First examples of methylene insertion into the phosphorus(III)–nitrogen bond

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Abstract

The reaction of N-substituted phosphinous amides with paraformaldehyde leads to methylene insertion into the P–N bond, followed by the oxidation of phosphorus from P(III) to P(V) state. The product, Ph3P(O)CH2NHPh was characterised by a single-crystal X-ray diffraction study. The reaction not only depends on the acidic proton on the nitrogen, but also on the oxidation state of phosphorus and it is considered to proceed through Staudinger–Wittig pathway.

Keywords: Insertion; Phosphinoamine; Phosphine oxide; Paraformaldehyde

1. Introduction

Insertion of CO, alkene, alkyne, CO2, CS2, etc., into the M–X bond (M = metal or metalloid; X = P, C, N, S, O, halide) are well documented in the literature [1–5]. The insertion of small molecules into C–H, N–H, O–H bonds with or without metal mediation is versatile in organic synthesis. Insertion of CO, alkene, etc., is an important step in many catalytic reactions, such as hydrogenation, hydroformylation [6]. Phosphines (R2PH, RPH3) and secondary amines undergo nucleophilic addition reaction when treated with paraformaldehyde to give phoshinoalcohols (R2PCH2OH, RP(CH2OH)3) and methylolamines, respectively. However, in the case of amines, the products undergo further condensation to give diamines. So far as the P–N bond is concerned, insertion into the P–N bond is scarcely seen in the literature [7–9].

As a part of our interest in designing and exploring multifunctional phosphorus-based ligands [10], we report here the reaction of N-diphenylphosphinoaniline with paraformaldehyde that leads to methylene insertion into the P–N bond followed by the oxidation of phosphorus from trivalent to pentavalent state instead of the anticipated amino alcohols of the type A (Scheme 1).

2. Experimental

All manipulations were performed under rigorously anaerobic conditions using Schlenk techniques. The monophosphinoamine, PhN(H)PPh2 was prepared according to the literature procedure with slight modification [11]. Solvents were dried and distilled under nitrogen atmosphere prior to use. Petroleum ether (60–80°C), toluene, benzene and diethylether were distilled over Na–benzophenone and dichloromethane from calcium hydride. The 1H and 31P NMR spectra were recorded on a VXR 300S spectrometer operating at the appropriate frequencies using tetramethyilsilane and 85% H3PO4 as internal and external references, respec-

![Scheme 1](image-url)
tively. Positive shifts lie downfield of the standard in all cases. Infrared spectra were recorded on a Nicolet Impact 400 FT IR instrument in KBr disk. Microanalyses were performed on a Carlo Erba model 1106 elemental analyser.

2.1. Synthesis of Ph₂P(O)/CH₂N(H)/Ph (2)

Method (a): To a solution of N-diphenylphosphinoaniline (1) (0.5 g, 1.8 mmol) in toluene (10 ml), paraformaldehyde (0.057 g, 1.8 mmol) was added heated under reflux conditions for 4 h. The solution was then cooled to room temperature, concentrated to 4 ml and kept for 7 h to give crystalline product of 2 in 81% (0.450 g).

Method (b): A mixture of N-diphenylphosphinoaniline (0.5 g, 1.8 mmol) and paraformaldehyde (0.057 g, 1.8 mmol) placed in a round-bottomed flask fitted with a condenser was heated with stirring in an oil bath maintained at 95–100°C for 2 h. The resultant clear melt was subjected to vacuum to remove any volatile material, then washed with hexane, filtered and dried under vacuum to obtain a white solid. The compound was crystallised from CH₂Cl₂ and n-hexane (2:1) at 0°C. Yield: 91% (0.51 g), m.p. 136–138°C. Anal.: Calc. for Ph₂P(O)/CH₂N(H)/Ph, C₁₀₉H₁₈NOP: C, 74.26; H, 5.90; N, 4.55%. Found: C, 74.44; H, 6.03; N, 3.95%. IR (KBr disk) cm⁻¹: 3255s, 3124m, 3052m, 2789m, 1598s, 1493s, 1433s, 1315s, 1210m, 1171s, 1124s, 867m, 755s, 696s, 578m, 532m. ³¹P NMR (299.9 MHz, CDCl₃, 298 K): δ 6.5–7.8 (m, phenyl, 15 H), 4.26 (br.s, NH, 1H), 3.94 (dd, CH₂, 2H, 2JₚH = 8.8 Hz, 3JₚH = 3.8 Hz). ³¹P[¹H] NMR (121.427 MHz, CDCl₃, 298 K); δ 30.2. HRMS: m/z = 307.12.

