Stereoselective Synthesis of Cyclopentanones by Reductive Cleavage of 6-Oxonorbornane-2-carboxylates and Its Application to the Synthesis of 1α,25-Dihydroxyvitamin D_3 CD Ring

Kazuo Nagasawa, Naoto Matsuda, Yasuo Noguchi, Masahiro Yamanashi, Yoshiro Zako, and Isao Shimizu*

Department of Applied Chemistry, School of Science and Engineering, Waseda University, Ookubo 3-4-1, Shinjuku-ku, Tokyo 169, Japan

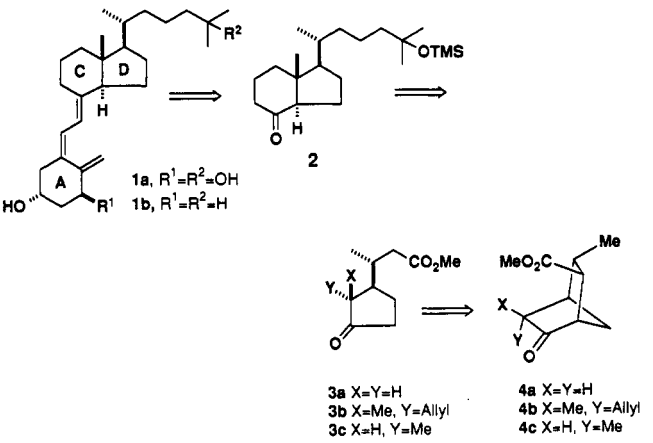
Received September 18, 1992

A novel chiral synthesis of the CD-ring **2** of 1α,25-dihydroxyvitamin D_3 (**1a**) is described. The optically active D-ring keto ester **3c** was prepared by reductive cleavage of 6-oxonorbornane-2-carboxylate **4c** with lithium naphthalenide. 1,2-Transposition of enone **15**, which was obtained by Robinson annulation of **14**, was accomplished via thermolysis of the allylic carbonate **29** at 100 °C to give enone **16**. Reduction of ketone **16** with $NaBH_4$–$CeCl_3$ followed by hydrogenation with $RhCl(PPh_3)_3$ catalyst gave *trans*-indanol **32**, which was transformed to intermediate **2**.

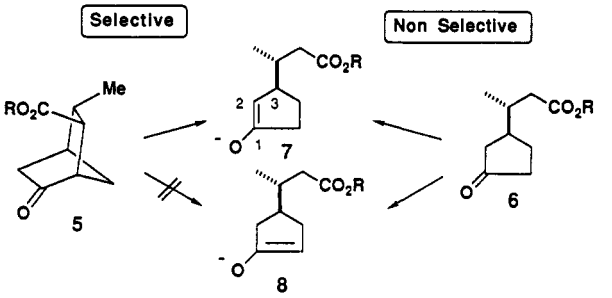
Introduction

Cyclopentanoids which have vicinal asymmetric carbon centers on both their cyclopentane rings and side chains are ubiquitous in natural terpenoids and steroids.[1] Several methods have been reported to introduce these asymmetric carbon centers.[2,3a] Norbornanones are known to be useful precursors for cyclopentanoids,[4] but very little is known about the reductive cleavage of norbornanones to afford cyclopentanoids.[5] In our studies on the synthesis of the hormonally active form of vitamin D_3 (**1b**) and its analogues,[3] we focused our attention on the reductive cleavage of norbornanones which are accessible from asymmetric Diels–Alder adducts. Thus, desired stereochemistries for the cyclopentanoids are fixed during the construction of the bicyclic systems. By selective cleavage of the remainder of the ring, the formation of the side chain is controlled, thus providing a promising method for controlling the stereochemistry of both cyclopentanone rings and the side chains. In this paper, we report a new synthetic method for the preparation of the 1α,25-dihydroxyvitamin D_3 CD-ring synthon **2** based on this reductive cleavage strategy for cyclopentanoids.

Scheme I



Scheme II



Results and Discussion

Synthesis of 2,3-Disubstituted Cyclopentanones by Reductive Cleavage of 6-Oxonorbornane-2-carboxylates. We have chosen oxonorbornanecarboxylates **4** as the bicyclic compounds which were transformed to cyclopentanones **3** by reductive cleavage. Reduction of **4a** was carried out with an excess lithium in liquid ammonia to give **3a** in 80% yield. It should be noted that the norbornanone **5** is considered to be a masked form of 3-substituted cyclopent-2-en-1-olate **7**. Since it is difficult to form the enolate of 2-norbornanones at the bridge head, formation of the enolate from **5** is site selective, which generates a synthetically equivalent enolate **7**. On the other hand, selective formation of the enolate **7** from the corresponding cyclopentanone **6** is difficult (Scheme II).

(1) *Natural Products Chemistry*; Nakanishi, K., Goto, T.; Ito, S., Natori, S., Nozoe, S., Eds.; Kodansha Scientific: Tokyo, 1974; Vol. 1.

(2) For recent works, see: (a) Nemoto, H.; Ando, M.; Fukumoto, K. *Tetrahedron Lett.* **1990**, *31*, 6205. (b) Yamada, H.; Shimizu, K.; Nisar, M.; Takahashi, T.; Tsuji, J. *Tetrahedron Lett.* **1990**, *31*, 2407. (c) Haynes, R. K.; Vonwiller, S. C.; Hambley, T. *J. Org. Chem.* **1989**, *54*, 5162. (d) Brandes, E.; Grieco, P. A.; Garner, P. *J. Chem. Soc., Chem. Commun.* **1988**, 500. (e) Haynes, R. K.; Vonwiller, S. C. *J. Chem. Soc., Chem. Commun.* **1987**, 92. (f) Mukaiyama, T.; Tamura, M.; Kobayashi, S. *Chem. Lett.* **1987**, 743. (g) Nemoto, H.; Kurobe, H.; Fukumoto, K.; Kametani, T. *J. Org. Chem.* **1986**, *51*, 5311. (h) Takahashi, T.; Miyazawa, M.; Ueno, H.; Tsuji, J. *Tetrahedron Lett.* **1986**, *27*, 3811. (i) Hutchinson, J. H.; Money, T. *J. Chem. Soc., Chem. Commun.* **1986**, 288. (j) Taber, D. F.; Krewson, K. R.; Raman, K.; Rheingold, A. L. *Tetrahedron Lett.* **1984**, *25*, 5283. (k) Ziegler, F. E.; Lim, H. *J. Org. Chem.* **1984**, *49*, 3278. (l) Hatakeyama, S.; Numata, H.; Takano, S. *Tetrahedron Lett.* **1984**, *25*, 3617. (m) Desmaele, D.; Ficini, J.; Guingant, A.; Touzin, A. M. *Tetrahedron Lett.* **1983**, *24*, 3079. (n) Ziegler, F. E.; Mencel, J. T. *Tetrahedron Lett.* **1983**, *24*, 1859.

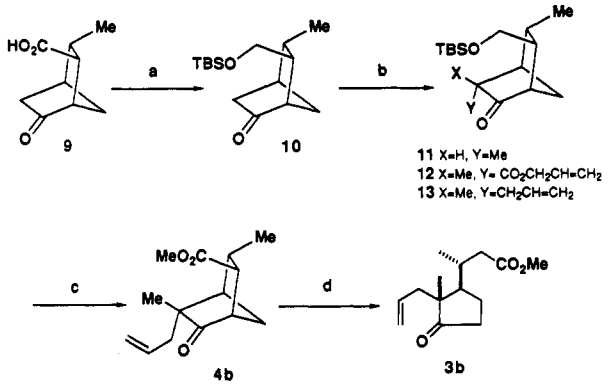
(3) (a) Shimizu, I.; Aida, F. *Chem. Lett.* **1988**, 601. (b) Shimizu, I.; Matsuda, N.; Noguchi, Y.; Zako, Y.; Nagasawa, K. *Tetrahedron Lett.* **1990**, *31*, 4899. (c) Nagasawa, K.; Zako, Y.; Ishihara, H.; Shimizu, I. *Tetrahedron Lett.* **1991**, *32*, 4937.

(4) (a) Trost, B. M.; Bernstein, P. R.; Funfschilling, P. C. *J. Am. Chem. Soc.* **1979**, *101*, 4378. (b) Grieco, P. A.; Takigawa, T.; Moore, D. R. *Ibid.* **1979**, *101*, 4380. (c) Stevens, R. V.; Lawrence, D. S. *Tetrahedron* **1985**, *41*, 93.

(5) Gassman, P. G.; Creary, X. *J. Chem. Soc., Chem. Commun.* **1972**, 1214.

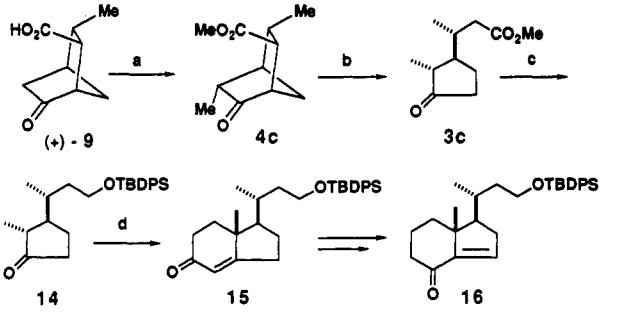
0022-3263/93/1958-1483$04.00/0

Scheme III[a]



[a] (a) (1) $LiAlH_4$, Et_2O, 0 °C to rt, 90%, (2) TBDMSCl, imidazole, DMF, rt., 95%, (3) PDC, CH_2Cl_2, rt., 92%; (b) (1) LDA, MeI, THF, 0 °C, 81%, (2) LDA, $ClCO_2CH_2CH{=}CH_2$, THF, 0 °C, 60% (3) $Pd(OAc)_2$, PPh_3, THF, 60 °C, 65%; (c) (1) Jones reagent, acetone, 0 °C; (2) MeOH, H_2SO_4, reflux, 70% for the two steps; (d) Li, NH_3, -78 °C, 71%.

Scheme IV[a]



[a] (a) (1) LDA (2.4 equiv), MeI, THF, -20 °C, (2) MeOH, *p*-TsOH, reflux, 78% overall; (b) Li, naphthalene, THF, -60 °C, 74%, (c) (1) $LiAlH_4$, Et_2O, 0 °C, 100%, (2) $NaBrO_2$, H_2O–AcOH, rt, 76%, (3) TBDPSCl, imidazole, DMF, rt, 98%; (d) methyl vinyl ketone, NaOH, MeOH, rt to reflux, 60%.

