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The unexpected conversion of a thiophene ring into a pyrrole ring via a putative nitrene intermediate

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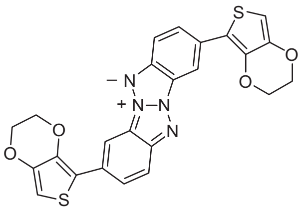
Thiophenes
Polythiophenes

A B S T R A C T

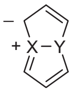
Triethylphosphite induced reductive cyclisation of 1-(2-nitrophenyl)-3,5-di(2-thienyl)pyrazole **6** afforded the expected 1,3-di(2-thienyl)pyrazolo[1,2-*a*]benzotriazole **7** (14%) together with an unexpected product which was shown to be a 2-(2-thienyl)pyrazolo[1,5-*a*]pyrrolo[2,1-*c*]quinoxaline **8** derivative (27%). A mechanism for the extrusion of sulfur during the transformation of heterocycle **6** into product **8** is proposed.

The synthesis and properties of thiophene-containing conducting polymers have attracted considerable interest.[1–4] We recently reported the synthesis of monomer **1** and have studied its electropolymerisation which yielded a polymer with optical and electrochemical band-gaps of 2.35 and 2.34 eV, respectively.[5] Monomer **1** is an example of a Type B heterocyclic mesomeric betaine (HMB)[6] and as such, is associated with the general core structure in which the heteroatoms X and Y are located at the bridge-head positions and formally contribute a pair of electrons to the π-system as depicted in formula **2**. The polymer derived from monomer **1** is, to our knowledge, the first example of a thiophene-containing material built upon a Type B HMB scaffold. In contrast to Type B HMBs, the Type A HMBs are associated with heteroatoms X and Y that are located at non-bridgehead positions as shown in formula **3**. Several examples of thiophene-containing conducting polymers which possess this structural motif have been reported such as polymers derived from the thienyl-substituted thieno[3,4-*c*][1,2,5]thiadiazole **4** (E_g = 0.9 eV)[7] and related systems.[8] An important feature of both Type A and Type B HMBs is that their highest occupied molecular orbital is topologically and energetically similar to a non-bonding molecular orbital.[6] Consequently, the frontier molecular orbital energy separation in these systems is relatively small and this property can be used beneficially for the construction of low band-gap polymers such as those noted above.

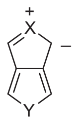
In view of our interest in thiophene-containing Type B HMBs as precursors to potential low band-gap polymers, we report in this Letter an investigation of the reductive cyclisation of compound **6** as a potential route to the Type B HMB **7**.



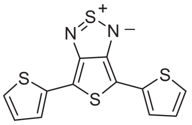
1



Type B
2



Type A
3



4

The reaction of compound **5**[9] with 2-nitrophenylhydrazine afforded 1-(2-nitrophenyl)-3,5-di(2-thienyl)pyrazole (**6**) (Scheme 1).[10] In view of several known examples of the triethylphosphite mediated reductive cyclisations of 1-(2-nitrophenyl)pyrazole derivatives yielding Type B HMBs based upon the pyrazolo[1,2-*a*]benzotriazole ring system,[11] heterocycle **6** was treated with hot triethylphosphite with the expectation that the required Type B HMB **7** would be formed. However, two products were formed from this reaction; the required pyrazolo[1,2-*a*]benzotriazole HMB derivative **7** was produced as anticipated together with an unexpected product which

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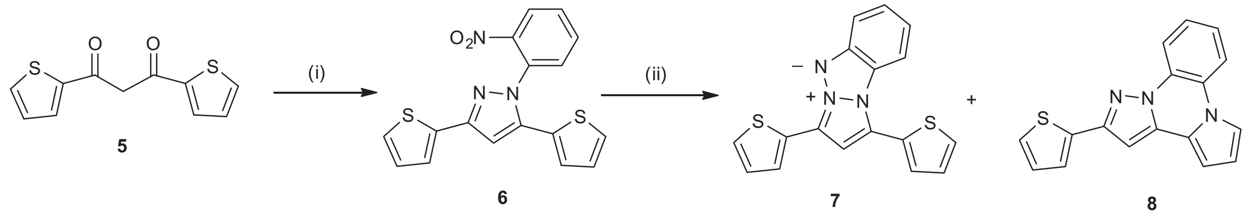


Scheme 1. Synthesis of heterocycles **7** and **8**. Reagents and conditions: (i) 2-nitrophenylhydrazine, AcOH, EtOH, concd H_2SO_4 (cat.), reflux (33%); (ii) $P(OEt)_3$, 110 °C, 28 h [**7** (14%) + **8** (27%)].

