Stereocontrolled Synthesis of Exocyclic Olefins Using Arene Tricarbonyl Chromium Complex-Catalyzed Hydrogenation. I. Efficient Synthesis of Carbacyclin and Its Analogs

Mikiko SODEOKA,[a] Yuji OGAWA,[a] Yoshie KIRIO,[b] and Masakatsu SHIBASAKI*,[a]

Sagami Chemical Research Center,[a] Nishi-Ohnuma, Sagamihara, Kanagawa 229, Japan and Faculty of Pharmaceutical Sciences, Hokkaido University,[b] Sapporo 060, Japan. *Received August 20, 1990*

An efficient synthesis of carbacyclin and its analogs (2—7) is described in which the stereospecific 1,4-hydrogenation of a 1,3-diene to an internal monoene plays a key role. That is, arene·$Cr(CO)_3$ complex-catalyzed 1,4-hydrogenation of the dienes 13 and 58, obtainable from the Corey lactone in good yields, under high H_2 pressure afforded the exocyclic olefins 14 and 61 stereospecifically in excellent yields, and these intermediates were converted to therapeutically useful carbacyclin (2) and its analogs 3—7 in a usual way.

Keywords 1,3-diene; 1,4-hydrogenation; arene tricarbonyl chromium complex; Corey lactone; carbacyclin; prostacyclin; antiulcer drug; circulatory disease; exocyclic olefin

Carbacyclin (**2**) is one of the potent, chemically stable analogs of prostacyclin (PGI_2, **1**), which is a naturally occurring bioregulator having remarkable platelet aggregation-inhibiting activity. Some ω-chain derivatives **3** and **5** are being studied in clinical trials as therapeutic agents for cardiovascular and circulatory diseases. Although many groups have succeeded in the synthesis of these important compounds,[1] none of the syntheses has involved the completely stereocontrolled construction of a 5*E*-trisubstituted olefin (PG numbering).[2] Therefore, formation of a considerable amount of the biologically much less active 5*Z*-isomer and extremely troublesome separation of the stereoisomers were unavoidable, making the industrial-scale preparation of the carbacyclin analogs fairly difficult. We started our research with the aim of developing a practical synthetic route which would involve the completely stereocontrolled construction of an exocyclic olefin.[3]

Wittig reaction, semihydrogenation of alkynes, combination of hydro- or carbometalation of alkynes and cross-coupling reaction, and so on are known as methods for the stereocontrolled synthesis of olefins. These methods, however, could not be applied to carbacyclin synthesis involving the stereocontrolled construction of an exocyclic olefin. We gave attention to the 1,4-hydrogenation of conjugated dienes to *cis*-olefins catalyzed by arene·$Cr(CO)_3$ complex. This reaction was first reported in 1968.[4] Subsequent mechanistic studies using simple substrates suggested that the regio- and stereochemistry of the products were controlled by the bidentate coordination of a diene in *s-cis* conformation to the chromium atom.[5] However, few applications of this reaction to the syntheses of rather complex molecules have been reported.[6] Although the scope and limitations of this hydrogenation were not clear, we anticipated that this remarkable reaction could be used for the stereocontrolled synthesis of an exocyclic olefin moiety in carbacyclin and its analogs. That is, it was expected that the conjugate diene **9** would be stereospecifically converted to the exocyclic trisubstiuted olefin **10**, a key intermediate for the synthesis of carbacyclin and its analogs, by this 1,4-hydrogenation. Furthermore, application of this methodology to the cyano-substituted diene **58** would enable us to synthesize cyanocarbacyclins (**6** and **7**), new carbacyclin analogs which were expected to have a similar biological profile to that of nileprost (**8**). Nileprost (**8**) may be of therapeutic value for gastric ulcer because of its potent antiulcer effect with weak antiaggregatory and vasodilating

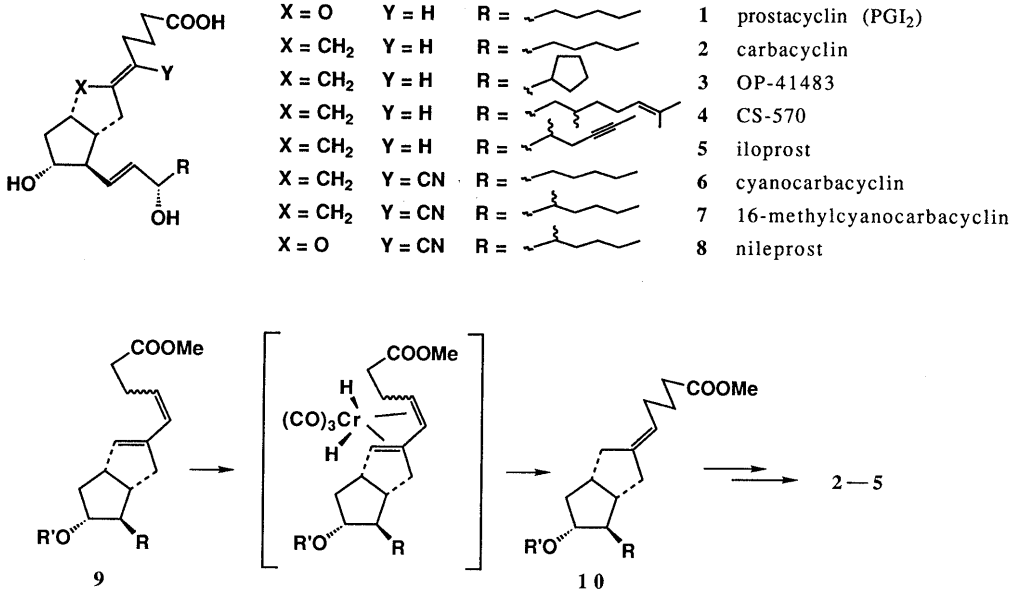


Chart 1

activities.

This account describes the stereospecific synthesis of carbacyclins (**2**—**5**) and cyanocarbacyclins (**6** and **7**).

Synthesis of Carbacyclin and Its Analogs It was well known that the most favorable stereochemistry of double bonds for the 1,4-hydrogenation was *E,E*.[5] Therefore, in the first place, the 1,4-hydrogenation of the conjugated diene **11** with an *E*-disubstituted olefin, which was stereospecifically synthesized from the well-known Corey lactone in *ca.* 27% overall yield by using an intramolecular thermal ene reaction as a key step,[7a,c] was undertaken. Hydrogenation of **11** in acetonitrile (70 kg/cm^2 of H_2 pressure, 130 °C, 12 h) using (methyl benzoate)$Cr(CO)_3$ as a catalyst (20 mol%) gave the desired *E*-exocyclic olefin **12** stereospecifically in 66% yield. None of the other possible products was observed except for the recovery of **11** (21%). The stereochemistry of **12** was unequivocally determined by comparison with an authentic sample[1] (gas liquid chromatography (GLC) analysis). Thus, the stereospecific synthesis of a 5*E*-trisubstituted olefin as found in carbacyclin (**2**) and its analogs **3**—**5** was realized for the first time. In order to improve the chemical yield, solvent effects were investigated, and acetone, which has weaker coordination ability to chromium than acetonitrile, was found to be an excellent solvent. That is, treatment of **11** with (methyl benzoate)$Cr(CO)_3$ (20 mol%) in acetone under 70 kg/cm^2 of H_2 pressure (120 °C, 15 h) provided **12** in nearly quantitative yield.

Next we turned our attention to the *Z*-rich 1,3-diene **13** (*Z*:*E*=2.2:1), which was prepared from the Corey lactone in much better overall yield (69%) by using an intramolecular aldol condensation as a key step.[7a,b] Hydrogenation of the *Z*-rich diene **13** in acetone (70 kg/cm^2 of H_2 pressure, 120 °C, 12 h) using (methyl benzoate)$Cr(CO)_3$ as a catalyst (20 mol%) gave the desired *E*-exocyclic olefin **14** in nearly quantitative yield. Careful GLC analysis of the hydrogenated product, however, indicated contamination with a trace amount of the regioisomer **15** (<2%). Treatment of **14** with tetrabutylammonium fluoride (TBAF) afforded the alcohol **16**, which was a versatile intermediate for the synthesis of carbacyclin and its analogs, in 95% yield, and at this stage the minor regioisomer **17** was found to be easily separated by silica gel chromatography (1.9%). Furthermore, when

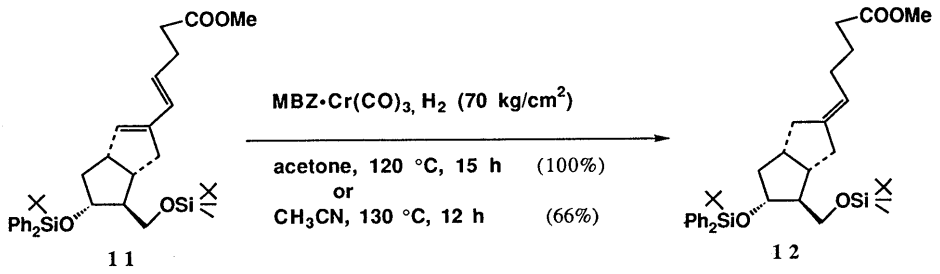


Chart 2

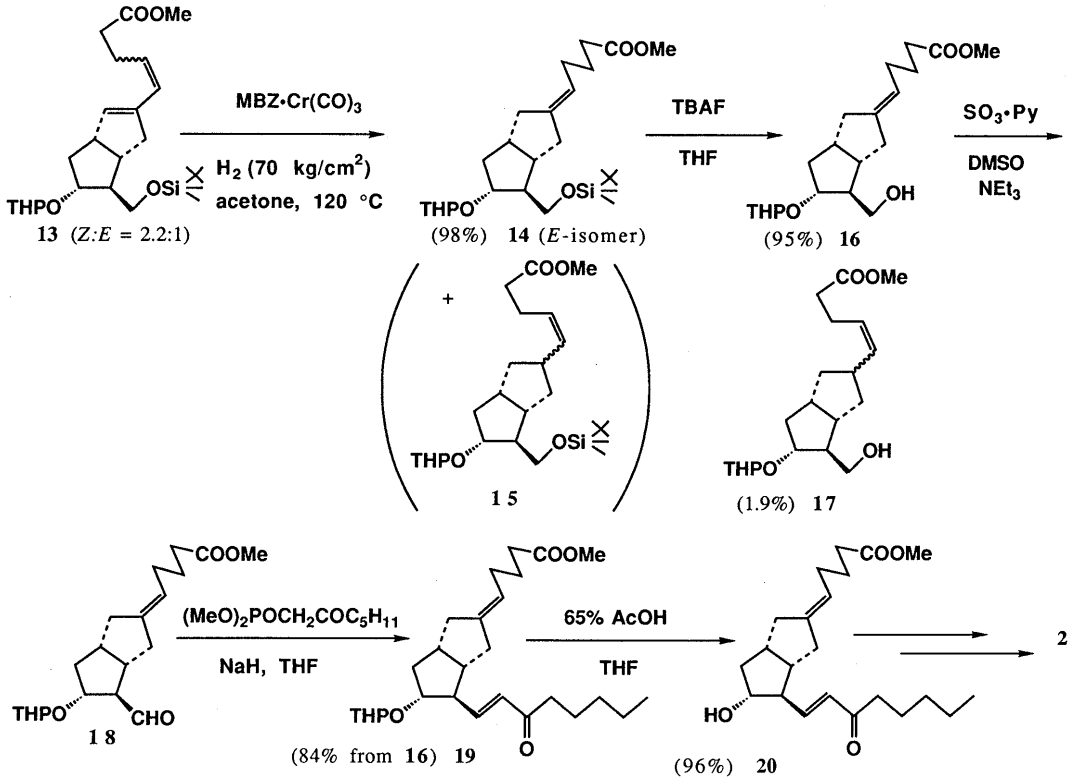
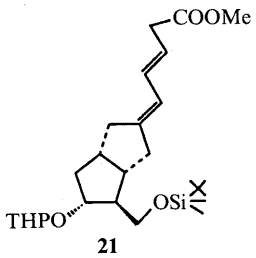


Chart 3

TABLE I. Hydrogenation of **13** ($Z:E=2.2:1$)



21

MBZ = methyl benzoate
NP = naphthalene
TOL = toluene
Ar = argon

Run	Catalyst[a]	Solvent	Pressure (kg/cm^2)	Temp. (°C)	Time (h)	Yield (%) 14	21	15	Recovery 13 Z	E
1	MBZ·$Cr(CO)_3$	Acetone	H_2 70	120	16	98	—	+[b]	—	—
2	NP·$Cr(CO)_3$	THF	H_2 70	45	23	95	—	+[b]	—	—
3	MBZ·$Cr(CO)_3$	CH_3CN	H_2 70	130	12	28	27	+[b]	37	—
4	MBZ·$Cr(CO)_3$	CH_3CN	H_2 130	120	24	83	—	+[b]	—	—
5	TOL·$Cr(CO)_3$	Acetone	H_2 70	130	13	81	4	+[b]	—	—
6	MBZ·$Cr(CO)_3$	CH_3CN	Ar 70	130	12	—	32	—	25	29
7	MBZ·$Cr(CO)_3$	Acetone	Ar 70	130	25	—	28	—	17	21

a) In each case, 20 mol% of catalyst was used. *b*) TLC analysis showed the presence of an extremely small amount of **15**.

naphthalene·$Cr(CO)_3$ complex was used as a catalyst in tetrahydrofuran (THF), the hydrogenation proceeded smoothly at 45 °C to give **14** stereospecifically in 95% yield. Thus, a highly efficient synthesis of the key intermediate for **2**—**5** was developed.

The alcohol **16** was then transformed to the enone **20** in a usual manner. Oxidation of **16** with SO_3·pyridine complex and triethylamine in dimethyl sulfoxide (DMSO) gave the aldehyde **18**, which was directly treated with the phosphonate carbanion derived from dimethyl (2-oxoheptyl)phosphonate and sodium hydride in THF to provide **19** in 84% overall yield. Deprotection of a 2-tetrahydropyranyl (THP) group in **19** afforded **20** in 96% yield, and **20** has been transformed to carbacyclin (**2**) in *ca.* 80% yield.[1k] The overall yield of carbacyclin (**2**) from the Corey lactone was *ca.* 40%, and using this route, the various ω-chain analogs **3**—**5** were also synthesized efficiently.

Reaction Pathway of the Hydrogenation Using 13 In contrast to the aforesaid successful results, hydrogenation of **13** in acetonitrile (70 kg/cm^2 of H_2 pressure, 130 °C, 12 h) using (methyl benzoate)$Cr(CO)_3$ as a catalyst (20 mol%) gave two main products (Table I, run 3). One was the desired 1,4-reduction product **14** (28%), and the other was the stereochemically homogeneous (3*E*, 5*E*) exocyclic conjugated diene **21** (27%), probably formed through a 1,5-hydrogen shift. In addition the starting diene containing only the 4*Z*-stereoisomer was recovered (37%). The exocyclic conjugated diene **21** was found to be formed just by heating **13** in the presence of a catalytic amount of (methyl benzoate)$Cr(CO)_3$ (20 mol%) in acetonitrile or acetone under an argon atmosphere in proportion to the consumption of the 4*Z*-isomer of **13** (runs 6 and 7). On the other hand, treatment of **21** with a catalytic amount of (methyl benzoate)$Cr(CO)_3$ in acetone under an argon atmosphere for 20 h at 130 °C afforded the 4*Z*-isomer of **13** (38%) together with **21** (62%). These results strongly implied that only one part (4*Z*) of the conjugated diene **13** and the exocyclic conjugated diene **21** were in a state of equilibrium through the η^5-pentadienylhydridochromium intermediate **22**. No other isomerized product was obtained in any case, showing that this 1,5-hydrogen shift catalyzed by (methyl benzoate)$Cr(CO)_3$ proceeded in a strictly stereocontrolled manner.[8] In marked contrast to the 4*Z*-isomer, no isomerization of the 4*E*-isomer having no readily abstractable hydrogen was found to occur.

