Efficient Synthesis of 1,3,4-Oxadiazoles Conjugated to Thiophene or Furan Rings via an Ethenyl Linker

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Abstract: A novel and efficient synthesis of 5-substituted 2-[2-(2-furyl)ethenyl]-1,3,4-oxadiazoles and 2-[2-(2-thienyl)ethenyl]-1,3,4-oxadiazoles by cyclocondensation of the appropriate 3-(2-furyl)- and 3-(2-thienyl)acrylohydrazides with triethyl orthoesters in the presence of glacial acetic acid is reported. The formation of symmetrically substituted 2,5-bis[2-(2-furyl)ethenyl]-1,3,4-oxadiazole and 2,5-bis[2-(2-thienyl)ethenyl]-1,3,4-oxadiazole from the corresponding *N*,*N*′-diacylhydrazines under the influence of phosphorus oxychloride is also described.

Key words: cyclization, heterocycles, furans, thiophenes, 1,3,4-oxadiazoles

During the past 20 years, there has been a significant increase of interest in organic compounds exhibiting luminescent properties.[1] An optimised organic luminophore is usually an extended π-conjugated chromophore system showing the proper electron- and hole-transporting properties, a high external quantum efficiency, and both thermal and chemical stability.[2] A literature survey reveals examples of the modification of luminophore electron-transporting properties by direct or indirect conjugation with other electron-deficient systems such as pyridines, furans, thiophenes, selenophenes or tellurophenes.[3] It has been proven that the ability of these arrangements to electropolymerise to linear PPV-type conducting systems and the resulting strong electroluminescence qualifies them as materials with potential applications in polymer and material science. Amongst the aromatic compounds used widely in the production of new materials for optoelectronics, particularly in organic light-emitting diodes (OLEDs), derivatives of 1,3,4-oxadiazole substituted with heteroaryl groups at the 2- and 5-positions play an important role.[3a,4]

1,3,4-Oxadiazoles belong to the group of five-membered, non-naturally occurring heterocycles. These compounds were first mentioned in the literature during the late 1950s as the products of the reaction between aryl carboxylic acid hydrazides and orthoesters.[5] 1,3,4-Oxadiazoles are well known for their biological interactions.[6] Many 1,3,4-oxadiazoles are used to fight infections involving AIDS and exhibit antibacterial, anticonvulsant and anticancer activities.[7a–c] They are also applied in agriculture as herbicides, fungicides or insecticides.[7d,e] Conjugated macrocyclic arrangements based on the 1,3,4-oxadiazole fragment exhibit interesting electron-transfer or luminescent properties and are used in OLEDs, scintillators and photosensitive materials. They are also applied in the production of heat-resistant polymers, blowing agents, laser dyes and optical brighteners.[4]

The most popular methods to synthesise 1,3,4-oxadiazoles involve the use of acid hydrazides as cyclocondensation substrates with carboxylic acids,[8] aromatic aldehydes[7c] and orthoesters.[9] The reactions of diacylhydrazines[10] with a range of cyclodehydrating agents, heterocyclization of semicarbazide, thiosemicarbazide and selenosemicarbazide derivatives,[11] or transformations involving another ring, such as 1,2,4-oxadiazole[12a] or tetrazole,[12b,c] may also be employed.

The aim of this work was to study the synthesis of new, extended heterocyclic 1,3,4-oxadiazole scaffold based arrangements that are conjugated through an ethenyl linker to other heteroaromatic fragments such as thiophene or furan. These fragment hybrids are promising monomers for optoelectronic applications because they combine different electron-deficient rings featuring excellent electron-transporting properties with high luminous efficiencies. To the best of our knowledge, the synthesis of 1,3,4-oxadiazoles that are derived from α,β-unsaturated acid hydrazides and triethyl orthoesters, and are conjugated via an ethenyl linker to thiophene or furan rings, has not been previously reported. This approach seemed to be quite promising due to the fact that, contrary to other synthons used in the formation of 1,3,4-oxadiazoles, orthoesters possess three easy-leaving alkoxy groups, which ensures the cyclization occurs readily and under relatively mild conditions.

Hydrazides of α,β-unsaturated acids were used as precursors to the 1,3,4-oxadiazole hybrids. The starting hydrazides, 3-(2-furyl)acrylohydrazide (**5a**) and 3-(2-thienyl)acrylohydrazide (**5b**), were prepared from the appropriate commercially available heteroaromatic aldehydes according to a short synthetic procedure (Scheme 1).

