Tetrahedron Letters No.5, pp. 307-309, 1969. Pergamon Press. Printed in Great Britain.

7a(H)-Eremophila-1,11-dien-9-one. A New Sesquiterpene of the Eremophilane Type.

G. L. Chetty and L. H. Zalkow[1]

School of Chemistry, Georgia Institute of Technology,
Atlanta, Georgia, U.S.A.

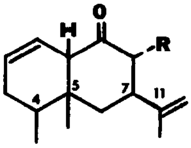
and

R. A. Massy-Westropp

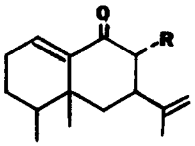
Department of Organic Chemistry, University of
Adelaide, Adelaide, South Australia, Australia

(Received in USA 29 October 1968; received in UK for publication 8 December 1968)

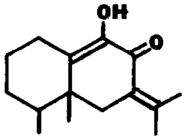
The first members of the eremophilane group of sesquiterpenes, a group which does not follow the isoprene rule, were isolated from *Eremophila mitchelli*, a small tree indigenous to Australia.[2] More recently[3], 8a-hydroxy-7a(H)-eremophila-1,11-dien-9-one (I) and 8a-hydroxy-7a(H)-eremophila-10,11-dien-9-one (II) were found to be present in this plant in addition to the previously reported[3] eremophilone (III), hydroxydihydroeremophilone (7a(H)eremophil-11-ene-9-one, IV) and hydroxydihydroeremophilone (V). We now wish to report the isolation of a sixth sesquiterpene of this class from *Eremophila mitchelli*; namely, 7a(H)-eremophila-1,11-dien-9-one (VI).



I R = OH, VI R = H
IV Δ^1-Dihydro-I



II R = OH
III R = H



V

An eremophilone rich fraction, obtained by chromatography of the cold ether extract of the wood of *Eremophila mitchelli* on alumina, followed by distillation (b.p. 125-140°/0.05 mm), showed on gas chromatographic analysis 65% eremophilone and 35% of the new sesquiterpene now identified as 7a(H)-eremophila-1,11-dien-9-one (VI). An examination of the total petroleum ether and ethyl ether extracts of the wood of *Eremophila mitchelli* some two years after the initially obtained sample, mentioned above, showed only trace amounts of eremophila-1,11-dien-9-one. The variation of content of VI does not arise from the conversion of eremophilone (III) to 7a(H)-eremophila-1,11-

dien-9-one under the conditions of isolation but appears to be related to the plant source in some way. Chromatography of the eremophilone-eremophila-1,11-dien-9-one mixture (65:35) on silica gel gave first eremophila-1,11-dien-9-one and then eremophilone in the petroleum ether--ethyl ether eluent (85:15). The eremophila-1,11-dien-9-one thus obtained (94% pure by glc) was further purified by preparative gas chromatography on a Ucon LB-550X column to give the analytical sample in >99% purity. $C_{15}H_{22}O$ requires: C, 82.57; H, 10.09. Found C, 82.47; H, 9.98%. M. p. 43-44°; $\nu_{max}^{CHCl_3}$ 1710, 1642, 892 cm^{-1}; $\lambda_{max}^{CH_3OH}$ 285 mμ, $\varepsilon = 151$; δ (CCl_4): 0.82 (3H,d,J = 6.0 cps), 0.96 (3H,s), 1.75 (3H,bs,$W_{1/2h}$ 3), 3.40 (2H,m); 4.73 (2H,m); RD (C, 0.09; CH_3OH), $[\Phi]_{589}$ + 214°, $[\Phi]_{389}$ - 1012°, $[\Phi]_{268}$ + 6549, a = -75.6.

Hydrogenation of VI in ethanol in the presence of platinum oxide, gave cis-tetrahydroeremophilone identical by glc, IR, nmr and RD with an authentic specimen.[4] 8a-Hydroxy-7a(H)-eremophila-1,11-dien-9-one (I) on acetylation and calcium ammonia reduction has been reported[3] to give a product with structure VI, which on treatment with base gave eremophilone (III). A comparison of the IR spectrum of the product obtained from I, as described above, with the spectrum of VI isolated from *Eremophila mitchelli* showed that the two were identical. Thus the structure of the newly isolated sesquiterpene is firmly established as 7a(H)-eremophila-1,11-dien-9-one (VI).

Ketone VI is an example of a molecule possessing a non-conjugated dissymmetric chromophore[5] in which the n→π* transition is not appreciably strengthened due to improper disposition of the carbonyl group and double bond. The situation is analogous to that of verbenalin.[5] The negative amplitude (a-39)[6] observed for cis-tetrahydroeremophilone (tetrahydro-VI) in its RD curve has been ascribed[7] to the contribution of C-2 in a front negative octant. Since VI shows a negative Cotton effect of even greater amplitude than cis-tetrahydroeremophilone, the double bond at C-1, C-2 appears to make an even greater negative contribution than the saturated C-C bond at this position.

A comparison of the nmr spectra of VI and III is instructive. The secondary methyl group at C-4 in eremophilone (III) appears at δ0.92 (J = 6 cps) showing a deshielding of ~0.1 ppm relative to the corresponding methyl group in 7a(H)-eremophila-1,11-dien-9-one (III). An examination of Dreiding models indicates that the C-4 methyl group in III is approximately 0.4Å closer to the bridgehead methyl group at C-5 than the analogous situation in VI and this steric congestion leads to deshielding.[8] The anticipated mutual deshielding of the C-5 methyl group in III is not observed, apparently, because of the counter shielding effect of the carbonyl group.

Acknowledgement: We wish to thank the National Institutes of Health (AM-10099) for financial support of this research and to express our appreciation to the University System of Georgia for Quality Improvement Funds used for the purchase of the JASCO ORD-CD instrument used in this study.

REFERENCES

1. Terpenes XXVI. Terpenes XXV: The Structure and Stereochemistry of a New Sesquiterpene of the Acorane Type. R. J. McClure, K. S. Schorno, J. A. Bertrand and L. H. Zalkow, Chem. Commun. (London), 1135 (1968).
2. J. Simonsen and D. H. R. Barton, "The Terpenes." Vol. III, p. 212, Cambridge University Press 1952.
3. R. A. Massy-Westropp and G. D. Reynolds, Aust. J. Chem., 19, 303 (1966).
4. C. Djerassi, R. Mauli and L. H. Zalkow, J. Am. Chem. Soc., 81, 3424 (1959).
5. A. Moscowitz, K. Mislow, R. A. W. Glass and C. Djerassi, J. Am. Chem. Soc., 84, 1945 (1962).
6. L. H. Zalkow, A. M. Shaligram, Shih-En Hu and Carl Djerassi, Tetrahedron, 22, 337 (1966).
7. C. Djerassi and W. Klyne, J. Chem. Soc., 4929 (1962).
8. N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, Inc., San Francisco, 1964, p. 37.