Synthesis of Polycyclic Cyclobutane Derivatives by Tandem Intramolecular Michael-Aldol Reaction under Two Complementary Conditions: TBDMSOTf-Et₃N and $TMSI-(TMS)_2NH$

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Abstract: The treatment of α,β -unsaturated esters having a ketone function at an appropriate position with either TBDMSOTf in the presence of Et₃N or TMSI in the presence of (TMS)₂NH provided, via a tandem intramolecular Michael-aldol reaction sequence, several different types of cyclobutane derivatives. The two reaction conditions were complementary. Tricyclo[4.2.1.0^{3,8}]nonanes 34 and 55, tricyclo[5.1.1.0^{4,8}]nonane 40, tricyclo[5.4.0.0^{3,7}]undecane 51, tetracyclo[5.4.0.0^{3,7}.0^{9,11}]undecane 45, and the bicyclo[3.2.0]heptanes 56, 57, and 58, which have structures either partially or completely similar to those of endiandric acids A (1a), B (1b), and C (2), trihydroxydecipiadiene (3), lintenone (4), italicene (5), and filifolone (6), were stereoselectively synthesized by the tandem reaction.

A number of polycyclic compounds possessing a cyclobutane, such as endiandric acids A (1a),¹ B (1b),¹ and C (2),¹ trihydroxydecipiadiene (3),²lintenone (4),³italicene (5),⁴ and filifolone (6),⁵ are found in nature (Chart I). Among the synthetic methods available for the synthesis of cyclobutanes, [2+2] cycloaddition is the most commonly used.⁶ As an extension of our study of the intramolecular double Michael reaction,7-10 we envisaged the formation of polycyclic ring systems fused to a cyclobutane by

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the tandem intramolecular Michael-aldol reaction of α,β unsaturated esters carrying a ketone function at an appropriate position. For example, the partial structure 8 of endiandric acid C (2) could be constructed from the γ -substituted cyclohexanone 7, while the frameworks 10 and 12 of trihydroxydecipiadiene (3) and italicene (5) could be formed from the β - and α -substituted cyclohexanones 9 and 11, respectively. Furthermore, the skeleton 14 of filifolone (6) could be assembled from the keto ester 13 (see Scheme I). The key to achieving these transformations is the trapping of the hydroxy anion formed by the tandem reaction to drive the aldol reaction to completion. Here we report a novel construction of polycyclic cyclobutanes by the above approach,

Scheme I. Plan for the Construction of Polycyclic Systems Fused to a Cyclobutane



carried out under two different conditions, which are complementary.11

Results and Discussion

Preparation of Substrates for Tandem Intramolecular Michael-Aldoi Reaction. The requisite α,β -unsaturated esters, functionalized with a keto group, were prepared using standard chemistry as outlined in Scheme II. The γ -substituted cyclohexanone 7 was synthesized from phenethyl alcohol 15 in four steps. The Eand Z-isomers of 7, formed in a 15:1 ratio, were readily separated by chromatography.

The synthesis of β -substituted cyclohexanone 18 was started by conjugate addition¹² to the enone 16.13 Similarly, the cyclopentanone derivative 22 was prepared from 19.14 Deprotection of the acetal group was carried out during the alcohol 21 stage in order to avoid an intramolecular aldol reaction. The Wittig reaction using a stabilized ylide, followed by oxidation with the Dess-Martin periodinane,¹⁵ provided a separable 18:1 mixture of (E)- and (Z)-22.

Bicyclo[3.1.0] hexanone 28 was synthesized as an α' -blocked α -substituted cyclohexanone derivative. After allylation of cyclohexanone, α -hydroxylation¹⁶ of the resulting ketone gave 24, which was subjected to oxidative cleavage with $Pb(OAc)_4$ in MeOH. The derived olefin 25 was converted into 27 via addition

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Scheme II. Preparation of Substrates for Tandem Intramolecular Michael-Aldol Reaction^a



^a Materials and conditions: (a) Li, liquid NH₃, Bu^tOH, then aqueous $(CO_2H)_2$; (b) H₂, 10% Pd-C; (c) PCC; (d) Ph₃P-CHCO₂Me; (e) [2-(2,6dioxanyl)ethyl]magnesium bromide, CuBr·SMe2, TMSCl, HMPA; (f) dilute HCl; (g) NaBH₄; (h) dilute HClO₄; (i) Dess-Martin periodinane; (j) pyrrolidine, PTSA, then allyl bromide; (k) LDA, MoOPH; (l) Pb(OAc)₄, MeOH, then NH₄Cl, MeOH; (m) KOH; (n) (COCl)₂, pyridine; (o) CH₂N₂; (p) Cu; (q) dilute AcOH; (r) LDA, HMPA, 4,4dimethoxybutyl bromide; (s) aqueous (CO2H)2; (t) (CF3CH2O)2POCH2-CO₂Me, KN(TMS)₂, 18-crown-6; (u) DIBALH; (v) MeMgI.

Scheme III. Tandem Intramolecular Michael-Aldol Reaction Using TBDMSOTf- Et_3N^a



^a Materials and conditions: (a) TBDMSOTf, Et₃N; (b) LiN(TMS)₂; (c) ZnCl₂, TMSCl, Et₃N, heat, then dilute HClO₄; (d) DIBALH; (e) Bu^a₄NF; (f) dilute AcOH; (g) Ac₂O, DMAP, pyridine.

of a carbene.¹⁷ The unsaturated ester **28** was obtained as a 7:1 mixture of two diastereoisomers, separable by high-performance liquid chromatography (HPLC).

The α' -unblocked α -substituted cyclohexanones 11 were prepared from 29. The *E*-unsaturated ester 11 was obtained using the ordinary Wittig reaction, while (*Z*)-11 was selectively synthesized by Still's method.¹⁸

Keto esters 13 and 33 were prepared from ϵ -caprolactone 31 and its methylated derivative 32¹⁹ in four steps, respectively.

Tandem Intramolecular Michael-Aldol Reaction. Treatment with TBDMSOTf-Et₃N. The tandem reaction of the symmetrical ketone 7 to afford cyclobutane 8, which has the partial framework of 2, was investigated first (Scheme III). The desired cyclization was achieved upon treatment with TBDMSOTf in the presence of Et_3N ,^{10,20} which gave 34 in 48% yield and the silyl enol ether 35 in 49% yield. The same compound 34 was obtained in 47%

Scheme IV. Treatment of Keto Ester 11 with TBDMSOTf- Et_3N



yield from the Z-isomer of 7 under similar reaction conditions. Further treatment of the silyl enol ether 35 with TBDMSOTf and Et_3N provided 34 in a similar yield. These results indicate a stepwise process.

Reaction of 7 with LiN(TMS)₂⁸ in THF gave a 3:1 mixture of the intramolecular Michael adducts **36** and **37**, which were also obtained in a 10:1 ratio by heating 7 with ZnCl₂, TMSCl, and Et₃N^{9,21} in toluene in a sealed tube at 160 °C for 17 h, followed by treatment with acid. Reaction of **34** with dilute acetic acid caused deprotection of the TBSDMS group accompanied by a retro aldol reaction, affording **37** as a single stereoisomer. This latter result is consistent with the cyclobutane structure of **34**. The TBDMS group could be removed without fragmentation of the cyclobutane ring by first reducing the ester to the primary alcohol with DIBALH, followed by treatment with Buⁿ₄NF. Thus, **34** was transformed into diol **39** in 78% overall yield.

Treatment of the β -substituted cyclohexanone 18 with TB-DMSOTf in the presence of Et₃N provided no cyclobutane derivative, perhaps a consequence of steric hindrance with the gem-dimethyl group. However, the desired cyclization of the corresponding cyclopentanone 22 proceeded to some extent. Upon its addition to a refluxing solution of TBDMSOTf and Et₃N in CH_2Cl_2 , followed by reflux for 15 min, 40 was obtained in 20% yield. It was noteworthy that the silyl enol ether 41 with a deconjugated ester was also isolated in 32% yield from this reaction. The Z-isomer of 22 was also transformed into 40 in 11% yield together with 41 in 45% yield. The TBDMS group of 40 was removed with Bun₄NF (66% yield) to give 43 after DIBALH reduction (86% yield) of the ester. As observed for keto ester 7, heating (E)-22 with ZnCl₂, Et₃N, and TMSCl in a sealed tube at 160 °C for 12 h, followed by acidic treatment, furnished a 1:1.5 diastereomeric mixture of the intramolecular Michael adduct 44 in 48% yield.

The tandem reaction of cyclopropane derivative 28 took place rapidly and quantitatively upon treatment of either diastereoisomer with TBDMSOTf in the presence of Et₃N to produce 45 as a single stereoisomer. The stereochemistry of 45 was determined by observation of NOEs between the CH₂ group attached to C(2) and the cyclopropyl H at C(11) and between the Bu⁴Me₂SiO at C(1) and the cyclobutyl H at C(2) of 46, formed by reduction of 45 with DIBALH. Formation of the tetracyclo[5.4.0.0^{3,7}.0^{9,11}]undecane ring system 45 is remarkably facile, as evidenced by the conversion in 39% yield of 28 into 47 upon heating with ZnCl₂, Et₃N, and TMSCl in CH₂Cl₂, followed by treatment with acid. The presence of an alcohol in 47 was confirmed by its conversion into the acetate 48 in 75% yield.

In the above cases, regioselectivity during enolsilane formation was not an issue since either an α' -blocked or symmetrical ketone was used as the substrate. In order to establish a widely applicable methodology, the tandem reaction of ketones possessing two different types of hydrogens at the α - and α' -positions was further investigated. Exposure of 11 to TBDMSOTf in the presence of Et₃N in CH₂Cl₂ resulted in the exclusive formation of the kinetically controlled silyl enol ethers 49, accompanied by deconjugation of the ester (Scheme IV). Two requirements must therefore be met to achieve the desired transformation: (i)

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Figure 1. ORTEP representation of diol 52.

regioselective formation of the thermodynamically controlled enolate and (ii) trapping of the hydroxy anion formed in the aldol reaction. These requirements can be met as described in the following section.

Treatment with TMSI-(TMS)₂NH. Upon treatment with TMSI in the presence of excess (TMS)₂NH²² at room temperature, 11 was completely converted into a mixture of the thermodynamically controlled silyl enol ether 50 and the tricyclic product 51 within 30 min. The ratio of 51 to 50 gradually increased with time, and the yield of 51 was shown to be solvent dependent. After the reaction had been run for 7 h, 51 was obtained in 70, 64, 14, and 11% yield from (E)-11 in reactions carried out in ClCH₂CH₂Cl, CH₂Cl₂, CCl₄, and ClHC=CCl₂, respectively. The same product (51) was produced in 68% yield by treatment of (Z)-11 with TMSI in the presence of $(TMS)_2NH$ in ClCH₂CH₂Cl. These results again support a stepwise mechanism through a common intermediate. The stereo structure of 51 was assigned on the basis of a comparison of its spectral data with those from compounds 45 and 47. The bent cyclobutane structure was firmly established by X-ray crystallographic analysis after transformation into the diol 52 (Figure 1). The diol 52 was further converted into the methyl compound 54 in two steps (Scheme V).

Treatment of 7 with TMSI and $(TMS)_2NH$ provided tricyclo-[4.2.1.0^{3,8}]nonane **55**, which was transformed into **39**. These conditions gave a modest improvement in yield (57%), compared to the use of TBDMSOTf-Et₃N to give **34** (48%).

