Tetrahedron Letters No. 47, pp 4823 - 4826, 1972. Pergamon Press. Printed in Great Britain.

OXIDATIONS BY THIONYL CHLORIDE. IV. BENZO[b]THIOPHENES AND OXOINDENO[2,3-d]BENZO[b]THIOPHENES VIA SULFENYL CHLORIDES[1]

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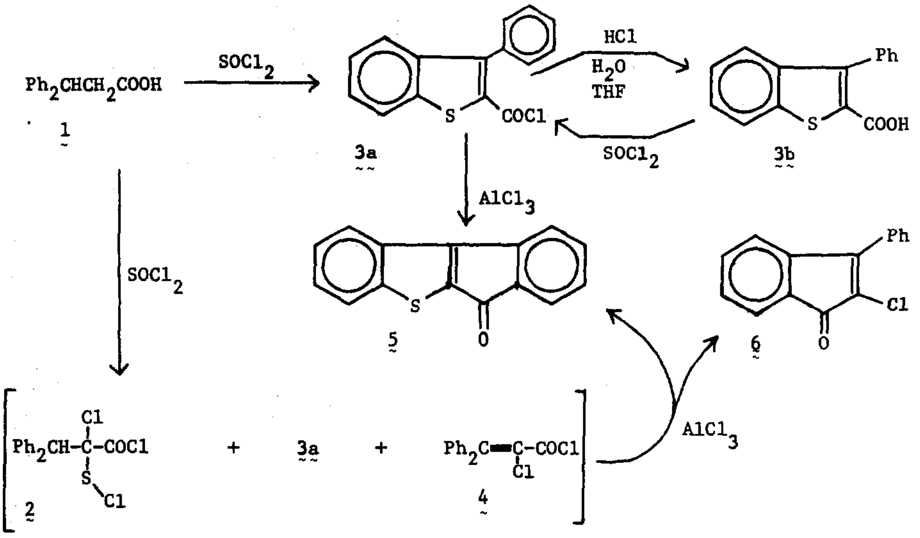
(Received in USA 25 September 1972; received in UK for publication 23 October 1972)

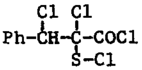
The reaction of hot thionyl chloride, in the presence of catalytic amounts of pyridine, on 3-phenylpropanoic acids constitutes one of the most direct routes to benzo[b]thiophenes.[2] It was of particular interest to us to extend this reaction to a variety of propanoic acids because the method showed promise of being a one-step synthesis of 3-alkyl- or 3-aryl-substituted benzo[b]thiophenes. The preparation of 3-phenylbenzo[b]thiophene-2-carboxylic acid, **3b**, by this route seemed to offer a practical challenge, since the previous synthesis of **3b** involved a six-step sequence starting from 2-chloro-5-nitrobenzoic acid.[3]

When 3,3-diphenylpropanoic acid, **1**, was treated with an excess of thionyl chloride in the presence of pyridine at 120-130° over a period of 3 hr, **3a** was obtained in quantitative yield as a viscous yellow oil. (The infrared spectrum of this oil was identical to that of the product obtained from the mild reaction of **3b** with thionyl chloride.) Oil **3a** was converted to **3b** (65%, mp[3] 199-200°) by heating it at reflux for 3 hr with 2.5% hydrochloric acid in aqueous tetrahydrofuran.



The intermediate in this sequence was shown to be the expected α-chloro-α-chlorosulfenyl derivative, 2, by heating 1 under reflux for 21 hr with an excess of thionyl chloride and 0.12 equivalent of pyridine. The viscous yellow oil obtained as the product was composed of 2 [72%, nmr ($CDCl_3$)τ2.70 (m) and 4.75 (s)], 3a, and 4. When it was attempted to convert crude 2 to 3a by the action of anhydrous aluminum chloride in dry methylene chloride at 0° for 1 hr, red crystalline 5 [63% from 1, mp 194.5-196°; ir (KBr) 5.80, 5.88, and 6.22 μm; nmr ($CDCl_3$)τ1.97-2.94 (m); m/e[4] 237 (P + 1), 236 (M^+, base) and 208 (-CO); calcd for $C_{15}H_8OS$, 236.02958; found, 236.02948] and 6 [12% from 1, mp[5] 100.5-101°; ir (KBr) 5.83 and 6.26 μm; m/e[4] 242 (P + 2), 240 (M^+, base) and 205 (-Cl)] were found to have formed instead.

