

Chemistry Laboratories, Indiana University

Benzo[b]thiophene Derivatives. VII. An Abnormal Substitution

Product From 3-Chloromethylbenzo[b]thiophene (1)

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

The alkylation of cyanide ion with 3-chloromethylbenzo[b]thiophene gave a higher yield of benzo[b]thiophene-3-acetonitrile in dimethyl sulfoxide than in alcohol, and in addition 2-cyano-3-methylbenzo[b]thiophene was obtained as a by-product in this solvent. The abnormal product was prepared by an alternative, unequivocal synthesis. The isomers were hydrolyzed to their respective acids, which were reduced to 3-(β -hydroxyethyl)benzo[b]thiophene and 2-hydroxymethyl-3-methylbenzo[b]thiophene. The ultraviolet and nuclear magnetic resonance spectra of these compounds are reported.

In connection with another problem it was necessary to prepare 3- β -hydroxyethylbenzo[b]thiophene (VI). Cagniant first prepared this alcohol by the reaction of 3-benzo[b]thienylmagnesium bromide with ethylene oxide (3). One of the procedures investigated in the present work was the reduction of benzo[b]thiophene-3-acetic acid (Va). This compound was derived from the acid hydrolysis of benzo[b]thiophene-3-acetonitrile (III) which in turn was prepared from sodium cyanide and 3-chloromethylbenzo[b]thiophene (II) in dimethyl sulfoxide.

When Va was treated with lithium aluminum hydride and the product isolated by distillation, compound VI was obtained as expected. Toward the end of the distillation a higher boiling material distilled and solidified in the condenser. Analyses of this white solid indicated that it was isomeric with VI. The melting point and spectral characteristics of this isomer identified it as 2-hydroxymethyl-3-methylbenzo[b]thiophene (X) (4, 5). The isomer was found to be identical to an authentic sample of X prepared by the lithium aluminum hydride reduction of 3-methylbenzo[b]thiophene-2-carboxylic acid (VIIa), and melted in agreement with the value reported in the literature (4, 5).

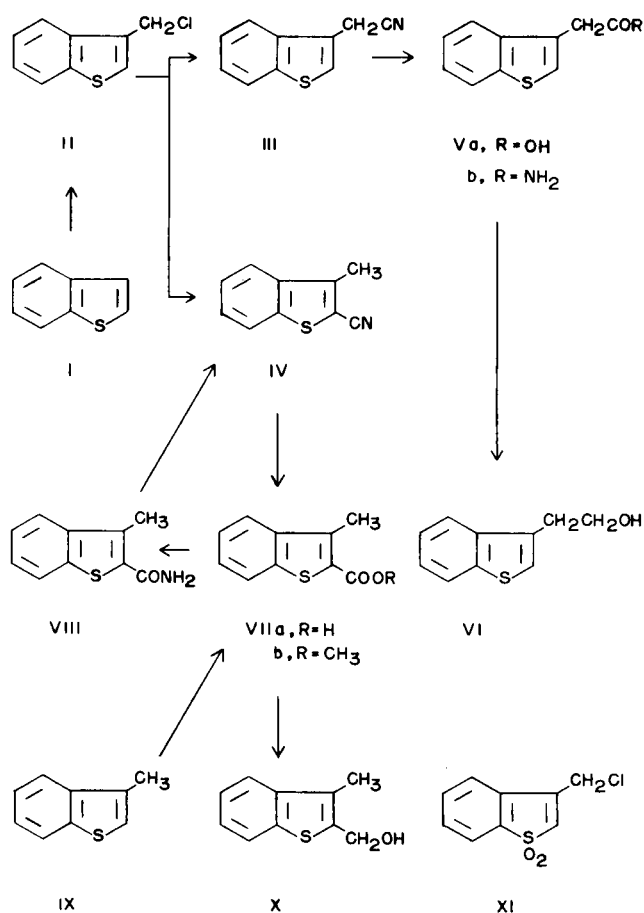
Since the acid, Va, which was reduced had not been purified and it was unlikely that rearrangement of Va could occur during reduction, the presence of VIIa as an impurity seemed probable. When the reduction was repeated on a sample of Va, purified by repeated recrystallization and melting in accordance with the reported value (6, 7), chromatography of the reaction mixture indicated the presence of only the normal product, VI. The reduction of pure VIIa likewise yielded only the expected product, X.

