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A NOVEL ALLYLIC OXIDATION USING A COMBINATION OF FORMIC ACID AND SELENIUM DIOXIDE

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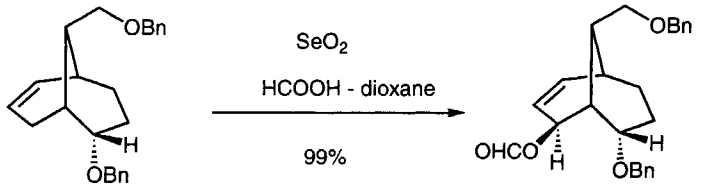
Abstract: A combination of formic acid and selenium dioxide in dioxane has been found to be an efficient system for the allylic oxygenation of olefins, in particular for sterically hindered ones, leading to the corresponding allylic alcohols or formates.

Although oxidation using selenium dioxide is one of the most efficient methods for the functionalization of the allylic carbon of olefinic compounds,[1] it is very sensitive to the stereochemical environment which sometimes brings about undesired side reactions or total recovery of starting materials when hindered substrates are employed.

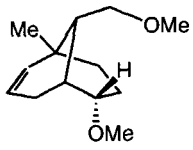
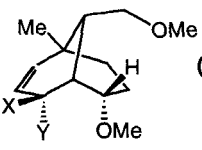
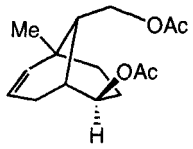
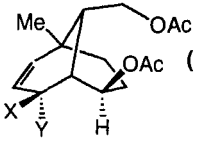
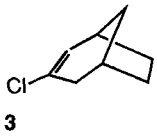
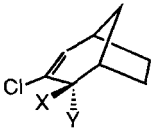
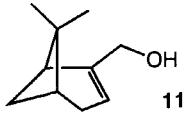
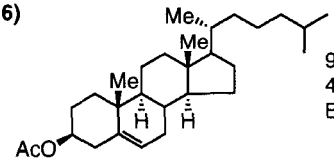
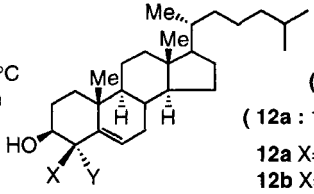
In the total synthesis of upial,[2,3] we have found that the allylic oxidation of a bicyclic olefin, being less reactive under conventional conditions, could be remarkably accelerated in the presence of formic acid to furnish the allyl formate in an excellent yield in regio- and stereoselective manners. (Scheme 1)



Scheme 1

Since we are very interested in the acceleration of the allylic oxidation resulted by employing a combination of selenium dioxide and formic acid, we investigated general applicability of this oxidation system by using some typical olefinic substrates. Herein we wish to report observation indicating the oxidation system employed may be judged to be compatible or to be superior to the conventional procedures. Thus, oxidation of two substrates having bicyclo[3.3.1]nonene framework was first examined under these conditions. As expected, the allylic oxidation proceeded smoothly in each compound to give the corresponding oxidation product in an excellent yield (entries 1-2). Under these conditions virtually no transesterification occurred even in the presence of an excess formic acid. Moreover, the substrate having a chlorine atom on the olefinic bond of the bicyclo[3.2.1]octene system afforded the oxidation product in high yield, though higher temperature (90 °C , 4 h)

Table Allylic oxidation of bicyclic olefins

Entry	Substrate	Reaction Conditions	Product	Yield (%) [Isomeric Ratio]
1)	 1	60°C 2 h A		97% (7a : 7b = 92 : 8) 7a: X=OCHO, Y=H 7b: X=H, Y=OCHO
2)	 2	60°C 7 h A		96% (8a : 8b = 83 : 17) 8a: X=OCHO, Y=H 8b: X=H, Y=OCHO
3)	 3	90°C 4 h A		88% (9a : 9b = 85 : 15) 9a: X=OCHO, Y=H 9b: X=H, Y=OCHO
4)	 4	60°C 4 h B	 10	80% (lit.[7] 57%)
5)	 5	60°C 4 h B*	 11	51% (lit.[8] 25%)
6)	 6	90°C 4 h B*		57% (lit.[9] 25-30%) (12a : 12b = 3 : 1) 12a X=OH, Y=H 12b X=H, Y=OH

Conditions A: HCOOH : dioxane (2 : 1) as solvent was used.

