Bicyclo[3.3.1]nonanes as Synthetic Intermediates. XVII.[1] A Novel Interconversion between Bicyclo-[4.3.1]decane and Tricyclo[4.3.1.0]decane Systems *via* the Dual Mode of Aldol Cyclization of Bicyclo-[4.3.1]decane-3,8-dione[2]

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The characteristic intramolecular aldol cyclization of bicyclo[4.3.1]decanedione to two novel tricyclic systems, protoadamantanone and isotwistanone, is described. Both systems were reconverted to bicyclo[4.3.1]decanones by the Grob fragmentation.

Keywords ring expansion; bicyclo[3.3.1]nonane-3,7-dione; aldol cyclization; bicyclo[4.3.1]decane-3,8-dione; tricyclo[4.3.1.0]-decane; isotwistane; protoadamantane

Despite its dipole-dipole repulsion between the two facing carbonyl groups, bicyclo[3.3.1]nonane-3,7-dione (**1**) is known to adopt the twin chair conformation.[4] Owing to the proximity of these two "fork head" sites, facile intramolecular cyclization was reported to occur, giving the oxaadamantane (**2**) or noradamantane (**3**) skeleton depending on the reaction conditions. Ionic conditions usually favor the former skeleton, as in the reaction of **1** with Grignard reagents[5] or some other nucleophiles,[6] while under radical conditions[7] **1** gave the latter skeleton.

In the preceding paper,[1] we described the characteristic behavior of the homologous diketones bicyclo[4.3.1]decane-2,7- and -3,7-dione (**4** and **5**) under ionic conditions, where the intramolecular aldol cyclization occurred to give 7-hydroxyisotwistan-2-one (**6**) and 3-hydroxyprotoadamantan-7-one (**7**), respectively. On the acid treatment of another isomeric diketone, bicyclo[4.3.1]decane-3,8-dione (**8**),[2] both 8-hydroxyprotoadamantan-4-one (**9**) and 3-hydroxyisotwistan-8-one (**10**) were obtained with predominance of the latter, in contrast to Alford and McKervey's finding[8] that **9** was the sole product in the cyclization of **8**.

In this paper we present a full account of the experiments aimed at clarifying the origin of the isotwistane (**10**), and the regeneration of the bicyclo[4.3.1]decane system by Grob fragmentation of the two glycols, *exo*-ptotoadamantane-4,8-diol (**11**) and *exo*-isotwistane-3,8-diol (**12**), and we also compare the characteristic behavior of the two "facing carbonyl" moieties between **1** and **8** under ionic and radical conditions.

Dual Mode of Cyclization of 8 into an Isotwistanone or a Protoadamantanone Skeleton Treatment of 3-aminomethyloxaadamantanol (**13**)[8,9] with sodium nitrite in aqueous acetic acid at 0 °C gave a solid, which was homogeneous on gas-liquid partition chromatography (GLPC) and thin-layer chromatography (TLC) analysis.

