resulting solution was then warmed to room temperature and was extracted with $CHCl_3$ (15 mL). The $CHCl_3$ solution was extracted with $NaHCO_3$ solution (10%, 2 × 5 mL), acidified with cold 10% HCl solution, and extracted with $CHCl_3$ (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and the solvents removed in vacuo. Recrystallization of the residue from acetone–petroleum ether afforded 0.015 g (79%) of 2-hydroxytetronic acid **4**, mp 238–239 °C (lit.[12] mp 235 °C).

Method II. To a solution of 2-(phenylmethoxy)tetronic acid **15** (0.05 g, 0.18 mmol) in EtOH (4 mL) were added 10% Pd/C (0.05 g) and cyclohexene (0.37 mL, 3.6 mmol). The resulting mixture was refluxed for 15 min under argon, filtered, and concentrated in vacuo and the residue taken up in Et_2O (30 mL). The Et_2O solution was extracted with $NaHCO_3$ solution (10%, 2 × 10 mL), which was acidified with cold 10% HCl solution and extracted with $CHCl_3$ (2 × 10 mL). The $CHCl_3$ extracts were combined and dried (Na_2SO_4). Removal of the solvents in vacuo, followed by recrystallization from acetone–petroleum ether, gave 0.031 g (91%) of 2-hydroxytetronic acid **4**.

Method III. 2-Hydroxytetronate **23** (4.0 g, 20.2 mmol) was stirred with HBr solution (48%, 80.0 mL) at 45 °C for 12 h. The reaction mixture was diluted with ice-cold H_2O (300 mL) and extracted with Et_2O (100 mL). The organic extract was extracted with $NaHCO_3$ solution (10%, 3 × 50 mL), which was acidified with cold 10% HCl solution. The resulting solid was filtered, dried, and recrystallized from acetone–petroleum ether to give crystalline 2-hydroxytetronic acid **4** (2.2 g, 60%).

3,4-Dihydroxy-1-oxaspiro[4.4]non-3-en-2-one (5). Method I. Treatment of the enol acetate **18** (0.02 g, 0.09 mmol) with a 1 M solution of BBr_3 in CH_2Cl_2 (0.44 mL, 0.44 mmol), followed by the workup for **4** (method I) and recrystallization from acetone–petroleum ether, gave 0.012 g (80%) of 2-hydroxytetronic acid **5**: mp 211–212 °C; IR (KBr) 1640 (C=C), 1728 (C=O), 3320 (OH) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.4–2.2 (m, 8 H, $(CH_2)_4$), 3.34 (brs, 1 H, OH), 10.16 (very brs, 1 H, OH). Anal. Calcd for $C_8H_{10}O_4$: C, 56.46; H, 5.92. Found: C, 56.53; H, 5.84.

Method II. Treatment of 2-(phenylmethoxy)tetronic acid **16** (0.05 g, 0.19 mmol) with 10% Pd/C (0.05 g) and cyclohexene (0.39 mL, 3.8 mmol), followed by the workup for **4** (method II) and recrystallization from acetone–petroleum ether, afforded 0.029 g (89%) of 2-hydroxytetronic acid **5**.

Method III. Treatment of 2-hydroxytetronate **24** (4.0 g, 21.7 mmol) with HBr solution (48%, 55.0 mL) at 45 °C for 12 h, followed by the workup for **4** (method III) and recrystallization from acetone–petroleum ether, gave 2.03 g (55%) of 2-hydroxytetronic acid **5**.

Stereospecificity of the Photorearrangement of Nitronate Anions and Its Utilization for Stereospecific Cleavage of Cyclic Compounds

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We have reported high regioselectivity of the photorearrangement of nitronate anions in preceding papers.[1-3] The nitronate anions are transformed to hydroxamic acids by irradiation with a low-pressure mercury lamp. These rearrangements are controlled by the number of substituents at the β-carbon atoms, and in the case of the same number of substituents the β-carbon atom with an electron-withdrawing group migrates to the nitrogen atom.

Scheme I

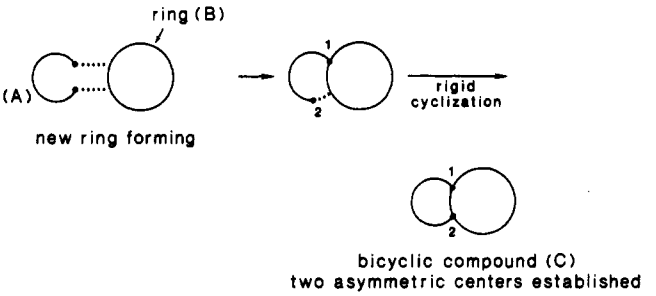

Table I. Retention of the Photorearrangement

entry	chemical yield,[a] %	ratio of the major diastereomer: before reaction, % (form)	ratio of the major diastereomer: after reaction, % (form)
1	14	91[b] (*R*)	90
2	47	99 (**2a**)	99 (**2b**)
3	81	96 (**3a**)	99 (**3b**)
4	62	99 (**4a**)	99 (**4ab**)
5	42	99 (**5a**)	99 (**5b**)

[a] Isolated yield. [b] Ratio of the major enantiomer.

