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Total Synthesis of Upial, a Marine Sesquiterpene Possessing Bicyclo[3.3.1]nonane Ring System

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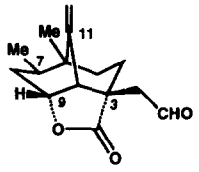
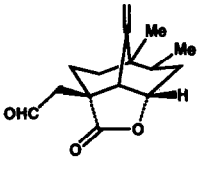
Abstract: *The total synthesis of marine sesquiterpene upial was achieved starting from D-mannitol via sequential Michael reaction of the lithium enolate of* **5** *with methyl (E,S)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-pentenoate ((E)-***6***), fragmentation reaction of tricyclic compound* **22** *and samarium(II) iodide-induced cyclization of diformate* **3**.

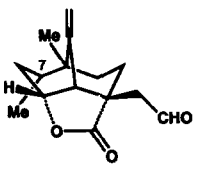
Upial, isolated from the sponge *Dysidea fragilis* at Kaneohe Bay, Oahu, by Scheuer *et al.* in 1979, is a nonisoprenoid sesquiterpene possessing a rare bicyclo[3.3.1]nonane ring system with five asymmetric carbon centers.[1] Its structure was elucidated by spectral analysis, mainly of the high field NMR spectrum of upial and lanthanide-induced shift study of upiol obtained by $NaBH_4$ reduction of upial, and chemical transformations.[1] In 1985, Taschner *et al.* reported the total synthesis of (-)-upial [(-)-**1**, the antipode of natural upial] from (-)-carvone.[2] The absolute configuration of upial was shown to be **1** by this synthesis.[2] In 1987, the synthesis of (±)-7-epiupial (**2**) utilizing manganese(III) γ-lactone annulation as the key step in the synthetic strategy was reported by Paquette *et al.*[3]



1 upial



(-)-1



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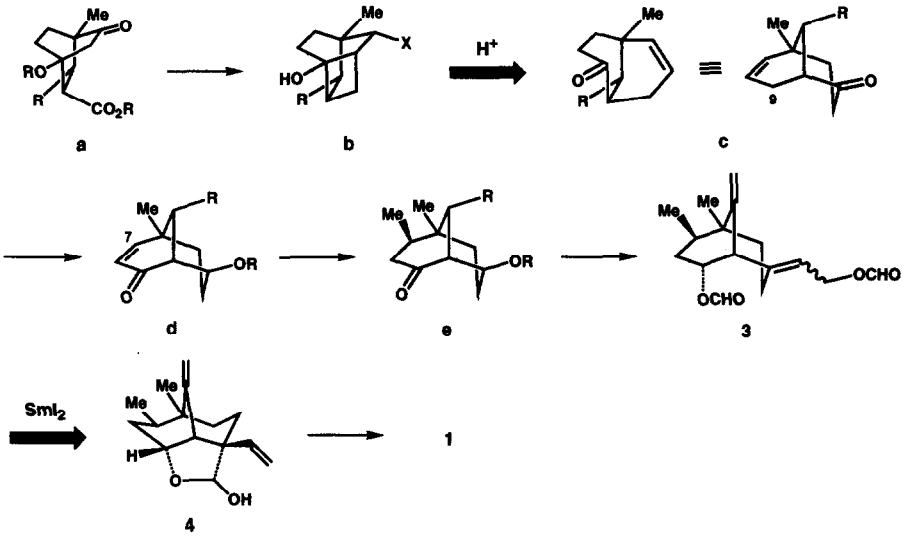
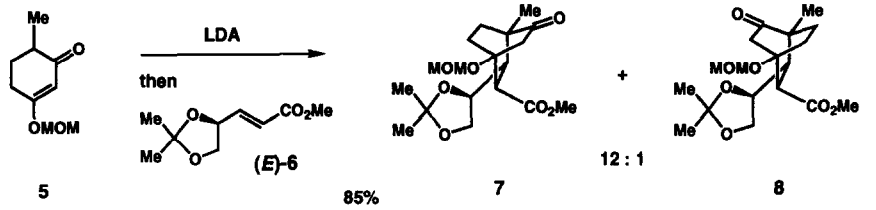
In the course of our investigation on the synthesis of highly functionalized bicyclic natural products using fragmentation reaction of tricyclic cage compounds as a key step,[4] the applicability of the method to the synthesis of this architecturally unique marine natural product was studied. Upial (**1**) was stereoselectively synthesized in natural form by using a combination of fragmentation reaction and samarium(II) iodide-induced C-C bond formation. Our synthetic strategy involves enantioselective synthesis of bicyclo[2.2.2]octane derivative **a**, transformation of **a** to tricyclic compound **b** (the first key intermediate), acid-induced fragmentation reaction of **b** to give bicyclo[3.3.1]nonane derivative **c**, allylic oxidation of the C-9[5] position,

Fig. 1



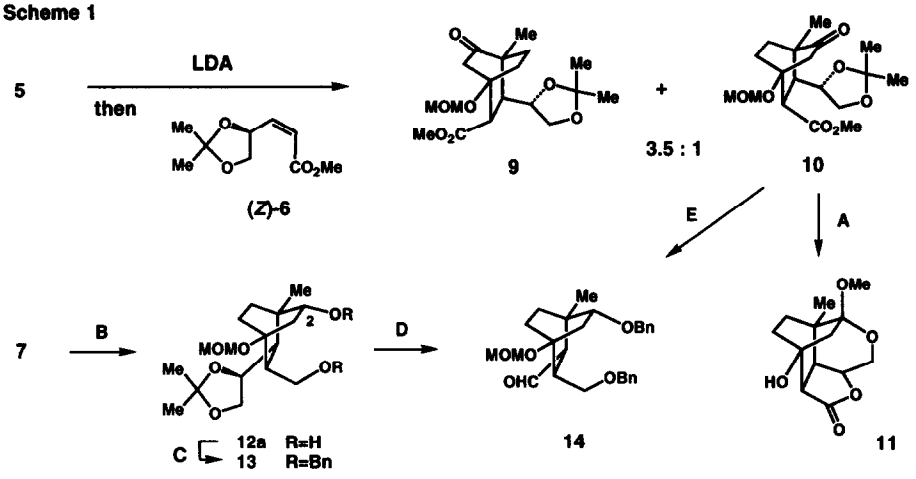
stereoselective introduction of the methyl group onto C-7[5] in **d** and samarium(II) iodide-induced intramolecular cyclization[6] of diformate **3** (the second key intermediate) to furnish **4** bearing the carbon skeleton of upial, as shown in Figure 1. A part of this work was appeared in a previous communication[7] and the present paper discusses the synthesis in detail.

Suitably functionalized optically active bicyclo[2.2.2]octane derivative **7**, corresponding to **a**, was synthesized *via* sequential Michael reaction[8] using methyl (*E*,*S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-pentenoate ((*E*)-**6**)[9] readily available from D-mannitol. Reaction of the kinetic enolate of 6-methyl-3-methoxymethyloxy-2-cyclohexenone (**5**)[4c] with (*E*)-**6** in THF at -78°C for 1 h, -50°C for 1 h, -40°C for 1.5 h, -30°C for 12 h and -20°C for 2 h gave predominantly keto ester **7** accompanied by the formation of a small amount of **8** in 85% yield (**7**:**8**=12:1).[10] The major isomer **7** was easily separated by recrystallization from ether. The



stereochemistries of **7** and **8** were determined by chemical correlation with **10**, obtained by reaction of the lithium enolate of **5** with methyl (*Z*,*S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-pentenoate ((*Z*)-**6**). The stereochemistry of **10** was clearly determined by transforming **10** to lactone acetal **11** as shown in Scheme 1.[11] Keto ester **7** was transformed to aldehyde **14** *via* **12a** and **13** in four steps: i) $LiAlH_4$ reduction to give the corresponding diols **12a** (2α-OH)[12] (76%) and **12b** (2β-OH)[12] (18%); ii) benzylation of the hydroxyl groups in the major isomer **12a** to give **13**; iii) acid hydrolysis of the acetonide group in **13** and iv) $NaIO_4$ oxidation.

Scheme 1



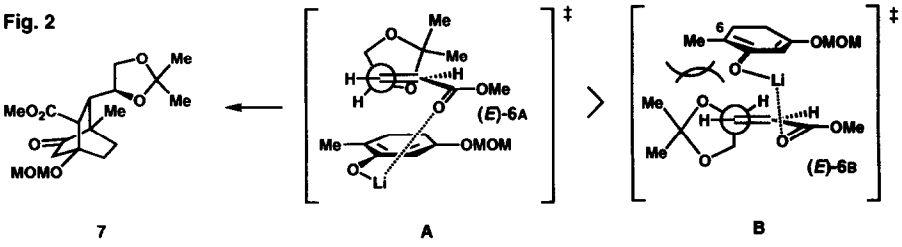
Reagents: A. MeOH, *p*-TsOH, 70°C, 91%; **B.** i) $LiAlH_4$, THF, **12a** (2α-OH) (76%), **12b** (2β-OH) (18%); ii) separation by silica gel column chromatography; **C.** BnBr, NaH, DMF, 25°C, 90%; **D.** i) 80%AcOH, 25°C, 83%; ii) $NaIO_4$, MeOH-H_2O (2:1), 0°C, 92%; **E.** i) L-selectride, THF, -78°C, 92%; ii) $LiAlH_4$, THF, 88%; iii) BnBr, NaH, DMF, 25°C, 96%; iv) 80%AcOH, 25°C, 4 h, 76%; v) $NaIO_4$, MeOH-H_2O (2:1), 0°C, 92%; vi) NaOH, EtOH, 25°C, 87%

Aldehyde **14** was also obtained from **10** in six steps: i) stereoselective reduction of the ketone with L-selectride; ii) reduction of the ester with $LiAlH_4$; iii) benzylation of the hydroxyl groups; iv) acid hydrolysis of

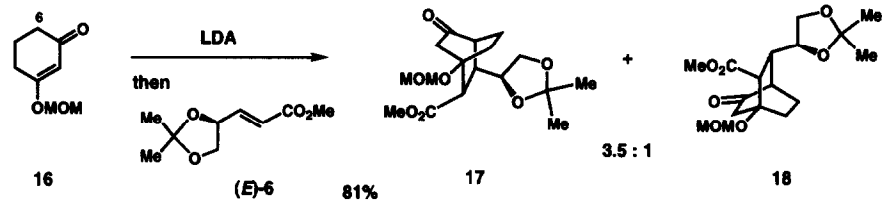
Reagents: A. i) 80%AcOH, 25°C, 85%; ii) $NaIO_4$, MeOH-H_2O, 25°C, 63%; **B.** i) *t*-BuOK, THF-DMSO (2:1), 25°C, 70%; ii) 80%AcOH, 25°C; iii) $NaIO_4$, MeOH-H_2O, 25°C, 93% (2 steps).

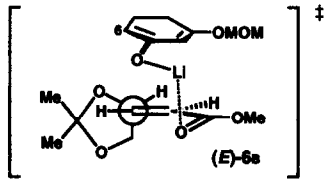
the acetonide; v) $NaIO_4$ oxidation and vi) epimerization of formyl group. Keto ester **8** was transformed to aldehyde **(-)-15** by acid hydrolysis of the acetonide group followed by $NaIO_4$ oxidation, whose antipode

Fig. 2



(+)-**15** was obtained from **10** as follows: i) epimerization of the methoxycarbonyl group with potassium *tert*-butoxide in a 2:1 mixture of THF and DMSO; ii) acid hydrolysis of the acetonide group and iii) $NaIO_4$ oxidation. Stereoselectivity in reaction of **5** with (*E*)-**6** can be explained by considering transition state **A** as shown in Figure 2. In this state, the dienolate of **5** approaches (*E*)-**6** having the conformation (*E*)-**6A**,[13] from

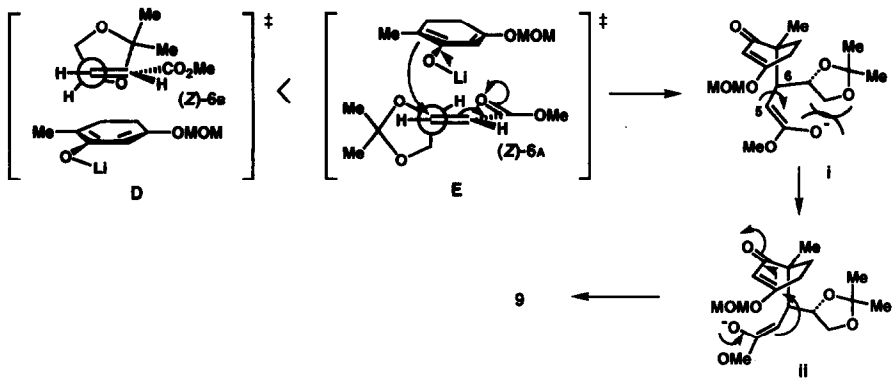




C

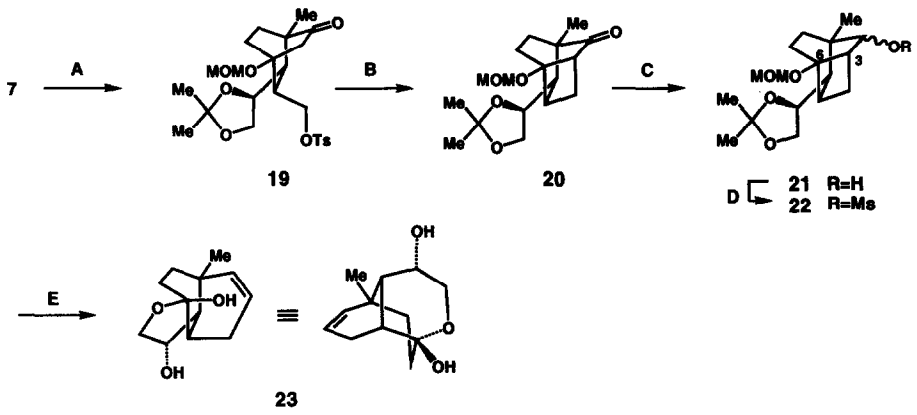
the less hindered side with coordination[14] between the lithium cation in enolate of **5** and the carbonyl oxygen of (*E*)-**6**. Similar sequential Michael reaction of enone **16**, without a methyl group at C-6, with (*E*)-**6** gives major adduct **17** *via* transition state **C** as previously reported.[11,15] However, in the former case, transition state **B** corresponding to **C** is disfavored since there is steric repulsion between the methyl group at C-6 and allylic oxygen. The mechanism for the formation of **9** from **5** and (*Z*)-**6** is not clear, but the route shown in Figure 3 appears to have a likely possibility. In this case, transition state **E** (corresponding to **B**) is superior to **D** (corresponding to **A**), because there is extremely strong steric repulsion between the methoxycarbonyl group and allylic oxygen in (*Z*)-**6B**. Following the first Michael addition, the C-C bond between C-5 and C-6[16] in **i** rotated to form **ii** which subsequently underwent the second Michael addition.

Fig. 3



The resulting bicyclo[2.2.2]octane derivative **7** was then converted to keto tosylate **19** by three step sequence: i) $LiAlH_4$ reduction to the corresponding diol; ii) selective tosylation of the primary hydroxyl group and iii) PDC oxidation[17] (Scheme 2). Treatment of **19** with 1.2 equiv of potassium *tert*-butoxide in a 1:1 mixture of THF and *N,N*-dimethylformamide for 1 h at 0°C gave cyclobutane **20** in 93% yield. Reduction of the ketone in **20** with $LiAlH_4$ in THF at -78°C to give **21** followed by mesylation gave the first key intermediate **22** as a 2:1 epimeric mixture in 85% overall yield. Both isomers could be used for the fragmentation reaction. Cleavage of the C(3)-C(6) bond was successfully carried out by treating of **22** with 2*N* HCl in acetonitrile at 25°C for 24 h to afford hemiacetal **23** bearing the same carbon ring system as that of upial in 91% yield.

