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N-(Dialkylphosphinoyl)hydroxylamines : Preparation using *N,O*-Bis(trimethylsilyl)hydroxylamine and Migration of Simple Alkyl Groups in the Rearrangements of their *O*-*p*-Nitrobenzenesulphonates[1]

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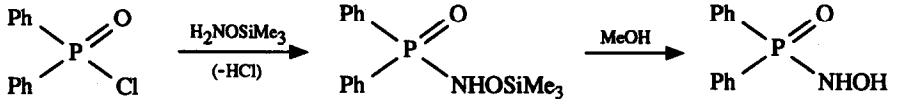
Abstract : Treatment of $Pr^i_2P(O)Cl$ with $Me_3SiNHOSiMe_3$ gives $Pr^i_2P(O)NHOSiMe_3$, which is desilylated by methanol giving $Pr^i_2P(O)NHOH$. The *O*-*p*-nitrobenzenesulphonyl derivative of this rearranges with $KOBu^t$ in Bu^tOH, an isopropyl group migrating from P to N and the phosphonamidate $Pr^iP(O)(OBu^t)NHPr^i$ being formed quantitatively. Rearrangement also occurs in other alcohols (MeOH, EtOH, Pr^iOH), but not quite as cleanly. In Bu^tNH_2 the phosphinoylhydrazine $Pr^i_2P(O)NHNHBu^t$ is formed as well as the rearrangement product, $Pr^iP(O)(NHBu^t)NHPr^i$. The *p*-nitrobenzenesulphonyl derivatives of $Et_2P(O)NHOH$ and $Pr^iMeP(O)NHOH$, prepared similarly with $Me_3SiNHOSiMe_3$, also rearrange quantitatively with Bu^tOH - $KOBu^t$. In the latter case, the migratory aptitudes of the two alkyl groups (Pr^i and Me) are almost identical.

Diphenylphosphinic chloride **1** reacts with the hydroxyl group of hydroxylamine, rather than the amino group, giving *O*-(diphenylphosphinoyl)hydroxylamine.[2] To obtain the *N*-phosphinoyl compound **2** it is necessary that this reaction be blocked. Using $H_2NOSiMe_3$ (and Et_3N or pyridine to scavenge the liberated HCl) it has been possible to prepare **2** and other *N*-phosphinoylhydroxylamines (Scheme 1),[3,4] including those in which one of the phenyl groups is replaced by benzyl or a simple alkyl group (Me, Et,

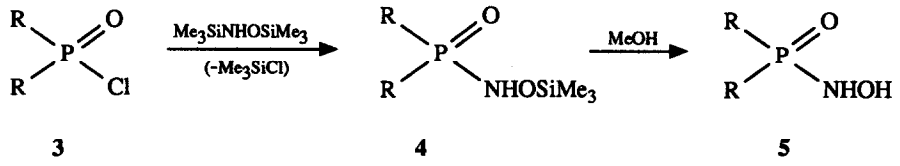


1 **2**

Scheme 1

Pr^i).[5,6] However, repeated attempts to extend the method to *N*-phosphinoylhydroxylamines with two simple alkyl groups on phosphorus have failed, the closest we could get being a dibenzyl compound.[7] This is particularly unfortunate in relation to the Lossen-like rearrangement of *O*-sulphonyl-*N*-phosphinoyl-hydroxylamines,[3-7] as it has precluded examination of the ability of a simple alkyl group to migrate from phosphorus to nitrogen.

In looking for a possible alternative route to *N*-(dialkylphosphinoyl)hydroxylamines, we noted Michalski's use of *N*-(trimethylsilyl)imidazole for converting phosphorus acid chlorides into *N*-phosphoroylimidazoles.[8] It seemed possible that phosphinic chlorides would react with $Me_3SiNHOSiMe_3$ in a similar way, eliminating Me_3SiCl and forming a P–N bond (Scheme 2). There are, of course, two silyl groups in $Me_3SiNHOSiMe_3$, but the one on nitrogen seemed likely to be the more



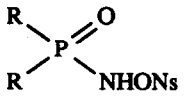
Scheme 2

reactive. Some encouragement was drawn from carbonyl chemistry, in particular the reactions of $Me_3SiNMeOSiMe_3$ with ketones[9] and $(Me_3Si)_2NOSiMe_3$ with acyl chlorides;[10] in both of these, an *N*-silyl group is eliminated, a C–N bond is formed, and the *O*-silyl group remains in place.

RESULTS AND DISCUSSION

Preparation of Substrates

Diethylphosphinic chloride **3** (R = Et) reacted readily with $Me_3SiNHOSiMe_3$ (1.25 mol equiv.) in a concentrated CH_2Cl_2 solution (δ_p 76 → 62.5). On the assumption that the *N*-phosphinoyl-*O*-silylhydroxylamine **4** (R = Et) had been formed, and that Me_3SiCl was present as a byproduct, the volatile material was removed *in vacuo* and the residue, dissolved in fresh CH_2Cl_2, was desilylated by treatment with MeOH. The result was an oily substance that began to decompose (CAUTION)[11] on attempted purification. Given that **5** (R = Et) might well be a liquid at room temperature [the parent phosphinic acid, $Et_2P(O)OH$, has m.p. 19 °C],[12] and that practically all the *N*-phosphinoylhydroxylamines prepared to date have decomposed at their melting points,[3-7] such instability would not be too surprising. The desilylated material was therefore subjected only to brief superficial purification, and was not characterised; instead, it was derivatised without delay. We have generally worked with *O*-methanesulphonyl derivatives,[3-7] but in this case the *p*-nitrobenzenesulphonate (nosylate) seemed to offer advantages. There should be more chance of it being obtained as a solid, stable enough for purification and characterisation, and it should be particularly well disposed towards a Lossen-like rearrangement[13] in which the sulphonate group must depart as the anion. Using *p*-nitrobenzenesulphonyl chloride (NsCl) and Et_3N, a crystalline product [m.p. 119 - 120 °C (decomp.)] was obtained, and was shown (^1H NMR and IR spectroscopy; elemental analysis) to be the hoped-for nosylate **6** (R = Et) (55 % overall yield from the phosphinic chloride). Starting from isopropyl(methyl)phosphinic chloride, a very similar procedure led to the nosylate **7** [m.p. 127 - 128 °C (decomp.)] (54 % overall). Here too, the intermediate compounds were obtained as oils that were not characterised.



