1,1’-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl)diethanone as a Building Block in Heterocyclic Synthesis. Novel Synthesis of Some Pyrazole and Pyrimidine Derivatives

Yahia Nasser Mabkhot 1,*, Abdullah Mohammed Al-Majid 1, Assem Barakat 1,*, Saeed Alshahrani 1 and Yamin Siddiqui 2

1 Department of Chemistry, Faculty of Science, King Saud University, P. O. Box 2455, Riyadh 11451, Saudi Arabia
2 Department of Chemistry, Faculty of Science, Taibah University, P.O. Box 344, Medina 41411, Saudi Arabia

* Authors to whom correspondence should be addressed; E-Mails: Yahia@ksu.edu.sa (Y.N.M.); ambarakat@ksu.edu.sa (A.B.); Tel.: +96614675884; Fax: +96614675992.

Received: 20 June 2011; in revised form: 25 July 2011 / Accepted: 29 July 2011 / Published: 3 August 2011

Abstract: A series of new bis(heterocycles) featuring thieno[2,3-b]thiophene rings was synthesized in a combinatorial manner. Intramolecular cyclization of enaminone derivatives with appropriate N-nucleophiles afforded the target compounds. All compounds were characterized by 1H-, 13C-NMR, GCMS, IR, and UV-Vis spectrometry. These compounds represent a new class of sulfur- and nitrogen-containing heterocycles that should also be of interest as new materials.

Keywords: thienothiophene; enaminones; bis-heterocycles; intramolecular cyclization; DMF-DMA

1. Introduction

We have recently reported a short and expedient route to various bis(heterocycles) [1,2]. The method consists of sequential directed nucleophilic addition, side chain deprotonation, nucleophilic addition, and cyclization using a nitrogen or sulfur moiety as internal nucleophile. The importance of bis(heterocycles) can be appreciated from the numerous reports in the literature in which the chemistry...
and biological activities of these compounds were reviewed [3-11]. Thus, thienothiophene derivatives exhibit biological activities, e.g., antitumor, antiviral [12-18], and as antibiotic, antiglaucoma drugs, or as inhibitors of platelet aggregation [19-23]. Substituted thienothiophenes have been used as building blocks in the synthesis of polycondensed systems which include sulfur analogues of electronic devices, due to their many fundamental advantages over their inorganic counterparts in achieving low-cost, large area and mechanically flexible electronics [24-27]. More recently thienothiophenes, in particular the the thieno[2,3-b]thiophene scaffold, have attracted considerable attention as the moieties offer some significant advantages such as centrosymmetry and higher rigidity, in the design of novel NLO systems by incorporating this nucleus with in unsymmetrically functionalized cyclophane [13]. On the other hand, imidazopyrimidine and triazolopyrimidine compounds have been shown antimicrobial effects [28-32]. Our research has been devoted to the development of new classes of bis(heterocycle) systems which incorporate the theinothiophene moiety in the hope that they may be biologically active. We report herein the use of enaminoine 3 for the synthesis of new pyrimidine, pyrazole, triazolopyrimidine and imidazopyrimidine derivatives.

2. Results and Discussion

The starting materials used in the synthesis, for instance, benzoylacetone (1), dimethylformamide dimethylacetal (DMF-DMA), 4-amino-1,2,4-triazole, and 2-aminobenzimidazole were easily available. The previously unreported 1,1’-(3-methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl)diethanone (2) was synthesized starting from benzoylacetone. Deprotonation of the active methylene proton of the latter using a K₂CO₃ in DMF, then trapping with a C-nucleophile such as CS₂ and finally reaction with chloroacetone afforded the product 2 (Scheme 1). The formation of the latter was confirmed by its spectral data (IR, MS, NMR) and elemental analysis. For example, the ¹H-NMR (DMSO-d₆) spectra revealed two singlets signal at δ 1.84, 1.96 assignable to CH₃ protons beside multiplet signal at δ 7.55 ppm assignable for 5H of the benzene ring.