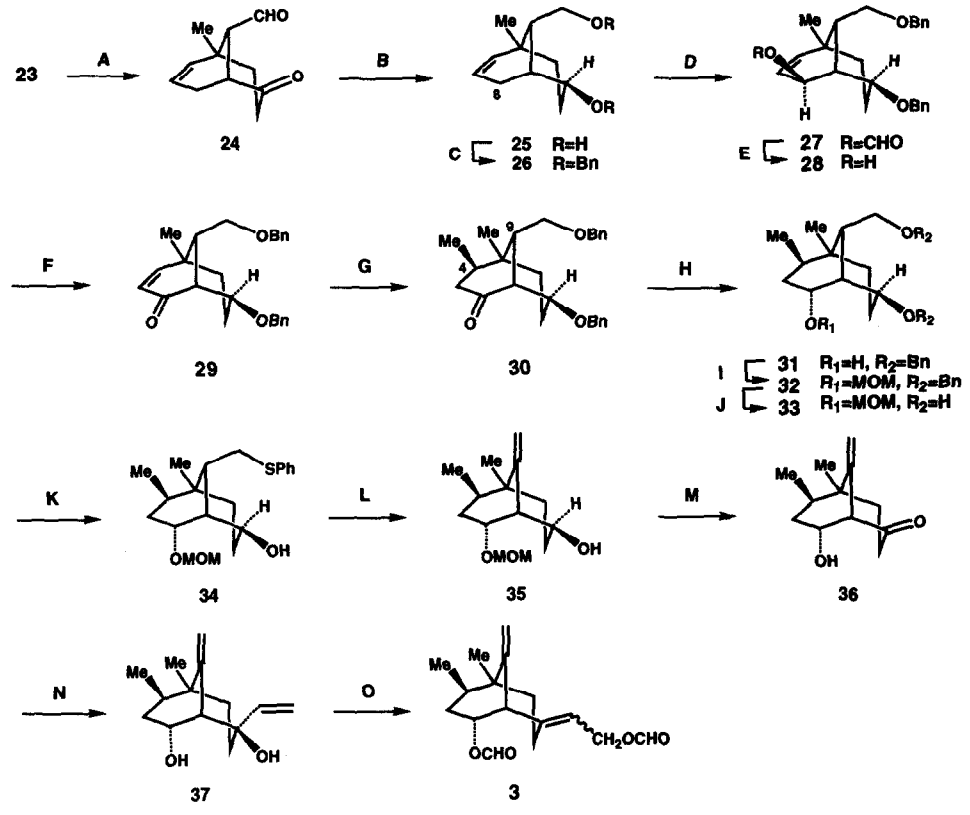
Scheme 2



Reagents: A. i) $LiAlH_4$, THF, 0°C to 23°C, (94%, 2α-OH:2β-OH=4:1); ii) TsCl, Py, 25°C, 80%; iii) PDC, 4Å MS, CH_2Cl_2, 25°C, 90%; **B.** t-BuOK, THF-DMF, 0°C, 1 h, 93%; **C.** $LiAlH_4$, THF, 97%; **D.** MsCl, DMAP, Py, 0°C to 25°C, 97%; **E.** 2*N* HCl, CH_3CN, 22°C, 24 h, 91%

Prior to allylic oxidation, **23** was converted to dibenzyl ether **26** in three steps: i) $NaIO_4$ oxidation in acetonitrile-water (2:3) at 22°C to give the corresponding keto aldehyde **24**; ii) Li-liquid ammonia reduction to give diol **25** as a single stereoisomer and iii) protection of the hydroxyl groups as benzyl ether (Scheme 3). The allylic position (C-8) in **26** was smoothly oxidized with selenium dioxide[18] in a 2:1 mixture of formic acid and 1,4-dioxane at 60°C for 1.5 h to form **27** in 99% yield. The configuration of introduced formyloxy group in **27** was estimated on the basis of preferential attack of selenium dioxide from the less screened face of the olefin. Use of acetic acid instead of formic acid as solvent in this oxidation caused the reaction time to be longer and decrease in the yield of the oxidized product. Successive hydrolysis of the formate in **27** with saturated ammonia in methanol to give alcohol **28** and PDC oxidation gave enone **29**. 1,4-Conjugated addition of **29** with dimethyl-copperlithium proceeded from the less hindered face with the consequent introduction of the desirable β-oriented methyl group to give **30** in 99% yield. The configuration of the newly introduced methyl group was confirmed by NOE correlation between the methyl proton at C-4 and methine proton at C-9. The ketone in **30** was reduced with sodium cyanoborohydride[19] in the presence of 2*N* hydrochloric acid to give α-alcohol **31** as a single isomer[20] whose hydroxyl group was protected as MOM ether and whose benzyl

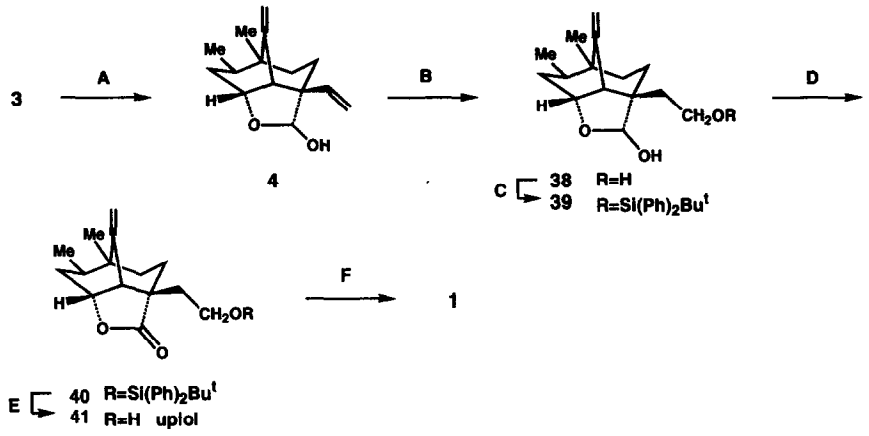
Scheme 3



Reagents: **A.** i) $NaIO_4$, CH_3CN-H_2O, 22°C, 99%; **B.** Li, liq.NH_3-THF-EtOH (4:2:1), -34°C, 93%; **C.** BnBr, NaH, DMF, 25°C, 96%; **D.** SeO_2, HCO_2H-1,4-dioxane (2:1), 60°C, 1.5 h, 99%; **E.** 10% NH_3, MeOH, 25°C, 99%; **F.** PDC, 4Å MS, CH_2Cl_2, 25°C, 73%; **G.** Me_2CuLi, Et_2O, -78° to -34°C, 99%; **H.** $NaBH_3CN$, 2*N* HCl, THF-MeOH (2:1), 0°C, 98%; **I.** i) $MeOCH_2Cl$, *i*-Pr_2NEt, 98%; **J.** Na, liq. NH_3-THF-EtOH (20:5:1), -34°C, 94%; **K.** i) PhSSPh, Bu_3P, Py, 80°C, 91%; **L.** i) MCPBA, $NaHCO_3$, CH_2Cl_2, -78°C, 99%; ii) 140°C, i-Pr_2NEt, 1,2-dichlorobenzene, 95%; **M.** i) PDC, 4Å MS, CH_2Cl_2, 24°C, 83%, ; ii) 6*N* HCl, AcOH, 23°C, 71%; **N.** CH_2=$CHMgBr$, Et_2O, 0°C to 25°C, 88%; **O.** i) AcOCHO, Py, CH_2Cl_2, 0°C, 94%; ii) HCO_2H-1,4-dioxane (2:1), 22°C, 87%

groups were removed by Na-liq. ammonia reduction to give **33**. *Exo*-olefin present in upial was constructed as follows: selective phenylsulfination of the primary hydroxyl group in **33** with phenyl disulfide and tributylphosphine in pyridine at 80°C to give **34**,[21] oxidation by treatment of **34** with *m*-chloroperbenzoic acid at -78°C to obtain the corresponding sulfoxide, and pyrolysis at 140°C in the presence of *N,N*-diisopropylethylamine to give **35** in 87% overall yield from **33**. The second key intermediate **3** having the requisite functional groups was elaborated from **35** to construct the skeleton of upial. Oxidation of **35** with PDC and subsequent acid hydrolysis of MOM ether produced hydroxy ketone **36**. Reaction of **36** with vinylmagnesium bromide in ether smoothly proceeded to afford allyl alcohol **37** as a single isomer, whose secondary hydroxyl group was formylated by treatment with acetyl formate[22] in pyridine to give the corresponding monoformate. It was then exposed to formic acid with consequent 1,3-rearangement of the

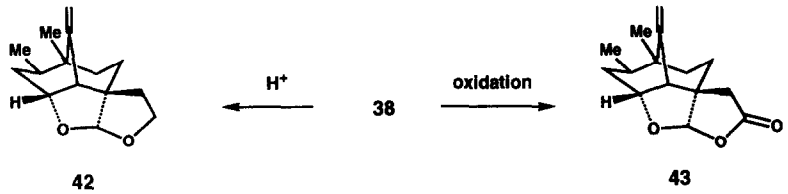
Scheme 4



Reagents: **A.** SmI_2, THF-HMPA (1:2), 25°C, 30 min, 76%; **B.** thexylborane, THF, 0°C, 1 h, 25°C, 1.5 h then $NaBO_3$, $NaHCO_3$, H_2O, 25°C; **C.** Ph_2(t-Bu)SiCl, DMAP, Et_3N, DMF, 77% (2 steps); **D.** i) PDC, 4Å MS, CH_2Cl_2, 25°C, 77%; **E.** Bu_4NF, AcOH, THF, 25°C, 94%; **F.** PDC, 4Å MS, CH_2Cl_2, 25°C, 87%.

allylic hydroxyl group to give diformate **3** as a 2:1 geometrical isomer.

One crucial step in the synthesis, *i. e.* cyclization of **3** to tricyclic hemiacetal **4**, was conducted in 76% yield by reaction of **3** with 3 equiv of SmI_2 in 2:1 THF-HMPA at 25°C for 30 min.[6] The final task to complete the synthesis of **1** was transformation of vinyl group to acetaldehyde appendage. After several attempts at selective hydroboration of the vinyl group, reaction of **4** with thexylborane followed by treatment with sodium perborate[23] provided **38**. The resulting diol **38** was quite sensitive to acid and even unstable to silica gel to give acetal **42**. Attempts at the direct transformation of the diol to upial by various oxidation procedures were unsuccessful. For example, the oxidation of **38** with tetrapropylammonium perruthenate[24] gave lactone acetal **43**. Thus, the primary hydroxyl group was immediately protected as silyl ether to give **39**. PDC oxidation of



42 **43**

the hemiacetal in **39**, deprotection of silyl ether using Bu_4NF in THF containing 5 equiv of acetic acid and PDC oxidation completed the synthesis of upial (**1**), $[\alpha]_D^{25}$ +36.1° (*c* 0.39, $CHCl_3$). ^1H- and ^{13}C-NMR spectra and the sign of optical rotation of synthesized **1** were identical to those of natural upial. The absolute value of optical rotation of synthetic upial (**1**) differed from that of naturally obtained upial, $[\alpha]_D^{25}$ +92.6° (*c* 0.27, $CHCl_3$),[1] but was essentially the same as that of optically pure (-)-upial, $[\alpha]_D$ -37° (*c* 1.50, $CHCl_3$), synthesized by Taschner *et al.*[2]

Experimental

Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. Optical rotations were measured with either a JASCO DIP-4 polarimeter or a JASCO DIP-370 polarimeter using a sodium lamp (589 nm, D line). Infrared (IR) spectra were recorded on a Shimazu IR-435 spectrometer. ^{1}H-NMR spectra were recorded at 270 MHz on a JEOL GSX-270 spectrometer. ^{13}C-NMR spectra were recorded at 67.5 MHz on a JEOL GSX-270. Chemical shifts are given on a δ (ppm) scale with tetramethylsilane (TMS) as an internal standard (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad). Electron impact mass (EIMS) spectra and high resolution mass spectra (HRMS) were taken with a JEOL JMS-D300 mass spectrometer. Elemental analyses were performed by a Yanako MT-3. Column chromatography was carried out on Fuji-Davison BW 820-MH (silica gel, 70-200 mesh), and preparative thin layer chromatography (PTLC) was carried out on Merck Kieselgel 60 F_{254} TLC plates. Ether, tetrahydrofuran (THF) and benzene were distilled from sodium-benzophenone ketyl under argon. Dichloromethane (CH_2Cl_2) was distilled from P_2O_5 under argon. *N,N*-Dimethylformamide (DMF), dimethyl sulfoxide (DMSO), hexamethylphosphoramide (HMPA), 1,4-dioxane, pyridine, triethylamine (NEt_3), *N,N*-diisopropylethylamine (*i*-Pr_2NEt) and diisopropylamine were distilled from calcium hydride under reduced pressure.

Methyl (1*S*, 2*R*, 3*R*, 4*R*, 4'*S*)-1-Methoxymethyloxy-4-methyl-3-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)-5-oxobicyclo[2.2.2]octane-2-carboxylate (7) and Methyl (1*R*, 2*R*, 3*R*, 4*S*, 4'*S*)-1-Methoxymethyloxy-4-methyl-3-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)-5-oxobicyclo-[2.2.2]octane-2-carboxylate (8): To a cold (-78°C) solution of lithium diisopropylamide [prepared from diisopropylamine (33.9 g, 336 mmol) and butyl lithium (1.6 M in hexane, 180 ml, 288 mmol)] in THF (400 ml) was added dropwise over 40 min a solution of 6-methyl-3-methoxymethyloxy-2-cyclohexenone (**5**) (40.8 g, 240 mmol) in THF (200 ml). After 2 h at this temperature, methyl (*E,S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-pentenoate ((*E*)-**6**) (67.0 g, 360 mmol) in THF (200 ml) was added dropwise over 20 min. The mixture was stirred for 1 h at -78°C, for 1 h at -50°C, for 1.5 h at -40°C, for 12 h at -30°C and for 2 h at -20°C, and was allowed to warm to 0°C. Saturated NH_4Cl solution (400 ml) was added to the mixture with stirring, and then the organic layer was separated. The aqueous layer was thoroughly extracted with ethyl acetate. The combined organic layers were washed with saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=3:1, 2:1, 1:1) to give a 12:1 mixture of **7** and **8** (71.8 g, 85% yield from **5**) as colorless solid. The ratio of **7** and **8** in the mixture was determined by a ^{1}H-NMR spectrum in $CDCl_3$. Recrystallization of the mixture from ether afforded pure 51 g of **7** as colorless crystals: mp 65-6°C; $[\alpha]_D^{25}$ -85.0° (c 2.0, $CHCl_3$); IR ($CHCl_3$) 2935, 1722,1371, 1165 and 1034 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.00 (3H, s), 1.35 (3H, s), 1.38 (1H, m), 1.40 (3H, s), 1.88 (1H, ddd, *J* = 12.4, 11.7, 5.4 Hz), 2.00 (1H, dddd, *J* = 12.4, 11.7, 5.4, 2.9 Hz), 2.12 (1H, dddd, *J* = 7.3, 4.4, 1.9 Hz), 2.21 (1H, ddd, *J* = 13.7, 11.7, 5.4 Hz), 2.47 (1H, dd, *J* = 18.5, 1.9 Hz), 3.06 (1H, dd, *J* = 18.5, 2.9 Hz), 3.20 (1H, dd, *J* = 7.3, 1.9 Hz), 3.32 (3H, s), 3.43 (1H, t, *J* = 7.8 Hz), 3.71 (3H, s), 3.97 (1H, dd, *J* = 7.8, 6.8 Hz), 4.27 (1H, ddd, *J* = 7.8, 6.8, 4.4 Hz), 4.59 (1H, d, *J* = 7.8 Hz) and 4.91 (1H, d, *J* = 7.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 16.7 (q), 25.4 (q), 26.2 (q), 26.3 (t), 31.0 (t), 43.2 (d), 44.4 (t), 45.0 (s), 47.7 (d), 52.1 (q), 55.3 (q), 68.2 (t), 74.1 (d), 76.7 (s), 91.0 (t), 109.0 (s), 174.7 (s), and 210.7 (s); EIMS m/z (relative intensity): 356 (M^+, 2.5), 341 (22) and 101 (100); Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.92. Found: C, 60.53; H, 7.98. Sample of the minor isomer **8** for spectroscopic analysis and for chemical transformations was prepared as follows. To a cold (0°C) solution of a

