

A New Synthesis of 4-Hydroxybenzo[*b*]thiophene

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We wish to report a convenient method for the preparation of 4-hydroxybenzo[*b*]thiophene (**4**) (**1**). The simplicity of this new method allows the formation of large quantities of **4**. Fieser and Kennelly (**2**) have previously reported a preparation of **4** which employed thiophene as a starting material with consequent cyclization of the Friedel-Crafts derived γ -(2-thienyl)butyric acid followed by aromatization.

Our route avoids several problems associated with the aromatic substitution reaction on thiophene especially when carried out on a large scale. We felt that the addition of mercaptoacetaldehyde diethylacetal to 2-cyclohexen-1-one (**3,4**), followed by an intramolecular aldol condensation of the hydrolysis product would afford 4-oxo-2,4,5,6,7,7a-hexahydrobenzo[*b*]thiophene (**2**), a precursor of phenol **4**. Tilak and co-workers (**5**) have reported a related reaction whereby ethylmercaptoacetate was added to methyl vinyl ketone to give 2-carboethoxy-3-hydroxy-3-methyl-tetrahydrothiophene which was in turn dehydrated to 2-carboethoxy-3-methyl-2,5-dihydrothiophene.

The Michael addition of mercaptoacetaldehyde diethylacetal (**6**) with 2-cyclohexen-1-one readily formed 3-(2,2-diethoxyethylthio)cyclohexanone (**1**). Acetal **1** was subsequently hydrolysed and cyclized to afford 4-oxo-

2,4,5,6,7,7a-hexahydrobenzo[*b*]thiophene (**2**). Ketone **2** represented the successful construction of the benzo[*b*]thiophene ring skeleton from readily obtainable aliphatic starting materials.

Ketone **2** was oxidized with sulfur in diphenyl ether (**7**) to give 4-hydroxybenzo[*b*]thiophene (**4**). The overall yield of **4** from **2** was improved by oxidation of **2** to 4-oxo-4,5,6,7-tetrahydrobenzo[*b*]thiophene (**3**) with chloranil (**8**). Ketone **3** exhibited an infrared spectrum identical in all respects with authentic material (**2**), and was subsequently converted to **4** by treatment with sulfur.

EXPERIMENTAL (10)

3-(2,2-Diethoxyethylthio)cyclohexanone (**1**).

A solution of 126.0 g. (1.31 moles) of 2-cyclohexen-1-one, 207.0 g. (1.38 moles) of mercaptoacetaldehyde diethylacetal, and 20 drops of piperidine was heated at 80° for 22 hours. Ether (100 ml.) was added and the solution was extracted successively with 100 ml. of cold 10% hydrochloric acid, 100 ml. of water, 100 ml. of cold 5% sodium bicarbonate and 125 ml. of brine. The organic phase was dried (Drierite) and concentrated to give an oil which was distilled to afford 181.0 g. (73%) of **1**, b.p. 114° at 0.05 mm; infrared cm^{-1} , 2945 (s), 1710 (vs), 1125 (b), 1060 (s); NMR (neat) δ 1.54 (6H, triplet), 2.70 (11H, multiplet), 3.90 (4H, quintet), 4.95 (1H, triplet).

Anal. Calcd. for $\text{C}_{12}\text{H}_{22}\text{O}_3\text{S}$: C, 58.50; H, 9.00; S, 13.01. Found: C, 58.40; H, 8.87; S, 13.20.

4-Oxo-2,4,5,6,7,7a-hexahydrobenzo[*b*]thiophene (**2**).

