Asymmetric Heck Reaction−Carbanion Capture Process. Catalytic Asymmetric Total Synthesis of (−)-$\Delta^{9(12)}$-Capnellene

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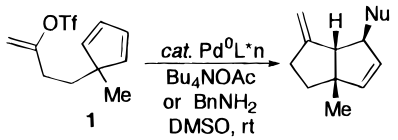
Abstract: An asymmetric Heck reaction−carbanion capture process was realized for the first time, making possible the catalytic asymmetric synthesis of various functionalized bicyclo[3.3.0]octane derivatives **6** in up to 94% ee. Sodium bromide had interesting effects on this asymmetric Heck reaction−carbanion capture process, and these effects were useful for improving the enantiomeric excess. Furthermore, the *catalytic* asymmetric synthesis of (−)-$\Delta^{9(12)}$-capnellene (**7**) was achieved for the first time, using **6b** as a key intermediate and a radical cyclization as a key step.

Introduction

The synthesis of optically active compounds is extremely important because enantiomer recognition plays an important role in many biological systems. Many methods are known for catalytic asymmetric reductions and oxidations,[1] but several successful catalytic asymmetric C−C bond-forming reactions[2] have been reported only recently. The development of new methods for catalytic asymmetric C−C bond formation is now a major interest of many synthetic chemists.

The first examples of the asymmetric Heck reaction were reported in 1989, by ourselves[3a] and later by Overman and co-workers.[3b] Since then, we[4] and others[5] have demonstrated that this type of catalytic asymmetric C−C bond-forming reaction

Scheme 1



is useful for the synthesis of various optically active compounds. In 1991, using alkenyl triflate **1** as a prochiral substrate, we also succeeded in demonstrating the first example of an asymmetric Heck reaction−acetate anion capture process to give **2** with 80% ee and an amine capture process to give **3** with 81% ee (Scheme 1).[6] Compound **2** was successfully converted to $\Delta^{9(12)}$-capnellene-3β,8β,10α-triol and $\Delta^{9(12)}$-capnellene-3β,8β,-10α,14-tetrol. To extend the usefulness of the above reactions, we decided to further examine the reaction of **1** with various carbanions.[7] The features of this asymmetric Heck reaction−carbanion capture process are that a one-pot cascade C−C bond-forming reaction occurs readily and various functionalized carbon chains can be introduced to the bicyclic π-allyl−Pd(II) complex **5** in a regio- and stereocontrolled manner to give **6** (Scheme 2). We describe here the catalytic asymmetric cyclization of triflate **1** in the presence of a variety of carbanions and the successful conversion of **6b**, one of the cyclization products, to (−)-$\Delta^{9(12)}$-capnellene (**7**) (Figure 1). We also discuss the effects of additives such as sodium bromide on the asymmetric Heck reaction−carbanion capture process.

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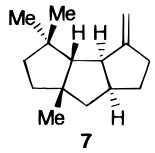

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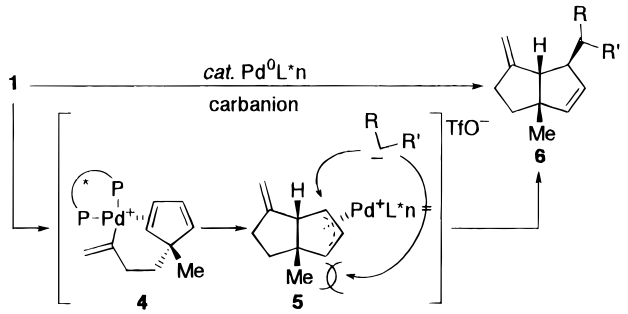
Figure 1.

Scheme 2



Results and Discussion

Improved Synthesis of Prochiral Triflate 1. As a key step in an earlier paper,[6] triflate **1** was prepared via selective acetalization of triketone **8**[8] by Noyori's method[9] using 1,2-bis((trimethylsilyl)oxy)ethane. However, isomerization of **9** to **10** sometimes occurred in a large-scale reaction. To overcome this problem, we undertook selective acetalization with 2,3-bis-((trimethylsilyl)oxy)butane instead of 1,2-bis((trimethylsilyl)-oxy)ethane, which we expected to prevent the isomerization of acetal, to produce **11** in a high yield even in a large-scale reaction. In fact, treatment of **8** (3.37 g scale) with 2,3-bis-((trimethylsilyl)oxy)butane (*dl*:*meso* = *ca*. 3:1) in the presence of TMSOTf (trimethylsilyl trifluoromethanesulfonate) at −78 °C gave only **11** in 95% yield. Using this method, triflate **1** was readily prepared in 57% overall yield starting from **8**, as shown in Scheme 3.

Preliminary Results of Asymmetric Heck Reaction−Carbanion Capture Process. Treatment of **1** with $Pd(OAc)_2$ (5 mol %), (*S*)-BINAP[10] (6.3 mol %), and the sodium enolate of dimethyl malonate (2 equiv) in DMSO at 20 °C for 2 h gave the cyclic product **6a** in 68% ee and 77% yield as the sole product. The structure of **6a** was determined by NOE experiments and the ^{1}H-NMR spectrum, which showed $J_{ab} = \sim 0$ Hz. The absolute configuration of **6a** was determined as follows. The allylic acetate **2** (80% ee), the absolute configuration of which had been determined previously,[6] was treated with $[Pd(allyl)Cl]_2$ (2.5 mol %), 1,4-bis(diphenylphosphino)butane (6 mol %), and the sodium enolate of dimethyl malonate (2 equiv) in DMSO at 20 °C for 16 h to give **6a** in 68% yield with double inversion of the configuration.[11] The sign of the optical rotation of the former sample of **6a** (above) was consistent with that of the latter, and the absolute configuration of **6a** was established unequivocally. Moreover, the enantiomeric excess of **6a** was determined by means of the ^{1}H-NMR spectrum using $Eu(hfc)_3$ (Scheme 4).

To obtain a much higher enantiomeric excess, solvent effects as well as ligand effects were carefully examined. After several attempts, we eventually found that DMSO and BINAP gave the best results as shown in Tables 1 and 2. Furthermore, other carbanions such as lithium enolate of dimethyl malonate had little effect on the asymmetric induction.

Table 1. Effects of Solvents on the Asymmetric Synthesis of **6a**[a]

entry	solvent	time (h)	yield (%)	ee (%)
1	DMSO	1.0	77	68
2	HMPA	1.0	trace	
3	DMF	21.5	61	14
4	NMP	29.0	11	31
5	MeCN	2.5	79	<5
6	diglyme	1.0	69	15
7	THF	25.0	40	16

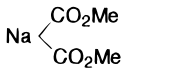
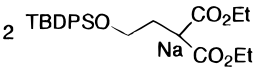
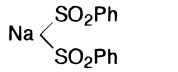
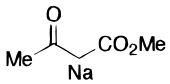
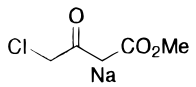
[a] Reactions were carried out using $Pd(OAc)_2$ (5 mol %), (*S*)-BINAP (6.3 mol %), and the sodium enolate of dimethyl malonate (2.0 equiv) at rt.

Table 2. Effects of Ligands on the Asymmetric Synthesis of **6a**[a]

entry	solvent	time (h)	yield (%)	ee (%)
1	(*S*)-BINAP	1.0	77	68
2	(*S*)-BINAPO	1.0	69	<5
3	(*R*,*R*)-DIOP	0.5	77	<5
4	(*S*,*S*)-CHIRAPHOS	65.0	trace	
5	(−)-NORPHOS	1.5	62	<5
6	(*R*,*R*)-BPPM	0.5	70	30[b]
7	(*S*,*R*)-BPPFA	0.5	67	27

[a] Reactions were carried out using $Pd(OAc)_2$ (5 mol %), ligand (6.3 mol %), and the sodium enolate of dimethyl malonate (2.0 equiv) in DMSO at rt. [b] The mirror image enantiomer was formed.

Table 3. Effects of Carbanions on the Asymmetric Cyclization of **1**[a]

entry	nucleophile	product	yield (%)	ee (%)
1		**6a**	87	70
2		**6b**	75	66
3		**6c**	75	66
4		**6d**	91	74
5[b]		**6e**	67[c]	80

[a] Reactions were carried out using $Pd(OAc)_2$ (5 mol %), (*S*)-BINAP (6.3 mol %), and carbanion (2.0 equiv) in DMSO at rt. [b] Reaction was carried out using $[Pd(allyl)Cl]_2$ (5 mol %), (*S*)-BINAP (12 mol %), methyl 4-chloro-3-oxobutyrate (2.0 equiv), and $NaN(SiMe_3)_2$ (2.0 equiv) in DMSO at rt. [c] A mixture of **6e** and **24** was obtained.

