VILNIUS UNIVERSITY

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DEVELOPMENT OF SYNTHETIC ROUTES TOWARDS β'-HYDROXY- OR α-SUBSTITUTED ENONES AND EVALUATION OF STRUCTURE – ANTIPROLIFERATIVE ACTIVITY RELATIONSHIP OF SYNTHESIZED COMPOUNDS

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Scientific supervisor:

Prof. Dr. Inga Čikotienė (Vilnius University, Physical Sciences, Chemistry 03P)

VILNIAUS UNIVERSITETAS

FIZINIŲ IR TECHNOLOGIJOS MOKSLŲ CENTRAS

IEVA KARPAVIČIENĖ

β‘-HIDROKSI- ARBA α-PAKEISTŲ ENONŲ SINTEZĖS METODŲ KŪRIMAS IR SUSINTETINTŲ JUNGINIŲ STRUKTŪROS - PRIEŠVĖŽINIO AKTYVUMO SĄRYŠIO ĮVERTINIMAS

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LIST OF ABBREVIATIONS

Ac	acetyl
Bn	benzyl
bt	boiling temperature
*i*Bu	isobutyl
*n*Bu	*n*-butyl
*t*Bu	*tert*-butyl
DABCO	1,4-diazabicyclo[2.2.2]octane
DCM	dichloromethane
DRS	death receptors stimulation
EA	Ethyl acetate
Et	ethyl
eq.	equivalent
GI_{50}	Growth inhibition of 50%
*c*Hex	cyclohexyl
*n*Hex	*n*-hexyl
HO-1	hemeoxygenase-1
*n*Hp	*n*-heptyl
IC_{50}	half maximal inhibitory concentration
IκB	Inhibitor of κB
Keap1	Kelch-like ECH associated protein

LA	Lewis acid
LDA	lithium diisopropylamide
LiHMDS	lithium hexamethyldisilazide
LPS	lipopolysaccharide
MBHA	Morita-Baylis-Hillman adduct
Me	methyl
NCS	*N*-chlorosuccinimide
NF-κB	nuclear factor kappa-light-chain-enhancer of activated B cells
NMR	nuclear magnetic resonance
*n*Non	*n*-nonyl
Nrf2	Nuclear factor (erythroid-derived 2)-like 2
*n*Okt	*n*-oktyl
Oxone	potassium peroxymonosulfate
PARP	poly (ADP-ribose) polymerase
*n*Pe	*n*-pentyl
Ph	phenyl
*i*Pr	isopropyl
*n*Pr	*n*-propyl
Py	pyridine
RaNi	Raney nickel
R_f	retention factor

ROS	reactive oxygen species
rt	room temperature
SAR	structure–activity relationship
SRB	sulphorhodamine B
TFA	trifluoroacetic acid
TIPS	triisopropylsisyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TNF-α	tumor necrosis factor alpha

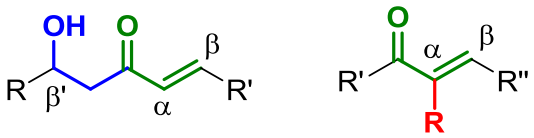
INTRODUCTION

α,β-Unsaturated ketones are not only important precursors for synthetic manipulations but also consist in a variety of natural products. It is known that these compounds display enormous number of biological activities [1]. It has been shown that natural α,β-unsaturated ketones and their derivatives exhibit pharmacological properties including antiinflammatory, antibacterial and anticarcinogen activities and the most important cytotoxicity against tumor cell lines [2]. The conjugated ketone functional group has been hypothesized to work in cancer chemotherapy *via* thiol alkylation without interaction with amino or hydroxyl groups of cellular constituents, and therefore, enones could have remarkable advantages over classical alkylators since these compounds probably could not cause genotoxic effects associated with a number of anticancer drugs [3]. Moreover, the antitumor activity of the enone framework containing materials is linked with various effects including inhibition on NF-κB [4] or mitochondrial mediated [5] pathways, stimulation of death receptors (DRS) of the tumor necrosis factor (TNF) [6], inhibition of cyclin-depended kinases [7] or DNA topoisomerase II [8] and so forth. Biological activity and selectivity towards different cell lines may be influenced by variation of α,β-unsaturated ketones structural scaffold. Some time ago, it was shown that β'-hydroxy-α,β-unsaturated ketones and α-substituted α,β-unsaturated ketones exhibited remarkable antiproliferative activities in human solid tumor cell lines and some of them could be more potent pharmacophores than simple α,β-unsaturated ketones [9].

The development of synthetic methods of α,β-unsaturated ketones had been started since 19th century and had been developed in very different ways. The most common classical synthesis of α,β-unsaturated ketones was aldol-type condensation [10] and its analogues reactions like the Claisen-Schmidt [11] or the Knoevenagel condensations [12]. The Wittig reaction [13] and its variation the Horner-Wadsworth-Emmons olefination [14] also were used in preparation of the desired compounds. More recently some modern synthetic protocols

were reported, such as the palladium-mediated Suzuki [15] or the carbonilative Heck couplings [16], catalytic alkene [17] or alkyne – carbonyl metatheses [18] and the Meyer-Schuster and the Rupe rearrangements of propargylic alcohols to the α,β-unsaturated carbonyl compounds [19]. These methods have their scope but they are sometimes problematic because of limited selectivity, formation of waste or harsh reaction conditions. Moreover the synthetic approach usually differs considering substituents on the main scaffold.

The main aim of the present work was dedicated to the development of synthetic approaches of two main structural scaffolds – β'-hydroxy-α,β-unsaturated ketones and α-substituted α,β-unsaturated ketones together with their structure-anticancer activity relationship evaluation.



Main tasks for the achievement of the aim:

- To investigate possible synthetic ways to β'-hydroxy-α,β-unsaturated ketones.
- To study an alkyne-carbonyl metathesis reaction between functionalized alkynes and aldehydes for preparation of various α-substituted α,β-unsaturated ketones.
- To evaluate structure – antiproliferative activity relationship of synthesized compounds.

Thus the dissertation is divided into 3 main chapters. In the first chapter studied synthetic approaches to β'-hydroxy-α,β-unsaturated ketones *via* iron (III) halide mediated reactions between aldehydes and pent-4-yn-2-ol or *via* reductive cleavage of Δ^2-isoxazolines are described. The second chapter represents the most intriguing and fundamental part of the dissertation; it deals with study of alkyne-carbonyl metathesis reactions between alkynes and aldehydes and with mechanistic investigation of some unique observed reactions. And finally, the third chapter deals with evaluation of

antiproliferative activity data of synthesized products together with estimation of structure – activity relationships.

In terms of significance of the work it is stated that:

- Study on iron (III) chloride mediated reactions between aldehydes and pent-4-yn-2-ol did not show enough potency for wide application of these transformations for synthesis of β'-hydroxy-α,β-unsaturated ketones.
- An *in situ* prepared aluminum-copper couple can be used an efficient and economical reductant of nonconjugated Δ^2-isoxazolines to the corresponding β-hydroxy ketones. However, $Mo(CO)_6$ was proved to be the only selective reductant for conjugated Δ^2-isoxazolines.
- Reactions between 3-arylprop-2-ynyl esters and aldehydes undergo unprecedentedly with formation of *E*- and *Z*-2-aroyl-3-arylallyl carboxylates and/or Morita-Baylis-Hillman carboxylates. These reactions proceed either *via* classical alkyne-carbonyl metathesis route, or *via* new nucleophilic addition-rearrangement cascade.
- The formation of the Morita-Baylis-Hillman adducts always proceed *via* a new addition-rearrangement cascade, which includes a nucleophilic attack of alkyne to Lewis acid-activated aldehyde, followed by an intramolecular nucleophilic addition to the vinylic carbocation by the ester carbonyl group and concomitant formation of a six-membered zwitterion. An acyl group transfer completes this cascade by formation of the kinetic Morita-Baylis-Hillman carboxylates. Uniquely, this new 1,3-acyl shift pathway in propargylic esters is induced by addition of electrophilic aldehydes and does not require alkyne activation by transition metal catalysis.
- In reactions between 3-arylprop-2-ynyl esters and aldehydes, electron-deficient benzaldehydes are able to switch from the classical alkyne-carbonyl metathesis pathway *via* four-membered intermediates to the newly discovered addition-rearrangement cascade *via* six-membered zwitterions. Therefore, the present synthetic method provides a useful

approach to Morita-Baylis-Hillman derivatives that have been difficult to access by classical MBH reactions.

- Evaluation of antiproliferative activities of synthesized compounds let to establish some SAR and to find several lead compounds exhibiting submicromolar GI_{50}‘s. The conjugated double bond is crucial for anticancer activity. It is possible to obtain a selective cell growth inhibition by varying substituents in α-position of α,β-unsaturated ketones.

Chapter I

INVESTIGATION OF POSSIBLE SYNTHETIC APPROACHES TO β'-HYDROXY-α,β-UNSATURATED KETONES

Introduction

The β'-hydroxy-α,β-unsaturated ketone fragment may be important pharmacophore in determining selective compound anticancer activity. Compounds with this fragment are found in ginger [20] and avocado fruits [21]. Recently, the Padron group reported on several synthetic compounds [9] as powerful A2780, SW1573 and WiDr solid tumor cell lines growth inhibitors (Fig. 1).

R = *n*Hex, *c*Hex, *t*Bu, *i*Bu, Ph, $(CH_2)_{10}Br$

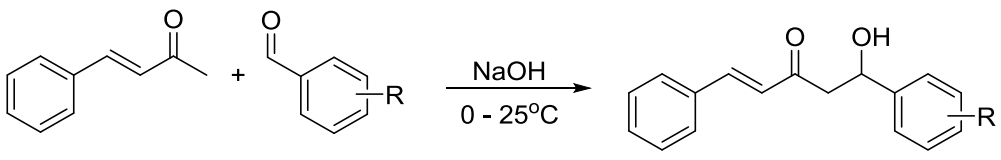
R_1 = Ph, 4-MeC_6H_4. R_2 = H

R_1 = 4-BrC_6H_4, R_2 = Me

Figure 1. Synthetic lead compounds from [9].

When our team started a collaborative project with the Padron group, it was decided to synthesize similar compounds with bigger variety of substituents, and also to check the importance of hydroxy group and double bond for biological activity.

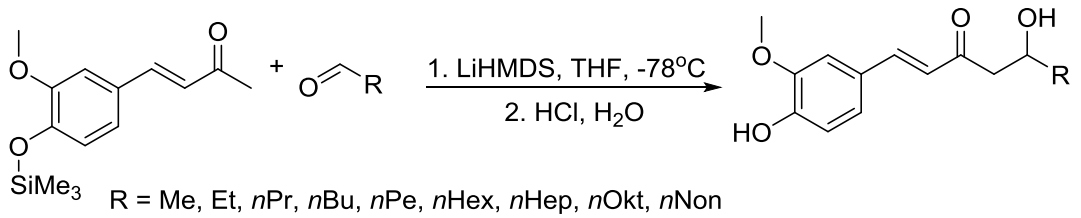
It is known from the literature, that the first syntheses of β'-hydroxy-α,β-unsaturated ketones were obtained by an aldol type condensation of benzylideneacetone and various benzaldehydes [22] (Scheme 1).



R = 2-Cl, 4-Cl

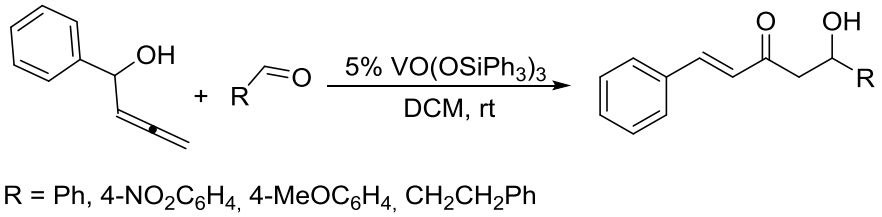
Scheme 1.

Later on, more selective approach to hydroxyl ketones was used via lithium enolates [23] (Scheme 2). After years this classical methodology had been broadly used in synthesis of β-hydroxy ketones using various lithium containing bases (*n*-BuLi [24], LDA [25], LiHMDS [26]). It should be noted that sometimes dehydration [23a] or intramolecular cyclization to tetrahydropyranones [27] occurred.



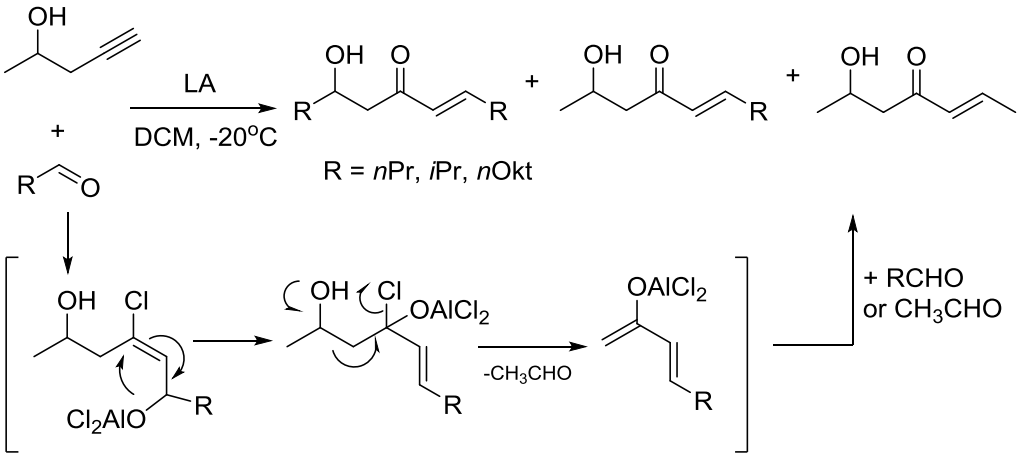
Scheme 2.

In addition to the mentioned condensations, there are some more elegant approaches resulting in simultaneous formation of all three functionalities (C=O, C=C and OH). The first one represented vanadium mediated additions of allenic alcohols to aldehydes [28] (Scheme 3). Later, similar procedure was presented demonstrating reaction of aromatic and aliphatic allenic alcohols with various aldehydes in the presence of indium chloride [29].



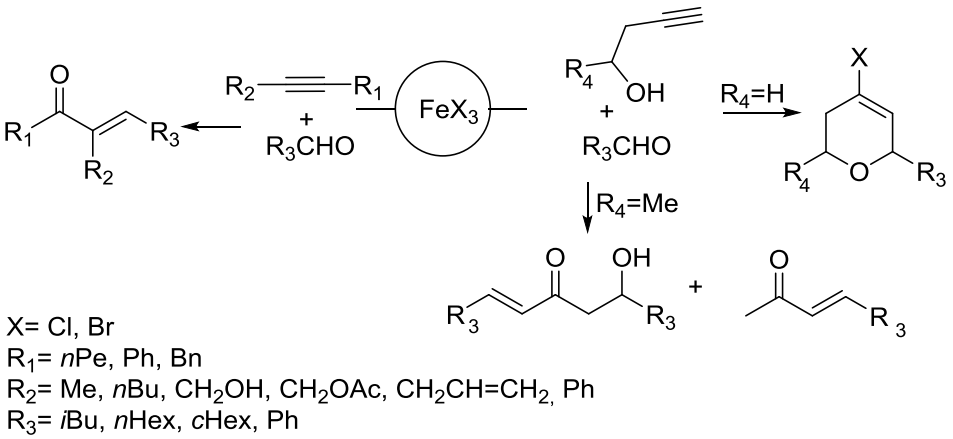
Scheme 3.

The second method demonstrated electrophilic condensation of aldehydes and pent-4-yn-2-ol to β'-hydroxy-α,β-unsaturated ketones catalyzed by Lewis acid $AlCl_3$ or $TiCl_4$ [30] (Scheme 4). Unfortunately, this reaction afforded a mixture of products due to its complicate mechanism. As authors suggested, first an activated aldehyde attached to the triple bond, then after several rearrangements formed acetaldehyde concurred in reaction with substrate.



Scheme 4.

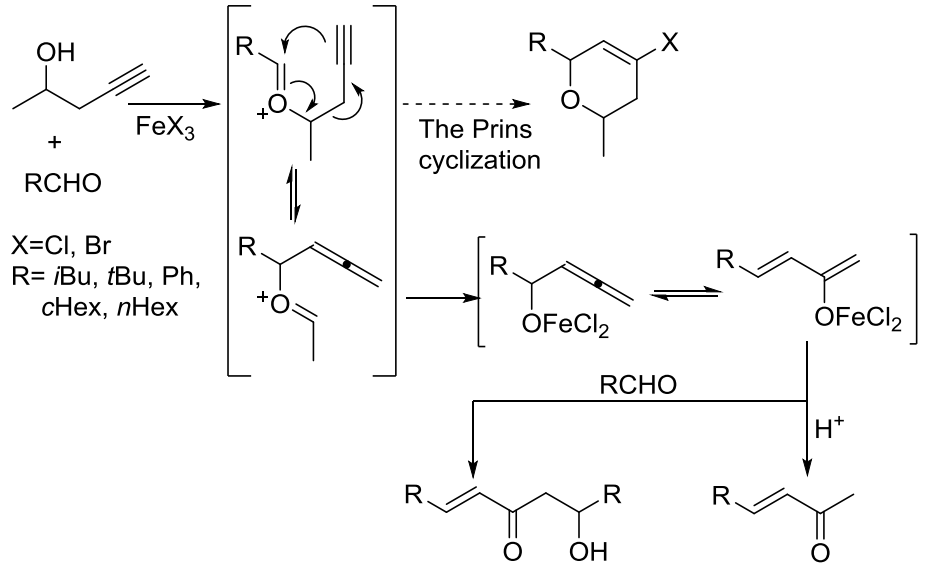
Later some possibilities of iron (III) halide mediated alkyne and aldehyde transformations to various conjugated products were demonstrated (Scheme 5) [31]. One of the routes led to the formation of α,β-unsaturated ketones via alkyne-carbonyl metathesis reaction and another one – to the formation of β'-hydroxy-α,β-unsaturated ketones instead of expected Prins-type cyclization products.



Scheme 5.

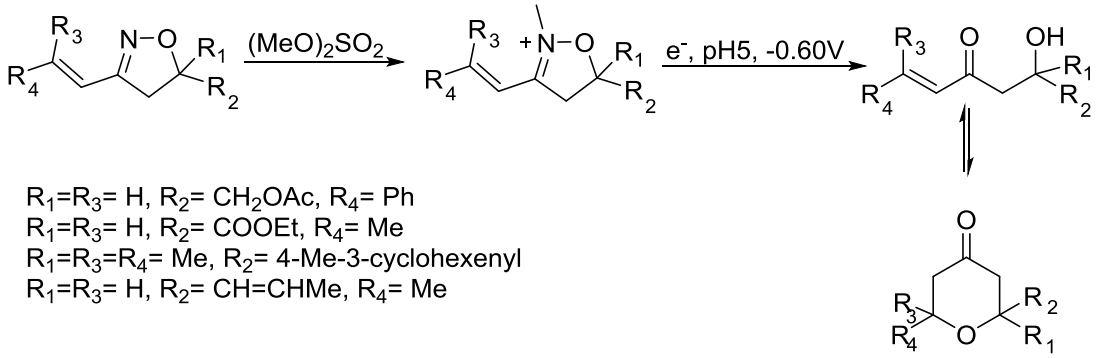
In comparison with earlier presented work [30], these authors created their own version of the reaction mechanism (Scheme 6) [32]. The authors proposed that first of all an oxonium ion was generated during addition of homopropargylic alcohol to an aldehyde promoted by ferric halide. Next, an oxonium-[3,3]-sigmatropic rearrangement, instead of the expected Prins cyclization, took place to give an allenoate. The subsequent coupling of the intermediate

allenoate with the aldehyde or protonation resulted in formation of final unsaturated ketones.



Scheme 6.

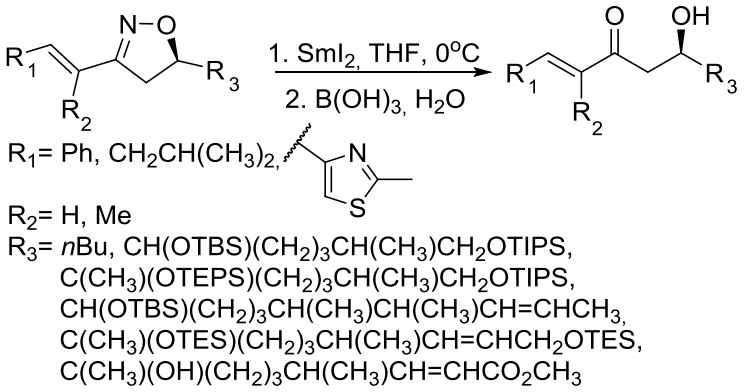
Another specific method for formation of β'-hydroxy-α,β-unsaturated ketones is reduction of Δ^2-isoxazolines. Reduction of α,β-unsaturated Δ^2-isoxazolines needs specific reduction agents, as classical RaNi catalyst reduces both Δ^2-isoxazoline and double bond fragments [33]. In 1990, an electrochemical reduction of conjugated Δ^2-isoxazolines to the β'-hydroxy-α,β-unsaturated ketones was presented [34] (Scheme 7). In this work an oxa-Michael cyclization of main products under reaction conditions was also demonstrated.



Scheme 7.

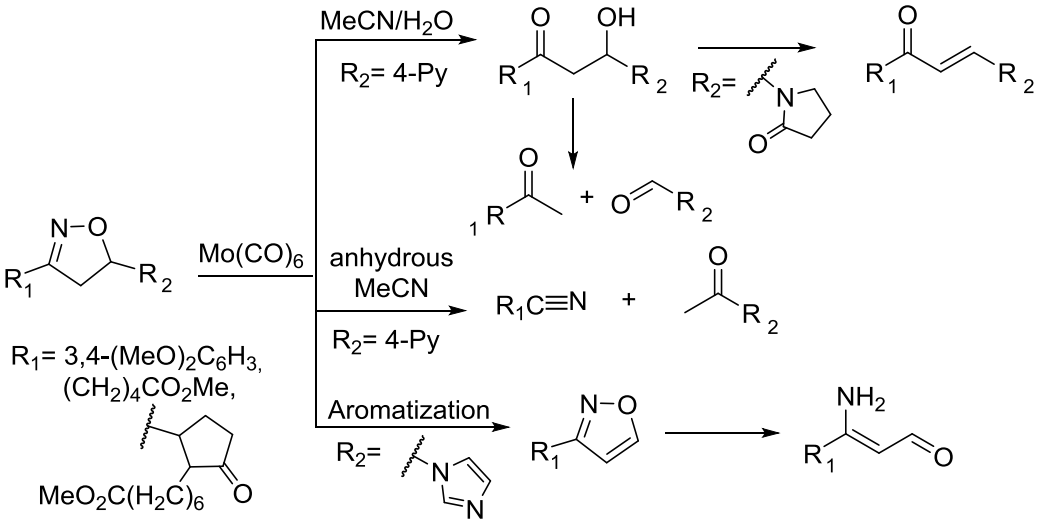
Later, the selective reduction of conjugated Δ^2-isoxazolines to unsaturated compounds using samarium diiodide was presented by the Carrierra group

(Scheme 8) [35]. Moreover, in this work it was showed that Δ^2-isoxazolines with alkyl or aryl substituents in the position 3 of the ring could not be reduced in SmI_2 mediated process. More recently, the same group demonstrated that the reduction of the isoxazoline ring together with the conjugated double bond can be achieved by using the same reductant in THF and water mixture [36]. It should be noted that this type of reduction found its appliance in the total synthesis of (±)-diospongin A through oxa-Michael cyclization in a 6-*endo-trig* manner of β'-hydroxy-α,β-unsaturated ketones [37].



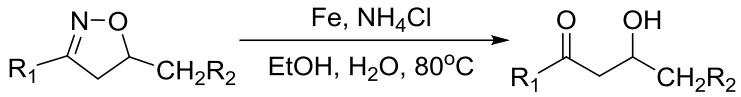
Scheme 8.

Another mediator of Δ^2-isoxazolines reduction is molybdenum hexacarbonyl in water acetonitrile mixture [38]. However, during heating of the reaction mixtures dehydration products usually form [39]. Moreover, use of substrates having heterocyclic ring can lead to decomposition, decyclization, retro aldol condensation or aromatization reactions (Scheme 9) [40].



Scheme 9.

Reduction of α,β-unsaturated Δ^2-isoxazolines can be also accomplished by Fe/NH_4Cl system. This reaction was performed in ethanol water mixture and resulted in formation of the desired products in moderate or good yields (Scheme 10) [41].



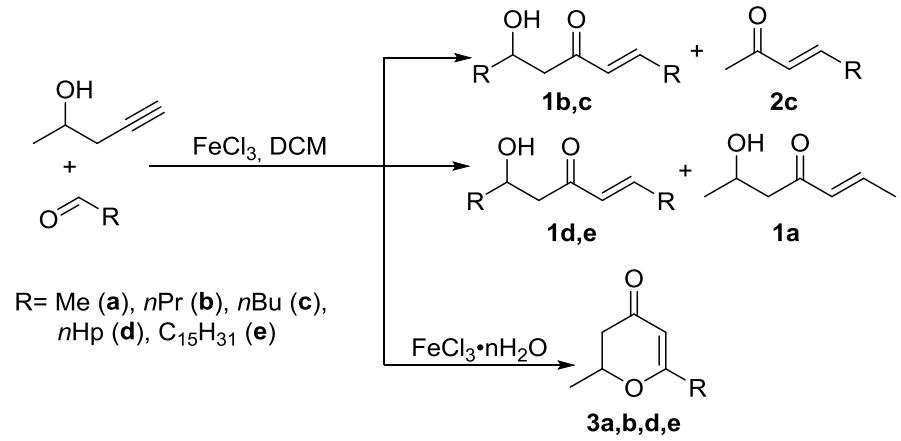
R_1= Ph, 4-ClC_6H_4, 4-$MeOC_6H_4$, 4-MeC_6H_4, 2-$BnOC_6H_4$, *n*Pr, CH=CHPh
R_2= Ph, 4-MeC_6H_4, 2-Py, 3-Py, 2-ClC_6H_4, 4-PhC_6H_4, 4-$CHOC_6H_4$, OMe, OH

Scheme 10.

I.1 Study of the Reaction between Pent-4-yn-2-ol and Aldehydes

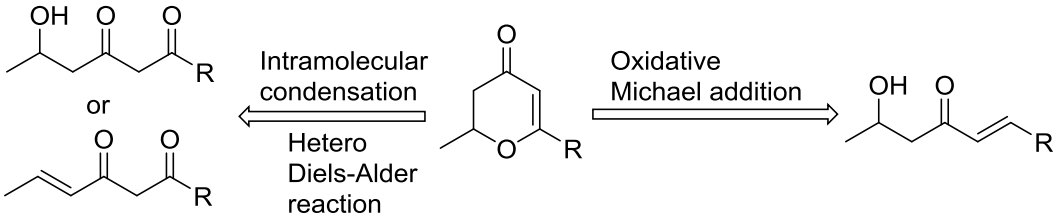
During investigation of synthetic ways for preparation of β'-hydroxy-α,β-unsaturated ketones first of all we chose the reaction between aldehydes and pent-4-yn-2-ol as previously described useful and economic one-pot method [31]. We used previously found optimal reaction conditions: an equivalent of $FeCl_3$ in dry DCM.

Thus, we chose several aliphatic aldehydes (having C_1, C_3, C_4, C_7 and C_{15} linear carbon chains) for this reaction. Unfortunately, reactions were not as predictable as we expected and as it was reported before (Scheme 11). When butanal and pentanal were used, we obtained the desired products **1b** and **1c** in low yields (22 % and 19 %, respectively). Side product **2c** was isolated in 12% yield during reaction between pentanal and pent-4-yn-2-ol. When aldehydes with longer aliphatic chains (octanal and palmitaldehyde) were used, mixtures of products **1d** or **1e** and 2-hydroxy-5-hepten-4-one (**1a**) were isolated in 1 : 1.5 ratio. Moreover it was found that the presence of water in reaction mixtures gave precedent to formation of cyclic products 2,3-dihydro-4*H*-pyran-4-ones **3** in 3 – 11% yields without desired β'-hydroxy-α,β-unsaturated ketones.



Scheme 11.

The impact of moisture on reaction outcome was tested in reaction between pent-4-yn-2-ol and butanal using iron (III) chloride hexahydrate. The reaction proceeded slowly and the yield of isolated product reached only 3% together with formation of tars. Considering the formation of dihydropyranones, there are several possible reaction pathways through conversion of similar linear molecules to the cyclic ones by the intramolecular condensation or hetero-Diels-Alder reactions [42] or palladium catalyzed oxidative Michael-type addition [43] (Scheme 12).



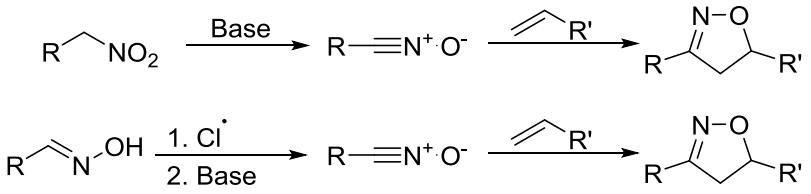
Scheme 12.

As shown in review article [44], $FeCl_3$ initiates various addition reactions to double or triple bond, and $FeCl_3 \cdot nH_2O$ mediates C-H or double bond oxidations. This process also needs additional oxidant as hydrogen peroxide [45] or organic peroxides [46], although there are some examples of oxidation of dihydropyridines to pyridines [47] and iron (III) chloride mediated oxidative C-C coupling [48] without extra oxidants. These facts did not clarify possible pathway of forming dihydropyranones. Unfortunately, it was impossible to find more reliable conditions for tested reaction.

All further experiments with this reaction were unselective and very unspecific and products were isolated only in low yields. After these unsatisfactory results we decided to change our strategy and to evaluate reductive cleavage of Δ^2-isoxazolines.

I.2 Investigation of Reductive Cleavage of Δ^2-Isoxazolines

Usually, Δ^2-isoxazolines are synthesized by [2+3] cycloaddition reaction between aldoximes or nitro compounds with alkenes. Starting aldoximes or nitro compounds form reactive intermediates nitrile oxides (Scheme 13).

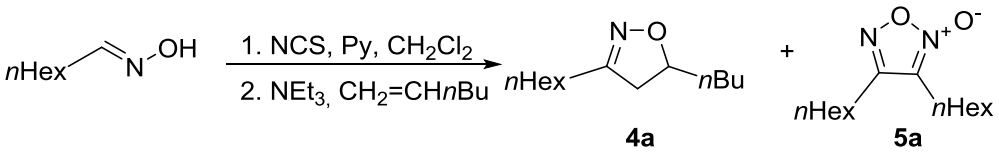


Scheme 13.

Methylene group next to the nitro group is very important in formation of nitrile oxides. Therefore, nitromethylene group limits variety of starting materials for this reaction, although used bases (DABCO, NaOH [49]) are easily available. In contrast, aldoximes are simply synthesized from aldehydes in good yields [50]. Then, nitrile oxides are prepared using chlorinating agents NCS [51], NaOCl [52] in basic media. Recently a new approach with *in situ* generated hypochlorous acid was presented as environmentally benign procedure for preparation of isoxazolines and isoxazoles [53].

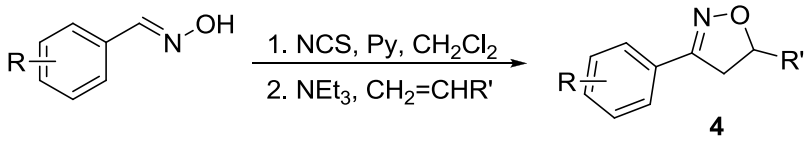
First, saturated substituents bearing Δ^2-isoxazoline **4a** was synthesized for evaluation of double bond importance in biological activity of β'-hydroxy-α,β-unsaturated ketones (Scheme 14). It was interesting to note, that this reaction gave two cyclization products: Δ^2-isoxazoline **4a** and furoxan **5a** in 43% and 40% yields, respectively. As it is known from the literature, nitrile oxides may cyclize into symmetric 1,4,2,5-dioxadiazines or 1,2,4-oxadiazole-4-oxides

[54]. But according ^{1}H and ^{13}C NMR spectra data compared with the literature data [55], the second cyclic structure was determined as furoxan **5a**.



Scheme 14.

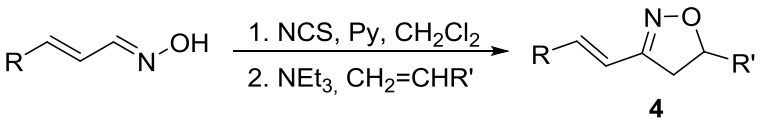
Next, in order to check an aromatic substituent influence on antiproliferative activities of Δ^2-isoxazolines, a series of 3-aryl-Δ^2-isoxazolines were synthesized from the corresponding benzaldoximes in 47 to 72 % yields (Scheme 15).



4b R= H, R'= *n*Bu;
4c R= H, R'= *t*Bu;
4d R= 4-Cl, R'= *n*Bu;
4e R= 4-Cl, R'= *t*Bu;
4f R= 4-NO_2, R'= *c*Hex;
4g R= 4-*n*Pe, R'= *n*Bu;
4h R= 4-OMe, R'= *n*Bu;
4i R= 4-OMe, R'= *t*Bu;
4j R= 4-OMe, R'= *c*Hex;
4k R= 3,4-OCH_2O, R'= *c*Hex.

Scheme 15.

And lastly, the third group of synthesized Δ^2-isoxazolines was prepared from cynamoyl- and crotonaldoximes by reactions with aliphatic alkenes in moderate yields (Scheme 16).

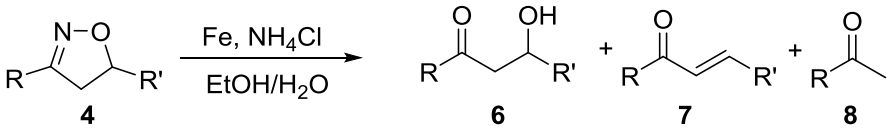


4l R= Me, R'= *n*Bu;
4m R= Me, R'= *t*Bu;
4n R= Me, R'= *c*Hex;
4o R= Ph, R'= *n*Bu;
4p R= Ph, R'= *t*Bu;
4q R=Ph, R'= *c*Hex;
4r R= 4-$MeOC_6H_4$, R'= *c*Hex.

Scheme 16.

After having the requisite isoxazoline compounds in hands, we chose Chen et al described reductive system: Fe/NH_4Cl in ethanol/water mixture [41].

Unfortunately, we found that besides the desired compounds **6**, formation of side-products **7** and **8** usually occurred (Table 1, Scheme 17). Dehydration products **7** were isolated due to formation of more stable conjugated product during heating of the reaction mixtures for prolonged times (at least for 6 hours) (Table 1, entries 5, 7, 9 – 11). An unexpected retro-aldol reaction took place during reduction of compounds having donating substituents on the aromatic ring (Table 1, entries 7 – 11). In the literature there are only few examples of retro-aldol reaction during Δ^2-isoxazoline reduction by metal carbonyl catalysts as iron pentacarbonyl [56] or molybdenum hexacarbonyl [40]. In the case of 5-cyclohexyl-3-(4-nitrophenyl)-4,5-dihydroisoxazole (**4f**), instead of reductive cleavage of the isoxazoline ring, reduction of the nitro group took place and product **4f-2** was isolated in 25 % yield (Table 1, entry 6). In all reactions the yields of β-hydroxy ketones varied from 20 to 50 %, though reduction yields of α,β-unsaturated-Δ^2-isoxazolines diminished drastically (Table 1, entries 12 – 15). Even partial reduction of the double bond was observed in the case of 5-butyl-3-(prop-1-en-1-yl)-4,5-dihydroisoxazole (**4l**) (Table 1, entry 12).



Scheme 17.

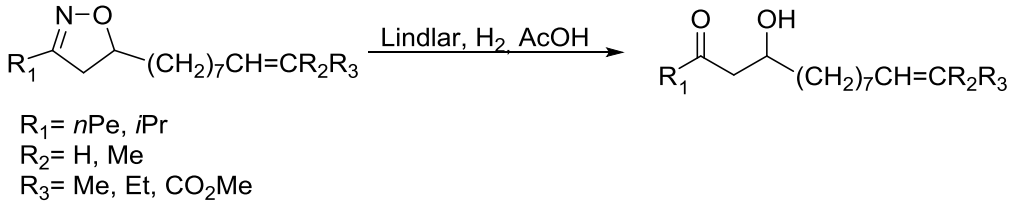
Table 1. The outcome of Δ^2-isoxazolines reduction with Fe/NH_4Cl.

Entry	Isoxazoline	R	R‘	Product (ratio 6:7:8)	Yield, %
1	**4a**	*n*Hex	*n*Bu	**6a**	50
2	**4b**	Ph	*n*Bu	**6b**	36
3	**4c**	Ph	*t*Bu	**6c**	22
4	**4d**	4-ClC_6H_4	*n*Bu	**6d**	16
5	**4e**	4-ClC_6H_4	*t*Bu	**6e, 7e** (1:1)	38
6	**4f**	4-$NO_2C_6H_4$	*c*Hex	**4f-2**[a]	25
7	**4g**	4-*n*-PeC_6H_4	*n*Bu	**6g, 7g, 8g** (9:10:3)	59
8	**4h**	4-$MeOC_6H_4$	*n*Bu	**6h, 8h** (12:7)	38
9	**4i**	4-$MeOC_6H_4$	*t*Bu	**6i, 8i** (1:1)	52
10	**4j**	4-$MeOC_6H_4$	*c*Hex	**6j, 7j, 8j** (31:37:7)	75
11	**4k**	3,4-$OCH_2OC_6H_3$	*c*Hex	**6k, 7k, 8k** (43:36:8)	87

12	**4l**	CH=CHCH$_3$	*n*Bu	**6l**	5[b]
13	**4m**	CH=CHCH$_3$	*t*Bu	-	0
14	**4o**	CH=CHPh	*n*Bu	**6o, 8o** (5:3)	32
15	**4q**	CH=CHPh	*c*Hex	**6q**	20

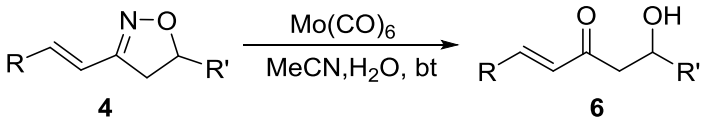
[a] The nitro group reduction product 4-(5-cyclohexyl-4,5-dihydroisoxazol-3-yl)aniline **4f-2** was isolated.
[b] Additionally, saturated β-hydroxy ketone 6-hydroxydecan-4-one (**6l-2**) was isolated in 5% yield.

From the literature review it is known that only several possible reduction systems ($Mo(CO)_6$ in MeCN or SmI_2 in dry THF) may be used for reduction of conjugated Δ^2-isoxazolines. There is also one example about use of the Lindlar catalyst in reductive cleavage of double bond having isoxazoline (Scheme 18) [57]. In order to find optimal reduction conditions for reductive cleavage of our synthesized α,β-unsaturated Δ^2-isoxazolines, we evaluated all of these methods.



Scheme 18.

All different conditions were tested on α,β-unsaturated Δ^2-isoxazoline with aliphatic substituents **4l** as reduction of these compounds was the most problematic (Table 1, entries 12, 13). During the first experiments it was found that Lindlar catalyst/H_2 in methanol did not reduce conjugated Δ^2-isoxazoline and starting material was fully recovered. Secondly, after reaction between **4l** and SmI_2 in dry THF compounds **6l** and **6l-2** (6-hydroxydecan-4-one) were isolated in 1:1 ratio in 40% yield like in previous reaction with Fe/NH_4Cl system. Moreover, 50% of starting material was recovered. The best results were obtained during reduction by $Mo(CO)_6$ in MeCN when β'-hydroxy-α,β-unsaturated ketone **6l** was isolated in 38 % yield without any trace of double bond reduction product. So, other α,β-unsaturated-Δ^2-isoxazolines were reduced with $Mo(CO)_6$/MeCN with several drops of water during reflux till full conversion of the starting material occurred (Scheme 19, Table 2).



4 **6**

Scheme 19.

Table 2. The reduction of on α,β-unsaturated Δ^2-isoxazolines with $Mo(CO)_6$.

Entry	Isoxazoline	R	R‘	Product	Yield, %
1.	**4l**	Me	*n*Bu	**6l**	38
2.	**4n**	Me	*c*Hex	**6n**	54
3.	**4p**	Ph	*t*Bu	**8p**[a]	15
4.	**4q**	Ph	*c*Hex	**6q**	38
5.	**4r**	4-$MeOC_6H_4$	*c*Hex	**6r**	29

[a] The retro aldol product (*E*)-4-phenylbut-3-en-2-one was isolated.

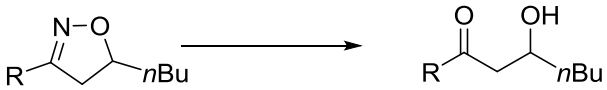
Unfortunately, this method did not significantly improve reaction yields (Table 1, entries 12 and 15 *vs* Table 2, entries 1 and 4). The reduction of Δ^2-isoxazoline **4p** led to formation of retro-aldol reaction product **8p** (Table 2, entry 3).

Then we turned our attention to the possible use of bimetallic systems for development of new, fast, economic and environmentally-friendly ways of N-O bond reduction that could be used instead of the previously tested reducing systems.

Bimetallic reductive systems such as Fe/Pd, Fe/Cu, Fe/Co, Zn/Cu, Pd/Ag, Pt/Cu, Al/Cu, etc. are known as effective catalysts mainly for dechlorination of various chlorinated hydrocarbons, and they were studied particularly for potent groundwater remediation [58]. We chose an *in situ* preparation of several inexpensive couples such as Fe/Cu, Zn/Cu, and Al/Cu and tested their reactivity towards the reductive cleavage of the isoxazolines with aliphatic (**4a**) and aromatic (**4b**) substituents (Scheme 20, Table 3).

The reductive systems Al/Cu, Zn/Cu and Fe/Cu were prepared *in situ* by adding an aqueous solution of copper (II) salts to mixtures of starting isoxazolines and the corresponding metal in methanol. No reaction was observed by TLC when we tried to use aluminum cuttings and copper (II)

sulfate (Table 3, entry 1). Addition of sodium chloride to the reaction mixture solved this problem probably by destroying the aluminum oxide layer. So the complete consumption of starting material was reached in five minutes (Table 3, entry 2). Using copper (II) chloride instead of the combination $CuSO_4$/NaCl slightly increased the yield of the product and, logically, the use of aluminum dust gave a better result in comparison to aluminum cuttings (Table 3, entries 3, 4). However, the Zn/Cu system was not so effective – the conversion of **4a** was only 25 % (Table 3, entry 5) and, moreover, the couple Fe/Cu was inactive at all (Table 3, entry 6). It should be noted that 5-butyl-3-phenyl-4,5-dihydroisoxazole (**4b**) was recovered unchanged after the treatment with Al/$CuCl_2$ or Zn/$CuCl_2$ systems (Table 3, entries 7, 8). So these experiments led to the conclusion that the Al (dust)/$CuCl_2$ system in methanol-aqueous media was the best reaction conditions for the reductive cleavage of nonconjugated isoxazolines.



4a, 4b **6a, 6b**

Scheme 20.

Table 3. Reaction conditions for the reductive cleavage of Δ^2-isoxazolines **4a,b**.

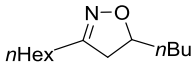
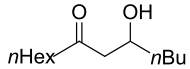
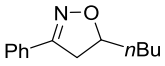
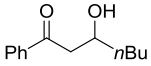
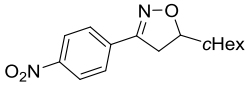
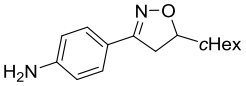
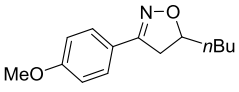
Entry	**Δ^2-Isoxazoline**	**Reaction conditions**	**Conv., %**	**Product 6 yield, %**
1.	**4a**, R= Me	Al (cuttings), $CuSO_4 \cdot 5H_2O$, MeOH-H_2O, rt	0	-
2.	**4a**	Al (cuttings), $CuSO_4 \cdot 5H_2O$, NaCl, MeOH-H_2O, rt	100	73
3.	**4a**	Al (cuttings), $CuCl_2 \cdot 2H_2O$, MeOH-H_2O, rt	100	76
4.	**4a**	Al (dust), $CuCl_2 \cdot 2H_2O$, MeOH-H_2O, rt	100	82
5.	**4a**	Zn (dust), $CuCl_2 \cdot 2H_2O$, MeOH-H_2O, rt	25[a]	18[b]
6.	**4a**	Fe, $CuCl_2 \cdot 2H_2O$, MeOH-H_2O, rt	0	-
7.	**4b**, R= Ph	Al (dust), $CuCl_2 \cdot 2H_2O$, MeOH-H_2O, rt	5[a]	-
8.	**4b**	Zn (dust), $CuCl_2 \cdot 2H_2O$, MeOH-H_2O, rt	0	-

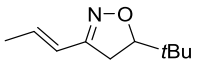
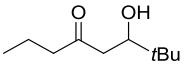
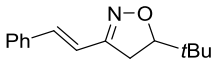
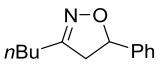
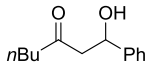
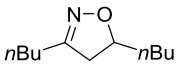
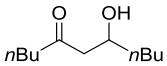
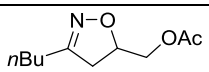
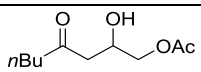
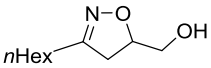
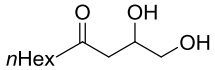
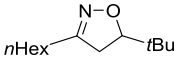
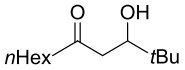
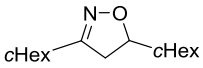
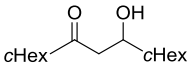
[a] Conversions determined from NMR of crude mixtures.

[b] Yield of pure product.

Encouraged by these results we decided to perform the reduction of various Δ^2-isoxazolines using this new method. The results are summarized in Table 4. All nonconjugated starting isoxazolines additionally prepared for this reaction underwent smooth reductive ring cleavage (Table 4, entries 1, 7 – 13). As it was observed earlier, the starting materials bearing aryl moiety in the 3-position of the isoxazoline ring were unreactive in these reaction conditions (Table 4, entries 2 – 4). The effect of conjugation is clearly seen from the comparison of the reduction of two isomeric compounds – 5-butyl-3-phenyl-4,5-dihydroisoxazole **4b** and 3-butyl-5-phenyl-4,5-dihydroisoxazole **4s** (Table 4, entries 2, 7). In the case of 5-cyclohexyl-3-(4-nitrophenyl)-4,5-dihydroisoxazole (**4f**), complete reduction of the nitro group was observed while the heterocyclic ring remained unchanged like in reaction with Fe/NH_4Cl (Table 4, entry 3 and Table 1, entry 6). In the case of 5-*tert*-butyl-3-(1-propenyl)-4,5-dihydroisoxazole (**4m**), the reduction of the C=C bond was also observed (Table 4, entry 5). But 5-*tert*-butyl-3-(2-phenylethenyl)-4,5-dihydroisoxazole (**4p**) remained unaffected during the reaction (Table 4, entry 6). When 5-hydroxymethyl Δ^2-isoxazoline **4v** was subjected to the reductive conditions, the reaction occurred smoothly and cleanly, as observed by TLC (Table 4, entry 10). However, the corresponding product **6v** was not stable, and about 15 % of it underwent hydroxyl elimination and subsequent condensation to form 2-hexylfuran during purification procedure.

Table 4. Data on the synthesis of β-hydroxy ketones by the $Al/CuCl_2 \cdot 2H_2O$, MeOH-H_2O.

Entry	Starting material	Product	Yield, %
1.	 **4a**	 **6a**	84
2.	 **4b**	 **6b**	14[a]
3.	 **4f**	 **4f-2**	80
4.	 **4h**	No reaction	-

5.	 **4m**	 **6m-2**	71
6.	 **4p**	No reaction	-
7.	 **4s**	 **6s**	72
8.	 **4t**	 **6t**	52
9.	 **4u**	 **6u**	76
10.	 **4v**	 **6v**	82[b]
11.	 **4w**	 **6w**	74[c]
13.	 **4x**	 **6x**	89

[a] Incomplete conversion of starting material.

[b] The product was unstable and 15 % of it turned into 2-hexylfurane during workup.

[c] The product was unstable and 20 % of it turned into 2,2-dimethyl-3-undec-5-ene.

SUMMARY OF THE CHAPTER I

Synthesis of β'-hydroxy-α,β-unsaturated ketones are usually performed in several step manner, though there are some methods preparing desired compounds in one step. First of all we tried one step condensation reaction of two aliphatic aldehydes and pent-4-yn-2-ol in presence of iron (III) chloride forming β'-hydroxy-α,β-unsaturated ketones **1**. Unfortunately, this reaction gave a lot of side products next to the desired compounds. Several of them were identified as aldehyde aldol condensation products. Moreover, condensation product of pent-4-yn-2-ol and acetaldehyde formed when aldehydes with longer chains were used. The use of slightly wet $FeCl_3$ gave unprecedented products, 2,3-dihydro-4*H*-pyran-4-ones **3**. Unfortunately, yields

of products **3** were very poor and we could not find optimal conditions for preparation of none of the above compounds.

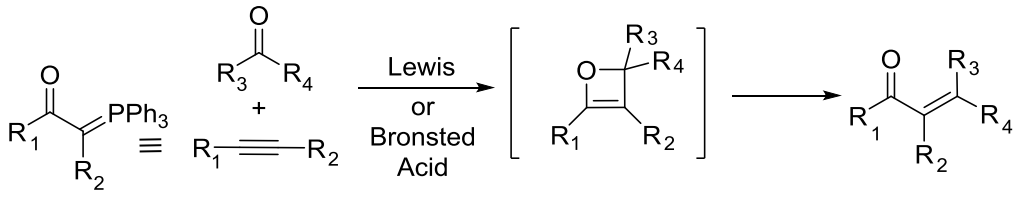
Reduction of simple α,β-unsaturated Δ^2-isoxazolines was usually complicated. Conjugated isoxazolines with aliphatic substituents in the most cases were reduced to saturated β-hydroxy ketones. Aromatic substituents having substrates were more stable, though water elimination was often observed. The reduction using Fe/NH_4Cl could be used in various substitution patterns of isoxazolines in moderate yields; also retro-aldol reactions often took place. The optimal results in reduction of α,β-unsaturated Δ^2-isoxazolines were reached using $Mo(CO)_6$. The new reduction using $Al/CuCl_2$ provided a facile, economical, and efficient protocol for the preparation of β-hydroxy ketones from nonconjugated Δ^2-isoxazolines. Moreover, this was the first example of using an *in situ* prepared aluminum/copper couple in organic synthesis. Advantages of the presented method included low cost, neutral media, and short reaction times (up to 10 min).

Chapter II

INVESTIGATION OF ALKYNE-CARBONYL METATHESIS REACTION BETWEEN ALKYNES AND ALDEHYDES FOR THE SYNTHESIS OF α-SUBSTITUTED α,β-UNSATURATED KETONES

Introduction

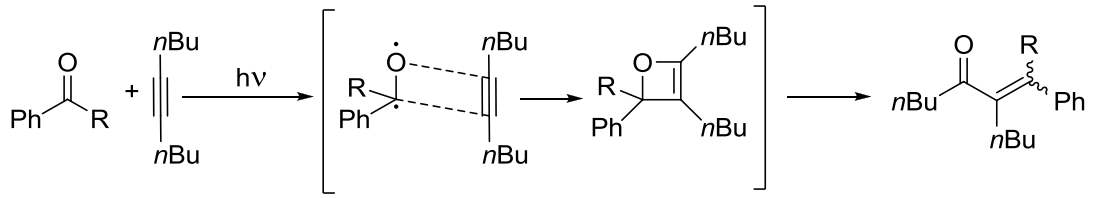
The synthetic approaches towards α,β-unsaturated ketones were briefly discussed in the introduction section. One of the best options for the synthesis of target compounds arose from an atom economic metathesis reaction between aldehydes and alkynes forming double bond and carbonyl group simultaneously. The metathesis reaction generally proceeds via formal [2+2] cycloaddition and cycloreversion pathways. Moreover, carbonyl olefination with alkynes mediated by Lewis and Bronsted acids has emerged as an alternative to the conventional Wittig olefination. The reactions between alkynes and carbonyl compounds are expected to proceed *via* intermediacy of four-membered oxete rings with following electrocyclic opening to enones (Scheme 21). Alkyne functionality in this reaction serves as a synthetic equivalent to stabilized phosphonium ylide in the Wittig reaction. However, in contrast to the Wittig reaction, this process does not afford any by-products as all atoms of the two reactants are incorporated into one product. Furthermore, the diastereoselectivity of the process would be controlled by electrocyclic opening of the oxetene intermediate forming energetically more stable *E* isomer.



Scheme 21.

In 1956, G. Buchi with co-workers reported on synthesis of unsaturated ketones when mixtures of benzaldehyde and 5-decyne or acetophenone and 5-

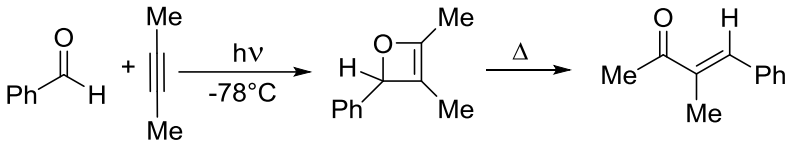
decyne were irradiated with mercury resonance arc at 40°C for 96 or 84 hours correspondingly (Scheme 22) [59]. Nevertheless products were isolated in low yields; this report represented the first example of a reaction between an alkyne and a carbonyl compound to give an olefination product. The reaction was proposed to proceed *via* π-π*excitation of the carbonyl group, followed by [2+2] cycloaddition. Electrocyclic ring opening of the oxetene afforded mixtures of *E*- and *Z*-enones.



R = H, Me

Scheme 22.

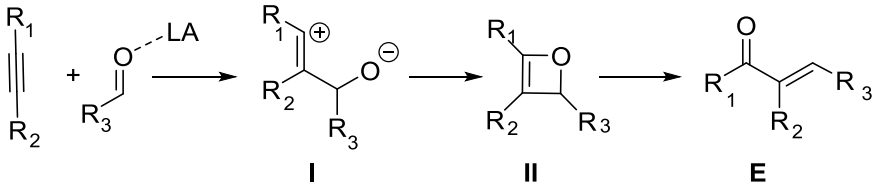
Although the generation of an oxete ring was accepted by others, no experimental evidence was presented until 1973, when L.E. Friedrich with J.D. Bower reported the detection of oxetene at low temperature by NMR spectroscopy [60] (Scheme 23). First of all, reaction mixture of benzaldehyde and 2-butyne was irradiated at room temperature affording a mixture of *E*- and *Z*-enones (ratio 1:2). A similar irradiation at –78 °C, followed by NMR analysis at room temperature, showed the presence of *E* isomer. After several independent experiments the conclusion was that enone was not photochemically generated at –78 °C, but rather was stereospecifically formed from oxetene in a thermal process on warming. In an attempt to actually observe the intermediate oxetene, after irradiation of solution at –78 °C most of the solvent and excess of 2-butyne was removed at –45 °C under reduced pressure. Following ^{1}H NMR analysis at the same temperature revealed characteristic peaks of oxetene, which disappeared on warming and did not reappear on cooling.



