TRANSPOSITION OF ALLYLIC ALCOHOLS CONTROLLED BY THE Ph2PO GROUP:
## REAGENTS FOR α-HYDROXY-DIENE SYNTHESIS BY THE HORNER-WITTIG REACTION

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4-Hydroxy-2-alkenyldiphenylphosphine oxides, prepared by a phosphorus-controlled allylic rearrangement, give dianions and hence α-hydroxydienes (substituted penta-2,4-dienols) by the Horner-Wittig reaction.

Esters (2) from α-hydroxydienes (diene alcohols, substituted penta-2,4-dienols, e.g. 1) give Diels-Alder products (3) whose stereo- and regiochemistry is controlled by the intramolecular nature of the reaction.[1] We report a connective synthesis (scheme) of α-hydroxydienes from three fragments: an aldehyde or ketone, an enal, and an alkyl diphenylphosphine oxide, using the Horner-Wittig reaction in the last step.
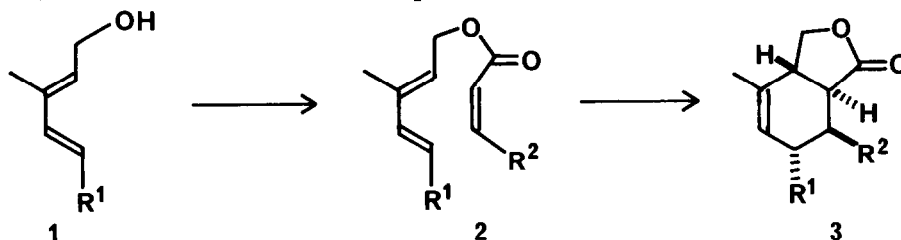

We have used allyl phosphine oxides[2] and dianions (4) of hydroxyalkyl phosphine oxides[3] in stereo-controlled syntheses of dienes and unsaturated alcohols by the Horner-Wittig reaction: dianions (5) of hydroxyallyl phosphine oxides were therefore good candidates for the synthesis of α-hydroxydienes (1) via adducts (6) with aldehydes or ketones. Addition[4] of phosphine oxide anions to α,β-unsaturated aldehydes and ketones gives adducts[5] (7) related to the required starting materials (9) by an allylic transposition.
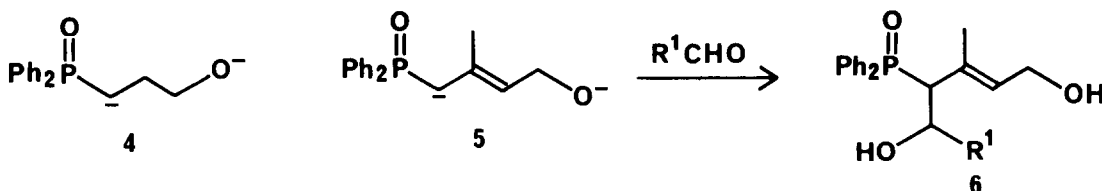

Unsymmetrically substituted allylic alcohols (12) can be transposed[6] to the isomer (15) with the more highly substituted double bond by acid catalysed rearrangement of the alcohol[6], via oxidation with an acidic reagent such as PCC,[7] or by acid-catalysed rearrangements of the esters (13).[8] The acid-

catalysed rearrangement of alcohol and ester are thought to have the allyl cation (14) as an intermediate.[9]

