Base induced rearrangement reactions of *N*-phosphinoyl-*O*-sulfonylhydroxylamines. Observation of a phosphonamidic–sulfonic anhydride intermediate by NMR spectroscopy [1]

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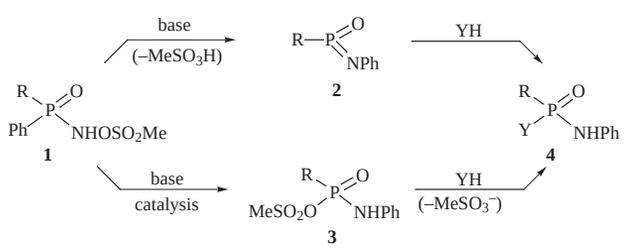
The hydroxylamine derivative PhRP(O)NHOSO$_2$Me (R = PhMeCH) reacts with Bu^{t}NH$_2$ to give the rearrangement product RP(O)(NHPh)NHBu^t by way of a reactive but non-transient intermediate. At low amine concentrations the intermediate can be observed by ^{31}P NMR spectroscopy; it is thought to be the mixed anhydride RP(O)(NHPh)-OSO$_2$Me as it has the same chemical shift as an authentic sample generated from RP(O)(NHPh)Cl and AgOSO$_2$Me. The intermediate is formed with high (or complete) stereospecificity but it reacts with Bu^{t}NH$_2$ with low stereospecificity.

N-Phosphinoylhydroxylamines are the phosphorus analogues of hydroxamic acids and when suitably activated they undergo base-induced rearrangement reactions. With the *O*-methylsulfonyl derivative **1** (R = Ph), for example, a phenyl group migrates from phosphorus to nitrogen.[2] The initial product may be a transient metaphosphonimidate **2** (Scheme 1), analogous



Scheme 1

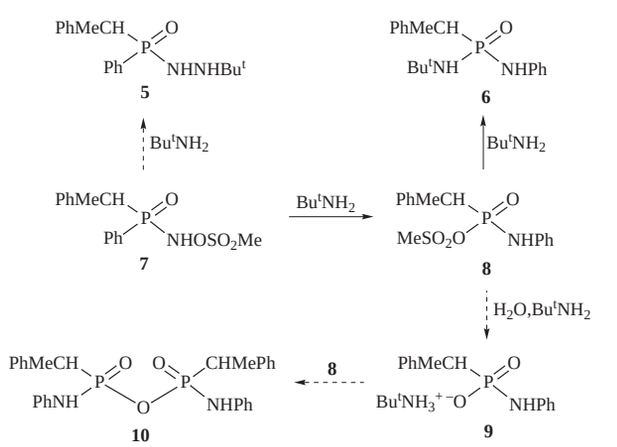
to the isocyanate formed in a Lossen rearrangement,[3] but the observed product is a phosphonamidic acid derivative, *e.g.* **4** (Y = MeO) with methoxide as base or **4** (Y = Bu^{t}NH) with *tert*-butylamine.[2] Alkyl groups are reluctant to migrate and **1** (R = alkyl) gives only the product **4** corresponding to migration of the phenyl group.[4,5] A stereochemical study, using a substrate **1** in which R is a chiral alkyl group, found that reaction with MeNH$_2$ gives **4** (Y = MeNH) stereospecifically with retention of configuration at phosphorus.[6] Stereospecificity is difficult to reconcile with a planar (trigonal) intermediate **2** as the product-forming species. A possible alternative involves rearrangement of the substrate **1** to a phosphonamidic–sulfonic mixed anhydride **3** (Scheme 1) which is then converted into **4** by nucleophilic attack at phosphorus. The stereochemistry could then be accounted for if both the formation of the mixed anhydride and its subsequent reaction proceed with inversion of the configuration at phosphorus. The reaction with Bu^{t}NH$_2$ was also found to be largely stereospecific in the absence of solvent but on dilution there were increasingly pronounced deviations from stereospecificity.

The substrate in the stereochemical study had a bulky alkyl group (PhMeCH) on the P atom and Bu^{t}NH$_2$ is a relatively non-nucleophilic (bulky) amine. With very low concentrations of amine the postulated phosphonamidic–sulfonic anhydride **3** might survive long enough to be observed directly. As well as confirming the involvement of the anhydride, it might also be possible to tell if *all* the product **4** is formed *via* the anhydride intermediate and whether deviations from stereospecificity arise in its formation or its conversion into product. These possibilities are examined in this paper.