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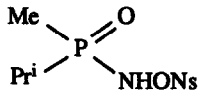

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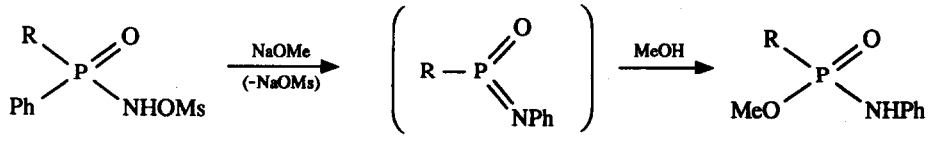
Having two bulky alkyl groups on phosphorus, diisopropylphosphinic chloride **3** (R = Pr^i) reacted only reluctantly with $Me_3SiNHOSiMe_3$. By use of an extremely concentrated reaction mixture (3 M substrate) and a slightly elevated temperature (30 °C) it was possible to effect complete consumption of the substrate (δ_P 85.9 → 63.3) within 22 h, although not without the formation of a significant amount of a side product (δ_P 54.3). The first few percent of reaction seemed to be particularly slow, suggesting some form of autocatalysis. Perhaps the Me_3SiCl formed during the reaction activates the P=O group of the phosphinic chloride to nucleophilic attack.[14] The product, after evaporation of the volatile material, was in this case a solid, and simply washing with ether afforded the silylated phosphinoylhydroxylamine **4** (R = Pr^i) in a spectroscopically pure state: δ_H ($CDCl_3$) 5.45 br (1H, NH) and 0.16 (9 H, s, $SiMe_3$); *m/z* 237 (M^+, 8 %); $\nu_{max.}$ (Nujol) 3110 cm^{-1} (NH).

The isolation and characterisation of the silylated phosphinoylhydroxylamine highlights a major advantage of the use of $Me_3SiNHOSiMe_3$: the chlorine displaced from the substrate becomes bound up in easily removed Me_3SiCl. Using the $H_2NOSiMe_3$ method, by contrast, the displaced chlorine becomes the anion of a salt (Et_3NHCl or pyridineHCl), and complete separation of this from the silylated phosphinoylhydroxylamine is not easy. Indeed, our many attempts to do so, with different phosphinoyl groups, have invariably been thwarted by extensive desilylation and/or decomposition. It is only now, with **4** (R = Pr^i), that we have direct evidence that the initial product really is the *O*-silyl-*N*-phosphinoyl-hydroxylamine.

Desilylation of **4** (R = Pr^i) with methanol gave the *N*-phosphinoylhydroxylamine **5** (R = Pr^i), δ_H ($CDCl_3$) 6.3 br (2 H, NHOH); *m/z* 165 (M^+, 6 %); $\nu_{max.}$ (Nujol) 3215 and 3165 cm^{-1} (NHOH), which was obtained analytically pure by crystallisation. Thus an *N*-phosphinoylhydroxylamine having only simple alkyl groups on phosphorus was fully characterised for the first time. It was converted into the nosylate **6** (R = Pr^i) without difficulty.

Base-induced Rearrangements in t-Butyl Alcohol

Previous work with *N*-(diphenylphosphinoyl)hydroxylamine has shown that the *O*-methanesulphonyl derviative **8** (R = Ph) readily undergoes a base-induced Lossen-like rearrangement in MeOH.[3] The metaphosphonimidate may be an intermediate (Scheme 3), but the observed product is the phosphonamidate



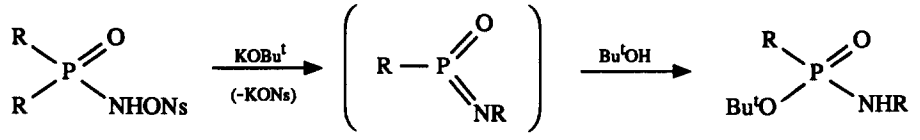
8 **9**

Scheme 3

9 (R = Ph). For the unsymmetrical substrates **8** (R ≠ Ph) the group that migrates can (in principle) be either Ph or R, so there are two possible pathways for rearrangement. Both are observed when R is an aryl group, albeit that the aptitude for migration is markedly reduced by a powerful electron-withdrawing substituent (p-NO_2).[4] When R is an alkyl group (Me, Et, Pr^i), however, only the Ph group migrates.[6] No trace of alkyl migration has been observed with any alkyl(phenyl)phosphinoyl substrate. This is rather surprising, both in itself[15] and because alkyl groups migrate at least as readily as phenyl in the Curtius-like photochemical rearrangements of the corresponding phosphinic azides [$RPhP(O)N_3$; R = Et, Pr^i, Bu^t].[16] Could it be that some unrecognised mechanistic feature of the Lossen-like rearrangement makes migration of a simple alkyl group impossible? Having now found a method of obtaining substrates containing only simple alkyl groups attached to phosphorus, this question can at last be addressed.

So that base-induced rearrangement of the nosylate should have as much chance as possible, without undue competition from possible nucleophilic attack, the reactions were examined in t-butyl alcohol rather than methanol. The nosylates displayed little solubility at room temperature, but when potassium t-butoxide (1.5 mol equiv.) was added they gradually dissolved (reacted). Although it took up to 15 min. for all the substrate to pass into solution, the reaction of dissolved substrate seemed to be rapid.

For each of the symmetrical substrates **6** (R = Et) and **6** (R = Pr^i), the ^{31}P NMR spectrum indicated a single product, at a sufficiently high field (δ_P 31.3 and 32.0 respectively) to suggest that only one of the original alkyl groups was still attached to phosphorus. The ^1H NMR spectra of the products, after isolation and purification by distillation (R = Et) or sublimation (R = Pr^i), afforded good evidence for one alkyl group on nitrogen [δ_H 1.14 (3 H, t, J_{HH} 7 Hz, $NCH_2\mathit{Me}$) or 1.16 (6 H, d, J_{HH} 6.5 Hz, $NCH\mathit{Me}_2$] and one on phosphorus [δ_H 1.11 (3 H, dt, J_{PH} 21, J_{HH} 7.5 Hz, $PCH_2\mathit{Me}$) or 1.13 and 1.12 (both 3 H, dd, J_{PH} 18, J_{HH} 7 Hz, $PCH\mathit{Me}_2$) (diastereotopic Me groups)] as well as an O-t-butyl group [δ_H 1.49 (9 H, s)]. Prominent ions in the mass spectra corresponding to (M^+ - Me) and (M^+ - Me - C_4H_8) were also consistent with the presence of N-ethyl or isopropyl and O-t-butyl groups. There seems no doubt that rearrangement occurs (Scheme 4), giving the phosphonamidate **10** (R = Et or Pr^i).

