Isomeric Products in the Diacetylation of Dibenzothiophene

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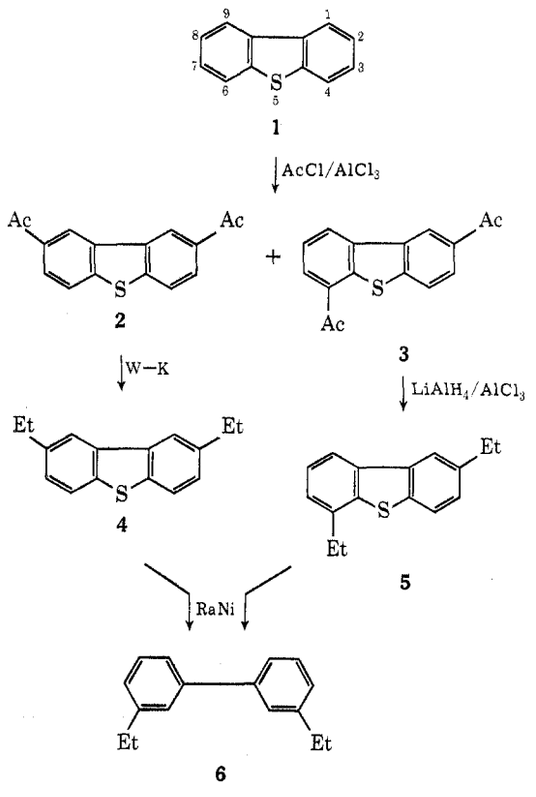
In the course of our work, it was necessary to prepare 2,8-diacetyldibenzothiophene (**2**), previously synthesized by Burger, *et al.*,[1] in a single-step Friedel–Crafts diacetylation reaction. These workers also prepared **2** in a stepwise fashion by employing two successive monoacetylation reactions, first preparing 2-acetyldibenzothiophene and subsequently converting the monoacetyl derivative into **2**. Later Burger and Bryant[2] investigated the mixture of ketones obtained in the monoacetylation of dibenzothiophene. In addition to the major product, 2-acetyldibenzothiophene, they were able to characterize a second monoacetylated isomer, 4-acetyldibenzothiophene. It was noted earlier by these workers that mixtures of ketones were also obtained in the diacetylation reaction. Considering the previous evidence, it was then realistic to anticipate the presence of the 2,6-disubstituted isomer in the diacetylation reaction.

Our original goal was to improve the synthesis of **2** in a single-step diacetylation by varying the reaction conditions. This was accomplished when methylene chloride was used as the reaction solvent and gave 47% of **2**. Continuing our investigation, we chose tetrachloroethane as the reaction solvent from which 11% of a pure diacetylated material could be isolated. Although this compound melted near the reported melting point of **2**, its nmr spectrum was considerably different from that of **2** and the mixture melting point with **2** was depressed. This paper is concerned with the structure proof of this new diacetyl dibenzothiophene, shown to be 2,6-diacetyldibenzothiophene (**3**) by chemical transformation and nmr spectroscopy.

The sequence of reactions used to elucidate the structure of **3** is shown in Scheme I. The course chosen was to convert **2** and **3** to the same biphenyl derivative. The initial attempt to convert both compounds to 3,3′-diacetylbiphenyl was only partially successful in that **2** was readily desulfurated but **3** was resistant to desulfurization. The next approach was to reduce **2** and **3** to 2,8-diethyldibenzothiophene (**4**) and 2,6-diethyldibenzothiophene (**5**), respectively. The Wolff–Kishner reduction of **2** gave **4**. Under identical conditions, **3** was not reduced to **5** but instead a yellow solid, mp > 300°, was obtained. The conversion of **3** to **5** was finally achieved by modifying the $LiAlH_4/AlCl_3$ reduction procedure of Nystron and Burger.[3] Compounds **4** and **5** were subsequently desulfurated with T-1 Raney nickel catalyst[4] to the known 3,3′-diethylbiphenyl (**6**).[5,6] The ir, uv, and nmr spectra of **6** obtained from both **4** and **5** were identical.

