Regio- and Stereoselective Synthesis of Alkyl Allylic Ethers via Gold(I)-Catalyzed Intermolecular Hydroalkoxylation of Allenes with Alcohols

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Experimental procedures, spectroscopic and analytical data for new compounds, scans of HPLC traces, and NMR spectra for allenes and allylic ethers (33 pages).

Experimental

General Methods. Reactions were performed under a nitrogen atmosphere employing standard Schlenk and/or drybox techniques unless specified otherwise. NMR spectra were obtained on Varian spectrometers operating at 400 MHz for ^{1}H NMR and 101 MHz for ^{13}C NMR in $CDCl_3$ at 25 °C unless noted otherwise. IR spectra were obtained on a Nicolet Avatar 360-FT IR spectrometer. Gas chromatography was performed on a Hewlett-Pakard 5890 gas chromatography equipped with a 15 m or 25 m polydimethylsiloxane capillary column and FID detector. Chiral HPLC was performed on a Hewlett-Packard 1090II chromatograph equipped with a 25 cm Chiralpak AD-H column. Column chromatography was performed employing 230-400 mesh silica gel (Silicycle). Thin layer chromatography (TLC) was performed on silica gel 60 F_{254} (EMD Chemicals Inc.). Catalytic reactions were performed in sealed glass tubes under an atmosphere of dry nitrogen unless noted otherwise. Elemental analyses were performed by Complete Analysis Laboratories (Parsippany, NJ). Room temperature is 23 °C.

All solvents were purchased from Aldrich or Acros in anhydrous form and used as received. All reagents were purchased from major suppliers and used as received. 3-Methyl-1,2-butadiene (**2**), ethyl 2,3-butadienoate (**8**), 2,4-dimethyl-2,3-pentadiene (**22**), (*R*)-(+)-3-butyn-2-ol, and (*R*)-1-phenyl-1-propanol were purchased from Aldrich and used as received. (*S*)-2-(Benzyloxy)propional was purchased from Toronto Research Chemicals, Inc. and used as received. Ethyl 3-vinylidenenonanoate (**16**) was prepared according to the procedure reported by Trost.[1]

Allenes

Dimethyl 2-(2,3-butadienyl)malonate (6).[2] Dimethyl propargylmalonate (8.50 g, 50.0 mmol) was added to a suspension of formaldehyde (3.00 g, 100 mmol), diisopropylamine (10.10 g, 100 mmol), and CuBr (2.88 g, 20.0 mmol) in dioxane (150 mL). The suspension was refluxed at 110 °C for 20 h and concentrated under vacuum. The residue was diluted with ether (150 mL), filtered through silica gel, and eluted with ether (150 mL). The filtrate was concentrated under vacuum and the residue was

chromatographed (SiO_2; hexanes–EtOAc = 30:1 → 10:1) to give **6** (9.20 g, 41%) as a pale yellow oil. TLC (hexanes–EtOAc = 2:1): R_f = 0.64. ^{1}H NMR: δ 5.10 (quint, *J* = 6.4 Hz, 1 H), 4.69 (t, *J* = 6.4 Hz, 1 H), 4.73 (t, *J* = 7.0 Hz, 1 H), 3.70 (s, 6 H), 3.47 (t, *J* = 8.0 Hz, 1 H), 2.58-2.53 (m, 2 H). ^{13}C{^{1}H} NMR: δ 209.0, 169.5, 86.9, 76.6, 52.8, 51.5, 27.7.

Dimethyl 2-(4,5-hexadienyl)malonate (7).[3] Allene **7** was synthesized in 56% yield as a colorless oil from homologation of dimethyl 2-(4-pentynyl)malonate[4] employing a procedure analogous to that used to synthesize **6**. TLC (hexanes–EtOAc = 2:1): R_f = 0.70. ^{1}H NMR: δ 5.01 (quintet, *J* = 6.8 Hz, 1 H), 4.60 (td, *J* = 3.2, 6.8 Hz, 2 H), 3.68 (s, 6 H), 3.31 (t, *J* = 7.4 Hz, 1 H), 2.02-1.93 (m, 2 H), 1.91-1.85 (m, 2 H), 1.42-1.35 (m, 2 H).