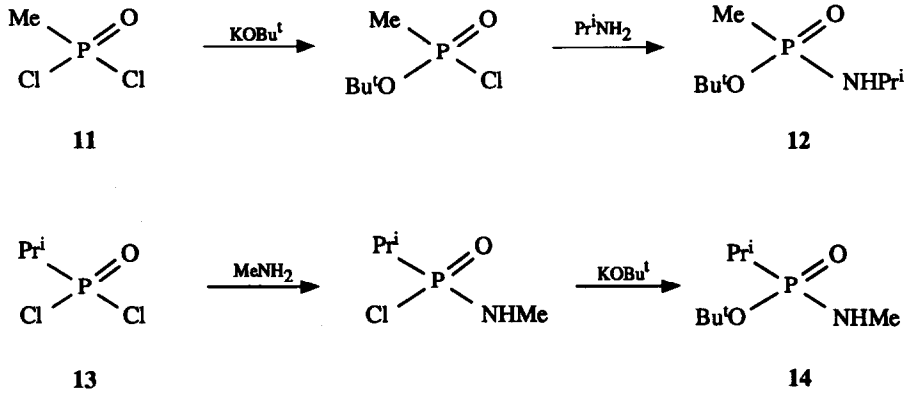


6 **10**

Scheme 4

The unsymmetrical substrate **7** gave an equal mixture of two products (δ_P 26.5 and 34.3) with KOBu^t - Bu^{t}OH. The ^1H NMR spectrum (300 MHz) of the mixture was rather complex (overlap of signals δ_H 1.1 - 1.2), but it was possible to establish the presence of two O-t-butyl groups (δ_H 1.49 and 1.495), two methyl groups [2.62, dd, J_{PH} 10.5, J_{HH} 6 Hz (PNHMe) and 1.43, d, J_{PH} 16.5 Hz (PMe)], and two isopropyl groups [3.38, m (NHCHMe$_2$) and 1.85, d x septet, J_{PH} 17.5, J_{HH} 7 Hz (PCHMe$_2$)]. This is clearly suggestive of a mixture of the rearrangement products **12** and **14**. For confirmation, authentic samples of these compounds were prepared from the appropriate phosphonic dichlorides **11** and **13** (Scheme 5). They showed the ^1H NMR features seen in the spectrum of the rearrangement product mixture, and had identical

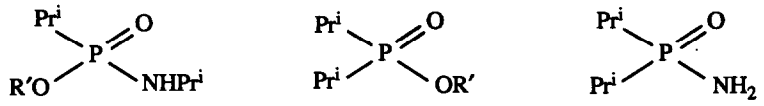
capillary GLC retention times.



Scheme 5

Other Base-induced Rearrangements

To assess the scope of the rearrangement, and to allow further comparisons with azide photochemical reactions,[17] the behaviour of the substrate **6** (R = Pr^i) was examined in other alcohols. With both Pr^{i}OH - NaOPr^i and EtOH - NaOEt the rearrangement product **15** (R′ = Pr^i or Et) was formed in high yield (> 95 % and ~ 94 % respectively of the total GLC - observable product). Several minor products were detected, but on comparison with authentic samples it was seen that these did not include the phosphinic ester **16** (R′ = Pr^i or Et) or the phosphinic amide **17**. The latter observation is particularly noteworthy; in the photolysis of the corresponding phosphinic azide [**6** (R = Pr^i) with N_3 in place of NHONs] the phosphinic amide **17** was the

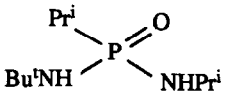


15 **16** **17**

major product in ethanol, and the only one in isopropyl alcohol.[17] For preparing phosphonamidates it seems clear that the Lossen-like rearrangement is of more general value than the photochemical Curtius-like reaction. In methanol, the base-induced rearrangement of **6** (R = Pr^i) was rather less clean (85 % one product by GLC), but gave the phosphonamidate **15** (R′ = Me) as the principal product. Some of the phosphinic ester **16** (R′ = Me) was formed in this case, but still very little (2 - 3 %). With the sterically less hindered substrate **6** (R = Et), however, reaction with MeOH - NaOMe gave comparable amounts of the phosphonamidate rearrangement product EtP(O)(OMe)NHEt and the phosphinic ester $Et_2P(O)OMe$. Nonetheless, this is still at least as good as the azide photolysis[17] for obtaining the phosphonamidate.

On the other hand, when a phosphonic diamide is sought by rearrangement, the azide reaction may be the more successful. Thus the photolysis of diisopropylphosphinic azide in t-butylamine gave the diamide **18** as the only substantial product (74 % isolated),[17] whereas the nosylate **6** (R = Pr^i) in t-butylamine (base as well as solvent) gave two principal products, in comparable yield. One of these was the diamide **18** but

the other was plainly unrearranged (^{1}H NMR : no *N*-Pr^i, 2 equivalent *P*-Pr^i groups), even though the sulphonate had been displaced and the amine incorporated [M^+ 220; δ_H 3.05 (s, NH) and 1.06 (9H, s)]. The



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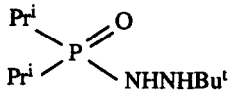

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presence of a second NH (δ_H 4.10, d, J_{PH} 11 Hz), together with solubility in aqueous acid, points to the second product being the phosphinoylhydrazine **19**. Clearly nucleophilic attack at nitrogen now competes with the base-induced rearrangement of the nosylate. Dilution of the amine with an inert solvent (CH_2Cl_2) did not diminish the importance of nucleophilic attack. On the contrary, the proportion of phosphinoylhydrazine in the product was greatly increased, and the phosphonic diamide rearrangement product was obtained in only 10 % yield.