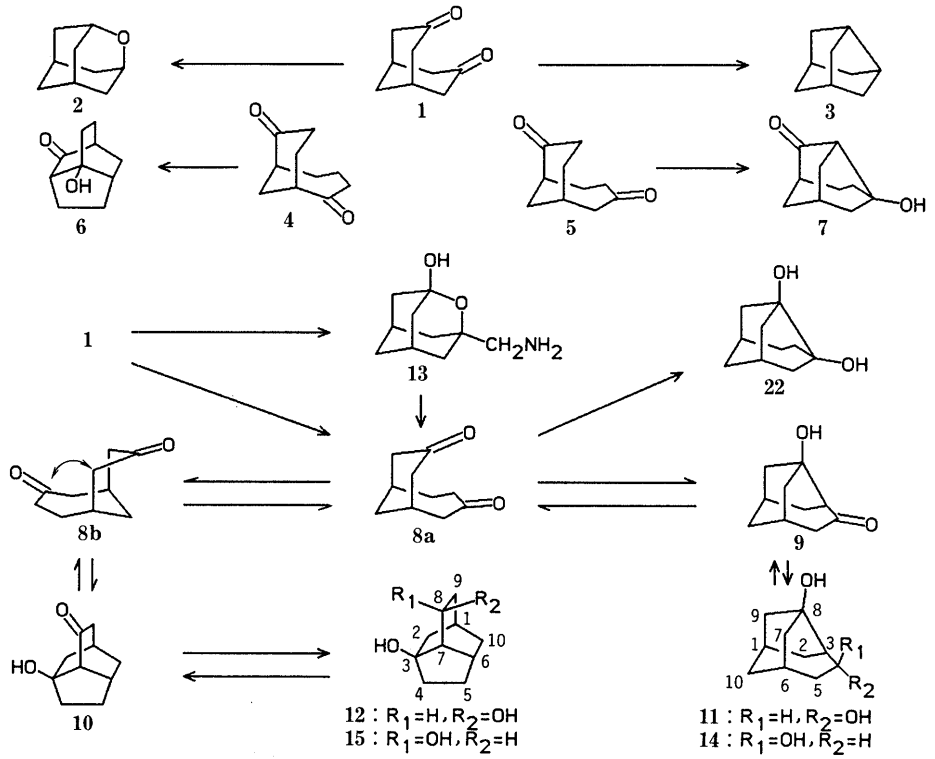

Chart 1

Alford and McKervey[8] reported that the product at this stage was the ketol (**9**) and that the subsequent lithium aluminum hydride (LAH) reduction gave a mixture of two isomeric glycols, *exo*- and *endo*-protoadamantane-4,8-diol (**11** and **14**), with melting points of 208.5—210 °C and 302—304 °C, respectively. We repeated the sequence and were able to isolate two glycols whose melting points were in good accordance with those reported.[8] Unexpectedly, a significant amount (34%) of a poorly separable mixture of two other glycols was obtained as additional components by preparative thin-layer chromatography (PTLC) of the reduction product. On the basis of spectral investigation and derivation to a known product, we concluded that the glycol (having the highest *Rf* value on TLC) of mp 208.5—210 °C was not **11** but another novel tricyclic compound, an isotwistane (**12**), possibly derived from the second mode of aldol cyclization involving interaction between C(3) and C(7). The *exo*-protoadamantanediol (**11**) was found to be present concomitantly with the isomer of **12**, *endo*-isotwistane-3,8-diol (**15**), in the fraction of the lowest *Rf* value on TLC.

The Jones oxidation of **14** and **12** gave the parent ketols, **9** and **10**, respectively. Although infrared (IR), mass (MS), and proton nuclear magnetic resonance (^{1}H-NMR) spectra were of no use for characterization of **9** and **10**, ^{13}C-NMR analysis was found effective to discriminate between these two compounds, even for the aldol mixture. Attempted determination of the melting points caused gradual conversion of each ketol into its counterpart, and resulted in the formation of an equilibrium mixture of **9** and **10** with a predominance of the former.

The LAH reduction of **10** gave two glycols (**12** and **15**) in the ratio of *ca.* 5:2. Their separation was effected by column chromatography over silica gel, and the major isomer was identical in its physical and spectroscopic properties with the glycol of mp 208—209 °C obtained originally *via* the diazotization of **13**. The configuration of the hydroxyl at C(8) in **15** could not readily be determined from its ^{1}H-NMR spectrum, because the coupling patterns of the C<u>H</u>OH signal for **12** and **15** were quite similar to each other owing to the symmetric character of the skeleton. The characteristic pattern of a triplet of doublets reveals appreciable coupling of this proton with another ($J_{8,9syn}$= 10.0 Hz), and the Dreiding models of both **12** and **15** show a dihedral angle approaching 0° between 8-H and one of the protons on C(9), which is consistent with the observed large coupling constants.

The LAH reduction of another ketol (**9**) gave **11** and **14** in the ratio of *ca.* 4:3, and the minor isomer (**14**) was identical with the glycol of mp 301—303 °C obtained *via* the diazotization of **13**. Although the previous workers[8] reported the C<u>H</u>OH signal for **14** as a broad, poorly resolved multiplet, a quartet-like signal with relatively small coupling constants ($W_{1/2}$=7.0 Hz) was observed at δ4.22 in our NMR studies. The large coupling constant ($J_{4,5}$=9.0 Hz) in the signal at δ4.08 due to the C<u>H</u>OH of **11** is consistent with the putative dihedral angle based on inspection of the Dreiding model.

