Rearrangement Approaches to Cyclic Skeletons. IX. Stereoselective Total Synthesis of (±)-Camphorenone Based on a Ring-Contraction of Bicyclo[3.2.1]oct-6-en-2-one. Reliable One-Step Diazo Transfer Followed by a Wolff Rearrangement # [1)]

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A direct diazo transfer reaction to bicyclo[3.2.1]oct-6-en-2-ones and related compounds was accomplished by treatments with 2,4,6-triisopropylbenzenesulfonyl azide and potassium *t*-butoxide at −78 °C in THF. A Wolff rearrangement of the resulting α-diazoketones in the presence of water gave ring-contraction products, bicyclo[2.2.1]heptenecarboxylic acids. Using these two transformations the total synthesis of (±)-camphorenone was achieved stereoselectively, starting from 1-methoxybicyclo[2.2.2]oct-5-en-2-one.

The total syntheses of bicyclo[2.2.1]heptane terpenes was achieved mainly by using the Diels–Alder methodology.[2,3)] In connection with our studies on rearrangement approaches from bridged polycyclic compounds to [m−n] fused-ring natural products,[4)] we were interested in studying the rearrangement routes to a substituted bicyclo[2.2.1]heptane, such as (−)-camphorenone (**1**) (Chart 1).[5,6)] In this paper we report on the development of a rearrangement route to bicyclo[2.2.1]heptenes (**5**) starting from 1-methoxybicyclo-[2.2.2]oct-5-en-2-ones (**2**) through 3-diazobicyclo[3.2.1]-oct-6-en-2-ones (**4**), shown in Scheme 1, and its application to a total synthesis of (±)-**1**.

Results and Discussion

The route in shown Scheme 1 was proposed on the basis of the following knowledge. The stepwise alkylation of a bicyclo[2.2.2]oct-5-en-2-one, such as a ketone **2a**, has already been demonstrated to proceed stereoselectively.[4h)] The transformation of **2** into bicyclo[3.2.1]oct-6-en-2-ones **3** should be achieved by a successive treatment with CH_3MgX, and then

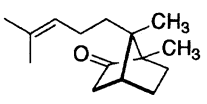

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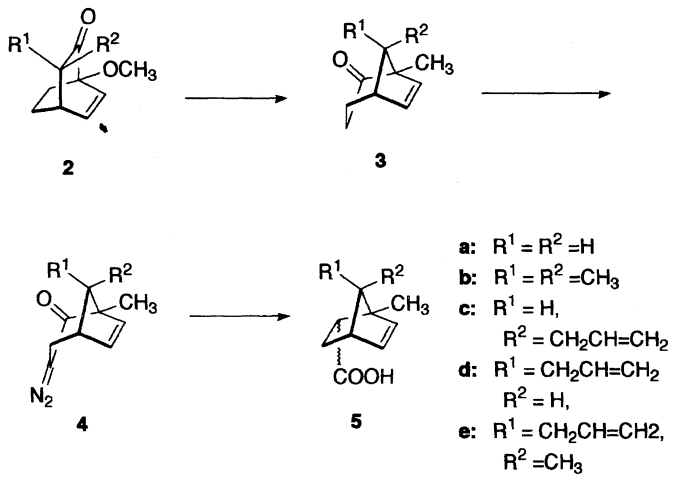
Chart 1.

with *p*-toluenesulfonic acid (TsOH) to cause a pinacol rearrangement.[4g,7)] The known procedure would be applied to the conversion of ketones **3** into acids **5** through α-diazoketones **4**, followed by a photochemical Wolff rearrangement Scheme 1. It is an important feature of this route that the stereochemical configuration of the C_1 bridge of **5** is controllable at the stage of the second alkylation of **2a**.

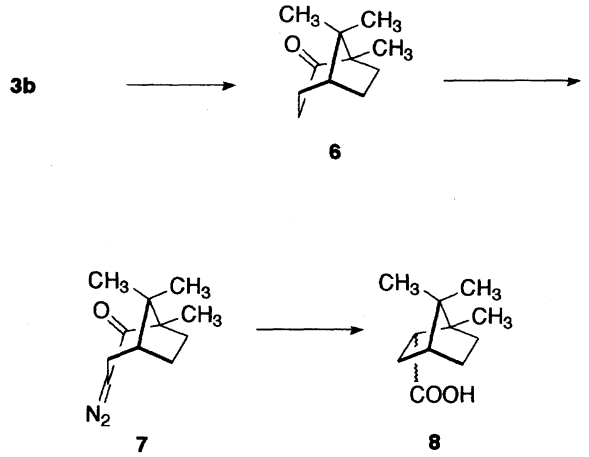
First, we employed ketones **3b** and **6** as model substrates for the ring contraction. A successive treatment of **2a** with excess potassium *t*-butoxide and methyl iodide in THF, methylmagnesium bromide followed by column chromatography, and TsOH in boiling benzene, gave ketone **3b**. The catalytic hydrogenation of **3b** gave a saturated ketone **6**.

A diazo transfer reaction from *p*-toluenesulfonyl azide to a β-dicarbonyl compound proceeds efficiently.[8)] Formylation followed by a deformylating diazo transfer reaction seems to be a practical method for preparing an α-diazo derivative of a simple ketone.[8,9)] In the case of a methyl ketone, the trifluoromethyl acylation of the kinetic enolate was recommended instead of formylation.[10)] A novel method for a direct diazo transfer reaction from sulfonyl azide to an α-position of a cyclic ketone has been carried out under phase-transfer conditions, the use of 2,4,6-triisopropylbenzenesulfonyl azide is recommended.[11)] We carefully applied this method to prepare diazoketones **4b** and **7** from ketones **3b** and **6**, respectively (Scheme 2). Unfortunately, the reproducibility of the yields of α-diazoketones by this procedure was not satisfactory.

#This paper is dedicated to Professor Takashi Toda on the occasion of his 65th birthday.



Scheme 1. Preparation and ring-contraction of bicyclo[3.2.1]oct-6-en-ones.



Scheme 2. Preparation and ring-contraction of bicyclo[3.2.1]octan-2-ones.

Ultimately, a direct diazo transfer reaction was successfully achieved under homogeneous conditions: the slow addition of an equimolar mixture of a ketone and triisopropylbenzenesulfonyl azide[12] to a solution of *t*-BuOK in tetrahydrofuran (THF) at −78 °C. α-Diazoketones **4b** and **7** were derived by this method in 81 and 96% yields, respectively. A Wolff rearrangement of **7** in THF–H_2O gave carboxylic acids **8**, as a mixture of the *exo* and *endo* isomers, in 87% yield by irradiation using a high-pressure Hg lamp (100 W) through a quartz wall. A similar treatment of the diazoketone **4b** gave carboxylic acids **5b** in 75% yield. Thus, the transformation of bicyclo[3.2.1]octan-2-ones into 2-bicyclo[2.2.1]heptanecarboxylic acids has been achieved.

Next, the ketone **2a** was chosen as the starting material for a total synthesis of (±)-**1**. A reaction of the lithium enolate of **2a** with allyl iodide in a mixture THF–HMPA (hexamethylphosphoric triamide) at −78 °C gave a mixture of monoallylated ketones **2c** and **2d** in 80% yield. Stereoselective methylation of this mixture was achieved by a treatment with *t*-BuOK and methyl iodide in THF at −78 °C to form only **2e** in 92% yield. The stereostructure of **2e** was estimated from the stereoselectivity of the methylation of a similarly substituted bicyclo[2.2.2]oct-5-en-2-one.[4h]

A reaction of **2e** with CH_3MgBr in THF at −78 °C gave a mixture of *exo* and *endo*-alcohols, **9** and **10**, respectively. Alcohols **9** and **10** were isolated by flash chromatography in 83 and 9% yields, respectively. The stereostructures of **9** and **10** were defined as shown on the basis of NMR studies including the NOE experiments (Fig. 1). A stereospecific transformation of the *exo*-alcohol **9** to a bicyclo[3.2.1]oct-6-en-2-one **3e** was accomplished in 98% yield by heating under reflux with TsOH in benzene.