The most likely point of origin of the 2-substituted compounds seemed to be the reaction of II with sodium cyanide. Bordwell (8) has demonstrated that a variety of nucleophiles attack the 2-position of 3-chloromethylbenzo[b]thiophene 1,1-dioxide (XI). Compound XI, however, contains an olefinic C₂-C₃ double bond (9) and the strongly electron attracting

sulfonyl group in the γ -position of the allylic system reduces the electron density at this bond and favors reaction of nucleophilic reagents at the 2-position. While abnormal products have been observed from the reaction of Grignard reagents derived from II (4), nucleophilic reactions of II have not been reported to give this result. Abnormal products have been obtained when furfuryl trimethylammonium iodide (10), α - and β -furfuryl chloride (11, 12) and 1-methylgramine methiodide (13) are treated with sodium cyanide. In the thiophene series, Lecocq (14) has shown that warming cuprous cyanide or sodium cyanide with 5-methyl-2-thenyl bromide resulted in a quantitative rearrangement with the formation of 2,5-dimethyl-3-bromothiophene. Therefore, the reaction of sodium cyanide with II was investigated.

A slight excess of sodium cyanide dissolved in dimethyl sulfoxide was treated with chromatographically pure II without external heating. The ratio of the areas of the two peaks observed when a sample of the reaction mixture was injected into the gas chromatograph indicated 98% of the major component and about 2% of the minor component. The qualitative nature of the peaks was established by the augmentation of the respective signals upon the serial addition of authentic pure samples of III and 2-cyano-3-methylbenzo[b]thiophene (IV). In this manner the major component was shown to be III and the minor component to be IV. Collection of the minor component obtained from serial injections into the chromatograph provided sufficient material to demonstrate that its infrared absorption spectrum was identical to that of authentic IV. Comparison of the infrared spectra of III and its isomer IV revealed a shift of the nitrile absorption band of 39 cm⁻¹ toward lower wave numbers in IV, indicating conjugation of the cyano group to the aromatic nucleus in the latter compound.

The ultraviolet spectrum (Table I) of the normal product, III, and that of Va are, as expected, very similar to that of compound IX. Likewise, the absorptions of X are quite similar to those of 2,3-



dimethylbenzo[b]thiophene (15). The abnormal product IV, however, has a spectrum exhibiting an additional absorption with bathochromic shifting attributed to the conjugation of the nitrile group with the aromatic nucleus. The methyl ester, VIIb, has ultraviolet absorption much like that of IV with greater shift to the red due to carbonyl conjugation. This similarity further supports the structure of the abnormal product. Finally, the n.m.r. spectral properties (Table I) are compatible with the assigned structures. It is noted that the 3-methyl protons in IX are split into a doublet by the hydrogen atom at the 2-position. When the 2-position is substituted (as in X, IV and VIIb) the splitting is not observed. A similar splitting of the methylene group protons in III is observed and this effect together with mutual methylene group splitting in VI produces a complex multiplet. The absence of splitting of the 3-methyl group protons in IV provides additional support for the assigned structure.

Compound III distilled at 148–150°/2 mm. and compound IV at 150–152°/2 mm. Distillation and attempted fractional distillation of the product obtained from reaction of II with sodium cyanide failed to resolve the isomers. The major product was obtained chromatographically pure after two recrystallizations.

Compound IV was prepared from the dehydration

of 3-methylbenzo[b]thiophene-2-carboxamide (VIII) whose structure has been established unequivocally (16). The acid, VIIa, was the sole product isolated when IV was hydrolyzed with mineral acid. This compound was further characterized as its methyl ester, VIIb.

The alkylation of cyanide by II has been reported by several workers (4,7,17) who used aqueous alcohol for the reaction solvent. There was no report of abnormal substitution products in these reactions. When a 50% aqueous ethanol solution was used as solvent in this reaction, the yield of III was lower, in spite of more vigorous conditions, but abnormal product was not indicated by gas chromatography. The sodium salt of 2-mercaptobenzothiazole reacted smoothly with II to yield the corresponding sulfide.