4:1 mixture of **7** and **8** (obtained from the mother solution of recrystallization of the 12:1 mixture of **7** and **8**) (14.3 g, 40.0 mmol) in THF (300 ml) was added portionwise lithium aluminum hydride ($LiAlH_4$) (3.0 g, 80 mmol) under an argon atmosphere. The reaction mixture was stirred for 2 h at 0°C and for 12 h at room temperature. This mixture was diluted with ether (600 ml), and then saturated NH_4Cl solution (10 ml) was added. After being stirred for 2 h, the mixture was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=3:1) to give (1*S*, 2*S*, 4*R*, 5*S*, 6*R*, 4'*S*)-5-hydroxymethyl-4-methoxymethyloxy-1-methyl-6-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)bicyclo[2.2.2]octan-2-ol (**44**) (2.2 g, 17% yield) (colorless oil, Rf value: 0.38, silica gel PTLC eluted with hexane-acetone=5:3): $[\alpha]_D^{25}$ +23.1° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3426, 2922, 1462, 1441 and 1380 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.97 (3H, s), 1.20 (1H, m), 1.33-1.44 (2H, m), 1.42 (3H, s), 1.50 (3H, s), 1.59 (1H, ddd, *J* = 13.7, 6.8, 3.4 Hz), 1.74 (1H, ddd, *J* = 13.7, 9.3, 1.9 Hz), 1.88 (1H, m), 2.18 (1H, dtd, *J* = 9.3, 5.4, 1.9 Hz), 2.51 (1H, dd, *J* = 12.7, 10.3 Hz), 3.31 (1H, ddd, *J* = 10.3, 9.3, 5.4 Hz), 3.36 (3H, s), 3.41 (1H, brd, *J* = 9.3 Hz), 3.50 (1H, tdd, *J* = 11.7, 6.8, 1.9 Hz), 3.76 (1H, t, *J* = 8.8 Hz), 3.88 (1H, d, *J* = 11.7 Hz), 3.91 (1H, d, *J* = 10.3 Hz), 3.97 (1H, dd, *J* = 8.8, 5.9 Hz), 4.35 (1H, ddd, *J* = 8.8, 5.9, 1.9 Hz), 4.72 (1H, d, *J* = 7.3 Hz) and 4.77 (1H, d, *J* = 7.3 Hz); EIMS m/z (relative intensity): 330 (M^+, 2.6), 315 (4) and 101 (100); Anal. Calcd for $C_{17}H_{30}O_6$: C, 61.80; H, 9.15. Found: C, 61.70; H, 9.25, (1*R*, 2*R*, 4*S*, 5*S*, 6*R*, 4'*S*)-5-hydroxymethyl-4-methoxymethyloxy-1-methyl-6-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)bicyclo[2.2.2]octan-2-ol (**12a**) (7.3 g, 55% yield) (colorless oil, Rf value: 0.33, silica gel PTLC eluted with hexane-acetone=5:3): $[\alpha]_D^{25}$ -5.1° (*c* 2.5, $CHCl_3$); IR ($CHCl_3$) 3396, 2925, 1462, 1378, and 1202 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.88 (3H, s), 1.20 (1H, m), 1.37 (3H, s), 1.42 (3H, s), 1.65-1.77 (2H, m), 1.77-1.94 (3H, m), 2.10 (1H, m), 2.23 (1H, ddd, *J* = 13.7, 9.7, 1.9 Hz), 2.49 (1H, brs), 3.08 (1H, brs), 3.36 (3H, s), 3.53 (1H, m), 3.58 (1H, t, *J* = 8.3 Hz), 3.75 (1H, m), 3.88 (1H, dd, *J* = 10.7, 6.8 Hz), 3.99 (1H, dd, *J* = 8.3, 5.8 Hz), 4.17 (1H, dt, *J* = 8.3, 5.8 Hz), 4.68 (1H, d, *J* = 7.3 Hz) and 4.77 (1H, d, *J* = 7.3 Hz); ^{13}C-NMR ($CDCl_3$) δ 22.2 (q), 25.8 (q), 26.6 (q), 28.4 (t), 30.9 (t), 35.5 (s), 37.9 (t), 39.5 (d), 43.4 (d), 55.4 (q), 64.1 (t), 68.7 (t), 75.6 (d), 76.0 (d), 77.7 (s), 90.5 (t) and 108.1 (s); EIMS m/z (relative intensity): 330 (M^+, 3.4), 315 (12) and 101 (100); Anal. Calcd for $C_{17}H_{30}O_6$: C, 61.80; H, 9.15. Found: C, 61.68; H, 9.37, and (1*R*, 2*S*, 4*S*, 5*S*, 6*R*, 4'*S*)-5-hydroxymethyl-4-methoxymethyloxy-1-methyl-6-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)bicyclo[2.2.2]octan-2-ol (**12b**) (1.7 g, 13% yield) (Rf value: 0.28, silica gel PTLC eluted with hexane-acetone=5:3): $[\alpha]_D^{25}$ +0.52° (c 2.5, $CHCl_3$); IR ($CHCl_3$) 3431, 3418, 2925, 1378, 1224 and 1149 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.81 (3H, s), 1.00 (1H, ddd, *J* = 5.8, 5.4, 2.4 Hz), 1.37 (3H, s), 1.43 (3H, s), 1.5-2.0 (5H, m), 2.19 (1H, ddt, *J* = 8.1, 2.4, 5.4 Hz), 2.40 (1H, ddd, *J* = 13.7, 10.8, 3.9 Hz), 3.36 (3H, s), 3.41 (1H, dd, *J* = 10.3, 5.4 Hz), 3.51 (1H, ddd, *J* = 12.2, 9.8, 1.4 Hz), 3.57 (1H, t, *J* = 8.3 Hz), 3.81 (1H, ddd, *J* = 10.3, 8.1, 1.4 Hz), 4.05 (1H, dd, *J* = 8.3, 5.8 Hz), 4.23 (1H, dt, *J* = 8.3, 5.8 Hz), 4.68 (1H, d, *J* = 7.3 Hz) and 4.78 (1H, d, *J* = 7.3 Hz); ^{13}C-NMR ($CDCl_3$) δ 20.0 (q), 23.5 (t), 25.7 (q), 26.5 (q), 30.7 (t), 35.9 (s), 38.1 (t), 44.3 (d), 46.9 (d), 55.5 (q), 65.9 (t), 69.3 (t), 73.6 (d), 75.5 (d), 78.1 (s), 90.6 (t) and 108.1 (s); EIMS m/z (relative intensity): 330 (M^+, 5.2), 315 (18) and 101 (100); Anal. Calcd for $C_{17}H_{30}O_6$: C, 61.80; H, 9.15. Found: C, 61.50; H, 9.31. To a mixture of **44** (3.30g, 10.0 mmol) and powdered 4Å molecular sieves (20 g) in CH_2Cl_2 (50 ml) was added portionwise pyridinium dichromate (PDC) (6.0 g, 16 mmol). After being stirred for 24 h at 25°C, the mixture was diluted with ether and passed through a silica gel short column. The eluate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-acetone=20:20:1, 15:15:1) to give

the corresponding keto aldehyde (1.32 g, 40% yield) as colorless oil: $[\alpha]_D^{25}$ -89.5° (c 1.0, $CHCl_3$); IR (KBr) 2926, 1714,1374, 1145 and 1034 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.09 (3H, s), 1.24 (3H, s), 1.41 (3H, s), 1.48 (1H, ddd, *J* = 12.4, 11.7, 2.4 Hz), 1.66 (1H, ddd, *J* = 12.4, 11.7, 5.4 Hz), 1.74 (1H, ddd, *J* = 12.4, 11.7, 2.4 Hz), 1.88 (1H, dddd, *J* = 12.4, 11.7, 5.4, 2.4 Hz), 2.50 (1H, dd, *J* = 4.9, 2.4 Hz), 2.55 (1H, d, *J* = 17.6 Hz), 2.83 (1H, dd, *J* = 17.6, 2.4 Hz), 3.10 (1H, dd, *J* = 4.9, 2.4 Hz), 3.30 (1H, dd, *J* = 8.8, 6.8 Hz), 3.41 (3H, s), 3.93 (1H, dd, *J* = 8.8, 6.8 Hz), 4.23 (1H, td, *J* = 6.8, 6.8, 2.9 Hz), 4.82 (1H, d, *J* = 7.8 Hz), 4.88 (1H, d, *J* = 7.8 Hz) and 10.17 (1H, s); EIMS m/z (relative intensity): 326 (M^+, 0.3), 325 (0.1) 311 (30), 279 (24) and 101 (100); HRMS Found: 326.1717. $C_{17}H_{26}O_6$ (M^+) requires; 326.1729; Anal. Calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.63; H, 8.21. To a cold (10°C) solution of the keto aldehyde (1.30 g, 4.00 mmol) and sodium dihydrogen phosphate ($NaH_2PO_4 \cdot 12H_2O$) (382 mg, 1.07 mmol) and 35% hydrogen peroxide (0.4 ml) in acetonitrile (4 ml) was added sodium chlorite[25] (90% in water, 0.56 g, 5.6 mmol) dropwise over 10 min, keeping the temperature at 10°C with water cooling. After stirring for 12 h at 25°C, a small amount of $NaHSO_3$ was added to destroy the unreacted NaOCl and H_2O_2. The mixture was thorougly extracted with ethyl acetate. The combined extracts were washed with saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give crude carboxylic acid (1.36 g). To a cold (0°C) solution of the product (1.36 g) in ether (10 ml) was added the solution of diazomethane, freshly prepared from *N*-nitrosomethylurea (5 g) and 50% potassium hydroxide solution (15 ml). The mixture was concentrated under reduced pressure and chromatographed on a silica gel column (eluted with hexane-acetone=5:1) to give **8** (1.40 g, 98% yield) as colorless crystals: mp 68-9°C; $[\alpha]_D^{25}$ -65.4° (c 1.0, $CHCl_3$); IR (KBr) 2977, 1722, 1190, 1143 and 1032 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.07 (3H, s), 1.26 (3H, s), 1.40 (3H, s), 1.51 (1H, ddd, *J* = 12.4, 11.7, 3.9 Hz), 1.73 (1H, dddd, *J* = 12.4, 11.7, 4.8, 1.9 Hz), 1.92 (1H, ddd, *J* = 12.4, 11.7, 4.8 Hz), 2.21 (1H, dddd, *J* = 12.4, 11.7, 3.9, 3.4 Hz), 2.28 (1H, dd, *J* = 5.8, 2.9 Hz), 2.53 (1H, d, *J* = 18.1 Hz), 2.69 (1H, dd, *J* = 18.1, 3.4 Hz), 3.11 (1H, dd, *J* = 5.8, 1.9 Hz), 3.35 (3H, s), 3.44 (1H, dd, *J* = 8.3, 6.8 Hz), 3.75 (3H, s), 3.94 (1H, dd, *J* = 8.3, 6.8 Hz), 4.17 (1H, td, *J* = 6.8, 6.8, 2.9 Hz), 4.66 (1H, d, *J* = 7.8 Hz) and 4.89 (1H, d, *J* = 7.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 17.3 (q), 24.6 (q), 25.9 (q), 26.2 (t), 31.2 (t), 45.1 (s), 46.5 (d), 46.8 (d), 49.2 (t), 52.2 (q), 55.4 (q), 66.8 (t), 73.5 (d), 76.6 (s), 91.2 (t), 109.3 (s), 174.7 (s) and 211.0 (s); EIMS m/z (relative intensity): 356 (M^+, 2.8), 341 (78) and 101 (100); HRMS Found: 356.1831. $C_{18}H_{28}O_7$ (M^+) requires: 356.1835; Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.82. Found: C, 60.68; H, 8.04.

Methyl (1*R*, 2*S*, 3*S*, 4*S*, 4'*S*)-1-Methoxymethyloxy-4-methyl-3-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)-5-oxobicyclo[2.2.2]octane-2-carboxylate (9) and Methyl (1*S*, 2*R*, 3*S*, 4*R*, 4'*S*)-1-Methoxymethyloxy-4-methyl-3-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)-5-oxobicyclo[2.2.2]octane-2-carboxylate (10): To a cold (-78°C) solution of lithium diisopropylamide [prepared from diisopropylamine (1.41 g, 14.0 mmol) and butyl lithium (1.6 M in hexane, 7.2 ml, 12 mmol)] in THF (15 ml) was added dropwise over 10 min a solution of 6-methyl-3-methoxymethyloxy-2-cyclohexenone (**5**) (1.67 g, 10 mmol) in THF (10 ml). After 2 h at this temperature, methyl (*Z*,*S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-pentenoate ((*Z*)-**6**) (2.79 g, 15.0 mmol) in THF (10 ml) was added over 5 min. The mixture was stirred for 2 h at -78°C and allowed to warm gradually to 0°C over 12 h. Saturated NH_4Cl solution (20 ml) was added to the mixture with stirring, and then the organic layer was separated. The aqueous layer was thoroughly extracted with ethyl acetate. The combined organic layers were washed with saturated

NaCl solution, dried over anhydrous $MgSO_4$ filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=1:3, 1:2, 1:1) to give a 3.5:1 mixture of **9** and **10** (2.93 g, 83% yield from **5**) as colorless solid. The ratio of **9** and **10** in the mixture was determined by a ^{1}H-NMR spectrum in $CDCl_3$. Sample of **9** for spectroscopic analysis was prepared by recrystallization from ether as colorless crystals: mp 101-4°C; $[\alpha]_D^{25}$ +121.2° (c 1.0, $CHCl_3$); IR (KBr) 2966, 1715, 1372, 1033 and 990 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.03 (3H, s), 1.32 (3H, s), 1.36 (3H, s), 1.46 (1H, dddd, *J* = 14.1, 10.8, 4.0, 1.9 Hz), 1.72 (1H, ddd, *J* = 14.1, 10.8, 5.4 Hz), 1.88 (1H, dddd, *J* = 12.2, 10.8, 4.0, 1.9 Hz), 1.96 (1H, ddd, *J* = 12.2, 10.8, 5.4 Hz), 2.50 (1H, dd, *J* = 18.5, 1.9 Hz), 2.51 (1H, dd, *J* = 7.8, 1.9 Hz), 2.75 (1H, dd, *J* = 7.8, 1.9 Hz), 3.16 (1H, dd, *J* = 18.5, 1.9 Hz), 3.31 (3H, s), 3.64 (1H, dd, *J* = 8.3, 7.8 Hz), 3.71 (3H, s), 4.05 (1H, dd, *J* = 7.8, 5.8 Hz), 4.23 (1H, ddd, *J* = 8.3, 7.8, 5.8 Hz), 4.59 (1H, d, *J* = 7.8 Hz) and 4.85 (1H, d, *J* = 7.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 17.3 (q), 25.5 (q), 26.1 (q), 26.3 (t), 31.2 (t), 42.9 (d), 44.0 (t), 44.5 (s), 48.7 (d), 52.0 (q), 55.3 (q), 65.9 (t), 75.1 (d), 76.4 (s), 91.0 (t), 108.4 (s), 174.0 (s) and 210.1 (s); EIMS m/z (relative intensity): 356 (M^+, 0.9), 341 (19), 297 (1.5), 237 (21) and 101 (100); Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.92. Found: C, 60.48; H, 7.99. Sample of **10** for spectroscopic analysis and for chemical transformations was prepared as follows. To a cold solution (0°C) of 3:1 mixture of **9** and **10** (1.38 g, 3.87 mmol) in dry THF (14 ml) was added dropwise L-selectride (1.0 M solution of THF, 15 ml, 15 mmol) at -78°C under an argon atmosphere. The reaction mixture was stirred for 2 h at this temperature, allowed to warm to 0°C and stirred for 2 h at 0°C. To the mixture was added saturated NH_4Cl solution (5 ml) and ether (300 ml). After being stirred for 30 min, the mixture was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-acetone=8:8:1) to give 947 mg of the hydroxy ester **45** corresponding to **9** as a colorless oil and 388 mg of the hydroxy ester **46** corresponding to **10** as colorless crystals. **45**: $[\alpha]_D^{25}$ +86.1° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3432, 2929, 1708, 1370 and 1215 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.00 (3H, s), 1.3 (1H, m), 1.33 (3H, s), 1.37 (3H, s), 1.46-1.85 (3H, m), 1.93 (1H, ddd, *J* = 13.7, 2.4, 1.9 Hz), 2.28 (1H, ddd, *J* = 13.7, 9.8, 2.4 Hz), 2.51 (1H, dd, *J* = 6.4, 1.9 Hz), 2.69 (1H, td, *J* = 6.4, 2.4 Hz), 3.25 (1H, d, *J* = 9.3 Hz), 3.30 (3H, s), 3.49 (1H, ddd, *J* = 9.8, 9.3, 2.4 Hz), 3.62 (1H, t, *J* = 7.8 Hz), 3.73 (3H, s), 4.06 (1H, dd, *J* = 7.8, 6.4 Hz), 4.19 (1H, dt, *J* = 7.8, 6.4 Hz), 4.58 (1H, d, *J* = 7.3 Hz) and 4.77 (1H, d, *J* = 7.3 Hz); EIMS m/z (relative intensity): 358 (M^+, 1.9), 343 (49), and 101 (100); Anal. Calcd for $C_{18}H_{30}O_7$: C, 60.32; H, 8.44. Found: C, 60.10; H, 8.33. **46**: mp 116-8° (ether), $[\alpha]_D^{25}$ +35.0° (*c* 1.0, $CHCl_3$); IR (KBr) 3423, 2887, 1703, 1200 and 1051 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.12 (3H, s), 1.30 (3H, s), 1.36 (3H, s), 1.24-1.5 (2H, m), 1.63-1.75 (1H, m), 1.80 (1H, ddd, *J* = 13.2, 2.4, 1.9 Hz), 1.91 (1H, brd, *J* = 14.7 Hz), 2.02 (1H, ddd, *J* = 12.2, 11.2, 1.9 Hz), 2.27 (1H, ddd, *J* = 14.7, 11.2, 1.9 Hz), 3.15 (1H, dd, *J* = 10.8, 1.9 Hz), 3.31 (3H, s), 3.44 (1H, t, *J* = 7.8 Hz), 3.54 (1H, ddd, *J* = 10.8, 10.3, 1.9 Hz), 3.72 (3H, s), 3.72 (1H, dd, *J* = 7.8, 5.4 Hz), 4.61 (1H, d, *J* = 7.8 Hz), 4.67 (1H, d, *J* = 7.8, 5.4, 1.9 Hz), 4.74 (1H, d, *J* = 10.3 Hz) and 4.79 (1H, d, *J* = 7.8 Hz); EIMS m/z (relative intensity): 358 (M^+, 2.3), 343 (58), 300 (58) and 268 (100); Anal. Calcd for $C_{18}H_{30}O_7$: C, 60.32; H, 8.44. Found: C, 60.10; H, 8.33. To a mixture of alcohol **45** (501 mg, 1.4 mmol) and powdered 4Å molecular sieves (3.32 g) in dry CH_2Cl_2 (6 ml) was added portionwise PDC (830 mg, 2.2 mmol). After being stirred for 4 h at 25°C, the mixture was diluted with ether and passed through a silica gel short column. The eluate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=7:1) to give **10** (436 mg, 87% yield) as colorless crystals: mp 105-6°C (ether); $[\alpha]_D^{25}$ -8.5° (*c* 1.0, $CHCl_3$); IR (KBr) 2922, 1710, 1192, 1146 and

1022 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.13 (3H, s), 1.25 (3H, s), 1.36 (3H, s), 1.59 (1H, ddd, *J* = 13.6, 11.7, 5.8 Hz), 1.77 (1H, ddd, *J* = 13.6, 11.7, 3.9 Hz), 1.95 (1H, dddd, *J* = 12.2, 11.7, 5.8, 2.9 Hz), 2.04 (1H, ddd, *J* = 12.2, 11.7, 3.9 Hz), 2.25 (1H, dd, *J* = 11.2, 8.3 Hz), 2.56 (1H, dd, *J* = 18.0, 1.9 Hz), 3.06 (1H, dd, *J* = 18.0, 2.9 Hz), 3.26 (1H, dd, *J* = 11.2, 1.9 Hz), 3.33 (3H, s), 3.52 (1H, t, *J* = 7.8 Hz), 3.67 (3H, s), 3.72 (1H, dd, *J* = 7.8, 6.3 Hz), 4.12 (1H, ddd, *J* = 8.3, 7.8, 6.3 Hz), 4.64 (1H, d, *J* = 7.8 Hz) and 4.79 (1H, d, *J* = 7.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 18.7 (q), 25.0 (q), 26.6 (q), 30.2 (t), 32.4 (t), 45.2 (t), 46.0 (s), 46.9 (d), 49.8 (d), 51.9 (q), 55.5 (q), 67.7 (t), 75.4 (d), 76.2 (s), 91.1 (t), 108.9 (s), 172.0 (s), and 210.8 (s); EIMS m/z (relative intensity): 356 (M^+, 2.4), 341 (100), 298 (26) and 266 (38); Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.82. Found: C, 60.49; H, 7.90.

