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ALLYLIC PHOSPHINE OXIDES AS PRECURSORS OF DIENES OF DEFINED GEOMETRY: SYNTHESIS OF 3-DEOXYVITAMIN D_2

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The observation, that geometrically homogeneous allylic phosphonium bromides can be used in Wittig reactions to give conjugated dienes in which the original (Z)- or (E)-geometry is retained, was first made[1] during synthesis of dienes related to vitamin D. The method has since been used successfully in other fields[2], although its application may have been restricted by difficulties sometimes found[3] in preparing the required homogeneous phosphonium salts. We now report methods for the preparation of geometrically homogeneous allylic diphenylphosphine oxides, which we have used in Horner[4] reactions to provide an efficient and convenient synthesis of conjugated dienes of defined geometry.

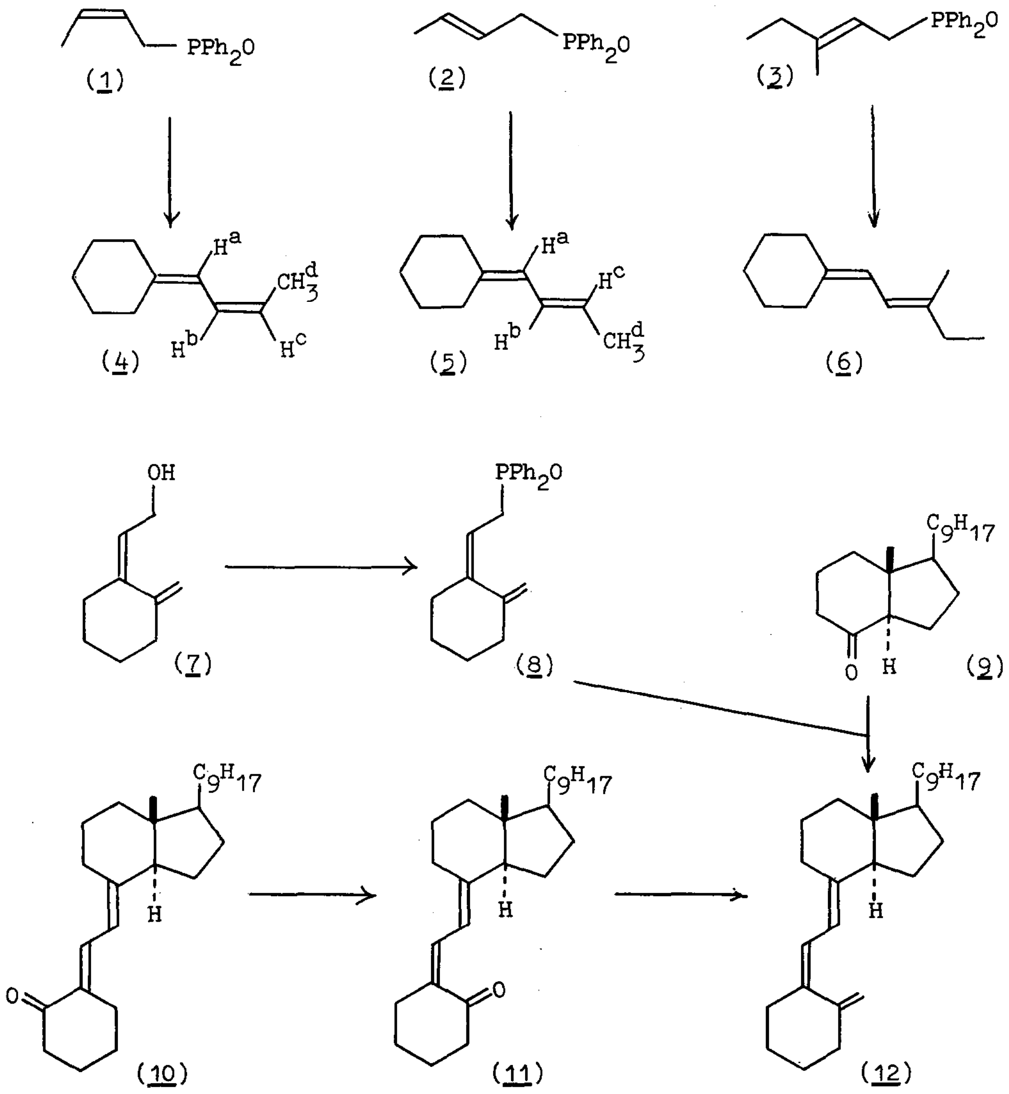
Our work concerns allyl derivatives unsubstituted at C_α, and with one or two substituents at C_γ. At the outset, only one allylic phosphine oxide had been used for diene synthesis[5]. We found that the ylids, generated using butyl-lithium, reacted at C_α; reaction at C_γ[6] was unimportant. It was not necessary to isolate, and later decompose[7], a hydroxy phosphine oxide; the initial adduct eliminated lithium diphenylphosphinate completely within 2 hr. at 25°. Thus cyclohexylidene-ethyl diphenylphosphine oxide and cyclohexanone gave dicyclohexylidene-ethane directly in 80% yield.

