

A Novel Synthesis of Acyl Cyanides from Diethyl Phosphorocyanidate and Some 1-Substituted Imidazole Carboxylic Acids including a D-Ribofuranoside

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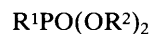
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Reaction of 5-[(dimethylamino)methylene]amino-1-t-butyl (or 2,3-*O*-isopropylidene-β-D-ribofuranosyl) imidazole-4-carboxylic acids (**8b**) and (**8d**) respectively with diethyl phosphorocyanidate and triethylamine in ethyl acetate at room temperature gave the crystalline 5-[(dimethylamino)methylene]amino-1-t-butyl (or 2,3-*O*-isopropylidene-β-D-ribofuranosyl) imidazole-4-carbonyl cyanides (**9a**) and (**9b**) respectively.

The reaction of carboxylic acids with diethyl phosphorocyanidate (DEPC) (**1**) and triethylamine, by analogy with the formation of acyl azides from carboxylic acids and diphenyl phosphorazidate (DPPA) (**2**), was expected to produce acyl cyanides.¹ However, attempts to prepare benzoyl or 3-phenylpropionyl cyanide in this way led to the formation of the dimers (**3**) and (**4**) in good yield. On the assumption that dimers are formed from the acyl cyanide and strong base, reaction of the hindered 2,4,6-trimethylbenzoic acid and DEPC was examined but in this case only the stable acyl phosphate (**5**) was obtained in good yield.¹ The formation of acyl cyanides has also been proposed, but without any supporting evidence, as intermediates in the *C*-acylation of nitromethane using an acid, DEPC, and triethylamine.² We now report the first formation of an acyl cyanide from a carboxylic acid, DEPC, and triethylamine.

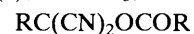
Reaction of *t*-butylamine with the imidate³ (**6**) gave the crystalline benzyl 1-*t*-butyl-5-aminoimidazole-4-carboxylate (**7a**) which when heated in acetonitrile with dimethylform-

amide dimethyl acetal gave a high (98%) yield of the crystalline formamidine (**8a**) m.p. 87 °C, hydrogenation of which, using palladium-carbon, gave a high (98%) yield of the carboxylic acid (**8b**) (M^+ 238). Treatment of (**8b**) with DEPC and triethylamine in ethyl acetate at room temperature gave a bright yellow solution. Chromatography of the product using silica gel and chloroform-methanol (9:1) as the eluting



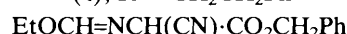
(**1**); $\text{R}^1 = \text{CN}$, $\text{R}^2 = \text{Et}$

(**2**); $\text{R}^1 = \text{N}_3$, $\text{R}^2 = \text{Ph}$

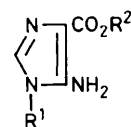


(**3**); $\text{R} = \text{Ph}$

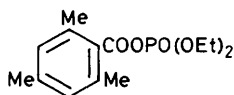
(**4**); $\text{R} = \text{CH}_2\text{CH}_2\text{Ph}$



(**6**)



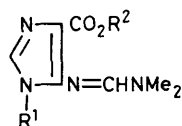
(**7**)



(**5**)

a; $\text{R}^1 = \text{But}$, $\text{R}^2 = \text{CH}_2\text{Ph}$

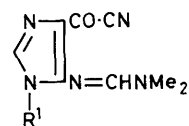
b; $\text{R}^1 = 2,3\text{-O-isopropylidene-}\beta\text{-D-ribofuranosyl}$, $\text{R}^2 = \text{CH}_2\text{Ph}$



(8)

- a; R¹ = Bu^t, R² = CH₂Ph
 b; R¹ = Bu^t, R² = H
 c; R¹ = 2,3-*O*-isopropylidene-β-D-ribofuranosyl, R² = CH₂Ph
 d; R¹ = 2,3-*O*-isopropylidene-β-D-ribofuranosyl, R² = H

solvent gave a good (62%) yield of the acyl cyanide (**9a**) as large bright yellow prisms, m.p. 149 °C. The structure was confirmed by elemental analysis, u.v. [λ_{\max} 248 (ϵ 18 450), 392 (ϵ 5 970) nm], i.r. [ν_{\max} 2 220 cm⁻¹ (CN)], mass (e.g. M^+ 247), and ¹H-n.m.r. spectroscopy [e.g. δ (CDCl₃) 1.7 (9H, s, CMe₃), 3.1–3.3 (6H, d, NMe₂), 7.4 (1H, s, 2-H), and 8.65 (1H, s, N=CHNMe₂)]. In a similar manner reaction of the benzyl ester (**7b**)³ with dimethylformamide dimethyl acetal gave an excellent yield of the formamidine (**8c**), hydrogenation of which in ethyl acetate solution using palladium–carbon produced the carboxylic acid (**8d**). Reaction of (**8d**) with DEPC and triethylamine at room temperature gave the crystalline acyl cyanide (**9b**) m.p. 152 °C. The structure assigned to the compound was confirmed by elemental analysis, u.v. absorption (λ_{\max} 250, 392 nm), i.r. [ν_{\max} 2 200 cm⁻¹ (CN)], mass (e.g. M^+ 363), and ¹H-n.m.r. [e.g. δ (CDCl₃) 1.35, 1.58, (6H, 2 × s, CMe₂), 3.1–3.19 (6H, d,



(9)

- a; R = Bu^t
 b; R = 2,3-*O*-isopropylidene-β-D-ribofuranosyl

NMe₂) 8.0 (1H, s, 2-H), 9.1 (1H, s, N=CHNMe₂) and full assignment of all other protons] spectra.

The ease of reaction of these particular imidazole carboxylic acids is in contrast to results obtained with other carboxylic acids and should help us to understand the specific requirements for acyl cyanide formation involving compounds such as DEPC. Satisfactory analytical, t.l.c., and spectral data were obtained for all new compounds.

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References

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