Synthesis of Polycyclic Cyclobutane Derivatives by Tandem Intramolecular Michael–Aldol Reaction under Two Complementary Conditions: TBDMSOTf–Et_3N and TMSI–$(TMS)_2NH$

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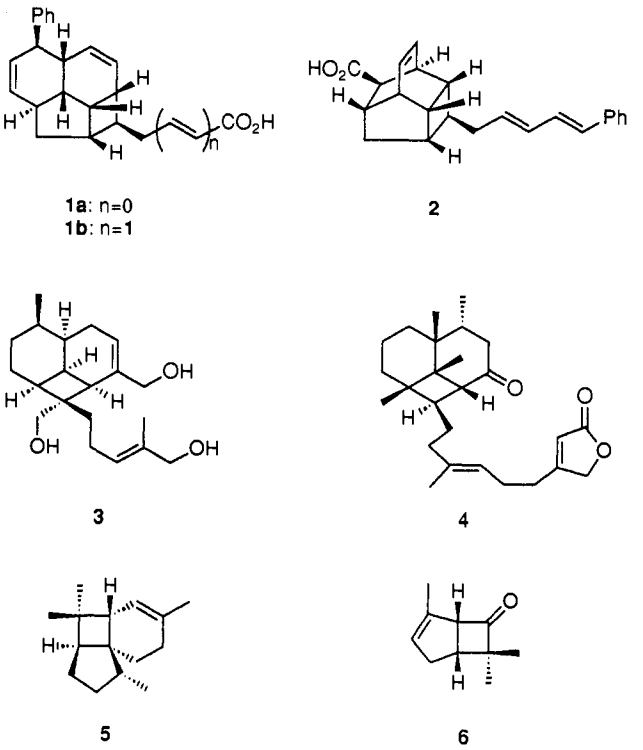
Abstract: The treatment of α,β-unsaturated esters having a ketone function at an appropriate position with either TBDMSOTf in the presence of Et_3N or TMSI in the presence of $(TMS)_2NH$ provided, *via* a tandem intramolecular Michael-aldol reaction sequence, several different types of cyclobutane derivatives. 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**),[2] lintenone (**4**),[3] italicene (**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 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,

Chart I



† Pharmaceutical Institute, Tohoku University.
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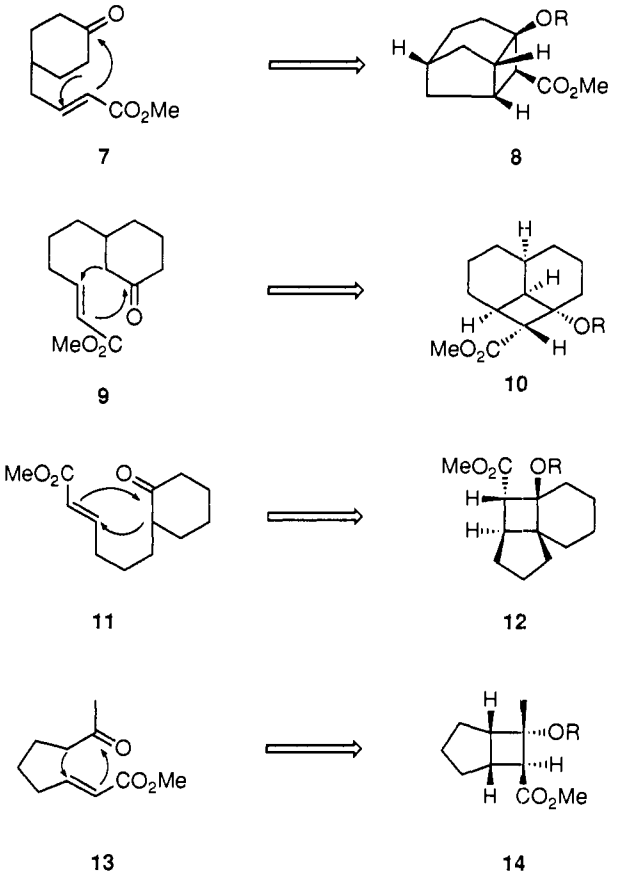
Scheme I. Plan for the Construction of Polycyclic Systems Fused to a Cyclobutane