(1*S*, 2*R*, 5*S*, 6*S*, 7*R*, 8*R*)-8,5-(Epoxymethano)-1-hydroxy-8-methoxy-7-methyl-4-oxatricyclo[5.2.2.0^{2,6}]undecan-3-one (11) A mixture of the keto ester **(10)** (88 mg, 0.247 mmol) and a catalytic amount of *p*-toluenesulphonic acid monohydrate (*p*-TsOH·H_2O) (4 mg) in methanol (3 ml) was refluxed for 24 h. The reaction mixture was concentrated under reduced pressure and diluted with ether (15 ml). The organic layer was washed with saturated $NaHCO_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=10:3) to give 57 mg (91% yield) of the lactone ether **11** as colorless crystals: mp. 133-5°C (ether-hexane); $[\alpha]_D^{25}$ +9.4° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3495, 2934, 1750, 1351 and 1071 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.13 (3H, s), 1.45 (1H, ddd, *J* = 12.2, 11.2, 3.4 Hz), 1.55 (1H, ddd, *J* = 12.2, 11.2, 1.9 Hz), 1.65 (1H, td, *J* = 11.2, 3.4 Hz), 1.97 (1H, td, *J* = 12.2, 5.4 Hz), 1.98 (1H, m), 2.02 (1H, td, *J* = 12.2, 5.4 Hz), 2.68 (1H, dd, *J* = 12.2, 1.9 Hz), 2.78 (1H, dd, *J* = 12.2, 8.8 Hz), 3.68 (1H, brs), 3.30 (3H, s), 3.83 (1H, dd, *J* = 13.7, 1.0 Hz), 4.22 (1H, dd, *J* = 13.7, 1.9 Hz) and 4.86 (1H, ddd, *J* = 8.8, 1.9, 1.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 21.1 (q), 31.7 (t), 33.2 (s), 33.9 (t), 39.9 (d), 46.2 (d), 46.8 (t), 48.1 (q), 64.0 (t), 71.2 (s), 78.7 (d),100.6 (s) and 177.8 (s); EIMS m/z (relative intensity): 254 (M^+, 63), 237 (83), 223 (25), and 97 (100); Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.13. Found: C, 61.34; H, 7.23.

(1*R*, 2*R*, 4*S*, 5*S*, 6*R*, 4'*S*)-5-Hydroxymethyl-4-methoxymethyloxy-1-methyl-6-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)bicyclo[2.2.2]octan-2-ol (12a) and (1*R*, 2*S*, 4*S*, 5*S*, 6*R*, 4'*S*)-5-Hydroxymethyl-4-methoxymethyloxy-1-methyl-6-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)-bicyclo[2.2.2]octan-2-ol (12b): To a cold (0°C) solution of keto ester **7** (46.2 g, 130 mmol) in THF (1.0 l) was added portionwise lithium aluminum hydride ($LiAlH_4$) (10 g, 0.26 mol) under an argon atmosphere. The reaction mixture was stirred for 2 h at 0°C and for 12 h at room temperature. This mixture was diluted with ether (2 l), and saturated NH_4Cl solution (30 ml) was added. After being stirred for 2 h, the mixture was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=3:1) to give 35.1 g (76% yield) of alcohol **12a** (2α-OH) as a colorless oil and 8.3 g (18% yield) of alcohol **12b** (2β-OH) as a colorless oil.

(1*S*, 2*S*, 3*R*, 4*R* 5*R*, 4'*S*)-5-Benzyloxy-2-benzyloxymethyl-1-methoxymethyloxy-4-methyl-3-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)bicyclo[2.2.2]octane (13): To a cold (0°C) solution of the diol **12a** (396 mg, 1.20 mmol) in dry DMF (4 ml) were added sodium hydride (50% dispersion in mineral oil,

192 mg, 4.0 mmol) and benzyl bromide (0.475 ml, 4.0 mmol) under an argon atmosphere. The reaction mixture was stirred for 10 min at this temperature and for 7 h at room temperature, and then MeOH (2 ml) was added. After being stirred for 20 min, the mixture was diluted with ether, washed successively with water, saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with ether-hexane=1:4) to give 549 mg (89% yield) of the dibenzyl ether **13** as a colorless oil: $[\alpha]_D^{25}$ -37.2° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 2863, 1367, 1144 and 1023 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.94 (3H, s), 1.1 (1H, m), 1.34 (3H, s), 1.42 (3H, s), 1.52 (1H, m), 1.8-2.0 (4H, m), 2.09 (1H, m), 2.25 (1H, ddt, *J* = 8.8, 1.9, 3.9 Hz), 3.26 (1H, dd, *J* = 7.8, 2.9 Hz), 3.31 (3H, s), 3.60 (1H, t, *J* = 8.8 Hz), 3.78 (1H, dd, *J* = 8.3, 6.4 Hz), 3.80 (1H, dd, *J* = 8.8, 3.9 Hz), 4.02 (1H, t, *J* = 8.3 Hz), 4.21 (1H, ddd, *J* = 8.3, 6.4, 1.9 Hz), 4.33 (1H, d, *J* = 12.2 Hz), 4.39 (1H, d, *J* = 12.2 Hz), 4.46 (1H, d, *J* = 12.2 Hz), 4.61 (1H, d, *J* = 12.2 Hz), 4.63 (1H, d, *J* = 7.3 Hz), 4.78 (1H, d, *J* = 7.3 Hz), and 7.20-7.35 (10H, m); ^{13}C-NMR ($CDCl_3$) δ 22.6 (q), 25.9 (q), 26.6 (q), 29.2 (t), 30.7 (t), 35.3 (t), 39.3 (d), 41.2 (d), 55.3 (q), 67.8 (t), 70.2 (t), 73.2 (t), 74.7 (d), 76.4 (s), 82.3 (d), 90.7 (t), 108.1 (s), 127.2 (d), 127.37 (d), 127.41 (d), 127.5 (d), 127.7 (d), 128.0 (d), 128.2 (d), 128.3 (d), 138.9 (s), and 138.8 (s); EIMS m/z (relative intensity): 510 (M^+, 2.5), 419 (3.2), 357 (100), and 329 (15); Anal. Calcd for $C_{31}H_{42}O_6$: C, 72.91; H, 8.29. Found: C, 73.14; H, 8.45.

(1*R*, 2*R*, 3*S*, 4*S*, 6*R*)-6-Benzyloxy-3-benzyloxymethyl-4-methoxymethyloxy-1-methylbicyclo[2.2.2]octane-2-carbaldehyde (14) from 13: A solution of the acetonide **13** (300 mg, 1.2 mmol) in 80% acetic acid (8 ml) was stirred for 24 h at 25°C. The reaction mixture was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=10:3) to give 245 mg (83% yield) of the corresponding diol as a colorless oil. To a cold (0°C) solution of the diol (193 mg, 0.41 mmol) in MeOH (2 ml) was added dropwise a solution of sodium periodate (175 mg, 0.82 mmol) in water (1 ml). After being stirred for 1.5 h at this temperature, the reaction mixture was diluted with AcOEt and the insoluble material was filtered off. The filtrate was washed successively with water and saturated NaCl solution, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether = 3:1) to give 165 mg (92% yield) of the aldehyde **14** as a colorless oil: $[\alpha]_D^{25}$ -138.0° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2919, 1714, 1143 and 1089 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.26 (1H, m), 1.51-1.87 (4H, m), 2.01 (1H, ddd, J = 13.7, 8.8, 1.9 Hz), 2.69 (1H, ddt, J = 12.2, 5.4, 1.9 Hz), 3.12 (1H, dt, *J* = 5.4, 1.9 Hz), 3.27 (1H, dd, *J* = 9.3, 2.9 Hz), 3.31 (3H, s), 3.53 (1H, t, *J* = 8.8 Hz), 3.72 (1H, dd, *J* = 8.8, 3.9 Hz), 4.38 (1H, d, *J* = 12.2 Hz), 4.41 (1H, d, *J* = 12.2 Hz), 4.47 (1H, d, *J* = 12.2 Hz), 4.62 (1H, d, *J* = 7.3 Hz), 4.63 (1H, d, *J* = 12.2 Hz), 4.76 (1H, d, *J* = 7.3 Hz), 7.20-7.35 (10H, m) and 9.86 (1H, d, J = 1.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 21.6 (q), 28.3 (t), 30.9 (t), 35.3 (t), 36.3 (s), 39.1 (d), 53.5 (d), 55.3 (q), 70.2 (t), 70.3 (t), 72.9 (t), 75.3 (s), 81.1 (d), 90.6 (t), 127.3 (d), 127.5 (d), 128.2 (d), 128.3 (d), 138.5 (s), 138.6 (s) and 204.6 (s); EIMS m/z (relative intensity): 438 (M^+, 1.5), 410 (3), 393 (28), 287 (55) and 91 (100); Anal. Calcd for $C_{27}H_{34}O_5$: C, 73.95; H, 7.81. Found: C, 73.79; H, 8.00.

Aldehyde 14 from 10: To a cold solution (0°C) of hydroxy ester **45** (427 mg, 1.19 mmol) prepared from **10** in THF (10 ml) was added portionwise $LiAlH_4$ (146 mg, 3.84 mmol) under an argon atmosphere. The reaction mixture was stirred for 15 min at 0°C, for 2 h at 25°C and for 1 h at 50°C. To the mixture were added

ether (90 ml) and saturated NH_4Cl solution (1 ml). The resulting mixture was stirred for 30 min, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:2) to give 346 mg (88% yield) of the corresponding diol **47** as colorless crystals: mp 109-110°C (hexane-CH_2Cl_2); $[\alpha]_D^{25}$ +50.1° (*c* 2.5, $CHCl_3$); IR (KBr) 3192, 2936, 1154, 1029 and 1004 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 1.13 (3H, s), 1.31-1.54 (2H, m), 1.35 (3H, s), 1.49 (3H, s), 1.63-1.93 (3H, m), 2.12-2.28 (3H, m), 3.06 (1H, brs), 3.37 (3H, s), 3.54 (1H, brd, *J* = 9.3 Hz), 3.80 (1H, m), 3.81 (1H, dd, *J* = 7.8, 7.3 Hz), 4.00 (1H, brs), 4.10 (1H, dd, *J* = 7.8, 7.3 Hz), 4.16 (1H, dt, *J* = 11.2, 5.9 Hz), 4.64 (1H, td, *J* = 7.3, 3.9 Hz), 4.72 (1H, d, *J* = 7.8 Hz) and 4.75 (1H, d, *J* = 7.8 Hz); Anal. Calcd for EIMS m/z (relative intensity): 330 (M^+, 0.7), 315 (0.8), 397 (6) and 101 (100); $C_{17}H_{30}O_6$: C, 61.80; H, 9.15. Found: C, 61.66; H, 9.35. To a cold (0°C) solution of diol **47** (328 mg, 0.72 mmol) in DMF (2.4 ml) was added portionwise sodium hydride (50% dispersion in mineral oil, 104 mg, 2.16 mmol) under an argon atmosphere. The resulting mixture was stirred for 15 min at 0°C and benzyl bromide (0.26 ml, 2.16 mmol) was added dropwise. The reaction mixture was stirred for 10 min at this temperature and for 6 h at 25°C, and then methanol (1 ml) was added. After being stirred for 30 min, the mixture was diluted with ether, washed successively with water, saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with ether-hexane=1:3) to give 351 mg (96% yield) of the dibenzyl ether **48** as a colorless oil: $[\alpha]_D^{25}$ +4.8° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2921, 2870, 1451, 1377 and 1141 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 1.12 (3H, s), 1.19-1.47 (2H, m), 1.27 (3H, s), 1.38 (3H, s), 1.52-1.87 (4H, m), 1.92 (1H, dd, *J* = 10.3, 9.8 Hz), 2.27 (1H, dd, *J* = 9.8, 5.4 Hz), 3.27 (1H, dd, *J* = 5.4, 3.9 Hz), 3.31 (3H, s), 3.62 (1H, dd, *J* = 10.3, 1.9 Hz), 3.68 (1H, dd, *J* = 8.8, 6.8 Hz), 3.74 (1H, dd, *J* = 10.3, 5.4 Hz), 4.08 (1H, dd, *J* = 8.8, 5.9 Hz), 4.32 (1H, d, *J* = 11.7 Hz), 4.33 (3H, s), 4.57 (1H, d, *J* = 11.7 Hz), 4.63 (1H, d, *J* = 7.3 Hz), 4.64 (1H, m), 4.79 (1H, d, *J* = 7.3 Hz), and 7.2-7.4 (10H, m); Anal. Calcd for $C_{31}H_{42}O_6$: C, 72.91; H, 8.29. Found: C, 73.03 H, 8.42. A solution of dibenzyl ether **48** (255 mg, 0.5 mmol) in 80% acetic acid (5 ml) was stirred for 4 h at 25°C. The reaction mixture was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:1) to give 178 mg (76% yield) of the diol as a colorless oil. To a cold (0°C) solution of the resulting diol (120 mg, 0.255 mmol) in MeOH (4 ml) was added dropwise a solution of sodium periodate (86 mg, 0.4 mmol) in water (2 ml). The mixture was stirred for 1.5 h at room temperature, diluted with AcOEt and the insoluble material was filtered off. The filtrate was washed successively with water and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluting with hexane-acetone=5:1) to give 103 mg (92% yield) of the corresponding aldehyde **49** as a colorless oil: $[\alpha]_D^{25}$ -56.3° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2913, 2870, 1699, 1451 and 1140 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.90 (3H, s), 1.41-1.56 (2H, m), 1.69-1.80 (2H, m), 1.96 (1H, ddd, J = 13.7, 2.9, 1.9 Hz), 2.10 (1H, ddd, J = 13.7, 9.3, 1.9 Hz), 2.39 (1H, ddd, J = 10.8, 5.9, 0.9 Hz), 2.52 (1H, dddd, J = 10.8, 10.3, 3.9, 1.9 Hz), 3.31 (3H, s), 3.44 (1H, ddd, *J* = 9.3, 2.9, 0.9 Hz), 3.77 (1H, dd, *J* = 9.3, 3.9 Hz), 4.10 (1H, dd, *J* = 10.3, 9.3 Hz), 4.35 (1H, d, *J* = 11.7 Hz), 4.39 (1H, d, *J* = 10.3 Hz), 4.42 (1H, d, *J* = 11.7 Hz), 4.63 (1H, d, *J* = 10.3 Hz), 4.64 (1H, d, *J* = 7.3 Hz), 4.72 (1H, d, *J* = 7.3 Hz), 7.20-7.35 (10H, m) and 9.81 (1H, d, J = 5.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 21.8 (q), 30.7 (t), 33.0 (t), 35.3 (t), 36.6 (s), 42.5 (d), 55.4 (q), 56.4 (d), 66.1 (t), 70.8 (t), 73.2 (t), 74.9 (s), 80.1 (d), 90.7 (t), 127.4 (d), 127.56 (d), 127.60 (d), 128.3 (d), 128.4 (d), 137.9 (s), 138.1 (s) and 204.8 (d); EIMS m/z (relative intensity): 410 (M^+-CO, 24), 393 (37) and 287 (100); Anal. Calcd

for $C_{27}H_{34}O_5$: C, 73.95; H, 7.81. Found: C, 74.00; H, 8.00. To a stirred solution of aldehyde **49** (30 mg, 0.068 mmol) in ethanol (1 ml) was added sodium hydroxide (80 mg, 2 mmol). After being stirred for 2 h at room temperature, the mixture was diluted with ether, washed successively with saturated NH_4Cl solution and saturated NaCl solution, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=3:1) to give 26 mg (87% yield) of the aldehyde **14**.

