Lossen-like Rearrangement of *N*-[α-Methylbenzyl(phenyl)phosphinoyl]-*O*-methylsulfonylhydroxylamine with Methylamine: Retention of Configuration at Phosphorus as revealed by X-Ray Crystallography

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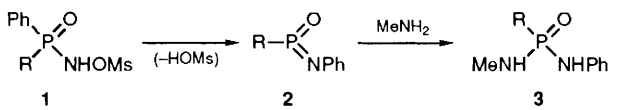
The diastereoisomers of the title compound **6** rearrange with high stereospecificity on treatment with $MeNH_2$, giving PhMeCHP(O)(NHMe)NHPh in which the migrating phenyl group has been replaced by $MeNH_2$ with retention of configuration at phosphorus.

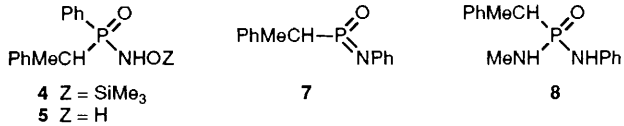
N-Phosphinoylhydroxylamines are the phosphorus analogues of hydroxamic acids, and the *O*-sulfonyl derivatives **1** (R = phenyl or alkyl) undergo a Lossen-like rearrangement with base (Scheme 1).[1] This involves migration of a phenyl group from phosphorus to nitrogen, and gives rise to a phosphonamide product such as **3**. The monomeric metaphosphonimidate **2** is a plausible intermediate, being analogous to the isocyanate formed in a Lossen rearrangement.[2] There is no direct evidence, however, and indirect attempts to demonstrate that a metaphosphonimidate is the product-forming species have not been conclusive.[3] With the aim of clarifying the role of metaphosphonimidate intermediates in the rearrangement, we have now examined the stereochemistry.



1 **2** **3**

Scheme 1 Ms = SO_2Me

The phosphinoylhydroxylamine **5** is chiral at carbon as well as phosphorus, and therefore exists as diastereoisomers. Treatment of α-methylbenzyl(phenyl)phosphinic chloride (from the known phosphinic acid[4] and oxalyl chloride) with $Me_3SiONHSiMe_3$ (1.25 mol equiv.) in CH_2Cl_2 (14 mol equiv., *T ca.* 35 °C) gave the silylated phosphinoylhydroxylamine **4**. Although the two diastereoisomers of **4** were formed in comparable amounts, one (A; δ_P 42.0) was markedly more soluble in CH_2Cl_2 than the other (B; δ_P 41.0), ν_{max} (Nujol)



4 Z = $SiMe_3$
5 Z = H
6 Z = SO_2Me

7 **8**

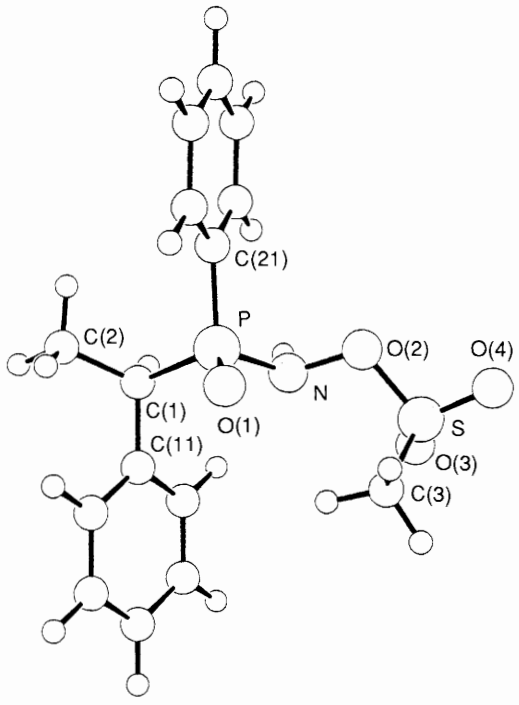


Fig. 1 X-ray structure of substrate **6**: relative configurations at phosphorus and carbon. Selected bond lengths (Å) and angles (°): P–C(1) 1.824(3), P–C(21) 1.786(2), P–N 1.690(2), N–O(2) 1.459(3), C(1)–P–C(21) 109.8(1), C(21)–P–N 109.4(1), N–P–C(1) 98.6(1), C(1)–P–O(1) 115.0(1), C(21)–P–O(1) 111.4(1), N–P–O(1) 111.9(1), P–N–O(2) 111.3(2).