![Scheme 1](image)

Condensation of 2 with dimethylformamide dimethyl acetal (DMF-DMA) under reflux for 10 h in the presence of xylene furnished enaminoine 3 (Scheme 2). The ¹H-NMR (DMSO-d₆) spectrum of 3 displayed a singlet signal at δ 2.99 ppm due to the N,N-dimethyl group and a singlet at δ 1.96 ppm due to methyl protons. Two doublets signal at δ 4.53, 5.38 ppm with coupling constant J = 12 Hz were assignable to olefinic protons (CH=CH) in a trans configuration.
Scheme 2. Synthesis of enaminone derivative 3.

Reaction of enaminone 3 with an N-nucleophile such as urea in dioxane or EtOH/DMF mixture under reflux for 4–6 h in the presence of a catalytic amount of ZnCl₂ as a Lewis acid afforded 4a (Scheme 3). The structure of the product was confirmed by the ¹H-NMR (DMSO-d₆) spectrum which displayed a new pair of doublets signals at δ 5.38, 7.65 with J = 7.8 Hz corresponding to pyrimidinol besides a singlet peak at δ 6.5 ppm assignable to OH. The formation of compound 4a would involve an initial addition of the amino group in urea to the activated double bond in enaminone derivative 3, followed by deamination to an intermediate which then undergoes cyclization and aromatization via loss of water affording the final isolable product (Scheme 4).

Scheme 3. Synthesis of bis-pyrimidine derivatives 4a–c.

Next, reaction of enaminone 3 with thiourea in refluxing DMF/Ethanol mixture afforded the corresponding dipyrimidin-2-thiol derivatives 4b (Scheme 3). The ¹H-NMR spectrum (DMSO-d₆) of compound 4b revealed two doublets at δ 5.36 ppm (1H, d) and 7.62 ppm (1H, d) which were readily assigned to the hydrogen attached at C₅ and C₄ of the pyrimidine ring respectively, and a singlet at δ 6.5 ppm (1H, s) assigned to the –SH attached at C₂ of the pyrimidine ring. Nevertheless, when enaminone derivative 3 was reacting with guanidine under similar reaction conditions to give
dipyrimidin-2-amine derivative 4c (Scheme 3). The structure of dipyrimidin-2-amine derivatives was established on the basis of their elemental analysis and spectral data (see Experimental).

Similarly, enaminone derivative 3 cyclized with hydrazine compounds in refluxing absolute ethanol for 6 h. The novel bispyrazole 5a was assumed to be formed via addition of the amino group in the hydrazine to the activated double bond of the enamine derivative, followed by deamination, dehydration and subsequently nucleophilic cyclization to afford the final product (Scheme 5). The IR spectrum of compound 5a indicated the characteristic absorption band at 3402 cm$^{-1}$ for the NH group. In particular, the $^1$H-NMR spectra (DMSO-$d_6$) of compound 5a revealed two doublets at δ 6.45 (1H, d) and 7.81 ppm (1H, d) which were readily assigned to the hydrogen attached at C$_4$ and C$_3$ of the pyrazole ring respectively, and a singlet at δ 13.01 ppm (1H, s) assigned to the –NH attached at C$_2$ of the pyrazole ring. Nevertheless, when enaminone derivative 3 was reacted with phenyl hydrazine under similar reaction conditions it gave N-phenyl pyrazole derivative 5b (Scheme 5). The structure of latter compound was established on the basis of their elemental analysis and spectral data (see Experimental).

Scheme 5. Synthesis of bis-pyrazole derivatives 5a,b.

The utility of enaminone 3 in the synthesis of annelated heterocycles was further explored via its reaction with 4-amino-1,2,4-triazole in absolute ethanol under reflux for 7 h in the presence of a catalytic amount of ZnCl$_2$. It is assumed that the product 6 was formed via initial formation of a nonisolable hydrazonal followed by elimination of water to give the desired product 6 (Scheme 6). Spectral data (IR, NMR, MS) and elemental analysis were consistent with isolated product 6. For example, the $^1$H-NMR (DMSO-$d_6$) displayed a characteristic a pair of doublets at δ 8.17, 8.99 ppm assigned to the hydrogen at C$_5$, and C$_4$ of the pyrimidine ring respectively and a singlet at δ 8.67 ppm assigned to the triazole proton, respectively.