The structure determination and the configurational assignment for **11** and **12** were achieved by their conversion into known bicyclic compounds, bicyclo[4.3.1]decan-8-one (**16**)[10] and bicyclo[4.3.1]decan-3-one (**17**),[11] respectively.

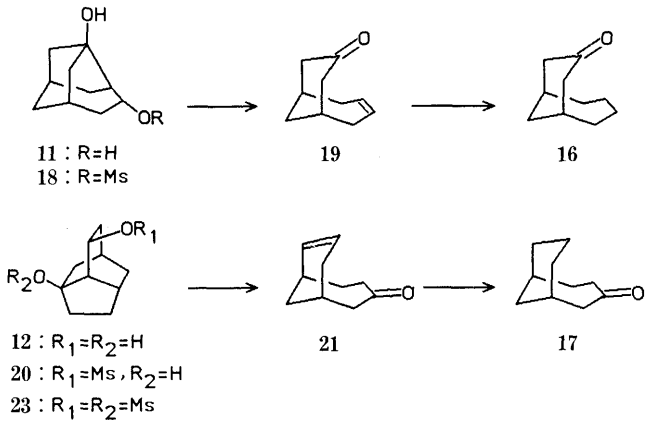

Chart 2

Mesylation of **11** and subsequent base-catalyzed fragmentation of the resulting monomesylate (**18**) gave bicyclo-[4.3.1]dec-3-en-8-one (**19**) as colorless crystals. The ^{1}H-NMR spectrum showed a multiplet, at δ5.72, due to two olefinic protons, and the relatively simple pattern of the signals suggests that the molecule is highly symmetrical. Catalytic hydrogenation of **19** over 5% palladium on carbon (Pd/C) afforded **16** quantitatively. The physical and spectral properties of **16** were completely in accordance with those obtained *via* an alternative method.[10]

Application of the same sequence to another *exo*-glycol (**12**) gave the isomeric ketone (**17**) in good yield. The monomesylate (**20**) of **12** was labile and easily converted into bicyclo[4.3.1]dec-7-en-3-one (**21**) in 75% yield. The feature of ten independent signals in its ^{13}C-NMR spectrum suggests that the compound is asymmetrical. Catalytic hydrogenation of **21** gave **17** in good yield, and the identification was achieved by comparison of its physical and spectral properties with those of an authentic specimen[11] obtained by the ring-enlargement of bicyclo-[3.3.1]nonan-2-one.

Synthesis of Bicyclo[4.3.1]decane-3,8-dione (8) and Its Selective Transformation into an Isotwistane or a Protoadamantane Skeleton Although diketone (**8**) is so labile as to be converted into a mixture of the ketols **9** and **10** even at room temperature, careful work-up of the diazotization mixture enabled us to isolate **8** as colorless crystals in quantitative yield. Its ^{13}C-NMR spectrum showed ten peaks including two carbonyl and two methine carbon resonances, which were completely different from those of the ketols (**9** and **10**).

When the diketone (**8**) was treated with *p*-toluenesulfonic acid (*p*-TsOH) in acetone below 0 °C, the aldol cyclization was found to proceed in a selective way to a considerable extent. The process was monitored by ^{13}C-NMR measurement, and the product at the first stage was found to be **10** (Fig. 1; a). Single crystallization of the product from ether–pentane (4:1) gave pure isotwistanone (**10**) in 66% yield. When **8** was treated with the acid in MeOH or in $CHCl_3$, no selectivity was observed, and a mixture of **9** and **10** was obtained (Fig. 1; b, c).

The specific construction of a protoadamantane skeleton from **8** was established by subjecting **8** to the Birch reduction to give a bridgehead α-glycol, tricyclo[4.3.1.$0^{3,8}$]decane-3,8-diol (**22**), in 90% yield. Two tertiary carbons in **22** resonated at the same frequency, appearing as one singlet, which was