1-Phenyl-1,2-butadiene (12).[5] MeLi (24.0 mL, 1.6 M in ether, 38.0 mmol) was added via syringe to a stirred solution of (2,2-dibromocyclopropylmethyl)-benzene[6] (9.46 g, 32.0 mmol) in ether (10 mL) at –78 °C. The reaction mixture was stirred for 1 min and quenched with 10% HCl (10 mL), extracted with ether (20 mL), and dried ($MgSO_4$). Distillation of the oily residue (30 °C, 0.5 Torr) gave **12** as a colorless oil (3.75 g, 88%). TLC (hexanes): R_f = 0.82. ^{1}H NMR: δ 7.35-7.27 (m, 4 H), 7.22-7.16 (m, 1 H), 6.10 (dq, *J* = 6.3, 3.2 Hz, 1 H), 5.55 (q, *J* = 7.0 Hz, 1 H), 1.79 (dd, *J* = 3.2, 7.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 206.1, 135.2, 128.7, 126.8, 94.1, 89.7, 14.2.

2,3-Pentadienyl benzoate (13). A solution of benzoyl chloride (21.1 g, 150 mmol) in CH_2Cl_2 (100 mL), pyridine (39.5 g, 500 mmol), and 4-(dimethylamino)pyridine (1.83 g, 15 mmol) were added sequentially to a solution of 2,3-pentadien-1-ol[7] (4.2 g, 50 mmol) in CH_2Cl_2 (200 mL) at 0 °C and the resulting solution was stirred for 6 h. The resulting mixture was quenched with 6 N HCl, the layers were separated, and the aqueous layer was extracted with ether (3 × 50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated under vacuum. Column chromatography of the residue (SiO_2; hexanes–CH_2Cl_2 = 5:1 → 3:1) gave **13** (8.0 g, 90%) as a yellow liquid. TLC (hexanes–CH_2Cl_2 = 1:1): R_f = 0.46. ^{1}H NMR: δ 8.05-7.39 (m, 5 H), 5.36-5.20 (m, 2 H), 4.78 (dd, *J* = 2.4, 6.8 Hz, 2 H), 1.67 (dd, *J* = 3.2, 7.2 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 206.4, 166.5, 133.1,

130.5, 129.8, 128.5, 87.9, 86.6, 63.4, 14.1. IR (neat, cm^{-1}): 2971, 2929, 2856, 1741, 1583, 1450, 1378, 1118, 840, 699. Anal. calcd (found) for $C_{12}H_{12}O_2$: C, 76.57 (76.52); H, 6.43 (6.51).

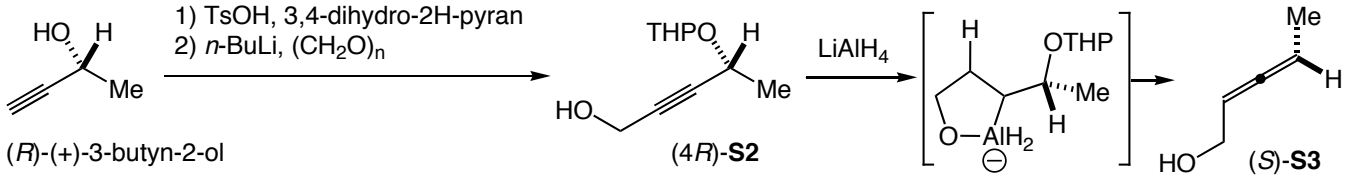
(*S*)-2,3-Pentadienyl benzoate [(*S*)-13]. A solution of $TsOH \cdot H_2O$ (11 mg, 0.058 mmol), (*R*)-(+)-3-butyn-2-ol (2.73 g, 39.0 mmol), and 3,4-dihydro-*2H*-pyran (3.94 g, 46.9 mmol) in CH_2Cl_2 (30 mL) was stirred for 2 h at 0 °C. The resulting mixture was diluted with Et_2O (20 mL) at 0 °C, quenched with saturated $NaHCO_3$ (40 mL), and extracted with ether (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated. Chromatography of the resulting oily residue (pentene–Et_2O = 10:1 → 5:1) gave (*R*)-2-(3-butyn-2-yloxy)-tetrahydro-2*H*-pyran [(*R*)-**S1**] as a colorless oil.

