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THE ABSOLUTE CONFIGURATION OF SANTOLINA ALCOHOL FROM ORMENIS MULTICAULIS[1]

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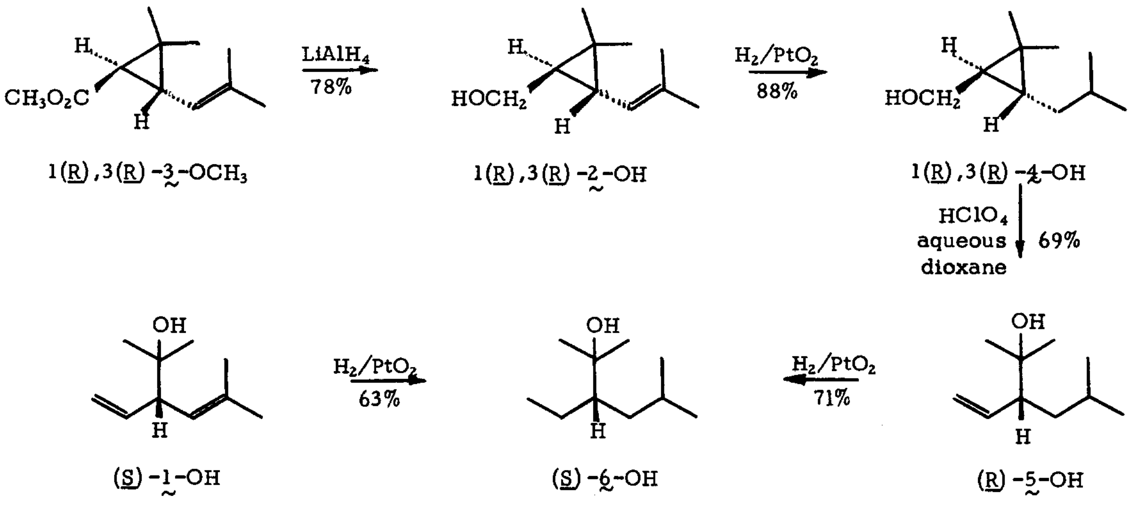
In vitro studies[3] have now established that santolinyl monoterpenes can be obtained from chrysanthemyl derivatives via carbonium ion intermediates in accord with suggested biogenetic pathways.[4] If naturally occurring santolina alcohol (1-OH)[5] is derived from chrysanthemyl pyrophosphate (2-OPP), the absolute configuration at C_3 of 2-OPP should be retained when the cyclopropane ring is opened. Although naturally occurring derivatives of 2-OH are not known, 1(R),3(R)-chrysanthemic acid[6] (3-OH) is presumably an oxidation product of 2-OH which retains configuration at C_1 and C_3. Therefore, as a corollary to the proposed biosynthetic mechanisms,[4] both 1-OH and 3-OH should have the same absolute configuration at C_3.[7] We now describe experiments which relate the configurations at C_3 of naturally occurring 1-OH and 3-OH.

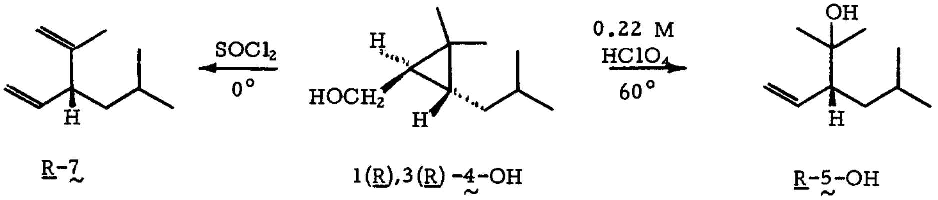
2-OPP

1-OH

Santolina alcohol, $[\alpha]^{23}_{D}$ + 11.8° (c. 1.2, cyclohexane), lit.[5] + 13.5°, was isolated from the essential oil of Ormenis multicaulis[8] by glpc (10' x 1/4" Carbowax 20M on Anakrom ABS) and converted to tetrahydrosantolina alcohol, 6-OH, $[\alpha]^{23}_{D}$ - 8.78° (c. 0.7, cyclohexane), by



hydrogenation in acetic acid.[9,10] Lithium aluminum hydride reduction of methyl 1(*R*),3(*R*)-*trans*-chrysanthemate [1(*R*),3(*R*)-**3**-OCH_3],[11] $[\alpha]_D^{23}$ + 24.4° (c. 3.2, cyclohexane), to 1(*R*),3(*R*)-**2**-