3130 cm^{-1}, *m/z* 333 (M^+, 30%). It was therefore possible to obtain samples of **4** substantially enriched in one or other of the diastereoisomers. These samples were separately converted into the phosphinoylhydroxylamine **5**, δ_P ($CDCl_3$) 41.9 and 40.1 (diastereoisomers), *m/z* 261 (M^+, 5%), by desilylation with MeOH in CH_2Cl_2. Treatment with $MeSO_2Cl$–Et_3N in CH_2Cl_2 then gave, after crystallisation (CH_2Cl_2–light petroleum), samples of the methanesulfonate **6** having diastereoisomer compositions of 80:20 (sample A), m.p. 154–157.5 °C, *m/z* (CI) 340 ($M + H^+$, 35%); major component, δ_P ($CDCl_3$) 39.6, δ_H ($CDCl_3$) (in part) 8.45 (d, J_{PH} 7, NH), 3.10 (s, SO_2Me) and 1.70 (dd, J_{PH} 16, J_{HH} 7.5, PhCH*Me*); and 3:97 (sample B), m.p. 177–179 °C (decomp.); major component δ_P($CDCl_3$) 38.1, δ_H ($CDCl_3$) (in part) 7.14 (d, J_{PH} 4, NH), 2.70 (s, SO_2Me) and 1.55 (dd, J_{PH} 18, J_{HH} 7.5, PhCH*Me*).†

Both samples of the methanesulfonate **6** reacted rapidly with $MeNH_2$ (large excess, no solvent) at *ca.* −5 °C. The product from sample A (80:20) was a 79:21 mixture of the diastereoisomers of the phosphonic diamide **8**, *m/z* 274 (M^+, 40%); major component, δ_P (CH_2Cl_2) 26.2, δ_H ($CDCl_3$) (in part) 2.51 (dd, J_{PH} 11.5, J_{HH} 6, NH*Me*) and 1.56 (dd, J_{PH} 17.5, J_{HH} 7.5, PhCH*Me*); and from sample B (3:97) it was a 7:93 mixture of the diastereoisomers of **8**, crystallised from CH_2Cl_2–light petroleum, m.p. 132–133 °C, $\nu_{max.}$ (Nujol) 3220, 3190 cm^{-1} (NH), δ_P (CH_2Cl_2) 25.7, δ_H ($CDCl_3$) (in part) 2.59 (dd, J_{PH} 11.5, J_{HH} 5.5, NH*Me*) and 1.62 (dd, J_{PH} 17.5, J_{HH} 7.5, PhCH*Me*). The rearrangement thus proceeds with a high degree of stereospecificity, and the free metaphosphonimidate **7** cannot be the principle product-forming species; the chirality at phosphorus is lost in **7**, and both diastereoisomers of the substrate would give the same mixture of the diastereoisomers of the product.

† All compounds were racemates, our concern being only the relative configurations at phosphorus and carbon in the substrate and product. The new compounds **4**, **5**, **6** and **8** were fully characterised by spectroscopy and elemental analysis or accurate mass measurement.

