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2-(1-CHLORO-2-HYDROXYETHYL)-4,4-DIMETHYLCYCLOHEXA-2,5-DIENONE: A PRECURSOR OF 4,5-DIMETHYLBENZO[*b*]FURAN FROM THE RED ALGA *DESMIA HORNEMANNI*

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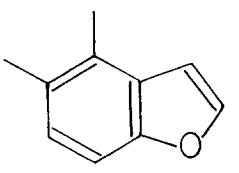
Abstract: A labile compound isolated from *D. hornemanni* was characterized as the title cyclohexadienone and shown to be a precursor of 4,5-dimethylbenzofuran.

A number of halogenated monoterpenes of myrcene and ochtodene types have been reported from the red alga *Desmia* (syn. *Chondrococcus*) *hornemanni* from geographically diverse areas of the Pacific.[1] In our earlier study with the alga from Okinawa we have isolated 4,5-dimethylbenzo[*b*]furan (1)[2] along with other metabolites. When a fresh collection of the alga was promptly processed, we obtained no benzofurans, but a series of new ochtodene-type compounds.[3] One of them was characterized as 2-(1-chloro-2-hydroxyethyl)-4,4-dimethylcyclohexa-2,5-dienone (2), a labile compound which was spontaneously transformed into 1 at room temperature.

The alga collected at Cape Zampa, Okinawa in May, 1983 was extracted with acetone. The methylene chloride soluble oil of the extract was rapidly separated on a silica gel column. The fractions eluted with 7:3 hexane-acetone were repeatedly purified by flash chromatography using TLC grade silica gel to give 2 as a pale yellow oil in a 0.07% yield (of wet alga), $[\alpha]_D^{21}$ -87.2° (c 1.29, CH_2Cl_2). The EIMS [m/z 165 (19), 158 (13), 156 (40), 150 (9), 148 (24), 136 (100), 122 (22), 120 (26), and 92 (44%)] of 2 showed no molecular ions, but a pair of isotopic peaks at m/z 158 and 156 (-CH_3, -CHO) clearly demonstrated the presence of a Cl atom. The formula $C_{10}H_{13}ClO_2$ for 2 was established by a combustion analysis on the stable acetate (3).[4] The UV [EtOH, λmax 237 nm (ε 8900)] and IR spectra (film, 1665 and 1627 cm^{-1}) indicated the presence of a cyclohexadienone chromophore. The 2-substituted 4,4-dimethylcyclohexa-2,5-dienone constellation was further substantiated by ^1H NMR [$CDCl_3$, δ7.08 (1H, d, J=2.9 Hz, H-3), 6.83 (1H, dd, J=9.9, 2.9 Hz, H-5), 6.18 (1H, d, J=9.9 Hz, H-6), 1.27 (3H, s) and 1.25 (3H, s)] and ^{13}C NMR data [$CDCl_3$, δ183.5 (s, C-1), 156.6 (d, C-3 or 5), 153.3 (d, C-5 or 3), 133.5 (s,



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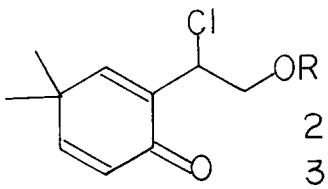
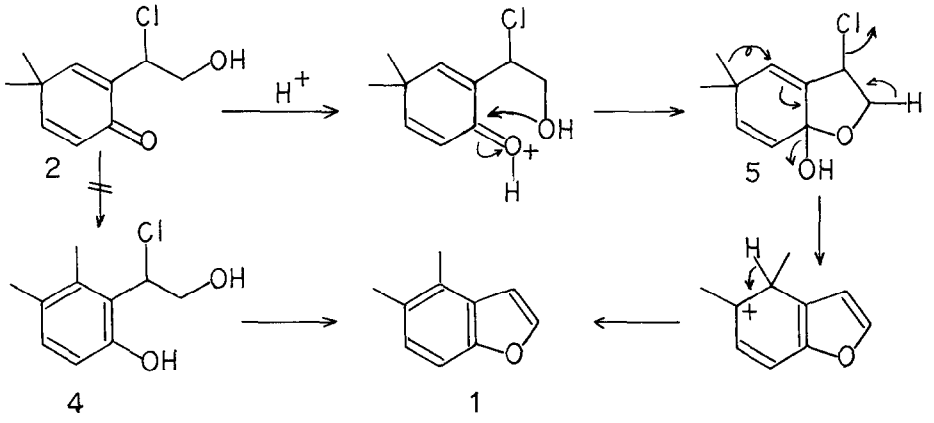


2 R=H
3 R=Ac

C-2), 126.3 (d, C-6), 38.0 (s, C-4), and 26.1 (2q, 2 Me)]. These spectral data were comparable to those reported for 2,4,4-trimethylcyclohexa-2,5-dienone.[5] The side chain could be assigned as -CHCl-CH_2OH by an IR band at 3420 cm^{-1}, three mutually coupling ^{1}H NMR signals [δ5.14 (1H, dd, J=6.0, 3.2 Hz), 3.88 (1H, dd, J=11.8, 3.2 Hz), and 3.72 (1H, dd, J=11.8, 6.3 Hz)] and by the ^{13}C NMR data (δ65.6t and 58.0d). The primary nature of the hydroxyl group was confirmed by observing a 2H doublet at δ4.35 for the methylene protons of 3.[4]

Although a pure sample of 2 could be kept unchanged for several hours at room temperature, prolonged standing destroyed the compound. It was extremely sensitive to a trace of an acid or heat. When a solution of 2 and a trace of hydrochloric acid in $CDCl_3$ in an NMR tube was warmed at about 50 °C for several minutes, complete transformation into 1 was observed by NMR measurement. On the other hand, the acetate 3 and a related compound[3] with Br in the place of OH in 2 were found to be stable under these conditions. Not only this difference in stability of these compounds but also the fact that 5,6-dimethylbenzofuran was not formed by the transformation strongly suggested that the dienone-phenol rearrangement[6] to form phenolic intermediates such as 4 was not the first step of the reaction. A plausible mechanism is to involve the initial cyclization to the hemiketal 5 followed by synchronized aromatization of the both rings. The acetate 3 showed potent antiviral activity against HSV-1 and VSV.



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References and Notes

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2. The bezofuran 1 has also been isolated from a Hawaiian collection. F. X. Woolard, Ph.D. Dissertation, 1977, University of Hawaii. I thank Prof. R. E. Moore for this information.

3. Isolation and structures of other related compounds will be reported elsewhere.

4. 3: $[\alpha]_D^{21}$ -56.8° (c 0.84, CH_2Cl_2); IR (film) 2970, 1742, 1660, 1632, 1230, 1035, and 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ7.05 (1H, dd, J=2.9, 0.8 Hz), 6.82 (1H, dd, J=10.0, 2.9 Hz), 6.18 (1H, d, J=10.0 Hz), 5.24 (1H, td, J=5.8, 0.8 Hz), 4.35 (2H, d, J=5.8 Hz), 2.08 (3H, s), 1.32 (3H, s), and 1.28 (3H, s). Found: C, 59.44; H, 6.25; Cl, 14.68%. Calcd for $C_{12}H_{15}ClO_3$: C, 59.39; H, 6.23; Cl, 14.61%.

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