

Pietro Cogoli, Filippo Maiolo, Lorenzo Testaferri, Marcello Tiecco and Marco Tingoli

Istituto di Chimica Organica, Facoltà di Farmacia, Università di Perugia, Italy

Received April 2, 1979

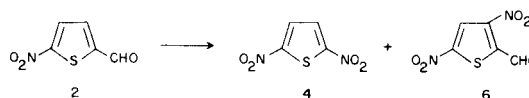
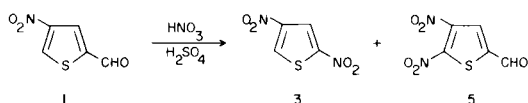
Nitration of 4-nitro-2-thiophenealdehyde afforded 2,4-dinitrothiophene and small quantities of 4,5-dinitro-2-thiophenealdehyde; 5-nitro-2-thiophenealdehyde gave instead 3,5-dinitro-2-thiophenealdehyde as the main product and some 2,5-dinitrothiophene. The two dinitrothiophenes form through a nitrodeformylation reaction which represents an interesting example of the nitration at an ipso position in a strongly deactivated substrate.

J. Heterocyclic Chem., **16**, 1495 (1979).

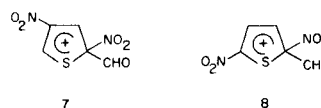
Attack of nitronium ions at an ipso position of an aromatic substrate is a well documented process (1); the ipso σ -complex formed can give a series of reactions among which the most frequently encountered is the loss of the group originally linked to the ipso carbon atom, *i.e.* ipso substitution. The large majority of the examples reported (1) refer to homoaromatic substrates activated towards electrophilic attack by the presence of electron-releasing substituents.

We report in this note that ipso nitration easily occurs in thiophenes even in the presence of strongly electron-withdrawing substituents such as nitro and formyl. The nitration of 2-thiophenealdehyde with nitric acid-sulfuric acid afforded the expected 4-nitro-2-thiophenealdehyde (1) and 5-nitro-2-thiophenealdehyde (2) together with a considerable amount of 2,4-dinitrothiophene (3) and smaller quantities of 2,5-dinitrothiophene (4). Similar results were obtained by Gronowitz and Dahlgren (2) in the nitration of 3-bromo-2-thiophenealdehyde from which a mixture of the 3-bromo derivatives of compounds 1-4 was obtained.

The formation of 3 and 4 suggests that a nitrodeformylation reaction occurs in compounds 1 and 2, respectively, and this was experimentally confirmed by nitrating the two aldehydes. Treatment of 4-nitro-2-thiophenealdehyde (1) with nitric acid-sulfuric acid afforded a mixture of 3 (73%) and of 4,5-dinitro-2-thiophenealdehyde (5) (23%); similarly, the aldehyde (2) gave the ipso substitution product (4) (18%) and the 3,5-dinitro-2-thiophenealdehyde (6) (61.5%) (3). In the nitration of 4-nitro-5-chloro-2-thiophenealdehyde, under similar experimental conditions, it has been reported that the 2,4-dinitro-5-chlorothiophene is formed in 85% yields (4); in this case the 5-position is occupied by chlorine and the only process occurring is the ipso substitution of the formyl group.



Nitrodeformylation thus occurs in both the nitroaldehydes investigated, but while in 1 it represents the most important process, in 2 it can be considered a secondary reaction. These results can be rationalized by considering that the ipso intermediate (7) is the more stable of the possible σ -complexes which can be formed from 1; in the case of 2, however, attack at the 3-position is favoured rather than the attack at the ipso position to give 8. These two ipso intermediates easily



evolve to 3 and 4 by loss of H^+ and CO . Nitration of the 4-nitro- and 5-nitro-2-carbomethoxythiophene gives only the products of nitration at the 5- and 3- position, respectively (5,6); in these cases also, attack at the 2-position probably occurs but is made reversible because the CO_2Me group cannot be easily expelled from the ipso intermediates.

The nitrodeformylation reactions described above, besides representing interesting examples of ipso substitution, can find useful applications in the syntheses of 2-nitro derivatives of thiophenes containing other electron-withdrawing substituents. These reactions also very likely occur with other aromatic substrates.

EXPERIMENTAL

Ir spectra were taken with a Beckman Acculab TM5 spectrophotometer. Nmr were recorded on a Jeol C60HL instrument, in deuteriochloroform. The progress of the reactions was monitored by tlc and glc (Hewlett-Packard 5830A with a 10% UCW 982 column); quantitative determinations of the reaction products were effected by nmr and glc.

Nitration of 2-Thiophenealdehyde.

To a stirred solution of 2-thiophenealdehyde (10 g.) in concentrated sulfuric acid (13.2 ml.), a mixture of nitric acid ($d = 1.52$; 14.2 ml.) and concentrated sulfuric acid (8.8 ml.) was added dropwise at -10° . The cooling bath was removed and stirring was continued for 0.5 hour. The mixture was poured on ice and extracted with ether; the organic layer was separated, washed with water, dried and evaporated. Column chromatography on silica gel using a mixture of light petroleum (b.p. $40-60^\circ$) and ethyl ether (9:1) as eluent afforded the following products.

