Rearrangement reactions of *N*-phosphinoyl-*O*-sulfonylhydroxylamines with amines: detection of a phosphonamidic–sulfonic mixed anhydride intermediate by nuclear magnetic resonance spectroscopy

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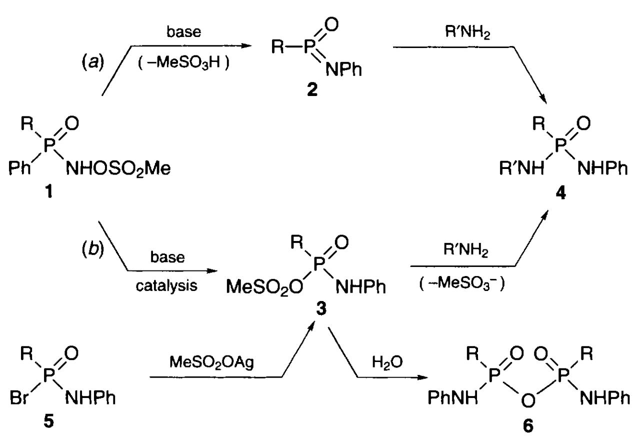
An intermediate can be detected by ^{31}P NMR spectroscopy when PhRP(O)NHOSO$_2$Me (R = PhMeCH) forms the rearrangement product RP(O)(NHBu^t)NHPh with Bu^{t}NH$_2$ in dilute solution; the intermediate has been identified as the mixed anhydride RP(O)(OSO$_2$Me)NHPh by comparison with an authentic sample.

Suitable derivatives of *N*-phosphinoylhydroxylamines undergo rearrangement with base. Thus, for example, the *O*-methanesulfonate **1** (R = alkyl or phenyl) reacts with an amine R′NH$_2$ to give the phosphonic diamide **4** in which a phenyl group has migrated from phosphorus to nitrogen.[1,2] By analogy with the isocyanate formed in a Lossen rearrangement, it may be supposed that a metaphosphonimidate **2** is the initial result of rearrangement.[3] Some observations accord well with a highly reactive and unselective three-coordinate P^V intermediate[4] being the product-forming species [Scheme 1, path (*a*)], but others are more readily reconciled with a phosphonamidic–sulfonic mixed anhydride **3** as the intermediate [Scheme 1, path (*b*)].[5] Attempts to detect a mixed anhydride intermediate have failed, however, and only the results of a recent stereochemical study have lent it some credibility.[6] In particular, methanesulfonate **1** having R = PhMeCH was found to react stereospecifically with MeNH$_2$, giving **4** (R = PhMeCH, R′ = Me) with retention of configuration at phosphorus. Stereospecificity would not be expected for reaction *via* a planar three-coordinate species **2**, but is compatible with a mixed anhydride intermediate if its formation and subsequent reaction are both stereospecific.

The substrate **1** (R = PhMeCH) has a bulky alkyl group at the phosphoryl centre. If the amine nucleophile is also bulky, and present in low concentration, then the phosphonamidic–sulfonic anhydride, if formed, should undergo substitution relatively slowly: it might even survive long enough to be detected. The reaction of **1** (R = PhMeCH) in a dilute solution of Bu^{t}NH$_2$ was therefore examined by ^{31}P NMR spectroscopy.



Scheme 1

Using just a small excess of Bu^{t}NH$_2$ (2.5 equiv.) as a dilute solution in CH$_2$Cl$_2$ (initial concentration 0.21 mol dm^{-3}), the methanesulfonate **1** (R = PhMeCH), a 4:1 mixture of diastereoisomers (δ_P 40.8 and 39.6), was consumed over 50 min (Fig. 1). The product was the expected phosphonic diamide **4** (R = PhMeCH, R′ = Bu^t)[6] (δ_P 21.7 and 21.4; two diastereoisomers) although there was also a substantial amount of a byproduct (δ_P ~ 24, several peaks). This is apparently the symmetrical phosphonamidic anhydride **6** (R = PhMeCH) (several diastereoisomers)† since a comparable ^{31}P NMR signal was observed for an authentic sample. Of particular interest was the appearance of a barely-resolved pair of peaks having δ_P 27.7 and 27.5. These peaks are clearly caused by an intermediate—they appeared and disappeared as reaction proceeded (Fig. 1)—and their chemical shift is not unreasonable for a phosphonamidic–sulfonic anhydride such as **3** (R = PhMeCH) (two diastereoisomers). Some support for the identity of the intermediate came from the ^1H NMR spectra of reaction mixtures (in CDCl$_3$). Singlets were observed around δ_H 3 (*Me*SO$_3$), not only for the substrate [δ_H 3.15 (major diastereoisomer) and 2.73] and the sulphonate anion (δ_H 2.78), but also for the intermediate [δ_H 3.32 (major diastereoisomer) and 2.92].

