

OXIDATIONS BY THIONYL CHLORIDE. III. MECHANISM OF
BENZO[b]THIOPHENE FORMATION FROM SULFENYL CHLORIDES (1)

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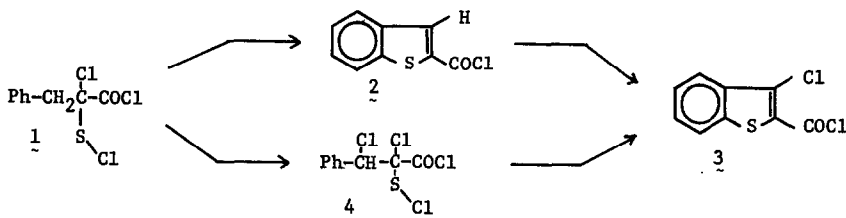
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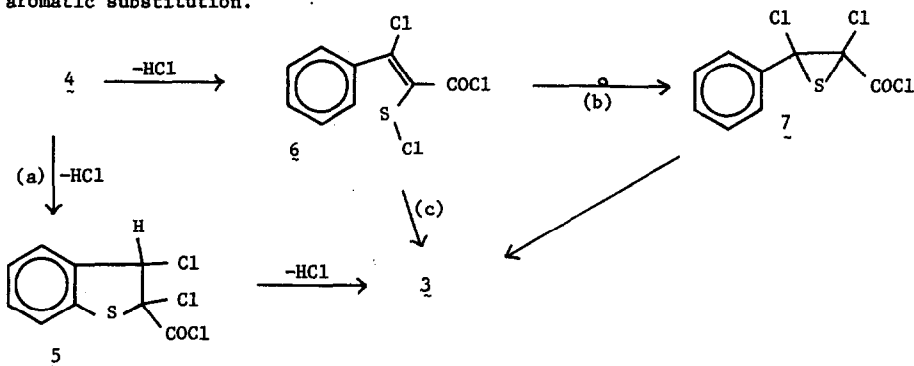
Recently studies of the oxidation of carbon atoms by thionyl chloride have shown that carboxylic acids and certain ketones can be converted to benzo[b]thiophenes (2), and methyl ketones can be converted to 3-thietanones (3). Although the mechanism of the latter event seemed rather straightforward, the sequence for a portion of the former was by no means clear. It appeared initially that the intermediate sulfenyl chloride, 1, was undergoing an electrophilic aromatic substitution reaction to form benzo[b]thiophene, 2, which upon further reaction with thionyl chloride formed the ultimate benzo[b]thiophene, 3.

We tested this proposal by preparing 2 by an unambiguous method (treatment of 1 with anhydrous aluminum chloride in dry methylene chloride at 0° for 1 hr, furnishing 2, mp 236-238°, in 61% yield) and subjecting it to the identical conditions that converted 1 to 3. The poor yield and slow rate of formation of 3 from 2 ruled against the intermediacy of 2. When, however, proposed intermediate, 4 (prepared by treating cinnamic acid with thionyl chloride in the presence of traces of pyridine at an oil bath temperature of 88° for 24 hr, affording 4, bp 107°/0.08 mm, in 19% yield) was heated with pyridine hydrochloride at 130° for 5 hr, a mixture of 3, 4, and α -chlorocinnamoyl chloride was obtained (ratio by nmr of 38:32:30), from which 3 was isolated

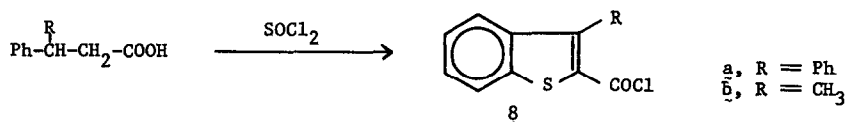
in 36% yield. This result strongly supported **4** as an intermediate.



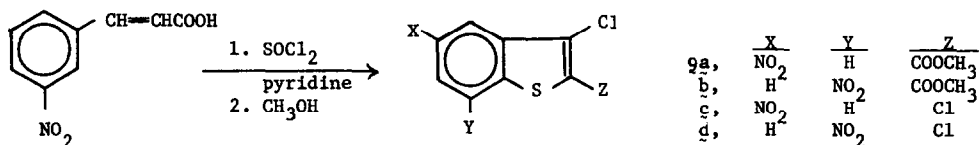
At least three mechanisms could now be proposed to account for ring closure of **4** to **3**: (a) An electrophilic aromatic substitution reaction would afford **5** which upon loss of hydrogen chloride would furnish **3**. (b) Formation of **6** and subsequent rearrangement of **6** to episulfide **7** would permit sulfur to attack the aromatic ring in either a concerted process or a nucleophilic aromatic substitution step to give **3**. (c) Sulfonyl chloride, **6**, could give **3** directly by electrophilic aromatic substitution.



