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A Synthesis of 7-Substituted Benzo[b]thiophene Derivatives

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In order to develop a method for synthesizing 7-substituted derivatives of benzo[b]-thiophene, the benzo[b]thiophene analog of 1-tetralone, 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene has been synthesized using as starting material the readily accessible 3-bromothiophene. The structure of this ketone has been verified by elemental analysis, spectra and conversion to derivatives of benzo[b]thiophene of known structure. Several hitherto unreported 7-substituted derivatives of benzo[b]thiophene have been prepared from the cyclic ketone.

Although a great number of substituted benzo[b]-thiophenes have been recorded in the literature (1), the number of 7-substituted benzo[b]thiophenes is relatively small. Tilak and co-workers have prepared 7-methoxybenzo[b]thiophene (2), 7-hydroxybenzo[b]thiophene (2), 7-methylbenzo[b]thiophene (3), and 7-bromobenzo[b]thiophene (4) by the acid-catalyzed cyclization of the appropriate *ortho*-substituted phenyl-2,2-dimethoxyethyl sulfides. 7-Cyanobenzo[b]thiophene and benzo[b]thiophene-7-carboxylic acid were prepared respectively from the 7-bromo compound by reaction with cuprous cyanide in pyridine followed by hydrolysis of the nitrile (5). Badger and co-workers (6) report a different synthesis of benzo[b]thiophene-7-carboxylic acid.

The present paper reports an alternative synthesis of 7-substituted benzo[b]thiophenes using the hitherto unreported 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene as a precursor from which these derivatives become readily available by simple chemical transformations involving one or two steps. The synthesis of 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene was accomplished as follows (Figure 1). 3-Bromothiophene (I) (7) was converted to the corresponding nitrile (II) in 86% yield by treatment with cuprous cyanide in quinoline. Use of *N*-methylpyrrolidone following the method of Newman (8) gave only 46% yield of the nitrile. Reaction of the nitrile with methylmagnesium iodide afforded the corresponding methyl ketone (III) in 72% yield. Bromination of the ketone gave bromomethyl-3-thienyl ketone (IV) in 82% yield and reaction of the bromo compound with diethyl malonate gave the expected monoketomalonate (V) together with a small amount of the disubstituted malonic ester, Va. Saponification of the mono-substituted malonic ester using aqueous potassium hydroxide solution at room temperature gave the corresponding malonic acid, VI. The malonic acid was decarboxylated by heating in diethylene glycol at 170-180° to give γ -oxo(3-thienyl)butyric acid (VII) in 53% yield calculated on the basis of the bromo-ketone. Wolfe-Kishner reduction of the γ -oxo(3-thienyl)butyric acid gave γ -(3-thienyl)butyric acid (VIII) in 86% yield. Similar reduction of the malonic acid also afforded γ -(3-thienyl)butyric acid in 57% yield. Treatment of the acid (VIII) with thienyl

chloride in an attempt to form the corresponding acid chloride prior to cyclization to the desired ketone (IX), afforded no chlorine-containing compound, but only the cyclic ketone (IX) in 78% yield.

This result contrasts sharply with that of Fieser and Kennelly (9) who found that γ -(2-thienyl)butyric acid could not be cyclized directly, but only by prior formation of the corresponding acid chloride followed by stannic chloride-catalyzed cyclization to the corresponding ketone, 4-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene. The great facility of cyclization of the γ -(3-thienyl)butyric acid may be explained on the basis of the greater ease of electrophilic substitution at the 2-position in the thiophene nucleus as compared with the 3-position. In addition, the inductive effect of the alkyl substituent in the 3-position further activates the 2-position towards electrophilic substitution (10).

In order to further confirm the structure of the 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene, it was converted by Wolff-Kishner reduction to 4,5,6,7-tetrahydrobenzo[b]thiophene (X) in 65% yield (Figure 2). The reduction product was compared with an authentic specimen prepared by a similar reduction of 4-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene and found to be identical in all respects (11).