The bicyclic compound 56 was the major product along with three other stereoisomers in a 6.8:1.3:1:1 ratio in 83% yield from the acyclic unsaturated ester 13. A mixture of two diastereoisomers of the corresponding angularly methylated compounds 57 and 58 in a 2:1 ratio was obtained in 91% yield by the reaction of 33 under the same conditions. The relative stereochemistry of the products 56, 57, and 58 was determined by observation of NOEs between hydrogens as shown in Scheme V. Both 56 and 57 were converted into diols 59 and 60, respectively. Treatment of 13 or 33 with TBDMSOTf in the presence of Et₃N produced only the corresponding deconjugated silyl enol ethers.

Thus, the carbon skeleton of italicene $(5)^4$ and filifolone $(6)^5$ and the partial skeletons of endiandric acids A (1a),¹ B (1b),¹ and C (2),¹ trihydroxydecipiadiene (3),² and lintenone $(4)^3$ were readily constructed by the above procedure. The tandem intramolecular reaction employing two complementary conditions, TBDMSOTf– Et₃N and TMSI–(TMS)₂NH, provides a useful approach for preparation of a variety of polycyclic compounds fused to a cyclobutane ring.

Experimental Section

General Procedure. All reactions were carried out under a positive atmosphere of dry Ar unless otherwise indicated. Solvents were distilled (22) Miller, R. D.; McKean, D. R. Synthesis 1979, 730–732.

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^a Materials and conditions: (a) IMSI, (IMS)₂NH; (b) DIBALH; (c) Bu^a₄NF; (d) (PhS)₂, Bu^a₃P, pyridine; (e) Li, liquid NH₃, Bu^bOH.

prior to use: THF, DME, Et₂O, benzene, and toluene were freshly distilled from Na benzophenone; CH₂Cl₂ and MeCN were distilled from CaH₂ and kept over 4-Å molecular sieves; HMPA was distilled from Na benzophenone under reduced pressure and kept over 4-Å molecular sieves. Unless otherwise noted, all extracts were dried over MgSO₄ and the solvent was removed by rotary evaporation under reduced pressure. Silica gel column chromatography was carried out with Merck Kieselgel 60 Art. 7734, while Merck Kieselgel 60 Art. 9835 was used for flash chromatography. HPLC was carried out using a Gilson HPLC system (Model 302/303) equipped with a 10 × 250 mm column of Dynamax Microsorb silica (5 μ m) and monitored by using UV and refractive index detectors.

4-[(2Z)- and (2E)-3-(Methoxycarbonyl)-2-propenyl]cyclohexan-1-one (7). To a solution of p-methoxyphenethyl alcohol (15) (437 mg, 3.11 mmol), Bu^tOH (2.5 mL, 26.51 mmol), and THF (1.5 mL) in liquid NH₃ (15 mL) was added Li (206 mg, 29.7 mmol). After 2 h of stirring, MeOH (1 mL) and H₂O (7.5 mL) were added to the reaction mixture. After having been allowed to stand overnight at ambient temperature, the mixture was partitioned between H₂O and benzene. The organic phase was washed with brine, dried, and evaporated to give an oil, which was used in the following reaction.

The above product was treated for 4 h at 40 °C with a mixture of $(CO_2H)_2$ (392 mg, 3.11 mmol) and MeOH-H₂O (4:1 v/v, 50 mL). After neutralization with NaHCO₃ (260 mg, 3.11 mmol), the mixture was concentrated. The residue was partitioned between brine and AcOEt. The organic phase was washed with brine, dried, and evaporated. The residue was purified by flash chromatography, with acetone-benzene (1:4 v/v) as eluent, to afford β,γ -unsaturated ketone (230 mg, 53% overall yield) as an oil: IR (neat, cm⁻¹) 3400, 1713; ¹H NMR (60 MHz, CCl₄) δ 5.50 (br s, 1H), 3.75 (t, J = 6.5 Hz, 2H), 3.20 (br s, 1H), 2.90 (br s, 2H), 2.50-2.15 (m, 6H); MS m/z (M⁺) 140.

The mixture of β , γ -unsaturated ketone (188 mg, 1.32 mmol) and 10% Pd-C (30 mg) in AcOEt (15 mL) was stirred for 19 h under a H₂ atmosphere. After filtration through Celite, followed by concentration under reduced pressure, the residue was subjected to flash chromatography. Elution with acetone-benzene (1:4 v/v) gave the saturated keto alcohol (122 mg, 64%) as an oil: IR (CHCl₃, cm⁻¹) 3405, 1713; ¹H NMR (500 MHz, CDCl₃) δ 3.74 (t, J = 6.6 Hz, 2H), 2.42–2.31 (m, 4H), 2.13–2.08 (m, 2H), 1.99–1.90 (m, 1H), 1.72 (br s, 1H), 1.62–1.58 (m, 2H), 1.50–1.40 (m, 2H); MS m/z (M⁺) 142.

To a stirred mixture of PCC (950 mg, 4.41 mmol) and Florisil (1.8 g) in dry CH_2Cl_2 (12 mL) was added at room temperature a solution of unsaturated keto alcohol (237 mg, 1.67 mmol) in dry CH_2Cl_2 (18 mL). After 4 h of stirring at the same temperature, followed by dilution with Et₂O, the mixture was filtered through Celite. After evaporation of the solvent, the residue was used in the following reaction.

A mixture of the crude product and Ph₃P=CHCO₂Me (430 mg, 1.29 mmol) in dry MeCN (24 mL) was stirred for 12 h at room temperature and heated for 1 h under reflux. After removal of the solvent under reduced pressure, the residue was subjected to flash chromatography. Elution with AcOEt-hexane (3:7 v/v) provided (Z)-7 (5.4 mg, 4% overall yield) as a colorless oil: IR (neat, cm⁻¹) 1723, 1650; ¹H NMR (90 MHz, CDCl₃) δ 6.28 (dt, J = 11.6, 7.8 Hz, 1H), 5.85 (dt, J = 11.6, 1.5 Hz, 1H), 3.72 (s, 3H), 2.71 (ddt, J = 7.8, 7.8, 1.5 Hz, 2H), 2.47-2.25 (m, 4H), 2.15 (br s, 1H), 2.10-1.90 (m, 2H), 1.60-1.30 (m, 2H); MS m/z (M⁺) calcd 196.1099, obsd 196.1106.

Further elution with the same solvents gave (*E*)-7 (81 mg, 60% overall yield) as a colorless oil: IR (neat, cm⁻¹) 1720, 1655; ¹H NMR (500 MHz, CDCl₃) δ 6.97 (dt, *J* = 16.0, 7.8 Hz, 1H), 5.87 (dt, *J* = 16.0, 1.5 Hz, 1H), 3.74 (s, 3H), 2.42–2.31 (m, 4H), 2.25 (ddt, *J* = 7.8, 1.5, 1.0 Hz, 2H), 2.10–2.05 (m, 2H); MS *m/z* (M⁺) calcd 196.1099, obsd 196.1067. Anal. Calcd for C₁₁H₁₆O₃: C, 67.32; H, 8.22. Found: C, 67.25; H, 8.42.

2,2-Dimethyl-5-[2-(1,3-dioxa-2-cyclohexyl)ethyl]cyclohexan-1-one (17). To a hot mixture of activated Mg (59 mg, 2.42 mmol) and a catalytic amount of I₂ in dry THF (0.5 mL) was added a solution of 2-(2bromoethyl)-1,3-dioxane (0.28 mL, 2.02 mmol) in dry THF (1.25 mL), and the mixture was stirred for 3 h at room temperature. To a stirred mixture of CuBr-SMe₂ (12 mg, 0.06 mmol) and HMPA (0.5 mL, 2.88 mmol) in dry THF (1.5 mL) at -78 °C was slowly added the above mixture. After 45 min of stirring at -78 °C, a solution of enone 1613 (150 mg, 1.21 mmol) and TMSCl (0.3 mL, 2.42 mmol) in dry THF (2 mL) was added over 10 min to the resulting mixture at -78 °C. After 40 min of stirring at the same temperature, followed by additions of AcOH (0.28 mL, 4.89 mmol) and THF (1.5 mL), the mixture was stirred for 1.5 h at room temperature. After neutralization with a mixture of NH₄Cl- NH_4OH (pH 8), the resulting mixture was partitioned between H_2O and Et₂O. The organic layer was washed with saturated NaHCO₃ and brine, dried, and evaporated. Flash chromatography of the residue with AcOEthexane (1:7 v/v) as eluent gave 17 (178 mg, 61%) as a colorless oil: IR (neat, cm⁻¹) 1702; ¹H NMR (500 MHz, CDCl₃) δ 4.50 (t, J = 4.7 Hz, 1H), 4.10 (dd, J = 12.0, 5.0 Hz, 2H), 3.75 (m, 2H), 2.33 (dd, J = 13.0, 3.0 Hz, 1H), 2.23 (dd, J = 13.0, 12.0 Hz, 1H), 2.12–2.01 (m, 1H), 1.77-1.68 (m, 4H), 1.65-1.31 (m, 6H), 1.13 (s, 3H), 1.05 (s, 3H); MS m/z (M⁺) calcd 239.1647, obsd 239.1666.

2,2-Dimethyl-5-[(3Z)- and (3E)-4-(methoxycarbonyl)-3-butenyl]cyclohexan-1-one (18). A mixture of 17 (446 mg, 1.94 mmol) and 2.5% HCl (6.2 mL) in acetone (12.5 mL) was stirred for 5 h at room temperature. After dilution with Et₂O-hexane (1:1 v/v), the mixture was neutralized with 10% NH₄OH. The organic phase was washed with brine, dried, and evaporated to give the crude aldehyde, which was used in the next reaction.

A mixture of the above product and Ph_3P —CHCO₂Me (778 mg, 2.33 mmol) in dry MeCN (60 mL) was stirred for 12 h at room temperature. Evaporation of the solvent gave a residue which was subjected to flash chromatography. Elution with AcOEt-hexane (1:8 v/v) produced (Z)-18 (6 mg, 1.3% overall yield) as a colorless oil: IR (neat, cm⁻¹) 1723,

1705, 1655; ¹H NMR (90 MHz, CDCl₃) δ 6.20 (dt, J = 11.3, 7.4 Hz, 1H), 5.78 (dt, J = 11.3, 1.0 Hz, 1H), 3.72 (s, 3H), 2.37–2.20 (m, 4H), 1.80–1.40 (m, 7H), 1.13 (s, 3H), 1.05 (s, 3H); MS m/z (M⁺) calcd 238.1568, obsd 238.1554.

Additional eluate gave (*E*)-**18** (120 mg, 26% overall yield) as a colorless oil: IR (neat, cm⁻¹) 1723, 1705, 1655; ¹H NMR (500 MHz, CDCl₃) δ 6.92 (dt, *J* = 15.0, 7.5 Hz, 1H), 5.82 (dt, *J* = 15.0, 1.0 Hz, 1H), 3.72 (s, 3H), 2.33 (ddd, *J* = 13.0, 4.4, 2.0 Hz, 1H), 2.26–2.20 (m, 3H), 1.78– 1.70 (m, 3H), 1.59–1.41 (m, 4H), 1.13 (s, 3H), 1.05 (s, 3H); MS *m/z* (M⁺) calcd 238.1568, obsd 238.1552.

