VILNIUS UNIVERSITY
CENTER FOR PHYSICAL SCIENCES AND TECHNOLOGY

Aurelija
URBANAITĖ

Study on Cyclization and Rearrangement Reactions of Functionalized Alkynes

DOCTORAL DISSERTATION

Life Sciences,
Chemistry N 003

VILNIUS 2019

This dissertation was written between 2014 and 2018 at Vilnius University, Faculty of Chemistry and Geosciences. The research was supported by Research Council of Lithuania.
Grants – DOK-15135, DOK-16407, DOK-17348, P-DAP-18-345.
Projects – VP1-3.1-ŠMM-07-K-01-002, MIP-15016.

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This doctoral dissertation will be defended in a public meeting of the Dissertation Defence Panel:
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The dissertation shall be defended at a public meeting of the Dissertation Defence Panel at 2 p. m. on 17th May 2019 in the Inorganic chemistry lecture hall (NChA, number 141) of the Faculty of Chemistry and Geosciences, Vilnius University.
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VILNIAUS UNIVERSITETAS
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URBANAITĖ

Funkcionalizuotų alkinų ciklizacijos ir persigrupavimų reakcijų tyrimas

DAKTARO DISERTACIJA

Gamtos mokslai,
Chemija N 003

VILNIUS 2019

Disertacija rengta 2014 – 2018 metais Vilniaus universitete, Chemijos ir geomokslų fakultete.
Mokslinius tyrimus rėmė Lietuvos mokslo taryba:
Stipendija už akademinius pasiekimus – DOK-15135, DOK-16407, DOK-17348, P-DAP-18-345.
Projektai – VP1-3.1-ŠMM-07-K-01-002, MIP-15016.

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prof. dr. Vytas Martynaitis (Kauno technologijos universitetas, gamtos mokslai, chemija – N 003).

Disertacija ginama viešame Gynimo tarybos posėdyje 2019 m. gegužės mėn. 17 d. 14 val. Vilniaus universiteto, Chemijos ir geomokslų fakulteto Neorganinės chemijos auditorijoje (NChA nr. 141). Adresas: Naugarduko g. 24, Vilnius, Lietuva, tel. +3705 219 3105 ; el. paštas info@chgf.vu.lt .

Disertaciją galima peržiūrėti Vilniaus universiteto, Fizinių ir technologijos mokslų centro bibliotekose ir VU interneto svetainėje adresu: https://www.vu.lt/naujienos/ivykiu-kalendorius

ABOUT THE AUTHOR

Aurelija Urbanaitė was born in Panevėžys, Lithuania in 1989. In 2008 she finished Mykolas Karka secondary school in Panevėžys. After four years of studying in Vilnius University and practice in Tuebingen University, Germany she graduated from Vilnius University, obtaining her Bachelor degree in Chemistry. In 2014 she received Master of Science degree in Chemistry. In the same year she started Ph.D. studies in group of prof. dr. I. Čikotienė. Aurelija's research interests include reactivity of functionalized alkynes, new synthetic routes of organic molecules and heterocyclic chemistry.

ACKNOWLEDGEMENTS

First of all, I would like to thank my supervisor Inga Čikotienė from the whole heart for her endless patience, great ideas and strong ability to motivate. Secondly, I am very thankful to Algirdas Brukštus for encouragement during hard times and his unfading positivity. Also I am grateful for the family of 113 lab, which part I could be. Thank you Rita Bukšnaitienė, Ieva Karpavičienė, Justina Šulgaitė, Mantas Jonušis, Justas Pošiūnas, Herkus Petrikas, Indrė Misiūnaitė, Girius Kisielius, Paulina Kaziukonytė, Kamilė Mociūnaitė. Special thanks to Simonas Balkaitis and Lukas Šteinys who contributed to the scope of experiments. Moreover, I express my gratitude to Lukas Taujenis for HRMS analysis, Marijona Birutė Krenevičienė for NMR analysis, Audronė Karosienė and Gražina Petraitytė for IR analysis. In addition, I would like to thank my mom, dad and brother who were very supportive and always were proud of me. And last but not least, I would like to thank my love Martynas Zlatkus, who has been with me since my scientific journey begun and survived my tears during failures also laughed together during moments of luck.

I would like to thank the Research Council of Lithuania for scholarship (2015 – 2018; DOK-15135, DOK-16407, DOK-17348, P-DAP-18-345).

The research was partially funded by the European Social Fund under the Global Grant measure (Grant No. VP1-3.1-ŠMM-07-K-01-002) and by a grant (No. MIP-15016) from the Research Council of Lithuania.

TABLE OF CONTENTS

LAYOUT OF THE THESIS

The thesis is divided into four main parts. List of papers describes contribution to each publication. Introduction details the goal of the thesis, main tasks, significance of the work and defensive statements. Review of the papers represents the outlook of four manuscripts. Experimental part specifies main methods of the synthesis and analysis. Additional parts include: conclusions, summary, list of publications in proceedings or books of abstracts, references and copies of the papers.

LIST OF ABBREVIATIONS

COSY – correlation spectroscopy
HMBC – heteronuclear multiple bond correlation
HOMO – highest occupied molecular orbital
HRMS – high resolution mass spectrometry
HSQC – heteronuclear single quantum coherence
LUMO – lowest unoccupied molecular orbital
Me – methyl group
NBS – *N*-bromosuccinimide
NMR – nuclear magnetic resonance
NOESY – Nuclear Overhauser effect spectroscopy
PPARδ – peroxisome proliferator-activated receptor delta
t-Bu – *tert*-butyl group
TLC – thin layer chromatography
UV – ultraviolet

LIST OF PAPERS

This thesis is based on the following publications. The papers can be found at the end of the doctoral thesis.

Papers Included in the Thesis

1. R. Bukšnaitienė, A. Urbanaitė, I. Čikotienė, Formation of Condensed 1*H*-Pyrrol-2-ylphosphonates and 1,2-Dihydropyridin-2-ylphosphonates *via* Kabachnik−Fields Reaction of Acetylenic Aldehydes and Subsequent 5-*exo*-dig or 6-*endo*-dig Cyclizations, *J. Org. Chem*., **2014**, *79*, 6532 − 6553.

2. A. Urbanaitė, M. Jonušis, R. Bukšnaitienė, S. Balkaitis, I. Čikotienė, Electrophile-Mediated Reactions of Functionalized Propargylic Substrates, *Eur. J. Org. Chem.*, **2015**, *2015* (32), 7091 – 7113.
3. A. Urbanaitė, I. Čikotienė, Synthesis of Polysubstituted Pyrroles through the Tandem 1,3-Addition/5-*Endo*-Dig Cyclization of 1-(1-Alkynyl)Cyclopropyl Imines, *Eur. J. Org. Chem.*, **2016**, *2016*, (31), 5294 – 5300.
4. A. Urbanaitė, L. Šteinys, A. Brukštus, I. Čikotienė, Addition of Primary Amines to 2-(1-Alkynyl)-2-cycloalken-1-ones, *Eur. J. Org. Chem.*, **2017**, *2017* (12), 1624 – 1627.

Contribution to the Papers

1. The first paper discloses the Kabachnik-Fields reactions between 2-alkynylcyclopent-1-enecarbaldehydes, 2-alkynylcyclohex-1-enecarbaldehydes, 2-alkynylbenzaldehydes, 2-alkynylindole-3-carbaldehydes, 2-alkynylpyridine-3-carbaldehydes, 2-alkynylquinoline-3-carbaldehydes, anilines and dimethylphosphite together with the following Lewis acid catalyzed or iodine mediated cyclizations. In addition to that, optimization of all reaction conditions is described in the paper. I was responsible for the synthesis and cyclization reactions of nonaromatic cyclohexene, aromatic indole, pyridine and benzene ring containing α-acetylenic anilinomethylphosphonates. Also, I did the assignment of NMR and IR signals for all my synthesized compounds in the experimental section.
2. The second paper discusses about electrophile-mediated reactions of propargylic amides, carbamates, ureas, thioureas and esters as well as about detailed reaction condition optimization processes. I performed synthesis of propargylic carbamates and optimized cyclization reaction conditions of these materials as well as expanded the electrophilic cyclizations scope of carbamates with different electrophilic sources such as iodine, NBS, phenyl hypochloroselenoite, oxocarbenium ions and various triple bond substituents. In addition, propargylic thioureas, 1,3-thiazines and 4,5-dihydrothiazoles were synthesized and characterized by bachelor student S. Balkaitis under my supervision. Moreover, I characterized the structures of starting carbamates, side products, final oxazinones and oxazolidinones assigning NMR and IR signals during preparation of the experimental part.
3. The third paper represents synthesis and 1,3-addition/cyclization reaction of 1-(1-alkynyl)cyclopropyl imines with polar covalent bond containing compounds giving polysubstituted pyrroles. I did synthesis of the

most starting materials, optimization experiments and cyclization reactions. To add, I performed NMR and HRMS analysis and wrote the experimental section of the paper.

4. The fourth paper talks about unusual behaviour of the 2-(1-alkynyl)-2-cycloalken-1-ones during the reaction with primary amines which leads to the formation of (*Z*)-*β*-enaminones. I contributed to the paper by synthesizing starting materials, performing the optimization of the addition-cyclization reaction conditions and by extending the reaction scope with 2-(1-alkynyl)-2-cycloalken-1-ones containing phenyl, 4-methoxyphenyl and *n*-butyl substituent next to the triple bond. All the reactions and NMR characterization regarding 2-((4-fluorophenyl)ethynyl)alk-2-enone were conducted by bachelor student L. Šteinys under my supervision. Besides that, I performed NMR, HRMS and IR analysis and prepared the experimental section. And finally, I participated in writing and layouting of the manuscript.

Short Review Not Included in the Thesis

A. Urbanaitė, I. Čikotienė, Synthesis of 4*H*-Thiazines, *Chem. Heterocycl. Compd*., **2016**, *52*, 1 – 3.

INTRODUCTION

Functionalized alkynes have huge potential in the designing of new carbocyclic and heterocyclic scaffolds and exploring undiscovered reaction pathways for fundamental research. In terms of cyclic molecules, functionalized triple bond containing compounds are precursors for the synthesis of *N*-, *O*- or *S*-heterocycles such as pyrrole, 1,2-dihydropyridine, oxazinone, oxazolidinone, oxazine, oxazole, thiazine, thiazole and many others. For example, pyrrole and its derivatives are well known for anticancer [1], anti-inflammatory [2], antioxidant [3], antifungal [4], antiviral [1a], [5], anti-diabetic [6], antibacterial [5a], [7], anti-hypertensive [8] or anti-HIV [9] activity and constitute a part of drugs such as Lamellarin O [10], Pyrrolnitrin 3 [11], Licofelone 4 [12], Tofacitinib [13], Ketorolac [14], Tolmetin [15] or Ribociclib [16]. 1,2-Dihydropyridine can be a part of antifungal [17] and anticancer [18] agents. Oxazinone motifs present in antitumor [19] molecules or can serve as building blocks in organic synthesis [20]. Oxazolidinones are used in synthesis of some drugs [21]. Oxazines are employed as antimicrobial [22] agents or precursors in therapeutic applications [23]. Oxazoles also own interesting pharmaceutical properties [24]. Thiazines are great synthons for analgesic, anti-inflammatory [25], antihypotensive [26], antibacterial [27] or antitubercular [28] compounds. Thiazoles are potential PPARδ agonists [29] also showing antifungal activities [30].

The most popular approach to heterocyclizations of functionalized alkynes is using strong bases or transition-metal salt catalysts such as Au (I), Au (III), Ag (I), Cu (I), Cu (II), Pd (II) [31].

Rising interest in mild, environmentally friendly and efficient reactions have opened the way to electrophile-promoted cyclizations of alkynes [32]. Very important feature of the electrophile-mediated cyclizations is that obtained compounds containing halogen or chalcogen functionalities could be used in the further modifications. Not only cyclizations are common process, skeletal rearrangements also play a role in chemistry of alkynes [33]. Despite the fact that propargylic substrates are attractive precursors, electrophile-promoted reactions are still not frequent in the literature [34].

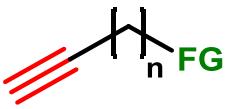
The interest in the field of propargylic compounds transformations was started in our laboratory several years ago [35].

Encouraged by the literature survey results and the results obtained in our laboratory this thesis was dedicated for the detailed investigation of electrophile-mediated together with Lewis acid catalysed reactions of fuctionalized propargylic substrates and other alkynes having internal

nucleophilic group. Moreover, during the investigation some unexpected results were faced, analysed and described.

Aim and main tasks

The aim of the present work was to investigate intramolecular cyclization or rearrangement reactions of functionalized alkynes.



The main tasks to achieve the aim are following:

- To investigate the transition metal catalysed cyclizations of acetylenic α-anilinomethylphosphonates.
- To study the electrophile-triggered reactions of propargylic substrates.
- To investigate the reactions between cyclopropyl-tethered 3-alkynyl imines and polar covalent bond containing compounds.
- To study the reaction between 2-(1-alkynyl)-2-cycloalken-1-ones and amines.

Significance of the Work

Three-component Kabachnik−Fields reaction was applied for the synthesis of acetylenic α-anilinomethylphosphonates. Nonaromatic α-amino (2-alkynyl) methylphosphonates regioselectively reacted to give pyrrole ring containing compounds. Pyridine or quinoline based acetylenic α-anilinomethylphosphonates exclusively formed 6-aryl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonates and dimethyl 2-aryl-1,2-dihydrobenzo[b][1,6]naphthyridin-1-ylphosphonates *via* tandem imine formation−6-*endo*-dig cyclization processes. Acetylenic α-anilinophenylmethylphosphonates reacted through 5-*exo*-dig mode when $AuBr_3$ or $PdCl_2$ was used as catalyst, whereas AgOTf promoted the formation of six membered ring. New method for iodine-mediated synthesis of pyrrol-1-ylphosphonates bearing 1-iodoalkenyl, aroyl or formyl substituents was discovered. Metal-free, effective and facile synthesis of oxazinones, 4*H*-1,3-oxazines, 4*H*-1,3-thiazines, 4,5-dihydrothiazoles and α-substituted enones from electrophile-induced cyclizations of functionalized propargylamines and propargyloxy group bearing substrates was established.

6-*Endo*-dig regioselectivity was achieved when propargylamines (except of propargylic thiourea) with electron-rich arylethynyl moieties were used as the substrates in halogen, chalcogen and oxocarbenium ion mediated reactions. Meanwhile, regioselective 5-*exo*-dig ring closure was possible when unsubstituted propargylic benzamides, ureas and thioureas were used in molecular iodine and phenyl hypochloroselenoite induced reactions. Also, it was showed that the outcome of the reaction depends on the nucleophilicity of the internal functionality, electronic nature of alkyne and electrophilic reagent. New mild and concise method of preparation of halogen, chalcogen, azide, alkoxy or aryloxy substituted pyrroles from cyclopropyl-tethered 3-alkynyl imines reaction with polar covalent bond containing compounds was developed. Powerful, atom-economic and straightforward double bond migration-nucleophilic addition reaction of 2-(1-alkynyl)-2-cycloalken-1-ones with primary amines forming (*Z*)-*β*-enaminones was found.

Defensive Statements

- Nonaromatic 2-alkynylcyclohex-1-enecarbaldehydes, 2-alkynylcyclopent-1-enecarbaldehydes, aromatic 2-alkynylbenzaldehydes and electron-rich 1-benzyl-2-alkynylindole-3-carbaldehydes react in a $BF_3 \cdot Et_2O$ mediated three-component reaction with dimethylphosphite and aromatic amines forming Kabachnik−Fields adducts.
- 5-*Exo*-dig or 6-*endo*-dig cyclization mode of acetylenic α-anilinomethylphosphonates strongly depends on the substrate framework and electronic density on it. Transition metal catalyst influences the regioselectivity of the cyclizations only in the case of α-amino (2-alkynylphenyl) methylphosphonates.
- Molecular iodine is able to induce cyclization reaction of carbocyclic α-amino (2-alkynyl) methylphosphonates.
- Functionalized oxazinones, 4*H*-1,3-oxazines, 4*H*-1,3-thiazines, 4,5-dihydrothiazoles and α-substituted enones can be synthesized utilizing *N*- and *O*-propargylic compounds with no need of Lewis acid catalysis.
- The outcome and regioselectivity of the propargylic benzamides, carbamates, ureas, thioureas and esters reactions, mediated with electrophiles depend on the nature of electrophile, electronic density at the alkyne terminus and the structure of the functional nucleophilic group.
- Cyclopropyl-tethered 3-alkynyl imines react with polar covalent bond containing compounds *via* 1,3-addition/5-*endo*-dig cyclization process in the absence of transition metal catalysts.

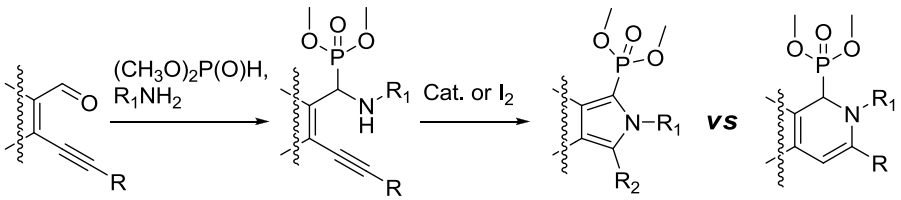
- 2-(1-Alkynyl)-2-cycloalken-1-ones react with primary amines through double bond migration-nucleophilic addition sequence allowing the formation of (*Z*)-*β*-enaminones in stereo- and regioselective manner.

REVIEW OF THE PAPERS

In this part of the thesis I will summarize each paper.

1.1 Paper 1. *Formation of Condensed 1H-Pyrrol-2-ylphosphonates and 1,2-Dihydropyridin-2-ylphosphonates via Kabachnik−Fields Reaction of Acetylenic Aldehydes and Subsequent 5-exo-dig or 6-endo-dig Cyclizations*

Pyrrole and 1,2-dihydropyridine core containing molecular scaffolds play a huge role in medicinal chemistry due to their bioactivity [1-18]. Moreover, α-aminophosphonates are known as the analogues of α-amino acids having broad biological applications [36]. About a decade ago several manuscripts about Lewis acid catalyzed cyclizations of α-amino (2-alkynylphenyl)methylphosphonates have been published [37]. To the best of our knowledge there are no information about reactivity and reactions of heteroaromatic or nonaromatic analogues of acetylenic α-anilinomethylphosphonates in the literature. Keeping in mind that regioselectivity of the cyclization reaction depends not only on the catalyst, but also on the structure of the starting material, the transition metal catalyzed or iodine-mediated cyclization reactions of various carbocyclic and heterocyclic α-acetylenic anilinomethylphosphonates were investigated (scheme 1).



Scheme 1. Cyclizations of α-aminomethylphosphonates derived from acetylenic aldehydes

Firstly, 5-*exo*-dig and 6-*endo*-dig cyclization modes can be explained by *Baldwin rules* [38]. The digit means the number of the atoms in the forming cycle, *exo* shows that double bond, formed from triple bond, after cyclization is outside the ring, meanwhile *endo* represents that double bond is in the formed cycle. Last three letters *dig* shows the *sp* hybridization of the triple bond carbons (figure 1).

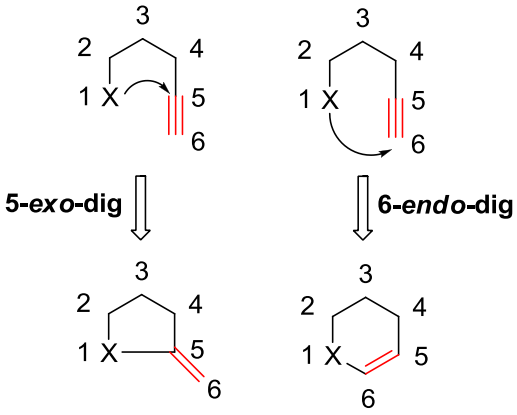
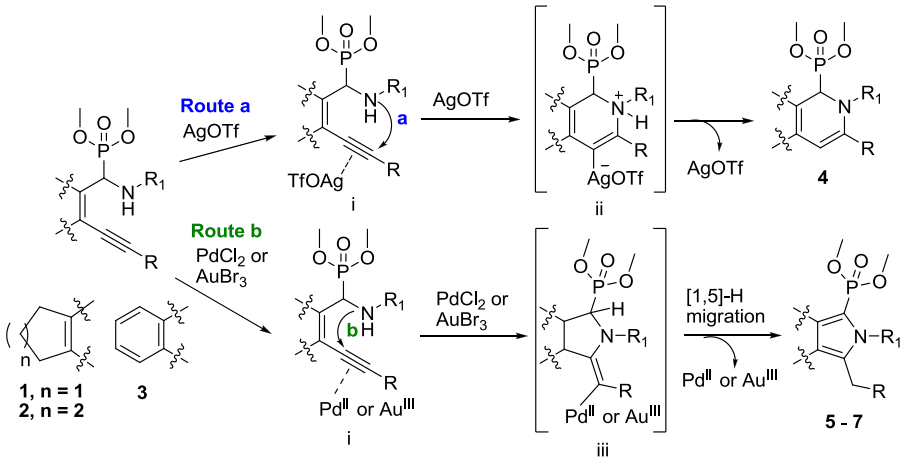


Figure 1. Ring closure modes: 5-*exo*-dig versus 6-*endo*-dig

In our study, carbocyclic Kabachnik-Fields adducts were synthesized from acetylenic aldehides, amines and dimethylphosphite *via* three-component reaction. This useful multicomponent reaction between amine, carbonyl compound and phosphoric acid diester was first discovered almost seventy years ago [39] and it is known to be promoted by different catalysts [40]. In our work three-component reaction products were subjected to the cyclization reaction catalyzed by transition metal salts such as AgOTf, $PdCl_2$ or $AuBr_3$. The mechanism of the cyclization reaction was proposed and it is similar to Wu *et al* assumptions [37]. However, nonaromatic α-acetylenic anilinomethylphosphonates **1**, **2** showed different reactivity in Lewis acid catalyzed transformations. Cyclization proceeds through two different routes depending on the catalyst and the starting material. It is generally accepted that metal coordinates triple bond forming metal-triple bond complex *i*, which then is prone to participate in the intramolecular cyclization. Nucleophilic amine moiety regioselectively attacs electron-poor triple bond producing intermediates *ii* or *iii*. In the case of α-amino (2-alkynylphenyl)methylphosphonates (**3**), 6-*endo*-dig mode is operating when Ag(I) salts are used (route a), whereas Pd(II) or Au(III) promotes 5-*exo*-dig cyclization (route b). Next, unstable cyclic compound *ii* transforms to 1,2-dihydropyridine product **4** (route a), while *iii* undergoes [1,5]-H migration to afford pyrrole ring containing compound **5** (route b). It is noteworthy that nonaromatic Kabachnik-Fields adducts **1**, **2** regioselectively reacted only in 5-*exo*-dig manner (route b). Interestingly, according to our findings, nonaromatic core containing phosphonates **1**, **2** cyclized exclusively to condensed pyrrole analogues **6**, **7** even when AgOTf, which promotes 6-*endo*-dig cyclization of benzene derivatives **3** was used, clearly indicating

that reaction mode depends on the structure of the starting material, but not only on the catalyst (scheme 2).

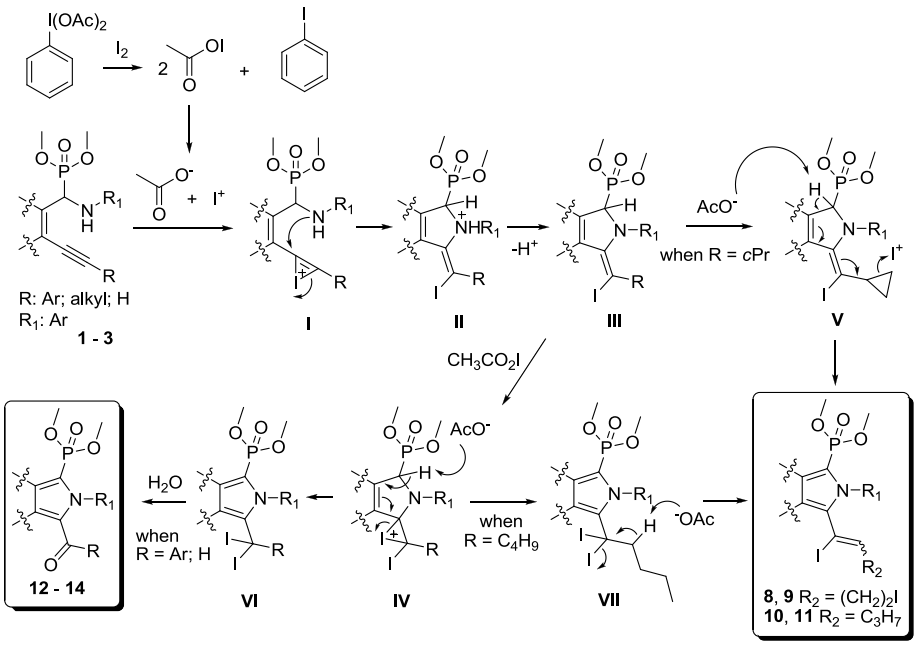


Scheme 2. Possible reaction mechanism of Lewis acid catalyzed cyclizations of carbocyclic α-acetylenic anilinomethylphosphonates **1** – **3**

In cyclizations of phenyl methylphosphonates **3** catalyst plays the biggest role in cyclization mode. Even though, all Lewis acids used are soft and has the affinity to carbon-carbon unsaturated bonds, they differ in charge and atomic radius. Ag(I) has smaller atomic radius and ionic charge than Pd(II) or Au(III), which might be one of the factor affecting the cyclization mode. It shoud be stressed out that the cyclization mode of nonaromatic analogues **1**, **2** is determined not by the catalyst itself, but by the framework of substrate. One factor that affects cyclization might be the conformation of the core – cyclohexene or cyclopentene rings are not planar comparing with benzene analogue. Although, literature revealed that in the metal salts promoted alkyne cyclizations, the nature of the triple bond substituent has clear impact on the ring closure pattern, in our findings, both aryl and alkyl substituents gave the same outcome.

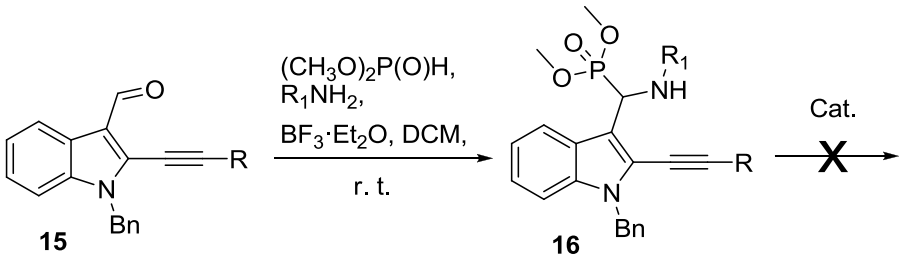
Since electrophilic iodine mediated cyclizations of functionally substituted alkynes are attractive and cheap methods to obtain functionalized heterocycles suitable for further modifications [41], cyclizations of nonaromatic methylphosphonates **1**, **2** and phenyl methylphosphonates **3** using molecular iodine were carried out. In all cases 5-membered pyrrole derivatives **8** – **14** were obtained. According to plausible mechanism molecular iodine is activated by converting it to more electrophilic source – acetyl hypoiodite [42]. I_2 is oxidized with (diacetoxyiodo)benzene, producing 2 equivalents of acetyl hypoiodite and iodobenzene, thus both

iodine atoms are transformed to I^+. Next, the triple bond of α-anilinomethylphosphonate **1** – **3** reacts with iodine forming iodonium cation **I**. This reactive species is then regioselectively attacked by neighbouring nucleophilic nitrogen and after deprotonation of **II** affords intermediate **III**, which acts in two different ways, depending on substituent on triple bond. When *R* is a cyclopropyl group, acetate anion abstracts proton from **V** leading to the opening of the three atom membered ring and iodine incorporation (products **8**, **9**). Meanwhile, iodine from other equivalent of acetyl hypoiodite could create iodonium cation with double bond of **III** forming intermediate **IV**. Proton loss and aromatization of heterocyclic ring then affords unstable diiodinated intermediates **VI** and **VII**. Compound with alkyl substituent tend to form iodoalkenyl products **10**, **11**, whereas water present in the solvent could react with intermediate **VI** when *R* is aryl or H, thus obtaining 5-*exo*-dig products **12** – **14**. Although, substitution pattern at alkyne terminus did not have the effect on cyclization mode, substrates bearing arylethynyl **1a**, **2a**, **3a** or ethynyl **1b**, **3b** moieties led to formation of condensed pyrroles **12** – **14** with carbonyl functionality. While phosphonates **1c**, **2c**, containing alkylethynyl group gave 1-iodoalkenyl products **8** – **11** as a mixtures of Z/E isomers (scheme 3).



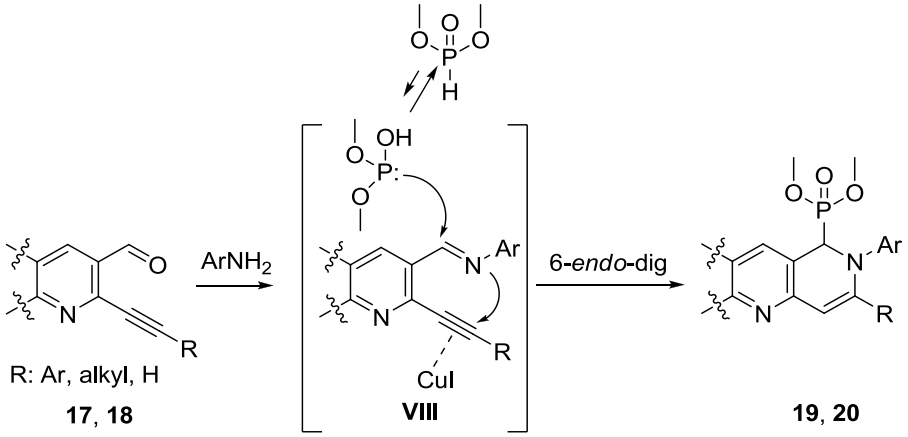
Scheme 3. Plausible reaction mechanism of the iodine-promoted cyclization of acetylenic α-anilinomethylphosphonates **1** – **3**

Next topic discussed in the paper is heterocyclic Kabachnic-Fields aducts and their cyclization reactions. Electron donating 2-(alkynyl)-1-benzyl-1*H*-indole-3-carbaldehyde (**15**) was able to form the corresponding phosphonate **16**, but unfortunately, it was not active enough to participate in intramolecular cyclization reaction (scheme 4).



Scheme 4. 2-(Alkynyl)-1-benzyl-1*H*-indole-3-carbaldehyde (**15**) and corresponding phosphonate **16** reactivity

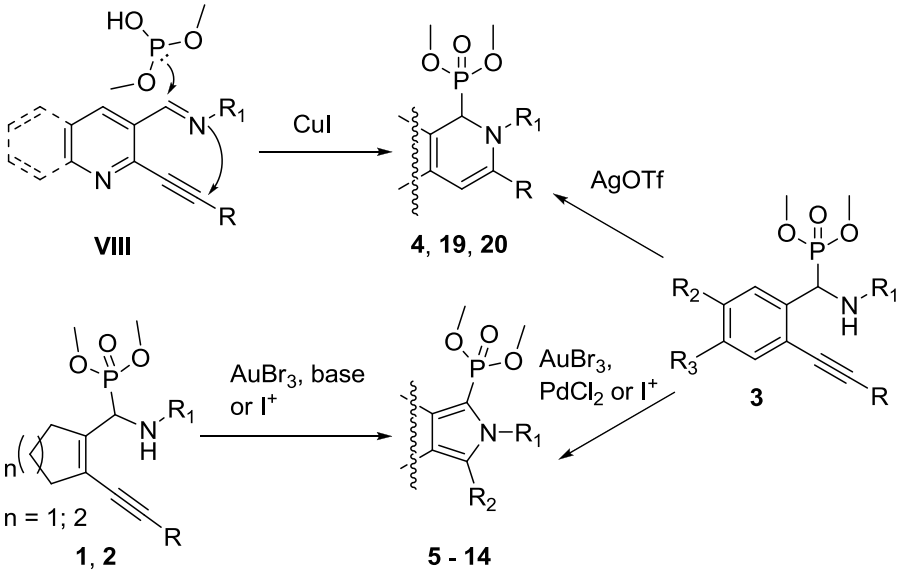
Therefore an electron-poor 2-alkynylpyridine-3-carbaldehyde **17** and 2-alkynylquinoline-3-carbaldehyde **18** were chosen. Surprisingly, 6-*endo*-dig cyclization product **19**, **20** instead of α-aminomehylphosphonate was obtained when heteroaromatic carbaldehyde **17** or **18** was subjected to the three-component reaction with amine and dimethylphosphite. It has to be mentioned that the full conversion of the reaction was possible only when CuI was used as a catalyst. It is believed, that triple bond is strongly activated due to electron withdrawing effect of the piridine or quinoline rings and metal-triple bond complex formation (intermediate **VIII**). Because of that, after imine formation, the consequent dimethylphosphite [43] attack to sp^2 carbon and nucleophilic cyclization to dihydro-1,6-naphthyridinylphosphonate **19**, **20** takes place (scheme 5). The formation of intermediate imine was proved by NMR of reaction mixture before the addition of copper iodide.



Scheme 5. Mechanism of the one pot dihydro-1,6-naphthyridinylphosphonate **19**, **20** synthesis

To conclude the findings described in the paper 1 it has been shown that three component Kabachnik-Fields reaction is suitable for the synthesis of carbocyclic core and electron-rich indole framework containing phosphonates **1** – **3**, **16**, whereas electron withdrawing 2-alkynylpyridine-3-carbaldehyde **17** or 2-alkynylquinoline-3-carbaldehyde **18** in the reaction of arylamine and dimethylphosphite straightforwardly cyclizes to 6-*endo*-*dig* product **19**, **20**. Dependance of the cyclization mode has been studied using different catalysts and core structures of the α-aminomehylphosphonates.

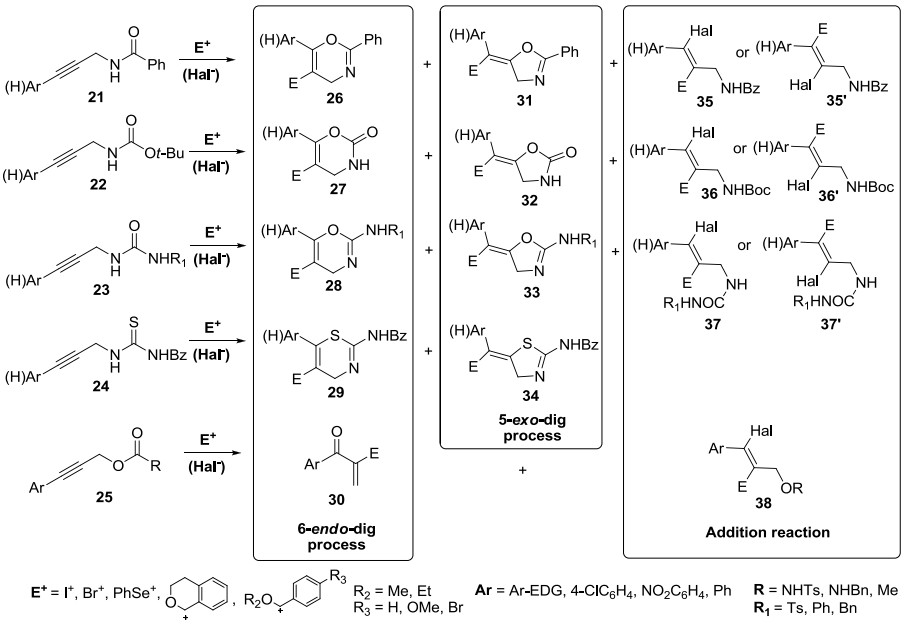
To summarize, nonaromatic cycloalkene derivatives containing phosphonates **1**, **2** cyclize only in 5-*exo*-dig mode, while aromatic phenyl core containing phosphonates **3** are able to change their reactivity, 5-*exo*-dig or 6-*endo*-dig depending on the catalyst used. On the one hand, it has been shown that cyclizations of electron-donating indole ring compounds are not possible, meanwhile, electron-defficient pyridine or quinoline ring containing molecules **17**, **18** smoothly cyclize in 6-*endo*-dig manner. Finally, iodine-promoted synthesis of pyrrole phosphonates **8** – **14** with 1-iodoalkenyl, aroyl or formyl substituents has been discovered. Summarized results are depicted in the scheme 6.



Scheme 6. Outcome of the α-aminomethylphosphonates **1** – **3** and imines **VIII** (from **17**, **18**) cyclizations

1.2 Paper 2. *Electrophile-Mediated Reactions of Functionalized Propargylic Substrates*

An enormous amount of publications concerning transition-metal catalyzed cyclizations of alkynes are presented in the literature [31]. Notwithstanding, there are some disadvantages related to transition-metal initiated transformations such as high cost or the unfriendliness to the environment. Therefore, scientists turned their attention to the electrophile-mediated reactions of alkyne motif containing compounds [32]. An emerging increase of electrophile-induced reactions of alkynes prompted us to investigate the reactivity of propargylic compounds. However, literature review revealed that electrophile-mediated cyclizations of propargylic substrates are not as common process as could be expected [34]. Thus, in the paper 2 electrophile-mediated reactions of functionalized propargylic substrates were studied (scheme 7).



Scheme 7. Electrophile-promoted transformations of propargylic compounds **21** – **25**

There are three types of intramolecular alkyne cyclizations, which include electrophile. Electrophilic cyclization is such type of ring closure where triple bond atacks internal electrophile (type a), while EPNC stands for electrophile promoted nucleophilic cyclizations (type b), which means, that the external electrofile is activating triple bond toward attack of neighbouring nucleophile [44]. Type c abbreviates as NPEC [45], which means nucleophile promoted electrophilic closures, where external nucleophile attacs triple bond, which is then prone to react with electrophile situated in close proximity (figure 2). Paper 2 deals with ring closures of type b only.

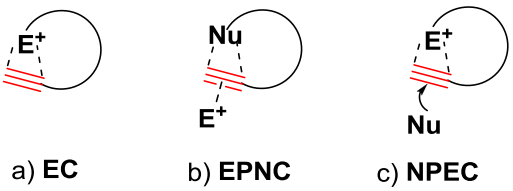


Figure 2. Types of alkyne cyclizations

In EPN cyclizations, external electrophile coordinates alkyne forming new LUMO from π-bond HOMO and empty E^+ orbital. It is very important, that

newly formed LUMO has the same symmetry as HOMO of the original triple bond, which then facilitates attack of the internal nucleophile in either *exo* or *endo* modes (figure 3a), whilst in the classical anionic cyclizations *endo* ring closures are disfavored, because the angle of the attacking nucleophile to the triple bond is ~120° (figure 3b) [46]. This divergence between nucleophilic ring closures (NC) and electrophile promoted nucleophilic cyclizations clearly shows that regioselectivity depends on the both alkyne and stereoelectronic effects of the internal nucleophilic functionality.

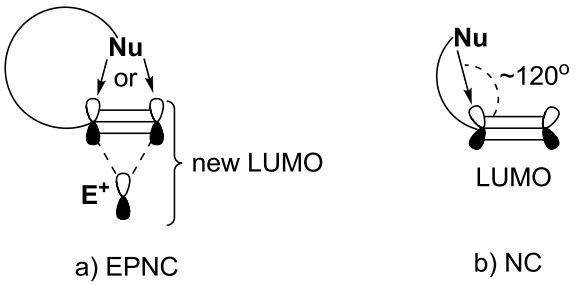


Figure 3. Different cyclization modes

Other meaningful factor in EPNC is polarization of the triple bond, which can be modulated using alkyne substituents with the different electronic properties. On one hand, electron withdrawing group at the alkyne terminus (β-carbon) diminishes electron density at the α-carbon, therefore *exo*-dig closure becomes favorable. On the other hand, donor group increases partial negative charge on the α-carbon, thus promoting *endo*-dig attack (figure 4).

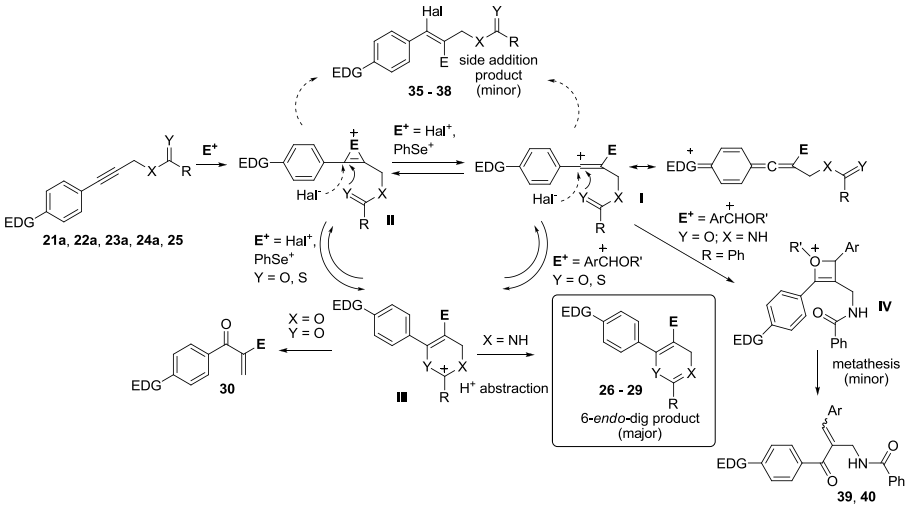
Figure 4. Triple bond substitution effect on regioselectivity of the cyclization

In addition to that, if the alkyne substituent does not have clearly expressed electronic properties, then 5-*exo*-dig / 6-*endo*-dig modes compete and regioselectivity could depend on the stability of the formed product. It means that formation of the compound with aromatic stabilization is more favorable.

In paper 2 propargylic benzamides **21**, carbamates **22**, ureas **23**, thioureas **24** and esters **25** with different substituents on the alkyne terminus were selected as the model substrates for electrophilic transformations. Molecular iodine, NBS, PhSeCl, cyclic and acyclic acetals were chosen to produce an electrophile. It should be noted that acetals require separate step to obtain actual electrophile. As it is seen from the scheme 7, there is different outcome of the propargylic substrate reaction with the electrophile. 5-*exo*-dig or 6-*endo*-dig ring closures as well as rearrangement or addition to the triple bond reactions could take place. Insights to the possible reaction mechanisms should unmask why different functionalities having propargylic compounds react in certain way.

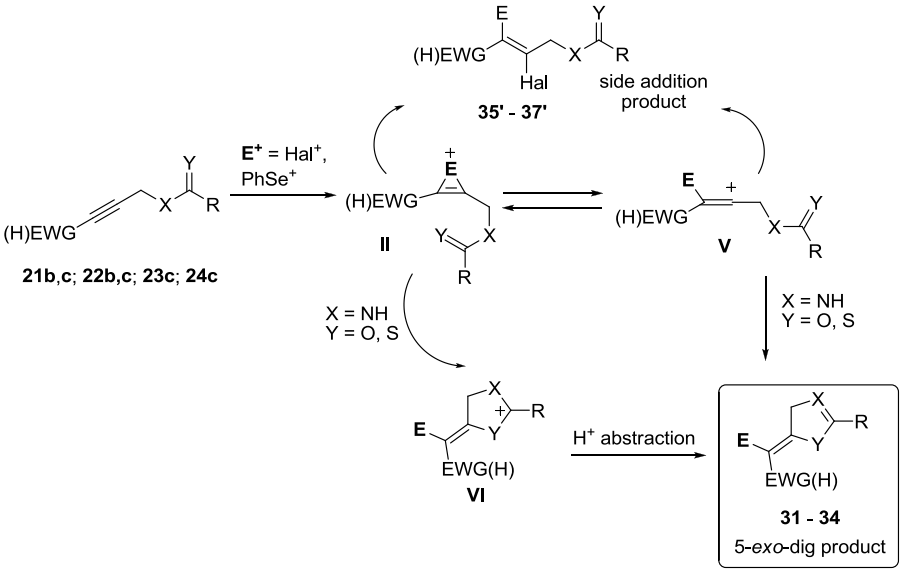
Possible reaction mechanism, which is depicted in the scheme 8, shows that propargylic substrates **21a**, **22a**, **23a**, **24a**, **25** bearing electron-rich aryl group could react with halogens or PhSeCl by forming haloirenium or selenirenium ions **II** which are in the equilibrium with the open-chain carbocations **I** [47]. Electron-rich aryl group next to the triple bond plays a role in the stabilization of vinylic carbocation (intermediate **I**) and thus 6-*endo*-dig cyclization becomes favorable. Cyclic derivative **III** then forms final products **26** – **29** or **30** depending on the X and Y functionality. When X = NH, Y = O or S, proton abstraction occurs providing 6-membered compounds **26** – **29**. Notably, reactions of **22a**, **23a**, **24a** and **25** with oxocarbenium ions proceed through the cyclic intermediate **III**, except of propargylic amides **21a** (X = NH, Y = O, R = Ph), which reaction with oxocarbenium species could proceed not only through 6-*endo*-dig pathway, but also *via* 1,2-dihydrooxetium intermediate **IV**, forming enones **39**, **40** [48]. Meanwhile, when X = Y = O, cationic intermediate **III** is unstable and rearranges to α-substituted enone **30**. This type of reactivity was previously observed in our laboratory [35a].

Nevertheless, in some cases the side electrophilic addition reaction was observed. During the reactions with molecular iodine or PhSeCl, counterions compete with internal nucleophile of propargylic substrate. When counterions are stronger nucleophiles than internal functional groups, side addition reaction takes place (dashed line in the scheme 8) forming products **35** – **38**. Otherwise, propargylic ureas **23a** and thioureas **24a** only undergo ring-closure process due to stronger nucleophilicity.



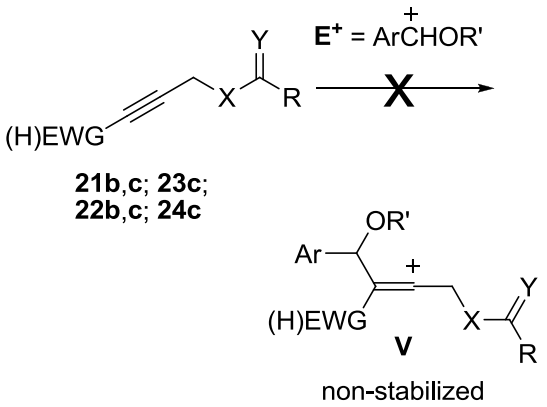
Scheme 8. Possible reaction mechanism of propargylic substrates **21a**, **22a**, **23a**, **24a**, **25** bearing electron-donating aryl group

Different reaction rate and regioselectivity was observed when electron-poor aryl group having substrates **21b**, **22b** or substrates with the terminal triple bond **21c**, **22c**, **23c**, **24c** were subjected to the reaction with electrophiles (scheme 9). As it is known, Hal^+ or $PhSe^+$ reacts with triple bond forming bridged ion **II**, which is in the equilibrium with the intermediate **V**. Vinylic carbocation **V** is stabilized by the inductive effect of CH_2FG and thus is more prone to react in 5-*exo*-dig way obtaining cyclic carbocation **VI**, which after abstraction of the proton, transforms into the final product **31 – 34**. Side electrophilic addition reaction is possible due to the same reasons as discussed in the previous paragraph.



Scheme 9. Possible reaction mechanism of unsubstituted propargylic substrates **21c**, **22c**, **23c**, **24c** or propargylic substrates bearing electron-poor **21b**, **22b** aryl group

It is very important to mention that propargylic compounds with terminal triple bond **21c**, **22c**, **23c**, **24c**, or electron withdrawing aryl group on the triple bond **21b**, **22b** were not able to react with oxocarbenium electrophiles (scheme 10). It is hypothesized that haloirenium or selenirenium ions **II** are crucial for the partial stabilization of the vinylic carbocations, but in the case of oxocarbenium electrophiles, formation of intermediates **II** are not possible causing the lack of stabilization.



Scheme 10. Electron-poor or unsubstituted propargylic substrates **21b**, **22b**, **21c**, **22c**, **23c**, **24c** and oxocarbenium ions

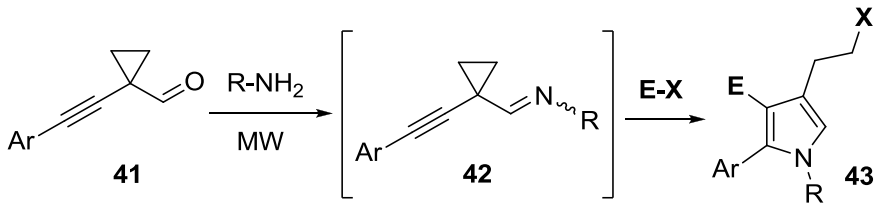
Overviewing the study of electrophilic transformations, it was observed that reaction rates of substrates **21a**, **22a**, **23a**, **24a**, **25** containing electron-donating groups next to the alkyne were accelerated, contrariwise electron-poor aryl substituents diminished the rates and in order to reach the full conversion of the reaction, prolonged time of the reaction was required. In addition to that, 6-*endo*-dig ring closure was usually noticed, when electron-rich groups were incorporated in the starting material. It is thought that vinylic carbocation which is formed during the first step of the electrophilic activation is stabilized by resonance, whereas substrates **21b**, **22b** bearing electron-withdrawing groups have different regioselectivity probably due to the both inductive and mesomeric effect on stability of the vinylic carbocation. Also, unactivated propargylic compounds **21b, 22b, 21c, 22c, 23c, 24c** are absolutely unreactive towards oxocarbenium ion mediated reactions due to the lack of stabilization of the intermediate vinylic carbocation. Additionally, only sulfur and carbonyl oxygen atoms acted as the nucleophiles and no nucleophilicity of *NH* group was observed in contrast to metal catalyzed cyclizations of carbamate analogues [49]. Furthermore, the electrophilic addition to the triple bond can take place when haloirenium or selenirenium ions are attacked by halogen counterion which competes with the internal nucleophile.

To sum up, metal-free halogen, chalcogen and oxocarbenium ion mediated yne-carbonyl or yne-thioxo conversions to various of 1,3-oxazines **26**, **28**, oxazinones **27**, 1,3-thiazines **29**, 4,5-dihydrothiazoles **34** and α-functionalized enones **30**, **39**, **40** have been developed. It has been shown that outcome of the reaction depends on the strength of the internal

nucleophile, substitution patern next to the triple bond, which affects the stability of the cationic intermediate and the nature of the electrophile.

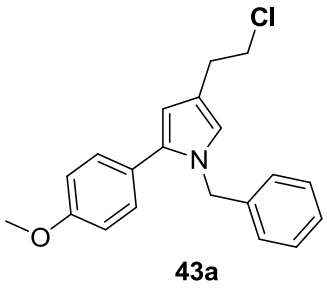
1.3 Paper 3. *Synthesis of Polysubstituted Pyrroles through the Tandem 1,3-Addition/5-Endo-Dig Cyclization of 1-(1-Alkynyl)Cyclopropyl Imines*

Polysubstituted pyrroles are broadly studied class of organic molecules having versatile biological [50], photophysical and chemical properties [51]. About ten years ago cyclopropyl-tethered functionalyzed alkynes were first applied to the synthesis of heterocyclic compounds [52]. The basic research areas covered furan synthesis, while preparation of pyrrole from 1-cyclopropylalkynyl imines were not as frequent [53]. Continuing the work in the field of electrophile-induced cyclizations, we were keen to prepare imines from 1-(1-alkynyl)cyclopropyl carbaldehydes and to investigate their reactions with electrophiles. Thus, paper 3 represents the study of 1-(1-alkynyl)cyclopropyl imine **42** reaction with polar covalent bond containing compounds **E-X** (scheme 11). Nevertheless, the reactivity that was observed cannot be described as electrophilic transformation.



Scheme 11. Synthesis of 1-(1-alkynyl)cyclopropyl imines **42** and their reaction with polar covalent bond containing compounds

Firstly, it was found that 1-(1-alkynyl)cyclopropyl carbaldehydes **41** react with amines *in situ* forming cyclopropyl-tethered imines **42**, which can further undergo cyclization reaction promoted by HCl which was present in the solvent as an impurity, obtaining pyrrole **43a** with incorporated halogen in the side chain (figure 5).



43a

Figure 5. Pyrrole **43a** with incorporated halogen

This could be explained by proton-induced 5-*endo*-dig cyclization of *in situ* formed imine **42** and cyclopropane ring opening assisted by nucleophilic Cl^-. General intramolecular 5-*endo*-dig cyclization of functionalized alkynes is depicted in figure 6.

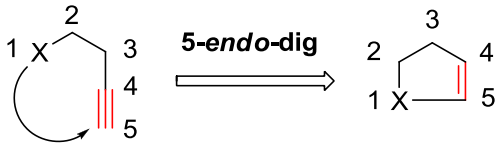
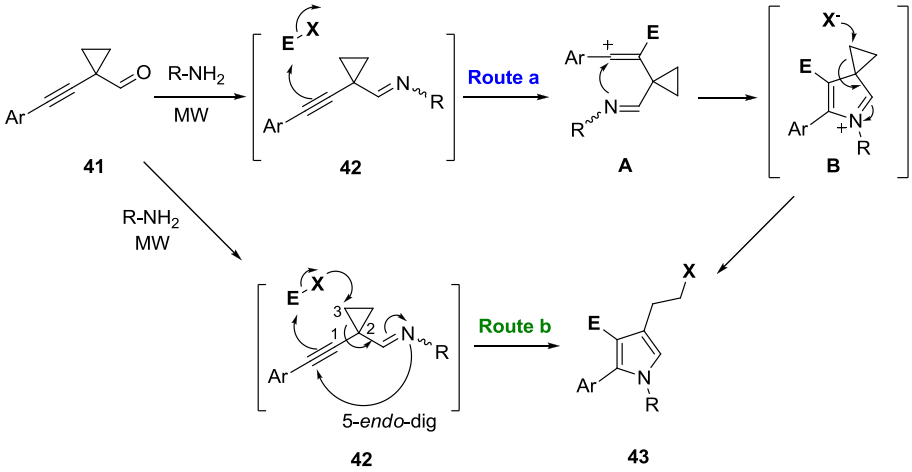


Figure 6. *Endo*-dig cyclization to 5-membered ring

Molecular iodine and reagents with unsymmetrical covalent bonds such as iodine monochloride, PhSeCl, freshly prepared IN_3, acetyl hypoiodite or even alcohols were chosen after finding the interesting reactivity of 1-(1-alkynyl)cyclopropyl imines **42**. The strategy of preparing imines in microwave reactor, followed by the evaporation of the solvent together with excess of amine, redissolving of the *in situ* prepared alkynylimine in MeCN and then testing its reactivity towards molecules containing polar covalent bonds was applied. This methodology was adjusted for the imines with phenyl, 4-methoxyphenyl or *p*-tolyl substituents next to the triple bond and *tert*-butyl, benzyl, cyclohexyl or isopropyl substituents next to the imine functionality.

Afterwards, the plausible reaction mechanism was proposed, showing that two reaction routes are possible. In route a, starting aldehyde **41** reacts with amine obtaining 3-alkynyl imine **42**, which interacts with the electrophile, forming vinylic carbocation **A**. Then, nucleophilic imine functionality attacks carbocation **A**, obtaining cyclopropyl-tethered cyclic intermediate **B**. Later on, an anion present in the media induces cyclopropyl opening, thus giving the pyrrole **43**. To test whether the cyclopropane ring opening occurs after the electrophilic activation of triple bond resulting 5-*endo*-dig ring

closure, as it was proposed for the synthesis of furans from 1-(1-alkynyl)-cyclopropyl ketones [54], an excess of external nucleophiles such as piperidine, indole, sodium azide, potassium iodide or methanol were added to the stirring mixture of imine and polar covalent bond containing reagent. After the reaction, NMR and HRMS analysis revealed that no fragment of the external nucleophile was present in the products indicating that this unique reaction proceeds *via* different route. It is assumed that polar covalent bond containing reagent **E-X** is attached to the alkyne-cyclopropane fragment by a formal 1,3-addition reaction and then subsequent 5-*endo*-dig cyclization becomes feasible forming the polysubstituted pyrrole **43** as the final product (route b, scheme 12).



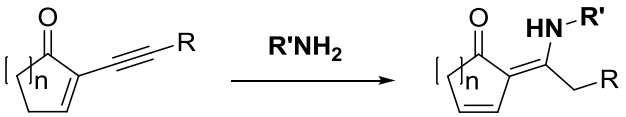
Scheme 12. Possible mechanism for the synthesis of polysubstituted pyrroles **43**

It should be pointed out that the answer which mechanism will be operating, could depend on the structure of the cyclopropyl-tethered imine. Therefore, unsubstituted cyclopropyl moiety having substrates tend to react in 1,3-addition process and subsequent intramolecular cyclization, whereas bulky substituents next to the cyclopropyl ring empower the electrophile-promoted ring-closure as it seen in [53] manuscript.

In conclusion, the new methodology for the efficient synthesis of polysubstituted pyrroles **43** with incorporated hydrogen, halogen, chalcogen, azide, or alkoxy/aryloxy moieties has been invented.

1.4 **Paper 4.** *Addition of Primary Amines to 2-(1-Alkynyl)-2-cycloalken-1-ones*

There is no doubt that electron-deficient 1,3-conjugated enynes are attractive precursors in organic synthesis [55]. The products of the reaction between 2-(1-alkynyl)-2-alken-1-ones and nucleophiles are five-membered furan derivatives [56]. The literature analysis revealed that pyrrole synthesis from imines of 2-(1-alkynyl)-alken-1-ales or 2-(1-alkynyl)-alken-1-one oximes are uncommon process [57]. For that reason, the goal was to prepare imines of 2-(1-alkynyl)-alken-1-ones and to investigate their cyclization reactions to pyrrole derivatives. However, our plans turned to the different direction after the unique reactivity of 2-(1-alkynyl)-alken-1-ones was observed. Thus, paper 4 deals with the study of the reaction between primary amines and 2-(1-alkynyl)-2-cycloalken-1-ones (**44**, **45**) (scheme 13).



n = 1 **44**
n = 2 **45**

n = 1 **46**
n = 2 **47**

Scheme 13. Reaction between 2-(1-alkynyl)-2-cycloalken-1-ones (**44**, **45**) and amines

It was found that the reaction of 2-(1-alkynyl)-2-cyclohexen-1-one **45** and amine leads to unprecedented regio- and stereoselective formation of (*Z*)-2-[1-(amino)-2-arylethylidene]cyclohex-3-enone **47**. Interestingly, no production of imine was observed. The structure of new product was proven by HSQC, HMBC and NOESY NMR spectra. The latter experiment disclosed the stereochemistry of the formed *β*-enaminone. The NOESY spectrum shows the cross-peaks of those hydrogen-hydrogen couplings which are next to each other through space. In this case, the cross-peak between *β*-H which is in vicinity to the double bond in the cyclohex-3-enone ring, and hydrogens from CH_2Aryl fragment was observed, demonstrating the *Z* configuration of the product (figure 7).

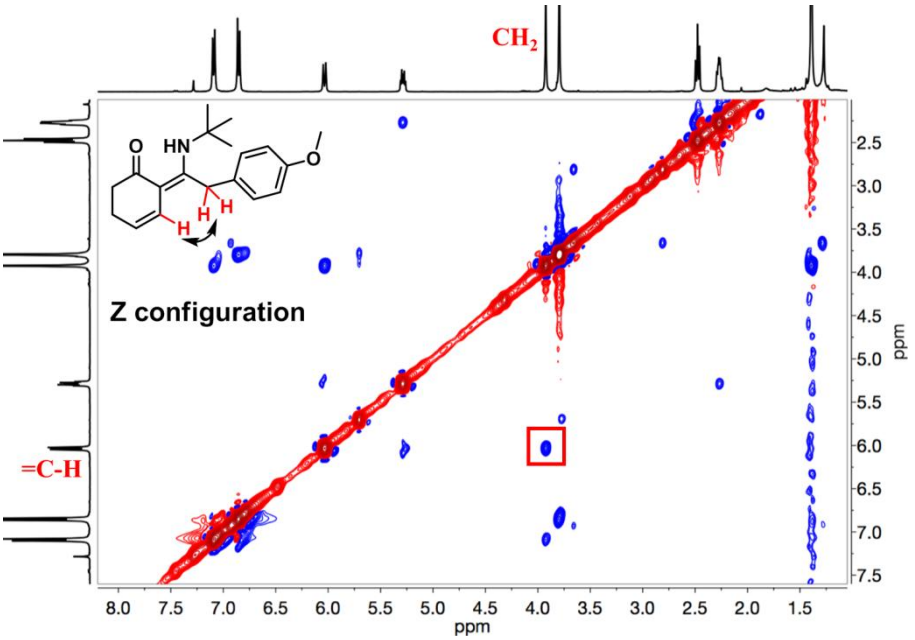
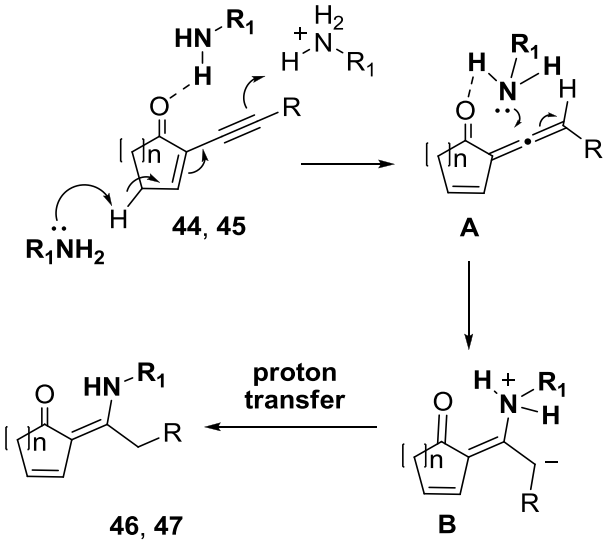


Figure 7. NOESY spectrum of *β*-enaminone **47a**

The scope of this cascade reaction was broadened with 2-(1-alkynyl)-2-cyclopenten-1-ones **44**. It should be pointed out that in order to reach the full conversion, harsh reaction conditions were required.

Furthermore, different kinds of amines were selected for the transformation. Luckily, 2-(1-alkynyl)-2-cyclohexen-1-ones **45** reaction with cyclic, bulky or linear primary aliphatic amines was smooth and efficient. On the contrary, aromatic amines were unreactive due to the lack of nucleophilicity, while secondary amines led to the decomposition of the starting material.

This specific formation of *β*-enaminones **46**, **47** could be explained as follows. Firstly, amine and ketone **44**, **45** forms hydrogen bond, then amine acts as a base and eliminates *γ* proton from the starting material. Afterwards, triple bond attacks proton and simultaneous double bond isomerization to allene **A** takes place. Lastly, the nucleophilic addition of amine to allene **A** forms the intermediate **B** and final (*Z*)-*β*-enaminone **46**, **47** in a stereo- and regioselective way (scheme 14). The analogous selectivity was supported by Sugita et al for the addition of amines to conjugated allene ketones or esters [58].



Scheme 14. Possible reaction mechanism of the reaction between 2-(1-alkynyl)-2-cycloalken-1-ones (**44**, **45**) and amines

To sum up, a unique tandem isomerization–addition reaction of 2-(1-alkynyl)-2-alken-1-ones (**44**, **45**) and primary aliphatic amines has been found. Notably, this mild and atom-economical transformation enables to synthesize (*Z*)-*β*-enaminones **46**, **47**, which serve as building blocks for heteroatom containing compounds [59], natural [60] or therapeutic [61] products.

EXPERIMENTAL PART

General information. IR spectra were run in KBr discs on a Perkin-Elmer FT spectrophotometer Spectrum BX II. ^{1}H and ^{13}C NMR spectra were recorded with a Varian Unity Inova (300 MHz) and Bruker (400 MHz) spectrometers in chloroform-d, dimethylsulfoxide-d_6 or acetonitrile-d_3 using the residual solvent signal as internal standard. Signal multiplicity as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet). Unambiguous assignment of signals was made using a combination of NMR experiments, including HSQC, HMBC, COSY, and, NOESY. HRMS spectra were obtained on a mass spectrometer Dual-ESI Q-TOF 6520 (Agilent Technologies). Microwave assisted reactions were carried out in scientific microwave oven CEM Focused Microwave™ Synthesis System, Discover® SP. Melting points were determined in open capillaries with a Stuart SMP10 digital melting point apparatus. All reactions and the purity of the synthesized compounds were monitored by TLC using Silica gel 60 F254 aluminium plates (Merck). Visualization was accomplished by UV light and by treating the plates with vanillin or $KMnO_4$ stains followed by heating. Final purification of synthesized compounds was performed on Flash Chromatography system CombiFlash (Teledyne Isco), using hexane – ethyl acetate mixtures or by column chromatography using toluene – ethyl acetate, methanol – dichloromethane or methanol – ethyl acetate mixtures.

All the procedures for the preparation of compounds as well as their characterization are written in the papers, except of the paper 4, which characterization of the compounds is provided in supporting information. NMR spectra of the synthesized molecules are also presented in the supporting information that it can be found at the following links:

- For paper 1
https://pubs.acs.org/doi/suppl/10.1021/jo501011u/suppl_file/jo501011u_si_001.pdf
- For paper 2
https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Fejoc.201501063&file=ejoc_201501063_sm_miscellaneous_information.pdf

- For paper 3

https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Fejoc.201600985&file=ejoc201600985-sup-0001-SupMat.pdf

- For paper 4

https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Fejoc.201700119&file=ejoc201700119-sup-0001-SupMat.pdf

CONCLUSIONS

1. It was found that carbocyclic 2-alkynylcyclopent-1-enecarbaldehydes, 2-alkynylcyclohex-1-enecarbaldehydes, 2-alkynylbenzaldehydes and electron-rich 1-benzyl-2-alkynylindole-3-carbaldehydes react during $BF_3 \cdot Et_2O$ mediated three-component Kabachnik−Fields reaction with dimethylphosphite and aromatic amines forming *α*-amino [2-(alkynyl)cyclopent-1-enyl]methylphosphonates (**1**), *α*-amino [2-(alkynyl)cyclohex-1-enyl]methylphosphonates (**2**), *α*-amino (2-alkynylphenyl)methylphosphonates (**3**) and *α*-amino [1-benzyl-2-(alkynyl)-1*H*-indol-3-yl]methylphosphonates (**16**) respectively.

2. It was showed that copper (I) iodide catalyzed reaction between electron-defficient 2-alkynylpyridine-3-carbaldehyde (**17**) or 2-alkynylquinoline-3-carbaldehyde (**18**), dimethylphosphite and arylamine proceeds *via* tandem imine formation−6-*endo*-dig cyclization sequence forming dimethyl 6-aryl-7-substituted 5,6-dihydro-1,6-naphthyridin-5-ylphosphonates (**19**) or dimethyl 2-aryl-3-substituted 1,2-dihydrobenzo-[*b*][1,6]naphthyridin-1-ylphosphonates (**20**) *in situ*.

3. The relationship between *α*-aminomethylphosphonates structure and outcome of the reaction was found. Therefore, only benzene ring containing phosphonates **3** were capable to switch their reactivity from 5-*exo*-dig to 6-*endo*-dig and *vice versa* by using different catalyst. Whereas nonaromatic cyclopentene **1** or cyclohexene **2** derivatives underwent 5-*exo*-dig cyclization processes forming fused five-membered products **5** – **14**. Contrariwise, compounds bearing electron-poor pyridine **17** or quinoline **18** ring exclusively reacted in a 6-*endo*-dig manner obtaining polysubstituted 1,6-naphthyridine frame containing phosphonates **19**, **20**.

4. It was found that pyrrol-1-ylphosphonates **8** – **14** having 1-iodoalkenyl, aroyl or formyl moieties can be synthesized applying iodine-mediated cyclization reaction of carbocyclic α-amino (2-alkynyl)methylphosphonates **1** – **3**.

5. Novel, efficient, metal-free synthesis of oxazinones **27**, 4*H*-1,3-oxazines **26**, **28**, 4*H*-1,3-thiazines **29** and 4,5-dihydrothiazoles **34** from electrophile-induced cyclization of *N*-(3-alkynylprop-2-ynyl)benzamides (**21**), *tert*-butyl 3-arylprop-2-ynylcarbamates (**22**), 1-substituted 3-(3-substituted prop-2-ynyl)ureas (**23**) and *N*-(3-arylprop-2-ynylcarbamothioyl)benzamides (**24**) was developed. The mechanistic study revealed that the result of the reactions between functionalized propargylic substrates and electrophilic reagents depends on the electronic effect on the

alkyne, the electrophile used, and the structure of the functional nucleophilic group.

6. It was showed that 1-(1-alkynyl)cyclopropyl imines **42** formed *in situ* from 1-(1-alkynyl)cyclopropyl ketones **41** react with molecules containing polar covalent bonds in a mild and efficient way obtaining polysubstituted pyrroles **43**.

7. The useful stereo- and regioselective approach to (*Z*)-*β*-enaminones (**46**, **47**) from 2-(1-alkynyl)-2-cycloalken-1-ones (**44**, **45**) and primary aliphatic amines was provided.

SUMMARY / SANTRAUKA

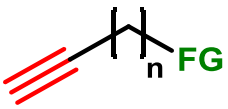
ĮVADAS

Funkcionalizuoti alkinai – tai organinių junginių klasė, įdomi savo cheminėmis savybėmis ir naudinga tikslinėje karbo- ir heterociklinių junginių sintezėje. *N*-, *O*- ar *S*-heterocikliniai dariniai tokie kaip pirolas, 1,2-dihidropiridinas, oksazinonas, oksazolidinonas, oksazinas, oksazolas, tiazinas, tiazolas ir daugelis kitų, yra sintetinami iš trigubąjį ryšį turinčių junginių. Šie heterocikliniai dariniai pasižymi vertingomis biologinėmis savybėmis ir yra aptinkami vaistinių preparatų struktūrose. Pavyzdžiui, pirolas įeina į vaistų: lamelarino, pirolnitrino, likofelono, tofacitinibo, ketorolako, tolmetino ar ribociklibo sudėtį.

Funkcionalizuotų alkinų heterociklizacijos dažniausiai yra atliekamos naudojant stiprias bazes ar pereinamųjų metalų katalizatorius tokius kaip Au (I), Au (III), Ag (I), Cu (I), Cu (II), ar Pd (II) druskos. Tačiau taip pat yra žinoma, kad elektrofiliniai reagentai gali reaguoti su trigubuoju ryšiu ir taip paskatinti greta esančios funkcinės grupės nukleofilinę ataką. Tokiu principu sintetinami junginiai savo sudėtyje turi halogeno ar chalkogeno funkcines grupes, todėl gali būti naudojami tolimesnėms modifikacijoms. Kaip ir ciklizacijos, skeletiniai persigrupavimai taip pat užima svarbią vietą alkinų chemijoje. Propargiliniai substratai yra patrauklūs pradiniai junginiai elektrofilų inicijuotose ciklizacijose, tačiau nepaisant to, šio tipo reakcijos literatūroje nėra dažnos. Prieš keletą metų mūsų laboratorijoje buvo pradėti funkcionalizuotų alkinų savybių tyrimai. Ši disertacija yra skirta fukcionalizuotų propargilinių substratų ir kitų alkinų, gretimoje padėtyje turinčių nukleofilinę grupę, elektrofilų inicijuotoms ir Liuiso rūgščių katalizuojamoms reakcijoms.

Disertacijos tikslas ir užduotys

Darbo tikslas – ištirti funkcionalizuotų alkinų intramolekulines ciklizacijos ar persigrupavimo reakcijas.



Tikslui įgyvendinti iškelti šie uždaviniai:

- Ištirti acetileninių α-anilinmetilfosfonatų ciklizacijas katalizuojamas pereinamųjų metalų druskomis.
- Ištirti elektrofilų inicijuojamas propargilinių substratų reakcijas.
- Ištirti reakcijas tarp 1-(1-alkinil)ciklopropiliminų ir polinį kovalentinį ryšį turinčių junginių.
- Ištirti reakcijas tarp 2-(1-alkinil)-2-cikloalken-1-onų ir aminų.

Mokslinį naujumą atskleidžiantys darbo rezultatai

Šio darbo metu acetileniniams α-anilinmetilfosfonatams sintetinti buvo pritaikyta trikomponentinė Kabachniko−Fieldso reakcija. Parodyta, kad nearomatiniai α-amino (2-alkinil)metilfosfonatai regioselektyviai sudaro pirolo žiedą turinčius junginius. Tuo tarpu piridino ar chinolino žiedą turintys acetileniniai α-anilinmetilfosfonatai tandeminės imino susidarymo–6-*endo*-dig ciklizacijos metu suformuoja 6-aril-5,6-dihidro-1,6-naftiridin-5-ilfosfonatus ir dimetil-2-aril-1,2-dihidrobenzo[b][1,6]naftiridin-1-ilfosfonatus. Acetileniniai α-anilinfenilmetilfosfonatai reaguoja 5-*egzo*-dig ciklizacijos būdu, kai katalizatoriais yra naudojami $AuBr_3$ ar $PdCl_2$, tuo tarpu AgOTf katalizuoja šešianario žiedo susidarymą. Atrastas metodas sintetinti 1-pirolilfosfonatus turinčius 1-jodalkenil-, aroil- ar formilpakaitus. Parodyta, kad oksazinonai, 4*H*-1,3-oksazinai, 4*H*-1,3-tiazinai, 4,5-dihidrotiazolai ir α-pakeisti enonai gali būti efektyviai sintetinami iš funkcionalizuotų propargilaminų ir propargilalkoholių nenaudojant metalų katalizatorių, pritaikant elektrofilų inicijuojamas ciklizacijos reakcijas. Propargilaminai, išskyrus propargiltiokarbamidą, turintys elektronų donorines ariletinilgrupes, reaguoja halogenų, chalkogenų ar oksokarbenio jonų inicijuojamose reakcijose regioselektyviai sudarant 6-*endo*-dig ciklizacijos produktus. Tuo tarpu 5-*egzo*-dig regioselektyvumas yra pasiekiamas vykstant molekulinio jodo ar fenilhipochloroselenoito inicijuojamai nepakeistų propargilinių benzamidų, karbamidų ar tiokarbamidų ciklizacijos reakcijai. Taip pat parodyta, kad reakcijos rezultatas priklauso nuo propargilinių darinių vidinės funkcinės grupės nukleofiliškumo, alkino elektroninio tankio ir elektrofilinio reagento. Surastas naujas būdas sintetinti halogeno, chalkogeno, azido, alkoksi- ar ariloksigrupėmis pakeistus pirolus iš 1-(1-alkinil)ciklopropiliminų ir polinį kovalentinį ryšį turinčių junginių. Atrasta stereo- ir regioselektyvi dvigubojo ryšio migracijos–nukleofilinio prijungimo reakcija tarp 2-(1-alkinil)-2-cikloalken-1-onų ir pirminių aminų susidarant (*Z*)-*β*-enaminonams.

Ginamieji teiginiai

- Nearomatiniai 2-alkinilcikloheks-1-enkarbaldehidai, 2-alkinilciklopent-1-enkarbaldehidai, aromatiniai 2-alkinilbenzaldehidai ir elektronų turtingi 1-benzil-2-alkinilindol-3-karbaldehidai reaguoja $BF_3 \cdot Et_2O$ katalizuojamoje trikomponentinėje reakcijoje su dimetilfosfitu ir aromatiniais aminais susidarant Kabachniko-Fieldso aduktams.
- Acetileninių α-anilinmetilfosfonatų ciklizacijos būdas: 5-*egzo*-dig ar 6-*endo*-dig, priklauso nuo substrato struktūros ir elektroninio tankio ties alkino funkcine grupe. Pereinamųjų metalų katalizatoriai įtaką reakcijos krypčiai turi tik α-amino (2-alkinilfenil) metilfosfonatų atveju.
- Karbocikliniai α-amino (2-alkinil)metilfosfonatai reaguoja su molekuliniu jodu susidarant jodintiems pirolo dariniams.
- Funkcionalizuoti oksazinonai, 4*H*-1,3-oksazinai, 4*H*-1,3-tiazinai, 4,5-dihidrotiazolai ir α-pakeisti enonai gali būti sintetinami iš *N*- ir *O*- propargilinių darinių nenaudojant Liuiso rūgščių katalizatorių.
- Elektrofilais inicijuojamų propargilinių benzamidų, karbamatų, karbamidų, tiokarbamidų ir esterių reakcijų rezultatas priklauso nuo naudojamo elektrofilo, elektroninio tankio ties alkinu ir nukleofilinės grupės struktūros.
- 1-(1-Alkinil)ciklopropiliminai 1,3-prijungimo/5-*endo*-dig ciklizacijos proceso metu reaguoja su polinį kovalentinį ryšį turinčiais junginiais nenaudojant pereinamųjų metalų katalizatorių.
- 2-(1-Alkinil)-2-cikloalken-1-onai regio- ir stereoselektyviai reaguoja su pirminiais aminais, dvigubojo ryšio migracijos–nukleofilinio prijungimo keliu, susidarant (*Z*)-*β*-enaminonams.

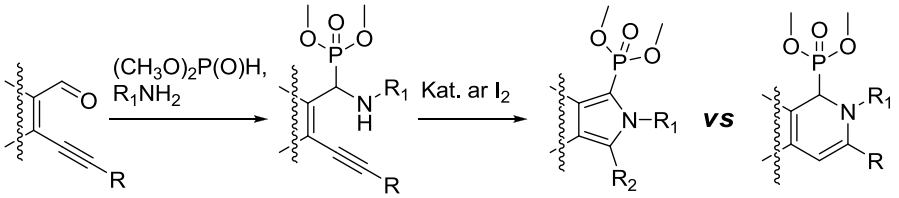
Santraukos išdėstymas

Santrauką sudaro keturios dalys – įžanga, straipsnių apžvalga, eksperimentinė dalis ir išvados. Įžangoje kalbama apie disertacijos tikslą, pagrindinius uždavinius, darbo reikšmingumą ir ginamuosius teiginius. Straipsnių apžvalgos dalyje supažindinama su keturiomis publikacijomis. Eksperimentinėje dalyje trumpai aprašomi sintezės ir analizės metodai. Paskutinėje dalyje pristatomos pagrindinės disertacijos išvados. Santraukoje taip pat pateikiamas doktorantės gyvenimo aprašymas.

Šioje dalyje bus apžvelgiamas kiekvienas straipsnis.

1.1 Straipsnis 1. *Formation of Condensed 1H-Pyrrol-2-ylphosphonates and 1,2-Dihydropyridin-2-ylphosphonates via Kabachnik−Fields Reaction of Acetylenic Aldehydes and Subsequent 5-exo-dig or 6-endo-dig Cyclizations*

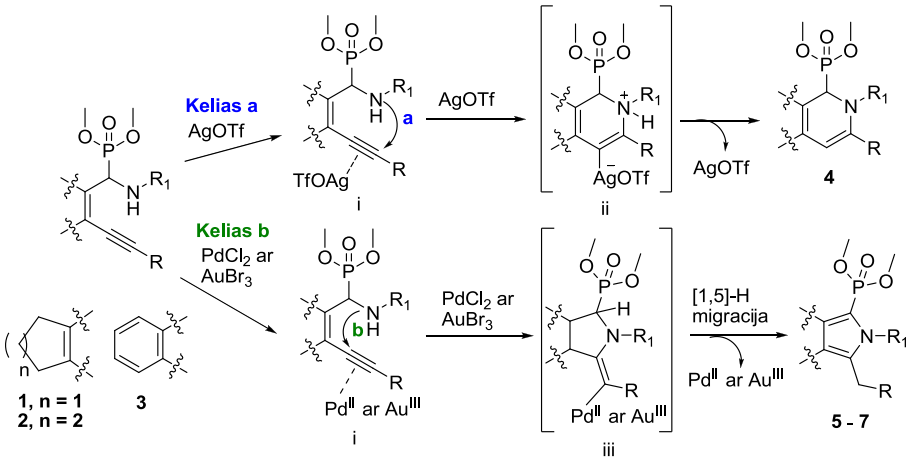
Prieš dešimtmetį literatūroje pasirodė keletas publikacijų apie Liuiso rūgščių katalizuojamas α-amino (2-alkinilfenil)metilfosfonatų ciklizacijos reakcijas. Išanalizavus literatūros duomenis pasirodė, kad heteroaromatinių ir nearomatinių acetileninių α-anilinometilfosfonatų reakcijos dar nėra ištirtos. Turint omenyje, kad ciklizacijos regioselektyvumas gali priklausyti nuo ne tik nuo naudojamo katalizatoriaus, bet ir nuo substrato struktūros, buvo nuspręsta ištirti pereinamųjų metalų katalizuojamas ir jodu inicijuojamas įvairių karbo- ir heterociklinių α-acetileninių anilinometilfosfonatų ciklizacijos reakcijas (schema 1). Taigi straipsnio 1 apžvalgoje pateikiami svarbiausi šios temos rezultatai.



