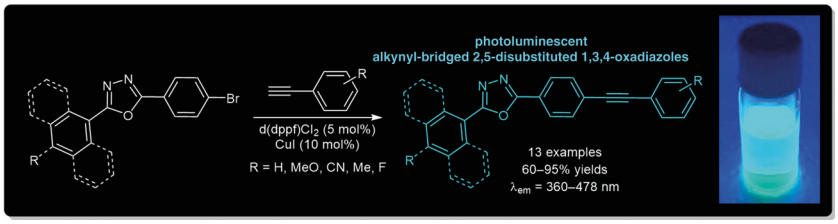
Synthesis A. Paun et al. Paper

Synthesis of New Alkynyl-Bridged 2,5-Disubstituted 1,3,4-Oxadiazoles

Anca Paun[1]
Codruta C. Paraschivescu[1]
Mihaela Matache*
Vasile I. Parvulescu*

University of Bucharest, Faculty of Chemistry, Department of Organic Chemistry, Biochemistry, and Catalysis, 90–92 Panduri Street, 050663 Bucharest, Romania
vasile.parvulescu@chimie.unibuc.ro
mihaela.matache@g.unibuc.ro



Received: 04.09.2015
Accepted after revision: 11.11.2015
Published online: 04.01.2016
DOI: 10.1055/s-0035-1560387; Art ID: ss-2015-t0519-op

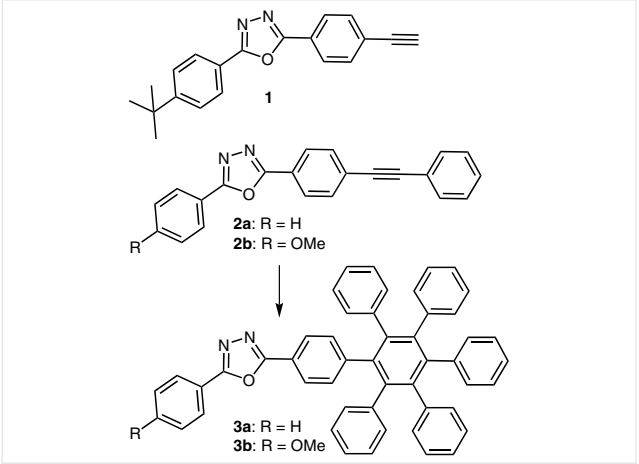
Abstract A synthesis of new alkynyl-derived 2,5-disubstituted 1,3,4-oxadiazoles through palladium/copper-catalyzed Sonogashira cross-coupling between oxadiazole-substituted phenyl bromides and various arylacetylenes is described. Investigation of the absorption and emission spectra of the target compounds indicates emission profiles in the near-blue and blue region and high luminescence intensities. The presented approach is very convenient for the synthesis of luminescent small-molecules or precursors of other complex derivatives that are useful in the preparation of OLEDs as electron-transporting components.

Key words 2,5-disubstituted 1,3,4-oxadiazoles, palladium-catalyzed Sonogashira reaction, cross-coupling, ethynyl-bridged compounds, electron-deficient heterocycles

The electron-transporting behavior of the 1,3,4-oxadiazole core has justified its utility in the manufacture of organic light-emitting diodes (OLEDs).[2] In particular, the chemistry of the 2,5-disubstituted 1,3,4-oxadiazoles[3] has evolved during the past two decades in an effort to synthesize and characterize new organic small molecules that exhibit enhanced optoelectronic properties.

On this ground, a number of interesting ethynyl-bridged 2,5-disubstituted 1,3,4-oxadiazoles were studied for their luminescence,[4] as fluorescent liquid crystals,[5] selective sensors for nitro compounds,[6] or ligands for coordination polymers with one-, two-, or three-dimensional structures.[7] Influence of the extended conjugation through the alkynyl chain was also investigated for various oligoyne-bridged 2,5-diphenyl-1,3,4-oxadiazole molecules.[8]

In addition, alkyne-substituted 1,3,4-oxadiazoles like **1** (Scheme 1) found use as building block for the synthesis of further π-extended functional molecules.[9] Notably, internal alkynes **2** were used in a Diels–Alder cycloaddition reaction to generate compounds **3** that exhibit emissions in the UV region with very high fluorescence quantum yields (0.91 for **3a** and 0.85 for **3b** measured using quinine as reference). Blue electrophosphorescent devices with high efficiencies also resulted when used as host materials.[10]



Scheme 1 Relevant examples of terminal or internal ethynyl-bridged 2,5-disubstituted 1,3,4-oxadiazoles (compounds **1** and **2**) with improved properties or precursors for compounds **3**

Hence, the design of new ethynyl-bridged 1,3,4-oxadiazoles bearing various combinations of electron-donating or -withdrawing functional groups, both on the alkyne and the oxadiazole core, is still challenging in order to obtain molecules with improved optoelectronic properties.

The Sonogashira reaction[11] has evolved as a very powerful tool for the Csp^2–Csp bond formation and, consequently, provides a suitable method for the synthesis of compounds of type **1**[4,9] and **2**.[10] Pd and Cu(I) are widely reported to catalyze in tandem cross-coupling alkynylations of aryl iodides under very mild conditions (i.e., at room temperature

and for short reaction times). Differently, the bromide analogues display a lower reactivity.[11b,c,12] This behavior is mainly attributed to a lower rate of the oxidative addition step, which may be enhanced by use of higher temperatures or presence of electron-withdrawing groups that could provide a more electrophilic character to the reacting molecule. However, the bromides show significant advantages over the iodides justified by their readily availability and higher stability.

Based on this state-of-the art, the aim of the present study was to design and prepare an extended series of alkynyl-bridged 2,5-disubstituted 1,3,4-oxadiazoles **2** that display enhanced photophysical properties and constitute proper candidates as OLEDs precursors. The synthetic approach uses a simple and convenient procedure, having as key intermediates 5-aryl-2-(4-bromophenyl)-1,3,4-oxadiazoles **4** (Scheme 2). Compounds **4**, once synthesized, are used as electrophiles in Sonogashira cross-couplings with various alkynes, others than phenylacetylene.[10]

