

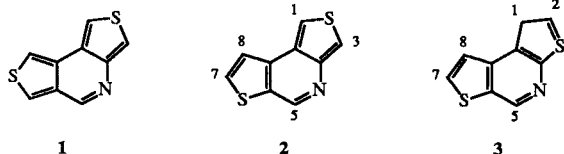
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The nitration of dithieno[3,4-*b*:3',2'-*d*]pyridine (**2**) and dithieno[2,3-*b*:3',2'-*d*]pyridine (**3**) has been studied. Nitration of **2** occurred in both positions of the *c*-fused thiophene ring, while **3** was predominantly substituted in the 2-position. The structures of the nitro derivatives were proven by extensive use of ¹H and ¹³C nmr spectroscopy.

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In connection with our interest in the effect of the mode of annelation on reactivity and orientation in electrophilic substitution of tricyclic heterosystems, we have previously studied the nitration of dithieno[3,4-*b*:3',4'-*d*]pyridine (**1**) [1]. Of the nine isomers, this is the only one in which the two thiophene rings are *c,c*-fused to the pyridine ring. The Wheland intermediates and the transition states for its nitration were calculated at the ab initio 3-21G* level. The energies for the transition state complexes were in good agreement with the experimental findings [1]. We have now studied the nitration of one of the [*b,c*]-fused systems, namely dithieno[3,4-*b*:3',2'-*d*]pyridine (**2**), and one of the [*b,b*]-fused systems, dithieno[2,3-*b*:3',2'-*d*]pyridine (**3**).



Compound **2** was nitrated in trifluoroacetic acid (TFA) with concentrated nitric acid at room temperature. We believe that under these conditions the protonated forms are nitrated, as nitrate salts can be precipitated by adding nitric acid to the ethereal solutions. Two mononitro derivatives, with mp of 230-232° and 219-221°, were isolated in approximately equal amounts (21% and 20% yield) on chromatography on silica gel.

The presence of a *J*₇₈ coupling in both mononitro isomers showed that the nitro group was in the *c*-fused ring. The lower melting isomer was shown by ¹H and ¹³C nmr spectra to be the 3-isomer. A DNOE effect of 6% was observed for the proton at 8.20 ppm on irradiation at the 8-hydrogen at 7.82 identifying the former as hydrogen 1. In the other isomer, which therefore must be the 1-isomer, the characteristic downfield shift of about one ppm of the 8-hydrogen (8.87 ppm) was observed, showing the presence of a nitro group in the 1-position. The large downfield shift of the proton resonance of the angular peri hydrogen was previously observed in nitro derivatives of some thieno-fused analogues of phenanthridine *N*-oxides [2].

The nitration of **3** had to be carried out under more rigorous conditions. Excess nitric acid was used and the mixture had to be refluxed for four hours. One major isomer, mp 229-231°, was isolated in 37% yield together with a minor isomer (12% yield, mp 212-213°). The major isomer was identified as the 2-nitro isomer of **3**, as its ¹³C spectrum showed two C-H couplings of 181-182 Hz, characteristic of β-CH groups [3] and furthermore, the presence of the characteristic long-range coupling *J*₅₈ of 0.8 Hz in its ¹H nmr spectrum [3]. The minor isomer was identified as the 1-isomer as its ¹H nmr spectrum also showed this coupling, and in the ¹³C spectrum two C-H couplings of 197.5 and 190.8 Hz were observed. Again the 8-hydrogen was shifted downfield to 8.45 ppm. The ¹H and ¹³C nmr spectra of the nitro derivatives are given in Tables 1 and 2.

From our results it is evident that a *c*-fused ring is more reactive in nitration than a *b*-fused ring, and mild methods

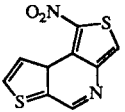
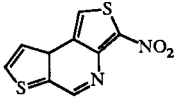
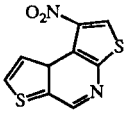
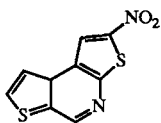
Table 1
Proton NMR Shifts (ppm) and Coupling Constants (Hz)
in Deuteriochloroform

| | H ¹ | H ² | H ³ | H ⁵ | H ⁷ | H ⁸ | <i>J</i> ₇₈ | <i>J</i> ₅₈ |
|--|----------------|----------------|----------------|----------------|----------------|----------------|------------------------|------------------------|
| | — | | 8.40 | 9.11 | 7.94 | 8.87 | 5.4 | 0.8 |
| | 8.20 | | — | 9.40 | 8.00 | 7.82 | 4.2 | 0.8 |
| | — | 8.78 | | 9.20 | 7.97 | 8.45 | 5.5 | 0.8 |
| | 8.51 | — | | 9.24 | 8.02 | 7.78 | 5.3 | 0.8 |

[a] DNOE effect 6%.