To confirm the identity of the intermediate, an authentic sample was required. For this the method recently developed by Wasiak and Michalski[7] proved successful. Thus, treatment of the phosphonamidic bromide **5** (R = PhMeCH)‡ with MeSO$_2$OAg in MeCN gave the mixed anhydride **3** (R = PhMeCH)

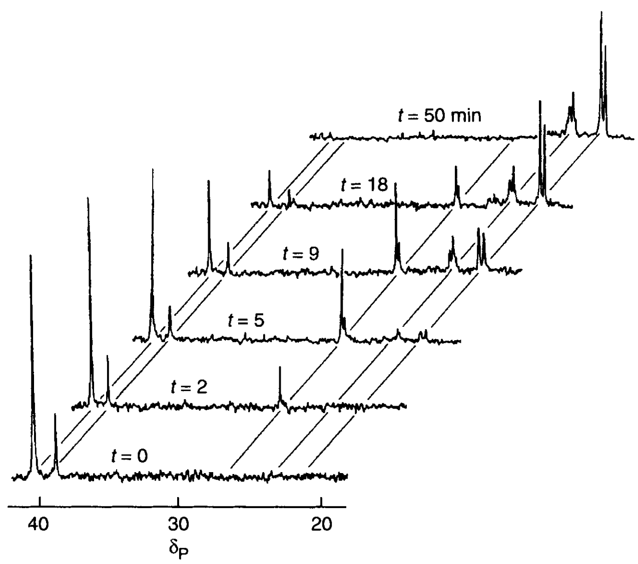


Fig. 1 ^{31}P NMR spectra (36.2 MHz; ^1H decoupled) for the reaction of **1** (R = PhMeCH) with Bu^{t}NH$_2$ in CH$_2$Cl$_2$ at room temperature. For each spectrum (except *t* = 0) data were accumulated for 1–2 min either side of the time shown.

as a mixture of diastereoisomers, δ_P (MeCN) 28.1 (two poorly resolved peaks); δ_H ($CDCl_3$) 7.4–6.7 (m, Ph $\times$ 2), 6.05 and 5.55 (broad, NH), 3.75–3.45 (m, PhMeC*H*), 3.31 and 2.90 (both s, *Me*SO_2O), and 1.74 and 1.63 (both dd, J_{PH} 21 Hz, J_{HH} 7.5 Hz; Ph*Me*CH); *m/z* 339 (M^+, 60%), 139 (95) and 105 (100). Addition of this material to a rearrangement reaction mixture increased the intensity of the ^{31}P NMR signals associated with the intermediate. Not surprisingly, the mixed anhydride **3** proved to be extremely reactive; even the authentic sample could not be isolated entirely free of the symmetrical phosphonamidic anhydride **6**, the product of its reaction with traces of moisture, and the byproduct of the rearrangement reaction.

Granted that the phosphonamidic–sulfonic mixed anhydride is an intermediate, some details of the reaction of **1** (R = PhMeCH) with Bu^tNH_2 remain to be addressed. The fact that the mixed anhydride was formed to an appreciable extent (Fig. 1, t = 2 min) before any of the diamide product (or the byproduct) could be detected (Fig. 1, t = 5 min) suggests that it is the sole product-forming species, *i.e.* that the reaction proceeds entirely by path (*b*) in Scheme 1. As regards stereochemistry, it seems (within the limitations of the spectra in Fig. 1) that the diastereoisomer ratio of the phosphonamidic–sulfonic anhydride is similar to that of the substrate (4 : 1), in which case it may be that its formation is stereospecific; use of a sample of the substrate in which the other (highfield) diastereoisomer was dominant certainly reversed the stereochemical make-up of the anhydride (highfield diastereoisomer now predominant). If the anhydride intermediate is indeed formed stereospecifically, then its reaction with Bu^tNH_2 (at low concentrations) must be substantially non-stereospecific, since the diastereoisomer ratio of the phosphonic diamide product (*ca.* 1.3 : 1) is clearly different from that of the substrate (Fig. 1). This is not unreasonable; like a phosphonamidic chloride,[8] a phosphonamidic–sulfonic anhydride will tend to depart from the $S_N2(P)$ pathway and react with a hindered amine by a non-stereospecific dissociative elimination–addition mechanism. A metaphosphonimidate may therefore still participate in the reaction, if not as the initial product of rearrangement then as an intermediate in the substitution that converts the phosphonamidic-sulfonic anhydride into the final diamide product.§

Footnotes

† Moisture was excluded as far as possible. However, given the low concentration of the amine (Bu^tNH_2) and its low nucleophilicity (steric hindrance), and the high nucleophilicity of water towards phosphoryl centres in basic media, some interference from traces of moisture is probably unavoidable. Formation of the byproduct **6** is, it seems, a price that must be paid for extending the lifetime of the intermediate.

‡ $PhMeCHP(O)Br_2$ (δ_P 33.0) was prepared from PhMeCHBr and PBr_3–$AlBr_3$; with $PhNH_2$ it gave the phosphonamidic bromide **5** (δ_P 38.3 and 35.8; mixture of diastereoisomers).

§ A metaphosphonimidate may actually be involved in the formation of the phosphonamidic–sulfonic anhydride, so long as the sulfonate anion displaced from N by the migrating phenyl group bonds to P more quickly than the metaphosphonimidate tumbles (stereospecific inversion of configuration at P; *c.f.* ref. 6). However, it seems at least as likely that there is some concertedness between the transfer of sulfonate from N to P and the migration of phenyl from P to N.

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