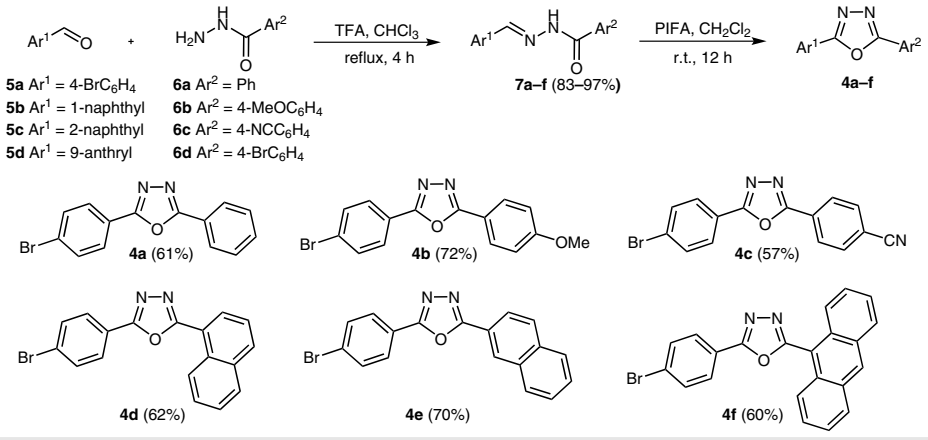
Viewed from the perspective of an oxadiazole-substituted aryl halide and considering a presumptive behavior of the heterocycle core as an electron-deficient group, the 2,5-disubstituted 1,3,4-oxadiazole bromides **4** would qualify as excellent electrophilic partners in Sonogashira reaction for the synthesis of the ethynyl-bridged 1,3,4-oxadiazoles. Thus, our substrates **4** were synthesized first. We chose to prepare the 5-aryl-2-(4-bromophenyl)-1,3,4-oxadiazoles **4** (Scheme 2) bearing a variety of unsubstituted or *para*-substituted aryls with electron-donating or -withdrawing groups.

Functional groups, such as methoxy or cyano, can be easily grafted on the phenyl rings of the oxadiazole core, in order to obtain compounds bearing opposite electronic effects. Moreover, the naphthyl and anthryl moieties were selected as a result of the growing interest to synthesize compounds with good electron transport properties and utility in fabrication of OLEDs or polymers.[13]

The oxadiazole heterocyclic ring is usually obtained[14] through dehydrative cyclization of *N*,*N*′-diacylhydrazines,[14b] oxidative cyclization of *N*′-acylhydrazones,[14c] or Huisgen reaction of tetrazoles and acid chlorides.[14d] Among the numerous methods described,[14] our attention was turned to the oxidative cyclization using hypervalent iodine reagents due to the readily availability of the *N*′-acylhydrazones from aldehydes and hydrazides, as well as the mild conditions required for the oxadiazole ring closure.[15]

The 2,5-disubstituted 1,3,4-oxadiazole substrates **4a**–**f** were synthesized following a two-step procedure (Scheme 2). Condensation of 4-bromobenzaldehyde (**5a**), naphthyl carbaldehydes **5b**,**c**, and anthracene-9-carbaldehyde (**5d**) with one of the corresponding hydrazides **6a**–**d** yielded under acidic catalysis (trifluoroacetic acid) the *N*′-acylhydrazones **7a**–**f** in good to excellent yields (83–97%). Further treatment of these compounds with bis(trifluoroacetoxy)iodobenze (PIFA) at room temperature in dichloromethane led to the oxadiazoles **4a**–**f** in good to very good yields (57–72%). All compounds were purified and characterized by spectral analysis. The obtained data corresponded with previously described reports for known compounds.[13c,15a,16]

With the substrates **4a**–**f** in hand, the cross-coupling experiments, modifying previously described procedures for Sonogashira couplings of aryl bromides, were conducted.[17] $Pd(dppf)Cl_2$ (5 mol%) was chosen as the palladium source, considering the general advantages of a bulky diphosphine ligand for aryl bromides cross-couplings,[18] mainly to better stabilize Pd(0) catalytic species over monodentate ligands. This is highly desirable when inactivation of the catalyst competes with the oxidative addition step of the cross-coupling reaction.[19] Furthermore, CuI (10 mol%) was used as the co-catalyst, tetrahydrofuran as the polar aprotic solvent, and triethylamine as the base. The reaction time was kept at 12 hours for all assays, under an inert atmosphere, using 1.5 equivalents of phenylacetylene.



Scheme 2 Synthetic scheme for the 2,5-disubstituted 1,3,4-oxadiazole substrates **4a**–**f**

Performing the coupling reactions of substrates **4a**–**c** at room temperature (Scheme 3) furnished no target coupling products. Increasing the temperature to solvent reflux gave the products **2a**–**c** in 70%, 83%, and 75% yield, respectively (Scheme 3). One can note that the substituent in *para*-position of the phenyl moiety has no significant influence on the coupling efficiency. In addition, we remark that the coupling reactions require higher temperature in order to occur, suggesting that the electron-deficient oxadiazole core does not sufficiently activate the bromides to undergo couplings at room temperatures.[11b,c,12] Very good to excellent yields of products **2d**–**f** (75–91%) (Scheme 3) were also obtained in the case of the substrates bearing the naphthyl and anthryl moieties.

The interest in more simple experimental protocols of the Sonogashira cross-coupling, concomitant with preservation of high product yields, has led to reports showing experiments conducted under aerobic conditions and, consequently, copper-free procedures,[11c] in order to reduce formation of the homocoupled diyne side-product.[20]

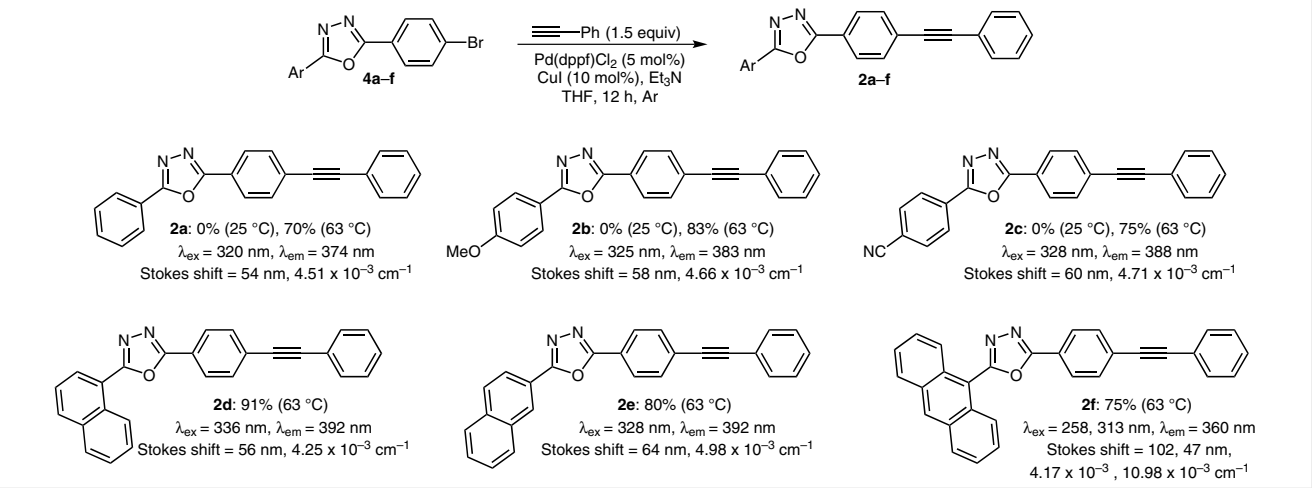
We were tempted to see whether in our case, with our particular substrates and using $Pd(dppf)Cl_2$ the coupling reactions with phenylacetylene under aerobic conditions would efficiently occur. The copper-free reaction of the methoxy-substituted compound **4b** was first performed using 1.5 equivalents of the alkyne in DMF at room temperature (Table 1, entry 1), which gave no coupling product. However, diphenylbutadiyne[21] was isolated in 79% yield (see Supporting Information). When the temperature was raised to 63 °C and an alkyne excess was used (3 equiv, entry 2), the coupling product could be detected in 26% yield (as inferred from the ^1H NMR spectrum) as an unseparable mixture with the starting material, along with the diyne side-product. Adding copper iodide to the reaction mixture and changing the solvent to THF (entry 3) yielded the coupling product in 87%.

