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Mori, Akira
Institute of Advanced Material Study Kyushu University

Takeshita, Hitoshi
Institute of Advanced Material Study Kyushu University

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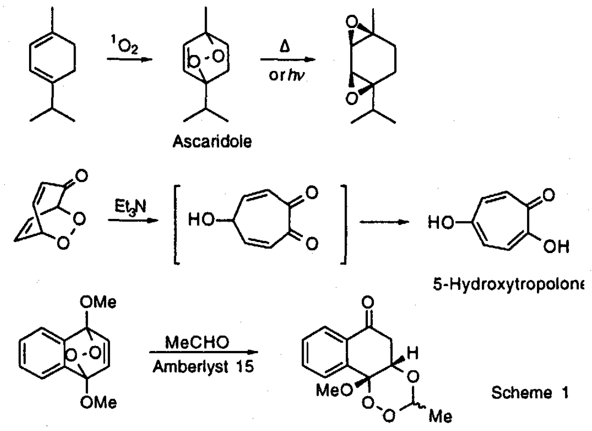
Acid-Catalyzed Rearrangement of Tropone Endoperoxides. An 8,9-Dioxabicyclo[3.2.2]nona-3,6-diene Derivative to an 8-Oxabicyclo[3.2.1]octane Derivative

Akira MORI and Hitoshi TAKESHITA

Tropone endoperoxides rearranged to 8-oxabicyclo[3.2.1]octane derivatives by acid. In *m*-chloroperbenzoic acid-oxidation, an epoxy ring would assist the O-O bond cleavage to give a γ-hydroxyketone, which cyclized to 8-oxabicyclo[3.2.1]octane derivatives.

Bicyclic endoperoxides, which are easily accessible by the [4+2] addition of singlet oxygen to cyclic 1,3-dienes, have been paid much attentions in respect with theoretical, preparative, and biological points of view.1) The fascinating endoperoxide-diepoxide rearrangement has been observed in the transformation of ascaridole to the diepoxide.2) Adam and Balci3) have utilized the endoperoxide-diepoxide rearrangement to synthesize three trioxides of 1,3,5-cycloheptatriene.4) Base-catalyzed rearrangements of endoperoxides have provided γ-hydroxy-α,β-unsaturated ketones, which gave enediones by oxidation, as observed in the reaction of tropone endoperoxide to 5-hydroxytropolone.5)



Scheme 1

On the other hand, acid-catalyzed rearrangements of endoperoxides have been postulated in anthracene systems to give a mixture of *o*- and *p*-quinones and the aldehyde ester.6) Jefford et al. have observed that the endoperoxide of 1,4-dimethoxynaphthalene reacted with carbonyl compounds to give 1,2,4-trioxanes in the presence of amberlyst-15 resin as catalyst.7) In this paper, we will report the acid-catalyzed rearrangement of an 8,9-dioxabicyclo[3.2.2]nona-3,6-diene derivative to an 8-oxabicyclo[3.2.1]octane derivative, which was found in the epoxidation and acetalization reactions of tropone endoperoxides.

When 8,9-dioxabicyclo[3.2.2]nona-3,6-diene-2-spiro-2'-dioxolane (**1**)8) was oxidized with *m*-chloroperbenzoic acid (*m*-CPBA, 2.8 equiv.) in chloroform, three products (**2**, **3**, and **4**) were obtained in 46, 7 and 7 % yields, respectively. The structure of the main product **2** was determined by the spectral data; the ^{1}H-NMR spectrum indicated the presence of an epoxide ring and a double bond. The IR spectrum showed an absorption band at 3470 cm^{-1}. The ^{13}C-NMR spectrum revealed two olefinic carbon atoms, two acetal carbon atoms at δ 100.5 (s) and 102.6 (s), and two acetal carbon atoms at δ 66.1 (t) and 66.5 (t) as well as two epoxide ring carbons at δ 51.5 (d) and 57.1 (d). These data implied that the structure of **2** must be a bicyclo[3.2.1]octane derivative. The coupling constant (9.5 Hz) of the olefinic protons indicated that the double bond should locate in the six-membered ring. The stereochemistry of the epoxide ring was assigned to be *exo* from the coupling pattern of the epoxide ring protons at δ 3.63 (d, J=3.2 Hz) and 3.70 (d, J=3.2 Hz). The compound **2** afforded the acetate (**5**) in 78% yield by a typical acetylation procedure.