Results and discussion

Samples of the hydroxylamine derivative **7** having diastereoisomer ratios 80:20 (sample A) and 3:97 (sample B) were available from the earlier stereochemical study.[6] The 4:1 mixture of diastereoisomers (sample A) was first examined using a modest excess of Bu^{t}NH$_2$ (2.5 equiv.) as a dilute solution in CH$_2$Cl$_2$ (initial amine concentration 0.21 mol dm^{-3}).†

Monitoring by ^{31}P NMR spectroscopy (36.2 MHz) showed the substrate **7** (δ_P 40.8 and 39.6; diastereoisomer ratio 80:20 initially) being converted into the phosphonic diamide rearrangement product **6** (δ_P 21.7 and 21.4; diastereoisomer ratio 56:44) over a period of 50 minutes. A substantial byproduct (δ_P ~24; several peaks), thought to be the symmetrical phosphonamidic anhydride **10** (several diastereoisomers) was also seen (Scheme 2). Crucially, the spectra also



Scheme 2

† Although they were diastereoisomerically enriched the substrate samples were racemic. The relative configurations at phosphorus and carbon for the major diastereoisomer in each sample, and for the major diastereoisomer of the derived product **6**, are known from X-ray crystallography (reference 6).

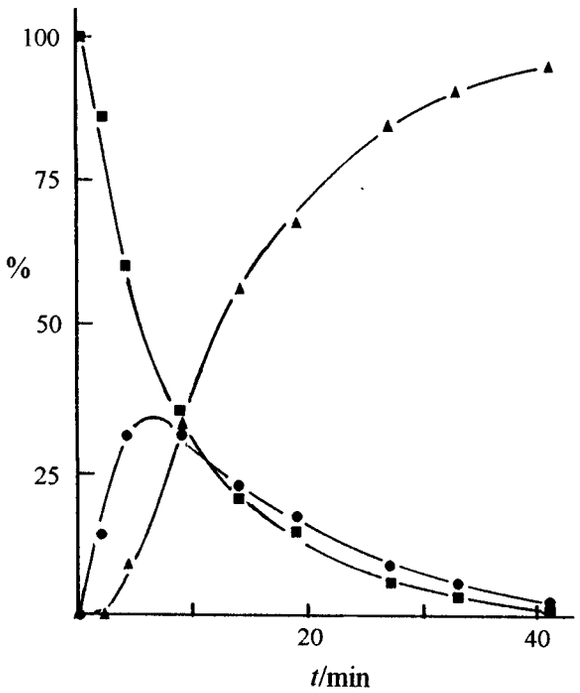
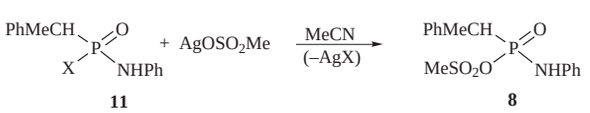


Fig. 1 Reaction of **7** (sample A) with Bu^tNH_2 (0.21 mol dm^{-3} initial concentration) in CH_2Cl_2. Contributions (%) of substrate **7** (■), intermediate **8** (●) and product **6** + byproduct **10** (▲) to the ^{31}P NMR spectrum (36.2 MHz; ^1H decoupled) of the reaction mixture at different times.

displayed a pair of peaks, only partially resolved, having δ_P 27.7 and 27.5. These peaks were not present before the amine was added ($t = 0$) or when reaction was complete ($t = 50$ min) but at $t = 5$ and $t = 9$ min they accounted for some 30% of the total reaction mixture (Fig. 1).‡ Clearly they must be due to an intermediate; and significantly, they were appreciable (15%) even at $t = 2$ min when the diamide product **6** (and the byproduct) could not yet be detected. The implication seems clear; the diamide rearrangement product (and the byproduct) is formed *via* a non-transient intermediate, and that intermediate constitutes the only substantial route from the substrate to the product. As to the identity of the intermediate, the ^{31}P chemical shift is not unreasonable for a phosphonamidic–sulfonic mixed anhydride such as **8** (two diastereoisomers) and the ^1H NMR spectrum of a reaction mixture (in $CDCl_3$) afforded some support: singlets attributable to $MeSO_3$ groups (δ_H ~3) were seen not only for unreacted substrate [δ_H 3.15 (major diastereoisomer) and 2.73] and the methanesulfonate anion (δ_H 2.78) but also for the intermediate [δ_H 3.32 (major diastereoisomer) and 2.92].

There seemed no prospect of isolating and purifying the intermediate, given its high reactivity, so for confirmation of its identity an authentic sample was required. The mixed anhydrides of phosphorus and sulfonic acids have attracted considerable attention in recent years, and several methods have been developed for their preparation.[7,8] None, however, has been applied to anhydrides having an NH group attached directly to the phosphorus atom. After a number of failures the new method of Wasiak and Michalski[9] was examined. This involved treating the phosphonamidic halide **11** (X = Br or Cl) with $AgOSO_2Me$ in MeCN solution (Scheme 3). The bromide



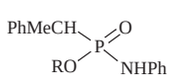
11 **8**

Scheme 3

‡ Representative ^{31}P NMR spectra (36.2 MHz) recorded at different times are displayed in the preliminary communication (reference 1).

reacted readily at room temperature but the chloride required several hours at 55 °C (the original work had no success with chlorides[9]). The phosphonamidic–sulfonic anhydride **8** was obtained as a mixture of diastereoisomers, δ_P ($CDCl_3$) 28.9 and 28.7, even when a single diastereoisomer of the halide **11** (X = Cl) was employed, presumably because of equilibration (sulfonate exchange) at the phosphorus centre. Attempted purification was negated by hydrolysis but the crude product was sufficiently pure (85–90%) for reasonable characterisation by ^1H NMR spectroscopy [especially singlets δ_H ($CDCl_3$) 3.31 and 2.90 for the $MeSO_3$ groups of the two diastereoisomers of **8**] and mass spectrometry [M^+ 339 (60%)]. When this material was added to a rearrangement reaction mixture the ^{31}P NMR signals associated with the intermediate increased in intensity.

