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SYNTHESIS OF SINGLE ISOMERS (E OR Z) OF UNSATURATED ALCOHOLS BY THE HORNER-WITTIG REACTION

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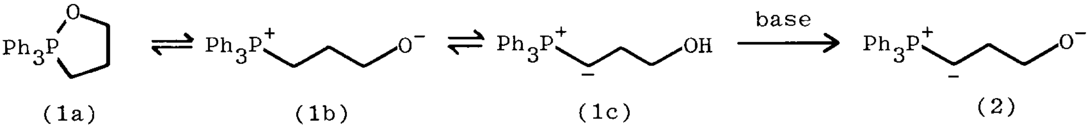
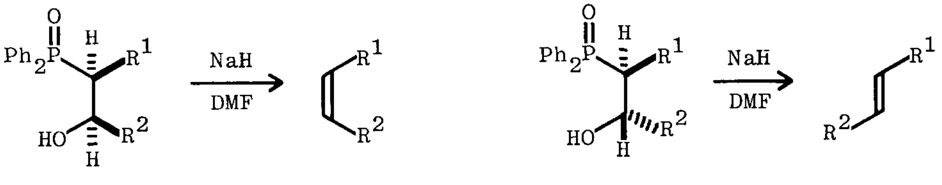
Single isomers (E or Z) of homoallylic and higher alcohols can be synthesised from ω-hydroxyalkyldiphenylphosphine oxides and aldehydes, or from alkyldiphenylphosphine oxides and lactones

Homoallylic alcohols may be made by the Wittig reaction from compound (1), one of whose tautomers (1c) is an ylid, with virtually no control over the geometry of the double bond,[1] though silyl ethers of such ylids give Z-selective, and anions (2) give E-selective olefination.[2] Longer chain alcohols have been made from protected hydroxyalkyl ylids[3] or anions[4] homologous to (2).



Our version[5,6,7] of the Horner-Wittig reaction allows the synthesis of single geometrical isomers of alkenes by stereospecific elimination of $Ph_2PO_2^-$ from pure erythro (3a) or threo (3b) intermediates each synthesised by a different stereoselective route. We now report the effects of hydroxyl, protected hydroxyl, and oxy-anion substituents on the stereoselectivity of these reactions and the synthesis of single geometrical isomers of homoallylic and higher unsaturated alcohols.[8]



(3a) (3b)

The acylation of a phosphine oxide anion by a lactone,[9] the reduction of the hydroxyketone (4), and elimination of $Ph_2PO_2^-$ from the pure threo alcohols (5) is the simplest and most reliable route to E-isomers of unsaturated alcohols (6) (table 1). Stereoselectivity increases with n in the series (5a-c) in agreement with Felkin's model for the stereoselectivity.[7]

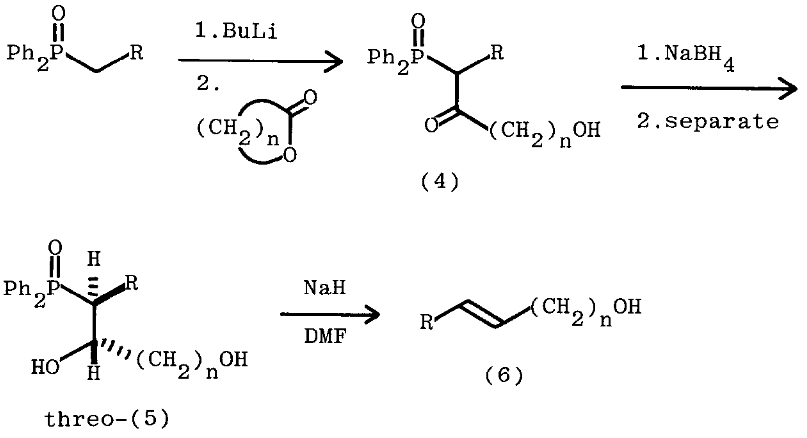
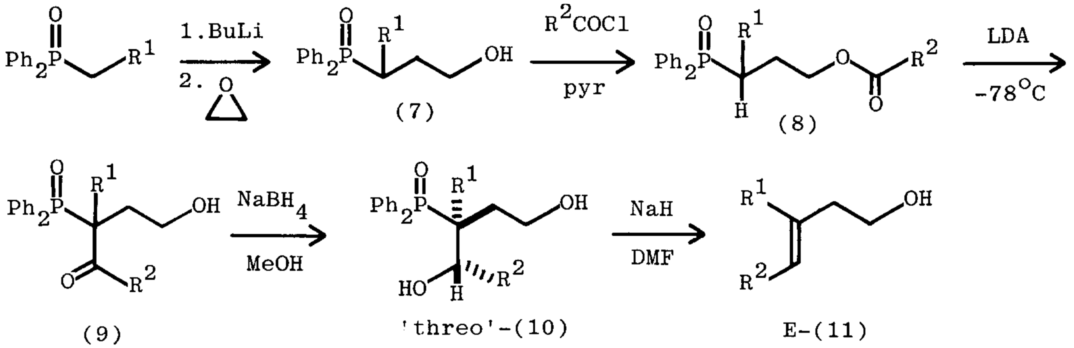


