Sulfonylation in the rearrangement of an *N*-phosphinoyl-*O*-sulfonylhydroxylamine: demonstration of a phosphonamidic-sulfonic anhydride intermediate and ^{18}O-labelling evidence on how it may be formed

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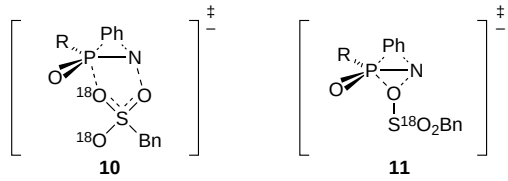
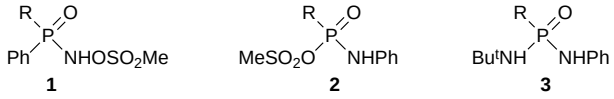
The rearrangement reaction of R(Ph)P(O)NHOSO$_2$Bn (R = PhMeCH) (57% enriched with one ^{18}O atom in the SO$_2$ group) with Bu^{t}NH$_2$ in CH$_2$Cl$_2$ gives the sulfonamide BnSO$_2$NHBu^t (43.7% enriched with one ^{18}O atom) as one of the products; this indicates a phosphonamidic-sulfonic anhydride intermediate [R(BnSO$_2$O)P(O)NHPh], formed with partial equilibration of the sulfonate oxygen atoms and attacked (in part) at the sulfonyl group.



10 **11**

N-Phosphinoylhydroxylamines are the phosphorus analogues of hydroxamic acids, and their *O*-sulfonyl derivatives **1** (R = alkyl or phenyl) undergo rearrangement with base,[1] *e.g.* **1** gives **3** with Bu^{t}NH$_2$. The product-forming species may be a transient metaphosphonimidate [RP(O)=NPh], analogous to the isocyanate in a Lossen rearrangement,[2] although some evidence points instead to a phosphonamidic-sulfonic mixed anhydride **2**.[3,4] In principle this anhydride could react with a nucleophile at sulfur rather than phosphorus,[5] but in practice such products have not hitherto been seen. We now report the first direct chemical evidence for a mixed anhydride intermediate in the rearrangement, and ^{18}O-labelling information on how it may be formed.



1 **2** **3**

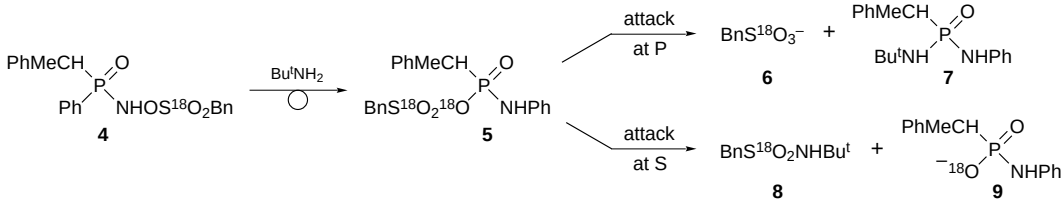
The benzylic sulfonyl derivative **4** was prepared by treating PhMeCH(Ph)P(O)NHOH (mixture of diastereoisomers)[3] with ^{18}O-enriched BnSO$_2$Cl in pyridine (ice cooling). It was obtained as a mixture of diastereoisomers [δ_P(CDCl$_3$) 42.6 and 41.0 (ratio 5:1); δ_H(CDCl$_3$) 4.61 (major) and 4.19 (both AB; $\Delta\delta$ 0.12 or 0.14 ppm, J_{AB} 14 Hz; SO$_2$C*H*$_2$Ph)] having 57% of the molecules enriched with one ^{18}O atom in the sulfonyl (SO$_2$) group [*m/z* (FAB) 416 and 418 (M + H)$^+$; negligible amount of double-labelled material]. With 2 mol dm^{-3} Bu^{t}NH$_2$ (40 equiv.) in CH$_2$Cl$_2$ it gave mainly the 'normal' phosphonamide rearrangement product **7** [δ_P(CDCl$_3$) 22.7 and 22.4 (diastereoisomers, ratio 3:1)] together with the sulfonate anion **6** [δ_H(CDCl$_3$) 4.07 (s, PhC*H*$_2$SO$_3^-$)]. Significantly, however, it also gave a substantial amount (*ca.* 17%) of the sulfonamide product **8** [δ_H(CDCl$_3$) 4.25 (s, PhC*H*$_2$SO$_2$) and 1.36 (s, NBu^t)] together with the phosphonamidate anion **9** [δ_P(CDCl$_3$) 19.5].

This behaviour is clearly indicative of a phosphonamidic-sulfonic anhydride intermediate **5** and competing attack at the P and S atoms by the Bu^{t}NH$_2$ nucleophile (Scheme 1).

Mass spectrometric examination of the products, after esterification with diazaomethane in the case of the anions, indicated their isotopic enrichment (±0.5%):† **6** had 57.6% one ^{18}O atom [methyl ester, *m/z* (EI) 186 and 188 (M$^+$)], **7** had no enrichment [*m/z* (EI) 316 (M$^+$)], **8** had 43.7% one ^{18}O atom [*m/z* (CI) 245 and 247 (M + NH$_4$)$^+$] and **9** had 13.7% one ^{18}O atom [methyl ester, *m/z* (EI, GC–MS) 275 and 277 (M$^+$)].