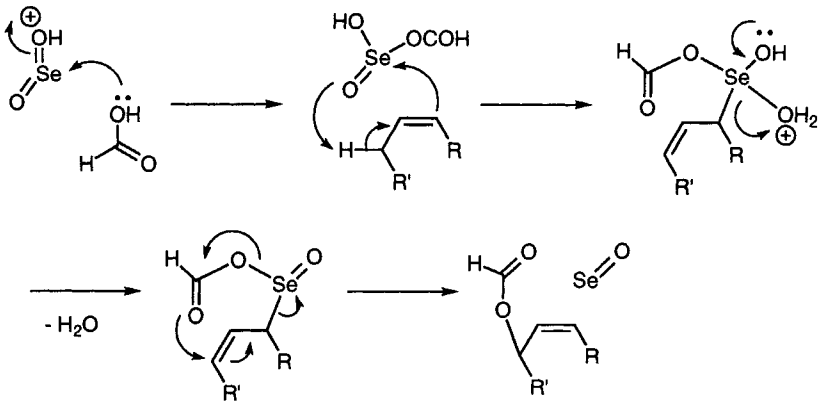
Conditions B: 1 molar equivalent amount of HCOOH in dioxane was used.

* Exposure of oxidation products to LAH gave the corresponding alcohols.

was required (entry 3). The oxidation of this compound was sluggish under conventional conditions: the use of selenium dioxide in acetic acid at 90 °C for 10 h or selenium dioxide and tert-butyl hydroperoxide in dichloromethane at room temperature for 48 h gave only a trace of the oxidation product. These obtained formates **7a**, **8a**, **9a** and **9b** were easily transformed into the corresponding alcohols **7c**, **8c**, **9c** and **9d** in an excellent yield upon exposure to saturated ammonia in methanol.

Since optically active 1-hydroxydicyclopentadiene has been recently recognized to be a versatile chiral synthon for the synthesis of natural product,[4] we next examined the oxidation using dicyclopentadiene as a starting material. Application of the same conditions, which involved an excess amount of formic acid, resulted in the concomitant formation of formyloxylation product of double bonds.[5,6] In the presence of one molar equivalent of formic acid, however, the reaction proceeded in an expected way to give the exo alcohol in a satisfactory yield. The present conditions were much superior to those reported (entry 4).[7] This procedure could be also suitable to transform α-pinene into myrtenol (entry 5).[8] In the case of cholesteryl acetate, the allylic oxidation occurred regioselectively under these conditions to give a mixture of two allylic alcohols in much higher yield than the reported procedure (entry 6).[9] The pathway of present reactions is presumed that selenium dioxide initially reacts with formic acid to form an active selenium formate intermediate which undergoes the ene reaction. The subsequent [3,3]sigmatropic rearrangement leads to allyl formate as shown in Scheme 2.[10-12]

In conclusion, the present procedure may be useful as a substitute for the conventional ones.



Scheme 2

Experimental Section

^{1}H-NMR spectra were recorded at 270 MHz on a JEOL GSX-270 spectrometer. ^{13}C-NMR spectra were recorded at 67.5 MHz on a JEOL GSX-270 spectrometer. IR spectra were recorded on a JASCO VALOR-III. Low resolution mass spectra (MS) and high resolution mass spectra (HRMS) were recorded on a JEOL JMS-D-300 mass spectrometer instrument. Elemental analyses were performed by Yanako MT-3. Optical rotations were measured on a JASCO DIP-370 polarimeter. Melting points were determined with a Yanagimoto micro melting point apparatus. All melting points are uncorrected. THF was freshly distilled from sodium benzophenone ketyl before use. 3-Chlorobicyclo[3.2.1]oct-2-ene (purity 98%) was purchased from Aldrich Chemical Company, Inc. (1R)-(+)-α-Pinene (purity 95%; $[\alpha]_D^{25}$ +32° (neat)) was purchased from Tokyo Chemical Industry Co.,Ltd. Dicyclopentadiene (purity 90%), cholesteryl acetate, selenium dioxide (purity 97%), formic acid (purity

99%) and all other reagents were of commercial quality and purchased from Wako Pure Chemical Industries, Ltd. The dimethyl ether **1** and the diacetate **2** were prepared from diols **14a** and **14b** respectively, which were obtained by reduction of ketoaldehyde **13** with lithium aluminum hydride (LAH). Column chromatography was carried out with Merck silica gel 0.063-0.2mm, 70-230 mesh.