Methyl (1*R*, 2*R*, 3*R*, 4*S*)-3-Formyl-1-methoxymethyloxy-4-methyl-5-oxobicyclo[2.2.2]-octan-2-carboxylate ((-)-15) from **8**: A solution of acetonide **8** (300 mg, 0.84 mmol) in 80% acetic acid (20 ml) was stirred for 16 h at 25°C. The mixture was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:2, 5:3) to give 227 mg (85% yield) of diol as a colorless oil. To a cold (0°C) solution of the diol (206 mg, 0.65 mmol) in MeOH (2 ml) was added dropwise a solution of sodium periodate (278 mg, 1.3 mmol) in water (1 ml). After being stirred for 2 h at 25°C, the mixture was diluted with AcOEt and filtered through a pad of Celite. The filtrate was washed successively with saturated $Na_2S_2O_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:1) to give 116 mg (63% yield) of the aldehyde (-)-**15** as a colorless oil: $[\alpha]_D^{25}$ -96.0° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3414, 2929, 1717, 1145 and 1034 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.23 (3H, s), 1.59 (1H, ddd, *J* = 13.5, 12.2, 3.4 Hz), 1.79 (1H, tdd, *J* = 12.2, 4.8, 1.9 Hz), 2.07 (1H, ddd, *J* = 13.5, 12.2, 4.8 Hz), 2.27 (1H, tdd, *J* = 12.2, 3.4, 2.9 Hz), 2.54 (1H, dd, *J* = 18.5, 2.9 Hz), 2.63 (1H, d, *J* = 18.5 Hz), 3.17 (1H, dd, *J* = 5.8, 1.9 Hz), 3.35 (3H, s), 3.39 (1H, dd, *J* = 5.8, 1.9 Hz), 3.74 (3H, s), 4.69 (1H, d, *J* = 7.8 Hz), 4.87 (1H, d, *J* = 7.8 Hz) and 9.63 (1H, d, *J* = 1.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 17.2 (q), 26.0 (t), 30.7 (t), 44.7 (d), 45.5 (s), 49.5 (t), 52.4 (q), 55.4 (d), 55.6 (q), 75.7 (s), 91.3 (t), 172.9 (s), 199.7 (d) and 209.1 (s); EIMS m/z (relative intensity): 284 (M^+, 1.3), 256 (4.9), 255 (2.7) and 170 (100); Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.08; H, 7.25.

Methyl (1*S*, 2*S*, 3*S*, 4*R*)-3-Formyl-1-methoxymethyloxy-4-methyl-5-oxobicyclo[2.2.2]-octan-2-carboxylate ((+)-15) from **10**: To a cold (0°C) solution of keto ester **10** (107 mg, 0.30 mmol) in THF (1.8 ml) and DMSO (0.6 ml) was added potassium *tert*-butoxide (135 mg, 1.2 mmol) under an argon atmosphere. The mixture was stirred at 25°C and the progress of isomerization of the carbomethoxyl group of **10** was monitored by TLC to check the disappearance of the starting material. After about 20 min, the mixture was diluted with ether, washed successively with saturated NH_4Cl solution and saturated NaCl solution, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=1:1) to give 87 mg (81% yield) of the epimer of **10** as a colorless oil: $[\alpha]_D^{25}$ +99.7° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 2929, 1718, 1435, 1264, 1224 and 1035 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.03 (3H, s), 1.27 (3H, s), 1.36 (3H, s), 1.55 (1H, ddd, *J* = 13.7, 12.2, 3.9 Hz), 1.82 (1H, tdd, *J* = 12.2, 12.2, 3.9, 1.7 Hz), 1.93 (1H, ddd, *J* = 13.7, 12.2, 3.9 Hz), 2.39 (1H, tdd, *J* = 12.2, 12.2, 3.9, 3.2 Hz), 2.51 (1H, dd, *J* = 18.6, 3.2 Hz), 2.68 (1H, d, *J* = 18.6 Hz), 2.70 (1H, dd, *J* = 7.8, 1.7 Hz), 2.79 (1H, dd, *J* = 7.8, 4.8 Hz), 3.28 (1H, dd, *J* = 8.1, 7.8 Hz), 3.34 (3H, s), 3.74 (3H, s), 3.78 (1H, dd, *J* = 8.1, 7.1 Hz), 4.15 (1H, ddd, *J* = 7.8, 7.1, 4.8 Hz), 4.66 (1H, d, *J* = 7.8 Hz), and 4.89 (1H, d, *J* = 7.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 17.5 (q), 24.7 (q), 24.9 (t), 26.3 (q), 31.7 (t), 45.1 (s), 45.4 (d), 48.5 (d), 49.6 (t), 52.0 (q),

55.4 (q), 64.7 (t), 75.1 (d), 75.9 (s), 91.3 (t), 108.6 (s), 173.8 (s) and 211.8 (s); EIMS m/z (relative intensity): 356 (M^+, 0.5), 341 (67) and 101 (100); Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.82. Found: C, 60.58; H, 8.13. A solution of the product (72 mg, 0.20 mmol) in 80% acetic acid (1.5 ml) was stirred for 48 h at room temperature. The mixture was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:2, 5:3) to give diol as a colorless oil. To a cold (0°C) solution of the diol (39.5 mg, 0.125 mmol) in MeOH (0.4 ml) was added dropwise a solution of sodium periodate (53.5 mg, 0.25 mmol) in water (0.2 ml). After being stirred for 1.5 h at 25°C, the mixture was diluted with AcOEt and filtered through a pad of Celite. The filtrate was washed successively with saturated $Na_2S_2O_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:1) to give 33 mg (93% yield) of the aldehyde (+)-**15** as a colorless oil: $[\alpha]_D^{25}$ +105.8° (c 0.6, $CHCl_3$); Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 58.89; H, 7.19.

(1*R*, 4*S*, 5*S*, 6*R*, 4'*S*)-4-Methoxymethyloxy-1-methyl-6-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)-5-*p*-toluenesulfonyloxymethylbicyclo[2.2.2]octan-2-one (19): To a cold (0°C) solution of diol **12** (4:1 mixture of **12a** and **12b**) (42 g, 127 mmol) in pyridine (250 ml) was added portionwise *p*-toluenesulfonyl chloride (26.7 g, 140 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 10 h, and then concentrated under reduced pressure. The residue was partitioned between ether and water. The organic layer was washed sequentially with 10% $KHSO_4$ solution, saturated $NaHCO_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-acetone=7:7:1, 4:4:1) to give 49.2 g (80% yield) of mono tosylate (2α:2β=4:1) as colorless crystals. Recrystallization of the mixture from ether-hexane gave one of the isomers as colorless crystals: mp 64-6°C, $[\alpha]_D^{25}$ +4.5° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3540, 2946, 1370, 1351 and 1169 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.87 (3H, s), 1.16 (1H, tdd, *J* = 12.4, 6.8, 2.4 Hz), 1.33 (6H, s), 1.51-1.95 (5H, m), 2.10 (1H, ddd, *J* = 14.2, 10.3, 2.4 Hz), 2.21 (1H, m), 2.43 (3H, s), 3.24 (3H, s), 3.55 (1H, dd, *J* = 9.8, 2.4 Hz), 3.62 (1H, t, *J* = 8.3 Hz), 3.87 (1H, dd, *J* = 8.3, 6.4 Hz), 4.11 (1H, ddd, *J* = 8.3, 6.4, 3.9 Hz), 4.26 (1H, dd, *J* = 9.3, 3.9 Hz), 4.44 (1H, dd, *J* = 9.3, 6.8 Hz), 4.57 (1H, d, *J* = 7.3 Hz), 4.63 (1H, d, *J* = 7.3 Hz), 7.33 (1H, d, *J* = 8.3 Hz) and 7.80 (1H, d, *J* = 8.3 Hz); ^{13}C-NMR ($CDCl_3$) δ 21.6 (q), 22.2 (q), 25.8 (q), 26.4 (t), 28.5 (t), 30.7 (t), 35.5 (s), 38.5 (t), 39.5 (d), 40.3 (d), 55.3 (q), 68.4 (t), 71.5 (t), 74.9 (d), 75.4 (d), 76.6 (s), 90.6 (t), 108.2 (s), 128.1 (d), 128.1 (d), 129.7 (d), 129.7 (d), 133.1 (s) and 144.7 (s); EIMS m/z (relative intensity): 469 (M^+-CH_3, 34), 355 (43), 295 (61) and 101 (100); Anal. Calcd for $C_{24}H_{36}SO_8$: C, 59.48; H, 7.49. Found: C, 59.24; H, 7.53. To a solution of the hydroxy tosylate (2α:2β=4:1) (37.0 g, 76.4 mmol) and 4Å molecular sieves (130 g) in dry methylene chloride (370 ml) was added portionwise PDC (42.9 g, 114 mmol). The mixture was stirred for 6 h at 25°C, diluted with ether and filtered through a short silica gel column. The filtrate was concentrated under reduced pressure and chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-acetone=8:8:1) to give 28.7 g (78% yield) of keto tosylate **19** as a colorless oil: $[\alpha]_D^{25}$ +4.9° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2926, 1718, 1363, 1171 and 1033 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.93 (3H, s), 1.34 (3H, s), 1.35 (1H, s), 1.39 (1H, m), 1.49 (1H, m), 1.82-2.13 (3H, m), 2.39 (1H, m), 2.44 (3H, s), 2.48 (1H, dd, *J* = 18.6, 2.4 Hz), 2.60 (1H, dd, *J* = 18.6, 2.4 Hz), 3.27 (3H, s), 3.51 (1H, dd, *J* = 8.3, 7.8 Hz), 3.92 (1H, dd, *J* = 8.3, 6.3 Hz), 4.16-4.29 (3H, m), 4.63 (1H, d, *J* = 7.3 Hz), 4.69 (1H, d, *J* = 7.3 Hz), 7.34 (1H, d, *J* = 7.8 Hz) and 7.75

(1H, d, J = 7.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 17.4 (q), 21.6 (q), 25.5 (q), 26.19 (q), 26.20 (t), 30.5 (t), 41.4 (d), 42.3 (d), 45.2 (t), 45.6 (s), 55.5 (q), 68.6 (t), 70.0 (t), 74.2 (d), 75.4 (s), 91.0 (t), 108.6 (s), 127.9 (d), 127.9 (d), 129.8 (d), 129.8 (d), 132.8 (s), 144.9 (s) and 211.1 (s); EIMS m/z (relative intensity): 482 (M^+, 0.8), 467 (57) and 101 (100); Anal. Calcd for $C_{24}H_{34}SO_8$: C, 59.73; H, 7.10. Found: C, 59.44; H, 7.27.

(1*R*, 2*R*, 5*R*, 7*R*, 9*R*, 4'*S*)-2-Methoxymethyloxy-5-methyl-9-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)tricyclo[3.3.1.0^{2,7}]nonan-6-one (20): To a cold (0°C) solution of keto tosylate **19** (15.9 g, 33.0 mmol) in THF (100 ml) and DMF (100 ml) under an argon atmosphere was added portionwise potassium tert-butoxide (4.48 g, 40.0 mmol). After stirring for 1.5 h at this temperature, saturated NH_4Cl solution was added. The mixture was concentrated under reduced pressure and partitioned between ether and water. The aqueous layer was thoroughly extracted with ether. The combined organic layers were washed sequentially with saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-acetone=9:9:1) to give 9.2 g (90% yield) of **20** as colorless crystals: mp 54-6°C (ether-hexane); $[\alpha]_D^{25}$ -82.6° (c 2.0, $CHCl_3$); IR (KBr) 2953, 1713, 1462, 1374, 1266 and 1221 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.10 (3H, s), 1.29-1.49 (2H, m), 1.37 (3H, s), 1.43 (3H, s), 1.65 (1H, ddd, J = 13.3, 11.7, 2.9 Hz), 1.76 (1H, dd, J = 2.9, 2.4 Hz), 1.98 (1H, ddd, J = 13.3, 11.7, 2.9 Hz), 2.15 (1H, ddd, J = 13.3, 11.7, 4.8 Hz), 2.75 (1H, t, J = 6.3 Hz), 2.95-3.06 (2H, m), 3.43 (3H, s), 3.52 (1H, t, J = 8.3 Hz), 4.06 (1H, dd, J = 8.3, 6.3 Hz), 4.30 (1H, ddd, J = 8.3, 6.3, 2.4 Hz), and 4.79 (2H, s); ^{13}C-NMR ($CDCl_3$) δ 18.2 (q), 25.1 (t), 25.7 (q), 26.5 (q), 28.8 (t), 33.0 (t), 39.6 (d), 47.5 (s), 49.5 (d), 55.67 (d), 55.72 (q), 69.2 (t), 73.5 (d), 84.0 (s), 92.5 (t), 109.4 (s) and 213.6 (s); EIMS m/z (relative intensity): 310 (M^+, 4.6), 295 (20), 207 (100), 190 (50) and 101 (84); Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44. Found: C, 65.63; H, 8.41.

(1*R*, 4*R*, 8*R*, 9*R*, 10*S*)-4-Methyl-2-oxatricyclo[6.4.0.0^{4,9}]-5-dodecen-1,10-diol (23): To a cold (0°C) solution of ketone **20** (18.6 g, 60.0 mmol) in THF (200 ml)was added portionwise $LiAlH_4$ (1.14 g, 30 mmol) under an argon atmosphere. After being stirred for 1 h at this temperature, the reaction mixture was allowed to warm to room temperature. The mixture was diluted with ether (1 l) and saturated NH_4Cl solution (5 ml), stirred for 1 h, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-acetone=8:8:1) to give 18.4 g (98% yield) of the corresponding alcohol **21** as a 2:1 diastereomeric mixture (colorless oil): IR ($CHCl_3$) 3434, 2929, 1377, 1230 and 1142 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.95 and 0.99 (1:2, 3H, both s), 1.34 and 1.35 (1:2, 3H, both s), 1.40 (3H, s), and 3.41 and 3.42 (2:1 3H, both s); Anal. Calcd for $C_{17}H_{28}O_5$: C, 65.36; H, 9.03. Found: C, 65.15; H, 9.03. To a cold (0°C) solution of alcohol (5.0 g, 16 mmol) and *N,N*-dimethylaminopyridine (DMAP) (125 mg, 2.0 mmol) in pyridine (40 ml) was added dropwise methane-sulfonyl chloride (3.7 ml, 5.5 g, 48 mmol). The mixture was stirred for 12 h at this temperature and concentrated *in vacuo*. The residue was diluted with ether, washed with water, 10% $KHSO_4$ solution, saturated $NaHCO_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=6:1) to give 6.08 g (97% yield) of the mesylate **22** as a 2:1 diastereomeric mixture (colorless oil): IR ($CHCl_3$) 2928, 1470, 1455, 1371, 1355 and 1225 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.03 and 1.06 (1:2, 3H,

both s), 1.34 and 1.35 (1:2, 3H, both s), 1.40 and 1.41 (1:2, 3H, both s), 2.99 and 3.03 (1:2, 3H, both s), and 3.41 (3H, s). To a solution of mesylate **22** (1.7 g, 4.35 mmol) in acetonitrile (8.5 ml) was added 2*N*-HCl (25.5 ml). After being stirred for 24 h at 25°C, the mixture was neutralized with sodium hydrogen carbonate ($NaHCO_3$), diluted with AcOEt, washed with saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:2, 5:3) to give 832 mg (91% yield) of the hemiketal **23** as colorless crystals: mp 97-8°C; $[\alpha]_D^{25}$ +13.2° (c 1.0, $CHCl_3$); IR (KBr) 3322, 2920, 2884, 1437, 1361 and 1336cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.00 (3H, s), 1.27 (1H, m), 1.49-1.75 (4H, m), 2.07 (1H, m), 2.18-2.37 (2H, m), 3.2 (1H, brs, OH), 3.63 (1H, d, *J* = 5.4 Hz), 3.65 (1H, d, *J* = 5.4 Hz), 4.0 (1H, brs, OH), 4.08 (1H, t, *J* = 5.4 Hz), 5.46 (1H, dt, *J* = 9.8, 2.4 Hz) and 5.71 (1H, ddd, *J* = 9.8, 5.4, 2.4 Hz); ^{13}C-NMR ($CDCl_3$) δ 23.2 (t), 25.6 (q), 30.4 (t), 32.4 (s), 33.9 (t), 41.0 (d), 45.0 (d), 66.0 (t), 77.6 (d), 108.1 (s), 125.0 (d) and 135.2 (d); EIMS m/z (relative intensity): 210 (M^+, 2.1) and 179 (100); HRMS Found: 210.1258, $C_{12}H_{18}O_3$ (M^+) requires; 210.1256; Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.29; H, 8.66.

