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THE WITTIG-HORNER ROUTE TO TRI-SUBSTITUTED ALKENES : SYNTHESIS OF Z-α-BISABOLENE

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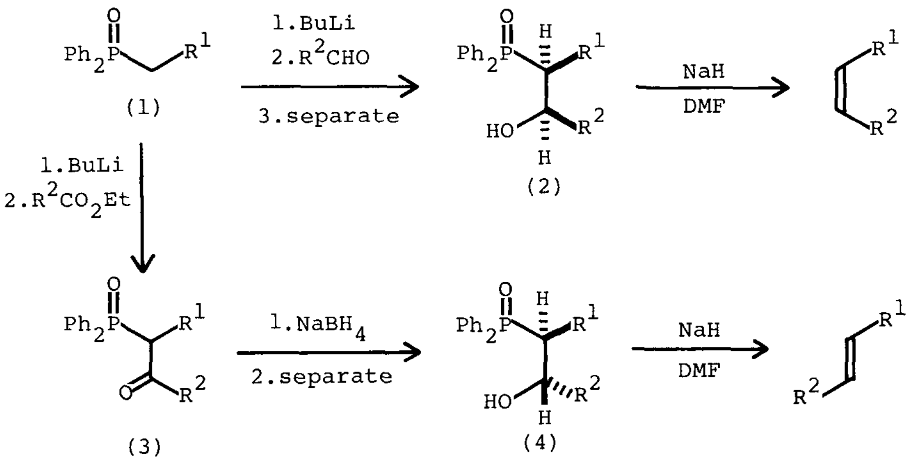
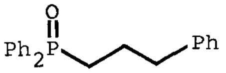
E and Z isomers of trisubstituted alkenes may separately be prepared by the Wittig-Horner reaction. Z-α-bisabolene has been made by this route.

Single geometrical isomers of disubstituted alkenes may be made stereoselectively by the Wittig-Horner reaction.[1] Direct addition of aldehydes to the anions of primary alkyl phosphine oxides (1) gives *erythro* alcohols (2) whilst reduction of ketones (3) gives *threo* alcohols (4) with high stereoselectivity in both cases. Chromatography and crystallisation give pure samples of (2) and (4) which eliminate $Ph_2PO_2^-$ stereospecifically on treatment with base to give *Z* and *E* alkenes respectively. We now report that this method may be extended to the synthesis of trisubstituted alkenes. The separation of diastereoisomers and the stereospecific elimination are unimpaired though the extra substituent generally lowers the stereoselectivity of the earlier steps.



The extra substituent may be added by alkylation[2] of a primary alkyl phosphine oxide. Methylation[3] of (5) gives (6) which adds to acetaldehyde to give a nearly 1:1 mixture of (7a) (38%) and (7b) (43%) in good yield. Separation by flash chromatography[4] and elimination gave *Z*-(9) and *E*-(9) whose structures were assigned by n.O.e. experiments. Acylation of secondary alkyl phosphine oxides with esters[5] gives poor yields, but acetyl chloride reacted cleanly with the copper derivative of (6) to give ketone (8). Reduction of (8) gave a 1:2 mixture of (7a) and (7b) in 98% yield.



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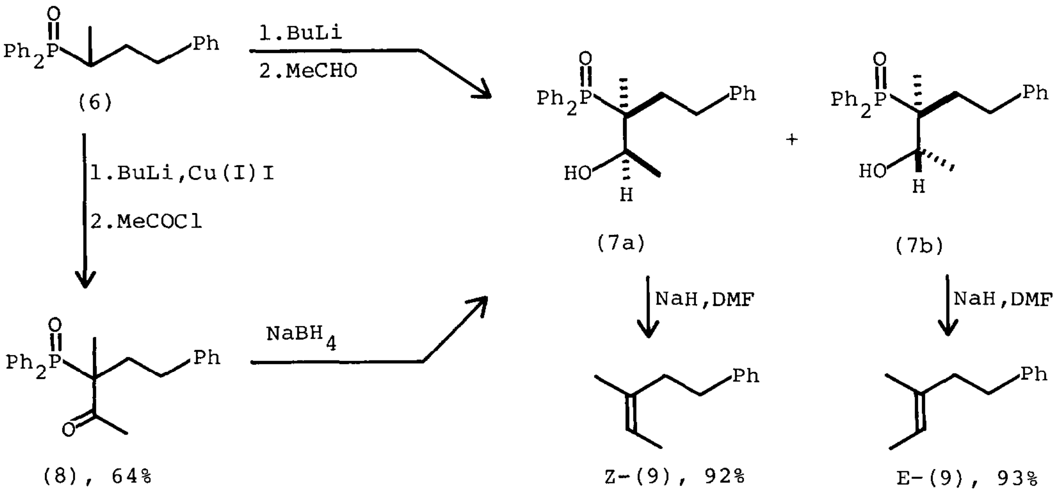
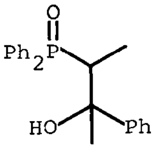