(1*R*, 5*S*, 9*R*)-9-Formyl-5-methylbicyclo[3.3.1]-6-nonen-2-one (13)

This compound was prepared as described in the literature[3]

(1*R*, 2*S*, 5*S*, 9*R*)-9-Hydroxymethyl-5-methylbicyclo[3.3.1]-6-nonen-2-ol (14a) and (1*R*, 2*R*, 5*S*, 9*R*)-9-Hydroxymethyl-5-methylbicyclo[3.3.1]-6-nonen-2-ol (14b)

To an ice-cooled and stirred solution of ketoaldehyde **13** (676 mg, 3.8 mmol) in THF (17 ml) was added portionwise LAH (152 mg, 4 mmol) under argon atmosphere. After being stirred at 0°C for 15 min, the mixture was diluted with Et_2O (70 ml) and sat. aq. NH_4Cl (0.5 ml) and stirred for 30 min in order to destroy the excess of LAH. The mixture was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (20 g, elution with 1 : 5 v/v acetone-hexane) to give two separable isomers of alcohol **14a** (147 mg, 22%) and **14b** (507 mg, 72%) as colorless solids. Spectral data of **14a** were identical with those of reported.[3] A sample **14b** was recrystallized from hexane to give a colorless needle for analysis, mp 87-89°C. $[\alpha]_D^{25}$ -20.9° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} (cm^{-1}): 3613 (OH), 3347 (OH), 3011, 2956, 2872, 1460; ^{1}H-NMR ($CDCl_3$) δ: 0.91-

0.99 (m, 1H), 1.02 (s, 3H), 1.48-1.57 (m, 1H), 1.64 (brt, J=6.8 Hz, 1H), 1.75 (ddd, J=13.2, 4.8, 3.4 Hz, 1H), 1.81-1.97 (m, 2H), 2.27-2.34 (m, 1H), 2.39 (dddd, J=17.6, 6.8, 2.7, 2.4 Hz, 1H), 3.74 (dd, J=11.2, 5.1 Hz, 1H), 3.79 (brd, J=2.7 Hz, 1H), 4.01 (dd, J=11.2, 8.1 Hz, 1H), 5.29 (ddd, J=9.8, 2.2, 1.9 Hz, 1H), 5.63 (ddd, J=9.8, 3.6, 2.7 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ: 26.50 (q), 26.68 (t), 27.74 (t), 31.85 (t), 34.14 (s), 36.16 (d), 43.86 (d), 62.87 (t), 71.58 (d), 125.62 (d), 137.56 (d); EIMS m/z (relative intensity): 182 (M^+, 21), 164 (M^+-H_2O, 47), 93 (100); HRMS Found: 182.1305, $C_{11}H_{18}O_2$ (M^+) requires; 182.1307. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.34; H, 10.12.

(1*R*, 5*S*, 8*S*, 9*R*)-8-Methoxy-9-methoxymethyl-5-methyl-bicyclo[3.3.1]-3-nonene (1)

To an ice-cooled and stirred solution of diol **14a** (182 mg, 1 mmol) in dry DMF (4 ml) was added sodium hydride (144 mg, 3 mmol) under argon atmosphere. After being stirred at 0°C for 5 min, iodomethane (355 mg, 2.5 mmol) was added. The reaction mixture was allowed to warm to room temperature, stirred for 1 h, and diluted with sat. aq. NH_4Cl (30 ml) and Et_2O (5 ml). The organic layer was separated and the aqueous layer was extracted with Et_2O (2x5 ml). The combined organic layers were washed with water (3x15 ml) and sat. aq. NaCl (15 ml), and dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (10 g, elution with 1 : 5 v/v CH_2Cl_2-hexane) to give dimethyl ether **1** (196 mg, 93%) as a colorless oil. $[\alpha]_D^{25}$ -66.3° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν max (cm^{-1}): 3008, 2931, 2875, 1456, 1094; ^{1}H-NMR ($CDCl_3$) δ: 0.98 (s, 3H),

1.24 (m, 1H), 1.36-1.56 (m, 2H), 1.71 (m, 1H), 1.89 (m, 1H), 2.05 (ddd, J=18.9, 5.8, 5.4 Hz, 1H), 2.29 (ddd, J=18.9, 3.4,1.4 Hz, 1H), 2.45 (m, 1H), 3.30 (s, 3H), 3.35 (m, 1H), 3.36 (s, 3H), 3.44 (t, J=9.5 Hz, 1H), 3.53 (dd, J=9.5, 5.8 Hz, 1H), 5.30 (dt, J=9.8, 2.2 Hz, 1H), 5.75 (dt, J=9.8, 3.4 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ: 25.18 (t), 25.78 (t), 26.40 (q), 31.92 (d), 32.34 (t), 33.37 (s), 44.30 (d), 55.52 (q), 58.82 (q), 71.51 (t), 77.41 (d), 128.06 (d), 136.60 (d); EIMS m/z (relative intensity): 178 (M^+-MeOH, 62), 146 (M^+-2MeOH, 36), 105 (100); HRMS Found: 178.1355, $C_{12}H_{18}O$ (M^+-MeOH) requires; 178.1358. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.34; H, 10.49.

