VILNIUS UNIVERSITY

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PYRROLO[2,3-*d*]PYRIMIDINE-BASED π-CONJUGATED FLUOROPHORES WITH 1,2,3-TRIAZOLE AND ETHYNYL LINKERS: SYNTHESIS AND PHOTOPHYSICAL PROPERTIES

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VILNIAUS UNIVERSITETAS

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PIROLO[2,3-*d*]PIRIMIDINO π-KONJUGUOTŲ FLUOROFORŲ, TURINČIŲ 1,2,3-TRIAZOLO IR ETINIL JUNGTUKUS, SINTEZĖ IR FOTOFIZIKINĖS SAVYBĖS

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List of Abbreviations and Physical Units

Å - angstrom

AAC – azide-alkyne cycloaddition

acac – acetylacetonate

Ad – adamantyl

ATRP – atom transfer radical polymerization

Bn - benzyl

Boc – *tert*-butoxycarbonyl

Bu – butyl

B3LYP - Becke, 3-parameter, Lee-Yang-Parr

CuAAC – copper (I)-catalyzed alkyne-azide cycloaddition

CT – charge transfer

CV - cyclic voltammetry

Cy – cyclohexane

D – debye

dba – dibenzylideneacetone

DCM – dichloromethane

DFT – density functional theory

DIPEA – diisopropylethylamine

DMF – *N*,*N*-dimethylformamide

DMSO – dimethyl sulfoxide

DNA – deoxyribonucleic acid

dppe – 1,2-bis(diphenylphosphino)ethane

dppf – 1,1’-bis(diphenylphosphino)ferocene

dppp – 1,3-bis(diphenylphosphino)propane

FMO – frontier molecular orbital

GC – gas chromatography

GIAO - gauge-independent atomic orbital

HMBC – Heteronuclear multiple-bond correlation spectroscopy

HOMO – highest occupied molecular orbital

HRMS – high resolution mass spectrometry

HSQC – Heteronuclear Single Quantum Coherence

IEFPCM – integral equation formalism polarizable continuum

LUMO – lowest unoccupied molecular orbital

MS – mass spectrometry

MW – microwave irradiation

NaAsc – sodium ascorbate

NBS – *N*-bromosuccinimide

NMR – nuclear magnetic resonance

NOESY – nuclear Overhauser effect spectroscopy

PES – potential energy surface

Ph – phenyl

PMDTA - *N*,*N*,*N′*,*N′*,*N″*-pentamethyldiethylenetriamine

PPA – polyphosphoric acid

ppm – parts per million

SCRF – self consistent reaction field

TBTA – tris(benzyltriazolyl)methyl amine

TBDMS – *tert*-butyldimethylsilyl

THF – tetrahydrofuran

THPTA – tris(3-hydroxypropyltriazolylmethyl)amine

TMS – trimethylsilyl or tetramethylsilane

TMSA – trimethylsilylacetylene

TLC – thin layer chromatography

UV-Vis – ultraviolet-visible spectroscopy

δ – chemical shift

Φ_F – fluorescence quantum yield

1. INTRODUCTION

Over recent years, organic molecules with a π-conjugated backbone have received much attention in both academic and industry due to their applications in a wide range of electronic and optoelectronic devices [1–6]. Introduction of heteroaryl moieties into the backbone of extended π-systems considerably influences molecular orbitals, stereochemical structure and linking topology of the substituents. In this regard, pyrimidine ring containing heterocycles owing to their aromaticity, significant π-deficiency and ability of nitrogen atoms to take part in the chelation processes, are desired structural units to be incorporated in more complex organic structures targeted for numerous applications [7–11]. Pyrimidine moiety has already been incorporated into linear, star- and banana-shaped oligomers that show good light emitting properties and two-photon absorption [11–18]. Pyrimidine ring is frequently used in push–pull structures as a strong electron-withdrawing unit and together with electron-donating moieties results in intramolecular charge transfer character, which plays a key role in important applications, such as nonlinear optics [12], polarity or pH sensors [12,14,15], bioimaging [16] and metal sensors [9,19–22] (Fig. 1.1).

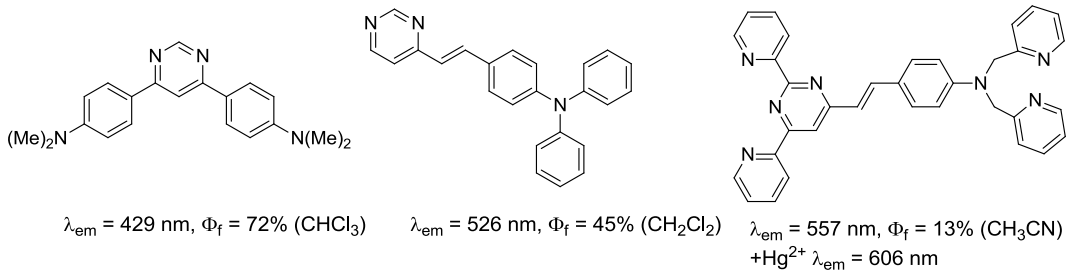


Figure 1.1. Pyrimidine-based push-pull fluorophores.

Generally, these push–pull chromophores have an A–π–D structure, where A is an electron-withdrawing moiety and D is an electron-donating group connected by a π-conjugated linker and upon excitation charge-polarized or charge-seperated states occur. Moreover, the applications of intramolecular charge

transfer complexes have recently attracted attention due to invention of delayed fluorescence emitters, possessing nitrogen heterocycles [23–25].

Pyrrolo[2,3-*d*]pyrimidine (7-deazapurine), which is structurally very similar to purine, is associated with biological activity. Substituted pyrrolo[2,3-*d*]pyrimidines exhibit antitumor [26], anti-inflammatory [27], cytostatic activity [28–30] and inhibit thymidylate synthase [31], dihydrofolate reductase [32], protein [33–35] and mycobacterial adenosine kinases [36]. Moreover, previous studies on pyrrolo[2,3-*d*]pyrimidines with π-conjugated aromatic assemblies revealed that such compounds exhibit strong UV-blue fluorescence and are promising candidates as fluorescent functional materials [37–39] (Fig. 1.2).

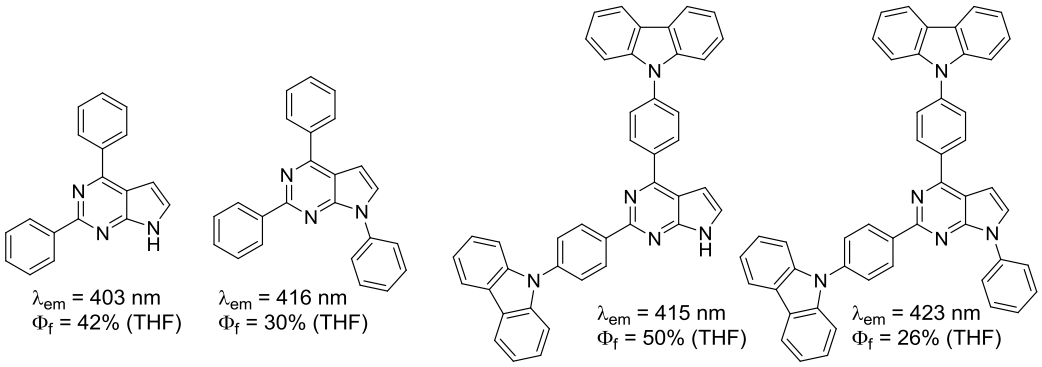


Figure 1.2. Pyrrolo[2,3-*d*]pyrimidine based fluorophores

However, preliminary quantum chemical calculations revealed that directly attached aryl moieties at the 4th position of pyrrolo[2,3-*d*]pyrimidines are twisted out of plane with the rest of the molecule, thus lowering the degree of conjugation. In reference to preliminary quantum chemical studies, such structural twisting may be overcome by the introduction of rigid π-linkers between aromatic side chains and heterocyclic scaffold (Fig. 1.3).

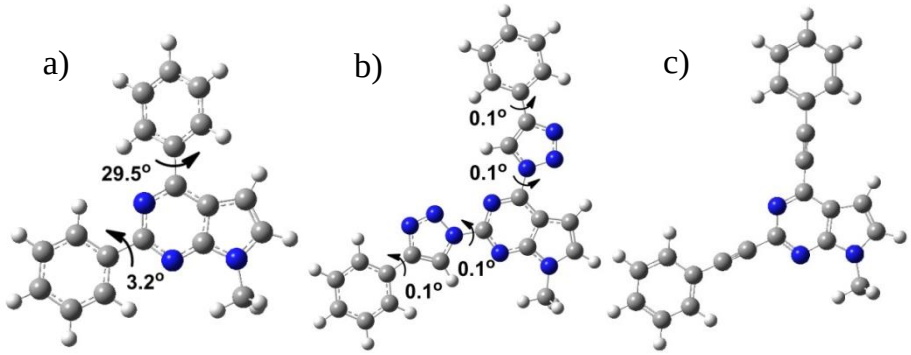


Figure 1.3. Optimized geometries of 2,4-diphenylpyrrolo[2,3-*d*]pyrimidines without (a) and with 1,2,3-triazole (b) and ethynyl (c) linkers.

Generally, ethynyl, ethenyl, 1,2,3-triazole or 1,3,4-oxadiazole units are most commonly used linkers. Taking into account that these moieties have been successfully employed as linkers in other aromatic and heteroaromatic systems [40–48] and that in current literature both triazolylpyrrolo[2,3-*d*]pyrimidines and alkynylpyrrolo[2,3-*d*]pyrimidines received very little attention, carbon-carbon triple bond and 1,2,3-triazole units were chosen as π-linkers in this work.

The aim of the present work was to synthesize pyrrolo[2,3-*d*]pyrimidine-core based oligoarylenes with 1,2,3-triazole and ethynyl linkers and to evaluate their photophysical properties.

The tasks proposed for the achievement of the above stated aim were as follows:

- to study the Cu(I) catalyzed azide-alkyne cycloadition reaction of 2,4-diazido-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine with arylethynes.

- to study the regioselectivity of the Sonogashira and Stille alkynylation reactions of 2,4-dichloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine and to elaborate efficient method for the synthesis of 4-arylethynyl-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines.

- to investigate synthetic routes for the preparation of pyrrolo[2,3-*d*]pyrimidines bearing the same and different arylethynyl moieties in positions

2 and 4 of the heterocycle and to elaborate efficient methods for the synthesis of the corresponding derivatives of the heterocycle.

- to develop an efficient method for the introduction of aryl moieties into position 2 of pyrrolo[2,3-*d*]pyrimidine and to synthesize a series of 2-aryl-4-arylethynylpyrrolo[2,3-*d*]pyrimidines.

- to study photophysical properties and to evaluate influence of electronic nature, structure and linking topology of the substituents on the photophysical and electronic characteristics of the synthesized pyrrolo[2,3-*d*]pyrimidines.

Scientific novelty: The copper(I)-catalysed azide-alkyne cycloaddition reaction of 2,4-diazido-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine with diverse arylethynes was studied and novel 2,4-bis(4-aryl-1,2,3-triazol-1-yl)pyrrolo[2,3-*d*]pyrimidines were synthesized and characterized. A comparative study of the palladium-catalysed alkynylation reactions of 2,4-dichloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine using arylethynes and (arylethynyl)tributylstannanes was carried out and efficient methods for the preparation of novel 4-arylethynyl-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines and 2,4-bis(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines bearing different or similar arylethynyl moieties were developed. Palladium-catalyzed Stille reaction of 4-arylethynyl-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines with (aryl)tributylstannanes was studied and novel 2-aryl-4-(arylethynyl)pyrrolo[2,3-*d*]pyrimidines were synthesized. An economic one pot method for the preparation of the key starting material – 2-(2-thienyl)benzoic acid for the synthesis of indeno[1,2-*b*]thiophen-4-one and improved procedures and 4,4-dialkyl-4*H*-indeno[1,2-*b*]thiophenes have been established. New 4,4-dialkyl-4*H*-indeno[1,2-*b*]thiophenes and their 2-bromo and 2-tributylstannyl derivatives were prepared and employed for the synthesis of pyrrolo[2,3-*d*]pyrimidine derivatives bearing indeno[1,2-*b*]thiophene moiety in position 2 of the heterocycle. Influence of electronic nature, structure, linking topology and extent of π-conjugated system on the photoluminiscent

characteristics of the pyrrolo[2,3-*d*]pyrimidine derivatives was evaluated with reference to quantum chemical calculations.

Main statements for the defense:

- In the copper(I)-catalyzed azide-alkyne cycloaddition reaction of 2,4-diazido-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine with aryl ethynes 1,4-disubstituted-1,2,3-triazoles are formed along with some amounts of 1,5-disubstituted isomers.
- Palladium catalyzed alkynylation of 2,4-dichloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine at position 4 of the heterocycle can be achieved by both Sonogashira and Stille reactions.
- $Pd(PPh_3)_2Cl_2/AsPh_3$ is a suitable catalytic system for both Stille alkynylation and arylation reactions of 4-(arylethynyl)-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine providing 2-arylethynyl- and 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines in good yields.
- Fine tuning of HOMO and LUMO values of the 2,4-bis(4-aryl-1,2,3-triazol-1-yl)pyrrolo-7-methyl-7*H*-[2,3-*d*]pyrimidines may be achieved by the introduction of diverse aromatic substituents.
- Photoluminescent properties of the synthesized novel pyrrolo[2,3-*d*]pyrimidines depend on the solvent polarity, electronic nature of substituents, linking topology, structure and extent of π-conjugated system.

The main results of the present work were published in 5 articles in the peer-reviewed scientific journals and were presented at 10 scientific conferences.

2. LITERATURE REVIEW

2.1. Copper-catalyzed azide-alkyne cycloaddition reaction: concept, regioselectivity and pyrrolo[2,3-*d*]pyrimidines as reactive partners

In this review a short outline on development of copper-catalysed azide-alkyne cycloadition reaction to furnish 1,4-disubstituted-1,2,3-triazoles with the emphasis of their importance in various fields will be presented. Along with most popular catalyst systems and conditions, cases of lower regioselectivity will be discussed, as well. Finally, attempts to use pyrrolo[2,3-*d*]pyrimidines as reactive partners in the copper-catalyzed azide-alkyne cycloaddition reactions will be reviewed.

The thermally induced 1,3-dipolar cycloaddition between alkynes and organic azides (AAC, Fig. 2.1) was discovered in 1893 [49] and extensively studied by Huisgen and coworkers in the middle of the last century [50–52]. However, the reaction was never widely exploited by synthetic chemists presumably because it usually generates a mixture of 1,4-disubstituted-1,2,3-triazoles (**1**) and 1,5-disubstituted-1,2,3-triazoles (**2**). Everything turned upside down in 2002 when Meldal [53] and Sharpless [54] independently discovered the Cu(I) catalysed version (CuAAC) of the AAC reaction.

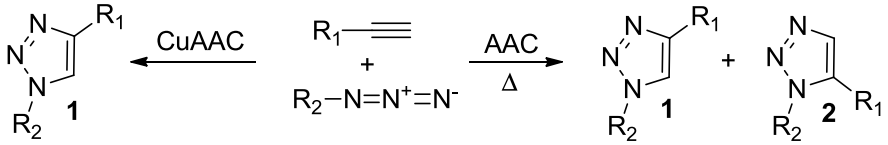


Figure 2.1. Generation of 1,4-disubstituted-1,2,3-triazoles by AAC and CuAAC reactions.

Compared with the thermal AAC process, the rate of the CuAAC reaction is increased up to 10^7 times [55], making the reaction conveniently fast at room temperature. Also, reaction is usually not significantly affected by steric and electronic properties of groups attached to azide and alkyne reactive centers. Reaction is unaffected by water and tolerates most organic and inorganic functional groups, thus eliminating the need of protecting-group chemistry.

Due to these features, the CuAAC methodology has become the “flagship reaction” of “click chemistry” [56].

The 1,4-disubstituted-1,2,3-triazole fragment itself possess interesting structural and electronic features. Early workers recognized that disubstituted 1,2,3-triazoles are excellent amide mimics [57]. Some structural differences between triazoles and amide bonds, of course, exist. Most notable is the extra atom in triazole backbone, which leads to increased distance between R_1-R_2 (Fig. 2.2). Also, the positioning of three electronegative nitrogen atoms on one side of the heterocycle leads to a large 5D dipole moment. On the other hand, this may actually enhance peptide bond mimicry by increasing hydrogen bond donor and acceptor properties of the triazole. Strong dipole moment can polarize C-5 proton to such a degree that it can function as a hydrogen-bond donor, like the amide proton.

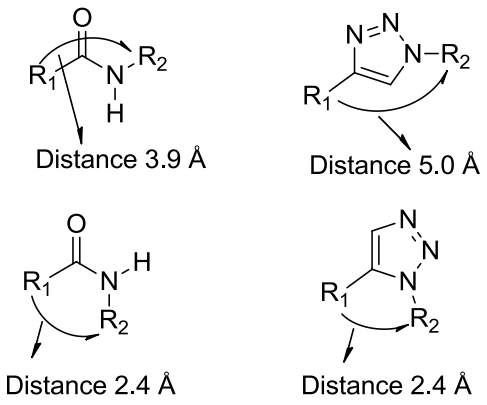


Figure 2.2. Structural similarity between the amide and 1,2,3-triazole moieties.

Hydrogen-bond accepting/donating ability together with high chemical stability, strong dipole moment and heteroaromatic character enables triazole ring to productively interact in several ways with biological molecules, organic and inorganic surfaces and other materials. These features together with relatively easy preparation made CuAAC reaction a method of choice in many different areas of chemistry including bioconjugation [58,59], polymers [60,61], drug discovery [62], interlocked architectures [63], material science [47], coordination [64] and supramolecular chemistry [65]. For example,

compounds based on 1,2,3-triazole moiety found their use as anionic receptors [66], metal sensors [67] or tunable light emitters [68] (Fig. 2.3).

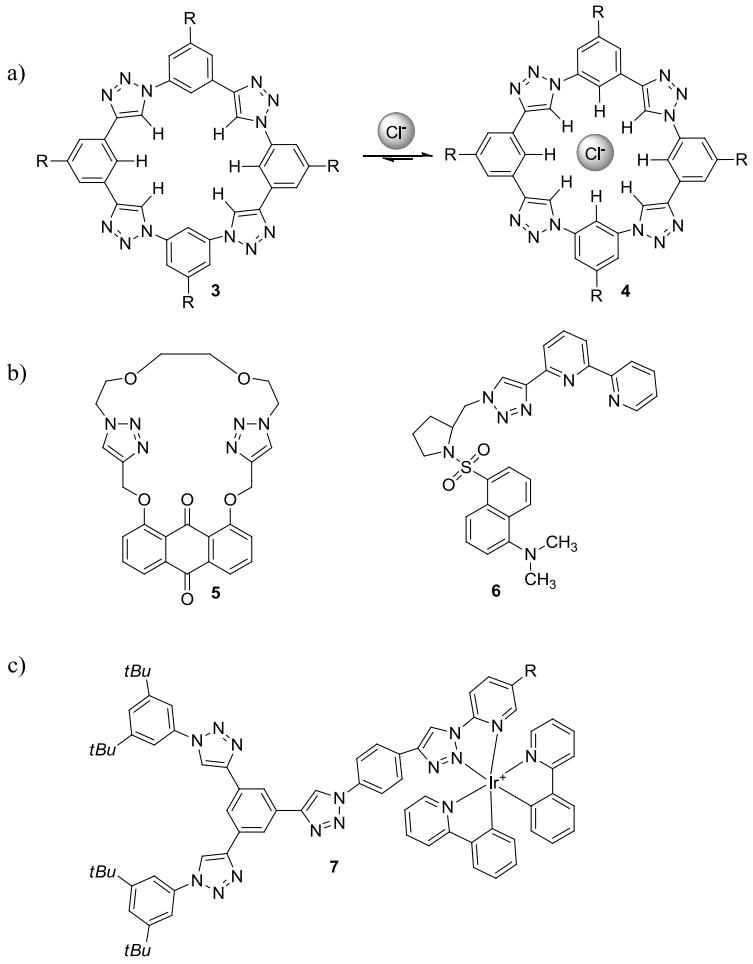


Figure 2.3. Examples of 1,4-disubstituted-1,2,3-triazoles a) anionic receptor b) metal sensors c) tunable wavelength light emitters.

Moreover, the triazole moiety is nitrogen-rich, strongly electron deficient heterocycle which, according to X-ray crystalography [69] and molecular modelling [70], is known to be flat. For this reason, triazole is also frequently used as rigid π-linker to connect various (hetero)aromatic/chromophoric units into one conjugated or covalently bonded assembly leading to materials with useful properties. For example, CuAAC approach opens access to a wide library of fluorescent nucleosides/oligonucleotides (**8**-**10**) [71–73] and various D-π-A systems otherwise known as push-pull systems (**11**-**13**) [15,44,46] (Fig. 2.4). In these

systems strongly electron donating moiety is conjugated through a π-linker to strong electron-withdrawing moiety. Push-pull chromophores received much interest due to their non-linear optical properties [74], in particular in optoelectronics [75], biomolecular imaging [76] and dye-sensitized solar cells [77]. These push-pull dyes are also interesting as fluorophores and most of them act as fluorescent sensors, as they have emission response that depends on their environment [78]. Moreover, push-pull system is one of the main requirements for thermally activated delayed fluorescent materials which are used in the third generation organic light emitting diodes [24].

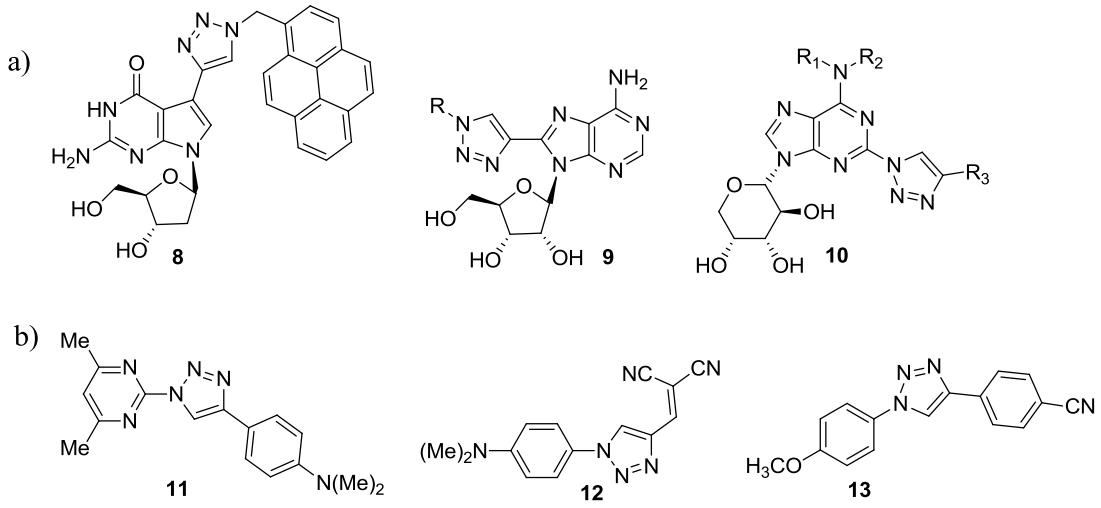
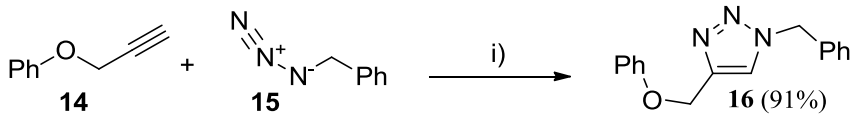


Figure 2.4. Examples of triazole based a) fluorescent nucleosides b) push-pull systems.

A wide range of experimental conditions for the CuAAC reaction have been employed since its discovery, underscoring robustness of the process and its compatibility with most functional groups, solvents and additives regarding to the source of copper. The choice of catalyst is dictated by the particular requirements of the experiment, and usually many combinations will produce desired results. On the other hand, there is no obvious correlation between method used and yield of the reaction and case-to-case optimisation is essential for the success of the experiment. The most important factor seems to be maintaining the reactants in solution and keeping Cu(I) at high level during the reaction. That's why, the use of Cu(II) source with addition of a reducing agent

in a large excess is one of the preferred methods [54] (Scheme 2.1).



Scheme 2.1. *Reagents and conditions* i) $CuSO_4$•$5H_2O$ 1 mol%, NaAsc 5 mol%, H_2O/*t*-BuOH 2:1, rt, 8 h.

The presence of a reducing agent renders the reaction much less susceptible to oxygen, and these reactions have often been carried out in open-air conditions. This may be the reason that the combination of $CuSO_4$/NaAsc in aqueous alcoholic mixtures is the most common catalytic system used in CuAAC reactions. However, the main drawback of this catalytic system is solubility issue of reactants. Other frequently used Cu(I) sources are copper halide salts, particularly CuI or CuBr. CuI alone is inefficient catalyst for CuAAC. In most cases it is used as a combination of CuI/NR_3, in which the tertiary amine is an essential additive. Naturally, CuI occurs in polymeric structure, therefore for the formation of copper acetylide it must be dissociated by amines to yield the "active" Cu(I) species. The tertiary amine additive functions as both ligand and a base and also could promote coupling of copper acetylide or substitution of 5-cuprated-1,2,3-triazole to yield undesired by-products **17-21** (Fig. 2.5).

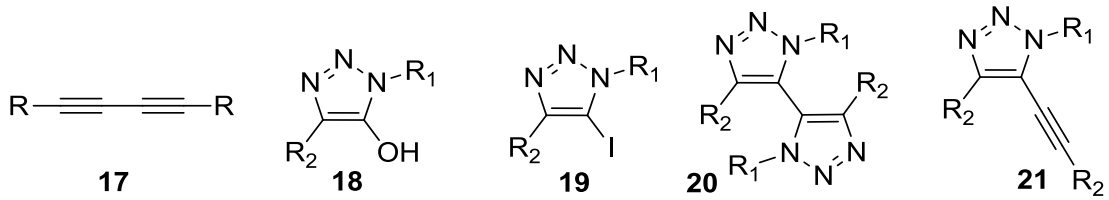


Figure 2.5. Possible undesired by-products formed from the C-Cu bond containing intermediates.

By-product formation issue can be easily overcome by using improved acid-base jointly promoted procedure [79]. Addition of AcOH to CuI/NR_3

catalytic system accelerates the conversion of C-Cu bond intermediates and prohibits formation of undesired products together with a reaction rate enhancement. Moreover, CuI may be obtained in highly pure form and it is partially soluble in polar and intermediate polarity solvents such as CH_3CN, THF, acetone, pyridine and DMSO. For this reason, CuI is often preferred in polymer reactions, peptide chemistry and for reactants that are sensitive to aqueous conditions. The reaction can also be catalyzed by Cu(I) species supplied by elemental copper, thus by simply stirring the piece of copper wire, turnings or nanoparticles in the reaction mixture, frequently followed by the addition of $CuSO_4$ to accelerate the reaction. Though, addition of Cu(II) species is not necessary as copper oxides, carbonates or the patina on metal surface are sufficient to initiate the catalytic cycle. Although, the procedure based on copper metal requires longer reaction times, it usually provides access to very pure triazole products with low levels of copper contamination and is often used in synthesis of compound libraries for biological screening. Finally, there is a range of other copper sources that have been introduced for variety of reasons. For example $[Cu(CH_3CN)_4]PF_6$ [80,81], $(EtO)_3P$:CuI [82], $CuBr(Ph_3P)_3$ [82,83], $Cu(CH_3CN)_4OTf$ [84] are used because of increased solubility in organic solvents. $Cu(OAc)_2$ [85] showed improved reactivity compared to $CuSO_4$. Solid supported CuI on zeolites [86] or on Al_2O_3 [87] also showed favourable activity.

Ligands are also employed in CuAAC reactions both to enhance the rate of reaction and to protect the Cu(I) from oxidation in the presence of adventurous oxygen, though ligands are by no means necessary for the catalytic effect of Cu(I) in triazole formation. However, ligands are mostly used in bioconjugation field, as the rate of CuAAC reaction in the absence of accelerating ligands is simply not high enough when concentrations of reactants are low. The first general solution to bioconjugation problem was provided by tris(benzyltriazolyl)methyl amine **22** (TBTA, Fig. 2.6), prepared using the CuAAC reaction and introduced shortly after its discovery [81]. This ligand was shown to significantly accelerate the reaction and stabilizes the

Cu(I) oxidation state in water containing mixtures. The poor solubility of TBTA in water prompted the development of more polar analogues such as **23** (THPTA) [88]. The polydentate trimethylamine theme has been extended to benzimidazole, benzothiazole, oxazoline and pyridine substituents [89]. Several of them have provided significantly faster catalysis when quantitative rates are measured, particularly the pendant ester and water-soluble acid derivatives of tris(benzimidazole) motif **24** and **25**. Further combinatorial search for alternatives led to the identification of the commercially available sulfonated bathophenanthroline (**26**) as the ligand component of the fastest water-soluble CuAAC catalyst under dilute aqueos conditions [90].

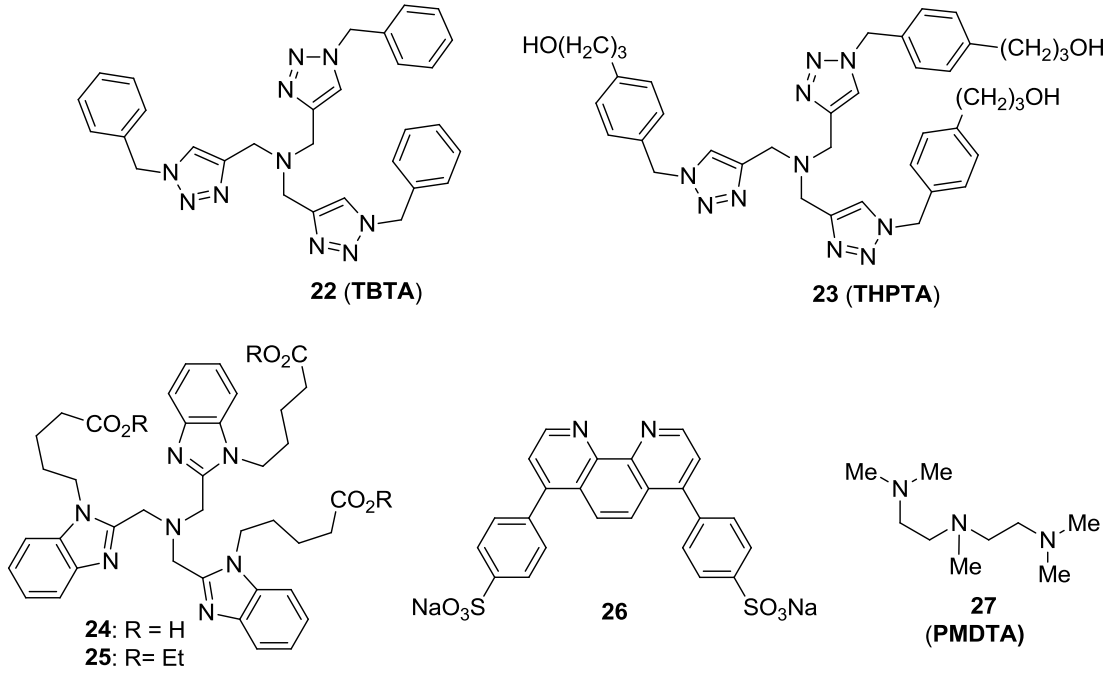
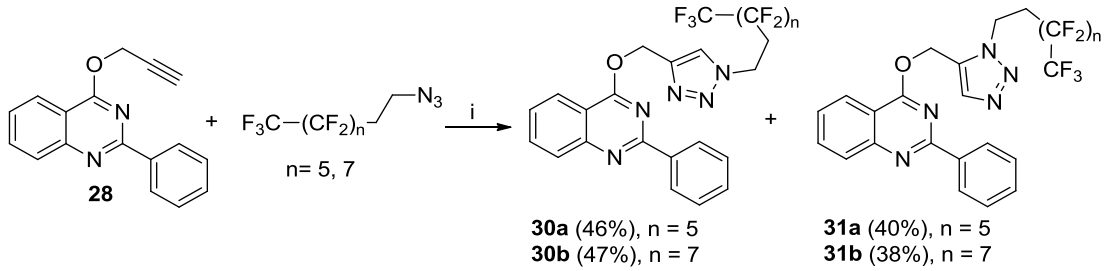


Figure 2.6. Most common ligands used to enhance the Cu(I)-catalysed triazole formation

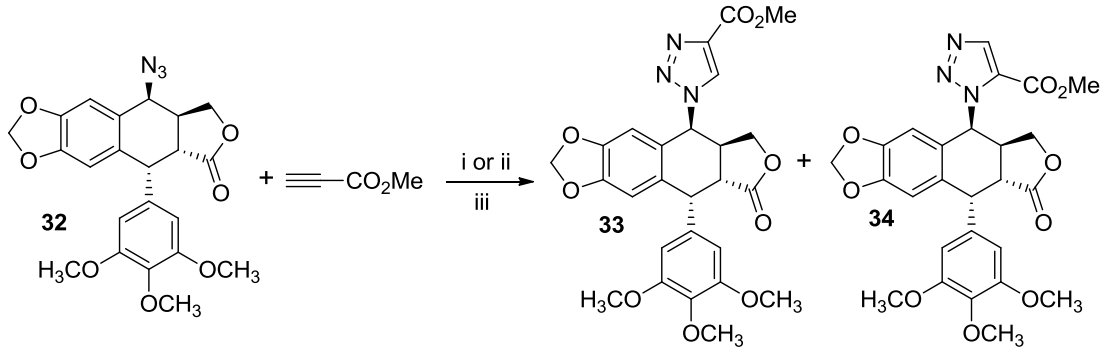
However, Cu-**26** complexes are strongly electron-rich and are therefore highly susceptible to oxidation in air. Predominant ligand in polymer-based CuAAC reactions is pentamethyldiethylenetriamine (**27**, PMDTA) [91]. This is probably due to well established efficiency of CuBr/PMDTA in polymerization processes such as ATRP.

Despite the fact that in most cases CuAAC reaction produces 1,4-disubstituted-1,2,3-triazoles as the only regioisomers, there are few reports in the literature when regioselectivity is not maintained. P. M. Chandrika et al. reported formation of both isomers **30** and **31** at approximate 1:1 ratio in reaction between 2-phenyl-4-(prop-2-yn-1-yloxy)quinazoline (**28**) and perfluoroalkylazides by using 5.5 mol% of CuI in THF at room temperature (Scheme 2.2). However, theoretical calculations suggested that formation of 1,4-isomer is more feasible and stable than 1,5-isomer both kinetically and thermodynamically [92].



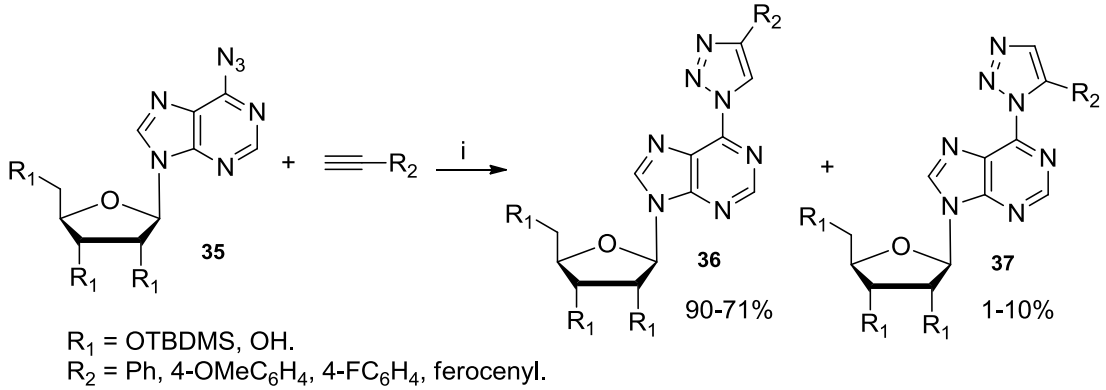
Scheme 2.2. *Reagents and conditons* i*)* 5.5 mol% CuI, THF, rt.

Screening for optimal CuAAC reaction conditions of 4-*β*-azido-podophyllotoxin **32** and methylpropiolate revealed that both isomers are formed if pyridine/CuI in $CHCl_3$ or 2,6-lutidine/$CuSO_4$•$5H_2O$ in a mixture of *t*-BuOH/H_2O were used. Nevertheless, 2,6-lutidine/CuI catalyst system in $CHCl_3$ produced 1,4-isomer **33** solely in high 90% yield [93] (Scheme 2.3).



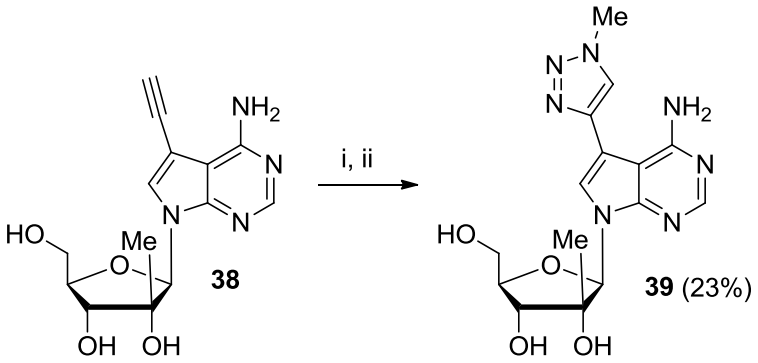
Scheme 2.3. *Reagents and conditions* i) 5 mol% CuI, 1 equiv. pyridine, $CHCl_3$, 25 ^oC, 12 h, **33** – 20%, **34** – 17%; ii) 4 mol% $CuSO_4$•$5H_2O$, 1 equiv. 2,6-lutidine, 1:1 *t*-BuOH/H_2O, 25 ^oC, 2 h, **33** – 15%, **34** – 10%; iii) 5 mol% CuI, 1 equiv. 2,6-lutidine, $CHCl_3$, 25 ^oC, 12 h, **33** – 90%, **34** – 0%.

Reaction of azidopurine nucleosides **35** with a range of alkynes under $CuSO_4$/NaAsc catalyst system produced 1,5-isomers as minor products (Scheme 2.4). It was determined, that formation of these isomers also arise *via* catalytic process, as no product formation was observed by simply stirring alkynes and azidopurine nucleoside **35** in CH_2Cl_2/H_2O at room temperature for 48 h [94]. Authors claim that this may arise from steric factors of bulky *tert*-butyldimethylsilyl (TBDMS) group. However, no clear evidence is given as in some cases formation of both isomers is also observed with azidopurine nucleoside which does not possess bulky TBDMS groups.



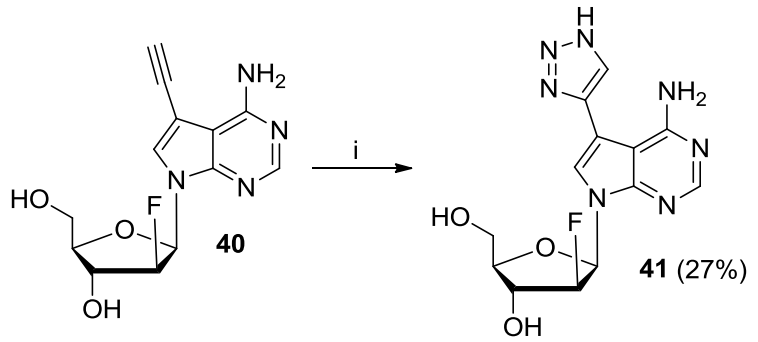
Scheme 2.4. *Reagents and conditions* i) 5 mol% $CuSO_4 \cdot 5H_2O$, 10 mol% NaAsc, CH_2Cl_2/H_2O 1:1, rt, 48 h.

Compounds containing pyrrolo[2,3-*d*]pyrimidine moiety has not been utilized in CuAAC reactions widely. Up to date, there are only few publications involving (alkynyl)pyrrolo[2,3-*d*]pyrimidines as ligation partners. One of them reports the synthesis of pyrrolo[2,3-*d*]pyrimidine nucleoside **39** starting from alkyne **38** by two steps approach [95]. At first, alkyne **38** reacted with trimethylsilyl azide ($TMSCH_2N_3$) by using $CuSO_4$/NaAsc catalyst system in a mixture of *t*-BuOH/H_2O and followed by the deprotection of trimethylsilyl group with NaOH. Nucleoside **39** was obtained in 23% overall yield (Scheme 2.5). $TMSCH_2N_3$ was used instead of methyl azide because of safety precautions, as methyl azide is known to be highly explosive, especially at elevated temperatures.



Scheme 2.5. *Reagents and conditions* i) 3 equiv. $TMSCH_2N_3$, 5 mol% $CuSO_4 \bullet 5H_2O$, 50 mol% NaAsc, 1:1 *t*-BuOH/H_2O , 50 ^oC, overnight; ii) 5 equiv. 1M aq NaOH, 1:1 MeOH/H_2O, 50 ^oC, 2 h.

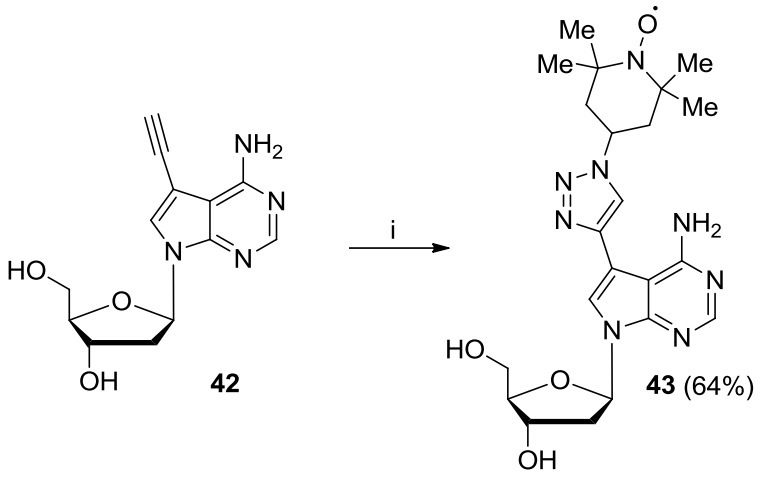
Hocek M. *et al.* reported the synthesis of very similar nucleoside **40** by using $TMSN_3$ as ligation partner [96]. CuI was used as a copper source in a mixture of DMF/MeOH for cycloaddition reaction. Nevertheless, the target nucleoside was obtained in very similar 27% yield (Scheme 2.6).



Scheme 2.6. *Reagents and conditions* i) 3 equiv. $TMSN_3$, 5 mol% CuI, DMF/MeOH, 100 ^oC, 24 h.

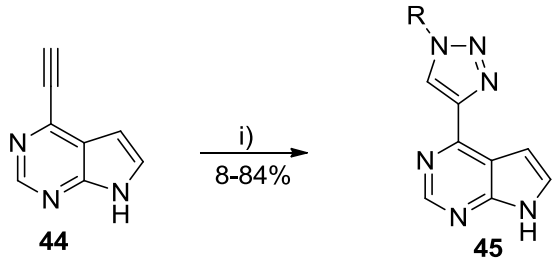
The 7-ethynyl nucleoside **42** was functionalized with 4-azido-2,2,6,6-tetramethylpiperidine 1-oxyl radical by the click reaction to give the conjugate **43** in the presence of CuI in a 3:1:1 mixture of THF/*t*-BuOH/H_2O. The addition of DIPEA was essential for the completion of the reaction in 4 h. CuI was used as the copper (I) source instead of the $CuSO_4$/NaAsc system to avoid reduction of the nitroxide radical by ascorbic acid to the diamagnetic hydroxylamine

derivative during the click reaction. The spin labeled nucleoside **43** was obtained in 64% yield [97] (Scheme 2.7).



Scheme 2.7. *Reagents and conditions* i) 1.2 equiv. 4-azido-TEMPO, 1.5 equiv. CuI, 1 equiv. DIPEA, 3:1:1 THF/H_2O/*t*-BuOH, rt, 4 h.

A large library of various 4-(1,2,3-triazol-4-yl)-7*H*-pyrrolo[2,3-*d*]pyrimidines as potent Janus kinase family inhibitors were prepared starting from 4-ethynylpyrrolo[2,3-*d*]pyrimidine [98]. One pot technique was used for the preparation of azides and cycloaddition step. The target compounds **45** were obtained in 8-89% yield (Scheme 2.8).

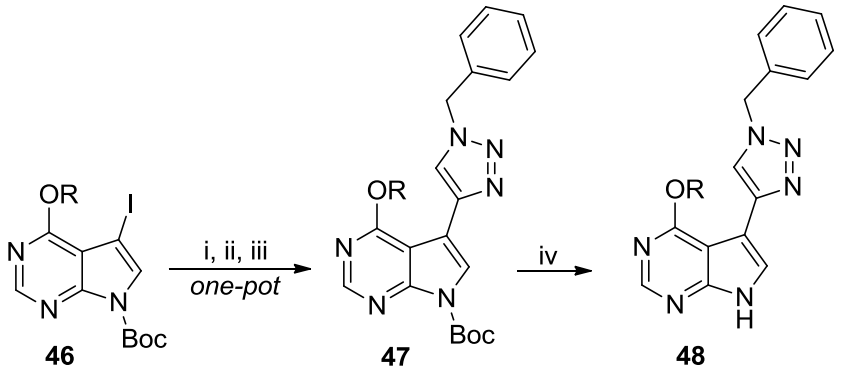


R = -Bn, 4-F-Bn; 4-Cl-Bn; 4-Br-Bn; 4-I-Bn; 3-F-Bn; 3-Cl-Bn; 3-Br-Bn; 3-I-Bn; 2-F-Bn; 2-Cl-Bn; 2-Br-Bn; 2-I-Bn; Bz; -$CH_2CH{=}CH_2$; C_5H_{11}; -$CH_2CH_2CH_2CN$; -Boc; -CH_2COOEt; -CH_2-cyclopropane.

Scheme 2.8. *Reagents and conditions* i) 1.0 equiv. alkyl halogenide, 1.05 equiv. NaN_3, 5 mol% $CuSO_4$, 10 mol% NaAsc, 1:1 *t*-BuOH:H_2O, rt, 24 h.

Muller T. J. J. *et al* reported a very convenient method for the preparation of triazolyl substituted NH-heterocycles *via* one-pot Sonogashira coupling-TMS-deprotection-CuAAC sequence. The corresponding N-Boc protected 5-iodopyrrolo[2,3-*d*]pyrimidines **46** were reacted with

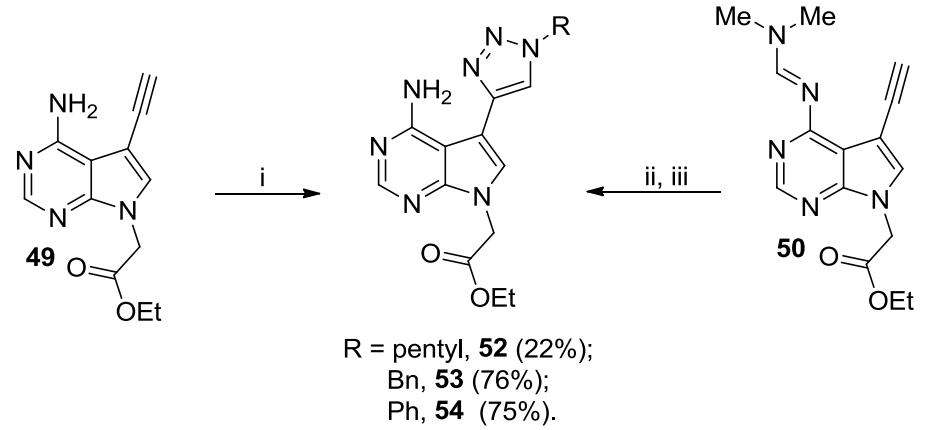
trimethylsilylacetylene. Deprotection of TMS group was carried out by using tetrabutylammonium fluoride and followed by the addition of azide. Moreover, no further addition of CuI was required, in the CuAAc step. Deprotection of Boc group was performed with K_2CO_3 in MeOH and target compounds **48** were obtained in overall 41-54% yield [99] (Scheme 2.9).



R = -Me; -$(CH_2)_2$OMe.