Reaction of the ketone IX with phenylmagnesium bromide gave the alcohol XI, in 82% yield. Treatment of the alcohol with sulfur at 230° yielded 7-phenylbenzo[b]thiophene XII, in 76% yield. Substantiation of the structure assigned to XII was provided by elemental analysis and the infrared spectrum which showed the absence of hydroxyl and aliphatic carbon-hydrogen stretching bands.

The ketone IX readily underwent the Reformatsky reaction with ethyl bromoacetate to give a mixture of esters, XIII and XIV in 81% yield. Structural assignments for the esters were made on the basis of elemental analysis and the infrared spectrum. Two absorption bands were found to be present in the carbonyl region, a strong band at 1705 cm^{-1} and a weaker band at 1737 cm^{-1} . The former band was attributed to the $\alpha\beta$ -unsaturated ester XIV. Saponification of the mixed esters gave an acid XV, in 69% yield. The presence of an absorption band at 1680 cm^{-1} is in agreement with the assignment of an $\alpha\beta$ -

FIGURE 1

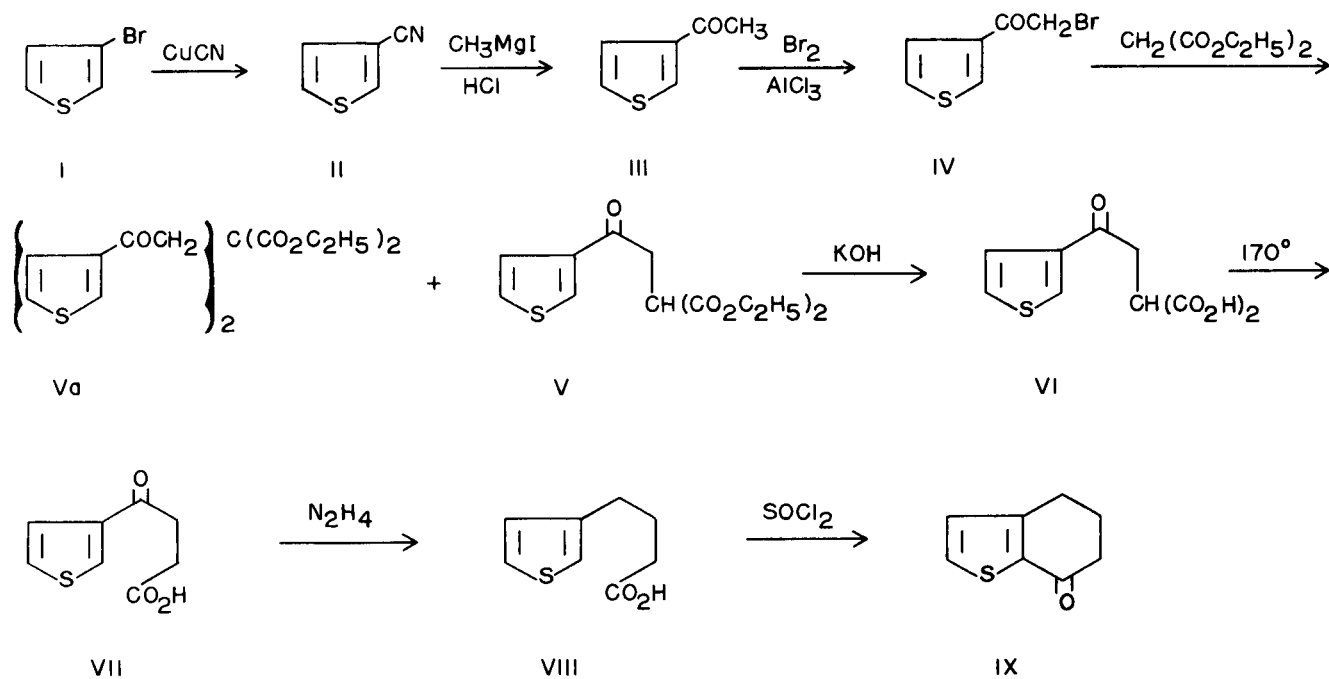
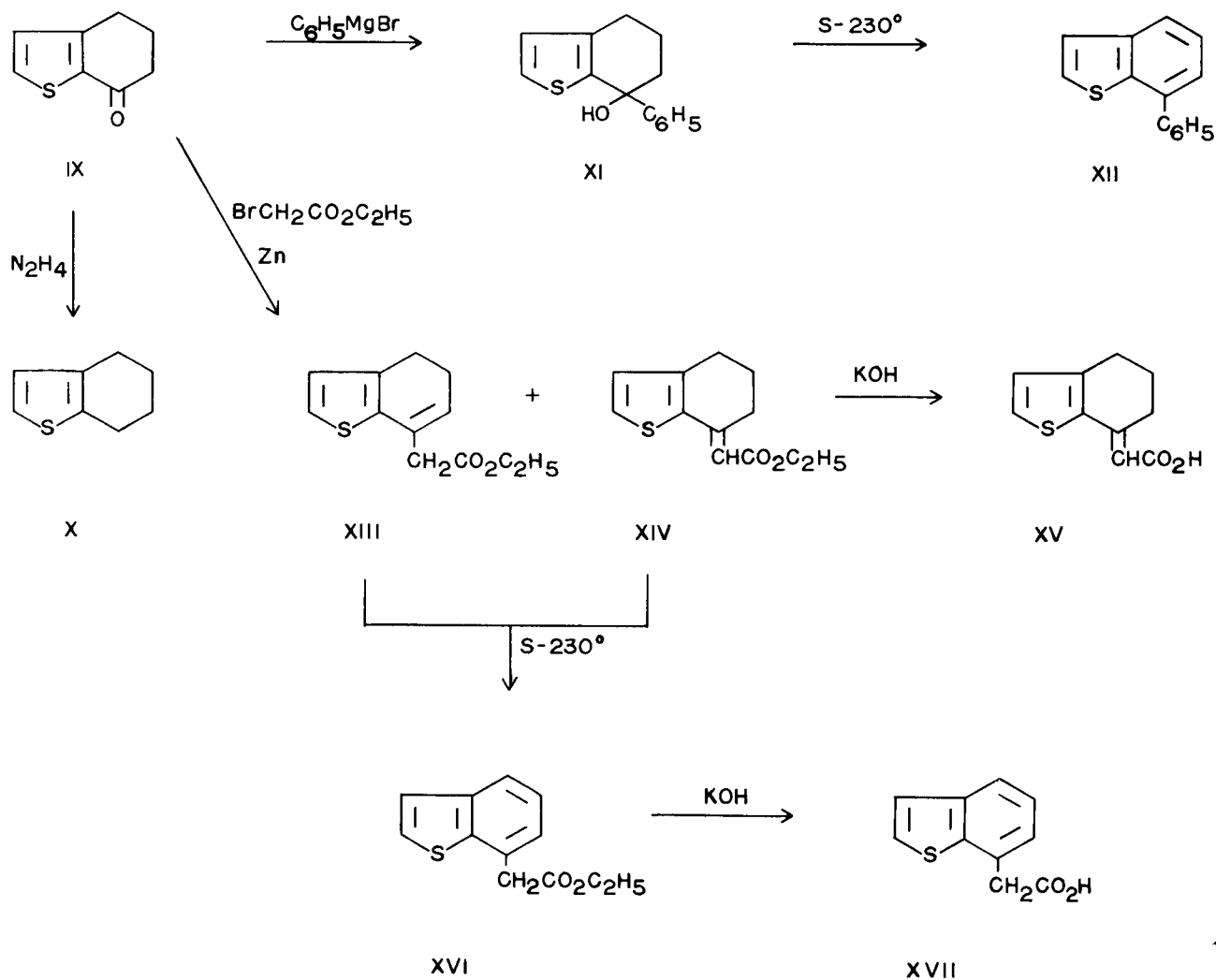


FIGURE 2



unsaturated acid structure to XV. Dehydrogenation of the mixture of esters using chloranil following the method of Kloetzel (12) afforded no useful product. Treatment of the ester mixture with sulfur for one hour at 230° afforded ethyl 7-benzo[b]thiopheneacetate (XVI) in 64% yield. Saponification of this ester yielded 7-benzo[b]thiopheneacetic acid (XVII) in 70% yield. Kefford and Kelso (13) report the synthesis of 7-benzo[b]thiopheneacetic acid by an Arndt-Eistert homologization of benzo[b]thiophene-7-carboxylic acid. They report a melting point of 119° for this acid together with a satisfactory neutralization equivalent. No elemental analyses are reported. The melting point of the 7-benzo[b]thiopheneacetic acid obtained in the present work is 155-156° and the discrepancy between these two values has not been resolved.

