

Acknowledgment. We thank the NSF for a graduate fellowship to E. L. H., F. A. L. Anet for the use of his 251-MHz nmr spectrometer, and the Office of Naval Research for partial support of this work.

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Contribution No. 3093

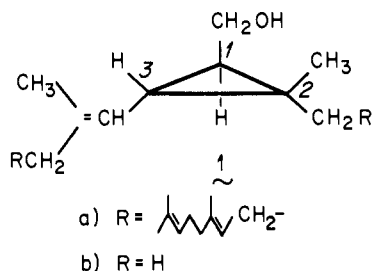
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Received December 8, 1972

Absolute Configuration of Presqualene Alcohol¹

Sir:

The structure of presqualene alcohol was shown to be that of a substituted cyclopropanecarbinol (**1a**)^{2,3} and



was confirmed by chemical synthesis.⁴⁻⁶ Studies in our laboratory reduced the eight possible stereoisomers of this alcohol to one of two enantiomers: 1*R*,2*R*,3*R* or 1*S*,2*S*,3*S*.^{3,7}

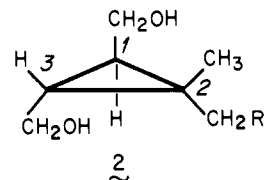
It was demonstrated first by Popják, *et al.*,⁸ that presqualene pyrophosphate was optically active with a plain positive optical rotatory dispersion curve (ORD) as far as 280 nm; presqualene alcohol was shown to behave similarly.³ Rilling, *et al.*,⁹ made a correlation between the absolute configuration of presqualene alcohol and chrysanthemum alcohol (**1b**), prepared from natural chrysanthemum monocarboxylic acid, the absolute configuration of which is known to be 1*R*,3*R*.^{7,10} They have stated, without presentation of experimental data, that whereas both **1a** and **1b** were dextrorotatory, **1a** gave a "plain positive CD curve" and **1b** a "similar but negative curve." Hence, they concluded that the absolute configuration of presqualene alcohol was enantiomeric to that of chrysanthemum alcohol.

The correlation reported by Rilling, *et al.*,⁹ is inconclusive because presqualene alcohol contains three asymmetric centers, whereas *trans*-(*R*)-chrysanthemum alcohol contains only two. Further, the effects of the

two large branched-chain olefinic substituents in presqualene alcohol on the optical properties of the substance are not immediately predictable.

Nakanishi and his colleagues¹¹ have exploited successfully the Cotton effect of benzoates for the determination of the absolute configuration of cyclic secondary alcohols and glycols. Harada and Nakanishi stated in a footnote to one of their papers that benzoates of asymmetric primary alcohols exhibit also the characteristic Cotton effect "provided the optical center is not too far removed from the hydroxyl group."¹² Thus, it seemed likely that a comparison of the optical properties of the benzoates of presqualene and *trans*-(*R*)-chrysanthemum alcohol and of their degradation products would provide further evidence as to the absolute configuration of presqualene alcohol.

We have prepared, therefore, the benzoates of **1a** and **1b**¹³ and the benzoates of their ozonolysis products, **2a**



and **2b**, which correspond to the "triacetate" and the "diacetate"¹⁴ ozonolysis products of **1a** and **1b**, respectively, and reported previously.³ We record here briefly some of the optical properties of these benzoates. Figure 1A shows the CD curves of the benzoates of **1a** and **1b** and Figure 1B the similar curves given by the tribenzoate of **2a** and the dibenzoate of **2b**. All four substances gave negative CD curves with minima in the range of 230–237 nm indicating that they belong to the same optical series. The correlation between the benzoates of **2a** and **2b** is particularly significant. We have found previously that the triacetate of **2a** was optically active;³ hence its two asymmetric centers must have the same absolute configuration, either *R* or *S*. Since the absolute configuration of the two asymmetric centers in **2b** is *R*, it follows from the identical CD curves of the benzoates of **2a** and **2b** that their absolute configuration is also identical. These correlations imply that the absolute configuration of presqualene alcohol at positions 1 and 3 in **1a** is the same as in natural chrysanthemumic acid, *i.e.*, *R,R*. Since the position of the methyl group on the cyclopropane ring in **1a** was deduced to be *syn* to the carbinol carbon,³ it also follows that the absolute configuration of **1a** at its third asymmetric center is also *R*.

(1) This research was supported by United States Public Health Service Research Grant HE-12745 from the National Heart and Lung Institute.

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(3) J. Edmond, G. Popják, S. M. Wong, and V. P. Williams, *J. Biol. Chem.*, **246**, 6254 (1971).

