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SYNTHESIS OF E-HOMOALLYLIC ALCOHOLS, γ-HYDROXYKETONES, AND CYCLOPROPYL KETONES FROM 3-DIPHENYLPHOSPHINOYL (Ph_2PO) PROPANOLS BY ACYL TRANSFER

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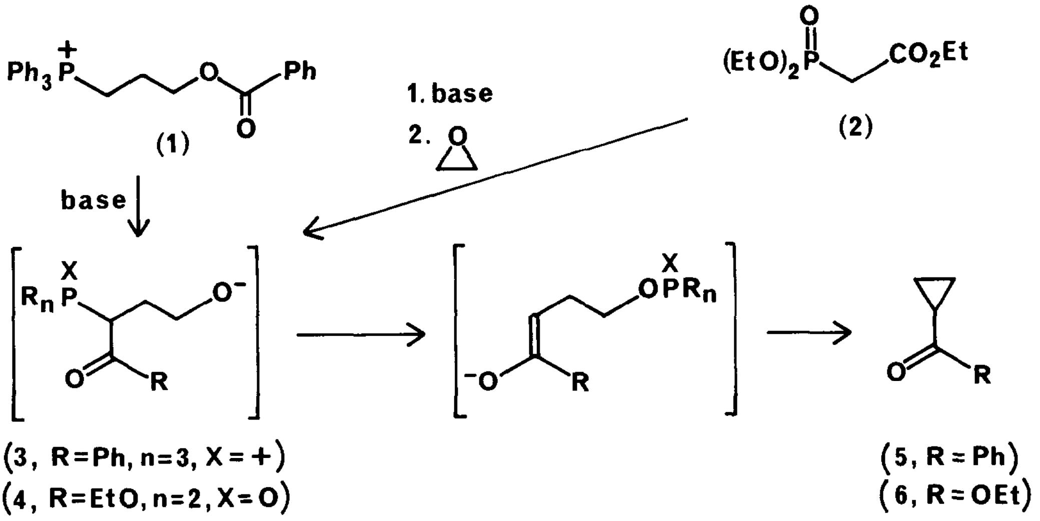
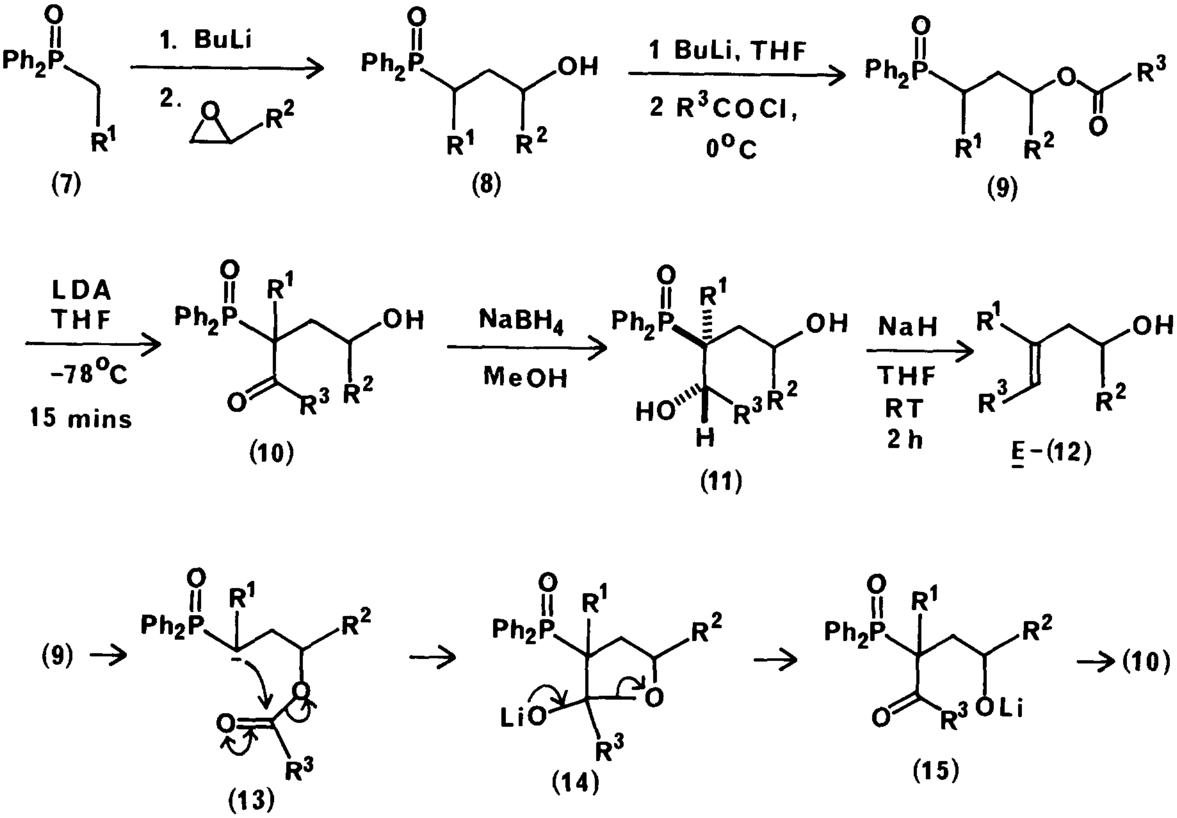
Carboxyl transfer (O→C) on 3-Ph_2PO propyl esters (9) gives an intermediate (10) from which the Ph_2PO group may be removed by the Horner-Wittig reaction or by Ph_2PO transfer (C→O) to give the title compounds.