Scheme 6. Synthesis of annelated heterocycles 6,7.
The study was extended to investigate the behavior of enaminone derivatives 3 with different nucleophiles like 2-aminobenzimidazole with a view to synthesizing various heterocyclic ring systems. Thus, the reaction of 3 with this compound in refluxing ethanol in the presence of catalytic amount of ZnCl₂ furnished the corresponding product 7 (Scheme 6). The structure of the product was confirmed on the basis of its elemental analysis and spectral data. The $^1$H-NMR (DMSO-$d_6$) spectrum of the compound 7 revealed two doublets signal at $\delta$ 8.16, 8.80 assigned to the hydrogen at $C_5$, and $C_4$ of the pyrimidine ring, respectively.

3. Experimental

3.1. General

All melting points were measured on a Gallenkamp melting point apparatus in open glass capillaries and are uncorrected. IR spectra were measured as KBr pellets on a Perkin Elmer FT 1000 spectrophotometer. The NMR spectra were recorded on a Varian Mercury Jeol-400 NMR spectrometer. $^1$H-NMR (400 MHz) and $^{13}$C-NMR (100 MHz) were run in deuterated dimethylsulphoxide (DMSO-$d_6$). Chemical shifts ($\delta$) are referred in terms of ppm and $J$-coupling constants are given in Hz. Abbreviations for multiplicities are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 eV. Elemental analysis was carried out on an Elementar Vario EL analyzer.

3.2. 1,1'-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl)diethanone (2)

A mixture of benzoylacetone 1 (16.2 g, 0.1 mol) and anhydrous potassium carbonate (25 g) in DMF (30–40 mL) was stirred vigorously at room temperature for 5 min, then carbon disulfide (7.6 mL, 0.1 mol) was added with continued stirring for 30 min. The resulting reaction mixture were cooled in ice bath, then chloroacetone (18.5 mL, 0.2 mol) was added with continued stirring for 15 min, then cooling bath subsequently removed and the mixture was stirred for further 30 min. The solid product was collected by filtration and washed with water, dried and the crude product was recrystallized from glacial acetic acid to give a pale green crystals. Yield: 87%; m.p. 204–206 °C; IR ($\nu$ max): 1645 (C=O) cm$^{-1}$; $^1$H-NMR $\delta$ (ppm): 1.84 (s, 6H, CH$_3$), 1.96 (s, 3H, CH$_3$), 7.551–7.61 (m, 5H, C$_6$H$_5$); $^{13}$C-NMR $\delta$ (ppm): 14.49 (CH$_3$), 29.37–30.55 (COCH$_3$), 192.2 (C=O), 129.23, 129.55, 129.87, 134.79, 138.82, 141.84, 147.68 (Ar–C); MS m/z (%): 314 [M+, 70%], 299 (100), 226 (37), 184 (14); Anal. calcd. for C$_{17}$H$_{14}$O$_2$S$_2$: C, 64.94; H, 4.49; S, 20.40; Found: C, 64.95; H, 4.44; S, 20.43.

3.3. 1,1'-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl)bis(3-(dimethylamino)prop-2-en-1-one) (3)

A mixture of compound 2 (1.75 g, 5 mmol), DMF-DMA (1.19 mL, 0.01 mol) was refluxed in m-xylene (15 mL) for 10 h. After cooling, the resulting solid product was collected by filtration to give a dark yellow crystals. Yield: 73%; m.p. 250 °C; IR ($\nu$_max): 1622 (C=O) cm$^{-1}$; $^1$H-NMR $\delta$ (ppm): 1.96 (s, 3H, CH$_3$), 2.99 (s, 12H, CH$_3$), 4.53 (d, 1H, $J$ = 12 Hz, CH), 5.38 (d, 1H, $J$ = 12 Hz, CH), 7.41–7.65 (m, 5H, C$_6$H$_5$); $^{13}$C-NMR $\delta$ (ppm): 14.9 (–CH$_3$), 44.79 (–N=(CH$_3$)$_2$), 109.8 (–CO–CH=), 153.9 (=CH–N), 180 (C=O); MS m/z (%): 424 [M+, 57%], 380 (51), 336 (18), 309 (18), 98 (100); Anal. calcd. for C$_{23}$H$_{24}$N$_2$O$_2$S$_2$: C, 65.06; H, 5.70; N, 6.60; S, 15.10; Found: C, 65.10; H, 5.68; S, 15.07.
3.4. General Procedure for the Synthesis of Compounds 4a–c (GP1)