In the synthesis of organic compounds having asymmetric carbons it is necessary that reactions take place regioselectively and stereospecifically. From this viewpoint, the stereospecificity of the photoreaction was investigated by using nitro compounds **1a–5a**. In all cases, the reaction showed complete retention of stereochemistry. In this manner normally inaccessible lactams such as 2-azabicyclo[3.2.1]octan-3-ones and 3-azabicyclo[3.2.1]octan-2-ones[4] were synthesized easily without loss of stereochemistry. Hydrolysis of lactams and **2c** and **3c** gave 1,3-disubstituted cyclopentane amino acid methyl esters that have several asymmetric centers.

Steric hindrance and stereoelectronic effects are effective in controlling the stereochemistry of the generated diastereomers; however, it is impossible to control them perfectly. In order to get a single diastereomer, it is necessary to choose a rigid polycyclic compound and to cleave the rings by a stereospecific method. Many natural products were synthesized by this methodolgy recently.[5-8] According to Scheme I the bicyclic compound (C) is synthesized by ring (B) and (A). If the bicyclic compound (C) is rigid and has no plane of symmetry, the number (k) of asymmetric centers is $2(N - 1)$ (N equals the number of rings). For example, bicyclic compound **2a** can exist in only the 1*R*,4*S* or 1*S*,4*R* form, as the 1*S*,4*S* and 1*R*,4*R* forms would be impossibly strained. So rigid bicyclo[2.2.1]heptanes have a pair of asymmetric centers ($k = 2(2 - 1) = 2$). Similarly **3a–5a** have two asymmetric carbons produced by the relationship.

Compound **1a** (82% ee[9]), prepared by the method of Mukaiyama et al.,[10] was irradiated in sodium meth-

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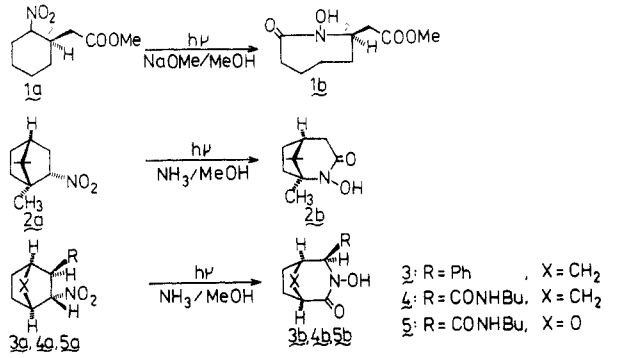
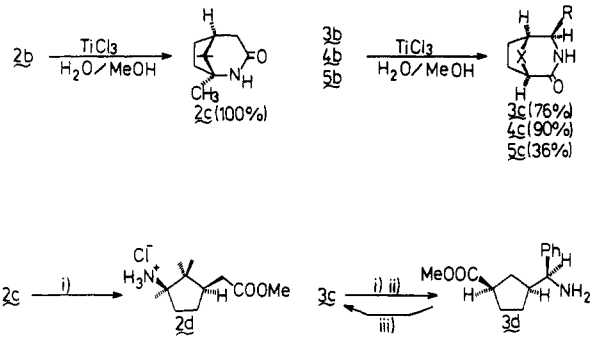
0022-3263/87/1952-2327$01.50/0

Scheme II



Scheme III



oxide/methanol by using a low-pressure mercury lamp, to afford **1b** in 79% ee. From this, it was clear that this photorearrangement proceeded stereospecifically; however, at this stage it was not apparent whether the reaction proceeded by retention or inversion at C-2. Therefore, the reaction was applied to nitro compounds with several asymmetric centers, which permits determination of the ratio of diastereomeric products formed. Hence nitro compound **2a**,[11] which has two asymmetric centers, was irradiated in ammonia/methanol to give *N*-hydroxylactam **2b**[3,12] after purification by column chromatography. Similarly **3a**, **4a**, and **5a**, which have three asymmetric carbon atoms, were prepared and irradiated. Bicyclic compound **3a** was obtained by hydrogenation of the Diels–Alder adduct.[13] Compound **4a** was prepared by amidation[14] of the hydrogenated Diels–Alder adduct,[13] and **5a** was synthesized by amidation of 3-nitro-7-oxabicyclo[2.2.1]heptane-2-carboxylic acid.[15]

The results of the photorearrangement are depicted in Scheme II and Table I. The ratio of diastereomers of starting material (**2a–5a**) was determined by ^{1}H NMR[16] spectroscopy utilizing the H–C(–NO_2) and H–C(–R) signal. The ratio of products (**2b–5b**) was determined by using the signal of H-4, the structure of the products being based on chemical shifts and coupling constants. The results indicated almost complete retention of the stereochemistry.