In addition to the site selectivities, carbon–carbon bond formation at the α-position of the cyclopentanone is also expected to proceed stereoselectively. As an application, a known intermediate of the steroid D-ring **3b**[6] was synthesized (Scheme III). Reduction of the carboxylic acid **9** with $LiAlH_4$ in ether at room temperature, followed by protection of the primary alcohol with *tert*-butyldimethylsilyl chloride using imidazole in DMF, and subsequent oxidation of the secondary alcohol with PDC gave the ketone **10** in 78% yield from **9** (Scheme IV). The ketone **10** was transformed to its enolate with LDA and allowed to react with methyl iodide to give **11** in 81% yield. Allylation of **11** to **13** with allyl bromide using LDA as a base did not proceed; therefore the palladium-catalyzed decarboxylative allylation method was adopted.[7] Enolate formation from **11** with LDA followed by reaction with allyl chloroformate gave keto ester **12** in 60% yield. Reaction of **12** in the presence of a catalytic amount of $Pd(OAc)_2$–PPh_3 in THF at reflux temperature gave the α-allyl ketone **13** in 65% yield, which was then converted to the keto ester **4b** by Jones oxidation and Fischer esterification with methanol in 70% yield. Reductive cleavage of keto ester **4b** with an excess lithium in liquid ammonia afforded the 2-allyl-2-methylcyclopentanone **3b** in 71% yield as one diastereomer, and whose stereochemistry was determined by ^1H NMR analysis. The signal showing the methyl group on the α-position appeared at δ 0.97 as a singlet,[6] which indicates that the allyl group was introduced from the less hindered convex face of the norbornanone **10**.

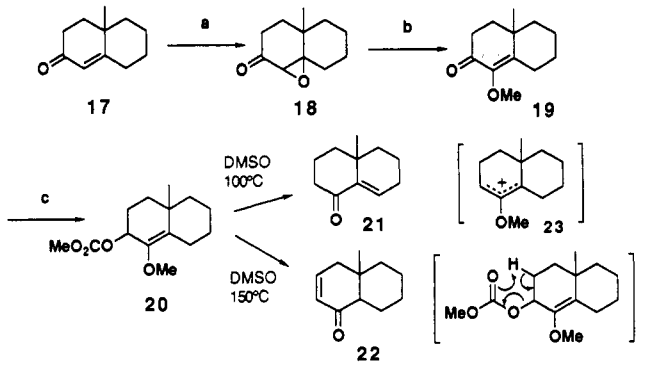
Synthesis of 1α,25-Dihydroxyvitamin D_3 CD-Ring 2 from the Cyclopentanone (+)-3c via Robinson Annulation and Transposition of the α,β-Unsaturated Ketone. 1α,25-Dihydroxyvitamin D_3 (**1a**) is known to play an important role in maintaining calcium homeostasis.[8] Recently, this hormone was found to induce cellular differentiation of human myeloid leukemia cells.[9] These potent biological activities have prompted a lot of synthetic efforts in recent years. Since we are interested in the structure–activity relationships of this hormone, asymmetric synthetic methods have been investigated in our laboratory. The procedure we have developed for the synthesis of 2,3-disubstituted cyclopentanones by the reductive cleavage of bicyclic compounds is applicable to synthesizing the steroid D rings. We have synthesized the CD-ring **2**, a key intermediate of Lythgoe's vitamin D_3 synthesis,[10] from (−)-**3c** obtained by reductive cleavage of the optically active (+)-**4c**.

The starting keto carboxylic acid (+)-**9** was prepared from the optically active norbornene carboxylic acid[11] according to the method reported by Beckmann.[12] Thus, iodo lactonization, followed by alkaline dehydroiodation and subsequent hydrolysis gave keto carboxylic acid **9** in 90% yield. The dianion prepared from the keto carboxylic acid **9** with LDA (2.4 equiv) was treated with methyl iodide,[13] which was followed by esterification with methanol using a catalytic amount of *p*-toluenesulfonic acid to give (+)-**4c** in 78% yield from **9**. Reductive cleavage of keto ester **4c** was carried out with an excess lithium in liquid ammonia to give cyclopentanone **3c** in 54% yield. When ester **4c** was treated with lithium naphthalenide at −60 °C, the yield of **3c** increased to 74%. Keto ester **3c** was reduced to the diol with $LiAlH_4$, which was followed by selective oxidation of the secondary alcohol with $NaBrO_2$[14] and protection of the primary alcohol with *tert*-butyldiphenylsilyl chloride to give ketone **14** in 74% yield from **3c**. Steroid CD-ring **15** was synthesized by Robinson annulation of cyclopentanone **14**.[2c,g,15] Ketone **14** was treated with freshly distilled methyl vinyl ketone and sodium hydroxide followed by dehydration to give indenone **15** in 60% yield, and the unreacted cyclopentanone **14** was recovered in 19% yield.

(6) Ziegler, F. E.; Mencel, J. J. *Tetrahedron Lett.* **1983**, *24*, 1859.
(7) Tsuji, J.; Yamada, T.; Minami, I.; Yuhara, M.; Nisar, M.; Shimizu, I. *J. Org. Chem.* **1987**, *52*, 2988.

(8) (a) Norman, A. W. *Vitamin D, "The Calcium Homeostatic Steroid Hormone"*; Academic Press: New York, 1979. (b) *Comprehensive Medicinal Chemistry*; DeLuca, H. F., Burmester, J., Darwish, H.; Krisinger, J., Eds.; Pergamon Press: New York, 1990; Vol. 3.
(9) (a) Abe, E.; Miyaura, C.; Sakagami, H.; Takeda, M.; Konno, K.; Yamazaki, T.; Yoshiki, S.; Suda, T. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *78*, 4990. (b) Ikekawa, N.; Fujimoto, Y. *J. Synth. Org. Chem. Jpn.* **1988**, *46*, 455 and references therein.
(10) Baggiolini, E. G.; Iacobelli, J. A.; Hennessy, B. M.; Batcho, A. D.; Sereno, J. F.; Uskokovic, M. R. *J. Org. Chem.* **1986**, *51*, 3098.
(11) (a) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238. (b) Poll, T.; Abdel Hady, A. F.; Karge, R.; Linz, G.; Weetman, J.; Helmchen, G. *Tetrahedron Lett.* **1989**, *30*, 5595.
(12) Beckmann, S.; Geiger, H.; Schaber-Kiechle, M. *Chem. Ber.* **1959**, *92*, 2419.
(13) Pfeffer, P. E.; Silbert, L. S.; Chirinko, J. M. *J. Org. Chem.* **1972**, *37*, 451.
(14) Kageyama, T.; Ueno, Y.; Okawara, M. *Synthesis* **1983**, 815.
(15) (a) Wovkulich, P. M.; Barcelos, F.; Batcho, A. D.; Sereno, J. F.; Baggiolini, E. G.; Hennessy, B. M.; Uskokovic, M. R. *Tetrahedron* **1984**, *40*, 2283. (b) Daniewski, A. R.; Kiegiel, J. *J. Org. Chem.* **1988**, *53*, 5534. (c) Suzuki, T.; Sato, E.; Unno, K.; Kametani, T. *J. Chem. Soc., Chem. Commun.* **1988**, 724.

Scheme V[a]



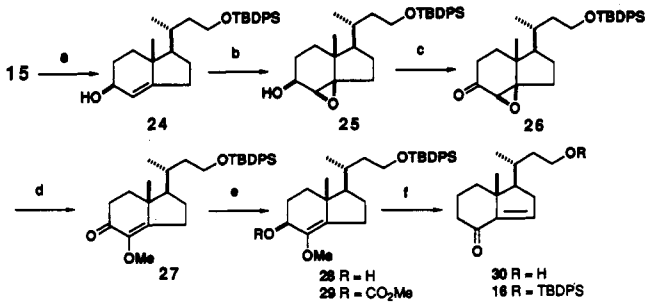
[a] (a) 6 N NaOH, 30% H_2O_2, MeOH, 0 °C, 84%; (b) KOH, MeOH, reflux, 53%; (c) (1) $LiAlH_4$, Et_2O, 0 °C, 83%, (2) $ClCO_2CH_3$, pyridine, DMAP, 0 °C, 92%.

In order to transform **15** to Grundmann ketone **2**, 1,2-transposition of the carbonyl group and hydrogenation of the olefin to the trans-fused indanone were necessary.[16] Recently, Okamura reported the stereoselective hydrogenation of an indenone similar to **16** via the α-hydroxy allylic alcohol using $RhCl(PPh_3)_3$ catalyst.[16f,17] Prior to the synthesis of **16** from **15**, the 1,2-enone transposition was investigated using the octalone **17**. Reaction of enone **17** (Scheme V) with hydrogen peroxide in alkaline methanol solution gave epoxide **18** in 84% yield. Epoxide **18** was then treated with methanol in the presence of potassium hydroxide at reflux temperature to give methoxy enone **19** in 53% yield. This methoxy enone upon reduction with $NaBH_4$–$CeCl_3$ followed by methoxycarbonylation with methyl chloroformate gave allylic carbonate **20** in 77% yield from **19**. At first, we tried the demethoxycarboxylation of **20** using a palladium catalyst.[18] However, satisfactory results were not obtained. Fortunately we then found out that the thermal demethoxycarboxylation proceeds with high selectivity. Thus, reaction of carbonate **20** in DMSO at 100 °C for 12 h gave the desired enone **21** in 96% yield.

The regioselectivity of thermal reaction is dependent on the temperature as evidenced by the predominant formation of the regioisomer **22** at 150 °C. The difference in the regioselectivity can be explained as follows. The thermal reaction at 100 °C proceeds via the stable allylic cation **23** formed by elimination of the (methoxycarbonyl)-oxy leaving group. However, it is possible that at 150 °C the thermal pericyclic retro-ene-type reaction of the carbonate **20** takes place predominantly by migration of the vicinal hydrogen.