Scheme: Synthesis of α-hydroxydienes by the Horner-Wittig reaction
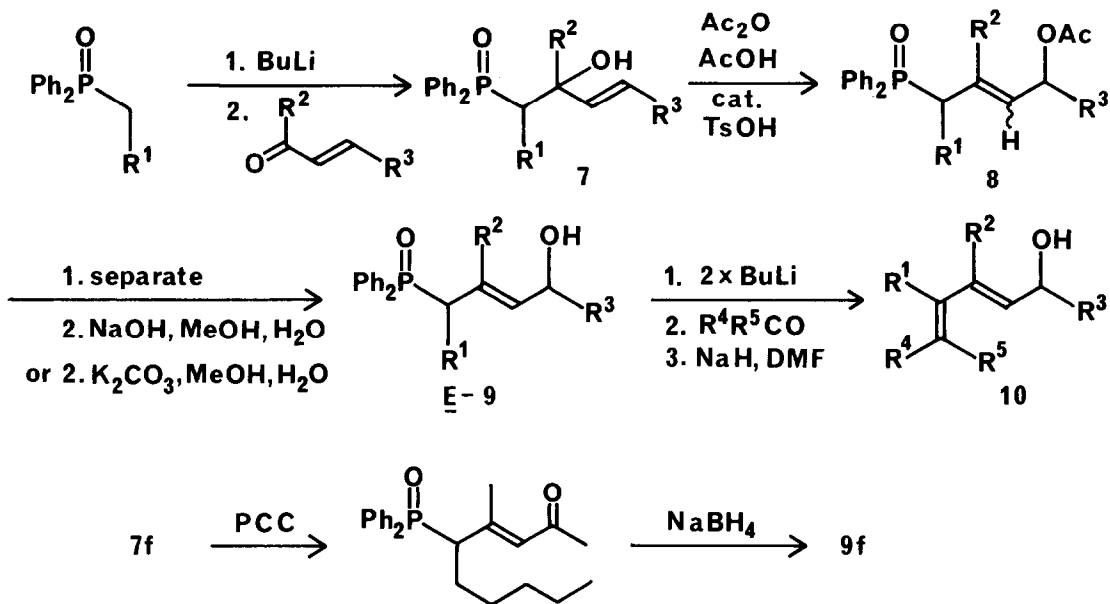
For the Ph_2PO-substituted allylic alcohols (7), direct rearrangement gave poor yields (7f, table), elimination being the main side-reaction. Oxidation with PCC gave a reasonable yield of the ketone (11) but our preferred method is the acid-catalysed rearrangement of the acetates[8] which gives consistently good yields of rearranged acetates (8), easily hydrolysed to the alcohols (9).
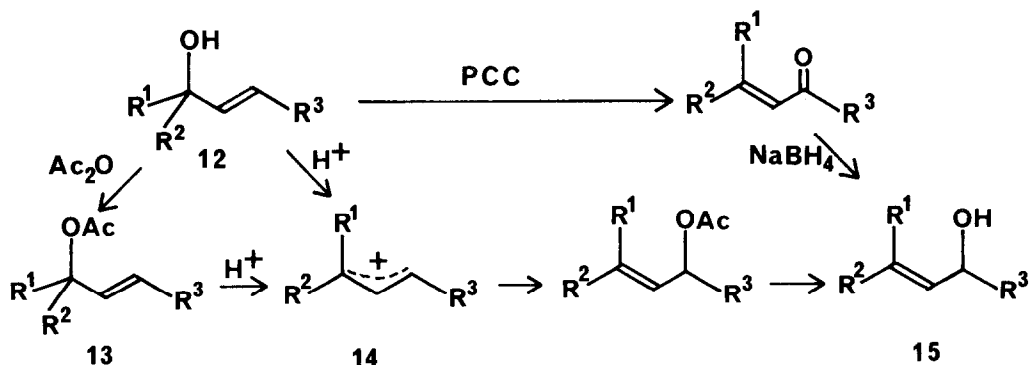
The tertiary alcohols (7, R^2=Me) rearranged readily under these conditions whether the product is the ester of a primary (8c) or a secondary (8d,f) alcohol. More remarkably, secondary alcohols (7, R^2=H) also rearranged completely to (8, R^2=H), directed only by the Ph_2PO group: we suppose this to be a steric rather than an electronic effect. The unsubstituted compound (7a) refused to rearrange under any conditions; presumably the allyl cation intermediate is too unstable.

Table: Allylic Rearrangement of Alcohols (7)

Compound	Yield (7)	R^1	R^2	R^3	Method	Yield (8)	Stereo (8)	Yield (9)
(7a)	85%	H	H	H	A,B	0%[a]	–	–
(7b)	88%	H	H	Me	A	83%	E only	86%
(7c)	80%	H	Me	H	A	90%	E:Z 1:1	76% E
								62% Z
(7d)	84%	H	Me	Me	A	95%	E:Z 1:1	90% E
								80% Z
(7e)	98%	n–C_5H_{11}	H	Me	A	98%	E only[b]	86% E
(7f)	65%	n–C_5H_{11}	Me	Me	A	77%	E only[b]	100% E
					B	16%	E	16% E
					C	60%[c]	E:Z 7:1[c]	–

Method A: Ac_2O, AcOH, cat. TsOH, $0^\circ C$, 15 min ($R^2 \neq H$)
    or room temperature, 24 h., (R^2=H).
Method B: HCl, H_2O, dioxan, room temperature, 15 mins.
Method C: PCC, CH_2Cl_2, room temperature, 3 h.