SCHEME I



The aromatic region of the nmr spectra of compounds **2** through **5** are shown in Figures 1 and 2. The two patterns of symmetrically substituted **2** and **4** and unsymmetrically substituted **3** and **5** are readily apparent. The former are assigned the 2,8 structure and the latter are assigned the 2,6 structure. These assignments are based on the detailed interpretation of the nmr spectra[7] and the chemical transformation outlined in Scheme I. In all compounds, the area ratios of aromatic to aliphatic protons, as well as the relative intensities of the separated aromatic peaks, agreed with theory.

The assignment of the 2,8 structure for the symmetrically substituted compounds is obvious. The assignment of the 2,6 structure to the unsymmetrical compounds is based on the observance of both an ABX and ABC pattern for the aromatic protons of **3** and **5** and the conversion to 3,3′-diethylbiphenyl. The 4,6-disubstituted isomer, which could also be converted to the 3,3′-diethylbiphenyl, would show *only* an ABC pattern in the nmr spectrum. The possibility that **3** and **5** are actually the 1,8-disubstituted dibenzothiophene, which would have a similar nmr spectrum, is eliminated by the chemical conversion of **5** into a 3,3′-disubstituted biphenyl.

The aliphatic region of the nmr spectra also re-

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(7) The detailed interpretation of the nmr spectra will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-72-3355. Remit $3.00 for photocopy or $2.00 for microfiche.

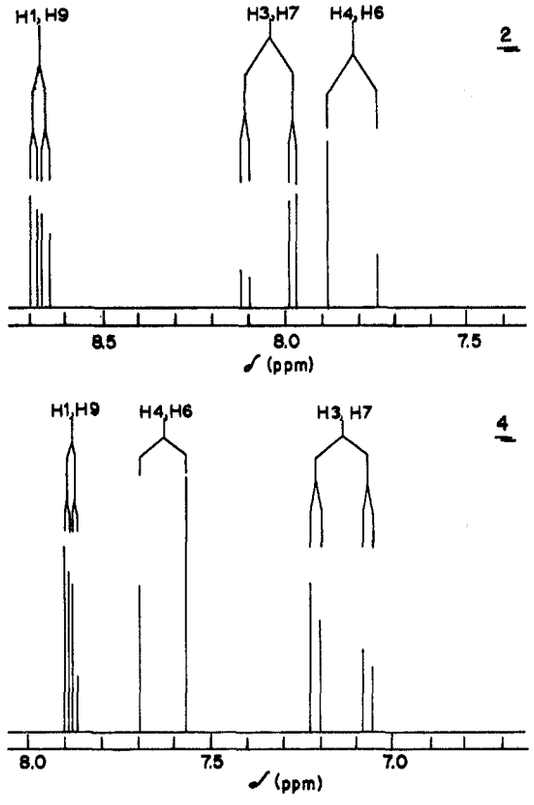

Figure 1.—Nmr spectra of aromatic region of **2** and **4**.

flects the symmetry of substitution. The unsymmetrical compounds **3** and **5** show an additional methyl and ethyl resonance shifted *ca.* 0.1 ppm downfield from the single resonances observed for **2** and **4**. Thus it is possible to determine the symmetry of substitution from examination of the high-field region of these nmr spectra. The ultimate structural assignment must be determined by the detailed analysis of the aromatic region of these spectra and appropriate chemical transformation.

The sulfones **7** and **8** were also prepared. A rigorous interpretation of their nmr spectra was of no additional value in establishing structure.

Experimental Section

All melting points were determined in open capillary tubes using a Thomas–Hoover apparatus and are uncorrected. All boiling points are uncorrected. The infrared spectra were recorded on a Perkin-Elmer 521 recording spectrophotometer. The ultraviolet spectra were recorded on a Perkin-Elmer 350 recording spectrophotometer. The nuclear magnetic resonance spectra were obtained from $CDCl_3$ solution unless otherwise noted at 60 MHz on a Varian A-60A spectrometer. Tetramethylsilane (TMS) was used as the internal standard and all signals are given in parts per million (δ) relative to TMS. Indices of refraction were determined on a Carl Zeiss Model A Abbe refractometer.