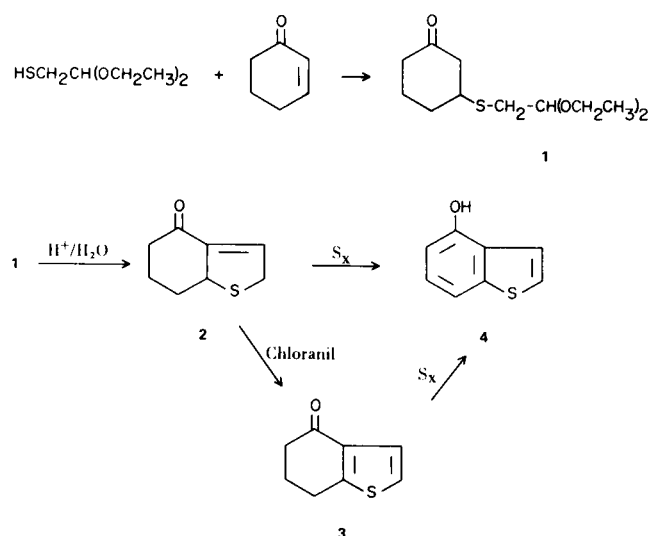
To a stirred solution of 9.0 g. (0.037 mole) of 3-(2,2-diethoxyethylthio)cyclohexanone in 30 ml. of xylene at 96° was added 2.8 ml. of 10% hydrochloric acid. Heating and stirring were continued for one hour. After cooling, the layers were separated and the aqueous phase washed with 30 ml. of xylene. The combined organic layers were stripped of solvent and the resultant liquid was distilled at 86° (0.5 mm) to afford 4.6 g. (82%) of **2** which crystallized on standing. Recrystallization from 30-60° petroleum ether furnished pure **2**, m.p. 49-51°; infrared cm^{-1} , 2945 (s), 1699 (vs), 1630 (s), 1255 (m), 1240 (w), 923 (w), 892 (w); NMR (carbon tetrachloride) δ 2.10 (6H), 3.75 (2H), 4.40 (1H), 6.45 (1H).

Anal. Calcd. for $\text{C}_8\text{H}_{10}\text{OS}$: C, 62.30; H, 6.54. Found: C, 62.12; H, 6.51.

4-Oxo-4,5,6,7-tetrahydrobenzo[*b*]thiophene (**3**).

A mixture of 9.8 g. (0.064 mole) of **2**, 15.7 g. (0.063 mole) of chloranil, and 200 ml. of xylene was heated with stirring at 90° for 3 hours. The temperature was raised to 100° for 5.5 hours

FIGURE 1



before another 1.0 g. of chloranil was added and heating was continued at 100° for 1.5 hours. The mixture was cooled and filtered and the filtrate was treated with 5% sodium hydroxide, washed with water, dried (magnesium sulfate), and evaporated to give an oil. Distillation at 92° (1.0 mm) furnished 9.7 g. (63%) of **3** which crystallized on standing, m.p. 36°, [lit (2) 35.5-37°]; infrared cm^{-1} , 2995 (s), 1689 (vs), 1540 (m), 1410 (s), 1275 (s), 1200 (m), 935 (m), 750 (w), 715 (w).

4-Hydroxybenzo[*b*]thiophene (**4**).

A.

A mixture of 1.0 g. (0.0065 mole) of **2**, 0.42 g. of sulfur and 10 ml. of diphenyl ether was heated at 247° for one hour and then vacuum distilled. Ether (50 ml.) was added and the solution was extracted with 10% sodium hydroxide. The aqueous layer was separated, acidified with 10% hydrochloric acid, and extracted with benzene. The organic layer was separated, washed with 5% sodium bicarbonate solution, dried (Drierite), and concentrated to afford 0.24 g. (25%) of **4**, m.p. 80-81°, [lit (2) 80-81°]; infrared cm^{-1} , 3400 (vs), 1580 (s), 1430 (m), 1383 (m), 935 (s), 750 (m). The *N*-methyl urethan of **4** had m.p. 129-130° [m.m.p. 129-130° with authentic urethan (9)].

B.

A mixture of 15.2 g. (0.1 mole) of **3**, 3.2 g. of sulfur and 150 ml. of diphenyl ether was heated at 247° for one hour and the product was isolated as in A to afford 9.1 g. (60%) of **4**, identical to product obtained by method A.

Acknowledgment.

The authors wish to thank Dr. John R. Kilsheimer and Dr. Sheldon Chibnik for helpful discussions.

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Received July 3, 1969

Edison, New Jersey 08817

Revised February 2, 1970