The *N*-hydroxylactams **2b–5b** were reduced to lactams **2c–5c** by the method of Miller et al.[17] Acid-catalyzed solvolysis of **2c** and **3c** gave the methyl esters of amino acids **2d** and **3d**. Product **2d** was represented by only one isomer (Scheme III) on the bases of ^{1}H and ^{13}C NMR spectrometers.[18] Refluxing **3d** in benzene yielded lactam **3c** in 88% yield,[19] thus proving that the stereochemistry of **3d** was not changed in the solvolysis.

The above observation permits the following conclusion. The nitro group is an essential element in a three-step cleavage process of bicyclic compounds to monocyclic products. The stereochemistry of the products follows from the stereochemistry at the bridgehead carbons of the rigid bicyclic starting materials. In this way it has been shown that there is formed only one of two possible diastereomers.

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(18) There is no signal of other diastereomer on these NMR charts.
(19) The same stereochemistry was evident from the ^{1}H NMR spectrum.

Experimental Section

^{1}H NMR spectra were recorded on Hitachi R-24B and R-600 spectrometers and JEOL JNM-GX270 and JNM-FX270 spectrometers. ^{13}C NMR spectra were recorded on JEOL JNM-GX270 and JNM-FX270 spectrometers. Tetramethylsilane was used as an internal standard. Low-resolution mass spectra were recorded on a Hitachi M-60 spectrometer, and high-resolution mass spectra were recorded on a Hitachi RMU-7M spectrometer. The optical rotations were measured with a Jasco DIP-140 polarimeter. Melting points were obtained on a Yanako MP-S3 appartus, and values are uncorrected. Merck 7731, type 60G, was used for centrifugal chromatography, and Wakogel C-200, 100–200 mesh, was used for column chromatography. Photo reaction was performed by a low-pressure mercury lamp (Ushio, 80 W).

***N*-Hydroxy-7-[(methoxycarbonyl)methyl]hexahydroazepin-2-one (1b).** Compound **1a** (318 mg, 1.70 mmol: 82% ee, $[\alpha]^{26}_D$ −23.5° (*c* 0.54, in chloroform)) was dissolved in 400 mL of 0.1 M sodium methoxide in methanol and irradiated by using a low-pressure mercury lamp for 2 h. The solvent was removed in vacuo, and the residue was separated by silica gel column chromatography (ethyl acetate). Compound **1a** (98.3 mg) was recovered and **1b** (43.8 mg, 13.8%) was afforded: R_f 0.7 (ethyl acetate); IR ($CHCl_3$) 3200, 1740, 1630, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.50–2.00 (m, 6 H), 2.40–2.90 (m, 4 H), 3.68 (s, 3 H), 4.40 (m, 1 H), 7.80 (broad, 1 H); MS, *m/e* (rel intensity) 201 (3.8), 187 (8.1), 169 (36.4), 152 (13.6), 124 (18.0), 109 (16.6), 82 (92.6), 55 (100), 41 (75.6), 27 (19.5); high-resolution mass spectrum, *m/e* 201.1006 (calcd for $C_9H_{15}NO_4$, 201.1000; $[\alpha]^{26}_D$ +11.1° (*c* 0.06 in chloroform); 79% ee.

2-Hydroxy-1,8,8-trimethyl-2-azabicyclo[3.2.1]octan-3-one (2b). Compound **2a** (1.06 g, 6.35 mmol) was dissolved in 400 mL of ammonia/methanol (pH 13.5). The solution was stirred at room temperature under argon atmosphere. After 30 min, the solution was irradiated by using a low-pressure mercury lamp for 4 h. The solvent was removed under reduced pressure. The photoproducts were separated by silica gel (15 g) column chromatography (chloroform/methanol, 9:1). Product **2b** (496 mg, 46.8%, R_f 0.45 (chloroform/methanol, 9:1)) was obtained, and the spectra were identical with the authentic 2-hydroxy-1,8,8-trimethyl-2-azabicyclo[3.2.1]octan-3-one.[1,2]