It was of quite interest to understand why the exocyclic conjugated diene **21** or its 1,4-hydrogenated product **15** was scarcely formed from **13** under the reaction conditions mentioned above (runs 1 and 2). Even in the case of acetonitrile as the solvent, a simple increase in H_2 pressure to 130 kg/cm^2 afforded none of the exocyclic diene **21** (run 4). On the other hand, hydrogenation of **13** in acetone using toluene·$Cr(CO)_3$, a slightly less active catalyst compared with (methyl benzoate)$Cr(CO)_3$, also afforded a small amount of **21** (4%). We assumed the following mechanism (Chart 4). Under all the hydrogenation conditions used, while the 4*E*-isomer of **13** was exclusively hydrogenated to give the desired product **14**, the 4*Z*-isomer of **13** was isomerized very rapidly, being in a state of equilibrium between *Z*-**13** and **21**. However, owing to the extremely slow 1,4-hydrogenation of **21** to **15**, the 4*Z*-isomer of **13** was transformed into **14** in high yield. The reason why 1,4-hydrogenation of **21** to **15** was quite slow is not clear at present. Thus, the 5*E*-trisubstituted olefin **14** was formed in high yield under the well-suited hydrogenation conditions. This assumption was strongly supported by the experimental fact that hydrogenation of the exocyclic conjugated diene **21** in acetone using (methyl benzoate)-$Cr(CO)_3$ as a catalyst (20 mol%) (70 kg/cm^2 of H_2 pressure, 120 °C, 16 h) gave the 5*E*-trisubstituted olefin **14** in 94% yield accompanied with a trace amount of **15**.

1,4-Hydrogenation of the Dienes with an ω-Chain Next we turned our attention to the 1,4-hydrogenation of the conjugated dienes having an ω-chain **36**—**39**. As shown in Chart 5, the dienes **36**—**39** were synthesized from **13** in a usual manner. In the case of the dienes **36**—**38**, the stereospecific hydrogenation proceeded quite smoothly, and the desired exocyclic olefins **40**—**42** were obtained stereospecifically in nearly quantitative yields. The stereochemistry of the exocyclic olefins was unequivocally

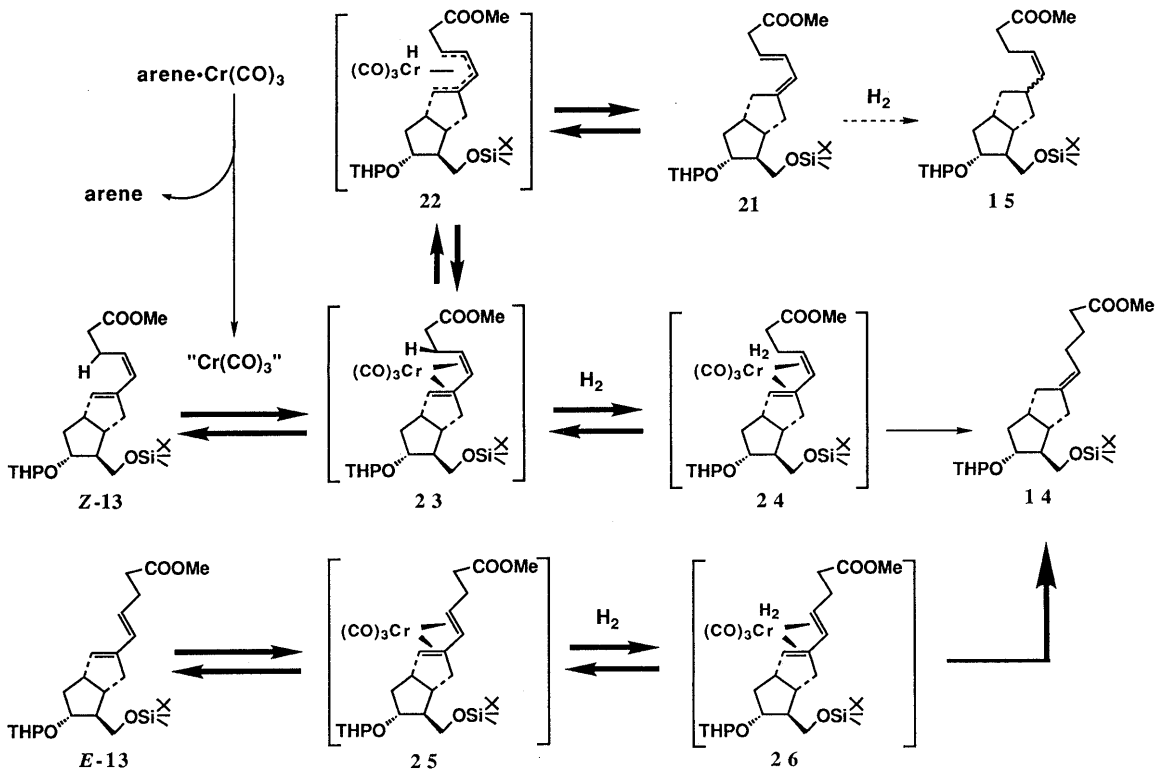


Chart 4

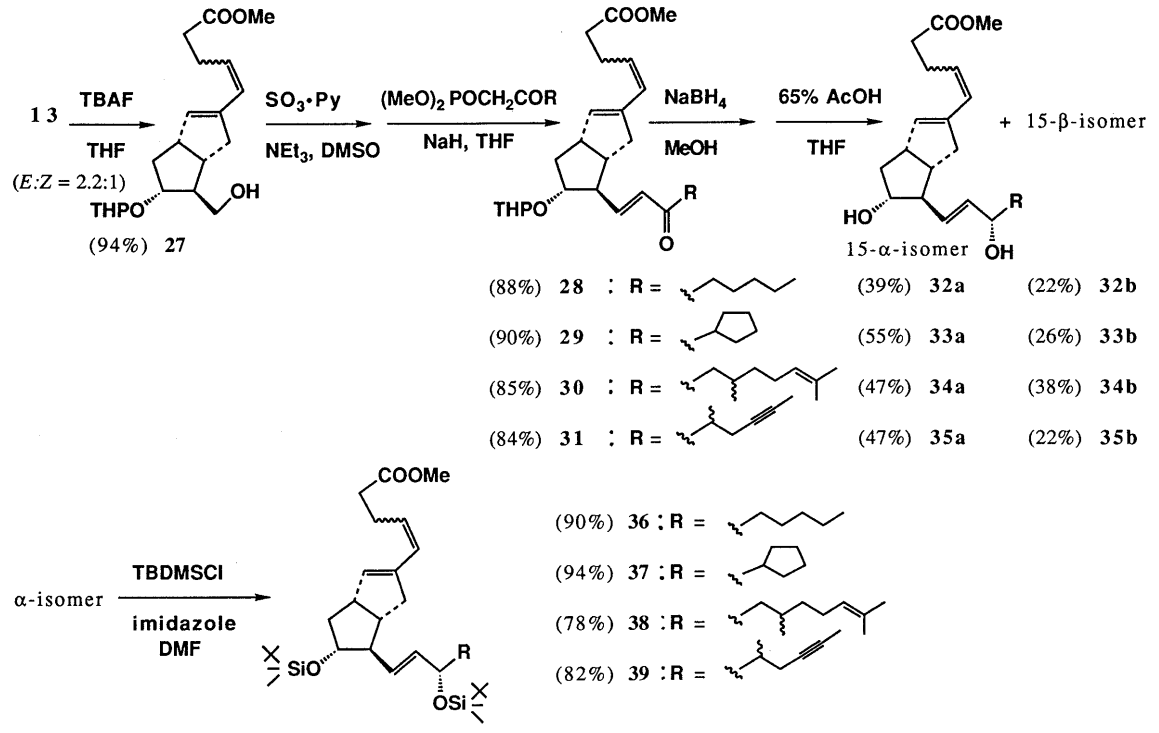


Chart 5

determined by comparison with authentic samples.[1] On the other hand, the hydrogenation of the diene **39** was complicated by the partial reduction of a triple bond. Namely, hydrogenation of the diene **39** in acetone (70 kg/cm^2 of H_2 pressure, 120 °C, 15 h) using (methyl benzoate)$Cr(CO)_3$ as a catalyst (20 mol%) gave the four products **43**—**46**. The yield of the desired product **43** was only 33%. Furthermore, the hydrogenation of the enone **29** was found to afford the saturated ketone **47** exclusively (100%). These new catalytic activities of arene·$Cr(CO)_3$ for the conversion of alkynes to *cis*-alkenes and enones to saturated ketones have already been reported in detail.[9]

The hydrogenation products **40**—**43** were then converted to the corresponding carbacyclin analogs **2**—**5** as shown in

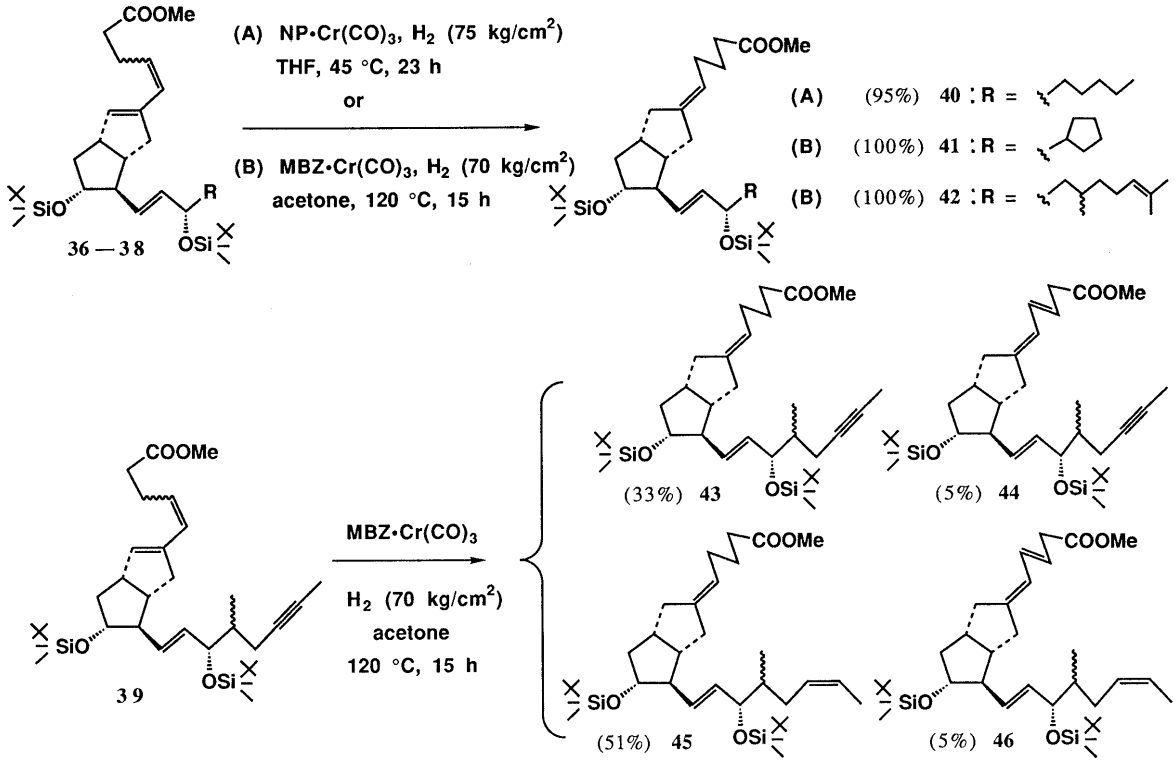


Chart 6

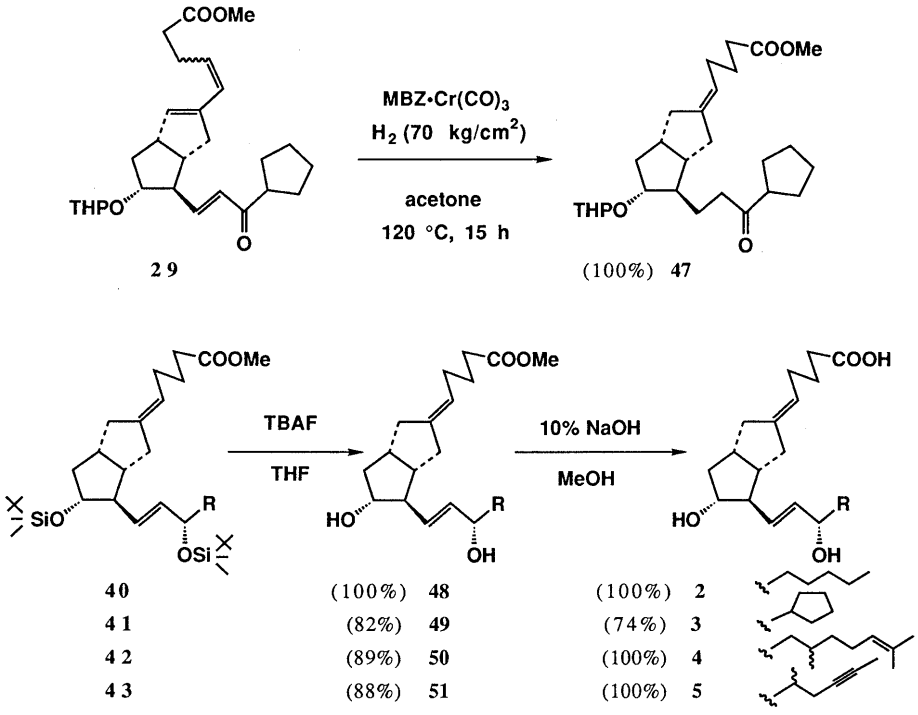


Chart 7

Chart 7. Since the synthetic routes to the conjugated dienes having an ω-chain from furfural or optically active 4-hydroxy-2-cyclopentenone were already established,[7a,10] the results described above should pave the way for the stereocontrolled synthesis of carbacyclin and its analogs from various starting materials.

Synthesis of Cyanocarbacyclin and Its Analogs Having established an efficient synthesis of carbacyclin and its analogs, we then turned our attention to the stereocontrolled synthesis of exocyclic tetrasubstituted olefins. Cyanocarbacyclins (**6** and **7**) were selected as target molecules with an exocyclic tetrasubstituted olefin moiety. In order to accomplish the stereocontrolled synthesis of cyanocarbacyclins (**6** and **7**) by using the 1,4-hydrogenation as a key step, the requisite conjugated diene **58** with a cyano functionality at the C-5 position was efficiently synthesized from **52** as

shown in Chart 8. The α,β-unsaturated aldehyde **52**, prepared from the Corey lactone in 73% overall yield,[7a,b] was first reduced to the allylic alcohol **53** diisobutyalminum hydride (DIBAH) in 98% yield. After conversion of **53** to the bromide **54** (PPh_3 and CBr_4 in CH_2Cl_2 at -60——$-25\,°C$, 89% yield), **54** was treated with KCN and 18-crown-6 in CH_3CN to give the allylic cyanide **55** in 99% yield. The α-chain was regiospecifically introduced by the coupling reaction of **55** and the aldehyde **56**[11] (lithium diisopropylamide (LDA) in THF at $-78\,°C$, then **56**), furnishing a diastereoisomeric mixture of the cyano-alcohols **57** in 82% yield. Subsequently these cyano-alcohols **57** were treated with methanesulfonyl chloride and triethylamine in CH_2Cl_2. Under these reaction conditions elimination occurred spontaneously to afford an easily separable mixture of the diene **58a** (83%) and **58b** (6%). The stereochemistry of both **58a** and **58b** was determined on the basis of the chemical shifts of the vinyl protons in their nuclear magentic resonance (NMR) spectra[12] (**58a**: δ 6.10 ppm, *trans* to nitrile, **58b**: δ 6.20, *cis* to nitrile). Furthermore, the chemical reactivity of **58a** and **58b** in the 1,4-hydrogenation reaction supported the above-mentioned stereochemistry.