The transformation of **3e** into a diazoketone **4e** proceeded smoothly under very similar conditions to those mentioned before. The diazoketone **4e** was isolated in 91% yield. A Wolff rearrangement of **4e** was conducted in THF–H_2O (1:1) containing $NaHCO_3$ by the above-mentioned method. A 1:4 mixture of *exo*- and *endo* carboxylic acids **5e** was obtained in 90% yield.

A functional-group transformation from carboxylic acids **5e** to nitriles **12** through amides **11** was performed in 85% overall yield by a sequential treatment with thionyl chloride, aqueous ammonia, and *N*,*N*-diethyl-*N*-[[(methylcarboxy)amino]sulfonyl]ethanaminium hydroxide inner salt ($CH_3OC(O)N^-$–SO_2–$N^+(C_2H_5)_3$).[13] The lithium anion of nitriles **12** was generated by a treatment with LDA at −78 °C and carefully reacted with dry oxygen. A reductive work-up of the reaction mixture with aqueous Na_2SO_3 gave a ketone **13** in 72% yield (Chart 2).

The carbonyl group of **13** was protected as an ethylene acetal **14** in 60% yield. Hydroboration of **14** with 9-borabicyclo[3.3.1]nonane (9-BBN) followed by oxidation with H_2O_2–NaOH selectively gave a primary alcohol **15** in 83% yield. A cleavage of the protecting group of **15** with pyridinium *p*-toluenesulfonate (PPTS) in aqueous acetone gave a hydroxyketone **16** in 98% yield.

Protection of the carbonyl group of **13** as an acetal seemed to be a sterically less favorable transformation.

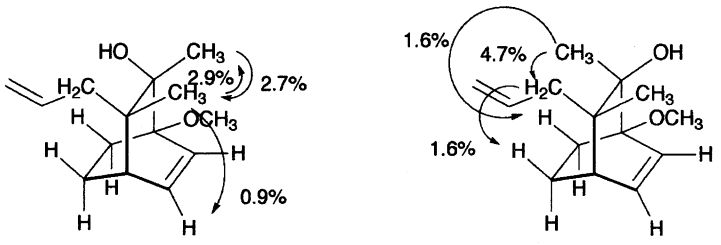


Fig. 1. Key interactions obtained from the NOE difference spectra.

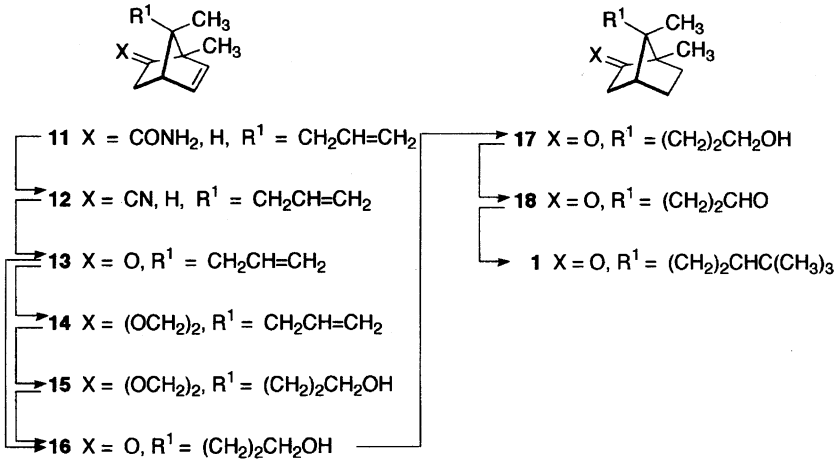


Chart 2.

This suggested that the carbonyl group was less reactive to bulky metal-hydride reagents. We thus attempted a direct hydroboration of **13** by using 9-BBN. The hydroxyketone **16** was obtained in 78% yield.

Ketone **16** was converted into a saturated hydroxyketone **17** in 98% yield by catalytic hydrogenation. A treatment of **17** with pyridinium chlorochromate (PCC), followed by a Wittig reaction with isopropylidenetriphenylphosphorane, gave a ketone containing a homoprenyl group in 35% yield. The spectroscopic characteristics of the ketone are identical with those of (±)-**1**.

In conclusion, it has been demonstrated that the rearrangement approach to bicyclo[2.2.1]hept-5-enes on the basis of the two-step ring-contraction of bicyclo[3.2.1]-oct-6-en-2-ones is a practical methodology for a natural-product synthesis.

Experimental

General. The ^{1}H NMR spectra were measured at 300 and 600 MHz in $CDCl_3$ using TMS [$(CH_3)_4Si$] as the internal standard. COSY and NOESY experiments were frequently employed for assigning the stereostructures. THF and diethyl ether were distilled from benzophenone ketyl under argon immediately prior to use. Dichloromethane was distilled from CaH_2 under argon immediately prior to use. All of the reactions were monitored by analytical TLC using Merck pre-coated silica-gel $60F_{254}$ plates. Column chromatography was carried out with Merck silica-gel 60 (70—230 mash ASTM). Flash chromatography was carried out with Cica–Merck silica-gel 60 (230—400 mash ASTM). Semi-preparative HPLC was performed using a Merck Hiber® prepacked column RT (250×10 mm).

1-Methoxy-3,3-dimethylbicyclo[2.2.2.]oct-5-en-2-one(2b). To a stirred solution of *t*-BuOK (6.671 g, 59.4 mmol) in THF (75 cm^3) was added dropwise a solution of a ketone **2a** (2.270 g 15.0 mmol) in THF (50 cm^3) at 0 °C under argon. After the addition was complete, iodomethane (4.70 cm^3, 75.0 mmol) was added dropwise to this mixture. After stirring overnight, the reaction mixture was first treated with a saturated aqueous NH_4Cl solution, and then extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (80 g, 3 : 1 hexane–ethyl acetate) gave a ketone **2b** (2.103 g, 11.7 mmol, 77%): A colorless oil; IR (neat) 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=6.51 (1H, dd, $J_{5,6}$=8.4 and $J_{5,4}$=6.5 Hz, H_5), 6.15 (1H, d, $J_{6,5}$=8.4 Hz, H6), 3.26 (3H, s. CH_3O–), 2.53 (1H, m, H_4), 2.08 (1H, dddd, $J_{8exo,8endo}$=12.8, $J_{8exo,7exo}$=9.6, $J_{8exo,7endo}$=3.3, and $J_{8exo,4}$=3.0 Hz, H_{8exo}), 1.86 (1H, ddd, $J_{7exo,7endo}$=12.3, $J_{7exo,8exo}$=9.6, and $J_{7exo,8endo}$=5.7 Hz, H_{7exo}), 1.71 (1H, ddd, $J_{7endo,7exo}$=12.3, $J_{7endo,8endo}$= 12.0, and $J_{7endo,8exo}$=3.3 Hz, H_{7endo}), 1.50 (1H, dddd, $J_{8endo,8exo}$=12.8, $J_{8endo,7endo}$=12.0, $J_{8endo,7exo}$=5.7, and $J_{8endo,4}$=2.7 Hz, H_{7endo}, 1.12 (3H, s, 3*exo*- or 3*endo*-CH_3), and 1.08 (3H, s, 3*exo*- or 3*endo*-CH_3). Found: *m/z* 180.1152. Calcd for $C_{11}H_{16}O_2$: 180.1150.

