Anal. Calcd. for $C_{12}H_8Cl_2$: C, 64.6; H, 3.6. Found: C, 64.8; H, 3.7.

The monobromobiphenyls were purchased from K and K Laboratories. The terphenyls were purchased from Eastman. The α-phenylnaphthalene was purchased from the Aldrich Chemical Co. All compounds used as starting materials in the isomerizations were purified until gas chromatographically pure.

Isomerization of Halogenated Biphenyls.—A mixture of 1 g. of compound and 0.01 g. of aluminum chloride (B and A, anhydrous, sublimed) in a 6-in. test tube was placed in an oil bath. Anhydrous hydrogen chloride was bubbled through the mixture throughout the reaction. The reaction time and temperature are described in Tables I and II. After cooling, *n*-pentane was added to the mixture and the organic phase washed with water. The organic layer was dried over magnesium sulfate, filtered, and evaporated to an oily residue which was analyzed directly by gas chromatography as described in ref. 14.

Isomerization of α-Phenylnaphthalene. Anhydrous hydrogen chloride was bubbled through a solution of 0.01 mole of α-phenylnaphthalene in 10 ml. of benzene to which had been added 0.05 g. of aluminum chloride. The reaction time was 15 min. at 70°. The product was prepared for analysis as described above. Gas chromatography indicates an equilibrium distribution of 3% α-phenylnaphthalene and 97% β-phenylnaphthalene. The same mixture is obtained starting with β-phenylnaphthalene.[15]

No naphthalene or diphenylnaphthalene peaks were observed on the gas chromatograms.

Isomerization of *o*-Terphenyl.—Anhydrous hydrogen chloride was bubbled through a mixture of 1 g. of *o*-terphenyl and 0.01 g. of aluminum chloride held at 160° for 30 min. The product was prepared for analysis as described above. Gas chromatographic analysis indicated an equilibrium mixture of 64% *m*-terphenyl and 36% *p*-terphenyl.

---

[15] β-Phenylnaphthalene was obtained from the α-phenylnaphthalene isomerization after sublimation and recrystallization, m.p. 102.4–102.7°.

Anal. Calcd. for C, 93.8; H, 6.0. Found: C, 94.0; H, 6.1.

The Friedel-Crafts Isopropylation of Benzo[*b*]thiophene[1]

S. F. BEDELL,[2] EARL C. SPAETH, AND J. M. BOBBITT[3]

Department of Chemistry, University of Connecticut, Storrs, Conn.

Received August 14, 1961

Benzo[*b*]thiophene has been isopropylated with several reagents using various methods and catalysts. In each case, a mixture of the 2- and 3-substituted products was obtained in which the 2-isomer predominated. The authentic compounds, 2-isopropyl- and 3-isopropylbenzo[*b*]thiophene, were each synthesized by two different routes and were, in addition, degraded to known compounds. The results are discussed.

The Authentic Compounds.—For a study of this type, the identity and purity of the authentic compounds are extremely important. Thus, 2-isopropyl-(I) and 3-isopropylbenzo[*b*]thiophene (II), the major compounds which would result from the monoalkylation of benzo[*b*]thiophene, were synthesized by two different routes, each thought to be unequivocal. The isomers were prepared by ring closure methods to ensure purity, but a second synthesis from the known 2- and 3-carboxylic acid esters was used to ensure identity. The synthetic reactions are outlined in the chart. In each case, the isomers derived from the different paths were identical.

The syntheses were reconfirmed by the desulfurization[11] of the 2- and 3-isomers to the corresponding hydrocarbons, 3-methyl-1-phenylbutane, (XVI), and 2-methyl-3-phenylbutane (XVII). The reference hydrocarbons XVI and XVII were synthesized by the procedures of Gilman and Beaber[12] and Klages,[13] respectively. The infrared spectra and physical constants of the prepared hydrocarbons were identical with those of the hydrocarbons derived from the benzo[*b*]thiophene derivatives. 2-Isopropyl- and 3-isopropylbenzo[*b*]thiophene were characterized as 2,4,7-trinitrofluorenone derivatives.[14]

Alkylation Experiments.—Benzo[*b*]thiophene was isopropylated using a variety of Lewis acid catalysts and alkylating agents. The alkylation procedures were dictated by the physical constants of the reactants and the desired temperatures, were of seven types and are described in the Ex-

---

(1) This investigation was partially supported by a Frederick Gardner Cottrell Grant from the Research Corporation.

(2) Abstracted in part, from the Ph.D. thesis of S. F. Bedell, University of Connecticut, 1959. Present address: Monsanto Chemical Company, Research and Engineering Division, Special Products Department, Everett, Mass.

(3) To whom inquiries should be sent.

(4) H. D. Hartough and A. I. Kosak, *J. Am. Chem. Soc.*, **68**, 2639 (1946).

(5) The experiments, III to VI, were carried out as a modification of the experiments first performed by C. B. Germain, Ph.D. dissertation, University of Connecticut, 1953.

(6) The conversions, VI to I, were carried out in a manner analogous to the preparation of 4-hydroxybenzo[*b*]thiophene; L. F. Fieser and R. G. Kennelly, *J. Am. Chem. Soc.*, **57**, 1611 (1935).

