SHORT COMMUNICATIONS

SOME REACTIONS OF O,O-DIPHENYLPHOSPHORYL AZIDE

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Abstract

Diphenylphosphoryl azide, in contrast to N,N'-disubstituted phosphorodiamidic azides, undergoes nucleophilic displacement of the azido group by reaction with water, butanol, ammonia, and amines. Possible mechanisms for the conversion of diphenylphosphoryl azide into urethanes and amides are briefly discussed. Pyrolysis of N,N'-dicyclohexylphosphorodiamidic azide gave the phosphenimidic amide dimer.

O,O-Diphenylphosphoryl azide (1) has been obtained by reaction of the phosphorochloridate with sodium azide. This compound undergoes pseudohalogen replacement of the azido group by treatment with nucleophilic reagents, such as water, butanol, ammonia, and various amines. Thus with aniline, the corresponding N-phenylphosphoramidate (2; R = Ph) was formed in high yield:

\[
\text{(PhO)}_2\text{P(O)N}_3 \xrightarrow{\text{RNH}_2} \text{(PhO)}_2\text{P(O)NHR} + \text{HN}_3
\]

With strong bases, like ammonia and aliphatic amines, the reaction was rapid and exothermic at room temperature; but with weaker bases, like aniline, there was no apparent reaction at room temperature.

The reactivity of the azide (1) towards nucleophiles resembled the behaviour of sulphonyl azides,\(^1\) but differed markedly from that of N,N'-disubstituted phosphorodiamidic azides which were very stable towards nucleophilic substitution at phosphorus.\(^2\)

However, efforts to obtain a phosphoryl nitrile insertion reaction, by heating the azide (1) with boiling o-xylene under similar conditions to those successfully used for the analogous reaction with sulphonyl azides,\(^1\) were unsuccessful.

The stability of the azide (1) towards heating was shown by its distillation at 157\(^\circ\),\(^3\) and by the fact that vigorous evolution of nitrogen was not observed until a temperature of 175\(^\circ\) had been reached.

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1 Cremllyn, R. J. W., J. chem. Soc. (C), 1965, 1132.

The publication of these reactions of $O,O$-diphenylphosphoryl azide has been prompted by the recent report\(^3\) of the use of this compound as a reagent for the synthesis of peptides by virtue of its reactions with carboxylic acids leading to either the urethane (3) or the amide (4):

\[
\text{RCO}_2\text{H} + \text{(PhO)}_2\text{P(O)}\text{N}_3 \rightarrow \text{RNHCO}_2\text{R'} \quad (3)
\]

\[
\text{RNH}_2\text{E}_2\text{N} \rightarrow \text{RCONHR'} \quad (4)
\]

The formation of the urethane (3) is particularly valuable since it works with carboxylic acids which fail to undergo the Schmidt reaction, and is believed\(^3\) to involve transfer of the azido group from (1) to the carboxylic acid. It is now suggested that this reaction proceeds through the intermediate mixed anhydride (5), resulting from attack by the nucleophilic carboxylate anion on the phosphorus atom, with expulsion of the azide ion. The latter then attacks the carbonyl carbon atom, to give the acyl azide (6) and loss of the diphenyl phosphate anion, known\(^4\) to be a good leaving group. Finally the acyl azide (6) reacts in the normal manner to give the urethane (3).

\[
\text{(PhO)}_2\text{P}\text{N}_3 \rightarrow \text{(PhO)}_2\text{P} \text{-} \text{O} \text{-} \text{R} \rightarrow \text{RCON}_3 \quad (1)
\]

\[
\text{N}_3 \rightarrow \text{N} \rightarrow \text{N} \rightarrow \text{RCONHR'} \quad (5)
\]

The present studies show that diphenylphosphoryl azide (1) reacts with amines giving the corresponding phosphoramidates (2); it therefore appears that formation of the amide (4) similarly involves the intermediate anhydride (5), followed by nucleophilic substitution by the amine:

\[
\text{(PhO)}_2\text{P} \text{-} \text{N}_3 \rightarrow \text{(PhO)}_2\text{P} \text{-} \text{N} \text{-} \text{R} \rightarrow \text{RCONHR'} \quad (6)
\]

Pyrolysis of $N,N'$-dicyclohexylphosphorodiamidic azide gave the dimeric phosphenimidic amide, as was observed\(^2\) in the analogous reaction with $N,N'$-dibenzylphosphorodiamidic azide.

**Experimental**

Mass spectra were determined with an A.E.I. MS9 spectrometer at 70 eV. I.r. spectra were generally determined as Nujol mulls with a Perkin-Elmer 257 spectrometer. N.m.r. spectra were measured with a Varian A60A spectrometer with tetramethylsilane as internal standard. The $^{31}\text{P}$ n.m.r. spectra were measured with a Perkin-Elmer R10 high resolution spectrometer using 85% phosphoric acid as external standard. Melting points were determined with a Kofler hot-stage apparatus.