The symmetrical phosphonamidic anhydride **10** (Scheme 2) is relatively unreactive and an authentic sample was prepared simply by treating the phosphonamidic chloride **11** (X = Cl) with a salt **9** of the phosphonamidic acid. It was obtained as a complex mixture of stereoisomers (structure **10** has 4 stereogenic centres) showing several peaks in the ^{31}P NMR spectrum [δ_P (CH_2Cl_2) 23–24] and seven distinct NH signals in the ^1H NMR spectrum. It seems almost certain that this anhydride **10** is the byproduct [δ_P (CH_2Cl_2) ~ 24] seen in the rearrangement, where it would result from reaction of the phosphonamidate anion (salt **9** in Scheme 2) with the phosphonamidic–sulfonic mixed anhydride intermediate **8**. The anion would be formed, together with $MeSO_2NHBu^t$, if the mixed anhydride intermediate were to react with Bu^tNH_2 at sulfur rather than at phosphorus. However, there was no sign of $MeSO_2NHBu^t$ [δ_H 3.02 ($MeSO_2$) for an authentic sample] in the ^1H NMR spectrum of the crude reaction product. More likely is that the phosphonamidate anion arises from reaction of the mixed anhydride with adventitious traces of moisture. Indeed, when the amine concentration was especially low (0.1 mol dm^{-3}) and the exclusion of moisture not so rigorous the phosphonamidate salt **9** was isolated as a minor product [identified by conversion into the free acid **12** (R = H) and the methyl ester **12** (R = Me)]. At higher concentrations of Bu^tNH_2, or with a more nucleophilic amine, the mixed anhydride intermediate will be converted rapidly and cleanly into the phosphonic diamide product; but under conditions designed to prolong the existence of the intermediate there is almost bound to be competition, both from traces of moisture giving the salt **9** and from the phosphonamidate anion of **9** giving the symmetrical anhydride **10**.



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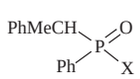

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A side reaction, not involving rearrangement, was apparent in the reactions of the hydroxylamine derivative **7** (sample B; diastereoisomer ratio 3:97) at low concentrations of Bu^tNH_2. It gave rise to a product δ_P ($CDCl_3$) 35.3 that was thought at first to be the phosphinic amide **13** (X = NH_2). After isolation (extraction into aqueous acid), however, its spectra (^1H NMR and MS) suggested rather the hydrazide **5** (one of the diastereoisomers). This was confirmed by comparison with an authentic sample [mixture of diastereoisomers, δ_P ($CDCl_3$) 36.9 and 35.3] prepared from the phosphinic chloride **13** (X = Cl) and H_2NNHBu^t. Comparable hydrazide formation has been observed before, but only when the substrate has no aryl group on the phosphorus atom and is reluctant to rearrange.[10] Here, uniquely, nucleophilic attack at the nitrogen atom of the substrate is competitive with migration of a phenyl group.

To learn more about the phosphonamidic–sulfonic anhydride intermediate—its formation and its breakdown—the reactions

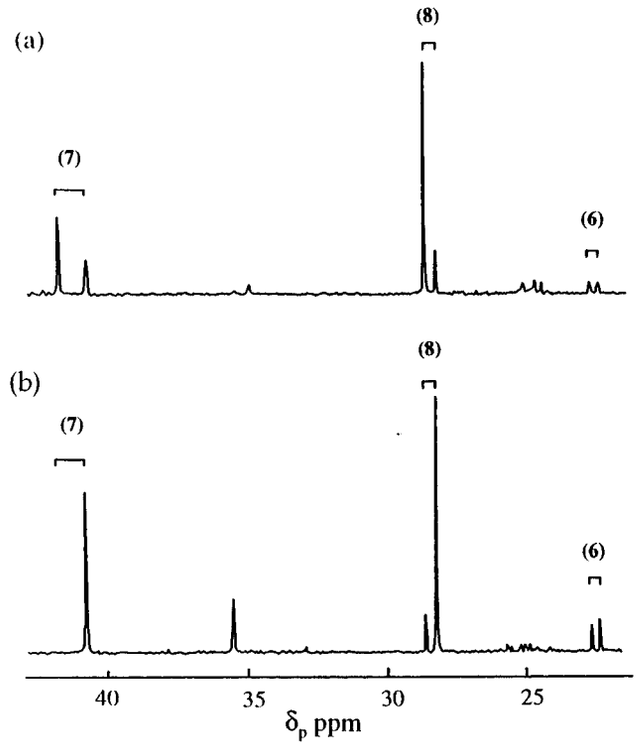


Fig. 2 Reaction of **7** with Bu^tNH_2 (0.09 mol dm^{-3} initial concentration) in $CDCl_3$. ^{31}P NMR spectra (101.3 MHz; ^1H decoupled) at *ca.* 75% conversion for (a) sample A (80:20 mixture of diastereoisomers) (t = 25 min) and (b) sample B (3:97 mixture of diastereoisomers) (t = 40 min) showing the intermediate **8** and product **6**.