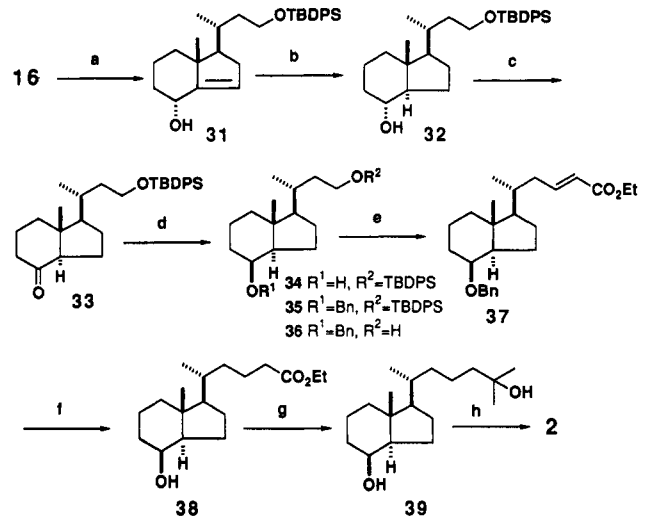
1,2-Transposition of enone **15** to **16** was carried out by a procedure similar to that described for octalone **17**. However, unlike octalone **17**, enone **15** could not be epoxidized with alkaline hydrogen peroxide. An alternative route to the epoxy ketone was therefore employed. Ketone **15** was reduced with $NaBH_4$ in the presence of $CeCl_3$ to give an 85% yield of allylic alcohol **24**, which was

Scheme VI[a]



[a] (a) $NaBH_4$, $CeCl_3$, EtOH, −78 °C, 85%; (b) *tert*-butyl hydroperoxide, $VO(acac)_2$, benzene, 0 °C, 80%; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 96%; (d) KOH, MeOH, reflux, 77%; (e) (1) $LiAlH_4$, Et_2O, 0 °C, 100%, (2) $ClCO_2CH_3$, pyridine, DMAP, 0 °C, 84%; (f) (1) DMSO, 100 °C, 75%, (2) TBDPSCl, imidazole, DMF, rt, 60%.

Scheme VII[a]



[a] (a) $NaBH_4$, $CeCl_3$, EtOH, −78 °C, 85%; (b) $RhCl(PPh_3)_3$, H_2, CH_2Cl_2, rt, 80% (c) PDC, CH_2Cl_2, rt, 88%; (d) (1) $LiAlH_4$, Et_2O, 0 °C, 100%, (2) BnBr, KH, THF, 0 °C, 100%; (3) Bu_4NF, THF, rt, 95%; (e) (1) PDC, CH_2Cl_2, rt, 84%; (2) $(EtO)_2P(=O)CH_2CO_2Et$, NaH, THF, 0 °C, 89%; (f) 5% Pd–C, H_2, EtOH, rt, 72%; (g) CH_3MgI (4 equiv), Et_2O, 0 °C, 86%; (h) (1) PDC, CH_2Cl_2, rt, 91%, (2) TMS-imidazole, CH_2Cl_2 rt, 77%.

epoxidized with *tert*-butyl hydroperoxide using $VO(acac)_2$ as catalyst[19] (Scheme VI). Subsequent Swern oxidation[20] of epoxy alcohol gave **26** in 77% yield from **24**. Methanolysis of keto epoxide **26** gave a 77% yield of methyl enol ether **27**, which was reduced with $LiAlH_4$ to give the β-alcohol **28** selectively in 100% yield. Methoxycarbonylation of **28** was carried out by treatment with methyl chloroformate and pyridine and thermolysis of the resulting allylic carbonate **29** at 100 °C in DMSO gave enone **30** in 63% yield from **28**. The hydroxy group of **30** deprotected during thermolysis was protected again by treatment with *tert*-butyldiphenylsilyl chloride and imidazole which gave enone **16** in 60% yield.

Enone **16** was then converted to the Grundmann ketone **2**. Reduction with $NaBH_4$ in the presence of $CeCl_3$ gave α-alcohol **31** selectively in 85% yield (Scheme VII). Catalytic hydrogenation of the allylic alcohol **31** with RhCl-

(16) (a) Lythgoe, B.; Roberts, D. A.; Waterhouse, I. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2608. (b) Baggiolini, E. G.; Iacobelli, J. A.; Hennessy, B. M.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 2945. (c) Desmaele, D.; Ficini, J.; Guingant, A.; Touzin, A. M. *Tetrahedron Lett.* **1983**, *24*, 3083. (d) Daniewski, A. R.; Kiegiel, J. *J. Org. Chem.* **1988**, *53*, 5534. (e) Mandai, T.; Matsumoto, T.; Kawada, M.; Tsuji, J. *J. Org. Chem.* **1992**, *57*, 1326. (f) Fernandez, B.; Martinez Perez, J. A.; Granja, J. R.; Mouriño, A. *J. Org. Chem.* **1992**, *57*, 3173.

(17) Hoeger, C. A.; Okamura, W. H. *J. Am. Chem. Soc.* **1985**, *107*, 268.

(18) Takahashi, T.; Nakagawa, N.; Minoshima, T.; Yamada, H.; Tsuji, J. *Tetrahedron Lett.* **1990**, *31*, 4333.

(19) (a) Sharpless, K. B.; Michaelson, R. *J. Am. Chem. Soc.* **1973**, *95*, 6136. (b) Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. *J. Am. Chem. Soc.* **1979**, *101*, 159. (c) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.

(20) Mancuso, A. J.; Huang, S. L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

$(PPh_3)_3$ in CH_2Cl_2 gave **32** exclusively,[17] which was determined by ^1H NMR analysis. The stereochemistry of **32** was confirmed by oxidation with PDC to ketone **33**, whose ^1H NMR spectrum showed the 18-methyl group as a singlet at δ 0.60 (versus δ 1.05 for the cis isomer of **33**).[21]

Reduction of ketone **33** with $LiAlH_4$ gave the β-alcohol **34**, which was then protected as a benzyl ether with benzyl bromide and potassium hydride in THF to give **35** from **33** quantitatively. Elimination of the *tert*-butyldiphenylsilyl group with Bu_4NF, followed by oxidation of the alcohol with PDC gave the corresponding aldehyde, which was subjected to Horner–Emmons reaction with $(EtO)_2P(O)CH_2CO_2Et$ and sodium hydride to give unsaturated ester **37** in 71% yield from **35**. Hydrogenation of the olefin and removal of the benzyl group were carried out simultaneously with palladium on carbon as catalyst. Methylation of **38** with 4 equiv of CH_3MgI gave the diol **39** in 62% yield from **37**. Finally, oxidation of the secondary alcohol with PDC followed by protection of the tertiary alcohol with TMS-imidazole gave **2**[10] in 70% yield from **39**, whose ^1H NMR, ^{13}C NMR, and IR spectral data were identical with those of the authentic sample.[22]

Conclusion

The reductive cleavage of 6-oxonorbornane-2-carboxylates provides a useful method for producing α,β-disubstituted cyclopentanones, which is applicable to the synthesis of 1α,25-dihydroxyvitamin D_3 CD-ring synthon **2**.

Experimental Section

General Methods. Optical rotations were measured at 589 nm in a 1-mL quartz sample cell. ^1H NMR spectra were recorded in $CDCl_3$ at 400 or 100 MHz unless specified otherwise. THF was distilled from benzophenone ketyl. CH_2Cl_2 was distilled from P_2O_5. DMSO was distilled from CaH_2. TLC was performed using Merck silica gel 60F glass plates (Art. 5715, 0.25 mm thick). Flash chromatography was performed using Wakogel C-300.

Methyl (1*S,2*R**,3*S**,4*S**)-3-Methyl-6-oxobicyclo[2.2.1]heptane-2-carboxylate (4a).** This compound was prepared by esterification of (±)-**9** in refluxing methanol for 1 h using a catalytic amount of H_2SO_4 in 77% yield (270 mg): ^1H NMR (60 MHz, CCl_4) δ 3.59 (s, 3 H), 2.76–1.06 (m, 8 H), 1.10 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (22.5 MHz) δ 214.00, 173.27, 54.21, 51.89, 51.62, 44.78, 41.40, 38.87, 35.67, 21.31; IR (neat) 1740 cm^{-1}.

(3*S)-3-[(1*R**)-2-(Methoxycarbonyl)-1-methylethyl]cyclopentanone (3a).** Lithium turnings (100 mg) were added to dry NH_3 (distilled from Na, 30 mL). To the mixture was added a solution of the keto ester **4a** (250 mg, 1.36 mmol) in THF (2 mL) at −78 °C, the resulting mixture was stirred for 30 min, and excess lithium was quenched by the addition of isoprene. To the mixture was added saturated NH_4Cl. The organic layer was extracted with ethyl acetate, and the extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel to give the cyclopentanone **3a** (200 mg, 80%); ^{13}C NMR (22.5 MHz) δ 218.15, 173.06, 51.46, 42.93, 42.68, 39.46, 38.94, 35.39, 27.64, 18.16; IR (neat) 1780, 1730 cm^{-1}; MS (CI) 185 (MH^+); HRMS calcd for $C_9H_{13}O_2$ (M^+ − OMe) 153.0916, found 153.0926.

(1*S,4*S**,5*S**,6*R**)-6-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-5-methylbicyclo[2.2.1]heptan-2-one (10).** To a solution of the carboxylic acid **9** (480 mg, 2.85 mmol) in ether (15 mL) was added $LiAlH_4$ (542 mg, 14.3 mmol) at 0 °C, and the mixture was stirred for 1 h at rt. To the reaction mixture was added H_2O (0.5 mL), 15% NaOH (0.5 mL), and H_2O (1.5 mL) successively at 0 °C. The mixture was diluted with ether, $MgSO_4$ was added, and the resultant mixture was stirred for 1 h at rt. The resulting mixture was filtered and concentrated in vacuo to give the diol (400 mg, 90%): ^1H NMR δ 4.17 (m, 1 H), 3.75 (br s, 2 H), 2.22 (br s, 1 H), 2.04 (m, 1 H), 1.81 (br d, 1 H), 1.64 (m, 2 H), 1.45 (dd, J = 1.4, 10.3 Hz, 1 H), 1.27 (d, J = 10.1 Hz, 1 H), 1.19 (t, J = 6.9 Hz, 1 H), 0.94 (d, J = 6.6 Hz, 3 H); ^{13}C NMR δ 72.60, 60.83, 51.57, 47.03, 43.24, 38.95, 37.24, 35.41, 20.93; IR (neat) 3274, 2949 cm^{-1}.

A mixture of the diol (400 mg, 2.56 mmol), imidazole (272 mg, 4.0 mmol), and *tert*-butyldimethylsilyl chloride (430 mg, 2.86 mmol) in CH_2Cl_2 (2 mL) was stirred at rt for 10 min. The reaction mixture was quenched with water, and the aqueous layer was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 5% ether–hexane to give the silyl ether (660 mg, 95%): ^1H NMR δ 4.08 (m, 1 H), 3.88 (dd, J = 2.2, 11.3 Hz, 1 H), 3.82 (dd, J = 4.4, 11.3 Hz, 1 H), 2.23 (br s, 1 H), 2.08 (m, 1 H), 1.81 (br d, J = 4.8 Hz, 1 H), 1.59 (m, 2 H), 1.44 (m, 1 H), 1.29–1.24 (m, 2 H), 0.91 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR δ 73.13, 62.07, 51.56, 47.93, 43.43, 40.06, 37.30, 35.67, 25.75, 20.92, 18.23, −5.69; IR (neat) 3422, 2950, 2858, 1471 cm^{-1}.