Scheme 23.

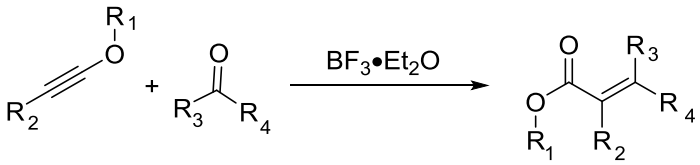
Since the first report in 1956, many photochemical reactions between alkynes and aldehydes have been reported. However, due to limited efficiency, scope and diastereoselectivity, these methods did not find any broad application.

The first work on Lewis acid promoted olefination of carbonyl compounds with alkynes was reported by Vieregge and co-workers in 1959 [61]. The authors proposed a mechanism that involved three steps: 1) nucleophilic attack of the alkyne to the LA activated aldehyde with formation of ion-pair intermediate **I**, 2) electrocyclic ring closure to give an oxete intermediate **II**, 3) cycloreversion to the corresponding α,β-unsaturated ketone **E** (Scheme 24).



Scheme 24.

Later their group presented a series of Lewis acid promoted reactions of activated alkoxy alkynes with range of carbonyl compounds [62]. These transformations typically required the presence of stoichiometric amount of a strong LA, for example boron trifluoride diethyl etherate. Under these conditions ethoxyacetylene and disubstituted acetylenes were able to react not only with aldehydes and ketones, but also with esters and amides (Scheme 25). The reactions typically displayed high E-diastereoselectivity, which would be controlled by the ring opening of the initially produced oxetene.

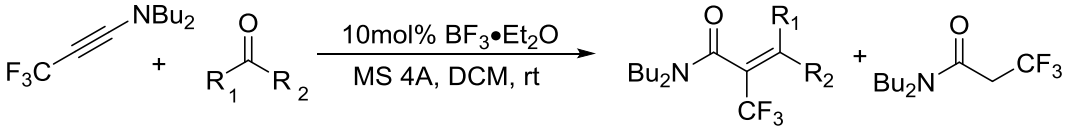


R_1 = Me, Et, *i*Pr, CH_2*t*Bu
R_2 = H, Me, Pr, *i*Pr, *n*Bu, *n*Pe

R_3 = H, R_4 = Me, Et, Ph, p-$NO_2C_6H_4$, p-$MeOC_6H_4$, CH=CH_2, CH=CHMe, CH=CHPh, OEt, CCl_3, NMe_2
R_3 = Me, R_4 = Et, *i*Bu, Ph, OEt, COMe, CH_2CO_2Et
R_3 = R_4 = Me, Et, -$(CH_2)_n$-, n = 4, 5, 6

Scheme 25.

Another group of activated alkynes *N*,*N*-dialkyl(3,3,3-trifluoro-1-propynyl)amines reacted smoothly with a variety of aldehydes or ketones in the presence of a catalytic amount of BF_3·Et_2O and molecular sieves 4Å at ambient temperature to produce the corresponding α-(trifluoromethyl)-α,β-unsaturated amides in good to excellent yields with high *Z*-stereoselectivity (Scheme 26) [63]. Addition of water to the triple bond was also observed in several cases.



68 - 97 % 2 - 23 %

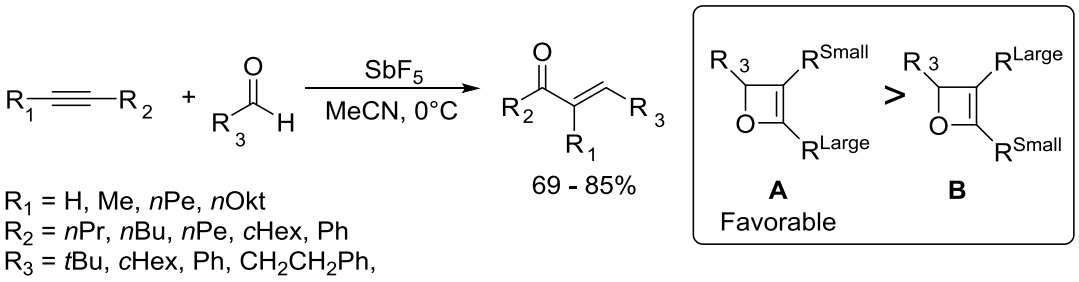
R_1 = H, R_2 = nPr, iPr, tBu, nHex, cHex, CMe=CH_2, CH=CHMe, CH=CHPh, CF=CHPh Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-ClC_6H_4, 2-furyl, 2-thienyl, 1-naphthyl
R_1 = R_2 = Me, Et, -$(CH_2)_5$-
R_1 = Me, R_2 = Ph

Scheme 26.

The reaction mechanism was supported by Middleton in 1965. The corresponding stable oxete intermediate was isolated from the reaction between ethoxyacetylene and hexafluoroacetone in low temperature [64]. Moreover, it was shown that the isolated oxete underwent cycloreversion to form the final unsaturated ester. The plausibility of the suggested three-step mechanism was also confirmed by computational methods in 2001 [65], albeit only for formation of methyl acrylate from formaldehyde and methoxyacetylene at the HF/6-31G* and B3LYP/6-31G* level of theory. The

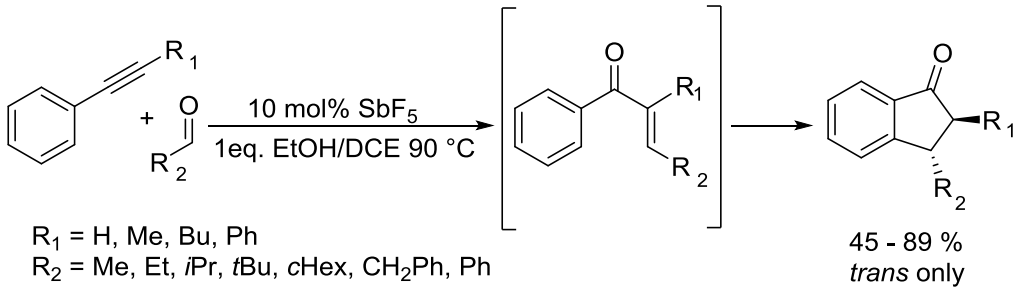
authors provided arguments in favor of a pathway that involved the formation of the C–C bond in the oxete intermediate.

In 1995, the Yamaguchi group reported coupling between nonactivated aliphatic alkynes and aliphatic aldehydes promoted with SbF_5 in acetonitrile [66] (Scheme 27). The *E*-configuration of compounds was determined by the measurement of coupling constant and nOe experiments. Authors also suggested regioselectivity in the enone synthesis as preferential formation of oxete **A** over **B**.



Scheme 27.

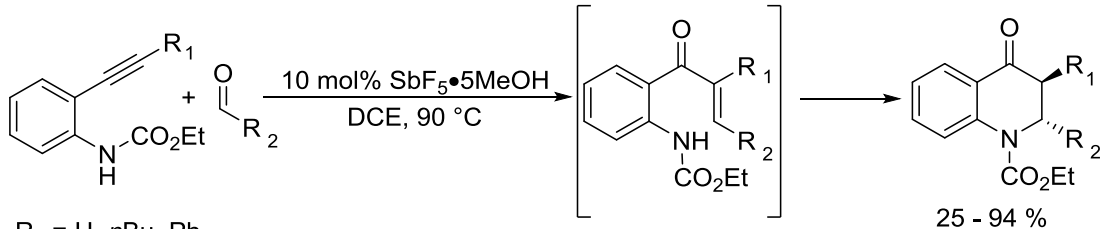
The same catalyst was also used by the Saito and Hanzawa work group. They applied SbF_5-alcohol complex to catalyze synthesis of indanones through alkyne-carbonyl metathesis and the subsequent Nazarov cyclization [67] (Scheme 28).



Scheme 28.

Next step of their work was synthesis of 2,3-disubstituted dihydroquinolinones with high *trans* selectivity through metathesis of *o*-alkynylaniline derivatives and aldehydes [68] (Scheme 29). Saito et al. showed that this type of reactions could be promoted only by oxophilic Lewis acids (TfOH, $BF_3{\cdot}Et_2O$, SbF_5, $AgSbF_6$, $In(OTf)_3$) and carbophilic ones ($PtCl_2$, $PtCl_4$, $AuCl_3$) were not

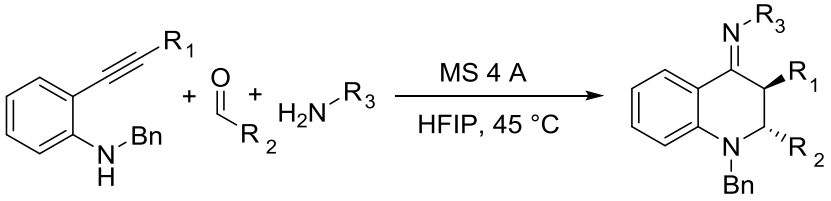
effective. The best ratio results and yields were reached with $SbF_5 \cdot 5MeOH$. It should be noted that only 2-alkynylphenylcarbamates gave quantitative results and other amine compounds (-NH_2, -NHBn, -NHTs) gave complex mixtures. In both cases intermediate α,β-unsaturated ketone was isolated performing reactions at lower temperature.



R_1 = H, *n*Bu, Ph
R_2 = *t*Bu, *n*Hex, *c*Hex, Ph, 4-$NO_2C_6H_4$

Scheme 29.

After a year Saito and Hanzawa managed to synthesize *trans*-2,3-disubstituted 2,3-dihydro-4-iminoquinolines in a complete *trans*-selective manner *via* three-component alkyne-imine metathesis without any catalyst [69] (Scheme 30). It is important to note, that their new procedure required use of hexafluoroisopropanol (HFIP) as solvent, for better activation of the imine. In the reaction with 4-nitrobenzaldehyde or anilines bearing a strong electron-withdrawing group (NO_2 or CN) the desired product did not form and only addition of water to the triple bond was observed.

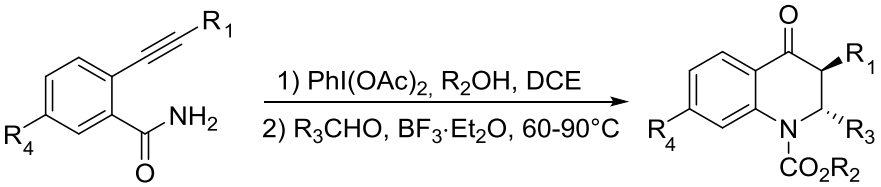


R_1 = *n*Bu, Ph
R_2 = Ph, 4-MeC_6H_4, 4-FC_6H_4, 4-$MeOC_6H_4$, 3-$MeOC_6H_4$, 2-$MeOC_6H_4$
R_3 = Ph, 4-MeC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-$MeOC_6H_4$

Scheme 30.

Another group of scientists also demonstrated synthesis of *trans*-2,3-disubstituted 2,3-dihydro-4-quinolinones through tandem Hofmann-type rearrangement of 2-alkynylbenzamides, nucleophilic addition of alcohols to the isocyanate intermediates, intermolecular alkyne – carbonyl metathesis, and intramolecular aminocyclization of nitrogen of carbamates to the α,β-

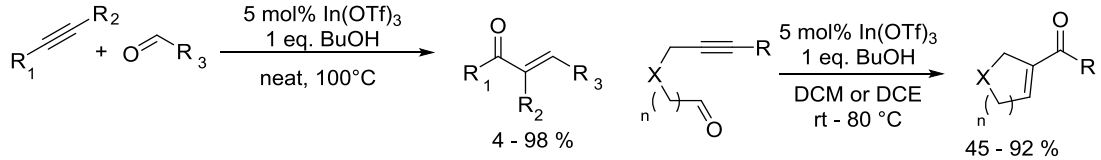
unsaturated ketones [70] (Scheme 31). It was noticed that electron-withdrawing nitro group in 2-alkynylbenzamide slowed [2+2] addition reaction and only Hofmann-type rearrangement product was isolated. Moreover, 4-nitro and 4-cyanobenzaldehydes formed *E*-α,β-unsaturated ketones in optimal conditions, fortunately higher reaction temperature lead to desired *trans* – products of the same reactions.



R_1 = H, *n*Bu, Ph
R_2 = Me, Et, Bn
R_3 = *n*Hex, *c*Hex, Ph, 4-MeC_6H_4, 3-MeC_6H_4, 2-MeC_6H_4, 4-FC_6H_4, 4-$MeOC_6H_4$, 4-$NO_2C_6H_4$, 4-NCC_6H_4
R_4 = H, F, OMe

Scheme 31.

$In(OTf)_3$ was also used as catalyst for metathesis reaction. Nevertheless first examples resulted in low product yields [18], the Hosomi group reported about crucial role of an alcohol additive for improvement of the yield (Scheme 32) [71]. However, reaction yield drastically diminished when phenylacetylene having an electron withdrawing $–CF_3$ group on phenyl ring was used.

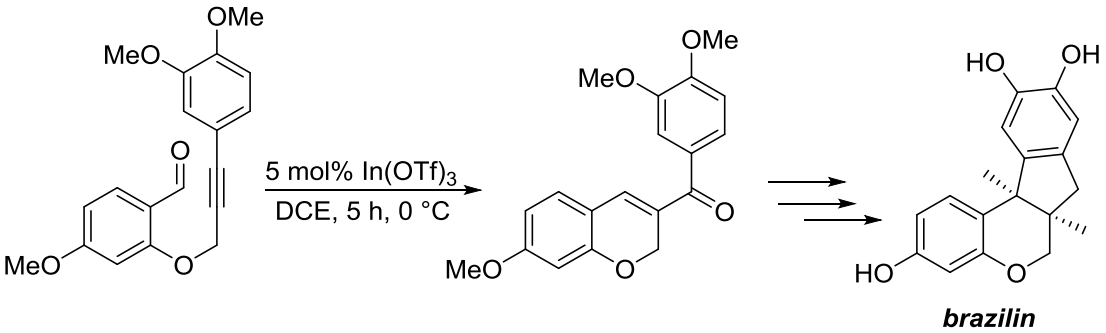


R_1 = Ph, 4-$MeOC_6H_4$, 4-MeC_6H_4, 2-MeC_6H_4, 4-$F_3CC_6H_4$
R_2 = H, Me
R_3 = cHex, Ph, 4-$MeOC_6H_4$, 4-BrC_6H_4

n = 1 - 3
X = O, CH_2
R = *n*Hex, Ph, 4-$MeOC_6H_4$, CH=CHPh

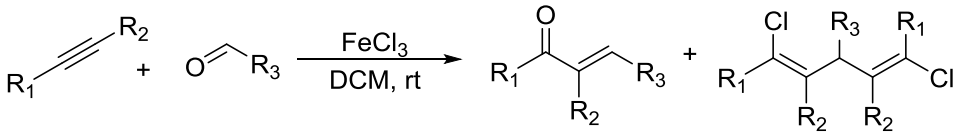
Scheme 32.

Indium (III) triflate without any additives was successfully used in the total synthesis of brazilin (Scheme 33) [72]. The screening of the optimal conditions for intramolecular metathesis reaction revealed that the best yield (97 %) was reached using 5 mol% of $In(OTf)_3$ in DCE at 0 °C temperature.



Scheme 32.

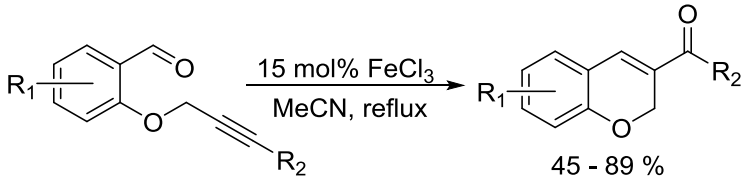
Iron (III) chloride was reported in 2005 as a cheap and environmentally friendly initiator of metathesis reaction [31]. Authors demonstrated olefination between various terminal and disubstituted alkynes with aliphatic aldehydes. Terminal alkynes formed not only α,β-unsaturated ketones but also *E*,*Z*-1,5-dihalo-1,4-dienes (Scheme 34).



R_1 = *n*Bu, *n*Pe, Bn, Ph
R_2 = H, Me, *n*Bu, CH_2OH, CH_2OAc, $CH_2CH{=}CH_2$, Ph
R_3 = *i*Bu, *n*Hex, *c*Hex, Ph

Scheme 34.

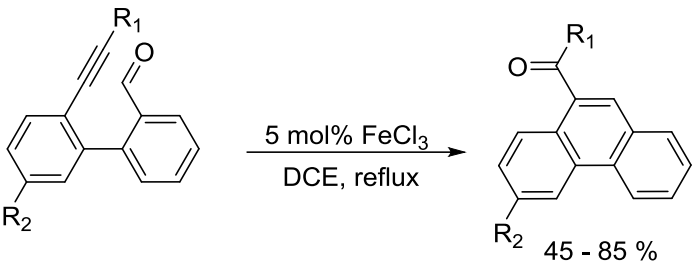
The Jana group used $FeCl_3$ for intramolecular metathesis synthesizing various hetero- and carbocyclic compounds. First of all, they reported on synthesis of functionalized 2*H*-chromenes by refluxing substrate with 15 mol% of Lewis acid in acetonitrile [73] (Scheme 35). Reaction yields diminished about 10 – 20 % during reactions with aliphatic substituents next to the triple bond and no reaction was observed with terminal alkynes.



R_1 = H, 5-Cl, 3,5-diCl, 5-Br, 3-OMe, 5-Ph
R_2 = H, Me, nPr, Ph, 4-FC_6H_4, 4-BrC_6H_4, 4-$MeOC_6H_4$

Scheme 35.

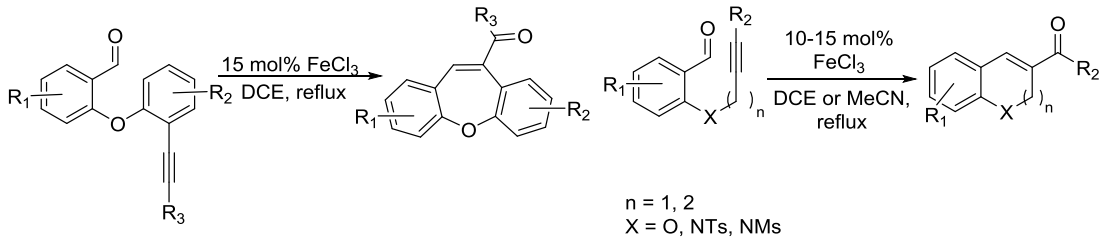
Next work of the same group represented synthesis of substituted phenanthrenes [74] (Scheme 36). Substituents in biphenyls did not show any influence on reaction yields. Aliphatic substituents next to the triple bond slightly diminished reaction yields compared with aromatic substituents. Authors also demonstrated coupling between alkyne and ketone in good yield using 10 mol% of $FeCl_3$ instead of 5 mol%.



R_1 = nHex, cHex, CH_2CH_2OMe, Ph, 4-MeC_6H_4, 4-ClC_6H_4, 3-$NO_2C_6H_4$, 6-MeO-2-naphthyl
R_2 = H, Me, OMe, F, Cl, CO_2Et

Scheme 36.

In more recent works the Jana group reported on intramolecular alkyne-carbonyl metathesis reaction forming dibenzo[b,f]oxepines and benzo[b]oxepines [75] and 1,2-dihydroquinolines and dihydrobenzo[b]azepines [76] (Scheme 37).



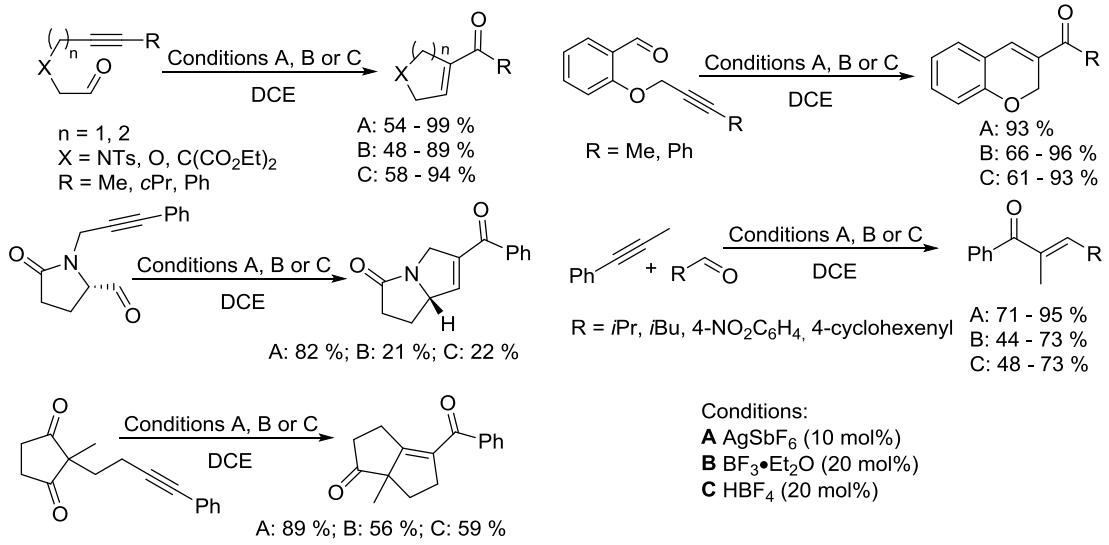
R_1 = H,4-C≡CPh, 5-NO_2, 6-OMe
R_2 = H, 4-Me, 4-OMe
R_3 = Ph, 4-ClC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 6-MeO-2-naphthyl

n = 1, 2
X = O, NTs, NMs
R_1 = H, 3,5-diCl, 3-OMe, 5-Br, 5-Cl
R_2 = Me, Pr, Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-ClC_6H_4, 3-BrC_6H_4, 4-$EtO_2CC_6H_4$, 4-$MeO_2CC_6H_4$, 3-thienyl

Scheme 37.

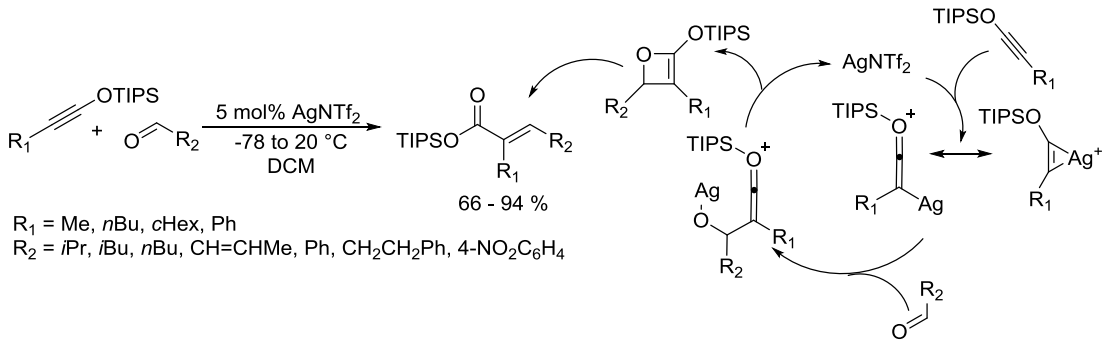
Silver and gold compounds are another group of catalysts used in alkyne-carbonyl system. This is a class of carbophilic activators. One of the first uses of Ag salt was reported by J. U. Rhee and M. J. Krische. They compared catalytic properties of newly presented cationic silver ($AgSbF_6$) with corresponding Bronsted (HBF_4) and Lewis ($BF_3{\cdot}Et_2O$) acids in intra- and

intermolecular alkyne-carbonyl metathesis reactions [77]. ^{13}C NMR spectroscopic analysis of an equimolar mixture of 1-phenylpropyne and isobutyraldehyde revealed a substantial upfield shift of the alkyne carbon signals upon addition of $AgSbF_6$, while signals corresponding to isobutyraldehyde exhibited a negligible change. Though product formed as in "oxophilic" Lewis acid catalyzed reaction, spectroscopic analysis showed an alternative catalytic mechanism potentially promoted through the use of a "carbophilic" Lewis acid in formation of an oxete intermediate. In all demonstrated cases only *E*-trisubstituted enones formed in good to moderate yields using all catalytic systems. Newly presented $AgSbF_6$-catalyzed process was moderately more efficient in certain cases, especially in intermolecular reactions and forming aliphatic bicycles (Scheme 38).



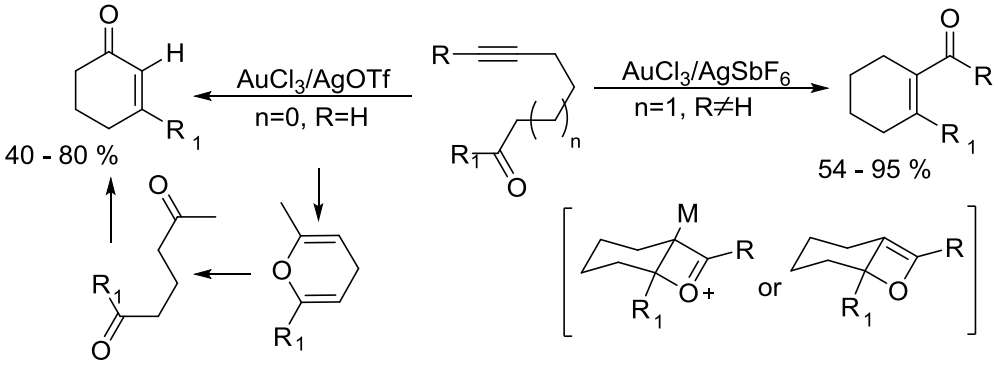
Scheme 38.

Different silver salt ($AgNTf_2$) was used as a catalyst in reactions between aldehydes and siloxyalkynes [78] (Scheme 39). While on one hand an olefination reaction using siloxyalkynes having methyl- and butyl- substituents remained in high diastereoselectivity; on the other hand, poor diastereoselectivity was reached using cyclohexyl- and phenyl- substituted siloxyalkynes. Authors also proposed reaction mechanism *via* activation of the triple bond.



Scheme 39.

T. Jin and Y. Yamamoto found conditions for intramolecular reaction between ketones and alkynes catalyzed with Ag/Au mixture [79]. The outcome of reaction depended on starting substrate; authors found that terminal alkynes reacted in different way than internal ones (Scheme 40).



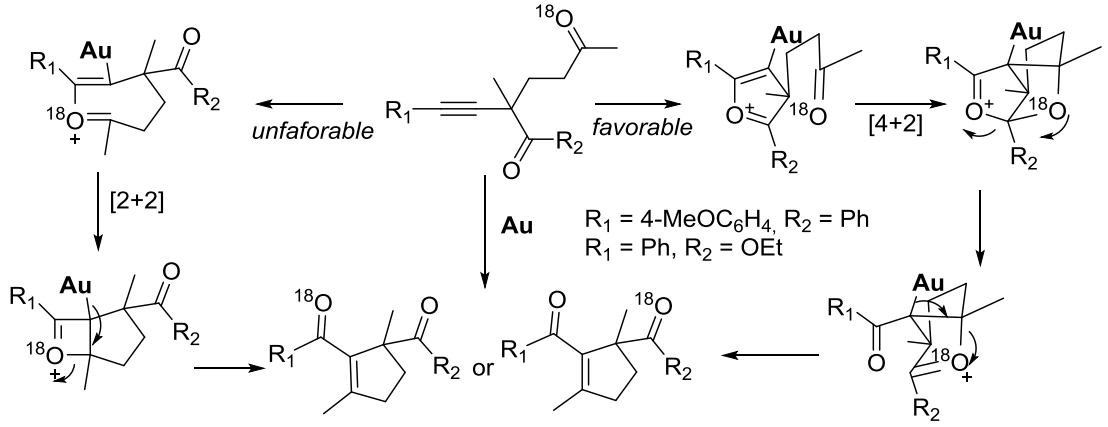
Scheme 40.

Hammond and co-workers found that gold-catalyzed oxygen transfer reaction proceeded very smoothly when using 2-alkynyl-1,5-diketones or 2-alkynyl-5-ketoesters as substrates under very mild conditions (Scheme 41) [80]. Indeed, this reaction completed in 5 minutes at room temperature to give the five-membered cyclic enones cleanly in good to excellent yields. The large reactivity difference between similar substrates presented by other authors [81] prompted the Hammond group to propose an alternative [4+2] mechanism for this transformation, rather than the previously proposed and well-accepted [2+2] pathway for oxygen transfer reactions.

R_1 = Me, *i*Pr, *t*Bu, *n*Hex, CH_2cHex, Bn, Ph, 4-$MeOC_6H_4$, 4-ClC_6H_4
R_2 = Me, Bn
R_3 = Ph, Me, OEt
R_4 = Me, Et, Ph

Scheme 41.

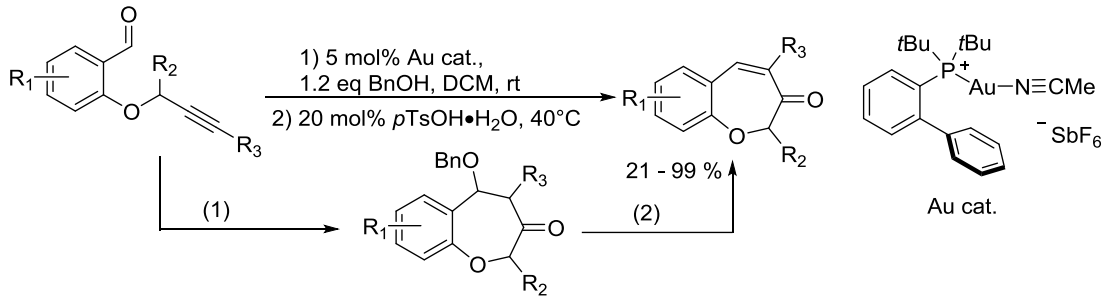
An isotopic labeling experiment was designed to elucidate the pathway responsible for the gold-catalyzed intramolecular oxygen transfer of both substrates. By introducing an ^{18}O atom into one of the carbonyls of the starting material, and using the ^{13}C NMR spectra of the substrate and product to locate the ^{18}O atom, the authors could elucidate the more favorable mechanistic pathway (Scheme 42). The discovery of a [4+2] cycloaddition of a furanium intermediate to a carbonyl group was further verified by quantum chemical calculations.



Scheme 42.

Chan and co-workers developed a gold-catalyzed tandem intramolecular rearrangement of 2-(prop-2-ynyloxy)benzaldehydes to benzo[*b*]oxepin-3(2*H*)-ones with good regioselectivity (Scheme 43) [82]. This transformation was effectively promoted by the addition of benzyl alcohol and the sequential addition of 4-toluenesulfonic acid. However, in the absence of 4-toluenesulfonic acid, benzyl ether was isolated as the major product. This

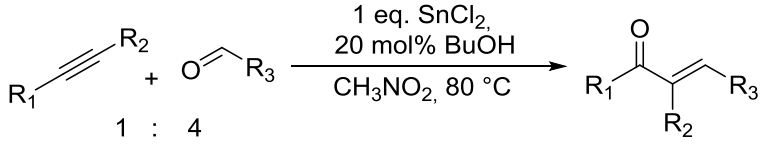
compound was considered to be an intermediate in the reaction and moreover, the isolated ether could be transformed into the final product under the mediation of 4-toluenesulfonic acid.



R_1 = H, 3-Cl, 3-F, 3-*t*Bu, 3-Ph, 3-OMe, 3-Me, 4-Me, 5-Me, 3,5-diCl, 3,5-dIl, 3,5-diF, 3,5-di*t*Bu, 3,5-diNO_2, 3,5-diBr
R_2 = H, Me
R_3 = H, Me, Et

Scheme 43.

Masuyama with co-workers used weak Lewis acid $SnCl_2$ with alcohol for coupling aldehydes and alkynes to form *E*-α,β-unsaturated ketones (Scheme 44) [83]. According to accomplished experiments with labeled hydrogen isotopes authors presumed that the coupling reactions between alkynes and aldehydes in the presence of tin (II) chloride proceeded *via* nucleophilic addition of the alkynes to aldehydes. In fact, the actual role of butanol was not exactly determined.

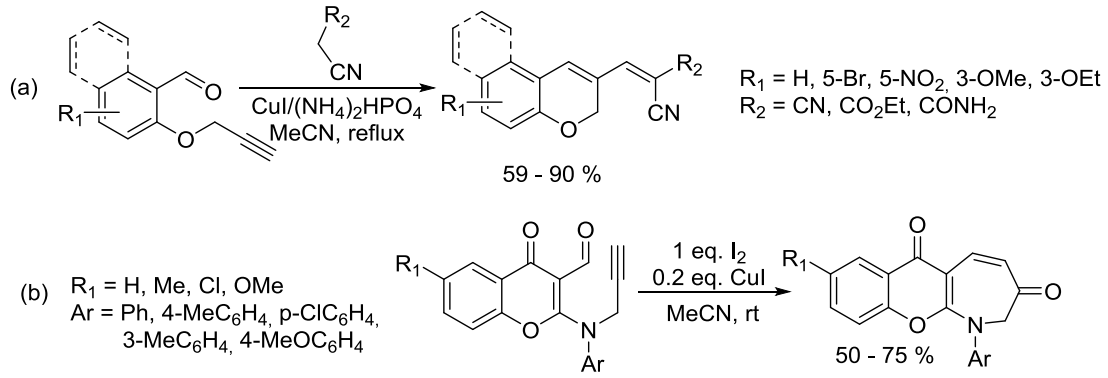


R_1 = Ph, 4-MeC_6H_4, 4-FC_6H_4, nHex
R_2 = H, Me, Pr
R_3 = cHex, Ph, 2-ClC_6H_4, 3-BrC_6H_4, 4-MeC_6H_4, 4-MeOC_6H_4, 4-FC_6H_4, 4-NCC_6H_4, 4-$NO_2C_6H_4$

Scheme 44.

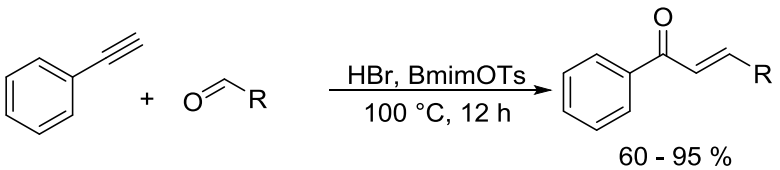
Recently two different scientist groups reported on an intramolecular olefination of terminal alkynes with aldehydes using CuI. Interestingly, these two groups reported formation of different size of cycles, though tested systems structurally were very similar. Firstly, Singh with co-workers reported on formation of 2*H*-chromen-3-yl derivatives *via* CuI/$(NH_4)_2HPO_4$ catalyzed reaction of *O*-propargyl salicylaldehydes (Scheme 45, a) [84]. Authors

separated alkyne-carbonyl metathesis product and proposed a plausible mechanism including formation of 2*H*-chromene-3-carbaldehyde and the following Knoevenagel condensation. Later, Bandyopadhyay with co-workers reported on the synthesis of chromeno[2,3-*b*]azepinones by cyclization of 2-(*N*-aryl-*N*-prop-2-ynyl)aminochromone-3-carbaldehydes catalyzed by I_2/CuI system (Scheme 45, b) [85]. They proposed that I_2 and CuI activated both the carbonyl and alkyne components and mediated the alkyne-carbonyl metathesis. This catalytic system could be used only with terminal alkynes forming seven-membered rings in contrast to previous described work.



Scheme 45.

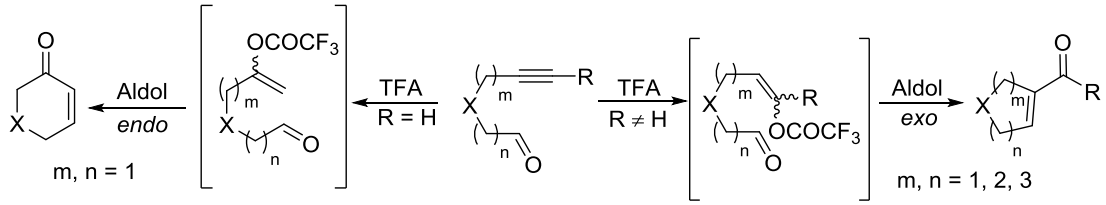
The alkyne-carbonyl metathesis reaction could be also mediated by Bronsted acids. The reaction between phenylacetylenes and aldehydes catalyzed by HBr in ionic liquid 1-butyl-3-methyl-1*H*-imidazolium 4-methylbenzenesulfonate (BmimOTs) represented the first example of this transformation (Scheme 46) [86]. It should be stated that aliphatic acetylenes or diphenylacetylene were unreactive under these conditions. Authors proposed mechanism consisting of addition of hydrogen bromide to the triple bond, followed by hydration and aldol-type condensation process.



R = Ph, 4-MeC_6H_4, 4-ClC_6H_4, 4-$NO_2C_6H_4$, 2-ClC_6H_4, 2-$MeOC_6H_4$, 3-$MeOC_6H_4$, 4-BrC_6H_4, CH_2CH_2Ph

Scheme 46.

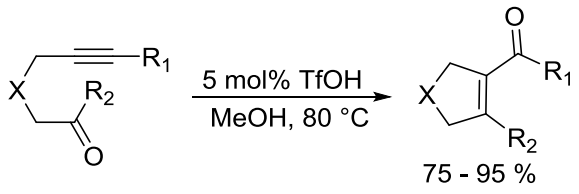
Very similar Bronsted acid mediated intramolecular reaction approach to the formation of cyclic enones was reported by Saa and co-workers. This group investigated carbocyclizations considered as tandem alkyne hydration/aldol condensation processes, where the efficient TFA-promoted *exo* carbocyclizations of nonterminal 5-, 6-, and 7-alkynals and *endo* carbocyclizations of terminal 5-alkynals gave cyclic enones in good to excellent yields (Scheme 47) [87].



X = CH_2, $C(CO_2Me)_2$, NTs
R = H, Me, Et, *n*Bu, *n*Pe, *n*Okt, Ph

Scheme 47.

Yamamoto and co-workers also attempted to utilize their protocol to build five-membered cyclic enones [88]. After optimizing the reaction conditions, the authors found that TfOH was the best catalyst for this oxygen transfer reaction in methanol (Scheme 48) as in their previous work the best conditions were reached using metal catalysts [79].



X = CHPh, $C(CO_2Me)_2$
R_1 = Ph, 4-MeC_6H_4, 4-ClC_6H_4, 2-naphthyl, 2-thiophenyl, 2-furanyl
R_2 = Me, *i*Pr

Scheme 48.

In conclusion, the alkyne-carbonyl metathesis reaction can be mediated by either Lewis or Bronsted acid and despite the fact that demonstrated mechanisms are different, these reactions result in the same product with high *E*-stereoselectivity. This synthetic approach can be equally applied to intra-

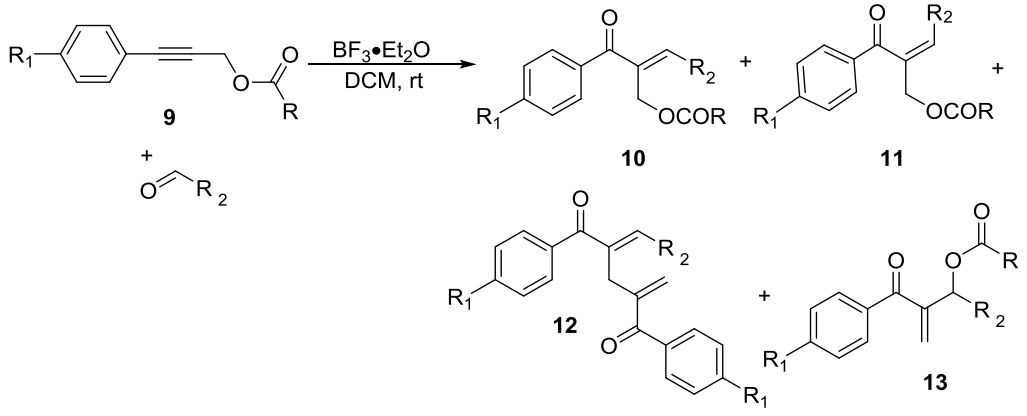
and intermolecular reactions. Oxophilic Lewis acids usually are used in reactions with heteroatom activated triple bond or arene-substituted alkynes. Carbophilic Lewis acids are combined with a bigger variety of acetylenes, though the use of the certain LA depends on substitution pattern of the triple bond. In the most cases, alkyne-carbonyl metathesis reactions are given with aldehydes, but also there are few examples of using ketones in these reactions.

II.1 Alkyne-Carbonyl Metathesis Reactions Between 3-Arylprop-2-ynyl Carboxylates and Aldehydes

First of all we prepared the starting 3-arylprop-2-ynyl carboxylates **9** by means of the classical Sonogashira coupling [89] between aryliodides and propargyl acetates or benzoates. Then we tested their reactivity toward the Lewis acid catalyzed coupling reaction with aldehydes. Several Lewis acids such as $BF_3{\cdot}Et_2O$, $FeCl_3$, $AlCl_3$, $AgSbF_6$, SbF_5, $AuCl_3$, AgOTf, $AgOCOCF_3$, different solvents (DCM, DCE, CH_3CN, THF, CH_3NO_2), and different reaction temperatures were examined. It was found that carbophilic Lewis acids were inactive and only oxophilic ones initiated reactions. Using $FeCl_3$ (Table 5, entries 1 – 5), nucleophilic exchange reaction of acetate group to chlorine occurred in several cases (Table 5, entries 1, 3) and the presence of moisture resulted in very low product yields (compounds **10ab**, **10ad**). Using SbF_5, reaction was very fast and exothermic and resulted in low yields. The self-condensation of aliphatic aldehyde as main reaction was obtained using $AlCl_3$. Reaction rate decreased in acetonitrile and any reaction did not take place in THF using both aliphatic and aromatic aldehydes. Good results were obtained in nitromethane, but unfortunately, an undesired condensation of benzaldehydes with solvent proceeded (Table 5, entry 11). After this brief search of the most suitable reaction conditions, we came to conclusion that 1 equivalent of $BF_3{\cdot}Et_2O$ in dichloromethane at rt gave the best results.

We became deeply intrigued by the fact, that reactions between 3-arylprop-2-ynyl carboxylates and aldehydes were not so predictable and usually several

possible products **10** – **13** were obtained. The data for the reactions between selected substrates under the optimal conditions (unless marked otherwise) are summarized in Table 5 (Scheme 49). It should be noted that the rate of the reactions strongly depended on the substituents on the arene moiety of 3-arylprop-2-ynyl carboxylates **9**. Thus, the reaction of unsubstituted 3-phenylprop-2-ynyl carboxylates **9a,b** with various aldehydes generally required one to several days for full conversion of the starting materials (Table 5, entries 1 – 28). Unfortunately, introduction of an electron-withdrawing chloro or nitro group into the 3-arylprop-2-ynyl carboxylate structure (compounds **9c,d**) deactivated the starting material toward coupling with aldehydes (entries 29 – 35). In the 3-(4-chlorophenyl)prop-2-ynyl acetate **9c** case reaction time prolonged to minimum 5 days (Table 5, entries 29 – 31) and with the 3-(4-nitrophenyl)prop-2-ynyl benzoate **9d** the starting material was recovered after the workup of reaction mixtures. On the other hand, the presence of an electron-donating methoxy group in 3-arylprop-2-ynyl carboxylates (**9e,f**) shortened the reaction time up to 1 hour (Table 5, entries 36 – 49).



Scheme 49.

Table 5. The outcome of reactions between 3-arylprop-2-ynyl carboxylates **9** and aldehydes.

Entry	Alkyne	Aldehyde R_2	Reaction time	Products	Ratio 10:11:12:13	Overall yield, %
1.	**9a:** R_1=H, R= Me	Me	30 min[a]	**10aa, 10ja**[b]	1:0:0:0	31
2.	**9a**	*n*Pr	10 min[a]	**10ab**	1:0:0:0	7
3.	**9a**	*n*Bu	15 min[a]	**10ac, 10jc**[c]	1:0:0:0	25
4.	**9a**	*n*Hp	30 min[a]	**10ad**	1:0:0:0	6
5.	**9a**	$C_{15}H_{31}$	80 min[a]	**10ae**	1:0:0:0	37

6.	**9a**	*c*Hex	24 h	**10af**	1:0:0:0	49
7.	**9a**	$CHEt_2$	72 h	**10ag**	1:0:0:0	39
8.	**9a**	Ph	18 h[d]	**10ah, 11ah, 12ah**	3:1:3:0	26
9.	**9a**	2-FC_6H_4	6 h[d]	**10ai, 11ai, 12ai**	3:1:1.1:0	66
10.	**9a**	4-FC_6H_4	72 h	**10aj, 11aj, 12aj**	3.3:1:3.6:0[e]	48
11.	**9a**	2-ClC_6H_4	6 h[d]	**10ak, 11ak**	1:1:0:0[f]	53
12.	**9a**	4-ClC_6H_4	24 h	**10al, 11al, 12al**	6:1:4:0	34
13.	**9a**	2,4-$Cl_2C_6H_3$	30 h	**10am, 11am**	2:1:0:0	69
14.	**9a**	2-BrC_6H_4	72 h	**10an, 11an**	3:1:0:0	79
15.	**9a**	4-$MeOC_6H_4$	1 h[g]	**12ao**	0:0:1:0	12
16.	**9a**	4-MeC_6H_4	120 h	**12ap**	0:0:1:0	22
17.	**9a**	4-$BzOC_6H_4$	72 h	**12aq**	0:0:1:0	14
18.	**9a**	2-$NO_2C_6H_4$	72 h	**10ar, 11ar**	2.8:1:0:0	38
19.	**9a**	4-$NO_2C_6H_4$	48 h	**10as, 11as, 13as**	5:1.6:0:1[h]	61
20.	**9a**	C_6F_5	48 h	**11at, 13at**	0:1:0:3.3[i]	47
21.	**9a**	2,4-$(NO_2)_2C_6H_3$	24 h	**10au, 13au**	1:0:0:2[i]	49
22.	**9b**: R_1=H, R= Ph	*c*Hex	24 h	**10bf**	1:0:0:0	24
23.	**9b**	2,4-$Cl_2C_6H_3$	48 h	**10bm, 11bm**	4.5:1:0:0	61
24.	**9b**	2-$NO_2C_6H_4$	24 h	**10br, 11br, 13br**	4.8:4:0:1[j]	45
25.	**9b**	4-$NO_2C_6H_4$	48 h	**10bs, 11bs, 13bs**	2:1:0:1.1[k]	49
26.	**9b**	C_6F_5	48 h	**13bt**	0:0:0:1	40
27.	**9b**	2,4-$(NO_2)_2C_6H_3$	24 h	**13bu**	0:0:0:1	67
28.	**9b**	2-NO_2-4-$CF_3C_6H_3$	48 h	**10bv, 11bv, 13bv**	1:2.6:0:1.5[i]	77
29.	**9c**: R_1=Cl, R=Me	*c*Hex	96 h	**10cf**	1:0:0:0	34
30.	**9c**	4-ClC_6H_4	96 h	**10cl, 11cl, 12cl**	2.2:1:1.7:0	64
31.	**9c**	2,4-$Cl_2C_6H_3$	96 h	**10cm, 11cm**	2.5:1:0:0	42
32.	**9c**	C_6F_5	168 h	**10ct, 11ct, 13ct**	1:4.6:0:2[i]	21
33.	**9d**: R_1=NO_2, R=Ph	*c*Hex	n.r.	-	-	-
34.	**9d**	C_6F_5	n.r.	-	-	-
35.	**9d**	2,4-$(NO_2)_2C_6H_3$	n.r.	-	-	-
36.	**9e**: R_1=OMe, R=Me	Me	5 min	**10ea**	1:0:0:0	52
37.	**9e**	Ph	1h	**10eh, 11eh, 12eh**	2:1:1:0[k]	70

38.	**9e**	*c*Hex	20 min	**10ef, 13ef**	1.3:0:0:1	66
39.	**9e**	$CHEt_2$	1 h	**10eg, 13eg**	1:0:0:1.6	58
40.	**9e**	2-FC_6H_4	5 min	**10ei, 13ei**	1.1:0:0:1	65
41.	**9e**	2,4-$Cl_2C_6H_3$	5 min	**13em**	0:0:0:1	86
42.	**9e**	4-$BzOC_6H_4$	15 min	**10eq, 11eq, 12eq**	1.25:1:2.3:0[k]	24
43.	**9e**	4-$NO_2C_6H_4$	5min	**13es**	0:0:0:1	82
44.	**9f**: R_1=OMe, R=Ph	Me	2 min	**10fa, 13fa**	1:0:0:1	45
45.	**9f**	*c*Hex	20 min	**10ff, 13ff**	1:0:0:7	63
46.	**9f**	$CHEt_2$	20 min	**10fg, 13fg**	1:0:0:9	41
47.	**9f**	2,4-$Cl_2C_6H_3$	10 min	**13fm**	0:0:0:1	88[l]
48.	**9f**	4-MeC_6H_4	30 min	**10fp, 11fp, 12fp**	2:1:4.7:0[k]	41
49.	**9f**	4-$NO_2C_6H_4$	5 min	**13fs**	0:0:0:1	70[l]

[a] 1 equivalent of $FeCl_3$ was used in reaction as Lewis acid.
[b] The acetate group substitution with chlorine appeared in 6 % yield forming **10ja**.
[c] The acetate group substitution with chlorine appeared in 4 % yield forming **10jc**.
[d] Reactions performed in nitromethane.
[e] **11aj** was isolated in a mixture with **10aj** in 10% yield due to the similar R_f's. Their ratio was determined from ^{1}H NMR spectrum.
[f] 2-chlorobenzaldehyde condensation with nitromethane product 1-(2-dichlorophenyl)-2-nitroethan-1-ol was separated with compound **10ak** in 1:1 ratio in 26 % yield.
[g] Reaction conditions: 1eq. of $FeCl_3$, DCM, bt.
[h] **10as** and **13as** were isolated as a mixture due to the same R_f's. Their ratio was determined from ^{1}H NMR spectrum.
[i] Products were isolated as a mixture due to the same R_f's. Their ratio was determined from ^{1}H NMR spectrum.
[j] **11br** and **13br** were isolated as a mixture due to the same R_f's. Their ratio was determined from ^{1}H NMR spectrum.
[k] **10** and **11** were isolated as a mixture due to the same R_f's. Their ratio was determined from ^{1}H NMR spectrum.
[l] Hydrolysis of **13** took place forming product **14**, see Table 6.

Next, the general dependence between the product formed and the structure of the aldehyde was deduced. In cases where aliphatic carbaldehydes were used (Table 5, entries 1 – 7, 22, 29, 36) the selective formation of *E*-configurated alkyne-carbonyl metathesis products **10** took place in low or moderate yields, as aliphatic aldehydes undergo a self-condensation reaction in the presence of Lewis acids; therefore, the yields of alkyne-carbonyl metathesis products were not satisfactory. However, the mixtures of *E* (**10**) and *Z* (**11**) isomers of the corresponding α,β-unsaturated ketones were formed during reaction of **9a,b,c** with aromatic aldehydes, especially those having an *ortho*-substituent (Table 5, entries 9, 11, 13, 14, 18, 20, 23, 24, 30 – 32). Also no reactions took place

while heterocyclic aldehydes such as indole-3-carbaldehyde, thiophene-2-carbaldehyde or pyridine-2-carbaldehyde were used.

The formed and isolated stereoisomers were identified by ^{1}H NMR nuclear Overhauser effect spectroscopy (NOESY) method using compounds **10am** and **11am**. Figure 3 represents structures of *E* and *Z* isomers and their NOESY spectra data, where interaction between =CH and CH_2 groups in *E* isomer is absent and in *Z* isomer is clearly visible. Also the structure of compound **11am** was confirmed by X-ray crystallographic method (Fig. 2). Stereoisomers of other compounds were identified by CH_2 group characteristic peak multiplicity (d, ^{4}J = 0.8 – 1.5 Hz for Z isomers and s for E isomers) and chemical shifts in the ^{1}H and ^{13}C NMR spectra.

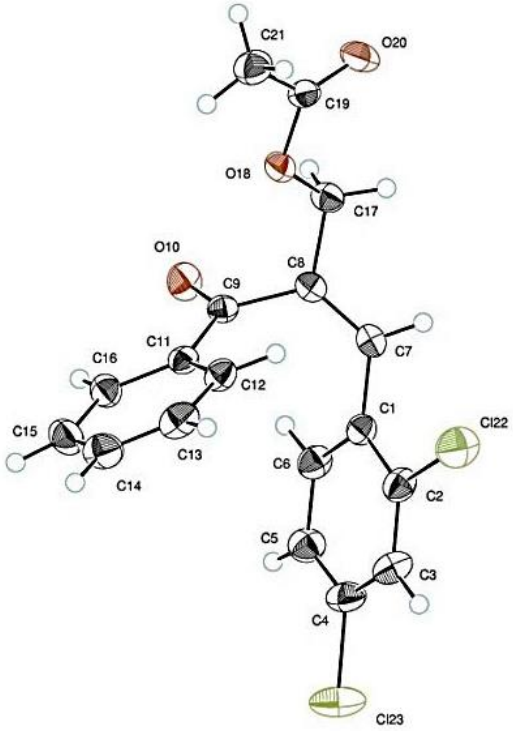


Figure 2. X-ray crystallographic structure of compound **11am**.