1,8,8-Trimethyl-2-azabicyclo[3.2.1]octan-3-one (2c). Compound **2b** (279 mg, 1.67 mmol) was dissolved in 8 mL of methanol. Sodium acetate (1.62 g) and water (5.5 mL) were added. The mixture was stirred under nitrogen while 2.25 mL of 20% $TiCl_3$ solution in water was added dropwise. After 1.5 h, the suspension was poured into 20 mL of water and extracted with five 10-mL portions of ethyl acetate. The combined solution was washed with 5% sodium carbonate in water, to remove acetic acid, and dried with anhydrous sodium sulfate. The soltuion was concentrated and separated by silica gel (5.5 g) column chromatography (chloroform/methanol, 50:1). Product **2c** (252 mg, 99.9%) was obtained. The spectra were identical with the authentic sample: R_f 0.4 (chloroform/methanol, 9:1); mp 156–158 °C (lit.[4a] mp 156–160 °C).

***endo*-2-Nitro-*exo*-3-phenylbicyclo[2.2.1]heptane (3a).** *endo*-2-Nitro-*exo*-3-phenylbicyclo[2.2.1]hept-5-ene (992 mg, 4.61 mmol) was dissolved in 30 mL of ethanol. Powder of 5% palladium–carbon (320 mg) was used as catalyst. After hydrogen-

ation, the catalyst and the solvent were removed. The product (1.37 g) was separated by silica gel (10 g) column chromatography (benzene/hexane, 1:1, R_f 0.55). It gave **3a** (885 mg, 88.5%). The ^{1}H NMR spectrum of this product was identical with that of an authentic sample:[20] ^{1}H NMR (CCl_4) δ 1.30–2.20 (m, 6 H), 2.60 (s, 1 H), 2.91 (m, 1 H), 3.50 (dd, J = 5, 2 Hz, 0.96 H), 3.80 (m, 0.04 H), 4.50 (m, 0.04 H), 4.70 (t, J = 5 Hz, 0.96 H), 7.17 (s, 5 H).

3-Hydroxy-*exo*-4-phenyl-3-azabicyclo[3.2.1]octan-2-one (3b).[2] Compound **3a** (885 mg, 4.08 mmol) was dissolved in 500 mL of ammonia/methanol (pH 12.8). The solution was stirred for 30 min at room temperature under argon and irradiated by using a low-pressure mercury lamp for 10 h. The solvent was evaporated in vacuo. The residue (1.15 g) was separated by silica gel (40 g) centrifugal chromatography (chloroform). Compound **3a** (52 mg) was recovered and **3b** (716 mg) was obtained (80.9%): ^{1}H NMR (CCl_4) δ 1.10–1.50 (m, 2 H), 1.80–2.20 (m, 4 H), 2.40–2.60 (m, 1 H), 2.80 (m, 1 H), 4.53 (s, 1 H), 7.24 (s, 5 H).

***exo*-4-Phenyl-3-azabicyclo[3.2.1]octan-2-one (3c). 3b** (504 mg, 2.32 mmol) was dissolved in 20 mL of methanol. Then 7.50 mL of water and sodium acetate (2.52 g) were added. While 4.56 mL of 20% $TiCl_3$ in water was added dropwise, the solution was stirred under nitrogen. The solution was stirred for 30 min. The suspension was poured into 15 mL of water and extracted with five 10-mL portions of ethyl acetate. The combined solution was washed with 5% sodium carbonate in water to remove acetic acid and dried with anhydrous sodium sulfate. The solution was concentrated. The product (802 mg) was separated by silica gel (10 g) column chromatography (chloroform/methanol, 9:1). Lactam **3c** (356 mg, 76.3%) was obtained: R_f 0.65 (chloroform/methanol, 9:1); mp 159–160 °C (carbon tetrachloride); IR ($CHCl_3$) 3240, 3000, 2975, 1660, 1455, 1345, 1280, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.13–1.50 (m, 2 H), 1.80–2.30 (m, 4 H), 2.40–2.60 (broad, 1 H), 2.75 (m, 1 H), 4.40 (s, 1 H), 5.96–6.30 (broad, 1 H), 7.20–7.50 (m, 5 H); MS, m/e (rel intensity) 201 (95.5), 160 (47.4), 132 (32.2), 106 (100), 104 (44.2), 91 (35.3), 77 (40.7), 68 (35.6), 67 (43.4), 55 (49.0), 39 (30.4). Anal. Calcd for $C_{12}H_{14}NO$: C, 77.58; H, 7.52; N, 6.96. Found: C, 76.98; H, 7.44; N, 6.92.