The reaction of alkyl halides with metallic cyanides in dimethyl sulfoxide has been reported to result in greater yields of product under shorter and milder reaction conditions (18,19). It seems likely that the solvolysis of II is greatly enhanced in this highly polar solvent and that the small amount of abnormal substitution product is a result of the delocalization of the positive charge of the benzylic methylene group through resonance with the sulfur atom. This would tend to contribute to the stability of an electrophilic center at the 2-position. A similar argument has been advanced for the abnormal product obtained in the cyanide alkylation by the analogous structure 1-methylgramine methiodide (13).

EXPERIMENTAL

The melting points reported were determined in a Mel-Temp heated block and are corrected. The infrared spectra were determined in pressed potassium bromide disks with a Perkin Elmer Model 137-B Infracord Spectrophotometer. Gas chromatography was performed with an F and M Scientific Corporation Model 500 Gas Chromatograph using a 6 foot Silicone Oil 550 on Haloport F column and programmed at a rate of 4° per minute from 180–220° with a helium flow rate of 68 ml. min. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Indiana.

3-Chloromethylbenzo[b]thiophene (II).

The method of Blicke and Sheets (7) gave an 80.6% yield of product on a one mole scale when treatment with dry hydrogen chloride gas was extended to a six hour period. The clear, lachrymatory liquid distilled at 133–136°/2 mm. and melted at 39–40° after recrystallization from petroleum ether (30–60°). This compound is reported to melt at 42° (20). The recrystallization product provided a single peak upon chromatography.

2-(3-Benzo[b]thenyl)mercaptobenzothiazole.

Two grams (0.11 mole) of II, 1.85 g. (0.11 mole) of 2-mercaptobenzothiazole and 1 g. of sodium bicarbonate were heated for one hour on the steam bath, cooled and treated with excess 20% phosphoric acid. The yellow oil was separated and slowly solidified in the refrigerator. After recrystallization from benzene, 2.8 g. (82%) of white needles were obtained which melted at 82–83°.

Anal. Calcd. for $\text{C}_{18}\text{H}_{11}\text{NS}_3$: C, 61.30; H, 3.54; S, 30.69. Found: C, 61.25; H, 3.75; S, 30.51.

Alkylation of Sodium Cyanide with II.

(a) In Dimethyl sulfoxide. Sodium cyanide (73.5 g., 1.5 moles) was added with stirring to 400 ml. of dimethyl sulfoxide in a one liter round-bottomed flask and heated to 60° with stirring to effect solution. After the solution had cooled to 30°, 250 g. (1.365 moles) of redistilled, chromatographically pure II was added dropwise with vigorous stirring and cooling as necessary to maintain a reaction temperature of 40–50°.

TABLE I
Spectral Properties of Benzo[b]thiophene Derivatives

Compound	Ultraviolet Spectrum (a)		N. M. R. Spectrum (b)		
	λ max ($m\mu$)	ϵ	Proton Ratio	τ - value	Assignment
IX	231	4.53	3	7.66 (d)	-CH ₃
	262	3.64			
	267 (sh.) (c)	3.62	5	2.18-3.06 (m)	Aromatic hydrogen
	290	3.42			
	299	3.50			
III	229.5	4.21	3	6.22 (d)	-CH ₂ -
	259	3.38			
	265 (sh.)	3.32	5	2.09-2.83 (m)	Aromatic hydrogen
	290	2.84			
	298	3.05			
VI	231	4.34	5	6.17-7.32 (m)	-CH ₂ -CH ₂ -O-H
	262	3.43			
	266 (sh.)	3.42	5	2.18-3.12 (m)	Aromatic hydrogen
	291.5	3.11			
	299.5	3.17			
Va	229	4.47	2	6.20 (d)	-CH ₂ -
	262	3.72			
	267 (sh.)	3.71	5	2.13-2.90 (m)	Aromatic hydrogen
	290	3.40			
	299	3.41			
1,2-dimethylbenzo- [b]thiophene (d)	232	4.47	3	7.67 (s)	3-CH ₃
	267	3.88	3	7.87 (s)	2-CH ₃
	290.5	3.43	4	2.38-2.97 (m)	Aromatic hydrogen
	300	3.33			
X (e)	233.5	4.38	3	7.75 (s)	-CH ₃
	266	3.64	1	7.46 (s)	-O-H
	292	3.16	2	5.22 (s)	-CH ₂ -O
	301	3.12	4	2.20-2.86 (m)	Aromatic hydrogen
IV	232.5	4.02	3	7.52 (s)	-CH ₃
	242	3.98			
	274.5	3.88	4	2.19-2.71 (m)	Aromatic hydrogen
	283.5	3.97			
	308	3.23			
	319	3.21			
VIIb	235	4.06	3	7.28 (s)	-CH ₃
	246	4.11	3	6.12 (s)	-OCH ₃
	281	3.97	4	2.15-2.81 (m)	Aromatic hydrogen
	290.5	4.03			
	315	3.29			
	326 (sh.)	3.25			

