Communications to the Editor

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CYANOPHOSPHORYLATION OF KETONES AND ALDEHYDES USING DIETHYL PHOSPHOROCYANIDATE (DEPC)[1)]

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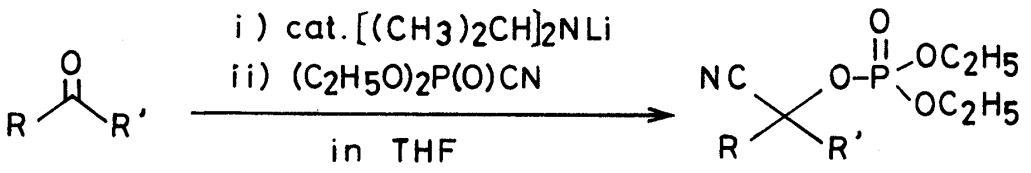
A novel one-pot and high-yield cyanophosphorylation of carbonyl compounds is achieved by treatment of ketones or aldehydes with diethyl phosphorocyanidate (DEPC) in the presence of a catalytic amount of lithium diisopropylamide in tetrahydrofuran.

KEYWORDS—— cyanophosphorylation; diethyl phosphorocyanidate; cyanophosphate; lithium diisopropylamide; α-hydroxycarboxylic acid

Diethyl phosphorocyanidate [DEPC, $(C_2H_5O)_2P(O)CN$][2)] has been extensively utilized as a versatile reagent for cyanation under mild and non-aqueous reaction conditions. Our recent efforts on the use of DEPC for cyanation have developed novel syntheses of α-aminonitriles,[3)] a modified Reissert-Henze reaction,[4)] and a new synthesis of thiocyanates from sulfinic acids.[5)]

It is well known that trimethylsilyl cyanide reacts with carbonyl compounds to give trimethylsilyloxy nitriles which have been proven to be useful precursors for the preparation of carbonyl anion synthons, cyanohydrins, β-amino alcohols, and the like.[6)] Recently, Horner et al. reported the cyanophosphinoylation of carbonyl compounds[7)] which is analogous to cyanosilylation. We now have an interest in the preparation of cyanophosphates using DEPC. Some of them are of particular utility as agricultural chemicals,[8)] for example, as biocides——insecticides, fungicides, nematocides, and the like. Cyanophosphates have hitherto been obtained by treating cyanohydrins with dialkyl phosphorochloridates.[8)] The present communication describes a novel one-pot and high-yield cyanophosphorylation of ketones and aldehydes by reaction with DEPC in the presence of a catalytic amount of lithium diisopropylamide.



A typical experimental procedure for the preparation of cyanophosphates is as follows; n-Butyl lithium (15 % hexane solution, 0.19 ml, 0.3 mmol) was added dropwise to a solution of diisopropylamine (30 mg, 0.3 mmol) in tetrahydrofuran (THF) (4 ml) at -10°C under argon, and the mixture was stirred for 20 min at -10°C. Ketone (3 mmol) in THF (4 ml) was then added to this solution, and the mixture was stirred for 20 min at -10°C. After DEPC (538 mg, 3.3 mmol) was added dropwise at -10°C ∿ -5°C, the resulting solution was stirred for 10 min at -10°C and then for 1 h at room temperature. The reaction was quenched by the addition of water, and concentrated in vacuo. The residue was dissolved in benzene - ethyl acetate (1:1, 50 ml) and washed with water (10 ml x 3) and saturated aqueous sodium chloride (10 ml x 1). Drying over sodium sulfate followed by concentration gave the crude cyanophosphate, which was purified by silica gel column chromatography. The results of our experiments are summarized in Table I.