A mixture of the alcohol (550 mg, 2.0 mmol) and pyridinium dichromate (1.53 g, 4.0 mmol) in CH_2Cl_2 (15 mL) was stirred for 1 h at rt. The reaction mixture was filtered through a Florisil column, and the filtrate was concentrated in vacuo to give the ketone **10** (493 mg, 92%): ^1H NMR δ 3.50 (dd, J = 6.6, 10.2 Hz, 1 H), 3.39 (dd, J = 6.9, 10.2 Hz, 1 H), 2.52 (br d, J = 3.3 Hz, 1 H), 2.20 (br d, J = 2.9 Hz, 1 H), 2.00 (dd, J = 4.8, 17.6 Hz, 1 H), 1.83–1.72 (m, 3 H), 1.59 (dd, J = 1.4, 10.2 Hz, 1 H), 1.47 (m, 1 H), 1.09 (d, J = 7.0 Hz, 3 H), 0.84 (s, 9 H), 0.00 (s, 3 H), −0.01 (s, 3 H); ^{13}C NMR δ 216.63, 64.25, 53.56, 49.89, 45.59, 41.40, 38.68, 35.36, 25.78, 21.58, 18.16, −5.62; IR (neat) 2954, 2885, 1741, 1471 cm^{-1}. Anal. Calcd for $C_{15}H_{28}O_2Si$: C, 67.11; H, 10.52. Found: C, 66.89; H, 10.52.

(1*S,3*R**,4*S**,5*S**,6*R**)-6-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-3,5-dimethylbicyclo[2.2.1]heptan-2-one (11).** The silyl ether **10** (1.8 g, 6.7 mmol) was added to a solution of LDA (prepared from *n*-BuLi 1.6 M in hexane, 4.6 mL, and diisopropylamine, 1.0 mL) in THF (50 mL) at 0 °C. After the mixture was stirred for 5 min, iodomethane (32 mmol, 2 mL) was added. The mixture was stirred for 30 min at 0 °C. Water was added to the mixture, and the resultant mixture was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel to give **11** (1.54 g, 81%): ^1H NMR (60 MHz, CCl_4) δ 3.41 (d, J = 7.0 Hz, 2 H), 2.50–0.91 (m, 12 H), 0.89 (s, 9 H), 0.00 (s, 6 H).

Allyl (1*S,2*R**,4*S**,5*R**,6*S**)-5-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-2,6-dimethyl-3-oxobicyclo[2.2.1]heptane-2-carboxylate (12).** The ketone **11** (1.5 g, 5.3 mmol) was added to a solution of LDA (prepared from *n*-BuLi 1.6 M in hexane, 3.9 mL, and diisopropylamine, 0.87 mL, 6.3 mmol) in THF (20 mL) at 0 °C, and the mixture was stirred for 5 min. The allyl chloroformate (1.3 g, 10.6 mmol) was added to the mixture, and the resulting mixture was stirred for 30 min. Water was added to the mixture, and the resultant mixture was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel to give the allyl ester **12** (1.1 g, 60%): ^1H NMR (60 MHz, CCl_4) δ 6.23–5.10 (m, 3 H), 4.60 (d, J = 7.0 Hz, 2 H), 3.70–3.30 (m, 2 H), 2.50–0.90 (m, 9 H), 1.15 (s, 3 H), 0.89 (s, 9 H), 0.00 (s, 6 H); IR (neat) 1770, 1750 cm^{-1}.

(1*S,3*S**,4*R**,5*S**,6*R**)-3-Allyl-6-[[(*tert*-Butyldimethylsilyl)oxy]methyl]-3,5-dimethylbicyclo[2.2.1]heptan-2-one (13).** A mixture of the ester **12** (500 mg, 1.14 mmol), $Pd(OAc)_2$ (24 mg, 0.11 mmol), and PPh_3 (57 mg, 0.22 mmol) in THF (10 mL) was heated to reflux for 1 h, and the reaction mixture was concentrated in vacuo. The residue was chromatographed on silica gel to give the α-allyl ketone **13** (392 mg, 85%): ^1H NMR (60 MHz, CCl_4) δ 5.90–4.80 (m, 3 H), 3.90–3.20 (m, 4 H), 2.50–0.90 (m, 12 H), 0.85 (s, 9 H), 0.00 (s, 6 H).

(21) The cis isomer was obtained from **15**, (1) $HSCH_2CH_2SH$, BF_3·Et_2O; (2) TBDMSCl, imidazole, (29%, 2 steps); (3) Li-NH_3, 58%; (4) BH_3-Me_2S, H_2O_2, 77%; (5) PCC, 53%. Related compounds, see: Paker, K. A.; Iqbal, T. *J. Org. Chem.* **1982**, *47*, 337 and ref 16f.

(22) Recently an efficient preparative method for the ketone **2** from vitamin D_3 has reported: Kiegiel, J.; Wovklich, P. M.; Uskokovic, M. R. *Tetrahedron Lett.* **1991**, *32*, 6057.

Methyl (1S*,2R*,3S*,4R*,5R*)-5-Allyl-3,5-dimethyl-6-oxobicyclo[2.2.1]heptane-2-carboxylate (4b). Jones oxidation reagent (1.4 N, 2 mL, 2.8 mmol) was added slowly to a solution of **13** (300 mg, 1.06 mmol) in acetone (20 mL) at 0 °C. The reaction mixture was quenched with 2-propanol and diluted with water. Acetone was evaporated in vacuo, and the residue was extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was diluted with methanol (30 mL), and a catalytic amount of H_2SO_4 was added to the solution. The mixture was stirred for 1 h at reflux. The reaction mixture was quenched with K_2CO_3 and concentrated in vacuo. The residue was diluted with water and extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel to give the ester **4b** (176 mg, 70%): ^1H NMR (60 MHz, CCl_4) δ 5.90–4.80 (m, 3 H), 3.65 (s, 3 H), 2.85–1.60 (m, 8 H), 1.19 (s, 3 H), 1.10 (d, J = 6.0 Hz, 3 H); ^{13}C NMR (22.5 MHz) δ 218.63, 173.24, 133.37, 118.35, 54.58, 53.07, 52.04, 49.62, 40.11, 32.85, 32.59, 21.69, 17.22.

(2R*,3R*)-2-Allyl-3-[(1R)-2-(methoxycarbonyl)-1-methyl]-3-methylcyclopentanone (3b). By a procedure similar to **4a**, **4b** (70 mg, 0.29 mmol) was converted to **3b** (50 mg, 71%): ^1H NMR (60 MHz, CCl_4) δ 5.90–4.80 (m, 3 H), 3.69 (s, 3H), 2.61–1.25 (m, 10 H), 1.07 (d, J = 6.0 Hz, 3 H), 0.97 (s, 3 H); ^{13}C NMR (22.5 MHz) δ 222.78, 173.54, 134.38, 118.52, 52,18, 51.57, 46.12, 42.02, 39.89, 37.68, 32.14, 23.88, 19.37, 17.92; HRMS calcd for $C_{14}H_{22}O_3$ 238.1569, found 238.1591.

Methyl (1S,2R,3S,4R,5R)-3,5-Dimethyl-6-oxobicyclo[2.2.1]heptane-2-carboxylate (4c). To a solution of diisopropylamine (17.1 mL, 122.3 mmol) in THF (300 mL) was added *n*-BuLi (1.6 M in hexane, 73.4 mL, 117.4 mmol) at −20 °C. The optically active carboxylic acid **9**[11,12] (8.22 g, 48.9 mmol) in THF (30 ml) was added over 20 min while the temperature was maintained below 0 °C. The milky white solution was warmed to rt and stirred for 30 min. After the mixture was cooled to 0 °C, iodomethane (12.2 mL, 196 mmol) was added rapidly to the mixture, and the resulting mixture was stirred for 20 min at 0 °C and then for 1.5 h at rt. The reaction mixture was quenched with ice-cold 3 N HCl, and the aqueous layer was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue (10.7 g) was dissolved in methanol (80 mL), and the mixture was stirred for 2 h at reflux in the presence of a catalytic amount of *p*-toluenesulfonic acid. To the reaction mixture was added saturated $NaHCO_3$, and most of the solvent was removed under reduced pressure. The residue was extracted with ether, and the extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 15% ethyl acetate–hexane to give the keto ester **4c** (7.45 g, 78%): $[\alpha]^{24}_D$ = +41° (*c* 1.6, $CHCl_3$); ^1H NMR δ 3.65 (s, 3 H), 2.73 (m, 1 H), 2.45 (t, J = 4.7 Hz, 1 H), 2.20 (ddq, J = 1.1, 4.7, 6.9 Hz, 1 H), 2.03 (m, 1 H), 1.95 (qd, J = 2.9, 7.6 Hz, 1 H), 1.85–1.82 (m, 2 H), 1.18 (d, J = 6.9 Hz, 3 H), 1.08 (d, J = 1.2 Hz, 3 H); ^{13}C NMR (22.5 MHz) δ 216.28, 173.04, 53.58, 51.35, 50.83, 47.65, 47.40, 39.64, 32.28, 20.83, 13.62; IR (neat) 1730, 1743 cm^{-1}; MS *m/z* 196 (M^+), 168, 165; HRMS(CI) calcd for $C_{11}H_{17}O_3$ (MH^+) 197.1177, found 197.1210.

(2R,3R)-3-[(1R)-2-(Methoxycarbonyl)-1-methylethyl]-2-methylcyclopentanone (3c). A mixture of naphthalene (12.2 g, 94.9 mmol) and lithium powder (632 mg, 91.1 mmol) in THF (190 mL) were stirred for 1 h at rt. The resulting mixture was cooled to −60 °C. The keto ester **4c** (7.45 g, 37.95 mmol) in THF (10 mL) was added to the solution, and the mixture was stirred for 30 min. The reaction mixture was quenched with 3 N HCl, and the aqueous layer was extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 15% ethyl acetate–hexane to give the cyclopentanone **3c** (5.55 g, 74%): $[\alpha]^{24}_D$ = −57° (*c* 1.4, $CHCl_3$); ^1H NMR δ 3.47 (s, 3 H), 2.24 (dd, J = 4.3, 14.6 Hz, 1 H), 2.14 (ddd, J = 1.0, 9.2, 17.0 Hz, 1 H), 2.02–1.82 (m, 4 H), 1.64 (ddt, J = 0.9, 6.8, 18.0 Hz, 1 H), 1.52 (qd, J = 5.8, 16.6 Hz, 1 H), 1.28 (dq, J = 9.7, 11.7 Hz, 1 H), 0.90 (d, J = 6.8 Hz, 3 H), 0.85 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (22.5 MHz) δ 219.83, 172.95, 51.08, 49.11, 46.53, 37.31, 36.67, 31.87, 23.11, 17.80, 13.67; IR (neat) 1781, 1736 cm^{-1}; HRMS (CI) calcd for $C_{11}H_{19}O_3$(MH^+) 199.1333, found 199.1324.