of the substrate **7** were examined by ^{31}P NMR at higher field (101.3 MHz; $CDCl_3$ solvent). The enhanced resolution allowed the individual diastereoisomers of the intermediate to be seen more clearly and the increased sensitivity allowed the concentration of Bu^tNH_2 to be reduced (0.09 mol dm^{-3}), and the lifetime of the intermediate extended, without foregoing an excess of the amine (2.4 equiv.). Representative spectra for samples A and B of the substrate are shown in Fig. 2 (a) and (b) and our deductions are noted below (δ_P values are for $CDCl_3$ solutions; they differ by ~1 ppm from the values for CH_2Cl_2 solutions).

1. The lowfield diastereoisomer of the substrate (δ_P 41.7) reacts more quickly than the other (δ_P 40.7) so that with a mixture of diastereoisomers the composition of the unreacted substrate changes as reaction proceeds. For sample A the initial 80:20 diastereoisomer ratio had become 70:30 at 75% conversion [t = 25 min; Fig. 2 (a)] and 55:45 at 90% conversion (t = 45 min; not shown), and for sample B the initial 3:97 diastereoisomer ratio had become ≤1:99 at 75% conversion [t = 40 min; Fig. 2 (b)].

2. The non-rearrangement side reaction that produces the phosphinic hydrazide **5** (δ_P 37.0 or 35.4) occurs more readily for the highfield diastereoisomer of the substrate. Since this is the diastereoisomer that rearranges less readily, the competition from hydrazide formation is (much) more serious in the case of the highfield diastereoisomer. Thus the hydrazide (δ_P 35.4) constitutes some 15% of the total product in Fig. 2 (b) whereas in Fig. 2 (a) the diastereoisomeric hydrazide (δ_P 37.0) is barely detectable.

3. The diastereoisomer ratio of the phosphonamidic–sulfonic mixed anhydride intermediate **8** (δ_P 28.6 and 28.3) at any time does not properly reflect the stereochemistry of the rearrangement. Because of differences in reactivity (points 1 and 2 above) the substrate that has actually undergone rearrangement at any time is disproportionately the lowfield diastereoisomer. Since the lowfield diastereoisomer of the substrate forms predominantly the lowfield diastereoisomer of the mixed anhydride [Fig. 2 (a)], and *vice versa* [Fig. 2 (b)], the mixed anhydride will be enriched in the lowfield diastereoisomer. In the case of substrate sample A (80:20 initially) the 85:15 diastereoisomer ratio of the mixed anhydride at 75% conversion [Fig. 2 (a)] may be compatible with stereospecific rearrangement. In the case of sample B (3:97 initially), however, the 12:88 diastereoisomer ratio [Fig. 2 (b)] seems not to be.

4. Stereoisomerisation of the mixed anhydride intermediate may be of some importance. Under conditions designed to prolong the existence of the intermediate [low concentration and low reactivity (steric hindrance) of amine nucleophile] any tendency it has to equilibrate, by epimerisation at the P atom, will inevitably be amplified. This, together with the other factors noted above, may account for the rather large amount of the minor (lowfield) diastereoisomer seen in the mixed anhydride intermediate in the reaction of substrate sample B [Fig. 2 (b)]. The possibility that the rearrangement process itself is stereospecific cannot be discounted.

5. Under the conditions employed (Bu^tNH_2 at very low concentration) the stereochemistry of the phosphonic diamide product **6** (δ_P 22.7 and 22.4) is largely independent of the stereochemistry of the substrate. At completion ($t \geq 2.8$ h) the diamide diastereoisomer ratio was 55:45 for substrate sample A (80:20) and 50:50 for sample B (3:97). The overall reaction is therefore almost completely non-stereospecific. The stereochemistry of the diamide product is also largely independent of the stereochemistry of the phosphonamidic–sulfonic mixed anhydride intermediate [Fig. 2 (a) and (b)]. It is the conversion of the mixed anhydride into the final product that is non-stereospecific rather than the initial rearrangement of the substrate.

Conclusion

The phosphinoylhydroxylamine derivative **7** forms the phosphonic diamide rearrangement product **6** by way of a phosphonamidic–sulfonic anhydride intermediate **8**. The stereochemistry overall depends on the stereochemistry of the separate stages, anhydride formation and anhydride reaction. In this particular case (Bu^tNH_2 at low concentration) the anhydride intermediate is formed with a high degree of stereospecificity. Indeed, given the probability of some stereoisomerisation of the anhydride after it has been formed, the actual rearrangement process (**7**→**8**) may well be completely stereospecific. If that is true here, where overall (**7**→**6**) the stereospecificity is low, it would be surprising if it were any less true where overall the stereospecificity is greater (higher concentrations and/or more nucleophilic amine). Stereospecificity in the rearrangement of **7** to **8** is consistent with a concerted mechanism in which the sulfonate group migrates from nitrogen to phosphorus at the same time as the phenyl group migrates from phosphorus to nitrogen (Fig. 3).