Table 1: E-Alcohols (6) by the Lactone Route

Entry	R	n	Yield (4)	Yield Threo(5)	Threo: Erythro	Yield E-(6)
1	n-C_5H_{11}	3	79%	(5a) 43%	1:1	-
2	n-C_4H_9	4	87%	(5b) 68%	3:1	96%[a]
3	Et	5	81%	(5c) 85%	6:1	98%[b]

a. The product is a pheromone of the peach twig borer moth. The threo alcohol was isolated by crystallisation: chromatography of the mother liquor gave 14% of the erythro alcohol and after elimination, 98% of Z-dec-5-en-1-ol, whose acetate is a pheromone of the male turnip moth.

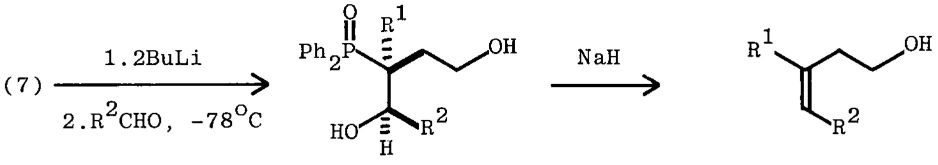
b. The product is a pheromone of the Mediterranean fruit fly.



E-Homoallylic alcohols are better[10] constructed with the hydroxyl group already on the phosphine oxide (7). Esters (8) form carbanions with i-Pr_2NLi (LDA) which rearrange by O to C acyl transfer to give hydroxy-ketones (9) as mixtures of diastereoisomeric hemiketals. Reduction stereoselectively gives threo (10) and hence E-alcohols (11). As expected[5] the stereoselectivity of reduction is decreased when the product (11b) is a trisubstituted alkene.

Table 2: E-Homoallylic Alcohols by Acyl Transfer

Starting Alcohol	R^1	R^2	Yield (8)	Yield (9)	Yield threo-(10)	threo: erythro	Yield E-(11)
(7a)	H	Ph	92%	96%	92%	19:1	82%
(7b)	Me	Ph	85%	92%	76%	4:1	80%
(7c)	H	Me	93%	83%	66%	3:1	-



erythro-(10)

(10a) R^1=H, R^2=Ph, 69%

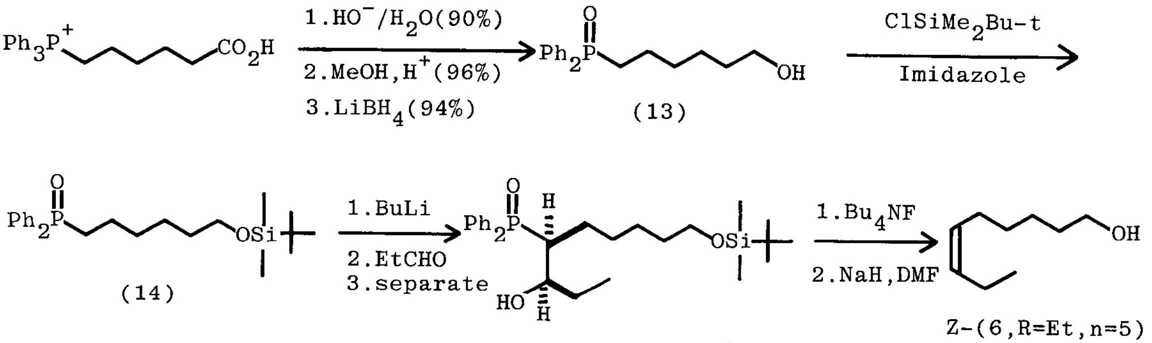
(10b) R^1=Me, R^2=Ph, 60%

Z-(11)