1,8,8-Trimethylbicyclo[3.2.1]oct-6-en-2-one (3b). To a stirred solution of ketone **2b** (563.9 mg, 3.11 mmol) in

THF (15 cm^3) was added dropwise a solution of 1.0 M (1 M=1 mol dm^{-3}) CH_3MgBr (6.00 cm^3, 6.00 mmol) in THF at −78 °C under argon. This mixture was stirred for 2.5 h and allowed to warm to room temperature. The reaction mixture was first treated with saturated an aqueous NH_4Cl solution, and then extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (20 g, 9 : 1 hexane–ethyl acetate) gave the *exo*-alcohol (515.1 mg, 2.63 mmol, 85%) and the *endo* alcohol (85.0 mg. 0.43 mmol, 13%).

A solution consisting of the *exo*-alcohol (448.7 mg, 2.29 mmol), TsOH (monohydrate, 431.0 mg, 2.29 mmol) and dry benzene (8 cm^3) was heated at 80 °C (bath temperature) for 30 min. The reaction mixture was first treated with a saturated aqueous $NaHCO_3$ solution, and then extracted with three portions of ether. The combined extracts were washed with saturated brine and dried over Na_2SO_4. Evaporation of the solvent gave **3b** (371.1 mg, 2.26 mmol, 99%) as a white solid.

3b: Colorless needles (hexane); mp 140—141 °C; IR (KBr) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.12 (1H, dd, $J_{6,7}$=5.7 and $J_{6,5}$=2.7 Hz, H_6), 5.54 (1H, d, $J_{7,6}$=5.7 Hz, H_7), 2.63 (1H, ddd, $J_{3exo,3endo}$=17.8, $J_{3exo,4endo}$=9.9, and $J_{3exo,4exo}$=8.1 Hz, H_{3exo}), 2.36—2.34 (1H, m, H_5), 2.19 (1H, dd, $J_{3endo,3exo}$=17.8 and $J_{3endo,4exo}$=7.8 Hz, H_{3endo}), 2.01 (1H, dddd, $J_{4exo,4endo}$=13.5, $J_{4exo,3exo}$=8.1, $J_{4exo,3endo}$=7.8, and $J_{4exo,5}$=3.6 Hz, H_{4exo}), 1.65 (1H, ddd, $J_{4endo,4exo}$=13.5, $J_{4endo,3exo}$=9.9, and $J_{4endo,5}$=3.2 Hz, H_{4endo}), 1.01 (3H, s, 8*endo*-CH_3), 0.99 (3H, s, 1-CH_3), and 0.89 (3H, s, 8*exo*-CH_3). Found: C, 80.54; H, 9.95%. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.81%.

1,8,8-Trimethylbicyclo[3.2.1]octan-2-one (6). To a solution of **3b** (163.3 mg, 0.994 mmol) in ethyl acetate (5 cm^3) was added 5% Pt–C (78 mg). The mixture was stirred under H_2 for 2.5 h. The resulting mixture was filtered through a silica-gel layer and washed with ethyl acetate. Evaporation of the solvent gave a crystalline solid. Chromatography of the solid on silica gel (10 g, 7 : 1 hexane–ethyl acetate) gave **6** (153.8 mg, 0.930 mmol, 94%) as a colorless solid.

6: Colorless prisms (hexane); mp 174—175 °C; IR (KBr) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.51—2.39 (1H, m), 2.25—2.12 (2H, m), 2.04—1.88 (2H, m), 1.79—1.53 (4H, m), 0.96 (3H, s), 0.94 (3H, s), and 0.83 (3H, s). Found: C, 79.78; H, 11.01%. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91%

3-Diazo-1,8,8-trimethylbicyclo[3.2.1]octan-2-one (7). (a) To a stirred solution of *t*-BuOK (296 mg, 2.64 mmol) in THF (12 cm^3) was added dropwise a solution of a ketone **6** (221.4 mg, 1.33 mmol) and 2,4,6-triisopropylbenzenesulfonyl azide[12] (458 mg, 1.50 mmol) in THF (6 cm^3) at −78 °C under argon. The mixture was first stirred for 20 min, and then treated with a saturated aqueous NH_4Cl solution. The resulting cold mixture was extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (50 g, 5 : 1 hexane–ethyl acetate) gave **7** (244.1 mg, 1.27 mmol, 96% yield) as a yellow oil.

(b) In a flask (200 cm^3) equipped with a mechanical stirrer were placed a ketone **6** (181.8 mg, 1.09 mmol), tetrabutylammonium bromide (122.8 mg, 0.380 mmol), 18-crown-6 (15.8 mg), 2,4,6-triisopropylbenzenesulfonyl azide (861.7 mg, 2.50 mmol), and benzene (22 cm^3). To the mixture was added a 66% aqueous KOH solution (22 cm^3). The resulting mixture was vigorously stirred at 35 °C for 6 h. Additional 2,4,6-triisopropylbenzenesulfonyl azide (175.0 mg, 0.54 mmol) was added to the reaction mixture, and then vigorously stirred for 19 h. The mixture was diluted with water and extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (80 g, 7 : 1 hexane–ethyl acetate) gave **7** (161.7 mg, 0.84 mmol, 66% yield) as a yellow oil.

7: UV (CH_3OH) 495 (sh, ε 6.7), 400 (sh, 45), 288 (7200), and 255 nm (sh, 5600); IR (neat) 2030 (−N_2) and 1640 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=2.95 (1H, ddd, J=13.2, 4.2, and 1.5 Hz, H_{4exo}), 2.43 (1H, dd, J=13.2 and 2.1 Hz, H_{4endo}), 2.17—1.99 (2H, m, H_5 and H_6), 1.90 (1H, ddd, J=13.8, 9.6, and 3.9 Hz, H_7), 1.77 (1H, ddd, J=13.8, 11.7, and 5.4 Hz, H_6), 1.51 (1H, ddd, J=13.5, 9.6, and 5.4 Hz, H_7), 1.08 (3H, s, 8-CH_3), 1.00 (3H, s, 1-CH_3), and 0.94 (3H, s, 8-CH_3); ^{13}C NMR ($CDCl_3$) δ=199.8 (C-2), 58.7 (C-3), 56.4 (C-1), 43.7 (C-8), 43.2 (C-5), 37.1 (C-7), 28.1 (C-6), 27.6 (C-4), 23.9 (8-CH_3), 18.9 (8-CH_3), and 12.9 (1-CH_3). Found: C, 68.55; H, 8.68; N, 14.47%. Calcd for $C_{11}H_{16}N_2O$; C, 68.71; H, 8.35; N, 14.57%.

3-Diazo-1,8,8-trimethylbicyclo[3.2.1]oct-6-en-2-one (4b). An α-diazoketone **4b** (176.7 mg, 0.930 mmol) was derived from a ketone **3b** (171.4 mg, 1.04 mmol) in 89% yield by a similar treatment under homogeneous conditions to that used for preparing **6**.

