Asymmetric Induction in the Base Induced Rearrangement of *N*-(Diphenylphosphinoyl)-*O*-(camphor-10-sulfonyl)hydroxylamine

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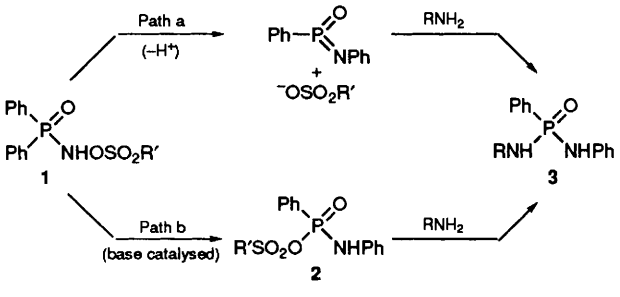
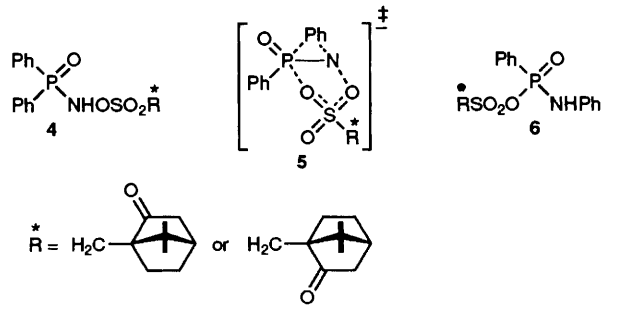
The derivatives of $Ph_2P(O)NHOH$ obtained using (+) and (−)-camphor-10-sulfonyl chloride rearrange with RNH_2 (R = Bu^t or Me) to give PhP(O)(NHPh)NHR having a small excess of the (+) or (−) enantiomer; this asymmetric induction is consistent with the initial product of rearrangement being a phosphonamidic–sulfonic mixed anhydride.

When suitably activated, *N*-phosphinoylhydroxylamines undergo a base-induced rearrangement in which a group migrates from phosphorus to nitrogen.[1,2] Thus, for example, the *O*-methylsulfonyl derivative **1** (R′ = Me) is converted into the phosphonic diamide **3** (R = Me or Bu^t) on treatment with $MeNH_2$ or Bu^tNH_2 (Scheme 1).[1,3] The initial product of rearrangement could be a short-lived monomeric metaphosphonimidate (path a) analogous to the isocyanate formed in a Lossen rearrangement.[4] Some observations accord well with a product-forming species of high reactivity/low selectivity,[3] but others are more easily understood if the initial product of rearrangement is a phosphonamidic-sulfonic mixed anhydride **2** (path b).[3,5]

A distinguishing feature of the two pathways in Scheme 1 is the geometry of the intermediate: the metaphosphonimidate in path a is trigonal at phosphorus but the anhydride **2** in path b is tetrahedral. The anhydride will therefore exist as stereoisomers. So long as the sulfonyl group is achiral (*e.g.* R′ = Me), the stereoisomers will just be enantiomers; they will be formed in equal amounts, and the diamide product **3** will be racemic even if it is formed by pathway b. If the sulfonyl group is chiral, however, the distinction between the two pathways might become apparent. The metaphosphonimidate (path a) will be no different, but the phosphonamidic-sulfonic mixed anhydride will now exist as diastereoisomers; these will not necessarily be formed in exactly equal amounts, so any product formed *via* the anhydride (path b) will not necessarily be racemic. With a view to clarifying the mechanism of the rearrangement, we have looked for evidence of asymmetric induction in the reactions of a substrate **1** having chirality in the sulfonyl group.



Scheme 1



Treatment of $Ph_2P(O)NHOH$ with (−)-camphor-10-sulfonyl chloride (1.35 equiv.)[6] in pyridine (12 equiv.) (10 min at 5–10 °C) gave one enantiomer of the camphorsulfonate **4**, crystallised from EtOH–H_2O, mp 150–152 °C (decomp.), δ_P ($CDCl_3$) 29.6, $[\alpha]_D$ −11° (*c* 0.85 in MeOH), *m/z* (FAB) 448 (M + H$^+$, 100%); treatment with (+)-camphor-10-sulfonyl chloride gave the other enantiomer, $[\alpha]_D$ + 11°.