A mixture of compound 3 (0.212 g, 0.5 mmol), urea derivatives (2 equiv., 1 mmol) refluxed in dioxane (20 mL) for 4–6 h after in the presence of 0.5 mL of TEA and catalytic amount of ZnCl₂. After cooling, the resulting solid products were filtered off, washed with ethanol, dried and recrystallized from DMF/EtOH, afford the corresponding derivatives 4a–c, respectively.

4.4’-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl) dipyrimidin-2-ol (4a). Compound 4a was prepared from urea following GP1 as a pale yellow crystalline powder. Yield: 67%; m.p. 248 °C; IR (νmax): 3444 (OH), 1624 (C=N) cm⁻¹; ¹H-NMR δ (ppm): 1.96 (s, 3H, CH₃), 5.38 (d, 1H, J = 7.8 Hz, CH), 6.5 (s, 1H, O–H), 7.65 (d, 1H, J = 7.8 Hz, CH), 7.41–7.65 (m, 5H, C₆H₅); MS m/z (%): 418 [M⁺, 2%]; Anal. calcd. for C₂₁H₁₄N₄O₂S₂: C, 60.27; H, 3.37; N, 13.39; O, 7.65; S, 15.32; Found: C, 60.24; H, 3.31; N, 13.38; S, 15.32.

4.4’-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl) dipyrimidin-2-thiol (4b). Compound 4b was prepared from thiourea following GP1 as a pale yellow crystalline powder. Yield: 68%; m.p. 247 °C; IR (νmax): 1625 (C=N) cm⁻¹; ¹H-NMR δ (ppm): 1.96 (s, 3H, CH₃), 5.36 (d, 1H, J = 7.8 Hz, CH), 6.5 (s, 1H, S–H), 7.41–7.65 (m, 5H, C₆H₅), 7.62 (d, 1H, J = 7.8 Hz, CH); MS m/z (%): 450 [M⁺, 2%]; Anal. calcd. for C₂₁H₁₄N₄S₄: C, 55.97; H, 3.13; N, 12.43; S, 28.46; Found: C, 55.98; H, 3.12; N, 12.41; S, 28.41.

4.4’-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl) dipyrimidin-2-amine (4c). Compound 4c was prepared from guanidine following GP1 as a yellow crystalline powder. Yield: 72%; m.p. 246 °C; IR (νmax): 3419 (NH₂), 1624 (C=N) cm⁻¹; ¹H-NMR δ (ppm): 1.96 (s, 3H, CH₃), 4.50–4.53 (d, 2H, NH₂), 5.39 (d, 1H, J = 11.7 Hz, CH), 7.41–7.52 (m, 5H, C₆H₅), 7.66 (d, 1H, J = 11.7 Hz, CH); ¹³C-NMR δ (ppm): 14.99, 19.12, 56.58, 94.12, 108, 128, 129, 130, 136, 154, 179; MS m/z (%): 416 [M⁺, 2%]; Anal. calcd. for C₂₁H₁₆N₆S₂: C, 60.55; H, 3.87; N, 20.18; S, 15.40; Found: C, 60.58; H, 3.85; N, 20.15; S, 15.38.

3.5. General Procedure for the Synthesis of Compounds 5a–b (GP2)

A mixture of compound 3 (1 mmol), and an excess of hydrazine derivatives (1 mL) refluxed in EtOH (20 mL) for 6 h. After cooling, the resulting solid products were filtered off, washed with ethanol, dried and recrystallized from MeOH, afforded the corresponding derivatives 5a–b.