(7) R. Weissgerber and O. Kruber, *Ber.*, **53**, 1551 (1920).

(8) The major route (through XV) was the general method of E. G. G. Werner, *Rec. trav. chim.*, **68**, 519 (1949).

(9) Prepared by the general method of W. D. McPhee and E. Klingsberg, *Org. Syntheses*, Coll. Vol. III, 119 (1955).

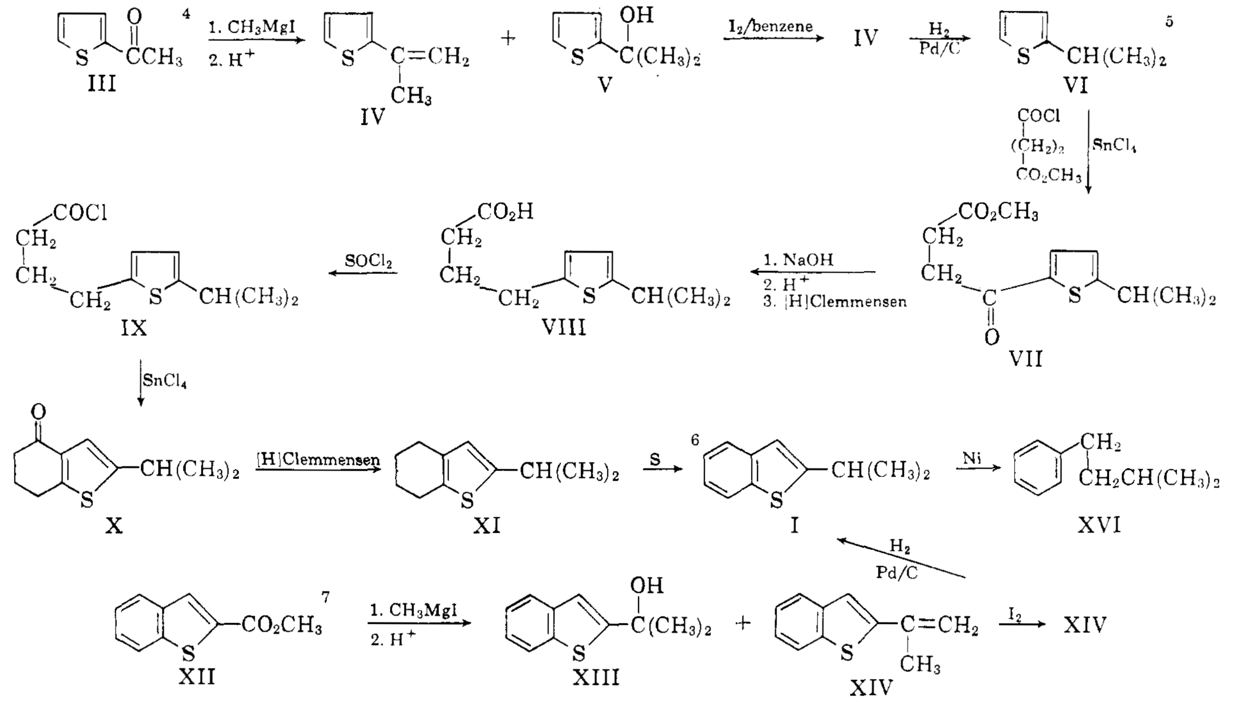
(10) G. Komppa and S. Weckman, *J. prakt. Chem.*, **138**, 109 (1933); *Chem. Abstr.*, **27**, 5326 (1933).

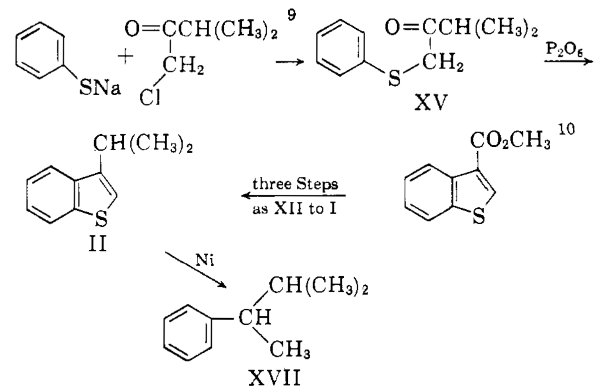
(11) F. F. Blicke and D. G. Sheets, *J. Am. Chem. Soc.*, **71**, 4010 (1949).

(12) H. Gilman and N. J. Beaber, *J. Am. Chem. Soc.*, **47**, 518 (1925).

(13) A. Klages, *Ber.*, **36**, 3688 (1903).

