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SOLVOLYSIS OF N-METHYL-4-(CHRYSANTHEMYLOXY) PYRIDINIUM IODIDE -- A MODEL FOR NON-HEAD-TO-TAIL MONOTERPENE BIOSYNTHESIS[1]

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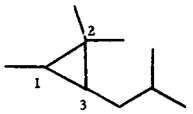
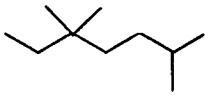
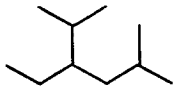
Closely related members of the Compositae family are apparently an exclusive source of non-head-to-tail monoterpenes which have chrysanthemyl, artemisyl and and santolinyl carbon skeletons.



chrysanthemyl



artemisyl

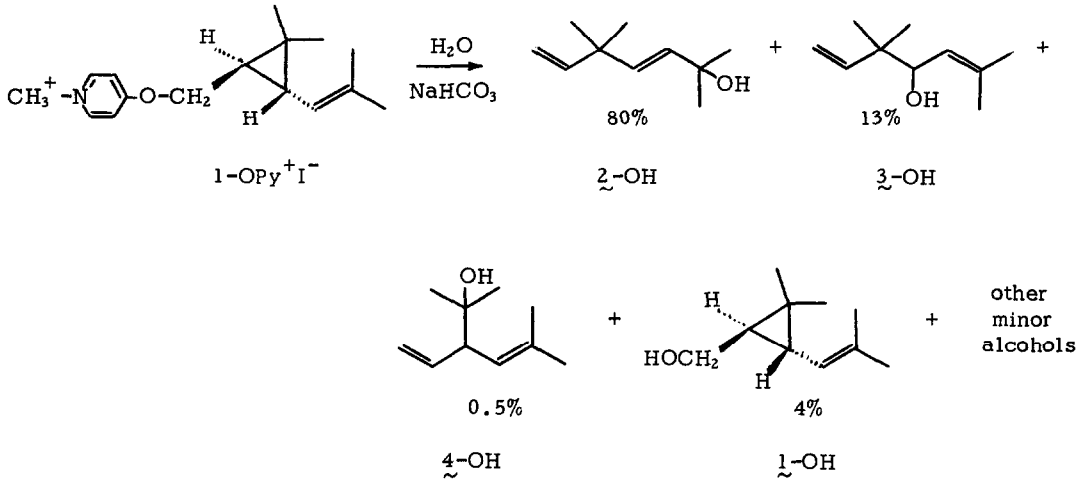


santolinyl

This obvious genetic link, as well as the established solvolytic properties of cyciopropylcarbinyl derivatives, has led several groups[3] to suggest biogenetic pathways which link chrysanthemyl to artemisyl and santolinyl monoterpenoids. By structural analogy to presqualene pyrophosphate,[4,5] ionization of trans-chrysanthemyl pyrophosphate (1-OPP) followed by cleavage of the appropriate bond would give the observed monoterpene products. Several in vitro studies have established the ease of cleavage between C_1 and C_3,[3a,6] but there have been no reports of rupture between C_1 and C_2 to give santolinyl products.[7] However, some of the earlier studies[3a,6a] were contradictory, presumably due to severe reaction conditions or an improper choice of leaving groups. We have circumvented these problems as well as those of acyl-oxygen cleavage and internal return with

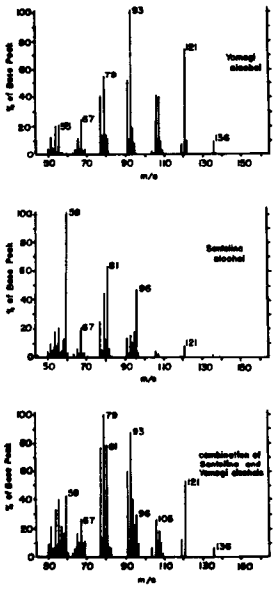
N-methyl-4-(trans-chrysanthemyloxy)pyridinium iodide ($\underset{\sim}{1}$-OPy$^+$I$^-$) and now report that both artemisyl and santolinyl monoterpenes are among the hydrolysis products of $\underset{\sim}{1}$-OPy$^+$I$^-$.

