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Direct Conversion of Diethyl Hydrogen Phosphate into Diethyl Phosphoramides

Short Communication

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The effective, one-step transformation of diethyl hydrogen phosphate into diethyl phosphoramides by using hexamethyltriaminodibromophosphorane prepared "*in situ*" is described.

(Keywords: Hexamethyltriaminodibromophosphorane; Intermolecular dehydration)

Direkte Umwandlung von Diethylhydrogenphosphat in Diethylphosphoramid (Kurze Mitteilung)

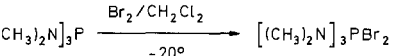
Es wird eine effiziente, einstufige Umwandlung von Diethylhydrogenphosphat in Diethylphosphoramid unter Verwendung von *in situ* erzeugten Hexamethyltriaminodibromphosphoran beschrieben.

Direct transformation of organophosphorus acids into the corresponding amides is a preparative problem which has not been properly solved so far. The only reported procedure[1] involving application of the four component system: phosphoric acid/triphenylphosphine/carbon tetrachloride/amine suffers from rather low yields and notoriously affords impure products. Such situation is due to the pronounced tendency of organophosphorus acids to form preferentially the corresponding anhydrides under the action of various conventional dehydrating agents.

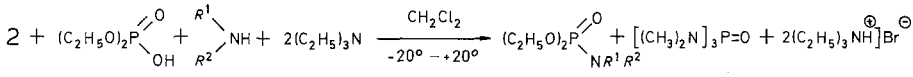
In the course of our studies on organophosphorus compounds which can be used as potential activators of an OH group we found that hexamethyltriaminodibromophosphorane (**2**) prepared "*in situ*" can be applied for direct amidation of diethyl hydrogen phosphate (**3**). Reagent

2 is obtained upon addition of an equimolar amounts of hexamethyltriaminophosphine (**1**) to the solution of bromine in dichloromethane at —20°. When the resultant solution of **2** is treated successively with the respective primary or secondary amine (**4**) and then with the mixture of diethyl hydrogen phosphate (**3**; 1 mol) and triethylamine (2 mole) an exothermic reaction occurs and the desired diethyl phosphoramide (**5**) is formed in high yield (Scheme 1). Such procedure (method A) can be conveniently used for the preparation of analytically pure **5** directly from diethyl hydrogen phosphate (**3**) and secondary amines, aromatic amines, or primary alipathic amines with an amino group linked to secondary carbon. For primary aliphatic amines with an amino group linked to primary carbon a slightly modified procedure (method B) should be applied to secure high yield and analytical purity of **5**.

Scheme 1



1 2



3 4 5

The reaction is particularity sensitive to the experimental conditions. All deviations from the given optimized procedures lead unevitably to inferior results, mainly the formation of considerable amounts of tetraethyl pyrophosphate (**8**). Such behaviour of the reacting system seems to be justified in terms of the presented mechanistic proposal (Scheme 2) considering the existence of at least two concomitant side processes. The main reaction pathway is assumed to involve ligand exchange between the ionized form of **2** and diethyl hydrogen phosphate anion (**6**) leading to the mixed anhydride type intermediate (**7**) which can subsequently react with an amine to give the desired diethyl phosphoramide (**5**). Concurrent $S_N2(P)$ reaction of **7** with the anion **6** leads unevitably to tetraethyl pyrophosphate (**8**). Hexamethyltriaminodibromophosphorane (**2**) can also react with an amine **4** to form the corresponding aminophosphonium salt (**9**). Both **8** and **9** are stable under the reaction conditions and cannot be transformed into **5**.

