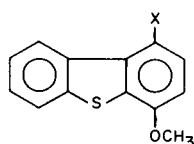


Some Substitution Reactions of 4-Methoxydibenzothiophene (1)

E. Campaigne, L. Hewitt and John Ashby

The Chemistry Laboratories of Indiana University

Gilman (2) has reported that nitration of 4-methoxydibenzothiophene (1a) yields a mixture of 1-nitro-4-methoxydibenzothiophene (1b) (66%) and the 2-isomer (5%). The isomers were identified by reduction to the corresponding amines and fractional crystallization, thus the original nitration product represented a mixture of isomers. Assignment of the major component to the 1-nitro structure was by analogy to the nitration of 4-methoxydibenzofuran which nitrates exclusively in the 1-position (3). In the light of our recent investigation of the substitution reactions of 4-methoxydibenzothiophene (4) where it was shown that nitration, acetylation and succinylation occurred in the 2-position, and bromination in the 2- and 3-positions, we decided to reinvestigate the electrophylic substitutions of 1a.



- 1a) X = H
 b) X = NO₂
 c) X = Br
 d) X = CHO

Repeating the nitration as described by Gilman (2) yielded a product in similar yield and of the same melting point as previously described. Gas-liquid chromatography showed this material to be a single substance. The nmr spectrum of the crude product was likewise identical in every detail to that of highly purified material. We were thus unable to find any evidence of a second nitration product. The product obtained was shown to have the previously assigned structure, 1-nitro-4-methoxydibenzothiophene, by analysis of its 100 MHz nmr spectrum. Bromination of 1a gave 1-bromo-4-methoxydibenzothiophene (1c) in good yield. The structure of the latter was assigned by analysis of the nmr spectrum of the derived aldehyde (1d).

The 100 MHz nmr spectrum of 1a showed doublets ($J = 8$ Hz) for H-1 and H-3 at δ 7.7 and 6.82, respectively and, due to identical coupling constants between H-2 and H-1, and H-2 and H-3, a triplet at δ 7.32 for H-2. Upon expansion of the spectrum a *meta*-coupling of *ca.* 0.8 Hz was observed between H-1 and H-3. These assignments were confirmed by irradiation of the H-2 triplet, causing the H-1 and H-3 doublets to collapse to singlets. The spectrum of the nitration product (1b) showed doublets for

H-2 and H-3 at δ 7.94 and 6.85, respectively ($J = 9$ Hz), confirming the structure assignment made by Gilman (2). Again these resonance assignments were confirmed by irradiation of either doublet causing the other to collapse to a singlet. The multiplets associated with H-6,7 and 8 of the unsubstituted ring of 1b were each deshielded by *ca.* 0.1 ppm from those in 1a. A similar effect was noted with dibenzothiophenes bearing an electron withdrawing substituent in the 3-position (5). The H-9 multiplet in 1b was however deshielded by 0.25 ppm from the resonance of H-9 in 1a. In the light of shifts to be discussed later this enhanced effect is probably due to deshielding through space by the adjacent nitro group.

The spectrum of 1d was similar to that of 1b, doublets at δ 7.84 and 6.86 associated with H-2 and H-3, respectively, confirming 1-substitution. Of particular interest in the spectrum of 1d was the appearance of the H-9 multiplet at δ 9.12, being deshielded by 1.05 ppm from the corresponding resonance in 1a. This behaviour can be explained by the H-9 proton lying in the deshielding cone of the aldehyde function; models show this to be possible. This surprising behaviour, exhibited to a lesser extent by the nitro compound, proves conclusively that 1a nitrates and brominates in the 1-position, and illustrates the close proximity of the 1- and 9-positions of dibenzothiophene. The difference in behaviour between 4-methoxy and 4-methoxydibenzothiophene (4) may be attributed to the stronger tautomeric *para*-orientating effect of the methoxy group.

EXPERIMENTAL

Melting points were measured on a Meltemp apparatus and are corrected. The 100 MHz nmr spectra were determined in deuteriochloroform on a Varian HA 100 instrument at 20°, TMS being used as internal standard throughout. In reporting the nmr spectra the following abbreviations have been made: s = singlet, d = doublet, dd = double doublet, t = triplet and m = multiplet (δ values refer to the center of the multiplet). Ether solutions were dried with anhydrous magnesium sulfate.

4-Hydroxydibenzothiophene.

Butyllithium (300 ml., 0.488 mole, 15% solution in hexane) was added to a stirred solution of dibenzothiophene (50 g., 0.272 mole) in sodium dried ether (400 ml.) at 0° over 15 minutes. The mixture was refluxed for 18 hours, cooled to 0° and butylmagnesium bromide [from 6.62 g., (0.272 mole) of magnesium and 37.2 g. of *n*-butyl bromide] in ether (100 ml.) added to the stirred solution over 15 minutes. Dry oxygen was then passed through the mixture for 4 hours at -5 to 0°. The reaction mixture was

poured over ice (500 g.) and hydrochloric acid and stirred overnight. The organic phase was separated and the aqueous phase extracted with ether (3 x 100 ml.). The combined ether extracts were extracted with a 10% solution of sodium hydroxide (6 x 200 ml.), the alkaline solution acidified, and the precipitate extracted into ether (3 x 150 ml.). The combined extracts were dried and evaporated leaving a brown solid (26.0 g. 48%) m.p. 134-150°. Crystallization from aqueous ethanol raised the m.p. to 163-165° (Lit. (6) m.p. 167°); nmr δ 8.12 (m, H-9), 7.85 (m, H-6), 7.78 (d, $J_{1,2}$ 7 Hz, H-1), 7.4 (m, H-2,7,8), 6.87 (d, $J_{3,2}$ 7 Hz, H-3) and 5.5 (broad singlet, OH).