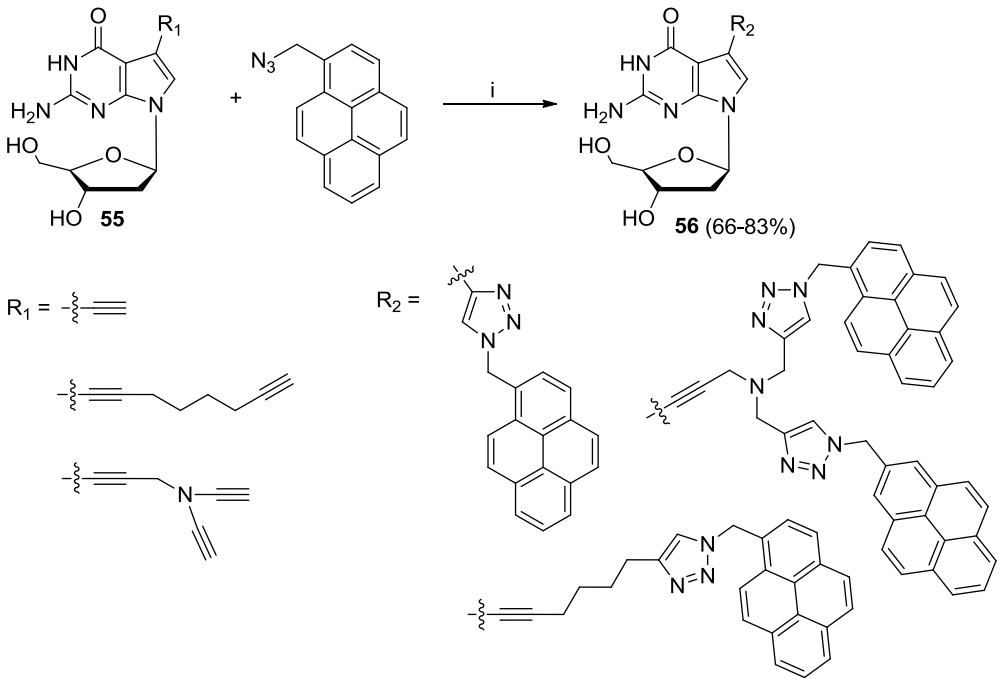
Scheme 2.9. *Reagents and conditions* i) 1.5 equiv. TMSA, 2 mol% $Pd(PPh_3)_2Cl_2$, 4 mol% CuI, 2.0 equiv. NEt_3; THF, rt, 2 h; ii) 1.5 equiv. TBAF, rt, 0.5 h; iii) 1.0 equiv. BnN_3, MeOH, rt, 115 h; iv) 2.5 equiv. K_2CO_3, MeOH, rt, 50 ^oC, 1 h.

Fluorescent base analogues **52-54**, as DNA structure probes, were synthesized by two different approaches [100]. In order to minimize formation of by-products best copper source for these reactions was found to be Cu/C. Compounds **52** and **53** possessing alkyl substituents were synthesized by stirring **49** with an excess of alkyl azides, Cu/C and Et_3N in EtOAc. Authors have chosen different, one pot azide formation and CuAAC approach, for the synthesis of **54**, possessing phenyl substituent. Reaction mixture consisting of phenyl iodide, NaN_3, NaAsc, L-proline, Cu/C in DMSO/H_2O was heated at 130^oC by microwave irradiation for 30 min. However, when **49** was used as starting material, Ullman reaction product predominated. For this reason, an alternative route involving *N*-protected compound **50** was employed to furnish triazole **54** in 75% yield (Scheme 2.10).



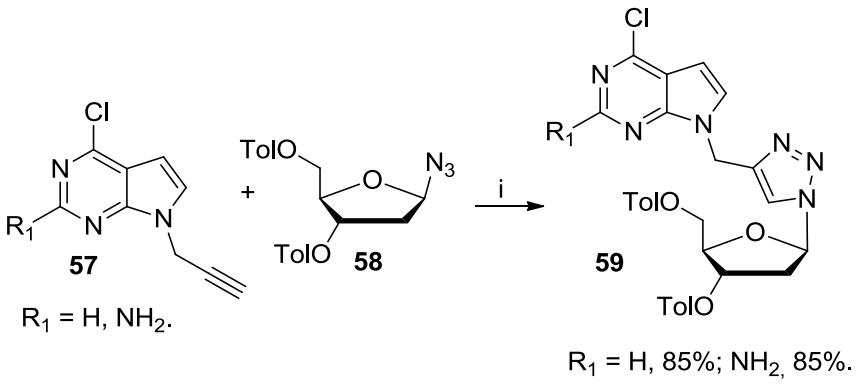
Scheme 2.10. *Reagents and conditions* i) 16.1 equiv. alkyl azide, 40 mol% Cu/C, 1 equiv. Et_3N, EtOAc, rt, 18 h; ii) 1.2 equiv. C_6H_5I, 1.2 equiv. NaN_3, 40 mol% NaAsc, 20 mol% L-proline, 40 mol% Cu/C, 1:1 DMSO/H_2O, MW 130 ^oC, 30 min; iii) NH_3-MeOH, rt, 2 h.

In a series of papers [72,101–103] Frank Seela's group described the synthesis of various nucleoside pyrene conjugates **56** (Scheme 2.11)**.** Compounds **56** were obtained in 66-83% yield and were screened as fluorescent DNA structure probes.



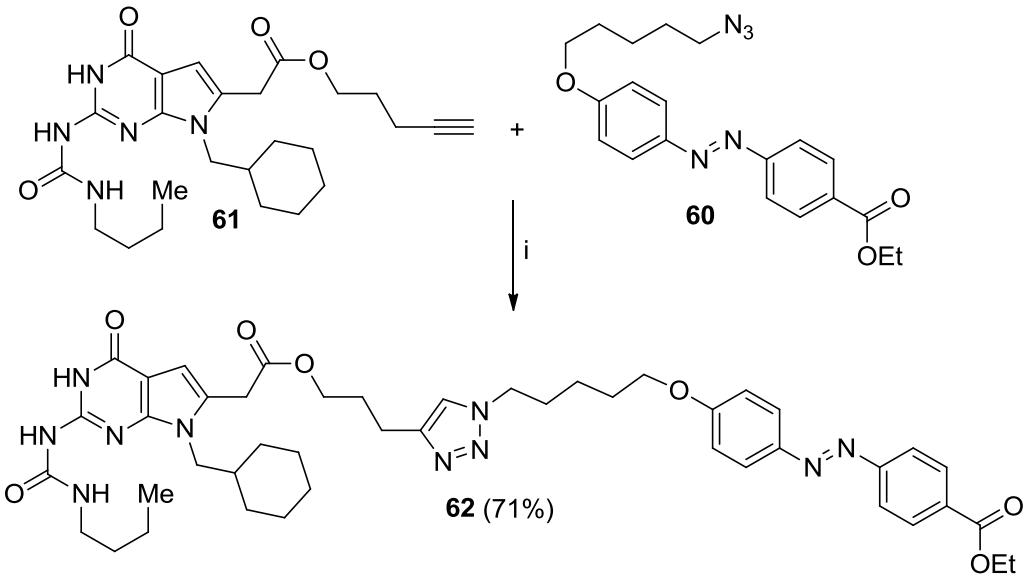
Scheme 2.11. *Reagents and conditions* i) up to 25 mol% $CuSO_4$•$5H_2O$, up to 1 equiv. NaAsc, 3:1:1 THF/H_2O/*t*-BuOH, rt.

P. Chittepu et al. reported synthesis of 1,2,3-triazole nucleosides that are linked to nucleobases as recognition element. Intermediate compounds **59** were obtained in 85% yield from 7-(propyn-3-yl)pyrrolo[2,3-*d*]pyrimidines **57** and azido sugar **58** by using well established $CuSO_4$/NaAsc catalytic system in a mixture of THF/H_2O/*t*-BuOH [104] (Scheme 2.12).



Scheme 2.12. *Reagents and conditions* i) 14 mol% $CuSO_4 \cdot 5H_2O$, 57 mol% NaAsc, 3:1:1 THF/H_2O/*t*-BuOH, 24 h, rt.

The same catalytic system in CH_2Cl_2/H_2O was applied for coupling of azobenzene dye **60** to the module of the pyrrolo[2,3-*d*]pyrimidin-4-one urea **61**. Triazole **62** was obtained in 71% yield and was successfully used as colorimetric indicator for specific quadruple hydrogen-bonding interactions with polymers modified with 2,7-diamido-1,8-naphthyridine moieties [105] (Scheme 2.13).



Scheme 2.13. *Reagents and conditions* i) 5 mol% $CuSO_4 \bullet 5H_2O$, 2 equiv. NaAsc, 9:1 CH_2Cl_2/H_2O, rt, 24 h.

In summary, this review shortly outlines development of copper catalysed azide-alkyne cycloadition reaction together with a scope of applications of the 1,4-disubstituted 1,2,3-triazoles. CuAAC reaction is an efficient tool for functionalization of compounds with biochemical, medicinal or material science applications. These reactions proceed under mild conditions and tolerate a wide range of functional groups and usually furnish isomerically pure 1,4-disubstituted-1,2,3-triazoles. However, in some cases detailed evaluation of byproducts reveals that superb regioselectivity should not be taken as self-evident process. Pyrrolo[2,3-*d*]pyrimidines as reactive partners in CuAAC have not received much attention. Moreover, it has never been attempted to use azidopyrrolo[2,3-*d*]pyrimidines in CuAAC reactions.

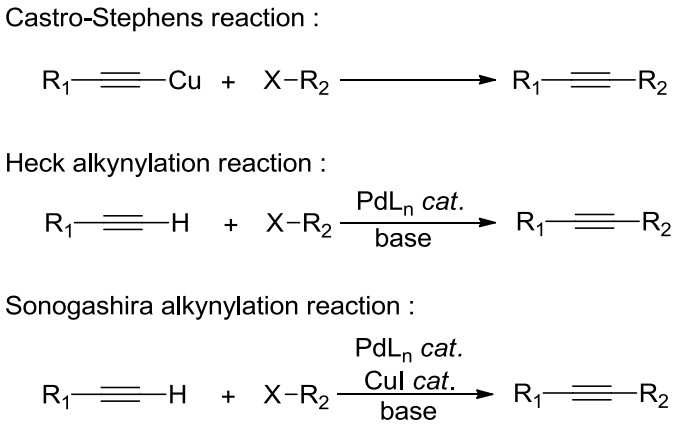
2.2 Palladium-catalysed alkynylation methods and alkynylation of pyrrolo[2,3-*d*]pyrimidine derivatives

In this part, a short overview of the development of the palladium-catalysed alkynylation reactions together with a short outline of scope and limitations of these reactions is presented. Literature data on alkynylation reactions of the pyrrolo[2,3-*d*]pyrimidine derivatives will be discussed, as well.

The carbon-carbon triple bond of alkynes is one of the basic functional groups. In the past decades, acetylene-chemistry has experienced a renaissance due to not only its occurrences in the molecules in the frontiers of organic chemistry such as biochemistry or materials sciences, but also as building blocks or versatile intermediates for the synthesis of a vast array of chemicals [106]. This boost to the alkyne chemistry has been fuelled mainly by the development of new synthetic methodologies based on transition metal catalysis, a field where palladium always occupies a leading position. Carbon-carbon triple bond is a highly valuable and versatile functional group in many natural and bioactive compounds [107–109]. Recently, the acetylene axis has been extensively employed as a linker in the construction of various molecular scaffolds because it connects two moieties linearly at an aproximate interval of 4.0 Å with the least steric demand. Thus, triple bond as a π-linker has been exploited for the range of functional materials with valuable photophysical, photoelectric [40,42,110] or liquid crystal properties [111–113]. Moreover, use of acetylenic linker was adopted in the fields of molecular machines and devices [114], molecular receptors [115] or optical chemosensors of explosives detection [116].

Over the past decade palladium-catalysed alkynylation has emerged as one of the most general and reliable methods for the synthesis of substituted alkynes. One of the first, effective alkynylation was described by C. E. Castro and R. D. Stephens [117] by using stoichiometric amount of cuprous acetylides and aryliodides. However, the scope of the reaction is limited by harsh reaction conditions and by difficulties in preparation of cuprous acetylides. After a decade, in 1975, palladium-catalysed alkynylations have been independently

reported by three groups. The former two methods [118,119] have been developed as an extension of the Heck reaction and the latter [120] became the most widely used alkynylation procedure and is known as Sonogashira-coupling (Scheme 2.14). This reaction considered generally superior to either the Castro-Stephens reaction or the alkyne version of Heck reaction, which is more prominent as copper free Sonogashira-coupling, and it is normally used without checking the comparative merits among them, even though the Heck alkynylation protocol has been shown to be highly satisfactory in a number of cases [121,122].



Scheme 2.14. The Castro-Stephens, Heck and Sonogashira alkynylation reactions.

The Sonogashira reaction provides the most straightforward access to aryl alkynes and related enynes by the use of C(sp^2) halides (I, OTf, Br, Cl) and terminal acetylenes in the presence of catalytic amounts of palladium-complex, CuI and a base. The classical Sonogashira-coupling conditions are a combination of 1-10 mol% of $Pd(PPh_3)_2Cl_2$ or $Pd(PPh_3)_4$ (sometimes generated *in situ*), CuI 2-20 mol% and tertiary or secondary amines which are usually used as solvent either. Although, other catalysts with monodentate or bidentate ligands such as $Pd(MeCN)_2Cl_2$, $Pd(PCy_3)_2Cl_2$, $Pd(acac)_2$, $Pd(dppe)Cl_2$, $Pd(dppp)Cl_2$, $Pd(dppf)Cl_2$ have been employed [123–128]. Solvents such as THF or DMF are also often used and in some cases dramatic rate enhancements are observed [129]. Moreover, the Sonogashira coupling may be performed in aqueous or biphasic conditions [130] or even performed in a ball

mill without any solvent [131], thus significantly simplifying the procedure and eliminating the need of dry solvents. For clarity, simplified Sonogashira reaction mechanism is given in Fig. 2.7.

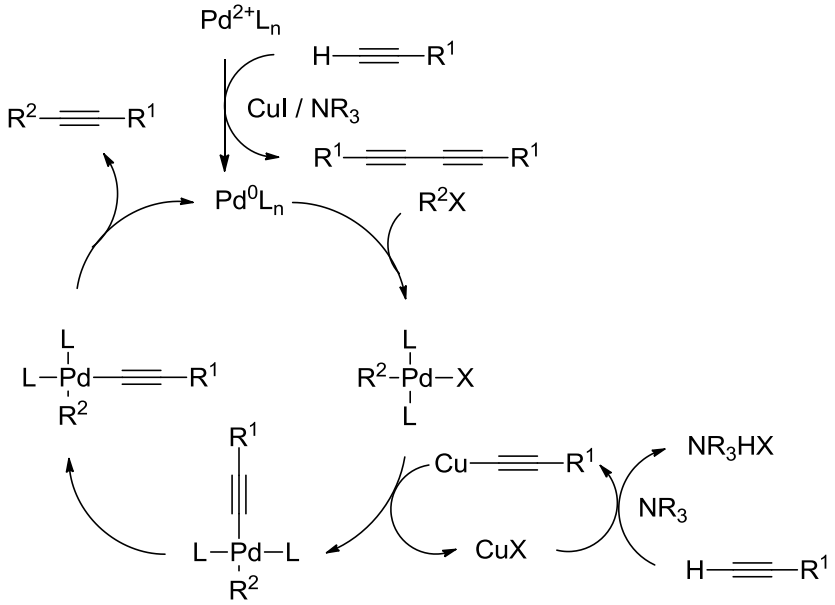


Figure 2.7. Mechanism of the Sonogashira coupling.

As addressed by a recent review [132] finding optimal conditions for the Sonogashira coupling is not an easy task. Though, from studies of the electron distribution and the bulkiness of the substrate and catalysts the following general rules for the palladium-catalysed cross-coupling reactions were published by Hartwig in 2007 [133]:

i) The oxidative addition in Ar-X is promoted by electron-withdrawing groups at the aryl halide.

ii) Steric bulk of phosphines or N-heterocyclic carbenes coordinated to palladium promotes the formation of a monoligated complex, which turns to be highly active for oxidative addition.

iii) There is a pronounced steric effect in the transmetalation, while the ligand bite angle and electronic effects are less important.

iv) Reductive elimination tends to be more favoured by less electron donating ligands and steric bulk.

Plenio et al. carried out a number of studies of substrate/ligand –activity relationships for Sonogashira reactions by using variously substituted aryl bromides and arylacetylenes as well as using phosphine ligands with an increasing bulkiness such as PCy_3, $AdPCy_3$, *t*-$BuPCy_2$, *t*-Bu_2PCy, *t*-Bu_3P, Ad_2PCy_2, *etc.* [134–137]. Moreover, important conclusions were made concerning bulkiness and electronic nature of substituents in arylbromides, arylacetylenes and ligands:

i) Electron-withdrawing groups on either aryl bromide or arylacetylene lead to significant increase in the rate of the Sonogashira reaction. Moreover, this rate is more pronounced for arylethynes than for aryl bromides with electron-withdrawing groups.

ii) Steric bulk on aryl bromides is more detrimental for the reaction than steric bulk on the acetylene. On the other hand, steric bulk on arylacetylene is crucial for choosing a ligand. In short, if steric bulk on the arylacetylene is high, most efficient transformation is achieved when ligands with lower bulk are used. In other words, ideal combination of steric bulk at the acetylene and the phosphine has to be found.

iii) The higher reactivity is achieved with electron-rich phosphines.

Other ligands instead of phosphines are also employed in the Sonogashira coupling. For example, formation of $C(sp^3)$-C(sp) bonds from unactivated alkyl iodides or bromides became possible by using *N*-heterocyclic carbenes as ligands [138] (Fig. 2.8). Moreover, by using Cu-nitrogen, Cu-oxygen or bidentate ligands such as modified ethylenediamines, phenantrolines, acetylacetonates or hydroxyquinoline [139] enabled to perform cross-coupling in absence of palladium species.

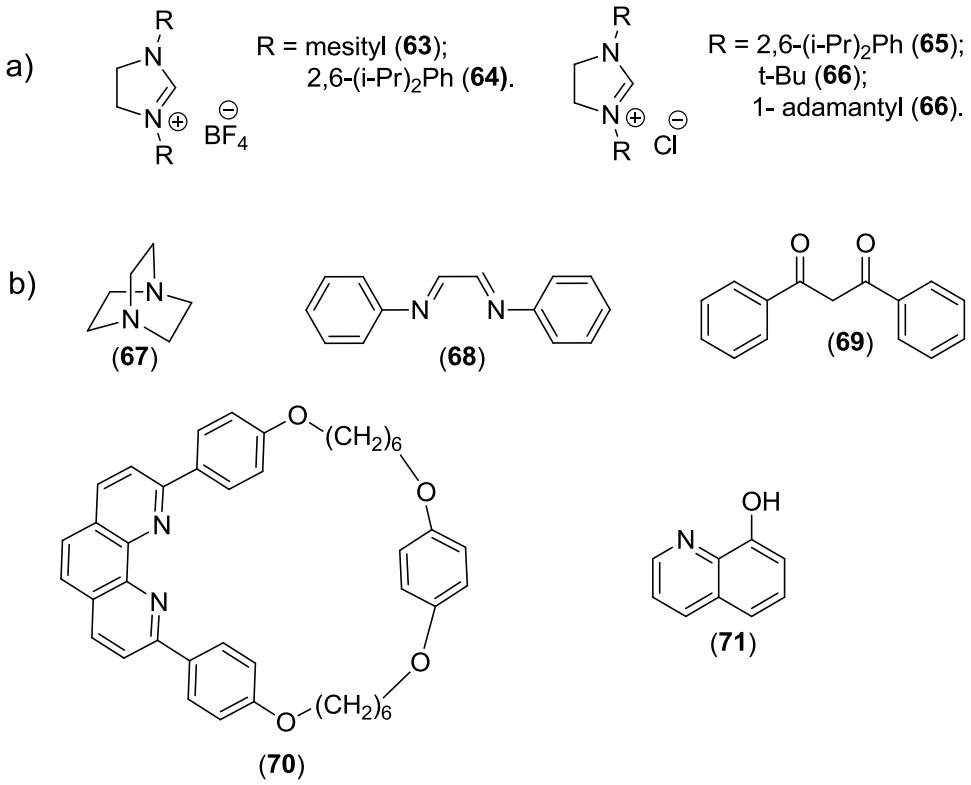
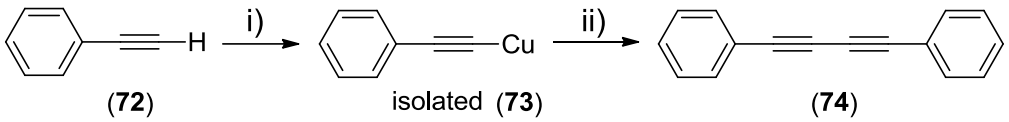


Figure 2.8. Non-phosphine ligands used in the Sonogashira coupling a) N-heterocyclic carbenes; b) copper ligands for palladium-free coupling.

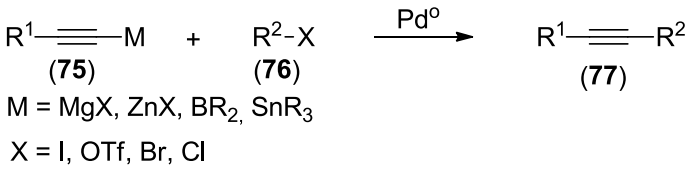
Despite its efficiency with aryl iodides, bromides or triflates and straightforward approach, the Sonogashira reaction has also revealed some significant limitations. Most important of them are formation of diynes by Glaser-type homocoupling (Scheme 2.15) of arylethynes in the presence of copper species [140] and struggling of coupling of aryl/heteroaryl chlorides, especially with the unactivated ones. Glaser homocoupling is usually initiated even by small amounts of oxygen or radicals, thus sometimes leading to a large excess usage of arylacetylenes. Moreover, it may be difficult to purify alkynylated products from formed diynes or, if thermally unstable, its decomposition products. Copper free Sonogashira protocol usually overcomes diyne formation issue, though coupling of unactivated aryl/heteroaryl chlorides is still challenging.



(**72**) isolated (**73**) (**74**)

Scheme 2.15. The Glaser coupling. *Reagents and conditions:* i) CuCl, NH_4OH, EtOH; ii) O_2, NH_4OH, EtOH.

In addition to the copper salts and palladium, other metal catalysts such as iron [141], ruthenium [142], cobalt [143], nickel [144], silver [145], gold [146], indium [147] and zinc [148] were also used. These reactions are usually limited to aryl iodides or activated aryl bromides. Thus, these catalytic procedures are not widely employed and as alternative to the Sonogashira coupling reactions with alkynylmetals containing Mg [149,150], Zn [151], B [152–154] or Sn [109,155,156] (Scheme 2.16) are more often used.

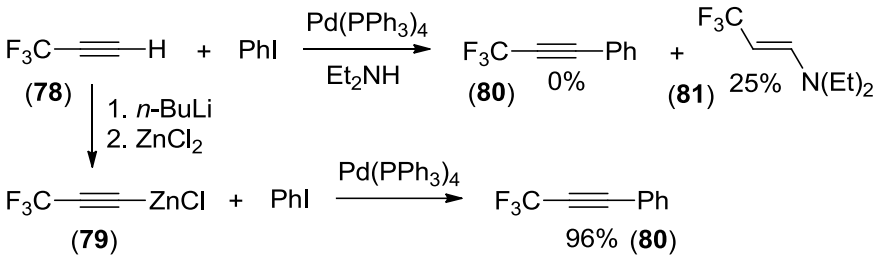


Scheme 2.16. Kumada, Negishi, Suzuki and Stille alkynylation reactions.

Cross coupling reactions with alkynylmagnesium derivatives can be performed by either nickel or palladium catalysis [157]. The advantage of using Grignard reagents as nucleophilic coupling partners is their easy and low-cost availability. Nevertheless, main disadvantages are moisture sensitivity and limited functional group tolerance of highly electrophilic moieties. Inasmuch as most of other alkynylmetals are prepared *via* alkynylmetals containing Mg, Li or Na, the reaction of alkynylmagnesium derivatives in particular should be considered first before converting them into other derivatives.

Alkynylzinc reagents are often superior to alkynylmagnesium, mostly because of higher chemoselectivity, higher catalytic activity and higher pair selectivity in the direct ethynylation [158]. Moreover, the Negishi alkynylation overcomes most of the Sonogashira reaction limits. The Sonogashira coupling

usually fails or produces products in very low yields when alkynes with directly attached electron-withdrawing groups are used. For example, coupling of 3,3,3-trifluoropropyne with iodobenzene does not occur by the Sonogashira protocol (Scheme 2.17). However, if 3,3,3-trifluoropropynylzinc chloride is used in the reaction, coupling product is obtained in 96% yield [159].

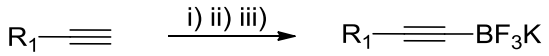


Scheme 2.17. Cross-Coupling of 3,3,3-trifluoropropyne and iodobenzene by Sonogashira and Negishi protocols.

However, despite a fact that Negishi alkynylation is superior in most cases, preparation of alkynylzincs requires an additional step and usage of hydroscopic zinc salts. Moreover, obtained alkynylzinc reagents, as well as alkynylmagnesium derivatives, are highly moisture sensitive, thus they cannot be stored for prolonged time and have to be prepared individually before every cross-coupling reaction.

The Suzuki-Miyaura cross-coupling is arguably the most widely applied transition metal catalysed carbon-carbon forming reaction to date. However, coupling with alkynylboron species is not widely employed as simplest reagents - alkynylboronic acids or boranes are highly unstable. However, examples of alkynylation with alkynyl boranes [152] boronic esters [160] or borates [160,161] can be found in the literature. The most promising Suzuki-Miyaura alkynylation reagent seems to be potassium alkynyl trifluoroborates [153,154,162], which are air stable and can be easily purified by recrystallization (Scheme 2.18). Coupling of alkynyl trifluoroborates is still not sufficiently explored, though it seems that higher yields of alkynylated products are obtained with activated aryl bromides or triflates. Deactivated aryl bromides or, especially aryl chlorides show dramatic decrease in reactivity.

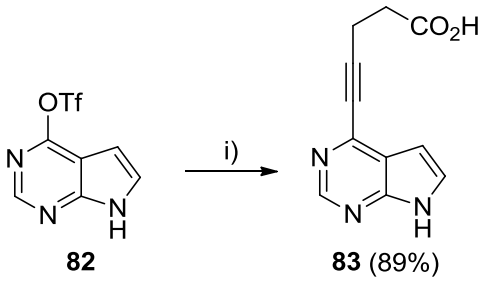
Nevertheless, high stability under normal conditions, easy purification and scale-up feasibility [162] of alkynyl trifluoroborates makes the Suzuki-Miyaura cross-coupling a reasonable method of choice.



Scheme 2.18. Synthesis of alkynyl trifluoroborates. *Reagents and conditions* i) 1 equiv. *n*-BuLi, -78^{0}C, THF, 1 h.; ii) 1.5 equiv. $B(OMe)_3$, -78^{o}C to -20^{o}C, 1 h.; iii) 6 equiv. KHF_2/H_2O, -20^{o}C to rt, 1h.

Organotin reagents are one of the most versatile organometallic species in palladium-catalysed coupling reactions. Organotin reagents are usually air and moisture stable organometallics, which can be prepared by a number of methods [163–167] and can be conveniently purified and stored. Since they do not react with most common functional groups, the use of protecting groups is almost unnecessary. Moreover, alkynylstannanes usually couple smoothly with a variety of electrophiles and this class of stannanes are the most reactive of all, according to Stille [168]. Also, the reaction is often neither air nor moisture sensitive. In some cases, water and oxygen have been shown to promote the coupling [169]. The reaction initially described by Stille is often carried out under rather drastic conditions, however developed ligands $AsPh_3$ and (2-furyl)$_3$P [170] have solved some of the problems associated with low reactivity. The utility and mildness of Stille reaction are demonstrated by its frequent use in the final stages of complex natural products synthesis [171]. Main drawbacks of Stille coupling are low atom efficiency and toxicity of organotin derivatives. However, despite the toxicity issue this reaction enjoys fourth place on named metal-catalysed cross-coupling reactions in the terms of publications and patents in the last decade [172].

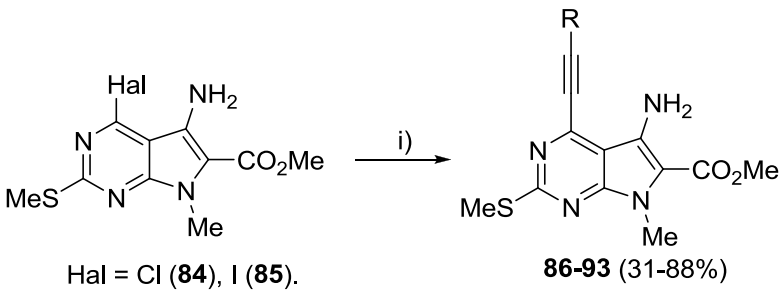
First palladium catalyzed alkynylation at position 4 of the pyrrolo[2,3-*d*]pyrimidine was reported in 1991 by S. Cacchi [173]. The pyrrolo[2,3-*d*]pyrimidine-4-triflate (**82**) was employed in the reaction with 4-pentynecarboxylic acid using $Pd(OAc)_2(PPh_3)_2$/CuI/*i*-Pr_2NH as the catalyst system. The target compound **83** was obtained in 89% yield (Scheme 2.19).



82 **83** (89%)

Scheme 2.19. *Reagents and conditions* i) 5 mol% $Pd(OAc)_2(PPh_3)_2$, 2.5 mol% CuI, *i*-Pr_2NH, DMSO, rt, 22 h.

More extensive study on the Sonogashira coupling of 4-halopyrrolo[2,3-*d*]pyrimidines **84-85**, bearing various functional groups in the molecule, with different terminal alkynes was carried out [174,175]. It was found that the reaction was very sluggish with 4-chloropyrrolo[2,3-*d*]pyrimidines **23**. In order to achieve full conversion, a large excess of alkynes (up to 10 equiv.) has to be used. Glaser type homocoupling by-products were often observed. Palladium and copper catalysts has been used in reasonable amounts (up to 10 mol% $PdCl_2(PPh_3)_2$ and 20 mol% CuI). However, when 4-iodopyrrolo[2,3-*d*]pyrimidine **85** was used, the cross-coupling reaction proceeded at room temperature using 2-3 mol% of $Pd(PPh_3)Cl_2$ and the target compounds were obtained in better yields (Scheme 2.20).



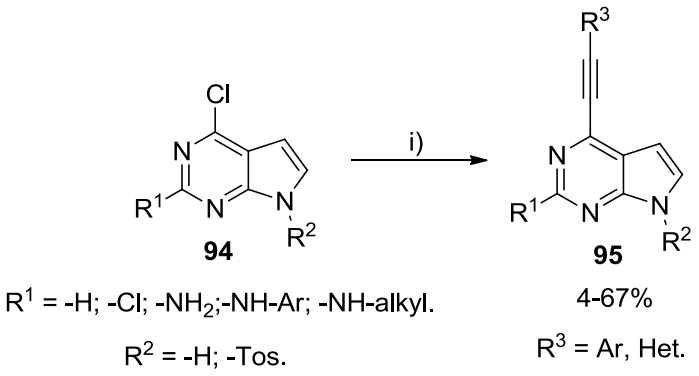
Hal = Cl (**84**), I (**85**).

86-93 (31-88%)

R = Ph (**86**), 4-MeC_6H_4 (**87**), 4-FC_6H_4 (**88**), 2-$H_2NC_6H_4$ (**89**), 2-$(EtO_2CNH)C_6H_4$ (**90**), C_4H_9 (**91**), $SiMe_3$ (**92**),CH_2OH (**93**).

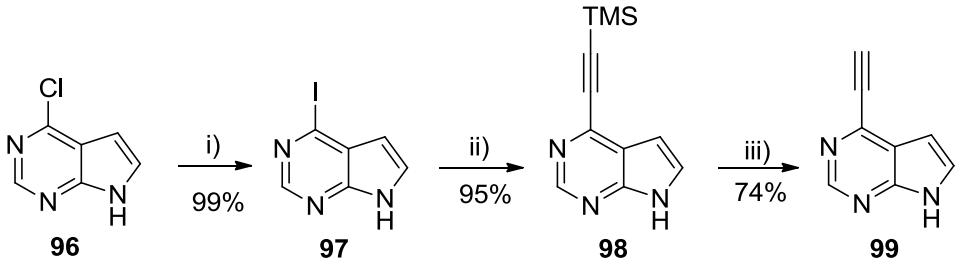
Scheme 2.20. *Reagents and conditions* i) 1.2-10 equiv. of terminal alkyne, 2-10 mol% $Pd(PPh_3)_2Cl_2$, 10-20 mol% CuI, Et_3N, rt to 70 ^oC, 1-48 h.

Patent claimed by Targe-gen Inc. [176] describes the synthesis of various 4-alkynylpyrrolo[2,3-*d*]pyrimidines as potent protein kinase inhibitors (Scheme 2.21). 4-Aryl(hetaryl)ethynyl derivatives **95** were synthesized from the corresponding 4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidines or 2,4-dichloro-7-tosyl-pyrrolo[2,3-*d*]pyrimidine by employing $Pd(PPh_3)Cl_2/PPh_3$/CuI catalyst system in a mixture of NEt_3 and THF or DMF. Products were obtained in 4-67% yield. However, the best yields were obtained when 2,4-dichloro-7-tosyl-pyrrolo[2,3-*d*]pyrimidine was used as starting material.



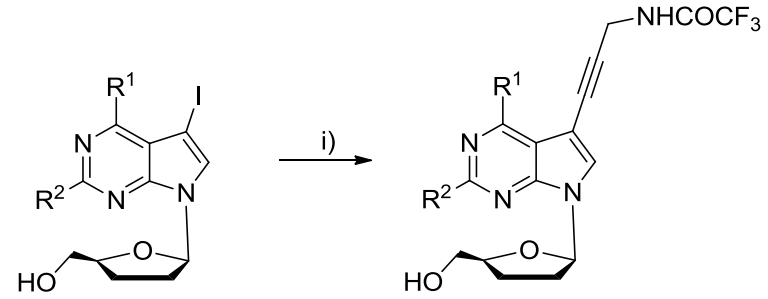
Scheme 2.21. *Reagents and conditions* i) 1.1 equiv. of terminal alkyne, 0.5-10 mol% $Pd(PPh_3)_2Cl_2$, 1-10 mol% PPh_3, 1-10 mol% CuI, 2:1 NEt_3/THF or DMF, 60-80 ^oC, 1-18 h.

S. A. Laufer reported an efficient synthesis of 4-ethynyl-7*H*-pyrrolo[2,3-*d*]pyrimidine **99** as an intermediate precursor for a synthesis of a library of Janus kinase family inhibitors [98]. Synthesis was started from commercially available 4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidine, a halogen exchange under acidic conditions using aqueous hydrogen iodide furnished iodo derivative **97**. The heteroaryl iodide **97** was subsequently coupled with trimethylsilylacetylene under classic Sonogashira conditions and finally deprotected with KF to afford 4-ethynyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**99**) in 70% overall yield (Scheme 2.22).



Scheme 2.22. *Reagents and conditions* i) HI_{aq} (58%), rt, 80 h.; ii) 1.2 equiv. trimethylsilylacetylene, 1.5 mol% $Pd(PPh_3)_2Cl_2$, 3 mol% CuI, NEt_3, 45 ^oC, 6 h.; iii) 1.2 equiv. KF, MeOH, rt, 5 h.

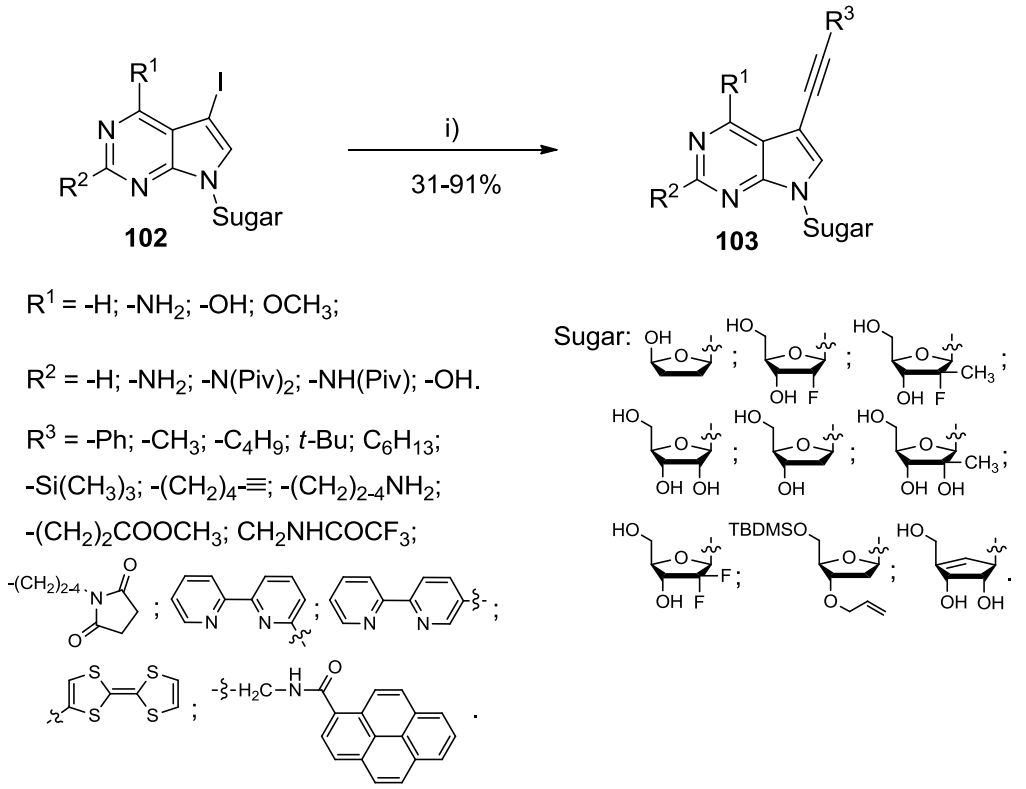
First alkynylation report at position 5 of pyrrolo[2,3-*d*]pyrimidine nucleosides using Sonogashira reaction conditions was reported in 1989 by F. Hobbs [177]. 5-Iodopyrrolo[2,3-*d*]pyrimidine nucleoside analogs **100** reacted with *N*-(prop-2-yn-1-yl)trifluoroacetamide in the presence of $Pd(PPh_3)_4$/CuI/Et_3N in DMF (Scheme 2.23). It was found that ratio of Pd(0) to Cu(I) is crucial and should be sustained at 1:2 in order to obtain modified nucleoside analogs **101** in good yields. Obtained compounds are important as tagged substrates for DNA polymerases.



Scheme 2.23. *Reagents and conditions* i) 3 equiv. N-propargyltrifluoroacetamide, 2 equiv. NEt_3, 10 mol% $Pd(PPh_3)_4$, 5 mol% CuI; DMF, rt, 4 h.

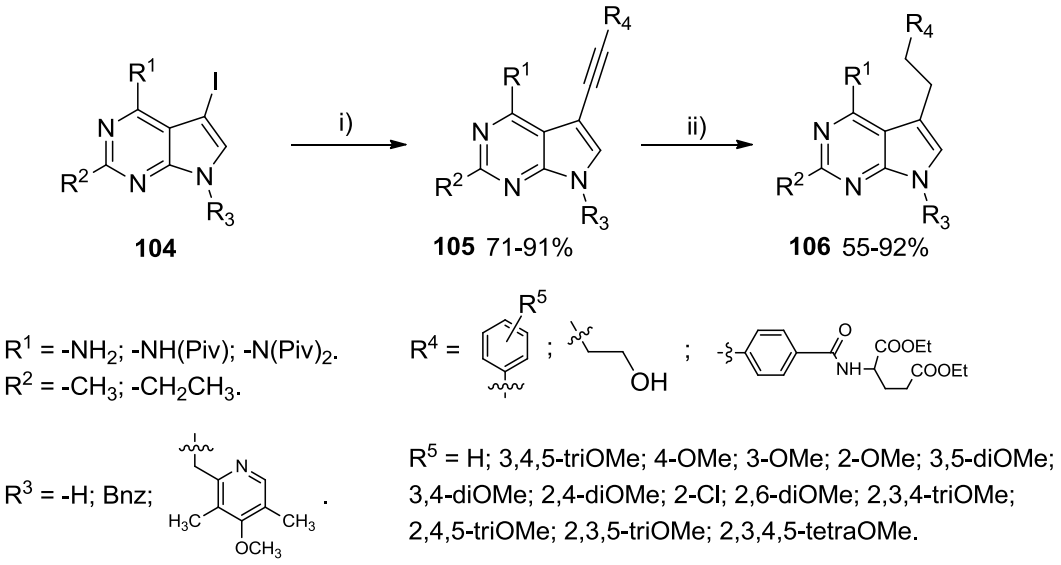
Over the recent years, following the same procedure described by F. Hobbs a large library of 5-alkynylpyrrolo[2,3-*d*]pyrimidine nucleosides with different substituents at 2, 4, 5 and 7 positions of the heterocycle were synthesized [20,30,95,96,178–200] (Scheme 2.24). The synthesized

compounds exhibited a significant antitumor, antiviral and antibacterial activities.



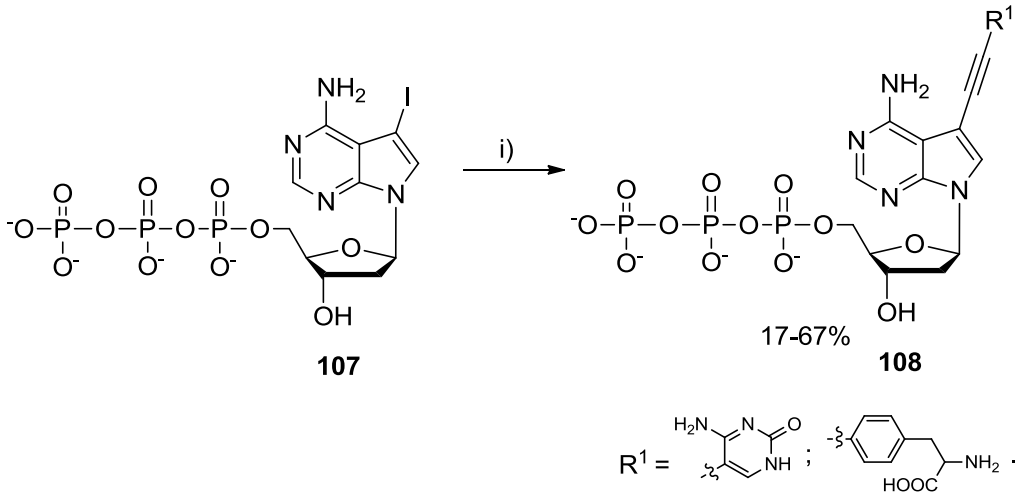
Scheme 2.24. *Reagents and conditions* i) 1.5-6 equiv. of alkyne, 7-18 mol% $Pd(PPh_3)_4$, 10-36 mol% CuI, NEt_3, THF or DMF, rt – 90 ^oC, 4-20 h.

Another important class of pyrrolo[2,3-*d*]pyrimidine-based compounds are inhibitors of folate-dependent biochemical processes **106** (Scheme 2.25). These analogues demonstrated a range of antitumor activities, for example a drug *Pemetrexed* has been approved for treatment of locally advanced and metastatic non-small cell lung cancer. Their synthesis relies on alkynylation of 5-iodopyrrolo[2,3-*d*]pyrimidines followed by a hydrogenation of the triple bond [201–206].



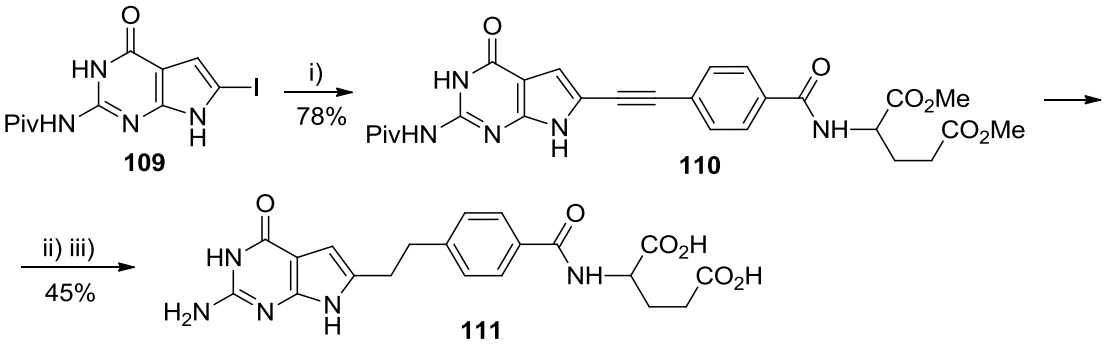
Scheme 2.25. *Reagents and conditions* i) 2.5-3 equiv. alkyne, 10-16 mol% $Pd(PPh_3)_4$, 16-20 mol% CuI, NEt_3, DCE, THF or DMF, rt.-100 ^oC, 10 min. - 24 h; ii) 5% Pd/C, 1:1 DCM:MeOH, H_2 50 psi, 3-24 h.

Sonogashira type alkynylation of 5-iodopyrrolo[2,3-*d*]pyrimidine nucleoside triphosphates **107** can be carried out under aqueous conditions in the presence of $Pd(OAc)_2$, $P(C_6H_4\text{-}3\text{-}SO_3Na)_3$, CuI and *i*$Pr_2$NEt (Scheme 2.26). Obtained compounds **108** are useful as substrates for DNA polymerase [194,207].



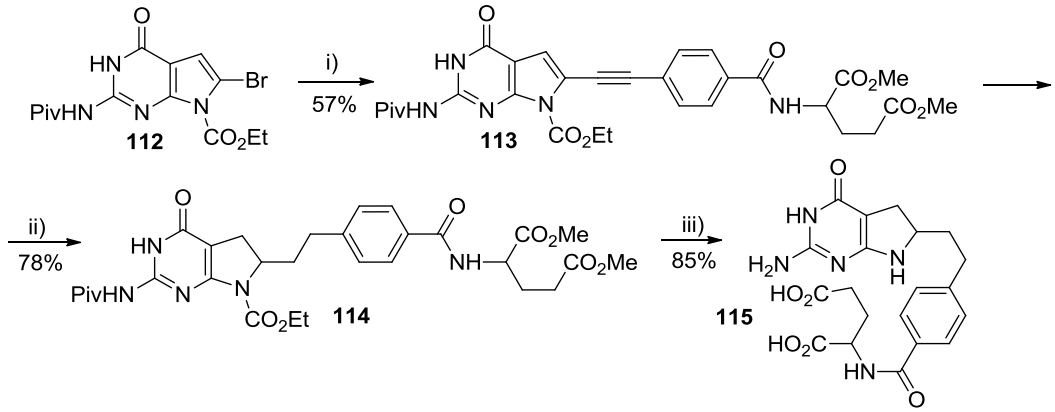
Scheme 2.26. *Reagents and conditions* i) 2 equiv. alkyne, 10 mol% $Pd(OAc)_2$, 20 mol% CuI, 50 mol% $P(C_6H_4\text{-}3\text{-}SO_3Na)_3$, *i*-$Pr_2$Net, 2:1 H_2O:CH_3CN, 60 ^oC, 1 h.

Synthesis of C_6 regioisomer of a drug pemetrexed **111** was reported by E. C. Taylor. This method involves the Sonogashira coupling of 6-iodopyrrolo[2,3-*d*]pyrimidine **109** with 4-ethynylbenzoylglutamate followed by the reduction of the triple bond to afford **111** in 35% total yield [208] (Scheme 2.27).



