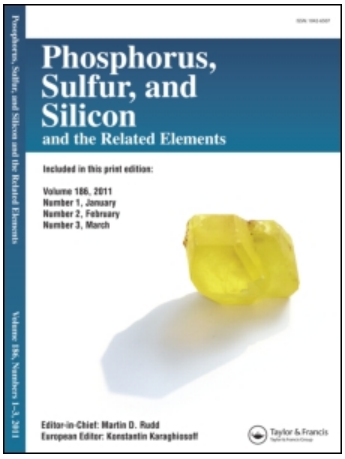

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

IMPROVED SYNTHESIS OF CYANOHYDRIN PHOSPHATES AND ITS REACTION MECHANISM

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Online publication date: 16 August 2010

Phosphorus, Sulfur, and Silicon, 179:1361–1364, 2004

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500490463501

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(Received August 31, 2003; accepted November 20, 2003)

Cyanohydrin phosphates ***2a–2c*** *were prepared in high yield from ketones (or aldehyde), diethyl phosphorochloridate, and sodium cyanide by using acetonitrile as solvent. GC analysis proved that the two reactions of cyanohydrin sodium with diethyl phosphorochloridate and with diethyl phosphorocyanidate resulted in the formation of cyanohydrin phosphates.*

Keywords: Cyanohydrin phosphate; phosphorochloridate; phosphorocyanidate

Cyanohydrin phosphates have been widely utilized as versatile intermediates for the synthesis of agricultural chemicals,[1] nitriles,[2] carbon anion synthons,[3] α-hydroxycarboxylic acids,[2a] and methylene groups.[4] Cyanohydrin phosphates were first prepared from cyanohydrin and phosphorochloridate.[1] Another approach[2b] employed reaction of ketones with three equivalent diethyl phosphorocyanidate (DEPC) and lithium cyanide. Mico[5] afforded a successful preparation in THF by employing diethyl phosphorochloridate (DEPCl) in stead of DEPC, but the expensive lithium cyanide was still necessary.

We have stated in our prior report[6] that an unexpected acetone cyanohydrin phosphate (ACHP) was obtained from the reaction of DEPCl with sodium cyanide in acetone (Figure 1). Herein, we wish to carry out the object of ascertaining the reaction mechanism.

RESULTS AND DISCUSSION

It can be deduced from Figure 1 that: a) DEPCl can react with sodium cyanide into DEPC in acetone; b) all of the DEPC formed in the system becomes ACHP at the end of the reaction; and c) since DEPC and

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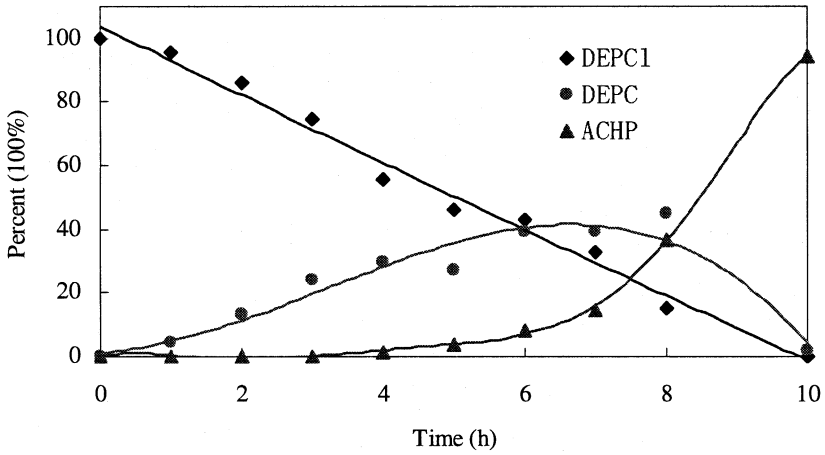


FIGURE 1 Reaction of DEPCl with sodium cyanide in acetone.

acetone would not react without sodium cyanide,* ACHP can only be the product of reaction of DEPC or/and DEPCl with cyanohydrin sodium which can be produced in situ[7] by acetone and sodium cyanide.

To testify the deduction, the following three reactions were examined: a) the first reaction was between cyanohydrin sodium** and DEPC in acetone, and ACHP was soon produced; b) the second one was between cyanohydrin sodium and DEPCl, and the same result as the first one was found; and c) the third one was to mix equivalent DEPC, DEPCl, and cyanohydrin sodium. At the end of the reaction, all of the cyanohydrin sodium became ACHP, but both DEPC and DEPCl remained half. That is to say, there was no obvious difference between the first two reaction rates.