(2R,3R)-3-[(1R)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-2-methylcyclopentanone (14). To a solution of the ketone **3c** (232 mg, 1.17 mmol) in ether (8 mL) was added $LiAlH_4$ (220 mg, 5.85 mmol) at 0 °C. After stirring for 30 min, the reaction was quenched by the successive addition of H_2O (0.2 mL), 15% NaOH (0.2 mL), and H_2O (0.6 mL). The mixture was diluted with ether (10 mL), and $MgSO_4$ was added. The mixture was stirred at rt for 1 h. The resulting mixture was filtered and concentrated in vacuo to give the diol (200 mg, 100%): ^1H NMR δ 3.61 (m, 2 H), 3.52 (m, 1 H), 3.11 (br s, 1 H), 2.94 (br s, 1 H), 1.78–1.40 (m, 7 H), 1.24 (m, 2 H), 0.94 (d, J = 6.9 Hz, 3 H), 0.86 (d, J = 6.6 Hz, 3 H); IR (neat) 3343, 2953 cm^{-1}.

The diol (90 mg, 0.52 mmol) and $NaBrO_2$ (65%, 458 mg, 15.8 mmol) were dissolved in 5 mL of water–acetic acid (50:1), and the mixture was stirred for 7 h at rt. The reaction mixture was quenched with aqueous $Na_2S_2O_3$ and extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 60% ethyl acetate–hexane to give the cyclopentanone (68 mg, 76%): $[\alpha]^{24}_D$ = −67° (*c* 1.4, $CHCl_3$); ^1H NMR δ 3.77 (m, 1 H), 3.66 (m, 1 H), 2.35 (dd, J = 8.0, 17.8 Hz, 1 H), 2.11 (d, J = 17.8 Hz, 1 H), 2.03 (m, 2 H), 1.93 (dd, J = 6.6, 11.4 Hz, 1 H), 1.83 (m, 1 H), 1.73 (m, 1 H), 1.70 (m, 1 H), 1.51 (dq, J = 11.4, 10.0 Hz, 1 H), 1.38 (m, 1 H), 1.10 (d, J = 6.9 Hz, 3 H), 1.02 (d, J = 6.6 Hz, 3 H); ^{13}C NMR δ 221.54, 61.08, 50.15, 46.79, 37.20, 35.15, 31.03, 23.15, 17.69, 13.88; IR (neat) 3434, 2926, 1732 cm^{-1}.

A solution of the cyclopentanone (68 mg, 0.40 mmol), imidazole (61 mg, 0.89 mmol), and *tert*-butyldiphenylsilyl chloride (0.13 mL, 0.50 mmol) in DMF (0.5 mL) was stirred for 1 h at rt. The mixture was cooled over ice, and water was added to the mixture. The mixture was extracted with ether, and the organic layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 5% ether–hexane to give **14** (160 mg, 98%): $[\alpha]^{24}_D$ = −16.0° (*c* 1.0, $CHCl_3$); ^1H NMR δ 7.67–7.65 (m, 4 H), 7.42–7.35 (m, 6 H), 3.76 (ddd, J = 4.8, 6.9, 10.2 Hz, 1 H), 3.68 (ddd, J = 5.9, 6.2, 10.2 Hz, 1 H), 2.32 (dd, J = 8.8, 18.7 Hz, 1 H), 2.07 (dt, J = 9.5, 11.3 Hz, 1 H), 1.93 (m, 1 H), 1.84 (m, 2 H), 1.73–1.62 (m, 2 H), 1.42 (ddd, J = 8.8, 11.7, 23.4 Hz, 1 H), 1.27 (m, 1 H), 1.05 (s, 9 H), 1.04 (d, J = 5.5 Hz, 3 H), 0.92 (d, J = 6.9 Hz, 3 H); ^{13}C NMR δ 221.45, 135.51, 133.82, 129.57, 127.59, 62.05, 50.16, 46.79, 37.21, 34.79, 30.58, 26.85, 22.90, 19.13, 17.81, 13.69; IR (neat) 2927, 1734 cm^{-1}; HRMS (CI) calcd for $C_{26}H_{37}O_2Si$ (MH^+) 409.2562, found 409.2561.

[1R-(1α,7aα)]-1-[(1R)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-1,2,3,6,7,7a-hexahydro-7a-methyl-5*H*-inden-5-one (15). To a solution of potassium hydroxide (48 mg, 0.87 mmol) in 3 mL of methyl alcohol–water (30:1) was added **14** (237 mg, 0.58 mmol) at 0 °C. The mixture was cooled to −20 °C, freshly distilled methyl vinyl ketone was slowly added to the solution, and the mixture was stirred for 14 h at rt and then for 4 h at reflux. The reaction was quenched by the addition of saturated NH_4Cl. The resulting solution was extracted with ether, and the combined organic layers were dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by flash chromatography through silica gel with 15–25% ethyl acetate–hexane to give the enone **15** (160 mg, 60%) and some unreacted ketone **14** (45 mg 19%). Enone **15**: $[\alpha]^{24}_D$ = +37.0° (*c* 2.5, $CHCl_3$); ^1H NMR δ 7.64–7.65 (m, 4 H), 7.42–7.35 (m, 6 H), 5.72 (br s, 1 H), 3.73 (ddd, J = 4.8, 7.3, 10.3 Hz, 1 H), 3.69 (ddd, J = 6.6, 8.0, 10.3 Hz, 1 H), 2.61 (ddt, J = 2.2, 10.6, 19.8 Hz, 1 H), 2.51 (ddd, J = 5.1, 14.7, 17.9 Hz, 1 H), 2.39 (m, 1 H), 2.29 (m, 1 H), 2.19 (ddd, J = 1.8, 5.1, 13.2 Hz, 1 H), 1.95 (m, 1 H), 1.82 (dt, J = 5.1, 13.5 Hz, 2 H), 1.72 (m, 1 H), 1.48 (m, 1 H), 1.39 (m, 1 H), 1.26 (m, 1 H), 1.06 (d, J = 5.8 Hz, 3 H), 1.05 (s, 9 H), 0.88 (d, J = 6.6 Hz, 3 H); ^{13}C NMR δ 199.27, 179.98, 135.57, 133.92, 129.58, 127.61, 121.61, 121.43, 61.44, 55.86, 45.03, 38.07, 36.93, 33.49, 31.19, 28.83, 26.86, 26.64, 19.16, 18.84, 16.04; IR (neat) 2929, 1668, 1471 cm^{-1}. Anal. Calcd for $C_{30}H_{40}O_2Si$: C, 78.12; H, 8.78. Found: C, 78.26; H, 8.99.

[1R-(1α,5α,7aα)]-1-[(1R)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-2,3,5,6,7,7a-hexahydro-7a-methyl-1*H*-inden-5-ol (24). To a solution of **15** (130 mg, 0.28 mmol) in EtOH (5 mL) was added $CeCl_3 \cdot 7H_2O$ (186 mg, 0.5 mmol), and the mixture

was stirred for 20 min at rt. The mixture was cooled to −78 °C, and $NaBH_4$ (19 mg, 0.5 mmol) in ethyl alcohol (1 mL) was added. After being stirred for 20 min, the reaction mixture was quenched by the addition of saturated NH_4Cl, and the organic layer was extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$, filtered, and evaporated in vacuo. The residue was purified by flash chromatography through silica gel with 25% ethyl acetate–hexane to give **24** (114 mg, 85%): $[\alpha]^{23}_D$ = +20.1° (*c* 1.7, $CHCl_3$); ^1H NMR δ 7.69–7.65 (m, 4 H), 7.42–7.35 (m, 6 H), 5.25 (quintet, *J* = 1.1 Hz, 1 H), 4.22 (ddt, *J* = 1.1, 2.6, 5.5 Hz, 1 H), 3.72 (ddd, *J* = 4.8, 7.7, 10.3 Hz, 1 H), 3.68 (ddd, *J* = 6.6, 7.7, 10.3 Hz, 1 H), 2.35 (tq, *J* = 13.2, 2.2 Hz, 1 H), 2.04 (m, 1 H), 1.96 (m, 1 H), 1.92–1.73 (m, 3 H), 1.66–1.52 (m, 2 H), 1.38 (dd, *J* = 1.5, 13.2 Hz, 1 H), 1.34 (ddd, *J* = 5.5, 11.0, 19.4 Hz, 1 H), 1.24 (m, 1 H), 1.15 (m, 1 H), 1.04 (s, 9 H), 0.94 (s, 3 H), 0.83 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR δ 153.56, 135.57, 134.07, 129.50, 127.57, 120.44, 68.43, 61.67, 56.15; 43.40, 38.17, 36.96, 31.93, 29.96, 27.30, 26.85, 26.61, 19.16, 18.75, 17.46; IR (neat) 3342, 2932, 1427 cm^{-1}. Anal. Calcd for $C_{30}H_{42}O_2Si$: C, 77.87; H, 9.16. Found: C, 77.57; H, 9.30.

[1*R*-(1α,3aα,4α,5α,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-3a,4-epoxyoctahydro-7a-methyl-1*H*-inden-5-ol (25). To a mixture of the alcohol **24** (114 mg, 0.24 mmol) and $VO(acac)_2$ (6.8 mg, 0.025 mmol) in benzene (4 mL) at 0 °C was added *tert*-butyl hydroperoxide (4.6 M in dichloroethane, 0.1 mL, 0.46 mmol), and the mixture was stirred for 1 h. The reaction mixture was quenched by the addition of Me_2S, and the resulting mixture was extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ and brine and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by flash chromatography through silica gel with 40% ethyl acetate–hexane to give the epoxy alcohol **25** (91 mg, 80%): $[\alpha]^{23}_D$ = +9.0° (*c* 1.6, $CHCl_3$); ^1H NMR δ 7.68–7.65 (m, 4 H), 7.42–7.37 (m, 6 H), 3.88 (dd, *J* = 5.5, 9.2 Hz, 1 H), 3.73 (ddd, *J* = 4.7, 7.7, 10.3 Hz, 1 H), 3.67 (ddd, *J* = 6.6, 8.1, 10.3 Hz, 1 H), 3.17 (d, *J* = 0.74 Hz, 1 H), 1.90–1.56 (m, 8 H), 1.50–1.34 (m, 2 H), 1.24 (m, 1 H), 1.14 (m, 1 H), 1.05 (s, 9 H), 0.91 (s, 3 H), 0.83 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR δ 135.56, 133.97, 129.53, 127.58, 74.53, 69.66, 64.39, 61.66, 56.53, 39.79, 37.69, 36.68, 30.96, 29.36, 26.83, 26.12, 25.30, 19.13, 19.01, 14.56; IR (neat) 3404, 2957, 1471 cm^{-1}. Anal. Calcd for $C_{30}H_{42}O_3Si$: C, 75.26; H, 8.85. Found: C, 75.47; H, 9.00.