(14) N. D. Cheronis and J. B. Entrikin, "Semimicro Qualitative Organic Analysis," 2nd ed., Interscience Publishers, Inc., New York, 1957, p. 487.





perimental section. The data concerning ratios of the reactants, temperatures, times, the alkylating agents, and the catalysts are given in Table I. After suitable treatment, the reaction mixtures were distilled to obtain the fraction containing the monoalkylated products. This fraction consisted of 2- and 3-isopropylbenzo[*b*]thiophene and a trace of what was presumed to be some benzo[*b*]thiophene isopropylated in the benzene ring. These trace products made the originally planned infrared analysis inexact. Nevertheless, the results of the infrared study were in general agreement with the more accurate gas chromatographic method which was ultimately used. Since the alkylation mixtures boiled too high for convenient gas chromatography, they were desulfurized[11] to the corresponding hydrocarbons and analyzed. This desulfurization method was similar to the one used in the analysis of the diisopropylthiophenes[15] and was thoroughly tested using synthetic mixtures of the two isomers. These synthetic mixtures were desulfurized (90–96%), and the resulting hydrocarbon mixtures were resolved by gas chromatography. In each case the values were within 1% of the starting mixtures. The data obtained from the actual alkylations are given in Table I.

The yields of monoalkylated products varied from 10–67% and were highest when the catalyst was 75 to 80% sulfuric acid. Sulfuric acid was followed, in order of decreasing yields, by phosphoric acid, boron trifluoride etherate, boron trifluoride, hydrogen fluoride, aluminum bromide in carbon disulfide, and aluminum chloride in carbon disulfide. The degree of polymerization increased in the same order. Monoalkylated products could not be isolated when the following catalysts were employed: aluminum chloride in nitromethane, aluminum chloride alone, aluminum bromide alone, ferric chloride, antimony trichloride, antimony pentachloride, zinc chloride, titanium tetrachloride, zirconium tetrachloride, stannic chloride in nitromethane, stannic chloride alone, and iodine. In most of these cases, polymeric products were obtained.

The catalytic activity of sulfuric acid of various concentrations (60–90%) was investigated. At the lower values, yields of monoalkylated products were negligible and at higher concentrations, sulfonation predominated. In no case does the concentration of acid affect the isomer ratio to any great extent.

In all of the alkylations, the 2-isomer is predominant, varying from 78 to 92%. Since the reaction conditions (mainly temperature and reactant ratios) were not constant over all of the experiments, any

---

[15] W. G. Appleby, A. F. Sartor, S. H. Lee, Jr., and S. W. Kapranos, *J. Am. Chem. Soc.*, **70**, 1552 (1948).

TABLE I

THE ALKYLATION OF BENZO[*b*]THIOPHENE[a]

Alkylating Agent	Catalyst	Benzo[*b*]-thiophene–Alkylating Agent, Molar Ratio	Catalyst–Alkylating Agent, Molar Ratio	Temp.	Time, hr.	Mono-alkylated Benzo[*b*]-thiophene, %	2-Isopropyl-[i] benzo[*b*]-thiophene, %	Procedure
Isopropyl chloride	$AlCl_3$[b]	1	1	0–52[d]	12	13	91	A
Propene	$AlCl_3$[c]	1	1	25–40	1	21	92	B
Isopropyl chloride	$AlBr_3$[c]	1	0.015	25–52	0.5	14	91	C
Propene	$AlBr_3$[c]	1	1	25–50	1	17	91	B
Isopropyl alcohol	$BF_3 \cdot Et_2O$	2	0.2	60–120[e]	1	42	86	G
Propene	$BF_3 \cdot Et_2O$	3	0.286	80–120[e]	1	44	86	E
Isopropyl alcohol	BF_3	2	0.133	150	1	26	85	F
Propene	BF_3	2	0.133	25–80[f]	1	29	85	D
Propene	75% H_2SO_4	3	1.14	35[g]	1	56	79	E
Propene	80% H_2SO_4	3	1.14	35[g]	1	67	79	E
Propene	85% H_3PO_4	3	0.86	125	1	22	79	D
Propene	100% H_3PO_4	3	0.86	140	1	40	78	D
Propene	100% H_3PO_4	3	0.86	150[g]	1	62	79	E
Isopropyl alcohol	100% H_3PO_4	2	1	150[g]	2	42	79	G
Propene	HF	1	12.5	0–25[h]	12	25	89	H
Isopropyl alcohol	HF	1	12.5	0–30[h]	12	16	91	H

[a] In all cases where alkylation was successful, a duplicate experiment was performed. The data agreed within 2%. [b] Carbon disulfide (400 ml. to 0.2 mole of catalyst) was solvent. [c] Carbon disulfide (200 ml. to 0.2 mole of catalyst) was solvent. [d] The reaction mixture was kept at 0° during halide addition. [e] The temperature rose to 120° during the course of reaction. [f] The temperature rose to 80° during the course of reaction. [g] Under 200 p.s.i. pressure. [h] The mixtures were kept at 0° for two hr. [i] The 3-isomer accounts for the difference between these per cent yields and 100%.

interpretation of the difference between the 78 and 92% values would not be valid.

Theoretical Considerations.—The existing data on isomer distribution in the electrophilic substitution of benzo[*b*]thiophene are far from satisfactory. The literature abounds in individual reports wherein the desired isomer was obtained, but only one rigorous study of the actual isomer distribution exists. However, it is relatively certain that the 3-isomer predominates in nitration,[16] halogenation,[17] and chloromethylation.[18] Sulfonation[19] appears to give a single isomer which may be either 2- or 3-. A comprehensive study by Farrer and Levine[20] leaves little doubt that acid-catalyzed acetylation occurs in the 3-position in a ratio of three to one. The acid-catalyzed alkylation of thianaphthene with isobutene has been reported[21] to give 100% of the 3-isomer, but no proof of structure is given for the product. The same reaction has also been reported[22] to yield 75% of the pure 3-isomer with no mention of any 2-isomer. The structure proof is based upon the physical constants of Conary and McCleary[21] and upon desulfurization to a known hydrocarbon. The hydrocarbons are proved to be identical not through infrared or ultraviolet spectra but one crystalline derivative. No yields are given on the derivative preparation.