1-Oxoindeno[2,3-d]benzo[b]thiophene, 5, was assumed to have formed by cyclization of 2 to 3a followed by a Friedel-Crafts cyclization of 3a to 5. Support for this supposition was obtained by treating 3a with aluminum chloride in methylene chloride in the same manner as described above; there was observed a 93% conversion of 3a to 5, and a 40% recovery of 3b. Compound 5 could also be obtained by stirring 7[2a] with aluminum chloride in benzene (1 hr, 10-15°, 42% yield). Presumably 6 is formed by a Friedel-Crafts cyclization of 4.[5]



$$\text{Ph-}\overset{\text{Cl}}{\text{CH}}\text{-}\underset{\text{S-Cl}}{\overset{\text{Cl}}{\text{C}}}\text{-COCl}$$

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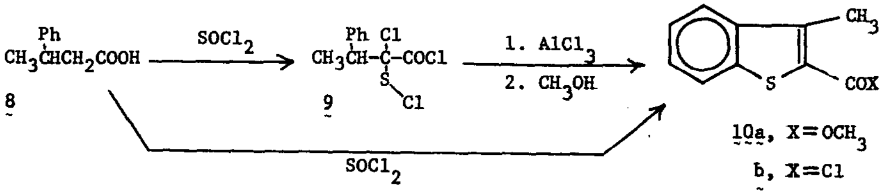
Additional evidence for the **1** to **2** to **3a** sequence was obtained indirectly by treating 3-phenylbutanoic acid, **8**, with thionyl chloride (pyridine, reflux, 21 hr), as described for the formation of **2**. Sulfenyl chloride, **9** [nmrτ2.72 (m, aromatic protons), 5.98 and 6.09 (two sets of quartets, methine proton), and 8.42 and 8.53 (two sets of doublets, methyl protons); ir (neat) 5.60, 5.70 sh, 6.72, 6.90, 7.37, 9.58, and 9.77 μm], was found to constitute 90% of the product mixture. The nmr spectrum was somewhat novel in that it showed clearly that **9** was a 1:1 mixture of diastereomers. Further treatment of **9** with aluminum chloride in methylene chloride, followed by a methanolic work-up, afforded **10a** [66%, mp[6] 102.5-103°; nmr ($CDCl_3$)τ2.29 and 2.67 (m, 4H), 6.14 (s, 3H), and 7.32 (s, 3H)] as yellow needles. Heating of **8** with thionyl chloride (pyridine, 8 hr at 120-130°) was found to be an impractical route to **10b**. The acid chloride **10b** could be isolated in only small amounts (16%, crude) from a mixture that consisted of mostly **9**. The slow cyclization of **8** to **10b** is unusual, and is an important clue to the mechanism of cyclization.[2a]



We feel that the action of thionyl chloride on 3-phenylpropanoic acids is a route of great promise for facile entry into a variety of complex products, including benzo[b]thiophenes and 1-oxoindeno[2,3-d]benzo[b]thiophenes. The 3-phenylpropanoic acid route to benzo[b]thiophenes is of especial importance because it should permit the introduction of substituents of choice in the 3-position of benzo[b]thiophenes. In contrast, the cinnamic acid route[2,7,8] is limited to only a 3-chloro substituent.

We are continuing our investigations of the high potential of sulfenyl chlorides, prepared by the oxidation of carboxylic acids by thionyl chloride, as synthetic intermediates.

FOOTNOTES AND REFERENCES

1. Taken in part from the Ph.D. dissertation of T. H., The Ohio State University, 1971.
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4. We thank Mr. Dick Weissenberger for the mass spectral measurements, and the National Science Foundation for a grant (GP-5202) to the chemistry department of The Ohio State University for the mass spectrometer.

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