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# BASE-INDUCED REARRANGEMENT OF SPHAEROCOCCENOL A

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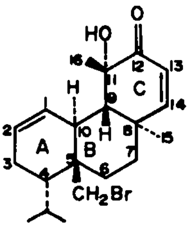
**Abstract**—On the basis of chemical and spectroscopic evidence structure 2 has been assigned to compound obtained from Sphaerococcenol A by treatment with alkali. A mechanism involving an acyloin rearrangement followed by an intramolecular nucleophilic displacement has been proposed.

Three related bromoditerpenes with an unprecedented tricyclic skeleton, sphaerococcenol A (1),[1] bromosphaerol[2] and bromosphaerodiol,[3] have been recently isolated from the red seaweed *Sphaerococcus coronopifolius* (Sphaerococcaceae). During the chemical investigation of this alga we had occasion to observe that treatment of sphaerococcenol A with base induces ready dehydrobromination. In the present paper we wish to report the structure of the product obtained by base-catalysed rearrangement of sphaerococcenol A and the mechanism of its formation.

When heated with 10% ethanolic potassium hydroxide, sphaerococcenol A afforded, in 90% yield, compound 2, m.p. 138–139°, $[\alpha]_D + 1.3°$. Exact mass determination and elemental analysis gave the molecular formula $C_{20}H_{28}O_2$. The IR spectrum showed OH (3420 cm$^{-1}$) and CO (1700 cm$^{-1}$) groups, accounting for both O atoms. The lack of UV absorption in the enone region proved that the CO group was not conjugated while deuterium exchange evidenced the absence of enolyzable protons on the adjacent C atoms. Sodium borohydride reduction of 2 gave a mixture of two epimeric diols (3). One of these could be isolated in pure form ($M^+$ 302, m.p. 158–159°, $[\alpha]_D - 1.6°$) and gave a positive Malaprade test for *vic*-diols, thus showing that in 2 the two oxygen functions are vicinal. On catalytic hydrogenation at room temperature, 2 absorbed 2 mol hydrogen to give hydroxyketone 4, MW 304 (MS) indicating a tetracyclic structure. In addition, ketone 5 was also obtained, MW 288 (MS) in which the allylic OH group was eliminated.

The NMR spectrum of 2 showed in the low-field region a further coupled AB quartet at $\delta$ 6.25 and 5.75 (J = 10 Hz) for the vinyl protons H-1 and H-2, and another AB pattern at 5.45 and 5.49 (J = 10 Hz), which was devoid of any further spin coupling, for the olefinic protons H-13 and H-14. The high-field region showed a broad 1H singlet at $\delta$ 2.35, which by decoupling experiments could be attributed to H-10, two doublets at 0.67



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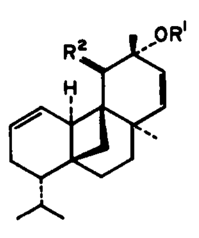
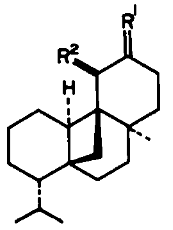


2 $R^1 = H,\ R^2 = O$

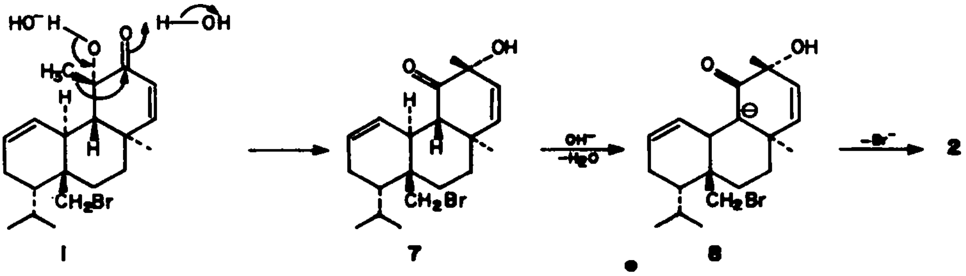
3 $R^1 = H,\ R^2 = <^{OH}_{H}$

6 $R^1 = Ac,\ R^2 = O$



4 $R^1 = <^{CH_3}_{OH},\ R^2 = O$

5 $R^1 = <^{CH_3}_{H},\ R^2 = O$



and 0.88 (J = 7 Hz) for the methyls of the isopropyl group, a singlet at 1.04 for the 15-Me and a singlet Me signal at 1.32 indicative of attachment to quaternary C atom bearing OH group. Attempted oxidation with Jones reagent and acetylation with acetic anhydride also failed, thus confirming this assignment. In more drastic conditions, i.e. with acetyl chloride in hot xylene, **2** yielded the acetate **6** ($M^+$ 342, $\nu_{max}$ 1718 $cm^{-1}$, m.p. 131–133°, $[\alpha]_D - 46°$). Comparison of the spectrum of **6** with that of **2** revealed that not only the 16-Me signal in the parent compound moved downfield on acetylation (from 1.32 to 1.37), but also the 15-Me signal which shifted from 1.04 to 1.25. Inspection of the model revealed that this Me is indeed in close proximity of the ester CO.

