Synthetic Studies on the Taxane Skeleton: Construction of Eight-membered Carbocyclic Rings by the Intramolecular *B*-Alkyl Suzuki-Miyaura Cross-coupling Reaction

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General Information. ^1H and ^{13}C NMR spectra were recorded on a JEOL AL-400 and AL-300 spectrometer. ^1H and ^{13}C chemical shifts are reported in ppm downfield from tetramethylsilane (TMS, δ scale) with the solvent resonances as internal standards. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; band, several overlapping signals; br, broad. IR spectra were recorded on a JASCO FT/IR-8300. Melting points (mp) are uncorrected, recorded on a Yamato capillary melting point apparatus. Optical rotations were measured using a 2 ml cell with a 1 dm path length on a JASCO DIP-1000. Mass spectra and elemental analyses were provided at the Materials Characterization Central Laboratory, Waseda University. All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and phosphomolybdic acid and heat as developing agents. E. Merck silica gel (60, particle size 0.040-0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on self-made 0.3 mm E. Merck silica gel plates (60F-254).

Materials. THF was distilled from sodium/benzophenone ketyl, and methylene chloride (CH_2Cl_2), and acetonitrile from calcium hydride. Toluene was distilled from sodium. DMF was distilled from CaH_2 under reduced pressure.

1-(2-Iodo-phenyl)-hex-5-en-1-ol (a)

IR (thin film) ν_{max} : 3356, 2940, 1640, 1462, 1436, 1010, 914, 754 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.79 (d, $J = 7.3$ Hz, 1H), 7.51 (d, $J = 7.3$ Hz, 1H), 7.37 (dd, $J = 7.3, 7.3$ Hz, 1H), 6.97 (dd, $J = 7.3, 7.3$ Hz,

1H), 5.87-5.77 (m, 1H), 5.03 (d, $J = 17.1$ Hz, 1H), 4.96 (d, $J = 10.3$ Hz, 1H), 4.92-4.90 (m, 1H), 2.17-2.08 (m, 2H), 1.94-1.93 (m, 1H), 1.79-1.69 (m, 1H), 1.67-1.61 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 146.5, 139.0, 138.4, 128.9, 128.4, 126.8, 114.6, 97.6, 77.1, 37.3, 33.5, 25.0; HRMS (FAB) $[\text{M}-\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{14}\text{OI}$: 301.0089, found: 301.0109. ; $R_f = 0.38$ (hexane/AcOEt = 4 / 1).

1-Iodo-2-(1-methoxymethoxy-hex-5-enyl)-benzene (1)

IR (thin film) ν_{max} : 3064, 2944, 1642, 1564, 1464, 1436, 1152, 1098, 1032, 1010, 918, 756 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.79 (d, $J = 7.8$ Hz, 1H), 7.41 (d, $J = 7.8$ Hz, 1H), 7.35 (dd, $J = 7.8, 7.2$ Hz, 1H), 6.96 (dd, $J = 7.8, 7.2$ Hz, 1H), 5.87-5.77 (m, 1H), 5.02 (d, $J = 17.1$ Hz, 1H), 4.95 (d, $J = 10.0$ Hz, 1H), 4.84 (dd, $J = 4.8, 4.8$ Hz, 1H), 4.55 (d, $J = 6.7$ Hz, 1H), 4.48 (d, $J = 6.7$ Hz, 1H), 3.39 (s, 3H), 2.17-2.08 (m, 2H), 1.72-1.65 (m, 3H), 1.51 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 144.6, 139.2, 138.5, 129.0, 128.4, 127.4, 114.6, 98.5, 94.7, 81.0, 55.9, 36.7, 33.5, 25.2; HRMS (FAB) $[\text{M}]^+$ calcd for $\text{C}_{14}\text{H}_{19}\text{O}_2\text{I}$: 346.0430, found: 346.0403 ; $R_f = 0.62$ (hexane/AcOEt = 4 / 1).