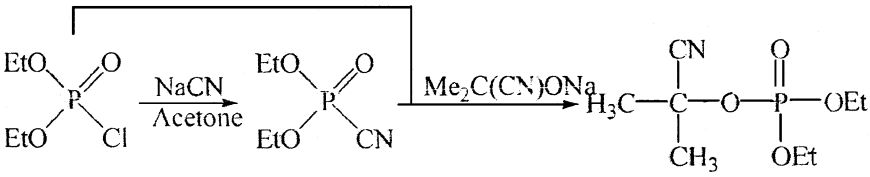
Therefore, it can be concluded that at the beginning, the very limited sodium cyanide dissolved in acetone first reacted with DEPCl to form DEPC; But along with the decrease of DEPCl, part of the dissolved sodium cyanide was transformed into cyanohydrin sodium which soon reacted with DEPC and DEPCl at the same time to give the final product—ACHP (Scheme 1).

In order to extend the application, we employed acetonitrile*** as solvent in the above reaction and obtained satisfactory results. Therefore,

*The mixture of DEPC and acetone (without sodium cyanide) was stirred at room temperature for 3 h, but GC/MS analysis showed no changes during the entire process.

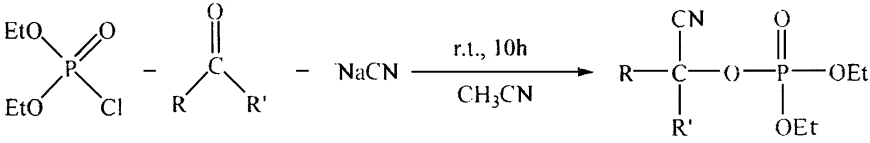
Cyanohydrin sodium can be easily prepared by sodium and cyanohydrin (preparation see *Org. Synth.*, **II, 7, 1943).

***Acetonitrile was chosen mainly due to its good properties in liquid-solid two-phase reactions according to our prior experiments.[6]



SCHEME 1

an economical and efficient cyanophosphorylation of ketones (or aldehydes) was performed by reaction with DEPCl and sodium cyanide in acetonitrile (Scheme 2).



SCHEME 2

The results of synthesis of cyanohydrin phosphates **2a–2c** from equal mole of DEPCl, ketones (or aldehydes), and sodium cyanide was shown in Table I.

EXPERIMENTAL

GC was recorded on a Varian 3800 spectrometer; IR on a Bio-Rad FTS185 spectrometer; ^{1}H and ^{13}C-NMR on a Varian UNITY500 spectrometer; MS on a Finnigan Mat TSQ70 spectrometer.

Cyanohydrin Phosphates 2a–2c

Diethyl phosphorochloridate[8] (0.2 mmol) and ketone (0.2 mmol) were added to sodium cyanide (0.4 mmol) in 100 mL actonitrile. The mixture was stirred vigorously at room temperature for 8–10 h. After filtration, the filtrate was concentrated in *vacuo* and then distilled to give the products.

Acetone cyanohydrin phosphate 2a. Yield 91%; b.p. 86–88° (0.5 mm); IR 2283 (C≡N), 1256 (P=O); ^{1}H-NMR ($CDCl_3$, 500MHz) 1.37 (6H, 2t, 6.5Hz), 1.85 (6H, s), 4.18 (4H, q, 7.5Hz); ^{13}C-NMR ($CDCl_3$, 125MHz) 18.0, 30.7, 66.5, 73.4, 121.4; MS 222 (M + 1).

Benzaldehyde cyanohydrin phosphate 2b. Yield 88%; b.p. 146–148° (1.0 mm); IR 1271 (P=O); ^{1}H-NMR ($CDCl_3$, 500MHz) 1.23 (3H, 2t, 7Hz);

TABLE I Synthesis of Cyanohydrin Phosphates **2a–2c**

Products	R	R′	Yield (%)
2a	CH_3	CH_3	91
2b	C_6H_5	H	88
2c	$-CH_2CH_2$	CH_2CH_2-(cyclopentone)	85

1.39 (3H, 2t, 7Hz), 4.02 (2H, 2q, 7.5Hz), 4.21 (2H, 2q, 7.5Hz), 6.07 (1H, d, 9Hz), ∼7.50 (5H, m); ^{13}C-NMR ($CDCl_3$, 125MHz) 6.5, 65.3, 67.1, 116.8, 130.2 (m); MS 270 (M + 1).

Cyclopentone cyanohydrin phosphate 2c. Yield 85%; b.p. 107–109° (0.5 mm); IR 2243 (C≡N), 1278 (P=O); ^{1}H-NMR ($CDCl_3$, 500MHz) 1.38 (6H, 2t, 7Hz), 1.90 (4H, m), 2.22 (2H, m), 2.45 (2H, m), 4.18 (4H, 2t, 8Hz); ^{13}C-NMR ($CDCl_3$, 125MHz) 116.5, 23.0, 40.5, 64.9, 79.4, 119.6; MS 248 (M + 1).

Reaction of Diethyl Phosphorochloridate with Sodium Cyanide in Acetone

Diethyl phosphorochloridate (0.1 mmol) and sodium cyanide (0.2 mmol) was added into 50 mL ketone. The mixture was stirred at room temperature for 10 h, during which sample was taken every hour for GC analysis.

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