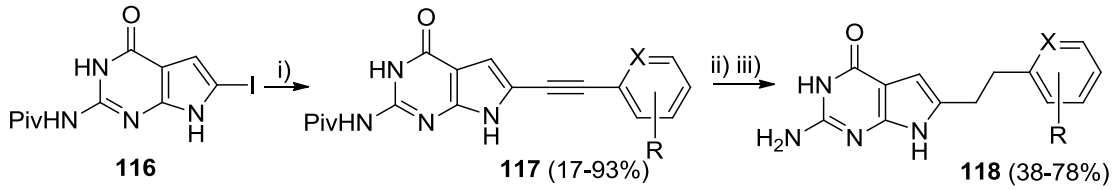
Scheme 2.27. *Reagents and conditions* i) 1.5 equiv. dimethyl 4-ethynylbenzoylglutamate, 5 mol% $Pd(PPh_3)_4$, 20 mol% CuI, 2.5 eq NEt_3, DMF, 60 ^oC, 4 h; ii) 5% Pd/C 80 wt%, H_2 50 psi., MeOH; iii) 1M NaOH.

Few years later, the same group reported on the synthesis of *Pemetrexed* drug C_6 analogue with hydrogenated pyrrole ring [209]. Synthesis was performed by using 6-bromo N-7 ethoxycarbonyl protected derivative **112**. Classical Pd-catalyzed alkynylation of 6-bromo derivative **112** provided **113** in 57% yield. Catalytic reduction of the acetilenic and pyrrole systems afforded **114** in 78% yield (Scheme 2.28). It was determined that presence of tosyl or ethoxycarbonyl protecting groups is essential for hydrogenation of the pyrrole ring. Finally, deprotection with dilute alkali afforded the target compound **115**.



Scheme 2.28. *Reagents and conditions* i) 1.5 equiv. dimethyl 4-ethynylbenzoylglutamate, 5 mol% $Pd(PPh_3)_4$, 2.5 mol% CuI, NEt_3, MeCN, reflux 6 h; ii) 10% Pd/C 100 wt%, H_2, MeOH; iii) 1M NaOH.

A. Gangjee *et al.* designed and synthesized several 6-substituted pyrrolo[2,3-*d*]pyrimidines **118** as potential inhibitors of Thymidylate Synthase [210]. Sonogashira coupling reaction of **116** with appropriate alkyne was one of the synthetic steps of target compound **118** (Scheme 2.29).



R = -H; 4-OMe; 4-CH_3; 2-Cl; 2,5-diOMe; 2,3-C_4H_4; 3,4-C_4H_4
X = CH; N.

Scheme 2.29. *Reagents and conditions* i) 1.5 equiv. alkyne, 9 mol% $Pd(PPh_3)_4$, 21 mol% CuI, NEt_3, DMF, rt, 72 h; ii) 5% Pd/C 100 wt%, 50 psi H_2, 4 drops of NH_4OH, DMF/THF, 20 h; iii) 1M NaOH.

The Sonogashira cross-coupling reaction undoubtedly is one of the most straightforward methods for the introduction of alkynyl groups on the aromatic or heteroaromatic scaffolds. In the pyrrolo[2,3-*d*]pyrimidine series, this reaction has been employed mainly for the synthesis of the 5-alkynylpyrrolo[2,3-*d*]pyrimidine nucleosides, which are interesting as antisense therapy nucleotides, substrates for DNA polymerases and fluorescent labels for nucleic acids. However, literature survey revealed that the introduction of alkynyl groups onto the pyrrolo[2,3-*d*]pyrimidine scaffold was

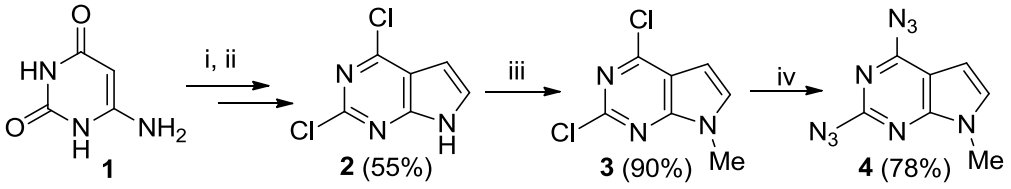
always performed *via* Sonogashira reaction protocol, while other palladium-catalysed alkynylation methods were not applied. Moreover, there are limited data about the synthesis of 2- and 4-alkynylpyrrolo[2,3-*d*]pyrimidines and this field remains explored insufficiently.

3. RESULTS AND DISCUSSION

3.1. Synthesis of 2,4-bis(4-aryl-1,2,3-triazol-1-yl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines

3.1.1. Synthesis and tautomerism of 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine

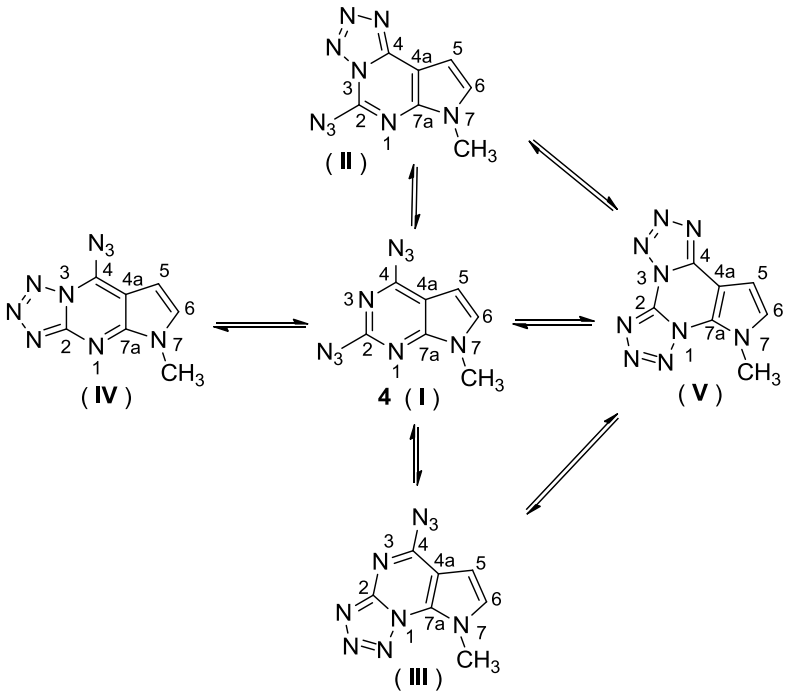
For the synthesis of 2,4-bis(4-aryl-1,2,3-triazol-1-yl)-7-methyl-pyrrolo[2,3-*d*]pyrimidines 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine (**4**) was chosen as starting material. Synthesis of diazide **4** was started from the commercially available 6-aminouracil (**1**) (Scheme 3.1). 2,4-Dichloropyrrolo[2,3-*d*]pyrimidine (**2**) was obtained in 55% yield following the two step procedure described in the literature [211, 212]. Compound **2** was treated with NaH and CH_3I in THF to produce 2,4-dichloro-7-methylpyrrolo[2,3-*d*]pyrimidine (**3**). Finally, 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine (**4**) was obtained in 78% yield by nucleophilic substitution of **3** with NaN_3 in DMF at ambient temperature (Scheme 1). It should be mentioned that great care should be taken working with organic azides, which do not follow the rule $(N_C+N_O)/N_N \leq 3$ (N = number of atoms) [213], to prevent potential explosion hazard. Nevertheless, diazide **4** appeared to be unstable only on standing at daylight or at elevated temperatures and could be stored for longer period of time in the dark bellow 5 ^oC.



Scheme 3.1. *Reagents and conditions* i) $ClCH_2CHO$, NaOAc, H_2O, 80 ^oC to rt; ii) $PhPOCl_2$, 165 ^oC, 2 h; iii) NaH, CH_3I, THF, 0 ^oC to rt; iv) NaN_3, DMF, rt.

It is known that organic azides, in which the azido group is adjacent to an endocyclic nitrogen atom, can undergo spontaneous cyclization to form tetrazole ring. The azide-tetrazole equilibrium is often observed in π-deficient heterocycles such as azidopyrimidines [15,16,214] and azido purines [94,215]. However, earlier reports on the synthesis of 4-azidopyrrolo[2,3-*d*]pyrimidines

indicate that these compounds exist as a tetrazole tautomers [216–219]. In the context of copper catalysed azide-alkyne cycloadition reactions azide-tetrazole tautomeric studies seem to be important, as it is known that existence of tetrazole form may dramatically influence outcome of CuAAC reaction. For example 4-azidoquinazoline mainly exists as tetrazolo[1,5-*c*]quinazoline and does not undergo ligation in CuAAC reactions at all [94]. For this reason it was decided to carry out tautomeric study of diazide **4**. Theoretically, 2,4-diazidopyrrolo[2,3-*d*]pyrimidine (**4**) can exist in five tautomeric forms **I-V** (Scheme 3.2). However, in the IR spectrum of compound **4** two absorbtion bands of both azido groups at 2152 cm^{-1} and 2115 cm^{-1} in KBr, and 2147 cm^{-1} and 2132 cm^{-1} in $CHCl_3$ are observed. In the ^1H NMR spectra recorded in $CDCl_3$, $(CD_3)_2CO$ and DMSO-D_6 two sets of signals for protons of compound **4** with varying ratio were observed. This indicates that two tautomeric forms - diazide and another possible tetrazole tautomer exist in solutions. As determined from ^1H NMR spectra a ratio of diazide form (major) and possible tetrazole tautomer (minor) was found to be 99:1 in chloroform, 20:1 in $(CD_3)CO$, and 6.25:1 in DMSO-D_6.



Scheme 3.2. Possible tautomeric forms **I-V** of 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine (**4**).

In order to determine which tetrazole tautomeric form is observed in solutions experimental chemical shifts in the ^{1}H NMR and ^{13}C NMR spectra were compared with the calculated ones. All ^{1}H and ^{13}C peaks were identified on the basis of HSQC and HMBC experiments in DMSO-D_6. Density functional theory (DFT) calculations were carried out by using Gaussian 09 program package [220]. Geometry optimizations of tautomers **I-V** were performed using the exchange – correlation hybrid functional B3LYP with the 6-311G** basis set. The *in vacuo* structures were further optimized by applying self – consistent reaction field (SCRF) under polarizable continuum model (IEFPCM) incorporating DMSO as solvent. Absolute shielding values were calculated by GIAO method. TMS was used as a reference in calculating ^{1}H and ^{13}C chemical shifts from absolute shielding values. 5-H and 6-H peaks of major tautomer are located at 6.45 ppm and 7.41 ppm in DMSO-D_6, respectively (Table 3.1). These peaks of minor tautomeric form are shifted downfield and observed at 7.01 ppm and 7.59 ppm. Greater downfield shift of the 5-H peak indicates that chain-ring isomerization takes place at the 4th position of pyrrolo[2,3-*d*]pyrimidine, as electron-withdrawing tetrazole group exhibits deshielding effect.

Table 3.1. Experimental and calculated chemical shifts of ^{1}H and ^{13}C NMR of azide and tetrazolyl tautomers **I-V.**

Entry	Tautomeric	^{1}H NMR			^{13}C NMR						
	Form	5H	6H	CH_3	CH_3	C_{7a}	C_2	C_4	C_{4a}	C_5	C_6
1	Major (**I**)[a]	6.45	7.41	3.75	31.6	153.2	154.3	154.0	105.5	98.3	130.8
2	Minor (**II**)[a]	7.01	7.59	3.91	32.5	141.7	137.5	148.0	100.9	99.7	128.9
3	**I**[b]	6.54	7.22	3.72	29.5	156.5	158.3	158.3	109.6	102.5	133.8
4	**II**[b]	7.24	7.49	3.93	30.8	146.1	139.1	152.8	104.8	105.5	133.2
5	**III**[b]	6.77	7.12	4.17	37.2	136.9	158.0	158.9	109.5	105.0	132.6
6	**IV**[b]	6.77	7.54	3.84	29.8	156.4	158.1	134.9	108.3	101.8	140.2
7	**V**[b]	7.33	7.33	4.28	37.9	131.5	147.9	151.7	104.3	107.2	133.4

[a]Experimental chemical shifts in DMSO-D_6. [b]Calculated chemical shifts by GIAO method.

Moreover, experimentally obtained ^{1}H and ^{13}C chemical shifts of major tautomer (Table 3.1, entry 1) showed very good agreement with calculated shifts for tautomeric form **I** (Table 3.1, entry 3). Comparison of ^{13}C shifts of major and minor forms revealed that peaks of C_{7a} and C_2 of minor tautomer are up-field shifted (Table 3.1, entry 2). Such shift in theoretical values is seen only for tautomeric forms **II** and **V** (Table 3.1, entry 4, 7). Nevertheless, experimental chemical shifts of all proton and carbon nucleus of minor tautomer better match with calculated chemical shifts of tautomer **II** - 5-azidopyrrolo[3,2-*e*]tetrazolo[1,5-*c*]pyrimidine (Table 3.1, entry 4). Moreover, comparison of potential energies of tautomeric forms **I-V** indicates that the smallest difference is between tautomeric forms **I** and **II** (ΔE=2.9 kcal/mol) what is also consistent with the NMR identification results (Fig. 3.1)**.**

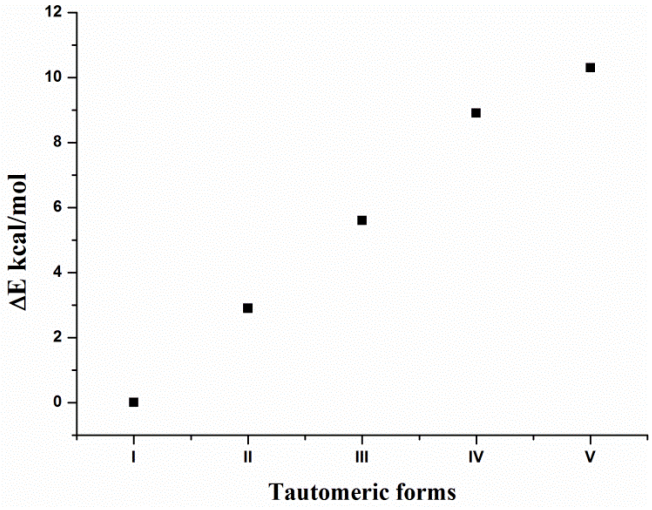


Figure 3.1. Potential energy differences of tautomeric forms **I-V**.

3.1.2. Study of the CuAAC reaction between 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine and arylethynes

With successfully prepared 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine in hand its ability to participate in the CuAAC reaction was examined. For this purpose a set of fourteen terminal alkynes (**5a-n**) has been chosen (Fig. 3.2).

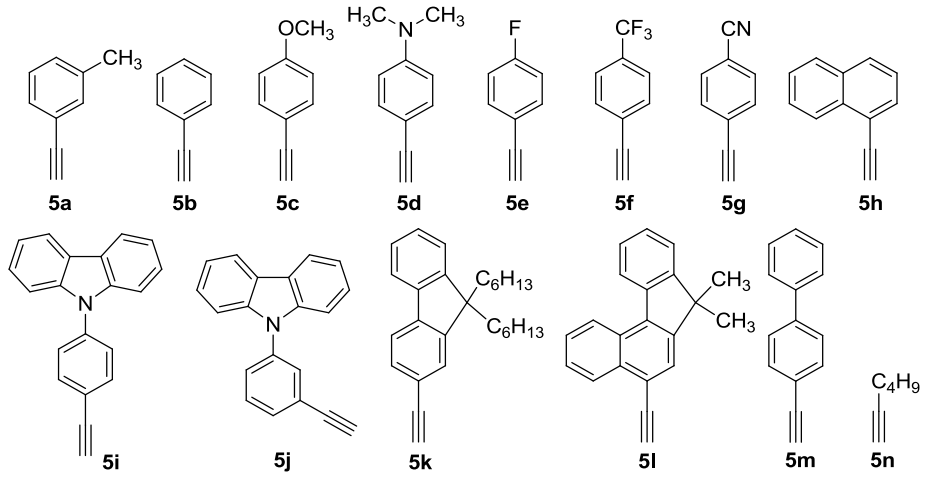
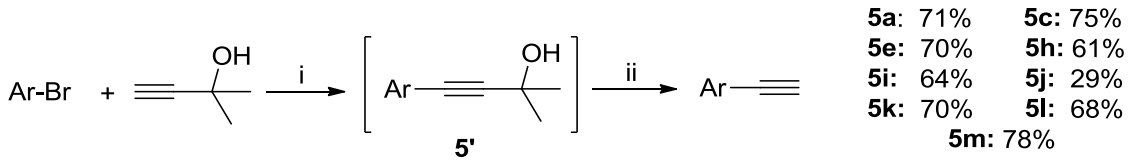


Figure 3.2. Terminal alkynes selected for the CuAAC reaction.

Alkynes **5b**, **5d**, **5f**, **5g**, **5n** were commercially available and were used as purchased. Other terminal alkynes were prepared following similar procedures described in the literature [129,221–224]. Intermediate compounds **5'** were obtained by Pd/Cu-catalysed cross-coupling reaction of aryl bromides with the 2-methyl-3-butyn-2-ol, followed by the retro-Favorsky elimination of acetone from obtained alcohol **5'** with powdered potassium hydroxide in toluene (Scheme 3.3).

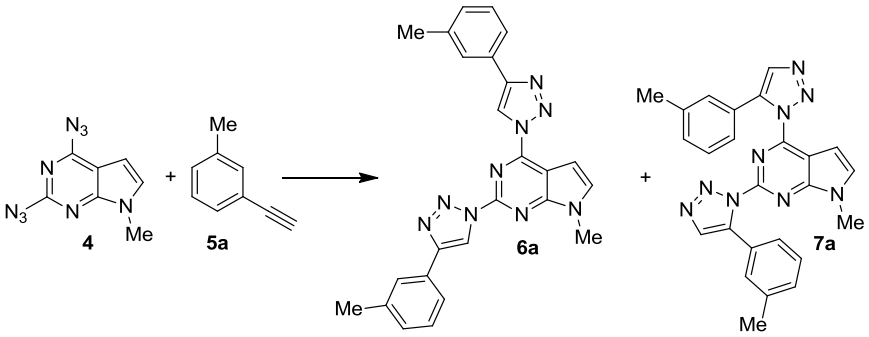


Scheme 3.3. *Reagents and conditions* i) 2 mol% $Pd(PPh_3)Cl_2$, 4 mol% PPh_3, 4 mol% CuI, 2 equiv NEt_3, THF, reflux; ii) 0.6 equiv. KOH, touene, 80-110 ^oC.

Further, on the example of reaction of diazide **4** with 3-ethynyltoluene (**5a**) formation of 2,4-bis(triazolyl)pyrrolo[2,3-*d*]pyrimidine was investigated (Table 3.2). Optimisation was started with the most popular catalyst systems. However, no ligation product was observed using well established $CuSO_4$/NaAsc catalyst system at ambient temperature in *t*-BuOH/H_2O (Table 3.2, entry 1). The target compound **6a** was obtained in 18% yield only when the reaction temperature was raised up to 70 °C (Table 3.2, entry 2). Low yield,

probably, arises from low stability of diazide **2** at elevated temperatures. Next, catalyst system was switched to CuI/NEt_3 and the reaction was examined in different solvents. Cycloadition reaction did not occur in DMF and DMSO. After prolonged stirring of the reaction mixture at ambient temperature only decomposition products of diazide **4** were observed in the reaction mixture. The same catalyst system in THF produced a trace amount of **6a** after 96 hours. To our surprise, switching of THF to CH_2Cl_2 furnished two regioisomers **6a** and possibly **7a** in overall 30% yield with a ratio 71:29 (Table 3.2, entry 6), as determined from ^{1}H NMR spectrum (regioisomer identification will be discussed later in this chapter). Addition of acetic acid, which is known to accelerate C-Cu bond protonation [79], raised the overall yield of products up to 48% (Table 3.2, entry 7).

Table 3.2. The model CuAAC reaction between 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine (**4**) and 3-ethynyltoluene (**5a**).



Entry	Copper source/additive	Solvent	Temp. (^{o}C), time (h)	**6a** : **7a**[a]	Overall yield, % (**6a** + **7a**)
1	$CuSO_4$/NaAsc	*t*-BuOH/H_2O 2:1	rt, 72h	-	no reaction
2	$CuSO_4$/NaAsc	*t*-BuOH/H_2O 2:1	70, 48h	-	18[b]
3	CuI/NEt_3	DMSO	rt, 48h	-	dec. products of **4**
4	CuI/NEt_3	DMF	rt, 48h	-	dec. products of **4**
5	CuI/NEt_3	THF	rt, 96h	-	trace
6	CuI/NEt_3	CH_2Cl_2	rt, 96h	71:29	30
7	CuI/NEt_3/AcOH	CH_2Cl_2	rt, 72h	73:27	48
8	CuI/DIPEA/AcOH	CH_2Cl_2	rt, 72h	70:30	78
9	-	CH_2Cl_2	rt, 168h	-	no reaction
10	DIPEA/AcOH	CH_2Cl_2	rt, 168h	-	no reaction

[a] ^{1}H NMR ratio of the crude product. [b] Regioselectivity was not determined, yield is given for **6a**.

Switching base from NEt_3 to DIPEA raised the overall yield of regioisomeric mixture up to 78% (table 2, entry 8). In all cases stated above regioisomeric ratio in the cycloaddition reaction of **4** with 3-ethynyltoluene was almost the same, so regioselectivity of this reaction seems to be not affected by the reaction conditions. To our knowledge, there are only few reports on the formation of 1,5-isomers in CuAAC reaction [92–94]. 1,5-Disubstituted 1,2,3-triazoles as by-products can be formed by a competitive non-catalysed thermal Huisgen cycloaddition, therefore, experiments were conducted in the absence of copper source and additives (table 2, entry 9-10). However, no traces of the reaction products were observed by TLC even after 7 days. This leads to a conclusion that both isomers are formed by CuAAC process. Perharps, presence of copper catalyst lowers activation energy barriers of both isomers formation [225]. Possible reaction mechanism (adapted from reference [94]) is given in Fig. 3.3. However, it is unclear why minor isomer formed is **7a** as there is a possibility of formation of two "mixed" isomers (Fig. 3.5).

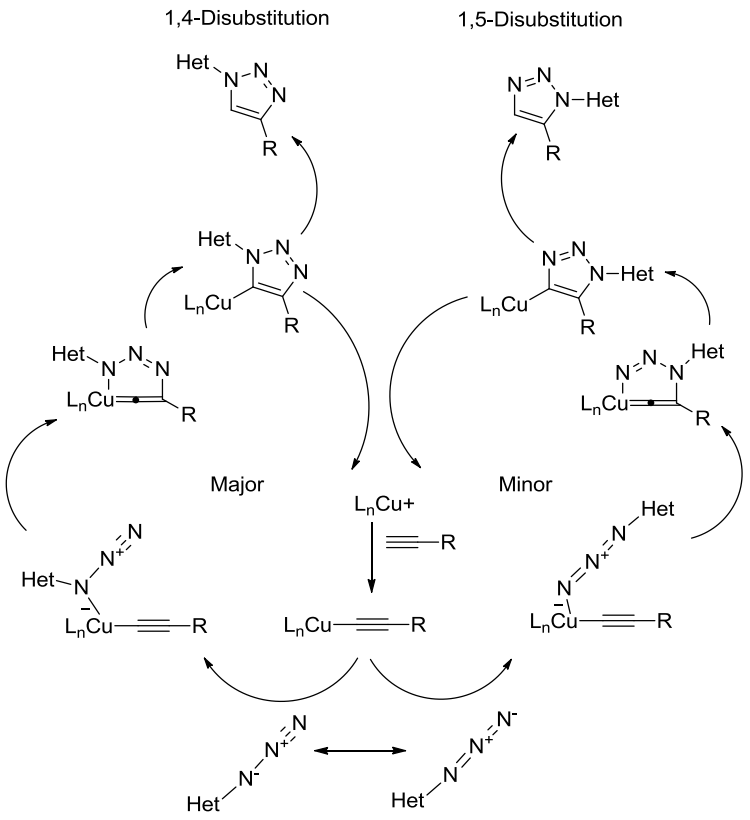


Figure 3.3.. Plausible mechanistic pathways leading to two regioisomeric products

Theoretically, the cycloaddition reaction of diazide **4** with alkynes can lead to the formation of four isomeric ditriazoles. The regiochemistries of the formed 2,4-bis(triazolyl)pyrrolo[2,3-*d*]pyrimidines were assigned on the basis of the characteristic ^{1}H NMR chemical shifts for positions C4-H and C5-H of the triazole moieties. Structural assignment of the formed regioisomers is illustrated on the example of compounds **6d** and **7d**, because none of the 5-H/4-H peaks of 1,2,3-triazole in the ^{1}H NMR spectra of its isomeric mixture were overlapped (Fig. 3.4). For clarity, in Fig. 3.5 structures of all possible isomers of 4-(dimethylamino)phenyl derivative **6d** are presented. It is known that 5-H signal in the ^{1}H NMR spectra of 1,4-disubstituted-1,2,3-triazoles is usually observed in lower fields than 4-H peak of 1,5-disubstituted-1,2,3-triazoles [46,94,226,227].

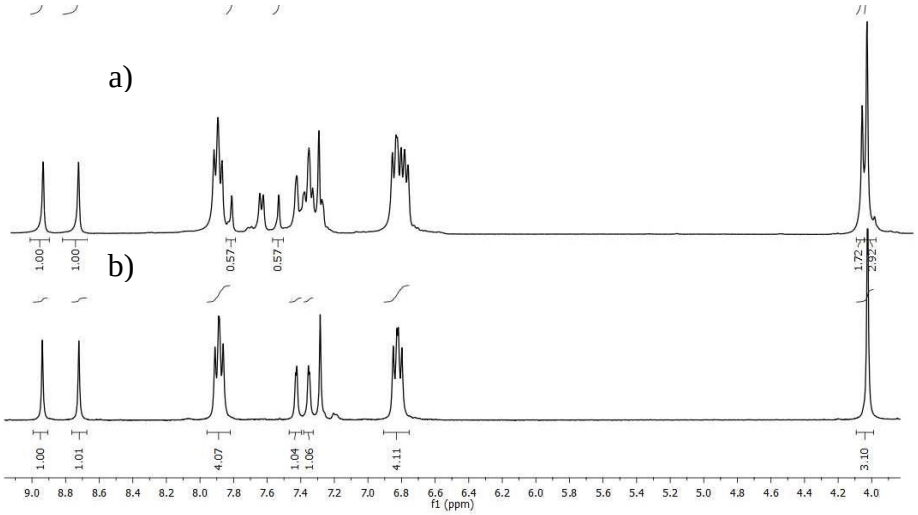


Figure 3.4. a) ^{1}H NMR of crude **6d**/**7d** mixture. b) ^{1}H NMR of pure **6d**.

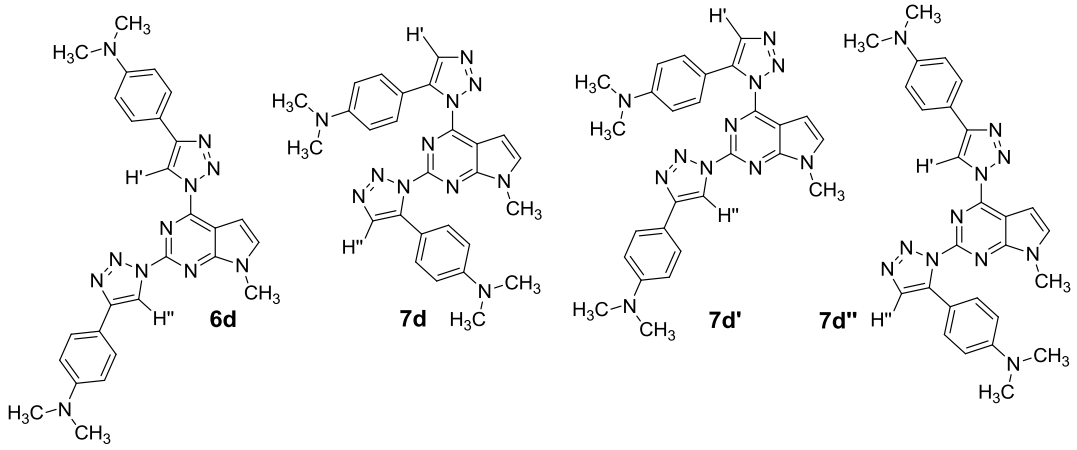


Figure 3.5. Structures of all possible regioisomers **6d**, **7d**, **7d'**, **7d''**.

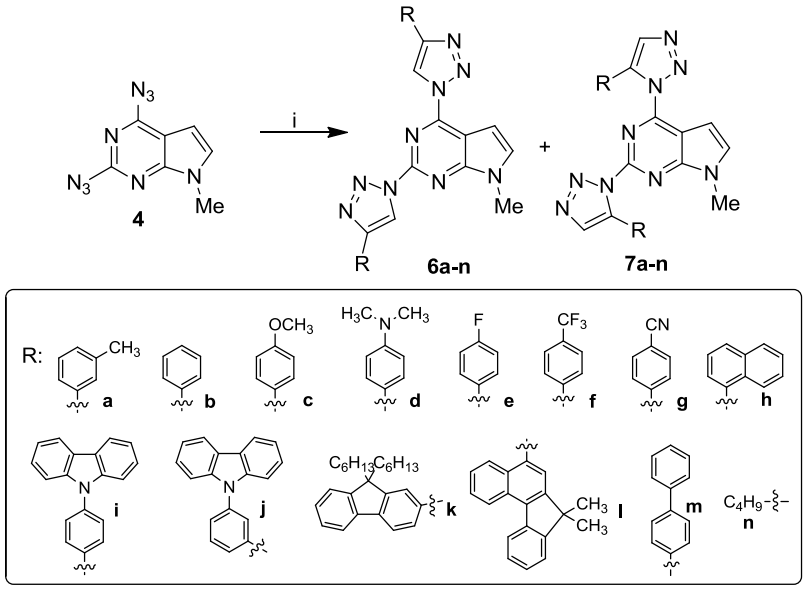
Analogous relationship was observed in the ^{1}H NMR spectra of compounds **6d** and **7d**. For example, in the ^{1}H NMR spectrum of a mixture of **6d** and **7d** both 5-H peaks of isomer **6d** are observed at 8.93 ppm and 8.72 ppm, while the 4-H peaks of **7d** are located at 7.80 ppm and 7.52 ppm, respectively (Table 3.3). It is logical to assume that in case of any "mixed" isomer (**7d'** or **7d''**) only one of the peaks would be shifted to higher fields. In addition, geometries of all regioisomers **6d, 7d, 7d'** and **7d''** were optimized by DFT/B3LYP/6-311G** level of theory and shielding values of the corresponding 4-H and 5-H of 1,2,3-triazole moieties were computed by GIAO method. Comparison of the calculated chemical shifts of 4-H and 5-H of the triazole rings for compounds **6d, 7d, 7d' and 7d''** with the experimental values (Table 3.3) also indicates that in the reaction of diazide **4** with 4-(dimethylamino)phenylethyne the corresponding 1,4-disubstituted (**6d**) and 1,5-disubstituted 1,2,3-triazoles (**7d**) were formed.

Table 3.3. Calculated and experimental 4H/5H chemical shifts δ of 1,2,3-triazole moiety for possible isomers **6d**, **7d**, **7d'**, **7d''**.

	Calculated δ, ppm				Experimental δ, ppm	
	6d	**7d**	**7d'**	**7d''**	Major (**6d**)	Minor (**7d**)
H'	9.28	7.73	7.66	9.15	8.93	7.80
H''	8.98	7.53	8.90	7.69	8.72	7.52

Having established that the optimal CuAAC reaction conditions were CuI/DIPEA/AcOH/CH_2Cl_2 attention was turned to the scope of the cycloaddition of diazide **4** with a range of arylethynes (Scheme 3.4). In most cases, alkynes **5a-n** underwent ligation with diazide **4** to give mixtures of bis-triazoles **6** and **7** with overall yields varying from 62% to 89% (Table 3.4). Cycloaddition of **4** proceeds faster with arylethynes bearing electron-withdrawing substituents (Table 3.4, entries 5-7). Regioselectivity favors the formation of 1,4-isomer. The lowest regioselectivity (63:37) and the lowest

yield of 1,4-isomer was obtained when 4-(dimetylamino)phenylethyne bearing strong electron donating group was employed in the reaction (Table 3.4, entry 4). However, in the reaction of **4** with phenyl-, *p*-fluorophenyl, *p*-cianophenyl, 9,9-dihexyl-2-fluorenyl- and 7,7-dimethylbenzo[*c*]fluoren-5-ylethynes formation of 1,5-disubstituted triazoles was not detected by NMR technique (Table 3.4, entries 2, 5, 7, 11, 12). Due to similar R_f values of isomeric triazoles **6** and **7** mixtures could not be separated into both individual isomers by column chromatography. Only one pure 1,5-disubstituted triazole **7i** was isolated in 9% yield (Table 3.4, entry 9). Nevertheless, all major 1,4-disubstituted triazoles **6a-l** were isolated and purified by fractional crystallization of the crude mixture of isomers from 2-PrOH or toluene.



Scheme 3.4. *Reagents and conditions* i) 3 equiv. alkyne, 20 mol% CuI, 1.1 equiv DIPEA, 1.1 equiv. AcOH, CH_2Cl_2, rt, 8-144 h.

Table 3.4. Synthesis of bistriazoles **6a-n** by CuAAC.

Entry	Reaction time, h	Regioisomeric ratio[a] (**6**:**7**)	Overall yield[b] (**6**+**7**), %	Yield,[c] %
1	72	70 : 30	78	46 (**6a**)
2	48	-[d]	-	48 (**6b**)
3	72	83 : 17	79	58 (**6c**)
4	72	63 : 37	74	35 (**6d**)
5	12	-[d]	-	61 (**6e**)
6	12	93 : 7	89	79 (**6f**)
7	8	-[d]	-	75 (**6g**)
8	120	79 : 21	68	38 (**6h**)
9	144	85 : 15	62	53 (**6i**) 9 (**7i**)
10	96	90 : 10	78	43 (**6j**)
11	96	-[d]	-	56 (**6k**)
12	120	-[d]	-	60 (**6l**)
13	96	69 : 31	45 (**6m**+**7m**)	-
14	70	74 : 26	61(**6n**+**7n**)	-

[a]Determined from the ^{1}H NMR spectra of obtained isomeric mixture. [b]Yield of crude mixture of isomers. [c]Isolated yield. [d]Formation of regioisomer **7** was not observed.

3.1.3. Quantum chemical calculations and cyclic voltammetry study of 2,4-bis(4-aryl-1,2,3-triazol-1-yl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines

Density functional theory calculations were carried out using Gaussian 09 program packages. The geometries of the studied compounds (**6a-l**) were optimized by using the B3LYP/6-311G** level of theory. It was determined that there are several local minima and in order to get correctly optimized structure potential energy surface scan (PES) of dihedral angle at the 4th position of the heterocycle was performed with a step of 5 degrees (Fig. 3.6).

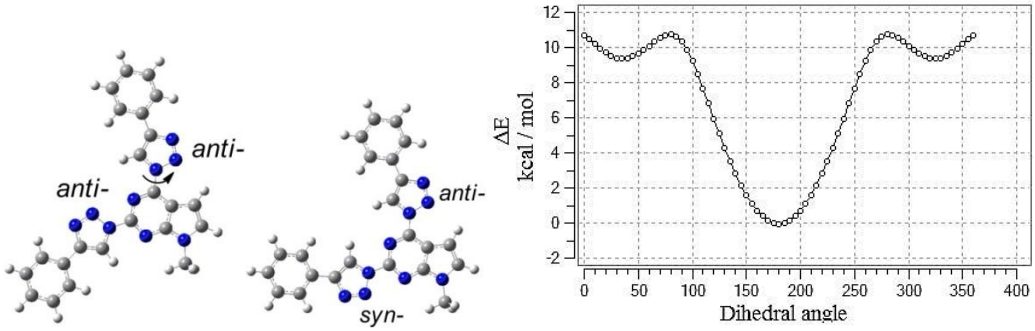
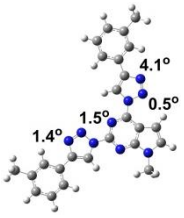
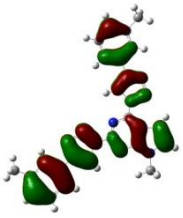
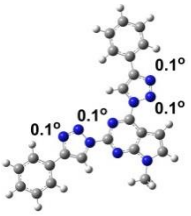
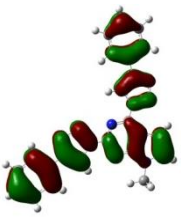
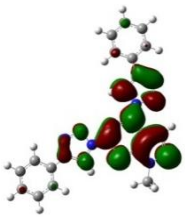
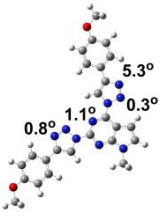
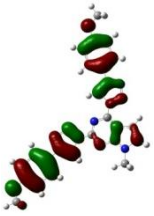
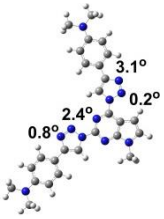
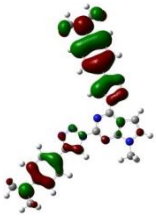
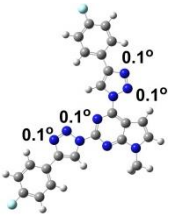
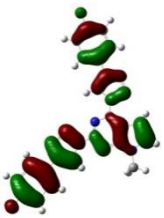
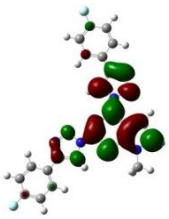


Figure 3.6. *Anti-anti, anti-syn* conformations and potential energy surface scan of compound **6b**.

The scan of 4th position of the heterocycle revealed that two local minima exist at dihedral angle at 40^{o} and 320^{o} degrees and global minima positioned at coplanar geometry with anti-orientation of the 1,2,3-triazole ring. 1,2,3-Triazole ring at the 2nd position of the heterocycle could adopt syn or anti orientation (in the respect of the pyrrolo[2,3-*d*]pyrimidine ring). Thus, potential energy comparison of both structures indicated that anti orientation is energetically more favored by 0.64 kcal/mol. Further examination of geometry of the optimized structures revealed that compounds possessing phenyl (**6a-g**) and 9,9-dihexyl-2-fluorenyl (**6k**) moieties connected to 1,2,3-triazolyl linker are almost coplanar. While compounds with more bulky fragments exhibit twisted geometry. For example, for compounds **6h** and **6l** naphthyl and benzofluorenyl moieties are out of plane with the rest of the molecule with dihedral angle of 36^{o} and for compounds **6i-j** carbazolyl moieties are twisted by 57^{o} (Fig. 3.7).

The DFT computed frontier molecular orbitals (FMO's) of compounds **6a-l** are presented in Fig. 3.7. A comparison of electronic structures revealed that for all the homologues LUMO is positioned on pyrrolo[2,3-*d*]pyrimidine core with an extension to the coplanar 1,2,3-triazolyl moieties. The main differences may be noticed in localization of HOMO. For compounds **6a-b** and **6e-g** possessing electron-withdrawing substituents HOMO is localized over the entire molecule, enclosing the pyrrolo[2,3-*d*]pyrimidine core. Introduction of substituents with increasing electron-donating properties (**6c-d**) results in

enhanced intramolecular charge transfer, which is obvious from localization of the HOMO on the electron-donating moieties. On the other hand the introduction of bulky aromatic substituents (**6h-j**, **l**), resulting in twisted geometry, yields non-symmetric localization of the HOMO on the sole substituent attached at the 4th position of the pyrimidine moiety and thus manifests intramolecular charge transfer character of the states. Compound **6k** possessing fluorenyl moiety, nevertheless showing planar geometry, exhibits intermediate positioning of HOMO, comprising both substituents at the 2nd and 4th positions and partially extending to the pyrrolo[2,3-*d*]pyrimidine.

GEOMETRY	***HOMO***	***LUMO***
 **6a**		
 **6b**		
 **6c**		
 **6d**		
 **6e**		

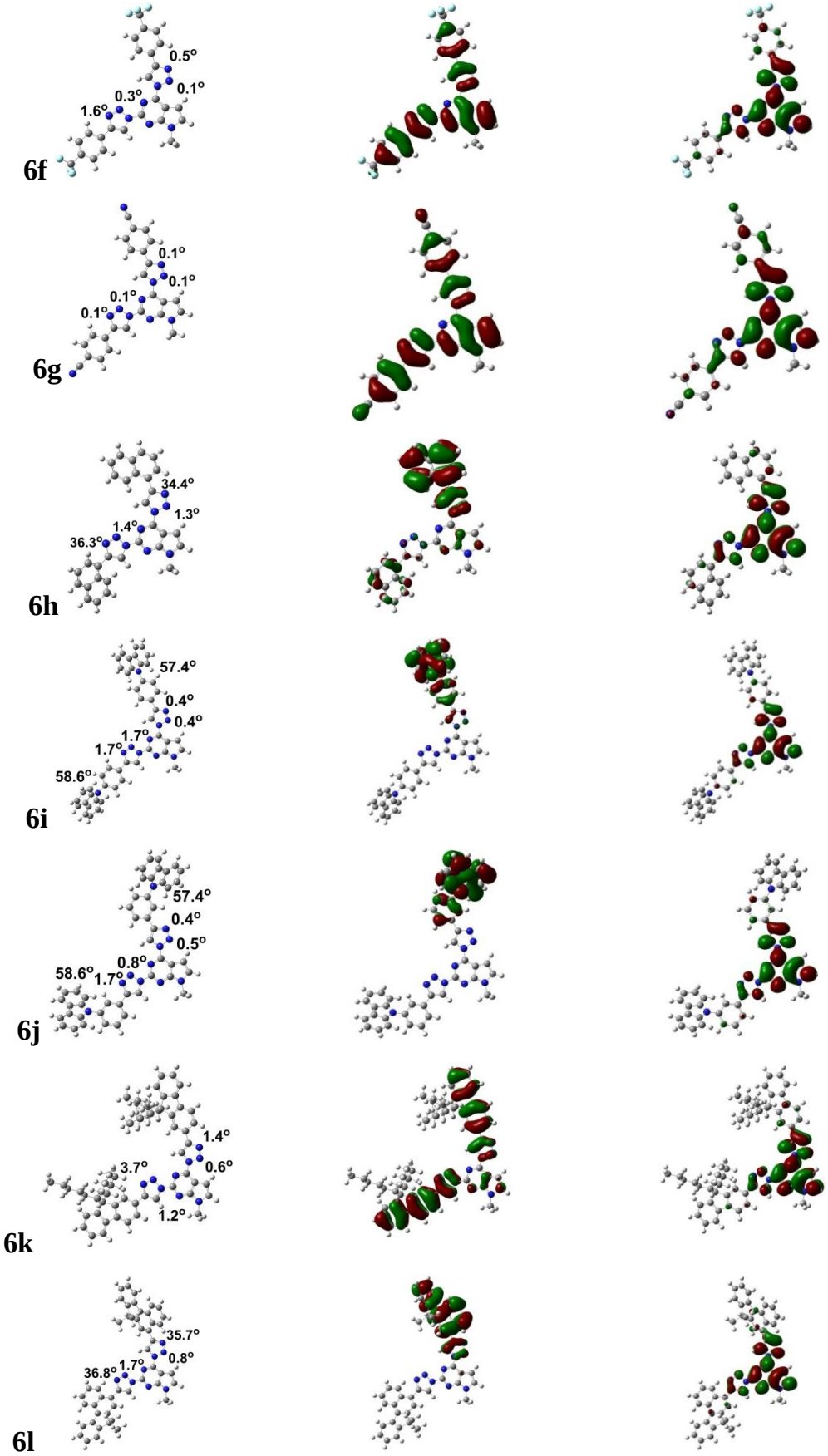


Figure 3.7. Global minima geometry and localization of FMO's for compounds **6a-l.**

Comparison of calculated energies of FMO's revealed the influence of substituents (Fig. 3.8). The energy of the HOMO steadily decreases from -5.08 eV to -6.69 eV with decreasing electron-donating character of the attached substituents (compounds **6d** and **6e**, respectively). Same observations are seen for energy of LUMO, which steadily decreases by the same regularities from -1.95 eV to -2.71 eV. The resulting energy gap increases from 3.13 eV to 4.04 eV. Incorporation of bulky substituents (Fig. 3.8) results in the increase of the HOMO energy with increasing size of aryl substituents (from -5.85 eV to -5.5 eV for compounds **6h** and **6l**). The energy of the LUMO state slightly decreases with increasing size of the conjugated system from -2.24 eV to -2.29 eV, thus the corresponding band gaps decrease from 3.61 eV to 3.21 eV.

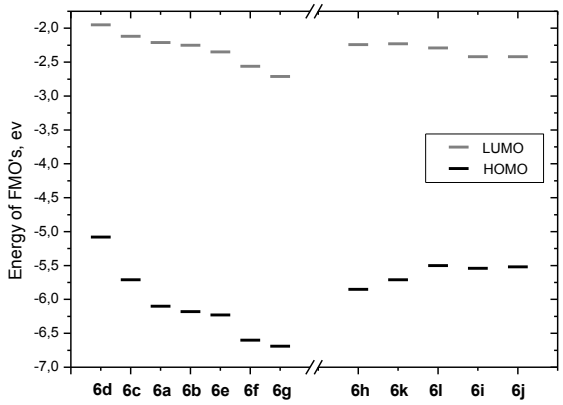


Figure 3.8. Diagram of calculated FMOs energy values of compounds **6a-l.**

The cyclic voltammetry measurements[1] (CV) were carried out with a glassy carbon electrode in dichloromethane (DCM) or dimethylformamide (DMF) solutions containing 0.1 M tetrabutylammonium hexafluorophosphate as electrolyte and Ag/Ag^+ as a reference electrode at the 50 mV/s scan rate. Each measurement was calibrated with ferocene as internal standard. The LUMO energies were calculated from the first signal onset of reduction using formula LUMO = $-(1.19 \cdot E(red)_{onsvsFc}+4.78)$ [228]. All compounds exhibited one irreversible reduction wave. HOMO values were calculated from the optical band gaps and LUMO values using formula $E_{HOMO} = E_{Lumo} - E_g^{opt}$.

[1] CV measurements were performed by Dr. G. Bagdžiūnas at Kaunas University of Technology

Typical voltammograms are shown in Fig. 3.9. HOMO and LUMO energies obtained from cyclic voltammetry studies are summarized in Table 3.5.

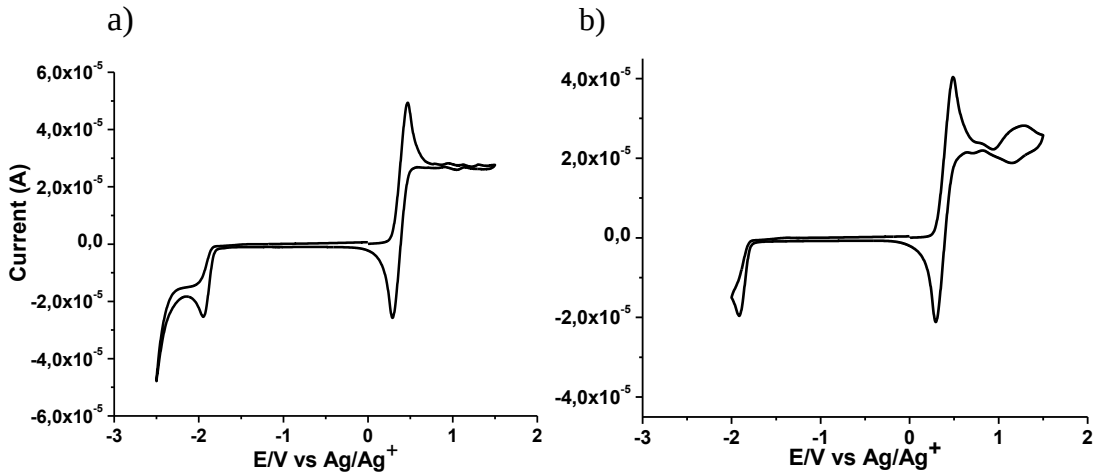


Figure 3.9. Typical CV voltammogram of a) compound **6a**, b) compound **6b**.

Table 3.5. Experimentally calculated energy values (eV) of HOMO and LUMO.