EXPERIMENTAL

All temperature readings are uncorrected. All elemental analyses were done by Galbraith Laboratories, Knoxville, Tennessee. The infrared spectra were recorded on the Perkin-Elmer Model 21 and Perkin-Elmer "Infracord" Model 137 spectrophotometers.

2,3,5-Tribromothiophene, b.p. 132-134° (12 mm.) was prepared by the method of Troyanowsky (14) in 86% yield, lit. value (14), 135-138° (17 mm.).

3-Bromothiophene (I), b.p. 159-161°, was prepared in 74% yield by reduction of 2,3,5-tribromothiophene following the method of Gronowitz (7).

3-Cyanothiophene (II) was prepared according to the procedure of Newman (15) using quinoline as solvent in 86% yield, b.p. 104-105° (32 mm.); (lit. (16) b.p. 59° at 3 mm.). The infrared spectrum (neat) of this compound showed a strong absorption at 2250 cm⁻¹, (CN). This compound was also prepared in 46% yield using N-methylpyrrolidone as solvent using the procedure of Newman and Boden (8).

Methyl 3-Thienyl Ketone (III) was prepared in 72% yield by the interaction of 3-cyanothiophene with methylmagnesium iodide. The product boiled at 78-79° (5 mm.) and crystallized from petroleum ether (b.p. 85-90°) as colorless needles, m.p. 61-62° (lit. (17) 58-59°).

Bromomethyl 3-Thienyl Ketone (IV).

In a 500 ml. three-necked round-bottomed flask provided with an addition funnel and two stoppers were added methyl 3-thienyl ketone (107 g., 0.85 mole), anhydrous ether (300 ml.), and anhydrous aluminum chloride (1.00 g., 0.075 mole). After solution was effected, the flask was submerged in an ice bath and to this mixture bromine (43.6 ml., 0.85 mole) was added dropwise. When the addition was complete, the ether and hydrogen bromide were then removed by bubbling a stream of air through the solution. The yellow solid remaining was immediately washed with 100 ml. of cold water, transferred to a filter funnel, and the excess water removed by suction.

The crude product was recrystallized from petroleum ether (b.p. 65-67°) and yielded 143 g. (82%) of white plates which melted at 62-63°. This compound was found to exhibit both lachrymatory and vesicatory properties.

Anal. Calcd. for C₆H₅BrOS: C, 35.14; H, 2.46; S, 15.64; Br, 38.97. Found: C, 35.36; H, 2.48; S, 15.92; Br, 38.74.

Alkylation of Diethyl Malonate with Bromomethyl 3-Thienyl Ketone.

Into a dry 500 ml. three-necked round-bottomed flask equipped with a condenser surmounted by a nitrogen inlet tube, an addition funnel, and a stirrer were added sodium hydride (2.32 g., 0.096 mole) and anhydrous tetrahydrofuran (20 ml.). The flask was swept with nitrogen, placed in an ice bath, and diethyl malonate (16.0 g., 0.100 mole) was added dropwise with stirring. When the addition was complete, a clear pale-yellow solution resulted. To this was added slowly with stirring a solution of bromomethyl 3-thienyl ketone (19.7 g., 0.096 mole) in 100 ml. of anhydrous tetrahydrofuran. The solution immediately became cloudy due to the presence of precipitated sodium bromide. When the addition was complete, the ice bath was removed and the mixture was stirred for an additional hour at room temperature.