Schema 1. α-Aminometilfosfonatų, susintetintų iš acetileninių aldehidų, ciklizacijos reakcijos

Atliekamame tyrime Kabachniko-Fieldso aduktai buvo sintetinami iš acetileninių aldehidų, aminų ir dimetilfosfito trikomponentinės reakcijos metu. Susidarę acetileniniai α-aminometilfosfonatai toliau dalyvavo ciklizacijos reakcijoje naudojant AgOTf, $PdCl_2$ ar $AuBr_3$ katalizatorius. Pasiūlytas reakcijos mechanizmas yra panašus į Wu *et al* siūlomą mechanizmą *α*-amino (2-alkinilfenil)metilfosfonatams. Visgi, nearomatiniai α-acetileniniai aminometilfosfonatai **1**, **2** reagavo kitaip negu aromatiniai analogai. Ciklizacija vyksta dvejais skirtingais keliais priklausomai nuo pradinio junginio struktūros ir naudojamo katalizatoriaus. Manoma, kad metalas koordinuoja trigubąjį ryšį sudarant metalo-trigubojo ryšio kompleksą *i*, kuris gali toliau dalyvauti ciklizacijoje. Nukleofilinė amino

grupė regioselektyviai atakuoja elektronų deficitinį trigubąjį ryšį, susidarant tarpiniams junginiams *ii* ar *iii*. *α*-Amino (2-alkinilfenil)metilfosfonatų (**3**) atveju, 6-*endo*-dig ciklizacija vyksta, kai katalizatoriumi naudojamos Ag(I) druskos (kelias a), tuo tarpu Pd(II) ar Au(III) įgalina 5-*egzo*-dig ciklizaciją (kelias b). Nestabilus ciklinis darinys *ii* transformuojasi į 1,2-dihidropiridino produktą **4** (kelias a), o *iii* dalyvauja [1,5]-H migracijoje sudarant pirolo žiedą turintį junginį **5** (kelias b). Svarbu paminėti, kad nearomatiniai Kabachniko-Fieldso aduktai **1**, **2** regioselektyviai sudaro tik 5-*egzo*-dig ciklizacijos produktus (kelias b). Įdomu tai, kad nearomatinį karkasą turintys fosfonatai **1**, **2** ciklizuojasi išskirtinai į kondensuotus pirolo **6**, **7** darinius net kai katalizatoriumi naudojmas AgOTf, kuris katalizuoja 6-*endo*-dig ciklizaciją benzeno dariniuose **3**. Tai aiškiai parodo, kad reakcijos kelias priklauso ne tik nuo katalizatoriaus, bet ir nuo pradinio junginio struktūros (schema 2).

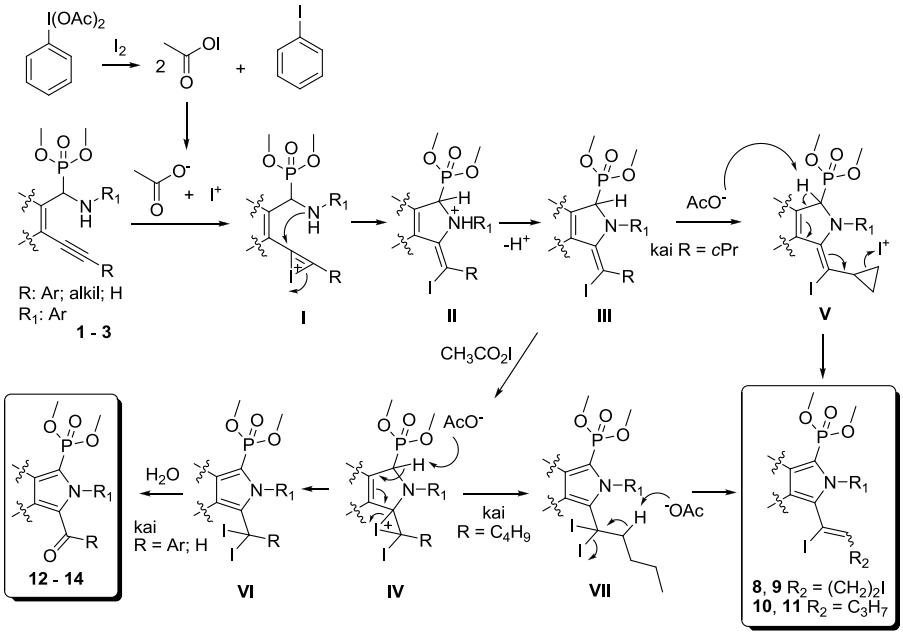


Schema 2. Liuiso rūgštimis katalizuojamų karbociklinių α-acetileninių anilinometilfosfonatų **1** – **3** galimas reakcijos mechanizmas

Fenilmetilfosfonatų **3** ciklizacijos reakcijose katalizatorius nulemia ciklizacijos eigą. Nors visos naudotos Liuiso rūgštys yra minkštosios ir yra gimininges C-C nesočioms jungtims, bet šios rūgštys skiriasi krūviu ir atomo spinduliu. Ag(I) turi mažesnį atomo spindulį ir joninį krūvį negu Pd(II) ar Au(III). Tai galėtų būti viena iš priežasčių, kodėl naudojant skirtingus katalizatorius skiriasi reakcijos rezultatas. Tačiau reikia pabrėžti, kad nearomatinių analogų **1**, **2** ciklizacijos kryptį lemia ne katalizatorius, bet substrato struktūra. Cikloheksenо ir ciklopenteno žiedai nėra vienoje plokštumoje lyginant su benzeno analogu. Nors literatūroje sutinkamose

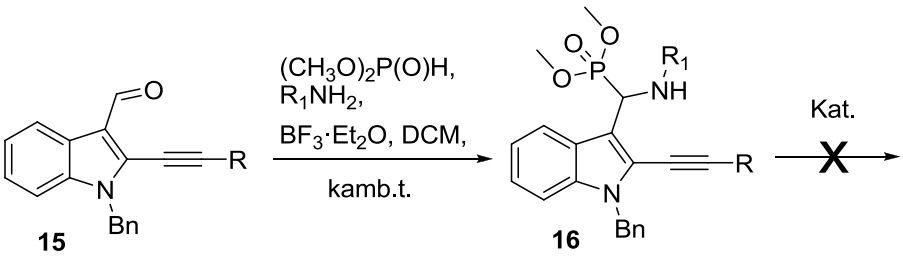
metalų katalizuojamose alkinų ciklizacijose, pakaito prie trigubojo ryšio prigimtis lemia žiedo užsidarymo būdą, mūsų tyrimuose tokia tendencija nebuvo pastebėta, tiek aril-, tiek alkilpakaitai nulėmė tą pačią reakcijos kryptį.

Toliau straipsnyje 1 kalbama apie elektrofilinio jodo inicijuojamas ciklizacijos reakcijas, kurios leidžia funkcionalizuotus heterociklus sintetinti patogiu ir pigiu būdu. Nearomatinių metilfosfonatų **1**, **2** ir fenilmetilfosfonatų **3** ciklizacijos metu, inicijuojant molekuliniam jodui, buvo stebimas tik penkianarių pirolo darinių **8** – **14** susidarymas. Molekulinis jodas yra aktyvuojamas paverčiant jį į labiau elektrofilinį darinį – acetilhipojoditą. I_2 yra oksiduojamas (diacetoksijod)benzenu, susidarant 2 ekvivalentams acetilhipojodito ir jodbenzeno. Toliau, α-anilinometilfosfonatų **1** – **3** trigubasis ryšys reaguoja su I^+, suformuojant jodonio katijoną **I**. Ši reaktyvi dalelė yra atakuojama kaimyninio azoto ir po **II** darinio deprotonizacijos, sudaro tarpinį produktą **III**, kuris gali reaguoti dvejais skirtingais keliais priklausomai nuo pakaito prie trigubojo ryšio. Kai *R* yra ciklopropilgrupė, acetato anijonas atplėšia protoną iš **V**, trinaris žiedas atsiveria ir prisijungus jodą, susidaro produktai **8**, **9**. I^+ taip pat gali sudaryti jodonio katijoną su darinio **III** dvigubuoju ryšiu, ko pasekoje susiformuoja tarpinė dalelė **IV**, kuri po aromatizacijos virsta į nestabilius darinius **VI** ir **VII**. Junginys su alkilpakaitu sudaro jodalkenilintus produktus **10**, **11**, o kai *R* yra arilpakaitas arba H, vanduo esantis tirpiklyje reaguoja su dariniu **VI** sudarant produktus **12** – **14**. Nors, pakaito prie trigubojo ryšio prigimtis nelėmė ciklizacijos krypties, tačiau substratai su ariletinil- **1a**, **2a**, **3a** ar etinilpakaitais **1b**, **3b** suformavo kondensuotus pirolus **12** – **14** su karbonilo funkcine grupe. Tuo tarpu fosfonatai **1c**, **2c** turintys alkiletinilgrupę, reagavo į 1-jodalkenilintus produktus **8** – **11** (schema 3).



Schema 3. Jodo inicijuojamų α-acetileninių anilinometilfosfonatų **1** – **3** galimas ciklizacijos mechanizmas

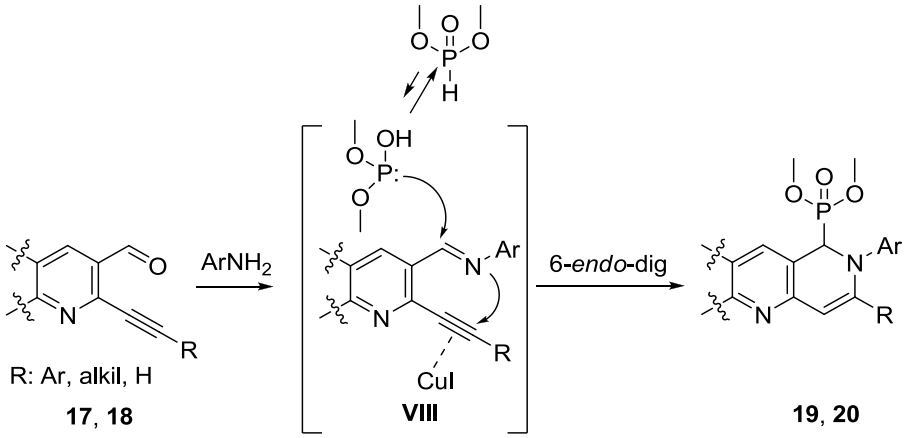
Kita tema aptariama straipsnyje yra heterocikliniai Kabachniko-Fieldso aduktai ir jų ciklizacijos reakcijos. Buvo nustatyta, kad elektronų donorinis 2-(alkinil)-1-benzil-1*H*-indol-3-karbaldehidas (**15**) geba suformuoti atitinkamą fosfonatą **16**, tačiau jis nėra pakankamai aktyvus ciklizacijos reakcijoje (schema 4).



Schema 4. 2-(Alkinil)-1-benzil-1*H*-indol-3-karbaldehido (**15**) ir atitinkamo fosfonato **16** reaktingumas

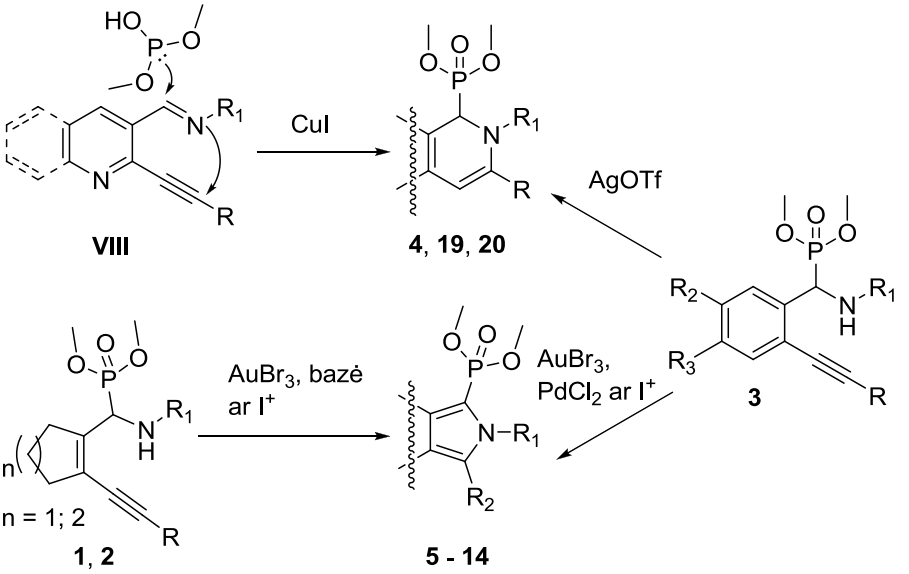
Taigi, tolimesniems tyrimams buvo pasirinkti elektronų deficitiniai 2-alkinilpiridin-3-karbaldehidai **17** ir 2-alkinilchinolin-3-karbaldehidai **18**, kurie trikomponentinės reakcijos metu su aminu ir dimetilfosfitu, iš karto ciklizavosi į 6-*endo*-dig ciklizacijos produktus **19**, **20**. Pilna reakcijos

konversija buvo pasiekta naudojant CuI katalizatorių. Manoma, kad trigubasis ryšys yra smarkiai aktyvuojamas dėl elektronus ištraukiančio piridino ir chinolino žiedo efekto ir metalo-trigubojo ryšio komplekso susidarymo (tarpinis darinys **VIII**). Dėl šios priežasties, po imino susiformavimo, dimetilfosfitas iškart atakuoja sp^2 anglies atomą ir įvyksta nukleofilinė ciklizacija susidarant dihidro-1,6-naftiridinilfosfonatams **19**, **20** (schema 5). Tarpinio imino susiformavimas buvo įrodytas BMR spektroskopijos pagalba.



Schema 5. Dihidro-1,6-naftiridinilfosfonatų **19**, **20** sintezės vienoje kolboje mechanizmas

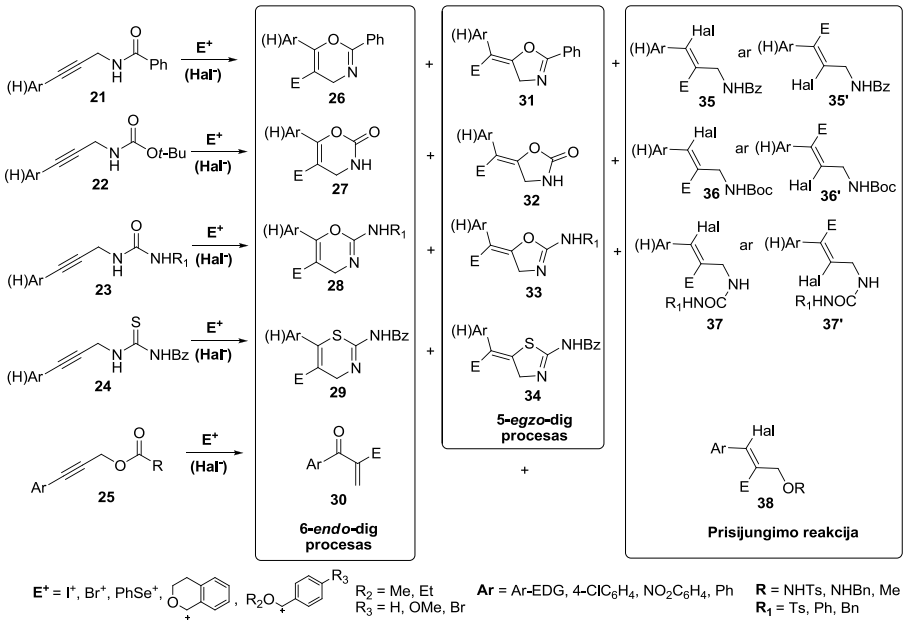
Apibendrinant straipsnyje 1 pateiktus duomenis, buvo parodyta, kad trikomponentinė Kabacniko-Fieldso reakcija yra tinkama karbociklinį karkasą ar elektronų donorinį indolo žiedą turintiems fosfonatams **1** – **3**, **16** sintetinti. Tuo tarpu elektronų deficitiniai 2-alkinilpiridin-3-karbaldehidai **17** ir 2-alkinilchinolin-3-karbaldehidai **18** reakcijoje su arilaminu ir dimeilfosfitu iškarto ciklizuojasi į 6-*endo*-dig produktus **19**, **20**. Ciklizacijos krypties nustatymo tyrimai buvo atliekami pasirinkus skirtingos struktūros α-aminometilfosfonatus. Nearomatiniai cikloalkeno žiedą turintys fosfonatai **1**, **2** ciklizuojasi 5-*egzo*-dig būdu, o benzeno žiedą turintys fosfonatai **3**, sudaro penkianarius arba šešianarius produktus priklausomai nuo naudojamo katalizatoriaus. Parodyta, kad elektronų donorinį indolo žiedą turinčių fosfonatų ciklizacijos nėra įmanomos, tuo tarpu elektronų deficitiniai piridino ir chinolino dariniai **17**, **18** ciklizuojasi 6-*endo*-dig būdu. Nustatyta, kad jodo inicijuojamose ciklizacijose susidaro pirolo fosfonatai **8** – **14** su 1-jodoalkenil-, aroil- ar formilpakaitais (schema 6).



Schema 6. α-Aminometilfosfonatų **1** – **3** ir iminų **VIII** (iš **17**, **18**) ciklizacijų kryptys

1.2 Straipsnis 2. *Electrophile-Mediated Reactions of Functionalized Propargylic Substrates*

Straipsnis 2 yra skirtas elektrofilų inicijuojamiems funkcionalizuotų propargilinių junginių reakcijų tyrimams (schema 7).



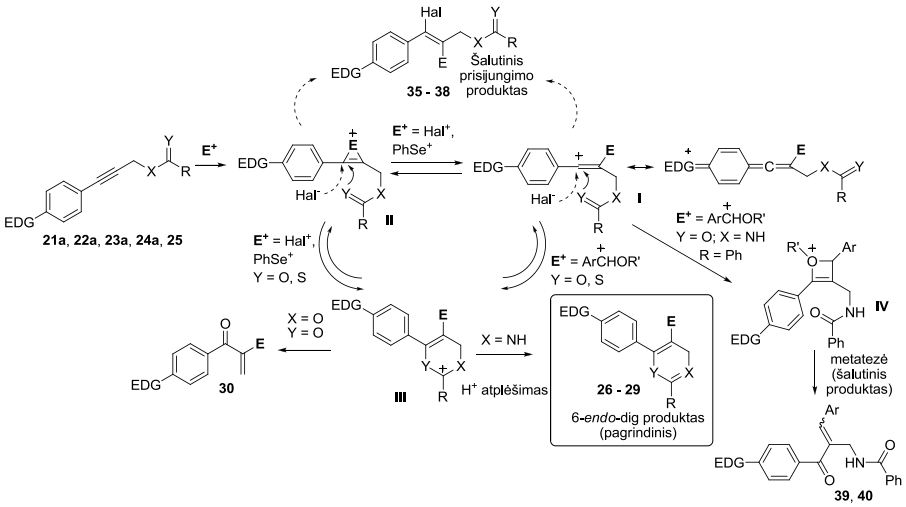
Schema 7. Elektrofilų inicijuojamos propargilinių darinių **21** – **25** transformacijos

Tiriant propargilinių darinių elektrofilų inicijuotas reakcijas, pradiniais substratais buvo pasirinkti propargiliniai benzamidai **21**, karbamatai **22**, karbamidai **23**, tiokarbamidai **24** ir esteriai **25** su skirtingais pakaitais prie trigubojo ryšio. Elektrofiliniais šaltiniais pasirinkti molekulinis jodas, NBS, PhSeCl, cikliniai ir acikliniai acetaliai. Reikia paminėti, kad norint gauti elektrofilinę dalelę, acetaliai turėjo būti modifikuojami. Kaip matoma schemoje 7, propargilinių substratų reakcijos su elektrofilais rezultatas gali būti 5-*egzo*-dig, 6-*endo*-dig ciklizacijos, persigrupavimo ar prisijungimo prie trigubojo ryšio produktas. Todėl yra būtina ištirti kaip skirtingos funkcinės grupės gali įtakoti reakcijos kryptis.

Galimas reakcijos mechanizmas yra pateiktas schemoje 8. Propargiliniai substratai **21a**, **22a**, **23a**, **24a**, **25** turintys elektronų donorines arilgrupes prie trigubojo ryšio reaguoja su halogenais ar PhSeCl suformuodami haloirenio ar selenirenio jonus **II**, kurie yra pusiausvyroje su atviros grandinės karbokatijonais **I**. Prie trigubojo ryšio esanti elektronų donorinė arilgrupė stabilizuoja vinilinį karbokatijoną **I**, todėl palankesnė tampa 6-*endo*-dig ciklizacija. Priklausomai nuo X ir Y funkcinių grupių, darinys **III** virsta į produktus **26** – **29** arba **30**. Kai X = NH, Y = O ar S, susidaro šešianariai junginiai **26** – **29**. Tuo tarpu, kai X = Y = O tarpinis junginys **III** yra nestabilus ir persigrupuoja į α-pakeistą enoną **30**. Kaip matome pradinių

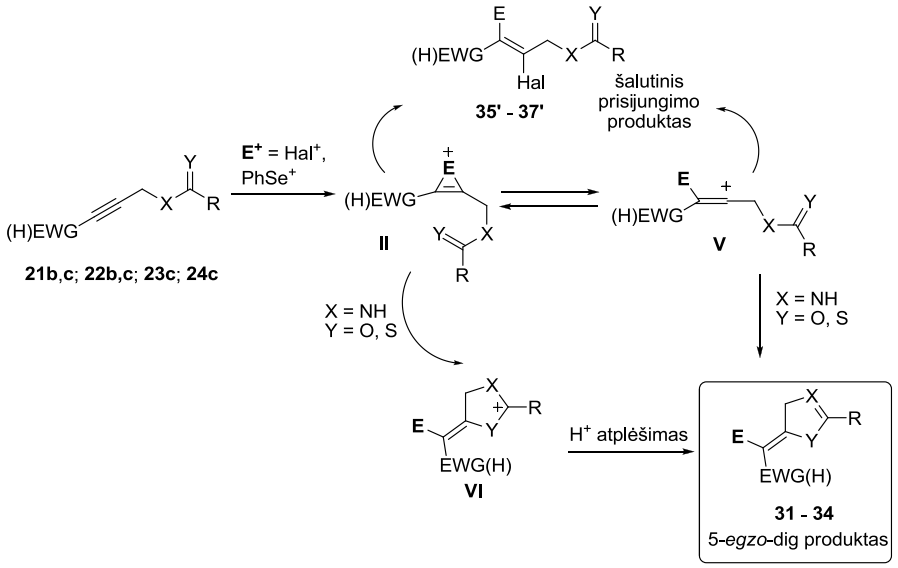
junginių **22a**, **23a**, **24a**, **25** reakcijos vyko per tarpinį ciklinį darinį **III**. Taip pat buvo nustatyta, kad propargilinių amidų **21a** (X = NH, Y = O, R = Ph) reakcija su oksokarbenio jonu gali vykti ne tik 6-*endo*-dig keliu, bet ir per tarpinę 1,2-dihidrooksetinio dalelę **IV**, susidarant enonams **39** ir **40**. Šio tipo reaktingumas buvo pastebėtas mūsų laboratorijoje jau anksčiau.

Kai kuriais etvejais buvo stebima šalutinė elektrofilo prisijungimo prie trigubojo ryšio reakcija. Vykstant reakcijai su jodu ar PhSeCl, priešjoniai konkuruoja su vidiniu propargilinio substrato nukleofilu. Pašalinė prisijungimo reakcija vyksta, kai priešjonis yra stipresnis nukleofilas už vidinį (punktyrinė linija schemoje 8). Taip susiformuoja produktai **35** – **38**. Tačiau verta paminėti, kad dėl didesnio nukleofiliškumo karbamidai **23a** ir tiokarbamidai **24a** dalyvauja išskirtinai tik ciklizacijos reakcijoje.



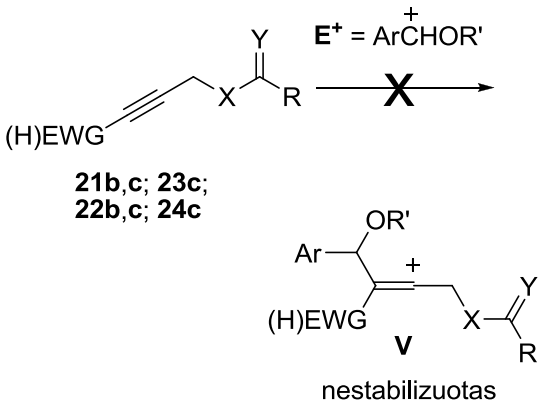
Schema 8. Propargilinių substratų **21a**, **22a**, **23a**, **24a**, **25** su elektronų donorine arilgrupe galimas reakcijos mechanizmas

Naudojant elektronų deficitines arilgrupes turinčius propargilinius substratus **21b**, **22b** arba substratus su terminaliniu trigubuoju ryšiu **21c**, **22c**, **23c**, **24c**, buvo stebimas tiek regioselektyvumo, tiek reakcijos greičio pasikeitimas (schema 9). Hal^+ ar $PhSe^+$ reaguoja su trigubuoju ryšiu sudarant joną **II**, kuris yra pusiausvyroje su viniliniu karbokatijonu **V**. Ši dalelė gali būti stabilizuojama CH_2FG grupės indukciniu efektu ir yra linkusi reaguoti 5-*egzo*-dig būdu susidarant cikliniam karbokatijonui **VI**, kuris transformuojasi į galutinius produktus **31 – 34**. Šiuo atveju taip pat galima šalutinė prisijungimo prie trigubojo ryšio reakcija.



Schema 9. Nepakeistų propargilinių substratų **21c**, **22c**, **23c**, **24c** ir substratų su elektronų akceptorinėmis arilgrupėmis **21b**, **22b** galimas reakcijos mechanizmas

Taip pat svarbu paminėti, kad propargiliniai dariniai su terminaliniu trigubuoju ryšiu **21c**, **22c**, **23c**, **24c** ar elektronų deficitinėmis arilgrupėmis **21b**, **22b** nereagavo su oksokarbenio elektrofilais (schema 10). Manoma, kad haloirenio ar selenirenio jonai **II** yra būtini vinilinio karbokatijono dalinei stabilizacijai. Reakcijų su oksokarbenio jonais atveju, tarpinė dalelė **II** susidaryti negali, dėl ko vinilinis karbokatijonas nėra stabilizuojamas ir reakcija nevyksta.



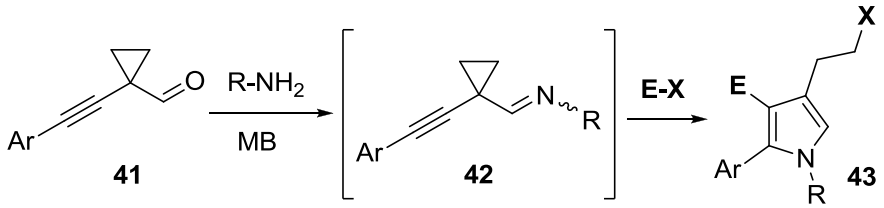
Schema 10. Elektronų deficitiniai ar nepakeisti propargiliniai junginiai **21b**, **22b**, **21c**, **22c**, **23c**, **24c** ir oksokarbenio jonai

Tiriant propargilinių darinių elektrofilines transformacijas pastebėta, kad reakcijos vyksta greičiau, kuomet naudojami substratai **21a**, **22a**, **23a**, **24a**, **25** su elektronų perteklinėmis grupėmis šalia trigubojo ryšio. Priešingai, elektronų deficitiniai arilpakaitai reakcijų greitį mažina. Taip pat nustatyta, kad esant elektronų donoriniams pakaitams, reakcija paparastai vyksta 6-*endo*-dig keliu. Spėjama, kad vinilinis karbokatijonas yra stabilizuojamas rezonanso pagalba, tuo tarpu substratai **21b**, **22b** su elektronus ištraukiančiomis grupėmis pasižymi skirtingu regioselektyvumu, galbūt dėl indukcinio ir mezomerinio efekto įtakos viniliniam karbokatijonui. Neaktyvuoti propargiliniai dariniai **21b**, **22b**, **21c**, **22c**, **23c**, **24c** nereaguoja su oksokarbenio elektrofilais dėl stabilizacijos trūkumo. Įdomus faktas yra tai, kad elektrofilų inicijuojamose reakcijose, tik siera ir karbonilinės grupės deguonis atlieka nukleofilo vaidmenis, kai tuo tarpu metalų katalizuojamose karbamatų analogų reakcijose, yra stebimas ir *NH* grupės nukleofiliškumas. Ištirta, kad elektrofilo prisijungimas prie trigubojo ryšio yra galimas tuomet, kai haloirenio ar selenirenio jonai yra atakuojami halogeno priešjonio, kuris konkuruoja su nukleofilu esančiu propargiliniame substrate.

Apibendrinant straipsnį 2, galima teigti, kad ištirta nauja, halogenų, chalkogenų ar oksokarbenio jonų inicijuojama įvairių 1,3-oksazinų **26**, **28**, oksazinonų **27**, 1,3-tiazinų **29**, 4,5-dihidrotiazolų **34** ir α-funkcionalizuotų enonų **30**, **39**, **40** sintezė, kuriai nereikalingi pereinamųjų metalų katalizatoriai. Parodyta, kad reakcijos rezultatas labai priklauso nuo vidinio nukleofilo stiprumo, trigubojo ryšio pakeitimo ir elektrofilo prigimties.

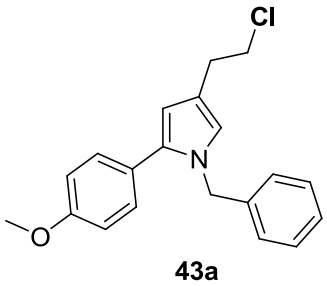
1.3 Straipsnis 3. *Synthesis of Polysubstituted Pyrroles through the Tandem 1,3-Addition/5-Endo-Dig Cyclization of 1-(1-Alkynyl)Cyclopropyl Imines*

Tęsiant darbus elektrofilais inicijuotų ciklizacijų srityje, buvo nuspręsta ištirti 1-(1-alkinil)ciklopropiliminų reakcijas su elektrofilais. Visgi pastebėjus šios reakcijos ypatybes, elektrofilus tikslingiau būtų vadinti polinį kovalentinį ryšį turinčiais junginiais. Todėl straipsnyje 3 yra analizuojamos 1-(1-alkinil)ciklopropiliminų **42** reakcijos su **E-X** tipo junginiais (schema 11).



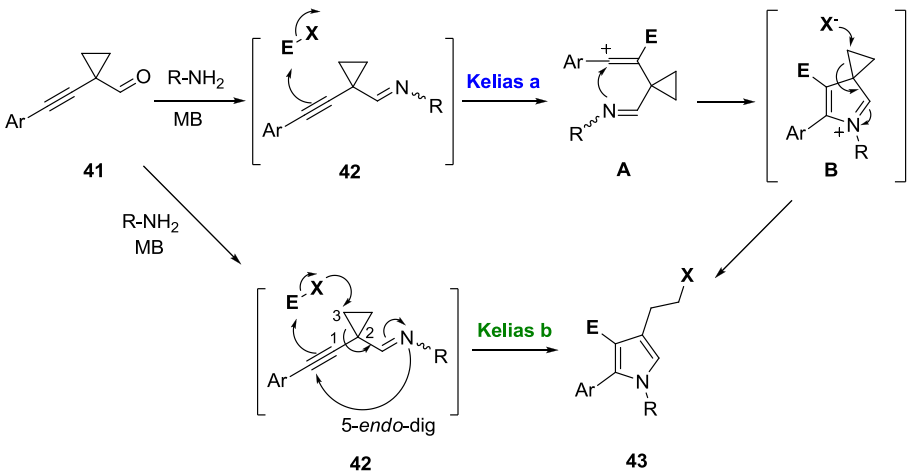
Schema 11. 1-(1-Alkinil)ciklopropiliminų **42** sintezė ir jų reakcija su **E-X** tipo junginiais

Pirmiausiai buvo bandoma atlikti 1-(1-alkinil)ciklopropilimino **42** sintezę iš 1-(1-alkinil)ciklopropilkarbaldehido **41**, tačiau nustatyta, kad vietoje imino susidaro ciklinis produktas – pirolas **43a** su halogeno grupe šoninėje grandinėje (pav. 1). Manoma, kad heterociklinio darinio susidarymą paskatino priemaišinis HCl, kuris galėjo būti reakcijos tirpiklyje 1,2-dichloretane. Reakcija vyksta protonui inicijuojant imino **42** 5-*endo*-dig ciklizaciją, po kurios, nukleofilinis Cl^- atveria ciklopropano žiedą.



Pav. 1. Pirolas **43a** su halogeno grupe šoninėje grandinėje

Pastebėjus šį įdomų reaktingumą, buvo tiriamos reakcijos su molekuliniu jodu ir junginiais turinčiais nesimetrinį kovalentinį ryšį (ICl, PhSeCl, IN_3, AcOI, ROH). Iminai **42** buvo sintetinami mikrobangų reaktoriuje (MB), tuomet nugarinus tirpiklį ir perteklinį aminą, likutis buvo tirpinamas MeCN ir pridedama reagento **E-X**. Ciklizacijos reakcija buvo atlikta su junginiais turinčiais fenil-, 4-metoksifenil-, *p*-tolilpakaitus prie trigubojo ryšio ir *tret*-butil-, benzil-, cikloheksil- ar izopropilpakaitus prie imino funkcinės grupės.
Taip pat buvo pasiūlytas galimas reakcijos mechanizmas, kuris rodo, kad reakcija gali vykti dvejais keliais. Kelyje a, iminas **42**, susiformavęs iš aldehido **41** ir amino, reaguoja su elektrofilu, sudarydamas vinilinį karbokatijoną **A**, tuomet vyksta 5-*endo*-dig ciklizacija, susiformuojant tarpiniam dariniui **B**. Tada anijonas, esantis tirpale atakuoja ciklopropano žiedą, kuriam atsivėrus susidaro pirolas **43**. Panašus mechanizmas buvo pasiūlytas Huango ir jo grupės, furanams iš 1-(1-alkinil)-ciklopropilketonų sintetinti. Norint išsiaiškinti ar ciklopropano žiedas atsiveria po elektrofilinės aktyvacijos ir iškart vykstančios ciklizacijos, į reakcijos mišinį su iminu **42** ir junginiu **E-X** buvo pridedama papildomų nukleofilų – piperidino, indolo, NaN_3, KI ar MeOH. Po reakcijos atlikus susidariusio junginio BMR ir HRMS analizę paaiškėjo, kad susidariusiame junginyje papildomo nukleofilo fragmento nėra. Tai parodo, kad reakcija vyksta kitu keliu. Manoma, kad polinį kovalentinį ryšį turintis junginys **E-X** prisijungia prie trigubojo ryšio, kartu atverdamas ciklopropano žiedą formaliu 1,3-prisijungimo būdu ir įvykus 5-*endo*-dig ciklizacijai susidaro galutinis pirolas **43** (kelias b, schema 12).

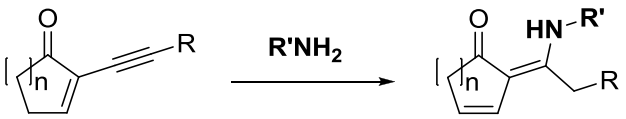


Schema 12. Galimas pirolų **43** susidarymo mechanizmas

Reikėtų pabrėžti, kad norint atsakyti į klausimą, kuris mechanizmas dominuos, būtina atsižvelgti į ciklopropilgrupę turintį alkiniliminą. Nepakeistą ciklopropilgrupę turintys substratai linkę reaguoti 1,3-prijungimo keliu paskatinant intramolekulinę ciklizaciją, tuo tarpu erdviškai dideli pakaitai šalia ciklopropilgrupės lemia elektrofilo inicijuojamą žiedo užsidarymo reakciją, taip kaip matoma mokslininko Huango straipsnyje.
Abibendrinus straipsnį 3, matome, kad surastas naujas metodas sintetinti polipakeistiems pirolams **43** turintiems halogeno, chalkogeno, azido, alkoksi-, ariloksigrupes šoninėje grandinėje.

1.4 Straipsnis 4. *Addition of Primary Amines to 2-(1-Alkynyl)-2-cycloalken-1-ones*

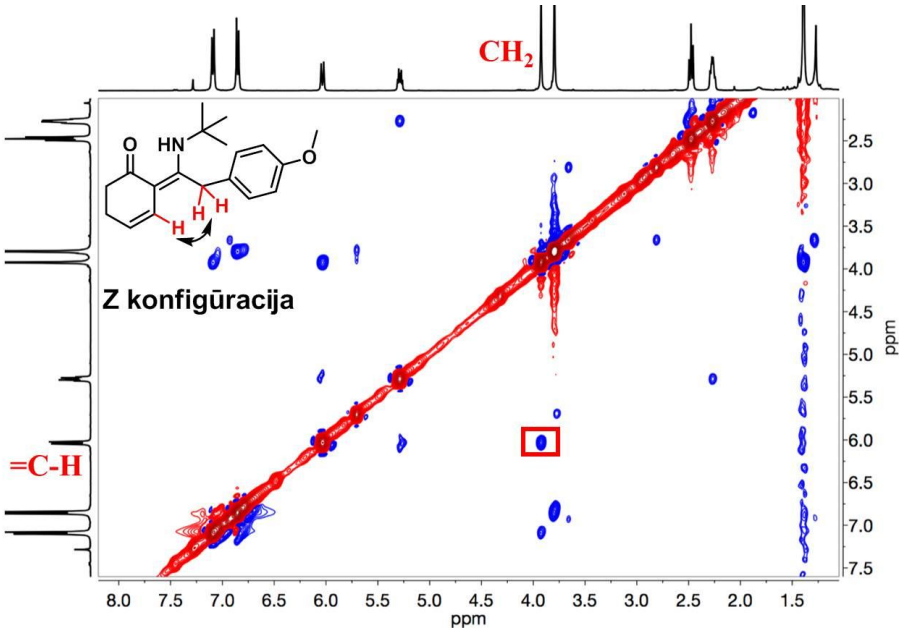
Pirminis tikslas buvo susintetinti 2-(1-alkinil)-alkeniminus iš 2-(1-alkinil)-alken-1-onų ir ištirti jų ciklizacijos reakcijas susidarant pirolo dariniams. Visgi reakcija vyko kitaip, negu tikėtasi, todėl straipsnyje 4 kalbama apie unikalią reakciją tarp 2-(1-alkinil)-cikloalken-1-onų (**44**, **45**) ir pirminių aminų (schema 13).



n = 1 **44** n = 1 **46**
n = 2 **45** n = 2 **47**

Schema 13. Reakcija tarp 2-(1-alkinil)-2-cikloalken-1-onų (**44**, **45**) ir aminų

Buvo pastebėta, kad reakcija tarp 2-(1-alkinil)-2-cikloheksen-1-ono **45** ir amino vyksta susiformuojant (*Z*)-2-[1-(amino)-2-ariletiliden]cikloheks-3-enonui **47** regio- ir stereoselektyviu būdu. Produkto struktūra buvo įrodyta remiantis HSQC, HMBC ir NOESY BMR spektrais. NOESY spektras parodo sąveikas tarp protonų, kurie yra netoli vienas kito ne per ryšius, o per erdvę. Spektre matoma sąveika tarp *β*-H, esančio prie dvigubojo ryšio cikloheksenо žiede ir vandenilių iš *CH_2Aril* fragmento, taip patvirtinant susidariusio *β*-enaminono *Z* konfigūraciją (pav. 7).

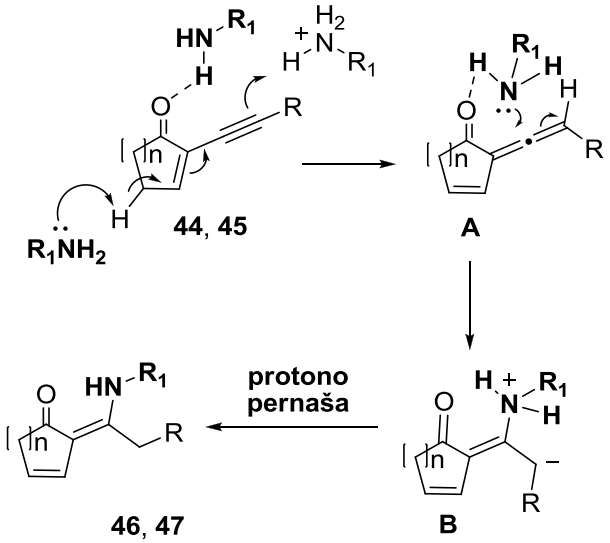


Pav. 7. *β*-Enaminono **47a** NOESY spektras

Taip pat buvo atliktos reakcijos ir su 2-(1-alkinil)-2-ciklopenten-1-onais **44**. Tačiau verta paminėti, kad norint pasiekti pilną reakcijos konversiją, buvo reikalingos griežtos reakcijos sąlygos.

Išbandžius skirtingus aminus paaiškėjo, kad 2-(1-alkinil)-2-cikloheksen-1-onų **45** reakcijos su aminais metu yra toleruojami tiek linijiniai, tiek cikliniai, tiek erdviškai dideli pirminiai aminai. Nustatyta, kad aromatiniai aminai nėra aktyvūs dėl per mažo nukleofiliškumo, o antriniai aminai lemia pradinio junginio degradaciją.

Šis specifinis *β*-enaminonų **46**, **47** susiformavimas gali būti paaiškintas remiantis reakcijos mechanizmu. Pirmiausiai aminas ir ketonas **44**, **45** suformuoja vandenilinį ryšį, tuomet aminas atplėšia *γ* protoną iš pradinio junginio. Trigubajam ryšiui protonizuojantis vyksta dvigubojo ryšio izomerizacija susidarant alenui **A**. Tuomet, nukleofilinis aminas jungiasi prie aleno **A**, stereo- ir regioselektyviu būdu, suformuojant tarpinį darinį **B**, kuris po protono pernašos virsta į (*Z*)-*β*-enaminoną **46**, **47** (schema 14).



Schema 14. Galimas 2-(1-alkinil)-2-cikloalken-1-onų (**44**, **45**) ir aminų reakcijos mechanizmas

Atrasta unikali, tandeminė persigrupavimo-prisijungimo reakcija tarp 2-(1-alkinil)-2-cikloalken-1-onų (**44**, **45**) ir pirminių aminų. Susidarę (*Z*)-*β*-enaminonai **46**, **47** gali būti naudojami kaip tarpiniai dariniai heterociklų ar natūralių produktų sintezėje.

EKSPERIMENTINĖ DALIS

Pagrindinė informacija. IR spektrai registruoti Perkin-Elmer Spectrum BX II spektrofotometru KBr tabletėse. ^{1}H ir ^{13}C BMR spektrai užrašyti su Varian Unity Inova (300 MHz) ir Bruker (400 MHz) spektrometrais, chloroformo-d, dimetilsulfoxido-d_6 ar acetonitrilo-d_3 tirpikliuose, vidiniu standartu naudojant deuteruotų tirpiklių likutines vertes. Cheminių poslinkių reikšmės pateiktos δ skalėje. Aprašant ^{1}H BMR spektrus naudojami pažymėjimai: s – singletas, d – dubletas, t – tripletas, q – kvadrupletas, quint – kvintetas, m – multipletas. Signalų priskirimas buvo atliktas pasitelkiant HSQC, HMBC, COSY ir NOESY BMR eksperimentus. HRMS spektrai užrašyti masių spektrometru Dual-Esi Q-TOF 6520 (Agilent Technologies). Mikrobangomis inicijuojamos reakcijos buvo atliekamos profesionalioje mikrobangų krosnelėje CEM Focused Microwave™ Synthesis System, Discover® SP. Junginių lydymosi temperatūros nustatytos atviruose kapiliaruose prietaisu Stuart SMP10. Reakcijų eiga stebima plonasluoksnės chromatografijos metodu, naudojant TLC Silica gel 60 F254 aliuminio

plokšteles (Merck). TLC dėmių vizualizavimas buvo atliktas UV šviesoje arba naudojant vanilino ar $KMnO_4$ tirpalus. Susintetintų junginių gryninimui naudota Flash chromatografijos sistema CombiFlash (Teledyne Isco). Eliuentai: heksano – etilacetato, tolueno – etilacetato, metanolio – dichlormetano ar metanolio – etilacetato mišiniai.

Sintezės metodikų aprašymai ir junginių charakterizavimas yra pateiktas straipsniuose, išskyrus junginius priklausančius ketvirtam straipsniui. Šie junginiai ir jų sintezės eiga yra aprašyta priede (*angl.* Supporting information). Susintetintų molekulių BMR spektrai taip pat pateikti prieduose, kurie prie disertacijos nepridedami, bet gali būti randami naudojant nuorodas:

- Straipsnio 1 priedas
https://pubs.acs.org/doi/suppl/10.1021/jo501011u/suppl_file/jo501011u_si_001.pdf
- Straipsnio 2 priedas
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IŠVADOS

1. Nustatyta, kad karbocikliniai 2-alkinilciklopent-1-enkarbaldehidai, 2-alkinilcikloheks-1-enkarbaldehidai, 2-alkinilbenzaldehidai ir elektronų turtingi 1-benzil-2-alkinilindol-3-karbaldehidai reaguoja $BF_3 \cdot Et_2O$ katalizuojamoje trikomponentinėje Kabachniko-Fieldso reakcijoje su dimetilfosfitu ir aromatiniais aminais susidarant *α*-amino [2-(alkinil)ciklopent-1-enil]metilfosfonatams (**1**), *α*-amino [2-(alkinil)cikloheks-1-enil]metilfosfonatams (**2**), *α*-amino (2-alkinilfenil)metilfosfonatams (**3**) ir *α*-amino [1-benzil-2-(alkinil)-1*H*-indol-3-il]metilfosfonatams (**16**).

2. Parodyta, kad vario (I) jodidas katalizuoja tandeminę imino suformavimo-6-*endo*-dig ciklizacijos reakciją tarp elektronus ištraukiančio 2-alkinilpiridin-3-karbaldehido (**17**) ar 2-alkinilchinolin-3-karbaldehido (**18**), dimetilfosfito ir arilaminų, *in situ* susidarant dimetil-6-aril-7-pakeistiems 5,6-dihidro-1,6-naftiridin-5-ilfosfonatams (**19**) ar dimetil-2-aril-3-pakeistiems 1,2-dihidrobenzo-[*b*][1,6]naftiridin-1-ilfosfonatams (**20**).
3. Surastas sąryšis tarp *α*-aminometilfosfonatų struktūros ir reakcijos rezultato. Pademonstruota, kad tik benzeno žiedą turintys fosfonatai **3** geba pakeisti savo reaktingumą iš 5-*egzo*-dig į 6-*endo*-dig ir atvirkščiai, naudojant skirtingus katalizatorius. Tuo tarpu nearomatiniai ciklopenteno **1** ar cikloheksено **2** dariniai ciklizuojasi 5-*egzo*-dig būdu į penkianarius produktus **5** – **14**. Priešingai, elektronų deficitiniai piridino **17** ar chinolino **18** junginiai dalyvauja išskirtinai 6-*endo*-dig ciklizacijoje suformuojant polipakeistus 1,6-naftiridino karkasą turinčius fosfonatus **19**, **20**.
4. Nustatyta, kad pirol-1-ilfosfonatai **8** – **14** turintys 1-jodalkenil-, aroil- ar formilgrupes gali būti sintetinami pritaikant karbociklinių α-amino (2-alkinil)metilfosfonatų **1** – **3** jodociklizacijos reakciją.
5. Pasiūlytas naujas, efektyvus ir paprastas, pereinamųjų metalų katalizės nereikalaujantis oxazinonų **27**, 4*H*-1,3-oksazinų **26**, **28**, 4*H*-1,3-tiazinų **29** ir 4,5-dihidrotiazolų **34** sintezės kelias panaudojant elektrofilų inicijuojamas *N*-(3-alkinilprop-2-inil)benzamidų (**21**), *tret*-butil-3-arilprop-2-inilkarbamatų (**22**), 1-pakeistų 3-(3-pakeistų prop-2-inil)karbamidų (**23**) ir *N*-(3-arilprop-2-inilkarbamotioil)benzamidų (**24**) žiedo suformavimo reakcijas. Buvo nustatyta, kad funkcionalizuotų propargilinių substratų ir elektrofilinių reagentų reakcijos rezultatas priklauso nuo alkino elektroninio efekto, naudojamo elektrofilo ir nukleofilinės grupės struktūros.
6. Parodyta, kad 1-(1-alkinil)ciklopropiliminai **42**, suformuoti *in situ* iš 1-(1-alkinil)ciklopropilketonų **41**, reaguoja su molekulėmis turinčiomis polinį kovalentinį ryšį, 1,3-prijungimo/5-*endo*-dig ciklizacijos būdu. Šis būdas įgalina sintetinti polipakeistus pirolus **43** švelniomis ir efektyviomis sąlygomis.
7. Surasta naudinga stereo- ir regioselektyvi (*Z*)-*β*-enaminonų (**46**, **47**) sintezė iš 2-(1-alkinil)-2-cikloalken-1-onų (**44**, **45**) ir pirminių alifatinių aminų.

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LIST OF PUBLICATIONS IN PROCEEDINGS OR BOOKS OF ABSTRACTS

1. A. Urbanaitė, M. Jonušis, R. Bukšnaitienė, J. Pošiūnas, S. Balkaitis, I. Čikotienė, Synthesis of *N*-Containing heterocycles from functionalized alkynes. "International Conference on Organic Synthesis BOS 2018", Tallinn, Estonia, July 2 – 4, **2018**, p. 155.
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3. A. Urbanaitė, I. Čikotienė, Synthesis of polysubstituted pyrroles *via* tandem 1,3-addition-5-*endo*-dig cyclization of 1-(1-alkynyl)cyclopropyl imines. Open Readings 2017, Vilnius, **2017**.
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8. S. Balkaitis, A. Urbanaitė, I. Čikotienė, *N*-(3-arilprop-2-inilkarbamotioil)benzamidų sintezė ir elektrofilinių ciklizacijos reakcijų tyrimas. Sixth young scientists conference: Physical and Technology Sciences Interdisciplinary Research, Vilnius, Lithuania, February 10, **2016**, p. 11 – 12.
9. A. Urbanaitė, M. Jonušis, R. Bukšnaitienė, J. Pošiūnas, S. Balkaitis, I. Čikotienė, Synthesis and Electrophile-Mediated Cyclization Reactions of Functionalized Propargylic Substrates. International Conference "Paul

Walden 9th Symposium on Organic Chemistry“, Riga, Latvia, May 21 – 22, **2015**, p. 74.

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Paper 1

Formation of Condensed 1*H*-Pyrrol-2-ylphosphonates and 1,2-Dihydropyridin-2-ylphosphonates *via* Kabachnik−Fields Reaction of Acetylenic Aldehydes and Subsequent 5-*exo*-dig or 6-*endo*-dig Cyclizations

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Journal of Organic Chemistry **2014**, *79* (14), pp 6532–6553
DOI: 10.1021/jo501011u
https://pubs.acs.org/doi/10.1021/jo501011u

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Formation of Condensed 1*H*-Pyrrol-2-ylphosphonates and 1,2-Dihydropyridin-2-ylphosphonates via Kabachnik–Fields Reaction of Acetylenic Aldehydes and Subsequent 5-*exo*-*dig* or 6-*endo*-*dig* Cyclizations

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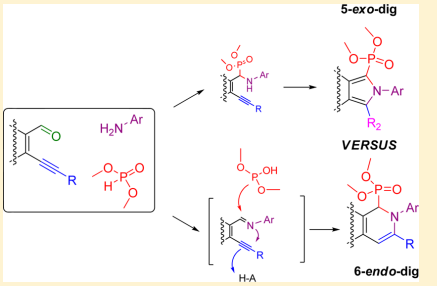
Supporting Information

ABSTRACT: Kabachnik–Fields reactions of various carbocyclic or heterocyclic acetylenic aldehydes together with subsequent Lewis acid catalyzed cyclizations have been studied. It was found that 5-*exo*-*dig* versus 6-*endo*-*dig* cyclization mode strongly depends on the structure of starting materials. Thus, nonaromatic acetylenic α-anilinomethylphosphonates underwent gold(III)-catalyzed or iodine-mediated 5-*exo*-*dig* cyclization to 1*H*-pyrrol-2-ylphosphonates. In contrast, electron-withdrawing heteroaromatic substrates formed 1,2-dihydropyridin-2-ylphosphonate ring containing materials via an exclusive 6-*endo*-*dig* ring-closure process. The dual mode of cyclization is possible only for α-amino (2-alkynylphenyl)methylphosphonates containing a benzene ring .



INTRODUCTION

Both heterocyclic pyrrole[1] and 1,2-dihydropyridine[2] ring systems are important skeletons in natural and synthetic bioactive products. Also, it is well-known that α-aminophosphonates attract attention as analogues of α-amino acids possessing a variety of important biological activities.[3] Combination of pyrrole and dihydropyridine rings together with the phosphonate functionality would represent a class of cyclic α-aminophosphonates with promising biological applications.[4]

In 2007 several manuscripts about the formation of dialkyl 1*H*-pyrrol-2-ylphosphonates and 1,2-dihydropyridin-2-ylphosphonates (Figure 1) via Lewis acid catalyzed cyclizations

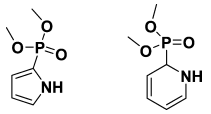
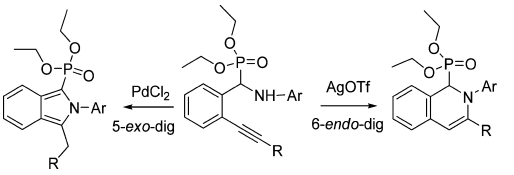


Figure 1. Structures of 1*H*-pyrrol-2-ylphosphonate and 1,2-dihydropyridin-2-ylphosphonate.

of α-amino (2-alkynylphenyl)methylphosphonates were published by Ding et al.[5] The authors proved that, in principle, both cyclization modes are possible and showed that 5-*exo*-*dig* versus 6-*endo*-*dig* cyclization regioselectivity could be simply switched by changing the catalyst (Scheme 1).[5a]

However, we envisioned that the cyclization regioselectivity of acetylenic α-anilinomethylphosphonates could also depend

Scheme 1. Results of Ding et al. Published in 2007[5a]



on the structure of starting material, due to different electronic densities on triple bond carbons. For the evaluation of this idea we chose a variety of carbocyclic and heterocyclic acetylenic α-anilinomethylphosphonates and tested their cyclization reactions.

In this work we present the results of our investigations.

RESULTS AND DISCUSSION

The corresponding 2-alkynylcyclopent-1-enecarbaldehydes **1**, 2-alkynylcyclohex-1-enecarbaldehydes **2**, 2-alkynylbenzaldehydes **3**, 2-alkynylindole-3-carbaldehydes **4**, 2-alkynylpyridine-3-carbaldehydes **5**, and 2-alkynylquinoline-3-carbaldehydes **6** (Figure 2) were reacted by the classical Sonogashira coupling[6] between 2-bromocyclopent-1-enecarbaldehyde,[7] 2-bromocyclohex-1-enecarbaldehyde,[8] and commercially available 2-bromobenzaldehyde, 2-bromo-1*H*-indole-3-carbaldehyde, 2-bromo-

Received: May 9, 2014
Published: June 23, 2014

   dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532–6553

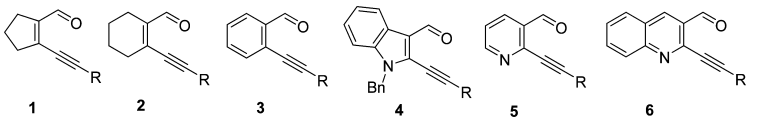
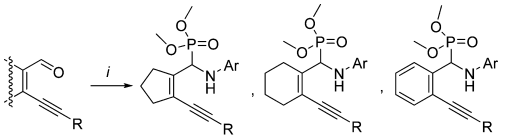


Figure 2. Starting acetylenic aldehydes. **1a**: R = Ph; **1b**: R = 4-MeC_6H_4; **1c**: R = 4-EtC_6H_4; **1d**: R = Bu; **1e**: R = C_5H_{11}; **1f**: R = *c*-Pr; **1g**: R = TMS. **2a**: R = Ph; **2b**: R = 4-MeC_6H_4; **2c**: R = Pr; **2d**: R = Bu; **2e**: R = C_5H_{11}; **2f**: R = *c*-Pr. **3a**: R = Ph; **3b**: R = TMS. **4a**: R = Ph; **4b**: R = Bu; **4c**: R = *c*-Pr. **5a**: R = Ph; **5b**: R = Pr; **5c**: R = *c*-Pr; **5d**: R = H; **5e**: R = CH_2OTHP. **6a**: R = Ph; **6b**: R = Bu; **6c**: R = Pr; **6d**: *c*-Pr.

pyridine-5-carbaldehyde, 2-chloroquinoline-3-carbaldehyde, and terminal acetylenes. The reactions proceeded smoothly in THF at room temperature under argon atmosphere in the presence of 4 mol % $PdCl_2(PPh_3)_2$ and 2 mol % CuI and 2 equiv of triethylamine. Then with the synthesized acetylenic aldehydes in hand, we utilized the Kabachnik–Fields reaction[9] between starting materials, anilines, and dimethylphosphite and screened synthetic approaches for the preparation of various phopshonated pyrrole or dihydropyridine core contacting compounds.

Synthetic Utility of Carbocyclic Acetylenic Aldehydes for the Preparation of Materials Having Pyrrole-1-phosphonate Functionalities. The Kabachnik–Fields reaction is a three-component process forming α-aminophosphonates from carbonyl compounds, amines, and dialkyl phosphonates. Despite a variety of method variations,[10] the presence of a Lewis acid in solution or in solvent-free conditions is usually required. After a brief search of optimal reaction conditions, we found that 1 equiv of $BF_3{\cdot}OEt_2$ in dichloromethane at room temperature gave the best results and did not cause polymerization of chemically unstable aldehydes **1** and **2**. Thus, when carbocyclic aldehydes **1**–**3** were stirred with anilines and dimethylphosphite in dichloromethane in the presence of 1 equiv of $BF_3{\cdot}OEt_2$ at room temperature, the corresponding acetylenic α-anilinomethylphosphonates **7**–**9** were formed in moderate or good yields (Scheme 2).

Scheme 2. Kabachnik–Fields Reaction of Carbocyclic Acetylenic Aldehydes 1–3[a]

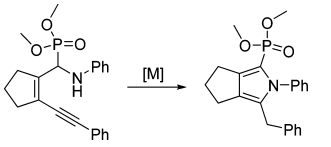


[a]Reagents and conditions: (i) $ArNH_2$ (1 equiv), dimethylphosphite (1.1 equiv), $BF_3{\cdot}OEt_2$ (1 equiv), DCM, rt, 12–24 h. Structures of **7**–**9** are depicted in Tables 4 and 5.

Next, the cyclization reaction of dimethyl (phenylamino)[2-(phenylethynyl)cyclopent-1-enyl]methylphosphonate **7a** was chosen for optimization of conditions. The aromatic substrate dimethyl (phenylamino)[2-(phenylethynyl)phenyl]-methylphosphonate **9a** was used as a model substrate for comparison. The data obtained are depicted in Tables 1 and 2.

First of all, it should be noted that in all successful cases the starting material **7a** underwent regioselective 5-*exo*-*dig* cyclization followed by aromatization and formation of the tetrahydrocyclopenta[*c*]pyrrole core. No 6-*endo*-*dig* cyclization product was observed by TLC and NMR monitoring of crude mixtures. Screening of Lewis acids revealed that copper(I) iodide was totally ineffective for the cyclization and the starting material **7a** was isolated after the workup of reaction mixture (Table 1, entry 1). When $PdCl_2$ was utilized as a catalyst in

Table 1. Screening of the Cyclization Reaction of Dimethyl (Phenylamino)[2-(phenylethynyl)cyclopent-1-enyl]methylphosphonate 7a



7a **10a**

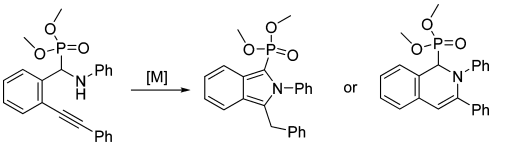
entry	reaction conditions	time, h	yield **10a**, %	recovered **7a**, %
1	CuI (10 mol %), $CHCl_3$, rt	48		95
2	$PdCl_2$ (10 mol %), $CHCl_3$, rt	48	10	79
3	$PdCl_2$ (10 mol %), CH_3CN, rt	48	11	78
4	$PdCl_2(PPh_3)_2$ (10 mol %), $CHCl_3$, rt	48	30	42
5	$AgNO_3$ (10 mol %), $CHCl_3$, rt	48	20	36
6	CF_3CO_2Ag (10 mol %), $CHCl_3$, rt	48	8	74
7	CF_3SO_3Ag (10 mol %), $CHCl_3$, rt	48	13	68
8	$AuBr_3$ (5 mol %), $CHCl_3$, rt	48	45	45
9	$AuBr_3$ (10 mol %), $CHCl_3$, rt	48	70	
10	**$AuBr_3$ (10 mol %), KO*t*Bu (1 equiv), $CHCl_3$, rt**	**0.5**	**99**	

chloroform or acetonitrile solutions, poor conversion of **7a** was reached and compound **10a** was isolated in 10% and 11% yields (Table 1, entries 2, 3). $PdCl_2(PPh_3)_2$ as well as various silver salts ($AgNO_3$, CF_3CO_2Ag, and CF_3SO_3Ag) also were not very effective, and after insufficient conversion of the starting material, pyrrole derivative **10a** was isolated in 20%, 8%, and 13% yields, respectively (Table 1, entries 4–7). After treatment of the starting alkyne by 5 mol % gold(III) bromide in chloroform at room temperature, 50% conversion of **7a** was reached in 48 h, affording 45% of final **10a** (Table 1, entry 8). Increasing the amount of $AuBr_3$ to 10 mol % resulted in full conversion of the starting material in 48 h, and **10a** was obtained in 70% yield (Table 1, entry 9). To our delight, addition of 1 equiv of potassium *tert*-butanoate speeded up the reaction, and high-yielding formation of **10a** was achieved after 30 min of stirring at room temperature (Table 1, entry 10).[11]

In contrast, aromatic dimethyl (phenylamino)(2-phenylethynylphenyl)methylphosphonate **9a** is able to undergo either 5-*exo*-*dig* or 6-*endo*-*dig* cyclizations. This dual reactivity of dialkyl (arylamino)(2-alkynylphenyl)methylphosphonates was described by Ding et al. in 2007.[5a] The authors showed that on one hand, palladium chloride in acetonitrile initiated regioselective 5-*exo*-*dig* cyclization followed by [1,5]-H shift

dx.doi.org/10.1021/jo501011u | *J. Org. Chem.* 2014, 79, 6532–6553

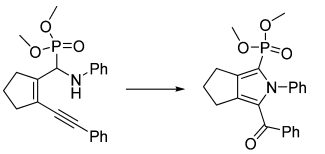
Table 2. Data of 5-*exo*-*dig* or 6-*endo*-*dig* Cyclization Reactions of Dimethyl (phenylamino)(2-phenylethynylphenyl)methylphosphonate 9a



9a **11a** **12a**

entry	reaction conditions	time, h	product	yield, %
1	$AuBr_3$ (10 mol %), KO^{t}Bu (1 equiv), $CHCl_3$, rt	24	**11a**	53
2	$PdCl_2$ (5 mol %), CH_3CN, 60−70 °C	32	**11a**	72
3	CF_3SO_3Ag (5 mol %), CH_3CN, 60−70 °C	72	**12a**	86

Table 3. Screening of the Iodine-Mediated Cyclization Reaction of Dimethyl (Phenylamino)[2-(phenylethynyl)cyclopent-1-enyl]methylphosphonate 7a



7a **13a**

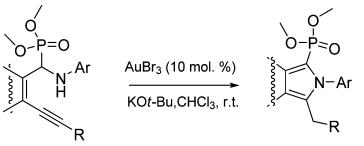
entry	reaction conditions	time, h	yield **13a**, %	recovered **7a**, %
1	I_2 (4 equiv), $CHCl_3$, rt	12	12	
2	I_2 (1 equiv), KO^{t}Bu (1 equiv), $CHCl_3$, 0 °C → rt	12	11	
3	I_2 (1 equiv), K_2CO_3 (1 equiv), $CHCl_3$, 0 °C → rt	12	48	
4	I_2 (1 equiv), K_2CO_3 (1 equiv), acetone, rt	12	24	24
5	I_2 (1 equiv), K_2CO_3 (1 equiv), CH_3CN, rt	12	30	32
6	I_2 (1 equiv), K_2CO_3 (1 equiv), CH_3NO_2, rt	12	28	43
7	I_2 (1 equiv), K_2CO_3 (1 equiv), CH_3OH, rt	12		85
8	I_2 (1 equiv), K_2CO_3 (1 equiv), $C_6H_5CH_3$, rt	12		
9	I_2 (1 equiv), $NaHCO_3$ (1 equiv), $CHCl_3$, 0 °C → rt	12	65	
10	I_2 (1 equiv), K_3PO_4 (1 equiv), $CHCl_3$, 0 °C → rt	12	67	
11	Py_2IBF_4 (1 equiv), $CHCl_3$, rt	12		49
12	**I_2 (1 equiv), PhI(OAc)$_2$ (2 equiv), $CHCl_3$, 0 °C → rt**	**1**	**89**	

to the corresponding 2,3-disubstituted-2*H*-isoindol-1-ylphosphonates. On the other hand, silver triflate catalyzed 6-*endo*-*dig* cyclization reaction to 2,3-disubstituted-1,2-dihydroisoquinolin-1-ylphosphonates. Indeed benzene derivative **9a** was able to undergo both cyclization processes as it was reported by Ding et al. (Table 2, entries 2 and 3).[5a] These methods required prolonged heating in acetonitrile. It should be noted that gold(III) bromide together with 1 equiv of potassium *tert*-butanoate in chloroform also initiated 5-*exo*-*dig* cyclization process at room temperature and final **11a** was formed in 53% yield (Table 2, entry 1).

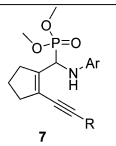
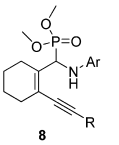
Thus, gold(III) bromide was able to initiate exclusive 5-*exo*-*dig* cyclization reactions of carbocyclic acetylenic α-anilinomethylphosphonates. With these promising results in hands and having in mind literature facts that various intramolecular transformations of functionally substituted alkynes can be carried out with either gold catalysts or iodine electrophiles to access the same core unit,[12] we decided to evaluate the usefulness of iodine electrophiles in this cyclization. Indeed, we found, that molecular iodine was able to mediate the cyclization process of (phenylamino)[2-(phenylethynyl)cyclopent-1-enyl]-methylphosphonate **7a**. In all cases dimethyl 3-benzoyl-2-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate **13a** bearing a carbonyl functionality instead of a methylene group was formed. Full conversion of the starting material **7a** was reached in 12 h. However, use of an excess of molecular iodine (Table 3, entry 1), as well as 1 equiv of molecular iodine together with 1 equiv of potassium *tert*-butanoate at 0 °C temperature (Table 3, entry 2) facilitated the formation of tars, and only minor quantities of **13a** were isolated. While use of potassium carbonate (Table 3, entry 3), sodium bicarbonate (Table 3, entry 9), and potassium phosphate (Table 3, entry 10) in chloroform at 0 °C temperature improved yield of the cyclization product, potassium carbonate in acetone (Table 3, entry 4), acetonitrile (Table 3, entry 5), and nitromethane (Table 3, entry 6) led to insufficient conversion of the starting alkyne. It also should be noted that combination of equivalent amounts of the starting material, molecular iodine, and potassium carbonate in methanol (Table 3, entry 7) or toluene (Table 3, entry 8) did not give the desired product, and 85% of starting alkyne was recovered or full decomposition of it was observed, respectively. The Barluenga reagent[13] was not able to mediate the cyclization process, and 49% of the starting material was recovered (Table 3, entry 11). Then, the electrophilicity of iodine was improved by adding hypervalent iodine oxidant.[14] To our delight, the combination of 1 equiv of

dx.doi.org/10.1021/jo501011u | *J. Org. Chem.* 2014, 79, 6532−6553

Table 4. Data on the Synthesis of Polysubstituted Pyrrol-1-ylphosphonates via Gold(III) Bromide Mediated Cyclization



7-8 10, 14

Entry	Starting material	Product	Yield, %
1	 7 **7a**: R = Ph, Ar = Ph	**10a**	98
2	**7b**: R = Ph, Ar = 4-MeOC$_6$H$_4$	**10b**	73
3	**7c**: R = Ph, Ar = 4-EtOC$_6$H$_4$	**10c**	74
4	**7d**: R = Ph, Ar = 4-FC$_6$H$_4$	**10d**	86
5	**7e**: R = Ph, Ar = 4-ClC$_6$H$_4$	**10e**	73
6	**7f**: R = 4-MeC$_6$H$_4$, Ar = Ph	**10f**	58
7	**7g**: R = 4-MeC$_6$H$_4$, Ar = 4-MeOC$_6$H$_4$	**10g**	76
8	**7h**: R = 4-EtC$_6$H$_4$, Ar = 4-MeOC$_6$H$_4$	**10h**	96
9	**7i**: R = C$_4$H$_9$, Ar = Ph	**10i**	96
10	**7j**: R = C$_4$H$_9$, Ar = 4-MeOC$_6$H$_4$	**10j**	78
11	**7k**: R = C$_4$H$_9$, Ar = 4-FC$_6$H$_4$	**10k**	80
12	**7l**: R = C$_4$H$_9$, Ar = 4-ClC$_6$H$_4$	**10l**	76
13	**7m**: R = C$_5$H$_{11}$, Ar = Ph	**10m**	90
14	**7n**: R = C$_5$H$_{11}$, Ar = 4-MeOC$_6$H$_4$	**10n**	63
15	**7o**: R = *cyclo*Pr, Ar = Ph	**10o**	77
16	**7p**: R = *cyclo*Pr, Ar = 4-MeOC$_6$H$_4$	**10p**	73
17	**7r**: R = *cyclo*Pr, Ar = 4-EtOC$_6$H$_4$	**10r**	90
18	**7s**: R = H, Ar = Ph	**10s**	66
19	 8 **8a**: R = Ph, Ar = Ph	**14a**	82
20	**8b**: R = Ph, Ar = 4-MeOC$_6$H$_4$	**14b**	95
21	**8c**: R = Ph, Ar = 4-FC$_6$H$_4$	**14c**	56
22	**8d**: R = Ph, Ar = 4-ClC$_6$H$_4$	**14d**	68
23	**8e**: R = 4-MeC$_6$H$_4$, Ar = Ph	**14e**	92
24	**8f**: R = 4-MeC$_6$H$_4$, Ar = 4-MeOC$_6$H$_4$	**14f**	79
25	**8g**: R = C$_3$H$_7$, Ar = Ph	**14g**	89
26	**8h**: R = C$_3$H$_7$, Ar = 4-MeOC$_6$H$_4$	**14h**	99
27	**8i**: R = C$_3$H$_7$, Ar = 4-FC$_6$H$_4$	**14i**	81
28	**8j**: R = C$_4$H$_9$, Ar = Ph	**14j**	88
29	**8k**: R = C$_4$H$_9$, Ar = 4-MeOC$_6$H$_4$	**14k**	82
30	**8l**: R = *cyclo*Pr, Ar = Ph	**14l**	83
31	**8m**: R = *cyclo*Pr, Ar = 4-MeOC$_6$H$_4$	**14m**	92
32	**8n**: R = *cyclo*Pr, Ar = 4-ClC$_6$H$_4$	**14n**	92

molecular iodine together with 2 equiv of phenyliodine diacetate in chloroform at 0 °C temperature resulted in full conversion of the starting alkyne and smooth formation of **13a** in 89% yield (Table 3, entry 12).

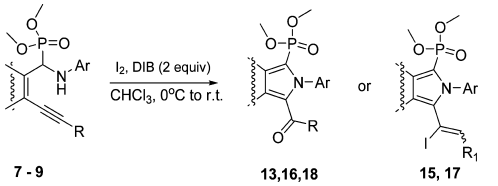
Optimized reaction conditions (Table 1, entry 10 and Table 3, entry 12) were applied for the synthesis of polysubstituted pyrrol-1-ylphosphonates **10** and **13**−**18**. The results are summarized in Tables 4 and 5. As is seen from Table 4, both starting substrates **7** and **8** having cyclopentene and cyclohexene rings underwent smooth and high-yielding formation of pyrrol-1-ylphosphonates **10** and **14** via gold(III) bromide catalyzed process (entries 1−32).

Molecular iodine mediated cyclizations proceeded smoothly for substrates **7a**−**h**,**j**,**s** (Table 5, entries 1−10), **8a**,**b**,**o**,**p** (Table 5, entries 13−15), and **9b**,**c** (Table 5, entries 18, 19) having arylethynyl or ethynyl functionality. The corresponding ketones **13a**−**g**,**h**,**j**, **16a**,**b**,**o**, **18b** and aldehydes **13s** and **18c** were isolated in moderate or good yields. However, derivatives **7i**, **7o** (Table 5, entries 11, 12) and **8k**, **8l** (Table 5, entries 16, 17) bearing an alkylethynyl substituent cyclized into pyrrol-1-ylphosphonates bearing 1-iodoalkenyl substituents. The latter four compounds were isolated as mixtures of *E* and *Z* isomers.

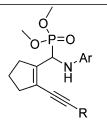
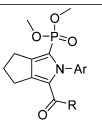
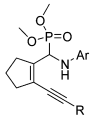
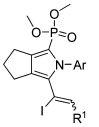
The plausible mechanism of the iodine-mediated cyclization is depicted in Scheme 3. We believe that at the first step, molecular iodine is converted to 2 equiv of acetyl hypoiodite during oxidation by phenyliodine diacetate.[14] Thus, an electrophilic I^+ is generated in an efficient and atom-economic way. The formation of byproduct iodobenzene was proved by NMR and MS methods. Next, after direct iodonium activation (intermediate **I**) of the triple bond of the starting substrate, the intramolecular 5-*exo*-*dig* nucleophilic attack of the neighboring arylamino group takes place, leading to intermediate **II**, and loss of a proton gives neutral intermediate **III**. Next, the second electrophilic iodine attack of the exocyclic double bond occurs,

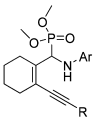
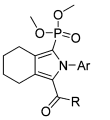
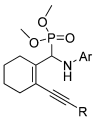
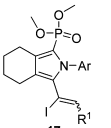
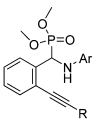
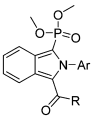
dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532−6553

Table 5. Data on the Synthesis of Polysubstituted Pyrrol-1-ylphosphonates 13 and 15−18 via Iodine-Mediated Cyclization



7 - 9 13,16,18 15, 17

Entry	Starting material	Product	Yield, %
1	 7	 13	89
	7a: R = Ph, Ar = Ph	**13a**	
2	**7b**: R = Ph, Ar = 4-MeOC$_6$H$_4$	**13b**	67
3	**7c**: R = Ph, Ar = 4-EtOC$_6$H$_4$	**13c**	70
4	**7d**: R = Ph, Ar = 4-FC$_6$H$_4$	**13d**	58
5	**7e**: R = Ph, Ar = 4-ClC$_6$H$_4$	**13e**	51
6	**7g**: R = 4-MeC$_6$H$_4$, Ar = 4-MeOC$_6$H$_4$	**13g**	56
7	**7h**: R = 4-EtC$_6$H$_4$, Ar = 4-MeOC$_6$H$_4$	**13h**	54
9	**7j**: R = 4-EtC$_6$H$_4$, Ar = 4-ClC$_6$H$_4$	**13j**	44
10	**7s**: R = H, Ar = Ph	**13s**	42
11	 7	 15	58
	7i: R = C$_4$H$_9$, Ar = Ph	**15i**: R^1 = C$_3$H$_7$, Ar = Ph	
12	**7o**: R = *cyclo*Pr, Ar = Ph	**15o**: R^1 = (CH$_2$)$_2$I, Ar = Ph	49

Entry	Starting material	Product	Yield, %
13	 8	 16	61
	8a: R = Ph, Ar = Ph	**16a**	
14	**8b**: R = Ph, Ar = 4-MeOC$_6$H$_4$	**16b**	60
15	**8o**: R = 4-MeC$_6$H$_4$, Ar = 4-ClC$_6$H$_4$	**16o**	69
16	 8	 17	25
	8k: R = C$_4$H$_9$, Ar = 4-MeOC$_6$H$_4$	**17k**: R^1 = C$_3$H$_7$, Ar = 4-MeOC$_6$H$_4$	
17	**8l**: R = *cyclo*Pr, Ar = Ph	**17l**: R^1 = (CH$_2$)$_2$I, Ar = Ph	83
18	 9	 18	44
	9b: R = Ph, Ar = 4-ClC$_6$H$_4$	**18b**	
19	**9c**: R = H, Ar = 4-MeOC$_6$H$_4$	**18c**	56

thus affording intermediate **IV**. Abstraction of a proton leads to aromatization of the pyrrole ring and formation of di-iodo intermediates **VI** and **VII**. However, when starting compound has a cyclopropyl functionality next to the triple bond, during the iodination-aromatization processes cleavage of the cyclopropane ring occurs, giving di-iodo derivatives **15** and **17**. Intermediate **VI** can undergo nucleophilic displacement reaction with water, forming carbonyl group bearing products **13**, **16**, **18**. In contrast, intermediate **VII**, bearing a CH_2R^1 group, undergoes base-mediated elimination reaction to compounds **15** and **17**.

The role of water in formation of products **13**, **16**, and **18** was proved by addition of ^{18}O-labeled water to the reaction mixture. Stirring of **7a** with 1 equiv of molecular iodine and 2 equiv of phenyliodine diacetate in chloroform in the presence of 3 equiv of ^{18}O-labeled water resulted in smooth formation of **13a-^{18}O** in 86% yield. The HRMS spectrum of **13a-^{18}O** confirmed absolute incorporation of ^{18}O in final ketone. Moreover, an observed δ 0.04 ppm (4 Hz) upfield chemical shift was found for ketone carbonyl carbon in ^{13}C NMR spectrum of **13a-^{18}O**, thus confirming position of ^{18}O.[15]

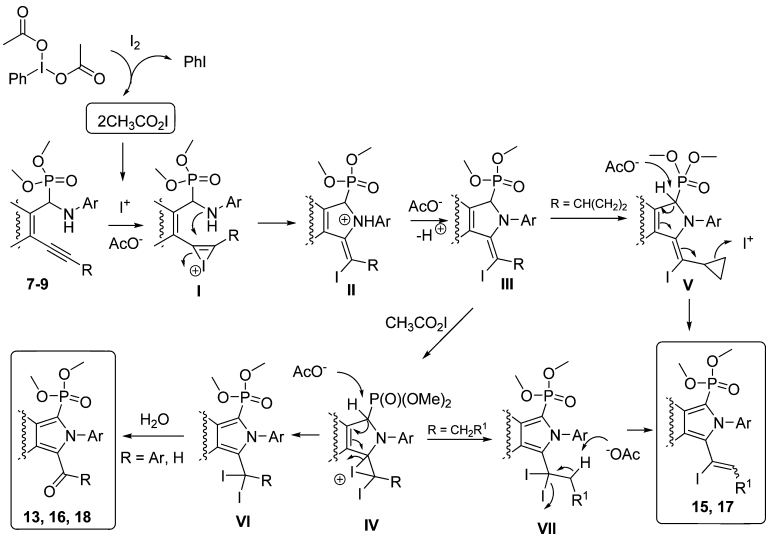
Kabachnik−Fields Reactions of Heterocyclic Aldehydes and Cyclization Reaction of Obtained Adducts. After exploring the reactivity of carbocyclic acetylenic aldehydes and their Kabachnik−Fields adducts, we turned our attention to heterocyclic substrates. Electron-rich 2-(alkynyl)-1-benzyl-1*H*-indole-3-carbaldehydes (**4**) reacted under the Kabachnik−Fields reaction condition and formed the corresponding adducts **19** in moderate yields (Scheme 4).