Compound	E_{LUMO}, eV[a]	E_{HOMO}, eV[b]	Eg^{opt}, eV[c]
6a[d]	-2.16	-5.54	3.38
6b[d]	-2.18	-5.58	3.40
6c[d]	-2.24	-5.50	3.26
6d[d]	-2.17	-5.04	2.87
6e[d]	-2.23	-5.60	3.37
6f[d]	-[e]	-[e]	3.35
6g[d]	-2.30	-5.72	3.42
6h[f]	-2.30	-5.67	3.37
6i[f]	-2.34	-5.59	3.25
6j[f]	-2.35	-5.7	3.35
6k[d]	-2.64	-5.96	3.32
6l[d]	-2.26	-5.40	3.14

[a]Calculated by the formula: $E_{LUMO} = -(1.19 \cdot E(red)_{onsvsFc} + 4.78)$. [b]Calculated by the formula: $E_{HOMO} = E_{LUMO} - E_g^{opt}$. [c]Obtained from the intersection of UV/vis and fluorescence spectra. [d]CV measurements were performed in DCM. [e]Could not be measured because of low solubility. [f]CV measurements were performed in DMF.

Variation of the experimentally obtained values induced by electronic effects of substituents is significantly smaller due to an opposite effect resulting from the polarity of the surrounding media. Note, that the cyclic voltammetry results were obtained in dichloromethane or in highly polar DMF

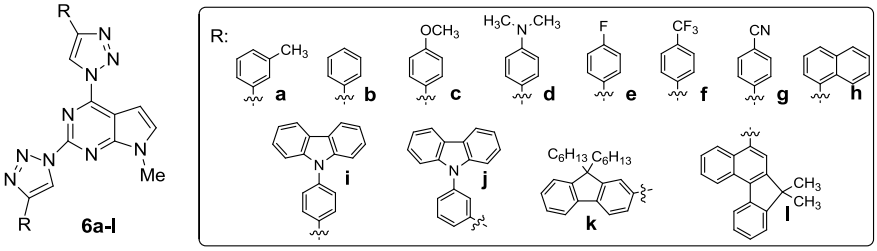
surrounding, in contrast to the theoretical calculations simulating vacuum conditions. Thus, the shift of the LUMO level energy induced by substituent polarity is, probably, diminished by the solvatic shift of energy levels (Table 3.5).

3.1.4. Photophysical properties of 2,4-bis(4-aryl-1,2,3-triazol-1-yl)-7-methylpyrrolo[2,3-*d*]pyrimidines.

Optical properties of the synthesized compounds **6a-l** were assessed by performing absorption and fluorescence spectroscopy, fluorescence lifetime and fluorescence quantum yield measurements in $CHCl_3$, THF and DMF solutions[2]. Absorption and fluorescence data of 2,4-bis(4-aryl-1,2,3-triazol-1-yl)pyrrolo[2,3-*d*]pyrimidines (**6a-l**) together with emission lifetimes (τ), radiative (τ_r) and non-radiative (τ_{nr}) decay lifetimes are collected in table 3.6. The studied compounds exhibit strong UV absorption in dilute solutions with their absorption maxima positioned in a region from 245 to 365 nm. Most of the synthesized compounds show two specific absorption bands located at around 260 nm and 310 nm which are characteristic of pyrrolo[2,3-*d*]pyrimidine units [229]. Slight modifications of the spectra are induced by the substituents attached to the pyrrolo[2,3-*d*]pyrimidine core. Compounds possessing electron-donating substituents (**6c-d**) show decreasing oscillator strength and red shift of the lowest energy absorption band. For example, compound **6d** possessing dimethylamino substituents results in the red shift of the absorption bands to 365 nm (table 3.6).

2 Photophysical measurements were performed by prof. habil. Dr. S. Juršėnas, Dr. K. Kazlauskas, L. Skardžiūtė at the Institute of Applied Research, Vilnius University.

Table 3.6. UV-Vis absorption and PL data for the series of compounds **6a-l** in 10^{-5}M $CHCl_3$, THF and DMF solutions.



		6a	6b	6c	6d	6e	6f	6g	6h	6i	6j	6k	6l
$CHCl_3$	λ_{abs},nm	255 309	264 311	268 318	308 365	249 312	253 310	277 311	245 298	247 293 313 329 341	253 293 314 326 340	245 293 319	246 334 348
	λ_{em},nm	402	402	405	530	403	404	408	404	453	454	422	459
	Φ_F, %	52	49	27	52	49	44	52	27	55	6	34	28
	Stokes shift, nm	93	91	87	165	91	93	97	106	112	114	103	111
	τ, ns	5.2	5.4	2.9	12.3	5.8	6.7	6.4	3.5	9.0	17.8(86%) 3.4(10%) 0.1(4%)	2.6	3.3
	τ_R, ns	10.9	10.7	8.7	23.6	11.4	12.0	13.4	4.7	16.4	-	7.6	11.9
	τ_{NR}, ns	10.0	11.1	4.2	25.6	11.9	15.3	12.4	12.8	20.0	-	3.9	4.6
THF	λ_{abs},nm	256 309	262 309	266 321	310 366	250 312	255 312	270 290	247 297	249 295 312 324 342	251 295 312 328 341	246 293 320	246 334 348
	λ_{em},nm	416	417	418	569	418	422	422	418	459	422	417	455
	Φ_F, %	55	73	31	38	61	43	67	32	50	17	32	25
	Stokes shift, nm	107	108	97	203	106	110	132	121	117	81	97	107
	τ, ns	7.3	7.5	3.8	9.8	7.8	7.8	7.5	5.5	8.7	15.2(71%) 1.3(17%) 0.3(12%)	3.0	3.7
	τ_R, ns	13.2	10.3	12.2	25.9	12.8	18.2	11.1	17.1	17.6	-	9.3	14.8
	τ_{NR}, ns	16.1	27.8	5.5	15.9	20.0	13.7	22.8	8.0	17.6	-	4.4	4.9
DMF	λ_{abs},nm	311	311	320	309 370	311	314	279 312	299	298 315 330 345	297 316 326 346	295 324	335 348
	λ_{em},nm	424	423	436	650	431	436	435	432	530	435	436	492
	Φ_F, %	71	62	21	3	56	50	56	31	27	5	41	19
	Stokes shift, nm	113	112	116	279	120	122	123	133	185	89	112	144
	τ, ns	9.3	9.8	6.3	2.2	10.4	10.6	9.8	7.7	12.5(74%) 20.4(26%)	1.8(44%) 0.5(56%)	6.3	4.8
	τ_R, ns	10.2	15.8	30.2	75.0	18.5	21.2	17.6	24.9	-	-	15.4	25.5
	τ_{NR}, ns	25.1	25.8	8.0	2.3	23.6	21.2	22.3	11.2	-	-	10.7	6.0

The absorption spectra of compounds **6i-j** show absorption bands at 290 nm 340 nm, which are typically assigned to the carbazolyl moieties [230]. Solvent polarity does not have significant influence on the absorption maxima of the studied compounds.

In Fig. 3.10 typical fluorescence spectra of the dilute solutions of compounds **6b-d** in solvents of different polarity ($CHCl_3$, THF, DMF) together with fluorescent decay profiles are shown.

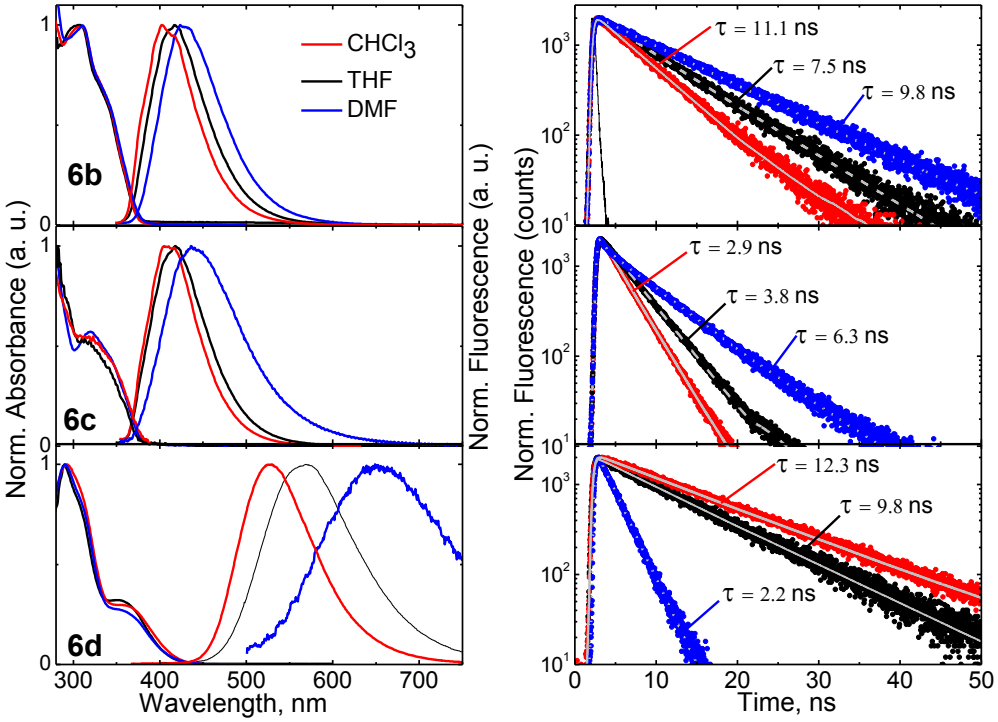


Figure 3.10. UV-Vis absoption and fluorescence spectra together with fluorescence decay profiles in dilute $CHCl_3$, THF and DMF of compounds a) **6b**; b) **6c**; c) **6d**.

Compounds possessing substituted phenyl fragments show broad structureless fluorescence spectra in the region from 402 to 649 nm depending on the electronic nature of the substituents and the polarity of the surrounding media. Weak fluorescence peak dependence on solvent polarity, in the range of 402 nm to 436 nm, was observed for compounds possessing weak electron-donating (**6a**) and electron-withdrawing groups (**6b, e-g**). Incorporation of strong electron-donating dimethylamino moiety (**6d**) resulted in prominent batochromic shift in dilute $CHCl_3$ solution from 402 nm to 530 nm. Thus, broadening and enhanced Stokes shift from 93 nm to 280 nm of the

fluorescence spectra was observed by changing surrounding media, which can be explained by intramolecular charge transfer character of the excited state. In accordance with the charge transfer nature of the transitions, the enhancement of the surrounding media polarity results in even higher red-shifting of the fluorescence spectra up to 650 nm in dilute DMF solution (**6d**, table 3.6).

Most of the compounds demonstrated efficient blue fluorescence with quantum yields up to 0.71. Derivatives **6a-b**, **6e-g** demonstrated fluorescence quantum yields varying from 0.44 to 0.52 in $CHCl_3$, while the higher polarity of the surrounding media resulted in higher efficiencies from 0.5 to 0.71 (in DMF). Much more prominent variation depending on solvent polarity is observed for excitation relaxation rates. The single exponential profiles of the decay transients enabled the estimation of radiative and non-radiative decay lifetimes by the equations $\Phi_F = \tau/\tau_r$ and $1/\tau = 1/\tau_r + 1/\tau_{nr}$. For compounds possessing weak electron-donating (**6a**) and electron-withdrawing groups (**6b, e-g**) both radiative and non-radiative decay lifetimes show almost two fold increase in more polar DMF, as compared to $CHCl_3$, which is evident by the significant slowdown of the fluorescence decay transients (Fig. 3.10). Thus, compounds bearing electron-donating substituents (**6c-d**) showed more than 3 times increase of the radiative decay lifetimes in the solutions of DMF. Such a pronounced variation of both radiative and non-radiative decay lifetimes indicates the charge transfer induced intramolecular twisting reactions, determined by solvation shell [231]. The increase of the radiative decay lifetimes was about 30% for other derivatives (**6a-b**, **6e-g**), with less pronounced CT nature. In general, the non-radiative rates are 2 or 3 times higher in the polar surrounding for all of the compounds, with the exception of **6d**, where the non-radiative decay rate undergoes a 10-fold increase. Thus, the resulting fluorescence quantum yield of differently substituted derivatives, comprising electron-accepting pyrrolo[2,3-*d*]pyrimidine core, depends on competition between both decreased radiative and non-radiative decay rates.

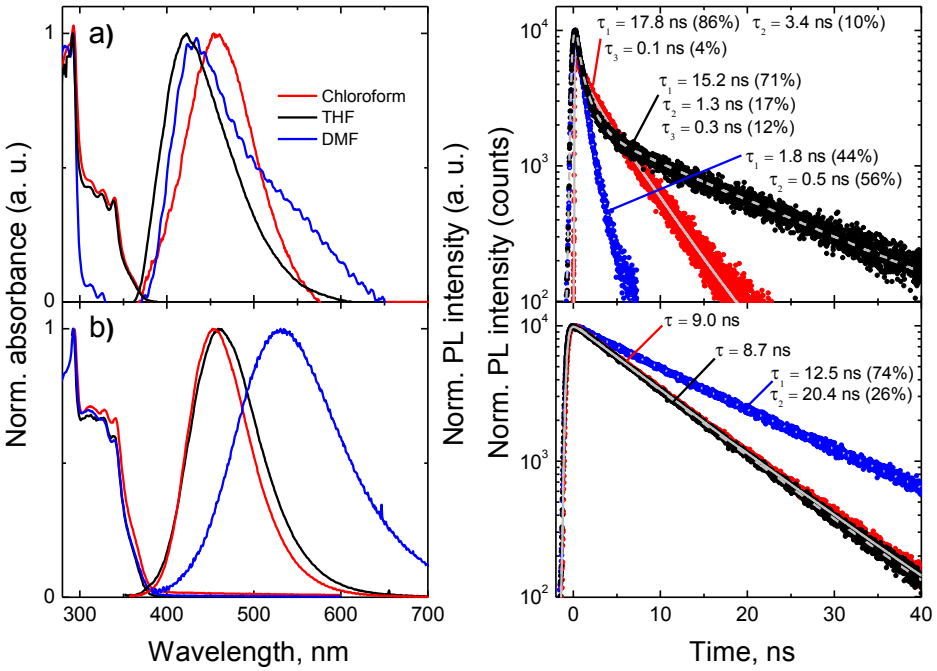


Figure 3.11. UV-Vis absorption and fluorescence spectra together with fluorescence decay profiles in dilute $CHCl_3$, THF and DMF of compounds a) **6j** b) **6i**.

Compounds bearing bulky aromatic substituents revealed similar trends of solvent polarity dependencies of the radiative and non-radiative decay trends with 2-fold increase of the radiative decay lifetime, accompanied by the significant increase of the non-radiative decay lifetimes up to 2.5 times, resulting in slightly lower fluorescence quantum yields, ranging from 0.19 to 0.41. Incorporation of electron-donating carbazolyl units at the para position of the aryl fragments (**6i**) results in fluorescence quantum yield of 0.55, which decreases to 0.27 in polar surrounding. Interestingly, attachment of the same carbazolyl unit at the meta position (**6j**) results in a dramatic decrease of the fluorescence efficiency to 0.06, which might be attributed to the broken symmetry of donor and acceptor moieties, resulting in dual-fluorescence nature of the excited states, clearly visible not only in the fluorescence spectra, but also prominent in the non-exponential decay transients in both non-polar and polar surrounding media (Fig. 3.11)

In summary, novel chromophores - 2,4-bis(4-aryl-1,2,3-triazol-1-yl)pyrrolo[2,3-*d*]pyrimidines were prepared by CuAAC reaction of 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine with diverse ethynylarenes at room

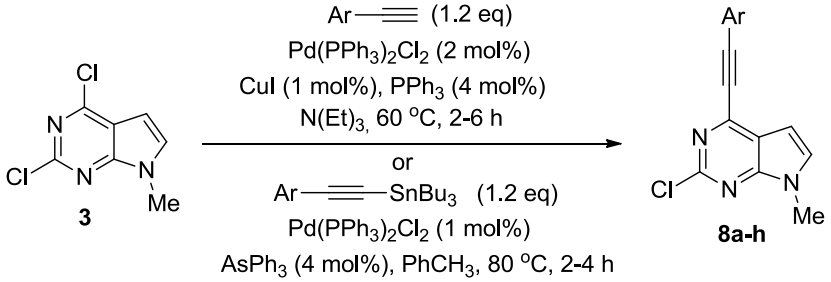
temperature in dichloromethane using CuI/DIPEA/AcOH catalyst system. It was demonstrated that in the CuAAC reaction of 2,4-diazidopyrrolo[2,3-*d*]pyrimidine along with 1,4-disubstituted 1,2,3-triazoles some amounts of 1,5-disubstituted isomers were formed. Synthesized 2,4-bis(4-aryl-1,2,3-triazol-1-yl)pyrrolopyrimidines exhibit efficient fluorescence in the range from 402 nm to 650 nm. The introduction of various substituents enables tuning of HOMO and LUMO energies: the attachment of polar substituents in the para position of phenyl group with increasing electron-donating character results in lower HOMO and LUMO energies (from -6.69 eV to -5.08 eV for HOMO and from -2.71 eV to -1.95 eV for LUMO), while the addition of more bulky aryl substituents caused the reduction of HOMO energy (from - 5.85 eV to -5.50 eV). DFT calculations revealed that LUMO of all derivatives are located on the pyrrolo[2,3-*d*]pyrimidine moiety and includes triazole fragments. This leads to the extension of the LUMO localization and enhanced electron-accepting properties of heterocyclic part of molecules. The bulky aryl substituents show mostly electron donating character and influence the energy levels of HOMO state. Variation of the size, polarity and geometry of the substituents alters the charge transfer character of the transitions, influencing the properties of the fluorescence spectra and fluorescence quantum yield. Intramolecular charge transfer of the excited state has a considerable influence on the dynamics of radiative and non-radiative decay in polar surroundings. Both processes slow down and the competition between the radiative and non-radiative decay pathways results in smaller fluorescence quantum yields for compounds possessing electron-donating substituents or substituents with twisted geometry. The highest quantum yield of 73% was observed for a pyrrolo[2,3-*d*]pyrimidine derivative **6b** with non-polar substituents in medium polarity surrounding media.

3.2. Synthesis of alkynylpyrrolo[2,3-*d*]pyrimidines

3.2.1 Synthesis of 2-aryl-4-(arylethynyl)- and 2,4-bis(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines

Initially, for the synthesis of the alkynyl[2,3-*d*]pyrrolopyrimidines, the Sonogashira coupling of 2,4-dichloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**3**) with different arylethynes **8a-8f** was investigated. After brief optimization it was found out that 4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines can be obtained in reasonable yields by using 2 mol% $Pd(PPh_3)_2Cl_2$ / 4 mol% PPh_3 / 1 mol% CuI in NEt_3 at 60°C (Table 3.7). Use of solvents such as DMF or THF, or higher catalyst loadings did not improve the yields of target compounds. Moreover, it is worth mentioning that increasing the amount of CuI in the reaction resulted in the decreased yields of the alkynylated products due to the dimerization of arylethynes.

Table 3.7. Synthesis of 4-(arylethynyl)-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines **8a-h** by Sonogashira and Stille reactions



Entry	Compdound	Ar	Yield, (%)	
			Sonogashira	Stille
1	**8a**	Ph	68	88
2	**8b**	3-MeC_6H_4	73	84
3	**8c**	4-FC_6H_4	58	70
4	**8d**	4-$Me_2NC_6H_4$	24	64
5	**8e**	4-$MeOC_6H_4$	46	71
6	**8f**	4-$CF_3C_6H_4$	60	36
7	**8g**	4-(9-carbazolyl)C_6H_4	-[a]	74
8	**8h**	9,9-dihexyl-2-fluorenyl	-[a]	52

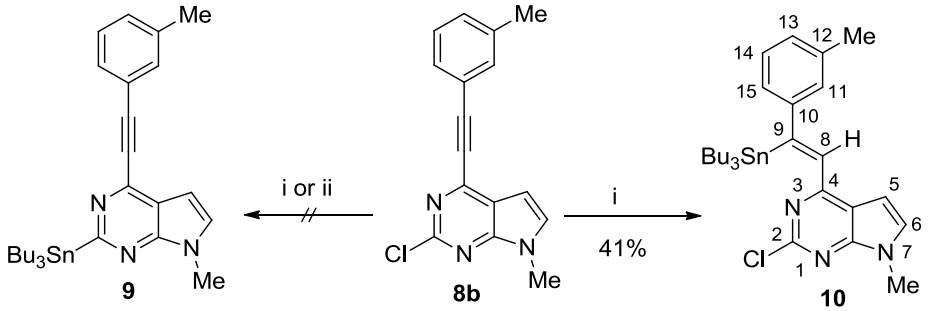
[a]Reactions were not carried out under the Sonogashira conditions.

However, it was impossible to prepare 2,4-bis(arylethynyl)pyrrolopyrimidines **14** or **15** (see general structures in Scheme

3.8 and table 3.10) *via* the 2nd Sonogashira coupling at position 2 of pyrrolopyrimidines **8**. The similar inertness of 2-chloro and even 2-iodo groups in Sonogashira reactions was previously observed in pyrimidines and quinazolines [232,233].

Moreover, in contrast to earlier reports on the synthesis of 2,4-diarylpyrrolopyrimidines [37, 38], the 2-chloro group in compounds **8** appeared to be unreactive in the Suzuki coupling with arylboronic acids. For example, in the Suzuki reaction of **8a** with phenylboronic acid, different catalysts [$Pd(OAc)_2$, $Pd(PPh_3)_2Cl_2$, $Pd(dppf)Cl_2$], ligands (Ph_3P, 2-biPhCy_2P), bases (Na_2CO_3, Cs_2CO_3, K_3PO_4) and solvents (THF, toluene, 1,4-dioxane) were employed, however, the desired 2-phenyl derivative **12a** was obtained in low yields (15–20%), only in the presence of $Pd(PPh_3)_2Cl_2/Ph_3P/Na_2CO_3$ or K_3PO_4 as the catalyst system, using a threefold excess of phenylboronic acid.

Consequently, in order to develop a method for the synthesis of 2-aryl-4-(arylethynyl)pyrrolopyrimidines **12**, different pathways using the Stille coupling were studied. According to one of these, the corresponding organotin derivative **9** might be useful as an intermediate for the synthesis of 2-substituted pyrrolo[2,3-*d*]pyrimidines (Scheme 3.5).

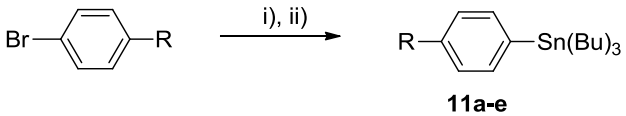


Scheme 3.5. *Reagents and conditions* i) $Bu_3SnSnBu_3$, *n*-BuLi, THF, -78°C to rt; ii) $Bu_3SnSnBu_3$, 4 mol% $Pd(PPh_3)_2Cl_2$, THF, reflux.

2-Tributylstannyl derivatives of pyrimidine and other diazines can be obtained by reactions of halogenated azines with (tributylstannyl)lithium [234–236]. However, the reaction of pyrrolopyrimidine **8b** with (tributylstannyl)lithium, derived from hexabutyldistannane and *n*-butyllithium,

did not gave the desired product **9**. Instead, addition of (tributylstannyl)lithium to the triple bond of 4-(*m*-tolylethynyl)pyrrolopyrimidine **8b** occurred to afford isomerically pure compound **10** in 41% yield. The structure of **10** was established by ^{1}H, ^{13}C NMR and NOESY spectroscopy. In the NOESY spectrum, intense cross peaks due to the vinyl-H/C_5-H and vinyl-H/C_{11}/C_{15}-H protons were observed. The values of the spin–spin coupling constants between the vinyl proton and tin ($^{3}J_{Sn–H}$ = 101 Hz and 97 Hz) are characteristic for *anti*-addition isomers [237–239]. The regioselectivity of the addition of the tributyltin anion to the triple bond of **8b** was confirmed on the basis of the $^{2}J_{Sn–C}$ and $^{3}J_{Sn–C}$ coupling between the tin atom and the C_{10} ($^{2}J_{Sn–C}$ = 24.0 Hz), C_{11}/C_{15} ($^{3}J_{Sn–C}$ = 15.3 Hz), and C_4 ($^{3}J_{Sn–C}$ = 18.6 Hz) carbon nucleus. Such regioselectivity of the addition reaction can be explained by stabilization of the vinyl anion formed by the π-deficient pyrimidine ring of **8b**. These results are consistent with those obtained for a series of diarylethynes [238]. Another attempt to obtain compound **9** by the palladium-catalysed stannylation reaction of **8b** with hexabutyldistannane led to the formation of a complex mixture of products and tars.

Therefore, an alternative route for the synthesis of compounds **12** based on the palladium-catalysed Stille cross-coupling reaction of 4-(arylethynyl)-2-chloropyrrolopyrimidines **8** with (aryl)tributylstannanes was investigated. For this reason, five (aryl)tributylstannanes **11a-e** were prepared by addition of *n*-BuLi to the cooled solution of corresponding arylbromides in THF and followed by the addition of tributyltin chloride (Scheme 3.6).

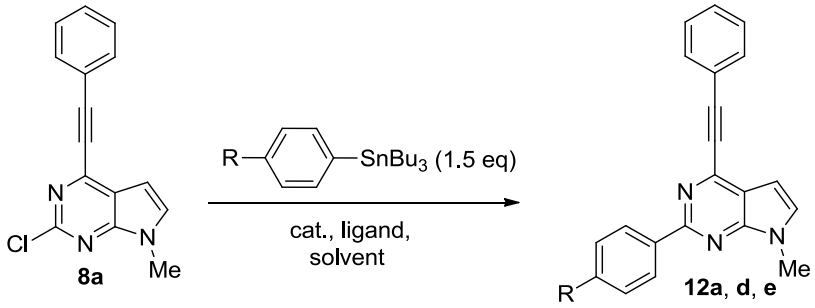


11a-e

R = -H (**11a**, 97%); -F (**11b,** 95%);-CF_3 (**11c**, 91%); -OCH_3 (**11d**, 96%); -$N(Me)_2$ (**11e**, 92%).

Scheme 3.6. *Reagents and conditions* i) 1.1 equiv. *n*-BuLi, THF, -78 ^{o}C, 30 min; ii) 1.0 equiv. $Sn(Bu)_3Cl$, -78 ^{o}C to rt.

Table 3.8. Optimization of Stille arylation reaction of **8a** with (aryl)tributylstannanes.



R = -H (**a**); -OMe (**d**); -N(Me)$_2$ (**e**).

Entry	Catalyst[a]	Ligand[a]	Solvent	Time, h	Product	Yield[b], (%)
1	$Pd(PPh_3)_2Cl_2$	-	toluene	120	**12a**	48
2	$Pd(PPh_3)_2Cl_2$	PPh_3	toluene	120	**12a**	64
3	$Pd(PPh_3)_2Cl_2$	PPh_3	*p*-xylene	96	**12a**	68
4	$Pd(PPh_3)_2Cl_2$	PPh_3	toluene	120	**12d**	21
5	$Pd(PPh_3)_2Cl_2$	PPh_3	*p*-xylene	96	**12d**	27
6	$Pd(PPh_3)_2Cl_2$	PPh_3	toluene	120	**12e**	18
7	$Pd(PPh_3)_2Cl_2$	PPh_3	*p*-xylene	96	**12e**	25
8	$Pd(PPh_3)_2Cl_2$	PPh_3	THF	96	-	N.R.[c]
9	$Pd(PPh_3)_2Cl_2$	PPh_3	DMF[d]	96	-	N.R.
10	$Pd(dppf)Cl_2$	-	toluene	96	-	N.R.
11	$Pd_2(dba)_3$	PPh_3	toluene	96	**12a**	trace
12	$Pd(PPh_3)_2Cl_2$	$AsPh_3$	toluene	48	**12a**	82
13	$Pd(PPh_3)_2Cl_2$	$AsPh_3$	toluene	72	**12d**	44
14	$Pd(PPh_3)_2Cl_2$,	$AsPh_3$	toluene	72	**12e**	42
15	$Pd(PPh_3)_2Cl_2$[e]	$AsPh_3$[e]	toluene	48	**12a**	55
16	$Pd(PPh_3)_2Cl_2$[f]	$AsPh_3$[f]	toluene	48	**12a**	38
17	$Pd_2(dba)_3$	$AsPh_3$	toluene	96	**12a**	trace
18	$PdCl_2$	$AsPh_3$	toluene	96	**12a**	trace
19	$Pd(OAc)_2$	$AsPh_3$	toluene	96	**12a**	trace
20	$Pd(PPh_3)_2Cl_2$	$AsPh_3$	*p*-xylene	72	**12d**	42
21	$Pd(PPh_3)_2Cl_2$	$AsPh_3$	*p*-xylene	72	**12e**	39

[a]Unless otherwise specified, all reactions were carried out using 5 mol% of catalyst and 20 mol% of ligand at reflux. [b]Isolated yields. [c]No reaction. [d]Reaction was carried out at 130 ^oC. [e]Amount of catalyst – 2.5 mol%, ligand – 10 mol%. [f]Amount of catalyst – 1 mol%, ligand – 4 mol%.

Optimization of the Stille coupling with (aryl)tributylstannanes was performed using compound **8a** (table 3.8). It was found that $Pd(PPh_3)_2Cl_2$ alone catalysed the reaction; after prolonged heating at reflux temperature in toluene, compound **12a** was obtained in a moderate 48% yield (table 3.8, entry 1).

Addition of an excess of triphenylphosphine (20 mol%) as the ligand resulted in an increased yield (64%) of **12a** (table 3.8, entry 2). However, lower yields were obtained when (aryl)tributylstannanes with electron-donating groups (**11d-e**) were used (Table 3.8, entries 4 and 6). Increasing the reaction temperature by using *p*-xylene as the solvent instead of toluene resulted in slightly increased yields of the cross-coupled products **12a**, **12d**, and **12e**, and reduced the reaction time (Table 3.8, entries 3, 5 and 7). It is noteworthy, that employing THF and DMF as solvents (Table 3.8, entries 8 and 9), or $Pd(dppf)Cl_2$ and $Pd_2(dba)_3$ (Table 8, entries 10 and 11) as catalysts did not give positive results. It is known that ligands of low donor ability such as tri(2-furyl)phosphine [$(2\text{-furyl})_3P$] and triphenylarsine ($AsPh_3$) increase the rate of Stille cross-coupling reactions and have small free ligand inhibition factors [170,240]. Thus, switching the ligand from PPh_3 to $AsPh_3$ led to higher yields of products and markedly reduced reaction times (Table 3.8, entries 12–14). When the loading of the catalyst was decreased to 1 mol%, the yield of **12a** decreased dramatically from 82% to 38% (Table 3.8, compare entries 12, 15 and 16), thus illustrating that the minimum amount of catalyst needed for this reaction to be efficient was 5 mol%. Any further variation of the catalysts (Table 3.8, entries 17–19) and solvents (Table 3.8, entries 20 and 21) did not improve the results.

Having established optimum reaction conditions ($Pd(PPh_3)_2Cl_2$ (5 mol%), $AsPh_3$ (20 mol%) as the catalyst system, toluene as the solvent) attention was turned to the scope of the Stille arylation of 4-(arylethynyl)-2-chloro-7-methylpyrrolo[2,3-*d*]pyrimidines **8a**–**c** with a range of (aryl)tributylstannanes. The reactions proceeded smoothly to afford products **12a**–**o** in moderate to high yields (Table 3.9).

Table 3.9. Synthesis of 2-Aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**12a**–**o**).

Entry	Compound	Ar^1	Ar^2	Yield, (%)
1	**12a**	Ph	Ph	82
2	**12b**	Ph	4-FC_6H_4	76
3	**12c**	Ph	4-$CF_3C_6H_4$	80
4	**12d**	Ph	4-$MeOC_6H_4$	44
5	**12e**	Ph	4-$Me_2NC_6H_4$	42
6	**12f**	3-MeC_6H_4	Ph	81
7	**12g**	3-MeC_6H_4	4-FC_6H_4	88
8	**12h**	3-MeC_6H_4	4-$CF_3C_6H_4$	85
9	**12i**	3-MeC_6H_4	4-$MeOC_6H_4$	48
10	**12j**	3-MeC_6H_4	4-$Me_2NC_6H_4$	43
11	**12k**	4-FC_6H_4	Ph	87
12	**12l**	4-FC_6H_4	4-FC_6H_4	85
13	**12m**	4-FC_6H_4	4-$CF_3C_6H_4$	86
14	**12n**	4-FC_6H_4	4-$MeOC_6H_4$	45
15	**12o**	4-FC_6H_4	4-$Me_2NC_6H_4$	42

The Sonogashira and Stille couplings of 2,4-dichloro-7-methylpyrrolo[2,3-*d*]pyrimidine occur first at position 4 of the pyrrolopyrimidine. This is consistent with the regioselectivity of the palladium-catalysed cross-couplings of multiply halogenated pyrimidines and related nitrogen heterocycles [37,38,232,241–244]. Additionally, evidence for such regioselectivity is supported by a single crystal X-ray structural analysis of compound **12m** (Figure 3.12).

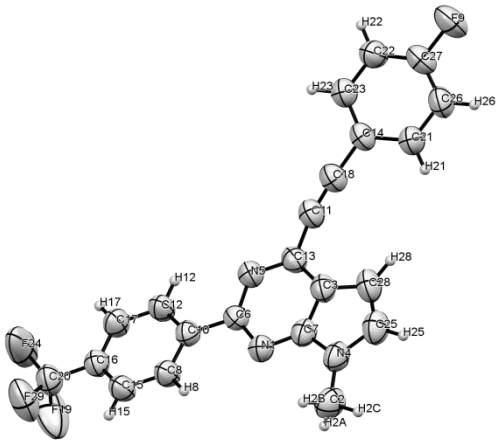
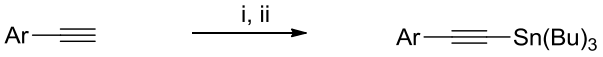


Figure 3.12. ORTEP view of X-ray structure of compound **12m** with the atom numbering labels and at 50% thermal ellipsoids probability.

The obtained results and the fact that the Stille coupling using alkynylstannanes in a heteroaromatic series, including fused pyrimidine heterocycles, has not been explored sufficiently prompted us to apply the $Pd(PPh_3)_2Cl_2/AsPh_3$ catalyst system for the synthesis of 2,4-bis(arylethynyl)pyrrolopyrimidines. However, only (phenylethynyl)tributylstannane was commercially available. For this reason nine (arylethynyl)tributylstannanes **13a-i** were prepared by addition of *n*-BuLi to the cooled solution of the corresponding arylethynes in THF and followed by the addition of tributyltin chloride (Scheme 3.7).



Ar: 3-MeC_6H_4- (**13a**, 96%); 4-FC_6H_4- (**13b**, 94%); 4-$Me_2NC_6H_4$- (**13c**, 95%); 4-$MeOC_6H_4$- (**13d**, 96%); 4-$CF_3C_6H_4$- (**13e**, 75%); 4-(9-carbazolyl)C_6H_4- (**13f**, 89%); 9,9-dihexylfluoren-2-yl (**13g**, 92%); 3-(9-carbazolyl)C_6H_4- (**13h**, 87%); 1-naphtyl (**13i**, 90%).

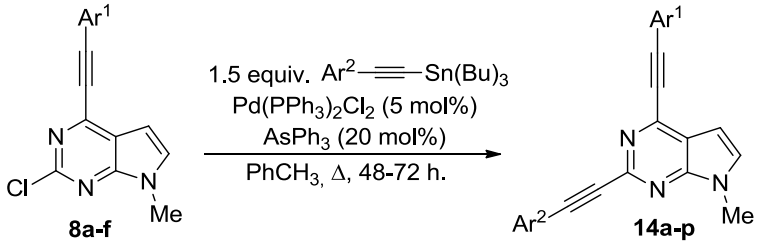
Scheme 3.7. *Reagents and conditions* i) 1.1 equiv. *n*-BuLi, THF, -78 ^oC, 45 min; ii) 1.0 equiv. $Sn(Bu)_3Cl$, -78 ^oC to rt.

At first, the comparative synthesis of compounds **8a**–**h** by Stille coupling of **3** with (arylethynyl)tributylstannanes was investigated (Table 3.7). Performing the reaction of compound **3** with a slight excess of

(phenylethynyl)tributylstannane at reflux temperature in toluene in the presence of $Pd(PPh_3)_2Cl_2$ (5 mol%) and $AsPh_3$ (20 mol%) led to the formation of product **8a** in 75% yield. However, bis(phenylethynyl)pyrrolopyrimidine **15a** (see general structure in Table 3.11) was isolated as a side product in 8% yield. Lowered catalyst loading from 5 mol% to 1 mol%, and of $AsPh_3$ to 4 mol% resulted in increased yield of **8a** (80%) and only a negligible amount of **15a** was detected. Furthermore, performing the reaction at a lower temperature (80 °C) afforded the desired product **8a** in 88% yield as the only reaction product. Using the latter conditions, [$Pd(PPh_3)_2Cl_2$ (1 mol%)/$AsPh_3$ (4 mol%), toluene, 80 °C], compound **3** was found to react with a range of (arylethynyl)tributylstannanes to give products **8a**–**h** (Table 3.7). It is noteworthy, that in most cases the Stille coupling furnished compounds **8** in higher yields when compared with those obtained by the Sonogashira protocol. The lower yield of compound **8f** (36%) can be explained by the poor stability of tributyl[(4-trifluoromethylphenyl)ethynyl]stannane (**13e**) at elevated temperatures. This stannane was observed to undergo degradation on storage at room temperature.

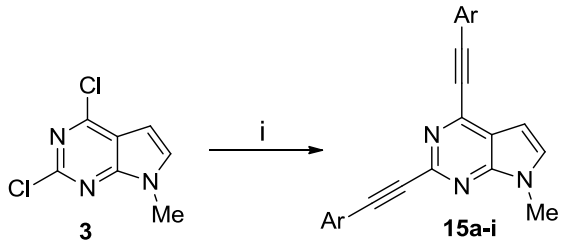
Additionally, treatment of selected 4-(arylethynyl)-2-chloropyrrolo[2,3-*d*]pyrimidines **8a-e** with (arylethynyl)tributylstannanes afforded compounds **14a**–**p** bearing different arylethynyl substituents at positions 2 and 4 of the heterocycle (Table 3.10). Displacement of the 2-chloro group with arylethynyl groups was achieved by performing the Stille coupling over a longer period of time (48–72 h) at reflux temperature in toluene, using $Pd(PPh_3)_2Cl_2$ (5 mol%) and $AsPh_3$ (20 mol%). As in previous cases, the lowest yields were obtained when tributyl[(4-trifluoromethylphenyl)ethynyl]stannane (**13e**) was used in the cross-coupling reaction (Table 3.10, entries 4, 14 and 16).

Table 3.10. Synthesis of 2,4-Bis(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**14a-p**).



Entry	Compound	Ar^1	Ar^2	Yield (%)
1	**14a**	Ph	4-FC_6H_4	80
2	**14b**	Ph	4-$MeOC_6H_4$	69
3	**14c**	Ph	4-$Me_2NC_6H_4$	46
4	**14d**	Ph	4-$CF_3C_6H_4$	25
5	**14e**	3-MeC_6H_4	Ph	68
6	**14f**	4-FC_6H_4	Ph	82
7	**14g**	4-FC_6H_4	4-$MeOC_6H_4$	79
8	**14h**	4-FC_6H_4	4-$Me_2NC_6H_4$	47
9	**14i**	4-$CF_3C_6H_4$	Ph	67
10	**14j**	4-$CF_3C_6H_4$	4-$MeOC_6H_4$	55
11	**14k**	4-$CF_3C_6H_4$	4-$Me_2NC_6H_4$	36
12	**14l**	4-$MeOC_6H_4$	Ph	81
13	**14m**	4-$MeOC_6H_4$	4-FC_6H_4	73
14	**14n**	4-$MeOC_6H_4$	4-$CF_3C_6H_4$	17
15	**14o**	4-$Me_2NC_6H_4$	4-FC_6H_4	62
16	**14p**	4-$Me_2NC_6H_4$	4-$CF_3C_6H_4$	7

Similarly, double Stille coupling of compound **3** was carried out by using 2.6 equivalents of (arylethynyl)tributylstannanes to give 2,4-bis(arylethynyl)pyrrolo[2,3-*d*]pyrimidines **15a**–**i** (Scheme 3.8, Table 3.11).



Scheme 3.8. *Reagents and conditions* i) 2.6 equiv. Ar-C≡C-$Sn(Bu)_3$, 5 mol% $Pd(PPh_3)_2Cl_2$, 20 mol% $AsPh_3$, $PhCH_3$, Δ, 48-72 h.

Table 3.11. Synthesis of 2,4-Bis(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**15a-i**).

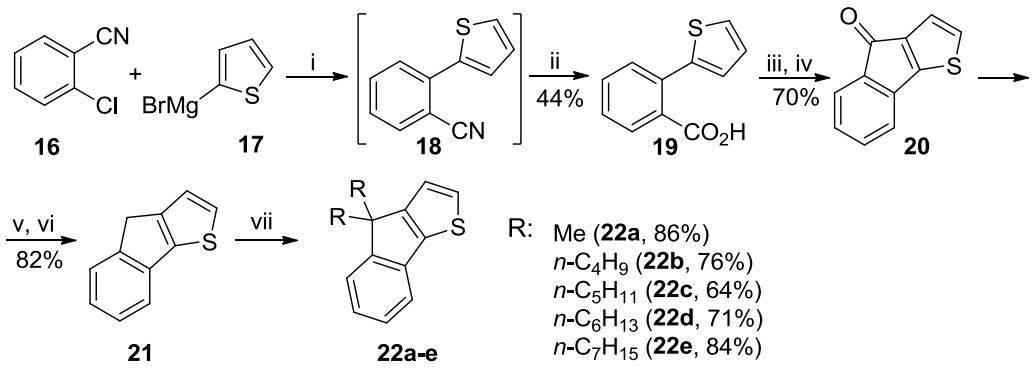
Entry	Compound	Ar	Yield (%)
1	**15a**	Ph	71
2	**15b**	3-MeC_6H_4	69
3	**15c**	4-$MeOC_6H_4$	56
4	**15d**	4-$Me_2NC_6H_4$	32
5	**15e**	4-FC_6H_4	61
6	**15f**	1-naphthyl	52
7	**15g**	4-(9-carbazolyl)C_6H_4	60
8	**15h**	3-(9-carbazolyl)C_6H_4	44
9	**15i**	9,9-dihexyl-2-fluorenyl	57

3.2.2 Synthesis of 2-(4,4-dialkyl-4*H*-indeno[1,2-*b*]thiophen-2-yl)-7-methyl-4-(arylethynyl)-7*H*-pyrrolo[2,3-*d*]pyrimidines

4*H*-Indeno[1,2-*b*]thiophene is an attractive molecule with potentially interesting properties owing to its unique structure highly reminiscent to fluorene. Compounds possessing this heterocyclic moiety were found to display a wide range of functional material properties and are useful for the construction of sensitizers for dye-sensitized solar cells [245,246], *p*-type organic semiconductors for organic thin film transistors [247,248], chromophores in luminescent materials [249], or as spacers in D-π-A [250] dyes for liquid or solid state solar cells. Taking into account all of these properties, it was decided to introduce 4*H*-indeno[1,2-*b*]thiophene moeity into position 2 of 4-(arylethynyl)pyrrolo[2,3-*d*]pyrimidines as chromophoric unit.

For the construction of 4*H*-indeno[1,2-*b*]thiophene ring system, 2-(2-thienyl)benzoic acid or the corresponding benzoates are the most often used starting materials [247,251]. These compounds, as well as their precursor, 2-(2-thienyl)benzonitrile, can be obtained by the Ullmann coupling [251], palladium-catalysed desulfitative [252,253] or Stille [254,255] reactions, or using manganese-catalysed oxidative cross coupling of the corresponding Grignard reagents [256].

Taking into account that manganese-catalysed reactions require large excess of one of the components, it was decided to establish a more economical synthetic method, suitable for the preparation of 4,4-disubstituted-4*H*-indeno[1,2-*b*]thiophenes on a multigram scale. In this connection, for the synthesis of 2-(2-thienyl)benzoic acid (**19**) it was decided to apply the Kumada-type Ni(0)-catalysed cross-coupling reaction between 2-chlorobenzonitrile (**16**) and 2-thienylmagnesium bromide (**17**) (scheme 9). Upon optimization of the reaction conditions, it was noticed that the success of the cross-coupling reaction depends on the amount of catalyst. When 2 mol% $NiCl_2(PPh_3)_2$ were used only 10% conversion of nitrile **16** to the desired product **18** was observed. Increase of catalyst loading up to 4 mol% raised the conversion to 30%, and 2-chlorobenzonitrile (**16**) was completely consumed in 8 h when 8 mol% $NiCl_2(PPh_3)_2$ was employed in the reaction. Formation of compound **18** was confirmed, and conversion of the starting material was estimated by GC/MS (*m*/*z* 185.1 $[M]^+$). Distillation of the crude product under reduced pressure gave a mixture consisting of 2-(2-thienyl)-benzonitrile (**18**) and triphenylphosphine. This mixture was used in the next step without any further purification. Hydrolysis of compound **18** with KOH in ethylene glycol furnished 2-(2-thienyl)benzoic acid (**19**) in overall two-step yield 44%.



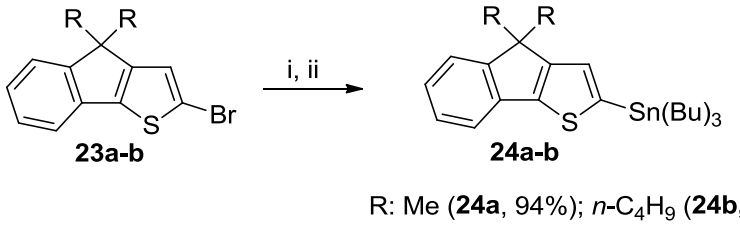
Scheme 3.9. *Reagents and conditions* i) 8 mol% $Ni(PPh_3)_2Cl_2$, 16 mol% PPh_3, 8 mol% Zn, THF, 30 ^oC; ii) KOH, H_2O, MEG, 130-140 ^oC; iii) 1.0 equiv. $SOCl_2$, DCE, Δ, 8 h; iv) 1.0 equiv. $AlCl_3$, 2.7 equiv $MeNO_2$, -18 ^oC to rt; v) 1.6 equiv N_2H_4, DEG, 110 ^oC, 3 h; vi) KOH, DEG, 110 ^oC, 4 h; vii) 3 equiv. *t*-BuOK, rt, 1 h. then 3 equiv. alkylhalogenide, 1 h.

Literature survey revealed that the synthesis of the key intermediate, 4*H*-indeno[1,2-*b*]thiophen-4-one (**20**) is explored insufficiently. To our knowledge, the only synthesis method of compound **20** from benzoic acid **19** described in the literature is transformation into the corresponding benzoyl chloride and its is subsequent cyclization with $SnCl_4$ in dry benzene [247,251]. Therefore, it was decided to investigate other well-known cyclization reactions. First, it was tried to apply the direct cyclization reactions using $POCl_3$ or PPA. However, the reaction of compound **19** with $POCl_3$ did not yield even traces of product. Heating of compound **19** with PPA at 100°C afforded 4*H*-indeno[1,2-*b*]thiophen-4-one (**20**) in low yield (18%). Further, the corresponding chloroanhydride was obtained by treating compound **19** with $SOCl_2$. Various Lewis acids were tested in intramolecular Friedel–Crafts acylation reaction. Using $FeCl_3$, $AlCl_3$, and $TiCl_4$ in dichloroethane afforded compound **20** in 36%, 46%, and 52% yields, respectively. The best result was achieved using *in situ* generated $AlCl_3$–$MeNO_2$ complex: indenothiophenone **20** was obtained in 70% yield over two steps (Scheme 3.9). Wolff–Kishner reduction of compound **20** afforded 4*H*-indeno[1,2-*b*]thiophene (**21**) in 82% yield. Methylation of compound **21** with methyl iodide using phase transfer catalyst benzyltriethylammonium chloride in the two-phase solvent system after 96 h of stirring at room temperature afforded compound **22a** in 82% yield. Alkylation of compound **21** under the same reaction conditions with alkyl halides, which had longer carbon chains, showed even longer reaction times, and 4,4-dialkyl-4*H*-indeno[1,2-*b*]thiophenes **22b**-**e** could not be separated from the monoalkylated by-products. In order to reduce the reaction time and increase yields of dialkylated compounds **22a**-**e**, the alkylation reaction using an excess of potassium *tert*-butoxide with alkyl halides was carried out (Scheme 3.9). This method produced 4,4-dialkyl-4*H*-indeno[1,2-*b*]thiophenes **22a**-**e** in good yields without any traces of monoalkylated by-products. The total reaction time was 2 h. The method seemed to work well with both alkyl bromides and alkyl iodides.