Further, when the unsubstituted compound **4a** (Table 1, entries 4 and 5) was treated in the same conditions using only 1.5 equivalents of the alkyne the product was obtained in 36% yield, while use of 3 equivalents of the alkyne led to 60% yield. In the case of the cyano-substituted substrate **4c** (entries 6 and 7), the target product **2c** was isolated in only 47% yield using 3 equivalents of phenylacetylene, at refluxing temperature of DMF.

We also performed the coupling reactions under aerobic conditions of the substrates **4d**–**f** with phenylacetylene and obtained moderate yields (Table 1, entries 8–11), irrespective of the solvent used in some cases.

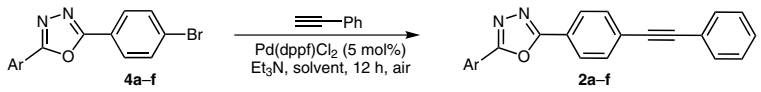
Once the optimum reaction conditions were found, the synthesis of a diverse-substituted series of new alkynyl-bridged 1,3,4-oxadiazoles was successfully achieved under inert conditions as shown in Scheme 4. One can notice that the coupling reactions occurred in very good to excellent yields for all our substrates and the alkynes used. The bromo derivative **4b** was used to synthesize compounds **2g**–**i** through coupling with 4-ethynyltoluene, 2-ethynylanisole, and 4-ethynylbenzonitrile, respectively (60–95%) (Scheme 4). Moreover, alkynes bearing both electron-donating and -withdrawing substituents such as the ones mentioned above as well as 4-ethynylfluorobenzene were coupled with the phenyl bromides bearing naphthyl and anthryl substituted oxadiazoles, providing compounds **2j**–**m** in very good yields (64–93%) (Scheme 4).

Preliminary studies of the absorption and emission properties of compounds **2a**–**m** (see Schemes 3 and 4 for the excitation and emission wavelengths, as well as the Supporting Information for the excitation and emission spectra of the compounds) indicate various profiles of the optoelectronic features. For example, Figure 1 shows the spectra profile of some selected compounds **2c**,**f**,**i**,**k**,**l** having a different substitution pattern. In general, compounds **2** have similar absorption profiles, with the excitation maxi-



Scheme 3 Cross-coupling reaction of substrates **4a**–**f** with phenylacetylene, structure of products **2a**–**f** (yields of isolated products after column chromatography, absorption and emission experiments were performed in $CHCl_3$: **2a**: 5×10^{-7} M, **2b**,**d**,**e**: 1×10^{-8} M, **2c**,**f**: 1×10^{-7} M)

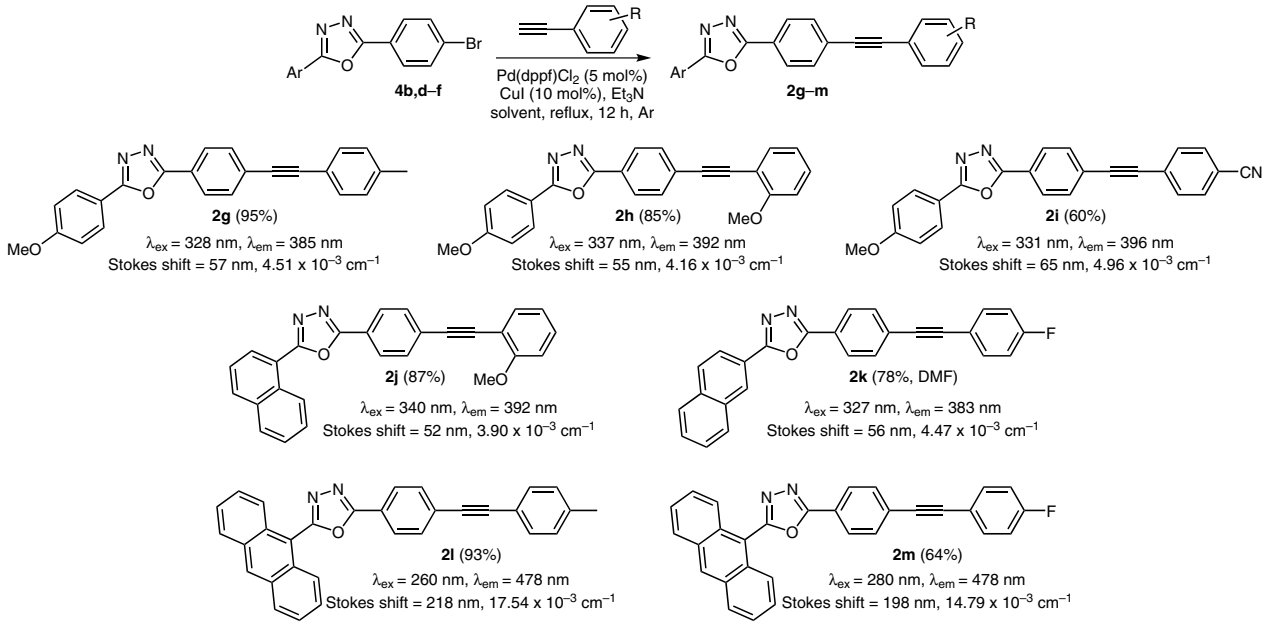
Table 1 Coupling Reactions between Substrates **4a–f** and Phenylacetylene under Aerobic Conditions



Entry	4	Solvent	Co-catalyst (mol%)	Temp (°C)	Alkyne (equiv)	Product	Yield (%)[a]
1	**4b**	DMF	–	25	1.5	**2b**	–[b]
2	**4b**	DMF	–	63	3	**2b**	26[c]
3	**4b**	THF	CuI (10)	63	3	**2b**	87
4	**4a**	THF	CuI (10)	63	1.5	**2a**	36
5	**4a**	THF	CuI (10)	63	3	**2a**	60
6	**4c**	THF	CuI (10)	63	3	**2c**	–
7	**4c**	DMF	CuI (10)	130	3	**2c**	47
8	**4d**	THF	CuI (10)	63	3	**2d**	55
9	**4e**	THF	CuI (10	63	3	**2e**	42
10	**4e**	DMF	CuI (10)	130	3	**2e**	51
11	**4f**	THF	CuI (10)	63	3	**2f**	35

[a] Yields of isolated products after purification by column chromatography.
[b] Yield of the isolated diyne was 79%, no coupling product was detected.
[c] Yield calculated from the ^{1}H NMR spectrum performed on unseparable mixture of the starting material and the coupling product.

ma between 320–340 nm, except the compounds bearing the anthryl moiety, for which the most intense maximum varies between 260–280 nm. The emission spectra indicate high luminescence intensities at low concentrations, in the nanomolar range, with emission maxima near the blue region, varying between 360 and 396 nm. One can note the different behavior of the anthryl derivatives **2l** and **2m**, which emit in the late blue-near green region and have $\lambda_{em,\,max}$ = 478 nm, unlike the unsubstituted compound **2f** for which $\lambda_{em,\,max}$ = 360 nm. The Stokes shifts are moderate for all compounds except **2l** and **2m**, which have very large values (218 nm for **2l** and 198 nm for **2m**).



