Thienopentathiepins and pentathiepinofuran

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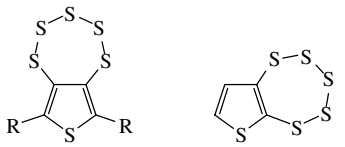
Thienopentathiepins and pentathiepinofuran were synthesised by the reaction of thiophenes and 2,5-dimethylfuran with S_2Cl_2 and *N*-ethyldiisopropylamine in chloroform at low temperature; thienopentathiepin 2 reacts with methyl propiolate and triphenylphosphine to give a pair of regioisomers.

1,2,3,4,5-Pentathiepins have attracted much attention amongst polysulfur heterocycles.[1] Recently, they have been investigated as anticancer, antimicrobial and antifungal agents and their activity resulted from the polysulfur moiety.[1–3] Pentathiepins are proposed for use as cathodic material in battery systems.[4] We found that treatment of nitrogen-containing heterocycles, such as pyrroles and indoles, with disulfur dichloride and 1,4-diazabicyclo[2.2.2]octane (DABCO) in chloroform at room temperature provides a simple one-pot synthesis of heterocyclic fused pentathiepins.[5–7] We believe that the strategy proposed can be useful for preparation of condensed pentathiepins from other aromatic heterocycles, *e.g.*, thiophenes and furans. Pentathiepins, fused to γ- (**1**) or β-bond (**2**) of thiophene, are known (Figure 1).[6,8–11] Pentathiepinofurans were not described so far.

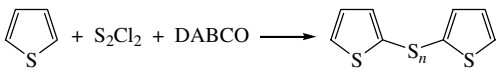


1 **2**

R = H, Cl, NEt_2, $S^-PPh_4^+$

Figure 1

We investigated the reaction of commercially available thiophene, furan and their 2,5-dimethyl derivatives with S_2Cl_2 and bases. The treatment of thiophene with S_2Cl_2 (5 equiv.) and DABCO (5 equiv.) in chloroform under argon at room temperature gave one spot according to TLC data, which is a mixture of bis(thiophenes) **3** connected by two, three and four sulfur atoms (NMR and mass spectral data) (Scheme 1).

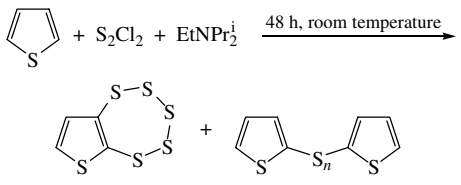


3a $n = 2$
3b $n = 3$
3c $n = 4$

Scheme 1

Thiophene is known to react with S_2Cl_2 giving **3a**,[12] and in the presence of kaolinitic clay catalyst a mixture of **3a** and **3b**.[13] The use of DABCO did also not afford cyclic polysulfur heterocycles, *e.g.*, pentathiepins. We decided to use a more active base, triethylamine or *N*-ethyldiisopropylamine, which in combination with S_2Cl_2 may facilitate β-substitution in the thiophene ring and finally construct the pentathiepin ring.

However, thiophene extensively decomposed by treatment with S_2Cl_2 and triethylamine, and we failed to isolate individual products. The reaction with *N*-ethyldiisopropylamine was successful and gave **2**, although in a low yield (Scheme 2); a mixture of bis(thiophenes) **3** was obtained as the main product. The influence of the quantity of reagents and the reaction temperature on the yield of **2** was studied, and the best yield (22%)



2, 10% **3a–c**

Scheme 2

was obtained when thiophene was treated with an equilibrated mixture of S_2Cl_2 (2.5 equiv.) and *N*-ethyldiisopropylamine (2.5 equiv.) at –10 °C for 48 h.‡ These conditions were employed for 2,5-dimethylthiophene and 2,5-dimethylfuran giving corresponding fused pentathiepins **4** and **5** in somewhat lower yields

† Professor Charles W. Rees, one of the most outstanding organic chemists and former President of The Royal Society of Chemistry (1992–1994), died on 21st September 2006.

‡ *General procedure for the preparation of pentathiepins* **2**, **4** *and* **5**. Disulfur dichloride (1 ml, 12.5 mmol) was added dropwise at –35 to –25 °C to a stirred solution of anhydrous *N*-ethyldiisopropylamine (1.6 g, 12.5 mmol) in chloroform (100 ml) under argon. The mixture was stirred at this temperature for 1 h. The corresponding heterocycle (5 mmol) in chloroform (10 ml) was added, the mixture was stirred for 48 h at –10 °C, filtered and the solvent was evaporated. The residue was separated by column chromatography (Silica gel Merck 60, light petroleum and then light petroleum–CH_2Cl_2 mixtures).

Synthesis of dithiin **6**. A solution of triphenylphosphine (2.2 g, 8.4 mmol) in dichloromethane (15 ml) was added dropwise to a stirred solution of pentathiepin **2** (0.34 g, 1.4 mmol) and methyl propiolate (0.59 g, 7 mmol) in dichloromethane (15 ml) at room temperature. The reaction mixture was stirred for 1 h, the solvent was evaporated under reduced pressure, and the corresponding dithiin was separated by column chromatography.

New compounds were characterised by elemental analysis, ^{1}H and ^{13}C NMR and mass spectra and HMRS.