4b: Pale yellow oil; UV (CH_3OH) 410 (sh, ε 28), 335 (sh, 95), 295 (sh, 4000), 275 (4700), and 225 nm (sh, 4800); IR (neat) 2030 (C=N_2) and 1630 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=6.10 (1H, ddd, $J_{6,7}$=5.4 and $J_{6,5}$=3.0 Hz, H_6), 5.63 (1H, d, $J_{7,6}$=5.4 Hz, H_7), 2.92 (1H, dd, $J_{4exo,4endo}$=13.8 and $J_{4exo,5}$=1.8 Hz, H_{4exo}), 2.45 (1H, ddd, $J_{4endo,4exo}$=13.8 and $J_{4endo,5}$=4.5 Hz, H_{4endo}), 2.38 (1H, m, H_5), 1.11 (3H, s, 1-CH_3), 1.07 (3H, s, 8-CH_3), and 0.99 (3H, s, 8-CH_3); ^{13}C NMR ($CDCl_3$) δ=196.1 (C-2), 137.9 (C-7), 134.6 (C-6), 61.2 (C-1), 59.6 (C-3), 47.8 (C-5), 47.7 (C-8), 24.0 (8-CH_3), 23.5 (C-4), 18.0 (8-CH_3), and 9.3 (1-CH_3). Found: C, 69.22; H, 7.64; N, 14.66%. Calcd for $C_{11}H_{14}N_2O$: C, 69.44; H, 7.41; N, 14.72%.

1,7,7-Trimethylbicyclo[2.2.1]heptane-2-carboxylic Acids (8). A solution consisting of an α-diazoketone **7** (371.8 mg, 1.94 mmol), $NaHCO_3$ (631.0 mg), and 1 : 4 THF–H_2O (40 cm^3) was placed in an immersion well equipped with a quartz filter. The solution was irradiated for 1 h with a 100-W Ushio Hg lamp under argon. After evaporation of THF, the remaining mixture was diluted with an aqueous KOH solution and extracted with ether. The aqueous layer was acidified with 5% HCl and extracted with three portions of ether. The combined extracts were washed with saturated brine and dried over Na_2SO_4. Evaporation of the solvent gave **8** (303.7 mg, 1.66 mmol, 87%) as a 11 : 2 mixture of the *endo* and the *exo* isomers.

8 (the *endo* isomer): Mp 73—75.5 °C; IR (KBr) 3200—2400 (OH) and 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ= 2.69 (1H, ddd, $J_{2exo,3exo}$=11.1 and $J_{2exo,3endo}$=5.1 Hz, and $J_{2exo,6}$=2.4 Hz, H_{2exo}), 1.93 (1H, dddd, $J_{3exo,2endo}$= 13.0, $J_{3exo,3exo}$=11.1, $J_{3exo,4}$=4.5, and $J_{3exo,5exo}$=3.3 Hz, H_{3exo}), 1.77—1.66 (2H, m, H_4 and H_{3endo}), 1.54—1.39 (2H,

m, H_6), 1.34—1.21 (2H, m, H_5), 1.04 (3H, s, 1-CH_3), 0.90 (3H, s, 7-CH_3), and 0.89 (3H, s, 7-CH_3). Found: C, 72.42; H, 10.11%. Calcd for $C_{11}H_{18}O_2$: C, 72.48; H, 9.95%.

1,7,7-Trimethylbicyclo[2.2.1]hept-5-ene-2-carboxylic acids (5b). A photochemical reaction of an α-diazoketone **4b** (153.0 mg, 0.804 mmol) by a similar method to that used for preparing **8** gave **5b** (108.6 mg, 0.602 mmol) in 75% yield as a 7.3:1 mixture of the *endo* and the *exo* isomers.

5b (the *endo* isomer): Mp 58—61 °C; IR (KBr) 3600—2400 (OH) and 1690 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ= 6.08 (1H, ddd, $J_{5,6}$=5.8 and $J_{5,4}$=3.3 Hz, H_5), 5.66 (1H, d, $J_{6,5}$=5.8 Hz, H_6), 2.78 (1H, dd, $J_{2exo,3exo}$=5.7 and $J_{2exo,3endo}$=3.9 Hz, H_{2exo}), 2.37 (1H, m, H_4), 2.13 (1H, ddd, $J_{3exo,3endo}$=12.6, $J_{3exo,2exo}$=8.7, and $J_{3exo,4}$=3.9 Hz, H_{3exo}), 1.42 (1H, ddd, $J_{3exo,3endo}$=12.6 and $J_{3endo,2exo}$= 3.9 Hz, H_{3endo}), 1.22 (3H, s, 1-CH_3), 0.84 (3H, s, 7*endo*-CH_3), and 0.83 (3H, s, 7*exo*-CH_3); ^{13}C NMR ($CDCl_3$) δ= 181.7 (COOH), 136.0 (C-5), 135.7 (C-6), 59.0 (C-1), 57.0 (C-7), 51.5 (C-4), 47.6 (C-2), 29.5 (C-3), 19.5 (7-CH_3), 19.4 (7-CH_3), and 12.1 (1-CH_3). Found: C, 73.02; H, 9.05%. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.94%.

***exo*-3-Allyl-1-methoxy-*endo*-3-methylbicyclo[2.2.2]oct-5-en-2-one (2e).** To a stirred solution of LDA (14.8 mmol) in THF (20 cm^3) was added dropwise a solution of a ketone **2a** (1.886 g, 12.4 mmol) in THF (10 cm^3) at −78 °C under argon. The mixture was stirred for 15 min. To this mixture was added dropwise a solution of allyl iodide (3.29 g, 19.5 mmol) and HMPA (6.5 cm^3, 37.2 mmol) in THF (10 cm^3) at −78 °C. The mixture was stirred for 2 h, allowed to warm to room temperature, and treated with a saturated aqueous NH_4Cl solution. This mixture was extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Flash chromatography (5:1 hexane–ethyl acetate) of this oil gave a ca. 3:1 mixture of ketones **2c** and **2d** (1.91 g, 9.96 mmol, 80%) and the α,α-bisallylated compound (134 mg, 0.57 mmol, 4.6%).

2c: ^{1}H NMR ($CDCl_3$) δ=6.37 (1H, dd, $J_{5,6}$=8.7 and $J_{5,4}$= 6.3Hz, H_5), 6.19 (1H, d, $J_{6,5}$=8.7 Hz, H_6), 5.83—5.69 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.07—4.98 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 3.53 (3H, s, OCH_3), 2.89–2.83 (1H, m, H_4), 2.60—2.51 (1H, m), and 2.09—1.60 (6H, m).

To a stirred solution of *t*-BuOK (2.33 g, 20.7 mmol) in THF (70 cm^3) was added dropwise a solution of a mixture of ketones **2c** and **2d** (2.54 g, 13.2 mmol) in THF (50 cm^3) at −78 °C under argon over a period of 1 h. The mixture was stirred for 5 min at −78 °C. To this solution was add dropwise iodomethane (1.60 cm^3, 26.4 mmol) at −78 °C. After stirring for 4 h this reaction mixture was allowed to warm to room temperature, and then stirred until the ketones were consumed. The resulting mixture was treated with a saturated aqueous NH_4Cl solution and extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Flash chromatography of this oil on silica gel (200 g, 8:1 hexane–ethyl acetate) gave **2e** (2.52 g, 12.2 mmol, 92%): Colorless oil; IR (neat) 1720 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=6.51 (1H, dd, $J_{5,6}$=8.4 and $J_{5,4}$=6.6 Hz, H_5), 6.18 (1H, d, $J_{6,5}$=8.4 Hz, H_6), 5.88—5.74 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.16—5.10 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 3.53 (3H, s, OCH_3), 2.63 (1H, m, H_4), 2.33 (1H, dd, J=14.1 and 7.2 Hz, CH_2=CH–C<u>H</u>H–), 2.14—1.91 (2H, m, H_{8exo} and CH_2=CH–CH<u>H</u>–), 1.88 (1H, ddd, $J_{7exo,7endo}$=12.3, $J_{7exo,8exo}$=9.8, and $J_{7exo,8endo}$=5.7 Hz, H_{7exo}), 1.73 (1H, ddd, $J_{7endo,7exo}$=12.3, $J_{7endo,8endo}$=12.3, $J_{7endo,8exo}$=3.3 Hz, H_{7endo}), 1.48 (1H, dddd, $J_{8endo,8exo}$= 12.6, $J_{8endo,7endo}$=12.3, $J_{8endo,7exo}$=5.7, and $J_{8endo,4}$= 2.7 Hz, H_{8endo}), and 1.04 (3H, s, 3*endo*-CH_3); ^{13}C NMR ($CDCl_3$) δ=213.2 (C-2), 136.8 (C-5), 132.5 (CH_2=C<u>H</u>–), 130.0 (C-6), 118.5 (C<u>H</u>$_2$=CH–), 84.3 (C-1), 52.9 (OCH_3), 46.3 (C-3), 40.4 (=CH–C<u>H</u>$_2$–), 39.6 (C-4), 25.8 (C-7), 23.4 (2*endo*-CH_3), and 20.9 (C-8). Found; C, 75.41; H, 8.57%. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79%. Found: *m/z* 206.1309. Calcd for $C_{13}H_{18}O_2$: M, 206.1307.