[a] Method A gave the unrearranged acetate.
[b] As a mixture of diastereoisomers (1:1 for 8e, 1:1.7 for 8f).
[c] Ketone (11)

The geometry of the double bond in the products (8) is determined by the number of substituents. With $R^1 \neq H$ only the E product is formed (8e,f). With $R^1 = R^2 = H$, again only the E product is formed (8b), but if R^1=H and R^2=Me, a 1:1 mixture of E and Z isomers is formed (8c,d). The geometrical isomers of the acetates (8) separate easily on silica chromatography. Diastereoisomeric mixtures result in all cases where R^1 and $R^3 \neq H$ whose composition does not reflect the diastereoisomeric composition of the starting alcohol (7), as expected for a mechanism involving an allyl cation[9]
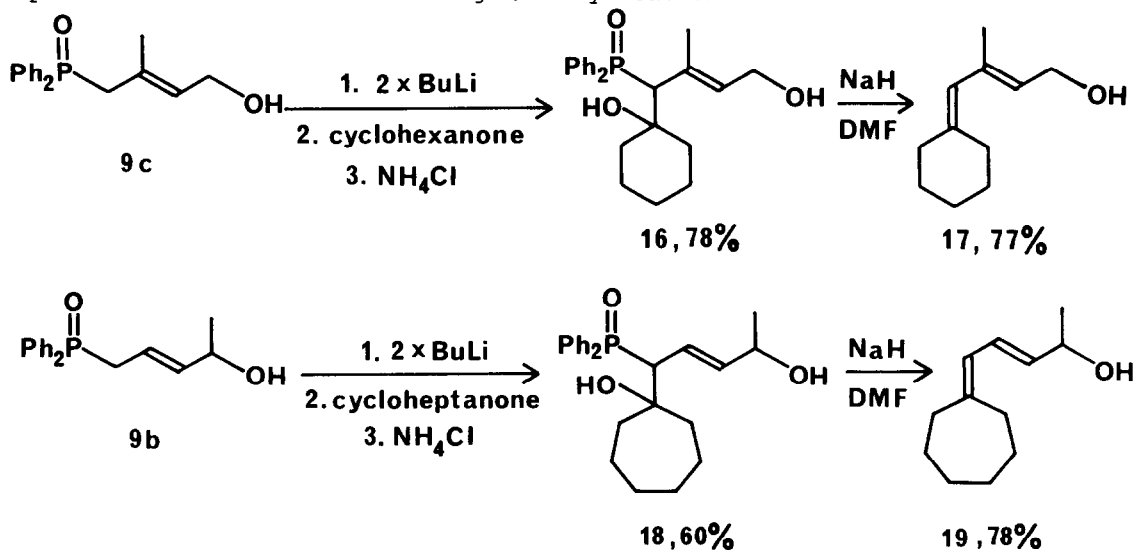
Dianions from the E alcohols (9) were formed on treatment with two equivalents of BuLi at −78°C. These combined with aldehydes or ketones to give diols (e.g. 16, 18), the latter as a mixture of diastereoisomers, but giving a single olefin (17, 19) on elimination. The geometry of the double bond in (9) is unchanged during these Horner–Wittig reactions. We had hoped to control the geometry of the second double bond in the diene alcohols by making the Horner–Wittig reaction stereoselective. However, addition of EtCHO to the dianion of (9c) gave a 1:1 (NMR) mixture of diastereoisomers (20, R=H) which could not be separated by chromatography, even by HPLC. The bis acetate (20, R=Ac) and the bis silyl ether (20, R=t-BuMe$_2$Si) were no better. The unsubstituted compound (9a, R^1=R^2=R^3=H) has been used in a one-step Horner–Wittig reaction giving low yields.[10] Dianions of Z alcohols (9c) and (9d) did not add to aldehydes or ketones, perhaps because of the basic cis oxyanion. Fortunately it is the E-diene alcohols e.g. (17) or (19) which are useful in Diels–Alder reactions.[1]
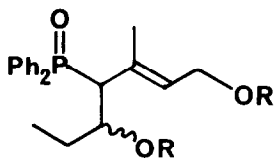
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