Synthesis of (±)-Hotrienol and (±)-Santolina Alcohol *via* Cyclopropenes

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A short synthesis of the title monoterpenols *via* cyclopropylcarbinyl–homoallyl rearrangement of adducts which are themselves produced by tandem addition of vinylmagnesium bromide and an appropriate carbonyl compound to the cyclopropenes (**1**) is described.

It was recently shown[1] that vinylmagnesium halides add to cyclopropenes to give vinylcyclopropyl Grignard reagents. Such Grignard reagents are ideal building blocks for preparing vinylcyclopropyl methanols which by acid catalysis can undergo the well known cyclopropylcarbinyl–homoallyl rearrangement.[2] With appropriately substituted alcohols this rearrangement has great potential for the construction of different types of isoprenoids. The synthetic value of this approach is illustrated here by the simple preparation of two racemic monoterpenols, namely hotrienol (**5**) of the linear head-to-tail type, and the terpene santolina alcohol (**6**) (Scheme 1). The smooth and high yield rearrangement of the tertiary alcohol (**4**) into santolina alcohol (**6**) is noteworthy since earlier approaches[3] have given complex mixtures and one synthesis of (**6**) is described without details.[4]

The Grignard reagent (**2a**) obtained from 0.1 mol of methylcyclopropene (**1a**) and 0.12 mol of vinylmagnesium bromide in tetrahydrofuran (THF) solution at −10 °C for 30 min and then at 45 °C for 1 h was treated (0 °C; 1 h) with 2-methylpropenal (0.12 mol) to give an 8 : 1 diastereomeric mixture (detected by g.l.c.) of the secondary alcohols (**3**) in 38% yield. The predominant isomer was isolated by column chromatography on neutral alumina (gradient elution from hexane to hexane–ether, 85 : 15 v/v) as a colourless liquid:† b.p. 64 °C at 2 Torr; n_D^{20} 1·4804; δ (CCl_4) 0.6—1.0 (m, 3H, cyclopropyl), 1.15 (s, 3H, cyclopropyl methyl), 1.70 (br s, 3H, MeC=C), 3.55 (br d, *J* 8 Hz, 1H, *H*C–OH), 4.6—5.1 (m, 4H, H_2C=C), and 5.66 (dd, *J* 18 and 10 Hz, 1H, *H*C=CH_2).

Similarly, starting from 0.1 mol of vinylmagnesium bromide, 65 mmol of dimethylcyclopropene (**1b**), and 0.1 mol of acetone the tertiary alcohol (**4**) was prepared in *ca.* 20% yield as a colourless liquid:† b.p. 63 °C at 12 Torr; n_D^{20} 1.4571; δ (CCl_4) 0.5—0.9 (m, 2H, cyclopropyl), 1.07 and 1.29 (s, 6H, cyclopropyl methyl), 1.25 (s, 6H, Me_2C–O), 4.7—5.2 (m, 2H, H_2C=C), and 5.7—6.4 (m, 1H, *H*C=CH_2).

The stereochemistry shown in (**2**)—(**4**) was assigned taking into account the well established *cis*-addition of organomagnesium compounds to cyclopropenes[1,5,6] and the fact that retention of configuration of the cyclopropyl C–Mg bond is maintained in electrophilic reactions.[7] The regiospecificity of the reaction observed in the case of methylcyclopropene (**1a**) is in accordance with the previous data on similar tandem additions to the olefin (**1a**).[5] It also follows from the isomerization of (**3**) into the trienol (**5**).‡ The reaction proceeds smoothly in THF solution in the presence of a catalytic amount of 30% $HClO_4$ at 25 °C for *ca.* 1 h (g.l.c. monitoring). (±)-Hotrienol (**5**) thus obtained in *ca.* 70% yield had b.p. 62 °C at 2 Torr; n_D^{20} 1.4915. The spectral properties found for (**5**) correspond to

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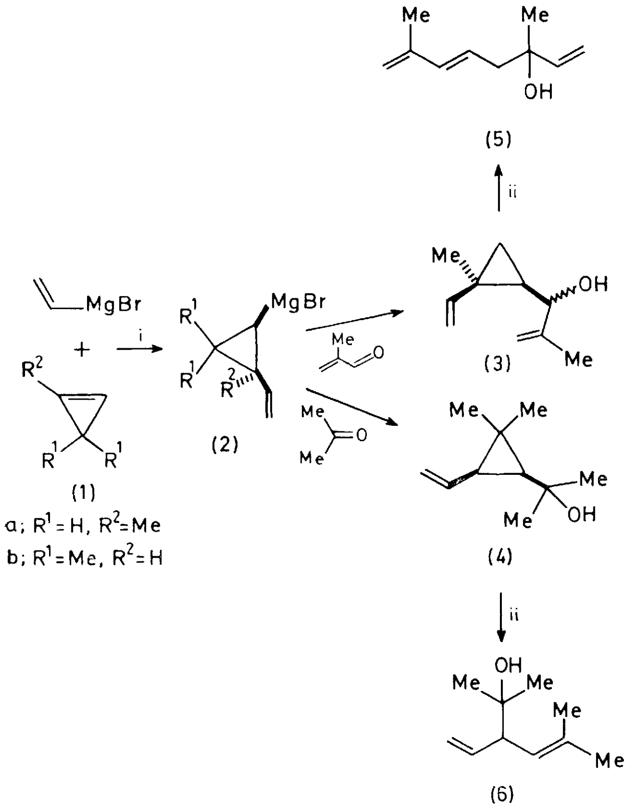
† Satisfactory elemental analysis data were obtained for this compound.

‡ Didehydro-geraniol and -nerol (*ca.* 1 : 1 mixture) were identified as minor products in this reaction.



Scheme 1. Reagents and conditions: i, THF, —10 then +45 °C; ii, 30% $HClO_4$, THF, 25 °C.

those described for the natural product[8] and for synthetic[9] hotrienol.

Similarly, the acid-catalysed rearrangement of the tertiary alcohol (**4**) gave (±)-santolina alcohol (**6**) in 87% yield, b.p. 70 °C at 10 Torr; n_D^{20} 1.4612. Its i.r., ^1H n.m.r., and mass spectral data matched those reported[10] for the alcohol found in the essential oil of *Ormenis multicaulis*.

Thus, the tandem addition of a Grignard reagent and the appropriate carbonyl compound to the cyclopropene C=C bond followed by homoallylic rearrangement of the cyclopropyl alcohols formed opens up a simple route to some functionalized terpenols.

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