***exo*-3-Allyl-1-methoxy-*endo*-2,*endo*-3-dimethylbicyclo[2.2.2]oct-5-en-exo-2-ol (9) and -*exo*-2,*endo*-3-dimethylbicyclo[2.2.2]oct-5-en-endo-2-ol (10).** To a stirred solution of a ketone **2e** (3.132 g, 15.2 mmol) in THF (50 cm^3) was added dropwise a solution of 0.95 M (1 M=1 mol dm^{-3}) CH_3MgBr (19.1 cm^3, 18.2 mmol) in THF at −78 °C under argon. After 2.5 h stirring, the mixture was allowed to warm to room temperature, and then stirred until **2e** was consumed. The reaction mixture was first treated with saturated aqueous NH_4Cl solution, and then extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (50 g, 9:1 hexane–ethyl acetate) gave **9** (2.90 g, 13.1 mmol, 86%) and **10** (438.9 mg, 1.97 mmol, 12%).

9: Colorless needles; mp 50—51 °C (hexane); IR (neat) 3500 cm^{-1} (OH); ^{1}H NMR ($CDCl_3$) δ=6.25 (1H, dd, $J_{5,6}$= 8.7 and $J_{5,4}$=6.3 Hz, H_5), 6.17 (1H, d, $J_{6,5}$=8.7 Hz, H_6), 5.99—5.85 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.09—5.00 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 3.36 (3H, s, OCH_3), 2.42 (1H, broad dd, CH_2=CH–C<u>H</u>H–), 2.21 (1H, broad dd, CH_2=CH–CH<u>H</u>–), 2.11—2.06 (1H, m, H_4), 2.05—1.93 (2H, m, H_{7exo} and H_{8exo}), 1.91 (1H, broad s, OH), 1.46—1.38 (1H, m, H_{7endo}), 1.15 (1H, dddd, $J_{8endo,8exo}$=12.0, $J_{8endo,7endo}$= 12.0, $J_{8endo,7exo}$=4.5, and $J_{8endo,4}$=3.0 Hz, H_{8endo}), 1.08 (3H, s, 2*endo*-CH_3), and 0.85 (3H, s, 3*endo*-CH_3); ^{13}C NMR ($CDCl_3$) δ=137.1 (CH_2=C<u>H</u>–), 134.5 (C-5), 131.0 (C-6), 116.4 (C<u>H</u>$_2$=CH–), 82.9 (C-1), 78.7 (C-2), 51.5 (OCH_3), 42.7 (C-4), 41.2 (C-3), 40.7 (=CH–C<u>H</u>$_2$–), 25.4 (3*endo*-CH_3), 23.6 (2*endo*-CH_3), 20.5 (C-8), and 19.6 (C-7). Found: C, 75.33; H, 10.11%. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97%.

10: Colorless needles; mp 45—45.5 °C (hexane); IR (KBr) 3470 cm^{-1} (OH); ^{1}H NMR ($CDCl_3$) δ=6.39 (1H, dd, $J_{5,6}$=8.7 and $J_{5,4}$=6.6 Hz, H_5), 6.25 (1H, d, $J_{6,5}$= 8.7 Hz, H_6), 5.91—5.77 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.10—5.04 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 3.05 (3H, s, OCH_3), 2.03—2.14 (3H, m, H_4 and CH_2=CH–C<u>H</u>H–), 1.98 (1H, broad s, OH), 1.86 (1H, dddd, $J_{8exo,8endo}$=12.6, $J_{8exo,7endo}$=9.6, $J_{8exo,7endo}$=3.3, and $J_{8exo,4}$=3.0 Hz, H_{8exo}), 1.58 (1H, ddd, $J_{7endo,7exo}$=12.5, $J_{7endo,8endo}$=12.5, and $J_{7endo,8exo}$=3.3 Hz, H_{7endo}), 1.47 (1H, ddd, $J_{7exo,7endo}$=12.5, $J_{7exo,8exo}$= 9.6, and $J_{7exo,8endo}$=5.4 Hz, H_{7exo}), 1.24 (3H, s, 2*exo*-CH_3), 1.14 (1H, dddd, $J_{8endo,8exo}$=12.6, $J_{8endo,7endo}$= 12.5, $J_{8endo,7exo}$=5.4, and $J_{8endo,4}$=3.0 Hz, H_{8endo}), and 0.90 (3H, s, 3*endo*-CH_3); ^{13}C NMR ($CDCl_3$) δ=135.5 (CH_2=C<u>H</u>–), 134.8 (C-5), 131.2 (C-6), 117.4 (C<u>H</u>$_2$=CH–), 82.9 (C-1), 80.0 (C-2), 51.7 (OCH_3), 45.2 (C-3), 42.2 (C-4), 39.3 (=CH–C<u>H</u>$_2$–), 22.3 (C-7), 21.9 (3*endo*-CH_3), 20.7 (C-8), and 18.4 (2*exo*-CH_3).

***exo*-8-Allyl-1,*endo*-8-dimethylbicyclo[3.2.1]oct-6-en-2-one (3e).** A solution consisting of an alcohol **9** (1.156 g, 5.19 mmol), TsOH (monohydrate, 82 mg, 0.43 mmol) and dry benzene (15 cm^3) was heated at 80 °C (bath temperature) for 1 h. The reaction mixture was first treated with a saturated aqueous $NaHCO_3$ solution, and then extracted with three portions of ether. The combined extracts were washed with saturated brine and dried over Na_2SO_4. Evaporation of the solvent gave **3e** (972 mg, 5.11 mmol, 98%) as a colorless oil.

