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NEW METHODS AND REAGENTS IN ORGANIC SYNTHESIS. 12.[1] REACTION OF DIETHYL PHOSPHOROCYANIDATE(DEPC) WITH AROMATIC AMINE OXIDES. A MODIFIED REISSERT-HENZE REACTION

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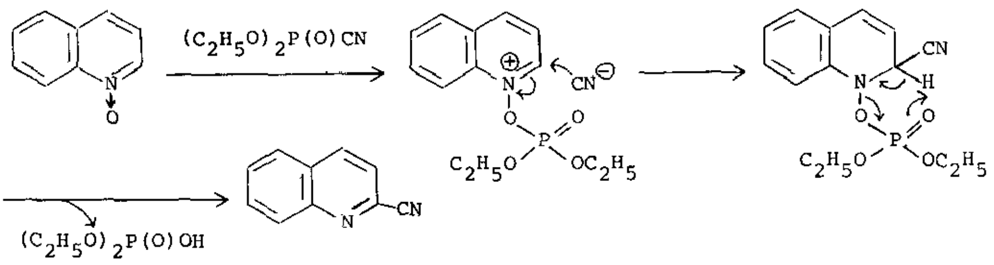
Abstract——— Diethyl phosphorocyanidate(DEPC) reacts with aromatic amine oxides in the presence of triethylamine to give α-cyanated compounds; the reaction may be called a modified Reissert-Henze reaction.

Diethyl phosphorocyanidate(DEPC, $(C_2H_5O)_2P(O)CN)$[2] has been proven to be a useful reagent in organic synthesis, especially for condensation reactions.[3] Recent reports from our laboratories have demonstrated that DEPC can be used for the cyanation of enamines[4] and the Strecker's α-amino nitrile synthesis.[5] Our systematic investigations in this area have led to a new method for the cyanation of aromatic amine oxides.

The cyanation of aromatic amine oxides is usually carried out by the action of benzoyl chloride and potassium cyanide, which is an application of the Reissert reaction to aromatic amine oxides and called the Reissert-Henze reaction.[6,7] We conceived that DEPC would substitute for a mixture of benzoyl chloride and potassium cyanide as a new reagent for the Reissert-Henze reaction, as shown in Chart 1 for the cyanation of quinoline 1-oxide.

Chart 1.



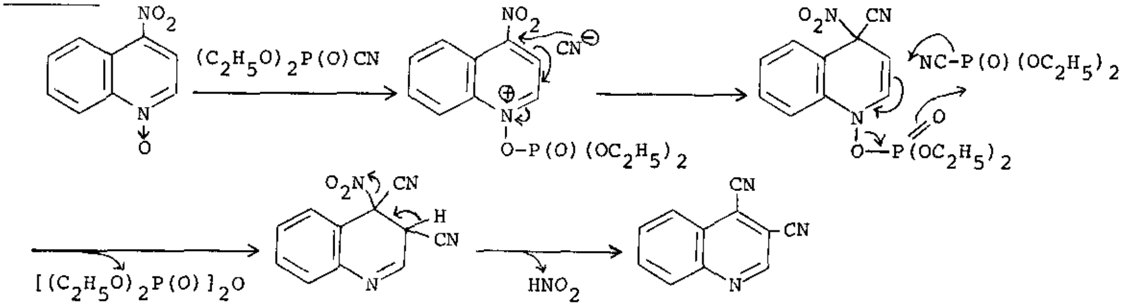
In fact, various aromatic N-oxides react with DEPC in the presence of triethylamine in refluxing acetonitrile to give deoxygenated α-cyano compounds.

A typical experimental procedure for the modified Reissert-Henze reaction is as follows: A mixture of isoquinoline 2-oxide·1/4 H_2O(150 mg, 1 mM), DEPC(489 mg, 3 mM), and triethylamine(101 mg, 1 mM) in acetonitrile(15 ml) was stirred at reflux for 18 h. After evaporation, the residue was purified by column chromatography over silica gel(14 g) with benzene-ethyl acetate(30:1) to give 1-cyanoisoquinoline (125 mg, 81 %).