Acyl transfer occurs in two established routes to cyclopropyl carbonyl compounds (5,6). The ylid from (1) undergoes[1] O→C benzoyl transfer to give (3). Both (3) and the phosphonate analogue[2] (4) prefer C→O phosphorus transfer to the alternative acyl (RCO) transfer and cyclopropane rings are formed. Each sequence [(1) to (5) and (2) to (6)] occurs as an uninterrupted homologous Wittig reaction. We report that the individual steps occur separately when phosphine oxides[3] are used with the advantage that three series of products may be prepared from the same intermediate under different conditions.



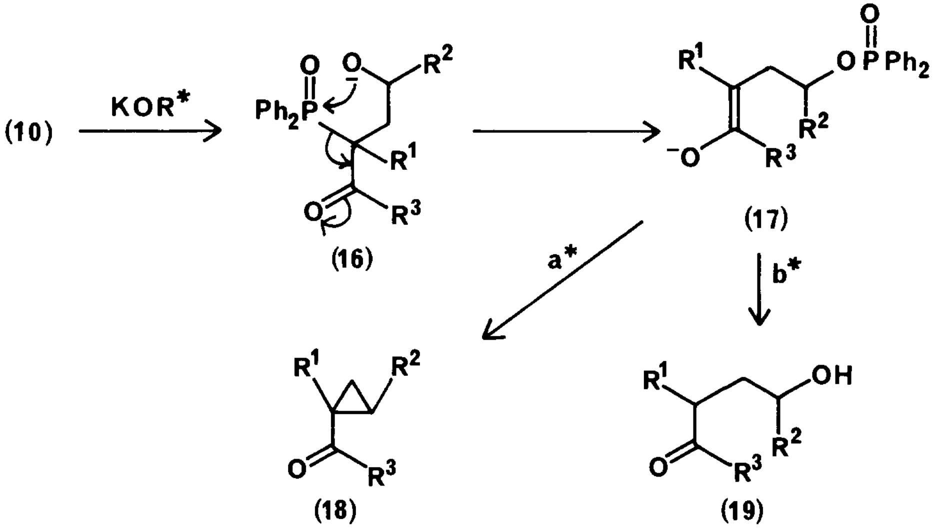
The starting materials (8) can be prepared by a variety of methods[4] including epoxide addition to alkyl phosphine oxides (7), and O-acylated to give the carboxylate esters (9). Acyl transfer [C→O *via* a five-membered cyclic intermediate (14)] was initiated by LDA and gave good yields of the hydroxyketones (10) (Table) whether the transferred group (R^3CO) or the product, e.g. (15, R^1=H), was enolisable or not. The OLi bond in (14) or (15) evidently prevents further reaction, as it does in the Ph_2PO version of the Horner-Wittig reaction.[5]