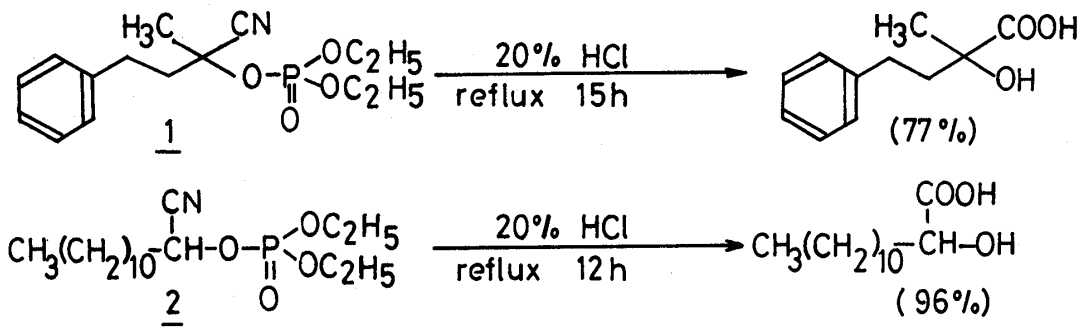
Table I. Preparation of Cyanophosphates[a] Using DEPC

Run	Carbonyl compounds	DEPC(eq)	Reaction conditions Temp.(°C)[b]	Time(min)	Yield (%)	bp(°C)/mmHg or [mp(°C)]
1	cyclohexanone	1.1	-10	10	85	136-139/3
2	cyclooctanone	3.0	rt	60	90	158/2
3	cyclododecanone	3.0	i) -10	10	75	[48-52]
			ii) rt	60		
4	5α-cholestan-3-one	1.1	-10	10	76[c]	[102-109]
5	2-adamantanone	3.0	i) -10	10	92	130/5[d]
			ii) rt	30		
6	acetophenone	1.1	i) -10	20	87	177/5
			ii) rt	90		
7	propiophenone	1.1	i) -10	10	84	oil[e]
			ii) rt	60		
8	α-tetralone	3.0	i) -10	10	75	oil[e]
			ii) rt	120		
9	benzophenone	1.3	i) -10	10	93	190/3
			ii) rt	60		
10	4-phenyl-2-butanone	1.1	i) -10	10	93	145/2
			ii) rt	60		
11	cyclohexanecarbaldehyde	1.1	i) -10	10	80	158-159/5
			ii) rt	60		
12	benzaldehyde	1.1	-10	10	56	149/3
13	dodecanal	3.0	i) -10	10	56.5	204/5
			ii) rt	60		

a) All the products have been identified by IR, ^{1}H-NMR, ^{13}C-NMR, mass spectra, and elemental analyses (except for runs 7 and 8). b) rt: room temperature. c) The configuration at C-3 position remains undetermined. d) By Kugelrohr distillation. e) Determined by spectroscopic data because of its thermal instability for distillation.

Although about one equivalent of DEPC is generally used, three equivalents are effective when the reaction proceeds sluggishly. Various cyclic and aromatic ketones react with DEPC to give cyanophosphates in high yields. It is interesting to note that even in the case of conjugated or hindered ketones such as α-tetralone or benzophenone,[9] which are known not to give cyanohydrins under usual reaction conditions,[10] DEPC reacts smoothly to give cyanophosphates. 2-Adamantanone and 4-phenyl-2-butanone caused no trouble to provide cyanophosphates. Furthermore, the method can be readily extended to aldehydes, giving cyanophosphates in satisfactory yields.

Cyanophosphates 1 and 2 smoothly gave α-hydroxycarboxylic acids on treatment with 20 % HCl.[11] Thus, the present method provides a useful synthetic means to α-hydroxycarboxylic acids. In addition, the cyanophosphates 1 is reconverted to the original ketone in 60 % yield by treatment with 20 % NaOH in methanol at 0°C for 0.5 h. These results suggest the synthetic utility of cyanophosphates.



In conclusion, the reaction of DEPC with carbonyl compounds offers a convenient, good yield and a mild method for the preparation of cyanophosphates, and may be applicable to a wide scope of structural types. Its further utilization is now actively under investigation.

REFERENCES AND NOTES

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