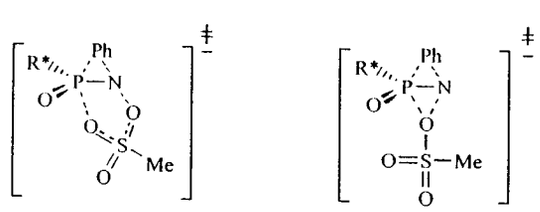
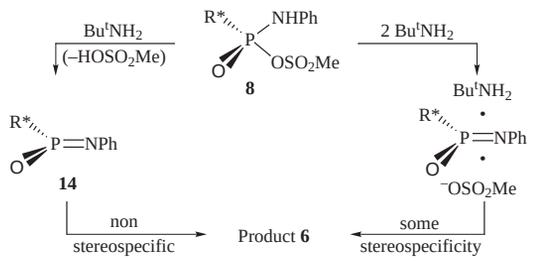


Fig. 3 Possible transition states (R* = PhMeCH) for stereospecific formation of phosphonamidic–sulfonic anhydride intermediate **8** by concerted rearrangement of substrate **7** (conjugate base).

If the anhydride intermediate is formed stereospecifically its subsequent reaction with the nucleophile (**8**→**6**) will determine the final outcome. The phosphonamidic chloride **11** (X = Cl) should be a reasonable model for **8** and although it has not been studied in detail some other phosphonamidic chlorides have.[11]

For them, and by implication for **11** and the phosphonamidic–sulfonic anhydride **8**, substitution can proceed not only by the normal associative $S_N2(P)$ mechanism (stereospecific inversion of configuration) but also by dissociative elimination–addition (EA). The EA mechanism, moreover, may involve a free metaphosphonimidate intermediate **14** (complete non-stereospecificity) or one that is unliberated [preassociation;[12] varying (concentration-dependent) degrees of stereospecificity] (Scheme 4). For a given substrate the $S_N2(P)$ pathway may well



Scheme 4

be dominant with a powerful nucleophile ($MeNH_2$) but EA will be significant when $S_N2(P)$ is sterically retarded (Bu^tNH_2).§ The preassociative form of the EA mechanism will be relatively more important at higher concentrations because it is second order in amine (base and nucleophile). Thus the varying degrees of stereospecificity seen here and in the earlier study[6] can be reconciled with complete stereospecificity in the rearrangement process itself.

Experimental

Mps were determined using a Kofler hot-stage apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 90 MHz on a Varian EM 390 spectrometer or (where indicated) at 300 MHz on a Bruker AM-300 (Me_4Si internal standard; coupling constants, *J*, given in Hz) and ^{31}P NMR spectra (^{1}H decoupled) were recorded at 36.2 MHz on a JEOL JNM-FX90Q spectrometer or at 101.3 MHz on a Bruker ARX 250 spectrometer. Mass spectra were obtained in EI mode on a VG 16-B or Kratos Concept spectrometer. GLC analyses were performed using a Philips PU 4500 chromatograph (helium carrier gas; flame-ionisation detector) fitted with an OV 1701 widebore capillary column (1 μm film; 15 m × 0.53 mm). *tert*-Butylamine was dried over KOH and $CDCl_3$ over 4 Å molecular sieves; CH_2Cl_2 was distilled from CaH_2. Light petroleum refers to the fraction with bp 60–80 °C unless otherwise indicated and ether to diethyl ether. The phosphinic chloride **13** (X = Cl) and the phosphonamidic chloride **11** (X = Cl) were as previously described.[6]

Reactions of *N*-[phenyl(1-phenylethyl)phosphinoyl]-*O*-methylsulfonylhydroxylamine 7

Two diastereoisomerically enriched samples of the hydroxylamine derivative **7** were available from previous work: sample A (diastereoisomer ratio 80:20) and sample B (3:97).[6] These had not deteriorated after prolonged storage at −20 °C and were used as the substrates in the present study.

(a) The substrate **7** (sample A) (27 mg, 0.08 mmol) was dissolved in CH_2Cl_2 (0.95 ml) in a 10 mm NMR tube and Bu^tNH_2 (0.20 mmol) was added. A concentric 5 mm tube containing D_2O provided the lock signal. The ^{31}P NMR spectrum (36.2 MHz; ^{1}H decoupled) was recorded as soon as possible (*t* = 2 min) and again at intervals (*t* = 4, 9, 14, 19, 27, 33, 41 min) until no further change occurred (*t* = 52 min) (the time *t* corresponds to the midpoint of the 2–4 min period during which data were accumulated).

(b) The substrate **7** (sample A or B) (6.5 mg, 0.02 mmol) was dissolved in $CDCl_3$ (0.5 ml) in a 5 mm NMR tube. The ^{31}P NMR spectrum (101.3 MHz; ^{1}H decoupled) was recorded before (*t* = 0) and after (*t* = 25, 40, 55 *etc.* min) the addition of Bu^tNH_2 (0.048 mmol); the ^{1}H NMR spectrum (250 MHz) was recorded at *t* = 0 and *t* = 50 min.