(1*R*, 2*S*, 5*S*, 8*S*, 9*R*)-2-Formyloxy-8-methoxy-9-methoxymethyl-5-methylbicyclo[3.3.1]-3-nonene (7a) and (1*R*, 2*R*, 5*S*, 8*S*, 9*R*)-2-Formyloxy-8-methoxy-9-methoxymethyl-5-methylbicyclo[3.3.1]-3-nonene (7b)

To a solution of dimethyl ether **1** (105 mg, 0.5 mmol) in dry dioxane (1 ml) were added selenium dioxide (SeO_2) (114 mg, 1 mmol) and formic acid (HCOOH) (2 ml). The reaction mixture was heated at 60°C for 2 h with stirring. After completion of reaction, the reaction mixture was diluted with water (20 ml) and Et_2O (5 ml), and the insoluble material was removed by filtration through a pad of Cerite. The organic layer was separated and the aqueous layer was extracted with Et_2O (3x3 ml). The combined organic layers were washed with water (3x10 ml), sat. aq. $NaHCO_3$ (10 ml) and sat. aq. NaCl (5 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel (5 g, elution with 1 : 5 v/v Et_2O-hexane)

to give an inseparable 92 : 8 mixture of formate esters **7a** and **7b** as a colorless oil, total yield 123 mg (97%). IR ($CHCl_3$) ν_{max} (cm^{-1}): 3010, 2930, 2877, 1712 (C=O), 1459, 1374; ^{1}H-NMR ($CDCl_3$) Major isomer **7a**: δ: 1.04 (s, 3H), 1.22 (ddt, J=12.2, 4.3, 1.9Hz, 1H), 1.34 (td, J=12.2, 4.3 Hz, 1H), 1.42-1.60 (m, 1H), 1.68-1.79 (m, 1H), 2.09 (m, 1H), 2.52 (m, 1H), 3.36 (s, 6H), 3.42 (t, J=9.5 Hz, 1H), 3.45-3.50 (m, 1H),3.53 (dd, J=9.5, 5.9 Hz, 1H), 5.51 (brd, J=4.2 Hz, 1H), 5.64 (dd, J=9.8, 0.7 Hz, 1H), 5.91 (ddd, J=9.8, 4.2, 1.5 Hz, 1H), 8.05 (d, J=1.2 Hz, 1H); Minor isomer **7b**: δ: 0.88 (s, 3H), 3.33 (s, 3H), 3.36 (s, 3H), 8.09 (d, J=1.2 Hz, 1H); ^{13}C-NMR ($CDCl_3$) Major isomer **7a**: δ: 25.29 (t), 25.71 (q), 29.96 (t), 33.96 (s), 38.36 (d), 40.27 (d), 56.05 (q), 58.84 (q), 67.02 (d), 70.59 (t), 74.41 (d), 125.20 (d), 142.51 (d), 160.57 (d); Minor isomer **7b**: δ: 23.31 (q), 24.17 (t), 28.38 (t), 34.97 (s), 35.76 (d), 39.83 (d), 55.92 (q), 58.84 (q), 70.59 (t), 74.94 (d), 75.51 (d), 127.49 (d), 133.96 (d), 161.19 (d); EIMS m/z (relative intensity): 222 (M^+-MeOH, 18), 208 (M^+-HCOOH, 44), 190 (M^+-2MeOH, 12), 71 (100); HRMS Found: 222.1236, $C_{13}H_{18}O_3$ (M^+-MeOH) requires; 222.1256. Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72. Found: C, 65.96; H, 8.78.

(1*R*, 2*S*, 5*S*, 8*S*, 9*R*)-8-Methoxy-9-methoxymethyl-5-methyl-bicyclo[3.3.1]-3-nonen-2-ol (7c)

To a solution of a mixture of formates **7a** and **7b** (90 mg, 0.35 mmol) in MeOH (1 ml) was added saturated methaniolic ammonia (3 ml). After being stirred for 40 min at room temperature, the reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel (10 g, elution with 1 : 5 v/v acetone-