(4) R. V. M. Campbell, L. Crombie, and G. Pattenden, *Chem. Commun.*, 218 (1971).

(5) L. J. Altman, D. C. Kowerski, and H. C. Rilling, *J. Amer. Chem. Soc.*, **93**, 1782 (1971).

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(7) The numbering of positions follows the numbering of the cyclopropane ring in formula 1.

(8) G. Popják, J. Edmond, K. Clifford, and V. Williams, *J. Biol. Chem.*, **244**, 1897 (1969).

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(10) L. Crombie and M. Elliott, *Fortschr. Chem. Org. Naturst.*, **19**, 120 (1961).

(11) N. Harada and K. Nakanishi, *Accounts Chem. Res.*, **5**, 257 (1972), and references cited therein.

(12) N. Harada and K. Nakanishi, *J. Amer. Chem. Soc.*, **90**, 7351 (1968); *cf.* footnote 8.

(13) The *trans*-(*R*)-chrysanthemum alcohol (**1b**) was made by the reduction with LiAlH₄ of methyl *trans*-(*R*)-chrysanthemum monocarboxylate prepared from a specimen of a concentrate of natural pyrethrins. The pmr and mass spectra of this optically active alcohol ([α]₅₀₀ +71°, max [α]₂₁₀ +10,800°) were indistinguishable from the reported³ spectra of the racemic *trans*-chrysanthemum alcohol.

(14) We propose naming the product of the "reductive" ozonolysis of **1b**, *i.e.*, the product obtained by the reduction of the ozonide of **1b** with LiAlH₄, *trans*-(*R*)-caronic alcohol, in analogy with caronic acid which is the product of the oxidative cleavage of the ozonide of chrysanthemumic acid.

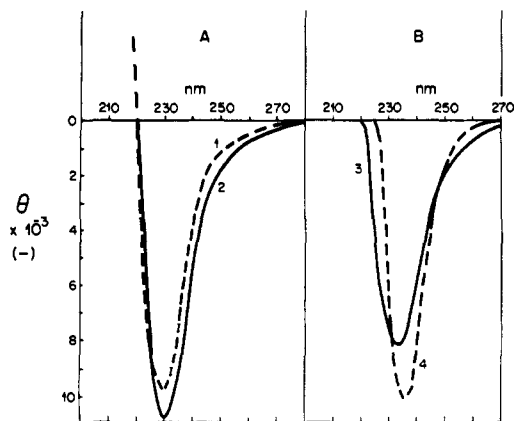


Figure 1. CD spectra of the benzoate of presqualene alcohol (A, curve 1) and of *trans*-(*R*)-chrysanthemum alcohol (A, curve 2), of the dibenzoate of *trans*-(*R*)-caronic alcohol¹⁴ (B, curve 3), and of the tribenzoate of an ozonolysis product **2a** of presqualene alcohol (B, curve 4). The spectra were taken in ethanol in a Cary 60 spectropolarimeter fitted with a CD attachment. The CD spectrum of presqualene benzoate shown appears to represent one-half of the split Cotton effect resulting from the interaction of the primary benzoate with a cyclopropyl olefinic chromophore, whereas for all other compounds the effects of isolated "chiral" benzoate groups are seen. The measurements could not be extended to below 215 nm on account of the strong uv absorption of the specimens even in very dilute solutions.

A full account of this work will be presented elsewhere.

Acknowledgments. We thank Mrs. Toby Altshuler for her assistance in the enzymic preparation and purification of presqualene alcohol and Dr. Kai Fang of the Chemistry Department on our campus for taking pmr spectra and ORD and CD measurements on our specimens. We are also grateful to S. B. Penick and Company, New York, N. Y. 10007, for a gift of pyrethrin concentrate.

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Received January 22, 1973

Photochemical Reactions of Benzoic Acid. Cycloaddition, Hydrogen Abstraction, and Reverse Type II Elimination

Sir:

The photochemistry of aromatic aldehydes and ketones has received intensive study, especially during the past decade, and the behavior of the $n \rightarrow \pi^*$ triplet excited states of these molecules is now fairly well understood.^{1,2} On the other hand, the photochemical behavior of carboxylic acids has been scarcely investigated. Aliphatic α,β -unsaturated acids are known to undergo *cis*-*trans* isomerization and addition of alcohols to the double bond.³⁻⁵ Aliphatic acids are reported to decarboxylate when irradiated with light of short

(1) P. J. Wagner, *Advan. Photochem.*, **5**, 23 (1968).

(2) A. A. Lamola and N. J. Turro, "Energy Transfer and Organic Photochemistry," Wiley-Interscience, New York, N. Y., 1969, Chapter 3.

