Synthesis, spectral characteristics and electrochemistry of symmetrically-substituted hybrids derived from 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole under Suzuki cross-coupling reaction

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Abstract
New symmetrically substituted derivatives of 2,5-bis(4-arylphenyl)-1,3,4-oxadiazole were prepared from 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole and various thiophene-, furan-, pyridine- or benzene-containing boronic acids by a palladium catalyzed Suzuki cross-coupling reaction under the conditions of the phase transfer catalysis. The structure of the products, the absorption and emission spectra and their electrochemistry were also studied.

Keywords: Heterocycles, Suzuki cross-coupling, 1,3,4-oxadiazoles, phase-transfer catalysis, photoluminescence

Introduction

Organic conducting or semiconducting compounds based on extended π-conjugated systems have been the subject of intensive studies over the past several years.[1-4] Functionalized hybrids of this type featuring increased photo- and electroluminescent properties, attract exceptional interest of material sciences as active components for electroluminescent diodes, displays, and photovoltaic cells. Amongst heteroaromatic compounds used widely in the production of new materials for optoelectronics, derivatives of 1,3,4-oxadiazole play an important role.[5-8] One of the most widely studied representatives of electron-injection/hole-blocking materials from this class is 2-(4-biphenylyl)-5-(4-tertbutylphenyl)-1,3,4-oxadiazole (PBD), exhibiting high photoluminescence quantum yield and good thermal and chemical stabilities.[9,10] A literature survey revealed some other examples of π-conjugated 1,3,4-oxadiazole hybrids connected directly or indirectly to other

aromatic systems, such as pyridine and pyrimidine,[11] benzene,[12] phenoxazine,[13] naphthalene,[14] thiophene[15-17] and fluorene.[18] Besides being of interest to the material sciences, these non-naturally occurring heterocycles also exhibit a broad spectrum of biological activity, such as antibacterial, anticonvulsant, antidepressive, anticancer and antifungal activities, which makes them potentially useful agents in medicine and agriculture.[19-27] The leading 1,3,4-oxadiazoles are usually prepared from acid hydrazides as cyclocondensation substrates with carboxylic acids,[28] aromatic aldehydes,[29] orthoesters[30] or by transformations involving other rings, such as 1,2,4-oxadiazole.[31] However, the most popular methodology involves reactions of diacylhydrazines with a range of cyclodehydrating agents, just to mention polyphosphoric acid, boron trifluoride-diethyl etherate, thionyl chloride, phosphorus oxychloride or the Burgess reagent.[32-37]

Bearing in mind excellent electron properties of both five- and six membered heterocyclic rings, such as thiophene, furan or pyridine and 1,3,4-oxadiazole, it was decided to combine these scaffolds in order to get new organic hybrids and to study their spectroscopic and electrochemical properties. Nowadays, one of the most versatile and effective method for the formation of new carbon-carbon bonds is the palladium-catalyzed Suzuki cross-coupling reaction.[38,39] It makes use of aromatic or vinyl halides or triflates and a range of boronic acids, and it may be conducted in a conventional way, by means of the phase-transfer catalysis, under the influence of microwaves or ultrasounds. The reaction is usually accompanied with the presence of a base to activate boronic acid and to facilitate the transmetallation step.

In this paper we describe the efficient synthesis and characterization of novel 1,3,4-oxadiazole-based derivatives conjugated to thiophene, furan, pyridine and benzene rings via phenylene linker by means of the Suzuki cross-coupling reaction. To the best of our knowledge, these fragment hybrids, not described in literature so far, are potentially interesting monomers for optoelectronic applications, because they combine different aromatic rings featuring excellent electron-transporting properties with high luminous efficiencies.

Results and Discussion

The leading scaffold - 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole (**3**) - was obtained in a two-step transformation from the commercially available 4-bromobenzoyl chloride (**1**). The initial chloride **1** treated with hydrazine hydrate in the presence of triethylamine gave the adequate *N,N'*-diacylhydrazine (**2**), which heated with phosphorus oxychloride in non-polar solvent led to the desired compound **3** in excellent yield (Scheme 1).
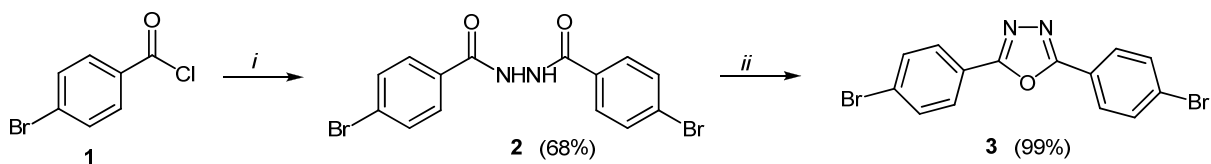
Scheme 1. Synthesis of 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole (**3**) scaffold. Reagents and conditions: (*i*) N$_2$H$_4$•H$_2$O, TEA, CHCl$_3$, rt, 4 h; (*ii*) POCl$_3$, toluene, reflux, 11 h.

The resulted dibromo derivative **3**, bifunctional compound for the Suzuki cross-coupling reaction, was heated with 2-thiopheneboronic acid (**4a**) in the homogenous aqueous-ethanol solution and in the presence of a catalyst: tetrakis(triphenylphosphine) palladium $Pd(PPh_3)_4$. The initial optimization involved the addition of a non-polar solvent, such as toluene, the application of different phase transfer catalysts (NBu_4Cl, NBu_4Br), the influence of a base concentration on the reaction yield, and finally the ratio of substrates (Scheme 2). The first attempts involving the few-hour heating of the reaction mixture in a basic media (K_2CO_3) on an oil-bath resulted in the formation of the final product **5a** in low yields (5%, entry 1, Table 1). Better results were obtained when the reaction was conducted in a two-phase system under the phase-transfer catalysis.
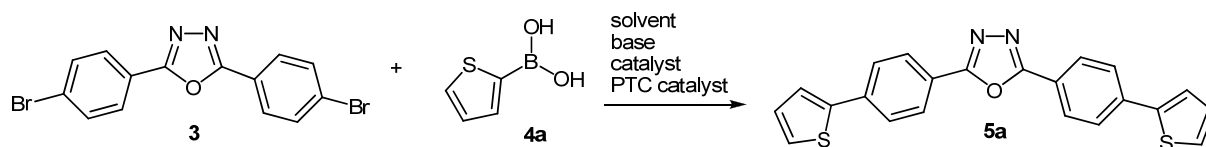
Scheme 2. Synthesis of 3,5-bis(4-(2-thienyl)phenyl)-1,3,4-oxadiazole (**5a**).