3e: IR (neat) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.13 (1H, dd, $J_{6,7}$=5.7 and $J_{6,5}$=3.0 Hz, H_6), 5.80 (1H, ddt, J=18.0, 9.3, and 7.2 Hz, CH_2=C<u>H</u>–CH_2–), 5.53 (1H, d, $J_{7,6}$=5.7 Hz, H_7), 5.12—5.06 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 2.66 (1H, ddd, $J_{3exo,3endo}$=17.7, $J_{3exo,4endo}$=9.9, and $J_{3exo,4exo}$=7.8 Hz, H_{3exo}), 2.47 (1H, ddd, $J_{5,4endo}$=3.2, $J_{5,6}$=3.0, and $J_{5,4exo}$=2.9 Hz, H_5), 2.24 (1H, dd, $J_{3endo,3exo}$=17.7 and $J_{3endo,4exo}$=7.8 Hz, H_{3endo}), 2.08 (1H, dddd, $J_{4exo,4endo}$= 13.2, $J_{4exo,3exo}$=7.8, $J_{4exo,3endo}$=7.8, and $J_{4exo,5}$=3.2 Hz, H_{4exo}), 1.99 (2H, d, J=7.2 Hz, CH_2=CH–C<u>H</u>$_2$–), 1.63 (1H, ddd, $J_{4endo,4exo}$=13.2, $J_{4endo,3exo}$=9.9, and $J_{4endo,5}$=3.2 Hz, H_{4endo}), 1.01 (6H, s, 1-CH_3 and 8*exo*-CH_3); ^{13}C NMR ($CDCl_3$) δ=212.2 (C-2), 136.2 (C-6), 136.0 (C-7), 133.7 (CH_2=<u>C</u>H–), 117.6 (<u>C</u>H$_2$=CH–), 64.5 (C-1), 52.8 (C-8), 47.8 (C-5), 37.2 (=CH–<u>C</u>H$_2$–), 34.1 (C-3), 21.0 (C-4), 20.0 (8-CH_3), and 10.1 (1-CH_3). Found; *m/z* 190.1370. Calcd for $C_{13}H_{18}O$: M, 190.1358.

***exo*-8-Allyl-3-diazo-1,*endo*-8-dimethylbicyclo-[3.2.1]oct-6-en-2-one (4e).** To a stirred solution of *t*-BuOK (1.031 g, 9.26 mmol) in THF (50 cm^3) was added dropwise a solution of a ketone **3e** (931 mg, 4.30 mmol) and 2,4,6-triisopropylbenzenesulfonyl azide (1.638 g, 5.10 mmol) in THF (20 cm^3) at −78 °C under argon. The mixture was first stirred for 30 min, and then treated with a saturated aqueous NH_4Cl solution. The resulting cold mixture was extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (80 g, 8:1 hexane–ethyl acetate) gave **4e** (544. mg, 3.90 mmol, 91%) and an identified product (66 mg).

4e: Pale yellow oil; UV (CH_3OH) 291 (ε 6900), 275 (sh, 6700), and 220 nm (4500); IR (neat) 2080 (–N_2) and 1640 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=6.04 (1H, dd, $J_{6,7}$=5.6 and $J_{6,5}$=3.0 Hz, H_6), 5.91—5.77 (1H, dddd, J=16.8, 10.2, 7.7, and 6.9 Hz, CH_2=C<u>H</u>–CH_2–), 5.64 (1H, d, $J_{7,6}$=5.6 Hz, H_7), 5.16—5.09 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 2.98 (1H, dd, $J_{4exo,4endo}$=13.8 and $J_{4exo,5}$=1.5 Hz, H_{4exo}), 2.51 (1H, m, H_5), 2.44 (1H, dd, $J_{4endo,4exo}$=13.8 and $J_{4endo,5}$= 1.8 Hz, H_{4endo}), 2.39 (1H, dd, J=14.4 and J=6.9 Hz, CH_2=CH–C<u>H</u>H–), 2.12 (1H, dd, J=14.4 and J=7.7 Hz, CH_2=CH–C<u>H</u>H–, H_{4endo}), 1.14 (3H, s, 1-CH_3), and 1.02 (3H, s, 8*exo*-CH_3); ^{13}C NMR ($CDCl_3$) δ=195.9 (C-2), 138.1 (C-7), 134.4 (C-6 or <u>C</u>H$_2$=CH–), 134.2 (<u>C</u>H$_2$=CH– or C-6), 117.8 (<u>C</u>H$_2$=CH–), 61.8 (C-1), 60.0 (C-3), 50.3 (C-8), 45.8 (C-5), 36.6 (=CH–<u>C</u>H$_2$–), 23.3 (C-4), 20.8 (8-CH_3), and 10.0 (1-CH_3). Found: C, 71.91; H, 7.60; N, 12.83%. Calcd for $C_{13}H_{16}N_2O$: C, 72.19; H, 7.45; N, 12.95%.

***exo*-7-Allyl-1,*endo*-7-dimethylbicyclo[2.2.1]hept-5-ene-2-carboxylic Acids (5e).** The photochemical reaction of an α-diazoketone **4e** (543 mg, 2.51 mmol) by a similar method to that used for preparing **8** gave **5e** (463.8 mg, 2.25 mmol, 90%) as a 4:1 mixture of the *endo* and *exo* isomers. Fractional crystallization of the mixture from hexane gave the *endo* isomer: Mp 80—81 °C (hexane); IR (neat); IR (neat) 3400—2400 (broad) and 1700 cm^{-1} (COOH); ^1H NMR ($CDCl_3$) δ=6.06 (1H, dd, $J_{5,6}$=5.7 and $J_{5,4}$=3.3 Hz, H_5), 5.85—5.70 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.68 (1H, d, $J_{6,5}$=5.7 Hz, H_6), 5.07—4.99 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 2.85 (1H, dd, $J_{2exo,3exo}$=9.0 and $J_{2exo,3endo}$=3.9 Hz, H_{2exo}), 2.48 (1H, dd, $J_{4,3exo}$=3.7 and $J_{4,5}$=3.3 Hz, H_4), 2.11 (1H, ddd, $J_{3exo,3endo}$=12.5, $J_{3exo,2exo}$=9.0 and $J_{3exo,4}$=3.7 Hz, H_{3exo}), 2.00 (1H, dd, J=13.4 and 6.9 Hz, CH_2=CH–C<u>H</u>H–), 1.83 (1H, dd, J=13.4 and 7.4 Hz, CH_2=CH–CH<u>H</u>–), 1.46 (1H, dd, $J_{3endo,3exo}$=12.5 and $J_{3endo,2exo}$=3.9 Hz, H_{3endo}), 1.25 (3H, s, 1-CH_3), and 0.84 (3H, s, 7*endo*-CH_3); ^{13}C CNR ($CDCl_3$) δ=180.7 (COOH), 136.5 (C-5), 135.2 (C-6), 134.8 (CH_2=<u>C</u>H–), 116.7 (<u>C</u>H$_2$=CH–), 61.4 (C-1), 57.4 (C-7), 48.8 (C-4), 47.7 (C-2), 37.3 (=CH–<u>C</u>H$_2$–), 28.7 (C-3), 16.1 (C-CH_3), and 12.3 (7-CH_3). Found: C, 75.43; H, 9.09%. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79%.

***exo*-7-Allyl-1,*endo*-7-dimethylbicyclo[2.2.1]hept-5-ene-2-carboxamides (11).** A mixture of acids **5e** (209.8 mg, 1.01 mmol) and thionyl chloride (2.0 cm^3, 27.4 mmol) was heated under reflux for 20 min at 110 °C (bath temperature). After the reaction mixture was dissolved in THF (5 cm^3), it was added dropwise to precooled aqueous ammonia at 0 °C with vigorous stirring. This mixture was stirred for 30 min, and then extracted with three portions of ether. The combined extracts were washed with saturated brine and dried over Na_2SO_4. Evaporation of the solvent gave **11** (201.8 mg, 0.980 mmol, 97%) as a white solid. Fractional crystallization of the mixture from hexane gave the *endo* isomer: Mp 79—81.5 °C (hexane); IR (KBr) 3440, 3350, 3310, 3210, 3070 (NH), and 1670 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ=6.14 (1H, dd, $J_{5,6}$=5.7 and $J_{5,4}$=3.3 Hz, H_5), 5.84—5.71 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.73 (1H, d, $J_{6,5}$=5.7 Hz, H_6), 5.59—5.28 (2H, broad, NH_2), 5.07—5.01 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 2.77 (1H, dd, $J_{2exo,3exo}$=8.9 and $J_{2exo,3endo}$=4.2 Hz, H_{2exo}), 2.51 (1H, dd, $J_{4,3exo}$=3.6 and $J_{4,5}$=3.3 Hz, H_4), 2.18 (1H, ddd, $J_{3exo,3endo}$=12.8, $J_{3exo,2exo}$=8.9 and $J_{3exo,4}$=3.6 Hz, H_{3exo}), 2.04 (1H, dd, J=14.0 and 6.9 Hz, CH_2=CH–CH<u>H</u>–), 1.86 (1H, dd, J=14.0 and 4.2 Hz, CH_2=CH–C<u>H</u>H–), 1.30 (1H, dd, $J_{3endo,3exo}$= 12.8 and $J_{3endo,2exo}$=4.2 Hz, H_{3endo}), 1.22 (3H, s, 1-CH_3), and 0.86 (3H, s, 7*endo*-CH_3).