The application of classical resonance and inductive theories to the electrophilic substitution of benzo[*b*]thiophene[20,23] predicts that the 3-isomer should predominate. This prediction is probably fulfilled in the nitration, halogenation, and chloromethylation experiments and is certainly substantiated in the acetylation, although 25% of the 2-isomer was found in the latter reaction. However, the data reported in this paper show a definite preponderance of the 2-isomer when benzo[*b*]thiophene is isopropylated under acidic conditions. This could be rationalized in two ways. First, the 3-isomer may actually be formed in the larger amount and may be selectively destroyed by polymerization or further alkylation. There does appear to be material in the analysis samples which represents further alkylation. Secondly, perhaps a thermodynamic equilibrium is established in which the 2-isomer or the reaction intermediates leading to the 2-isomer are more stable than the 3-isomer. Both of these rationals would appear to be negated by the fact that the 3-isomer (theoretically the more unstable one) is not changed by 100% phosphoric acid or by 80% sulfuric acid.[24] Thus, no reaction path is obvious and we do not wish to suggest a new one based upon a single set of experiments. We do not plan to pursue this work any further.

---

(16) For general discussion and references, see H. D. Hartough and S. L. Meisel, "Compounds with Condensed Thiophene Rings," Interscience Publishers, Inc., New York, 1954, p. 48.

(17) Ref. 16, p. 45.

(18) Ref. 16, p. 46. Compare S. Avakian, J. Moss, and C. J. Martin, *J. Am. Chem. Soc.*, **70**, 3075 (1948).

(19) M. Pailer and E. Romberger, *Monatsh. Chem.*, **92**, 677 (1961).

(20) M. W. Farrer and R. Levine, *J. Am. Chem. Soc.*, **72**, 4433 (1950).

(21) R. E. Conary and R. F. McCleary, U. S. Patent 2,652,405, September 15, 1953; *Chem. Abstr.*, **48**, 12178 (1954).

(22) B. B. Corson, H. E. Tiefenthal, G. H. Atwood, W. J. Heintzelman, and W. L. Reilly, *J. Org. Chem.*, **21**, 584 (1956).

(23) Ref. 16, p. 4.

(24) We would like to thank the referee for suggesting these equilibration experiments.

Experimental

The melting points were taken in capillary tubes and are corrected. The analyses were performed by Dr. Carl Tiedke's Laboratory of Microchemistry, Teaneck, N. J., and Drs. Weiler and Strauss in Oxford, England.

2-Isopropylthiophene (VI).[5] A solution of 151.2 g. of freshly distilled 2-acetylthiophene (Matheson Co.) in 250 ml. of anhydrous ether was slowly added to a stirred, cooled solution of methylmagnesium iodide (from 1.08 moles of methyl iodide and 1.1 g.-atoms of magnesium) in 350 ml. of ether. The yellow semisolid complex which formed was transferred to a large beaker and hydrolyzed with 550 ml. of saturated ammonium chloride solution. The ether layer was decanted and the aqueous layer was extracted twice with ether. The combined ether layers were dried over sodium sulfate, and the solvent was distilled to yield a mixture of 2-isopropenylthiophene and 2-thienyldimethylcarbinol. The dehydration was completed by refluxing the mixture with 80 ml. of dry benzene using a 25-ml. Gibbs Phase Separator until no more water was removed. The volume of benzene and the volume of the Phase Separator are important since they determined, to some extent, the reaction temperature. The benzene was distilled and the remaining 2-isopropenylthiophene was distilled through a 12-cm. Vigreux column attached to a Claisen flask. The fraction boiling at 55–56° (10 mm.), $n^{20}\text{D}$ 1.5565, lit.[25] b.p. 98–99° (25 mm.), was collected and amounted to 98 g. (66%).

The 2-isopropenylthiophene (98 g.) was dissolved in 200 ml. of methanol and hydrogenated (3 atm.) using 3 g. of 10% palladium-on-carbon as a catalyst. After 2 hr., the catalyst was removed by centrifugation and the solvent was distilled through a 150-cm. helices packed column. The residue was distilled at reduced pressure through an 18-cm. Vigreux column to yield 90 g. (90%) of 2-isopropylthiophene, b.p. 48–49° (14 mm.), $n^{20}\text{D}$ 1.5035, lit., b.p. 154–155° (760 mm.)[26] $n^{20}\text{D}$ 1.5040[26] 1.5030.[27]