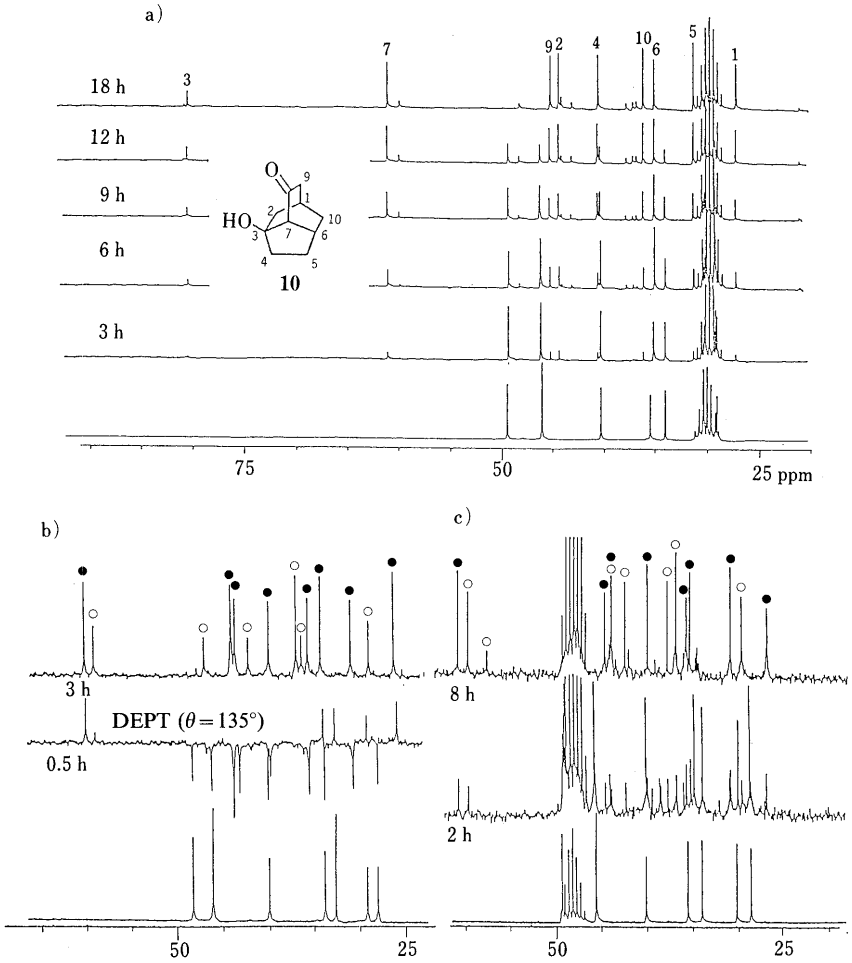

Fig. 1. ^{13}C-NMR Spectra of the Diketone (**8**) and the Reaction Mixture of **8** and *p*-Toluenesulfonic Acid under Various Conditions

Spectra of **8** (bottom) and the mixture measured after an elapse of time at (a) 0 °C in $(CD_3)_2CO$, (b) −60 °C in $CDCl_3$, and (c) −30 °C in CD_3OD. ○ and ● signals for **9** and **10**, respectively. DEPT; distortionless enhancement by potarization transfer.

separated into two by the addition of a shift reagent.

Consequently, the behavior of the diketone (**8**) under ionic conditions was found to be completely different from that of **1**, and the predominant formation of the less stable isomer (**10**), inevitably *via* the transient boat conformation of the cyclohexanone ring rather than of the cycloheptanone half of the bicyclo system (**8**), suggests that the reaction is under kinetic control and provides a new synthetic route to tricyclo[4.3.1.0^{3,7}]decane derivatives.[12] On the other hand, direct linkage of two carbonyl carbons was found to occur exclusively under radical conditions as was experienced in the case of **1**.[7] The conformational analysis of bicyclo[4.3.1]decane derivatives by use of ^{13}C-NMR will be the subject of a subsequent study.

Experimental

Melting points (mp) are uncorrected. IR spectra were taken with a Hitachi 260-30 or a Shimadzu IR-435 grating spectrometer. ^{1}H-NMR spectra were recorded on a Hitachi R-22 (90 MHz) or a JEOL JNM-FX 200 (200 MHz) spectrometer with tetramethylsilane as an internal standard. Coupling constants (*J*) are given in hertz, and the following abbreviations are used; s=singlet, d=doublet, t=triplet, q=quartet, quint=quintet, m=multiplet, br=broad peak. ^{13}C-NMR (50 MHz) spectra were taken on a JEOL JNM-FX 200 spectrometer, and the NMR spectra were taken for $CDCl_3$ solutions unless otherwise mentioned. MS were taken on a Hitachi RMU-6E or a Hitachi M-70 mass spectrometer. High-resolution mass spectra (HRMS) were taken on a JEOL JMS-D300 or a JEOL JMS-HX100 mass spectrometer. All the column chromatographies were performed on Mallinckrodt silicic acid. All the organic extracts were dried over anhydrous magnesium sulfate prior to evaporation.