Elution with AcOEt-hexane (1:7 v/v) yielded 17 (260 mg, 56%).

2,2-Dimethyl-4-[2-(1,3-dioxa-2-cyclohexyl)ethyl]cyclopentan-1-one (20). To a stirred mixture of the Grignard reagent, prepared from Mg (1.40 g, 57.5 mmol) and 2-(2-bromoethyl)-1,3-dioxane (6.60 mL, 49.7 mmol), a catalytic amount of I2, CuBr-SMe2 (390 mg, 1.90 mmol), and HMPA (13.3 mL, 76.4 mmol) in dry THF (135 mL) at -78 °C was added over 30 min a solution of 1914 (4.20 g, 38.2 mmol) and TMSCl (9.70 mL, 76.4 mmol) in dry THF (60 mL), and the mixture was stirred for 40 min at ~78 °C. After addition of AcOH (6.80 mL, 118.0 mmol) and THF (56.7 mL), the resulting mixture was worked up as described for 17. The crude product was purified by chromatography on silica gel with AcOEt-hexane (1:3 v/v) as eluent to give 20 (5.66 g, 66%) as a colorless oil: IR (neat, cm⁻¹) 1736; ¹H NMR (500 MHz, CDCl₃) δ 4.53 (t, J = 5.2 Hz, 1H), 4.10 (dd, J = 11.0, 4.9 Hz, 2H), 3.77 (dt, J = 12.2, 2.4 Hz, 2H), 2.51 (ddd, J = 18.6, 7.3, 2.1 Hz, 1H), 2.20-2.03 (m, 2H), 1.96 (ddd, J = 12.5, 12.5)6.3, 1.8 Hz, 1H), 1.84 (dd, J = 18.3, 11.6 Hz, 1H), 1.70-1.48 (m, 4H), 1.40–1.31 (m, 2H), 1.06 (s, 3H), 1.01 (s, 3H); MS m/z (M⁺) calcd 226.1569, obsd 226.1574. Anal. Calcd for C13H22O3: C, 68.99; H, 9.80. Found: C, 68.82; H, 9.74.

2,2-Dimethyl-4-[2-(1,3-dioxa-2-cyclohexyl)ethyl]cyclopentan-1-ol (21). To a stirred solution of **20** (325 mg, 1.44 mmol) in MeOH (10 mL) at room temperature was slowly added NaBH₄ (109 mg, 2.88 mmol), and the mixture was stirred for 10 min. After addition of H₂O, the mixture was thoroughly extracted with Et₂O. The extracted was washed with brine, dried, and evaporated. Chromatography of the residue on silica gel with AcOEt-hexane (3:7 v/v) as eluent yielded **21** (321 mg, 98%) as a 1:1.5 mixture of two stereoisomers: IR (neat, cm⁻¹) 3450; ¹H NMR (500 MHz, CDCl₃) δ 4.49 and 4.48 [each t, each J = 6.0 Hz, 1H, (1.5: 1)], 4.10 (dd, J = 12.0, 4.4 Hz, 2H), 3.80–3.72 (m, 2H), 3.72 and 3.62 [each t, J = 7.0, 6.0 Hz, respectively, 1H (1.5:1)], 0.98 and 0.97 [each s, 3H (1.5:1)], 0.90 (s, 3H); MS m/z (M⁺ - H) calcd 227.1651. Anal. Calcd for C₁₃H₂₄O₃: C, 68.38; H, 10.59. Found: C, 68.49; H, 10.58.

2,2-Dimethyl-4-[(3Z)- and (3E)-4-(methoxycarbonyl)-3-butenyl]cyclopentan-1-one (22). A mixture of 21 (377 mg, 1.65 mmol) in 10% HClO₄-THF (1:1 v/v, 30 mL) was stirred for 12 h at 30 °C. After dilution with Et₂O, the organic phase was washed with saturated NaHCO₃ and brine, dried, and evaporated. The residue was dissolved in dry MeCN (100 mL) and treated with Ph₃P=CHCO₂Me (551 mg, 1.65 mmol) for 12 h at room temperature. Removal of the solvent gave a residue, which was subjected to silica gel chromatography with AcOEt-hexane (1:9 v/v) as eluent to afford the epimeric mixture of α,β -unsaturated esters (256 mg, 69% overall yield) as a colorless oil: IR (neat, cm⁻¹) 3440, 1721, 1654; ¹H NMR (500 MHz, CDCl₃) δ 6.99–6.92 (m, 1H), 5.82 (d, J = 15.8 Hz, 1H), 3.72 (s, 3H), 3.65 (t, J = 6.0 Hz, 1H), 2.23–1.00 (m, 10H), 0.98 and 0.97 [each s, 3H (1.5:1)], 0.93 and 0.92 [each s, 3H (1.5:1)]; MS m/z (M⁺) calcd 226.1568, obsd 226.1559.

To a stirred solution of DMP¹⁵ (1.08 g, 2.55 mmol) in dry CH₂Cl₂ (15 mL) at room temperature was added a solution of the above alcohols (384 mg, 1.70 mmol) in dry CH₂Cl₂ (3 mL), and the mixture was stirred for 10 min at the same temperature. After dilution with Et₂O, the mixture was poured into saturated NaHCO₃ containing Na₂S₂O₃ and was stirred for 20 min at room temperature. The organic layer was washed with saturated NaHCO₃ and brine, dried, and evaporated. The residue was subjected to chromatography on silica gel with AcOEt-hexane (3:17 v/v) to give (*Z*)-22 (19.5 mg, 5%) as a colorless oil: IR (neat, cm⁻¹) 1735, 1720, 1655; ¹H NMR (500 MHz, CDCl₃) δ 6.23 (dt, *J* = 12.0, 7.5 Hz, 1H), 5.79 (d, *J* = 12.0 Hz, 1H), 3.71 (s, 3H), 2.53 (ddd, *J* = 18.0, 7.0, 3.0 Hz, 1H), 1.38 (t, *J* = 12.5 Hz, 1H), 1.07 (s, 3H), 1.00 (s, 3H); MS *m/z* (M⁺) calcd 224.1413, obsd 224.1412.

Further elution afforded (*E*)-22 (345 mg, 91%) as a colorless oil: IR (neat, cm⁻¹) 1730, 1720, 1655; ¹H NMR (500 MHz, CDCl₃) δ 6.96 (dt, J = 15.9, 7.3 Hz, 1H), 5.84 (d, J = 15.9 Hz, 1H), 3.73 (s, 3H), 2.52 (ddd, J = 18.3, 7.3, 1.8 Hz, 1H), 2.26 (dd, J = 15.3, 7.3 Hz, 2H), 2.22–2.12 (m, 1H), 2.00 (ddd, J = 12.2, 6.1, 1.8 Hz, 1H), 1.84 (dd, J = 18.3, 11.0

Hz, 1H), 1.60 (dd, J = 15.3, 7.3 Hz, 2H), 1.37 (t, J = 12.2 Hz, 1H), 1.07 (s, 3H), 1.01 (s, 3H); MS m/z (M⁺) calcd 224.1413, obsd 224.1424.

6-Allyl-2-hydroxycyclohexan-1-one (24). A mixture of cyclohexanone (23) (49 g, 0.5 mol), pyrrolidine (71 g, 1.0 mol), and p-TsOH (150 mg, 0.79 mmol) in dry benzene (500 mL) was heated for 24 h under reflux in a Dean-Stark apparatus. After evaporation, the residue was washed with a small amount of dry benzene. A mixture of the product and allyl bromide (73 g, 0.6 mol) in BuⁿOH (125 mL) was heated for 12 h under reflux. After evaporation of the solvent, followed by addition of H₂O (200 mL), the mixture was heated for 3 h under reflux. After being cooled, the mixture was thoroughly extracted with Et₂O. The extract was dried and evaporated to give a residue, which was distilled to give 2-allylcyclohexan-1-one (38 g, 55%), bp 90-99 °C (200 mmHg), as a colorless oil.

To a LDA-THF solution (30 mL), prepared from Pri₂NH (2.1 mL, 15.0 mmol) and 1.54 M BunLi-hexane (8.44 mL, 13.0 mmol), was added at -78 °C a solution of 2-allylcyclohexan-1-one (1.46 g, 10.6 mmol) in dry THF (20 mL). After 1 h of stirring at -78 °C, the resulting mixture was transferred into a stirred mixture of MoOPH¹⁶ (7.8 g, 18.0 mmol) in dry THF (30 mL) at -78 °C. After 1 h of stirring at -78 °C, to the mixture was added saturated Na₂S₂O₃ (30 mL). After further addition of H₂O, the resulting mixture was thoroughly extracted with Et₂O. The extract was washed with 5% HCl and brine, dried, and evaporated. Chromatography on silica gel using AcOEt-hexane (1:9 v/v) as eluent afforded 2-allylcyclohexan-1-one (116 mg) and an epimeric mixture of 24 (907 mg, 56%) as a pale yellow oil: IR (neat, cm⁻¹) 3540; ¹H NMR (500 MHz, CDCl₃) δ 5.83-5.74 and 5.71-5.62 [each m, 1H (3:7)], 5.11-5.01 (m, 2H), 4.26 and 4.11 [each dd, each J = 12.0 and 6.5 Hz, 1H (7:3)], 3.70 and 3.60 [each s, 1H (7:3)]; MS m/z (M⁺) calcd 154.0994, obsd 154.0998.

Methyl 2-Allyl-6,6-dimethoxyhexanoate (25). To a stirred solution of 24 (953 mg, 6.19 mmol) in hexane–MeOH (3:1 v/v, 40 mL) at 0 °C was slowly added Pb(OAc)₄ (2.75 g, 6.20 mmol). After 1 h of stirring, followed by additions of saturated NaHCO₃ and Et₂O, the mixture was filtered through Celite. The organic phase was washed with brine, dried, and evaporated to give a residue, which was used in the next reaction without purification.

A mixture of the product and NH₄Cl (10 mg, 0.18 mmol) in MeOH (20 mL) was heated for 1 h under reflux. Evaporation of the solvent gave a residue, which was partitioned between saturated NaHCO₃ and Et₂O. The organic layer was dried and evaporated to afford a residue, which was subjected to silica gel chromatography. Elution with AcOEt-hexane (1:9 v/v) provided **25** (990 mg, 70%) as a colorless oil: IR (neat, cm⁻¹) 1740; ¹H NMR (500 MHz, CDCl₃) δ 5.78–5.64 (m, 1H), 5.04–4.95 (m, 2H), 4.30 (t, J = 6.0 Hz, 1H), 3.64 (s, 3H), 3.26 (s, 6H); MS m/z (M⁺ – H) calcd 229.1440, obsd 229.1438.

3-Allyl-1-diazo-7,7-dimethoxyheptan-2-one (26). A mixture of 25 (497 mg, 2.16 mmol) and KOH (200 mg, 3.6 mmol) in MeOH-H₂O (5:1 v/v, 6 mL) was heated for 6 h under reflux. After addition of 10% KHSO₄ with cooling, the mixture was thoroughly extracted with CH₂Cl₂. The extract was washed with brine, dried, and evaporated to give a residue, which was used in the following reaction without purification.

