

SELECTIVE CLEAVAGE OF POLYCYCLIC CYCLOPROPANES BY ELECTROCHEMICAL OXIDATION

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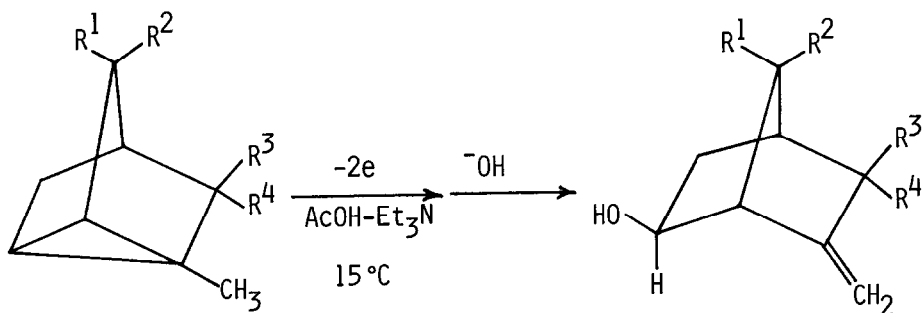
Summary: Anodic Oxidation in acetic acid of polycyclic cyclopropanes, namely tricyclene, cyclofenchene, and longicyclene, followed by hydrolysis brought about stereo- and regioselective formation of the corresponding homoallylic alcohols as the main product in good yields.

Extensive studies<sup>1,2</sup> have been focused on oxidative cleavage of cyclopropane rings by electrochemical methods in recent years because of unique reactivity of the strained  $\sigma$ -bonds, easy availability of cyclopropyl compounds and much usefulness of the products in organic synthesis.

In this study, we wish to report stereo- and regioselective cleavage of naturally-occurring polycyclic methylcyclopropanes **1a-c** by anodic oxidation in acetic acid followed by hydrolysis to give the corresponding homoallylic alcohols **2a-c** as the main product in good yields. The present electrochemical method can also provide with a facile and efficient synthesis of *exo*-2,2-dimethyl-3-methylenebicyclo[2.2.1]heptane-5-ol (**1a**)<sup>3</sup>, named as "Nojigiku Alcohol", which was isolated from the essential oil of *chrysanthemum japonense*<sup>4</sup>, and has been shown to be of much use as an important olfactory component of floral perfume and fragrance composition<sup>5</sup>.

A typical procedure was as follow: Into 80ml of glacial acetic acid containing 3.03 g (0.03 mole) of triethylamine was added 2.72 g (0.02 mole) of tricyclene (**1a**), and the solution was electrochemically oxidized in an undivided cell equipped with carbon rod electrodes as an anode and a cathode at 25-30°C with stirring under the constant-current conditions (current density; 17-20 mA/cm<sup>2</sup>). After 4.0 F/mol of electricity was passed through the system, the mixture was worked up according to usual procedure to give ca. 2.80 g of an oily material, which was subsequently subjected to base-catalyzed hydrolysis. Fractional distillation, column chromatography (silica gel, elute: hexane-ethyl

acetate(6:1) and/or a preparative gas chromatography(column:5% PEG-20M 2m) of the product mixture gave *exo*-2,2-dimethyl-3-methylenebicyclo[2.2.1]heptan-5-ol (**2a**)<sup>3</sup> in a 70% yield, accompanied with small amounts of the *endo* isomer(**3a**)<sup>6</sup> (8% yield) of **2a**, 2,2,3-trimethylbicyclo[2.2.1]heptan-3,5 $\beta$ -diol(**4a**) (8% yield)<sup>7,8</sup> and 2,2,3-trimethylbicyclo[2.2.1]heptan-3,5 $\alpha$ -diol(**5a**) (3% yield)<sup>7,8</sup>. Anodic oxidation of **1a** at 15°C brought about some increase in the yield of **2a** up to 76%.