[1*R*-(1α,3aα,4α,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-3a,4-epoxyoctahydro-7a-methyl-5*H*-inden-5-one (26). To a solution of oxalyl chloride (30 μL, 0.38 mmol) in CH_2Cl_2 (2 mL) at −78 °C was added DMSO (67 μL, 0.95 mmol). The mixture was stirred for 10 min, and a solution of the alcohol **25** (88 mg, 0.184 mmol) in CH_2Cl_2 (3 mL) was added. After being stirred for 1 h, the reaction mixture was treated with triethylamine (0.26 mL, 1.91 mmol) and then allowed to warm to rt. The resulting mixture was quenched with water and extracted with ether. The extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 12% ethyl acetate–hexane to give **26** (84 mg, 96%): $[\alpha]^{23}_D$ = +29.8° (*c* 1.8, $CHCl_3$); ^1H NMR δ 7.67–7.65 (m, 4 H), 7.42–7.38 (m, 6 H), 3.73 (ddd, *J* = 4.7, 7.3, 10.3 Hz, 1 H), 3.68 (ddd, *J* = 6.6, 8.1, 10.3 Hz, 1 H), 3.07 (s, 3 H), 2.73 (dt, *J* = 5.5, 13.9 Hz, 1 H), 1.97–1.67 (m, 8 H), 1.51 (m, 2 H), 1.25 (m, 2 H), 1.10 (s, 3 H), 1.05 (s, 9 H), 0.83 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR δ 209.28, 135.55, 133.89, 129.58, 127.60, 80.09, 62.46, 61.46, 56.01, 40.84, 40.19, 37.50, 32.23, 30.87, 28.98, 26.84, 19.14, 18.87, 14.64; IR (neat) 2961, 1715, 1471 cm^{-1}; HRMS (CI) calcd for $C_{30}H_{41}O_3Si$ (MH^+) 477.2824, found 477.2827.

[1*R*-(1α,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-1,2,3,6,7,7a-hexahydro-4-methoxy-7a-methyl-5*H*-inden-5-one (27). A mixture of the epoxy ketone **26** (84 mg, 0.176 mmol) and potassium hydroxide (15 mg, 0.275 mmol) in methyl alcohol (3.6 mL) was stirred for 9 h at reflux. The reaction mixture was quenched with saturated NH_4Cl. The mixture was diluted with water and extracted with ethyl acetate. The organic layer was dried over $MgSO_4$, filtered, and evaporated in vacuo. The residue was purified by flash chromatography through silica gel with 16% ethyl acetate–hexane to give the ketone **27** (66 mg, 77%): $[\alpha]^{23}_D$ = +75.4° (*c* 1.4, $CHCl_3$); ^1H NMR δ 7.68–7.66 (m, 4 H), 7.42–7.35 (m, 6 H), 3.73 (ddd, *J* = 4.8, 7.3, 10.3 Hz, 1 H), 3.68 (ddd, *J* = 6.6, 8.1, 10.3 Hz, 1 H), 3.63 (s, 3 H), 2.62 (ddd, *J* = 5.1, 14.6, 17.9 Hz, 1 H), 2.52 (d, *J* = 8.8 Hz, 1 H), 2.51 (d, *J* = 9.2 Hz, 1 H), 2.38 (ddd, *J* = 2.2, 5.1, 17.9 Hz, 1 H), 2.14 (ddd, *J* = 2.2, 5.1, 12.8 Hz, 1 H), 1.94 (m, 1 H), 1.86–1.67 (m, 2 H), 1.45 (m, 2 H), 1.27 (m, 2 H), 1.08 (s, 3 H), 1.05 (s, 9 H), 0.87 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR δ 194.40, 162.51, 145.41, 135.54, 133.89, 129.55, 127.59, 61.41, 59.36, 56.51, 45.94, 38.08, 36.64, 34.88, 31.02, 27.27, 26.82, 24.98, 19.13, 18.82, 16.37; IR (neat) 2928, 1676, 1471 cm^{-1}.

[1*R*-(1α,5α,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-2,3,5,6,7,7a-hexahydro-4-methoxy-7a-methyl-1*H*-inden-5-ol (28). To a solution of the enone **27** (46 mg, 0.094 mmol) in ether (4 mL) at 0 °C was added $LiAlH_4$ (3.7 mg, 0.1 mmol). After being stirred for 10 min, the reaction mixture was quenched by the successive addition of H_2O (0.1 mL), 15% NaOH (0.1 mL), and H_2O (0.3 mL). The mixture was diluted with ether (4 mL), and $MgSO_4$ was added. The mixture was stirred at rt for 30 min. The resulting mixture was filtered and concentrated in vacuo to give the alcohol **28** (47 mg, 100%): $[\alpha]^{24}_D$ = +17.6° (*c* 1.2, $CHCl_3$); ^1H NMR δ 7.66 (dd, *J* = 1.1, 6.6 Hz, 4 H), 7.41–7.35 (m, 6 H), 4.28 (dt, *J* = 1.8, 7.8 Hz, 1 H), 3.72 (ddd, *J* = 4.8, 7.3, 10.3 Hz, 1 H), 3.68 (ddd, *J* = 6.6, 8.1, 10.3 Hz, 1 H), 3.61 (s, 3 H), 2.27 (tt, *J* = 1.8, 7.7 Hz, 2 H), 2.05 (ddd, *J* = 3.7, 6.9, 13.6 Hz, 1 H), 1.89–1.72 (m, 4 H), 1.61 (m, 1 H), 1.38 (m, 2 H), 1.23 (m, 2 H), 1.04 (s, 9 H), 0.95 (s, 3 H), 0.84 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR δ 147.25, 135.60, 134.60, 134.06, 133.05, 129.52, 127.56, 66.65, 61.66, 58.40, 56.69, 44.82, 38.26, 36.27, 31.54, 29.33, 27.63, 26.83, 23.18, 19.15, 18.87, 18.11; IR (neat) 3418, 2932, 1690, 1471 cm^{-1}; HRMS (CI) calcd for $C_{31}H_{45}O_3Si$ (MH^+) 493.3137, found 493.3131.

[1*R*-(1α,5α,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-2,3,5,6,7,7a-hexahydro-4-methoxy-5-[(methoxycarbonyl)oxy]-7a-methyl-1*H*-indene (29). To a mixture of the alcohol **28** (46 mg, 0.093 mmol), 4-(dimethylamino)pyridine (1 mg, 9.4 μmol), and pyridine (0.03 mL, 0.39 mol) in CH_2Cl_2 (2 mL) at 0 °C was added methyl chloroformate (15 μL, 0.19 mmol), and the mixture was stirred for 40 min. The reaction was quenched with water, and the resulting mixture was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 10% ethyl acetate–hexane to give the methoxy carbonate **29** (41 mg, 84%): ^1H NMR δ 7.67–7.65 (m, 4 H), 7.41–7.35 (m, 6 H), 5.34 (dt, *J* = 7.7, 1.8 Hz, 1 H), 3.78 (s, 3 H), 3.73 (ddd, *J* = 4.8, 7.3, 10.3 Hz, 1 H), 3.69 (ddd, *J* = 6.6, 8.1, 10.3 Hz, 1 H), 3.53 (s, 3 H), 2.30 (m, 2 H), 2.17 (m, 2 H), 1.86 (m, 2 H), 1.77 (m, 1 H), 1.61 (m, 1 H), 1.42 (m, 2 H), 1.26 (m, 2 H), 1.04 (s, 9 H), 0.96 (s, 3 H), 0.84 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR δ 155.92, 143.60, 138.32, 135.57, 134.02, 129.51, 127.57, 73.74, 61.65, 58.67, 56.73, 54.57, 44.34, 38.23, 36.33, 31.43, 26.83, 26.60, 23.31, 19.15, 18.87, 17.66; IR (neat) 2956, 1746, 1694 cm^{-1}. Anal. Calcd for $C_{32}H_{46}O_4Si$: C, 73.51; H, 8.87. Found: C, 73.76; H, 8.88.

[1*R*-(1α,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-1,2,5,6,7,7a-hexahydro-7a-methyl-4*H*-inden-4-one (16). A solution of the carbonate **29** (41 mg, 0.078 mmol) in DMSO (1 mL) was stirred for 2 h at 100 °C. The reaction mixture was diluted with ethyl acetate, washed with brine, and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by flash chromatography through silica gel with 60% ethyl acetate–hexane to give the alcohol **30** (13 mg, 75%): ^1H NMR δ 6.46 (dd, *J* = 1.8, 3.3 Hz, 1 H), 3.75 (m, 1 H), 3.70 (m, 1 H), 2.48 (tq, *J* = 16.5, 3.6 Hz, 1 H), 2.22 (m, 1 H), 2.11 (dt, *J* = 9.9, 3.6 Hz, 1 H), 1.95 (m, 1 H), 1.83 (m, 2 H), 1.75 (dd, *J* = 5.8, 13.2 Hz, 1 H), 1.59 (dt, *J* = 4.0, 12.8 Hz, 2 H), 1.33 (m, 2 H), 1.12 (m, 1 H), 1.01 (d, *J* = 6.2 Hz, 3 H), 0.99 (s, 3 H); ^{13}C NMR δ 200.19, 150.34, 135.17, 60.53, 59.45, 48.50, 42.64, 39.97, 38.66, 35.40, 30.91, 20.88, 18.73, 17.91.