5-Methoxymethoxy-5,6,7,8,9,10-hexahydro-benzocyclooctene (2)

IR (thin film) ν_{max} : 2932, 1734, 1452, 1210, 1154, 1098, 1040, 758 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.44 (d, $J = 7.6$ Hz, 1H), 7.24 (ddd, $J = 7.6, 7.3, 1.7$ Hz, 1H), 7.19 (ddd, $J = 7.3, 7.3, 1.7$ Hz, 1H), 7.09 (d, $J = 7.3$ Hz, 1H), 5.06 (dd, $J = 4.6, 4.6$ Hz), 4.61 (d, $J = 6.6$ Hz, 1H), 4.58 (d, $J = 6.6$ Hz, 1H), 3.40 (s, 3H), 2.83-2.72 (m, 2H), 2.13-2.06 (m, 1H), 1.99-1.92 (m, 1H), 1.63-1.52 (m, 3H), 1.41-1.36 (m, 2H), 0.94-0.89 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 140.7, 140.2, 128.9, 127.0, 126.3, 124.5, 94.3, 73.3, 55.5, 39.1, 32.7, 32.6, 26.6, 23.7; HRMS (FAB) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2\text{Na}$: 243.1361, found: 243.1354. ; $R_f = 0.62$ (hexane/AcOEt = 4 / 1).

dl-carbonate (4)

IR (KBr) $\nu_{\max}$: 2940, 1798, 1286, 1208, 1020 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 7.45 (d, $J = 7.5$ Hz, 1H), 7.29-7.18 (m, 3H), 5.57 (s, 1H), 2.96 (dd, $J = 21.1, 14.7$ Hz, 1H), 2.68 (dd, $J = 21.1, 14.7$ Hz, 2H), 2.48-2.37 (m, 1H), 2.34-2.24 (m, 2H), 2.20-1.90 (m, 1H), 1.45 (s, 3H), 1.33-1.26 (m, 1H), 1.18 (s, 3H), 0.71 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 154.2, 138.6, 135.0, 134.4, 131.1, 130.3, 128.0, 126.2, 123.7, 92.5, 79.5, 39.8, 34.2, 28.8, 25.2, 23.0, 20.9, 19.7; HRMS (FAB) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{23}\text{O}_3$, 299.1647, found, 299.1650. ; $R_f = 0.60$ (hexane/AcOEt = 2 / 1).

***dl*-(1*S*,2*S*)-12,15,15-Trimethyl-tricyclo[9.3.1.0^{3,8}]pentadeca-3,5,7,11-tetraene-1,2-diol (5)**

IR (KBr) $\nu_{\max}$: 3390, 2922, 1458, 1376, 1020, 750 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 7.62 (d, $J = 7.3$ Hz, 1H), 7.20 (ddd, $J = 7.3, 7.3, 1.7$ Hz, 1H), 7.10 (dd, $J = 7.3, 1.7$ Hz, 1H), 7.03 (ddd, $J = 7.3, 7.3, 1.3$ Hz, 1H), 4.72 (s, 1H), 2.86 (d, $J = 1.5$ Hz, 1H), 2.83 (dd, $J = 4.6, 4.0$ Hz, 1H), 2.79-2.68 (m, 1H), 2.49 (s, 1H), 2.43 (d, $J = 4.4$ Hz, 1H), 2.40 (d, $J = 5.3$ Hz, 1H), 2.37-2.31 (m, 1H), 1.37 (s, 3H), 1.33-1.19 (m, 3H), 1.08 (s, 3H), 0.47 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 143.5, 139.0, 133.0, 131.7, 129.9, 126.3, 125.7, 124.3, 80.0, 71.4, 41.3, 34.4, 29.4, 29.3, 26.2, 25.7, 19.8, 19.3; HRMS (FAB) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2\text{Na}$, 295.1674, found, 295.1695 ; $R_f = 0.46$ (hexane/AcOEt = 2 / 1).