The obtained 4,4-dialkylindeno[1,2-*b*]thiophenes **22a-e** were selectively brominated at position 2 by NBS in DMF under exclusion of light to give compounds **23a-e** in high yields (Scheme 3.10).

Scheme 3.10. *Reagents and conditions* i) 1.1 equiv. NBS, DMF, 0 ^{o}C, 2 h.

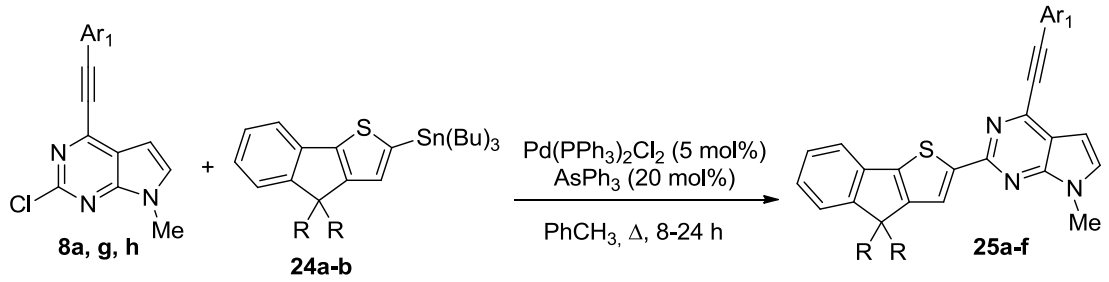
Further, two of the obtained compounds **23a-b** were selected for the synthesis of corresponding organotin derivatives. Compounds **24a-b** were prepared by treatment of cooled solutions of **23a-b** in THF with *n*-BuLi and followed by the addition of Bu_3SnCl (Scheme 3.11).



Scheme 3.11. *Reagents and conditions* i) 1.1 equiv. *n*-BuLi, THF, -78 ^{o}C, 30 min; ii) 1.0 equiv. Bu_3SnCl, -78 ^{o}C to rt.

For the introduction 4*H*-indeno[1,2-*b*]thiophene moeity into position 2 of 4-(arylethynyl)pyrrollo[2,3-*d*]pyrimidines three 4-(arylethynyl)-2-chloro-7-methylpyrrolo[2,3-*d*]pyrimidines **8a, g, h** were chosen. Stille cross-coupling reactions were carried out employing the same reaction conditions as for the synthesis of 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines. The target compounds **25a-f** were obtained in 67-88% yield (Table 3.12).

Table 3.12. Synthesis of 2-(4,4-dialkyl-4*H*-indeno[1,2-*b*]thien-2-yl)-7-methyl-4-(arylethynyl)-7*H*-pyrrolo[2,3-*d*]pyrimidines **25a-f**.



Entry	Compound	Ar^1	R	Yield, (%)
1	**25a**	Ph	Me	88
2	**25b**	4-(9-carbazolyl)C_6H_4	Me	71
3	**25c**	9,9-dihexyl-2-fluorenyl	Me	67
4	**25d**	Ph	*n*-C_4H_9	78
5	**25e**	4-(9-carbazolyl)C_6H_4	*n*-C_4H_9	80
6	**25f**	9,9-dihexyl-2-fluorenyl	*n*-C_4H_9	82

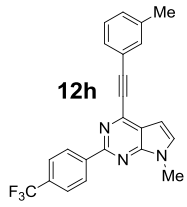
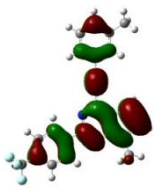
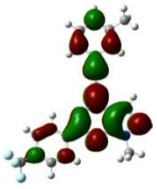
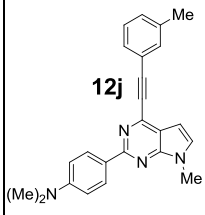
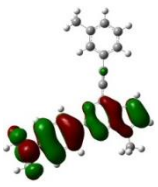
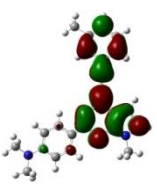
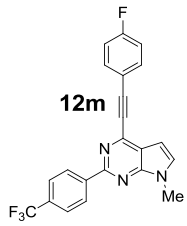
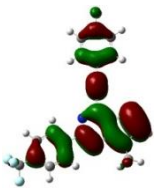
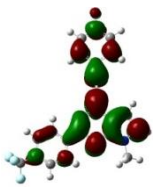
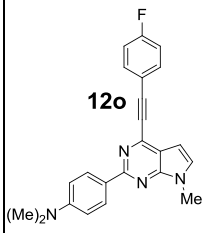
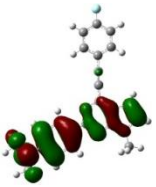
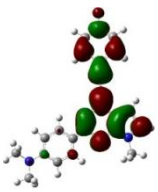
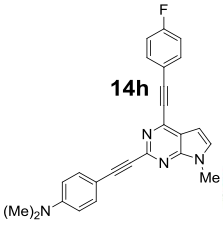
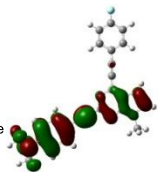
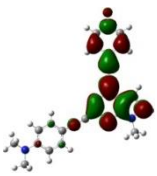
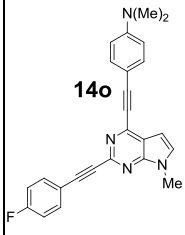
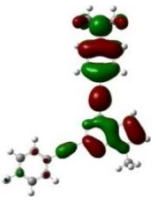
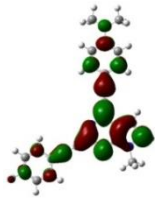
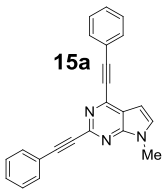
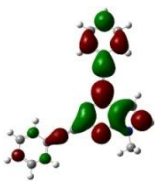
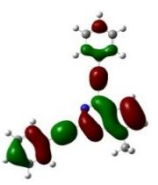
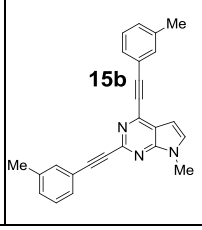
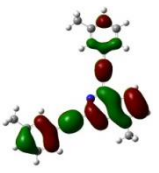
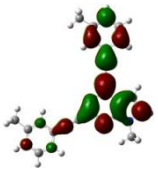
3.2.3 Quantum chemical calculations and photophysical properties of 2-aryl-4-(arylethynyl)- and 2,4-bis(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines

For further studies compounds differing by the electronic nature of the substituents and by the linker from previously synthesized 2,4-bis(4-aryl-1,2,3-triazol-1-yl)pyrrolopyrimidines were selected.

The geometries of the selected compounds **12h, 12j, 12m, 12o, 14h, 14o, 15a-i** were optimized by using the DFT/B3LYP/6-311G** level of theory. Examination of geometry of optimized structures revealed that almost all compounds exhibit coplanar geometry, with the exception of compounds **15g** and **15h**, wherein carbazole moieties are twisted out of plane of the rest of the molecule with dihedral angle of 55-58^o.

The DFT computed frontier molecular orbitals (FMO's) of the studied compounds are presented in Fig. 3.13. A comparison of FMO's localization revealed that for compounds **15a-i** LUMO is positioned on the pyrrolo[2,3-*d*]pyrimidine core with an extension to the substituents at 4th position of the heterocycle, while HOMO is localized on the pyrrolo[2,3-*d*]pyrimidine core and on the substituents at the 2nd position of the heterocycle together with a partial distribution to the moieties at the 4th position, thus reveling weak ICT

character. However, for compounds **15g** and **15h** HOMO is localized mainly on the carbazolyl and phenyl moieties at the 2nd position. Further comparison of compounds possessing different substituents at the 2nd and 4th positions, revealed that incorporation of electron-withdrawing moieties to the 2nd position of the heterocycle extends HOMO and LUMO distributions over entire molecule (see FMO's of **12h** and **12m**). The same extension of FMO's can be observed even when electron-donating moiety is incorporated at the 4th position (**14o**). Interestingly, incorporation of electron-donating moiety into the 2nd position results in positioning of HOMO on the substituents at the 2nd position and pyrrolo[2,3-*d*]pyrimidine core. LUMO is located on substituents at the 4th position with an extension to the heterocycle, thus revealing ICT enhancing capabilities by tuning electronic nature of the substituents (**12j**, **12o**, **14h**).

	HOMO	***LUMO***		***HOMO***	***LUMO***
12h 			**12j** 		
12m 			**12o** 		
14h 			**14o** 		
15a 			**15b** 		

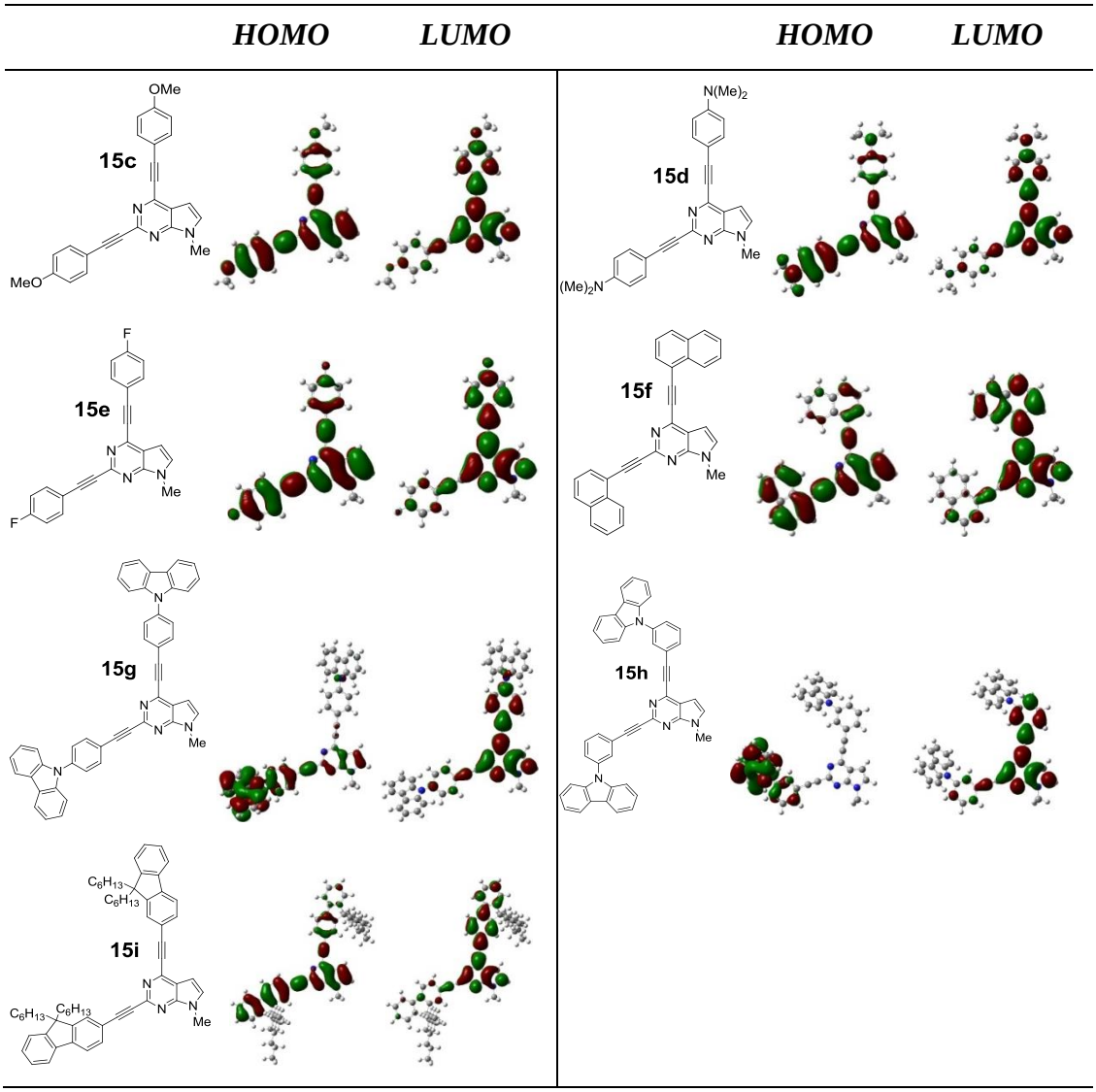


Figure 3.13. Calculated spatial distributions of FMO's for compounds **12h, 12j, 12m, 12o, 14h, 14o** and **15a-i.**

Comparison of calculated energies of FMO's revealed the influence of substituents (Table 3.13). Lower calculated values of HOMO and LUMO were obtained, when electron-withdrawing moiety is attached at the 2nd position, when compared with the FMOs energy values for compounds possessing electron-donating moieties at the 2nd position of the heterocycle (Table 3.13, entries 1-4). Comparison of FMOs energy values for isomeric compounds **14h** and **14o** revealed that higher HOMO and lower LUMO value has an isomer **14h**, which possesses electron-donating substituent at the 2nd position, thus resulting in lower band gap (Table 3.13, entries 5-6). Insignificant influence of substituents on FMOs energy values is observed for compounds **15a, 15b** and

15e (Table 3.13, entries 7, 8, 11). However, incorporation of electron donating moieties (**15c** and **15d**) results in increased values of FMO's and lower band gap (Table 3.13, entries 9-10). HOMO values for compounds possessing different bulky aromatic substituents estimated herein were found to be in the range from -5.60 eV to -5.24 eV and LUMO in the range from -2.28 eV to 1.85 eV, thus resulting into very similar band gaps ranging from 3.26 eV to 3.39 eV. E_g^{opt} was calculated from the intersection of UV/Vis and fluorescence spectra. The same variation regularities induced by electronic effects of the substituents are observed for experimentally obtained E_g^{opt} as compared with the theoretically calculated E_{gap}. Note, that the E_g^{opt} was determined in THF, in contrast to the theoretical calculations simulating vacuum conditions, thus resulting in lower E_g^{opt} values.

Table 3.13. Calculated values of FMOs, E_{gap} and E_g^{opt}.

Entry	Compound	E_{HOMO}, eV	E_{LUMO}, eV	E_{gap}, eV	E_g^{opt}, eV[a]
1	**12h**	-6.03	-2.23	3.80	3,26
2	**12j**	-5.07	-1.81	3.26	2,90
3	**12m**	-6.10	-2.30	3.80	3,24
4	**12o**	-5.11	-1.89	3.22	2,98
5	**14h**	-5.20	-1.96	3.24	2,94
6	**14o**	-5.40	-1.84	3.56	3,05
7	**15a**	-5.76	-2.07	3.69	3,24
8	**15b**	-5.69	-2.02	3.67	3,25
9	**15c**	-5.42	-1.83	3.59	3,26
10	**15d**	-4.93	-1.57	3.36	2,98
11	**15e**	-5.84	-2.16	3,68	3,28
12	**15f**	-5.60	-2.22	3,38	3,13
13	**15g**	-5.55	-2.28	3,27	3,14
14	**15h**	-5.54	-2.28	3,26	3,19
15	**15i**	-5.24	-1.85	3,39	3,16

[a]Obtained from the intersection of UV/Vis and fluorescence spectra.

Optical properties of the studied compounds **12h, 12j, 12m, 12o, 14h, 14o** and **15a-I** were assessed by performing absorption and fluorescence spectroscopy, fluorescence lifetime and fluorescence quantum yield measurements in THF solutions. Absorption and fluorescence data together with emission lifetimes (τ), radiative (τ_r) and non-radiative (τ_{nr}) decay lifetimes are collected in Table 3.14. The studied compounds exhibit strong UV

absorption in dilute solutions with their absorption maxima positioned in a region from 290 to 390 nm and emission maxima positioned in the range of 419-547 nm with quantum yields 10-49%.

Table 3.14. UV-Vis absorption and PL data for compounds **12h, 12j, 12m, 12o, 14h, 14o** and **15a-i** in10^{-5}M THF solutions.

Compd.	λ_{abs}, nm	λ_{em}, nm	Φ_F	Stokes Shift, nm	τ, ns	τ_r, ns	τ_{nr}, ns
12h	290 330	433	25	103	5.3	21.2	7.1
12j	326 368	536	12	168	7.7	64.2	8.8
12m	291 332	432	35	100	5.9	16.9	9.1
12o	326 368	537	10	169	7.3	73.0	8.1
14h	292 339	547	10	208	5.3	53.0	5.9
14o	291 329 391	476	10	85	2.2	22.0	2.4
15a	296 324	428	22	104	4	18.2	5.1
15b	297 327	424	28	97	4.7	16.8	6.5
15c	319	419	30	100	3.5	11.7	5.0
15d	290 368	485	20	117	3.4	17.0	4.2
15e	295 329	426	24	97	5.2	21.7	6.8
15f	338	437	45	99	4.7	10.4	8.5
15g	291 342	435	49	93	3.2	6.5	6.3
15h	293 325 339	437	23	98	7	30.4	9.1
15i	343	432	49	89	3.3	6.7	6.5

Comparison of compounds possessing substituents with different electronic nature (**12h** and **12j**, **12m** and **12o)** and isomeric compounds (**14h** and **14o**), indicates that incorporation of electron-donating moieties into the 2nd position of the hetereocycle results in prominent batochromic shift of emission maxima and enhanced Stokes shift up to 208 nm (**12j**, **12o**, **14h**). This can be explained by enhanced intramolecular charge transfer character of the exited

state with reference to DFT studies. However, significant increase of radiative decay lifetimes up to 4 times is observed, whilst no notable change was noticed in non-radiative decay lifetimes, thus resulting in decreased quantum yields. Compounds **12o** and **14h**, which differ only by the presence of ethynyl linker, demonstrated similar fluorescence quantum yields (10%). Moreover, emission maxima of compound **14h** is red shifted only by 10 nm compared to **12o**, thus indicating negligible influence of presence of ethynyl linker at the 2nd position.

A series of compounds **15a-i** exhibit efficient fluorescence in the range of 419-437 nm, with an exception for compound **15d** (λ_{em} = 485 nm), which possesses strong electron-donating groups. Fluorescence quantum yields of compounds possesing substituted phenyl fragments (**15a-e**) were found to be in the range of 20-30%. A noticable increase in quantum yields up to 49% was observed when well known naphtyl (**15f**), carbazolyl (**15g**) or fluorenyl (**15i**) chromophores were incorporated into the molecule. However, comparison of two isomeric compounds **15g** (Φ_F = 49%) and **15h** (Φ_F = 23%) shows that the enhancing effect of carbazolyl chromophore is diminished if carbazolyl moeity is connected to the *meta*-position of benzene ring. Moreover, fluorescence lifetime of *meta*-isomer **15h** (τ = 7.0 ns) is two times larger than that of *para*-isomer **15g** (τ = 3.2 ns). These differences can be explained by better stabilization of the excited state and weaker electronic coupling of the ground state of *meta*-isomer **15h** [257].

In summary, a comparative study of Sonogashira and Stille reactions as well as Suzuki and Stille reactions for the introduction of alkynyl and aryl moieties onto pyrrolo[2,3-*d*]pyrimidine has been carried out. The synthesis of 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines and 2,4-bis(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines bearing different substituents can be accomplished by applying two-step processes: Sonogashira – Stille or Stille – Stille. Moreover, 2,4-bis(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines bearing the same substituents can be obtained by one step Stille coupling starting from 2,4-dichloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine. $Pd(PPh_3)_2Cl_2/AsPPh_3$ has emerged as suitable catalyst system for

Stille alkynylation and arylation reactions providing the desired products in good yields. The developed protocol allows a wide library of novel 2-aryl-4-(arylethynyl)pyrrolo[2,3-*d*]pyrimidines and 2,4-bis(arylethynyl)pyrrolo[2,3-*d*]pyrimidines to be generated, including those with different arylethynyl groups in positions 2 and 4 of the heterocycle.

As demonstrated, variation in substituent electronic nature and their position in the heterocyclic system have a significant influence on the photophysical properties of these compounds. Thus, understanding the topology-properties relationship allows tuning of the desired properties by simply modifying, introducing linker or changing linkage position of the substituents.

4. EXPERIMENTAL PART

4.1 Instrumentation

Melting points were determined in open capillaries with a digital melting point IA9100 series apparatus (ThermoFischer Scientifc).

All reactions and purity of the synthesized compounds were monitored by TLC using Silica gel 60 F_{254} aluminum plates (Merck). Visualization was accomplished by UV light. Column chromatography was performed using Silica gel 60 (0.040–0.063 mm) (Merck).

Mass spectra and conversion of compounds were acquired on an Agilent 5975 GC/MS instrument with EI ionization (70 eV).

Elemental analysis was performed on a Flash 2000 Elemental Analyzer (ThermoFischer Scientific).

NMR spectra were recorded on a Bruker Ascend 400 spectrometer (400 MHz and 100 MHz for ^{1}H and ^{13}C, respectively). ^{1}H NMR and ^{13}C NMR were referenced to residual solvent peaks.

Infrared spectra (IR) were recorded on an IR spectrophotometer Spectrum BX II (Perkin Elmer).

High Resolution Mass Spectrometry (HRMS) analyses were carried out on a quadrupole, time-of-flight mass spectrometer (microTOF-Q II, Bruker Daltonik GmbH, Bremen, Germany) or on ESI TOF 6230 (Agilent Technologies) mass spectrometers.

All quantum chemical calculations were carried out using Gaussian 09 program package. Geometries were optimized at DFT/B3LYP/6-311G** level of theory. Structures for calculations of shielding values were further optimized by applying self-consistent reaction field (SCRF) under the polarizable continuum model (IEFPCM) incorporating DMSO as solvent, absolute shielding values were calculated by GIAO method. TMS was used as a reference in calculating ^{1}H and ^{13}C chemical shifts from absolute shielding values.

Electrochemical investigation was carried out using BioLogic SAS and a micro-AUTOLAB Type III potentiostat-galvanostat. The solutions of the synthesized compounds with the concentration of 1mg/1mL were used for cyclic voltammetry (CV) measurements. The experiments were calibrated with the standard ferrocene/ferrocenium redox system.

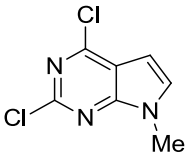
The absorption spectra were recorded on a Perkin-Elmer UV-Vis-NIR spectrophotometer Lambda 950.

Fluorescence of the sample solutions was excited by 320 nm wavelength light-emitting diode and measured using backthinned CCD spectrometer (Hamamatsu PMA-11). The fluorescence quantum yield of the solutions was estimated by comparing wavelength-integrated fluorescence intensity of the solution with that of the reference. Quinine sulfate in 0.1 M H_2SO_4 was used as a reference. Optical densities of the reference and the sample solutions were ensured to be below 0.05 to avoid reabsorption effects. Estimated quantum yield was verified by using an alternative method of an integrating sphere (Sphere Optics), which was coupled to the CCD spectrometer by an optical fiber. Fluorescence transients of the sample solutions were measured using time-correlated single photon counting system (PicoQuant PicoHarp 300). Fluorescence lifetime estimated at λ_{em}.

Single crystal X-ray data were collected on a Rikagu XtaLab mini diffractometer using graphite monochromated MoKα radiation and the data were processed with Rikagu CrystalClear, CrystalStructure and SHELXL-97 software.

4.2. Materials and methods

2,4-Dichloro-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**3**)

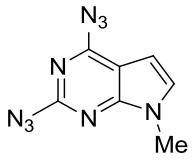


To a solution of 2,4-dichloro-7*H*-pyrrolo[2,3-*d*]pyrimidine **(2)** [212] (3.0 g, 16 mmol) in THF (30 mL) 60% NaH (0.77 g, 19.2 mmol) was added in

small portions at 0 ^{o}C. After addition was complete, the resulting mixture was stirred at 0 ^{o}C for 30 min. followed by addition of MeI (1.3 mL, 20.8 mmol). The mixture was stirred at room temperature overnight and poured into brine (70 mL), extracted with $CHCl_3$ (3x50mL). Organic phase was dried with Na_2SO_4 and filtered. Solvent was evaporated under reduced pressure to yield crude residue, which was purified by silica gel chromatography (eluent $CHCl_3$) to give 2.9 g (90%) of compound **3**. White solid, mp 151-152 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (3H, s, NCH_3), 6.62 (1H, d, *J* = 3.6 Hz, 5-H), 7.21 (1H, d, *J* = 3.6 Hz, 6-H). ^{13}C NMR (400 MHz, $CDCl_3$): δ = 31.8, 99.9, 116.3, 130.8, 151.9, 152.2, 152.6.

Lit. [258]: yield 84%, mp 151 ^{o}C.

2,4-Diazido-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**4**)



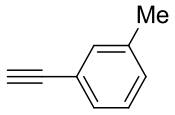
A mixture of compound **3** (1.0 g, 4.95 mmol) and NaN_3 (0.708 g, 10.89 mmol) in DMF (35 mL) was stirred at room temperature for 24 h. Then the reaction mixture was poured into water (100 mL). Precipitate was filtered off, washed with MeOH (10 mL), dried at room temperature and stored in a vessel protected from sunlight. Product was obtained as white solid (0.83 g, 78%), mp 118–119 ^{o}C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.80 (3H, s, NCH_3), 6.51 (1H, d, *J* = 3.6 Hz, 5-H), 7.00 (1H, d, *J* = 3.6 Hz, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.6, 99.0, 105.7, 128.5, 153.6, 155.13, 155.14; IR (KBr): 2152 cm^{-1} (N_3), 2115 cm^{-1} (N_3); HRMS (ESI): calculated for $C_7H_5N_9Na$ $[M + Na]^+$ = 238.0560, found 238.0560.

General procedure for the synthesis of ethynylarenes **5a, 5c, 5e, 5h-m.**

A mixture of the corresponding arylbromide, 2-methylbut-3-yn-2-ol (1.3 equiv.), $Pd(PPh_3)_2Cl_2$, (2 mol%), PPh_3 (4 mol%), CuI (4 mol%), NEt_3 (2 equiv.) in THF (50-100 mL) was refluxed under argon for 8 h. Then the reaction mixture was poured into water and extracted with CH_2Cl_2. Organic

layer was dried with Na_2SO_4 and filtered. Solvent was evaporated under reduced pressure to yield yellow oil, which was dissolved in toluene and powdered KOH (0.6 equiv.) was added. The obtained mixture was stirred at 80-100 ^oC for 6-16 h. The reaction mixture was cooled to rt., poured into water and extracted with toluene. Solvent was evaporated under reduced pressure to yield crude product, which was purified by silica gel chromatography or recrystallization.

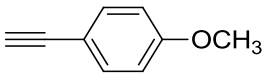
1-Ethynyl-3-methylbenzene (**5a**)



Compound **5a** was synthesized from 3-bromotoluene (8.5 g, 0.05 mol) and purified by silica gel column chromatography, eluent – hexane. Yield 4.1 g (71%). Yellow liquid; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.38 (3H, s, CH_3), 3.10 (1H, s, C≡C-H), 7.21 (1H, d, *J* = 7.6 Hz, 4-H), 7.26 (1H, t, *J* = 7.6 Hz. 5-H), 7.36 (1H, d, *J* = 7.6 Hz, 6-H), 7.38 (1H, s, 2-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 76.8, 83.9, 121.9, 128.2, 129.2, 129.7, 132.7, 138.0.

Lit. [259]: yield 72%.

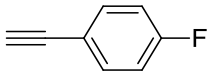
1-Ethynyl-4-methoxybenzene (**5c**)



Compound **5c** was synthesized from 1-bromo-4-methoxybenzene (7.5 g, 0.04 mol) and purified by silica gel column chromatography, eluent – hexane. Yield 4.0g (75%). Yellow liquid; ^1H NMR (400 MHz, $CDCl_3$): δ = 3.03 (1H, s, C≡C-H), 3.83 (3H, s, OCH_3), 6.86 (2H, d, *J* = 8.4 Hz, 3,5-H), 7.46 (2H, d, *J* = 8.4 Hz, 2,6-H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2, 75.8, 83.6, 113.9, 114.1, 133.6, 159.9.

Lit. [260]: yield 96%.

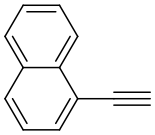
1-Ethynyl-4-fluorobenzene (**5e**)



Compound **5e** was synthesized from 1-bromo-4-fluorobenzene (7.0 g, 0.04 mol) and purified by silica gel column chromatography, eluent – hexane. Yield 3.4 g (70%). Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.07 (1H, s, C≡C-H), 7.04 (2H, dd, ^{3}J = 8.8 Hz, $^{3}J_{H\text{-}F}$ = 8.4 Hz, 3,5-H), 7.50 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H\text{-}F}$ = 5.2 Hz, 2,6-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 76.9, 82.6, 115.6 (d, $^{2}J_{C\text{-}F}$ = 22 Hz), 118.2 (d, $^{4}J_{C\text{-}F}$ = 3 Hz), 134.1 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 162.8 (d, $^{1}J_{C\text{-}F}$ = 248 Hz).

Lit. [261]: yield 79%.

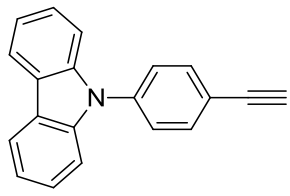
1-Ethynylnaphthalene (**5h**)



Compound **5h** was synthesized from 1-bromonaphtalene (6.2 g, 0.03 mol) and purified by silica gel column chromatography, eluent – hexane. Yield 2.8 g (61%). Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): 3.55 (1H, s, C≡C-H); 7.47 (1H, t, *J* = 7.6 Hz, 3-H); 7.58-7.65 (2H, m, 6,7-H); 7.81 (1H, d, *J* = 7.2 Hz, 2-H); 7.90 (2H, d, *J* = 8.0 Hz, 4,5-H); 8.44 (1H, d, *J* = 8.0 Hz, 8-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 81.8, 82.0, 119.8, 125.1, 126.1, 126.5, 127.0, 128.3, 129.3, 131.2, 133.1, 133.5.

Lit. [224]: yield 73%.

9-(4-Ethynylphenyl)-9H-carbazole (**5i**)

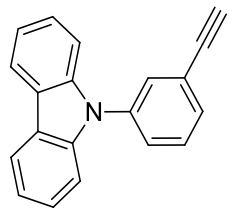


Compound **5i** was synthesized from 9-(4-bromophenyl)-9*H*-carbazole (6.4 g, 0.02 mol) and purified by recrystallization from 2-PrOH. Yield 3.4 g (64%). White solid, mp 103-105 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.22

(1H, s, C≡C-H), 7.29-7.32 (2H, m, 3,6-H), 7.34-7.46 (4H, m, 1,2,7,8-H), 7.59 (2H, d, *J* = 8.0 Hz, ArH), 7.77 (2H, d, *J* = 8.0 Hz, ArH), 8.18 (2H, d, *J* = 7.6 Hz, 4,5-H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 78.3, 83.1, 109.9, 120.5, 120.6, 121.0, 123.8, 126.3, 127.0, 133.9, 138.4, 140.7.

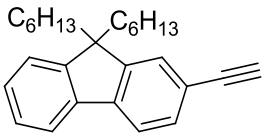
Lit. [262]: yield 81%, mp 102-103 ^{o}C.

9-(3-Ethynylphenyl)-9H-carbazole (**5j**)



Compound **5j** was synthesized from 9-(3-bromophenyl)-9*H*-carbazole (6.4 g, 0.02 mol) and purified by recrystallization from hexane. Yield 3.6 g (68%). Off-white solid, mp 67-70 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.20 (1H, s, C≡C-H), 7.33 (2H, ddd, ^{3}J = 7.6 Hz, ^{3}J = 5.6 Hz, ^{4}J = 0.8 Hz, 3,6-H), 7.42-7.48 (4H, m, 1,2,7,8-H), 7.58-7.64 (3H, m, ArH), 7.75 (1H, s, ArH), 8.18 (2H, d, *J* = 7.6 Hz, 4,5-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 78.5, 82.6, 109.6, 120.2, 120.3, 123.5, 124.0, 126.0, 127.7, 129.9, 130.6, 131.1, 137.9, 140.6. HRMS (ESI): calculated for $C_{20}H_{14}N$ $[M+H]^{+}$ = 268.1120; found: 268.1121.

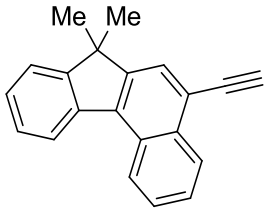
2-Ethynyl-9,9-dihexyl-9H-fluorene (**5k**)



Compound **5k** was synthesized from 2-bromo-9,9-dihexyl-9*H*-fluorene (6.2 g, 0.015 mol) and purified by silica gel column chromatography, eluent – hexane. Yield 3.7 g (70%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57-0.65 (4H, m, 2xCH_2), 0.79 (6H, t, *J* = 7.2 Hz, 2xCH_3), 1.02-1.16 (12H, m, 6xCH_2), 1.95-1.99 (4H, m, 2xCH_2), 3.16 (1H, s, C≡C-H), 7.33-7.38 (3H, m, 6,7,8-H), 7.49-7.52 (2H, m, 3,4-H), 7.66-7.72 (2H, m, 1,5-H). ^{13}C NMR (100

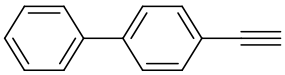
MHz, $CDCl_3$): δ = 13.9, 22.5, 23.6, 29.7, 31.5, 40.3, 55.1, 76.9, 84.7, 119.5, 120.0, 120.1, 122.9, 126.5, 126.8, 127.6, 131.1, 140.2, 141.94, 150.7, 151.0.
Lit. [263]: yield 87%.

5-Ethynyl-7,7-dimethyl-7H-benzo[c]fluorene (**5l**)



Compound **5l** was synthesized from 5-bromo-7,7-dimethyl-7*H*-benzo[*c*]fluorene (4.8 g, 0.015 mol) and purified by recrystallization from hexane. Yield 1.2 g (29%). Yellow solid, mp 121-124 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.59 (6H, s, 2xCH_3), 3.60 (1H, s, C≡C-H), 7.43 (1H, td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, H-2), 7.50 (1H, td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, H-3), 7.58 (1H, dd, *J* = 7.6 Hz, *J* = 0.8 Hz, H-8), 7.64-7.74 (2H, m, H-9, H-10), 7.94 (1H, s, H-6), 8.39 (1H, d, *J* = 7.6 Hz, H-1), 8.56 (1H, dd, ^3J = 8.4 Hz, ^4J = 1.2, H-11), 8.83 (1H, d, *J* = 7.6 Hz, H-4). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.6, 46.6, 82.3, 82.6, 119.3, 122.6, 123.4, 124.2, 126.1, 126.3, 127.0, 127.1, 127.31, 127.38, 129.4, 133.7, 134.8, 139.6, 151.3, 155.0. HRMS (ESI): calculated for $C_{21}H_{17}$ $[M+H]^+$ = 269.1325; found: 269.1328.

4-Ethynylbiphenyl (**5m**)



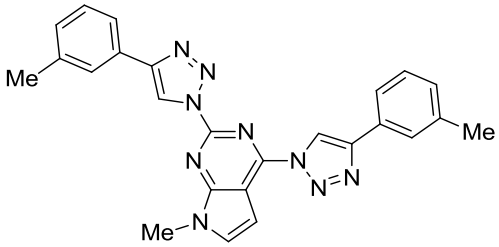
Compound **5m** was synthesized from 4-bromobiphenyl (9.3 g, 0.04 mol) and purified by recrystallization from 2-PrOH. Yield 5.5 g (78%). White solid, mp 86-88 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = δ 3.13 (s, 1H, C≡C-H), 7.36 (1H, t, *J* = 7.2 Hz, 4'-H), 7.45 (2H, t, *J* = 7.2 Hz, 3',5'-H), 7.56 (4H, m, 2,6,2',6'-H), 7.58 (2H, d, *J* = 7.6 Hz, 3,5-H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 77.7, 83.5, 120.9, 127.0, 127.7, 128.8, 130.6, 132.5, 140.2, 141.5.

Lit. [264]: yield 89%, mp 86-87 ^{o}C.

***General procedure for the synthesis of compounds* 6a-l, 7i.**

A mixture of compound 2,4-diazido-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**4**) (100 mg, 0.46 mmol), corresponding alkyne (1.4 mmol), CuI (17 mg, 0.09 mmol), DIPEA (89 µL, 0.51 mmol) and acetic acid (29 µL, 0.51 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature. End of the reaction was determined by TLC. Then the reaction mixture was poured into water (20 mL) and extracted with CH_2Cl_2 (3x10 mL). The extracts were combined, dried over Na_2SO_4 and filtered. After removal of the solvent the residue was purified by silica gel column chromatography (eluent - hexane/EtOAc) to give a crude isomeric mixture. Further purification was performed by recrystallization from 2-PrOH or toluene.

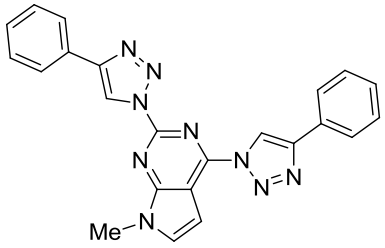
***7-Methyl-2,4-bis[4-(m-tolyl)-1H-1,2,3-triazol-1-yl]-7H-pyrrolo[2,3-d]-pyrimidine* (6a)**



Compound **6a** was purified by silica gel column chromatography (eluent hexane/EtOAc (1:5)) and recrystallized from 2-PrOH. Yield 94 mg (46%); white solid mp 220 ^{o}C dec. (from 2-PrOH); λ_{max} ($CHCl_3$)/nm 255 and 309 (ε/dm^{-3}mol^{-1}cm^{-1} 15104 and 8320). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.49 (6H, s, 2xCH_3), 4.07 (3H, s, NCH_3), 7.22-7.30 (2H, m, ArH), 7.40-7.48 (3H, m, ArH, 5-H), 7.49 (1H, d, *J* = 3.6 Hz, 6-H), 7.84 (2H, t, *J* = 8.8 Hz, ArH) 7.90 (2H, s, ArH), 8.91 (1H, s, triazole-H), 9.14 (1H, s, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (2 peaks overlapped), 31.9, 103.2, 106.9, 117.5, 118.3, 123.11, 123.16, 126.6, 126.7, 128.7, 128.9, 129.34, 129.36 129.6, 129.8, 132.3, 138.6, 138.7,

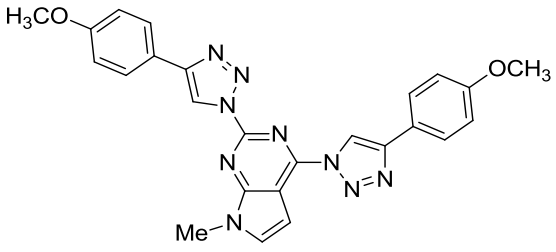
147.1, 147.6, 147.7, 147.9, 154.1. HRMS (ESI): calculated for $C_{25}H_{21}N_9Na$ $[M+Na]^+$ = 470.1812; found: 470.1824.

7-Methyl-2,4-bis(4-phenyl-1H-1,2,3-triazol-1-yl)-7H-pyrrolo[2,3-d]-pyrimidine (**6b**)



Compound **6b** was purified by silica gel column chromatography (eluent hexane/EtOAc (1:5)) and recrystallized from 2-PrOH. Yield 92 mg (48%); white solid, mp 237 ^oC dec. (from 2-PrOH); λ_{max} ($CHCl_3$)/nm 264 and 311 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 8784 and 7798). ^1H NMR (400 MHz, $CDCl_3$): δ = 4.07 (3H, s, NCH_3), 7.42-7.47 (3H, m, ArH, 5-H), 7.49 (1H, d, *J* = 3.6 Hz, 6-H), 7.51-7.56 (4H, m, ArH), 8.04-8.07 (4H, m, ArH), 8.93 (1H, s, triazole-H), 9.14 (1H, s, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.0, 103.4, 107.4, 117.7, 118.5, 126.11, 126.14, 128.6, 128.91, 128.94, 129.1, 129.6, 130.1, 132.5, 147.4, 147.8, 147.9, 148.0, 154.3. HRMS (ESI): calculated for $C_{23}H_{17}N_9$ $[M+H]^+$ = 420.1680; found: 420.1694.

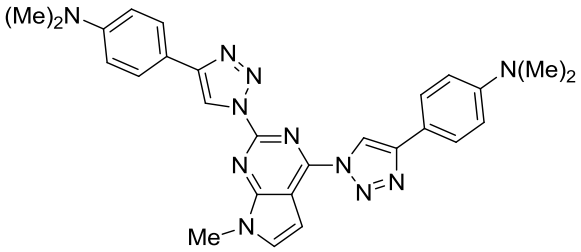
2,4-Bis[4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**6c**)



Compound **6c** was purified by silica gel column chromatography (eluent EtOAc) and recrystallized from toluene. Yield 128 mg (58%); yellow solid; mp 247 ^oC dec.; λ_{max} ($CHCl_3$)/nm 268 and 318 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 7060 and 5585). ^1H NMR (400 MHz, $CDCl_3$): δ = 3.91 (3H, s,

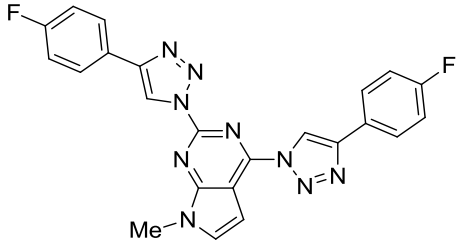
OCH_3), 3.92, (3H, s, OCH_3), 4.06 (3H, s, NCH_3), 7.06 (2H, d, *J* = 8.8 Hz, ArH), 7.07 (2H, d, *J* = 8.8 Hz, ArH), 7.42 (1H, d, *J* = 3.6 Hz, 5-H), 7.48 (1H, d, *J* = 3.6 Hz, 6-H), 7.97 (2H, d, *J* = 8.8 Hz, ArH), 7.99 (2H, d, *J* = 8.8 Hz, ArH), 8.84 (1H, s, triazole-H), 9.07 (1H, s, triazole-H). ^{13}C NMR (100 MHz, d_6-DMSO, 80^{o}C): δ = 32.1, 55.8 (2 peaks overlapped), 102.0, 106.8, 114.9, 115.0, 118.6, 119.8, 122.6, 123.1, 127.5, 127.7, 134.6, 146.9, 147.31, 147.8, 147.64, 154.5, 160.1, 160.3. HRMS (ESI): calculated for $C_{25}H_{22}N_9O_2$ $[M+H]^+$ = 480.1891; found: 480.1905.

2,4-Bis[4-(4-dimethylaminophenyl)-1H-1,2,3-triazol-1-y]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**6d**)



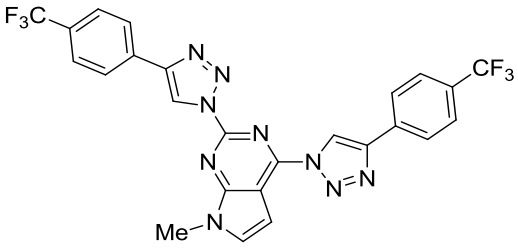
Compound **6d** was purified by silica gel column chromatography (eluent hexane/EtOAc (1:4)) and recrystallized from toluene. Yield 81 mg (35%); yellow solid; mp 225 ^{o}C dec.; λ_{max} ($CHCl_3$)/nm 308 and 365 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 14827 and 6182). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.03 (6H, s, $N(CH_3)_2$), 3.05 (6H, s, $N(CH_3)_2$), 4.02 (3H, s, NCH_3), 6.81 (2H, d, *J* = 8.8 Hz, ArH), 6.84 (2H, d, *J* = 8.8 Hz, ArH), 7.35 (1H, d, *J* = 3.2 Hz, 5-H), 7.43 (1H, d, *J* = 3.2 Hz, 6-H), 7.87 (2H, d, *J* = 8.8 Hz, ArH), 7.90 (2H, d, *J* = 8.8 Hz, ArH), 8.72 (1H, s, triazole-H), 8.94 (1H, s, triazole-H). ^{13}C NMR (100 MHz, d_6-DMSO, 80^{o}C): δ = 31.8, 40.41, 40.43, 103.4, 106.9, 112.3, 112.4, 115.7, 116.7, 117.5, 118.1, 127.0, 127.1, 132.0, 147.4, 147.9, 148.1, 148.3, 150.6, 150.7, 154.1. HRMS (ESI): calculated for $C_{27}H_{28}N_{11}$ $[M+H]^+$ = 506.2524; found: 506.2536.

2,4-Bis[4-(4-fluorophenyl)-1H-1,2,3-triazol-1-y])-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**6e**)



Compound **6e** was purified by silica gel column chromatography (eluent hexane/EtOAc (1:1)) and recrystallized from 2-PrOH. Yield 127 mg (61%); white solid; mp 232 ^{o}C dec.; λ_{max} ($CHCl_3$)/nm 249 and 312 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 19602 and 7777). ^{1}H NMR (400 MHZ, $CDCl_3$): δ = 4.02 (3H, s, NCH_3), 7.17-7.23 (4H, m, ArH), 7.38 (1H, d, *J* = 3.6 Hz, 5-H), 7.41 (1H, d, *J* = 3.6 Hz, 6-H), 7.96-8.01 (4H, m, ArH), 8.82 (1H, s, triazole-H)), 9.04 (1H, s, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.9, 103.9, 107.0, 115.9 (d, $^{2}J_{C\text{-}F}$ = 21Hz), 116.1 (d, $^{2}J_{C\text{-}F}$ = 21Hz), 117.4, 118.1, 125.7 (d, $^{4}J_{C\text{-}F}$ = 4Hz), 126.2 (d, $^{4}J_{C\text{-}F}$ = 4Hz), 127.8 (d, $^{3}J_{C\text{-}F}$ = 8Hz), 127.9 (d, $^{3}J_{C\text{-}F}$ = 8Hz), 132.5, 146.8, 147.10, 147.16, 147.6, 154.1, 162.9 (d, $^{1}J_{C\text{-}F}$ = 247Hz), 163.1 (d, $^{1}J_{C\text{-}F}$ = 247Hz). HRMS (ESI): calculated for $C_{23}H_{15}F_2N_9Na$ $[M+Na]^+$ = 478.1311; found: 478.1321.

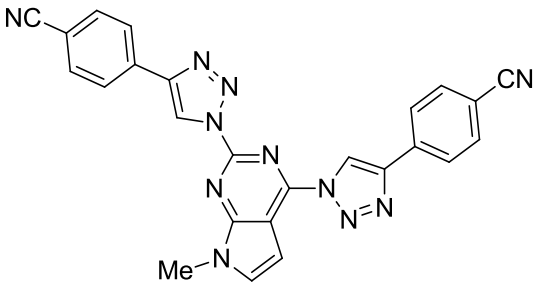
7-Methyl-2,4-bis[4-(4-trifluoromethylphenyl)-1H-1,2,3-triazol-1-yl]-7H-pyrrolo[2,3-d]pyrimidine (**6f**)



Compound **6f** was filtered from the reaction mixture and washed with CH_2Cl_2 and water. Yield 201 mg (79%); yellow solid; mp 228 ^{o}C dec.; λ_{max} ($CHCl_3$)/nm (ε/$dm^{-3}mol^{-1}cm^{-1}$ 19761 and 8730). ^{1}H NMR (400 MHz, $CDCl_3$): 4.09 (3H, s, NCH_3), 7.47 (1H, d, *J* = 3.6 Hz, 5-H), 7.50 (1H, d, *J* = 3.6 Hz, 6-H), 7.78-7.81 (4H, m, ArH), 8.17 (2H, d, *J* = 8.0 Hz, ArH)

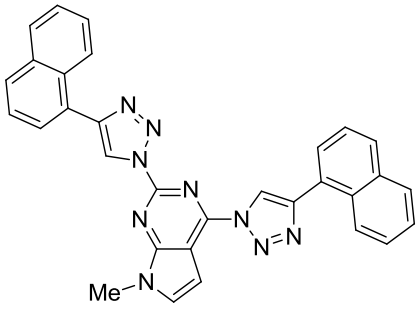
8.19 (2H, d, *J* = 8.0 Hz, ArH), 9.01 (1H, s, triazole-H), 9.26 (1H, s, triazole-H). ^{13}C NMR could not be obtained because of very low solubility in common deuterated solvents. HRMS (ESI): calculated for $C_{25}H_{15}F_6N_9Na$ $[M+Na]^+$ = 578.1247; found: 578.1248.