Asymmetric Heck Reactions Using Various Carbanions. Considering this interesting result, the reaction of **1** with $Pd(OAc)_2$ (5 mol %), (*S*)-BINAP (6.3 mol %), and various sodium enolates (2 equiv) in DMSO was further investigated (Table 3). All of these reactions gave various functionalized cyclic products **6** in high chemical yields (up to 91%) and in moderate to good optical yields (up to 80% ee). However, the optical yields of **6** were slightly lower than those of **2** and **3**. In a previous paper,[6] the asymmetric Heck reaction of alkenyl iodide **16** in the absence of a silver salt provided cyclic product **20** with only low ee (Scheme 5), which is consistent with the hypothesis that the asymmetric Heck reaction proceeded via a 16-electron Pd^+ intermediate (like **4**) but not via neutral palladium intermediates such as **18** and **19** to give products with

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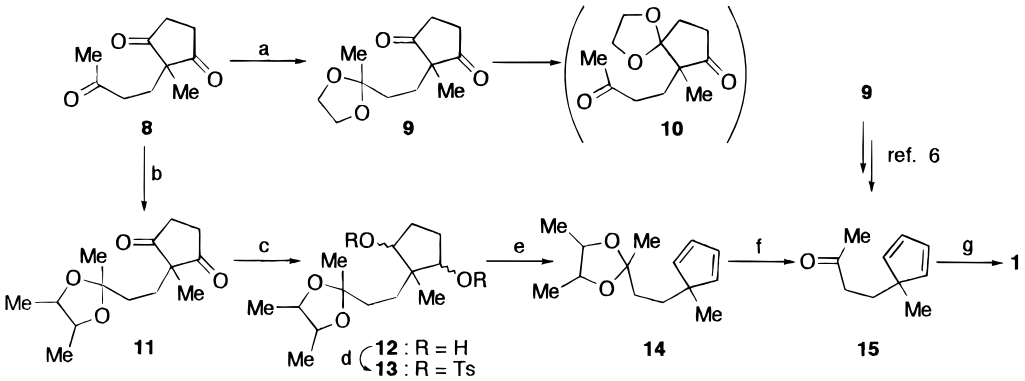
(9) Tsuda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357.
(10) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345.
(11) Trost, B. M.; Weber, L. *J. Am. Chem. Soc.* **1975**, *97*, 1611. Trost, B. M.; Weber, L.; Strege, P. E.; Fullerton, T. J.; Dietsche, T. *J. Am. Chem. Soc.* **1978**, *100*, 3416. Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1978**, *100*, 3435. Hayashi, T.; Hagihara, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1983**, *105*, 7767. Hayashi, T.; Konishi, M.; Kumada, M. *J. Chem. Soc., Chem. Commun.* **1984**, 107.

Scheme 3[a]



[a] Reaction conditions: (a) 1,2-bis((trimethylsilyl)oxy)ethane (1.13 equiv), TMSOTf (0.1 equiv), CH_2Cl_2, −78 °C (77%); (b) 2,3-bis((trimethylsilyl)oxy)butane (1.13 equiv), TMSOTf (0.1 equiv), CH_2Cl_2, −78 °C (95%); (c) $NaBH_4$ (1.2 mol equiv), MeOH, 0 °C to rt; (d) TsCl (4.3 equiv), DMAP (0.3 equiv), pyridine, 0 °C to rt; (e) DBU (4 equiv), toluene, reflux (three steps 90%); (f) TSOH·H_2O (1.7 mol %), acetone, rt (94%); (g) LDA (1.2 equiv), $PhNTf_2$ (1.3 equiv), THF, −78 °C to rt (71%).

Scheme 4

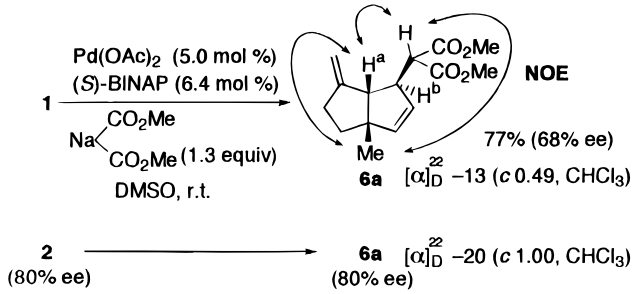


Table 4. Effects of Additives on the Asymmetric Synthesis of **6d**[a]

entry	additive	yield (%)	ee (%)
1		94	70
2	NaCl	79	78
3	NaBr	74	83
4	NaI	73	78
5	$NaClO_4$	81	73
6	Na_2SO_4	61	74

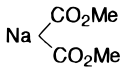
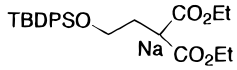
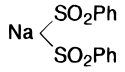
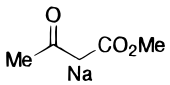
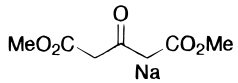
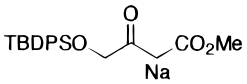
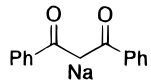
[a] Reactions were carried out using $[Pd(allyl)Cl]_2$ (2.5 mol %), (*S*)-BINAP (6.3 mol %), sodium enolate of methyl acetoacetate (2.0 equiv), and additive (2.0 equiv) in DMSO at rt.

high ee[3−6]. These results appeared to indicate that counteranion exchange occurred between the hard triflate anion and the soft enolate anion (**4** → **22** and/or **23**) to result in the formation of **6** with a slightly lower enantiomeric excess, as shown in Scheme 6.

Quite interestingly, the use of methyl 4-chloro-3-oxobutyrate instead of methyl 3-oxobutyrate increased the optical yield from 74% to 80% ee (Table 3, compare entries 4 and 5). As soon as sodium enolate of methyl 4-chloro-3-oxobutyrate was generated, partial dimerization occurred to give dimer **24** and sodium chloride (Scheme 7). Therefore, it was presumed that sodium chloride affected the undesired counteranion exchange. Thus, we next examined the effects of additivies such as sodium chloride on counteranion exchange in this reaction (**1** → **6d**).

Effects of Additives. We first found that, as expected, addition of 2 equiv of NaCl (1 equiv to carbanion) to the reaction mixture (Table 4, compare entries 1 and 2) increased the optical yield of **6d** from 70% to 78% ee. Encouraged by this result, we then examined the effects of a variety of sodium salts (entries 3−6). NaBr had the greatest effect and gave **6d** in 83% ee (entry 3). Since the addition of 5 equiv of NaBr gave the same optical yield, an excess of NaBr was not required in this reaction system. In contrast, $NaClO_4$ and Na_2SO_4 had almost no effects

Table 5. Effects of Carbanions on the Asymmetric Cyclization of **1**[a]

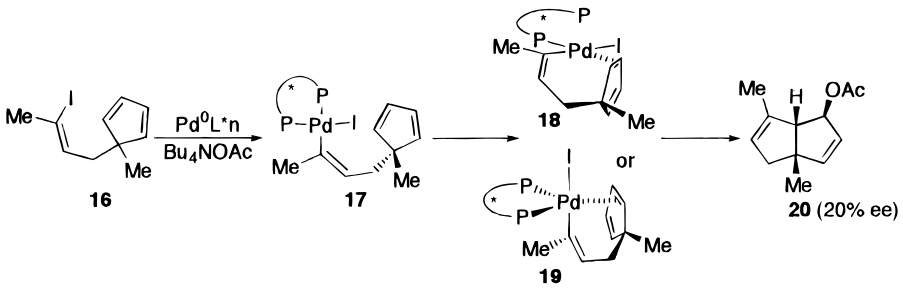
entry	nucleophile	product	yield(%)	ee(%)
1		**6a**	92	83
2		**6b**	77	87
3		**6c**	83	94
4		**6d**	74	83
5		**6f**	81	82
6		**6g**	72	82
7		**6h**	90	80

[a] Reactions were carried out using $[Pd(allyl)Cl]_2$ (2.5 mol %), (*S*)-BINAP (6.3 mol %), NaBr (2.0 equiv), and carbanion (2.0 equiv) in DMSO at rt.

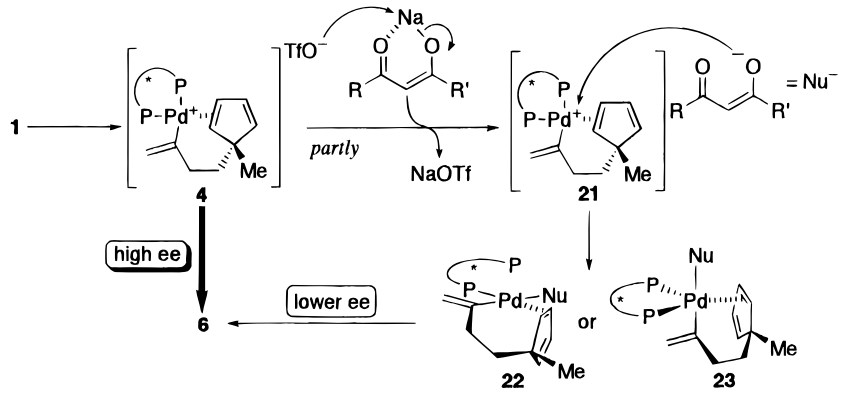
on the reaction (entries 5 and 6). If even partial counteranion exchange occurred between a triflate anion and a bromide anion, the enantiomeric excess of the products **6** would decrease.[4a,j] Thus, it appears that sodium bromide prevents counteranion exchange between the triflate anion and the enolate anion by complexing with sodium enolate (Scheme 8). The reaction of **1** with $[Pd(allyl)Cl]_2$ (2.5 mol %), (*S*)-BINAP (6.3 mol %), NaBr (2 equiv), and various sodium enolates (2 equiv) in DMSO was further investigated (Table 5). These studies showed that the addition of NaBr improved the optical yields (up to 94% ee, entry 3) without decreasing the chemical yield in all cases. The possible transition states leading to **6** are shown in Scheme 9. The transition state (*R*)-**4** is notable for the high probability of severe steric repulsion between the cyclopentadiene moiety and a bezene ring of the BINAP ligand, a factor which is not present in the transition state (*S*)-**4**; this may account for the predominance of the (*S*)-**5** enantiomer in the product.