***dl*-(*S*)-((*S*)-3-iodo-1-(methoxymethoxy)-2,2,4-trimethylcyclohex-3-enyl)(2-vinylphenyl)methanol (b)**

IR (thin film) $\nu_{\max}$: 2924, 1458, 1388, 1150, 1022, 890, 826, 770 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.68 (d, $J = 7.7$ Hz, 0.09H), 7.57 (d, $J = 7.3$ Hz, 0.91H), 7.44 (d, $J = 7.7$ Hz, 0.09H), 7.41 (d, $J = 7.6$ Hz, 0.91H), 7.32-7.23 (m, 2H), 5.60 (d, $J = 17.3$ Hz, 0.91H), 5.58 (d, $J = 17.3$ Hz, 0.09H), 5.38 (d, $J = 3.9$ Hz, 0.09H), 5.32 (d, $J = 11.0$ Hz, 0.91H), 5.30 (d, $J = 11.0$ Hz, 0.09H), 5.20 (d, $J = 8.5$ Hz, 0.91H), 4.93 (d, $J = 6.8$ Hz, 0.91H), 4.79 (d, $J = 6.8$ Hz, 0.91H), 4.17 (d, $J = 7.5$ Hz, 0.09H), 4.13 (d, $J = 7.5$ Hz, 0.09H), 3.53 (s, 2.73H), 3.25 (s, 0.27H), 2.03-1.85 (m, 1H), 1.93 (s, 0.27H), 1.90-1.86 (m, 1H), 1.83 (s, 2.73H), 1.76-1.69 (m, 1H), 1.65-1.60 (m, 1H), 1.34 (s, 2.73H), 1.30 (s, 2.73H), 1.24 (s, 0.27H), 1.22 (s, 0.27H); HRMS (FAB) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{27}\text{O}_3\text{I}$, 465.0903, found, 465.0922 ; $R_f = 0.42$ (hexane/AcOEt = 4 / 1).

1-Hydroxymethyl-3-iodo-2,2,4-trimethyl-cyclohex-3-enol (7)

IR (thin film) $\nu_{\max}$: 3410, 2975, 1457, 1375, 1202, 1102, 1043, 894, 661 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 3.76 (d, J = 11.0 Hz, 1H), 3.53-3.50 (m, 1H), 2.33 (dt, J = 17.8, 6.6 Hz, 1H), 2.21 (dd, J = 6.4, 6.1 Hz, 1H), 2.16 (br, 1H), 2.09 (br, 1H), 1.90 (s, 3H), 1.88-1.76 (m, 2H), 1.20 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 137.3, 115.8, 74.6, 65.6, 45.7, 31.0, 30.5, 26.7, 26.5, 26.1; HRMS (FAB) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{10}\text{H}_{17}\text{IO}_2\text{Na}$, 319.0171, found, 319.0183; R_f = 0.29 (hexane/AcOEt = 1 / 1).

Acetic acid 1-hydroxy-3-iodo-2,2,4-trimethyl-cyclohex-3-enylmethyl ester (c)

IR (thin film) $\nu_{\max}$: 3492, 2976, 1742, 1458, 1384, 1246, 1038, 896 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 4.28 (d, J = 11.7 Hz, 1H), 4.10 (d, J = 11.7 Hz, 1H), 2.31 (dt, J = 17.8, 6.1 Hz, 1H), 2.19-2.15 (m, 1H), 2.21 (s, 3H), 1.90 (s, 3H), 1.87-1.74 (m, 2H), 1.21 (s, 3H), 1.13 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.3, 137.2, 114.9, 73.5, 68.0, 45.8, 30.9, 30.6, 27.2, 26.9, 25.8, 21.0; HRMS (FAB) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{19}\text{IO}_3$, 339.0457, found, 339.0444; R_f = 0.51 (hexane/ AcOEt = 1 / 1).

Acetic acid 3-iodo-1-methoxymethoxy-2,2,4-trimethyl-cyclohex-3-enylmethyl ester (d)

IR (thin film) $\nu_{\max}$: 2984, 1748, 1458, 1382, 1234, 1152, 1108, 1044, 920, 894 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 4.83 (d, J = 7.3 Hz, 1H), 4.79 (d, J = 7.3 Hz, 1H), 4.28 (d, J = 12.2 Hz, 1H), 4.21 (d, J = 12.2 Hz, 1H), 2.27-2.10 (m, 3H), 2.08 (s, 3H), 1.95-1.89 (m, 1H), 1.87 (s, 3H), 1.19 (s, 3H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.7, 136.9, 114.6, 91.5, 78.2, 67.4, 55.6, 46.8, 31.0, 30.6, 27.2, 25.7, 23.1, 21.1; HRMS (FAB) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{14}\text{H}_{24}\text{IO}_4$, 383.0719, found, 383.0742; R_f = 0.67 (hexane/ AcOEt = 1 / 1).