**1a**: R<sup>1</sup>=R<sup>2</sup>=H, R<sup>3</sup>=R<sup>4</sup>=CH<sub>3</sub> (tricyclene)

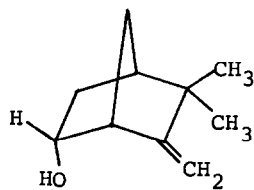
**2a**: Y=76%

**b**: R<sup>1</sup>=R<sup>2</sup>=CH<sub>3</sub>, R<sup>3</sup>=R<sup>4</sup>=H (cyclofenchene)

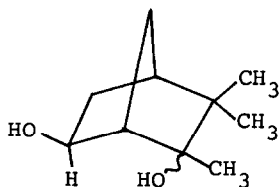
**b**: Y=77%

**c**: R<sup>1</sup>=H, R<sup>4</sup>=CH<sub>3</sub> R<sup>2</sup>-R<sup>3</sup>=-C(CH<sub>3</sub>)<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-  
(longicyclene)

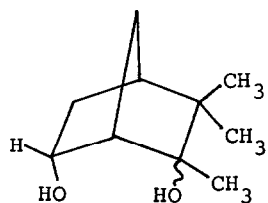
**c**: Y=85%



**3a** (8%)



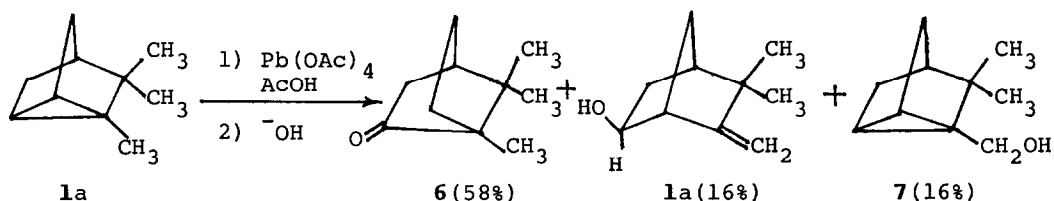
**4a** (8%)



**5a** (3%)

Similarly, electrochemical oxidation of cyclofenchene(**1b**) and longicyclene (**1c**) afforded *exo*-7,7-dimethyl-2-methylenebicyclo[2.2.1]heptan-6-ol(**2b**)<sup>7</sup> and *exo*-3,3,7-trimethyl-8-methylenetricyclo[5.4.0.0<sup>2,9</sup>]undecan-10-ol(**2c**)<sup>7</sup> in 77% and 85% yields, respectively.

The present electrochemical oxidation shows sharp contrast to conventional oxidation using a metal-salt oxidizing agent. Thus, oxidation of tricyclene (**1a**) in acetic acid with lead tetracetate followed by hydrolysis gave camphor (**6**), nojigiku alcohol(**2a**) and tricyclenyl alcohol(**7**) as principle products in 58%, 16% and 16% yields, respectively.<sup>9</sup> Therefore, high stereo- and regio-selectivities in cleavage of a carbon-carbon bond of a cyclopropane ring in polycyclic compounds **1a-c** may be noteworthy in this anodic oxidation, though the detail of these selectivities does not seem simple.



As one of attractive explanation for the regioselectivity, it may be proposed that higher electron density<sup>10</sup> of the more substituted carbon-carbon bond of the cyclopropane ring of 1a-c takes the most important role and the second effect seems steric repulsion<sup>11</sup> between the bulky dialkyl group of 1a-c and an anode on electron transfer from the substrate to the anode.

Stereoselective formation of an *exo* olefinic alcohol 2a-c may be elucidated by generation of a norbornyl-type cationic intermediate after electron transfer, followed by predominant *exo*-attack of an acetate anion from the reverse side toward the carbon-carbon bond to be cleaved, as is well conceived in solvolysis of *exo*-2-norbornyl brosylate.<sup>12</sup> It may be also interesting that the homoallylic alcohols possessing an *exo*-methylene group, 2a and 3a, were obtained preferentially in comparison with little formation of saturated dialcohols, 4a and 5a ( the ratio of [2a + 3a]/[4a + 5a] : ca. 7/1).