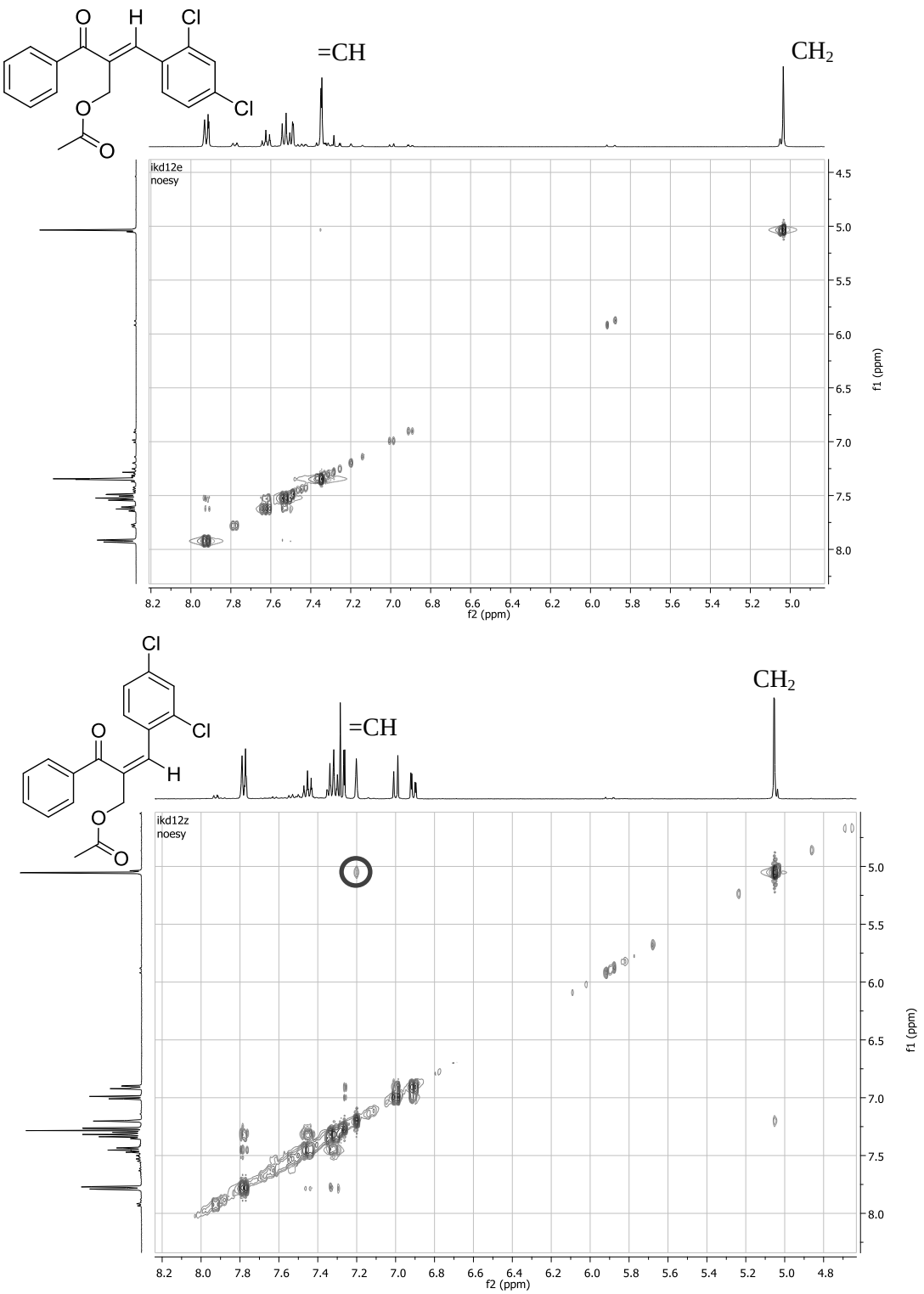
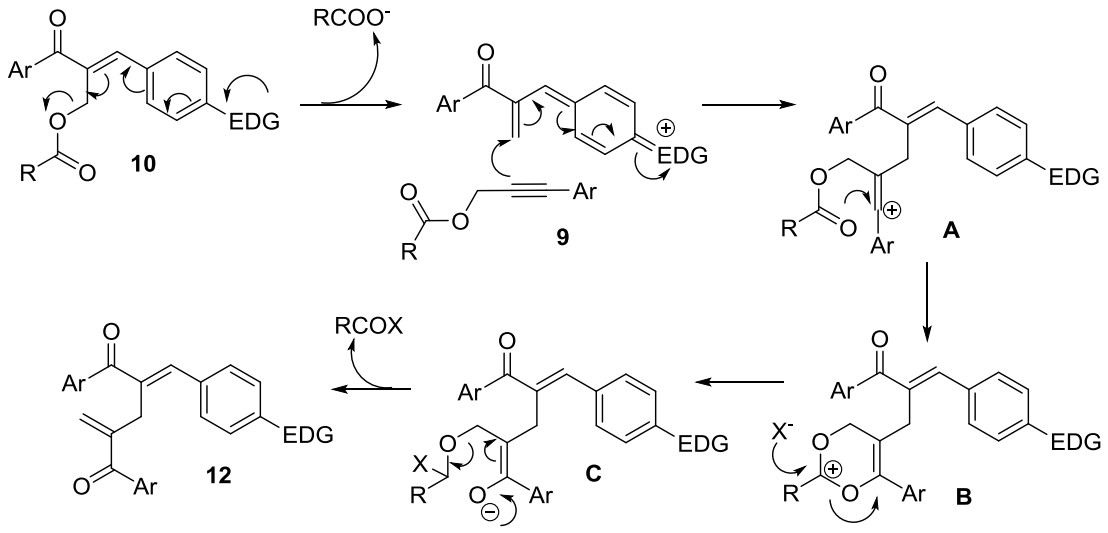


Figure 3. NOESY spectra of compounds **10am** and **11am**.

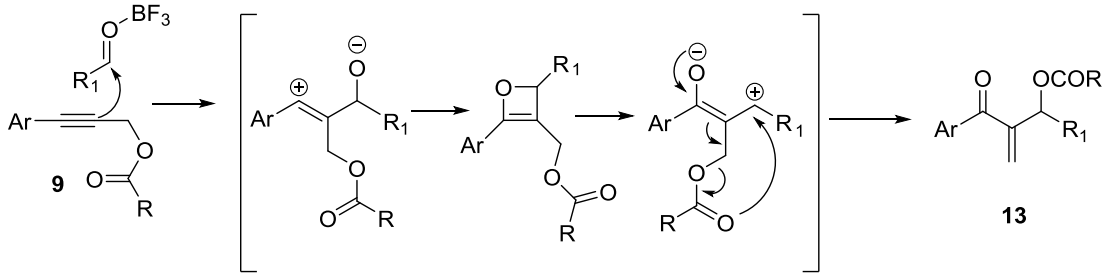
The reactions of **9** with benzaldehydes bearing an electron-donating group in the *para*-position (Table 5, entries 15 – 17, 42, and 48) were complicated, due to formation of big amounts of tars, and required a longer reaction time for full conversion of the alkyne. After workup of the reaction mixtures, 2:1 adducts

12ao, **12ap**, **12aq**, **12eq**, **12fp** were isolated in poor yields as sole or major reaction products. The formation of 2:1 adducts was also observed in reactions with 4-halobenzaldehydes (Table 5, entries 10, 12, 30, 37). Interesting result was obtained performing reaction in the CEM Focused Microwave™ Synthesis System, Discover® SP (in dichloroethane, 100 °C, 15 min). In the reaction between 3-phenylprop-2-ynyl acetate **9a** and 2,4-dichlorobenzaldehyde considerable amount of 2:1 adduct **12am** (16%) formed comparing with other reaction conditions (Table 5, entry 13), where it was not even observed. We also proved that 2:1 adducts formed from coupling *E*-enones with starting alkynes by performed control experiment, where formation of **12al** was observed chromatographically in the reaction between enone **10al** and alkyne **9a** in presence of $BF_3 \cdot Et_2O$. We supposed, that electron donating group at *para* position of 3-aryl moiety facilitated elimination of RCOO- group (cleavage of CH_2-O bond) (Scheme 50). Then, the nucleophilic attack of the second 3-arylprop-2-ynyl carboxylate **9** molecule (intermediate **A**) took place, followed by the intramolecular oxygen transfer from the carboxylate moiety (intermediate **B**). Rearrangement of **B** resulted in formation of **12** and elimination of RCOX molecule (X could be OH^- from water, F^- from LA or $RCOO^-$ formed during the first stage of rearrangement).



Scheme 50.

The reaction of **9a** with 4-nitrobenzaldehyde led to the formation of three products: the major one, **10as**, which had the same R_f as impurity, resulting in unsuccessful purification, and the *Z*-isomer **11as** (Table 5, entry 19). In the ^{1}H NMR spectrum of the impure compound **10as** there were two doublets at 5.94 ppm (1H, d, J = 0.9 Hz) and 6.15 ppm (1H, d, J = 1.5 Hz) together with broad singlet at 6.92 ppm (1H, br.s.). The ^{13}C NMR of the same mixture showed the presence of a tertiary CH–O carbon (signal at 73.07 ppm). After careful study of the spectral data we came to the conclusion that the impurity could be acetylated Morita-Baylis-Hillman adduct (MBHA) **13as**. During the reaction of **9a** with 2,3,4,5,6-pentafluorobenzaldehyde, the mixture of two products (*Z* isomer **11at** and the major product acetylated MBHA **13at**) was formed (Table 5, entry 20). Similar results were obtained after reaction between **9a** and 2,4-dinitrobenzaldehyde, except this time mixture of *E* isomer and MBHA was isolated (Table 5, entry 21). We were intrigued by these results and decided to investigate the scope of the reaction and the reasons of formation of MBHAs. During first brief evaluation it seemed obvious, that the formation of **13as**, **13at** and **13au** occurred during migration of the acetoxy group during reaction pathway (Scheme 51). We envisioned that the migration of the benzoyloxy group could be more favored due to stabilization of the intermediate carbocation by the neighboring phenyl group.



Scheme 51.

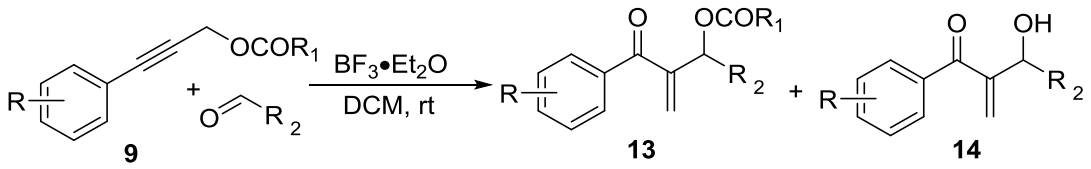
Reactions of **9b** with 2-nitrobenzaldehyde, 4-nitrobenzaldehyde or 2-nitro-4-trifluoromethylbenzaldehyde led to the formation of three compounds (*E* (**10**), *Z* (**11**) and MBHA **13**) (Table 5, entries 24, 25, 28); and it should be noted, that relative amounts of formed MBHAs were bigger than amounts of MBHAs,

formed during reactions between **9a** and nitrobenzaldehydes (Table 5, entries 18, 19). Moreover, the use of more electron-poor 2,4-dinitrobenzaldehyde or 2,3,4,5,6-pentafluorobenzaldehyde (Table 5, entries 26, 27) gave the desired benzoylated MBHAs **13bt**, **13bu** as sole reaction products.

We were pleasantly surprised in finding that the reactions between starting 3-(4-methoxyphenyl)prop-2-ynyl carboxylates (**9e**, **9f**) and dichloro or nitro substituted benzaldehydes were smooth and selective, leading to good-yielding formation of MBHAs **13em**, **13es**, **13fm**, and **13fs** (Table 5, entries 41, 43, 47, 49), though hydrolysis of products **13fm** and **13fs** occurred leading to products **14**. The most intriguing was observed fact that MBHA formed together with *E* isomer in reactions between **9e** and aliphatic aldehydes or 2-fluorobenzaldehyde approximately in 1:1 ratio (Table 5, entries 38 – 40). MBHA was also the major product in reactions of **9f** and aliphatic aldehydes (Table 5, entries 44 – 46) even without use of electron deficient aldehyde.

In summary, the outcome of the reaction was dictated by the structures of both starting 3-arylprop-2-ynyl carboxylates and aldehydes. While the use of aliphatic aldehydes led to the *E* isomer of α,β-unsaturated ketone, the reaction with aromatic aldehydes gave mixtures of *E* and *Z* isomers. The presence of an electron-donating group on benzaldehydes diminished the reaction rates and induced the formation of a 2:1 adduct. The combination of an electron-donating group onto starting 3-arylprop-2-ynyl carboxylates with an electron-withdrawing group on benzaldehydes afforded a very smooth and selective formation of the acetylated or benzoylated Morita-Baylis-Hillman adducts. Therefore, various 2-aroyl-1-arylallyl carboxylates **13** were prepared by the presented method (Scheme 52). Interestingly, considerable amount of hydrolyzed product **14** were isolated after reactions between 3-(4-methoxyphenyl)prop-2-ynyl benzoate **9f** and aldehydes whereas in other reactions between **9b**, **9e** or **9g** and aldehydes, hydrolysis of carboxylate group was not observed. The results are summarized in Table 6. When we tried to enhance yield of product **13fk** from the reaction between 3-(4-

methoxyphenyl)prop-2-ynyl benzoate **9f** and 2-chlorobenzaldehyde, we found, that after prolonged stirring of starting materials, *E* and *Z*-enones **10fk** and **11fk** were isolated instead of MBH adduct (Table 6, entry10). This observation led to hypothesis, that MBHAs form first and after some time rearrange into more thermodynamically stable *E* and *Z*-enones.



Scheme 52.

Table 6. Synthesis of MBHAs *via* reactions between 3-arylprop-2-ynyl carboxylates **9** and aldehydes.

Entry	Alkyne	Aldehyde, R_2	Reaction time	Product, (Yield, %)
1.	**9b**: R=H, R_1=Ph	C_6F_5	48 h	**13bt** (40)
2.	**9b**	2,4-$(NO_2)_2C_6H_3$	24 h	**13bu** (67)
3.	**9e**: R=4-OMe, R_1=Me	2,4-$Cl_2C_6H_3$	5 min	**13em** (86)
4.	**9e**	4-$NO_2C_6H_4$	5 min	**13es** (82)
5.	**9e**	C_6F_5	1 h	**13et** (60)
6.	**9e**	2,4-$(NO_2)_2C_6H_3$	5 min	**13eu** (68)
7.	**9e**	2-NO_2-4-$CF_3C_6H_3$	5 min	**13ev** (87)
8.	**9e**	3-$NO_2C_6H_4$	5 min	**13ew** (54)
9.	**9f**: R=4-OMe, R_1=Ph	2-FC_6H_4	20 min	**13fi** (42), **14fi** (9)
10.[a]	**9f**	2-ClC_6H_4	5 min	**13fk** (46), **14fk** (13)
11.	**9f**	2,4-$Cl_2C_6H_3$	10 min	**13fm** (56), **14fm** (32)
12.	**9f**	2-$NO_2C_6H_4$	20 min	**13fr** (22), **14fr**[b] (47)
13.	**9f**	4-$NO_2C_6H_4$	10 min	**13fs** (43), **14fs** (27)
14.	**9f**	C_6F_5	30 min	**13ft** (28), **14ft** (38)
15.	**9f**	2,4-$(NO_2)_2C_6H_3$	10 min	**13fu** (31), **14fu** (59)
16.	**9g:** R=2,4-diOMe, R=Me	2-$NO_2C_6H_4$	5min	**13gr** (32)
17.	**9g**	4-$NO_2C_6H_4$	3min	**13gs** (21)

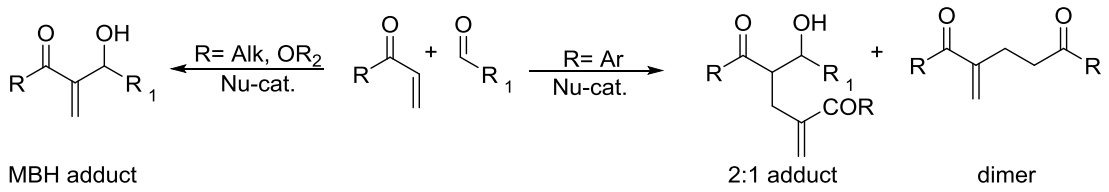
[a] After prolonged stirring (24 hours) of reaction mixture compounds **10fk** (33%) and **11fk** (20%) were isolated.
[b] A mixture of compounds **13fr** and **14fr** was isolated in 1:0.7 ratio, as it was determined from ^{1}H NMR spectrum.

In conclusion, during investigation of the synthesis of various biologically important unsaturated ketones *via* alkyne-carbonyl metathesis reactions, we observed the unique reactivity of some substrates. We noticed that during Lewis acid catalyzed reactions between 3-arylprop-2-ynyl carboxylates and aromatic aldehydes, four possible products could be obtained. In some cases

the derivatives of Morita-Baylis-Hillman adduct formed as main reaction products. Keeping in mind that 2-aroyl-1-arylallyl carboxylates are privileged structures and they are not easily synthetically available, we studied reactions between 3-arylprop-2-ynyl carboxylates and aldehydes and determined the factors dictating the outcome of the reactions.

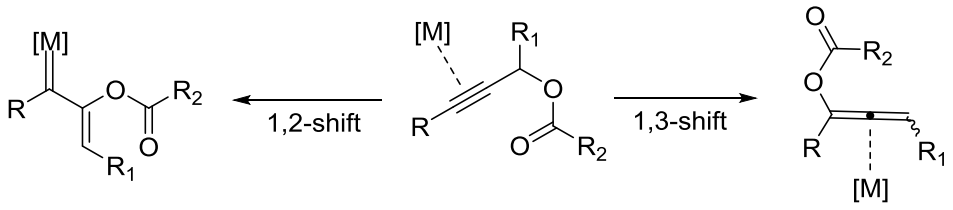
II.2 Mechanistic Investigation of Reactions Between 3-Arylprop-2-ynyl Carboxylates and Aldehydes

Unprecedented and selective formation of products **13** in reactions between 3-arylprop-2-ynyl carboxylates and aldehydes led to the opportunity to synthesize acetylated or benzoylated Morita–Baylis–Hillman adducts which are unavailable by traditional MBH reactions from aryl vinyl ketones because of the high reactivity of the starting materials in fast follow-up processes (Scheme 53) [90].



Scheme 53.

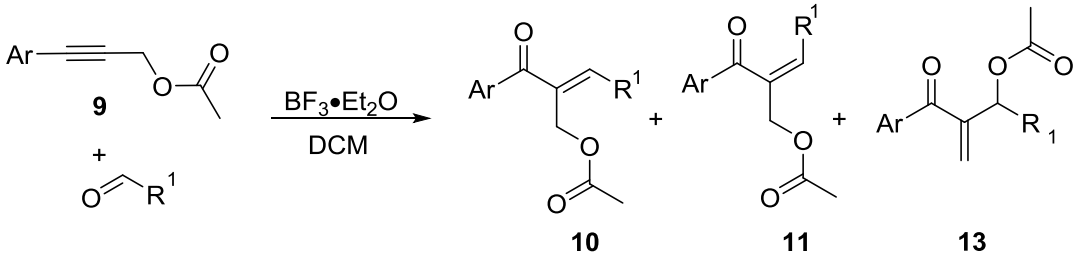
It should be noted that the usual outcome of the intermolecular alkyne–carbonyl metathesis reaction is the formation of thermodynamically stable *E* enones as mentioned above. Propargylic esters are known as a specific class of alkynes with interesting chemical properties. In literature, migration of acyloxy group is usually initiated by gold carbophilic activation of the alkyne unit. This is the dominant synthetic application which leads to 1,2- or 1,3-acyloxy shifts and formation of metal vinyl carbenoid species or metal-complexed allenic intermediates, respectively (Scheme 54) [91].



Scheme 54.

But nothing is known about the mechanistic course of the oxophilic Lewis acid mediated alkyne–carbonyl metathesis of esters **9** and the formation of the MBH adducts in these reactions is still not clearly understood. For this reason additional control experiments and extensive mechanistic experiments with ^{18}O-labeled aldehydes and propargylic esters were performed in order to investigate divergent mechanistic pathways that lead to the formation of either α,β-unsaturated ketones **10** and **11** or MBH adducts **13**. The results are discussed below.

Both the aldehydes and the starting alkynes **9** were carefully chosen for the current study to cover the full reactivity spectrum indicated above (Table 7, Scheme 55).



Scheme 55.

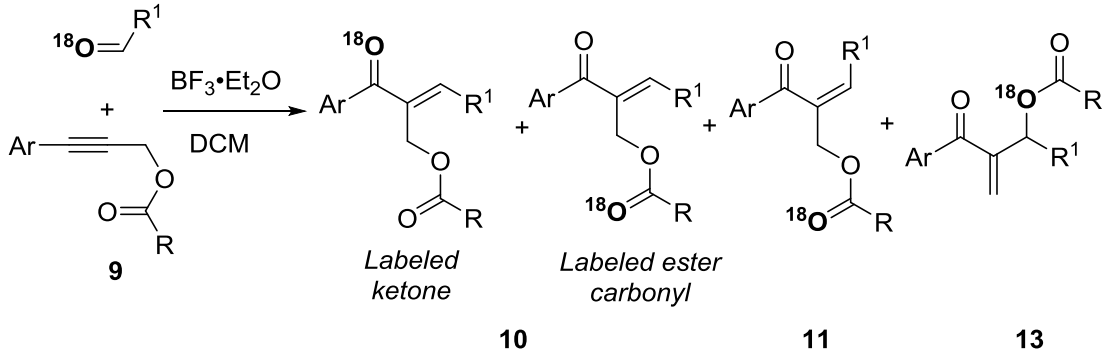
Table 7. Influence of conditions on outcome of the reactions between 3-arylprop-2-ynyl acetates and aldehydes.

Entry	**Alkyne Ar**	**Aldehyde R_1**	**Additive**	**T, °C**	**Reaction time**	**Product, ratio (10:11:13)**	**Overall yield, %**
1.	**9a**, Ar=Ph	Me	–	20	24 h	**10aa** (1:0:0)	26
2.	**9a**	Me	TMSOTf	–10	30 min.	**10aa, 13aa** (1:0:0.3)	16
3.	**9a**	2-FC_6H_4	–	20	24 h	**10ai, 11ai** (2:1:0)	77

4.	**9a**	2-FC_6H_4	TMSOTf	–10	30 min.	**10ai, 11ai, 13ai** (5.3:1.1:1)	69
5.	**9a**	2,4-$Cl_2C_6H_3$	–	20	24 h	**10am, 11am** (2:1:0)	69
6.	**9a**	2,4-$Cl_2C_6H_3$	TMSOTf	–10	30 min.	**10am, 13am** (1:0:1.5)	55
7.	**9e**, Ar=4-$MeOC_6H_4$	4-$NO_2C_6H_4$	–	20	5 min.	**13es** (0:0:1)	82
8.	**9e**	4-$NO_2C_6H_4$	–	10	25 min.	**10es, 13es** (1:0:1)	51
9.	**9e**	4-$NO_2C_6H_4$	–	20	24 h	**10es, 11es** (1.3:1:0)	64

As it was shown earlier, the reactions between **9a** and aldehydes under the optimal conditions ($BF_3 \cdot Et_2O$ (1 eq.), DCM, rt) were slow and took 24 h for the full conversion of the starting alkyne (Table 7, entries 1, 3, and 5). The major products of these three reactions were α,β-unsaturated ketones **10** and **11**. To solve the problem of slow reactivity of the starting materials at lower temperatures we used 1 equivalent of the synergistic couple of $BF_3 \cdot Et_2O$ and TMSOTf. It is known, that these two Lewis acids form much stronger activator BF_2OTf *in situ.* [92]. However, when this couple was used at lower temperature (–10°C), the previously unobserved MBH adducts **13** formed competitively to the major *E*- and *Z*-enones **10** and **11** (Table 7, entries 2, 4, and 6). 3-(4-Methoxyphenyl)prop-2-ynyl acetate (**9e**) reacted very smoothly with 4-nitrobenzaldehyde in the presence of $BF_3 \cdot Et_2O$ (1 eq.) at room temperature and **13es** was isolated as the main product (Table 7, entry 7). Lowering the reaction temperature to 10°C resulted in slower conversion of the starting material, and the mixture of **10es** and **13es** formed in 1:1 ratio (Table 7, entry 8). It was interesting to note that a mixture of **10es** and **11es** formed during prolonged stirring of **9e** and 4-nitrobenzaldehyde in the presence of $BF_3 \cdot Et_2O$ (1 eq.) at room temperature for 24 h (Table 7, entry 9). The same result was obtained when pure **13es** was stirred in CH_2Cl_2 in the presence of $BF_3 \cdot Et_2O$. These results indicated that firstly MBH adduct should be formed in reactions between propargylic esters and aldehydes and then, rearrangement to

more stable *E*- and *Z*-enones take place, as reverse process was not observed. To elucidate the pathway of the reaction from all our imagined possible ways next part of study was performed using isotopic oxygen labeling experiments. ^{18}O-Labeled aldehydes (R^1 = Me, 2-FC_6H_4, 2,4-$Cl_2C_6H_3$ and 4-$NO_2C_6H_4$) were prepared by an exchange reaction between aldehydes and $H_2{}^{18}O$. The data obtained are presented in Table 8 and Scheme 56.



Scheme 56.

Table 8. Reactions of selected 3-arylprop-2-ynyl esters **9** with ^{18}O-labeled aldehydes.

Entry	Alkyne		Aldehyde	Reaction time	Reaction yield, %	Products	10		11	13
	Ar	R	R^1				Labeled ketone	Labeled ester carbonyl		
1.	Ph	Me	Me	24 h	27	**10aa***	1	1.8	-	-
2.	Ph	Me	2-FC_6H_4	24 h	65	**10ai***, **11ai***	0.5	1.5	1	-
3.	Ph	Me	2,4-$Cl_2C_6H_3$	24 h	71	**10am*** **11am***	-	2	1	-
4.	4-$MeOC_6H_4$	Me	4-$NO_2C_6H_4$	5 min	89	**10es***, **13es***	-	0.15	-	1
5.	4-$MeOC_6H_4$	Ph	4-$NO_2C_6H_4$	5 min	78	**13fs***[a]	-	-	-	1

[a] Hydrolyzed **14fs*** with the ^{18}O-label in the hydroxyl group was also isolated in 12% yield.

The reaction between 3-phenylprop-2-ynyl acetate (**9a**) and ^{18}O-acetaldehyde provided ^{18}O-labeled *E* enone **10aa*** as the exclusive product. The ^{18}O atom was incorporated in both the ester carbonyl and keto groups in a 1.8:1 ratio (Table 8, entry 1). The reaction between **9a** and ^{18}O-2-fluorobenzaldehyde led to formation of both enones **10ai*** and **11ai*** in a 2:1 ratio. After isolation and purification of the products it was found that the ^{18}O atom was incorporated

into both carbonyl groups of **10ai*** . The ratio of labeled ketone and labeled ester groups in **10ai*** was 1:3. In contrast, the ^{18}O label was found only in the ester carbonyl group of **11ai*** (Table 8, entry 2).

The experiments with the more electron-poor aldehyde substrates revealed exclusive incorporation of the ^{18}O label in the ester groups of products **10**–**13**. Specifically, the reaction between **9a** and ^{18}O-2,4-dichlorobenzaldehyde provided compounds **10am*** and **11am*** with labeled ester carbonyl groups (Table 8, entry 3). Reactions between **9e** or **9f** and ^{18}O-4-nitrobenzaldehyde displayed a divergent outcome (Table 8, entries 4 and 5). Alkyne **9e** and 4-nitrobenzaldehyde were stirred in DCM in the presence of $BF_3 \cdot Et_2O$ (1 eq.) at room temperature to provide **13es*** and a small amount of **10es*** (Table 8, entry 4). It was proven that the ^{18}O atom was incorporated into the ester carbonyl group of **10es*** and the sp^3 hybridized oxygen atom of the ester functionality in **13es***. In contrast, the reaction between **9f** and the same aldehyde led to the exclusive formation of the MBH adduct **13fs***. Besides the main product **13fs***, 12% of hydrolyzed compound **14fs*** with a free-hydroxyl group was also isolated. The aldehyde oxygen atom was incorporated into the CH-^{18}O(C=O)Ph and CH-^{18}OH positions.

The incorporation of the ^{18}O atom into the products was proven by ^{13}C NMR spectroscopy [93]. Inverse-gated ^{13}C NMR decoupling experiments [94] were used to allow integration of the areas of the carbonyl signals. Upfield chemical shifts of approximately 0.04 ppm (4 Hz) were found for the ^{18}O-carbonyl carbon atoms in both **10aa*** and **10ai***. Similarly, 4 Hz upfield shifts were observed in the ^{13}C NMR spectra for the ester carbonyl groups of **10am***, **10es***, and **11am***, whereas no change in chemical shift occurred at the ketone carbon atoms. The examples are demonstrated in Figure 4. ^{13}C NMR spectra of **13es*** and **13fs*** showed upfield-shifted values for both carbon atoms of the ^{18}O-labeled CH-**O**(C=O)R functionalities. Moreover, IR spectra of **10aa*** and **10ai*** clearly showed a shift of the carbonyl bands to lower wavenumbers, specifically from ν = 1738 to 1708 cm^{-1} for the ester carbonyl bands and from

ν = 1652 to 1646 cm^{-1} for the ketone carbonyl bands. Similar shifts of the ester carbonyl bands to lower wavenumbers (ν = 1738 and 1732 cm^{-1} to ν = 1714 and 1711 cm^{-1}, respectively) were observed in the IR spectra of **10am***, **10es***, and **11am***.

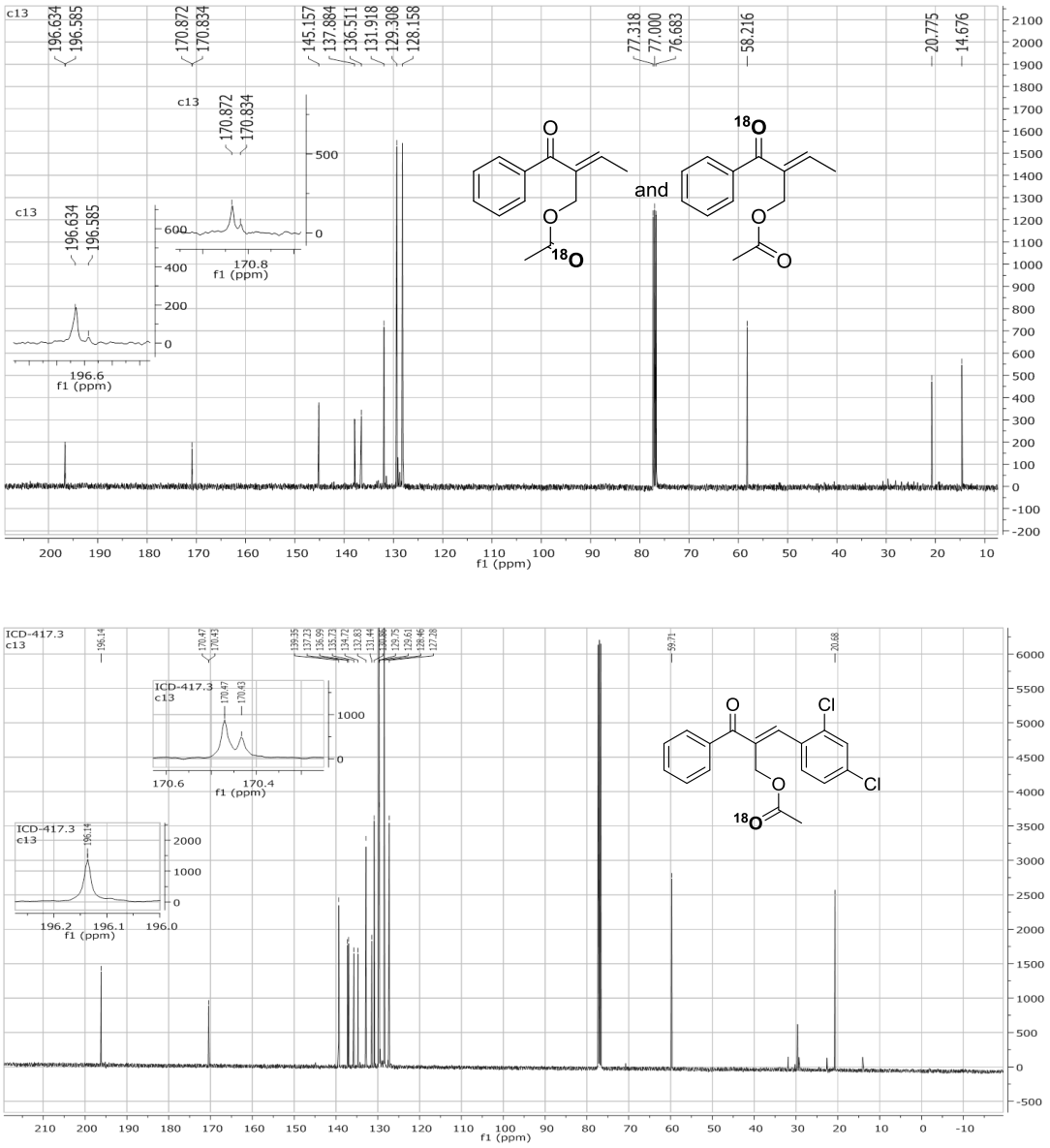
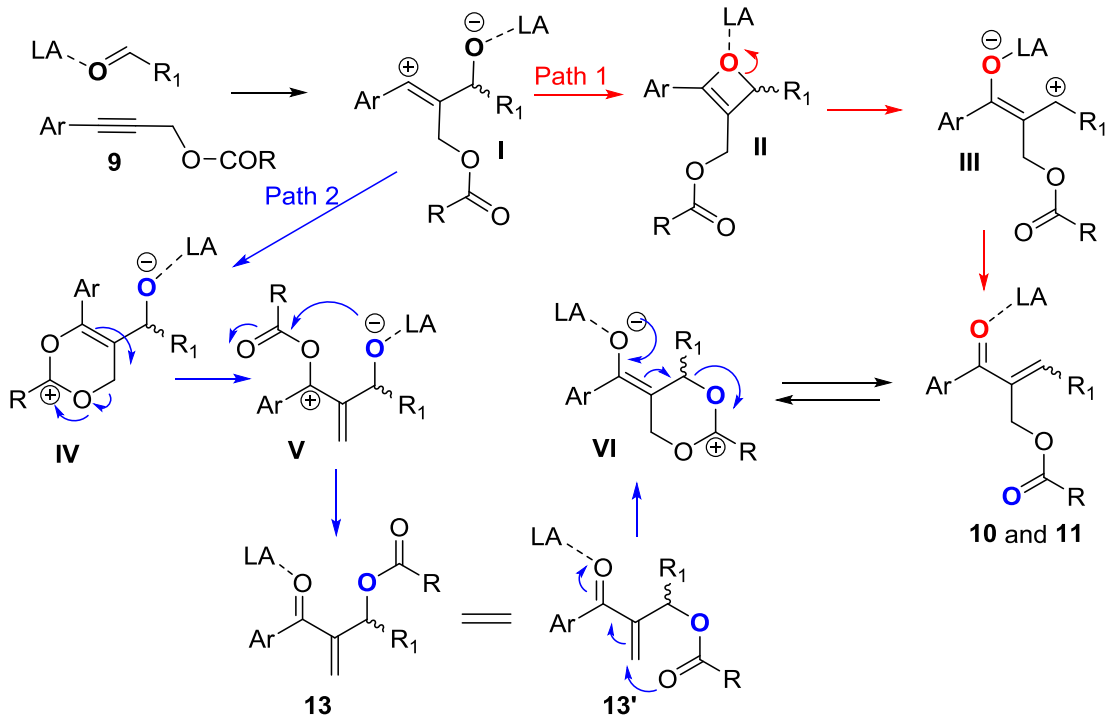


Figure 4. ^{13}C NMR spectra data of compounds **10aa*** and **10am***.

The data presented in Table 8 indicate that at least two competing reaction pathways operate leading to the formation of the observed products. Path 1 explains the formation of *E* enones **10** by the classical alkyne–carbonyl metathesis route, which consists of a formal [2+2] reaction *via* intermediates **I** and **II** (Scheme 55). In contrast, the location of the ^{18}O label in the ester groups

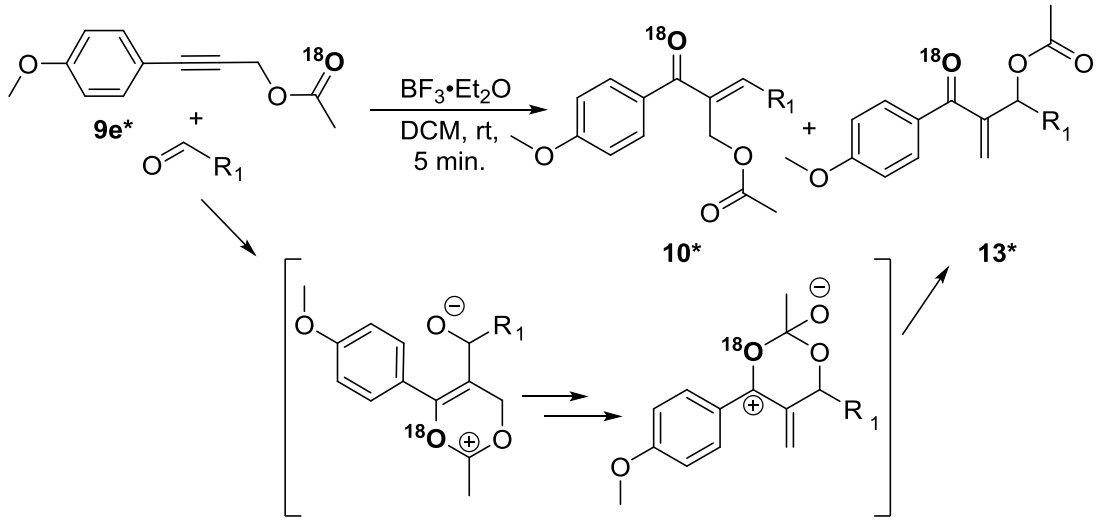
of **10**–**13** cannot be explained by this pathway, but suggests a mechanism that includes intramolecular nucleophilic attack of the ester group onto the initial ion-pair intermediate **I** to form a six-membered zwitterion **IV**, which stabilizes by an acyl group transfer *via* **V** and **VI** to the products (Scheme 57, path 2).



Scheme 57.

To gain support for path 2, additional experiments with ^{18}O labeled 3-(4-methoxyphenyl)prop-2-ynyl acetate **9e*** were performed (Scheme 58, Table 9). The aldehydes were used the same like in previous reactions. After reaction between **9e*** and acetaldehyde besides the main *E* enone **10e*a** a small amount of MBH adduct **13e*a** was isolated (Table 9, entry 1). After reactions with aromatic aldehydes the main products were MBHA **13e*m** and **13e*s**, unfortunately *E* enones also formed and could not be separated due to same R_f values (Table 9, entries 2, 3). Despite this fact, the incorporation of ^{18}O atom in keto group was clearly observed by 4 Hz upfield shifts in the ^{13}C NMR spectra of all compounds, whereas no change in chemical shift occurred for the ester carbonyl atoms. These experiments confirmed the exclusive Path 2 reaction

pathway *via* six-membered intermediate of activated 3-arylprop-2-ynyl carboxylates even with aliphatic aldehydes.



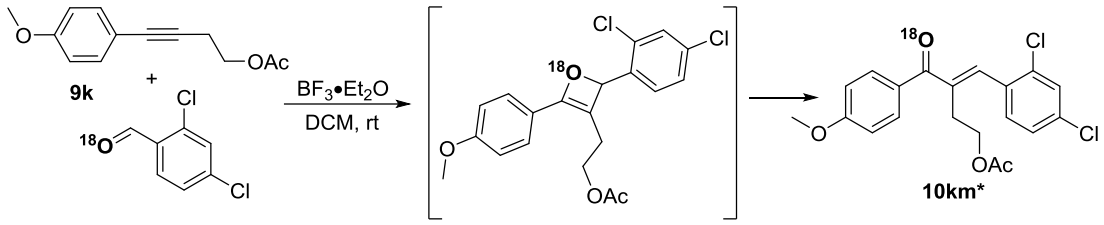
Scheme 58.

Table 9. Reactions of ^{18}O-labeled-3-(4-methoxyphenyl)prop-2-ynyl acetate **9j*** with selected aldehydes.

Entry	Aldehyde, R_1	Products	Ratio of products (10:13)	Overall yield, %
1.	Me	**10e*a, 13e*a**	4 : 1	57
2.	2,4-$Cl_2C_6H_3$	**10e*m, 13e*m**[a]	1 : 4.4	65
3.	4-$NO_2C_6H_4$	**10e*s**[b], **13e*s**	1 : 2.5	50

[a] The inseparable mixture of compounds **10e*m** and **13e*m** was obtained due to same R_f values. The product ratio was determined from the ^{1}H NMR spectrum.
[b] Compound **10e*s** was separated in a mixture with **13e*s** in 26 % yield. The product ratio was determined from the ^{1}H NMR spectrum and recalculated for overall reaction.

Additionally to prove the role of the propargylic ester group in the formal alkyne–carbonyl metathesis reaction, 4-(4-methoxyphenyl)but-3-ynyl acetate (**9k**) was applied in the $BF_3 \cdot Et_2O$ catalyzed reaction with ^{18}O-labeled 2,4-dichlorobenzaldehyde (Scheme 59). Introduction of the additional methylene group should effectively shut down the path 2, because the formation of 6-membered intermediate **IV** would not be possible. In the event, (*E*)-4-(2,4-dichlorophenyl)-3-(4-methoxybenzoyl)but-3-enyl acetate (**10km***) was formed as the exclusive product of the reaction.



Scheme 59.

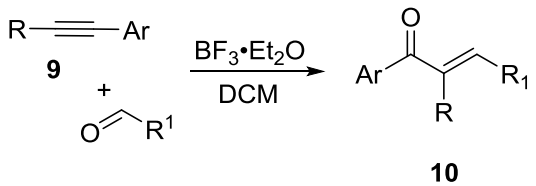
The ^{13}C NMR spectrum of isolated **10km*** revealed a 0.05 ppm (5 Hz) upfield shift of the ketone carbonyl resonance, whereas the ester carbonyl carbon atom remained unshifted. This indicated that the ^{18}O atom was incorporated in the keto group and the classical alkyne–carbonyl metathesis proceeded *via* the oxete intermediate.

Reactions between 3-arylprop-2-ynyl esters and aldehydes leading to the formation of various α,β-unsaturated ketones were studied by using ^{18}O-labeling experiments and confirmed by computational methods during collaboration with prof. L. Rulíšek group (Institute of Organic Chemistry and Biochemistry Gilead Sciences Research Center & IOCB Academy of Sciences of the Czech Republic). The obtained computational results suggested that both mechanisms, either *via* a four- or six-membered intermediate, were plausible and energetically feasible, which explained the observed mechanistic dichotomy. It was also proved that the formation of the MBH adducts always proceeded by a new addition–rearrangement cascade, which included nucleophilic attack of the alkyne to the Lewis acid activated aldehyde, followed by an intramolecular nucleophilic stabilization of the vinylic carbocation by the ester carbonyl group and concomitant formation of a six-membered zwitterion. An acyl group transfer completed this cascade by formation of the kinetic MBH carboxylates. Uniquely, this new 1,3-acyl shift in propargylic esters was induced by addition of electrophilic aldehydes and did not require alkyne activation by transition metal catalysis. Thus acceptor-substituted benzaldehydes and/or donor-substituted alkynes were shown to dramatically switch from the classical alkyne–carbonyl metathesis pathway *via* four-membered intermediates to the newly discovered addition–rearrangement

cascade *via* six-membered zwitterions. Therefore, on one hand, the present synthetic method provided a useful approach to MBH derivatives that had been difficult to access by classical MBH reactions. On the other hand, prolonged reaction times allowed the synthesis of thermodynamically more stable 2-aroyl-3-arylallyl acetates.

II.3. Alkyne-Carbonyl Metathesis Reactions between Various Substituted Arylalkynes and Aldehydes

Previously synthesized compounds were tested for their antiproliferative activity on cancer cell lines and showed interesting results, presented in the next chapter. To obtain a particular influence of α-substituents for the anticancer activity it was decided to extend a variety of alkynes, especially propargylic ones in the alkyne-carbonyl reactions. In contrast to the chemistry of propargylic esters, reactions of phenylacetylene **9h**, 4-(4-methoxyphenyl)but-3-ynyl acetate **9k**, 5-(4-methoxyphenyl)pent-4-yn-2-yl acetate **9l**, alkynes **9m-n** or *N*-(3-(4-methoxyphenyl)prop-2-ynyl)-*N*-methylbenzamide **9o** and various aldehydes resulted in exclusive formation of *E*-enones (**10**) in moderate or good yields (Scheme 60, Table 10). The only exceptions were reactions between diphenyl acetylene **9i** and aldehydes, when due to steric factors *Z*-enones also formed (Table 10, entries 3, 4). Reactions between **9h**, **9i** and **9j** were slow and usually took several days. Due to prolonged time of the reactions yields diminished.



Scheme 60.

Table 10. Data on the reactions between alkynes **9h-o** and aldehydes.

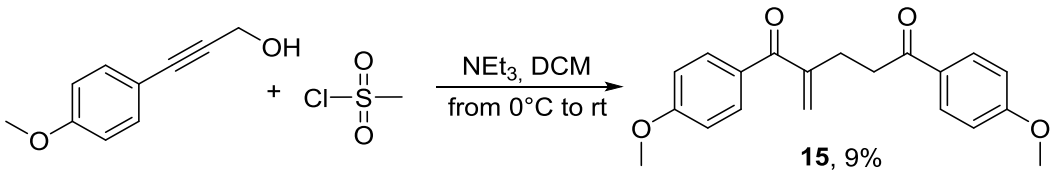
Entry	Alkyne	Ar	R	R_1	Product	Yield, %
1.	**9h**	Ph	H	*c*Hex	**10hf**	16
2.	**9h**			2,4-$Cl_2C_6H_3$	**10hm**	42
3.	**9i**	Ph	Ph	*c*Hex	**10if, 11if**[a]	40
4.	**9i**			2,4-$Cl_2C_6H_3$	**11im**	24

5.	**9j**	Ph	CH_2Cl	*c*Hex	**10jf**	34
6.	**9j**			Ph	**10jh**	50
7.	**9j**			4-ClC_6H_4	**10jl**	32
8.	**9j**			2,4-$Cl_2C_6H_3$	**10jm**	55
9.	**9j**			4-MeC_6H_4	**10jp**	9
10.	**9k**	4-$MeOC_6H_4$	CH_2CH_2OAc	*c*Hex	**10kf**	40
11.	**9k**			$CHEt_2$	**10kg**	21
12.	**9k**			2-FC_6H_4	**10ki**	50
13.	**9k**			2-ClC_6H_4	**10kk**	55
14.	**9k**			4-ClC_6H_4	**10kl**	25
15.	**9k**			2,4-$Cl_2C_6H_3$	**10km**	61
16.	**9k**			4-$NO_2C_6H_4$	**10ks**	53
17.	**9k**			C_6F_5	**10kt**	21
18.	**9l**	4-$MeOC_6H_4$	$CH_2CHMeOAc$	*c*Hex	**10lf**	30
19.	**9l**			4-ClC_6H_4	**10ll**	21
20.	**9l**			2,4-$Cl_2C_6H_3$	**10lm**	70
21.	**9l**			C_6F_5	**10lt**	8
22.	**9m**	4-$MeOC_6H_4$	CH_2CHMe_2	4-ClC_6H_4	**10ml**	46
23.	**9m**			2,4-$Cl_2C_6H_3$	**10mm**	70
24.	**9m**			4-$NO_2C_6H_4$	**10ms**	76
25.	**9m**			4-$F_3CC_6H_4$	**10mx**	71
26.	**9n**	4-$MeOC_6H_4$	CH_2*c*Hex	2,4-$Cl_2C_6H_3$	**10nm**	50
27.	**9n**			4-$F_3CC_6H_4$	**10nx**	54
28.	**9o**	4-$MeOC_6H_4$	CH_2NMeBz	*c*Hex	**10of**	49
29.	**9o**			2,4-$Cl_2C_6H_3$	**10om**	51

[a] Ratio of isomers obtained is 2:1 (**10**:**11**).

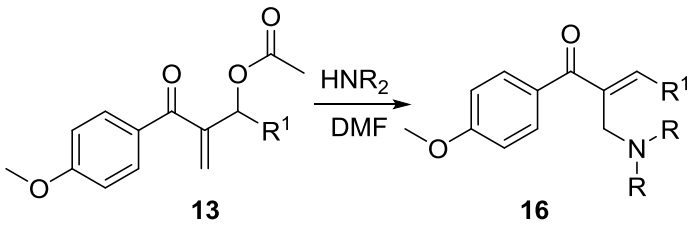
Unfortunately, reactions with *N*-(3-(4-methoxyphenyl)prop-2-ynyl)benzamide **9p** and various aldehydes led to very unstable products. Chromatographically formation of two compounds was observed, but after purification, these products decomposed in two days. (3-(Benzyloxy)prop-1-ynyl)benzene **9q** or 4-phenylbut-3-yn-2-yl benzoate **9s** and aldehydes underwent ambiguous reactions and no dominant product was observed in any previously tested conditions. After reaction of diethyl (3-phenylprop-2-ynyl) phosphate **9t** and 2,4-dichlorobenzaldehyde hydrolyzed *E*-enone was isolated in low 16 % yield, also full conversion of alkyne was not reached. Using more active diethyl (3-(4-methoxyphenyl)prop-2-ynyl) phosphate **9u** in the same reaction no dominant product was observed. The last tested compounds were 3-arylprop-2-ynyl methanesulfonates. No reaction between 3-phenylprop-2-ynyl methanesulfonate **9v** and aliphatic aldehydes was observed, and when benzaldehyde was used, the only 2:1 adduct **12ah** was isolated in 9% yield under standard reaction conditions. During preparation of 3-(4-

methoxyphenyl)prop-2-ynyl methanesulfonate **9w** instead of desired product adduct **15** formed in 9% yield (Scheme 61).



Scheme 61.

To further functionalize the α-substituent of the synthesized enones, some of the isolated Morita-Baylis-Hillman adducts **13** were transformed into the corresponding amino functionalized α-substituted α,β -unsaturated ketones **16** by reacting with amines [95] as presented in Scheme 62. All the reactions performed proceeded smoothly, and the products were isolated in moderate to good yields. Unfortunately, a lot of products **16** decomposed over time, and therefore were not stable enough to be tested (Table 11, entries 2, 4, 5, 7).



Scheme 62.

Table 11. Data on the reactions between compounds **13** and secondary amines.

Entry	Compound 14	R_1	Amine	Product	Yield, %
1	**13es**	4-$NO_2C_6H_4$	diethylamine	**16a**	48
2			piperidine	**16b**	80[a]
3			morpholine	**16c**	77
4			aniline	**16d**	99[a]
5	**13em**	2,4-$Cl_2C_6H_3$	diethylamine	**16e**	84[a]
6			morpholine	**16f**	53
7			aniline	**16g**	70[a]

[a] Solid products were stable only during several days at room temperature.

SUMMARY OF THE CHAPTER II

The general methodology of the alkyne-carbonyl metathesis reaction allowed the quick production of a variety of *E*-α-substituted α,β-unsaturated ketones useful for the discovery of novel bioactive compounds. Though this reaction had some limitations related to the structure of starting materials, especially using heteroaromatic substituents. Also it was noticed that donating substituents in arylalkynes accelerated reaction rate as electron-withdrawing groups contrariwise diminished it.

The most intriguing discovery was unprecedented reactions between 3-arylprop-2-ynyl carboxylates and aldehydes, leading to the formation of *E* and *Z* enones (**10** and **11**), 2:1 adduct (**12**) and MBHA (**13**). It was also found, that the outcome of the reaction was dictated by the structures of both starting materials. While the use of aliphatic aldehydes led to the *E* isomer of α,β-unsaturated ketone, and the reaction with aromatic aldehydes gave mixtures of *E* and *Z* isomers. The presence of an electron-donating group on benzaldehydes diminished the reaction rates and stimulated the formation of a 2:1 adduct. The combination of an electron-donating group onto starting 3-arylprop-2-ynyl carboxylates with an electron-withdrawing group on benzaldehydes afforded a very smooth and selective formation of the acetylated or benzoylated Morita-Baylis-Hillman adducts.

Due to the scope of reactions between 3-arylprop-2-ynyl esters and aldehydes that lead to the formation of various α,β-unsaturated ketones, they have been studied by using ^{18}O-labeling experiments and confirmed by computational methods done by the prof. L. Rulíšek working group (Institute of Organic Chemistry and Biochemistry Gilead Sciences Research Center & IOCB Academy of Sciences of the Czech Republic). The obtained results showed that these substrates underwent through two competing energetically feasible reaction pathways, *via* either a four- or six-membered intermediate. It was also proved that the formation of the MBH adducts always proceeded by a new

addition–rearrangement cascade. Uniquely, this new 1,3-acyl shift in propargylic esters was induced by addition of electrophilic aldehydes. Thus acceptor-substituted benzaldehydes and/or donor-substituted alkynes were shown to dramatically switch from the classical alkyne–carbonyl metathesis pathway to the newly discovered addition–rearrangement cascade.

Chapter III

ANTIPROLIFERATIVE ACTYVITIES OF SYNTHESIZED α,β-UNSATURATED KETONES AND EVALUATION OF STRUCTURE-ACTIVITY RELATIONSHIP

Introduction

In nature α,β-unsaturated ketone fragment is often found in secondary plant constituents flavonoids, which are chemoprotective or cytotoxic to tumor cell lines [96]. As it was shown, natural chalcones and their synthetic analogues also exhibited anticancirogen and chemoprotective properties [1,97]. The main pathway of pharmacological activity was explained *via* covalent reactivity of α,β-unsaturated carbonyl compounds with highly reactive sulfhydryl group of a molecule of biological sensor, that recognized the inducers and signaled the enhanced transcription of phase 2 genes, in such way induced enzymes protected against carcinogenesis [98]. One of main target was thought to be Kelch-like ECH-associated protein 1 (Keap1) which is rich of cysteine groups. Their modification could lead to induction of Nrf2 (the transcription factor called nuclear factor (erythroid-derived 2)-like 2) pathway. Unfortunately, it remained unclear which was main activity model– direct covalent modification of Keap1 or redox cycling induced by generated reactive oxygen species (ROS) [99]. Later chemical and biological activities of synthetic α,β-unsaturated carbonyl compounds were compared and analyzed establishing a model of the compound reactivity [100]. Firstly, this study estimated the reactivity of different synthetic chalcones and other α,β-unsaturated carbonyl compounds with *N*-acetylcysteine, checked human dermal fibroblasts viability and formation of ROS in these cells. Test results showed that reactivity of the studied compounds with *N*-acetylcysteine depends on substitutions in chalcones; moreover, all tested substances did not significantly induce or inhibit ROS formation and also showed low toxicity. Secondly, biological activity was evaluated by determining induction of hemeoxygenase-1 (HO-1). In summary, study results showed that biological activity depended on

chemical reactivity and lipophilicity of the substances. One more important aspect has been clarified, that initiation of Nrf2 pathway through oxidation of Keap1 with ROS was likely of minor importance.

Natural compound curcumin (**I**) extracted from rhizome of turmeric had been already used in clinical trials from various health conditions (Fig. 5) [101]. In a review article [102] author summarized *in vitro* and *in vivo* cancer related properties of curcumin and analyzed possible mechanisms in chemopreventive and chemotherapeutic activities, which were related to its abilities to control cellular levels of ROS. In another study, tetrahydrocurcumin showed lack of activity suggesting that double bond in α,β-unsaturated ketones was important for pre-oxidant activity of curcumin [103]. Synthetic analogues of curcumin (**II-III**) (Fig. 5) showed better activity than their natural congeners. Compound **II** inhibited cancer cell proliferation, induced tumor cell apoptosis by increasing PARP-mediated apoptotic activation, and stimulated the anti-tumor activity of TNF-α [20]. Tests with compound **III** metabolites confirmed importance of α,β-unsaturated ketone fragment for efficacious antitumor activity [104].

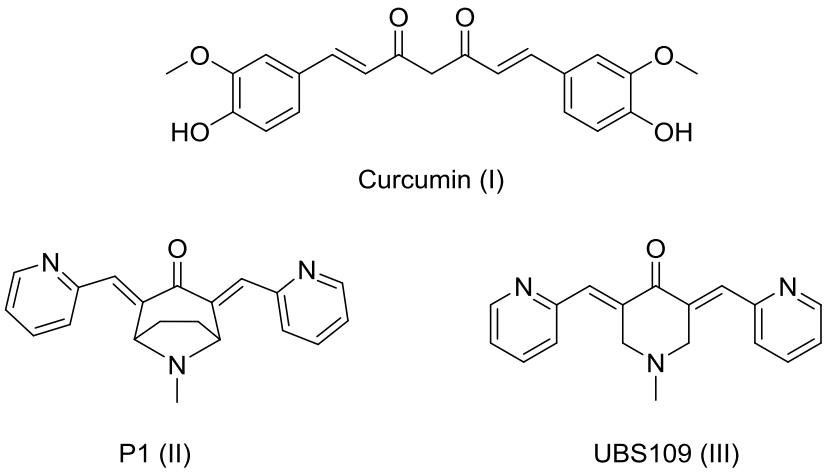


Figure 5. Curcumin and its synthetic analogues.