OH,[4c] $[\alpha]_D^{23}$ + 46.9° (c. 1.7, methylcyclohexane), followed by hydrogenation in acetic acid[9] gave 1(*R*),3(*R*)-**4**-OH,[4c] $[\alpha]_D^{23}$ + 10.5° (c. 4.2, cyclohexane). Crombie and coworkers[4b] had previously reported that 1(*R*),3(*R*)-**4**-OH gave a modest yield of diene *R*-**7** when treated with thionyl chloride at 0°. In accord with previous experience[12] we found that 1(*R*),3(*R*)-**4**-OH cleanly isomerized to homoallylic alcohol *R*-**5**-OH,[13] $[\alpha]_D^{23}$ - 29.3° (c. 0.7, cyclohexane), when treated with aqueous perchloric acid. Glpc analysis on a 500' column (Carbowax 20M) indicated that *R*-**5**-OH comprised more than 95% of the final product mixture. Hydrogenation of *R*-**5**-OH using the same conditions employed for **1**-OH and 1(*R*),3(*R*)-**2**-OH[9] gave an alcohol whose IR spectrum, glpc retention time (by coinjection) and sign of rotation[14] were identical to those of **6**-OH obtained from hydrogenation of naturally occurring santolina alcohol.

Since our reaction sequence did not alter the stereochemistry at C_3 of santolina alcohol or methyl *trans*-chrysanthemate, both naturally occurring **1**-OH and **3**-OH have the same absolute configuration at that carbon.[15] This observation had been predicted as a consequence of a biogenetic pathway in which *trans*-chrysanthemyl pyrophosphate is the precursor for chrysanthemyl, santolinyl and artemisyl monoterpenes. We are now investigating other non-head-to-tail monoterpenes of unknown absolute configuration.

REFERENCES

* Author to whom inquiries should be addressed.

1. This research was supported by the Research Corporation; the donors of the Petroleum Research Fund, administered by the American Chemical Society; and the University of Utah Research Fund.

2. Research Corporation undergraduate fellow.

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4. (a) R. B. Bates and S. K. Paknikar, *Tetrahedron Letters*, 1453 (1965); (b) L. Crombie, R. P. Houghton and D. K. Woods, *ibid*., 4553 (1967).

5. Y. Chretien-Bessiere, L. Peyron, L. Benezet and J. Garnero, *Bull. Chim. Soc., France*, 2018 (1968).

6. L. Crombie, J. Crossley and D. A. Mitchard, *J. Chem. Soc*., 4957 (1963).

7. While both enantiomers of some head-to-tail monoterpenes occur naturally, only one enantiomer of each non-head-to-tail monoterpene is presently known.

8. We wish to thank Mme. Bessiere and Dr. Peyron for a sample of the essential oil of *Ormenis multicaulis*.

9. O. N. Devgan, M. M. Bokadia, A. K. Bose, G. K. Trivedi, and K. K. Chakravarti, *Tetrahedron*, **25**, 3217 (1969).

10. IR (CCl_4) 3600, 3390, 2960, 1385, 1370 cm^{-1}; NMR (CCl_4) 0.82-1.80 (15,m), 1.09 (6,s, carbinyl methyls), and 1.39 ppm (1,s,hydroxyl group). All chemical shifts are reported as δ, relative to TMS internal standard.

11. We wish to thank FMC Corporation for a generous sample of 1(*R*),3(*R*)-*trans*-chrysanthemoyl chloride from which 1(*R*),3(*R*)-**3**-OCH_3 was prepared.

12. (a) C. D. Poulter, E. C. Friedrich and S. Winstein, *J. Amer. Chem. Soc.*, **92**, 4274 (1970); (b) C. D. Poulter and S. Winstein, *ibid.*, **92**, 4282 (1970); (c) C. D. Poulter and S. Winstein, *ibid.*, in press.

13. IR (CCl_4) 3450, 3050, 2950, 1640, 1380, 1370, 1004, 939, 915 cm^{-1}; NMR (CCl_4) 0.77-1.52 (9,m), 1.07 (6,s,carbinyl methyls), 1.58 (1,s,hydroxyl group), 1.71-2.16 (1,m, allylic H), and 4.73-5.63 ppm (3,m,olefinic H).

14. $[\alpha]_D^{23}$ - 9.03° (c. 1.3, cyclohexane).

15. 1(*R*),3(*R*)-*trans*-Chrysanthemum dicarboxylic acid is also the naturally occurring enantiomer.[6]