A solution of *n*-BuLi (2.5 M in hexanes, 21.8 mL, 54.6 mmol) was added over 30 min to a solution of (*R*)-**S1** (all material obtained in previous step) in THF (115 mL) at –78 °C. The resulting mixture was warmed to 0 °C and treated sequentially with HMPA (8.3 mL) and paraformaldehyde (2.34 g, 78.0 mmol). The reaction mixture was warmed slowly to room temperature and stirred for 2 h. The resulting mixture was cooled to 0 °C, diluted with ether, quenched with saturated aqueous NH_4Cl, and extracted with ether (3 × 50 mL). The ether extracts were dried ($MgSO_4$) and concentrated. The resulting residue was chromatographed (EtOAc–hexanes = 10:1 → 1:2) to yield (4*R*)-4-(tetrahydro-2*H*-pyran-2-yloxy)pent-2-yn-1-ol [(4*R*)-**S2**] as a yellow oil.

A solution of (4*R*)-**S2** (all material obtained in previous step) in ether (30 mL) was added to a stirred suspension of $LiAlH_4$ (2.85 g, 75.0 mmol) in ether (100 mL) at 0 °C and warmed to room temperature overnight. The reaction mixture was cooled to 0 °C and quenched by successive addition of water (4.2 mL), 15 % NaOH [(w/w), 4.2 mL], and water (4.2 mL). The resulting white suspension was filtered through Celite, eluted with ether, and concentrated under vacuum to give crude (*S*)-2,3-pentadien-1-ol [(*S*)-**S3**] as pale yellow oil that was used in the subsequent step without further purification.

A solution of benzoyl chloride (11.8 g, 84.0 mmol) in CH_2Cl_2 (15 mL), pyridine (22.1 g, 280 mmol), and 4-(dimethylamino)pyridine (1.03 g, 8.40 mmol) were added sequently to the solution of (*S*)-

S3 (all material obtained in previous step) in CH_2Cl_2 (150 mL) at 0 °C and stirred for 6 h. The resulting mixture was quenched with 6 N HCl. The layers were separated and the aqueous layer was extracted with ether (3 × 50 mL). The combined ether extracts were washed with brine, dried ($MgSO_4$), and concentrated under vacuum. Column chromatography of the residue (hexanes–CH_2Cl_2 = 5:1 → 3:1) gave (*S*)-**13** (2.46 g, 34% from (*R*)-(+)-3-butyn-2-ol) as a yellow liquid with 97% ee (Figure S1). The absolute configuration of the allene is set by delivery of the hydride to the same face as the THP leaving group via trans addition of the Al–H bond across the C≡C bond followed by anti elimination (Scheme S1).[8]



(*R*)-(+)-3-butyn-2-ol (4*R*)-**S2** (*S*)-**S3**

Scheme S1

1-(Benzyloxy)-2-(5-methyl-3,4-hexadienyl)benzene (18). 2-Benzyloxyphenylmagnesium bromide (1.0 M THF, 20.0 mL, 20.0 mmol) was added dropwise to a suspension of copper (I) iodide (1.52 g, 8.00 mmol) in THF (20.0 mL). The resulting mixture was stirred at –20 °C for 1 h and then treated with a solution of 5-methyl-3,4-hexadienyl 4-methylbenzenesulfonate[9] (1.71 g, 6.42 mmol) in THF (20.0 mL), added dropwise. The reaction mixture was warmed slowly to room temperature, stirred overnight, cooled to –20 °C, quenched with saturated aqueous NH_4Cl, and extracted with ether (3 × 25 mL). The organic extracts were dried ($MgSO_4$) and concentrated. The resulting residue was chromatographed (CH_2Cl_2–hexanes = 1:5 → 1:3) to yield **18** as a colorless oil (1.3 g, 73%). TLC (CH_2Cl_2-hexanes = 1:1): R_f = 0.80. ^{1}H NMR: δ 7.47-7.31 (m, 5 H), 7.21-7.14 (m, 2 H), 6.93-6.89 (m, 2 H), 5.10 (s, 2 H), 5.05-4.99 (m, 1 H), 2.80 (t, *J* = 7.6 Hz, 2 H), 2.33-2.28 (m, 2 H), 1.64 (d, *J* = 3.2 Hz, 6 H). ^{13}C{^{1}H} NMR: δ 202.0, 156.8, 137.8, 131.1, 130.3, 128.7, 127.8, 127.2, 127.1, 120.8, 111.8, 95.3,