(c) The identity of the intermediate in the reaction of **7** with Bu^tNH_2 was confirmed by addition of authentic phosphonamidic–sulfonic anhydride **8** to a reaction mixture similar to that in (b) (sample A); the peaks δ_P 28.6 and 28.3 (diastereoisomers) were seen to increase in intensity.

(d) The phosphonic diamide rearrangement product **6** (mixture of diastereoisomers) was as previously reported.[6] Minor products were identified as follows.

Phosphinic hydrazide 5. The reaction mixture from **7** (sample B) with Bu^tNH_2 (0.1 mol dm^{-3}) in CH_2Cl_2 was extracted with aqueous acid. The extract was basified and the liberated product was extracted into CH_2Cl_2. Examination by GLC (t_R 4.0 min at 220 °C), NMR spectroscopy [δ_P ($CDCl_3$) 35.3; δ_H ($CDCl_3$) 3.92, 3.45, 1.41, 0.87] and mass spectrometry (*m*/*z* as for authentic) showed it to be the same as the minor diastereoisomer in the authentic sample (see below) of the hydrazide **5** (t_R 4.0 and 5.0 min).

Phosphonamidic acid salt 9. A reaction mixture from **7** (sample A) with 0.1 mol dm^{-3} Bu^tNH_2 in CH_2Cl_2 included a peak δ_P 18.0 which was removed by washing with water. The aqueous portion was acidified and the liberated material was back-extracted into CH_2Cl_2, δ_P ($CDCl_3$) 30.6, ^{1}H NMR spectrum similar to that of the authentic phosphonamidic acid **12** (R = H). The corresponding reaction of **7** (sample B) was worked up in the same way and the liberated material was treated with diazomethane. Analysis by GLC indicated a 1:1 mixture of the diastereoisomers of the methyl phosphonamidate **12** (R = Me), t_R 5.7 and 6.4 min at 230 °C as for the authentic sample.

With the aid of authentic samples it was shown that neither the phosphinic amide **13** (X = NH_2) [authentic (mixture of diastereoisomers): δ_P ($CDCl_3$ + Bu^tNH_2) 34.3 and 32.3; t_R 3.2 and 3.6 min at 220 °C] nor Bu^tNHSO_2Me [authentic: δ_H ($CDCl_3$ + Bu^tNH_2) 3.02 (SO_2*Me*)] were formed in the reactions of **7** with Bu^tNH_2.

Authentic samples of potential reaction products

Phosphonamidic-sulfonic anhydride 8. *N*-Phenyl-*P*-(1-phenylethyl)phosphonamidic chloride **11** (X = Cl) (56 mg, 0.20 mmol) was heated with a small excess of silver methanesulfonate (0.25 mmol) in MeCN (0.45 ml). Reaction (δ_P 43.5→28.5) was 80% complete after 2.7 h at 55 °C. On completion the mixture was diluted with CH_2Cl_2 (1.5 ml) and filtered. The filtrate was concentrated and the residue was extracted with CH_2Cl_2. The extract was concentrated to an oil which on trituration with ether afforded the crude *phosphonamidic–sulfonic anhydride* **8** as a mixture of diastereoisomers, δ_P ($CDCl_3$) 28.9 (major) and 28.7; *m*/*z* 339 (M^+, 60%), 139 ($PhNHPO^+$, 95) and 105 ($PhMeCH^+$, 100). This material could not be purified (hydrolysis) but the ^{1}H NMR spectrum contained signals consistent with structure **8** (mixture of diastereoisomers): δ_H ($CDCl_3$) 7.4–6.7 (*Ph*CHMe and *Ph*NH), 6.00 (major) and 5.55 (both br d, J_{PH} 8, NH), 3.75–3.45 (m, PhC*H*Me), 3.31 and 2.90 (major) (both s, SO_2Me) and 1.74 and 1.63 (major) (both dd, J_{PH} 21, J_{HH} 7.5, PhCH*Me*). The anhydride **8** was also obtained

§ Steric effects in the nucleophile seem to be very important in attack at a tetrahedral P=O centre, *e.g.* in competition experiments with $Ph_2P(O)Cl$ as substrate, Bu^tNH_2 is almost 100-fold less nucleophilic than Pr^iNH_2 which in turn is at least 50-fold less nucleophilic than $MeNH_2$ (M. J. P. Harger and A. Smith, *J. Chem. Soc.*, *Perkin Trans. 1*, 1990, 2507).

from the phosphonamidic bromide **11** (X = Br) and AgO-SO_2Me in MeCN (90% conversion in 12 min at room temperature). [The phosphonamidic bromide was used initially because it seemed unlikely that the chloride would prove satisfactory.[9] However, the reaction using the chloride was subsequently found to be just as good, albeit much slower. Details of the rather tedious preparation and purification of the phosphonamidic bromide, δ_P ($CDCl_3$) 38.3 and 35.8 (diastereoisomers), *m*/*z* 325, 323 (M^+, 35%), and its precursor PhMeCHP(O)Br_2 (δ_P 33.0) are therefore not included].

