A novel approach to 4*H*-thieno[3,2-*b*]pyrroles

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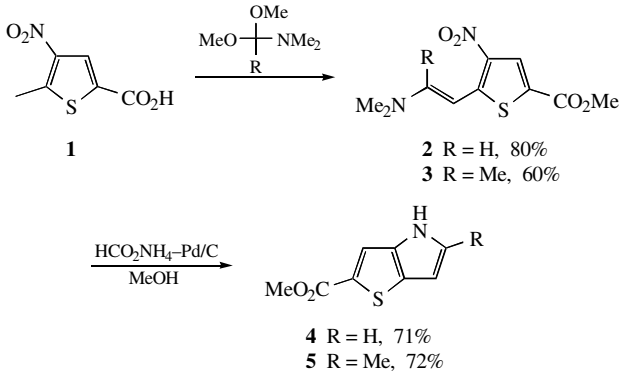
The condensation of 3-nitro-5-carboxy-2-methylthiophene with acetals of amides proceeds smoothly, and further ammonium formate–Pd/C reduction of nitroenamines thus obtained affords 2-carboxythieno-(5-R)-[3,2-*b*]pyrroles (R = H, Me) in good yields.

Thieno[3,2-*b*]pyrroles, close indole analogues, are of particular interest as biologically active compounds[1] and the moieties of photochromic compounds.[2–4] The most common synthetic methods of construction of the thieno[3,2-*b*]pyrrole core[5] employ cyclisation of azidovinyl thiophene derivatives,[6] condensation of nitromethylthiophenes with diethyl oxalate with further reduction of obtained nitrothienylpyruvic acids with either Fe^{II}, $SnCl_2$ or $NaHSO_3$,[7] reduction of nitrovinylthiophenes with trialkyl phosphites,[8] and also Fischer-reminiscent cyclisation of hydrazinothiophenes.[5] Each of the above methods has some drawbacks. Moreover, none of them leads to 2-carboxy-5-alkylthieno[3,2-*b*]-pyrroles. Thus, the construction of these compounds is still of prime interest.

In our search for a convenient preparative method for the synthesis of thieno[3,2-*b*]pyrroles, we noted the Batcho and Leimgruber indole synthesis,[9–11] which employs condensation of substituted *o*-nitrotoluenes with *N*,*N*-dimethylformamide dimethyl acetal followed by the reduction of the resulting nitroenamines to the corresponding indoles. We found that this reaction can be extended to methyl nitrothiophenes, which possess a considerable CH acidity of the methyl group. 3-Nitro-5-carboxy-2-methylthiophene **1** was chosen as an expedient starting compound. Reactions of **1** with dimethyl acetals of *N*,*N*-dimethylformamide and *N*,*N*-dimethylacetamide provides enamines **2** and **3** in 80% and 60% yields, respectively. Condensation is followed by the conversion of a carboxylic acid into its methyl ester. Compounds **2** and **3** are reduced easily with ammonium formate–Pd/C to form corresponding thienopyrroles **4** and **5**† in 71 and 72% yields, respectively.

Taking into account the availability of **1** and amide acetals and the possibility of introducing different alkyl groups into the 5-position of thienopyrrole by varying the amide acetal, good yields of products, and simplicity of experiments, the above method can be considered as useful and universal for the synthesis of thienopyrroles.



1

2 R = H, 80%
3 R = Me, 60%

4 R = H, 71%
5 R = Me, 72%

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† Compounds **2**–**5** were characterised using spectroscopic methods and elemental analysis.

*(*E*)-2-(2-Dimethylamino)vinyl-3-nitro-5-methoxycarbonylthiophene* **2**: mp 155–158 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.05 (s, 6H), 3.87 (s, 3H), 6.54 (d, 1H, *J* 14.6 Hz), 7.30 (d, 1H, *J* 14.6 Hz), 8.10 (s, 1H). MS, *m*/*z*: 258 (M^+ + 2), 257 (M^+ + 1), 256 (M^+), 224, 150, 86. Found (%): C, 46.75; H, 4.65; N, 10.68; S, 12.42. Calc. for $C_{10}H_{12}N_2O_4S$ (%): C, 46.86; H, 4.71; N, 10.93; S, 12.51.

2-(2-Dimethylamino-2-mehyl)vinyl-3-nitro-5-methoxycarbonylthiophene **3**: mp 203 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 2.39 (s, 3H), 3.17 (s, 6H), 3.87 (s, 3H), 7.02 (s, 1H), 8.22 (s, 1H). MS, *m*/*z*: 272 (M^+ + 2), 271 (M^+ + 1), 270 (M^+), 164, 100. Found (%): C, 48.75; H, 5.35; N, 10.38; S, 11.52. Calc. for $C_{11}H_{14}N_2O_4S$ (%): C, 48.87; H, 5.22; N, 10.36; S, 11.86.

*4*H-*thieno[3,2-*b*]pyrrole-2-carboxylic acid methyl ester* **4**: mp 123–124 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.90 (s, 3H), 6.49 (s, 1H), 7.19 (t, 1H, *J* 2.76 Hz), 7.70 (s, 1H), 8.65 (s, 1H). IR (KBr, ν_{max}/cm^{-1}): 3280, 1664. MS, *m*/*z*: 183 (M^+ + 2), 182 (M^+ + 1), 181 (M^+), 150, 122. Found (%): C, 53.02; H, 3.67; N, 7.89; S, 17.85. Calc. for $C_8H_7NO_2S$ (%): C, 53.02; H, 3.89; N, 7.72; S, 17.69.

*5-Methyl-4*H-*thieno[3,2-*b*]pyrrole-2-carboxylic acid methyl ester* **5**: mp 175–178 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 2.43 (s, 3H), 3.88 (s, 3H), 6.17 (s, 1H), 7.60 (s, 1H), 8.20 (s, 1H). IR (KBr, ν_{max}/cm^{-1}): 3320, 1684. MS, *m*/*z*: 197 (M^+ + 2), 196 (M^+ + 1), 195 (M^+), 164, 136. Found (%): C, 55.30; H, 4.45; N, 7.14; S, 16.20. Calc. for $C_9H_9NO_2S$ (%): C, 55.36; H, 4.64; N, 7.17; S, 16.42.

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