3,3’-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl)bis(1H-pyrazole) (5a). Compound 5a was prepared from hydrazine hydrate following GP2 as white crystals. Yield: 72%; m.p. 246 °C; IR (νmax): 3419 (NH₂), 1624 (C=N) cm⁻¹; ¹H-NMR δ (ppm): 1.96 (s, 3H, CH₃), 4.50–4.53 (d, 2H, NH₂), 5.39 (d, 1H, J = 11.7 Hz, CH), 7.41–7.52 (m, 5H, C₆H₅), 7.66 (d, 1H, J = 11.7 Hz, CH); ¹³C-NMR δ (ppm): 14.99, 19.12, 56.58, 94.12, 108, 128, 129, 130, 136, 154, 179; MS m/z (%): 416 [M⁺, 2%], 336(100), 324(47), 153(8); Anal. calcd. for C₂₁H₁₆N₆S₂: C, 60.55; H, 3.87; N, 20.18; S, 15.40; Found: C, 60.58; H, 3.85; N, 20.15; S, 15.38.

3,3’-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl)bis(1-phenyl-1H-pyrazole) (5b). Compound 5b was prepared from phenyl hydrazine following GP2 as brown crystals. Yield: 64%; m.p. 199 °C;
IR (\(\nu_{\text{max}}\)): 1606 (C=N) cm\(^{-1}\); \(^1\)H-NMR \(\delta\) (ppm): 1.86 (s, 3H, CH\(_3\)), 6.48 (d, 1H, \(J = 4.5\) Hz, CH), 6.53–7.20 (m, 15H, C\(_6\)H\(_5\)), 7.55 (d, 1H, \(J = 4.5\) Hz, CH); \(^13\)C-NMR \(\delta\) (ppm): 14.03 (CH\(_3\)), 102 (CH), 143 (N=CH), 128.52, 129.23, 129.94, 130.38, 130.54, 136.38, 147.33, 152.84 (Ar–C); MS \(m/z\) (%): 514 [M\(^+\), 1\%]; 169 (5), 107 (100), 92 (55), 90 (35); Anal. calcd. for C\(_{31}\)H\(_{22}\)N\(_4\)S\(_2\): C, 72.34; H, 4.31; N, 10.89; S, 12.46; Found: C, 72.36; H, 4.29; N, 10.86; S, 12.43.

3.6. General Procedure for the Synthesis of Compounds 6,7 (GP3)

To a solution of compound 3 (212 mg, 0.5 mmol) in DMF (2 mL), substituted amine (2 equiv., 1 mmol) in EtOH (20 mL, 99.9%) was added, then the resulting reaction mixture was heated under reflux for 7 h in the presence of catalytic amount of ZnCl\(_2\). After cooling, the solid product was collected by filtration, washed with ethanol, dried and recrystallized from DMF/EtOH, to afford the corresponding derivatives 6,7, respectively.

7,7’-(3-Methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl)di-[1,2,4]triazolo[1,5-a]pyrimidine (6).

According to GP3, 6 was obtained from 4-amino-1,2,4-triazole (84 mg) as yellow crystals. Yield: 67%; m.p. 245 °C; IR (\(\nu_{\text{max}}\)): 1624 (C=N) cm\(^{-1}\); \(^1\)H-NMR \(\delta\) (ppm): 1.96 (s, 3H, CH\(_3\)), 7.41–7.56 (m, 5H, C\(_6\)H\(_5\)), 8.17 (d, 1H, \(J = 8.5\) Hz, CH, pyrimidyl), 8.67 (s, 1H, CH, triazole), 8.99 (d, 1H, \(J = 12.5\) Hz, CH, pyrimidyl); \(^13\)C-NMR \(\delta\) (ppm): 14.29 (–CH\(_3\)), 115.38, 125, 129.11, 129.98, 130.21, 132.81, 135.8, 152.8, 154.43, 159.98, 162.88 (Ar–C); MS \(m/z\) (%): 466 [M\(^+\),45\%]; Anal. calcd. for C\(_{23}\)H\(_{14}\)N\(_8\)S\(_2\): C, 59.21; H, 3.02; N, 24.02; S, 13.75; Found: C, 59.19; H, 3.03; N, 24.04; S, 13.71.

2,2’-(3-methyl-4-phenylthieno[2,3-b]thiophene-2,5-diyl)bis(benzo[4,5]imidazo [1,2-a]pyrimidine) (7).