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

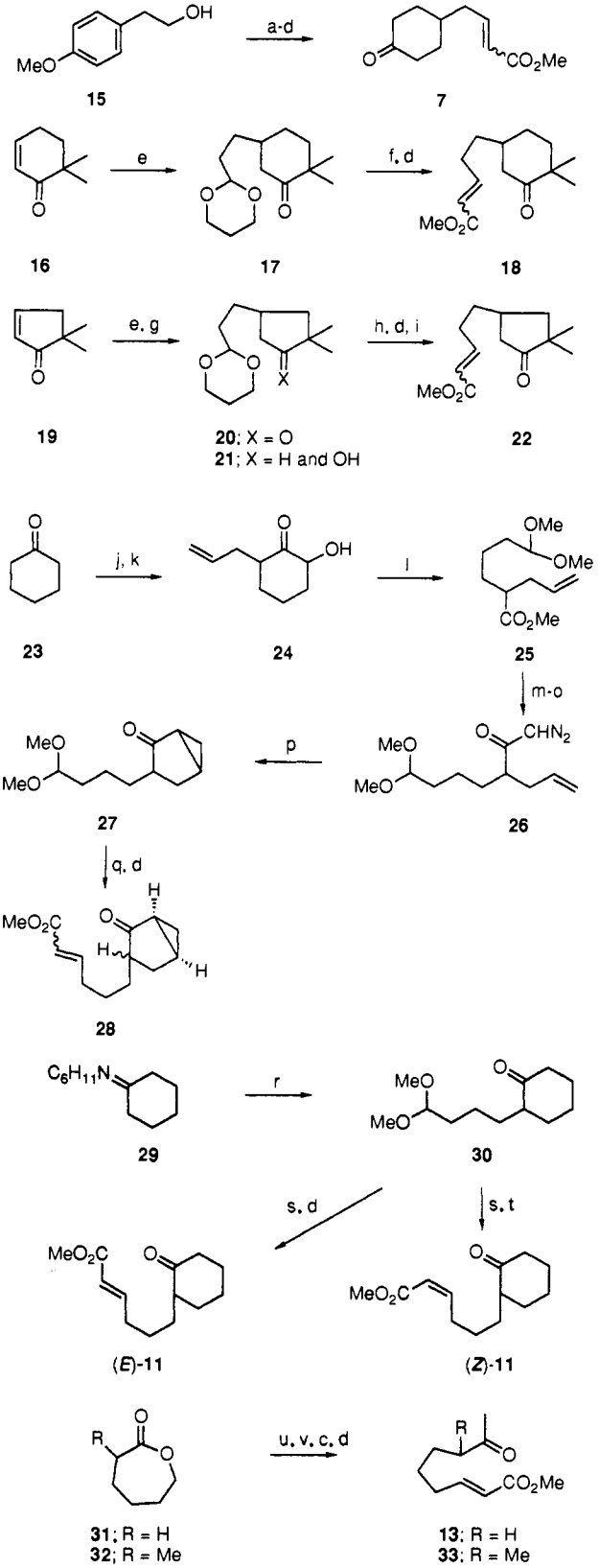
Results and Discussion

Preparation of Substrates for Tandem Intramolecular Michael–Aldol 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 *E*- and *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 addition[12] 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-hydroxylation[16] 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

Scheme II. Preparation of Substrates for Tandem Intramolecular Michael–Aldol Reaction[a]



[a] Materials and conditions: (a) Li, liquid NH_3, Bu^{t}OH, then aqueous $(CO_2H)_2$; (b) H_2, 10% Pd–C; (c) PCC; (d) $Ph_3P{=}CHCO_2Me$; (e) [2-(2,6-dioxanyl)ethyl]magnesium bromide, CuBr·SMe_2, TMSCl, HMPA; (f) dilute HCl; (g) $NaBH_4$; (h) dilute $HClO_4$; (i) Dess–Martin periodinane; (j) pyrrolidine, PTSA, then allyl bromide; (k) LDA, MoOPH; (l) $Pb(OAc)_4$, MeOH, then NH_4Cl, MeOH; (m) KOH; (n) $(COCl)_2$, pyridine; (o) CH_2N_2; (p) Cu; (q) dilute AcOH; (r) LDA, HMPA, 4,4-dimethoxybutyl bromide; (s) aqueous $(CO_2H)_2$; (t) $(CF_3CH_2O)_2POCH_2CO_2Me$, KN$(TMS)_2$, 18-crown-6; (u) DIBALH; (v) MeMgI.