Conclusions

Two important conclusions can be drawn from this study. First, some *N*-phosphinoylhydroxylamines that could not be obtained with $H_2NOSiMe_3$ can be prepared using $Me_3SiNHOSiMe_3$. The method is quite straightforward, and $Me_3SiNHOSiMe_3$ may become the preferred reagent for making *N*-phosphinoylhydroxylamines in general. Second, for simple alkyl groups, as for benzyl, there is no insurmountable barrier to migration in the Lossen-like rearrangement of the *O*-sulphonyl derivatives of *N*-phosphinoylhydroxylamines. Alkyl migration cannot compete when phenyl migration is also possible, but if no phenyl group is available, rearrangement still occurs quite readily. In some cases rearrangement has to compete with nucleophilic attack on the substrate, at phosphorus or at nitrogen, but this is unimportant so long as the base is strong and not particularly nucleophilic.

EXPERIMENTAL

Instrumentation.– M.p.s were determined using a Kofler hot-stage apparatus and are uncorrected. IR spectra were obtained with a Perkin-Elmer 298 instrument. ^{1}H NMR spectra were recorded at 90 MHz on a Varian EM 390 spectrometer or at 300 MHz on a Brucker AM-300 (Me_4Si internal standard), and ^{31}P NMR spectra (^{1}H decoupled) were recorded at 36.2 MHz on a JEOL JNM-FX90Q spectrometer (positive chemical shifts downfield from external 85 % H_3PO_4). Mass spectra were obtained in EI (70 eV) or CI (NH_3) mode using VG 12-253, 16-B, or ZAB-E (high resolution) spectrometers. GLC analyses were carried out using a 12 m x 0.53 mm SE 54 (1.2 μm film) column in a Philips PU4500 chromatograph fitted with a flame ionization detector (helium carrier gas, linear flow 0.40 m s^{-1}).

Solvents and Reagents.– Methanol and ethanol were dried by distillation from their magnesium salts, and isopropyl and t-butyl alcohols by repeated treatment with powdered 3 A molecular sieve. Light petroleum refers to the fraction b.p. 60 - 80 °C unless otherwise indicated. Potassium t-butoxide was sublimed immediately before use. Diethyl and diisopropylphosphinic acids were available from earlier work.[18,19] *N,O*-Bis(trimethylsilyl)hydroxylamine was prepared by silylation of free hydroxylamine[20] with

trimethylsilyl chloride.[21]

Isopropyl(methyl)phosphinic Acid.[22] – A solution of *N,N*-dimethyl-*P*-isopropylphosphonamidic chloride (4.60 g, 27.2 mmol) in ether (25 ml) was added dropwise over 15 min. to a stirred solution of methylmagnesium chloride (30 mmol; 10 ml of 3.0 M THF solution) in ether (60 ml). An oil separated. The mixture was heated under reflux for 1.5 h. Ammonium chloride (0.3 g) was added to destroy any remaining Grignard reagent and the solvent was evaporated. Dichloromethane (60 ml) and water (4 ml) were added, and insoluble solid material was removed by filtration. The filtrate contained the required phosphinic amide [$Pr^iMeP(O)NMe_2$] (δ_P 53), but also a substantial impurity (δ_P 60) (possibly unchanged substrate). These were separated by concentration to a small volume, extraction of the phosphinic amide into water (5 ml) [the impurity remained in the organic phase], and re-extraction from water with several larger portions of dichloromethane (40 ml, 3 x 15 ml). The organic extracts were evaporated and the residual phosphinic amide was hydrolysed in 2 M hydrochloric acid (8 ml) at room temperature (36 h, but reaction probably complete in much less time). The solution was concentrated (to 2 ml) and extracted with dichloromethane (25 ml, 4 x 2 ml). The extracts were evaporated, water was removed by azeotroping ($CHCl_3$), and the product was extracted into ether. Isopropyl(methyl)phosphinic acid (1.81 g, 55 %) was obtained spectroscopically pure, δ_P ($CDCl_3$) 61.0; δ_H ($CDCl_3$) 11.80 (1 H, s), 1.83 (1 H, m), 1.40 (3 H, d, J_{PH} 14 Hz), and 1.15 (6 H, dd, J_{PH} 17, J_{HH} 7 Hz).

Phosphinic Chlorides. – These were prepared as previously described [**3** (R = Pr^i)],[19] or by adding an excess of oxalyl chloride in portions (quite vigorous gas evolution) to a stirred solution of the phosphinic acid in dichloromethane or ether at *ca.* 5 °C. After 0.5 h at room temperature, volatile material was evaporated and (to remove last traces of oxalyl chloride) benzene was added to, and evaporated from, the residue. After pumping *in vacuo*, the phosphinic chloride (pure by ^{31}P NMR spectroscopy) was used without further purification.

N-*(Diisopropylphosphinoyl)hydroxylamine* (**5**; R = Pr^i).– *N,O*-Bis(trimethylsilyl)hydroxylamine (1.1 g, 6.2 mmol) was added to a solution of diisopropylphosphinic chloride (5.0 mmol) in dichloromethane (1.5 ml). The vessel was stoppered in a way that would allow pressure to be vented, and was maintained at 30 °C. Reaction was complete (δ_P 85.9 → 63.3) (substantial byproduct, δ_P 54.3) in 22 h. Volatile material was removed *in vacuo* and the resutling solid was washed with ether to give N-*(diisopropylphosphinoyl)*-O-*(trimethylsilyl)hydroxylamine* (**4**; R = Pr^i) (0.91 g, 77 %), m.p. 88 - 91 °C; *m/z* 237 (M^+, 8 %); $\nu_{max.}$ (Nujol) 3110 cm^{-1}; δ_H($CDCl_3$) 5.45 br (1 H, NH), 2.21 (2 H, d x septet, J_{PH} 11, J_{HH} 7 Hz), 1.23 (6 H, dd, J_{PH} 17, J_{HH} 7 Hz), 1.22 (6 H, dd, J_{PH} 16, J_{HH} 7 Hz), and 0.16 (9 H, s); δ_P ($CDCl_3$) 64.1 (Found : M^+, 237.1314. $C_9H_{24}NO_2PSi$ requires M, 237.1314). Desilylation was achieved using methanol (1 ml) in dichloromethane (4 ml) (δ_P 64.4 → 63.3) for 6 h. The solution was concentrated to a small volume (no heat), and ether was added to precipitate N-*(diisopropylphosphinoyl)hydroxylamine* (**5**; R = Pr^i) (0.49 g, 60 % overall), m.p. 97 - 101 °C (decomp.) (from CH_2Cl_2 - ether); *m/z* 165 (M^+, 6 %), 149 (40), and 64 (100); $\nu_{max.}$ (Nujol) 3215 and 3165 cm^{-1}; δ_H($CDCl_3$) 6.3 br (2 H, s, NHOH), 2.18 (2 H, d x septet, J_{PH} 11, J_{HH} 7 Hz), and 1.25 (12 H, dd, J_{PH} 16, J_{HH} 7 Hz); δ_P ($CDCl_3$) 62.1 (Found : C, 43.8; H, 9.7; N, 8.6. $C_6H_{16}NO_2P$ requires C, 43.6; H, 9.8; N, 8.5 %).