For preparing the phosphine oxides, the appropriate geometric form of the allylic alcohol was first converted into the 2,6-dichlorobenzoate[8] by reaction with the acid and dimethylformamide dineopentyl acetal[9]. Treatment (THF; -20°) with lithium diphenylphosphide, followed by oxidation with hydrogen peroxide, gave material from which pure phosphine oxide (yield >80%) was readily obtained[10]. Thus the (Z)-isomer (1), m.p. 112·5°, was obtained from (Z)-crotyl alcohol, uncontaminated by the (E)-isomer (2), m.p. 119°; and the pure (E)-isomer (3), m.p. 119°, was similarly obtained [from (E)-3-methylpent-2-enol], uncontaminated by its (Z)-isomer, m.p. 113°.

Geometry was best maintained when the ylids were generated, and treated with the carbonyl compound, at *ca*. -70° (THF); the mixture was then brought gradually to 25°. In this way, the (Z)-compound (1) and cyclohexanone gave (yield, 72%) the (Z)-diene (4) containing (g.l.c.) <3% of the (E)-diene (5), which was obtained in a similar state of purity from the (E)-phosphine oxide (2). The (Z)-diene (4) had $\lambda_{max.}^{EtOH}$ 241 nm (ε 27,700) (sh. at 234 and 249), whereas (5) had $\lambda_{max.}^{EtOH}$ 233, 240 (ε 32,000) (sh. at 247 nm); for n.m.r. data, see the Table. The (E)-diene (6) (>95% pure) was similarly obtained from the phosphine oxide (3).

Table. Isomeric Crotylidenecyclohexanes: N.m.r. Data ($CDCl_3$) obtained at 90 MHz with the aid of spin-decoupling experiments

Compound	H^a	H^b	H^c	H^d
(4)	τ 3·96, d; J_{ab} 12 Hz	τ 3·8 dd of q's; J_{ab} 12, J_{bc} 10, J_{bd} 1·5 Hz	τ 4·6 dq; J_{bc} 10, J_{cd} 7 Hz	τ 8·25 dd; J_{cd} 7, J_{bd} 1·5 Hz
(5)	τ 4·25, d; J_{ab} 10·5 Hz	τ 3·7 dd of q's; J_{ab} 10·5, J_{bc} 15, J_{bd} 1·5 Hz	τ 4·4 dq; J_{bc} 15, J_{cd} 6·5 Hz	τ 8·23 dd; J_{cd} 6·5, J_{bd} 1·5 Hz



The value of the new methods is further shown by their application to the (Z)-dienol (7)[11], which was so converted into the phosphine oxide (8), m.p. 98°. The corresponding ylid reacted with the ketone (9)[12] to give (yield 70%) 3-deoxy-vitamin D_2 (12), m.p. 41°, $\lambda_{max.}$ (EtOH with a little hexane) 263·5 nm (ε 17,600);

$\nu_{max.}^{film}$ 1645m, 1630m, 1605w, 892vs cm^{-1}; τ_{CDCl_3} 3·88, dd, *J* 11·5 (H-6 and -7); 4·79, m, $W_{1/2}$ 9·5 (H-22 and -23): 5·01, d, *J* 1·5 (H-19); 5·23, d, *J* 2·5 Hz (H-19) 9·42, s, (CH_3-18); $[\alpha]_D^{22}$ + 13·0° ($CHCl_3$)[13]. The deoxyvitamin was identified by comparison with material obtained by an earlier, photochemical, route[14]. Reaction of Heilbron's[15] C_{21} αβ-unsaturated aldehyde and cyclohexanone gave the (*E*)-dienone (10), m.p. 63-64°; its (*Z*)-isomer (11), obtained by irradiation[14], was converted into (12) by the Wittig method.

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