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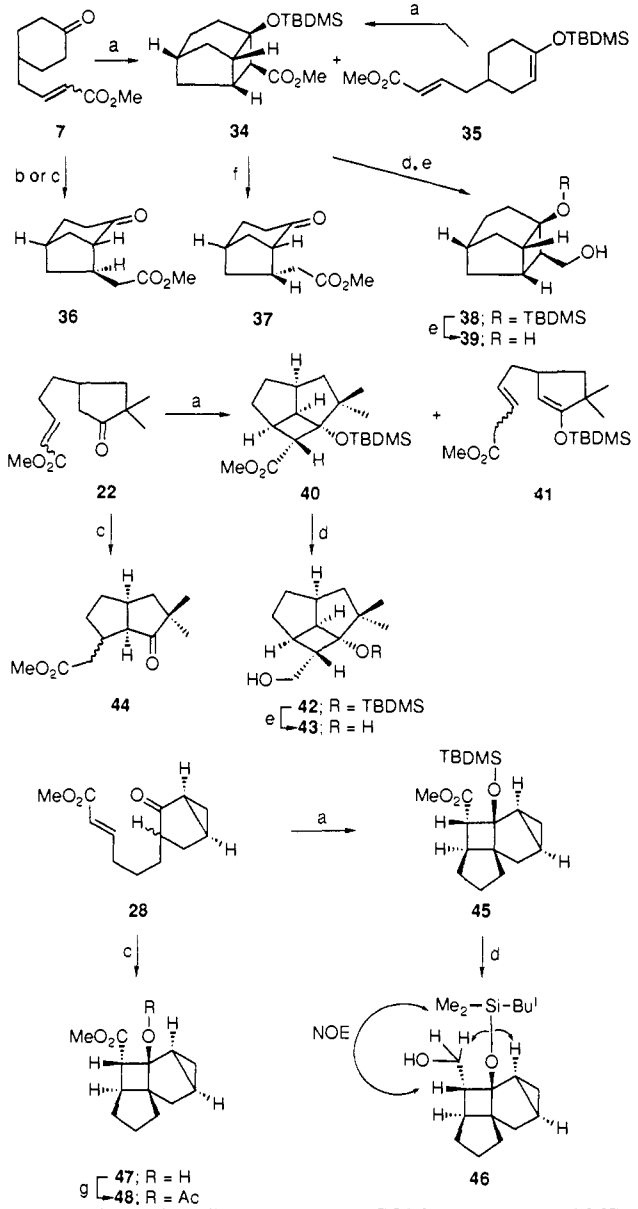
Scheme III. Tandem Intramolecular Michael–Aldol Reaction Using TBDMSOTf–Et_3N[a]



[a] Materials and conditions: (a) TBDMSOTf, Et_3N; (b) $LiN(TMS)_2$; (c) $ZnCl_2$, TMSCl, Et_3N, heat, then dilute $HClO_4$; (d) DIBALH; (e) Bu^n_4NF; (f) dilute AcOH; (g) Ac_2O, DMAP, pyridine.

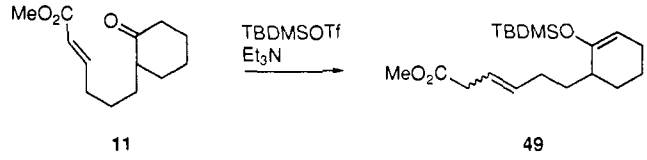
of a carbene.[17] The unsaturated ester **28** was obtained as a 7:1 mixture of two diastereoisomers, separable by high-performance liquid chromatography (HPLC).

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 **32**[19] in four steps, respectively.

Tandem Intramolecular Michael–Aldol Reaction. Treatment with TBDMSOTf–Et_3N. 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% 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.

Scheme IV. Treatment of Keto Ester **11** with TBDMSOTf–Et_3N



Reaction of **7** with $LiN(TMS)_2$[8] 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 $ZnCl_2$, TMSCl, and Et_3N[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 Bu^n_4NF. Thus, **34** was transformed into diol **39** in 78% overall yield.