Another group of natural compounds from ginger (**IV-VI**) showed various biological activities (Fig. 6). Non-conjugated ketone group having [6]-gingerol (**IV**) inhibited lung metastases of B16F10 melanoma in an experimental mouse model due to its anti-angiogenic properties [105].

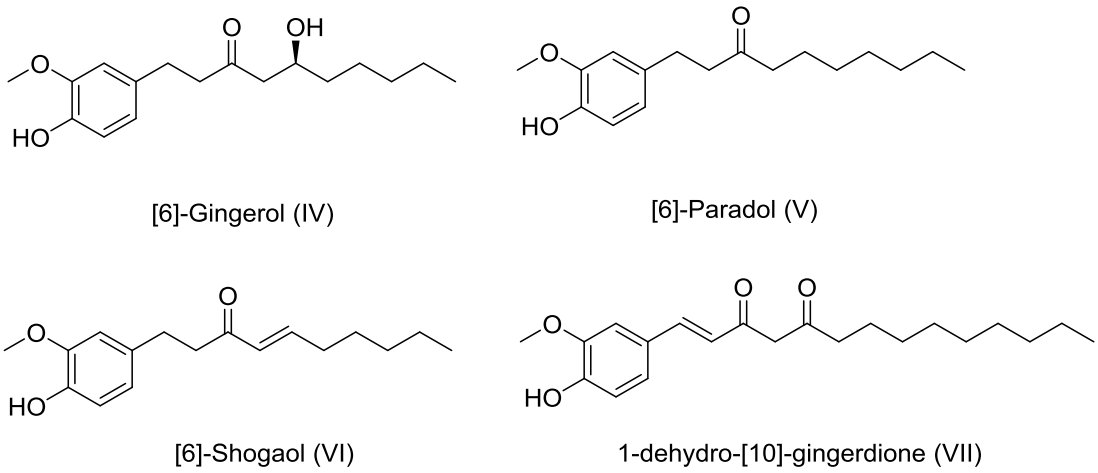


Figure 6. Constituents of ginger.

While compound **IV** inhibited cell growth, [6]-paradol (**V**) induced apoptosis and forced cell necrosis in higher concentration [106]. It was shown that [6]-shogaol (**VI**) exhibited greater cell growth inhibitory effects in several cell lines, A549, SK-OV-3, SK-MEL-2, and HCT15, than gingerol [107]. In search of the activity pathway of [6]-shogaols (**VI**), the growth inhibition of the human colorectal carcinoma cells COLO205 was investigated. Authors demonstrated possible apoptotic pathway through increased production of ROS, first apoptosis signaling receptor activation, and coordinative modulation of DNA damage-inducible gene 153 expression [108]. Investigated metabolites of [6]-shogaol showed that its Michael addition product with cysteine had comparable biological activity and was less toxic in normal cells [109]. Later observations indicated that this metabolite could serve as carrier of compound **VI** before exerting its activity [110].

1-Dehydro-[10]-gingerdione (**VII**) turned out to be more effective in inhibiting the production of nitric oxide in lipopolysaccharide (LPS) activated macrophages than [6]-shogaol (**VI**) and other constituents of ginger [111]. Detailed study of the compound **VII** revealed its molecular target an IκB kinase β, which was involved in the suppression of NF-κB-regulated gene expression in LPS-activated macrophages; this suggested compound **VII** to have therapeutic potential in NF-κB-associated inflammation and autoimmune disorders [112]. Investigation of synthetic analogues of gingerdione revealed

the importance of the double bond in molecular scaffold for the biological activity. This was proved by 1-(3,4-dimethoxyphenyl)-3,5-dodecenedione, an inhibitor of cell proliferation in human promyelocytic leukemia HL-60 cells. This compound arrested cell cycle in G1 phase and induced apoptosis, while other synthetic gingerdiones without double bond showed lack of activity [113].

Constituents of avocado fruit persenone A (**VIII**), persenone B (**IX**) and persin (**X**) suppressed nitric oxide and superoxide generation in cells (Fig. 7) [21].

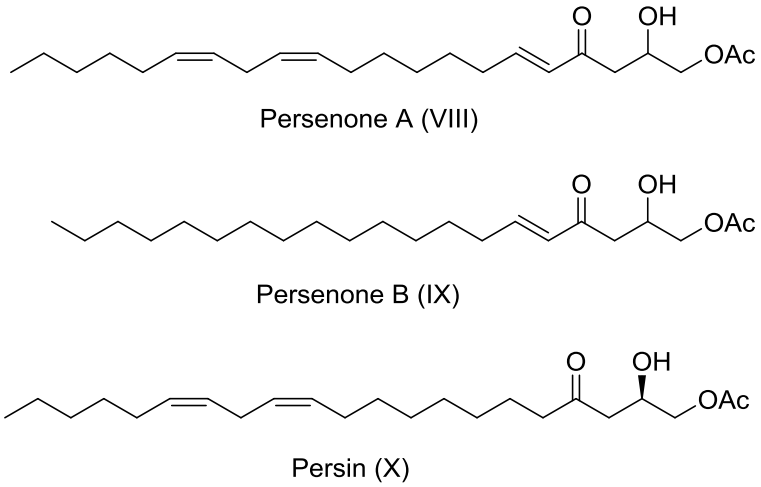


Figure 7. Constituents of avocado fruits.

Detailed investigations showed, that the α,β-unsaturated ketone fragment was important pharmacophore for this type of activity. [19b]. Thus, persin (**X**) induced G2/M phase arrest in human breast cancer cell lines MCF-7 and T-47D cells, however did not significantly affect cell cycle distribution of the human breast cancer cell line MDA-MB-231 [114]. Synthetic analogues of persenones, β'-hydroxy-α,β-unsaturated ketones, α,β-unsaturated ketones and α-substituted α,β-unsaturated ketones had an induced growth inhibition of human solid tumor cells [9, 115]. They also induced apoptosis and arrested cell cycle mostly in G2/M phase on T-47D, H28, H2452, LPc006 and HAPC cancer cells [115 ,116].

Newly found compound chromomoric acid C-I (**XI**) isolated from *Chromolaena odorata* also induced Nrf2 pathway and HO-1, inhibited NF-κB activity and cell proliferation. Though the structure of the substances was very

similar with the other isolated phytoprostanes, this activity was explained by *E*-α,β-unsaturated carbonyl moiety in compound **XI** (Fig. 8). It was thought that due to its active structure chromomoric acid C-I could undergo an electrophilic attack of cysteine residues of Keap1 and thereby activate Nrf2 signaling [117] similarly as previously mentioned chalcones and other α,β-unsaturated carbonyl compounds.

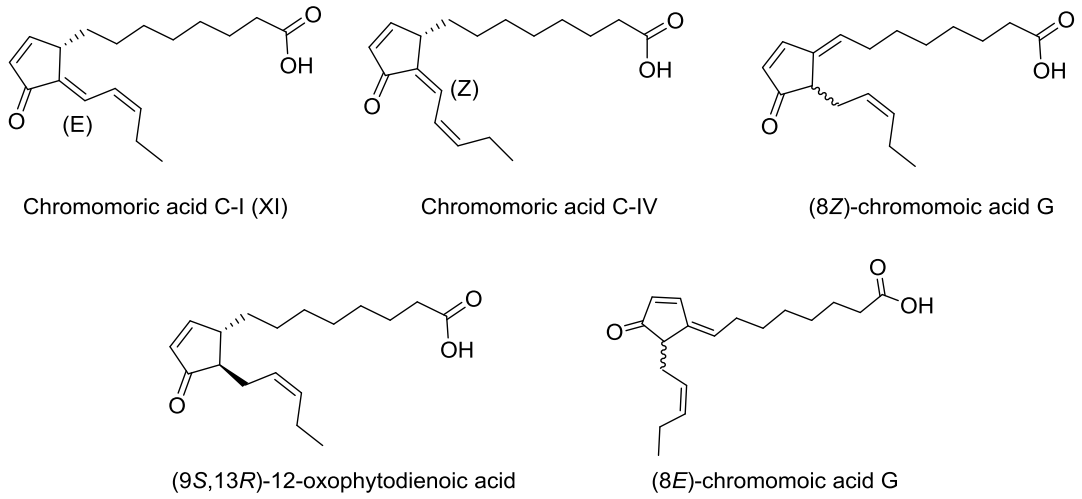


Figure 8. Constituents of *Chromolaena odorata*.

In conclusion, a number of natural α,β-unsaturated carbonyl compounds and their analogues showed broad scope of chemopreventive and anticancer activity. Mechanisms of action of some molecules or their activity centers were investigated and possible application was considered. For this reason the α,β-unsaturated ketone pharmacophore was chosen for the present investigation.

III.1 Structure-Activity Relationship Evaluation of β'-Hydroxy-α,β-unsaturated Ketones

Synthesized β'-hydroxy-α,β-unsaturated ketones and their analogues were tested for their antiproliferative activity using five different human solid cancer cell lines: HBL-100 breast carcinoma cell line, HeLa cervix epitheloid carcinoma cell line, SW1573 non-small lung cancer cell line (alveolar cell carcinoma), T-47D ductal breast epithelial cell line, and WiDr colon adenocarcinoma cell line. The results expressed as GI_{50} were obtained using

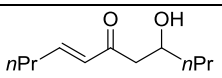
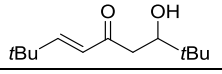
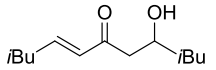
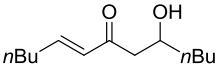
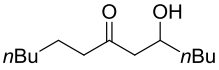
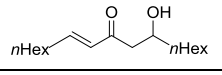
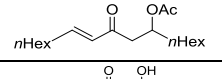
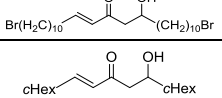
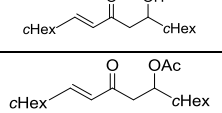
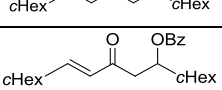
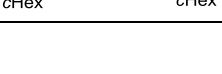
the SRB assay [118], and the results are given in Table 12. The standard anticancer drugs cisplatin and etoposide were used as positive controls.

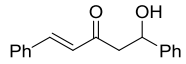
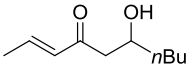
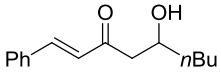
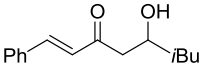
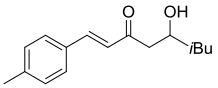
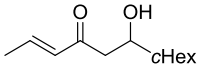
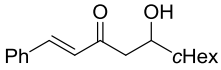
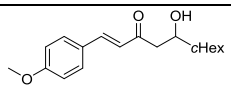
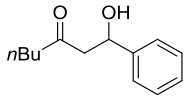
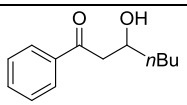
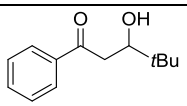
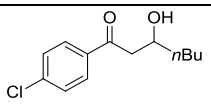
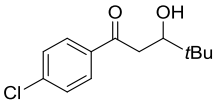
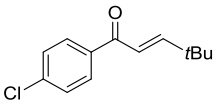
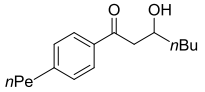
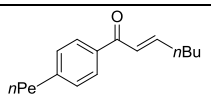
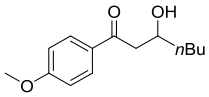
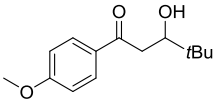
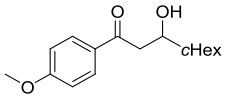
The analysis of the GI_{50} values allowed us to establish several qualitative SARs. Several isoxazolines **4** and 2,3-dihydro-4*H*-pyran-4-ones **3** were also tested for their biological activity as possible structure analogues, though they all appeared inactive. In this reason they were not included in given data. Newly synthesized compounds antiproliferative activity was compared with previously presented compounds of the Padron group [9, 115] (Table 12, entries 2, 3, 6 – 12, 15, 16). The analysis of GI_{50} values of β'-hydroxy-α,β-unsaturated ketones with same aliphatic substituents around the main scaffold revealed that the length of aliphatic chain had no significant difference in biological activity and cyclohexyl substituents remained leading group in enhanced antiproliferative activity (Table 12, entries 1 – 4, 6 – 9). Also biphenyl-β'-hydroxy-α,β-unsaturated ketone ***7f*** demonstrated better antiproliferative activity than its analogues with different substituents even with cyclohexyl fragment (**6q**, **6r**) (Table 12, entries 12, 14 – 16, 18, 19). Comparing activity of compound **6o** with *n*-butyl fragment and compound **6q** with cyclohexyl fragment only slight increase of activity was observed of compound **6q** at all cell lines (Table 12, entries 14, 18). Compound **6r** was inactive at all cell lines though its analogue **6q** exhibited moderate activity and the only difference of these two compounds was methoxy group in phenyl ring (Table 12, entries 18, 19).Though similar compounds with methyl group instead of phenyl one (**6l**, **6n**) showed considerable difference in activity. This example also demonstrated pronounced activity of compound having cyclohexyl substituent compared with *n*-butyl fragment on HBL-100, HeLa, T-47D and WiDr cell lines (Table 12, entries 13, 17).

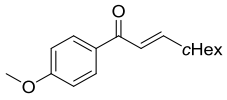
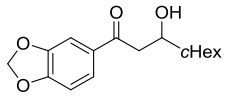
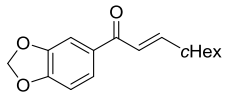
The research showed that conjugated carbonyl group is crucial for biological activity of β-hydroxy ketones (Table 12, entries 4, 5 and 25, 26). Thus activity of phenyl substituted β-hydroxy ketones strongly depended on aliphatic chain and substitution pattern in phenyl ring (Table 12, entries 26 – 38). Phenyl and

4-chlorophenyl substituents diminished antiproliferative activity compared with compounds with donating substituents (Table 12, entries 26, 28 *vs* 31, 33). The best results in this group of compounds were obtained with cyclohexyl substituents (Table 12, entries 35 *vs* 33, 34). Variation of donating substituents in phenyl ring gave no marked difference in antiproliferative activity (Table 12, entries 35, 37). Elimination of hydroxyl group forming α,β-unsaturated ketones had minor influence to the growth inhibition and their activity remained very similar compared with analogues β-hydroxy ketones (Table 12, entries 31, 32, 35 – 38). As an exception was compound **7k** with greater growth inhibition of SW1573 cell line (in comparison to compound **6k**). The pronounced antiproliferative activity of α,β-unsaturated ketone **7e** was also observed as compared to its inactive β-hydroxy ketone analogue **6e** on HBL-100, HeLa and SW1573 cell lines (Table 12, entries 29, 30).

Table 12. In vitro antiproliferative activity of compounds **1**, **6** and **7** against human cancer cell lines (GI_{50} in μM).

	Compound	Structure	GI 50% (μM)				
			HBL-100	HeLa	SW1573	T-47D	WiDr
1.	**1b**		25	27	30	22	29
2.	***7e***[a]		n.t.	n.t.	26 (±4.1)	n.t.	59 (±14)
3.	***7d***[a]		n.t.	n.t.	27 (±4.9)	n.t.	21 (±1.0)
4.	**1c**		25	42	33	30	66
5.	**6a**		>100	>100	>100	n.t.	>100
6.	***7a***[a] (***16a***)[b]		n.t.	n.t.	25 (±4.2)	> 100	31 (±6.2)
7.	***16b***[b]		n.t.	n.t.	23 (±2.4)	18 (±2.6)	18 (±2.4)
8.	***7c***[a]		n.t.	n.t.	30 (±6.4)	n.t.	32 (±8.0)
9.	***7b***[a] (***17a***)[b]		2.3 (±0.3)	n.t.	3.1 (±0.7)	17 (±6.7)	2.9 (±1.5)
10.	***17b***[b]		1.8 (±0.7)	n.t.	2.2 (±0.5)	2.0 (±0.9)	3.9 (±1.6)
11.	***17c***[b]		1.6 (±0.8)	n.t.	3.2 (±1.4)	1.7 (±0.8)	3.1 (±0.2)

12.	***7f***[a]		n.t.	n.t.	4.3 (±1.3)	n.t.	14 (±0.8)
13.	**6l**		70 (±0.7)	56 (±62)	24 (±7.5)	29 (±13)	64 (±51)
14.	**6o**		23	25	23	n.t.	26
15.	***7g***[a]		n.t.	n.t.	13 (±3.4)	n.t.	16 (±6.3)
16.	***7h***[a]		n.t.	n.t.	12 (±5.8)	n.t.	15 (±5.0)
17.	**6n**		17 (±0.3)	25 (±5.9)	23 (±2.5)	20 (±1.9)	35 (±4.6)
18.	**6q**		15 (±3.5)	22 (±22)	20 (±6.9)	11 (±5.2)	19 (±11)
19.	**6r**		>100	>100	>100	>100	>100
25.	**6s**		>100	>100	>100	>100	>100
26.	**6b**		38	>100	35	n.t.	>100
27.	**6c**		>100	>100	>100	n.t.	>100
28.	**6d**		>100	>100	>100	n.t.	>100
29.	**6e**		>100	>100	>100	n.t.	>100
30.	**7e**		26	70	28	n.t.	>100
31.	**6g**		18	20	17	n.t.	29
32.	**7g**		17	23	18	n.t.	30
33.	**6h**		>100	62	34	n.t.	>100
34.	**6i**		32	70 (±15)	42 (±3.3)	63 (±13)	>100
35.	**6j**		13	18	5.3	12	18

36.	**7j**		15	17	7.8	13	19
37.	**6k**		17	19	15	18	23
38.	**7k**		15	18	7.5	16	21

[a] Data taken from [9], leaving a number of compound from literature source.
[b] Data taken form [115], leaving a number of compound from literature source.

III.2 Structure-Activity Relationship Evaluation of α-Substituted α,β-Unsaturated Ketones

Chalcones represent a class of flavonoids that occur naturally in fruits and vegetables and possess valuable biological activity [119]. Despite the fact that pharmacological activity and mechanisms of action of naturally occurring and synthetic chalcones have been clarified, there is still room for exploring the pharmacological potential of chalcones by modifications of the molecular scaffold [120]. In this particular context, our co-workers have reported earlier that α-branched α,β-unsaturated ketones (Fig. 9) prepared *via* iron (III) catalyzed tandem processes showed remarkable biological activity towards human cancer cell lines and demonstrated antiproliferative activity dependence on substituents in α position [9, 115]. These findings initiated our research on structure-activity relationship of α-substituted α,β-unsaturated ketones.

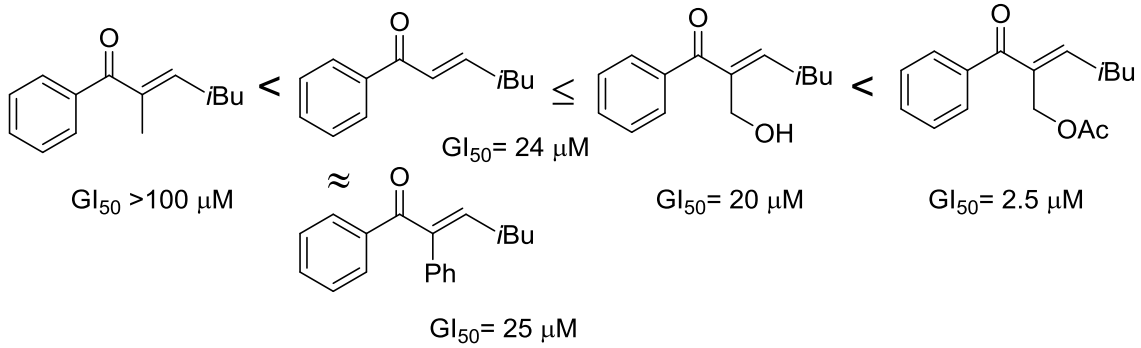


Figure 9. Antiproliferative activity dependence on α-substituents in α,β-unsaturated ketones. GI_{50} values are given in average rating on three different cell lines presented in [9, 115].

All synthesized pure and stable α-substituted α,β-unsaturated ketones were tested *in vitro* for their antiproliferative activity. For a better evaluation of structure-activity relationship, the compounds were divided into three groups: the first group containing α-substituted chalcones **10**, **11** and 1**6**, the second group representing 2:1 adducts **12,** and the third group including Morita-Baylis-Hillman's adducts **13** and **14**. Due to some reasons, antiproliferative activity tests were performed in two different institutions: BioLab, Instituto Canario de Investigacion del Cancer (Chapter III.2.1) and Department of Molecular Cell Biology, Institute of Biochemistry, Vilnius University (Chapter III.2.2).

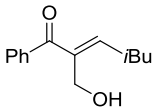
III.2.1 Antiproliferative Activity of α-Branched α,β-Unsaturated Ketones on Human Solid Tumor Cells

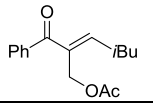
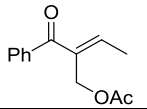
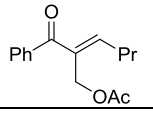
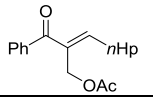
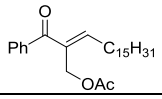
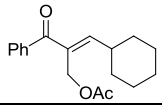
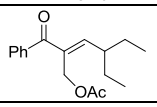
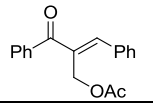
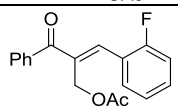
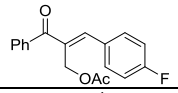
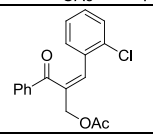
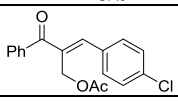
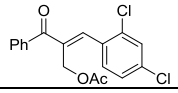
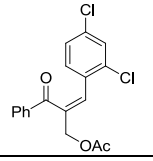
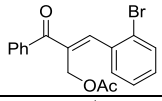
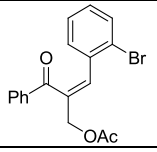
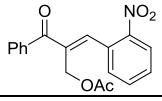
The *in vitro* activity of the first part of synthesized compounds was assessed in HBL-100 (breast), HeLa (cervix), SW1573 (non-small cell lung cancer, NSCLC), T-47D (breast) and WiDr (colon cancer) human solid tumor cells (BioLab, Instituto Canario de Investigacion del Cancer). The results expressed as GI_{50} were obtained using the SRB assay [118], and the results are given in Tables 13 and 14. Overall, the data on antiproliferative activity showed that all tested compounds exhibited growth inhibition in at least two of the cell lines of the panel. For the most active compound of the series **12ao** the GI_{50} values were in the range 0.32 – 0.53 μM.

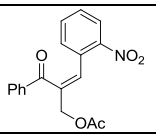
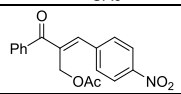
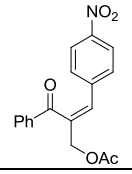
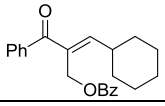
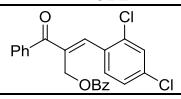
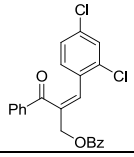
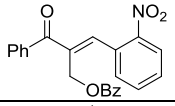
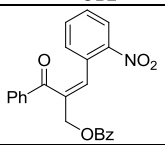
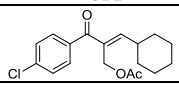
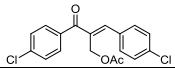
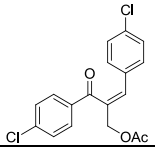
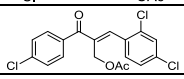
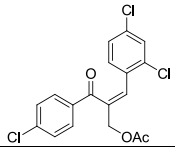
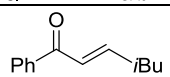
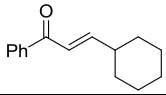
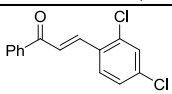
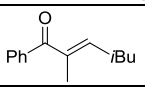
The analysis of the GI_{50} values allowed us to establish some SARs. A first comparison was done between *E* (**10**) and *Z* (**11**) isomers. In most cases, *E* isomers (**10am**, **10ar**, **10as**, **10br**, **10cm, 10if**) appeared more active than the corresponding *Z* isomer (**11am**, **11ar**, **11as**, **11br**, **11cm**, **11if**). However, *E* compounds **10an**, **10bm** and **10cl** did not show a clear enhanced activity when compared to the corresponding *Z* analogues **11an**, **11bm** and **11cl**, respectively. When considering the substituent at the β position of the unsaturated ketone, an alkyl side chain produced loss of activity (**10ag**) when

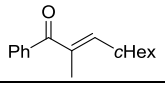
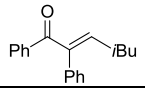
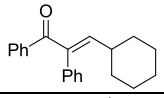
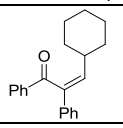
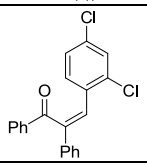
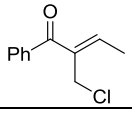
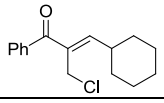
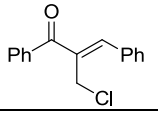
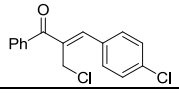
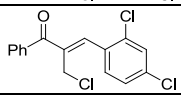
compared to *c*Hex (**10af**, **10cf**) and other linear aliphatic chains (**10aa** – **10ae**). This result was consistent with previously presented observations as demonstrated in Table 13, entries 1, 2. Also aromatic substituents at the β position demonstrated enhanced antiproliferative activity compared with their aliphatic analogues, especially on the HBL-100 and SW1573 cell lines (Table 13, entries 3 – 8 *vs* 9 – 11, 13, 14, 20; 22 *vs* 23, 25; 27 *vs* 28 - 30; 42 *vs* 43 – 45). In the same context, the presence of halogenated substituents on the aryl ring tended to ameliorate the antiproliferative activity (**10jm** > **10jl** > **10jh**; **10al** > **10ah**) if they were located at the *para*-position. In contrast, a substituent in the *ortho*-position (**10ah** *vs* **10ai, 10an**) did not influence positively the antiproliferative effect. Next, the presence of acetoxymethyl (**10am, 10cm**), benzoyloxymethyl (**10bm**), chloromethyl (**10jm**) groups in α position of chalcone moiety enhanced the antiproliferative activity compared to the compound with no substituent (**10hm**) (Table 13, entries 34 *vs* 14, 23, 30, 45). Although in compounds with cyclohexyl substituent at the β position these groups at the α position demonstrated similar growth inhibition compared with no substituent, but –Me and –Ph groups visibly diminished antiproliferative activity (Table 13, entries 7, 22, 27, 33, 36, 38, 42). Finally, a chlorine atom in *para* position of the phenyl ring next to the ketone did not produce a significant effect on the activity (**10al**, **10af**, **10am** *vs* **10cl**, **10cf**, **10cm**). A direct comparison of the GI_{50} data of *E* (**10**) chalcones with the previously reported data for analogue ***8b*** (Table 13, entry 2) indicated that compounds **10al**, **10cl** and **10cm** showed an improved biological activity only in the most resistant cell line T-47D.

Table 13. In vitro antiproliferative activity of compounds **10, 11** against human cancer cell lines (GI_{50} in μM).

Entry	Compound	Structure	GI 50% (μM)				
			HBL-100	HeLa	SW1573	T-47D	WiDr
1.	***10c***[a]		n.t.	n.t.	24 (±3.3)	38 (±5.3)	19 (±8.7)

2.	***8b*[b]**		n.t.	n.t.	1.8 (±1.4)	25 (±0.2)	3.5 (±2.1)
3.	**10aa**		17	16	16	14	17
4.	**10ab**		17	17	18	18	16
5.	**10ad**		20	17	15	15	17
6.	**10ae**		31	10	23	23	28
7.	**10af**		21 (±1.3)	21 (±2.1)	19 (±3.3)	22 (±1.5)	21 (±2.3)
8.	**10ag**		>100	50 (±6.0)	77 (±17)	89 (±9.8)	52 (±2.0)
9.	**10ah**		17 (±4.2)	20 (±8.5)	4.8 (±0.9)	16 (±3.2)	17 (±4.9)
10.	**10ai**		17 (±3.3)	22 (±0.8)	6.1 (±1.4)	18 (±1.6)	19 (±5.8)
11.	**10aj**		17 (±3.9)	25 (±4.2)	4.2 (±0.5)	14 (±2.8)	13 (±1.3)
12.	**11ak**		21 (±3.8)	24 (±4.5)	14 (±0.8)	19 (±1.2)	22 (±4.5)
13.	**10al**		2.3 (±0.5)	3.2 (±0.7)	2.6 (±0.7)	5.3 (±2.5)	4.8 (±1.5)
14.	**10am**		3.1 (±1.2)	16 (±3.7)	3.5 (±0.3)	9.5 (±1.8)	14 (±1.9)
15.	**11am**		23 (±2.6)	22 (±2.5)	22 (±3.5)	20 (±1.8)	19 (±1.4)
16.	**10an**		22 (±4.3)	20 (±2.7)	14 (±1.7)	17 (±2.2)	21 (±3.0)
17.	**11an**		21 (±2.2)	19 (±1.4)	21 (±3.7)	18 (±1.0)	18 (±4.8)
18.	**10ar**		26 (±3.9)	25 (±2.6)	18 (±1.7)	21 (±6.5)	18 (±6.3)

19.	**11ar**		>100	78 (±5.8)	>100	52 (±3.7)	>100
20.	**10as**		10 (±3.3)	26 (±4.6)	3.8 (±0.5)	16 (±4.8)	23 (±1.0)
21.	**11as**		41 (±7.7)	36 (±5.4)	32 (±6.5)	36 (±4.8)	83 (±18)
22.	**10bf**		23 (±5.2)	24 (±2.4)	17 (±3.3)	20 (±0.7)	19 (±2.5)
23.	**10bm**		3.1 (±0.6)	20 (±1.0)	3.3 (±0.5)	17 (±5.8)	17 (±4.0)
24.	**11bm**		26 (±4.6)	8.3 (±1.3)	29 (±6.3)	5.4 (±0.5)	8.7 (±3.9)
25.	**10br**		3.9 (±1.4)	22 (±7.3)	4.3 (±1.8)	16 (±2.2)	18 (±1.8)
26.	**11br**		>100	30 (±6.8)	>100	18 (±6.1)	21 (±1.9)
27.	**10cf**		31 (±14)	24 (±2.6)	18 (±3.9)	18 (±2.9)	21 (±5.5)
28.	**10cl**		4.0 (±1.6)	19 (±3.5)	3.4 (±0.5)	5.4 (±1.5)	18 (±3.2)
29.	**11cl**		16 (±0.9)	5.7 (±1.2)	5.3 (±1.8)	12 (±3.3)	17 (±1.4)
30.	**10cm**		3.2 (±0.8)	4.6 (±0.9)	3.4 (±0.6)	5.2 (±0.9)	8.1 (±1.9)
31.	**11cm**		22 (±4.0)	19 (±0.4)	21 (±3.9)	20 (±1.4)	20 (±1.1)
32.	***10a***[a]		n.t.	n.t.	20 (±3.1)	31 (±1.1)	22 (±11)
33.	**10hf**		18 (±2.9)	21 (±2.5)	10 (±4.7)	15 (±4.3)	21 (±3.9)
34.	**10hm**		17 (±1.1)	18 (±0.3)	12 (±1.5)	14 (±1.6)	20 (±1.8)
35.	***10b***[a]		n.t.	n.t.	>100	>100	>100

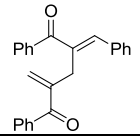
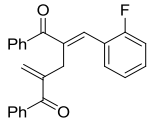
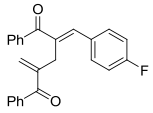
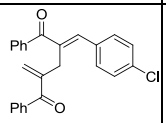
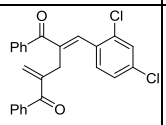
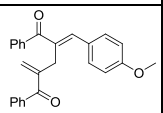
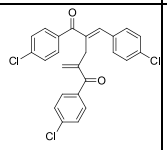
36.	***10e*[a]**		n.t.	n.t.	28 (±4.5)	36 (±5.7)	41 (±25)
37.	***10d*[a]**		n.t.	n.t.	21 (±6.2)	33 (±4.0)	21 (±8.8)
38.	**10if**		57 (±2.6)	47 (±16)	29 (±8.0)	39 (±4.5)	34 (±3.7)
39.	**11if**		59 (±6.7)	63 (±6.5)	64 (±1.0)	74 (±30)	64 (±22)
40.	**10im**		>100	47 (±14)	41 (±16)	52 (±13)	46 (±15)
41.	**10ja**		19	26	24	21	24
42.	**10jf**		22 (±1.8)	30 (±5.1)	23 (±3.9)	29 (±9.2)	22 (±1.5)
43.	**10jh**		12 (±1.9)	23 (±1.8)	3.6 (±0.3)	18 (±3.5)	18 (±3.7)
44.	**10jl**		3.2 (±0.7)	22 (±3.7)	3.9 (±0.6)	17 (±4.9)	19 (±1.6)
45.	**10jm**		3.1 (±0.8)	15 (±2.7)	3.8 (±0.6)	6.3 (±0.7)	13 (±1.8)

[a] Data taken from [9], leaving a number of compound from literature source.
[b] Data taken form [115], leaving a number of compound from literature source.

From the synthesized 2:1 adducts in our investigations, the best results of antiproliferative activity were obtained for adduct **12ao** (Table 14, entry 6), which was found as the most potent compound from the whole study. These adducts possess an additional α,β-unsaturated arylketone group in their structure. When considering the GI_{50} data of adducts **12ah**, **12ai, 12aj, 12al**, **12am** and **12cl**, they did not improve the results of their corresponding analogues *E*-enones (**10**) (Table 14, entries 1 – 5, 7 *vs* Table 13, entries 9 – 11, 13, 14, 28). However, analogue **12ao** was the only compound of the series with a methoxy group in *para* position of the phenyl ring at the β position of the unsaturated ketone and the corresponding *E* and *Z* chalcones were not obtained by the reported methodology. Thus, it was not possible to establish the role in

the activity of methoxy group, although we speculate that it should be favorable.

Table 14. In vitro antiproliferative activity of compounds **12** against human cancer cell lines (GI_{50} in μM).

Entry	Compound	Structure	GI 50% (μM)				
			HBL-100	**HeLa**	**SW1573**	**T-47D**	**WiDr**
1.	**12ah**		10 (±5.0)	19 (±5.7)	3.0 (±1.1)	15 (±4.5)	18 (±4.8)
2.	**12ai**		15 (±3.2)	20 (±6.0)	3.5 (±0.6)	14 (±2.6)	17 (±3.8)
3.	**12aj**		14 (±1.9)	18 (±5.0)	3.5 (±0.5)	15 (±3.0)	19 (±3.2)
4.	**12al**		17 (±2.6)	22 (±2.8)	6.1 (±2.4)	19 (±3.5)	20 (±2.9)
5.	**12am**		12 (±1.9)	19 (±8.7)	4.4 (±1.5)	11 (±7.6)	20 (±1.9)
6.	**12ao**		0.53 (±0.28)	0.32 (±0.02)	0.45 (±0.25)	0.37 (±0.04)	0.47 (±0.05)
7.	**12cl**		16 (±1.1)	21 (±3.4)	5.3 (±1.1)	17 (±5.0)	24 (±4.6)

III.2.2 Antiproliferative Activity of α-Branched α,β-Unsaturated Ketones on Human Hematological and Solid Cancer Cell Lines

First part of antiproliferative activity tests demonstrated enhanced tumor cell growth inhibition of α,β-unsaturated ketones with aromatic substituents having

functional groups linked in α-position. Next part of this work investigation was designed on exploring possible substitutions in α-position and importance of β-substitution pattern for biological activity. Other part of synthesized compounds was tested *in vitro* for their antiproliferative activity using three different human cancer cell lines: NB4 acute promyelocytic leukemia cells, A549 lung cancer cell line and MCF-7 breast cancer cells (Department of Molecular Cell Biology, Institute of Biochemistry, Vilnius University). After 48 h treatment, the effect of compounds was evaluated using XTT assay according to the manufacturer's instructions.

The data presented of three main groups of compounds in Tables 15 – 17 revealed that the A549 cancer cell line was the most resistant, and therefore almost all compounds showed weak or moderate antiproliferative activities against this cell line. In contrast, the NB4 hematological cell line was extremely sensitive to the majority of the tested compounds.

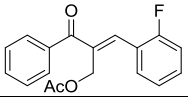
The analysis of the IC_{50} values allowed establishing of several SARs. Among compounds of the Group 1 (Table 15), *E*-α,β-unsaturated ketone α-methyl carboxylate analogues exhibited notable antiproliferative activities. Moreover, *E*-enones showed better activities than their corresponding *Z*-isomers against the NB4 and MCF-7 cell lines, as shown in the comparisons of **10ai**, **10am** and **10fk** *vs* **11ai**, **11am** and **11fk**, respectively (Table 15, entries 1, 2, 4 – 7). This result was consistent with our previously discussed observation. However, the *E*-chalcones **10ai** and **10am** (Table 15, entries 1, 4) were less potent than the respective *Z*-isomers **11ai** and **11am** (Table 15, entries 2, 5) towards the A549 cell line. Also, *E*-enones bearing alkyl substituent in β-position did not show any significant activity against the A549 cell line, while displayed moderate antiproliferative activities against the other cell lines (Table 15, entries 8 – 12). Incorporation of benzoyloxy functionality at the α-substituent seemed to favor antiproliferative activity towards all cancer cell lines, as exemplified by comparing **10ff** to its counterpart **10ef** (Table 15, entry 9, 10). Elongation of the α-substituent by one CH_2 group, as in **10kl – 10kt** (Table 15, entries 13 –

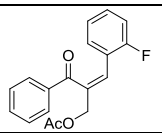
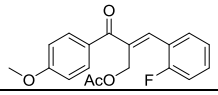
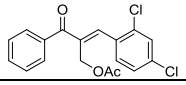
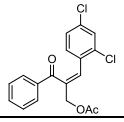
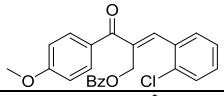
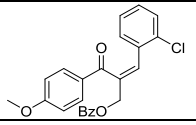
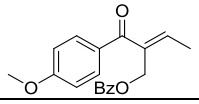
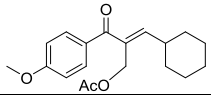
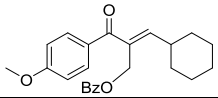
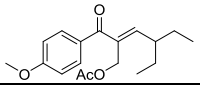
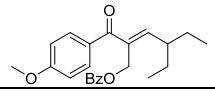
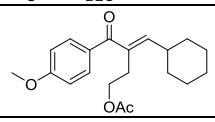
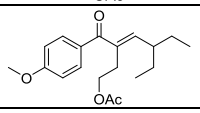
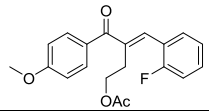
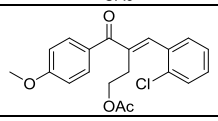
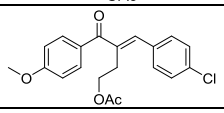
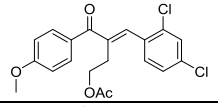
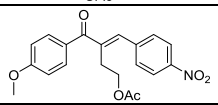
20) led to a substantial loss of activity for all cell lines. Introduction of the $CH_2CH(CH_3)OAc$ moiety at the α-position of the α,β-unsaturated ketone framework or replacement of the ester group in the α-substituent by the *N*-methylbenzamide functionality gave compounds with modest to negligible activities (Table 15, entries 21 – 26).

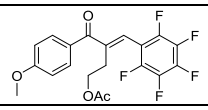
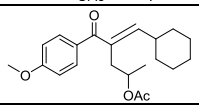
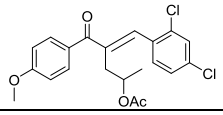
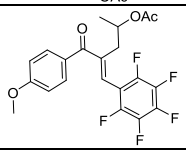
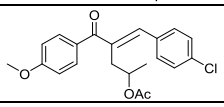
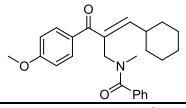
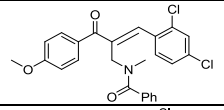
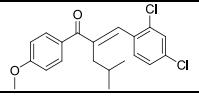
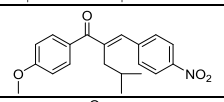
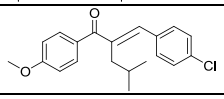
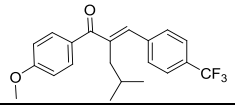
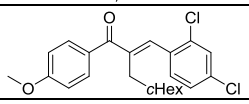
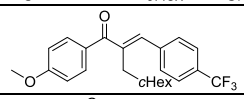
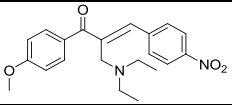
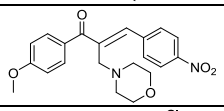
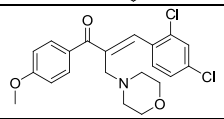
Interestingly, *E*-chalcones **10** bearing a branched aliphatic substituent (isobutyl or cyclohexylmethyl groups) at the α-position displayed a selective activity towards the leukemia cancer cell line (Table 15, entries 27 – 32), with **10ms** (entry 28) being active at submicromolar concentration. However, the presence of the more bulky cyclohexylmethyl substituent caused a decrease in potency against the above cancer cells, as exemplified by comparing **10mm** (entry 27) *vs* **10nm** (entry 31) and **10mx** (entry 30) *vs* **10nx** (entry 32). Moreover, benzene ring C4-methoxy substitution adjacent to the carbonyl function in combination with C4-substitution on the β-phenyl moiety with nitro, chloro and trifluoromethyl groups led to a very effective growth inhibition of the leukemia cancer cells, as evidenced by compounds **10ml**, **10ms** and **10mx**.

Incorporation of a tertiary amino functionality in α-position along with a combination of electron-donating (methoxy) and electron withdrawing (nitro) groups on the aromatic rings of the chalcone scaffold, as in **16a** and **16c** (Table 15, entries 33, 34), gave an effective growth inhibition of both leukemic (NB4) and breast (MCF-7) cancer cell lines. Compound **16f** (entry 35) bearing dichlorophenyl portion in β-position was less active against the MCF-7 cell line, but retained satisfactor activity and selectivity towards the leukemic cell line (NB4).

Table 15. In vitro antiproliferative activity of compounds **10**, **11** and **16** against human cancer cell lines (IC_{50} in μM).

Entry	Compound	Structure	IC 50% (μM)		
			NB4	A549	MCF-7
1.	**10ai**		5.8 (±1.2)	68.7 (±0.04)	14.6 (±2.16)

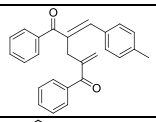
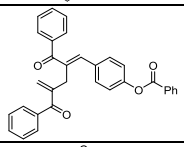
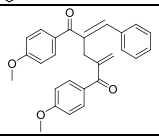
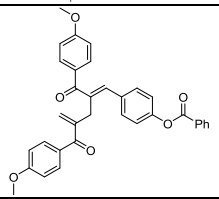
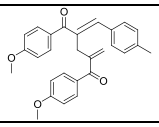
2.	**11ai**		8.3 (±0.55)	20.3 (±0.15)	39.8 (±0.67)
3.	**10ei**		8.2 (±1.24)	22.5 (±0.17)	30 (±0.27)
4.	**10am**		6.6 (±0.84)	97 (±0.13)	8.7 (±1.01)
5.	**11am**		12.6 (±0.72)	74.5 (±0.13)	31.7 (±0.68)
6.	**10fk**		7 (±0.76)	20.1 (±1.01)	9 (±0.05)
7.	**11fk**		18 (±0.69)	52 (±0.15)	36 (±0.93)
8.	**10fa**		16.2 (±1. 18)	> 100	29.8 (±0.29)
9.	**10ef**		23.3 (±0.29)	90 (±0.22)	24 (±0.30)
10.	**10ff**		10.2 (±1.09)	36 (±0.19)	13.7 (±0.75)
11.	**10eg**		9.5 (±0.22)	> 100	13.7 (±0.94)
12.	**10fg**		26.8 (±0.06)	> 100	28 (±0.35)
13.	**10kf**		> 100	> 100	> 100
14.	**10kg**		91.1 (±0.09)	> 100	> 100
15.	**10ki**		> 100	> 100	> 100
16.	**10kk**		51.6 (±0.06)	> 100	> 100
17.	**10kl**		36.3 (±0.28)	86 (±0.09)	> 100
18.	**10km**		34.8 (±0.19)	69.2 (±0.04)	83.4 (±0.03)
19.	**10ks**		> 100	> 100	> 100

20.	**10kt**		28.5 (±0.20)	58.1 (±0.08)	> 100
21.	**10lf**		33.4 (±0.17)	98 (±0.09)	> 100
22.	**10lm**		36.8 (±0.09)	40.3 (±0.10)	> 100
23.	**10lt**		49 (±0.10)	91.7 (±0.11)	> 100
24.	**10ll**		62 (±0.17)	73.2 (±0.13)	> 100
25.	**10of**		39.7 (±0.22)	69.7 (±0.01)	32.7 (±0.18)
26.	**10om**		24 (±0.38)	32.4 (±0.22)	> 100
27.	**10mm**		14.6 (±0.05)	80.3 (±0.27)	> 100
28.	**10ms**		0.6 (±0.02)	> 100	> 100
29.	**10ml**		12.1 (±0.07)	> 100	> 100
30.	**10mx**		12.6 (±0.01)	> 100	> 100
31.	**10nm**		48.9 (±0.21)	> 100	> 100
32.	**10nx**		18.2 (±0.06)	> 100	> 100
33.	**16a**		1.2 (±0.99)	22 (±0.18)	4.3 (±1.06)
34.	**16c**		5.6 (±1.01)	70.1 (±0.06)	7 (±0.88)
35.	**16f**		8.5 (±0.32)	> 100	42.3 (±0.59)

Group 2 of the tested compounds includes a small number of 2:1 adducts **12** (Table 16), which exhibited satisfactory micromolar growth inhibitory activity

against the leukemic cancer cells (NB4), the most active and selective being the bis(methoxy) substituted analogue **12eq** (Table 16, entry 4). However, its unsubstituted counterpart **12aq** was less selective and showed weak activities towards the A549 and MCF-7 solid cancer cells (Table 16, entry 2). Noticeably, enhanced anti-A549 and MCF-7 activities were observed in the cases of compounds **12ap**, **12eh** and **12fp** (Table 16, entries 1, 3, 5), indicating that the absence of the benzoate functionality had a favorable effect on the antiproliferative activity over the A549 and MCF-7 cell lines.

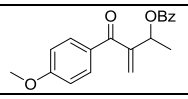
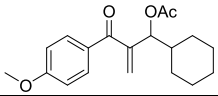
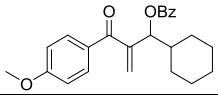
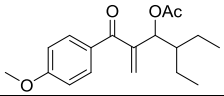
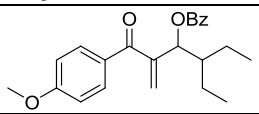
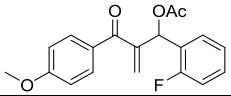
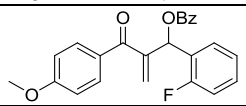
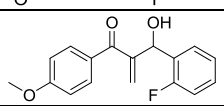
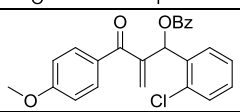
Table 16. In vitro antiproliferative activity of compounds **12** against human cancer cell lines (IC_{50} in μM).

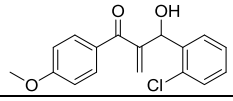
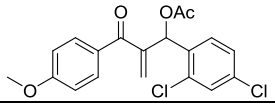
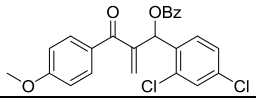
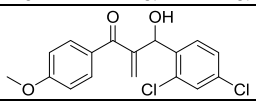
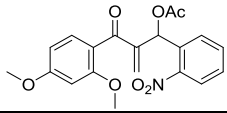
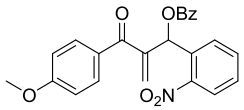
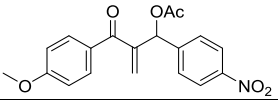
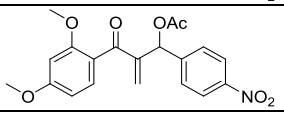
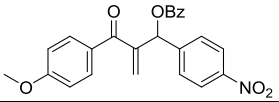
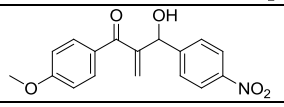
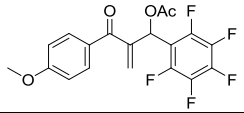
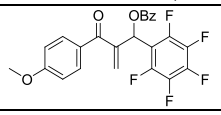
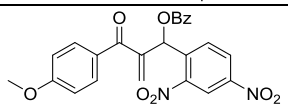
Entry	Compound	Structure	IC 50% (μM)		
			NB4	A549	MCF-7
1	**12ap**		7.6 (±1.04)	20.9 (±0.04)	15.9 (±1.11)
2	**12aq**		8 (±0.79)	44.4 (±0.06)	61.6 (±0.17)
3	**12eh**		7.4 (±0.74)	22.9 (±0.47)	27.1 (±0.65)
4	**12eq**		6.7 (±0.25)	> 100	> 100
5	**12fp**		11.4 (±1.07)	43.8 (±0.57)	26.9 (±0.43)

The third group of the tested compounds represents the class of Morita-Baylis-Hillman adducts **13** and **14** (Table 17), which were found to be the most potent over all cancer cell lines, although their majority showed low to moderate growth inhibitory activities against the A549 cell line. It is evident from Table 17 that the presence of the *ortho*-halogenaryl portion in the α-substituent was responsible for enhanced anti-NB4 activity (Table 17, entries 6, 8 – 11).

Furthermore, the acetylated derivatives (Table 17, entries 6, 11, 16) were more potent than their respective benzoylated counterparts (Table 17, entries 7, 12, 18). Dimethoxyphenyl moiety present in compounds **13gr** and **13gs** had a negative effect on their antiproliferative activity towards the A549 and MCF-7 cancer cell lines (Table 17, e.g. entry 16 *vs* entry 17). Changing the aromatic component in the α-substituent for an aliphatic residue did not inhibit the cell growth to a considerable extent (Table 17, entries 1 – 5). Compounds with electron deficient aryl moieties at the α-substituent along with acetyloxy or hydroxyl functionalities gave improved growth inhibitory activity against the MCF-7 cell line (Table 17, entries 11, 13, 16, 20), while the benzoyloxy functionalized analogues displayed significantly lower antiproliferative activity over the same cell line (Table 17, entries 12, 18, 21, 22).

Table 17. In vitro antiproliferative activity of compounds **13** and **14** against human cancer cell lines (IC_{50} in μM).

Entry	Compound	Structure	IC 50% (μM)		
			NB4	A549	MCF-7
1.	**13fa**		15.7 (±0.34)	> 100	14.5 (±0.63)
2.	**13ef**		10.5 (±0.57)	> 100	14 (±1.73)
3.	**13ff**		10 (±1.07)	62.1 (±0.02)	34.3 (±0.01)
4.	**13eg**		11.8 (±0.31)	32.9 (±0.33)	38.9 (±0.19)
5.	**13fg**		13 (±0.56)	35.2 (±0.25)	17.9 (±0.56)
6.	**13ei**		9.5 (±1.43)	67.3 (±0.07)	18 (±0.54)
7.	**13fi**		14.3 (±0.47)	73.7 (±0.12)	34.2 (±0.18)
8.	**14fi**		6.9 (±0.78)	15.7 (±0.08)	30.9 (±0.04)
9.	**13fk**		8.5 (±0.85)	30.5 (±0.14)	36 (±0.94)

10.	**14fk**		8.1 (±0.80)	28.5 (±0.11)	29.6 (±1.20)
11.	**13em**		5.4 (±1.01)	17.6 (±0.01)	8.3 (±0.78)
12.	**13fm**		9.7 (±0.28)	79.2 (±0.09)	26.8 (±0.27)
13.	**14fm**		26.1 (±0.33)	70 (±0.07)	9 (±0.07)
14.	**13gr**		8.8 (±2.23)	> 100	70.1 (±0.36)
15.	**13fr**		12.7 (±0.42)	45.5 (±0.14)	11.8 (±0.48)
16.	**13es**		10.3 (±1.19)	21.3 (±0.27)	6.1 (±0.86)
17.	**13gs**		5 (±1.53)	43.5 (±0.04)	10.4 (±0.79)
18.	**13fs**		13.2 (±0.83)	66.6 (±0.16)	56.1 (±2.03)
19.	**14fs**		5.4 (±0.76)	23.8 (±0.14)	11 (±0.73)
20.	**13et**		12.6 (±1.12)	14.8 (±1.19)	6.7 (±0.79)
21.	**13ft**		12.9 (±0.74)	32.1 (±0.32)	45.3 (±0.17)
22.	**13fu**		10 (±1.07)	13 (±0.41)	> 100

Additional experiments of the most potent and selective agent towards the hematological cell line NB4 *E*-1-(4-Methoxyphenyl)-4-methyl-2-(4-nitrobenzylidene)pentan-1-one **10ms** showed that this compound did not induce apoptosis but blocked cell cycle in the G0/G1 phase. It was also demonstrated that **10ms** activity in NB4 cells may be associated with a promotion of leukemia cells to differentiation. Some other tested compounds, such as **10am**, **10fk, 16a** and **16c,** exhibited marked growth inhibition of the

NB4 and MCF-7 cancer cells; moreover, the apoptotic effect of these compounds was observed.

Using the QSAR computational techniques from our obtained structure – antiproliferative activity data Dr. V. Kairys group (Department of Bioinformatics, Institute of Biotechnology, Vilnius University) have successfully developed and validated models that provide foundation for the computational design of new molecules with improved inhibitory properties on NB4, MCF-7 and A549 cell lines.

SUMMARY OF THE CHAPTER III

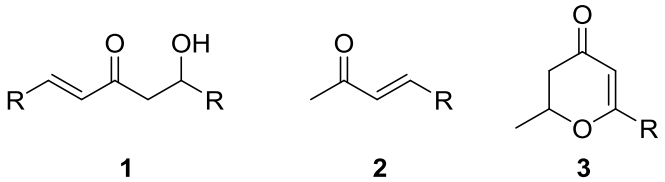
Various α,β-unsaturated ketones ability to inhibit cancer cell growth was evaluated and some structure – activity relationships have been derived. In summary, the aliphatic β'-hydroxy-α,β-unsaturated ketones exhibited moderate activity and theirs lead substituent was cyclohexyl fragment. The conjugation of carbonyl group was crucial for biological activity of β-hydroxy ketones. Esterification of hydroxyl group had positive impact only on T-47D cell line, other cell lines growth inhibition was not influenced by this change. Aromatic substituents around main scaffold indicated better selective activity on SW1573 cell line. Though a mixture of aliphatic and aromatic substituents around β'-hydroxy-α,β-unsaturated ketone scaffold did not show the same dependence on cancer cell lines like compounds with aliphatic substituents and demonstrated only moderate growth inhibition. The change of double bond into phenyl group forming 3-substituted 3-hydroxy-1-arylpropan-1-one was possible in retaining biological activity. It was demonstrated, that only compounds with donating substituents in phenyl ring exhibited moderate activity. Moreover, cyclohexyl group remained important in growth inhibition potency of cancer cell lines like in aliphatic β'-hydroxy-α,β-unsaturated ketones. The compound *E*-1,5-dicyclohexyl-5-hydroxypent-1-en-3-one remained in lead position and various changes of substituents on main scaffold only diminished antiproliferative activity.

