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Synthetic Photochemistry. XXI.[1] The Sensitized Photooxygenation of Calarene. A Facile Hock Cleavage of an Allylhydroperoxide and Structure Revision for Aristolenols

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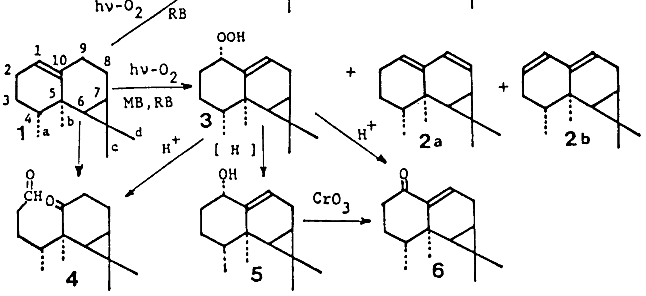
Synopsis. An allylic hydroperoxide formed by the sensitized photooxidation of calarene causes a Hock cleavage. A revised stereochemistry of an aristolenol is given on the basis of the direction of oxygenation.

Calarene (**1**),[2] an unconjugated vinyl cyclopropane, should be incapable of forming a dioxetane in a sensitized photooxygenation,[3] but its structural complexity may reveal some other features in the reactions. In fact, a keto aldehyde formed in the Methylene Blue (MB)-sensitized photooxidation of **1** was a Hock cleavage product.

When **1** and MB were irradiated in a mixture of chloroform and methanol (30 : 1) under an oxygen atmosphere by means of a tungsten lamp, a neat reaction occurred. The silica gel column separation of products yielded, together with an inseparable mixture of aristoladienes (**2a** and **2b**),[4,5] an allylic hydroperoxide (**3**), the major product, and a keto aldehyde (**4**). The separation of **2** from the hydrocarbon mixture was achieved by silver nitrate-impregnated silica-gel chromatography, and it was shown that the selenium dioxide oxidation of **1** also gave **2**. The structure of **3**, a colorless oil, was obtained by NMR [δ:[6] 0.59—0.85 (2H, m), 1.00 (3H, d, J=7 Hz), 1.03 (6H, s), 1.15 (3H, s), 1.1—2.7 (7H, m), 4.28 (1H, m), 5.56 (1H, m), and 7.62 (1H, s, OOH)] spectroscopy and chemical correlations; the sodium borohydride reduction of **3** yielded an oily allylic alcohol (**5**), which was further converted to an α,β-unsaturated ketone (**6**).[4] On the other hand, **4** was identical with the osmium(VIII) oxide-oxidation product of **1**. However, the photochemical formation of **4** is not related to a dioxetane; it was formed from **3** by either a contact with an acidic silica gel for 8 h or gentle heating in a chloroform solution, indicating it to be a Hock-cleavage product.[7,8]

Next, the Rose Bengal (RB)-sensitized oxygenation of **1** in a mixture of methanol and chloroform (1 : 30) mainly produced an ene-reaction product; a work-up after the sodium borohydride reduction yielded **5** (67%) and another allylic alcohol (**7**) (8.5%), which was subsequently oxidized to a known 1(10)-aristolen-2-one (**8**).[9-11] The stereochemistry of the hydroxy group of **7** is likely to be α-equatorial, judging from the large spin splittings revealed in its NMR spectrum, but it would be difficult to conclude the point from the limited evidence available at present. The absence of *cis*-glycol in this case also ruled out the intermediacy of dioxetane.[12] An attempted oxygenation in the dark resulted in the complete recovery of the starting material.



Scheme 1.

For the structure of crystalline allylic alcohol, **A** (designated as **1** in the original paper[4]), isolated from *Nardostachys chinensis* Betalin, Rücker and Kretzchmar have given the structure that we have assigned to **5**. However, the NMR spectrum of **5** taken in dimethyl-d_6 sulfoxide was different from that of **A**,[13] and so **5** might be an isomer of **A**. Mainly, the formulation **A** was deduced from the conformational analysis of the equatorial hydroxyl group. However, for the preferable conformation, an alternative may be possible. On the other hand, the β-configuration of the *gem*-dimethyl cyclopropane ring should prohibit the sterically hindered β-side attack of the oxygen, much as in the case of 2-carene.[14,15] This was supported by the chemical-shift difference for the methyl groups[16,17] on the ring-juncture of **3**, **5**, and **6**; two of the three sets of chemical-shift differences for the singlet methyls between **3** and **5**, $\Delta\delta_n$(3–5), were very small, but $\Delta\delta_b$(3–5), the difference of between the lowest methyl signals which are ascribable to the angular methyls, was significantly large, 1.15—1.23=−0.08. The $\Delta\delta_b$(5–6) value, the difference between **5** and **6**, is +0.16 or +0.24, in accord with only the α-orientation for the oxygen function. Otherwise, the $\Delta\delta_b$(5–6) is estimated to be less than +0.02.