***exo*-7-Allyl-1,*endo*-7-dimethylbicyclo[2.2.1]hept-5-ene-2-carbonitriles (12).** To a solution of amides **11** (350.5 mg, 1.71 mmol) in CH_2Cl_2 (5 cm^3) was added *N,N*-diethyl-*N*-[[(methylcarboxy)amino]sulfonyl]ethanaminium-hydroxide, inner salt[13] (540 mg, 2.05 mmol) under argon, it was then stirred overnight at room temperature. This reaction mixture was diluted with ethyl acetate and chromatographed on alumina (1:1 hexane–ethyl acetate) gave **12** (280.6 mg, 1.50 mmol, 88%) as a mixture of the *endo* and *exo* isomers. Fractional crystallization of the mixture from hexane gave the *endo* isomer: Mp 38—39.5 °C (hexane); IR (neat) 2220 cm^{-1} (CN); ^1H NMR ($CDCl_3$) δ=6.22 (1H, dd, $J_{5,6}$=5.7 and $J_{5,4}$=3.3 Hz, H_5), 5.90 (1H, d, $J_{6,5}$= 5.7 Hz, H_6), 5.80—5.56 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.07—5.00 (2H, m, C<u>H</u>$_2$=CH–CH_2–), 2.81 (1H, dd, $J_{2exo,3exo}$=9.0 and $J_{2exo,3endo}$=3.9 Hz, H_{2exo}), 2.57 (1H, dd, $J_{4,3exo}$=3.6 and $J_{4,5}$=3.3 Hz, H_4), 2.30 (1H, ddd, $J_{3exo,3endo}$=12.3, $J_{3exo,2exo}$=9.0, and $J_{3exo,4}$=3.6 Hz, H_{3exo}), 1.85—1.81 (2H, m, CH_2=CH–C<u>H</u>$_2$–), 1.36 (1H, dd, $J_{3endo,3exo}$=12.3 and

$J_{3endo,2exo}$=3.9 Hz, H_{3endo}), 1.24 (3H, s, 1-CH_3), and 0.88 (3H, s, 7*endo*-CH_3). Found: C, 83.49; H, 9.18; N, 7.52%. Calcd for $C_{13}H_{17}N$: C, 83.37; H, 9.18; N, 7.47%.

***exo*-7-Allyl-1,*endo*-7-dimethylbicyclo[2.2.1]hept-5-en-2-one (13).** To a stirred solution of LDA (3.36 mmol) in THF (5.0 cm^3) prepared under argon was added dropwise a solution of a nitrile **12** (482.2 mg, 2.57 mmol) in THF (5 cm^3) at −78 °C. The mixture was stirred for 10 min at −78 °C. Dry oxygen was bubbled into the solution for 80 min at −78 °C. This mixture was stirred for an additional hour under oxygen and transferred into ice-cooled 1 M sodium sulfite solution (20 cm^3) through a double-ended needle. After stirring overnight, it was extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Flash chromatography (8:1 hexane–ethyl acetate) of this oil gave **13** (326.5 mg, 1.85 mmol, 72%): A colorless oil; IR (neat) 1740 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=6.45 (1H, dd, $J_{5,6}$=5.4 and $J_{5,4}$=3.0 Hz, H_5), 5.85—5.71 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.59 (1H, d, $J_{6,5}$=5.4 Hz, H_6), 5.10—5.01 (2H, m, C<u>H_2</u>=CH–CH_2–), 2.77 (1H, dd, $J_{4,3exo}$=3.3 and $J_{4,5}$=3.0 Hz, H_4), 2.18 (1H, dd, $J_{3exo,3endo}$=16.8 and $J_{3exo,4}$=3.3 Hz, H_{3exo}), 2.01—1.85 (2H, m, CH_2=CH–C<u>H_2</u>–), 1.94 (1H, d, $J_{3endo,3exo}$=16.8 Hz, H_{3endo}), 1.08 (3H, s, 7*endo*-CH_3), and 1.03 (3H, s, 1-CH_3). Found: *m/z* 176.1209. Calcd for $C_{12}H_{16}O$: M, 176.1201.

***exo*-7-Allyl-1,*endo*-7-dimethylbicyclo[2.2.1]hept-5-en-2-one Ethylene Acetal (14).** A solution consisting of a ketone **13** (197.1 mg, 1.12 mmol), ethylene glycol (1.0 cm^3, 17.9 mmol), TsOH (monohydrate, 181.0 mg, 0.960 mmol), and benzene (4 cm^3) was heated under reflux for 86 h at 140 °C (bath temperature) while removing water by a Dean-Stark trap. After a saturated aqueous $NaHCO_3$ solution was added to the reaction mixture, and it was extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (8:1 hexane–ethyl acetate) gave **14** (147.9 mg, 0.670 mmol, 60%): A colorless oil; IR (neat) 1640 cm^{-1} (C=C); ^{1}H NMR ($CDCl_3$) δ=6.14 (1H, dd, $J_{5,6}$=5.7 and $J_{5,4}$=3.3 Hz, H_5), 5.91—5.74 (1H, m, CH_2=C<u>H</u>–CH_2–), 5.82 (1H, d, $J_{6,5}$= 5.7 Hz, H_6), 5.09—4.98 (2H, m, C<u>H_2</u>=CH–CH_2–), 4.00—3.71 (4H, m, –OCH_2CH_2O–), 2.78 (1H, broad dd, J=15.0 and 6.3 Hz, CH_2=CH–C<u>H</u>H–), 2.50 (1H, dd, $J_{4,3exo}$=3.5 and $J_{4,5}$=3.3 Hz, H_4), 2.06 (1H, dd, $J_{3exo,3endo}$=12.6 and $J_{3exo,4}$=3.5 Hz, H_{3exo}), 1.93 (2H, broad dd, J=15.0 and 7.5 Hz, CH_2=CH–CH<u>H</u>–), 1.49 (1H, d, $J_{3endo,3exo}$=12.6 Hz, H_{3endo}), 0.97 (3H, s, 1-CH_3), and 0.93 (3H, s, 7*endo*-CH_3).