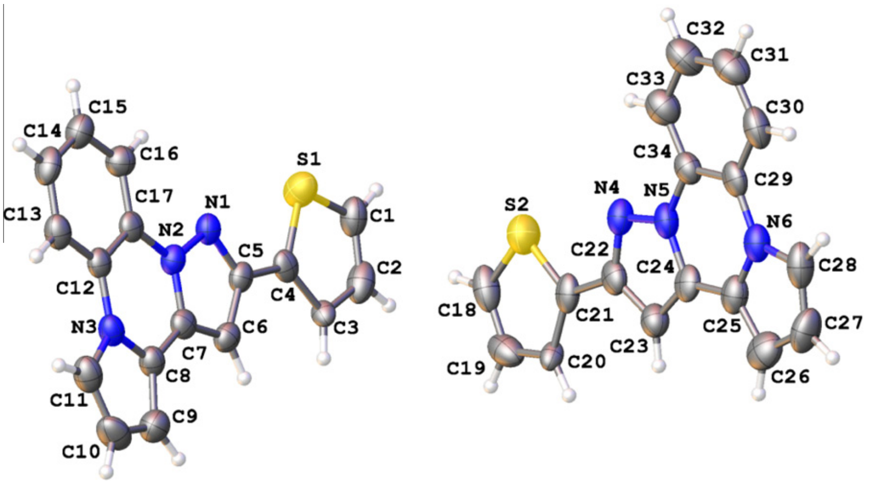


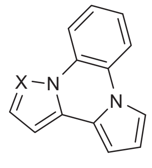
Figure 1. X-ray crystal structure of heterocycle **8** (ORTEP representation). Ellipsoids are shown at the 50% probability level.

was identified as 2-(2-thienyl)pyrazolo[1,5-*a*]pyrrolo[2,1-*c*]quinoxaline (**8**).[12] The structure of compound **8** was confirmed by X-ray crystallography (Fig. 1).[13] The asymmetric unit consists of two crystallographically independent molecules, in an approximately coplanar arrangement. Both molecules are completely planar and pack with a herringbone style arrangement, forming five intermolecular C–H· · ·π interactions.

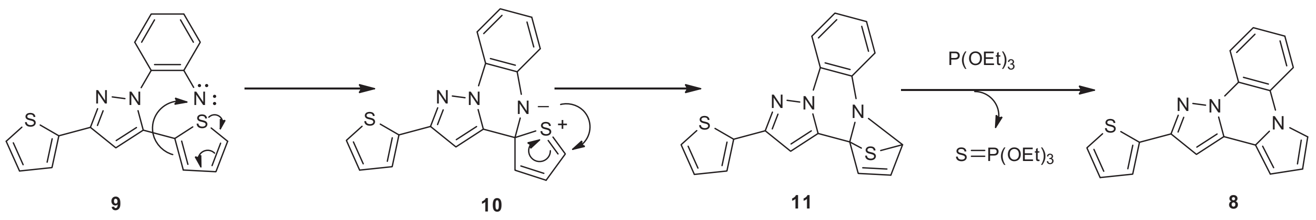
A plausible mechanism which accounts for the formation of heterocycle **8** is depicted in Scheme 2. Reduction of the nitro compound **6** by triethylphosphite gives a putative intermediate nitrene **9** (or an equivalent species) from which the HMB **7** is formed by nitrogen–nitrogen bond formation. In order to account for the formation of heterocycle **8**, the electrophilic nitrene **9** might also have reacted at the 2-position of the appositely located electron-rich thiophene ring yielding a dipolar intermediate **10** from which the bridged sulfide **11** is formed (Scheme 2). Extrusion of sulfur from compound **11**, presumably by its reaction with triethylphosphite, then affords the heterocycle **8**.

To our knowledge, compound **8** is the first example of a derivative of the novel pyrazolo[1,5-*a*]pyrrolo[2,1-*c*]quinoxaline heterocyclic ring system **12**. The dipyrrolo[1,2-*a*:2′,1′-*c*]quinoxaline **13** and some related derivatives have been reported recently as conformationally restricted 2,2′-bipyrrole analogues.[14]

In conclusion, we have prepared a novel heterocyclic ring system which has been formed by an unexpected mechanism. A thiophene ring has effectively been converted into a pyrrole-ring during this process. The Type B HMB **7** has been successfully prepared but in view of its relatively low yield and the requirement of chromatography for its purification, this heterocycle is unlikely to find use as a polythiophene precursor.