The crucial 1,4-hydrogenation of **58a** proceeded smoothly *via* the transition state **60** by using (methyl benzoate)-$Cr(CO)_3$ (20 mol%) as a catalyst in acetone to afford the stereochemically homogeneous *Z*-tetrasubstituted olefin **61** in quantitative yield (70 kg/cm^2 of H_2 pressure, 120 °C,

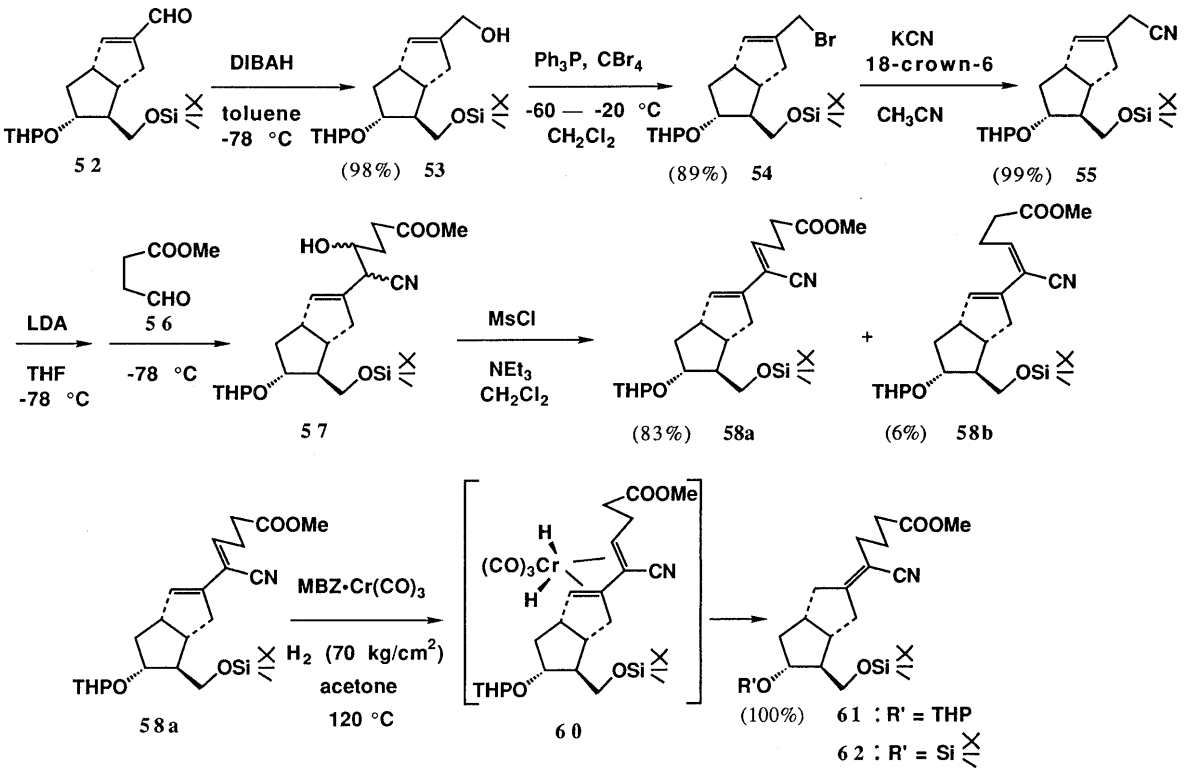


Chart 8

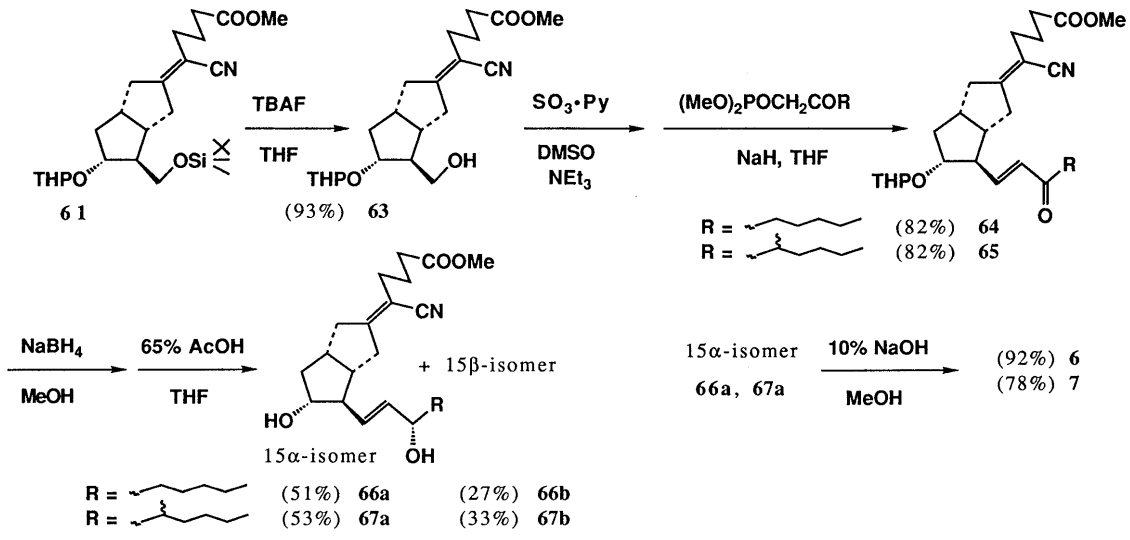


Chart 9

15 h). It was also found that the hydrogenation proceeded under milder conditions by the use of naphthalene·$Cr(CO)_3$ (20 mol%) as a catalyst in THF (70 kg/cm^2 of H_2 pressure, 45 °C, 21 h) to give **61** stereospecifically in 97% yield.[13] On the other hand, the 1,4-hydrogenation of **58b**, available in very low yield, remained unchanged under the various 1,4-hydrogenation conditions probably due to steric hindrance around the diene moiety.

Introduction of an ω-chain into the hydrogenation product **61** was accomplished according to the general procedure (Chart 9), and cyanocarbacyclin (**6**) and its 16-methyl analog **7** were obtained in 36 and 32% overall yields from **61**, respectively.

On the contrary, the stereoselective synthesis of the 5*E*-stereoisomer **68** was achieved by the Pd–C-catalyzed hydrogenation of **58**.[14] That is, treatment of **58** with 10% Pd–C in toluene (1 atm of hydrogen pressure, −40 °C) afforded **68** stereoselectively (**68**:**61** = 6.7:1) *via* reduction-isomerization. After desilylation, the 5*E*-isomer **72** was isolated from the alcohol derived from **70**. This selectivity might be explained by the steric effect and/or the intramolecular coordination of a cyano group to Pd in the π-allyl intermediate **71**. It is of particular interest that the stereoselectivity of the product can be reversed depending on the catalyst used. The stereochemistry of the newly formed double bonds of **61** and **68** was determined to be *Z* and *E*, respectively, from nuclear Overhauser effect (NOE) experiments on **62** derived from **61** (i. Et_2AlCl, ii. *tert*-butyldimethylchlorosilane (TBDMSCl), imidazole in dimethylformamide (DMF), 75% yield in two steps) and **69** derived from **72** (i. 65% AcOH, ii. TBDMSCl, imidazole, DMF, 45% in two steps) (Fig. 1 in the experimental section).

The absence of the 5*E*-stereoisomers **73** and **74** in the cyanocarbacyclins (**6**, **7**) was confirmed by the following experiments. Thus, **72** was transformed into 5*E*-cyanocarbacyclin (**73**, **74**) by a similar procedure to that described above (Chart 10). Careful thin layer chromatography (TLC) analysis of both **73**, **74** and **6**, **7** showed clearly that the cyanocarbacyclins (**6** and **7**) were stereochemically homogeneous, indicating that isomerization of an α,β-conjugated cyanide functionality did not occur during the ω-chain introduction. On the basis of the arguments present above, it was concluded that the 1,4-hydrogenation of 1,3-dienes bearing a cyano functionality at the C-2 position provides a useful method for the stereospecific construction of versatile exocyclic tetrasubstituted olefins.[15]

Biological Activity Preliminary results of the biological testing of cyanocarbacyclins **6** and **7**, and the dienecarbacyclin analogs **75**—**78** prepared by the hydrolysis of **32**—**35** are shown in Table II. Contrary to expectation, the platelet aggregation-inhibiting and cytoprotective effects of the cyanocarbacyclins **6** and **7** were both very weak. On the other hand, the new prostacyclin analogs 75—78 were as potent as the known carbacyclin analogs in inhibiting human platelet aggregation induced by adenosine diphosphate (ADP).[16] These new prostacyclin analogs might be of therapeutic value for occlusive peripheral vascular diseases.[17]

As described above, we have shown that the arene·$Cr(CO)_3$-catalyzed hydrogenation of conjugated dienes can

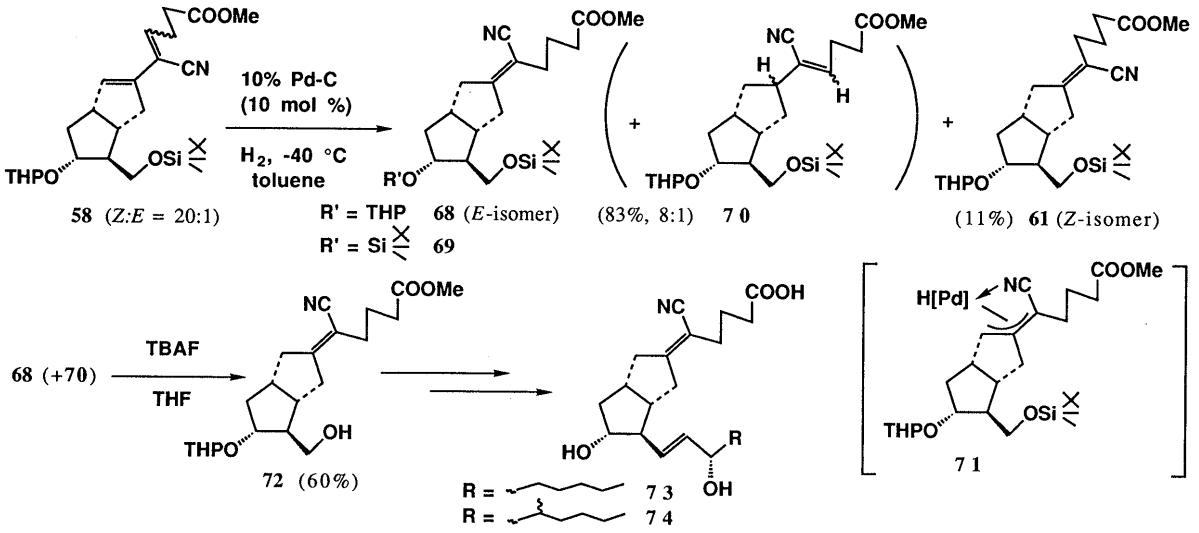


Chart 10

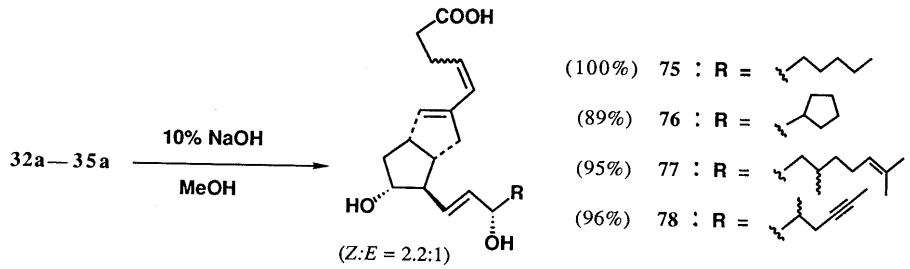


Chart 11

Table II. Biological Activities of Carbacyclin Analogs

Compound	ADP induced human platelet aggregation *in vitro* inhibition (%)						Cytoprotective effect[a] inhibition (%)	
	Drug concentration (M)						dose (μg/kg)	
	10^{-4}	10^{-5}	10^{-6}	10^{-7}	10^{-8}	10^{-9}	250	5
3				99	47	6		
5				99	89	35		
6	100	0					20	
7		91	15				27	
75				100	44			
76				100	64	16		
77				100	25	13		
78					100	59		77

a) Cytoprotective effects on HCl-induced gastric mucosal lesion in rats.

be an excellent method for the stereocontrolled synthesis of exocyclic olefins. The synthesis presented in this paper offers the most efficient synthetic route to carbacyclins. Carbacyclins and several synthetic intermediates are now being produced on a commercial basis.[18]

Experimental

General Methods Infrared (IR) spectra were measured on a JASCO A-202 diffraction grating infrared spectrophotometer. ^{1}H-NMR spectra were recorded with a Varian EM 390 NMR spectrometer or a Hitachi R-90H Fourier-transform NMR spectrometer or a Bruker ASX-500 spectrometer with tetramethylsilane as an internal standard. Low-resolution mass spectra (MS) were obtained with a Hitachi RUM-6MG mass spectrometer. Optical rotation was measured on a Horiba SEPA-200 high-sensitivity polarimeter. In general, reactions were carried out in dry solvents under an argon atmosphere unless otherwise mentioned.

In a similar manner to the previously reported[7a] intramolecular ene reaction route, the diene **11** was synthesized from methyl (*Z*)-7-[(1*R*,2*S*,3*R*)-2-*tert*-butyldimethylsilyloxymethyl-5-methylene-3-tetrahydropyranyloxycyclopentyl]hept-5-enoate. Yield and spectral data of the intermediates were as follows.

Methyl (*Z*)-7-[(1*R*,2*S*,3*R*)-2-*tert*-Butyldimethylsilyloxymethyl-3-*tert*-butyldiphenylsilyloxy-5-methylenecyclopentyl]hept-5-enoate Yield from methyl (*Z*)-7-[(1*R*,2*S*,3*R*)-2-*tert*-butyldimethylsilyloxymethyl-5-methylene-3-tetrahydropyranyloxycyclopentyl]hept-5-enoate was 87%. IR (neat): 1743, 1660 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.86 (s, 9H), 1.10 (s, 9H), 1.20—2.60 (m, 12H), 3.50 (d, J=6 Hz, 2H), 3.68 (s, 3H), 4.12 (m, 1H), 4.83 (br s, 2H), 5.50 (m, 2H), 7.20—7.60 (m, 6H), 7.60—7.90 (m, 4H). MS *m/z*: 563 ($M^+ - tert$-Bu), 296, 295, 294, 293, 255, 240, 239 (base peak), 237, 215. HR-MS *m/z*: (M^+ − Me) Calcd for $C_{36}H_{53}O_4Si_2$ 605.3479, Found 605.3475. $[\alpha]_D^{20}$: −22° (c=1.50, MeOH).

Methyl (*Z*)-7-[(1*S*,2*S*,3*R*,5*S*)-2-*tert*-Butyldimethylsilyloxymethyl-3-*tert*-butyldiphenylsilyloxy-5-hydroxymethylcyclopentyl]hept-5-enoate Yield was 78%. IR (neat): 3475, 1745, 740, 705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.14 (s, 6H), 0.85 (s, 9H), 1.17 (s, 9H), 1.50—2.50 (m, 13H), 3.00—3.50 (m, 3H), 3.70 (s, 3H), 3.75 (m, 2H), 4.18 (m, 1H), 5.42 (m, 2H), 7.20—7.50 (m, 6H), 7.50—7.90 (m, 4H). MS *m/z*: 581 ($M^+ - tert$-Bu), 365, 271, 251, 234, 233, 221, 219, 209, 201, 73 (base peak). HR-MS *m/z*: (M^+) Calcd for $C_{37}H_{58}O_5Si_2$ 638.3820, Found 638.3847. $[\alpha]_D^{20}$: +16° (c=1.98, MeOH).

Methyl (*Z*)-7-[(1*S*,2*S*,3*R*,5*S*)]-2-*tert*-Butyldimethylsilyloxymethyl-3-*tert*-butyldiphenylsilyloxy-5-formylcyclopentyl]hept-5-enoate Yield was 100%. IR (neat): 1740, 1720, 740, 700 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.07 (s, 6H), 0.88 (s, 9H), 1.14 (s, 9H), 1.30—2.50 (m, 12H), 2.70 (m, 1H), 3.50 (m, 2H), 3.74 (s, 3H), 4.20 (m, 1H), 5.47 (m, 2H), 7.20—7.60 (m, 6H), 7.60—7.90 (m, 4H), 10.05 (d, J=3 Hz, 1H). MS *m/z*: 580, 579 ($M^+ - tert$-Bu), 368, 313, 272, 271, 249, 235, 231, 217, 211, 210, 209, 200, 73 (base peak). HR-MS *m/z*: ($M^+ - tert$-Bu) Calcd for $C_{33}H_{47}O_5Si_2$ 579.2959, Found 579.2931. $[\alpha]_D^{20}$: +7° (c=1.34, MeOH).

Methyl (1*R*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-7-*tert*-butyldiphenylsilyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (11) Yield from methyl (*Z*)-7-[(1*S*,2*S*,3*R*,5*S*)-2-*tert*-butyldimethylsilyloxymethyl-3-*tert*-butyldiphenylsilyloxy-5-formylcyclopentyl]hept-5-enoate was 57%. IR (neat): 1745, 740, 700 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.07 (s, 9H), 1.50—2.00 (m, 2H), 2.00—2.70 (m, 8H), 2.90 (m, 1H), 3.30—4.20 (m, 3H), 3.70 (s, 3H), 5.50 (m, 2H), 6.25 (d, J=16.5 Hz, 1H), 7.25—7.50 (m, 6H), 7.50—7.80 (m, 4H). MS *m/z*: 561 ($M^+ - tert$-Bu), 271, 231, 209, 205 (base peak). HR-MS *m/z*: ($M^+ - tert$-Bu) Calcd for $C_{33}H_{45}O_4Si_2$ 561.2854, Found 561.2871.

