Methyl (2*R*),(3*S*)-2,5-Dimethyl-3-vinylhex-4-enoate (Methyl Santolinate) a New Irregular Monoterpene Constituent of ***Artemesia tridentada tridentada***

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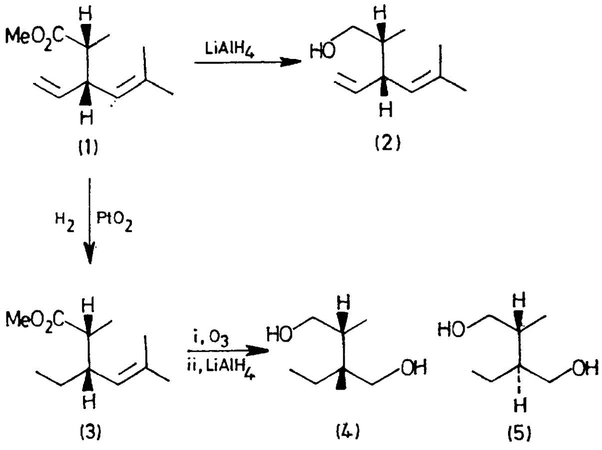
Summary Evidence establishing structure (**1**) (including stereochemistry) to a new, irregular monoterpene of the santolinyl carbon series and the implications of the structure and stereochemistry in relation to the biogenesis of irregular monoterpenes are presented.

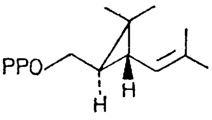
There has been a good deal of interest recently[1] in the biogenesis of irregular monoterpenes as biosynthetic models for the important non-cyclic triterpene, squalene, and its immediate precursor, presqualene pyrophosphate. We have been screening plants of the *Compositae* family, *Anthemideae* tribe as possible sources for cell-free enzyme systems for study of these biosynthetic pathways. The sagebrush group (*Artemesia*) of the above plant species is available locally, and we report here on one component obtained from *Artemesia tridentada tridentada*, big sage.

The leaves, stems, and flowers of *Artemesia tridentada tridentada*, collected near Price, Utah, were extracted with pentane and the volatile oils isolated by a closed system vacuum distillation. The volatile portions were analysed by g.l.c.–mass spectroscopy. The material[†] with *m/e* 182, $C_{11}H_{18}O_2$, which was separated and purified by preparative gas chromatography had $[\alpha]_D + 10{\cdot}6°$ (*c* 0·76, MeOH), ν_{max} (neat), 1735, 1665, 1640, 992, 910, and 828 cm^{-1}; u.v. end absorption; δ ($CDCl_3$), 1·11 (3H, d), 1·61 (3H, s) 1·69 (3H, s), 2·41 (1H, m), 3·13 (1H, m) 3·60 (3H, s), 4·97 (3H, m), and 5·63 (1H, m). These data suggested the presence of a CO_2Me carbonyl system, $-CH{=}CH_2$ and $-CH{=}CMe_2$ olefinic systems as well as a >CHMe grouping, leaving only a ⩾CH grouping. These units can be assembled in three ways but the most satisfying biogenetically is (**1**) (no stereochemistry considered), which we have named methyl santolinate.

Structure (**1**) was confirmed by chemical means. Reduction of (**1**) with $LiAlH_4$ gave the alcohol (**2**), as an oil, $[\alpha]_D$ $-10{\cdot}1°$ (*c* 2·09, MeOH), the spectral data for which are consistent with loss of one carbon and conversion of the ester carbonyl into an alcohol group. The vinyl double bond of (**1**) could be preferentially reduced using PtO_2–H_2



(1) (2) (3) (4) (5)



(6)

[†] A substance which is identical by comparison to (**1**) has been isolated independently from a Montana sagebrush (E. H. Hoerger, *Proc. Montana Acad. Sci.*, 1973, **33**, 97.)

to give (**3**) with loss of the 1665, 992, and 910 cm^{-1} i.r. bands.

Compound (**3**) was degraded to the known *threo*-3-ethyl-2-methylbutane-1,4-diol (**4**) by ozonization followed by reduction with $LiAlH_4$. Both the *threo*- and *erythro*-isomers, (**4**) and (**5**), respectively, were synthesized by $LiAlH_4$ reduction of the corresponding dicarboxylic acids for comparison.[2] The spectral (i.r. and n.m.r.) and g.l.c. properties of the two racemic diastereoisomers are distinctly different and, when compared with degraded methyl santolinate, confirmed the proposed structure as well as established the relative stereochemistry at C-2 and C-3 as indicated in (**1**).

Brockmann and Muller-Enoch[3] have established that the (−)-*threo*-3-ethyl-2-methylbutane-1,4-diol has the (2*S*), (3*S*) absolute stereochemistry. Since (**4**) obtained by degradation of (**1**) is (+) rotating, the absolute stereochemistry of (**1**) is as shown, *i.e.* (2*R*),(3*S*). The (*S*) absolute stereochemistry at the 3-position is that expected[1] if (1*R*),(3*R*)-chrysanthemyl pyrophosphate (**6**) is the biosynthetic precursor to the non-head-to-tail monoterpenes in general and the santolinyl skeleton in particular and thus must be considered as evidence in favour of this hypothesis.

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[2] J. H. Golden and R. P. Linstead, *J. Chem. Soc.*, 1958, 1732.

[3] H. Brockmann and D. Muller-Enoch, *Ber.*, **1971**, **104**, **3704**.