Table 1. Initial optimization of the coupling reaction to afford **5a**

Entry	**3 : 4a** ratio (equiv.)	Solvents	Base K_2CO_3 (equiv.)	Catalyst $Pd(PPh_3)_4$ (equiv.)	PTC catalyst (equiv.)	Yield[a] (%)
1	1 : 2	$EtOH/H_2O$	4	0.01	-	5
2	1 : 2	$EtOH/H_2O$/toluene	4	0.01	NBu_4Cl 0.1 eq	30
3	1 : 2	$EtOH/H_2O$/toluene	10	0.01	NBu_4Cl 0.1 eq	32
4	1 : 2	$EtOH/H_2O$/toluene	10	0.05	NBu_4Cl 0.1 eq	37
5	1 : 2	$EtOH/H_2O$/toluene	10	0.05	NBu_4Br 0.1 eq	46
6	1 : 2.5	$EtOH/H_2O$/toluene	10	0.05	NBu_4Br 0.1 eq	74

[a] Yield with respect to the starting 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole (**3**). Conditions: oil bath: 130 °C, reaction time: 7 h.

It was found that from the two PTC catalysts studied, tetrabutylammonium bromide acted better than its chloride counterpart (entries 4,5, Table 1). One should also notice the beneficial effect of high K_2CO_3 concentrations on the reaction yield. The role of base in Suzuki cross-coupling reactions is still under investigation.[40] However, there is no doubt that it plays at least a dual action in the whole transformation. The base participates both in exchanging halogen ions in the molecule of the starting halide **3** at the surface of catalyst and in activating boronic acid **4** to facilitate transmetallation step, which requires increased amounts of this reagent. In addition, the

considerable increase in yield was observed for an excess amount of boronic acid **4a** and larger amounts of the palladium catalyst (74%, entry 6, Table 1). One of the reactions gave also a nonsymmetrical product, being the result of mono-coupling transformation **6** (Table 2).

Thus, optimized reaction conditions were applied in the synthesis of other 2,5-bis(4-arylphenyl)-1,3,4-oxadiazole **5b–g** hybrids (Scheme 3). The leading 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole (**3**) was heated on the oil-bath with an excess amount of the selected heterocyclic five- and six-membered boronic acids **4a–f** and with phenylboronic acid (**4g**) in the presence of the 5 mol % palladium catalyst Pd(PPh₃)₄. The reactions were conducted under the phase transfer catalysis in a two-phase solvent system (EtOH/H₂O/toluene) and by means of NBu₄Br as the phase transfer catalyst. The progress of the transformation was monitored by TLC until the initial 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole (**3**) was fully consumed.

Ar = 2-thienyl, 3-thienyl, 2-furyl, 3-furyl, 4-pyridyl, 3-pyridyl, C₆H₅
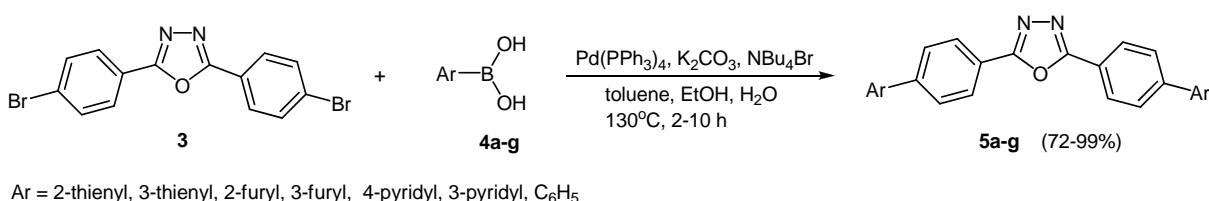
Scheme 3. Synthesis of 2,5-bis(4-arylphenyl)-1,3,4-oxadiazole **5a–g** hybrids. Reagents and conditions: aryl dichloride **3** (1.00 mmol), boronic acid **4** (2.50 mmol), Pd(PPh₃)₄ (0.05 mmol), NBu₄Br (0.10 mmol), K₂CO₃ (10 mmol), toluene/H₂O/EtOH (10:6:3 mL), 130 °C, 2-10 h.

The study afforded novel symmetrical 2,5-diphenyl-1,3,4-oxadiazole derivatives substituted at the position 4 of the benzene rings with heteroaryl and phenyl groups in high yields (72–99%, Table 2). The best result was obtained in the case of a reaction where phenylboronic acid was applied (**5g**, 99%, Table 2). The products containing terminal both electron deficient and electron rich heterocyclic arrangements were produced in relatively lower yields (Table 2). One should also note the effect of the position of the heteroatom in the cycle on the reaction yield. Moreover, heteroaryl derivatives substituted at the position 3 (**5b,d**) were formed more readily than their 2-substituted isomers (**5a**,**c**). The structures of conjugated hybrids **5a–g** obtained in the Suzuki cross-coupling reactions from the initial 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole (**3**) were confirmed with elemental analyses and typical spectroscopic methods (^{1}H and ^{13}C NMR, UV, HRMS, IR). Generally, 2,5-bis(4-arylphenyl)-1,3,4-oxadiazoles **5a–g** are highly melting and sparingly soluble solids. In the ^{1}H spectra of 2,5-bis(4-arylphenyl)-1,3,4-oxadiazoles **5a–g**, one can observe a reduced number of proton signals due to the fact that compounds like these possess a symmetrical structure. The most characteristic peaks in the ^{1}H NMR spectra are associated with the protons adjacent to phenylene linkers at the positions 2 and 5 of the 1,3,4-oxadiazole ring and appear as a doublet. Two phenylene protons H2' and H6' are shifted in the ^{1}H NMR spectra to low fields and appear between 8.15 and 8.29 ppm. Such significant changes in the chemical shifts could result from their proximity to the ring's nitrogen and oxygen atoms. The remaining H3' and H5' proton signals occur in the range of 7.65–7.83 ppm. Similarly to ^{1}H NMR spectra, the spectra of ^{13}C NMR also show a

decreased number of signals. Here, the diagnostic peak comes from C2 and C5 carbon atoms of the 1,3,4-oxadiazole scaffold and appears in the narrow range between 164.3–164.5 ppm.

