

MECHANISM OF THE ABNORMAL REACTION OF THIONYL CHLORIDE

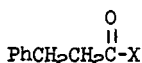
WITH CARBOXYLIC ACIDS (1)

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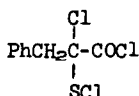
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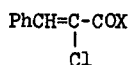
In a recent paper (3) the authors suggested that the abnormal reaction of thionyl chloride with 4-nitro-2,5-dimethoxyphenylacetic acid to give a sulfenyl chloride proceeded by means of a mechanism which involved oxidation of a benzylic position. Although it was equally probable in this case that the oxidation was a result of the carbon atom being adjacent to a carbonyl group rather than an aromatic ring, this alternate possibility apparently was not considered (3). We wish to present definitive evidence herein that the oxidation occurs at the  $\alpha$ -carbon atom of the carbonyl group rather than at a benzylic position. Further, we wish to demonstrate that the reaction is of a much more general (and consequential) nature than had been supposed heretofore, and to suggest mechanisms for this reaction and for the further reactions which the sulfenyl chloride undergoes under the reaction conditions.



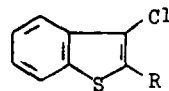
1 a, X = OH  
b, X = Cl



2



3 a, X = Cl  
b, X = OH

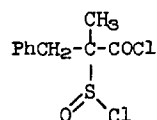
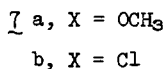
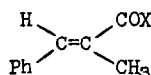
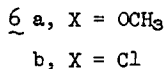
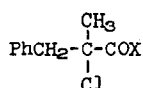
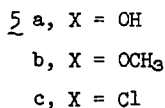
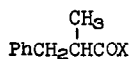


4 a, R = COCl  
b, R = COOH  
c, R = H

When 1a was heated under reflux for 14 hr. with excess thionyl chloride and 0.08 equiv. of pyridine, it gave rise to 3-phenylpropanoyl chloride (1b), 11%, and a yellow liquid, b.p. 92-94° (0.14 mm), 61%, which on the basis of exact mass, mass, NMR, and IR spectra (4) was regarded as the sulfenyl chloride 2. Conversion of 2 to phenylpyruvic acid by basic hydro-

lysis confirmed the structural assignment. In addition, treatment of 1a with thionyl chloride and pyridine at 115-127° for 2.5 hr. afforded 1b, 5%, and 2, 2%, as well as 2-chloro-3-phenylpropenoyl chloride (3a), b.p. 97-102° (0.33 mm), 22.4%; 3-chloro-2-chlorocarbonylbenzo[b]thiophene (4a), m.p. 114.4-115.1°, 31.4%; and sulfur. The structures of these products were established (i) by basic hydrolysis of 3a to the known (5) 3b and (ii) by hydrolysis (aqueous dioxane) of 4a and decarboxylation (copper chromite) of the resulting 4b to the known (6) 3-chlorobenzo[b]thiophene (4c). The ultraviolet spectrum (4) of 4c was essentially identical to the reported (7) spectrum of 3-bromobenzo[b]thiophene.

From the experimental results it appeared that a logical sequence for these events followed the path 1a to 1b to 2 to 3a and 4a. On the basis of this surmise and with the aim of observing these individual events, the reaction of 1a with pyridine and refluxing thionyl chloride was studied over a 36-hr. period. Both IR and NMR spectroscopy demonstrated the initial, rapid, and complete conversion of 1a to 1b, followed by the formation of 2 and the slow formation of 3a and 4a as 1b disappeared. In addition, in a separate experiment, the sulfonyl chloride, 2, was converted to 3a and 4a with thionyl chloride (2 equiv.) and pyridine (0.1 equiv.) at 120° for four hours; the NMR spectrum revealed the product to be a mixture of 2, 3a, and 4a in the ratio of 25:41:34.



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A study of the reaction of 2-methyl-3-phenylpropanoic acid (5a) with refluxing thionyl chloride and pyridine gave rise to similar results. In this case, decomposition of the reaction mixture with methanol provided ester 5b, 10%; the reported (8) methyl 2-chloro-2-methyl-3-phenylpropanoate (6a), 29%; and the known (9) methyl ester 7a, 26%. Closer examination of this reaction by IR spectroscopy for 13 days over the temperature range of 46 to 85° provided additional insight into the mechanism of the sequence. Acid chloride 5c (5.57μ) was observed to form initially, rapidly, and completely. Significantly, as absorption due to 5c diminished, other absorption due to 7b (6.18μ) and what seems to be sulfinyl chloride 8 (8.55μ) (10) appeared and increased gradually in intensity.



(13). The evidence suggests that the role of pyridine is to promote enolization, for in the absence of pyridine, 1a still gives rise to 2 but at a much reduced rate.

These data unequivocally establish that the abnormal reaction of thionyl chloride with carboxylic acids proceeds by a mechanism which involves oxidation of the  $\alpha$ -carbon atom rather than the reported (3) oxidation of a carbon atom adjacent to an aromatic ring. We have found no evidence whatsoever in support of the latter contention. Furthermore, our continuing studies on the scope of this reaction reveal it to be general for even saturated carboxylic acids as well as a variety of other carbonyl-containing compounds. In some cases the reaction proceeds exothermically at room temperature (4). Clearly, thionyl chloride as a reagent in organic chemistry must be used with extreme caution, especially if it is used in excess and pyridine (or, presumably, another tertiary amine) is used as a catalyst.

#### FOOTNOTES AND REFERENCES

1. This investigation was supported in part by a Grant-in-Aid from the College of Arts and Sciences of The Ohio State University.
2. Grantee of the Ryukyuan Scholarship Program, sponsored by the Department of the Army.
3. M. S. Simon, J. B. Rogers, W. Saenger, and J. Z. Gougoutas, J. Am. Chem. Soc., 89, 5838 (1967).
4. Details of the spectral data of all compounds reported herein and of the reactions of thionyl chloride with a variety of carbonyl compounds will be presented in a forthcoming paper.
5. J. R. A. Pollock and R. Stevens, Eds., "Dictionary of Organic Compounds," 4th ed., Vol. 2, Eyre and Spottiswoode, Publishers, Ltd., London, 1965, p. 610.
6. A. H. Schlesinger and D. T. Mowry, J. Am. Chem. Soc., 73, 2614 (1951).
7. A. S. Angeloni and M. Tramontini, Ann. Chim. (Rome), 53, 1665 (1963).
8. A. V. Dombrovsky, A. P. Terentyev, and A. M. Yurkevich, J. Gen. Chem. USSR, 27, 473 (1957).
9. H. Kasiwagi, N. Nakagawa and J. Niwa, Bull. Chem. Soc. Jap., 36, 410 (1963).
10. H. E. Simmons, D. C. Blomstrom, and R. D. Vest, J. Am. Chem. Soc., 84, 4782 (1962).
11. F. G. Bordwell and B. M. Pitt, J. Am. Chem. Soc., 77, 572 (1955).
12. (a) H.-D. Becker, J. Org. Chem., 29, 1358 (1964); (b) S. Oae, T. Kitoa, S. Kawamura, and Y. Kitaoka, Tetrahedron, 19, 817 (1963).
13. Thionyl chloride adds to the double bond of the acid chloride of trans-cinnamic acid when the latter is treated with pyridine and refluxing thionyl chloride for 2.5 hr. The products which are isolated are 3a, 13%, and 4a, 61% (unpublished results from This Laboratory).
14. P. W. Schenk and R. Steudel, Angew. Chem., 77, 437 (1965).