Scheme 4 Synthesis of diverse-substituted ethynyl-bridged 1,3,4-oxadiazoles **2g**–**m**. Yields of isolated products after purification by column chromatography. Reactions were performed in refluxing THF as solvent, unless otherwise stated. Absorption and emission experiments were performed in $CHCl_3$: **2g**–**i**,**k**,**l**: 1 × 10^{-7} M, **2j**: 1 × 10^{-8} M, **2m**: 5 × 10^{-7} M.

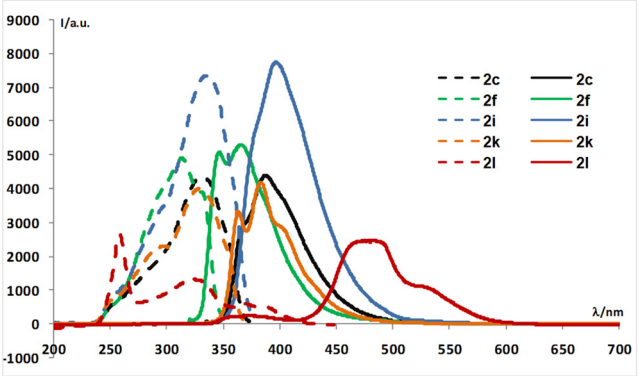


Figure 1 Excitation (dotted lines) and emission (plain lines) spectra of selected compounds **2** (performed in $CHCl_3$ at 1×10^{-7} M)

Thus, a wide spectral range can be covered and the optoelectronic properties of the compounds can, therefore be tuned, through selection of proper substituent both on the oxadiazole and the alkyne cores. Another interesting observation would be that the moderate Stokes shifts are, however, accompanied by high luminescence intensities. Deeper investigations of the luminescence behavior (such as the quantum yields, etc.) may reveal some other interesting features and these are currently under way.

In conclusion, we have described synthesis of new ethynyl-bridged 2,5-diaryl-1,3,4-oxadiazoles using a simple three-step protocol, involving the synthesis of *N*′-acylhydrazones, their oxidative cyclization to form the oxadiazole ring and, finally, the alkynylation reaction of the resulting oxadiazole-aryl bromides. The target compounds were designed and synthesized to contain various electron-donating or -withdrawing functional groups. The alkynylation approach followed the Sonogashira coupling procedure between bromophenyl-1,3,4-oxadiazole derivatives and various substituted arylacetylenes, bearing activating or deactivating functional groups. The coupling reactions occurred in good to excellent yields, indicating a convenient strategy to synthesize new decorated 2,5-disubstituted 1,3,4-oxadiazoles as potential OLEDs precursors. The heterocyclic ring behaves as a moderate electron-deficient group of aryl bromides as suggested by the low reaction performance at room temperature. The coupling reactions of the 1,3,4-oxadiazole substrates with phenylacetylene also occur in aerobic conditions in moderate to very good yields, using an alkyne excess, along with the diyne side-product in considerable amounts. Preliminary studies indicate that the target internal oxadiazole alkynes are compounds that bear luminescent properties in the near-blue or blue region and have high luminescence intensities. A systematic and more detailed study regarding the influence of the structural particularities over the displayed luminescent properties may reveal other interesting features. In addition, such compounds may also be used as building blocks in the synthesis of new small molecules, more complex from a structural point of view, in the attempt to generate enhanced optoelectronic properties.

The solvents and reagents were purchased from commercial suppliers and used without further purification. Anhydrous THF was distilled from Na and benzophenone. Petroleum ether (PE) used refers to the hydrocarbon mixture with a boiling range of 40–60 °C. Reactions conducted under argon were performed in oven-dried Schlenk tubes using anhydrous solvent. The NMR spectra were recorded on Bruker spectrometers operating at 300 MHz, 500, and 600 MHz for ^{1}H and 75 MHz, 125 and 150 MHz, respectively, for ^{13}C. Chemical shifts (δ) are reported in parts per million (ppm) using residual solvent peak as internal reference. High-resolution mass spectra were recorded on a ThermoScientific (LTQ XL Orbitrap) spectrometer using APCI technique and Orbital Ion Trap mass analyzer. TLC was performed on silica gel 60 coated aluminum F_{254} plates and preparative column chromatography was performed on Merck silica gel 60 (0.040–0.063 mm). All plates were visualized by UV irradiation at 254 nm. Melting points were determined in open capillary tubes using a Stuart SMP3 electric melting point apparatus and are uncorrected. Hydrazides **6** were either commercially available or synthesized from the corresponding carboxylic acids, through esterification and further reaction with hydrazine hydrate.

N′-Acylhydrazones 7a–f; General Procedure

The corresponding aldehyde **5** (5 mmol) and the corresponding hydrazide **6** (5 mmol) were dissolved in $CHCl_3$ (50 mL). To this solution was added trifluoroacetic acid (2 drops) and the mixture was stirred at reflux for 4 h and then at r.t. overnight. Evaporation of almost half of the solvent volume led to massive precipitation of the product, which was filtered, thoroughly washed with Et_2O, and dried to yield pure product **7**.

N′-(4-Bromobenzylidene)benzohydrazide (7a)

Yield: 1.25 g (83%); white solid; mp 189–190 °C (Lit.[16e] mp 190–191 °C); R_f = 0.38 (EtOAc–PE, 1:2).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 11.91 (s, 1 H, NH), 8.46 (s, 1 H, CH=N), 7.87 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 7.77–7.73 (m, 4 H, H_{Ar}), 7.48–7.45 (m, 3 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.2, 148.1, 134.2, 132.5, 131.5, 130.2, 129.7, 128.9, 127.1, 125.5.

N′-(4-Bromobenzylidene)-4-methoxybenzohydrazide (7b)

Yield: 1.55 g (93%); white solid; mp 207–209 °C; R_f = 0.31 (EtOAc–PE, 1:2).

^{1}H NMR (600 MHz, DMSO-d_6): δ = 11.79 (s, 1 H, NH), 8.38 (s, 1 H, CH), 7.85 (d, ^3J = 8.46 Hz, 2 H, H_{Ar}), 7.75 (d, ^3J = 8.46 Hz, 2 H, H_{Ar}), 7.68 (d, ^3J = 8.64 Hz, 2 H, H_{Ar}), 7.03 (d, ^3J = 8.64 Hz, 2 H, H_{Ar}), 3.81 (s, 3 H, OCH_3).