(3-Iodo-1-methoxymethoxy-2,2,4-trimethyl-cyclohex-3-enyl)-methanol (e)

IR (thin film) $\nu_{\max}$: 3476, 2980, 1464, 1360, 1148, 1106, 1042, 894, 668 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 4.96 (d, $J = 7.7$ Hz, 1H), 4.57 (d, $J = 7.7$ Hz, 1H), 3.71 (d, $J = 10.1$ Hz, 1H), 3.58 (d, $J = 10.1$ Hz, 1H), 2.29-2.20 (m, 2H), 2.13-2.07 (m, 1H), 1.89 (s, 3H), 1.75-1.68 (m, 1H), 1.16 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 136.9, 115.2, 90.4, 81.3, 64.6, 55.6, 46.3, 30.8, 30.6, 27.0, 26.0, 21.2; HRMS (FAB) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{22}\text{IO}_3$, 341.0613, found, 341.0602; $R_f = 0.53$ (hexane/ AcOEt = 2 / 1).

(S)-3-Iodo-1-methoxymethoxy-2,2,4-trimethyl-cyclohex-3-enecarbaldehyde ((+)-8)

$[\alpha]_{\text{D}}^{27.4} +76.2$ (c 0.98, CHCl_3); IR (thin film) $\nu_{\max}$: 2889, 1724, 1458, 1154, 1023, 917, 776 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 9.76 (s, 1H), 4.75 (d, $J = 7.3$ Hz, 1H), 4.64 (d, $J = 7.3$ Hz, 1H), 2.25-2.21 (m, 2H), 2.12-2.04 (m, 1H), 1.94 (dd, $J = 5.4, 4.4$ Hz, 1H), 1.91 (s, 3H), 1.38 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 202.9, 137.1, 114.1, 91.9, 83.4, 56.0, 45.3, 30.9, 29.2, 27.3, 26.6, 20.4; HRMS (FAB) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{20}\text{IO}_3$, 339.0457, found, 339.0451; $R_f = 0.60$ (hexane/ AcOEt = 2 / 1).

dl-1-((S)-(benzyloxy)((S)-3-iodo-1-(methoxymethoxy)-2,2,4-trimethylcyclohex-3-enyl)methyl)-2-vinyl benzene (9)

IR (thin film) $\nu_{\max}$: 2932, 1738, 1454, 1374, 1242, 1150, 1102, 1028, 918, 700 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.75-7.68 (br, 1H), 7.46-7.38 (br, 1H), 7.28-7.15 (m, 7H), 7.01-6.94 (m, 1H), 5.68 (d, $J = 17.1$ Hz, 1H), 5.35 (d, $J = 10.7$ Hz, 1H), 4.90 (s, 1H), 4.75 (d, $J = 7.1$ Hz, 1H), 4.56 (d, $J = 7.1$ Hz, 1H), 4.27 (d, $J = 11.2$ Hz, 1H), 4.15 (d, $J = 11.2$ Hz, 1H), 3.29 (s, 3H), 2.44-2.40 (m, 1H), 1.97-1.93 (m, 1H), 1.85 (s, 1H), 1.72-1.69 (m, 1H), 1.28 (s, 1H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 138.4, 137.8, 136.6, 136.5, 134.7, 129.4, 128.2, 128.1, 127.9, 127.7, 127.5, 125.7, 118.6, 116.9, 92.4, 82.9, 79.8, 70.1, 55.7, 48.2, 31.3, 29.7, 29.4, 27.4, 24.2; HRMS (FAB) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{33}\text{O}_3\text{INa}$, 555.1372, found, 555.1390; $R_f = 0.60$ (hexane/AcOEt = 4 / 1).

***dl*-1-((*R*)-(benzyloxy)((*S*)-3-iodo-1-(methoxymethoxy)-2,2,4-trimethylcyclohex-3-enyl)methyl)-2-vinyl benzene (f)**

IR (thin film) $\nu_{\max}$: 2928, 1454, 1360, 1150, 1070, 1044, 1022, 920, 886 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.57-7.50 (m, 2H), 7.37-7.20 (m, 8H), 5.63 (d, $J = 17.3$ Hz, 1H), 5.34 (d, $J = 10.7$ Hz, 1H), 5.15 (s, 1H), 4.11 (s, 2H), 3.99 (d, $J = 7.8$ Hz, 1H), 3.87 (d, $J = 7.8$ Hz, 1H), 3.14 (s, 3H), 2.54-2.46 (m, 1H), 2.37-2.31 (m, 1H), 2.27-2.19 (m, 1H), 2.13-2.06 (m, 1H), 1.82 (s, 3H), 1.33 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 139.3, 138.1, 136.6, 136.2, 135.4, 128.3, 128.1, 127.8, 127.5, 127.3, 127.2, 126.2, 116.3, 115.7, 91.1, 82.6, 79.8, 70.5, 55.8, 47.8, 31.3, 29.7, 28.6, 28.0, 20.4; HRMS (FAB) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{27}\text{H}_{34}\text{O}_3\text{I}$, 533.1553, found, 533.1543 ; $R_f = 0.67$ (hexane/AcOEt = 4 / 1).