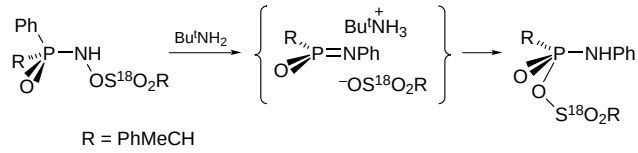
For the products of attack at the phosphorus atom of the mixed anhydride, the results are as expected: all the label originally in the substrate **4** ends up in the sulfonate anion **6** and none in the phosphonamide rearrangement product **7**. Of more interest are the products of attack at sulfur, since it is from these that the distribution of the label in the mixed anhydride intermediate can be inferred. With 76% of the available ^{18}O label ending up in the sulfonamide product **8**, and only 24% in the phosphonamidate anion **9**, it would seem that, on rearrangement, the label in the sulfonyl group of the substrate **4** is transferred to the bridging and non-bridging positions of the mixed anhydride **5** in a ratio of 24:76.

Concerted rearrangement of the substrate, after removal of a proton (N*H*) by the amine, would most plausibly involve a transition state resembling **10**. This would give rise to a bridging:non-bridging ^{18}O ratio of 50:50 in the mixed anhydride. Subsequent scrambling of the label, after formation of the anhydride but before its conversion into product, might reduce the ratio, but not beyond the statistical value of 33:67; the experimentally observed value of 24:76 could never be attained. At the other extreme, if concerted rearrangement involved a transition state resembling **11**, the mixed anhydride would be formed with none of the label in the bridging position (ratio 0:100). In this case, however, subsequent scrambling could give rise to an (average) ratio of 24:76, so long as it occurred at approximately the same rate as the conversion of the



4 **5** **6** **7** **8** **9**

Scheme 1



Scheme 2

anhydride into product. Such scrambling is certainly not unreasonable; like a phosphonamidic chloride,[6] the phosphonamidic-sulfonic anhydride will tend to react with Bu^tNH_2 at phosphorus by a dissociative substitution mechanism (stepwise preassociative elimination-addition).[7] Nonetheless, the geometry of the transition state **11** makes this concerted pathway seem rather improbable.

The alternative to these is a non-concerted mechanism (Scheme 2), in which the sulfonate group becomes completely detached from the nitrogen atom before it begins to bond to phosphorus. At the limit this must result in a uniform (statistical) distribution of the label between the three sulfonate oxygen atoms of the mixed anhydride (ratio 33 : 67). Initially, however, the sulfonate oxygen atom (unlabelled) released from the N–O bond will not be equivalent to the other two, because of differences in solvation (by CH_2Cl_2 or Bu^tNH_2) and/or association (with $Bu^tNH_3^+$). If the new bond to phosphorus is formed before equilibration of the oxygen atoms is complete, and makes preferential use of this (unlabelled) oxygen atom, the mixed anhydride will be formed with less than a third of the available ^{18}O label located in the bridging position. The observed result (24% of the available ^{18}O in the bridging position) could then reflect a rather modest bias for incorporation of the unlabelled oxygen atom in the new P–O bond, or a strong bias with some subsequent scrambling. There is at least one precedent for a rearrangement involving migration of a sulfonate anion in which the oxygen atom released by bond breaking is preferentially employed in subsequent bond making;[8] in that case, however, it is a cation with which the sulfonate anion recombines, not an uncharged species.

Two conclusions can be drawn from the present study: a phosphonamidic-sulfoninc mixed anhydride **5** is involved in the rearrangement reactions of the hydroxylamine derivative **4**, even at a high amine concentration,‡ and the transformation of **4** into **5** is most probably non-concerted (Scheme 2). Some of the initial metaphosphonimidate intermediate may go directly to the phosphonamide product, by reaction with Bu^tNH_2, but some—perhaps most—rapidly recombines with the sulfonate anion to form the mixed anhydride.

I am grateful to Dr G. Eaton for recording mass spectra and Professor P. M. Cullis for advice and encouragement.

Footnotes

† In all mass spectrometric measurements of ^{18}O enrichment, allowance was made for ^{34}S and natural abundance ^{18}O by comparing directly the spectrum of the enriched material with that of a natural abundance sample.

‡ A high concentration of Bu^tNH_2 was used for two reasons. First, it affords a rigorous test of the generality of mixed anhydride formation; at very low amine concentrations a metaphosphonimidate intermediate might have an atypically high disposition towards recombination with the sulfonate anion. Second, it limits the complications associated with the phosphonamidate anion **9** that is released when the amine attacks the mixed anhydride **5** at sulfur. This anion is a powerful nucleophile and competes with Bu^tNH_2 for another molecule of **5** (attack at the P atom of **5** produces a symmetrical phosphonamidic anhydride).

References

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3 M. J. P. Harger and R. Sreedharan-Menon, *J. Chem. Soc., Perkin Trans. 1*, 1994, 3261 and references cited therein.
4 M. J. P. Harger and R. Sreedharan-Menon, *Chem. Commun*., 1996, 867. (A very low concentration of Bu^tNH_2 had to be used in this study; the conclusions might not be valid under more normal conditions.)
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8 U. Gessner, A. Heesing, L. Keller and W. K. Homann, *Chem. Ber*., 1982, **115**, 2865 (see especially rearrangement in methanol).

Received, 27th November 1996; Com. 6/08043J