Both enantiomers of **4** reacted rapidly and cleanly with Bu^tNH_2 (20 equiv.) as a 1.0 mol dm^{-3} solution in CH_2Cl_2 to give the rearrangement product **3** (R = Bu^t), δ_P ($CDCl_3$) 12.7. The sample obtained from (−) **4** showed a slight (−) rotation and that from (+) **4** a slight (+) rotation, but the magnitudes ($[\alpha]_D$ *ca.* 1° in $CHCl_3$) were too small to be of quantitative value, even if $[\alpha]_D$ for a pure single enantiomer had been known. Analysis by ^{1}H NMR spectroscopy was more helpful. The two product samples, and for comparison one obtained from the methanesulfonate **1** (R′ = Me), were examined using (−)-PhMeP(S)OH (1.0 equiv.) as a chiral solvating agent.[7] Even at 90 MHz, the N–Bu^t signals (9 H, s) of the enantiomers of **3** (R = Bu^t) were well separated [$\Delta\delta$ ($CDCl_3$) 0.10 ppm]. As expected, the product from the methanesulfonate (Fig. 1b) gave signals of equal intensity (racemic), but the products from the camphorsulfonates (Fig. 1a,c) showed a small excess (8–10%) of either the lowfield or the highfield enantiomer. With other concentrations of Bu^tNH_2 (0.05, 0.3, 3 mol dm^{-3} and neat) the (−)-camphorsulfonate again gave the product **3**

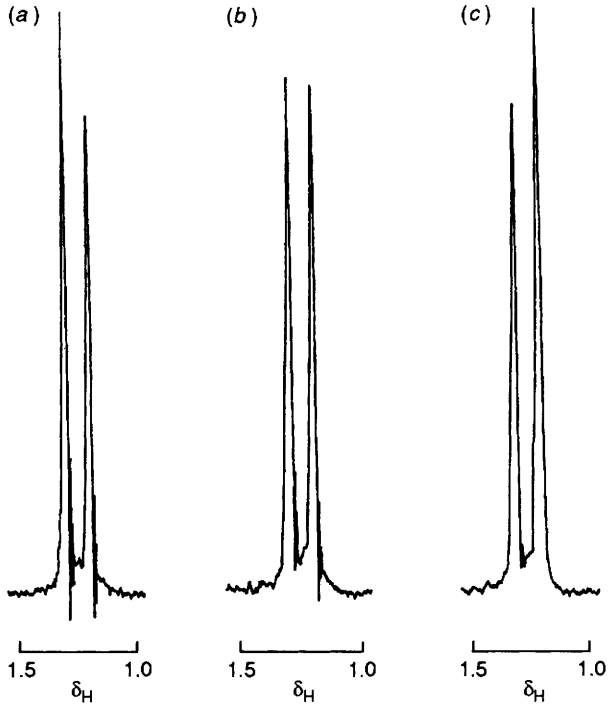


Fig. 1 ^{1}H NMR Spectra (90 MHz) of the rearrangement product PhP(O)(NHPh)NHBu^t with added (−)-PhMeP(S)OH; N–Bu^t signals for the two enantiomers: (*a*) product from (−)-camphorsulfonate: (*b*) product from methanesulfonate; (*c*) product from (+)-camphorsulfonate

