

A CONVENIENT METHOD FOR THE PREPARATION OF CARBOXYLIC ACID FLUORIDES

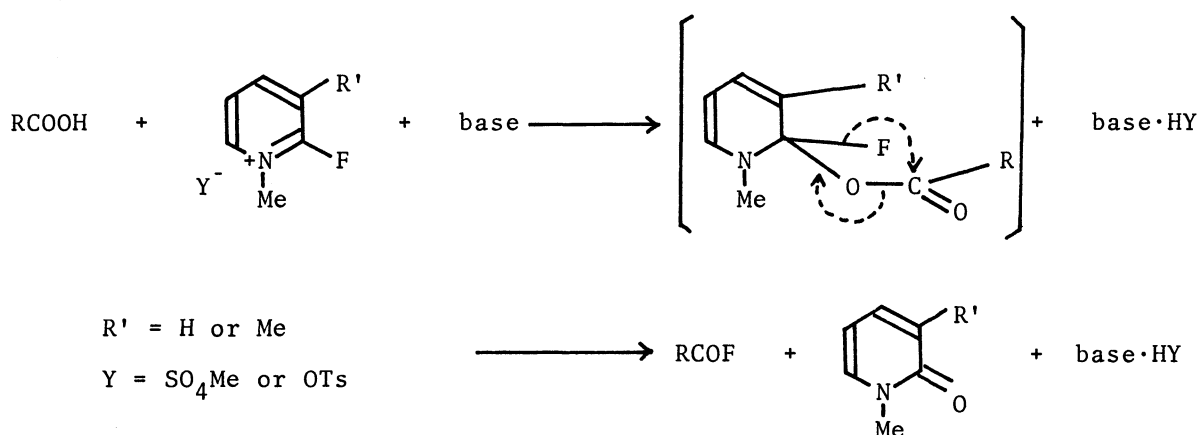
Teruaki MUKAIYAMA and Toshio TANAKA

Department of Chemistry, Faculty of Science,
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

Various carboxylic acid fluorides are prepared in good yields by treating carboxylic acids with 2-fluoro-1,3-dimethylpyridinium salts in the presence of tertiary amines such as triethylamine.

In the preceding papers, it was reported that carboxylic acids reacted rapidly with an equimolar amount of various alcohols or amines in the presence of 2-halopyridinium salts and bases to provide the corresponding carboxylic esters¹⁾ or carboxamides²⁾, respectively, in good yields. Further developments³⁾ of useful synthetic reactions by utilizing the onium salts of azaaromatics were also reported. In the course of our investigation on the reaction mechanism of the esterification or amidation, it was found that carboxylic acids reacted easily with 2-fluoropyridinium salts in the presence of such bases as triethylamine to give the corresponding carboxylic acid fluorides in good yields.

In a typical procedure for the preparation of carboxylic acid fluorides, a solution of triethylamine (0.6 g, 6 mmol) in dichloromethane (1 ml) was slowly added at room temperature under an argon atmosphere to a stirred mixture of lauric acid (1.0 g, 5 mmol) and 2-fluoro-1,3-dimethylpyridinium tosylate (1.8 g, 6 mmol) in dichloromethane (2 ml), and then the reaction mixture was stirred at room temperature for an additional 10 min. After removal of the solvent at atmospheric pressure, the residue was directly distilled to give lauroyl fluoride in quantitative yield (1.0 g, 5 mmol); b.p. 114 ~ 116°C/17 mmHg. In a similar manner, various carboxylic acid fluorides were successfully prepared from carboxylic acids and 2-fluoro-1,3-dimethylpyridinium tosylate as summarized in the table.



In this reaction, the base was found to be essential for the formation of carboxylic acid fluorides. On addition of the base at room temperature to a mixture of carboxylic acid and pyridinium salt such as 2-fluoro-1,3-dimethylpyridinium tosylate, 2-fluoro-1-methylpyridinium tosylate, or 2-fluoro-1,3-dimethylpyridinium methylsulfate, the ir and uv spectroscopic measurements exhibited the complete formation of the carboxylic acid fluoride and the corresponding pyridone in the reaction mixture, respectively. Thus, it was thought that the carboxylic acid fluoride was immediately yielded by the intramolecular nucleophilic displacement of fluorine in the intermediate formed by the addition of carboxylate anion to 2-fluoropyridinium salt at the carbon attached to fluorine as sketched in the scheme similar to the cases of 2,4-dinitrofluorobenzene⁴⁾⁵⁾ or cyanuric fluoride.⁶⁾ When 2-chloropyridinium salts were used instead of 2-fluoropyridinium salts in the above experiment, carboxylic acids were predominantly led to acid anhydrides. The formation of acid anhydrides in the case of 2-chloropyridinium salts can be rationalized by assuming that acid chlorides are too reactive toward the remaining carboxylic acids to survive in the presence of bases.