7-Methyl-2,4-bis[4-(4-cianophenyl)-1H-1,2,3-triazol-1-yl]-7H-pyrrolo[2,3-d]pyrimidine (**6g**)



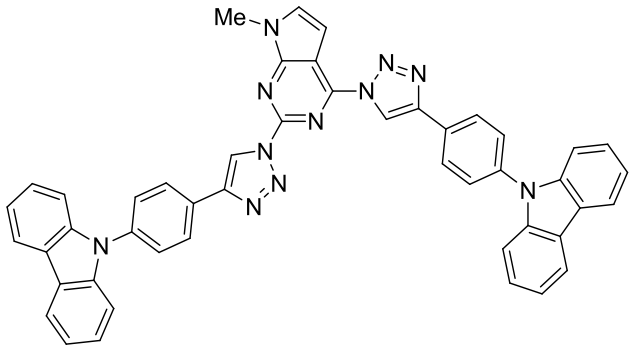
Compound **6g** was purified by silica gel column chromatography (eluent EtOAc) and recrystallized from DMF. Yield 162 mg (75%); white solid; mp 274 ^{o}C dec.; λ_{max} ($CHCl_3$)/nm 277 and 311 (ε/dm^{-3}mol^{-1}cm^{-1} 20300 and 10716). ^{1}H NMR (400 MHz, d_6-DMSO, 80^{o}C): δ = 4.01 (3H, s, NCH_3), 7.23 (1H, d, *J* = 3.2 Hz, 5-H), 7.86 (1H, d, *J* = 3.2 Hz, 6-H), 7.95 (4H, d, *J* = 6.8 Hz, ArH), 8.20-8.27 (4H, m, ArH), 9.62 (1H, s, triazole-H), 9.73 (1H, s, triazole-H). ^{13}C NMR (100 MHz, d_6-DMSO, 80^{o}C): δ = 32.0, 102.0, 107.3, 111.4, 111.8, 118.90, 118.96, 121.3, 122.3, 126.8, 127.0, 133.33, 133.36, 134.5, 135.0, 135.1, 145.8, 145.9, 146.7, 147.4, 154.6. HRMS (ESI): calculated for $C_{25}H_{15}N_{11}Na$ $[M+Na]^+$ = 492.1404; found: 492.1411.

7-Methyl-2,4-bis[4-(naphth-1-yl)-1H-1,2,3-triazol-1-yl]-7H-pyrrolo[2,3-d]-pyrimidine (**6h**)



Compound **6h** was purified by silica gel column chromatography (eluent hexane/EtOAc (1:2)) and recrystallized from 2-PrOH. Yield 90 mg (38%); yellow solid; mp 216 ^{o}C dec.; λ_{max} ($CHCl_3$)/nm 245 and 298 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 16158 and 12867). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.07 (3H, s, NCH_3), 7.44 (1H, d, *J* = 3.6 Hz, 5-H), 7.54 (1H, d, *J* = 3.6 Hz, 6-H), 7.55-7.61 (6H, m, ArH), 7.86-7.97 (6H, m, ArH), 8.49-8.54 (2H, m, ArH), 8.96 (1H, s, triazole-H), 9.19 (1H, s, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.0, 103.4, 107.1, 120.7, 121.6, 125.33, 125.37,125.38, 125.4, 126.1, 126.2, 126.82, 126.97, 126.98, 127.4, 127.5, 127.6, 128.50, 128.56, 129.3, 129.5, 131.09, 131.2, 132.6, 133.92, 133.94, 147.22, 147.27, 147.3, 147.8, 154.33. HRMS (ESI): calculated for $C_{31}H_{22}N_9$ $[M+H]^+$ = 520.1993; found: 520.2005.

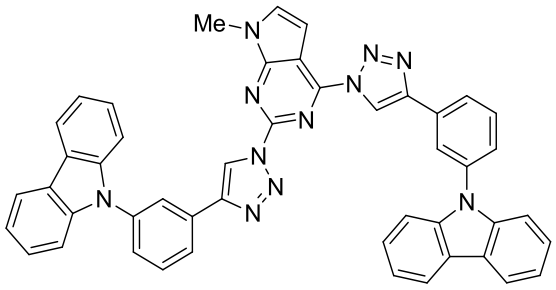
7-Methyl-2,4-bis{4-[4-(9-carbazolyl)phenyl]-1H-1,2,3-triazol-1-yl}-7H-pyrrolo[2,3-d]pyrimidine (**6i**)



Compound **6i** was purified by silica gel column chromatography (eluent EtOAc) and recrystallized from 2-toluene. Yield 182 mg (53%);

yellow solid, mp 268 ^{o}C dec.; λ_{max} ($CHCl_3$)/nm 247, 293, 313, 329 and 341 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 42093, 25031, 17628, 17233 and 16471). ^{1}H NMR (400 MHz, d_6-DMSO): δ = 4.04 (3H, s, NCH_3), 7.29-7.34 (5H, m, 5-H, carbazole-H), 7.45-7.52 (8H, m, ArH, carbazole-H), 7.86 (4H, t, *J* = 8.0 Hz, carbazole-H), 7.97 (1H, d, *J* = 3.6 Hz, 6-H), 8.28 (4H, d, *J* = 7.6 Hz, ArH), 8.38-8.43 (4H, m, carbazole-H), 9.87 (1H, s, triazole-H), 9.99 (1H, s, triazole-H). ^{13}C NMR = (100 MHz, $CDCl_3$): δ = 32.0, 103.4, 107.3, 109.7, 109.8, 117.9, 118.7, 120.15, 120.19, 120.41, 120.42, 123.53, 123.56, 123.61, 126.06, 126.08, 127.54, 127.59, 127.6, 128.6, 129.1, 132.7, 138.0, 138.2, 140.6, 140.7, 147.1, 147.3, 147.4, 147.7, 154.3. HRMS (ESI): calculated for $C_{47}H_{31}N_{11}Na$ $[M+Na]^+$ = 772.2656; found: 772.2659.

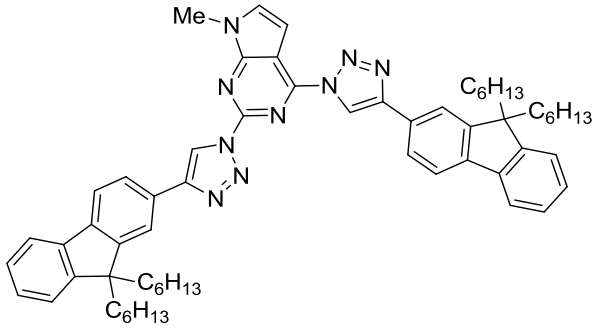
7-Methyl-2,4-bis{4-[3-(9-carbazolyl)phenyl]-1H-1,2,3-triazol-1-yl}-7H-pyrrolo[2,3-d]pyrimidine (**6j**)



Compound **6j** was purified by silica gel column chromatography, eluent hexane/EtOAc (1:3) and recrystallized from 2-toluene. Yield 148 mg (43%); white solid, mp 234 ^{o}C dec.; λ_{max} ($CHCl_3$)/nm 253, 293, 314, 326 and 340 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 35488, 26491, 12013, 11255 and 10549). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.98 (3H, s, NCH_3), 7.25-7.28 (5H, m, 5-H, carbazole-H), 7.36-7.46 (10H, m, carbazole-H, ArH), 7.54 (1H, d, *J* = 8.0 Hz, carbazole-H), 7.58 (1H, d, *J* = 8.0 Hz, carbazole-H), 7.68 (1H, d, *J* = 8.0 Hz, carbazole-H), 7.72 (1H, , *J* = 8.0 Hz, carbazole-H), 8.08-8.14 (6H, m, ArH, 6-H, carbazole-H), 8.23 (1H, s, ArH), 8.88 (1H, s, triazole-H); 9.12 (1H, s, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =

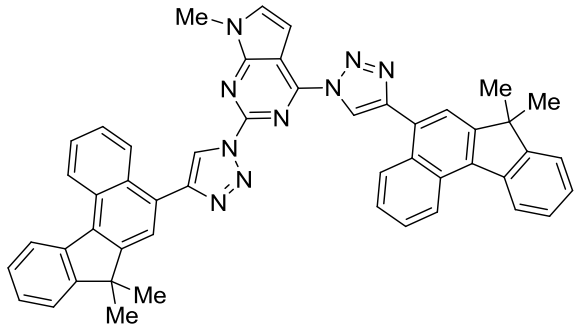
31.9, 103.3, 107.1, 109.72, 109.74, 118.2, 119.0, 120.02, 120.07, 120.24, 120.25, 123.3, 123.4, 124.57, 124.58, 124.9, 125.0, 125.9, 126.0, 127.1, 127.3, 130.5, 130.6, 131.5, 132.0, 132.5, 138.3, 138.5, 140.7, 140.8, 146.84, 146.89, 147.0, 147.3, 154.1. HRMS (ESI): calculated for $C_{47}H_{31}N_{11}Na$ $[M+Na]^+$ = 772.2656; found 772.2653.

7-Methyl-2,4-bis[4-(9,9-dihexylfluoren-2-yl)-1H-1,2,3-triazol-1-yl]-7H-pyrrolo[2,3-d]pyrimidine (**6k**)



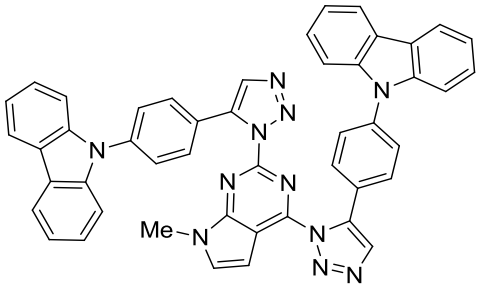
Compound **6k** was purified by silica gel column chromatography, eluent hexane/EtOAc (3:1) and recrystallized from 2-PrOH. Yield 240 mg (56%). Yellow solid, mp 102-104 ^oC; λ_{max} ($CHCl_3$)/nm 245, 293 and 319 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 13769, 23487 and 26245). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.67-0.79 (20H, m, $4CH_2CH_3$), 1.06-1.16 [24H, m, $4(CH_2)_3$], 2.02-2.16 (8H, m, $4CH_2$), 4.10 (3H, s, NCH_3), 7.34-7.41 (6H, m, ArH), 7.44 (1H, d, *J* = 3.6 Hz, 5-H), 7.52 (1H, d, *J* = 3.6 Hz, 6-H), 7.77 (2H, d, *J* = 7.2 Hz, ArH); 7.85 (2H, t, *J* = 8.0 Hz, ArH), 7.99-8.08 (4H, m, ArH). 9.00 (1H, s, triazole-H), 9.24 (1H, s, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (2 signals overlapped), 22.6 (2 signals overlapped), 23.8 (2 signals overlapped), 29.7 (2 signals overlapped), 31.5, 40.4 (2 signals overlapped), 40.5 (2 signals overlapped), 55.3 (2 signals overlapped), 103.4, 107.2, 117.5, 118.4, 119.8, 119.9, 120.1, 120.2, 120.42, 120.48, 122.9, 124.94, 124.95, 126.85, 126.86, 127.3, 127.4, 128.1, 128.6, 132.4, 140.5, 140.6, 141.7, 142.0, 147.4, 147.9, 148.2, 148.4, 148.6, 151.01, 151.07, 151.62, 152.67, 154.28. HRMS (ESI): calculated for $C_{61}H_{74}N_9$ [M+H] = 932.6062; found 932.6056

7-Methyl-2,4-bis[4-(7,7-dimethylbenzo[c]fluoren-5-yl)-1H-1,2,3-triazol-1-yl]-7H-pyrrolo[2,3-d]pyrimidine **(6l)**



Compound **6l** was purified by silica gel column chromatography, eluent hexane/EtOAc (1:1) and recrystallized from toluene. Yield 207 mg (60%). Yellow solid, mp 220 ^{o}C dec.; λ_{max} ($CHCl_3$)/nm 246, 334 and 348 (ε/$dm^{-3}mol^{-1}cm^{-1}$ 39131, 20724 and 25790). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.64 (6H, s, $2CH_3$), 1.65 (6H, s, $2CH_3$), 4.07 (3H, s, NCH_3), 7.40-7.75 (12H, m, ArH, 5-H, 6-H), 8.01 (1H, s, ArH), 8.06 (1H, s, ArH), 8.36-8.42 (2H, m, ArH), 8.54 (1H, d, *J* = 8.4 Hz, ArH), 8.61 (1H, d, *J* = 8.4 Hz, ArH), 8.84-8.90 (2H, m, ArH), 8.99 (1H, s, triazole-H), 9.25 (1H, s, triazole-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 26.7 (2 signals overlapped), 31.9, 46.9 (2 signals overlapped), 103.4, 107.1, 120.9, 121.9, 122.5, 122.6, 122.8, 122.9, 123.3, 123.4, 124.2, 124.3, 125.8, 126.0, 126.5, 126.6, 126.74, 126.79, 126.81, 126.85, 126.87, 127.23, 127.26, 127.3, 130.0, 130.1, 131.2, 131.4, 132.6, 134.3, 134.7, 139.7, 139.8, 147.3, 147.5, 147.7, 151.6, 151.7, 154.25, 154.27, 154.9, 155.0. HRMS (ESI): calculated for $C_{49}H_{38}N_9$ $[M+H]^+$ = 752.3245; found 752.3252.

***7-Methyl-2,4-bis{5-[4-(9-carbazolyl)phenyl]-1H-1,2,3-triazol-1-yl}-7H-pyrrolo[2,3-d]pyrimidine* (7i)**



Compound **7i** was purified by silica gel column chromatography, eluent EtOAc and recrystallized from 2-PrOH. Yield 31 mg (9%). White solid, mp 249 ^{o}C dec.; ^{1}H NMR (400 MHz, d_6-DMSO): δ = 4.03 (3H, s, NCH_3), 7.13 (1H, d, *J* = 3.2 Hz, 5-H), 7.16-7.25 (6H, m, carbazole-H), 7.29-7.37 (6H, m, 6-H, carbazole-H), 7.46 (2H, t, *J* = 8.0 Hz, carbazole-H), 7.82 (2H, d, *J* = 7.6 Hz, ArH), 7.93 (2H, d, *J* = 7.6 Hz, ArH), 7.97-8.00 (3H, m, carbazole-H), 8.16 (2H, d, *J* = 7.6 Hz, ArH), 8.25 (2H, d, *J* = 7.6 Hz, ArH), 8.44 (1H, s, triazole-H), 8.48 (1H, s, triazole-H). ^{13}C NMR (100 MHz, d_6-DMSO): δ = 32.1, 101.9, 109.7, 110.0, 110.1, 119.7, 120.6, 120.7, 120.91, 120.96, 123.2, 123.3, 126.6, 126.68, 126.7, 126.8, 127.2, 127.3, 128.9, 131.7, 135.2, 135.4, 137.0, 138.2, 138.5, 140.1, 140.3, 146.4, 146.8, 147.85, 154.42. HRMS (ESI): calculated for $C_{47}H_{31}N_{11}Na$ $[M+Na]^+$ = 772.2656; found: 772.2655

***General Procedures for the synthesis of 4-(Arylethynyl)-2-chloro-7-methyl-7H-pyrrolo[2,3-d]pyrimidines* 8a-h**

Method A (Sonogashira coupling):

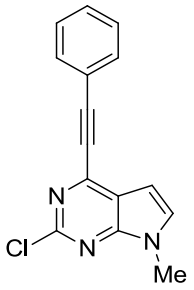
A solution of 2,4-dichloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**3**) (400 mg, 1.98 mmol) in anhydrous Et_3N (20 mL) was flushed with argon and $Pd(PPh_3)_2Cl_2$ (28.0 mg, 0.04 mmol), Ph_3P (21.0 mg, 0.08 mg), CuI (3.8 mg, 0.02 mmol) and the corresponding arylacetylene (2.38 mmol) were added. The mixture was stirred under argon at 60^{o} C for 2-6 h. After cooling, the mixture was poured into water (40 mL) and extracted with $CHCl_3$. The extract was dried over Na_2SO_4, filtered and the solvent was removed on a rotary

evaporator. The residue was purified by column chromatography (eluent – $CHCl_3$) to afford **8a-f**.

Method B (Stille coupling):

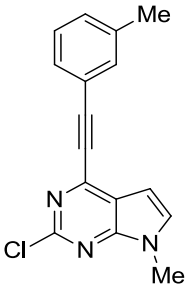
A solution of 2,4-dichloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**3**) (400 mg, 1.98 mmol) in anhydrous toluene (10 mL) was flushed with argon and the corresponding (arylethynyl)tributylstannane (2.38 mmol) was added. The mixture was stirred under argon at 80 ^oC for 2 h. After cooling, the mixture was poured into aqueous K_2CO_3 solution (0.5 M, 25 mL) containing CsF (50 mg), stirred for 30 min and the extracted with $CHCl_3$. The extract was dried over Na_2SO_4, filtered and the $CHCl_3$ removed on a rotary evaporator. The residue was purified by column chromatography (eluent – $CHCl_3$) to afford **8a-h**.

2-Chloro-7-methyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**8a**)



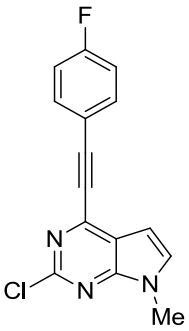
Yield 360 mg (68%) by **method A** (Sonogashira coupling) and 465 mg (88%) by **method B** (Stille coupling); Yellow solid, mp 175-176 ^oC (2-PrOH). IR (KBr): 2213 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.89 (3H, s, NCH_3), 6.72 (1H, d, *J* = 3.6 Hz, 5-H), 7.23 (1H, d, *J* = 3.6 Hz, 6-H), 7.44 (3H, m, ArH), 7.69 (2H, dd, *J* = 8.0 Hz, *J* = 1.6 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 85.2, 96.7, 100.1, 118.9, 121.3, 128.5, 129.9, 131.0, 132.5, 142.5, 152.4, 153.3. HRMS (ESI): *m/z* $[M+H]^+$ calcd. for $C_{15}H_{11}ClN_3$: 268.0636; found 268.0642.

2-Chloro-7-methyl-4-(m-tolylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (8b)



Yield 407 mg (73%) by **method A** (Sonogashira coupling) and 468 mg (84%) by **method B** (Stille coupling); Yellow solid, mp 184-185 °C (2-PrOH). IR (KBr): 2203 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.39 (3H, s, CH_3), 3.87 (3H, s, NCH_3), 6.71 (1H, d, *J* = 3.6 Hz, 5-H), 7.22 (1H, d, *J* = 3.6 Hz, 6-H), 7.25-7.32 (2H, m, ArH), 7.48 (1H, d, *J* = 8.8 Hz, ArH), 7.49 (1H, s, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 31.4, 84.9, 97.1, 100.2, 118.8, 121.1, 128.4, 129.6, 130.91, 130.98, 133.0, 138.3, 143.5, 152.4, 153.3. HRMS (ESI): *m/z* $[M+H]^+$ calcd. for $C_{16}H_{13}ClN_3$: 282.0793; found 282.0798.

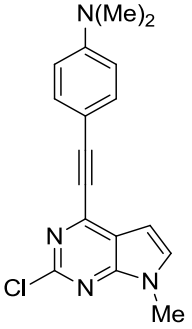
***2-Chloro-4-[(4-fluorophenyl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine* (8c)**



Yield 328 mg (58%) by **method A** (Sonogashira coupling) and 396 mg (70%) by **method B** (Stille coupling); White solid, mp 158–160 °C. IR (KBr): 2211 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.87 (3 H, s, NCH_3), 6.68 (1H, d, *J* = 3.6 Hz, 5-H), 7.12 (2H, dd, ^{3}J = 8.8 Hz, $^{3}J_{H-F}$ = 8.6 Hz, ArH), 7.22 (1H, d, *J* = 3.6 Hz, 6-H), 7.66 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H-F}$ = 5.2 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 85.0, 95.5, 100.0, 116.0 (d, $^{2}J_{C-F}$ = 22 Hz), 117.4 (d, $^{4}J_{C-F}$ = 4 Hz), 118.7, 131.1, 134.5 (d, $^{3}J_{C-F}$ = 9 Hz), 143.2, 152.4, 153.3, 163.5 (d, $^{1}J_{C-F}$ = 251 Hz).

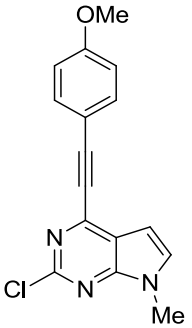
^{19}F NMR (376 MHz, $CDCl_3$): δ = –107.7. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{15}H_{10}ClFN_3$: 286.0542; found: 286.0541.

2-Chloro-4-{[4-(dimethylamino)phenyl]ethynyl}-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**8d**)



Yield 148 mg (24%) by **method A** (Sonogashira coupling) and 393 mg (64%) by **method B** (Stille coupling); Orange solid, mp 212–213 °C (2-PrOH). IR (KBr): 2193 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.04 [6H, s, $N(CH_3)_2$], 3.85 (3H, s, NCH_3), 6.67 (2H, d, *J* = 8.8 Hz, ArH), 6.68 (1H, d, *J* = 3.6 Hz, 5-H), 7.16 (1H, d, *J* = 3.6 Hz, 6-H), 7.55 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 40.0, 84.7, 100.0, 100.3, 107.3, 111.5, 118.1, 130.2, 134.0, 144.4, 151.1, 152.1, 153.3. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{17}H_{16}ClN_4$: 311.1058; found: 311.1066.

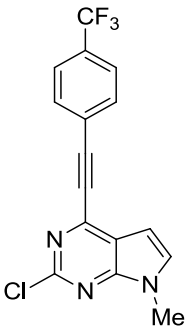
2-Chloro-4-[(4-methoxyphenyl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**8e**)



Yield 271 mg (46%) by **method A** (Sonogashira coupling) and 418 mg (71%) by **method B** (Stille coupling); Yellow solid, mp 156–157 °C (*2*-PrOH). IR (KBr): 2204 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.87 (6H, s, NCH_3, OCH_3), 6.70 (1H, d, *J* = 3.6 Hz, 5-H), 6.94 (2H, d, *J* = 8.8 Hz, ArH), 7.20 (1H, d, *J* = 3.6 Hz, 6-H), 7.63 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100

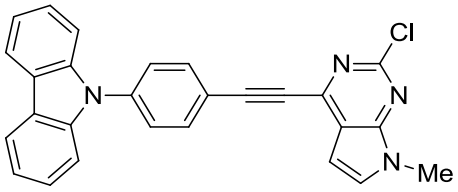
MHz, $CDCl_3$): δ = 31.4, 55.4, 84.5, 97.4, 100.2, 113.3, 114.2, 118.5, 130.7, 134.2, 143.9, 152.3, 153.3, 161.0. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{13}ClN_3O$: 298.0742; found: 298.0731.

***2-Chloro-7-methyl-4-{[4-(trifluoromethyl)phenyl]ethynyl}-7H-pyrrolo[2,3-d]pyrimidine* (8f)**



Yield 398 mg (60%) by **method A** (Sonogashira coupling) and 239 mg (36%) by **method B** (Stille coupling); White solid, mp 148–149 °C. IR (KBr): 2220 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.88 (3H, s, NCH_3), 6.69 (1H, d, *J* = 3.6 Hz, 5-H), 7.25 (1H, d, *J* = 3.6 Hz, 6-H), 7.66 (2H, d, *J* = 8.0 Hz, ArH), 7.76 (2H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 86.9, 94.3, 99.9, 119.01, 123.6 (q, ^1J = 271 Hz), 125.1, 125.5 (q, ^3J = 4 Hz), 131.46 (q, ^2J = 33 Hz), 131.49, 132.6, 142.6, 152.5, 153.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –63.0. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{16}H_{10}ClF_3N_3$: 336.0510; found: 336.0508.

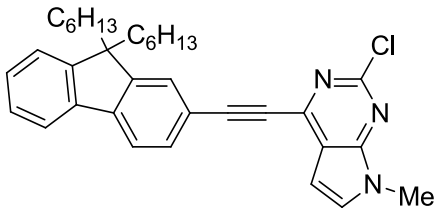
***4-{[4-(9-Carbazolyl)phenyl]ethynyl}-2-chloro-7-methyl-7H-pyrrolo[2,3-d]pyrimidine* (8g)**



Yield 643 mg (74%) by **method B** (Stille coupling); Yellow solid, mp 256–258 °C. IR (KBr): 2206 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.90 (3H, s, NCH_3), 6.77 (1H, d, *J* = 3.6 Hz, 5-H), 7.26 (1H, d, *J* = 3.6 Hz, 6-H), 7.34 (2H, td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, Cbz-H), 7.46 (2H, td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, Cbz-H), 7.51 (2H, d, *J* = 7.6Hz, Cbz-H), 7.68 (2H, d, *J* = 8.8 Hz,

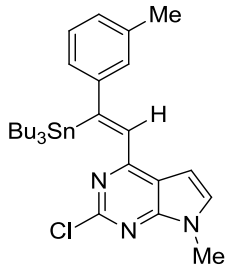
ArH), 7.93 (2H, d, *J* = 8.8 Hz, ArH), 8.17 (2H, d, *J* = 7.6 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.5, 86.0, 95.8, 100.1, 109.7, 118.97, 120.0, 120.4, 120.5, 123.7, 126.1, 126.8, 131.1, 134.0, 139.2, 140.3, 143.2, 152.5, 153.4. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{27}H_{18}ClN_4$: 433.1215; found: 433.1218.

2-Chloro-4-[(9,9-dihexyl-9H-fluoren-2-yl)ethynyl]-7-methyl-7Hpyrrolo[2,3-d]pyrimidine (**8h**)



Yield: 539 mg (52%) by method B (Stille coupling); Yellow solid, mp 129–130 °C (2-PrOH). IR (KBr): 2210 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.56–0.68 (4H, m, 2×CH_2), 0.78 (6H, t, *J* = 7.2 Hz, 2×CH_3), 1.01–1.16 [12H, m, 2×$(CH_2)_3$], 2.00 (4H, t, *J* = 8.0 Hz, 2×CH_2), 3.90 (3H, s, NCH_3), 6.79 (1H, d, *J* = 3.6 Hz, 5-H), 7.25 (1H, d, *J* = 3.6 Hz, 6-H), 7.35–7.41 (3H, m, ArH), 7.66–7.69 (2H, m, ArH), 7.73–7.75 (2H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.5, 23.7, 29.6, 31.4, 31.5, 40.3, 55.2, 85.4, 98.2, 100.2, 118.6, 119.2, 119.7, 120.3, 122.9, 127.0, 127.1, 128.0, 130.8, 131.5, 140.0, 143.1, 143.7, 150.9, 151.3, 152.5, 153.4. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{34}H_{39}ClN_3$: 524.2827; found: 524.2826.

(Z)-2-Chloro-7-methyl-4-[2-(m-tolyl)-2-(tributylstannyl)vinyl]-7H-pyrrolo[2,3-d]pyrimidine (**10**)



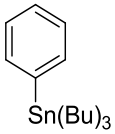
To a mixture of hexabutyldistannane ($Bu_3SnSnBu_3$) (215 μL, 0.43 mmol) in anhydrous THF (10 mL) was added a solution of *n*-butyllithium (295 μL, 1.6 M in hexane, 0.47 mmol) at –20 °C under an atmosphere of argon.

After the addition was complete, the mixture was stirred at –20 °C for 30 min. The mixture was cooled to –78 °C and a solution of compound **8b** (100 mg, 0.36 mmol) in anhydrous THF (2 mL) was added. After stirring for 2 h. at –78 °C, the mixture was slowly warmed to r.t. and was then poured into brine (25 mL) and extracted with $CHCl_3$ (3×25 mL). The extract was dried over Na_2SO_4, filtered and the $CHCl_3$ removed on a rotary evaporator. The residue was purified by column chromatography ($CHCl_3$) to afford 83 mg (41%) of compound **10**. Pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.06 (6H, t, *J* = 8.4 Hz, 3×$SnCH_2$), 1.19–1.28 (6H, m, 3×CH_2), 1.34–1.46 (6H, m, 3×CH_2), 2.41 (3H, s, CH_3), 3.86 (3H, s, NCH_3), 6.65 (1H, d, *J* = 3.6 Hz, 5-H), 6.98 (1H, d, *J* = 7.6 Hz, ArH), 6.99 (1H, s, ArH), 7.08 (1H, d, *J* = 7.6 Hz, ArH), 7.14 (1H, d, *J* = 3.6 Hz, 6-H), 7.27 (1H, m, ArH), 7.43 (1H, s, satellite d^{Sn119}, satellite d^{Sn117} $^3J_{Sn–H}$ = 101/97 Hz, C=CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.8, 13.6, 21.5, 27.4, 29.1, 31.3, 99.2, 115.7, 123.5 (satellite d, $^3J_{Sn–C}$ = 15.3 Hz), 127.0, 127.1 (satellite d, $^3J_{Sn–C}$ = 15.3 Hz), 127.9, 129.6, 134.0, 137.5, 147.9 (satellite d, $^2J_{Sn–C}$ = 24.0 Hz), 152.7, 152.9, 156.2 ($^3J_{Sn–C}$ = 18.6 Hz), 166.9. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{28}H_{41}ClN_3Sn$: 574.2004; found: 574.2002.

***General procedure for the synthesis of (aryl)tributylstannanes* 11a-e:**

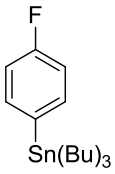
To a mixture of corresponding aryl bromide in anhydrous THF (10 mL) was added a solution of *n*-butyllithium (1.1 equiv.) at –78 °C under an atmosphere of argon. After the addition was complete, the mixture was stirred at –78 °C for 30 min. and tributyltin chloride (1.0 equiv.) was added. After stirring for 30 min. at –78 °C, the mixture was slowly warmed to room temperature and was then poured into brine (25 mL) and extracted with $CHCl_3$ (3×50 mL). The extract was dried over Na_2SO_4, filtered and the $CHCl_3$ removed on a rotary evaporator. The obtained compounds **11a-e** were used further without additional purification.

Phenyltributylstannane (**11a**)



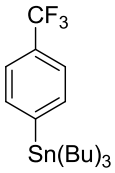
Compound **11a** was synthesized from bromobenzene (3 g, 0.019 mol). Yield 6.7 g (97%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.08 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.30-142 (6H, m, 3×CH_2), 1.54-1.63 (6H, m, 3×CH_2), 7.32-7.50 (5H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.5, 13.7, 27.4, 29.1, 128.5, 128.7, 136.9, 141.3.
Lit. [164]: yield 96%.

Tributyl(4-fluorophenyl)stannane (**11b**)



Compound **11b** was synthesized from 1-bromo-4-fluorobenzene (2 g, 0.011 mol). Yield 4.0 g (95%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.06 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.35 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.51-1.60 (6H, m, 3×CH_2), 7.03-7.10 (2H, m, ArH), 7.37-7.50 (2H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.6, 13.6, 27.3, 29.0, 115.1 (d, $^{2}J_{C\text{-}F}$ = 19 Hz), 136.7 (d, $^{4}J_{C\text{-}F}$ = 4 Hz), 137.8 (d, $^{3}J_{C\text{-}F}$ = 6 Hz), 163.2 (d, $^{1}J_{C\text{-}F}$ = 244 Hz).
Lit. [265]: yield 70%.

Tributyl(4-(trifluoromethyl)phenyl)stannane (**11c**)

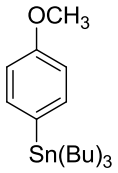


Compound **11c** was synthesized from 1-bromo-4-(trifluoromethyl)benzene (2 g, 8.88 mmol). Yield 3.5 g (91%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.12 (6H, t, *J* =

8.0 Hz, 3×$SnCH_2$), 1.29-1.41 (6H, m, 3×CH_2), 1.49-1.61 (6H, m, 3×CH_2), 7.55-7.67 (4H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.6, 13.6, 27.3, 29.0, 124.4 (q, $^1J_{C-F}$ = 270 Hz) 124.1 (q, $^3J_{C-F}$ = 4 Hz), 128.6, 130.4 (q, $^2J_{C-F}$ = 32 Hz), 136.0.

Lit. [166]: yield 56%.

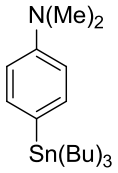
Tributyl(4-methoxyphenyl)stannane (**11d**)



Compound **11d** was synthesized from 1-bromo-4-methoxybenzene (2 g, 0.01 mol). Yield 4.1 g (96%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.07 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.32-1.42 (6H, m, 3×CH_2), 1.52–1.66 (6H, m, 3×CH_2), 3.83 (3H, s, OCH_3), 6.94 (2H, d, *J* = 8.8 Hz, ArH), 7.41(2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.6, 13.6, 27.4, 29.1, 54.9, 113.9, 131.9, 137.5, 159.7.

Lit. [166]: yield 96%.

N,N-dimethyl-4-(tributylstannyl)aniline (**11e**)



Compound **11e** was synthesized from 4-bromo-*N*,*N*-dimethylaniline (2 g, 0.01 mol). Yield 3.7 g (92%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.04 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.36 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.51–1.65 (6H, m, 3×CH_2), 2.97 [6H, s, $N(CH_3)_2$], 6.78 (2H, d, *J* = 8.8 Hz, ArH), 7.36 (2H, d, *J* = 8.8 Hz, ArH).

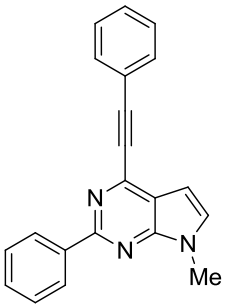
^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.5, 13.7, 27.4, 29.1, 40.3, 112.6, 126.4, 137.2, 150.4.

Lit. [166]: yield 61%.

***General procedure for the synthesis of 2-aryl-4-(arylethynyl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidines* 12a–o.**

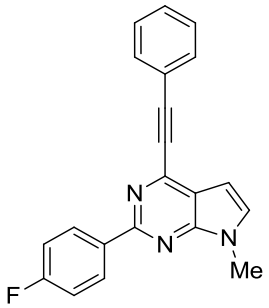
A solution of corresponding 4-(arylethynyl)-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine **8** (0.3 mmol) in anhydrous toluene (2 mL) was flushed with argon and $Pd(PPh_3)_2Cl_2$ (10.5 mg, 0.015 mmol), $AsPh_3$ (18.4 mg, 0.06 mmol) and corresponding (aryl)tributyltin (0.45 mmol) were added. The mixture was refluxed under argon for 48-72 h. After cooling reaction mixture was poured into 0.5M K_2CO_3 (20 mL) solution consisting 50 mg of CsF, stirred for 30 min. and extracted with $CHCl_3$. Extract was dried over Na_2SO_4, filtered and chloroform was removed by rotary evaporator. The crude product was purified by column chromatography (eluent $CHCl_3$) to afford **12a-o**.

***7-Methyl-2-phenyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine* (12a)**



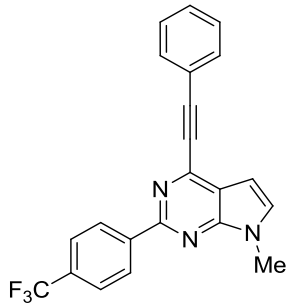
Yield 76 mg (82%); Yellow solid, mp 132-133^{o}C. IR (KBr), ν, cm^{-1}: 2212 (C≡C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.96 (3H, s, NCH_3), 6.72 (1H, d, *J* = 3.2 Hz, 5-H), 7.23 (1H, d, *J* = 3.2 Hz, 6-H), 7.42-7.49 (4H, m, ArH), 7.52 (2H, t, *J* = 7.6 Hz, ArH), 7.73-7.75 (2H, m, ArH), 8.61 (2H, d, *J* = 7.6 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.1, 86.5, 94.5, 99.7, 118.5, 122.0, 128.1, 128.40, 128.48, 129.4, 129.7, 130.4, 132.4, 138.5, 142.2, 152.0, 158.2 ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{21}H_{16}N_3$: 310.1339; found: 310.1344.

2-(4-Fluorophenyl)-7-methyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**12b**)



Yield 75 mg (76%); Yellow solid, mp 152–154 °C. IR (KBr): 2212 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.95 (3H, s, NCH_3), 6.71 (1H, d, *J* = 3.6 Hz, 5-H), 7.17–7.21 (2H, m, ArH), 7.23 (1H, d, *J* = 3.6 Hz, 6-H), 7.43–7.45 (3H, m, ArH), 7.72–7.75 (2H, m, ArH), 8.61 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H\text{-}F}$ = 5.6Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.0, 86.4, 94.6, 99.7, 115.2 (d, $^{2}J_{C\text{-}F}$ = 22Hz), 118.4, 121.9, 128.5, 129.5, 130.1 (d, $^{3}J_{C\text{-}F}$ = 9 Hz), 130.5, 132.4, 134.7 (d, $^{4}J_{C\text{-}F}$ = 3 Hz), 142.2, 152.0, 157.3, 164.1 (d, $^{1}J_{C\text{-}F}$ = 247 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –112.2. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{21}H_{15}FN_3$: 328.1244; found: 328.1239

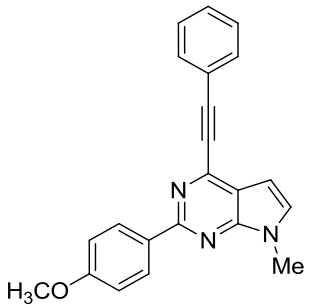
7-Methyl-4-(phenylethynyl)-2-[4-(trifluoromethyl)phenyl]-7H-pyrrolo[2,3-d]pyrimidine (**12c**)



Yield: 90 mg (80%); Off-white solid mp 105–107 °C. IR (KBr): 2214 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.97 (3H, s, NCH_3), 6.74 (1H, d, *J* = 3.6 Hz, 5-H), 7.27 (1H, d, *J* = 3.6 Hz, 6-H), 7.43–7.47 (3H, m, ArH), 7.73–7.77 (4H, m, ArH), 8.72 (2H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.0, 86.2, 94.9, 99.9, 118.9, 121.8, 124.3 (q, $^{1}J_{C\text{-}F}$ = 271 Hz), 125.2 (q, $^{3}J_{C\text{-}F}$ = 3 Hz), 128.3, 128.5, 129.6, 131.0, 131.2 (q, $^{2}J_{C\text{-}F}$ = 32 Hz),

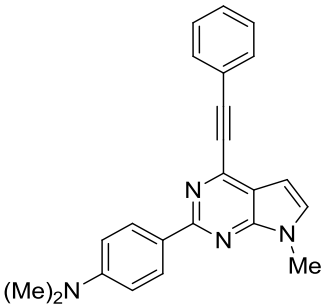
132.4, 141.9, 142.3, 151.8, 156.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.4. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{22}H_{15}F_3N_3$: 378.1212; found: 378.1215.

2-(4-Methoxyphenyl)-7-methyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine **(12d)**



Yield 45 mg (44%); Yellow solid; mp 147–149 °C (2-PrOH). IR (KBr): 2214 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (3H, s, NCH_3), 3.94 (3H, s, OCH_3), 6.69 (1H, d, *J* = 3.6 Hz, 5-H), 7.03 (2H, d, *J* = 8.8 Hz, ArH), 7.19 (1H, d, *J* = 3.6 Hz, 6-H), 7.43–7.45 (3H, m, ArH), 7.72–7.74 (2H, m, ArH), 8.56 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.9, 55.3, 86.6, 94.3, 99.6, 113.7, 118.0, 122.1, 128.4, 129.4, 129.6, 130.1, 131.3, 132.3, 142.1, 152.1, 158.1, 161.1. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{22}H_{18}N_3O$: 340.1444; found: 340.1452

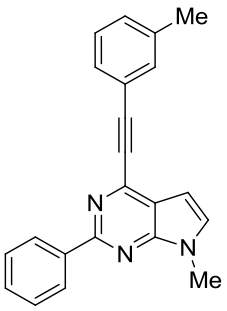
2-[4-(Dimethylamino)phenyl]-7-methyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine **(12e)**



Yield 44 mg (42%); Orange solid, mp 182–183 °C (2-PrOH). IR (KBr): 2212 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.07 [6H, s, $N(CH_3)_2$], 3.92 (3H, s, NCH_3), 6.66 (1H, d, *J* = 3.6 Hz, 5-H), 6.83 (2H, d, *J* = 8.8 Hz, ArH), 7.15 (1H, d, *J* = 3.6 Hz, 6-H), 7.42–7.44 (3H, m, ArH), 7.72–7.75 (2H, m, ArH), 8.51 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.8, 40.3,

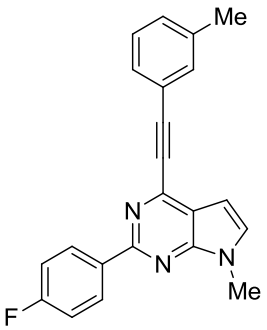
86.8, 93.9, 99.5, 111.7, 117.6, 122.2, 126.6, 128.4, 129.30, 129.31, 129.5, 132.3, 142.1, 151.6, 152.2, 158.8. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{23}H_{21}N_4$: 353.1761; found: 353.1770.

***7-Methyl-2-phenyl-4-(m-tolylethynyl)-7H-pyrrolo[2,3-d]pyrimidine* (12f)**



Yield 79 mg (81%); Pale yellow solid, mp 103–105 °C (2-PrOH). IR (KBr): 2219 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.42 (3H, s, CH_3), 3.97 (3H, s, NCH_3), 6.73 (1H, d, *J* = 3.6 Hz, 5-H), 7.24–7.27 (2H, m, 6-H, ArH), 7.33 (1H, t, *J* = 7.6 Hz, ArH), 7.45–7.56 (5H, m, ArH), 8.61 (2H, d, *J* = 7.2 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 31.0, 86.2, 94.8, 99.7, 118.5, 121.8, 128.1, 128.3, 128.4, 129.5, 129.7, 130.3, 130.4, 132.9, 138.2, 138.6, 142.3, 152.1, 158.2. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{22}H_{18}N_3$: 324.1495; found: 324.1496.

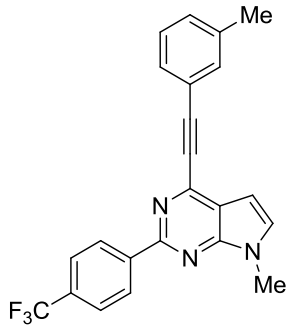
***2-(4-Fluorophenyl)-7-methyl-4-(m-tolylethynyl)-7H-pyrrolo[2,3-d]pyrimidine* (12g)**



Yield 90 mg (88%); Pale yellow solid, mp 147–148 °C. IR (KBr): 2208 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.42 (3H, s, CH_3), 3.95 (3H, s, NCH_3), 6.71 (1H, d, *J* = 3.6 Hz, 5-H), 7.18 (2H, dd, ^3J = 8.8 Hz, $^3J_{H\text{-}F}$ = 8.6 Hz,

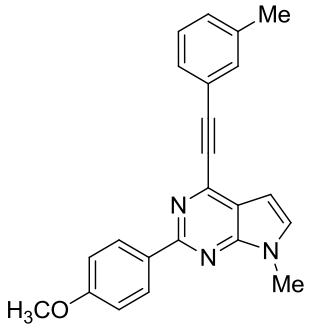
ArH), 7.23 (1H, d, *J* = 3.6 Hz, 6-H), 7.26 (1H, d, *J* = 7.6 Hz, ArH), 7.33 (1H, t, *J* = 7.6 Hz, ArH), 7.51–7.57 (2H, m, ArH), 8.61 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H\text{-}F}$ = 5.2 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 31.0, 86.1, 94.9, 99.7, 115.1 (d, $^{2}J_{C\text{-}F}$ = 21 Hz), 118.4, 121.7, 128.3, 129.5, 130.1 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 130.4, 132.9, 134.7, 134.8, 138.2, 142.4, 152.0, 157.3, 164.1 (d, $^{1}J_{C\text{-}F}$ = 248 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –112.2. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{22}H_{17}FN_3$: 342.1401; found: 342.1393.

7-Methyl-4-(m-tolylethynyl)-2-[4-(trifluoromethyl)phenyl]-7H-pyrrolo[2,3-d]pyrimidine (**12h**)



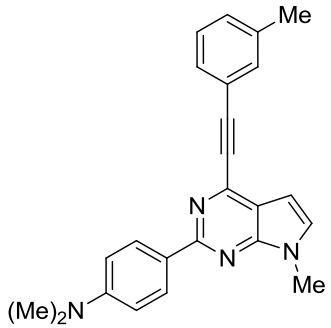
Yield 100 mg (85%); Pale yellow solid, mp 104–106 °C. IR (KBr): 2218 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.42 (3H, s, CH_3), 3.96 (3H, s, NCH_3), 6.74, (1H, d, *J* = 3.6 Hz, 5-H), 7.27 (1H, d, *J* = 3.6 Hz, 6-H), 7.33 (1H, t, *J* = 7.6 Hz, ArH), 7.50–7.58 (2H, m, ArH), 7.76 (2H, d, *J* = 8.4 Hz, ArH), 8.72 (2H, d, *J* = 8.4 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 31.0, 85.9, 95.2, 99.9, 118.9, 121.6, 122.3 (q, $^{1}J_{C\text{-}F}$ = 270 Hz), 125.2 (q, $^{3}J_{C\text{-}F}$ = 4 Hz), 128.3, 129.5, 130.5, 131.0, 131.2 (q, $^{2}J_{C\text{-}F}$ = 32 Hz), 132.9, 138.2, 141.93, 141.94, 142.4, 151.8, 156.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.4. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{23}H_{17}F_3N_3$: 392.1369; found: 392.1380.

2-(4-Methoxyphenyl)-7-methyl-4-(m-tolylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**12i**)



Yield: 48 mg (48%); Yellow solid, mp 132–133 °C (2-PrOH). IR (KBr): 2209 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.42 (3H, s, CH_3), 3.91 (3H, s, NCH_3), 3.95 (3H, s, OCH_3), 6.70 (1H, d, *J* = 3.6 Hz, 5-H), 7.03 (2H, d, *J* = 8.8 Hz, ArH), 7.20 (1H, d, *J* = 3.6 Hz, 6-H), 7.20 (1H, d, *J* = 7.6 Hz, ArH), 7.32 (1H, t, *J* = 7.6 Hz, ArH), 7.50–7.56 (2H, m, ArH), 8.56 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 30.9, 55.3, 86.2, 94.6, 99.7, 113.7, 118.0, 121.9, 128.3, 129.4, 129.6, 129.9, 130.3, 131.3, 132.9, 138.1, 142.3, 152.1, 158.1, 161.1. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{23}H_{20}N_3O$: 354.1601; found: 354.1609.

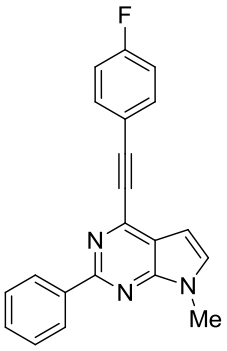
2-[4-(Dimethylamino)phenyl]-7-methyl-4-(m-tolylethynyl)-7H-pyrrolo[2,3-d]pyrimidine **(12j)**



Yield 47 mg (43%); Orange solid, mp 180–182 °C (2-PrOH). IR (KBr): 2218 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.42 (3H, s, CH_3), 3.07 [6H, s, $N(CH_3)_2$], 3.93 (3H, s, NCH_3), 6.66 (1H, d, *J* = 3.6 Hz, 5-H), 8.83 (2H, d, *J* = 8.8 Hz, ArH), 7.15 (1H, d, *J* = 3.6 Hz, 6-H), 7.25 (1H, d, *J* = 7.6 Hz, ArH), 7.32 (1H, t, *J* = 7.6 Hz, ArH), 7.50–7.58 (2H, m, ArH), 8.50 (2H, d, *J* =

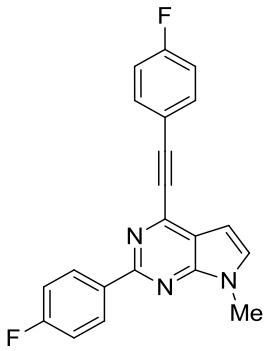
8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 30.8, 40.3, 86.5, 94.2, 99.6, 111.7, 117.6, 122.0, 126.6, 128.3, 129.2, 129.4, 129.5, 130.2, 132.9, 138.1, 142.2, 151.6, 152.2, 158.8. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{23}N_4$: 367.1917; found: 367.1925.