Unfortunately, the presence of an electron-rich indole ring deactivated isolated compounds **19** toward the cyclization reaction. No changes of the starting materials **19** were observed by TLC or NMR monitoring during prolonged stirring or refluxing of compounds **19** in dichloroethane, in the presence of gold(III) bromide, palladium(II) chloride, silver(I) triflate, or I_2/DIB.

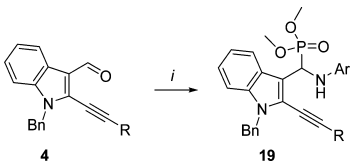
However, when we tried to perform the Kabachnik−Fields reaction of electron-defficient pyridine or quinoline substrates **5** and **6**, we surprisingly found that these reactions were not so

dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532−6553

Scheme 3. Plausible Mechanism of the Iodine-Mediated Cyclization of Acetylenic α-Anilinomethylphosphonates



Scheme 4. Kabachnik–Fields Reaction of 2-Alkynylindole-3-carbaldehydes 4[a]



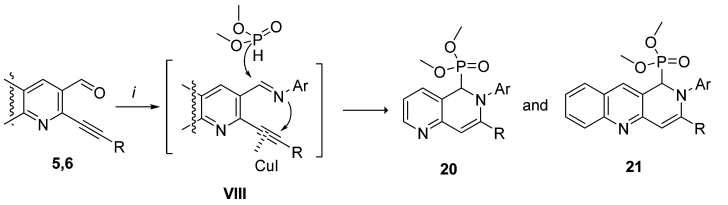
[a]Reagents and conditions: (i) aniline (1 equiv), dimethylphosphite (1.1 equiv), $BF_3{\cdot}OEt_2$ (1 equiv), DCM, rt, 24 h. **19a**: R = Ph, Ar = Ph; **19b**: R = Bu, Ar = 4-$CH_3OC_6H_4$-; **19c**: R = *c*Pr, Ar = Ph.

straightforward and $BF_3{\cdot}OEt_2$ did not mediate an exclusive formation of the Kabachnik–Fields adducts. Reactions proceeded slowly, and after NMR analysis of crude mixtures we found that after 12–24 h there were products of 6-*endo*-*dig* cyclization process **20** or **21** together with the corresponding imines **VIII**. After a brief searching of the most suitable reaction conditions for the full conversion to cyclized **20** and **21**, we came to conclusion that 10 mol % copper iodide (in comparison to gold(III) bromide, palladium(II) chloride, or silver(I) triflate) in DCE at room temperature gave the best results. Thus, the corresponding dimethyl 6-aryl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonates **20** and dimethyl 2-aryl-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonates **21** were isolated in good yields after stirring of reaction mixtures at room temperature for 2–4 h. (Scheme 5, Table 6). We believe that after formation of intermediate imines **VIII**, tandem dimethylphosphite addition–6-*endo*-*dig* cyclization reactions took place. An immediate nucleophilic attack of imine group is facilitated by decreased electron density on the triple bond of intermediates **VIII**.

The mechanism presented in Scheme 5 was supported by isolation of intermediate **22** (Figure 3) after the reaction between starting 2-phenylethynylquinolin-3-carbaldehyde **6a** and 4-methoxyaniline in chloroform in the presence of 3Å MS. Then, after stirring of compound **22** with dimethylphosphite in DCE in the presence of 10 mol % CuI, smooth 6-*endo*-*dig* cyclization process proceeded, and final product **21a** was isolated in 64% yield.

Moreover, we succeeded in synthesizing the Kabachnik–Fields reaction product **23** during reaction between starting aldehyde **6c** with 4-methoxyaniline and dimethylphosphite in dichloromethane in the presence of 10 mol % gold(III)

Scheme 5. Three-Component Reaction between Electron-Defficient Aldehydes 5 and 6, Anilines, and Dimethylphosphite[a]



[a]Reagents and conditions: (i) aniline (1 equiv), dimethylphosphite (1.1 equiv), CuI (10 mol %), DCM, rt, 2–4 h.

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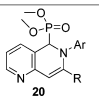
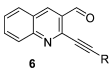
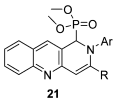
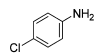
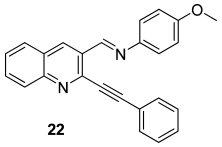
Table 6. Data on the Synthesis of Dimethyl 6-Aryl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonates 20 and Dimethyl 2-Aryl-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonates 21[a]

Entry	Starting material	$ArNH_2$	Product	Yield, %
1	 **5**		 **20**	58
	5a: R = Ph		**20a**	
2	**5a**: R = Ph		**20b**	61
3	**5b**: R = C_3H_7		**20c**	52
4	**5c**: R = *cyclo*Pr		**20d**	63
5	**5c**: R = *cyclo*Pr		**20e**	59
6	**5d**: R = H		**20f**	50
7	**5e**: R = CH_2OTHP		**20g**	51
8	**5e**: R = CH_2OTHP		**20h**	48
9	 **6**		 **21**	48
	6a R = Ph		**21a**	
10	**6b**: C_4H_9		**21b**	48
11	**6b**: C_4H_9		**21c**	45
12	**6b**: C_4H_9		**21d**	52
13	**6c**: C_3H_7		**21e**	69
14	**6d**: R = *cyclo*Pr		**21f**	67
15	**6d**: R = *cyclo*Pr		**21g**	67
16	**6d**: R = *cyclo*Pr		**21h**	48

[a]Reactions between starting materials, the corresponding aniline (1 equiv), and dimethylphosphite (1.1 equiv) were carried out in DCM at rt in the presence of CuI (10 mol %) for 2−4 h.



22

Figure 3. (*E*)-4-Methoxy-*N*-{[2-(phenylethynyl)quinolin-3-yl]-methylene}aniline **22**.

bromide (Scheme 6). Together with compound **23**, the corresponding cyclized 1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonate **21e** was formed. After isolation and purification of **23**, we tested its reactivity toward various Lewis acids ($AuBr_3$, AgOTf, CuI, I_2 in neutral and basic media) and found that in all cases slow formation of 6-*endo-dig* cyclization product **21e** with incomplete conversion of compound **23** took place. Thus, it was showed that reaction of electron-withdrawing heterocyclic acetylenic aldehydes with anilines and dimethylphosphite likely does not proceed via the Kabachnik−Fields reaction adducts, but mainly via imines **VIII**. The triple bond of intermediates **VIII** is activated by neighboring electron-withdrawing pyridine and quinoline rings, and therefore smooth tandem dimethylphosphite attack−6-*endo-dig* cyclization reactions take place.

CONSLUSION

Kabachnik−Fields reactions between 2-alkynylcyclopent-1-enecarbaldehydes, 2-alkynylcyclohex-1-enecarbaldehydes, 2-alkynylbenzaldehydes, 2-alkynylindole-3-carbaldehydes, 2-alkynylpyridine-3-carbaldehydes, and 2-alkynylquinoline-3-carbaldehydes have been studied. It has been found that substrates having carbocyclic and electron-rich indole ring successfully undergo $BF_3{\cdot}OEt_2$-mediated reactions with anilines and dimethylphoshphite, yielding the corresponding Kabachnik−Fields adducts. In contrast, electron-defficient 2-alkynylpyridine-3-carbaldehydes and 2-alkynylquinoline-3-carbaldehydes undergo smooth tandem imine formation−6-*endo-dig* cyclization processes forming the corresponding dimethyl 6-aryl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonates and dimethyl 2-aryl-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonates.

A variety of Lewis acids have been investigated for the cyclization processes of all isolated acetylenic α-anilinomethylphosphonates (Scheme 7).

An important conclusion of this study is that 5-*exo-dig* and 6-*endo-dig* cyclization processes can be switched by using a different catalyst only in the case of starting benzene derivatives. However, while on one hand substrates having nonaromatic cyclopentene or cyclohexene rings undergo exclusive 5-*exo-dig* cyclization processes to form polysubstituted pyrrole derivatives, on the other hand, substrates having electron-defficient pyridine or quinoline rings always undergo 6-*endo-dig* cyclization processes. Finally, substrates bearing an electron-donating indole ring are totally unreactive toward Lewis acid catalyzed cyclization processes.

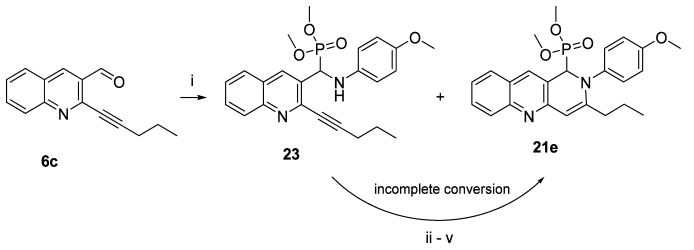
Additionally, during this study, a new iodine-mediated synthetic method of aroyl- or formyl-substituted pyrrole-1-phosphonates has been developed.

EXPERIMENTAL SECTION

General Information. IR spectra were run in KBr discs. ^1H and ^{13}C NMR spectra were recorded at either 300 or 400 MHz in chloroform-*d* or dimethylsulfoxide-d_6, using the residual solvent signal

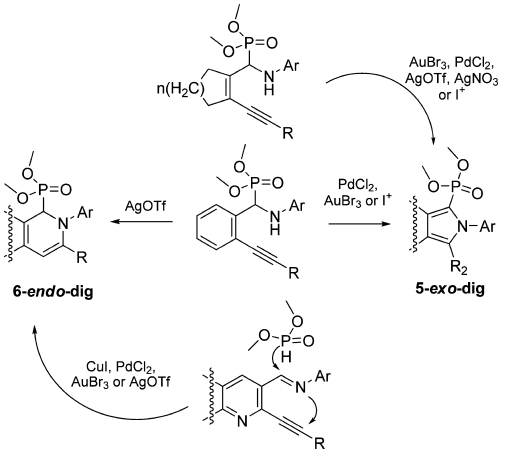
dx.doi.org/10.1021/jo501011u | *J. Org. Chem.* 2014, 79, 6532−6553

Scheme 6[a]



[a]Reagents and conditions: (i) 4-methoxyaniline (1 equiv), dimethylphosphite (1.1 equiv), $AuBr_3$ (10 mol %), DCM, rt, 3 h. (ii) $AuBr_3$ (10 mol %), DCM, rt 24 h. (iii) AgOTf (10 mol %), DCM, rt 24 h. (iv) CuI (10 mol %), DCM, rt 24 h. (v) I_2 (1 equiv), K_3PO_4 (1 equiv), $CHCl_3$, 0 °C → rt, 10 h.

Scheme 7. Dependence of the Cyclization Mode on the Structures of the Starting Acetylenic α-Anilinomethylphosphonates



as internal standard. Signal multiplicity is denoted as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet). Unambiguous assignment of signals was made using a combination of NMR experiments, including COSY, HSQC, and HMBC. High resolution mass spectra were recorded on a Dual-ESI Q-TOF 6520 mass spectrometer by electrospray ionization. All reactions and purity of the synthesized compounds were monitored by TLC using silica gel 60 F254 aluminum plates. Visualization was accomplished by UV light and by treating the plates with vanillin stain followed by heating.

Synthesis of 2-alkynylcyclopent-1-enecarbaldehydes **1**,[16] 2-alkynylcyclohex-1-enecarbaldehydes **2**,[15] 2-alkynylbenzaldehydes **3**,[17] 2-alkynylindole-3-carbaldehydes **4**,[18] 2-alkynylpyridine-3-carbaldehydes **5**,[19] 2-alkynylquinoline-3-carbaldehydes **6**,[20] dimethyl 3-benzyl-2-phenyl-2*H*-isoindol-1-ylphosphonate (**11a**),[5a] and dimethyl 2,3-diphenyl-1,2-dihydroisoquinolin-1-ylphosphonate (**12a**)[5a] were performed by methods reported in the literature.

General Procedure for the Preparation of Compounds 7–9 and 19. To a solution of starting corresponding acetylenic aldehyde **1**–**4** (2 mmol) was added the corresponding aniline (2 mmol) and dimethylphosphite (0.242 g, 2.2 mmol) in dry dichloromethane (5 mL) boron trifuoride etherate (0.284 g, 2 mmol). The resulting solution was stirred at room temperature. When the completion of the reaction was observed by TLC (after 12–24 h), the solution was quenched with aqueous sodium bicarbonate. The organic layer was separated, washed with water (2 × 20 mL), and dried over anhydrous Na_2SO_4. After the evaporation of solvent under reduced pressure, the residue was purified by flash column chromatography eluting with hexane–ethyl acetate mixtures.

Dimethyl (Phenylamino)(2-(phenylethynyl)cyclopent-1-enyl)methylphosphonate (7a). Yellow solid, mp114–115 °C. Yield 0.48 g, 63%. IR (KBr): υ_{max} 3488 (NH), 2200 (C≡C) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.77–1.99 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.37–2.50 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.56–2.68 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.80 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.85 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.02 (1H, d, $^3J_{H,P}$ = 24.9 Hz, CH), 6.70–6.78 (3H, m, ArH), 7.15–7.20 (2H, m, ArH), 7.33–7.37 (3H, m, ArH), 7.48–7.51 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.2 (CH_2), 32.6 (CH_2), 36.7 (d, $^5J_{C,P}$ = 2.1 Hz, CH_2), 51.3 (d, $^1J_{C,P}$ = 153.6 Hz, CH), 53.6 (d, $^2J_{C,P}$ = 7.2 Hz, OCH_3), 53.8 (d, $^2J_{C,P}$ = 6.6 Hz, OCH_3), 84.9 (d, $^4J_{C,P}$ = 5.1 Hz, C-sp), 96.0 (d, $^5J_{C,P}$ = 2.4 Hz, C-sp), 113.9 (ArC), 118.9 (ArC), 123.1 (ArC), 124.2 (d, $^3J_{C,P}$ = 12.9 Hz, C-sp^2), 128.3 (ArC), 128.4 (ArC), 129.2 (ArC), 131.3 (ArC), 144.9 (d, $^2J_{C,P}$ = 4.7 Hz, C-sp^2), 145.9 (d, $^3J_{C,P}$ = 15.3 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 404.1830. $C_{22}H_{24}NNaO_3P$ requires 404.1836.

Dimethyl (4-Methoxyphenylamino)(2-(phenylethynyl)-cyclopent-1-enyl)methylphosphonate (7b). Yellow solid, mp 121–122 °C. Yield 0.44 g, 54%. IR (KBr): υ_{max} 3436 (NH), 2200 (C≡C) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.76–1.98 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.38–2.49 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.56–2.68 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.80 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.85 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 4.94 (1H, d, $^3J_{H,P}$ = 24.6 Hz, CH), 6.67–6.77 (4H, m, ArH), 7.32–7.36 (3H, m, ArH), 7.45–7.50 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.2 (CH_2), 32.6 (CH_2), 36.7 (d, $^5J_{C,P}$ = 2.0 Hz, CH_2), 52.2 (d, $^1J_{C,P}$ = 153.8 Hz, CH), 53.5 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 53.8 (d, $^2J_{C,P}$ = 6.6 Hz, OCH_3), 55.5 (OCH_3), 85.0 (d, $^4J_{C,P}$ = 6.9 Hz, C-sp), 95.9 (d, $^5J_{C,P}$ = 2.7 Hz, C-sp), 114.7 (ArC), 115.3 (ArC), 123.1 (ArC), 124.1 (d, $^3J_{C,P}$ = 11.9 Hz, C-sp^2), 128.3 (ArC), 128.4 (ArC), 131.3 (ArC), 139.9 (d, $^3J_{C,P}$ = 13.8 Hz, ArC), 145,1 (d, $^2J_{C,P}$ = 6.7 Hz, C-sp^2), 152.9 (ArC) ppm. HRMS (ESI): MNa^+, found 434.1497. $C_{23}H_{26}NNaO_4P$ requires 434.1492.

Dimethyl (4-Ethoxyphenylamino)(2-(phenylethynyl)-cyclopent-1-enyl)methylphosphonate (7c). Yellow solid, mp 139–141 °C. Yield 0.49 g, 57%. IR (KBr): υ_{max} 3443 (NH), 2198 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.35 (3H, t, ^3J = 6.8 Hz, CH_3), 1.78–1.96 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.38–2.47 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.56–2.65 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.80 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.84 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.93 (2H, q, ^3J = 6.8 Hz, $\underline{CH_2}CH_3$) 4.93 (1H, d, $^3J_{H,P}$ = 24.4 Hz, CH), 6.66–6.69 (2H, m, ArH), 6.73–6.77 (2H, m, ArH), 7.32–7.37 (3H, m, ArH), 7.47–7.49 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.0 (CH_3), 22.3 (CH_2), 32.7 (d, $^3J_{C,P}$ = 1.2 Hz, CH_2), 36.8 (d, $^5J_{C,P}$ = 2.2 Hz, CH_2), 52.2 (d, $^1J_{C,P}$ = 153.8 Hz, CH), 53.6 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 53.9 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 63.9 ($O\underline{CH_2}CH_3$), 85.1 (d, $^4J_{C,P}$ = 5.3 Hz, C-sp), 96.0 (d, $^5J_{C,P}$ = 2.6 Hz, C-sp), 115.3 (ArC), 115.5

dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532–6553

(ArC), 123.2 (d, $^{6}J_{C,P}$ = 1.1 Hz, ArC), 124.1 (d, $^{3}J_{C,P}$ = 12.8 Hz, C-sp^2), 128.3 (ArC), 128.4 (ArC), 131.4 (ArC), 140.0 (d, $^{3}J_{C,P}$ = 16.0 Hz, ArC), 145.3 (d, $^{2}J_{C,P}$ = 4.7 Hz, C-sp^2), 152.3 (ArC) ppm. HRMS (ESI): MNa^+, found 448.1669. $C_{24}H_{28}NNaO_4P$ requires 448.1648.

Dimethyl (4-Fluorophenylamino)(2-(phenylethynyl)-cyclopent-1-enyl)methylphosphonate (7d). Yellow solid, mp 102−104 °C. Yield 0.56 g, 70%. IR (KBr): υ_{max} 3453 (NH), 2220(C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.79−1.97 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.34−2.44 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.57−2.63 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.80 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 3.85 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 4.93 (1H, d, $^{3}J_{H,P}$ = 24.8 Hz, CH), 6.62−6.65 (2H, m, ArH), 6.84−6.90 (2H, m, ArH), 7.33−7.36 (3H, m, ArH), 7.46−7.49 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3 (CH_2), 32.6 (d, $^{3}J_{C,P}$ = 1.2 Hz, CH_2), 36.8 (d, $^{5}J_{C,P}$ = 2.3 Hz, CH_2), 51.9 (d, $^{1}J_{C,P}$ = 154.0 Hz, CH), 53.7 (d, $^{2}J_{C,P}$ = 7.2 Hz, OCH_3), 53.9 (d, $^{2}J_{C,P}$ = 6.8 Hz, OCH_3), 84.9 (d, $^{4}J_{C,P}$ = 5.3 Hz, C-sp), 96.2 (d, $^{5}J_{C,P}$ = 2.6 Hz, C-sp), 114.8 (d, $^{3}J_{C,F}$ = 7.4 Hz, ArC), 115.7 (d, $^{2}J_{C,F}$ = 22.3 Hz, ArC), 123.0 (d, $^{6}J_{C,P}$ = 0.9 Hz, ArC), 124.4 (d, $^{3}J_{C,P}$ = 12.7 Hz, C-sp^2), 128.5 (ArC), 131.4 (ArC), 142.5 (dd, $^{3}J_{C,P}$ = 16.3 Hz, $^{4}J_{C,F}$ = 2.0 Hz, ArC), 144.9 (d, $^{2}J_{C,P}$ = 4.9 Hz, C-sp^2), 156.5 (d, $^{1}J_{C,F}$ = 234.9 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 422.1283. $C_{22}H_{23}FNNaO_3P$ requires 422.1292.

Dimethyl (4-Chlorophenylamino)(2-(phenylethynyl)-cyclopent-1-enyl)methylphosphonate (7e). Yellow solid, mp 129−131 °C. Yield 0.49 g, 59%. IR (KBr): υ_{max} 3418 (NH), 2215 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.79−1.97 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.34−2.43 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.58−2.63 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.80 (3H, d, $^{3}J_{H,P}$ = 10.4 Hz, OCH_3), 3.84 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 4.94 (1H, d, $^{3}J_{H,P}$ = 24.8 Hz, CH), 6.13−6.65 (2H, m, ArH), 7.09−7.13 (2H, m, ArH), 7.33−7.37 (3H, m, ArH), 7.46−7.49 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.2 (CH_2), 32.6 (d, $^{3}J_{C,P}$ = 1.1 Hz, CH_2), 36.7 (d, $^{5}J_{C,P}$ = 2.4 Hz, CH_2), 51.3 (d, $^{1}J_{C,P}$ = 153.9 Hz, CH), 53.6 (d, $^{2}J_{C,P}$ = 7.2 Hz, OCH_3), 53.8 (d, $^{2}J_{C,P}$ = 6.8 Hz, OCH_3), 84.8 (d, $^{4}J_{C,P}$ = 5.3 Hz, C-sp), 96.3 (d, $^{5}J_{C,P}$ = 2.6 Hz, C-sp), 114.9 (ArC), 123.0 (d, $^{6}J_{C,P}$ = 0.9 Hz, ArC), 124.4 (d, $^{3}J_{C,P}$ = 12.7 Hz, C-sp^2), 128.4 (ArC), 128.4 (ArC), 129.0 (ArC), 131.3 (ArC), 144.5 (d, $^{2}J_{C,P}$ = 5.0 Hz, C-sp^2), 144.8 (d, $^{3}J_{C,P}$ = 15.8 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 438.0999. $C_{22}H_{23}ClNNaO_3P$ requires 438.0996.

Dimethyl (Phenylamino)(2-(*p*-tolylethynyl)cyclopent-1-enyl)methylphosphonate (7f). Yellow solid, mp 143−145 °C. Yield 0.65 g, 82%. IR (KBr): υ_{max} 3402 (NH), 2179 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.78−1.96 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.37 (3H, s, CH_3), 2.40−2.47 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.57−2.67 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.80 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 3.84 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 5.01 (1H, d, $^{3}J_{H,P}$ = 24.8 Hz, CH), 6.70−6.77 (3H, m, ArH), 7.15−7.19 (4H, m, ArH), 7.37−7.39 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5 (CH_3), 22.2 (CH_2), 32.6 (d, $^{3}J_{C,P}$ = 1.5 Hz, CH_2), 36.7 (d, $^{5}J_{C,P}$ = 2.3 Hz, CH_2), 51.1 (d, $^{1}J_{C,P}$ = 153.6 Hz, CH), 53.6 (d, $^{2}J_{C,P}$ = 7.1 Hz, OCH_3), 53.8 (d, $^{2}J_{C,P}$ = 6.7 Hz, OCH_3), 84.4 (d, $^{4}J_{C,P}$ = 5.3 Hz, C-sp), 96.2 (d, $^{5}J_{C,P}$ = 2.8 Hz, C-sp), 113.7 (ArC), 118.6, (ArC), 120.0 (d, $^{6}J_{C,P}$ = 1.1 Hz, ArC), 124.1 (d, $^{3}J_{C,P}$ = 12.6 Hz, C-sp^2), 129.1 (ArC), 129.2 (ArC), 131.2 (ArC), 131.3 (ArC), 138.5 (ArC), 144.6 (d, $^{2}J_{C,P}$ = 4.7 Hz, C-sp^2), 146.2 (d, $^{3}J_{C,P}$ = 14.0 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 418.1542. $C_{23}H_{26}NNaO_3P$ requires 418.1543.

Dimethyl (4-Methoxyphenylamino)(2-(*p*-tolylethynyl)-cyclopent-1-enyl)methylphosphonate (7g). Yellow solid, mp 110−112 °C. Yield 0.63 g, 74%. IR (KBr): υ_{max} 3488 (NH), 2197 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.77−1.95 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.36 (3H, s, CH_3), 2.39−2.45 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.55−2.66 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.72 (3H, s, OCH_3), 3.79 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 3.84 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 4.80 (1H, d, $^{3}J_{H,P}$ = 24.4 Hz, CH), 6.68 (2H, d, ^{3}J = 8.8 Hz, ArH), 7.15 (2H, d, ^{3}J = 8.8 Hz, ArH), 7.15 (2H, d, ^{3}J = 7.6 Hz, ArH), 7.37 (2H, d, ^{3}J = 8.0 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5 (CH_3), 22.3 (CH_2), 32.6 (d, $^{3}J_{C,P}$ = 1.1 Hz, CH_2), 36.8 (d, $^{5}J_{C,P}$ = 2.2 Hz, CH_2), 52.1 (d, $^{1}J_{C,P}$ = 153.6 Hz, CH), 53.6 (d, $^{2}J_{C,P}$ = 7.1 Hz, OCH_3), 53.9 (d, $^{2}J_{C,P}$ = 6.7 Hz, OCH_3), 55.6 (OCH_3), 84.5 (d, $^{4}J_{C,P}$ = 5.4 Hz, C-sp), 96.2 (d, $^{5}J_{C,P}$ = 2.7 Hz, C-sp), 114.7 (ArC), 115.3, (ArC), 120.1 (d, $^{6}J_{C,P}$ = 0.1 Hz, ArC), 124.3 (d, $^{3}J_{C,P}$ = 12.8 Hz, C-sp^2), 129.2 (ArC), 131.3 (ArC), 138.6 (ArC), 140.1 (^{3}d, $J_{C,P}$ = 16.4 Hz, ArC), 144.8 (d, $^{2}J_{C,P}$ = 4.8 Hz, C-sp^2) ppm. HRMS (ESI): MNa^+, found 448.1642. $C_{24}H_{28}NNaO_4P$ requires 448.1648.

Dimethyl (2-((4-Ethylphenyl)ethynyl)cyclopent-1-enyl)(4-methoxyphenylamino)methylphosphonate (7h). Yellow solid, mp 93−95 °C. Yield 0.35 g, 40%. IR (KBr): υ_{max} 3448 (NH), 2202 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (3H, t, ^{3}J = 7.6 Hz, $CH_2\underline{CH_3}$), 1.77−1.95 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.37−2.46 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.55−2.62 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.66 (2H, q, ^{3}J = 7.6 Hz, $\underline{CH_2}CH_3$), 3.72 (3H, s, OCH_3), 3.79 (3H, d, $^{3}J_{H,P}$ = 10.4 Hz, OCH_3), 3.84 (3H, d, $^{3}J_{H,P}$ = 10.4 Hz, OCH_3), 4.94 (1H, d, $^{3}J_{H,P}$ = 24.8 Hz, CH), 6.68 (2H, d, ^{3}J = 9.2 Hz, ArH), 6.75 (2H, d, ^{3}J = 8.8 Hz, ArH), 7.18 (2H, d, ^{3}J = 8.4 Hz, ArH), 7.40 (2H, d, ^{3}J = 8.4 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.3 (CH_3), 22.2 (CH_2), 28.8 (CH_2), 32.6 (d, $^{3}J_{C,P}$ = 1.1 Hz, CH_2), 36.7 (d, $^{5}J_{C,P}$ = 2.2 Hz, CH_2), 52.1 (d, $^{1}J_{C,P}$ = 153.6 Hz, CH), 53.5 (d, $^{2}J_{C,P}$ = 7.1 Hz, OCH_3), 53.8 (d, $^{2}J_{C,P}$ = 6.7 Hz, OCH_3), 84.4 (d, $^{4}J_{C,P}$ = 5.4 Hz, C-sp), 96.2 (d, $^{5}J_{C,P}$ = 2.6 Hz, C-sp), 114.7 (ArC), 115.2, (ArC), 120.3 (d, $^{6}J_{C,P}$ = 1.1 Hz, ArC), 124.3 (d, $^{3}J_{C,P}$ = 12.9 Hz, C-sp^2), 127.9 (ArC), 131.3 (ArC), 140.0 (d, $^{3}J_{C,P}$ = 16.8 Hz, ArC), 144.7 (d, $^{2}J_{C,P}$ = 4.6 Hz, C-sp^2), 144.8 (ArC), 152.9 (ArC) ppm. HRMS (ESI): MNa^+, found 462.1808. $C_{25}H_{30}NNaO_4P$ requires 462.1805.

Dimethyl (2-(Hex-1-ynyl)cyclopent-1-enyl)(phenylamino)-methylphosphonate (7i). Yellowish oil. Yield 0.36 g, 50%. IR (KBr): υ_{max} 3440 (NH), 2214 (C≡C) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (3H, t, ^{3}J = 7.2 Hz, $CH_2(CH_2)_2\underline{CH_3}$), 1.42−1.63 (4H, m, $CH_2\underline{(CH_2)_2}CH_3$), 1.69−1.91 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.29−2.55 (6H, m, $\underline{CH_2}CH_2\underline{CH_2}$ and $\underline{CH_2}(CH_2)_2CH_3$), 3.77 (3H, d, $^{3}J_{H,P}$ = 10.5 Hz, OCH_3), 3.82 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 4.78 (1H, d, $^{3}J_{H,P}$ = 24.6 Hz, CH), 6.66−6,69 (2H, m, ArH), 6.71−6.76 (1H, m, ArH), 7.13−7.18 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.5 (CH_3), 19.3 (CH_2), 21.9 (CH_2), 22.0 (CH_2), 32.0 (CH_2), 36.9 (d, $^{5}J_{C,P}$ = 2.1 Hz, CH_2), 50.9 (d, $^{1}J_{C,P}$ = 154.2 Hz, CH), 53.5 (d, $^{2}J_{C,P}$ = 7.3 Hz, OCH_3), 53.6 (d, $^{2}J_{C,P}$ = 6.9 Hz, OCH_3), 76.2 (d, $^{4}J_{C,P}$ = 5.4 Hz, C-sp), 97.3 (d, $^{5}J_{C,P}$ = 2.2 Hz, C-sp), 113.7 (ArC), 118.5 (ArC), 124.9 (d, $^{3}J_{C,P}$ = 13.0 Hz, C-sp^2), 129.1 (ArC), 142.3 (d, $^{2}J_{C,P}$ = 4.4 Hz, C-sp^2), 146.2 (d, $^{3}J_{C,P}$ = 15.5 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 384.1698. $C_{20}H_{28}NNaO_3P$ requires 384.1704.

Dimethyl (2-(Hex-1-ynyl)cyclopent-1-enyl)(4-methoxyphenylamino)methylphosphonate (7j). Yellowish oil. Yield 0.46 g, 59%. IR (KBr): υ_{max} 3418 (NH), 2211 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (3H, t, ^{3}J = 7.6 Hz, $CH_2(CH_2)_2\underline{CH_3}$), 1.43−1.61 (4H, m, $CH_2\underline{(CH_2)_2}CH_3$), 1.69−1.88 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.26−2.56 (6H, m, $\underline{CH_2}CH_2\underline{CH_2}$ and $\underline{CH_2}(CH_2)_2CH_3$), 3.72 (3H, s, OCH_3), 3.76 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 3.81 (3H, d, $^{3}J_{H,P}$ = 10.8 Hz, OCH_3), 4.83 (1H, d, $^{3}J_{H,P}$ = 24.4 Hz, CH), 6.62 (2H, d, ^{3}J = 9.2 Hz, ArH), 6.74 (2H, d, ^{3}J = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 19.3 (CH_2), 21.9 (CH_2), 22.0 (CH_2), 32.0 (d, $^{3}J_{C,P}$ = 1.0 Hz, CH_2), 36.9 (d, $^{5}J_{C,P}$ = 2.3 Hz, CH_2), 51.7 (d, $^{1}J_{C,P}$ = 154.2 Hz, CH), 53.4 (d, $^{2}J_{C,P}$ = 7.1 Hz, OCH_3), 53.6 (d, $^{2}J_{C,P}$ = 6.7 Hz, OCH_3), 55.5 (OCH_3), 76.3 (d, $^{4}J_{C,P}$ = 5.2 Hz, C-sp), 97.1 (d, $^{5}J_{C,P}$ = 2.5 Hz, C-sp), 114.6 (ArC), 115.0 (ArC), 124.9 (d, $^{3}J_{C,P}$ = 13.0 Hz, C-sp^2), 140.2 (d, $^{3}J_{C,P}$ = 16.6 Hz, ArC), 142.6 (d, $^{2}J_{C,P}$ = 4.5 Hz, C-sp^2), 152.7 (ArC) ppm. HRMS (ESI): MNa^+, found 414.1785. $C_{21}H_{30}NNaO_4P$ requires 414.1810.

Dimethyl (4-Fluorophenylamino)(2-(hex-1-ynyl)cyclopent-1-enyl)methylphosphonate (7k). Yellow solid, mp 68−70 °C. Yield 0.42 g, 55%. IR (KBr): υ_{max} 3469 (NH), 2216 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (3H, t, ^{3}J = 7.6 Hz, $CH_2(CH_2)_2\underline{CH_3}$), 1.43−1.52 (2H, m, $CH_2\underline{CH_2}CH_2CH_3$), 1.54−1.61 (2H, m, $CH_2CH_2\underline{CH_2}CH_3$), 1.70−1.89 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.25−2.34 (1H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 2.41−2.57 (5H, m, $\underline{CH_2}CH_2\underline{CH_2}$ and $\underline{CH_2}(CH_2)_2CH_3$), 3.77 (3H, d, $^{3}J_{H,P}$ = 10.4 Hz, OCH_3), 3.82 (3H, d, $^{3}J_{H,P}$ = 10.4 Hz, OCH_3), 4.83 (1H, d, $^{3}J_{H,P}$ = 24.4 Hz, CH), 6.58−6.61 (2H, m, ArH), 6.83−6.88 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 19.3 (CH_2), 21.9 (CH_2), 22.1 (CH_2), 30.9 (CH_2), 32.0 (d, $^{3}J_{C,P}$ = 1.0 Hz, CH_2), 36.9 (d, $^{5}J_{C,P}$ = 2.3 Hz, CH_2), 51.5 (d, $^{1}J_{C,P}$ = 154.3 Hz, CH), 53.5 (d, $^{2}J_{C,P}$ = 7.1 Hz, OCH_3), 53.6 (d, $^{2}J_{C,P}$ = 6.8 Hz, OCH_3), 76.2 (d, $^{4}J_{C,P}$ = 5.2 Hz, C-sp), 97.4 (d, $^{5}J_{C,P}$

= 2.5 Hz, C-sp), 114.7 (d, $^3J_{C,F}$ = 7.4 Hz, ArC), 115.5, (d, $^2J_{C,F}$ = 22.2 Hz, ArC), 125.3 (d, $^3J_{C,P}$ = 12.9 Hz, C-sp^2), 142.1 (d, $^2J_{C,P}$ = 4.6 Hz, C-sp^2), 142.5 (dd, $^3J_{C,P}$ = 16.2 Hz, $^4J_{C,F}$ = 1.8 Hz, ArC), 156.3 (d, $^1J_{C,F}$ = 234.7 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 402.1603. $C_{20}H_{27}FNNaO_3P$ requires 402.1605.

Dimethyl (4-Chlorophenylamino)(2-(hex-1-ynyl)cyclopent-1-enyl)methylphosphonate (7l). Yellow solid, mp 73−75 °C. Yield 0.36 g, 45%. IR (KBr): υ_{max} 3433 (NH), 2213 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.94 (3H, t, ^3J = 7.2 Hz, $CH_2(CH_2)_2\underline{CH_3}$), 1.42−1.51 (2H, m, $CH_2\underline{CH_2}CH_2CH_3$), 1.53−1.61 (2H, m, $CH_2CH_2\underline{CH_2}CH_3$), 1.70−1.89 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.26−2.31 (1H, m, $\underline{CH_2}CH_2CH_2$), 2.41−2.55 (5H, m, $\underline{CH_2}CH_2CH_2$ and $\underline{CH_2}(CH_2)_2CH_3$), 3.76 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.81 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 4.84 (1H, d, $^3J_{H,P}$ = 24.8 Hz, CH), 6.58 (2H, d, ^3J = 9.2 Hz, ArH), 7.09 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 19.2 (CH_2), 21.9 (CH_2), 22.0 (CH_2), 30.9 (CH_2), 32.0 (d, $^3J_{C,P}$ = 1.1 Hz, CH_2), 36.8 (d, $^5J_{C,P}$ = 2.2 Hz, CH_2), 51.0 (d, $^1J_{C,P}$ = 154.3 Hz, CH), 53.5 (d, $^2J_{C,P}$ = 4.3 Hz, OCH_3), 53.6 (d, $^2J_{C,P}$ = 3.9 Hz, OCH_3), 76.1 (d, $^4J_{C,P}$ = 5.3 Hz, C-sp), 97.5 (d, $^5J_{C,P}$ = 2.4 Hz, C-sp), 114.9 (ArC), 123.1 (ArC), 125.4 (d, $^3J_{C,P}$ = 12.9 Hz, C-sp^2), 128.9 (ArC), 141.8 (d, $^2J_{C,P}$ = 4.6 Hz, C-sp^2), 144.8 (d, $^3J_{C,P}$ = 16.6 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 418.1301. $C_{20}H_{27}ClNNaO_3P$ requires 418.1309.

Dimethyl (2-(Hept-1-ynyl)cyclopent-1-enyl)(phenylamino)-methylphosphonate (7m). Yellowish oil. Yield 0.31 g, 41%. IR (KBr): υ_{max} 3409 (NH), 2216 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (3H, t, ^3J = 7.6 Hz, $CH_2(CH_2)_3\underline{CH_3}$), 1.30−1.39 (2H, m, $CH_2(CH_2)_2\underline{CH_2}CH_3$), 1.40−1.48 (2H, m, $CH_2\underline{CH_2}CH_2CH_2CH_3$), 1.60 (2H, quint, ^3J = 7.2 Hz, $CH_2\underline{CH_2}CH_2CH_2CH_3$), 1.71−1.89 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.31−2.59 (6H, m, $\underline{CH_2}CH_2CH_2$ and $\underline{CH_2}(CH_2)_3CH_3$), 3.77 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.82 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 4.92 (1H, d, $^3J_{H,P}$ = 24.8 Hz, CH), 6.67 (2H, d, ^3J = 7.6 Hz, ArH), 6.74 (1H, t, ^3J = 7.6 Hz, ArH), 7.16 (2H, t, ^3J = 7.6 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (CH_3), 19.6 (CH_2), 22.0 (CH_2), 22.2 (CH_2), 28.5 (CH_2), 31.0 (CH_2), 32.0 (d, $^3J_{C,P}$ = 1.0 Hz, CH_2), 36.9 (d, $^5J_{C,P}$ = 2.3 Hz, CH_2), 50.9 (d, $^1J_{C,P}$ = 154.0 Hz, CH), 53.5 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 76.2 (d, $^4J_{C,P}$ = 5.3 Hz, C-sp), 97.3 (d, $^5J_{C,P}$ = 2.5 Hz, C-sp), 113.7 (ArC), 118.5 (ArC), 124.9 (d, $^3J_{C,P}$ = 13.0 Hz, C-sp^2), 129.1 (ArC), 142.3 (d, $^2J_{C,P}$ = 4.5 Hz, C-sp^2), 146.2 (d, $^3J_{C,P}$ = 15.4 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 398.1851. $C_{21}H_{30}NNaO_3P$ requires 398.1856.

Dimethyl (2-(Hept-1-ynyl)cyclopent-1-enyl)(4-methoxyphenylamino)methylphosphonate (7n). Yellowish oil. Yield 0.41 g, 50%. IR (KBr): υ_{max} 3450 (NH), 2221 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (3H, t, ^3J = 7.2 Hz, $CH_2(CH_2)_3\underline{CH_3}$), 1.30−1.37 (2H, m, $CH_2(CH_2)_2\underline{CH_2}CH_3$), 1.39−1.47 (2H, m, $CH_2CH_2\underline{CH_2}CH_2CH_3$), 1.59 (2H, quint, ^3J = 7.2 Hz, $CH_2\underline{CH_2}CH_2CH_2CH_3$), 1.70−1.88 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.30−2.56 (6H, m, $\underline{CH_2}CH_2CH_2$ and $\underline{CH_2}(CH_2)_3CH_3$), 3.73 (3H, s, OCH_3), 3.77 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.82 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 4.84 (1H, d, $^3J_{H,P}$ = 24.4 Hz, CH), 6.65 (2H, d, ^3J = 9.2 Hz, ArH), 6.75 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (CH_3), 19.6 (CH_2), 22.1 (CH_2), 22.2 (CH_2), 28.5 (CH_2), 31.0 (CH_2), 32.0 (CH_2), 36.9 (d, $^5J_{C,P}$ = 2.2 Hz, CH_2), 51.9 (d, $^1J_{C,P}$ = 154.3 Hz, CH), 53.5 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 6.7 Hz, OCH_3), 55.6 (OCH_3), 76.2 (d, $^4J_{C,P}$ = 5.3 Hz, C-sp), 97.3 (d, $^5J_{C,P}$ = 2.5 Hz, C-sp), 114.6 (ArC), 115.4 (ArC), 125.1 (d, $^3J_{C,P}$ = 13.1 Hz, C-sp^2), 139.8 (d, $^3J_{C,P}$ = 16.2 Hz, ArC), 142.3 (d, $^2J_{C,P}$ = 4.6 Hz, C-sp^2), 152.9 (ArC) ppm. HRMS (ESI): MNa^+, found 428.1958. $C_{22}H_{32}NNaO_4P$ requires 428.1961.

Dimethyl (2-(Cyclopropylethynyl)cyclopent-1-enyl)-(phenylamino)methylphosphonate (7o). Yellow solid, mp 143−145 °C. Yield 0.37 g, 53%. IR (KBr): υ_{max} 3407 (NH), 2211 (C≡C) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.73−0.78 (2H, m, $CH(\underline{CH_2})_2$), 0.85−0.92 (2H, m, $CH(\underline{CH_2})_2$), 1.41−1.50 (1H, m, $\underline{CH}(CH_2)_2$), 1.67−1.89 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.27−2.58 (4H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.77 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.82 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 4.86 (1H, d, $^3J_{H,P}$ = 24.9 Hz, CH), 6.63−6.67 (2H, m, ArH), 6.71−6.76 (1H, m, ArH), 7.12−7.19 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3 ($\underline{CH}(CH_2)_2$), 8.9 ($CH(\underline{CH_2})_2$), 9.0 ($CH(\underline{CH_2})_2$), 22.0 (CH_2), 32.1 (CH_2), 36.8 (d, $^5J_{C,P}$ = 2.2 Hz, CH_2), 50.9 (d, $^1J_{C,P}$ = 154.2 Hz, CH), 53.5 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 6.7 Hz, OCH_3), 71.3 (d, $^4J_{C,P}$ = 5.1 Hz, C-sp), 100.4 (d, $^5J_{C,P}$ = 2.5 Hz, C-sp), 113.6 (ArC), 118.4 (ArC), 124.6 (d, $^3J_{C,P}$ = 13.2 Hz, C-sp^2), 129.1 (ArC), 142.8 (d, $^2J_{C,P}$ = 4.5 Hz, C-sp^2), 146.3 (d, $^3J_{C,P}$ = 16.6 Hz, ArC) ppm. HRMS (ESI): MH^+, found 346.1569. $C_{19}H_{25}NO_3P$ requires 346.1567.

Dimethyl (2-(Cyclopropylethynyl)cyclopent-1-enyl)(4-methoxyphenylamino)methylphosphonate (7p). Yellowish oil. Yield 0.41 g, 55%. IR (KBr): υ_{max} 3451 (NH), 2211 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.73−0.77 (2H, m, $CH(\underline{CH_2})_2$), 0.86−0.90 (2H, m, $CH(\underline{CH_2})_2$), 1.42−1.48 (1H, m, $\underline{CH}(CH_2)_2$), 1.69−1.87 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.27−2.56 (4H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.73 (3H, s, OCH_3), 3.76 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.82 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 4.79 (1H, d, $^3J_{H,P}$ = 24.4 Hz, CH), 6.61 (2H, d, ^3J = 9.2 Hz, ArH), 6.75 (1H, d, ^3J = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.42 ($\underline{CH}(CH_2)_2$), 8.9 ($CH(\underline{CH_2})_2$), 9.0 ($CH(\underline{CH_2})_2$), 22.1 (CH_2), 32.2 (d, $^3J_{C,P}$ = 1.2 Hz, CH_2), 36.9 (d, $^5J_{C,P}$ = 2.1 Hz, CH_2), 51.8 (d, $^1J_{C,P}$ = 154.0 Hz, CH), 53.4 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 6.7 Hz, OCH_3), 55.6 (OCH_3), 71.4 (d, $^4J_{C,P}$ = 5.3 Hz, C-sp), 100.4 (d, $^5J_{C,P}$ = 2.3 Hz, C-sp), 114.6 (ArC), 115.1 (ArC), 124.6 (d, $^3J_{C,P}$ = 13.0 Hz, C-sp^2), 140.2 (d, $^3J_{C,P}$ = 16.4 Hz, ArC), 143.0 (d, $^2J_{C,P}$ = 4.5 Hz, C-sp^2), 152.7 (ArC) ppm. HRMS (ESI): MNa^+, found 398.1487. $C_{20}H_{26}NNaO_4P$ requires 398.1492.

Dimethyl (2-(Cyclopropylethynyl)cyclopent-1-enyl)(4-ethoxyphenylamino)methylphosphonate (7r). Yellow solid, mp 139−141 °C. Yield 0.44 g, 57%. IR (KBr): υ_{max} 3460 (NH), 2212 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.73−0.77 (2H, m, $CH(\underline{CH_2})_2$), 0.85−0.90 (2H, m, $CH(\underline{CH_2})_2$), 1.35 (3H, t, ^3J = 7.2 Hz, $OCH_2\underline{CH_3}$), 1.41−1.48 (1H, m, $\underline{CH}(CH_2)_2$), 1.68−1.87 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.26−2.54 (4H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.76 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.82 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.94 (2H, q, ^3J = 7.2 Hz, $O\underline{CH_2}CH_3$), 4.79 (1H, d, $^3J_{H,P}$ = 24.4 Hz, CH), 6.59 (2H, d, ^3J = 8.8 Hz, ArH), 6.74 (1H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.38 ($\underline{CH}(CH_2)_2$), 8.9 ($CH(\underline{CH_2})_2$), 9.0 ($CH(\underline{CH_2})_2$), 14.9 ($OCH_2\underline{CH_3}$), 22.1 (CH_2), 32.2 (d, $^3J_{C,P}$ = 1.0 Hz, CH_2), 36.9 (d, $^5J_{C,P}$ = 2.3 Hz, CH_2), 51.7 (d, $^1J_{C,P}$ = 154.1 Hz, CH), 53.4 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 6.7 Hz, OCH_3), 63.8 ($O\underline{CH_2}CH_3$), 71.4 (d, $^4J_{C,P}$ = 5.4 Hz, C-sp), 100.3 (d, $^5J_{C,P}$ = 2.4 Hz, C-sp), 115.0 (ArC), 115.4 (ArC), 124.5 (d, $^3J_{C,P}$ = 12.9 Hz, C-sp^2), 140.2 (d, $^3J_{C,P}$ = 16.4 Hz, ArC), 143.1 (d, $^2J_{C,P}$ = 4.5 Hz, C-sp^2), 152.0 (ArC) ppm. HRMS (ESI): MH^+, found 390.1844. $C_{21}H_{29}NO_4P$ requires 390.1829.

Dimethyl (Phenylamino)(2-((trimethylsilyl)ethynyl)-cyclopent-1-enyl)methylphosphonate (7s-TMS). Yellow solid, mp 141−143 °C. Yield 0.41 g, 54%. IR (KBr): υ_{max} 3437 (NH), 2134 (C≡C), cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.24 (9H, s, $Si(CH_3)_3$), 1.73−1.91 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.35−2.60 (4H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.78 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.83 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 4.93 (1H, d, $^3J_{H,P}$ = 24.8 Hz, CH), 6.68 (2H, d, ^3J = 7.6 Hz, ArH), 6.76 (1H, t, ^3J = 7.6 Hz, ArH), 7.15−7.19 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.0 ($Si(\underline{CH_3})_3$), 22.2 (CH_2), 32.5 (d, $^3J_{C,P}$ = 1.2 Hz, CH_2), 36.5 (d, $^5J_{C,P}$ = 2.1 Hz, CH_2), 50.9 (d, $^1J_{C,P}$ = 153.3 Hz, CH), 53.5 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 53.8 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 101.0 (d, $^4J_{C,P}$ = 5.0 Hz, C-sp), 101.3 (d, $^5J_{C,P}$ = 2.1 Hz, C-sp), 113.7 (ArC), 118.6 (ArC), 124.2 (d, $^3J_{C,P}$ = 12.6 Hz, C-sp^2), 129.2 (ArC), 146.1 (d, $^3J_{C,P}$ = 15.2 Hz, ArC), 146.5 (d, $^2J_{C,P}$ = 4.2 Hz, C-sp^2) ppm. HRMS (ES): MNa^+, found 400.1464. $C_{19}H_{28}NNaO_3PSi$ requires 400.1468.

Dimethyl (2-Ethynylcyclopent-1-enyl)(phenylamino)-methylphosphonate (7s). This compound was synthesized from **7s-TMS** by treating by 2 equiv of $KF_2{\cdot}H_2O$ in methanol at room temperature for 2 h. After evaporation of solvent, the residue was purified by column chromatography. Yellow solid, mp 118−119 °C. Yield 0.27 g, 83%. IR (KBr): υ_{max} 3452 (NH), 2088 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.74−1.92 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.34−2.40 (1H, m, $\underline{CH_2}CH_2CH_2$), 2.49−2.61 (3H, m, $\underline{CH_2}CH_2\underline{CH_2}$), 3.38 (1H, br. s, C≡$\underline{CH}$), 3.78 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.83 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 4.93 (1H, d, $^3J_{H,P}$ = 24.8 Hz, CH), 6.64−6.67

dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532−6553

(2H, m, ArH), 6.73−6.77 (1H, m, ArH), 7.14−7.19 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0 (CH_2), 32.4 (d, $^3J_{C,P}$ = 1.1 Hz, CH_2), 36.6 (d, $^5J_{C,P}$ = 2.3 Hz, CH_2), 50.9 (d, $^1J_{C,P}$ = 153.5 Hz, CH), 53.5 (d, $^2J_{C,P}$ = 7.2 Hz, OCH_3), 53.8 (d, $^2J_{C,P}$ = 6.7 Hz, OCH_3), 79.4 (d, $^4J_{C,P}$ = 5.2 Hz, C-sp), 83.9 (d, $^5J_{C,P}$ = 2.6 Hz, C-sp), 113.6 (ArC), 118.6 (ArC), 123.1 (d, $^3J_{C,P}$ = 12.7 Hz, C-sp^2), 129.2 (ArC), 146.1 (d, $^3J_{C,P}$ = 15.4 Hz, ArC), 146.9 (d, $^2J_{C,P}$ = 4.6 Hz, C-sp^2) ppm. HRMS (ESI): MH^+, found 306.1261. $C_{16}H_{21}NO_3P$ requires 306.1254.

Dimethyl (Phenylamino)(2-(phenylethynyl)cyclohex-1-enyl)methylphosphonate (8a). Light Orange solid, mp 139−140 °C. Yield 0.39 g, 49%. IR (KBr): υ_{max} 2200 (C≡C) 3405 (NH),cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54−1.62 (4H, m, 2 × CH_2), 2.04−2.17 (1H, m, CHH), 2.32−2.34 (3H, m, CHH, CH_2), 3.80 (3H, d, $^3J_{H,P}$ = 6.8 Hz, OCH_3), 3.83 (3H, d, $^3J_{H,P}$ = 6.8 Hz, OCH_3), 5.29 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.70−6.76 (3H, m, ArH), 7.16−7.20 (2H, m, ArH), 7.33−7.35 (3H, m, ArH), 7.47−7.49 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9 (CH_2), 22.0 (CH_2), 24.8 (d, $^3J_{C,P}$ = 1.5 Hz, CH_2), 30.4 (d, $^4J_{C,P}$ = 1.9 Hz, CH_2), 53.7 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.8 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 54.8 (d, $^1J_{C,P}$ = 150.5 Hz, CH), 88.5 (d, $^4J_{C,P}$ = 5.2 Hz, C_{sp}), 94.6 (d, $^5J_{C,P}$ = 2.2 Hz, C_{sp}), 113.5 (ArC), 118.3 (ArC), 120.8 (d, $^3J_{C,P}$ = 12.4 Hz, C_{sp^2}), 123.3 (ArC), 128.2 (ArC), 128.4 (ArC), 129.3 (ArC), 131.3 (ArC), 139.5 (d, $^2J_{C,P}$ = 3.7 Hz, C_{sp^2}), 146.3 (d, $^3J_{C,P}$ = 16.0 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 418.1547. $C_{23}H_{26}NNaO_3P$ requires 418.1543.

Dimethyl (4-Methoxyphenylamino)(2-(phenylethynyl)-cyclohex-1-enyl)methylphosphonate (8b). Brownish solid, mp 142−141 °C. Yield 0.43 g, 51%. IR (KBr): υ_{max} 3343 (NH), 2202 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52−1.65 (4H, m, 2 × CH_2), 2.02−2.08 (1H, m, CHH), 2.31−2.39 (3H, m, CHH, CH_2), 3.73 (3H, s, OCH_3), 3.79 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.83 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.22 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.67 (2H, d, J = 8.8 Hz, ArH), 6.76 (2H, d, J = 9.2 Hz, ArH), 7.31−7.35 (3H, m, ArH), 7.46−7.49 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9 (CH_2), 22.0 (CH_2), 24.8 (d, $^3J_{C,P}$ = 1.2 Hz, CH_2), 30.4 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 53.6 (d, $^2J_{C,P}$ = 2.6 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 2.9 Hz, OCH_3), 55.6 (d, $^1J_{C,P}$ = 150.8 Hz, CH), 55.6 (OCH_3), 88.6 (d, $^4J_{C,P}$ = 5.0 Hz, C_{sp}), 94.5 (d, $^5J_{C,P}$ = 2.2 Hz, C_{sp}), 114.8 (ArC), 114.9 (ArC), 120.9 (d, $^3J_{C,P}$ = 12.4 Hz, C_{sp^2}), 123.3 (ArC), 128.2 (ArC), 128.4 (ArC), 131.3 (ArC), 139.6 (d, $^2J_{C,P}$ = 3.6 Hz, C_{sp^2}), 140.1 (d, $^3J_{C,P}$ = 16.9 Hz, ArC), 152.7 (ArC) ppm. HRMS (ESI): MNa^+, found 448.1641. $C_{24}H_{28}NNaO_4P$ requires 448.1648.

Dimethyl (4-Fluorophenylamino)(2-(phenylethynyl)-cyclohex-1-enyl)methylphosphonate (8c). Brownish solid, mp 158−159 °C. Yield 0.46 g, 56%. IR (KBr): υ_{max} 3295 (NH), 2158 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.51−1.67 (4H, m, 2 × CH_2), 1.98−2.01 (1H, m, CHH), 2.32−2.35 (3H, m, CHH, CH_2), 3.80 (3H, d, $^3J_{H,P}$ = 8.4 Hz, OCH_3), 3.83 (3H, d, $^3J_{H,P}$ = 8.8 Hz, OCH_3), 5.21 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.63 (2H, dd, J = 13.2; 4.4 Hz, ArH), 6.88 (2H, t, J = 8.8 Hz, ArH), 7.33−7.36 (3H, m, ArH), 7.46−7.48 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9 (CH_2), 22.0 (CH_2), 24.8 (d, $^3J_{C,P}$ = 1.5 Hz, CH_2), 30.4 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 53.6 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 55.3 (d, $^1J_{C,P}$ = 150.9 Hz, CH), 88.4 (d, $^4J_{C,P}$ = 5.0 Hz, C_{sp}), 94.7 (d, $^5J_{C,P}$ = 2.2 Hz, C_{sp}), 114.5 (d, $^3J_{C,F}$ = 7.4 Hz, ArC), 115.7 (d, $^2J_{C,F}$ = 22.3 Hz, ArC), 121.2 (d, $^3J_{C,P}$ = 12.4 Hz, C_{sp^2}), 123.2 (ArC), 128.3 (ArC), 128.4 (ArC), 131.3 (ArC), 139.2 (d, $^2J_{C,P}$ = 3.9 Hz, C_{sp^2}), 142.5 (dd, $^3J_{C,P}$ = 16.7 Hz, $^4J_{C,F}$ = 1.8 Hz, ArC), 156.3 (d, $^1J_{C,F}$ = 234.6 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 436.1444. $C_{23}H_{25}FNNaO_3P$ requires 436.1448.

Dimethyl (4-Chlorophenylamino)(2-(phenylethynyl)-cyclohex-1-enyl)methylphosphonate (8d). Yellowish solid, mp 139−140 °C. Yield 0.38 g, 44%. IR (KBr): υ_{max} 3296 (NH), 2201 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50−1.66 (4H, m, 2 × CH_2), 1.98−1.99 (1H, m, CHH), 2.32−2.33 (3H, m, CHH, CH_2), 3.80 (3H, d, $^3J_{H,P}$ = 6.4 Hz, OCH_3), 3.83 (3H, d, $^3J_{H,P}$ = 6.4 Hz, OCH_3), 5.22 (1H, d, $^2J_{H,P}$ = 26.0 Hz, CHNH), 6.63 (2H, d, J = 8.8 Hz, ArH), 7.11 (2H, d, J = 8.8 Hz, ArH), 7.33−7.35 (3H, m, ArH), 7.46−7.48 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9 (CH_2), 24.8 (d, $^3J_{C,P}$ = 1.4 Hz, CH_2), 30.3 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 53.6 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 54.9 (d, $^1J_{C,P}$ = 151.0 Hz, CH), 88.3 (d, $^4J_{C,P}$ = 5.1 Hz, C_{sp}), 94.8 (d, $^5J_{C,P}$ = 2.2 Hz, C_{sp}), 114.7 (ArC), 121.2 (d, $^3J_{C,P}$ = 12.4 Hz, C_{sp^2}), 123.0 (ArC), 123.1 (d, $^6J_{C,P}$ = 0.8 Hz, ArC), 128.3 (ArC), 128.4 (ArC), 129.1 (ArC), 131.3 (ArC), 138.9 (d, $^2J_{C,P}$ = 4.0 Hz, C_{sp^2}), 144.9 (d, $^3J_{C,P}$ = 16.3 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 452.1145. $C_{23}H_{25}ClNNaO_3P$ requires 452.1153.

Dimethyl (Phenylamino)(2-(p-tolylethynyl)cyclohex-1-enyl)-methylphosphonate (8e). Light orange solid, mp 133−134 °C. Yield 0.43 g, 53%. IR (KBr): υ_{max} 3304 (NH), 2201 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54−1.65 (4H, m, 2 × CH_2), 2.05−2.08 (1H, m, CHH), 2.33 (3H, br. s, CHH, CH_2), 2.36 (3H, s, CH_3), 3.80 (3H, d, $^3J_{H,P}$ = 6.4 Hz, OCH_3), 3.82 (3H, d, $^3J_{H,P}$ = 6.4 Hz, OCH_3), 5.29 (1H, d, $^2J_{H,P}$ = 26.0 Hz, CHNH), 6.70−6.76 (3H, m, ArH), 7.16 (4H, dd, J = 13.3; 7.6 Hz ArH), 7.37 (2H, d, J = 7.6 Hz ArH), 7.47−7.49 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5 (CH_3), 22.0 (2 × CH_2), 24.8 (CH_2), 30.4 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 53.6 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 53.8 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 54.7 (d, $^1J_{C,P}$ = 150.2 Hz, CH), 87.9 (d, $^4J_{C,P}$ = 5.2 Hz, C_{sp}), 94.8 (d, $^5J_{C,P}$ = 1.8 Hz, C_{sp}), 113.5 (ArC), 118.3 (ArC), 120.3 (ArC), 120.9 (d, $^3J_{C,P}$ = 12.6 Hz, C_{sp^2}), 129.2 (ArC), 129.3 (ArC), 131.2 (ArC), 138.4 (ArC), 139.0 (d, $^2J_{C,P}$ = 4.0 Hz, C_{sp^2}), 146.3 (d, $^3J_{C,P}$ = 15.8 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 432.1699. $C_{24}H_{28}NNaO_3P$ requires 432.1699.

Dimethyl (4-Methoxyphenylamino)(2-(*p*-tolylethynyl)-cyclohex-1-enyl)methylphosphonate (8f). Light orange solid, mp 96−97 °C. Yield 0.39 g, 44%. IR (KBr): υ_{max} 3503 (NH), 2197 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50−1.66 (4H, m, 2 × CH_2), 2.01−2.08 (1H, m, CHH), 2.28−2.31 (3H, m, CHH, CH_2), 2.36 (3H, s, CH_3), 3.72 (3H, s, OCH_3), 3.79 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.82 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.22 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.67 (2H, d, J = 9.2 Hz ArH), 6.76 (2H, d, J = 9.2 Hz ArH), 7.14 (2H, d, J = 8.0 Hz ArH), 7.36 (2H, d, J = 8.0 Hz ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5 (CH_3), 22.0 (2 × CH_2), 24.8 (d, $^3J_{C,P}$ = 1.1 Hz, CH_2), 30.4 (d, $^4J_{C,P}$ = 1.7 Hz, CH_2), 53.7 (d, $^2J_{C,P}$ = 3.8 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 3.9 Hz, OCH_3), 55.6 (d, $^1J_{C,P}$ = 150.6 Hz, CH), 55.6 (OCH_3), 88.0 (d, $^4J_{C,P}$ = 5.2 Hz, C_{sp}), 94.7 (d, $^5J_{C,P}$ = 2.0 Hz, C_{sp}), 114.8 (ArC), 115.0 (ArC), 120.3 (ArC), 121.1 (d, $^3J_{C,P}$ = 12.4 Hz, C_{sp^2}), 129.2 (ArC), 131.2 (ArC), 138.4 (ArC), 139.1 (d, $^2J_{C,P}$ = 3.6 Hz, C_{sp^2}), 140.1 (d, $^3J_{C,P}$ = 15.9 Hz, ArC), 152.7 (ArC) ppm. HRMS (ESI): MNa^+, found 462.1795. $C_{25}H_{30}NNaO_4P$ requires 462.1805.

Dimethyl (2-(Pent-1-ynyl)cyclohex-1-enyl)(phenylamino)-methylphosphonate (8g). Light orange solid, mp 65−66 °C. Yield 0.18 g, 25%. IR (KBr): υ_{max} 3434 (NH), 2216 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (3H, t, J = 7.6 Hz, CH_3), 1.46−1.56 (4H, m, 2 × CH_2), 1.62 (2H, sexst., C≡CCH$_2$CH$_2$), 1.95−2.01 (1H, m, CHH), 2.17−2.20 (2H, m, CH_2), 2.27 (1H, dd, J = 20.0; 4.0 Hz CHH), 2.40 (2H, t, J = 7.2 Hz, C≡CCH$_2$CH$_2$), 3.78 (3H, d, $^3J_{H,P}$ = 8.8 Hz, OCH_3), 3.80 (3H, d, $^3J_{H,P}$ = 9.2 Hz, OCH_3), 5.21 (1H, d, $^2J_{H,P}$ = 26.0 Hz, CHNH), 6.66−6.69 (2H, m, ArH), 6.73 (1H, t, J = 7.6 Hz, ArH), 7.16 (2H, dd, J = 8,4; 7.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 21.6 (CH_2), 22.0 (CH_2, 2 × CH_{2chex}), 22.4 (CH_2), 24.4 (d, $^3J_{C,P}$ = 1.5 Hz, CH_2), 30.8 (d, $^4J_{C,P}$ = 1.9 Hz, CH_2), 53.4 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 54.5 (d, $^1J_{C,P}$ = 150.9 Hz, CH), 80.0 (d, $^4J_{C,P}$ = 4.9 Hz, C_{sp}), 95.5 (d, $^5J_{C,P}$ = 2.0 Hz, C_{sp}), 113.6 (ArC), 118.2 (ArC), 121.5 (d, $^3J_{C,P}$ = 12.6 Hz, C_{sp^2}), 129.2 (ArC), 136.9 (d, $^2J_{C,P}$ = 3.5 Hz, C_{sp^2}), 146.2 (d, $^3J_{C,P}$ = 16.0 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 384.1695. $C_{20}H_{28}NNaO_3P$ requires 384.1699.

Dimethyl (4-Methoxyphenylamino)(2-(pent-1-ynyl)-cyclohex-1-enyl)methylphosphonate (8h). Brownish solid, mp 92−93 °C. Yield 0.51 g, 65%. IR (KBr): υ_{max} 3308 (NH), 2216 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (3H, t, J = 7.2 Hz, CH_3), 1.41−1.55 (4H, m, 2 × CH_2), 1.61 (2H, sexst., J = 7.2 Hz, C≡CCH$_2$CH$_2$), 1.92−1.98 (1H, m, CHH), 2.15−2.18 (2H, m, CH_2), 2.24−2.29 (1H, m, CHH), 2.39 (2H, t, J = 6.8 Hz, C≡CCH$_2$CH$_2$), 3.73 (3H, s, OCH_3), 3.77 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.80 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.14 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.63 (2H, d, J = 9.2 Hz, ArH), 6.75 (2H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 21.6 (CH_2), 22.0 (2 × CH_{2chex}), 22.4 (CH_2), 24.4 (d, $^3J_{C,P}$ = 1.3 Hz, CH_2), 30.8 (d, $^4J_{C,P}$ = 1.8

Hz, CH_2), 53.5 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 53.6 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 55.3 (d, $^1J_{C,P}$ = 151.2 Hz, CH), 55.6 (OCH_3), 80.0 (d, $^4J_{C,P}$ = 4.9 Hz, C_{sp}), 95.4 (d, $^5J_{C,P}$ = 2.1 Hz, C_{sp}), 114.7 (ArC), 115.0 (ArC), 121.6 (d, $^3J_{C,P}$ = 12.7 Hz, C_{sp^2}), 136.9 (d, $^2J_{C,P}$ = 3.4 Hz, C_{sp^2}), 140.1 (d, $^3J_{C,P}$ = 16.5 Hz, ArC), 152.6 (ArC) ppm. HRMS (ESI): MNa^+, found 414.1811. $C_{21}H_{30}NNaO_4P$ requires 414.1805.

Dimethyl (4-Fluorophenylamino)(2-(pent-1-ynyl)cyclohex-1-enyl)methylphosphonate (8i). Brownish solid, mp 97−98 °C. Yield 0.27 g, 35%. IR (KBr): υ_{max} 3315 (NH), 2216 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.03 (3H, t, J = 7.2 Hz, CH_3), 1.45−1.63 (6H, 2m (overlap.), C≡CCH_2CH_2, 2 × CH_2), 1.89−1.94 (1H, m, CHH), 2.15−2.18 (2H, m, CH_2), 2.26−2.28 (1H, m, CHH), 2.39 (2H, t, J = 7.2 Hz, C≡CCH_2CH_2), 3.77 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.80 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.13 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.59 (2H, dd, J = 8.8 Hz, $^3J_{H,F}$ = 4.4 Hz, ArH), 6.86 (2H, t, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 21.5 (CH_2), 22.0 (2 × CH_{2chex}), 22.4 (CH_2), 24.3 (d, $^3J_{C,P}$ = 1.4 Hz, CH_2), 30.7 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 53.4 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 55.0 (d, $^1J_{C,P}$ = 151.3 Hz, CH), 79.9 (d, $^4J_{C,P}$ = 4.9 Hz, C_{sp}), 95.6 (d, $^5J_{C,P}$ = 2.0 Hz, C_{sp}), 114.5 (d, $^3J_{C,F}$ = 7.3 Hz, ArC), 115.6 (d, $^2J_{C,F}$ = 22.2 Hz), 121.9 (d, $^3J_{C,P}$ = 12.6 Hz, C_{sp^2}), 136.5 (d, $^2J_{C,P}$ = 3.5 Hz, C_{sp^2}), 142.4 (dd, $^3J_{C,P}$ = 17.3 Hz, $^4J_{C,F}$ = 1.3 Hz, ArC), 156.2 (d, $^1J_{C,F}$ = 234.4 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 402.1598. $C_{20}H_{27}FNNaO_3P$ requires 402.1605.

Dimethyl (2-(Hex-1-ynyl)cyclohex-1-enyl)(phenylamino)-methylphosphonate (8j). Yellowish solid, mp 55−56 °C. Yield 0.37 g, 49%. IR (KBr): υ_{max} 3514 (NH), 2214 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.97 (3H, t, J = 7.2 Hz, CH_3), 1.46−1.60 (8H, m, C≡CCH_2CH_2CH_2, 2 × CH_2), 1.96−2.01 (1H, m, CHH), 2.18−2.19 (2H, m, CH_2), 2.25−2.30 (1H, m, CHH), 2.43 (2H, t, J = 6.4 Hz, C≡CCH_2CH_2CH_2), 3.78 (3H, d, $^3J_{H,P}$ = 9.6 Hz, OCH_3), 3.80 (3H, d, $^3J_{H,P}$ = 9.6 Hz, OCH_3), 5.20 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.68 (2H, dd, J = 8.4; 0.8 Hz, ArH), 6.73 (1H, tt, J = 7.6; 1.2 Hz, ArH), 7.16 (2H, dd, J = 8,4; 7.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 19.2 (CH_2), 22.0 (CH_2, 2 × CH_{2chex}), 24.4 (d, $^3J_{C,P}$ = 1.5 Hz, CH_2), 30.8 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 31.0 (CH_2), 53.4 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 7.2 Hz, OCH_3), 54.6 (d, $^1J_{C,P}$ = 150.7 Hz, CH), 79.9 (d, $^4J_{C,P}$ = 4.8 Hz, C_{sp}), 95.6 (d, $^5J_{C,P}$ = 2.0 Hz, C_{sp}), 113.6 (ArC), 118.2 (ArC), 121.5 (d, $^3J_{C,P}$ = 12.6 Hz, C_{sp^2}), 129.2 (ArC), 136.8 (d, $^2J_{C,P}$ = 3.6 Hz, C_{sp^2}), 146.2 (d, $^3J_{C,P}$ = 16.0 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 398.1858. $C_{21}H_{30}NNaO_3P$ requires 398.1856.

Dimethyl (2-(Hex-1-ynyl)cyclohex-1-enyl)(4-methoxyphenylamino)methylphosphonate (8k). Light brown solid, mp 72−71 °C. Yield 0.45 g, 56%. IR (KBr): υ_{max} 3307 (NH), 2213 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.93 (3H, t, J = 7.2 Hz, CH_3), 1.43−1.60 (8H, m, C≡CCH_2CH_2CH_2, 2 × CH_2), 1.93−1.98 (1H, m, CHH), 2.14−2.17 (2H, m, CH_2), 2.24−2.29 (1H, m, CHH), 2.41 (2H, t, J = 6.4 Hz, C≡CCH_2CH_2CH_2), 3.73 (3H, s, OCH_3), 3.77 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.80 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.13 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.63 (2H, d, J = 9.2 Hz, ArH), 6.75 (2H, d, J = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 19.2 (CH_2), 21.9 (CH_2), 22.0 (2 × CH_{2chex}), 24.4 (d, $^3J_{C,P}$ = 1.4 Hz, CH_2), 30.8 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 31.0 (CH_2), 53.5 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 53.6 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 55.3 (d, $^1J_{C,P}$ = 151.1 Hz, CH), 55.6 (OCH_3), 79.9 (d, $^4J_{C,P}$ = 4.9 Hz, C_{sp}), 95.5 (d, $^5J_{C,P}$ = 2.0 Hz, C_{sp}), 114.7 (ArC), 114.9 (ArC), 121.6 (d, $^3J_{C,P}$ = 12.6 Hz, C_{sp^2}), 136.9 (d, $^2J_{C,P}$ = 3.4 Hz, C_{sp^2}), 140.1 (d, $^3J_{C,P}$ = 16.9 Hz, ArC), 152.6 (ArC) ppm. HRMS (ESI): MNa^+, found 428.1953. $C_{22}H_{32}NNaO_4P$ requires 428.1961.

Dimethyl (2-(Cyclopropylethynyl)cyclohex-1-enyl)-(phenylamino)methylphosphonate (8l). Yellowish solid, mp 125−124 °C. Yield 0.26 g, 36%. IR (KBr): υ_{max} 3308 (NH), 2207 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.74−0.77 (2H, m, CH(CH_2)$_2$), 0.85−0.89 (2H, m, CH(CH_2)$_2$), 1.51−1.58 (5H, m, CH(CH_2)$_2$, 2 × CH_2), 1.95−2.00 (1H, m, CHH), 2.15−2.17 (2H, m, CH_2), 2.21−2.28 (1H, m, CHH), 3.77 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.81 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.14 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.65 (2H, d, J = 7.6 Hz, ArH), 6.74 (1H, t, J = 7.6 Hz, ArH), 7.33−7.35 (2H, dd, J = 8.4; 7.6 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.3 (CH(CH_2)$_2$), 8.8 (CH(CH_2)$_2$), 9.0 (CH-(CH_2)$_2$), 22.0 (2 × CH_2), 24.5 (d, $^3J_{C,P}$ = 1.6 Hz, CH_2), 30.6 (d, $^4J_{C,P}$ = 1.7 Hz, CH_2), 53.5 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 7.1 Hz, OCH_3), 54.6 (d, $^1J_{C,P}$ = 150.8 Hz, CH), 74.9 (d, $^4J_{C,P}$ = 5.0 Hz, C_{sp}), 98.9 (d, $^5J_{C,P}$ = 2.0 Hz, C_{sp}), 113.6 (ArC), 118.2 (ArC), 121.3 (d, $^3J_{C,P}$ = 12.4 Hz, C_{sp^2}), 129.2 (ArC), 137.3 (d, $^2J_{C,P}$ = 3.5 Hz, C_{sp^2}), 146.3 (d, $^3J_{C,P}$ = 15.7 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 382.1542. $C_{20}H_{26}NNaO_3P$ requires 382.1543

Dimethyl (2-(Cyclopropylethynyl)cyclohex-1-enyl)(4-methoxyphenylamino)methylphosphonate (8m). Yellowish solid, mp 98−99 °C. Yield 0.45 g, 58%. IR (KBr): υ_{max} 3306 (NH), 2213 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.72−0.76 (2H, m, CH(CH_2)$_2$), 0.85−0.89 (2H, m, CH(CH_2)$_2$), 1.41−1.58 (5H, m, CH(CH_2)$_2$, 2 × CH_2), 1.91−1.97 (1H, m, CHH), 2.13−2.16 (2H, m, CH_2), 2.23−2.28 (1H, m, CHH), 3.74 (3H, s, OCH_3), 3.76 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.81 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.07 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.60 (2H, d, J = 8.8 Hz, ArH), 6.76 (2H, d, J = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.3 (CH(CH_2)$_2$), 8.8 (CH(CH_2)$_2$), 9.0 (CH(CH_2)$_2$), 22.0 (2 × CH_2), 24.5 (CH_2), 30.6 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 53.5 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.6 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 55.2 (d, $^1J_{C,P}$ = 150.7 Hz, CH), 55.7 (OCH_3), 75.0 (d, $^4J_{C,P}$ = 5.0 Hz, C_{sp}), 98.7 (d, $^5J_{C,P}$ = 2.0 Hz, C_{sp}), 114.7 (ArC), 114.8 (ArC), 121.3 (d, $^3J_{C,P}$ = 12.5 Hz, C_{sp^2}), 137.5 (d, $^2J_{C,P}$ = 3.6 Hz, C_{sp^2}), 140.2 (d, $^3J_{C,P}$ = 17.0 Hz, ArC), 152.5 (ArC) ppm. HRMS (ESI): MNa^+, found 412.1640. $C_{21}H_{28}NNaO_4P$ requires 412.1648.

Dimethyl (4-Chlorophenylamino)(2-(cyclopropylethynyl)-cyclohex-1-enyl)methylphosphonate (8n). Brownish solid, mp 114−115 °C. Yield 0.44 g, 56%. IR (KBr): υ_{max} 3295 (NH), 2212 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.71−0.75 (2H, m, CH(CH_2)$_2$), 0.86−0.89 (2H, m, CH(CH_2)$_2$), 1.41−1.47 (1H, m, CH(CH_2)$_2$), 1.49−1.56 (3H, m, CH_2), 1.88−1.93 (1H, m, CHH), 2.13−2.16 (2H, m, CH_2), 2.19−2.26 (1H, m, CHH), 3.76 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.80 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.07 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.57 (2H, d, J = 9.2 Hz, ArH), 7.10 (2H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.3 (CH(CH_2)$_2$), 8.8 (CH(CH_2)$_2$), 9.0 (CH(CH_2)$_2$), 22.0 (2 × CH_2), 24.5 (d, $^3J_{C,P}$ = 1.4 Hz, CH_2), 30.6 (d, $^4J_{C,P}$ = 1.8 Hz, CH_2), 53.4 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 54.6 (d, $^1J_{C,P}$ = 151.1 Hz, CH), 74.8 (d, $^4J_{C,P}$ = 4.9 Hz, C_{sp}), 99.1 (d, $^5J_{C,P}$ = 2.0 Hz, C_{sp}), 114.7 (ArC), 121.7 (d, $^3J_{C,P}$ = 12.5 Hz, C_{sp^2}), 122.9 (ArC), 129.0 (ArC), 136.7 (d, $^2J_{C,P}$ = 3.9 Hz, C_{sp^2}), 144.9 (d, $^3J_{C,P}$ = 16.3 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 416.1150. $C_{20}H_{25}ClNNaO_3P$ requires 416.1153.

Dimethyl (4-Chlorophenylamino)(2-(p-tolylethynyl)-cyclohex-1-enyl)methylphosphonate (8o). Yellowish solid, mp 112−113 °C. Yield 0.47 g, 53%. IR (KBr): υ_{max} 3309 (NH), 2118 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.52−1.65 (4H, m, 2 × CH_2), 1.97−2.03 (1H, m, CHH), 2.31−2.34 (3H, m, CHH, CH_2), 2.36 (3H, s, CH_3), 3.79 (3H, d, $^3J_{H,P}$ = 6.0 Hz, OCH_3), 3.82 (3H, d, $^3J_{H,P}$ = 6.0 Hz, OCH_3), 5.22 (1H, d, $^2J_{H,P}$ = 25.6 Hz, CHNH), 6.63 (2H, d, J = 8.8 Hz, ArH), 7.11 (2H, d, J = 8.8 Hz, ArH), 7.15 (2H, d, J = 7.6 Hz, ArH), 7.36 (2H, d, J = 8.0 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4 (CH_3), 21.9 (CH_2), 22.0 (CH_2), 24.7 (d, $^3J_{C,P}$ = 1.4 Hz, CH_2), 30.3 (d, $^4J_{C,P}$ = 1.7 Hz, CH_2), 53.6 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.8 (d, $^2J_{C,P}$ = 7.2 Hz, OCH_3), 54.9 (d, $^1J_{C,P}$ = 150.9 Hz, CH), 87.7 (d, $^4J_{C,P}$ = 5.1 Hz, C_{sp}), 95.0 (d, $^5J_{C,P}$ = 2.2 Hz, C_{sp}), 114.7 (ArC), 120.0 (ArC), 121.4 (d, $^3J_{C,P}$ = 12.4 Hz, C_{sp^2}), 123.0 (ArC), 129.1 (ArC), 129.2 (ArC), 131.1 (ArC), 138.4 (d, $^2J_{C,P}$ = 4.0 Hz, C_{sp^2}), 138.5 (ArC), 144.9 (d, $^3J_{C,P}$ = 16.3 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 466.1307. $C_{24}H_{27}ClNNaO_3P$ requires 466.1309.