***dl*-acetone (11)**

IR (KBr) $\nu_{\max}$: 2983, 1458, 1373, 1240, 1223, 1087, 1048 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 7.56 (d, $J = 7.7$ Hz, 1H), 7.19 (dd, $J = 7.7, 7.3$ Hz, 1H), 7.14 (d, $J = 7.0$ Hz, 1H), 7.07 (dd, $J = 7.3, 7.0$ Hz, 1H), 4.94 (s, 1H), 2.86 (dd, $J = 13.4, 7.7$ Hz, 1H), 2.77 (ddd, $J = 13.4, 11.8, 7.0$ Hz, 1H), 2.60 (ddd, $J = 12.7, 11.8, 7.7$ Hz, 1H), 2.41 (dd, $J = 12.7, 7.0$ Hz, 1H), 2.21 (ddd, 13.2, 12.2, 4.4 Hz, 2H), 1.68-1.62 (m, 1H), 1.57 (s, 3H), 1.41 (s, 3H), 1.40 (s, 3H), 1.21-1.13 (m, 1H), 1.10 (s, 3H), 0.64 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 139.0, 138.4, 132.9, 131.8, 130.5, 126.6, 125.7, 124.2, 105.8, 87.6, 76.8, 39.8, 34.4, 29.4, 29.0, 28.5, 26.6, 25.8, 25.7, 20.6, 19.7; HRMS (FAB) $[\text{M}]^+$ calcd for $\text{C}_{21}\text{H}_{28}\text{O}_2$, 312.2089, found, 312.2068 ; $R_f = 0.43$ (hexane/AcOEt = 10 / 1).

***dl*-(1*S*,2*S*)-2-Benzoyloxy-1-methoxymethoxy-12,15,15-trimethyl-tricyclo[9.3.1.0^{3,8}]pentadeca-3,5,7,11-tetraene (12)**

IR (thin film) $\nu_{\max}$: 2928, 1458, 1384, 1154, 1110, 1066, 1030, 918, 758, 738, 698 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.57 (d, $J = 7.4$ Hz, 1H), 7.31-7.25 (m, 5H), 7.14 (dd, $J = 8.1, 7.0$ Hz, 1H), 7.11 (d, $J = 7.4$ Hz, 1H), 7.02 (dd, $J = 8.1, 7.0$ Hz, 1H), 5.28 (d, $J = 7.9$ Hz, 1H), 4.66 (d, $J = 7.9$ Hz, 1H), 4.39 (s, 1H), 4.17 (d, $J = 2.9$ Hz, 2H), 2.47-2.31 (m, 3H), 2.27-2.19 (m, 1H), 2.11-2.04 (m, 1H), 1.38 (s, 3H), 1.36-1.33 (m, 1H), 1.08 (s, 3H), 0.43 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 142.2, 140.2, 138.6, 132.9, 131.7, 129.9, 128.1, 127.5, 127.1, 126.2, 125.7, 125.0, 93.8, 85.0, 81.3, 71.1, 55.4, 42.3, 34.4, 29.5, 29.2, 26.8, 20.4, 19.6, 19.5; HRMS (FAB) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{34}\text{O}_3\text{Na}$, 424.2406, found, 429.2435; $R_f = 0.66$ (hexane/AcOEt = 4 / 1).