The alternative approach puts the extra substituent on the other carbon atom as in adducts of primary alkyl phosphine oxides with ketones. With some compounds this arrangement led to difficulties. Adducts of aromatic ketones, e.g. (10), reverted to starting materials on treatment with base. The diastereoisomers of (11) were separated but each gave the same alkene. Adduct (12), which gives (9) on elimination, could not be separated into diastereoisomers. Adducts of benzyl phopshine oxides,e.g. (13), decomposed to alkenes under the condition of their formation, even at - 50°C, so that mixed alkenes were inevitably formed.



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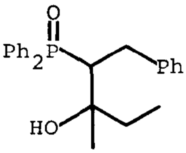

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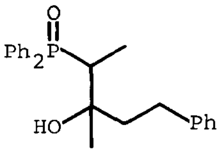

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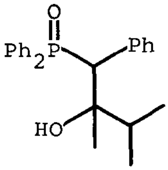

(13)

This alternative approach was, however, successful in a synthesis of *Z*-α-bisabolene (18), the perfumery compound[6] from oil of *Opopanax*. The starting materials were both made from isoprene; the phosphine oxide (16) *via* prenyl bromide[7] (14), and ketone (15) by a Lewis-acid catalysed Diels-Alder reaction.[8] The anion of (16) added to (15) to give a 53% yield of mixed '*erythro*' adducts (17), easily separated from 4% of mixed '*threo*' adducts. The chromatography is dominated, as expected, by the chiral centres bearing polar groups. Elimination of $Ph_2PO_2^-$ from (17) gave *Z*-α-bisabolene (18) uncontaminated by the *E* isomer. The only impurity detectable by chromatography was a trace of ketone (15). The stereochemistry of (18) and of the *E* isomer, made from the *threo* isomers of (17), was confirmed by 400 MHz proton NMR.[6] The Wittig reaction between (15) and the phosphonium salt corresponding to (16) gives 25% of a 93:7 mixture of *Z* and *E*-α-bisabolenes.[6]

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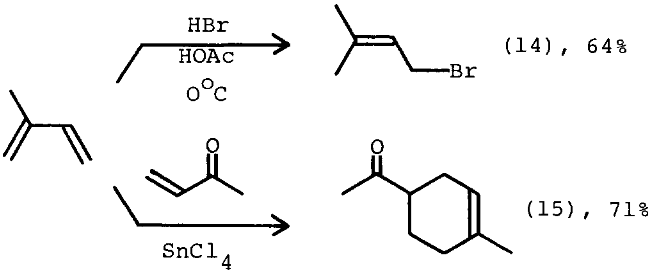

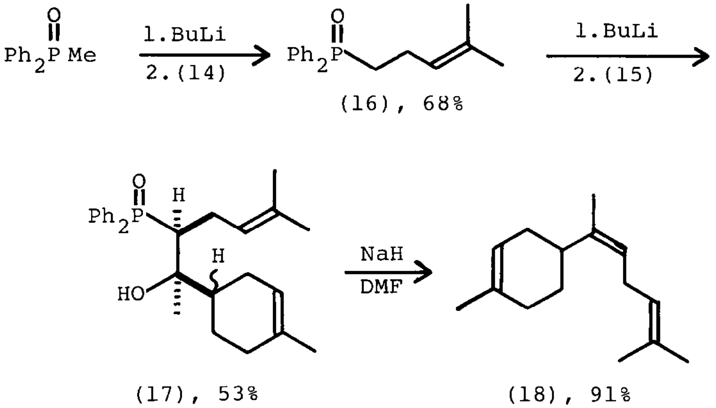

References and Notes

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3. TMEDA is normally added during these alkylations.[2] In this case it causes dimethylation and a better yield of (6) is obtained in the absence of TMEDA.
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