12 X = N
13 X = CH



Scheme 2. Proposed mechanism for the formation of heterocycle **8**.

Acknowledgments

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10. To a solution of compound **5** (8.0 g, 33.9 mmol) in EtOH (50 mL) and AcOH (45 mL) containing concd H_2SO_4 (10 drops) was added 2-nitrophenylhydrazine [stabilised with H_2O (30%); 6.7 g, 30.1 mmol]. The mixture was stirred under reflux (7 h), allowed to cool to room temperature and poured into H_2O (ca. 200 mL). The mixture was extracted with CH_2Cl_2 (2 × ca. 50 mL) and the combined organic layers washed with H_2O (50 mL), dried ($MgSO_4$) and evaporated giving a maroon coloured solid (12.7 g). Recrystallisation from EtOH gave compound **6** as maroon coloured needles (3.6 g, 33%), mp 122–123 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.02 (1H, dd, *J* = 2 and 8 Hz), 7.55–7.72 (3H, m), 7.41 (1H, dd, *J* = 1.5 and 4 Hz), 7.28 (2H, dt, *J* = 1.5 and 6 Hz), 7.07 (1H, dd, *J* = 6 and 8 Hz), 6.93 (1H, dd, *J* = 6 and 8 Hz), 6.84 (1H, dd, *J* = 1.5 and 4 Hz), 6.81 (1H, s); HRMS (ESI) $C_{17}H_{12}O_2N_3S_2$ [M+H]$^+$: calculated 354.0365, measured 354.0370.
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12. A mixture of compound **6** (1.0 g, 2.8 mmol) and $P(OEt)_3$ (3.0 mL) was heated (110 °C, 28 h) with stirring under nitrogen atmosphere. The mixture was allowed to cool to room temperature and the excess $P(OEt)_3$ was evaporated under reduced pressure (Kugelrohr). The resulting dark residue was purified by column chromatography [silica gel; eluent EtOAc: petroleum ether (bp 40–60 °C), 1:10 changing to 1:5] giving a yellow solid (0.35 g) which was shown to be a mixture (approximately 4:7) of compounds **7** (14%) and **8** (27%) by ^{1}H NMR spectroscopy. Chromatography over silica gel eluting with CH_2Cl_2 enabled the separation of analytical samples of pure products. Compound **7** (ca. 20 mg, eluted second): mp 178–180 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.91 (1H, dd, *J* = 2 and 4 Hz), 7.79 (1H, br d, *J* = 11 Hz), 7.67 (1H, br d, *J* = 11 Hz), 7.45–7.49 (2H, m), 7.32–7.43 (2H, m), 7.17–7.25 (2H, m), 7.02 (1H, s), 6.96 (1H, dt, *J* = 1.5 and 11 Hz); HRMS (APCI) $C_{17}H_{12}N_3S_2$ [M+H]$^+$: calculated 322.0467, measured 322.0469. Compound **8** (ca. 60 mg, eluted first): mp 192–193 °C; IR (diamond anvil): ν_{max}/cm^{-1} 1630, 1494, 1382, 1343; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.42 (1H, m), 7.72 (1H, m), 7.64 (1H, dd, *J* = 2 and 4 Hz), 7.50 (1H, dd, *J* = 1.5 and 3.5 Hz), 7.35–7.41 (2H, m), 7.32 (1H, dd, *J* = 2 and 8 Hz), 7.11 (1H, dd, *J* = 6 and 8 Hz), 6.81 (1H, s), 6.74 (1H, dd, *J* = 1.5 and 4 Hz), 6.67 (1H, dd, *J* = 3 and 4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 136.3, 133.6, 127.7, 126.0, 125.7, 125.6, 125.3, 125.3, 125.0, 121.6, 117.1, 114.9, 114.1, 112.9, 104.8, 95.6; HRMS (ESI) $C_{17}H_{12}N_3S$ [M+H]$^+$: calculated 290.0746, measured 290.0749. Intermediate fractions contained a mixture of products **7** and **8**.
13. Recrystallisation (MeOH) of a sample of compound **8** gave crystals suitable for X-ray analysis. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, CCDC857991. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (international) +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk].
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