A mixture of the alcohol **30** (13 mg, 0.058 mmol), imidazole (12 mg, 0.18 mmol), and *tert*-butyldiphenylsilyl chloride (60 μL, 0.23 mmol) in DMF (0.2 mL) was stirred for 1 h at rt. The reaction mixture was quenched with water, and the mixture was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 10% ether–hexane to give the silylated ketone **16** (16 mg, 60%): ^1H NMR δ 7.67–7.65 (m, 4 H), 7.41–7.35 (m, 6 H), 6.42 (dd, *J* = 1.8, 3.3 Hz, 1 H),

3.74 (ddd, J = 4.7, 7.3, 10.3 Hz, 1 H), 3.70 (ddd, J = 6.6, 8.1, 10.3 Hz, 1 H), 2.40 (m, 1 H), 2.34 (m, 2 H), 2.17 (ddd, J = 2.8, 8.5, 7.2 Hz, 1 H), 2.03 (m, 1 H), 1.94 (m, 1 H), 1.83 (m, 1 H), 1.75 (m, 2 H), 1.52 (dt, J = 4.0, 12.8 Hz, 1 H), 1.25 (m, 2 H), 1.06 (s, 9 H), 1.05 (s, 3 H), 0.87 (d, J = 5.8 Hz, 3 H); ^{13}C NMR δ 200.43, 150.23, 135.59, 134.11, 133.96, 129.49, 127.56, 61.56, 59.27, 48.40, 39.91, 38.56, 38.33, 35.35, 30.72, 26.51, 20.84, 18.98, 18.78, 17.81; IR (neat) 2929, 1668, 1471 cm^{-1}.

[1*R*-(1α,4β,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]-2,4,5,6,7,7a-hexahydro-7a-methyl-1*H*-inden-4-ol (31). To a solution of **16** (13 mg, 0.028 mmol) in EtOH (1 mL) was added $CeCl_3 \cdot 7H_2O$ (37 mg, 0.1 mmol), and the mixture was stirred for 10 min at rt. The mixture was cooled to −78 °C, and $NaBH_4$ (3.7 mg, 0.1 mmol) in ethyl alcohol (0.5 mL) was added. After the mixture was stirred for 1 h, the reaction was quenched by the addition of saturated NH_4Cl, and the mixture was extracted with ethyl acetate. The extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 20% ethyl acetate–hexane to give the alcohol **31** (11 mg, 85%): $[\alpha]^{23}_D$ = −22.0° (c 0.4, $CHCl_3$): ^{1}H NMR δ 7.68–7.65 (m, 4 H), 7.43–7.35 (m, 6 H), 5.41 (br s, 1 H), 4.17 (dt, J = 1.5, 4.7 Hz, 1 H), 3.74 (ddd, J = 4.7, 7.3, 10.3 Hz, 1 H), 3.69 (ddd, J = 6.6, 8.1, 10.3 Hz, 1 H), 2.29 (dddd, J = 1.4, 2.9, 7.7, 15.7 Hz, 1 H), 2.05 (m, 1 H), 1.94 (m, 1 H), 1.87 (m, 1 H), 1.75 (m, 2 H), 1.60 (m, 2 H), 1.27 (m, 2 H), 1.18 (m, 2 H), 1.04 (s, 9 H), 0.90 (s, 3 H), 0.82 (d, J = 6.6 Hz, 3 H); ^{13}C NMR δ 153.67, 135.60, 134.11, 129.51, 127.58, 116.16, 68.84, 61.80, 59.34, 48.83, 41.59, 38.50, 36.64, 35.29, 30.61, 26.89, 21.61, 19.18, 18.99, 17.00; IR (neat) 3418, 2929 cm^{-1}; HRMS (CI) calcd for $C_{30}H_{43}O_2Si$ (MH^+) 463.3031, found 463.2993.

[1*R*-(1α,3aα,4β,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]octahydro-7a-methyl-1*H*-inden-4-ol (32). A mixture of the alcohol **31** (10 mg, 0.029 mmol) and $RhCl(PPh_3)_3$ (13.7 mg, 0.015 mmol) in CH_2Cl_2 (2 mL) was stirred under an atmospheric pressure of hydrogen for 22 h at rt. The reaction mixture was filtered through a pad of Celite, and the solvent was evaporated in vacuo. The residue was purified by flash chromatography through silica gel with 20% ethyl acetate–hexane to give the alcohol **32** (8 mg, 80%): $[\alpha]^{23}_D$ = +16.7° (c 0.3, $CHCl_3$); ^{1}H NMR δ 7.66 (d, J = 7.7 Hz, 4 H), 7.42–7.35 (m, 6 H), 3.71 (ddd, J = 4.7, 7.3, 10.3 Hz, 1 H), 3.67 (ddd, J = 6.9, 8.1, 10.3 Hz, 1 H), 3.57 (dt, J = 4.7, 10.3 Hz, 1 H), 1.98 (m, 1 H), 1.82 (m, 4 H), 1.53 (m, 5 H), 1.30–1.14 (m, 5 H), 1.04 (s, 9 H), 0.81 (d, J = 6.2 Hz, 3 H), 0.65 (s, 3 H); ^{13}C NMR δ 135.59, 134.11, 129.49, 127.56, 71.13, 61.78, 57.24, 56.61, 44.73, 39.11, 38.60, 35.86, 32.25, 27.86, 26.86, 23.38, 21.78, 19.17, 18.74, 11.88; IR (neat) 3418, 2930, 1471 cm^{-1}; HRMS (CI) calcd for $C_{30}H_{45}O_2Si$ (MH^+) 465.3187, found 465.3230.

[1*R*-(1α,3aβ,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]octahydro-7a-methyl-4*H*-inden-4-one (33). A mixture of the alcohol **32** (15 mg, 0.032 mmol) and pyridinium dichromate (61 mg, 0.161 mmol) in CH_2Cl_2 (2 mL) was stirred for 1 h at rt. The reaction mixture was filtered through a Florisil column, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 10% ethyl acetate–hexane to give the ketone **33** (13 mg, 88%): $[\alpha]^{23}_D$ = −3.0° (c 1.0, $CHCl_3$); ^{1}H NMR δ 7.73–7.65 (m, 4 H), 7.42–7.35 (m, 6 H), 3.72 (ddd, J = 4.7, 7.3, 10.3 Hz, 1 H), 3.66 (ddd, J = 6.6, 8.1, 10.3 Hz, 1 H), 2.40 (dd, J = 7.7, 11.7 Hz, 1 H), 2.25 (dt like, 1 H), 2.18 (dt like, 1 H), 2.05 (br s, 1 H), 1.96 (m, 1 H), 1.87 (m, 2 H), 1.73 (m, 2 H), 1.53 (m, 3 H), 1.41 (q, J = 9.5 Hz, 1 H), 1.24 (m, 2 H), 1.06 (s, 9 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.60 (s, 3 H); ^{13}C NMR δ 212.21, 135.56, 134.77, 129.57, 127.56, 61.95, 61.60, 56.71, 49.92, 40.90, 38.86, 38.34, 32.37, 27.40, 26.83, 26.51, 24.01, 19.02, 18.86, 12.35; IR (neat) 2957, 1712, 1472 cm^{-1}; HRMS (CI) calcd for $C_{30}H_{42}O_2Si$ (MH^+) 463.3031, found 463.3009.

[1*R*-(1α,3aβ,4α,7aα)]-1-[(1*R*)-3-[(*tert*-Butyldiphenylsilyl)oxy]-1-methylpropyl]octahydro-7a-methyl-1*H*-inden-4-ol (34). To a solution of the ketone **33** (52 mg, 0.11 mmol) in ether (2 mL) at 0 °C was added $LiAlH_4$ (11 mg, 0.3 mmol). After being stirred for 10 min, the reaction mixture was quenched by the successive addition of H_2O (0.1 mL), 15% NaOH (0.1 mL), and H_2O (0.3 mL). The mixture was diluted with ether (5 mL), and $MgSO_4$ was added. The mixture was stirred at rt for 30 min. The resulting mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 10% ethyl acetate–hexane to give the alcohol **34** (52 mg, 100%): $[\alpha]^{24}_D$ = +15.8° (c 0.8, $CHCl_3$); ^{1}H NMR δ 7.72–7.68 (m, 4 H), 7.41–7.35 (m, 6 H), 4.05 (d, J = 2.2 Hz, 1 H), 3.72 (ddd, J = 4.7, 7.3, 10.3 Hz, 1 H), 3.66 (ddd, J = 6.6, 8.0, 10.3 Hz, 1 H), 1.97 (br d, 1 H), 1.82–1.71 (m, 4 H), 1.46 (m, 2 H), 1.42 (m, 4 H), 1.33–1.11 (m, 4 H), 1.04 (s, 9 H), 0.90 (s, 3 H), 0.80 (d, J = 6.2 Hz, 3 H); ^{13}C NMR δ 135.59, 134.15, 129.47, 127.55, 69.41, 61.82, 56.72, 52.58, 41.86, 40.30, 38.43, 33.52, 32.22, 26.85, 26.52, 22.49, 19.16, 18.74, 17.39, 13.37; IR (neat) 3426, 2998, 1471 cm^{-1}.

[1*R*-(1α,3aβ,4α,7aα)]-4-(Benzyloxy)-1-[(1*R*)-3-[(*tert*-butyldiphenylsilyl)oxy]-1-methylpropyl]octahydro-7a-methyl-1*H*-indene (35). To a solution of the alcohol **34** (16 mg, 0.034 mmol) and KH (washed with hexane, 20 mg, 0.5 mmol) in THF (1 mL) at 0 °C was added benzyl bromide (6 μL, 0.05 mmol), and the mixture was stirred for 30 min and then for 2 h at rt. The reaction was cooled to 0 °C and quenched with water (1 mL) and saturated NH_4Cl (1 mL). The aqueous layer was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 3% ether–hexane to give **35** (20 mg, 100%): $[\alpha]^{23}_D$ = +21.6° (c 0.5, $CHCl_3$); ^{1}H NMR δ 7.75 (dd, J = 1.4, 8.1 Hz, 2 H), 7.67 (dd, J = 1.4, 6.9 Hz, 2 H), 7.43–7.31 (m, 11 H), 4.60 (d, J = 12.4 Hz, 1 H), 4.35 (d, J = 12.4 Hz, 1 H), 3.69 (m, 3 H), 1.96 (br t, 2 H), 1.75 (m, 4 H), 1.52 (m, 1 H), 1.41–1.28 (m, 3 H), 1.26–1.15 (m, 4 H), 1.10 (m, 1 H), 1.04 (s, 9 H), 0.94 (s, 3 H), 0.81 (d, J = 6.6 Hz, 3 H); ^{13}C NMR δ 139.97, 135.60, 134.19, 129.46, 128.11, 127.55, 126.88, 126.77, 71.13, 61.90, 56.86, 52.80, 42.11, 40.69, 38.52, 32.41, 29.24, 27.34, 26.90, 26.47, 22.77, 19.18, 18.83, 17.94, 13.48; IR (neat) 2927, 1471, 1463 cm^{-1}.