To a mixture of the product and pyridine (0.177 mL, 2.21 mmol) in dry benzene (5 mL) at 0 °C was slowly added a solution of $(COCl)_2$ (0.175 mL, 2.01 mmol) in dry benzene (1 mL), and the mixture was stirred for 1 h at room temperature. The mixture was filtered through Celite using benzene. Evaporation of the filtrate gave a residue, which was subjected to the next reaction without purification.

To a solution of excess CH₂N₂ in Et₂O (20 mL) at 0 °C was slowly added a solution of the above product in dry benzene (5 mL), and the mixture was stirred for 12 h at room temperature. After evaporation, the residue was subjected to chromatography on silica gel with protection from light. Elution with AcOEt-hexane (1:9 v/v) afforded **26** (268 mg, 52%) as a yellowish oil: IR (neat, cm⁻¹) 2100, 1640; ¹H NMR (60 MHz, CDCl₃) δ 6.20–5.40 (m, 1H), 5.25–4.80 (m, 2H), 4.30 (t, J = 6.0 Hz, 1H), 3.30 (s, 6H); MS m/z (M⁺ – CHN₂) calcd 199.1334, obsd 199.1374.

3-(4,4-Dimethoxybutyl)bicyclo[3.1.0]hexan-2-one (27). To a stirred hot mixture of Cu (250 mg, 3.9 mmol) in dry cyclohexane (10 mL) was slowly added a solution of 26 (201 mg, 0.84 mmol) in dry cyclohexane (10 mL), and the mixture was heated for 1 h under reflux. After dilution with Et₂O, the mixture was filtered through Celite. Evaporation of the filtrate gave a residue, which was chromatographed on silica gel. Elution with AcOEt-hexane (1:9 v/v) provided 27 (148 mg, 83%) as an epimeric mixture: IR (neat, cm⁻¹) 1720; ¹H NMR (500 MHz, CDCl₃) δ 4.30 (dd, J = 12.0, 6.0 Hz, 1H), 3.28 (s, 6H), 1.23–1.08 (m, 2H), 0.95–0.91 and 0.76–0.72 [each m, 1H (7:1)]; MS m/z (M⁺ – OMe) calcd 181.1229, obsd 181.1190. 3-[(4E)-5-(Methoxycarbonyl)-4-pentenyl]bicyclo[3.1.0]hexan-2-one (28). A mixture of 27 (219 mg, 1.04 mmol) in AcOH-H₂O (4:1 v/v, 5 mL) was stirred for 3 h at room temperature. After neutralization with saturated NaHCO₃ with cooling, the mixture was thoroughly extracted with Et_2O . The extract was washed with brine, dried, and evaporated to give a residue, which was used in the following reaction without purification.

A mixture of the product and Ph₃P=CHCO₂Me (1.17 g, 3.5 mmol) in dry MeCN (20 mL) was stirred for 24 h at room temperature. After evaporation, the residue was taken up into CH₂Cl₂. The organic solution was washed with brine, dried, and evaporated. Chromatography of the residue on silica gel with AcOEt-hexane (1:9 v/v) as eluent gave a 7:1 mixture of **28** (134 mg, 74%) as a colorless oil: IR (neat, cm⁻¹) 1720, 1660; ¹H NMR (500 MHz, CDCl₃) δ 6.94 (dt, J = 16.0 and 7.0 Hz, 1H), 5.82 (dt, J = 16.0, 1.5 Hz, 1H), 3.72 (s, 3H), 1.22–1.12 (m, 2H), 0.99– 0.95 and 0.90–0.85 [each m, 1H (7:1)]; ¹³C NMR (125 MHz, CDCl₃, ppm) 215.7, 167.1, 149.1, 121.3, 51.5, 40.3, 32.3, 30.3, 29.3, 27.6, 26.0, 20.1, 14.6; MS m/z (M⁺) calcd 222.1256, obsd 222.1266. Two stereoisomers were separable by HPLC on Si 80-199-C5 with AcOEthexane (1:4 v/v) as eluent (4 mL min⁻¹), the major isomer ($t_R = 11.2$ min) and the minor one ($t_R = 13.2$ min).

2-(4,4-Dimethoxybutyl)cyclohexan-1-one (30). To a stirred LDA-THF solution (60 mL), prepared from Pri₂NH (4.6 mL, 33.0 mmol) and 1.56 M BuⁿLi-hexane (18.5 mL, 29.0 mmol), was slowly added at 0 °C a solution of N-cyclohexylidenecyclohexylamine (29) (4.0 g, 22.0 mmol) in dry THF (10 mL). After 30 min of stirring at 0 °C, followed by addition of HMPA (5.0 mL, 29.0 mmol), a solution of 4-bromo-1,1dimethoxybutane (5.70 g, 29.0 mmol) in dry THF (10 mL) was added. After 1 h of stirring at 0 °C, the mixture was diluted with Et₂O. The organic solution was washed with saturated NH₄Cl, H₂O, and brine, dried, and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with Et_2O -hexane (1:3 v/v) afforded 30 (4.1 g, 86%) as a colorless oil: IR (neat, cm⁻¹) 1710; ¹H NMR (300 MHz, CDCl₃) δ 4.36 (t, J = 5.9 Hz, 1H), 3.31 (s, 6H), 2.42-2.21 (m, 3H), 2.15-1.94 (m, 2H), 1.88-1.73 (m, 2H), 1.70-1.54 (m, 3H), 1.43–1.13 (m, 5H); MS m/z (M⁺ – MeOH) calcd 182.1306, obsd 182.1311.

2-[(4E)- and (4Z)-5-(Methoxycarbonyl)-4-pentenyl]cyclohexan-1-one (11). (A) A mixture of 30 (2.0 g, 9.3 mmol) and $(CO_2H)_2$ -2H₂O (11.5 g, 93.0 mmol) in THF-H₂O (1:1 v/v, 40 mL) was stirred for 3 h at room temperature. After dilution with Et₂O, the mixture was neutralized with saturated NaHCO₃ with cooling. The organic phase was washed with H₂O and brine, dried, and evaporated to give the crude aldehyde (1.7 g), which was used in the next reaction without purification.

A mixture of the above product (1.7 g) and Ph₃P=CHCO₂Me (4.0 g, 12.1 mmol) in dry MeCN (40 mL) was stirred for 12 h at room temperature. After evaporation, the residue was chromatographed on silica gel with Et₂O-hexane (1:3 v/v) as eluent to afford a 16:1 mixture of (*E*)- and (*Z*)-11 (1.8 g, 86% overall yield) as a colorless oil.

(B) To a mixture of 18-crown-6 (1.4 g, 5.20 mmol) and (CF₃-CH₂O)₂P(=O)CH₂CO₂Me (0.286 mL, 1.35 mmol) in dry THF (3.5 mL) was added at -78 °C 0.5 M KN(TMS)₂-toluene (2.2 mL, 1.14 mmol). After 30 min of stirring at -78 °C, a solution of the crude aldehyde (175 mg) in dry THF (1 mL) was added to the mixture. After 1 h of stirring at -78 °C, the resulting mixture was diluted with Et₂O. The organic solution was washed with saturated NH₄Cl, H₂O, and brine, dried, and evaporated to give a residue, which was subjected to silica gel chromatography. Elution with Et₂O-hexane (1:3 v/v) afforded a 1:22.5 mixture of (*E*)- and (*Z*)-11 (170 mg, 81% overall yield) as a colorless oil.

Data for (*E*)-11: IR (neat, cm⁻¹) 1720, 1710, 1660; ¹H NMR (300 MHz, CDCl₃) δ 6.96 (dt, J = 15.8, 6.6 Hz, 1H), 5.83 (dt, J = 15.8, 1.1 Hz, 1H), 3.72 (s, 3H), 2.43–2.16 (m, 5H), 2.15–1.97 (m, 2H), 1.92–1.73 (m, 2H), 1.72–1.62 (m, 2H), 1.52–1.33 (m, 3H), 1.27–1.16 (m, 1H); MS m/z (M⁺) calcd 224.1411, obsd 224.1410.

Data for (Z)-11: IR (neat, cm⁻¹) 1720, 1710, 1640; ¹H NMR (500 MHz, CDCl₃) δ 6.28 (dt, J = 11.6, 7.3 Hz, 1H), 5.89 (dt, J = 11.6, 1.2 Hz, 1H), 3.71 (s, 3H), 2.72 (ddd, J = 7.3, 7.3, 1.2 Hz, 2H), 2.44–2.29 (m, 4H), 2.11–2.03 (m, 2H), 1.98–1.88 (m, 1H), 1.57–1.46 (m, 2H); ¹³C NMR (125 MHz, CDCl₃, ppm) 213.2, 166.8, 150.5, 119.4, 51.0, 50.4, 42.1, 34.0, 29.1, 29.0, 28.1, 26.6, 24.9; MS m/z (M⁺) calcd 224.1411, obsd 224.1431. Anal. Calcd for C₁₃H₂₀O₃: C, 69.61; H, 8.99. Found: C, 69.55; H, 9.13.

Methyl 8-Oxo-2-nonenate (13). To a solution of ϵ -caprolactone (1.5 g, 13.0 mmol) in CH₂Cl₂-DME (1:1 v/v, 40 mL) was slowly added at -78 °C 0.93 M DIBALH-hexane (15.5 mL, 14.5 mmol), and the mixture was stirred for 45 min at -78 °C. After additions of Et₂O (300 mL) and

 H_2O (15 mL), the mixture was stirred for 1.5 h at room temperature. The organic phase was dried and evaporated to give the crude aldehyde (1.5 g), which was subjected to the following reaction without purification.

To a stirred solution of the above product (1.5 g) in dry THF (40 mL) was slowly added at 0 °C 0.98 M MeMgI-Et₂O (4.1 mL, 40.0 mmol). After 8 h of stirring at room temperature, the resulting mixture was partitioned between Et₂O and H₂O. The organic layer was washed with brine, dried, and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with AcOEt-hexane (1:1 v/v) provided the diol (851 mg, 49% overall yield) as a colorless oil: IR (neat, cm⁻¹) 3360; ¹H NMR (300 MHz, CDCl₃) δ 3.83–3.75 (m, 1H), 3.65 (br t, J = 5.1 Hz, 2H), 1.62–1.53 (m, 1H), 1.49–1.22 (m, 7H), 1.19 (d, J = 6.2 Hz, 3H); MS m/z (M⁺ – 1) 131, (M⁺ – 1 – H₂O) 113.

To a solution of the diol (400 mg, 3.0 mmol) in ClCH₂CH₂Cl (16 mL) were added 4-Å molecular sieves (2.3 g) and PCC (1.5 g, 7.0 mmol), and the mixture was stirred for 1 h at room temperature. After dilution with Et₂O, the mixture was filtered through silica gel. Evaporation of the filtrate gave the keto aldehyde (370 mg). A mixture of the product (370 mg) and Ph₃P=CHCO₂Me (1.3 g, 3.8 mmol) in dry MeCN (16 mL) was stirred for 16 h at room temperature. After removal of the solvent, the residue was purified by silica gel chromatography. Elution with Et₂Ohexane (1:2 v/v) yielded 13 (280 mg, 50% overall yield) as a colorless oil: IR (neat, cm⁻¹) 1715, 1705, 1650; ¹H NMR (500 MHz, CDCl₃) δ 6.94 (dt, J = 15.9, 7.0 Hz, 1H), 5.83 (dt, J = 15.9, 1.2 Hz, 1H), 3.72(s, 3H), 2.45 (t, J = 7.3 Hz, 2H), 2.24–2.19 (m, 2H), 2.14 (s, 3H), 1.63-1.57 (m, 2H), 1.50-1.43 (m, 2H); ¹³C NMR (75 MHz, CDCl₃, ppm) 208.3, 166.8, 148.7, 121.1, 51.3, 43.2, 31.9, 29.8, 27.4, 23.1; MS m/z (M⁺) 185. Anal. Calcd for C₁₀H₁₆O₃: C, 65.19; H, 8.75. Found: C, 65.18; H, 8.71.