Finally, from the viewpoint of high selectivity, good yield, practical utility of products and simplicity of procedure, the present electrochemical oxidation may give a useful technique in synthetic organic chemistry.

#### References and Notes

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3. For hitherto known methods for synthesis of 2a, see a) H. G. Richery, T. G. Garbacik, D. L. Dull, and J. E. Grant, *J. Org. Chem.*, **29**, 3095 (1964); b) D. G. Patil, J. S. Yadav, H. P. S. Chawla, and S. Dev, *Indian J. Chem., Sect. B*, **22**, 183 (1983); c) M. Gaionde, P. A. Vakencherry and S. Dev, *Tetrahedron Lett.*, **1964**, 2007.
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5. Kuraray Co. Ltd. and Osaka City, *Japan Kokai Koho* 84-155308.
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7. All of the products isolated in this study were identified by comparison of their gas chromatographic and spectroscopic behaviors with those of authentic

samples<sup>3,6</sup> or by spectroscopic analyses.

- 4a:** mp 143-144°C; <sup>1</sup>H-NMR(CDCl<sub>3</sub>, ppm) δ 0.82, 0.97 (two s, 6H, gem-CH<sub>3</sub>), 1.08 (d.d.d., 1H, J=3.5, 7.0, 14.0 Hz, C<sub>7</sub>-H<sub>syn</sub>), 1.13 (s, 3H, C<sub>3</sub>-(OH)CH<sub>3</sub>), 1.42, 2.00 (m, 2H, C<sub>6</sub>-H<sub>2</sub>), 1.69 (d.d, 1H, J=1.5, 3.5 Hz, C<sub>1</sub>-H), 1.91 (s, 1H, C<sub>4</sub>-H), 2.09 (d.d.d, 1H, J=3.5, 7.0, 14.0 Hz, C<sub>7</sub>-H<sub>anti</sub>), 3.94 (d.d, 1H, J=1.5, 7.0 Hz, C<sub>5</sub>-(OH)H); <sup>13</sup>C-NMR(CDCl<sub>3</sub>, ppm) δ 21.61 (q, CH<sub>3</sub>), 23.65, 25.46 (two q, gem-CH<sub>3</sub>), 31.18 (t, C<sub>7</sub>), 37.14 (t, C<sub>6</sub>), 43.74 (s, C<sub>2</sub>), 50.28 (d, C<sub>1</sub>), 60.79 (d, C<sub>4</sub>), 70.43 (d, C<sub>5</sub>), 78.95 (s, C<sub>3</sub>); IR(KBr) 3320, 1030 cm<sup>-1</sup> (-OH); MASS m/e 152 (M<sup>+</sup>-H<sub>2</sub>O), 137 (M<sup>+</sup>-H<sub>2</sub>O-CH<sub>3</sub>).
- 5a:** mp 105-108°C; <sup>1</sup>H-NMR(CDCl<sub>3</sub>, ppm) δ 0.89, 1.01 (two s, 6H, gem-CH<sub>3</sub>), 1.13 (s, 3H, C<sub>3</sub>-(OH)CH<sub>3</sub>), 1.73 (br. d, 1H, J=3.0 Hz, C<sub>1</sub>-H), 4.15 (d, 1H, J=6.5 Hz, C<sub>5</sub>-(OH)H); IR(KBr) 3320, 1045 cm<sup>-1</sup> (-OH); MASS m/e 155 (M<sup>+</sup>-CH<sub>3</sub>), 152 (M<sup>+</sup>-H<sub>2</sub>O), 137 (M<sup>+</sup>-H<sub>2</sub>O-CH<sub>3</sub>).