Dimethyl (Phenylamino)(2-(phenylethynyl)phenyl)-methylphosphonate (9a). White solid, mp 154−155 °C. Yield 0.34 g, 44%. IR (KBr): υ_{max} 3348 (NH), 2212 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.44 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.85 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.59 (1H, d, $^2J_{H,P}$ = 24.4 Hz, CHNH), 6.67−6.72 (3H, m, ArH), 7.09−7.13 (2H, m, ArH), 7.25- 7.35 (2H, m, ArH), 7.38−7.41 (3H, m, ArH), 7.57−7.64 (4H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.9 (d, $^1J_{C,P}$ = 151.0 Hz, CH), 53.8 (d, $^2J_{C,P}$ = 6.3 Hz, OCH_3), 53.9 (d, $^2J_{C,P}$ = 6.2 Hz, OCH_3), 86.8 (d, $^4J_{C,P}$ =

dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532−6553

2.0 Hz, C_{sp}), 95.1 (C_{sp}), 113.8 (ArC), 118.6 (ArC), 122.9 (ArC), 123.2 (d, $^3J_{C,P}$ = 8.7 Hz, ArC), 127.4 (d, $^3J_{C,P}$ = 4.4 Hz, ArC), 127.9 (d, $^5J_{C,P}$ = 3.1 Hz, ArC), 128.5 (ArC), 128.7 (ArC), 129.0 (d, $^4J_{C,P}$ = 3.1 Hz, ArC), 129.2 (ArC), 131.5 (ArC), 132.2 (d, $^4J_{C,P}$ = 2.1 Hz, ArC), 137.7 (d, $^2J_{C,P}$ = 1.8 Hz, ArC), 145.7 (d, $^3J_{C,P}$ = 14.8 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 414.1228. $C_{23}H_{22}NNaO_3P$ requires 414.1230.

Dimethyl (4-Chlorophenylamino)(2-(phenylethynyl)phenyl)-methylphosphonate (9b). Yellowish solid, mp 149−150 °C. Yield0.51 g, 60%. IR (KBr): υ_{max} 3508 (NH), 2213 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.44 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.85 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 4.44 (1H, br. s, NH), 5.53 (1H, d, $^2J_{H,P}$ = 24.4 Hz, CHNH), 6.59 (2H, d, J = 8.8 Hz, ArH), 7.05 (2H, d, J = 8.8 Hz, ArH), 7.28−7.35 (2H, m, ArH), 7.38−7.40 (3H, m, ArH), 7.57−7.61 (4H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.0 (d, $^1J_{C,P}$ = 151.5 Hz, CH), 53.8 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.9 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 86.7 (d, $^4J_{C,P}$ = 2.0 Hz, C_{sp}), 95.3 (C_{sp}), 114.9 (ArC), 122.8 (ArC), 123.2 (ArC), 123.2 (d, $^6J_{C,P}$ = 7.0 Hz, ArC), 127.3 (d, $^3J_{C,P}$ = 4.3 Hz, ArC), 128.0 (d, $^5J_{C,P}$ = 3.0 Hz, ArC), 128.5 (ArC), 128.8 (ArC), 129.0 (d, $^4J_{C,P}$ = 3.1 Hz, ArC), 129.1 (ArC), 131.5 (ArC), 132.3 (d, $^4J_{C,P}$ = 2.2 Hz, ArC), 137.2 (d, $^2J_{C,P}$ = 2.1 Hz, ArC), 144.4 (d, $^3J_{C,P}$ = 15.1 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 448.0836. $C_{23}H_{21}ClNNaO_3P$ requires 448.0840.

Dimethyl (4-Methoxyphenylamino)(2-((trimethylsilyl)-ethynyl)phenyl)methylphosphonate (9c-TMS). Yellowish solid, mp 115−116 °C. Yield 0.59 g, 71%. IR (KBr): υ_{max} 2157 (C≡C), 3287 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.30 (9H, s, CH_3), 3.43 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 3.68 (3H, s, OCH_3), 3.84 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.46 (1H, d, $^2J_{H,P}$ = 24.8 Hz, CHNH), 6.62 (2H, d, J = 8.8 Hz, ArH), 6.70 (2H, d, J = 9.2 Hz, ArH), 7.20 (1H, tt, J = 7.6 Hz; 1.6 Hz, ArH), 7.30 (1H, t, J = 7.6 Hz, ArH), 7.47 (1H, d, J = 7.6 Hz, ArH), 7.58 (1H, d, J = 7.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.1 (CH_3), 53.4 (d, $^1J_{C,P}$ = 150.2 Hz, CH), 53.7 (d, $^2J_{C,P}$ = 6.1 Hz, OCH_3), 53.8 (d, $^2J_{C,P}$ = 6.2 Hz, OCH_3), 55.6 (OCH_3), 100.3 (C_{sp}), 102.7 (C_{sp}), 114.7 (ArC), 115.2 (ArC), 123.2 (d, $^3J_{C,P}$ = 7.5 Hz, ArC), 127.4 (ArC), 127.7 (d, $^5J_{C,P}$ = 2.4 Hz, ArC), 129.2 (d, $^4J_{C,P}$ = 3.0 Hz, ArC), 132.3 (d, $^4J_{C,P}$ = 1.9 Hz, ArC), 138.1 (ArC), 139.4 (ArC), 152.9 (ArC) ppm. HRMS (ES): MNa^+, found 440.1419. $C_{21}H_{28}NNaO_4PSi$ requires 440.1417.

Dimethyl (2-Ethynylphenyl)(4-methoxyphenylamino)-methylphosphonate (9c). This compound was synthesized from **9c-TMS** by treating with 2 equiv of $KF_2{\cdot}H_2O$ in methanol at room temperature for 2 h. After evaporation of solvent, the residue was purified by column chromatography. White solid, mp 171−172 °C. Yield 0.38 g, 78%. IR (KBr): υ_{max} 3504 (NH), 2101 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.44 (4H, d and s (overlap.), $^3J_{H,P}$ = 10.8 Hz, OCH_3, CH), 3.68 (3H, s, OCH_3), 3.85 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.44 (1H, d, $^2J_{H,P}$ = 24.0 Hz, CHNH), 6.64 (2H, d, J = 8.8 Hz, ArH), 6.69 (2H, d, J = 9.2 Hz, ArH), 7.24 (1H, tt, J = 7.6 Hz; 1.6 Hz, ArH), 7.34 (1H, t, J = 7.2 Hz, ArH), 7.52 (1H, d, J = 7.6 Hz, ArH), 7.63 (1H, d, J = 7.6 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.7 (d, $^1J_{C,P}$ = 151.1 Hz, CH), 53.8 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 54.0 (d, $^2J_{C,P}$ = 6.8 Hz, OCH_3), 55.6 (OCH_3), 81.2 (d, $^4J_{C,P}$ = 1.9 Hz, C_{sp}), 82.8 (C_{sp}), 114.7 (ArC), 115.7 (ArC), 122.2 (d, $^3J_{C,P}$ = 7.2 Hz, ArC), 127.5 (d, $^3J_{C,P}$ = 4.2 Hz, ArC), 127.9 (d, $^5J_{C,P}$ = 3.0 Hz, ArC), 129.5 (d, $^4J_{C,P}$ = 3.0 Hz, ArC), 132.9 (d, $^4J_{C,P}$ = 2.1 Hz, ArC), 138.0 (ArC), 138.9 (ArC), 153.2 (d, $^6J_{C,P}$ = 1.2 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 368.1022. $C_{18}H_{20}NNaO_4P$ requires 368.1022.

Dimethyl (1-Benzyl-2-(phenylethynyl)-1*H*-indol-3-yl)-(phenylamino)methylphosphonate (19a). Yellowish solid, mp156−157 °C. Yield 0.44 g, 42%. IR (KBr): υ_{max} 3316 (NH), 2214 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.50 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.88 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.47 (1H, d, $^2J_{H,P}$ = 24.4 Hz, CHNH), 5.47 (2H, s, NCH_2), 6.71 (1H, t, J = 7.2 Hz, ArH), 6.81 (2H, d, J = 8.0 Hz, ArH), 7.09- 7.26 (10H, m, ArH), 7.40−7.41 (3H, m, ArH), 7.55−7.58 (2H, m, ArH), 8.03 (1H, d, J = 6.4 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 48.0 (NCH_2), 49.4 (d, $^1J_{C,P}$ = 160.2 Hz, CH), 53.6 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 7.0 Hz, OCH_3), 79.6 (d, $^4J_{C,P}$ = 3.5 Hz, C_{sp}), 99.6 (d, $^5J_{C,P}$ = 1.5 Hz, C_{sp}), 110.1 (ArC), 114.1 (2 × ArC), 114.9 (d, J = 1.6 Hz, ArC), 118.4 (ArC), 120.7 (ArC), 121.7 (d, $^3J_{C,P}$ = 10.1 Hz, ArC), 122.1 (ArC), 123.7 (ArC), 125.9 (d, $^2J_{C,P}$ = 3.0 Hz, ArC), 126.5 (ArC), 127.4 (ArC), 128.5 (ArC), 128.6 (ArC), 128.9 (ArC), 129.0 (ArC), 131.4 (ArC), 136.9 (ArC), 137.3 (ArC), 146.3 (d, $^3J_{C,P}$ = 14.9 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 543.1807. $C_{32}H_{29}N_2NaO_3P$ requires 543.1808.

Dimethyl (1-Benzyl-2-(hex-1-ynyl)-1*H*-indol-3-yl)(4-methoxyphenylamino)methylphosphonate (19b). Yellowish solid, mp 132−133 °C. Yield 0.24 g, 46%. IR (KBr): υ_{max} 3480 (NH), 2214 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.93 (3H, t, J = 7.2 Hz, CH_3), 1.46 (2H, sext., J = 7.2 Hz, C≡CCH$_2$CH$_2$CH$_2$), 1.58−1.65 (2H, m, C≡CCH$_2$CH$_2$CH$_2$), 2.55 (2H, t, J = 7.2 Hz, C≡CCH$_2$CH$_2$CH$_2$), 3.46 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.68 (3H, s, OCH_3), 3.85 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.25 (1H, d, $^2J_{H,P}$ = 24.0 Hz, CHNH), 5.37 (2H, s, NCH_2), 6.53−6.72 (4H, m, ArH), 6.96−6.98 (2H, m, ArH), 7.11- 7.12 (3H, m, ArH), 7.20−7.21 (3H, m, ArH), 7.94−7.97 (1H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 19.5 (CH_2), 21.9 (CH_2), 30.6 (CH_2), 47.8 (NCH_2), 50.5 (d, $^1J_{C,P}$ = 161.0 Hz, CH), 53.6 (d, $^2J_{C,P}$ = 5.4 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 55.6 (OCH_3), 71.1 (d, $^4J_{C,P}$ = 3.2 Hz, C_{sp}), 101.1 (d, $^5J_{C,P}$ = 1.4 Hz, C_{sp}), 109.9 (ArC), 113.4 (ArC), 114.5 (ArC), 115.8 (ArC), 120.4 (ArC), 120.6 (ArC), 122.9 (d, $^3J_{C,P}$ = 10.5 Hz, ArC), 123.1 (ArC), 125.8 (d, $^2J_{C,P}$ = 2.7 Hz, ArC), 126.3 (ArC), 127.2 (ArC), 128.5 (ArC), 136.4 (ArC), 137.5 (ArC), 140.3 (d, $^3J_{C,P}$ = 15.9 Hz, ArC), 152.8 (ArC) ppm. HRMS (ESI): MNa^+, found 553.2218. $C_{31}H_{35}N_2NaO_4P$ requires 553.2227.

Dimethyl (1-Benzyl-2-(cyclopropylethynyl)-1*H*-indol-3-yl)-(phenylamino)methylphosphonate (19c). Yellowish solid, mp 106−107 °C. Yield 0.31 g, 32%. IR (KBr): υ_{max} 3314 (NH), 2219 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.16−1.19 (2H, m, CH(CH$_2$)$_2$), 1.29−1.32 (2H, m, CH(CH$_2$)$_2$), 1.89−1.95 (1H, m, CH(CH$_2$)$_2$), 3.78 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 4.18 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.65 (1H, d, $^2J_{H,P}$ = 24.4 Hz, CHNH), 5.70 (2H, s, NCH_2), 7.03 (1H, t, J = 7.2 Hz, ArH), 7.08 (2H, d, J = 8.0 Hz, ArH), 7.34- 7.57 (10H, m, ArH), 8.27−8.29 (1H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 0.5 (CH(CH$_2$)$_2$), 9.3 (2 × CH(CH$_2$)$_2$), 47.8 (NCH_2), 49.3 (d, $^1J_{C,P}$ = 160.7 Hz, CH), 53.6 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 53.7 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 65.8 (d, $^4J_{C,P}$ = 3.3 Hz, C_{sp}), 104.5 (d, $^4J_{C,P}$ = 1.1 Hz, C_{sp}), 110.0 (ArC), 113.8 (ArC), 114.1 (2 × ArC), 118.4 (ArC), 120.4 (ArC), 122.6 (d, $^3J_{C,P}$ = 10.4 Hz, ArC), 123.2 (ArC), 125.8 (d, $^2J_{C,P}$ = 2.8 Hz, ArC), 126.4 (ArC), 127.3 (ArC), 128.5 (ArC), 128.9 (ArC), 136.4 (ArC), 137.5 (ArC), 146.4 (d, $^3J_{C,P}$ = 15.0 Hz, ArC) ppm. HRMS (ESI): MNa^+, found 507.1793. $C_{29}H_{29}N_2NaO_3P$ requires 507.1808.

General Procedure for the Preparation of Compounds 10 and 14. To a solution of the corresponding acetylenic α-anilinomethylphosphonate **7** were added **8** (1 mmol) in dry chloroform (5 mL) and potassium *tert*-butanoate (0.112 g, 1 mmol), together with gold(III) bromide (43.7 mg, 0.1 mmol). The resulting solution was stirred at room temperature. When the completion of the reaction was observed by TLC (after 0.5−2 h), the solution was evaporated under reduced pressure, and the residue was purified by flash column chromatography eluting with hexane−ethyl acetate mixtures.

Dimethyl 3-Benzyl-2-phenyl-2,4,5,6-tetrahydrocyclopenta-[c]pyrrol-1-ylphosphonate (10a). Yellowish oil. Yield 0.37 g, 98%. ^1H NMR (400 MHz, $CDCl_3$): δ 2.24−2.32 (2H, m, CH$_2$CH$_2$CH$_2$), 2.35−2.38 (2H, m, CH$_2$CH$_2$CH$_2$), 2.84−2.87 (2H, m, CH$_2$CH$_2$CH$_2$), 3.42 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.65 (2H, br. s, CH_2), 6.91−6.93 (2H, m, ArH), 7.12−7.21 (5H, m, ArH), 7.35−7.39 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8 (CH_2), 26.6 (CH_2), 30.3 (CH_2), 32.3 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.6 Hz, OCH_3), 110.2 (d, $^1J_{C,P}$ = 234.2 Hz, C-sp^2), 126.0 (ArC), 128.1 (ArC), 128.3 (ArC), 128.3 (ArC), 128.5 (ArC), 128.8 (ArC), 129.4 (d, $^3J_{C,P}$ = 14.2 Hz, C-sp^2), 131.5 (d, $^4J_{C,P}$ = 8.5 Hz, C-sp^2), 138.5 (ArC), 138.7 (ArC), 144.5 (d, $^2J_{C,P}$ = 17.4 Hz, C-sp^2) ppm. HRMS (ESI): MNa^+, found 404.1388. $C_{22}H_{24}NNaO_3P$ requires 404.1386.

Dimethyl 3-Benzyl-2-(4-methoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10b). Yellow-

dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532−6553

ish oil. Yield 0.30 g, 74%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.23−2.30 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.34−2.37 (2H, m, $\underline{CH_2}CH_2CH_2$), 2.82−2.86 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.51 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.63 (2H, br. s, CH_2), 3.82 (3H, s, OCH_3), 6.86 (2H, d, ^3J = 9.2 Hz, ArH), 6.92−6.94 (2H, m, ArH), 7. Ten (2H, d, J = 9.2 Hz, ArH), 7.14−7.21 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8 (CH_2), 26.6 (CH_2), 30.3 (CH_2), 32.3 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 55.3 (OCH_3), 110.1 (d, $^1J_{C,P}$ = 234.7 Hz, C-sp^2), 113.4 (ArC), 126.0 (ArC), 128.1 (ArC), 128.6 (ArC), 129.1 (d, $^3J_{C,P}$ = 14.2 Hz, C-sp^2), 129.8 (ArC), 131.5 (ArC), 131.9 (d, $^4J_{C,P}$ = 8.5 Hz, C-sp^2), 138.6 (ArC), 144.2 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2), 159.2 (ArC) ppm. HRMS (ESI): MNa^+, found 434.1497. $C_{23}H_{26}NNaO_4P$ requires 434.1492.

Dimethyl 3-Benzyl-2-(4-ethoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10c). Yellowish oil. Yield 0.32 g, 76%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (3H, t, ^3J = 6.8 Hz, $OCH_2\underline{CH_3}$), 2.23−2.31 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.34−2.37 (2H, m, $\underline{CH_2}CH_2CH_2$), 2.82−2.86 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.50 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.63 (2H, br. s, CH_2), 4.04 (2H, q, ^3J = 6.8 Hz, $O\underline{CH_2}CH_3$), 6.85 (2H, d, ^3J = 8.8 Hz, ArH), 6.93−6.95 (2H, m, ArH), 7. Ten (2H, d, ^3J = 8.8 Hz, ArH), 7.14−7.21 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.7 (CH_3), 24.8 (CH_2), 26.6 (CH_2), 30.3 (CH_2), 32.3 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 63.5 ($O\underline{CH_2}CH_3$), 110.2 (d, $^1J_{C,P}$ = 234.4 Hz, C-sp^2), 113.9 (ArC), 126.0 (ArC), 128.1 (ArC), 128.6 (ArC), 129.0 (d, $^3J_{C,P}$ = 14.3 Hz, C-sp^2), 129.8 (ArC), 131.3 (ArC), 131.8 (d, $^4J_{C,P}$ = 8.6 Hz, C-sp^2), 138.6 (ArC), 144.2 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2), 158.6 (ArC) ppm. HRMS (ESI): MNa^+, found 448.1649. $C_{24}H_{28}NNaO_4P$ requires 448.1648.

Dimethyl 3-Benzyl-2-(4-fluorophenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10d). Yellowish oil. Yield 0.32 g, 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.25−2.33 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.38−2.41 (2H, m, $\underline{CH_2}CH_2CH_2$), 2.82−2.86 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.52 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.64 (2H, br. s, CH_2), 6.89−6.91 (2H, m, ArH), 7.01−7.05 (2H, m, ArH), 7.12−7.21 (5H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8 (CH_2), 26.6 (CH_2), 30.4 (CH_2), 32.3 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.6 Hz, OCH_3), 110.4 (d, $^1J_{C,P}$ = 234.6 Hz, C-sp^2), 115.2 (d, $J_{C,F}$ = 22.6 Hz, ArC), 126.1 (ArC), 128.2 (ArC), 128.5 (ArC), 129.6 (d, $^3J_{C,P}$ = 14.2 Hz, C-sp^2), 130.5 (d, $^3J_{C,F}$ = 8.7 Hz, ArC), 131.7 (d, $^4J_{C,P}$ = 8.4 Hz, C-sp^2), 134.7 (d, $^4J_{C,F}$ = 3.1 Hz, ArC), 138.4 (ArC), 144.5 (d, $^2J_{C,P}$ = 17.3 Hz, C-sp^2), 162.2 (d, $^1J_{C,F}$ = 246.6 Hz, ArH) ppm. HRMS (ESI): MH^+, found 400.1473. $C_{22}H_{24}FNO_3P$ requires 400.1472.

Dimethyl 3-Benzyl-2-(4-chlorophenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10e). Yellowish oil. Yield 0.3 g, 73%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.25−2.32 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.37−2.40 (2H, m, $\underline{CH_2}CH_2CH_2$), 2.82−2.86 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.52 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.64 (2H, br. s, CH_2), 6.90−6.92 (2H, m, ArH), 7. Eleven (2H, d, ^3J = 8.8 Hz, ArH), 7.15−7.22 (3H, m, ArH), 7.32 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.8 (CH_2), 26.6 (CH_2), 30.4 (CH_2), 32.3 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.6 Hz, OCH_3), 110.3 (d, $^1J_{C,P}$ = 234.2 Hz, C-sp^2), 126.2 (ArC), 128.3 (ArC), 128.5 (ArC), 128.6 (ArC), 129.8 (d, $^3J_{C,P}$ = 14.1 Hz, C-sp^2), 130.1 (ArC), 131.5 (d, $^4J_{C,P}$ = 8.4 Hz, C-sp^2), 134.2 (ArC), 137.3 (ArC), 138.3 (ArC), 144.7 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2) ppm. HRMS (ESI): MH^+, found 416.1185. $C_{22}H_{24}ClNO_3P$ requires 416.1182.

Dimethyl 3-(4-Methylbenzyl)-2-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10f). Yellowish oil. Yield 0.23 g, 58%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26−2.31 (5H, m, $CH_2\underline{CH_2}CH_2$ and CH_3), 2.33−2.37 (2H, m, $\underline{CH_2}CH_2CH_2$), 2.83−2.87 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.49 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.60 (2H, br. s, CH_2), 6.82 (2H, d, ^3J = 8.0 Hz, ArH), 7. 00 (2H, d, ^3J = 7.6 Hz, ArH), 7.20−7.22 (2H, m, ArH), 7.37−7.39 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9 (CH_3), 24.8 (CH_2), 26.5 (CH_2), 30.3 (CH_2), 31.8 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 109.9 (d, $^1J_{C,P}$ = 234.7 Hz, C-sp^2), 128.3 (ArC), 128.3 (ArC), 128.4 (ArC), 128.7 (ArC), 128.8 (ArC), 129.2 (d, $^3J_{C,P}$ = 14.2 Hz, C-sp^2), 131.8 (d,, $^4J_{C,P}$ = 8.5 Hz, C-sp^2), 135.4 (ArC), 135.4 (ArC), 138.7 (ArC), 144.5 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2) ppm. HRMS (ESI): MNa^+, found 418.1541. $C_{23}H_{26}NNaO_3P$ requires 418.1543.

Dimethyl 2-(4-Methoxyphenyl)-3-(4-methylbenzyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10 g). Yellowish oil. Yield 0.32 g, 76%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.25−2.30 (5H, m, $CH_2\underline{CH_2}CH_2$ and CH_3), 2.33−2.37 (2H, m, $\underline{CH_2}CH_2CH_2$), 2.81−2.85 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.51 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.58 (2H, br. s, CH_2), 3.83 (3H, s, OCH_3), 6.83 (2H, d, ^3J = 8.0 Hz, ArH), 6.87 (2H, d, ^3J = 8.8 Hz, ArH), 7.01 (2H, d, ^3J = 8.0 Hz, ArH), 7.12 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9 (CH_3), 24.9 (CH_2), 26.6 (CH_2), 30.3 (CH_2), 31.8 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 55.3 (OCH_3), 110.0 (d, $^1J_{C,P}$ = 234.3 Hz, C-sp^2), 113.4 (ArC), 128.5 (ArC), 128.8 (ArC), 128.9 (ArC), 129.1 (ArC), 129.8 (ArC), 131.5 (ArC), 132.1 (d, $^4J_{C,P}$ = 8.5 Hz, C-sp^2), 135.5 (ArC), 144.3 (d, $^2J_{C,P}$ = 17.6 Hz, C-sp^2), 159.2 (ArC) ppm. HRMS (ESI): MNa^+, found 448.1643. $C_{24}H_{28}NNaO_4P$ requires 448.1648.

Dimethyl 3-(4-Ethylbenzyl)-2-(4-methoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10h). Yellowish oil. Yield 0.42 g, 96%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.19 (3H, t, ^3J = 7.6 Hz, CH_3), 2.23−2.30 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.35−2.38 (2H, m, $\underline{CH_2}CH_2CH_2$), 2.58 (2H, q, ^3J = 7.6 Hz, $\underline{CH_2}CH_3$), 2.81−2.85 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.50 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.59 (2H, br. s, CH_2), 3.83 (3H, s, OCH_3), 6.84−6.87 (4H, m, ArH), 7.03 (2H, d, ^3J = 8.4 Hz, ArH), 7.11 (2H, d, ^3J = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.6 (CH_3), 24.8 (CH_2), 26.6 (CH_2), 28.3 (CH_2), 30.3 (CH_2), 31.8 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 55.3 (OCH_3), 109.8 (d, $^1J_{C,P}$ = 235.1 Hz, C-sp^2), 113.4 (ArC), 127.6 (ArC), 128.5 (ArC), 129.0 (d, $^3J_{C,P}$ = 14.2 Hz, C-sp^2), 129.8 (ArC), 131.5 (ArC), 132.3 (d, $^4J_{C,P}$ = 8.6 Hz, C-sp^2), 135.8 (ArC), 141.9 (ArC), 144.4 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2), 159.2 (ArC) ppm. HRMS (ESI): MNa^+, found 462.1808. $C_{25}H_{30}NNaO_4P$ requires 462.1805.

Dimethyl 3-Pentyl-2-phenyl-2,4,5,6-tetrahydrocyclopenta-[*c*]pyrrol-1-ylphosphonate (10i). Yellowish oil. Yield 0.31 g, 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.79 (3H, t, ^3J = 7.2 Hz, $CH_2(CH_2)_3\underline{CH_3}$), 1.09−1.21 (4H, m, $CH_2CH_2\underline{(CH_2)_2}CH_3$), 1.42 (2H, quint, ^3J = 7.6 Hz, $CH_2\underline{CH_2}(CH_2)_2CH_3$), 2.27 (2H, t, ^3J = 7.6 Hz, $\underline{CH_2}CH_2(CH_2)_2CH_3$), 2.36 (2H, quint, ^3J = 7.2 Hz, $CH_2CH_2\underline{CH_2}$), 2.65 (2H, t, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_2$), 2.84 (2H, td, $^3J_{HH}$ = 6.8 Hz, $^4J_{HP}$ = 1.2 Hz, $CH_2CH_2\underline{CH_2}$), 3.48 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.26−7.28 (2H, m, ArH), 7.39−7.44 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8 (CH_3), 22.1 (CH_2), 25.1 (CH_2), 26.0 (CH_2), 26.5 (CH_2), 27.8 (CH_2), 30.4 (CH_2), 31.3 (CH_2), 51.9 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 109.3 (d, $^1J_{C,P}$ = 234.8 Hz, C-sp^2), 128.0 (d, $^3J_{C,P}$ = 14.4 Hz, C-sp^2), 128.2 (ArC), 128.3 (ArC), 128.6 (ArC), 133.6 (d, $^4J_{C,P}$ = 8.4 Hz, C-sp^2), 138.9 (ArC), 144.6 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2) ppm. HRMS (ESI): MNa^+, found 384.1697. $C_{20}H_{28}NNaO_3P$ requires 384.1699.

Dimethyl 2-(4-Methoxyphenyl)-3-pentyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10j). Yellowish oil. Yield 0.3 g, 78%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.80 (3H, t, ^3J = 6.8 Hz, $CH_2(CH_2)_3\underline{CH_3}$), 1.13−1.22 (4H, m, $CH_2CH_2\underline{(CH_2)_2}CH_3$), 1.42 (2H, quint, ^3J = 7.6 Hz, $CH_2\underline{CH_2}(CH_2)_2CH_3$), 2.26 (2H, t, ^3J = 8.0 Hz, $\underline{CH_2}CH_2(CH_2)_2CH_3$), 2.32 (2H, quint, ^3J = 7.2 Hz, $CH_2\underline{CH_2}CH_2$), 2.63 (2H, t, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_2$), 2.82−2.86 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.50 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.83 (3H, s, OCH_3), 6.91 (2H, d, ^3J = 8.8 Hz, ArH), 7.18 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8 (CH_3), 22.2 (CH_2), 25.2 (CH_2), 26.0 (CH_2), 26.5 (CH_2), 27.9 (CH_2), 30.4 (CH_2), 31.3 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 55.3 (OCH_3), 109.4 (d, $^1J_{C,P}$ = 235.0 Hz, C-sp^2), 113.4 (ArC), 127.8 (d, $^3J_{C,P}$ = 14.3 Hz, C-sp^2), 129.7 (ArC), 131.8 (ArC), 134.0 (d, $^4J_{C,P}$ = 8.4 Hz, C-sp^2), 144.3 (d, $^2J_{C,P}$ = 17.6 Hz, C-sp^2), 159.1 (ArC) ppm. HRMS (ESI): MNa^+, found 414.1806. $C_{21}H_{30}NNaO_4P$ requires 414.1805.

Dimethyl 2-(4-Fluorophenyl)-3-pentyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10k). Yellowish oil. Yield 0.3 g, 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81 (3H, t, ^3J = 6.8 Hz, $CH_2(CH_2)_3\underline{CH_3}$), 1.10−1.22 (4H, m, $CH_2CH_2\underline{(CH_2)_2}CH_3$), 1.42 (2H, quint, ^3J = 7.6 Hz, $CH_2\underline{CH_2}(CH_2)_2CH_3$), 2.26 (2H, t, ^3J = 7.6 Hz, $\underline{CH_2}CH_2(CH_2)_2CH_3$), 2.33 (2H, quint, ^3J = 6.8 Hz, $CH_2\underline{CH_2}CH_2$), 2.63 (2H, t, ^3J = 6.8 Hz,

$CH_2CH_2CH_2$), 2.83 (2H, td, $^3J_{HH}$ = 7.0 Hz, $^4J_{HP}$ = 1.6 Hz, $CH_2CH_2CH_2$), 3.52 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.07−7.12 (2H, m, ArH), 7.23−7.26 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8 (CH_3), 22.2 (CH_2), 25.1 (CH_2), 26.0 (CH_2), 26.5 (CH_2), 27.9 (CH_2), 30.4 (CH_2), 31.4 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 109.4 (d, $^1J_{C,P}$ = 235.8 Hz, C-sp^2), 115.3 (d, $^2J_{C,F}$ = 22.6 Hz, ArC), 128.3 (d, $^3J_{C,P}$ = 14.3 Hz, C-sp^2), 130.4 (d, $^3J_{C,F}$ = 8.7 Hz, ArC), 133.9 (d, $^4J_{C,P}$ = 8.2 Hz, C-sp^2), 134.9 (d, $^4J_{C,F}$ = 3.1 Hz, ArC), 144.8 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2), 162.1 (d, $^1J_{C,F}$ = 246.5 Hz, ArC) ppm. HRMS (ESI): MH$^+$, found 380.1791. $C_{20}H_{28}FNO_3P$ requires 380.1785.

Dimethyl 2-(4-Chlorophenyl)-3-pentyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10l). Yellowish oil. Yield 0.3 g, 76%. ^1H NMR (400 MHz, $CDCl_3$): δ 0.81 (3H, t, ^3J = 6.8 Hz, $CH_2(CH_2)_3CH_3$), 1.12−1.21 (4H, m, $CH_2CH_2(CH_2)_2CH_3$), 1.42 (2H, quint, ^3J = 7.6 Hz, $CH_2CH_2(CH_2)_2CH_3$), 2.26 (2H, t, ^3J = 7.6 Hz, $CH_2CH_2(CH_2)_2CH_3$), 2.33 (2H, quint, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.64 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.83 (2H, td, $^3J_{HH}$ = 7.0 Hz, $^4J_{HP}$ = 1.6 Hz, $CH_2CH_2CH_2$), 3.52 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.21 (2H, d, ^3J = 8.8 Hz, ArH), 7.39 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8 (CH_3), 22.2 (CH_2), 25.1 (CH_2), 26.0 (CH_2), 26.5 (CH_2), 27.9 (CH_2), 30.4 (CH_2), 31.4 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.6 Hz, OCH_3), 109.4 (d, $^1J_{C,P}$ = 235.0 Hz, C-sp^2), 128.5 (d, $^3J_{C,P}$ = 14.2 Hz, C-sp^2), 128.6 (ArC), 130.0 (ArC), 133.7 (d, $^4J_{C,P}$ = 8.2 Hz, C-sp^2),134.1 (ArC), 137.5 (ArC), 144.9 (d, $^2J_{C,P}$ = 17.4 Hz, C-sp^2) ppm. HRMS (ESI): MH$^+$, found 396.1500. $C_{20}H_{28}ClNO_3P$ requires 396.1490.

Dimethyl 3-Hexyl-2-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]-pyrrol-1-ylphosphonate (10m). Yellowish oil. Yield 0.3 g, 80%. ^1H NMR (400 MHz, $CDCl_3$): δ 0.82 (3H, t, ^3J = 6.8 Hz, $CH_2(CH_2)_4CH_3$), 1.14−1.21 (6H, m, $CH_2CH_2(CH_2)_3CH_3$), 1.34−1.46 (2H, m, $CH_2CH_2(CH_2)_3CH_3$), 2.28 (2H, t, ^3J = 8.0 Hz, $CH_2(CH_2)_4CH_3$), 2.34 (2H, quint, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.65 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.83−2.87 (2H, m, $CH_2CH_2CH_2$), 3.48 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.26−7.28 (2H, m, ArH), 7.39−7.43 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (CH_3), 22.4 (CH_2), 25.2 (CH_2), 26.1 (CH_2), 26.5 (CH_2), 28.2 (CH_2), 28.9 (CH_2), 30.5 (CH_2), 31.3 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.6 Hz, OCH_3), 109.2 (d, $^1J_{C,P}$ = 235.2 Hz, C-sp^2), 128.1 (d, $^3J_{C,P}$ = 14.3 Hz, C-sp^2), 128.2 (ArC), 128.4 (ArC), 128.7 (ArC), 133.8 (d, $^4J_{C,P}$ = 8.4 Hz, C-sp^2), 139.0 (ArC), 144.8 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2) ppm. HRMS (ESI): MNa$^+$, found 398.1862. $C_{21}H_{30}NNaO_3P$ requires 398.1856.

Dimethyl 3-Hexyl-2-(4-methoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10n). Yellowish oil. Yield 0.26 g, 63%. ^1H NMR (400 MHz, $CDCl_3$): δ 0.82 (3H, t, ^3J = 6.8 Hz, $CH_2(CH_2)_4CH_3$), 1.14−1.24 (6H, m, $CH_2CH_2(CH_2)_2CH_3$), 1.37−1.45 (2H, m, $CH_2CH_2(CH_2)_3CH_3$), 2.26 (2H, t, ^3J = 7.6 Hz, $CH_2(CH_2)_4CH_3$), 2.32 (2H, quint, ^3J = 6.8 Hz, $CH_2CH_2CH_2$), 2.63 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.81−2.85 (2H, m, $CH_2CH_2CH_2$), 3.50 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.83 (3H, s, OCH_3), 6.91 (2H, d, ^3J = 8.8 Hz, ArH), 7.18 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (CH_3), 22.4 (CH_2), 25.1 (CH_2), 26.0 (CH_2), 26.5 (CH_2), 28.2 (CH_2), 28.9 (CH_2), 30.4 (CH_2), 31.3 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.4 Hz, OCH_3), 55.3 (OCH_3), 109.3 (d, $^1J_{C,P}$ = 235.0 Hz, C-sp^2), 113.4 (ArC), 127.8 (d, $^3J_{C,P}$ = 14.4 Hz, C-sp^2), 129.7 (ArC), 131.7 (ArC), 134.0 (d, $^4J_{C,P}$ = 8.4 Hz, C-sp^2), 144.4 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2) ppm. HRMS (ESI): MNa$^+$, found 428.1963. $C_{22}H_{32}NNaO_4P$ requires 428.1961.

Dimethyl 3-(Cyclopropylmethyl)-2-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10o). Yellowish oil. Yield 0.26 g, 76%. ^1H NMR (300 MHz, $CDCl_3$): δ −0.04−0.00 (2H, m, $CH(CH_2)_2$), 0.38−0.43 (2H, m, $CH(CH_2)_2$), 0.76−0.89 (1H, m, $CH(CH_2)_2$), 2.18 (2H, d, ^3J = 6.8 Hz, CH_2), 2.31−2.38 (2H, m, $CH_2CH_2CH_2$), 2.73 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.87 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 3.48 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.26−7.28 (2H, m, ArH), 7.38−7.42 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.0 (CH_2), 9.6 (CH), 25.5 (CH_2), 26.5 (CH_2), 30.4 (CH_2), 31.4 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 109.5 (d, $^1J_{C,P}$ = 234.3 Hz, C-sp^2), 128.2 (ArC), 128.4 (ArC), 128.5 (C-sp^2), 128.7 (ArC), 133.2 (d, $^4J_{C,P}$ = 8.4 Hz, C-sp^2), 138.9 (ArC), 144.7 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2). HRMS (ESI): MNa$^+$, found 368.1387. $C_{19}H_{24}NNaO_3P$ requires 368.1386.

Dimethyl 3-(Cyclopropylmethyl)-2-(4-methoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10p). Yellowish oil. Yield 0.26 g, 76%. ^1H NMR (300 MHz, $CDCl_3$): δ −0.03−0.00 (2H, m, $CH(CH_2)_2$), 0.39−0.43 (2H, m, $CH(CH_2)_2$), 0.76−0.86 (1H, m, $CH(CH_2)_2$), 2.17 (2H, d, ^3J = 7.2 Hz, CH_2), 2.33 (2H, quint, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.71 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.85 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 3.50 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.82 (3H, s, OCH_3), 6.90 (2H, d, ^3J = 8.4 Hz, ArH), 7.18 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.0 (CH_2), 9.7 (CH), 25.5 (CH_2), 26.5 (CH_2), 30.3 (CH_2), 31.3 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 55.2 (OCH_3), 109.6 (d, $^1J_{C,P}$ = 234.3 Hz, C-sp^2), 113.4 (ArC), 128.0 (d, $^3J_{C,P}$ = 14.2 Hz, C-sp^2), 129.7 (ArC), 131.7 (ArC), 133.5 (d, $^4J_{C,P}$ = 8.3 Hz, C-sp^2), 144.4 (d, $^2J_{C,P}$ = 17.7 Hz, C-sp^2), 159.1 (ArC). HRMS (ESI): MNa$^+$, found 398.1494. $C_{20}H_{26}NNaO_4P$ requires 398.1492.

Dimethyl 3-(Cyclopropylmethyl)-2-(4-ethoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (10r). Yellowish oil. Yield 0.23 g, 59%. ^1H NMR (300 MHz, $CDCl_3$): δ −0.03−0.00 (2H, m, $CH(CH_2)_2$), 0.38−0.43 (2H, m, $CH(CH_2)_2$), 0.76−0.86 (1H, m, $CH(CH_2)_2$), 1.42 (3H, t, ^3J = 7.2 Hz, OCH_2CH_3), 2.17 (2H, d, ^3J = 7.2 Hz, CH_2), 2.38 (2H, quint, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.71 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.85 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 3.50 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 4.04 (3H, q, ^3J = 7.2 Hz, OCH_2CH_3), 6.88 (2H, d, ^3J = 8.8 Hz, ArH), 7.16 (2H, d, ^3J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.0 (CH_2), 9.7 (CH), 14.7 (CH_3), 25.5 (CH_2), 26.5 (CH_2), 30.3 (CH_2), 31.4 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 63.5 (OCH_3), 109.6 (d, $^1J_{C,P}$ = 234.6 Hz, C-sp^2), 113.9, 128.0 (d, $^3J_{C,P}$ = 14.3 Hz, C-sp^2), 129.7 (ArC), 131.6 (ArC), 133.5 (d, $^4J_{C,P}$ = 8.5 Hz, C-sp^2), 144.4 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2), 158.6 (ArC). HRMS (ESI): MNa$^+$, found 412.1646. $C_{21}H_{28}NNaO_4P$ requires 412.1648.

Dimethyl 3-Methyl-2-phenyl-2,4,5,6-tetrahydrocyclopenta-[*c*]pyrrol-1-ylphosphonate (10s). Yellowish oil. Yield 0.2 g, 66%. ^1H NMR (400 MHz, $CDCl_3$): δ 1.93 (3H, s, CH_3), 2.34 (2H, quint, ^3J = 6.8 Hz, $CH_2CH_2CH_2$), 2.60 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.86 (2H, td, $^3J_{H,H}$ = 7.2 Hz, $^4J_{H,P}$ = 1.2 Hz, $CH_2CH_2CH_2$), 3.49 (6H, d, $^3J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 7.26−7.28 (2H, m, ArH), 7.37−7.45 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.6 (CH_3), 24.4 (CH_2), 26.8 (CH_2), 30.4 (CH_2), 52.1 (d, $^2J_{C,P}$ = 5.5 Hz, OCH_3), 109.4 (d, $^1J_{C,P}$ = 235.1 Hz, C-sp^2), 128.2 (ArC), 128.4 (ArC), 128.5 (ArC), 128.8 (d, $^3J_{C,P}$ = 14.3 Hz, C-sp^2), 129.0 (d, $^4J_{C,P}$ = 8.8 Hz, C-sp^2), 139.0 (ArC), 144.6 (d, $^2J_{C,P}$ = 17.5 Hz, C-sp^2) ppm. HRMS (ESI): MH$^+$, found 306.1263. $C_{16}H_{21}NO_3P$ requires 306.1254.

Dimethyl 3-Benzyl-2-phenyl-2*H*-isoindol-1-ylphosphonate (11a). Light orange solid, mp 82−83 °C. Yield 0.28 g, 72%. ^1H NMR (400 MHz, $CDCl_3$): δ 3.53 (6H, d, $^3J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 4.14 (2H, s, CH_2), 6.82−6.85 (2H, m, ArH), 7.09−7.15 (5H, m, ArH), 7.22- 7.24 (1H, m, ArH), 7.37−7.49 (4H, m, ArH), 7.57−7.64 (4H, m, ArH), 7.56−7.61 (1H, m, ArH), 8.11 (1H, dt, J = 8.8; 0.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.1 (d, $^4J_{C,P}$ = 1.1 Hz, CH_2), 52.2 (d, $^2J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 106.5 (d, $^1J_{C,P}$ = 235.4 Hz, ArC), 119.7 (ArC), 120.3 (ArC), 121.7 (ArC), 123.3 (d, $^3J_{C,P}$ = 13.6 Hz, ArC), 125.0 (d, $^4J_{C,P}$ = 0.4 Hz, ArC), 126.3 (ArC), 128.1 (ArC), 128.2 (ArC), 128.3 (2 × ArC), 129.2 (ArC), 131.9 (d, $^2J_{C,P}$ = 8.6 Hz, ArC), 132.1 (d, $^2J_{C,P}$ = 18.2 Hz, ArC), 138.0 (ArC), 138.4 (d, $^5J_{C,P}$ = 0.7 Hz, ArC) ppm. HRMS (ESI): MH$^+$, found 392.1410. $C_{23}H_{23}NO_3P$ requires 392.1410.

Dimethyl 2,3-Diphenyl-1,2-dihydroisoquinolin-1-ylphosphonate (12a). Light orange solid, mp 128−129 °C. Yield 0.34 g, 86%. ^1H NMR (400 MHz, $CDCl_3$): δ 3.69 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.76 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.57 (1H, d, $^1J_{H,P}$ = 18.8 Hz, CH), 6.62 (1H, s, $C_{sp^2}H$), 6.91−6.95 (1H, m, ArH), 7.16−7.17 (3H, m, ArH), 7.21−7.28 (4H, m, ArH), 7.30−7.34 (4H, m, ArH), 7.65−7.67 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 53.1 (d, $^2J_{C,P}$ = 6.4 Hz, OCH_3), 53.2 (d, $^2J_{C,P}$ = 6.2 Hz, OCH_3), 63.8 (d, $^1J_{C,P}$ = 162.2 Hz, CH), 111.9 ($C_{sp^2}H$), 122.4 (ArC), 122.6 (d, $J_{C,P}$ = 2.0 Hz, ArC), 124.3 (d, $^2J_{C,P}$ = 2.6 Hz, ArC), 125.2 (d, $J_{C,P}$ = 3.1 Hz, ArC),

dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532−6553

126.6 (d, $J_{C,P}$ = 1.9 Hz, ArC), 127.1 (d, $J_{C,P}$ = 5.9 Hz, ArC), 127.5 (ArC), 128.0 (ArC), 128.3 (ArC), 128.3 (d, $^{2}J_{C,P}$ = 3.1 Hz, ArC), 128.5 (ArC), 132.8 (d, $^{3}J_{C,P}$ = 3.2 Hz, ArC), 137.0 (ArC), 142.0 (d, $J_{C,P}$ = 1.6 Hz, ArC), 147.4 (d, $^{3}J_{C,P}$ = 7.0 Hz, ArC) ppm. HRMS (ESI): MNa^{+}, found 414.1222. $C_{23}H_{22}NNaO_3P$ requires 414.1230.

Dimethyl 3-Benzyl-2-phenyl-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14a). Yellowish oil. Yield 0.32 g, 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.77−1.79 (4H, m, 2 × CH_2), 2.46 (2H, t, J = 5.6 Hz, CH_2), 2.88 (2H, t, J = 5.6 Hz, CH_2), 3.46 (6H, d, $^{3}J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.67 (2H, s, CH_2), 6.79−6.81 (2H, m, ArH), 7.07 (2H, dd, J = 8.2; 1.6 Hz, ArH), 7.10−7.16 (3H, m, ArH), 7.27−7.34 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8 (d, $^{3}J_{C,P}$ = 1.1 Hz, CH_2), 23.1 (CH_2), 23.3 (CH_2), 23.5 (CH_2), 30.6 (d, $^{4}J_{C,P}$ = 1.0 Hz, CH_2), 51.7 (d, $^{2}J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 112.9 (d, $^{1}J_{C,P}$ = 230.2 Hz, ArC), 118.7 (d, $^{3}J_{C,P}$ = 14.7 Hz, ArC), 125.8 (ArC), 128.0 (ArC), 128.1 (2 × ArC), 128.2 (ArC), 128.8 (ArC), 133.9 (d, $^{2}J_{C,P}$ = 19.1 Hz, ArC), 134.8 (d, $^{3}J_{C,P}$ = 9.8 Hz, ArC), 138.6 (ArC), 138.7 (ArC) ppm. HRMS (ESI): MNa^{+}, found 418.1548. $C_{23}H_{26}NNaO_3P$ requires 418.1543.

Dimethyl 3-Benzyl-2-(4-methoxyphenyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14b). Brownish solid, mp 108−109 °C. Yield 0.4 g, 95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.76−1.78 (4H, m, 2 × CH_2), 2.45 (2H, t, J = 5.6 Hz, CH_2), 2.86 (2H, t, J = 5.6 Hz, CH_2), 3.48 (6H, d, $^{3}J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.66 (2H, s, CH_2), 3.80 (3H, s, OCH_3), 6.79 (2H, d, J = 8.8 Hz, ArH), 6.81−6.83 (2H, m, ArH), 6.97 (3H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8 (d, $^{3}J_{C,P}$ = 1.0 Hz, CH_2), 23.2 (CH_2), 23.4 (CH_2), 23.6 (CH_2), 30.7 (d, $^{4}J_{C,P}$ = 1.0 Hz, CH_2), 51.8 (d, $^{2}J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 55.3 (OCH_3), 113.0 (d, $^{1}J_{C,P}$ = 230.3 Hz, ArC), 113.2 (ArC), 118.6 (d, $^{3}J_{C,P}$ = 14.8 Hz, ArC), 125.8 (ArC), 128.1 (2 × ArC), 129.8 (ArC), 131.3 (ArC), 133.7 (d, $^{2}J_{C,P}$ = 19.2 Hz, ArC), 135.2 (d, $^{3}J_{C,P}$ = 9.9 Hz, ArC), 138.9 (ArC), 159.2 (ArC) ppm. HRMS (ESI): MNa^{+}, found 448.1645. $C_{24}H_{28}NNaO_4P$ requires 448.1648.

Dimethyl 3-Benzyl-2-(4-fluorophenyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14c). Yellowish solid, mp 95−96 °C. Yield 0.23 g, 56%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.77−1.79 (4H, m, 2 × CH_2), 2.48−2.49 (2H, m, CH_2), 2.85−2.86 (2H, m, CH_2), 3.49 (6H, d, $^{3}J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.66 (2H, s, CH_2), 6.78−6.80 (2H, m, ArH), 6.93−7.01 (4H, m, ArH), 7.11−7.17 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8 (d, $^{3}J_{C,P}$ = 1.0 Hz, CH_2), 23.1 (CH_2), 23.3 (CH_2), 23.5 (CH_2), 30.6 (d, $^{4}J_{C,P}$ = 1.1 Hz, CH_2), 51.8 (d, $^{2}J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 113.2 (d, $^{1}J_{C,P}$ = 230.2 Hz, ArC), 115.0 (d, $^{2}J_{C,F}$ = 22.5 Hz, ArC), 119.0 (d, $^{3}J_{C,P}$ = 14.7 Hz, ArC), 126.0 (ArC), 128.0 (ArC), 128.2 (ArC), 130.5 (d, $^{3}J_{C,F}$ = 8.7 Hz, ArC), 133.9 (d, $^{2}J_{C,P}$ = 19.0 Hz, ArC), 134.6 (d, $^{4}J_{C,P}$ = 3.0 Hz, ArC), 135.0 (d, $^{3}J_{C,P}$ = 9.8 Hz, ArC), 138.6 (ArC), 162.1 (d, $^{1}J_{C,F}$ = 246.5 Hz, ArC) ppm. HRMS (ESI): MNa^{+}, found 436.1452. $C_{23}H_{25}FNNaO_3P$ requires 436.1448.

Dimethyl 3-Benzyl-2-(4-chlorophenyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14d). Yellowish oil. Yield 0.29 g, 68%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.77−1.78 (4H, m, 2 × CH_2), 2.46−2.48 (2H, m, CH_2), 2.84−2.86 (2H, m, CH_2), 3.49 (6H, d, $^{3}J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 3.66 (2H, s, CH_2), 6.78−6.80 (2H, m, ArH), 6.97 (2H, d, J = 8.4 Hz, ArH), 7.10−7.18 (3H, m, ArH), 7.25 (2H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7 (d, $^{3}J_{C,P}$ = 1.1 Hz, CH_2), 23.1 (CH_2), 23.3 (CH_2), 23.4 (CH_2), 30.6 (d, $^{4}J_{C,P}$ = 1.0 Hz, CH_2), 51.9 (d, $^{2}J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 113.1 (d, $^{1}J_{C,P}$ = 229.9 Hz, ArC), 119.1 (d, $^{3}J_{C,P}$ = 14.6 Hz, ArC), 126.0 (ArC), 127.9 (ArC), 128.2 (ArC), 128.3 (ArC), 130.1 (ArC), 134.1 (d, $^{2}J_{C,P}$ = 18.9 Hz, ArC), 134.1 (ArC), 134.9 (d, $^{3}J_{C,P}$ = 9.7 Hz, ArC), 137.2 (ArC), 138.5 (ArC) ppm. HRMS (ESI): MNa^{+}, found 452.1157. $C_{23}H_{25}ClNNaO_3P$ requires 452.1153.

Dimethyl 3-(4-Methylbenzyl)-2-phenyl-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14e). Yellowish oil. Yield 0.38 g, 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.76−1.78 (4H, m, 2 × CH_2), 2.27 (3H, s, CH_3), 2.43−2.47 (2H, m, CH_2), 2.87−2.89 (2H, m, CH_2), 3.47 (6H, d, $^{3}J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.63 (2H, s, CH_2), 6.70 (2H, d, J = 8.0 Hz, ArH), 6.96 (2H, d, J = 8.0 Hz, ArH), 7.08−7.10 (2H, m, ArH), 7.28−7.35 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9 (CH_3), 21.8 (d, $^{3}J_{C,P}$ = 1.0 Hz, CH_2), 23.2 (CH_2), 23.4 (CH_2), 23.5 (CH_2), 30.2 (d,, $^{4}J_{C,P}$ = 1.1 Hz, CH_2), 51.8 (d, $^{2}J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 112.7 (d, $^{1}J_{C,P}$ = 230.7 Hz, ArC), 118.7 (d, $^{3}J_{C,P}$ = 14.9 Hz, ArC), 127.9 (ArC), 128.1 (ArC), 128.2 (ArC), 128.8 (2 × ArC), 134.0 (d, $^{2}J_{C,P}$ = 19.2 Hz, ArC), 135.2 (d, $^{3}J_{C,P}$ = 9.9 Hz, ArC), 135.3 (ArC), 135.7 (ArC), 138.7 (ArC) ppm. HRMS (ESI): MNa^{+}, found 432.1706. $C_{24}H_{28}NNaO_3P$ requires 432.1699.

Dimethyl 2-(4-Methoxyphenyl)-3-(4-methylbenzyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14e). Yellowish oil. Yield 0.35 g, 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.75−1.77 (4H, m, 2 × CH_2), 2.27 (3H, s, CH_3), 2.42−2.45 (2H, m, CH_2), 2.85−2.87 (2H, m, CH_2), 3.49 (6H, d, $^{3}J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 3.62 (2H, s, CH_2), 3.81 (3H, s, OCH_3), 6.72 (2H, d, J = 7.6 Hz, ArH), 6.80 (2H, d, J = 8.8 Hz, ArH), 6.96−7.00 (4H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9 (CH_3), 21.8 (d, $^{3}J_{C,P}$ = 1.1 Hz, CH_2), 23.2 (CH_2), 23.4 (CH_2), 23.6 (CH_2), 30.2 (d,, $^{4}J_{C,P}$ = 1.0 Hz, CH_2), 51.9 (d, $^{2}J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 55.3 (OCH_3), 112.6 (d, $^{1}J_{C,P}$ = 230.5 Hz, ArC), 113.2 (ArC), 118.5 (d, $^{3}J_{C,P}$ = 14.8 Hz, ArC), 127.9 (ArC), 128.8 (ArC), 129.8 (ArC), 131.3 (ArC), 133.9 (d, $^{2}J_{C,P}$ = 19.2 Hz, ArC), 135.3 (ArC), 135.5 (d, $^{3}J_{C,P}$ = 10.0 Hz, ArC), 135.8 (ArC), 159.2 (ArC) ppm. HRMS (ESI): MNa^{+}, found 462.1795. $C_{25}H_{30}NNaO_4P$ requires 462.1805.

Dimethyl 3-Butyl-2-phenyl-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14g). Yellowish oil. Yield 0.32 g, 89%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.72 (3H, t, J = 7.2 Hz, CH_3), 1.11 (2H, sexst., J = 7.2 Hz, CH_2), 1.22−1.26 (2H, m, CH_2), 1.74−1.77 (4H, m, 2 × CH_{2chex}), 2.27 (2H, t, J = 7.6 Hz, CH_2), 2.48 (2H, br. s, CH_{2chex}), 2.83 (2H, br. s, CH_{2chex}), 3.45 (6H, d, $^{3}J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.22−7.25 (2H, m, ArH), 7.39−7.41 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 21.7 (d, $^{3}J_{C,P}$ = 1.2 Hz, CH_2), 22.3 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 23.5 (CH_2), 24.3 (d, $^{4}J_{C,P}$ = 1.1 Hz, CH_2), 31.0 (CH_2), 51.8 (d, $^{2}J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 112.0 (d, $^{1}J_{C,P}$ = 230.8 Hz, ArC), 117.6 (d, $^{3}J_{C,P}$ = 14.8 Hz, ArC), 128.2 (2 × ArC), 128.8 (ArC), 134.0 (d, $^{2}J_{C,P}$ = 19.2 Hz, ArC), 137.4 (d, $^{3}J_{C,P}$ = 9.7 Hz, ArC), 138.9 (ArC) ppm. HRMS (ESI): MNa^{+}, found 384.1695. $C_{20}H_{28}NNaO_3P$ requires 384.1699.

Dimethyl 3-Butyl-2-(4-methoxyphenyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14h). Yellowish oil. Yield 0.39 g, 99%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.74 (3H, t, J = 7.2 Hz, CH_3), 1.13 (2H, sexst., J = 7.2 Hz, CH_2), 1.20−1.29 (2H, m, CH_2), 1.74−1.76 (4H, m, 2 × CH_{2chex}), 2.26 (2H, t, J = 7.6 Hz, CH_2), 2.47 (2H, br. s, CH_{2chex}), 2.82 (2H, br. s, CH_{2chex}), 3.48 (6H, d, $^{3}J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.83 (3H, s, OCH_3), 6.90 (2H, d, J = 8.8 Hz, ArH), 7.14 (2H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 21.7 (CH_2), 22.3 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 23.5 (CH_2), 24.3 (CH_2), 31.1 (CH_2), 51.8 (d, $^{2}J_{C,P}$ = 5.3 Hz, 2 × OCH_3), 55.3 (OCH_3), 111.8 (d, $^{1}J_{C,P}$ = 231.3 Hz, ArC), 113.3 (ArC), 117.4 (d, $^{3}J_{C,P}$ = 14.9 Hz, ArC), 129.7 (ArC), 131.6 (ArC), 133.8 (d, $^{2}J_{C,P}$ = 19.4 Hz, ArC), 137.7 (d, $^{3}J_{C,P}$ = 9.7 Hz, ArC), 159.1 (ArC) ppm. HRMS (ESI): MNa^{+}, found 414.1801. $C_{21}H_{30}NNaO_4P$ requires 414.1805.

Dimethyl 3-Butyl-2-(4-fluorophenyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14i). Yellowish oil. Yield 0.31 g, 81%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.73 (3H, t, J = 7.2 Hz, CH_3), 1.12 (2H, sexst., J = 7.2 Hz, CH_2), 1.21−1.25 (2H, m, CH_2), 1.72−1.76 (4H, m, 2 × CH_{2chex}), 2.25 (2H, t, J = 8.0 Hz, CH_2), 2.46 (2H, br. s, CH_{2chex}), 2.80 (2H, br. s, CH_{2chex}), 3.48 (6H, d, $^{3}J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.06−7.10 (2H, m, ArH), 7.19−7.22 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 21.7 (d, $^{3}J_{C,P}$ = 1.2 Hz, CH_2), 22.4 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 23.5 (CH_2), 24.4 (CH_2), 31.1 (CH_2), 51.9 (d, $^{2}J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 112.2 (d, $^{1}J_{C,P}$ = 230.8 Hz, ArC), 115.2 (d, $^{2}J_{C,F}$ = 22.6 Hz, ArC), 117.8 (d, $^{3}J_{C,P}$ = 14.8 Hz, ArC), 130.5 (d, $^{3}J_{C,F}$ = 8.6 Hz, ArC), 134.1 (d, $^{2}J_{C,P}$ = 19.2 Hz, ArC), 134.0 (d, $^{4}J_{C,P}$ = 3.2 Hz, ArC), 137.6 (d, $^{3}J_{C,P}$ = 9.5 Hz, ArC), 162.2 (d, $^{1}J_{C,F}$ = 246.4 Hz, ArC) ppm. HRMS (ESI): MNa^{+}, found 402.1610. $C_{20}H_{27}FNNaO_3P$ requires 402.1605.

Dimethyl 3-Pentyl-2-phenyl-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14j). Brownish oil. Yield 0.33 g, 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.75 (3H, t, J = 7.2 Hz, CH_3), 1.05−1.15 (4H, m, 2 × CH_2), 1.22−1.29 (2H, m, CH_2), 1.74−1.77 (4H, m, 2 × CH_{2chex}), 2.26 (2H, t, J = 7.6 Hz, CH_2), 2.48 (2H, br. s, CH_{2chex}), 2.83 (2H, br. s, CH_{2chex}), 3.45 (6H, d, $^{3}J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.22−

7.24 (2H, m, ArH), 7.39−7.41 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7 (CH_3), 21.7 (d, $^3J_{C,P}$ = 1.2 Hz, CH_2), 22.0 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 23.5 (CH_2), 24.6 (d, $J_{C,P}$ = 0.9 Hz, CH_2), 28.4 (CH_2), 31.3 (CH_2), 51.7 (d, $^2J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 112.0 (d, $^1J_{C,P}$ = 231.0 Hz, ArC), 117.6 (d, $^3J_{C,P}$ = 14.9 Hz, ArC), 128.2 (2 × ArC), 128.8 (ArC), 134.0 (d, $^2J_{C,P}$ = 19.3 Hz, ArC), 137.4 (d, $^3J_{C,P}$ = 9.7 Hz, ArC), 138.9 (ArC) ppm. HRMS (ESI): MNa^+, found 398.1845. $C_{21}H_{30}NNaO_3P$ requires 398.1856.

Dimethyl 2-(4-Methoxyphenyl)-3-pentyl-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14k). Light brown oil. Yield 0.33 g, 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.77 (3H, t, J = 7.2 Hz, CH_3), 1.08−1.15 (4H, m, 2 × CH_2), 1.22−1.30 (2H, m, CH_2), 1.75 (4H, br. s, 2 × CH_{2chex}), 2.25 (2H, t, J = 7.6 Hz, CH_2), 2.46 (2H, br. s, CH_{2chex}), 2.82 (2H, br. s, CH_{2chex}), 3.47 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.83 (3H, s, OCH_3), 6.90 (2H, d, J = 8.8 Hz, ArH), 7.14 (2H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7 (CH_3), 21.7 (d, $^3J_{C,P}$ = 0.9 Hz, CH_2), 22.1 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 23.5 (CH_2), 24.6 (d, $^4J_{C,P}$ = 0.7 Hz, CH_2), 28.5 (CH_2), 31.4 (CH_2), 51.8 (d, $^2J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 55.3 (OCH_3), 112.0 (d, $^1J_{C,P}$ = 231.1 Hz, ArC), 113.3 (ArC), 117.4 (d, $^3J_{C,P}$ = 14.8 Hz, ArC), 129.7 (ArC), 131.6 (ArC), 133.8 (d, $^2J_{C,P}$ = 19.3 Hz, ArC), 137.6 (d, $^3J_{C,P}$ = 9.7 Hz, ArC), 159.1 (ArC) ppm. HRMS (ESI): MNa^+, found 428.1969. $C_{22}H_{32}NNaO_4P$ requires 428.1961.

Dimethyl 3-(Cyclopropylmethyl)-2-phenyl-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14l). Yellowish oil. Yield 0.3 g, 83%. ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.16 (2H, q, J = 4.8 Hz, $CH(CH_2)_2$), 0.26−0.30 (2H, m, $CH(CH_2)_2$), 0.57−0.67 (1H, m, $CH(CH_2)_2$), 1.76 (4H, t, J = 3.2 Hz, 2 × CH_2), 2.21 (2H, d, J = 6.8 Hz, CH_2), 2.52 (2H, br. s, CH_2), 2.85 (2H, br. s, CH_2), 3.45 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.24−7.25 (2H, m, ArH), 7.37−7.41 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.8 ($CH(CH_2)_2$), 10.2 ($CH(CH_2)_2$), 21.9 (d, $^3J_{C,P}$ = 1.1 Hz, CH_{2chex}), 23.1 (CH_{2chex}), 23.4 (2 × CH_{2chex}), 29.4 (d, $^4J_{C,P}$ = 1.60 Hz, CH_2), 51.7 (d, $^2J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 112.3 (d, $^1J_{C,P}$ = 230.4 Hz, ArC), 117.7 (d, $^3J_{C,P}$ = 14.8 Hz, ArC), 128.1 (ArC), 128.2 (ArC), 128.9 (ArC), 133.9 (d, $^2J_{C,P}$ = 19.3 Hz, ArC), 136.9 (d, $^3J_{C,P}$ = 9.5 Hz, ArC), 139.0 (ArC) ppm. HRMS (ESI): MNa^+, found 382.1541. $C_{20}H_{26}NNaO_3P$ requires 382.1543.

Dimethyl 3-(Cyclopropylmethyl)-2-(4-methoxyphenyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14m). Yellowish oil. Yield 0.36 g, 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.15 to −0.11 (2H, m, $CH(CH_2)_2$), 0.27−0.31 (2H, m, $CH(CH_2)_2$), 0.61−0.65 (1H, m, $CH(CH_2)_2$), 1.75 (4H, br. s, 2 × CH_2), 2.19 (2H, d, J = 6.8 Hz, CH_2), 2.51 (2H, br. s, CH_2), 2.83 (2H, br. s, CH_2), 3.47 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.82 (3H, s, OCH_3), 6.89 (2H, d, J = 8.8 Hz, ArH), 7.15 (2H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.8 ($CH(CH_2)_2$), 10.3 ($CH(CH_2)_2$), 21.9 (d, $^3J_{C,P}$ = 1.0 Hz, CH_{2chex}), 23.1 (CH_{2chex}), 23.4 (CH_{2chex}), 23.5 (CH_{2chex}), 29.5 (d, $^4J_{C,P}$ = 0.7 Hz, CH_2), 51.7 (d, $^2J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 55.2 (OCH_3), 112.2 (d, $^1J_{C,P}$ = 230.8 Hz, ArC), 113.2 (ArC), 117.5 (d, $^3J_{C,P}$ = 14.8 Hz, ArC), 129.9 (ArC), 131.6 (ArC), 133.8 (d, $^2J_{C,P}$ = 19.4 Hz, ArC), 137.3 (d, $^3J_{C,P}$ = 9.6 Hz, ArC), 159.2 (ArC) ppm. HRMS (ESI): MNa^+, found 412.1650. $C_{21}H_{28}NNaO_4P$ requires 412.1648.

Dimethyl 2-(4-Chlorophenyl)-3-(cyclopropylmethyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (14n). Yellowish oil. Yield 0.36 g, 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ −0.15 to −0.11 (2H, m, $CH(CH_2)_2$), 0.28−0.33 (2H, m, $CH(CH_2)_2$), 0.55−0.65 (1H, m, $CH(CH_2)_2$), 1.74−1.76 (4H, m, 2 × CH_2), 2.20 (2H, d, J = 6.8 Hz, CH_2), 2.51 (2H, br. s, CH_2), 2.82 (2H, br. s, CH_2), 3.49 (6H, d, $^3J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 7.19 (2H, d, J = 8.8 Hz, ArH), 7.37 (2H, d, J = 8.4 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.9 ($CH(CH_2)_2$), 10.3 ($CH(CH_2)_2$), 21.9 (d, $^3J_{C,P}$ = 1.2 Hz, CH_{2chex}), 23.1 (CH_{2chex}), 23.3 (CH_{2chex}), 23.4 (CH_{2chex}), 29.4 (d, $^4J_{C,P}$ = 1.0 Hz, CH_2), 51.8 (d, $^2J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 112.5 (d, $^1J_{C,P}$ = 230.3 Hz, ArC), 118.1 (d, $^3J_{C,P}$ = 14.8 Hz, ArC), 128.4 (ArC), 130.3 (ArC), 134.2 (d, $^2J_{C,P}$ = 20.0 Hz, ArC), 134.2 (ArC), 137.0 (d, $^3J_{C,P}$ = 9.4 Hz, ArC), 137.6 (ArC) ppm. HRMS (ESI): MNa^+, found 416.1161. $C_{20}H_{25}ClNNaO_3P$ requires 416.1153.

General Procedure for the Preparation of Compounds 13 and 15−18. To a cooled solution of the corresponding acetylenic α-anilinomethylphosphonate **7**−**9** (1 mmol) in dry chloroform (5 mL) was added molecular iodine (0.254 g, 1 mmol) at 0 °C, together with phenyliodine diacetate (0.644 g, 2 mmol). The resulting stirring solution was allowed to warm to room temperature. When the completion of the reaction was observed by TLC (after 0.5−1 h), the solution was quenched with aqueous sodium thiosulfate. The organic layer was separated, washed with aqueous sodium thiosulfate (2 × 20 mL) and then with water (2 × 20 mL), and dried over anhydrous Na_2SO_4. After the evaporation of solvent under reduced pressure, the residue was purified by flash column chromatography eluting with hexane−ethyl acetate mixtures.

Dimethyl 3-Benzoyl-2-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13a). Yellowish oil. Yield 0.35 g, 89%. IR (KBr): υ_{max} 1644 (C═O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.21−2.31 (2H, m, $CH_2CH_2CH_2$), 2.42 (2H, t, ^3J = 6.9 Hz, $CH_2CH_2CH_2$), 2.89 (2H, td, $^3J_{H,H}$ = 7.3 Hz, $^4J_{H,P}$ = 1.5 Hz, $CH_2CH_2CH_2$), 3.53 (6H, d, $^3J_{H,P}$ = 11.4 Hz, 2 × OCH_3), 7.35−7.38 (5H, m, ArH), 7.40−7.44 (2H, m, ArH), 7.49−7.54 (1H, m, ArH), 7.71−7.74 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.7 (CH_2), 27.7 (CH_2), 30.1 (CH_2), 52.4 (d, $^2J_{C,P}$ = 5.7 Hz, OCH_3), 119.7 (d, $^1J_{C,P}$ = 225.4 Hz, C-sp^2), 127.9 (ArC), 128.2 (ArC), 128.2 (2 × ArC), 129.0 (ArC), 130.2 (d, $^4J_{C,P}$ = 9.0 Hz, C-sp^2), 132.2 (ArC), 138.7 (ArC), 139.2 (d, $^3J_{C,P}$ = 13.8 Hz, C-sp^2), 139.6 (ArC), 143.4 (d, $^2J_{C,P}$ = 17.1 Hz, C-sp^2), 186.3 (C═O) ppm. HRMS (ESI): MNa^+, found 418.1176. $C_{22}H_{22}NNaO_4P$ requires 418.1179.

Dimethyl 3-Benzoyl-2-(4-methoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13b). Yellowish oil. Yield 0.28 g, 67%. IR (KBr): υ_{max} 1645 (C═O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.25 (2H, quint, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.40 (2H, t, ^3J = 7.6 Hz, $CH_2CH_2CH_2$), 2.87 (2H, td, $^3J_{H,H}$ = 7.2 Hz, $^4J_{H,P}$ = 1.2 Hz, $CH_2CH_2CH_2$), 3.56 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.80 (3H, s, OCH_3), 6.87 (2H, d, ^3J = 9.2 Hz, ArH), 7.28 (2H, d, ^3J = 8.8 Hz, ArH), 7.38−7.42 (2H, m, ArH), 7.49−7.53 (1H, m, ArH), 7.71−7.73 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.6 (CH_2), 27.7 (CH_2), 30.1 (CH_2), 52.4 (d, $^2J_{C,P}$ = 5.7 Hz, OCH_3), 55.2 (OCH_3), 113.3 (ArC), 119.8 (d, $^1J_{C,P}$ = 225.9 Hz, C-sp^2), 126.8 (ArC), 128.1 (ArC), 129.0 (ArC), 129.0 (ArC), 130.3 (d, $^4J_{C,P}$ = 8.8 Hz, C-sp^2), 132.2 (ArC), 138.8 (ArC), 138.9 (d, $^3J_{C,P}$ = 14.0 Hz, C-sp^2), 143.0 (d, $^2J_{C,P}$ = 17.0 Hz, C-sp^2), 159.1 (ArC), 186.3 (C═O) ppm. HRMS (ESI): MNa^+, found 448.1287. $C_{23}H_{24}NNaO_5P$ requires 448.1284.

Dimethyl 3-Benzoyl-2-(4-ethoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13c). Yellowish oil. Yield 0.31 g, 70%. IR (KBr): υ_{max} 1643 (C═O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (3H, t, ^3J = 6.8 Hz, OCH_2CH_3), 2.25 (2H, quint, ^3J = 6.8 Hz, $CH_2CH_2CH_2$), 2.40 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.87 (2H, td, $^3J_{H,H}$ = 7.6 Hz, $^4J_{H,P}$ = 1.2 Hz, $CH_2CH_2CH_2$), 3.55 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 4.02 (2H, q, ^3J = 7.2 Hz, OCH_2CH_3), 6.86 (2H, d, ^3J = 8.8 Hz, ArH), 7.26 (2H, d, ^3J = 9.2 Hz, ArH), 7.38−7.42 (2H, m, ArH), 7.49−7.53 (1H, m, ArH), 7.71−7.77 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.7 (OCH_2CH_3), 26.7 (CH_2), 27.7 (CH_2), 30.1 (CH_2), 52.4 (d, $^2J_{C,P}$ = 5.7 Hz, OCH_3), 63.4 (OCH_2CH_3), 113.8 (ArC), 119.8 (d, $^1J_{C,P}$ = 226.1 Hz, C-sp^2), 128.1 (ArC), 129.0 (ArC), 129.0 (ArC), 130.3 (d, $^4J_{C,P}$ = 8.8 Hz, C-sp^2), 132.2 (ArC), 136.3 (ArC), 138.8 (ArC), 139.0 (d, $^3J_{CP}$ = 13.2 Hz, C-sp^2), 143.0 (d, $^2J_{C,P}$ = 17.0 Hz, C-sp^2), 158.6 (ArC), 186.3 (C═O) ppm. HRMS (ESI): MNa^+, found 462.1439. $C_{24}H_{26}NNaO_5P$ requires 462.1441.

Dimethyl 3-Benzoyl-2-(4-fluorophenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13d). Yellowish oil. Yield 0.24 g, 58%. IR (KBr): υ_{max} 1640 (C═O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (2H, quint, ^3J = 6.8 Hz, $CH_2CH_2CH_2$), 2.41 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2CH_2$), 2.87 (2H, td, $^3J_{H,H}$ = 7.2 Hz, $^4J_{H,P}$ = 1.2 Hz, $CH_2CH_2CH_2$), 3.57 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.06 (2H, t, ^3J = 8.4 Hz, ArH), 7.33−7.36 (2H, m, ArH), 7.42 (2H, t, ^3J = 7.6 Hz, ArH), 7.53 (1H, t, ^3J = 8.8 Hz, ArH), 7.71−7.73 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.8 (CH_2), 27.9 (CH_2), 30.3 (CH_2), 52.6 (d, $^2J_{C,P}$ = 6 Hz, OCH_3), 115.3 (d, $^2J_{C,F}$ = 23 Hz, ArC), 120.0 (d, $^1J_{C,P}$ = 226 Hz, C-sp^2), 128.4 (ArC), 129.2 (ArC), 129.9 (d, $^3J_{C,F}$ = 8 Hz, ArC), 130.4 (d, $^4J_{C,P}$ = 9 Hz, C-sp^2), 132.5 (ArC), 135.7 (d, $^4J_{C,F}$ = 4 Hz, ArC), 138.8 (ArC),

139.5 (d, $^3J_{C,P}$ = 14 Hz, C-sp^2), 143.5 (d, $^2J_{C,P}$ = 17 Hz, C-sp^2), 162.3 (d, $^1J_{C,F}$ = 246 Hz, ArH), 186.4 (C=O) ppm. HRMS (ESI): MNa^+, found 436.1077. $C_{22}H_{21}FNNaO_4P$ requires 436.1084.

Dimethyl 3-Benzoyl-2-(4-chlorophenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13e). Yellow solid, mp 108−109 °C. Yield 0.22 g, 51%. IR (KBr): υ_{max} 1641 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (2H, quint, ^3J = 7.2 Hz, $CH_2\underline{CH_2}CH_2$), 2.41 (2H, t, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_2$), 2.87 (2H, td, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,P}$ = 1.6 Hz, $CH_2CH_2\underline{CH_2}$), 3.58 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.29−7.36 (4H, m, ArH), 7.42 (2H, t, ^3J = 7.6 Hz, ArH), 7.53 (2H, t, ^3J = 7.2 Hz, ArH), 7.71−7.73 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.7 (CH_2), 27.9 (CH_2), 30.2 (CH_2), 52.7 (d, $^2J_{C,P}$ = 5.7 Hz, OCH_3), 119.9 (d, $^1J_{C,P}$ = 225.4 Hz, C-sp^2), 128.4 (ArC), 128.6 (ArC), 129.1 (ArC), 129.4 (ArC), 130.3 (d, $^4J_{C,P}$ = 8.5 Hz, C-sp^2), 132.6 (ArC), 134.2 (ArC), 138.2 (ArC), 138.7 (ArC), 139.7 (d, $^3J_{C,P}$ = 13.9 Hz, C-sp^2), 143.8 (d, $^2J_{C,P}$ = 16.8 Hz, C-sp^2), 186.3 (C=O) ppm. HRMS (ESI): MNa^+, found 452.0786. $C_{22}H_{21}ClNNaO_4P$ requires 452.0789.

Dimethyl 2-(4-Methoxyphenyl)-3-(4-methylbenzoyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13g). Yellowish oil. Yield 0.25 g, 56%. IR (KBr): υ_{max} 1639 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (2H, quint, ^3J = 7.2 Hz, $CH_2\underline{CH_2}CH_2$), 2.39 (3H, s, CH_3), 2.43 (2H, t, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_2$), 2.85−2.89 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.55 (6H, d, $^3J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 6.87 (2H, d, ^3J = 8.8 Hz, ArH), 7.21 (2H, d, ^3J = 8.0 Hz, ArH), 7.28 (2H, d, ^3J = 9.2 Hz, ArH), 7.65 (2H, d, ^3J = 8.0 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6 (CH_3), 26.7 (CH_2), 27.7 (CH_2), 30.1 (CH_2), 52.4 (d, $^2J_{C,P}$ = 5.7 Hz, OCH_3), 55.2 (OCH_3), 113.2 (ArH), 119.4 (d, $^1J_{C,P}$ = 226.1 Hz, C-sp^2), 128.9 (ArC), 129.0 (ArC), 129.3 (ArC), 130.6 (d, $^4J_{C,P}$ = 8.8 Hz, C-sp^2), 132.4 (ArC), 136.1 (ArC), 138.3 (d, $^3J_{C,P}$ = 14.0 Hz, C-sp^2), 143.0 (ArC), 143.0 (d, $^2J_{C,P}$ = 17.0 Hz, C-sp^2), 159.1 (ArC), 186.1 (C=O) ppm. HRMS (ESI): MNa^+, found 462.1436. $C_{24}H_{26}NNaO_5P$ requires 462.1441.

Dimethyl 3-(4-Ethylbenzoyl)-2-(4-methoxyphenyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13h). Yellowish oil. Yield 0.24 g, 54%. IR (KBr): υ_{max} 1639 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (3H, t, ^3J = 7.6 Hz, $CH_2\underline{CH_3}$), 2.25 (2H, quint, ^3J = 7.2 Hz, $CH_2\underline{CH_2}CH_2$), 2.46 (2H, t, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_2$), 2.68 (2H, q, ^3J = 7.6 Hz, $\underline{CH_2}CH_3$), 2.87 (2H, t, ^3J = 7.2 Hz, $CH_2CH_2\underline{CH_2}$), 3.55 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 6.86 (2H, d, ^3J = 8.8 Hz, ArH), 7.23 (2H, d, ^3J = 8.0 Hz, ArH), 7.27 (2H, d, ^3J = 8.8 Hz, ArH), 7.67 (2H, d, ^3J = 8.4 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.1 (CH_3), 26.6 (CH_2), 27.7 (CH_2), 28.8 (CH_2), 30.1 (CH_2), 52.4 (d, $^2J_{C,P}$ = 5.7 Hz, OCH_3), 55.2 (OCH_3), 113.2 (ArC), 119.2 (d, $^1J_{C,P}$ = 226.4 Hz, C-sp^2), 127.6 (ArC), 128.9 (ArC), 129.4 (ArC), 130.6 (d, $^4J_{C,P}$ = 8.7 Hz, C-sp^2), 132.3 (ArC), 136.2 (ArC), 138.3 (d, $^3J_{C,P}$ = 14.0 Hz, C-sp^2), 143.0 (d, $^2J_{C,P}$ = 17.0 Hz, C-sp^2), 149.3 (ArC), 159.0 (ArC), 186.0 (C=O) ppm. HRMS (ESI): MNa^+, found 476.1592. $C_{25}H_{28}NNaO_5P$ requires 476.1597.