^{13}C NMR (150 MHz, DMSO-d_6): δ = 166.3, 164.9, 148.0, 131.8, 131.5, 129.7, 128.8, 126.8, 126.6, 114.4, 55.3.

N′-(4-Bromobenzylidene)-4-cyanobenzohydrazide (7c)

Yield: 1.59 g (97%); white solid; mp 255–257 °C; R_f = 0.37 (EtOAc–PE, 1:2).

^{1}H NMR (500 MHz, DMSO-d_6): δ = 12.13 (s, 1 H, NH), 8.43 (s, 1 H, CH=N), 8.06 (d, ^3J = 8.5 Hz, 2 H, H_{Ar}), 8.03 (d, ^3J = 8.5 Hz, 2 H, H_{Ar}), 7.70 (d, ^3J = 8.5 Hz, 2 H, H_{Ar}), 7.67 (d, ^3J = 8.5 Hz, 2 H, H_{Ar}).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 161.8, 147.5, 137.4, 133.4, 132.6, 131.9, 129.1, 128.5, 123.6, 118.3, 114.1.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{11}BrN_3O$: 328.0080, 360.0060; found: 328.0107, 330.0087.

4-Bromo-*N*′-(naphthalen-1-ylmethylene)benzohydrazide (7d)

Yield: 1.61 g (91%); white solid; mp 227–229 °C; R_f = 0.47 (EtOAc–PE, 1:2).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.01 (s, 1 H, NH), 9.10 (s, 1 H, CH=N), 8.87 (d, ^3J = 8.4 Hz, 1 H, H_{Ar}), 8.05–8.02 (m, 2 H, H_{Ar}), 7.95–7.92 (m, 3 H, H_{Ar}), 7.78 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 7.71–7.59 (m, 3 H, H_{Ar}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.1, 148.1, 133.6, 132.5, 131.6, 130.7, 130.2, 129.8, 129.5, 128.9, 127.9, 127.4, 126.4, 125.6, 124.3.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{14}BrN_2O$: 353.0284, 355.0264; found: 353.0297, 355.0288.

4-Bromo-*N*′-(naphthalen-2-ylmethylene)benzohydrazide (7e)

Yield: 1.67 g (95%); white solid; mp 265–267 °C; R_f = 0.44 (EtOAc–PE, 1:2).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.02 (s, 1 H, NH), 8.60 (s, 1 H, CH=N), 8.17 (s, 1 H, H_{Ar}), 8.03–7.93 (m, 4 H, H_{Ar}), 7.90 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 7.77 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 7.60–7.56 (m, 2 H, H_{Ar}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.2, 148.1, 133.8, 132.9, 132.5, 132.0, 131.6, 129.8, 128.9, 128.6, 128.4, 127.8, 127.2, 126.8, 125.6, 122.7.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{14}BrN_2O$: 353.0284, 355.0264; found: 353.0313, 355.0294.

N′-(Anthracen-9-ylmethylene)-4-bromobenzohydrazide (7f)

Yield: 1.71 g (85%); yellow solid; mp 293–294 °C; R_f = 0.43 (EtOAc–PE, 1:2).

^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.18 (s, 1 H, NH), 9.67 (s, 1 H, CH=N), 8.77–8.75 (m, 3 H, H_{Ar}), 8.17 (d, ^3J = 8.3 Hz, 2 H, H_{Ar}), 7.98 (d, ^3J = 8.3 Hz, 2 H, H_{Ar}), 7.83 (d, ^3J = 8.3 Hz, 2 H, H_{Ar}), 7.69–7.57 (m, 4 H, H_{Ar}).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 162.1, 147.4, 132.5, 131.7, 130.9, 129.8, 129.7, 129.1, 127.3, 125.7, 125.6, 124.9, 124.9.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{16}BrN_2O$: 403.0441, 405.0420; found: 403.0471, 405.0450.

2,5-Disubstituted 1,3,4-Oxadiazoles 4a–f; General Procedure

The corresponding *N*′-acylhydrazone **7** (3 mmol) and bis(trifluoroacetoxy)iodobenze (1.42 g, 3.3 mmol, 1.1 equiv) was dissolved in CH_2Cl_2 (15 mL) and the resulting solution was stirred at r.t. overnight. The solvent was removed under vacuum and the residue was purified by column chromatography on silica gel to yield the respective pure product **4**.

2-(4-Bromophenyl)-5-phenyl-1,3,4-oxadiazole (4a)

Yield: 550 mg (61%); white solid; mp 169–170 °C (Lit.[16c] mp 169–170 °C); R_f = 0.62 (EtOAc–PE, 1:4).

2-(4-Bromophenyl)-5-(4-methoxyphenyl)-1,3,4-oxadiazole (4b)

Yield: 710 mg (72%); white solid; mp 158–160 °C (Lit.[15a] mp 154–155 °C); R_f = 0.5 (EtOAc–PE, 1:4).

4-[5-(4-Bromophenyl)-1,3,4-oxadiazol-2-yl]benzonitrile (4c)

Yield: 560 mg (57%); white solid; mp 227–229 °C (Lit.[16d] mp 220.3–221.8); R_f = 0.32 (EtOAc–PE, 1:4).

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_9BrN_3O$: 325.9924, 327.9903; found: 325.9932, 327.9904.

2-(4-Bromophenyl)-5-(naphthalen-1-yl)-1,3,4-oxadiazole (4d)

Yield: 650 mg (62%); white solid; mp 148–149 °C (Lit.[13c] mp 139 °C); R_f = 0.5 (EtOAc–PE, 1:4).

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{12}BrN_2O$: 351.0128, 353.0107; found: 351.0122, 353.0095.

2-(4-Bromophenyl)-5-(naphthalen-2-yl)-1,3,4-oxadiazole (4e)

Yield: 740 mg (70%); white solid; mp 169–170 °C; R_f = 0.55 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.60 (s, 1 H, H_{Ar}), 8.18 (d, ^3J = 8.6 Hz, 1 H, H_{Ar}), 8.04 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 7.97 (d, ^3J = 8.2 Hz, 2 H, H_{Ar}), 7.89 (d, ^3J = 8.6 Hz, 1 H, H_{Ar}), 7.69 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 7.61–7.56 (m, 2 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.1, 164.1, 134.9, 132.9, 132.6, 129.3, 128.9, 128.5, 128.2, 128.1, 127.5, 127.3, 126.6, 123.3, 122.9, 121.1.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{12}BrN_2O$: 351.0128, 353.0107; found: 351.0127, 353.0100.

2-(Anthracen-9-yl)-5-(4-bromophenyl)-1,3,4-oxadiazole (4f)

Yield: 720 mg (60%); yellow solid; mp 257–259 °C (Lit.[13c] mp 261 °C); R_f = 0.44 (EtOAc–PE, 1:4).