***N*-Butyl-*endo*-3-nitrobicyclo[2.2.1]heptane-*exo*-2-carboxamide (4a).** 3-Nitroacrylic acid (1.51 g, 12.9 mmol) was dissolved in 20 mL of dry ether, and the solution was stirred at −15 °C. Cyclopentadiene (1.58 mL, 19.2 mmol) in 10 mL of ether was added dropwise. After 30 min, the temperature of the reaction mixture was raised to room temperature and the solution was stirred for 1 h. The solvent was evaporated in vacuo. The solid (2.36 g) was recrystallized from chloroform: white crystal (1.69 g, 71.3%); mp 99–100 °C (lit.[13] mp 95–96 °C).

3-Nitrobicyclo[2.2.1]hept-5-ene-2-carboxylic acid (3.24 g, 17.7 mmol) in 30 mL of ethanol was hydrogenated with 5% palladium–carbon (502 mg). The solvent and the catalyst were removed. The solid (3.12 g) was recrystallized from chloroform. 3-Nitrobicyclo[2.2.1]heptane-2-carboxylic acid (2.71 g, 82.8%) was obtained: mp 85–86 °C.

3-Nitrobicyclo[2.2.1]heptane-2-carboxylic acid (2.71 g, 14.6 mmol) was dissolved in 20 mL of dry THF. DCC (*N*,*N*-dicyclohexylcarbodiimide) (4.51 g, 21.9 mmol) in 10 mL of THF was added to the solution. White precipitate appeared. After 10 min, 2.16 mL (21.9 mmol) of *n*-butylamine was added. The solution was stirred for 4 h at room temperature. Acetic acid (0.43 mL) was added to quench the reaction. The solution was filtered with suction. The filtrate was concentrated, and the solid was dissolved in 20 mL of ethyl acetate. The solution was washed with 1 N hydrochloric acid and 10% potassium bicarbonate in water. The solution was dried with anhydrous sodium sulfate and concentrated. The solid (4.43 g) was separated by silica gel (70 g) centrifugal chromatography (chloroform). It gave 3.34 g (95.3%) of **4a**: R_f 0.25 (chloroform); IR ($CHCl_3$) 3500–3300, 2970, 2900, 1680, 1540, 1465, 1385, 1330, 1315, 1240, 905 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80–1.20 (m, 3 H), 1.20–2.00 (m, 10 H), 2.52 (s, 1 H), 2.96 (m, 2 H), 3.15–3.45 (m, 2 H), 5.30 (t, J = 5 Hz, 1 H), 6.00–6.50 (broad, 1 H); MS, m/e (rel intensity) 240 (6.3), 198 (12.9), 194 (54.6), 168 (11.7), 150 (13.8), 128 (16.6), 122 (12.2), 121 (100), 95 (13.9), 93 (38.1), 81 (20.0), 67 (31.5), 66 (51.1), 57 (43.8), 41 (62.2), 39 (30.8), 29 (34.5).

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***N*-Butyl-3-hydroxy-4-oxo-3-azabicyclo[3.2.1]octane-*exo*-2-carboxamide (4b).** Compound **4a** (530 mg, 2.21 mmol) was dissolved in 200 mL of ammonia/methanol (pH 13.1). The solution was stirred for 30 min under argon at room temperature and irradiated by using a low-pressure mercury lamp for 8 h. The solvent was removed, and the resulting residue was separated by silica gel (20 g) column chromatography (chloroform/methanol, 9:1). Product **4b** (326 mg, 61.5%) was afforded: R_f 0.20 (chloroform/methanol, 9:1); mp 153–154 °C (carbon tetrachloride); IR ($CHCl_3$) 3450–3250, 3010, 2975, 2900, 1650, 1530, 1460, 1300, 1125, 955 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.70–1.10 (m, 6 H), 1.70–2.10 (m, 4 H), 2.77 (s, 1 H), 2.90–3.50 (m, 4 H), 3.91 (s, 1 H), 6.98 (m, 1 H); MS, m/e (rel intensity) 240 (10.4), 140 (100), 124 (7.3), 112 (17.7), 95 (2.7), 79 (15.2), 67 (10.4), 57 (7.0), 41 (12.1), 29 (5.1); high-resolution mass spectrum, m/e 240.1459 (calcd for $C_{12}H_{20}N_2O_3$, 240.1472).