88.8, 69.9, 30.3, 29.6, 20.9. IR (neat, cm^{-1}): 2911, 1595, 1494, 1450, 1379, 1237, 1111, 1023, 855, 745, 695, 621. Anal. calcd (found) for $C_{20}H_{22}O$: C, 86.29 (86.12); H, 7.97 (7.88).

((5-Ethyl-3,4-heptadienyloxy)methyl)benzene (19). A Solution of 3-ethyl-1-pentyn-3-ol (15.00 g, 133.7 mmol), propionic acid (500 mg, 6.75 mmol), and triethylorthoacetate (34.20 g, 210.8 mmol) was heated at reflux for 3 days. The reaction mixture was cooled to room temperature and treated with 1 M HCl (100 mL) and extracted with ether (150 mL). The ether extracts were washed with saturated $NaHCO_3$ (2 x 100 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated. The resulting residue was chromatographed (hexanes–EtOAc = 10:1) to give ethyl 5-ethyl-3,4-heptadienoate (**S4**) as a colorless oil (1.48 g, 6%). TLC (hexanes–EtOAc = 4:1): R_f = 0.65. ^{1}H NMR: 5.32-5.23 (m, 1 H), 4.13 (q, J = 7.0 Hz, 2 H), 2.97 (d, J = 7.2 Hz, 2 H), 1.93 (dq, J = 3.1, 7.3 Hz, 4 H), 1.24 (t, J = 7.2 Hz, 3 H), 0.98 (t, J = 7.5 Hz, 6 H). ^{13}C{^{1}H} NMR: 201.6, 172.0, 109.7, 86.2, 60.6, 35.9, 25.6, 14.3, 12.3. IR (neat, cm^{-1}): 2969, 1737, 1155, 1083. Anal calcd (found) for $C_{11}H_{18}O_2$: C, 72.49 (72.33); H, 9.95 (9.92).

A solution of **S4** (1.016 g, 5.574 mmol) in ether (25 mL) was added to a stirred suspension of $LiAlH_4$ (466 mg, 12.3 mmol) in ether (50 mL) at 0 °C and the resulting mixture was stirred for 4 h. The reaction mixture was quenched by successive addition of water (0.65 mL), 15 % NaOH [(w/w), 0.65 mL], and water (0.65 mL) at 0 °C. The resulting white suspension was filtered through Celite, extracted with ether, and concentrated to give crude 5-ethyl-3,4-heptadien-1-ol (**S5**) as a colorless oil that was used in the subsequent step without further purification.

A solution of benzyl bromide (0.672 g, 3.93 mmol) in DMF (5 mL) and a solution of **S5** (all material obtained in previous step) in DMF (5 mL) were added sequentially to a suspension of NaH (94.3 mg, 3.93 mmol) in DMF (20 mL) at 0 °C. The resulting mixture was warmed slowly to room temperature, stirred for 8 h, and quenched with water (75 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under vacuum. Column chromatography of the residue (hexanes–EtOAc = 20:1) gave **19** (500 mg, 39% from **S4**) as a colorless oil. TLC (hexanes–CH_2Cl_2 = 1:1): R_f = 0.54. ^{1}H NMR (Figure S2): δ 7.41-7.25 (m, 5 H), 5.23-5.16 (m, 1 H), 4.53 (s, 2 H), 3.55 (t, J