Table 2. 2,5-Bis(4-arylphenyl)-1,3,4-oxadiazoles **5a**−**g** and intermediate **6** prepared in Suzuki cross-coupling reactions
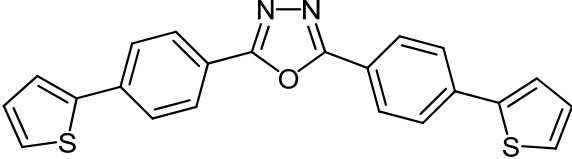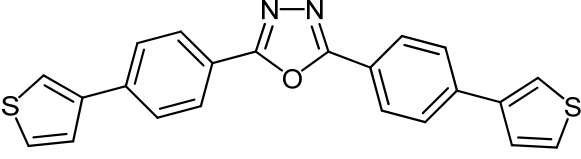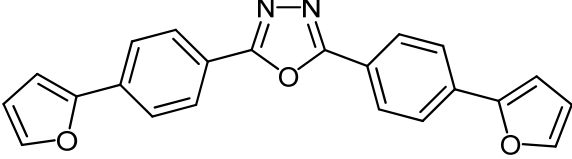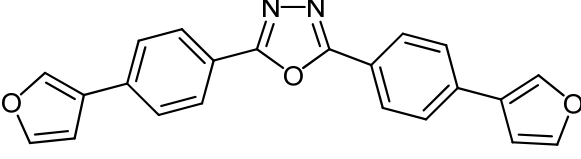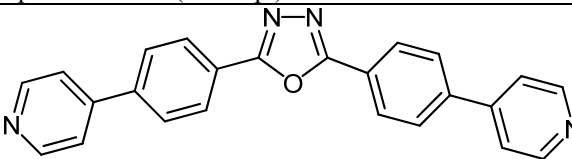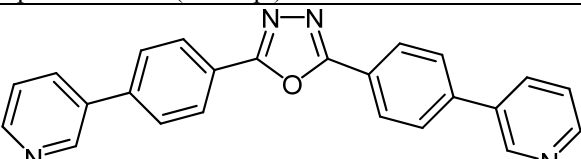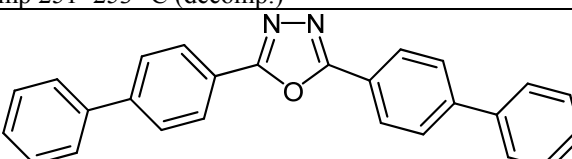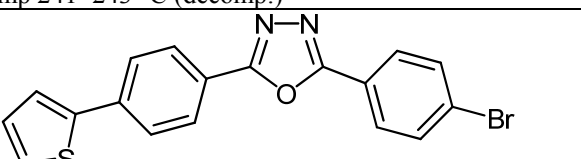
5a (74%); Time 5 h	**5b** (89%); Time 4 h
mp 250–252 °C (decomp.)	mp 313–315 °C (decomp.)
5c (72%); Time 10 h	**5d** (85%); Time 7 h
mp 210–212 °C (decomp.)	mp 238–240 °C (decomp.)
5e (95%); Time 2 h	**5f** (94%); Time 3 h
mp 251–253 °C (decomp.)	mp 241–243 °C (decomp.)
5g (99%); Time 5 h	**6** (4%); Time 7 h
mp 239–240 °C (lit.: [41] mp 234–236 °C)	mp 193–194 °C (decomp.)

Figure 1 presents UV spectra of the target compounds **5a**−**g** registered in the methanol solution at room temperature at the same molar concentration. One can clearly see the existence of two (**5d**−**g**) or three absorption maxima (**5a**−**c**), depending on the nature of the terminal aryl substituent. In addition, the five-membered terminal substituents (**5a**−**d**) present at the studied hybrids are shifted to the longer wavelengths from 5 up to 30 nm, in contrast to the model 3,5-bis(4-biphenylyl)-1,3,4-oxadiazole (**5g**), while for the pyridine derivatives (**5e**,**f**) the reversed trend is observed. One may also observe distinct differences in the position of absorption maximum for 2-substituted thienyl and furyl derivatives (**5a**,**c**, Table 3) and their 3-substituted counterparts (**5b**,**d**, Table 3). This might be probably attributed to the existence of the additional interaction between hydrogen of the phenylene linker and the terminal 2-substituted heteroaryl group strengthening