***exo*-7-(3-Hydroxypropyl)-1,*endo*-7-dimethylbicyclo[2.2.1]hept-5-en-2-one Ethylene Acetal (15).** To a solution of a ketone **14** (131.2 mg, 0.595 mmol) in THF (3.0 cm^3) was added 9-BBN (0.51 M THF solution, 1.4 cm^3, 0.71 mmol) under argon. The mixture was stirred at room temperature for 70 min. To this solution was added methanol (0.5 cm^3), followed by the addition of a 5% aqueous NaOH solution (1.0 cm^3) and 30% hydrogen peroxide (0.5 cm^3). The resulting mixture was heated under reflux for 1 h. This mixture was treated with a saturated aqueous NH_4Cl solution and extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (1:1 hexane–ethyl acetate) gave **15** (117.4 mg, 0.492 mmol, 83%): A colorless oil; IR (neat) 3600—3200 (OH) and 1640 cm^{-1} (C=C); ^{1}H NMR ($CDCl_3$) δ=6.15 (1H, dd, $J_{5,6}$=5.7 and $J_{5,4}$=3.3 Hz, H_5), 5.82 (1H, d, $J_{6,5}$=5.7 Hz, H_6), 4.00—3.70 (4H, m, –OCH_2CH_2O–), 3.67—3.61 (2H, m, HOC<u>H_2</u>), 2.51 (1H, broad dd, $J_{4,3exo}$= 3.3 and $J_{4,5}$=3.3 Hz, H_4), 2.01 (1H, dd, $J_{3exo,3endo}$=12.6 and $J_{3exo,4}$=3.6 Hz, H_{3exo}), 1.67—1.40 (4H, m), 1.49 (1H, d, $J_{3endo,3exo}$=12.6 Hz, H_{3endo}), 0.97 (3H, s, 1-CH_3), and 0.94 (3H, s, 7*endo*-CH_3).

***exo*-7-(3-Hydroxypropyl)-1,*endo*-7-dimethylbicyclo[2.2.1]hept-5-en-2-one (16).** (a) To a solution of a ketone **13** (70.7 mg, 0.401 mmol) in THF (3.0 cm^3) was added 9-BBN (0.51 M THF solution, 1.76 cm^3, 0.880 mmol) under argon. The mixture was stirred at room temperature for 2 h. Additional 9-BBN (0.5 mmol) was added to the solution, since **13** remained by this stage. The reaction mixture was stirred at room temperature for 1 h. To the reaction mixture were added methanol (0.5 cm^3), a 5% aqueous NaOH solution (1.0 cm^3), and 30% hydrogen peroxide (0.5 cm^3). The resulting mixture was heated under reflux for 1 h. After a saturated aqueous NH_4Cl solution was added, the mixture was extracted with three portions of ether. The combined extracts were washed with saturated brine, dried over Na_2SO_4, and concentrated to an oil. Chromatography of this oil on silica gel (10 g, 1:1 hexane–ethyl acetate) gave **16** (60.0 mg, 0.310 mmol, 78%) as a colorless oil.

(b) A solution consisting of an acetal **15** (165.4 mg, 0.693 mmol), PPTS (83 mg, 0.33 mmol), and 4:1 acetone–H_2O (5 cm^3) was heated under reflux for 3 h. To the reaction mixture was added a saturated aqueous $NaHCO_3$ solution, and this mixture was then extracted with three portions of ether. The combined extracts were washed with saturated brine and dried over Na_2SO_4. Evaporation of the solvent gave **16** (132.0 mg, 0.680 mmol, 98%): IR (neat) 3600—3200 (OH) and 1740 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=6.46 (1H, dd, $J_{5,6}$=5.7 and $J_{5,4}$=3.0 Hz, H_5), 5.59 (1H, d, $J_{6,5}$=5.7 Hz, H_6), 3.61 (2H, m, HOC<u>H_2</u>), 2.80 (1H, broad dd, $J_{4,3exo}$= 3.3 and $J_{4,5}$=3.0 Hz, H_4), 2.13 (1H, dd, $J_{3exo,3endo}$=16.8 and $J_{3exo,4}$=3.3 Hz, H_{3exo}), 1.93 (1H, d, $J_{3exo,3endo}$=16.8 H_{3endo}), 1.54—1.43 (1H, m), 1.38—1.31 (1H, broad), 1.29—1.18 (2H, m, H_8), 1.08 (3H, s, 7-CH_3), and 1.02 (3H, s, 1-CH_3). Found: *m/z* 194.1311. Calcd for $C_{12}H_{18}O_2$: M, 194.1307.

***exo*-7-(3-Hydroxypropyl)-1,*endo*-7-dimethylbicyclo[2.2.1]heptan-2-one (17).** To a solution of **16** (132.0 mg, 0.680 mmol) in ethyl acetate (5 cm^3) was added 5% Pd–C (77 mg). The mixture was first stirred under H_2 for 3.5 h, and then filtered through a silica-gel layer. Evaporation of the filtrate gave a crystalline solid. Chromatography of the solid on silica gel (10 g, 1:1 hexane–ethyl acetate) gave **17** (131.9 mg, 0.678 mmol, 98%): A colorless oil; IR (neat) 3600—3200 (OH) and 1742 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=3.63—3.85 (2H, m, HOC<u>H_2</u>), 2.31—2.22 (2H, m), 1.95—1.82 (2H, m), 1.79—1.64 (2H, m), 1.56—1.45 (1H, m), 1.43—1.32 (3H, m), 1.22—1.02 (2H, m), 0.97 (3H, s, 7-CH_3), and 0.92 (3H, s, 1-CH_3). Found: C, 73.42; H, 10.45%. Calcd for $C_{12}H_{20}O_2$: C, 73.42; H, 10.26%.

(±)-Camphorenone (±)-(1). To a mixture of PCC (120 mg, 0.556 mmol), celite (1.411 g), and dichloromethane (26 cm^3) was added a solution of **17** (69.4 mg, 0.353 mmol) in dichloromethane (2 cm^3) at room temperature under ar-

gon. The mixture was first stirred for 2 h, and then filtered through a florisil layer. The concentration of the filtrate gave a colorless oil. Chromatography of the oil on silica gel (25 g, 3:1 hexane–ethyl acetate) gave *exo*-7-formylethyl-1,*endo*-7-dimethylbicyclo[2.2.1]heptan-2-one (**18**, 52.4 mg, 0.270 mmol, 77%) as a colorless oil. To a solution of isopropyltriphenylphosphonium iodide (450 mg, 1.04 mmol) in ether (3 cm^3) was added dropwise 1.65 M butyllithium in hexane (0.51 cm^3, 0.84 mmol) at 0 °C under argon. After 50 min stirring, a solution of **18** (39.9 mg, 0.21 mmol) in ether (3 cm^3) was added dropwise to the reaction mixture and stirred for 30 min. The resulting mixture was filtered, and the solid was washed well with ether. The filtrate was washed with water and with saturated brine, and then dried over Na_2SO_4. Evaporation of the solvent gave a colorless oil. Flash chromatography of the oil on silica gel (50 g, 9:1 hexane–ethyl acetate) gave (±)-**1** (21.4 mg, 0.097 mmol, 46% from **18**): A colorless oil; IR (neat) 1742 (C=O) and 835 cm^{-1} (trisubstited alkene); ^1H NMR ($CDCl_3$) δ=5.08—5.02 (1H, m), 2.31—2.24 (2H, m), 2.15—2.03 (1H, m), 1.97—1.80 (2H, m), 1.74—1.69 (2H, m), 1.66 (3H, s), 1.59 (3H, s), 1.45—1.26 (2H, m), 1.17—0.87 (2H, m), 0.97 (3H, s), and 0.90 (3H, s); ^{13}C NMR ($CDCl_3$) δ=219.5 (C-2), 131.5 ($(CH_3)_2\underline{C}$=CH), 124.1 (C=$\underline{C}$H–CH_2–), 58.6 (C-1), 48.5 (C-7), 42.6 (C-3), 39.6 (C-4), 33.9 (7-CH_2–), 29.9 (C-6), 26.8 (C-5), 25.5 ($\underline{C}H_3$–C=), 23.7 (=CH–$\underline{C}H_2$–), 17.4 ($\underline{C}H_3$–C=), 15.8 (7-CH_3), and 9.1 (1-CH_3). Found: C, 81.90; H, 11.20%. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.97%.

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