Scheme 1



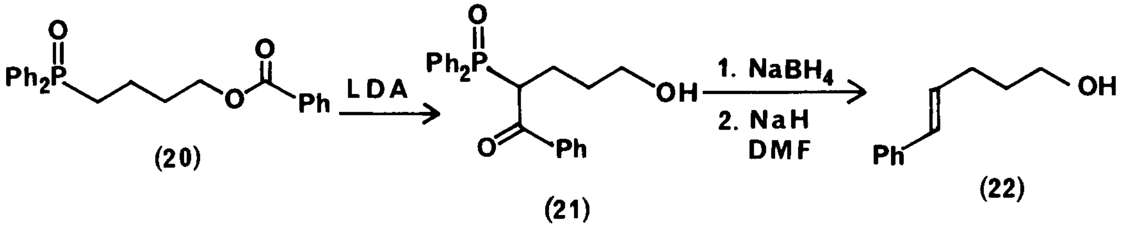
Threo-selective reduction and treatment of the diol (11) with a sodium base (NaH) completed the Horner-Wittig reaction to give[6] the *E*-homoallylic alcohols (12). When the same hydroxy ketone (10) was treated with a potassium base, the homologous Horner-Wittig reaction occurred by C→O Ph_2PO transfer to give the enolate (17) which eliminated $Ph_2PO_2^-$ to give the cyclopropyl ketones (18) (table). In water with a more nucleophilic base (KOH), the enolate was protonated and the phosphinate ester hydrolysed to free the γ-hydroxy ketone (19) with some cyclisation to (18) as a side reaction.

Scheme 2



*Conditions (a) (t-BuOK, t-BuOH, 30 °C, 2h) or (b) (KOH, H_2O, EtOH, 60 °C, 2h) were chosen to give products (18) or (19) as required.

The homologue (20) also undergoes the O→C acyl transfer <u>via</u> a six-membered cyclic intermediate and can be used to make the <u>E</u>-unsaturated alcohol (22). The C→O Ph_2PO transfer could not be induced on (21): vigorous conditions led to deacylation.

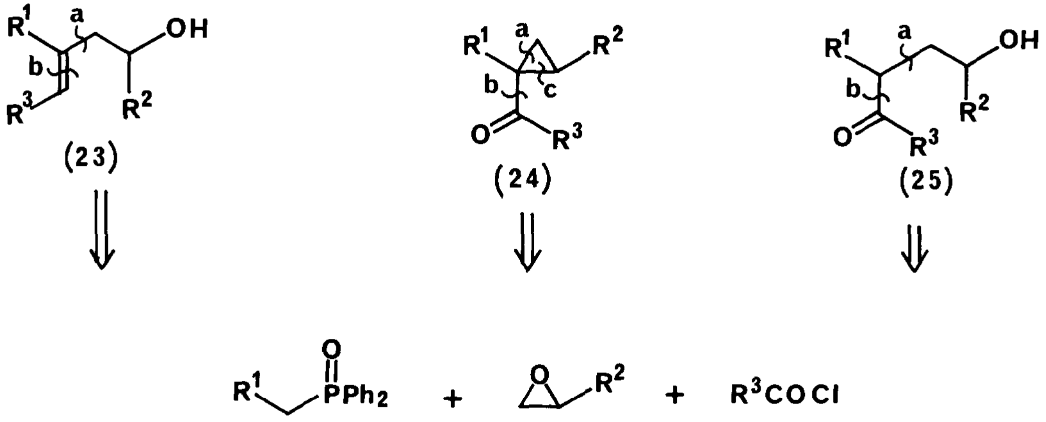


TABLE

Starting Material				Products						
	R^1	R^2	R^3	(9)	(10)	(11)[a]	<u>threo</u>:<u>erythro</u>	(12)	(18)	(19)
(8a)	H	H	Me	93%	83%	66%	75:25	85%	95%	65%
(8b)	H	H	Et	93%	73%	[95%][b]	75:25	-	100%[c]	60%
(8c)	H	H	Ph	92%	96%	92%	95:5	82%	100%	69%
(8d)	Me	H	Ph	85%	82%	76%	76:24	90%	77%	-
(8e)	H	Me	n-C_6H_{13}	90%	80%	[90%][b]	-	-	91%	65%
(8f)	H	Ph	△	80%	73%	-	-	-	99%[d]	-

a. Yield of pure <u>threo</u>-(11)
b. Yield of mixed isomers which were not separated
c. Isolated as 2,4-dinitrophenylhydrazone
d. Trans by N.M.R.

The Ph_2PO group is used to make at least two new C-C bonds in these syntheses, corresponding to disconnections (a) and (b) in (23)-(25). The strategy of disconnection (b) is to transform an easily made C-O bond into a C-C bond by rearrangement and these reactions belong to a family which includes the Fries[7] and Claisen[8] rearrangements and the base-catalysed rearrangement of esters of o-hydroxyacetophenones.[9]



(23) (24) (25)

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