Thus, the starting aldehydes, 2-furancarboxaldehyde (**1a**) and 2-thiophenecarboxaldehyde (**1b**), were each treated with malonic acid in pyridine in the presence of catalytic amounts of piperidine. Knoevenagel condensation and successive decarboxylation of the intermediate dicarbox-

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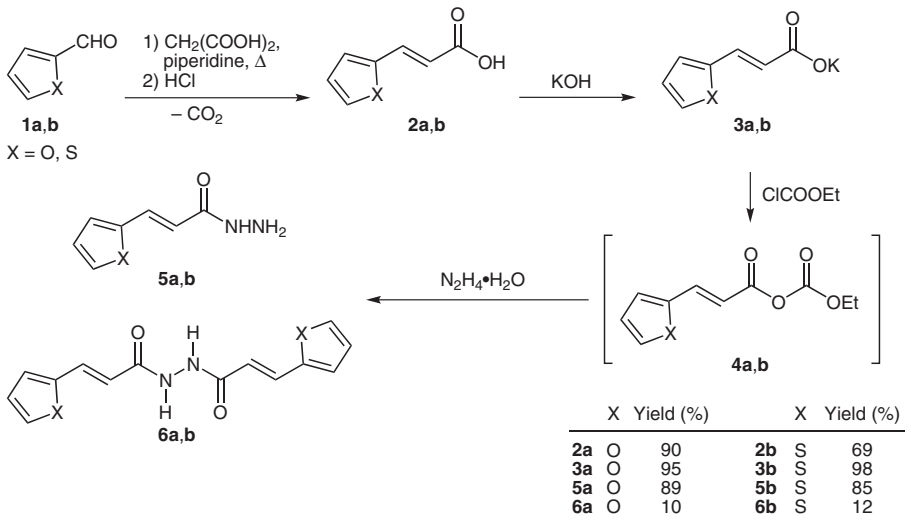


	X	Yield (%)		X	Yield (%)
2a	O	90	**2b**	S	69
3a	O	95	**3b**	S	98
5a	O	89	**5b**	S	85
6a	O	10	**6b**	S	12

Scheme 1

ylic acids resulted in the formation of the α,β-unsaturated monocarboxylic acids, 3-(2-furyl)acrylic acid (**2a**) and 3-(2-thienyl)acrylic acid (**2b**), in high yields. They were transformed into the hydrazides **5a**,**b**, via the mixed anhydrides **4a**,**b**, produced in a one-pot, two-step procedure.

First, the potassium salt **3a**,**b** of the corresponding acid was treated with ethyl chloroformate, and then hydrazine hydrate was added to obtain the desired product **5a**,**b**; however, the main reaction was accompanied by the formation of significant quantities of high-melting *N*,*N*′-diacylhydrazines **6a**,**b**. These products arose from the bidentate nucleophile hydrazine hydrate mediated substitution of the anhydrides **4a**,**b**. An increase of the molar ratio between the hydrazine hydrate and salt/ethyl chloroformate system resulted in high yields of the desired hydrazide **5a** (Table 1, entry 2). Unfortunately, the number of solvents applicable here was rather limited because the intermediate anhydride **4** is a relatively reactive compound. However, it should also be noted that the formation of hydrazide **5a** proceeded more effectively in a polar solvent such as acetonitrile (Table 1, entry 4). Thus, the synthesis of the second key starting material, 3-(2-thienyl)acrylohydrazide (**5b**), was successfully conducted with excess hydrazine hydrate in acetonitrile solution.

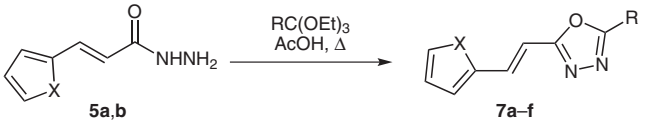
Table 1 Optimisation of the Reaction Conditions for the Preparation of 3-(2-Furyl)acrylohydrazide (**5a**)

Entry	Molar ratio **3a**/$ClCO_2Et$/$N_2H_4·H_2O$	Solvent	Yield[a] (%) of **5a**
1	1:1:1	CH_2Cl_2	35
2	1:1:2	CH_2Cl_2	58
3	1:1:2	THF	86
4	1:1:2	MeCN	89

[a] Yield with respect to the starting 3-(2-furyl)acrylic acid (**2a**).