***N*-Phenyl-*P*-(1-phenylethyl)phosphonamidic acid 12 (R = H).** The phosphonamidic chloride **11** (X = Cl) (110 mg, 0.39 mmol) was heated (steam bath) with 1 mol dm^{-3} NaOH solution (1 ml) for 1 h. The cooled reaction mixture was filtered, acidified to pH 1 (HCl), and extracted with CH_2Cl_2. The extract was concentrated and the residue was triturated with ether to give the *phosphonamidic acid* **12** (R = H), mp 125.5–127 °C (from CH_2Cl_2–light petroleum); δ_P ($CDCl_3$) 30.3; δ_H ($CDCl_3$) 8.5 (2 H, very broad, OH and NH), 7.4–6.6 (10 H, m), 3.32 (1 H, dq, J_{PH} 19.5, J_{HH} 7.5) and 1.49 (3 H, dd, J_{PH} 18, J_{HH} 7.5); ν_{max}(Nujol)/cm^{-1} 3235 (NH), 2700, 2360, 1650 br (OH) and 1155 (P=O) (Found: C, 64.2; H, 6.2; N, 5.5. $C_{14}H_{16}NO_2P$ requires C, 64.4, H, 6.2; N, 5.4%).

Phosphonamidic anhydride 10. An equimolar mixture of *N*-phenyl-*P*-(1-phenylethyl)phosphonamidic chloride **11** (X = Cl) (mixture of diastereoisomers) and the *tert*-butylammonium salt **9** of the phosphonamidic acid **12** (R = H) in CH_2Cl_2 was gradually transformed into the *phosphonamidic anhydride* **10** (several diastereoisomers), crystallised from CH_2Cl_2–light petroleum, mp 155–161 °C, *m*/*z* 504 (M^+, 20%), 412 (M^+ − NHPh, 15), 105 ($PhCHMe^+$, 100) and 93 ($PhNH_2^+$, 60); ν_{max}(Nujol)/cm^{-1} 3170 br (NH), 1240 (P=O) and 950 (several maxima) (P–O–P); δ_P ($CDCl_3$) 25.65, 25.33, 24.91, 24.27 and 24.23; δ_H ($CDCl_3$, 300 MHz) 7.4–6.7 (20 H, m), 6.25–5.35 (2 H; a series of 7 br signals, exchangeable with D_2O; NH), 3.6–3.15 (2 H, m, PhC*H*Me) and 1.75–1.25 (6 H, m, Ph*Me*CH) (Found: C, 66.4; H, 6.05; N, 5.7. $C_{28}H_{30}N_2O_3P_2$ requires C, 66.7; H, 6.0; N, 5.55%).

Methyl *N*-phenyl-*P*-(1-phenylethyl)phosphonamidate 12 (R = Me). The phosphonamidic chloride **11** (X = Cl) (73 mg, 0.26 mmol; mixture of diastereoisomers) was added to a solution of NaOMe (0.4 mmol) in MeOH (1 ml). The excess methoxide was quenched (NH_4Cl), the solvent was evaporated, and the residue was partitioned between ether and water. The organic portion afforded the *methyl phosphonamidate* **12** (R = Me) (50 mg, 69%) as a mixture of diastereoisomers after crystallisation from light petroleum containing a very little CH_2Cl_2; mp 101.5–103 °C; δ_P ($CDCl_3$) 31.0 and 30.8 (major); δ_H ($CDCl_3$, 300 MHz) 7.45–6.8 (10 H, m), 6.185 (major) and 5.80 (total 1 H; both d, J_{PH} 5.3 or 5.0, NH), 3.76 and 3.61 (major) (total 3 H; both d, J_{PH} 11, OMe), 3.42 and 3.355 (major) (total 1 H; both dq, J_{PH} 19, J_{HH} 7.5) and 1.645 and 1.515 (major) (total 3 H; both dd, J_{PH} 18 or 19, J_{HH} 7.5); *m*/*z* 275 (M^+, 100%), 171 (M^+ − PhCH=CH_2, 20), 170 (M^+ − PhMeCH, 25), 105 ($PhMeCH^+$, 70) and 93 ($PhNH_2^+$, 45); ν_{max}(Nujol)/cm^{-1} 3140 (NH) and 1210 (P=O) (Found: M^+ 275.1073. $C_{15}H_{18}NO_2P$ requires *M* 275.1075).

