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STEREOSELECTIVE PERACID EPOXIDATION OF ALLYLIC AND δ-HYDROXYALLYLIC DIPHENYLPHOSPHINE OXIDES

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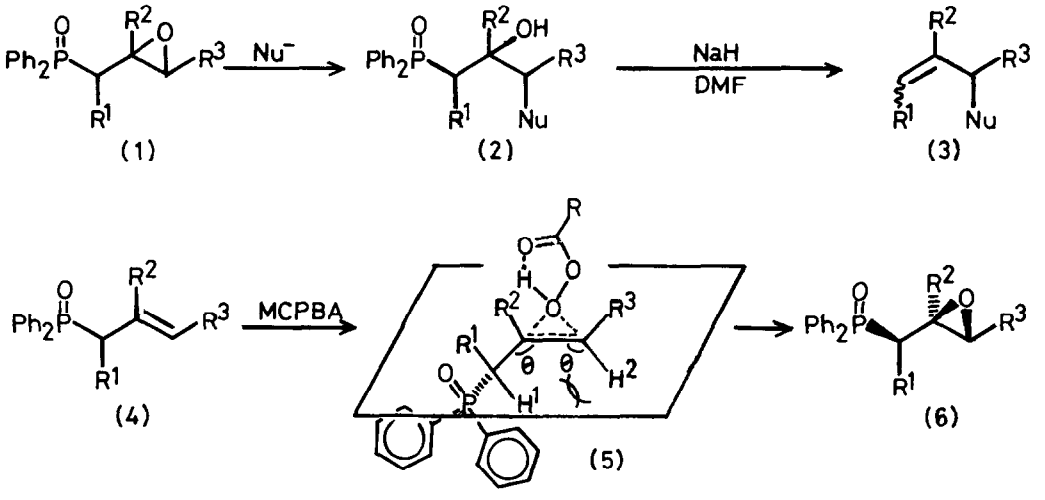
The title compounds were epoxidised by m-chloroperbenzoic acid with high stereoselectivity induced by the Ph_2PO or hydroxyl groups.

Epoxides of allylic diphenyl phosphine oxides (4) are potentially useful synthetic intermediates.[1] Nucleophilic opening[2] of the epoxides (1) produces β-hydroxyalkylphosphine oxides (2) and completion of the Horner-Wittig reaction could lead to a variety of allylically substituted compounds (3). Since both the S_N2 opening of the epoxide[2] and syn elimination[3] of $Ph_2PO_2^-$ are stereospecific, a single diastereoisomer of epoxide (1) should give a single isomer (E or Z) of the product (3). The usefulness of the sequence depends on the diastereoselectivity attainable in the epoxidation step. Both diastereo- and enantioselectivity of epoxidation have been studied[4] for other classes of compound.



Epoxidation of allylic phosphine oxides[5] (4) with m-chloroperbenzoic acid (MCPBA) gave the required epoxides (1) in good yield and with high stereoselectivity (table 1). This stereoselectivity must be controlled by the chiral centre α to phosphorus, and can be rationalised by a transition state[7] with minimised steric interactions such as (5). As epoxidation proceeds, the bond angles θ decrease (120° - 117°) so the preferred conformation places the

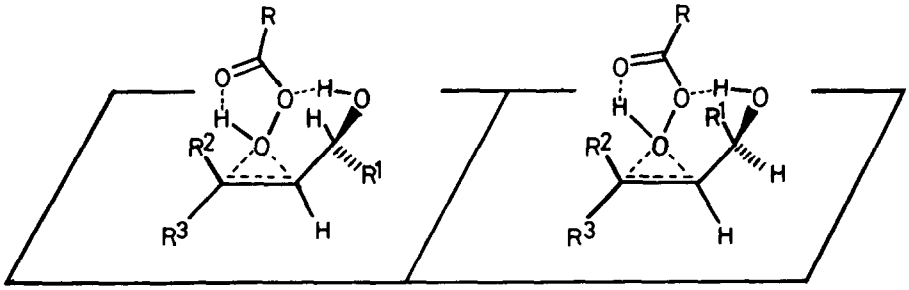
smallest group on the chiral centre (H^1 in 5) towards the approaching epoxide proton H^2 to minimise the $A^{1,3}$ steric strain.[8] With this constraint, the diastereoisomeric transition state (5) with the peracid remote from the bulky diphenylphosphinoyl (Ph_2PO) group favours the major isomer (6). This is supported by the reduced steroselectivity on epoxidation of (4c) where the increased $A^{1,2}$ strain (R^2=Et) competes with the $A^{1,3}$ interaction.

Table 1: Epoxidation of Allylic Phosphine Oxides (4) with MCPBA

Compound	R^1	R^2	R^3	Stereo-selectivity	Yield (%)	Major Product
(4a)	$n\text{-}C_5H_{11}$	Me	Me	10:1	71	(6a)[a]
(4b)	Me	Me	i-Pr	9:1	89	(6b)[b]
(4c)	Me	Et	Me	4:1	79[c]	(6c)
(4d)	n-Pr	H	Me	6:1	100	(6d)

a. Stereochemistry of (1a) determined by X-ray crystal structure.
b. Stereochemistry of (1b) determined by stereospecific conversion to a Z allyl sulphide (3b, Nu=PhS).
c. From $Ph_2PO.Et$ and Et_2CO without isolation of intermediate (4c).[1]

The importance of $A^{1,3}$ interactions in peracid epoxidations has been reported.[10,11] The allylic hydroxyl group coordinates to the incoming peracid, forcing an unfavourable $A^{1,3}$ interaction between R^1 and R^2 in the erythro transition state (7b) and favouring threo transition state (7a). If R^1=R^2=alkyl, this causes 95% stereoselectivity for the threo epoxide. If R^2=H, the reduced $A^{1,3}$ interaction gives only about 65% selectivity.