= 7.0 Hz, 2 H), 2.31 (q, *J* = 6.8 Hz, 2 H), 1.94 (dq, *J* = 3.1, 7.3 Hz, 4 H), 0.99 (t, *J* = 7.3 Hz, 6 H). $^{13}C\{^1H\}$ NMR (Figure S3): δ 200.9, 138.8, 128.5, 127.8, 127.7, 108.5, 89.5, 73.1, 70.5, 30.2, 25.8, 12.5. IR (neat, cm^{-1}): 2964, 2870, 1721, 1453, 1362, 1318, 1272, 1205, 1104, 1027, 806, 736, 697. HRMS calcd (found) for $C_{16}H_{22}O$ (M^+): 230.1671 (230.1669).

Allylic Ethers

(1-(3-Methyl-2-butenyloxy)propyl)benzene (3). A mixture of (**5**)AuCl (6.2 mg, 0.010 mmol) and AgOTf (2.6 mg, 0.010 mmol) in toluene (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **2** (13.6 mg, 0.20 mmol) and 1-phenyl-1-propanol (30.0 mg, 0.22 mmol) in toluene (0.3 mL) and the resulting suspension was stirred at room temperature for 4 h. Column chromatography of the crude reaction mixture (CH_2Cl_2-hexanes = 1:5 → 1:2) gave **3** (35.8 mg, 88%) as a colorless oil. TLC (CH_2Cl_2–hexanes = 1:1): R_f = 0.56. ^1H NMR: δ 7.33-7.21 (m, 5 H), 5.36-5.32 (m, 1 H), 4.11 (t, *J* = 6.8 Hz, 1 H), 3.82 (dd, *J* = 6.6, 11.6 Hz, 1 H), 3.73 (dd, *J* = 7.2, 11.2 Hz, 1 H), 1.87-1.76 (m, 1 H), 1.70 (s, 3 H), 1.69-1.58 (m, 1 H), 1.52 (s, 3 H), 0.85 (t, *J* = 7.6 Hz, 3 H). $^{13}C\{^1H\}$ NMR: δ 143.0, 137.1, 128.4, 127.5, 127.0, 121.5, 83.2, 65.3, 31.4, 26.0, 18.1, 10.6. IR (neat, cm^{-1}): 2965, 2927, 2860, 1675, 1451, 1378, 1202, 1060, 1028, 982, 833, 755, 701. Anal. calcd (found) for $C_{14}H_{20}O$: C, 82.30 (82.19); H, 9.87 (9.87). HRMS calcd (found) for $C_{12}H_{15}O$ ($[M\text{-}Et]^+$): 175.1123 (175.1123).

All remaining intermolecular hydroalkoxylation reactions were performed employing a procedure analogous to that used to synthesize **3** unless noted otherwise.

(1-(2-Methyl-3-buten-2-yloxy)propyl)benzene (4). A mixture of (**1**)AuCl (10.6 mg, 0.020 mmol) and AgOTs (5.6 mg, 0.20 mmol) in toluene (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **2** (81.6 mg, 1.20 mmol) and 1-phenyl-1-propanol (54.5 mg, 1.40 mmol) in toluene (0.3 mL), and the resulting suspension was stirred at room temperature for 48 h. Column chromatography of the crude reaction mixture (CH_2Cl_2–hexanes = 1:5 → 1:2) gave **4** (16.3 mg, 20%) as a colorless oil. TLC (CH_2Cl_2–hexanes = 1:1): R_f = 0.62. ^1H NMR (Figure S4): δ 7.31-7.16 (m, 5 H), 5.79 (dd, *J* = 10.8,

17.6 Hz, 1 H), 5.07 (dd, *J* = 1.2, 17.6 Hz, 1 H), 5.01 (dd, *J* = 1.2, 10.8 Hz, 1 H), 4.24 (dd, *J* = 5.6, 7.2 Hz, 1 H), 1.71-1.51 (m, 2 H), 1.26 (s, 3 H), 1.08 (s, 3 H), 0.83 (t, *J* = 7.2 Hz, 3 H). $^{13}C\{^{1}H\}$ NMR (Figure S5): δ 146.6, 145.1, 128.1, 126.7, 126.5, 113.4, 76.7, 76.4, 33.1, 27.8, 26.2, 10.8. IR (neat, cm^{-1}): 2930, 2862, 1450, 1380, 1059, 1028, 757, 700. HRMS calcd (found) for $C_{12}H_{15}O$ ($[M\text{-}Et]^+$): 175.1123 (175.1117).