Thieno[2,3-f][1,2,3,4,5]pentathiepin **2**: yellow oil. ^{1}H NMR [$(CD_3)_2CO$] δ: 7.36 (d, 1H, CH, *J* 5.5 Hz), 7.64 (d, 1H, CH, *J* 5.5 Hz). ^{13}C NMR [$(CD_3)_2CO$] δ: 130.16 and 134.05 (2CH), 141.475 and 144.7 (2 sp^2 tertiary C). MS, *m/z* (%): 242 (M^+, 65), 178 ($M^+ - S_2$, 100), 146 (46), 114 (47). Found M^+, 241.8483; $C_4H_2S_6$ requires 241.8481. Found (%): C, 22.82; H, 1.01. Calc. for $C_4H_2S_6$ (%): C, 23.21; H, 0.87.

6,8-Dimethylthieno[3,4-f][1,2,3,4,5]pentathiepin **4**: colourless oil. ^{1}H NMR ($CDCl_3$) δ: 2.54 (s, 6H, Me). ^{13}C NMR ($CDCl_3$) δ: 15.37 (Me), 143.13 and 177.18 (2 sp^2 tertiary C). MS, *m/z* (%): 270 (M^+, 30), 206 ($M^+ - S_2$, 100), 173 (40), 110 (10). Found M^+, 269.8795; $C_6H_6S_6$ requires 269.8794. Found (%): C, 26.97; H, 2.50. Calc. for $C_6H_6S_6$ (%): C, 26.64; H, 2.24.

6,8-Dimethyl[1,2,3,4,5]pentathiepino[6,7-c]furan **5**: colourless oil. ^{1}H NMR ($CDCl_3$) δ: 2.48 (s, 6H, Me). ^{13}C NMR ($CDCl_3$) δ: 13.45 (Me), 153.45 and 165.23 (2 sp^2 tertiary C). MS, *m/z* (%): 254 (M^+, 25), 190 ($M^+ - S_2$, 100), 158 (44), 94 (12). Found M^+, 253.9025; $C_6H_6S_5O$ requires 253.9022. Found (%): C, 28.42; H, 2.55. Calc. for $C_6H_6S_5O$ (%): C, 28.36; H, 2.38.

Methyl thieno[2,3-b][1,4]dithiin-2-carboxylate **6a** *and methyl thieno[2,3-b][1,4]dithiin-3-carboxylate* **6b**: yellow solid, mp 45–49 °C. ^{1}H NMR ($CDCl_3$) δ: 3.82 (s, 3H, Me, **6a** + **6b**), 6.71 (d, 1H, CH thiophene, *J* 5.3 Hz, **6b**), 6.75 (d, 1H, CH thiophene, *J* 5.3 Hz, **6a**), 7.33 (d, 1H, CH thiophene, *J* 5.3 Hz, **6b**), 7.35 (d, 1H, CH thiophene, *J* 5.3 Hz, **6a**), 7.47 (s, 1H, CH dithiin, **6a**), 7.59 (s, 1H, CH dithiin, **6b**). MS, *m/z* (%): 230 (M^+, 28), 198 (9), 171 (42), 127 (39), 69 (100). Found (%): C, 41.54; H, 2.52. Calc. for $C_8H_6O_2S_3$ (%): C, 41.72; H, 2.63.

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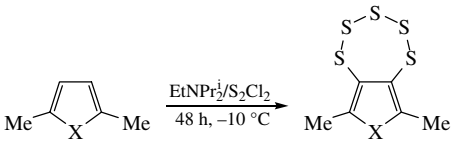
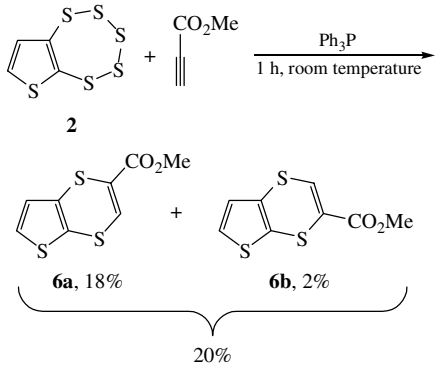


4 X = S, 13%
5 X = O, 11%

Scheme 3

(Scheme 3). In the case of furan, pentathiepinofuran was not isolated. Although the reaction yields are low, this new procedure may be useful for the insertion of a pentathiepin ring to other aromatic heterocycles.

Given ready one-pot synthesis of thienopentathiepin **2**, we wished to study its reaction with an unsymmetrical alkyne, methyl propiolate, which could lead to one or a pair of regioisomers. Treatment of thienopentathiepin **2** with methyl propiolate and triphenylphosphine at room temperature for 1 h gave a mixture of two regioisomers (Scheme 4) in an overall yield of 20%. All our attempts to isolate pure isomers were unsuccessful; they have similar R_f on TLC and crystallised as a mixture of isomers in the same ratio as obtained from the reaction. The molecular



Scheme 4

formula of isomers **6** was based on elemental analysis and mass spectrometry; the ratio of isomers was determined from the ^{1}H NMR spectrum. The exact structure of isomers **6a** and **6b** was finally proved by X-ray analysis of their mixture.[§] Note that the reaction of unsymmetrical pyrrolopentathiepins with methyl propiolate is much more selective giving one regioisomer in a higher yield[14] with the mode of junction as in isomer **6a**.

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