3-(2-Isopropyl-5-thenoyl)propanoic Acid (VII). Freshly distilled anhydrous stannic chloride (163 g.) was added to a cooled, stirred mixture (0°) of 56 g. of 2-isopropylthiophene, VI, 84 g. of 3-carbomethoxypropanoyl chloride,[28] and 440 ml. of thiophene-free, anhydrous benzene in a dry system. The addition time was one hour. The cooling bath was removed and the mixture was stirred for 1 hr. and decomposed with ice and 6 *N* hydrochloric acid. The benzene and unchanged 2-isopropylthiophene were removed by steam distillation and the residue, which partially solidified on cooling, was extracted with ether. The ether was distilled from the extract and the residue was saponified by refluxing for 2 hr. with 500 ml. of 10% potassium hydroxide in ethanol. The mixture was diluted with water and the ethanol was distilled. The hot solution was filtered, cooled, and acidified with concentrated hydrochloric acid. The keto acid, 90 g. (90%), was removed by filtration and recrystallized from 60% aqueous alcohol to give an analytical sample, m.p. 105–106°.

Anal. Calcd. for $C_{11}H_{14}O_3S$: C, 58.38; H, 6.24; S, 14.17. Found: C, 58.19; H, 6.50; S, 14.23.

4-(2-Isopropyl-5-thienyl)butanoic Acid (VIII).—The keto acid (VII) (106 g.) was added to 600 g. of amalgamated zinc in 1000 ml. of hydrochloric acid and the mixture was allowed to stand for 50 hr. with occasional swirling. During this time, 500-ml. portions of 6 *N* hydrochloric acid were added at 12-hr. intervals. The reaction mixture was then refluxed for 90 min., allowed to cool, and extracted three times with ether. The extract was washed twice with water and dried over calcium chloride and the ether was removed by distillation. The residual oil was distilled through a 90-cm., vacuum-jacketed Vigreux column under reduced pressure to yield 84 g. (85%) of product, b.p. 116–117° (0.25 mm.), $n^{20}\text{D}$ 1.5100, $d^{25}{}_4$ 1.0640.

Anal. Calcd. for $C_{11}H_{16}O_2S$ C, 62.26; H, 7.55; S, 15.09. Found: C, 62.73; H, 7.99; S, 14.70.

This compound was also prepared (82%) by a modified Wolff-Kishner reduction.

2-Isopropyl-4-keto-4,5,6,7-tetrahydrobenzo[*b*]thiophene (X).—The acid chloride (IX) of VIII was prepared by mixing 111 g. with thionyl chloride (85.3 g.), ether (120 ml.), and pyridine (16 drops). The mixture was refluxed for 5 hr. and the ether and excess thionyl chloride were removed under vacuum. The residue was distilled through a 90-cm., vacuum-jacketed Vigreux column under reduced pressure to give 105 g. (88%) of acid chloride, b.p. 120° (1 mm.), which was used, without further purification, in the next reaction. A solution of 134 g. of anhydrous stannic chloride and 650 ml. of freshly distilled carbon disulfide in an anhydrous system was cooled to 0° and 100 g. of acid chloride (IX) in 200 ml. of carbon disulfide was added dropwise, with stirring, during 40 min. The reaction mixture was refluxed for 2.5 hr., 500 g. of ice was added, and stirring was continued for 1.5 hr. During the hydrolysis, the mixture turned from deep red to light yellow. The reaction mixture was steam distilled. After the solvent was removed, the product codistilled with about 6 l. of water. The steam-distillate was extracted three times with ether; the extract was dried over calcium chloride and the solvent was removed by distillation. The residue was fractionated through a Wheeler semimicro distillation column to yield 71 g. (85%) of product, b.p. 88–89° (0.05 mm.), $n^{20}\text{D}$ 1.5582, $d^{25}{}_4$ 1.1008.

Anal. Calcd. for $C_{11}H_{14}OS$: C, 68.00; H, 7.21; S, 16.49. Found: C, 67.79; H, 7.40; S, 16.54.

2-Isopropyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (XI).—Zinc amalgam (12 g.) was washed with water and covered with 30 ml. of glacial acetic acid and 18 ml. of hydrochloric acid. The cyclic ketone (X) (1.03 g.) was added and the mixture was allowed to stand for 15 hr. with occasional shaking and warming (to 50°). To complete the reaction, 8 ml. of toluene was added and the mixture was warmed to 80° for 8 hr. The layers were separated, and the organic layer was washed with dilute sodium bicarbonate and dried over anhydrous sodium sulfate. The solvent was removed from the combined layers from fifty[29] such experiments and the residue was distilled under vacuum through a Wheeler column. The fraction boiling at 55° (0.05 mm.) was collected to yield 39 g. (82%) of product, $n^{20}\text{D}$ 1.5268, $d^{25}{}_4$ 0.9926. The infrared spectrum showed no carbonyl absorption.

Anal. Calcd. for $C_{11}H_{16}S$: C, 74.10; H, 7.97; S, 17.98. Found: C, 74.23; H, 7.85; S, 17.91.

2-Isopropylbenzo[*b*]thiophene (I).—An intimate mixture of XI (18 g.) and sulfur (7.3 g.) was stirred and heated to 235–245° for 5 hr. The reaction mixture was cooled and benzene was added. The organic layer was separated, washed with 10% sodium sulfite solution, and dried over anhydrous calcium chloride. The benzene was distilled and the residual oil was fractionated under vacuum through the Wheeler column. The fraction boiling at 71.5–72.0° (0.5 mm.) was collected to yield 15 g. (85%) of product, $n^{20}\text{D}$ 1.5895, $d^{25}\text{D}$ 1.0526.