Treatment of 3-Aminomethyl-2-oxaadamantan-1-ol (13) with Nitrous Acid Sodium nitrite (1.3 g, 18.8 mmol) was added to a solution of **13** (0.84 g, 4.6 mmol) and acetic acid (0.7 ml) in water (8 ml) under ice-cooling, and the mixture was stirred at 0 °C for 3 h, and at room temperature for another 3 h, then neutralized, saturated with sodium bicarbonate, and extracted with ether. The extract was washed with brine, and evaporated to give 700 mg of a mixture of 8-hydroxyprotoadamantan-4-one (**9**) and 3-hydroxyisotwistan-8-one (**10**) as a colorless solid, which was subjected to LAH reduction without further purification.

When the diazotization was carried out at 0 °C and the mixture was worked-up below 20 °C, practically pure bicyclo[4.3.1]decane-3,8-dione (**8**) was obtained as a colorless solid in 98% yield.

8: IR ($CHCl_3$) cm^{-1}: 2930, 1708, 1442, 1412, 1358, 1348, 1330, 1295, 1235, 1146, 1120, 1098. ^{1}H-NMR (200 MHz) δ: 1.60—2.00 (3H, m), 2.16 (1H, td, J=14.0, 4.2), 2.26—2.42 (4H, m), 2.42—2.74 (6H, m). ^{13}C-NMR δ: 29.0 (t), 29.6 (d), 33.4 (d), 33.9 (t), 40.4 (t), 46.5 (t), 46.7 (t), 48.6 (t), 211.0 (s), 212.6 (s).

LAH Reduction of a Mixture of Ketols 9 and 10 A suspension consisting of LAH (150 mg), a mixture of ketols (**9** and **10**, 565 mg), and dry tetrahydrofuran (THF, 30 ml) was stirred at room temperature for 3 h. The excess hydride was decomposed with ethyl acetate. To this mixture, 10% aqueous sodium hydroxide solution was added, and the resulting gel was collected by filtration with suction, and washed with THF several times. The filtrate and the washings were combined, and evaporated to give 550 mg of a colorless solid, which on preparative thin layer chromatography [PTLC, eluent; chloroform–acetone (4:1, v/v)] gave 246 mg (43%) of *exo*-isotwistane-3,8-diol (**12**), 107 mg (19%) of *endo*-protoadamantane-4,8-diol (**14**), and 194 mg (34%) of a mixture of *exo*-protoadamantane-4,8-diol (**11**) and *endo*-isotwistane-3,8-diol (**15**).

12: Colorless needles (from *n*-hexane after sublimation), mp 208—209 °C.[13] IR (KBr) cm^{-1}: 3400, 2950, 2875, 1453, 1345, 1110, 1090,

1073, 1041, 950. ^{1}H-NMR (200 MHz, CD_3OD) δ: 1.06 (1H, td-like, J=13.0, 3.0), 1.16—1.32 (1H, m), 1.36—2.14 (11H, m), 4.16 (1H, td, J=10.0, 3.5). ^{13}C-NMR (CD_3OD) δ: 26.3 (d), 31.3 (t), 34.1 (d), 36.1 (t), 39.4 (t), 41.3 (t), 47.2 (t), 47.7 (d), 67.7 (d), 78.6 (s). MS m/z (%): 150 (M^+-18, 29), 92 (100). *Anal.* Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.01; H, 9.74.

14: Colorless needles (from acetone), mp 301—303 °C, lit.,[8] mp 302—304 °C. IR (KBr) cm^{-1}: 3380, 2945, 2875, 1455, 1355, 1330, 1303, 1163, 1122, 1070, 1045, 1020. ^{1}H-NMR (200 MHz) δ: 1.10—1.38 (2H, m), 1.42—2.12 (7H, m), 2.12—2.40 (4H, m), 3.36 (2H, bs, OH), 4.22 (1H, m). ^{13}C-NMR δ: 29.0 (d), 35. 1(t), 35.9 (d), 37.2 (t), 38.2 (t), 40.4 (t), 48.8 (t), 48.9 (d), 70.4 (d), 77.5 (s). MS m/z (%): 150 (M^+-18, 39), 92 (100). *Anal.* Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.2; H, 9.86.

