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TERPENOIDS LXXIII.[1] SINULARENE, A SESQUITERPENE HYDROCARBON BASED ON A NOVEL SKELETON FROM THE SOFT CORAL, *SINULARIA MAYI*.

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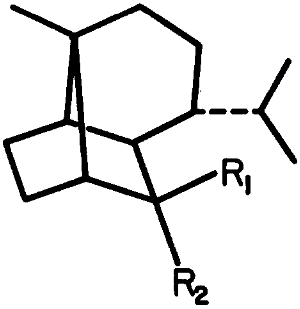
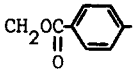
Interesting sesquiterpenes, including a number with new structures, have been reported from Alcyonacea[3,4,5] and from the closely related Gorgonacea.[6] We now wish to record the structure elucidation of sinularene (1), a naturally occurring sesquiterpene based on a hitherto unknown skeleton which cannot be derived by direct cyclization of a farnesol precursor.

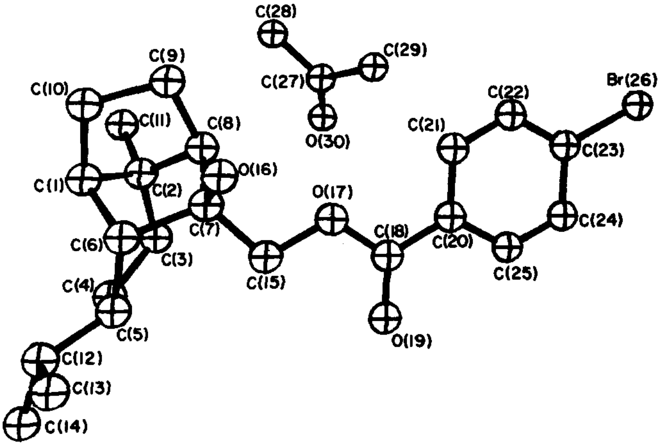


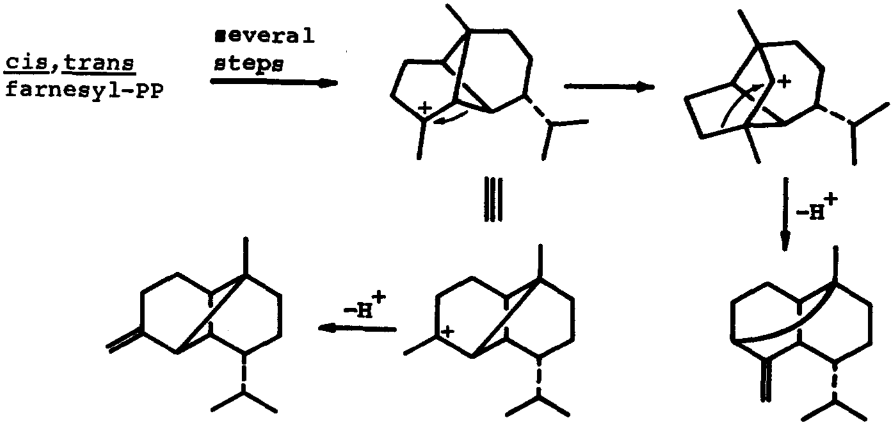
1, $R_1R_2 = CH_2$
2, $R_1R_2 = O$
3, $R_1 = CH_2OH$, $R_2 = H$
4, $R_1 = CH_2OH$, $R_2 = OH$
5, R_1 =  $CH_2OC(=O)C_6H_4Br$, $R_2 = OH$

Dried, shredded colonies of *Sinularia mayi* (Coelenterata, Anthozoa, Alcyonaria, Alcyonacea), were extracted at ambient temperature with hexane. Silica gel column chromatography yielded in the hexane fractions a number of sesquiterpene hydrocarbons;[7] the major ones were isolated by preparative gas chromatography [OV-17 (12%) on Chrom W A/W, 120-150°] and yielded about 180 mg (0.010% yield based on the dried animal material) of the most abundant sesquiterpene hydrocarbon, sinularene: $[\alpha]_D^{20°}$ -142° (c 0.55 in CCl_4); MS (70 e.v.) M^+ 204(17) $C_{15}H_{24}$ with prominent peaks at 105(100), 91(95), 161(93); IR (neat) 3076 cm^{-1}, 1660, 1382, 1365, 870 isopropyl and exocyclic methylene; ^{1}H NMR ($CDCl_3$) δ 0.90 (d, J 6.4 Hz, 3H, isopropyl methyl), 0.92 (d, J 6.4, 3H, isopropyl methyl), 0.915 (s, 3H, tertiary methyl), 2.1-2.25 (unres. m, 2H, allylic protons), 4.59 and 4.79 (broad singlets, 1H each, exocyclic methylene); ^{13}C NMR ($CDCl_3$) three CH_3 (20.67, 20.67, 21.41 ppm), five CH_2 (22.37, 25.99, 30.21, 31.70, 101.08 vinylidene), five CH (29.09, 42.94, 49.21, 50.21, 53.29), and two C (46.90, 162.92 vinylidene). Ozonolysis (or OsO_4/$NaIO_4$) yielded 2: MS M^+ 206(100) $C_{14}H_{22}O$; IR (neat) 1740 cm^{-1} indicating a cyclopentanone; ORD (methanol) $[\Phi]_{589}$ -96°, $[\Phi]_{303}$ -2700°, $[\Phi]_{272}$ +750°; CD (methanol) $[\theta]_{317.5}$ +220, $[\theta]_{287}$ -2500. Hydroboration-oxidation of 1 gave the primary alcohol 3: MS M^+ 222(28) $C_{15}H_{26}O$, 95(100); IR (neat) 3340 cm^{-1} OH; NMR ($CDCl_3$) δ 3.74, m, 2H, $C\underline{H_2}$-OH. Osmium tetroxide oxidation of 1 gave one diol 4: MS M^+ 238(12) $C_{15}H_{26}O_2$, 41(100); IR (neat) 3400 cm^{-1} OH; ^{1}H NMR ($CDCl_3$) δ 3.68 and 3.91 (doublets, J 11.0, 2H total, $C\underline{H_2}$-OH). Reaction of 4 with p-Br-benzoyl chloride led to 5: m.p. 48-49° crystallized from acetone-H_2O; ^{1}H NMR (CCl_4) δ 4.42 and 4.60 (doublets, J 11.0, 2H total, $C\underline{H_2}$-O), 7.56 and 7.88 (doublets, J 8.4 Hz, 4 protons total, aromatic).

