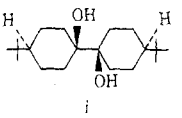
tion for singlet oxygen are the subject of much current interest: (a) N. M. Hasty and D. R. Kearns, *J. Am. Chem. Soc.*, **95**, 3380 (1973); (b) A. P. Schaap and G. R. Faler, *ibid.*, **95**, 3381 (1973); (c) P. A. Burns and C. S. Foote, *ibid.*, **96**, 4339 (1974); (d) L. N. Stephenson, D. E. McClure, and P. K. Sysak, *ibid.*, **95**, 7888 (1973).

(6) (a) Investigation of photooxygenation: G. O. Schenck and K. H. Schulte-Elte, *Justus Liebigs Ann. Chem.*, **618**, 185 (1958). (b) In benzene *t*-Bu absorptions of starting material and products are well separated and can be monitored accurately using wide sweep widths. Although they cannot be detected by the ^{1}H NMR method under these conditions other products are certainly present. Crude photooxygenation mixtures in boiling dioxane with 9,10-dibromoanthracene chemiluminesce well. When photooxygenated in methylene chloride using Methylene Blue as sensitizer, **1** after reduction gave 5–10% glycol i, likely arising from reduc-



i

tion of a 1,2-dioxetane. In a reinvestigation of the photooxygenation of cyclohexylidenecyclohexane, after reduction with $NaBH_4$ there was found in addition to the previously reported 1-(1-cyclohexenyl)-1-cyclohexanol the glycol and the epoxide of cyclohexylidenecyclohexane in the ratio 98:1:1 (by GPC).

(7) See also (a) W. F. Brill, *J. Am. Chem. Soc.*, **87**, 3286 (1965); (b) G. O. Schenck, O. A. Neumüller, and W. Eisfeld, *Justus Liebigs Ann. Chem.*, **618**, 202 (1958).

(8) Dienes are formed. Note that loss of water from **3a** and **4a** leads to two isomeric dienes.

(9) Spectral data were in accord with the proposed structures, in particular a single vinylic proton was observed in the ^{1}H NMR spectra. Satisfactory analytical data have been obtained for all new compounds except **3a** and **4a**.

(10) (a) K. Savard, *J. Biol. Chem.*, **202**, 457 (1953); (b) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953); (c) S. Winstein and N. S. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955); (d) E. W. Garbisch, Jr., and D. B. Patterson, *ibid.*, **85**, 3228 (1963).

(11) Compare with R. P. Thummel and B. Rickborn, *J. Am. Chem. Soc.*, **92**, 2064 (1970).

(12) E. Koch, *Tetrahedron*, **24**, 6295 (1968).

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(14) D. Y. Curtin, *Record. Chem. Progr.*, **15**, 111 (1954).

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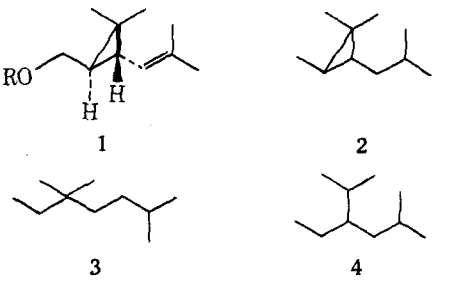
Received April 23, 1975

Studies on the Biogenesis of Non-Head-to-Tail Monoterpenes. The Isolation of (1*R*,3*R*)-Chrysanthemol from *Artemesia ludoviciana*[1]

Summary: The isolation of optically pure (1*R*,3*R*)-chrysanthemol from the leaves of *Artemesia ludoviciana* supports the hypothetical involvement of the corresponding pyrophosphate as a cruical intermediate in the biosynthesis of non-head-to-tail monoterpenes.

Sir: As part of a continuing study of the biosynthesis of the biologically important triterpene, squalene, we have been investigating the simpler but presumably analogous non-head-to-tail monoterpenes. Although there has been little experimental verification of any biosynthetic pathway, the available data[2] coupled with biogenetic analogies to presqualene alcohol and the known chemical[3] interconversions of the chrysanthemyl carbon skeleton with other non-head-to-tail monoterpene carbon skeletons have led to a unified hypothesis for the biosynthesis of these compounds.[4] This hypothesis requires (1*R*,3*R*)-chrysanthemyl pyrophosphate (**1**, R = pyrophosphate) as a key intermediate in the formation of the chrysanthemyl (**2**), artemesyl (**3**), and santolinyl (**4**) types of irregular monoterpenes. With the ubiquitous occurrence of phosphatases in plants, it might be expected that any plants producing **1** (R = pyrophosphate) would also have the corresponding alcohol, (1*R*,3*R*)-chrysanthemol (**1**, R = H), present.



1 **2** **3** **4**

In support of the proposed biosynthetic scheme, we wish to report the isolation of **1** (R = H) from the leaves of the sage brush, *Artemesia ludoviciana*, and further in accord with the hypothesis the natural chrysanthemol is optically pure possessing the 1*R*,3*R* absolute configuration.

The essential oils from 4 kg of fresh leaves of *A. ludoviciana* collected near Salt Lake City[5] were obtained by extraction of the plant material with pentane. Removal of the solvent and vacuum, bulb-to-bulb distillation of the remaining volatiles gave 12.5 ml of a mixture containing approximately 2% chrysanthemol as evidenced by VPC comparison to known **1** (R = H) on a 500-ft capillary column. The mixture was subjected to a vacuum distillation on a 60-cm annular spinning band column and the fractions enriched in **1** (R = H) were combined and further separated by a succession of high-pressure liquid chromatographies on a 170–200 mesh Florisil column using 1:10 ethyl acetate–hexane as the eluting solvent system. VPC analysis indicated an increase from 70 to 90 to 98% purity in the successive runs. The final purification was accomplished by preparative VPC on a 20 ft × ⅜ in. Carbowax 20M column to give 25 mg of 100% pure chrysanthemol. Spectral comparisons (NMR and ir) with authentic material as well as VPC coinjections confirmed the structure. Synthetic **1** (R = H) prepared by reduction of 97% (1*R*,3*R*)-chrysanthemic acid via its methyl ester[6] possessed an $[\alpha]_D$ of +46.9° (*c* 1.7, methylcyclohexane) while the isolated material had $[\alpha]_D$ +49.7° (*c* = 1.1, methylcyclohexane), indicating that the natural chrysanthemol is essentially 100% 1*R*,3*R*.

Evidence that the isolated **1** (R = H) could have been derived in vivo from the corresponding pyrophosphate was provided by allied studies in which we have clearly demonstrated enzymatic including phosphatase activity in leaf preparations of *A. ludoviciana*. In particular we have observed the facile conversion of known **1** (R = pyrophosphate) to **1** (R = H) in vitro by these leaf preparations.

References and Notes

(1) This work was supported by a grant from the National Institutes of Health (R01 GM20196).

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(5) Voucher Specimen 84025 of the University of Utah Herbarium contains a pressed sample of the *Artemesia ludoviciana* used in this study.

(6) We wish to thank Professor C. D. Poulter of this department for the sample used in our comparisons.

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Received June 3, 1975