

Synthesis of an Unstable Allyl Sulphide from an Allyl Phosphine Oxide

Richard S. Torr and Stuart Warren *

University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW

The epoxide (8) reacts with PhSLi to give Horner–Wittig intermediate (9) and hence the allyl sulphide (10). The stereochemistry and reactions of the intermediates are described.

Allyl phenyl sulphides and sulphoxides¹ are useful intermediates in organic synthesis. We have prepared² allyl sulphides of type (2) by rearrangement of alcohols (1) but the less stable isomer (3) is at most a minor product and rearranges quickly to olefin (4) by a [1,3] PhS shift.³ Only with a silicon atom to accelerate the rearrangement and to direct the position of the double bond can isomers (3) be made by the rearrangement route.⁴ We now report the synthesis of one such compound (10) via the more stable isomer (7) of the corresponding phosphine oxide by a route which therefore involves a formal [1,3] transposition of functionality.

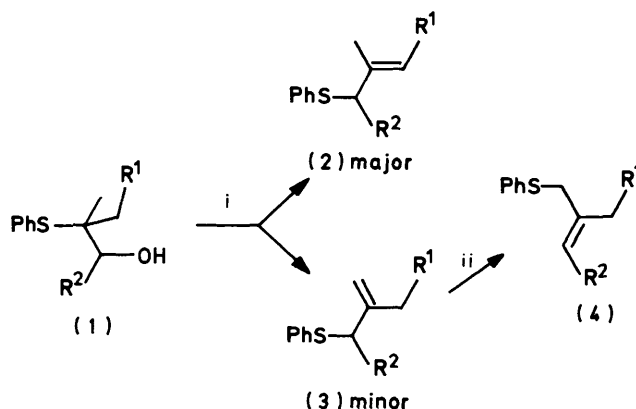
The allyl phosphine oxide (7) can be synthesised by regio-specific dehydration of alcohol (6), the more substituted double bond being formed exclusively within the six-membered ring, as expected from previous work.⁵ Epoxidation under standard conditions gave a high yield of crystalline epoxide (8). Treatment of (8) with PhSNa gave a 76% yield of the adduct (9) with some of the allyl sulphide (10), but PhSLi in THF (tetrahydrofuran) gave 89% of crystalline (8) as the only product.

Alcohol (9) is a Horner–Wittig intermediate and on treatment with NaH in THF gives some phosphine oxide (5) (16%) and a 79% yield of the allyl sulphide (10) which could be purified by preparative t.l.c. on silica in a foil-covered tank. The product (10) was stable in the dark but had rearranged quantitatively to the more stable isomer (11) in daylight within three days. Attempts to make the intermediate (9) by Horner–Wittig reaction between the phosphine oxide (5) and 2-(phenylthio)cyclohexanone are likely to lead to proton exchange.⁶

The epoxide (8) has an ABP system in its ¹H n.m.r. spectrum for the diastereotopic PCH₂ group (J_{AB} 14 Hz) and the epoxide proton appears as a doublet of doublets (1 H, dd, J_{ca} 1, 4 Hz). The alcohol (9) again has an ABP system (J_{AB} 16 Hz) in its ¹H n.m.r. spectrum but H_C (12) appears as a broad triplet, J_{ca} 4 Hz, as expected if the large Ph₂P(O)CH₂ group is equatorial. In the related compound (13), simply made by PhSLi addition to cyclohexane oxide, the proton next to sulphur (H_C) is now axial and appears as a double triplet with $J_{AC} = J_{CD} = 10$ Hz, J_{BC} 4 Hz.

Dehydration of the alcohol (9) in acid gave a 1:1 mixture of the allyl sulphides (14) and (15) but none of the vinyl sulphide (17). This is explained² if the thiiranium ion (16) is an intermediate—it should form easily from intermediate (12) in which both OH and PhS substituents are axial. The vinyl phosphine oxide (14) has J_{PH} 29 Hz for the vinyl proton in its ¹H n.m.r. spectrum. Treatment of the epoxide (8) with hydroxide or methoxide ion gives vinyl phosphine oxide (19) via anion (18). The ¹H n.m.r. spectrum of compound (19) has J_{PH} 27 Hz for the vinyl proton. Allyl sulphide (14) and allyl alcohol (19) are both single geometrical isomers, presumably *E*.