The resulting acid hydrazides **5a**,**b** were subjected to heating with an excess of the triethyl orthoesters (orthoacetate, orthopropionate or orthobenzoate; R = Me, Et, Ph) in glacial acetic acid, yielding the 2-[2-(2-furyl)ethenyl]-1,3,4-oxadiazoles **7a**–**c** and the 2-[2-(2-thienyl)ethenyl]-1,3,4-oxadiazoles **7d**–**f** substituted at the 5-position with a phenyl or an alkyl group (Table 2). The highest yields were obtained in the reactions with triethyl orthobenzoate, where extended and stable conjugated arrangements were formed (**7c**: 84%, **7f**: 89%). In contrast to the previously examined 2-styryl-1,3,4-oxadiazoles, prepared in the reaction of cinnamic acid hydrazide and triethyl orthoesters,[9c] the α,β-unsaturated acid hydrazides conjugated with a furan or thiophene ring were much more reactive than their phenyl-containing counterpart. The reactions between hydrazides **5a**,**b** and the alkyl-group-bearing orthoesters (R = Me, Et) were complete after 3–4 hours at

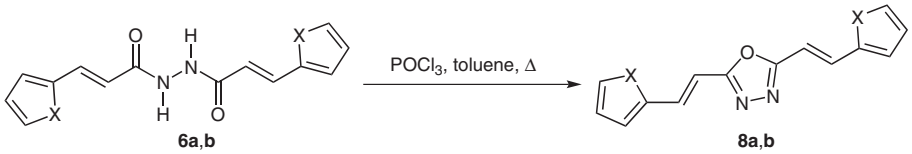
Table 2 Reaction of 3-(2-Furyl)acrylohydrazide (**5a**) or 3-(2-Thienyl)acrylohydrazide (**5b**) with Triethyl Orthoesters



X	R	Temp (°C)	Time (h)	Product	Yield[a] (%)	Mp (°C)
O	Me	120	4.0	**7a**	68	110–112
O	Et	125	3.0	**7b**	76	90–92
O	Ph	150	1.5	**7c**	84	117–119
S	Me	120	3.5	**7d**	72	101–103
S	Et	125	3.0	**7e**	83	61–63
S	Ph	150	1.5	**7f**	89	108–110

[a] Yield with respect to the starting hydrazide **5a**,**b**.

Table 3 Preparation of 2,5-Bis-[2-(2-furyl)ethenyl]-1,3,4-oxadiazole (**8a**) and 2,5-Bis[2-(2-thienyl)ethenyl]-1,3,4-oxadiazole (**8b**) from the Corresponding *N*,*N*′-Diacylhydrazines **6a**,**b**



X	Temp (°C)	Time (h)	Product	Yield[a] (%)	Mp (°C)
O	110	1	**8a**	72	179–181
S	110	1	**8b**	89	173–176

[a] Yield with respect to the starting *N*,*N*′-diacylhydrazine **6a**,**b**.

reflux, while cinnamic acid hydrazide required up to 40 hours of conventional heating in glacial acetic acid to react.[9c]

As already noted, reaction of the potassium salts **3a**,**b** of the α,β-unsaturated acids with ethyl chloroformate and hydrazine hydrate resulted not only in the desired products **5a**,**b** but also in the formation of side products, namely the corresponding *N*,*N*′-diacylhydrazines **6a**,**b** (Scheme 1). This particular group of compounds, usually prepared from acid chlorides or acid anhydrides and hydrazides or simply hydrazine hydrate, is widely exploited in the synthesis of 1,3,4-oxadiazoles. The reactions are conducted under the influence of typical dehydrating agents such as polyphosphoric acid, phosphorus oxychloride, thionyl chloride and boron trifluoride–diethyl ether complex.[11] The great advantage of the methods making use of phosphorus oxychloride or thionyl chloride and proceeding in non-polar solvents is the ease of the post-reaction workup. Thus, *N*,*N*′-diacylhydrazines **6a**,**b**, obtained from the corresponding α,β-unsaturated acids **2a**,**b**, were heated at reflux with phosphorus oxychloride in toluene for a short time to obtain other conjugated aromatic products, the symmetrically substituted 2,5-bis[2-(2-heteroaryl)ethenyl]-1,3,4-oxadiazoles **8a**,**b**, in high yields (72–89%; Table 3).

In conclusion, we have demonstrated an easy and efficient synthesis of both unsymmetrical and symmetrical 1,3,4-oxadiazole–furan and 1,3,4-oxadiazole–thiophene hybrids, compounds with potential useful applications in optoelectronics. The methods presented here have the advantage of providing the desired products rapidly and in high yields, which makes them useful additions to the existing synthetic protocols.

All solvents and reagents were purchased from commercial sources and were used without additional purification. Melting points were measured using a Stuart SMP3 melting point apparatus and are uncorrected. Elemental analyses were performed with a Vario EL analyser. UV spectra were recorded on a Jasco V-650 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 and $CDCl_3$ solutions using TMS as the internal standard on a Varian Inova 300, a Varian 600 or an Agilent 400-MR spectrometer. Thin-layer chromatography was performed on Merck silica gel 60 F_{254} TLC plates using benzene–EtOAc (1:3 v/v) or MeOH–$CHCl_3$ (1:4 v/v) as the mobile phase. FT-IR spectra were recorded between 4000 and 650 cm^{-1} on a Nicolet 6700 FT-IR apparatus with a Smart iTR accessory. Mass spectra were obtained on a GC/MS Agilent Technologies 7890A/5975C System with a Triple Axis Detector using the EI technique (70 eV).