hexane) to give alcohol as a colorless oil, total yield 79 mg (99%). The major isomer **7c** was separated as a single isomer. $[\alpha]_D^{25}$ 24.9° (c 1.15, $CHCl_3$); IR ($CHCl_3$) ν_{max} (cm^{-1}): 3601 (OH), 3432 (OH), 3010, 2932, 2875, 2827; ^{1}H-NMR ($CDCl_3$) δ: 1.01 (s, 3H), 1.14-1.36 (m, 1H), 1.41-1.55 (m, 1H), 1.61-1.73 (m, 1H), 1.85 (m, 1H), 2.03 (m, 1H), 2.45 (m, 1H), 3.28 (m, 1H), 3.35 (s, 6H), 3.39 (d, J=9.5 Hz, OH, 1H), 3.41 (t, J=9.7 Hz, 1H), 3.54 (dd, J=9.7, 6.1 Hz, 1H), 4.25 (m, 1H), 5.51 (dd, J=9.8, 1.0 Hz), 5.91 (ddd, J=9.8, 4.2, 1.5 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ: 25.12 (t), 25.87 (q), 30.27 (t), 34.11 (s), 39.81 (d), 41.84 (d), 55.94 (q), 58.73 (q), 63.92 (d), 71.16 (t), 75.16 (d), 129.34 (d), 140.10 (d); EIMS m/z (relative intensity): 194 (M^+-MeOH, 64), 162 (M^+-2MeOH, 100); HRMS Found: 194.1312, $C_{12}H_{18}O_2$ (M^+-MeOH) requires; 194.1307. Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.73; H, 9.72.

(1*R*, 5*S*, 8*R*, 9*R*)-8-Acetyloxy-9-acetyloxymethyl-5-methyl-bicyclo[3.3.1]-3-nonene (2)

To a stirred solution of diol **14b** (182 mg, 1 mmol) and N,N-dimethylaminopyridine (1.2 mg, 0.01 mmol) in pyridine (2 ml) was added acetic anhydride (306 mg, 3 mmol). After stirring at room temperature for 12 h, the mixture was diluted with Et_2O (10 ml) and water (15 ml). The organic layer was separated, washed with 1N $KHSO_4$ (3x10 ml) and sat. aq. NaCl (10 ml), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on silica gel (10 g, elution with 1 : 5 v/v Et_2O-hexane) to give diacetate **2** (263 mg, 98%) as a colorless oil. $[\alpha]_D^{25}$ -26.6° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} (cm^{-1}): 3023, 2957, 2934, 2875, 1729 (C=O),

1369; ^{1}H-NMR ($CDCl_3$) δ: 1.04 (s, 3H), 1.05-1.09 (m, 1H), 1.54-1.95 (m, 5H), 2.02 (s, 3H), 2.04 (s, 3H), 2.38 (m, 1H), 2.45 (dt, J=7.4, 2.4 Hz, 1H), 4.29 (dd, J=11.4, 7.4 Hz, 1H), 4.35 (dd, J=11.4, 7.9 Hz, 1H), 4.78 (m, 1H), 5.33 (dd, J=9.8, 2.4 Hz, 1H), 5.69 (ddd, J=9.8, 4.9, 2.4 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ: 21.05 (q), 21.49 (q), 24.72 (t), 26.79 (t), 27.10 (q), 31.02 (t), 32.88 (d), 33.68 (s), 41.75 (d), 64.98 (t), 74.10 (d), 126.0 (d), 136.84 (d), 170.27 (s), 171.18 (s); EIMS m/z (relative intensity): 206(M^+-AcOH, 24), 146 (M^+-2AcOH, 100); HRMS Found: 206.1303, $C_{13}H_{18}O_2$ (M^+-AcOH) requires; 206.1307. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found: C, 67.66; H, 8.50.

(1*R*, 2*S*, 5*S*, 8*R*, 9*R*)-8-Acetyloxy-9-acetyloxymethyl-2-formyloxy-5-methylbicyclo[3.3.1]-3-nonene (8a) and (1*R*, 2*R*, 5*S*, 8*R*, 9*R*)-8-Acetyloxy-9-acetyloxymethyl-2-formyloxy-5-methylbicyclo[3.3.1]-3-nonene (8b)

To a stirred solution of diacetate **2** (133 mg, 0.5 mmol) in dioxane (1 ml) were added SeO_2 (114 mg, 1 mmol) and HCOOH (2 ml) and the mixture was heated at 60°C for 7 h. After completion of reaction, the reaction mixture was diluted with water (20 ml) and ether (5 ml), and then the insoluble material was removed by filtration through a pad of Cerite. The organic layer was separated and the aqueous layer was extracted with Et_2O (3x5 ml). The combined organic layers were washed with water (2x10 ml), sat. aq. $NaHCO_3$ (10 ml) and sat. aq. NaCl (10 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was chromatographed on silica gel (10 g, elution with 1 : 5, 2 : 5 v/v Et_2O-hexane) to give an inseparable 83 : 17 mixture of formate