8-Hydroxyprotoadamantan-4-one (9) A slight excess of Jones' reagent was added dropwise to a solution of **14** (278 mg, 1.65 mmol) in purified acetone (5 ml), followed by stirring at room temperature for 1 h. The excess oxidant was decomposed with isopropanol, and the resulting mixture was made alkaline with anhydrous potassium carbonate and extracted with ethyl acetate. The extract was washed with brine, and evaporated to give 270 mg (98%) of **9** as a colorless solid, mp 168—172 °C (from *n*-hexane).[14] IR (KBr) cm^{-1}: 3420, 2950, 2875, 1710, 1460, 1443, 1323, 1282, 1072, 1035. ^{1}H-NMR (200 MHz) δ: 1.56—2.68 (14H, m). ^{13}C-NMR δ: 29.4 (d), 37.0 (t), 37.1 (t), 37.4 (d), 43.0 (t), 44.1 (t), 47.7 (t), 58.6 (d), 81.0 (s), 214.5 (s). MS m/z (%): 166 (M^+, 23), 108 (100). *Anal.* Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.33; H, 8.55.

3-Hydroxyisotwistan-8-one (10) A solution of **12** (280 mg, 1.7 mmol) was treated with Jones' reagent in the same manner as described for the preparation of **9**. Work-up and removal of the solvent gave 254 mg (92%) of **10** as a colorless solid, mp 240—255 °C (from benzene–petroleum ether).[14] IR (KBr) cm^{-1}: 3370, 2945, 2875, 1700, 1467, 1445, 1415, 1400, 1335, 1310, 1297, 1235, 1210, 1123, 1110, 1062. ^{1}H-NMR (200 MHz) δ: 1.28—1.50 (2H, m), 1.66—2.26 (11H, m), 2.36 (1H, m). ^{13}C-NMR δ: 26.8 (d), 31.1 (t), 34.8 (d), 35.9 (t), 40.6 (t), 44.4 (t), 44.8 (t), 60.9 (d), 80.8 (s), 216.3 (s). MS m/z (%): 166 (M^+, 36), 108 (100). HRMS m/z: 166.0999 (requires 166.0994 for $C_{10}H_{14}O_2$).

LAH Reduction of 10 A suspension consisting of **10** (155 mg, 0.93 mmol), LAH (130 mg), and dry THF (10 ml) was stirred at room temperature for 3 h. Work-up in a manner similar to that used in the case of reduction of a mixture of **9** and **10** gave 140 mg of a colorless solid, which, on column chromatography [eluent; chloroform–acetone (4 : 1, v/v)], gave 95 mg (61%) of **12** and 38 mg (24%) of **15**. The physical and spectroscopic properties of the major component (**12**) were completely in accordance with those of the specimen obtained *via* the diazotization of **13**.

15: Colorless solid (from chloroform–carbon tetrachloride), mp 237—239 °C. IR (KBr) cm^{-1}: 3320, 2940, 2870, 1468, 1455, 1345, 1320, 1300, 1278, 1120, 1070, 1020, 1008. ^{1}H-NMR (200 MHz, CD_3OD) δ: 0.98—1.30 (3H, m), 1.44—2.00 (9H, m), 2.26 (1H, m), 4.14 (1H, td, J=10.0, 3.5). ^{13}C-NMR (CD_3OD) δ: 27.3 (d), 31.1 (d), 31.2 (t), 36.8 (t), 38.8 (t), 41.4 (t), 45.7 (t), 50.3 (d), 65.0 (d), 78.3 (s). MS m/z (%): 168 (M^+, 35), 95 (100). HRMS m/z: 168.1154 (requires 168.1151 for $C_{10}H_{16}O_2$).

LAH Reduction of 9 A suspension consisting of **9** (175 mg, 1.1 mmol), LAH (150 mg), and dry THF (10 ml) was stirred at room temperature for 3 h. Work-up in a manner similar to that described in the case of reduction of a mixture of **9** and **10** gave 150 mg of a colorless solid, which, on PTLC [eluent; chloroform–acetone (4 : 1, v/v)], gave 79 mg of **11** and 60 mg of **14**. The physical and spectroscopic properties of the minor component (**14**) were completely in accordance with those of the specimen obtained *via* the diazotization of **13**.

