

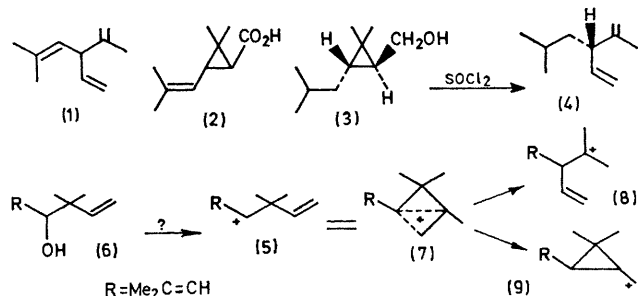
Rearrangement of the Artemisia Skeleton to the Santolina Skeleton: a 1,2-Shift of the Vinyl Group

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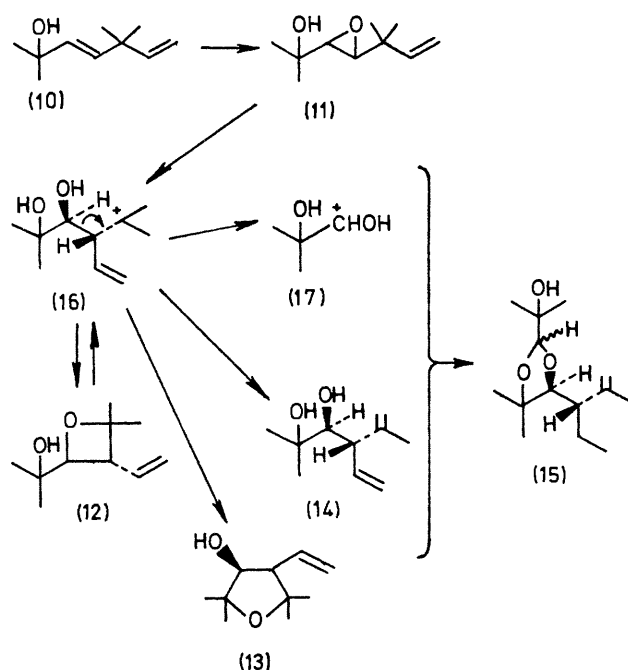
Summary An acid-catalysed 1,2-vinyl shift of 3,3-dimethylpenta-1,4-diene monoepoxides, leading to derivatives of 3-methyl-2-vinylbut-3-en-1-ol, makes possible the synthesis of the santolenyl group of monoterpenes from the artemisia group, a result of possible biogenetic significance.

It has been suggested¹ that the santolina group of monoterpenes, comprising santolinatriene (**1**)² and two of its hydroxylated derivatives,³ the artemisyl group, and the lavandulyl group of monoterpenes, might arise biogenetically from a specific ring-fission of a chrysanthemic acid (**2**) derivative. A cyclopropylcarbinyll compound (**3**) has been converted into a reduced santolina compound (**4**) with



retention of configuration at the asymmetric centre.⁴ The intervention of a cyclopropyl compound in order to produce the homoallyl carbonium ion (**5**) is not essential, and in view of recent speculations concerning the biogenesis of substances related to artemisia alcohol⁵ via a [2,3]-sigmatropic rearrangement of di-isoprenyl ether,⁶ a study was made to see whether the artemisia skeleton [*e.g.* artemisia alcohol, (**6**)] could be converted directly into the santolinyl skeleton. For example, if the homoallyl ion (**5**) does not immediately lose a hydrogen ion (as it does in the presence of pyridine⁷),

participation by the double bond will lead, through ion (**7**)[†] to either the santolinyl (**8**), chrysanthemyl (**9**), or artemisyl (**5**) skeletons.



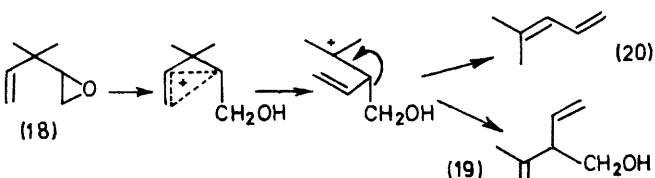
Yomogi alcohol (**10**)⁹ is related allylically to artemisia alcohol (**6**), and it was felt that ring-opening of its epoxide (**11**) might generate the desired homoallylic carbonium ion. In fact, treatment of this epoxide (**11**) with certain acidic reagents gave products derived only from the santolinyl skeleton. Somewhat surprising was the presence of the oxetan (**12**), which could, itself, be converted into the two other main products (**13**) and (**14**) by suitable acid treatment.

[†] Ions of this type are well-known; for recent structural work by n.m.r. spectrometry, see ref. 8.

Experimentally, when the epoxide (**11**) is stirred for 5 h in dry ether with Dowex 50 ion exchange resin, 40% of the material is converted into three products, the oxetan representing over 70% of these. Isolated gas chromatographically, this oxetan (**12**) is recognizable by the characteristic n.m.r. signal[†] at 4.03 p.p.m. (doublet, $J = 7.5$ Hz, due to the ring proton adjacent to oxygen¹⁰), the remainder of the spectrum supporting the structure. This oxetan (**12**) is slowly converted into the two other substances on heating with Dowex 50. The first of these (**13**) had m.p. 126—127° and had (n.m.r.) four methyl groups on saturated carbon atoms and a vinyl group on a carbon atom also carrying a hydrogen atom. The hydroxyl group was probably secondary, since it was easily acetylated with acetic anhydride in pyridine [unlike the hydroxyl of the oxetan (**12**)], and was assigned a *cis*-configuration with respect to the vinyl group because the acetate is stable up to 500°, when an acetate with a neighbouring *cis*-hydrogen atom would lose acetic acid. A compound with much longer retention time on a polar column was also isolated and shown to be one of the possible isomers of 2,5-dimethyl-4-vinylhex-5-en-2,3-diol (**14**) by its n.m.r. spectrum, which also showed that there were five protons on unsaturated carbon, compared with three in the cyclic products.

When the reaction was carried out by heating the epoxide (**11**) in benzene with toluene-*p*-sulphonic acid, the same compounds (**12**), (**13**), (**14**) were obtained, but were contaminated by two others, shown by mass spectra and microanalysis to have the formula $C_{14}H_{24}O_3$. The n.m.r.

and mass spectra were very similar, and led to the conclusion that they were the two possible isomers of an acetal (**15**) formed from the single glycol (**14**).



These facts are readily explained by considering the formation of an ion like (7) with $R = Me_2C(OH)CHOH$, all the products arising from the carbonium ion corresponding to (8) [*i.e.* (**16**)] by either ring closure [(**12**) and (**13**)] or loss of a hydrogen ion (**14**). Evidently under certain circumstances fission in the sense shown by the arrow on formula (**16**) can occur, leading to the protonated aldehyde (**17**) that forms the acetals (**15**). In support of the latter fission, I have found that when the monoepoxide (**18**) of 3,3-dimethylpenta-1,4-diene is treated with Dowex 50, the main products are the expected alcohol from vinyl rearrangement [*i.e.* (**19**)], together with 2-methylpenta-2,4-diene (**20**).

The 1,2-shift of the vinyl group described here makes the santolinyl group of monoterpenes readily accessible, and lends support to the postulate that they might arise biogenetically from artemisyl precursors.

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† All n.m.r. spectra were measured on a Varian model A-60 instrument in CCl_4 with Me_4Si as internal reference.

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¹⁰ For typical n.m.r. spectra of oxetans, see *e.g.* S. H. Schroeter and C. M. Orlando, Jr., *J. Org. Chem.*, 1969, **34**, 1181.