(2*R*,4*aR*,8*aS*)-hexahydro-4*a*-methyl-2-phenylbenzo[d][1,3]dioxin-5-one (14)

$[\alpha]^{28.2}_{\text{D}} +73.0$ (c 1.03, CHCl_3); mp 71-73 $^{\circ}\text{C}$; IR (KBr) $\nu_{\max}$: 2953, 1703, 1378, 1216, 1067, 764, 696 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.50-7.49 (m, 2H), 7.39-7.33 (m, 3H), 5.49 (s, 1H), 4.11 (d, $J = 11.5$ Hz, 1H), 4.02 (d, $J = 11.5$ Hz, 1H), 3.86 (dd, $J = 11.2, 4.4$ Hz, 1H), 2.65 (ddd, $J = 14.9, 14.4, 6.6$ Hz, 1H), 2.22 (dd, $J = 14.9, 4.7$ Hz, 1H), 2.08-1.92 (m, 3H), 1.72-1.60 (m, 1H), 1.50 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 212.1, 137.8, 129.0, 128.3, 126.1, 102.4, 82.2, 73.3, 48.7, 36.9, 25.5, 21.0, 16.1; HRMS (FAB) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{19}\text{O}_3$, 247.1334, found, 247.1318; $R_f = 0.69$ (hexane / AcOEt = 3 / 1).

(2*R*,4*aR*,8*aS*)-4*a*,7,8,8*a*-tetrahydro-5-iodo-4*a*-methyl-2-phenyl-4H-benzo[d][1,3]dioxine (15)

$[\alpha]^{28.8}_{\text{D}} -66.6$ (c 1.03, CHCl_3); mp 54-56 $^{\circ}\text{C}$; IR (KBr) $\nu_{\max}$: 1459, 1375, 1225, 1092, 909, 754, 696 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 7.52-7.50 (m, 2H), 7.40-7.32 (m, 3H), 6.28 (dd, $J = 3.4, 3.2$ Hz, 1H), 5.54 (s, 1H), 3.93 (t, $J = 8.1$ Hz, 1H), 3.89 (d, $J = 10.6$ Hz, 1H), 3.58 (d, $J = 10.6$ Hz, 1H), 2.35-2.15 (m, 2H), 1.94-1.88 (m, 2H), 1.32 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 137.8, 137.7, 129.0, 128.3, 126.2, 103.2,

103.1, 81.1, 80.1, 40.8, 28.4, 23.1, 18.0; HRMS (FAB) $[M+H]^+$ calcd for $C_{15}H_{18}O_2I$, 357.0352, found, 357.0338; R_f = 0.31 (hexane / AcOEt = 3 / 1).

((1*R*,6*S*)-6-(benzyloxy)-2-iodo-1-methylcyclohex-2-enyl)methanol (g)

$[\alpha]^{27.4}_D$ -28.4 (c 0.99, $CHCl_3$); IR (thin film) ν_{max} : 3456, 2944, 2880, 1454, 1102, 1042, 734, 698 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 7.35-7.27 (m, 5H), 6.47 (t, J = 3.9 Hz, 1H), 4.68 (d, J = 11.7 Hz, 1H), 4.50 (d, J = 11.7 Hz, 1H), 3.91 (dd, J = 12.1, 3.3 Hz, 1H), 3.62 (dd, J = 10.5, 8.6 Hz, 1H), 3.49 (d, J = 10.5 Hz, 1H), 2.12 (dt, J = 8.3, 3.9 Hz, 2H), 2.02 (dt, J = 12.1, 3.9 Hz, 1H), 1.80-1.70 (m, 1H), 1.44 (br, 1H), 0.97 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 140.9, 138.5, 128.3, 127.6, 109.3, 75.1, 71.5, 68.8, 49.3, 28.5, 22.5, 17.6; HRMS (FAB) $[M+H]^+$ calcd for $C_{15}H_{20}O_2I$, 359.0508, found, 359.0487; R_f = 0.44 (hexane/AcOEt = 3 / 1).

(1*S*,6*S*)-6-(benzyloxy)-2-iodo-1-methylcyclohex-2-enecarbaldehyde (h)

$[\alpha]^{24.3}_D$ + 33.9 (c 1.05, $CHCl_3$); IR (thin film) ν_{max} : 2940, 2332, 1734, 1456, 1366, 1100, 1028, 738, 698 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 9.31 (s, 1H), 7.35-7.26 (m, 5H), 6.60 (dd, J = 4.7, 3.3 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.42 (d, J = 12.0 Hz, 1H), 3.92 (dd, J = 10.3, 3.2 Hz, 1H), 2.30-2.21 (m, 1H), 2.18-2.09 (m, 1H), 2.01-1.94 (m, 1H), 1.84-1.74 (m, 1H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.2, 140.9, 137.8, 128.3, 127.7, 127.6, 97.4, 75.9, 71.3, 58.8, 27.8, 22.0, 16.6; HRMS (FAB) $[M+H]^+$ calcd for $C_{15}H_{18}O_2I$, 357.0352, found, 357.0322; R_f = 0.56 (hexane/ AcOEt = 3 / 1).