Dimethyl 2-(4-Chlorophenyl)-3-(4-ethylbenzoyl)-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13j). Yellowish oil. Yield 0.2 g, 44%. IR (KBr): υ_{max} 1637 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.25 (3H, t, ^3J = 7.6 Hz, $CH_2\underline{CH_3}$), 2.27 (2H, quint, ^3J = 7.2 Hz, $CH_2\underline{CH_2}CH_2$), 2.46 (2H, t, ^3J = 7.6 Hz, $\underline{CH_2}CH_2CH_2$), 2.69 (2H, q, ^3J = 7.6 Hz, $\underline{CH_2}CH_3$), 2.88 (2H, td, $^3J_{H,H}$ = 7.0 Hz, $^4J_{H,P}$ = 1.2 Hz, $CH_2CH_2\underline{CH_2}$), 3.57 (6H, d, $^3J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 7.24 (2H, d, ^3J = 8.4 Hz, ArH), 7.28−7.34 (4H, m, ArH), 7.67 (2H, d, ^3J = 8.0 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.5 (CH_2), 26.8 (CH_2), 27.9 (CH_2), 29.0 (CH_2), 30.3 (CH_2), 52.6 (d, $^2J_{C,P}$ = 5.8 Hz, OCH_3), 119.4 (d, $^1J_{C,P}$ = 225.7 Hz, C-sp^2), 127.9 (ArC), 128.5 (ArC), 129.4 (ArC), 129.5 (ArC), 130.6 (d, $^4J_{C,P}$ = 8.5 Hz, C-sp^2), 134.1 (ArC), 136.1 (ArC), 138.3 (ArC), 139.1 (d, $^3J_{C,P}$ = 13.9 Hz, C-sp^2), 143.8 (d, $^2J_{C,P}$ = 16.0 Hz, C-sp^2), 149.7 (ArC), 186.1 (C=O) ppm. HRMS (ESI): MNa^+, found 480.1100. $C_{24}H_{25}ClNNaO_4P$ requires 480.1102.

Dimethyl 3-Formyl-2-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (13s). Yellowish oil. Yield 0.13 g, 42%. IR (KBr): υ_{max} 1666 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.41 (2H, quint, ^3J = 7.2 Hz, $CH_2\underline{CH_2}CH_2$), 2.85 (2H, td, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,P}$ = 1.2 Hz, $\underline{CH_2}CH_2CH_2$), 2.94 (2H, t, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_2$), 3.52 (6H, d, $^3J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 7.38−7.40 (2H, m, ArH), 7.45−7.47 (3H, m, ArH), 9.34 (1H, s, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.2 (CH_2), 26.4 (CH_2), 30.3 (CH_2), 52.6 (d, $^2J_{C,P}$ = 5.7 Hz, OCH_3), 119.7 (d, $^1J_{C,P}$ = 224.4 Hz, C-sp^2), 128.6 (ArC), 128.8 (ArC), 129.3 (ArC), 130.6 (d, $^4J_{C,P}$ = 8.4 Hz, C-sp^2), 137.5 (ArC), 140.3 (d, $^3J_{C,P}$ = 13.7 Hz, C-sp^2), 143.7 (d, $^2J_{C,P}$ = 16.5 Hz, C-sp^2), 180.6 (d, $^4J_{C,P}$ = 1.4 Hz, C=O) ppm. HRMS (ESI): MNa^+, found 342.0872. $C_{16}H_{18}NNaO_4P$ requires 342.0866.

Dimethyl 3-Benzoyl-2-phenyl-2,4,5,6-tetrahydrocyclopenta-[*c*]pyrrol-1-ylphosphonate (13a-^{18}O). Yellowish oil. Yield 0.34 g, 86%. IR (KBr): υ_{max} 1640 (C=O^{18}) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.29 (2H, pent, J = 7.1 Hz,, $CH_2\underline{CH_2}CH_2$), 2.45 (2H, t, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_2$), 2.92 (2H, td, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,P}$ = 1.5 Hz, $CH_2CH_2\underline{CH_2}$), 3.56 (6H, d, $^3J_{H,P}$ = 11.4 Hz, 2 × OCH_3), 7.37−7.42 (5H, m, ArH), 7.43−7.47 (2H, m, ArH), 7.52−7.57 (1H, m, ArH), 7.76 (2H, dd, J = 8.3, 1.3 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.7 (CH_2), 27.7 (CH_2), 30.1 (CH_2), 52.4 (d, $^2J_{C,P}$ = 5.7 Hz, OCH_3), 119.7 (d, $^1J_{C,P}$ = 225.4 Hz, C-sp^2), 127.9 (ArC), 128.2 (ArC), 128.2 (2 × ArC), 129.0 (ArC), 130.2 (d, $^4J_{C,P}$ = 9.0 Hz, C-sp^2), 132.2 (ArC), 138.7 (ArC), 139.2 (d, $^3J_{C,P}$ = 13.8 Hz, C-sp^2), 139.6 (ArC), 143.4 (d, $^2J_{C,P}$ = 17.1 Hz, C-sp^2), 186.26 (C=O^{18})ppm. HRMS (ESI): MNa^+, found 420.1230. $C_{22}H_{22}NNaO_3{}^{18}OP$ requires 420.1227.

Dimethyl 3-(1-Iodopent-1-enyl)-2-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (15i) (mixture of E and Z isomers). Yellowish oil. Yield 0.28 g, 58%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.72, 0.82 (3H, 2t, ^3J = 7.2 Hz, ^3J = 7.2 Hz, CH_3), 1.18 (2H, sext, ^3J = 7.2 Hz, $\underline{CH_2}CH_3$), 1.99 (2H, q, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_3$), 2.31−2.38 (2H, 2m (overlapped), CH_2), 2.64 (2H, t, ^3J = 7.2 Hz, $\underline{CH_2}CH_2CH_2$), 2.84−2.87 (2H, m, $CH_2CH_2\underline{CH_2}$), 3.50 (6H, d, $^3J_{HP}$ = 11.6 Hz, 2 × OCH_3), 5.49, 6.32 (1H, 2t, ^3J = 6.8 Hz, ^3J = 7.2 Hz, CH), 7.29−7.40 (5H, m ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4, 13.5 (CH_3), 21.0 (CH_2), 25.5 (CH_2), 26.8 (CH_2), 30.0 (CH_2), 35.0, 38.5 (CH_2), 52.2 (d, $^2J_{HP}$ = 5.6 Hz, 2 × OCH_3), 82.6, 90.3 (IC-sp^2), 111.7 (d, $^1J_{CP}$ = 232.3 Hz, C-sp^2), 128.0 (ArC), 128.2 (ArC), 128.7 (ArC), 131.3 (d, $^3J_{CP}$ = 13.7 Hz, C-sp^2), 133.7 (d, $^4J_{CP}$ = 9.2 Hz, C-sp^2), 138.9 (ArC), 143.8 (d, $^2J_{CP}$ = 16.7 Hz, C-sp^2), 143.9, 148.8 (HC-sp^2) ppm. HRMS (ESI): MNa^+, found 508.0515. $C_{20}H_{25}INNaO_3P$ requires 508.0509.

Dimethyl 3-(1,4-Diiodobut-1-enyl)-2-phenyl-2,4,5,6-tetrahydrocyclopenta[*c*]pyrrol-1-ylphosphonate (15o) (mixture of E and Z isomers). Yellowish oil. Yield 0.29 g, 49%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34−2.39 (2H, m, $CH_2\underline{CH_2}CH_2$), 2.60−2.68 (4H, 2m, CH_2 and $\underline{CH_2}CH_2CH_2$), 2.84−2.90 (4H, m, $CH_2CH_2\underline{CH_2}$andCH_2), 3.50 (6H, d, $^3J_{HP}$ = 11.2 Hz, 2 × OCH_3), 5.59, 6.25 (1H, 2t, ^3J = 6.8 Hz, ^3J = 7.2 Hz, CH), 7.31−7.41 (5H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 1.5, 1.7 (CH_2), 25.6 (CH_2), 26.7 (CH_2), 30.0 (CH_2), 40.1 (CH_2), 52.2 (d, $^2J_{C,P}$ = 5.6 Hz, 2 × OCH_3), 85.4, 92.6 (CIsp^2), 112.4 (d, $^1J_{C,P}$ = 231.5 Hz, CH), 128.1 (ArC), 128.3 (ArC), 128.7 (ArC), 131.7 (d, $^3J_{C,P}$ = 13.7 Hz, Csp^2), 133.0 (d, $^4J_{C,P}$ = 9.4 Hz, Csp^2), 138.7 (ArC), 141.6, 146.0 (CHsp^2), 143.8 (d, $^2J_{C,P}$ = 16.9 Hz, Csp^2) ppm. HRMS (ESI): MNa^+, found 619.9309. $C_{19}H_{22}I_2NNaO_3P$ requires 619.9319.

Dimethyl 3-Benzoyl-2-phenyl-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (16a). Yellowish oil. Yield 0.25 g, 61%. IR (KBr): υ_{max} 1646 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60−1.66 (2H, m, CH_2), 1.74−1.80 (2H, m, CH_2), 2.31 (2H, t, J = 6.4 Hz, CH_2), 2.89 (2H, t, J = 6.4 Hz, CH_2), 3.51 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.27 (4H, br. s, ArH), 7.34−7.38 (3H, m, ArH), 7.46−7.50 (1H, m, ArH), 7.66 (2H, dd, J = 8.2; 1.6 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.9 (CH_2), 23.0 (CH_2), 23.1 (CH_2), 23.5 (CH_2), 52.2 (d, $^2J_{C,P}$ = 5.6 Hz, 2 × OCH_3), 120.7 (d, $^1J_{C,P}$ = 222.7 Hz, ArC), 127.1 (d, $^3J_{C,P}$ = 14.5 Hz, ArC), 128.0 (ArC), 128.2 (ArC), 128.3 (ArC), 128.9 (ArC), 129.2 (ArC), 132.5 (ArC), 133.3 (d, $^2J_{C,P}$ = 18.8 Hz, ArC), 134.7 (d, $^3J_{C,P}$ = 9.6 Hz, ArC), 139.0 (ArC), 139.1 (ArC), 188.4 (d, $^4J_{C,P}$ = 1.4 Hz, CO) ppm. HRMS (ESI): MNa^+, found 432.1333. $C_{23}H_{24}NNaO_4P$ requires 432.1335.

Dimethyl 3-Benzoyl-2-(4-methoxyphenyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (16b). Brownish oil. Yield

dx.doi.org/10.1021/jo501011u | *J. Org. Chem.* 2014, 79, 6532−6553

0.26 g, 60%. IR (KBr): υ_{max} 1644 (C═O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.59−1.64 (2H, m, CH_2), 1.72−1.78 (2H, m, CH_2), 2.28 (2H, t, J = 6.0 Hz, CH_2), 2.87 (2H, t, J = 6.0 Hz, CH_2), 3.53 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 3.75 (3H, s, OCH_3), 6.77 (2H, d, J = 8.8 Hz, ArH), 7.18 (2H, d, J = 8.8 Hz, ArH), 7.36 (3H, t, J = 7.6 Hz, ArH), 7.48 (1H, t, J = 7.6 Hz, ArH), 7.65−7.67 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.8 (CH_2), 23.0 (2 × CH_2), 23.4 (CH_2), 52.2 (d, $^2J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 55.2 (OCH_3), 113.1 (ArC), 120.7 (d, $^1J_{C,P}$ = 222.8 Hz, ArC), 126.7 (d, $^3J_{C,P}$ = 14.6 Hz, ArC), 128.2 (ArC), 129.2 (2 × ArC), 131.7 (ArC), 132.5 (ArC), 132.9 (d, $^2J_{C,P}$ = 19.0 Hz, ArC), 134.7 (d, $^3J_{C,P}$ = 9.6 Hz, ArC), 138.9 (ArC), 159.1 (ArC), 188.5 (d, $^4J_{C,P}$ = 1.3 Hz CO) ppm. HRMS (ESI): MH^+, found 440.1627. $C_{24}H_{26}NO_5P$ requires 440.1621.

Dimethyl 2-(4-Chlorophenyl)-3-(4-methylbenzoyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (16o). Yellowish solid, mp 99−100 °C. Yield 0.32 g, 69%. IR (KBr): υ_{max} 1652 (C═O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.60−1.63 (2H, m, CH_2), 1.73−1.77 (2H, m, CH_2), 2.27 (2H, t, J = 6.4 Hz, CH_2), 2.39 (3H, s, CH_3), 2.87 (2H, t, J = 6.0 Hz, CH_2), 3.55 (6H, d, $^3J_{H,P}$ = 11.2 Hz, 2 × OCH_3), 7.19−7.27 (6H, m, ArH), 7.60 (2H, d, J = 8.4 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7 (CH_3), 22.8 (CH_2), 22.9 (CH_2), 23.0 (CH_2), 23.6 (CH_2), 52.2 (d, $^2J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 120.5 (d, $^1J_{C,P}$ = 222.6 Hz, ArC), 126.8 (d, $^3J_{C,P}$ = 14.5 Hz, ArC), 128.2 (ArC), 129.1 (ArC), 129.4 (ArC), 129.5 (ArC), 133.4 (d, $^2J_{C,P}$ = 18.7 Hz, ArC), 134.0 (ArC), 134.8 (d, $^3J_{C,P}$ = 9.4 Hz, ArC), 136.1 (ArC), 137.7 (ArC), 143.8 (ArC), 187.9 (d, $^4J_{C,P}$ = 1.1 Hz, CO) ppm. HRMS (ESI): MNa^+, found 480.1096. $C_{24}H_{25}ClNNaO_4P$ requires 480.1102.

Dimethyl 3-(1-Iodopent-1-enyl)-2-(4-methoxyphenyl)-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (17k). Yellowish oil. Yield 0.12 g, 22%. Compound exists as the geometrical isomers, which were not isolated due to the same R_f. ^1H NMR (400 MHz, $CDCl_3$): δ 0.79; 0.84 (3H, 2t, J = 7.2 Hz, J = 7.2 Hz, CH_3), 1.25−1.33 (2H, m, C═$CHCH_2C\underline{H_2}$), 1.73−1.76 (4H, 2m (overlap.), 2 × CH_{2chex}), 2.03 (2H, q, J = 7.2 Hz, C═$CHC\underline{H_2}CH_2$), 2.42 (2H, t, J = 5.6 Hz, CH_{2chex}), 2.81 (2H, br. s, CH_{2chex}), 3.49−3.55 (6H, 2m (overlap.), 2 × OCH_3), 3.82; 3.83 (3H, 2s, OCH_3), 5.58; 6.37 (1H, 2t, J = 6.8 Hz, J = 7.2 Hz, CH), 6.86 (2H, d, J = 8.8 Hz, ArH), 7.18 (2H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4; 13.6 (CH_3), 21.1; 21.6 (CH_2), 22.1 (CH_2), 22.9; 23.0 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 35.1; 38.5 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.4 Hz, 2 × OCH_3), 55.3; 55.3 (OCH_3), 82.8; 90.5 (2d, $^4J_{C,P}$ = 1.6 Hz, $^4J_{C,P}$ = 1.6 Hz, IC$_{sp}$2), 113.0 (ArC), 114.4 (d, $^1J_{C,P}$ = 197.7 Hz, ArC), 119.8 (d, $^3J_{C,P}$ = 14.3 Hz, ArC), 129.9 (ArC), 131.4 (ArC), 133.0 (d, $^2J_{C,P}$ = 18.8 Hz, ArC), 137.4 (d, $^3J_{C,P}$ = 10.7 Hz, ArC), 145.1; 149.5 (C$_{sp}$2H), 159.1; 159.2 (ArC) ppm. HRMS (ESI): MH^+, found 530.0959. $C_{22}H_{30}INO_4P$ requires 530.0952.

Dimethyl 3-(1,4-Diiodobut-1-enyl)-2-phenyl-4,5,6,7-tetrahydro-2*H*-isoindol-1-ylphosphonate (17l). Yellowish oil. Yield 0.51 g, 83%. Compound exists as the geometrical isomers, which were not isolated due to the same R_f. ^1H NMR (400 MHz, $CDCl_3$): δ 1.76 (4H, 2br. s (overlap.), 2 × CH_{2chex}), 2.46 (2H, br. s, CH_{2chex}), 2.65 (2H, q, J = 6.8 Hz, C═$CHC\underline{H_2}CH_2$), 2.83 (2H, br. s, CH_{2chex}), 2.93 (2H, t, J = 6.8 Hz, C═$CHCH_2C\underline{H_2}$), 3.46−3.52 (6H, 2m (overlap.), 2 × OCH_3), 5.69; 6.31 (1H, 2t, J = 6.8 Hz, J = 6.8 Hz, CH), 7.28−7.30 (2H, m, ArH), 7.37−7.38 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0; 22.2 (CH_2), 22.8; 22.9 (CH_2), 23.0 (CH_2), 23.2; 23.3 (CH_2), 36.6 (CH_2), 40.0 (CH_2), 52.0 (d, $^2J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 85.5; 92.7 (2d, $^4J_{C,P}$ = 1.6 Hz, $^4J_{C,P}$ = 1.5 Hz, IC$_{sp}$2), 114.8 (d, $^1J_{C,P}$ = 227.4 Hz, ArC), 120.3 (d, $^3J_{C,P}$ = 14.2 Hz, ArC), 128.0; 128.1 (ArC), 128.2; 128.4 (ArC), 128.9 (ArC), 133.3 (d, $^2J_{C,P}$ = 18.7 Hz, ArC), 136.4 (d, $^3J_{C,P}$ = 10.7 Hz, ArC), 138.4; 138.5 (ArC), 143.2; 147.1 (C$_{sp}$2H) ppm. HRMS (ESI): MNa^+, found 633.9469. $C_{20}H_{24}I_2NNaO_3P$ requires 633.9475.

Dimethyl 3-Benzoyl-2-(4-chlorophenyl)-2*H*-isoindol-1-ylphosphonate (18b). Yellowish solid, mp 57−58 °C. Yield 0.19 g, 44%. IR (KBr): υ_{max} 1649 (C═O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.64 (6H, d, $^3J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 7.09 (2H, m, ArH), 7.23−7.27 (1H, m, ArH), 7.33−7.41 (4H, m, ArH), 7.45 (2H, t, J = 7.6 Hz, ArH), 7.58 (1H, t, J = 7.6 Hz, ArH), 7.77−7.79 (2H, m, ArH), 8.23 (1H, d, J = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.7 (d, $^2J_{C,P}$ = 5.5 Hz, 2 × OCH_3), 117.3 (d, $^1J_{C,P}$ = 223.8 Hz, ArC), 120.3 (ArC), 121.1 (ArC), 125.1 (ArC), 125.3 (ArC), 127.6 (d, $^3J_{C,P}$ = 13.1 Hz, ArC), 128.4 (ArC), 128.5 (ArC), 129.0 (d, $^3J_{C,P}$ = 8.3 Hz, ArC), 129.0 (ArC), 129.7 (ArC), 131.8 (d, $^2J_{C,P}$ = 17.4 Hz, ArC), 132.9 (ArC), 135.1 (ArC), 137.4 (d, $^3J_{C,P}$ = 1.1 Hz, ArC), 139.1 (ArC), 186.0 (d, $^4J_{C,P}$ = 1.0 Hz, CO) ppm. HRMS (ESI): MNa^+, found 462.0640. $C_{23}H_{19}ClNNaO_4P$ requires 462.0632.

Dimethyl 3-Formyl-2-(4-methoxyphenyl)-2*H*-isoindol-1-ylphosphonate (18c). Brownish solid, mp 117−118 °C. Yield 0.2 g, 56%. IR (KBr): υ_{max} 1655 (CHO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.63 (6H, d, $^3J_{H,P}$ = 11.6 Hz, 2 × OCH_3), 3.89 (3H, s, OCH_3), 7.02 (2H, d, J = 8.8 Hz, ArH), 7.34−7.45 (4H, m, ArH), 8.18 (1H, d, J = 8.4 Hz, ArH), 8.41 (1H, dt, J = 8.4 Hz; 0.8 Hz, ArH), 9.55 (1H, s, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.8 (d, $^2J_{C,P}$ = 5.6 Hz, 2 × OCH_3), 55.5 (OCH_3), 113.8 (ArC), 118.5 (d, $^1J_{C,P}$ = 221.7 Hz, ArC), 120.7 (ArC), 120.9 (ArC), 126.0 (ArC), 127.3 (ArC), 127.4 (ArC), 128.9 (2 × ArC), 129.2 (ArC), 131.3 (d, $^2J_{C,P}$ = 17.0 Hz, ArC), 160.6 (ArC), 180.0 (d, $^4J_{C,P}$ = 1.7 Hz, CHO) ppm. HRMS (ESI): MNa^+, found 382.0810. $C_{18}H_{18}NNaO_5P$ requires 382.0815.

General Procedure for the Preparation of Compounds 20 and 21. A solution of starting corresponding acetylenic aldehyde **5**, **6** (1 mmol), aniline (1 mmol), and dimethylphosphite (0.121 g, 1.1 mmol) in dry dichloromethane (5 mL) was stirred at room temperature. When the consumption of starting aldehyde was observed by TLC, 10 mol % copper(I) iodide (19.05 mg, 0.1 mmol) was added. When the full completion of the reaction was observed by TLC (after 1−4 h), the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography eluting with hexane−ethyl acetate mixtures.

Dimethyl 6,7-Diphenyl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonate (20a). Brownish solid, mp 146−147 °C. Yield 0.23 g, 58%. ^1H NMR (400 MHz, DMSO-d_6): δ 3.56 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.69 (3H, d, $^3J_{H,P}$ = 10.8 Hz, OCH_3), 5.94 (1H, d, $^1J_{H,P}$ = 18.8 Hz, CH), 6.67 (1H, br. s, $C_{sp^2}H$), 6.91 (1H, t, J = 7.2 Hz, ArH), 7.05 (2H, d, J = 7.6 Hz, ArH), 7.15 (2H, t, J = 7.6 Hz, ArH), 7.24−7.33 (4H, m, ArH), 7.57 (2H, d, J = 6.8 Hz, ArH), 7.63 (1H, d, J = 6.0 Hz, ArH), 8.73 (1H, br. s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 52.9 (d, $^2J_{C,P}$ = 4.1 Hz, OCH_3), 53.0 (d, $^2J_{C,P}$ = 4.2 Hz, OCH_3), 62.0 (d, $^1J_{C,P}$ = 158.9 Hz, CH), 103.6 ($^4C_{sp^2}H$), 112.7 (ArC), 122.8 (3 × ArC), 127.5 (ArC), 128.4 (ArC), 128.6 (2 × ArC), 129.0 (ArC), 134.5 (ArC), 136.5 (ArC), 146.0 (ArC), 146.6 (d, $^3J_{C,P}$ = 6.7 Hz, ArC), 148.0 (ArC), 151.5 ($^3C_{sp^2}$) ppm. HRMS (ESI): MNa^+, found 415.1178. $C_{22}H_{21}N_2NaO_3P$ requires 415.1182.

Dimethyl 6-(4-Methoxyphenyl)-7-phenyl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonate (20b). Yellow oil. Yield 0.26 g, 61%. ^1H NMR (400 MHz, DMSO-d_6): δ 3.56 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.61 (3H, s, OCH_3), 3.68 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.73 (1H, d, $^1J_{H,P}$ = 19.6 Hz, CH), 6.51 (1H, br. s, $C_{sp^2}H$), 6.73 (2H, d, J = 8.8 Hz, ArH), 7.01 (2H, d, J = 8.4 Hz, ArH), 7.23−7.32 (4H, m, ArH), 7.55 (3H, d, J = 6.4 Hz, ArH), 8.45 (1H, br. s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 52.9 (d, $^2J_{C,P}$ = 2.0 Hz, OCH_3), 53.0 (d, $^2J_{C,P}$ = 2.1 Hz, OCH_3), 55.0 (OCH_3), 62.7 (d, $^1J_{C,P}$ = 161.8 Hz, CH), 111.5 ($^4C_{sp^2}H$), 113.9 (ArC), 121.6 (ArC), 124.6 (d, $^4J_{C,P}$ = 1.2 Hz, ArC), 127.6 (ArC), 128.4 (ArC), 128.6 (ArC), 129.1 (ArC), 134.5 (d, $^3J_{C,P}$ = 4.4 Hz, ArC), 136.6 (ArC), 140.3 (d, $^3J_{C,P}$ = 7.3 Hz, ArC), 146.4 (ArC), 148.7 (ArC), 151.5 ($^3C_{sp^2}$), 155.3 (ArC) ppm. HRMS (ESI): MNa^+, found 445.1282. $C_{23}H_{23}N_2NaO_4P$ requires 445.1288.

Dimethyl 6-Phenyl-7-propyl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonate (20c). Brownish oil. Yield 0.17 g, 52%. ^1H NMR (400 MHz, DMSO-d_6): δ 0.83 (3H, t, J = 7.2 Hz, CH_3), 1.46 (2H, sext., J = 7.2 Hz, CH_2), 2.11−2.19 (1H, m, C$\underline{H}$H), 2.23−2.31 (1H, m, CH$\underline{H}$), 3.56 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 3.66 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH_3), 5.56 (1H, d, $^2J_{H,P}$ = 18.4 Hz, CH), 6.13 (1H, br. s, $C_{sp^2}H$), 7.13 (1H, t, J = 7.2 Hz, ArH), 7.24 (2H, d, J = 8.0 Hz, ArH), 7.32−7.36 (2H, m, ArH), 7.43−7.50 (2H, m, ArH), 8.45 (1H, br. s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.6 (CH_3), 20.7 (CH_2), 35.0 (CH_2), 52.7 (d, $^2J_{C,P}$ = 7.2 Hz, OCH_3), 53.0 (d, $^2J_{C,P}$ = 6.9 Hz, OCH_3), 63.6 (d, $^1J_{C,P}$ = 161.0 Hz, CH), 109.7 ($^4C_{sp^2}H$), 120.6 (ArC), 124.2 (ArC), 124.2 (ArC), 128.9 (ArC), 129.4 (ArC), 134.2 (d, $^3J_{C,P}$ = 5.0 Hz, ArC), 145.9 (d, $^3J_{C,P}$ = 5.7 Hz, ArC), 148.4 (2 × ArC), 151.7

dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532−6553

($^3C_{sp^2}$) ppm. HRMS (ESI): MH$^+$, found 359.1526. $C_{19}H_{23}N_2O_3P$ requires 359.1519.

Dimethyl 7-Cyclopropyl-6-phenyl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonate (20d). Brownish solid, mp 144−145 °C. Yield 0.22 g, 63%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.71−0.75 (2H, m, CH(C$\underline{H}_2$)$_2$), 0.80−0.84 (2H, m, CH(C$\underline{H}_2$)$_2$), 1.33 (1H, p, J = 6.4 Hz, C$\underline{H}$(CH$_2$)$_2$), 3.60 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH$_3$), 3.65 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH$_3$), 5.64 (1H, d, $^2J_{H,P}$ = 18.8 Hz, CH), 5.90 (1H, br. s, C_{sp^2}H), 7.06 (1H, br. s, ArH), 7.12−7.14 (1H, m, ArH), 7.32−7.37 (4H, m, ArH), 7.45 (1H, d, J = 6.0 Hz, ArH), 8.35 (1H, br. s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 8.4 (C$\underline{H}$(CH$_2$)$_2$), 10.9 (CH(C$\underline{H}_2$)$_2$), 14.2 (CH(C$\underline{H}_2$)$_2$), 53.0 (d, $^2J_{C,P}$ = 6.9 Hz, 2 × OCH$_3$), 62.5 (d, $^1J_{C,P}$ = 159.3 Hz, CH), 104.2 ($^4C_{sp^2}$H), 120.3 (ArC), 123.8 (ArC), 123.8 (ArC), 128.8 (ArC), 129.1 (ArC), 134.1 (d, $^3J_{C,P}$ = 4.3 Hz, ArC), 146.0 (d, $^3J_{C,P}$ = 5.5 Hz, ArC), 148.4 (ArC), 150.9 (ArC), 151.8 ($^3C_{sp^2}$) ppm. HRMS (ESI): MH$^+$, found 357.1369. $C_{19}H_{22}N_2O_3P$ requires 357.1363.

Dimethyl 7-Cyclopropyl-6-(4-methoxyphenyl)-5,6-dihydro-1,6-naphthyridin-5-ylphosphonate (20e). Brownish solid, mp 111−112 °C. Yield 0.27 g, 59%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.62−0.82 (4H, m, CH(C$\underline{H}_2$)$_2$), 1.22−1.24 (1H, m, C$\underline{H}$(CH$_2$)$_2$), 3.59 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH$_3$), 3.63 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH$_3$), 3.73 (3H, s, OCH$_3$), 5.49 (1H, d, $^2J_{H,P}$ = 17.6 Hz, CH), 5.78 (1H, br. s, C_{sp^2}H), 6.91 (2H, d, J = 8.4 Hz, ArH), 7.04 (1H, d, J = 8.4 Hz, ArH), 7.29 (2H, d, J = 8.0 Hz, ArH), 7.39−7.52 (1H, m, ArH), 8.36 (1H, br. s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 7.7 (C$\underline{H}$(CH$_2$)$_2$), 10.7 (CH(C$\underline{H}_2$)$_2$), 14.2 (CH(C$\underline{H}_2$)$_2$), 53.0 (d, $^2J_{C,P}$ = 4.5 Hz, OCH$_3$), 53.0 (d, $^2J_{C,P}$ = 4.7 Hz, OCH$_3$), 55.2 (OCH$_3$), 63.2 (d, $^1J_{C,P}$ = 159.4 Hz, CH), 102.0 ($^4C_{sp^2}$H), 114.1 (ArC), 120.2 (ArC), 126.4 (ArC), 128.7 (ArC), 134.1 (d, $^3J_{C,P}$ = 4.8 Hz, ArC), 139.2 (d, $^3J_{C,P}$ = 5.1 Hz, ArC), 148.3 (ArC), 151.7 (ArC), 152.3 ($^3C_{sp^2}$), 156.4 (ArC) ppm. HRMS (ESI): MH$^+$, found 387.1462. $C_{20}H_{24}N_2O_4P$ requires 387.1468.

Dimethyl 6-Phenyl-5,6-dihydro-1,6-naphthyridin-5-ylphosphonate (20f). Brownish oil. Yield 0.16 g, 50%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.52 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH$_3$), 3.56 (3H, d, $^3J_{H,P}$ = 10.4 Hz, OCH$_3$), 5.90 (1H, d, J = 6.4 Hz, C_{sp^2}H), 6.08 (1H, d, $^2J_{H,P}$ = 13.6 Hz, CH), 7.04 (1H, t, J = 7.2 Hz, ArH), 7.08−7.10 (2H, m, ArH, C_{sp^2}H), 7.26 (2H, d, J = 8.0 Hz, ArH), 7.36 (2H, t, J = 7.6 Hz, ArH), 7.53 (1H, d, J = 7.2 Hz, ArH), 8.33 (1H, br. s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 52.8 (d, $^2J_{C,P}$ = 7.3 Hz, OCH$_3$), 52.9 (d, $^2J_{C,P}$ = 7.2 Hz, OCH$_3$), 57.6 (d, $^1J_{C,P}$ = 152.6 Hz, CH), 106.4 (d, $^3J_{C,P}$ = 1.4 Hz, $^4C_{sp^2}$H), 117.2 (d, $^4J_{C,P}$ = 1.4 Hz, ArC), 119.6 (ArC), 120.7 (ArC), 121.8 (ArC), 129.0 (ArC), 134.3 (d, $^3J_{C,P}$ = 2.2 Hz, ArC), 134.6 (d, $^3J_{C,P}$ = 6.0 Hz, ArC), 144.2 ($^3C_{sp^2}$), 148.6 (ArC), 151.4 (ArC) ppm. HRMS (ESI): MH$^+$, found 317.1046. $C_{16}H_{18}N_2O_3P$ requires 317.1050.

Dimethyl 6-Phenyl-7-((tetrahydro-2*H*-pyran-2-yloxy)-methyl)-5,6-dihydro-1,6-naphthyridin-5-ylphosphonate (20g). Brownish oil. Yield 0.22 g, 51%. Compound exists as the diastereomers, which were not isolated due to the same R_f. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.34−1.52 (4H, 2m (overlap.), 2 × CH$_2$), 1.53−1.68 (2H, m, CH$_2$), 3.23−3.36 (2H, m, CH$_2$), 3.60; 3.63 (3H, 2d, $^3J_{H,P}$ = 8.8 Hz, $^3J_{H,P}$ = 8.8 Hz, OCH$_3$), 3.66; 3.67 (3H, 2d, $^3J_{H,P}$ = 10.4 Hz, $^3J_{H,P}$ = 10.4 Hz, OCH$_3$), 4.02; 4.06 (1H, 2d, J = 8.4 Hz, J = 8.4 Hz, =CC$\underline{H}$HO), 4.21; 4.27 (1H, 2d, J = 13.6 Hz, J = 14.0 Hz, =CCH$\underline{H}$O), 4.43; 4.71 (1H, 2br. s, O-CH-O), 5.57; 5.62 (1H, 2d, $^2J_{H,P}$ = 10.8 Hz, $^2J_{H,P}$ = 11.2 Hz, PCH), 6.29 (1H, br. s, C_{sp^2}H), 7.13−7.16 (2H, 2m (overlap.), 2 × ArH), 7.27−7.30 (2H, m, ArH), 7.33−7.37 (2H, m, ArH), 7.48 (1H, d, J = 6.8 Hz, ArH), 8.40 (1H, br. s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 18.6; 18.7 (CH$_2$), 24.8; 24.9 (CH$_2$), 29.8; 29.9 (CH$_2$), 52.9; 53.1 (2d, $^2J_{C,P}$ = 7.1 Hz, $^2J_{C,P}$ = 7.0 Hz, OCH$_3$), 53.2; 53.2 (2d, $^2J_{C,P}$ = 3.0 Hz, $^2J_{C,P}$ = 3.1 Hz, OCH$_3$), 60.6; 61.0 (CH$_2$), 62.6 (d, $^1J_{C,P}$ = 160.9 Hz, PCH), 64.1; 65.0 (=C$\underline{C}$H$_2$O), 96.0; 97.7 (O-CH-O), 110.3; 110.5 ($^4C_{sp^2}$H), 119.8 (ArC), 121.3 (ArC), 123.7; 124.2 (ArC), 124.4; 124.6 (ArC), 129.0; 129.0 (ArC), 134.5 (d, $^3J_{C,P}$ = 3.8 Hz, ArC), 144.6; 145.0 (2d, $^3J_{C,P}$ = 1.7 Hz, $^3J_{C,P}$ = 1.9 Hz, ArC), 145.5; 145.7 (2d, $^3J_{C,P}$ = 5.6 Hz, $^3J_{C,P}$ = 5.6 Hz, $^3C_{sp^2}$), 148.7 (ArC), 151.0 (ArC) ppm. HRMS (ESI): MH$^+$, found 431.1728. $C_{22}H_{28}N_2O_5P$ requires 431.1730.

Dimethyl 6-(4-Methoxyphenyl)-7-((tetrahydro-2*H*-pyran-2-yloxy)methyl)-5,6-dihydro-1,6-naphthyridin-5-ylphosphonate (20h). Yellowish oil. Yield 0.22 g, 48%. Compound exists as the diastereomers, which were not isolated due to the same R_f. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.38−1.47 (4H, 2m (overlap.), 2 × CH$_2$), 1.52−1.69 (2H, m, CH$_2$), 3.42−3.48 (2H, m, CH$_2$), 3.59; 3.62 (3H, 2d, $^3J_{H,P}$ = 10.8 Hz, $^3J_{H,P}$ = 10.8 Hz, OCH$_3$), 3.65; 3.65 (3H, 2d, $^3J_{H,P}$ = 10.4 Hz, $^3J_{H,P}$ = 10.4 Hz, OCH$_3$), 3.73 (3H, s, OCH$_3$), 3.93; 3.97 (1H, 2d, J = 6.8 Hz, J = 6.8 Hz, =CC$\underline{H}$HO), 4.12; 4.18 (1H, 2d, J = 13.6 Hz, J = 13.6 Hz, =CCH$\underline{H}$O), 4.40; 4.69 (1H, 2t, J = 3.2 Hz, J = 3.2 Hz, O-CH-O), 5.42; 5.46 (1H, 2d, $^2J_{H,P}$ = 6.8 Hz, $^2J_{H,P}$ = 6.8 Hz, PCH), 6.09; 6.15 (1H, 2br. s, C_{sp^2}H), 6.91; 6.91 (2H, 2d, J = 9.2 Hz, J = 8.8 Hz, ArH), 7.09 (1H, J = 5.6 Hz, ArH), 7.24; 7.25 (2H, 2d, J = 8.8 Hz, J = 8.8 Hz, ArH), 7.42 (1H, d, J = 7.6 Hz, ArH), 8.31 (1H, br. s, ArH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 18.6; 18.6 (CH$_2$), 24.8; 24.9 (CH$_2$), 29.8 (CH$_2$), 52.8; 53.0 (2d, $^2J_{C,P}$ = 7.0 Hz, $^2J_{C,P}$ = 6.8 Hz, POCH$_3$), 53.0; 53.1 (2d, $^2J_{C,P}$ = 6.5 Hz, $^2J_{C,P}$ = 6.7 Hz, POCH$_3$), 55.2 (OCH$_3$), 60.6; 60.9 (CH$_2$), 63.0 (d, $^1J_{C,P}$ = 160.0 Hz, CH), 64.3; 65.1 (=C$\underline{C}$H$_2$O), 96.0; 97.6 (O-CH-O), 107.9; 108.2 ($^4C_{sp^2}$H), 114.1; 114.2 (ArC), 118.8 (ArC), 120.9 (ArC), 126.3 (ArC), 126.7 (ArC), 134.3; 134.4 (2d, $^3J_{C,P}$ = 2.7 Hz, $^3J_{C,P}$ = 2.9 Hz ArC), 138.6; 138.7 (2d, $^3J_{C,P}$ = 5.3 Hz, $^3J_{C,P}$ = 5.3 Hz, ArC), 145.2; 145.6 (2d, $^3J_{C,P}$ = 2.2 Hz, $^3J_{C,P}$ = 2.0 Hz, $^3C_{sp^2}$), 148.6 (ArC), 151.2; 151.3 (2d, $^3J_{C,P}$ = 3.1 Hz, $^3J_{C,P}$ = 3.2 Hz, ArC), 156.7; 156.8 (ArC) ppm. HRMS (ESI): MH$^+$, found 461.1837. $C_{23}H_{30}N_2O_6P$ requires 461.1836.

Dimethyl 2-(4-Methoxyphenyl)-3-phenyl-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonate (21a). Yellow solid, mp 188−190 °C. Yield 0.27 g, 48%. ^{1}H NMR (300 MHz, CDCl$_3$): δ 3.63 (3H, d, $^3J_{HP}$ = 10,5 Hz, OCH$_3$), 3.65 (3H, s, OCH$_3$), 3.76 (3H, d, $^3J_{HP}$ = 10,8 Hz, OCH$_3$), 5.50 (1H, d, $^1J_{HP}$ = 20.1 Hz, C$_1$H), 6.66 (2H, d, ^3J = 9.0 Hz, ArH), 6.80 (1H, s, C$_4$H), 7.49 (2H, d, ^3J = 9.0 Hz, ArH), 7.25−7.29 (3H, m, ArH), 7.41 (1H, td, ^3J = 7.3 Hz, ^4J = 0.9 Hz, ArH), 7.63−7.67 (3H, m, ArH), 7.71 (1H, d, ^3J = 8.1 Hz, ArH), 7.81 (1H, d, $^4J_{HP}$ = 3.3 Hz, ArH), 8.06 (1H, d, ^3J = 8.4 Hz, ArH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ 53.3 (d, $^2J_{CP}$ = 7.3 Hz, OCH$_3$), 53.6 (d, $^2J_{CP}$ = 6.5 Hz, OCH$_3$), 55.2 (OCH$_3$), 65.0 ($^1J_{CP}$ = 163.5 Hz, CH), 110.2 (C$_4$-sp^2), 114.0 (ArC), 120.7 (ArC), 125.4 (ArC), 125.4 (ArC), 127.2 ($^4J_{CP}$ = 2.4 Hz, ArH), 127.6 (ArC), 127.8 (ArC), 128.3 (ArC), 128.4 (ArC), 128.9 (ArC), 129.1 (ArC), 130.0 (ArC), 134.2 (d, $^3J_{CP}$ = 9.0 Hz, ArC), 136.5 (ArC), 140.7 (d, $^3J_{CP}$ = 5.7 Hz, ArC), 147.8 (ArC), 151.8 (ArC), 156.2 (C$_3$-sp^2) ppm. HRMS (ESI): MH$^+$, found 473.1626. $C_{27}H_{26}N_2O_4P$ requires 473.1625.

Dimethyl 3-Butyl-2-phenyl-1,2-dihydrobenzo[*b*][1,6]-naphthyridin-1-ylphosphonate (21b). Yellow solid, mp 149−151 °C. Yield 0.2 g, 48%. ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.82 (3H, t, ^3J = 7.2 Hz, CH$_3$), 1.24−1.35 (2H, m, CH$_2$), 1.50−1.60 (2H, m, CH$_2$), 2.18−2.39 (2H, m, CH$_2$), 3.60 (3H, d, $^3J_{HP}$ = 10,5 Hz, OCH$_3$), 3.72 (3H, d, $^3J_{HP}$ = 10,5 Hz, OCH$_3$), 5.30 (1H, dd, $^1J_{HP}$ = 19.2 Hz, $^4J_{HH}$ = 0.6 Hz, C$_1$H), 6.34 (1H, s, C$_4$H), 7.13−7.19 (1H, m, ArH), 7.30−7.37 (5H, m, ArH), 7.57−7.66 (2H, m, ArH), 7.70 (1H, d, $^4J_{HP}$ = 3.0 Hz, ArH), 7.97 (1H, d, ^3J = 8.4 Hz, ArH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ 13.7 (CH$_3$), 22.2 (CH$_2$), 30.0 (CH$_2$), 33.5 (CH$_2$), 53.2 (d, $^2J_{CP}$ = 7.2 Hz, OCH$_3$), 53.5 (d, $^2J_{CP}$ = 7.2 Hz, OCH$_3$), 65.7 ($^1J_{CP}$ = 161.4 Hz, CH), 108.3 (C$_4$-sp^2), 119.3 (ArC), 124.9 (ArC), 125.3 (ArC), 125.4 (ArC), 127.0 ($^4J_{CP}$ = 2.1 Hz, ArC), 127.5 (ArC), 127.8 (ArC), 129.1 (ArC), 129.8 (ArC), 133.6 (d, $^3J_{CP}$ = 8.4 Hz, ArC), 146.2 (d, $^3J_{CP}$ = 4.8 Hz, ArC), 147.8 (ArC), 152.1 (ArC), 153.1 (C$_3$-sp^2) ppm. HRMS (ESI): MH$^+$, found 423.1835. $C_{24}H_{28}N_2O_3P$ requires 423.1838.

Dimethyl 3-Butyl-2-(4-methoxyphenyl)-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonate (21c). Yellow solid, mp 48−50 °C. Yield 0.18 g, 40%. ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.81 (3H, t, ^3J = 7.2 Hz, CH$_3$), 1.20−1.35 (2H, m, CH$_2$), 1.47−1.57 (2H, m, CH$_2$), 2.09−2.30 (2H, m, CH$_2$), 3.58 (3H, d, $^3J_{HP}$ = 10,5 Hz, OCH$_3$), 3.70 (3H, d, $^3J_{HP}$ = 10,8 Hz, OCH$_3$), 3.77 (3H, s, OCH$_3$), 5.19 (1H, dd, $^1J_{HP}$ = 19.0 Hz, $^4J_{HH}$ = 0.6 Hz, C$_1$H), 6.20 (1H, s, C$_4$H), 6.83 (2H, d, ^3J = 9.3 Hz, ArH), 7.25−7.35 (3H, m, ArH), 7.55−7.67 (3H, m, ArH), 7.97 (1H, d, ^3J = 8.4 Hz, ArH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ 13.7 (CH$_3$), 22.1 (CH$_2$), 29.9 (CH$_2$), 33.5 (CH$_2$), 53.2 (d, $^2J_{CP}$ = 6.6 Hz, OCH$_3$), 53.2 (d, $^2J_{CP}$ = 7.2 Hz, OCH$_3$), 55.4

dx.doi.org/10.1021/jo501011u | J. Org. Chem. 2014, 79, 6532−6553

(OCH_3), 64.9 ($^1J_{CP}$ = 160.6 Hz, CH), 106.1 (C_4-sp^2), 114.2 (ArC), 119.2 (ArC), 124.6 (ArC), 126.9 ($^4J_{CP}$ = 2.1 Hz, ArC), 127.5 (ArC), 127.6 (2 × ArC), 129.7 (ArC), 133.5 (d, $^3J_{CP}$ = 8.4 Hz, ArC), 139.2 (d, $^3J_{CP}$ = 4.3 Hz, ArC), 147.7 (ArC), 152.3 (ArC), 153.8 (C_3-sp^2), 157.6 (ArC) ppm. HRMS (ESI): MH^+, found 453.1941. $C_{25}H_{30}N_2O_4P$ requires 453.1938.

Dimethyl 3-Butyl-2-(4-fluorophenyl)-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonate (21d). Yellow oil. Yield 0.24 g, 52%. ^1H NMR (300 MHz, $CDCl_3$): δ 0.82 (3H, t, ^3J = 7.5 Hz, CH_3), 1.19−1.39 (2H, m, CH_2), 1.54 (2H, quint, ^3J = 7.8 Hz, CH_2), 2.12−2.31 (2H, m, CH_2), 3.60 (3H, d, $^3J_{HP}$ = 10,5 Hz, OCH_3), 3.71 (3H, d, $^3J_{HP}$ = 10,8 Hz, OCH_3), 5.21 (1H, d, $^1J_{HP}$ = 19.2 Hz, C_1H), 6.27 (1H, s, C_4H), 6.97−7.03 (2H, m, ArH), 7.29−7.37 (3H, m, ArH), 7.57−7.66 (2H, m, ArH), 7.70 (1H, d, $^4J_{HP}$ = 3.6 Hz, ArH), 7.95 (1H, d, ^3J = 8.7 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.6 (CH_3), 22.2 (CH_2), 29.9 (CH_2), 33.5 (CH_2), 53.3 (d, $^2J_{CP}$ = 7.3 Hz, OCH_3), 53.4 (d, $^2J_{CP}$ = 7.4 Hz, OCH_3), 64.8 ($^1J_{CP}$ = 161.6 Hz, CH), 107.6 (C_4-sp^2), 115.9 (d $^2J_{CF}$ = 22.5 Hz, ArC), 119.2 (ArC), 124.9 (ArC), 127.0 (ArC), 127.5 (ArC), 127.6 (d, $^3J_{CF}$ = 8.5 Hz, ArC), 127.8 (ArC), 129.8 (ArC), 133.6 (d, $^3J_{CP}$ = 8.1 Hz, ArC), 142.2 (ArC), 147.7 (ArC), 152.0 (ArC), 153.0 (C_3-sp^2), 160.4 (d $^1J_{CF}$ = 244.7 Hz, ArC) ppm. HRMS (ESI): MH^+, found 457.1441 $C_{24}H_{27}ClN_2O_3P$ requires 457.1442.

Dimethyl 2-(4-Methoxyphenyl)-3-propyl-1,2-dihydrobenzo-[*b*][1,6]naphthyridin-1-ylphosphonate (21e). Yellow solid, mp 47−49 °C. Yield 0.3 g, 68%. ^1H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, ^3J = 7.6 Hz, CH_3), 1.54−1.56 (2H, m, CH_2), 2.11−2.15 and 2.20−2.23 (2H, 2m, CH_2), 3.58 (3H, d, $^3J_{HP}$ = 10,4 Hz, OCH_3), 3.70 (3H, d, $^3J_{HP}$ = 10,4 Hz, OCH_3), 3.76 (3H, s, OCH_3), 5.18 (1H, d, $^1J_{HP}$ = 19.2 Hz, C_1H), 6.19 (1H, s, C_4H), 6.82 (2H, d, ^3J = 9.0 Hz, ArH), 7.25 (2H, d, ^3J = 8,4 Hz, ArH), 7.31 (1H, t, ^3J = 8,4 Hz, ArH), 7.57 (1H, t, ^3J = 8,4 Hz, ArH), 7.62 (1H, d, ^3J = 8.1 Hz, ArH), 7.65 (1H, d, ^4J = 3.6 Hz, ArH), 7.92 (1H, d, ^3J = 8.4 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8 (CH_3), 21.1 (CH_2), 36.01 (CH_2), 53.3 (d, $^2J_{CP}$ = 7.3 Hz, OCH_3), 53.4 (d, $^2J_{CP}$ = 7.3 Hz, OCH_3), 55.4 (OCH_3), 64.5 ($^1J_{CP}$ = 161.6 Hz, CH), 106.4 (C_4-sp^2), 114.3 (ArC), 124.6 (ArC), 126.9 (J_{CP} = 2.1 Hz, ArC), 127.5 (ArC), 127.6 (2 × ArC), 127.8 (ArC), 129.6 (ArC), 133.4 (J_{CP} = 8.5 Hz, ArC), 139.3 ($^4J_{CP}$ = 4.6 Hz, ArC), 147.9 (ArC), 152.3 (ArC), 153.4 (C_3-sp^2), 157.6 (ArC) ppm. HRMS (ESI): MH^+, found 439.1791. $C_{24}H_{28}N_2O_4P$ requires 439.1787.

Dimethyl 3-Cyclopropyl-2-(4-methoxyphenyl)-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonate (21f). Yellow solid, mp 60−61 °C. Yield 0.29 g, 67%. ^1H NMR (300 MHz, $CDCl_3$): δ 0.72−0.83 (3H, m, $CH(\underline{CH_2})_2$), 1.00−1.06 (1H, m, $CH(\underline{CH_2})_2$), 1.28−1.35 (1H, m, $\underline{CH}(CH_2)_2$), 3.60 (3H, d, $^3J_{HP}$ = 10.8 Hz, OCH_3), 3.74 (3H, d, $^3J_{HP}$ = 10.5 Hz, OCH_3), 3.78 (3H, s, OCH_3), 5.29 (1H, d, $^1J_{HP}$ = 18.6 Hz, C_1H), 5.91 (1H, s, C_4H), 6.85 (2H, d, ^3J = 9.0 Hz, ArH), 7.32 (1H, t, ^3J = 7.2 Hz, ArH), 7.38 (2H, d, ^3J = 9.0 Hz, ArH), 7.55−7.66 (3H, m, ArH), 7.92 (1H, d, ^3J = 8.1 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 8.4 ($CH(\underline{CH_2})_2$), 11.5 ($CH(\underline{CH_2})_2$), 14.7 ($\underline{CH}(CH_2)_2$), 53.2 (d, $^2J_{CP}$ = 7.4 Hz, OCH_3), 53.7 (d, $^2J_{CP}$ = 6.3 Hz, OCH_3), 55.4 (OCH_3), 65.0 (d, $^1J_{CP}$ = 160.2 Hz, C_1H), 99.7 (C_4-sp^2), 114.1 (ArC), 119.5 (ArC), 124.6 (ArC), 126.7 (ArC), 127.4 (ArC), 127.4 (2 × ArC), 129.8 (ArC), 133.4 (d, $^3J_{CP}$ = 8.3 Hz, ArC), 139.3 (d, $^3J_{CP}$ = 4.5 Hz, ArC), 147.5 (ArC), 152.4 (ArC), 156.0 (C_3-sp^2), 157.4 (ArC) ppm. HRMS (ESI): MH^+, found 437.1633. $C_{24}H_{26}N_2O_4P$ requires 437.1625.

Dimethyl 3-Cyclopropyl-2-(4-fluorophenyl)-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonate (21g). Yellow solid, mp 60−61 °C. Yield 0.28 g, 67%. ^1H NMR (300 MHz, $CDCl_3$): δ 0.77−0.89 (3H, m, $CH(\underline{CH_2})_2$), 1.03−1.10 (1H, m, $CH(\underline{CH_2})_2$), 1.27−1.36 (1H, m, $\underline{CH}(CH_2)_2$), 3.63 (3H, d, $^3J_{HP}$ = 10.8 Hz, OCH_3), 3.76 (3H, d, $^3J_{HP}$ = 10.5 Hz, OCH_3), 5.30 (1H, dd, $^1J_{HP}$ = 18.3 Hz, ^3J = 0.6 Hz, C_1H), 6.04 (1H, s, C_4H), 7.00−7.06 (2H, m, ArH), 7.34−7.39 (1H, m, ArH), 7.46−7.48 (2H, m, ArH), 7.59−7.67 (2H, m, ArH), 7.71 (1H, d, $^4J_{HP}$ = 3.6 Hz, ArH), 8.00 (1H, d, ^3J = 8.4 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 8.7 ($CH(\underline{CH_2})_2$), 11.8 ($CH(\underline{CH_2})_2$), 14.8 ($\underline{CH}(CH_2)_2$), 53.3 (d, $^2J_{CP}$ = 7.4 Hz, OCH_3), 53.8 (d, $^2J_{CP}$ = 6.7 Hz, OCH_3), 64.8 (d, $^1J_{CP}$ = 161.0 Hz, C_1H), 100.4 (C_4-sp^2), 115.8 (d $^2J_{CF}$ = 22.5 Hz, ArC), 119.6 (ArC), 125.0 (ArC), 126.6 (ArC), 127.1 (ArC), 127.4 (ArC), 127.5 (ArC), 127.5 (ArC), 130.1 (ArC), 133.8 (d, $^3J_{CP}$ = 7.1 Hz, ArC), 142.1 (ArC), 151.8 (C_3-sp^2), 160.3 (d $^2J_{CF}$ = 244.8 Hz, ArC) ppm. HRMS (ESI): MH^+, found 425.1424. $C_{23}H_{23}FN_2O_3P$ requires 425.1425.

Dimethyl 2-(4-Chlorophenyl)-3-cyclopropyl-1,2-dihydrobenzo[*b*][1,6]naphthyridin-1-ylphosphonate (21h). Yellow solid, mp 78−80 °C. Yield 0.22 g, 50%.^1H NMR (300 MHz, $CDCl_3$): δ 0.79−0.92 (3H, m, $CH(\underline{CH_2})_2$), 0.99−1.05 (1H, m, $CH(\underline{CH_2})_2$), 1.29−1.38 (1H, m, $\underline{CH}(CH_2)_2$), 3.61 (3H, d, $^3J_{HP}$ = 10.5 Hz, OCH_3), 3.74 (3H, d, $^3J_{HP}$ = 10.8 Hz, OCH_3), 5.31 (1H, d, $^1J_{HP}$ = 18.3 Hz, C_1H), 6.04 (1H, s, C_4H), 7.26−7.39 (5H, m, ArH), 7.57−7.66 (2H, m, ArH), 7.69 (1H, d, $^4J_{HP}$ = 3.3 Hz, ArH), 7.81 (1H, d, ^3J = 8.4 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.0 ($CH(\underline{CH_2})_2$), 11.9 ($CH(\underline{CH_2})_2$), 14.7 ($\underline{CH}(CH_2)_2$), 53.3 (d, $^2J_{CP}$ = 7.4 Hz, OCH_3), 53.8 (d, $^2J_{CP}$ = 6.9 Hz, OCH_3), 64.5 (d, $^1J_{CP}$ = 161.3 Hz, C_1H), 102.2 (C_4-sp^2), 119.7 (ArC), 125.0 (ArC), 126.3 (ArC), 126.7 (ArC), 127.5 (d, J_{CP} = 3.3 Hz, ArC), 129.1 (ArC), 129.9 (ArC), 130.4 (ArC), 133.6 (d, $^3J_{CP}$ = 8.1 Hz, ArC), 144.6 (d, $^3J_{CP}$ = 4.2 Hz, ArC), 147.5 (ArC), 151.8 (ArC), 154.8 (C_3-sp^2) ppm. HRMS (ESI): MH^+, found 441.1147. $C_{23}H_{23}ClN_2O_3P$ requires 441.1129.

Synthesis of (*E*)-4-Methoxy-*N*-{[2-(phenylethynyl)quinolin-3-yl]methylene}aniline (22). A mixture of 2-phenylethynylquinoline-3-carbaldehyde **6a** (100 mg, 0.389 mmol), 4-methoxyaniline (47.84 mg, 0.389 mmol), and 3 Å MS (100 mg) was stirred in dry chloroform (5 mL). When completion of the reaction was observed by TLC, the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography eluting with hexane−ethyl acetate mixtures to afford 0.16 g (88%) of yellow solid. Mp 175−176 °C. IR (KBr): υ_{max} 2219 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.89 (3H, s, OCH_3), 7.02 (2H, d, ^3J = 8.9 Hz, ArH), 7.40 (2H, d, ^3J = 8.9 Hz, ArH), 7.42−7.47 (3H, m, ArH), 7.61 (1H, ddd, ^3J = 8.1 and 6.9 Hz, ^4J = 1.1 Hz, ArH), 7.70−7.72 (2H, m, ArH), 7.80 (1H, ddd, ^3J = 8.4 and 6.9 Hz, ^4J = 1.4 Hz, ArH), 7.96 (1H, d, ^3J = 7.9 Hz, ArH), 8.18 (1H, d, ^3J = 8.5 Hz, ArH), 9.06 (1H, s, ArH), 9.28, s, CH═N) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.5 (OCH_3), 86.68 (C_{sp}), 94.55 (C_{sp}), 114.2 (ArC), 121.8 (ArC), 122.6 (ArC), 127.2 (ArC), 127.7 (ArC), 128.6 (ArC), 128.8 (ArC), 129.2 (ArC), 129.5 (ArC), 130.2 (ArC), 131.3 (ArC), 132.2 (ArC), 134.3 (ArC), 143.6 (ArC), 144.6 (ArC), 149.0 (ArC), 154.8 (ArC), 158.9 (ArC) ppm. HRMS (ESI): MH^+, found 363.1500. $C_{25}H_{19}N_2O$ requires 363.1497.

Synthesis of Dimethyl (4-Methoxyphenylamino)[2-(pent-1-ynyl)quinolin-3-yl]methylphosphonate (23). To a solution of 2-(pent-1-ynyl)quinoline-3-carbaldehyde **6c** (100 mg, 0.448 mmol), 4-methoxyaniline (55.15 mg, 0.448 mmol), and dimethylphoshite (54.21 mg, 0.493 mmol) was added gold(III) bromide (19.58 mg, 0.0448 mmol). When the completion of the reaction was observed by TLC, the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography eluting with hexane−ethyl acetate mixtures to afford 0.16 g (83%) of yellow solid. Mp 118−119 °C. IR (KBr): υ_{max} 3298 (NH), 2211 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.12 (3H, t, ^3J = 7.2 Hz, CH_3), 1.76 (2H, sext, ^3J = 7.2 Hz, CH_2), 2.59 (2H, t, ^3J = 7.2 Hz, CH_2), 3.44 (3H, d, $^3J_{HP}$ = 10.8 Hz, OCH_3), 3.65 (3H, s, OCH_3), 3.88 (3H, d, $^3J_{HP}$ = 10.8 Hz, OCH_3), 4.81 (1H, br. s, NH), 5.57 (1H, d, $^1J_{HP}$ = 24.4 Hz, CH), 6.60 (2H, d, ^3J = 8.8 Hz, ArH), 6.67 (2H, d, ^3J = 8.8 Hz, ArH), 7.47 (1H, t, ^3J = 7.2 Hz, ArH), 7.66 (1H, t, ^3J = 7.2 Hz, ArH), 7.73 (1H, d, ^3J = 8.0 Hz, ArH), 8.05 (1H, d, ^3J = 8.4 Hz, ArH), 8.33 (1H, d, $^3J_{HP}$ = 2.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 21.6 (CH_2), 21.8 (CH_2), 52.6 (d, $^1J_{CP}$ = 152.6 Hz, CH), 53.7 (d, $^2J_{CP}$ = 7.3 Hz, OCH_3), 54.1 (d, $^2J_{CP}$ = 6.8 Hz, OCH_3), 55.6 (OCH_3), 78.6 (Csp^3), 97.0 (Csp^3), 114.8 (ArC), 114.9 (ArC), 127.0 (d, $^4J_{CP}$ = 2.9 Hz, ArC), 127.1 (ArC), 127.7 (ArC), 128.6 (ArC), 130.2 (ArC), 130.9 (ArC), 134.9 (ArC), 139.3 (d, $^3J_{CP}$ = 15.3 Hz, ArC), 143.5 (ArC), 147.2 (ArC), 152.8 (ArC) ppm. HRMS (ESI): MH^+, found 439.1789. $C_{24}H_{28}N_2O_4P$ requires 439.1781.

dx.doi.org/10.1021/jo501011u | *J. Org. Chem.* 2014, 79, 6532−6553

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of the reported compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The research was funded by the European Social Fund under the Global Grant measure (Grant No. VP1-3.1-ŠMM-07-K-01-002).

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Paper 2

Electrophile-Mediated Reactions of Functionalized Propargylic Substrates

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European Journal of Organic Chemistry (**2015**) 2015: 7091-7113
DOI: 10.1002/ejoc.201501063
https://onlinelibrary.wiley.com/doi/10.1002/ejoc.201501063

EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201501063

Electrophile-Mediated Reactions of Functionalized Propargylic Substrates

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Keywords: Alkynes / Electrophilic addition / Cyclization / Nitrogen heterocycles / Sulfur heterocycles / Regioselectivity

Metal-free halogen, chalcogen, or oxocarbenium ion mediated yne-carbonyl or yne-thioxo transformations of a range of *N*- and *O*-propargylic compounds have been studied. This investigation has led to the development of a mild, economic, and effective method for the synthesis of functionalized 4*H*-1,3-oxazines, 4*H*-1,3-thiazines, 4,5-dihydrothiazoles, and α-substituted enones. The structure of the propargylic substrate and the nature of electrophile influence both the outcome and regioselectivity of processes.

Introduction

In the past decade an explosive increase of interest in electrophile-mediated cyclizations of alkynes has taken place.[1] These methodologies have become an original field of carbo- and heterocycle synthesis and have enabled the formation of halogen- or chalcogen-substituted compounds. The obtained materials are suitable for further synthetic transformations. Electrophilic cyclizations of alkynes may be defined as processes that involve addition of an electrophilic source to sp-carbon centers and subsequent formation of cyclic compounds through attack of neighboring nucleophilic functionality through either *endo* or *exo* modes. The mode of cyclization normally depends on chain length, substitution pattern on the chain, and on the electrophile employed. Functionalized propargylic substrates are a specific class of alkynes with attractive chemical properties. It is known that these materials can undergo a number of skeletal rearrangements and cyclization reactions and these processes are usually mediated by activation of the triple bond by transition-metal salts.[2] Despite the fact that electrophilic cyclization reactions of alkynes bearing an internal nucleophile have emerged as a very efficient process to obtain a variety of prefunctionalized compounds, this type of activation is still not common for functionalized propargylic substrates.[3] Recently, we have found that electrophilic reagents (iodine or *N*-iodo succinimide, aldehydes or oxocarbenium ions) can be used to induce 1,3-acyloxy shifts in propargylic esters.[4] Moreover, at the beginning of 2015, we presented an electrophilic cyclization of *N*-(3-arylprop-2-ynyl)amides to functionalized 4*H*-1,3-oxazines.[5] These preliminary findings prompted us to study the scope of electrophile-mediated transformations of functionally substituted propargylic substrates. In this work, we present the results of our recent and more detailed investigations.

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Supporting Information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201501063.

Results and Discussion

As starting propargylic substrates we chose six classes of compounds: amides **1**, carbamates **2** and **5**, ureas **3**, thioureas **4**, and esters **6**. We utilized known methods for the preparation of these compounds. The strategy of their synthesis is presented in the Supporting Information. Structures of the starting materials are shown in Figure 1.

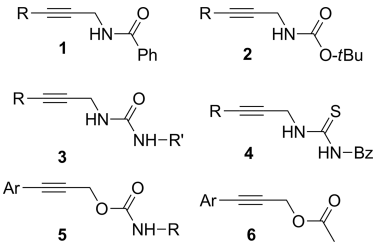
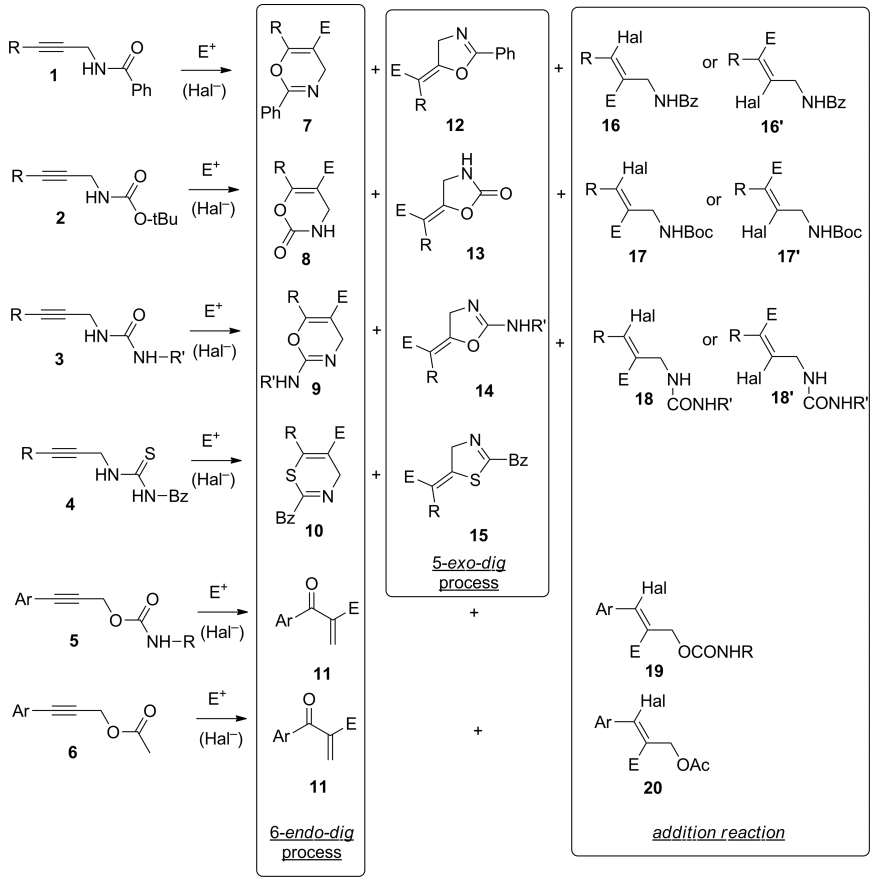


Figure 1. Structures of the starting materials. **1**: R = 4-$MeOC_6H_4$ (**a**); R = 4-$EtOC_6H_4$ (**b**); R = 3,4-$(MeO)_2C_6H_3$ (**c**); R = 3,4,5-$(MeO)_3C_6H_2$ (**d**); R = 4-MeC_6H_4 (**e**); R = Ph (**f**); R = 4-ClC_6H_4 (**g**); R = 4-$O_2NC_6H_4$ (**h**); R = H (**i**). **2**: R = 4-$MeOC_6H_4$ (**a**); R = 3,4-$(MeO)_2C_6H_3$ (**b**); R = 3,4-$(OCH_2O)C_6H_3$ (**c**); R = 4-MeC_6H_4 (**d**); R = Ph (**e**); R = 4-ClC_6H_4 (**f**); R = 4-$O_2NC_6H_4$ (**g**); R = H (**h**). **3**: R = 4-$MeOC_6H_4$; R′ = Ts (**a**); R = 4-$MeOC_6H_4$; R′ = Ph (**b**); R = 4-$MeOC_6H_4$; R′ = Bn (**c**); R = 3,4-$(MeO)_2C_6H_3$; R′ = Ts (**d**); R = 4-MeC_6H_4; R′ = Bn (**e**); R = 4-MeC_6H_4; R′ = Ts (**f**); R = Ph; R′ = Ts (**g**); R = 4-ClC_6H_4; R′ = Ts (**h**); R = H; R′ = Ts (**i**); R = H; R′ = Ph (**j**); R = H; R′ = Bn (**k**). **4**: R = 4-$MeOC_6H_4$ (**a**); R = 4-ClC_6H_4 (**b**); R = Ph (**c**); R = H (**d**). **5**: Ar = 4-$MeOC_6H_4$; R = Ts (**a**); Ar = 4-$MeOC_6H_4$; R = Bn (**b**). **6**: Ar = 4-$MeOC_6H_4$ (**a**); Ar = Ph (**b**).

With synthesized propargylic substrates in hand, we explored the scope of electrophile-mediated reactions. For the



Scheme 1. General outcomes of electrophile-mediated reactions of propargylic substrates.

chosen model substrates and electrophile sources, we performed detailed optimization processes, including an investigation of solvent, temperature, base, and stoichiometry; the results of optimization study are presented in the Supporting Information (Table S1). With appropriate reactions conditions for halogen-, chalcogen-, and oxocarbenium ion mediated reactions established, we synthesized a wide range of functionalized heterocyclic compounds and α-substituted enones. The results are presented in chapters 1–3 together with some concluding remarks on the reactions, which are presented in chapter 4. The general trends of reactivity of the studied propargylic substrates are shown in Scheme 1.

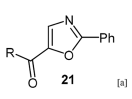
1. Halogen-Mediated Reaction of Propargylic Substrates

Reactions between propargylic substrates and iodine electrophile sources proceeded well and resulted in the formation of iodo-substituted 4*H*-1,3-oxazines **7**–**9**, 4*H*-1,3-thiazines **10**, and α-iodoenones **11** as main reactions products. Whereas amides **1** and carbamates **5** underwent smooth and chromatographically clean transformations with *N*-iodosuccinimide (NIS) in CH_2Cl_2 at ambient temperature, other substrates required some modification of the procedure (see Table S1). Thus, two equivalents of molecular iodine in either CH_2Cl_2 or acetonitrile at 0 °C were the best conditions for iodocyclizations of carbamates **2** and ureas **3**. Ester **6a** participated in competitive electrophilic addition reaction during NIS or molecular iodine[4a] mediated transformation and therefore the yield of isolated iodinated enone **11aa** was low (Table 1, entry 41). *N*-Bromosuccinimide (NBS) was not efficient for such transformations. Whereas carbamates **2** formed six-membered bromoderivatives **8** in low yields (entries 11, 13, 16, 18, and 20), NBS-mediated reactions of amides **1**, ureas **3**, carbamates **5**, and esters **6** were problematic and resulted in low conversions of the starting materials (data not shown). *N*-Chlorosuccinimide was completely ineffective.

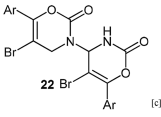
As seen from Table 1, substrates bearing an electron-rich aryl group next to the triple bonds (amides **1a**–**f**, carbamates **2a**–**f** and **5a**,**b**, ureas **3a**,**c**–**g**, and ester **6a**; entries 1–

Table 1. Data on the halogen-mediated reactions of substrates.

Entry	Starting material	Reaction conditions	E^+	Products		
				6-*endo*-*dig*	5-*exo*-*dig*	Addition or side reaction
				(yield, %)	(yield, %)	(yield, %)
1	**1a**: R = 4-MeOC$_6$H$_4$		I^+	**7aa** (72)	–	–
2	**1b**: R = 4-EtOC$_6$H$_4$		I^+	**7ba** (58)	–	–
3	**1c**: R = 3,4-(MeO)$_2$C$_6$H$_3$		I^+	**7ca** (52)	–	–
4	**1d**: R = 3,4,5-(MeO)$_3$C$_6$H$_2$		I^+	**7da** (60)	–	–
5	**1e**: R = 4-MeC$_6$H$_4$	NIS (1.1 equiv.), DCM, r.t.	I^+	**7ea** (58)	–	–
6	**1f**: R = C$_6$H$_5$		I^+	**7fa** (52)	–	–
7	**1g**: R = 4-ClC$_6$H$_4$		I^+	**7ga** (20)	**12ga** (41), **21ga**[a] (18)	–
8	**1h**: R = 4-O$_2$NC$_6$H$_4$		I^+	**7ha** (24)	**21ha**[a] (16)	–
9	**1i**: R = H		I^+	–	**21ia**[a] (16)	**16ia** (Hal = I) (41)[b]
10	**2a**: R = 4-MeOC$_6$H$_4$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	**8aa** (68)	–	–
11	**2a**	NBS (1.1 equiv.), DCM, r.t.	Br^+	**8ab** (30)	–	–
12	**2b**: R = 3,4-(MeO)$_2$C$_6$H$_3$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	**8ba** (67)	–	–
13	**2b**	NBS (1.1 equiv.), DCM, r.t.	Br^+	**8bb** (53)	–	–
14	**2c**: R = 3,4-(OCH$_2$O)C$_6$H$_3$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	**8ca** (60)	–	–
15	**2d**: R = 4-MeC$_6$H$_4$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	**8da** (65)	–	–
16	**2d**	NBS (1.1 equiv.), DCM, r.t.	Br^+	**8db** (39)	–	**22db** (7)[c]
17	**2e**: R = C$_6$H$_5$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	**8ea** (52)	–	**17ea** (Hal = I) (9)
18	**2e**	NBS (1.1 equiv.), DCM, r.t.	Br^+	**8eb** (39)	–	**22eb** (7)[c]
19	**2f**: R = 4-ClC$_6$H$_4$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	**8fa** (54)	–	–
20	**2f**	NBS (1.1 equiv.), DCM, r.t.	Br^+	**8fb** (24)	–	**22fb** (14)[c]
21	**2g**: R = 4-O$_2$NC$_6$H$_4$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	traces	**13ga** (17)	–
22	**2g**	NBS (1.1 equiv.), DCM, r.t.	Br^+	traces	**13gb** (11)	–
23	**2h**: R = H	I$_2$ (2 equiv.), DCM, 0 °C	I^+	–	traces	**17ha** (Hal = I) (26)
24	**3a**: R = 4-MeOC$_6$H$_4$; R' = Ts		I^+	**9aa** (73)	–	–
25	**3c**: R = 4-MeOC$_6$H$_4$; R' = Bn		I^+		mixture of products	
26	**3d**: R = 3,4-(MeO)$_2$C$_6$H$_3$; R' = Ts		I^+	**9da** (55)	–	–
27	**3e**: R = 4-MeC$_6$H$_4$; R' = Bn		I^+		mixture of products	
28	**3f**: R = 4-MeC$_6$H$_4$; R' = Ts	I$_2$ (2 equiv.), MeCN, 0 °C	I^+	**9fa** (93)		
29	**3g**: R = C$_6$H$_5$; R' = Ts		I^+	**9ga** (59)	traces	–
30	**3i**: R = H; R' = Ts		I^+	–	**14ia** (71)	**18ia** (Hal = I) (16)
31	**3j**: R = H; R' = Ph		I^+	–	**14ja** (47)	–
32	**3k**: R = H; R' = Bn		I^+	–	**14ka** (49)	–
33	**4a**: R = 4-MeOC$_6$H$_4$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	**10aa** (59)	traces	–
34	**4a**	NBS (1.1 equiv.), DCM, r.t.	Br^+	**–**	**15ab** (68)	–
35	**4b**: R = 4-ClC$_6$H$_4$	NBS (1.1 equiv.), DCM, r.t.	Br^+		**15bb** (44)	–
36	**4c**: R = C$_6$H$_5$	I$_2$ (2 equiv.), DCM, 0 °C	I^+	**10ca** (18)	**15ca** (25)	–
37	**4c**	NBS (1.1 equiv.), DCM, r.t.	Br^+		**15cb** (67)	–
38	**4d**: R = H	I$_2$ (2 equiv.), DCM, 0 °C	I^+		**15da** (20)	–
39	**5a**: Ar = 4-MeOC$_6$H$_4$; R = Ts	NIS (1.1 equiv.), DCM, r.t.	I^+	**11aa** (52)	–	traces
40	**5b**: Ar = 4-MeOC$_6$H$_4$; R = Bn		I^+	**11aa** (60)	–	–
41	**6a**: Ar = 4-MeOC$_6$H$_4$	NIS (1.1 equiv.), DCM, r.t.	I^+	**11aa** (36)		**20aa** (27)[b]



21 [a]



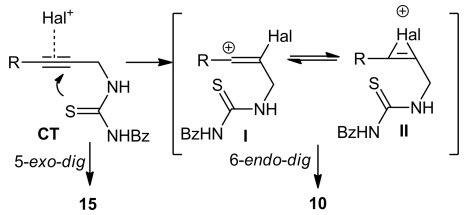
22 [c]

[a] Aryl(2-phenyloxazol-5-yl)methanones **21ga** and **21ha**, and 2-phenyloxazole-5-carbaldehyde **21ia** were isolated. [b] The same compound was obtained by using molecular iodine in CH_2Cl_2 at room temp. [c] 6,6′-Diaryl-5,5′-dibromo-3′,4′-dihydro-2′*H*-3,4′-bi(1,3-oxazine)-2,2′(4*H*)-diones **22** formed as minor products.

6, 10–18, 24, 26, 28, 29, and 39–41) underwent regioselective and dominant 6-*endo-dig* processes under halonium ion mediated reactions. Iodine-mediated reactions of starting materials with electron-poor aryl groups next to the triple bond (**1g**, **1h**, and **2g**) proceeded slowly and ineffectively. Thus, *N*-[3-(4-chloro or 4-nitrophenyl)prop-2-ynyl]benzamides **1g** and **1h** formed a mixture of six-membered and five-membered heterocyclic products **7**, **12**, and **21** in NIS-mediated cyclizations (entries 7 and 8). By using starting *tert*-butyl 3-(4-nitrophenyl)prop-2-ynylcarbamate **2g** (entries 21 and 22) or 1-substituted-3-(prop-2-ynyl)ureas **3j** and **3k** (entries 31 and 32), regioselective formation of 5-*exo-dig* cyclization products in halogen-mediated reactions was observed. In some cases, terminal propargylic substrates in halogen-mediated reactions formed mixtures of isoxazole ring containing compounds and products of electrophilic addition reactions (entries 9, 23 and 30).

In contrast to the chemistry of amides, carbamates and ureas, iodine-mediated cyclizations of electron-rich thioureas **4** were unselective (entries 33 and 36) and we were surprised when these starting materials underwent ring-closure through the 5-*exo-dig* mode exclusively during halogen-mediated cyclizations (entries 34, 35, and 37). The structures of all six- and five-membered cyclic products were established based on NMR spectroscopic analysis. In particular, after assignment of carbon signals by using a combination of COSY, HSQC, and HMBC experiments, the analysis of HMBC spectra of all cyclic products was performed. In the case of compounds **15**, the presenting cross-peaks between *ortho* protons of C(6)-Ar and C_{sp2}-Br or C_{sp2}-I nuclei indicated a five-membered core. In the HMBC spectra of six-membered cyclic compounds **10**, cross-peaks between *ortho* protons of C(6)-Ar and C_{sp2}-Br or C_{sp2}-I nuclei were absent.

It is known that because of the large size and ready polarization, sulfur is a stronger nucleophile than oxygen; therefore, cyclizations of thioureas **4** proceeded more readily than analogous reactions of amides **1**, carbamates **2**, and ureas **3**. We presume that in bromine-mediated cyclizations of thioureas **4**, nucleophilic attack occurs just after the initial formation of the charge-transfer complex between the bromonium ion and the triple bond.[6] The carbon–carbon triple bond in charge transfer (CT) complexes between alkyne and halogen remains linear; therefore, nucleophilic sulfur attack occurs through the 5-*exo-dig* mode. From the results obtained, we hypothesized that during the iodonium-mediated reaction, two possible pathways are possible: 5-*exo-dig* cyclization reaction occurs after formation of a CT complex and competing 6-*endo-dig* cyclization takes place after conversion of the CT complex into open iodovinyl (**I**) or bridged iodirenium[7] (**II**) ions (Scheme 2).



Scheme 2. Possible mechanisms of halogen-mediated 5-*exo-dig* and 6-*endo-dig* cyclizations of thioureas **4**.