Methyl (1*S*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*E*-Δ$^{3,\delta}$pentanoate (14) The diene **13** (495 mg, 1.07 mmol) and (methyl benzoate)$Cr(CO)_3$ (58 mg, 0.21 mmol) were dissolved in acetone (15 ml). The solution was degassed by three freeze-pump-thaw cycles, and then transferred into an autoclave with glass insert (100 ml) under an argon atmosphere. The autoclave was purged repeatedly with hydrogen. The solution was stirred at 120 °C for 16 h under 70 kg/cm^2 of hydrogen pressure. After cooling to room temperature, the reaction mixture was exposed to air and light to decompose the catalyst. Removal of the solvent gave a dark green residue, which was purified by silica gel column chromatography (ether–hexane, 1 : 10—1 : 5) to afford the desired exocyclic olefin **14** (486 mg, 98%) as a colorless oil. The GLC analysis (OV-1, 1.5%, 1.5 m, 228 °C, 1.0 kg/cm^2 of N_2 pressure) of the product showed the absence of the 5*Z*-isomer of **14**, starting material and exocyclic conjugated diene, but revealed contamination with a trace amount of regioisomer **15** (retention time: 5*E*-isomer **14**, 6.5 min; 5*Z*-isomer, 5.9 min; regioisomer **15**, 5.3 min; starting material **13**, 4*Z*-isomer, 6.2 min; 4*E*-isomer, 7.5 min; exocyclic conjugated diene **21**, 8.1 min). Spectral data of **14**: IR (neat): 2970, 2880, 1747, 840 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.30—2.60 (m, 21H), 3.30—4.10 (m, 5H), 3.70 (s, 3H), 4.66 (m, 1H), 5.23 (t, J=7 Hz, 1H). MS *m/z*: 466 (M^+), 325, 233, 201, 159, 131, 117, 105, 91, 89, 86, 85 (base peak), 75, 73, 67, 57, 43, 41. HR-MS *m/z*: (M^+) Calcd for $C_{26}H_{46}O_5Si$ 466.3112, Found 466.3138.

In a similar manner, the hydrogenations described in Chart 2 and Table I were carried out. The spectral data of **12** and **21** were as follows.

Methyl (1*S*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-7-*tert*-butyldiphenylsilyloxybicyclo[3.3.0]octane-*E*-Δ$^{3,\delta}$-pentanoate (12) IR (neat): 1745, 740, 703 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.04 (s, 6H), 0.90 (s, 9H), 1.08 (s, 9H), 1.20—2.60 (m, 15H), 3.20—3.80 (m, 2H), 3.68 (s, 3H), 3.80—4.10 (m, 1H), 5.25 (br t, J=7 Hz, 1H), 7.30—7.60 (m, 6H), 7.60—7.80 (m, 4H). MS *m/z*: 564, 563 ($M^+ - tert$-Bu), 531, 313, 307, 273, 272, 271, 235, 234, 233 (base peak). HR-MS *m/z*: ($M^+ - tert$-Bu) Calcd for $C_{33}H_{47}O_4Si_2$ 563.3009, Found 563.2998. $[\alpha]_D^{20}$: −17° (c=1.32, $CHCl_3$).

Methyl (1*S*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*E*-Δ$^{3,\delta}$-*E*-β-pentenoate (21) IR (neat): 2960, 1745, 840 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.20—2.00 (m, 8H), 2.00—2.80 (m, 7H), 3.13 (d, J=7 Hz, 2H), 3.30—4.10 (m, 5H), 3.71 (s, 3H), 4.63 (m, 1H), 5.64 (dt, J=15.5, 7 Hz, 1H), 5.96 (d, J=11 Hz, 1H), 6.25 (dd, J=15.5, 11 Hz, 1H), MS *m/z*: 464 (M^+), 323, 305, 231, 159, 157, 89, 85 (base peak), 75, 73. HR-MS *m/z*: (M^+) Calcd for $C_{26}H_{44}O_5Si$ 464.2956, Found 464.2973.

Methyl (1*S*,5*S*,6*S*,7*R*)-6-Hydroxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*E*-Δ$^{3,\delta}$-pentanoate (16) Tetrabutylammonium fluoride (1 M solution in THF, 1.56 ml) was added to a solution of **14** (486 mg, 1.04 mmol) in THF (5 ml), and the mixture was stirred for 11.5 h at 23 °C. The reaction was quenched by the addition of brine, followed by extraction with ether. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (ether–hexane, 3 : 2) to give the alcohol (**16**) (349 mg, 95%) and the more polar regioisomer **17** (7 mg, 1.9%). Spectral data of **16**: IR (neat): 3480, 2950, 1741 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00—2.60 (m, 21H), 2.60—3.30 (m, 1H), 3.30—4.20 (m, 5H), 3.65 (s, 3H), 4.65 (m, 1H), 5.22 (br t, J=7 Hz, 1H). MS *m/z*: 352 (M^+), 334 ($M^+ - H_2O$), 268 (M^+ − DHP), 250, 232, 219, 91, 86, 85 (base peak), 79, 67, 57, 55, 43, 41. HR-MS *m/z*: (M^+) Calcd for $C_{20}H_{32}O_5$ 352.2247, Found 352.2225. Spectral data of **17**: IR (neat): 3480, 2950, 1740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.80—3.10 (m, 21H), 3.30—4.30 (m, 5H), 3.68 (s, 3H), 4.68 (m, 1H), 5.32 (m, 2H). MS *m/z*: 352 (M^+), 334 ($M^+ - H_2O$), 268 (M^+ − DHP), 250, 233, 219, 201, 173, 159, 149, 105, 91, 86, 85 (base peak), 84, 79, 67, 57, 55, 43, 41. HR-MS *m/z*: (M^+) Calcd for $C_{20}H_{32}O_5$ 352. 2247, Found 352.2252.

Methyl (1*S*,5*S*,6*R*,7*R*)-6-(3-Oxo-*E*-1-octenyl)-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*E*-Δ$^{3,\delta}$-pentanoate (19) A solution of SO_3–pyridine complex (201 mg, 1.26 mmol) in DMSO (3 ml) was added to a stirred solution of the alcohol **16** (49 mg, 0.14 mmol) and triethylamine (0.36 ml) in DMSO (1.5 ml), and the mixture was stirred at 23 °C for 2.5 h. The reaction mixture was poured into ice-water, and extracted with ether. The ether extracts were washed with water and brine, and dried over $MgSO_4$. Removal of the solvent gave the crude aldehyde **18**. Sodium hydride (60%

in oil, 8 mg, 0.20 mmol) was washed with pentane, and suspended in THF (1.4 ml). A solution of dimethyl (2-oxoheptyl)phosphonate (47 mg, 0.21 mmol) in THF (0.2 ml) was added to the suspension, and the mixture was stirred at 23 °C for 30 min. Then, a solution of the crude aldehyde **18** in THF (0.6 ml) was dropped into a solution of the phosphonate carbanion, and the whole mixture was stirred for 30 min. The reaction was quenched by the addition of saturated aqueous NH_4Cl, followed by extraction with ether. The combined ether extracts were washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification by silica gel column chromatography (ether–hexane, 2 : 5) afforded the enone **19** (52 mg, 84%) as a colorless oil. IR (neat): 2950, 1740, 1700, 1675, 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, J=6 Hz, 3H), 1.00—2.70 (m, 29H), 3.30—4.20 (m, 3H), 3.68 (s, 3H), 4.55, 4.65 (each br s, total 1H), 5.25 (t, J=7 Hz, 1H), 6.13, 6.17 (each d, J=16 Hz, total 1H), 6.75 (m, 1H). MS m/z: 362 (M^+ − DHP), 344 (M^+ − THPOH), 318, 279, 205, 167, 149, 85 (base peak), 74, 73, 61, 59, 57, 45 (base peak), 43. HR-MS m/z: (M^+ − DHP) Calcd for $C_{22}H_{34}O_4$ 362.2455, Found 362.2462.

Methyl (1*R*,5*S*,6*R*,7*R*)-7-Hydroxy-6-(3-oxo-*E*-1-octenyl)bicyclo[3.3.0]-octane-*E*-$\Delta^{3,\delta}$-pentanoate (20) A 65% aqueous solution of acetic acid (0.9 ml) was added to a solution of **19** (50 mg, 0.11 mmol) in THF (0.9 ml), and the mixture was stirred at 50 °C for 2 h, then poured into saturated aqueous $NaHCO_3$, and extracted with ether. The ether extracts were washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification by silica gel column chromatography (ether–hexane, 3 : 2) afforded the alcohol **20** (39 mg, 96%) as a colorless oil. IR (neat): 3450, 2950, 1740, 1695, 1675, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, J=7 Hz, 3H), 1.00—2.70 (m, 24H), 3.70 (s, 3H), 3.92 (m, 1H), 5.28 (br t, J=7 Hz, 1H), 6.22 (d, J=15 Hz, 1H), 6.76 (dd, J=15, 7 Hz, 1H). MS m/z: 362 (M^+), 344 ($M^+ - H_2O$), 318, 273 (base peak), 119, 105, 99, 91, 79, 71, 55, 43, 4. $[\alpha]_D^{20}$: +53° (c=0.77, MeOH). The spectral data of **20** were identical with those of an authentic sample prepared by the known method.[1)]

Methyl (1*R*,5*S*,6*S*,7*R*)-6-Hydroxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (27) Tetrabutylammonium fluoride (1 M solution in THF, 0.32 ml) was added to a solution of **13** (100 mg, 0.22 mmol), and the mixture was stirred at 23 °C for 13 h. The reaction was quenched by the addition of brine, followed by extraction of the mixture with ether. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (ether–hexane, 3 : 2) to give the alcohol **27** (71 mg, 94%) as a colorless oil. IR (neat): 3480, 2950, 1740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00—2.00 (m, 8H), 2.00—2.80 (m, 8H), 3.00 (m, 2H), 3.00—4.30 (m, 5H), 3.68 (s, 3H), 4.62 (m, 1H), 5.35 (m, 1H), 5.58 (br s, 1H), 6.00 (d, J=12 Hz, 2.2/3.2H), 6.26 (d, J=15 Hz, 1/3.2H). MS m/z: 350 (M^+), 266 (M^+-DHP), 248, 230, 217, 177, 117, 91, 85 (base peak). HR-MS m/z: (M^+) Calcd for $C_{20}H_{30}O_5$ 350.2090, Found 350.2081.

Methyl (1*R*,5*S*,6*R*,7*R*)-6-(3-Oxo-*E*-1-octenyl)-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (28) A solution of SO_3–pyridine complex (94 mg, 0.59 mmol) in DMSO (1.6 ml) was added to a stirred solution of the alcohol **27** (69 mg, 0.2 mmol) and triethylamine (0.16 ml) in DMSO (2.3 ml), and the mixture was stirred at 23 °C for 30 min. The reaction mixture was poured into ice-water, and extracted with ether. The ether extracts were washed with water and brine, and dried over $MgSO_4$. Removal of the solvent gave the crude aldehyde. Sodium hydride (60% in oil, 10 mg, 0.25 mmol) was washed with pentane, and suspended in THF (2 ml). A solution of dimethyl (2-oxoheptyl)phosphonate (47 mg, 0.21 mmol) in THF (0.3 ml) was added to the suspension, and the mixture was stirred at 23 °C for 30 min. Then, a solution of the crude aldehyde in THF (1 ml) was dropped into the solution of the phosphonate carbanion, and the whole mixture was stirred at 23 °C for 40 min. The reaction was quenched by the addition of saturated aqueous NH_4Cl, followed by extraction of the mixture with ether. The combined ether extracts were washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification of the residue by silica gel column chromatography (ether–hexane, 2 : 5) afforded the enone **28** (77 mg, 88%) as a colorless oil. IR (neat): 2950, 1740, 1680, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, J=6 Hz, 3H), 1.00—2.00 (m, 12H), 2.00—3.00 (m, 12H), 3.10 (m, 1H), 3.30—4.20 (m, 3H), 3.67 (s, 3H), 4.60 (m, 1H), 5.00—5.70 (m, 2H), 5.80—6.40 (m, 2H), 6.75 (m, 1H). MS m/z: 444 (M^+), 360 (M^+ − DHP), 342 (M^+ − THPOH), 316, 246, 99, 85 (base peak), 67, 57, 43, 41, HR-MS m/z: (M^+) Calcd for $C_{27}H_{40}O_5$ 444.2873, Found 444.2873.

In a similar manner, **29**—**31** were synthesized from **27** and the corresponding ketophosphonates. The spectral data were as follows.

Methyl (1*R*,5*S*,6*R*,7*R*)-6-(3-Cyclopentyl-3-oxo-*E*-1-propenyl)-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (29) IR (neat): 2960, 1740, 1700, 1670, 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20—2.00 (m, 14H), 2.00—2.90 (m, 10H), 3.10 (m, 2H), 3.30—4.20 (m, 3H), 3.68 (s, 3H), 4.60 (m, 1H), 5.00—5.70 (m, 2H), 5.80—6.50 (m, 2H), 6.80 (m, 1H). MS m/z: 442 (M^+), 411 (M^+ − MeO), 358 (M^+ − DHP), 340 (M^+ − THPOH), 244, 97, 85 (base peak), 69, 67, 57, 55, 43, 41. HR-MS m/z: (M^+) Calcd for $C_{27}H_{38}O_5$ 442.2716, Found 442.2713.

Methyl (1*R*,5*S*,6*R*,7*R*)-6-(5,9-Dimethyl-3-oxo-*E*-1,8-decadienyl)-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (30) IR (neat): 2950, 1740, 1695, 1680, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (d, J=6 Hz, 3H), 1.00—1.80 (m, 15H), 1.80—2.90 (m, 14H), 3.10 (m, 1H), 3.30—4.20 (m, 3H), 3.70 (s, 3H), 4.65 (m, 1H), 4.90—5.70 (m, 3H), 5.80—6.50 (m, 2H), 6.80 (m, 1H). MS m/z: 498 (M^+), 414 (M^+ − DHP), 396 (M^+ − THPOH), 246, 230, 178, 153, 131, 129, 117, 109, 85 (base peak), 69, 67. HR-MS m/z: (M^+) Calcd for $C_{31}H_{46}O_5$ 498.3342, Found 498.3335.

Methyl (1*R*,5*S*,6*R*,7*R*)-6-(4-Methyl-3-oxo-*E*-1-octen-6-ynyl)-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (31) IR (neat): 2950, 1740, 1695, 1680, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20 (d, J=7 Hz, 3H), 1.30—1.70 (m, 6H), 1.75 (t, J=2 Hz, 3H), 1.90—2.80 (m, 12H), 3.00 (m, 2H), 3.30—4.20 (m, 3H), 3.68 (s, 3H), 4.60 (m, 1H), 5.00—5.70 (m, 2H), 5.80—6.50 (m, 2H), 6.65—7.15 (m, 1H). MS m/z: 454 (M^+), 370 (M^+ − DHP), 352 (M^+ − THPOH), 326, 246, 202, 178, 169, 161, 155, 143, 129, 124, 117, 109, 105, 91, 85 (base peak). HR-MS m/z: (M^+) Calcd for $C_{28}H_{38}O_5$ 454.2717, Found 454.2723.

Methyl (1*R*,5*S*,6*R*,7*R*)-6-(3-Hydroxy-*E*-1-octenyl)-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate An excess amount of sodium borohydride was added to a stirred solution of the enone **28** (73 mg, 0.16 mmol) in methanol (2.6 ml) at −25 °C, and the mixture was stirred at the same temperature for 40 min. The reaction was quenched by the addition of acetone, and then saturated aqueous NH_4Cl was added to the reaction mixture. After evaporation of the organic solvents, the water layer was extracted with ether. The combined ether extracts were dried over $MgSO_4$, and concentrated to give the alcohol as an epimeric mixture (81 mg). Spectral data of the alcohol: IR (neat): 3470, 2950, 1745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (m, 3H), 1.00—2.90 (m, 24H), 3.00 (m, 1H), 3.30—4.30 (m, 5H), 3.70 (s, 3H), 4.67 (m, 1H), 5.10—5.75 (m, 4H), 6.00 (d, J=11 Hz, 2.2/3.2H), 6.28 (d, J=16 Hz, 1/3.2H). MS m/z: 446 (M^+), 230, 217, 157, 156, 143, 129, 128, 117, 115, 91, 79, 78 (base peak), 77, 52. HR-MS m/z:(M^+) Calcd for $C_{27}H_{42}O_5$ 446.3029, Found 446.3006.