Treatment of the β-substituted cyclohexanone **18** with TBDMSOTf in the presence of Et_3N 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 Et_3N 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 Bu^n_4NF (66% yield) to give **43** after DIBALH reduction (86% yield) of the ester. As observed for keto ester **7**, heating (*E*)-**22** with $ZnCl_2$, Et_3N, 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 Et_3N to produce **45** as a single stereoisomer. The stereochemistry of **45** was determined by observation of NOEs between the CH_2 group attached to C(2) and the cyclopropyl H at C(11) and between the Bu^tMe_2SiO 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 $ZnCl_2$, Et_3N, and TMSCl in CH_2Cl_2, 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 enol silane 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 Et_3N in CH_2Cl_2 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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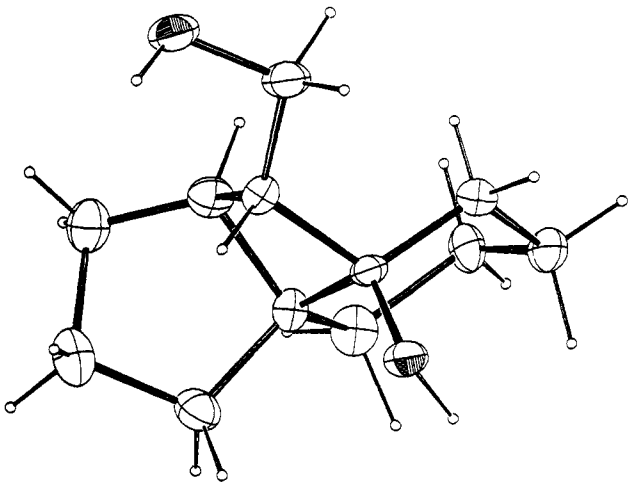

Figure 1. ORTEP representation of diol **52**.

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 $(TMS)_2NH$[22] 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 $ClCH_2CH_2Cl$, CH_2Cl_2, CCl_4, and $ClHC{=}CCl_2$, respectively. The same product (**51**) was produced in 68% yield by treatment of (*Z*)-**11** with TMSI in the presence of $(TMS)_2NH$ in $ClCH_2CH_2Cl$. 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–Et_3N 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 Et_3N 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–Et_3N 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 prior to use: THF, DME, Et_2O, benzene, and toluene were freshly distilled from Na benzophenone; CH_2Cl_2 and MeCN were distilled from CaH_2 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 $MgSO_4$ 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 μm) and monitored by using UV and refractive index detectors.

4-[(2*Z*)- and (2*E*)-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 NH_3 (15 mL) was added Li (206 mg, 29.7 mmol). After 2 h of stirring, MeOH (1 mL) and H_2O (7.5 mL) were added to the reaction mixture. After having been allowed to stand overnight at ambient temperature, the mixture was partitioned between H_2O and benzene. The organic

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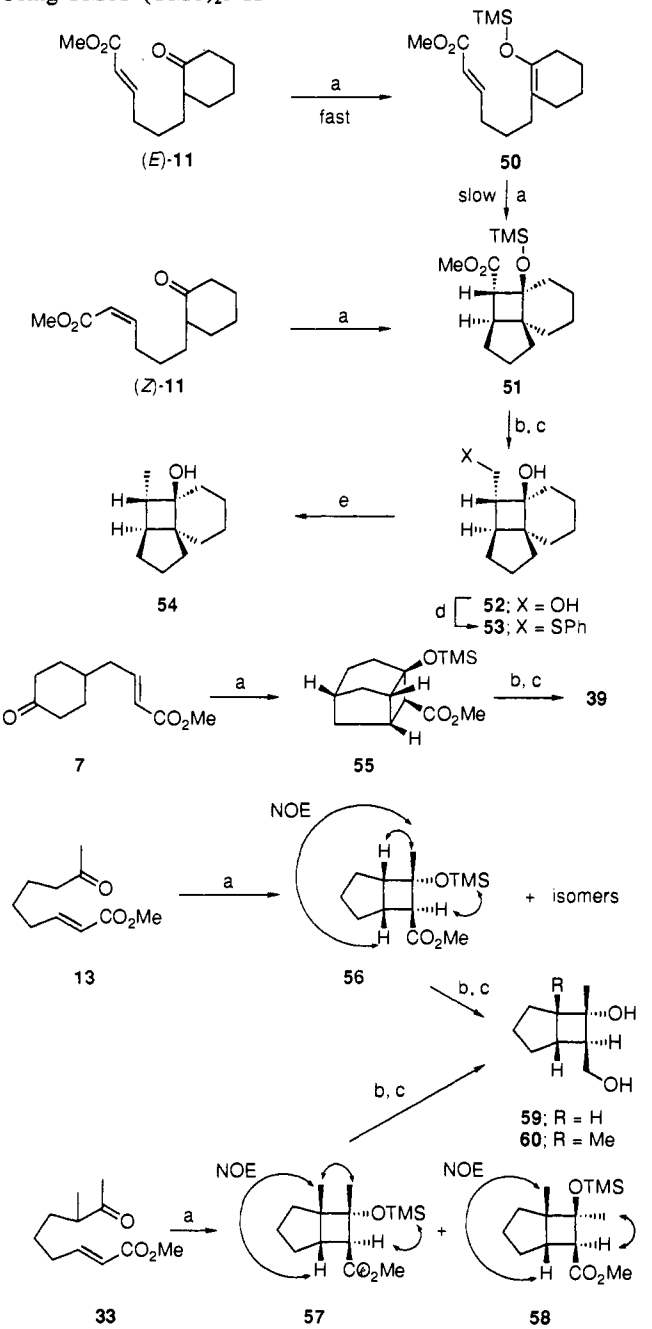
Scheme V. Tandem Intramolecular Michael–Aldol Reaction Using TMSI–$(TMS)_2NH$[a]