3-Methylheptane-2,7-diol. α -Methyl- ϵ -caprolactone¹⁹ (1.5 g, 11.7 mmol) was reduced with 0.93 M DIBALH-hexane (13.9 mL, 12.9 mmol) in CH₂Cl₂-DME (1:1 v/v, 40 mL) as above to give the crude aldehyde (1.5 g). Reaction of the product (1.5 g) with 0.98 M MeMgI-Et₂O (27 mL, 26.5 mmol) in dry THF, followed by workup as above, gave the diol (1.4 g, 82% overall yield) as a colorless oil: IR (neat, cm⁻¹) 3350; ¹H NMR (300 MHz, CDCl₃) δ 3.77–3.67 (m, 0.57H), 3.64 (t, J = 6.2 Hz, 2H), 3.54–3.40 (m, 0.43H), 1.93 (br s, 1H), 1.78 (br s, 1H), 1.62–1.27 (m, 5.7H), 1.22–1.13 (m, 0.3H), 1.14 (d, J = 6.2 Hz, 1.7H), 1.13 (d, J = 6.2 Hz, 1.3H), 0.95–0.87 (m, 1H), 0.89 and 0.88 [each d, each J = 6.6 Hz, 3H (1.7:1.3)]; MS m/z (M⁺ + 1) calcd 147.1384, obsd 147.1359.

Methyl 7-Methyl-8-oxo-2-nonenate (33). The above diol (546 mg, 3.7 mmol) was oxidized using 4-Å molecular sieves (2.8 g) and PCC (1.9 g, 8.6 mmol) in ClCH₂CH₂Cl (22 mL) as above to afford the keto aldehyde (530 mg), which was transformed, by the reaction with Ph₃P=CHCO₂-Me (1.6 g, 4.8 mmol) in MeCN (1.5 mL) as above, to provide 33 (380 mg, 51% overall yield) as a colorless oil: IR (neat, cm⁻¹) 1720, 1710, 1650; ¹H NMR (300 MHz, CDCl₃) δ 6.94 (dt, J = 15.9, 6.9 Hz, 1H), 5.82 (dt, J = 15.9, 1.5 Hz, 1H), 3.73 (s, 3H), 2.51 (dd, J = 13.8, 6.9 Hz, 1H), 2.24–2.15 (m, 2H), 2.14 (s, 3H), 1.72–1.63 (m, 1H), 1.49–1.32 (m, 3H), 1.10 (d, J = 6.9 Hz, 3H); MS m/z (M⁺) calcd 198.1255, obsd 198.1275. Anal. Calcd for C₁₁H₁₈O₃: C, 66.64; H, 9.15. Found: C, 66.60; H, 9.04.

(±)-(1R*,2S*,3R*,6S*,8S*)-3-(tert-Butyldimethylsiloxy)-2-(methoxycarbonyl)tricyclo[4.2.1.0^{3,8}]nonane (34). (A) To a stirred solution of (E)-7 (20 mg, 0.10 mmol) in dry CH₂Cl₂ (2 mL) were added at room temperature Et₃N (0.1 mL, 0.72 mmol) and TBDMSOTf (0.1 mL, 0.44 mmol), and the reaction mixture was stirred for 1 h. After dilution with hexane, the mixture was washed with 5% KHSO4 and saturated NaHCO₃, dried, and evaporated to give a residue which was subjected to flash chromatography on silica gel. Elution with Et₂Ohexane (3:97 v/v) gave 34 (15 mg, 48%) as a colorless oil: IR (neat, cm⁻¹) 1740; ¹H NMR (500 MHz, CDCl₃) δ 3.68 (s, 3H), 2.87 (dd, J = 8.2, 4.8 Hz, 1H), 2.82 (d, J = 3.2 Hz, 1H), 2.79 (ddd, J = 8.4, 8.4, 3.2 Hz, 1H), 2.21 (ddd, J = 8.2, 4.7, 4.7 Hz, 1H), 1.99-1.91 (m, 1H), 1.80 (d, J = 12.6 Hz, 1H), 1.69 (dddd, J = 12.6, 8.2, 4.7, 1.7 Hz, 1H), 1.63-1.58 (m, 2H), 1.37–1.28 (m, 2H), 1.26 (br d, J = 12.6 Hz, 1H), 0.83 (s, 9H), 0.09 (s, 3H), 0.05 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, ppm) 173.6, 75.5, 55.8, 51.5, 47.9, 39.3, 33.0, 31.5, 30.9, 30.5, 25.9, 25.6, 17.9, -2.5, -2.7; MS m/z (M⁺ – Me) calcd 295.1729, obsd 295.1728.

Further elution afforded **35** (15.2 mg, 49%) as a colorless oil: IR (neat, cm⁻¹) 1725, 1670, 1650; ¹H NMR (90 MHz, CDCl₃) δ 6.95 (dt, J = 16.0, 7.0 Hz, 1H), 5.82 (dt, J = 16.0, 1.5 Hz, 1H), 4.83 (br s, 1H), 3.72 (s, 3H), 2.30–1.20 (m, 9H), 0.91 (s, 9H), 0.15 (s, 6H); MS m/z (M⁺ – 1) calcd 309.1886, obsd 309.1853.

(B) Using the same procedure as above, (Z)-7 (9.5 mg, 0.05 mmol) was converted into 34 (7.1 mg, 47%), which was identical with the above product in all respects.

(±)-(15°,5R°,7R^{*})- and (15°,5R^{*},7S^{*})-7-[(Methoxycarbonyi)methyl]bicyclo[3.2.1]octan-2-one (36 and 37). (A) To a stirred mixture of 1 M LiN(TMS)₂-THF (0.18 mL, 0.18 mmol) in dry THF (1 mL) was slowly added at -78 °C a solution of (E)-7 (17 mg, 0.09 mmol) in dry THF (1 mL), and the mixture was stirred for 5.5 h at -78 °C and for 9.5 h at room temperature. After dilution with benzene, the mixture was washed with 5% KHSO₄ and brine, dried, and evaporated. Flash chromatography of the residue with AcOEt-hexane (1:3 v/v) as eluent gave a 3:1 mixture of 36 and 37 (4.3 mg, 39%) as a colorless oil: IR (neat, cm⁻¹) 1738, 1710; ¹H NMR (500 MHz, CDCl₃) δ 3.68 (s, 3H), 2.74–2.62 (m, 0.5H), 2.56– 2.22 (m, 7.25H), 2.16 (ddd, J = 18.0, 11.5, 9.0 Hz, 0.25H), 2.04 (ddd, J = 14.0, 8.0, 2.0 Hz, 0.75H), 1.98–1.92 (m, 1H), 1.84–1.64 (m, 3H), 1.24 (dd, J = 13.0, 6.0 Hz, 0.25H); MS m/z (M⁺) calcd 196.1099, obsd 196.1093.

(B) A mixture of (E)-7 (21 mg, 0.11 mmol), $ZnCl_2$ (162 mg, 1.23 mmol), Et_3N (0.15 mL, 1.08 mmol), and TMSCl (0.15 mL, 1.18 mmol) in dry toluene (7.5 mL) was heated for 17 h at 160 °C in a scaled tube. The mixture was partitioned between 5% HCl and benzene. The organic phase was washed with saturated NaHCO₃ and brine, dried, and evaporated to give a residue, which was dissolved in THF (1 mL) and treated for 20 min with 10% HClO₄. After dilution with Et_2O -benzene (1:1 v/v), the mixture was washed with saturated NaHCO₃ and brine, dried, and evaporated. The residue was purified by flash chromatography with AcOEt-hexane (1:4 v/v) as eluent to give a 10:1 mixture of 36 and 37 (4.1 mg, 19%): ¹H NMR (500 MHz, CDCl₃) δ 2.16 (ddd, J = 18.0, 11.5, 9.0 Hz, 0.09H), 2.04 (ddd, J = 14.0, 8.0, 2.0 Hz, 0.91H).

(C) To a solution of 34 (13 mg, 0.04 mmol) in THF (0.5 mL) was added AcOH-H₂O (1:1 v/v, 1 mL), and the mixture was heated for 15 h at 60 °C and for 6 h at 110 °C. After addition of AcOH (0.5 mL), the mixture was further heated at 110 °C. Removal of solvents gave a residue, which was taken up into Et₂O-benzene (1:1 v/v). The organic solution was washed with H₂O and brine, dried, and evaporated. The residue was subjected to flash chromatography with AcOEt-hexane (1:4 v/v) as eluent to give 37 (4.1 mg, 51%) as a colorless oil: IR (neat, cm⁻¹) 1738, 1710; ¹H NMR (500 MHz, CDCl₃) δ 3.68 (s, 3H), 2.74–2.62 (m, 2H), 2.41 (dd, J = 16.0, 6.0 Hz, 1H), 2.25 (dd, J = 16.0, 9.0 Hz, 1H), 2.16 (ddd, J = 18.0, 11.5, 9.0 Hz, 1H), 1.98–1.92 (m, 1H), 1.82–1.71 (m, 3H), 1.24 (dd, J = 13.0, 6.0 Hz, 1H); MS m/z (M⁺) calcd 196.1099, obsd 196.1111.

(±)-(1R*,2S*,3R*,6S*,8S*)-3-(tert-Butyldimethylsiloxy)-2-(hydroxymethyl)tricyclo[4.2.1.0^{3,8}]nonane (38). To a stirred solution of 34 (77 mg, 0.25 mmol) in dry DME (6 mL) was added at 0 °C 1 M DIBALH-hexane (0.75 mL, 0.75 mmol), and the mixture was stirred for 3 h at 0 °C. After additions of Et₂O (20 mL) and H₂O (0.75 mL), the mixture was stirred for 30 min at room temperature. After dilution with Et_2O -benzene (1:1 v/v), the organic solution was filtered through Celite, dried, and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with AcOEt-hexane (1:20 v/v)afforded 37 (58 mg, 83%) as a colorless oil: IR (neat, cm⁻¹) 3575; ¹H NMR (500 MHz, CDCl₃) δ 3.94 (t, J = 11.0 Hz, 1H), 3.61 [br d, (dd with D_2O , J = 11.5, 5.0 Hz, 1H], 2.90 (br s, disappeared with D_2O , 1H), 2.66 (t, J = 6.0 Hz, 1H), 2.22–2.17 (m, 1H), 2.12 (ddd, J = 11.0, 5.0,1.6 Hz, 1H), 1.99 (dt, J = 8.0, 1.6 Hz, 1H), 1.91 (dt, J = 13.4, 8.2, 1H), 1.80 (d, J = 12.0 Hz, 1H), 1.65–1.57 (m, 2H), 1.54 (dd, J = 12.0, 8.0 Hz, 1H), 1.42-1.34 (m, 1H), 1.28-1.23 (m, 2H), 0.79 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, ppm) 77.2, 64.7, 51.1, 46.3, 39.6, 33.0, 31.5, 30.90, 30.8, 26.0, 25.9, 17.9, -2.4, -2.7; MS m/z (M⁺) calcd 282.2015, obsd 282.2032.