N-*(Diethylphosphinoyl)hydroxylamine* (**5**; R = Et).– *N,O*-Bis(trimethylsilyl)hydroxylamine (220 mg, 1.25 mmol) was added to a solution of diethylphosphinic chloride (141 mg, 1.0 mmol) in dicholoromethane (1.0 ml). Reaction was complete (δ_P 76 → 62.5) in 15 min. Volatile material was removed *in vacuo*, and (to ensure no Me_3SiCl remained) some benzene (1 ml) was added to, and pumped from, the oily residue. This was then dissolved in dichloromethane (0.8 ml) containing methanol (96 mg, 3 mmol). Desilylation (δ_P 61.5 → 59.9) was *ca.* 90 % complete in 18 min., at which time the solution was immediately cooled ($T \leqslant 10$ °C) and most of the solvent removed. With continued cooling, ether (2 ml) and light petroleum (2 ml) were added and partially evaporated (to remove traces of MeOH). The remaining solvent was decanted from the oily *N*-phosphinoylhydroxylamine (**5**; R = Et) that had separated (CAUTION).[11] After washing with a little ether, this was immediately converted into the *p*-nitrobenzenesulphonyl derivative (see below).

N-*[Isopropyl(methyl)phosphinoyl]hydroxylamine*.– The silylated phosphinoylhydroxylamine was prepared (δ_P 75.1 → 61.5), isolated, and desilylated (δ_P 61.1 → 59.3) in the same way as for the diethylphosphinoyl compound except that the desilylation was slower and was allowed to proceed for 40 min. [A decomposition product (δ_P 61.2) became apparent in the later stages of the desilylation]. *N*-[Isopropyl(methyl)phosphinoyl]hydroxylamine was obtained as an oil (CAUTION),[11] and was immediately converted into the *p*-nitrobenzenesulphonyl derivative (see below).

N-*(Diisopropylphosphinoyl)*-O-p-*nitrobenzenesulphonylhydroxylamine* (**6**; R = Pr^i).– A suspension of the *N*-phosphinoylhydroxylamine (495 mg, 3.0 mmol) in dichloromethane (5 ml) was stirred and cooled in ice while *p*-nitrobenzenesulphonyl chloride (795 mg, 3.6 mmol) and triethylamine (303 mg, 3.0 mmol) were added. Stirring was continued at room temperature for 15 min. (reaction complete by ^{31}P NMR spectroscopy). The solvent was evaporated and the solid residue was washed thoroughly with ether and cold aqueous methanol to give the p-*nitrobenzenesulphonate* (**6**; R = Pr^i) (787 mg, 75 %), crystallised from aqueous methanol, m.p. 159 - 160 °C (decomp.); *m/z* 350 (M^+, 20 %) and 186 (100); $\nu_{max.}$(Nujol) 3100 - 2750 cm^{-1} (NH); δ_H ($CDCl_3$) 8.30 (1H, s, NH), 8.21 (4 H, AA′ BB′ pattern), 2.10 (2 H, d x septet, J_{PH} 10, J_{HH} 7 Hz), and 1.09 (12 H, dd, J_{PH} 16, J_{HH} 7 Hz); δ_P ($CDCl_3$) 66.0 (Found : C, 41.2; H, 5.4; N, 8.0; S, 9.3. $C_{12}H_{19}N_2O_6PS$ requires C, 41.4; H, 5.5; N, 8.0; S, 9.15 %).

N-*(Diethylphosphinoyl)*-O-p-*nitrobenzenesulphonylhydroxylamine* (**6**; R = Et).– The crude phosphinoylhydroxylamine (from 1.0 mmol phosphinic chloride; see above) was dissolved in ice-cold dichloromethane (1.0 ml). *p*-Nitrobenzenesulphonyl chloride (267 mg, 1.2 mmol) was immediately added, followed by triethylamine (120 mg, 1.2 mmol) in three portions at 1 min. intervals. Solid soon began to separate. After 15 min. at room temperature, the product was isolated as above to give the p-*nitrobenzenesulphonate* (**6**; R = Et) (177 mg, 55 % overall), crystallised from aqueous methanol; m.p. 119 - 120 °C (decomp.) (from methanol - ether); $\nu_{max.}$ (Nujol) 3100 - 2750 cm^{-1} (NH); δ_H (CD_3OD) 8.28 (4 H, AA′ BB′ pattern), 1.76 (4 H, dq, J_{PH} 14, J_{HH} 7 Hz), and 1.07 (6 H, dt, J_{PH} 17, J_{HH} 7 Hz); δ_P(CD_3OD) 60.3 (Found : C, 37.15; H, 4.7; N, 8.65. $C_{10}H_{15}N_2O_6PS$ requires C, 37.3; H, 4.7; N, 8.7 %).

N-[*Isopropyl(methyl)phosphinoyl*]-O-p-*nitrobenzenesulphonylhydroxylamine* (**7**).– The crude

phosphinoylhydroxylamine (see above) was treated in the same way as the diethylphosphinoyl compound to give the p-*nitrobenzenesulphonate* (**7**) (54 % overall), crystallised from ethanol, m.p. 127 - 128 °C (decomp.); $\nu_{max.}$ (Nujol) 3100 - 2700 cm^{-1} (NH); δ_H (CD_3OD) 8.36 (4 H, AA′ BB′ pattern), 2.02 (1 H, d x septet, J_{PH} 13, J_{HH} 7 Hz), 1.41 (3 H, d, J_{PH} 13 Hz), and 1.14 (6 H, dd, J_{PH} 17, J_{HH} 7 Hz); δ_P (CD_3OD) 59.8 (Found : C, 37.4; H, 4.6; N, 8.9. $C_{10}H_{15}N_2O_6PS$ requires C, 37.3; H, 4.7; N, 8.7 %).