[a] Materials and conditions: (a) TMSI, $(TMS)_2NH$; (b) DIBALH; (c) Bu^n_4NF; (d) $(PhS)_2$, Bu^n_3P, pyridine; (e) Li, liquid NH_3, Bu^tOH.

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–H_2O (4:1 v/v, 50 mL). After neutralization with $NaHCO_3$ (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, CCl_4) 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 H_2 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 ($CHCl_3$, cm^{-1}) 3405, 1713; ^1H NMR (500 MHz, $CDCl_3$) 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 Et_2O, 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 $Ph_3P{=}CHCO_2Me$ (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, $CDCl_3$) 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, $CDCl_3$) 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 $C_{11}H_{16}O_3$: 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 I_2 in dry THF (0.5 mL) was added a solution of 2-(2-bromoethyl)-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 $CuBr{\cdot}SMe_2$ (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 **16**[13] (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 NH_4Cl–NH_4OH (pH 8), the resulting mixture was partitioned between H_2O and Et_2O. The organic layer was washed with saturated $NaHCO_3$ and brine, dried, and evaporated. Flash chromatography of the residue with AcOEt–hexane (1:7 v/v) as eluent gave **17** (178 mg, 61%) as a colorless oil: IR (neat, cm^{-1}) 1702; ^1H NMR (500 MHz, $CDCl_3$) 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-[(3*Z*)- and (3*E*)-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 Et_2O–hexane (1:1 v/v), the mixture was neutralized with 10% NH_4OH. 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 $Ph_3P{=}CHCO_2Me$ (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, $CDCl_3$) 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, $CDCl_3$) 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 I_2, $CuBr{\cdot}SMe_2$ (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 **19**[14] (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, $CDCl_3$) 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, 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 $C_{13}H_{22}O_3$: 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 $NaBH_4$ (109 mg, 2.88 mmol), and the mixture was stirred for 10 min. After addition of H_2O, the mixture was thoroughly extracted with Et_2O. 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, $CDCl_3$) 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 227.1611, obsd 227.1651. Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.49; H, 10.58.