Phenyl(1-phenylethyl)phosphinic amide 13 (X = NH_2). A solution of the phosphinic chloride **13** (X = Cl) in CH_2Cl_2 was added cautiously to an excess of anhydrous NH_3 dissolved in ether. Volatile material was evaporated and the residue was partitioned between CH_2Cl_2 and water. The organic portion was concentrated and the crude product was crystallised from CH_2Cl_2–light petroleum to give the *phosphinic amide* **13** (X = NH_2) (49%) as a mixture of diastereoisomers, mp 140–142 °C (resolidifies and melts again at 151–153 °C), δ_P ($CDCl_3$) 35.1 and 32.9; δ_H ($CDCl_3$) 8.0–6.9 (10 H, m), 3.5–2.9 (1 H, m), 2.80 (2 H, br s, NH_2; exchanges with D_2O), and 1.48 and 1.40 (total 3 H; both dd, J_{PH} 17, J_{HH} 7); *m*/*z* 245 (M^+, 55%), 141 (M^+ − PhCH=CH_2, 45), 140 (M^+ − PhCHMe, 100) and 105 ($PhMeCH^+$, 60); ν_{max}(Nujol)/cm^{-1} 3330, 3240, 3130 (NH) and 1175 (P=O) (Found: C, 68.4; H, 6.8; N, 5.7. $C_{14}H_{16}NOP$ requires C, 68.6; H, 6.6; N, 5.7%).

***N*-*tert*-Butyl-*N*′-[phenyl(1-phenylethyl)phosphinoyl]hydrazine 5.** The phosphinic chloride **13** (X = Cl) (455 mg, 1.85 mmol) was added to a solution of *tert*-butylhydrazine (6 mmol) in CH_2Cl_2 (7 ml). After 30 min all volatile material was evaporated and the residue was partitioned between ether and water. The organic portion was extracted with 0.5 mol dm^{-3} hydrochloric acid, the aqueous extract was basified, and the liberated hydrazine derivative was back-extracted into CH_2Cl_2. The crude product (310 mg, 55%) was crystallised from CH_2Cl_2–light petroleum to give the *phosphinic hydrazide* **5** as a mixture of diastereoisomers, mp 170–171 °C, t_R 4.0 and 5.0 (major) min at 220 °C; δ_P ($CDCl_3$) 36.9 (major) and 35.3; δ_H ($CDCl_3$, 300 MHz) 7.95–7.05 (10 H, m), 4.13 (major) and 3.91 (total 1 H; both d, J_{PH} 14.5 or 13.5, NH), 3.605 (major) and 3.445 (total 1 H; both dq, J_{PH} 16.5 or 13, J_{HH} 7.5), 3.07 (major) and 2.94 (total 1 H; both br s, NH), 1.66 (major) and 1.41 (total 3 H; both dd, J_{PH} 16 or 17, J_{HH} 7.5), and 1.07 (major) and 0.87 (total 9 H; both s); ν_{max}(Nujol)/cm^{-1} 3150 (NH) and 1185 (P=O); *m*/*z* 316 (M^+, 25%), 301 (M^+ − Me, 30) and 105 ($PhMeCH^+$, 100) (Found: C, 67.7; H, 7.9; N, 8.75; M^+ 316.1705. $C_{18}H_{25}N_2OP$ requires C, 68.3; H, 8.0; N, 8.85%; *M* 316.1705).

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References

1 Preliminary communication: M. J. P. Harger and R. Sreedharan-Menon, *J. Chem. Soc.*, *Chem. Commun.*, 1996, 867.
2 M. J. P. Harger, *J. Chem. Soc.*, *Perkin Trans. 1*, 1983, 2699.
3 E. S. Wallis and R. D. Dripps, *J. Am. Chem. Soc.*, 1933, **55**, 1701; H. L. Yale, *Chem. Rev.*, 1943, **33**, 209; L. Bauer and O. Exner, *Angew. Chem.*, *Int. Ed. Engl.*, 1974, **13**, 376.
4 M. J. P. Harger and A. Smith, *J. Chem. Soc.*, *Perkin Trans. 1*, 1987, 683; *J. Chem. Res.* (*S*), 1991, 358.
5 M. J. P. Harger and P. A. Shimmin, *Tetrahedron*, 1992, **48**, 7539.
6 M. J. P. Harger and R. Sreedharan-Menon, *J. Chem. Soc.*, *Perkin Trans. 1*, 1994, 3261.
7 W. Dabkowski, J. Michalski, C. Radziejewski and Z. Skrzypczynski, *Chem. Ber.*, 1982, **115**, 1636; W. Dabkowski, J. Michalski and Z. Skrzypczynski, *Chem. Ber.*, 1985, **118**, 1809; J. Baraniak and W. J. Stec, *J. Chem. Soc.*, *Perkin Trans. 1*, 1987, 1645.
8 J. Michalski, W. Dabkowski and J. Wasiak, *Pol. J. Chem.*, 1992, **66**, 879.
9 J. Wasiak and J. Michalski, *Tetrahedron Lett.*, 1994, **35**, 9473.
10 M. J. P. Harger and A. Smith, *J. Chem. Soc.*, *Perkin Trans. 1*, 1985, 2651; 1990, 1447.
11 S. Freeman and M. J. P. Harger, *J. Chem. Soc.*, *Perkin Trans. 2*, 1988, 81; *J. Chem. Soc.*, *Perkin Trans. 1*, 1988, 2737.
12 W. P. Jencks, *Acc. Chem. Res.*, 1980, **13**, 161; *Chem. Soc. Rev.*, 1981, **10**, 345.

Paper 8/09267B