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PREPARATION OF ESTERS AND AMIDES USING HEXAFLUORO-1,2-EPOXYPROPANE—TRIETHYLAMINE SYSTEM

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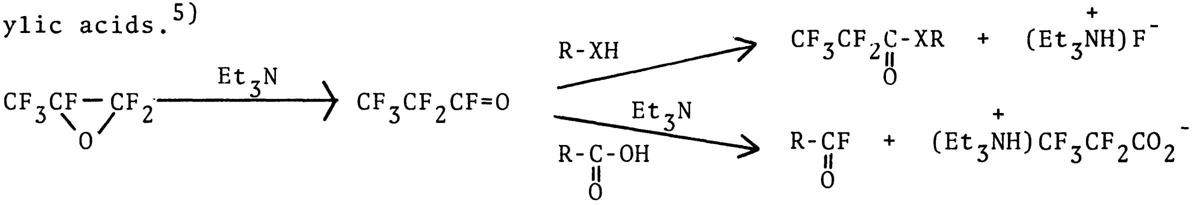
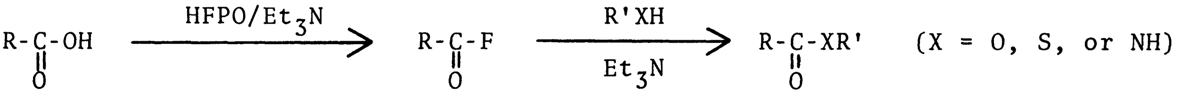
Hexafluoro-1,2-epoxypropane-triethylamine system was found to be a useful condensing agent for the preparation of esters, thioesters, and amides.

It is well known that hexafluoro-1,2-epoxypropane (HFPO, hexafluoropropylene oxide) rearranges into pentafluoropropionyl fluoride by the action of base.[1-3] Applying this reaction, we have reported a convenient method for the preparation of pentafluoropropionic acid derivatives,[4] and of fluorides of non-fluorinated carboxylic acids.[5]



Extending these works, we found that the HFPO-Et_3N system works as an effective dehydrating agent for the esterification and amidation of carboxylic acids.



$$R\text{-}\underset{\overset{\|}{O}}{C}\text{-}OH \xrightarrow{HFPO/Et_3N} R\text{-}\underset{\overset{\|}{O}}{C}\text{-}F \xrightarrow[Et_3N]{R'XH} R\text{-}\underset{\overset{\|}{O}}{C}\text{-}XR' \quad (X = O,\ S,\ \text{or } NH)$$

By allowing carboxylic acids to react with butanol, phenol, thiophenol, or amines in acetonitrile in the presence of HFPO and triethylamine for a short period at room temperature, esters, thioesters and amides were obtained in good yields. For example, a mixture of benzoic acid (2.44 g, 20 mmol), triethylamine (3.03 g, 30 mmol) and acetonitrile (30 ml) was placed in a glass-made pressure vessel, and cooled to -75°C by a dry ice-acetone bath. Liquefied HFPO (bp -27°C, 2.91 g, 17.5 mmol) was introduced into the vessel, and the whole was brought to room temperature (10 min). After 30 min of stirring, aniline (1.86 g, 20 mmol) was added and stirring was continued for an additional 30 min. The reaction mixture was thrown into water and precipitate was collected by filtration. After washing with a dilute aqueous solution of sodium hydroxide, benzoyl anilide (mp 161-163°C, 2.95 g, 86%) was obtained. Recrystallization from benzene gave a pure product, mp 164-165°C. Propionic, isobutyric, and benzoic acid were subjected to condensation with butanol, phenol, thiophenol or aniline in similar manners. When phenol was used, the reaction time was extended to 60 min because of its low nucleophilicity (Table 1).

Esters and amides are generally prepared by treating alcohols or amines with carboxylic acid anhydrides or halides. For the sake of condensation between free

Table 1. Preparation of carboxylic acid derivatives (RCO_2H : R'XH : HFPO = 1 : 1 : x)

RCO_2H	R'XH	HFPO (x)	Product R-CO-X-R' B.p. °C/mm or [M.p. °C] (lit)	Yield*(%)
$EtCO_2H$	n-BuOH	0.97	80-82/83 (146)[a]	70
	PhOH	0.99	100-101/20 (211)[b]	83
	PhSH	1.00	130-131/20 (112-113/10)[c]	82
	$PhNH_2$	0.92	[106-107](105-107)[d]	95
$i\text{-}PrCO_2H$	n-BuOH	1.00	84-85/65 (154-155)[e]	76
	PhOH	0.95	110/22 (211/707)[f]	79
	PhSH	1.00	135-136/20[g]	81
	$PhNH_2$	0.95	[105-106](105)[h]	80
$PhCO_2H$	n-BuOH	0.97	104-105/9 (248.5-249.5)[i]	80
	PhOH	0.91	[70-71](70-71)[j]	87
	PhSH	1.00	[57-58](56)[k]	89
	$n\text{-}PrNH_2$	0.94	[83-84](84.5)[l]	78
	$PhNH_2$	0.88	[164-165](163)[m]	86

* Yields are based on the amounts of HFPO used. Those of the products purified by distillation and/or recrystallization are shown. a) "Beilsteins Handbuch der Organischen Chemie," 4th Ed., 2, p.241. b) Ibid., 6,EIII, p.559. c) T. Endo, S. Ikegawa, and T. Mukaiyama, Bull. Chem. Soc., Jpn., 43, 2632 (1970). d) "Beilstein," 12, 250. e) K. C. Brannock and G. R. Lappin, J. Am. Chem. Soc., 77, 6052 (1955). f) H. Huber and K. Brunner, Monatsh., 56, 322 (1930). g) Found, C, 66.83, H, 6.60%; Calcd for $C_{10}H_{12}OS$, C, 66.63, H, 6.71%. h) "Beilstein," 12,EII, p.147,. i) Ibid., 9, p.112. j) Ibid., 9, EII, p.96. k) Ibid., 9, p.421. l) Ibid., 12, EIII, p.152. m) Ibid., 9, p.203.

carboxylic acids and alcohols or amines, strong dehydrating agents, such as N,N-carbonyldiimidazole,[6] 1,3-dicyclohexylcarbodiimide,[7] or 1-methyl-2-halopyridinium iodides,[8] were recently used. The method using HFPO-Et_3N described here seems to be another candidate for the agent for these dehydrating condensations because it works well under mild conditions. By this method, as shown in the examples, even phenol or aniline having low nucleophilicity gave esters or amides in good yields.

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