Anal. Calcd. for $C_{11}H_{12}S$: C, 74.95; H, 6.86; S, 18.19. Found: C, 75.06; H, 6.95; S, 18.34.

A **2,4,7-trinitrofluorenone** derivative was prepared by mixing hot, equimolar solutions of 2,4,7-trinitrofluorenone and 2-isopropylbenzo[*b*]thiophene in minimum amounts of glacial acetic acid. The derivative, m.p. 112–115°, crystallized from the cooled solution. It was not sufficiently

---

(25) V. Thomas, *Bull. soc. chim.* [4] **5**, 730 (1909).

(26) W. M. Kutz and B. B. Corson, *J. Am. Chem. Soc.*, **68**, 1477 (1946).

(27) H. Scheibler and M. Schmidt, *Ber.*, **54B**, 139 (1921).

(28) This compound was prepared by the action of phosphorous pentachloride on methyl hydrogensuccinate [J. Cason, *Org. Syntheses*, Coll. Vol. III, 169 (1955)] according to the method of Cason [J .Cason, *J. Am. Chem. Soc.*, **64**, 1106 (1942)].

(29) The yields in this reaction were much better on the described small scale than on a larger one.

stable to allow further purification but was dried and analyzed.

Anal. Calcd. for $C_{24}H_{17}N_3O_7S$: C, 58.65; H, 3.49; N, 8.55; S, 6.52. Found: C, 58.44; H, 3.55; N, 8.61; S, 6.78.

2-Isopropylbenzo[*b*]thiophene from Methyl Benzo[*b*]thiophene-2-carboxylate.—A solution of methyl benzo[*b*]thiophene-2-carboxylate[7] (38.4 g.) in 125 ml. of dry ether was added, during 0.5 hr., to a cooled, stirred solution of methylmagnesium iodide (from 12 g. of magnesium and 71 g. of methyl iodide) in 150 ml. of ether. The mixture was stirred under reflux for 1 hr. The yellow semisolid complex was hydrolyzed with 400 ml. of saturated ammonium chloride solution and the ether layer was separated. The aqueous layer was washed twice with ether and the combined ether portions were washed twice with water and dried over sodium sulfate. The solid residue obtained when the ether was distilled was a mixture of XIII and XIV.

The dehydration was completed by boiling the mixture with 30 ml. of dry benzene and 15–20 mg. of iodine under a Gibbs Phase Separator until no more water was formed (about 2 hr.). The benzene solution was washed twice with sodium thiosulfate solution, dried over sodium sulfate, and evaporated to dryness under vacuum to yield white crystalline 2-isopropenylbenzo[*b*]thiophene, m.p. 52–56°, which was too unstable to purify. The olefin was dissolved in 200 ml. of methanol and hydrogenated (3 atm.) using 2 g. of 10% palladium-on-carbon as catalyst. After 2 hr., the reaction mixture was centrifuged to remove the catalyst and the methanol was removed by distillation through a 150 cm., helices-packed column. The residue was fractionated through the Wheeler column and the fraction, 29 g. (83%), boiling at 63–63.5° (0.1 mm.) was collected. The **2,4,7-trinitrofluorenone** derivative melted at 109.5–112°.

Chloromethyl Isopropyl Ketone.—A solution of 20.6 g. of isobutyryl chloride in 100 ml. of dry ether was added, during 35 min., to a cooled (0°), stirred solution of 24 g. of diazomethane[30] in 1500 ml. of ether. The diazomethane solution had been previously dried over potassium hydroxide and the entire operation was kept anhydrous. After the addition was complete, the solution was allowed to stir at room temperature for 1 hr. and was reduced to 400 ml. by distillation. Anhydrous hydrogen chloride was passed into the stirred, cooled (0°) solution for about 1 hr. The ether was distilled and the residue was distilled under vacuum through a 24-cm. helices-packed column. The fraction boiling at 50–52° (13 mm.), lit.[31] 53° (13 mm.) was collected to yield 16.4 g. (70%) of product.

Phenylmercaptomethyl Isopropyl Ketone (XV).—Chloromethyl isopropyl ketone (53.0 g.) was added during 30 min. to a stirred and cooled solution of 48.4 g. of benzenethiol dissolved in 70 ml. of 30% sodium hydroxide. During the addition, the temperature was maintained at 20°. The organic layer was separated and the aqueous phase was extracted twice with ether. The combined organic phase and ether layers were washed with water and dried over anhydrous sodium sulfate. The solvents were distilled and the residue was fractionated through the Wheeler column. The fraction boiling at 99–100° (0.4 mm.) was collected to yield 62 g. (72%) of product, $n^{20}\mathrm{D}$ 1.5680, $d^{25}{}_4$ 1.1071. The compound was characterized as a **hydantoin,** which was prepared by the method of Henze and Speer[32] and melted at 204–205°.