Catalytic Asymmetric Total Synthesis of (−)-Δ$^{9(12)}$-Capnellene (7) from Bicyclic Compound (+)-(*S*,*S*,*S*)-6b. Having

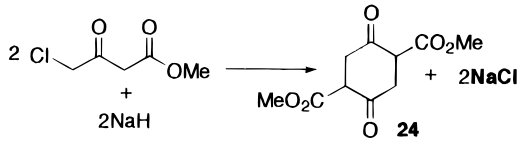
Scheme 5



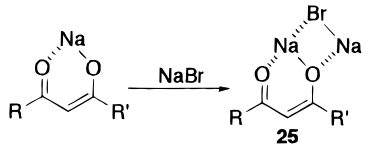
Scheme 6



Scheme 7



Scheme 8



achieved the catalytic asymmetric synthesis of bicyclic compound **6a**−**h** with high ee, we then sought to demonstrate the usefulness of this class of compounds as asymmetric building blocks. We planned to transform the key intermediate **6b** into natural (−)-$\Delta^{9(12)}$-capnellene (**7**). (−)-$\Delta^{9(12)}$-Capnellene (**7**) is found in the soft coral *Capnella imbricata* and is believed to be the biosynthetic precursor to the capnellane family of nonisoprenoid sesquiterpenes.[12a] These compounds display biological activities similar to those of their terrestrial counterparts, the hirsutanes, which possess antibacterial and antitumor properties.[12b] Capnellanes appear to serve as chemical defense agents within the coral reef biomass toward algae and microbial growth and to prevent larvae settlement.[13] Interest in these substances has inspired several synthetic studies.[14] However, despite the efficient asymmetric syntheses of (+)-**7**[15a] and (−)-**7**,[15b] the *catalytic* asymmetric total synthesis of (−)-**7** has not yet been achieved.

Decarboxylation of diester (+)-(*S*,*S*,*S*)-**6b** (87% ee) produced monoester **26** in 84% yield. Reduction of **26** with diisobutylaluminum hydride in CH_2Cl_2 gave alcohol **27** in 96% yield, which was protected as its benzoyl ester to afford **28** quantitatively. Deprotection of the TBDPS (*tert*-butyldiphenylsilyl) ether **28** was achieved by treatment with tetrabutylammonium fluoride in THF to give alcohol **29** in 97% yield, and **29** was successively treated with methanesulfonyl chloride and triethylamine in CH_2Cl_2 and NaI in acetone to furnish iodide **31** quantitatively from **29**. Radical cyclization of **31** was performed with tributyltin hydride and 2,2′-azobis(isobutyronitrile) in refluxing benzene to give the tricyclic compound **32**, which was then treated with NaOH in methanol to give alcohol **33** in 96% yield from **31**. Exocyclic olefin **33** was treated with excess diethylzinc and diiodomethane in toluene at 60 °C to give cyclopropane **34** in 95% yield. Subsequent hydrogenation of **34** with a catalytic amount of PtO_2 in acetic acid under a

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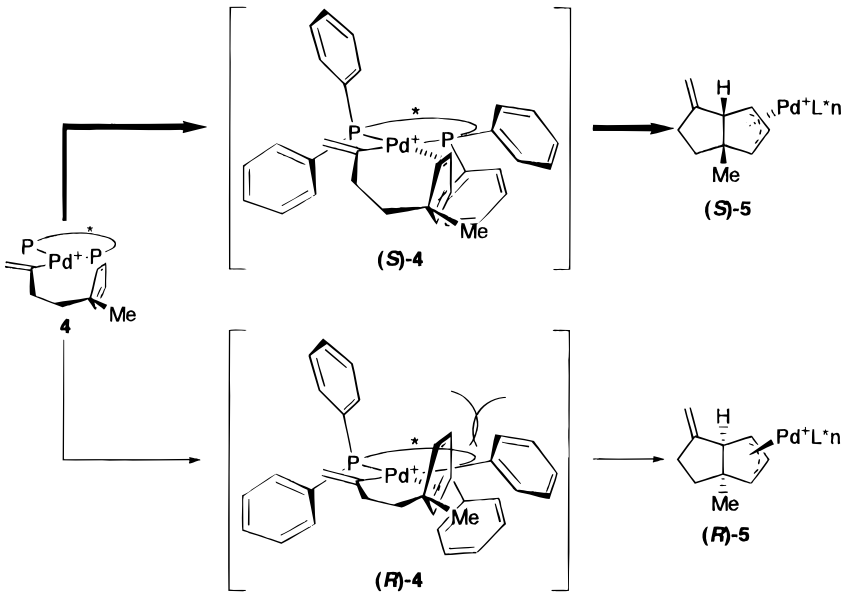
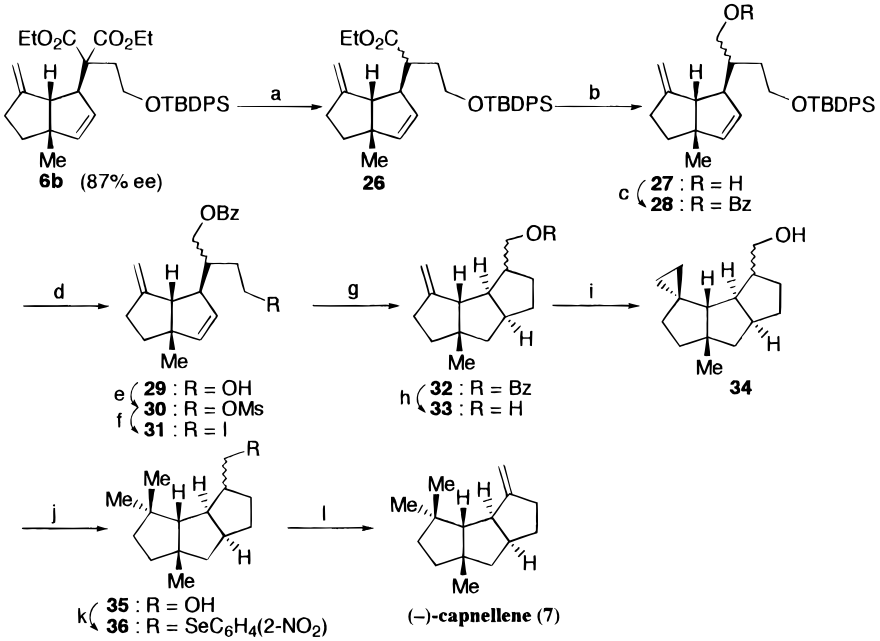
Scheme 9



Scheme 10[a]



[a] Reaction conditions: (a) LiCl (2 equiv), H_2O (1 equiv), DMSO, reflux (84%); (b) DIBALH (3 equiv), CH_2Cl_2 −78 °C to rt (96%); (c) BzCl (2 equiv), DMAP (0.1 equiv), pyridine, CH_2Cl_2, 0 °C to rt (quantitative) (d) TBAF (1 equiv), THF, rt (97%); (e) MsCl (10 equiv), Et_3N (15 equiv), CH_2Cl_2, −23 to 0 °C; (f) NaI (5 equiv), acetone, rt (quantitative); (g) Bu_3SnH (2 equiv), AIBN (0.2 equiv), benzene, reflux; (h) NaOH, MeOH, rt (two steps 96%); (i) Et_2Zn (5 eq), CH_2I_2 (10 equiv), toluene, 60 °C (95%); (j) PtO_2 (0.2 equiv), H_2 (1 atm), AcOH, rt (80); (k) 2-nitrophenyl selenocyanate (3 equiv), Bu_3P (3 equiv), pyridine, rt; (l) H_2O_2, K_2CO_3 (10 equiv), THF, rt (two steps 78%).

hydrogen atmosphere gave **35** in 80% yield. The last stage in this synthesis was transformation of the primary alcohol of **35** to the exocyclic olefin **7**. This was realized through the oxidation of a selenenyl compound. Alcohol **35** was treated with 2-nitrophenyl selenocyanate[16] and tributylphosphine in pyridine to give **36**, and **36** was oxidized with aqueous hydrogen peroxide solution in THF in the presence of potassium carbonate to give the title compound **7** in 78% yield from **35** without isomerization of exocyclic olefin to endocyclic olefin (Scheme 10). The spectral data were identical to those previously reported.[12] The optical rotation of the synthetic product ($[\alpha]^{26}_D$ −120, 87% ee) was well within the limits of polarimetric error for the reported value[12] of the natural product ($[\alpha]_D$ −145).

Conclusions

We have developed a new method for the catalytic asymmetric synthesis of bicyclo[3.3.0]octane derivatives **6** with excellent asymmetric induction (up to 94% ee) using the first example of an asymmetric Heck reaction−carbanion capture process. Using (+)-(*S*,*S*,*S*)-**6b** as an asymmetric building block, we have achieved the first *catalytic* asymmetric total synthesis of (−)-$\Delta^{9(12)}$-capnellene (**7**) in 19 steps and in 20% overall yield from commercially available starting material **8**. Furthermore, we have found that sodium bromide has interesting effects on this asymmetric Heck reaction−carbanion capture process.