2,2-Dimethyl-4-[(3*Z*)- and (3*E*)-4-(methoxycarbonyl)-3-butenyl]cyclopentan-1-one (22). A mixture of **21** (377 mg, 1.65 mmol) in 10% $HClO_4$–THF (1:1 v/v, 30 mL) was stirred for 12 h at 30 °C. After dilution with Et_2O, the organic phase was washed with saturated $NaHCO_3$ and brine, dried, and evaporated. The residue was dissolved in dry MeCN (100 mL) and treated with $Ph_3P{=}CHCO_2Me$ (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, $CDCl_3$) 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 DMP[15] (1.08 g, 2.55 mmol) in dry CH_2Cl_2 (15 mL) at room temperature was added a solution of the above alcohols (384 mg, 1.70 mmol) in dry CH_2Cl_2 (3 mL), and the mixture was stirred for 10 min at the same temperature. After dilution with Et_2O, the mixture was poured into saturated $NaHCO_3$ containing $Na_2S_2O_3$ and was stirred for 20 min at room temperature. The organic layer was washed with saturated $NaHCO_3$ 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, $CDCl_3$) 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), 2.24–2.10 (m, 3H), 2.02 (ddd, J = 11.0, 7.5, 3.0 Hz, 1H), 1.86 (dd, J = 18.0, 11.0 Hz, 1H), 1.60–1.53 (m, 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, $CDCl_3$) 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 Bu^nOH (125 mL) was heated for 12 h under reflux. After evaporation of the solvent, followed by addition of H_2O (200 mL), the mixture was heated for 3 h under reflux. After being cooled, the mixture was thoroughly extracted with Et_2O. 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 Pr^i_2NH (2.1 mL, 15.0 mmol) and 1.54 M Bu^nLi–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 MoOPH[16] (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 $Na_2S_2O_3$ (30 mL). After further addition of H_2O, the resulting mixture was thoroughly extracted with Et_2O. 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, $CDCl_3$) 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 $NaHCO_3$ and Et_2O, 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 NH_4Cl (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 $NaHCO_3$ and Et_2O. 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, $CDCl_3$) 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–H_2O (5:1 v/v, 6 mL) was heated for 6 h under reflux. After addition of 10% $KHSO_4$ with cooling, the mixture was thoroughly extracted with CH_2Cl_2. 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 CH_2N_2 in Et_2O (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, $CDCl_3$) 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 ($M^+ - CHN_2$) 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 Et_2O, 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, $CDCl_3$) 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-[(4*E*)-5-(Methoxycarbonyl)-4-pentenyl]bicyclo[3.1.0]hexan-2-one (28). A mixture of **27** (219 mg, 1.04 mmol) in AcOH–H_2O (4:1 v/v, 5 mL) was stirred for 3 h at room temperature. After neutralization with saturated $NaHCO_3$ 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 $Ph_3P{=}CHCO_2Me$ (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 CH_2Cl_2. 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, $CDCl_3$) 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)]; ^{13}C NMR (125 MHz, $CDCl_3$, 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 AcOEt–hexane (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 Pr^i_2NH (4.6 mL, 33.0 mmol) and 1.56 M Bu^nLi–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-1,1-dimethoxybutane (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 Et_2O. The organic solution was washed with saturated NH_4Cl, H_2O, 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, $CDCl_3$) 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-[(4*E*)- and (4*Z*)-5-(Methoxycarbonyl)-4-pentenyl]cyclohexan-1-one (11). (A) A mixture of **30** (2.0 g, 9.3 mmol) and $(CO_2H)_2{\cdot}2H_2O$ (11.5 g, 93.0 mmol) in THF–H_2O (1:1 v/v, 40 mL) was stirred for 3 h at room temperature. After dilution with Et_2O, the mixture was neutralized with saturated $NaHCO_3$ with cooling. The organic phase was washed with H_2O 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 $Ph_3P{=}CHCO_2Me$ (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 Et_2O–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 $(CF_3CH_2O)_2P(=O)CH_2CO_2Me$ (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 Et_2O. The organic solution was washed with saturated NH_4Cl, H_2O, and brine, dried, and evaporated to give a residue, which was subjected to silica gel chromatography. Elution with Et_2O–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, $CDCl_3$) 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, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$, 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 $C_{13}H_{20}O_3$: 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 CH_2Cl_2–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 Et_2O (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–Et_2O (4.1 mL, 40.0 mmol). After 8 h of stirring at room temperature, the resulting mixture was partitioned between Et_2O and H_2O. 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, $CDCl_3$) 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, ($M^+ - 1 - H_2O$) 113.

To a solution of the diol (400 mg, 3.0 mmol) in $ClCH_2CH_2Cl$ (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 Et_2O, 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 $Ph_3P{=}CHCO_2Me$ (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 Et_2O–hexane (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, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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 $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.18; H, 8.71.

3-Methylheptane-2,7-diol. α-Methyl-ϵ-caprolactone[19] (1.5 g, 11.7 mmol) was reduced with 0.93 M DIBALH–hexane (13.9 mL, 12.9 mmol) in CH_2Cl_2–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–Et_2O (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, $CDCl_3$) 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 $ClCH_2CH_2Cl$ (22 mL) as above to afford the keto aldehyde (530 mg), which was transformed, by the reaction with $Ph_3P{=}CHCO_2$-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, $CDCl_3$) 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 $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.60; H, 9.04.

(±)-(1*R,2*S**,3*R**,6*S**,8*S**)-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 CH_2Cl_2 (2 mL) were added at room temperature Et_3N (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% $KHSO_4$ and saturated $NaHCO_3$, dried, and evaporated to give a residue which was subjected to flash chromatography on silica gel. Elution with Et_2O–hexane (3:97 v/v) gave **34** (15 mg, 48%) as a colorless oil: IR (neat, cm^{-1}) 1740; ^1H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$, 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, $CDCl_3$) 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.