(1*R*, 5*S*, 9*R*)-9-Formyl-5-methylbicyclo[3.3.1]-6-nonen-2-one (24): To a cold (0°C) solution of hemiacetal **23** (1.05 g, 5 mmol) in acetonitrile (20 ml) was added dropwise a solution of sodium periodate (2.14 g, 10 mmol) in water (30 ml). After being stirred for 2 h at 25°C, the mixture was diluted with AcOEt and filtered through a pad of Celite. The filtrate was washed successively with water and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:1) to give keto aldehyde **24** (881 mg, 99% yield) as colorless crystals: mp 68-70°C; $[\alpha]_D^{25}$ -200.0° (*c* 1.0, $CHCl_3$); IR (KBr) 2901, 1708, 1456, 1430 and 1398 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.38 (3H, s), 1.64 (1H, ddt, *J* = 13.7, 6.8, 2.4 Hz), 1.76 (1H, ddd, *J* = 13.7, 9.8, 6.8 Hz), 2.11 (1H, dd, *J* = 19.0, 4.4 Hz), 2.32 (1H, dd, *J* = 9.8, 6.8 Hz), 2.36 (1H, ddd, *J* = 9.8, 2.4, 1.4 Hz), 2.46 (1H, ddt, *J* = 19.0, 6.8, 2.4 Hz), 2.79 (1H, dd, *J* = 3.9, 1.4 Hz), 2.88 (1H, brd, *J* = 6.8 Hz), 5.53 (1H, dt, *J* = 9.8, 2.4 Hz), 5.83 (1H, ddd, *J* = 9.8, 4.4, 2.4 Hz) and 10.02 (1H, d, *J* = 1.4 Hz); EIMS m/z (relative intensity): 178 (M^+, 14) 150 (69), 135 (35) and 93 (100); Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.85; H, 8.08.

(1*R*, 2*S*, 5*S*, 9*R*)-9-Hydroxymethyl-5-methylbicyclo[3.3.1]-6-nonen-2-ol (25): To a solution of ketone (430 mg, 2.4 mmol) in a mixture of liquid ammonia (40 ml), THF (20 ml) and ethanol (10 ml), lithium (550 mg) was added portionwise and the mixture was stirred for 1 h. After addition of NH_4Cl, the volatile material was evaporated. The residue was partitioned between AcOEt and water, and aqueous layer was extracted with AcOEt. The combined organic layers were washed sequentially with saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=10:3) to give 405 mg (93% yield) of diol **25** as colorless crystals: mp 109-111°C (ether-hexane); $[\alpha]_D^{25}$ -34.6° (c 2.0, $CHCl_3$); IR (KBr) 3264, 2920, 2863, 1708, 1495 and 1450 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.01 (3H, s), 1.29 (1H, m), 1.42-1.69 (3H, m), 1.80 (1H, m), 2.09 (1H, dddd, *J* = 18.9, 6.8, 2.4, 1.9 Hz), 2.27-2.45 (2H, m), 3.71 (1H, ddd, *J* = 10.8, 8.3, 5.4 Hz), 3.84-3.97 (2H, m), 5.31 (1H, ddd, *J* = 9.8, 2.4, 1.9 Hz) and 5.77 (1H, ddd, *J* = 9.8, 3.4, 2.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 25.8 (t), 26.4 (q), 28.0 (t), 32.5 (t), 33.2 (s),

35.1 (d), 47.3 (d), 60.8 (t), 68.3 (d), 128.0 (d) and 136.8 (d); EIMS m/z (relative intensity): 182 (M^+, 1.5), 164 (15), 146 (19) and 93 (100); Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.24; H, 10.21.

(1*R*, 2*S*, 5*S*, 9*R*)-2-Benzyloxy-9-benzyloxymethyl-5-methylbicyclo[3.3.1]-6-nonene (26): To a cold (0°C) solution of diol **25** (1.16 g, 6.4 mmol) in dry DMF (20 ml) were added sodium hydride (50% dispersion in mineral oil, 920 mg, 19.2 mmol) and benzyl bromide (1.9 ml, 16 mmol) under an argon atmosphere. The reaction mixture was allowed to warm to room temperature and stirred for 8 h, and then MeOH was added. After 15 min, the mixture was concentrated under reduced pressure, diluted with ether, washed successively with water, saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with: hexane-CH_2Cl_2=2:1, 1:1) to give 2.30 g (99% yield) of dibenzyl ether **24** as a colorless oil: $[\alpha]_D^{25}$ -47.0° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 2896, 1451, 1365, 1091, 1067 and 693 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.97 (3H, s), 1.21 (1H, m), 1.41 (1H, dd, *J* = 12.7, 3.9 Hz), 1.47-1.74 (2H, m), 1.97 (1H, m), 2.09 (1H, ddd, *J* = 18.9, 7.3, 2.4 Hz), 2.43 (1H, ddd, *J* = 18.9, 3.9, 1.9 Hz), 2.59 (1H, m), 3.49 (1H, dd, *J* = 9.3, 8.8 Hz), 3.54 (1H, dd, *J* = 10.8, 5.4 Hz), 3.61 (1H, dd, *J* = 9.3, 5.4 Hz), 4.41 (1H, d, *J* = 12.2 Hz), 4.43 (1H, d, *J* = 12.2 Hz), 4.52 (1H, d, *J* = 12.2 Hz), 4.54 (1H, d, *J* = 12.2 Hz), 5.30 (1H, ddd, *J* = 9.7, 2.4, 1.9 Hz), 5.77 (1H, ddd, *J* = 9.7, 3.9, 2.9 Hz) and 7.23-7.40 (10H, m); ^{13}C-NMR ($CDCl_3$) δ 25.6 (t), 26.0 (t), 26.5 (q), 32.1 (d), 32.5 (t), 33.4 (s), 44.5 (d), 68.8 (t), 69.6 (t), 73.1 (t), 75.4 (d), 127.3 (d) 127.5 (d), 127.6 (d), 127.8 (d), 128.2 (d), 128.3 (d), 128.4 (d), 136.6 (d), 138.6 (s) and 139.2 (d); EIMS m/z (relative intensity): 362 (M^+, 1.2), 271 (71), 180 (59) and 91 (100); Anal. Calcd for $C_{25}H_{30}O_2$: C, 82.83; H, 8.34. Found: C, 82.57; H, 8.40.

(1*R*, 2*R*, 5*S*, 8*S*, 9*R*)-8-Benzyloxy-9-benzyloxymethyl-2-formyloxy-5-methylbicyclo-[3.3.1]-3-nonene (27): To a solution of dibenzyl ether **26** (2.17 g, 6.00 mmol) in dioxane (12 ml) and formic acid (99% purity, 24 ml) was added selenium dioxide (777 mg, 7.00 mmol). After being stirred for 2 h at 60°C, the mixture was diluted with water and ether and then the insoluble material was filtered through a pad of Celite. The organic layer was separated and aqueous layer extracted with ether. The combined organic layers were washed with saturated $Na_2S_2O_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=5:1) to give 2.42 g (99% yield) of formate **27** as a colorless oil. $[\alpha]_D^{25}$ +9.0° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 2905, 1710, 1451, 1364, 1177, 1070 and 692 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.02 (3H, s), 1.19 (1H, m), 1.35-1.58 (2H, m), 1.67 (1H, m), 2.16 (1H, m), 2.66 (1H, m), 3.44 (1H, dd, *J* = 9.8, 9.3 Hz), 3.52 (1H, m), 3.60 (1H, dd, *J* = 9.8, 5.4 Hz), 4.41 (1H, d, *J* = 12.2 Hz), 4.43 (1H, d, *J* = 12.2 Hz), 4.55 (1H, d, *J* = 12.2 Hz), 4.65 (1H, d, *J* = 12.2 Hz), 5.68-5.61 (2H, m), 5.92 (1H, ddd, *J* = 9.8, 4.4, 1.9 Hz), 7.22-7.38 (10H, m) and 8.06 (s); ^{13}C-NMR ($CDCl_3$) δ 25.7 (t), 25.8 (q), 30.1 (t), 34.0 (s), 38.6 (d), 40.5 (d), 67.3 (d), 67.8 (t), 70.2 (t), 72.4 (d), 73.1 (t), 125.2 (d) 127.4 (d), 127.5 (d), 127.6 (d) 127.7 (d) 127.8 (d) 128.2 (d) 128.3 (d), 128.4 (d), 138.3 (s), 138.7 (s), 142.5 (d) and 160.6 (s); EIMS m/z (relative intensity): 406 (M^+, 0.6), 315 (23), 224 (11) and 91 (100); Anal. Calcd for $C_{26}H_{30}O_4$: C, 76.82; H, 7.44. Found: C, 76.76; H, 7.64.

(1*R*, 2*R*, 5*S*, 8*S*, 9*R*)-8-Benzyloxy-9-benzyloxymethyl-5-methylbicyclo[3.3.1]-3-nonen-2-ol (28): To a solution of formate **27** (2.15 g, 5.30 mmol) in methanol (10 ml) was added saturated methanolic ammonia (30 ml). After 40 min, the reaction mixture was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:2) to give 2.0 g (99% yield) of alcohol **28** as a colorless oil: $[\alpha]_D^{25}$ -6.0° (c 2.0, $CHCl_3$); IR ($CHCl_3$) 3565, 3410, 2987, 2857, 1451, 1364 and 1068 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.00 (3H, s), 1.12-1.50 (3H, m), 1.63 (1H, m), 2.08 (1H, m), 2.56 (1H, m), 3.45 (1H, dd, *J* = 9.8, 8.8 Hz), 3.51 (1H, dd, *J* = 11.3, 5.8 Hz), 3.61 (1H, dd, *J* = 9.8, 5.8 Hz), 4.38 (1H, dd, *J* = 5.4, 4.4 Hz), 4.43 (1H, d, *J* = 12.2 Hz), 4.53 (1H, d, *J* = 11.7 Hz), 4.55 (1H, d, *J* = 12.2 Hz), 4.57 (1H, d, *J* = 11.7 Hz), 5.51 (1H, d, *J* = 9.8 Hz), 5.92 (1H, ddd, *J* = 9.8, 4.4, 1.9 Hz) and 7.24-7.39 (10H, m); EIMS m/z (relative intensity): 378 (M^+, 1.9), 287 (62), 195 (17) and 91 (100); Anal. Calcd for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found: C, 79.12; H, 8.12.

(1*R*, 5*S*, 8*S*, 9*R*)-8-Benzyloxy-9-benzyloxymethyl-5-methylbicyclo[3.3.1]-3-nonen-2-one (29): To a mixture of alcohol **28** (3.78 g, 10 mmol) and 4Å molecular sieves (15 g) in CH_2Cl_2 (40 ml) was added portionwise PDC (5.64 g, 15 mmol). The resulting slurry was stirred for 4 h at room temperature, diluted with ether and filtered through a silica gel short column. The filtrate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether =3:1, 2:1) to give 2.71 g (73% yield) of enone **29** as a colorless oil: $[\alpha]_D^{25}$ -90.0° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 2901, 1670, 1451, 1364 and 1099 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.13 (3H, s), 1.34 (1H, m), 1.49-1.75 (2H, m), 1.82 (1H, m), 2.43 (1H, m), 3.26 (1H, m), 3.43 (1H, dd, *J* = 9.8, 8.3 Hz), 3.56 (1H, dd, *J* = 9.8, 5.8 Hz), 3.64 (1H, dt, *J* = 11.2, 5.8 Hz), 4.41 (1H, d, *J* = 12.2 Hz), 4.42 (1H, d, *J* = 12.2 Hz), 4.50 (1H, d, *J* = 12.2 Hz), 4.80 (1H, d, *J* = 12.2 Hz), 6.16 (1H, d, *J* = 9.8 Hz), 6.56 (1H, d, *J* = 9.8 Hz) and 7.24-7.39 (10H, m); EIMS m/z (relative intensity): 377 (M^++1, 4.3), 285 (32) and 91 (100); Anal. Calcd for $C_{25}H_{28}O_3$: C, 79.76; H, 7.50. Found: C, 79.48; H, 7.57.

(1*R*, 4*R*, 5*S*, 8*S*, 9*R*)-8-Benzyloxy-9-benzyloxymethyl-4,5-dimethylbicyclo[3.3.1]nonan-2-one (30): To a cold (0°C) suspension of copper(I) iodide (2.86 g, 15.0 mmol) in ether (40 ml), methyl lithium (1.05 M solution in ether, 28.6 ml, 30.0 mmol) was added dropwise until it became a colorless solution. After 10 min at this temperature, the solution was cooled to -78°C, and then enone **29** (1.13 g, 3.00 mmol) in ether (16 ml) was added dropwise. After being allowed to warm to -35°C over 2 h, the mixture was poured into a mixture of saturated NH_4Cl solution and 28% NH_4OH (2:1), and blue aqueous layer was thoroughly extracted with ether. The combined organic layers were washed with saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=2:1) to give 1.17 g (99% yield) of ketone **30** as a oil. $[\alpha]_D^{25}$ -10.9° (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) 2901, 1697, 1451, 1364 and 1098 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.88 (3H, s), 0.97 (3H, *J* = 7.3 Hz), 1.58-2.13 (5H, m), 2.30 (1H, m), 2.27 (1H, d, *J* = 17.6 Hz), 2.92 (1H, dd, *J* = 17.6, 8.8 Hz), 3.30 (1H, m), 3.48 (1H, dd, *J* = 15.6, 9.3 Hz), 3.51 (1H, dd, *J* = 15.6, 9.3 Hz), 3.81 (1H, ddd, *J* = 10.8, 6.8, 5.4 Hz), 4.38 (1H, d, *J* = 11.7 Hz), 4.39 (1H, d, *J* = 11.7 Hz), 4.50 (1H, d, *J* = 11.7 Hz), 4.69 (1H, d, *J* = 11.7 Hz) and 7.15-7.39 (10H, m); ^{13}C-NMR ($CDCl_3$) δ 19.3 (q), 25.9 (q), 28.2 (t), 33.7 (s), 35.8 (t), 39.7 (d), 41.5 (d), 49.2 (t), 50.9 (d), 68.2 (t), 69.7 (t), 71.4 (d), 73.2 (t), 127.5 (d), 127.6 (d), 127.9 (d), 128.3 (d), 128.4 (d), 138.2 (s), 138.3 (s) and 211.2 (s); EIMS

m/z (relative intensity): 392 (M^+, 0.6), 301 (32) and 91 (100); Anal. Calcd for $C_{26}H_{32}O_3$: C, 79.56; H, 8.22. Found: C, 79.32; H, 8.34.

(1*R*, 2*R*, 4*R*, 5*S*, 8*S*, 9*R*)-8-Benzyloxy-9-benzyloxymethyl-4,5-dimethylbicyclo[3.3.1]-nonan-2-ol (31): Ketone **30** (1.17 g, 3.00 mmol) and sodium cyanoborohydride (377 mg, 6.00 mmol) were dissolved in a mixture of MeOH (8 ml) and THF (16 ml) containing a trace amount of Methyl Orange, and cooled to 10°C. A solution of 2*N* HCl (3 ml) was added dropwise in order to maintain the red color. After being stirred for 30 min at this temperature (no more change in red color), the mixture was neutralized with saturated $NaHCO_3$ solution and concentrated under reduced pressure. The residue was partitioned between ether and water. The organic layer was washed with saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered, concentrated under reduced pressure and chromatographed on a silica gel column (eluted with hexane-ether=2:1) to give 1.16 g (99% yield) of alcohol **31** as a colorless oil: $[\alpha]_D^{25}$ -27.3° (c 2.0, $CHCl_3$); IR ($CHCl_3$) 3450, 2898, 1490, 1451, 1364 and 1260 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.77 (3H, s), 0.99 (3H, *J* = 7.3 Hz), 1.43-1.76 (3H, m), 1.82 (1H, dd, *J* = 13.7, 6.4 Hz), 1.95-2.09 (3H, m), 2.25 (1H, td, *J* = 13.7, 7.3 Hz), 2.78 (1H, m), 3.40 (1H, t, *J* = 9.3 Hz), 3.50 (1H, dd, *J* = 9.3, 5.4 Hz), 3.87-4.07 (1H, m), 4.33 (1H, d, *J* = 9.3 Hz), 4.40 (1H, d, *J* = 11.7 Hz), 4.53 (1H, d, *J* = 11.7 Hz), 4.55 (2H, s) and 7.23-7.39 (10H, m); EIMS m/z (relative intensity): 392 (M^+, 0.6), 303 (70) and 91 (100); Anal. Calcd for $C_{26}H_{34}O_3$: C, 79.15; H, 8.69. Found: C, 79.13; H, 8.89.