***N*-Butyl-4-oxo-3-azabicyclo[3.2.1]octane-*exo*-2-carboxamide (4c).** Compound **4b** (211 mg, 0.972 mmol) was dissolved in 4.0 mL of methanol. Water (3.0 mL) and sodium acetate (853 mg) were added. The solution was stirred under nitrogen while 1.35 mL of 20% $TiCl_3$ in water was added dropwise. The suspended solution was poured into 10 mL of water. A few drops of concentrated hydrochloric acid was added, and the solution was extracted with five 15-mL portions of ethyl acetate. The combined solution was washed with 5% sodium carbonate in water. The organic phase was dried with anhydrous sodium sulfate and concentrated. The residual solid was recrystallized from chloroform. Product **4c** (176 mg, 90.1%) was yielded: mp 192–193 °C (chloroform); IR ($CHCl_3$) 3500–3200, 2975, 2900, 1660, 1530, 1405, 1385, 1180, 1130, 1105, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80–1.10 (m, 3 H), 1.10–1.70 (m, 6 H), 1.70–2.15 (m, 4 H), 2.65 (s, 1 H), 2.90 (m, 1 H), 3.30 (m, 2 H), 3.69 (s, 1 H), 7.27 (m, 2 H); MS, m/e (rel intensity) 224 (2.4), 124 (100), 97 (3.2), 81 (15.8), 79 (19.9), 67 (4.6), 57 (5.4), 41 (14.6), 30 (21.4); high-resolution mass spectrum, m/e 224.1529 (calcd for $C_{12}H_{20}N_2O_2$, 224.1523).

***N*-Butyl-*endo*-3-nitro-7-oxabicyclo[2.2.1]heptane-*exo*-2-carboxamide (5a).** 3-Nitro-7-oxabicyclo[2.2.1]heptane-2-carboxylic acid (1.46 g, 7.81 mmol) in a 100-mL flask equipped with a tube of calcium chloride was dissolved in 30 mL of dry THF, and 2.44 g (11.8 mmol) of DCC was added to the solution. After 10 min, *n*-butylamine (1.15 mL, 11.7 mmol) was added to the solution dropwise. After the addition was completed, the reaction mixture was stirred for 4 h; the reaction was quenched by addition of acetic acid (0.3 mL). The white precipitate was filtered, and the solvent was removed under reduced pressure. The resulting solid was dissolved in 20 mL of ethyl acetate and washed with 1 N hydrochloric acid and aqueous 10% sodium bicarbonate solution. The solution was dried with anhydrous sodium sulfate and concentrated in vacuo. The residual solid (2.60 g) was separated by centrifugal chromatography on 70 g of silica gel, eluting with chloroform. Product **5a** (1.65 g, 87.3%) was obtained: R_f 0.10 (chloroform); mp 65–66 °C (benzene); IR ($CHCl_3$) 3460, 3350, 3010, 2975, 2870, 1675, 1545, 1475, 1380, 1315, 1230, 1015, 925, 860, 820 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.95–1.05 (m, 3 H), 1.20–1.60 (m, 4 H), 1.60–2.10 (m, 4 H), 3.10–3.50 (m, 3 H), 4.86 (s, 1 H), 5.00–5.15 (m, 1 H), 5.41 (t, J = 4.8 Hz, 1 H), 6.20–6.55 (m, 1 H); MS, m/e (rel intensity) 242 (17.8), 227 (13.7), 213 (21.2), 200 (31.2), 185 (83.0), 140 (21.4), 126 (15.5), 112 (7.1), 98 (57.3), 83 (28.7), 68 (36.2), 57 (52.5), 56 (100), 44 (51.0), 41 (66.5), 30 (76.0); high-resolution mass spectrum, m/e 242.1244 (calcd for $C_{11}H_{18}N_2O_4$, 242.1265).

***N*-Butyl-3-hydroxy-4-oxo-3-aza-8-oxabicyclo[3.2.1]octane-*exo*-2-carboxamide (5b).** Compound **5a** (509 mg, 2.10 mmol) was dissolved in 150 mL of ammonia/methanol (pH 12.6) at 0 °C. The solution was stirred for 45 min at 0 °C under argon, and the solution was irradiated by using a low-pressure mercury lamp for 7 h. The solvent was evaporated under reduced pressure, and the residue was separated by column chromatography on silica gel (10 g), eluting with chloroform/methanol (9:1). Product **5b** (212 mg, 41.7%) was afforded: R_f 0.20 (chloroform/methanol, 9:1); mp 174–175 °C (benzene); IR ($CHCl_3$) 3430, 3200, 3020, 2975, 2950, 2890, 1670, 1540, 1475, 1285, 1085, 1060, 1020, 850 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85–1.15 (m, 3 H), 1.36–1.76 (m, 4 H), 2.09–2.40 (m, 4 H), 3.20–3.60 (m, 2 H), 4.07 (m, 1 H), 4.66 (m, 1 H), 5.04 (m, 1 H), 7.02–7.40 (m, 1 H), 7.00–8.50 (m, 1 H); MS, m/e (rel intensity) 242 (26.6), 184 (10.2), 174 (18.0), 142 (26.1), 126 (43.7),

114 (100), 97 (29.7), 83 (15.9), 72 (16.3), 57 (52.0), 41 (60.1), 29 (38.8); high-resolution mass spectrum, *m/e* 242.1266 (calcd for $C_{11}H_{18}N_2O_4$, 242.1265).