1-(((1*S*,2*R*)-3-iodo-2-methyl-2-vinylcyclohex-3-enyloxy)methyl)benzene (16)

$[\alpha]^{27.3}_D$ +60.1 (c 0.61, $CHCl_3$); IR (thin film) ν_{max} : 2944, 2872, 1454, 1098, 1074, 924, 736, 698 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 7.33-7.26 (m, 5H), 6.49 (t, J = 4.0 Hz, 1H), 5.64 (dd, J = 17.3, 10.5 Hz, 1H), 5.22 (d, J = 10.5 Hz, 1H), 5.15 (d, J = 17.3 Hz, 1H), 4.60 (d, J = 11.8 Hz, 1H), 4.47 (d, J = 11.8 Hz, 1H), 3.53 (dd, J = 7.4, 2.6 Hz, 1H), 2.26-2.17 (m, 1H), 2.04-1.95 (m, 1H), 1.93 (m, 2H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.2, 138.8, 138.5, 128.2, 127.6, 127.4, 115.7, 109.0, 79.6, 71.8, 50.2, 26.8, 22.9,

21.8; HRMS (FAB) $[M+H]^+$ calcd for $C_{16}H_{20}OI$, 355.0559, found, 355.0571; $R_f = 0.63$ (benzene/ AcOEt = 20 / 1).

(S)-((5S,6S)-5-benzyloxy-6-methyl-6-vinylcyclohex-1-enyl)((S)-3-iodo-1-(methoxymethoxy)-2,2,4-trimethylcyclohex-3-enyl)methanol (i)

$[\alpha]^{20.4}_D +28.1$ (c 0.32, $CHCl_3$); IR (thin film) ν_{max} : 3572, 2948, 1456, 1158, 1094, 1028, 918, 886, 788 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, $J = 4.2$ Hz, 4H), 7.27-7.23 (m, 1H), 6.10 (dd, $J = 4.9, 2.9$ Hz, 1H), 5.64 (dd, $J = 17.4, 10.6$ Hz, 1H), 5.22 (d, $J = 17.4$ Hz, 1H), 5.19 (d, $J = 10.6$ Hz, 1H), 4.92 (d, $J = 6.8$ Hz, 1H), 4.71 (d, $J = 6.8$ Hz, 1H), 4.62 (d, $J = 2.0$ Hz, 1H), 4.48 (d, $J = 2.0$ Hz, 1H), 4.06 (d, $J = 9.7$ Hz, 1H), 3.43-3.38 (m, 1H), 3.41 (s, 3H), 2.98 (d, $J = 9.7$ Hz, 1H), 2.38-1.66 (m, 8H), 1.85 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 144.6, 139.0, 136.8, 128.0, 127.3, 127.1, 124.6, 117.8, 115.6, 92.7, 82.7, 81.7, 71.4, 71.3, 56.3, 48.7, 47.7, 31.2, 30.6, 28.9, 28.6, 25.4, 24.2, 22.4, 18.1; HRMS (FAB) $[M+H]^+$ calcd for $C_{28}H_{40}IO_4$, 567.1971, found, 567.1945; $R_f = 0.24$ (hexane/ AcOEt = 4/1).

1-(((S)-((5S,6S)-5-benzyloxy-6-methyl-6-vinylcyclohex-1-enyl)((S)-3-iodo-1-(methoxymethoxy)-2,2,4-trimethylcyclohex-3-enyl)methoxy)methyl)benzene (17)