Z-(11a), 95%

Z-(11b), 95%

Pure Z-alcohols were made from the minor isomers of all these adducts but overall yields were necessarily low. Z-Homoallylic alcohols are made in good yield from the dianions of alcohols (7) and aldehydes. Stereoselectivity is low (3:1 for 10a and 2:1 for 10b) but still favours erythro-(10)[11]: pure Z-homoallylic alcohols Z-(11a) and Z-(11b) were obtained by elimination. The alternative route to non-6-en-1-ol (cf entry 3, table 1) requires hydroxyalkyl phosphine oxide (13). The dianion of (13) added to EtCHO but the diastereoisomers of the adduct could not be separated. The silyl ether (14) added with poor selectivity (1.8:1) but the diastereoisomers of (15) could be separated: removal of the silyl group from erythro-(15a) and elimination gave pure Z-alcohol in 94% yield.



(13)

(14)

Z-(6,R=Et,n=5)

erythro(15a),55%
(+threo(15b),30%)

Table 3: Stereoselectivity in the Horner-Wittig Reaction with Functionalised Phosphine Oxides

Entry	R^1	Substituent -X or =Y	Position	R^2	Yield Adducts (3)	*erythro* :*threo* (3a):(3b)	*Z*-Alkene from *erythro*	*E*-Alkene from *threo*
1[a]	CH_2CH_3	-	-	Ph	86%	5.7:1	79%	89%
2[b]	OMe	OMe	C-1	An*	85%	1.2:1	70%	88%
3[c]	CH_2X	$N(CH_2)_5$	C-2	Ph	80%	1.1:1	72%	86%
4	$(CH_2)_2X$	OLi	C-3	Ph	69%	3.0:1	82%	82%
5[d]	$(CH_2)_3CYMe$	OCH_2CH_2O	C-4	Ph	72%	3.8:1	90%	83%
6[e]	$(CH_2)_4CYMe$	OCH_2CH_2O	C-5	Et	71%	1.5:1	-	-
7	$(CH_2)_6X$	$OSiMe_2Bu$-t	C-6	Et	85%	1.8:1	94%[f]	92%[f]

* An=*p*-$MeOC_6H_4$
a. ref. 6
b. C. Earnshaw, C.J. Wallis, and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1979, 3099.
c. D. J. Cavalla and S. Warren, *Tetrahedron Lett.*, 1982, 23, 4505.
d. C. A. Cornish and S. Warren, *Tetrahedron Lett.*, 1983, **24**, 2603.
e. C. A. Cornish and S. Warren, *unpublished observations*.
f. Deprotected with n-Bu_4NF in THF before elimination.

Stereoselectivity in all these cases is well below that observed for the unsubstituted compounds [all straight chain alkyldiphenylphosphine oxides add to benzaldehyde with 5-6:1 selectivity in favour of *erythro*(3a)[6]]. Other functionalised phosphine oxides (table 3) show a similarly decreased selectivity. These effects cannot be explained simply by steric effects and we suggest some coordination to lithium in the transition state.[6]

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References

1. A. R. Hands and A. J. H. Mercer, *J. Chem. Soc. (C)*, 1968, 1099; 2448.
2. W. G. Salmond, M. A. Barta, and J. L. Havens, *J. Org. Chem.*, 1978, **43**, 790.
3. H. H. Inhoffen, K. Brückner, and H-J. Hess, *Chem. Ber.*, 1955, **88**, 1850.
4. I. T. Harrison and B. Lythgoe, *J. Chem. Soc.*. 1958, 843; A. G. Martinez and M. O. Ruiz, *Synthesis*, 1983, 663.
5. A. D. Buss and S. Warren, *J. Chem. Soc., Chem. Commun.*, 1981, 100; *Tetrahedron Lett.*, 1983, **24**, 111.
6. A. D. Buss and S. Warren, *Tetrahedron Lett.*, 1983, **24**, 3931.
7. A. D. Buss, R. Mason, and S. Warren, *Tetrahedron Lett.*, 1983, **24**, 0000.
8. *E*-Isomers of allylic alcohols may be made from allyldiphenylphosphine oxides; R. R. Arndt and S. Warren *Tetrahedron Lett.*, 1978, 4089.
9. R. S. Torr and S. Warren, *J. Chem. Soc. Pak.*, 1979, 1, 15; *J. Chem. Soc., Perkin Trans. 1*, 1983, 1173.
10. A β-lactone would be required to make (5, n=2).
11. In contrast to the dianions of 2-amidoalkylphosphine oxides which give *threo*-selective addition to benzaldehyde, D. J. Cavalla and S. Warren, *Tetrahedron Lett.*, 1983, **24**, 295.

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