

## Spiro Meisenheimer Compounds in the Thiophene Series

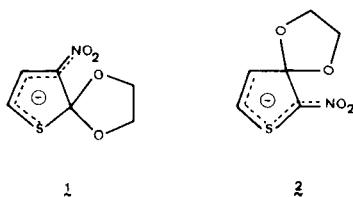
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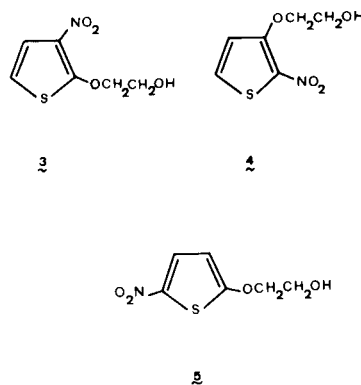
As part of our current interest in the chemistry of thiophene and in particular on the interaction of nitrothiophenes with bases (1), we report on the first evidence of spiro Meisenheimer complex (1 and 2) formation from five-membered ring substrates, 2-(2'-hydroxyethoxy)-3-nitrothiophene (3) and 3-(2'-hydroxyethoxy)-2-nitrothiophene (4). Up to now we have no evidence for the formation of any adduct from 2-(2'-hydroxyethoxy)-5-nitrothiophene (5).



The alcohols 3 and 4 were prepared from equimolar amounts of the corresponding bromonitrothiophenes and sodium glycolate in ethylene glycol (2). The alcohol 3 (m.p. 80°) shows pmr peaks, in solution (0.2 M) of dried DMSO-d<sub>6</sub>, at  $\tau$  2.63 (1H, d, J 6.25 Hz), 3.08 (1H, d, J 6.25 Hz), 4.93 (1H, t, J 5.25 Hz), 5.64 (2H, t, J 4.60 Hz), 6.18 (2H, m). The alcohol 4 (m.p. 95°) shows pmr peaks, in solution (0.2 M) of dried DMSO-d<sub>6</sub>, at  $\tau$  2.06 (1H, d, J 6.15 Hz), 2.73 (1H, d, J 6.15 Hz), 5.05 (1H, t, J 5.25 Hz), 5.64 (2H, t, J 4.85 Hz), 6.24 (2H, m).

The alcohol 5 (m.p. 71°) was prepared in several steps: substitution reaction of 2-iodothiophene with sodium glycolate, acetylation, nitration, separation of the two isomers and hydrolysis (2). It shows pmr peaks, in solution (0.2 M) of dried DMSO-d<sub>6</sub>, at  $\tau$  2.04 (1H, d, J 4.75 Hz), 3.44 (1H, d, J 4.75 Hz), 4.94 (1H, t, J 5.40 Hz), 5.72 (2H, t, J 4.60 Hz), 6.24 (2H, m).

The alcohol 3 was submitted to the following reactions: (i) a solution (0.2 M) in dried DMSO-d<sub>6</sub> was treated with an equimolar amount of a solution of sodium methoxide (2.56 M) in methanol; (ii) a solution (3 M) in benzene-methanol was treated with an equimolar amount of sodium methoxide (5.12 M) in methanol under nitrogen; the precipitate was washed with benzene and anhydrous ether



and dried *in vacuo* over phosphorus pentoxide. The pmr spectrum of a solution in DMSO-d<sub>6</sub> of the precipitate obtained *via* (ii) showed two doublets at  $\tau$  3.82 (1H) and 4.27 (1H) with J 7.00 Hz, similar to those of the corresponding non spiro Meisenheimer complex (3); the methylene protons showed an unresolved multiplet centered at  $\tau$  6.0. The reaction mixture obtained *via* (i) showed an analogous spectrum. Addition of a drop of trifluoroacetic acid afforded 3 in quantitative yield, as determined by analysis of the resulting pmr spectrum. The pmr data, together with the quantitative restoration of the starting compound are fully consistent with the proposed spiro structure 1.

The alcohol 4 was also submitted to reactions (i) and (ii). The pmr spectrum of a solution in DMSO-d<sub>6</sub> of the precipitate obtained *via* (ii) showed two doublets at  $\tau$  3.61 and 4.58 with J 6.50 Hz. The methylene protons showed an AA'BB' system with  $\tau_A$  5.76,  $\tau_B$  6.13,  $J_{AA'}$  =  $J_{BB'}$  =  $6.622 \pm 0.032$ ,  $J_{AB}$  =  $J_{A'B'}$  =  $-6.505 \pm 0.032$  and  $J_{AB'}$  =  $J_{A'B}$  =  $5.878 \pm 0.027$  (computer generated and experimental spectra were in good agreement). The reaction mixture obtained *via* (i) showed an analogous spectrum. Addition of a drop of trifluoroacetic acid restored 4 in quantitative yield. The pmr data together with the quantitative restoration of the starting compound are fully consistent with the proposed spiro structure 2.

The compound 2 is the first example of a Meisenheimer-type adduct at C<sub>3</sub> in the thiophene series. In fact, as

determined by other authors (3), 3-methoxy-2-nitrothiophene under the same conditions used to prepare **2** via (i) reacts with sodium methoxide to furnish an adduct at C<sub>5</sub>. Further studies are in progress on the equilibrium and kinetic constants of the formation reactions of **1** and **2**.

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