(a) The ultraviolet spectra were determined in 95% ethanol with a Bausch and Lomb Spectronic 505 Recording Spectrophotometer. (b) The nuclear magnetic resonance (N. M. R.) spectral data were determined in deuteriochloroform with a Varian Associates Model A-60 High Resolution N. M. R. spectrometer operating at 60 megacycles per sec. Chemical shifts are recorded on the frequency independent τ scale relative to an internal tetramethylsilane reference. The following abbreviations have been used to indicate the multiplicity of the signals: s = singlet, d = doublet, m = complex multiplet. (c) sh. refers to a shoulder. (d) The ultraviolet spectra of 1,2-dimethylbenzo[b]thiophene was reported by D. Cagniant, P. Faller and P. Cagniant, *Bull. soc. Chim.*, 2410 (1961) and the N. M. R. spectrum (carbon tetrachloride) by F. G. Bordwell and T. W. Cutshall, *J. Org. Chem.*, 29, 2020 (1964). These values are included for comparison with compounds X, IV and VIIb. (e) F. G. Bordwell (*ibid*) has reported the N. M. R. spectrum of this compound in carbon tetrachloride: 2.38-2.98 (m) for aromatic hydrogen, 5.40 (s) for the methylene group, 6.83 (s) for the hydroxylic hydrogen, and 7.83 (s) for the methyl group.

The reaction mixture turned red upon initiation of the addition and became progressively darker throughout the addition of II. After 90 minutes, the addition was complete and the dark red solution was stirred for three hours at room temperature and let stand overnight.

A sample of the reaction mixture was injected into the gas chromatograph. In addition to air and solvent peaks, two other peaks were present. The ratio of the areas of these peaks indicated that the major peak represented 98% of the sample and the minor peak about 2%. The qualitative nature of the peaks was determined by the augmentation of the respective signals upon addition to samples of the reaction mixture of highly purified 3-cyanomethylbenzo[b]thiophene (III) and authentic 2-cyano-3-methylbenzo[b]thiophene (IV). In this manner, the major product was shown to be III and the minor, abnormal product to be IV.

The reaction mixture was poured into 2.5 l. of cold water and a brown precipitate separated. The aqueous phase was decanted and extracted with three 250 ml. portions of ether and the brown precipitate was dissolved in an additional liter of ether. The combined ether solutions were washed with salt water and dried with anhydrous sodium sulfate. Chromatography of the residue after removal of most of the solvent indicated the same isomer distribution. The minor component (IV) had a retention time of 12 minutes and was well resolved from III which had a retention time of 16.2 minutes. Repeated injections of 10 microliter samples of the reaction mixture were used to collect a sufficient amount of the minor peak component at the exit valve of the chromatograph for the determination of its infrared spectra. This spectra, though weak, showed a nitrile peak at 4.53 μ and was identical in each absorption to that of authentic alternately prepared IV. After complete removal of the solvent, the residual tan solid was distilled with a long Vigreux column. A clear, colorless distillate weighing 205 g. (86.5% yield) was collected at 150–152°/2 mm. The product crystallized in the receiving vessel as a white solid. Several attempts to separate the minor, abnormal product by fractional distillation failed. The product was recrystallized from benzene and petroleum ether (30–60°) as white crystals which melted at 65–66°. A further recrystallization gave III melting at 66.5–67°. Compound III is reported to melt at 66–67° (7). Evaporation of the mother liquors gave a material which exhibited a strong nitrile peak at 4.45 μ (aliphatic nitrile) and a very weak absorption at 4.53 μ (aryl nitrile). Attempts to resolve this mixture of isomers failed. Compound III, shown to be pure by chromatography, had a strong infrared nitrile absorption at 4.45 μ .