Concerning another group of compounds, α-substituted α,β-unsaturated ketones, they showed remarkable biological activity towards human cancer cell lines. Overall, the compounds showed activity against the resistant breast cancer cell line T-47D. The following structural features of unsaturated ketones were shown to lead to the improved activity and selectivity: (a) the aryl group in the β-position of enone fragment was always a better option compared to the aliphatic chain or cyclohexyl ring; (b) the presence of the methylene linker between the α-position and the acetoxy, benzoyloxy, dialkylamino, chlorine or branched alkyl group was important for the notable antiproliferative activities of compounds **10** and **16**; (c) in some cases selectivity between human tumor cell lines could be reached by choosing *E* or *Z* isomers of the same compounds (d) Morita-Baylis-Hillman adducts **13** were generally more active towards tested cancer cell lines, but they were less selective; (e) compounds **13** and **14** bearing unprotected hydroxyl or acetyloxy groups showed improved activity towards all tested cancer cell lines; (f) the presence of *ortho*-halogenaryl group could be associated with improved activities towards NB4 cells; (g) motifs containing electron-poor aryl groups were responsible for better activities towards MCF-7 cells. In particular, the lead compound **12ao** displayed similar activity profile against drug sensitive (HBL-100, HeLa and SW1573) and resistant (T-47D and WiDr) cell lines and compound **10ms** was the most potent and selective agent towards the hematological cell line NB4.

EXPERIMENTAL SECTION

General information. IR spectra were run in KBr discs. ^{1}H and ^{13}C NMR spectra were recorded at either 300 MHz (Varian Unity INOVA) or 400 MHz (Brucker Ascend 400) in chloroform-d, using 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 COSY, HSQC and HMBC. High resolution mass spectra were recorded on a mass spectrometer Dual-ESI Q-TOF 6520 Agilent Technologies by electrospray ionization. All reactions and purity of the synthesized compounds monitored by TLC using Silica gel 60 F_{254} aluminum plates. Visualization was accomplished by UV light and by treating the plates with vanillin stain followed by heating.

Reactions between Pent-4-yn-2-ol and Aldehydes



General procedure

$FeCl_3$ (0.81 g, 5.0 mmol) was added to the solution of pent-4-yn-2-ol (0.42 g, 5.0 mmol) and appropriate aldehyde (10.0 mmol) in dry DCM (5 ml). The resultant solution was stirred at room temperature for 5 minutes, then quenched with 10 ml of water and vigorously stirred for another 10 min. Organic layer was separated, washed with water (2×20 ml) and dried with anhydrous Na_2SO_4. The solvent was evaporated in reduced pressure and the residue was purified by flash column chromatography (hexane/ethyl acetate).

***(E)*-8-Hydroxyundec-4-en-6-one 1b**

Yellowish oil. Yield 22%.

^{1}H NMR (300 MHz, $CDCl_3$): 0.86 – 0.92 (6H, m, 2×CH_3), 1.35 – 1.51 (6H, m, 3×CH_2), 2.17 (2H, qd, $^{3}J_{H,H}$= 7.5 Hz, $^{4}J_{H,H}$= 1.5 Hz, C^{3}H$_2$), 2.59 (1H, dd, $^{1}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 8.7 Hz, C^{7}H<u>H</u>), 2.70 (1H, dd, $^{1}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 3.3 Hz, C^{7}H<u>H</u>), 3.28 (1H, br. s, OH), 4.04 (1H, m, HCOH), 6.06 (1H, dt, $^{3}J_{H,H}$= 15.9 Hz, $^{4}J_{H,H}$= 1.5 Hz, =C^{5}H), 6,83 (1H, dt, $^{3}J_{H,H}$= 15.9 Hz, $^{3}J_{H,H}$= 6.9 Hz, =C^{4}H).^{13}C NMR (75 MHz, $CDCl_3$): 13.89, 14.21, 18.91, 21.47, 34.70, 38.88, 46.27, 67.65, 130.98, 148.85, 201.47.

Spectral data are consistent with reported in the literature [30].

***(E)*-9-Hydroxetridec-5-en-7-one 1c**

Yellowish oil. Yield 19%.

IR (ν, cm^{-1}): 3446 (OH), 1716 (C=O).^{1}H NMR (300 MHz, $CDCl_3$): 0.90 – 0.97 (6H, m, 2×CH_3), 1.34 – 1.48 (10H, m, 5×CH_2), 2.25 (2H, qd, $^{3}J_{H,H}$= 6.3 Hz, $^{4}J_{H,H}$= 1.5 Hz, C^{4}H$_2$), 2.53 (1H, dd, $^{1}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 9.3 Hz, C^{8}<u>H</u>H), 2,77 (1H, dd, $^{1}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 3.0 Hz, C^{8}H<u>H</u>), 3.41 (1H, br. s, OH), 4.09 (1H, m, HCOH), 6.12 (1H, dt, $^{3}J_{H,H}$= 15.9 Hz, $^{4}J_{H,H}$= 1.5 Hz, =C^{6}H), 6.89 (1H, dt, $^{3}J_{H,H}$= 15.9 Hz, $^{3}J_{H,H}$= 6,9 Hz, =C^{5}H). ^{13}C NMR (75 MHz, $CDCl_3$): 14.05, 14.29, 22.49, 22.89, 27.93, 30.34, 32.46, 36.42, 46.18, 68.04, 130.85, 149.23, 201.65.

Spectral data are consistent with reported in the literature [121].

***(E)*-Oct-3-en-2-one 2c**

Colourless oil. Yield 12%.

^{1}H NMR (300 MHz, $CDCl_3$): 0.91 (3H, t, $^{3}J_{H,H}$= 7.2 Hz, CH_3), 1.25 – 1.45 (4H, m, 2×CH_2), 2.19 – 2.24 (5H, m, C^{5}H$_2$, CH_3), 6.06 (1H, dt, $^{3}J_{H,H}$= 15.9 Hz, $^{4}J_{H,H}$= 1.5 Hz, =C^{3}H), 6.80 (1H, dt, $^{3}J_{H,H}$= 15.9 Hz, $^{3}J_{H,H}$= 6,9 Hz, =C^{4}H). ^{13}C NMR (75 MHz, $CDCl_3$): 14.03, 22.45, 27.01, 30.39, 32.37, 131.50, 148.88, 199.01.

Spectral data are consistent with reported in the literature [122].

2,6-Dimethyl-2,3-dihydro-4*H*-pyran-4-one 3a

Colourless oil. Yield 11%.

IR (ν, cm^{-1}): 1720 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 1.42 (3H, d, $^{3}J_{H,H}$= 6.6 Hz, CH_3), 1.98 (3H, d, $^{4}J_{H,H}$= 0,6 Hz, CH_3), 2.38 (2H, m, CH_2), 4.48 (1H, m, HCO), 5.29 (1H, d, $^{4}J_{H,H}$= 0.6 Hz, =CH).^{13}C NMR (75 MHz, $CDCl_3$): 20.61, 21.32, 42.56, 75.87, 104.84, 174.92, 193.41.

Spectral data are consistent with reported in the literature [123].

2-Methyl-6-propyl-2,3-dihydro-4*H*-pyran-4-one 3b

Yellowish oil. Yield 11%.

^{1}H NMR (300 MHz, $CDCl_3$): 0.98 (3H, t, $^{3}J_{H,H}$= 7.5 Hz, CH_3), 1.48 (3H, d, $^{3}J_{H,H}$= 6,3 Hz, CH_3), 1.62 (2H, m, $CH_2\underline{CH_2}CH_3$), 2.24 (2H, td, $^{3}J_{H,H}$= 7.5 Hz, $^{2}J_{H,H}$= 2.1 Hz, $\underline{CH_2}CH_2CH_3$), 2.43 (2H, m, CH_2), 4.52 (1H, m, HCO), 5.35 (1H, d, $^{4}J_{H,H}$= 0.3 Hz, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 13.82, 19.99, 20.62, 37.00, 42.77, 75.83, 104.19, 178.37, 193.80.

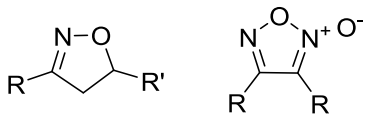
Spectral data are consistent with reported in the literature [40].

2-Mehyl-6-heptyl-2,3-dihydro-4*H*-pyran-4-one 3d

Yellowish oil. Yield 8%.

IR (ν, cm^{-1}): 1731 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 0.89 (3H, t, $^{3}J_{H,H}$= 6,9 Hz, CH_3), 1.27 – 1.55 (13H, m, CH_3, $CH_2\underline{(CH_2)_5}CH_3$), 2.23 (2H, t, $^{3}J_{H,H}$= 7,5 Hz, $\underline{CH_2}(CH_2)_5CH_3$), 2.40 (2H, m, CH_2), 4.51 (1H, m, HCO), 5.32 (1H, s, =CH).^{13}C NMR (75 MHz, $CDCl_3$): 14.29, 20.61, 22.83, 26.60, 29.16, 29.24, 31.88, 35.07, 42.75, 75.83, 104.04, 178.59, 193.70.

Synthesis of Δ^2-Isoxazolines 4 and Formation of Furoxanes 5



4 **5**

General procedure

NCS (0.22 g, 1.65 mmol) and pyridine (1,3 μL, 1.65 μmol) were added to the solution of aldoxime (1.65 mmol) in THF (5 ml), then stirred at 60^0C temperature. After completion of the reaction (observed by TLC), the mixture was cooled down to 40^0C and solution of alkene (1.65 mmol) and NEt_3 (0.23 ml, 1.65 mmol) in THF (1 ml) was added in stirring. After completion of the reaction (observed by TLC), the solvent was evaporated at reduced pressure, the residue dissolved in chloroform (15 ml) and washed with water (3×20 ml). The organic layer was separated, dried over anhydrous Na_2SO_4, the solvent evaporated in reduced pressure and the residue purified by column chromatography (hexane/ethyl acetate or toluene/ethyl acetate).

5-*n*-Butyl-3-*n*-hexyl-4,5-dihydroisoxazole 4a

Yellowish Oil. Yield 43%.

^{1}H NMR (300 MHz, $CDCl_3$): 0.77 – 0.84 (6H, m, 2×CH_3), 1.21 – 1.65 (14H, m, $\underline{(CH_2)}_3CH_3$, $CH_2\underline{(CH_2)}_4CH_3$), 2.24 (2H, t, $^3J_{H,H}$= 7.5 Hz, $\underline{CH_2}(CH_2)_4CH_3$), 2.45 (1H, dd, $^2J_{H,H}$= 16.8 Hz, $^3J_{H,H}$= 8.1 Hz, C^{4}H), 2.88 (1H, dd, $^2J_{H,H}$= 16.5 Hz, $^3J_{H,H}$= 10.2 Hz, C^{4}H), 4.41 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 14.11, 14.14, 22.65, 22.71, 26.50, 27.88, 27.96, 29.05, 31.62, 35.14, 42.20, 80.15, 159.00. Elemental analysis, found C 73.88 %, H 11.92 %. $C_{13}H_{25}NO$ requires C 74.50 %, H 11.89 %.

5-Butyl-3-phenyl-4,5-dihydroisoxazole 4b

White solid; m. p. = 43 – 45 ^{0}C. Yield 63%. Lit. data [124]: m. p. = 40 – 42 ^{0}C.

^{1}H NMR (300 MHz, $CDCl_3$): 0,96 (3H, t, $^{3}J_{H,H}$= 7.2 Hz, CH_3), 1.42 – 1.90 (6H, m, $(CH_2)_3CH_3$), 2.99 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 8.4 Hz, C^{4}H), 3.42 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 10.2 Hz, C^{4}H), 4.79 (1H, m, HCO), 7.41 – 7.43 (3H, m, ArH), 7.68 – 7.72 (2H, m, ArH).^{13}C NMR (75 MHz, $CDCl_3$): 14.27, 22.83, 27.91, 35.30, 40.17, 81.75, 126.83, 128.92, 130.14, 156.67.

5-*t*-Butyl-3-phenyl-4,5-dihydroisoxazole 4c

Colourless oil. Yield 57%..

^{1}H NMR (300 MHz, $CDCl_3$): 1.00 (9H, s, 3×CH_3), 3.11 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 9.3 Hz, C^{4}H), 3.42 (1H, dd, $^{2}J_{H,H}$= 16.8 Hz, $^{3}J_{H,H}$= 11.1 Hz, C^{4}H), 4.48 (1H, dd, $^{3}J_{H,H}$= 11.1 Hz, $^{3}J_{H,H}$= 9.3 Hz, HCO), 7.40 – 7.44 (3H, m, ArH), 7.69 – 7.72 (2H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.35, 34.36, 35.75, 89.59, 126.78, 128.92, 129.32, 130.15, 156.46.

Spectral data are consistent with reported in the literature [125]

5-*n*-Butyl-3-(4-chlorophenyl)-4,5-dihydroisoxazole 4d

White solid; m. p. = 72 – 74 ^{0}C. Yield 46%. Lit. data [126]: m. p. 74^{0}C.

^{1}H NMR (300 MHz, $CDCl_3$): 0.95 (3H, t, $^{3}J_{H,H}$= 7.2 Hz, CH_3), 1.40 – 1.85 (6H, m, $(CH_2)_3CH_3$), 2.96 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 8.1 Hz, C^{4}H), 3.38 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 10.2 Hz, C^{4}H), 4.77 (1H, m, HCO), 7.39 (2H, d, $^{3}J_{H,H}$= 6,6Hz, ArH), 7.62 (2H, d, $^{3}J_{H,H}$= 6,6Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.24, 22.79, 27.88, 35.26, 40.02, 82.06, 128.06, 128.71, 129.18, 136.05, 155.74.

5-*t*-Butyl-3-(4-chlorophenyl)-4,5-dihydroisoxazole 4e

White solid; m. p. = 75 – 76 ^{0}C. Yield 58%.

^{1}H NMR (300 MHz, $CDCl_3$): 1.00 (9H, s, 3×CH_3), 3.08 (1H, dd, $^{2}J_{H,H}$= 16.8 Hz, $^{3}J_{H,H}$= 9.0 Hz, C^{4}H), 3.23 (1H, dd, $^{3}J_{H,H}$= 16.8 Hz, $^{3}J_{H,H}$= 11.1 Hz, C^{4}H), 4.50 (1H, dd, $^{3}J_{H,H}$= 11.1 Hz, $^{3}J_{H,H}$= 9.3 Hz, HCO), 7.40 (2H, d, $^{3}J_{H,H}$= 8.7 Hz,

ArH), 7.63 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.32, 34.36, 35.61, 89.90, 128.02, 128.65, 129.17, 135.97, 155.55. Elemental analysis, found C 66.93 %, H 7.03 %. $C_{13}H_{16}ClNO$ requires C 65.68 %, H 6.78 %.

5-Cyclohexyl-3-(4-nitrophenyl)-4,5-dihydroisoxazole 4f

White solid; m. p. = 113 – 115 ^{0}C. Yield 43%.

^{1}H NMR (300 MHz, $CDCl_3$): 1.03 – 1.29 (5H, m, *c*Hex), 1.56 – 1.80 (5H, m , *c*Hex), 1.90 – 1.94 (1H, m, CH), 3.07 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 9.0 Hz, C^{4}H), 3.31 (1H, dd, $^{2}J_{H,H}$= 16.8 Hz, $^{3}J_{H,H}$= 10.8 Hz, C^{4}H), 4.57 (1H, ddd, $^{3}J_{H,H}$= 10.8 Hz, $^{3}J_{H,H}$= 9.0 Hz, $^{3}J_{H,H}$= 6.8 Hz, HCO), 7.82 (2H, d, $^{3}J_{H,H}$= 9.0 Hz, ArH), 8.24 (2H, d, $^{3}J_{H,H}$= 9.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.56, 25.73, 26.19, 28.37, 28.38, 36.74, 42.36, 86.89, 123.89, 127.14, 135.98, 148.22, 154.81.

5-*n*-Butyl-3-(4-*n*-pentylphenyl)-4,5-dihydroisoxazole 4g

Yellowish solid; m. p. = 41 – 42 ^{0}C. Yield 54%.

^{1}H NMR (300 MHz, $CDCl_3$): 0.91 – 0.97 (6H, m, 2×CH_3), 1.35 – 1.82 (12H, m, $\underline{(CH_2)}_3CH_3$ and $CH_2\underline{(CH_2)}_3CH_3$), 2.65 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, $\underline{CH_2}(CH_2)_3CH_3$), 2.98 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 8.1 Hz, C^{4}H), 3.41 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 10.2 Hz, C^{4}H), 4.74 (1H, m, HCO), 7.24 (2H, d, $^{3}J_{H,H}$= 8.1 Hz, ArH), 7.61 (2H, d, $^{3}J_{H,H}$= 8.1 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.30, 22.80, 22.85, 27.93, 31.26, 31.70, 35.31, 36.08, 40.32, 81.55, 126.80, 127.53, 128.98, 145.38, 156.66.

5-*n*-Butyl-3-(4-methoxyphenyl)-4,5-dihydroisoxazole 4h

White solid; m. p. = 67 – 69 ^{0}C. Yield 63%. Lit. data [127]: m. p. = 85 ^{0}C

^{1}H NMR (300 MHz, $CDCl_3$): 0.92 (3H, t, $^{3}J_{H,H}$= 6.9 Hz, CH_3), 1.31 – 1.51 (4H, m, 2×CH_2), 1.55 – 1.67 (1H, m, CH), 1.73 – 1.83 (1H, m, CH), 2.93 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 8.1 Hz, C^{4}H), 3.36 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 10.2

Hz, C^{4}H), 3.83 (3H, s, OCH_3), 4.63 – 4.74 (1H, m, HCO), 6.91 (2H, d, $^3J_{H,H}$= 9.0 Hz, ArH), 7.60 (2H, d, $^3J_{H,H}$= 9.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 13.97, 22.54, 27.68, 35.00, 40.17, 55.31, 81.15, 114.02, 122.50, 128.05, 155.95, 160.85.

5-*t*-Butyl-3-(4-methoxyphenyl)-4,5-dihydroisoxazole 4i

White solid; m. p. = 132 – 134 ^{0}C. Yield 56%.

^{1}H NMR (300 MHz, $CDCl_3$): 0.99 (9H, s, 3×CH_3), 3.07 (1H, dd, $^2J_{H,H}$= 16.8 Hz, $^3J_{H,H}$= 9.3 Hz, C^{4}H), 3.24 (1H, dd, $^2J_{H,H}$= 16.8 Hz, $^3J_{H,H}$= 10.8 Hz, C^{4}H), 3.86 (3H, s, OCH_3), 4.44 (1H, dd, $^3J_{H,H}$= 10.8 Hz, $^3J_{H,H}$= 9.3 Hz, HCO), 6.94 (2H, d, $^3J_{H,H}$= 9.0 Hz, ArH), 7.64 (2H, d, $^3J_{H,H}$= 9.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.06, 34.02, 35.71, 55.29, 88.97, 113.97, 122.42, 127.95, 155.67, 160.76.

5-Cyclohexyl-3-(4-methoxyphenyl)-4,5-dihydroisoxazole 4j

Yellowish solid; m. p. = 107 – 109 ^{0}C. Yield 71%.

^{1}H NMR (300 MHz, $CDCl_3$): 0.97 – 1.33 (5H, m, *c*Hex), 1.50 – 1.79 (5H, m, *c*Hex), 1.89 – 1.95 (1H, m, CH), 3.01 (1H, dd, $^2J_{H,H}$= 16.5 Hz, $^3J_{H,H}$= 9.0 Hz, C^{4}H), 3.25 (1H, dd, $^2J_{H,H}$= 16.5 Hz, $^3J_{H,H}$= 10.5 Hz, C^{4}H), 3.82 (3H, s, OCH_3), 4.43 (1H, ddd, $^3J_{H,H}$= 10.5 Hz, $^3J_{H,H}$= 9.0 Hz, $^3J_{H,H}$= 6.9 Hz, HCO), 6.90 (2H, d, $^3J_{H,H}$= 9.0 Hz, ArH), 7.60 (2H, d, $^3J_{H,H}$= 9.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.65, 25.83, 26.28, 28.50, 28.55, 37.64, 42.41, 55.27, 85.38, 113.98, 122.45, 127.98, 155.85, 160.80.

5-Cyclohexyl-3-(3,4-methylendioxyphenyl)-4,5-dihydroisoxazole 4k

Yellowish solid; m. p. = 99 – 101 ^{0}C. Yield 60%.

^{1}H NMR (300 MHz, $CDCl_3$): 0.98 – 1.28 (5H, m, *c*Hex), 1.49 – 1.77 (5H, m, *c*Hex), 1.89 – 1.93 (1H, m, CH), 2.98 (1H, dd, $^2J_{H,H}$= 16.5 Hz, $^3J_{H,H}$= 9.0 Hz, C^{4}H), 3.22 (1H, dd, $^2J_{H,H}$= 16.5 Hz, $^3J_{H,H}$= 10.5 Hz, C^{4}H), 4.38 – 4.47 (1H, m, HCO), 5.98 (2H, s, OCH_2O), 6.79 (1H, d, $^3J_{H,H}$= 8.1 Hz, ArH), 7.02 (1H, dd,

$^{3}J_{H,H}$= 8.1 Hz, $^{4}J_{H,H}$= 1.5 Hz, ArH), 7.26 (1H, d, $^{4}J_{H,H}$= 1.5 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.61, 25.79, 26.25, 28.45, 28.48, 37.61, 42.37, 85.57, 101.35, 106.30, 108.04, 121.19, 123.96, 147.96, 149.02, 155.89.

_(E)_-5-Butyl-3-(prop-1-en-1-yl)-4,5-dihydroisoxazole 4l

Colourless oil. Yield 52 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.85 (3H, t, $^{3}J_{H,H}$= 6.9 Hz, CH_3), 1.20 – 1.68 (6H, m, 3×CH_2), 1.82 (3H, dd, $^{3}J_{H,H}$= 6.7 Hz, $^{4}J_{H,H}$= 1.6 Hz, CH_3), 2.62 (1H, dd, $^{2}J_{H,H}$= 16.2, $^{3}J_{H,H}$= 8.22 Hz, C^{4}H), 3.04 (1H, dd, $^{2}J_{H,H}$= 16.2 Hz, $^{3}J_{H,H}$= 10.2 Hz, C^{4}H), 4.56 – 4.44 (1H, m, HCO), 5.91 (1H, qd, $^{3}J_{H,H}$= 15.8, $^{3}J_{H,H}$= 6.7 Hz, =CH), 6.31 (1H, dt, $^{3}J_{H,H}$= 15.8 Hz, $^{4}J_{H,H}$= 1.6 Hz, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.14, 18.71, 22.71, 27.81, 35.15, 38.98, 81.10, 121.84, 134.65, 157.40. HRMS (ES): M + H^+, found 168.1391. $C_{10}H_{18}NO$ requires,168.1383.

5-_t_-Butyl-3-(prop-1-en-1-yl)-4,5-dihydroisoxazole 4m

Colourless oil. Yield 20 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.91 (9H, s, 3×CH_3), 1.87 (3H, dd, $^{3}J_{H,H}$= 6.7 Hz, $^{3}J_{H,H}$= 1.6 Hz, CH_3), 2.78 (1H, dd, $^{2}J_{H,H}$= 16.7 Hz, $^{3}J_{H,H}$= 9.0 Hz, C^{4}H), 2.93 (1H, dd, $^{2}J_{H,H}$= 16.7 Hz, $^{3}J_{H,H}$= 10.9 Hz, C^{4}H), 4.29 (1H, dd, $^{3}J_{H,H}$= 10.9 Hz, $^{3}J_{H,H}$= 9.0 Hz, HCO), 5.96 (1H, dq, $^{3}J_{H,H}$= 15.8 Hz, 6.7 Hz, =CH), 6.35 (1H, dq, $^{3}J_{H,H}$= 15.8 Hz, $^{4}J_{H,H}$= 1.6 Hz, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 18.78, 25.25, 34.24, 34.62, 88.99, 121.89, 134.46, 157.27.

Spectral data are consistent with reported in the literature [128].

5-Cyclohexyl-3-(prop-1-en-1-yl)-4,5-dihydroisoxazole 4n

Colourless oil. Yield 38 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.91 – 1.75 (10H, m, *c*Hex), 1.81 – 1.86 (4H, m, CH_3, CH), 2.73 (1H, dd, $^{2}J_{H,H}$= 16.3 Hz, $^{3}J_{H,H}$= 8.7 Hz, C^{4}H), 2.97 (1H, dd, $^{2}J_{H,H}$= 16.3 Hz, $^{3}J_{H,H}$= 10.5 Hz, C^{4}H), 4.29 (1H, ddd, $^{3}J_{H,H}$= 10.5 Hz, $^{3}J_{H,H}$= 8.7

Hz, $^{3}J_{H,H}$= 6.8 Hz, HCO), 5.93 (1H, dq, $^{3}J_{H,H}$= 15.8 Hz, $^{3}J_{H,H}$= 6.7 Hz, =CH), 6.34 (1H, dq, $^{3}J_{H,H}$= 15.0 Hz, $^{4}J_{H,H}$= 0.8 Hz, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 18.76, 25.90, 26.07, 26.53, 28.67, 28.71, 36.51, 42.64, 85.39, 121.86, 134.54, 157.38. HRMS (ES): M + H^+, found 194.1516. $C_{12}H_{20}NO$ requires, 194.1539.

***(E)*-5-Butyl-3-styryl-4,5-dihydroisoxazole 4o**

Colourless oil. Yield 50 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.93 (3H, t, $^{3}J_{H,H}$= 7.0 Hz, CH_3), 1.31 – 1.50 (4H, m, $CH_2(\underline{CH_2})_2CH_3$), 1.55–1.83 (2H, m, $\underline{CH_2}(CH_2)_2CH_3$), 2.82 (1H, dd, $^{2}J_{H,H}$= 16.1 Hz, $^{3}J_{H,H}$= 8.2 Hz, C^{4}H), 3.24 (1H, dd, $^{2}J_{H,H}$= 16.1 Hz, $^{3}J_{H,H}$= 10.2 Hz, C^{4}H), 4.62–4.73 (1H, m, HCO), 6.71 (1H, d, $^{3}J_{H,H}$= 16,4 Hz, =CH), 7.08 (1H, d, $^{3}J_{H,H}$= 16,4 Hz, =CH), 7.27 – 7.40 (3H, m, ArH), 7.43 – 7.49 (2H, m, ArH).^{13}C NMR (75 MHz, $CDCl_3$): 14.26, 22.81, 27.89, 35.27, 38.75, 81.93, 118.66, 127.17, 129.10, 129.21, 136.15, 136.22, 157.90.

Spectral data are consistent with reported in the literature [129].

***(E)*-5-*t*-Butyl-3-styryl-4,5-dihydroisoxazole 4p**

White solid; m. p. = 79 – 80 °C. Yield 35 %. Lit. data [128]: m. p. = 79–81 °C.

^{1}H NMR (300 MHz, $CDCl_3$): 1.00 (9H, s, 3×CH_3), 2.97 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 9.0 Hz, C^{4}H), 3.12 (1H, dd, $^{2}J_{H,H}$= 16.5 Hz, $^{3}J_{H,H}$= 10.9 Hz, C^{4}H), 4.44 (1H, dd, $^{3}J_{H,H}$= 10.9 Hz, $^{3}J_{H,H}$= 9.1 Hz, HCO), 6.76 (1H, d, $^{3}J_{H,H}$= 16.4 Hz, =CH), 7.11 (1H, d, $^{3}J_{H,H}$= 16.4 Hz, =CH), 7.31 – 7.56 (5H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.34, 34.36, 89.77, 118.61, 127.16, 129.08, 129.12, 129.36, 136.03, 136.16, 157.74.

***(E)*-5-Cyclohexyl-3-styryl-4,5-dihydroisoxazole 4q**

White solid; m. p. = 92 – 93 °C. Yield 57 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.99 – 1.38 (6H, m, *c*Hex), 1.65 – 1.87 (4H, m, *c*Hex), 1.91 – 1.99 (1H, m, CH), 2.94 (1H, dd, $^{2}J_{H,H}$= 16.3 Hz, $^{3}J_{H,H}$= 8.7 Hz, C^{4}H), 3.18 (1H, dd, $^{2}J_{H,H}$= 16.2 Hz, $^{3}J_{H,H}$= 10.5 Hz, C^{4}H), 4.47 (1H, ddd, $^{3}J_{H,H}$= 10.5 Hz, $^{3}J_{H,H}$= 8.7 Hz, $^{3}J_{H,H}$= 6.8 Hz, HCO), 6.75 (1H, d, $^{3}J_{H,H}$= 16.4 Hz, =CH), 7.11 (1H, d, $^{3}J_{H,H}$= 16.4 Hz, =CH), 7.28 – 7.48 (5H, m, ArH).^{13}C NMR (75 MHz, $CDCl_3$): 25.94, 26.12, 26.58, 28.73, 28.80, 36.26, 42.73, 86.18, 100.23, 118.63, 127.16, 129.10, 136.11, 136.16, 157.86. HRMS (ES): M + H^+, found 256.1664. $C_{17}H_{22}NO$ requires, 256.1696.

***(E)*-5-Cyclohexyl-3-(4-methoxystyryl)-4,5-dihydroisoxazole 4r**

Colourless solid; m. p. 118 – 119 °C. Yield 39 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.97–1.34 (5H, m, *c*Hex), 1.50 – 1.82 (5H, m, *c*Hex) 1.87 – 1.95 (1H, m, CH), 2.89 (1H, dd, $^{2}J_{H,H}$= 16.2 Hz, $^{3}J_{H,H}$= 8.7 Hz, C^{4}H), 3.13 (1H, dd, $^{2}J_{H,H}$= 16.2 Hz, $^{3}J_{H,H}$= 10.6 Hz, C^{4}H), 3.83 (3H, s, OCH_3), 4.41 (1H, ddd, $^{3}J_{H,H}$= 10.5 Hz, $^{3}J_{H,H}$= 8.8 Hz, $^{3}J_{H,H}$= 6.9 Hz, HCO), 6.67 (1H, d, $^{3}J_{H,H}$= 16.4 Hz, =CH), 6.89 (2H, d, $^{3}J_{H,H}$= 8.8 Hz, ArH), 6.94 (1H, d, J = 16.4 Hz, =CH), 7.40 (2H, d, $^{3}J_{H,H}$= 8.8 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.95, 26.12, 26.58, 28.74, 28.82, 36.36, 42.73, 55.60, 85.96, 114.54, 116.45, 128.53, 128.97, 135.71, 158.00, 160.43. HRMS (ES): M + H^+, found 286.1797. $C_{18}H_{24}NO_2$ requires, 286.1802.

3-*n*-Butyl-5-phenyl-4,5-dihydroisoxazole 4s

Yellowish oil. Yield 70 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.92 (3H, t, $^{3}J_{H,H}$= 7.5 Hz, CH_3), 1.30 – 1.42 (2H, m, CH_2) 1.49 – 1.60 (2H, m, CH_2), 2.36 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, CH_2), 2.86 (1H, ddt, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 8.1 Hz, $^{5}J_{H,H}$= 0.6 Hz, C^{4}H), 3.33 (1H, ddt, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 10.8 Hz, $^{5}J_{H,H}$= 0.9 Hz, C^{4}H), 5.51 (1H, dd, $^{3}J_{H,H}$= 10.8 Hz, $^{3}J_{H,H}$= 8.1 Hz, HCO), 6.89 (5H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 13.49, 22.07, 27.10, 28.18, 45.08, 80.92, 125.45, 127.68, 128.38, 141.18, 158.33.

Spectral data are consistent with reported in the literature [130].

3,5-Dibutyl-4,5-dihydroisoxazole 4t

Yellowish oil. Yield 64 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.82 – 0.88 (6H, m, 2×CH_3), 1.22 – 1.31 (6H, m, 3×CH_2) 1.40 – 1.65 (4H, m, 2×CH_2), 2.22 – 2.28 (2H, m, CH_2), 2.45 (1H, dd, $^{2}J_{H,H}$= 16.8 Hz, $^{3}J_{H,H}$= 8.1 Hz, C^{4}H), 2.88 (1H, dd, $^{2}J_{H,H}$= 16.8 Hz, $^{3}J_{H,H}$= 10.2 Hz, C^{4}H), 4.36 – 4.48 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 13.46, 13.71, 22.09, 22.31, 27.27, 27.50, 28.25, 34.73, 41.86, 79.79, 158.64.

Spectral data are consistent with reported in the literature [131].

(3-Butyl-4,5-dihydroisoxazol-5-yl)methyl acetate 4u

Colourless oil. Yield 45 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.82 (3H, t, $^{3}J_{H,H}$= 7.5 Hz, CH_3), 1.20 – 1.33 (2H, m, CH_2), 1.39 – 1.50 (2H, m, CH_2), 1.97 (3H, s, H_3CC=O), 2.22 – 2.28 (2H, m, CH_2), 2.63 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 6.9 Hz, C^{4}H), 2.95 (1H, ddt, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 10.5 Hz, $^{5}J_{H,H}$= 0.9 Hz, C^{4}H), 3.97 (1H, dd, $^{2}J_{H,H}$= 11.7 Hz, $^{3}J_{H,H}$= 6.0 Hz, HCOAc), 4.05 (1H, dd, $^{2}J_{H,H}$= 11.7 Hz, $^{3}J_{H,H}$= 4.2 Hz, HCOAc), 4.61 – 4.71 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 13.40, 20.45, 21.96, 26.87, 28.12, 39.01, 64.81, 76.47, 158.39, 170.46.

(3-Hexyl-4,5-dihydroisoxazol-5-yl)methanol 4v

Colourless oil. Yield 46 %.

IR (ν, cm^{-1}): 3395 (OH). ^{1}H NMR (300 MHz, $CDCl_3$): 0.81 – 0.86 (3H, m, CH_3), 1.22 – 1.33 (6H, m, 3×CH_2), 1.46 – 1.55 (2H, m, CH_2), 2.29 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, CH_2), 2.64 - 2.83 (2H, m, C^{4}H, OH), 2.93 (1H, dd, $^{2}J_{H,H}$= 16.8 Hz, $^{3}J_{H,H}$= 10.5 Hz, C^{4}H), 3.52 (1H, dd, $^{2}J_{H,H}$= 12.3 Hz, $^{3}J_{H,H}$= 4.8 Hz, HCOH), 3.69 (1H, dd, $^{2}J_{H,H}$= 12.3 Hz, $^{3}J_{H,H}$= 3.3 Hz, HCOH), 4.56 – 4.65 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 13.88, 22.35, 26.15, 27.49, 28.74, 31.29, 38.34, 63.47, 79.76, 159.59.

5-*t*-Butyl-3-hexyl-4,5-dihydroisoxazole 4w

Yellowish oil. Yield 21 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.83 – 0.87 (12H, m, 4×CH_3), 1.23 – 1.33 (6H, m, 3×CH_2) 1.46 – 1.56 (2H, m, CH_2), 2.28 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, CH_2), 2.63 (1H, ddt, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 9.0 Hz, $^{5}J_{H,H}$= 0.6 Hz, C^{4}H), 2.77 (1H, ddt, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 10.8 Hz, $^{5}J_{H,H}$= 0.6 Hz, C^{4}H), 4.21 (1H, dd, $^{3}J_{H,H}$= 10.8 Hz, $^{3}J_{H,H}$= 9.0 Hz, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 13.96, 22.43, 24.98, 26.32, 27.70, 28.83, 31.40, 33.88, 37.55, 87.77, 158.50.

3,5-Dihexyl-4,5-dihydroisoxazole 4x

Brownish solid; m. p. = 48 – 50 °C Yield 42 %.

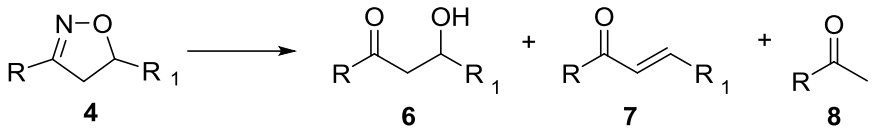
^{1}H NMR (300 MHz, $CDCl_3$): 0.91 – 1.03 (2H, m, CH_2), 1.09 – 1.34 (8H, m, 4×CH_2) 1.38 – 1.49 (1H, m, CH), 1.56 – 1.85 (10H, m, 5×CH_2), 2.33 – 2.42 (1H, m, CH), 2.60 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 8.7 Hz, C^{4}H), 2.84 (1H, ddd, $^{2}J_{H,H}$= 16.8 Hz, $^{3}J_{H,H}$= 10.5 Hz, $^{5}J_{H,H}$= 0.6 Hz, C^{4}H), 4.17 – 4.26 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 25.68, 25.73, 25.86, 26.30, 28.48, 28.51, 30.37, 37.36, 37.71, 42.44 84.02, 162.47.

3,4-Dihexylfuroxane 5a

Yellow oil. Yield 40%.

IR (ν, cm^{-1}): 1601, 1467. ^{1}H NMR (300 MHz, $CDCl_3$): 0.84 – 0.90 (6H, m, 2×CH_3), 1.28 – 1.76 (16H, m, 2×$CH_2\underline{(CH_2)_4}CH_3$), 2.48 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, $\underline{CH_2}(CH_2)_4CH_3$), 2.62 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, $\underline{CH_2}(CH_2)_4CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): 14.16, 14.16, 22.58, 22.663, 22.64, 25.56, 25.82, 26.84, 28.92, 29.01, 31.49, 31.54, 116.22, 158.26. MS: m/z M + H^{+}, found 255.2066. $C_{14}H_{26}N_2O_2$ requires 255.2067.

Reductive cleavage of Δ^2-Isoxazolines



Method A: Reduction with Fe/NH_4Cl

Iron dust (0.27g, 5.0 mmol) was added to the solution of appropriate isoxazoline **4** (0.5 mmol) and ammonium chloride (0.26 g, 5.0 mmol) in ethanol and water mixture (ratio 1:1, 5ml). The resulting solution was refluxed for 6 – 8 hours till full conversion of the starting material (observed by TLC). Then the solvent was evaporated under reduced pressure, residue diluted with chloroform and filtered through silica gel layer, obtained clear solution was washed with water (2×20 ml). The separated organic layer dried with anhydrous Na_2SO_4, evaporated under the reduced pressure and reaction products separated by column chromatography (hexane/ethyl acetate).

Method B: Reduction with $Mo(CO)_6$

The solution of appropriate isoxazoline **4** (0.371 mmol) and $Mo(CO)_6$ (0.074 g, 0.278 mmol) in acetonitrile (3 ml) and water mixture (5 – 6 drops) was refluxed about 2,5 hours till full conversion of starting material (observed by TLC). Then the solvent evaporated in the reduced pressure and the residue purified by column chromatography (hexane/ethyl acetate).

Method C: Reduction with SmI_2

The solution of isoxazoline **4** (0.371 mmol) in absolute THF (10 ml) was degased in the ultrasound bath for 30 min, flushed with Ar, cooled to the 0 °C temperature and then SmI_2 solution in THF (10 ml, 0.1 M, 4 eq.) was added. Another portion of SmI_2 solution (1.25 ml, 0.1 M, 0.5 eq.) was added after 20 min of stirring in ice bath. After another 20 min reaction mixture was flushed with O_2 (the solution changed its color form dark blue to yellow), water solution of $B(OH)_3$ added and reaction mixture stirred for 30 min at room

temperature. Next, THF was evaporated under the reduced pressure; the residue extracted with diethyl ether and washed with water. The organic layer was separated and dried with anhydrous Na_2SO_4, evaporated under the reduced pressure and the residue purified by column chromatography (hexane/ethyl acetate).

Method D: Reduction with Al/$CuCl_2$

To the mixture of the corresponding isoxazoline **4** (1 mmol) and Al dust (0.81 g, 30 mmol) in MeOH (5 ml) a solution of $CuCl_2 \times 2H_2O$ (1.75 g, 10 mmol) in water (5 ml) was added dropwise under vigorous stirring. After the evolution of hydrogen and full consumption of the starting material (observed by TLC, approximately after 5 – 10 min), the mixture was diluted with H_2O (30 ml), and the product was extracted with chloroform (2×30 ml). The organic layer was dried over anhydrous Na_2SO_4, evaporated under the reduced pressure, and the residue purified by column chromatography (hexane/ethyl acetate) to give product.

5-Hydroxytridecan-7-one 6a

Colourless solid; m. p. = 39 – 41 ^{0}C. Method A: yield 50 %, method D: yield 84 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.88 – 0.92 (6H, m, 2×CH_3), 1.28 – 1.59 (14H, m, ($\underline{CH_2}$)$_3$$CH_3$, CH_2($\underline{CH_2}$)$_4$$CH_3$), 2.43 (2H, t, $^3J_{H,H}$= 7.5 Hz, $\underline{CH_2}$(CH_2)$_4$$CH_3$), 2.50 (1H, dd, $^3J_{H,H}$= 17.7 Hz, $^3J_{H,H}$= 9.0 Hz, C^{6}H), 2.61 (1H, dd, $^3J_{H,H}$= 17.7 Hz, $^3J_{H,H}$= 3.0 Hz, C^{6}H), 3.03 (1H, br. s, OH), 4.03 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 14.26, 22.71, 22.86, 23.80, 27.88, 29.06, 31.80, 36.38, 43.90, 49.18, 67.86, 212.92.

Spectral data are consistent with reported in the literature [132].

3-Hydroxy-1-phenylheptan-1-one 6b

Yellowish oil. Method A: yield 36 %, method D: yield 14 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.94 (3H, t, $^{3}J_{H,H}$= 6.9 Hz, CH_3), 1.36 – 1.69 (6H, m, $(\underline{CH_2})_3CH_3$), 3.02 – 3.23 (3H, m, C^2H_2, OH), 4.24 (1H, m, HCO), 7.46 – 7.63 (3H, m, ArH), 7.96 – 7.99 (2H, m, ArH).^{13}C NMR (75 MHz, $CDCl_3$): 14.32, 22.94, 28.01, 36.48, 45.29, 68.00, 128.32, 128.92, 133.77, 137.04, 201.31.

Spectral data are consistent with reported in the literature [133].

3-Hydroxy-4,4-dimethyl-1-phenylpentan-1-one 6c

Colourless oil. Method A: yield 22 %.

^{1}H NMR (300 MHz, $CDCl_3$): 1.02 (9H, s, 3×CH_3), 2.96 – 3.27 (3H, m, CH_2, OH), 3.93 (1H, dd, $^{3}J_{H,H}$= 7.2 Hz, $^{3}J_{H,H}$= 1.8 Hz, HCO), 7.47 – 7.61 (3H, m, ArH), 7.98 – 8.01 (2H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 26.07, 34.64, 40.30, 75.28, 128.36, 128.91, 133.68, 137.30, 201.85.

Spectral data are consistent with reported in the literature [134].

1-(4-Chlorophenyl)-3-hydroxyheptan-1-one 6d

Colourless oil. Method A: yield 16 %.

IR (ν, cm^{-1}): 3452 (OH), 1680 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 0.95 (3H, t, $^{3}J_{H,H}$= 7.2 Hz, CH_3), 1.37 – 1.63 (6H, m, $(\underline{CH_2})_3CH_3$), 3.00 – 3.18 (3H, m, C^2H_2, OH), 4.23 (1H, m, HCO), 7.39 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH), 7.62 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.30, 22.92, 27.99, 36.49, 45.34, 67.95, 129.26, 129.76, 135.40, 140.26, 199.95.

1-(4-Chlorophenyl)-3-hydroxy-4,4-dimethylpentan-1-one 6e

White solid; m. p. = 68 – 70 ^{0}C. Method A: yield 18 %.

IR (ν, cm^{-1}): 3509 (OH), 1673 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 1.01 (9H, s, 3×CH_3), 2.94 – 3.19 (3H, m, CH_2, OH), 3.92 (1H, dd, $^{3}J_{H,H}$= 9.9 Hz, $^{3}J_{H,H}$= 1.8 Hz, HCO), 7.47 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH), 7.93 (2H, d, $^{3}J_{H,H}$= 8.7 Hz,

ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 26.06, 34.66, 40.33, 75.22, 129.22, 129.78, 135.48, 140.13, 200.47.

4-(5-Cyclohexyl-4,5-dihydroisoxazol-3-yl)aniline 4f-2

Yellow oil. Method A: yield 25%, method D: yield 80 %.

^{1}H NMR (300 MHz, DMSO-d_6): 0.93 – 1.23 (5H, m, *c*Hex), 1.38 – 1.49 (1H, m, CH), 1.59 – 1.79 (5H, m, *c*Hex), 2.99 (1H, dd, $^2J_{H,H}$= 16.8 Hz, $^3J_{H,H}$= 8.7 Hz, C^{4}H), 3.23 (1H, dd, $^2J_{H,H}$= 16.8 Hz, $^3J_{H,H}$= 10.2 Hz, C^{4}H), 4.22 – 4.31 (1H, m, CHO), 5.52 (2H, br. s, NH_2), 6.55 (2H, d, $^3J_{H,H}$= 8.4 Hz, ArH), 7.31 (2H, d, $^3J_{H,H}$= 8.4 Hz, ArH). ^{13}C NMR (75 MHz, DMSO-d_6): 25.27, 25.41, 25.94, 28.03, 28.09, 37.34, 41.86, 83.98, 113.37, 116.63, 127.71, 150.45, 156.22.

3-Hydroxy-1-(4-*n*-pentylphenyl)heptan-1-one 6g

Yellowish oil. Method A: yield 24 %.

IR (ν, cm^{-1}): 3477 (OH), 1671 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 0.89 – 0.97 (6H, m, 2×CH_3), 1.33 – 1.71 (12H, m, ($\underline{CH_2}$)$_3$$CH_3$, CH_2($\underline{CH_2}$)$_3$$CH_3$), 2.69 (2H, t, $^3J_{H,H}$= 7.5 Hz, $\underline{CH_2}$(CH_2)$_3$$CH_3$), 3.02 (1H, dd, $^2J_{H,H}$= 17.7 Hz, $^3J_{H,H}$= 9.0 Hz, C^{2}H), 3.19 (1H, dd, $^3J_{H,H}$= 17.7 Hz, $^3J_{H,H}$= 2.7 Hz, C^{2}H), 3.36 (1H, br. s, OH), 4.23 (1H, m, HCO), 7.30 (2H, d, $^3J_{H,H}$= 8.4 Hz, ArH), 7.90 (2H, d, $^3J_{H,H}$= 8.4 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.2, 14.3, 22.7, 22.9, 28.0, 31.0, 31.6, 36.2, 36.4, 45.0, 68.0, 128.4, 128.9, 134.7, 149.6, 201.0.

3-Hydroxy-1-(4-methoxyphenyl)heptan-1-one 6h

Colourless oil. Method A: yield 24 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.90 (3H, t, $^3J_{H,H}$= 7.2 Hz, CH_3), 1.32 – 1.61 (6H, m, 2×CH_2), 2.95 (1H, dd, $^2J_{H,H}$= 17.4 Hz, $^3J_{H,H}$= 9.0 Hz, C^{2}H), 3.03 – 3.14 (2H, m, C^{2}H, OH), 3.85 (3H, s, OCH_3), 4.14 – 4.19 (1H, m, HCO), 6.91 (2H, d, $^3J_{H,H}$= 9.0 Hz, ArH), 7.91 (2H, d, $^3J_{H,H}$= 9.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.00, 22.62, 27.68, 36.17, 44.44, 55.42, 67.80, 113.70, 129.78, 130.32, 163.71, 199.53.

1-(4-Methoxyphenyl)-3-hydroxy-4,4-dimethylpentan-1-one 6i

Yellow oil. Method A: yield 26 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.98 (9H, s, 3×CH_3), 2.84 – 2.93 (2H, m, C^{2}H, OH), 3.17 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 1.8 Hz, C^{2}H), 3.84 – 3.88 (4H, m, CHO, OCH_3), 6.93 (2H, d, $^{3}J_{H,H}$= 9.0 Hz, ArH), 7.94 (2H, d, $^{3}J_{H,H}$= 9.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.80, 34.33, 39.44, 55.46, 75.11, 113.73, 130.38, 130.76, 163.71, 200.12.

3-Cyclohexyl-3-hydroxy-1-(4-methoxyphenyl)propan-1-one 6j

Pink solid; m. p. = 63 – 65 ^{0}C. Method A: yield 31 %.

^{1}H NMR (300 MHz, $CDCl_3$): 1.03 – 1.23 (5H, m, *c*Hex), 1.38 – 1.49 (1H, m, *c*Hex), 1.64 – 1.79 (4H, m, *c*Hex), 1.86 – 1.94 (1H, m, CH), 2.87 – 3.00 (2H, m, C^{2}H, OH), 3.12 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 2.4 Hz, C^{2}H), 3.84 (3H, s, OCH_3), 3.91 – 3.97 (1H, m, CHO), 6.91 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH), 7.92 (2H, d, $^{3}J_{H,H}$= 9.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 26.07, 26.18, 26.42, 28.30, 28.94, 41.51, 43.01, 55.40, 71.87, 113.68, 129.93, 130.32, 163.68, 199.87.

3-Cyclohexyl-3-hydroxy-1-(3,4-methylendioxyphenyl)propan-1-one 6k

Yellow oil. Method A: yield 43 %.

^{1}H NMR (300 MHz, $CDCl_3$): 1.04 – 1.32 (5H, m, *c*Hex), 1.39 – 1.46 (1H, m, *c*Hex), 1.65 – 1.80 (4H, m, *c*Hex), 1.86 – 1.94 (1H, m, CH), 2.65 (1H, br. s, OH), 2.94 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 9.3 Hz, C^{2}H), 3.09 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 2.7 Hz, C^{2}H), 3.91 – 3.97 (1H, m, CHO), 6.03 (2H, s, OCH_2O), 6.83 (1H, d, $^{3}J_{H,H}$= 8.4 Hz, ArH), 7.41 (1H, d, $^{4}J_{H,H}$= 1.8 Hz, ArH), 7.55 (1H, dd, $^{3}J_{H,H}$= 8.1 Hz, $^{4}J_{H,H}$= 1.8 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 26.09, 26.20, 26.44, 28.32, 28.96, 41.74, 43.02, 71.87, 101.87, 107.72, 107.83, 124.49, 131.76, 148.18, 152.02, 154.12, 199.31.

***(E)*-6-Hydroxydec-2-en-4-one 6l**

Colourless oil. Method A: yield 5 %, method B: yield 38 %, method C: yield 20 %.

IR (ν, cm^{-1}): 3448 (OH), 1664 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 0.85 – 0.95 (3H, m, CH_3), 1.20 – 1.47 (6H, m, 3×CH_2), 1.91 (3H, dd, $^{3}J_{H,H}$= 6.8 Hz, $^{4}J_{H,H}$= 1.6 Hz, CH_3), 2.59 (1H, dd, $^{2}J_{H,H}$= 17.3 Hz, $^{3}J_{H,H}$= 9.0 Hz, $C^{5}H$), 2.74 (1H, dd, $^{2}J_{H,H}$= 17.3 Hz, $^{3}J_{H,H}$= 2.7 Hz, $C^{5}H$), 2.78 (1H, br.s, OH), 4.01 – 4.10 (1H, m, HCO), 6.12 (1H, qd, $^{3}J_{H,H}$= 15.8 Hz, $^{4}J_{H,H}$= 1.6 Hz, =CH), 6.89 (1H, qd, $^{3}J_{H,H}$= 15.8 Hz, $^{3}J_{H,H}$= 6.8 Hz, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.30, 18.61, 22.91, 27.94, 36.44, 46.15, 68.00, 132.49, 144.23, 201.39. HRMS (ES): M + Na^{+}, found 193.1205. $C_{10}H_{18}O_2$ requires, 193.1199.

6-Hydroxydecan-4-one 6l-2

Colourless oil. Method A: yield 5 %, method C: yield 20%, method D: yield 13 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.79 – 0.89 (6H, m, 2×CH_3), 1.30 – 1.40 (6H, m, 3×CH_2), 1.54 (2H, dd, $^{3}J_{H,H}$= 14.8 Hz, $^{3}J_{H,H}$= 7.3 Hz, CH_2), 2.34 (2H, t, $^{3}J_{H,H}$= 7.3 Hz, CH_2), 2.42 (1H, dd, $^{2}J_{H,H}$= 17.5 Hz, $^{3}J_{H,H}$= 8.9 Hz, $C^{5}H$), 2.54 (1H, dd, $^{2}J_{H,H}$= 17.5 Hz, $^{3}J_{H,H}$= 2.9 Hz, $C^{5}H$), 2.85 (1H, br. s, OH), 3.97 – 4.06 (m, 1H, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 13.92, 14.28, 17.33, 22.88, 27.88, 36.38, 45.79, 49.19, 67.87, 212.79.

Spectral data are consistent with reported in the literature [135].

6-Hydroxy-7,7-dimethyloctan-4-one 6m-2

Colourless oil. Method D: yield 71 %.

IR (ν, cm^{-1}): 3493 (OH), 1707 (C=O).^{1}H NMR (300 MHz, $CDCl_3$): 0.85 – 0.92 (12H, m, 4×CH_3), 1.59 (2H, sext, $^{3}J_{H,H}$= 7.2 Hz, CH_2), 2.36 – 2.46 (3H, m, CH_2, $C^{5}H$), 2.58 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 2.1 Hz, $C^{5}H$), 2.80 (1H, br. s,

OH), 3.70 (1H, dd, $^{3}J_{H,H}$= 10.5 Hz, $^{3}J_{H,H}$= 2.1 Hz, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 13.62, 17.02, 25.59, 34.11, 43.97, 45.63, 74.85, 212.87.

***(E)*-1-Cyclohexyl-1-hydroxyhex-4-en-3-one 6n**

Colourless oil. Method B: yield 54 %.

IR (ν, cm^{-1}): 3478 (OH), 1667 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 1.28 – 1.92 (11H, m, *c*Hex), 1.95 (3H, dd, $^{3}J_{H,H}$= 6.8 Hz, $^{4}J_{H,H}$= 1.6 Hz, CH_3), 2.65 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 9.3 Hz, C^{2}H), 2.79 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 2.5 Hz, C^{2}H), 3.16 (1H, br. s, OH), 3.87 (1H, ddd, $^{3}J_{H,H}$= 9.0 Hz, $^{3}J_{H,H}$= 6.0 Hz, $^{3}J_{H,H}$= 2.5 Hz, HCO), 6.16 (1H, dq, $^{3}J_{H,H}$= 15.8 Hz, $^{4}J_{H,H}$= 1.6 Hz, =CH), 6.93 (1H, dq, $^{3}J_{H,H}$= 15.8 Hz, $^{3}J_{H,H}$= 6.8 Hz, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 18.60, 26.37, 26.48, 26.74, 28.60, 29.17, 43.28, 43.33, 72.10, 132.54, 144.08, 201.18. HRMS (ES): M + Na^{+}, found 219.1383. $C_{12}H_{20}O_2$ requires, 219.1356.