Methyl (1*R*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-*E*-1-octenyl]bicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (32a) The crude alcohol (epimeric mixture, 80 mg) was dissolved in a mixture of 65% aqueous acetic acid (1.3 ml) and THF (0.13 ml), and the mixture was stirred at 50 °C for 2 h, then poured into saturated aqueous $NaHCO_3$, and extracted with ether. The ether extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (ether–hexane, 3 : 1→ether) to afford the desired 15α-diol (**32a**) (23 mg, 39%) as a more polar fraction and the 15β-diol (**32b**) (13 mg, 22%) as a less polar fraction. Spectral data of **32a**: IR (neat): 3400, 2950, 1742 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (m, 3H), 1.10—2.95 (m, 20H), 3.02 (m, 1H), 3.70 (s, 3H), 3.70 (m, 1H), 4.10 (m, 1H), 5.00—5.70 (m, 4H), 6.02 (d, J=11 Hz, 2.2/3.2 H), 6.30 (d, J=15 Hz, 1/3.2H). MS m/z: 362 (M^+), 344, 300, 273, 230, 220, 192, 191, 178, 167, 149, 143, 131, 129, 128, 119, 118, 117, 105, 99, 91, 79, 71, 67, 57, 55, 43 (base peak), 41. HR-MS m/z: (M^+) Calcd For $C_{22}H_{34}O_4$ 362.2454, Found 362.2451. $[\alpha]_D^{20}$: −35° (c=0.466, MeOH). The spectral data of **32b** were nearly identical with those of **31a** except for the optical rotation.

In a similar manner, **29**—**31** were converted to the corresponding diols **33a**—**35a**. The spectral data were as follows.

Methyl (1*R*,5*S*,6*R*,7*R*)-6-(3-Cyclopentyl-3-hydroxy-*E*-1-propenyl)-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate IR (neat): 3500, 2970, 1742 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00—2.90 (m, 23H), 3.02 (m, 1H), 3.30—4.10 (m, 7H), 3.70 (s, 3H), 4.70 (m, 1H), 5.10—5.80 (m, 4H), 6.00 (d, J=11 Hz, 2.2/3.2H), 6.28 (d, J=16 Hz, 1/3.2H). MS m/z: 444 (M^+), 342, 298, 220, 178, 85 (base peak), 69, 67, 57. HR-MS m/z: (M^+) Calcd for $C_{27}H_{40}O_5$ 444.2873, Found 444.2885.

Methyl (1*R*,5*S*,6*R*,7*R*)-6-[3(*R*)-Cyclopentyl-3-hydroxy-*E*-1-propenyl]-7-hydrobicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (33a) IR (neat): 3400, 2950, 1740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10—2.80 (m, 21H), 3.02 (m, 1H), 3.40—4.00 (m, 2H), 3.65 (s, 3H), 5.17—5.75 (m, 4H), 5.95 (d, J=11 Hz, 2.2/3.2H), 6.22 (d, J=15 Hz, 1/3.2H). MS m/z: 360 (M^+), 342, 324, 298, 273, 220, 178, 131, 117, 105, 97, 91, 79, 69 (base peak), 67, 41. HR-MS m/z: (M^+) Calcd for $C_{22}H_{32}O_4$ 360.2298, Found 360.2293. $[\alpha]_D^{20}$: −30° (c=1.16, MeOH).

Methyl (1*R*,5*S*,6*R*,7*R*)-6-(3-Hydroxy-5,9-dimethyl-*E*-1,8-decadienyl)-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate IR (neat):

3500, 2950, 1745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (d, J=6 Hz, 3H), 1.10—2.80 (m, 30H), 3.04 (m, 1H), 3.50—4.05 (m, 3H), 3.69 (s, 3H), 4.20 (m, 1H), 4.68 (m, 1H), 5.00—5.50 (m, 2H), 5.62 (m, 3H), 6.00 (d, J=11 Hz, 2.2/3.2H), 6.26 (d, J=15 Hz, 1/3.2H). MS m/z: 500 (M^+), 482, 416 (M^+ − DHP), 399, 398 (M^+ − THPOH), 380, 232, 231, 230, 131, 117, 109, 105, 95, 91, 86, 85 (base peak), 81, 79, 69, 67, 57, 55. HR-MS m/z: (M^+) Calcd for $C_{31}H_{48}O_5$ 500.3499, Found 500. 3539.

Methyl (1*R*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3-(*S*)-hydroxy-5,9-dimethyl-*E*-1,8-decadienyl]bicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (34a) IR (neat): 3400, 2920, 1740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.95 (d, J=6 Hz, 3H), 1.10—1.60 (m, 6H), 1.62 (s, 3H), 1.70 (s, 3H), 1.80—2.80 (m, 1H), 2.80—3.50 (m, 3H), 3.70 (s, 3H), 3.70 (m, 1H), 4.14 (m, 1H), 5.12 (t, J=7 Hz, 1H), 5.20—5.80 (m, 4H), 6.00 (d, J=12 Hz, 2.2/3.2H), 6.25 (d, J=15 Hz, 1/3.2H). MS m/z: 416 (M^+), 398 ($M^+ - H_2O$), 380 ($M^+ - 2H_2O$), 313, 230, 178, 143, 131, 129, 117, 109, 105, 95, 91, 81, 79, 68, 67, 55, 43, 41 (base peak). HR-MS m/z: (M^+) Calcd for $C_{26}H_{40}O_4$ 416.2923, Found 416.2909.

Methyl (1*R*,5*S*,6*R*,7*R*)-6-(3-Hydroxy-4-methyl-*E*-1-octen-6-ynyl)-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoate IR (neat): 3500, 2950, 1745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (m, 3H), 1.10—2.80 (m, 23H), 3.04 (m, 1H), 3.60—4.40 (m, 4H), 3.71 (s, 3H), 4.60 (m, 1H), 5.20—5.80 (m, 4H), 6.02 (d, J=12 Hz, 2.2/3.2H), 6.30 (d, J=16 Hz, 1/3.2H). MS m/z: 372 (M^+ − DHP), 354 (M^+ − THPOH), 310, 301, 220, 143, 117, 105, 91, 86, 85 (base peak), 81, 79, 77, 67, 57, 55, 53. HR-MS m/z: (M^+ − DHP) Calcd for $C_{23}H_{32}O_4$ 372.2298, Found 372.2285.

Methyl (1*R*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*R*)-hydroxy-4-methyl-*E*-1-octen-6-ynyl]bicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (35a) IR (neat): 3400, 2940, 1740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (m, 3H), 1.10—2.80 (m, 16H), 1.78 (t, J=2 Hz, 3H), 3.03 (m, 1H), 3.30—4.30 (m, 2H), 3.68 (s, 3H), 5.00—5.70 (m, 3H), 6.00 (d, J=12 Hz, 2.2/3.2H), 6.25 (d, J=16 Hz, 1/3.2H). MS m/z: 372 (M^+), 354 ($M^+ - H_2O$), 336 ($M^+ - 2H_2O$), 310, 220, 178, 155, 145, 143, 131, 129, 119, 118, 117, 105, 91, 81 (base peak), 79, 77, 67, 55, 53. HR-MS m/z: (M^+) Calcd for $C_{23}H_{32}O_4$ 372.2299, Found 372.2302.

Methyl (1*R*,5*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-6-[3(*S*)-*tert*-butyldimethylsilyloxy-*E*-1-octenyl]bicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (36) Imidazole (12 mg, 0.18 mmol) and *tert*-butyldimethylsilyl chloride (27 mg, 0.18 mmol) were added to a stirred solution of the diol **32a** (21 mg, 0.06 mmol) in DMF (0.08 ml) at 0 °C. The mixture was stirred at 23 °C for 1 h, and then saturated aqueous NH_4Cl was added. The reaction mixture was extracted with ether, washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification of the residue by silica gel column chromatography (ether–hexane, 1 : 10) afforded **36** (31 mg, 90%) as a colorless oil. IR (neat): 2950, 1750, 840 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.03 (s, 12H), 0.87 (t, J=7 Hz, 3H), 0.90 (s, 18H), 1.10—2.80 (m, 18H), 2.97 (m, 1H), 3.69 (s, 3H), 3.70 (m, 1H), 4.07 (m, 1H), 5.51 (m, 4H), 6.02 (d, J=12 Hz, 2.2/3.2H), 6.27 (d, J=16 Hz, 1/3.2H). MS m/z: 590 (M^+), 533 (M^+ − *tert*-Bu), 519, 458, 427, 401, 301, 75, 73 (base peak). HR-MS m/z: (M^+ − *tert*-Bu) Calcd for $C_{30}H_{53}O_4Si_2$ 533.3484, Found 533.3490.

In a similar manner, **33a**—**35a** were converted to the corresponding silyl ether **37**—**39**. The spectral data were as follows.

Methyl (1*R*,5*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-6-[3(*R*)-*tert*-butyldimethylsilyloxy-3-cyclopentyl-*E*-1-propenyl]bicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (37) IR (neat): 2960, 1745, 838 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.90 (s, 9H), 0.95 (s, 9H), 1.00—2.75 (m, 19H), 3.00 (m, 1H), 3.65—4.00 (m, 2H), 3.68 (s, 3H), 5.05—5.80 (m, 4H), 6.01 (d, J=11 Hz, 2.2/3.2H), 6.25 (d, J=16 Hz, 1/3.2H). MS m/z: 588 (M^+), 573.531 (M^+ − *tert*-Bu), 519, 387, 361, 299, 171, 147, 117, 105, 91, 79, 75, 73 (base peak), 67. HR-MS m/z: (M^+) Calcd for $C_{34}H_{60}O_4Si_2$ 588.4030, Found 588.4020.

Methyl (1*R*,5*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-6-[3(*S*)-*tert*-butyldimethylsilyloxy-5,9-dimethyl-*E*-1,8-decadienyl]bicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (38) IR (neat): 2960, 2940, 1745, 835 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.91 (m, 21H), 1.00—1.75 (m, 6H), 1.60 (s, 3H), 1.66 (s, 3H), 1.75—2.80 (m, 11H), 3.00 (m, 1H), 3.55—3.90 (m, 1H), 3.68 (s, 3H), 5.10 (t, J=7 Hz, 1H), 5.15—5.60 (m, 4H), 5.90 (d, J=11 Hz, 2.2/3.2H), 6.20 (d, J=15 Hz, 1/3.2H). MS m/z: 644 (M^+), 587 (M^+ − *tert*-Bu), 588, 519, 455, 387, 381, 361, 355, 217, 177, 147, 117, 109, 81, 75, 73 (base peak), 69. HR-MS m/z: (M^+) Calcd for $C_{38}H_{68}O_4Si_2$ 644.4652, Found 644.4621.

Methyl (1*R*,5*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-6-[3(*R*)-*tert*-butyldimethylsilyloxy-4-methyl-*E*-1-octen-6-ynyl]bicyclo[3.3.0]oct-2-ene-3-γ-pentenoate (39) IR (neat): 2960, 2940, 1745, 840 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.90 (m, 21H), 1.05—2.70 (m, 13H), 1.75 (t, J=2 Hz, 3H), 3.00 (m, 1H), 3.25—4.20 (m, 2H), 3.65 (s, 3H), 5.05—5.70 (m, 4H), 5.97 (d, J=11 Hz, 2.2/3.2H), 6.23 (d, J=15 Hz, 1/3.2H). MS m/z: 600 (M^+), 543 (M^+ − *tert*-Bu), 519, 387, 361, 171, 155, 147, 131, 119, 117, 105, 91, 89, 81, 79, 75, 73 (base peak), 59. HR-MS m/z: (M^+) Calcd for $C_{35}H_{60}O_4Si_2$ 600.4027, Found 600.4052.

The 1,4-hydrogenations of **36**—**39** and **29** were carried out in a similar manner to that described in the case of the diene **13**. The spectral data were as follows.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-6-[3(*S*)-*tert*-butyldimethylsilyloxy-*E*-1-octenyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (40) IR (neat): 2950, 1745, 835, 755 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.88 (s, 9H), 0.90 (s, 9H), 1.00—2.50 (m, 26H), 3.40—3.80 (m, 1H), 3.65 (s, 3H), 4.02 (m, 1H), 5.18 (br t, J=7 Hz, 1H), 5.40 (m, 2H). MS m/z: 535 (M^+ − *tert*-Bu), 503, 460, 403, 389, 329, 297, 215, 201, 179, 171, 149, 147, 117, 105, 91, 79, 75, 73 (base peak), 67. HR-MS m/z: (M^+ − *tert*-Bu) Calcd for $C_{30}H_{51}O_4Si_2$ 535.3639, Found 535.3642.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-6-[3(*R*)-*tert*-butyldimethylsilyloxy-3-cyclopentyl-*E*-1-propenyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (41) IR (neat): 2950, 1745, 835, 775 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 6H), 0.03 (s, 6H), 0.88 (s, 9H), 0.98 (s, 9H), 1.00—2.70 (m, 24H), 3.50—4.00 (m, 2H), 3.68 (s, 3H), 5.23 (t, J=7 Hz, 1H), 5.50 (m, 2H). MS m/z: 533 (M^+ − *tert*-Bu), 521, 458, 389, 363, 327, 213, 201, 179, 171, 147, 133, 131, 129, 119, 117, 105, 91, 79, 75, 73 (base peak), 67. HR-MS m/z: (M^+ − *tert*-Bu) Calcd for $C_{30}H_{53}O_4Si_2$ 533.3479, Found 533.3477.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-6-[3(*S*)-*tert*-butyldimethylsilyloxy-5,9-dimethyl-*E*-1,8-decadienyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (42) IR (neat): 2960, 2940, 1745, 835, 775 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.90 (m, 21H), 1.00—2.70 (m, 22H), 1.63 (s, 3H), 1.74 (s, 3H), 3.75 (m, 1H), 3.70 (s, 3H), 4.18 (m, 1H), 5.18 (m, 2H), 5.50 (m, 2H). MS m/z: 631 (M^+ − Me), 590, 589 (M^+ − *tert*-Bu), 514, 457, 389, 384, 363, 201, 179, 171, 147, 109, 105, 95, 81, 75, 73 (base peak), 69, 41. HR-MS m/z: (M^+ − *tert*-Bu) Calcd for $C_{34}H_{61}O_4Si_2$ 589.4105, Found 589.4137.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-6-[3(*R*)-*tert*-butyldimethylsilyloxy-4-methyl-*E*-1-octen-6-ynyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (43) Spectral data of **43**: IR (neat): 2960, 2940, 1745, 840, 780 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.87 (m, 21H), 1.00—2.80 (m, 9H), 1.74 (t, J=2 Hz, 3H), 3.60—4.20 (m, 2H), 3.62 (s, 3H), 5.20 (br t, J=7 Hz, 1H), 5.45 (m, 2H). MS m/z: 602 (M^+), 546, 545 (M^+ − *tert*-Bu), 521, 470, 389, 363, 225, 171, 147, 117, 105, 91, 79, 75, 73 (base peak). HR-MS m/z: (M^+ − *tert*-Bu) Calcd for $C_{31}H_{53}O_4Si_2$ 545.3480, Found 545.3498. Spectral data of **44**: IR (neat): 2960, 2940, 1745, 840, 780 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.90 (m, 21H), 1.00—2.70 (m, 18H), 1.78 (t, J=2 Hz, 3H), 3.12 (d, J=7 Hz, 2H), 3.50—4.30 (m, 2H), 3.71 (s, 3H), 5.40—5.80 (m, 3H), 5.95 (d, J=11 Hz, 1H), 6.25 (dd, J=15, 11 Hz, 1H). MS m/z: 600 (M^+), 585 (M^+ − Me), 559, 543 (M^+ − *tert*-Bu), 468, 177, 171, 147, 117, 75, 73 (base peak). HR-MS m/z: (M^+) Calcd for $C_{35}H_{60}O_4Si_2$ 600.4030, Found 600.4039. Spectral data of **45**: IR (neat): 2960, 2950, 1745, 840, 780 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.90 (m, 21H), 1.00—2.60 (m, 18H), 1.60 (t, J=6 Hz, 3H), 3.65 (s, 3H), 3.70 (m, 1H), 3.95 (m, 1H), 5.20 (br t, J=7 Hz, 1H), 5.48 (m, 4H). MS m/z: 589 (M^+ − Me), 547 (M^+ − *tert*-Bu), 521, 515, 389, 363, 309, 257, 225, 201, 171, 147, 105, 75, 73 (base peak), 55. HR-MS m/z: (M^+ − *tert*-Bu) Calcd for $C_{31}H_{55}O_4Si_2$ 547.3635, Found 547.3629. Only NMR data of **46** are shown, because **46** was inseparable from **45**: ^{1}H-NMR ($CDCl_3$) δ: 0.00 (s, 12H), 0.90 (m, 21H), 1.00—2.70 (m, 15H), 3.08 (d, J=8 Hz, 2H), 3.60—4.20 (m, 2H), 3.62 (s, 3H), 5.00—6.50 (m, 7H).