- 2b:** mp 60-62°C (3,5-dinitrobenzoate mp 115-116°C); <sup>1</sup>H-NMR(CDCl<sub>3</sub>, ppm) δ 0.94, 1.24 (two s, 6H, gem-CH<sub>3</sub>), 2.30 (d, 1H, J=6.0 Hz, C<sub>5</sub>-H), 3.95 (d.d, 1H, J=3.5, 8.0 Hz, C<sub>6</sub>-(OH)H), 4.72, 4.93 (two d.d, 2H, J=1.5, 4.0 Hz, =CH<sub>2</sub>); <sup>13</sup>C-NMR(CDCl<sub>3</sub>, ppm) δ 22.13, 22.83 (two q, gem-CH<sub>3</sub>), 35.86 (t, C<sub>5</sub>), 41.23 (t, C<sub>3</sub>), 45.73 (d, C<sub>4</sub>), 45.96 (s, C<sub>7</sub>), 61.96 (d, C<sub>1</sub>), 76.15 (d, C<sub>6</sub>), 105.76 (t, C<sub>2</sub>), 152.07 (s, C<sub>8</sub>); MASS m/e 152 (M<sup>+</sup>), 137 (M<sup>+</sup>-CH<sub>3</sub>), 134 (M<sup>+</sup>-H<sub>2</sub>O), 119 (M<sup>+</sup>-CH<sub>3</sub>-H<sub>2</sub>O).
- 2c:** mp 79-80°C (3,5-dinitrobenzoate mp 150-151°C); <sup>1</sup>H-NMR(CDCl<sub>3</sub>, ppm) δ 1.00 (three s, 9H, CH<sub>3</sub>), 2.64 (m, 1H, C<sub>9</sub>-H), 3.75 (m, 1H, C<sub>10</sub>-(OH)H), 4.55, 4.90 (two s, 2H, =CH<sub>2</sub>); <sup>13</sup>C-NMR(CDCl<sub>3</sub>, ppm) δ 21.14 (t, C<sub>10</sub>), 29.43, 30.31, 30.54 (three q, CH<sub>3</sub>), 31.59 (s, C<sub>8</sub>), 33.29 (s, C<sub>2</sub>), 36.91 (t, C<sub>9</sub>), 38.48 (t, C<sub>11</sub>), 43.21 (t, C<sub>6</sub>), 44.97 (d, C<sub>1</sub>), 57.52 (d, C<sub>7</sub>), 57.94 (d, C<sub>4</sub>), 74.46 (d, C<sub>5</sub>), 102.55 (t, C<sub>12</sub>), 163.22 (s, C<sub>3</sub>); IR(KBr) 3300, 1052 cm<sup>-1</sup> (-OH), 980, 882 cm<sup>-1</sup> (=CH<sub>2</sub>); MASS 220 (M<sup>+</sup>).
8. Although stereochemistry of the C<sub>3</sub>-hydroxyl group in 4a and 5a has not been determined as yet, gas chromatographic analysis indicated that both of products consist of their corresponding stereoisomers in the ratio of ca. 4/1 to 5/1.
9. H. Iwamuro, M. Kanehiro, O. Okabe, and Y. Matsubara, *Nippon Nogeikagaku Kaishi*, **57**, 1097 (1983).
10. It has been reported that a carbon-carbon bond of a cyclopropane ring with higher electron density is exclusively cleaved in anodic oxidation of bicyclic cyclopropyl compounds. See references 1a and 1b.
11. Stereoselectivity caused by steric repulsion between a bulky alkyl group and an electrode on electron transfer of a substrate to an anode has been observed in similar electrochemical oxidation. See a) T. Shono and A. Ikeda, *J. Am. Chem. Soc.*, **94**, 7892 (1972); b) L. Ebersson and H. Sternerup, *Acta Chem. Scand.*, **26**, 1431 (1972).
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