Anal. Calcd. for $C_{10}H_7NS$: S, 18.50. Found: S, 18.78.

(b) In dilute alcohol. The procedure of Avakian, Moss and Martin (17) was used without modification. Chromatography of the ether extract of the reaction mixture indicated the presence of III and no signal for IV. Upon distillation of the crude product, a 47% yield of III was obtained which had identical melting and spectral properties to that of III prepared in dimethyl sulfoxide.

Phenylthiopropone.

Thiophenol (1.0 mole) was treated with chloroacetone (according to the procedure of Werner (21) to provide a 71% yield of the β -keto sulfide which distilled at 94–95°/0.5 mm. The clear distillate solidified to a white solid upon cooling and was recrystallized from a petroleum ether (30–60°) chloroform mixture as white needles which melted at 33–34°. This compound is reported to melt at 34–35° (21).

Anal. Calcd. for C_9H_9OS : C, 65.02; H, 6.06. Found: C, 64.98; H, 6.08.

The semicarbazone derivative was prepared by the usual procedure (23) as white needles which melted at 151–152°.

Anal. Calcd. for $C_{10}H_{13}N_3OS$: C, 53.78; H, 5.87; S, 14.36. Found: C, 53.89; H, 6.04; S, 14.55.

3-Methylbenzo[b]thiophene (IX).

It was found that the method of Werner (21) was inconvenient for large scale preparation of this compound, as a violently exothermic reaction took place at 170°. In a modification of Werner's procedure, 100 g. (0.6 mole) of phenylthiopropone, 800 g. of polyphosphoric acid and 40 g. of phosphorus pentoxide were stirred and heated at 120–125° for 5.5 hours. When the reaction mixture had cooled to 85°, it was slowly added with stirring to two liters of cold water in an ice bath. After standing overnight, the organic layer was separated and the aqueous phase was washed with two 100 ml. portions of salt water and dried with anhydrous sodium sulfate. After removal of the solvent and distillation of the residue, 70 g. (79%) of a pale yellow liquid boiling at 80–81°/1 mm. was obtained. When this procedure was repeated on a 1.8 mole scale, a 76% yield of IX was obtained.

Anal. Calcd. for C_9H_8S : C, 72.94; H, 5.44; S, 21.62. Found: C, 73.03; H, 5.63; S, 21.40.

Compound IX was further characterized by oxidation to 3-methylbenzo[b]thiophene-1,1-dioxide. A mixture of 10 g. (0.0675 mole) of

IX, 50 ml. of acetic acid, 50 ml. of acetic anhydride and 50 ml. of 30% hydrogen peroxide was carefully warmed to reflux temperature. The initial reaction on warming was quite vigorous. The reaction mixture was allowed to reflux for one hour, 200 ml. of water was added and the reaction vessel was allowed to cool in the refrigerator overnight. Six grams (49%) of shiny white platelets was obtained which melted at 143–145°. The product was recrystallized from ethanol as white platelets that melted at 145–146°. Werner (21) reported this compound to melt at 146–146.5°.

3-Methylbenzo[b]thiophene-2-carboxylic Acid (VIIa).

One and four-tenths moles of IX provided a 73% yield of VIIa by minor modifications of the method of Shirley (16). After recrystallization from glacial acetic acid, white needles were obtained which melted at 244–245°. The reported melting point is 244–246°; λ max (KBr) 3.3–4.0 μ (bonded OH), 5.98 μ (aryl acid carbonyl group).

Anal. Calcd. for $C_{10}H_8O_2S$: S, 16.67. Found: S, 16.37.

Methyl 3-Methylbenzo[b]thiophene-2-carboxylate (VIIb).

A suspension of 38.4 g. (0.2 mole) of VIIa in 450 ml. of dry methanol was treated with 6 drops of concentrated sulfuric acid and allowed to reflux for 20 hours. The hot solution was filtered and the crystals which separated from the cooled filtrate were collected, washed with 200 ml. of 5% sodium bicarbonate solution and then with 50 ml. of water. After two recrystallizations from methanol, 24 g. (59% yield) of tiny, pale-yellow needles were obtained which melted at 105–106°; λ max (KBr) 3.33 μ (=C-H), 3.45 μ (=CH₃), 5.84 μ (aryl ester carbonyl), 7.88 μ , 3.52 μ , 9.03 μ (C-O).