The results of our experiments are compiled in Table I. Three molar excess of DEPC is necessary to conduct the reaction smoothly. Without triethylamine, the reaction sluggishly proceeds. In contrast to the aqueous conditions for the usual Reissert-Henze reaction, the non-aqueous conditions[8] have been employed in the modified one.

Quinoline 1-oxide reacted with DEPC to give 2-cyanoquinoline together with a small amount of 2-ethoxyquinoline, the ethoxy group of which was apparently derived from the ethoxy group of DEPC. Although the usual Reissert-Henze reaction of 4-nitroquinoline 1-oxide has been reported[9] to give 4-chloro-2-cyanoquinoline, the modified reaction using DEPC gave 3,4-dicyanoquinoline[ir in $CHCl_3$ ν_{max}: 2230 cm^{-1}(CN); ^1H-nmr in $CDCl_3$ δ: 9.17 ppm(1H, s, C_2-H); ^{13}C-nmr in $CDCl_3$ δ: 149.1 ppm(doublet by the off-resonance ^1H decoupling, C_2)] though in low yield. The mechanism for this reaction will be presumably as shown in Chart 2.

Chart 2.

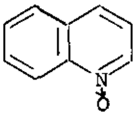
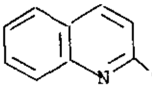
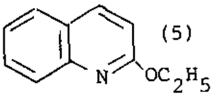
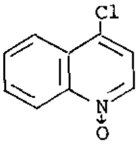
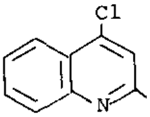
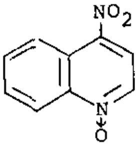
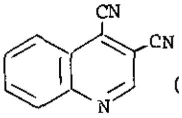
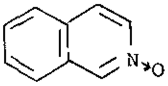
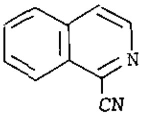
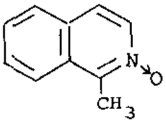
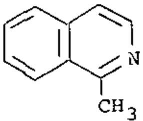
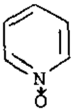
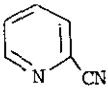
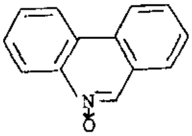
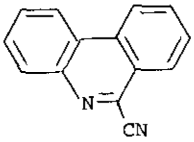
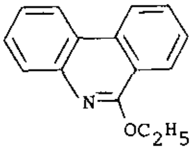


Interestingly, 1-methylisoquinoline 2-oxide did not undergo the cyanation reaction with DEPC but mainly afforded the deoxygenated product. Pyridine 1-oxide is known[9] to resist the reaction with benzoyl chloride-potassium cyanide completely, but Hamana and co-workers reported[10] that 2-cyanopyridine was obtained from pyridine-1-oxide in 18.3 % yield by the action of tosyl chloride and potassium cyanide in aqueous ethanol. DEPC also reacted with pyridine-1-oxide in the presence of tri-

Table I. Reaction of DEPC with Aromatic Amine Oxides[a]

$$\text{Aromatic Amine Oxide} \xrightarrow[(C_2H_5)_3N(1\ eq)]{(C_2H_5O)_2P(O)CN(3\ eq)} \text{Product}$$

in CH_3CN, Reflux, 18 h

N-Oxide	Product[b] (Yield, %)	
	 (57)	 (5)
	 (40)[c]	
	 (17)[c,d]	
	 (81)	
	 (40)	
	 (24.5)	
	 (60)	 (19)[e]

a: Each reaction was carried out as in the typical experimental procedure.

b: New compounds have been identified by ir and nmr measurements as well as elemental analysis. Known compounds have been identified by comparisons of their melting points with the reported ones as well as by ir and nmr measurements.

c: The starting N-oxide was recovered in 57 % yield.

d: Mp 205-206°C.

e: Mp 54.5-55.5°C.

ethylamine to give 2-cyanopyridine in 24.5 % yield. In the usual Reissert-Henze reaction of phenanthridine 5-oxide, 6-phenanthridone instead of 6-cyanophenanthridine has been reported[11] as the main product. The modified Reissert-Henze reaction using DEPC, however, afforded 6-cyanophenanthridine as the main product. The method described here may have a broad application and promise flexibility in the Reissert-Henze reaction.

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