(*E*)-Dimethyl 2-(4-phenethoxy-2-butenyl)malonate (9a). Colorless oil, 81%. TLC (CH_2Cl_2): R_f = 0.30. ^{1}H NMR: δ 7.27-7.15 (m, 5 H), 5.63 (td, *J* = 4.8, 15.6 Hz, 1 H), 5.58 (td, *J* = 5.6, 15.6 Hz, 1 H), 3.89-3.88 (m, 2 H), 3.68 (s, 6 H), 3.57 (t, *J* = 7.2 Hz, 2 H), 3.41 (t, *J* = 7.6 Hz, 1 H), 2.85 (t, *J* = 7.4 Hz, 2 H), 2.63-2.60 (m, 2 H). $^{13}C\{^{1}H\}$ NMR: δ 169.3, 139.0, 130.0, 129.0, 128.9, 128.5, 126.3, 71.2, 72.1, 52.6, 51.6, 36.5, 31.6. IR (neat, cm^{-1}): 3025, 2951, 2854, 1737, 1437, 1228, 1155, 1101, 973, 748, 700. Anal. calcd (found) for $C_{17}H_{22}O_5$: C, 66.65 (66.51); H, 7.24 (7.22). HRMS calcd (found) for $C_{17}H_{22}O_5$ (M^+): 306.1467 (306.1464).

The *E*-stereochemistry of **9a**, **9b**, **9c**, **10a**-**10d**, **11a**, **11b**, and **14a**-**14d**, were assigned on the basis of the large C=C coupling constants in the ^{1}H NMR spectrum (J_{HH} ≈ 15.5 Hz).

(*E*)-Dimethyl 2-(4-(1-phenylpropoxy)-2-butenyl)malonate (9b). Colorless oil, 83%. TLC (CH_2Cl_2): R_f = 0.40. ^{1}H NMR: δ 7.33-7.21 (m, 5 H), 5.61 (ddd, *J* = 5.2, 6.0, 15.6 Hz, 1 H), 5.54 (td, *J* = 6.4, 15.6 Hz, 1 H), 4.11 (t, *J* = 6.6 Hz, 1 H), 3.80 (ddd, *J* = 1.0, 5.2, 12.4 Hz, 1 H), 3.70 (s, 6 H), 3.66 (ddd, *J* = 0.8, 6.0, 12.4 Hz, 1 H), 3.41 (t, *J* = 7.6 Hz, 1 H), 2.61 (t, *J* = 7.2 Hz, 2 H), 1.85-1.58 (m, 2 H), 0.84 (t, *J* = 7.4 Hz, 3 H). $^{13}C\{^{1}H\}$ NMR: δ 169.4, 142.6, 130.3, 128.7, 128.5, 127.6, 127.0, 83.0, 68.8, 52.7, 51.7, 31.7, 31.2, 10.4. IR (neat, cm^{-1}): 2957, 2855, 1737, 1438, 1227, 1155, 1110, 1055, 973, 758, 702. Anal. calcd (found) for $C_{18}H_{24}O_5$: C, 67.48 (67.43); H, 7.55 (7.64). HRMS calcd (found) for $C_{18}H_{24}O_5$ (M^+): 320.1624 (320.1625).