(±)-(1*S,5*R**,7*R**)- and (1*S**,5*R**,7*S**)-7-[(Methoxycarbonyl)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% $KHSO_4$ 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, $CDCl_3$) 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 sealed tube. The mixture was partitioned between 5% HCl and benzene. The organic phase was washed with saturated $NaHCO_3$ and brine, dried, and evaporated to give a residue, which was dissolved in THF (1 mL) and treated for 20 min with 10% $HClO_4$. After dilution with Et_2O–benzene (1:1 v/v), the mixture was washed with saturated $NaHCO_3$ 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, $CDCl_3$) 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–H_2O (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 Et_2O–benzene (1:1 v/v). The organic solution was washed with H_2O 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, $CDCl_3$) 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.

(±)-(1*R,2*S**,3*R**,6*S**,8*S**)-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 Et_2O (20 mL) and H_2O (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, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$, 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 Bu^n_4NF–THF (0.5 mL, 0.5 mmol) in THF (1.75 mL) was stirred for 15 min at room temperature. After dilution with Et_2O–benzene (1:1 v/v), the mixture was washed with 5% $KHSO_4$ and saturated $NaHCO_3$, 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, $CDCl_3$) 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 CH_2Cl_2 (0.3 mL) as above. The crude product (10 mg) was treated with 1 M Bu^n_4NF–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[5.1.1.0^{4,8}]nonane (40). (A) To a stirred solution of Et_3N (0.3 mL, 2.1 mmol) and TBDMSOTf (0.3 mL, 1.3 mmol) in dry CH_2Cl_2 (3 mL) was slowly added under reflux a solution of (*E*)-**22** (49 mg, 0.22 mmol) in dry CH_2Cl_2 (2 mL), and the mixture was heated for 15 min under reflux. After dilution with hexane, the mixture was washed with saturated $NaHCO_3$ 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, $CDCl_3$) 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, 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); ^{13}C NMR (125 MHz, $CDCl_3$, 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, $CDCl_3$) 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.

(±)-(1S*,4S*,7S*,8S*,9S*)-1-(*tert*-Butyldimethylsiloxy)-2,2-dimethyl-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, $CDCl_3$) 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^n_4NF–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, $CDCl_3$) 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^+ – H_2O) 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 sealed tube. After dilution with Et_2O, the mixture was washed with 5% HCl, saturated $NaHCO_3$, 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, $CDCl_3$) 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)], 1.06 and 0.99 [each s, 3H (1.5:1)]; MS *m/z* (M^+) calcd 224.1411, obsd 224.1412.

(±)-(1R*,2S*,3S*,7R*,9S*,11S*)-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 Et_3N (0.019 mL, 0.135 mmol) in dry CH_2Cl_2 (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 CH_2Cl_2, the mixture was washed with saturated $NaHCO_3$, 5% $KHSO_4$, 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, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$, 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 3*R**-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.

(±)-(1R*,2R*,3S*,7R*,9S*,11S*)-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, $CDCl_3$) 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 s, 1H), 1.06 (ddd, *J* = 12.3, 12.3, 7.1 Hz, 1H), 0.89 (s, 9H), 0.66 (dddd, *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); ^{13}C NMR (125 MHz, $CDCl_3$, ppm) 76.9, 63.7, 60.5, 49.4, 43.7, 42.2, 32.6, 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), $ZnCl_2$ (300 mg, 2.20 mmol), Et_3N (0.3 mL, 2.15 mmol), and TMSCl (0.3 mL, 2.37 mmol) in dry CH_2Cl_2 (3 mL) was heated for 24 h at 160 °C in a sealed tube. After dilution with Et_2O, the mixture was washed with 5% HCl, saturated $NaHCO_3$, and brine, dried, and evaporated. The residue was treated for 30 min at room temperature with 10% $HClO_4$–THF (1:1 v/v, 5 mL). After dilution with Et_2O, the mixture was washed with saturated $NaHCO_3$ 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, $CDCl_3$) δ 3.72 (s, 3H), 2.64 (d, *J* = 6.7 Hz, 1H), 2.39 (dd, *J* = 6.7, 6.7 Hz, 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, 4.8, 1.2 Hz, 1H), 0.12 (ddd, *J* = 4.2, 4.2, 4.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$, 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.