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{14}BrN_2O$: 401.0284, 403.0264; found: 401.0278, 403.0255.

Cross-Coupling Reaction Between Aryl Bromides Bearing the Substituted 1,3,4-Oxadiazole Moiety 4a–f and Arylacetylenes; General Procedure

The corresponding aryl bromide **4a**–**f** (0.125 mmol–0.166 mmol) was dissolved in solvent (anhydrous THF or DMF for reactions performed under an inert atmosphere, 1–3 mL). To the resulting solution the following were sequentially added: $Pd(dppf)Cl_2$ (5 mol%), CuI (10 mol%), Et_3N (10 equiv), and the alkyne (1.5 equiv for reactions performed under argon and 3 equiv for reactions performed under air, unless otherwise stated). The reactions were left to stir for 12 h at solvent reflux temperature, then the solvent was evaporated, and the residue was purified by column chromatography on silica gel to afford the respective pure product **2**.

2-Phenyl-5-[4-(phenylethynyl)phenyl]-1,3,4-oxadiazole (2a)[10]

Yield: 37.4 mg (70%); white solid; mp 194–196 °C; R_f = 0.59 (EtOAc–PE, 1:4).

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{15}N_2O$: 323.1179; found: 323.1170.

2-(4-Methoxyphenyl)-5-[4-(phenylethynyl)phenyl]-1,3,4-oxadiazole (2b)[10]

Yield: 44 mg (83%); white solid; mp 177–178 °C; R_f = 0.26 (EtOAc–PE, 1:4).

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{17}N_2O_2$: 353.1285; found: 353.1285.

4-{5-[4-(Phenylethynyl)phenyl]-1,3,4-oxadiazol-2-yl}benzonitrile (2c)

Yield: 40 mg (75%); white solid; mp 244–246 °C; R_f = 0.31 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.27 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 8.14 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 7.85 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 7.70 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 7.58–7.56 (m, 2 H, H_{Ar}), 7.39–7.38 (m, 3 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.1, 163.3, 133.1, 132.5, 131.9, 129.1, 128.6, 127.8, 127.6, 127.5, 127.2, 122.8, 122.7, 118.0, 115.4, 93.0, 88.5.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{14}N_3O$: 348.1131; found: 348.1139.

2-(Naphthalen-1-yl)-5-[4-(phenylethynyl)phenyl]-1,3,4-oxadiazole (2d)

Yield: 48.1 mg (91%); white solid; mp 121–123 °C; R_f = 0.35 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.30 (d, ^3J = 8.4 Hz, 1 H, H_{Ar}), 8.29 (d, ^3J = 7.3 Hz, 1 H, H_{Ar}), 8.19 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 8.07 (d, ^3J = 8.4 Hz, 1 H, H_{Ar}), 7.96 (d, ^3J = 8.4 Hz, 1 H, H_{Ar}), 7.74–7.71 (m, 3 H, H_{Ar}), 7.64–7.61 (m, 2 H, H_{Ar}), 7.60–7.57 (m, 2 H, H_{Ar}), 7.40–7.37 (m, 3 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.9, 163.9, 134.0, 132.9, 132.4, 131.9, 130.3, 128.9, 128.9, 128.6, 128.4, 127.1, 126.9, 126.4, 125.0, 123.4, 122.8, 120.6, 92.6, 88.7.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{17}N_2O$: 373.1335; found: 373.1339.

2-(Naphthalen-2-yl)-5-[4-(phenylethynyl)phenyl]-1,3,4-oxadiazole (2e)

Yield: 42.4 mg (80%); white solid; mp 162–164 °C; R_f = 0.38 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.65 (s, 1 H, H_{Ar}), 8.23 (dd, ^3J = 8.6 Hz, ^4J = 1.7 Hz, 1 H, H_{Ar}), 8.19 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 8.00 (d, ^3J = 8.0 Hz, 2 H, H_{Ar}), 7.92 (d, ^3J = 8.6 Hz, 1 H, H_{Ar}), 7.71 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 7.63–7.57 (m, 4 H, H_{Ar}), 7.40–7.38 (m, 3 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.1, 164.5, 134.9, 133.0, 132.4, 131.9, 129.3, 129.0, 128.9, 128.6, 128.2, 128.2, 127.6, 127.3, 127.0, 123.4, 123.4, 122.8, 121.2, 92.6, 88.7.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{17}N_2O$: 373.1335; found: 373.1337.

2-(Anthracen-9-yl)-5-[4-(phenylethynyl)phenyl]-1,3,4-oxadiazole (2f)

Yield: 39.7 mg (75%); yellow solid; mp 193–195 °C; R_f = 0.52 (EtOAc–PE, 1:4).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.71 (s, 1 H, H_{Ar}), 8.19 (d, ^3J = 8.3 Hz, 2 H, H_{Ar}), 8.12–8.04 (m, 4 H, H_{Ar}), 7.71 (d, ^3J = 8.3 Hz, 2 H, H_{Ar}), 7.60–7.56 (m, 6 H, H_{Ar}), 7.39–7.37 (m, 3 H, H_{Ar}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6, 163.4, 132.5, 131.9, 131.7, 131.6, 131.2, 128.9, 128.6, 127.9, 127.2, 127.2, 125.9, 125.2, 123.4, 122.8, 117.2, 92.6, 88.7.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{19}N_2O$: 423.1492; found: 423.1496.

2-(4-Methoxyphenyl)-5-[4-(*p*-tolylethynyl)phenyl]-1,3,4-oxadiazole (2g)

Yield: 52.5 mg (95%); white solid; mp 181–183 °C; R_f = 0.25 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 8.08 (d, ^3J = 9.0 Hz, 2 H, H_{Ar}), 7.66 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 7.45 (d, ^3J = 8.0 Hz, 2 H, H_{Ar}), 7.18 (d, ^3J = 8.0 Hz, 2 H, H_{Ar}), 7.04 (d, ^3J = 9.0 Hz, 2 H, H_{Ar}), 3.90 (s, 3 H, OCH_3), 2.39 (s, 3 H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.8, 163.9, 162.6, 139.2, 132.2, 131.8, 129.4, 128.9, 126.9, 126.8, 123.4, 119.8, 116.5, 114.7, 92.7, 88.2, 55.6, 29.8.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{19}N_2O_2$: 367.1441; found: 367.1437.

2-(4-Methoxyphenyl)-5-{4-[(2-methoxyphenyl)ethynyl]phenyl}-1,3,4-oxadiazole (2h)

Yield: 49 mg (85%); white solid; mp 147–148 °C; R_f = 0.13 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 (d, ^3J = 8.8 Hz, 2 H, H_{Ar}), 8.08 (d, ^3J = 9.0 Hz, 2 H, H_{Ar}), 7.70 (d, ^3J = 8.8 Hz, 2 H, H_{Ar}), 7.52 (d, ^3J = 8.5 Hz, 1 H, H_{Ar}), 7.35 (t, ^3J = 8.5 Hz, 1 H, H_{Ar}), 7.04 (d, ^3J = 9.0 Hz, 2 H, H_{Ar}), 6.97 (t, ^3J = 8.5 Hz, 1 H, H_{Ar}), 6.93 (d, ^3J = 8.5 Hz, 1 H, H_{Ar}), 3.94 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.8, 163.9, 162.6, 160.2, 133.8, 132.4, 130.5, 128.9, 127.1, 126.8, 123.4, 120.7, 116.5, 114.7, 112.0, 110.9, 92.8, 88.9, 56.0, 55.6.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{19}N_2O_3$: 383.1390; found: 383.1398.