coplanarization of the molecule and enhancing conjugation which results in considerable shifting of the long-wave absorption maximum. UV spectra of the investigated compounds in dichloromethane (Figure 2) consist of a single, unstructured band attributed to a π-π* electron transition in the conjugated bond network. Conversely, fluorescence spectra comprise three individual signals, two of which manifest as distinct peaks, with the third signal overlapping to the point of constituting an inflection on the low energy slope of the central emission peak. In comparison to 2,5-bis(4-biphenylyl)-1,3,4-oxadiazole (**5g**), the absorption and emission maxima of **5a−d** derivatives are red-shifted. The occurrence of this effect, upon replacing of the terminal phenyl substituents by thiophene or furan rings, implies enhanced conjugation between the core and its substituents. This can be explained by the interaction of the heteroatom, present within these rings, with the phenylene hydrogen atoms of the core moiety, leading to co-planarization of the two rings.
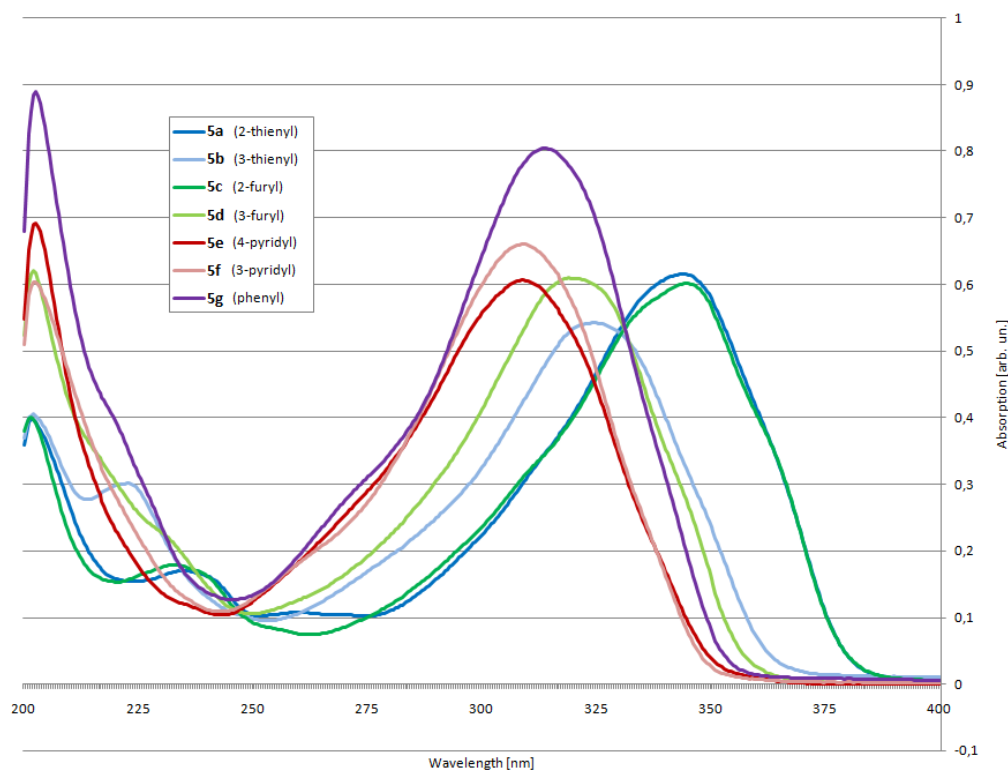

Figure 1. Experimental absorption spectra of 2,5-bis(4-arylphenyl)-1,3,4-oxadiazoles **5a−g**. Measurement conditions: $C=1.2 \cdot 10^{-5}\,M$, solvent: methanol, rt.

The observed Stokes shifts (Δ) imply that the changes to the geometry of the molecules, brought on by the transition from their ground state to the first excited state, are relatively small. Arranging these compounds by the magnitude of the observed shifts gives the sequence **5c**<**5a**<**5d**<**5f**<**5g**<**5e**<**5b**, with larger Stokes shifts being more desirable, as re-absorption of the emitted photons is minimized.[42] The investigated 1,3,4-oxadiazole derivatives **5a−g** show strong photoluminescence, with measured quantum yields Φ_f ranging from 0.67 for 3-thienyl containing arrangement **5b** up to 0.91 for its 3-furyl counterpart **5d** (Table 3). Generally, replacing thienyl

substituents with furyl one resulted in an increase of the fluorescence quantum yield, a phenomenon called the "heavy atom effect".[43]

Table 3. Absorption and fluorescence spectral parameters of investigated compounds **5a−g**

Compound	Absorption maximum λ_{max} [nm]	Onset of the $\pi-\pi^*$ absorption λ_{onset} [nm]	Optical orbital energy gap[a] [eV]	Excitation wavelength λ_{ex} [nm]	Emission wavelength λ_{em} [nm]	Stokes shift[b] Δ [nm]	Quantum yield Φ_f
5a	344	383	3.24	340	383, 402, 426(E)[c]	39	0.71
5b	318	366	3.39	317	367(E), 383, 404(E)	49	0.67
5c	346	382	3.25	345	382, 401, 425(E)	36	0.86
5d	319	360	3.44	315	359, 376, 394(E)	40	0.91
5e	311	352	3.51	307	356, 372, 390(E)	45	0.86
5f	313	353	3.51	309	355, 372, 391(E)	42	0.81
5g	316	355	3.49	312	359, 376, 394(E)	43	0.86

[a] Calculated for spectra registered in dichloromethane (Figure 3). [b] Stokes shift from the equation $\Delta=\lambda_{em}-\lambda_{max}$.[44] [c] E − shoulder. [d] 9,10-Diphenylanthracene in cyclohexane (for **5b,d,e,f,g**) and 1,4-diphenylbutadiene in hexane (for **5a**,**c**) were used as standards.[45-48]

The electrochemical investigation of the synthesized 1,3,4-oxadiazole derivatives **5a−g**, except for **5a**, show a distinct reduction signal and an onset of an oxidative process, which can be attributed to the supporting electrolyte, due to reaching the limits of its operating potential window. Although it was possible to identify the reduction onset potential (E_{red}) for every compound (Table 4), oxidation onset potentials (E_{ox}) were determined only for **5a**,**c**,**d** and **5g**. In the case of **5b**,**e** and **5f**, the oxidation peak onset was located beyond the boundary of the operating potential window of the supporting electrolyte. Electrochemical redox potentials provide a good estimate of the ionization potential (IP) and electron affinity (EA) parameters.[49] Minor shifts in E_{red} have been observed, indicating that the electrochemically generated negative charge is located primarily on the electron-accepting 1,3,4-oxadiazole moiety,[50] with some contribution of the electron-donating 4-arylphenyl substituents. Oxidation peaks of most compounds are not observed for compounds **5b−g** in the potential window of the utilized supporting electrolyte, concurrent with the estimated energies of the electron transitions, believed to be HOMO-LUMO transitions, observed via UV-Vis spectroscopy. Conversely, in the case of **5a**, a clear anodic peak is observed. The electrochemical orbital energy gap of this compound can be estimated at 2.3 eV, which should give rise to an optical