***(E)*-5-Hydroxy-1-phenylnon-1-en-3-one 6o**

Yellow oil. Method A: yield 20 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.92 (3H, t, $^{3}J_{H,H}$= 6.9 Hz, CH_3), 1.28 – 1.41 (4H, m, 2×CH_2), 1.49 – 1.63 (2H, m, CH_2), 2.75 – 2.83 (2H, m, C^{4}H, OH), 2.93 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 2.7 Hz, C^{4}H), 4.13 – 4.21 (1H, m, HCO), 6.76 (1H, d, $^{3}J_{H,H}$= 16.2 Hz, =CH), 7.42 – 7.45 (3H, m, ArH), 7.57 – 7.63 (3H, m, =CH, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.35, 22.95, 27.98, 36.49, 47.09, 68.13, 126.59, 128.68, 129.28, 131.06, 134.43, 143.84, 201.37.

Spectral data are consistent with reported in the literature [29].

***(E)*-5-Cyclohexyl-5-hydroxy-1-phenylpent-1-en-3-one 6q**

Yellowish oil. Method A: yield 20 %, method B: yield 38 %.

^{1}H NMR (300 MHz, $CDCl_3$): 1.10 – 1.33 (5H, m, *c*Hex), 1.41 – 1.51 (1H, m, *c*Hex), 1.69 – 1.84 (4H, m, *c*Hex), 1.90 – 1.98 (1H, m, CH), 2.80 (1H, dd,

$^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 9.3 Hz, C^{4}H), 2.92 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 2.7 Hz, C^{4}H), 3.19 (1H, d, $^{3}J_{H,H}$= 3.6 Hz, OH), 3.91 – 3.98 (1H, m, HCO), 6.78 (1H, d, $^{3}J_{H,H}$= 16.2 Hz, =CH), 7.42 – 7.44 (3H, m, ArH), 7.57 – 7.63 (3H, m, ArH, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 26.39, 26.50, 26.75, 28.61, 29.23, 43.35, 44.35, 72.22, 126.69, 128.66, 128.79, 129.26, 131.00, 134.49, 143.66, 201.64.

Spectral data are consistent with reported in the literature [29].

***(E)*-5-Cyclohexyl-5-hydroxy-1-(4-methoxyphenyl)pent-1-en-3-one 6r**

Brownish oil. Method B: yield 29 %.

IR (ν, cm^{-1}): 3443 (OH), 1599 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 1.15 – 1.87 (10H, m, *c*Hex), 1.89 – 1.96 (1H, m, CH), 2.77 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 9.3 Hz, C^{4}H), 2.90 (1H, dd, $^{2}J_{H,H}$= 17.1 Hz, $^{3}J_{H,H}$= 2.6 Hz, C^{4}H), 3.30 (1H, br. s, OH), 3.87 (3H, s, OCH_3), 3.89 – 3.95 (1H, m, HCO), 6.66 (1H, d, $^{3}J_{H,H}$= 16.2 Hz, =CH), 6.94 (2H, d, $^{3}J_{H,H}$= 9.0 Hz, ArH), 7.52–7.59 (3H, m, ArH, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 26.39, 26.51, 26.76, 28.63, 29.22, 43.34, 44.08, 55.67, 72.32, 114.72, 124.28, 127.13, 130.43, 143.51, 162.06, 201.67. HRMS (ES): M + Na^{+}, found 311.1601 $C_{18}H_{24}O_3$ requires, 311.1618.

1-Hydroxy-1-phenyl-heptan-3-one 6s

Yellowish oil. Method D: yield 72 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.89 (3H, t, $^{3}J_{H,H}$= 7.2 Hz, CH_3), 1.24 – 1.36 (2H, m, CH_2), 1.50 – 1.61 (2H, m, CH_2), 2.42 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, CH_2), 2.77 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 3.9 Hz, C^{2}H), 2.85 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 8.4 Hz, C^{2}H), 3.15 (1H, br. s, OH), 5.14 (1H, dd, $^{3}J_{H,H}$= 8.7 Hz, $^{3}J_{H,H}$= 3.9 Hz, HCO), 7.24–7.35 (5H, m, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 13.77, 22.18, 25.55, 43.36, 50.93, 69.86, 125.55, 127.55, 128.45, 142.78, 211.66.

Spectral data are consistent with reported in the literature [136].

7-Hydroxyundecan-5-one 6t

Colourless oil. Method D: yield 52 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.87 – 0.92 (6H, m, 2×CH_3), 1.25 – 1.60 (10H, m, 5×CH_2), 2.39 – 2.52 (4H, m, CH_2, C^{6}H, OH), 2.60 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 3.3 Hz, C^{6}H), 3.98 – 4.06 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 13.79, 14.00, 22.25, 22.61, 25.69, 27.62, 36.12, 43.37, 48.90, 67.62, 212.63.

Spectral data are consistent with reported in the literature [137].

2-Hydroxy-4-oxooctyl acetate 6u

Colourless oil. Method D: yield 76 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.86 (3H, t, $^{3}J_{H,H}$= 7.2 Hz, CH_3), 1.20 – 1.33 (2H, m, CH_2), 1.46 – 1.56 (2H, m, CH_2), 2.05 (3H, s, H_3CC=O), 2.41 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, CH_2), 2.57 (1H, d, $^{3}J_{H,H}$= 1.5 Hz, C^{3}H), 2.60 (1H, d, $^{3}J_{H,H}$= 4.5 Hz, C^{3}H), 3.19 (1H, br. s, OH), 4.00 (1H, dd, $^{2}J_{H,H}$= 11.4 Hz, $^{3}J_{H,H}$= 6.0 Hz, C^{1}H), 4.06 (1H, dd, $^{2}J_{H,H}$= 11.4 Hz, $^{3}J_{H,H}$= 4.2 Hz, C^{1}H), 4.22 – 4.30 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 13.69, 20.73, 22.10, 25.48, 43.23, 45.12, 65.77, 67.16, 170.97, 210.79.

1,3-Dicyclohexyl-3-hydroxypropan-1-one 6x

Colourless oil. Method D: yield 89 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.94 – 1.38 (11H, m, *c*Hex), 1.60 – 1.84 (10H, m, *c*Hex), 2.26 – 2.35 (1H, m, CH), 2.49 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 9.3 Hz, C^{2}H), 2.61 (1H, dd, $^{2}J_{H,H}$= 17.4 Hz, $^{3}J_{H,H}$= 2.7 Hz, C^{2}H), 3.11 (1H, br. s, OH), 3.72 – 3.78 (1H, m, HCO). ^{13}C NMR (75 MHz, $CDCl_3$): 25.50, 25.71, 26.02, 26.13, 26.39, 28.23, 28.80, 42.90, 43.87, 51.40, 71.59, 215.95.

Spectral data are consistent with reported in the literature [138].

***(E)*-1-(4-Chlorophenyl)-4,4-dimethylpent-2-en-1-one 7e**

Yellow solid; m. p. = 60 – 61 ^{0}C. Method A: yield 20%.

^{1}H NMR (300 MHz, $CDCl_3$): 1.17 (9H, s., 3×CH_3), 6.76 (1H, d, $^{3}J_{H,H}$= 15.6 Hz, =CH), 7.10 (1H, d, $^{3}J_{H,H}$= 15.6 Hz, =CH), 7.46 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH), 7.90 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 28.97, 34.53, 120.72, 129.06, 130.20, 136.72, 139.21, 160.49, 190.45.

Spectral data are consistent with reported in the literature [139].

***(E)*-1-(4-*n*-Pentylphenyl)hept-2-en-1-one 7g**

Yellowish oil. Method A: yield 8%.

IR (ν, cm^{-1}): 1699 (C=O). ^{1}H NMR (300 MHz, $CDCl_3$): 0.90 – 0.98 (6H, m, 2×CH_3), 1.34 – 1.68 (10H, m, $CH_2(\underline{CH_2})_2CH_3$, $CH_2(\underline{CH_2})_3CH_3$), 2.35 (2H, m, $\underline{CH_2}(CH_2)_2CH_3$), 2.69 (2H, t, $^{3}J_{H,H}$= 7.8 Hz, $\underline{CH_2}(CH_2)_3CH_3$), 6.91 (1H, dt, $^{3}J_{H,H}$= 15.3 Hz, $^{4}J_{H,H}$= 1.5 Hz, =CH), 7.09 (1H, dt, $^{3}J_{H,H}$= 15.3 Hz, $^{3}J_{H,H}$= 6.9 Hz, =CH), 7.30 (2H, d, $^{3}J_{H,H}$= 8.4 Hz, ArH), 7.89 (2H, d, $^{3}J_{H,H}$= 8.4 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.15, 14.28, 22.60, 22.77, 30.58, 31.11, 31.70, 32.81, 36.23, 126.06, 128.82, 128.93, 135.83, 148.59, 149.83, 190.79.

***(E)*-3-Cyclohexyl-1-(4-methoxyphenyl)prop-2-en-1-one 7j**

Red solid; m. p. = 57 – 59 ^{0}C. Method A: yield 37 %.

^{1}H NMR (300 MHz, $CDCl_3$): 1.15 – 1.34 (5H, m, *c*Hex), 1.64 – 1.84 (5H, m, *c*Hex), 2.18 – 2.27 (1H, m, CH), 3.85 (3H, s, OCH_3), 6.82 (1H, dd, $^{3}J_{H,H}$= 15.3 Hz, $^{4}J_{H,H}$= 1.2 Hz, =CH), 6.90 – 7.02 (3H, m, =CH, ArH), 7.93 (2H, d, $^{3}J_{H,H}$= 9.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.71, 25.91, 31.85, 40.93, 55.37, 113.62, 122.92, 127.96, 130.72, 153.77, 163.15, 189.48.

***(E)*-3-Cyclohexyl-1-(3,4-methylendioxyphenyl)prop-2-en-1-one 7k**

Orange solid; m. p. = 56 – 59 ^{0}C. Method A: yield 36 %.

^{1}H NMR (300 MHz, $CDCl_3$): 1.18 – 1.34 (5H, m, *c*Hex), 1.65 – 1.84 (5H, m, *c*Hex), 2.17 – 2.28 (1H, m, CH), 6.03 (2H, s, OCH_2O), 6.77 (1H, dd, $^{3}J_{H,H}$= 15.3 Hz, $^{4}J_{H,H}$= 1.2 Hz, =CH), 6.84 (1H, d, $^{3}J_{H,H}$= 8.1 Hz, ArH), 6.98 (1H, dd, $^{3}J_{H,H}$= 15.3 Hz, $^{3}J_{H,H}$= 6.9 Hz, =CH), 7.43 (1H, d, $^{4}J_{H,H}$= 1.5 Hz, ArH), 7.53 (1H, dd, $^{3}J_{H,H}$= 8.1 Hz, $^{4}J_{H,H}$= 1.5 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 25.72, 25.92, 31.84, 40.96, 101.73, 107.74, 108.42, 122.82, 124.57, 148.08, 151.42, 154.12, 189.04.

4-*n*-Pentylacetophenone 8g

Colourless oil. Method A: yield 27 %.

^{1}H NMR (300 MHz, $CDCl_3$): 0.92 (3H, t, $^{3}J_{H,H}$= 7.2 Hz, CH_3), 1.32 – 1.37 (4H, m, $CH_2CH_2\underline{CH_2}\underline{CH_2}CH_3$), 1.62 – 1.69 (2H, m, $CH_2\underline{CH_2}CH_2CH_2CH_3$), 2.61 (3H, s, CH_3), 2.69 (2H, t, $^{3}J_{H,H}$= 7.5 Hz, $\underline{CH_2}(CH_2)_3CH_3$), 7.30 (2H, d, $^{3}J_{H,H}$= 8.4 Hz, ArH), 7.91 (2H, d, $^{3}J_{H,H}$= 8.4 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 14.27, 22.76, 26.84, 31.08, 31.69, 36.22, 128.72, 128.86, 135.12, 149.10, 198.18.

Spectral data are consistent with reported in the literature [140].

4-Methoxyacetophenone

Yellow oil. Method A: **8h** yield 14 %, **8i** yield 25 %, **8j** yield 7 %. Lit. data [141]: m. p. = 31 – 33 °C.

^{1}H NMR (300 MHz, $CDCl_3$): 2.55 (3H, s, CH_3), 3.86 (3H, s, OCH_3), 6.93 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH), 7.93 (2H, d, $^{3}J_{H,H}$= 8.7 Hz, ArH).

3,4-Methylendioxyacetophenone 8k

Yellow solid; m. p. = 74 – 76 ^{0}C. Method A: yield 8 %. Lit. data [142]: m. p. = 84 – 87 ^{0}C.

^{1}H NMR (300 MHz, $CDCl_3$): 2.54 (3H, s, CH_3), 6.04 (3H, s, OCH_2O), 6.85 (1H, d, $^{3}J_{H,H}$= 8.1 Hz, ArH), 7.43 (1H, d, $^{4}J_{H,H}$= 1.8 Hz, ArH), 7.55 (1H, dd, $^{3}J_{H,H}$= 8.1 Hz, $^{4}J_{H,H}$= 1.8 Hz, ArH).

***(E)*-4-Phenylbut-3-en-2-one 8o/8p**

Yellowish oil. Method A (**8o**): yield 12 %, method B (**8p**): yield 15 %.

^{1}H NMR (300 MHz, $CDCl_3$): 2.43 (3H, s, CH_3), 6.76 (1H, d, $^{3}J_{H,H}$= 16.3 Hz, =CH), 7.41 – 7.47 (3H, m, ArH), 7.52–7.60 (3H, m, ArH, =CH). ^{13}C NMR (75 MHz, $CDCl_3$): 27.81, 127.40, 128.53, 129.24, 130.81, 134.64, 143.78, 198.81.

Spectral data are consistent with reported in the literature [143].

Synthesis of Starting Alkynes 9

3-Phenylprop-2-ynol, **9h** and **9i** were purchased commercially from Sigma-Aldrich and were not purified additionally. Acetylation and benzoylation reactions were performed according literature procedures [144,145] synthesizing **9a**, **9b**, **9s**, prop-2-ynyl acetate, prop-2-ynyl benzoate, but-3-ynyl acetate, pent-4-yn-2-yl acetate, *N*-(prop-2-ynyl)acetamide, *N*-methyl-*N*-(prop-2-ynyl)acetamide. Chlorination of 3-phenylprop-2-ynol synthesizing **9j** was performed according procedure [146]. **9c-g** and **9k-p** and 3-(4-methoxyphenyl)prop-2-ynol were prepared by Sonogashira coupling procedure [147] and as described below. Propargylic phosphates **9t**, **9u** were prepared according procedure [148]. **9v** was prepared according mesylation procedure [149] and **9q** was prepared according benzylation procedure [150].

General procedure for the synthesis of alkynes 9c-g and 9k-p

Under argon atmosphere, the appropriate terminal alkyne (2.1 mmol) was added to a mixture of aryliodide (2.0 mmol), $[PdCl_2(PPh_3)_2]$ (0.28 g, 0.4 mmol) and triethylamine (6mmol) in THF (5 mL). After stirring the resultant mixture at rt for 5 min, copper (I) iodide (38 mg, 0.2 mmol) was added. The mixture was stirred under argon at rt for 1 – 4 h. After completion of the reaction

(observed by TLC), the solvent was evaporated under reduced pressure and the crude residue was purified by flash column chromatography (hexane/ethyl acetate).

Synthesis of *^{18}O-labeled*-3-(4-methoxyphenyl)prop-2-ynyl acetate 9e*

I. $H_2{}^{18}O$ (0.07 mL) was added to the cooled to the 0°C temperature freshly distilled acetyl chloride (0.24 mL, 3.4 mmol) in stirring. After 10 min the mixture was stirred in room temperature for the 0.5 h, then DCM (1 mL) and anhydrous Na_2SO_4 were added to the mixture, filtered from salt with additional wash of it with DCM (2×1 mL).

II. The solution of 3-(4-methoxyphenyl)prop-2-ynol (0.5 g, 3.1 mmol) and DMAP (0.04 g, 0.3 mmol) in DCM (8 mL) was cooled to the 0°C. Then extract of labeled acetic acid prepared in procedure (I) was added to the stirred solution of the alcohol followed by addition of DCC (0.76 g, 3.7 mmol). After 10 min the stirred mixture was warmed to the room temperature and after completion of the reaction (observed by TLC), the mixture was filtered from residues, then the solvent evaporated under reduced pressure and the crude residue purified by flash column chromatography (hexane/ethyl acetate) obtaining yellow oil in 90 % yield.

IR (KBr): ν_{max} = 2233 (C≡C), 1745 (O-C=O), 1714 (O-C=^{18}O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.10 (3H, s, CH_3CO), 3.78 (3H, s, OCH_3), 4.87 (2H, s, CH_2O), 6.81 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.37 (2H, d, $^3J_{H,H}$ = 8.4 Hz, ArH) ppm. ^{13}C NMR (100 Hz, $CDCl_3$) δ: 20.69, 52.87, 55.14, 81.49, 86.37, 113.83, 114.06, 133.38, 159.88, 170.19 (O-C=^{18}O), 170.22 (O-C=O) ppm. HRMS (ES): M + Na^+, found 227.0676 and 229.0720. $C_{12}H_{12}NaO_3$ and $C_{12}H_{12}NaO_2{}^{18}O$ require 227.0679 and 229.0721.

General method for the preparation of compounds 10 – 14

To a stirred solution of alkyne (0.5 mmol) and aldehyde (0.5 mmol) in dry dichloromethane (3 mL), boron trifluoride diethyl etherate (0.071 g, 0.065 mL,

0.5 mmol) was added. Stirring was continued at room temperature till the reaction was completed (monitored by TLC). The mixture was then quenched with sodium bicarbonate solution, and 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.

(*E*)-2-Benzoylbut-2-en-1-yl acetate 10aa

Yellowish oil. Yield 26%.

IR (KBr): ν_{max} = 1737 (O-C=O), 1653 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.03 (3H, d, $^3J_{H,H}$ = 6.9 Hz, C^4H_3), 2.08 (3H, s, $COCH_3$), 5.05 (2H, s, OCH_2), 6.63 (1H, q, $^3J_{H,H}$ = 6.9 Hz, =CH), 7.46 – 7.59 (3H, m, ArH), 7.69 – 7.72 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.02, 21.11, 58.53, 128.49, 129.65, 132.26, 136.81, 138.19, 145.56, 171.25, 196.99 ppm. Elemental analysis: found C 71.88 %, H 6.21 %, $C_{13}H_{14}O_3$ requires C 71.54 %, H 6.47 %.

^{18}O-labeled*-(*E*)-2-benzoylbut-2-enyl acetate 10aa

Yellowish oil. Yield 28 %.

IR (KBr): ν_{max} = 1738 (O-C=O), 1708 (O-C=O^{18}), 1652 (C=O), 1646 (C=O^{18}) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.02 (3H, d, $^3J_{H,H}$ = 7.2 Hz, CH_3), 2.07 (3H, s, CH_3CO), 5.04 (2H, s, CH_2OAc), 6.62 (1H, q, $^3J_{H,H}$ = 7.2 Hz, =CH), 7.45 (2H, t, $^3J_{H,H}$ = 8.0 Hz, ArH), 7.55 (1H, t, $^3J_{H,H}$ = 7.6 Hz, ArH), 7.68 – 7.71 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.74, 20.83, 58.18, 128.23, 129.38, 131.99, 136.58, 137.95, 145.22, 170.91 (O-C=O^{18}), 170.94 (O-C=O), 196.66 (C=O^{18}), 196.71 (C=O) ppm. HRMS (ES): M + Na^+, found 241.0836 and 243.0878. $C_{13}H_{14}NaO_3$ and $C_{13}H_{14}NaO_2{}^{18}O$ require 241.0841 and 243.0883.

(*E*)-2-Benzoylhex-2-en-1-yl acetate 10ab

Colourless oil. Yield 7%.

IR (KBr): ν_{max} = 1738 (O-C=O), 1655 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.98 (3H, t, $^3J_{H,H}$ = 7.5 Hz, $CH_2CH_2\underline{CH_3}$), 1.52 (2H, sex, $^3J_{H,H}$ = 7.5 Hz, $CH_2\underline{CH_2}CH_3$), 2.07 (3H, s, $COCH_3$), 2.39 (2H, q, $^3J_{H,H}$ = 7.5 Hz, $\underline{CH_2}CH_2CH_3$), 5.03 (2H, s, OCH_2), 6.51 (1H, t, $^3J_{H,H}$ = 7.5 Hz, =CH), 7.45 – 7.57 (3H, m, ArH), 7.70 – 7.73 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.11, 21.14, 22.28, 31.17, 58.83, 128.50, 129.72, 132.31, 135.77, 138.20, 150.45, 171.22, 197.13 ppm.

(*E*)-2-Benzoylhept-2-en-1-yl acetate 10ac

Yellowish oil. Yield 21%.

IR (KBr): ν_{max} = 1739 (O-C=O), 1653 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.94 (3H, t, $^3J_{H,H}$ = 7.2 Hz, $CH_2CH_2CH_2\underline{CH_3}$), 1.37 – 1.47 (4H, m, $CH_2\underline{CH_2}\underline{CH_2}CH_3$), 2.07 (3H, s, $COCH_3$), 2.42 (2H, q, $^3J_{H,H}$ = 7.5 Hz, $\underline{CH_2}CH_2CH_2CH_3$), 5.03 (2H, s, OCH_2), 6.52 (1H, t, $^3J_{H,H}$ = 7.5 Hz, =CH), 7.45 - 7259 (3H, m, ArH), 7.70 – 7.74 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.08, 21.14, 22.70, 29.00, 31.12, 58.83, 128.49, 129.72, 132.28, 135.58, 138.22, 150.68, 171.20, 197.12 ppm. Elemental analysis: found C 74.51%, H 7.61%, $C_{16}H_{20}O_3$ requires C 73.82 %, H 7.74 %.

(*E*)-2-Benzoyldec-2-en-1-yl acetate 10ad

Yellow oil. Yield 6%.

IR (KBr): ν_{max} = 1741 (O-C=O), 1654 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.90 (3H, t, $^3J_{H,H}$ = 7.2 Hz, $CH_2(CH_2)_5\underline{CH_3}$), 1.28 – 1.47 (10H, m, $CH_2(\underline{CH_2})_5CH_3$), 2.07 (3H, s, $COCH_3$), 2.40 (2H, q, $^3J_{H,H}$ = 7.5 Hz, $\underline{CH_2}(CH_2)_5CH_3$), 5.02 (2H, s, OCH_2), 6.51 (1H, t, $^3J_{H,H}$ = 7.5 Hz, =CH), 7.43 – 7.59 (3H, m, ArH), 7.69 – 7.73 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.31, 21.13, 22.83, 29.00, 29.27, 29.31, 29.57, 31.93, 58.82,

128.49, 129.72, 132.28, 135.55, 138.22, 150.79, 171.18, 197.10 ppm. Elemental analysis: found C 73.29%, H 8.44%, $C_{19}H_{26}O_3$ requires C 75.46 %, H 8.67 %.

(*E*)-2-Benzoyloctadec-2-en-1-yl acetate 10ae

White solid; m.p. = 21°C. Yield 37%.

IR (KBr): ν_{max} = 1739 (O-C=O), 1657 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.90 (3H, t, $^3J_{H,H}$ = 6.9 Hz, $CH_2(CH_2)_{13}\underline{CH_3}$), 1.28 – 1.48 (26H, m, $CH_2(\underline{CH_2})_{13}CH_3$), 2.07 (3H, s, $COCH_3$), 2.39 (2H, q, $^3J_{H,H}$ = 7.5 Hz, $\underline{CH_2}(CH_2)_{13}CH_3$), 5.03 (2H, s, OCH_2), 6.52 (1H, t, $^3J_{H,H}$ = 7.5 Hz, =CH), 7.42 – 7.59 (3H, m, ArH), 7.70 – 7.74 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.37, 21.13, 22.94, 24.93, 29.01, 29.32, 29.50, 29.63, 29.76, 29.86, 29.91, 29.94, 32.17, 34.21, 58.85, 128.49, 129.73, 132.29, 135.53, 138.22, 150.82, 179.72, 197.15 ppm.

(*E*)-2-Benzoyl-3-cyclohexylallyl acetate 10af

Yellowish oil. Yield 49%.

IR (KBr): ν_{max} = 1738 (O-C=O), 1657 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.04–1.38 (5H, m, *c*Hex), 1.60–1.75 (5H, m, *c*Hex), 2.01 (3H, s, $COCH_3$), 2.49–2.63 (1H, m, *c*Hex), 4.98 (2H, s, CH_2OAc), 6.26 (1H, d, $^3J_{H,H}$ = 10.2 Hz, =CH), 7.41 (2H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.51 (1H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.66 (2H, d, $^3J_{H,H}$ = 6.9 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.81, 25.15, 25.54, 32.11, 32.18, 32.21, 38.21, 58.77, 128.10, 129.44, 131.94, 133.05, 137.83, 154.79, 170.82, 196.92 ppm. HRMS (ES): M + Na^+, found 309.1449. $C_{18}H_{22}NaO_3$ requires 309.1461.

(*E*)-2-Benzoyl-4-ethylhex-2-enyl acetate 10ag

Yellowish oil. Yield 39%.

IR (KBr): ν_{max} = 1740 (O-C=O), 1655 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.87 (6H, t, $^3J_{H,H}$ = 7.5 Hz, $CH(CH_2\underline{CH_3})_2$), 1.18–1.33 (2H, m,

CH(CH$_2$CH$_3$)(CH$_2$CH$_3$)), 1.46– 1.60 (2H, m, CH(CH$_2$CH$_3$)(CH$_2$CH$_3$)), 2.01 (3H, s, COCH$_3$), 2.39–2.51 (1H, m, CH(CH$_2$CH$_3$)$_2$), 4.98 (2H, s, CH$_2$OAc), 6.15 (1H, d, $^3J_{H,H}$ = 10.5 Hz, =CH), 7.42 (2H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.52 (1H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.67–7.70 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ: 11.87, 20.80, 27.58, 42.76, 58.83, 128.16, 129.36, 131.97, 135.58, 137.92, 154.39, 170.77, 196.81 ppm. HRMS (ES): M + Na$^+$, found 297.1463. $C_{17}H_{22}NaO_3$ requires 297.1461.

(*E*)-2-Benzoyl-3-phenylallyl acetate 10ah

Yellowish oil . Yield 24%.

IR (KBr): ν_{max} = 1739 (O-C=O), 1652 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 2.05 (3H, s, COCH$_3$), 5.15 (2H, s, CH$_2$OAc), 7.37 (1H, s, =CH), 7.38–7.43 (5H, m, ArH), 7.47 (2H, t, $^3J_{H,H}$ = 7.2 Hz, ArH), 7.57 (1H, t, $^3J_{H,H}$ = 6.9 Hz, ArH), 7.81–7.84 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ: 20.77, 59.79, 128.27, 128.65, 129.26, 129.46, 129.53, 132.25, 134.01, 134.95, 137.57, 145.15, 170.64, 196.87 ppm. HRMS (ES): M + Na$^+$, found 303.0993. $C_{18}H_{16}NaO_3$ requires 303.0992.

(*E*)-2-Benzoyl-3-(2-fluorophenyl)allyl acetate 10ai

Yellowish oil. Yield 51%.

IR (KBr): ν_{max} = 1741 (O-C=O), 1657 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 2.00 (3H, s, COCH$_3$), 5.09 (2H, s, CH$_2$OAc), 7.07–7.13 (1H, m, ArH), 7.20 (1H, td, $^3J_{H,H}$ = 7.65 Hz, $^4J_{H,H}$ = 3.9 Hz, ArH), 7.37–7.44 (3H, m, =CH, ArH), 7.48 (2H, t, $^3J_{H,H}$ = 7.35 Hz, ArH), 7.58 (1H, t, $^3J_{H,H}$ = 7.35 Hz, ArH), 7.84–7.87 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, CDCl$_3$) δ: 20.69, 60.04, 115.71 (d, $^2J_{C,F}$ = 21.45 Hz), 122.18 (d, $^2J_{C,F}$ = 13.80 Hz), 124.25 (d, $^4J_{C,F}$ = 3.67 Hz), 128.38, 129.66, 130.16 (d, $^3J_{C,F}$ = 2.40 Hz), 131.28 (d, $^3J_{C,F}$ = 8.40 Hz), 132.58, 136.73, 137.01, 137.27, 160.19 (d, $^1J_{C,F}$ = 248.92 Hz), 170.56, 196.36 ppm. HRMS (ES): M + Na$^+$, found 321.0881. $C_{18}H_{15}FNaO_3$ requires 321.0897.

^{18}*O-labeled*-(*E*)-2-benzoyl-3-(2-fluorophenyl)allyl acetate 10ai*

Yellowish oil. Yield 37 %.

IR (KBr): ν_{max} = 1740(O-C=O), 1711 (O-C=O^{18}), 1655 (C=O), 1648 (C=O^{18}) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.00 (3H, s, $COCH_3$), 5.09 (2H, s, CH_2OAc), 7.08 – 7.13 (1H, m, ArH), 7.20 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 0.8 Hz, ArH), 7.35 – 7.43 (3H, m, =CH, ArH), 7.48 (2H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.58 (1H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.84 – 7.87 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.69, 60.06 (d, $^{5}J_{C,F}$ = 1.2 Hz), 115.72 (d, $^{2}J_{C,F}$ = 21.4 Hz), 122.19 (d, $^{2}J_{C,F}$ = 13.8 Hz), 124.25 (d, $^{4}J_{C,F}$ = 3.7 Hz), 128.39, 129.67, 130.17 (d, $^{3}J_{C,F}$ = 2.3 Hz), 131.28 (d, $^{3}J_{C,F}$ = 8.3 Hz), 132.58, 136.66, 136.70, 136.71, 137.04, 137.29, 160.20 (d, $^{1}J_{C,F}$ = 248.7 Hz), 170.52 (O-C=O^{18}), 170.56 (O-C=O), 196.42 (C=O^{18}), 196.46 (C=O) ppm. HRMS (ES): M + Na^+, found 321.0898 and 323.0939. $C_{18}H_{15}FNaO_3$ and $C_{18}H_{15}FNaO_2O^{18}$ require 321.0897 and 323.0945.

(*E*)-2-Benzoyl-3-(4-fluorophenyl)allyl acetate 10aj

Yellowish oil. Yield 16%.

IR (KBr): ν_{max} = 1739 (O-C=O), 1651 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.06 (3H, s, $COCH_3$), 5.11 (2H, s, CH_2OAc), 7.08–7.14 (2H, m, ArH), 7.31 (1H, s, =CH), 7.37–7.42 (2H, m, ArH), 7.48 (2H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.58 (1H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.79–7.82 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.81, 59.74, 115.92 (d, $^{2}J_{C,F}$ = 21.6 Hz), 128.38, 129.57, 130.24 (d, $^{4}J_{C,F}$ = 3.4 Hz), 131.40 (d, $^{3}J_{C,F}$ = 8.4 Hz), 132.36, 134.98, 137.60, 143.87, 163.26 (d, $^{1}J_{C,F}$ = 249.6 Hz), 170.68, 196.80 ppm. HRMS (ES): M + Na^+, found 321.0874. $C_{18}H_{15}FNaO_3$ requires 321.0897.

(*E*)-2-Benzoyl-3-(2-chlorophenyl)allyl acetate 10ak

Yellow oil. Yield 26%.

IR (KBr): ν_{max} = 1740 (O-C=O), 1652 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.99 (3H, s, $COCH_3$), 5.02 (2H, s, CH_2OAc), 7.30–7.35 (4H, m, ArH), 7.42 (1H, s, =CH), 7.49 (2H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.59 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.89–7.92 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.69, 59.83, 127.49, 128.40, 129.63, 129.76, 130.12, 130.38, 132.71, 132.87, 133.93, 136.57, 137.13, 141.00, 170.65, 196.50 ppm. HRMS (ES): M + Na^{+}, found 337.0607. $C_{18}H_{15}ClNaO_3$ requires 337.0602.

(*E*)-2-Benzoyl-3-(4-chlorophenyl)allyl acetate 10al

Yellowish oil . Yield 21%.

IR (KBr): ν_{max} = 1740 (O-C=O), 1651 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.05 (3H, s, $COCH_3$), 5.10 (2H, s, CH_2OAc), 7.28 (1H, s, =CH), 7.31–7.41 (4H, m, ArH), 7.48 (2H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.58 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.79–7.82 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.80, 59.69, 128.39, 129.00, 129.58, 130.61, 132.45, 132.50, 135.60, 137.47, 143.44, 170.64, 196.68 ppm. HRMS (ES): M + Na^{+}, found 337.0603. $C_{18}H_{15}ClNaO_3$ requires 337.0602.

(*E*)-2-Benzoyl-3-(2,4-dichlorophenyl)allyl acetate 10am

Yellowish oil. Yield 46%.

IR (KBr): ν_{max} = 1738 (O-C=O), 1659 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.99 (3H, s, $COCH_3$), 5.00 (2H, s, CH_2OAc), 7.31–7.32 (3H, m, =CH, ArH), 7.45–7.52 (3H, m, ArH), 7.59 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.89 (2H, d, $^{3}J_{H,H}$ = 6.9 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.65, 59.67, 127.23, 128.42, 129.56, 129.71, 130.83, 131.39, 132.78, 134.67, 135.67, 136.94, 137.18, 139.30, 170.41, 196.07 ppm. HRMS (ES): M + H^{+}, found 349.0381. $C_{18}H_{15}Cl_2O_3$ requires 349.0393.

^{18}O-labeled*-(*E*)-2-benzoyl-3-(2,4-dichlorophenyl)allyl acetate 10am

Yellowish oil. Yield 39 %.

IR (KBr): ν_{max} = 1738 (O-C=O), 1714 (O-C=O^{18}), 1659 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.00 (3H, s, CH_3CO), 5.01 (2H, s, CH_2OAc), 7.32 – 7.33 (3H, m, =CH, ArH), 7.46 – 7.52 (3H, m, ArH), 7.58 – 7.62 (1H, m, ArH), 7.89 - 7.91 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.68, 59.71, 127.28, 128.46, 129.61, 129.75, 130.86, 131.44, 132.83, 134.72, 135.73, 136.99, 137.23, 139.35, 170.43 (O-C=O^{18}), 175.47 (O-C=O), 196.14 (C=O) ppm. HRMS (ES): M + Na^+, found 371.0219 and 373.0252. $C_{18}H_{14}{}^{35}Cl_2NaO_3$ and $C_{18}H_{14}{}^{35}Cl_2NaO_2{}^{18}O$ require 371.0217 and 373.0260.

(*E*)-2-Benzoyl-3-(2-bromophenyl)allyl acetate 10an

Yellow oil. Yield 59%.

IR (KBr): ν_{max} = 1741 (O-C=O), 1656 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.99 (3H, s, $COCH_3$), 5.02 (2H, d, $^{4}J_{H,H}$ = 0.3 Hz, CH_2OAc), 7.21–7.27 (1H, m, ArH), 7.33–7.37 (3H, m, ArH, =CH), 7.47–7.52 (2H, m, ArH), 7.57–7.64 (2H, m, ArH), 7.93–7.97 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.70, 59.75, 123.89, 127.42, 128.38, 129.79, 130.19, 130.44, 132.69, 132.78, 134.78, 136.40, 137.11, 142.82, 170.50, 196.36 ppm. HRMS (ES): M + Na^+, found 381.0086. $C_{18}H_{15}BrNaO_3$ requires 381.0097.

(*E*)-2-Benzoyl-3-(2-nitrophenyl)allyl acetate 10ar

Yellow oil. Yield 28%.

IR (KBr): ν_{max} = 1736 (O-C=O), 1655 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.93 (3H, s, $COCH_3$), 4.91 (2H, s, CH_2OAc), 7.37 (1H, d, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.49–7.61 (4H, m, ArH), 7.63 (1H, br. s, =CH), 7.70 (1H, td, $^{3}J_{H,H}$ = 7.5 Hz, $^{4}J_{H,H}$ = 1.5 Hz, ArH), 7.98 (2H, d, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 8.23 (1H, dd, $^{3}J_{H,H}$ = 8.1 Hz, $^{4}J_{H,H}$ = 1.2 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.63, 59.56, 125.12, 128.47, 130.65, 130.80, 132.81, 133.83, 136.18, 136.77, 140.77, 147.08, 170.43, 195.96 ppm. HRMS (ES): M + Na^+, found 348.0858. $C_{18}H_{15}NNaO_5$ requires 348.0842.

(*E*)-2-Benzoyl-3-(4-nitrophenyl)allyl acetate 10as

Yellow oil. Yield 48%.

IR (KBr): ν_{max} = 1739 (O-C=O), 1657 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.03 (3H, s, $COCH_3$), 5.08 (2H, s, CH_2OAc), 7.29 (1H, br. s, =CH), 7.49 (2H, t, $^3J_{H,H}$ = 7.2 Hz, ArH), 7.57 (2H, d, $^3J_{H,H}$ = 8.7 Hz, ArH), 7.65 (1H, t, $^3J_{H,H}$ = 7.2 Hz, ArH), 7.82–7.85 (2H, m, ArH), 8.26 (2H, d, $^3J_{H,H}$ = 8.7 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.64, 59.57, 123.82, 128.51, 129.32, 129.60, 129.93, 132.88, 136.81, 138.32, 140.50, 147.77, 170.44, 196.03 ppm. HRMS (ES): M + Na^+, found 348.0854. $C_{18}H_{15}NNaO_5$ requires 348.0842.

(*E*)-2-Benzoyl-3-cyclohexylallyl benzoate 10bf

Yellow solid; m. p. = 66–68^oC . Yield 24%.

IR (KBr): ν_{max} = 1716 (O-C=O), 1651 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.09–1.35 (5H, m, *c*Hex), 1.71–1.75 (5H, m, *c*Hex), 2.62–2.75 (1H, m, *c*Hex), 5.26 (2H, s, CH_2OBz), 6.33 (1H, d, $^3J_{H,H}$ = 9.9 Hz, =CH), 7.37–7.46 (4H, m, ArH), 7.50–7.56 (2H, m, ArH), 7.70–7.74 (2H, m, ArH), 7.97–8.00 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 25.19, 25.59, 32.22, 38.35, 59.34, 128.20, 128.27, 129.53, 129.57, 130.02, 132.02, 132.89, 133.21, 137.96, 154.79, 166.36, 197.06 ppm. HRMS (ES): M + Na^+, found 371.1612. $C_{23}H_{24}NaO_3$ requires 371.1618.

(*E*)-2-Benzoyl-3-(2,4-dichlorophenyl)allyl benzoate 10bm

Yellowish oil . Yield 50%.

IR (KBr): ν_{max} = 1721 (O-C=O), 1658 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 5.28 (2H, d, $^3J_{H,H}$ = 0.6 Hz, CH_2OBz), 7.30 (1H, dd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.1 Hz, ArH), 7.34–7.40 (4H, m, =CH, ArH), 7.44 (1H, d, $^4J_{H,H}$ = 2.1 Hz, ArH), 7.48–7.54 (3H, m, ArH), 7.57–7.63 (1H, m, ArH), 7.88–7.96 (4H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 60.27, 127.30, 128.26, 128.47,

129.52, 129.57, 129.72, 130.81, 131.46, 132.81, 133.04, 134.66, 135.68, 137.01, 137.30, 139.25, 165.92, 196.16 ppm. HRMS (ES): M + Na^+, found 433.0398. $C_{23}H_{16}Cl_2NaO_3$ requires 433.0369.

(*E*)-2-Benzoyl-3-(2-nitrophenyl)allyl benzoate 10br

Yellow oil . Yield 22%.

IR (KBr): ν_{max} = 1715 (O-C=O), 1651 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 5.20 (2H, s, CH_2OBz), 7.35 (2H, t, $^3J_{H,H}$ = 7.2 Hz, ArH), 7.43–7.64 (7H, m, =CH, ArH), 7.69 (1H, td, $^3J_{H,H}$ = 7.5 Hz, $^4J_{H,H}$ = 1.2 Hz, ArH), 7.84–7.87 (2H, m, ArH), 8.00–8.04 (2H, m, ArH), 8.21 (1H, td, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 1.2 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 60.12, 125.21, 128.27, 128.55, 129.49, 129.53, 129.83, 130.76, 130.91, 132.85, 133.05, 133.92, 136.30, 136.89, 140.72, 147.05, 165.94, 196.14 ppm. HRMS (ES): M + K^+, found 426.0738. $C_{23}H_{17}KNO_5$ requires 426.0738.

(*E*)-2-(4-Chlorobenzoyl)-3-cyclohexylallyl acetate 10cf

Yellow oil. Yield 34%.

IR (KBr): ν_{max} = 1739 (O-C=O), 1654 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.09–1.34 (5H, m, *c*Hex), 1.66–1.75 (5H, m, *c*Hex), 2.01 (3H, s, $COCH_3$), 2.49–2.62 (1H, m, *c*Hex), 4.96 (2H, s, CH_2OAc), 6.22 (1H, d, $^3J_{H,H}$ = 10.2 Hz, =CH), 7.39 (2H, d, $^3J_{H,H}$ = 8.7 Hz, ArH), 7.62 (2H, d, $^3J_{H,H}$ = 8.7 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.82, 25.15, 25.54, 32.13, 38.24, 58.74, 128.47, 130.86, 133.03, 136.13, 138.36, 154.78, 170.79, 195.67 ppm. HRMS (ES): M + Na^+, found 343.1073. $C_{18}H_{21}ClNaO_3$ requires 343.1071.

(*E*)-2-(4-Chlorobenzoyl)-3-(4-chlorophenyl)allyl acetate 10cl

Yellow oil. Yield 29%.

IR (KBr): ν_{max} = 1738 (O-C=O), 1651 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.05 (3H, s, $COCH_3$), 5.08 (2H, s, CH_2OAc), 7.23 (1H, br. s, =CH), 7.33 (2H, d, $^3J_{H,H}$ = 8.7 Hz, ArH), 7.39 (2H, d, $^3J_{H,H}$ = 8.7 Hz, ArH), 7.45 (2H,

d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 7.75 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.77, 59.69, 128.75, 129.08, 130.65, 130.99, 132.30, 135.48, 135.70, 135.82, 138.92, 143.29, 170.59, 195.42 ppm. HRMS (ES): M + Na^+, found 371.0206. $C_{18}H_{14}Cl_2NaO_3$ requires 371.0212.

(*E*)-2-(4-Chlorobenzoyl)-3-(2,4-dichlorophenyl)allyl acetate 10cm

White solid; m. p. = 80–82^{o}C. Yield 30%.

IR (KBr): ν_{max} = 1740 (O-C=O), 1662 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.99 (3H, s, $COCH_3$), 4.99 (2H, s, CH_2OAc), 7.28 (1H, br. s, =CH), 7.32 (2H, m, ArH), 7.45–7.49 (3H, m, ArH), 7.84 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.66, 59.64, 127.32, 128.82, 129.65, 130.84, 131.14, 134.72, 135.24, 135.89, 137.02, 139.19, 139.34, 170.40, 194.86 ppm. HRMS (ES): M + Na^+, found 404.9818. $C_{18}H_{13}Cl_3NaO_3$ requires 404.9822.

(*E*)-2-(4-Methoxybenzoyl)but-2-enyl acetate 10ea

Yellow oil . Yield 52 %.

IR (KBr): ν_{max} = 1736 (O-C=O), 1647 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.95 (3H, d, $^{3}J_{H,H}$ = 7.2 Hz, $=CHCH_3$), 1.99 (3H, s, CH_3CO), 3.82 (3H, s, OCH_3), 4.96 (2H, s, CH_2OAc), 6.47 (1H, q, $^{3}J_{H,H}$ = 7.2 Hz, =CH), 6.88 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 7.68 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.78, 21.07, 55.69, 59.01, 113.73, 130.53, 132.08, 136.66, 143.07, 163.21, 171.17, 195.75 ppm. HRMS (ES): M + Na^+, found 271.0929. $C_{14}H_{16}NaO_4$ requires 271.0941.

***^{18}O-labeled*-((*E*)-2-(4-methoxybenzoyl)but-2-enyl acetate 10e*a**

Yellow oil. Yield 46 %.

IR (KBr): ν_{max} = 1737 (O-C=O), 1646 (C=O), 1600 ($C=O^{18}$) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.95 (3H, d, $^{3}J_{H,H}$ = 7.2 Hz, $=CHCH_3$), 2.00 (3H, s, CH_3CO), 3.83 (3H, s, OCH_3), 4.97 (2H, s, CH_2OAc), 6.48 (1H, q, $^{3}J_{H,H}$ = 7.2

Hz, =CH), 6.89 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.69 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.41, 20.71, 55.34, 58.66, 113.40, 130.22, 131.74, 136.36, 142.64, 162.88, 170.81, 195.35 (C=O^{18}), 195.39 (C=O) ppm. HRMS (ES): M + Na^+, found 271.0944 and 273.0988. $C_{14}H_{16}NaO_4$ and $C_{14}H_{16}NaO_3O^{18}$ require 271.0941 and 273.0989.

(*E*)-3-Cyclohexyl-2-(4-methoxybenzoyl)allyl acetate 10ef

Colorless oil. Yield 37 %.

IR (KBr): ν_{max} = 1738 (O-C=O), 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.07 – 1.19 (3H, m, *c*Hex), 1.27 – 1.38 (2H, m, *c*Hex), 1.65 – 1.74 (5H, m, *c*Hex), 1.99 (3H, s, $OCOCH_3$), 2.49 – 2.59 (1H, m, *c*Hex), 3.84 (3H, s, OCH_3), 4.97 (2H, s, CH_2OCOMe), 6.18 (1H, d, $^{3}J_{H,H}$ = 10.0 Hz, =CH), 6.90 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.70 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.80, 25.20, 25.59, 32.24, 38.05, 55.34, 59.24, 113.40, 130.30, 131.86, 133.00, 152.61, 162.91, 170.82, 195.73 ppm. HRMS (ES): M + Na^+, found 339.1576. $C_{19}H_{24}NaO_4$ requires 339.1567.

(*E*)-4-Ethyl-2-(4-methoxybenzoyl)hex-2-en-1-yl acetate 10eg

Yellowish oil. Yield 22 %.

IR (KBr): ν_{max} = 1737 (O-C=O), 1647 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (6H, t, $^{3}J_{H,H}$ = 7.6 Hz, $CH(CH_2\underline{CH_3})_2$), 1.21 – 1.32 (2H, m, $\underline{CH_2}CH_3$), 1.48 – 1.59 (2H, m, $\underline{CH_2}CH_3$), 2.00 (3H, s, $OCOCH_3$), 2.38 – 2.48 (1H, m, $\underline{CH}(CH_2CH_3)_2$), 3.85 (3H, s, OCH_3), 4.97 (2H, s, CH_2OCOMe), 6.07 (1H, d, $^{3}J_{H,H}$ = 10.8 Hz, =CH), 6.93 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) 7.73 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.92, 20.85, 27.66, 42.63, 55.40, 59.32, 113.45, 130.35, 131.81, 135.53, 152.29, 162.92, 170.85, 195.69 ppm. HRMS (ES): M + Na^+, found 327.1571. $C_{18}H_{24}NaO_4$ requires 327.1567.

(*E*)-3-(2-Fluorophenyl)-2-(4-methoxybenzoyl)allyl acetate 10ei

Yellowish oil. Yield 34 %.

IR (KBr): ν_{max} = 1737 (O-C=O), 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.98 (3H, s, $OCOCH_3$), 3.87 (3H, s, OCH_3), 5.07 (2H, s, CH_2OCOMe), 6.97 (2H, d, 6.18 $^{3}J_{H,H}$ = 9.2 Hz, ArH), 7.07 – 7.12 (1H, m, ArH), 7.19 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 0.8 Hz, ArH), 7.27 (1H, s, =CH), 7.33 – 7.43 (2H, m, ArH), 7.89 (2H, d, $^{3}J_{H,H}$= 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.67, 55.43, 60.46, 113.69, 115.68 (d, $^{2}J_{C,F}$= 21.4 Hz), 122.32 (d, $^{2}J_{C,F}$= 14.0 Hz), 124.21 (d, $^{3}J_{C,F}$= 3.7 Hz), 129.76, 130.20 (d, $^{3}J_{C,F}$= 2.4 Hz), 131.02 (d, $^{4}J_{C,F}$= 8.4 Hz), 132.15, 134.62 (d, $^{3}J_{C,F}$= 3.6 Hz), 137.26, 160.20 (d, $^{1}J_{C,F}$= 248.3 Hz), 163.42, 170.57, 195.06 ppm. HRMS (ES): M + Na^{+}, found 351.1007. $C_{19}H_{17}FNaO_4$ requires 351.1003.

^{18}O-labeled*-(*E*)-2-(4-methoxybenzoyl)-3-(4-nitrophenyl)allyl acetate 10es

Colorless oil. Yield 51 %.

IR (KBr): ν_{max} = 1741 (O-C=O), 1711 (O-C=O^{18}), 1657 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.04 (3H, s, CH_3CO), 3.92 (3H, s, CH_3O), 5.11 (2H, s, CH_2), 7.01 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH), 7.23 (1H, br. s. =CH), 7.59 (2H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.90 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.28 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.72, 55.58, 60.12, 113.91, 123.93, 129.39, 129.95, 132.22, 138.49, 138.77, 140.83, 147.79, 163.75, 170.52 (O-C=O^{18}), 170.56 (O-C=O), 194.79 (C=O) ppm. HRMS (ES): M + Na^{+}, found 378.0945 and 380.1005. $C_{19}H_{17}NNaO_6$ and $C_{19}H_{17}NNaO_5{}^{18}O$ require 378.0954 and 380.0996.

(*E*)-2-Benzoylbut-2-en-1-yl benzoate 10fa

Colourless oil. Yield 22%.

IR (KBr): ν_{max} = 1715 (O-C=O), 1644 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.05 (3H, d, $^{3}J_{H,H}$ = 7.2 Hz, CH_3), 3.85 (3H, s, OCH_3), 5.26 (2H, s,

CH_2OCOPh), 6.54 (1H, q, $^3J_{H,H}$ = 7.2 Hz, =CH), 6.92 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.39 (2H, t, $^3J_{H,H}$ = 7.6 Hz, ArH), 7.52 (1H, t, $^3J_{H,H}$ = 7.6 Hz, ArH), 7.75 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.97 – 7.99 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.63, 55.43, 59.28, 113.49, 129.62, 129.98, 130.35, 131.86, 132.92, 136.56, 142.72, 162.95, 166.43, 195.59 ppm. HRMS (ES): M + Na^+, found 333.1100. $C_{19}H_{18}NaO_4$ requires 333.1097.

(*E*)-3-Cyclohexyl-2-(4-methoxybenzoyl)allyl benzoate 10ff

Yellowish oil. Yield 8 %.

IR (KBr): ν_{max} = 1717 (O-C=O), 1646 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.14 – 1.20 (3H, m, *c*Hex), 1.29 – 1.35 (2H, m, *c*Hex), 1.66 – 1.75 (5H, m, *c*Hex), 2.61 – 2.71 (1H, m, *c*Hex), 3.86 (3H, s, OCH_3), 5.24 (2H, s, CH_2OCOPh), 6.24 (1H, d, $^3J_{H,H}$ = 10.0 Hz, =CH), 6.93 (2H, d, $^3J_{H,H}$ = 7.6 Hz, ArH), 7.39 (2H, t, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.52 (1H, t, $^3J_{H,H}$ = 7.6 Hz, ArH), 7.76 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.97 (2H, d, $^3J_{H,H}$ = 7.6 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.25, 25.64, 32.35, 38.20, 55.43, 59.82, 113.49, 128.28, 129.58, 130.05, 130.43, 131.96, 132.89, 133.12, 152.71, 162.97, 166.40, 195.93 ppm. HRMS (ES): M + Na^+, found 401.1730. $C_{24}H_{26}NaO_4$ requires 401.1723.

(*E*)-4-Ethyl-2-(4-methoxybenzoyl)hex-2-en-1-yl benzoate 10fg

Yellowish oil. Yield 4 %.

IR (KBr): ν_{max} = 1717 (O-C=O), 1647 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (6H, t, $^3J_{H,H}$ = 7.6 Hz, $CH(CH_2\underline{CH_3})_2$), 1.26 – 1.34 (2H, m, $\underline{CH_2}CH_3$), 1.52 – 1.58 (2H, m, $\underline{CH_2}CH_3$), 2.50 – 2.59 (1H, m, $\underline{CH}(CH_2CH_3)_2$), 3.87 (3H, s, OCH_3), 5.24 (2H, s, CH_2OCOMe), 6.13 (1H, d, $^3J_{H,H}$ = 10.4 Hz, =CH), 6.94 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.38 (2H, t, $^3J_{H,H}$ = 7.2 Hz, ArH), 7.52 (1H, t, $^3J_{H,H}$ = 7.2 Hz, ArH), 7.78 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.96 – 7.98 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.99, 27.72, 42.71, 55.45, 59.86, 113.54, 128.28, 129.61, 130.07, 130.50, 131.87, 132.87, 135.64, 152.27,

162.98, 166.34, 195.80 ppm. HRMS (ES): M + Na^+, found 389.1730. $C_{23}H_{26}NaO_4$ requires 389.1723.

(*E*)-3-(2-Chlorophenyl)-2-(4-methoxybenzoyl)allyl benzoate 10fk

Colourless solid m. p. = 94 – 96 ^oC. Yield 33 %.

IR (KBr): ν_{max} = 1715 (O-C=O), 1651 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.88 (3H, s, OCH_3), 5.29 (2H, d, $^4J_{H,H}$ = 0.8 Hz, CH_2OCOPh), 6.99 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.29 – 7.32 (2H, m, ArH), 7.33 – 7.38 (3H, m, ArH, =CH), 7.42 – 7.46 (2H, m, ArH), 7.50 (1H, t, $^3J_{H,H}$ = 7.6 Hz, ArH), 7.88 – 7.90 (2H, m, ArH), 8.01 (2H, d, $^3J_{H,H}$ = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.46, 60.78, 113.76, 126.90, 128.24, 129.56, 129.65, 129.73, 129.76, 130.18, 130.21, 132.28, 132.92, 133.11, 133.94, 136.94, 138.68, 163.53, 166.03, 195.14 ppm. HRMS (ES): M + Na^+, found 429.0859. $C_{24}H_{19}ClNaO_4$ requires 429.0864.

(*E*)-3-Cyclohexyl-1-phenylprop-2-en-1-one 10hf

Yellow oil. Yield 16%.

^1H NMR (300 MHz, $CDCl_3$) δ: 1.19–1.35 (5H, m, *c*Hex), 1.76–1.86 (5H, m, *c*Hex), 2.20–2.30 (1H, m, *c*Hex), 6.83 (1H, dd, $^3J_{H,H}$ = 15.6 Hz, $^4J_{H,H}$ = 1.2 Hz, =CH), 7.01 (1H, dd, $^3J_{H,H}$ = 15.6 Hz, $^3J_{H,H}$ = 6.6 Hz, =CH),7.45 (2H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.55 (1H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.90–7.93 (2H, m, ArH) ppm.