2.2. Structure determination

Crystals of the compound 2 obtained as described above were mounted on Pyrex filaments with epoxy resin. General procedures for crystal alignment and collection of intensity data on the Enraf–Nonius CAD-4 diffractometer have been published [12]. Details of the crystal and data collection for 2: C₁₀₉H₁₈NOP, M = 307.31, monoclinic, a (Å) = 9.5474(5), b (Å) = 15.3265(11), c (Å) = 11.8320(10), β (deg) = 107.452(6), Z = 4, V (Å³) = 1651.7(2), T (K) = 293(2). Space group P2₁/n, D (calc) (g/cm³) = 1.236. μ (Mo-Kα) = 0.168 mm⁻¹, 3124 reflections collected, 2940 unique (R (int) = 0.0348). The final R₁ was 0.0348 (all data) and wR₂ = 0.0891 (all data). Periodic monitoring of check reflections showed stability of the intensity data. All calculations were performed with the SHELXTL PLUS [13] program package. The data are deposited in the Cambridge Crystallographic Data Center and the CCDC reference number is 150093.

3. Results and discussion

The reaction of N-diphenylphosphinoaniline (1) with paraformaldehyde in toluene under reflux for 4 h afforded the methylene-inserted product, Ph₂P(O)/CH₂N(H)/Ph (2), in good yield. The ³¹P NMR spectrum of 2 shows a singlet at 30.2 ppm. The ¹H NMR spectrum shows a singlet at δ 4.26 which is D₂O exchangeable and is assigned to NH, and a doublet of doublets at δ 3.94 with a 2JₚH value of 8.8 Hz is assigned to the CH₂ protons. The IR spectrum shows ν NH at 3255 cm⁻¹, which is about 50 cm⁻¹ lower in frequency when compared to the phosphinous amide (ν NH = 3302 cm⁻¹), indicates the participation of the NH bond in either intra- or intermolecular interactions. The elemental analysis and HRMS could not explain the low-frequency shift of the NH bond and also the ³¹P NMR data did not rule out the possibility of structure A as there is no significant difference in P(III) and P(V) chemical shifts. However, the single-crystal X-ray studies confirmed that the product is not A and it is the methylene-inserted compound 2 (Fig. 1). The low-frequency shift of ν NH when compared to phosphinous amide is due to the intermolecular N···H … O=P hydrogen bonding between H(1N) and O of adjacent molecules [d₉₋O = 2.866(3) Å, d₉₋O…O = 2.02(2) Å, N–H(1N) … O bond angle is 173(1)°] as the compound 2 exists as a dimer (Fig. 2). The anti conformation of the NH and the P=O of adjacent molecules facilitates this strong intermolecular hydrogen bonding. The P–O (1.481 Å) and P–C(av) (1.804 Å) bond lengths agree well with the literature [14].

![Fig. 1. Perspective view of the compound (2).](image-url)

**References**

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**Fig. 1. Perspective view of the compound (2).**
The phosphorus is in a slightly distorted tetrahedral environment.

Mukaiyama and Yokota [15] and Hudson and co-workers [7] have reported the de-oxygenation reactions of isocyanates by the cyclic phosphoramidite (2-phenyl-1,3,2-oxazaphospholidine) and acyclic phosphoramidite (diethyl-N-phenylphosphoramidite) to give the corresponding phosphen oxide and isonitrile which involves the preferential interaction of the oxygen and phosphorus atoms. Ivanov et al. [16] have obtained the same product (2) via the Arbuzov reaction of RR’NCH2OAc (R = R’ = Et; R = H, R’ = Ac, Bz, Ph) with PhR’PNEt3 (R” = Ph, NEt3) as shown in Scheme 1.

From the earlier reports [7,8], it was found that the hydrogen atom on nitrogen greatly accelerates the reaction. Also, no reaction occurred when the diphenylphosphinoamines containing P=O, P=S or P=Se bonds was treated with paraformaldehyde. This indicates that the reaction depends not only on the active hydrogen on nitrogen, but also on the oxidation state of phosphorus, i.e. the reaction occurs only if the phosphorus is in trivalent state. The mechanism of the reaction follows the Staudinger–Wittig pathway, which involves proton transfer from nitrogen to phosphorus giving the intermediate Ph3P(O)H as shown in the proposed mechanism (Scheme 2). This may probably be due to the interaction of oxygen atom of the zwitterionic intermediate with the electrophilic phosphorus.

To summarise, the P(III)–N bond undergoes methylene insertion followed by the oxidation of P(III) to P(V) when treated with paraformaldehyde. Similar results were obtained with a chiral amine derivative such as PhCH(Me)NHPPH2 [17]. We found that this method is very convenient to make this type of compound in high yield. Further, these compounds can be reacted with phosphorus(III) reagents to obtain heterodifunctional ligands containing soft P(III) and hard oxygen donor centers which can serve as potential homogeneous catalysts in organic synthesis [18]. Further research in this direction is in progress.

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References

V.V. Grushin, J. Am. Chem. Soc. 121 (1999) 5831;