2,8-Diacetyldibenzothiophene (2).—A stirred mixture of 196 g (2.5 mol) of acetyl chloride, 280 g (2.1 mol) of $AlCl_3$ and 2 l. of CH_2Cl_2 was cooled in an ice bath while a solution of 184 g (1.0 mol) of dibenzothiophene (J. T. Baker) in 1 l. of CH_2Cl_2 was added dropwise over a period of 1 hr. The reaction mixture was stirred overnight at room temperature, refluxed for 1 hr, cooled, and then decomposed by pouring onto ice–concentrated HCl. The crude product was crystallized from butanone to yield 127 g (47%) of **2**: mp 204–205.5° (lit.[1] mp 208–209°); uv max ($CHCl_3$) 262 mμ (ϵ 67,600); ir (KBr) 1675 cm^{-1} (C=O); nmr.[7]

2,6-Diacetyldibenzothiophene (3).—The above reaction was repeated with $(CHCl_2)_2$ as solvent and the crude product was crystallized from $(CHCl_2)_2$ to give 30 g (11%) of **3**: mp 205–206°; uv max ($CHCl_3$) 257 mμ (ϵ 45,500); ir (KBr) 1675, 1665 cm^{-1} (C=O); nmr.[7]

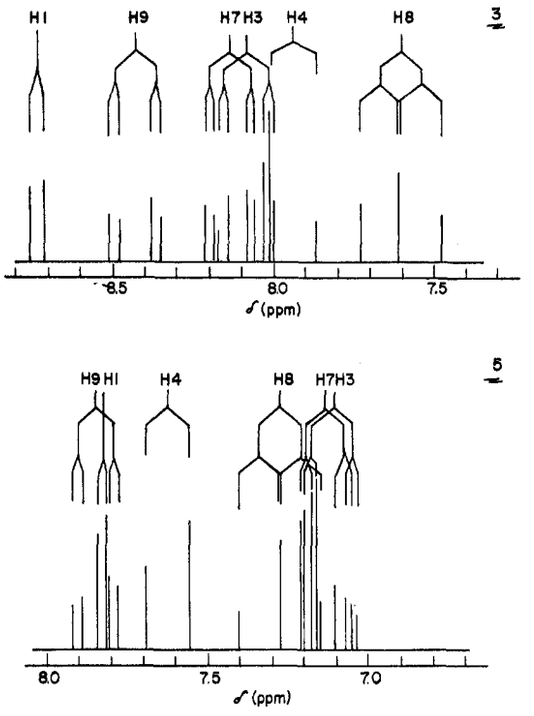

Figure 2.—Nmr spectra of aromatic region of **3** and **5**.

Anal. Calcd for $C_{16}H_{12}O_2$: C, 71.63; H, 4.51; S, 11.93. Found: C, 71.57; H, 4.44; S, 11.88.

The mixture melting point of **2** and **3** is 170–185°.

2,8-Diethyldibenzothiophene (4).—A mixture of 5.0 g of **2**, 25 ml of 85% H_2NNH_2, and 100 ml of diethylene glycol was stirred and heated at 110° for 1 hr in an open flask, followed by the addition of 18 g of KOH. After stirring at reflux for 18 hr, the mixture was poured into 1 l. of H_2O and then extracted with benzene. The benzene extracts were combined, washed with water and saturated NaCl solution, dried ($MgSO_4$), and evaporated *in vacuo* on a steam bath. The residue obtained was vacuum distilled. The yield of **4** was 1.8 g (40%): bp 193–195° (2.0 mm); uv max (95% EtOH) 238 mμ (ϵ 53,100); ir (neat) 2960, 2925, 2865 (aliphatic CH), 1550 cm^{-1} (C=C); nmr.[7]

Anal. Calcd for $C_{16}H_{16}S$: C, 79.94; H, 6.71; S, 13.34. Found: C, 79.86; H, 6.62; S, 13.12.