Methyl (1*S*,5*S*,6*R*,7*R*)-6-(3-Cyclopentyl-3-oxopropyl)-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (47) IR (neat): 2960, 1742, 1715 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00—3.10 (m, 34H), 3.20—4.10 (m, 3H), 3.66 (s, 3H), 4.62 (br s, 1H), 5.20 (br t, J=7 Hz, 1H). MS m/z: 362 (M^+ − DHP), 344 (M^+ − THPOH), 233, 232, 179, 149, 145, 131, 85 (base peak), 69, 67, 57, 43, 41. HR-MS m/z: (M^+ − DHP) Calcd for $C_{22}H_{34}O_4$ 362.2454, Found 362.2449.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-*E*-1-octenyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (48) Tetrabutylammonium fluoride (1 M solution in THF, 0.39 ml) was added to a solution of **40** (80 mg, 0.13 mmol) in THF (1 ml), and the mixture was stirred at 23 °C for 13 h. The reaction was quenched by the addition of brine, followed by extraction with ethyl acetate. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (ether) to give the diol **48** (59 mg, 100%) as a colorless oil. The spectral data of **48** thus obtained were identical with those of an authentic sample.[1k] In a similar manner, **41**—**43** were converted to the corresponding diols **49**—**51**.

Methyl (1*S*,5*S*,6*R*,7*R*)-6-[3(*R*)-Cyclopentyl-3-hydroxy-*E*-1-propenyl]-7-hydroxybicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (49) IR (neat): 3400, 2960, 1742 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00—2.50 (m, 24H), 2.72 (s, 2H), 3.50—3.90 (m, 2H), 3.67 (s, 3H), 5.20 (t, J=7 Hz, 1H), 5.50 (m, 2H). MS m/z: 344 (M^+-H_2O), 326 (M^+-2H_2O), 300, 275, 257, 247, 179, 149, 145, 131, 119, 117, 105, 97, 95, 91, 81, 79, 77, 69 (base peak), 67, 57, 55. HR-MS m/z: (M^+-H_2O) Calcd for $C_{22}H_{32}O_3$ 344.2349, Found 344.2366.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-5,9-dimethyl-*E*-1,8-decadienyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (50) IR (neat): 3400, 2940, 1745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (d, J=6 Hz, 3H), 1.00—2.60 (m, 22H), 1.60 (s, 3H), 1.68 (s, 3H), 2.90 (br s, 2H), 3.68 (m, 1H), 3.68 (s, 3H), 4.15 (m, 1H), 5.26 (m, 2H), 5.50 (m, 2H). MS m/z: 400 (M^+-H_2O), 382 (M^+-2H_2O), 339, 315, 247, 246, 245, 233, 232, 219, 201, 179, 147, 131, 119, 117, 109, 105, 93, 91, 81, 79, 69 (base peak), 55, 41. HR-MS m/z: (M^+-H_2O) Calcd for $C_{26}H_{40}O_3$ 400.2975, Found 400.2978.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*R*)-hydroxy-4-methyl-*E*-1-octen-6-ynyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoate (51) IR (neat): 3400, 2940, 1742 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (m, 3H), 1.06—2.70 (m, 20H), 1.78 (t, J=2 Hz, 3H), 3.66 (s, 3H), 3.67 (m, 1H), 4.06 (m, 1H), 5.24 (t, J=7 Hz, 1H), 5.55 (m, 2H). MS m/z: 374 (M^+), 356 (M^+-H_2O), 338 (M^+-2H_2O), 312, 205, 167, 150, 149 (base peak), 105, 104, 83, 76, 71, 70, 69, 57, 56, 55, 43, 41. HR-MS m/z: (M^+) Calcd for $C_{23}H_{34}O_4$ 374.2478, Found 374.2478.

(1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-*E*-1-octenyl]bicyclo[3.3.0]-octane-*E*-$\Delta^{3,\delta}$-pentanoic Acid (2) A 10% NaOH aqueous solution (1.0 ml, 2.5 mmol) was added to a stirred solution of the diol **48** (45 mg, 0.12 mmol) in methanol (1 ml) at 0 °C, and the mixture was stirred at the same temperature for 13 h. The reaction mixture was diluted with ether, and neutralized by adding 10% aqueous HCl, followed by evaporation of the organic solvents. Then the remaining water layer was acidified to pH 3—4 by adding 10% aqueous HCl, followed by extraction with ethyl acetate. The combined organic layers were washed with brine, and dried over $MgSO_4$. Removal of the solvent afforded carbacyclin (**2**) (43 mg, 100%). The spectal data of **2** thus obtained were identical with those of an authentic sample.[1k] In a similar manner, the diols **49**—**51** and **32a**—**35a** were hydrolyzed to the carboxylic acids **3**—**5 and 75**—**78**. The IR and NMR data were as follows.

(1*S*,5*S*,6*R*,7*R*)-6-[3(*R*)-Cyclopentyl-3-hydroxy-*E*-1-propenyl]-7-hydroxybicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentenoic Acid (3) IR (neat): 3350, 2940, 1705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00—2.52 (m, 24H), 3.28—3.96 (m, 5H), 5.22 (br t, J=7 Hz, 1H), 5.42 (m, 2H).

(1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-5,9-dimethyl-*E*-1,8-decadienyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoic Acid (4) IR (neat): 3400, 2940, 1712 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (d, J=6 Hz, 3H), 1.00—2.70 (m, 22H), 1.60 (s, 3H), 1.68 (s, 3H), 3.70 (m, 1H), 4.15 (m, 1H), 4.90—5.40 (m, 2H), 5.40—5.90 (m, 4H).

(1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*R*)-hydroxy-4-methyl-*E*-1-octen-6-ynyl]-bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-pentanoic Acid (5) IR (neat): 3400, 2950, 1712 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.96, 1.00 (each d, J=7 Hz, total 3H), 1.10—2.70 (m, 18H), 1.80 (t, J=2 Hz, 3H), 3.15 (m, 3H), 3.76 (m, 1H), 4.10 (m, 1H), 5.26 (t, J=7 Hz, 1H), 5.60 (m, 2H).

(1*R*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-*E*-1-octenyl]bicyclo[3.3.0]-oct-2-ene-3-γ-pentenoic Acid (75) IR (neat): 3350, 2950, 1715 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (m, 3H), 1.10—2.90 (m, 19H), 3.10 (m, 1H), 3.70—4.40 (m, 3H), 5.45 (m, 1H), 5.65 (m, 3H), 6.06 (d, J=11 Hz, 2.2/3.2H), 6.34 (d, J=16 Hz, 1/3.2H).

(1*R*,5*S*,6*R*,7*R*)-6-[3(*R*)-Cyclopentyl-3-hydroxy-*E*-1-propenyl]-7-hydroxybicyclo[3.3.0]oct-2-ene-3-γ-pentenoic Acid (76) IR (neat): 3350, 2950, 1715 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10—2.90 (m, 20H), 3.10 (m, 1H), 3.65—4.60 (m, 3H), 5.43 (m, 1H), 5.54 (m, 3H), 6.04 (d, J=12 Hz, 2.2/3.2 H), 6.32 (d, J=16 Hz, 1/3.2H).

(1*R*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-5,9-dimethyl-*E*-1,8-decadienyl]bicyclo[3.3.0]oct-2-ene-3-γ-pentenoic Acid (77) IR (neat): 3350, 2950, 1715 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (d, J=6 Hz, 3H), 1.00—3.30 (m, 23H), 1.61 (s, 3H), 1.68 (s, 3H), 3.82 (m, 1H), 4.24 (m, 1H), 5.12 (t, J=7 Hz, 1H), 5.28—5.72 (m, 4H), 6.02 (d, J=11 Hz, 2.2/3.2H), 6.30 (d, J=16 Hz, 1/3.2H).

(1*R*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*R*)-hydroxy-4-methyl-*E*-1-octen-6-ynyl]-bicyclo[3.3.0]oct-2-ene-3-γ-pentenoic Acid (78) IR (neat): 3350, 2950, 1715 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.98, 1.01 (each d, J=7 Hz, total 3H), 1.60—3.30 (m, 19H), 1.81 (t, J=2 Hz, 3H), 3.70—4.30 (m, 2H), 5.20—5.90 (m, 4H), 6.04 (d, J=11 Hz, 2.2/3.2H), 6.32 (d, J=16 Hz, 1/3.2H).

(1*R*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-3-hydroxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene (53) A solution of diisobutylaluminum hydride in hexane (1.76 M, 2.9 ml, 5.17 mmol) was added to a stirred solution of the aldehyde **52**[7a] (1.66 g, 4.36 mmol) in toluene (8 ml) at −70 °C. Stirring was continued at the same temperature for 45 min, and the reaction was quenched by the addition of methanol. After dilution of the mixture with ether, saturated aqueous NaCl was added. Stirring was continued at 23 °C until the organic layer became clear. The aqueous layer was extracted with ether, and the organic layers were combined and dried over $MgSO_4$. Removal of the solvent afforded the alcohol **53** (1.64 g, 98%) as a colorless oil. IR (neat): 3430, 2950, 838, 778 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.00—2.00 (m, 9H), 2.00—2.80 (m, 4H), 3.00 (m, 1H), 3.25—4.05 (m, 5H), 4.12 (s, 2H), 4.62 (m, 1H), 5.56 (br s, 1H). MS m/z: 382 (M^+), 298 (M^+−DHP), 241, 223, 159, 149, 131, 91, 85, (base peak), 75. HR-MS m/z: (M^+−DHP) Calcd for $C_{16}H_{30}O_3Si$ 298.1962, Found 298.1946.

(1*R*,5*S*,6*S*,7*R*)-3-Bromomethyl-6-*tert*-butyldimethylsilyloxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene (54) Carbon tetrabromide (1.57 g, 4.74 mmol) was added to a stirred solution of the alcohol **53** (1.48 g, 3.87 mmol) and triphenylphosphine (1.24 g, 4.74 mmol) in methylene chloride (25 ml) at −60 °C, and the mixture was stirred at −25 °C for 1 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$, followed by extraction of the mixture with ether. The combined ether extracts were washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification by silica gel column chromatography (ether–hexane, 1 : 20) afforded the bromide **54** (1.54 g, 89%) as a colorless oil. IR (neat): 2950, 838, 776 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.00—2.00 (m, 8H), 2.00—2.70 (m, 4H), 3.00 (m, 1H), 3.25—4.00 (m, 5H), 4.00 (s, 2H), 4.60 (m, 1H), 5.70 (br s, 1H), MS m/z: 362 (M^+−DHP), 360 (M^+−DHP), 345 (M^+−THPOH), 343 (M^+−THPOH), 281, 213, 211, 159, 149, 131, 91, 89, 85 (base peak), 75, 67, HR-MS m/z: (M^+−DHP) Calcd for $C_{16}H_{29}BrO_2Si$ 362.1099, 360.1118, Found 362.1107, 360.1094.

(1*R*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-3-cyanomethyl-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene (55) Potassium cyanide (97%, 113 mg, 1.68 mmol) was added to a stirred solution of the bromide **53** (500 mg, 1.12 mmol) and 18-crown-6 (444 mg, 1.68 mmol) in acetonitrile (25 ml), and the mixture was stirred at 23°C for 2 h. After evaporation of the acetonitrile, saturated aqueous $NaHCO_3$ was added. The mixture was extracted with ether. The combined ether extracts were washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification by silica gel column chromatography (ether–hexane, 1 : 3) afforded the cyanide **55** (435 mg, 99%) as a colorless oil. IR (neat): 2950, 2260, 1735, 1260, 840, 780 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.00—2.00 (m, 8H), 2.00—2.80 (m, 4H), 3.05 (s, 2H), 3.05 (m, 1H), 3.25—4.10 (m, 5H), 4.60 (m, 1H), 5.68 (br s, 1H). MS m/z: 307 (M^+−DHP), 290, 159, 158, 86, 85 (base peak), 75, 73. HR-MS m/z: (M^+−DHP) Calcd for $C_{17}H_{29}NO_2Si$ 307.1965, Found 307.1948.

Methyl (1*R*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-δ-cyano-γ-hydroxypentanoate (57) A solution of lithium diisopropylamide prepared from diisopropylamine (71 μl, 0.51 mmol), butyllithium (1.50 M, 0.3 ml, 0.46 mmol) and THF (0.63 ml) was added to a stirred solution of the cyanide **55** (100 mg, 0.26 mmol) in THF (2 ml) at −78 °C, and the mixture was stirred at the same temperature for 25 min. A solution of the aldehyde **56** (59 mg, 0.51 mmol, bp 39 °C/1.3 mmHg) in THF (3 ml) was added to this pale yellow solution at −78 °C, and the reaction mixture was stirred at the same temperature for 20 min. The reaction was quenched by the addition of saturated aqueous NH_4Cl, followed by extraction of the mixture with ether. The combined organic layers were washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification by silica gel column chromatography (ether–hexane, 1 : 3–1 : 1) afforded the desired coupling products **57** (108 mg, 82%, mixture of the diastereomers) as a colorless oil. IR (neat): 3490, 2950, 2240, 1738, 835, 775 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.10—2.70 (m, 16H), 2.70—4.20 (m, 9H), 3.66 (s, 3H), 4.50 (m, 1H), 5.75 (m, 1H). MS m/z: 424 (M^++H–DHP), 406 (M^++H–THPOH), 392, 374, 348, 334, 316, 307, 242, 232, 201, 196, 160, 159, 158, 145, 117, 115, 89, 86, 85 (base peak), 75, 73, 67, 59, 57, 43, 41. HR-MS m/z: (M^++H–DHP) Calcd for $C_{22}H_{38}NO_5Si$ 424.2517, Found 424.2546.

Methyl (1*R*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]oct-2-ene-3-δ-cyano-γ-pentenoate (58) Mesyl chloride (0.19 ml, 2.45 mmol) was added to a stirred solution of **57** (300 mg, 0.16 mmol) and triethylamine (1.03 ml, 7.35 mmol) at 0 °C, and the mixture was stirred at 23 °C for 20 min. The reaction was quenched by the addition of brine, followed by extraction of the mixture with ether. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (ether–hexane, 1 : 4) to give

the 4*Z*-diene **58a** (240 mg, 83%) as a less polar fraction and the 4*E*-diene **58b** (18 mg, 6%) as a more polar fraction. Spectral data of **58a**: IR (neat): 2930, 2220, 1735, 828, 770 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.00—2.10 (m, 8H), 2.10—2.90 (m, 8H), 3.10 (m, 1H), 3.25—4.15 (m, 5H), 3.70 (s, 3H), 4.60 (m, 1H), 6.05 (br s, 1H), 6.10 (t, J=7 Hz, 1H). MS *m/z*: 458 (M^+ −MeO), 406 (M^+ +H−DHP), 388 (M^+ +H−THPOH), 349, 348, 330, 256, 224, 196, 159, 85 (base peak), 75, 73. HR-MS *m/z*: (M^+ +H−DHP) Calcd for $C_{22}H_{36}NO_4Si$ 406.2412, Found 406.2412. Spectral data of **58b**: IR (neat): 2950, 2230, 1740, 1620, 840, 780 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.10—2.10 (m, 8H), 2.10—2.90 (m, 8H), 3.06 (m, 1H), 3.30—4.30 (m, 5H), 3.68 (s, 3H), 4.60 (m, 1H), 5.98 (bs, 1H), 6.20 (t, J=7 Hz, 1H). MS *m/z*: 458 (M^+ −MeO), 406 (M^+ +H−DHP), 388 (M^+ +H−THPOH), 349, 348, 256, 196, 159, 85 (base peak), 75, 73. HR-MS *m/z*: (M^+ +H−DHP) Calcd for $C_{22}H_{36}NO_4Si$ 406.2412, Found 406.2423.

Methyl (1*S*,5*S*,6*S*,7*R*)-6-*tert*-Butyldimethylsilyloxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoate (61) The diene **58a** (85 mg, 0.17 mmol) and (methyl benzoate)$Cr(CO)_3$ (10 mg, 0.035 mmol) were dissolved in acetone (10 ml). The solution was degassed by three free-pump-thaw cycles, and then transferred into an autoclave with glass insert (100 ml) under an argon atmosphere. The autoclave was purged repeatedly with hydrogen. The solution was stirred at 120 °C for 15 h under 70 kg/cm^2 of hydrogen pressure. After cooling to room temperature, the reaction mixture was exposed to air and light to decompose the catalyst. Removal of the solvent gave a dark green residue, which was purified by silica gel column chromatography (ether–hexane, 2 : 3) to afford the desired exocyclic olefin **61** (86 mg, 100%) as a colorless oil. IR (neat): 2950, 2200, 1740, 1640, 835, 775 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.90 (s, 9H), 1.10—2.00 (m, 10H), 2.00—2.80 (m, 11H), 3.30—4.10 (m, 5H), 3.66 (s, 3H), 4.60 (m, 1H). MS *m/z*: 434 (M^+ −*tert*-Bu), 390 (M^+ −THPO), 389 (M^+ −THPOH), 350, 332, 226, 159, 85 (base peak), 75, 73. HR-MS *m/z*: (M^+ −*tert*-Bu) Calcd for $C_{23}H_{36}NO_5Si$ 434.2361, Found 434.2365. TLC (ether–hexane, 4 : 1, silica gel, two times development): *Rf* **61** (*Z*-isomer) 0.29, **68** (*E*-isomer) 0.26.