(1*R*, 2*R*, 4*R*, 5*S*, 8*S*, 9*R*)-8-Benzyl-9-benzyloxymethyl-2-methoxymethyloxy-4,5-dimethylbicyclo[3.3.1]nonane (32): To a cold (0°C) solution of **31** (1.54 g, 3.90 mmol) and diisopropylethylamine (756 mg, 5.85 mmol) in 1,2-dichloroethane (3 ml) was added dropwise methoxymethyl chloride (377 mg, 4.68 mmol). After being stirred for 12 h at 50 °C, the mixture was partitioned between ether and water, and aqueous layer was thoroughly extracted with ether. The combined organic layers were washed sequentially with 10% $KHSO_4$ solution, saturated $NaHCO_3$ solution and saturated NaCl solution, filtered, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=2:1) to give 1.68 g (98% yield) of methoxymethyl ether **32** as a colorless oil: $[\alpha]_D^{25}$ -4.4° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 2870, 1451, 1141 and 1099 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.76 (3H, s), 1.00 (3H, d, *J* = 6.8 Hz), 1.48 (1H, dd, *J* = 14.6, 7.3 Hz), 1.54-1.78 (3H, m), 1.60 (1H, dd, *J* = 13.7, 7.3 Hz), 1.70 (1H, dd, *J* = 13.7, 6.8 Hz), 1.85-2.13 (3H, m), 2.41 (1H, ddd, *J* = 13.7, 12.2, 6.8 Hz), 2.78 (1H, m), 3.37 (3H, s), 3.39 (1H, t, *J* = 9.3 Hz), 3.48 (1H, dd, *J* = 9.3, 5.8 Hz), 3.75 (1H, ddd, *J* = 11.7, 6.8, 4.3 Hz), 4.03 (1H, ddd, *J* = 12.2, 6.8, 5.4 Hz), 4.39 (1H, d, *J* = 12.2 Hz), 4.47 (1H, d, *J* = 12.2 Hz), 4.48 (1H, d, *J* = 12.2 Hz), 4.60 (1H, d, *J* = 12.2 Hz), 4.61 (1H, d, *J* = 6.8 Hz), 4.84 (1H, d, *J* = 6.8 Hz) and 7.15-7.40 (10H, m); EIMS m/z (relative intensity): 438 (M^+, 0.5), 347 (4.4), 315 (54), 299 (50) and 91 (100); Anal. Calcd for $C_{28}H_{38}O_4$: C, 76.68; H, 8.73. Found: C, 76.70; H, 8.89.

(1*R*, 2*S*, 5*S*, 6*R*, 8*R*, 9*R*)-9-Hydroxymethyl-8-methoxymethyloxy-5,6-dimethylbicyclo-[3.3.1]nonan-2-ol (33): To a cold (-34°C) solution of **32** (1.69 g, 3.85 mmol) in liquid ammonia (160 ml), THF (32 ml) and ethanol (8 ml), sodium (0.98 g, 42.6 mmol) was added portionwise until it maintain the blue color over a period of 30 min. After addition of NH_4Cl, ammonia was evaporated. The resulting mixture

was concentrated under reduced pressure, partitioned between ether and water, and aqueous layer was extracted with ether. The combined organic layers were washed sequentially with saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-acetone=5:3) to give 935 mg (94% yield) of diol **33** as colorless crystals: mp 60-2°C (ether-hexane): $[\alpha]_D^{25}$ -7.9° (c 2.0, $CHCl_3$); IR (KBr) 3432, 3400, 2924, 1437 and 1044 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.81 (3H, s), 0.99 (3H, *J* = 7.3 Hz), 1.43-1.56 (2H, m), 1.59-2.12 (5H, m), 2.36 (1H, ddd, *J* = 13.7, 12.2, 7.3 Hz), 2.58 (1H, dd, *J* = 7.3, 3.9 Hz), 3.39 (3H, s), 3.62-3.83 (2H, m), 3.98 (1H, m), 4.15 (1H, td, *J* = 12.2, 6.8 Hz), 4.17 (1H, d, *J* = 9.3 Hz), 4.66 (1H, d, *J* = 6.8 Hz) and 4.70 (1H, d, *J* = 6.8 Hz); EIMS m/z (relative intensity): 226 (M^+-CH_3OH, 9.3), 208 (14) and 121 (100); Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.09; H, 10.14. Found: C, 65.14; H, 10.24.

(1*R*, 2*S*, 5*S*, 6*R*, 8*R*, 9*R*)-8-Methoxymethyloxy-5,6-dimethyl-9-phenylthiomethylbicyclo-[3.3.1]nonan-2-ol (34): A mixture of diol **33** (930 mg, 3.60 mmol), diphenyldisulfide (1.96 g, 9.00 mmol) and tributylphosphine (2.21 ml, 9.00 mmol) in pyridine (1.5 ml) was stirred for 2 h at 80°C under an argon atmosphere. The mixture was diluted with ether, washed sequentially with 10% NaOH solution, water, 10% $KHSO_4$ solution, saturated $NaHCO_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2=1:1 and then with hexane-ether=3:2) to give 1.14 g (91% yield) of thioether **34** as a colorless oil: $[\alpha]_D^{25}$ -51.3° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3468, 2932, 2890, 1581, 1463 and 1438 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.83 (3H, s), 0.93 (3H, d, *J* = 7.3 Hz), 1.50 (1H, dd, *J* = 14.6, 6.8 Hz), 1.66 (1H, dd, *J* = 12.7, 7.3 Hz), 1.71-1.90 (3H, m), 1.94 (1H, dd, *J* = 12.7, 5.8 Hz), 2.06 (1H, ddd, *J* = 14.6, 7.3, 6.8 Hz), 2.35 (1H, ddd, *J* = 13.7, 12.7, 7.3 Hz), 2.71 (1H, dd, *J* = 7.8, 3.9 Hz), 2.89 (1H, t, *J* = 12.2 Hz), 3.10 (1H, dd, *J* = 12.2, 4.8 Hz), 3.39 (3H, s), 3.96-4.11 (2H, m), 4.16 (1H, d, *J* = 8.8 Hz), 4.65 (1H, d, *J* = 6.8 Hz), 4.70 (1H, d, *J* = 6.8 Hz) and 7.13-7.39 (5H, m); EIMS m/z (relative intensity): 351 (M^++1, 7.9), 319 (63) and 123 (100); Anal. Calcd for $C_{14}H_{26}O_4$: C, 68.53; H, 8.63; S, 9.15. Found: C, 68.36; H, 8.82; S, 9.20.

(1*R*, 2*S*, 5*S*, 6*R*, 8*R*)-8-Methoxymethyloxy-5,6-dimethyl-9-methylenebicyclo[3.3.1]nonan-2-ol (35): To a cold (-78°C) suspension of **34** (1.14 g, 3.25 mmol) and $NaHCO_3$ (382 mg, 4.55 mmol) in CH_2Cl_2 (25 ml) was added portionwise mCPBA (882 mg, 3.58 mmol). After 40 min at this temperature, triethylamine (0.6 ml) was added. The mixture was diluted with ether, washed sequentially with 1N NaOH solution, saturated $Na_2S_2O_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-ether=1:1:1 and then with hexane-acetone=5:2) to give 1.18 g (99% yield) of the corresponding sulfoxide as a diastereomeric mixture. The sample for the spectral analysis was separated by silica gel PTLC (eluted with hexane-acetone=5:2). The polar sulfoxide: $[\alpha]_D^{25}$ -96.1° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3453, 2929, 1462, 1440 and 1148 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 0.75 (3H, s), 0.91 (1H, td, *J* = 13.7, 7.8 Hz), 0.92 (1H, dd, *J* = 15.6, 7.8 Hz), 1.02 (3H, d, *J* = 7.3 Hz), 1.34-1.74 (2H, m), 1.75-2.14 (2H, m), 2.30 (1H, m), 2.40 (1H, dd, *J* = 13.7, 7.8 Hz), 2.71 (1H, dd, *J* = 13.7, 11.2 Hz), 2.76 (1H, m), 2.81 (1H, dd, *J* = 13.7, 4.4 Hz), 3.40 (3H, s), 4.10 (1H, ddt, *J* = 15.6, 8.8, 3.9 Hz), 4.22 (1H, ddd, *J* = 12.2, 5.8, 5.3 Hz), 4.33 (1H, d, *J* = 8.8 Hz), 4.68 (1H, d, *J* = 6.8 Hz), 4.72 (1H, d, *J* = 6.8 Hz) and 7.50-7.70 (5H,

m). The less polar sulfoxide: $[\alpha]_D^{25}$ +90.9° (c 1.0, $CHCl_3$); IR ($CHCl_3$) 3461, 2937, 2890, 1462 and 1440 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.75 (3H, s), 0.99 (3H, d, *J* = 7.3 Hz), 1.45-1.63 (2H, m), 1.72-2.07 (4H, m), 1.34-1.74 (2H, m), 2.12-2.26 (2H, m), 2.32 (1H, ddd, *J* = 13.7, 7.3, 5.4 Hz), 2.78 (1H, dd, *J* = 13.7, 5.4 Hz), 2.88 (1H, dd, *J* = 13.7, 6.3 Hz), 3.36 (3H, s), 3.92 (1H, ddt, *J* = 16.2, 8.8, 3.9 Hz), 4.08 (1H, d, *J* = 8.8 Hz), 4.09 (1H, ddd, *J* = 12.2, 5.8, 5.4 Hz), 4.61 (2H, s) and 7.48-7.69 (5H, m). A mixture of the sulfoxide (770 mg, 2.1 mmol) and diisopropylethylamine (1.0 ml, 742 mg, 5.74 mmol) in 1,2-dichlorobenzene (5 ml) was stirred for 4 h at 140°C under an argon atmosphere. The mixture was concentrated *in vacuo*. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2=1:1 and then with hexane-ether=1:1) to give 480 mg (95% yield) of olefin **35** as a colorless oil: $[\alpha]_D^{25}$ +5.2° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3475, 2899, 1447, 1414 and 1378 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.86 (3H, d, *J* = 6.8 Hz), 0.94 (3H, s), 1.49 (1H, m), 1.74-1.89 (3H, m), 1.99-2.11 (2H, m), 2.41 (1H, ddd, *J* = 13.7, 12.2, 6.8 Hz), 3.04 (1H, t, *J* = 4.4 Hz), 3.40 (3H, s), 3.83 (1H, qd, *J* = 9.3, 4.4 Hz), 4.11 (1H, dd, *J* = 12.2, 6.8 Hz), 4.16 (1H, d, *J* = 9.3 Hz), 4.65 (1H, d, *J* = 6.8 Hz), 4.67 (1H, d, *J* = 1.4 Hz), 4.69 (1H, d, *J* = 6.8 Hz) and 4.97 (1H, d, *J* = 1.4 Hz); Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06. Found: C, 69.95; H, 10.24.

(1*S*, 5*S*, 6*R*, 8*R*)-8-Hydroxy-5,6-dimethyl-9-methylenebicyclo[3.3.1]nonan-2-one (36): To a mixture of alcohol **35** (480 mg, 2.00 mmol) and 4Å molecular sieves (3 g) in dry CH_2Cl_2 (5 ml) was added PDC (1.12 g, 3 mmol). After being stirred for 4 h at 25°C, the mixture was diluted with ether and filtered through a silica gel short column. The filtrate was concentrated under reduced pressure and chromatographed on a silica gel column (eluted with hexane-ether=3:1) to give 414 mg (86% yield) of the corresponding ketone as colorless crystals: mp 44-6°C (hexane); $[\alpha]_D^{25}$ +57.1° (*c* 2.0, $CHCl_3$); IR (KBr) 2931, 1701, 1634, 1469, 1415 and 1376 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.95 (3H, d, *J* = 6.8 Hz), 1.08 (3H, s), 1.71 (1H, dt, *J* = 13.7, 9.3 Hz), 1.86 (1H, dd, *J* = 13.7, 6.3 Hz), 1.92 (1H, m), 1.98 (1H, ddd, *J* = 13.7, 8.3, 3.9 Hz), 2.15 (1H, ddd, *J* = 13.7, 12.2, 6.3 Hz), 2.50 (1H, ddd, *J* = 18.5, 8.3, 3.9 Hz), 2.59 (1H, ddd, *J* = 18.5, 9.3, 8.3 Hz), 3.37 (3H, s), 3.49 (1H, d, *J* = 6.3 Hz), 3.98 (1H, dt, *J* = 12.2, 6.3 Hz), 4.60 (1H, d, *J* = 6.8 Hz), 4.75 (1H, d, *J* = 6.8 Hz), 4.78 (1H, s) and 5.01 (1H, s); EIMS m/z (relative intensity): 238 (M^+, 0.3) and 168 (100); Anal. Calcd for $C_{14}H_{24}O_3$: C, 70.56; H, 9.30. Found: C, 70.28; H, 9.36. To a solution of the product (166 mg, 0.70 mmol) in acetic acid (4 ml) was added 6*N* HCl (0.117 ml, 0.70 mmol). After being stirred for 35 min at 25°C, the mixture was neutralized with saturated $NaHCO_3$ solution, and extracted thoroughly with ether. The combined organic layers were washed with saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=1:1 and then with hexane-acetone=10:3) to give 160 mg (71% yield) of keto alcohol **36** as colorless crystals: mp 128-131°C (ether-hexane); $[\alpha]_D^{25}$ +103.3° (*c* 1.5, $CHCl_3$); IR (KBr) 3371, 2956, 2920, 2880, 1684 and 1468 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.92 (3H, d, *J* = 6.8 Hz), 1.15 (3H, s), 1.64-1.95 (5H, m), 2.38 (1H, ddd, *J* = 16.6, 6.8, 5.4 Hz), 2.51 (1H, dt, *J* = 16.6, 9.3 Hz), 2.94 (1H, dd, *J* = 7.8, 3.9 Hz), 3.24 (1H, d, *J* = 5.8 Hz), 3.96 (1H, dddd, *J* = 12.2, 7.8, 5.8, 5.4 Hz), 4.88 (1H, s) and 5.04 (1H, s); EIMS m/z (relative intensity): 194 (M^+, 25), 177 (13) and 124 (100); Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.07; H, 9.33.

(1*S*, 2*R*, 5*S*, 6*R*, 8*R*)-5,6-dimethyl-9-methylene-4-vinylbicyclo[3.3.1]nonan-2,8-diol (37): To a cold (0°C) solution of **36** (150 mg, 0.77 mmol) in ether (20 ml) was added dropwise vinylmagnesium bromide (1.0 M solution in THF, 2.3 ml, 2.3 mmol) under an argon atmosphere. After being stirred for 5 min at this temperature and for 30 min at 25°C, the reaction mixture was partitioned between ether and saturated NH_4Cl solution, and aqueous layer was extracted with ether. The combined organic layers were washed with saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-ether=1:1:1 and then with hexane-acetone=10:3) to give 151 mg (88% yield) of diol **37** as colorless crystals: mp 110-2°C (ether-hexane); $[\alpha]_D^{25}$ -36.3° (*c* 1.0, $CHCl_3$); IR (KBr) 3403, 3253, 3074, 2968, 2900, 1640 and 1492 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.88 (3H, d, *J* = 6.8 Hz), 0.95 (3H, s), 1.49 (1H, td, *J* = 13.7, 6.8 Hz), 1.71-1.93 (4H, m), 2.35 (1H, ddd, *J* = 13.7, 12.2, 6.8 Hz), 2.48 (1H, ddd, *J* = 13.7, 12.2, 6.8 Hz), 2.67 (1H, d, *J* = 4.9 Hz), 3.50 (1H, s), 3.90 (1H, m), 4.08 (1H, m), 4.71 (1H, d, *J* = 1.4 Hz), 4.90 (1H, d, *J* = 1.4 Hz), 5.01 (1H, dd, *J* = 10.7, 1.4 Hz), 5.25 (1H, dd, *J* = 17.1, 1.4 Hz) and 6.11 (1H, dd, *J* = 17.1, 10.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 18.4 (q), 24.8 (q), 36.8 (t), 38.9 (t), 39.0 (s), 39.6 (t), 39.8 (d), 55.9 (d), 73.2 (d), 78.5 (s), 110.2 (t), 111.0 (t), 144.4 (d) and 149.6 (s); EIMS m/z (relative intensity): 223 (M^++1, 2.6), 204 (30), 186 (77), 171 (99) and 133 (100); Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.64; H, 10.06.

(1*S*, 2*S*, 4*R*, 5*S*)-2-Formyloxy-8-(2'-formyloxyethylidene)-5,6-dimethyl-9-methylenebicyclo[3.3.1]nonane (3): To a cold (0°C) solution of **37** (116 mg, 0.52 mmol) in CH_2Cl_2 (0.5 ml) and pyridine (0.4 ml) was added dropwise acetyl formate (132 mg, 1.5 mmol). After 7 h at this temperature, the mixture was diluted with ether, washed sequentially with water, 10% $KHSO_4$ solution, saturated $NaHCO_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=2:1) to give 122 mg (94% yield) of the corresponding mono formate as a colorless oil: $[\alpha]_D^{25}$ +10.0° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3552, 2914, 1721, 1642, 1450 and 1379 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.93 (3H, d, *J* = 7.3 Hz), 0.98 (3H, s), 1.56 (1H, td, *J* = 13.7, 6.8 Hz), 1.72-1.97 (4H, m), 2.22 (1H, td, *J* = 13.7, 6.8 Hz), 2.58 (1H, td, *J* = 13.7, 6.8 Hz), 2.72 (1H, d, *J* = 5.3 Hz), 3.11 (1H, s), 4.80 (1H, d, *J* = 0.9 Hz), 4.98 (1H, d, *J* = 0.9 Hz), 5.00 (1H, dd, *J* = 10.7, 1.4 Hz), 5.30 (1H, dd, *J* = 17.1, 1.4 Hz), 5.36 (1H, dd, *J* = 12.2, 6.8, 5.3 Hz), 6.04 (1H, dd, *J* = 17.1, 10.7 Hz) and 8.09 (1H, s); EIMS m/z (relative intensity): 250 (M^+, 2.3), 232 (5.9), 204 (22) and 121 (100); Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.82; H, 9.08. To a cold (0°C) solution of the product (96 mg, 0.38 mmol) in 1,4-dioxane (2 ml) was added formic acid (99% purity, 4 ml). After being stirred for 2 h at 25°C, the mixture was diluted with ether, washed successively with water, saturated $NaHCO_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=3:1) to give 92 mg (87% yield) of diformate **3** as a 2:1 mixture of geometrical isomers (colorless oil): IR ($CHCl_3$) 2915, 1712, 1168, 1121 and 892 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.94 and 0.95 (2:1, 3H, both d, *J* = 6.8 Hz), 1.00 (3H, s), 5.32 (2/3H, td, *J* = 6.8, 2.4 Hz), 5.49 (1/3H, td, *J* = 6.8, 2.4 Hz), 8.01 (1H, s) and 8.05 (1H, s); Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.29; H, 8.11.