11: Colorless needles (from chloroform), mp 293—295 °C. IR (KBr) cm^{-1}: 3350, 2935, 2870, 1460, 1400, 1340, 1325, 1310, 1290, 1203, 1123, 1094, 1080, 1033, 972. ^{1}H-NMR (200 MHz, CD_3OD) δ: 1.20—1.96 (9H, m), 2.00—2.28 (4H, m), 4.08 (1H, dt, J=9.0, 4.0). ^{13}C-NMR (CD_3OD) δ: 30.2 (d), 31.3 (t), 36.0 (d), 36.4 (t), 38.5 (t), 39.6 (t), 49.0 (t), 49.9 (d), 66.7 (d), 78.9 (s). MS m/z (%): 168 (M^+, 48), 95 (100). HRMS m/z: 158.1141 (required 158.1151 for $C_{10}H_{16}O_2$).

4-*exo*-Mesyloxyprotoadamantan-8-ol (18) A solution of methanesulfonyl chloride (0.10 ml) in dichloromethane (1 ml) was added dropwise to a stirred solution of **11** (60 mg, 0.36 mmol) in dry pyridine (5 ml) at −20—−15 °C, and the mixture was stirred for 10 h, diluted with water, and extracted with chloroform. The combined extract was washed with 1 N hydrochloric acid, and then with water, and evaporated to give 72 mg (82%) of **18** as a colorless oil, which was subjected to the next reaction without further purification. IR ($CHCl_3$) cm^{-1}: 3620, 2950, 2875, 1460, 1350, 1330, 1160, 930, 903. ^{1}H-NMR (90 MHz) δ: 1.20—2.60 (14H, m), 3.00 (3H, s), 5.06 (1H, m).

Bicyclo[4.3.1]dec-3-en-8-one (19) A solution of **18** (69 mg, 0.28 mmol) in diisopropylamine (5 ml) was heated under reflux for 3 h. After being cooled, the mixture was made acid to Congo red with 5% sulfuric acid, and extracted with ether. The extract was washed with brine and evaporated to give a pale brown solid, which, on column chromatography, gave 23 mg (55%) of **19** as a colorless solid, mp 208—211 °C (sublimed at 150 °C/760 mmHg). IR (CCl_4) cm^{-1}: 3040, 2940, 2905, 2853, 1718, 1456, 1440, 1418, 1358, 1315, 1225, 1160, 1118, 1099, 1080, 1054. ^{1}H-NMR (200 MHz) δ: 1.90 (1H, quint of d, J=14.0, 2.0), 2.12—2.56 (11H, m), 5.72 (2H, m). ^{13}C-NMR δ: 31.6 (d), 35.4 (t), 37.3 (t), 46.1 (t), 131.9 (d), 211.3 (s). MS m/z (%): 150 (M^+, 50), 92 (100). HRMS m/z: 150.1022 (requires 150.1045 for $C_{10}H_{14}O$).

Bicyclo[4.3.1]decan-8-one (16) A suspension consisting of **19** (23 mg), 5% Pd/C (200 mg), and absolute ethanol (10 ml) was hydrogenated at room temperature under atmospheric pressure until absorption of hydrogen ceased. The catalyst was filtered off, and the filtrate was concentrated to give 24 mg (quantitative) of **16** as a colorless solid, the physical and spectroscopic properties of which were completely in accordance with those of an authentic specimen.[10]

Treatment of 12 with Methanesulfonyl Chloride to Give Bicyclo[4.3.1]dec-7-en-3-one (21) and 3,8-*exo*-Bismesyloxyisotwistane (23) A solution of methanesulfonyl chloride (0.27 ml) in dichloromethane (5 ml) was added to a solution of **12** (478 mg, 2.8 mmol) in dry pyridine (5 ml) under ice-cooling, and the mixture was stirred at room temperature for 6 h. Work-up in a manner similar to that used for the preparation of **18** gave a waxy solid, which, on column chromatography (eluent: chloroform), gave 320 mg (75%) of **21** and 66 mg (7%) of **23**.