Methyl (1*S*,5*S*,6*S*,7*R*)-6-Hydroxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoate (63) Tetrabutylammonium fluoride (1 M solution in THF, 0.41 ml) was added to a solution of **61** (133 mg, 0.27 mmol) in THF (2 ml), and the mixture was stirred at 23 °C for 3 h. The reaction was quenched by the addition of brine, followed by extraction of the mixture with ether. The combined organic layers were dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (ether–hexane, 1 : 4) to give the alcohol **63** (95 mg, 93%) as a colorless oil. IR (neat): 3500, 2950, 2350, 2210, 1740, 1642 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00—3.10 (m, 22H), 3.10—4.10 (m, 5H), 3.68 (s, 3H), 4.60 (m, 1H). MS *m/z*: 293 (M^+ −DHP), 275 (M^+ −THPOH), 257, 244, 243, 226, 225, 135, 117, 105, 91, 86, 85 (base peak), 84, 79, 77, 67, 57, 55, 43, 41. HR-MS *m/z*: (M^+ −DHP) Calcd for $C_{16}H_{23}NO_4$ 293.1625, Found 293.1622.

Methyl (1*S*,5*S*,6*S*,7*R*)-6-Hydroxymethyl-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-δ-cyano-γ-pentanoate (72) A suspension of 10% Pd on C (241 mg, 10 mol%) in toluene (40 ml) was stirred at 23 °C for 1 h under a hydrogen atmosphere (1 atm). A solution of the diene **58** (1.11 g, 2.27 mmol), in toluene (40 ml) was added at −40 °C, and the mixture was stirred at the same temperature for 6 h. After filtration through a silica gel pad to remove the catalyst, the filtrate was concentrated and purified by silica gel column chromatography (ethyl acetate–hexane, 1 : 7) to afford a mixture of the 5*E*-exocyclic olefin **68** and the regioisomer **70** (929 mg, 83%, **68** : **70** = 8 : 1) and the 5*Z*-exocyclic olefin **61** (118 mg, 11%) as a colorless oil. Tetrabutylammonium fluoride (1 M solution in THF, 2.77 ml) was added to a solution of the mixture of **68** and **70** (906 mg) in THF (8 ml), and the mixture was stirred at 23 °C for 1.5 h. The reaction was quenched by the addition of saturated aqueous NH_4Cl, followed by extraction of the mixture with ethyl acetate. The combined organic layers were dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (ethyl acetate–hexane, 3 : 1) to give the alcohol **72** (428 mg, 62%) as a colorless oil. IR (neat): 3460, 2940, 2200, 1740, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.16—3.04 (m, 22H), 3.32—4.21 (m, 5H), 3.68 (s, 3H), 4.60 (m, 1H). MS *m/z*: 293 (M^+ −DHP), 275 (M^+ −THPOH), 257, 244, 226, 117, 85, 67, 57, 43 (base peak). HR-MS *m/z*: (M^+ −DHP) Calcd for $C_{16}H_{23}NO_4$ 293.1627, Found 293.1647.

NMR (500 MHz) Data of 62 and 69 **62** (5*Z*-Stereoisomer): H_a 3.67 (s, 3H), H_b 2.34 (t, J=7.1 Hz, 2H), H_c 1.86 (tt, J=7.5, 7.1 Hz, 2H), H_d 2.21 (t, J=7.5 Hz, 2H), H_e 2.35 (m, 1H), H_f 2.60 (dd, J=18, 9.5 Hz, 1H), H_g 2.77 (dd, J=18, 8.5 Hz, 1H), H_h 2.67 (br d, J=18 Hz, 1H), H_i 2.50 (m, 1H), H_j 2.40 (td, J=8.5, 4 Hz, 1H), H_k 2.14 (ddd, J=13, 7.3, 7.3 Hz, 1H),

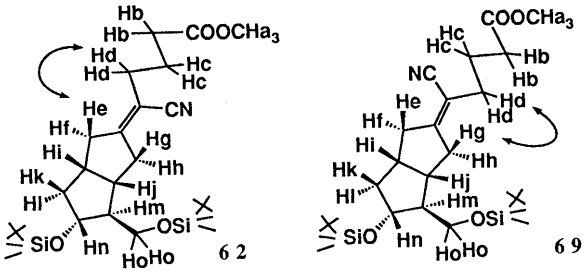


Fig. 1

H_l 1.30 (ddd, J=13, 7.1, 7.1 Hz, 1H), H_m 1.56 (ddt, J=7, 4, 4 Hz, 1H), H_n 3.98 (ddd, J=7.1, 7.1, 7.1 Hz, 1H), H_o 3.59 (d, J=4.4 Hz, 2H), *tert*-BuSi 0.89 (s, 9H), 0.85 (s, 9H), MeSi 0.04 (s, 6H), 0.03 (s, 3H), 0.02 (s, 3H).

69 (5*E*-Stereoisomer): H_a 3.67 (s, 3H), H_b 2.33 (t, J=7.3 Hz, 2H), H_c 1.85 (tt, J=7.3, 7.3 Hz, 2H), H_d 2.20 (t, J=7.3 Hz, 2H), H_e 2.82 (dd, J=17.9, 9.1 Hz, 1H), H_f 2.58 (dd, J=17.9, 4.2 Hz, 1H), H_g 2.42—2.48 (m, 1H), H_h 2.48—2.55 (m, 1H), H_i 2.43—2.52 (m, 1H), H_j 2.36—2.41 (m, 1H), H_k 2.13 (ddd, J=12.8, 7.0, 7.0 Hz, 1H), H_l 1.32 (ddd, J=12.8, 7.0, 7.0 Hz, 1H), H_m 1.52—1.57 (m, 1H), H_n 3.92 (ddd, J=7.0, 7.0, 7.0 Hz, 1H), H_o 3.55 (dd, J=10.8, 5.6 Hz, 1H), 3.61 (dd, J=10.8, 4.1 Hz, 1H), *tert*-BuSi 0.88 (s, 9H), 0.86 (s, 9H), MeSi 0.03 (s, 6H), 0.02 (s, 6H). Assignment of each signal was determined by correlated spectroscopy (COSY). The stereochemistry of the exocyclic olefin in **62** was assigned to be *Z* by nuclear Overhauser effect correlation spectroscopy (NOESY). Namely, strong NOE was observed between H_e and H_d, and no NOE was observed between H_g and H_d. On the other hand, no NOE was observed between H_e and H_d, and strong NOE was observed between H_g and H_d in the case of **69**.

Methyl (1*S*,5*S*,6*R*,7*R*)-6-(3-Oxo-*E*-1-octenyl)-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoate (64) A solution of SO_3-pyridine complex (104 mg, 0.65 mmol) in DMSO (1.6 ml) was added to a stirred solution of the alcohol **62** (82 mg, 0.22 mmol) and triethylamine (0.19 ml) in DMSO (2.4 ml), and the mixture was stirred at 23 °C for 40 min, then poured into ice-water, and extracted with ether. The ether extracts were washed with water and brine, and dried over $MgSO_4$. Removal of the solvent gave the crude aldehyde. Sodium hydride (60% in oil, 12 mg, 0.31 mmol) was washed with pentane, and suspended in THF (2.2 ml). A solution of dimethyl (2-oxoheptyl)phosphonate (73 mg, 0.33 mmol) in THF (1.4 ml) was added to this suspension, and the mixture was stirred at 23 °C for 50 min. Then, a solution of the crude aldehyde in THF (1 ml) was dropped into the solution of the sodium ketophosphonate, and the whole mixture was stirred at 23 °C for 30 min. The reaction was quenched by the addition of saturated aqueous NH_4Cl, followed by extraction of the mixture with ether. The combined ether extracts were washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification by silica gel column chromatography (ether–hexane, 4 : 3) afforded the enone **64** (84 mg, 82%) as a colorless oil. IR (neat): 2950, 2350, 2210, 1740, 1699, 1675, 1628 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, J=6 Hz, 3H), 1.00—2.05 (m, 16H), 2.05—3.00 (m, 13H), 3.45 (m, 1H), 3.69 (s, 3H), 3.80 (m, 2H), 4.51, 4.61 (each br s, total 1H), 6.17, 6.20 (each d, J=16 Hz, total 1H), 6.72, 6.78 (each dd, J=16, 7.5 Hz, total 1H). MS *m/z*: 440 (M^+ −MeO), 388, 387 (M^+ −DHP), 370, 369, 355, 343, 338, 327, 288, 256, 238, 151, 131, 130, 99, 91, 86, 85 (base peak), 71, 67, 57, 55, 43, 41. HR-MS *m/z*: (M^+ −DHP) Calcd for $C_{23}H_{33}NO_4$ 387.2407, Found 387.2402.

In a similar manner, the 5*E*-stereoisomer was synthesized from **72** in 64% yield. Spectral data of the 5*E*-stereoisomer of **64**: IR (neat): 2960, 2220, 1740, 1695, 1670, 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.99 (t, J=6 Hz, 3H), 1.08—2.05 (m, 16H), 2.05—3.20 (m, 13H), 3.42 (m, 1H), 3.60—4.22 (m, 2H), 3.68 (s, 3H), 4.55, 4.64 (each br s, total 1H), 6.14, 6.17 (each d, J=16 Hz, total 1H), 6.72, 6.80 (each dd, J=16, 7.5 Hz, total 1H). MS *m/z*: 387 (M^+ −DHP), 369, 355, 338, 327, 288, 256, 229, 213, 165, 151, 99, 85 (base peak), 71, 67, 57, 43. HR-MS *m/z*: (M^+ −DHP) Calcd for $C_{23}H_{33}NO_4$ 387.2410, Found 387.2421. TLC (ether–hexane, 4 : 3, silica gel): *Rf* **64** (*Z*-isomer) 0.24, *E*-isomer of **64** 0.33.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-*E*-1-octenyl]bicyclo[3.3.0]octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoate (66a) An excess amount of sodium borohydride was added to a stirred solution of the enone **64** (83 mg, 0.18 mmol) in methanol (3 ml) at −20 °C, and the mixture was stirred at the same temperature for 1.5 h. The reaction was quenched by the addition of acetone, and then saturated aqueous NH_4Cl was added to the reaction mixture. After evaporation of the organic solvents, the water layer was extracted with ether. The combined ether extracts were dried over $MgSO_4$,

and concentrated to give the alcohol as an epimeric mixture (83 mg). Spectral data of the alcohol: IR (neat): 3480, 2940, 2210, 1738, 1641 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (br t, J=6 Hz, 3H), 1.05—2.90 (m, 33H), 3.50 (m, 1H), 3.60—4.20 (m, 3H), 3.68 (s, 3H), 4.63 (br s, 1H), 5.56 (m, 2H). MS m/z: 371 (M^+ −THPOH), 353, 327, 117, 99, 86, 85 (base peak), 67, 57, 43, 41. HR-MS m/z: (M^+ −THPOH) Calcd for $C_{23}H_{33}O_3$ 371.2458, Found 371.2484. The alcohol thus obtained (epimeric mixture, 81 mg) was dissolved in a mixture of 65% aqueous acetic acid (1.3 ml) and THF (0.13 ml), and the mixture was stirred at 50 °C for 1 h, then poured into saturated aqueous $NaHCO_3$, and extracted with ether. The ether extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (ether) to afford the desired 15α-diol (**66a**) (34 mg, 51%) as a more polar fraction and the 15β-diol (**66b**) (28 mg, 42%) as a less polar fraction. Spectral data of **66a**: IR (neat): 3420, 2930, 2200, 1736, 1641 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (br t, J=6 Hz, 3H), 1.05—1.65 (m, 10H), 1.65—3.10 (m, 15H), 3.68 (s, 3H), 3.70 (m, 1H), 4.02 (m, 1H), 5.50 (m, 2H). MS m/z: 371 ($M^+ - H_2O$), 354, 353 ($M^+ - 2H_2O$), 327, 300, 295, 268, 226, 225, 159, 149, 131, 130, 117, 99, 91, 81, 79, 71, 67, 57, 55, 43 (base peak), 41. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{23}H_{33}NO_3$ 371.2458, Found 371.2439. $[\alpha]_D^{20}$: +1.4° (c=1.15, MeOH). Spectral data of **66b**: IR (neat): 3450, 2940, 2210, 1740, 1645 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (br t, J=6 Hz, 3H), 1.05—1.65 (m, 10H), 1.65—2.80 (m, 15H), 3.68 (s, 3H), 3.83 (m, 1H), 4.10 (m, 1H), 5.60 (m, 2H). MS m/z: 371 ($M^+ - H_2O$), 353 ($M^+ - 2H_2O$), 327, 300, 295, 269, 268, 226, 225, 159, 131, 117, 99 (base peak), 91, 81, 79, 71, 67, 57, 55, 43, 41. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{23}H_{33}NO_3$ 371.2458, Found 371.2484. $[\alpha]_D^{20}$: −12° (c=1.01, MeOH).

Methyl (1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-*E*-1-octenyl]bicyclo-[3.3.0]octane-*E*-$\Delta^{3,\delta}$-δ-cyanopentanoate A 65% aqueous solution of acetic acid (2 ml) was added to a solution of the *E*-isomer of the enone **64** (122 mg, 0.26 mmol) in THF (1 ml), and the mixture was stirred at 65 °C for 10 h, then neutralized with saturated aqueous $NaHCO_3$, and extracted with ethyl acetate. The organic layers were washed with brine, and dried over Na_2SO_4. Removal of the solvent and purification of the residue by silica gel column chromatography (ethyl acetate–hexane, 1 : 1) afforded the alcohol (98 mg, 98%) as a colorless oil. IR (neat): 3450, 2950, 2220, 1740, 1690, 1665, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (br t, J=6 Hz, 3H), 1.08—3.20 (m, 24H), 3.68 (s, 3H), 4.01 (ddd, J=9, 7, 7 Hz, 1H), 6.20 (dd, J=16, 1 Hz, 1H), 6.72 (dd, J=16, 8 Hz, 1H). MS m/z: 387 (M^+), 369 ($M^+ - H_2O$), 338, 298, 256, 99 (base peak), 71, 43. HR-MS m/z: (M^+) Calcd for $C_{23}H_{33}NO_4$ 387.2410, Found 387.2421. $[\alpha]_D^{20}$: +103° (c=0.46, $CHCl_3$). A solution of diisobutylaluminum hydride in toluene (1 M, 2.40 ml) was added to a stirred solution of 2,6-di-*tert*-butyl-4-methylphenol (726 mg, 3.43 mmol) in toluene (3 ml) at −10 °C, and the mixture was stirred at the same temperature for 1 h. To this solution was added a solution of the alcohol obtained above (86 mg, 0.22 mmol) in toluene (5 ml) at −78 °C, and the whole mixture was stirred at −78—−10 °C for 3 h. The raction was quenched by the addition of brine, followed by extraction with ethyl acetate. The combined organic layers were washed with brine, and dried over Na_2SO_4. Removal of the solvent and purification by silica gel column chromatography (ethyl acetate–hexane, 3 : 1) afforded the 15α-diol (61 mg, 71%) as a more polar fraction and the 15β-diol (11 mg, 13%) as a less polar fraction. Spectral data of 15α-diol (5*E*-isomer): IR (neat): 3420, 2950, 2240, 1745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.83 (br t, J=6 Hz, 3H), 1.00—1.56 (m, 10H), 1.56—1.98 (m, 3H), 1.98—2.61 (m, 9H), 2.61—3.04 (m, 3H), 3.60—3.88 (m, 1H), 3.62 (s, 3H), 3.78—4.16 (m, 1H), 5.24—5.56 (m, 2H). MS m/z: 371 ($M^+ - H_2O$), 353 ($M^+ - 2H_2O$), 327, 300, 295, 268, 225, 99 (base peak), 71, 43. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{23}H_{33}NO_3$ 371.2461, Found 371.2460. $[\alpha]_D^{20}$: +92° (c=0.60, $CHCl_3$). TLC (ether–methanol, 50 : 1, silica gel): *Rf* **66a** (*Z*-isomer) 0.29, *E*-isomer of **66a** 0.38, **66b** 0.42, *E*-isomer of **66b** 0.48.