3-(2-Heteroaryl)acrylic Acids 2a,b; General Procedure

A mixture of an aldehyde **1a**,**b** (0.38 mol), malonic acid (93.6 g, 0.90 mol), pyridine (180 mL) and piperidine (3 mL) was heated in a steam bath, stirred for 2 h and boiled for 5 min. After cooling, the reaction mixture was poured into cold H_2O (80 mL) and treated with concd HCl (120 mL). The precipitate was collected by filtration, washed with H_2O and dried. The crude product was crystallised (EtOH) to yield the corresponding pure 3-(2-heteroaryl)acrylic acid **2a**,**b**.

3-(2-Furyl)acrylic Acid (2a)

Beige solid; yield: 47.2 g (90%); mp 138–141 °C (Lit.[13] 139–140 °C); R_f = 0.67 (benzene–EtOAc–AcOH, 6:2:1).

3-(2-Thienyl)acrylic Acid (2b)

White solid; yield: 40.4 g (69%); mp 147–149 °C (Lit.[14] 148–149 °C); R_f = 0.53 (benzene–EtOAc–AcOH, 6:2:1).

3-(2-Heteroaryl)acrylohydrazides 5a,b and *N*,*N*′-Diacylhydrazines 6a,b; General Procedure

The 3-(2-heteroaryl)acrylic acid **2a**,**b** (0.10 mol) was slowly added to a stirred soln of KOH (5.6 g, 0.10 mol) in H_2O (100 mL). The mixture was stirred for approximately 10 min and then concentrated using a rotary evaporator. The precipitate was washed with Et_2O (2 × 50 mL), collected by filtration and air-dried to give the corresponding crude potassium salt as a white solid; yield of **3a**: 16.7 g (95%); yield of **3b**: 18.8 g (98%).

To a stirred suspension of the potassium salt **3a**,**b** (0.09 mol) in MeCN (300 mL) were added ethyl chloroformate (9.8 g, 0.09 mol) and a 1% soln of pyridine in MeCN (30 mL). The reaction mixture was heated under reflux for 2 h and then slowly poured into a stirred, ice-cooled suspension of hydrazine hydrate (9.0 g, 0.18 mol) in MeCN (100 mL). After filtration, the filtrate was kept in an ice-box overnight. After cooling, the light-yellow precipitate was collected by filtration, washed with Et_2O (2 × 50 mL) and air-dried, yielding the corresponding pure *N*,*N*′-diacylhydrazines **6a**,**b**. The filtrate was washed with sat. aq Na_2CO_3 soln (2 × 50 mL), dried over $MgSO_4$ and concentrated using a rotatory evaporator. The crude product was purified by silica gel column chromatography (benzene–EtOAc, 1:3) to give the 3-(2-heteroaryl)acrylohydrazides **5a**,**b**.

3-(2-Furyl)acrylohydrazide (5a)

Yellow solid; yield: 12.2 g (89%); mp 108–109 °C (Lit.[15] 108–110 °C); R_f = 0.18 (benzene–EtOAc, 1:3).

3-(2-Thienyl)acrylohydrazide (5b)
Yellow solid; yield: 12.9 g (85%); mp 105–107 °C; R_f = 0.11 (benzene–EtOAc, 1:3).

IR (ATR): 3259, 3170, 2162, 1980, 1683, 1656, 1515, 1494, 1421, 1358, 1320, 1278, 1263, 1222, 1196, 1128, 1085, 1041, 938, 870, 829, 787, 746, 692 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 4.55 (br s, 2 H, NH_2), 6.29 (d, J = 15.3 Hz, 1 H, α-CH=), 7.08 (dd, J_1 = 3.6 Hz, J_2 = 5.1 Hz, 1 H, C4′-H), 7.35 (d, J = 3.6 Hz, 1 H, C3′-H), 7.57 (d, J = 5.1 Hz, 1 H, C5′-H), 7.60 (d, J = 15.3 Hz, 1 H, β-CH=), 9.31 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 119.0, 127.7, 128.3, 130.4, 131.2, 139.9, 164.2.

MS (EI, 70 eV): m/z (%) = 40.1 (22), 43.9 (49), 63.0 (15), 64.9 (22), 108.0 (29), 108.9 (60), 135.0 (46), 137.0 (100), 152.9 (37), 168.0 (15) [M^+].

UV (MeOH): λ_{max} (ε) = 203.5 (10660), 306.5 nm (19120).

Anal. Calcd for $C_7H_8N_2OS$: C, 49.98; H, 4.78; N, 16.65. Found: C, 49.93; H, 4.84; N, 16.67.

