

Chemistry Laboratories, Indiana University

Benzo[b]thiophene Derivatives. VI. A Symmetrical Fused Heptacyclic System Containing Oxygen, Sulfur, Aromatic and Carbocyclic Rings (I)

E. Campaigne and E. S. Neiss (2)

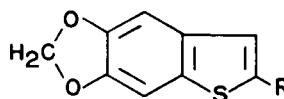
In a continuation of our work (3-8) in the synthesis and reactions of alkoxy substituted benzo[b]thiophene derivatives, it was desirable to prepare 2-chloromethyl-5,6-methylenedioxybenzo[b]thiophene (Id). 5,6-Methylenedioxybenzo[b]thiophene-2-carboxylic acid (Ib) was reduced in good yield by lithium aluminum hydride to the corresponding alcohol (Ic). It was anticipated that Ic could be converted to the chloromethyl compound Id and then to the acetonitrile derivative, Ie.

When Ic was treated with thionyl chloride in dry benzene, tan crystals were obtained. Upon attempted recrystallization from ethanol a portion of the crystal mass dissolved in a large amount of boiling ethanol and crystallized as long white needles, which proved to be the ethyl ether If. Apparently Id contains an extremely reactive methylene derivative, since If could only be obtained by reaction with the recrystallization solvent. That portion which did not dissolve in ethanol was also insoluble in common organic solvents, but could be purified by repeated solution in dimethylformamide and precipitation by the addition of water. In this manner a white solid was obtained which decomposed without melting up to 400°, and had a molecular weight of 374±4. Analyses were in agreement with the formula C₂₀H₁₂O₄S₂. The ultraviolet spectrum of this compound has maxima which were both bathochromic and hyperchromic with respect to compound Ia (Table I). Additionally, a simple NMR spectrum of two singlets and an aromatic multiplet, in a ratio of 1:1:1, support the structural assignment 6,12-dihydrobenzo[1,2-b:4,5-b']bis-5,6-methylenedioxybenzo[b]thiophene (II) for this compound.

It is postulated that the stabilization of the carbonium ion generated from Id is augmented by resonance involving the participation of the oxygen atom at the 6-position, which has been shown to direct electrophilic substitution to the 2-position in Ia (6,7). 2-Chloromethylbenzo[b]thiophene has been prepared in good yield from 2-hydroxymethylbenzo[b]thiophene (9) without apparent side-products. It is likely that II was produced by the attack of Id on the relatively nucleophilic 3-position of Ic to yield a product (III) which is geometrically favored to attack the 3-position of the newly attached benzo[b]thiophene moiety. If this were the case, II should also form by simply heating Ic in a polar solvent with a catalytic amount of mineral acid. When Ic was allowed to reflux in

dimethoxyethane in the presence of a small amount of polyphosphoric acid, a 75% yield of II was obtained.

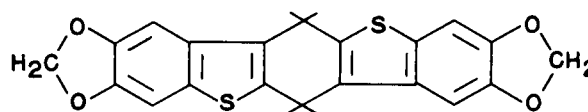
The only compound similar to II previously reported was the anthraquinone-type vat dye 3-chloro-1-methyl-6,12-dioxobenzo[1,2-b:4,5-b']bisbenzo[b]thiophene (10). This compound was prepared by conventional Friedel-Crafts reaction. It was of



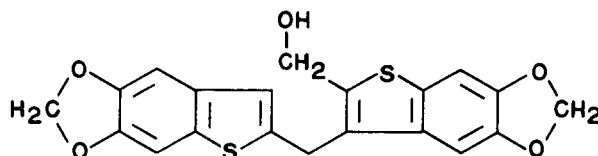
I a-f

I-a. R = H

I-b. R = COOH

I-c. R = CH₂OHI-d. R = CH₂ClI-e. R = CH₂CNI-f. R = CH₂OC₂H₅

II



III

TABLE I

Spectral Properties of 5,6-Methylenedioxybenzo[b]thiophene Derivatives (a)