O,O-Diphenylphosphoryl Azide (I)

Diphenylphosphorochloridate (13 g) in acetone (20 ml) was stirred with a solution of sodium azide (6.6 g, 2 mol equiv.) in water (20 ml) for 3 hr. The acetone was removed under vacuum, and the residual oil extracted with ether (200 ml), to give the phosphoryl azide as a pale yellow oil (8 g) (lit.3 b.p. 157°/0.17 mm) (Found: C, 52.2; H, 3.7; N, 14.2; P, 11.0. Calc. for C_{12}H_{10}N_{3}O_{3}P: C, 52.4; H, 3.6; N, 14.4; P, 11.3%). v_\text{max} (\text{CHCl}_{3}) 2180 (N, asym. str.), 1595 (arom. C=C), 1290, 1270 (N_3 sym. str.), 1180 (P=O) cm\textsuperscript{-1}.

Effect of heating.—When the azide (200 mg) was heated bubbling began at 165°, and became vigorous, with darkening at 175°. At 230° rapid decomposition was observed, the liquid becoming a dark red-brown; the increasing heating was accompanied by progressive decrease in the size of the azide band in the i.r. spectra of the decomposition products.

Reactions of Diphenylphosphoryl Azide (I) with Various Nucleophiles

(i) Water.—The azide (1 g) was boiled under reflux with water (15 ml) and dioxan (15 ml) for 6 hr to give diphenyl hydrogen phosphate dihydrate (0.8 g), m.p. 58-60° (lit.5 61-62°). v_\text{max} 3440, 3240 (NH), 1220 (P=O) cm\textsuperscript{-1}; 31P n.m.r. (DMSO) +6.0 p.p.m. (doublet) (lit? +6.3, 7.1).

(ii) Ammonia.—The azide (1 g) by shaking with ammonia (2 ml of 0.88) and ethanol (10 ml) gave a solution which became warm and a precipitate began to form After 2 hr, the crystalline product was filtered off to give diphenylphosphoramidate (2; R = H) (0.8 g), m.p. 151° (lit.6 149.5-150°); v_\text{max} 3440, 3240 (NH), 1220 (P=O) cm\textsuperscript{-1}; 31P n.m.r. (DMSO) +6.0 p.p.m. (doublet) (lit? +6.3, 7.1).

(iii) Aniline.—The azide (1.4 g) was boiled under reflux with aniline (1 g, 2 mol equiv.) in ethanol (15 ml) for 3 hr to give the N-phenylphosphoramidate (2; R = Ph) (1.1 g), m.p. 130-132° (lit.' 129-130°); v_\text{max} 3180 (NH), 1600 (arom. GC), 1220, 1180 (P=O) cm\textsuperscript{-1}; 31P n.m.r. (DMSO) +6.0 p.p.m. (doublet) (lit? +6.3, 7.1).

(iv) Benzylamine.—The azide (1 g) was treated with benzylamine (1.2 ml, 2 mol equiv.) in ethanol (5 ml); the liquid became hot and a solid was precipitated; the suspension was boiled under reflux for 1 hr to give the N-benzylphosphoramidate (2; R = PhCH\textsubscript{2}) as needles (0.9 g), m.p. 103-104° (lit.8 102-102.5°).

(v) Cyclohexylamine.—The azide (1 g) was mixed with cyclohexylamine (1 ml, 2 mol equiv.) in methanol (5 ml); an exothermic reaction occurred with the precipitation of a solid. Recrystallization (aqueous ethanol) gave the N-cyclohexylphosphoramidate (2; R = CycH\textsubscript{11}) as plates (0.8 g), m.p. 103-105° (lit.8 101-102.5°).

(vi) Butanol.—The azide (3.0 g) was boiled under reflux with butanol (10 ml) for 6 hr. The butanol was evaporated under vacuum, and the residue extracted with ether (200 ml) to give butyl-diphenyl phosphate (3.4 g), b.p. 178-181°/3 mm (lit.9 181-182°/3 mm) (Found: C, 62.1; H, 5.9; P, 10.4). Calc. for C\textsubscript{16}H\textsubscript{10}O\textsubscript{4}P: C, 62.4; H, 5.2; P, 10.1%.

Decomposition of N,N'-Dicyclohexylphosphorodiamidic Azide

The azide (1.5 g) was heated at 170° under reduced pressure (13 mm) for 1 hr to give N,N'-dicyclohexylphosphorodiamidic amide dimer, as prisms from ethanol (200 mg), m.p. >300° (Found: C, 59.3; H, 9.3; N, 11.4; P, 12.9. C\textsubscript{12}H\textsubscript{23}N\textsubscript{2}OP requires C, 59.5; H, 9.5; N, 11.6; P, 12.8%). v_\text{max} 3180 (NH), 1220 (P=O) cm\textsuperscript{-1}. The mass spectrum showed the molecular ion (M, 484).

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