From the foregoing data it can be deduced that under the action of base C ring in sphaerococcenol A undergoes an acyloin rearrangement. Since C-9 in **2** is tetrasubstituted, it follows that the further modification induced by alkali is due to an intramolecular nucleophilic displacement of the bromine from carbanion **8**. On the basis of this mechanism (Scheme), stereostructure **2** could be assigned to the product obtained from sphaerococcenol A by treatment with base.

## EXPERIMENTAL

*Treatment of sphaerococcenol A with base.* **1** (600 mg) was heated at reflux with 10% KOH (in EtOH–$H_2O$ 1:4; 5 ml) for 5 hr. The EtOH was removed and the residue diluted with water and extracted with ether (3 × 30 ml). The extract was evaporated to give a crystalline solid (**2**, 526 mg) which was recrystallized from EtOH, m.p. 138–139°, $[\alpha]_D + 1.3°$ (*c*, 1 in $CHCl_3$). (Found: C, 79.38; H, 9.29. $C_{20}H_{28}O_2$ requires: C, 79.95; H, 9.39%); *m/e* 300.2085 (100%; $C_{20}H_{28}O_2$ requires: 300.2089), 285 (7%), 282 (28%), 272 (100%), 267 (21%), 257 (75%), 243 (28%), 229 (56%), $\lambda_{max}^{MeOH}$ 302 nm, $\epsilon$ 64.

*Deuterium exchange experiment.* Na (20 mg) was dissolved in $CD_3OD$ (1 ml) and $D_2O$ (0.5 ml), and **2** (6 mg) was then added. The mixture was heated at 70° in sealed tube for 24 hr. After removal of $CD_3OD$, $D_2O$ (2 ml) was added and the suspension acidified with 1M DCl in $D_2O$. Ether extraction and evaporation of the solvent gave a residue (4 mg) which was examined by mass spectrometry. A parent ion at *m/e* 301 revealed that only the OH group had suffered isotopic exchange.

*Reduction of **2** with sodium borohydride.* $NaBH_4$ (30 mg) was added to a soln of **2** (64 mg) in EtOH (10 ml) and the mixture was kept at room temp. for 1 hr. After dilution with water and destruction of excess borohydride by addition of AcOH, the soln was extracted with ether. Evaporation of the solvent gave 62 mg of solid material, which was shown (tlc) to be a mixture of two compounds. Chromatographic separation (tlc on silica gel; $CHCl_3$–EtOH (99:1) as the solvent) allowed the isolation in pure form of the more abundant compound (30 mg), m.p. 158–159°, $[\alpha]_D - 1.6°$ (*c*, 1 in $CHCl_3$), MW 302 (MS); $\delta$ ($CDCl_3$) 5.97 (2H, m, H-1 and H-2), 5.33 and 5.28 (1H each, AB system, J = 10 Hz, H-13 and H-14), 4.0 (1H, s, H-11), 1.17 (3H, s, 16-Me), 1.10 (3H, s, 15-Me), 0.88 and 0.63 (3H each, d, J = 7 Hz, 19-Me and 20-Me).

*Catalytic hydrogenation of* **2**. **2** (190 mg) was hydrogenated over Pd/C (20 mg) in EtOH (10 ml) at room temp. and 1.5 atm for 12 hr. After removal of the catalyst and evaporation of the solvent, the residue was chromatographed (tlc; benzene–ether 9:1 as the eluent) thus giving two compounds. The less polar compound (**5**, mixture of diastereoisomers) had molecular formula $C_{20}H_{32}O$ ($M^+$ 288), while the more polar (**4**) had formula $C_{20}H_{32}O_2$ ($M^+$ 304), $[\alpha]_D + 5.1°$ (*c*, 1 in $CHCl_3$) $\nu_{max}$ 3480 and 1686 $cm^{-1}$, $\delta$ ($CCl_4$), 1.22 (3H, s, 16-Me), 0.92 (3H, s, 15-Me), 0.91 and 0.79 (3H each, d, J = 6 Hz, 19-Me and 20-Me).

*Acetylation of* **2**. **2** (76 mg) and acetyl chloride (1.5 ml) in anhyd. xylene (10 ml) was heated to reflux for 4 hr. Evaporation and tlc (benzene–ether 7:3) gave **6** (27 mg) m.p. 131–133° (EtOH); MW 342 (MS); $[\alpha]_D - 46°$ (*c*, 1 in $CHCl_3$); IR $\nu_{max}$ 1750 and 1718 $cm^{-1}$; $\delta$ ($CDCl_3$) 6.35 (1H, bd, J = 10 Hz, H-1), 5.60 (1H, bd, J = 10 Hz, H-2), 5.52 and 5.39 (1H each, AB quartet, J = 10 Hz, H-13 and H-14), 1.99 (3H, s, $CH_3$–C=O), 1.37 (3H, s, 16-Me), 1.25 (3H, s, 15-Me), 0.86 and 0.64 (3H each, d, J = 7 Hz, 19- and 20-Me).

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