***N*,*N*′-Bis[3-(2-furyl)-2-propenoyl]hydrazine (6a)**
Light-yellow solid; yield: 2.4 g (10%); mp >350 °C; R_f = 0.65 (MeOH–$CHCl_3$, 1:4).

IR (ATR): 3181, 3019, 2597, 2162, 2039, 1980, 1647, 1583, 1563, 1471, 1420, 1389, 1324, 1279, 1261, 1221, 1152, 1122, 1096, 1019, 986, 969, 928, 882, 839, 755, 694 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.51 (d, J = 15.6 Hz, 1 H, α-CH=), 6.60 (dd, J_1 = 1.8 Hz, J_2 = 3.3 Hz, 1 H, C4′-H), 6.83 (d, J = 3.3 Hz, 1 H, C5′-H), 7.34 (d, J = 15.6 Hz, 1 H, β-CH=), 7.81 (d, J = 1.8 Hz, 1 H, C3′-H), 10.46 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 112.5, 114.5, 116.4, 127.3, 145.1, 150.8, 163.0.

UV (MeOH): λ_{max} (ε) = 310.5 nm (74640).

Anal. Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.78; H, 4.63; N, 10.27.

***N*,*N*′-Bis[3-(2-thienyl)-2-propenoyl]hydrazine (6b)**
Light-yellow solid; yield: 3.3 g (12%); mp 290–295 °C; R_f = 0.70 (MeOH–$CHCl_3$, 1:4).

IR (ATR): 3133, 2814, 2590, 1662, 1634, 1597, 1524, 1468, 1413, 1393, 1309, 1269, 1228, 1207, 1182, 1074, 1043, 967, 944, 929, 882, 828, 755, 719, 663 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.49 (d, J = 15.3 Hz, 1 H, α-CH=), 7.12 (dd, J_1 = 3.6 Hz, J_2 = 5.1 Hz, 1 H, C4′-H), 7.43 (d, J = 3.6 Hz, 1 H, C3′-H), 7.64 (d, J = 5.1 Hz, 1 H, C5′-H), 7.69 (d, J = 15.3 Hz, 1 H, β-CH=), 10.42 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 117.9, 128.1, 128.4, 131.1, 133.1, 139.6, 162.8.

UV (MeOH): λ_{max} (ε) = 204.5 (17232), 319.0 nm (43457).

Anal. Calcd for $C_{14}H_{12}N_2O_2S_2$: C, 55.24; H, 3.97; N, 9.20. Found: C, 55.28; H, 3.90; N, 9.15.

5-Substituted 2-[2-(2-Heteroaryl)ethenyl]-1,3,4-oxadiazoles 7a–f; General Procedure
The starting hydrazide **5a**,**b** (10.0 mmol) was added to a mixture of the triethyl orthoester (15.0 mmol) and glacial AcOH (10 mL). The mixture was kept under reflux until the starting hydrazide was fully consumed (monitored by TLC, 1–4 h). After cooling, the excess orthoester and AcOH were evaporated under reduced pressure. The crude product **7a**–**f** was subjected to silica gel column chromatography (benzene–EtOAc, 1:3) or was crystallised (benzene–hexane mixtures).

2-[2-(2-Furyl)ethenyl]-5-methyl-1,3,4-oxadiazole (7a)
White solid; yield: 1.2 g (68%); mp 110–112 °C (Lit.[16] 114–115 °C); R_f = 0.55 (benzene–EtOAc, 1:3).

2-Ethyl-5-[2-(2-furyl)ethenyl]-1,3,4-oxadiazole (7b)
White solid; yield: 1.4 g (76%); mp 90–92 °C; R_f = 0.50 (benzene–EtOAc, 1:3).

IR (ATR): 3133, 3113, 3070, 2985, 2941, 2162, 1980, 1788, 1730, 1650, 1632, 1586, 1521, 1471, 1443, 1391, 1375, 1317, 1292, 1259, 1191, 1153, 1082, 1066, 1029, 972, 927, 847, 820, 727, 665 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.41 (t, J = 7.5 Hz, 3 H, CH_3), 2.90 (q, J = 7.5 Hz, 2 H, CH_2), 6.48 (dd, J_1 = 1.8 Hz, J_2 = 3.3 Hz, 1 H, C4′-H), 6.57 (d, J = 3.3 Hz, 1 H, C5′-H), 6.89 (d, J = 16.2 Hz, 1 H, α-CH=), 7.26 (d, J = 16.2 Hz, 1 H, β-CH=), 7.50 (d, J = 1.8 Hz, 1 H, C3′-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.7, 19.1, 108.0, 112.2, 113.2, 125.1, 144.3, 151.0, 164.3, 167.1.