esters **8a** and **8b** as colorless solids, total yield 149 mg (96%). Recrystallization of the mixture from Et_2O-hexane afforded a single isomer **8a** as a colorless needle, mp 74-76°C. $[\alpha]_D^{25}$ 77.6° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} (cm^{-1}): 3028, 2959, 2935, 2876, 1733 (C=O), 1368; ^{1}H-NMR ($CDCl_3$) δ: 1.10 (s, 3H), 1.02-1.17 (m, 1H), 1.56-1.72 (m, 3H), 2.02 (s, 3H), 2.05 (s, 3H), 2.06-2.14 (m, 1H), 2.40 (brs, 1H), 4.29 (dd, J=11.2, 8.3 Hz, 1H), 4.36 (dd, J=11.2, 7.3 Hz, 1H), 4.94 (brs, 1H), 5.15 (dd, J=4.1, 0.7 Hz, 1H), 5.84 (ddd, J=9.8, 4.1, 1.0 Hz, 1H), 5.69 (dd, J=9.8, 0.7 Hz, 1H), 8.04 (d, J=1.0 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ: 21.01 (q), 21.33 (q), 24.61 (t), 25.07 (t), 26.40 (q), 34.33 (s), 38.21 (d), 39.46 (d), 64.12 (t), 69.48 (d), 69.97 (d), 123.53 (d), 143.30 (d), 160.20 (d), 169.87 (s), 171.09 (s); EIMS m/z (relative intensity): 250 (M^+-AcOH, 8), 190 (M^+-2AcOH, 18) 144 (100); HRMS Found: 250.1196, $C_{14}H_{18}O_4$ (M^+-AcOH) requires; 250.1205. Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.14. Found: C, 61.79; H, 7.25; Minor isomer **8b**: ^{1}H-NMR ($CDCl_3$) δ: 0.98 (s, 3H), 4.82 (m, 1H), 5.13 (m, 1H), 6.13 (ddd, J=9.8, 6.3, 1.0 Hz, 1H), 8.10 (d, J=1.0 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ: 21.01 (q), 21.33 (q), 22.71 (t), 23.85 (q), 28.75 (t), 35.24 (s), 35.59 (d), 37.57 (d), 63.92 (t), 68.63 (d), 74.98 (d), 128.85 (d), 134.42 (d), 160.35 (d), 169.87 (s), 171.07 (s).

(1*R*, 2*S*, 5*S*, 8*R*, 9*R*)-8-Acetyloxy-9-acetyloxymethyl-5-methylbicyclo[3.3.1]-3-nonen-2-ol (8c)

To a solution of formate ester **8a** (50 mg, 0.16 mmol) in MeOH (0.5 ml) was added saturated methanolic ammonia (1.5 ml). After being stirred for 20 min at room temperature, the reaction mixture was concentrated

under reduced pressure. The residue was chromatographed on silica gel (1 g, elution with 3 : 10 v/v hexane-acetone) to give alcohol **8c** as a colorless oil, yield 44 mg (98%). $[\alpha]_D^{25}$ 36.1° (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} (cm^{-1}): 3600 (OH), 3471 (OH), 3019, 2958, 2935, 2875, 1727 (C=O), 1368; ^{1}H-NMR ($CDCl_3$) δ: 1.05 (m, 1H), 1.08 (s, 3H), 1.54-1.79 (m, 3H), 1.93 (m, OH, 1H) 2.03 (s, 3H), 2.05 (s, 3H), 2.06 (m, 1H), 2.34 (brs, 1H), 3.99 (brt, J=4.2 Hz, 1H), 4.27 (dd, J=11.2, 8.1 Hz, 1H), 4.38 (dd, J=11.2, 7.1 Hz, 1H), 4.87 (brs, 1H), 5.55 (dd, J=9.5, 0.7 Hz, 1H), 5.84 (ddd, J=9.5, 4.2, 1.2 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ: 21.05 (q), 21.42 (q), 24.63 (t), 25.16 (t), 26.55 (q), 34.49 (s), 37.55 (d), 42.63 (d), 64.52 (t), 67.90 (d), 70.74 (d), 127.38 (d), 141.04 (d), 170.19 (s), 171.22 (s); EIMS m/z (relative intensity): 222 (M^+-AcOH, 7), 162 (M^+-2AcOH, 100); HRMS Found: 222.1251, $C_{13}H_{18}O_3$ (M^+-AcOH) requires; 222.1256. Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 64.01; H, 8.02.