Concerning the preparation of carboxylic acid fluorides, there are a variety of methods⁶⁾, which involve, for example, halogen exchange from the corresponding acyl chlorides with various metal fluorides or fluorination of carboxylic acids with fluorinating reagents such as cyanuric fluoride⁶⁾, 2-chloro-1,1,2-trifluoro-triethylamine⁷⁾, or selenium tetrafluoride.⁸⁾ It is noted that the present fluorinating reagents, readily available and easily handled 2-fluoropyridinium salts⁹⁾, were found to convert carboxylic acids into carboxylic acid fluorides under mild conditions in good yields on treatment with bases. This method provides a new,

convenient, and general procedure for the preparation of various carboxylic acid fluorides.

Table Acid Fluorides by Fluorination of Carboxylic Acids
with 2-Fluoro-1,3-dimethylpyridinium Tosylate

Carboxylic acid	Acid fluoride ^{a)}	b.p.	Yield (%)
$\text{CH}_3(\text{CH}_2)_{10}\text{COOH}$	$\text{CH}_3(\text{CH}_2)_{10}\text{COF}$	114 ~ 116°C/17 mmHg	quant.
$\text{CH}_3(\text{CH}_2)_4\text{COOH}$	$\text{CH}_3(\text{CH}_2)_4\text{COF}$	120 ~ 122°C	84
$\text{PhCH}_2\text{CH}_2\text{COOH}$	$\text{PhCH}_2\text{CH}_2\text{COF}$	98 ~ 101°C/18 mmHg	88
PhCH_2COOH	PhCH_2COF	72 ~ 73.5°C/13 mmHg	80
PhCOOH	PhCOF	84 ~ 86°C/174 mmHg	93
$\text{PhCH}(\text{C}_2\text{H}_5)\text{COOH}$	$\text{PhCH}(\text{C}_2\text{H}_5)\text{COF}$	99 ~ 101°C/24 mmHg	87
$\text{PhCH}(\text{OCH}_3)\text{COOH}$	$\text{PhCH}(\text{OCH}_3)\text{COF}$	96 ~ 98°C/14 mmHg	87
$\text{CH}_3\text{CH}=\text{CHCOOH}$	$\text{CH}_3\text{CH}=\text{CHCOF}$	66 ~ 70°C	64
$\text{PhCH}=\text{CHCOOH}$	$\text{PhCH}=\text{CHCOF}$	114 ~ 115°C/23 mmHg	69
$\text{CH}_3(\text{CH}=\text{CH})_2\text{COOH}$	$\text{CH}_3(\text{CH}=\text{CH})_2\text{COF}$	57 ~ 58°C/24 mmHg	89
$\text{HOOC}(\text{CH}_2)_5\text{COOH}$	$\text{FCO}(\text{CH}_2)_5\text{COF}^{\text{b)}$	98 ~ 103°C/26 mmHg	93

a) Each product gave satisfactory spectral data.

b) Dicarboxylic acid was treated with each 2.4 molar amounts of pyridinium salt and triethylamine.

REFERENCES and NOTE

- 1) T. Mukaiyama, M. Usui, E. Shimada, and K. Saigo, Chem. Lett., 1045 (1975).
- 2) E. Bald, K. Saigo, and T. Mukaiyama, *ibid.*, 1163 (1975).
- 3) a) T. Mukaiyama, S. Ikeda, and S. Kobayashi, *ibid.*, 1159 (1975).
b) T. Mukaiyama, H. Toda, and S. Kobayashi, *ibid.*, 13 (1976).
c) T. Mukaiyama, M. Usui, and K. Saigo, *ibid.*, 49 (1976).
d) T. Mukaiyama, T. Aikawa, and S. Kobayashi, *ibid.*, 57 (1976).
e) T. Mukaiyama and K. Hojo, *ibid.*, 267 (1976).
- 4) R. Wittmann, Chem. Ber., 96, 771 (1963).
- 5) Carboxylic acid fluorides were also detected by the ir spectroscopic measurement in the reaction mixture of carboxylic acids with 2,4-dinitrofluorobenzene in the presence of a base.
- 6) G. A. Olah, M. Nojima, and I. Kerekes, Synthesis, 487 (1973) and references cited therein.
- 7) N. N. Yarovenko and M. A. Radsha, J. Gen. Chem. USSR (English Transl.), 29, 2125 (1959).
- 8) G. A. Olah, M. Nojima, and I. Kerekes, J. Amer. Chem. Soc., 96, 925 (1974).
- 9) These pyridinium salts are generally prepared by the equimolar reaction of 2-fluoropyridine or 2-fluoro-3-methylpyridine with alkylating reagents such as dimethyl sulfate, methyl p-toluenesulfonate, or triethyloxonium fluoroborate.

(Received February 6, 1976)