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Experimental Section

Infrared (IR) spectra were recorded on a JASCO A-300 diffraction grating infrared spectrometer. NMR spectra were measured in JEOL JNM-EX 270 spectrometer, operating at 270 MHz, for ^{1}H and 68 MHz for ^{13}C NMR. Chemical shifts were reported in the δ scale relative to $CHCl_3$ as an internal reference (7.26 ppm for ^{1}H and 77.00 ppm for ^{13}C). Mass spectra (MS) were measured on a JEOL JMS-DX303 or JEOL JMN-SX-102A instruments. Optical rotation was measured on a JASCO DIP-140 polarimeter. Thin layer chromatography (TLC) analyses were performed on commercial glass plates bearing 0.25 mm layer of Merck silica gel 60 F_{254} (Merck Art. No. 5715). Column chromatography was carried out with silica gel, Merck Type 60 (70-325 mesh ASTM) or Merck Type 60 (230−400 mesh ASTM). HPLC was carried out on a JASCO HPLC system consisting of the following: pump, 880-PU; detector, 875-UV, measured at 245 nm; column, DAICEL CHIRALPAK AS, AD, OD; mobile phase, hexane−2-propanol; flow rate, 0.5−1.0 mL/min. In general, reactions were carried out in dry solvents under an argon atmosphere, unless otherwise mentioned. IR, NMR, and MS data were obtained on all intermediates described herein using chromatographically homogeneous samples.

Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium benzophenone ketyl. Dichloromethane was distilled from calcium hydride.

2-(3,3-(1,2-Dimethylethylenedioxy)butyl)-2-methyl-1,3-cyclopentanedione (11). To a solution of **8**[8] (3.37 g, 18.5 mmol) and 2,3-bis((trimethylsilyl)oxy)butane (4.90 g, 20.9 mmol) in CH_2Cl_2 (19 mL) was gradually added TMSOTf (0.36 mL, 1.85 mmol) at −78 °C. The reaction mixture was stirred for 40 h at the same temperature, quenched by the addition of pyridine (2.2 mL), poured into saturated aqueous $NaHCO_3$ solution with vigorous stirring (−78 °C → room temperature (rt)), and extracted with Et_2O. The organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:5) to give **11** (4.47 g, 95%) as a colorless oil: IR (neat) 2978, 1724, 1378, 1244, 1094 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.61 (dq, J = 8.6, 5.9 Hz, 1 H), 3.47 (dq, J = 8.6, 5.9 Hz, 1 H), 2.75 (s, 4 H), 1.81−1.69 (m, 2 H), 1.57−1.49 (m, 2 H), 1.29 (s, 3 H), 1.20 (d, J = 5.9 Hz, 3 H), 1.19 (d, J = 5.9 Hz, 3 H), 1.10 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 216.05 (s, 2 C), 108.32 (s), 78.71 (d), 78.00 (d), 55.92 (s), 34.88 (t, 2 C), 34.48 (t), 29.40 (t), 25.23 (q), 18.74 (q), 17.05 (q), 16.35 (q); MS *m*/*z* (relative intensity) 255 (M^+ + H, 0.4), 239 (26), 115 (100); HR-MS calcd for $C_{14}H_{22}O_4$ 254.1519, found 254.1506. Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72. Found: C, 65.84; H; 8.63.

5-(3,3-(1,2-Dimethylethylenedioxy)butyl)-5-methylcyclopentanediene (14). To a stirred solution of **11** (593 mg, 2.33 mmol) in MeOH (4 mL) was added $NaBH_4$ (106 mg, 2.80 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C for 30 min and at rt for 30 min, quenched by the addition of acetone, and diluted with H_2O (0.4 mL) and excess Et_2O. The mixture was filtered through a silica gel pad and concentrated to give crude **12**. To the residual oil was added pyridine (3.8 mL, 46.6 mmol), TsCl (1.91 g, 10.0 mmol), and DMAP (8.5 mg, 0.7 mmol) at 0 °C. The reaction mixture was stirred at rt for 42 h, quenched by the addition of EtOH (1.2 mL) at 0 °C, diluted with CH_2Cl_2, and successively washed with saturated aqueous $CuSO_4$ solution, saturated aqueous $NaHCO_3$ solution, and brine. The CH_2Cl_2 layer was dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:3) to give diastereo mixture of **13** as a pale yellow oil. A solution of this mixture and DBU (1.4 mL, 9.3 mmol) in toluene (4 mL) was refluxed with stirring for 40 h. The reaction mixture was poured into saturated aqueous NH_4Cl solution and extracted with Et_2O. The organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:20) to give **14** (446.0 mg, three steps 90%) as a colorless oil: IR (neat) 2970, 1376, 1100, 753 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 6.19 (s, 4 H), 3.63 (dq, J = 8.6, 5.9 Hz, 1 H), 3.53 (dq, J = 8.6, 5.9 Hz, 1 H), 1.74−1.62 (m, 2 H), 1.51−1.43 (m, 2 H), 1.29 (s, 3 H), 1.22 (d, J = 5.9 Hz, 3 H), 1.21 (d, J = 5.9 Hz, 3 H), 1.15 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 145.32 (d, 2 C), 128.63 (d, 2 C), 109.20 (s), 78.74 (d), 77.97 (d), 55.73 (s), 35.65 (t), 29.92 (t), 25.59 (q), 20.72 (q), 17.13 (q), 16.52 (q); MS *m*/*z* (relative intensity) 222 (M^+, 17), 185 (15), 149 (100), 115 (90); HR-MS calcd for $C_{14}H_{22}O_2$ 222.1620, found 222.1614.

5-Methyl-5-(3-oxobutyl)cyclopentadiene (15). To a solution of **14** (132.9 mg, 0.598 mmol) in acetone (1.2 mL) was added $TsOH\cdot H_2O$ (2.3 mg, 0.01 mmol), the reaction mixture was stirred at rt for 48 h and diluted with hexane, and most of the acetone was evaporated under reduced pressure. This hexane solution was purified by silica gel column chromatography (Et_2O−hexane, 1:15) to give **15**[6] (84.1 mg, 94%) as a colorless oil.

General Procedure for the Asymmetric Heck Reaction−Carbanion Capture Process. [Pd(allyl)Cl]$_2$ (3.79 mg, 10.4 μmol), (*S*)-BINAP (16.24 mg, 26.1 μmol), and NaBr (85 mg, 0.828 mmol) were added to a solution of **1** (116.8 mg, 0.414 mmol) in DMSO (1.5 mL). After degassing, the sodium enolate of diethyl (2-((*tert*-butyldiphenylsilyl)oxy)ethyl)malonate[17] (0.33 M, in DMSO, 2.5 mL, 0.83 mmol) was gradually added to the mixture. The reaction mixture was stirred at rt for 1 h, diluted with Et_2O, washed with 1 N aqueous HCl and brine, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (Et_2O−hexane, 1:50) to give **6b** (183.0 mg, 77%, 87% ee) as colorless needles.

(1*S*,4*S*,5*S*)-4-(Bis(methoxycarbonyl)methyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (6a): $[\alpha]^{22}_D$ −13.3 (*c* 1.23, $CHCl_3$) (70% ee); IR (neat) 1738, 1249, 1151 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 5.56−5.52 (m, 2 H), 4.90−4.84 (m, 2 H), 3.77 (s, 3 H), 3.74 (s, 3 H), 3.31 (d, J = 10.0 Hz, 1 H), 3.21 (br-d, J = 10.0 Hz, 1 H), 2.40 (br-s, 1 H), 2.32−2.16 (m, 2 H), 1.71 (ddd, J = 12.5, 7.0, 3.0 Hz, 1 H), 1.50 (ddd, J = 12.5, 11.0, 7.5 Hz, 1 H), 1.20 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 168.86 (s), 168.64 (s), 157.47 (s), 141.38 (d), 129.33 (d), 105.86 (t), 57.88 (d), 57.29 (s), 56.53 (d), 55.10 (d), 52.36 (q), 52.29 (q), 38.37 (t), 33.19 (t), 27.60 (q); MS *m*/*z* (relative intensity) 265 (M^+ + H, 14), 205 (14), 132 (100). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.46; H; 7.47.