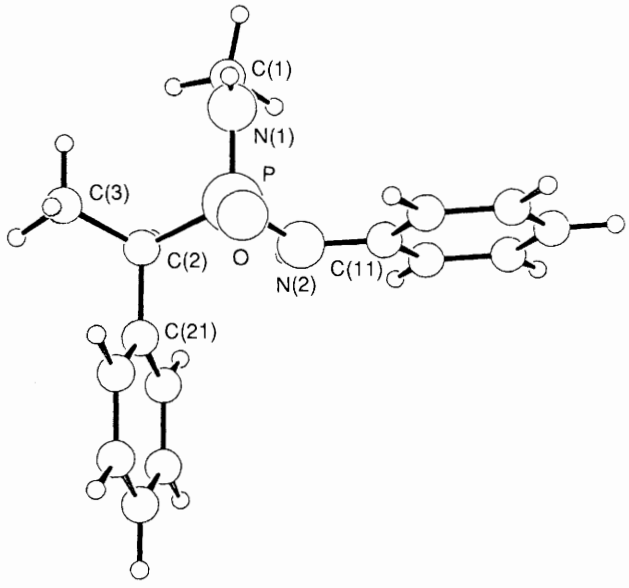


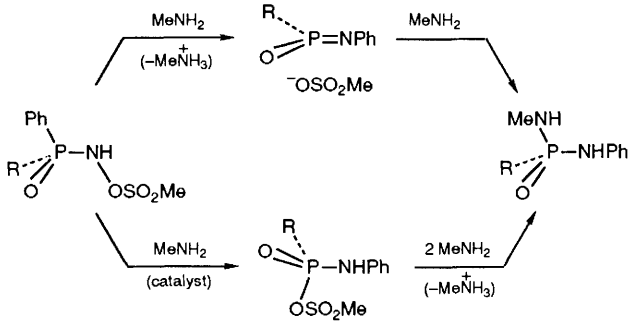
Fig. 2 X-ray structure of product **8**: relative configurations at phosphorus and carbon. Selected bond lengths (Å) and angles (°): P–C(2) 1.825(5), P–N(1) 1.624(6), P–N(2) 1.653(5), N(1)–C(1) 1.477(8), N(2)–C(11) 1.414(5), C(2)–P–N(1) 108.8(3), N(1)–P–N(2) 108.4(3), N(2)–P–C(2) 100.0(2), C(2)–P–O 114.4(2), N(1)–P–O 109.1(3), N(2)–P–O 115.6(2), P–N(1)–C(1) 124.4(5), P–N(2)–C(11) 128.6(4).

To ascertain the sense of the stereospecificity, the relative configurations at carbon and phosphorus, in both the substrate and product, were determined by X-ray crystallography.‡ Fig. 1 shows the structure of the dominant diastereoisomer in sample B of the substrate **6**, and Fig. 2 the dominant diastereoisomer of the product **8** that it forms on reaction with $MeNH_2$. The stereochemical relationship between substrate and product (Scheme 2) establishes that the nucleophile ($MeNH_2$) takes the place of the migrating phenyl group *with retention of configuration at phosphorus*.

Stereospecificity is obviously not compatible with a liberated metaphosphonimidate intermediate, although there is still the possibility of a metaphosphonimidate that combines with the nucleophile ($MeNH_2$) more quickly than it diffuses away from the leaving group ($\bar{O}SO_2Me$). Then the leaving group might shield one face of the metaphosphonimidate and direct the attacking nucleophile to the other, giving the product of retained configuration (Scheme 2, top pathway).

‡ *X-ray crystallography*. Data were measured on a Stöe STADI-2 diffractometer with graphite monochromated Mo-Kα radiation (λ 0.7107 Å) and ω scans. The data were corrected for Lorentz and polarisation effects. The structures were solved by direct methods. The phenyl and methyl hydrogen atoms were included in calculated positions with isotropic thermal parameters refined as groups (for **6**) or with a single fixed thermal parameter (for **8**). The remaining hydrogen atoms were refined as isotropic atoms. All other atoms were refined with anisotropic thermal parameters.

Crystal data: **6** (racemate): $C_{15}H_{18}NO_4PS$, M = 339.35. Monoclinic, space group *I2/a*, a = 20.132(16), b = 10.396(2), c = 17.814(14) Å, β = 117.8(1)°, U = 3299(5) Å^3, Z = 8, μ = 2.62 cm^{-1}, $F(000)$ = 1424, D_c = 1.37 g cm^{-3}, T = 293 K. Full-matrix least squares refinement of 187 parameters gave R = 0.047 and R_w = 0.049 for 2324 unique reflections with $I > 3\sigma(I)$. **8** (racemate): $C_{15}H_{19}N_2OP$, M = 274.3. Monoclinic, space group $P2_1/a$, a = 10.450(2), b = 13.204(14), c = 10.755(11) Å, β = 97.17(6)°, U = 1472(3) Å^3, Z = 4, μ = 1.41 cm^{-1}, $F(000)$ = 584, D_c = 1.24 g cm^{-3}, T = 293 K. Full-matrix least squares refinement of 166 parameters gave R = 0.056 and R_w = 0.059 for 1221 unique reflections with $I > 3\sigma(I)$. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.



Scheme 2 R = PhMeCH

Alternatively, reaction may proceed *via* a phosphonamidic-sulfonic anhydride (Scheme 2, bottom pathway), as tentatively suggested before.[3] The observed retention of configuration would then be a consequence of two inversions, in the formation of the anhydride and in its reaction with the nucleophile.

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