A small quantity of water was added to dissolve the sodium bromide and the excess solvent was removed by heating on a steam bath. To

the residue was added 200 ml. of a 10% aqueous potassium hydroxide solution and the resulting red-colored solution was stirred at room temperature for 10 hours. This low temperature saponification was employed because the solution darkened rapidly and showed signs of decomposition at elevated temperatures.

A small portion of the crude ester remained unsaponified after treatment with alkali and was recrystallized from ethanol to give a product which crystallized as white plates, m.p. 100-101°. On the basis of elemental analysis and infrared spectrum, this product is believed to be the dialkylated compound, Va.

Anal. Calcd. for C₁₈H₂₀O₆S₂: C, 55.86; H, 4.94; S, 15.70. Found: C, 55.65, 55.58; H, 4.98, 4.96; S, 15.59, 15.63.

Infrared spectrum (KBr): 1739 cm⁻¹ (ester CO) and 1678 (ketone CO).

Several Rast molecular weight determinations using camphor were attempted but in each case, the samples were found to darken at the required elevated temperature, suggesting that decomposition had taken place.

After removal of the unsaponified dialkylated ester Va described above, the red-colored solution was washed with 50 ml. of ether, poured into ice-cold 6 N hydrochloric acid and the crude dicarboxylic acid VI was precipitated and removed by filtration. The aqueous solution was then saturated with sodium chloride and extracted with ether. The extracts were dried, the ether was removed and the solid residue was combined with the precipitated acid. The yield of acid which melted at 165-168° was 18.4 g. (83%). This product was decarboxylated as described below without further purification.

A small portion of the dicarboxylic acid was purified for analysis by recrystallization from water (Norite) and finally from ethanol to give small white plates, m.p. 168-169°.

Anal. Calcd. for C₉H₈O₅S: C, 47.36; H, 3.53. Found: C, 47.45; H, 3.56. Neut. Equivalent: Calcd.: 114. Found: 115.

γ-Oxo-3-Thiophenebutyric Acid (VII).

The crude dicarboxylic acid (18 g.) was decarboxylated by heating in 100 ml. of diethylene glycol at 170-180° until the evolution of carbon dioxide had ceased. This solution was then added to a mixture of ice and water to which had been added a few drops of acetic acid. The crude keto-acid VII precipitated as a yellow-orange solid and was recrystallized from water using decolorizing charcoal to yield 9.3 g. of white product which melted at 143-147°. Recrystallization from acetone-petroleum ether (b.p. 85-90°) gave small white needles, m.p. 149-150°.

Anal. Calcd. for C₈H₆O₃S: C, 52.16; H, 4.38; S, 17.41. Found: C, 52.38; H, 4.22; S, 17.20. Neut. Equivalent: Calcd.: 184. Found: 186.

Infrared spectrum (KBr): 1670 cm⁻¹ (ketone CO) and 1702 cm⁻¹ (acid CO).

γ-3-Thiophenebutyric Acid (VIII).

In a 250 ml. three-necked round-bottomed flask were placed diethylene glycol (110 ml.) and potassium hydroxide (20 g., 0.36 mole). The mixture was heated gently to effect solution and then cooled to room temperature. To this solution was added γ-oxo-3-thiophenebutyric acid (18.4 g., 0.10 mole) and the solution was stirred as 95% hydrazine (5.06 g., 0.15 mole) was added dropwise. After the addition was complete, the solution was stirred for five minutes and then heated under reflux with continuous removal of the distillate until the temperature of the mixture had risen to 200°. After two hours at this temperature, the solution was cooled and poured over a mixture of ice and hydrochloric acid.

The acid precipitated as a solid but on warming turned into an oily liquid. The mixture was saturated with sodium chloride and extracted thoroughly with ether. The extracts were dried and the ether was removed on a steam bath. The oily residue was distilled under reduced pressure and the pale-yellow distillate boiling at 145-147° (2 mm.) was collected. The product weighed 14.6 g. (86%).

Anal. Calcd. for C₈H₁₀O₂S: C, 56.44; H, 5.92; S, 18.84. Found: C, 56.34; H, 5.72; S, 19.00.