Spectral data are consistent with reported in the literature [151].

(*E*)-3-(2,4-Dichlorophenyl)-1-phenylprop-2-en-1-one 10hm

Yellow solid; m. p. = 69–70^oC. Yield 42%.

^1H NMR (300 MHz, $CDCl_3$) δ: 7.30 (1H, ddd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.1 Hz, $^5J_{H,H}$ = 0.6 Hz, ArH), 7.45–7.54 (4H, m, =CH, ArH), 7.60 (1H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.68 (1H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.99–8.03 (2H, m, ArH), 8.10 (1H, dt, $^3J_{H,H}$ = 15.9 Hz, $^5J_{H,H}$ = 0.6 Hz, =CH) ppm.

Spectral data are consistent with reported in the literature [152].

(*E*)-3-Cyclohexyl-1,2-diphenylprop-2-en-1-one 10if

Yellowish oil. Yield 26%.

IR (KBr): ν_{max} = 1667 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.11–1.18 (5H, m, *c*Hex), 1.63–1.78 (5H, m, *c*Hex), 2.29–2.42 (1H, m, *c*Hex), 6.27 (1H, d, $^{3}J_{H,H}$ = 10.5 Hz, =CH), 7.24–7.28 (2H, m, ArH), 7.32–7.44 (5H, m, ArH), 7.51 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.76–7.80 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 25.14, 25.69, 32.34, 38.29, 127.37, 128.07, 128.19, 129.35, 129.68, 131.85, 136.34, 138.45, 139.43, 150.10, 197.52 ppm. HRMS (ES): M + Na^{+}, found 313.1572. $C_{21}H_{22}NaO$ requires 313.1563.

(*Z*)-2-(Chloromethyl)-1-phenylbut-2-en-1-one 10ja

Colourless oil. Yield 6%.

IR (KBr): ν_{max} = 1679 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.06 (3H, d, $^{3}J_{H,H}$ = 6.9 Hz, CH_3), 4.54 (2H, s, OCH_2), 6.60 (1H, q, $^{3}J_{H,H}$ = 6.9Hz, =CH), 7.44 – 7.71 (5H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.05, 37.11, 128.52, 129.59, 132.28, 138.12, 138.54, 145.33, 196.32 ppm.

(*Z*)-2-(Chloromethyl)-1-phenylhept-2-en-1-one 10jc

Colourless oil. Yield 4%.

IR (KBr): ν_{max} = 1693 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.95 (3H, t, $^{3}J_{H,H}$ = 7.2 Hz, $CH_2CH_2CH_2\underline{CH_3}$), 1.37 – 1.49 (4H, m, $CH_2\underline{CH_2}\underline{CH_2}CH_3$), 2.45 (2H, q, $^{3}J_{H,H}$ = 7.5 Hz, $\underline{CH_2}CH_2CH_2CH_3$), 4.53 (2H, s, OCH_2), 6.48 (1H, t, $^{3}J_{H,H}$ = 7,5 Hz, =CH), 7.45 – 7.73 (5H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.11, 22.79, 29.11, 30.91, 37.42, 128.53, 129.68, 132.36, 137.28, 138.16, 150.42, 196.58.

(*Z*)-2-(Chloromethyl)-3-cyclohexyl-1-phenylprop-2-en-1-one 10jf

Yellow oil. Yield 34%.

IR (KBr): ν_{max} = 1651 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.13–1.38 (5H, m, *c*Hex), 1.68–1.78 (5H, m, *c*Hex), 2.51–2.64 (1H, m, *c*Hex), 4.50 (2H, s, CH_2Cl), 6.24 (1H, d, $^{3}J_{H,H}$ = 9.9 Hz, =CH), 7.43 (2H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.54 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.66–7.70 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 25.22, 25.60, 31.93, 37.41, 38.47, 128.20, 129.49, 132.05, 134.87, 137.88, 154.35, 196.50 ppm. HRMS (ES): M + Na^+, found 285.1013. $C_{16}H_{19}ClNaO$ requires 285.1017.

(*Z*)-2-(Chloromethyl)-1,3-diphenylprop-2-en-1-one 10jh

Yellow oil. Yield 45%.

IR (KBr): ν_{max} = 1651 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.68 (2H, s, CH_2Cl), 7.29 (1H, s, =CH), 7.44–7.61 (8H, m, ArH), 7.81–7.84 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 38.99, 128.33, 128.86, 129.38, 129.59, 129.66, 132.34, 133.99, 136.35, 137.73, 144.36, 196.40 ppm. HRMS (ES): M + Na^+, found 279.0551. $C_{16}H_{13}ClNaO$ requires 279.0547.

(*Z*)-2-(Chloromethyl)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one 10jl

Yellowish oil. Yield 32%.

IR (KBr): ν_{max} = 1651 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.63 (2H, s, CH_2Cl), 7.21 (1H, s, =CH), 7.41–7.51 (6H, m, ArH), 7.59 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.78–7.82 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 38.72, 128.40, 129.17, 129.59, 130.70, 132.40, 132.48, 135.79, 136.80, 137.55, 142.84, 196.16 ppm. HRMS (ES): M + Na^+, found 313.0164. $C_{16}H_{12}Cl_2NaO$ requires 313.0157.

(*Z*)-2-(Chloromethyl)-3-(2,4-dichlorophenyl)-1-phenylprop-2-en-1-one 10jm

Orange oil. Yield 55%.

IR (KBr): ν_{max} = 1659 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.52 (2H, s, CH_2Cl), 7.27 (1H, s, =CH), 7.38 (1H, ddd, $^{3}J_{H,H}$ = 8.1 Hz, $^{4}J_{H,H}$ = 2.1 Hz, $^{5}J_{H,H}$

= 0.3 Hz, ArH), 7.46–7.52 (3H, m, ArH), 7.60 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.65 (1H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.85–7.89 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 38.64, 127.48, 128.45, 129.69, 129.73, 130.75, 131.19, 132.79, 134.88, 135.96, 137.11, 138.13, 138.79, 195.65 ppm. HRMS (ES): M + Na^+, found 346.9770. $C_{16}H_{11}Cl_3NaO$ requires 346.9768.

(*Z*)-2-(Chloromethyl)-3-(4-methylphenyl)-1-phenylprop-2-en-1-one 10jp

Yellow oil. Yield 9 %.

IR (KBr): ν_{max} = 1651 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.40 (3H, s, CH_3), 4.69 (2H, s, CH_2Cl), 7.26 – 7.28 (3H, m, =CH, ArH), 7.43–7.50 (4H, m, ArH), 7.58 (1H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.78–7.81 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.72, 39.42, 128.62, 129.92, 131.51, 132.51, 135.90, 138.27, 140.53, 145.26, 196.90 ppm. HRMS (ES): M + Na^+, found 293.0705. $C_{17}H_{15}ClNaO$ requires 293.0704.

(*E*)-4-Cyclohexyl-3-(4-methoxybenzoyl)but-3-enyl acetate 10kf

Bright yellow oil. Yield 40%.

IR (KBr): ν_{max} = 1736 (O-C=O), 1640 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.07 – 1.79 (11H, m, *c*Hex) 1.98 (3H, s, $OCOCH_3$), 2.83 (2H, t, $^{3}J_{H,H}$= 6.7 Hz, $=CCH_2$), 3.85 (3H, s, OCH_3), 4.17 (2H, t, $^{3}J_{H,H}$= 6.7 Hz, CH_2OCOMe), 6.09 (1H, d, $^{3}J_{H,H}$= 10.0 Hz, =CH), 6.89 – 6.93 (2H, m, ArH), 7.65 – 7.69 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.87, 25.42, 25.74, 26.82, 32.40, 38.12, 55.38, 63.46, 113.34, 130.90, 131.83, 134.33, 151.08, 162.68, 170.89, 197.45 ppm. HRMS (ESI^+): M + Na^+, found 353.1723. $C_{20}H_{26}NaO_4$ requires 353.1718.

(E)-5-Ethyl-3-(4-methoxybenzoyl)hept-3-enyl acetate 10kg

Bright yellow oil. Yield 21%.

IR (KBr): ν_{max} =1736 (O-C=O), 1639 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92 (6H, t, $^{3}J_{H,H}$= 7.5 Hz, $CH(CH_2\underline{CH_3})_2$), 1.22 – 1.35 (2H, m,

CH($\underline{CH_2}CH_3)_2$), 1.48 – 1.61 (2H, m, CH($\underline{CH_2}CH_3)_2$), 1.98 (3H, s, $OCOCH_3$), 2.40 (1H, m, $\underline{CH}(CH_2CH_3)_2$), 2.86 (2H, t, $^3J_{H,H}$= 6.9 Hz, $=CCH_2$), 3.87 (3H, s, OCH_3), 4.18 (2H, t, $^3J_{H,H}$= 6.9 Hz, CH_2OCOMe), 5.97 (1H, d, $^3J_{H,H}$=10.4 Hz, =CH), 6.91 – 6.97 (2H, m, ArH), 7.66 – 7.74 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.02, 20.93, 26.99, 27.73, 42.45, 55.43, 63.26, 113.40, 130.92, 131.78, 136.90, 150.33, 162.71, 170.97, 197.32 ppm. HRMS (ESI^+): M + Na^+, found 341.1723. $C_{19}H_{26}NaO_4$ requires 341.1723.

(*E*)-4-(2-Fluorophenyl)-3-(4-methoxybenzoyl)but-3-enyl acetate 10ki

Bright yellow oil. Yield 50%.

IR (KBr): ν_{max} = 1738 (O-C=O), 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.92 (3H, s, $OCOCH_3$), 3.01 (2H, t, $^3J_{H,H}$= 6.6 Hz, $=CCH_2$), 3.87 (3H, s, OCH_3), 4.25 (2H, t, $^3J_{H,H}$= 6.6 Hz, CH_2OCOMe), 6.94 – 7.00 (2H, m, ArH), 7.07 – 7.24 (3H, m, =CH, ArH), 7.30 – 7.38 (1H, m, ArH), 7.43 – 7.51 (1H, m, ArH), 7.86 – 7.91 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ20.62, 27.82, 55.34, 62.43, 113.49, 115.59 (d, $^2J_{C,F}$= 21.7 Hz), 123.12 (d, $^2J_{C,F}$= 14.3 Hz), 124.03 (d, $^3J_{C,F}$= 3.6 Hz), 129.87 (d, $^3J_{C,F}$= 2.8 Hz), 129.99, 130.23 (d, $^4J_{C,F}$= 8.3 Hz), 132.08, 133.40 (d, $^3J_{C,F}$= 3.2 Hz), 139.59, 159.97 (d, $^1J_{C,F}$= 247.1 Hz), 163.13, 170.65, 196.65 ppm. HRMS (ESI^+): M + Na^+, found 365.1160. $C_{20}H_{19}FNaO_4$ requires 365.1166.

(*E*)-4-(2-Chlorophenyl)-3-(4-methoxybenzoyl)but-3-enyl acetate 10kk

Yellow oil. Yield 55%.

IR (KBr): ν_{max} = 1739 (O-C=O), 1645 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.92 (3H, s, $OCOCH_3$), 2.96 (2H, t, $^3J_{H,H}$= 6.5 Hz, $=CCH_2$), 3.89 (3H, s, OCH_3), 4.19 (2H, t, $^3J_{H,H}$= 6.5 Hz, CH_2OCOMe), 6.96 – 7.01 (2H, m, ArH), 7.19 (1H, s, =CH), 7.28 – 7.35 (2H, m, ArH), 7.40 – 7.47 (2H, m, ArH), 7.93 – 7.99 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.80, 27.53, 55.50, 62.55, 113.65, 126.80, 129.61, 130.01, 130.06, 132.30, 132.56, 133.82,

134.17, 137.77, 139.17, 163.35, 170.76, 196.84 ppm. HRMS (ESI^+): M + Na^+, found 381.0864. $C_{20}H_{19}ClNaO_4$ requires 381.0868.

(*E*)-4-(4-Chlorophenyl)-3-(4-methoxybenzoyl)but-3-enyl acetate 10kl

Yellow solid; m.p. = 64 – 65^oC. Yield 25%.

IR (KBr): ν_{max} = 1739 (O-C=O), 1643 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.97 (3H, s, $OCOCH_3$), 3.08 (2H, t, $^3J_{H,H}$= 6.7 Hz, $=CCH_2$), 3.90 (3H, s, OCH_3), 4.29 (2H, t, $^3J_{H,H}$= 6.7 Hz, CH_2OCOMe), 6.95 – 7.01 (2H, m, ArH), 7.11 (1H, s, =CH), 7.36 – 7.43 (4H, m, ArH), 7.81 – 7.85 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.83, 27.66, 55.50, 62.66, 113.64, 128.90, 130.33, 130.35, 132.09, 133.67, 134.58, 138.24, 139.90, 163.16, 170.84, 197.08 ppm. HRMS (ESI^+): M + Na^+, found 381.0864. $C_{20}H_{19}ClNaO_4$ requires 381.0864.

(*E*)-4-(2,4-Dichlorophenyl)-3-(4-methoxybenzoyl)but-3-enyl acetate 10km

Yellowish oil. Yield 61 %.

IR (KBr): ν_{max} = 1740 (O-C=O), 1647 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.90 (3H, s, $COCH_3$), 2.09 (2H, t, $^3J_{H,H}$ = 6.4 Hz,$\underline{CH_2}CH_2OAc$), 3.87 (3H, s, OCH_3), 4.16 (2H, t, $^3J_{H,H}$ = 6.4 Hz,$CH_2\underline{CH_2}OAc$), 6.96 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.07 (1H, s, =CH), 7.30 (1H, dd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.0 Hz, ArH), 7.36 (1H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.44 (1H, d, $^4J_{H,H}$ = 2.0 Hz, ArH), 7.91 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.69, 27.58, 55.42, 62.32, 113.62, 127.14, 129.45, 129.79, 130.70, 132.18, 132.59, 134.52, 134.73, 136.19, 139.72, 163.36, 170.59, 196.42 ppm. HRMS (ES): M + Na^+, found 415.0472. $C_{20}H_{18}Cl_2NaO_4$ requires 415.0474.

^{18}O-labeled*-(*E*)-4-(2,4-dichlorophenyl)-3-(4-methoxybenzoyl)but-3-enyl acetate 10km

Yellowish oil. Yield 66 %.

IR (KBr): ν_{max} = 1739 (O-C=O), 1644 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.89 (3H, s, $COCH_3$), 2.89 (2H, t, $^3J_{H,H}$ = 6.8 Hz, $\underline{CH_2}CH_2OAc$), 3.85 (3H, s, OCH_3), 4.15 (2H, t, $^3J_{H,H}$ = 6.8 Hz, $CH_2\underline{CH_2}OAc$), 6.94 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.06 (1H, s, =CH), 7.28 (1H, dd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.0 Hz, ArH), 7.35 (1H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.42 (1H, d, $^4J_{H,H}$ = 2.4 Hz, ArH), 7.89 (2H, d, $^3J_{H,H}$ = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.62, 27.52, 55.35, 62.24, 113.54, 127.06, 129.35, 129.69, 130.64, 132.10, 132.51, 134.43, 134.63, 136.10, 139.64, 163.28, 170.49, 196.26 ($C=O^{18}$), 196.30 (C=O) ppm. HRMS (ES): M + Na^+, found 415.0478 and 417.0486. $C_{20}H_{18}Cl_2NaO_4$ and $C_{20}H_{18}Cl_2NaO_3O^{18}$ require 415.0474 and 417.0522.

(*E*)-3-(4-Methoxybenzoyl)-4-(4-nitrophenyl)but-3-enyl acetate 10ks

Brownish solid; m.p. = 121 – 122^{o}C. Yield 53%.

IR (KBr): ν_{max} = 1734 (O-C=O), 1636 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.94 (3H, s, $OCOCH_3$), 3.05 (2H, t, $^3J_{H,H}$= 6.6 Hz, $=CCH_2$), 3.88 (3H, s, OCH_3), 4.26 (2H, t, $^3J_{H,H}$= 6.6 Hz, CH_2OCOMe), 6.94 – 7.00 (2H, m, ArH), 7.12 (1H, s, =CH), 7.56 – 7.62 (2H, m, ArH), 7.81 – 7.87 (2H, m, ArH), 8.22 – 8.28 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.76, 27.94, 55.53, 62.39, 113.78, 123.84, 129.69, 129.76, 132.16, 137.54, 140.88, 141.84, 147.35, 163.49, 170.68, 196.39 ppm. HRMS (ESI^+): M + Na^+, found 392.1105. $C_{20}H_{19}NNaO_6$ requires 392.1107.

(*E*)-3-(4-Methoxybenzoyl)-4-(2,3,4,5,6-pentafluorophenyl)but-3-enyl acetate 10kt

Yellowish oil. Yield 21%.

IR (KBr): ν_{max} = 1741 (O-C=O), 1654 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.89 (3H, s, $OCOCH_3$), 2.80 (2H, m, $=CCH_2$), 3.91 (3H, s, OCH_3), 4.17 (2H, t, $^3J_{H,H}$= 6.4 Hz, CH_2OCOMe), 6.62 (1H, m, =CH), 6.97 – 7.04 (2H, m, ArH), 7.89 – 7.95 (2H, m, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.53, 29.50, 55.51, 61.74, 110.14 (m), 113.82, 122.05, 129.15, 132.26, 136.45

(m), 138.97 (m), 139.74 (m), 142.34 (m), 144.85 (m), 145.59, 163.77, 170.56, 195.08 ppm. HRMS (ESI^+): M + Na^+, found 437.0783. $C_{20}H_{15}F_5NaO_4$ requires 437.0790.

(*E*)-5-Cyclohexyl-4-(4-methoxybenzoyl)pent-4-en-2-yl acetate 10lf

Yellowish oil. Yield 30%.

IR (KBr): ν_{max} = 1736 (O-C=O), 1644 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.06 – 1.81 (10H, m, *c*Hex), 1.26 (3H, d, $^3J_{H,H}$= 6.2 Hz, $CH_2CH\underline{CH_3}$), 1.88 (3H, s, $OCOCH_3$) 2.45 – 2.57 (1H, m, =CHC<u>H</u>), 2.81 (2H, d, $^3J_{H,H}$= 6.2 Hz, $=CCH_2$), 3.87 (3H, s, OCH_3), 5.03 (1H, sext, $^3J_{H,H}$= 6.2 Hz, $CH_2\underline{CH}CH_3$) 6.04 (1H, d, $^3J_{H,H}$= 10.0 Hz, =CH) 6.90 – 6.95 (2H, m, ArH), 7.67 – 7.73 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.20, 21.23, 25.43, 25.48, 25.78, 32.27, 32.39, 33.21, 38.14, 55.41, 70.56, 113.37, 130.71, 131.94, 134.53, 150.30, 162.70, 170.49, 197.37 ppm. HRMS (ESI^+): M + Na^+, found 367.1880. $C_{21}H_{28}NaO_4$ requires 367.1882.

(*E*)-5-(4-Chlorophenyl)-4-(4-methoxybenzoyl)pent-4-en-2-yl acetate 10ll

Yellowish oil. Yield 21%.

IR (KBr): ν_{max} = 1644, 1736 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.31 (3H, d, $^3J_{H,H}$= 6.2 Hz, $CH_2CH\underline{CH_3}$), 1.85 (3H, s, $OCOCH_3$), 2.99 (1H, dd, $^2J_{H,H}$= 13.9 Hz, $^3J_{H,H}$= 5.0 Hz, $=C\underline{CH_2}$), 3.04 (1H, dd, $^2J_{H,H}$= 13.9 Hz, $^3J_{H,H}$= 8.7 Hz, $=C\underline{CH_2}$), 3.90 (3H, s, OCH_3), 5.18 (1H, dqd, $^3J_{H,H}$= 8.7 Hz, $^3J_{H,H}$= 6.2 Hz, $^3J_{H,H}$= 5.0 Hz, $CH_2C\underline{H}CH_3$), 6.95 – 6.99 (2H, m, ArH), 7.05 (1H, s, =CH), 7.39 – 7.41 (4H, m, ArH), 7.81 – 7.85 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.58, 21.12, 34.42, 55.50, 70.14, 113.63, 128.85, 130.07, 130.36, 132.16, 133.80, 134.45, 138.74, 139.18, 163.15, 170.36, 196.98 ppm. HRMS (ESI^+): M + Na^+, found 395.1021. $C_{21}H_{21}ClNaO_4$ requires 395.1024.

(*E*)-5-(2,4-Dichlorophenyl)-4-(4-methoxybenzoyl)pent-4-en-2-yl acetate 10lm

Yellowish oil. Yield 70%.

IR (KBr): ν_{max} = 1738 (O-C=O), 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.18 (3H, d, $^{3}J_{H,H}$= 6.2 Hz, $CH_2CH\underline{CH_3}$), 1.80 (3H, s, $OCOCH_3$), 2.88 (2H, d, $^{3}J_{H,H}$= 6.5 Hz, $=CCH_2$), 3.87 (3H, s, OCH_3), 5.02 (1H, tq, $^{3}J_{H,H}$= 6.5 Hz, $^{3}J_{H,H}$= 6.2 Hz, $CH_2\underline{CH}CH_3$), 6.94 – 6.99 (2H, m, ArH), 7.04 (1H, s, =CH), 7.31 (1H, dd, $^{3}J_{H,H}$= 8.31 Hz, $^{4}J_{H,H}$= 1.96 Hz, ArH), 7.38 (1H, d, $^{3}J_{H,H}$= 8.31 Hz, ArH), 7.45 (1H, d, $^{4}J_{H,H}$= 2.08 Hz, ArH), 7.90 – 7.95 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.26, 21.04, 34.12, 55.47, 69.64, 113.69, 127.18, 129.49, 129.54, 130.83, 132.28, 132.87, 134.62, 134.66, 135.67, 140.02, 163.40, 170.14, 196.25 ppm. HRMS (ESI^+): M + Na^+, found 429.0631. $C_{21}H_{20}Cl_2NaO_4$ requires 429.0632.

(*E*)-4-(4-Methoxybenzoyl)-5-(2,3,4,5,6-pentafluorophenyl)pent-4-en-2-yl acetate 10lt

Greenish oil. Yield 8%.

IR (KBr): ν_{max} = 1738 (O-C=O), 1651 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.20 (3H, d, *J*=6.4 Hz, $CH_2CH\underline{CH_3}$), 1.77 (3H, s, $OCOCH_3$), 2.72 (1H, dd, $^{2}J_{H,H}$= 14.1 Hz, $^{3}J_{H,H}$= 8.4 Hz, $=C\underline{CH_2}$), 2.76 (1H, dd, $^{2}J_{H,H}$= 14.1 Hz, $^{3}J_{H,H}$= 4.4 Hz, $=C\underline{CH_2}$), 3.90 (3H, s, OCH_3), 5.01 (1H, dqd, $^{3}J_{H,H}$= 8.4 Hz, $^{3}J_{H,H}$= 6.4 Hz, $^{3}J_{H,H}$= 4.4 Hz, $CH_2\underline{CH}CH_3$), 6.59 (1H, s, =CH), 6.96 – 7.02 (2H, m, ArH), 7.88 – 7.93 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.23, 20.77, 36.18, 55.48, 69.09, 110.28 (m), 113.83, 121.61, 128.89, 132.24, 136.46 (m), 138.99 (m), 139.71 (m), 142.32 (m), 144.83 (m), 145.74, 163.72, 170.09, 194.92 ppm. HRMS (ESI^+): M + Na^+, found 451.0939. $C_{21}H_{17}F_5NaO_4$ requires 451.0944.

(*E*)-2-(4-Chlorobenzylidene)-1-(4-methoxyphenyl)-4-methylpentan-1-one 10ml

Yellow oil. Yield 46 %.

IR (KBr): ν_{max} = 1644 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92 (6H, d, $^{3}J_{H,H}$ = 6.8 Hz, $CH(CH_3)_2$), 1.86 (1H, sept, $^{3}J_{H,H}$ = 6.8 Hz, $CH(CH_3)_2$), 2.63 (2H, d, $^{3}J_{H,H}$ = 7.2 Hz, CH_2), 3.87 (3H, s, OCH_3), 6.94 – 6.97 (3H, m, ArH, =CH), 7.29 (2H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.35 (2H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.87 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.76, 28.10, 36.72, 55.39, 113.54, 128.61, 130.28, 130.31, 132.08, 133.85, 134.32, 137.38, 142.60, 163.04, 197.66 ppm. HRMS (ES): M + Na^{+}, found 351.1117. $C_{20}H_{21}ClNaO_2$ requires 351.1122.

(*E*)-2-(2,4-Dichlorobenzylidene)-1-(4-methoxyphenyl)-4-methylpentan-1-one 10mm

Yellow oil. Yield 70 %.

IR (KBr): ν_{max} = 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.82 (6H, d, $^{3}J_{H,H}$ = 6.8 Hz, $CH(CH_3)_2$), 1.72 (1H, sept, $^{3}J_{H,H}$ = 6.8 Hz, $CH(CH_3)_2$), 2.49 (2H, dd, $^{3}J_{H,H}$ = 6.8 Hz, $^{4}J_{H,H}$ = 0.4 Hz, CH_2), 3.86 (3H, s, OCH_3), 6.95 – 6.98 (3H, m, ArH, =CH), 7.26 – 7.27 (2H, m, ArH), 7.42 – 7.43 (1H, m, ArH), 7.99 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.55, 27.40, 36.69, 55.35, 113.58, 126.88, 129.26, 129.82, 130.89, 132.21, 133.36, 134.14, 134.18, 134.51, 143.53, 163.26, 196.93 ppm. HRMS (ES): M + Na^{+}, found 385.0727. $C_{20}H_{20}Cl_2NaO_2$ requires 385.0733.

(*E*)-2-(4-Nitrobenzylidene)-1-(4-methoxyphenyl)-4-methylpentan-1-one 10ms

Yellow oil. Yield 76 %.

IR (KBr): ν_{max} = 1646 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89 (6H, d, $^{3}J_{H,H}$ = 6.8 Hz, $CH(CH_3)_2$), 1.82 (1H, sept, $^{3}J_{H,H}$ = 6.8 Hz, $CH(CH_3)_2$), 2.60

(2H, d, $^{3}J_{H,H}$ = 7.2 Hz, CH_2), 3.85 (3H, s, OCH_3), 6.95 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 6.99 (1H, s, =CH), 7.49 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.88 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.21 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.66, 27.98, 37.02, 55.35, 113.62, 123.55, 129.56, 129.60, 132.04, 135.11, 142.55, 145.06, 146.89, 163.28, 196.89 ppm. HRMS (ES): M + Na^+, found 362.1357. $C_{20}H_{21}NNaO_4$ requires 362.1363.

(*E*)-2-(4-Trifluoromethylbenzylidene)-1-(4-methoxyphenyl)-4-methylpentan-1-one 10mx

Yellow oil. Yield 71 %.

IR (KBr): ν_{max} = 1647 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92 (6H, d, $^{3}J_{H,H}$ = 6.4 Hz, $CH(CH_3)_2$), 1.86 (1H, sept, $^{3}J_{H,H}$ = 6.8 Hz, $CH(CH_3)_2$), 2.63 (2H, d, $^{3}J_{H,H}$ = 6.8 Hz, CH_2), 3.87 (3H, s, OCH_3), 6.97 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH), 7.01 (1H, br. s, =CH), 7.47 (2H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.64 (2H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.91 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.73, 28.08, 36.90, 55.38, 113.63, 123.99 (q, $^{1}J_{C\text{-}F}$ = 270.5 Hz), 125.31 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 129.18, 129.73 (q, $^{2}J_{C\text{-}F}$ = 32.4 Hz), 130.02, 132.13, 136.52, 139.58, 143.92, 163.24, 197.40 ppm. HRMS (ES): M + Na^+, found 385.1390. $C_{21}H_{21}F_3NaO_2$ requires 385.1386.

(*E*)-2-(Cyclohexylmethyl)-3-(2,4-dichlorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one 10nm

Yellow oil. Yield 50 %.

IR (KBr): ν_{max} = 1651 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.75 – 0.84 (2H, m, *c*Hex), 1.01 – 1.16 (3H, m, *c*Hex), 1.35 – 1.44 (1H, m, *c*Hex), 1.53 – 1.66 (5H, m, *c*Hex), 2.49 (2H, d, $^{3}J_{H,H}$ = 6.8 Hz, CH_2*c*Hex), 3.87 (3H, s, OCH_3), 6.96 – 6.98 (3H, m, ArH, =CH), 7.27 – 7.28 (2H, m, ArH), 7.44 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, ArH), 7.99 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.05, 26.19, 33.30, 35.41, 36.80, 55.41, 113.62, 126.91, 129.30, 129.93, 130.95, 132.25, 133.43, 134.16, 134.39, 134.55, 143.30,

163.28, 197.06 ppm. HRMS (ES): M + Na^+, found 425.1041. $C_{24}H_{25}Cl_2NaO_2$ requires 425.1046.

(*E*)-2-(Cyclohexylmethyl)-3-(4-trifluoromethylphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one 10nx

Bright yellow oil. Yield 54 %.

IR (KBr): ν_{max} = 1646 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.89 – 0.98 (2H, m, *c*Hex), 1.10 – 1.22 (3H, m, *c*Hex), 1.49 – 1.73 (6H, m, *c*Hex), 2.63 (2H, d, $^3J_{H,H}$ = 6.8 Hz, CH_2*c*Hex), 3.88 (3H, s, OCH_3), 6.97 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.01 (1H, s, =CH), 7.46 (2H, d, $^3J_{H,H}$ = 8.0 Hz, ArH), 7.64 (2H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.89 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.16, 26.21, 33.54, 35.66, 37.58, 55.42, 113.64, 124.00 (q, $^1J_{C\text{-}F}$ = 270.4 Hz), 125.33 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 129.20, 129.74 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 130.06, 130.22, 132.16, 136.69, 139.59, 143.68, 163.22, 197.46 ppm. HRMS (ES): M + Na^+, found 425.1690. $C_{24}H_{25}F_3NaO_2$ requires 425.1699.

(*E*)-*N*-(3-Cyclohexyl-2-(4-methoxybenzoyl)allyl)-*N*-methylbenzamide 10of

Yellow oil. Yield 49 %.

IR (KBr): ν_{max} = 1640, 1632 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.06 – 1.17 (4H, m, *c*Hex), 1.54 – 1.87 (6H, m, *c*Hex), 2.80 (1H, br. s, *c*Hex), 2.95 (3H, br. s, NCH_3), 3.83 (3H, s, OCH_3), 4.43 – 4.57 (2H, m, CH_2NMeCOPh), 6.11 (1H, d, $^4J_{H,H}$ = 9.6 Hz, =CH), 6.90 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.27 – 7.35 (5H, m, ArH), 7.64 – 7.80 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.19, 25.65, 32.16, 37.75, 38.68, 44.27, 55.34, 113.45, 113.81, 126.66, 128.23, 129.34, 130.57, 131.90, 136.36, 151.65, 162.96, 171.69, 197.38 ppm. HRMS (ES): M + Na^+, found 414.2043. $C_{25}H_{29}NNaO_3$ requires 414.2040.

(*E*)-*N*-(3-(2,4-Dichlorophenyl)-2-(4-methoxybenzoyl)allyl)-*N*-methylbenzamide 10om

Yellowish oil. Yield 51 %.

IR (KBr): ν_{max} = 1643, 1633 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.91 (3H, s, NCH_3), 3.85 (3H, s, OCH_3), 4.59 (2H, br. s, $CH_2NMeCOPh$), 6.95 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.04 – 7.08 (2H, m, ArH, =CH), 7.20 – 7.37 (5H, m, ArH), 7.43 (1H, d, $^{4}J_{H,H}$ = 1.6 Hz, ArH), 7.61 – 7.74 (1H, m, ArH), 7.99 (2H, d, $^{3}J_{H,H}$ = 7.6 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 39.39, 46.54, 55.40, 113.75, 113.87, 126.67, 127.08, 128.14, 129.29, 129.41, 129.81, 131.25, 132.12, 132.34, 134.38, 134.76, 135.80, 139.59, 163.65, 171.72, 196.32 ppm. HRMS (ES): M + Na^+, found 476.0787. $C_{25}H_{21}Cl_2NNaO_3$ requires 476.0791.

(*Z*)-2-Benzoyl-3-(2-fluorophenyl)allyl acetate 11ai

Yellowish oil. Yield 26%.

IR (KBr): ν_{max} = 1737 (O-C=O), 1642 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.99 (3H, s, $COCH_3$), 5.02 (2H, d, $^{4}J_{H,H}$ = 1.2 Hz, CH_2OAc), 6.76–6.80 (1H, m, ArH), 6.85–6.90 (1H, m, ArH), 7.01–7.07 (2H, m, ArH), 7.18 (1H, br. s, =CH), 7.26–7.30 (2H, m, ArH), 7.38–7.42 (1H, m, ArH), 7.80–7.82 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.69, 66.60, 115.18 (d, $^{2}J_{C,F}$ = 21.4 Hz), 122.66 (d, $^{3}J_{C,F}$ = 13.5 Hz), 123.74 (d, $^{4}J_{C,F}$ = 3.6 Hz), 128.36, 129.15, 129.71, 130.31 (d, $^{3}J_{C,F}$ = 2.2 Hz), 130.34 (d, $^{3}J_{C,F}$ = 8.40 Hz), 133.37, 136.05, 136.93, 159.89 (d, $^{1}J_{C,F}$ = 247.9 Hz), 170.42, 197.60 ppm. HRMS (ES): M + Na^+, found 321.0903. $C_{18}H_{15}FNaO_3$ requires 321.0897.

^{18}O-labeled*-(*Z*)-2-benzoyl-3-(2-fluorophenyl)allyl acetate 11ai

Yellowish oil. Yield 20 %.

IR (KBr): ν_{max} = 1743 (O-C=O), 1716 (O-C=O^{18}), 1655 (C=O), cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.00 (3H, s, $COCH_3$), 5.02 (2H, d, $^{4}J_{H,H}$ = 0.8 Hz, CH_2OAc), 6.77 – 6.81 (1H, m, ArH), 6.86 – 6.90 (1H, m, ArH), 7.02 – 7.10

(2H, m, ArH), 7.18 (1H, br. s, =CH), 7.29 (2H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.41 (1H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.80 – 7.82 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.73, 66.64, 115.22 (d, $^{2}J_{C,F}$ = 21.4 Hz), 122.72 (d, $^{3}J_{C,F}$ = 13.5 Hz), 123.78 (d, $^{4}J_{C,F}$ = 3.7 Hz), 127.07 (d, $^{3}J_{C,F}$ = 4.3 Hz), 128.40,129.20, 130.36 (d, $^{3}J_{C,F}$ = 2.7 Hz), 130.37 (d, $^{3}J_{C,F}$ = 8.3 Hz), 133.40, 136.10, 137.00, 159.94 (d, $^{1}J_{C,F}$ = 247.9 Hz), 170.48 (C=O), 170.44 (C=O^{18}), 197.65 ppm. HRMS (ES): M + Na^+, found 321.0894 and 323.0935. $C_{18}H_{15}FNaO_3$ and $C_{18}H_{15}FNaO_2O^{18}$ require 321.0897 and 323.0945.

(*Z*)-2-Benzoyl-3-(2-chlorophenyl)allyl acetate 11ak

Orange oil. Yield 27%.

IR (KBr): ν_{max} = 1742 (O-C=O), 1655 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.02 (3H, s, $COCH_3$), 5.04 (2H, d, $^{4}J_{H,H}$ = 1.5 Hz, CH_2OAc), 6.88 (1H, td, $^{3}J_{H,H}$ = 7.5 Hz, $^{4}J_{H,H}$ = 0.6 Hz, ArH), 6.98–7.04 (2H, m, =CH, ArH), 7.19–7.30 (4H, m, ArH), 7.36 (1H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.74–7.77 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.73, 66.21, 126.39, 128.11, 128.26, 129.03, 129.08, 129.66, 129.71, 130.75, 131.66, 133.26, 136.34, 137.04, 170.47, 197.53 ppm. HRMS (ES): M + H^+, found 315.0768. $C_{18}H_{16}ClO_3$ requires 315.0782.

(*Z*)-2-Benzoyl-3-(2,4-dichlorophenyl)allyl acetate 11am

White solid; m. p. = 96–97^{o}C. Yield 23%.

IR (KBr): ν_{max} = 1731, 1664 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.02 (3H, s, $COCH_3$), 5.03 (2H, d, $^{4}J_{H,H}$ = 1.2 Hz, CH_2OAc), 6.88 (1H, dd, $^{3}J_{H,H}$ = 8.4 Hz, $^{4}J_{H,H}$ = 2.4 Hz, ArH), 6.97 (1H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.17 (1H, br. s, =CH), 7.23 (1H, d, $^{4}J_{H,H}$ = 2.4 Hz, ArH), 7.26–7.32 (2H, m, ArH), 7.42 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.75 (2H, d, $^{3}J_{H,H}$ = 7.2 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.71, 35.36, 66.05, 126.79, 128.47, 129.02, 129.07, 130.01, 131.33, 131.96, 133.61, 133.95, 134.83, 136.08, 137.79, 170.41, 197.29 ppm. HRMS (ES): M + H^+, found 349.0378. $C_{18}H_{15}Cl_2O_3$ requires 349.0393. Crystal

structure analysis for **11am**: $C_{18}H_{15}Cl_2O_3$, M_r = 349.21 g mol^{-1}, monoclinic, space group P 21/c; a = 38.1445(2), b = 18.5345(3), c = 11.1260(3) Å, α = 90.00, β = 96.4938(9), γ =90.00, V = 1668.74(7) $Å^3$, ρ = 1.390 g/cm^3, F (000) = 720. X-ray diffraction data were collected on a Nonius Kappa CCD diffractometer at the temperature 293 K using graphite-monochromated MoK_λ radiation (λ = 0.71073 Å). Structure **11am** was solved by direct methods with SIR97 program and refined by full-matrix least squares techniques with anisotropic non-hydrogen atoms. Hydrogen atoms were refined in the riding model. The refinement calculations were carried out with the help of SHELX97 program. CCDC 991095 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

^{18}*O-labeled*-(*Z*)-2-benzoyl-3-(2,4-dichlorophenyl)allyl acetate 11am*

White solid; m. p. = 95 – 97 °C. Yield 19 %.

IR (KBr): ν_{max} = 1732 (O-C=O), 1711 (O-C=O^{18}), 1665 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.99 (3H, s, CH_3CO), 5.00 (2H, d, $^4J_{H,H}$ = 1.2 Hz, CH_2OAc), 6.85 (1H, dd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.4 Hz, ArH), 6.95 (1H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.15 (1H, br. s, =CH), 7.21 (1H, d, $^4J_{H,H}$ = 2.4 Hz, ArH), 7.24 – 7.30 (2H, m, ArH), 7.42 (1H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.73 (2H, d, $^3J_{H,H}$ = 7.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.71, 66.05, 126.79, 128.47, 129.03, 129.07, 130.01, 131.33, 131.96, 133.61, 133.95, 134.84, 136.08, 137.79, 170.37 (O-C=O^{18}), 170.41 (O-C=O), 197.29 (C=O) ppm. HRMS (ES): M + Na^+, found 371.0218 and 373.0254. $C_{18}H_{14}{}^{35}Cl_2NaO_3$ and $C_{18}H_{14}{}^{35}Cl_2NaO_2{}^{18}O$ require 371.0217 and 373.0260.

(*Z*)-2-Benzoyl-3-(2-bromophenyl)allyl acetate 11an

Yellow oil. Yield 20%.

IR (KBr): ν_{max} = 1743 (O-C=O), 1658 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.03 (3H, s, CH_3CO), 5.04 (2H, d, $^{4}J_{H,H}$ = 1.2 Hz, CH_2OAc), 6.88–6.95 (2H, m, =CH, ArH), 7.21–7.26 (3H, m, ArH,), 7.33–7.39 (3H, m, ArH), 7.73–7.76 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.73, 66.04, 123.35, 126.99, 128.21, 129.01, 129.75, 130.89, 132.23, 133.21, 133.76, 135.19, 136.38, 136.85, 170.45, 197.42 ppm. HRMS (ES): M + Na^+, found 381.0083. $C_{18}H_{15}BrNaO_3$ requires 381.0097.

(*Z*)-2-Benzoyl-3-(2-nitrophenyl)allyl acetate 11ar

Orange oil. Yield 10%.

IR (KBr): ν_{max} = 1741 (O-C=O), 1656 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.06 (3H, s, $COCH_3$), 5.06 (2H, d, $^{4}J_{H,H}$ = 1.2 Hz, CH_2OAc), 7.15–7.36 (6H, m, ArH), 7.44 (1H, br. s, =CH), 7.71 (2H, d, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.92 (1H, dd, $^{3}J_{H,H}$ = 8.1 Hz, $^{4}J_{H,H}$ = 1.5 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.74, 65.54, 124.63, 128.34, 128.80, 129.24, 131.28, 131.45, 132.05, 133.35, 133.37, 136.77, 137.37, 146.79, 170.41, 197.16 ppm. HRMS (ES): M + Na^+, found 348.0873. $C_{18}H_{15}NNaO_5$ requires 348.0842.

(*Z*)-2-Benzoyl-3-(4-nitrophenyl)allyl acetate 11as

Orange oil. Yield 13%.

IR (KBr): ν_{max} = 1745 (O-C=O), 1667 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.00 (3H, s, $COCH_3$), 5.02 (2H, d, $^{4}J_{H,H}$ = 1.2 Hz, CH_2OAc), 7.05 (1H, br. s, =CH), 7.28–7.36 (4H, m, ArH), 7.48 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.80–7.84 (2H, m, ArH), 7.97 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.69, 66.38, 123.54, 128.77, 129.25, 129.46, 130.57, 134.14, 135.42, 139.44, 140.90, 147.17, 170.42, 197.31 ppm. HRMS (ES): M + Na^+, found 348.0856. $C_{18}H_{15}NNaO_5$ requires 348.0842.

(*Z*)-2-Benzoyl-3-(2,4-dichlorophenyl)allyl benzoate 11bm

Yellowish oil . Yield 11%.

IR (KBr): ν_{max} = 1721 (O-C=O), 1663 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.27 (2H, d, $^{3}J_{H,H}$ = 1.5 Hz, CH_2OBz), 6.90 (1H, ddd, $^{3}J_{H,H}$ = 8.4 Hz, $^{4}J_{H,H}$ = 2.1 Hz, $^{5}J_{H,H}$ = 0.6 Hz, ArH), 7.03 (1H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.24 (1H, d, $^{4}J_{H,H}$ = 2.1 Hz, ArH), 7.26–7.32 (3H, m, =CH, ArH), 7.36 (2H, t, $^{3}J_{H,H}$ = 7.8 Hz, ArH), 7.43 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.52 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.80–7.83 (2H, m, ArH), 7.88–7.92 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 66.61, 126.83, 128.35, 128.51, 129.09, 129.54, 129.59, 129.84, 131.31, 131.93, 133.13, 133.65, 134.01, 134.85, 136.08, 137.87, 165.90, 197.42 ppm. HRMS (ES): M + Na^{+}, found 433.0376. $C_{23}H_{16}Cl_2NaO_3$ requires 433.0369.

(*Z*)-2-Benzoyl-3-(2-nitrophenyl)allyl benzoate 11br

Yellow oil. Yield 23%.

IR (KBr): ν_{max} = 1724 (O-C=O), 1659 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.31 (2H, d, $^{4}J_{H,H}$ = 1.2 Hz, CH_2OBz), 7.19–7.27 (4H, m, ArH), 7.31–7.39 (4H, m, ArH), 7.44 (1H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.50–7.55 (2H, m, =CH, ArH), 7.76–7.79 (2H, m, ArH), 8.92–8.96 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 66.087, 124.66, 128.35, 128.38, 128.53, 128.83, 129.27, 129.62, 130.07, 131.28, 131.44, 132.06, 133.11, 133.39, 133.42, 136.77, 137.38, 165.88, 197.22 ppm. HRMS (ES): M + Na^{+}, found 410.0995. $C_{23}H_{17}NaNO_5$ requires 410.0999.

(*Z*)-2-(4-Chlorobenzoyl)-3-(4-chlorophenyl)allyl acetate 11cl

Dark yellow oil. Yield 13%.

IR (KBr): ν_{max} = 1745 (O-C=O), 1660 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.97 (3H, s, $COCH_3$), 4.96 (2H, d, $^{4}J_{H,H}$ = 1.2 Hz, CH_2OAc), 7.00 (1H, br. s, =CH), 7.04 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 7.10 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 7.29 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 7.76 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.72, 66.90, 128.66, 129.00, 130.08, 130.63,

132.71, 132.90, 134.20, 134.67, 135.46, 140.26, 170.50, 196.92 ppm. HRMS (ES): M + Na^+, found 371.0206. $C_{18}H_{14}Cl_2NaO_3$ requires 371.0212.

(*Z*)-2-(4-Chlorobenzoyl)-3-(2,4-dichlorophenyl)allyl acetate 11cm

Yellow oil. Yield 12%.

IR (KBr): ν_{max} = 1746 (O-C=O), 1662 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.03 (3H, s, $COCH_3$), 5.00 (2H, d, $^4J_{H,H}$ = 1.5 Hz, CH_2OAc), 6.90 (1H, dd, $^3J_{H,H}$ = 8.1 Hz, $^4J_{H,H}$ = 1.8 Hz, ArH), 6.95, (1H, d, $^3J_{H,H}$ = 8.1 Hz, ArH), 7.17 (1H, d, $^4J_{H,H}$ = 1.2 Hz, =CH), 7.32 (2H, m, ArH), 7.24–7.29 (3H, m, ArH), 7.64 (2H, d, $^3J_{H,H}$ = 9.0 Hz, ArH), ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.70, 65.99, 126.95, 128.89, 129.26, 130.24, 130.37, 130.89, 131.27, 131.78, 133.95, 134.43, 135.18, 137.43, 140.19, 170.37, 196.08 ppm. HRMS (ES): M + Na^+, found 404.9820. $C_{18}H_{13}Cl_3NaO_3$ requires 404.9822.

^{18}O-labeled*-(*Z*)-2-(4-methoxybenzoyl)-3-(4-nitrophenyl)allyl acetate 11es

Colorless oil. Yield 23 %.

IR (KBr): ν_{max} = 1743 (O-C=O), 1714 (O-C=O^{18}), 1659 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.03 (3H, s, CH_3CO), 3.83 (3H, s, CH_3O), 5.02 (2H, d, $^4J_{H,H}$ = 1.2 Hz, CH_2), 6.81 (2H, d, $^3J_{H,H}$ = 8.0 Hz, ArH), 6.99 (1H, br. s. =CH), 7.35 (2H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.84 (2H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 8.01 (2H, d, $^3J_{H,H}$ = 8.0 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.73, 55.50, 66.50, 114.11, 123.60, 128.46, 129.45, 129.48, 131.80, 139.84, 141.11, 147.16, 164.42, 170.43 (^{18}O-C=O), 170.47 (O-C=O), 195.72 (C=O) ppm. HRMS (ES): M + Na^+, found 378.0947 and 380.0994. $C_{19}H_{17}NNaO_6$ and $C_{19}H_{17}NNaO_5{}^{18}O$ require 378.0954 and 380.0996.

(*Z*)-3-(2-Chlorophenyl)-2-(4-methoxybenzoyl)allyl benzoate 11fk

Colorless oil. Yield 20 %.

IR (KBr): ν_{max} = 1715 (O-C=O), 1651 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.76 (3H, s, OCH_3), 5.26 (2H, d, $^3J_{H,H}$ = 1.2 Hz, CH_2OBz), 6.74 (2H,

d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 6.93 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 0.8 Hz, ArH), 7.04 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 1.6 Hz, ArH), 7.13 (1H, dd, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 1.6 Hz, ArH), 7.24 (1H, dd, $^{3}J_{H,H}$ = 8.0 Hz, $^{4}J_{H,H}$ = 0.8 Hz, ArH), 7.30 (1H, br. s, =CH), 7.34 – 7.38 (2H, m, ArH), 7.51 (1H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.82 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.89 – 7.92 (2H, m, ArH) ppm. HRMS (ES): M + Na^{+}, found 429.0870. $C_{24}H_{19}ClNaO_4$ requires 429.0864.

(*Z*)-3-Cyclohexyl-1,2-diphenylprop-2-en-1-one 11if

Yellowish oil. Yield 14%.

IR (KBr): ν_{max} = 1670 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.13–1.19 (5H, m, *c*Hex), 1.58–1.78 (5H, m, *c*Hex), 2.00–2.09 (1H, m, *c*Hex), 6.07 (1H, d, $^{3}J_{H,H}$ = 10.2 Hz, =CH), 7.21–7.34 (5H, m, ArH), 7.41 (2H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.53 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.95–7.98 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 25.34, 25.75, 32.73, 38.86, 125.97, 127.54, 128.59, 128.65, 129.66, 133.39, 136.93, 137.28, 137.68, 138.90, 198.49 ppm. HRMS (ES): M + Na^{+}, found 313.1576. $C_{21}H_{22}NaO$ requires 313.1563.

(*Z*)-3-(2,4-Dichlorophenyl)-1,2-diphenylprop-2-en-1-one 11im

Yellow solid; m. p. = 69–71^{o}C. Yield 24%.

IR (KBr): ν_{max} = 1655 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.84 (1H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 6.94 (1H, dd, $^{3}J_{H,H}$ = 8.4 Hz, $^{4}J_{H,H}$ = 2.1 Hz, ArH), 7.22–7.30 (6H, m, =CH, ArH), 7.41 (1H, d, $^{4}J_{H,H}$ = 2.1 Hz, ArH), 7.45 (2H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.55 (1H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH),7.92– 7.95 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 126.71, 128.20, 128.36, 128.65, 129.30, 129.53, 129.98, 131.85, 132.48, 132.74, 133.70, 134.61, 135.09, 135.27, 137.15, 142.84, 196.79 ppm. HRMS (ES): M + Na^{+}, found 375.0311. $C_{21}H_{14}Cl_2NaO$ requires 375.0314.

(*E*)-2-Benzylidene-4-methylene-1,5-diphenylpentane-1,5-dione 12ah

White solid; m. p. = 45–47 ^{o}C. Yield 11%.

IR (KBr): ν_{max} = 1642, 1641 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.92 (2H, br. s, =C$\underline{CH_2}$C=), 5.69 (1H, t, $^{4}J_{H,H}$ = 1.2 Hz, =C$\underline{H}$H), 5.89 (1H, t, $^{4}J_{H,H}$ = 1.5 Hz, =CH$\underline{H}$), 7.37–7.56 (12H, m, =CH, ArH), 7.73–7.77 (2H, m, ArH) 7.79–7.82 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 30.51, 125.84, 128.10, 128.18, 128.31, 128.68, 129.11, 129.24, 129.56, 129.63, 131.92, 132.30, 134.95, 137.68, 138.28, 144.48, 145.40, 197.85, 198.27 ppm. HRMS (ES): M + Na^+, found 375.1339. $C_{25}H_{20}NaO_2$ requires 375.1356.

(*E*)-2-(2-Fluorobenzylidene)-4-methylene-1,5-diphenylpentane-1,5-dione 12ai

Yellowish oil. Yield 15%.

IR (KBr): ν_{max} = 1652 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.84 (2H, br. s, =C$\underline{CH_2}$C=), 5.66 (1H, br. s, =C$\underline{H}$H), 5.88 (1H, t, $^{4}J_{H,H}$ = 1.6 Hz, =CH$\underline{H}$), 7.05–7.12 (1H, m, ArH), 7.17–7.21 (1H, m, ArH), 7.37–7.41 (4H, m, =CH, ArH), 7.47 (2H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.51–7.58 (3H, m, ArH), 7.68–7.70 (2H, m, ArH), 7.82–7.84 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.74, 115.65 (d, $^{2}J_{C,F}$ = 21.5 Hz), 123.09 (d, $^{2}J_{C,F}$ = 13.9 Hz), 124.24 (d, $^{4}J_{C,F}$ = 3.8 Hz), 126.38, 128.16, 128.36, 129.34, 129.51, 129.58, 129.69, 129.75 (d, $^{3}J_{C,F}$ = 2.5 Hz), 130.76 (d, $^{3}J_{C,F}$ = 8.4 Hz), 132.22, 132.27, 137.35, 137.85, 139.75, 162.42 (d, $^{1}J_{C,F}$ = 181.1 Hz), 197.68, 197.74 ppm. HRMS (ES): M + Na^+, found 393.1264. $C_{25}H_{19}FNaO_2$ requires 393.1261.

(*E*)-2-(4-Fluorobenzylidene)-4-methylene-1,5-diphenylpentane-1,5-dione 12aj

Yellowish oil. Yield 22%.

IR (KBr): ν_{max} = 1655(C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.89 (2H, br. s, =C$\underline{CH_2}$C=), 5.68 (1H, br. s, =C$\underline{H}$H), 5.88 (1H, t, $^{4}J_{H,H}$ = 1.6 Hz, =CH$\underline{H}$), 7.07–7.12 (2H, m, ArH), 7.33 (1H, br. s, =CH), 7.41–7.49 (6H, m, ArH), 7.51–7.53 (2H, m, ArH), 7.73–7.76 (2H, m, ArH), 7.77–7.80 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.52, 115.80 (d, $^{2}J_{C,F}$ = 21.5 Hz), 125.95, 128.21,

128.34, 129.52, 129.63, 131.05 (d, $^{4}J_{C,F}$ = 3.4 Hz), 131.27 (d, $^{3}J_{C,F}$ = 8.3 Hz), 131.98, 132.40, 137.29, 137.49, 138.19, 143.07, 145.11, 162.95 (d, $^{1}J_{C,F}$ = 249.0 Hz), 197.81, 198.14 ppm. HRMS (ES): M + Na^{+}, found 393.1257. $C_{25}H_{19}FNaO_2$ requires 393.1261.

(*E*)-2-(4-Chlorobenzylidene)-4-methylene-1,5-diphenylpentane-1,5-dione 12al

Yellowish oil. Yield 12%.

IR (KBr): ν_{max} = 1648 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.88 (2H, br. s, =C$\underline{CH_2}$C=), 5.68 (1H, t, $^{4}J_{H,H}$ = 1.2 Hz, =C$\underline{H}$H), 5.88 (1H, t, $^{4}J_{H,H}$ = 1.5 Hz, =CH$\underline{H}$), 7.30 (1H, br. s, =CH), 7.38–7.53 (10H, m, ArH), 7.72–7.75 (2H, m, ArH), 7.77–7.80 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 30.62, 126.17, 128.22, 128.36, 128.93, 129.55, 129.62, 130.54, 132.07, 132.40, 133.38, 135.06, 137.27, 138.05, 138.26, 142.61, 145.01, 197.74, 198.03 ppm. HRMS (ES): M + Na^{+}, found 409.0953. $C_{25}H_{19}ClNaO_2$ requires 409.0966.

(*E*)-2-(4-Methoxybenzylidene)-4-methylene-1,5-diphenylpentane-1,5-dione 12ao

Brown solid; m. p. = 102–104 ^{o}C. Yield 12%.