Rearrangement of epoxide (8) in acid is one of the many ways to make ketone (20), whose acetal acts as a homoenolate equivalent in Horner–Wittig reactions.⁷



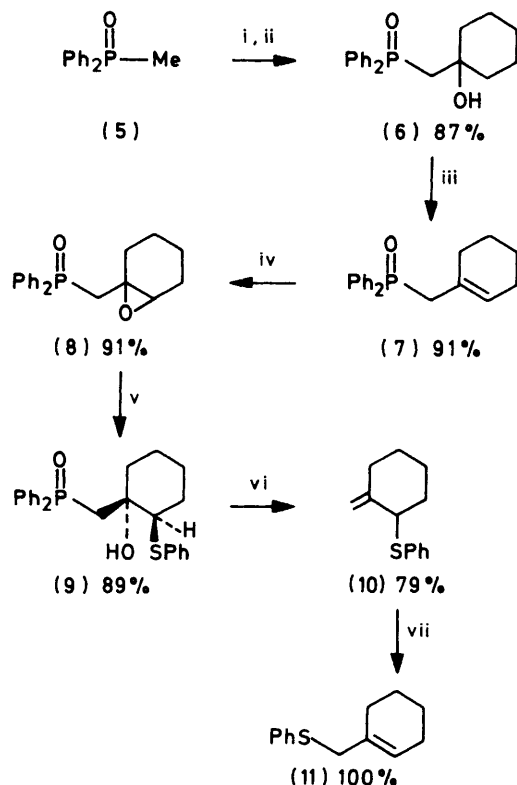
Reagents and conditions: i, H⁺; ii, hv or heat

Experimental

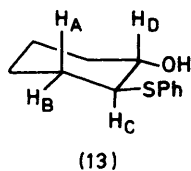
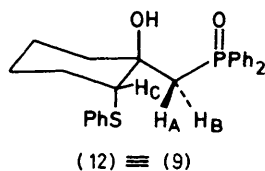
General Procedures are described in the following paper.⁸

1-(Diphenylphosphinoylmethyl)cyclohexanol (6).—Butyllithium (16.4 ml, 25.5 mmol) was added dropwise to a stirred solution of methyl diphenylphosphine oxide (5 g, 23.1 mmol) in dry THF (25 ml) under nitrogen at -78°C . After 10 min, cyclohexanone (2.50 g, 25.5 mmol) was added, the solution was allowed to warm to room temperature, and aqueous NH₄Cl (25 ml) was added. The layers were separated, the aqueous layer was extracted with EtOAc (3 × 25 ml), and the combined organic layers were dried (Na₂SO₄) and evaporated under reduced pressure to give a white solid. Recrystallisation from EtOAc gave the alcohol (6) (6.32 g, 87%), m.p. 162–164 °C (from EtOAc) (Found: C, 72.8; H, 7.30; P, 10.1. C₂₀H₂₃O₂P requires C, 72.6; H, 7.40; P, 9.8%); R_F 0.46 (EtOAc); δ (CDCl₃) 1.10–1.90 (10 H, m, 5 × ring CH₂), 2.60 (2 H, d, J_{PH} 10 Hz, PCH₂), 4.64 (1 H, s, OH), and 7.36–7.82 (10 H, m, Ph₂PO); ν_{max} 3 300 (OH), 1 435 (P–Ph), and 1 165 cm⁻¹ (P=O); m/z 314 (M^+ , 60%), 296 ($M - \text{H}_2\text{O}$, 60), 215 (Ph₂POCH₂⁺, 100), and 201 (Ph₂PO⁺, 95).