2. Phenyl Hypochloroselenoite Mediated Reaction of Propargylic Substrates

After investigation of halogen-mediated reactions, we turned our attention to phenyl hypochloroselenoite as a source of chalcogen-electrophile. It should be noted that the presence of base (*t*BuOK for amides **1** and $K_3PO_4 \cdot H_2O$ for carbamates **2**) is required for successful reactions (see the Supporting information, Table S1). In contrast, ureas **3** and thioureas **4** underwent phenyl hypochloroselenoite-triggered base-independent and selective reactions.

Propargylic amides **1** and Boc-protected propargylic amines **2** during reactions with phenyl hypochloroselenoite underwent smooth 6-*endo-dig* cyclizations. However, both classes of these substrates also underwent side addition reactions and (*E*)-*N*-[3-aryl-3-chloro-2-(phenylselanyl)allyl]-benzamides **16** (Table 2, entries 1–6) or (*E*)-*tert*-butyl 3-aryl-3-chloro-2-(phenylselanyl)allylcarbamates **17** formed (entries 10–14). When starting compounds **1i** and **2h**, with terminal alkyne groups, were used, the regioselectivity of the addition reaction differed and compounds **16′ib** and **17′hc** were isolated (entries 9 and 15).

Ureas **3** and thioureas **4**, having electron-rich aryl groups next to the triple bond, underwent regioselective phenyl hypochloroselenoite triggered base-free 6-*endo-dig* cyclizations, and electrophilic addition did not take place (Table 2, entries 16, 17, 19–21, and 25–27). However, terminal propargylic ureas **3j** and **3k**, and thiourea **4d** in the reaction with phenyl hypochloroselenoite formed 4,5-dihydrothiazoles **14** and **15** through 5-*exo-dig* cyclization (entries 23, 24, and 28). The exception was 4-methyl-*N*-(prop-2-ynylcarbamoyl)-benzenesulfonamide (**3i**), which did not participate in cyclization reaction and, after treatment with the reagent, converted into (*E*)-*N*-[2-chloro-3-(phenylselanyl)allylcarbamoyl]-4-methylbenzenesulfonamide (**18′ib**; entry 22).

Unfortunately, carbamate **5a** and ester **6a**, having *O*-propargyl functionality, did not undergo the expected rearrangement reaction with phenyl hypochloroselenoite, and high-yielding electrophilic addition reaction took place (Table 2, entries 29 and 30).

3. Oxocarbenium Ion Mediated Reaction of Propargylic Substrates

Another group of electrophiles that we studied were oxocarbenium ions formed from acetals through Lewis acid mediation. The data obtained are presented in Table 3 and Table 4.

Reactions between 1-methoxyisochroman and propargylic substrates proceeded smoothly and regioselectively. However, the activation of the triple bond by an electron-

Table 2. Data for the phenyl hypochloroselenoite mediated reactions of substrates.

Entry	Starting material	Reaction conditions	Products (E = PhSe-)		
			6-*endo-dig* (yield, %)	5-*exo-dig* (yield, %)	Addition (Hal = Cl) (yield, %)
1	**1a**: R = 4-MeOC$_6$H$_4$	PhSeCl (1 equiv.), *t*BuOK (1 equiv.), DCM, r.t.	**7ab** (66)	–	**16ab** (13)
2	**1b**: R = 4-EtOC$_6$H$_4$		**7bb** (65)	–	**16bb** (12)
4	**1c**: R = 3,4-(MeO)$_2$C$_6$H$_3$		**7cb** (68)	–	**16cb** (19)
5	**1d**: R = 3,4,5-(MeO)$_3$C$_6$H$_2$		**7db** (63)	–	traces
6	**1f**: R = C$_6$H$_5$		**7fb** (57)	–	traces
7	**1g**: R = 4-ClC$_6$H$_4$		mixture of products		
8	**1h**: R = 4-O$_2$NC$_6$H$_4$		no reaction		
9	**1i**: R = H		–	**12ib** (26)	**16'ib** (20)
10	**2a**: R = 4-MeOC$_6$H$_4$	PhSeCl (1 equiv.), K$_3$PO$_4$·H$_2$O (1 equiv.), MeCN, 0 °C	**8ac** (86)	–	**17ac** (9)
11	**2b**: R = 3,4-(MeO)$_2$C$_6$H$_3$		**8bc** (42)	–	**17bc** (18)
12	**2c**: R = 3,4-(OCH$_2$O)C$_6$H$_3$		**8cc** (56)	–	**17cc** (26)
13	**2d**: R = 4-MeC$_6$H$_4$		**8dc** (42)	–	**17dc** (31)
14	**2g**: R = 4-O$_2$NC$_6$H$_4$		**8gc** (10)	–	**17gc** (25)
15	**2h**: R = H		traces	–	**17'hc** (75)
16	**3a**: R = 4-MeOC$_6$H$_4$; R' = Ts	PhSeCl (1 equiv.), MeCN, 0 °C	**9ab** (82)	–	–
17	**3b**: R = 4-MeOC$_6$H$_4$; R' = Ph		**9bb** (92)	–	–
18	**3c**: R = 4-MeOC$_6$H$_4$; R' = Bn		mixture of products		
19	**3d**: R = 3,4-(MeO)$_2$C$_6$H$_3$; R' = Ts		**9db** (73)	–	–
20	**3f**: R = 4-MeC$_6$H$_4$; R' = Ts		**9fb** (80)	–	–
21	**3g**: R = C$_6$H$_5$; R' = Ts		**9gb** (63)	–	–
22	**3i**: R = H; R' = Ts		–	–	**18'ib** (94)
23	**3j**: R = H; R' = Ph		–	**14jb** (27)	
24	**3k**: R = H; R' = Bn		–	**14kb** (40)	–
25	**4a**: R = 4-MeOC$_6$H$_4$	PhSeCl (1 equiv.), DCM, 0 °C	**10ab** (73)	–	–
26	**4b**: R = 4-ClC$_6$H$_4$		**10bb** (51)	–	–
27	**4c**: R = C$_6$H$_5$		**10cb** (56)	traces	–
28	**4d**: R = H		–	**15db** (45)	–
29	**5a**: Ar = 4-MeOC$_6$H$_4$; R = Ts	PhSeCl (1 equiv.), DCM, r.t.	–	–	**19ab** (79)
30	**6a**: Ar = 4-MeOC$_6$H$_4$		–	–	**20ab** (78)

rich aryl group was required for successful 6-*endo-dig* reaction. Thus, functionalized aryl-substituted propargylic amides **1**, carbamates **2**, ureas **3**, or thioureas **4** in the present reaction formed 5-(isochroman-1-yl)-4*H*-1,3-oxazines or 5-(isochroman-1-yl)-4*H*-1,3-thiazines in good yields (Table 3, entries 1–6, 9–13, 16, 18–21, and 23–25). Compounds bearing either a terminal propargylic fragment or an electron-poor aromatic ring were not active towards 3,4-dihydroisochromenylium ion mediated reactions (entries 7, 8, 14, 15, 22, 26). 1-Benzyl-3-[3-(4-methoxyphenyl)prop-2-ynyl]urea (**3c**) in reaction with 1-methoxyisochroman formed a mixture of inseparable products (entry 17) and we suppose that this is dictated by the two nucleophilic atoms (carbonyl oxygen and the nitrogen of the benzylamino fragment) presenting in the functional group. Analogous unselective reactions of **3c** were observed for halogen- and phenyl hypochloroselenoite triggered reactions (Table 1, entries 25 and 27, and Table 2, entry 18).

Esters **6** and carbamates **5** underwent our previously reported[4a] 6-*endo-dig* rearrangement reactions to 1-aryl-2-(isochroman-1-yl)-1prop-2-en-1-ones **11** (Table 3, entries 27–30). It should be noted that parallel reactions between starting materials and Lewis acids without acetals were also performed. In almost all cases, slow decomposition of the starting materials occurred.

Reactions between propargylic amides **1** and acyclic acetals under the optimized conditions (Table S1) led to the formation of predominantly six-membered products **7**, with minor amounts of enones **23** and **24** (Table 4, entries 1–8). After the activation of acetals by oxophilic Lewis acids

Table 3. Data for the 3,4-dihydroisochromenylium ion mediated reactions of substrates.

Entry	Starting material	Reaction conditions	E^+	6-*endo-dig* process product (yield, %)
1	**1a**: R = 4-$MeOC_6H_4$	1-methoxyisochroman (1 equiv.), TMSOTf (1 equiv.), DCM, r.t.		**7ac** (78)
2	**1b**: R = 4-$EtOC_6H_4$			**7bc** (53)
3	**1c**: R = 3,4-$(MeO)_2C_6H_3$			**7cc** (70)
4	**1d**: R = 3,4,5-$(MeO)_3C_6H_2$			**7dc** (54)
5	**1e**: R = 4-MeC_6H_4			**7ec** (81)
6	**1f**: R = C_6H_5			**7fc** (78)
7	**1h**: R = 4-$O_2NC_6H_4$			**7hc** (14), together with 60% of **1h**
8	**1i**: R = H			no reaction
9	**2a**: R = 4-$MeOC_6H_4$	1-methoxyisochroman (1 equiv.), $BF_3{\cdot}OEt_2$ (1 equiv.), DCM, 0 °C		**8ad** (35)
10	**3b**: R = 3,4-$(MeO)_2C_6H_3$			**8bd** (55)
11	**3d**: R = 4-MeC_6H_4			**8dd** (49)
12	**3e**: R = C_6H_5			**8ed** (40)
13	**3f**: R = 4-ClC_6H_4			**8fd** (29)
14	**2g**: R = 4-$O_2NC_6H_4$			no reaction
15	**2h**: R = H			no reaction
16	**3a**: R = 4-$MeOC_6H_4$; R' = Ts	1-methoxyisochroman (1 equiv.), TMSOTf (1 equiv.), DCM, 0 °C		**9ac** (74)
17	**3c**: R = 4-$MeOC_6H_4$; R' = Bn			mixture of products
18	**3d**: R = 3,4-$(MeO)_2C_6H_3$; R' = Ts			**9dc** (88)
19	**3f**: R = 4-MeC_6H_4; R' = Ts			**9fc** (92)
20	**3g**: R = C_6H_5; R' = Ts			**9gc** (90)
21	**3h**: R = 4-ClC_6H_4; R' = Ts			**9hc** (62)
22	**3k**: R = H; R' = Ts			no reaction
23	**4a**: R = 4-$MeOC_6H_4$	1-methoxyisochroman (1 equiv.), $BF_3{\cdot}OEt_2$ (1 equiv.), MeCN, 0 °C		**10ad** (82)
24	**4b**: R = 4-ClC_6H_4			**10bd** (55)
25	**4c**: R = C_6H_5			**10cd** (64)
26	**4d**: R = H			no reaction
27	**5a**: Ar = 4-$MeOC_6H_4$; R = Ts	1-methoxyisochroman (1 equiv.), TMSOTf (1 equiv.), DCM, r.t.		**11ac** (59)
28	**5b**: Ar = 4-$MeOC_6H_4$; R = Bn			**11ac** (71)
29	**6a**: Ar = 4-$MeOC_6H_4$			**11ac** (90)
30	**6b**: Ar = C_6H_5			**11bc** (83)

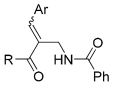
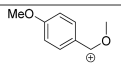
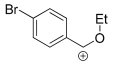
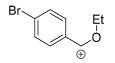
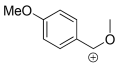
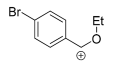
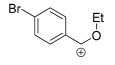
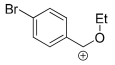
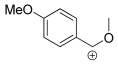
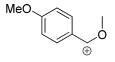
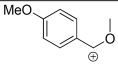
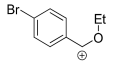
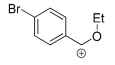
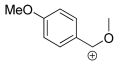
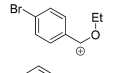
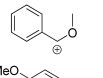
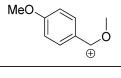
($BF_3{\cdot}OEt_2$ or TMSOTf) the formation of electrophilic oxocarbenium ions occur. After addition of the electrophile to the triple bond of amide **1**, two possible intramolecular reactions of the resulting ion **I** can then take place concurrently. The desired reaction (Route a) is 6-*endo-dig* O-nucleophilic attack resulting in cyclization products. The side reaction is ring closure to four-membered 1,2-dihydrooxetium intermediate **IV** and subsequent cycloreversion to enones[9] (Scheme 3).

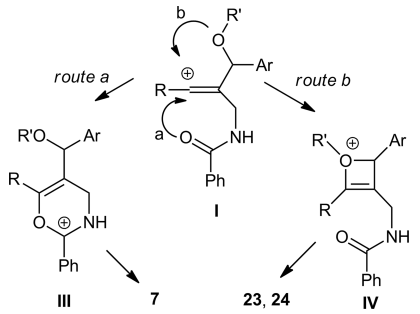
In contrast, *N*-(3-arylprop-2-ynylcarbamothioyl)benzamides **4** reacted with acyclic acetals selectively and formed *N*-{5-[alkoxy(aryl)methyl]-6-aryl-4*H*-1,3-thiazin-2-yl}benzamides **10** in good yield (Table 4, entries 11–18).

4. Factors Affecting the Outcome of Electrophile Mediated Reactions of Propargylic Substrates

Some general remarks on the investigated reactions can be made. First, almost all investigated propargylic substrates undergo cyclization or rearrangement reactions and these processes usually dominate over simple electrophilic addition reactions. Second, the outcomes of the studied reactions depend on three main factors: electron density on the alkyne, the electrophile used, and the structure of the functional nucleophilic group. Thus, the rates of the reactions as well as the regioselectivity of the processes depend strongly on the substituent next to the triple bond. Reac-

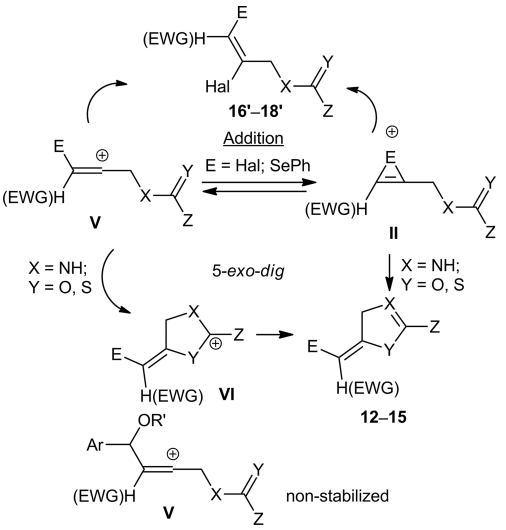
Table 4. Data for arylideneoxonium ion mediated reactions of substrates.

Entry	Starting material	Reaction conditions	E^+	Products	
				6-*endo-dig* (yield, %)	Metathesis  **23**(*E*), **24** (*Z*) (yield, %)
1	**1a**: R = 4-MeOC$_6$H$_4$	ArCH(OR')$_2$ (1.5 equiv.), BF_3·OEt$_2$ (1 equiv.), DCM, −10 °C		**7ad** (51);	**23ad** (10), **24ad** (11)
2	**1a**			**7ae** (54);	**23ae** (15), **24ae** (5)
3	**1c**: R = 3,4-(MeO)$_2$C$_6$H$_3$			**7ce** (49)	traces
4	**1e**: R = 4-MeC$_6$H$_4$			**7ed** (47)	**23ed** (11)
5	**1e**			**7ee** (48)	**23ee** (22), **24ee** (traces)
6	**1e**			**7ef** (50)	**23ef** (10)
7	**1f**: R = C$_6$H$_5$			**7fe** (54)	**23fe** (6)
8	**1g**: R = 4-ClC$_6$H$_4$			**7ge** (52)	**23ge** (11)
9	**1h**: R = 4-O$_2$NC$_6$H$_4$			no reaction	
10	**1i**: R = H			no reaction	
11	**4a**: R = 4-MeOC$_6$H$_4$	ArCH(OR')$_2$ (1.5 equiv.), TMSOTf (1 equiv.), DCM, −10 °C		**10ae** (76)	–
12	**4a**			**10af** (59)	–
13	**4a**			**10ag** (58)	–
14	**4b**: R = 4-ClC$_6$H$_4$			**10bf** (57)	–
15	**4b**			**10bg** (65)	–
16	**4c**: R = C$_6$H$_5$			**10ce** (81)	–
17	**4c**			**10cf** (60)	–
18	**4c**			**10cg** (57)	–
19	**4d**: R = H			no reaction	



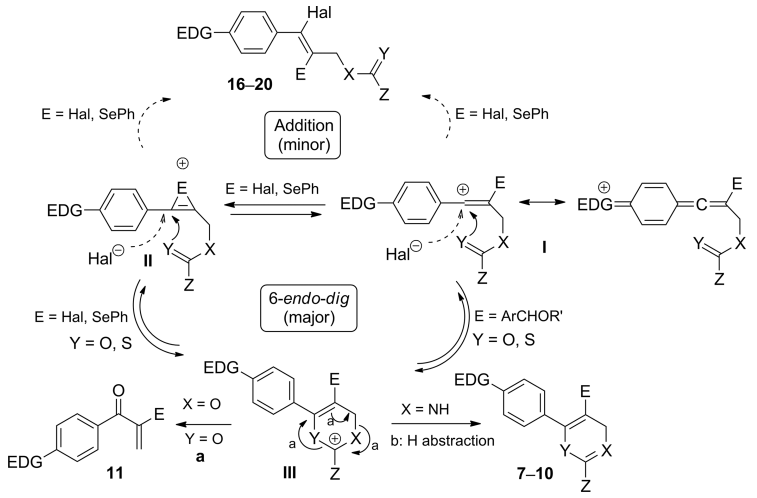
Scheme 3. Intermediates in reactions between propargylic amides with acyclic oxocarbenium electrophiles.

tions of substrates bearing electron-donating aryl groups proceeded smoothly and usually in selective 6-*endo-dig* mode. These observations could be logically explained by participation of the electron-donating aryl group in stabilization of the intermediate vinylic carbocation **I** formed during the first stage of the electrophilic activation (Scheme 4). Starting materials with electron-poor aryl groups (4-ClC_6H_4-, 4-$O_2NC_6H_4$-) next to the triple bond, or terminal propargylic substrates were not so active in electrophile-mediated reactions. These materials required prolonged reactions times for full conversion, and yields of isolated products were not high. Moreover, usually a change of cyclization mode from 6-*endo* into 5-*exo* was observed. The different regioselectivity can be explained by participation of CH_2FG groups in the inductive stabilization of the neighboring cationic center of the formed vinylic carbocation **V** (Scheme 5).



Scheme 5. Stabilization of vinylic carbocation **I** and subsequent 5-*exo-dig* processes of electron-poor propargylic substrates.

Undesired electrophilic additions can take place during halonium- or phenyl hypochloroselenoite mediated reactions, because nucleophilic anions are present in the media. Thus, during activation of the triple bond by Hal^+ or $PhSe^+$ ions, the formation of vinylic carbocations **I** can take place. The open-chain vinylic carbocations **I** can be in equilibrium with haloirenium or selenirenium ions **II**, which is consistent with recent experimental and theoretical studies.[7,8] Neither open-chain nor cyclic antiaromatic ions are very stable and the subsequent nucleophilic attack of the neigh-



Scheme 4. Stabilization of vinylic carbocation **I** and subsequent 6-*endo-dig* processes of electron-rich propargylic substrates.

boring functional group or halogen counterion takes place readily. We suppose that the dominant process is dictated by the nucleophilicity of the internal functional group and by the stability of cyclic intermediates **III**. When the nucleophilicity of the internal functional group is high (as for ureas **3** and thioureas **4**), usually an exclusive cyclization process occurs. In the opposite case, the halogen counterion acts as a nucleophile and formation of side addition products **16**–**20** takes place (Scheme 4). Notably, the stability of the six-membered cationic intermediates **III** depends on the type of heterocyclic cation. Thus, 4*H*-1,3-dioxin-2-ylium ions (X = Y = O) seem to be less stable than 4*H*-1,3-oxazin-3-ium (X = NH; Y = O) or 4*H*-1,3-thiazin-3-ium (X = NH; Y = S) ions. Therefore, electrophilic addition reactions of *O*-propargyl derivatives **5** and **6** can dominate in halonium and phenyl chloroselenoite mediated processes (Table 1, entry 41 and Table 2, entries 29 and 30).

Third, we observed that, in all successful cases, either the carbonyl oxygen or the thiocarbonyl sulfur acted as nucleophiles during the transformations. Fourth, the data obtained from these studies indicate the main difference in electrophile-mediated reactions between compounds bearing *O*- and *N*-propargyl functionality. Whereas compounds bearing *N*-propargyl groups (amides **1**, carbamates **2**, ureas **3**, and thioureas **4**) underwent electrophilic cyclization reactions quite easily, in the case of the corresponding *O*-propargyl derivatives (carbamates **5** and esters **6**), transformations into α-functionalized enones took place (Scheme 4).

It is worth mentioning that propargylic substrates **1h**,**i**, **2g**,**h**, **3k**, and **4d**, bearing a terminal or 4-nitrophenyl substituent, were completely unreactive towards oxocarbenium electrophiles (Table 3, entries 8, 14, 15, 22, and 26; Table 4, entries 9, 10, and 19). However, in contrast, reactions of these materials with iodine or phenylhypochloroselenoite proceeded, albeit ineffectively. This fact indicates that the ability to form cyclic haloirenium or selenirenium ions plays a role in the partial stabilization of vinylic carbocations. Therefore, unactivated propargylic substrates react with halogen- or chalcogen-based electrophiles, but do not undergo oxocarbenium ion mediated transformations because of the lack of stabilization (Scheme 5).

Conclusions

We have shown that substrates with various *N*- and *O*-propargil moieties can undergo electrophile-triggered reactions without the need for transition-metal catalysis. The scope and limitations of these processes were investigated by using a broad range of substrates. Based on our findings, efficient synthetic protocols for functionalized 4*H*-1,3-oxazines, 4*H*-1,3-thiazines, and 4,5-dihydrothiazoles have been developed. These methodologies permit one-step formation of heterocycle and simultaneous installation of halogen, chalcogen, or benzyl ether functionality onto the ring. Moreover, we proved that whereas propargylamine derivatives undergo electrophilic cyclization reactions, materials having a propargyloxy group can rearrange into α-functionalized enones. We expect that the presented processes will find applications in the synthesis of complex structures.

Experimental Section

General Information: IR spectra were recorded from KBr discs. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz in [D]chloroform or [D_6]dimethyl sulfoxide, using residual solvent signal as internal standard. Signal multiplicity is abbreviated as: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet). Unambiguous assignment of signals was made by using a combination of NMR experiments, including COSY, HSQC, and HMBC. High-resolution mass spectra were recorded with a Dual-ESI Q-TOF 6520 mass spectrometer with electrospray ionization. All reactions and the purity of the synthesized compounds were monitored by TLC using silica gel 60 F254 aluminum plates. Visualization was accomplished under UV light and by treating the plates with vanillin stain followed by heating.

General Procedures for Halogen-Mediated Reactions

Method A: To a solution of **1**, **5**, or **6** (1 mmol) in dichloromethane (5 mL), *N*-iodosuccinimide (0.25 g, 1.1 mmol) was added. The mixture was stirred at room temperature.

Method B: To a cooled solution of **2** or **4** (1 mmol) in anhydrous chloroform (5 mL) or **3** (1 mmol) in anhydrous acetonitrile (5 mL), molecular iodine (0.51 g, 2 mmol) was added at 0 °C. The resulting stirred solution was warmed to room temperature.

Method C: To a solution of **2** or **4** (1 mmol) in dichloromethane (5 mL), *N*-bromosuccinimide (0.19 g, 1.1 mmol) was added. The mixture was stirred at room temperature.

Isolation Procedures for All Products: When completion of the reaction was determined by TLC analysis, the reaction was quenched with aqueous sodium thiosulfate. The organic layer was separated, washed with aqueous sodium thiosulfate (2 × 20 mL), and then with water (2 × 20 mL), and dried with anhydrous Na_2SO_4. After the evaporation of solvent under reduced pressure, the residue was purified by flash column chromatography eluting with hexane/ethyl acetate mixtures.

5-Iodo-6-(4-methoxyphenyl)-2-phenyl-4*H*-1,3-oxazine (7aa): Yield 0.28 g (72%); white solid; m.p. 119–120 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, OCH_3), 4.56 (s, 2 H, CH_2), 6.96 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.48 (tt, ^3J = 7.6, ^4J = 2.4 Hz, 1 H, ArH), 7.63 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.95–7.97 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2 (CH_2), 55.4 (OCH_3), 69.8 (CI), 113.6 (ArC), 126.6 (ArC), 127.4 (ArC), 128.4 (ArC), 130.5 (ArC), 131.1 (ArC), 131.7 (ArC), 147.7 (Csp^2), 153.7 (Csp^2), 160.6 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{15}INO_2$ [M + H] 392.0142; found 392.0148.

6-(4-Ethoxyphenyl)-5-iodo-2-phenyl-4*H*-1,3-oxazine (7ba): Yield 0.24 g (58%); white solid; m.p. 108–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 4.08 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 4.55 (s, 2 H, CH_2), 6.94 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.39 (t, ^3J = 8.0 Hz, 2 H, ArH), 7.46 (tt, ^3J = 7.6, ^4J = 2.4 Hz, 1 H, ArH), 7.61 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.92–7.94 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9 (CH_3), 55.5 (CH_2), 63.6 (OCH_2CH_3), 69.9 (CI), 114.0 (ArC), 126.6 (ArC), 127.3 (ArC), 128.4 (ArC), 130.5 (ArC), 131.3 (ArC), 131.7 (ArC), 147.8 (Csp^2), 153.0 (Csp^2), 159.9 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{17}INO_2$ [M + H] 406.0298; found 406.0294.

6-(3,4-Dimethoxyphenyl)-5-iodo-2-phenyl-4*H*-1,3-oxazine (7ca): Yield 0.22 g (52%); white solid; m.p. 147–148 °C. ^{1}H NMR

(400 MHz, $CDCl_3$): δ = 3.93 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 4.56 (s, 2 H, CH_2), 6.92 (d, ^3J = 8.4 Hz, 1 H, ArH), 7.21 (d, ^4J = 2.0 Hz, 1 H, ArH), 7.27 (dd, ^3J = 8.6, ^4J = 2.0 Hz, 1 H, ArH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.48 (tt, ^3J = 7.6, ^4J = 2.4 Hz, 1 H, ArH), 7.94–7.96 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.1 (CH_2), 56.0 (CH_3), 56.1 (CH_3), 70.0 (CI), 110.6 (ArC), 112.2 (ArC), 122.1 (ArC), 126.7 (ArC), 127.3 (ArC), 128.4 (ArC), 131.3 (ArC), 131.5 (ArC), 147.7 (Csp^2), 148.4 (ArC), 150.1 (ArC), 153.4 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{18}H_{16}INNaO_3$ [M + Na] 444.0067; found 444.0060.

5-Iodo-2-phenyl-6-(3,4,5-trimethoxyphenyl)-4*H*-1,3-oxazine (7da): Yield 0.27 g (60%); white solid; m.p. 184–185 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.90 (s, 6 H, 2×OCH_3), 3.91 (s, 3 H, OCH_3), 4.56 (s, 2 H, CH_2), 6.90 (s, 2 H, ArH), 7.40 (t, ^3J = 8.0 Hz, 2 H, ArH), 7.49 (tt, ^3J = 7.6, ^4J = 2.4 Hz, 1 H, ArH), 7.92–7.94 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_2), 56.4 (2×OCH_3), 61.0 (OCH_3), 70.7 (CI), 106.6 (ArC), 127.2 (ArC), 128.4 (ArC), 129.6 (ArC), 131.4 (ArC), 131.6 (ArC), 139.2 (ArC), 147.8 (Csp^2), 152.8 (Csp^2), 159.9 (2×ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{19}H_{19}INO_4$ [M + H] 452.0353; found 452.0347.

5-Iodo-2-phenyl-6-*p*-tolyl-4*H*-1,3-oxazine (7ea): Yield 0.22 g (58%); white solid; m.p. 125–126 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, CH_3), 4.57 (s, 2 H, CH_2), 7.26 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.40 (t, ^3J = 8.0 Hz, 2 H, ArH), 7.49 (t, ^3J = 7.6 Hz, 1 H, ArH), 7.57 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.95–7.97 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6 (CH_3), 55.1 (CH_2), 70.3 (CI), 127.5 (ArC), 128.4 (ArC), 129.0 (ArC), 131.0 (ArC), 131.3 (ArC), 131.7 (ArC), 140.0 (ArC), 147.9 (Csp^2), 153.8 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{17}H_{15}INO$ [M + H] 376.0193; found 376.0189.

5-Iodo-2,6-diphenyl-4*H*-1,3-oxazine (7fa): Yield 0.18 g (52%); white solid; m.p. 105–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.57 (s, 2 H, CH_2), 7.38–7.48 (m, 6 H, ArH), 7.66–7.69 (m, 2 H, ArH), 7.93–7.95 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_2), 70.9 (CI), 127.2 (ArC), 128.2 (ArC), 128.3 (ArC), 129.1 (ArC), 129.7 (ArC), 131.3 (ArC), 131.6 (ArC), 134.4 (ArC), 148.0 (Csp^2), 152.8 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{13}INO$ [M + H] 362.0036; found 362.0036.

6-(4-Chlorophenyl)-5-iodo-2-phenyl-4*H*-1,3-oxazine (7ga): Yield 0.08 g (20%); white solid; m.p. 122–123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.55 (s, 2 H, CH_2), 7.37–7.43 (m, 4 H, ArH), 7.62 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.89–7.92 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_2), 71.4 (CI), 127.2 (ArC), 128.4 (ArC), 128.6 (ArC), 130.5 (ArC), 131.4 (ArC), 131.5 (ArC), 132.9 (ArC), 147.1 (Csp^2), 152.6 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{11}Cl^{35}INO$ [M + H] 395.9652; found 395.9616.

(*E*)-5-[(4-Chlorophenyl)iodomethylene]-2-phenyl-4,5-dihydrooxazole (12ga): Yield 0.16 g (41%); white solid; m.p. 141–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.55 (s, 2 H, CH_2), 7.37–7.43 (m, 4 H, ArH), 7.62 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.89–7.92 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (CH_2), 71.4 (CI), 127.2 (ArC), 128.4 (ArC), 128.6 (ArC), 130.5 (ArC), 131.4 (ArC), 131.5 (ArC), 132.9 (ArC), 147.1 (Csp^2), 152.6 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{11}Cl^{35}INO$ [M + H] 395.9652; found 395.9616.

(4-Chlorophenyl)(2-phenyloxazol-5-yl)methanone (21ga): Yield 49 mg (18%); white solid; m.p. 142–143 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1654 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.56 (m, 5 H, ArH), 7.89 (s, 1 H, CH), 7.96–7.98 (m, 2 H, ArH), 8.19 (dd, ^3J = 8.1, ^4J = 1.6 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 126.1 (ArC), 127.5 (ArC), 129.0 (ArC), 129.1 (ArC), 130.4 (ArC), 132.0 (ArC), 135.1 (ArC), 137.7 (ArC), 139.8 (ArC), 148.8 (ArC), 164.9 (ArC), 180.0 (C=O) ppm. HRMS (ES): *m/z* calcd. for $C_{16}H_{10}ClNNaO_2$ [M + Na] 306.0298; found 306.0299.

5-Iodo-6-(4-nitrophenyl)-2-phenyl-4*H*-1,3-oxazine (7ha): Yield 0.1 g (24%); white solid; m.p. 190–191 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.91 (s, 2 H, CH_2), 7.46 (t, ^3J = 7.2 Hz, 2 H, ArH), 7.56 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.86 (d, ^3J = 9.2 Hz, 2 H, ArH), 7.90–7.92 (m, 2 H, ArH), 8.23 (d, ^3J = 9.2 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 65.7 (CH_2), 67.3 (CI), 123.5 (ArC), 126.2 (ArC), 128.1 (ArC), 128.9 (ArC), 130.4 (ArC), 132.6 (ArC), 144.3 (ArC), 146.7 (Csp^2), 156.0 (Csp^2), 163.9 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{12}IN_2O_3$ [M + H] 406.9887; found 406.9889.

(4-Nitrophenyl)(2-phenyloxazol-5-yl)methanone (21ha): Yield 47 mg (16%); yellowish solid; m.p. 186–187 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.61 (m, 3 H, ArH), 7.94 (s, 1 H, ArH), 8.15–8.20 (m, 4 H, ArH), 8.41 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 124.1 (ArC), 125.9 (ArC), 127.8 (ArC), 129.3 (ArC), 130.1 (ArC), 132.5 (ArC), 138.8 (ArC), 141.8 (ArC), 148.6 (Csp^2), 150.4 (ArC), 165.6 (Csp^2), 179.5 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{11}N_2O_4$ [M + H] 295.0713; found 295.0713.

2-Phenyloxazole-5-carbaldehyde (21ia): Yield 27.7 mg (16%); solid; m.p. 103–104 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1668 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.58 (m, 3 H, ArH), 7.95 (s, 1 H, CH), 8.16–8.19 (m, 2 H, ArH), 9.81 (s, 1 H, CHO) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 126.0 (ArC), 127.8 (ArC), 129.2 (ArC), 132.4 (ArC), 139.2 (Csp^2), 149.7 (Csp^2), 165.6 (Csp^2), 176.4 (CHO) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_7NNaO_2$ [M + Na] 196.0369; found 196.0368.

(*E*)-*N*-(2,3-Diiodoallyl)benzamide (16ia): Yield 0.16 g (41%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.62 (d, ^3J = 3.2 Hz, 2 H, CH_2), 5.79 (t, ^3J = 3.2 Hz, 1 H, CH), 7.44 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.53 (t, ^3J = 7.6 Hz, 1 H, ArH), 7.94–7.97 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 47.5 (CH_2), 61.1 ($HC_{sp2}I$), 126.4 ($C_{sp2}I$), 128.2 (ArC), 128.7 (ArC), 132.3 (ArC), 157.8 (ArC), 164.2 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_9H_{11}I_2NO$ [M + H] 402.8930; found 402.8936.

5-Iodo-6-(4-methoxyphenyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8aa): Yield 0.24 g (68%); yellow solid; m.p. 174–175 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1747 (C=O), 3242 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 4.23 (d, ^3J = 1.2 Hz, 2 H, CH_2), 6.12 (br. s, 1 H, NH), 6.91 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.57 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.8 (CH_2), 55.3 (OCH_3), 62.8 (CI), 113.3 (ArC), 125.7 (ArC), 130.6 (ArC), 148.9 (Csp^2), 150.8 (NHCO), 160.6 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{11}H_{10}INNaO_3$ [M + Na] 353.9598; found 353.9595.

5-Bromo-6-(4-methoxyphenyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8ab): Yield 0.09 g (30%); yellow solid; m.p. 166–167 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1737 (C=O), 3271 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 4.23 (s, 2 H, CH_2), 6.61 (br. s, 1 H, NH), 6.92 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.64 (d, ^3J = 8.0 Hz, 2 H, ArH), ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 47.8 (CH_2), 55.3 (OCH_3), 92.3 (CBr), 113.4 (ArC), 123.8 (ArC), 130.2 (ArC), 146.1 (Csp^2), 150.8 (NHCO), 160.6 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{11}H_{10}{}^{79}BrNNaO_3$ [M + Na] 305.9736; found 305.9732.

6-(3,4-Dimethoxyphenyl)-5-iodo-3,4-dihydro-2*H*-1,3-oxazin-2-one (8ba): Yield 0.24 g (67%); brownish solid; m.p. 186–189 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1724 (C=O), 3246 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (s, 6 H, 2×OCH_3), 4.23 (d, ^3J = 1.6 Hz, 2 H, CH_2), 6.31 (br. s, 1 H, NH), 6.87 (d, ^3J = 8.4 Hz, 1 H, ArH), 7.12 (d, ^4J = 2.0 Hz, 1 H, ArH), 7.24 (dd, ^3J = 8.4, ^4J = 2.0 Hz, 1 H,

ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.8 (CH_2), 55.9 (OCH_3), 56.0 (OCH_3), 63.0 (CI), 110.2 (ArC), 111.9 (ArC), 122.5 (ArC), 125.8 (ArC), 148.3 (ArC), 148.8 (Csp^2), 150.2 (ArC), 150.8 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{12}H_{12}INNaO_4$ [M + Na] 383.9703; found 383.9708.

5-Bromo-6-(3,4-dimethoxyphenyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8bb): Yield 0.17 g (53%); yellowish white solid; m.p. 162–163 °C. IR (KBr): ṽmax = 1766 (C=O), 3251 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 4.22 (d, ^3J = 1.6 Hz, 2 H, CH_2), 6.71 (br. s, 1 H, NH), 6.87 (d, ^3J = 8.4 Hz, 1 H, ArH), 7.18 (d, ^4J = 2.0 Hz, 1 H, ArH), 7.30 (dd, ^3J = 8.4, ^4J = 2.0 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 47.8 (CH_2), 55.8 (OCH_3), 55.9 (OCH_3), 92.5 (CBr), 110.3 (ArC), 111.4 (ArC), 122.1 (ArC), 123.9 (ArC), 146.0 (ArC), 148.3 (Csp^2), 150.2 (ArC), 150.8 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{12}H_{12}{}^{79}BrNO_4$ 314.0022 [M + H]; found 314.0037.

6-(Benzo[*d*][1,3]dioxol-5-yl)-5-iodo-3,4-dihydro-2*H*-1,3-oxazin-2-one (8ca): Yield 0.21 g (60%); white solid; m.p. 203–204 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1737 (C=O), 3278 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 4.07 (d, ^3J = 1.2 Hz, 2 H, CH_2), 6.09 (s, 2 H, OCH_2O), 6.98 (d, ^3J = 7.6 Hz, 1 H, ArH), 7.03 (d, ^4J = 1.6 Hz, 1 H, ArH), 7.05 (br. s, 1 H, ArH), 7.91 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 50.6 (CH_2), 66.3 (CI), 101.6 (OCH_2O), 108.0 (ArC), 109.1 (ArC), 123.5 (ArC), 127.7 (ArC), 146.9 (ArC), 147.8 (Csp^2), 148.1 (ArC), 149.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{11}H_8INNaO_4$ [M + Na] 367.9390; found 367.9391.

5-Iodo-6-*p*-tolyl-3,4-dihydro-2*H*-1,3-oxazin-2-one (8da): Yield 0.2 g (65%); yellow solid; m.p. 183–184 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1747 (C=O), 3242 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.83 (s, 3 H, CH_3), 4.22 (d, ^3J = 1.6 Hz, 2 H, CH_2), 6.69 (br. s, 1 H, NH), 7.21 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.51 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 51.6 (CH_2), 63.5 (CI), 128.7 (ArC), 128.9 (ArC), 130.5 (ArC), 140.1 (ArC), 149.0 (Csp^2), 151.1 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{11}H_{10}INNaO_2$ [M + Na] 337.9648; found 337.9643.

5-Bromo-6-*p*-tolyl-3,4-dihydro-2*H*-1,3-oxazin-2-one (8db): Yield 0.1 g (39%); white solid; m.p. 160–161 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1754 (C=O), 3248 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 4.23 (d, ^3J = 1.6 Hz, 2 H, CH_2), 6.78 (br. s, 1 H, NH), 7.21 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.58 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 47.8 (CH_2), 93.0 (CBr), 128.5 (ArC), 128.6 (ArC), 128.7 (ArC), 140.1 (ArC), 146.3 (Csp^2), 150.9 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{11}H_{10}{}^{79}BrNNaO_2$ [M + Na] 289.9787; found 289.9787.

5,5′-Dibromo-6,6′-di-*p*-tolyl-3′,4′-dihydro-2′*H*-3,4′-bi(1,3-oxazine)-2,2′(4*H*)-dione (22db): Yield 18.6 mg (7%); white solid; m.p. 198–199 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1734 (C=O), 3234 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), 4.07 (d, ^2J = 14.4 Hz, 1 H, C*H*H), 4.19 (d, ^2J = 14.4 Hz, 1 H, CH*H*), 6.55 (d, ^3J = 3.2 Hz, 1 H, CH), 6.65 (d, ^3J = 2.8 Hz, 1 H, NH), 7.21 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.26 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.59 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.59 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 21.5 (CH_3), 45.7 (CH_2), 67.8 (CH), 90.5 (CBr), 92.2 (CBr), 127.6 (ArC), 127.8 (ArC), 128.4 (ArC), 128.6 (ArC), 128.8 (ArC), 129.0 (ArC), 140.4 (ArC), 141.3 (ArC), 146.0 (Csp^2), 148.5 (NHCO), 149.8 (NHCO), 151.3 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{18}{}^{79}Br_2N_2NaO_4$ [M + Na] 554.9526; found 554.9523.

5-Iodo-6-phenyl-3,4-dihydro-2*H*-1,3-oxazin-2-one (8ea): Yield 0.16 g (52%); yellow solid; m.p. 165–166 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1723 (C=O), 3386 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.24 (d, ^3J = 1.6 Hz, 2 H, CH_2), 6.70 (br. s, 1 H, NH), 7.39–7.42 (m, 3 H, ArH), 7.60–7.62 (m, 2 H, ArH), ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.6 (CH_2), 64.1 (CI), 128.0 (ArC), 129.1 (ArC), 130.0 (ArC), 133.4 (ArC), 148.9 (Csp^2), 151.0 (NHCO), ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_8INNaO_2$ [M + Na] 323.9492; found 323.9497.

(*E*)-*tert*-Butyl 2,3-Diiodo-3-phenylallylcarbamate (17ea): Yield 43.6 mg (9%); white solid; m.p. 103–104 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1685 (C=O), 3384 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.49 (s, 9 H, 3×CH_3), 4.33 (d, ^3J = 2.0 Hz, 2 H, CH_2), 4.97 (br. s, 1 H, NH), 7.20 (d, ^3J = 7.2 Hz, 2 H, ArH), 7.27–7.31 (m, 1 H, ArH), 7.36 (t, ^3J = 7.2 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4 (3×CH_3), 57.1 (CH_2), 80.0 [$C(CH_3)_3$], 96.3 (Csp^2I), 102.8 (Csp^2I), 128.1 (ArC), 128.5 (ArC), 131.7 (ArC), 147.5 (ArC), 155.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{14}H_{17}I_2NNaO_2$ [M + Na] 507.9241; found 507.9244.

5-Bromo-6-phenyl-3,4-dihydro-2*H*-1,3-oxazin-2-one (8eb): Yield 0.1 g (39%); white solid; m.p. 154–155 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1721 (C=O), 3380 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.24 (d, ^3J = 1.2 Hz, 2 H, CH_2), 7.05 (br. s, 1 H, NH), 7.40–7.42 (m, 3 H, ArH), 7.66–7.69 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 47.7 (CH_2), 93.6 (CBr), 128.0 (ArC), 128.6 (ArC), 129.9 (ArC), 131.4 (ArC), 146.1 (Csp^2), 151.0 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_8{}^{79}BrNNaO_2$ [M + Na] 275.9631; found 275.9635.

5,5′-Dibromo-6,6′-diphenyl-3′,4′-dihydro-2′*H*-3,4′-bi(1,3-oxazine)-2,2′(4*H*)-dione (22eb): Yield 17.6 mg (7%); white solid; m.p. 203–204 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1717 (C=O), 3288 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 4.24 (s, 2 H, CH_2), 6.30 (s, 1 H, CH), 7.49–7.52 (m, 6 H, ArH), 7.64–7.69 (m, 4 H, ArH), 9.00 (d, ^3J = 2.4 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 47.4 (CH_2), 68.2 (CH), 93.0 (CBr), 94.3 (CBr), 128.8 (ArC), 128.9 (2×ArC), 129.2 (ArC), 130.6 (ArC), 130.9 (ArC), 131.5 (ArC), 131.8 (ArC), 145.6 (Csp^2), 148.5 (2×NHCO), 150.3 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{20}H_{14}{}^{79}Br_2N_2NaO_4$ [M + Na] 526.9213; found 526.9212.

6-(4-Chlorophenyl)-5-iodo-3,4-dihydro-2*H*-1,3-oxazin-2-one (8fa): Yield 0.17 g (54%); yellow solid; m.p. 209–210 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1749 (C=O), 3141 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 4.10 (d, ^3J = 1.6 Hz, 2 H, CH_2), 7.53 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.58 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.95 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 50.6 (CH_2), 67.4 (CI), 128.3 (ArC), 130.8 (ArC), 132.9 (ArC), 134.2 (ArC), 147.0 (Csp^2), 149.0 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{11}H_{10}{}^{35}ClINNaO_2$ [M + Na] 372.9343; found 372.9340.

5-Bromo-6-(4-chlorophenyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8fb): Yield 0.07 g (24%); white solid; m.p. 203–204 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1758 (C=O), 3238 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 4.14 (d, ^3J = 1.6 Hz, 2 H, CH_2), 7.55 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.63 (d, ^3J = 8.4 Hz, 2 H, ArH), 8.14 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 46.8 (CH_2), 95.2 (CBr), 128.5 (ArC), 130.3 (ArC), 130.7 (ArC), 134.4 (ArC), 144.6 (Csp^2), 148.7 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{10}H_7{}^{79}Br^{35}ClNNaO_2$ [M + Na] 309.9241; found 309.9241.

5,5′-Dibromo-6,6′-bis(4-chlorophenyl)-3′,4′-dihydro-2′*H*-3,4′-bi-(1,3-oxazine)-2,2′(4*H*)-dione (22fb): Yield 40 mg (14%); white solid; m.p. 123–124 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1734 (C=O), 3175 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 4.22 (d, ^2J = 15.6 Hz, 1 H, C*H*H), 4.27 (d, ^2J = 15.2 Hz, 1 H, CH*H*), 6.28 (s, 1 H, CH), 7.57 (d, ^3J = 3.2 Hz, 2 H, ArH), 7.59 (d, ^3J = 3.6 Hz, 2 H, ArH), 7.68 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.71 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.59

(d, ^3J = 2.4 Hz, 2 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 47.1 (CH_2), 67.7 (CH), 93.0 (CBr), 94.6 (CBr), 128.5 (ArC), 128.6 (ArC), 129.8 (ArC), 130.2 (ArC), 130.3 (ArC), 130.7 (ArC), 134.8 (ArC), 135.0 (ArC), 144.1 (Csp^2), 147.8 (NHCO), 147.9 (NHCO), 148.8 (Csp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{20}H_{12}{}^{79}Br_2{}^{35}Cl_2KN_2O_4$ [M + K] 610.8172; found 610.8162.

(*E*)-5-[Iodo(4-nitrophenyl)methylene]oxazolidin-2-one (13ga): Yield 58.8 mg (17%); yellow solid; m.p. 203–204 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1812 (C=O), 3302 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.34 (s, 2 H, CH_2), 7.77 (d, ^3J = 9.2 Hz, 2 H, ArH), 8.23 (d, ^3J = 9.2 Hz, 2 H, ArH), 8.74 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.2 (CH_2), 68.7 (CI), 123.5 (ArC), 130.5 (ArC), 144.1 (ArC), 146.1 (ArC), 149.7 (Csp^2), 155.6 (NHCO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{10}H_7IN_2NaO_4$ [M + Na] 368.9343; found 368.9348.

(*E*)-5-[Bromo(4-nitrophenyl)methylene]oxazolidin-2-one (13gb): Yield 32.7 mg (11%); yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 1735 (C=O), 3302 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.48 (s, 2 H, CH_2), 6.18 (br. s, 1 H, NH), 7.90 (d, ^3J = 8.8 Hz, 2 H, ArH), 8.22 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 47.6 (CH_2), 93.4 (CBr), 123.5 (ArC), 129.4 (ArC), 140.1 (ArC), 145.6 (ArC), 147.0 (Csp^2), 155.6 (NHCO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{10}H_7{}^{79}BrN_2NaO_4$ [M + Na] 320.9481; found 320.9482.

(*E*)-*tert*-Butyl 2,3-Diiodoallylcarbamate (17ha): Yield 0.11 g (26%); white solid; m.p. 72–73 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1699 (C=O), 3379 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 (s, 9 H, 3 × CH_3), 4.00 (d, ^3J = 5.6 Hz, 2 H, CH_2), 4.88 (br. s, 1 H, NH), 7.02 (s, 1 H, Csp^{2}H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4 (3 × CH_3), 51.8 (CH_2), 80.0 [$C(CH_3)_3$], 80.4 (Csp^2HI), 102.0 (Csp^2I), 155.2 (NHCO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_8H_{13}I_2NNaO_2$ [M + Na] 431.8928; found 431.8926.

***N*-[5-Iodo-6-(4-methoxyphenyl)-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9aa):** Yield 0.35 g (73%); white solid; m.p. 190–195 °C (decomp.). IR (KBr): $\tilde{\nu}_{max}$ = 3278 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, CH_3), 3.88 (s, 3 H, OCH_3), 4.33 (s, 2 H, NCH_2), 6.93 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.17 (d, ^3J = 8.1 Hz, 2 H, ArH), 7.52 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.71 (d, ^3J = 8.2 Hz, 2 H, ArH), 9.13 (br. s, 1 H, HN) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5 (CH_3), 49.8 (NCH_2), 55.4 (OCH_3), 64.8 (CI), 113.4 (ArC), 124.2 (ArC), 126.9 (ArC), 129.2 (ArC), 130.9 (ArC), 139.2 (ArC), 142.8 (ArC), 147.2 (C-sp^2), 153.8 (HNC-sp^2), 160.9 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{17}IN_2NaO_4S$ [M + Na] 506.9846; found 506.9842.

***N*-[6-(3,4-Dimethoxyphenyl)-5-iodo-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9da):** Yield 0.28 g (55%); off-white powder; m.p. 211 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3003 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.32 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 4.15 (s, 2 H, CH_2), 7.04 (d, ^3J = 8.3 Hz, 1 H, ArH), 7.17 (d, ^3J = 8.2 Hz, 1 H, ArH), 7.20–7.34 (m, 3 H, ArH), 7.60 (d, ^3J = 7.6 Hz, 2 H, ArH), 9.19 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.3 (CH_3), 49.6 (CH_2), 56.0 (2 × OCH_3), 67.6 (IC-sp^2), 111.4 (ArC), 112.8 (ArC), 122.9 (ArC), 124.6 (ArC), 126.6 (ArC), 129.5 (ArC), 140.1 (ArC), 142.3 (ArC), 146.2 (ArC), 148.4 (IC*C*-sp^2), 150.5 (ArC), 153.1 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{19}H_{19}IN_2NaO_5S$ [M + Na] 536.9952; found 536.9950.

***N*-[5-Iodo-6-(*p*-tolyl)-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9fa):** Yield 0.44 g (93%); yellowish solid; m.p. 234 °C (decomp.). IR (KBr): $\tilde{\nu}_{max}$ = 3000 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.33 (s, 3 H, CH_3), 2.36 (s, 3 H, CH_3), 4.14 (br. s, 2 H, CH_2), 7.20–7.28 (m, 4 H, ArH), 7.30–7.38 (m, 2 H, ArH), 7.57 (d, ^3J = 7.9 Hz, 2 H, ArH), 9.15 (s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.3 (CH_3), 21.4 (CH_3), 49.5 (CH_2), 68.6 (CI), 126.6 (ArC), 129.1 (ArC), 129.3 (ArC), 129.5 (ArC), 129.7 (ArC), 140.4 (ArC), 140. 9 (ArC), 142.3 (ArC), 146.3 (C-sp^2), 152.9 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{18}IN_2O_3S$ [M + H] 469.0077; found 469.0072.

***N*-(5-Iodo-6-phenyl-4*H*-1,3-oxazin-2-yl)-4-methylbenzenesulfonamide (9ga):** Yield 0.27 g (59%); white solid; m.p. 204–208 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3284 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.33 (s, 3 H, CH_3), 4.17 (s, 2 H, CH_2), 7.21 (d, ^3J = 7.3 Hz, 2 H, ArH), 7.46 (br. s, 5 H, ArH), 7.58 (d, ^3J = 7.5 Hz, 2 H, ArH), 9.17 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.4 (CH_3), 49.5 (CH_2), 69.2 (IC-sp^2), 126.6 (ArC), 128.6 (ArC), 129.4 (ArC), 129.5 (ArC), 130.6 (ArC), 132.6 (ArC), 140.9 (ArC), 142.3 (ArC), 146.2 (IC*C*-sp^2), 152.8 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{15}IN_2NaO_3S$ [M + Na] 476.9740; found 476.9731.

(*E*)-*N*-[5-(Iodomethylene)-4,5-dihydrooxazol-2-yl]-4-methylbenzenesulfonamide (14ia): Yield 0.27 g (71%); white solid; m.p. 218–223 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3364 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.36 (s, 3 H, CH_3), 4.27 (s, 2 H, CH_2), 6.22 (s, 1 H, ICH), 7.35 (br. s, 2 H, ArH), 7.73 (br. s, 2 H, ArH), 9.40 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.4 (CH_3), 46.3 (CH_2), 54.1 (IC-sp^2), 126.6 (ArC), 129.8 (ArC), 140.0 (ArC), 142.9 (ArC), 151.1 (ICC-sp^2), 159.2 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{11}H_{12}IN_2O_3S$ [M + H] 378.9608; found 378.9611.

(*E*)-*N*-(2,3-Diiodoallylcarbamoyl)-4-methylbenzenesulfonamide (18ia): Yield 80.9 mg (16%); white solid; m.p. 184–187 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3234 (NH), 1691 (CO) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.34 (s, 3 H, CH_3), 3.80 (d, ^3J = 5.5 Hz, 2 H, CH_2), 6.86 (t, ^3J = 5.8 Hz, 1 H, NH), 7.30 (s, 1 H, CH), 7.41 (d, ^3J = 8.1 Hz, 2 H, ArH), 7.80 (d, ^3J = 8.3 Hz, 2 H, ArH), 10.76 (br. s, 1 H, NH) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{11}H_{12}I_2N_2NaO_3S$ [M + Na] 528.8550; found 528.8555.

(*E*)-5-(Iodomethylene)-*N*-phenyl-4,5-dihydrooxazol-2-amine (14ja): Yield 0.15 g (47%); white solid; m.p. 152–155 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3233(NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 4.38 (d, ^4J = 2.5 Hz, 2 H, CH_2), 5.88 (s, 1 H, CH), 6.95 (t, ^3J = 7.3 Hz, 1 H, ArH), 7.26 (t, ^3J = 7.9 Hz, 2 H, ArH), 7.55 (d, ^3J = 7.1 Hz, 2 H, ArH), 9.65 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 48.3 (IC-sp^2), 59.3 (CH_2), 118.2 (ArC), 122.2 (ArC), 129.2 (ArC), 139.9 (ArC), 155.3 (H_2CC-sp^2), 156.5 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{10}H_{10}IN_2O$ [M + H] 300.9832; found 300.9830.

(*E*)-*N*-Benzyl-5-(iodomethylene)-4,5-dihydrooxazol-2-amine (14ka): Yield 0.14 g (49%); white solid; m.p 103–105 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3442(NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 4.17 (d, ^4J = 2.4 Hz, 2 H, CH_2), 4.27 (s, 2 H, CH_2), 5.77 (s, 1 H, CH), 7.20–7.40 (m, 5 H, ArH), 7.48 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 45.7 (NCH_2), 47.7 (IC-sp^2), 58.7 ($HNCH_2$), 127.3 (ArC), 127.6 (ArC), 128.7 (ArC), 139.8 (ArC), 158.4 (H_2CC-sp^2), 159.7 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{11}H_{12}IN_2NaO$ [M + H] 337.9892; found 337.9894.

***N*-[5-Iodo-6-(4-methoxyphenyl)-4*H*-1,3-thiazin-2-yl]benzamide (10aa):** Yield 0.27 g (59%); yellow solid; m.p. 149–150 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1680 (C=O), 3238 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 4.52 (s, 2 H, CH_2), 6.92 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.35 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.43 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.52 (tt, ^3J = 7.6, ^4J = 1.2 Hz, 1 H, ArH), 8.08 (d, ^3J = 7.2 Hz, 2 H, ArH), 10.61 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 57.7 (CH_2), 78.1 (CI), 113.9

(ArC), 128.3 (ArC), 128.9 (ArC), 130.5 (ArC), 130.8 (ArC), 132.4 (ArC), 135.0 (ArC), 135.1 (Csp^2), 160.3 (ArC), 164.1 (Csp^2), 174.0 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{18}H_{16}IN_2O_2S$ [M + H] 450.9972; found 450.9980.

***N*-(5-Iodo-6-phenyl-4*H*-1,3-thiazin-2-yl)benzamide (10ca):** Yield 0.08 g (18%); white solid; m.p. 172–173 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1608 (C=O), 3406 (NH) cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 4.57 (s, 2 H, CH_2), 7.33–7.36 (m, 2 H, ArH), 7.42–7.50 (m, 5 H, ArH), 7.58 (t, ^3J = 7.6 Hz, 1 H, ArH), 8.00 (d, ^3J = 7.6 Hz, 2 H, ArH), 10.95 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 57.3 (CH_2), 82.9 (CI), 128.3 (ArC), 128.5 (ArC), 128.8 (ArC), 129.0 (ArC), 129.1 (ArC), 132.3 (ArC), 134.6 (Csp^2), 138.9 (ArC), 140.3 (ArC), 165.4 (Csp^2), 174.1 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{17}H_{13}IN_2OS$ [M + H] 420.9866; found 420.9873.

(*E*)-*N*-{5-[Iodo(phenyl)methylene]-4,5-dihydrothiazol-2-yl}benzamide (15ca): Yield 0.11 g (25%); yellow solid; m.p. 195–196 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1693 (C=O), 3138 (NH) cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 4.50 (s, 2 H, CH_2), 7.33–7.37 (m, 1 H, ArH), 7.42–7.49 (m, 6 H, ArH), 7.56 (t, ^3J = 7.2 Hz, 1 H, ArH), 8.01–8.03 (m, 2 H, ArH), 10.64 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 57.3 (CH_2), 82.5 (CI), 128.2 (ArC), 128.3 (ArC), 128.7 (2 × ArC), 128.8 (ArC), 132.3 (ArC), 134.6 (Csp^2), 139.8 (ArC), 142.6 (ArC), 163.3 (Csp^2), 172.2 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{17}H_{13}IN_2OS$ [M + H] 420.9866; found 420.9876.

(*E*)-*N*-{5-[Bromo(4-methoxyphenyl)methylene]-4,5-dihydrothiazol-2-yl}benzamide (15ab): Yield 0.27 g (68%); yellow solid; m.p. 195–196 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1687 (C=O), 3127 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 4.44 (s, 2 H, CH_2), 6.89 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.45–7.49 (m, 4 H, ArH), 7.57 (tt, ^3J = 7.6, ^4J = 1.2 Hz, 1 H, ArH), 7.91–7.93 (m, 2 H, ArH), 10.03 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3 (OCH_3), 61.3 (CH_2), 108.3 (Csp^2), 114.0 (ArC), 128.4 (ArC), 129.0 (ArC), 129.7 (ArC), 131.5 (ArC), 132.8 (ArC), 133.4 (ArC), 134.7 (Csp^2), 159.9 (ArC), 163.8 (Csp^2), 169.9 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{18}H_{16}{}^{79}BrN_2O_2S$ [M + H] 403.0110; found 403.0106.

(*E*)-*N*-{5-[Bromo(4-chlorophenyl)methylene]-4,5-dihydrothiazol-2-yl}benzamide (15bb): Yield 0.18 g (44%); yellow solid; m.p. 234–235 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1628 (C=O), 3419 (NH) cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 4.62 (s, 2 H, CH_2), 7.48 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.55–7.60 (m, 5 H, ArH), 8.02–8.05 (m, 2 H, ArH), 10.81 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 59.7 (CH_2), 105.0 (Csp^2), 128.4 (ArC), 128.6 (ArC), 128.9 (ArC), 130.0 (ArC), 130.6 (ArC), 132.5 (ArC), 133.5 (ArC), 134.3 (Csp^2), 137.7 (ArC), 161.2 (Csp^2), 169.1 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{17}H_{12}{}^{79}Br^{35}ClN_2OS$ [M + H] 405.9542; found 405.9543.

(*E*)-*N*-{5-[Bromo(phenyl)methylene]-4,5-dihydrothiazol-2-yl}-benzamide (15cb): Yield 0.25 g (67%); yellow solid; m.p. 190–191 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1688 (C=O), 3138 (NH) cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 4.61 (s, 2 H, CH_2), 7.40 (tt, ^3J = 7.2, ^4J = 1.2 Hz, 1 H, ArH), 7.45–7.54 (m, 6 H, ArH), 7.57 (t, ^3J = 7.2 Hz, 1 H, ArH), 8.03–8.05 (m, 2 H, ArH), 10.87 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 54.9 (CH_2), 106.7 (CBr), 128.1 (ArC), 128.3 (ArC), 128.7 (ArC), 128.8 (ArC), 129.1 (ArC), 132.4 (ArC), 134.4 (Csp^2), 137.1 (ArC), 138.8 (ArC), 167.9 (Csp^2), 174.2 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{17}H_{13}{}^{79}BrN_2OS$ [M + H] 371.9932; found 371.9935.

(*E*)-*N*-[5-(Iodomethylene)-4,5-dihydrothiazol-2-yl]benzamide (15da): Yield 0. 07 g (20%); white solid; m.p. 195–196 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1631 (C=O), 3421 (NH) cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 4.30 (d, ^4J = 2.8 Hz, 2 H, CH_2), 6.57 (t, ^4J = 2.8 Hz, 1 H, CH), 7.48 (t, ^3J = 7.2 Hz, 2 H, ArH), 7.57 (tt, ^3J = 7.2, ^4J = 1.2 Hz, 1 H, ArH), 8.05–8.08 (m, 2 H, ArH), 10.54 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 56.6 (CH_2), 65.9 (CH), 128.3 (ArC), 128.7 (ArC), 132.3 (ArC), 134.8 (Csp^2), 143.3 (ArC), 167.4 (Csp^2), 172.0 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{11}H_9IN_2OS$ [M + H] 344.9553; found 344.9544.

2-Iodo-1-(4-methoxyphenyl)prop-2-en-1-one (11aa): Yield 0.17 g (60%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 1653 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.91 (s, 3 H, OCH_3), 6.70 (d, $^2J_{H,H}$ = 2.4 Hz, 1 H, =CH), 6.77 (d, $^2J_{H,H}$ = 2.4 Hz, 1 H, =CH), 6.93 (d, $^3J_{H,H}$ = 9.2 Hz, 2 H, ArH), 7.90 (d, $^3J_{H,H}$ = 9.2 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.57 (OCH_3), 106.76 (=C-I), 113.91 (ArC), 126.15 (=CH_2), 132.57 (ArC), 135.82 (ArC), 163.91 (ArC), 190.63 (C=O) ppm. HRMS (ES): *m/z* calcd. for $C_{10}H_9INaO_2$ [M + Na]$^+$ 310.9539; found 310.9537.

(*E*)-2,3-Diiodo-3-(4-methoxyphenyl)allyl Acetate (20aa): Yield 0.12 g (27%); yellowish wax. IR (KBr): $\tilde{\nu}_{max}$ = 1726 (CO) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.17 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 5.06 (s, 2 H, OCH_2), 6.87 (d, ^3J = 8.8 Hz, 1 H, ArH), 7.19 (d, ^3J = 8.3 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9 (CH_3), 55.3 (OCH_3), 76.5 (OCH_2), 96.7 (Csp_2-I), 99.6 (Csp_2-I), 113.7 (ArC), 129.6 (ArC), 139.7 (ArC), 159.5 (ArC), 170.1 (C=O) ppm. HRMS (ESI): *m/z* calcd. for $C_{12}H_{13}I_2O_3$ [M + H] 458.8954; found 458.8966.

General Procedures for the Phenyl Hypochloroselenoite Mediated Reactions

Method A: To a solution of the corresponding *N*-(3-substituted prop-2-ynyl)benzamide **1** (0.5 mmol) in anhydrous dichloromethane (5 mL), phenyl hypochloroselenoite (95.96 mg, 0.5 mmol) together with potassium *tert*-butanoate (0.5 mmol) were added. The reaction mixture was stirred at room temperature.

Method B: To a solution of the corresponding *tert*-butyl prop-2-ynylcarbamate **2** (0.5 mmol) in anhydrous acetonitrile (5 mL), phenyl hypochloroselenoite (95.96 mg, 0.5 mmol) together with potassium phosphate monohydrate (0.5 mmol) were added. The reaction mixture was stirred at room temperature.

Method C: To a cooled solution of urea **3** (0.5 mmol) in anhydrous acetonitrile (5 mL) or to a cooled solution of thiourea **4** (0.5 mmol) in anhydrous dichloromethane, phenyl hypochloroselenoite (95.96 mg, 0.5 mmol) was added at 0 °C. The resulting mixtures were warmed and stirred at room temperature.

Isolation Procedures for All Products: When completion of the reaction was observed by TLC, the solution was evaporated under reduced pressure and the residue was purified by flash column chromatography eluting with hexane/ethyl acetate mixtures.

6-(4-Methoxyphenyl)-2-phenyl-5-(phenylselanyl)-4*H*-1,3-oxazine (7ab): Yield 0.14 g (66%); yellowish oil. ^1H NMR (400 MHz, [D$_6$]-DMSO): δ = 2.87 (s, 3 H, OCH_3), 3.29 (s, 2 H, CH_2), 6.10 (d, ^3J = 8.8 Hz, 2 H, ArH), 6.34–6.43 (m, 3 H, ArH), 6.51–6.57 (m, 4 H, ArH), 6.62 (t, ^3J = 7.6 Hz, 2 H, ArH), 6.68 (d, ^3J = 8.8 Hz, 2 H, ArH), 6.98–7.00 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 49.2 (CH_2), 55.3 (OCH_3), 98.7 (Csp^2), 113.6 (ArC), 125.3 (ArC), 126.9 (ArC), 127.3 (ArC), 128.4 (ArC), 128.6 (ArC), 129.7 (ArC), 130.1 (ArC), 130.8 (ArC), 131.1 (ArC), 131.4 (ArC), 150.2 (Csp^2), 151.8 (Csp^2), 160.2 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}NO_2Se$ [M + H] 422.0655; found 422.0647.

(*E*)-*N*-[3-Chloro-3-(4-methoxyphenyl)-2-(phenylselanyl)allyl]benzamide (16ab): Yield 29.7 mg (13%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 4.56 (d, ^3J = 5.6 Hz,

2 H, CH_2), 6.34 (br. s, NH), 6.89 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.24–7.26 (m, 3 H, ArH), 7.37 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.40–7.43 (m, 4 H, ArH), 7.49 (t, ^3J = 7.2 Hz, 2 H, ArH), 7.64–7.66 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.8 (CH_2), 55.4 (OCH_3), 113.5 (ArC), 125.9 (Csp^2), 127.0 (ArC), 128.1 (ArC), 128.6 (ArC), 129.4 (ArC), 129.6 (ArC), 130.6 (ArC), 131.52 (ArC), 131.59 (ArC), 133.0 (ArC), 134.4 (ArC), 135.2 (Csp^2), 160.2 (ArC), 166.9 (NHCO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{23}H_{20}ClNNaO_2Se$ [M + Na] 480.0238; found 480.0230.

6-(4-Ethoxyphenyl)-2-phenyl-5-(phenylselanyl)-4*H*-1,3-oxazine (7bb): Yield 0.14 g (65%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, ^3J = 6.8 Hz, 3 H, OCH_2CH_3), 4.08 (q, ^3J = 6.8 Hz, 2 H, OCH_2CH_3), 4.30 (s, 2 H, CH_2), 6.94 (d, ^3J = 9.2 Hz, 2 H, ArH), 7.26–7.28 (m, 3 H, ArH), 7.41 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.45–7.49 (m, 3 H, ArH), 7.62 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.97–7.99 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9 (OCH_2CH_3), 50.0 (CH_2), 63.6 (OCH_2CH_3), 99.5 (Csp^2), 113.9 (ArC), 125.9 (ArC), 127.33 (ArC), 127.36 (ArC), 128.3 (ArC), 128.7 (ArC), 129.4 (ArC), 130.2 (ArC), 131.1 (ArC), 131.90 (ArC), 131.96 (ArC), 150.0 (Csp^2), 152.9 (Csp^2), 159.9 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{22}NO_2Se$ [M + H] 436.0811; found 436.0802.

(*E*)-*N*-[3-Chloro-3-(4-ethoxyphenyl)-2-(phenylselanyl)allyl]benzamide (16bb): Yield 28.3 mg (12%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (t, ^3J = 6.8 Hz, 3 H, OCH_2CH_3), 4.05 (q, ^3J = 6.8 Hz, 2 H, OCH_2CH_3), 4.55 (d, ^3J = 5.6 Hz, 2 H, CH_2), 6.33 (br. s, NH), 6.87 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.14–7.26 (m, 3 H, ArH), 7.36 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.38–7.43 (m, 4 H, ArH), 7.49 (tt, ^3J = 7.2, ^4J = 2.0 Hz, 2 H, ArH), 7.63–7.66 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9 (OCH_2CH_3), 43.8 (CH_2), 63.6 (OCH_2CH_3), 114.0 (ArC), 125.8 (ArC), 127.0 (ArC), 128.1 (ArC), 128.6 (ArC), 129.5 (ArC), 129.6 (Csp^2), 130.6 (ArC), 131.3 (ArC), 131.5 (ArC), 133.1 (ArC), 134.4 (Csp^2), 135.3 (ArC), 159.7 (ArC), 166.9 (NHCO) ppm. HRMS (ES): *m*/*z* calcd.for $C_{24}H_{22}ClNNaO_2Se$ $[M + Na]^+$ 494.0395; found 494.0406.

6-(3,4-Dimethoxyphenyl)-2-phenyl-5-(phenylselanyl)-4*H*-1,3-oxazine (7cb): Yield 0.15 g (68%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 4.31 (s, 2 H, CH_2), 6.92 (d, ^3J = 8.0 Hz, 1 H, ArH), 7.21 (d, ^3J = 2.0 Hz, 1 H, ArH), 7.24–7.29 (m, 4 H, ArH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.45–7.49 (m, 3 H, ArH), 7.97–7.99 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.0 (CH_2), 56.00 (OCH_3), 56.01 (OCH_3), 99.7 (Csp^2), 110.4 (ArC), 111.9 (ArC), 121.7 (ArC), 126.2 (ArC), 127.2 (ArC), 127.3 (ArC), 128.3 (ArC), 128.8 (ArC), 129.5 (ArC), 131.2 (ArC), 131.84 (ArC), 131.88 (ArC), 148.3 (Csp^2), 149.8 (ArC), 150.0 (ArC), 159.9 (Csp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{22}NO_3Se$ [M + H] 452.0761; found 452.0756.

(*E*)-*N*-[3-Chloro-3-(3,4-dimethoxyphenyl)-2-(phenylselanyl)allyl]-benzamide (16cb): Yield 46.3 mg (19%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.56 (d, ^3J = 5.6 Hz, 2 H, CH_2), 6.37 (br. s, NH), 6.83 (d, ^3J = 8.4 Hz, 1 H, ArH), 6.93 (d, ^3J = 2.0 Hz, 1 H, ArH), 7.00 (dd, ^3J = 8.4, ^4J = 2.0 Hz, 1 H, ArH), 7.24–7.26 (m, 3 H, ArH), 7.38–7.43 (m, 4 H, ArH), 7.48 (tt, ^3J = 7.6, ^4J = 2.4 Hz, 1 H, ArH), 7.65–7.67 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.7 (CH_2), 56.00 (OCH_3), 56.03 (OCH_3), 110.4 (ArC), 112.1 (ArC), 122.0 (ArC), 126.1 (Csp^2), 127.0 (ArC), 128.1 (ArC), 128.6 (ArC), 129.5 (ArC), 129.6 (ArC), 131.6 (ArC), 133.0 (ArC), 134.3 (Csp^2), 139.4 (ArC), 148.4 (ArC), 148.8 (ArC), 166.9 (NHCO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{22}Cl^{35}NNaO_3Se$ [M + Na] 510.0344; found 510.0343.

2-Phenyl-5-(phenylselanyl)-6-(3,4,5-trimethoxyphenyl)-4*H*-1,3-oxazine (7db): Yield 0.15 g (63%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 6 H, 2 × OCH_3), 3.90 (s, 3 H, OCH_3), 4.30 (s, 2 H, CH_2), 6.89 (s, 2 H, ArH), 7.26–7.29 (m, 3 H, ArH), 7.41 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.45–7.50 (m, 3 H, ArH), 7.96–7.99 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.0 (CH_2), 56.2 (2 × OCH_3), 61.0 (OCH_3), 100.6 (Csp^2), 106.1 (ArC), 127.2 (ArC), 127.5 (ArC), 128.4 (ArC), 128.6 (ArC), 128.8 (ArC), 129.5 (ArC), 131.2 (ArC), 131.7 (ArC), 132.0 (ArC), 139.1 (ArC), 149.4 (Csp^2), 152.81 (Csp^2), 152.85 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{23}NNaO_4Se$ [M + Na] 504.0686; found 504.0687.

2,6-Diphenyl-5-(phenylselanyl)-4*H*-1,3-oxazine (7fb): Yield 0.11 g (57%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.32 (s, 2 H, CH_2), 7.27–7.30 (m, 3 H, ArH), 7.39–7.50 (m, 8 H, ArH), 7.66–7.69 (m, 2 H, ArH), 7.97–8.00 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.8 (CH_2), 101.0 (Csp^2), 127.3 (ArC), 127.5 (ArC), 128.1 (ArC), 128.3 (ArC), 128.4 (ArC), 129.8 (ArC), 129.5 (ArC), 129.6 (ArC), 131.2 (ArC), 131.8 (ArC), 132.1 (ArC), 133.6 (ArC), 149.8 (Csp^2), 152.8 (Csp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{22}H_{17}NNaOSe$ [M + Na] 414.0373; found 414.0380.

(*E*)-2-Phenyl-5-(phenylselanylmethylene)-4,5-dihydrooxazole (12ib): Yield 40.9 mg (26%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.09 (d, ^3J = 0.8 Hz, 2 H, CH_2), 6.78 (s, 1 H, CH), 7.26–7.31 (m, 3 H, ArH), 7.28–7.45 (m, 3 H, ArH), 7.52–7.54 (m, 2 H, ArH), 7.94–7.96 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6 (CH_2), 125.4 (ArC), 126.3 (ArC), 127.4 (ArC), 128.2 (ArC), 128.8 (ArC), 129.2 (ArC), 129.3 (ArC), 130.3 (sp^2), 134.6 (ArC), 149.5 (Csp^2), 161.4 (Csp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{13}NNaOSe$ [M + Na] 338.0055; found 338.0061.

(*E*)-*N*-[3-Chloro-2-(phenylselanyl)allyl]benzamide (16′ib): Yield 35 mg (20%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.45 (dd, ^3J = 5.6, ^4J = 1.2 Hz, 2 H, CH_2), 6.35 (br. s, 1 H, NH), 6.58 (t, ^3J = 1.2 Hz, 1 H, CH), 7.26–7.29 (m, 3 H, ArH), 7.37 (t, ^3J = 8.0 Hz, 2 H, ArH), 7.45–7.51 (m, 3 H, ArH), 7.59–7.62 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.0 (CH_2), 122.7 (Csp^2), 127.0 (ArC), 128.2 (ArC), 128.4 (ArC), 128.5 (ArC), 129.7 (ArC), 130.8 (ArC), 131.6 (ArC), 133.0 (ArC), 134.0 (Csp^2), 167.1 (NHCO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{14}Cl^{35}NNaOSe$ [M + Na] 373.9819; found 373.9826.

6-(4-Methoxyphenyl)-5-(phenylselanyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8ac): Yield 0.16 g (86%); yellow solid; m.p. 125–126 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1742 (C=O), 3420 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 3.99 (d, ^3J = 1.2 Hz, 2 H, CH_2), 6.49 (br. s, 1 H, NH), 6.90 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.27–7.29 (m, 3 H, ArH), 7.41–7.43 (m, 2 H, ArH), 7.55 (t, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.4 (CH_2), 55.3 (OCH_3), 97.3 (Csp^2), 113.2 (ArC), 125.0 (ArC), 127.7 (ArC), 128.3 (ArC), 129.5 (ArC), 130.4 (ArC), 131.9 (ArC), 150.7 (Csp^2), 151.4 (NHCO), 160.6 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{15}NNaO_3Se$ [M + Na] 384.0110; found 384.0111.

(*E*)-*tert*-Butyl 3-Chloro-3-(4-methoxyphenyl)-2-(phenylselanyl)allylcarbamate (17ac): Yield 20.3 mg (9%); white oil. IR (KBr): $\tilde{\nu}_{max}$ = 1714 (C=O), 3368 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 9 H, 3 × CH_3), 3.84 (s, 3 H, OCH_3), 4.23 (d, ^3J = 4.8 Hz, 2 H, CH_2), 4.84 (br. s, 1 H NH), 6.89 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.26–7.29 (m, 3 H, ArH), 7.35 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.40–7.43 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.3 (3 × CH_3), 44.1 (CH_2), 55.2 (OCH_3), 79.4 [$C(CH_3)_3$], 113.3 (ArC), 127.0 (Csp^2), 127.8 (ArC), 129.3 (ArC), 129.5 (ArC), 130.4 (ArC), 131.5 (ArC), 133.0 (ArC), 134.2 (Csp^2), 155.2 (NHCO), 160.0 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{21}H_{24}{}^{35}ClNNaO_3Se$ [M + Na] 476.0500; found 476.0504.

6-(3,4-Dimethoxyphenyl)-5-(phenylselanyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8bc): Yield 82.1 mg (42%); yellow solid; m.p. 138–139 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1732 (C=O), 3239 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 3.99 (d, ^3J = 1.2 Hz, 2 H, CH_2), 6.35 (br. s, 1 H, NH), 6.86 (d, ^3J = 8.4 Hz, 1 H, ArH), 7.13 (d, ^4J = 2.0 Hz, 1 H, ArH), 7.18 (dd, ^3J = 8.4, ^4J = 2.0 Hz, 1 H, ArH), 7.27–7.29 (m, 3 H, ArH), 7.42–7.44 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.5 (CH_2), 55.8 (OCH_3), 55.9 (OCH_3), 97.4 (CSe), 110.1 (ArC), 111.6 (ArC), 122.2 (ArC), 125.1 (ArC), 127.8 (ArC), 128.3 (ArC), 129.5 (ArC), 132.0 (ArC), 148.2 (ArC), 150.2 (ArC), 150.4 (Csp^2), 151.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{18}H_{17}NNaO_4Se$ [M + Na] 414.0216; found 414.0216.

(*E*)-*tert*-Butyl 3-Chloro-3-(3,4-dimethoxyphenyl)-2-(phenylselanyl)-allylcarbamate (17bc): Yield 43.5 mg (18%); yellowish brown solid; m.p. 76–77 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1696 (C=O), 3403 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, 3 × CH_3), 3.82 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.21 (d, ^3J = 4.8 Hz, 2 H, CH_2), 4.82 (br. s, 1 H, NH), 6.82 (d, ^3J = 8.4 Hz, 1 H, ArH), 6.87 (d, ^4J = 2.0 Hz, 1 H, ArH), 6.96 (dd, ^3J = 8.4, ^4J = 2.0 Hz, 1 H, ArH), 7.23–7.25 (m, 3 H, ArH), 7.37–7.40 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4 (3 × CH_3), 44.2 (CH_2), 55.9 (2 × OCH_3), 79.5 [$C(CH_3)_3$], 110.3 (ArC), 112.0 (ArC), 121.9 (ArC), 127.2 (Csp^2), 127.8 (ArC), 129.3 (ArC), 131.5 (ArC), 131.7 (ArC), 133.0 (ArC), 134.0 (Csp^2), 148.3 (ArC), 149.6 (ArC), 155.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{26}{}^{35}ClNNaO_4Se$ [M + Na] 506.0606; found 506.0601.

6-(Benzo[*d*][1,3]dioxol-5-yl)-5-(phenylselanyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8cc): Yield 0.11 g (56%); yellow solid; m.p. 155–156 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1748 (C=O), 3231 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.96 (d, ^3J = 0.8 Hz, 2 H, CH_2), 5.99 (s, 2 H, OCH_2O), 6.62 (br. s, 1 H, NH), 6.81 (d, ^3J = 8.4 Hz, 1 H, ArH), 7.07–7.09 (m, 2 H, ArH), 7.28–7.29 (m, 3 H, ArH), 7.41–7.43 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.3 (CH_2), 98.0 (Csp^2), 101.4 (OCH_2O), 107.7 (ArC), 109.1 (ArC), 123.5 (ArC), 126.3 (ArC), 127.9 (ArC), 128.0 (ArC), 129.5 (ArC), 132.2 (ArC), 147.2 (ArC), 148.7 (ArC), 150.0 (Csp^2), 151.4 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{17}H_{13}NNaO_4Se$ [M + Na] 397.9903; found 397.9901.