(1*S*,4*S*,5*S*)-4-(1,1-Bis(ethoxycarbonyl)-3-((*tert*-butyldiphenylsilyl)-oxy)propyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (6b): $[\alpha]^{24}_D$ +8.68 (*c* 1.32, $CHCl_3$) (87% ee); IR (KBr) 2956, 1724, 1225, 1108, 704 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.67−7.62 (m, 4 H), 7.45−7.35 (m, 6 H), 5.63 (dd, J = 5.6, 2.3 Hz, 1 H), 5.42 (dd, J = 5.6, 2.3 Hz, 1 H), 4.77−4.73 (br-s, 2 H), 4.09 (dq, J = 10.2, 7.0 Hz, 2 H), 4.03 (dq, J = 10.2, 6.3 Hz, 2 H), 3.74 (ddd, J = 10.1, 9.0, 6.2 Hz, 1 H), 3.67 (ddd, J = 10.1, 9.0, 6.2 Hz, 1 H), 3.21 (dt, J = 3.4, 2.3 Hz, 1 H), 2.51 (d, J = 3.4 Hz, 1 H), 2.38−2.08 (m, 4 H), 1.65 (ddd, J = 12.0, 7.3, 2.1 Hz, 1 H), 1.39 (td, J = 12.0, 6.9 Hz, 1 H), 1.16 (t, J = 7.0 Hz, 3 H), 1.14 (t, J = 7.0 Hz, 3 H), 1.10 (s, 3 H), 1.03 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 170.80 (s), 170.63 (s), 157.36 (s), 140.04 (d), 135.53 (d, 4 C), 133.78 (s, 2 C), 129.69 (d), 129.51 (d, 2 C), 127.57 (d, 4 C), 104.78 (t), 60.90 (t), 60.77 (t), 60.40 (t), 59.26 (s), 59.00 (d), 56.89 (s), 53.89 (d), 39.25 (t), 35.49 (t), 33.35 (t), 27.50 (q), 26.78 (q, 3 C), 19.12 (s), 13.96 (q), 13.87 (q); MS *m*/*z* (relative intensity) 574 (M^+, 0.1), 559 (0.1), 517 (15), 385 (12), 227 (6), 199 (20), 133 (100); mp 85 °C. Anal. Calcd for $C_{35}H_{46}O_5Si$: C, 73.13; H, 8.07. Found: C, 73.00; H, 8.13; The enantiomeric excess was determined by HPLC analysis (DAICEL CHIRALPAK AD+AD, hexane−2-propanol, 99.5:0.5, 0.5 mL/min, retention time: 19 min (−), 21 min (+)).

(1*S*,4*S*,5*S*)-1-Methyl-6-methylene-4-(bis(phenylsulfonyl)methyl)-bicyclo[3.3.0]oct-2-ene (6c): $[\alpha]^{26}_D$ +0.942 (*c* 1.72, $CHCl_3$) (94% ee); IR (KBr) 1321, 1154 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 8.06−7.88 (m, 4 H), 7.70−7.53 (m, 6 H), 5.62 (dd, J = 5.5, 2.6 Hz, 1 H), 5.23 (dd, J = 5.5, 2.2 Hz, 1 H), 4.73−4.69 (m, 2 H), 4.63−4.60 (br-s, 1 H), 3.47 (ddd, J = 5.5, 2.6, 2.2 Hz, 1 H), 3.09 (d, J = 5.5 Hz, 1 H), 2.35−2.20 (m, 2 H), 1.48−1.64 (m, 2 H), 1.26 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 156.06 (s), 142.26 (d), 140.40 (s), 137.50 (s), 134.52 (d), 134.11 (d), 129.72 (d, 2 C), 129.20 (d, 2 C), 129.09 (d, 2 C), 128.81 (d, 2 C), 124.49 (d), 105.43 (t), 86.27 (d), 59.43 (d), 56.96 (s), 53.32 (d), 39.37 (t), 33.41 (t), 26.09 (q); MS *m*/*z* (relative intensity) 429 (M^+ + H, 0.1), 287 (66), 145 (78), 57 (100); HR-MS (M^+ + H) calcd for $C_{23}H_{25}O_4S_2$ 429.1194, found 429.1201; mp 145 °C; The enantiomeric

(17) Diethyl (2-((*tert*-butyldiphenylsilyl)oxy)ethyl)malonate was prepared as follows. Hydrogenolysis (10% Pd/C catalyst, H_2, EtOH) of diethyl (2-(benzyloxy)ethyl)malonate (Padgett, H. C.; Csendes, I. G.; Rapoport, H. *J. Org. Chem.* **1974**, *39*, 1612.) gave the crude alcohol, which was redissolved in dichloromethane and treated directly with *tert*-butyldiphenylsilyl chloride, triethylamine, and 4-(dimethylamino)pyridine. After aqueous workup, the crude product was further treated with chlorotrimethylsilane in order to facilitate the removal from the target molecule of traces of *tert*-butyldiphenylsilanol, which had formed during the silylation step.

excess was determined by HPLC analysis (DAICEL CHIRALPAK AD, hexane−2-propanol, 90:10, 1.0 mL/min, retention time: 15 min (+), 19 min (−)).

(1*S*,4*S*,5*S*)-4-(1-(Methoxycarbonyl)-2-oxopropyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (6d): IR (neat) 2952, 1746, 1716, 1160 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 5.53 (s, 1 H), 5.52 (dd, J = 5.5, 2.2 Hz, 0.5 H), 5.46 (dd, J = 5.5, 2.2 Hz, 0.5 H), 4.88−4.85 (m, 2 H), 3.77 (s, 1.5 H), 3.73 (s, 1.5 H), 3.41 (d, J = 6.5 Hz, 0.5 H), 3.38 (d, J = 6.0 Hz, 0.5 H), 3.27−3.23 (m, 1 H), 2.30−2.28 (m, 1 H), 2.27 (s, 1.5 H), 2.24 (s, 1.5 H), 2.25−2.21 (m, 2 H), 1.73−1.68 (m, 1 H), 1.58−1.42 (m, 1 H), 1.22 (s, 1.5 H), 1.20 (s, 1.5 H); ^{13}C-NMR ($CDCl_3$) δ 202.07 (s), 169.07, 169.02 (s), 157.48, 157.32 (s), 141.44, 141.19 (d), 129.49, 129.11 (d), 106.02, 105.95 (t), 66.43, 66.17 (d), 57.27, 57.18 (s), 56.62, 56.34 (d), 54.92, 54.63 (d), 52.29, 52.22 (q), 38.24 (t), 33.14 (t), 29.62, 29.35 (q), 27.6 (q); MS *m*/*z* (relative intensity) 248 (M^+, 0.5), 205 (36), 189 (20), 173 (16), 145 (22), 132 (100); HR-MS (M^+ − Ac) calcd for $C_{13}H_{17}O_2$ 205.1229, found 205.1224; The enantiomeric excess was determined by its conversion to methyl ((1*S*,4*R*,5*R*)-4-hydroxy-5-methyl-8-methylene-α-oxobicyclo[3.3.0]oct-2-en-2-yl)acetate: $[\alpha]^{24}_D$ −101 (*c* 0.40, $CHCl_3$) (83% ee); IR (neat) 3418, 2956, 1738, 1681, 1152 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 6.96−6.93 (br-s, 1 H), 5.10−5.07 (br-s, 1 H), 4.96−4.91 (br-s, 1 H), 4.79−4.75 (br-s, 1 H), 3.89 (s, 3 H), 3.59−3.55 (br-s, 1 H), 2.43−2.34 (m, 2 H), 2.30−2.15 (br-s, 1 H), 1.89−1.78 (m, 1 H), 1.64−1.43 (m, 1 H), 1.16 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 183.29 (s), 162.64 (s), 150.66 (s), 150.24 (d), 142.17 (s), 109.45 (t), 83.27 (d), 59.43 (d), 55.58 (s), 52.74 (q), 37.47 (t), 33.17 (t), 20.13 (q); MS *m*/*z* (relative intensity) 236 (M^+, 18), 205 (18), 177 (60), 149 (78), 94 (100); HR-MS (M^+) calcd for $C_{13}H_{16}O_4$ 236.1048, found 236.1055. The enantiomeric excess was determined by HPLC analysis (DAICEL CHIRALPAK AS, hexane−2-propanol, 90:10, 1.0 mL/min, retention time: 10 min (+), 13 min (−)). See ref 18.

(1*S*,4*S*,5*S*)-4-(3-Chloro-1-(methoxycarbonyl)-2-oxopropyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (6e). A mixture of **6e** and **24** was obtained: IR (neat) 1673, 1443, 1343, 1213 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 5.58−5.40 (m, 2 H), 4.91−4.85 (m, 2 H), 4.28−4.23 (m, 2 H), 3.78 (s, 1.5 H), 3.74 (s, 1.5 H), 3.66 (d, J = 10.3 Hz, 1 H), 3.30 (d, J = 10.3 Hz, 1 H), 2.39−2.35 (br-s, 1 H), 2.28−2.20 (m, 2 H), 1.75−1.66 (m, 1 H), 1.54−1.42 (m, 1 H), 1.23 (s, 1.5 H), 1.21 (s, 1.5 H); MS *m*/*z* (relative intensity) 284 (M^+ (^{37}Cl), 0.2), 284 (M^+ (^{35}Cl), 0.3), 267 (4), 239 (3), 205 (42), 132 (100). The enantiomeric excess was determined by its conversion to **6d**.