The structures of the minor products **3** and **4** were determined to be the diepoxide from the spectral data: the stereochemistry of **3** was assigned to be *syn* by the comparison with the coupling constants of the *syn*-diepoxide (**6**)9) of 8-oxabicyclo[3.2.1]oct-2-one. The remaining **4** was, therefore, the *anti*-diepoxide.

The similar skeletal rearrangement has been observed in the preparation of **1** from 8,9-dioxabi-

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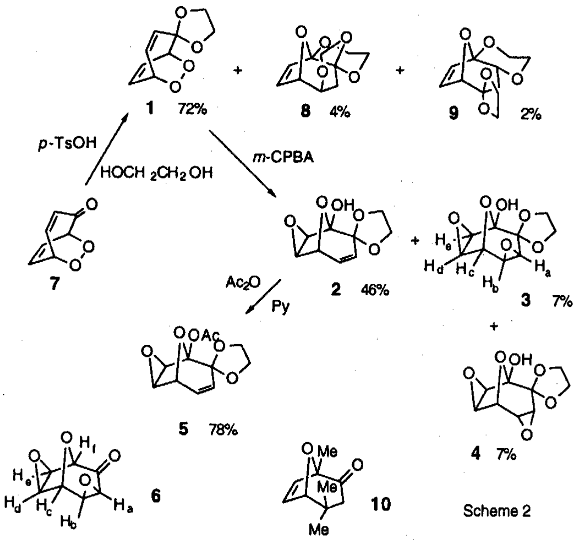
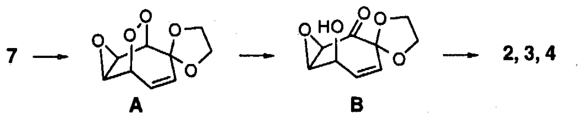
cyclo[3.2.2]nona-3,6-dien-2-one (**7**);[8] when **7** was allowed to react with ethylene glycol in benzene in the presence of *p*-TsOH, **1** was obtained in 72% yield as well as two bisacetals (**8** and **9**) in 4 and 2% yields, respectively. The ^{1}H-NMR spectrum of **8** showed two methylene protons besides two ethylene glycol moieties at δ 1.84 (dm, J=15.5 Hz) and 2.32 (dd, J=15.5, 6.0 Hz) and two olefinic protons at δ 6.09 and 6.42, which coupled each other with the coupling constant of 6.0 Hz. The latter further showed a splitting with the coupling constant of 2.0 Hz. These coupling patterns were quite similar to those of 1,4,4-trimethyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**10**),[10] in which two olefinic protons appeared at δ 6.30 (d, J=6 Hz) and 6.35 (dd, J=6, 2 Hz) and the bridgehead proton at δ 4.37 as a broad signal. The IR spectrum of **8** showed no OH and CO absorption bands. From these data, the structure of **8** was determined as shown in the Scheme 2. The second product **9**, which had the similar spectral data to **8**, was also as a bisacetal derivative. The structure of **9** should be as shown in Scheme 2.



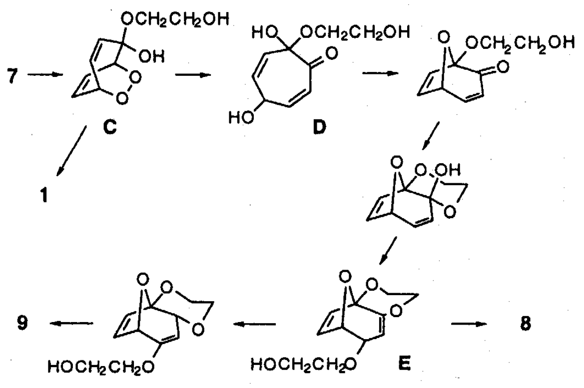
Scheme 2

Since *m*-CPBA oxidation was inert to **7**, the presence of the 1,3-dioxolane ring of **1** was essential to epoxidation, which induced the rearrangement of the 8,9-dioxabicyclo[3.2.2]nonadiene system to the 8-oxabicyclo[3.2.1]octene system. The first epoxidation would occur at the less hindered and the more electron rich double bond from the *exo* direction to give the epoxyendoperoxide **A**. The following O-O bond cleaved to give ketol **B**, which led to **2**, **3**, and **4**. This type of O-O bond cleavage is, however, commonly observed in base-catalyzed reactions. We speculated that the epoxy ring would assist the O-O bond cleavage.