Reactions with Potassium t-Butoxide in t-Butyl Alcohol

Freshly sublimed potassium t-butoxide (1.5 mol equiv.) was added to a suspension of the *N*-phosphinoyl-*O*-*p*-nitrobenzenesulphonylhydroxylamine **6** (R = Pr^i), **6** (R = Et), or **7** (1.0 mol equiv.) in t-butyl alcohol (7.5 ml per mmol substrate) under strictly anhydrous conditions. The mixture was shaken, and warmed just sufficiently to keep the solvent molten. Reaction proceeded as the substrate dissolved and was complete in *ca.* 15 min. A solid byproduct (KONs) precipitated. The mixture was examined by ^{31}P NMR spectroscopy (see below). Solid NH_4Cl (1 mol equiv.) was added to quench the excess t-butoxide. The mixture was filtered and the solid was washed with ether. The combined filtrate and washing was concentrated and the residue was partitioned between water and dichloromethane [or, for **6** (R = Pr^i), ether]. The organic portion was dried (Na_2SO_4) and the solvent evaporated.

Substrate **6** (R = Pr^i) gave as the only product, δ_P (Bu^tOH) 32.0, *t-butyl* N,P-*diisopropylphosphonamidate* (**10**; R = Pr^i), sublimed at 80 °C (oven temp.) at 0.4 mmHg; m.p. 125-6 °C (softens at ~105 °C); *m/z* 206 (15 %, M^+- Me) and 150 (100, M^+- Me - C_4H_8) (M^+ not observed); $\nu_{max.}$ (Nujol) 3220 cm^{-1} (NH); δ_H ($CDCl_3$; 300 MHz) 3.444 (1 H, d x d x septet, J_{PH} 9.3, J_{HH} 6.5, J_{HH} 6.5 Hz, PNHC*H*Me_2), 2.047 br (1 H, NH), 1.774 (1 H, d x septet, J_{PH} 17.2, J_{HH} 7.1 Hz), 1.492 (9 H, s), 1.162 (6 H, d, J_{HH} 6.5 Hz), 1.128 (3 H, dd, J_{PH} 17.8, J_{HH} 7.1 Hz), and 1.119 (3 H, dd, J_{PH} 18.0, J_{HH} 7.1 Hz); δ_P ($CDCl_3$) 33.0 (Found : C, 54.5; H, 10.6; N, 6.4. $C_{10}H_{24}NO_2P$ requires C, 54.3; H, 10.9; N, 6.3 %).

Substrate **6** (R = Et) gave as the only product, δ_P (Bu^tOH) 31.3, *t-butyl* N,P-*diethylphosphonamidate* (**10**; R = Et), b.p. 100 °C (oven temp.) at 0.1 mmHg; *m/z* (EI) 178 (15 %, M^+- Me), 138 (100), and 122 (75, M^+- Me - C_4H_8) (M^+ not observed); *m/z* (CI) 194 (20 %, M + H^+), 155 (55, M + NH_4^+ - C_4H_8), and 138 (100, M + H^+ - C_4H_8); $\nu_{max.}$ (film) 3210 cm^{-1} (NH); δ_H ($CDCl_3$; 300 MHz) 2.939 (2 H, m, PNHCH_2Me) (simplified by D_2O exchange), 2.55 br (1 H, NH) (exchanged with D_2O), 1.629 (2 H, m), 1.493 (9 H, s), 1.143 (3 H, t, J_{HH} 7.1 Hz), and 1.112 (3 H, dt, J_{PH} 20.8, J_{HH} 7.5 Hz); δ_P ($CDCl_3$) 32.6 (Found : M + H^+, 194.1310. $C_8H_{20}NO_2P$ requires M + H, 194.1310).

Substrate **7** gave a mixture of two products, δ_P (Bu^tOH) 26.5 and 34.3 (ratio 1 : 1.05) (also minor byproduct, δ_P 40), b.p. 110 °C (oven temp.) at 0.1 mmHg. The ^1H NMR spectrum ($CDCl_3$; 300 MHz) was consistent with a mixture of the phosphonamidates **12** [δ_H 3.381 (1 H, m), 1.497 (9 H, s), 1.425 (3 H, d, J_{PH} 16.4 Hz), and 1.2 - 1.1 (several peaks)] and **14** [δ_H 2.617 (3 H, dd, J_{PH} 10.6, J_{HH} 5.8 Hz), 1.849 (1 H, d x septet, J_{PH} 17.3, J_{HH} 7.2 Hz), 1.492 (9 H, s), and 1.2 - 1.1 (several peaks)]; δ_P (CH_2Cl_2) 26.9 and 35.2 (enhanced by addition of authentic **12** and **14** respectively); R_t 4.6 and 5.6 min. on SE 54 at 120 °C (enhanced by additon of authentic **12** and **14** respectively).

Authentic Samples of t-Butyl Phosphonamidates

(a) Potassium t-butoxide (108 mg, 0.97 mmol) was added to a solution of methylphosphonic dichloride (116 mg, 0.87 mmol)[18] in t-butyl alcohol. The mixture was shaken until all the t-butoxide had dissolved (reacted). A large excess of isopropylamine (*ca.* 5 mmol) was then added. When reaction was complete (^{31}P NMR spectroscopy), volatile material was evaporated and the residue was partitioned between dichloromethane and water. The organic portion afforded *t-butyl* N-*isopropyl*-P-*methyl-phosphonamidate* (**12**), b.p. 120 °C (oven temp.) at 1.0 mmHg, solidifies on cooling; *m/z* (EI) 193 (M^+, < 1 %), 178 (15, M^+ - Me), and 122 (100, M^+ - Me - C_4H_8); *m/z* (CI) 194 (M + H^+, 25 %), 155 (35, M + NH_4^+ - C_4H_8), and 138 (100, M + H^+ - C_4H_8); $\nu_{max.}$ (melt) 3195 cm^{-1} (NH); δ_H ($CDCl_3$; 300 MHz) 3.38 (1 H, m), 2.30 br (NH), 1.497 (9 H, s), 1.427 (3 H, d, J_{PH} 16.4 Hz), 1.171 (3 H, d, J_{HH} 6.4 Hz), and 1.154 (3 H, d, J_{HH} 6.4 Hz); δ_P(CH_2Cl_2) 26.9 (Found : M + H^+, 194.131. $C_8H_{20}NO_2P$ requires M + H, 194.131)