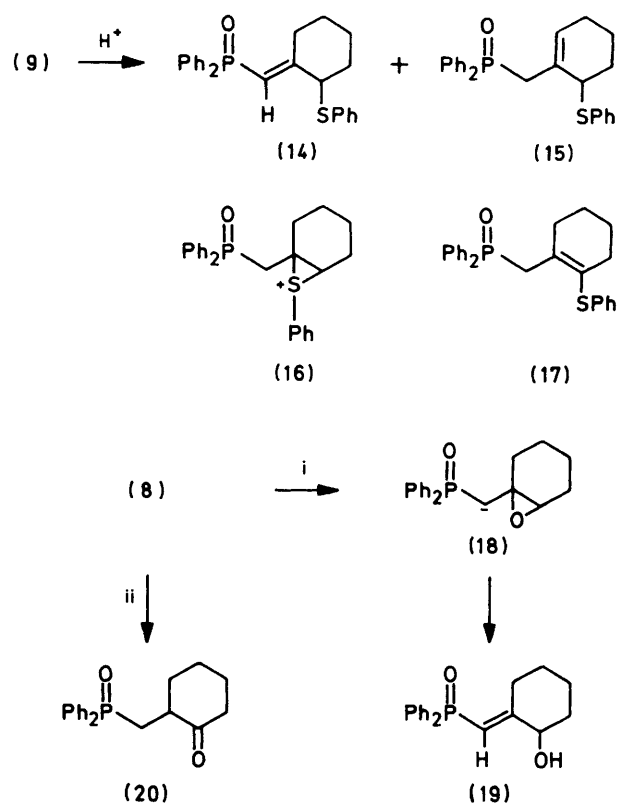
1-(Diphenylphosphinoylmethyl)cyclohexene (7).—The alcohol (6) (6.32 g, 20.1 mmol) was heated under reflux with an excess of trifluoroacetic acid (TFA) (25 ml) for 1 h and the solution was then cooled, poured into water (150 ml), and extracted with chloroform (3 × 50 ml). The combined extracts were washed in turn with saturated aqueous sodium hydrogen carbonate (3 × 50 ml) and water (2 × 50 ml), then dried (Na₂SO₄) and evaporated under reduced pressure to give a white solid. Recrystallisation from EtOAc gave the allyl phosphine oxide (7) (5.42 g, 91%), m.p. 141–142 °C (Found: C, 76.7; H, 7.15; P, 10.5; M^+ , 296.1339. C₁₉H₂₁OP requires C, 77.0; H, 7.15; P, 10.5%; M , 296.1330); R_F 0.36 (EtOAc); δ (CDCl₃) 1.40–1.60 (total 4 H, m, CH₂CH₂CH₂CH₂), 1.80–2.10 (total 4 H, m, CH₂CH₂CH₂CH₂), 3.00 (2 H, d, J_{PH} 14 Hz, PCH₂), 5.40 (1 H, m, C=CH), and 7.30–7.84 (10 H, m



Reagents and conditions: i, BuLi; ii, cyclohexanone; iii, $\text{CF}_3\text{CO}_2\text{H}$; iv, *m*-chloroperbenzoic acid- $\text{Na}_2\text{CO}_3\text{-CH}_2\text{Cl}_2$; v, PhSLi-THF; vi, NaH-THF; vii, hv



Ph_2PO (the signals at 1.80–2.10, 3.00, and 5.40 show fine splitting due to allylic and homoallylic coupling); ν_{max} 1 440 (P-Ph) and 1 185 cm^{-1} (P=O); m/z 296 (M^+ , 100%), 202 (Ph_2POH^+ , 55), and 201 (Ph_2PO^+ , 84).



Reagents: i, Base; ii, H^+

g, 3.5 mmol) in dry THF (20 ml) at room temperature, was added dropwise during 15 min to a stirred solution of the epoxide (8) (1.0 g, 3.2 mmol) in dry THF (20 ml) at room temperature under nitrogen. The mixture was stirred for a further 1 h, aqueous NH_4Cl (20 ml) was added, the layers were separated, and the aqueous layer was extracted with Et_2O (4×25 ml). The combined organic fractions were washed in turn with 3% aqueous sodium hydroxide (2×50 ml) and water (2×100 ml), dried (Na_2SO_4), and evaporated under reduced pressure to give a pale-yellow oil. Column chromatography on silica (EtOAc as eluant) followed by crystallisation from benzene gave the alcohol (9) (1.20 g, 89%), m.p. 147–148 $^\circ\text{C}$; R_F 0.46 (EtOAc); δ (CDCl_3) 1.10–2.30 (8 H, m, $4 \times$ ring CH_2), 2.78 (1 H, dd, $J_{\text{A,B}} = 16$, $J_{\text{A,C}} = 10$ Hz

(CDCl₃) 1.06—2.74 (8 H, m, 4 × ring CH₂), 3.90 (1 H, br t, J_{HH} ca. 4 Hz, PhSCH), 4.65 (2 H, s, =CH₂), and 7.35 (5 H, s, PhS).

Also obtained was 1-(diphenylphosphinoylmethylene)-2-(phenylthio)cyclohexane (14) (134 mg, 46%), m.p. 108—111 °C (from EtOAc): R_f 0.38 (EtOAc); δ (CDCl₃) 1.50—2.20