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NEW SYNTHETIC REACTION WITH THIONYL CHLORIDE

OXIDATION OF ACTIVE METHYL-COMPOUNDS TO THIOACYL CHLORIDES

Kitaro Oka* and Shoji Hara
Laboratory of Organic Chemistry, Tokyo College of Pharmacy
Horinouchi 1432-1, Hachioji, Tokyo 192-03, Japan

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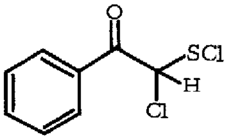
A great deal of interest has been generated in the reactions of thionyl chloride with a broad spectrum of organic functional groups, and these investigations have been extensively reviewed.[1a,b] However, in these reviews, there has been a little attention devoted to some of the lesser known but nevertheless rather general reactions of this reagent with active methylene (or methyl) groups, because these reactions, at first sight, appear to be extremely varied and complex.

It has been clearly shown by Simon, et al.[2] that the treatment of phenylacetic acid with excess thionyl chloride in the presence of 0.35 molar equivalent of pyridine at reflux temperature afforded α-chloro-α-chlorosulfenylphenylacetyl chloride. Subsequently Krubsack and Higa[3] and Ohoka, et al.[4] have synthesized the analogous compounds.

The object of the present paper is to apply this oxidation reaction to active methyl-compounds, since one might reasonably expect such α-chlorosulfenyl chlorides derived from methyl groups might be easily dehydrochlorinated to thioacyl chlorides. Such derivatives are not well-known chemical species[5] but seem to be of considerable synthetic significance as the starting materials for thioamides[5c] and sulfur-containing or non-sulfur-containing heterocycles. These applications will be reported elsewhere.

When acetophenone[6] was dissolved in 10-15 molar equivalents of thionyl chloride in the presence of 0.02 molar equivalent of pyridine[7] at 20°C, spontaneous evolution of hydrogen chloride and sulfur dioxide was observed. After two and a half hours, the excess thionyl chloride was evaporated at room temperature and products were purified on silica gel column eluted with benzene to give an inseparable mixture of equimolar amounts of two components in 95% yield. The NMR spectrum of the mixture revealed that one of the components was α-chloro-α-chlorosulfenylacetophenone (1, NMR ($CDCl_3$) δ 6.62 (ClS-CH-Cl), 7.35-7.60 (*m*-H_2 and *p*-H), 7.93 (*o*-H_2)) and the other one had no side chain-hydrogen (δ 7.35-7.60 (*m*-H_2 and *p*-H), 8.18 (*o*-H_2)). The mass spectrum of the mixture showed the strong peak at m/e 184 (C_8H_5ClOS), and the ir spectrum exhibited the C=S streching band at 1230 cm^{-1}. Furthermore, when the mixture was heated in thionyl chloride, the intensity of the multiplet at δ 8.18 gradually increased, while the singlet at δ 6.62 and the multiplet at δ 7.93 decreased. These facts indicated the formation of benzoylthioformyl chloride (2) from the sulfenyl chloride (1) by elimination of hydrogen chloride. Further elucidation of these structures was supported by the chemical conversion of the mixture into *N*,*N*-dimethyl-benzoylthioformamide (3, mp 84-85°; lit.[8] 86-87°) in 95% yield.



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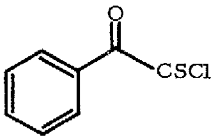

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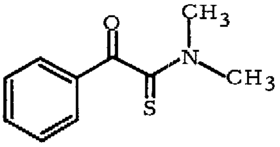

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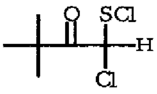

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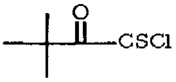

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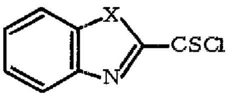
$MeOOC-\overset{O}{\overset{\|}{C}}-CSCl$

6



7a X=O
b X=S

To extend the scope of the reaction, several aliphatic and aromatic active methyl-compounds were subjected to this oxidation condition and the results are summarized in Table 1.

Table 1

Substrate	Product	Condition	Yield	δ (CDCl$_3$)		ν cm^{-1}(neat)	
			%	CH$_3$	ClSCHCl	C=O	C=S
Pinacolone	4 + 5	r.t., 2 days	96	1.23 1.46	6.15	1715	1215
Methyl pyruvate	6	reflux, 2.5 hrs	85	3.97	—	1743	1275
2-Methylbenzoxazole	7a	reflux, 3 hrs	75	—	—	—	1236
2-Methylbenzothiazole	7b	reflux, 3 hrs	80	—	—	—	1230

It is worth mentioning that the mechanism of the known synthesis of acyl chlorides from 6-methylnicotinic acid[9] and 2,4-dimethylthiazole-5-carboxylic acid[10] with excess thionyl chloride is now easily understandable in terms of an oxidative desulfurization of thioacyl chlorides by air at elevated temperatures for a long time.[11] The oxidation of thiobenzoyl chloride to benzoyl chloride with molecular oxygen has been already reported by Staudinger and Siegwart.[5a] The recently reported abnormal products from 4-methylnicotinic acid by Wenkert, et al.[12] or from *o*-ethylaniline by Davis, et al.[13] can be also elucidated logically *via* thioacyl chlorides as intermediates.

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