(±)-(1*R**,2*S**,3*R**,6*S**,8*S**)-3-Hydroxy-2-(hydroxymethyl)tricyclo-[4.2.1.0^{3,8}]nonane (39). (A) A mixture of 38 (13 mg, 0.05 mmol) and 1 M Buⁿ₄NF-THF (0.5 mL, 0.5 mmol) in THF (1.75 mL) was stirred for 15 min at room temperature. After dilution with Et₂O-benzene (1:1 v/v), the mixture was washed with 5% KHSO₄ and saturated NaHCO₃, dried, and evaporated. Chromatography of the residue on silica gel with AcOEt-hexane (1:1 v/v) as eluent gave 39 (7.9 mg, 94%) as a colorless powder, mp 43-44 °C: IR (neat, cm⁻¹) 3380; ¹H NMR (300 MHz, CDCl₃) δ 3.96 (dd, J = 11.0, 7.7 Hz, 1H), 3.82 (dd, J = 11.0, 4.0 Hz, 1H), 2.63 (br t, J = 5.1 Hz, 1H), 2.46 (br s, 2H), 2.25–2.11 (m, 2H), 2.08-2.02 (m, 1H), 2.01–1.88 (m, 1H), 1.82 (d, J = 12.1 Hz, 1H), 1.72– 1.61 (m, 1H), 1.59–1.50 (m, 2H), 1.44–1.33 (m, 1H), 1.32–1.19 (m, 2H); MS m/z (M⁺) calcd 168.1150, obsd 168.1152.

(B) Reduction of 55 (11 mg, 0.041 mmol) was carried out using 0.93 M DIBALH-hexane (0.097 mL, 0.09 mmol) in CH₂Cl₂ (0.3 mL) as above. The crude product (10 mg) was treated with 1 M Bu^a₄NF-THF (0.054 mL, 0.054 mmol) in THF (0.2 mL), and the product was purified as above to give 39 (6 mg, 87%) as a colorless powder, mp 43-44 °C, which was identical with the above compound.

(±)-(1S*,4S*,7S*,8R*,9R*)-1-(tert-Butyldimethylsiloxy)-2,2-dimethyl-9-(methoxycarbonyl)tricyclo[5.1.1.04,8]nonane (40). (A) To a stirred solution of Et₃N (0.3 mL, 2.1 mmol) and TBDMSOTf (0.3 mL, 1.3 mmol) in dry CH₂Cl₂ (3 mL) was slowly added under reflux a solution of (E)-22 (49 mg, 0.22 mmol) in dry CH₂Cl₂ (2 mL), and the mixture was heated for 15 min under reflux. After dilution with hexane, the mixture was washed with saturated NaHCO3 and brine, dried, and evaporated to give a residue, which was chromatographed on silica gel. Elution with Et_2O -hexane (1:99 v/v) provided 40 (15 mg, 20%) as a colorless oil: IR (neat, cm⁻¹) 1732; ¹H NMR (500 MHz, CDCl₃) δ 3.62 (s, 3H), 3.08 (dddd, J = 9.2, 8.6, 7.0, 3.2 Hz, 1H), 2.94 (dd, J = 8.6, 3.2 Hz, 1H)8.6 Hz, 1H), 2.75 (d, J = 7.0 Hz, 1H), 2.72–2.64 (m, 1H), 1.94 (dddd, J = 13.4, 9.9, 9.2, 3.2 Hz, 1H), 1.72–1.59 (m, 2H), 1.63 (dd, J = 13.4, 8.4 Hz, 1H), 1.56–1.46 (m, 1H), 1.26 (dd, J = 13.4, 10.0 Hz, 1H), 0.94 (s, 3H), 0.85 (s, 9H), 0.82 (s, 3H), 0.21 (s, 3H), 0.10 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, ppm) 172.6, 86.8, 54.1, 52.8, 51.4, 47.9, 43.6, 40.4, 34.5, 31.9, 31.2, 26.0, 23.3, 20.2, 18.2, -1.5, -3.0; MS m/z (M⁺) calcd 338.2277, obsd 338.2246.

Further elution afforded **41** (24 mg, 32%) as a colorless oil: IR (neat, cm⁻¹) 1745, 1640; ¹H NMR (500 MHz, CDCl₃) δ 5.61–5.57 (m, 1H), 5.54–5.50 (m, 1H), 4.38 (br s, 1H), 3.69 and 3.68 [each s, 3H (1:1.2)], 3.10 and 3.04 [each d, each J = 6.0 Hz, 2H)], 2.63–2.49 (m, 1H), 2.12–1.94 (m, 2H), 1.92–1.80 (m, 1H), 1.30–1.19 (m, 1H), 1.03 and 1.06 [each s, 3H (1.2:1)], 1.00 (s, 3H), 0.93 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H); MS m/z (M⁺) calcd 338.2277, obsd 338.2232.

(B) (Z)-22 (19 mg, 0.09 mmol) was converted, as above using Et_2N (0.1 mL, 0.77 mmol) and TBDMSOTf (0.1 mL, 0.4 mmol), into 40 (3.2 mg, 11%) and 41 (13 mg, 45%), which were identical with the above samples in all respects.

(±)-(15*,45*,75*,85*,95*)-1-(*tert*-Butyldimethylsiloxy)-2,2-dimethylsyl-9-(hydroxymethyl)tricyclo[5.1.1.0^{4,8}]nonane (42). Reduction of 40 (10 mg, 0.03 mmol) with 1 M DIBALH-hexane (0.1 mL, 0.1 mmol) in dry DME (2 mL) as previously described, followed by the similar workup procedure, gave 42 (8 mg, 86%) as a colorless oil: IR (neat, cm⁻¹) 3410; ¹H NMR (500 MHz, CDCl₃) δ 3.79 (t, J = 11.0 Hz, 1H), 3.61–3.39 (m, 1H), 2.91 (t, J = 9.0 Hz, 1H), 2.73–2.61 (m, 1H), 2.15–2.03 (m, 2H), 1.92–1.77 (m, 2H), 1.75–1.64 (m, 1H), 1.64–1.49 (m, 2H), 1.34 (d, J = 10.0 Hz, 1H), 1.31 (d, J = 10.0 Hz, 1H), 0.93 (s, 9H), 0.86 (s, 3H), 0.84 (s, 3H), 0.26 (s, 3H), 0.17 (s, 3H); MS m/z (M⁺) calcd 310.2326, obsd 310.2338.

(±)-($1S^*$, $4S^*$, $7S^*$, $8S^*$, $9S^*$)-2, 2-Dimethyl-1-hydroxy-9-(hydroxymethyl)tricyclo[5.1.1.0^{4,8}]nonane (43). Treatment of 42 (20 mg, 0.07 mmol) with 1 M Bu^a₄NF-THF (0.65 mL, 0.65 mmol), followed by workup as previously described and chromatography on silica gel, with AcOEt-hexane (3:17 v/v) as eluent, gave 43 (8.5 mg, 66%) as a colorless oil: IR (neat, cm⁻¹) 3430; ¹H NMR (500 MHz, CDCl₃) δ 3.84 (dd, J = 10.5, 8.0 Hz, 1H), 3.76 (dd, J = 6.5, 5.0 Hz, 1H), 2.68-2.55 (m, 3H), 2.00 (dt, J = 8.5, 6.0 Hz, 1H), 1.95-1.86 (m, 1H), 1.70-1.50 (m, 4H), 1.35 (dd, J = 13.5, 9.5 Hz, 1H), 0.90 (s, 3H), 0.86 (s, 3H); MS m/z (M⁺ – H₂O) calcd 178.1357, obsd 178.1358.

3,3-Dimethyl-8-[(methoxycarbonyl)methyl]bicyclo[3.3.0]octan-2-one (44). A mixture of (E)-22 (22 mg, 0.1 mmol), $ZnCl_2$ (160 mg, 1.2 mmol), Et_3N (0.15 mL, 1.1 mmol), and TMSCl (0.15 mL, 1.7 mmol) in dry toluene (7 mL) was heated for 12 h at 160 °C in a scaled tube. After dilution with Et_2O , the mixture was washed with 5% HCl, saturated NaHCO₃, and brine, dried, and evaporated. Chromatography of the residue on silica gel with AcOEt-hexane (1:4 v/v) gave a 1:1.5 mixture of 44 (16 mg, 48%) as an oil: IR (neat, cm⁻¹) 1734, 1729; ¹H NMR (500 MHz, CDCl₃) δ 3.70 and 3.68 [each s, 3H (1.5:1)], 2.24 and 2.22 [each dd, J = 5.8, 3.0 and 6.4, 3.6 Hz, respectively, 2H (1.5:1)], 1.04 and 1.12 [each s, 3H (1.5:1)], 1.05 and 0.99 [each s, 3H (1.5:1)]; MS m/z (M⁺) calcd 224.1411, obsd 224.1412.

(±)-(1*R**,2*S**,3*S**,7*R**,9*S**,11*S**)-1-(*tert*-Butyldimethylsiloxy)-2-(methoxycarbonyl)tetracyclo[5.4.0.0^{3,7},0^{9,11}]undecane (45). (A) To a stirred solution of 3*S**-isomer of 28 (10 mg, 0.045 mmol) and Et₃N (0.019 mL, 0.135 mmol) in dry CH₂Cl₂ (2 mL) was added at room temperature TBDMSOTf (0.026 mL, 0.113 mmol), and the mixture was stirred for 5 min. After dilution with CH₂Cl₂, the mixture was washed with saturated NaHCO₃, 5% KHSO₄, and brine, dried, and evaporated. Flash chromatograph of the residue, with AcOEt-hexane (1:19 v/v) as eluent, afforded 45 (15 mg, 99%) as a colorless oil: IR (neat, cm⁻¹) 1725; ¹H NMR (500 MHz, CDCl₃) δ 3.73 (s, 3H), 2.56 (d, *J* = 6.2 Hz, 1H), 2.37 (dd, *J* = 6.2, 6.2 Hz, 1H), 2.09 (ddd, *J* = 13.5, 6.2, 1.2 Hz, 1H), 1.88 (ddd, *J* = 12.8, 6.2, 1.6 Hz, 1H), 1.70–1.40 (m, 7H), 1.10 (ddd, *J* = 12.6, 10.8, 7.6 Hz, 1H), 0.90 (s, 9H), 0.66 (ddd, *J* = 8.2, 8.2, 4.4 Hz, 1H), 0.18 (ddd, *J* = 4.4, 4.4, 4.4 Hz, 1H), 0.15 (s, 3H), 0.13 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, ppm) 173.3, 83.9, 61.8, 51.9, 51.2, 42.1, 41.3, 31.8, 31.6, 28.9, 26.2, 26.0, 19.7, 18.4, 13.5, -3.4, -3.5; MS m/z (M⁺) calcd 336.2120, obsd 336.2107.

(B) The $3R^*$ -isomer of 28 (5 mg, 0.023 mmol) was similarly converted into 45 (7.5 mg, 99%), which was identical with the above compound in all respects.