According to GP3, 7 was obtained from 2-aminobenzimidazole (133 mg) as dark yellow crystals. Yield: 62%; m.p. 245 °C; IR (\(\nu_{\text{max}}\)): 1622 (C=N) cm\(^{-1}\); \(^1\)H-NMR \(\delta\) (ppm): 1.96 (s, 3H, CH\(_3\)), 7.42–7.65 (m, 8H, C\(_6\)H\(_5\), benzimidazole), 8.16 (d, 1H, \(J = 12.5\)Hz, CH, pyrimidyl), 8.39 (d, 1H, \(J = 8.5\)Hz, CH, benzimidazole), 8.80 (d, 1H, \(J = 12.5\) Hz, CH, pyrimidyl); \(^13\)C-NMR \(\delta\) (ppm): 14.81 (–CH\(_3\)), 112.05, 115.13, 122.5, 127.13, 128.1, 129.9, 131.31, 135.97, 139.1, 142.0, 148.4, 156 (Ar–C); MS \(m/z\) (%): 564 [M\(^+\), 1\%]; 488 (1.5), 380 (38), 336 (55), 324 (67), 98 (100); Anal. calcd. for C\(_{33}\)H\(_{20}\)N\(_6\)S\(_2\): C, 70.19; H, 3.57; N, 14.88; S, 11.36; Found: C, 70.21; H, 3.54; N, 14.85; S, 11.40.

4. Conclusions

In conclusion, the present investigation describes an efficient method for preparing novel bis(heterocycles), many of which may display potentially interesting biological activity in the field of medicinal chemistry.

Acknowledgments

The authors extend their appreciation to the Deanship of Scientific Research at King Saud University for funding the work through the research group project Number RGP- VPP- 007.

Conflict of Interest

The authors declare no conflict of interest.
References and Notes

1. Mabkhot, Y.N.; Kheder, N.A.; Al-Majid, A.M. Facile and convenient synthesis of new thieno[2,3-b]thiophene derivatives. *Molecules* **2010**, *15*, 9418-9426.

2. Mabkhot, Y.N. Synthesis and analysis of some bis-heterocyclic compounds containing sulphur. *Molecules* **2009**, *14*, 1904-1914.

3. Boydston, A.J.; Vu, P.D.; Dykhno, O.L.; Chang, V.; Wyatt, A.R.; Stockett, A.S.; Ritschdorff, E.T.; Shear, J.B.; Bielawski, C.W. Modular fluorescent benzobisimidazolium salts: Syntheses, photophysical analyses, and applications. *J. Am. Chem. Soc.* **2008**, *130*, 3143-3156.

4. Coady, D.J.; Khramov, D.M.; Norris, B.C.; Tennyson, A.G.; Bielawski, C.W. Modular fluorescent benzobisimidazolium salts: Syntheses, photophysical analyses, and applications. *J. Am. Chem. Soc.* **2008**, *130*, 3143-3156.

5. Tang, T.; Coady, D.J.; Boydston, A.J.; Dykhno, O.L.; Bielawski, C.W. Pro-ionomers: An anion metathesis approach to amphiphilic block ionomers from neutral precursors. *Adv. Mater.* **2008**, *20*, 3096-3099.

6. King, W.J.; Nord, F.F. Studies in the thiophene series. V. Wolff-Kishner reductions. *J. Org. Chem.* **1949**, *14*, 638-642.

7. Wu, C.; Decker, E.R.; Blok, N.; Bui, H.; You, T.J.; Wang, J.; Bourgoyne, A.R.; Knowles, V.; Berens, K.L.; Holland, G.W.; *et al.* Discovery, modeling, and human pharmacokinetics of N-(2-acetyl-4,6-dimethylphenyl)-3-(3,4-dimethylisoxazol-5-ylsulfamoyl)-thiophene-2-carboxamide (TBC3711), a second generation, ETA selective, and orally bioavailable endothelin antagonist. *J. Med. Chem.* **2004**, *47*, 1969-1986.

8. Dubus, S.; Levesque, I.; Brunette, M.; Corbeil, G.; Boissinot, M.; Boivin, G.; Bergeron, M.G.; Boudreau, D.; Leclerc, M. Fluorescent polymeric transducer for the rapid, simple, and specific detection of nucleic acids at the zeptomole level. *J. Am. Chem. Soc.* **2004**, *126*, 4240-4244.