(1*R*, 4*R*, 6*R*, 7S, 9*S*)-6,7-dimethyl-9-methylene-1-vinyl-3-oxatricyclo[5.2.2.0^{4,9}]undecan-2-ol (4): To a mixture of samarium diiodide (0.25 M solution in THF, 5.6 ml, 1.4 mmol) and HMPA (3.5 ml) was added diformyl ester **3** (109 mg, 0.40 mmol) in THF (1.4 ml) in one portion under an argon atmosphere. After being stirred for 20 min at 25°C, the mixture was diluted with saturated NH_4Cl solution and extracted thoroughly with ether. The combined organic extracts were washed with water and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane-ether=3:1, 1:1) to give 70 mg (76% yield) of hemiacetal **4** as colorless crystals: mp 61-6°C (hexane); $[\alpha]_D^{25}$ +42.1° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3570, 33349, 2906, 1637, 1447 and 1382 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.86 (3H, d, *J* = 6.8 Hz), 1.01 (3H, s), 1.25 (1H, ddd, *J* = 14.6, 10.8, 5.4 Hz), 1.30 (1H, ddd, *J* = 14.6, 13.7, 5.4 Hz), 1.57 (1H, ddd, *J* = 13.7, 5.4, 2.4 Hz), 1.69 (1H, ddd, *J* = 14.6, 5.4, 2.4 Hz), 1.78 (1H, ddd, *J* = 14.6, 5.4, 2.4 Hz), 1.96 (1H, td, *J* = 14.6, 5.4 Hz), 2.10 (1H, dqd, *J* = 10.8, 6.8, 5.4 Hz), 2.59 (1H, d, *J* = 2.4 Hz), 3.13 (1H, d, *J* = 9.8 Hz), 4.61 (1H, ddd, *J* = 9.8, 5.4, 2.4 Hz), 4.72 (1H, d, *J* = 1.4 Hz), 4.83 (1H, d, *J* = 1.4 Hz), 4.96 (1H, d, *J* = 2.4 Hz), 5.17 (1H, d, *J* = 10.7 Hz), 5.18 (1H, d, *J* = 18.0 Hz) and 5.92 (1H, dd, *J* = 18.0, 10.7 Hz); ^{13}C-NMR ($CDCl_3$) δ 18.8 (q), 22.9 (q), 27.6 (t), 33.8 (d), 37.1 (t), 38.0 (s), 39.6 (t), 48.8 (d), 53.9 (s), 79.4 (d), 103.7 (d), 107.9 (t), 114.8 (t), 140.0 (d) and 151.0 (s); EIMS m/z (relative intensity): 234 (M^+, 1.9), 216 (7.8), 188 (49), 173 (89) and 119 (100); Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.63; H, 9.58.

(1*R*, 4*R*, 6*R*, 7S, 9*S*)-1-Hydroxyethyl-6,7-dimethyl-8-methylene-3-oxatricyclo[5.2.2.-0^{4,9}]undecan-2-ol (39): To a cold (0°C) solution of **4** (40 mg, 0.17 mmol) in THF (0.2 ml) was added dropwise thexylborane (0.5 M solution in THF, 1.8 ml, 0.90 mmol) under an argon atmosphere, and the reaction mixture was stirred for 1h at this temperature and for 1.5 h at 25°C. After addition of water (2 ml), $NaHCO_3$ (168 mg, 2.0 mmol) and $NaBO_3$ (26 mg, 0.17 mmol), the mixture was stirred for 1.5 h and then partitioned between ether and water. The aqueous layer was extracted with ether. The combined organic layers were washed with saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give 42 mg of crude **38**. This product was used for the next reaction without further purification. To a solution of hemiacetal **38**, Et_3N (0.11 ml, 0.80 mmol) and *N,N*-dimethylaminopyridine (DMAP) (2 mg) in DMF (0.3 ml) was added *tert*-butyldiphenylsilyl chloride (TBDPSCl) (0.16 ml, 0.60 mmol). After 2 h at 25°C and 4 h at 40°C, Et_3N (0.22 ml, 1.6 mmol), DMAP (6 mg, 0.051 mmol) and TBDPSCl (0.16 ml, 0.60 mmol) was added. After 4 h at 45°C, the mixture was partitioned between ether and water, and the aqueous layer was extracted with ether. The combined organic layers were washed with saturated NH_4Cl solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-ether=4:1) to give 49 mg (77% yield) of silyl ether **39** as a colorless oil. $[\alpha]_D^{25}$ +6.0° (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3387, 2917, 1639, 1467 and 1447 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.84 (3H, d, *J* = 6.8 Hz), 0.97 (3H, s), 1.05 (9H, s), 1.20 (1H, td, *J* = 12.7, 5.4 Hz), 1.30 (1H, td, *J* = 9.8, 5.4 Hz), 1.39-1.79 (5H, m), 1.85 (1H, ddd, *J* = 15.1, 5.4, 2.9 Hz), 2.05 (1H, m), 2.79 (1H, d, *J* = 9.3 Hz), 3.65 (1H, brs), 3.71 (1H, td, *J* = 10.3, 3.9 Hz), 3.76 (1H, td, *J* = 10.3, 3.9 Hz), 4.58 (1H, ddd, *J* = 9.3, 5.4, 2.9 Hz), 4.64 (1H, d, *J* = 1.4 Hz), 4.75 (1H, d, *J* = 1.4 Hz), 5.12 (1H, brs), 7.35-7.50 (6H, m) and 7.60-7.75 (4H, m); ^{13}C-NMR ($CDCl_3$) δ 19.0 (q), 23.2 (q), 26.1 (t), 26.5 (s), 26.7 (q), 34.8 (d), 35.2 (t), 37.2 (t), 38.4 (s), 39.8 (t), 50.9 (s), 52.0 (d), 61.2 (t), 78.7 (d), 103.8 (d), 107.6 (t), 127.7 (d), 127.8 (d), 129.6 (d), 129.9 (d), 132.8 (s),

135.6 (d), 135.6 (d),134.8 (s) and 151.4 (s); EIMS m/z (relative intensity): 433 (M^+-*t*-Bu, 4.3), 415 (10) and 199 (100); HRMS Found: 433.2160, $C_{27}H_{33}O_3Si$ (M^+-C_4H_9) requires; 433.2199.

Reaction of Hemiacetal 38 with Silica Gel: The crude hemiacetal **38** (prepared from 40 mg of **4**) was chromatographed on a silica gel (1.0 g) column using hexane-ether=1:1 and hexane-acetone=5:2 as eluent to give 7 mg of **38** and 30 mg (84% yield from **4**) of acetal **42** as a colorless oil: $[\alpha]_D^{25}$ +31.3° (*c* 0.9, $CHCl_3$); IR (neat) 2914, 1642, 1445, 1366, 1136 and 1090 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.77 (3H, d, *J* = 6.8 Hz), 1.04 (3H, s), 1.45-2.03 (9H, m), 2.67 (1H, d, *J* = 8.3 Hz), 3.94 (1H, d, *J* = 10.8 Hz), 3.95 (1H, dd, *J* = 10.8, 2.9 Hz), 4.52 (1H, dt, *J* = 8.3, 6.8 Hz), 4.70 (1H, d, *J* = 1.4 Hz), 4.94 (1H, d, *J* = 1.4 Hz) and 5.43 (1H, s); ^{13}C-NMR ($CDCl_3$) δ 17.1 (q), 24.8 (q), 29.0 (t), 35.0 (t), 37.9 (s), 38.1 (t), 39.8 (d), 40.8 (t), 53.9 (d), 56.7 (s), 66.3 (t), 78.9 (d), 108.9 (t), 112.9 (d) and 149.3 (s); EIMS m/z (relative intensity): 234 (M^+, 21), 216 (14) and 164 (100); HRMS Found: 234.1622, $C_{15}H_{22}O_2$ (M^+) requires; 234.1620.

***O*-*tert*-Butyl(diphenyl)silylupiol (40)**: To a mixture of **39** (49 mg, 0.10 mmol) and 4Å molecular sieves (225 mg) in CH_2Cl_2 (1 ml) was added PDC (75 mg, 0.20 mmol). After being stirred for 4 h at 25°C, the mixture was diluted with ether and filtered through a silica gel short column. The filtrate was concentrated under reduced pressure and chromatographed on a silica gel column (eluted with hexane-ether=5:1) to give 37 mg (77% yield) of lactone **40** as a colorless oil. $[\alpha]_D^{25}$ +7.6° (c 1.5, $CHCl_3$); IR ($CHCl_3$) 2924, 1753, 1105, 1075 and 697 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.82 (3H, d, *J* = 6.8 Hz), 1.00 (3H, s), 1.03 (9H, s), 1.41-1.72 (4H, m), 1.77 (1H, dd, *J* = 14.2, 6.8 Hz), 1.77-1.93 (2H, m), 2.00 (1H, dd, *J* = 14.2, 6.8 Hz), 2.12 (1H, dt, *J* = 15.1, 6.4 Hz), 3.17 (1H, d, *J* = 9.3 Hz), 3.74 (2H, t, *J* = 6.8 Hz), 4.71 (1H, ddd, *J* = 9.3, 6.4, 5.4 Hz), 4.72 (1H, s), 4.82 (1H, s), 7.33-7.48 (6H, m) and 7.63-7.71 (4H, m); ^{13}C-NMR ($CDCl_3$) δ 19.6 (q), 20.0 (s), 25.3 (q), 27.7 (q), 27.7 (q), 27.7 (q), 32.0 (t), 37.2 (t), 38.8 (s), 39.3 (t), 39.9 (d), 40.3 (t), 48.7 (s), 48.9 (d), 61.0 (t), 78.1 (d), 111.3 (t), 128.6 (d), 128.6 (d), 128.6 (d), 128.6 (d), 130.6 (d), 130.6 (d), 134.3 (s), 134.4 (s), 136.5 (d), 136.5 (d), 136.5 (d), 136.5 (d), 148.6 (s) and 182.3 (s); EIMS m/z (relative intensity): 431 (M^+-*t*-Bu, 29), 387 (7), 199 (95) and 71 (100); HRMS Found: 431.2039, $C_{27}H_{31}O_3Si$ (M^+-C_4H_9) requires; 431.2034.

Oxidation of 38 with Tetrapropylammonium Perruthenate: To a mixture of the hemiacetal **38** (3.0 mg, 0.01 mmol), 4-methylmorpholine-*N*-oxide (3.5 mg, 0.03 mmol) and 4Å molecular sieves (30 mg) in CH_2Cl_2 (0.1 ml) was added tetrapropylammonium perruthenate (4.5 mg, 0.013 mmol) under an argon atmosphere. After being stirred for 20 min at 25°C, the mixture was diluted with ether and filtered through a silica gel short column. The filtrate was concentrated under reduced pressure and purified by silica gel PTLC (eluted with hexane-ether=1:1) to give 1.5 mg (60% yield) of lactone acetal **43** as a colorless oil: $[\alpha]_D^{25}$ -6.0° (*c* 0.05, $CHCl_3$); IR ($CHCl_3$) 2915, 1776, 1212, 1124 and 925 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.80 (3H, d, *J* = 6.8 Hz), 1.2 (1H, m), 1.02 (3H, s), 1.73 (1H, m), 1.76 (1H, dd, *J* = 13.7, 5.4 Hz), 1.84 (1H, dd, *J* = 12.2, 1.9 Hz), 1.89 (1H, dd, *J* = 12.2, 6.8 Hz), 1.96 (1H, dd, *J* = 14.7, 6.8 Hz), 1.76 (1H, dd, *J* = 13.7, 5.4 Hz), 2.07 (1H, ddd, *J* = 14.7, 6.8, 3.9 Hz), 2.46 (1H, d, *J* = 17.6 Hz), 2.68 (1H, d, *J* = 17.6 Hz), 2.70 (1H, d, *J* = 9.3 Hz), 4.71 (1H, ddd, *J* = 9.3, 5.4, 3.9 Hz), 4.79 (1H, d, *J* = 1.4 Hz), 4.95 (1H, d, *J* = 1.4 Hz) and 5.73 (1H, s); EIMS m/z (relative intensity): 248 (M^+, 18), 230 (22) 219 (53) and 174 (100); HRMS Found: 248.1408, $C_{15}H_{20}O_3$ (M^+) requires; 248.1412.

Upiol (41): To a cold (0°C) solution of **40** (37 mg, 0.075 mmol) and acetic acid (0.022ml, 0.38 mmol) in THF (0.9 ml) was added tetrabutylammonium fluoride (1 M solution in THF, 0.38 ml, 0.38 mmol). After being stirred for 3.5 h at 25°C, the mixture was diluted with ether, washed successively with water, saturated $NaHCO_3$ solution and saturated NaCl solution, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (eluted with hexane-CH_2Cl_2-ether=1:1:1) to give 17 mg (94% yield) of upiol (**41**) as a colorless oil: $[\alpha]_D^{25}$ +2.0° (*c* 0.75, $CHCl_3$); IR ($CHCl_3$) 3410, 2926, 1755, 1371, 1262, 1203, 1135 and 995 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.84 (3H, d, *J* = 6.8 Hz), 1.03 (3H, s), 1.47-2.01 (8H, m), 2.18 (1H, dt, *J* = 14.6, 6.8 Hz), 3.12 (1H, d, *J* = 8.8 Hz), 3.72 (1H, dt, *J* = 12.2, 6.3 Hz), 3.82 (1H, brs), 3.83 (1H, dt, *J* = 12.2, 6.3 Hz), 4.81 (1H, ddd, *J* = 8.8, 6.8, 2.4 Hz), 4.81 (1H, d, *J* = 1.4 Hz) and 5.00 (1H, d, *J* = 1.4 Hz); ^{13}C-NMR ($CDCl_3$) δ 18.7 (q), 24.4 (q), 29.9 (t), 36.2 (t), 36.6 (s), 38.1 (t), 38.90 (t), 38.93 (t), 48.0 (s), 49.3 (d), 58.7 (t), 77.8 (d), 110.8 (t), 147.0 (s) and 182.6 (s); EIMS m/z (relative intensity): 250 (M^+, 6), 232 (33), 217 (99), 206 (15) and 119 (100); HRMS Found: 250.1565, $C_{15}H_{22}O_3$ (M^+) requires; 250.1569.

Upial (1): To a mixture of upiol (15 mg, 0.06 mmol) and 4Å molecular sieves (140 mg) in CH_2Cl_2 (0.5 ml) was added PDC (45 mg, 0.12 mmol). After being stirred for 1 h at 25°C, the mixture was diluted with ether and filtered through a silica gel short column. The filtrate was concentrated under reduced pressure and chromatographed on a silica gel column (eluted with hexane-ether=5:1) to give 13 mg (87% yield) of **1** as a colorless oil: $[\alpha]_D^{25}$ +36.1° (*c* 0.39, $CHCl_3$); IR ($CHCl_3$) 2929, 1756, 1719, 1378, 1190, 1147, 1065, 976 and 905 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.83 (3H, d, *J* = 6.8 Hz), 1.04 (3H, s), 1.33-1.83 (5H, m), 1.92 (1H, sextet, *J* = 6.8 Hz), 2.22 (1H, ddd, *J* = 15.6, 6.8, 4.4 Hz), 2.75 (1H, d, *J* = 18.6 Hz), 2.90 (1H, d, *J* = 18.6 Hz), 3.03 (1H, d, *J* = 9.8 Hz), 4.81 (1H, d, *J* = 1.4 Hz), 4.94 (1H, d, *J* = 1.4 Hz), 4.97 (1H, ddd, *J* = 9.8, 5.4, 4.4 Hz) and 9.72 (1H, d, *J* = 0.5 Hz); ^{13}C-NMR ($CDCl_3$) δ 18.7 (q), 24.3 (q), 30.4 (t), 35.9 (t), 37.7 (s), 39.2 (t), 39.4 (d), 46.7 (s), 48.9 (d), 50.6 (t), 78.1 (d), 111.2 (t), 147.4 (s), 180.9 (s) and 199.5 (d); EIMS m/z (relative intensity): 248 (M^+, 6), 220 (27), 204 (61) and 105 (100); HRMS Found: 248.1407, $C_{15}H_{20}O_3$ (M^+) requires; 248.1412.

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