This compound was also obtained by a Wolff-Kishner reduction of the dicarboxylic acid. The crude dicarboxylic acid, which was prepared by the malonic ester synthesis previously described, was both reduced and decarboxylated under the reaction conditions in 57% yield of VIII, b.p. 135-140° (1.2 mm.).

The *p*-nitrobenzyl ester of this acid after three recrystallizations from ethanol was obtained as pale-yellow needles, m.p. 45-46°.

Anal. Calcd. for C₁₅H₁₅NO₄S: C, 59.00; H, 4.95; N, 4.59. Found: C, 58.82; H, 4.89; N, 4.70.

7-Oxo-4,5,6,7-Tetrahydrobenzo[b]thiophene (IX).

γ-3-Thiophenebutyric acid (17.8 g., 0.105 mole) and thionyl chloride (14.3 g., 0.120 mole) were mixed with four drops of pyridine and anhydrous ether (60 ml.). This solution was heated under reflux for 8 hours. The excess ether and thionyl chloride were removed by

distillation and the residue was distilled at reduced pressure. The clear, colorless distillate boiling at 99-100° (0.3 mm.) was collected and weighed 12.5 g. (78%). Recrystallization from petroleum ether (b. p. 85-90°) in the cold gave a white solid, m. p. 34-35°. The infrared spectrum of this compound (neat) showed a ketone carbonyl absorption at 1652 cm^{-1} .

Anal. Calcd. for $\text{C}_8\text{H}_8\text{OS}$: C, 63.12; H, 5.30; S, 21.07. Found: C, 62.97; H, 5.23; S, 21.01.

The 2,4-dinitrophenylhydrazone of this compound was prepared and crystallized from ethyl acetate, as tiny deep-violet needles, m. p. 263-263.5°.

Anal. Calcd. for $\text{C}_{14}\text{H}_{12}\text{N}_4\text{O}_4\text{S}$: C, 50.59; H, 3.64; N, 16.86. Found: C, 50.70; H, 3.71; N, 16.97.

4,5,6,7-Tetrahydrobenzo[b]thiophene (X).

This compound was prepared by a Wolff-Kishner reduction of 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene, as described by Cagniant and Cagniant (11). The product boiled at 87-88° (13 mm.), yield (65%), (lit. (11) b. p. 88° at 13.3 mm.).

The infrared spectrum of this compound (neat) was identical with that of the compound obtained by a Wolff-Kishner reduction of 4-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene.

7-Hydroxy-7-phenyl-4,5,6,7-tetrahydrobenzo[b]thiophene (XI).

This compound was prepared by a Grignard reaction with 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene. To a solution of phenylmagnesium bromide prepared in ether under dry nitrogen from 1.6 g. of magnesium and 10.4 g. of bromobenzene was added slowly with stirring, a solution of 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene (5.0 g., 0.033 mole) in anhydrous ether (30 ml.). A white complex formed immediately. The mixture was stirred at room temperature for four hours and was then hydrolyzed with 25 ml. of a saturated ammonium chloride solution. The layers were separated and the aqueous layer extracted once with 100 ml. of ether, the extract added to the organic layer and the combined layers dried over anhydrous magnesium sulfate.

The ether was removed on a steam bath and the yellow oily residue distilled under reduced pressure. The fraction boiling at 148-149° (1 mm.) was collected and weighed 6.2 g. (82%). The distillate solidified on cooling with dry-ice and a portion was recrystallized from ethanol in the cold giving white crystals which melted at 51-52°. The infrared spectrum of this compound in potassium bromide showed a strong, broad absorption at 3360 cm^{-1} indicating the presence of the hydroxyl group.

7-Phenylbenzo[b]thiophene (XII).

This synthesis employs a dehydration-dehydrogenation using sulfur following the procedure employed by Kloetzel (12). A mixture of 7-hydroxy-7-phenyl-4,5,6,7-tetrahydrobenzo[b]thiophene (5.5 g., 0.023 mole) and sulfur (1.05 g., 0.033 mole) contained in a 50 ml. distilling flask was heated in a salt bath at 230° for 20 minutes. Evolution of hydrogen sulfide and steam was noticed during this time. The temperature was then elevated to 250° and the reaction completed by heating at this temperature for 10 minutes. The residue was then distilled under reduced pressure, and the fraction boiling at 148-150° (1.3 mm.) collected and weighed 4.7 g. (94%). A portion of this compound was recrystallized from ethanol in the cold to yield a white crystalline product, m. p. 35.5-36.5°. The infrared spectrum of this compound (neat) showed the absence of the hydroxyl band.