Experimental

MB-sensitized Photooxidation of 1. *a)*: Calarene[18] (**1**, 546 mg) was dissolved in MeOH (1 cm^3) and $CHCl_3$ (30 cm^3) containing MB (77 mg) and irradiated by means of a 500-W tungsten lamp under an oxygen atmosphere for 7 h. Then the mixture was chromatgraphed on a silica gel (Wako Gel C 200) column. From the fractions eluted by hexane we obtained hydrocarbons (**1** and **2**) (147 mg, 27%) and subsequently two colorless oils, **3** (108 mg, 30.5%) [Found: M.W., 236.1772. Calcd for $C_{15}H_{24}O_2$: 236.1776. ν: 3360 cm^{-1}] and **4** (48 mg, 13.5%)[M. W., 236.1802. Calcd for $C_{15}H_{24}O_2$: 236.1776. δ: 0.85 (3H, s), 0.89 (3H, d, J=7 Hz), 1.01 (3H, s), 1.25 (3H, s), 1.1—2.7 (11H, m), and 9.76 (1H, t, J=2 Hz). ν: 2720, 1730, 1710 cm^{-1}]. The hydrocarbon fractions were separated by the use of an $AgNO_3$-impregnated silica-gel column to give **1** (150 mg, 27%) and **2** (a colorless oil, 10 mg, 2.7%) [*m*/*e*, 202 (M$^+$). δ: 0.92 (3H, s), 0.96 (3H, s), 1.00

(3H, d, J=7 Hz), 1.10 (3H, s), 5.25 (1H, m), 5.6—5.9 (2H, m). ν: 1640, 1610, 980 cm^{-1}. $\lambda_{\max}^{\mathrm{hex}}$: 238 nm ($\varepsilon$=27000), 245 (28000)].

b): A mixture of MeOH (1 cm^3), $CHCl_3$ (30 cm^3), **1** (817 mg) and MB (77 mg) was irradiated by means of a tungsten lamp for 13 h under an oxygen atomsphere. The mixture was then diluted with water, extracted with ether, and treated with $NaBH_4$ (20 mg). Subsequent silica-gel chromatography of the product gave, besides the hydrocarbon mixture, two colorless oils **5** (260 mg, 50%) [Found: 220.1827. Calcd for $C_{15}H_{24}O$: 220.1827. δ: 0.5—0.9 (2H, m), 1.00 (3H, d, J=7 Hz), 1.02 (6H, s), 1.23 (3H, s), 1.0—2.6 (8H, m), 4.17 (1H, m), and 5.42 (1H, m). δ $(CD_3)_2SO$: 0.5—0.8 (2H, m), 0.92 (3H, d, J=6.5 Hz), 0.98 (6H, s), 1.17 (3H, s), 1.07—2.45 (7H, m), 3.98 (1H, m), 4.29 (1H, d, J=2.3 Hz), and 5.28 (1H, m). ν: 3370 cm^{-1}] and **6** (25 mg, 5%) [Found: 218.1672. Calcd for $C_{15}H_{22}O$: 218.1671. δ: 0.6—0.85 (2H, m), 0.99—1.07 (12H, overlapped four methyls), 1.6—2.4 (7H, m), and 6.39 (1H, m). ν: 1690, 1623 cm^{-1}]. Further $AgNO_3$–silica-gel chromatography of the hydrocarbon fractions yielded **1** (333 mg, 41%) and **2** (32 mg, 6.7%).