Structure	Ultraviolet Spectra (b)		NMR Spectra (c)		
	λ max ($m\mu$)	ϵ	τ value	Assignment	Proton ratio
Ia	237	(24,000)	2.50-2.84 (m)	Arom. -C-H	2
	264	(8,900)	3.96	-OCH ₂ O-	1
	273	(9,100)			
	303	(3,400)			
	307	(3,750)			
	317	(3,900)			
Ic	241	(26,600)	2.75-2.95 (t)	Arom. -C-H	3
	268	(10,600)	4.02	-OCH ₂ O-	2
	277	(15,500)	5.19	-CH ₂ O-	2
	305	(4,620)	6.62	-O-H	1
	311	(5,200)			
	317	(5,400)			
If	241	(27,000)	2.93-3.15 (t)	Arom. -C-H	3
	267	(11,100)	4.06	-OCH ₂ O-	2
	277	(12,300)	5.42	-CH ₂ O-	2
	304	(4,820)	6.51 (q)	-CH ₂ -CH ₃	2
	310	(5,300)	8.83 (t)	-CH ₂ -CH ₃	3
	317	(5,780)			
II	267	(21,100)	2.70-3.10 (m)	Arom. -C-H	1
	280	(19,800)	4.00	-OCH ₂ O-	1
	286	(20,800)	7.13	-CH ₂ -	1
	310	(9,125)			
	315	(9,125)			
	320	(9,870)			

(a) Ultraviolet spectra were determined with a Cary 14 Recording Spectrophotometer in 95% ethanol, except compound II which was in dimethylformamide. The nuclear magnetic resonance spectra were obtained with a Varian Associates Model A-60 High Resolution NMR Spectrometer; all NMR spectra were taken in deuterioacetone. (b) The absorption maximum of compound II below 267 $m\mu$ was not recorded as dimethylformamide absorbs at 260 $m\mu$. (c) Abbreviations: m, multiplet; t, triplet; q, quadruplet.

interest to determine if compound II could be prepared directly from Ia through the Blanc chloromethylation reaction. This procedure produced a white solid which did not contain chlorine, melted at 184-185° and was not compound II. Van Zyl (11) has reported that the condensation of benzo[b]thiophene with formaldehyde results in a mixture of di-(3-benzo[b]thienyl)methane, 2,3-di-(3-benzo[b]thienyl)-benzo[b]thiophene and higher molecular weight compounds of unknown structure. On this basis, the present product was initially thought to be di-(5,6-methylenedioxy-2-benzo[b]thienyl)methane, but this is not supported by analyses and molecular weight determinations which are more compatible with the

formulae C₂₂H₁₄S₂O₈ or C₂₃H₂₀S₂O₈. The highly insoluble nature of the product prevented the study of its NMR spectra.

The recent report (12) that 1-methylindole-2-carbonyl chloride dimerized in dichloroethane in the presence of aluminum chloride to give a fair yield of 5,11-dimethylindolo[3,2-b]carbazole-6,12-(5H,11H)-dione prompted us to attempt a similar reaction on the acid chloride of Ib. Only intractable tars were obtained in this reaction. An attempt to aromatize II with chloranil in a similar fashion failed. Compound II gives a blue color in both sulfuric and tri-fluoroacetic acids.

EXPERIMENTAL

2-Hydroxymethyl-5,6-methylenedioxybenzo[b]thiophene (Ic).

A solution of 23.5 g. (0.107 mole) of 5,6-methylenedioxybenzo[b]thiophene-2-carboxylic acid (6) in 200 ml. of dry tetrahydrofuran was added dropwise with stirring to a slurry of 6 g. (0.158 mole) of lithium hydride in 140 ml. of dry tetrahydrofuran. The reaction mixture was allowed to reflux during the addition, and was heated to reflux for an hour after completion of this addition. After standing at room temperature overnight, the excess hydride was decomposed by the addition of ethyl acetate followed by the addition of 110 ml. of 5% hydrochloric acid solution. The reaction mixture was filtered through glass wool and the residue was washed with diethyl ether. The solvent from the combined ether solutions was removed under partial vacuum and the resulting grey solid was recrystallized from ethanol to yield 16 g. (72%) of small shiny white platelets which melted at 153-154°.