4-({4-[5-(4-Methoxyphenyl)-1,3,4-oxadiazol-2-yl]phenyl}ethynyl)benzonitrile (2i)

Yield: 16 mg (60%); white solid; mp 233–235 °C; R_f = 0.21 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.13 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 8.08 (d, ^3J = 8.9 Hz, 2 H, H_{Ar}), 7.68 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 7.67–7.62 (m, 4 H, H_{Ar}), 7.04 (d, ^3J = 8.9 Hz, 2 H, H_{Ar}), 3.90 (s, 3 H, OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.9, 163.7, 162.7, 133.2, 132.5, 132.3, 132.2, 128.9, 127.8, 126.9, 125.5, 124.4, 118.5, 116.3, 114.7, 92.9, 90.4, 55.6.

HRMS (ESI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{16}N_3O_2$: 378.1237; found: 378.1243.

2-{4-[(2-Methoxyphenyl)ethynyl]phenyl}-5-(naphthalen-1-yl)-1,3,4-oxadiazole (2j)

Yield: 49.6 mg (87%); white solid; mp 181–183 °C; R_f = 0.47 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.30 (d, ^3J = 8.4 Hz, 1 H, H_{Ar}), 8.29 (d, ^3J = 7.6 Hz, 1 H, H_{Ar}), 8.18 (d, ^3J = 8.4 Hz, 2 H, H_{Ar}), 8.07 (d, ^3J = 8.4 Hz, 1 H, H_{Ar}), 7.95 (d, ^3J = 8.4 Hz, 1 H, H_{Ar}), 7.75–7.71 (m, 3 H, H_{Ar}), 7.63–7.60 (m, 2 H, H_{Ar}), 7.53 (dd, ^3J = 7.6 Hz, ^4J = 1.7 Hz, 1 H, H_{Ar}), 7.58 (t, ^3J = 7.6 Hz, 1 H, H_{Ar}), 6.98 (t, ^3J = 7.6 Hz, 1 H, H_{Ar}), 6.94 (d, ^3J = 8.4 Hz, 1 H, H_{Ar}), 3.95 (s, 3 H, OCH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.9, 164.0, 160.3, 134.0, 133.8, 132.8, 132.4, 130.5, 130.3, 128.9, 128.6, 128.4, 127.4, 127.0, 126.9, 126.4, 125.0, 123.2, 120.7, 120.6, 92.8, 89.1, 56.0.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{19}N_2O_2$: 403.1441; found: 403.1446.

2-{4-[(4-Fluorophenyl)ethynyl]phenyl}-5-(naphthalen-2-yl)-1,3,4-oxadiazole (2k)

Yield: 48.2 mg (78%); white solid; mp 194–196 °C; R_f = 0.32 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.65 (s, 1 H, H_{Ar}), 8.22 (dd, ^3J = 8.5 Hz, ^4J = 1.6 Hz, 1 H, H_{Ar}), 8.19 (d, ^3J = 8.5 Hz, 2 H, H_{Ar}), 8.00 (d, ^3J = 8.5 Hz, 2 H, H_{Ar}), 7.92 (d, ^3J = 9.0 Hz, 1 H, H_{Ar}), 7.70 (d, ^3J = 8.5 Hz, 2 H, H_{Ar}), 7.63–7.59 (m, 2 H, H_{Ar}), 7.58–7.54 (m, 2 H, H_{Ar}), 7.08 (t, ^3J = 8.5 Hz, 2 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.1, 164.4, 162.9 (d, $^1J_{C,F}$ = 249.0 Hz), 134.9, 133.8 (d, $^3J_{C,F}$ = 8.4 Hz), 133.0, 132.3, 129.3, 129.0, 128.2, 128.1, 127.6, 127.3, 127.0, 126.8, 123.5, 123.4, 121.2, 118.9 (d, $^4J_{C,F}$ = 3.8 Hz), 116.0 (d, $^2J_{C,F}$ = 22.0 Hz), 91.5, 88.4.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{16}FN_2O$: 391.1241; found: 391.1242.

2-(Anthracen-9-yl)-5-[4-(*p*-tolylethynyl)phenyl]-1,3,4-oxadiazole (2l)

Yield: 50.7 mg (93%); yellow solid; mp 198–200 °C; R_f = 0.77 (EtOAc–PE, 1:4).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.71 (s, 1 H, H_{Ar}), 8.18 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 8.12 (d, ^3J = 7.6 Hz, 2 H, H_{Ar}), 8.06 (d, ^3J = 7.6 Hz, 2 H, H_{Ar}), 7.69 (d, ^3J = 8.6 Hz, 2 H, H_{Ar}), 7.59–7.54 (m, 4 H, H_{Ar}), 7.46 (d, ^3J = 8.0 Hz, 2 H, H_{Ar}), 7.19 (d, ^3J = 8.0 Hz, 2 H, H_{Ar}), 2.39 (s, 3 H, CH_3).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.6, 163.4, 139.2, 132.4, 131.8, 131.7, 131.6, 131.2, 129.4, 128.9, 127.9, 127.5, 127.1, 125.9, 125.2, 123.2, 119.7, 117.3, 29.9.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{21}N_2O$: 437.1648; found: 437.1639.

2-(Anthracen-9-yl)-5-{[4-(*p*-fluorophenyl)ethynyl]phenyl}-1,3,4-oxadiazole (2m)

Yield: 35.2 mg (64%); yellow solid; mp 209–211 °C; R_f = 0.43 (EtOAc–PE, 1:6).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.71 (s, 1 H, H_{Ar}), 8.19 (d, ^3J = 8.3 Hz, 2 H, H_{Ar}), 8.11 (dd, ^3J = 7.4 Hz, ^4J = 2.4 Hz, 2 H, H_{Ar}), 8.05 (d, ^3J = 7.9 Hz, 2 H, H_{Ar}), 7.69 (d, ^3J = 8.3 Hz, 2 H, H_{Ar}), 7.59–7.54 (m, 6 H, H_{Ar}), 7.08 (t, ^3J = 8.6 Hz, 2 H, H_{Ar}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.5, 163.4, 162.9 (d, $^1J_{C,F}$ = 249.0 Hz), 133.8 (d, $^3J_{C,F}$ = 8.4 Hz), 132.4, 131.73, 131.61, 131.18, 128.9, 127.9, 127.2, 127.0, 125.9, 125.2, 123.5, 118.9 (d, $^4J_{C,F}$ = 3.5 Hz), 117.2, 116.0 (d, $^2J_{C,F}$ = 22.0 Hz), 91.5, 88.4.