IR (KBr): ν_{max} = 1652 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.82 (3H, s, OCH_3), 3.93 (2H, br. s, =C$\underline{CH_2}$C=), 5.67 (1H, t, $^{4}J_{H,H}$ = 1.2 Hz, =C$\underline{H}$H), 5.86 (1H, t, $^{4}J_{H,H}$ = 1.5 Hz, =CH$\underline{H}$), 6.92 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 7.39–7.58 (9H, m, =CH, ArH), 7.75–7.81 (4H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 30.31, 55.26, 114.11, 125.27, 127.32, 128.12, 128.17, 129.37, 129.61, 131.27, 135.31, 137.33, 138.63, 145.00, 145.24, 160.40, 197.97, 198.35 ppm. HRMS (ES): M + H^{+}, found 383.1645. $C_{26}H_{23}O_2$ requires 383.1642.

(*E*)-2-(4-Methylbenzylidene)-4-methylene-1,5-diphenylpentane-1,5-dione 12ap

Yellow oil. Yield 22 %.

IR (KBr): ν_{max} = 1651, 1644 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.37 (3H, s, $CH_3C_6H_4$), 3.92 (2H, br. s, $=CCH_2C=$), 5.68 (1H, br. s, $=CH_2$), 5.87 (1H, t, $^{4}J_{H,H}$ = 1.5 Hz, $=CH_2$), 7.19 – 7.22 (3H, m, =CH, ArH), 7.34 (2H, d, $^{3}J_{H,H}$ = 8.1 Hz, ArH), 7.39 – 7.56 (8H, m, ArH), 7.75 – 7.81 (4H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.35, 30.44, 125.58, 128.17, 128.26, 129.40, 129.51, 129.65, 131.76, 132.07, 132.28, 136.77, 137.44, 138.49, 139.51, 1 44.95, 145.42, 197.92, 198.38 ppm. HRMS (ES): M + Na^+, found 389.1515. $C_{26}H_{22}NaO_2$ requires 389.1512.

(*E*)-4-(2,4-Dibenzoylpenta-1,4-dien-1-yl)phenyl benzoate 12aq

Yellowish oil. Yield 14 %.

IR (KBr): ν_{max} = 1738 (O-C=O), 1659, 1651 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.95 (2H, br. s, $=CCH_2C=$), 5.71 (1H, br. s, =C<u>H</u>H), 5.91 (1H, t, br. s, =CH<u>H</u>), 7.28 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.40 – 7.44 (3H, m, =CH, ArH), 7.46 – 7.59 (8H, m, ArH), 7.63 – 7.67 (1H, m, ArH), 7.75 – 7.77 (2H, m, ArH), 7.80 – 7.83 (2H, m, ArH), 8.19 – 8.22 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.55, 122.08, 126.00, 128.19, 128.32, 128.58, 129.19, 129.55, 129.61, 130.16, 130.62, 131.97, 132.32, 132.62, 133.73, 137.33, 137.77, 138.19, 143.25, 145.14, 151.39, 164.86, 197.76, 198.15 ppm. HRMS (ES): M + Na^+, found 495.1563. $C_{32}H_{24}NaO_4$ requires 495.1567.

(*E*)-2-(4-Chlorobenzylidene)-1,5-bis(4-chlorophenyl)-4-methylenepentane-1,5-dione 12cl

Yellow oil. Yield 22%.

IR (KBr): ν_{max} = 1648 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.84 (2H, br. s, =C<u>CH$_2$</u>C=), 5.65 (1H, t, $^{4}J_{H,H}$ = 1.2 Hz, =C<u>H</u>H), 5.85 (1H, t, $^{4}J_{H,H}$ = 1.5

Hz, =CHH), 7.36–7.41 (7H, m, =CH, ArH), 7.44 (2H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.67 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 7.72 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 30.76, 126.18, 128.61, 128.73, 129.01, 130.54, 130.94, 131.02, 133.11, 135.30, 135.43, 136.23, 137.94, 138.58, 138.98, 142.65, 144.75, 196.40, 196.78 ppm. HRMS (ES): M + H^+, found 455.0365. $C_{25}H_{18}Cl_3O_2$ requires 455.0367.

(*E*)-2-(4-Methylbenzylidene)-4-methylene-1,5-diphenylpentane-1,5-dione 12eh

Yellow oil. Yield 17 %.

IR (KBr): ν_{max} = 1651 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.85 (3H, s, OCH_3), 3.87 – 3.88 (5H, m, =CCH_2C=, OCH_3), 5.57 (1H, br. s, =CH), 5.78 (1H, br. s, =CH), 6.88 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH), 6.95 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.30 (1H, s, =CH), 7.34 – 7.41 (3H, m, ArH), 7.44 – 7.46 (2H, m, ArH), 7.78 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.85 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 31.40, 55.42, 55.46, 113.46, 113.57, 123.77, 128.65, 128.83, 129.21, 130.60, 132.07, 132.11, 135.16, 137.81, 142.42, 145.57, 162.92, 163.20, 196.69, 197.09 ppm. HRMS (ES): M + H^+, found 413.1743. $C_{27}H_{25}O_4$ requires 413.1747.

(*E*)-4-(2,4-Bis(4-methoxybenzoyl)penta-1,4-dien-1-yl)phenyl benzoate 12eq

Yellowish oil. Yield 12 %.

IR (KBr): ν_{max} = 1737 (O-C=O), 1658, 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.84 (3H, s, OCH_3), 3.88 (3H, m, OCH_3), 3.91 (2H, br. s, =CCH_2C=), 5.59 (1H, br. s, =CHH), 5.80 (1H, br. s, =CHH), 6.89 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH), 6.96 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.27 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH),7.30 (1H, s, =CH), 7.52 – 7.55 (4H, m, ArH), 7.65 (1H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.78 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.85 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.19 – 8.21 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 31.43, 55.39, 55.45, 113.48, 113.59, 122.02, 123.94, 128.59, 129.28, 129.77, 130.17, 130.49,

130.55, 132.07, 132.10, 132.84, 133.71, 137.94, 141.22, 145.30, 151.19, 162.96, 163.21, 164.92, 196.00, 196.98 ppm. HRMS (ES): M + Na^+, found 555.1776. $C_{34}H_{28}NaO_6$ requires 555.1778.

(*E*)-2-(4-Methylbenzylidene)-4-methylene-1,5-di(4-methoxyphenyl)pentane-1,5-dione 12fp

Yellowish oil. Yield 26 %.

IR (KBr): ν_{max} = 1715 (O-C=O), 1644 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.36 (3H, s, $\underline{CH_3}C_6H_4$), 3.85 (3H, s, OCH_3), 3.87 – 3.88 (5H, m, =C$\underline{CH_2}$C= and OCH_3), 5.56 (1H, br. s, =C$\underline{H}$H), 5.76 (1H, br. s, =CH$\underline{H}$), 6.89 (2H, d, $^3J_{H,H}$ = 8.7 Hz, ArH), 6.94 (2H, d, $^3J_{H,H}$ = 8.7 Hz, ArH), 7.20 (2H, d, $^3J_{H,H}$ = 8.1 Hz, ArH), 7.30 (1H, s, =CH), 7.35 (2H, d, $^3J_{H,H}$ = 8.1 Hz, ArH), 7.78 – 7.84 (4H, m, ArH) ppm. HRMS (ES): M + Na^+, found 449.1416. $C_{28}H_{26}NaO_4$ requires 449.1723.

1-(4-Nitrophenyl)-2-benzoylallyl benzoate 13bs

Yellow oil. Yield 13 %.

IR (KBr): ν_{max} = 1723 (O-C=O), 1654 (C=O), cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 5.97 (1H, d, $^4J_{H,H}$ = 0.6 Hz, =CH), 6.25 (1H, d, $^4J_{H,H}$ = 1.5 Hz, =CH), 7.14 (1H, br.s, CHOBz), 7.41 – 7.49 (4H, m, ArH), 7.53 – 7.63 (2H, m, ArH), 7.70 – 7.76 (4H, m, ArH), 8.07 – 8.10 (2H, m, ArH), 8.23 (2H, d, $^3J_{H,H}$ = 9.0 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 73.37, 123.36, 124.27, 126.78, 128.20, 128.44, 128.60, 129.31, 129.43, 129.71, 132.90, 133.60, 136.81, 145.34, 145.96, 164.87, 195.26 ppm. HRMS (ES): M + Na^+, found 410.1019. $C_{23}H_{17}NNaO_5$ requires 410.0999.

1-(2,3,4,5,6-Pentafluorophenyl)-2-benzoylallyl benzoate 13bt

Yellow oil. Yield 40 %.

IR (KBr): ν_{max} = 1734 (O-C=O), 1654 (C=O), cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.09 (1H, d, $^4J_{H,H}$ = 1.5 Hz, =CH), 6.43 (1H, d, $^4J_{H,H}$ = 0.9 Hz,

=CH), 7.38 (1H, br.s, CHOBz), 7.44 – 7.49 (4H, m, ArH), 7.56 – 7.63 (2H, m, ArH), 7.77 (2H, d, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 8.09 (2H, d, $^{3}J_{H,H}$ = 6.9 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 65.19, 111.99 (m), 127.25, 128.47, 128.60, 129.43, 129.79, 132.94, 133.35, 133.69, 135.88 (m), 136.83, 139.30 (m), 142.98, 143.80, 147.09 (m), 164.65, 195.12 ppm. HRMS (ES): M + K^+, found 471.0410. $C_{23}H_{13}F_5KO_3$ requires 471.0416.

1-(2,4-Dinitrophenyl)-2-benzoylallyl benzoate 13bu

White solid; m.p. = 94 – 95 °C. Yield 67 %.

IR (KBr): ν_{max} = 1723 (O-C=O), 1661 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.04 (1H, s, =CH), 6.08 (1H, d, $^{4}J_{H,H}$ = 1.1 Hz, =CH), 7.46 (2H, t, $^{3}J_{H,H}$ = 8.1 Hz, ArH), 7.58 (1H, t, $^{3}J_{H,H}$ = 8.1 Hz, ArH), 7.63 (1H, br.s, CHOBz), 7.77 (2H, d, $^{3}J_{H,H}$ = 6.9 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 70.41, 120.50, 127.27, 128.53, 128.67, 129.00, 129.51, 129.84, 130.83, 133.06, 133.86, 136.63, 140.10, 144.19, 147.52, 148.20, 164.74, 194.85 ppm. HRMS (ES): M + H^+, found 433.1024. $C_{23}H_{17}N_2O_7$ requires 433.1030.

***^{18}O labeled*-3-(4-methoxybenzoyl)but-3-en-2-yl acetate 13e*a**

Yellow oil. Yield 11 %.

IR (KBr): ν_{max} = 1739 (O-C=O), 1651 (C=O), 1598 (C=O^{18}) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.48 (3H, d, $^{3}J_{H,H}$ = 6.4 Hz, $CHCH_3$), 2.08 (3H, s, CH_3CO), 3.89 (3H, s, CH_3O), 5.61 (1H, br. s., =CH), 5.80 (1H, q, $^{3}J_{H,H}$ = 6.4 Hz, CHOAc), 5.92 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.95 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.83 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.13, 21.15, 55.48, 69.61, 113.59, 121.97, 129.38, 132.02, 148.48, 163.44, 169.97, 195.10 (C=^{18}O), 195.15 (C=O) ppm. HRMS (ES): M + Na^+, found 271.0943 and 273.0986. $C_{14}H_{16}NaO_4$ and $C_{14}H_{16}NaO_3{}^{18}O$ require 271.0941 and 273.0983.

1-Cyclohexyl-2-(4-methoxybenzoyl)allyl acetate 13ef

Yellowish oil. Yield 29 %.

IR (KBr): ν_{max} = 1732 (O-C=O), 1651 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.03 – 1.24 (5H, m, *c*Hex), 1.62 – 1.81 (6H, m, *c*Hex), 2.05 (3H, s, $OCOCH_3$), 3.85 (3H, s, OCH_3), 5.52 (1H, d, $^{3}J_{H,H}$ = 6.0 Hz, CHOCOMe), 5.63 (1H, s, =CH), 5.80 (1H, s, =CH), 6.91 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.79 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.93, 25.85, 25.96, 26.21, 27.97, 29.27, 40.70, 55.39, 77.42, 113.51, 123.75, 129.93, 131.98, 145.95, 163.28, 170.18, 194.85 ppm. HRMS (ES): M + Na^{+}, found 339.1571. $C_{19}H_{24}NaO_4$ requires 339.1567.

4-Ethyl-2-(4-methoxybenzoyl)hex-1-en-3-yl acetate 13eg

Yellowish oil. Yield 36 %.

IR (KBr): ν_{max} = 1741 (O-C=O), 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.85 (3H, t, $^{3}J_{H,H}$ = 7.2 Hz, $(CH_2\underline{CH_3})_2$), 0.89 (3H, t, $^{3}J_{H,H}$ = 7.2 Hz, $CH(CH_2\underline{CH_3})_2$), 1.23 – 1.34 (2H, m, $\underline{CH_2}CH_3$), 1.37 – 1.44 (1H, m, $\underline{CH_2}CH_3$), 1.46 – 1.53 (1H, m, $\underline{CH_2}CH_3$), 1.56 – 1.63 (1H, m, $\underline{CH}(CH_2CH_3)_2$), 2.07 (3H, s, $OCOCH_3$), 3.84 (3H, s, OCH_3), 5.64 (1H, s, =CH), 5.78 (1H, s, =CH), 5.83 (1H, d, $^{3}J_{H,H}$ = 4.8 Hz, CHOCOMe), 6.91 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) 7.79 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.28, 11.33, 20.92, 20.93, 22.12, 43.44, 55.38, 74.47, 113.51, 123.24, 129.87, 131.92, 146.36, 163.28, 170.07, 194.81 ppm. HRMS (ES): M + Na^{+}, found 327.1567. $C_{18}H_{24}NaO_4$ requires 327.1567.

1-(2-Fluorophenyl)-2-(4-methoxybenzoyl)allyl acetate 13ei

Colorless oil. Yield 31 %.

IR (KBr): ν_{max} = 1744 (O-C=O), 1651 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.09 (3H, s, $OCOCH_3$), 3.84 (3H, s, OCH_3), 5.76 (1H, d, $^{4}J_{H,H}$ = 0.8 Hz, =CH), 5.87 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.91 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH),

7.01 – 7.06 (2H, m, CHOCOMe, ArH), 7.13 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 0.8 Hz, ArH), 7.25 – 7.29 (1H, m, ArH), 7.43 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{3}J_{H,H}$ = 1.6 Hz, ArH), 7.79 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.85, 55.40, 69.29 (d, $^{3}J_{C,F}$= 2.8 Hz), 113.56, 115.74 (d, $^{2}J_{C,F}$= 21.2 Hz), 124.13 (d, $^{3}J_{C,F}$= 3.6 Hz), 124.19, 125.00 (d, $^{2}J_{C,F}$= 13.1 Hz), 129.27 (d, $^{3}J_{C,F}$= 3.6 Hz), 129.72, 130.13 (d, $^{4}J_{C,F}$= 8.3 Hz), 131.90, 145.57, 160.39 (d, $^{1}J_{C,F}$= 248.1 Hz), 143.41, 169.33, 194.06 ppm. HRMS (ES): M + Na^{+}, found 351.1005. $C_{19}H_{17}FNaO_4$ requires 351.1003.

1-(2,4-Dichlorophenyl)-2-(4-methoxybenzoyl)allyl acetate 13em

White solid; m.p. = 99 – 100 °C. Yield 86 %.

IR (KBr): ν_{max} = 1744 (O-C=O), 1649 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.12 (3H, s, CH_3CO), 3.87 (3H, s, OCH_3), 5.78 (1H, d, $^{4}J_{H,H}$ = 1.5 Hz, =CH), 5.84 (1H, d, $^{4}J_{H,H}$ = 0.9 Hz, =CH), 6.94 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 7.13 (1H, br.s, CHOAc), 7.25 – 7.35 (2H, m, ArH), 7.41 (1H, d, $^{4}J_{H,H}$ = 2.1 Hz, ArH), 7.44 (2H, d, $^{3}J_{H,H}$ = 9.0Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.70, 55.35, 70.99, 113.56, 125.51, 129.54, 129.58, 131.84, 132.16, 134.09, 134.23, 134.61, 144.88, 163.44, 169.07, 193.76 ppm. HRMS (ES): M + Na^{+}, found 401.0318. $C_{19}H_{16}NaO_4$ requires 401.0317.

1-(4-Nitrophenyl)-2-(4-methoxybenzoyl)allyl acetate 13es

Colorless oil. Yield 82 %.

IR (KBr): ν_{max} = 1744 (O-C=O), 1652 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.16 (3H, s, CH_3CO), 3.86 (3H, s, CH_3O), 5.85 (1H, d, $^{4}J_{H,H}$ = 1.5 Hz, =CH), 6.14 (1H, d, $^{4}J_{H,H}$ = 1.5 Hz, =CH), 6.88 (1H, br.s, CHOAc), 6.92 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 7.64 (2H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.73 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 8.19 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.80, 55.36, 73.05, 113.59, 123.60, 124.80, 128.10, 129.18, 129.82, 131.77, 145.27, 145.71, 163.49, 169.18, 193.72 ppm. HRMS (ES): M + Na^{+}, found 378.0945. $C_{19}H_{17}NNaO_6$ requires 378.0948.

^{18}*O-labeled*-1-(4-Nitrophenyl)-2-(4-methoxybenzoyl)allyl acetate 13es*

Colorless oil. Yield 82 %.

IR (KBr): ν_{max} = 1743 br. (O-C=O), 1712 (O-C=O^{18}), 1650, 1648 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.13 (3H, s, CH_3CO), 3.87 (3H, s, CH_3O), 5.82 (1H, d, $^{4}J_{H,H}$ = 1.5 Hz, =CH), 6.00 (1H, d, $^{4}J_{H,H}$ = 1.5 Hz, =CH), 6.85 (1H, br.s, CHOAc), 6.89 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.61 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.70 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.17 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.85, 55.41, 73.08 (CH^{18}OAc), 73.11 (CHOAc), 113.64, 123.66, 124.78, 128.14, 129.25, 129.86, 131.82, 145.29, 145.79, 163.55, 169.20 (^{18}O-C=O), 169.21 (O-C=O), 193.76 (C=O) ppm. HRMS (ES): M + Na^{+}, found 378.0960 and 380.1001. $C_{19}H_{17}NNaO_6$ and $C_{19}H_{17}NNaO_5{}^{18}O$ require 378.0954 and 380.0996.

^{18}*O-labeled*-1-(4-Nitrophenyl)-2-(4-methoxybenzoyl)allyl acetate 13e*s

Yellowish solid; m. p. = 92 – 94 °C. Yield 24 %.

IR (KBr): ν_{max} = 1746 (O-C=O), 1648 (C=O), 1599 (C=^{18}O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.14 (3H, s, CH_3CO), 3.84 (3H, s, CH_3O), 5.82 (1H, d, $^{4}J_{H,H}$ = 0.8 Hz, =CH), 6.00 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.86 (1H, br.s, CHOAc), 6.89 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH), 7.62 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.71 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.18 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.89, 55.45, 73.16, 113.69, 123.71, 124.77, 128.18, 129.30, 131.86, 145.33, 145.87, 147.61, 163.60, 169.24, 193.75 (C=^{18}O), 193.80 (C=O) ppm. HRMS (ES): M + Na^{+}, found 378.0942 and 380.0992. $C_{19}H_{17}NNaO_6$ and $C_{19}H_{17}NNaO_5{}^{18}O$ require 378.0948 and 380.0996.

1-(2,3,4,5,6-Pentafluorophenyl)-2-(4-methoxybenzoyl)allyl acetate 13et

Colorless solid; m.p. = 93 – 96°C. Yield 60 %.

IR (KBr): ν_{max} = 1754 (O-C=O), 1652 (C=O), cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.13 (3H, s, CH_3CO), 3.85 (3H, s, CH_3O), 5.92 (1H, d, $^4J_{H,H}$ = 1.6 Hz, =CH), 6.15 (1H, d, $^4J_{H,H}$ = 2.0 Hz, =CH), 6.91 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.07 (1H, br.s, CHOAc), 7.74 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.54, 55.40, 64.95, 111.98, 113.68, 125.26, 129.29, 131.84, 136.19, 138.70, 140.10, 142.84, 144.11, 146.59, 163.62, 169.13, 193.59 ppm. HRMS (ES): M + Na^+, found 423.0630. $C_{19}H_{13}F_5NaO_4$ requires 423.0626.

1-(2,4-Dinitrophenyl)-2-(4-methoxybenzoyl)allyl acetate 13eu

Yellowish solid; m.p. = 178 – 179°C. Yield 68 %.

IR (KBr): ν_{max} = 1741 (O-C=O), 1644 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$ + DMSO) δ: 1.92 (3H, s, CH_3CO), 3.66 (3H, s, CH_3O), 5.65 (1H, d, $^4J_{H,H}$ = 1.5 Hz, =CH), 5.71 (1H, br. s., =CH), 6.73 (2H, d, $^3J_{H,H}$ = 9.0 Hz, ArH), 7.13 (1H, br.s, CHOAc), 7.53 (2H, d, $^3J_{H,H}$ = 9.0 Hz, ArH), 7.73 (2H, d, $^3J_{H,H}$ = 8.9 Hz, ArH), 8.30 (1H, dd, $^3J_{H,H}$ = 8.6 Hz, $^4J_{H,H}$ = 2.3 Hz, ArH), 8.61 (1H, d, $^4J_{H,H}$ = 2.3 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO) δ: 20.08, 54.94, 68.89, 113.20, 119.68, 126.74, 126.85, 128.39, 130.17, 131.30, 138.52, 143.55, 146.80, 147.50, 163.08, 168.47, 192.75 ppm. HRMS (ES): M + Na^+, found 423.0793. $C_{19}H_{16}N_2NaO_8$ requires 423.0799.

1-(4-Trifluoromethyl-2-nitrophenyl)-2-(4-methoxybenzoyl)allyl acetate 13ev

Yellowish solid; m.p. = 126 – 128°C. Yield 87 %.

IR (KBr): ν_{max} = 1742 (O-C=O), 1645 (C=O) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.14 (3H, s, CH_3CO), 3.89 (3H, s, CH_3O), 5.83 (1H, d, $^4J_{H,H}$ = 0.8 Hz, =CH), 5.90 (1H, br. s., =CH), 6.95 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.36 (1H, br.s, CHOAc), 7.81 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.86 – 7.93 (2H, m, ArH), 8.28 (1H, s, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.69, 55.50, 70.14, 113.74, 122.21 (q, $^3J_{C,F}$ = 4 Hz), 122.60 (q, $^1J_{C,F}$ = 271 Hz), 126.79, 129.31,

129.62 (q, $^{3}J_{C,F}$ = 4 Hz), 130.27, 131.66 (q, $^{2}J_{C,F}$ = 34 Hz), 131.98, 137.39, 144.67, 148.15, 163.64, 169.17, 193.61 ppm. HRMS (ES): M + Na^{+}, found 446.0816. $C_{20}H_{16}F_{3}NNaO_{6}$ requires 446.0822.

1-(3-Nitrophenyl)-2-(4-methoxybenzoyl)allyl acetate 13ew

Yellowish oil. Yield 54 %.

IR (KBr): ν_{max} = 1744, 1654 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.14 (3H, s, CH_3CO), 3.84 (3H, s, CH_3O), 5.84 (1H, d, $^{4}J_{H,H}$ = 0.8 Hz, =CH), 6.04 (1H, d, $^{4}J_{H,H}$ = 1.6 Hz, =CH), 6.87 (1H, br.s, CHOAc), 6.90 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.51 (1H, t, $^{3}J_{H,H}$ = 8.0 Hz, ArH), 7.73 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.79 (1H, dt, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 1.2 Hz, ArH), 8.14 (1H, ddd, $^{3}J_{H,H}$ = 8.3 Hz, $^{4}J_{H,H}$ = 2.4 Hz, $^{4}J_{H,H}$ = 1.2 Hz, ArH), 8.30 (1H, t, $^{4}J_{H,H}$ = 1.6 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.95, 55.45, 73.06, 113.68 (m), 122.06, 123.23, 124.81, 129.32, 129.48, 131.86, 134.04, 140.30, 145.80, 148.31, 163.55, 169.30, 193.85 ppm. HRMS (ES): M + Na^{+}, found 378.0950. $C_{19}H_{17}NNaO_{6}$ requires 378.0948.

3-Benzoylbut-3-en-2-yl benzoate 13fa

Colorless oil. Yield 23%.

IR (KBr): ν_{max} = 1715 (O-C=O), 1649 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.60 (3H, d, $^{3}J_{H,H}$ = 6.4 Hz, CH_3), 3.86 (3H, s, OCH_3), 5.63 (1H, s, =CH), 5.99 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.02 (1H, q, $^{3}J_{H,H}$ = 6.4 Hz, CHOCOPh), 6.93 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.42 (2H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.55 (1H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.84 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.03 – 8.05 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.29, 55.43, 70.19, 113.55, 122.04, 128.33, 129.56, 129.90, 130.19, 132.00, 132.97, 148.46, 163.38, 165.41, 195.14 ppm. HRMS (ES): M + Na^{+}, found 333.1094. $C_{19}H_{18}NaO_{4}$ requires 333.1097.

1-Cyclohexyl-2-(4-methoxybenzoyl)allyl benzoate 13ff

White solid, m. p. = 87–89 ^{o}C. Yield 55 %.

IR (KBr): ν_{max} = 1702 (O-C=O), 1649 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.13 – 1.28 (5H, m, *c*Hex), 1.65 – 1.93 (6H, m, *c*Hex), 3.84 (3H, s, OCH_3), 5.68 (1H, s, =CH), 5.82 (1H, d, $^{3}J_{H,H}$ = 5.6 Hz, CHOCOPh), 5.90 (1H, s, =CH), 6.91 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.45 (2H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.56 (1H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.83 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.07 – 8.09 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 25.91, 25.99, 26.23, 27.86, 29.48, 40.95, 55.36, 77.65, 113.50, 123.92, 128.35, 129.53, 129.87, 130.18, 131.99, 132.95, 145.95, 163.22, 165.54, 194.86 ppm. HRMS (ES): M + Na^{+}, found 401.1718. $C_{24}H_{26}NaO_4$ requires 401.1723.

4-Ethyl-2-(4-methoxybenzoyl)hex-1-en-3-yl benzoate 13fg

Yellowish oil. Yield 37 %.

IR (KBr): ν_{max} = 1718 (O-C=O), 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92 – 0.98 (6H, m, $CH(CH_2\underline{CH_3})_2$), 1.36 – 1.53 (3H, m, $\underline{CH_2}CH_3$), 1.64 – 1.77 (2H, m, $\underline{CH_2}CH_3$, $\underline{CH}(CH_2CH_3)_2$), 3.85 (3H, s, OCH_3), 5.69 (1H, s, =CH), 5.86 (1H, d, , $^{4}J_{H,H}$ = 0.8 Hz, =CH), 6.14 (1H, d, $^{3}J_{H,H}$ = 4.4 Hz, CHOCOPh), 6.93 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.45 (2H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.57 (1H, t, $^{3}J_{H,H}$ = 7.2 Hz, ArH), 7.85 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.08 – 8.10 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.44, 11.55, 21.16, 22.43, 43.77, 55.39, 74.89, 113.56, 128.41, 129.58, 129.93, 130.14, 131.96, 133.02, 146.44, 163.30, 165.49, 194.84 ppm. HRMS (ES): M + Na^{+}, found 389.1722. $C_{23}H_{26}NaO_4$ requires 389.1723.

1-(2-Fluorophenyl)-2-(4-methoxybenzoyl)allyl benzoate 13fi

Yellowish oil. Yield 42 %.

IR (KBr): ν_{max} = 1721 (O-C=O), 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.84 (3H, s, OCH_3), 5.82 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.01 (1H, d,

$^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.92 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.04 – 7.09 (1H, m, ArH), 7.14 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{3}J_{H,H}$ = 0.8 Hz, ArH), 7.31 (1H, br. s., CHOCOPh), 7.41 (2H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.52 – 7.57 (2H, m, ArH), 7.84 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.05 – 8.08 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.38, 70.04 (d, $^{3}J_{C,F}$= 2.5 Hz), 113.57, 115.81 (d, $^{2}J_{C,F}$= 21.2 Hz), 124.12, 124.17 (d, $^{3}J_{C,F}$= 3.6 Hz), 124.95 (d, $^{2}J_{C,F}$= 13.0 Hz), 128.36, 129.39 (d, $^{3}J_{C,F}$= 3.5 Hz), 129.53, 129.68, 129.70, 130.20 (d, $^{4}J_{C,F}$= 8.2 Hz), 131.90, 133.15, 145.54, 160.50 (d, $^{3}J_{C,F}$= 248.2 Hz), 163.40, 164.88, 194.09 ppm. HRMS (ES): M + Na^+, found 413.1162. $C_{24}H_{19}FNaO_4$ requires 413.1160.

1-(2-Chlorophenyl)-2-(4-methoxybenzoyl)allyl benzoate 13fk

Yellowish oil. Yield 59 %.

IR (KBr): ν_{max} = 1724 (O-C=O), 1651 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.84 (3H, s, CH_3O), 5.83 (2H, m, =CH_2), 6.92 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 7.23 – 7.28 (2H, m, ArH), 7.37 – 7.43 (4H, m, CHOBz, ArH), 7.51 – 7.58 (2H, m, ArH), 7.86 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 8.03 – 8.07 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.40, 72.30, 113.60, 125.24, 126.95, 128.36, 128.82, 129.53, 129.64, 129.70, 129.71, 129.90, 131.93, 133.14, 133.46, 135.45, 145.39, 163.42, 164.86, 194.09 ppm. HRMS (ES): M + Na^+, found 429.0869. $C_{24}H_{19}ClNaO_6$ requires 429.0864.

1-(2,4-Dichlorophenyl)-2-(4-methoxybenzoyl)allyl benzoate 13fm

Yellowish solid; m.p. = 153 – 156°C. Yield 88 %.

IR (KBr): ν_{max} = 1725 (O-C=O), 1653 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.85 (3H, s, CH_3O), 5.86 (1H, d, $^{4}J_{H,H}$ = 0.9 Hz, =CH), 5.89 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.93 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 7.26 (2H, dd, $^{3}J_{H,H}$ = 8.4 Hz, $^{4}J_{H,H}$ = 2.1 Hz, ArH), 7.34 (1H, br. s, CHOBz), 7.39 – 7.44 (3H, m, ArH), 7.50 – 7.57 (2H, m, ArH), 7.84 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 8.03 – 8.06 (2H, m, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.40, 71.84, 113.65, 125.41, 127.31, 128.41, 129.41, 129.54, 129.69, 129.84, 131.91, 133.28,

134.20, 134.76, 144.94, 163.51, 164.78, 193.86 ppm. HRMS (ES): M + Na^+, found 463.0481. $C_{24}H_{18}Cl_2NaO_4$ requires 463.0474.

1-(2-Nitrophenyl)-2-(4-methoxybenzoyl)allyl benzoate 13fr

Yellowish solid; m.p. = 120 – 122^oC. Yield 22 %.

IR (KBr): ν_{max} = 1726 (O-C=O), 1651 (C=O) cm^{-1}.^1H NMR (400 MHz, $CDCl_3$) δ: 3.85 (3H, s, OCH_3), 5.81 (1H, d, $^4J_{H,H}$ = 1.2 Hz, =CH), 5.86 (1H, d, $^4J_{H,H}$ = 0.4 Hz, =CH), 6.93 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.42 (2H, t, $^3J_{H,H}$ = 7.6 Hz, ArH), 7.46 – 7.51 (1H, m, ArH), 7.56 (1H, t, $^3J_{H,H}$ = 7.6 Hz, ArH), 7.60 (1H, br. s, CHOCOPh), 7.63 (1H, td, $^3J_{H,H}$ = 7.6 Hz, $^4J_{H,H}$ = 1.2 Hz, ArH), 7.77 (1H, dd, $^3J_{H,H}$ = 8.0 Hz, $^4J_{H,H}$ = 1.2 Hz, ArH), 7.84 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 8.01 – 8.04 (3H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.44, 71.10, 113.67, 124.94, 126.01, 128.46, 129.14, 129.21, 129.33, 129.58, 129.76, 131.95, 133.36, 133.43, 145.59, 148.23, 163.49, 164.88, 193.97 ppm. HRMS (ES): M + Na^+, found 440.1089. $C_{24}H_{19}NNaO_6$ requires 440.1105.

1-(4-Nitrophenyl)-2-(4-methoxybenzoyl)allyl benzoate 13fs

Yellow oil. Yield 70 %.

IR (KBr): ν_{max} = 1725 (O-C=O), 1651 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.84 (3H, s, CH_3O), 5.88 (1H, d, $^4J_{H,H}$ = 0.6 Hz, =CH), 6.14 (1H, d, $^4J_{H,H}$ = 1.5 Hz, =CH), 6.91 (2H, d, $^3J_{H,H}$ = 9.0 Hz, ArH), 7.11 (1H, br.s, CHOBz), 7.43 – 7.48 (2H, m, ArH), 7.59 (1H, t, $^3J_{H,H}$ = 7.5 Hz, ArH), 7.71 – 7.78 (4H, m, ArH), 8.06 – 8.10 (2H, m, ArH), 8.20 (2H, d, $^3J_{H,H}$ = 9.0 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.42, 73.71, 113.70, 123.77, 124.83, 128.13, 128.53, 129.28, 129.65, 131.88, 133.51, 145.37, 145.91, 147.61, 163.59, 164.84, 193.85 ppm. HRMS (ES): M + Na^+, found 440.1096. $C_{24}H_{19}NNaO_6$ requires 440.1105.

^{18}O-labeled*-1-(4-nitrophenyl)-2-(4-methoxybenzoyl)allyl benzoate 13fs

Yellow oil. Yield 68 %.

IR (KBr): ν_{max} = 1723 (O-C=O), 1651 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.85 (3H, s, CH_3O), 5.88 (1H, d, $^{4}J_{H,H}$ = 0.6 Hz, =CH), 6.14 (1H, d, $^{4}J_{H,H}$ = 1.5 Hz, =CH), 6.92 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 7.11 (1H, br.s, CHOBz), 7.44 – 7.48 (2H, m, ArH), 7.59 (1H, tt, $^{3}J_{H,H}$ = 7.5 Hz, $^{4}J_{H,H}$ = 1.2 Hz ArH), 7.72 – 7.78 (4H, m, ArH), 8.07 – 8.10 (2H, m, ArH), 8.21 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.45, 73.71 ($CH^{18}OBz$), 73.74 (CHOBz), 113.73, 123.80, 124.85, 128.15, 128.56, 129.37, 129.68, 131.91, 133.54, 145.39, 145.97, 147.69, 163.62 (^{18}O-C=O), 163.69 (O-C=O), 164.85, 193.88 ppm. HRMS (ES): M + Na^{+}, found 440.1098 and 442.1155. $C_{24}H_{19}NNaO_6$ and $C_{24}H_{19}NNaO_5{}^{18}O$ require 440.1110 and 442.1152.

1-(2,3,4,5,6-Pentafluorophenyl)-2-(4-methoxybenzoyl)allyl benzoate 13ft

Yellowish oil. Yield 66 %.

IR (KBr): ν_{max} = 1731 (O-C=O), 1651 (C=O), cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.87 (3H, s, CH_3O), 5.99 (1H, d, $^{4}J_{H,H}$ = 2.0 Hz, =CH), 6.30 (1H, d, $^{4}J_{H,H}$ = 1.6 Hz, =CH), 6.95 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.35 (1H, br.s, CHOBz), 7.46 (2H, t, $^{3}J_{H,H}$ = 8.0 Hz, ArH), 7.60 (1H, t, $^{3}J_{H,H}$ = 7.6 Hz, ArH), 7.80 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.06 – 8.08 (2H, m, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.48, 65.47, 112.02, 113.78, 125.22, 128.59, 128.99, 129.38, 129.79, 131.93, 133.66, 136.28, 138.80, 140.23, 143.06, 144.21, 146.76, 163.69, 164.69, 193.69 ppm. HRMS (ES): M + H^{+}, found 485.0790. $C_{24}H_{15}F_5NaO_4$ requires 485.0783.

1-(2,4-Dinitrophenyl)-2-(4-methoxybenzoyl)allyl benzoate 13fu

Yellowish solid; m.p. = 153 – 156 ^{o}C. Yield 90 %.

IR (KBr): ν_{max} = 1726 (O-C=O), 1647 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.86 (3H, s, CH_3O), 5.96 (1H, s, =CH), 6.00 (1H, br. s, =CH), 6.93 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 7.44 (2H, t, $^{3}J_{H,H}$ = 7.5 Hz, ArH), 7.57 – 7.62 (2H, m, CHOBz, ArH), 7.80 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 8.00 – 8.03 (3H, m, ArH), 8.45 (1H, dd, $^{3}J_{H,H}$ = 8.7 Hz, $^{4}J_{H,H}$ = 2.1 Hz, ArH), 8.83 (1H, d, $^{4}J_{H,H}$ =

2.4 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.49, 70.71, 113.80, 120.38, 127.11, 127.22, 128.63, 129.14, 129.79, 130.10, 130.87, 132.00, 133.80, 140.15, 144.15, 147.41, 148.17, 163.75, 164.75, 193.46 ppm. HRMS (ES): M + Na^+, found 485.0962. $C_{24}H_{18}N_2NaO_8$ requires 485.0955.

1-(2-Nitrophenyl)-2-(2,4-dimethoxybenzoyl)allyl acetate 13gr

Yellow oil. Yield 52 %.

IR (KBr): ν_{max} = 1746 (O-C=O), 1652 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.06 (3H, s, CH_3CO), 3.76 (3H, s, CH_3O), 3.81 (3H, s, CH_3O), 5.65 (1H, d, $^4J_{H,H}$ = 1.2 Hz, =CH), 5.86 (1H, s, =CH), 6.43 (1H, d, $^4J_{H,H}$ = 2.0 Hz, ArH), 6.46 (1H, dd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.0 Hz, ArH), 7.33 (1H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.39 (1H, br.s, CHOAc), 7.43 – 7.47 (1H, m, ArH), 7.59 – 7.66 (2H, m, ArH), 7.96 (1H, dd, $^3J_{H,H}$ = 8.0 Hz, $^4J_{H,H}$ = 0.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.67, 55.41, 69.53, 98.57, 107.53, 120.67, 124.68, 127.56, 128.90, 129.26, 131.98, 133.08, 133.57, 147.11, 148.20, 159.47, 163.45, 169.15, 194.02 ppm. HRMS (ES): M + Na^+, found 408.1049. $C_{20}H_{19}NNaO_7$ requires 408.1053.

1-(4-Nitrophenyl)-2-(2,4-dimethoxybenzoyl)allyl acetate 13gs

Yellow oil. Yield 51 %.

IR (KBr): ν_{max} = 1745 (O-C=O), 1652 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.13 (3H, s, CH_3CO), 3.70 (3H, s, CH_3O), 3.82 (3H, s, CH_3O), 5.84 (1H, d, $^4J_{H,H}$ = 0.8 Hz, =CH), 6.02 (1H, d, $^4J_{H,H}$ = 1.2 Hz, =CH), 6.42 (1H, d, $^4J_{H,H}$ = 2.0 Hz, ArH), 6.46 (1H, dd, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 2.0 Hz, ArH), 6.90 (1H, br.s, CHOAc), 7.23 (1 H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.62 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 8.18 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.94, 55.46, 72.49, 98.71, 104.56, 120.49, 123.50, 126.01, 128.45, 131.88, 145.66, 147.46, 147.52, 159.48, 163.59, 169.18, 194.29 ppm. HRMS (ES): M + Na^+, found 408.1055. $C_{20}H_{19}NNaO_7$ requires 408.1053.

2-((2-Fluorophenyl)(hydroxy)methyl)-1-phenylprop-2-en-1-one 14fi

Yellowish oil. Yield 9 %.

IR (KBr): ν_{max} = 3433 (OH), 1643 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.85 (3H, s, OCH_3), 5.70 (1H, s, CHOH),5.89 (1H, br. s, =CH), 5.93 (1H, d, $^{3}J_{H,H}$ = 5.2 Hz, =CH), 6.90 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 6.99 – 7.04 (1H, m, ArH), 7.15 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 0.8 Hz, ArH), 7.22 – 7.28 (1H, m, ArH), 7.57 (1H, td, $^{3}J_{H,H}$ = 7.6 Hz, $^{4}J_{H,H}$ = 1.6 Hz, ArH), 7.75 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.47, 69.42 (d, $^{3}J_{C,F}$= 3.2 Hz), 113.62, 115.18 (d, $^{2}J_{C,F}$= 21.2 Hz), 124.30 (d, $^{3}J_{C,F}$= 3.5 Hz), 125.63, 128.09 (d, $^{3}J_{C,F}$= 3.9 Hz), 128.27 (d, $^{2}J_{C,F}$= 13.0 Hz), 129.29 (d, $^{4}J_{C,F}$= 8.2 Hz), 129.62, 132.16, 147.12, 159.82 (d, $^{1}J_{C,F}$= 244.9 Hz), 163.68, 197.52 ppm. HRMS (ES): M + Na^{+}, found 309.0896. $C_{17}H_{15}FNaO_3$ requires 309.0897.

2-((2-Chlorophenyl)(hydroxy)methyl)-1-(4-methoxyphenyl)prop-2-en-1-one 14fk

Yellow oil. Yield 13 %.

IR (KBr): ν_{max} = 3435 (OH), 1645 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.86 (3H, s, OCH_3), 5.69 (1H, s, =CH),5.73 (1H, s, =CH), 5.98 (1H, s, CHOH), 6.91 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 7.20 – 7.25 (1H, m, ArH), 7.29 – 7.37 (2H, m, ArH), 7.70 (1H, dd, $^{3}J_{H,H}$ = 7.5 Hz, $^{4}J_{H,H}$ = 1.5 Hz, ArH), 7.79 (2H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH) ppm. HRMS (ES): M + Na^{+}, found 325.0606. $C_{17}H_{15}ClNaO_3$ requires 325.0602.

2-((2,4-Dichlorophenyl)(hydroxy)methyl)-1-(4-methoxyphenyl)prop-2-en-1-one 14fm

Orange oil. Yield 32 %.

IR (KBr): ν_{max} = 3431 (OH), 1645 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.85 (3H, s, OCH_3), 5.70 (1H, s, =CH),5.73 (1H, d, $^{4}J_{H,H}$ = 0.9 Hz, =CH), 5.91 (1H, s, CHOH), 6.91 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 7.29 (1H, dd, $^{3}J_{H,H}$ = 8.4 Hz,

$^{4}J_{H,H}$ = 2.1 Hz, ArH), 7.36 (1H, d, $^{4}J_{H,H}$ = 2.1 Hz, ArH), 7.63 (1H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.77 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.49, 71.11, 113.72, 126.56, 127.36, 129.13, 129.15, 129.35, 132.24, 132.83, 133.92, 137.13, 146.43, 163.83, 197.60 ppm. HRMS (ES): M + Na^+, found 359.0220. $C_{17}H_{14}Cl_2NaO_3$ requires 359.0212.

2-[Hydroxy(4-nitrophenyl)methyl]-1-(4-methoxyphenyl)prop-2-en-1-one 14fs

Yellow oil. Yield 5 %.

IR (KBr): ν_{max} = 3440 (OH), 1644 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.86 (3H, s, CH_3O), 5.78 (1H, br. s., CHOH), 5.80 (1H, br.s., =CH), 6.02 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.90 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.62 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.71 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.19 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.53, 74.30, 113.80, 123.67, 126.33, 127.09, 129.27, 132.09, 147.42, 148.83, 163.92, 196.71 ppm. HRMS (ES): M + Na^+, found 336.0850. $C_{17}H_{15}NNaO_5$ requires 336.0848.

^{18}O-labeled*-2-[hydroxy(4-nitrophenyl)methyl]-1-(4-methoxyphenyl)prop-2-en-1-one 14fs

Yellow oil. Yield 10 %.

IR (KBr): ν_{max} = 3437 (OH), 1644 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.87 (3H, s, CH_3O), 5.80 (1H, br. s., CHOH), 5.82 (1H, br.s., =CH), 6.03 (1H, d, $^{4}J_{H,H}$ = 1.2 Hz, =CH), 6.92 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.63 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.72 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.20 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.53, 74.29 (CH-^{18}O), 74.32 (CH-O), 113.80, 123.67, 126.33, 127.09, 129.27, 132.09, 147.42, 148.83, 163.92, 196.71 ppm. HRMS (ES): M + Na^+, found 336.0850 and 338.0993. $C_{17}H_{15}NNaO_5$ and $C_{17}H_{15}NNaO_4{}^{18}O$ require 336.0848 and 338.0890.

2-((2,3,4,5,6-Pentafluorophenyl)(hydroxy)methyl)-1-(4-methoxyphenyl)prop-2-en-1-one 14ft

Yellow oil. Yield 38 %.

IR (KBr): ν_{max} = 3431 (OH), 1654 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.86 (3H, s, CH_3O), 5.89 (1H, d, $^{4}J_{H,H}$ = 1.6 Hz, =CH), 6.15 (1H, br. s, CHOH), 6.20 (1H, d, $^{4}J_{H,H}$ = 1.6 Hz, =CH), 6.92 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.75 (2H, d, $^{3}J_{H,H}$ = 9.2 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.48, 65.07, 113.74, 114.90 (m), 125.31, 128.43, 129.37, 130.11, 131.99, 136.24, 138.76, 139.66, 143.83, 146.01, 146.28, 163.75, 195.52 ppm. HRMS (ES): M + H^+, found 381.0524. $C_{17}H_{11}F_5NaO_3$ requires 381.0521.

2-((2,4-Dinitrophenyl)(hydroxy)methyl)-1-(4-methoxyphenyl)prop-2-en-1-one 14fu

Yellow oil. Yield 59 %.

IR (KBr): ν_{max} = 3436 (OH), 1639 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.85 (3H, s, CH_3O), 5.74 (1H, d, $^{4}J_{H,H}$ = 0.6 Hz, =CH), 5.75 (1H, s, =CH), 6.31 (1H, br. s, CHOCOPh), 6.89 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 7.70 (2H, d, $^{3}J_{H,H}$ = 9.0 Hz, ArH), 8.24 (1H, d, $^{3}J_{H,H}$ = 8.7 Hz, ArH), 8.48 (1H, dd, $^{3}J_{H,H}$ = 8.7 Hz, $^{4}J_{H,H}$ = 2.4 Hz, ArH), 8.79 (1H, d, $^{4}J_{H,H}$ = 2.4 Hz, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.50, 69.75, 113.81, 120.04, 126.93, 127.37, 128.67, 130.71, 132.20, 143.15, 146.31, 147.14, 147.57, 164.00, 196.72 ppm. HRMS (ES): M + Na^+, found 381.0698. $C_{17}H_{14}N_2NaO_7$ requires 381.0693.

Synthesis of 1,5-Bis(4-methoxyphenyl)-2-methylenepentane-1,5-dione 15

3-(4-Methoxyphenyl)prop-2-ynol (0.33 g, 2.03 mmol) and NEt_3 (0.70 ml, 5.1 mmol) were dissolved in the DCM (10 ml) and cooled to the 0 °C. Mesyl chloride (0.24 ml, 3.06 mmol) was slowly added to the stirred reaction mixture, after 15 min. reaction mixture was warmed to the room temperature. After completion of the reaction (observed by TLC) the mixture was washed with water (2×10 ml), then with 10 % HCl (2×10 ml), water (2×10 ml), saturated

solution of $NaHCO_3$ (2×10 ml). The organic layer was separated, dried over anhydrous Na_2SO_4, evaporated under reduced pressure and the residue was purified by Flash Column chromatography eluting with hexane–ethyl acetate mixtures.

Yellow oil. Yield 9 %.

IR (KBr): ν_{max} = 2054 (C=CH_2), 1672 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.87 (2H, t, $^3J_{H,H}$ = 7.2 Hz, CH_2), 3.15 (2H, t, $^3J_{H,H}$ = 7.2 Hz, CH_2), 3.85 (6H, s, CH_3O), 5.56 (1H, s, =CH), 5.83 (1H, d, $^4J_{H,H}$ = 0.8 Hz, =CH), 6.91 (4H, d, $^3J_{H,H}$ = 9.2 Hz, ArH), 7.78 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.94 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.01, 36.79, 55.41, 113.45, 113.68, 124.78, 129.82, 130.14, 130.34, 131.95, 146.99, 163.13, 163.41, 196.94, 197.85 ppm. HRMS (ES): M + Na^+, found 347.1253. $C_{20}H_{20}NaO_4$ requires 347.1254.

General Method for the Preparation of Compounds 16

A solution of the MBH adduct **13es** or **13em** (0.14 mmol) and appropriate amine (0.168 mmol) in dimethylformamide (2 mL) was stirred at room temperature till the reaction was completed (monitored by TLC). The mixture was then quenched with ethyl acetate (10 mL), and the organic solution was 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.

(*E*)-2-((Diethylamino)methyl)-1-(4-methoxyphenyl)-3-(4-nitrophenyl)prop-2-en-1-one 16a

Yellow solid, m. p. = 69 – 71 ^oC. Yield 48 %.

IR (KBr): ν_{max} = 1650 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.90 (6H, t, $^3J_{H,H}$ = 6.4 Hz, $N(CH_2CH_3)_2$), 2.48 (4H, q, $^3J_{H,H}$ = 6.4 Hz, $N(CH_2CH_3)_2$), 3.58 (2H, s, CH_2NEt_2), 3.88 (3H, s, OCH_3), 6.97 (2H, d, $^3J_{H,H}$ = 8.8 Hz, ArH), 7.06 (1H, s, =CH), 7.73 (2H, d, $^3J_{H,H}$ = 8.4 Hz, ArH), 7.90 (2H, d, $^3J_{H,H}$ = 8.4 Hz,

ArH), 8.24 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.24, 46.63, 50.59, 55.48, 113.69, 123.47, 129.71, 130.55, 131.98, 135.97, 142.17, 144.10, 147.28, 163.34, 196.65 ppm. HRMS (ES): M + H^+, found 369.1806. $C_{21}H_{25}N_2O_4$ requires 369.1809.

(*E*)-1-(4-Methoxyphenyl)-2-(morpholinomethyl)-3-(4-nitrophenyl)prop-2-en-1-one 16c

Yellow solid, m. p. = 107 – 109 ^{o}C. Yield 77 %.

IR (KBr): ν_{max} = 1656 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.45 (4H, br. s, N($\underline{CH_2}CH_2)_2O$), 3.49 (2H, s, $\underline{CH_2}N(CH_2CH_2)_2O$), 3.62 (4H, br. s, $N(CH_2\underline{CH_2})_2O$), 3.87 (3H, s, OCH_3), 6.96 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.17 (1H, s, =CH), 7.76 (2H, d, $^{3}J_{H,H}$ = 8.4 Hz, ArH), 7.87 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 8.24 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 53.37, 55.22, 55.47, 66.82, 113.77, 123.52, 129.35, 130.57, 131.98, 138.33, 141.57, 141.79, 147.40, 163.42, 196.12 ppm. HRMS (ES): M + H^+, found 383.1607. $C_{21}H_{23}N_2O_5$ requires 383.1601.

(*E*)-3-(2,4-Dichlorophenyl)-1-(4-methoxyphenyl)-2-(morpholinomethyl)prop-2-en-1-one 16f

Yellow solid, m. p. = 117 – 118 ^{o}C. Yield 53 %.

IR (KBr): ν_{max} = 1643 (C=O) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.39 (4H, br. s, N($\underline{CH_2}CH_2)_2O$), 3.44 (2H, s, $\underline{CH_2}N(CH_2CH_2)_2O$), 3.57 (4H, br. s, $N(CH_2\underline{CH_2})_2O$), 3.88 (3H, s, OCH_3), 6.97 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH), 7.14 (1H, s, =CH), 7.29 (1H, dd, $^{3}J_{H,H}$ = 8.0 Hz, $^{4}J_{H,H}$ = 2.0 Hz, ArH), 7.44 (1H, d, $^{4}J_{H,H}$ = 2.0 Hz, ArH), 7.61 (1H, d, $^{3}J_{H,H}$ = 8.0 Hz, ArH), 7.94 (2H, d, $^{3}J_{H,H}$ = 8.8 Hz, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 53.33, 55.03, 55.45, 66.82, 113.70, 126.91, 129.27, 129.54, 131.91, 132.14, 132.55, 134.58, 134.89, 163.41, 196.22 ppm. HRMS (ES): M + H^+, found 406.0977. $C_{21}H_{22}Cl_2NO_3$ requires 406.0971.

CONCLUSIONS

1. It was found that aliphatic aldehydes and pent-4-yn-2-ol in the presence of iron (III) chloride reacted ambiguously resulting in the formation of complex mixtures and therefore hardly can be applied for the synthesis of β'-hydroxy-α,β-unsaturated ketones.
2. The new reduction method of nonconjugated Δ^2-isoxazolines using $Al/CuCl_2$ couple was presented, providing a fast, economical, and efficient protocol for the preparation of β-hydroxy ketones.
3. The optimal results for the reduction of α,β-unsaturated Δ^2-isoxazolines were obtained using $Mo(CO)_6$. 3-alkyl or 3-aryl-Δ^2-isoxazolines also could be reduced using Fe/NH_4Cl couple. Moreover, Fe/NH_4Cl system initiated retro-aldol reaction especially in activated Δ^2-isoxazolines.
4. The reactions between 3-arylprop-2-ynyl carboxylates and aldehydes led to the formation of (*E*)- and (*Z*)-2-aroyl-3-substituted allyl carboxylates (**10** and **11**), (*E*)-2-arylidene-1,5-diaryl-4-methylenepentane-1,5-diones (**12**) and 1-substituted 2-aroylallyl carboxylates (**13**) and formation of products depended on the structures of both starting materials.
5. The mechanistic investigation revealed that 3-arylprop-2-ynyl esters and aldehydes underwent reactions through two competing energetically feasible pathways, *via* either a four- or six-membered intermediates. It was also proved that the formation of adducts **13** always proceeded *via* a new addition–rearrangement cascade. Thus acceptor-substituted benzaldehydes and/or donor-substituted alkynes were shown to dramatically switch from the classical alkyne–carbonyl metathesis pathway to the newly discovered addition–rearrangement cascade.
6. The presented synthetic method provided a useful approach to 1-substituted 2-aroylallyl carboxylate (**13**) derivatives that have been difficult to access by the classical MBH reactions. Prolonged reaction

times allowed the synthesis of thermodynamically more stable 2-aroyl-3-substituted allyl carboxylates (**10**, **11**).

7. Structure – anticancer activity relationship evaluation of β'-hydroxy-α,β-unsaturated ketones and their analogues revealed, that conjugation of carbonyl group is crucial for biological activity of β-hydroxy ketones. Also this group of synthesized compounds exhibited only moderate growth inhibition. The compound (*E*)-1,5-dicyclohexyl-5-hydroxypent-1-en-3-one remained in lead position and various changes of substituents on main scaffold only diminished antiproliferative activity.
8. Structure – anticancer activity relationship of α,β-unsaturated ketones with various α- and β-substituents was evaluated. It was shown that aromatic substituents were superior to aliphatic ones. Better selectivity between cell lines was reached varying α-substituents whereas the absence of β-substituents gave opposite effect. These results revealed a set of compounds as promising candidates for further biological evaluations.

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