Anal. Calcd. for $C_{10}H_8O_3S$: C, 57.67; H, 3.87; S, 15.40. Found: C, 57.85; H, 3.78; S, 15.09.

Reaction of Ic with thionyl chloride. (If and II).

Five grams (0.024 mole) of Ic was suspended in 25 ml. of dry benzene and treated with 3.57 g. (0.03 mole) of thionyl chloride. The reaction mixture immediately turned dark and hydrogen chloride was evolved. After the initial reaction, the solution was allowed to reflux for 4 hours after which the solvent was removed under partial vacuum. Dry benzene was added and distilled several times until the odor of thionyl chloride was gone. Then the dark residue was treated with 50 ml. of dry benzene and stored overnight in the refrigerator. The tan needles that were obtained had a metallic grey appearance after drying on a watch glass. Upon recrystallization from 100 ml. of boiling ethanol only part of this crystal mass went into solution. Long straw-colored needles which crystallized from ethanol were recrystallized as white needles (2.4 g., 43%) which melted at 67-68°. Analysis and spectral properties (Table I) support the assignment 2-ethoxymethyl-5,6-methylenedioxybenzo[b]thiophene (If).

Anal. Calcd. for $C_{12}H_{12}O_3S$: C, 60.99; H, 5.12; S, 13.57. Found: C, 61.13; H, 5.06; S, 13.82.

The tan precipitate which did not dissolve in hot ethanol weighed 0.6 g. and was insoluble in all common organic solvents except dimethylformamide. After several precipitations of this compound (Norite) from dimethylformamide by the addition of water, a white solid was obtained which charred but did not melt up to 400°. Two determinations of the molecular weight of this solid by the Rast method had good precision and indicated a molecular weight of 374 ± 4 (Calcd. for $C_{20}H_{12}O_4S_2$, 380.42). Analysis and spectral properties (Table I) of this compound support the assignment of structure II.

Anal. Calcd. for $C_{20}H_{12}O_4S_2$: C, 63.15; H, 3.18; O, 16.84; S, 16.83. Found: C, 63.09; H, 3.29; O, 17.05; S, 16.38.

6,12-Dihydrobenzo[1,2-b:4,5-b']bis-5,6-methylenedioxybenzo[b]thiophene (II).

One-half gram (0.0024 mole) of Ic was allowed to reflux for four hours in 20 ml. of dimethoxyethane containing 50 mg. of polyphosphoric acid. The hot reaction mixture was decanted from a small precipitate of tarry material and the solvent was removed. The brown residue was dissolved in dimethylformamide, treated with Norite, filtered and precipitated by the addition of water. After this process was repeated three times a white solid (345 mg., 75%) was obtained which had identical melting and spectral properties to that of II prepared above.

Attempted chloromethylation of Ia.

Two and two-tenths grams (0.0124 mole) of Ia (6), 1.2 g. (0.015 mole) of 37% formaldehyde and 1.5 g. of 36% hydrochloric acid were suspended in 15 ml. of glacial acetic acid and stirred vigorously while hydrogen chloride gas was bubbled into the reaction mixture. During this addition, the mixture warmed to 55° and became a pale blue suspension. After treatment with the hydrogen chloride gas for one hour, the mixture was poured into 200 ml. of water and a white precipitate separated. After three precipitations from dimethylformamide with water and two recrystallizations from acetone 1.4 g. of a white solid was obtained which melted at 184-185° with decomposition. A precipitate was not obtained with this material and alcoholic silver nitrate either before or after fusion with sodium.

Anal. Calcd. for $C_{22}H_{14}O_6S_2$: C, 56.15; H, 3.00; S, 13.62 (m.w. 470.46). Calcd. for $C_{23}H_{16}O_6S_2$: C, 56.57; H, 4.12; S, 13.13 (m.w. 488.5). Found: C, 56.40; H, 3.11; S, 13.73 (m.w. 429±30, Rast Method).

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Bloomington, Indiana 47405