MS (EI, 70 eV): m/z (%) = 57.0 (23), 65.0 (20), 78.0 (15), 79.0 (20), 121.0 (35), 149.0 (31), 189.0 (100), 190.1 (51) [M^+].

UV (MeOH): λ_{max} (ε) = 220.0 (4540), 314.0 nm (36410).

Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.22; H, 5.29; N, 14.77.

2-[2-(2-Furyl)ethenyl]-5-phenyl-1,3,4-oxadiazole (7c)
White solid; yield: 2.0 g (84%); mp 117–119 °C (Lit.[17] 118–119 °C); R_f = 0.74 (benzene–EtOAc, 1:3).

2-Methyl-5-[2-(2-thienyl)ethenyl]-1,3,4-oxadiazole (7d)
White solid; yield: 1.4 g (72%); mp 101–103 °C; R_f = 0.46 (benzene–EtOAc, 1:3).

IR (ATR): 3096, 3044, 2162, 2037, 1827, 1637, 1543, 1531, 1505, 1421, 1411, 1359, 1324, 1247, 1234, 1219, 1199, 1174, 1131, 1085, 1044, 970, 857, 826, 747, 732, 669, 653 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, CH_3), 6.79 (d, J = 16.2 Hz, 1 H, α-CH=), 7.06 (dd, J_1 = 3.6 Hz, J_2 = 5.1 Hz, 1 H, C4′-H), 7.23 (d, J = 3.6 Hz, 1 H, C3′-H), 7.37 (d, J = 5.1 Hz, 1 H, C5′-H), 7.60 (d, J = 16.2 Hz, 1 H, β-CH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.9, 108.8, 127.6, 128.0, 129.5, 131.0, 139.9, 162.9, 164.1.

MS (EI, 70 eV): m/z (%) = 121.0 (17), 137.0 (17), 191.0 (100), 192.0 (22) [M^+].

UV (MeOH): λ_{max} (ε) = 203.5 (9449), 315.0 nm (24781).

Anal. Calcd for $C_9H_8N_2OS$: C, 56.23; H, 4.19; N, 14.57. Found: C, 56.24; H, 4.23; N, 14.51.

2-Ethyl-5-[2-(2-thienyl)ethenyl]-1,3,4-oxadiazole (7e)
White solid; yield: 1.7 g (83%); mp 61–63 °C; R_f = 0.50 (benzene–EtOAc, 1:3).

IR (ATR): 3103, 3089, 2986, 2940, 2163, 1980, 1844, 1637, 1545, 1507, 1498, 1462, 1443, 1412, 1375, 1354, 1317, 1293, 1265, 1245, 1187, 1081, 1040, 1024, 968, 861, 848, 797, 691 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.41 (t, J = 7.5 Hz, 3 H, CH_3), 2.90 (q, J = 7.5 Hz, 2 H, CH_2), 6.80 (d, J = 16.2 Hz, 1 H, α-CH=), 7.05 (dd, J_1 = 3.9 Hz, J_2 = 4.8 Hz, 1 H, C4′-H), 7.23 (d, J = 3.9 Hz, 1 H, C3′-H), 7.36 (d, J = 4.8 Hz, 1 H, C5′-H), 7.60 (d, J = 16.2 Hz, 1 H, β-CH=).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.6, 19.0, 108.9, 127.6, 128.0, 129.4, 131.0, 139.9, 163.9, 167.0.

MS (EI, 70 eV): m/z (%) = 121.0 (15), 137.0 (15), 205.0 (100), 206.0 (23) [M^+].

UV (MeOH): λ_{max} (ε) = 222.0 (5347), 320.5 nm (26702).

Anal. Calcd for $C_{10}H_{10}N_2OS$: C, 58.23; H, 4.89; N, 13.58. Found: C, 58.27; H, 4.82; N, 13.61.

2-Phenyl-5-[2-(2-thienyl)ethenyl]-1,3,4-oxadiazole (7f)
White solid; yield: 2.3 g (89%); mp 108–110 °C; R_f = 0.61 (benzene–EtOAc, 1:3).

IR (ATR): 3062, 2162, 1980, 1636, 1609, 1563, 1548, 1482, 1449, 1418, 1293, 1274, 1253, 1127, 1090, 1071, 1018, 972, 959, 924, 857, 847, 824, 744, 728, 687 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.89 (d, J = 16.2 Hz, 1 H, α-CH=), 7.08 (dd, J_1 = 3.6 Hz, J_2 = 5.1 Hz, 1 H, C4′-H), 7.27 (d, J = 3.6 Hz, 1 H, C3′-H), 7.39 (d, J = 5.1 Hz, 1 H, C5′-H), 7.49–7.56 (m, 3 H, C3″-H, C4″-H, C5″-H), 7.74 (d, J = 16.2 Hz, 1 H, β-CH=), 8.09–8.12 (m, 2 H, C2″-H, C6″-H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 108.9, 123.9, 126.9, 127.9, 128.2, 129.0, 129.7, 131.5, 131.7, 140.1, 163.9, 164.0.