(±)-(1*R**,2*R**,3*S**,7*R**,9*S**,11*S**)-1-(*tert*-Butyldimethylsiloxy)-2-(hydroxymethyl)tetracyclo[5.4.0.0^{3,7}.0^{9,11}]undecane (46). Reduction of 45 (7 mg, 0.021 mmol) with 1 M DIBALH-hexane (0.1 mL, 0.1 mmol) in dry DME (1 mL), followed by workup as previously described and flash chromatography with AcOEt-hexane (3:47 v/v) as eluent gave 46 (6.4 mg, 100%) as a colorless oil: ¹H NMR (400 MHz, CDCl₃) δ 3.94 (dd, *J* = 10.6, 7.3 Hz, 1H), 3.80 (dd, *J* = 10.6, 7.8 Hz, 1H), 2.03 (ddd, *J* = 13.0, 6.3, 1.1 Hz, 1H), 1.87 (dd, *J* = 6.3, 6.3 Hz, 1H), 1.88-1.46 (m, 8H), 1.42 (ddddd, *J* = 8.0, 8.0, 6.3, 4.2, 1.1 Hz, 1H), 1.19 (br, 3.1H), 1.06 (ddd, *J* = 12.3, 12.3, 7.1 Hz, 1H), 0.89 (s, 9H), 0.66 (ddd, *J* = 8.5, 8.5, 4.2, 1.2 Hz, 1H), 0.16 (ddd, *J* = 4.2, 4.2, 4.2 Hz, 1H), 0.12 (s, 3H), 0.11 (s, 3H); ¹³C NMR (125 MHz, CDCl₃, pm) 76.9, 63.7, 60.5, 49.4, 43.7, 42.2, 23.6, 32.1, 27.5, 26.5, 26.0, 19.7, 18.4, 13.2, -2.9, -3.0; MS *m/z* (M⁺) calcd 308.2172, obsd 308.2168.

(±)-(1R*,2S*,3S*,7R*,9S*,11S*)-1-Hydroxy-2-(methoxycarbonyl)tetracyclo[5.4.0.0^{3,7}.0^{9,11}]undecane (47). A mixture of 28 (41 mg, 0.18 mmol), ZnCl₂ (300 mg, 2.20 mmol), Et₃N (0.3 mL, 2.15 mmol), and TMSCl (0.3 mL, 2.37 mmol) in dry CH₂Cl₂ (3 mL) was heated for 24 h at 160 °C in a sealed tube. After dilution with Et₂O, the mixture was washed with 5% HCl, saturated NaHCO₃, and brine, dried, and evaporated. The residue was treated for 30 min at room temperature with 10% HClO₄-THF (1:1 v/v, 5 mL). After dilution with Et_2O , the mixture was washed with saturated NaHCO3 and brine, dried, and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with AcOEt-hexane (1:9 v/v) provided 47 (16 mg, 39%) as a colorless oil: IR (neat, cm⁻¹) 3500, 1735; ¹H NMR (500 MHz, CDCl₃) δ 3.72 (s, 3H), 2.64 (d, J = 6.7 Hz, 1H), 2.39 (dd, J = 6.7, 6.7Hz, 1H), 2.14 (ddd, J = 13.5, 5.6, 1.0 Hz, 1H), 1.86 (br s, 1H), 1.84-1.44(m, 8H), 1.18 (ddd, J = 10.6, 9.2, 6.2 Hz, 1H), 0.71 (dddd, J = 8.4, 8.4, 8.4)4.8, 1.2 Hz, 1H), 0.12 (ddd, J = 4.2, 4.2, 4.2 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃, ppm) 173.1, 83.0, 60.4, 51.5, 50.6, 42.5, 41.0, 31.3, 31.1, 29.1, 26.3, 18.5, 12.1; MS m/z (M⁺) calcd 222.1256, obsd 222.1262.

(±)-(1 R^* ,2 S^* ,3 S^* ,7 R^* ,9 S^* ,11 S^*)-1-Acetoxy-2-(methoxycarbonyl)tetracyclo[5.4.0.0^{3,7},0^{9,11}]undecane (48). A mixture of 47 (8 mg, 0.035 mmol), DMAP (1 mg, 0.008 mmol), and Ac₂O (0.2 mL, 2.12 mmol) in pyridine (0.5 mL, 6.19 mmol) was stirred for 48 h at room temperature. The mixture was partitioned at 0 °C between Et₂O and 5% HCl. The organic phase was washed with brine, dried, and evaporated. Chromatography of the residue on silica gel with AcOEt-hexane (1:9 v/v) as eluent gave 48 (7 mg, 75%) as a colorless oil: IR (neat, cm⁻¹) 1735; ¹H NMR (500 MHz, CDCl₃) 3.72 (s, 3H), 2.63 (d, J = 7.0 Hz, 1H), 2.46–2.42 (m, 1H), 2.05 (s, 3H), 1.27–1.19 (m, 1H), 0.72–0.68 (m, 1H), 0.13 (dd, J = 8.0, 4.0 Hz, 1H); MS m/z (M⁺) calcd 264.1362, obsd 264.1386.

Treatment of 11 with TBDMSOTf and Et₃N. To a stirred solution of 11 (15 mg, 0.067 mmol) and Et₃N (0.093 mL, 0.67 mmol) in dry CH₂Cl₂ (0.3 mL) was added at room temperature TBDMSOTf (0.077 mL, 0.33 mmol), and the mixture was stirred for 30 min at room temperature. After dilution with Et₂O, the mixture was washed with H₂O and brine, dried, and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with Et₂O-hexane (1:20 v/v) containing Et₃N (3 v/v %) afforded a 1:1.3 mixture of (*E*)- and (*Z*)-49 (21 mg, 93%) as a colorless oil: IR (neat, cm⁻¹) 1740, 1665, 1660; 1H NMR (500 MHz, CDCl₃) δ 5.59–5.45 (m, 2H), 4.81 (ddd, *J* = 7.5, 3.5, 1.0 Hz, 1H), 3.68 (s, 1.3H), 3.67 (s, 1.7H), 3.09 (d, *J* = 6.1 Hz, 0.9H), 3.03 (dd, *J* = 6.5, 1.5 Hz, 1.1H), 2.14–1.93 (m, 5H), 1.80–1.30 (m, 6H), 0.93 (s, 5H), 0.91 (s, 4H), 0.124 (s, 3.4H), 0.120 (s, 2.6H); MS *m*/z (M⁺) calcd 338.2275, obsd 338.2290.

(±)-(1*R**,2*S**,3*S**,7*R**)-2-(Methoxycarbonyl)-1-(trimethylsiloxy)tricyclo[5.4.0.0^{3,7}]undecane (51). (A) To a solution of (*E*)-11 (40 mg, 0.18 mmol) and (TMS)₂NH (0.05 mL, 0.27 mmol) in dry ClCH₂CH₂Cl (1.2 mL) was added at 0 °C TMSI (0.03 mL, 0.21 mmol), and the mixture was stirred for 10 min at 0 °C and for 7 h at room temperature. After dilution with Et₂O, the mixture was washed with H₂O and brine, dried, and evaporated. Chromatography of the residue on silica gel with Et₂O-hexane (1:20 v/v) containing Et₃N (3 v/v %) as eluent gave 51 (37 mg, 70%) as a colorless oil: IR (neat, cm⁻¹) 1730; ¹H NMR (500 MHz, CDCl₃) δ 3.67 (s, 3H), 2.65 (d, J = 7.9 Hz, 1H), 2.39 (dd, J = 7.9, 4.9 Hz, 1H), 2.27 (ddd, J = 13.6, 7.6, 3.0 Hz, 1H), 1.81–1.28 (m, 12H), 1.13 (ddd, J = 13.4, 8.0, 8.0 Hz, 1H), 0.13 (s, 9H); ¹³C NMR (125 MHz, CDCl₃, ppm) 173.4, 76.2, 52.9, 51.1, 38.7, 35.0, 34.0, 32.1, 30.7, 25.3, 22.6, 19.9, 1.9; MS m/z (M⁺) calcd 296.1806, obsd 296.1804.

(B) Similarly, (Z)-11 (50 mg, 0.22 mmol) was converted, using

 $(TMS)_2NH$ (0.071 mL, 0.33 mmol) and TMSI (0.038 mL, 0.27 mmol) in ClCH₂CH₂Cl (1.3 mL), into **51** (45 mg, 68%), which was identical with the above sample in all respects.

(±)-(1*R**,2*R**,3*S**,7*R**)-1-Hydroxy-2-(hydroxymethyl)tricyclo-[5.4.0.0^{3,7}]undecane (52). Reduction of 51 (150 mg, 0.51 mmol) with 0.93 M DIBALH-hexane (1.2 mL, 1.1 mmol) in dry CH₂Cl₂ (4 mL), followed by treatment of the product with 1 M Buⁿ₄NF (0.68 mL, 0.68 mmol) in THF (4 mL) as above and chromatography on silica gel, with AcOEt-hexane (1:3 v/v) as eluent, yielded 52 (84 mg, 85% overall yield) as colorless crystals, mp 122–123 °C: IR (CHCl₃, cm⁻¹) 3400; ¹H NMR (300 MHz, CDCl₃) δ 3.74 (dd, J = 11.0, 9.5 Hz, 1H), 3.57 (dd, J = 11.0, 5.5 Hz, 1H), 2.83 (br s, 1H), 2.68 (br s, 1H), 2.24 (ddd, J = 13.6, 8.1, 5.9 Hz, 1H), 1.95 (ddd, J = 9.2, 7.8, 6.0 Hz, 1H), 1.86–1.66 (m, 5H), 1.65–1.18 (m, 9H); MS m/z (M⁺) 196. Anal. Calcd for C₁₂H₂₀O₂: C, 73.43; H, 10.27. Found: C, 73.48; H, 10.43.

(±)-(1*R**,2*S**,3*S**,7*R**)-1-Hydroxy-2-[(phenylthio)methyl]tricyclo-[5.4.0.0^{3,7}]undecane (53). A mixture of 52 (60 mg, 0.31 mmol), Buⁿ₃P (0.23 mL, 0.92 mmol), and (PhS)₂ (200 mg, 0.92 mmol) in dry pyridine (0.25 mL) was stirred for 1.5 h at room temperature. After dilution with Et₂O, the mixture was washed with 10% NaOH, H₂O, and brine, dried, and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with Et₂O-hexane (1:3 v/v) afforded 53 (86 mg, 98%) as a yellowish oil: IR (neat, cm⁻¹) 3400, ¹H NMR (500 MHz, CDCl₃) δ 7.33-7.28 (m, 4H), 7.18-7.14 (m, 1H), 3.12 (dd, *J* = 12.2, 7.3 Hz, 1H), 2.95 (dd, *J* = 12.2, 7.9 Hz, 1H), 2.17 (ddd, *J* = 13.4, 7.9, 4.9 Hz, 1H), 1.97 (dd, *J* = 15.3, 7.3 Hz, 1H), 1.84-1.55 (m, 10H), 1.50-1.45 (m, 1H), 1.41-1.21 (m, 3H); ¹³C NMR (125 MHz, CDCl₃), pm) 137.1, 129.0, 128.9, 125.8, 72.8, 52.5, 48.6, 43.0, 34.7, 33.6, 32.7, 32.4, 30.5, 25.9, 23.3, 20.1; MS *m/z* (M⁺) calcd 288.1547, obsd 288.1527.