Anal. Calcd. for $C_{11}H_{10}O_2S$: C, 64.05; H, 4.89; S, 15.54. Found: C, 63.97; H, 5.01; S, 15.53.

3-Methylbenzo[b]thiophene-2-carboxamide (VIII).

Twenty-five grams (0.13 mole) of VIIa was treated with 100 ml. of thionyl chloride and boiled for three hours. The excess thionyl chloride was distilled under reduced pressure and the residual solid was added in small portions to 200 ml. of ice-cold ammonium hydroxide solution. The white precipitate was collected, washed with three 100 ml. portions of water and recrystallized from 95% ethanol to yield 16.9 g. (68%) of small white needles which melted at 182–183°. The reported melting point is 181–183° (16). λ max (KBr) 2.99 μ , 3.16 μ (bonded N-H), 6.05 μ (primary amide carbonyl). Shirley (16) has desulfurized VIII to β -phenylbutyramide and converted the latter to its para nitro derivative, both of which melted in accordance with literature values.

Anal. Calcd. for $C_{10}H_9NOS$: N, 7.33; S, 16.75. Found: N, 7.33; S, 16.94.

2-Cyano-3-methylbenzo[b]thiophene (IV).

A mixture of 10 g. (0.0524 mole) of VIII and 10 g. of phosphorus pentoxide was placed in a 100 ml. round-bottomed flask connected to an air condenser with a receiver cooled in an ice bath. The apparatus was placed under a pressure of 20 mm. and the distillation flask was heated with a Fischer burner flame. A yellow liquid distilled and crystallized in the condenser. The condenser was washed with ether and the solvent was removed. The white product was redistilled at 148–150°/2 mm. After recrystallization from 95% ethanol, 4.6 g. (51% yield) of small white cubes were obtained which melted at 76–77°; λ max (KBr) 4.53 μ (aryl nitrile). The infrared spectrum of this product was identical in every major absorption to that of the minor product isolated by gas chromatography from the alkylation of sodium cyanide with II in dimethyl sulfoxide. A mixed melting point determination of IV with chromatographically pure III was depressed, 49–52°.

Anal. Calcd. for $C_{10}H_7NS$: C, 69.32; H, 4.07; S, 18.50. Found: C, 69.67; H, 4.26; S, 18.30.

A sample of IV was hydrolyzed by refluxing overnight in a 6 N hydrochloric acid solution. The cooled solution was made alkaline with 30% sodium hydroxide solution, treated with Norit and filtered hot. The cooled filtrate was acidified and the white solid was collected and recrystallized from glacial acetic acid to provide a 67% yield of white needles which melted at 244–245° and did not depress the melting point of VIIa prepared as described earlier.

2-Hydroxymethyl-3-methylbenzo[b]thiophene (X).

This compound was prepared as described by Gaertner (4). The lithium aluminum hydride reduction of VIIa provided a 72% yield of X which melted at 92–93° after two recrystallizations from hexane. Compound X is reported to melt at 90.6–91.6° (4) and at 90–91° (5); λ max (KBr) 3.05 μ (intermolecular hydrogen bonded hydroxyl).

A similar reduction of compound VIIb provided an 87% yield of X with identical infrared absorption spectra and melting point.

Benzo[b]thiophene-3-acetic Acid (Va).

The alkaline hydrolysis of III as reported by Blicke (7) gave a 51.6% yield of Va. Acid hydrolysis, as described by Wenner for the hydrolysis of benzyl cyanide to phenylacetic acid (22), was found more efficient.