MS (EI, 70 eV): *m*/*z* (%) = 77.0 (15), 97.0 (100), 110.0 (23), 254.0 (51) [M^+].

UV (MeOH): λ_{max} (ε) = 203.0 (20020), 262.5 (12770), 336.0 nm (30570).

Anal. Calcd for $C_{14}H_{10}N_2OS$: C, 66.12; H, 3.96; N, 11.02. Found: C, 66.08; H, 3.90; N, 11.07.

2,5-Bis[2-(2-heteroaryl)ethenyl]-1,3,4-oxadiazoles 8a,b; General Procedure
A soln of the *N*,*N*′-diacylhydrazine **6a**,**b** (3.7 mmol) and $POCl_3$ (10 mL) in anhyd toluene (20 mL) was heated under reflux for approximately 1 h. After cooling, the precipitate was collected by filtration, air-dried and crystallised (*i*-PrOH) to give the corresponding pure 2,5-bis[2-(2-heteroaryl)ethenyl]-1,3,4-oxadiazole **8a**,**b**.

2,5-Bis[2-(2-furyl)ethenyl]-1,3,4-oxadiazole (8a)
Brown solid; yield: 0.7 g (72%); mp 179–181 °C (Lit.[17] 126–127 °C); R_f = 0.43 (benzene–EtOAc, 1:3).

2,5-Bis[2-(2-thienyl)ethenyl]-1,3,4-oxadiazole (8b)
Beige solid; yield: 0.9 g (89%); mp 173–176 °C; R_f = 0.67 (benzene–EtOAc, 1:3).

IR (ATR): 3085, 2163, 2035, 1632, 1562, 1541, 1493, 1416, 1356, 1264, 1216, 1193, 1127, 1040, 989, 947, 854, 826, 707 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 6.96 (d, J = 16.2 Hz, 1 H, α-CH=), 7.17 (dd, J_1 = 3.6 Hz, J_2 = 5.1 Hz, 1 H, C4′-H), 7.56 (d, J = 3.6 Hz, 1 H, C3′-H), 7.72 (d, J = 5.1 Hz, 1 H, C5′-H), 7.84 (d, J = 16.2 Hz, 1 H, β-CH=).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 108.2, 128.6, 129.3, 130.4, 131.7, 139.5, 162.9.

MS (EI, 70 eV): *m*/*z* (%) = 65.0 (15), 109.0 (32), 137.0 (49), 285.0 (100), 286.0 (38) [M^+].

UV (MeOH): λ_{max} (ε) = 230.6 (8320), 309.4 (19850), 356.6 nm (28370).

Anal. Calcd for $C_{14}H_{10}N_2OS_2$: C, 58.72; H, 3.52; N, 9.78. Found: C, 58.66; H, 3.59; N, 9.74.