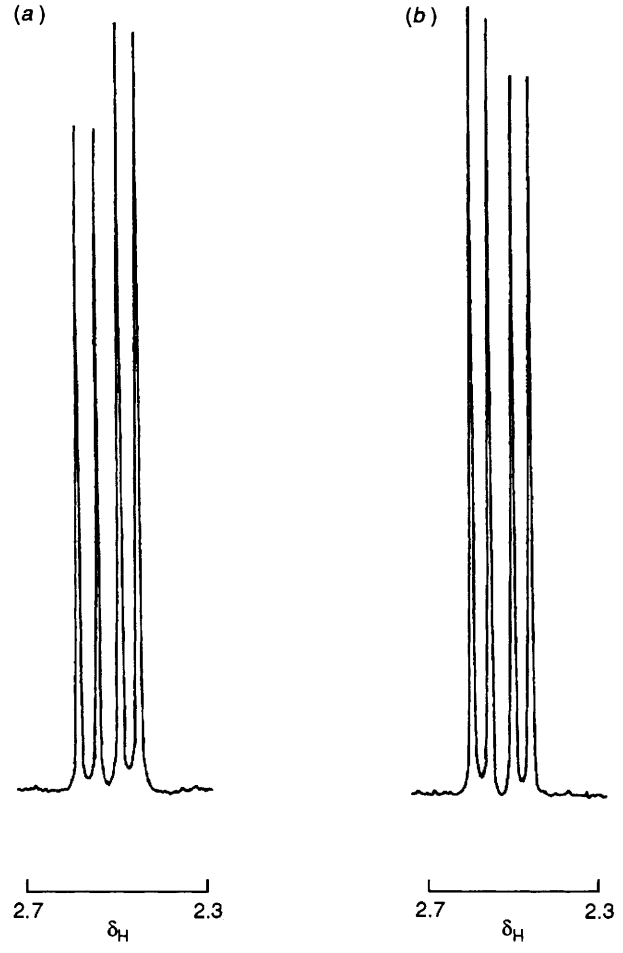


Fig. 2 ^{1}H NMR Spectra (300 MHz) of the rearrangement product PhP(O)(NHPh)NHMe with added (+)-PhBu^{t}P(S)OH; N–Me signals for the two enantiomers: (*a*) product from (−)-camphorsulfonate; (*b*) product from (+)-camphorsulfonate

(R = Bu^t) having, in every case, a small excess (6–12%) of the lowfield enantiomer. With $MeNH_2$ (1.0 mol dm^{-3} in CH_2Cl_2; 0 °C) also, there was clear evidence that the camphorsulfonates formed the rearrangement product **3** (R = Me), δ_P ($CDCl_3$) 17.4, as slightly unequal mixtures of enantiomers: Fig. 2 shows the product N–Me signals (3 H, d, J_{PH} 12.6 Hz) at 300 MHz with (+)-PhBu^{t}P(S)OH (1.3 equiv.) as the chiral solvating agent.[7] It thus seems clear that achiral $Ph_2P(O)$-NHOH, when activated with an enantiopure chiral sulfonylating agent, acquires the ability to rearrange with asymmetric induction. The sulfonate moiety of the activated substrate must therefore be more than just a leaving group that departs from nitrogen to make way for the migrating phenyl group.

Asymmetric induction does not automatically exclude the metaphosphonimidate pathway for rearrangement (path a, Scheme 1); the eliminated sulfonate anion might, by virtue of its chirality, exert a stereochemical influence on product formation simply by remaining in close proximity. There is, however, no charge on the metaphosphonimidate to keep it close to the sulfonate anion, and the asymmetric induction is not diminished by use of a very low concentration of the amine nucleophile, or by inclusion of sulfonate anion of the opposite configuration in the reaction medium. It is therefore more reasonable to suppose that the chiral sulfonyl group exerts its influence by bonding to phosphorus, and that the asymmetric induction originates as diastereoselectivity in the formation of the phosphonamidic–sulfonic mixed anhydride (path b, Scheme 1). The magnitude of the asymmetric induction is admittedly small,† but the diastereoisomeric mixed anhydrides **6**, and the transition states (possibly resembling **5**) leading to them, are unlikely to differ much in energy. That being so, it may be that much of the rearrangement, not just a small part, proceeds *via* the phosphonamidic–sulfonic mixed anhydride.

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Footnote

† It is possible that the product-forming reaction of the mixed anhydride with RNH_2 is not 100% stereospecific; in that case the diastereoselectivity of anhydride formation will be greater than we have inferred from the enantiomer excess of the phosphonic diamide product.

References

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