(*E*)-*tert*-Butyl 3-(Benzo[*d*][1,3]dioxol-5-yl)-3-chloro-2-(phenylselanyl)allylcarbamate (17cc): Yield 60.7 mg (26%); yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 1710 (C=O), 3243 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, 3 × CH_3), 4.17 (d, ^3J = 5.2 Hz, 2 H, CH_2), 4.79 (br. s, 1 H, NH), 5.98 (s, 2 H, OCH_2O), 6.77 (d, ^3J = 8.4 Hz, 1 H, ArH), 6.85–6.86 (m, 2 H, ArH), 7.24–7.28 (m, 3 H, ArH), 7.39–7.41 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.3 (3 × CH_3), 43.9 (CH_2), 79.4 [$C(CH_3)_3$], 101.4 (OCH_2O), 107.8 (ArC), 109.3 (ArC), 123.3 (ArC), 127.7 (Csp^2), 127.9 (ArC), 129.2 (ArC), 129.3 (ArC), 132.8 (ArC), 133.2 (ArC), 134.3 (Csp^2), 147.3 (ArC), 148.1 (ArC), 151.2 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{21}H_{22}{}^{35}ClNNaO_4Se$ [M + Na] 490.0293; found 490.0293.

5-(Phenylselanyl)-6-*p*-tolyl-3,4-dihydro-2*H*-1,3-oxazin-2-one (8dc): Yield 0.15 g (42%); yellow solid; m.p. 115–116 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1752 (C=O), 3246 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 3.99 (d, ^3J = 1.6 Hz, 2 H, CH_2), 6.44 (br. s, 1 H, NH), 7.20 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.28–7.30 (m, 3 H, ArH), 7.42–7.44 (m, 2 H, ArH), 7.49 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 46.4 (CH_2), 98.0 (Csp^2), 127.8 (ArC), 128.2 (ArC), 128.6 (ArC), 128.8 (ArC), 129.5 (ArC), 129.7 (ArC), 132.1 (ArC), 140.0 (ArC), 150.8 (Csp^2), 151.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{17}H_{15}NNaO_2Se$ [M + Na] 368.0161; found 368.0158.

(*E*)-*tert*-Butyl 3-Chloro-2-(phenylselanyl)-3-*p*-tolylallylcarbamate (17dc): Yield 67.7 mg (31%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 1715 (C=O), 3352 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.43 (s, 9 H, 3 × CH_3), 2.37 (s, 3 H, CH_3), 4.21 (d, ^3J = 4.8 Hz, 2 H, CH_2), 4.81 (br. s, 1 H NH), 7.17 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.26–7.28 (m, 5 H, ArH), 7.39–7.41 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (CH_3), 28.3 (3 × CH_3), 44.0 (CH_2), 79.4 [$C(CH_3)_3$], 127.3 (Csp^2), 127.8 (ArC), 128.76 (ArC), 128.78 (ArC), 129.3 (ArC), 129.4 (ArC), 133.0 (ArC), 134.3 (Csp^2), 136.3 (ArC), 139.1 (ArC), 155.2 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{21}H_{24}{}^{35}ClNNaO_2Se$ [M + Na] 460.0551; found 460.0549.

6-(4-Nitrophenyl)-5-(phenylselanyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8gc): Yield 18.8 mg (10%); yellow solid; m.p. 176–177 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1732 (C=O), 3252 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.05 (d, ^3J = 1.6 Hz, 2 H, CH_2), 6.11 (br. s, 1 H, NH), 7.31–7.33 (m, 3 H, ArH), 7.42–7.45 (m, 2 H, ArH), 7.81 (d, ^3J = 8.8 Hz, 2 H, ArH), 8.26 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.7 (CH_2), 102.0 (Csp^2), 123.2 (ArC), 127.1 (ArC), 128.5 (ArC), 129.8 (ArC), 129.9 (ArC), 132.6 (ArC), 138.5 (ArC), 148.0 (ArC), 148.2 (Csp^2), 150.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{16}H_{12}N_2NaO_4Se$ [M + Na] 398.9855; found 398.9854.

(*E*)-*tert*-Butyl 3-Chloro-3-(4-nitrophenyl)-2-(phenylselanyl)allylcarbamate (17gc): Yield 58.5 mg (25%); yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 1714 (C=O), 3430 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 9 H, 3 × CH_3), 4.25 (d, ^3J = 5.6 Hz, 2 H, CH_2), 4.87 (br. s, 1 H NH), 7.23–7.26 (m, 3 H, ArH), 7.30–7.33 (m, 2 H, ArH), 7.51 (d, ^3J = 8.4 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.3 (3 × CH_3), 44.0 (CH_2), 79.7 [$C(CH_3)_3$], 123.4 (ArC), 123.5 (ArC), 128.1 (ArC), 129.1 (Csp^2), 129.5 (ArC), 130.1 (ArC), 131.2 (Csp^2), 132.9 (ArC), 145.3 (ArC), 147.5 (ArC), 155.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{20}H_{21}{}^{35}ClN_2NaO_4Se$ [M + Na] 491.0246; found 491.0253.

(*E*)-*tert*-Butyl 2-Chloro-3-(phenylselanyl)allylcarbamate (17′hc): Yield 0.13 g (75%); yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 1686 (C=O), 3301 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.41 (s, 9 H, 3 × CH_3), 4.09 (d, ^3J = 5.6 Hz, 2 H, CH_2), 4.80 (br. s, 1 H NH), 6.39 (br. s, 1 H Csp^2H), 7.28–7.30 (m, 3 H, ArH), 7.47–7.50 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.2 (3 × CH_3), 41.2 (CH_2), 79.5 [$C(CH_3)_3$], 120.8 (Csp^2Cl), 128.0 (ArC), 128.2 (ArC), 129.4 (ArC), 132.2 (Csp^2), 133.2 (ArC), 155.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{14}H_{18}{}^{35}ClNNaO_2Se$ [M + Na] 370.0081; found 370.0081.

***N*-[6-(4-Methoxyphenyl)-5-(phenylselanyl)-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9ab):** Yield 0.21 g (82%); white solid; m.p. 218–222 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2997 (NH) cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 2.33 (s, 3 H, CH_3), 3.81 (s, 3 H, OCH_3), 3.86 (s, 2 H, CH_2), 7.01 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.25 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.30–7.38 (m, 3 H, ArH), 7.40–7.50 (m, 4 H, ArH), 7.63 (d, ^3J = 8.2 Hz, 2 H, ArH), 9.17 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 21.4 (CH_3), 44.4 (CH_2), 55.8 (OCH_3), 99.8 (SeC-sp^2), 113.9 (ArC), 123.8 (ArC), 126.6 (ArC), 128.1 (ArC), 128.4 (ArC), 129.6 (ArC), 130.3 (ArC), 130.9 (ArC), 132.2 (ArC), 140.9 (ArC), 142.4 (ArC), 148.7 (ArCC-sp^2), 153.1 (HNC-sp^2), 161.0 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{24}H_{23}N_2O_4SSe$ [M + H] 515.0539; found 515.0536.

6-(4-Methoxyphenyl)-*N*-phenyl-5-(phenylselanyl)-4*H*-1,3-oxazin-2-amine (9bb): Yield 0.2 g (92%); white solid; m.p. 166–170 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3426 (NH) cm^{-1}. ^1H NMR (400 MHz, [D_6]DMSO): δ = 3.80 (s, 3 H, OCH_3), 4.02 (s, 2 H, CH_2), 7.03 (s, 2 H, CH_2), 7.03 (d, ^3J = 8.6 Hz, 2 H, ArH), 7.25–7.50 (m, 8 H, ArH), 7.51–7.72 (m, 4 H, ArH), 11.87 (br. s, 1 H, NH) ppm. ^{13}C NMR

(100 MHz, [D$_6$]DMSO): δ = 44.3 (CH_2), 55.8 (OCH_3), 100.7 (SeC-sp^2), 114.1 (ArC), 123.3 (ArC), 124.4 (ArC), 127.3 (ArC), 128.0 (ArC), 129.9 (ArC), 130.3 (ArC), 131.0 (ArC), 132.0 (ArC), 134.5 (ArC), 148.1 (ArC*C*-sp^2), 154.0 (HNC-sp^2), 161.2 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{23}H_{21}N_2O_2Se$ [M + H] 437.0764; found 437.0760.

***N*-[6-(3,4-Dimethoxyphenyl)-5-(phenylselanyl)-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9db):** Yield 0.2 g (73%); white solid; m.p. 153–154 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3285 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.32 (s, 3 H, CH_3), 3.75 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 3.86 (br. s, 2 H, CH_2), 7.03 (d, ^3J = 8.4 Hz, 1 H, ArH), 7.13 (dd, ^3J = 8.3, ^4J = 2.2 Hz, 1 H,ArH), 7.25 (d, ^3J = 8.3 Hz, 2 H, ArH), 7.31–7.39 (m, 4 H, ArH), 7.44–7.50 (m, 2 H, ArH), 7.65 (d, ^3J = 8.2 Hz, 2 H, ArH), 9.22 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.3 (CH_3), 44.3 (CH_2), 55.9 (OCH_3), 56.0 (OCH_3), 100.0 (SeC-sp^2), 111.3 (ArC), 112.5 (ArC), 122.7 (ArC), 123.9 (ArC), 126.6 (ArC), 128.3 (ArC), 128.4 (ArC), 129.5 (ArC), 130.3 (ArC), 132.3 (ArC), 141.0 (ArC), 142.4 (ArC), 148.5 (ArC), 148.6 (ArCC-sp^2), 150.7 (ArC), 153.6 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{24}N_2NaO_5SSe$ [M + Na] 567.0464; found 567.0461.

4-Methyl-*N*-[5-(phenylselanyl)-6-(*p*-tolyl)-4*H*-1,3-oxazin-2-yl]benzenesulfonamide (9fb): Yield 0.2 g (80%); white solid; m.p. 224–226 °C. IR (KBr): $\tilde{\nu}_{max}$ = 2918(NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.33 (s, 3 H, CH_3), 2.35 (s, 3 H, CH_3), 3.85 (s, 2 H, CH_2), 7.21–7.29 (m, 4 H, ArH), 7.31–7.36 (m, 3 H, ArH), 7.36–7.40 (m, 2 H, ArH), 7.41–7.47 (m, 2 H, ArH), 7.62 (d, ^3J = 8.2 Hz, 2 H), 9.16 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 21.4 (2×CH_3), 44.3 (CH_2), 100.8 (SeC-sp^2), 126.6 (ArC), 127.9 (ArC), 128.5 (ArC), 128.8 (ArC), 129.0 (ArC), 129.1 (ArC), 129.5 (ArC), 130.3 (ArC), 132.5 (ArC), 140.5 (ArC), 140.9 (ArC), 142.4 (ArC), 148.6 (ArCC-sp^2), 153.1 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{22}N_2NaO_3SSe$ [M + Na] 521.0409; found 521.0417.

4-Methyl-*N*-[6-phenyl-5-(phenylselanyl)-4*H*-1,3-oxazin-2-yl]benzenesulfonamide (9gb): Yield 0.15 g (63%); white solid; m.p. 201–204 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3002 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.33 (s, 3 H, CH_3), 3.88 (s, 2 H, CH_2), 7.23 (d, ^3J = 7.7 Hz, 2 H, ArH), 7.34 (br. s, 3 H, ArH), 7.48 (br. s, 7 H, ArH), 7.61 (d, ^3J = 7.8 Hz, 2 H, ArH), 9.17 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.4 (CH_3), 44.3 (CH_2), 101.4 (SeC-sp^2), 126.6 (ArC), 127.8 (ArC), 128.5 (ArC), 128.6 (ArC), 129.3 (ArC), 129.5 (ArC), 130.3 (ArC), 130.6 (ArC), 131.7 (ArC), 132.5 (ArC), 140.9 (ArC), 142.4 (ArC), 148.4 (ArC*C*-sp^2), 153.0 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{23}H_{20}N_2NaO_3SSe$ [M + Na] 507.0252; found 507.0258.

(*E*)-*N*-{[2-Chloro-3-(phenylselanyl)allyl]carbamoyl}-4-methylbenzenesulfonamide (18′ib): Yield 0.21 g (94%); off-white solid; m.p. 148–149 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1685 (C=O), 3301, 3317 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.38 (s, 3 H, CH_3), 3.94 (d, ^3J = 5.4 Hz, 2 H, CH_2), 6.61 (s, 1 H, CH), 6.70 (t, ^3J = 5.6 Hz, 1 H, NH), 7.27–7.35 (m, 3 H, ArH), 7.36–7.47 (m, 4 H, ArH), 7.77 (d, ^3J = 8.2 Hz, 2 H, ArH), 10.64 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.5 (CH_3), 40.6 (CH_2), 121.5 (SeC-sp^2), 127.7 (ArC), 128.4 (ArC), 129.1 (ArC), 129.9 (ArC), 130.1 (ArC), 132.4 (ArC), 133.0 (ClC-sp^2), 137.7 (ArC), 144.1 (ArC), 151.7 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{17}ClN_2NaO_3SSe$ [M + Na] 466.9703, found 466.9704.

(*E*)-*N*-Phenyl-5-[(phenylselanyl)methylene]-4,5-dihydrooxazol-2-amine (14jb): Yield 44.6 mg (27%); white solid; m.p. 160–165 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3436 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 4.59 (d, ^4J = 2.2 Hz, 2 H, CH_2), 6.66 (s, 1 H, CH), 7.25–7.38 (m, 4 H, ArH), 7.43–7.55 (m, 6 H, ArH), 11.53 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 49.0 (CH_2), 90.7 (SeC-sp^2), 123.2 (ArC), 126.9 (ArC), 127.4 (ArC), 129.9 (ArC), 130.4 (2×ArC), 130.5 (ArC), 135.1 (ArC), 154.5 (H_2CC-sp^2), 158.5 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{16}H_{15}N_2OSe$ [M + H] 331.0345; found 331.0342.

(*E*)-*N*-Benzyl-5-[(phenylselanyl)methylene]-4,5-dihydrooxazol-2-amine (14kb): Yield 68.8 mg (40%); white solid; m.p. 171–176 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3436(NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 4.60 (s, 2 H, CH_2), 4.66 (br. s, 2 H, $HNCH_2$), 6.63 (s, 1 H, CH), 7.25–7.44 (m, 6 H, ArH), 7.45–7.60 (m, 4 H, ArH), 11.16 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 45.7 ($HNCH_2$), 47.8 (CH_2), 91.1 (SeC-sp^2), 127.5 (ArC), 128.3 (2×ArC), 129.0 (ArC), 130.0 (ArC), 130.4 (ArC), 130.6 (ArC), 136.4 (ArC), 153.9 (H_2CC-sp^2), 160.2 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{17}N_2OSe$ [M + H]$^+$ 345.0501; found 345.0501.

***N*-[6-(4-Methoxyphenyl)-5-(phenylselanyl)-4*H*-1,3-thiazin-2-yl]benzamide (10ab):** Yield 0.18 g (73%); yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 1681 (C=O), 3196 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 4.10 (s, 2 H, CH_2), 6.94 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.31–7.32 (m, 3 H, ArH), 7.39–7.41 (m, 3 H, ArH), 7.43–7.47 (m, 3 H, ArH), 7.49 (tt, ^3J = 7.2, ^4J = 1.2 Hz, 1 H, ArH), 7.15–7.17 (m, 2 H, ArH), 10.84 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.8 (CH_2), 55.3 (OCH_3), 113.8 (ArC), 116.0 (Csp^2), 128.1 (2×ArC), 128.4 (ArC), 129.0 (ArC), 129.2 (ArC), 129.6 (ArC), 130.9 (ArC), 132.1 (ArC), 133.2 (ArC), 134.2 (Csp^2), 136.0 (ArC), 160.4 (ArC), 168.4 (Csp^2), 176.0 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{21}N_2O_2SSe$ [M + H] 481.0484; found 481.0485.

***N*-[6-(4-Chlorophenyl)-5-(phenylselanyl)-4*H*-1,3-thiazin-2-yl]benzamide (10bb):** Yield 50.8 mg (21%); white solid; m.p. 59–60 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1678 (C=O), 3173 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.13 (s, 2 H, CH_2), 7.33–7.34 (m, 3 H, ArH), 7.40 (br. s, 4 H, ArH), 7.42–7.47 (m, 4 H, ArH), 7.51 (tt, ^3J = 7.6, ^4J = 1.2 Hz, 1 H, ArH), 8.13–8.15 (m, 2 H, ArH), 10.73 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 50.0 (CH_2), 118.0 (Csp^2), 128.2 (ArC), 128.4 (ArC), 128.5 (ArC), 128.8 (ArC), 129.2 (ArC), 129.8 (ArC), 130.9 (ArC), 132.3 (ArC), 133.0 (ArC), 133.4 (ArC), 134.7 (Csp^2), 135.6 (ArC), 135.8 (ArC), 167.6 (Csp^2), 175.8 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{23}H_{17}{}^{35}ClN_2OSSe$ [M + H] 484.9986; found 484.9988.

***N*-[6-Phenyl-5-(phenylselanyl)-4*H*-1,3-thiazin-2-yl]benzamide (10cb):** Yield 0.08 g (36%); yellow solid; m.p. 61–62 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1681 (C=O), 3193 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.13 (s, 2 H, CH_2), 7.30–7.34 (m, 3 H, ArH), 7.40–7.52 (m, 10 H, ArH), 8.14–8.16 (m, 2 H, ArH), 10.86 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 49.8 (CH_2), 117.1 (Csp^2), 128.1 (ArC), 128.2 (ArC), 128.5 (ArC), 128.8 (ArC), 129.2 (ArC), 129.5 (2×ArC), 129.7 (ArC), 132.1 (ArC), 133.3 (ArC), 134.2 (Csp^2), 135.9 (ArC), 136.3 (ArC), 168.1 (Csp^2), 175.9 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{23}H_{18}N_2OSSe$ [M + H] 451.0378; found 451.0388.

(*E*)-*N*-[5-(Phenylselanylmethylene)-4,5-dihydrothiazol-2-yl]benzamide (15db): Yield 74.8 mg (40%); yellow solid; m.p. 160–161 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1634 (C=O), 3410 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 4.45 (d, ^4J = 2.8 Hz, 2 H, CH_2), 6.82 (t, ^4J = 2.8 Hz, 1 H, CH), 7.26–7.30 (m, 1 H, ArH), 7.32–7.36 (m, 2 H, ArH), 7.45–7.50 (m, 4 H, ArH), 7.57 (tt, ^3J = 7.6, ^4J = 1.2 Hz, 1 H, ArH), 8.07–8.10 (m, 2 H, ArH), 10.43 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 51.9 (CH_2), 105.3 (Csp^{2}H), 127.0 (ArC), 128.3 (ArC), 128.7 (ArC), 129.5 (ArC), 130.4 (ArC), 130.5 (ArC), 132.2 (ArC), 135.0 (Csp^2), 141.2 (ArC), 168.2 (Csp^2),

172.3 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{14}N_2OSSe$ [M + H] 375.0065; found 375.0072.

(*E*)-3-Chloro-3-(4-methoxyphenyl)-2-(phenylselanyl)allyl Tosylcarbamate (19ab): Yield 0.22 g (79%); colorless oil. IR (KBr): $\tilde{\nu}_{max}$ = 1697 (C=O), 3345 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.44 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3),4.94 (s, 2 H, OCH_2), 6.90 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.18–7.23 (m, 3 H, ArH), 7.33–7.36 (m, 6 H, ArH), 7.96 (d, ^3J = 8.4 Hz, 2 H, ArH), 8.25 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5 (CH_3), 55.2 (OCH_3), 66.7 (OCH_2), 113.4 (ArC), 122.6 (ArC or C-sp^2), 126.3 (ArC or C-sp^2), 128.1 (ArC or C-sp^2), 128.3 (ArC or C-sp^2), 129.2 (ArC or C-sp^2), 129.5 (ArC or C-sp^2), 130.3 (ArC or C-sp^2), 130.7 (ArC or C-sp^2), 133.7 (ArC or C-sp^2), 135.4 (ArC or C-sp^2), 135.9 (ArC or C-sp^2), 144.9 (ArC or C-sp^2), 149.8 (ArC), 160.2 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{24}H_{22}{}^{35}ClNNaO_5SSe$ [M + Na] 573.9970; found 573.9973.

(*E*)-3-Chloro-3-(4-methoxyphenyl)-2-(phenylselanyl)allyl Acetate (20ab): Yield 0.15 g (78%); colorless oil. IR (KBr): $\tilde{\nu}_{max}$ = 1712 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.02 (s, 3 H, CH_3), 3.85 (s, 3 H, OCH_3), 5.01 (s, 2 H, OCH_2), 6.92 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.28–7.30 (m, 3 H, ArH), 7.43 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.47 (dd, ^3J = 7.4, ^4J = 2.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (CH_3), 55.3 (OCH_3), 65.1 (OCH_2), 113.5 (ArC), 123.9 (ArC or C-sp^2), 128.1 (ArC or C-sp^2), 129.2 (ArC or C-sp^2), 130.5 (ArC or C-sp^2), 131.2 (ArC or C-sp^2), 133.7 (ArC or C-sp^2), 135.6 (ArC or C-sp^2), 160.2 (ArC), 170.4 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{18}H_{17}{}^{35}ClNaO_3Se$ [M + Na] 418.9922; found 418.9917.

General Procedures for Oxocarbenium Ion Mediated Reactions

Method A: To a mixture of **1**, **3**, **5** or **6** (0.5 mmol) and 1-methoxyisochromane (90.2 mg, 0.55 mmol) in anhydrous dichloromethane (5 mL), trimethylsilyl triflate (0.09 mL, 0.5 mmol) was added either at room temperature (for **1**, **5**, and **6**) or at 0 °C (for **3**). The resulting solution was stirred at the same temperature.

Method B: To a cooled solution of **2** or **4** (0.5 mmol) and 1-methoxyisochromane (90.2 mg, 0.55 mmol) in either anhydrous dichloromethane (5 mL, for **2**) or anhydrous acetonitrile (5 mL, for **4**) boron trifluoride etherate (0.06 mL, 0.5 mmol) was added at 0 °C. The resulting solution was stirred at the same temperature.

Method C: To a cooled solution of **1** or **4** (0.5 mmol) and the corresponding dialkoxymethylarene (0.75 mmol) in anhydrous dichloromethane (5 mL), boron trifluoride etherate (0.5 mmol, for **1**) or trimethylsilyl triflate (0.5 mmol, for **4**) was added at –10 °C. The resulting solution was stirred at the same temperature.

Isolation Procedures for All Products: When completion of the reaction was observed by TLC, the reaction was quenched with aqueous sodium hydrogen carbonate solution. The organic layer was separated, washed with water (2×20 mL), and dried with anhydrous Na_2SO_4. After the evaporation of solvent under reduced pressure, the residue was purified by flash column chromatography eluting with hexane/ethyl acetate mixtures.

5-(Isochroman-1-yl)-6-(4-methoxyphenyl)-2-phenyl-4*H*-1,3-oxazine (7ac): Yield 0.16 g (78%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.63 (d, ^3J = 16.4 Hz, 1 H, CH_2), 3.09–3.17 (m, 1 H, CH_2), 3.76–3.83 (m, 1 H, CH_2), 3.84 (d, ^2J = 18.8 Hz, 1 H, CH_2), 3.85 (s, 3 H, OCH_3), 4.20 (d, ^2J = 18.8 Hz, 1 H, CH_2), 4.21–4.26 (m, 1 H, CH_2), 5.62 (s, 1 H, CH), 7.00 (d, ^3J = 9.2 Hz, 2 H, ArH), 7.10–7.15 (m, 2 H, ArH), 7.17–7.19 (m, 2 H, ArH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.46 (tt, ^3J = 7.2, ^4J = 2.8 Hz, 1 H, ArH), 7.64 (d, ^3J = 8.8 Hz, 2 H, ArH), 8.00–8.03 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 (CH_2), 42.7 (CH_2), 55.4 (OCH_3), 64.9 (CH_2), 75.2 (CH), 109.4 (Csp^2), 114.0 (ArC), 125.2 (ArC), 126.6 (ArC), 127.0 (ArC), 127.3 (ArC), 128.3 (ArC), 129.0 (ArC), 130.0 (ArC), 131.0 (ArC), 131.9 (ArC), 134.6 (ArC), 135.1 (ArC), 147.4 (Csp^2), 153.7 (Csp^2), 160.4 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{25}NNaO_4$ [M + Na] 438.1676; found 438.1674.

5-[Methoxy(4-methoxyphenyl)methyl]-6-(4-methoxyphenyl)-2-phenyl-4*H*-1,3-oxazine (7ad): Yield 0.11 g (51%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.32 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.98 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.22 (d, ^2J = 19.2 Hz, 1 H, CH_2), 5.10 (s, 1 H, CH), 6.89 (d, ^3J = 8.8 Hz, 2 H, ArH), 6.98 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.29 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.38 (t, ^3J = 7.2 Hz, 2 H, ArH), 7.44 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.48 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.95–7.98 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.0 (CH_2), 55.4 (OCH_3), 55.4 (OCH_3), 56.3 (OCH_3), 79.3 (CH), 108.7 (Csp^2), 113.9 (ArC), 114.0 (ArC), 125.3 (ArC), 127.3 (ArC), 127.6 (ArC), 128.3 (ArC), 130.1 (ArC), 131.0 (ArC), 131.5 (ArC), 132.1 (ArC), 147.6 (Csp^2), 153.5 (NCO), 159.1 (ArC), 160.3 (ArC) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{26}NO_4$ [M + H] 416.1856; found 416.1862.

(*E*)-*N*-[2-(4-Methoxybenzoyl)-3-(4-methoxyphenyl)allyl]benzamide (23ad): Yield 22 mg (10%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 3334 (NH), 1639 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 6 H, OCH_3), 3.87 (s, 3 H, OCH_3), 4.72 (d, ^3J = 5.6 Hz, 2 H, CH_2), 6.95 (d, ^3J = 8.8 Hz, 2 H, ArH), 6.97 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.16 (t, ^3J = 5.6 Hz, 1 H, NH), 7.26 (s, 1 H, CH), 7.38 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.46 (t, ^3J = 7.6 Hz, 1 H, ArH), 7.59 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.74–7.77 (m, 2 H, ArH), 7.80 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.2 (CH_2), 55.4 (OCH_3), 55.6 (OCH_3), 113.7 (ArC), 114.4 (ArC), 126.9 (ArC), 127.1 (ArC), 128.6 (ArC), 130.6 (ArC), 131.5 (ArC), 131.7 (ArC), 132.1 (ArC), 134.5 (ArC), 134.6 (Csp^2), 143.7 (Csp^2), 160.6 (ArC), 163.1 (ArC), 167.3 (NHCO), 198.7 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{23}NNaO_4$ [M + Na] 424.1519; found 424.1518.

(*Z*)-*N*-[2-(4-Methoxybenzoyl)-3-(4-methoxyphenyl)allyl]benzamide (24ad): Yield 23 mg (11%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 3326 (NH), 1652 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.69 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 4.41 (d.d, ^3J = 5.6, ^4J = 0.8 Hz, 2 H, CH_2), 6.63 (d, ^3J = 8.8 Hz, 2 H, ArH), 6.75–6.79 (m, 3 H, ArH, NH), 6.94 (s, 1 H, CH), 7.08 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.39 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.47 (t, ^3J = 7.6 Hz, 1 H, ArH), 7.71–7.73 (m, 2 H, ArH), 7.87 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.5 (CH_2), 55.2 (OCH_3), 55.5 (OCH_3), 113.8 (ArC), 114.0 (ArC), 127.0 (ArC), 127.6 (ArC), 128.6 (ArC), 128.9 (ArC), 130.5 (ArC), 131.6 (ArC), 132.0 (ArC), 132.2 (ArC), 134.3 (ArC or Csp^2), 134.4 (ArC or Csp^2), 159.5 (ArC), 164.1 (ArC), 167.6 (NHCO), 199.2 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{23}NNaO_4$ [M + Na] 424.1519; found 424.1518.

5-[(4-Bromophenyl)(ethoxy)methyl]-6-(4-methoxyphenyl)-2-phenyl-4*H*-1,3-oxazine (7ae): Yield 0.13 g (54%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 3.32–3.40 (m, 1 H, OCH_2CH_3), 3.56–3.64 (m, 1 H, OCH_2CH_3), 3.86 (s, 3 H, OCH_3), 3.92 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.21 (d, ^2J = 19.2 Hz, 1 H, CH_2), 5.21 (s, 1 H, CH), 6.99 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.27 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.38 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.43–7.48 (m, 5 H, ArH), 7.95–7.97 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.4 (OCH_2CH_3), 42.0 (CH_2), 55.4 (OCH_3), 64.0 (OCH_2CH_3), 77.2 (CH), 108.6 (Csp^2), 114.1 (ArC), 121.4 (ArC), 125.2 (ArC), 127.3 (ArC), 128.1 (ArC), 128.3 (ArC), 130.1 (ArC), 131.0 (ArC), 131.6 (ArC), 132.0 (ArC), 139.0 (ArC),

147.7 (Csp^2), 153.4 (NCO), 160.4 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{25}{}^{79}BrNO_3$ [M + H] 478.1018; found 478.1015.

(*E*)-*N*-[3-(4-Bromophenyl)-2-(4-methoxybenzoyl)allyl]benzamide (23ae): Yield 33.7 mg (15%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 3332 (NH), 1645 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, OCH_3), 4.64 (d, ^3J = 5.6 Hz, 2 H, CH_2), 6.95 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.11 (t, ^3J = 5.6 Hz, 1 H, NH), 7.16 (s, 1 H, CH), 7.37 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.45 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.50 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.57 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.71–7.73 (m, 2 H, ArH), 7.82 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 38.1 (CH_2), 55.5 (OCH_3), 113.8 (ArC), 123.5 (ArC), 126.9 (ArC), 128.5 (ArC), 130.1 (ArC), 131.1 (ArC), 131.5 (ArC), 132.0 (ArC), 132.1 (ArC), 133.3 (ArC), 134.2 (ArC), 137.5 (Csp^2), 141.1 (Csp^2), 163.4 (ArC), 167.3 (NHCO), 198.0 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{24}H_{20}Br^{79}NNaO_3$ [M + Na] 472.0519; found 472.0517.

(*Z*)-*N*-[3-(4-Bromophenyl)-2-(4-methoxybenzoyl)allyl]benzamide (24ae): Yield 11.2 mg (5%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 3325 (NH), 1647 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, OCH_3), 4.43 (dd, ^3J = 5.8, ^4J = 1.4 Hz, 2 H, CH_2), 6.71 (t, ^3J = 5.2 Hz, 1 H, NH), 6.77 (d, ^3J = 8.8 Hz, 2 H, ArH), 6.90 (s, 1 H, CH), 7.01 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.23 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.48 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.70–7.72 (m, 2 H, ArH), 7.85 (d, ^3J = 9.2 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.3 (CH_2), 55.6 (OCH_3), 114.2 (ArC), 122.3 (ArC), 127.0 (ArC), 128.6 (ArC), 128.7 (ArC), 130.4 (ArC), 130.5 (ArC), 131.5 (ArC), 131.7 (ArC), 132.0 (ArC), 134.0 (ArC or Csp^2), 134.2 (ArC or Csp^2), 137.6 (Csp^2), 164.4 (ArC), 167.7 (NHCO), 198.5 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{24}H_{20}Br^{79}NNaO_3$ [M + Na] 472.0519; found 472.0514.

6-(4-Ethoxyphenyl)-5-(isochroman-1-yl)-2-phenyl-4*H*-1,3-oxazine (7bc): Yield 0.11 g (53%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.44 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 2.63 (d, ^3J = 16.4 Hz, 1 H, CH_2), 3.09–3.17 (m, 1 H, CH_2), 3.76–3.82 (m, 1 H, CH_2), 3.82 (d, ^2J = 18.4 Hz, 1 H, CH_2), 4.08 (q, ^3J = 7.2 Hz, 2 H, OCH_2CH_3), 4.18 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.21–4.25 (m, 1 H, CH_2), 5.61 (s, 1 H, CH), 6.97 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.10–7.15 (m, 2 H, ArH), 7.16–7.19 (m, 2 H, ArH), 7.39 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.46 (tt, ^3J = 7.2, ^4J = 2.8 Hz, 1 H, ArH), 7.61 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.98–8.03 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9 (OCH_2CH_3), 28.8 (CH_2), 42.9 (CH_2), 63.6 (OCH_2CH_3), 64.9 (CH_2), 75.3 (CH), 109.3 (Csp^2), 114.5 (ArC), 125.1 (ArC), 125.3 (ArC), 126.7 (ArC), 127.0 (ArC), 127.3 (ArC), 128.3 (ArC), 129.0 (ArC), 130.0 (ArC), 130.9 (ArC), 132.2 (ArC), 134.7 (ArC), 135.3 (ArC), 148.6 (Csp^2), 153.4 (Csp^2), 169.8 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{27}H_{26}NO_3$ [M + Na] 412.1907; found 412.1914.

6-(3,4-Dimethoxyphenyl)-5-(isochroman-1-yl)-2-phenyl-4*H*-1,3-oxazine (7cc): Yield 0.15 g (70%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.62 (d, ^3J = 16.4 Hz, 1 H, CH_2), 3.08–3.17 (m, 1 H, CH_2), 3.76–3.82 (m, 1 H, CH_2), 3.83 (d, ^3J = 19.2 Hz, 1 H, CH_2), 3.92 (s, 6 H,2 × OCH_3), 4.17 (d, ^3J = 19.2 Hz, 1 H, CH_2), 4.21–4.26 (m, 1 H, CH_2), 5.62 (s, 1 H, CH), 6.94 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.08–7.14 (m, 2 H, ArH), 7.15–7.18 (m, 2 H, ArH), 7.23–7.28 (m, 2 H, ArH), 7.39 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.46 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.99–8.01 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 (CH_2), 42.8 (CH_2), 56.04 (OCH_3), 56.07 (OCH_3), 64.9 (CH_2), 75.3 (CH), 109.4 (Csp^2), 110.9 (ArH), 111.7 (ArC), 125.2 (ArC), 125.4 (ArC), 126.6 (ArC), 127.0 (ArC), 127.3 (ArC), 128.3 (ArC), 129.0 (ArC), 130.9 (ArC), 132.1 (ArC), 134.6 (ArC), 135.1 (ArC), 148.7 (Csp^2), 148.9 (ArC), 150.0 (ArC), 153.4 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{27}H_{26}NO_4$ [M + H] 428.1856; found 428.1859.

5-[(4-Bromophenyl)(ethoxy)methyl]-6-(3,4-dimethoxyphenyl)-2-phenyl-4*H*-1,3-oxazine (7ce): Yield 0.12 g (49%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 6.8 Hz, 3 H, OCH_2CH_3), 3.34–3.41 (m, 1 H, OCH_2CH_3), 3.56–3.63 (m, 1 H, OCH_2CH_3), 3.87 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 3.94 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.22 (d, ^2J = 19.2 Hz, 1 H, CH_2), 5.23 (s, 1 H, CH), 6.93 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.03 (d, ^3J = 2.0 Hz, 1 H, ArH), 7.09 (d.d, ^3J = 8.8, ^3J = 2.0 Hz, 1 H, ArH), 7.26 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.39 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.43–7.48 (m, 3 H, ArH), 7.95–7.98 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.4 (OCH_2CH_3), 42.0 (CH_2), 56.0 (OCH_3), 56.1 (OCH_3), 64.1 (OCH_2CH_3), 77.3 (CH), 108.8 (Csp^2), 111.0 (ArC), 111.7 (ArC), 121.5 (ArC), 121.6 (ArC), 125.3 (ArC), 127.3 (ArC), 128.2 (ArC), 128.3 (ArC), 131.1 (ArC), 131.6 (ArC), 138.9 (ArC), 147.6 (Csp^2), 149.1 (ArC), 150.0 (ArC), 153.5 (NCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{27}H_{27}{}^{79}BrNO_4$ [M + H] 508.1123; found 508.1129.

5-(Isochroman-1-yl)-2-phenyl-6-(3,4,5-trimethoxyphenyl)-4*H*-1,3-oxazine (7dc): Yield 0.25 g (54%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.63 (d, ^3J = 16.4 Hz, 1 H, CH_2), 3.10–3.18 (m, 1 H, CH_2), 3.78–3.84 (m, 1 H, CH_2), 3.83 (d, ^3J = 19.2 Hz, 1 H, CH_2), 3.90 (s, 6 H, 2 × OCH_3), 3.90 (s, 3 H, OCH_3), 4.16 (d, ^3J = 19.2 Hz, 1 H, CH_2), 4.23–4.28 (m, 1 H, CH_2), 5.64 (s, 1 H, CH), 6.94 (s, 2 H, ArH), 7.06–7.14 (m, 2 H, ArH), 7.15–7.18 (m, 2 H, ArH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.46 (tt, ^3J = 7.2, ^4J = 2.8 Hz, 1 H, ArH), 7.97–8.00 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 (CH_2), 42.9 (CH_2), 56.3 (2 × OCH_3), 61.0 (OCH_3), 64.9 (CH_2), 75.3 (CH), 105.9 (ArC), 109.8 (Csp^2), 125.1 (ArC), 126.7 (ArC), 127.0 (ArC), 127.3 (ArC), 128.1 (ArC), 128.3 (ArC), 129.1 (ArC), 131.0 (ArC), 132.0 (ArC), 134.5 (ArC), 134.9 (ArC), 139.0 (ArC), 148.9 (Csp^2), 153.25 (Csp^2), 159.29 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{28}H_{27}NNaO_5$ [M + Na] 480.1781; found 480.1779.

5-(Isochroman-1-yl)-2-phenyl-6-*p*-tolyl-4*H*-1,3-oxazine (7ec): Yield 0.15 g (81%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 2.63 (d, ^3J = 16.4 Hz, 1 H, CH_2), 3.09–3.17 (m, 1 H, CH_2), 3.75–3.81 (m, 1 H, CH_2), 3.83 (d, ^3J = 18.8 Hz, 1 H, CH_2), 4.21 (d, ^3J = 18.8 Hz, 1 H, CH_2), 4.21–4.25 (m, 1 H, CH_2), 5.61 (s, 1 H, CH), 7.10–7.15 (m, 2 H, ArH), 7.16–7.19 (m, 2 H, ArH), 7.28 (d, ^3J = 7.6 Hz, 2 H, ArH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.46 (tt, ^3J = 7.2, ^4J = 2.4 Hz, 1 H, ArH), 7.58 (d, ^3J = 8.0 Hz, 2 H, ArH), 8.00–8.02 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5 (CH_3), 28.8 (CH_2), 42.7 (CH_2), 64.9 (CH_2), 75.2 (CH), 109.9 (Csp^2), 125.2 (ArC), 126.7 (ArC), 127.0 (ArC), 127.4 (ArC), 128.3 (ArC), 128.5 (ArC), 129.0 (ArC), 129.3 (ArC), 129.9 (ArC), 131.1 (ArC), 131.8 (ArC), 134.7 (ArC), 135.1 (ArC), 139.5 (ArC), 148.6 (Csp^2), 153.9 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{24}NO_2$ [M + Na] 382.1802; found 382.1796.

5-[Methoxy(4-methoxyphenyl)methyl]-2-phenyl-6-*p*-tolyl-4*H*-1,3-oxazine (7ed): Yield 93.7 mg (47%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 3.33 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.99 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.24 (d, ^2J = 19.2 Hz, 1 H, CH_2), 5.11 (s, 1 H, CH), 6.89 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.26–7.30 (m, 4 H, ArH), 7.38 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.42–7.46 (m, 3 H, ArH), 7.96–7.98 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5 (CH_3), 41.9 (CH_2), 55.4 (OCH_3), 56.3 (OCH_3), 79.2 (CH), 109.1 (Csp^2), 113.9 (ArC), 127.3 (ArC), 127.5 (ArC), 128.3 (ArC), 128.7 (ArC), 129.3 (ArC), 130.1 (ArC), 130.9 (ArC), 131.4 (ArC), 132.1 (ArC), 139.4 (ArC), 147.8 (Csp^2), 153.5

(NCO), 159.1 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{26}NO_3$ [M + H] 400.1907; found 400.1914.

(*E*)-*N*-[3-(4-Methoxyphenyl)-2-(4-methylbenzoyl)allyl]benzamide (23ed): Yield 21.2 mg (11%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 3342 (NH),1638 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 4.74 (d, ^3J = 5.6 Hz, 2 H, CH_2), 6.97 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.13 (t, ^3J = 5.2 Hz, 1 H, NH), 7.27 (d, ^3J = 8.0 Hz, 2 H, ArH),7.31 (s, 1 H, CH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.47 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.60 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.68 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.75–7.78 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7 (CH_3), 38.0 (CH_2), 55.5 (OCH_3), 114.4 (ArC), 126.9 (ArC), 127.1 (ArC), 128.6 (ArC), 129.2 (ArC), 129.8 (ArC), 131.5 (ArC), 131.9 (ArC), 134.6 (ArC or Csp^2), 134.6 (ArC or Csp^2), 135.5 (ArC), 143.0 (ArC), 144.9 (Csp^2), 160.8 (ArC), 167.3 (NHCO), 199.8 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{25}H_{23}NNaO_3$ [M + Na] 408.1570; found 408.1574.

5-[(4-Bromophenyl)(ethoxy)methyl]-2-phenyl-6-*p*-tolyl-4*H*-1,3-oxazine (7ee): Yield 0.11 g (48%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 6.8 Hz, 3 H, OCH_2CH_3), 2.42 (s, 3 H, CH_3), 3.32–3.40 (m, 1 H, OCH_2CH_3), 3.92 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.21 (d, ^2J = 19.6 Hz, 1 H, CH_2), 5.21 (s, 1 H, CH), 7.26–7.29 (m, 4 H, ArH), 7.36–7.48 (m, 8 H, ArH), 7.95–7.97 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.4 (OCH_2CH_3), 21.5 (CH_3), 41.9 (CH_2), 64.0 (OCH_2CH_3), 77.1 (CH), 109.0 (Csp^2), 121.4 (ArC), 127.3 (ArC), 128.1 (ArC), 128.3 (ArC), 128.6 (ArC), 129.4 (ArC), 130.0 (ArC), 131.0 (ArC), 131.6 (ArC), 132.0 (ArC), 138.9 (ArC), 139.5 (ArC), 147.9 (Csp^2), 153.5 (NCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{25}{}^{79}BrNO_2$ [M + H] 462.1069; found 462.1070.

(*E*)-*N*-[3-(4-Bromophenyl)-2-(4-methylbenzoyl)allyl]benzamide (23ee): Yield 49.8 mg (22%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 3341 (NH), 1645 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 4.66 (dd, ^3J = 6.0, ^4J = 0.4 Hz, 2 H, CH_2), 7.10 (t, ^3J = 5.2 Hz, 1 H, NH), 7.22 (s, 1 H, CH), 7.27 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.38 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.46 (t, ^3J = 7.2 Hz, 1 H, ArH), 7.51 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.57 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.68 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.72–7.74 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7 (CH_3), 38.0 (CH_2), 123.7 (ArC), 127.0 (ArC), 128.6 (ArC), 129.3 (ArC), 129.9 (ArC), 131.2 (ArC), 131.6 (ArC), 132.1 (ArC), 133.3 (ArC), 134.3 (ArC), 135.1 (ArC), 137.6 (Csp^2), 142.5 (Csp^2), 143.5 (ArC), 167.4 (NHCO), 199.2 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{24}H_{20}Br^{79}NNaO_2$ [M + Na] 456.0570; found 456.0577.

5-[Methoxy(phenyl)methyl]-2-phenyl-6-*p*-tolyl-4*H*-1,3-oxazine (7ef): Yield 0.09 g (50%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.44 (s, 3 H, CH_3), 3.36 (s, 3 H, OCH_3), 3.97 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.25 (d, ^2J = 19.2 Hz, 1 H, CH_2), 5.17 (s, 1 H, CH), 7.27–7.30 (m, 3 H, ArH), 7.34–7.45 (m, 7 H, ArH), 7.47 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.96–7.99 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5 (CH_3), 41.9 (CH_2), 56.3 (OCH_3), 79.5 (CH), 109.0 (Csp^2), 126.3 (ArC), 127.3 (ArC), 127.6 (ArC), 128.3 (ArC), 128.5 (ArC), 128.7 (ArC), 129.4 (ArC), 130.1 (ArC), 130.9 (ArC), 132.1 (ArC), 139.4 (ArC), 139.4 (ArC), 148.0 (Csp^2), 153.4 (NCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{25}H_{24}NO_2$ [M + H] 370.1807; found 370.1809.

(*E*)-*N*-[2-(4-Methylbenzoyl)-3-phenylallyl]benzamide (23ef): Yield 17.8 mg (10%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 3254 (NH), 1645 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 4.72 (dd, ^3J = 6.0, ^4J = 0.4 Hz, 2 H, CH_2), 7.11 (t, ^3J = 5.2 Hz, 1 H, NH), 7.28 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.33 (s, 1 H, CH), 7.37–7.40 (m, 3 H, ArH), 7.43–7.48 (m, 2 H, ArH), 7.61 (d, ^3J = 7.2 Hz, 2 H, ArH), 7.71–7.75 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7 (CH_3), 38.0 (CH_2), 127.1 (ArC), 128.6 (ArC), 128.9 (ArC), 129.2 (ArC), 129.4 (ArC), 129.7 (ArC), 129.9 (ArC), 131.5 (ArC), 134.4 (ArC), 134.5 (ArC), 135.2 (ArC), 136.8 (Csp^2), 143.3 (ArC), 144.4 (ArC), 167.3 (NHCO), 199.5 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{24}H_{21}NNaO_2$ [M + Na] 378.1465; found 378.1467.

5-(Isochroman-1-yl)-2,6-diphenyl-4*H*-1,3-oxazine (7fc): Yield 0.14 g (78%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.63 (d, ^2J = 16.4 Hz, 1 H, CH_2), 3.14 (ddd, ^2J = 17.3, ^3J = 11.7 Hz, ^2J = 6.0 Hz, 1 H, CH_2), 3.79 (td, $^{2,3}J$ = 11.6, ^3J = 3.2 Hz, 1 H, CH_2), 3.86 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.23 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.22–4.27 (m, 1 H, CH_2), 5.63 (s, 1 H, CH), 7.11–7.15 (m, 2 H, ArH), 7.17–7.20 (m, 2 H, ArH), 7.38–7.24 (m, 2 H, ArH), 7.44–7.51 (m, 4 H, ArH), 7.69–7.22 (m, 2 H, ArH), 8.00–8.02 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 (CH_2), 42.8 (CH_2), 64.9 (CH_2), 75.1 (CH), 110.2 (Csp^2), 125.2 (ArC), 126.6 (ArC), 127.0 (ArC), 127.3 (ArC), 128.2 (ArC), 128.6 (2×ArC), 129.0 (ArC), 129.4 (ArC), 130.9 (ArC), 132.0 (ArC), 132.8 (ArC), 134.6 (ArC), 135.1 (ArC), 148.6 (Csp^2), 153.4 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{25}H_{22}NO_2$ [M + Na] 368.1645; found 368.1651.

5-[(4-Bromophenyl)(ethoxy)methyl]-2,6-diphenyl-4*H*-1,3-oxazine (7fe): Yield 0.12 g (54%); solid; m.p. 89–90 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 3.32–3.39 (m, 1 H, OCH_2CH_3), 3.56–3.64 (m, 1 H, OCH_2CH_3), 3.93 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.22 (d, ^2J = 19.2 Hz, 1 H, CH_2), 5.20 (s, 1 H, CH), 7.26 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.38 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.43–7.48 (m, 6 H, ArH), 7.52–7.54 (m, 2 H, ArH), 7.94–7.97 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.4 (OCH_2CH_3), 41.9 (CH_2), 64.0 (OCH_2CH_3), 77.1 (CH), 109.4 (Csp^2), 121.5 (ArC), 127.3 (ArC), 128.1 (ArC), 128.3 (ArC), 128.7 (ArC), 128.8 (ArC), 129.5 (ArC), 131.1 (ArC), 131.5 (ArC), 131.9 (ArC), 132.8 (ArC), 138.9 (ArC), 147.8 (Csp^2), 153.4 (NCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{25}H_{23}{}^{79}BrNO_2$ [M + H] 448.0912; found 448.0911.

(*E*)-*N*-[2-Benzoyl-3-(4-bromophenyl)allyl]benzamide (23fe): Yield 12.6 mg (6%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 4.67 (dd, ^3J = 6.0, ^4J = 0.8 Hz, 2 H, CH_2), 7.05 (t, ^3J = 5.6 Hz, 1 H, NH), 7.25 (s, 1 H, CH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.45–7.49 (m, 3 H, ArH), 7.53 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.56–7.60 (m, 3 H, ArH), 7.73–7.78 (m, 4 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.9 (CH_2), 123.9 (ArC), 127.1 (ArC), 128.6 (ArC), 128.7 (ArC), 129.7 (ArC), 131.3 (ArC), 131.7 (ArC), 132.2 (ArC), 132.6 (ArC), 133.2 (ArC), 134.3 (ArC), 137.5 (ArC or Csp^2), 137.9 (ArC or Csp^2), 143.4 (Csp^2), 167.4 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{19}{}^{79}BrNO_2$ [M + H] 420.0599; found 420.0597.

5-[(4-Bromophenyl)(ethoxy)methyl]-6-(4-chlorophenyl)-2-phenyl-4*H*-1,3-oxazine (7ge): Yield 0.13 g (52%); yellowish oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, ^3J = 6.8 Hz, 3 H, OCH_2CH_3), 3.32–3.39 (m, 1 H, OCH_2CH_3), 3.54–3.61 (m, 1 H, OCH_2CH_3), 3.92 (d, ^2J = 19.2 Hz, 1 H, CH_2), 4.22 (d, ^2J = 19.6 Hz, 1 H, CH_2), 5.14 (s, 1 H, CH), 7.24 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.39 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.44–7.49 (m, 7 H, ArH), 7.92–7.95 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.3 (OCH_2CH_3), 42.0 (CH_2), 64.1 (OCH_2CH_3), 77.1 (CH), 110.1 (Csp^2), 121.6 (ArC), 127.3 (ArC), 128.1 (ArC), 128.3 (ArC), 129.1 (ArC), 130.0 (ArC), 131.1 (ArC), 131.1 (ArC), 131.7 (ArC), 131.8 (ArC), 135.5 (ArC), 138.5 (ArC), 146.7 (Csp^2), 153.1 (NCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{25}H_{22}{}^{79}Br{}^{35}ClNO_2$ [M + H] 482.0522; found 482.0523.

(*E*)-*N*-[3-(4-Bromophenyl)-2-(4-chlorobenzoyl)allyl]benzamide (23ge): Yield 27.2 mg (11%); yellowish oil. ^1H NMR (400 MHz,

$CDCl_3$): δ = 4.65 (d, ^3J = 5.2 Hz, 2 H, CH_2), 7.00 (t, ^3J = 4.8 Hz, 1 H, NH), 7.19 (s, 1 H, CH), 7.39 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.43–7.49 (m, 3 H, ArH), 7.52 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.59 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.71–7.73 (m, 4 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.9 (CH_2), 124.1 (ArC), 127.0 (ArC), 128.7 (ArC), 128.9 (ArC), 131.1 (ArC), 131.3 (ArC), 131.7 (ArC), 132.2 (ArC), 133.0 (ArC), 134.2 (ArC), 136.1 (ArC), 137.7 (Csp^2), 139.1 (ArC), 143.1 (Csp^2), 167.5 (NHCO), 198.2 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{17}Br^{79}Cl^{35}NNaO_2$ [M + Na] 476.0023; found 476.0022.

5-(Isochroman-1-yl)-6-(4-nitrophenyl)-2-phenyl-4*H*-1,3-oxazine (7hc): Yield 28.8 mg (14%); yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.66 (d, ^3J = 16.4 Hz, 1 H, CH_2), 3.05–3.18 (m, 1 H, CH_2), 3.79 (td, $^{2,3}J$ = 11.4, ^3J = 3.2 Hz, 1 H, CH_2), 3.85 (d, ^3J = 19.6 Hz, 1 H, CH_2), 4.20 (d, ^3J = 19.2 Hz, 1 H, CH_2), 4.24–4.27 (m, 1 H, CH_2), 5.54 (s, 1 H, CH), 7.01–7.03 (m, 1 H, ArH), 7.14–7.21 (m, 3 H, ArH), 7.41 (t, ^3J = 7.2 Hz, 2 H, ArH), 7.48 (t, ^3J = 7.6 Hz, 1 H, ArH), 7.87 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.94–7.96 (m, 2 H, ArH), 8.33 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.7 (CH_2), 42.9 (CH_2), 64.9 (CH_2), 74.8 (CH), 113.2 (Csp^2), 123.9 (ArC), 124.9 (ArC), 126.8 (ArC), 127.3 (ArC), 127.3 (ArC), 128.4 (ArC), 129.3 (ArC), 129.5 (ArC), 131.3 (ArC), 131.6 (ArC), 134.3 (ArC), 134.6 (ArC), 139.0 (ArC), 146.5 (Csp^2), 148.2 (ArC), 152.7 (Csp^2) ppm. HRMS (ESI): *m/z* calcd. for $C_{25}H_{20}N_2NaO_4$ [M + Na] 435.1315; found 435.1314.

5-(Isochroman-1-yl)-6-(4-methoxyphenyl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8ad): Yield 59 mg (35%); white solid; m.p. 170–171 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1749 (C=O), 3266 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.60 (d, ^2J = 16.4 Hz, 1 H, CH_2), 3.01–3.10 (m, 1 H, CH_2), 3.52 (dd, ^2J = 14.8, ^3J = 1.6 Hz, 1 H, CH_2), 3.74 (td, $^{2,3}J$ = 11.6, ^3J = 2.8 Hz, 1 H, CH_2), 3.82 (s, 3 H, OCH_3), 3.95 (dd, ^2J = 14.8, ^3J = 1.6 Hz, 1 H, CH_2), 4.19 (ddd, ^2J = 10.0, ^3J = 6.0 Hz, ^3J = 1.2 Hz, 1 H, CH_2), 5.53 (s, 1 H, CH), 6.33 (br. s, 1 H, NH), 6.92 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.04–7.06 (m, 1 H, ArH), 7.10–7.12 (m, 1 H, ArH), 7.16–7.19 (m, 2 H, ArH), 7.55 (d, ^3J = 8.8 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5 (CH_2), 39.9 (CH_2), 55.2 (OCH_3), 64.8 (CH_2), 74.7 (CH), 108.2 (Csp^2), 113.7 (ArC), 124.2 (ArC), 125.0 (ArC), 126.6 (ArC), 127.1 (ArC), 129.0 (ArC), 130.0 (ArC), 134.4 (ArC), 134.6 (ArC), 149.0 (Csp^2), 151.6 (NHCO), 160.6 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{20}H_{19}NNaO_4$ [M + Na] 360.1206; found 360.1206.

6-(3,4-Dimethoxyphenyl)-5-(isochroman-1-yl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8bd): Yield 0.1 g (55%); yellow solid; m.p. 168–170 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1750 (C=O), 3334 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.60 (d, ^2J = 15.6 Hz, 1 H, CH_2), 3.01–3.10 (m, 1 H, CH_2), 3.53 (d, ^2J = 14.8 Hz, 1 H, CH_2), 3.75 (td, $^{2,3}J$ = 11.6, ^3J = 3.2 Hz, 1 H, CH_2), 3.88 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 3.95 (d, ^2J = 14.4 Hz, 1 H, CH_2), 4.20 (dd, ^2J = 11.2, ^3J = 6.0 Hz, 1 H, CH_2), 5.56 (s, 1 H, CH), 6.13 (br. s, 1 H, NH), 6.87 (d, ^3J = 8.4 Hz, 1 H, ArH), 7.03–7.06 (m, 1 H, ArH), 7.09–7.12 (m, 1 H, ArH), 7.16–7.20 (m, 4 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5 (CH_2), 40.0 (CH_2), 55.8 (OCH_3), 55.9 (OCH_3), 64.8 (CH_2), 74.8 (CH), 108.3 (Csp^2), 110.5 (ArC), 111.5 (ArC), 121.5 (ArC), 124.3 (ArC), 125.0 (ArC), 126.6 (ArC), 127.1 (ArC), 129.1 (ArC), 134.3 (ArC), 134.5 (ArC), 148.7 (ArC), 149.3 (Csp^2), 150.1 (ArC), 151.5 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{21}H_{21}NNaO_5$ [M + Na] 390.1312; found 390.1308.

5-(Isochroman-1-yl)-6-*p*-tolyl-3,4-dihydro-2*H*-1,3-oxazin-2-one (8dd): Yield 78.6 mg (49%); white solid; m.p. 141–142 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1751 (C=O), 3271 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 2.60 (d, ^2J = 15.6 Hz, 1 H, CH_2), 3.02–3.11 (m, 1 H, CH_2), 3.55 (dd, ^2J = 14.6, ^3J = 1.6 Hz, 1 H, CH_2), 3.75 (td, $^{2,3}J$ = 11.6, ^3J = 3.2 Hz, 1 H, CH_2), 3.99 (dd, ^2J = 14.8, ^3J = 1.2 Hz, 1 H, CH_2), 4.18–4.22 (m, 1 H, CH_2), 5.47 (br. s, 1 H, NH), 5.55 (s, 1 H, CH), 7.05–7.08 (m, 1 H, ArH), 7.10–7.14 (m, 1 H, ArH), 7.19–7.21 (m, 2 H, ArH), 7.22 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.51 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 28.6 (CH_2), 40.1 (CH_2), 64.9 (CH_2), 74.8 (CH), 108.6 (Csp^2), 125.1 (ArC), 126.7 (2 × ArC), 127.2 (ArC), 128.5 (ArC), 128.9 (ArC), 129.1 (ArC), 134.4 (ArC), 134.7 (ArC), 139.8 (ArC), 149.4 (Csp^2), 151.1 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{20}H_{19}NNaO_3$ [M + Na] 344.1257; found 344.1258.

5-(Isochroman-1-yl)-6-phenyl-3,4-dihydro-2*H*-1,3-oxazin-2-one (8ed): Yield 61.3 mg (40%); white solid; m.p. 189–190 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1751 (C=O), 3255 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.60 (d, ^2J = 16.4 Hz, 1 H, CH_2), 3.02–3.11 (m, 1 H, CH_2), 3.55 (dd, ^2J = 14.8, ^3J = 1.6 Hz, 1 H, CH_2), 3.74 (td, $^{2,3}J$ = 11.4, ^3J = 3.2 Hz, 1 H, CH_2), 3.99 (dd, ^2J = 14.8, ^3J = 1.2 Hz, 1 H, CH_2), 4.20 (ddd, ^2J = 11.4, ^3J = 6.0 Hz, ^3J = 1.2 Hz, 1 H, CH_2), 5.54 (s, 1 H, CH), 6.11 (br. s, 1 H, NH), 7.05–7.07 (m, 1 H, ArH), 7.10–7.13 (m, 1 H, ArH), 7.18–7.21 (m, 2 H, ArH), 7.41–7.43 (m, 3 H, ArH), 7.61–7.63 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.5 (CH_2), 40.0 (CH_2), 64.8 (CH_2), 74.6 (CH), 109.1 (Csp^2), 125.0 (ArC), 126.7 (ArC), 127.2 (ArC), 128.4 (ArC), 128.6 (ArC), 129.1 (ArC), 129.6 (ArC), 131.8 (ArC), 134.4 (ArC), 134.5 (ArC), 149.2 (Csp^2), 151.3 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{19}H_{17}NNaO_3$ [M + Na] 330.1101; found 330.1101.

6-(4-Chlorophenyl)-5-(isochroman-1-yl)-3,4-dihydro-2*H*-1,3-oxazin-2-one (8fd): Yield 49.5 mg (29%); white solid; m.p. 71–172 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1747 (C=O), 3278 (NH) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.60 (d, ^2J = 16.4 Hz, 1 H, CH_2), 2.90–2.99 (m, 1 H, CH_2), 3.29 (dd, ^2J = 15.2, ^3J = 1.6 Hz, 1 H, CH_2), 3.68 (td, $^{2,3}J$ = 11.2, ^3J = 3.2 Hz, 1 H, CH_2), 3.75 (dd, ^2J = 15.2, ^3J = 1.2 Hz, 1 H, CH_2), 4.10 (dd, ^2J = 11.4, ^3J = 4.8 Hz, 1 H, CH_2), 5.34 (s, 1 H, CH), 7.06–7.12 (m, 1 H, ArH), 7.15–7.22 (m, 3 H, ArH), 7.57 (br. s, 4 H, ArH), 7.81 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.9 (CH_2), 39.1 (CH_2), 64.1 (CH_2), 74.0 (CH), 110.0 (Csp^2), 124.9 (ArC), 126.6 (ArC), 127.1 (ArC), 128.8 (ArC), 129.1 (ArC), 130.2 (ArC), 130.7 (ArC), 134.3 (ArC), 137.6 (ArC), 134.4 (ArC), 147.6 (Csp^2), 149.7 (NHCO) ppm. HRMS (ESI): *m/z* calcd. for $C_{19}H_{16}{}^{35}ClNNaO_3$ [M + Na] 364.0711; found 364.0704.

***N*-[5-(Isochroman-1-yl)-6-(4-methoxyphenyl)-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9ac):** Yield 0.18 g (74%); white solid; m.p. 246 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3145 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 2.34 (s, 3 H, CH_3), 2.61 (m, 1 H, $ArCCH_2$), 2.95 (m, 1 H, $ArCCH_2$), 3.33 (m, 1 H, NCH_2), 3.66 (m, 1 H, OCH_2), 3.73 (m, 1 H, NCH_2), 3.82 (s, 3 H, OCH_3), 4.10 (m, 1 H, OCH_2), 5.41 (s, 1 H, CH), 7.03 (d, ^3J = 6.6 Hz, 1 H, ArH), 7.07 (d, ^3J = 8.7 Hz, 2 H, ArH), 7.15–7.23 (m, 3 H, ArH), 7.25 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.44 (d, ^3J = 8.6 Hz, 2 H, ArH), 7.63 (d, ^3J = 8.1 Hz, 2 H, ArH), 9.11 (s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 21.4 (CH_3), 28.3 ($ArCCH_2$), 38.1 (NCH_2), 55.8 (OCH_3), 64.6 (OCH_2), 74.2 (CH), 110.5 (H_2CC-sp2), 114.5 (ArC), 122.8 (ArC), 125.3 (ArC), 126.6 (ArC), 127.1 (ArC), 127.2 (ArC), 129.5 (ArC), 129.6 (ArC), 130.4 (ArC), 134.3 (ArC), 134.9 (ArC), 141.0 (ArC), 142.3 (ArC), 147.8 (C-sp^2), 153.5 (HNC-sp^2), 160.9 (ArC) ppm. HRMS (ESI): *m/z* calcd. for $C_{27}H_{27}N_2O_5S$ $[M + H]^+$ 491.1635; found 491.1639.

***N*-[6-(3,4-Dimethoxyphenyl)-5-(isochroman-1-yl)-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9dc):** Yield 0.23 g (88%); white needles; m.p. 141 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3300 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 2.32 (s, 3 H, CH_3), 2.61 (d, ^3J = 16.2 Hz, 1 H, $ArCCH_2$), 2.90–3.00 (m, 1 H, $ArCCH_2$), 3.28–3.34 (m, 1 H, NCH_2), 3.68–3.73 (m, 1 H, OCH_2), 3.74–3.76 (m, 1 H,

NCH$_2$), 3.80 (s, 3 H, OCH$_3$), 3.81 (s, 3 H, OCH$_3$), 4.11 (ddd, ^3J = 11.1, ^3J = 5.8 Hz, ^2J = 1.5 Hz, 1 H, OCH$_2$), 5.50 (s, 1 H, CH), 7.00–7.12 (m, 3 H, ArH), 7.16–7.26 (m, 5 H, ArH), 7.30 (br. s, 1 H, ArH), 7.64 (d, ^3J = 8.0 Hz, 2 H), 9.13 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.3 (CH$_3$), 28.3 (ArCCH$_2$), 38.1 (NCH$_2$), 55.9 (OCH$_3$), 56.0 (OCH$_3$), 64.6 (OCH$_2$), 74.2 (CH), 110.6 (H$_2$CC-sp^2), 111.9 (ArC), 112.3 (ArC), 121.8 (ArC), 122.9 (ArC), 125.3 (ArC), 126.6 (ArC), 127.1 (ArC), 127.7 (ArC), 129.5 (ArC), 129.6 (ArC), 134.4 (ArC), 134.9 (ArC), 141.1 (ArC), 142.2 (ArC), 148.1 (ArCC-sp^2), 149.0 (ArC), 150.7 (ArC), 153.6 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{28}H_{29}N_2O_6S$ [M + H]$^+$ 521.1741; found 521.1746.

***N*-[5-(Isochroman-1-yl)-6-(*p*-tolyl)-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9fc):** Yield 0.23 g (92%); white solid; m.p. 259–261 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3300 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.34 (s, 3 H, CH$_3$), 2.37 (s, 3 H, CH$_3$), 2.60 (d, ^3J = 16.4, Hz, 1 H, ArCCH$_2$), 2.89–3.00 (m, 1 H, ArCCH$_2$), 3.29–3.33 (m, 1 H, NCH$_2$), 3.67 (td, ^3J = 11.5, ^2J = 3.0 Hz, 1 H, OCH$_2$), 3.74 (dd, ^3J = 15.3, ^2J = 1.1 Hz, 1 H, NCH$_2$), 4.09 (dd, ^3J = 11.1, ^2J = 5.6 Hz, 1 H, OCH$_2$), 5.40 (s, 1 H, CH), 7.02 (d, ^3J = 6.5 Hz, 1 H, ArH), 7.15–7.28 (m, 5 H, ArH), 7.31 (d, ^3J = 8.1 Hz, 2 H, ArH), 7.36 (d, ^3J = 8.2 Hz, 2 H, ArH), 9.10 (s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.3 (CH$_3$), 21.4 (CH$_3$), 28.3 (ArC*C*H$_2$), 38.1 (NCH$_2$), 64.6 (OCH$_2$), 74.1 (CH), 111.1 (H$_2$C*C*-sp^2), 125.3 (ArC), 126.6 (ArC), 127.1 (ArC), 127.7 (ArC), 127.8 (ArC), 129.5 (ArC), 129.6 (ArC), 129.7 (ArC), 134.2 (ArC), 134.9 (ArC), 140.4 (ArC), 141.0 (ArC), 142.3 (ArC), 147.8 (ArC*C*-sp^2), 153.4 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{27}H_{26}N_2NaO_4S$ [M + Na]$^+$ 497.1505; found 497.1500.

***N*-[5-(Isochroman-1-yl)-6-phenyl-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9gc):** Yield 0.21 g (90%); white solid; m.p. 225–226 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3152 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.34 (s, 3 H, CH$_3$), 2.61 (d, ^3J = 16.4 Hz, 1 H, ArCCH$_2$), 2.95 (m, 1 H, ArCCH$_2$), 3.35 (d, ^2J = 15.4 Hz, 1 H, NCH$_2$), 3.68 (td, ^3J = 11.4, ^2J = 8.7 Hz, 1 H, OCH$_2$), 3.77 (d, ^2J = 15.4 Hz, 1 H, NCH$_2$), 4.10 (td, ^3J = 10.0, ^2J = 5.4 Hz, 1 H, OCH$_2$), 5.41 (s, 1 H, CH), 7.04 (d, ^3J = 6.3 Hz, 1 H, ArH), 7.14–7.29 (m, 5 H, ArH), 7.45–7.56 (m, 5 H, ArH), 7.61 (d, ^3J = 8.1 Hz, 2 H, ArH), 9.11 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.4 (CH$_3$), 28.3 (ArCCH$_2$), 38.2 (NCH$_2$), 64.6 (OCH$_2$), 74.1 (CH), 111.6 (H$_2$CC-sp^2), 125.3 (ArC), 126.6 (ArC), 127.1 (ArC), 127.8 (ArC), 128.9 (ArC), 129.1 (ArC), 129.5 (ArC), 129.6 (ArC), 130.6 (ArC), 134.1 (ArC), 134.9 (ArC), 141.0 (ArC), 142.3 (ArC), 147.7 (ArCC-sp^2), 153.4 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{25}N_2O_4S$ [M + H]$^+$ 461.1530; found 461.1536.

***N*-[6-(4-Chlorophenyl)-5-(isochroman-1-yl)-4*H*-1,3-oxazin-2-yl]-4-methylbenzenesulfonamide (9hc):** Yield 0.15 g (62%); white solid; m.p. 275–277 °C. IR (KBr): $\tilde{\nu}_{max}$ = 3124 (NH) cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.34 (s, 3 H, CH$_3$), 2.61 (d, ^3J = 16.2 Hz, 1 H, ArCCH$_2$), 2.88–2.99 (m, 1 H, ArCCH$_2$), 3.69 (d, ^3J = 11.6 Hz, 1 H, OCH$_2$), 3.75 (d, ^3J = 15.6 Hz, 1 H, NCH$_2$), 4.05–4.15 (m, 1 H, OCH$_2$), 5.38 (s, 1 H, CH), 7.03 (d, ^3J = 6.02 Hz, 1 H, ArH), 7.15–7.30 (m, 5 H, ArH), 7.35–7.45 (m, 1 H, ArH), 7.46–7.55 (m, 2 H, ArH), 7.56–7.67 (m, 4 H, ArH), 9.12 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 21.4 (CH$_3$), 28.3 (ArC*C*H$_2$), 38.3 (NCH$_2$), 64.5 (OCH$_2$), 73.9 (CH), 112.3 (H$_2$C*C*-sp^2), 125.4 (ArC), 126.6 (ArC), 127.1 (ArC), 127.8 (ArC), 129.3 (ArC), 129.5 (ArC), 129.6 (ArC), 130.7 (ArC), 133.5 (ArC), 134.0 (ArC), 134.9 (ArC), 135.4 (ArC), 141.0 (ArC), 142.4 (ArC), 146.7 (ArC), (ArC*C*-sp^2), 153.2 (HNC-sp^2) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{24}ClN_2O_4S$ [M + H] 495.1140; found 495.1143.

***N*-[5-(Isochroman-1-yl)-6-(4-methoxyphenyl)-4*H*-1,3-thiazin-2-yl]-benzamide (10ad):** Yield 0.19 g (82%); yellow solid; m.p. 78–79 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1676 (C=O), 3198 (NH) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.63 (d, ^2J = 15.2 Hz, 1 H, CH$_2$), 3.10–3.18 (m, 1 H, CH$_2$), 3.72 (td, $^{2,3}J$ = 11.6, ^3J = 3.2 Hz, 1 H, CH$_2$), 3.77 (d, ^2J = 15.2 Hz, 1 H, CH$_2$), 3.83 (s, 3 H, OCH$_3$), 3.96 (d, ^2J = 15.2 Hz, 1 H, CH$_2$), 4.22 (ddd, ^2J = 11.2, ^3J = 5.6, ^3J = 0.8 Hz, 1 H, CH$_2$), 5.51 (s, 1 H, CH), 6.96–6.98 (m, 3 H, ArH), 7.13–7.21 (m, 3 H, ArH), 7.38–7.42 (m, 2 H, ArH), 7.46–7.50 (m, 1 H, ArH), 7.53 (d, ^3J = 8.8 Hz, 2 H, ArH), 8.17–8.20 (m, 2 H, ArH), 11.0 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 28.5 (CH$_2$), 43.7 (CH$_2$), 55.3 (OCH$_3$), 64.8 (CH$_2$), 75.7 (CH), 114.2 (ArC), 125.2 (ArC), 126.7 (ArC), 126.8 (ArC), 127.3 (ArC), 127.4 (Csp^2), 128.0 (ArC), 129.1 (ArC), 129.3 (ArC), 130.8 (ArC), 131.9 (ArC), 134.2 (ArC), 134.9 (ArC), 135.3 (Csp^2), 136.5 (ArC), 160.4 (ArC), 169.5 (Csp^2), 176.7 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{27}H_{25}N_2O_3S$ [M + H] 457.1580; found 457.1585.

***N*-[6-(4-Chlorophenyl)-5-(isochroman-1-yl)-4*H*-1,3-thiazin-2-yl]-benzamide (10bd):** Yield 0.13 g (55%); yellow solid; m.p. 56–57 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1679 (C=O), 3197 (NH) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.64 (d, ^2J = 16.0 Hz, 1 H, CH$_2$), 3.10–3.18 (m, 1 H, CH$_2$), 3.73 (td, ^2J = 11.6, ^3J = 2.8 Hz, 1 H, CH$_2$), 3.78 (d, ^2J = 15.2 Hz, 1 H, CH$_2$), 3.96 (d, ^2J = 15.6 Hz, 1 H, CH$_2$), 4.22 (dd, ^2J = 11.4, ^3J = 5.2 Hz, 1 H, CH$_2$), 5.44 (s, 1 H, CH), 6.91 (d, ^3J = 7.2 Hz, 1 H, ArH), 7.13–7.25 (m, 4 H, ArH), 7.39–7.42 (m, 4 H, ArH), 7.52 (d, ^3J = 8.8 Hz, 2 H, ArH), 8.15–8.17 (m, 2 H, ArH), 10.9 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 28.5 (CH$_2$), 43.9 (CH$_2$), 64.9 (CH$_2$), 75.6 (CH), 125.1 (ArC), 126.4 (ArC), 126.8 (ArC), 127.2 (ArC), 127.4 (Csp^2), 128.1 (ArC), 128.9 (ArC), 129.1 (ArC), 129.2 (ArC), 129.3 (ArC), 130.8 (ArC), 132.0 (ArC), 133.2 (ArC), 134.3 (ArC), 134.5 (ArC), 135.5 (Csp^2), 164.8 (Csp^2), 174.2 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{21}{}^{35}ClN_2O_2S$ [M + H] 461.1085; found 461.1095.

***N*-[5-(Isochroman-1-yl)-6-phenyl-4*H*-1,3-thiazin-2-yl]benzamide (10cd):** Yield 0.14 g (64%); white solid; m.p. 89–90 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1682 (C=O), 3189 (NH) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.62 (d, ^2J = 15.2 Hz, 1 H, CH$_2$), 3.09–3.18 (m, 1 H, CH$_2$), 3.72 (td, ^2J = 11.6, ^3J = 3.2 Hz, 1 H, CH$_2$), 3.80 (d, ^2J = 15.2 Hz, 1 H, CH$_2$), 3.99 (d, ^2J = 15.2 Hz, 1 H, CH$_2$), 4.22 (ddd, ^2J = 11.2, ^3J = 5.4, ^3J = 1.2 Hz, 1 H, CH$_2$), 5.49 (s, 1 H, CH), 6.97 (d, ^3J = 7.2 Hz, 1 H, ArH), 7.13–7.21 (m, 3 H, ArH), 7.39–7.49 (m, 6 H, ArH), 7.58–7.60 (m, 2 H, ArH), 8.18–8.20 (m, 2 H, ArH), 10.9 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 28.5 (CH$_2$), 43.7 (CH$_2$), 64.8 (CH$_2$), 75.6 (CH), 125.2 (ArC), 126.7 (ArC), 127.3 (ArC), 128.0 (ArC), 128.1 (Csp^2), 128.8 (ArC), 129.1 (ArC), 129.2 (ArC), 129.3 (ArC), 129.4 (ArC), 131.9 (ArC), 134.2 (ArC), 134.7 (2 × ArC), 135.2 (Csp^2), 136.4 (ArC), 169.1 (Csp^2), 176.5 (CO) ppm. HRMS (ESI): *m*/*z* calcd. for $C_{26}H_{22}N_2O_2S$ [M + H] 427.1475; found 427.1484.

***N*-{5-[Methoxy(4-methoxyphenyl)methyl]-6-(4-methoxyphenyl)-4*H*-1,3-thiazin-2-yl}benzamide (10ae):** Yield 0.18 g (76%); yellow solid; m.p. 47–48 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1680 (C=O), 3194 (NH) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 3.30 (s, 3 H, OCH$_3$), 3.81 (s, 3 H, OCH$_3$), 3.84 (s, 3 H, OCH$_3$), 3.89 (d, ^2J = 15.2 Hz, 1 H, C*H*H), 4.08 (d, ^2J = 15.2 Hz, 1 H, CH*H*), 5.03 (s, 1 H, CH), 6.89 (d, ^3J = 8.8 Hz, 2 H, ArH), 6.94 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.22 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.38 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.41 (d, ^3J = 7.6 Hz, 2 H, ArH), 7.48 (tt, ^3J = 7.2, ^4J = 1.2 Hz, 1 H, ArH), 8.18–8.20 (m, 2 H, ArH), 11.07 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 42.4 (CH$_2$), 55.2 (OCH$_3$), 55.3 (OCH$_3$), 56.6 (OCH$_3$), 79.4 (CH), 114.0 (ArC), 114.3 (ArC), 126.8 (ArC), 127.2 (ArC), 127.9 (Csp^2), 128.0 (ArC), 129.4 (ArC), 130.8 (ArC),

131.1 (ArC), 131.9 (ArC), 134.0 (Csp^2), 136.5 (ArC), 159.2 (ArC), 160.3 (ArC), 170.0 (Csp^2), 176.8 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{27}H_{27}N_2O_4S$ [M + H] 475.1686; found 475.1687.

***N*-{5-[(4-Bromophenyl)(ethoxy)methyl]-6-(4-methoxyphenyl)-4*H*-1,3-thiazin-2-yl}benzamide (10af):** Yield 0.16 g (59%); yellow solid; m.p. 89–90 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1684 (C=O), 3203 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.21 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 3.29–3.37 (m, 1 H, $OCHHCH_3$), 3.52–3.59 (m, 1 H, $OCHHCH_3$), 3.84–3.87 (m, 4 H, CHH and OCH_3), 4.04 (d, ^2J = 15.2 Hz, 1 H, CHH), 5.13 (s, 1 H, CH), 6.94 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.19 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.35 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.38–7.42 (m, 2 H, ArH), 7.46–7.49 (m, 3 H, ArH), 8.16–8.18 (m, 2 H, ArH), 10.99 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2 (OCH_2CH_3), 42.5 (CH_2), 55.3 (OCH_3), 64.3 (OCH_2CH_3), 77.2 (CH), 114.3 (ArC), 125.7 (ArC), 126.6 (ArC), 127.6 (Csp^2), 127.7 (ArC), 128.1 (ArC), 129.3 (ArC), 130.7 (ArC), 131.7 (ArC), 132.0 (ArC), 133.6 (Csp^2), 134.2 (ArC), 138.5 (ArC), 160.3 (ArC), 169.4 (Csp^2), 176.6 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{27}H_{25}{}^{79}BrN_2O_3S$ [M + H] 536.0770; found 536.0768.

***N*-{5-[Methoxy(phenyl)methyl]-6-(4-methoxyphenyl)-4*H*-1,3-thiazin-2-yl}benzamide (10ag):** Yield 0.13 g (58%); yellow solid; m.p. 55–56 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1681 (C=O), 3195 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.32 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.88 (d, ^2J = 15.2 Hz, 1 H, CHH), 4.08 (d, ^2J = 15.2 Hz, 1 H, CHH), 5.09 (s, 1 H, CH), 6.95 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.30–7.32 (m, 3 H, ArH), 7.35–7.42 (m, 6 H, ArH), 7.48 (tt, ^3J = 7.6, ^4J = 1.6 Hz, 1 H, ArH), 8.17–8.19 (m, 2 H, ArH), 11.03 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.5 (CH_2), 55.3 (OCH_3), 55.6 (OCH_3), 79.6 (CH), 114.3 (ArC), 126.0 (ArC), 126.7 (ArC), 127.6 (ArC), 127.8 (Csp^2), 128.0 (ArC), 128.6 (ArC), 129.3 (ArC), 130.8 (ArC), 131.9 (ArC), 134.3 (Csp^2), 136.4 (ArC), 139.0 (ArC), 160.3 (ArC), 169.7 (Csp^2), 176.7 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{24}N_2O_3S$ [M + H] 445.1580; found 445.1574.