Finally, it is worth discussing acetalization of **7**; ethylene glycol would attack the carbonyl group to give the intermediate **C**, which led to **1**. The OCH_2CH_2OH group would assist the O-O bond cleavage to form the γ-hydroxyketone (**D**), which led to the intermediate **E** *via* dehydration and ring formation processes. From **E**, the minor products **8** and **9** were formed. Thus, we succeeded to prepare poly-oxygenated molecules by *m*-CPBA-oxidation of the tropone endoperoxide **1**.



Scheme 3



Scheme 4

Experimental

Elemental analyses were performed in this Institute, Kyushu University. The mps were measured with a Yanagimoto Micro mp apparatus and are not corrected. The NMR spectra were measured by JEOL FX 100 and GSX 270H spectrometers in $CDCl_3$, unless otherwise specified, and the chemical shifts expressed were in δ units. Mass spectra were measured with a JEOL 01SG-2 spectrometer. The IR spectra were taken as KBr disks for crystalline compounds or as liquid films inserted between NaCl plates for oily materials using a JASCO IR-A 102 spectrometer. The UV spectra were measured using Hitachi U-3200 and U-3410 spectrophotometers. The stationary phase for the column chromatography was Wakogel C-300 and the elution solvents were mixtures of hexane and ethyl acetate.

***m*-CPBA-Oxidation of 8,9-Dioxabicyclo[3.2.2]nona-3,6-diene-2-spiro-2'-dioxolane (1).** A chloroform solution (17 cm^3) of **1** (503 mg) and *m*-CPBA (1.348 g, 85% purity, 2.8 equiv.) was refluxed for 13 h. The precipitate was filtered and the filtrate was chromatographed on a silica-gel column to give **2** (272 mg, 46%), **3** (39 mg, 7%), and **4** (43 mg, 7%).

2: mp 145-147 °C. ^{1}H-NMR: δ=3.63 (1H, d, *J*=3.2 Hz), 3.70 (1H, d, *J*=3.2 Hz), 3.8-4.2 (4H, m), 4.46 (1H, d, *J*=4.0 Hz), 5.66 (1H, d, *J*=9.5 Hz), and 6.26 (1H, dd, *J*=9.5, 4.0 Hz). ^{13}C-NMR: δ=51.5 (d), 57.1 (d), 66.1 (t), 66.5 (t), 72.2 (d), 100.5 (s), 102.6 (s), 130.3 (d), and 133.0 (d). IR: ν 3470, 1645, 1385, 1370, 1265, 1195, 1180, 1035, 1015, 955, 930, 870, 830, and 790 cm^{-1}. MS m/z 198 (M$^+$, 0.55), 197 (3), 169 (51.5), 154 (11), 153 (100), 98 (54.1), and 81 (79.3). Found: C, 54.50; H, 5.10%. Calcd for $C_9H_{10}O_5$: C, 54.54; H, 5.09%.

3: mp 175-177 °C. ^{1}H-NMR: δ=3.03 (H, dd, *J*=4.0, 1.7 Hz), 3.38 (1H, d, *J*=4.0 Hz), 3.6-3.8 (2H, m), and 3.9-4.3 (6H, m). δ (CD$_3$OD) =3.04 (1H, dd, *J*=4.0, 1.7 Hz), 3.3 (1H, overlapped with CD$_3$OD), 3.63 (1H, d, *J*=3.0 Hz), 3.76 (1H, d, *J*=3.0 Hz), and 3.8-4.2 (5H, m). ^{13}C-NMR: δ=ca.49 (overlapped with CD$_3$OD), 52.7, 54.3, 55.0, 65.8, 66.9, 79.1, 99.9, and 102.0. IR: ν 3325, 1390, 1210, 1145, 1025, 890, and 860 cm^{-1}. MS m/z 215, 214 (M$^+$), 213, 197, 185, 113. Found: 214.0491. Calcd for $C_9H_{10}O_6$: 214.0477.