absorption signal centered at approximately 540 nm. In light of the lack of such an absorption signal, the absorption peaks comprising the UV spectra of each of the investigated compounds may arise not from the HOMO-LUMO transition, but rather from a more energetic transition, due to the orbital symmetry constraints. Repeated potential cycling of a **5a** solution, in a potential range incorporating the above-mentioned oxidation signal, brings about the evolution of another oxidation signal, located at less positive potentials (Figure 3). Consequent potential cycles yield a shift of the incipient oxidation peak towards more positive potentials implying that the electrode becomes increasingly isolated from the electrolyte solution, due to the deposition of an insoluble film of **oligo(5a)**. Upon cycling the potential of such a modified electrode in a pristine solution of the supporting electrolyte, the oxidation peak diminishes and shifts toward higher potentials, indicating a deterioration of the electrical properties of the investigated layer.
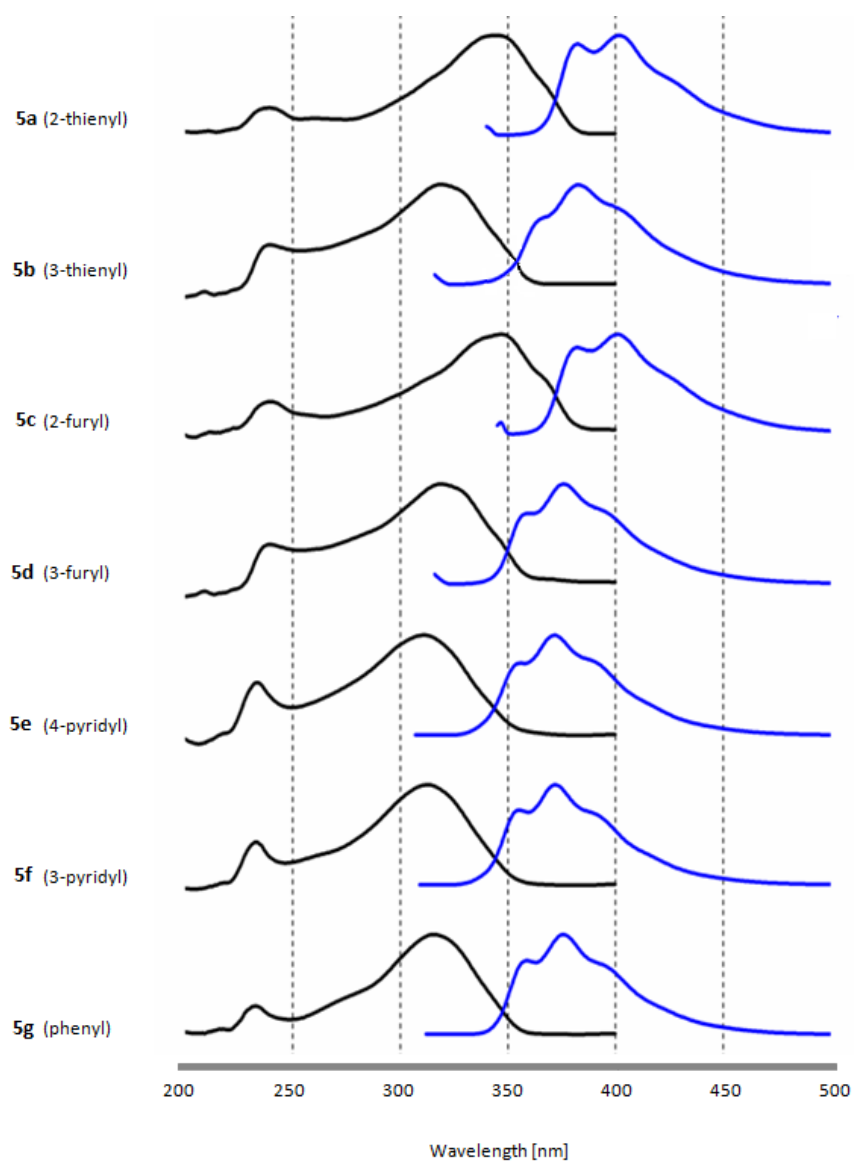

Figure 2. UV-Vis absorption and fluorescence spectra of 2,5-bis(4-arylphenyl)-1,3,4-oxadiazoles **5a−g**. Measurement conditions: C=1.0·10^{-7} M, solvent: dichloromethane, rt.

Table 4. Reduction potentials and electron affinities of compounds **5a−g**

Compound	Reduction potential[a] E_{red} [V]	Electron affinity[b] [eV]	Oxidation Potential E_{ox} [V]	Ionization potential[b] [eV]	Electrochemical orbital energy gap[c] [eV]	Optical orbital energy gap[d] [eV]
5a	-1.29	3.81	+1.01	6.11	2.30	3.27
5b	-1.13	3.97	-	7.39[c]	-	3.42
5c	-1.37	3.73	+0.72	5.82	2.09	3.28
5d	-1.07	4.03	+0.96	6.06	2.03	3.47
5e	-1.23	3.87	-	7.41[c]	-	3.54
5f	-1.18	3.92	-	7.48[c]	-	3.56
5g	-1.21	3.89	+0.89	5.99	2.10	3.52