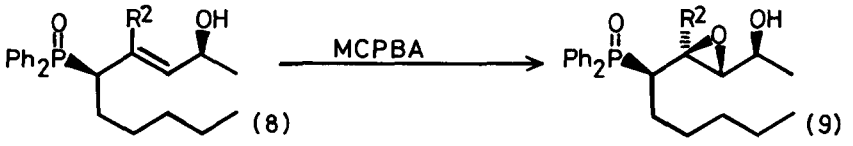
One group of Ph_2PO-substituted allylic alcohols is available by our allylic ester transposition.[12] These molecules have two chiral centres and single diastereoisomers (8) and (10) are available by the stereocontrolled version of the transposition[13] allowing us to assess the relative strength of the steric hindrance (Ph_2PO) and hydrogen bonding (OH) factors in the stereoselectivity of the epoxidation. Epoxidation by MCPBA gave epoxyalcohols (9) and (11) in good yield. The stereoselectivity (table 2) shows that the positive stereochemical control from the OH group completely overrides the negative hindrance by the Ph_2PO group. The stereoselectivity is excellent for R^2=Me, but not so good for

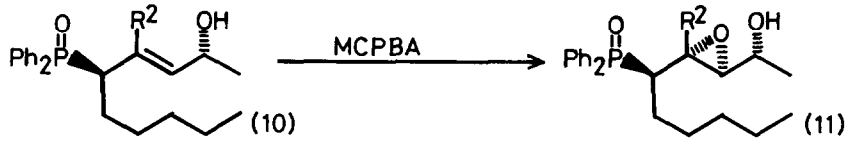
R^2=H. The stereoselectivity observed for (8b) and (10b) is much lower than that observed for the analogous compound (4d) lacking the OH group. These results can be rationalised by transition states (12a) and (12b): in (12a) the steric repulsion between the peracid and the Ph_2PO group is reduced by hydrogen bonding. Such secondary interactions have been reported only when an allylic alcohol is present.[14] Each diastereoisomer [(8a) and (10a)] gave a single diastereoisomer [(9a) and (11a)] of the epoxide with high stereoselectivity and the same is true for the diastereoisomers (8b) and (10b), though the stereoselectivity is lower. The threo transition state (12a) is favoured.

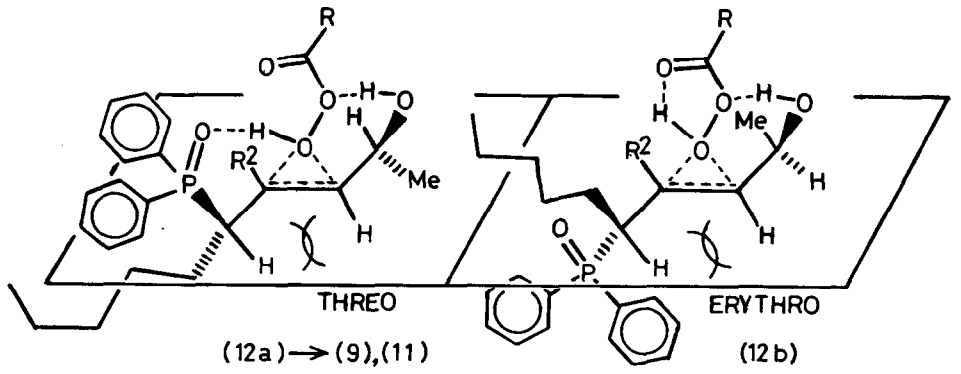
Table 2: Epoxidation of δ-hydroxyallylic phosphine oxides

Starting Material	R^2	Yield (%)	Stereo-selectivity	Major product
(8a)	Me	71[a]	10:1	(9a)[b]
(10a)	Me	87	13:1	(11a)
(8b)	H	95	1.3:1	(9b)[b]
(10b)	H	95	2.7:1	(11b)

a. Yield of major isomer. Other yields are combined yields.
b. Stereochemistry of product established by X-ray crystal structure.[9]







Attempted epoxidations of allylic alcohol (8b) with vanadium (II) catalysis [$VO(AcAc)_2$, t-BuOOH][15] gave only the corresponding enone and recovered starting material.

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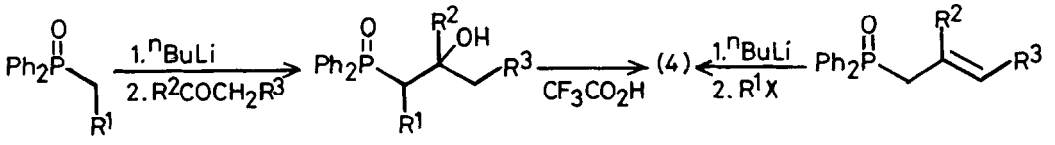

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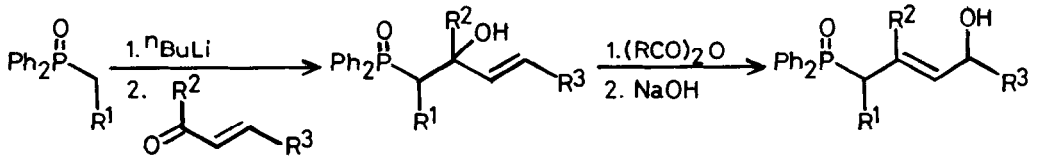

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