(1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-*E*-1-octenyl]bicyclo[3.3.0]-octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoic Acid (6) A 10% NaOH aqueous solution (0.4 ml, 1.0 mmol) was added to a stirred solution of the diol **66a** (20 mg, 0.05 mmol) in methanol (0.4 ml) at −5 °C, and the mixture was stirred at 0 °C for 12 h. The reaction mixture was diluted with ether, and neutralized by adding 10% aqueous HCl, followed by evaporation of the organic solvents. Then the remaining water layer was acidified to pH 3—4 by adding 10% aqueous HCl, followed by extraction with ethyl acetate. The combined organic layers were washed with brine, and dried over $MgSO_4$. Removal of the solvent afforded cyanocarbacyclin (**6**) (18 mg, 92%). IR (neat): 3400, 2950, 2210, 1700—1730, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (br t, J=6 Hz, 3H), 1.05—1.75 (m, 10H), 1.75—2.80 (m, 13H), 3.02 (m, 3H), 3.82 (ddd, J=7, 7, 7 Hz, 1H), 4.10 (dt, J=6, 6 Hz, 1H), 5.56 (m, 2H). MS m/z: 375 (M^+), 357 ($M^+ - H_2O$), 339 ($M^+ - 2H_2O$), 286, 268, 243, 225, 183, 173, 159, 143, 131, 117, 105, 99 (base peak), 93, 91, 81, 79, 71, 67, 55, 43, 41. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{22}H_{31}NO_3$ 357.2304, Found 357.2322. $[\alpha]_D^{20}$: −1.0° (c=0.348, MeOH).

In a similar manner, the 5*E*-stereoisomer **73** was synthesized from the corresponding ester in 45% yield. Spectral data of **73**: IR (neat): 3400, 2950, 2220, 1720, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (br t, J=6.5 Hz, 3H), 1.02—1.71 (m, 10H), 1.71—2.10 (m, 3H), 2.10—2.70 (m, 9H), 2.76—2.93 (m, 1H), 3.30—4.40 (m, 5H), 5.48 (dd, J=15, 8 Hz, 1H), 5.58 (dd, J=15, 7 Hz, 1H). MS m/z: 357 ($M^+ - H_2O$), 339 ($M^+ - 2H_2O$), 268, 243, 225, 147, 117, 99, 91, 71, 43 (base peak). HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{22}H_{31}NO_3$ 357.2304, Found 357.2284. $[\alpha]_D^{20}$: +74° (c=0.39, $CHCl_3$). TLC (ether–methanol, 15 : 1, silica gel): *Rf* **6** (*Z*-isomer) 0.11, **73** (*E*-isomer) 0.45.

In a similar manner, 16-methylcyanocarbacyclin **7** and its 5*E*-stereoisomer **74** were synthesized from **63** and **72**. The spectral data were as follows.

Methyl (1*S*,5*S*,6*R*,7*R*)-6-(4-Methyl-3-oxo-*E*-1-octenyl)-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoate (65) Yield was 82%. IR (neat): 2935, 2250, 2210, 1740, 1695, 1670, 1622 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (t, J=6 Hz, 3H), 1.10 (d, J=7 Hz, 3H), 1.10—2.10 (m, 16H), 2.10—3.00 (m, 12H), 3.20—4.30 (m, 3H), 3.68 (s, 3H), 4.51, 4.62 (each br s, total 1H), 6.18, 6.25 (each d, J=16 Hz, total 1H), 6.70 (m, 1H). MS m/z: 401 (M^+ −DHP), 383 (M^+ −THPOH), 288, 256, 113, 85 (base peak), 67, 57, 43, 41. HR-MS m/z: (M^+ −DHP) Calcd for $C_{24}H_{35}NO_4$ 401.2564, Found 401.2580.

Methyl (1*S*,5*S*,6*R*,7*R*)-6-(4-Methyl-3-oxo-*E*-1-octenyl)-7-tetrahydropyranyloxybicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-δ-cyanopentanoate Yield was 69%. IR (neat): 2950, 2210, 1740, 1695, 1625 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.86 (t, J=6 Hz, 3H), 1.10 (d, J=7 Hz, 3H), 1.10—2.04 (m, 16H), 2.04—3.14 (m, 12H), 3.22—4.22 (m, 3H), 3.66 (s, 3H), 4.53, 4.63 (each br s, total 1H), 6.28 6.32 (each d, J=16 Hz, total 1H), 6.78, 6.82 (each dd, J=16, 8 Hz, 1H). MS m/z: 401 (M^+ −DHP), 383 (M^+ −THPOH), 357, 288, 113, 85 (base peak). HR-MS m/z: (M^+ −DHP) Calcd for $C_{24}H_{35}NO_4$ 401.2566, Found 401.2573.

Methyl (1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-4-methyl-*E*-1-octenyl]bicyclo[3.3.0]octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoate (67a) Yield: **66a**, 52%, **66b**, 43% (in two steps). Spectral data of **67a**: IR (neat): 3425, 2940, 2220, 1740, 1642 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (m, 6H), 1.02—3.00 (m, 24H), 3.70 (s, 3H), 3.75—4.05 (m, 2H), 5.56 (m, 2H). MS m/z: 385 ($M^+ - H_2O$), 368, 367 ($M^+ - 2H_2O$), 318, 300, 269, 268 (base peak), 250, 242, 226, 225, 167, 159, 149, 113, 91, 85, 81, 79, 67, 57, 55, 43, 41. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{24}H_{35}NO_3$ 385.2615, Found 385.2618. $[\alpha]_D^{20}$: +2.9° (c=0.90, MeOH). Spectral data of **67b**: IR (neat): 3450, 2950, 2220, 1740, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (m, 6H), 1.00—3.00 (m, 24H), 3.70 (s, 3H), 3.80—4.10 (m, 2H), 5.62 (m, 2H). MS m/z: 385 ($M^+ - H_2O$), 367 ($M^+ - 2H_2O$), 318, 300, 269, 268 (base peak), 250, 242, 240, 226, 225, 159, 131, 130, 117, 112, 91, 85, 81, 79, 57, 55, 43, 41. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{24}H_{35}NO_3$ 385.2615, Found 385.2629. $[\alpha]_D^{20}$: −16° (c=0.67, MeOH).

Methyl (1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-4-methyl-*E*-1-octenyl]bicyclo[3.3.0]octane-*E*-$\Delta^{3,\delta}$-δ-cyanopentanoate Yield: 65% (in two steps). IR (neat): 3430, 2950, 2200, 1730, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.76—1.06 (m, 6H), 1.23—1.62 (m, 8H), 1.80—2.01 (m, 5H), 2.17—3.10 (m, 11H), 3.70 (s, 3H), 3.75—4.10 (m, 2H), 5.44—5.68 (m, 2H). MS m/z: 385 ($M^+ - H_2O$), 367 ($M^+ - 2H_2O$), 354, 341, 300, 268 (base peak), 159, 85, 43. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{24}H_{35}NO_3$ 385.2617, Found 385.2623.

(1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-4-methyl-*E*-1-octenyl]-bicyclo[3.3.0]octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoic Acid (7) Yield: 78%. IR (neat): 3400, 2980, 2220, 1720, 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (m, 6H), 1.05—3.20 (m, 25H), 3.90 (m, 1H), 5.55 (m, 2H). MS m/z: 389 (M^+), 371 ($M^+ - H_2O$), 353 ($M^+ - 2H_2O$), 286, 269, 268 (base peak), 250, 242, 159, 131, 113, 95, 85, 81, 67, 55, 43, 41. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{23}H_{33}NO_3$ 371.2460, Found 371.2451. $[\alpha]_D^{20}$: +8° (c=0.22, MeOH).

(1*S*,5*S*,6*R*,7*R*)-7-Hydroxy-6-[3(*S*)-hydroxy-4-methyl-*E*-1-octenyl]-bicyclo[3.3.0]octane-*Z*-$\Delta^{3,\delta}$-δ-cyanopentanoic Acid (74) Yield: 100%. IR (neat): 3400, 2970, 2230, 1720, 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.78—1.07 (m, 6H), 1.08—1.71 (m, 9H), 1.74—2.12 (m, 3H), 2.14—3.10 (m, 10H), 3.62—4.00 (m, 2H), 4.41—4.92 (m, 3H), 5.46—5.66 (m, 2H). MS m/z: 371 ($M^+ - H_2O$), 353 ($M^+ - 2H_2O$), 286, 268 (base peak), 159, 85, 43. HR-MS m/z: ($M^+ - H_2O$) Calcd for $C_{23}H_{33}NO_3$ 371.2460, Found 371.2442.

Acknowledgment We are grateful to Drs. K. Iseki, T. Kanayama and Y. Hayashi, Mitsubishi Kasei Corporation, for the tests of biological activity.

References and Notes

1) For nonstereoselective syntheses of carbacyclins, see: *a*) K. C. Nicolaou, W. J. Sipio, R. L. Magolda, S. Seitz, and W. E. Barnett, *J. Chem. Soc., Chem. Commun.*, **1978**, 1067; *b*) K. Kojima and K. Sakai, *Tetrahedron Lett.*, **1978**, 3743; *c*) M. Shibasaki, J. Ueda, and S. Ikagami, *ibid.*, **1979**, 433; *d*) D. R. Morton and F. C. Brokaw, *J. Org. Chem.*, **44**, 2880 (1979); *e*) Y. Konishi, M. Kawamura, Y. Arai, and M. Hayashi, *Chem. Lett.*, **1979**, 1437; *f*) A. Sugie, M. Shimomura, J. Katsube, and M. Yamamoto, *Tetrahedron Lett.*, **1979**, 2607; *g*) M. Shibasaki, K. Iseki, and S. Ikegami, *Chem. Lett.*, **1979**, 1299; h) A. Barco, S. Benetti, P. Pollini, P. G. Baraldi, and C. Gandolfi, *J. Org. Chem.*, **45**, 4776 (1980); *i*) M. Yamazaki, M. Shibasaki, and S. Ikegami, *Chem. Lett.*, **1981**, 1245; *j*) P. A. Aristoff, *J. Org. Chem.*, **46**, 1954 (1981); *k*) Y. Konishi, M. Kawamura, Y. Iguchi, Y. Arai, and M. Hayashi, *Tetrahedron*, **37**, 4391 (1981); *l*) W. Skuballa and H. Vorbrüggen, *Angew. Chem., Int. Ed. Engl.*, **20**, 1046 (1981); *m*) R. F. Newton and A. H. Wadsworth, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 823; *n*) K. Kojima, S. Amemiya, K. Koyama, and K. Sakai, *Chem. Pharm. Bull.*, **31**, 3775 (1983); *o*) S. Amemiya, K. Kojima, and K. Sakai, *ibid.*, **32**, 4746 (1984); *p*) K. Ueno, H. Suemune, and K. Sakai, *ibid.*, **32**, 3768 (1984); *q*) B. Bennua, H. Dahl, and H. Vorbrüggen, *Synthesis*, **1985**, 41 ; *r*) W. Skuballa, E. Schillinger, and C.-St. Stürzebecher, *J. Med. Chem.*, **29**, 313 (1986); *s*) Y. Nagao, T. Nakamura, M. Ochiai, K. Fuji, and E. Fujita, *J. Chem. Soc., Chem. Commun.*, **1987**, 267; *t*) P. Magnus and D. P. Becker, *J. Am. Chem. Soc.*, **109**, 7495 (1987); For attempts to achieve stereocontrol, see: *u*) S. Amemiya, K. Kojima, and K. Sakai, *Chem. Pharm. Bull.*, **32**, 1349 (1984); *v*) H.-G. Gais, G. Schmiedl, A. Ball, J. Bund, G. Hellmann, and I. Erdelmeier, *Tetrahedron Lett.*, **29**, 1773 (1988); *w*) H. Rehwinkel, J. Skupsh, and H. Vorbrüggen, *ibid.*, **29**, 1775 (1988); For attempts to recycle the useless *Z*-isomer, see: *x*) H. Vorbrüggen and B. Bennua, *Synthesis*, **1985**, 925.

2) After our preliminary communication, two stereocontrolled syntheses were reported: *a*) D. K. Hutchinson and P. L. Fuchs, *J. Am. Chem. Soc.*, **109**, 4755 (1987); *b*) I. Erdelmeier and H.-J. Gais, *ibid.*, **111**, 1125 (1989).

3) Preliminary communications: *a*) M. Shibasaki, M. Sodeoka, and Y. Ogawa, *J. Org. Chem.*, **49**, 4096 (1984); *b*) M. Shibasaki and M. Sodeoka, *Tetrahedron Lett.*, **26**, 3491 (1985).

4) *a*) E. N. Frankel, E. Selke, and C. A. Grass, *J. Am. Chem. Soc.*, **90**, 2446 (1968); *b*) M. Cais, E. N. Frankel, and A. Rejoan, *Tetrahedron Lett.*, **1968**, 1919.

5) For review, see: *a*) M. F. Farona, "Organometallic Reactions and Syntheses," Vol. 6, ed. by E. N. Becker and M. Tsutsui, Plenum Press, New York and London, 1977, p. 246; *b*) M. Shibasaki and M. Sodeoka, *Yuki Gosei Kagaku Kyokai Shi*, **43**, 877 (1985) and references cited therein.

6) At nearly the same time, one application to the synthesis of rather complex molecules was reported. See: P. Rosenmund and M. Casutt, *Tetrahedron Lett.*, **24**, 1771 (1983).

7) *a*) M. Sodeoka, Y. Ogawa, T. Mase, and M. Shibasaki, *Chem. Pharm. Bull.*, **37**, 586 (1989); *b*) M. Sodeoka and M. Shibasaki, *Chem. Lett.*, **1984**, 579; *c*) Y. Ogawa and M. Shibasaki, *Tetrahedron Lett.*, **25**, 1067 (1984); *d*) T. Mase, M. Sodeoka, and M. Shibasaki, *ibid.*, **25**, 5087 (1984).

8) In the absence of the catalyst no isomerization was observed at 130 °C. This fact rules out the possibility of thermal 1,5-sigmatropic rearrangement. We found that this stereospecific isomerization of conjugated dienes occurred even at 20 °C in acetone or THF when naphthalene·$Cr(CO)_3$ was used as a catalyst. We also succeeded in the stereocontrolled synthesis of aryl-substituted exocyclic olefins and silyl dienol ethers using this unique isomerization. See *a*) M. Sodeoka, S. Satoh, and M. Shibasaki, *J. Am. Chem. Soc.*, **110**, 4823 (1988); *b*) M. Sodeoka, H. Yamada, and M. Shibasaki, *ibid.*, **112**, 4906 (1990).

9) M. Sodeoka and M. Shibasaki, *J. Org. Chem.*, **50**, 1147 (1985).

10) *a*) T. Bannai, T. Toru, A. Hazato, T. Oba, T. Tanaka, N. Okumura, K. Watanabe, and S. Kurozumi, *Chem. Pharm. Bull.*, **30**, 1102 (1982); *b*) A. Hazato, T. Tanaka, K. Watanabe, T. Bannai, T. Toru, N. Okumura, K. Manabe, A. Ohtsu, F. Kamimoto, and S. Kurozumi, *ibid.*, **33**, 1815 (1985).

11) The aldehyde **56** was synthesized by hydrogenation of 3-carbomethoxypropionyl chloride. See: A. W. Burgstahler, L. O. Weigdand, and C. G. Shaffer, *Synthesis*, **1976**, 767. Since **56** is rather unstable, it is necessary to use freshly prepared **56**.

12) R. M. Silverstein, G. C. Bassler, and T. C. Morrill, "Spectrometric Identification of Organic Compounds," John Wiley & Sons, Inc.

13) About 7% of the product was obtained as its chromium complex. Although the structure was not clear, this complex was transformed into **61** quantitatively under exposure to air and light.

14) A. Takahashi, Y. Kirio, M. Sodeoka, H. Sasai, and M. Shibasaki, *J. Am. Chem. Soc.*, **111**, 643 (1989).

15) The cyano group is easily converted to a variety of functional groups such as aldehyde, carboxylic acid, ester, alcohol, amine, *etc.*

16) The stereoisomers of **39** could be separated by $AgNO_3$-impregnated silica gel column chromatography. The 4*Z*-stereoisomer of **78** is approximately one hundred times as potent as the 4*E*-stereoisomer in inhibiting human platelet aggregation. See: K. Iseki, M. Shinoda, C. Ishiyama, Y. Hayashi, S. Yamada, and M. Shibasaki, *Chem. Lett.*, **1986**, 559.

17) For other diene-carbacyclins, see: *a*) K. Iseki, T. Katayama, Y. Hayashi, and M. Shibasaki, *Chem. Pharm. Bull.*, **38**, 1769 (1990); *b*) M. Shibasaki, A. Takahashi, T. Aoki, H. Sato, and S. Narita, *ibid.*, **37**, 1647 (1989).

18) Nissan Chemical Industries, Ltd., Tokyo, Japan