(b) Anhydrous methylamine (390 mg, 12.5 mmol) in dichloromethane (5 ml) was added during 10 min. to a stirred ice-cold solution of isopropylphosphonic dichloride (1.01 g, 6.27 mmol)[23] in ether (16 ml). The mixture was filtered and the filtrate (δ_P 56.2) concentrated to give *P*-isopropyl-*N*-methyl-phosphonamidic chloride [δ($CDCl_3$) 3.80 (1 H, s, NH), 2.67 (3 H, d, J_{PH} 15 Hz), 2.27 (1 H, d x septet, J_{PH} 14, J_{HH} 7 Hz), 1.26 (3 H, dd, J_{PH} 22, J_{HH} 7 Hz), and 1.25 (3 H, dd, J_{PH} 21, J_{HH} 7 Hz)]. A portion of this was treated with 1 M potassium t-butoxide (1.5 mol equiv.) in t-butyl alcohol to give *t-butyl* P-*isopropyl*-N-*methylphosphonamidate* (**14**), b.p. 120 °C (oven temp.) at 1.0 mmHg; *m/z* (EI) 193 (M^+, < 1 %), 178 (10, M^+ - Me), 138 (100), and 57 (70); *m/z* (CI) 194 (M + H^+, 20 %), 155 (60, M + NH_4^+ - C_4H_8), and 138 (100, M + H^+ - C_4H_8); $\nu_{max.}$ (film) 3225 cm^{-1} (NH); δ_H ($CDCl_3$; 300 MHz) 2.613 (3 H, dd, J_{PH} 10.6, J_{HH} 5.5 Hz), 2.50 br (NH), 1.848 (1 H, d x septet, J_{PH} 17.3, J_{HH} 7.2 Hz), 1.492 (9 H, s), 1.142 (3 H, dd, J_{PH} 17.3, J_{HH} 7.1 Hz), and 1.108 (3 H, dd, J_{PH} 17.5, J_{HH} 7.2 Hz); δ_P (CH_2Cl_2) 35.2 (Found : M + H^+, 194.131. $C_8H_{20}NO_2P$ requires M + H, 194.131).

Other Base-induced Reactions

Authentic samples of the phosphinic esters **16** were prepared from diisopropylphosphinic acid and CH_2N_2 (R′ = Me) or diisopropylphosphinic chloride and NaOR′ (R′ = Et, Pr^i); their ^{1}H NMR spectra were as expected. An authentic sample of the phosphinic amide **17** was already available.[19]

(a) The *p*-nitrobenzenesulphonate **6** (R = Pr^i) in the appropriate alcohol (5 ml per mmol) was allowed to react with the sodium alkoxide (1.5 mol equiv.) for *ca.* 40 min. The excess base was neutralised (NH_4Cl) and the mixture was examined by GLC (SE 54 at 120 °C) with the aid of authentic samples. In each case one dominant product was accompanied by 3 or 4 minor products. In methanol the minor products included the phosphinic ester **16** (R′ = Me) (R_t 2.9 min., 2.5 %) and the phosphinic amide **17** (R_t 9.0 min., *ca.* 8 %). In ethanol and isopropyl alcohol the minor products (1 - 2 % each) did not include **16** (R′ = Et) (R_t 3.5 min.), **16** (R′ = Pr^i) (R_t 4.2 min), or **17**. The alcohol was evaporated and the residue was partitioned between water and dichloromethane. The organic portion afforded the alkyl phosphonamidate **15** (R′ = Me) (R_t 4.2) or **15** (R′ = Et) (R_t 4.9), identified by comparison (GLC, IR, ^{1}H NMR) with the samples available from azide photolysis,[17] or *isopropyl* N,P-*diisopropylphosphonamidate* (**15**; R′ = Pr^i) (R_t 5.4), *m/z* 207 (M^+, 2 %), 192 (40, M^+ - Me), 164 (10, M^+ - C_3H_7), and 150 (100, M^+ - Me - C_3H_6); δ_H ($CDCl_3$; 300 MHz) 4.672 (1 H, d x septet, J_{PH} 8.4, J_{HH} 6.2 Hz, OC*H*Me_2), 3.435 (1 H, m, NHC*H*Me_2), 2.17 br (1 H, s, NH), 1.835 (1 H, d x septet, J_{PH} 17.0, J_{HH} 7.2 Hz, PC*H*Me_2), 1.323 and 1.272 (both 3 H, d, J_{HH} 6.2 Hz, OCH*Me*$_2$), 1.176 and

1.164 (both 3 H, d; J_{HH} 6.0 and 6.3 Hz respectively; $NCHMe_2$), 1.152 and 1.148 (both 3 H, dd, J_{PH} 17.7, J_{HH} 7.2 Hz, $PCHMe_2$); $\nu_{max.}$ (Nujol) 3190 cm^{-1} (NH). The identity of the last of these was confirmed by comparison with an authentic sample of **15** (R′ = Pr^i) prepared from $Pr^iP(O)Cl_2$ by sequential treatment with Pr^iNH_2 and $NaOPr^i$; crystallised from light petroleum (b.p. 40 - 60 ° C) at -20 °C; m.p. 135 - 137 °C (softens at 90 ° C, turns to a glass at 105 - 120 °C) (Found : C, 52.0; H, 10.4; N, 6.8. $C_9H_{22}NO_2P$ requires C, 52.15; H, 10.7; N, 6.8 %).

