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

Hitoshi TAKESHITA,* Isao SHIMOODA, and Toshihide HATSUI

Research Institute of Industrial Science, 86, Kyushu University, Hakozaki, Fukuoka 812

(Received March 28, 1980)

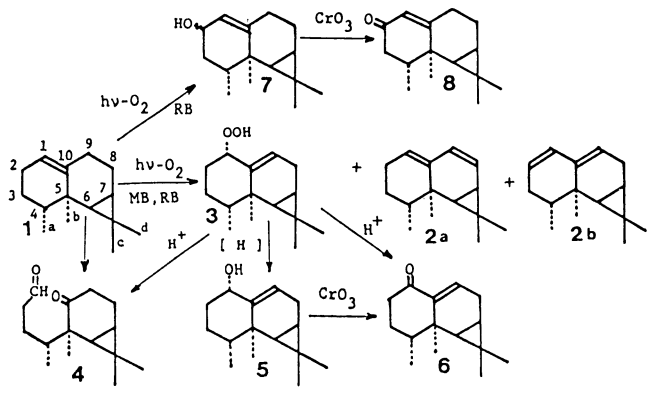
Synopsis. An allylic hydroperoxide formed by the sensitized photooxidation of calarene causes a Hock cleavage. A revised stereochemistry of an aristolenol is given on the basis of the direction of oxygenation.

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.

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.



Scheme 1.

Experimental

MB-sensitized Photooxidation of 1. a): Calarene[18] (**1**, 546 mg) was dissolved in MeOH (1 cm³) and $CHCl_3$ (30 cm³) 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}. λ_{max}^{hex}: 238 nm (ε=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]

References

1) Part XX: H. Takeshita, I. Shimooda, and T. Hatsui, *Kyushu Daigaku Sogo Rikogaku Kenkyuka Hokoku*, **2**, 23 (1980).

2) G. Buchi, F. Grenter, and T. Tokoroyama, *Tetrahedron Lett.*, **1962**, 827.

3) For a verification of the dioxetane intermediate in the singlet-oxygen oxidation of the vinylcyclopropanes, see H. Takeshita, T. Hatsui, and H. Mametsuka, *Heterocycles*, **11**, 323 (1978).

4) G. Rücker and U. Kretzuschmar, *Ann. Chem.*, **748**, 214 (1971).

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.

7) G. O. Schenck and K. H. Schulte-Elte, *Ann. Chem.*, **618**, 185 (1958).

8) K. Gollnick, "Advances in Photochemistry," **6**, 1 (1968).

9) G. Rücker, *Ann. Chem.*, **717**. 221 (1968).

10) R. Nishida and Z. Kumazawa, *Agric. Biol. Chem.*, **37**, 341 (1973).

11) G. Rücker and U. Kretzschmar, *Ann. Chem.*, **748**, 211 (1971).

12) H. Takeshita and T. Hatsui, *J. Org. Chem.*, **43**, 3080 (1978).

13) We are grateful to Professor G. Rücker for sending us copies of the spectral charts of **A** and the related compounds.

14) K. Gollnick and G. Schade, *Tetrahedron Lett.*, **1966**, 2335.

15) H. Takeshita and I. Kouno, *Kyushu Daigaku Seisan Kagaku Kenkyusho Hokoku*, **65**, 13 (1977).

16) a) W. Zürcher, *Helv. Chim. Acta*, **44**, 1380 (1961); **46**, 2054 (1963).

17) K. Tori and K. Aono, *Ann. Rept. Shionogi Research Lab.*, **14**, 136 (1964).

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.