2,6-Diethyldibenzothiophene (5).—A solution of 6.7 g of **3** in 400 ml of $CHCl_3$ was added dropwise to a stirred mixture of 6.7 g of $LiAlH_4$, 49.5 g of $AlCl_3$, and 400 ml of anhydrous Et_2O. After stirring at reflux for 18 hr, the reaction mixture was treated with H_2O, followed by concentrated HCl. The organic layer was separated, washed with H_2O and saturated NaCl solution, dried ($MgSO_4$), and evaporated *in vacuo* on a steam bath. The residue obtained was vacuum distilled. The yield of **5** was 4.1 g (69%): bp 174° (0.8 mm); mp 35–39°;[8] uv max (95% EtOH) 233 mμ (ϵ 52,900); ir (neat) 2970, 2935, 2880 (aliphatic CH), 1610, 1578, 1558 cm^{-1} (C=C); nmr.[7]

Anal. Calcd for $C_{16}H_{16}S$: C, 79.94; H, 6.71; S, 13.34. Found: C, 79.99; H, 6.65; S, 13.28.

Desulfurization of 4.—A mixture of 5.0 g of **4**, 100 g of T-1 Raney nickel catalyst,[8] and 100 ml of ethyl acetate was refluxed for 24 hr. After filtration to remove the catalyst, the filtrate was evaporated *in vacuo* on a steam bath. The residue obtained was vacuum distilled to give 2.4 g (55%) of 3,3′-diethylbiphenyl (**6**): bp 131–132° (0.5 mm); n^{20}D 1.5773; uv max (95% EtOH) 251 mμ (ϵ 16,100); ir (CS_2) 2960, 2925, 2870 (aliphatic CH), 885, 790, 705 cm^{-1} (aromatic meta substitution) [lit.[5,6] bp 154–155° (9–10 mm); n^{25}D 1.5768; uv max (95% EtOH) 251 mμ (ϵ 16,100); ir (CS_2) 2960, 2925, 2870, 890, 795, 710 cm^{-1}]; nmr ($CDCl_3$) δ 7.28 (m, 8, Ar), 2.68 (q, 4, J = 8 Hz, CH_2), 1.23 (t, 6, J = 8 Hz, CH_3).

(8) Corrected melting point determined using a Perkin-Elmer Differential Scanning Calorimeter Model DSC-1B.

Desulfurization of 5.—By the same procedure described for desulfurization of **4**, 3.0 g of **5** was desulfurated to yield 1.3 g (48%) of 3,3′-diethylbiphenyl (**6**): bp 135–137° (1.3 mm); n^{20}D 1.5762; uv max (95% EtOH) 251 mμ (ε 16,745). The ir and nmr were identical in all respects to the ir and nmr of **6** obtained in the desulfurization of **4**.

2,6-Diacetyldibenzothiophene 5,5-Dioxide (7).—A mixture of 3.0 g of **3**, 10 ml of 30% H_2O_2, and 50 ml of HOAc was refluxed for 1 hr and cooled to room temperature, and the product was filtered. Recrystallization from acetonitrile gave 3.1 g (92%) of **7**: mp 303° dec; uv max (DMF) 333 mμ (ε 844); ir (KBr) 1695, 1681 (C=O), 1310, 1162 cm^{-1} (sulfone); nmr (CF_3COOH/$CDCl_3$) δ 2.83 (s, 3, CH_3), 2.87 (s, 3, CH_3).

Anal. Calcd for $C_{16}H_{12}O_4S$: C, 63.99; H, 4.03; S, 10.67. Found: C, 64.19; H, 3.95; S, 10.72.

2,8-Diacetyldibenzothiophene 5,5-Dioxide (8).—By the same procedure used in the oxidation of **3**, 6.0 g of **2** was oxidized, yielding 5.7 g (84%) of **8** after crystallization from acetonitrile: mp 272–277°; uv max (DMF) 377 mμ (ε 1430); ir (KBr) 1690 (C=O), 1312, 1169 cm^{-1} (sulfone); nmr (CF_3CO_2H/$CDCl_3$) δ 2.87 (s, 6, CH_3).