(±)-(1R*,2S*,3S*,7R*,9S*,11S*)-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 Ac_2O (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 Et_2O 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, $CDCl_3$) 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 Et_3N. To a stirred solution of **11** (15 mg, 0.067 mmol) and Et_3N (0.093 mL, 0.67 mmol) in dry CH_2Cl_2 (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 Et_2O, the mixture was washed with H_2O and brine, dried, and evaporated to give a residue, which was subjected to chromatography on silica gel. Elution with Et_2O–hexane (1:20 v/v) containing Et_3N (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, $CDCl_3$) 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.

(±)-(1R*,2S*,3S*,7R*)-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 $ClCH_2CH_2Cl$ (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 Et_2O, the mixture was washed with H_2O and brine, dried, and evaporated. Chromatography of the residue on silica gel with Et_2O–hexane (1:20 v/v) containing Et_3N (3 v/v %) as eluent gave **51** (37 mg, 70%) as a colorless oil: IR (neat, cm^{-1}) 1730; ^1H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$, 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 $ClCH_2CH_2Cl$ (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 CH_2Cl_2 (4 mL), followed by treatment of the product with 1 M Bu^n_4NF (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 ($CHCl_3$, cm^{-1}) 3400; ^1H NMR (300 MHz, $CDCl_3$) 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 $C_{12}H_{20}O_2$: 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), Bu^n_3P (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 Et_2O, the mixture was washed with 10% NaOH, H_2O, 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 **53** (86 mg, 98%) as a yellowish oil: IR (neat, cm^{-1}) 3400, ^1H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$, ppm) 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–Bu^{t}OH (10:1 v/v, 3.3 mL) in liquid NH_3 (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 NH_4Cl (100 mg), followed by evaporation of the liquid NH_3, the residue was taken up into Et_2O. The organic solution was washed with 10% NaOH, H_2O, and brine, dried, and evaporated. Chromatography of the residue on silica gel with Et_2O–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, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$, 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,2*S**,3*R**,6*S**,8*S**)-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 $ClCH_2CH_2Cl$ (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 Et_2O–hexane (1:30 v/v) containing Et_3N (3 v/v %) provided **55** (31 mg, 57%) as a colorless oil: IR (neat, cm^{-1}) 1735; ^1H NMR (500 MHz, $CDCl_3$) 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* = 12.8 Hz, 1H), 1.68 (dddd, *J* = 12.5, 7.4, 4.7, 1.5 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 $ClCH_2CH_2Cl$ (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 Et_2O–hexane (1:10 v/v) containing Et_3N (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, C_6D_6) 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), 2.38 (ddd, *J* = 6.8, 6.8, 1.4 Hz, 1H), 2.18–2.13 (m, 1H), 1.78–1.71 (m, 2H), 1.53 (dd, *J* = 12.0, 6.0 Hz, 1H), 1.45 (s, 3H), 1.47–1.37 (m, 2H), 0.27 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6, 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.

(1*S,5*S**,6*R**,7*S**)- and (1*S**,5*S**,6*S**,7*S**)-5,6-Dimethyl-7-(meth-oxycarbonyl)-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 $ClCH_2CH_2Cl$ (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, C_6D_6) 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); ^{13}C NMR (125 MHz, C_6D_6, 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, $CDCl_3$) 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.

(1*S,5*S**,6*S**,7*R**)-6-Hydroxy-7-(hydroxymethyl)-6-methylbicyclo-[3.2.0]heptane (59).** To a stirred solution of **56** (25 mg, 0.098 mmol) in dry CH_2Cl_2 (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 Et_2O (15 mL) and H_2O (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^n_4NF–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 H_2O 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, $CDCl_3$) 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* ($M^+ - H_2O$) calcd 138.1044, obsd 138.1051.

(1*S,5*S**,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 CH_2Cl_2 (2 mL), followed by treatment of the product (55 mg) with 1 M Bu^n_4NF–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, $CDCl_3$) 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* ($M^+ - H_2O$) calcd 152.1200, obsd 152.1223.

X-ray Crystallographic Study of 52. A crystal with dimensions of 0.20 × 0.10 × 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 Kα radiation (λ = 0.710 69 Å). Crystal data are as follows: molecular formula $C_{12}H_{20}O_2$; molecular weight 196.1; monoclinic space group *Cc*; *a* = 8.615(1) Å, *b* = 11.584(2) Å, *c* = 21.706(3) Å, β = 92.89(1)°; *V* = 2163.4(7) Å^3; *Z* = 8; D_c = 1.205 g/cm^3; μ(Mo Kα) = 0.74 cm^{-1}; total of 2871 reflections within 2θ = 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 $|F_o| > 2\sigma(|F_o|)$.

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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.