$[\alpha]^{27.2}_D +66.0$ (c 0.45, $CHCl_3$); IR (thin film) ν_{max} : 2948, 1500, 1152, 1102, 1030, 918, 734, 698 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 7.31-7.21 (m, 10H), 6.30 (t, $J = 6.9$ Hz, 1H), 5.87 (dd, $J = 16.7, 10.5$ Hz, 1H), 5.13 (d, $J = 16.7$ Hz, 1H), 5.13 (d, $J = 10.5$ Hz, 1H), 4.76 (d, $J = 6.8$ Hz, 1H), 4.75 (d, $J = 6.8$ Hz, 1H), 4.64 (d, $J = 11.0$ Hz, 1H), 4.62 (d, $J = 11.5$ Hz, 1H), 4.45 (d, $J = 11.5$ Hz, 1H), 4.19 (d, $J = 11.0$ Hz, 1H), 4.03 (s, 1H), 3.41 (dd, $J = 7.8, 3.0$ Hz, 1H), 3.30 (s, 3H), 2.55 (ddd, $J = 17.8, 10.6, 7.1$ Hz, 1H), 2.41-2.32 (m, 1H), 2.25-2.16 (m, 1H), 2.04-1.95 (m, 2H), 1.88-1.79 (m, 2H), 1.86 (s, 3H), 1.62 (ddd, $J = 10.6, 7.6, 4.7$ Hz, 1H), 1.46 (s, 3H), 1.40 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.6, 139.1, 139.0,

138.1, 136.3, 129.8, 128.1, 127.9, 127.5, 127.2, 127.1, 126.8, 119.5, 113.9, 92.5, 83.3, 83.1, 80.6, 71.2, 69.4, 55.5, 48.5, 46.0, 31.4, 30.1, 30.0, 27.9, 26.6, 23.4, 21.5, 19.3; HRMS (FAB) $[M+Na]^+$ calcd for $C_{35}H_{45}IO_4Na$, 679.2260, found, 679.2249; R_f = 0.46 (hexane/ AcOEt = 4/1).

(1*S*,2*S*, 7*S*,8*S*)-2,7-Bis-benzyloxy-1-methoxymethoxy-8,12,15,15-tetramethyl-tricyclo[9.3.1.0^{3,8}]pentadeca-3,11-diene (18)

Vinyl iodide **17** (0.0295 g, 4.50×10^{-2} mmol) was treated with a solution of 0.5 N 9-BBN in THF (0.27 ml, 1.35×10^{-1} mmol) at 0°C, and the resulting mixture was refluxed for 3 h under an Ar atmosphere. After cooling to room temperature, to this mixture was added H₂O (0.45 ml) and the solution was stirred for 15 min. This solution was added to a solution of Pd(PPh₃)₄ (0.0260 g, 2.25×10^{-2} mmol) in a mixture of 3N NaOH (0.06 ml, 1.80×10^{-1} mmol) and MeCN (4.5 ml), and the resulting mixture was refluxed for 72 h under an Ar atmosphere. The reaction was quenched with a mixture of 3N NaOH (0.270 ml) and 30% H₂O₂ aqueous solution (0.135 ml) for 2 h at 0 °C. Then, the reaction mixture was diluted with H₂O (10 ml) and extracted with Et₂O (20 ml $\times$ 3). The combined organic layer was washed with brine (20 ml), and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO₂, hexane/ AcOEt (50:1)) to afford **18** (0.0202 g, 85 %) as a viscous oil.

$[\alpha]_D^{21.8} +99.3$ (c 0.65, CHCl₃); IR (thin film) ν_{max} : 2928, 1454, 1156, 1104, 1066, 1026, 918, 788, 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.40-7.23 (m, 10H), 5.77(dd, J = 4.9, 2.4 Hz, 1H), 5.14 (d, J = 7.7 Hz, 1H), 4.74 (d, J = 11.8 Hz, 1H), 4.50 (d, J = 7.7 Hz, 1H), 4.49 (d, J = 11.8 Hz, 1H), 4.45 (d, J = 11.0 Hz, 1H), 4.14 (d, J = 11.0 Hz, 1H), 3.79 (s, 1H), 3.73 (dd, J = 12.0, 3.8 Hz, 1H), 3.36 (s, 3H), 2.37-2.13 (m, 5H), 2.89-1.93 (m, 4H), 1.76-1.58 (m, 3H), 1.40 (s, 3H), 1.33 (s, 3H), 1.05 (s, 3H), 1.02 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 143.7, 139.4, 139.1, 134.3, 131.1, 128.3, 128.1, 127.9, 127.5, 127.2, 127.0, 118.5, 93.5, 87.0, 81.0, 75.8, 70.6, 69.7, 55.3, 42.0, 41.9, 33.3, 30.3, 28.2, 24.3, 24.2, 23.9, 22.3, 21.5, 20.9, 20.0; HRMS (FAB) $[M]^+$ calcd for $C_{35}H_{46}O_4$, 530.3396, found, 530.3390; R_f = 0.55 (hexane/ AcOEt = 4/1).