3-Chloro-4-*exo*-formyloxybicyclo[3.2.1]oct-2-ene (9a) and 3-Chloro-4-*endo*-formyloxybicyclo[3.2.1]oct-2-ene (9b)

To a solution of 3-chlorobicyclo[3.2.1]oct-2-ene **3** (291 mg, 2 mmol) in dioxane (1.5 ml) were added SeO_2 (458 mg, 4 mmol) and HCOOH (3 ml). The reaction mixture was stirred at 90°C for 4 h and then diluted with water (30 ml) and Et_2O (10 ml). The insoluble material was removed by filtration through a pad of Cerite. The organic layer was separated and the aqueous layer was extracted with Et_2O (3x5 ml). The combined organic layers were washed with water (3x5 ml), sat. aq. $NaHCO_3$ (5 ml), and sat. aq. NaCl (5 ml), and dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was

chromatographed on silica gel (10 g, elution with 1 : 20, 1 : 10 v/v CH_2Cl_2-hexane) to give an inseparable 85 : 15 mixture of formate esters **9a** and **9b** as a colorless oil, total yield 328 mg (88%). IR ($CHCl_3$) ν_{max} (cm^{-1}): 3030, 2953, 2875, 1719 (C=O); ^{1}H-NMR ($CDCl_3$) Major isomer **9a**: δ: 1.25-1.38 (m, 1H), 1.39-1.49 (m, 1H), 1.57-2.11 (m, 4H), 2.57 (m, 1H), 2.67 (m, 1H), 5.08 (brd, J=2.2 Hz), 6.29 (dd, J=7.3, 1.0 Hz, 1H), 8.12 (d, J=1.0 Hz, 1H); Minor isomer **9b**: δ: 5.76 (brd, J=4.9 Hz, 1H), 6.23 (dt, J=7.3, 1.0 Hz, 1H), 8.18 (d, J=1.2 Hz, 1H); ^{13}C-NMR ($CDCl_3$) Major isomer **9a**: δ: 24.28 (t), 30.80 (t), 31.19 (t), 36.30 (d), 38.87 (d), 76.30 (d), 127.21 (s), 137.37 (d), 160.16 (d); Minor isomer **9b**: δ: 22.00 (t), 32.16 (t), 36.53 (d), 37.31 (t), 39.44 (d), 76.83 (d), 127.70 (s), 136.39 (d), 160.38 (d); EIMS m/z (relative intensity): 186 (M^+, 31), 149 (M^+-HCl, 86), 140 (M^+-HCOOH, 22), 105 (100); HRMS Found: 186.0440, $C_9H_{11}O_2$ (M^+) requires; 186.0447.

3-Chloro-4-*exo*-hydroxybicyclo[3.2.1]oct-2-ene (9c) and 3-Chloro-4-*endo*-hydroxybicyclo[3.2.1]oct-2-ene (9d)

To a solution of a mixture of formates **9a** and **9b** (280 mg, 1.5 mmol) in MeOH (3 ml) was added saturated methanolic ammonia (7 ml). After being stirred for 25 min at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was chromatographed on silica gel (10 g, elution with 1 : 5 v/v Et_2O-hexane) to give exo-alcohol **9c** (201 mg, 84%) and endo-alcohol **9d** (36 mg, 15%) as a colorless oil, respectively. Major isomer **9c**: IR ($CHCl_3$) ν_{max} (cm^{-1}): 3595 (OH), 3437 (OH), 3015, 2950, 2873, 1635; ^{1}H-NMR ($CDCl_3$) δ: 1.24-1.37 (m, 2H), 1.58-1.97 (m, 4H), 2.31 (d, J=4.4 Hz, OH,

1H), 2.50-2.63 (m, 2H), 3.75 (dd, J=4.4, 2.9 Hz, 1H), 6.12 (dd, J=7.1, 0.7 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ: 24.55 (t), 30.68 (t), 30.88 (t), 36.43 (d), 40.52 (d), 76.46 (d), 132.00 (s), 134.40 (d); EIMS m/z (relative intensity): 158 (M^+, 5), 123 (M^+-Cl, 100); HRMS Found: 123.0809, $C_8H_{11}O$ (M^+-Cl) requires; 123.0810. Minor isomer **9d**: IR ($CHCl_3$) ν_{max} (cm^{-1}): 3592 (OH), 3454 (OH), 3016, 2950, 2871; ^{1}H-NMR ($CDCl_3$) δ: 1.54-1.77 (m, 4H), 1.82 (brd, J=12.0 Hz, 1H), 2.01-2.16 (m, 1H), 2.23 (d, J=3.4 Hz, OH, 1H), 2.49 (m, 1H), 2.60 (brq, J=5.4 Hz, 1H), 4.44 (dd, J=4.2, 3.4 Hz, 1H), 6.05 (dt, J=7.1, 1.2 Hz, 1H); EIMS m/z (relative intensity): 158 (M^+, 10), 123 (M^+-Cl, 100); HRMS Found: 123.0807, $C_8H_{11}O$ (M^+-Cl) requires; 123.0810.