***N*-Butyl-4-oxo-3-aza-8-oxabicyclo[3.2.1]octane-*exo*-2-carboxamide (5c).** Compound **5b** (307 mg, 1.27 mmol) was dissolved in methanol (6 mL). Water (4.3 mL) and sodium acetate (1.27 g) were added to the solution. The solution was stirred at room temperature under nitrogen while 1.96 mL of 20% $TiCl_3$ in water was added dropwise via syringe. After the addition was completed, the solution was stirred for 15 min. Then the solution was poured into 20 mL of water, and a few drops of concentrated hydrochloric acid was added to the solution. The solution was extracted with six 10-mL portions of ethyl acetate. The combined organic layers were washed with aqueous 5% sodium carbonate and dried with anhydrous sodium sulfate. The solvent was evaporated in vacuo. The solid was separated by column chromatography (chloroform/methanol, 9:1) on silica gel (5.0 g). It gave 104 mg (36.2%) of **5c**: R_f 0.20 (chloroform/methanol, 9:1); mp 177–178 °C (benzene); IR ($CHCl_3$) 3450, 3410, 3010, 2975, 2950, 2890, 1695, 1690, 1535, 1475, 1455, 1345, 1290, 1030, 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (t, J = 6.4 Hz, 3 H), 1.20–1.70 (m, 4 H), 2.00–2.35 (m, 4 H), 3.33 (q, J = 6 Hz, 2 H), 3.68 (d, J = 3.4 Hz, 1 H), 4.50 (m, 1 H), 4.91 (d, J = 5 Hz, 1 H), 7.00–7.40 (m, 2 H); MS, *m/e* (relative intensity) 226 (3.8), 184 (9.2), 155 (2.9), 127 (100), 109 (34.8), 98 (59.9), 81 (7.2), 70 (13.2), 57 (13.8), 43 (22.5), 30 (22.0); high-resolution mass spectrum, *m/e* 226.1328 (calcd for $C_{11}H_{18}N_2O_3$, 226.1316).

Solvolysis of 2c. Compound **2c** (119 mg, 0.713 mmol) was dissolved in 5 mL of 6 N hydrochloric acid. The solution was refluxed for 36 h. The solvent was removed under reduced pressure. After addition of methanol (5 mL), the solvent was evaporated at 50 °C, and this procedure was repeated 5 times. The residue (137 mg) was separated by silica gel (6 g) column chromatography (chloroform/methanol, 9:1). Product **2d** (monohydrate, 73.3 mg, 40.5%) was yielded: R_f 0.10 (chloroform/methanol, 9:1); mp 171–172 °C (benzene); IR ($CHCl_3$) 3600–3300, 2950, 1735, 1620, 1520, 1445, 1395, 1305, 1170, 990 cm^{-1}; ^1H NMR (CD_3OD) δ 0.89 (s, 3 H), 1.01 (s, 3 H), 1.34 (s, 3 H), 1.40–1.53 (m, 1 H), 1.78–1.89 (m, 1 H), 1.95–2.07 (m, 2 H), 2.16–2.30 (m, 2 H), 2.46 (d, J = 11 Hz, 1 H), 3.66 (s, 3 H); ^{13}C NMR (CD_3OD) δ 18.3 (q), 21.5 (q), 23.1 (q), 27.2 (t), 35.6 (t), 36.1 (t), 44.5 (d), 45.9 (s), 52.2 (q), 65.8 (s), 175.1 (s). Anal. Calcd for $C_{11}H_{21}NO_2 \cdot HCl \cdot H_2O$: C, 52.06; H, 9.53; N, 5.52. Found: C, 51.69; H, 9.33; N, 5.50.

Solvolysis of 3c. Compound **3c** (184 mg, 0.915 mmol) was dissolved in 6 mL of 2 N hydrochloric acid, and the solution was refluxed for 4 h. The water was evaporated, and 5 mL of methanol was added. The solution was refluxed for 1 h and concentrated. The residue (259 mg) was separated by alumina (10 g, Wako, 200 mesh) column chromatography (chloroform/methanol, 4:1). Product **3d** (191 mg (89.6%)) was obtained: R_f 0.25 (chloroform/methanol, 4:1); IR (CCl_4) 3400–3300, 1740, 1600, 1520, 1440, 1365, 1200, 1160, 700 cm^{-1}; ^1H NMR (CCl_4) δ 1.20–2.20 (m, 9 H), 2.45–2.90 (m, 1 H), 3.67 (s, 3 H), 3.65 (m, 1 H), 7.20 (s, 5 H); MS, *m/e* (rel intensity) 233 (0.8), 201 (21.6), 173 (4.3), 160 (10.1), 41 (10.8), 28 (10.3); high-resolution mass spectrum, *m/e* 233.1420 (calcd for $C_{14}H_{19}NO_2$, 233.1414).