[a] Reduction potential vs. Ferrocene/Ferrocinium standard redox couple.
[b] Calculated using equations: Electron affinity=$|e| \cdot (5.1 + E_{red})$; Ionization potential=$|e| \cdot (5.1 + E_{ox})$.
[c] Ionization potential estimated based on optical orbital energy gap.
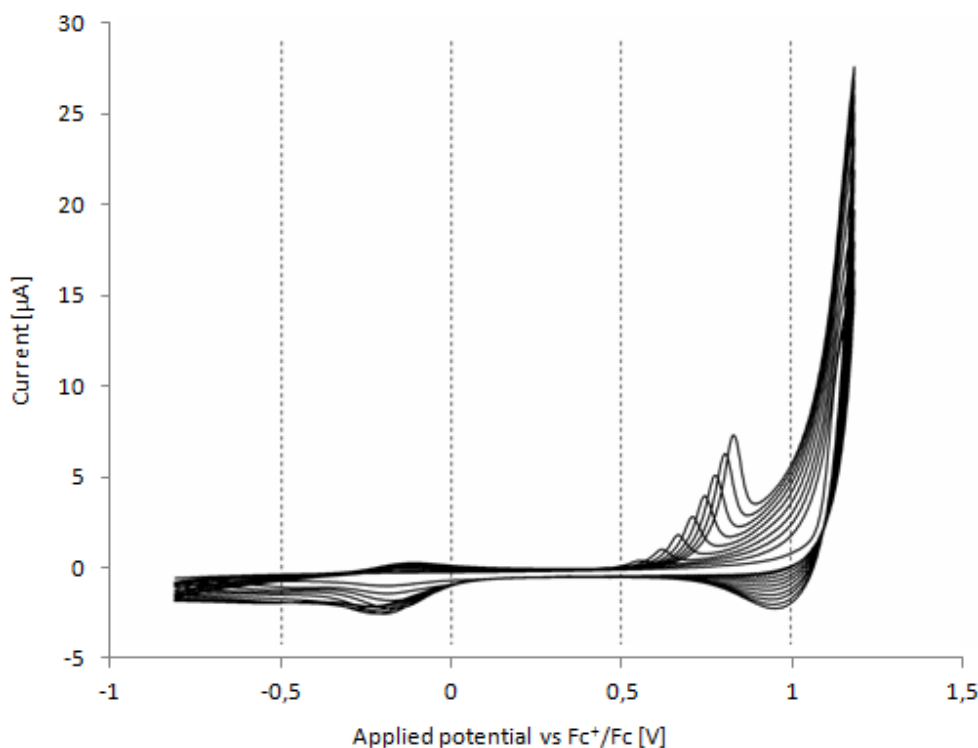[d] Calculated for spectra registered in methanol (Figure 1).

Figure 3. Evolution of **oligo(5a)** redox system upon repeated potential cycling of a **5a** solution. Measurement conditions: C=$1.0 \cdot 10^{-3}$ *M*, solvent: dichloromethane, supporting electrolyte: tetrabutylammonium hexafluorophosphate, C=0.1 *M*, potential sweep rate: 0.1 V·s^{-1}.

Conclusions

We have demonstrated an efficient methodology for the synthesis of conjugated 1,3,4-oxadiazoles substituted symmetrically with selected heteroaromatic and aromatic rings via a phenylene linker, compounds, which may find useful applications in material sciences. The application of the phase-transfer catalysis in the key Suzuki cross-coupling reaction of the 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole bifunctional moiety and boronic acids has got a beneficial effect on the reaction progress and yield. Strong fluorescence has been observed for all compounds, with emission spectra of the compounds revealing a vibronic structure typical to 1,3,4-oxadiazole derivatives. High fluorescence quantum yields were observed, reaching up to 91%, dependent on the nature of terminal substituents, suggesting conjugation extending over all five rings of the investigated systems. Electrochemical polymerization of a 2-thienyl derivative has been observed, however, it is followed by electro-deactivation of the deposit, possibly due to over-oxidation.

Experimental Section

General. Melting points were measured using a Stuart SMP3 melting point apparatus. The ^{1}H and ^{13}C NMR spectra were recorded on an Agilent 400-NMR spectrometer in DMSO-d_6 and CDCl$_3$ solutions using TMS as the internal standard. UV spectra were recorded on a Jasco V-650 spectrophotometer. FT-IR spectra were recorded between 4000 and 650 cm^{-1} on an FT-IR Nicolet 6700 apparatus with a Smart iTR accessory. Elemental analysis were performed with a VarioEL analyser. High-resolution mass spectra were obtained by means of a Waters ACQUITY UPLC/Xevo G2QT instrument. Thin-layer chromatography was performed on silica gel 60 F$_{254}$ (Merck) thin-layer chromatography plates using benzene/ethyl acetate (3:1 v/v) as the mobile phase. Fluorescence spectra were recorded at room temperature in dichloromethane solution using Hitachi F-2500 fluorescence spectrophotometer. Cyclic voltammetry studies were performed using a Metrohm-AUTOLAB PGSTAT20 potentiostat operating in argon atmosphere. Platinum wire was used as the working electrode, an Ag pseudoreference electrode was employed, being calibrated versus the ferrocene/ferrocinium standard redox couple.

N,N'-**Bis(4-bromobenzoyl)hydrazine (2).** To a magnetically agitated solution of hydrazine hydrate (2.4 mL, 0.05 mol), triethylamine (13.9 mL, 0.10 mol) in 100 mL of chloroform placed in an ice bath, 4-bromobenzoyl chloride (**1**, 21.95 g, 0.10 mol) was added, dissolved in 100 mL of chloroform. After the addition was completed, the mixture was stirred for 4 hours at room temperature. The solid precipitate was collected by filtration, washed with hexane, a large quantity of water, air-dried yielding pure *N,N'*-bis(4-bromobenzoyl)hydrazine (**2**). White solid (8.91 g, 79% yield); mp 316-318 °C (lit.:[51] mp 319–320 °C); R$_f$ (benzene/ethyl acetate, 1:3 v/v) 0.61.

2,5-Bis(4-bromophenyl)-1,3,4-oxadiazole (3). A mixture of *N,N'*-bis(4-bromobenzoyl) hydrazine (**2**, 7.96 g, 0.02 mol) and phosphorous oxychloride (18.5 mL, 0.20 mol) in 100 mL of dry toluene was refluxed until the initial compound **2** was fully consumed (TLC, 11 h). After cooling, the

precipitated crystals were filtered off to give pure 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole (**3**). The filtrate was concentrated on a rotary evaporator and then treated with ethanol. The solid precipitate was filtered off, washed with EtOH, air-dried yielding additional amounts of 2,5-bis(4-bromophenyl)-1,3,4-oxadiazole. White crystals (6.62 g, 99% yield); mp 259 °C (lit.:[51] mp 258 °C); R_f (benzene/ethyl acetate, 3:1 v/v) 0.62.