1-Hydroxydicyclopentadiene (10)

To a stirred suspension of SeO_2 (1.20 g, 10.5 mmol) in dioxane (10 ml) were added HCOOH (483 mg, 10.5 mmol) and a solution of dicyclopentadiene **4** (1.47 g, 10 mmol) in dioxane (10 ml). The reaction mixture was stirred at 60°C for 4 h and then diluted with water (50 ml) and Et_2O (20 ml). The insoluble material was removed by filtration through a pad of Cerite. The organic layer was separated and the aqueous layer was extracted with Et_2O (3x15 ml). The combined organic layers were washed with water (15 ml), sat. aq. $NaHCO_3$ (15 ml) and sat. aq. NaCl (15 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was chromatographed on silica gel (70 g, elution with 1 : 3, 1 : 1 v/v Et_2O-hexane) to give alcohol **10** as a pale yellow oil, yield 1.19g (80%). Spectral data and chromatographical behavior were identical with those of an authentic material.

(+)-Myrtenol (11)

To a suspension of SeO_2 (503 mg, 4.4 mmol) in dioxane (2 ml) was added HCOOH (186 mg, 4 mmol). After stirring for 5 min, to this mixture was added a solution of (+)-α-pinene **5** (574 mg, 4 mmol) in dioxane (4 ml). The resultant mixture was stirred at 60°C for 6 h, diluted with water (20 ml) and Et_2O (10 ml), and neutralized with $NaHCO_3$ (840 mg, 10 mmol). The insoluble material was removed by filtration through a pad of Cerite. The organic layer was separated and the aqueous layer was extracted with Et_2O (2x10 ml). The combined organic layers were washed with sat. aq. NaCl (20 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was chromatographed on silica gel (15 g, elution with hexane, 1 : 20 v/v Et_2O-hexane) to give (+)-myrtenal as a pale yellow oil, yield 419 mg (70%). To an ice-cooled and stirred solution of the above product (419 mg, 2.79 mmol) in Et_2O (10 ml) was added portionwise LAH (80 mg, 2.1 mmol) under argon atmosphere. After being stirred at 0°C for 1 h, the mixture was diluted with Et_2O (35 ml) and sat. aq. NH_4Cl (0.3 ml) and stirred for 30 min in order to destroy the excess of LAH. The mixture was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (20 g, elution with 1 : 6 v/v Et_2O-hexane) to give (+)-Myrtenol **11** as a pale yellow oil, yield 310 mg (51%) The product thus obtained was identical with an authentic sample of (-)-myrtenol in every respect except optical rotation. $[\alpha]_D^{25}$ 37.8° (c 1.0, $CHCl_3$) [lit. $[\alpha]_D^{22}$ 44.3° (c 3.21, $CHCl_3$),[8] Aldrich (-)-myrtenol $[\alpha]_D^{20}$ -51° (neat)].

(3*S*, 4*R*)-3,4-Dihydroxy-5-cholesten (12a) and (3*S*, 4*S*)-3,4-Dihydroxy-5-cholesten (12b)

To a solution of cholesteryl acetate **6** (214 mg, 0.5 mmol) in dioxane (3 ml) were added SeO_2 (126 mg, 1.1 mmol) and HCOOH (46 mg, 1.0 mmol). The reaction mixture was stirred at 90°C for 4 h, and then diluted with water (20 ml) and Et_2O (10 ml). The insoluble material was removed by filtration through a pad of Cerite. The organic layer was separated and the aqueous layer was extracted with Et_2O (3x5 ml). The combined organic layers were washed with water (10 ml), sat. aq. $NaHCO_3$ (5 ml) and sat. aq. NaCl (5 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure. To an ice-cooled and stirred solution of the residue in THF (5 ml) was added portionwise LAH (28 mg, 0.75 mmol) under argon atmosphere. The reaction mixture was allowed to warm to room temperature, stirred for 1 h and then diluted with AcOEt (30 ml) , Et_2O (15 ml) and sat. aq. NH_4Cl (0.5 ml) in order to destroy the excess of LAH. After being stirred for 30 min until a white free-flowing suspension formed, the mixture was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was chromatographed on silica gel (5 g, elution with 1 : 2, 1 : 1 v/v Et_2O-hexane, 2 : 5 v/v acetone-hexane) to give the corresponding diols **12a** (86 mg, 43%) and **12b** (29 mg, 14%) as white solids respectively. Spectral and physical data were identical with those of reported.[9]

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