9. Rost, C.; Karg, S.; Riess, W.; Loi, M.A.; Murgia, M.; Muccini, M. Ambipolar light-emitting organic field-effect transistor. *Appl. Phys. Lett.* **2004**, *85*, 1613-1615.

10. Vriezema, D.M.; Hoogboom, J.; Velonia, K.; Takazawa, K.; Christianen, P.C.M.; Maan, J.C.; Rowan, A.E.; Nolte, R.J. Vesicles and polymerized vesicles from thiophene-containing rod-coil block copolymers. *Angew. Chem. Int. Ed.* **2003**, *42*, 772-776.

11. Pullen, A.E.; Bushel, M.G.; Swager, T.M. Charge-specific interactions in segmented conducting polymers: An approach to selective ionoresistive responses. *Angew. Chem. Int. Ed.* **2004**, *43*, 3700-3703.

12. Heeney, M.; Bailey, C.; Genevicius, K.; Shkunov, M.; Sparrowe, D.; Tierney, S.; Mculloch, I. Stable polythiophene semiconductors incorporating thieno[2,3-b]thiophene. *J. Am. Chem. Soc.* **2005**, *127*, 1078-1079.

13. Mashraqui, S.H.; Sangvikar, Y.S.; Meetsma, A. Synthesis and structures of thieno[2,3-b]thiophene incorporated [3.3]dithiacyclophanes. Enhanced first hyperpolarizability in an unsymmetrically polarized cyclophane. *Tetrahedron Lett.* **2006**, *47*, 5599-5602.

14. Mashraqui, S.H.; Sangvikar, Y.S.; Ashraf, M.; Kumar, S.; Daub, E. Dipyridyl/pyridinium thieno[2,3-b]thiophenes as new atropisomeric systems. Synthesis, conformational analysis and energy minimization. *Tetrahedron* **2005**, *61*, 3507-3513.
15. Leriche, P.R.J.; Turbiez, M.M.; Monroche, V.; Allain, M.; Sauvage, F.X.; Roncali, J.; Frere, P.; Skabara, P.J. Linearly extended tetrathiafulvalene analogues with fused thiophene units as π-conjugated spacers. J. Mater. Chem. 2003, 13, 1324-1327.

16. Lee, B.; Seshadri, V.; Palko, H.; Sotzing, G.A. Ring-sulfonated poly(thienothiophene). J. Adv. Mater. 2005, 17, 1792-1795.

17. Lim, E.; Jung, B.J.; Lee, J.; Shim, H.K.; Lee, J.I.; Yang, Y.S.; Do, L.M. Thin-film morphologies and solution-processable field-effect transistor behavior of a fluorine-thieno[3,2-b]thiophene-based conjugated copolymer. Macromolecules 2005, 38, 4531-4535.

18. Kim, H.S.; Kim, Y.H.; Kim, T.H.; Noh, Y.Y.; Pyo, S.; Yi, M.H.; Kim, D.Y.; Kwon, S.K. Synthesis and studies on 2-hexylthieno[3,2-b]thiophene end-capped oligomers for OTFTs. Chem. Mater. 2007, 19, 2859-2868.

19. Jarak, I.; Kralj, M.; Piantanida, I.; Suman, L.; Zinic, M.; Pavletic, K.; Karminski-Zamola, G. Novel cyano- and amidino-substituted derivatives of thieno[2,3-b]- and thieno-[3,2-b]thiophene-2-carboxanilides and thieno[30,20:4,5]thieno- and thieno [20,30:4,5] thieno[2,3-c]quinolones: Synthesis, photochemical synthesis, DNA binding, and antitumor evaluation. Bioorg. Med. Chem. 2006, 14, 2859-2868.

20. Peters, D.; Hornfeldt, A.B.; Gronowitz, S. Synthesis of various 5-substituted uracils. J. Heterocycl. Chem. 1990, 27, 2165-2173.