Since the carbon analysis of this compound proved to be considerably lower than the calculated value, it was believed to be contaminated with either a small amount of sulfur or 7-hydroxy-7-phenyl-4,5,6,7-tetrahydrobenzo[b]thiophene. The compound (4.2 g.) was again heated at 230° with a small amount of sulfur for 2 hours and distilled. The portion distilling at 150-151° (1 mm.) was collected, taken up in a small amount of petroleum ether (b. p. 35-37°) and passed through a column containing alumina. The solvent was removed from the eluent leaving a clear liquid along with a yellow solid. This residue was taken up in acetone and the sulfur removed by filtration. The solution was concentrated to a volume of about 5 ml. and cooled to 0° for one hour. The yellow solid (sulfur) which separated was removed by filtration and the remainder of the acetone was removed leaving a clear, colorless liquid.

The liquid residue (3.8 g., 74%) was dissolved in a small amount of methanol and on cooling the solution to -20°, crystals were deposited. Recrystallization of this solid from methanol at this low temperature afforded an analytical sample, m. p. 37.5-38.5°.

Anal. Calcd. for $\text{C}_{14}\text{H}_{10}\text{S}$: C, 79.96; H, 4.79. Found: C, 79.79; H, 4.83.

Synthesis of the Esters XIII and XIV.

To a hot mixture of amalgamated zinc (24.0 g., 0.367 g-atom), ethyl bromoacetate (6 ml.), iodine (0.2 g.), dry benzene (100 ml.)

and dry ether (100 ml.) was added 7-oxo-4,5,6,7-tetrahydrobenzo[b]thiophene (8.0 g., 0.053 mole). While the mixture was heated under reflux for 2 hours, amalgamated zinc (24.0 g.) and iodine (0.2 g.) were added at each half-hour interval. The reaction mixture exhibited a green to yellow-green coloration at various times during the reaction. Finally, ethyl bromoacetate (6 ml.) was added and the mixture refluxed an additional two and one-half hours.

The mixture was cooled, decanted into a 1-liter separatory funnel containing 200 ml. of cold 10% hydrochloric acid and shaken. The organic layer was separated, combined with two benzene extracts of the aqueous layer, washed successively with 100 ml. of dilute aqueous ammonia and 50 ml. of water and dried for one hour over anhydrous magnesium sulfate.

The solvent was removed and the yellow residue was distilled under reduced pressure. The pale-yellow product distilled at 140-145° (0.8 mm.). Yield 9.4 g. (81%).

Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{O}_2\text{S}$: C, 64.83; H, 6.35. Found: C, 64.58; H, 6.29.

The infrared spectrum of this material (neat) showed two absorption bands in the carbonyl region at 1737 cm^{-1} and 1705 cm^{-1} , suggesting that a mixture of esters had been obtained. The spectrum also exhibited a strong absorption band at 1610 cm^{-1} characteristic of the carbon-carbon double bond stretching frequency.

Saponification of the Esters XIII and XIV.

The esters XIII and XIV (2.0 g., 0.009 mole) were heated with a 20% aqueous sodium hydroxide solution (50 ml.) until solution was effected, (4 hours). The solution was cooled, washed with ether and poured into ice-cold 6 N hydrochloric acid. The yellow acid which precipitated was separated by filtration, washed with 50 ml. of cold water and dried overnight in a desiccator.

The crude acid XV was taken up in a ether-petroleum ether (b. p. 85-90°) solution and the ether removed slowly on a steam bath until the solution became cloudy. The resulting solution was cooled to room temperature and the acid XV (1.2 g., 69%) crystallized as long white needles, m. p. 174.5-175°. Only one isomeric acid was obtained.

Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{O}_2\text{S}$: C, 61.83; H, 5.19. Found: C, 61.65; H, 5.16. Neut. Equivalent: Calcd.: 194. Found: 193.

Infrared spectrum (KBr): 1680 cm^{-1} ($\alpha\beta$ -unsaturated C=O), 1600 cm^{-1} (C=C).

Ethyl 7-benzo[b]thiophene Acetate (XVI).

This compound was prepared by dehydrogenation of the esters XIII and XIV using sulfur. The esters (2.22 g., 0.010 mole) and sulfur (0.50 g., 0.016 mole) were heated in a 10 ml. distilling flask at 230° for one hour. The mixture was then directly distilled under reduced pressure and the pale-yellow distillate boiling at 140-142° (0.9 mm.) was collected and weighed 1.4 g. (64%).

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_2\text{S}$: C, 65.42; H, 5.49. Found: C, 65.38; H, 5.75.

Infrared spectrum (neat); 1725 cm^{-1} (ester C=O).

7-Benzo[b]thiopheneacetic Acid (XVII).

A mixture of ethyl 7-benzo[b]thiophene acetate (1.0 g., 0.0045 mole) and 20% aqueous sodium hydroxide solution (25 ml.) was heated under reflux until solution was effected. After cooling, the solution was washed with ether and then poured into ice-cold 6 N hydrochloric acid. The precipitated acid was separated by filtration, washed with a small quantity of cold water and dried.

The crude acid was recrystallized once from ether-petroleum ether (b. p. 85-90°) and gave 0.6 g. (70%) of pure acid crystallizing as long white needles, m. p. 155-156°. Lit. 119° (13).

Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{O}_2\text{S}$: C, 62.48; H, 4.19. Found: C, 62.71; H, 4.17. Neut. Equivalent: Calcd.: 192. Found: 191.

Infrared spectrum (KBr): 1702 cm^{-1} (acid C=O).

REFERENCES

- (1) H. D. Hartough and S. L. Meisel, "Compounds with Condensed Thiophene Rings," Interscience Publishers, Inc., New York (1954).
- (2) A. V. Sunthakar and B. D. Tilak, *Proc. Indian Acad. Sci.*, **33A**, 35 (1951).
- (3) A. V. Sunthakar and B. D. Tilak, *ibid.*, **32A**, 396 (1950).
- (4) K. Rabindran and B. D. Tilak, *ibid.*, **32A**, 390 (1950).
- (5) R. B. Mitra, K. Rabindran and B. D. Tilak, *J. Sci. Ind. Res. (India)*, **158**, 627 (1956).
- (6) G. M. Badger, D. J. Clark, W. Davies, K. T. H. Farrer and N. P. Kefford, *J. Chem. Soc.*, 2624 (1957).
- (7) S. Gronowitz, *Acta Chem. Scand.*, **13**, 1045 (1959).
- (8) M. S. Newman and H. Boden, *J. Org. Chem.*, **26**, 2525 (1961).
- (9) L. F. Fieser and R. G. Kennelly, *J. Am. Chem. Soc.*, **57**, 1611 (1935).
- (10) S. Gronowitz, "Advances in Heterocyclic Chemistry," Editor

A. R. Katritzky, Academic Press Inc., New York, N. Y., 1963, Vol. I, p. 54.

(11) P. Cagniant and P. Cagniant, *Bull. Soc. Chim. France*, 62 (1953).

(12) M. C. Kloetzel, J. E. Little and D. M. Frisch, *J. Org. Chem.*, 18, 1511 (1953).

(13) N. P. Kefford and J. M. Kelso, *Australian J. Biol. Sci.*, 10, 80 (1957).

(14) C. Troyanowsky, *Bull. Soc. Chim. France*, 425 (1955).

(15) M. S. Newman, "Organic Synthesis," Collective Volume III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 631.

(16) E. Campaigne and H. L. Thomas, *J. Am. Chem. Soc.*, 77, 5368 (1955).

(17) S. Gronowitz, *Arkiv Kemi.*, 12, 533 (1958).

Received January 11, 1965

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