4-[(4-Fluorophenyl)ethynyl]-7-methyl-2-phenyl-7H-pyrrolo[2,3-d]pyrimidine (**12k**)



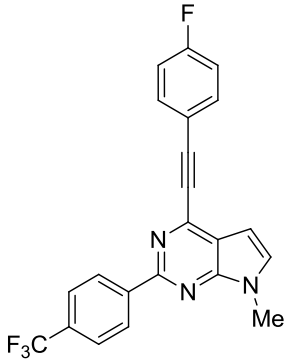
Yield 85 mg (87%); Off-white solid, mp 148–150 °C. IR (KBr): 2215 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.96 (3H, s, NCH_3), 6.70 (1H, d, *J* = 3.6 Hz, 5-H), 7.13 (2H, dd, ^3J = 8.8 Hz, $^3J_{H-F}$ = 8.4 Hz, ArH), 7.24 (1H, d, *J* = 3.6 Hz, 6-H), 7.47–7.54 (3H, m, ArH), 7.72 (2H, dd, ^3J = 8.8 Hz, $^4J_{H-F}$ = 5.2 Hz, ArH), 8.59–8.61 (2H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.0, 86.3, 93.3, 99.6, 115.9 (d, $^2J_{C-F}$ = 22 Hz), 118.1 (d, $^4J_{C-F}$ = 3 Hz), 118.4, 128.1, 128.4, 129.7, 130.5, 134.4 (d, $^3J_{C-F}$ = 8 Hz), 138.5, 142.0, 152.0, 158.2, 163.2 (d, $^1J_{C-F}$ = 250 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –108.7. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{21}H_{15}FN_3$: 328.1244; found: 328.1243.

2-(4-Fluorophenyl)-4-[(4-fluorophenyl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**12l**)



Yield 88 mg (85%); Yellow solid, mp 192–194 °C. IR (KBr): 2212 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.94 (3H, s, NCH_3), 6.69 (1H, d, *J* = 3.6 Hz, 5-H), 7.11–7.21 (4H, m, ArH), 7.22 (1H, d, *J* = 3.6 Hz, 6-H), 7.71 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H\text{-}F}$ = 5.2 Hz, ArH), 8.60 (2H, dd, ^{3}J = 9.2 Hz, $^{4}J_{H\text{-}F}$ = 5.6 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.0, 86.20, 86.21, 99.6, 115.2 (d, $^{2}J_{C\text{-}F}$ = 21 Hz), 115.9 (d, $^{2}J_{C\text{-}F}$ = 22 Hz), 118.1 (d, $^{4}J_{C\text{-}F}$ = 3 Hz), 118.3, 130.1 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 130.5, 134.4 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 134.7 (d, $^{4}J_{C\text{-}F}$ = 3 Hz), 142.0, 152.0, 157.3, 163.2 (d, $^{1}J_{C\text{-}F}$ = 250 Hz), 164.1 (d, $^{1}J_{C\text{-}F}$ = 247 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = -112.1, -108.6. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{21}H_{14}F_2N_3$: 346.1150; found: 346.1144.

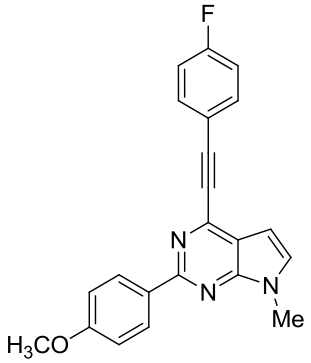
4-[(4-Fluorophenyl)ethynyl]-7-methyl-2-[4-(trifluoromethyl)phenyl]-7H-pyrrolo[2,3-d]pyrimidine (**12m**)



Yield: 102 mg (86%); Off-white solid, mp 148–150 °C. IR (KBr): 2208 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.96 (3H, s, NCH_3), 6.72 (1H, d, *J* = 3.6 Hz, 5-H), 7.11–7.17 (2H, m, ArH), 7.27 (1H, d, *J* = 3.6 Hz, 6-H), 7.70–

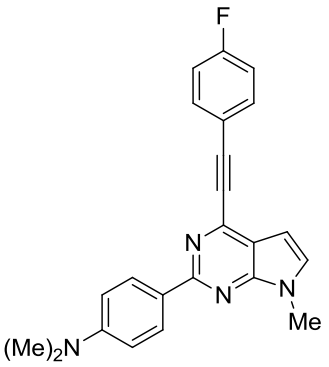
7.77 (4H, m, ArH), 8.71 (2H, d, J = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.0, 86.0, 93.7, 99.8, 116.0 (d, $^2J_{C\text{-}F}$ = 22 Hz), 118.0 (d, $^4J_{C\text{-}F}$ = 4 Hz), 118.9, 124.3 (q, $^1J_{C\text{-}F}$ = 271 Hz), 125.3 (q, $^3J_{C\text{-}F}$ = 4 Hz), 128.3, 131.1, 131.3 (q, $^2J_{C\text{-}F}$ = 32 Hz), 134.5 (d, $^3J_{C\text{-}F}$ = 8 Hz), 141.8, 142.1, 151.8, 156.6, 163.3 (d, $^1J_{C\text{-}F}$ = 250 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –108.4, –62.5. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{22}H_{14}F_4N_3$: 396.1118; found: 396.1118.

4-[(4-Fluorophenyl)ethynyl]-2-(4-methoxyphenyl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidine **(12n)**



Yield 48 mg (45%); Yellow solid, mp 152–155 °C. IR (KBr): 2214 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (3H, s, NCH_3), 3.95 (3H, s, OCH_3), 6.67 (1H, d, J = 3.6 Hz, 5-H), 7.03 (2H, d, J = 8.8 Hz, ArH), 7.11–7.15 (2H, m, ArH), 7.20 (1H, d, J = 3.6 Hz, 6-H), 7.71 (2H, dd, ^3J = 8.8 Hz, $^4J_{H\text{-}F}$ = 5.2 Hz, ArH), 8.55 (2H, d, J = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.9, 55.3, 86.3, 93.1, 99.5, 113.7, 115.8 (d, $^2J_{C\text{-}F}$ = 22 Hz), 118.0, 118.2 (d, $^4J_{C\text{-}F}$ = 4 Hz), 129.6, 130.1, 131.3, 134.4 (d, $^3J_{C\text{-}F}$ = 8 Hz), 142.0, 152.1, 158.1, 161.1, 163.2 (d, $^1J_{C\text{-}F}$ = 250 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –108.8. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{22}H_{17}FN_3O$: 358.1350; found: 358.1355.

***4-[(4-Fluorophenyl)ethynyl]-2-[4-(dimethylamino)phenyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine* (12o)**

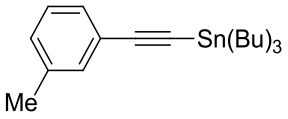


Yield 47 mg (42%); Orange solid, mp 189–191 °C. IR (KBr): 2212 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.06 [6H, s, $N(CH_3)_2$], 3.92 (3H, s, NCH_3), 6.64 (1H, d, *J* = 3.6 Hz, 5-H), 6.82 (2H, d, *J* = 8.8 Hz, ArH), 7.10–7.15 (3H, m, ArH, 6-H), 7.70 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H\text{-}F}$ = 5.2 Hz, ArH), 8.49 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.8, 40.3, 86.5, 92.7, 99.4, 111.7, 115.8 (d, $^{2}J_{C\text{-}F}$ = 23 Hz), 117.5, 118.3 (d, $^{4}J_{C\text{-}F}$ = 3 Hz), 126.5, 129.2, 129.6, 134.3 (d, $^{3}J_{C\text{-}F}$ = 9 Hz), 141.9, 151.6, 152.2, 158.8, 163.1 (d, $^{1}J_{C\text{-}F}$ = 250 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –109.0. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{23}H_{20}FN_4$: 371.1667; found: 371.1678.

***General procedure for the synthesis of (arylethynyl)tributylstannanes* 13a-i**

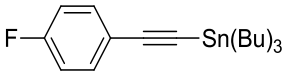
To a mixture of corresponding aryl acetylene in anhydrous THF (10 mL) was added a solution of *n*-butyllithium (1.1 equiv.) at –78 °C under an atmosphere of argon. After the addition was complete, the mixture was stirred at –78 °C for 45 min. and tributyltin chloride (1.0 equiv.) was added. After stirring for 30 min. at –78 °C, the mixture was slowly warmed to room temperature and was then poured into brine (25 mL) and extracted with $CHCl_3$ (3×50 mL). The extract was dried over Na_2SO_4, filtered and the $CHCl_3$ evaporated under reduced atmosphere. The obtained viscous oil was dissolved in hexane and filtered through a layer of silica gel. Hexane was removed on a rotary evaporator. The obtained compounds **13a-i** were used further without additional purification.

Tributyl(m-tolylethynyl)stannane (**13a**)



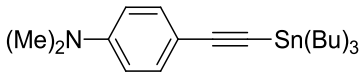
Compound **13a** was synthesized from 1-ethynyl-3-methylbenzene (1.0 g, 8.6 mmol). Yield 3.35 g (96%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.08 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.40 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.61–1.70 (6H, m, 3×CH_2), 2.34 (3H, s, CH_3) 7.11 (1H, d, *J* = 7.6 Hz, ArH), 7.19 (1H, t, *J* = 7.6 Hz, ArH), 7.28 (1H, d, *J* = 7.6 Hz, ArH), 7.31 (1H, s, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.1, 13.7, 27.0, 28.9, 92.7, 110.2, 123.8, 128.0, 128.7, 129.0, 132.5, 137.7.
Lit. [167]: yield 80%.

Tributyl[(4-fluorophenyl)ethynyl]stannane (**13b**)



Compound **13b** was synthesized from 1-ethynyl-4-fluorobenzene (1.5 g, 12.5 mmol). Yield 4.8 g (94%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.08 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.40 (6H, sex, *J* = 7.2 Hz, 3×CH_2), 1.60–1.69 (6H, m, 3×CH_2), 6.96-7.02 (m, 2H, ArH), 7.44 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H\text{-}F}$ = 5.2 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.1, 13.6, 26.9, 28.9, 92.9, 108.8, 115.3 (d, $^{2}J_{C\text{-}F}$ = 21 Hz), 120.1 (d, $^{4}J_{C\text{-}F}$ = 4 Hz), 133.7 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 162.3 (d, $^{1}J_{C\text{-}F}$ = 247 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = -111.6. Lit. [266]: yield 79%.

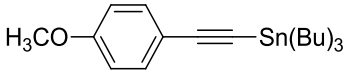
Tributyl[(4-dimethylaminophenyl)ethynyl]stannane (**13c**)



Compound **13c** was synthesized from 4-ethynyl-*N*,*N*-dimethylaniline (1.5 g, 10.3 mmol). Yield 4.3 g (95%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.06 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.39 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.58–1.69 (6H, m, 3×CH_2), 2.98 [6H, s, $N(CH_3)_2$], 6.63 (2H, d, *J* = 8.8 Hz, ArH), 7.34 (2H, d, *J* = 8.8 Hz,

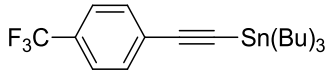
ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.2, 13.7, 27.0, 28.9, 40.2, 89.5, 111.3, 111.7, 133.0, 133.2, 149.8. Lit. [267]: yield 96%.

Tributyl[(4-methoxyphenyl)ethynyl]stannane (**13d**)



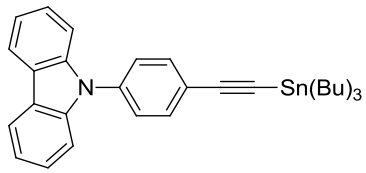
Compound **13d** was synthesized from 1-ethynyl-4-methoxybenzene (1.5 g, 11.3 mmol). Yield 4.6 g (96%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.07 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.40 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.60–1.71 (6H, m, 3×CH_2), 3.82 (3H, s, OCH_3), 6.83 (2H, d, *J* = 8.8 Hz, ArH), 7.41 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.2, 13.7, 27.0, 28.9, 55.2, 91.1, 110.0, 113.7, 116.3, 133.4, 159.3. Lit. [167]: yield 79%.

Tributyl{[4-(trifluoromethyl)phenyl]ethynyl}stannane (13e)



Compound **13e** was synthesized from 1-ethynyl-4-(trifluoromethyl)benzene (1.5 g, 8.8 mmol). Yield 3.0 g (75%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.11 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.40 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.59–1.70 (6H, m, 3×CH_2), 7.56 (4H, s, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.2, 13.6, 26.9, 28.9, 97.0, 108.4, 124.0 (q, $^1J_{C\text{-}F}$ = 270 Hz), 125 (q, $^3J_{C\text{-}F}$ = 4 Hz), 127.8, 129.4 (q, $^2J_{C\text{-}F}$ = 33 Hz), 132.1.

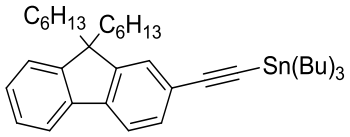
9-*{4-[(Tributylstannyl)ethynyl]phenyl}-9H-carbazole* (**13f**)



Compound **13f** was synthesized from 9-(4-ethynylphenyl)-9*H*-carbazole (2.0 g, 7.5 mmol). Yield 3.7 g (89%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.14 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.45 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.64-1.75 (6H, m,

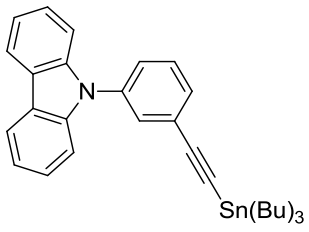
3×CH_2), 7.30-7.37 (2H, m, cbz-H), 7.41-7.46 (4H, m, cbz-H), 7.53 (2H, d, *J* = 8.8 Hz, ArH), 7.71 (2H, d, *J* = 8.8 Hz, ArH), 8.17 (2H, d, *J* = 7.6 Hz, cbz-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.2, 13.7, 27.0, 28.9, 94.8, 109.2, 109.7, 120.1, 120.3, 123.1, 123.5, 126.0, 126.7, 127.1, 133.4, 140.6. HRMS (ESI): calculated for $C_{32}H_{39}KNSn$ $[M+K]^+$ = 596.1741; found: 596.1734.

Tributyl[(9,9-dihexyl-9H-fluoren-2-yl)ethynyl]stannane (**13g**)



Compound **13g** was synthesized from 2-ethynyl-9,9-dihexyl-9*H*-fluorene (1.5 g, 4.2 mmol). Yield 2.5 g (92%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.55-0.67 (4H, m, 2xCH_2), 0.79 (6H, t, *J* = 7.6 Hz, 2xCH_3), 0.97 (9H, t, *J* = 7.2 Hz, 3xCH_3), 1.05-1.18 (18H, m, 9xCH_2), 1.42 (6H, sext, *J* = 7.2 Hz, 3xCH_2), 1.63-1.71 (6H, m, 3xCH_2), 1.92-2.01 (4H, m, 2xCH_2), 7.31-7.36 (3H, m, ArH), 7.44-7.51 (2H, m, ArH), 7.62 (1H, d, *J* = 7.6 Hz, ArH), 7.69 (1H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.2, 13.7, 13.9, 22.6, 27.0, 27.4, 28.9, 29.7, 31.5, 40.3, 55.0, 92.9, 111.2, 119.3, 119.9, 122.1, 122.8, 126.2, 126.7, 127.2, 131.0, 140.5, 141.0, 150.5, 151.0. HRMS (ESI): calculated for $C_{39}H_{60}KSn$ $[M+K]^+$ = 687.3355; found: 687.3346

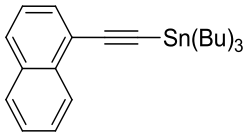
9-{3-[(Tributylstannyl)ethynyl]phenyl}-9H-carbazole (**13h**)



Compound **13h** was synthesized from 9-(3-ethynylphenyl)-9*H*-carbazole (2.0 g, 7.5 mmol). Yield 3.6 g (87%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.10 (6H, t, *J* = 8.0 Hz, 3×SnCH_2), 1.40 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.60-1.71 (6H, m,

3×CH_2), 7.30-7.36 (2H, m, cbz-H), 7.42-7.47 (4H, m, cbz-H), 7.51-7.61 (3H, m, ArH,), 7.69 (1H, s, ArH), 8.17 (2H, d, *J* = 7.6 Hz, cbz-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.2, 13.7, 26.9, 28.9, 95.3, 108.8, 109.6, 109.8, 120.0, 120.3, 123.4, 125.9, 126.7, 129.7, 130.5, 131.0, 137.7, 140.8. HRMS (ESI): calculated for $C_{32}H_{39}KNSn$ $[M+K]^+$ = 596.1731; found: 596.1749.

Tributyl(naphthalen-1-ylethynyl)stannane (**13i**)



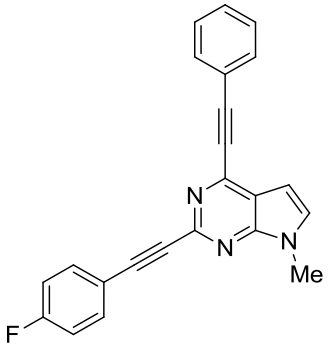
Compound **13i** was synthesized from 1-ethynylnaphthalene (500 mg, 3.3 mmol). Yield 1.3 g (90%). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (9H, t, *J* = 7.2 Hz, 3×CH_3), 1.16 (6H, t, *J* = 8.0 Hz, 3×$SnCH_2$), 1.45 (6H, sext, *J* = 7.2 Hz, 3×CH_2), 1.64-1.75 (6H, m, 3×CH_2), 7.42 (1H, t, *J* = 8.0 Hz, ArH), 7.45 (1H, t, *J* = 8.0 Hz Hz, ArH), 7.71-7.80 (2H, m, ArH), 7.88 (2H, d, *J* = 8.0 Hz, ArH), 8.45 (1H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.4, 13.7, 27.4, 29.3, 98.7, 107.8, 119.8, 125.2, 126.0, 126.5, 126.9, 128.1, 128.3, 129.7, 131.2, 133.1. HRMS (ESI): calculated for $C_{24}H_{34}KSn$ $[M+K]^+$ = 481.1317; found: 481.1309.

General procedure for the synthesis of 2,4-bis(arylethynyl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidines **14a-p**

A solution of 4-(Arylethynyl)-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine **8** (0.4 mmol) in anhydrous toluene (2 mL) was flushed with argon, after which $Pd(PPh_3)_2Cl_2$ (14 mg, 0.02 mmol), $AsPh_3$ (24.5 mg, 0.08 mmol) and the corresponding (arylethynyl)tributyltin (0.6 mmol) was added. The mixture was heated at reflux temperature under argon for 48–72 h. After cooling, the mixture was poured into K_2CO_3 solution (0.5 M, 20 mL) containing CsF (50 mg), stirred for 30 min and then extracted with $CHCl_3$. The extract was dried over Na_2SO_4, filtered and the $CHCl_3$ removed on a rotary

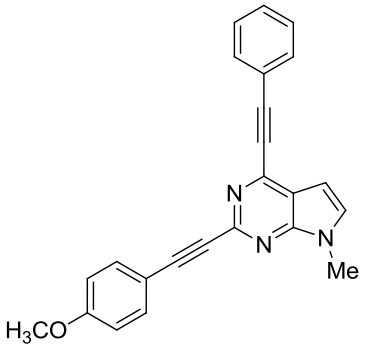
evaporator. The crude residue was purified by column chromatography ($CHCl_3$) to afford compounds **14a**–**p**.

2-[(4-Fluorophenyl)ethynyl]-7-methyl-4-(phenylethynyl)-7H-pyrrolo-[2,3-d]pyrimidine (**14a**)



Yield 112 mg (80%); Pale yellow solid, mp 173–174 °C. IR (KBr): 2210 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.93 (3H, s, NCH_3), 6.75 (1H, d, *J* = 3.6 Hz, 5-H), 7.05–7.11 (2H, m, ArH), 7.30 (1H, d, *J* = 3.6 Hz, 6-H), 7.39–7.45 (3H, m, ArH), 7.67–7.77 (4H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 84.7, 85.6, 88.7, 95.6, 100.2, 115.7 (d, $^2J_{C-F}$ = 22 Hz), 118.2 (d, $^4J_{C-F}$ = 4 Hz), 118.9, 121.6, 128.5, 129.7, 131.5, 132.4, 134.5 (d, $^3J_{C-F}$ = 8 Hz), 142.5, 145.2, 151.1, 163.0 (d, $^1J_{C-F}$ = 250 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –109.3. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{23}H_{15}FN_3$: 352.1244; found: 352.1249.

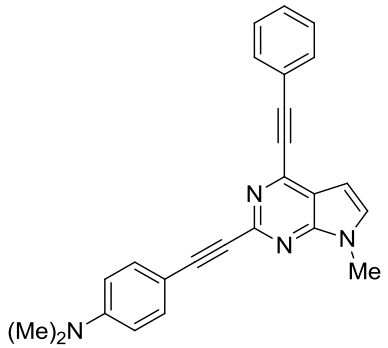
2-[(4-Methoxyphenyl)ethynyl]-7-methyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**14b**)



Yield 100 mg (69%); Yellow solid, mp 188–189 °C. IR (KBr): 2212 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.85 (3H, s, NCH_3), 3.93 (3H, s, OCH_3), 6.73 (1H, d, *J* = 3.6 Hz, 5-H), 6.91 (2H, d, *J* = 8.8 Hz, ArH), 7.28 (1H,

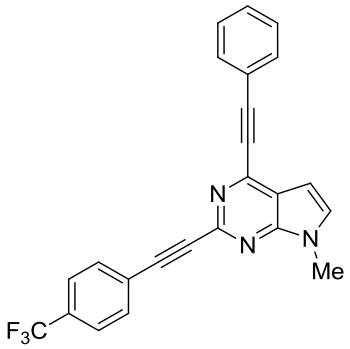
d, *J* = 3.6 Hz, 6-H), 7.39–7.44 (3H, m, ArH), 7.66 (2H, d, *J* = 8.8 Hz, ArH), 7.68–7.71 (2H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 55.3, 85.7, 86.2, 88.0, 95.4, 100.1, 113.9, 114.1, 118.7, 121.7, 128.5, 129.6, 131.3, 132.4, 134.1, 142.5, 145.7, 151.2, 160.2. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{18}N_3O$: 364.1444; found: 364.1452.

2-{[4-(Dimethylamino)phenyl]ethynyl}-7-methyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**14c**)



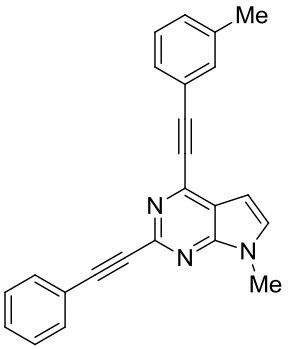
Yield 69 mg (46%); Orange solid, mp 203–205 °C. IR (KBr): 2200 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.02 [6H, s, $N(CH_3)_2$], 3.92 (3H, s, NCH_3), 6.68 (2H, d, *J* = 8.8 Hz, ArH), 6.72 (1H, d, *J* = 3.6 Hz, 5-H), 7.26 (1H, d, *J* = 3.6 Hz, 6-H), 7.39–7.46 (3H, m, ArH), 7.61 (2H, d, *J* = 8.8 Hz, ArH), 7.68–7.71 (2H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 40.1, 85.8, 87.7, 88.1, 95.2, 100.0, 108.4, 111.5, 118.4, 121.8, 128.5, 129.6, 131.0, 132.4, 133.9, 142.4, 146.2, 150.5, 151.3. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{25}H_{21}N_4$: 377.1761; found: 377.1765

7-Methyl-4-(phenylethynyl)-2-{[4-(trifluoromethyl)phenyl] ethynyl}-7H-pyrrolo[2,3-d]pyrimidine (**14d**)



Yield 40 mg (25%); Pale yellow solid, mp 210–212 °C (dec.). IR (KBr): 2211 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.95 (3H, s, NCH_3), 6.77 (1H, d, *J* = 3.6 Hz, 5-H), 7.33 (1H, d, *J* = 3.6 Hz, 6-H), 7.40-7.46 (3H, m, ArH), 7.65 (2H, d, *J* = 8.0 Hz, ArH), 7.69–7.71 (2H, m, ArH), 7.81 (2H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.5, 83.8, 85.5, 90.9, 95.9, 100.3, 119.1, 121.6, 123.8 (q, $^{1}J_{C\text{-}F}$ = 271 Hz), 125.2 (q, $^{3}J_{C\text{-}F}$ = 3 Hz), 125.9, 128.5, 129.8, 130.7 (q, $^{2}J_{C\text{-}F}$ = 32 Hz), 131.8, 132.4, 132.6, 142.6, 144.8, 151.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.8. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{15}F_3N_3$: 402.1212; found: 402.1221

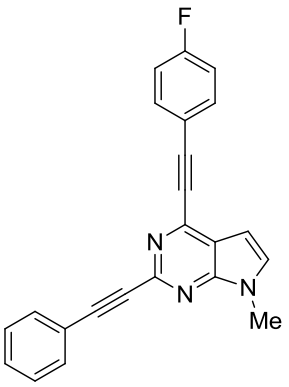
7-Methyl-2-(phenylethynyl)-4-(m-tolylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**14e**)



Yield 94 mg (68%); Yellow solid, mp 121–122 °C. IR (KBr): 2213 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (3H, s, CH_3), 3.94 (3H, s, NCH_3), 6.76 (1H, d, *J* = 3.2 Hz, 5-H), 7.25–7.33 (3H, m, 6-H, ArH), 7.37–7.44 (3H, m, ArH), 7.51 (1H, d, *J* = 8.8 Hz, ArH), 7.52 (1H, s, ArH), 7.69–7.73 (2H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 31.4, 85.4, 85.7, 89.0,

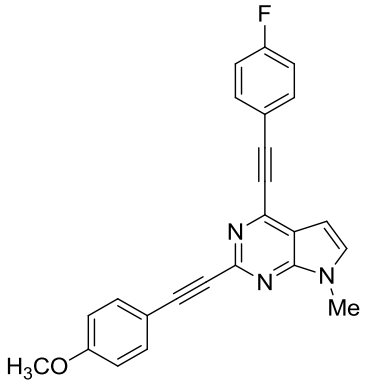
95.9, 100.2, 118.9, 121.5, 122.1, 128.2, 128.4, 129.0, 129.5, 130.6, 131.4, 132.5, 132.9, 138.2, 142.6, 145.4, 151.1. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{18}N_3$: 348.1495; found: 348.1492.

4-[(4-Fluorophenyl)ethynyl]-7-methyl-2-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**14f**)



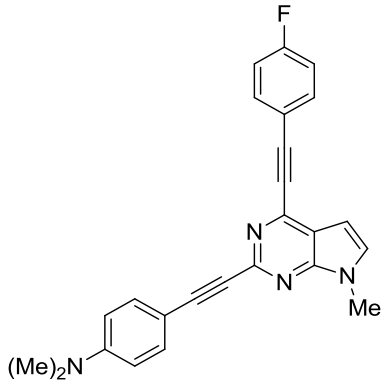
Yield 115 mg (82%); Yellow solid, mp 172–173 °C. IR (KBr): 2214 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.94 (3H, s, NCH_3), 6.73 (1H, d, *J* = 3.6 Hz, 5-H), 7.09-7.15 (2H, m, ArH), 7.30 (1H, d, *J* = 3.6 Hz, 6-H), 7.37-7.41 (3H, m, ArH), 7.76-7.72 (4H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 85.5, 85.8, 88.9, 94.4, 100.1, 116.0 (d, $^2J_{C\text{-}F}$ = 22 Hz), 117.8 (d, $^4J_{C\text{-}F}$ = 3 Hz), 118.8, 122.0, 128.3, 129.1, 131.5, 132.5, 134.5 (d, $^3J_{C\text{-}F}$ = 9 Hz), 142.3, 145.4, 151.1, 163.4 (d, $^1J_{C\text{-}F}$ = 250 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –108.2. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{23}H_{15}FN_3$: 352.1244; found: 352.1246.

4-[(4-Fluorophenyl)ethynyl]-2-[(4-methoxyphenyl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**14g**)



Yield 105 mg (79%); Yellow solid, mp 194-195^{o}C. IR (KBr): 2213 cm^{-1} (C≡C). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (3H, s, NCH_3), 3.92 (3H, s, OCH_3), 6.70 (1H, d, *J* = 3.6 Hz, 5-H), 6.91 (2H, d, *J* = 8.8 Hz, ArH), 7.08-7.14 (2H, m, ArH), 7.27 (1H, d, *J* = 3.6 Hz, 6-H), 7.63-7.69 (4H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 55.3, 85.5, 86.3, 88.0, 94.2, 100.0, 113.9, 114.0, 115.9 (d, $^{2}J_{C\text{-}F}$ = 22 Hz), 117.8 (d, $^{4}J_{C\text{-}F}$ = 4 Hz), 118.6, 131.3, 134.1, 134.5 (d, $^{3}J_{C\text{-}F}$ = 9 Hz), 142.3, 145.7, 151.7, 160.3, 163.3 (d, $^{1}J_{C\text{-}F}$ = 250 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = -108.3. ESI-HRMS: *m/z* $[M+H]^{+}$ calcd. for $C_{24}H_{17}FN_3O$: 382.1350; found: 382.1356.

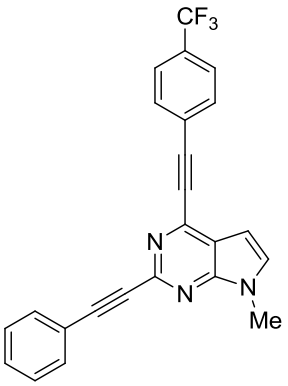
2-{[4-(Dimethylamino)phenyl]ethynyl}-4-[(4-fluorophenyl) ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**14h**)



Yield: 74 mg (47%); Brown solid, mp 216 °C (dec.). IR (KBr): 2198 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.02 [6H, s, $N(CH_3)_2$], 3.92 (3H, s, NCH_3), 6.66-6.70 (3H, m, 5-H, ArH), 7.09-7.16 (2H, m, ArH), 7.26 (1H, d, *J*

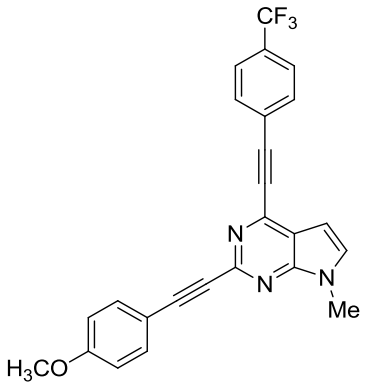
= 3.6 Hz, 6-H), 7.60 (2H, d, J = 8.8 Hz, ArH), 7.67 (2H, dd, ^{3}J = 8.4 Hz, $^{4}J_{H\text{-}F}$ = 5.6 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 40.1, 85.7, 87.6, 88.2, 94.0, 99.9, 108.4, 111.5, 116.1 (d, $^{2}J_{C\text{-}F}$ = 22 Hz), 117.9 (d, $^{4}J_{C\text{-}F}$ = 3 Hz), 118.3, 131.0, 133.9, 134.5 (d, $^{3}J_{C\text{-}F}$ = 9 Hz), 142.2, 146.2, 150.6, 151.3, 163.3 (d, $^{1}J_{C\text{-}F}$ = 251 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –108.4. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{25}H_{20}FN_4$: 395.1666; found: 395.1678.

7-Methyl-2-(phenylethynyl)-4-{[4-(trifluoromethyl)phenyl] ethynyl}-7H-pyrrolo[2,3-d]pyrimidine (**14i**)



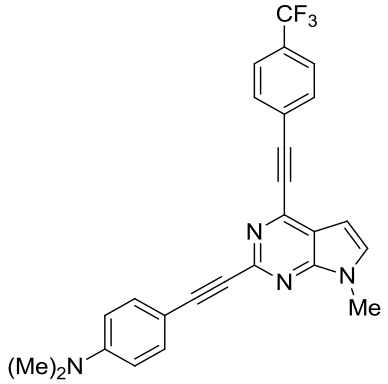
Yield 107 mg (67%); Yellow solid, mp 207–209 °C. IR (KBr): 2216 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.94 (3H, s, NCH_3), 6.73 (1H, d, J = 3.6 Hz, 5-H), 7.32 (1H, d, J = 3.6 Hz, 6-H), 7.37–7.41 (3H, m, ArH), 7.67 (2H, d, J = 8.0 Hz, ArH), 7.70–7.72 (2H, m, ArH), 7.79 (2H, d, J = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 86.0, 87.5, 88.8, 93.3, 100.0, 119.0, 121.9, 123.7, (q, $^{1}J_{C\text{-}F}$ = 271 Hz), 125.47 (q, $^{3}J_{C\text{-}F}$ = 4 Hz), 125.48, 128.3, 129.1, 131.3, (q, $^{2}J_{C\text{-}F}$ = 33 Hz), 131.9, 132.5, 132.6, 141.7, 145.4, 151.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.9. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{24}H_{15}F_3N_3$: 402.1212; found: 402.1213.

2-[(4-Methoxyphenyl)ethynyl]-7-methyl-4-{[4-(trifluoromethyl) phenyl]ethynyl}-7H-pyrrolo[2,3-d]pyrimidine (**14j**)



Yield 95 mg (55%); Yellow solid, mp 200–203 °C. IR (KBr): 2215 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (3H, s, NCH_3), 3.94 (3H, s, OCH_3), 6.73 (1H, d, *J* = 3.6 Hz, 5-H), 6.91 (2H, d, *J* = 8.8 Hz, ArH), 7.31 (1H, d, *J* = 3.6 Hz, 6-H), 7.64–7.69 (4H, m, ArH), 7.85 (2H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 55.3, 86.5, 87.6, 87.9, 93.2, 99.9, 113.9, 114.0, 118.8, 123.7 (q, $^{1}J_{C\text{-}F}$ = 270 Hz), 125.48, (q, $^{2}J_{C\text{-}F}$ = 3 Hz), 125.49, 131.2 (q, $^{2}J_{C\text{-}F}$ = 32 Hz), 131.7, 132.6, 134.1, 141.7, 145.7, 151.3, 160.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.9. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{25}H_{17}F_3N_3O$: 432.1318; found: 432.1322.

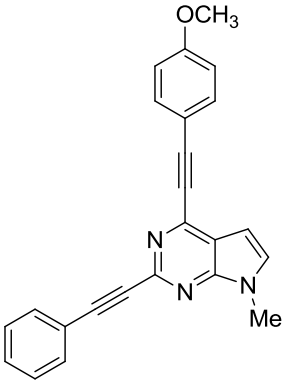
2-{[4-(Dimethylamino)phenyl]ethynyl}-7-methyl-4-{[4-(trifluoromethyl) phenyl]ethynyl}-7H-pyrrolo[2,3-d]pyrimidine (**14k**)



Yield 64 mg (36%); Light brown solid, mp 213 °C (dec.). IR (KBr): 2203 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.03 [6H, s, $N(CH_3)_2$], 3.94 (3H, s, NCH_3), 6.68 (2H, d, *J* = 8.8 Hz, ArH), 6.72 (1H, d, *J* = 3.6 Hz, 5-H), 7.29 (1H, d, *J* = 3.6 Hz, 6-H), 7.61 (2H, d, *J* = 8.8 Hz, ArH), 7.68 (2H, d, *J*

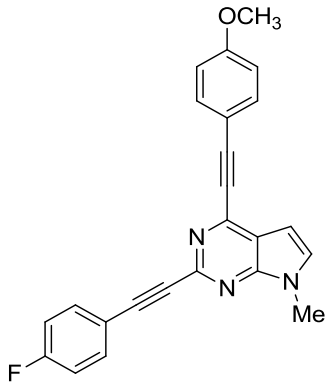
= 8.0 Hz, ArH), 7.80 (2H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 40.1, 87.6, 87.8, 88.4, 93.0, 99.9, 108.3, 111.5, 118.5, 123.7 (q, $^{1}J_{C\text{-}F}$ = 271 Hz), 125.4 (q, $^{3}J_{C\text{-}F}$ = 3 Hz), 125.6, 131.1 (q, $^{2}J_{C\text{-}F}$ = 32 Hz), 131.4, 132.6, 133.9, 141.7, 146.3, 150.6, 151.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –62.9. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{26}H_{20}F_3N_4$: 445.1634; found: 445.1644.

4-[(4-Methoxyphenyl)ethynyl]-7-methyl-2-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**14l**)



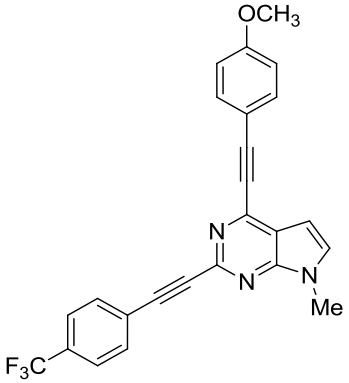
Yield 118 mg (81%); Yellow solid, mp 143–144 °C. IR (KBr): 2205 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (3H, s, NCH_3), 3.92 (3H, s, OCH_3), 6.72 (1H, d, *J* = 3.6 Hz, 5-H), 6.93 (2H, d, *J* = 8.8 Hz, ArH), 7.27 (1H, d, *J* = 3.6 Hz, 6-H), 7.36-7.39 (3H, m, ArH), 7.63 (2H, d, *J* = 8.8 Hz, ArH), 7.70-7.72 (2H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 55.3, 84.9, 85.6, 89.0, 96.2, 100.2, 113.6, 114.2, 118.6, 122.1, 128.2, 129.0, 131.2, 132.5, 134.1, 142.8, 145.4, 151.0, 160.7. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{24}H_{18}N_3O$: 364.1444; found: 364.1450.

2-[(4-Fluorophenyl)ethynyl]-4-[(4-methoxyphenyl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**14m**)



Yield 97 mg (73%); Yellow solid, mp 169-170 ^{o}C. IR (KBr): 2209 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (3H, s, NCH_3), 3.92 (3H, s, OCH_3), 6.72 (1H, d, *J* = 3.6 Hz, 5-H), 6.93 (2H, d, *J* = 8.8 Hz, ArH), 7.04-7.10 (2H, m, ArH), 7.27 (1H, d, *J* = 3.6 Hz, 6-H), 7.63 (2H, d, *J* = 8.8 Hz, ArH), 7.69 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H\text{-}F}$ = 5.2 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 55.3, 84.5, 84.9, 88.8, 96.3, 100.2, 113.6, 114.2, 115.7 (d, $^{2}J_{C\text{-}F}$ = 22 Hz), 118.2 (d, $^{4}J_{C\text{-}F}$ = 3 Hz), 118.7, 131.2, 134.1, 134.4 (d, $^{3}J_{C\text{-}F}$ = 8 Hz), 142.8, 145.2, 151.0, 160.8, 163.0 (d, $^{1}J_{C\text{-}F}$ = 249 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = -109.4. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{24}H_{17}FN_3O$: 382.1350; found: 382.1355.

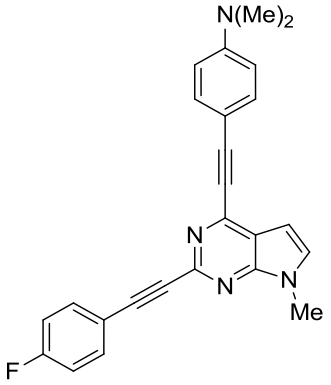
4-[(4-Methoxyphenyl)ethynyl]-7-methyl-2-{[4-(trifluoromethyl) phenyl]ethynyl}-7H-pyrrolo[2,3-d]pyrimidine (**14n**)



Yield 29 mg (17%); Light brown solid, mp 211–212 °C. IR (KBr): 2208 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (3H, s, NCH_3), 3.92 (3H, s, OCH_3), 6.73 (1H, d, *J* = 3.6 Hz, 5-H), 6.93 (2H, d, *J* = 8.8 Hz, ArH), 7.29 (1H,

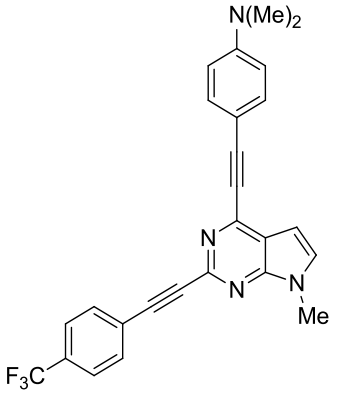
d, *J* = 3.6 Hz, 6-H), 7.61–7.65 (4H, m, ArH), 7.80 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 55.3, 83.7, 84.8, 91.0, 96.5, 100.3, 113.5, 114.2, 118.9, 123.8 (q, $^{1}J_{C\text{-}F}$ = 270 Hz), 125.2 (q, $^{3}J_{C\text{-}F}$ = 3 Hz), 126.0, 130.6 (q, $^{2}J_{C\text{-}F}$ = 32 Hz), 131.5, 132.6, 134.1, 142.9, 144.8, 150.9, 160.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.8. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{25}H_{17}F_3N_3O$: 432.1318; found: 432.1333.

2-[(4-Fluorophenyl)ethynyl]-4-{[4-(dimethylamino)phenyl] ethynyl}-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**14o**)



Yield 98 mg (62%); Orange solid, mp 227 °C (dec.). IR (KBr): 2192 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.03 [6H, s, $N(CH_3)_2$], 3.91 (3H, s, NCH_3), 6.68 (2H, d, *J* = 8.8 Hz, ArH), 6.72 (1H, d, *J* = 3.2 Hz, 5-H), 7.04–7.10 (2H, m, ArH), 7.24 (1H, d, *J* = 3.2 Hz, 6-H), 7.56 (2H, d, *J* = 8.8 Hz, ArH), 7.69 (2H, dd, ^{3}J = 8.8 Hz, $^{4}J_{H\text{-}F}$ = 5.2 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 40.0, 84.3, 84.8, 88.9, 98.6, 100.3, 107.8, 111.6, 115.6 (d, $^{2}J_{C\text{-}F}$ = 22 Hz), 118.37 (d, $^{4}J_{C\text{-}F}$ = 3 Hz), 118.39, 130.8, 133.9, 134.5 (d, $^{3}J_{C\text{-}F}$ = 9 Hz), 143.4, 145.2, 150.8, 151.0, 162.9 (d, $^{1}J_{C\text{-}F}$ = 249 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = –109.6. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{25}H_{20}FN_4$: 395.1666; found: 395.1667.

2-{[4-(Trifluoromethyl)phenyl]ethynyl}-4-{[4-(dimethylamino) phenyl]ethynyl}-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**14p**)

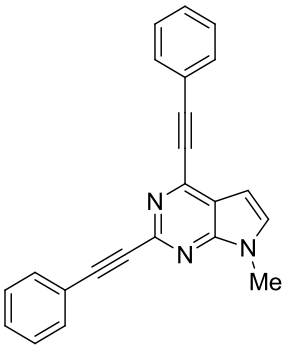


Yield 12.5 mg (7%); Brown solid, mp 246 °C (dec.). IR (KBr): 2197 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.04 [6H, s, $N(CH_3)_2$], 3.92 (3H, s, NCH_3), 6.69 (2H, d, *J* = 8.8 Hz, ArH), 6.75 (1H, d, *J* = 3.6 Hz, 5-H), 7.27 (1H, d, *J* = 3.6 Hz, 6-H), 7.57 (2H, d, *J* = 8.8 Hz, ArH), 7.64 (2H, d, *J* = 8.0 Hz, ArH), 7.81 (2H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 40.0, 83.5, 84.8, 91.2, 98.9, 100.4, 107.7, 111.6, 118.6, 123.8 (q, $^{1}J_{C\text{-}F}$ = 271 Hz), 125.2 (q, $^{3}J_{C\text{-}F}$ = 3 Hz), 126.1, 130.5 (q, $^{2}J_{C\text{-}F}$ = 32 Hz), 131.0, 132.6, 133.9, 143.5, 144.8, 150.8, 151.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.8. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{26}H_{20}F_3N_4$: 445.1634; found: 445.1641.

General procedure for the synthesis of 2,4-Bis(arylethynyl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidines **15a-i**

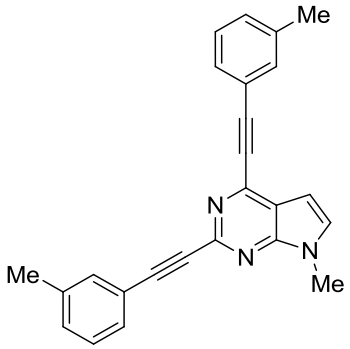
A solution of 2,4-dichloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**3**) (0.3 mmol) in anhydrous toluene (2 mL) was flushed with argon, after which $Pd(PPh_3)_2Cl_2$ (10.5 mg, 0.015 mmol), $AsPh_3$ (18.4 mg, 0.06 mmol) and the corresponding (arylethynyl)tributyltin (0.78 mmol) were added. The mixture was heated at reflux temperature under argon for 48–72 h. After cooling, the mixture was poured into aqous K_2CO_3 solution (0.5 M, 20 mL) containing CsF (50 mg), stirred for 30 min and extracted with $CHCl_3$. The extract was dried over Na_2SO_4, filtered and the $CHCl_3$ was removed on a rotary evaporator. The crude residue was purified by column chromatography ($CHCl_3$) to afford pure product **15a-i**.

7-Methyl-2,4-bis(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**15a**)



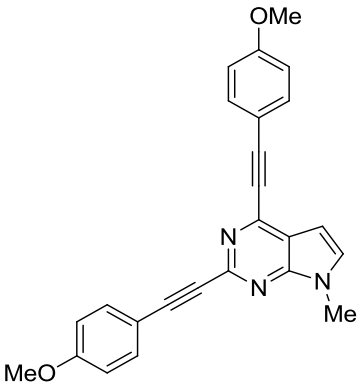
Yield 117 mg (71%), Yellow solid, mp 178-179 ^{o}C (2-PrOH). IR (KBr): 2214 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.94 (3H, s, NCH_3), 6.74 (1H, d, *J* = 3.6 Hz, 5-H), 7.30 (1H, d, *J* = 3.6 Hz, 6-H), 7.38-7.46 (6H, m, ArH), 7.69-7.73 (4H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 85.7, 85.8, 88.9, 95.6, 100.2, 118.9, 121.7, 122.1, 128.2, 128.5, 129.0, 129.7, 131.5, 132.4, 132.5, 142.5, 145.4, 151.1. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{23}H_{16}N_3$: 334.1339; found: 334.1346.

7-Methyl-2,4-bis(m-tolylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**15b**)



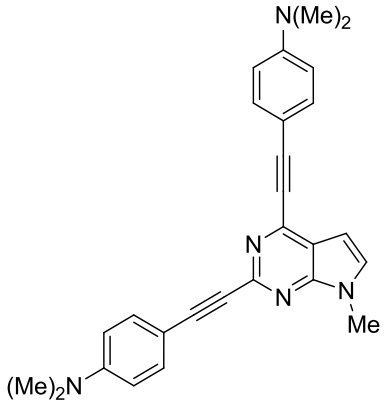
Yield 75 mg (69%); Off-white solid, mp 158–159 °C (2-PrOH). IR (KBr): 2204 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.37 (3H, s, CH_3), 2.40 (3H, s, CH_3), 3.93 (3H, s, NCH_3), 6.74 (1H, d, *J* = 3.6 Hz, 5-H), 7.20-7.27 (3H, m, 6-H, ArH), 7.29-7.33 (2H, m, ArH), 7.49-7.55 (4H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 (2 peaks overlapped), 31.4, 85.4, 86.0, 88.7, 95.8, 100.2, 118.8, 121.5, 121.9, 128.1, 128.4, 129.55, 129.59, 130.0, 130.6, 131.3, 132.9, 133.1, 137.9, 138.3, 142.6, 145.5, 151.2. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{25}H_{20}N_3$: 362.1652; found: 362.1662

2,4-Bis[(4-methoxyphenyl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**15c**)



Yield 66 mg (56%); Light brown solid, mp 197–198 °C (2-PrOH). IR (KBr): 2205 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.85 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.92 (3H, s, NCH_3), 6.72 (1H, d, *J* = 3.6 Hz, 5-H), 6.91 (2H, d, *J* = 8.8 Hz, ArH), 6.94 (2H, d, *J* = 8.8 Hz, ArH), 7.26 (1H, d, *J* = 3.6 Hz, 6-H), 7.64 (2H, d, *J* = 8.8 Hz, ArH), 7.66 (2H, d, *J* = 8.8 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 55.3, 55.4, 85.0, 86.1, 88.1, 96.1, 100.1, 113.7, 113.9, 114.1, 114.2, 118.4, 131.0, 134.12, 134.13, 142.8, 145.7, 151.1, 160.2, 160.7. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{25}H_{20}N_3O_2$: 394.1550; found: 394.1555.