(1*S*,4*S*,5*S*)-4-[1,3-Bis(methoxycarbonyl)-2-oxopropyl]-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (6f):[19] IR (neat) 2952, 1744, 1436, 1244, 1162 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 5.56−5.47 (m, 2 H), 5.22 (s, 0.1 H), 5.17 (s, 0.1 H), 4.95−4.75 (m, 2 H), 3.76, 3.75, 3.73, 3.72, 3.71 (s, 6 H), 3.65−3.51 (m, 2.4 H), 3.29−3.26 (m, 0.5 H), 3.25−3.22 (m, 0.5 H), 2.99 (d, J = 10.6 Hz, 0.1 H), 2.93 (d, J = 10.6 Hz, 0.1 H), 2.38−2.20 (m, 3 H), 1.76−1.65 (m, 1 H), 1.56−1.40 (m, 1 H), 1.21, 1.20, 1.19 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 196.55, 196.44 (s), 168.52, 168.43 (s), 166.94, 166.81 (s), 157.39, 157.25 (s), 141.71 (d), 129.09, 128.90 (d), 106.27, 106.16 (t), 65.59, 65.37 (d), 57.34 (s), 56.59, 56.37 (d), 55.06, 54.66 (d), 52.53, 52.47, 52.36 (q, 2 C), 48.52, 48.20 (t), 38.30 (t), 33.19 (t), 27.60 (q); MS *m*/*z* (relative intensity) 306 (M^+, 0.4), 205 (58), 132 (100). Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.54; H, 7.54. The enantiomeric excess was determined by its conversion to methyl ((1*S*,4*R*,5*R*)-4-hydroxy-5-methyl-8-methylene-α-oxobicyclo[3.3.0]oct-2-en-2-yl)acetate. See ref 18.

(1*S*,4*S*,5*S*)-4-(3-((*tert*-Butyldiphenylsilyl)oxy)-1-(methoxycarbonyl)-2-oxopropyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (6g): IR (neat) 2952, 1723, 1113, 758, 702 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.68−7.62 (m, 4 H), 7.49−7.36 (m, 6 H), 5.56 (dd, J = 5.6, 2.1 Hz, 0.5 H), 5.51 (dd, J = 5.6, 1.5 Hz, 0.5 H), 5.45 (dd, J = 5.5, 1.6 Hz, 0.5 H), 5.27 (dd, J = 5.5, 2.2 Hz, 0.5 H), 4.96−4.92 (br-s, 0.5 H), 4.91−4.87 (br-s, 0.5 H), 4.87−4.83 (m, 1 H), 4.31 (d, J = 12.5 Hz, 0.5 H), 4.29 (d, J = 13.0 Hz, 0.5 H), 4.27 (d, J = 12.5 Hz, 0.5 H), 4.24 (d, J = 13.0 Hz, 0.5 H), 3.78 (d, J = 9.2 Hz, 0.5 H), 3.69 (d, J = 10.3 Hz, 0.5 H), 3.68 (s, 1.5 H), 3.65 (s, 1.5 H), 3.33−3.23 (m, 1 H), 2.42−2.38 (br-s, 0.5 H), 2.29−2.19 (m, 2 H), 2.19−2.15 (br-s, 0.5 H), 1.74−1.64 (m, 1 H), 1.53−1.39 (m, 1 H), 1.19 (s, 1.5 H), 1.14 (s, 1.5 H), 1.11 (s, 4.5 H), 1.10 (s, 4.5 H); ^{13}C-NMR ($CDCl_3$) δ 203.56, 203.34 (s), 168.48, 168.37 (s), 157.52, 157.34 (s), 141.22, 141.08 (d), 135.53 (d, 4 C), 135.53, 132.35, 132.31 (s, 2 C), 129.97 (d, 2 C), 129.74, 129.38 (d), 127.84 (d, 4 C), 106.09, 106.02 (t), 69.92, 69.88 (t), 60.29, 59.91 (d), 57.20, 56.82 (s), 57.07, 56.28 (d), 54.74, 54.07 (d), 52.24, 52.11 (q), 38.35 (t), 33.19 (t), 27.64 (q), 26.63 (q, 3 C), 19.16 (s); MS *m*/*z* (relative intensity) 445 (M^+ − ^{t}Bu,2), 385 (1), 313 (15), 133 (100). Anal. Calcd for $C_{31}H_{38}O_4Si$: C, 74.06; H, 7.62. Found: C, 73.78; H, 7.66. The enantiomeric excess was determined by its conversion to methyl ((1*S*,4*R*,5*R*)-4-hydroxy-5-methyl-8-methylene-α-oxobicyclo[3.3.0]oct-2-en-2-yl)acetate. See ref 18.

(1*S*,4*S*,5*S*)-4-(Dibenzoylmethyl)-1-methyl-6-methylenebicyclo-[3.3.0]oct-2-ene (6h): $[\alpha]^{25}_D$ +69.3 (*c* 1.01, $CHCl_3$) (80% ee); IR (neat) 2949, 1698, 1596, 1448 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 8.02−7.97 (m, 4 H), 7.59−7.38 (m, 6 H), 5.54−5.47 (m, 2 H), 5.23 (d, J = 10.6 Hz, 1 H) 4.90−4.87 (br-s, 1 H), 4.85−4.82 (br-s, 1 H), 3.77 (br-d, J = 10.6 Hz, 1 H), 2.36−2.33 (br-s, 1 H), 2.30−2.14 (m, 2 H), 1.76−1.67 (m, 1 H), 1.54−1.40 (m, 1 H), 1.31 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 195.06 (s), 194.57 (s), 157.50 (s), 140.99 (d), 136.95 (s), 136.89 (s), 133.46 (d, 2 C), 130.75 (d), 128.95 (d, 4 C), 128.84 (d, 4 C), 106.51 (t), 64.62 (d), 57.34 (d), 57.00 (d), 56.84 (s), 38.21 (t), 33.23 (t), 27.85 (q); MS *m*/*z* (relative intensity) 356 (M^+, 0.2), 279 (0.3), 251 (63), 132 (50), 105 (100: HR-MS (M^+ − PhCO) calcd for $C_{18}H_{19}O$ 251.1436, found 251.1440. The enantiomeric excess was determined by HPLC analysis (DAICEL CHIRALPAK OD+OD, hexane-2-propanol, 99.5:0.5, 1.0 mL/min, retention time: 45 min (−), 50 min (+)).

(1*S*,4*S*,5*S*)-4-(3-((*tert*-Butyldiphenylsilyl)oxy)-1-(ethoxycarbonyl)-propyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (26). A solution of **6b** (280.7 mg, 0.488 mmol), LiCl (41.4 mg, 0.977 mmol), and H_2O (8.8 μL, 0.488 mmol) in DMSO (0.81 mL) was refluxed with stirring for 6 h. After being cooled, the reaction mixture was diluted with H_2O, extracted with Et_2O, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:50) to give **26** (205.1 mg, 84%) as a colorless oil: IR (neat) 2954, 1731, 1428, 1173, 1112, 702 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.69−7.63 (m, 4 H), 7.46−7.34 (m, 6 H), 5.58 (dd, J = 5.6, 2.3 Hz, 0.4 H), 5.51−5.47 (m, 1 H), 5.41 (dd, J = 5.6, 2.3 Hz, 0.6 H), 4.81−4.78 (br-s, 1 H), 4.76−4.72 (br-s, 0.4 H), 4.71−4.69 (br-s, 0.6 H), 4.20−4.00 (m, 2 H), 3.76−3.58 (m, 2 H), 2.81−2.74 (m, 1 H), 2.66−2.55 (m, 1 H), 2.42−2.37 (br-s, 1 H), 2.35−2.15 (m, 2 H), 2.02−1.73 (m, 2 H), 1.73−1.64 (m, 1 H), 1.54−1.41 (m, 1 H), 1.22 (t, J = 7.1 Hz, 1.8 H), 1.21 (t, J = 7.1 Hz, 1.2 H), 1.20 (s, 1.2 H), 1.19 (s, 1.8 H), 1.05 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 175.11, 174.99 (s), 158.54, 158.51 (s), 140.41, 140.16 (d), 135.54 (d, 4 C), 133.82, 133.76 (s, 2 C), 130.05, 129.94 (d), 129.56 (d, 2 C), 127.60 (d, 4 C), 104.94, 104.55 (t), 62.01 (t), 60.11 (t), 58.56, 58.26 (d) 57.27, 57.05 (s), 56.77, 56.19 (d), 48.23, 47.26 (d), 38.83, 38.73 (t), 33.43, 33.30 (t), 33.05, 32.98 (t), 27.64 (q), 26.81 (q, 3 C), 19.19 (s), 14.27 (q); MS *m*/*z* (relative intensity) 502 (M^+, 0.1), 445 (84), 227 (34), 133 (100); HR-MS (M^+) calcd for $C_{32}H_{42}O_3Si$ 502.2903, found 502.2919.

(1*S*,4*S*,5*S*)-4-(3-((*tert*-Butyldiphenylsilyl)oxy)-1-(hydroxymethyl)-propyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (27). To a stirred solution of **26** (60.7 mg, 0.121 mmol) in CH_2Cl_2 (1.2 mL) was added a solution of DIBALH (0.98 M, in hexane, 0.37 mL, 0.38 mmol) at −78 °C. After gradually being warmed to 0 °C and 15 min further of stirring, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl solution at the same temperature and excess Et_2O was added. The mixture was stirred at rt for 15 h, extracted with Et_2O, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:10) to give **27** (53.3 mg, 96%) as a colorless oil: IR (neat) 3410, 2931, 1717, 1428, 1362, 701 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.71−7.66 (m, 4 H), 7.48−7.36 (m, 6 H), 5.54−5.49 (m, 1 H), 5.49−5.44 (m, 1 H), 4.78−4.75 (br-s, 1 H), 4.74−4.70 (br-s, 0.4 H), 4.70−4.66 (br-s, 0.6 H), 3.87−3.59 (m, 4 H), 2.94−2.84 (br-s, 0.4 H), 2.84−2.71 (br-s, 0.6 H), 2.64−2.55 (m, 1 H), 2.37−2.13 (m, 3 H), 1.82−1.53 (m, 4 H), 1.53−1.40 (m, 1 H), 1.18 (s, 1.2 H), 1.17 (s, 1.8 H), 1.07 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 159.28, 159.07 (s), 139.71, 139.62 (d), 135.60 (d, 4 C), 133.24 (s, 2 C), 130.82, 130.64 (d), 129.76 (d, 2 C), 127.73 (d, 4 C), 104.15, 103.99 (t), 65.16, 64.82 (t), 63.18 (t), 58.11, 57.88 (d), 57.04, 57.00 (s), 56.89,

(18) Ohshima, T.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1993**, *34*, 8509.