***N*-{6-(4-Chlorophenyl)-5-[methoxy(phenyl)methyl]-4*H*-1,3-thiazin-2-yl}benzamide (10bg):** Yield 0.15 g (65%); yellow solid; m.p. 55–56 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1683 (C=O), 3196 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.32 (s, 3 H, OCH_3), 3.89 (d, ^2J = 15.6 Hz, 1 H, CHH), 4.09 (d, ^2J = 15.6 Hz, 1 H, CHH), 5.01 (s, 1 H, CH), 7.27–7.32 (m, 3 H, ArH), 7.35–7.44 (m, 8 H, ArH), 7.49 (tt, ^3J = 7.2, ^4J = 1.2 Hz, 1 H, ArH), 8.16–8.18 (m, 2 H, ArH), 10.94 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.6 (CH_2), 56.7 (OCH_3), 79.7 (CH), 125.9 (ArC), 128.0 (Csp^2), 128.1 (ArC), 128.7 (ArC), 129.0 (ArC), 129.2 (ArC), 129.3 (ArC), 130.8 (ArC), 132.0 (ArC), 133.2 (ArC and Csp^2), 135.5 (ArC), 136.1 (ArC), 138.7 (ArC), 168.7 (Csp^2), 176.4 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{25}H_{21}{}^{35}ClN_2O_2S$ [M + H] 449.1085; found 449.1076.

***N*-{5-[(4-Bromophenyl)(ethoxy)methyl]-6-(4-chlorophenyl)-4*H*-1,3-thiazin-2-yl}benzamide (10bf):** Yield 0.15 g (57%); yellow solid; m.p. 73–74 °C. IR (KBr): $\tilde{\nu}_{max}$ = 1682 (C=O), 3188 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.22 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 3.29–3.37 (m, 1 H, $OCHHCH_3$), 3.50–3.57 (m, 1 H, $OCHHCH_3$), 3.87 (d, ^2J = 15.6 Hz, 1 H, CHH), 4.05 (d, ^2J = 15.6 Hz, 1 H, CHH), 5.05 (s, 1 H, CH), 7.16 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.35–7.39 (m, 2 H, ArH), 7.41–7.43 (m, 3 H, ArH), 7.46–7.49 (m, 3 H, ArH), 7.51–7.56 (m, 1 H, ArH), 8.14–8.17 (m, 2 H, ArH), 10.88 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2 (OCH_2CH_3), 42.7 (CH_2), 64.5 (OCH_2CH_3), 77.3 (CH), 121.9 (ArC), 125.8 (ArC), 127.7 (ArC), 128.1 (ArC), 128.9 (Csp^2), 129.3 (2 × ArC), 129.7 (ArC), 130.7 (ArC), 131.8 (ArC), 132.1 (ArC), 133.1 (Csp^2), 135.6 (ArC), 138.2 (ArC), 168.3 (Csp^2), 176.3 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{22}{}^{35}Cl^{79}BrN_2O_2S$ [M + H] 540.0274; found 540.0271.

***N*-{5-[Methoxy(4-methoxyphenyl)methyl]-6-phenyl-4*H*-1,3-thiazin-2-yl}benzamide (10ce):** Yield 0.18 g (81%); yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 1680 (C=O), 3198 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.31 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.91 (d, ^2J = 15.6 Hz, 1 H, CHH), 4.09 (d, ^2J = 15.2 Hz, 1 H, CHH), 5.01 (s, 1 H, CH), 6.89 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.21 (d, ^3J = 7.6 Hz, 2 H, ArH), 7.38–7.46 (m, 7 H, ArH), 7.48 (tt, ^3J = 7.6, ^4J = 1.2 Hz, 1 H, ArH), 8.18–8.20 (m, 2 H, ArH), 11.03 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.4 (CH_2), 55.2 (OCH_3), 56.5 (OCH_3), 79.3 (CH), 114.0 (ArC), 127.1 (ArC), 128.0 (ArC), 128.5 (Csp^2), 128.8 (ArC), 129.2 (ArC), 129.3 (ArC), 129.4 (ArC), 130.9 (ArC), 132.0 (ArC), 133.9 (Csp^2), 134.7 (ArC), 136.3 (ArC), 159.1 (ArC), 169.4 (Csp^2), 176.6 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{24}N_2O_3S$ [M + H] 445.1580; found 445.1574.

***N*-{5-[(4-Bromophenyl)(methoxy)methyl]-6-phenyl-4*H*-1,3-thiazin-2-yl}benzamide (10cf):** Yield 0.15 g (60%); yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 1681 (C=O), 3167 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.21 (t, ^3J = 7.2 Hz, 3 H, OCH_2CH_3), 3.29–3.37 (m, 1 H, $OCHHCH_3$), 3.52–3.60 (m, 1 H, $OCHHCH_3$), 3.86 (d, ^2J = 15.6 Hz, 1 H, CHH), 4.05 (d, ^2J = 15.2 Hz, 1 H, CHH), 5.10 (s, 1 H, CH), 7.19 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.38–7.42 (m, 7 H, ArH), 7.46–7.48 (m, 3 H, ArH), 8.16–8.18 (m, 2 H, ArH), 10.96 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2 (OCH_2CH_3), 42.5 (CH_2), 64.3 (OCH_2CH_3), 77.1 (CH), 121.7 (ArC), 127.7 (ArC), 128.0 (ArC), 128.1 (Csp^2), 128.9 (ArC), 129.3 (2 × ArC), 131.6 (ArC), 132.0 (ArC), 134.1 (Csp^2), 134.6 (ArC), 136.2 (ArC), 138.4 (ArC), 168.8 (Csp^2), 176.3 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{23}{}^{79}BrN_2O_2S$ [M + H] 506.0664; found 506.0665.

***N*-{5-[Methoxy(phenyl)methyl]-6-phenyl-4*H*-1,3-thiazin-2-yl}benzamide (10cg):** Yield 0.12 g (57%); yellow oil. IR (KBr): $\tilde{\nu}_{max}$ = 1680 (C=O), 3189 (NH) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.33 (s, 3 H, OCH_3), 3.89 (d, ^2J = 15.2 Hz, 1 H, CHH), 4.09 (d, ^2J = 15.6 Hz, 1 H, CHH), 5.07 (s, 1 H, CH), 7.28–7.32 (m, 3 H, ArH), 7.35–7.38 (m, 2 H, ArH), 7.40–7.51 (m, 8 H, ArH), 8.18–8.20 (m, 2 H, ArH), 11.01 (br. s, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.5 (CH_2), 56.6 (OCH_3), 79.5 (CH), 125.9 (ArC), 127.8 (ArC), 128.0 (ArC), 128.2 (Csp^2), 128.9 (ArC), 129.2 (ArC), 129.3 (ArC), 129.4 (ArC), 131.9 (ArC), 134.2 (Csp^2), 134.7 (ArC), 136.3 (ArC), 138.9 (ArC), 169.3 (Csp^2), 176.5 (CO) ppm. HRMS (ESI): *m/z* calcd. for $C_{25}H_{22}N_2O_2S$ [M + H] 415.1475; found 415.1461.

2-(Isochroman-1-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (11ac): Yield 0.13 g (90%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 1654 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.85–3.00 (m, 2 H, CH_2), 3.90 (s, 3 H, OCH_3), 3.93 (ddd, $^2J_{H,H}$ = 11.3, $^3J_{H,H}$ = 6.3, $^2J_{H,H}$ = 4.9 Hz, 1 H, OCH_2), 4.17 (ddd, $^2J_{H,H}$ = 11.3, $^3J_{H,H}$ = 6.3, $^2J_{H,H}$ = 4.9 Hz, 1 H, OCH_2), 5.71 (s, 1 H, =CH), 5.79 (s, 1 H, =CH), 5.99 (s, 1 H, *CH*O), 6.97 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, ArH), 7.04 (d, $^3J_{H,H}$ = 7.0 Hz, 1 H, ArH), 7.17–7.22 (m, 3 H, ArH), 7.91 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.58 (CH_2), 55.44 (OCH_3), 62.13 (OCH_2), 74.84 (OCH), 113.53 (ArC), 125.83 (ArC), 126.01 (=CH_2), 126.53 (ArC), 126.70 (ArC), 128.88 (ArC), 130.00 (ArC), 132.11 (ArC), 134.12 (ArC), 135.19 (ArC), 148.81 (=*C*-C=O), 163.36 (ArC), 195.70 (C=O) ppm. HRMS (ES): *m/z* calcd. for $C_{19}H_{18}NaO_3$ [M + Na]$^+$ 317.1148; found 317.1149.

2-(Isochroman-1-yl)-1-phenylprop-2-en-1-one (11bc): Yield 0.11 g (83%); yellowish oil. IR (KBr): $\tilde{\nu}_{max}$ = 1660 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.87–2.95 (m, 2 H, CH_2), 3.95 (ddd, $^2J_{H,H}$ = 11.4, $^3J_{H,H}$ = 6.8, $^2J_{H,H}$ = 4.7 Hz, 1 H, OCH_2), 4.18 (ddd, $^2J_{H,H}$

= 11.4, $^3J_{H,H}$ = 6.8, $^2J_{H,H}$ = 4.7 Hz, 1 H, OCH_2), 5.81 (s, 1 H, =CH), 5.88 (s, 1 H, =CH), 6.03 (s, 1 H, *CH*O), 7.03 (d, $^3J_{H,H}$ = 7.0 Hz, 1 H, ArH), 7.16–7.24 (m, 3 H, ArH), 7.46–7.50 (m, 2 H, ArH), 7.57–7.61 (m, 1 H, ArH), 7.86–7.88 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.61 (CH_2), 62.27 (OCH_2), 74.45 (OCH), 125.91 (ArC), 126.43 (ArC), 126.75 (ArC), 127.97 (=CH_2), 128.28 (ArC), 128.92 (ArC), 129.67 (ArC), 132.56 (ArC), 134.17 (ArC), 135.27 (ArC), 137.46 (ArC), 148.82 (=*C*-C=O), 196.96 (C=O) ppm. HRMS (ES): *m*/*z* calcd. for $C_{18}H_{16}NaO_2$ $[M + Na]^+$ 287.1043l; found 287.1045.

Supporting Information (see footnote on the first page of this article): Experimental details for the preparation of the starting materials, the results of optimization studies, and copies of ^1H and ^{13}C NMR spectra.

Acknowledgments

The research was funded by the Research Council of Lithuania (grant number MIP-15016).

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Received: August 17, 2015
Published Online: October 12, 2015

Paper 3

Synthesis of Polysubstituted Pyrroles through the Tandem 1,3-Addition/5-*Endo*-Dig Cyclization of 1-(1-Alkynyl)Cyclopropyl Imines

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European Journal of Organic Chemistry (**2016**) 2016: 5294-5300
DOI:10.1002/ejoc.201600985
https://onlinelibrary.wiley.com/doi/10.1002/ejoc.201600985

ChemPubSoc Europe

DOI: 10.1002/ejoc.201600985

EurJOC European Journal of Organic Chemistry

Full Paper

Synthetic Methods

Synthesis of Polysubstituted Pyrroles through the Tandem 1,3-Addition/5-*endo-dig* Cyclization of 1-(1-Alkynyl)cyclopropyl Imines

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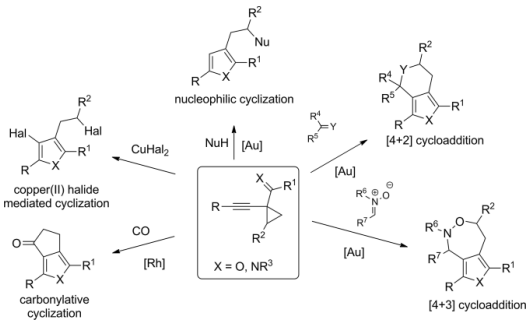
Abstract: Cyclopropyl-tethered 3-alkynyl imines react with polarized-covalent-bond-containing compounds to give polyfunctionalized pyrroles. This provides a mild and effective method for the simultaneous introduction of halogen, chalcogen, or hydrogen groups to the 3-position of the pyrrole ring, together with the incorporation of halogen, azide, or alkoxy/aryloxy groups into the ethyl side-chain.

Introduction

Pyrroles are an important class of heterocycles with valuable chemical, biological, and photophysical properties. This heterocycle is found in a number of natural products,[1] synthetic biologically active molecules,[2] and compounds used in materials science.[3] Although a wide variety of classical[4] or more modern transition-metal-mediated[5] methods for the synthesis of pyrroles are present in the literature, the development of new methods for the synthesis of polyfunctionalized pyrroles is highly desirable. Cyclopropyl-tethered functionalized alkynes can be useful synthons for the preparation of five-membered heteroaromatic compounds. Thus, 1-arylalkynylcyclopropyl carbaldehydes or ketones were recently introduced as suitable starting materials for the preparation of various furans. These compounds, due to their unique structure and reactivity, serve as all-carbon 1,4-carbon dipoles,[6] and can therefore undergo gold-catalyzed reactions with nucleophiles,[7] [4+2][6,8b] or [4+3][8] cycloadditions, rhodium-catalyzed carbonylative reactions,[9] and copper(II) halide mediated cyclization reactions[10] (Scheme 1). 1-Cyclopropylalkynyl imines or oximes are not used so often, but there are some reports in the literature about their transition-metal-mediated transformations to give pyrroles.[11] Electrophile-assisted cyclization reactions of cyclopropyl-tethered alkynyl ketones to give the corresponding furans were proposed some time ago by Huang et al., and, to the best of our knowledge, no further examples of this type of ring closure of 1-(1-alkynyl)cyclopropyl ketones have been reported.[12]

It is noteworthy that electrophile-assisted cyclizations have their uses, and have some benefits in organic synthesis; these methods do not require transition-metal catalysis, and the final products contain halogen, chalcogen, or alkoxyarylmethyl functional groups that can be used for further functionalizations.[13] In a continuation of our recent studies in the field of electrophile-mediated transformations of functionalized alkynes,[14] we decided to prepare some cyclopropyl-tethered imines, and to evaluate their reactivity towards electrophilic reagents. However, the results we obtained revealed a unique reactivity of 1-alkynylcyclopropyl imines towards molecules containing polar covalent bonds, so this process cannot be classified as an electrophile-assisted transformation. In this paper, we present the results of our investigations.



Scheme 1. Transition-metal-catalyzed reactions of cyclopropyl-tethered functionalized alkynes.

Results and Discussion

Starting 1-(arylalkynyl)cyclopropanecarbaldehydes **1** were prepared by known methods.[11a] With the starting aldehydes in hand, for the synthesis of the desired starting imines, we tried to use the classical reaction with primary amines. Thus, 1-[(4-methoxyphenyl)ethynyl]cyclopropanecarbaldehyde (**1a**) and benzylamine were chosen for the synthesis of cyclopropyl-tethered 3-alkynyl imine **3a**. However, no TLC-detectable product was formed when the aldehyde was heated with the amine in

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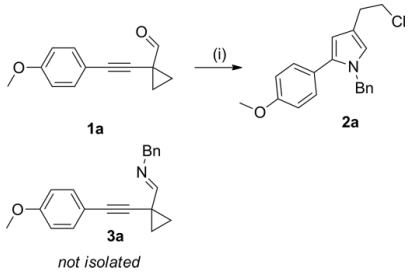
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201600985.

dichloromethane in the presence of magnesium sulfate in a sealed tube.[11a] Therefore, we decided to use microwave-assisted synthesis for smoother formation of the imine functionality. After irradiation of a solution of the starting aldehyde and benzylamine in 1,2-dichloroethane in the presence of activated molecular sieves (3 Å) at 120 °C, a spot corresponding to a new product was detected on TLC, together with a spot corresponding to unreacted starting material. Further irradiation of the reaction mixture did not improve this conversion. After preparative column chromatography, 57 % of the starting aldehyde (i.e., **1a**) was recovered, and the product (i.e., **2a**) was isolated in 29 % yield. To our great surprise, structural analysis of the product revealed that it was 1-benzyl-4-(2-chloroethyl)-2-(4-methoxyphenyl)-1*H*-pyrrole (**2a**), instead of the desired imine (i.e., **3a**; Scheme 2).



Scheme 2. Reaction between 1-[(4-methoxyphenyl)ethynyl]cyclopropanecarbaldehyde (**1a**) and benzylamine in dichloroethane. (i) benzylamine (1.1 equiv.), 1,2-dichloroethane, molecular sieves (3 Å), MW, 120 °C, 15 min.

We presumed that hydrogen chloride, present as an impurity in the solvent, reacted with the in-situ-formed imine. This reaction could lead to a tandem proton-assisted cyclization to give a five-membered heterocyclic ring, followed by chloride-mediated cyclopropane ring opening. Heating of a solution of 1-[(4-methoxyphenyl)ethynyl]cyclopropanecarbaldehyde (**1a**) and benzylamine in a saturated solution of hydrogen chloride in dichloroethane, resulted in a higher yield (72 %) of compound **2a**. Next, we changed the solvent to nonacidic acetonitrile, and monitored the formation of the imine by ^{1}H NMR spectroscopy. We noticed that the imine group formed successfully after heating the reaction solution at 120 °C in a microwave oven (MW) for 20 min. For full conversion of the aldehyde, 2 equiv. of the amine was required. However, attempted purification of the desired imine by column chromatography led to complete hydrolysis of the product to give the starting aldehyde.

So we decided to prepare cyclopropyl-tethered alkynyl imines in situ just before addition of the electrophilic reagent. First of all, we tried to perform iodo cyclization of the intermediate imine. Starting aldehyde **1a** was heated with excess *tert*-butylamine in acetonitrile at 120 °C in a microwave oven for 20 min, then the resulting solution was cooled to room temper-

Table 1. Data on the synthesis of polysubstituted pyrroles **2**.

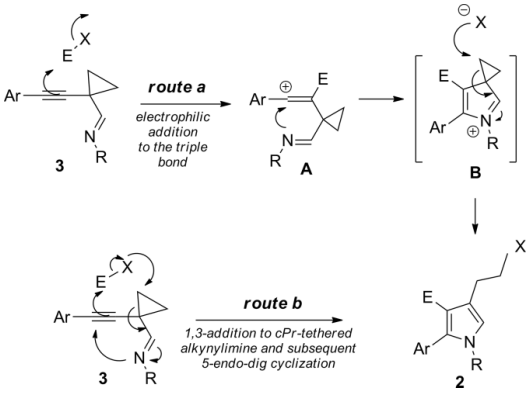
Entry	Starting aldehyde **1**	Amine RNH_2	E–X	Additive (3 equiv.)	Reaction conditions[a]	Product **2** (yield [%])
1	**1a**: Ar = 4-$MeOC_6H_4$	R = *t*Bu	I_2	–	Method A	**2b** (81); E = X = I
2	**1a**	R = *t*Bu	I_2	indole	Method A	**2b** (56)
3	**1a**	R = *t*Bu	I_2	piperidine	Method A	**2b** (59)
4	**1a**	R = *t*Bu	I_2	CH_3OH	Method A	**2b** (16)
5	**1a**	R = *t*Bu	I_2	NaN_3	Method A	**2b** (76)
6	**1a**	R = Bn	I_2	–	Method A	**2c** (78); E = X = I
7	**1b**: Ar = Ph	R = *t*Bu	I_2	–	Method A	**2d** (57); E = X = I
8	**1b**	R = Bu	I_2	–	Method A	**2e** (46); E = X = I
9	**1c**: Ar = 4-MeC_6H_4	R = *t*Bu	I_2	–	Method A	**2f** (58); E = X = I
10	**1c**	R = Bn	I_2	–	Method A	**2g** (59); E = X = I
11	**1c**	R = *c*Hex	I_2	–	Method A	**2h** (64); E = X = I
12	**1b**	R = *t*Bu	ICl	–	Method B	**2i** (52); E = I; X = Cl
13	**1c**	R = *c*Hex	ICl	–	Method B	**2j** (95); E = I; X = Cl
14	**1c**	R = *i*Pr	ICl	–	Method B	**2k** (55); E = I; X = Cl
15	**1b**	R = *t*Bu	PhSeCl	–	Method B	**2l** (53); E = PhSe; X = Cl
16	**1b**	R = *t*Bu	PhSeCl	KI	Method B	**2l** (48)
17	**1c**	R = *t*Bu	PhSeCl	–	Method B	**2m** (65); E = PhSe; X = Cl
18	**1b**	R = *c*Hex	IN_3	–	Method B	**2n** (56); E = I; X = N_3
19	**1c**	R = *t*Bu	IN_3	–	Method B	**2o** (76); E = I; X = N_3
20	**1b**	R = *t*Bu	IOAc	–	Method C	**2p** (21); E = I; X = OAc[b]
21	**1a**	R = Bn	$HOCH_3$	–	Method D	**2r** (49); E = H; X = OCH_3
22	**1a**	R = Bn	$HOCH_3$	KI	Method D	**2r** (47); E = H; X = OCH_3
23	**1b**	R = *t*Bu	HOPh	–	Method D	**2s** (56); E = H; X = OPh
24	**1c**	R = *t*Bu	HOC_3H_7	–	Method D	**2t** (63); E = H; X = OC_3H_7
25	**1c**	R = *c*Hex	$HOCH_3$	–	Method D	**2u** (70); E = H; X = OCH_3

[a] Method A: Starting aldehyde, appropriate amine (2 equiv.), acetonitrile, MW, 120 °C, 20 min; then addition of molecular iodine (1 equiv.) at room temp. Method B: Starting aldehyde, appropriate amine (2 equiv.), acetonitrile, MW, 120 °C, 20 min; then evaporation of the solvent and excess amine, redissolving in fresh acetonitrile, and addition of the appropriate reagent. Method C: Starting aldehyde, appropriate amine (2 equiv.), acetonitrile, MW, 120 °C, 20 min; then evaporation of the solvent and excess amine, redissolving in fresh chloroform (2 mL), and addition of the resulting mixture to a solution of freshly prepared acetyl hypoiodite (2 equiv.) in chloroform (1 mL). Method D: Starting aldehyde, appropriate amine (2 equiv.), appropriate alcohol (2 mL), MW, 120 °C, 50 min. [b] An additional product, 2-(1-*tert*-butyl-2,4-diiodo-5-phenyl-1*H*-pyrrol-3-yl)ethyl acetate (**4**), was isolated in 19 % yield.

ature, and molecular iodine was added. A very quick consumption of the starting material was observed by TLC, which showed the formation of a single product within 5 min. Spectroscopic analysis together with HRMS data for the isolated compound proved the structure of 1-*tert*-butyl-3-iodo-4-(2-iodoethyl)-2-(4-methoxyphenyl)-1*H*-pyrrole (**2b**; Table 1, Entry 1). The iodocyclization/cyclopropane ring-cleavage reactions also proceeded very smoothly with other substrates, resulting in the formation of diiodo derivatives **2c**–**2h** in good yields (Table 1, Entries 6–11). For the preparation of polysubstituted pyrroles bearing different functional groups on the pyrrole ring and the ethyl chain, we turned our attention to reagents containing unsymmetrical covalent bonds. Thus, the use of iodine monochloride resulted in the formation of 2-aryl-4-(2-chloroethyl)-3-iodo-1*H*-pyrroles (**2i**–**2k**; Table 1, Entries 12–14), phenylselenyl chloride gave the corresponding 2-aryl-4-(2-chloroethyl)-3-(phenylselanyl)-1*H*-pyrroles (i.e., **2l** and **2m**; Table 1, Entries 15 and 17). Reactions between imine intermediates and freshly prepared iodine azide or acetyl hypoiodite resulted in the formation of the corresponding 2-aryl-4-(2-azidoethyl)-3-iodo-1*H*-pyrroles (**2n** and **2o**), 2-(1-*tert*-butyl-4-iodo-5-phenyl-1*H*-pyrrol-3-yl)ethyl acetate (**2p**), and 2-(1-*tert*-butyl-2,4-diiodo-5-phenyl-1*H*-pyrrol-3-yl)ethyl acetate (**4**) (Table 1, Entries 18–20). Finally, we were pleasantly surprised to see that when solutions of starting aldehydes **1** and amines were irradiated in a microwave oven in the presence of alcohols or phenol, the selective formation of *N*-substituted 4-(2-alkoxyethyl)-2-aryl-1*H*-pyrroles (**2r**, **2t**, and **2u**) and 1-*tert*-butyl-4-(2-phenoxyethyl)-2-phenyl-1*H*-pyrrole (**2s**) took place (Table 1, Entries 21 and 23–25).

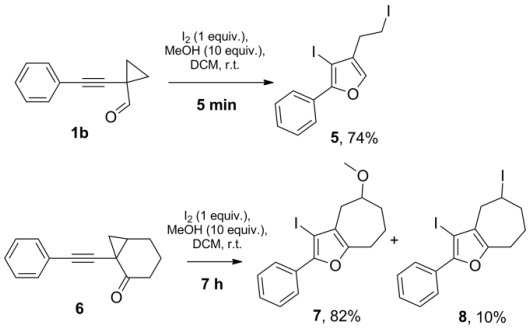
From the results obtained, the following mechanism can be proposed: after addition of the electrophile to the triple bond and formation of vinylic carbocation **A**, nucleophilic *anti* attack of the imine nitrogen atom takes place to give intermediate **B** (Scheme 3, route a). An analogous scenario was proposed by Huang et al. for the synthesis of functionalized furans.[12] However, the introduction of an excess of some external nucleophiles (indole, piperidine, methanol, sodium azide, or potassium iodide) to the reaction mixtures (Table 1, Entries 2–5, 16, and 22), did not result in the logical incorporation of the nucleophilic fragment into the ethyl chain of the final products. In each case, diiodo compound **2b** (Table 1, Entries 2–5), chloroethyl group containing compound **2l** (Entry 16), or methoxyethyl group containing compound **2r** (Entry 22) was isolated as the sole reaction product. Moreover, the rate of the cyclization reaction did not depend on the presence or absence of a strongly electron-donating methoxy group on the benzene ring, as is usually observed in reactions proceeding via vinyl carbocations.[14b,14c,15] These observations give support to route b (Scheme 3). Thus, we believe this reaction is promoted by a formal 1,3-addition reaction of the polar-covalent-bond-containing reagent to the C_{sp}–*c*Pr fragment, which then allows a subsequent 5-*endo-dig* cyclization to take place to give the final pyrroles (i.e., **2**; Scheme 3, route b).

Moreover, we carried out additional control experiments, including cyclization of starting 1-(phenylethynyl)cyclopropanecarbaldehyde (**1b**) and of Huang's 1-(phenylethynyl)bicyclo-



Scheme 3. Plausible mechanisms of the formation of polysubstituted pyrroles.

[4.1.0]heptan-2-one (**6**)[12] (Scheme 4). When compound **1b** was stirred in a methanol/dichloromethane mixture in the presence of 1 equiv. of iodine, a very smooth (5 min) and selective formation of 3-iodo-4-(2-iodoethyl)-2-phenylfuran (**5**) took place without any incorporation of a methoxy group from methanol into the product. In contrast, under the same conditions Huang's ketone **6** reacted more slowly (7 h), and two products were isolated after workup of the reaction mixture. The major product, as shown by Huang et al.,[12] was 3-iodo-5-methoxy-2-phenyl-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]furan (**7**), and the minor product contained an iodo group on the cycloheptane ring. The differences in rates as well as in the outcome of the reactions indicate that the cyclizations of cyclopropyl-tethered functionalized alkynes can take place by different mechanisms. An unsubstituted cyclopropyl tether favors the formal 1,3-addition process and smooth subsequent cyclization, while the presence of a bulky cyclohexane ring next to the cyclopropyl tether favors a classical electrophile-assisted cyclization with the incorporation of external nucleophiles. Unfortunately, Huang's ketone did not form any imine under the standard conditions, so we were not able to synthesize derivatives of 5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]pyrrole.



Scheme 4. Control experiments with 1-(arylalkynyl)cyclopropanecarbaldehyde **1b** and Huang's ketone **6**.

Conclusions

We have shown that 1-(1-alkynyl)cyclopropyl imines are able to react with polarized-covalent-bond-containing compounds, and that these reactions lead to a variety of polysubstituted pyrroles. This provides a mild and effective method for the simultaneous introduction of halogen, chalcogen, or hydrogen groups to the 3-position of the pyrrole ring, together with incorporation of halogen, azide, or alkoxy/aryloxy groups into the ethyl side-chain. This unique reactivity of cyclopropyl-tethered functionalized alkynes towards covalent-polar-bond-containing molecules points towards a broad and divergent synthetic applicability of analogous substrates.

Experimental Section

General Information: IR spectra were run as KBr discs with a Perkin–Elmer Spectrum BX II FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker (400 MHz) spectrometer in [D]chloroform, using the residual solvent signal as an internal standard. Signal multiplicities are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet). HR mass spectra were obtained with a Dual-ESI Q-TOF 6520 (Agilent Technologies) mass spectrometer. All reactions, and also the purity of the synthesized compounds, were monitored by TLC using silica gel 60 F254 aluminium plates (Merck). Plates were visualized with UV light and by treating the plates with vanillin stain followed by heating.

General Procedures for the Synthesis of Polysubstituted Pyrroles 2

Method A: A solution of the appropriate cyclopropanecarbaldehyde **1** (0.5 mmol) and amine (1 mmol.) in acetonitrile (2 mL) was irradiated in a closed vessel in a scientific microwave oven (CEM Focused Microwave™ Synthesis System, Discover® SP) at 150 W, 120 °C for 20 min. Then the reaction mixture was cooled to room temperature, and iodine (0.127 g, 0.5 mmol) was added. The resulting solution was stirred at room temperature, and the progress of the reaction was monitored by TLC. After all the starting material had been consumed, the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography, eluting with hexane/ethyl acetate (20:1).

Method B: A solution of the appropriate cyclopropanecarbaldehyde **1** (0.5 mmol) and amine (1 mmol) in acetonitrile (2 mL) was irradiated in a closed vessel in a scientific microwave oven (CEM Focused Microwave™ Synthesis System, Discover® SP) at 150 W, 120 °C for 20 min. Then the solvent and the amine were evaporated under reduced pressure. The residue was dissolved in acetonitrile (2 mL), and iodine monochloride (81.25 mg, 0.5 mmol), or phenyl hypochloroselenoite (95.5 mg, 0.5 mmol), or a solution of freshly prepared hypoiodyl azide[16] (1 mmol) was added. The resulting solution was stirred at room temperature, and the progress of the reaction was monitored by TLC. After all the starting material had been consumed, the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography, eluting with hexane/ethyl acetate (20:1).

Method C: Synthesis of 2-(1-*tert*-butyl-4-iodo-5-phenyl-1*H*-pyrrol-3-yl)ethyl acetate (**2p**) and 2-(1-*tert*-butyl-2,4-diiodo-5-phenyl-1*H*-pyrrol-3-yl)ethyl acetate (**4**). A solution of 1-(phenylethynyl)cyclopropanecarbaldehyde (**1b**; 67 mg, 0.4 mmol) and *tert*-butylamine (83.3 µL, 0.79 mmol, 2 equiv.) in acetonitrile (2 mL) was irradiated in a closed vessel in a scientific microwave oven (CEM Focused Microwave™ Synthesis System, Discover® SP) at 150 W, 120 °C for 20 min. Then the solvent and the *tert*-butylamine were evaporated under reduced pressure. The residue was dissolved in chloroform (2 mL), and the resulting solution was added to a freshly prepared solution of acetyl hypoiodite[17] (2 equiv.) in chloroform (1 mL). The resulting mixture was stirred in the dark at room temperature for 20 min. After the reaction was finished, the solution was diluted with CH_2Cl_2, and was washed with saturated sodium thiosulfate solution (2 × 10 mL), saturated sodium hydrogen carbonate solution (2 × 10 mL), and brine (2 × 10 mL). The organic layer was dried with sodium sulfate, and filtered, and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography, eluting with hexane/ethyl acetate (20:1).

Method D: A solution of the appropriate cyclopropanecarbaldehyde **1** (0.5 mmol) and amine (1 mmol) in the appropriate alcohol (2 mL) was irradiated in a closed vessel in a scientific microwave oven (CEM Focused Microwave™ Synthesis System, Discover® SP) at 100–150 W, 100–120 °C for 50 min. After all the starting material had been consumed, the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography, eluting with hexane/ethyl acetate (20:1).

1-Benzyl-4-(2-chloroethyl)-2-(4-methoxyphenyl)-1*H*-pyrrole (2a): Yellowish oil (47.1 mg, 29 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.99 (t, ^3J = 7.6 Hz, 2 H, CH_2), 3.72 (t, ^3J = 7.6 Hz, 2 H, CH_2Cl), 3.83 (s, 3 H, OCH_3), 5.09 (s, 2 H, CH_2Ph), 6.13 (s, 1 H, $CH_{pyrrole}$), 6.60 (br.s, 1 H, $NCH_{pyrrole}$), 6.90 (d, ^3J = 8.8 Hz, 2 H, ArH), 7.05 (d, ^3J = 7.2 Hz, 2 H, ArH), 7.26 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.28–7.35 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.0 (CH_2), 45.3 (CH_2Cl), 50.4 (CH_2Ph), 55.2 (OCH_3), 108.5 ($CH_{pyrrole}$), 113.8 (ArC), 120.0 (ArC), 120.3 ($NCH_{pyrrole}$), 125.5 (ArC), 126.4 (ArC), 127.2 (ArC), 128.6 (ArC), 130.0 (ArC), 134.8 (ArC), 138.8 (ArC), 158.8 (ArC) ppm. HRMS (ESI): calcd. for $C_{20}H_{21}{}^{35}ClNO$ [M + H] 326.1306; found 326.1306.

1-*tert*-Butyl-3-iodo-4-(2-iodoethyl)-2-(4-methoxyphenyl)-1*H*-pyrrole (2b): White solid (0.206 g, 81 %); m.p. 129–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 9 H, 3 CH_3), 3.01 (t, ^3J = 8.0 Hz, 2 H, CH_2), 3.33 (t, ^3J = 8.0 Hz, 2 H, CH_2I), 3.87 (s, 3 H, OCH_3), 6.87 (s, 1 H, $CH_{pyrrole}$), 6.94 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.19 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.1 (CH_2I), 31.5 (3 CH_3), 33.6 (CH_2), 55.2 (OCH_3), 58.0 [$C(CH_3)_3$], 72.5 (CI), 113.2 (ArC), 117.1 ($CH_{pyrrole}$), 122.8 (ArC), 128.3 (ArC), 133.6 (ArC), 135.0 (ArC), 159.4 (ArC) ppm. HRMS (ESI): calcd. for $C_{17}H_{22}{}^{127}I_2NO$ [M + H] 509.9785; found 509.9787.

1-Benzyl-3-iodo-4-(2-iodoethyl)-2-(4-methoxyphenyl)-1*H*-pyrrole (2c): Yellowish oil (0.211 g, 78 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.02 (t, ^3J = 8.0 Hz, 2 H, CH_2), 3.34 (t, ^3J = 8.0 Hz, 2 H, CH_2I), 3.83 (s, 3 H, OCH_3), 4.97 (s, 2 H, CH_2Ph), 6.69 (s, 1 H, $CH_{pyrrole}$), 6.91 (d, ^3J = 8.0 Hz, 2 H, ArH), 6.95 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.19 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.23–7.30 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.2 (CH_2I), 33.3 (CH_2), 51.7 (CH_2Ph), 55.2 (OCH_3), 67.5 (CI), 113.7 (ArC), 120.0 ($CH_{pyrrole}$), 124.3 (ArC), 125.0 (ArC), 126.6 (ArC), 127.5 (ArC), 128.6 (ArC), 132.1 (ArC), 135.8 (ArC), 138.0 (ArC), 159.5 (ArC) ppm. HRMS (ESI): calcd. for $C_{20}H_{20}I_2NO$ [M + H] 543.9634; found 543.9636.

1-*tert*-Butyl-3-iodo-4-(2-iodoethyl)-2-phenyl-1*H*-pyrrole (2d): White solid (0.137 g, 57 %); m.p. 100–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 9 H, 3 CH_3), 3.02 (t, ^3J = 8.0 Hz, 2 H, CH_2), 3.34 (t, ^3J = 8.0 Hz, 2 H, CH_2I), 6.88 (s, 1 H, $CH_{pyrrole}$), 7.28–7.30 (m, 2 H, ArH), 7.41–7.42 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.1 (CH_2I), 31.5 (3 CH_3), 33.6 (CH_2), 58.2 [$C(CH_3)_3$], 71.9 (CI), 117.2 ($CH_{pyrrole}$), 123.0 (ArC), 127.8 (ArC), 128.3 (ArC), 132.5 (ArC), 135.2 (ArC), 136.4 (ArC) ppm. HRMS (ESI): calcd. for $C_{16}H_{20}{}^{127}I_2N$ [M + H] 479.9680; found 479.9683.

1-Butyl-3-iodo-4-(2-iodoethyl)-2-phenyl-1*H*-pyrrole (2e): Colorless oil (0.11 g, 46 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79 (t, ^3J = 7.6 Hz, 3 H, CH_3), 1.15 (sext, ^3J = 7.6 Hz, 2 H, CH_{2nBu}), 1.52 (p, ^3J = 7.6 Hz, 2 H, CH_{2nBu}), 3.02 (t, ^3J = 8.0 Hz, 2 H, CH_2), 3.34 (t, ^3J = 8.0 Hz, 2 H, CH_2I), 3.78 (t, ^3J = 7.2 Hz, 2 H, CH_{2nBu}), 6.72 (s, 1 H, $CH_{pyrrole}$), 7.32–7.34 (m, 2 H, ArH), 7.34–7.46 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.2 (CH_2I), 13.5 (CH_3), 19.6 (CH_{2nBu}), 33.3 (CH_2), 33.4 (CH_{2nBu}), 48.0 (CH_{2cHex}), 66.8 (CI), 119.6 ($CH_{pyrrole}$), 124.7 (ArC), 128.1 (ArC), 128.3 (ArC), 130.8 (ArC), 132.5 (ArC), 135.4 (ArC) ppm. HRMS (ESI): calcd. for $C_{16}H_{20}I_2N$ [M + H] 479.9685; found 479.9689.

1-*tert*-Butyl-3-iodo-4-(2-iodoethyl)-2-*p*-tolyl-1*H*-pyrrole (2f): White solid (0.143 g, 58 %); m.p. 129–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 9 H, 3 CH_3), 2.42 (s, 3 H, CH_3), 3.01 (t, ^3J = 8.0 Hz, 2 H, CH_2), 3.33 (t, ^3J = 8.0 Hz, 2 H, CH_2I), 6.86 (s, 1 H, $CH_{pyrrole}$), 7.16 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.22 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.1 (CH_2I), 21.4 (CH_3), 31.5 (3 CH_3), 33.6 (CH_2), 58.1 [$C(CH_3)_3$], 72.0 (CI), 117.1 ($CH_{pyrrole}$), 122.9 (ArC), 128.6 (ArC), 132.3 (ArC), 133.3 (ArC), 135.3 (ArC), 138.1 (ArC) ppm. HRMS (ESI): calcd. for $C_{17}H_{22}I_2N$ [M + H] 493.9836; found 493.9841.

1-Benzyl-3-iodo-4-(2-iodoethyl)-2-*p*-tolyl-1*H*-pyrrole (2g): Colorless oil (0.155 g, 59 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, CH_3), 3.03 (t, ^3J = 8.0 Hz, 2 H, CH_2), 3.35 (t, ^3J = 8.0 Hz, 2 H, CH_2I), 4.98 (s, 2 H, CH_2Ph), 6.69 (s, 1 H, $CH_{pyrrole}$), 6.97 (d, ^3J = 6.4 Hz, 2 H, ArH), 7.16–7.21 (m, 4 H, ArH), 7.25–7.30 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.1 (CH_2I), 21.3 (CH_3), 33.3 (CH_2), 51.7 (CH_2Ph), 67.3 (CI), 120.0 ($CH_{pyrrole}$), 125.2 (ArC), 126.7 (ArC), 127.5 (ArC), 128.6 (ArC), 129.0 (2 ArC), 130.7 (ArC), 136.0 (ArC), 137.9 (ArC), 138.1 (ArC) ppm. HRMS (ESI): calcd. for $C_{20}H_{20}{}^{127}I_2N$ [M + H] 527.9685; found 527.9689.

1-Cyclohexyl-3-iodo-4-(2-iodoethyl)-2-*p*-tolyl-1*H*-pyrrole (2h): Colorless oil (0.166 g, 64 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.14–1.18 (m, 2 H, CH_{2cHex}), 1.52–1.65 (m, 4 H, CH_{2cHex}), 1.78–1.80 (m, 2 H, CH_{2cHex}), 1.91 (d, ^2J = 12.0 Hz, 2 H, CH_{2cHex}), 2.43 (s, 3 H, CH_3), 3.03 (t, ^3J = 8.0 Hz, 2 H, CH_2), 3.34 (t, ^3J = 8.0 Hz, 2 H, CH_2I), 3.78 (tt, ^3J = 12.0, ^3J = 3.6 Hz, 1 H, CH_{cHex}), 6.79 (s, 1 H, $CH_{pyrrole}$), 7.20 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.26 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.1 (CH_2I), 21.4 (CH_3), 25.3 (CH_{2cHex}), 25.7 (CH_{2cHex}), 33.6 (CH_2), 34.6 (CH_{2cHex}), 56.5 (CH_{cHex}), 66.5 (CI), 115.8 ($CH_{pyrrole}$), 124.6 (ArC), 129.0 (ArC), 129.6 (ArC), 130.7 (ArC), 134.8 (ArC), 137.8 (ArC) ppm. HRMS (ESI): calcd. for $C_{19}H_{24}{}^{127}I_2N$ [M + H] 519.9993; found 519.9987.

1-*tert*-Butyl-4-(2-chloroethyl)-3-iodo-2-phenyl-1*H*-pyrrole (2i): Brownish solid (0.101 g, 52 %); m.p. 147–148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 9 H, 3 CH_3), 2.91 (t, ^3J = 8.0 Hz, 2 H, CH_2), 3.69 (t, ^3J = 8.0 Hz, 2 H, CH_2Cl), 6.88 (s, 1 H, $CH_{pyrrole}$), 7.27–7.30 (m, 2 H, ArH), 7.41–7.42 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.5 (3 CH_3), 32.3 (CH_2), 44.3 (CH_2Cl), 58.2 [$C(CH_3)_3$], 72.4 (CI), 117.6 ($CH_{pyrrole}$), 120.0 (ArC), 127.8 (ArC), 128.3 (ArC), 132.5 (ArC), 135.2 (ArC), 136.5 (ArC) ppm. HRMS (ESI): calcd. for $C_{16}H_{20}{}^{35}ClI^{127}IN$ [M + H] 388.0323; found 388.0328.

4-(2-Chloroethyl)-1-cyclohexyl-3-iodo-2-*p*-tolyl-1*H*-pyrrole (2j): White solid (0.203 g, 95 %); m.p. 118–119 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16–1.18 (m, 2 H, CH_{2cHex}), 1.52–1.65 (m, 4 H, CH_{2cHex}), 1.78–1.79 (m, 2 H, CH_{2cHex}), 1.91 (d, ^2J = 12.0 Hz, 2 H, CH_{2cHex}), 2.43 (s, 3 H, CH_3), 2.93 (t, ^3J = 7.6 Hz, 2 H, CH_2), 3.69 (t, ^3J = 7.6 Hz, 2 H, CH_2Cl), 3.78 (tt, ^3J = 12.0, ^3J = 3.6 Hz, 1 H, CH_{cHex}), 6.79 (s, 1 H, $CH_{pyrrole}$), 7.20 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.26 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 25.3 (CH_{2cHex}), 25.7 (CH_{2cHex}), 32.4 (CH_2), 34.6 (CH_{2cHex}), 44.3 (CH_2Cl), 56.5 (CH_{cHex}), 66.9 (CI), 116.2 ($CH_{pyrrole}$), 121.6 (ArC), 129.1 (ArC), 129.6 (ArC), 130.7 (ArC), 134.8 (ArC), 137.9 (ArC) ppm. HRMS (ESI): calcd. for $C_{19}H_{24}ClIN$ [M + H] 428.0642; found 428.0641.

4-(2-Chloroethyl)-3-iodo-1-isopropyl-2-*p*-tolyl-1*H*-pyrrole (2k): White solid (0.106 g, 55 %); m.p. 121–122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (d, ^3J = 6.8 Hz, 6 H, CH_{3iPr}), 2.42 (s, 3 H, CH_3), 2.93 (t, ^3J = 7.6 Hz, 2 H, CH_2), 3.69 (t, ^3J = 8.0 Hz, 2 H, CH_2Cl), 4.23 (sept, ^3J = 6.8 Hz, 1 H, CH_{iPr}), 6.79 (s, 1 H, $CH_{pyrrole}$), 7.20 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.26 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (CH_3), 23.8 (CH_{3iPr}), 32.4 (CH_2), 44.3 (CH_2Cl), 48.6 (CH_{iPr}), 67.0 (CI), 115.3 ($CH_{pyrrole}$), 122.0 (ArC), 129.1 (ArC), 129.7 (ArC), 130.8 (ArC), 134.9 (ArC), 138.0 (ArC) ppm. HRMS (ESI): calcd. for $C_{16}H_{20}{}^{35}ClIN$ [M + H] 388.0323; found 388.0326.

1-*tert*-Butyl-4-(2-chloroethyl)-2-phenyl-3-(phenylselanyl)-1*H*-pyrrole (2l): White solid (0.111 g, 53 %); m.p. 122–123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 9 H, 3 CH_3), 2.95 (t, ^3J = 7.6 Hz, 2 H, CH_2), 3.60 (t, ^3J = 7.6 Hz, 2 H, CH_2Cl), 6.97 (s, 1 H, $CH_{pyrrole}$), 7.06–7.10 (m, 3 H, ArH), 7.12–7.16 (m, 2 H, ArH), 7.20–7.23 (m, 2 H, ArH), 7.27–7.29 (m, 2 H, ArH), 7.34 (t, ^3J = 7.2 Hz, 1 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.7 (CH_2), 31.7 (3 CH_3), 45.0 (CH_2Cl), 58.0 [$C(CH_3)_3$], 106.8 (ArC), 117.9 ($CH_{pyrrole}$), 121.4 (ArC), 125.0 (ArC), 127.3 (ArC), 128.0 (ArC), 128.1 (ArC), 128.7 (ArC), 132.1 (ArC), 135.3 (ArC), 135.7 (ArC), 139.1 (ArC) ppm. HRMS (ESI): calcd. for $C_{22}H_{25}{}^{35}ClNSe$ [M + H] 418.0834; found 418.0830.

1-*tert*-Butyl-4-(2-chloroethyl)-3-(phenylselanyl)-2-*p*-tolyl-1*H*-pyrrole (2m): White solid (0.14 g, 65 %); m.p. 137–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (s, 9 H, 3 CH_3), 2.37 (s, 3 H, CH_3), 2.94 (t, ^3J = 7.6 Hz, 2 H, CH_2), 3.58 (t, ^3J = 7.6 Hz, 2 H, CH_2Cl), 6.96 (s, 1 H, $CH_{pyrrole}$), 7.07–7.09 (m, 3 H, ArH), 7.10 (br.s, 4 H, ArH), 7.13–7.16 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (CH_3), 30.7 (CH_2), 31.7 (3 CH_3), 45.0 (CH_2Cl), 57.9 [$C(CH_3)_3$], 106.7 (ArC), 117.8 ($CH_{pyrrole}$), 121.3 (ArC), 125.0 (ArC), 128.1 (ArC), 128.7 (ArC), 131.9 (ArC), 132.6 (ArC), 135.3 (ArC), 137.7 (ArC), 139.2 (ArC) ppm. HRMS (ESI): calcd. for $C_{23}H_{27}{}^{35}ClNSe$ [M + H] 432.0990; found 432.0982.

4-(2-Azidoethyl)-1-cyclohexyl-3-iodo-2-phenyl-1*H*-pyrrole (2n): Yellowish oil (0.118 g, 56 %). IR (KBr): $\tilde{\nu}$ = 2098 ($N{=}N^+{=}N^-$) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16–1.20 (m, 2 H, CH_{2cHex}), 1.53–1.64 (m, 4 H, CH_{2cHex}), 1.78–1.80 (m, 2 H, CH_{2cHex}), 1.92 (d, ^2J = 12.4 Hz, 2 H, CH_{2cHex}), 2.77 (t, ^3J = 7.2 Hz, 2 H, CH_2), 3.47 (t, ^3J = 7.2 Hz, 2 H, CH_2N_3), 3.77 (tt, ^3J = 12.0, ^3J = 3.6 Hz, 1 H, CH_{cHex}), 6.80 (s, 1 H, $CH_{pyrrole}$), 7.31–7.35 (m, 2 H, ArH), 7.39–7.49 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2 (CH_{2cHex}), 25.7 (CH_{2cHex}), 28.4 (CH_2), 34.6 (CH_{2cHex}), 51.4 (CH_2N_3), 56.6 (CH_{cHex}), 67.1 (CI), 116.3 ($CH_{pyrrole}$), 121.3 (ArC), 128.1 (ArC), 128.3 (ArC), 130.9 (ArC), 132.7 (ArC), 134.9 (ArC) ppm. HRMS (ESI): calcd. for $C_{18}H_{22}{}^{127}IN_4$ [M + H] 421.0884; found 421.0901.

4-(2-Azidoethyl)-1-*tert*-butyl-3-iodo-2-*p*-tolyl-1*H*-pyrrole (2o): Yellowish solid (0.155 g, 76 %); m.p. 92–93 °C. IR (KBr): $\tilde{\nu}$ = 2096 ($N{=}N^+{=}N^-$) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.39 (s, 9 H, 3 CH_3), 2.42 (s, 3 H, CH_3), 2.75 (t, ^3J = 7.2 Hz, 2 H, CH_2), 3.46 (t, ^3J = 7.2 Hz, 2 H, CH_2N_3), 6.87 (s, 1 H, $CH_{pyrrole}$), 7.17 (d, ^3J = 8.0 Hz, 2 H, ArH), 7.22 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 28.4 (CH_2), 31.5 (3 CH_3), 51.4 (CH_2N_3), 58.1 [$C(CH_3)_3$], 72.5 (CI), 117.5 ($CH_{pyrrole}$), 119.4 (ArC), 128.6 (ArC), 132.3 (ArC), 133.4 (ArC), 135.4 (ArC), 138.1 (ArC) ppm. HRMS (ESI): calcd. for $C_{17}H_{22}N_4I$ [M + H] 409.0884; found 409.0890.

2-(1-*tert*-Butyl-4-iodo-5-phenyl-1*H*-pyrrol-3-yl)ethyl Acetate (2p): Yellow oil (43.2 mg, 21 %). IR (KBr): $\tilde{\nu}$ = 1738 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (s, 9 H, 3 CH_3), 2.09 ($COCH_3$), 2.77 (t, ^3J = 7.6 Hz, 2 H, CH_2CH_2O), 4.25 (t, ^3J = 7.6 Hz, 2 H, CH_2CH_2O), 6.83 (s, 1 H, $CH_{pyrrole}$), 7.27–7.29 (m, 2 H, ArH), 7.40–7.41 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 ($COCH_3$), 28.0

(CH_2CH_2O), 31.6 (3 CH_3), 58.1 [$C(CH_3)_3$], 64.4 (CH_2CH_2O), 72.9 (Cl), 117.2 ($CH_{pyrrole}$), 119.4 (ArC), 127.8 (ArC), 128.3 (ArC), 132.6 (ArC), 135.1 (ArC), 136.6 (ArC), 171.1 (CO) ppm. HRMS (ESI): calcd. for $C_{18}H_{23}{}^{127}INO_2$ [M + H] 412.076; found 412.0771.

1-Benzyl-4-(2-methoxyethyl)-2-(4-methoxyphenyl)-1*H*-pyrrole (2r): Yellowish wax (78.6 mg, 49 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.81 (t, ^3J = 7.2 Hz, 2 H, $CH_2CH_2OCH_3$), 3.41 (s, 3 H, $CH_2CH_2OCH_3$), 3.63 (t, ^3J = 7.2 Hz, 2 H, $CH_2CH_2OCH_3$), 3.81 (s, 3 H, OCH_3), 5.06 (s, 2 H, CH_2Ph), 6.12 (d, ^4J = 1.2 Hz, 1 H, $CH_{pyrrole}$), 6.57 (br.s, 1 H, $NCH_{pyrrole}$), 6.87 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.05 (d, ^3J = 7.6 Hz, 2 H, ArH), 7.24–7.33 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.5 ($CH_2CH_2OCH_3$), 50.3 (CH_2Ph), 55.1 (OCH_3), 58.5 ($CH_2CH_2OCH_3$), 73.7 ($CH_2CH_2OCH_3$), 108.7 ($CH_{pyrrole}$), 113.7 (ArC), 120.1 ($NCH_{pyrrole}$), 120.4 (ArC), 125.8 (ArC), 126.4 (ArC), 127.1 (ArC), 128.5 (ArC), 130.0 (ArC), 134.5 (ArC), 139.0 (ArC), 158.6 (ArC) ppm. HRMS (ESI): calcd. for $C_{21}H_{24}NO_2$ [M + H] 322.1802; found 322.1804.

1-*tert*-Butyl-4-(2-phenoxyethyl)-2-phenyl-1*H*-pyrrole (2s): White solid (89.3 mg, 56 %); m.p. 72–73 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (s, 9 H, 3 CH_3), 3.04 (t, ^3J = 7.4 Hz, 2 H, CH_2CH_2OPh), 3.04 (t, ^3J = 7.5 Hz, 2 H, CH_2CH_2OPh), 6.01 (d, ^4J = 1.9 Hz, 1 H, $CH_{pyrrole}$), 6.84 (d, ^4J = 1.8 Hz, 1 H, $NCH_{pyrrole}$), 6.97–7.01 (m, 3 H, ArH), 7.32–7.36 (m, 2 H, ArH), 7.38–7.39 (m, 3 H, ArH), 7.45–7.47 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.2 (CH_2CH_2OPh), 31.9 (3 CH_3), 56.9 [$C(CH_3)_3$], 68.8 (CH_2CH_2OPh), 112.2 ($CH_{pyrrole}$), 114.5 (ArC), 116.8 (ArC), 117.0 ($NCH_{pyrrole}$), 120.4 (ArC), 127.3 (ArC), 127.4 (ArC), 129.3 (ArC), 131.6 (ArC), 133.8 (ArC), 137.3 (ArC), 159.0 (ArC) ppm. HRMS (ESI): calcd. for $C_{22}H_{25}NO$ [M + H] 320.2014; found 320.2011.

1-*tert*-Butyl-4-(2-propoxyethyl)-2-*p*-tolyl-1*H*-pyrrole (2t): Yellowish oil (94.2 mg, 63 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, ^3J = 7.6 Hz, 3 H, $OCH_2CH_2CH_3$), 1.41 (s, 9 H, 3 CH_3), 1.63 (sext, ^3J = 7.2 Hz, 2 H, $OCH_2CH_2CH_3$), 2.39 (s, 3 H, CH_3), 2.77 (t, ^3J = 7.6 Hz, 2 H, CH_2CH_2O), 3.44 (t, ^3J = 6.8 Hz, 2 H, $OCH_2CH_2CH_3$), 3.64 (t, ^3J = 7.6 Hz, 2 H, CH_2CH_2O), 5.87 (d, ^4J = 2.0 Hz, 1 H, $CH_{pyrrole}$), 6.72 (d, ^3J = 2.0 Hz, 1 H, $NCH_{pyrrole}$), 7.14 (d, ^3J = 7.6 Hz, 2 H, ArH), 7.27 (d, ^3J = 8.0 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.6 ($OCH_2CH_2CH_3$), 21.2 (CH_3), 22.9 ($OCH_2CH_2CH_3$), 27.6 (CH_2CH_2O), 31.9 (3 CH_3), 56.8 [$C(CH_3)_3$], 71.9 (CH_2CH_2O), 72.5 ($OCH_2CH_2CH_3$), 112.2 ($CH_{pyrrole}$), 116.6 ($NCH_{pyrrole}$), 117.5 (ArC), 128.0 (ArC), 131.5 (ArC), 133.6 (ArC), 134.5 (ArC), 137.0 (ArC) ppm. HRMS (ESI): calcd. for $C_{20}H_{30}NO$ [M + H] 300.2322; found 300.2320.

1-Cyclohexyl-4-(2-methoxyethyl)-2-*p*-tolyl-1*H*-pyrrole (2u): Yellowish oil (0.104 g, 70 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19–1.27 (m, 2 H, CH_{2cHex}), 1.60–1.70 (m, 4 H, CH_{2cHex}), 1.83 (d, ^2J = 12.8 Hz, 2 H, CH_{2cHex}), 2.00 (d, ^2J = 12.8 Hz, 2 H, CH_{2cHex}), 2.41 (s, 3 H, CH_3), 2.81 (t, ^3J = 7.2 Hz, 2 H, CH_2CH_2O), 3.41 (s, 3 H, OCH_3), 3.63 (t, ^3J = 7.2 Hz, 2 H, CH_2CH_2O), 3.98 (tt, ^3J = 12.0, ^3J = 3.6 Hz, 1 H, CH_{cHex}), 6.00 (d, ^4J = 1.6 Hz, 1 H, $CH_{pyrrole}$), 6.70 (br.s, 1 H, $NCH_{pyrrole}$), 7.21 (d, ^3J = 8.4 Hz, 2 H, ArH), 7.25 (d, ^3J = 7.6 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1 (CH_3), 25.4 (CH_{2cHex}), 25.9 (CH_{2cHex}), 27.6 (CH_2CH_2O), 34.9 (CH_{2cHex}), 55.0 (CH_{cHex}), 58.5 (OCH_3), 73.8 (CH_2CH_2O), 108.3 ($CH_{pyrrole}$), 115.8 ($NCH_{pyrrole}$), 119.6 (ArC), 128.9 (ArC), 129.0 (ArC), 131.0 (ArC), 133.6 (ArC), 136.3 (ArC) ppm. HRMS (ESI): calcd. for $C_{20}H_{28}NO$ [M + H] 298.2165; found 298.2162.

2-(1-*tert*-Butyl-2,4-diiodo-5-phenyl-1*H*-pyrrol-3-yl)ethyl Acetate (4): Yellow oil (51 mg, 19 %). IR (KBr): $\tilde{\nu}$ = 1739 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.57 (s, 9 H, 3 CH_3), 2.09 ($COCH_3$), 2.92 (t, ^3J = 7.6 Hz, 2 H, CH_2CH_2O), 4.17 (t, ^3J = 7.6 Hz, 2 H, CH_2CH_2O), 7.19–7.22 (m, 2 H, ArH), 7.36–7.38 (m, 3 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 ($COCH_3$), 31.5 (CH_2CH_2O), 33.2 (3 CH_3), 62.1 [$C(CH_3)_3$], 63.3 (CH_2CH_2O), 67.2 (CI), 73.3 (CI), 127.9 (ArC), 128.2 (2 ArC), 131.6 (ArC), 138.8 (ArC), 140.4 (ArC), 171.0 (CO) ppm. HRMS (ESI): calcd. for $C_{18}H_{22}{}^{127}I_2NO_2$ [M + H] 537.9734; found 537.9745.

General Procedure for the Synthesis of Furans 5, 7, and 8: Methanol (0.202 mL, 5 mmol) and iodine (0.127 g, 0.5 mmol) were added to a solution of 1-(phenylethynyl)cyclopropanecarbaldehyde (**1b**) (85 mg, 0.5 mmol) or 1-(phenylethynyl)bicyclo[4.1.0]heptan-2-one (**6**) (105 mg, 0.5 mmol) in dichloromethane (2 mL). The resulting solution was stirred at room temperature, and the progress of the reaction was monitored by TLC. After all the starting material had been consumed, the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography, eluting with hexane/ethyl acetate (20:1).

3-Iodo-4-(2-iodoethyl)-2-phenylfuran (5): Yellow oil (0.157 g, 74 %. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.00 (t, ^3J = 7.5 Hz, 2 H, CH_2), 3.36 (t, ^3J = 7.5 Hz, 2 H, CH_2I), 7.36 (tt, ^3J = 7.2, ^4J = 2.0 Hz, 1 H, ArH), 7.42–7.46 (m, 3 H, ArH and CH_{furan}), 7.96–7.99 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.6 (CH_2I), 31.0 (CH_2), 66.5 (CI), 126.3 (ArC), 128.3 (ArC), 128.4 (ArC), 128.6 (ArC), 130.1 (ArC), 139.0 (CH_{furan}), 152.2 (ArC) ppm. HRMS (ESI): calcd. for $C_{12}H_{11}{}^{127}I_2O$ [M + H] 424.889; found 424.8902.

3-Iodo-5-methoxy-2-phenyl-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]furan (7): Colorless oil (0.151 g, 82 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.59–1.68 [m, 1 H, $CH_2CH(OCH_3)CH_2CH$*H*CH_2], 1.75–1.83 [m, 1 H, $CH_2CH(OCH_3)C$*H*$H(CH_2)_2$], 1.94–2.03 [m, 1 H, $CH_2CH(OCH_3)CH_2C$*H*HCH_2], 2.14–2.19 [m, 1 H, $CH_2CH(OCH_3)CH$*H*$(CH_2)_2$], 2.55 [dd, ^2J = 15.3, ^3J = 9.2 Hz, 1 H, C*H*$H_2CH(OCH_3)(CH_2)_3$], 2.74–2.81 [m, 1 H, $CH_2CH(OCH_3)(CH_2)_2CH$*H*], 2.84–2.90 [m, 2 H, CH*H*$CH(OCH_3)(CH_2)_2CH$*H*], 3.35 [tt, ^3J = 9.0, ^3J = 2.8 Hz, 1 H, $CH_2CH(OCH_3)(CH_2)_3$], 3.41 (s, 3 H, OCH_3), 7.30 (t, ^3J = 7.4 Hz, 1 H, ArH), 7.40 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.93–7.95 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.3 [$CH_2CH(OCH_3)CH_2CH_2CH_2$], 28.3 [$CH_2CH(OCH_3)CH_2CH_2CH_2$], 31.9 [$CH_2CH(OCH_3)(CH_2)_3$], 35.5 [$CH_2CH(OCH_3)CH_2(CH_2)_2$], 56.3 ($OCH_3$), 70.5 (CI), 78.9 [$CH_2CH(OCH_3)(CH_2)_3$], 119.7 (ArC), 125.9 (ArC), 127.6 (ArC), 128.3 (ArC), 130.6 (ArC), 148.7 (ArC), 152.7 (ArC) ppm. HRMS (ESI): calcd. for $C_{16}H_{18}{}^{127}I_2O$ [M + H] 369.0351; found 369.0358.

3-Iodo-4-(2-iodoethyl)-2-phenylfuran (8): White solid (23.2 mg, 10 %); m.p. 97–99 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.67–1.77 (m, 1 H, $CH_2CHICH_2CH_2CH_2$), 1.84–1.93 (m, 1 H, $CH_2CHICH_2CH_2CH_2$), 2.30–2.39 [m, 1 H, $CH_2CHICH_2(CH_2)_2$], 2.41–2.48 [m, 1 H, $CH_2CHICH_2(CH_2)_2$], 2.79–2.91 [m, 1 H, $CH_2CHICH_2(CH_2)_2$], 3.13 [dd, ^2J = 15.8, ^3J = 9.0 Hz, 1 H, $CH_2CHI(CH_2)_3$], 3.22 [dd, ^2J = 15.8, ^3J = 3.2 Hz, 1 H, $CH_2CHI(CH_2)_3$], 4.54 [tt, ^3J = 9.0, ^3J = 3.0 Hz, 2 H, $CH_2CHI(CH_2)_3$], 7.31 (t, ^3J = 7.4 Hz, 1 H, ArH), 7.41 (t, ^3J = 7.6 Hz, 2 H, ArH), 7.95–7.97 (m, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.5 ($CH_2CHICH_2CH_2CH_2$), 28.2 [$CH_2CHI(CH_2)_2CH_2$], 31.0 [$CH_2CHI(CH_2)_3$], 39.5 [$CH_2CHI(CH_2)_3$], 43.2 [$CH_2CHICH_2(CH_2)_2$], 69.4 (CI), 123.7 (ArC), 125.9 (ArC), 127.7 (ArC), 128.3 (ArC), 130.4 (ArC), 148.6 (ArC), 153.2 (ArC) ppm. HRMS (ESI): calcd. for $C_{15}H_{15}{}^{127}I_2O$ [M + H] 464.9212; found 464.9214.

Keywords: Alkynes · Small-ring systems · Cyclization · Nitrogen heterocycles · Imines

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Received: August 10, 2016
Published Online: September 29, 2016

Paper 4

Addition of Primary Amines to 2-(1-Alkynyl)-2-cycloalken-1-ones

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European Journal of Organic Chemistry (**2017**) 2017: 1624-1627
DOI:10.1002/ejoc.201700119
https://onlinelibrary.wiley.com/doi/10.1002/ejoc.201700119

ChemPubSoc Europe

DOI: 10.1002/ejoc.201700119

EurJOC European Journal of Organic Chemistry

Communication

Isomerization–Addition Cascade

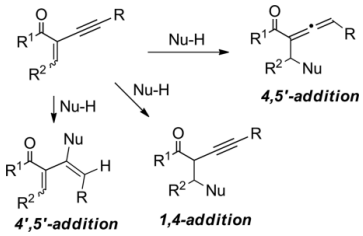
Addition of Primary Amines to 2-(1-Alkynyl)-2-cycloalken-1-ones

Aurelija Urbanaitė,[a] Lukas Šteinys,[a] Algirdas Brukštus,[a] and Inga Čikotienė*[a]

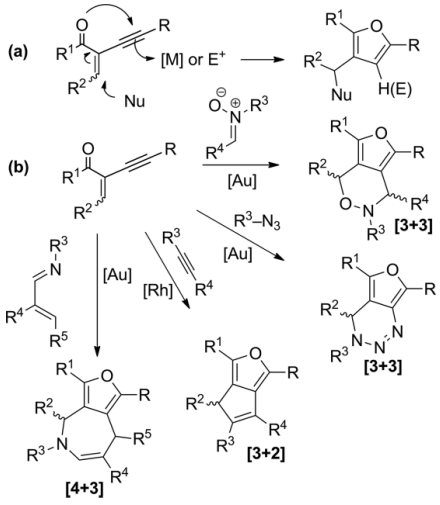
Abstract: The regio- and stereoselective nucleophilic addition of primary aliphatic amines to 2-(1-alkynyl)-2-alken-1-ones was found to proceed through double-bond migration. In particular, this is a mild and atom-economical route for the preparation of (*Z*)-β-enaminones having cycloalkene rings.

Introduction

2-(1-Alkynyl)-2-alken-1-ones are a readily available class of reactive compounds having carbonyl, alkynyl, and alkenyl functional groups.[1] Being a representative class of electron-deficient 1,3-conjugated enynes, these compounds are able to undergo catalytic or catalyst-free nucleophilic addition reactions. The regioselectivity of the addition depends on the nature of the nucleophile. Thus, the addition of carbon-centered nucleophiles proceeds through a 4,5′-addition mode and gives functionalized allenes, whereas the addition of oxygen and sulfur nucleophiles results in 1,4- and 4′,5′-addition reactions and the formation of functionalized alkynes and 1,3-dienes, respectively (Scheme 1).[2] The products of nucleophilic addition reactions are attractive precursors in organic synthesis. Undoubtedly, the main synthetic application of the interactions between 2-(1-alkynyl)-2-alken-1-ones and nucleophiles is the transition-metal-catalyzed[1,3] and electrophile-mediated[4,5] preparation of polysubstituted furan derivatives. These methods involve tandem nucleophilic addition–cyclization reactions[1,3,4] or gold- or rhodium-catalyzed [3+3], [3+2], and [4+3] cycloaddition–cyclization cascades[5] (Scheme 2). There are only a few examples of the metal-catalyzed construction of polysubstituted pyrroles from 2-(1-alkynyl)-alken-1-one oximes[6] or in situ formed imines of 2-(1-alkynyl)-alken-1-ales.[7] In continuation of our recent studies in the field of metal-catalyzed and electrophile-mediated transformations of functionally substituted alkynes,[8] we decided to prepare some imines of 2-(1-alkynyl)-alken-1-ones and to investigate their cyclization reactions to polyfunctional pyrrole derivatives. However, we found that the title compounds showed unique reactivity towards primary aliphatic amines and a hitherto unknown isomerization–addition process occurred. Herein, we present the results of our investigations.



Scheme 1. Reactions between 2-(1-alkynyl)-2-alken-1-ones and nucleophiles.



Scheme 2. Synthesis of polysubstituted furans from 2-(1-alkynyl)-2-alken-1-ones. (a) Tandem nucleophilic addition–cyclization reactions. (b) Cycloaddition–cyclization reactions cascades.

Results and Discussion

2-(1-Alkynyl)-2-cycloalken-1-ones **1** and **3** were prepared by a known method involving an iodination/Sonogashira coupling sequence starting from commercial cycloalkenones.[1] With the starting materials in hand, we chose 2-(phenylethynyl)cyclohex-

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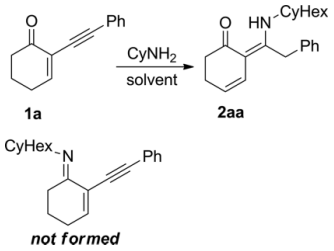
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201700119.

2-enone (**1a**) as a model substrate and investigated its reaction with cyclohexylamine. Notably, in all cases a new isomerization–nucleophilic addition reaction took place to give (*Z*)-2-[1-(cyclohexylamino)-2-phenylethylidene]cyclohex-3-enone (**2aa**) as the only product. The regio- and stereoselectivity of the addition was proven by HSQC, HMBC, and NOESY NMR spectroscopy experiments. All attempts to obtain *N*-[2-(phenylethynyl)cyclohex-2-enylidene]cyclohexanamine were unsuccessful (Scheme 3).



Scheme 3. Reaction between 2-(phenylethynyl)cyclohex-2-enone (**1a**) and cyclohexylamine. Cy = cyclohexyl.

First, we utilized a microwave-assisted synthesis for a smoother condensation reaction. Thus, we irradiated a solution of **1a** and cyclohexylamine (1.1 equiv.) in acetonitrile in a closed vessel in a scientific microwave oven. The reaction proceeded smoothly, and full conversion of the starting material was reached in 7 min (Table 1, entry 1). The yield of isolated product **2aa** was moderate, so we increased the amount of cyclohexylamine to 2 equivalents. In this case, the formation of **2aa** occurred within 3 min, and the final product was isolated in 70 % yield (Table 1, entry 2). Increasing the amount of cyclohexylamine to 10 equivalents and performing the reaction at room temperature in acetonitrile did not give substantially better results (Table 1, entries 3 and 4). Next, we switched our attention to some different solvents. The reaction between **1aa** and cyclohexylamine proceeded slowly in *n*-propanol at room temperature and gave good yields of final **2aa** (Table 1, entries 5 and 6). However, the use of methanol at room temperature or in a microwave oven was not promising (Table 1, entries 7 and 8). On the one hand, the reaction in 1,2-dichloroethane (DCE) led to incomplete conversion of the starting compound and the formation of tars (Table 1, entry 9), and on the other hand, a polar aprotic solvent such as dimethylformamide (DMF) facilitated the interaction between **1a** and cyclohexylamine, so smooth and chromatographically clean formation of **2aa** occurred in good yields either in a microwave oven or at room temperature (Table 1, entries 10 and 11).

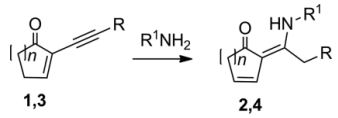
Table 1. Data for the reaction of 2-(phenylethynyl)cyclohex-2-enone (**1a**) with cyclohexylamine.

Entry	Amine [equiv.]	Reaction conditions	Time [min]	Yield [%] of **2aa**
1	1.1	MeCN, microwave, 120 °C	7	44
2	2	MeCN, microwave, 120 °C	3	70
3	10	MeCN, microwave, 120 °C	1	47
4	2	MeCN, r.t.	1440	49
5	2	*n*PrOH, K_2CO_3 (2 equiv.), Ar, r.t.	360	70
6	2	*n*PrOH, Ar, r.t.	360	60
7	2	MeOH, Ar, r.t.	60	21
8	2	MeOH, microwave, 100 °C	3	39
9	2	DCE, microwave, 120 °C	8	12
10	2	DMF, microwave, 120 °C	3	60
11	2	DMF, r.t.	30	69

Thus, it was found that the best reaction conditions included irradiation of a mixture of the 2-(1-alkynyl)-2-cycloalken-1-one with a primary amine (2 equiv.) in acetonitrile in a microwave oven or stirring the mixture in dimethylformamide at room temperature for 30 min.

Next, we investigated the scope of this reaction and used various 2-(1-alkynyl)-2-cyclohexen-1-ones **1**/2-(1-alkynyl)-2-cyclopenten-1-ones **3** and different amines. The results are summarized in Table 2. Notably, 2-(1-alkynyl)-2-cyclohexen-1-ones **1** reacted readily in all cases with a broad range of primary aliphatic amines (Table 2, entries 1–7, 10–21, 23–26). The reactions proceeded well either in a microwave oven in acetonitrile

Table 2. Data for the reaction between 2-(1-alkynyl)-2-alken-1-ones **1** or **3** and primary amines.



1,3 2,4

Entry	Starting compound	Amine[a]	Product (yield [%])
1	**1a** (*n* = 2; R = Ph)	$CyNH_2$	**2aa** (70)
2	**1a**	$tBuNH_2$	**2ab** (79)
3	**1a**	$iPrNH_2$	**2ac** (64)
4	**1a**	$cPrNH_2$	**2ad** (52)
5	**1a**	$BnNH_2$	**2ae** (56)
6	**1a**	$HC{\equiv}CCH_2NH_2$	**2af** (52)
7	**1a**	$iBuNH_2$	**2ag** (53)
8	**1a**	$PhNH_2$	no reaction
9	**1a**	4-$MeOC_6H_4NH_2$	no reaction
10	**1b** (*n* = 2; R = 4-$MeOC_6H_4$)	$CyNH_2$	**2ba** (60)
11	**1b**	$tBuNH_2$	**2bb** (53)
12	**1b**	$iPrNH_2$	**2bc** (50)
13	**1b**	$cPrNH_2$	**2bd** (48)
14	**1b**	$BnNH_2$	**2be** (51)
15	**1b**	$nBuNH_2$	**2bh** (61)
16	**1c** (*n* = 2; R = 4-FC_6H_4)	$CyNH_2$	**2ca** (81)
17	**1c**	$tBuNH_2$	**2cb** (71)
18	**1c**	$iPrNH_2$	**2cc** (72)
19	**1c**	$cPrNH_2$	**2cd** (65)
20	**1c**	$BnNH_2$	**2ce** (70)
21	**1c**	$nBuNH_2$	**2ch** (78)
22	**1c**	$PhNH_2$	no reaction
23	**1d** (*n* = 2; R = *n*Bu)	$CyNH_2$	**2da** (60)
24	**1d**	$iPrNH_2$	**2dc** (40)
25	**1d**	$BnNH_2$	**2de** (46)
26	**1d**	$iBuNH_2$	**2dg** (60)
27	**3a** (*n* = 1; R = Ph)	$CyNH_2$	**4aa** (31)
28	**3a**	$tBuNH_2$	**4ab** (56)
29	**3a**	$iPrNH_2$	**4ac** (43)
30	**3b** (*n* = 1; R = 4-$MeOC_6H_4$)	$CyNH_2$	**4ba** (33)
31	**3b**	$tBuNH_2$	**4bb** (53)
32	**3c** (*n* = 1; R = 4-FC_6H_4)	$CyNH_2$	**4ca** (28)
33	**3c**	$tBuNH_2$	**4cb** (29)

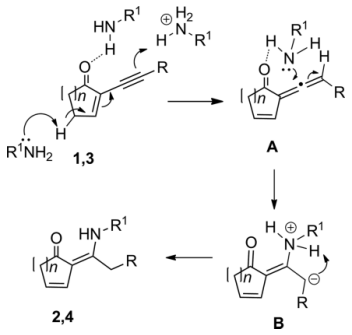
[a] Cy = cyclohexyl, *c*Pr = cyclopropyl.

solution or in dimethylformamide at room temperature. Linear and bulky primary aliphatic amines were well tolerated. However, compounds **1a** and **1c** did not react with weaker aniline nucleophiles (Table 2, entries 8, 9, and 22) and unchanged starting materials were isolated after workup of the reaction mixtures.

Reactions between 2-(1-alkynyl)-2-cyclopenten-1-ones **3** and primary amines required irradiation in a microwave oven to reach full conversion of the starting materials. Moreover, the yields of final products **4** were not very high (Table 2, entries 27–33), and in all cases, the formation of some tars occurred.

Finally, it is important to note that the use of secondary amines did not result in the formation of any detectable product. In all cases, smooth decomposition of the starting materials took place, even at room temperature.

From the data obtained, we suppose, that the reaction between 2-(1-alkynyl)-2-cycloalken-1-ones **1**/**3** and primary amines proceeds in the following manner (Scheme 4). First, abstraction of the acidic γ proton of compound **1** or **3** by the amine takes place. After abstraction of the proton, isomerization to intermediate allene **A** becomes possible. Then, very smooth addition of the nearby amine in a regio- and stereoselective manner finishes this process allowing the formation of (*Z*)-2-[1-(alkylamino)-2-substitutedethylidene]cycloalk-3-enones **2**/**4**. Unfortunately, we did not succeed in isolating or catching allene intermediate **A** by changing the reaction temperature, by using non-nucleophilic bases, or by monitoring of the reaction by ^{1}H NMR spectroscopy. However, given that analogous selectivity in the addition of amines to conjugated allene ketones and esters was previously described,[9] our proposed mechanism seems reasonable.



Scheme 4. Proposed mechanism for the reaction of 2-(1-alkynyl)-2-alken-1-ones **1** and **3** with primary amines.

Conclusions

In summary, it was shown that reactions between 2-(1-alkynyl)-2-alken-1-ones and primary aliphatic amines proceed through a unique isomerization–addition cascade. The method allowed the construction of (*Z*)-β-enaminones in a regio- and stereoselective manner. Given that β-enaminones are important compounds as building blocks for a variety of heterocycles,[10] we believe that our findings will find application in the synthesis of small scaffolds. Further investigation concerning the scope of the enaminones, demonstration of synthetic applications, and mechanistic details are currently ongoing in our group and will be published in due course.

Experimental Section

General Procedure for the Synthesis of (*Z*)-2-[1-(Amino)-2-ethylidene]cycloalk-3-enones 2 and 4

Method A: A solution of 2-(alkynyl)cyclopent-2-enone **3** or 2-(hex-1-ynyl)cyclohex-3-enone (**1d**) (1 mmol) and amine (2 equiv.) in DMF (2 mL) was irradiated in a closed vessel in a scientific microwave oven (CEM Focused Microwave™ Synthesis System, Discover® SP) at 150 W and 120 °C for 3 min. Then, the mixture was cooled to room temperature. The solution was diluted with CH_2Cl_2 and was washed with water (2 × 20 mL) and brine (1 × 20 mL). The organic layer was dried with sodium sulfate, filtered, and then concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/ethyl acetate, 4:1).

Method B: A solution of 2-(arylethynyl)cyclohex-2-enone **1a**–**c** (1 mmol) and amine (2 equiv.) in DMF (2 mL) was stirred at room temperature, and the progress of the reaction was monitored by TLC. After all the starting material was consumed, the solution was diluted with CH_2Cl_2 and was washed with water (2 × 20 mL) and brine (1 × 20 mL). The organic layer was dried with sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/ethyl acetate, 4:1).

Keywords: Alkynes · Amines · Domino reactions · Isomerization · Nucleophilic addition

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Received: January 25, 2017

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