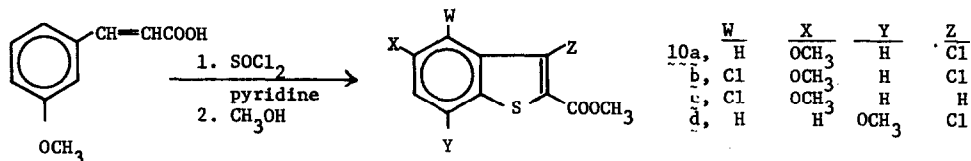
Both electrophilic aromatic substitution processes (a) and (c) were eliminated by the following experimental results. First, under conditions (heat in the presence of pyridine hydrochloride) in which **4** readily yielded **3**, **1** furnished only intractable tar rather than a benzo[*b*]thiophene. Secondly, 3,3-diphenylpropanoic acid, when treated with thionyl chloride and pyridine, produced benzo[*b*]thiophene, **8a**, in 65% yield, but 3-phenylbutanoic acid produced **8b** in only 16% yield (4). Thus where steric hindrance might be expected to lower the yield, the reaction proceeds far better. Thirdly, treatment of *m*-nitrocinnamic acid with thionyl



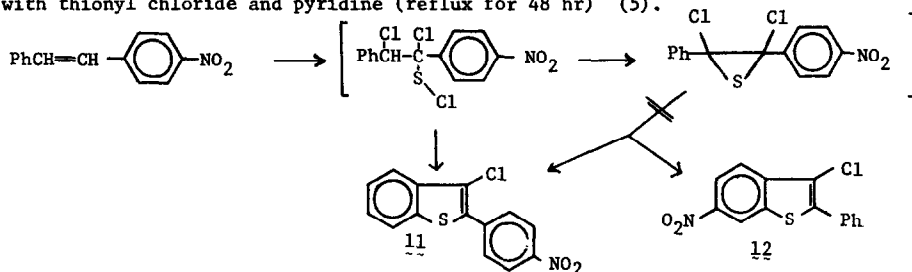
chloride in the presence of catalytic amounts of pyridine (135°, 1.5 hr) and then with methanol readily furnished the four benzo[*b*]thiophenes 9a (23%, mp 186–190°), 9b (23.4%, mp 196.5–197°), 9c (1%, mp 182–183.5°), and 9d (1.5%, mp 140–141°). Since the *m*-nitro group would be expected to prevent very effectively any type of electrophilic reaction, these results furnished strong evidence against such a process but suggested instead a nucleophilic reaction.



The intermediacy of an episulfide was therefore examined in two ways. First, *m*-methoxystilbene was allowed to react with thionyl chloride in the presence of catalytic amounts of pyridine. The fact that benzo[*b*]thiophenes 10a (26.4%, mp 115–116°), 10b (1.7%, mp 172–172.8°), and 10c (0.9%, mp 159–160°) were formed at 140° for 70 min, and 10a (54.4%), 10b (6%), and 10d (2%) were formed at 105° for 48 hr, both milder conditions than that used with the *m*-nitro derivative, argued against a nucleophilic reaction. Furthermore, an episulfide intermediate

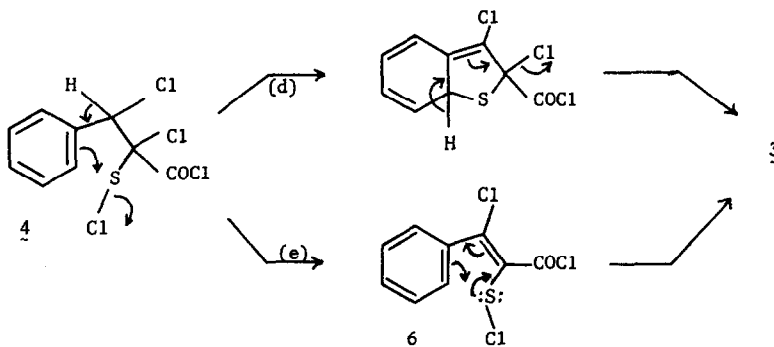


could explain neither the formation of 10c nor the formation of only 11 (15.2%, mp 154–155°, nmr AA'BB' pattern at τ 1.60 and 1.94, $J = 9.0$ Hz) and not also 12 when *p*-nitrostilbene was treated with thionyl chloride and pyridine (reflux for 48 hr) (5).



Some of these data, however, seemed to have special significance. These included the apparent dependency of the success of benzo[*b*]thiophene formation on the acidity of the benzylic hydrogen atom (e.g. when that position bears an additional phenyl group or a chlorine atom) (4), and the formation of a benzo[*b*]thiophene that is unsubstituted at the 3-position (e.g. 10c).

We feel that either one of two concerted-type mechanisms (to explain the lack of an obvious substituent effect) will satisfactorily explain all of the observed data. In mechanism (d) a concerted elimination-cyclization affords an intermediate which, upon loss of another molecule of hydrogen chloride through re-aromatization affords **3**. In mechanism (e), the conjugated 6π -electron system of intermediate **6** undergoes a concerted cyclization in what should be a thermally allowed process. The success of either mechanism is dependent in part on the benzylic hydrogen atom being acidic enough to be lost either simultaneous with or prior to cyclization.



These results, we believe, will play an important part in determining the direction that related studies^{5,6} of thionyl chloride reactions will take.

We are continuing our investigations with cinnamic and hydrocinnamic acids, and with stilbene derivatives, in order to further define the mechanisms of these reactions.⁷

FOOTNOTES AND REFERENCES

1. Taken in part from the Ph.D. dissertation of T. H., The Ohio State University, 1971.
2. A. J. Krubsack and T. Higa, *Tetrahedron Lett.*, 5149 (1968).
3. A. J. Krubsack, T. Higa, and W. E. Slack, *J. Amer. Chem. Soc.*, **92**, 5258 (1970).
4. A. J. Krubsack and T. Higa, *Tetrahedron Lett.*, in press.
5. For related work with stilbenes, see S. Nakagawa, J. Okumura, F. Sakai, H. Hoshi, and T. Naito, *Tetrahedron Lett.*, 3719 (1970).
6. For example, see W. B. Wright, Jr., and H. J. Brabander, *J. Heterocycl. Chem.*, **8**, 711 (1971); W. B. Wright, Jr., *J. Heterocycl. Chem.*, **9**, 879 (1972).
7. We thank the National Science Foundation for a grant (GP 31761 X) in partial support of this work.