(19) **6f** was obtained as an equilibrium mixture of the keto form and 2,3-enol form (*ca.* 8:2).

56.44 (d), 44.35, 43.78 (d), 39.12, 39.07 (t), 33.43 (t), 33.07, 32.96 (t), 27.66, 27.59 (q), 26.79 (q, 3 C), 19.09 (s); MS *m*/*z* (relative intensity) 461 ($M^+ + H$, 0.2), 443 (0.7), 403 (4), 385 (3), 373 (20), 325 (22), 199 (80), 133 (100). Anal. Calcd for $C_{30}H_{40}O_2Si$: C, 78.21; H, 8.75. Found: C, 77.97; H, 8.81.

(1*S*,4*S*,5*S*)-4-(1-((Benzoyloxy)methyl)-3-((*tert*-butyldiphenylsilyl)-oxy)propyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (28). To a solution of **27** (53.3 mg, 0.116 mmol) in CH_2Cl_2 (1.6 mL) were added pyridine (0.038 mL, 0.464 mmol), BzCl (0.027 mL, 0.232 mmol), and DMAP (1.4 mg, 0.012 mmol) at 0 °C. After being stirred at rt for 16 h, the reaction mixture was diluted with Et_2O, washed with 1 N aqueous HCl and saturated aqueous $NaHCO_3$ solution, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:20) to give **28** (65.1 mg, quant.) as a colorless oil: IR (neat) 2953, 1721, 1272, 1112 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 8.04−7.09 (m, 2 H), 7.70−7.64 (m, 4 H), 7.59−7.52 (m, 1 H), 7.46−7.32 (m, 8 H), 5.55 (dd, J = 5.6, 2.1 Hz, 1 H), 5.50 (dd, J = 5.6, 1.5 Hz, 1 H), 4.81−4.78 (br-s, 0.6 H), 4.77−4.73 (br-s, 1 H), 4.71−4.68 (br-s, 0.4 H), 4.40 (dd, J = 11.3, 5.0 Hz, 0.4 H), 4.33 (dd, J = 11.3, 5.2 Hz, 0.6 H), 4.28 (dd, J = 11.3, 5.3 Hz, 0.6 H), 4.27 (dd, J = 11.3, 5.5 Hz, 0.4 H), 3.89−3.76 (m, 2 H), 2.77−2.71 (m, 1 H), 2.46−2.41 (br-s, 1 H), 2.33−2.00 (m, 3 H), 1.92−1.63 (m, 3 H), 1.56−1.43 (m, 1 H), 1.22 (s, 1.8 H), 1.21 (s, 1.2 H), 1.06 (s, 9 H); ^{13}C-NMR ($CDCl_3$) δ 166.56, 166.52 (s), 158.99, 158.81 (s), 139.91 (d), 135.53 (d, 4 C), 133.80, 133.76 (s, 2 C), 132.76 (d), 130.37 (s), 130.28, 130.19 (d), 129.56 (t, 2 C), 129.52 (d, 2 C), 128.30 (d, 2 C), 127.62 (d, 4 C), 104.35, 104.22 (t), 66.74, 65.95 (t), 61.98, 61.87 (t), 57.85, 57.59 (d), 57.05, 56.93 (s), 56.89, 56.68 (d), 39.21, 38.96 (d), 39.09, 39.01 (t), 33.48, 33.41 (t), 32.83, 32.19 (t), 27.64, 27.53 (q), 26.85 (q, 3 C), 19.14 (s); MS *m*/*z* (relative intensity) 507 ($M^+ - {}^t$Bu, 3), 385 (4), 303 (46), 187 (60), 133 (70), 105 (100). Anal. Calcd for $C_{37}H_{44}O_3Si$: C, 78.68; H, 7.85. Found: C, 78.70; H, 7.71.

(1*S*,4*S*,5*S*)-4-(1-((Benzoyloxy)methyl)-3-hydroxypropyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (29). To a stirred solution of **28** (211.3 mg, 0.392 mmol) in THF (2 mL) was added a solution of TBAF (1.0 M, in THF, 0.40 mL, 0.38 mmol) at rt, and the resulting mixture was stirred at rt for 2 h. The mixture was poured into 1 N aqueous HCl, extracted with Et_2O, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:5) to give **29** (118.8 mg, 97%) as a colorless oil: IR(neat) 3420, 2949, 1719, 1273 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 8.05−8.00 (m, 2 H), 7.59−7.52 (m, 1 H), 7.47−7.40 (m, 2 H), 5.61−5.49 (m, 2 H), 4.80−4.70 (m, 2 H), 4.44 (dd, J = 11.4, 5.0 Hz, 0.4 H), 4.36 (d, J = 5.5 Hz, 1.2 H), 4.33 (d, J = 11.4, 5.7 Hz, 0.4 H), 3.84−3.75 (m, 2 H), 2.78−2.72 (m, 1 H), 2.46−2.41 (br-s, 1 H), 2.33−2.16 (m, 2 H), 2.09−1.94 (m, 1 H), 1.89−1.60 (m, 4 H), 1.55−1.42 (m, 1 H), 1.21 (s, 1.8 H), 1.20 (s, 1.2 H); ^{13}C-NMR ($CDCl_3$) δ 166.70 (s), 158.94, 158.83 (s), 140.14 (d), 132.94 (d), 130.21 (s), 130.05 (d), 129.52 (d, 2 C), 128.39 (d, 2 C), 104.35 (t), 66.61, 66.22 (t), 61.17, 60.99 (t), 57.97, 57.76 (d), 57.11, 57.04 (s), 56.71, 56.48 (d), 39.43, 39.37 (d), 39.03 (t), 33.46, 33.41 (t), 32.85, 32.63 (t), 27.51 (q); MS *m*/*z* (relative intensity) 326 (M^+, 0.1), 311 (0.2), 308 (0.1), 303 (0.2), 204 (29), 189 (32), 145 (46), 133 (47), 105 (100). Anal. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 76.91; H, 8.19.

(1*S*,4*S*,5*S*)-4-(1-((Benzoyloxy)methyl)-3-iodopropyl)-1-methyl-6-methylenebicyclo[3.3.0]oct-2-ene (31). To a solution of **29** (107.0 mg, 0.328 mmol) in CH_2Cl_2 (6.6 mL) was added Et_3N (0.68 mL, 4.92 mmol) and MsCl (0.25 mL, 3.28 mmol) at −23 °C, and the reaction mixture was stirred at the same temperature for 2 h and at 0 °C for 1 h. The reaction mixture was quenched by the addition of ice cold H_2O at 0 °C, extracted Et_2O, dried (Na_2SO_4), and concentrated to give crude mesylate **30**. A solution of this mesylate and NaI (246 mg, 1.64 mmol) in acetone (3.3 mL) was stirred at rt for 24 h. The reaction mixture was diluted with H_2O, extracted with Et_2O, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:50) to give **31** (143.8 mg, quantitative) as a pale yellow oil: IR (neat) 2949, 1721, 1451, 1271, 1113, 711 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 8.06−8.01 (m, 2 H), 7.61−7.53 (m, 1 H), 7.48−7.41 (m, 2 H), 5.58−5.51 (m, 2 H), 4.82−4.77 (br-s, 1 H), 4.77−4.73 (br-s, 0.6 H), 4.73−4.70 (br-s, 0.4 H), 4.45 (dd, J = 11.5, 4.0 Hz, 0.4 H), 4.39 (dd, J = 11.0, 4.0 Hz, 0.6 H), 4.28 (dd, J = 11.0, 5.0 Hz, 0.6 H), 4.26 (dd, J = 11.5, 5.0 Hz, 0.4 H), 3.44−3.21 (m, 2 H), 2.78−2.70 (m, 1 H), 2.46−2.41 (br-s, 1 H), 2.33−2.20 (m, 2 H), 2.15−1.93 (m, 3 H), 1.74−1.64 (m, 1 H), 1.56−1.42 (m, 1 H), 1.24 (s, 1.8 H). 1.21 (s, 1.2 H); ^{13}C-NMR ($CDCl_3$) δ 166.50 (s), 158.74, 158.58 (s), 140.54 (d), 133.01 (d), 130.08, 129.70 (s), 129.56 (d, 3 C), 128.43 (d, 2 C), 104.60, 104.51 (t), 65.73, 65.21 (t), 57.34, 56.98 (d), 57.14, 57.07 (s), 56.62, 56.57 (d), 43.51, 43.15 (d), 38.94 (t), 34.29, 33.98 (t), 33.43, 33.35 (t), 27.59, 27.51 (q), 4.75, 4.57 (t); MS *m*/*z* (relative intensity) 436 (M^+, 0.2), 421 (0.1), 314 (28), 299 (12), 187 (43), 159 (53), 105 (100). Anal. Calcd for $C_{21}H_{25}IO_2$: C, 57.81; H, 5.77. Found: C, 57.57; H, 5.75.