21. Kukolja, S.; Draheim, S.E.; Graves, B.J.; Hunden, D.C.; Pfeil, J.L.; Cooper, R.D.G.; Ott, J.L.; Couter, F.T. Orally absorbable cephalosporin antibiotics. 2. Structure-activity studies of bicyclic glycine derivatives of 7-aminodeacetoxycephalosporanic acid. J. Med. Chem. 1985, 28, 1896-1903.

22. Prugh, J.D.; Hartman, G.D.; Mallorga, P.J.; MeKeever, B.M.; Michelson, S.R.; Murcko, M.A.; Schwam, H.; Smith, R.L.; Sondey, J.M.; Springer, J.P.; et al. New isomeric classes of topically active ocular hypotensive carbonic anhydrase inhibitors: 5-substituted thieno[2,3-b]thiophene-2-sulfonamides and 5-substituted thieno[3,2-b]thiophene-2-sulfonamides. J. Med. Chem. 1991, 34, 1805-1818.

23. Egbertson, M.S.; Cook, J.J.; Bednar, B.; Prugh, J.D.; Bednar, R.A.; Gaul, S.L.; Gould, R.J.; Hartman, G.D.; Homnick, C.F.; Holahan, M.A.; et al. Centrally constrained thienothiophene α-sulfonamides are potent, long acting in vivo inhibitors of platelet aggregation. J. Med. Chem. 1999, 42, 2409-2421.

24. Allard, S.; Forster, M.; Souharce, B.; Thiem, H.; Scherf, U. Organic semiconductors for solution-processable field-effect transistors (OFETs). Angew. Chem. Int. Ed. 2008, 47, 4070-4098.

25. Wu, Z.-Q.; Ono, R.I.; Chen, Z.; Bielawski, C.W. Synthesis of poly(3-alkylthiophene)-block-poly(arylisocyanide): Two sequential, mechanistically distinct polymerizations using a single catalyst. J. Am. Chem. Soc. 2010, 132, 14000-14001.

26. Li, Z.; Ono, R.J.; Wu, Z.-Q.; Bielawski, C.W. Synthesis and self-assembly of poly(3-hexylthiophene)-block-poly(acrylic acid). Chem. Commun. 2011, 47, 197-199.

27. Wu, Z.-Q.; Ono, R.J.; Chen, Z.; Li, Z.; Bielawski, C.W. Polythiophene-block-poly(γ-benzyl L-glutamate): Synthesis and study of a new rod-rod block copolymer. Polym. Chem. 2011, 2, 300-302.

28. Sirringhaus, H.; Brown, P.J.; Friend, R.H.; Nielsen, M.M.; Bechgaard, K.; Langeveld-Voss, B.M.W.; Spiering, A.J.H.; Janssen, R.A.J.; Meijer, E.W.; Herwig, P.; et al. Two-dimensional charge transport in self-organized, high-mobility conjugated polymers. Nature 1999, 401, 685-688.
29. Schuett, W.; Raoort, H.S. The paralytic shellfish poison. Degradation to a pyrrolopyrimidine. *J. Am. Chem. Soc.* **1962**, *84*, 2266-2267.

30. Ho, Y.W. 5-(1-Pyrrolyl)-2-phenylthieno[2,3-d]pyrimidine as building block in heterocyclic synthesis: Novel synthesis of some pyrazoles, pyrimidines, imidazo[1,2-a]pyrimidines, pyrazolo[1,5-a]pyrimidines, pyrido-(pyrimido)pyrazolo[1,5-a]pyrimidines, 1,2,4-triazolo[1,5-a]pyrimidine and a 1,2,3,4-Tetrazolo[1,5-a]pyrimidine derivative. *J. Chin. Chem. Soc.* **2007**, *54*, 1075-1085.

31. Alexander, S.K.; Smith, L. Novel one pot synthesis of polysubstituted pyrazolo[1,5-a] and imidazo[1,2-a]pyrimidines. *Tetrahedron Lett.* **2006**, *47*, 2611-2614.

32. Riyadh, S.M. Enaminones as building blocks for the synthesis of substituted pyrazoles with antitumor and antimicrobial activities. *Molecules* **2011**, *16*, 1834-1853.

*Sample Availability*: Samples of the compounds *2–7* are available from the authors.

© 2011 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (http://creativecommons.org/licenses/by/3.0/).