21: Colorless solid, mp 54—56 °C. IR (CCl_4) cm^{-1}: 3025, 2925, 1700, 1440, 1343, 1182. ^{1}H-NMR (200 MHz) δ: 1.64—2.76 (12H, m), 5.64 (2H, m). ^{13}C-NMR δ: 26.6 (d), 28.1 (t), 29.5 (t), 31.2 (d), 35.7 (t), 40.9 (t), 50.6 (t), 127.7 (d), 129.6 (d), 214.0 (s). MS m/z (%): 150 (M^+, 17), 92 (100). HRMS m/z: 150.1040 (requires 150.1045).

23: Colorless needles (from ethanol–hexane), mp 107—108.5 °C. IR (KBr) cm^{-1}: 2935, 1346, 1328, 1185, 1172, 1163, 1010, 980, 942, 917, 892, 875, 849, 835, 810. ^{1}H-NMR (90 MHz) δ: 1.00—2.70 (13H, m), 3.01 (3H, s), 3.02 (3H, s), 5.12 (1H, m). *Anal.* Calcd for $C_{12}H_{20}O_6S_2$: C, 44.44; H, 6.22. Found: C, 44.04; H, 6.12.

Bicyclo[4.3.1]decan-3-one (17) A suspension consisting of **21** (50 mg), 5% Pd/C (50 mg), and absolute ethanol was hydrogenated until the hydrogen absorption ceased. Work-up in a manner similar to that used for the preparation of **16** gave a colorless solid, which, on column chromatography (eluent; chloroform), gave 45 mg (89%) of **17** as a colorless solid, the physical and spectroscopic properties of which were completely in accordance with those of an authentic specimen obtained *via* an alternative route.[11] mp 70—71 °C (in a sealed tube) (lit.,[11] mp 70—71 °C).

Selective Transformation of 8 into 10 Selective aldol cyclization of **8** into **10** was carried out according to the method previously reported in a communication.[2]

Protoadamantane-3,8-diol (22) A solution of **8** (500 mg, 3.0 mmol) in dry THF (10 ml) was added dropwise to a dark blue solution of lithium (416 mg, 60.2 mmol) in liquid ammonia (100 ml) at −78 °C, and the mixture was stirred for 6 h. A mixture of ethanol–methanol [10 ml, (1 : 1, v/v)] was added dropwise, and the stirring was continued for 1 h. The ammonia and the solvent were removed, and the residue was washed with hot THF several times. The combined washings were dried and evaporated to give 457 mg (90%) of **22** as a colorless solid, mp 209—211 °C (from petroleum ether–ether). IR (KBr) cm^{-1}: 3340, 2920, 2845, 1455, 1350, 1325, 1305, 1260, 1175, 1140, 1125, 1090, 1015, 970, 940, 705, 650, 570. ^{1}H-NMR (200 MHz) δ: 1.22—2.18 (14H, m), 2.78 (2H, br s, OH). ^{13}C-NMR δ: 27.7 (t), 28.8 (d), 30.3 (t), 31.7 (d), 38.0 (t), 39.9 (t), 46.4 (t), 76.2 (s). MS m/z (%): 168 (M^+, 85), 150 (40), 108 (90), 95 (100). HRMS m/z: 168.1142 (requires 168.1151 for $C_{10}H_{16}O_2$).

References and Notes

1) Part XVI: T. Momose, O. Muraoka, N. Shimada, C. Tsujimoto, and T. Minematsu, *Chem. Pharm. Bull.*, **37**, 1909 (1989).
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12) Isotwistanes have been highlighted since their use in sesquiterpene syntheses: see, for example, H. Yamamoto and H. L. Sham, *J. Am. Chem. Soc.*, **101**, 1609 (1979); E. J. Corey and M. Ishiguro, *Tetrahedron Lett.*, **1979**, 2745 (isocyanopupukeanane); H. Seto, S. Hirokawa, Y. Fujimoto, and T. Tatsuno, *Chem. Lett.*, **1983**, 989 (synthetic study on nakafuran-9).
13) The value reported by Alford and McKervey[8] (mp 208.5—210 °C) as the melting point of **11** is in good agreement with the present value.
14) The wide range of melting point observed was caused by concomitant isomer formation derived from the thermal equilibration between **9** and **10** on heating in a melting point apparatus.