Anal. Calcd. for $C_{13}H_{16}N_2O_2S$: C, 59.07; H, 6.10; N, 10.60. Found: C, 59.14; H, 5.82; N, 10.61.

3-Isopropylbenzo[*b*]thiophene (II).—A mixture of phenyl mercaptoisopropyl ketone (39 g.) and 13 g. of phosphorus pentoxide was stirred and heated to 180–195° in a dry atmosphere. After 1 hr., the mixture was allowed to cool and 50 ml. of water was added. The aqueous phase was extracted three times with ether and the combined ether extracts were washed with sodium carbonate solution and water and dried over anhydrous sodium sulfate. The ether was removed by distillation and the residue was distilled under vacuum through the Wheeler column. The fraction boiling at 69–70° (0.1 mm.) was collected to yield 29.8 g. (84%) of 3-isopropylbenzo[*b*]thiophene $n^{20}\mathrm{D}$ 1.5958, $d^{25}{}_4$ 1.0663.

Anal. Calcd. for $C_{11}H_{12}S$: C, 74.95; H, 6.86; S, 18.19. Found: C, 74.79; H, 6.69; S, 18.40.

A **2,4,7-trinitrofluorenone** derivative melted at 131–133°.

Anal. Calcd. for $C_{24}H_{17}N_3O_7S$: C, 58.65; H, 3.62; N, 8.55; S, 6.52. Found: C, 58.45; H, 3.62; N, 8.10; S, 6.25.

3-Isopropylbenzo[*b*]thiophene from Methyl Benzo[*b*]thiophene-3-carboxylate.—Methyl benzo[*b*]thiophene-3-carboxylate, b.p. 165° (17 mm.), lit.[10] 165–166 (17 mm.), was prepared according to Komppa and Weckman.[10] The reactions leading to II were identical to those in the second synthesis of I and the overall yield was 73%. The **2,4,7-trinitrofluorenone** derivative melted at 131–133°.

Desulfurization Procedure.—The same general procedure was used for the conversion of 2-isopropylbenzo[*b*]thiophene to 3-methyl-1-phenylbutane (XVI); for the conversion of 3-isopropylbenzo[*b*]thiophene to 2-methyl-3-phenylbutane, XVII; and for the desulfurization of the alkylation-product mixtures. A solution of the sulfur compound and Raney nickel[33] (7.5 g. per g. of substrate) in methanol (65 ml. per g. of substrate) was maintained at reflux for 5 hr. The solution was filtered and the solvent was removed by distillation through a helices-packed column. The residue was poured into water and the resulting phases were separated. The aqueous phase was extracted with ether and the combined organic solutions were dried over calcium chloride. The solvent was removed by distillation through a helices-packed column and the residue was distilled under vacuum through a semimicro Claisen head with a 7.5-cm. Vigreux column. The yields varied between 90 and 96%.

The 3-methyl-1-phenylbutane from 2-isopropylbenzo[*b*]thiophene boiled at 75–76° (10 mm.) with $n^{16}\mathrm{D}$ 1.4868 and the synthetic sample[12] boiled at 74–75° (9 mm.) with $n^{16}\mathrm{D}$ 1.4870. The 2-methyl-3-phenylbutane from 2-isopropylbenzo[*b*]thiophene boiled at 70–71° (15 mm.) with $n^{16}\mathrm{D}$ 1.4976 and the synthetic sample[13] boiled at 68–69° (13 mm.) with $n^{16}\mathrm{D}$ 1.4972. The appropriate infrared spectra were identical.

Alkylation Procedure A.—A mixture of benzo[*b*]thiophene and isopropyl chloride was slowly added to a cooled (0–5°), stirred mixture of aluminum chloride in 400 ml. of distilled, anhydrous carbon disulfide. The system had a reflux condenser and was kept anhydrous. When the addition was complete, the cooling bath was removed and the mixture was stirred at room temperature (25°) for 12 hr. The reaction mixture was poured, with vigorous stirring, onto 300 g. of ice and the resulting phases were separated. The aqueous layer was washed with three 150-ml. portions of ether. The combined organic solutions were washed once with water (200 ml.), twice with 10% sodium carbonate (150 ml.), once with saturated sodium chloride, and dried over sodium sulfate. The solvents and the unchanged isopropyl chloride were removed by distillation and the residue was distilled under vacuum through the Wheeler column to yield three fractions of b.p. 52°, 52° to 88°, and 88° to 93° (all at 1.75 mm.). The pot residue was discarded and the last two fractions (b.p. 52 to 93° at 1.75 mm.) were subsequently desulfurized and analyzed. The first fraction (b.p. 52° at 1.75 mm.) contained benzo[*b*]thiophene.

Alkylation Procedure B.—The gaseous propene used in this procedure was handled in a manner similar to that

---

(30) Prepared from 160 g. of *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide; T. J. DeBoer and H. J. Backer, *Rec. trav. chim.*, **73**, 229 (1954).

(31) F. W. Eastwood, G. K. Hughes, and E. Ritchie, *Australian J. Chem.*, **7**, 87 (1954).

(32) H. R. Henze and R. J. Speer, *J. Am. Chem. Soc.*, **64**, 522 (1942).