Lactamization of 3d. Compound **3d** (191 mg, 0.820 mmol) was dissolved in 1.0 mL of benzene, and the solution was refluxed for 15 min. The solution was concentrated in vacuo, and the residue (244 mg) was separated by silica gel (4 g) column chromatography (chloroform/methanol), 9:1). The separation gave **3c** (146 mg, 88.6%); mp 159–160 °C. The spectra were identical with those of authentic **3c**.

^1H NMR Study of the Photoproducts. To determine the stereochemistry of the product, the following experiments were attempted. 3-Nitro-7-oxabicyclo[2.2.1]heptane-2-carboxylic acid was reacemized by addition of aqueous sodium hydroxide (at pH 11.5, *exo*-4-carboxyl:*endo*-4-carboxyl = 71:29, from ^1H NMR). After methyl esterification of it with diazomethane, the ester was irradiated in ammonia/methanol. The separation of the products gave a hydroxamic acid (4-epimerized, 3-hydroxy-4-(methoxycarbonyl)-3-aza-8-oxabicyclo[3.2.1]octan-2-one): ^1H NMR ($CDCl_3$) δ 1.90–2.30 (m, 4 H), 3.25 (s, 0.24 H), 3.83 (s, 3 H), 4.06 (s, 0.76 H), 4.50–4.60 (m, 1 H), 4.70–4.90 (m, 1 H), 7.00–8.00 (broad, 1 H); IR ($CHCl_3$) 3350 (broad), 1740, 1640 cm^{-1}; high-resolution mass spectrum, *m/e* 201.0597 (calcd for $C_8H_{11}NO_2$, 201.0559). From ^1H NMR study, the ratio of the diastereomer was determined (*exo*-4-(methoxycarbonyl) (4-equatorial hydrogen):*endo*-4-(methoxycarbonyl) (4-axial hydrogen) = 76:24). In the same way, from the racemized acid, **5b** was made (^1H NMR of H-C(4) δ 3.25 (s, 0.29 H, axial hydrogen), 3.70 (d, J = 3.4 Hz, 0.71 H, equatorial hydrogen). So we can decide the ratio of the diastereomers of the hydroxamic acids. Actually none of the products (in Table I) had any axial hydrogen at C(4).

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Synthesis and Characterization of a Novel Calix[4]arene Tetramethyl Tetraether

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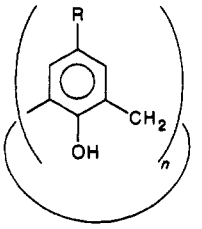
Calixarenes **1** are [1.*n*]metacyclophanes comprising cyclic arrays of phenolic residues attached by methylene units at the positions ortho to the hydroxy groups.[1] These



1, *n* = 4-8

materials have the ability to entrap other molecules within their central cavities. Thus, they are attractive models for mimicking enzyme–substrate interactions.[2] Structures with both inward- and outward-turned functional groups have been the object of synthetic efforts. The hydroxy inward-turned calix[4]arenes (cyclic tetramers) have been obtained either by base-induced condensation of *p*-alkylphenols with formaldehyde[3] or by stepwise syntheses.[1] The calix[4]arenes with outward-turned hydroxy groups have been synthesized by acid-catalyzed condensation of resorcinol with various aldehydes[4] and by the reaction of a bisphenol with paraformaldehyde.[5] Herein, we report an efficient synthesis of 6,10,18,22-tetramethoxy-4,12,16,24,25,26,27,28-octamethylpentacyclo-[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]-octacosa-1(25),3,5,7(28),9,11,13-(27),15,17,19(26),21,23-dodecaene (**2**) via a Lewis acid mediated tetramerization of a *p*-methoxybenzyl alcohol. This transformation reproducibly gives with selectivity a cyclic tetramer, in 80% yield, with methoxy groups adorning the outside periphery.

A solution of the known 2,6-dimethyl-4-methoxybenzyl alcohol[6] in dichloromethane was treated with 0.6 equiv of anhydrous aluminum chloride in five portions over a period of 2 h. As the reaction proceeded, the solution turned dark

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