(b) A similar experiment with **6** (R = Et) in methanol gave a mixture (*ca.* 1 : 1) of methyl diethylphosphinate[17] (R_f 3.5 min; SE 54 at 100 °C) and methyl *N,P*-diethylphosphonamidate (R_f 7.2); δ_H ($CDCl_3$) includes 3.68 (d, J_{PH} 10 Hz, OMe), 3.62 (d, J_{PH} 11 Hz, OMe), and 2.94 (ddq, $J_{PH} \sim J_{HH} \sim J_{HH}$ 7 Hz, $PNHCH_2Me$).

(c) The *p*-nitrobenzenesulphonate **6** (R = Pr^i) gradually dissolved (1 - 2 h) when treated with a large excess (25 mol equiv.) of t-butylamine, giving two principal products, δ_p (Bu^tNH_2) 31.7 and 53.8 (ratio *ca.* 1 : 1), R_f 3.4 and 7.4 min. (SE 54 at 150 °C) (minor product; δ_p 52.9, R_f 4.4 min.). Volatile material was evaporated and the residue was dissolved in dichloromethane. The solution was washed with water (to remove $Bu^tNH^+_3\bar{}ONs$) and was then extracted with 0.5 M hydrochloric acid. Concentration of the organic portion afforded *N*-t-butyl-*N′,P*-diisopropylphosphonic diamide (**18**), R_f 3.4 min. (contaminated with the minor product, R_f 4.4 min.), δ_p ($CDCl_3$) 31.6, ^1H NMR and IR spectra as for the product from the azide photolysis.[17] The aqueous portion was made strongly basic (NaOH), and was then extracted with dichloromethane. This extract, on concentration, gave N-*t-butyl*-N′-*(diisopropylphosphinoyl)hydrazine* (**19**), R_f 7.4 min. δ_P ($CDCl_3$) 52.6; washed with light petroleum (b.p. 40 - 60 °C) at -30 °C, m.p. 120 - 122 °C; *m/z* 220 (M^+, 30 %), 205 (100, M^+ - Me), and 164 (20, $M^+ - C_4H_8$); δ_H ($CDCl_3$) 4.10 (1 H, d, J_{PH} 11 Hz, NH), 3.05 (1 H, s, NH), 2.19 (2 H, d x septet, J_{PH} 14, J_{HH} 7 Hz), 1.23 (12 H, dd, J_{PH} 15, J_{HH} 7 Hz), and 1.06 (9 H, s); $\nu_{max.}$ (Nujol) 3140 cm^{-1} (NH) (Found : C, 54.6; H, 11.0; N, 12.95; M^+, 220.170. $C_{10}H_{25}N_2OP$ requires C, 54.5; H, 11.4; N, 12.7 %; M, 220.170).

The product ratio **18** : **19** decreased to *ca.* 1 : 8 when the reaction was repeated using a 1 M solution of t-butylamine in dichloromethane.

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REFERENCES AND NOTES

1. Preliminary communication : Harger, M. J. P.; Shimmin, P. A. *Tetrahedron Lett.* 1991, 4769.
2. Harger, M. J. P. *J. Chem. Soc., Perkin Trans. 1* 1981, 3284.
3. Harger, M. J. P. *J. Chem. Soc., Perkin Trans. 1* 1983, 2699.
4. Harger, M. J. P.; Smith, A. *J. Chem. Soc., Perkin Trans. 1* 1985, 1787.
5. Harger, M. J. P.; Smith, A. *J. Chem. Research (S)* 1991, 358.
6. Harger, M. J. P.; Smith, A. *J. Chem. Soc., Perkin Trans. 1* 1987, 683.
7. Harger, M. J. P.; Smith, A. *J. Chem. Soc., Perkin Trans. 1* 1990, 1447.
8. Dąbkowski, W.; Michalski, J.; Skrzypczyński, Z. *Phosphorus Sulfur* 1986, **26**, 321.

9. Hwu, J. R.; Robl, J. A.; Wang, N.; Anderson, D. A.; Ku, J.; Chen, E. *J. Chem. Soc., Perkin Trans. 1* 1989, 1823.
10. King, F. D.; Pike, S; Walton, D. R. M. *J. C. S. Chem. Comm.* 1978, 351; Kozyukov, V. P.; Feoktistov, A. E.; Mironov, V. F. *J. Gen. Chem. USSR (Engl. Transl.)* 1988, **58**, 1154.
11. *N*-Phosphinoylhydroxylamines generally decompose vigorously when they melt. Both $Et_2P(O)NHOH$ and $Pr^iMeP(O)NHOH$ were formed as unstable oils, even at room temperature. We experienced no problems, but strongly caution against their preparation on anything other than a small scale (≤ 2 mmol).
12. Kuchen, W.; Strolenberg, K.; Buchwald, H. *Chem. Ber.* 1962, **95**, 1703.
13. Yale, H. L. *Chem. Rev.* 1943, **33**, 209; Bauer, L.; Exner, O. *Angew. Chem., Int. Ed. Engl.* 1974, **13**, 376.
14. Interaction between phosphoryl (P=O) oxygen atoms and trimethylsilyl halides is known to be important in, for example, the conversion of alkyl phosphorus esters into trimethyl silyl esters: Woźniak, L.; Chojnowski, J. *Tetrahedron* 1989, **45**, 2465 and references cited therein.
15. Alkyl groups generally migrate without apparent difficulty in the Lossen rearrangement of hydroxamic acid (RCONHOH) derivatives : Bright, R. D.; Hauser, C. R. *J. Am Chem. Soc.* 1939, **61**, 618; Berndt, D. C.; Shechter, H. *J. Org. Chem.* 1964, **29**, 916.
16. Harger, M. J. P.; Westlake, S. *Tetrahedron* 1982, **38**, 3073.
17. Harger, M. J. P.; Stephen, M. A. *J. Chem. Soc., Perkin Trans. 1* 1981, 736.
18. Harger, M. J. P. *J. Chem. Soc., Perkin Trans. 1* 1983, 2127.
19 Harger, M. J. P.; Stephen, M. A. *J. Chem. Soc., Perkin Trans. 1* 1980, 705.
20. Hurd, C. D.; *Inorg. Synth.* 1939, **1**, 87.
21. Wannagat, U.; Smrekar, O. *Monatsh. Chem.* 1969, **100**, 750.
22. Crofts, P. C.; Fox, I. S. *J. Chem. Soc.* 1958, 2995.
23. Kinnear, A. M.; Perren, E. A. *J. Chem. Soc.* 1952, 3437.