(1*S*,2*S*,6*S*,8*S*)-11-(Hydroxymethyl)-6-methyl-3-methylenetricyclo-[6.3.0.0^{2,6}]undecane (33). To a solution of **31** (61.4 mg, 0.141 mmol) in benzene (7 mL) at reflux was added a solution of Bu_3SnH (0.076 mL, 0.282 mmol) and AIBN (4.6 mg, 0.028 mmol) in benzene (3.5 mL) in 10 portions at 30 min intervals. Reflux was continued for 30 min, and after cooling to rt, KF·2H_2O (80 mg) in CH_2Cl_2 (0.7 mL) was added and the mixture was stirred for 2 h, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (hexane → EtOAc−hexane, 1:20) to give crude benzoate **32**. To this crude benzoate was added a solution of NaOH (0.7%, in MeOH, 5.6 mL), and the reaction mixture was stirred at rt for 22 h. The reaction mixture was neutralized with saturated NH_4Cl solution, extracted EtOAc, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:5) to give **33** (27.8 mg, two steps 96%) as a colorless oil: IR (neat) 3318, 2944, 1456, 1025, 878 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 4.89−4.84 (m, 1.2 H), 4.83−4.78 (m, 0.8 H), 3.84 (dd, J = 11.3, 9.0 Hz 0.6 H), 3.69 (dd, J = 11.3, 6.0 Hz, 0.6 H), 3.61 (dd, J = 10.5, 6.2 Hz, 0.4 H), 3.48 (dd, J = 10.5, 7.8 Hz, 0.4 H), 2.80−2.29 (m, 3.6 H), 2.18−1.79 (m, 4.2 H), 1.78−1.52 (m, 2.4 H), 1.46−1.08 (m, 4.8 H), 1.06 (s, 1.2 H), 0.97 (s, 1.8 H); ^{13}C-NMR ($CDCl_3$) δ 158.76, 158.44 (s), 105.86, 105.00 (t), 66.54, 63.85 (t), 63.42, 58.44 (d), 57.00, 52.47 (d), 53.92, 52.89 (s), 49.67, 46.85 (d), 47.23, 46.98 (t), 43.74, 42.57 (d), 37.47, 35.55 (t), 32.62, 32.10 (t), 31.88, 30.82 (t), 30.17, 26.70 (t), 26.76, 25.36 (q); MS *m*/*z* (relative intensity) 206 (M^+, 13), 191 (100), 173 (30); HR-MS (M^+) calcd for $C_{14}H_{22}O$ 206.1671, found 206.1664.

(1*S*,2*S*,6*S*,8*S*)-3,3-Ethylene-11-(hydroxymethyl)-6-methyltricyclo-[6.3.0.0^{2,6}]undecane (34). To a stirred solution of **33** (19.9 mg, 0.0964 mmol) in toluene (2.4 mL) was added a solution of Et_2Zn (1.0 M, in hexane, 0.48 mL, 0.48 mmol) at rt. After warming to 60 °C, the reaction mixture was treated dropwise with CH_2I_2 (0.078 mL, 0.964 mmol) and stirred for 15 h at the same temperature. The reaction mixture was diluted with Et_2O, washed with 1 N aqueous HCl and saturated $NaHCO_3$ solution, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:10) to give **34** (20.2 mg, 95%) as a colorless oil: IR (neat) 3341, 2939, 2863, 1458, 1024 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.59 (dd, J = 10.2, 6.6 Hz, 0.6 H), 3.58 (dd, J = 10.5, 5.4 Hz, 0.4 H), 3.45 (dd, J = 10.2, 7.8 Hz, 0.6 H), 3.38 (dd, J = 10.5, 7.8 Hz, 0.4 H), 2.75−2.44 (m, 1.4 H), 2.09−1.23 (m, 13.6 H), 1.21 (s, 1.2 H), 1.17 (s, 1.8 H), 0.58−0.32 (m, 4 H); ^{13}C-NMR ($CDCl_3$) δ 66.40, 64.94 (t), 65.05, 59.28 (d), 54.25 (s), 53.95, 51.97 (d), 49.51, 46.38 (d), 49.29, 48.20 (t), 44.49, 44.15 (d), 40.06, 39.23 (t), 35.80, 35.67 (t), 31.39, 30.77 (t), 29.47 (s), 28.45 (q), 28.25 (t), 16.53, 15.67 (t), 7.19, 6.81 (t); MS *m*/*z* (relative intensity) 220 (M^+, 4), 205 (43), 191 (55), 107 (100); HR-MS (M^+) calcd for $C_{15}H_{24}O$ 220.1827, found 220.1836.

(1*S*,2*S*,6*S*,8*S*)-11-(Hydroxymethyl)-3,3,6-trimethyltricyclo[6.3.0.0^{2,6}]-undecane (35). A mixture of **34** (22.4 mg, 0.102 mmol) and PtO_2 (4.6 mg, 0.020 mmol) in acetic acid (2.0 mL) was hydrogenated at rt under atmospheric pressure for 3 days. The reaction mixture was filtered through a Celite pad, neutralized with saturated $NaHCO_3$ solution, extracted with EtOAc, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel column chromatography (EtOAc−hexane, 1:10) to give **35** (18.0 mg, 80%) as a colorless oil: IR (neat) 3374, 2935, 1028 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.72 (dd, J = 10.5, 6.7 Hz, 0.6 H), 3.68 (dd, J = 10.8, 4.2 Hz, 0.4 H), 3.54 (dd, J = 10.5, 7.9 Hz, 0.6 H), 3.42 (dd, J = 10.8, 7.1 Hz, 0.4 H), 2.66−2.40 (m, 1.4 H), 2.18−1.32 (m, 13.6 H), 1.22 (s, 1.2 H), 1.17 (s, 1.8 H), 1.00 (s, 1.2 H), 0.98 (s, 1.8 H), 0.95 (s, 1.8 H), 0.92 (s, 1.2 H); ^{13}C-NMR ($CDCl_3$) δ 67.57, 61.92 (d), 66.87, 65.41 (t), 53.62, 53.35 (s), 50.74, 49.40 (d), 49.72, 48.84 (t), 48.79, 46.90 (d), 46.40, 45.50 (d), 42.37, 42.16 (s), 41.42, 41.39 (t), 40.70, 40.63 (t), 32.20 (q), 31.23, 31.04 (t), 30.73,

30.30 (q) 29.56, 28.54 (t), 26.00, 25.68 (q); MS *m*/*z* (relative intensity) 222 (M^+, 14), 207 (8), 166 (56), 151 (54), 135 (100): HR-MS (M^+) calcd for $C_{15}H_{26}O$ 222.1983, found 222.1975.

(−)-$\Delta^{9(12)}$-Capnellene (7). A solution of **35** (17.0 mg, 0.0764 mmol) in pyridine (0.8 mL) containing 2-nitrophenyl selenocyanate (52 mg, 0229 mmol) was treated dropwise with Bu_3P (0.057 mL, 0.229 mmol) at rt. After being stirred for 20 h, the reaction mixture was quenched by the addition of H_2O, diluted with Et_2O, washed with 1 N aqueous HCl and saturated $NaHCO_3$ solution, dried (Na_2SO_4), and concentrated to give crude **36**. To the residual yellow solid were added THF (1.5 mL), K_2CO_3 (105 mg, 0.764 mmol), and 30% H_2O_2 (0.31 mL) at rt. The reaction mixture was stirred at rt for 20 h and directly filtered through a silica gel pad. This crude products were purified by silica gel column chromatography (EtOAc−hexane, 1:10) to give (−)-capnellene (**7**) (12.2 mg, two steps 78%) as a colorless oil: $[\alpha]^{26}_D$ −120 (*c* 0.325, $CHCl_3$) (87% ee); IR (neat) 3068, 2934, 2864, 1650, 1456, 1382, 1372, 1364, 874 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 4.91−4.88 (br-s, 1 H), 4.80−4.77 (br-s, 1 H), 2.68−2.62 (m, 1 H), 2.60−2.30 (m, 3 H), 1.78−1.64 (m, 3 H), 1.56−1.42 (m, 5 H), 1.20 (dd, J = 13.2, 9.5 Hz, 1 H), 1.15 (s, 3 H), 1.05 (s, 3 H), 0.98 (s, 3 H); ^{13}C-NMR ($CDCl_3$) δ 158.98 (s), 104.96 (t), 69.06 (d), 53.32 (s), 52.27 (d), 47.89 (t), 45.99 (d), 42.32 (s), 41.66 (t), 40.56 (t), 31.81 (q), 31.50 (t), 30.80 (q), 29.02 (t), 26.04 (q).

Supporting Information Available: ^{1}H- and ^{13}C-NMR spectra of all new compounds (37 pages). See any current masthead page for ordering and Internet access information.

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