2,5-Dinitrothiophene (4).

This compound had m.p. $79-80^\circ$ (lit. (7) m.p. $79.5-80^\circ$), (0.68 g.); nmr: δ 7.85 (s).

2,4-Dinitrothiophene (3).

This compound had m.p. $55-56^\circ$ (lit. (6) m.p. $55-56^\circ$) (3.5 g.); nmr: δ 8.35 (d, H_5), 8.2 (d, H_3 , $J = 1.5$ Hz).

4-Nitro-2-thiophenealdehyde (1).

This compound had m.p. $54-55^\circ$ (lit. (8) m.p. $55-56^\circ$) (3.9 g.); nmr: δ 9.8 (d, CHO, $J = 1.5$ Hz), 8.6 (dd, H_5), 8.2 (d, H_3 , $J_{3-5} = 1.5$ Hz).

5-Nitro-2-thiophenealdehyde (2).

This compound had m.p. $74-76^\circ$ (lit. (9) $75-76^\circ$) (2.5 g.); nmr: δ 9.8 (s, CHO), 7.85 (d, H_4), 7.65 (d, H_3 , $J = 4.5$ Hz).

Nitration of 4-Nitro-2-thiophenealdehyde (1).

The reaction was carried out under the same conditions described above; stirring at room temperature was continued until the starting product (0.5 g.) was completely consumed (2 hours). The nmr spectrum of the reaction mixture showed the presence of **3** and **5** in a ratio of 3:1. Column chromatography as described above, afforded 0.4 g. of 2,4-dinitrothiophene (**3**) and 0.15 g. of 4,5-dinitro-2-thiophenealdehyde (**5**) as an oil; nmr: δ 9.8 (s, CHO), 7.85 (s, H_3).

Anal. Calcd. for $C_5H_2N_2O_5S$: C, 29.71; H, 1.00; N, 13.86. Found: C, 29.9; H, 1.05; N, 13.95.

Nitration of 5-Nitro-2-thiophenealdehyde (2).

The reaction was carried out under the same experimental

conditions described for the 4-nitro isomer, using 0.5 g. of **2**. The reaction mixture was constituted by **4** and **6**, in a ratio of 1:3.5 (determined by nmr and glc). Column chromatography, as described above, afforded 0.1 g. of 2,5-dinitrothiophene (**4**) and 0.4 g. of 3,5-dinitro-2-thiophenealdehyde (**6**), m.p. $63-64^\circ$; nmr: δ 10.5 (s, CHO), 8.2 (s, H_4).

Anal. Found: C, 29.85; H, 1.03; N, 13.91.

Oxidation of this compound with tetrabutylammonium permanganate in pyridine (**10**) afforded 2,4-dinitrothiophene; it has already been observed, in fact, that the 3,5-dinitro-2-thiophene-carboxylic acid is easily decarboxylated (**6**).

Acknowledgment.

Financial support from the CNR-Rome is gratefully acknowledged.

REFERENCES AND NOTES

- (1) R. B. Moodie and K. Schofield, *Acc. Chem. Res.*, **9**, 287 (1976).
- (2) S. Gronowitz and K. Dahlgren, *Ark. Kemi*, **21**, 201 (1961); *Chem. Abstr.*, **59**, 12740e (1963).
- (3) The structures of the dinitroaldehydes **5** and **6** could be assigned by nmr. The J_{H_5-CHO} present in the starting compound (**1**), was no more observed in **5**, indicating that nitration occurs at position 5; the chemical shift of the aromatic proton was the same as that of 4,5-dinitro-2-carbomethoxythiophene (**5**). In compound **6** the aldehydic proton is considerably deshielded with respect to those of **1**, **2** and **5**, suggesting that a nitro group is present in the 3-position; moreover, oxidation and decarboxylation of **6** afforded the 2,4-dinitrothiophene.
- (4) S. Nishimura, A. Sakumoto and E. Imoto, *Nippon Kagaku Zasshi*, **82**, 1540 (1961); *Chem. Abstr.*, **57**, 15051b (1962).
- (5) M. Tiecco and co-workers, unpublished results.
- (6) I. J. Rinkes, *Rec. Trav. Chim.*, **52**, 538 (1933).
- (7) A. H. Blatt, S. Bach and L. W. Kresch, *J. Org. Chem.*, **22**, 1693 (1957).
- (8) G. Gever, *J. Am. Chem. Soc.*, **77**, 577 (1955).
- (9) T. M. Patrick and W. S. Emerson, *ibid.*, **74**, 1356 (1952).
- (10) T. Sala and M. V. Sargent, *J. Chem. Soc., Chem. Commun.*, 253 (1978).