4: mp 156-157 °C. ^{1}H-NMR: δ=3.20 (1H, d, *J*=4.0 Hz), 3.60 (1H, d, *J*=3.2 Hz), 3.66 (1H, d, *J*=3.2 Hz), 3.62 (OH, D$_2$O exchangeable), 3.68 (1H, dd, *J*=4.2, 4.0 Hz), 4.0-4.3 (4H, m), and 4.54 (1H, d, *J*=4.2 Hz). ^{13}C-NMR: δ=51.3 (d), 51.5 (d), 53.3 (d), 55.4 (d), 66.5 (t), 67.0 (t), 71.6 (d), 99.9 (s), and 103.2 (s). IR: ν 3350, 1390, 1355, 1210, 1170, 1050, 1017, 967, 867, 830, and 793 cm^{-1}. Found: C, 50.18; H, 4.66%. Calcd for $C_9H_{10}O_6$: C, 50.37; H, 4.71%.

***m*-CPBA-Oxidation of 8,9-Dioxabicyclo[3.2.2]nona-3,6-dien-2-one (7).** A chloroform solution (18 cm^3) of **7** (496.5 mg) and *m*-CPBA (1.756 g) was refluxed for 15 h. The ^{1}H-NMR spectrum of the mixture was identical with that of **7**.

Acetylation of 2. Compound **2** (21.5 mg) was stirred in a mixture of acetic anhydride (0.5 cm^3) and pyridine (0.5 cm^3) at room temperature overnight. The mixture was poured into water and extracted with chloroform. After the evaporation of solvent, the residue was recrystallized with methanol to give **5** (20.4 mg, 78%).

5: mp 145-145.5 °C. ^{1}H-NMR: δ=2.16 (3H, s), 3.72 (1H, d, *J*=3.0 Hz), 3.8-4.2 (4H, m), 4.40 (1H, d, *J*=3.0 Hz), 4.51 (1H, d, *J*=4.0 Hz), 5.63 (1H, d, *J*=9.5 Hz), and 6.26 (1H, dd, *J*=9.5, 4.0 Hz). ^{13}C-NMR: δ=21.8 (q), 51.1 (d), 58.2 (d), 65.8 (t), 66.5 (t), 71.8 (d), 103.2 (2C, s), 131.3 (d), 131.7 (d), and 167.4 (s). IR: ν 1760, 1055, 1025, and 958 cm^{-1}. Found: C, 54.83; H, 5.26%. Calcd for $C_{11}H_{12}O_6$: C, 55.00; H, 5.04%.

Acetalization of 7. A benzene solution (8 cm^3) of **7** (102 mg), ethylene glycol (1.5 cm^3), and *p*-TsOH was refluxed for 7 h with azeotropic removal of water. The mixture was then washed with aq. NaCl and water and the aq. layer was extracted with chloroform. The combined solvent was removed to give the residue, which was chromatographed on a silica-gel column to give **1** (97 mg, 72%), **8** (7 mg, 4%), and **9** (3.5 mg, 2%).

8: mp 98.5-101 °C. ^{1}H-NMR: δ=1.84 (1H, dm, *J*=15.5 Hz), 2.32 (1H, dd, *J*=15.5, 6.0 Hz), 3.54 (1H, dm, *J*=6.0 Hz), 3.6-4.5 (8H, m), 4.60 (1H, t, *J*=2.0 Hz), 6.09 (1H, d, *J*=6.0 Hz), and 6.42 (1H, dd, *J*=6.0, 2.0 Hz). ^{13}C-NMR: δ=37.2 (t), 62.0 (t), 64.9 (t), 65.2 (t), 66.4 (t), 70.2 (d), 83.3 (d), 103.6 (s), 105.5 (s), 133.3 (d), and 136.1 (d). Found: C, 58.25; H, 6.26%. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H. 6.24%.

9: mp 111-112 °C. ^{1}H-NMR: δ=1.79 (1H, dd, *J*=12.8, 10.5 Hz), 2.03 (1H, ddd, *J*=12.8, 6.5, 1.5 Hz), 3.45 (1H, dd, *J*=10.5, 6.5 Hz), 3.7-4.1 (8H, m), 4.40 (1H, br s), and 6.55 (2H, s). ^{13}C-NMR: δ=35.4 (t), 64.8 (t), 65.2 (t), 65.5 (t), 66.6 (t), 72.2 (d), 82.2 (d), 106.2 (s), 129.9 (d), and 134.9 (d). Found: C, 58.19; H, 6.23%. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H. 6.24%.

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