Table 2

Carbon-13 NMR Shifts (ppm) and Carbon-hydrogen Coupling Constants (Hz) in 80% Formic Acid 20% Acetone-d₆ Solvent System

| | | C ¹ | C ² | C ³ | C ^{3a} | C ⁵ | C ^{5a} | C ⁷ | C ⁸ | C ^{8a} | C ^{8b} |
|--|------------------------------|----------------|----------------|----------------|-----------------|----------------|-----------------|----------------|----------------|-----------------|-----------------|
|  | δ | 144.5 | — | 124.5 | 146.8 | 144.2 | 134.3 | 146.7 | 129.3 | 140.6 | 134.0 |
| | ¹ J _{CH} | — | | 197.9 | | 194.9 | | 188.2 | 181.2 | | |
| | ² J _{CH} | — | | — | | — | | 7.6 | 4.8 | | |
|  | δ | 131.4 | — | 137.0 | 145.5 | 146.9 | 131.0 | 152.1 | 124.8 | 130.9 | 127.7 |
| | ¹ J _{CH} | 198.6 | | | | 197.1 | | 191.0 | 178.2 | | |
| | ² J _{CH} | — | | | | — | | 7.2 | 4.4 | | |
|  | δ | 121.9 | 133.8 | — | 145.4 | 140.5 | 135.8 | 144.3 | 125.8 | 142.9 | 142.2 |
| | ¹ J _{CH} | | 197.5 | | | 194.3 | | 190.8 | 181.2 | | |
| | ² J _{CH} | | — | | | — | | 6.8 | 4.3 | | |
|  | δ | 121.8 | 127.4 | — | 151.0 | 142.5 | 133.7 | 143.9 | 122.0 | 145.2 | 136.4 |
| | ¹ J _{CH} | 181.9 | | | | 192.2 | | 190.2 | 181.2 | | |
| | ² J _{CH} | — | | | | — | | 6.8 | 4.3 | | |

must be used in order to avoid tar-formation. In the [b,b]-fused compound **3**, the thiophene ring fused to the pyridinic b-side is more reactive than the thiophene ring fused to the d-side. Theoretical calculations are in progress in order to explain this reactivity.

EXPERIMENTAL

The nmr spectra were recorded on a Varian XL-300 spectrometer. The high resolution mass spectral data were obtained on a Finnigan 4021 spectrometer.

Nitration of Dithieno[3,4-b:3',2'-d]pyridine.

To a solution of 0.20 g (1.04 mmoles) of dithieno[3,4-b:3',2'-d]pyridine [4] in 10 ml of trifluoroacetic acid (TFA). 0.18 ml of concentrated nitric acid was added and the mixture stirred for six hours at room temperature. The solvent was evaporated and the residue neutralized by the addition of sodium bicarbonate solution. Upon chromatography of the crude product on silica gel 60 (Merck), using dichloromethane-ethyl acetate (50:1) as eluent, 0.052 g (21%) of 1-nitrodithieno[3,4-b:3',2'-d]pyridine; ms: m/e 236, (M⁺), was obtained; nmr: cf. Tables 1-2.

1-Nitro-isomer.

Anal. Calcd. for C₉H₄N₂O₂S₂: C, 45.75; H, 1.70; N, 11.86. Found: C, 45.5; H, 1.6; N, 11.5.

3-Nitro-isomer.

Anal. Calcd. for C₉H₄N₂O₂S₂: C, 45.75; H, 1.70; N, 11.86. Found: C, 45.5; H, 1.5; N, 11.7.

Nitration of Dithieno[2,3-b:3',2'-d]pyridine.

To a solution of 0.49 g (2.56 mmoles) of dithieno[2,3-b:3',2'-d]

pyridine in 10 ml of TFA, 1.4 ml (33.3 mmoles) of concentrated nitric acid was added and the solution refluxed for four hours. The solvent was evaporated and the residue neutralized with sodium bicarbonate solution. Upon chromatography of the crude product on a silica gel 60 (Merck) column using chloroform-ethyl acetate (80:1) as eluent, 0.224 g (37%) of 2-nitrodithieno[2,3-b:3',2'-d]pyridine, mp 229-231°; ms: m/e 236 (M⁺), and 0.075 g (12%) of 1-nitrodithieno[2,3-b:3',2'-d]pyridine, mp 212-213°; ms: m/e 236 (M⁺), was obtained; nmr: Tables 1-2.

2-Nitro-isomer.

Anal. Calcd. for C₉H₄N₂O₂S₂: C, 45.75; H, 1.70; N, 11.86. Found: C, 45.4; H, 1.6; N, 11.9.

1-Nitro isomer.

Anal. Calcd. for C₉H₄N₂O₂S₂: C, 45.75; H, 1.70; N, 11.86. Found: C, 45.4; H, 1.7; N, 11.9.

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REFERENCES AND NOTES

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