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References

(1) (a) Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem. Int. Ed.* **1998**, *37*, 402. (b) Segura, J. L. *Acta Polym.* **1998**, *49*, 319. (c) Mitschke, U.; Bauerle, P. *J. Mater. Chem.* **2000**, *10*, 1471.
(2) (a) Schulz, B.; Bruma, M.; Brehmer, L. *Adv. Mater. (Weinheim, Ger.)* **1997**, *9*, 601. (b) Thelakkat, M.; Schmidt, H. W. *Polym. Adv. Technol.* **1998**, *9*, 429.
(3) (a) Wang, C.; Jung, G. Y.; Batsanov, A. S.; Bryce, M. R.; Petty, M. C. *J. Mater. Chem.* **2002**, *12*, 173. (b) Waskiewicz, K.; Gabański, R.; Żak, J.; Suwiński, J. *Electrochem. Solid-State Lett.* **2005**, *8*, E24. (c) Fuks-Janczarek, I.; Reshak, A. H.; Kuźnik, N.; Kityk, I. V.; Gabański, R.; Łapkowski, M.; Motyka, R.; Suwiński, J. *Spectrochim. Acta, Part A* **2009**, *72*, 394. (d) Łapkowski, M.; Motyka, R.; Suwiński, J.; Data, P. *Macromol. Chem. Phys.* **2012**, *231*, 29. (e) Data, P.; Łapkowski, M.; Motyka, R.; Suwiński, J. *Electrochim. Acta* **2012**, *59*, 567.
(4) (a) Schulz, B.; Orgzall, I.; Freydank, A.; Xii, C. *Adv. Colloid Interface Sci.* **2005**, *116*, 143. (b) Chen, Z. K.; Meng, H.; Lai, Y. H.; Huang, W. *Macromolecules* **1999**, *32*, 4351. (c) Tamoto, N.; Adachi, C.; Nagai, K. *Chem. Mater.* **1997**, *9*, 1077. (d) Sinigersky, V.; Wegner, G.; Schopov, I. *Eur. Polym. J.* **1993**, *29*, 617.
(5) Ainsworth, C. *J. Am. Chem. Soc.* **1955**, *77*, 1148.
(6) Suwiński, J.; Szczepankiewicz, W. *Comprehensive Heterocyclic Chemistry III*; Vol. 5; Katritzky, A. R.; Ramsden, C. A.; Scriven, E. F. V.; Taylor, R. J. K., Eds.; Chap. 6; Elsevier Science Ltd: Oxford, **2008**, 398.
(7) (a) Amir, M.; Shikha, K. *Eur. J. Med. Chem.* **2004**, *39*, 535. (b) Almasirad, A.; Tabatabai, S. A.; Faizi, M.; Kebriaeezadeh, A. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 6057. (c) Rajapakse, H. A.; Zhu, H.; Young, M. B.; Mott, B. T. *Tetrahedron Lett.* **2006**, *47*, 4827. (d) Zheng, X.; Li, Z.; Wang, Y.; Chen, W.; Huang, Q.; Liu, C.; Song, G. *J. Fluorine Chem.* **2003**, *123*, 163. (e) Zou, X. J.; Lai, L. H.; Zhang, Z. X. *J. Agric. Food Chem.* **2002**, *50*, 3757.
(8) Dabiri, M.; Salehi, P.; Baghbanzadeh, M.; Bahramnejad, M. *Tetrahedron Lett.* **2006**, *47*, 6983.
(9) (a) Kudelko, A.; Zieliński, W.; Ejsmont, K. *Tetrahedron* **2011**, *67*, 7838. (b) Kudelko, A. *Tetrahedron* **2012**, *68*, 3616. (c) Kudelko, A.; Zieliński, W. *Tetrahedron Lett.* **2012**, *53*, 76.
(10) (a) Tully, W. R.; Cardner, C. R.; Gillespie, R. J.; Westwood, R. *J. Med. Chem.* **1991**, *34*, 2060. (b) Cao, S.; Qian, X.; Song, G.; Huang, Q. *J. Fluorine Chem.* **2002**, *117*, 63. (c) El Kain, L.; Le Menestrel, I.; Morgentin, R. *Tetrahedron Lett.* **1998**, *39*, 6885. (d) Tandon, V. K.; Chhor, R. B. *Synth. Commun.* **2001**, *31*, 1727. (e) Brain, C. T.; Paul, J. M.; Loong, Y.; Oakley, P. J. *Tetrahedron Lett.* **1999**, *40*, 3275.
(11) (a) Shaker, R. M.; Mahmoud, A. F.; Abdel-Latif, F. F. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 397. (b) Zarghi, A.; Hajimahdi, Z.; Mohebbi, S.; Rashidi, H.; Mozaffari, S.; Sarraf, S.; Faizi, M.; Tabatabaee, S. A.; Shafiee, A. *Chem. Pharm. Bull.* **2008**, *56*, 509. (c) Xie, Y.; Liu, J.; Yang, P.; Shi, X.; Li, J. *Tetrahedron* **2011**, *67*, 5369.
(12) (a) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N. *J. Org. Chem.* **2002**, *67*, 6253. (b) Dupau, P.; Epple, R.; Thomas, A. A.; Fokin, V. V.; Sharpless, K. B. *Adv. Synth. Catal.* **2002**, *344*, 421. (c) Huisgen, R.; Sauer, J.; Sturm, H. J.; Markgraf, J. H. *Chem. Ber.* **1960**, *93*, 2106.
(13) Karminski-Zamola, G.; Jakopcic, K. *Croat. Chem. Acta* **1974**, *46*, 71.
(14) Singh, S.; Arthur, J. C. *Carbohydr. Res.* **1971**, *17*, 353.
(15) Yale, H. L.; Losee, K.; Martins, J.; Holsing, M.; Perry, F. M.; Bernstein, J. *J. Am. Chem. Soc.* **1953**, *75*, 1933.
(16) Sugihara, A.; Ito, M. *Yakugaku Zasshi* **1965**, *85*, 418; *Chem. Abstr.* **1965**, *63*, 5640.
(17) Karakhanov, R. A.; Kelarev, V. I.; Koshelev, V. N.; Morozova, G. V.; Dibi, A. *Chem. Heterocycl. Compd. (N.Y.)* **1995**, *31*, 208.