Anal. Calcd for $C_{16}H_{12}O_4S$: C, 63.99; H, 4.03; S, 10.67. Found: C, 64.24; H, 4.05; S, 10.64.

Registry No.—**1**, 132-65-0; **2**, 35105-75-0; **3**, 35105-76-1; **4**, 35105-77-2; **5**, 35105-78-3; **6**, 13049-38-2; **7**, 35105-80-7; **8**, 35105-81-8.

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Synthesis of 1-(*p*-Iodobenzenesulfonyl)-3,5-di-*n*-propyl Isocyanurate

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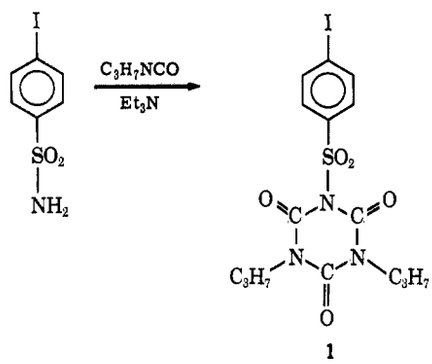
The base-catalyzed reaction of arylsulfonamides with alkyl isocyanates is a valuable synthetic method for the preparation of arylsulfonylureas. During studies aimed at the synthesis of 1-(*p*-iodobenzenesulfonyl)-3-*n*-propylurea-^{125}I, we found that a base-insoluble product was formed when the reaction was carried out with an excess of *n*-propyl isocyanate.[1] This base-insoluble product was identified as 1-(*p*-iodobenzenesulfonyl)-3,5-di-*n*-propyl isocyanurate (**1**).

Tri-N-substituted, di-N-substituted, and mono-N-substituted isocyanurates have been synthesized[2–4] and studied, but no 1-arylsulfonyl-3,5-dialkyl isocyanurates have been reported. The formation of **1**, therefore, represents not only a novel reaction but also a new chemical entity. The reaction most likely involves the base-catalyzed condensation of *p*-iodobenzenesulfonamide with a threefold excess of *n*-propyl isocyanate with the subsequent elimination of *n*-propylamine. The transient existence of a series of anionic intermediates can be justified on the basis of a delocalization of the developing negative charge as proposed by Ulrich[5] for analogous reactions.



1

No mass ion occurred in the high-resolution mass spectrum of this compound under normal conditions; however, a small peak did occur at *m/e* 479 when the instrument was overloaded with sample. The prominent high mass ion in the mass spectrum occurred at *m/e* 415. This differs by sulfur dioxide from the proposed structure. The loss of sulfur dioxide upon electron impact has previously been reported in sulfonylureas[6] and in *O*-alkyl-*N*-arylsulfonyl carbamates.[7] The prominent ions in the mass spectrum of **1** (Table I)

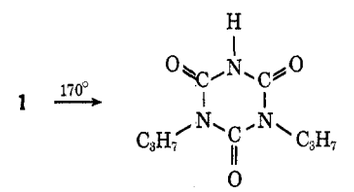
TABLE I

PROMINENT IONS IN THE MASS SPECTRUM OF 1-(*p*-IODOBENZENESULFONYL)-3,5-DI-*n*-PROPYL ISOCYANURATE

m/e	Ion	Per cent total ionization
415	$C_{15}H_{18}IN_3O_3^+$	12.50
374	$C_{12}H_{13}IN_3O_3^+$	8.75
332	$C_9H_7IN_3O_3^+$	2.70
288	$C_8H_5IN_2O_2^+$	13.25
267	$C_6H_4IO_2S^+$	22.50
245	$C_7H_4INO^+$	26.25
203	$C_6H_4I^+$	50.50
56	$C_2H_2NO^+$	51.25
43	$C_3H_7^+$	61.25

can be accounted for by fragmentation of the molecule in a manner analogous to that reported for tolbutamide[6] and for ethyl *N*-methyl-*N*-(*p*-toluenesulfonyl)carbamate.[7]

Heating **1** at 170° in DMF–H_2O afforded 1,3-di-*n*-propyl isocyanurate (**2**), thus providing chemical evidence in support of the proposed structure of **1**.



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