4-Methoxydibenzothiophene (Ia).

Methyl sulfate (11.2 ml., 0.118 mole) was added dropwise over 15 minutes to a solution of 4-hydroxydibenzothiophene (crude material, 23.6 g., 0.118 mole) and sodium hydroxide (4.72 g., 0.118 mole) in 100 ml. of water at 0°. The mixture was stirred at room temperature for 1 hour and the tan solid filtered, washed with water and dried, leaving the product as a brown solid (18.9 g., 75%) m.p. 100-110°. Recrystallization from ethanol-water raised the m.p. to 120-122° (Lit. (6) m.p. 123°); nmr δ 8.05 (m, H-9), 7.8 (m, H-6), 7.7 (d, $J_{1,2}$ 8 Hz, H-1), 7.36 (m, H-7,8), 7.32 (t, $J_{2,1}$ 8 Hz; $J_{2,3}$ 8 Hz, H-2), 6.82 (d, $J_{2,3}$ 8 Hz, H-3) and 3.94 (s, CH₃).

1-Nitro-4-methoxydibenzothiophene (Ib).

Nitric acid (1.6 ml., sp. gr. 1.50) was added with stirring to a solution of Ia (2.00 g., 0.00935 mole) in glacial acetic acid (35 ml.) at 15°. The mixture was kept at 20° for 20 minutes and the yellow product filtered (1.70 g., 70%) m.p. 157-158°. Crystallization from ethanol gave needles (1.55 g., 64%), m.p. 160-161° (Lit. (2) m.p. 161-162°). An analytical sample had m.p. 162-162.5°; nmr δ 8.3 (m, H-9), 7.94 (d, $J_{2,3}$ 8 Hz, H-2), 7.88 (m, H-6), 7.46 (m, H-7,8), 6.85 (d, $J_{3,2}$ 8 Hz, H-3) and 4.08 (s, CH₃).

Anal. Calcd. for C₁₃H₉NO₃S: C, 60.2; H, 3.5; S, 12.4. Found: C, 60.3; H, 3.6; S, 12.3.

1-Bromo-4-methoxydibenzothiophene (Ic).

Bromine (1.50 g., 0.51 ml., 0.00935 mole) in acetic acid (10 ml.) was added with stirring at room temperature to a solution of Ia (2.00 g., 0.00935 mole) in acetic acid (70 ml.) over 30

minutes. The solution was stirred for an additional 30 minutes and poured into water containing a small amount of sodium bisulfite. The product was collected as a tan solid (2.60 g., 95%), m.p. 99-102°. Recrystallization from ethanol gave needles (1.84 g., 67%), m.p. 111-112°. A further crop of needles was obtained from the mother liquor on standing (0.27 g., 7%), m.p. 110-112° (total yield 74%). An analytical sample had m.p. 112-112.5°.

Anal. Calcd. for C₁₃H₉BrOS: C, 53.3; H, 3.1; S, 10.9. Found: C, 53.2; H, 3.2; S, 10.6.

4-Methoxydibenzothiophene-1-carboxaldehyde (Id).

Butyllithium (2.40 ml., 0.00384 mole, 15% solution in hexane) was added to a solution of Ic (1.0 g., 0.00342 mole) in sodium dried ether under an atmosphere of dry nitrogen. The solution was stirred for 2 minutes and *N,N*-dimethylformamide (0.266 ml., 0.00342 mole) in ether (5 ml.) added and the mixture refluxed for 2 hours. The reaction mixture was poured over ice (100 g.) and ether added to dissolve the solid formed. The ether phase was separated and the aqueous phase extracted with ether (2 x 25 ml.). The combined ether extracts were dried and the solvent removed yielding the product as a pale yellow powder (0.73 g., 88%), m.p. 144-147°. An analytical sample from ethanol had m.p. 147°; nmr δ 10.36 (s, CHO), 9.12 (m, H-9), 7.84 (d, $J_{2,3}$ 8 Hz, H-2),

7.84 (m, H-6), 7.46 (m, H-7,8) and 6.86 (d, $J_{3,2}$ 8 Hz, H-3).

Anal. Calcd. for C₁₄H₁₀O₂S: C, 69.4; H, 4.2; S, 13.2. Found: C, 69.1; H, 4.4; S, 13.0.

REFERENCES

- (1) Contribution No 1723, supported by Public Health Service Research Grant GM-10366 to Indiana University.
- (2) H. Gilman and S. Avakian, *J. Am. Chem. Soc.*, **68**, 1514 (1946).
- (3) H. Gilman, A. L. Jacoby and J. Swislowky, *ibid.*, **61**, 954 (1939).
- (4) E. Campaigne, L. Hewitt and J. Ashby, *J. Heterocyclic Chem.*, **6**, 553 (1969).
- (5) E. Campaigne and J. Ashby, *ibid.*, **6**, 517 (1969).
- (6) H. Gilman and A. L. Jacoby, *J. Org. Chem.*, **3**, 108 (1938).

Received June 27, 1969

Bloomington, Indiana, 47401.