HRMS (APCI+, Orbitrap): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{18}N_2OF$: 441.1398; found: 441.1436

Acknowledgment

Financial support from the National Research Council (CNCS) of Romania, Grant PN-II-PT-PCCA-2013-4-0291 (contract no. 203/2014) is gratefully acknowledged.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560387.

References

(1) These authors contributed equally to this work.
(2) (a) Tao, Y.; Yang, C.; Qin, J. *Chem. Soc. Rev.* **2011**, *40*, 2943. (b) Hughes, G.; Bryce, M. R. *J. Mater. Chem.* **2005**, *15*, 94.
(3) Jakopin, Z.; Dolenc, M. S. *Curr. Org. Chem.* **2008**, *12*, 850.
(4) Cha, S. W.; Choi, S. H.; Kim, K.; Jin, J. I. *J. Mater. Chem.* **2003**, *13*, 1900.
(5) Cristiano, R.; Vieira, A. A.; Ely, F.; Gallardo, H. *Liq. Cryst.* **2006**, *33*, 381.
(6) Majumdar, K. C.; Shyam, P. K.; Biswas, A.; De, S. *J. Lumin.* **2013**, *143*, 321.
(7) Dong, Y. B.; Xu, H.-X.; Ma, J. P.; Huang, R. Q. *Inorg. Chem.* **2006**, *45*, 3325.
(8) (a) Wang, C.; Palsson, L.-O.; Batsanov, A. S.; Bryce, M. R. *J. Am. Chem. Soc.* **2006**, *128*, 3789. (b) Palsson, L.-O.; Wang, C.; Batsanov, A. S.; King, S. M.; Beeby, A.; Monkman, A. P.; Bryce, M. R. *Chem. Eur. J.* **2010**, *16*, 1470.
(9) (a) Wang, C.; Batsanov, A. S.; Bryce, M. R. *Chem. Commun.* **2004**, 578. (b) Hughes, G.; Kreher, D.; Wang, C.; Batsanov, A. S.; Bryce, M. R. *Org. Biomol. Chem.* **2004**, *2*, 3363. (c) Kreher, D.; Batsanov, A. S.; Wang, C.; Bryce, M. R. *Org. Biomol. Chem.* **2004**, *2*, 858.
(10) Chen, S.; Xu, X.; Liu, Y.; Qiu, W.; Yu, G.; Sun, X.; Zhang, H.; Qi, T.; Lu, K.; Gao, X.; Liu, Y.; Zhu, D. *J. Mater. Chem.* **2007**, *17*, 3788.
(11) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (b) Chinchilla, R.; Najera, C. *Chem. Rev.* **2007**, *107*, 874. (c) Chinchilla, R.; Najera, C. *Chem. Soc. Rev.* **2011**, *40*, 5084.
(12) Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46.
(13) (a) Kumar, A.; Tyagi, P.; Reddy, M. A.; Mallesham, G.; Bhanuprakash, K.; Rao, V. J.; Kamalasanan, M. N.; Srivastava, R. *RSC Adv.* **2014**, *4*, 12206. (b) Zhang, Z.; Jiang, W.; Ban, X.; Yang, M.; Ye, S.; Huang, B.; Sun, Y. *RSC Adv.* **2015**, *5*, 29708. (c) Hou, S.; Chan, W. K. *Macromolecules* **2002**, *35*, 850.
(14) (a) For a review describing synthetic methods of 1,3,4-oxadiazoles, see: Soares de Oliveira, C.; Lira, B. F.; Barbosa-Filho, J. M.; Fernandez Lorenzo, J. G.; Filgueiras de Athayde-Filho, P. *Molecules* **2012**, *17*, 10192. (b) For a recent example of dehydrative cyclization of *N*,*N*′-diacylhydrazines using $POCl_3$, see: Li, A. F.; Ruan, Y. B.; Jiang, Q. Q.; He, W. B.; Jiang, Y. B. *Chem. Eur. J.* **2010**, *16*, 5794. (c) For an example of oxidative cyclization of *N*′-acylhydrazones using CAN, see: Dabiri, M.; Salehi, P.; Baghbanzadeh, M.; Bahramnejad, M. *Tetrahedron Lett.* **2006**, *47*, 6983. (d) For an example of Huisgen reaction of tetrazole and acid chlorides, see: Yang, C.-C.; Hsu, C.-J.; Chou, P.-T.; Cheng, H. C.; Su, Y. O.; Leung, M. *J. Phys. Chem. B* **2010**, *114*, 756. (e) For oxidative cyclisation using molecular iodine, see: Majji, G.; Rout, S. K.; Guin, G.; Gogoi, A.; Patel, B. K. *RSC Adv.* **2014**, *4*, 5357. (f) Yu, W.; Huang, G.; Zhang, Y.; Liu, H.; Dong, L.; Yu, X.; Li, Y.; Chang, J. *J. Org. Chem.* **2013**, *78*, 10337.
(15) (a) Shang, Z. *Synth. Commun.* **2006**, *36*, 2927. (b) Dobrota, C.; Paraschivescu, C. C.; Dumitru, I.; Matache, M.; Baciu, I.; Ruta, L. L. *Tetrahedron Lett.* **2009**, *50*, 1879. (c) Paraschivescu, C.; Matache, M.; Dobrotă, C.; Nicolescu, A.; Maxim, C.; Deleanu, C.; Fărcășanu, I. C.; Hădade, N. D. *J. Org. Chem.* **2013**, *78*, 2670.
(16) (a) Sugiono, E.; Detert, H. *Synthesis* **2001**, 893. (b) Augustine, J. K.; Vairaperumal, V.; Narasimhan, S.; Alagarsamy, P.; Radhakrishnan, A. *Tetrahedron* **2009**, *65*, 9989. (c) Guin, S.;

Ghosh, T.; Rout, S. K.; Banerjee, A.; Patel, B. K. *Org. Lett.* **2011**, *13*, 5976. (d) Wielopolski, M.; Linton, K. E.; Marszałek, M.; Gulcur, M.; Bryce, M. R.; Moser, J. E. *Phys. Chem. Chem. Phys.* **2014**, *16*, 2090. (e) Dimmock, J. R.; Sidhu, K. K.; Tumber, S. D.; Basran, S. K.; Chen, M.; Quail, J. W.; Yang, J.; Rozas, I.; Weaver, D. F. *Eur. J. Med. Chem.* **1995**, *30*, 287.

(17) (a) Thorand, S.; Kraus, N. *J. Org. Chem.* **1998**, *63*, 8551. (b) Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, *2*, 1729.

(18) Birkholz (nee Gensow), M. N.; Freixa, Z.; van Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2009**, *38*, 1099.

(19) Beletskaya, I. P.; Cheprakov, A. V. *J. Organomet. Chem.* **2004**, *689*, 4055.

(20) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem. Int. Ed.* **2000**, *39*, 2632.

(21) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2014**, *114*, 1783.