(±)-(1*R**,2*R**,3*S**,7*R**)-1-Hydroxy-2-methyltricyclo[5.4.0.0^{3,7}]undecane (54). To a mixture of 53 (86 mg, 0.30 mmol) and THF-But-OH (10:1 v/v, 3.3 mL) in liquid NH₃ (50 mL) was added at -34 °C Li (50 mg, 7.2 mmol), and the mixture was stirred for 5 min at -34 °C. After addition of NH₄Cl (100 mg), followed by evaporation of the liquid NH₃, the residue was taken up into Et₂O. The organic solution was washed with 10% NaOH, H₂O, and brine, dried, and evaporated. Chromatography of the residue on silica gel with Et₂O-hexane (1:4 v/v) as eluent provide 54 (45 mg, 85%) as a colorless solid, mp 63-64 °C: IR (neat, cm⁻¹) 3370; ¹H NMR (500 MHz, CDCl₃) δ 2.13 (ddd, J = 14.0, 7.6, 6.4 Hz, 1H), 1.79-1.44 (m, 11H), 1.36-1.23 (m, 4H), 1.21 (dd, J = 14.0, 7.0 Hz, 1H), 0.94 (d, J = 6.7 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃, ppm) 72.5, 53.0, 44.3, 43.7, 34.7, 32.6, 32.2, 29.8, 26.0, 23.4, 20.3, 12.6; MS *m/z* (M⁺) calcd 180.1513, obsd 180.1528.

(±)-(1*R**,25*,3*R**,65*,85*)-2-(Methoxycarbonyl)-3-(trimethylsiloxy)tricyclo[4.2.1.0^{3,8}]nonane (55). To a stirred solution of 7 (40 mg, 0.20 mmol) and (TMS)₂NH (0.065 mL, 0.31 mmol) in dry ClCH₂CH₂Cl (1 mL) was added at 0 °C TMSI (0.035 mL, 0.25 mmol), and the mixture was stirred for 10 min at 0 °C and for 22 h at room temperature. After a workup similar to that described in the preparation of 51, chromatography on silica gel with Et₂O-hexane (1:30 v/v) containing Et₃N (3 v/v%) provided 55 (31 mg, 57%) as a colorless oil: IR (neat, cm⁻¹) 1735; ¹H NMR (500 MHz, CDCl₃) δ 3.68 (s, 3H), 2.92 (dd, J = 7.4, 5.0 Hz, 1H), 2.83 (d, J = 2.1 Hz, 1H), 2.78 (ddd, J = 7.4, 7.4, 2.1 Hz, 1H), 2.22 (ddd, J = 8.2, 8.2, 4.7 Hz, 1H), 1.98–1.92 (m, 1H), 1.80 (d, J = 12.5 Hz, 1H), 1.63–1.61 (m, 2H), 1.36–1.27 (m, 2H), 1.25 (d, J = 12.5 Hz, 1H), 0.09 (s, 9H); MS *m/z* (M⁺) calcd 268.1493, obsd 268.1515.

(1*R**,5*S**,6*S**,7*S**)-7-(Methoxycarbonyl)-6-methyl-6-(trimethylsiloxy)bicyclo[3.2.0]heptane (56). To a stirred solution of 13 (115 mg, 0.63 mmol) and (TMS)₂NH (0.197 mL, 0.94 mmol) in dry ClCH₂CH₂Cl (2.8 mL) was added at 0 °C TMSI (0.107 mL, 0.75 mmol), and the mixture was stirred for 10 min at 0 °C and for 2 h at room temperature. After the same workup as above, the product was purified by silica gel chromatography. Elution with Et₂O-hexane (1:10 v/v) containing Et₃N (3 v/v) gave a 6.8:1.3:1:1 mixture (132 mg, 83%), the major component being 56, which was isolated by preparative TLC: IR (neat, cm⁻¹) 1730; ¹H NMR (500 MHz, C₆D₆) δ 3.44 (s, 3H), 2.91 (ddd, J = 6.8, 6.8, 6.7 Hz, 1H), 2.81 (d, J = 6.7 Hz, 1H), 2.13 (dd, J = 12.0, 6.0 Hz, 1H), 1.45 (s, 3H), 1.47–1.37 (m, 2H), 0.27 (s, 9H); ¹³C NMR (125 MHz, C₆D₆, ppm) 172.4, 73.6, 55.1, 50.7, 50.6, 34.3, 32.0, 26.6, 26.4, 26.2, 2.0; MS m/z (M⁺) calcd 256.1493, obsd 256.1489.

 $(1S^*,5S^*,6R^*,7S^*)$ - and $(1S^*,5S^*,6S^*,7S^*)$ -5,6-Dimethyl-7-(methoxycarbonyl)-6-(trimethylsiloxy)bicyclo[3.2.0]heptane (57 and 58). To a stirred solution of 33 (50 mg, 0.25 mmol) and (TMS)₂NH (0.08 mL, 0.38 mmol) in dry ClCH₂CH₂Cl (1.3 mL) was added at 0 °C TMSI (0.043 mL, 0.30 mmol), and the mixture was stirred for 10 min at 0 °C

and for 1.5 h at room temperature. The same workup as above, followed by chromatography of the product on silica gel with Et_2O -hexane (1:20 v/v) containing Et_3N (3 v/v %) as eluent, afforded a 2:1 mixture of 57 and 58 (62 mg, 91%), which were separable by preparative TLC.

Data for 57: IR (neat, cm⁻¹) 1730; ¹H NMR (500 MHz, C₆D₆) δ 3.45 (s, 3H), 2.85 (d, J = 7.3 Hz, 1H), 2.47 (t, J = 7.3 Hz, 1H), 2.42 (ddd, J = 13.2, 8.1, 4.0 Hz, 1H), 1.88–1.72 (m, 2H), 1.71–1.64 (m, 1H), 1.51 (ddd, J = 9.4, 6.9, 2.5 Hz, 1H), 1.41 (s, 3H), 1.22 (ddd, J = 13.2, 9.2, 7.7 Hz, 1H), 1.04 (s, 3H), 0.28 (s, 9H); ¹³C NMR (125 MHz, C₆D₆, ppm) 172.5, 76.6, 54.8, 53.1, 50.6, 41.4, 35.2, 31.6, 26.9, 22.4, 21.8, 2.1; MS m/z (M⁺) calcd 270.1650, obsd 270.1643.

Data for 58: IR (neat, cm⁻¹) 1740; ¹H NMR (300 MHz, CDCl₃) δ 3.58 (s, 3H), 3.08 (t, J = 6.6 Hz, 1H), 2.44 (d, J = 7.3 Hz, 1H), 1.72–1.63 (m, 2H), 1.57–1.38 (m, 4H), 1.31 (s, 3H), 1.20 (s, 3H), 0.25 (s, 9H); MS m/z (M⁺) calcd 270.1650, obsd 270.1664.

 $(15^{\circ},55^{\circ},65^{\circ},7R^{\circ})$ -6-Hydroxy-7-(hydroxymethyl)-6-methylbicyclo-[3.2.0]heptane (59). To a stirred solution of 56 (25 mg, 0.098 mmol) in dry CH₂Cl₂ (0.8 mL) was added at -78 °C 0.93 M DIBALH-hexane (0.26 mL, 0.24 mmol), and the mixture was stirred for 1 h. After additions of Et₂O (15 mL) and H₂O (0.26 mL), the mixture was stirred for 1 h at room temperature. The organic solution was dried and evaporated to give a residue, which was used in the following reaction without purification.

A mixture of the product (22 mg) and 1 M Bu^a₄NF-THF (0.125 mL, 0.125 mmol) in THF (0.5 mL) was stirred for 30 min at room temperature. After dilution with AcOEt, the mixture was washed with H₂O and brine, dried, and evaporated. Chromatography on silica gel with AcOEt-hexane (1:1 v/v) as eluent gave **59** (14 mg, 92% overall yield) as a colorless solid, mp 103-104 °C: IR (neat, cm⁻¹) 3375; ¹H NMR (500 MHz, CDCl₃) δ 3.75 (ddd, J = 10.4, 8.5, 4.3 Hz, 1H), 3.62 (ddd, J = 10.4, 6.1, 4.3 Hz, 1H), 2.40 (t, J = 7.9 Hz, 1H), 2.05 (dd, J = 13.4, 6.7 Hz, 1H), 1.94-1.87 (m, 2H), 1.83-1.72 (m, 2H), 1.59-1.55 (m, 1H), 1.52-1.43 (m, 3H), 1.34 (s, 3H), 1.26 (br t, J = 5.5 Hz, 1H); MS *m/z* (M⁺ - H₂O) calcd 138.1044, obsd 138.1051.

(15°,55°,6*R*°,7*R*°)-5,6-Dimethyl-6-hydroxy-7-(hydroxymethyl)bicyclo-[3.2.0]heptane (60). Reduction of 57 (60 mg, 0.23 mmol) with 0.93 M DIBALH-hexane (0.63 mL, 0.59 mmol) in dry CH₂Cl₂ (2 mL), followed by treatment of the product (55 mg) with 1 M Bu^a₄NF-THF (0.32 mL, 0.32 mmol) in THF (1.5 mL) and purification as above, provided **60** (34 mg, 93%) as a colorless solid, mp 101-102 °C: IR (neat, cm⁻¹) 3350; ¹H NMR (500 MHz, CDCl₃) δ 3.71 (dd, J = 11.0, 9.2 Hz, 1H), 3.60 (dd, J = 11.0, 6.1 Hz, 1H), 2.14 (ddd, J = 13.4, 7.3, 4.9 Hz, 1H), 2.00 (br s, 1H), 1.92 (dt, J = 6.7, 4.9 Hz, 1H), 1.89-1.79 (m, 1H), 1.73 (br s, 1H), 1.71-1.64 (m, 1H), 1.54-1.49 (m, 1H), 1.29 (s, 3H), 1.24 (dt, J = 13.4, 7.9 Hz, 1H), 1.02 (s, 3H); MS m/z (M⁺ - H₂O) calcd 152.1200, obsd 152.1223.

X-ray Crystallographic Study of 52. A crystal with dimensions of 0.20 \times 0.10 \times 0.25 was used for the data collection on a Rigaku automated four-circle diffractometer, equipped with a rotating anode (50 kV, 200 mA) and using graphite-monochromated Mo K α radiation ($\lambda = 0.710$ 69 Å). Crystal data are as follows: molecular formula C₁₂H₂₀O₂; molecular weight 196.1; monoclinic space group Cc; a = 8.615(1) Å, b = 11.584(2) Å, c = 21.706(3) Å, $\beta = 92.89(1)^\circ$; V = 2163.4(7) Å³; Z = 8; $D_c = 1.205$ g/cm³; μ (Mo K α) = 0.74 cm⁻¹; total of 2871 reflections within 26 = 55°. The structure was solved by the direct method using a RANTAN 81 program with some modification. After the block-diagonal least-squares refinement for non-hydrogen atoms with anisotropic temperature factors, the hydrogen atoms were calculated geometrically and also verified from the difference Fourier map and then included in the refinement with isotropic temperature factors. The final R factor was 0.076 ($R_w = 0.071$) for 1886 reflections with $|F_0| > 2\sigma(|F_0|)$.

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Supplementary Material Available: Listings of final atomic coordinates, bond distances and angles, and thermal parameters for 52 and ¹H NMR (500 MHz) spectra of products of the tandem Michael-aldol reactions (17 pages). Ordering information is given on any current masthead page.