The disappearance of $\underset{\sim}{1}$-OPy$^+$I$^-$[8] (mp 129-131°, decomp) in water at 25°, k = (4.23 ± 0.22) x 10^{-5} sec^{-1}, was followed by monitoring the increase in absorption at 265 nm of solutions which were 7 x 10^{-5} M in $\underset{\sim}{1}$-OPy$^+$I$^-$ and 3 x 10^{-4} M in sodium bicarbonate. Our mild hydrolysis conditions[9] yielded yomogi alcohol ($\underset{\sim}{2}$-OH),[10] artemisia alcohol ($\underset{\sim}{3}$-OH),[11] trans-chrysanthemol ($\underset{\sim}{1}$-OH), and santolina alcohol ($\underset{\sim}{4}$-OH). The structures of $\underset{\sim}{1}$-OH and $\underset{\sim}{4}$-OH were established by coinjection[12]



(10' x 1/8" 3% SE-30 on Chromosorb W, 500' x 0.03" Carbowax 20M) and mass spectra. Santolina alcohol ($\underset{\sim}{4}$-OH) could not be completely separated from $\underset{\sim}{2}$-OH and we were not able to obtain a mass spectrum of uncontaminated $\underset{\sim}{4}$-OH from the solvolysis mixture. Both component alcohols have characteristic mass spectra, and the mass spectrum of the mixture could be accurately duplicated by assuming nearly equal amounts of $\underset{\sim}{2}$-OH and $\underset{\sim}{4}$-OH.[13] The structures of the minor alcohols are currently being investigated.

It has now been established that solvolysis of trans-chrysanthemyl derivatives leads to both artemisia and santolina monoterpenes without prior alteration of the natural substitution



pattern of the cyclopropylcarbinyl system. Although the distribution of non-head-to-tail C_{10} products varies widely among plant species, as one would expect, the transition state energy perturbations necessary for the predominance of 2-OH, 3-OH or 4-OH by a ratio of 99:1 are modest and should be within the capability of an enzyme system. In addition, we have been able to demonstrate that the asymmetric carbon atom in naturally occurring santolina alcohol (4-OH) has the same absolute configuration as C_3 in trans-chrysanthemic acid,[14] in accord with the hypothesis that both of the monoterpenes come from a common biogenetic precursor.

REFERENCES

* Author to whom inquiries should be addressed.

1. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society; the Research Corporation; and the University of Utah Research Fund for support of this research.

2. Petroleum Research Fund undergraduate scholar.

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

4. Cyclopropylcarbinyl pyrophosphates may be of pivotal importance in non-head-to-tail terpene biosynthesis.

5. H. C. Rilling, C. D. Poulter, W. W. Epstein and B. Larsen, J. Amer. Chem. Soc., 93, 1783 (1971).

6. (a) R. B. Bates and D. Feld, Tetrahedron Letters, 4875 (1967); (b) T. Sasaki, S. Eguchi, M. Ohno and T. Umemura, J. Org. Chem., 36, 1968 (1971).

7. Studies with dihydrochrysanthemol[3a] seem inappropriate to us since the electronic nature of the cyclopropylcarbinyl intermediate has obviously been drastically altered by removal of the double bond.

8. (a) M. Vogel and J. D. Roberts, J. Amer. Chem. Soc., 88, 2262 (1966); (b) G. H. Schmid and A. Brown, Tetrahedron Letters, 4695 (1968).

9. We found a similar product distribution for solvolysis of trans-chrysanthemyl dinitrobenzoate (1-ODNB) in 80% aqueous acetone at 100°. This is in contrast to the previous report[6a] that acetolysis of 1-OTs at 40-60° gave exclusively 1-OAc.

10. W. Sucrow, Tetrahedron Letters, 1431 (1970).

11. T. Takemoto and T. Nakajima, Yakugaku Zasshi, 77, 1307 (1957).

12. We wish to thank Dr. Sucrow for a sample of santolina alcohol.

13. We wish to thank Dr. J. D. Morrison for assistance with his computer program for determining the composition of the mixture from spectra of pure components.

14. C. D. Poulter, R. J. Goodfellow and W. W. Epstein, following paper.