(33) R. Mozingo, *Org. Syntheses*, Coll. Vol. III, 181 (1955).

used by Reichert and Niewland[34] except that a saturated sodium chloride solution was used to displace the propene. Benzo[*b*]thiophene was added to a stirred mixture of aluminum chloride in 200 ml. of carbon disulfide. Propene was passed slowly through a drying tower of silica gel and into the reaction mixture through a gas inlet tube extending as far into the reaction flask as possible. The reaction mixture was stirred at 40° for 1 hr. and then treated as described in Procedure A to isolate the products.

Alkylation Procedure C.—Aluminum bromide was added over a period of several minutes to a stirred mixture of benzo[*b*]thiophene, isopropyl chloride, and 200 ml. of carbon disulfide in an anhydrous system. After 0.5 hr. at reflux, the reaction mixture was hydrolyzed and the products were isolated as described in Procedure A.

Alkylation Procedure D.—Propene was passed slowly into a reaction mixture consisting of boron trifluoride in the benzo[*b*]thiophene. After the addition was complete, the mixture, which heated spontaneously to 80°, was stirred for 1 hr. and treated as described in Procedure A to isolate the products. In some experiments the reaction mixture was heated to the specified temperature before addition of the alkylating agent.

Alkylation Procedure E.—Benzo[*b*]thiophene and boron trifluoride etherate were placed in a 500-ml. Parr pressure apparatus and propene gas was admitted to a pressure of 200 p.s.i. The mixture which heated spontaneously to 120° was stirred for 30 min. and cooled and the products were isolated as described in Procedure A.

Alkylation Procedure F.—Boron trifluoride was passed into the Parr pressure apparatus containing benzo[*b*]thiophene and isopropyl alcohol until a pressure of 100 p.s.i. was reached. The temperature was raised to 150° before the addition of the catalyst. The mixture was stirred at 150° for 1 hr. and cooled. The products were isolated as described in Procedure A.

Alkylation Procedure G.—A mixture of benzo[*b*]thiophene, isopropyl chloride, and boron trifluoride etherate was stirred in the Parr pressure apparatus for 1 hr. The mixture was heated to 60° after which it heated spontaneously to 120°. After cooling the mixture, the products were isolated as described in Procedure A.

Alkylation Procedure H.—The reactions with hydrogen fluoride were carried out in a 1-l. stainless steel beaker with a cover equipped to accommodate a stirrer, a Weston thermometer, a gas inlet tube and a funnel. Except for the gas inlet tube, which was copper, everything was made of stainless steel. Benzo[*b*]thiophene was slowly added, over about 5 min., with stirring to the liquid hydrogen fluoride at 0°. The alkylating agent, either propene or isopropyl alcohol, was then added over about 1 hr. When the additions were complete, the cover was removed from the beaker and the catalyst was allowed to evaporate over night. Any remaining hydrogen fluoride was destroyed by the cautious addition of solid sodium carbonate. The mixture was then partitioned between ether and water and the products were isolated as described in Procedure A.

Analysis of the Desulfurized Mixtures.—The analytical chromatograms were recorded on a Model 154B Perkin-Elmer Vapor Fractometer using nitrogen as the carrier gas (9 p.s.i.). In the analyses, a 2-m. silicone vacuum grease on firebrick column was used. The temperature of the column was 200° and the vaporizer was at 225°. The detector voltage was 8 volts. The sample injections generally caused slight variations in the flow rate. Normally the flow rates were maintained at between 40 and 30 ml./min. After equilibrium was reached, a 7-microliter sample of the hydrocarbon mixture was injected. Depending on the flow rate, the analysis took between 12 and 15 min. Since the thermal conductivities of ethylbenzene and nitrogen are quite similar, ethylbenzene could not be detected when present in amounts of less than 5%. The percentages of 2-methyl-3-phenylbutane (from 3-isomer) and 3-methyl-1-phenylbutane (from 2-isomer) in the mixtures were obtained by determining the areas under their respective curves.

Equilibration Studies.—The two isomers, I and II, were treated with 80% sulfuric acid and with isopropyl alcohol and 100% phosphoric acid under conditions approximating procedures E and G, respectively. The reaction mixtures were poured into water and extracted with benzene. The benzene extracts were washed with water, 5% sodium bicarbonate, water, and saturated sodium chloride. The resulting solutions, dried over sodium sulfate, were analyzed directly on a model A-90, Aerograph gas-phase chromatography apparatus with helium (43 p.s.i.) as a carrier gas.[35] The temperature was 105° and a ten-foot 3% Carbowax 400 on Chromasorb W column was used. The retention times for benzo[*b*]thiophene, 2-isopropylbenzo[*b*]thiophene, and 3-isopropylbenzo[*b*]thiophene were 15.7, 30.4, and 33.6 min., respectively. The two isomers were followed on the chromatograms by a third peak which appeared to represent an unknown mixture.

Acknowledgment.—We would like to thank Dr. R. M. Roberts of the University of Texas and Drs. Roy J. Gritter and F. W. Wassmundt of The University of Connecticut for helpful theoretical discussions.

---

[34] J. A. Reichert and P. J. Niewland, *Org. Syntheses*, **I**, 230 (1941).

[35] This instrument was not available when the original work was done.