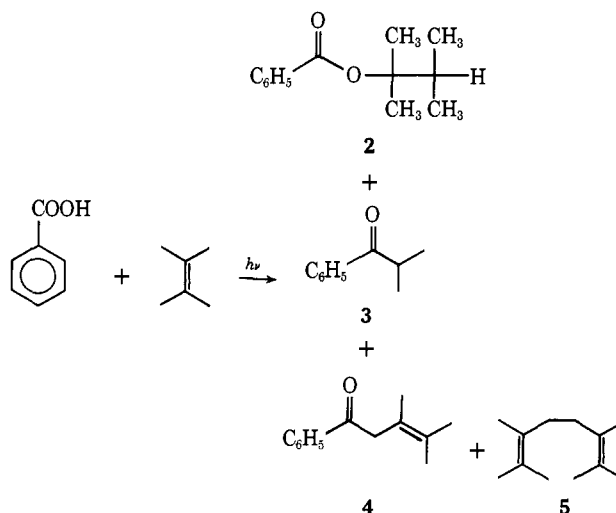
(3) M. J. Jorgenson, *Chem. Commun.*, 137 (1965).

(4) P. J. Kropp and H. J. Krauss, *J. Org. Chem.*, **32**, 3222 (1967).

(5) C. H. Nicholls and P. A. Leermakers, *ibid.*, **35**, 2754 (1970).

wavelength.⁶ We report here our results on the solution photochemistry of benzoic acid, which we have observed to undergo the several processes mentioned in the title.

Irradiation⁷ of a 1% solution of benzoic acid (**1**) and excess 2,3-dimethyl-2-butene in hexane until 35% of **1** was consumed (~ 2 hr) led to the isolation of four products: (a) 2,3-dimethyl-2-butyl benzoate (**2**, 46%), bp 73-75° (0.1 mm) [ir (film) 1711 cm^{-1} ; nmr τ 2.3 (2 H, m), 2.8 (3 H, m), 6.7 (1 H, septet, $J = 6.8$ Hz), 8.53 (6 H, s), and 9.00 (6 H, d, $J = 6.8$ Hz)], identified by comparison with an authentic sample;⁸ (b) isobutyrophenone (**3**, 22%); (c) 1-benzoyl-2,3-dimethyl-2-butene (**4**, 7%) [ir (film) 1681 cm^{-1} ; nmr τ 2.3-2.8 (5 H, m), 6.5 (2 H, s, br) 8.3 (6 H, s, br), and 8.4 (3 H, s, br); m/e 188 (P, 11), 173 (13), 106 (28), 105 (80), and 84 (100)]; and (d) diene **5**⁹ (25%) [τ 7.9 (4 H, s, br) and



8.4 (18 H, s, br)]. Ester **2**, the major product, is evidently formed by a process which is the reverse of the well-known type II elimination so often observed with alkyl and aryl alkyl ketones,¹⁰ and which has recently been observed in esters of simple aromatic acids.¹¹ Evidence for this mechanism was provided by the observation that irradiation of $\text{C}_6\text{H}_5\text{COOD}$ in excess olefin gave a monodeuterated ester **2** with the deuterium located at C-3 of the 2,3-dimethyl-2-butyl group as shown by its nmr spectrum. Irradiation of **2** itself gave benzoic acid and 2,3-dimethyl-2-butene; the position of equilibrium between the forward and reverse reactions could not be determined because of competing reactions of both **1** and **2**, such as formation of **3**. Irradiation of solutions of **1** and olefin until **1** was entirely consumed gave mainly **3**. Compound **3**, isobutyrophenone, is most simply rationalized as arising *via* retro **2** + **2** cleavage of an intermediate oxetane, a sequence which has analogy in some cases of ketone-derived oxetanes.¹²

(6) P. Ausloos and E. W. R. Steacie, *Can. J. Chem.*, **33**, 1530 (1955).

(7) Preparative irradiations were performed with a 15-fold excess of olefin, using light from a Hanovia 450-W medium-pressure mercury arc.

(8) The authentic material was prepared by sequential treatment of 2,3-dimethyl-2-butanol with 1 equiv of butyllithium and 1 equiv of benzoyl chloride.

(9) T. Midgley and A. L. Henne, *J. Amer. Chem. Soc.*, **52**, 2078 (1930).

(10) P. J. Wagner, *Accounts Chem. Res.*, **4**, 168 (1971).

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(12) D. R. Arnold, *Advan. Photochem.*, **6**, 301 (1968), and references given therein.