Into a three liter three-necked round-bottom flask fitted with a stirrer, reflux condenser and thermometer was placed 800 ml. of concentrated hydrochloric acid. With vigorous stirring 186 g. (1.075 moles) of melted III (containing 2% of IV) was added rapidly. During two hours of stirring on the steam bath at 40-45°, the reaction mixture remained heterogeneous. Near the end of the second hour the reaction mixture was a white slurry of material, presumably benzo[b]thiophene-3-acetamide. With continued vigorous stirring, 800 ml. of water was added and the reaction mixture was heated to its reflux temperature. The white slurry slowly became a yellow-orange oily dispersion. After refluxing for 6 hours, the reaction mixture was poured into a large beaker and was cooled at 5° overnight. White crystals separated from the solution and an oil at the bottom of the beaker solidified. The solid material was collected and dissolved in one liter of 10% sodium hydroxide solution. The basic solution was filtered to remove a small amount of unhydrolyzed material and the filtrate was heated with Norit, filtered, cooled and acidified with 6 N hydrochloric acid solution. After drying at reduced pressure in a desiccator, 187 g. (90.5%) of white solid was obtained which melted at 97-102°. A sample of this material was recrystallized twice from water to yield white crystals which melted at 110-111°. Compound Va is reported to melt at 108-109° (7).

Anal. Calcd. for $C_{10}H_8O_2S$: C, 62.47; H, 4.19; S, 16.68. Found: C, 62.65; H, 4.25; S, 16.58.

Benzo[b]thiophene-3-acetamide (Vb).

Ten grams (0.0522 mole) of Va was treated dropwise with 50 ml. of thionyl chloride and after the vigorous evolution of hydrogen chloride subsided, the reaction mixture was allowed to reflux for two hours. The excess thionyl chloride was removed by distillation under reduced pressure and the residue was treated with 50 ml. of dry benzene. The benzene was removed by distillation and replaced with a further 50 ml. of dry benzene. This solution was added dropwise with vigorous stirring and cooling to 150 ml. of ammonium hydroxide. The benzene and excess ammonium hydroxide were evaporated and the amide was collected and recrystallized twice from water to yield 8.2 g. (82.5%) of fine white needles which melted at 173-174°; λ max (KBr) 2.98 μ , 3.15 μ (bonded N-H), 6.03 μ (amide carbonyl). Compound Vb was reported to melt at 171-173° (7).

Anal. Calcd. for $C_{10}H_8NOS$: C, 62.79; H, 4.75; N, 7.33. Found: C, 62.71; H, 4.64; N, 7.27.

3-(β -Hydroxyethyl)benzo[b]thiophene (VD).

Into a three liter three-necked round-bottomed flask fitted with a stirrer, condenser with drying tube and an additional funnel was placed 24 g. of lithium aluminum hydride and 800 ml. of anhydrous ether. A solution of 120 g. (0.625 mole) of crude Va (containing some VIIa) in one liter of dry ether was added dropwise to the stirred metal hydride at a rate which maintained a gentle reflux of the solvent. After the addition was complete, the reaction mixture was stirred an additional 2 hours and then excess hydride was decomposed by the dropwise addition of ethyl acetate with cooling and vigorous stirring. The reaction mixture was treated slowly with 500 ml. of 3.8 N sodium hydroxide solution and the ether layer was separated. The aqueous phase was filtered and the residue was washed with 100 ml. of ether. The aqueous filtrate was extracted with three 100 ml. portions of ether. The combined ether solutions were dried with anhydrous sodium sulfate and the solvent was removed under reduced pressure. The residual oil was distilled to give 47 g. (42.4%) of clear, light yellow

liquid which boiled at 134-136°/0.2 mm.; λ max (Film) 3.0 μ (hydroxyl), 3.3 μ (=C-H), 3.45 μ , 3.50 μ (-CH₂-), 9.6 μ (C-O).

Anal. Calcd. for $C_{10}H_{10}OS$: S, 17.98. Found: S, 18.28.

At 150-155°/0.2 mm. a yellow liquid distilled which solidified in the condenser. This white solid weighed 1.4 g. and melted at 91-92° after recrystallization from hexane. The infrared spectrum of this compound was identical to that of X prepared by the lithium aluminum hydride reduction of VIIa and VIIb. A mixed melting point determination with the alternately prepared X was undepressed, 91-92°.

Anal. Calcd. for $C_{10}H_{10}OS$: S, 17.98. Found: S, 17.77.

When the above preparation was repeated on a highly purified sample of Va, melting at 110-111°, a 49% yield of VI was obtained, but no X distilled. Furthermore, gas chromatography of the reaction mixture before distillation indicated the presence of VI, but no signal for X.

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Bloomington, Indiana 47405