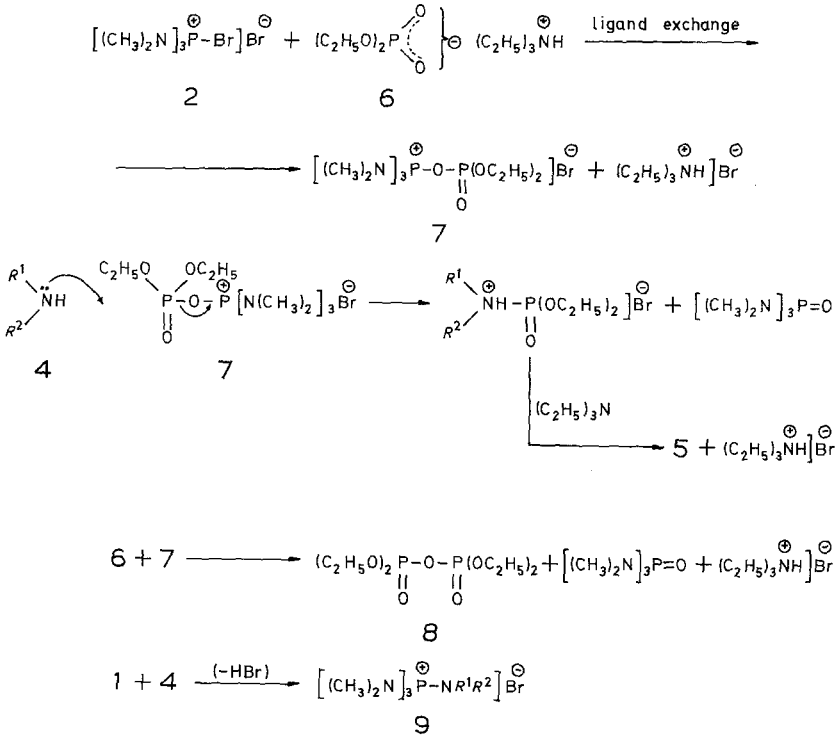
The reported procedure seems to be the method of choice for the preparation or pure **5** directly from the acid **3**. Yields and physical

Table 1. *Diethyl phosphoramides* (**5**)

R^1	R^2	Method	Yield (%)	^{31}P-NMR (δ, ppm)[a]	n_D^{20} [m.p.]	Literature data
C_6H_5	H	A	59	3.0	[93–95°][b]	m.p. 93–94.5°[2]
C—C_6H_{11}	H	A	85	8.8	[72–74°][b]	m.p. 71–72°[3]
n-C_3H_7	n-C_3H_7	A	91	9.8	1.4328	n_D^{22} = 1.4280[4]
C_6H_5—CH_2	H	B	91	9.1	1.4940	n_D^{20} = 1.4968[5]
n-C_4H_9	H	B	88	9.7	1.4317	n_D^{20} = 1.4350[6]
—$(CH_2)_4$—		A	89	8.5	1.4450	n_D^{20} = 1.4451[7]

[a] Measured in CCl_4 solutions at 36.43 MHz with a Bruker HFX 90 spectrometer using 85% H_3PO_4 as external reference.
[b] Crystallised from hexane.

Scheme 2



properties of diethyl phosphoramide (**5**) are summarized in Table 1. This approach cannot be, however, recommended for other organophosphorus acids, i.e. dibenzyl hydrogen phosphate, diethyl hydrogen thiophosphate, and diphenylphosphinic acid because the corresponding anhydrides are formed in all these cases predominantly, if not exclusively.

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Experimental

Preparation of diethyl phosphoramides (**5**). *General Procedure*

Method A:

A solution of hexamethyltriaminophosphine (**1**; 3.26 g, 0.2 mol) in 10 ml of CH_2Cl_2 was added dropwise at −20° with stirring and efficient external cooling (dry ice-acetone bath) to bromine (3.2 g, 0.2 mol) dissolved in 10 ml of CH_2Cl_2. The corresponding amine (**4**; 0.2 mol) was then introduced at −20° and the cooling bath was removed. A mixture of diethyl hydrogen phosphate (**3**; 3.08 g, 0.2 mol), triethylamine (4.04 g, 0.4 mol), and CH_2Cl_2 (30 ml) was then added dropwise during 30 min. The temperature of the reacting mixture rose gradually from −20° to + 20° and triethylamine hydrobromide precipitated. Stirring was then continued at room temperature for 2 h. The product was washed with 5% hydrochloric acid (25 ml) and water (2 × 25 ml), dried, and evaporated *in vacuo* to give crude phosphoramide **5** which was analytically pure according to ^{31}P-NMR.

Method B:

Reagent **2** was obtained as described above. After removal of a cooling bath the mixture of diethyl hydrogen phosphate (**3**; 0.2 mol), triethylamine (0.4 mol), and the amine **4** (0.2 mol) was added dropwise during 30 min. Stirring was then continued for 2 h at room temperature. The solvent was evaporated and the residue dissolved in CCl_4 (50 ml) and washed with 5% hydrochloric acid (25 ml) followed by water (2 × 25 ml). Upon evaporation of the solvent *in vacuo* the residual phosphoramide **5** was analytically pure (^{31}P-NMR).

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