The spectral data required that 1 ($C_{15}H_{24}$) be tricyclic and that it possess an isopropyl and a tertiary methyl and, as the only functional group, an exocyclic methylene on a five-membered ring. There had to be at least one allylic proton since the ^{13}C NMR data of 1 established the presence of only two quaternary carbons, one belonging to the vinylidene; integration of the distinct, broad, unresolved multiplet between δ 2.1-2.5 in ^{1}H NMR was consistent with there being two allylic protons. Ketone 2 did not give significant deuterium exchange (NaOD/D_2O/THF/4 days) indicating the allylic protons to be at bridgehead positions. An ^{1}H NMR shift reagent study on 3 using $Eu(Fod)_3$ with decoupling affirmed the above conclusions but failed to provide significant new information. The Baeyer-Villiger reaction using m-Cl-peroxybenzoic acid or trifluoroperoxyacetic acid was attempted a number of times without success, hindering a degradation study.

The structure was finally solved via X-ray diffraction studies at -60° of 5. The crystals were quite soft and difficult to work with; one with the approximate dimensions .2 x .4 x .1 mm was chosen for diffraction studies. The crystals are monoclinic, space group $C_2(C_2^3)$, with $\underline{a}$ = 17.923(19), $\underline{b}$ = 7.140(6), $\underline{c}$ = 18.628(9)A°, β = 101.60(7)°, Z = 4, elemental composition $C_{22}H_{29}BrO_3 \cdot CH_3COCH_3$ and calculated density 1.33 g/cc. Using graphite monochromated CuKα radiation a total of 1670 reflections were measured, and after correction for Lorenz, polarization and background effects only 1138 (68%) were judged observed ($F_o \geq 3\sigma(F_o)$). The bromine position was located from a Patterson map[8] and all other atom positions were located from subsequent difference Fourier maps. In the final X-ray model all nonhydrogen atoms are refined anisotropically and hydrogens, isotropically by full-matrix least-squares techniques. After correction for the anomalous scattering of the bromine the conventional crystallographic residual is 0.062 for the model shown and slightly higher for the enantiomer. Bond distances and angles agree well with generally accepted values. There is a hydrogen bond between the acetone oxygen and the hydroxyl hydrogen.





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The absolute configuration implicit in stereostructure 1 is based on the above-cited negative Cotton effect of 2 using the octant rule,[9] a conclusion which is consistent with the absolute configurations of other related sesquiterpene hydrocarbons[7] from S. mayi (e.g. (+)-β-copaene 6[10]). The carbon framework of sinularene is isoprenoid but does not have the standard head-to-tail (i.e. farnesolic) skeleton. (+)-β-Copaene (6), which follows the standard head-to-tail assembly of a farnesol precursor, and sinularene (1=7) could plausibly arise from the same precursor.[10] Further biogenetic implications will be considered in the full paper[7] which will describe the isolation and characterization of ten sesquiterpenes from S. mayi.

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REFERENCES

1. Terpenoids LXXII, Y. M. Sheikh, C. Djerassi, J. C. Braekman, D. Daloze, M. Kaisin, B. Tursch, and R. Karlsson, Tetrahedron (in press).
2. Camille and Henry Dreyfus Teacher-Scholar Grant Awardee 1972-1977.
3. B. Tursch, M. Colin, D. Daloze, D. Losman, and R. Karlsson, Bull. Soc. Chim. Belg., 84, 81 (1975).
4. Y. M. Sheikh, G. Singy, M. Kaisin, H. Eggert, C. Djerassi, B. Tursch, D. Daloze, and J. C. Braekman, Tetrahedron, 32, 1171 (1976).
5. R. Karlsson, Acta Crystallogr., Sect. B, 32, 2609 (1976).
6. L. S. Ciereszko and T. K. B. Karns in "Biology and Geology of Coral Reefs", Vol. II, O. A. Jones and R. Endean, Eds., Academic Press, Inc., New York, 1973, chapter 6.
7. To be published.
8. The following library of crystallographic programs was used: C. R. Hubbard, C. O. Quicksall, and R. A. Jacobson, "The Fast Fourier Algorithm and the Programs ALFF, ALFFOP, ALFFT and FRIEDEL", USAEC Report IS-2625, Iowa State University-Institute for Atomic Research, Ames, Iowa, 1971; W. R. Busing, K. O. Martin, and H. S. Levy, "A Fortran Crystallographic Least Square Program", USAEC Report ORNL-TM-305 Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965; C. Johnson, "ORTEP, A Fortran Thermal-Ellipsoid Plot Program", USAEC Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965.
9. W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, J. Amer. Chem. Soc., 83, 4013 (1961); T. D. Bouman and D. A. Lightner, ibid., 98, 3145 (1976).
10. R. M. Coates, Fortschr. Chem. Org. Naturst., 33, 73 (1976); see especially pages 145-151.