[1*R*-[1α(*R),3aβ,4α,7aα]]-4-(Benzyloxy)octahydro-γ,7a-dimethyl-1*H*-indene-1-propanol (36).** A mixture of the silyl ether **35** (28 mg, 0.05 mmol) and Bu_4NF (21 mg, 0.08 mmol) in THF (2 mL) was stirred for 3 h at rt. The reaction mixture was diluted with ether (20 mL), washed with water and brine, and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by flash chromatography through silica gel with 25% ethyl acetate–hexane to give the alcohol **36** (15 mg, 95%): $[\alpha]^{23}_D$ = +65.8° (c 1.0, $CHCl_3$); ^{1}H NMR δ 7.32–7.30 (m, 5 H), 4.60 (d, J = 12.4 Hz, 1 H), 4.34 (d, J = 12.4 Hz, 1 H), 3.69 (br d, 1 H), 3.68 (m, 1 H), 3.60 (m, 1 H), 1.99 (br dd, 1 H), 1.90–1.68 (m, 3 H), 1.52 (m, 1 H), 1.45–1.05 (m, 10 H), 0.96 (s, 3 H), 0.92 (d, J = 6.6 Hz, 3 H); ^{13}C NMR δ 139.84, 128.01, 126.81, 126.68, 76.46, 71.05, 60.72, 56.89, 52.69, 42.05, 40.64, 38.72, 32.56, 29.14, 27.36, 22.67, 18.75, 17.86, 13.43; IR (neat) 3332, 2933, 1446, 1463 cm^{-1}; HRMS calcd for $C_{21}H_{32}O_2$ 316.2402, found 316.2440.

[1*R*-[1α(*R),3aβ,4α,7aα]]-4-(Benzyloxy)octahydro-δ,7a-dimethyl-1*H*-indene-1-pentanoic Acid Ethyl Ester (37).** A mixture of the alcohol **36** (50 mg, 0.158 mmol) and pyridinium dichromate (225 mg, 0.6 mmol) in CH_2Cl_2 (5 mL) was stirred for 6 h at rt. The reaction mixture was filtered through a Florisil column, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 10% ethyl acetate–hexane to give the aldehyde (42 mg, 84%): $[\alpha]^{23}_D$ = +38.8° (c 1.7, $CHCl_3$); ^{1}H NMR δ 9.74 (dd, J = 1.1, 3.6 Hz, 1 H), 7.33–7.30 (m, 5 H), 4.60 (d, J = 12.4 Hz, 1 H), 4.35 (d, J = 12.4 Hz, 1 H), 3.71 (br d, J = 2.2 Hz, 1 H), 2.45 (dd, J = 1.8, 15.7 Hz, 1 H), 2.20–1.95 (m, 3 H), 1.78 (br q, 3 H), 1.45–1.10 (m, 6 H), 1.01 (d, J = 6.2 Hz, 3 H), 1.00 (s, 3 H); ^{13}C NMR δ 203.60, 139.83, 128.12, 126.93, 126.77, 71.14, 56.47, 52.73, 50.75, 42.21, 40.54, 31.39, 29.09, 27.57, 22.65, 19.93, 17.86, 13.60; IR (neat) 2932, 1727, 1454 cm^{-1}.

To a suspension of NaH (55 wt % oil dispersion, 52 mg, 1.02 mmol) in THF (10 mL), was added diethyl phosphonoacetate (0.2 mL, 1.02 mmol) at 0 °C, and the mixture was stirred for 10 min. To the solution was added the aldehyde (268 mg, 0.85 mmol) in THF (5 mL), and the mixture was stirred for 10 min. The reaction mixture was quenched with water, and the aqueous layer was extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 5% ethyl acetate–hexane to give the ester **37** (290 mg, 89%): $[\alpha]^{23}_D$ = +43.2° (c 0.4, $CHCl_3$); ^{1}H NMR δ 7.32–7.30 (m, 5 H), 6.94 (ddd, J = 6.6, 8.8, 15.4 Hz, 1 H), 5.81 (d, J = 15.4 Hz, 1 H), 4.60 (d,

J = 12.4 Hz, 1 H), 4.35 (d, J = 12.4 Hz, 1 H), 4.18 (q, J = 6.9 Hz, 2 H), 3.70 (br d, 1 H), 2.27 (m, 1 H), 1.98 (br d, 3 H), 1.88–1.70 (m, 3 H), 1.62 (m, 1 H), 1.45–1.05 (m, 7 H), 1.28 (t, J = 6.9 Hz, 3 H), 0.96 (s, 3 H), 0.93 (d, J = 6.6 Hz, 3 H); ^{13}C NMR δ 166.57, 148.14, 139.86, 128.12, 126.93, 126.17, 122.31, 75.84, 71.11, 60.05, 56.14, 52.66, 42.11, 40.45, 35.22, 29.12, 27.31, 22.67, 18.91, 17.85, 14.27, 13.59; IR (neat) 2932, 1720, 1651 cm^{-1}; HRMS (CI) calcd for $C_{25}H_{37}O_3$ (MH^+) 385.2742, found 385.2643.

[1*R*-[1α(*R),3aβ,4α,7aα]]-Octahydro-4-hydroxy-δ,7a-dimethyl-1*H*-indene-1-pentanoic Acid Ethyl Ester (38).** A mixture of the alcohol **37** (92 mg, 0.24 mmol) and 5% Pd–C (51 mg, 0.024 mmol) in ethanol (3 mL) was stirred for 24 h at rt under H_2 (1 atm). The reaction mixture was filtrated through a pad of Celite and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 12% ethyl acetate–hexane to give the alcohol **38** (51 mg, 72%): $[\alpha]^{24}_D$ = +51.2° (c 1.0, $CHCl_3$); ^{1}H NMR δ 4.10 (q, J = 6.9 Hz, 2 H), 4.06 (br d, J = 2.6 Hz, 1 H), 2.27 (dd, J = 6.6, 8.4 Hz, 1 H), 2.23 (m, 1 H), 1.98 (m, 1 H), 1.90–1.75 (m, 2 H), 1.69 (m, 1 H), 1.60–1.05 (m, 13 H), 1.25 (t, J = 6.9 Hz, 3 H), 0.92 (s, 3 H), 0.91 (d, J = 6.6 Hz, 3 H); ^{13}C NMR δ 173.89, 69.31, 60.13, 56.31, 52.56, 41.81, 40.32, 35.16, 34.97, 34.74, 33.54, 27.07, 22.47, 21.47, 18.40, 17.39, 14.21, 13.44; IR (neat) 3520, 2933, 1732 cm^{-1}; HRMS (CI) calcd for $C_{18}H_{33}O_3$ (MH^+) 297.2429, found 297.2426.

[1*R*-[1α(*R),3aβ,4α,7aα]]-Octahydro-4-hydroxy-α,α,ϵ,7a-tetramethyl-1*H*-indene-1-pentanol (39).** To a mixture of Mg (19.0 mg, 0.78 mmol) in ether (2 mL) was added iodomethane (53 mL, 0.86 mmol) at 0 °C. After the mixture was stirred for 20 min, a solution of the ester **38** (51 mg, 0.17 mmol) in ether (2 mL) was added, and the resultant mixture was stirred for 10 min at 0 °C and then for 20 min at rt. The reaction mixture was cooled to 0 °C and quenched with water (1 mL) and 3 N HCl (1 mL), and the aqueous layer was extracted with ether. The extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 30% ethyl acetate–hexane to give the alcohol **39** (42 mg, 86%): $[\alpha]^{23}_D$ = +44.1° (c 1.1, EtOH); ^{1}H NMR δ 4.06 (m, 1 H), 1.20 (s, 6 H), 0.92 (s, 3 H), 0.90, (d, J = 6.59 Hz, 3 H); ^{13}C NMR δ 71.10, 69.40, 56.62, 52.58, 44.39, 41.84, 40.37, 36.23, 35.25, 33.57, 29.36, 29.33, 29.18, 29.15, 27.17, 22.51, 20.75, 18.52, 17.42, 13.53, 13.50; IR (neat) 3330, 2931, 1468, 1376, 1238, 1161, 759 cm^{-1}; HRMS (CI) calcd for $C_{18}H_{35}O_2$ (MH^+) 283.2636, found 283.2585 [lit.[10] $[\alpha]^{21}_D$ = +44.7° (EtOH)].

[1*R*-(1α,3aβ,7aα)]-1-[(1*R*)-1,5-Dimethyl-5-[(trimethylsilyl)oxy]hexyl]octahydro-7a-methyl-4*H*-inden-4-one (2). A mixture of the alcohol **39** (31.5 mg, 0.112 mmol) and pyridinium dichromate (126 mg, 0.336 mmol) in CH_2Cl_2 (1 mL) was stirred for 4 h at rt. The reaction mixture was filtered through a Florisil column, and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 30% ethyl acetate–hexane to give the ketone (28.4 mg, 91%): $[\alpha]^{23}_D$ = +4.6° (c 1.38, $CHCl_3$); ^{1}H NMR δ 1.21 (s, 6 H), 0.96 (d, J = 6.2 Hz, 3 H), 0.63 (s, 3 H); ^{13}C NMR δ 212.18, 71.03, 61.97, 56.61, 49.92, 44.28, 40.95, 38.96, 36.21, 35.46, 29.38, 29.18, 27.51, 24.05, 20.69, 19.05, 18.69, 12.46; IR (neat) 3432, 2960, 1709 cm^{-1}; HRMS (CI) calcd for $C_{18}H_{33}O_2$ (MH^+) 281.2482, found 281.2485.

To a solution of alcohol (180 mg, 0.643 mmol) in CH_2Cl_2 (120 mL) was added TMS-imidazole (0.47 mL, 3.22 mmol), and the mixture was stirred for 68 h at rt. To the reaction mixture was added water, and the mixture was stirred for 30 min. The resulting mixture was extracted with CH_2Cl_2, and the extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by flash chromatography through silica gel with 10% ethyl acetate–hexane to give the ketone **2** (174 mg, 77%): $[\alpha]^{23}_D$ = +3.4° (c 0.5, $CHCl_3$); ^{1}H NMR δ 1.19 (s, 6 H), 0.95 (d, J = 6.2 Hz, 3 H), 0.63 (s, 3 H), 0.09 (s, 9 H); ^{13}C NMR δ 212.14, 74.00, 61.97, 56.73, 49.92, 45.12, 40.95, 38.96, 36.21, 35.50, 29.93, 29.90, 29.83, 29.80, 27.49, 24.05, 20.74, 19.04, 18.66, 12.46, 2.60; IR (neat) 2958, 1715 cm^{-1}; HRMS (CI) calcd for $C_{21}H_{41}O_2Si$ (MH^+) 353.2875, found 353.2859.

Acknowledgment. This work was supported by the Uehara Memorial Foundation.

Supplementary Material Available: ^{1}H NMR spectra (25 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.