2,4-Bis{[4-(dimethylamino)phenyl]ethynyl}-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**15d**)

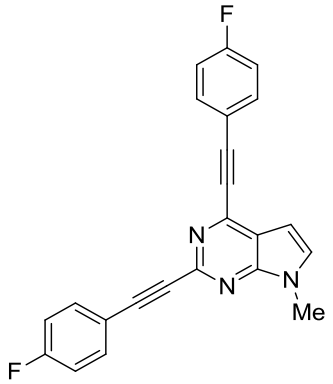


Yield 40 mg (32%); Light brown solid, mp 251–253 °C (2-PrOH). IR (KBr): 2197 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.02 [6H, s, $N(CH_3)_2$], 3.04 [6H, s, $N(CH_3)_2$], 3.90 (3H, s, NCH_3), 6.66–6.71 (5H, m, ArH, 5-H), 7.20 (1H, d, *J* = 3.6 Hz, 6-H), 7.57 (2H, d, *J* = 9.2 Hz, ArH), 7.60 (2H, d,

J = 9.2 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.3, 40.10 (2 peaks overlapped), 40.12 (2 peaks overlapped), 85.0, 87.7, 87.9, 98.1, 100.2, 108.1, 108.7, 111.5, 111.6, 117.9, 130.3, 133.8, 133.9, 143.4, 146.2, 150.5, 150.9, 151.0. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{27}H_{26}N_5$: 420.2183; found: 420.2178.

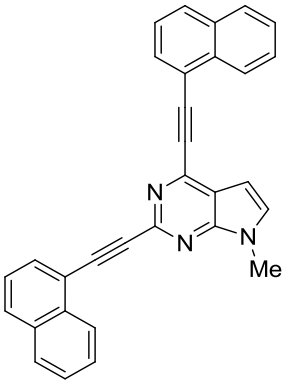
2,4-Bis[(4-fluorophenyl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine

(15e)



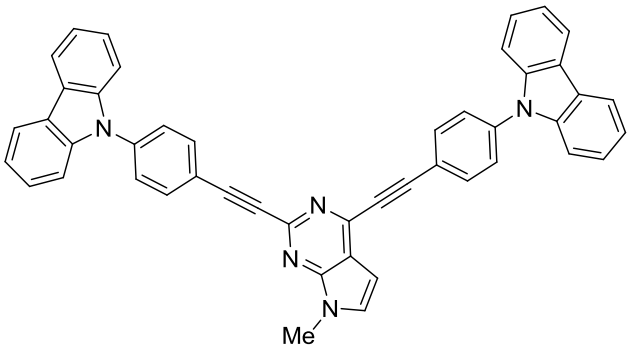
Yield 68 mg (61%); Yellow solid, mp 213–214 °C. IR (KBr): 2216 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.93 (3H, s, NCH_3), 6.72 (1H, d, *J* = 3.6 Hz, 5-H), 7.06-7.14 (4H, m, ArH), 7.30 (1H, d, *J* = 3.6 Hz, 6-H), 7.66-7.71 (4H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 84.7, 85.4, 88.6, 94.5, 100.1, 115.7 (d, $^2J_{C\text{-}F}$ = 22 Hz), 116.0 (d, $^2J_{C\text{-}F}$ = 22 Hz), 117.8 (d, $^4J_{C\text{-}F}$ = 3 Hz), 118.2 (d, $^4J_{C\text{-}F}$ = 3 Hz), 118.8, 131.6, 134.5 (d, $^3J_{C\text{-}F}$ = 9 Hz), 134.51 (d, $^3J_{C\text{-}F}$ = 9 Hz), 142.3, 145.2, 151.1, 163.0 (d, $^1J_{C\text{-}F}$ = 250 Hz), 163.3 (d, $^1J_{C\text{-}F}$ = 250 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = -109.3, -108.1. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{23}H_{14}F_2N_3$: 370.1150; found: 370.1156.

***7-Methyl-2,4-bis[(naphthalen-1-yl)ethynyl]-7H-pyrrolo[2,3-d]pyrimidine* (15f)**



Yield 68 mg (52%); Light brown solid, mp 218–220 °C (toluene). IR (KBr): 2205 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.98 (3H, s, NCH_3), 6.86 (1H, d, *J* = 3.6 Hz, 5-H), 7.35 (1H, d, *J* = 3.6 Hz, 6-H), 7.49–7.61 (4H, m, ArH), 7.64–7.71 (2H, m, ArH), 7.89–7.99 (6H, m, ArH), 8.60 (1H, d, *J* = 8.4 Hz, ArH), 8.67 (1H, d, *J* = 8.4 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 84.0, 90.5, 93.8, 93.9, 100.2, 119.1, 119.3, 119.8, 125.2, 125.3, 126.1, 126.5, 126.72, 126.73, 127.0, 127.3, 128.2, 128.4, 129.6, 130.3, 131.6, 131.7, 132.0, 133.1, 133.2, 133.3, 133.7, 142.7, 145.7, 151.2. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{31}H_{20}N_3$: 434.1652; found: 434.1668

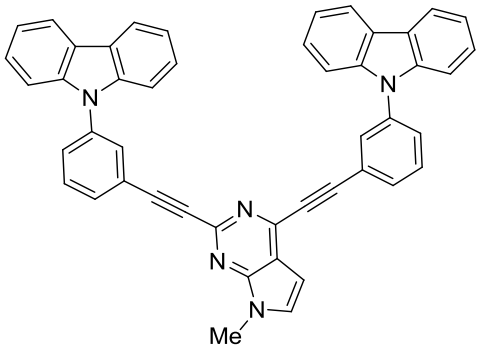
***2,4-Bis{[4-(9-carbazolyl)phenyl]ethynyl}-7-methyl-7H-pyrrolo[2,3-d]pyrimidine* (15g)**



Yield 119 mg (60%); Off-white solid, mp >310 °C (toluene). IR (KBr): 2212 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.00 (3H, s, NCH_3), 6.83 (1H, d, *J* = 3.2 Hz, 5-H), 7.32–7.38 (5H, m, 6-H, Cbz-H), 7.44–7.53 (8H, m, Cbz-H), 7.65 (2H, d, *J* = 8.4 Hz, ArH), 7.69 (2H, d, *J* = 8.4 Hz, ArH), 7.96 (2H, d, *J* = 8.4 Hz, ArH), 7.98 (2H, d, *J* = 8.4 Hz, ArH), 8.16–8.19 (4H, m,

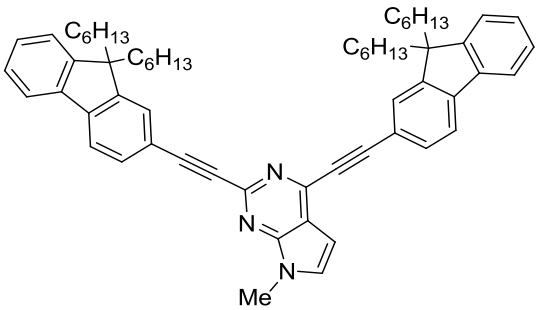
Cbz-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.5, 85.1, 86.5, 89.8, 94.8, 100.2, 109.7, 109.8, 119.1, 120.32, 120.37, 120.45, 120.47, 120.9, 123.6, 123.7, 126.1, 126.2, 126.7, 126.8, 131.7 (2 peaks overlapped), 134.0, 134.1, 138.4, 139.0, 140.4, 140.5, 142.3, 145.3, 151.2. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{47}H_{30}N_5$: 664.2496; found: 664.2488.

***2,4-Bis{[3-(9-carbazolyl)phenyl]ethynyl}-7-methyl-7H-pyrrolo[2,3-d]pyrimidine* (15h)**



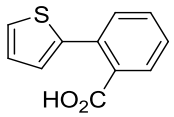
Yield: 88 mg (44%); Light brown solid, mp 238–241 °C (toluene). IR (KBr): 2213 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.93 (3H, s, NCH_3), 6.74 (1H, d, *J* = 3.6 Hz, 5-H), 7.30 (1H, d, *J* = 3.6 Hz, 6-H), 7.31–7.36 (4H, m, Cbz-H), 7.44-7.50 (8H, m, Cbz-H), 7.63-7.68 (4H, m, Cbz-H), 7.78-7.83 (2H, m, ArH), 7.93 (1H, s, ArH), 7.96 (1H, s, ArH), 8.18 (2H, d, *J* = 8.0 Hz, ArH), 8.19 (2H, d, *J* = 8.0 Hz, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 84.6, 86.6, 89.9, 94.2, 100.1, 109.6, 109.8, 119.1, 120.2, 120.32, 120.33, 120.4, 123.5, 123.6, 124.0, 126.0, 126.1, 127.8, 128.3, 128.5, 129.9, 130.2, 130.7, 130.8, 131.2, 132.3, 131.9, 137.9, 138.1, 140.6, 140.7, 142.0, 145.1, 151.1. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{47}H_{30}N_5$: 664.2496; found: 664.2500.

***2,4-Bis[(9,9-dihexyl-9H-fluoren-2-yl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine* (15i)**



Yield 145 mg (57%); Yellow solid, mp 78–81 °C. IR (KBr): 2209 (C≡C) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.57–0.61 (8H, m, 4×CH_2), 0.79 (12H, t, *J* = 6.8 Hz, 4×CH_3), 1.07-1.17 [24H, m, 4×$(CH_2)_3$], 1.97-2.03 (8H, m, 4×CH_2), 3.97 (3H, s, NCH_3), 6.82 (1H, d, *J* = 3.6 Hz, 5-H), 7.32 (1H, d, *J* = 3.6 Hz, 6-H), 7.34–7.39 (7H, m, ArH), 7.68–7.76 (7H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (2 peaks overlapped), 22.5 (2 peaks overlapped), 23.7 (2 peaks overlapped), 29.6 (2 peaks overlapped), 31.51, 31.53 (2 peaks overlapped), 40.3 (2 peaks overlapped), 55.1, 55.2, 85.9, 87.1, 89.0, 96.9, 100.3, 118.6, 119.5, 119.7, 120.14, 120.18, 120.2, 122.8, 122.9, 126.8, 126.9, 127.0, 127.3, 127.6, 127.9, 128.3, 131.2, 131.3, 131.4, 140.1, 140.3, 142.2, 142.7, 142.8, 145.7, 150.5, 150.8, 151.25, 151.27, 151.3. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{61}H_{72}N_3$: 846.5721; found: 846.5707.

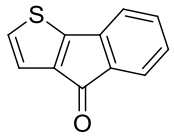
***2-(2-Thienyl)benzoic acid* (19)**.



A mixture of $NiCl_2(PPh_3)_2$ (144.5 g, 0.221 mol), PPh_3 (115.8 g, 0.442 mol), and Zn (14.3 g, 0.221 mol) was stirred at room temperature for 30 min under argon atmosphere till the reaction mixture became dark-red. Then a solution of 2-chlorobenzonitrile (379.5 g, 2.760 mol) in THF (1000 ml) was added to the reaction mixture. Thiophene Grignard reagent, prepared by reacting 2-bromothiophene (500 g, 3.07 mol) with magnesium turnings (76.5 g, 3.15 mol) in THF (1000 ml), was added dropwise to the reaction mixture at such a speed that temperature would not rise above 30°C. The reaction mixture

was stirred at room temperature for 2 h and left overnight, then poured into ice water, acidified with concentrated hydrochloric acid to pH 2-4, and extracted with CH_2Cl_2 (2×750 ml). The combined extracts were dried over Na_2SO_4 and filtered. After the removal of the solvent from the filtrate, the obtained viscous dark-brown residue was distilled under vacuum and the fraction with bp 145-155°C/1 mbar was collected to give 300.0 g of 2-(2-thienyl)benzonitrile as a viscous yellow oil. The obtained crude 2-(2-thienyl)benzonitrile was added to a mixture of ethylene glycol (1200 ml), water (50 ml), and KOH (320 g, 5.7 mol). The reaction mixture was stirred at 130-140°C for 24 h. After cooling to room temperature, the mixture was poured into water, acidified with concentrated HCl to pH 1-2, and extracted with CH_2Cl_2 (3×500 ml). After removal of the solvent, the brown residue was recrystallized from hexane to give 250 g (44%) of compound **19** as a white solid, mp 91-93 °C (hexane). Lit. [247]: mp 92-94 °C . ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.08-7.14 (2H, m, H-3,4 thienyl), 7.39 (1H, dd, ^3J = 4.8 Hz, ^4J = 1.6 Hz, H-5 thienyl), 7.41-7.54 (2H, m, H-4,5 Ph), 7.57 (1H, dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, H-3 Ph), 7.94 (1H, dd, ^3J = 7.6 Hz, ^4J = 1.6 Hz, H-6 Ph), 10.09 (1H, s, COOH). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 126.4, 127.1, 127.5, 128.1, 130.5, 130.8, 132.1, 132.2, 135.4, 141.9, 173.9. Found, %: C 64.32; H 3.96. $C_{11}H_8O_2S$. Calculated, %: C 64.69; H 3.95.

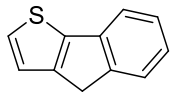
4H-Indeno[1,2-b]thiophen-4-one **(20)**.



A mixture of 2-(2-thienyl)benzoic acid (**19**) (150 g, 0.735 mol), $SOCl_2$ (88 g, 0.74 mol), and 1,2-dichloroethane (250 ml) was refluxed for 8 h. Then the reaction mixture was cooled to -18°C, and a solution of $AlCl_3$ (103 g, 0.75 mol) and $MeNO_2$ (122 g, 2 mol) in 1,2-dichloroethane (300 ml) was added dropwise within 1 h. After the addition was complete, the reaction mixture was left to warm to room temperature for 1 h. The mixture was poured into 5 M HCl (500 ml) and stirred for 30 min. The organic layer was separated, washed

twice with water, dried over Na_2SO_4, and filtered. After removal of the solvent from the filtrate, the obtained dark-brown residue was distilled under vacuum at 122°C/0.5 mbar and recrystallized from hexane to give 96 g (70%) of compound **20** as orange solid, mp 101-102°C (hexane). Lit [247]: yield 59%, mp 99-101°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13-7.22 (4H, m, H-2,3,6,8), 7.35 (1H, td, ^3J = 7.6 Hz, ^4J = 0.8 Hz, H-7), 7.46 (1H, dd, ^3J = 7.6 Hz, ^4J = 0.8 Hz, H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 119.5, 121.7, 123.9, 128.7, 129.3, 134.1, 136.7, 139.0, 142.2, 159.2, 187.5. Found, %: C 70.69; H 3.24. $C_{11}H_6OS$. Calculated, %: C 70.94; H 3.25.

***4H-Indeno[1,2-b]thiophene* (21)**.

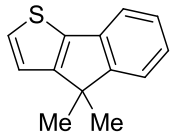


A mixture of 4*H*-indeno[1,2-*b*]thiophen-4-one (**20**) (40 g, 0.215 mol), hydrazine hydrate (36 g of 50% solution in water, 0.36 mol), and diethylene glycol (150 ml) was heated at 110°C for 3 h, then cooled to 40°C, and KOH (36 g, 0.645 mol) was added. The reaction mixture was heated to 110°C and stirred for 4 h. After cooling to room temperature, the mixture was poured into water (400 ml) and extracted with CH_2Cl_2 (3×150 ml). The organic layer was separated and washed with water until neutral reaction (pH 7). After removal of the solvent, the solid was recrystallized from hexane to give 32 g (82%) of compound **21** as a yellowish solid, mp 68-70°C (hexane). Lit [247]: yield 78%, mp 68-69°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (2H, s, CH_2), 7.16 (1H, d, *J* = 4.4, H-3), 7.24-7.34 (2H, m, H-5,8), 7.35 (1H, d, *J* = 4.4, H-2), 7.52-7.55 (2H, m, H-6,7). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 34.2, 119.0, 122.9, 125.0, 125.3, 127.1, 127.3, 139.1, 143.4, 146.3, 147.4. Mass spectrum, *m*/*z* (I_{rel}, %): 172 $[M]^+$ (100), 139 (10), 127 (20), 86 (14). Found, %: C 76.46; H 4.63. $C_{11}H_8S$. Calculated, %: C 76.70; H 4.68.

General procedure for the synthesis of 4,4-dialkyl-4H-indeno[1,2-b]-thiophenes (**22a-e**)

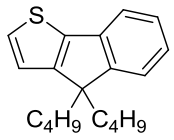
Potassium *tert*-butoxide (3.9 g, 34.8 mmol) was added to a solution of 4*H*-indeno[1,2-*b*]-thiophene (**21**) (2.0 g, 11.6 mmol) in THF (30 ml). The reaction mixture was stirred at room temperature for 1 h. Then the corresponding alkyl iodide (for compounds **22a**, **22b**, **22e**) or bromide (for compounds **22c**, **22d**) (34.8 mmol) was added, and the reaction mixture was stirred for an additional hour. The reaction was quenched with water and extracted with CH_2Cl_2 (3×50 ml); the organic layer was separated and washed with water until neutral reaction (pH 7). After evaporation of the solvent, the product was recrystallized from 2-PrOH (compound **22a**) or purified by silica gel column chromatography (eluent hexane, compounds **22b-e**).

4,4-Dimethyl-4H-indeno[1,2-b]thiophene (**22a**)



Yield 1.90 g (82%); White solid, mp 84-85°C (2-PrOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 (6H, s, 2xCH_3), 7.08 (1H, d, *J* = 5.2 Hz, H-3), 7.24-7.32 (2H, m, H-5,8), 7.34 (1H, d, *J* = 5.2, H-2), 7.48-7.50 (2H, m, H-6,7). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.3, 45.7, 119.1, 120.9, 122.6, 125.4, 127.2, 127.8, 136.8, 140.0, 156.5, 158.6. Found, %: C 77.45; H 6.04. $C_{13}H_{12}S$. Calculated, %: C 77.95; H 6.04.

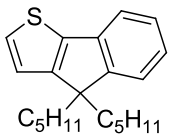
4,4-Dibutyl-4H-indeno[1,2-b]thiophene (**22b**)



Yield 2.5 g (76%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.69-0.85 (4H, m, 2xCH_2), 0.75-0.87 (6H, t, *J* = 7.6 Hz, 2xCH_3), 1.13-1.21 (4H, m, 2xCH_2), 1.89-1.99 (4H, m, 2xCH_2), 7.20 (1H, d, *J* = 4.8 Hz, H-3), 7.31-7.33 (3H, m, H-5,6,7), 7.38 (1H, d, *J* = 4.8 Hz, H-2), 7.45 (1H, d, *J* = 7.6 Hz, H-8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 23.3, 26.6, 39.0, 54.0, 118.8, 121.8,

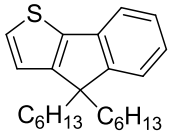
122.8, 125.2, 126.9, 127.3, 138.5, 141.4, 154.1, 155.6. Found, %: C 80.22; H 9.03. $C_{19}H_{24}S$. Calculated, %: C 80.22; H 8.59.

4,4-Dipentyl-4H-indeno[1,2-b]thiophene (**22c**)



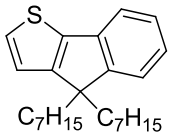
Yield 2.3 g (64%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.71-0.89 (4H, m, 2xCH_2), 0.83 (6H, t, *J* = 7.2 Hz, 2xCH_3), 1.14-1.23 (8H, m, 4xCH_2), 1.97-2.07 (4H, m, 2xCH_2), 7.04 (1H, d, *J* = 4.8 Hz, H-3), 7.30-7.36 (3H, m, H-5,6,7), 7.39 (1H, d, *J* = 4.8 Hz, H-2), 7.51 (1H, d, *J* = 7.2 Hz, H-8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.6, 24.1, 32.6, 39.3, 54.1, 118.9, 121.8, 122.8, 125.3, 127.0, 127.4, 138.6, 141.5, 154.2, 155.6. Mass spectrum, *m*/*z* (I_{rel}, %): 312 $[M]^+$ (70), 241 (90), 185 (100), 171 (35), 152 (14). Found, %: C 80.7; H 9.03. $C_{21}H_{28}S$. Calculated, %: C 80.71; H 9.03.

4,4-Dihexyl-4H-indeno[1,2-b]thiophene (**22d**).



Yield 2.8 g (71%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.72-0.89 (4H, m, 2xCH_2), 0.88 (6H, t, *J* = 7.6, 2xCH_3), 1.12-1.21 (12H, m, 6xCH_2), 1.96-2.06 (4H, m, 2xCH_2), 7.07 (1H, d, *J* = 4.8 Hz, H-3), 7.27-7.38 (3H, m, H-5,6,7), 7.38 (1H, d, *J* = 4.8 Hz, H-2), 7.51 (1H, d, 7.2 Hz, H-8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.9, 24.4, 30.0, 31.9, 39.3, 54.1, 118.9, 121.8, 122.8, 125.2, 127.0, 127.4, 138.6, 141.5, 154.1, 155.6. Mass spectrum, *m*/*z* (I_{rel}, %): 340 $[M]^+$ (63), 255 (85), 185 (100), 171 (32), 152 (12). Found, %: C 80.92; H 9.44. $C_{23}H_{32}S$. Calculated, %: C 81.11; H 9.47.

4,4-Diheptyl-4H-indeno[1,2-b]thiophene (**22e**)

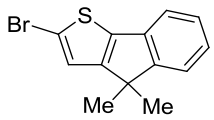


Yield 3.6 g (84%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.75-0.91 (4H, m, 2xCH_2), 0.91 (6H, t, *J* = 7.2 Hz, 2xCH_3), 1.17-1.29 (16H, m, 8xCH_2), 1.91-2.07 (4H, m, 2xCH_2), 7.03 (1H, d, *J* = 4.8 Hz, H-3), 7.24-7.36 (3H, m, H-5,6,7), 7.36 (1H, d, *J* = 4.8 Hz, H-2), 7.47 (1H, d, *J* = 7.2, H-8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.8, 24.4, 29.3, 30.3, 32.1, 39.3, 54.1, 118.9, 121.8, 122.8, 125.3, 127.0, 127.3, 138.5, 141.4, 154.1, 155.6. Found, %: C 80.96; H 9.87. $C_{25}H_{36}S$. Calculated, %: C 81.46; H 9.84.

General procedure for the synthesis of 2-bromo-4,4-dialkyl-4H-indeno[1,2-b]thiophenes (**23a-e**)

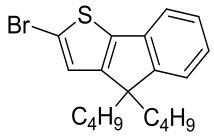
NBS (1.47 g, 8.25 mmol) was added in portions to a cooled (0^{o}C) and protected from a daylight solution of the corresponding 4,4-dialkylindeno[1,2-*b*]thiophene (**22**) (7.5 mmol) in DMF (25 mL), The reaction mixture was stirred at 0^{o}C for 2 h then allowed to reach room temperature. The reaction was quenched with water (100 ml) and extracted with CH_2Cl_2. After removal of the solvent, the products were purified by column chromatography on silica gel (eluent hexane).

2-Bromo-4,4-dimethyl-4H-indeno[1,2-b]thiophene (**23a**).



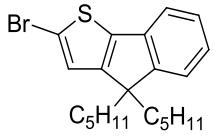
Yield 1.9 g (90%), white solid, mp 54-55°C (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (6H, s, 2xCH_3), 7.08 (1H, s, H-3), 7.25-7.33 (2H, m, H-5,6), 7.38-7.40 (2H, m, H-7,8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1, 46.7, 113.7, 119.0, 122.0, 124.2, 125.7, 127.3, 136.4, 140.2, 155.1, 157.4. Found, %: C 56.23; H, 3.98. $C_{13}H_{11}BrS$. Calculated, %: C 55.92; H 3.97.

2-Bromo-4,4-dibutyl-4H-indeno[1,2-b]thiophene (**23b**)



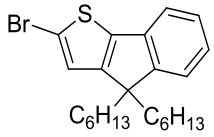
Yield 2.2 g (82%), white solid, mp 61-63°C (hexane). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.73-0.84 (4H, m, 2xCH_2), 0.77 (6H, t, *J* = 7.2 Hz, 2xCH_3), 1.12-1.17 (4H, m, 2xCH_2), 1.81-1.92 (4H, m, 2xCH_2), 7.02 (1H, s, H-3), 7.20-7.29 (2H, m, H-5,6), 7.31-7.39 (2H, m, H-7,8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 23.2, 26.5, 38.9, 55.0, 113.3, 118.8, 122.8, 124.8, 125.5, 127.1, 138.1, 141.7, 152.7, 154.4. Mass spectrum, *m*/*z* (I_{rel}, %): 364 $[M]^+$ (60), 307 (50), 251 (20), 226 (100), 198 (46), 184 (75), 139 (24). Found, %: C 63.13; H 6.55. $C_{19}H_{23}BrS$. Calculated, %: C 62.80; H 6.38.

2-Bromo-4,4-dipentyl-4H-indeno[1,2-b]thiophene (**23c**)



Yield 2.7 g (92%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.77-0.82 (4H, m, 2xCH_2), 0.81 (6H, t, *J* = 7.2 Hz, 2xCH_3), 1.11-1.16 (8H, m, 4xCH_2), 1.72-1.98 (4H, m, 2xCH_2), 7.01 (1H, s, H-3), 7.20-7.30 (2H, m, H-5,6), 7.31-7.41 (2H, m, H-7,8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 22.6, 24.0, 32.4, 39.1, 55.1, 113.3, 118.8, 122.8, 124.8, 125.5, 127.1, 138.1, 141.7, 152.7, 154.7. Found, %: C 64.92; H 7.06. $C_{21}H_{27}BrS$. Calculated, %: C 64.44; H 6.95.

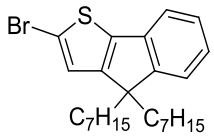
2-Bromo-4,4-dihexyl-4H-indeno[1,2-b]thiophene (**23d**)



Yield 2.8 g (89%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79-0.85 (4H, m, 2xCH_2), 0.82 (6H, t, *J* = 7.2 Hz, 2xCH_3), 1.15-1.22 (12H, m, 6xCH_2), 1.81-1.98 (4H, m, 2xCH_2), 7.03 (1H, s, H-3), 7.21-7.32 (2H, m, H-5,6), 7.37-7.44 (2H, m, H-7,8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 22.8,

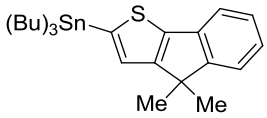
24.3, 29.8, 31.8, 39.0, 55.1, 113.3, 118.8, 122.8, 124.9, 125.5, 127.1, 138.1, 141.7, 152.7, 154.6. Found, %: C 65.69; H 7.43. $C_{23}H_{31}BrS$. Calculated, %: C 65.86; H 7.45.

2-Bromo-4,4-diheptyl-4H-indeno[1,2-b]thiophene (**22e**)



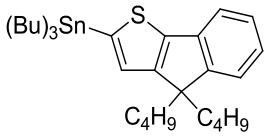
Yield 2.61 g (78%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78-0.84 (4H, m, 2xCH_2), 0.86 (6H, t, *J* = 7.2 Hz, 2xCH_3), 1.12-126 (16H, m, 8xCH_2), 1.78-1.95 (4H, m, 2xCH_2), 7.01 (1H, s, H-3), 7.20-7.30 (2H, m, H-5,6), 7.32-7.39 (2H, m, H-7,8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.8, 24.3, 29.2, 30.2, 32.0, 39.1, 55.1, 113.3, 118.8, 122.8, 124.9, 125.5, 127.1, 138.1, 141.7, 152.7, 154.5. Found, %: C 66.93; H 7.92. $C_{25}H_{35}BrS$. Calculated, %: C 67.10; H 7.88.

Tributyl(4,4-dimethyl-4H-indeno[1,2-b]thiophen-2-yl)stannane (**24a**)



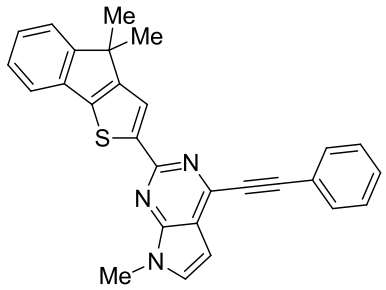
Compound **24a** was synthesized according to the procedure described for (aryl)tributylstannanes **11a-e**. Reaction was carried out starting from 2-bromo-4,4-dimethyl-4*H*-indeno[1,2-*b*]thiophene (**23a**) (1.0 g, 3.6 mmol). The obtained compound was used further without additional purification. Yield 1.6 g (94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (9H, t, *J* = 7.6 Hz, 3xCH_3), 1.16 (6H, t, *J* = 7.6 Hz, 3xCH_2), 1.34-1.45 (6H, m, 3xCH_2), 1.50 (6H, s, 2xCH_3); 1.59-1.68 (6H, m, 3xCH_2), 7.07 (1H, s); 7.17-7.34 (2H, m, H-6,7); 7.37 (1H, d, *J* = 7.2 Hz, H-5) 7.43 (1H, d, *J* = 7.2 Hz, H-8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.9, 13.7, 26.2, 27.3, 29.0, 44.8, 118.9, 122.4, 124.9, 126.8, 128.5, 136.6, 140.6, 145.6, 156.6, 160.4.

Tributyl(4,4-dibutyl-4H-indeno[1,2-b]thiophen-2-yl)stannane (**24b**)



Compound **24b** was synthesized according to the procedure described for (aryl)tributylstannanes **11a-e**. Reaction was carried out starting from 2-bromo-4,4-dimethyl-4*H*-indeno[1,2-*b*]thiophene (**23b**) (1.0 g, 2.75 mmol). The obtained compound was used further without additional purification. Yield 1.25 g (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.72-0.89 (10H, m, 2xCH_2, 2xCH_3), 0.92 (9H, t, *J* = 7.6 Hz, 3xCH_3), 1.10-1.22 (10H, m, 5xCH_2) 1.32-1.46 (6H, m, 3xCH_2), 1.68-1.88 (10H, m, 5xCH_2). 6.98 (1H, s, H-3, 7.15-7.33(3H, m, H-5,6,7), 7.41 (1H, d, *J* = 7.2 Hz, H-8). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.1, 13.4, 23.2, 26.2, 26.5, 27.5, 29.2, 38.9, 49.4, 118.8, 122.6, 125.3, 126.7, 128.7, 136.8, 140.6, 145.7, 156.8, 160.5.

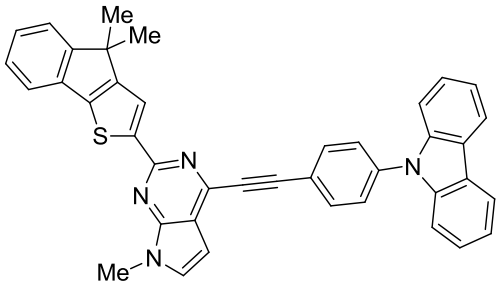
2-(4,4-Dimethyl-4H-indeno[1,2-b]thiophen-2-yl)-7-methyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**25a**)



Compound **25a** was synthesized according to the procedure described for 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**12a**–**o**). Reaction was carried out starting from 2-chloro-7-methyl-4-(phenylethynyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**8a**) (75 mg, 0.28 mmol). Yield 106 mg (88%). Yellow solid, mp 158-160 ^{o}C. IR (KBr): 2209 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (6H, s, 2xCH_3), 3.93 (3H, s, NCH_3), 6.70 (1H, d, *J* = 3.6 Hz, 5-H), 7.19 (1H, d, *J* = 3.6 Hz, 6-H), 7.26 (1H, td, ^{3}J = 7.2 Hz, ^{4}J = 1.2 Hz, 6'-H), 7.33 (1H, td, ^{3}J = 7.2 Hz, ^{4}J = 1.2 Hz, 7'-H), 7.42 (1H, d, *J* = 7.2 Hz, 5'-H), 7.43-7.45 (3H, m, ArH), 7.52 (1H, d, *J* = 7.2 Hz, 8'-H), 7.72-7.75 (2H, m,

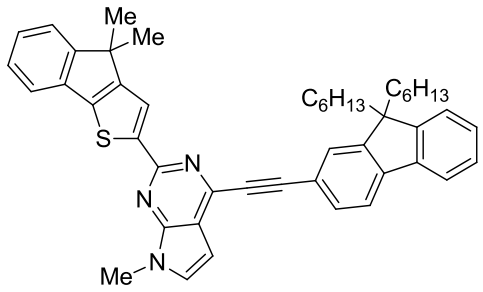
ArH), 8.10 (1H, s, 3'-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1, 31.0, 45.9, 86.2, 94.8, 100.1, 118.2, 119.3, 121.7, 122.0, 122.3, 125.7, 127.1, 128.5, 129.5, 130.2, 132.4, 136.8, 142.2, 142.6, 146.8, 151.6, 155.5, 156.3, 158.9. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{28}H_{22}N_3S$: 432.1529; found: 432.1526.

4-{[4-(9-Carbazolyl)phenyl]ethynyl}-2-(4,4-dimethyl-4H-indeno[1,2-b]thiophen-2-yl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**25b**)



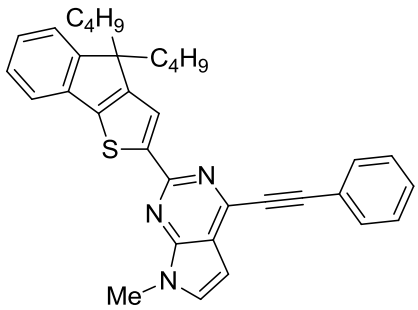
Compound **25b** was synthesized according to the procedure described for 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**12a–o**). Reaction was carried out starting from 4-{[4-(9-carbazolyl)phenyl]ethynyl}-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**8g**) (75 mg, 0.17 mmol). Yield 73 mg (71%). Yellow solid, mp 165-167 ^{o}C. IR (KBr): 2209 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.58 (6H, s, 2xCH_3), 3.96 (3H, s, NCH_3), 6.74 (1H, d, *J* = 3.6 Hz, 5-H), 7.20-7.25 (2H, m, 6-H, 6'-H), 7.32-7.37 (3H, m, 7'-H, cbz-H), 7.42-7.54 (6H, m, 5'-H, 8'-H, cbz-H), 7.69 (2H, d, *J* = 8.4 Hz, ArH), 7.97 (2H, d, *J* = 8.4 Hz, ArH), 8.13 (1H, s, 3'-H), 8.19 (2H, d, *J* = 7.6 Hz, cbz-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.0, 31.1, 45.9, 87.1, 94.0, 100.1, 109.8, 118.2, 119.3, 120.4, 120.8, 121.7, 122.4, 123.7, 125.7, 126.1, 126.8, 127.1, 128.3. 130.4, 133.9, 136.7, 138.8, 140.4, 141.9, 142.8, 146.7, 151.7, 155.6, 156.4, 158.9. HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{40}H_{29}N_4S$: 597.2107; found: 597.2104.

4-[(9,9-Dihexyl-9H-fluoren-2-yl)ethynyl]-2-(4,4-dimethyl-4H-indeno[1,2-b]thiophen-2-yl)-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**25c**)



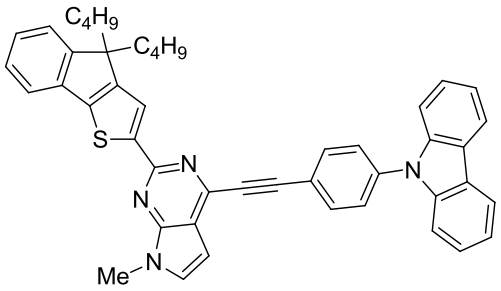
Compound **25c** was synthesized according to the procedure described for 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**12a–o**). Reaction was carried out starting from 2-chloro-4-[(9,9-dihexyl-9*H*-fluoren-2-yl)ethynyl]-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**8h**) (75 mg, 0.14 mmol). Yield 66 mg (67%). Yellow solid, mp 110-113 ^{o}C . IR (KBr): 2206 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.62-0.67 (4H, m, 2xCH_2), 0.79 (6H, t, *J* = 7.2 Hz, 2xCH_3), 1.04-1.17 (12H, m, 6xCH_2), 2.01-2.05 (4H, m, 2xCH_2), 3.95 (3H, s, NCH_3), 6.77 (1H, d, *J* = 3.6 Hz, 5-H), 7.22 (1H, d, *J* = 3.6 Hz, 6-H), 7.26 (1H, dt, *J* = 7.2 Hz, *J* = 1.2 Hz, 6'-H), 7.33 (1H, dt, *J* = 7.2 Hz, *J* = 1.2 Hz, 7'-H), 7.36-7.39 (3H, m, ArH), 7.42 (1H, d, *J* = 7.2 Hz, 5'-H), 7.52 (1H, d, *J* = 7.2 Hz, 8'-H), 7.72-7.77 (4H, m, ArH), 8.15 (1H, s, 3'-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.5, 23.7, 26.0, 26.9, 29.7, 31.0 31.5, 40.3, 45.9, 55.2, 86.2, 100.3, 118.0, 119.3, 119.7, 119.9, 120.2, 121.9, 122.4, 122.9, 125.7, 126.9, 127.0, 127.1, 127.9, 128.2, 129.0, 130.2, 131.5, 136.7, 140.2, 142.2, 142.7, 146.5, 150.8, 151.3, 151.7, 144.4, 156.4, 158.9. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{47}H_{50}N_3S$: 688.3720; found: 688.3720.

2-(4,4-Dibutyl-4H-indeno[1,2-b]thiophen-2-yl)-7-methyl-4-(phenylethynyl)-7H-pyrrolo[2,3-d]pyrimidine (**25d**)



Compound **25d** was synthesized according to the procedure described for 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**12a**–**o**). Reaction was carried out starting from 2-chloro-7-methyl-4-(phenylethynyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (**8a**) (75 mg, 0.28 mmol). Yield 112 mg (78%). Yellow solid, mp 90-92 ^{o}C. IR (KBr): 2212 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.74 (6H, t, *J* = 7.2 Hz, 2xCH_3), 0.85-0.97 (4H, m, 2xCH_2), 1.14 (4H, sex, *J* = 7.2 Hz, 2xCH_2), 1.90-2.09 (4H, m, 2xCH_2), 3.94 (3H, s, NCH_3), 6.70 (1H, d, *J* = 3.6 Hz, 5-H), 7.20 (1H, d, *J* = 3.6 Hz, 6-H), 7.24 (1H, dt, *J* = 7.2 Hz, *J* = 1.2 Hz, 6'-H) 7.30-7.34 (2H, m, 7'-H, 5'-H), 7.42-7.46 (3H, m, ArH), 7.50 (1H, d, *J* = 7.2 Hz, 8'-H), 7.73-7.76 (2H, m, ArH), 8.03 (1H, s, 3'-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 23.1, 26.3, 39.0, 54.3, 86.1, 95.1, 100.2, 118.1, 119.1, 121.9, 122.5, 122.6, 125.5, 126.8, 128.5, 129.5, 130.2, 132.4, 138.5, 142.1, 144.3, 146.2, 151.7, 153.9, 155.6, 155.9. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{34}H_{34}N_3S$: 516.2468; found: 516.2464.

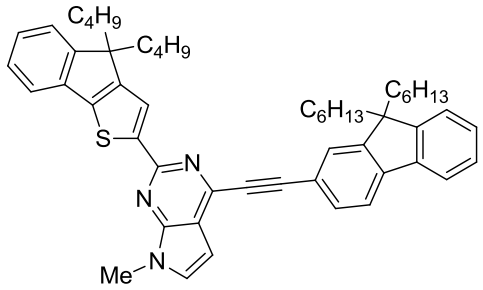
2-(4,4-Dibutyl-4H-indeno[1,2-b]thiophen-2-yl)-4-{[4-(9-carbazolyl)phenyl]ethynyl}--7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**25e**)



Compound **25e** was synthesized according to the procedure described for 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**12a**–**o**).

Reaction was carried out starting from 4-{[4-(9-carbazolyl)phenyl]ethynyl}-2-chloro-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**8g**) (75 mg, 0.17 mmol). Yield 93 mg (80%). Yellow solid, mp 134-136 ^{o}C. IR (KBr): 2211 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.79 (6H, t, *J* = 7.2 Hz, 2xCH_3), 0.88-1.01 (4H, m, 2xCH_2), 1.18 (4H, sex, *J* = 7.2 Hz, 2xCH_2), 1.94-2.12 (4H, m, 2xCH_2), 3.96 (3H, s, NCH_3), 6.75 (1H, d, *J* = 3.6 Hz, 5-H), 7.22-7.29 (2H, m, 6-H, 6'-H), 7.32-7.39 (4H, m, cbz-H), 7.46-7.55 (5H, m, 7'-H, 5'-H, 8'-H, cbz-H), 7.69 (2H, d, *J* = 8.4 Hz, ArH), 7.99 (2H, d, *J* = 8.4 Hz, ArH), 8.09 (1H, s, 3'-H), 8.20 (2H, d, *J* = 7.6 Hz, cbz-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 23.1, 26.3, 31.1, 39.1, 54.3, 87.1, 94.1, 100.1, 109.8, 118.2, 119.1, 120.4, 120.7, 122.5, 122.6, 123.7, 125.6, 126.2, 126.8, 126.9, 128.3, 130.4, 134.0, 138.4, 138.8, 140.4, 141.9, 144.5, 146.3, 151.8, 153.9, 155.7, 155.9. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{46}H_{41}N_4S$: 681.3046; found 681.3042.

2-(4,4-Dibutyl-4H-indeno[1,2-b]thiophen-2-yl)-4-[(9,9-dihexyl-9H-fluoren-2-yl)ethynyl]-7-methyl-7H-pyrrolo[2,3-d]pyrimidine (**25f**)



Compound **25f** was synthesized according to the procedure described for 2-aryl-4-(arylethynyl)-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidines (**12a–o**). Reaction was carried out starting from 2-chloro-4-[(9,9-dihexyl-9*H*-fluoren-2-yl)ethynyl]-7-methyl-7*H*-pyrrolo[2,3-*d*]pyrimidine (**8h**) (75 mg, 0.14 mmol). Yield 89 mg (82%). Yellow solid, mp 93-95 ^{o}C. IR (KBr): 2207 (C≡C) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.60-0.68 (4H, m, 2xCH_2), 0.74 (3H, t, *J* = 7.2 Hz, 2xCH_3), 0.81 (3H, t, *J* = 7.2 Hz, 2xCH_3), 0.90-0.95 (4H, m, 2xCH_2), 1.05-1.19 (16H, m, 8xCH_2), 1.92-2.09 (8H, m, 4xCH_2), 3.95 (3H, s, NCH_3), 6.77 (1H, d, *J* = 3.6 Hz, 5-H), 7.21 (1H, d, *J* = 3.6 Hz, 6-H), 7.25 (1H, dt, *J* = 7.2 Hz, *J* = 1.2 Hz, 6'-H), 7.31-7.40 (5H, m, 5'-H, 7'-H, ArH), 7.51 (1H, d, *J* =

7.2 Hz, 8'-H), 7.72-7.77 (4H, m, ArH), 8.07 (1H, s, 3'-H). ^{3}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.0, 22.5, 23.1, 23.7, 26.3, 29.7, 31.0, 31.5, 39.0, 40.4, 54.3, 55.2, 86.3, 96.4, 100.3, 118.0, 119.0, 119.7, 119.9, 120.2, 122.56, 122.57, 122.9, 125.5, 126.8, 126.9, 127.0 127.9, 130.1, 131.5, 138.5, 140.2, 142.3, 142.7, 144.3, 146.3, 150.8, 151.2, 151.7, 153.9, 155.6, 155. HRMS (ESI): *m*/*z* $[M+H]^+$ calcd for $C_{53}H_{62}N_3S$: 772.4659; found: 772.4662.

5. CONCLUSIONS

1. 2,4-Diazido-7-methylpyrrolo[2,3-*d*]pyrimidine was synthesized and its ring–chain tautomerism was investigated. The synthesized diazides were shown to exist as diazide (major) and 5-azidopyrrolo[3,2-*e*]tetrazolo[1,5-*c*]pyrimidine (minor) tautomers. The ratio of these tautomeric forms depends on the polarity of the solvent – proportion of the diazide isomer decreases with the increase of solvent polarity.

2. Novel D-π-A-π-D type fluorophores - 2,4-bis(4-aryl-1,2,3-triazol-1-yl)pyrrolo[2,3-*d*]pyrimidines were prepared by CuAAC reaction of 2,4-diazido-7-methylpyrrolo[2,3-*d*]pyrimidine with diverse arylethynes. It was demonstrated that in the CuAAC reaction of 2,4-diazidopyrrolo[2,3-*d*]pyrimidine along with 1,4-disubstituted 1,2,3-triazoles some amounts of 1,5-disubstituted isomers are formed. The ratio of these isomers does not depend on the catalyst system and relies on the nature of alkyne used in the reaction.

3. The alteration of substituents of 2,4-bis(4-aryl-1,2,3-triazol-1-yl)-7-methylpyrrolo[2,3-*d*]pyrimidines enables tuning of HOMO and LUMO energies: the attachment of polar substituents at the para position of phenyl group with decreasing electron-donating character results in lower HOMO and LUMO energies, whereas the more bulky aryl substituents resulted in the increase of HOMO energy.

4. Variation in size, polarity and geometry of the substituents of 2,4-bis(4-aryl-1,2,3-triazol-1-yl)pyrrolo-7-methyl[2,3-*d*]pyrimidines alters the charge transfer character of the transitions, influencing the properties of the fluorescence spectra and fluorescence quantum yield. Intramolecular charge transfer has a considerable influence on the dynamics of radiative and non-radiative decay in polar surroundings. Both processes slow down and the competition between the radiative and non-radiative decay pathways results in smaller fluorescence quantum yields for compounds possessing electron-donating substituents or substituents with twisted geometry. The highest quantum yield of 73% was observed for 7-methyl-2,4-bis(4-phenyl-1*H*-1,2,3-

triazol-1-yl)pyrrolo[2,3-*d*]pyrimidine in a solvent of medium polarity – THF. 2,4-Bis[4-(4-dimethylaminophenyl)-1*H*-1,2,3-triazol-1-y]-7-methylpyrrolo[2,3-*d*]pyrimidine exhibited the largest Stokes shift of 279 nm in DMF solution.

5. A comparative study of the palladium-catalysed alkynylation reaction of 2,4-dichloro-7-methylpyrrolo[2,3-*d*]pyrimidine using arylethynes and (arylethynyl)tributylstannanes has proved that introduction of alkynyl moieties into position 4 of the pyrrolo[2,3-*d*]pyrimidine can be achieved by both, Sonogashira and Stille reactions, whereas Stille coupling appeared to be the more suitable process to introduce aryl and alkynyl moieties into position 2 of the heterocycle. As demonstrated, $Pd(PPh_3)_2Cl_2/AsPh_3$ has emerged to be suitable catalyst system for both, alkynylation and arylation Stille reactions, providing the desired coupling products in good yields.

6. Incorporation of electron-donating moieties into the 2nd position of 2-aryl-4-(arylethynyl)-7-methylpyrrolo[2,3-*d*]pyrimidines or 2,4-bis(arylethynyl)-7-methylpyrrolo[2,3-*d*]pyrimidines, results in prominent bathochromic shift of emission maxima and enchanced Stokes shifts due to enhanced charge transfer character of the exited state.

7. Pyrrolo[2,3-*d*]pyrimidine-core based oligoarylenes possessing ethynyl linkers demonstrates a slight bathochromic shift of emission maxima and generally slightly lower fluorescence quantum yields in THF solutions if compared with similar pyrrolo[2,3-*d*]pyrimidine derivatives bearing 1,2,3-triazole linker.

8. Increase of fluorescence quantum yields of pyrrolo[2,3-*d*]pyrimidine-based oligoarylenes possessing ethynyl linker are mostly affected by extent of π-conjugated aromatic system, whilst quantum yields of pyrrolo[2,3-*d*]pyrimidines with 1,2,3-triazole linker are influenced by polarity of the substituents.

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