SeO_2 Oxidation of 1 to 2. To a dioxane solution (15 cm^3) of **1** (175 mg), freshly sublimed SeO_2 (120 mg) was added, after which the mixture was refluxed for 1 h. Then, powdered $Na_2S_2O_3$ was added to the mixture. After the removal of the Se (50 mg) by filtration, the mixture was chromatographed on silica gel to get a hydrocarbon mixture (150 mg). $AgNO_3$-impregnated silica-gel chromatography gave recovered **1** (4 mg) and **2**, a colorless oil (127 mg, 74%). The sample of **2** was identical with those obtained by the photooxygenations (NMR, $AgNO_3$–silica gel, and gas-liquid chromatogram[19]).

RB-sensitized Photooxidation of 1. A mixture of MeOH (1 cm^3), $CHCl_3$ (30 cm^3), **1** (253 mg), and RB (30 mg) was irradiated by means of a tungsten lamp for 8.5 h. After treatment with $NaBH_4$ (50 mg), the mixture was chromatographed on a silica-gel column to give **5** (100 mg, 67%), **7** (colorless crystals, mp 84—86 °C (23 mg, 15%) [M. W., 220.1838. Calcd for $C_{15}H_{24}O$: 220.1827. δ: 0.47—0.8 (2H, m), 0.92 (6H, s), 0.95 (3H, d, J=7 Hz), 1.05 (3H, s), 3.93 (1H, br. m, $W_{h/2}$=14 Hz), 4.51 (1H, d, J=5.5 Hz), and 5.15 (1H, m). ν: 3620—3000 cm^{-1}]) and the recovered **1** (114 mg, 45%).

Conversion of 3 to 4. *a)*: To a hexane solution (5 cm^3) of **3** (25.4 mg), silica gel (Wako Gel C 200, 5 g) was added after which the mixture was kept at room temperature for 7 h. Subsequent extraction with ether gave **4** (12.3 mg).

b): A $CHCl_3$ solution (4 cm^3) of **3** (22.3 mg) was refluxed for 20 min. Subsequent evaporation of the solvent *in vacuo* gave **4** (22 mg).

Osmium(VIII) Oxide Oxidation of 1 to 4. To a solution of **1** (93 mg) in MeOH (5 cm^3), OsO_4 (100 mg) was added, after which the mixture was kept for 24 h. After treatment with $NaIO_4$ (215 mg) and H_2S, the mixture was chromatographed on a silica-gel column to give **4** (43 mg, 40%) which was identical with the sample of photochemical origin.

Jones Oxidation of 5 to Give 6. To a solution of CrO_3 (61 mg) and H_2SO_4 (1 cm^3) in acetone (10 cm^3), **5** (40 mg) was added. After 5 min, the mixture was treated with 2-propanol and extracted with ether. The colorless oil obtained by silica-gel column chromatography was **6**[4] (9 mg, 22%).

Jones Oxidation of 7 to Give Aristolenone (8). Similarly, **7** (12.1 mg) was dissolved in acetone (10 cm^3) containing CrO_3 and H_2SO_4, after which the mixture was oxidized for 5 min. Then, the mixture was treated with 2-propanol and extracted with ether. Silica-gel chromatography of the extract gave colorless crystals (mp 46—47 °C (lit, 39—42 °C,[9] 46.5—47.5 °C[10])), identified as **8** (5.6 mg, 46%), whose NMR NMR [δ: 0.68 (1H, d, J=9 Hz), 0.96 (3H, s), 1.02 (3H, s), 1.06 (3H, d, J=7 Hz), 1.0—2.6 (8H, m), 1.23 (3H, s), and 5.72 (1H, m)] were in accord with the previously reported figures.[9,10]

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5) One of the isomers (**2b**) has been isolated from *Nardostachys chinensis Betalin.*[4]

6) All the NMR spectra, otherwise specified, were obtained in $CDCl_3$ solutions, and the chemical shifts were expressed in δ values from the internal standard, Me_4Si.

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18) The starting material, **1**, was isolated from an unspecified luan oil, a generous gift of Professor Kyoichi Suga and Dr. Shoji Watanabe, Chiba University, to whom our thanks are due.

19) Gas-liquid chromatography on a glass capillary column (tricresyl phosphate at 115 °C) showed two peaks. However, **2** was rather unstable under the preparative chromatographic conditions. An attempted separation by means of a high-pressure liquid chromatograph (Micropolasil–hexane) was unsuccessful.