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Preparation of Hindered Esters from Acid Chlorides and Alcohols in the Presence of Silver Cyanide

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Synopsis. Sterically hindered esters were prepared from the corresponding acyl chlorides and alcohols in the presence of silver cyanide. The method is superior to the conventional acyl chloride-alcohol-pyridine method as regards yield and the rapidity of reaction.

This report describes a rapid and convenient procedure for preparing sterically very crowded esters by the reaction between acyl chlorides and alcohols in the presence of silver cyanide. The results are summarized in Table 1.

The conventional acyl chloride–alcohol–pyridine method is useful for the preparation of the usual esters but it is too slow and incomplete for preparing the hindered esters. The method in which the acyl chlorides are treated with lithium alkoxides[1] and that in which the acids and alcohols are treated with trifluoroacetic anhydride[2] appear to be the most useful ones in view of the yield and the rapidity of the reaction. However, because of the strongly alkaline or acidic reaction conditions inherent to these methods, their applicability must be made with certain restrictions: in the alkoxide method, some reservation should be given to acid chlorides having α-hydrogen atoms;[1] the trifluoroacetic anhydride method is not suitable for aliphatic tertiary alcohols.[2] The present method can be applied to a wide variety of substrates with better yields. Esters of triphenylmethanol, however, can not be prepared by this method.

The reaction seems to proceed with the help of the electrophilic catalysis of silver ion though other silver salts such as silver carbonate or silver trifluoroacetate are ineffective for the ester formation. The intermediacy of the acyl cyanide as the main reaction pass might be excluded since the acyl cyanide has been reported to be less reactive to the nucleophiles than the corresponding acyl chloride.[3] Actually, in an experiment carried out with pivaloyl cyanide and 2-methyl-2-propanol in HMPA at 80 °C for 8 h, only a trace of ester could be observed. Addition of tributylamine[4] or DBU caused no acceleration in the reaction but rather retarded it.

Copper cyanide showed a similar effect but the yield of the ester was very low and the formation of a considerable amount of acid anhydride was observed.

Experimental

Silver cyanide was precipitated by mixing a potassium cyanide solution (1.95 g in 50 ml water) with a silver nitrate

TABLE 1. PERCENT YIELD OF HINDERED ESTERS

Acid chloride (0.5 mmol)	Alcohol (mmol)		Reaction conditions			Ester Yield (%)[a]
			Solvent (1 ml);	Temp;	Time	
Pivaloyl	2-Butanol	(0.5)	Benzene;	r. t.;	1 h	100
	2-Methyl-2-propanol	(0.6)	HMPA;	80 °C;	10 min	94
		(1.0)	Benzene;	80 °C;	30 min	100
	3-Ethyl-3-pentanol	(1.0)	HMPA;	80 °C;	10 min	57
		(1.0)	Benzene;	80 °C;	4 h	99[b]
	2,6-Dimethylphenol	(0.7)	HMPA;	80 °C;	4 h	61
		(0.5)	Benzene;	80 °C;	30 h	83[c]
2,2-Diethylbutyryl	2-Butanol	(0.5)	Benzene;	80 °C;	1 h	94
	2-Methyl-2-propanol	(1.0)	HMPA;	80 °C;	10 min	95
		(1.0)	Benzene;	80 °C;	4.5 h	90
	3-Ethyl-3-pentanol	(1.0)	HMPA;	80 °C;	30 min	75
		(1.0)	Benzene;	80 °C;	54 h	86
	2,6-Dimethylphenol	(0.5)	HMPA;	80 °C;	30 min	80
		(0.5)	Benzene;	80 °C;	75 h	90
2,4,6-Trimethylbenzoyl	2-Methyl-2-propanol	(0.5)	Benzene;	r. t.;	10 min	92
	3-Ethyl-3-pentanol	(1.0)	HMPA;	80 °C;	30 min	92
		(0.5)	Benzene;	80 °C;	3 h	82[c]
	2,6-Dimethylphenol	(0.5)	Benzene;	r. t.;	5 min	92
2-Methylpentanoyl	3-Ethyl-3-pentanol	(0.5)	Benzene;	r. t.;	3 h	95

a) Unless otherwise stated, the yields were determined by GLPC by comparison with the appropriate internal standards. b) An experiment carried out according to the trifluoroacetic anhydride method[2] gave the ester formation (13%, r. t., 1 h) but the ester gradually disappeared in eight hours. c) The yield was that of the product distilled after the work up.

Table 2. Analytical and NMR data of new esters

Ester	Found(Calcd)		NMR, δ
	C%	H%	
2,6-Dimethylphenyl pivalate	75.74 (75.69)	8.80 (8.80)	1.42(s, 9H), 2.14(s, 6H), 7.02(s, 3H)
2-Butyl 2,2-diethylbutyrate	72.32 (71.95)	12.19 (12.08)	0.76(t, 9H, J=7.9 Hz), 0.88(t, 3H, J=9.0 Hz), 1.19(d, 3H, J=6.0 Hz), 1.35—1.90 (m, 8H), 4.80(m, 1H)
t-Butyl 2,2-diethylbutyrate	71.67 (71.95)	12.06 (12.08)	0.77(t, 9H, J=7.2 Hz), 1.34(s, 9H), 1.55(m, 6H)
3-Ethyl-3-pentyl 2,2-diethylbutyrate	74.10 (74.32)	12.50 (12.48)	0.80(t, 9H), 0.83(t, 9H), 1.36—2.10 (m, 12H)
2,6-Dimethylphenyl 2,2-diethylbutyrate	77.34 (77.37)	9.74 (9.74)	0.93(t, 9H, J=7.1 Hz), 1.89(q, 6H), 2.16(s, 6H), 7.01(s, 3H)
3-Ethyl-3-pentyl 2,4,6-trimethylbenzoate	77.55 (77.82)	9.90 (9.99)	0.91(t, 9H, J=7.0 Hz), 1.98(q, 6H, J=7.0 Hz), 2.25(s, 3H), 2.34(s, 6H), 6.81(s, 2H)
3-Ethyl-3-pentyl 2-methylpentanoate	73.01 (72.84)	12.27 (12.23)	0.83(t, 12H, J=8.0 Hz), 1.12(q, 3H, J=7.0 Hz), 1.40(m, 4H), 1.84(q, 6H, J=8.0 Hz), 2.40(m, 1H)

solution (5.1 g in 100 ml water) at room temperature, which was then washed thoroughly with water and dried for twelve hours under 2 mmHg. Of the solvents examined, benzene and HMPA gave the best results. In HMPA, the reaction completed very rapidly but the yield was slightly reduced. The NMR spectra in $CDCl_3$ were used for identification of the esters. A typical example is given below.

t-Butyl Pivalate. Pivaloyl chloride (60 mg, 0.5 mmol) was added with use of a microsyringe to a stirred mixture of silver cyanide (134 mg, 1 mmol), 2-methyl-2-propanol (44 mg, 0.6 mmol) and HMPA (1 ml) with the exclusion of moisture, the mixture being then heated at 80 °C in an oil bath. Formation of the ester was followed by GLPC by the addition of an internal standard (xylene in this case). After ten minutes the amount of ester became constant with a 94% yield. For isolation of the ester, the reaction mixture was diluted with pentane (10 ml) without addition of xylene, filtered through a celite column, washed successively with a 10% aqueous sodium hydrogencarbonate solution and water, dried with calcium sulfate, and distilled at 150 °C (bath temperature).

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