General Synthesis of 2,5-Bis(4-arylphenyl)-1,3,4-oxadiazoles (5a-g). 2,5-Bis(4-bromophenyl)-1,3,4-oxadiazole (**3**, 0.38 g, 1.00 mmol), the appropriate boronic acid (**4a–g**, 2.50 mmol), tetrakis(triphenylphosphine)palladium(0) (0.06 g, 0.05 mmol), tetrabutylammomium bromide (0.03 g, 0.10 mmol) and K_2CO_3 (1.38 g, 10.00 mmol) were treated with a combination of toluene (10 mL), H_2O (6 mL) and the EtOH (3 mL) solvent system. The mixture was kept under reflux in the oil bath (120 °C) for 2–7 h (TLC). After cooling, 100 mL of $CHCl_3$ was added and the whole mixture was filtered through silica gel. The filtrate was separated, the organic layer was dried over anhydrous $MgSO_4$ and then concentrated on a rotary evaporator. The residue was treated with a mixture of benzene/ethyl acetate (3:1 v/v). The solid precipitate was filtered off, washed with benzene/ethyl acetate (3:1 v/v), air-dried to give pure 2,5-bis(4-arylphenyl)-1,3,4-oxadiazole (**5a–g**).

3,5-Bis[4-(2-thienyl)phenyl]-1,3,4-oxadiazole (5a). Yellow solid (0.28 g, 74% yield); mp 250–252 °C (decomp.); R_f (benzene/ethyl acetate, 3:1 v/v) 0.60. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (dd, J 5.2 Hz and 3.2 Hz, 2H), 7.38 (d, J 5.2 Hz, 2H), 7.45 (d, J 3.2 Hz, 2H), 7.78 (d, J 8.4 Hz, 4H, -C_6H_4-: H3', H5'), 8.15 (d, J 8.4 Hz, 4H, -C_6H_4-: H2', H6'); ^{13}C NMR (100 MHz, $CDCl_3$): δ 122.6, 124.4, 126.3, 127.0, 127.6, 128.4, 137.6, 143.0, 164.3; UV-Vis: λ_{max} (MeOH) 202 nm (ε·10^{-3} 33.0 cm^{-1}·M^{-1}), 234 (14.1), 344 (51.1); IR (ATR) ν: 3075, 2158, 2029, 1607, 1522, 1487, 1429, 1410, 1350, 1257, 1212, 1189, 1124, 1104, 1075, 1015, 960, 849, 840, 821, 745, 705, 681 cm^{-1}; Anal. Calcd for $C_{22}H_{14}N_2OS_2$: C, 68.37; H, 3.65; N, 7.25. Found: C, 68.39; H, 3.60; N, 7.21; HRMS calcd for ($C_{22}H_{14}N_2OS_2$+H$^+$): 387.0626; found: 387.0631.

3,5-Bis[4-(3-thienyl)phenyl]-1,3,4-oxadiazole (5b). Beige solid (0.34 g, 89% yield); mp 313–315 °C (decomp.); R_f (benzene/ethyl acetate, 3:1 v/v) 0.51. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.50 (m, 4H), 7.61 (br s, 2H), 7.77 (d, J 8.0 Hz, 4H, -C_6H_4-: H3', H5'), 8.19 (d, J 8.0 Hz, 4H, -C_6H_4-: H2', H6'); ^{13}C NMR (100 MHz, $CDCl_3$): δ 121.8, 122.5, 126.1, 126.8, 126.9, 127.5, 136.4, 141.1, 164.5; UV-Vis: λ_{max} (MeOH) 202 nm (ε·10^{-3} 33.6 cm^{-1}·M^{-1}), 222 (25.0), 324 (45.1); IR (ATR) ν: 3098, 2177, 2035, 1683, 1611, 1581, 1551, 1527, 1489, 1430, 1349, 1283, 1255, 1202, 1193, 1076, 1034, 1011, 964, 863, 843, 782, 740, 709, 688 cm^{-1}; Anal. Calcd for $C_{22}H_{14}N_2OS_2$: C, 68.37; H, 3.65; N, 7.25. Found: C, 68.32; H, 3.62; N, 7.27; HRMS calcd for ($C_{22}H_{14}N_2OS_2$+H$^+$): 387.0626; found: 387.0629.

3,5-Bis[4-(2-furyl)phenyl]-1,3,4-oxadiazole (5c). Beige solid (0.31 g, 72% yield); mp 210–212 °C (decomp.); R_f (benzene/ethyl acetate, 3:1 v/v) 0.54. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.53 (dd, J 3.2 Hz and 1.6 Hz, 2H), 6.82 (d, J 3.2 Hz, 2H), 7.54 (d, J 1.6 Hz, 2H), 7.83 (d, J 8.6 Hz, 4H, -C_6H_4-: H3', H5'), 8.16 (d, J 8.6 Hz, 4H, -C_6H_4-: H2', H6'); ^{13}C NMR (100 MHz, $CDCl_3$): δ 107.1, 112.1, 122.3, 124.1, 127.4, 129.1, 143.1, 152.8, 164.3; UV-Vis: λ_{max} (MeOH) 201 nm (ε·10^{-3} 33.8 cm^{-1}·M^{-1}), 233 (15.1), 344 (50.8); IR (ATR) ν: 3116, 2162, 1684, 1612, 1548, 1500, 1425, 1272, 1220,

1185, 1161, 1106, 1076, 1010, 963, 903, 886, 846, 802, 748, 723, 709, 667 cm^{-1}; Anal. Calcd for C$_{22}$H$_{14}$N$_2$O$_3$: C, 74.57; H, 3.98; N, 7.91. Found: C, 74.58; H, 3.95; N, 7.89; HRMS calcd for (C$_{22}$H$_{14}$N$_2$O$_3$+H$^+$): 355.1083; found: 355.1082.

3,5-Bis[4-(3-furyl)phenyl]-1,3,4-oxadiazole (5d). Yellow solid (0.37 g, 85% yield); mp 238–240 °C (decomp.); R$_f$ (benzene/ethyl acetate, 3:1 v/v) 0.51. ^{1}H NMR (400 MHz, CDCl$_3$): δ 6.77 (dd, J 1.6 Hz and 0.8 Hz, 2H), 7.53 (d, J 1.6 Hz, 2H), 7.65 (d, J 8.8 Hz, 4H, -C$_6$H$_4$-: H3', H5'), 7.85 (d, J 0.8 Hz, 2H), 8.15 (d, J 8.8 Hz, 4H, -C$_6$H$_4$-: H2', H6'); ^{13}C NMR (100 MHz, CDCl$_3$): δ 108.6, 122.3, 125.6, 126.3, 127.5, 135.9, 139.5, 144.2, 164.4; UV-Vis: λ$_{max}$ (MeOH) 202 nm (ε·10^{-3} 52.4 cm^{-1}·M^{-1}), 319 (51.5); IR (ATR) ν: 3149, 3058, 2961, 2031, 1614, 1584, 1540, 1511, 1478, 1418, 1190, 1160, 1122, 1108, 1074, 1054, 1016, 964, 921, 874, 844, 787, 747, 710 cm^{-1}; Anal. Calcd for C$_{22}$H$_{14}$N$_2$O$_3$: C, 74.57; H, 3.98; N, 7.91. Found: C, 74.52; H, 3.97; N, 7.93; HRMS calcd for (C$_{22}$H$_{14}$N$_2$O$_3$+H$^+$): 355.1083; found: 355.1085.

3,5-Bis[4-(4-pyridyl)phenyl]-1,3,4-oxadiazole (5e). White solid (0.49 g, 95% yield); mp 251–253 °C (decomp.); R$_f$ (benzene/ethyl acetate, 3:1 v/v) 0.55. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.57 (dd, J 5.2 Hz and 1.8 Hz, 4H), 7.81 (d, J 8.4 Hz, 4H, -C$_6$H$_4$-: H3', H5'), 8.27 (d, J 8.4 Hz, 4H, -C$_6$H$_4$-: H2', H6'), 8.73 (dd, J 5.2 Hz and 1.8 Hz, 4H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 121.5, 127.6, 127.7, 129.1, 141.4, 146.8, 150.5, 164.3; UV-Vis: λ$_{max}$ (MeOH) 202 nm (ε·10^{-3} 57.9 cm^{-1}·M^{-1}), 308 (50.7); IR (ATR) ν: 3038, 2160, 1960, 1596, 1548, 1507, 1484, 1406, 1077, 1028, 1014, 994, 964, 858, 814, 770, 752, 732, 707, 690, 664 cm^{-1}; Anal. Calcd for C$_{24}$H$_{16}$N$_4$O: C, 76.58; H, 4.28; N, 14.88. Found: C, 76.56; H, 4.23; N, 14.85; HRMS calcd for (C$_{24}$H$_{16}$N$_4$O+H$^+$): 377.1402; found: 377.1394.

3,5-Bis[4-(3-pyridyl)phenyl]-1,3,4-oxadiazole (5f). White solid (0.48 g, 94% yield); mp 241–243 °C (decomp.); R$_f$ (benzene/ethyl acetate, 3:1 v/v) 0.51. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.43 (dd, J 7.8 Hz and 4.8 Hz, 2H), 7.79 (d, J 8.8 Hz, 4H, -C$_6$H$_4$-: H3', H5'), 7.96 (ddd, J 7.8 Hz, 2.2 Hz and 1.6 Hz, 2H), 8.29 (d, J 8.8 Hz, 4H, -C$_6$H$_4$-: H2', H6'), 8.67 (dd, J 4.8 Hz and 1.6 Hz, 2H), 8.94 (d, J 2.2 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 123.5, 123.7, 127.6, 127.7, 127.8, 134.3, 141.2, 148.3, 149.4, 164.4; UV-Vis: λ$_{max}$ (MeOH) 202 nm (ε·10^{-3} 50.5 cm^{-1}·M^{-1}), 309 (55.3); IR (ATR) ν: 3038, 2159, 1922, 1612, 1587, 1569, 1549, 1500, 1473, 1429, 1400, 1073, 1023, 1001, 964, 847, 801, 773, 745, 708 cm^{-1}; Anal. Calcd for C$_{24}$H$_{16}$N$_4$O: C, 76.58; H, 4.28; N, 14.88. Found: C, 76.55; H, 4.27; N, 14.89; HRMS calcd for (C$_{24}$H$_{16}$N$_4$O+H$^+$): 377.1402; found: 377.1403.

3,5-Bis(4-biphenylyl)-1,3,4-oxadiazole (5g). White-pearl solid (0.56 g, 99% yield); mp 239–240 °C (lit.:[41] mp 234–236 °C); R$_f$ (benzene/ethyl acetate, 3:1 v/v) 0.63.

3-(4-Bromophenyl)-5-[4-(2-thienyl)phenyl]-1,3,4-oxadiazole (6). White solid (0.02 g, 4% yield); mp 193–194 °C (decomp.). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.14 (dd, J 4.8 Hz and 3.6 Hz, 1H), 7.38 (dd, J 4.8 Hz and 0.8 Hz, 1H), 7.45 (dd, J 3.6 Hz and 0.8 Hz, 1H), 7.69 (d, J 8.4 Hz, 2H), 7.78 (d, J 8.0 Hz, 2H), 8.02 (d, J 8.4 Hz, 2H), 8.14 (d, J 8.0 Hz, 2H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 108.9, 123.3, 125.1, 126.3, 127.1, 127.6, 128.3, 128.4, 132.5, 136.0, 138.6, 144.9, 164.6, 166.3; UV-Vis: λ$_{max}$ (MeOH) 202 nm (ε·10^{-3} 12.5 cm^{-1}·M^{-1}), 238 (4.7), 282 (6.7), 329 (15.0); IR (ATR) ν: 3084, 2923, 2568, 2168, 1922, 1602, 1577, 1522, 1488, 1477, 1427, 1402, 1350, 1279, 1214, 1191, 1095, 1071, 1009, 965, 853, 832, 820, 744, 737, 725, 701, 692 cm^{-1}; Anal. Calcd for C$_{18}$H$_{11}$N$_2$OSBr: C, 56.41; H, 2.89; N, 7.31. Found: C, 56.45; H, 2.80; N, 7.36; HRMS calcd for (C$_{18}$H$_{11}$N$_2$OS^{79}Br+H$^+$): 382.9854, (C$_{18}$H$_{11}$N$_2$OS^{81}Br+H$^+$): 384.9833; found: 382.9839, 384.9835 (1:1).

Acknowledgements

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