(*E*)-Dimethyl 2-(4-(cyclohexyloxy)-2-butenyl)malonate (9c). Colorless oil, 84%. TLC (hexanes–EtOAc = 5:1): R_f = 0.36. ^{1}H NMR: δ 5.63 (td, *J* = 4.8, 15.6 Hz, 1 H), 5.57 (td, *J* = 6.0, 15.6 Hz, 1 H), 3.88 (d, *J* = 4.6 Hz, 2 H), 3.68 (s, 6 H), 3.40 (t, *J* = 7.6 Hz, 1 H), 3.23-3.15 (m, 1 H), 2.59 (dd, *J*

= 5.6, 7.2 Hz, 2 H), 1.85-1.12 (m, 10 H). $^{13}C\{^1H\}$ NMR: δ 169.4, 130.8, 128.2, 76.9, 68.1, 52.6, 51.7, 32.4, 31.7, 25.9, 24.3. IR (neat, cm^{-1}): 2931, 2855, 1738, 1438, 1344, 1227, 1154, 1090, 1027, 973, 846. Anal. calcd (found) for $C_{15}H_{24}O_5$: C, 63.36 (63.18); H, 8.51 (8.42).

Hydroalkoxylation of 7 with 2-phenyl ethanol. A mixture of (**5**)AuCl (6.2 mg, 0.010 mmol) and AgOTf (2.6 mg, 0.010 mmol) in toluene (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **7** (42.4 mg, 0.20 mmol) and 2-phenyl ethanol (26.9 mg, 0.22 mmol) in toluene (0.3 mL) and the resulting suspension was stirred at room temperature for 1 h. Column chromatography of the crude reaction mixture (hexanes-EtOAc = 15:1 → 5:1) gave pure (*E*)-dimethyl 2-(6-phenethoxy-4-hexenyl)malonate (**10a**) (68%) and pure dimethyl 2-(4-phenethoxy-5-hexenyl)malonate (**S6**) (17%) as colorless oil.

For 10a: Colorless oil, 68%. TLC (hexanes–EtOAc = 5:1): R_f = 0.35. ^1H NMR: δ 7.28-7.16 (m, 5 H), 5.62 (td, *J* = 6.4, 15.6 Hz, 1 H), 5.53 (td, *J* = 6.0, 15.6 Hz, 1 H), 3.91 (d, *J* = 6.0 Hz, 2 H), 3.71 (s, 6 H), 3.60 (t, *J* = 7.2 Hz, 2 H), 3.34 (t, *J* = 7.6 Hz, 1 H), 2.87 (t, *J* = 7.4 Hz, 2 H), 2.05 (q, *J* = 6.8 Hz, 2 H), 1.92-1.86 (m, 2 H), 1.43-1.35 (m, 2 H). $^{13}C\{^1H\}$ NMR: δ 170.0, 139.1, 133.4, 129.1, 128.5, 127.3, 126.3, 71.7, 71.2, 52.6, 51.7, 36.5, 32.0, 28.5, 26.9. IR (neat, cm^{-1}): 2943, 2849, 1736, 1438, 1344, 1205, 1155, 1104, 972, 748, 700. Anal. calcd (found) for $C_{19}H_{26}O_5$: C, 68.24 (68.16); H, 7.84 (7.99).

For S6: Colorless oil, 17%. TLC (hexanes–EtOAc = 5:1): R_f = 0.42. ^1H NMR: δ 7.28-7.16 (m, 5 H), 5.62 (ddd, *J* = 7.8, 10.8, 16.4 Hz, 1 H), 5.14-5.09 (m, 2 H), 3.72 (s, 6 H), 3.70-3.65 (m, 1 H), 3.59 (td, *J* = 6.4, 7.2 Hz, 1 H), 3.46-3.40 (m, 1 H), 3.32 (t, *J* = 7.6 Hz, 1 H), 2,90-2.78 (m, 2 H), 1.87 (q, *J* = 7.8 Hz, 2 H), 1.63-1.23 (m, 4 H). $^{13}C\{^1H\}$ NMR: δ 170.1, 139.3, 139.2, 129.1, 128.5, 126.3, 117.1, 81.2, 69.6, 52.7, 51.9, 36.7, 35.1, 28.9, 23.4. IR (neat, cm^{-1}): 2986, 2870, 1737, 1437, 1352, 1139, 927, 673. Anal. calcd (found) for $C_{19}H_{26}O_5$: C, 68.24 (68.05); H, 7.84 (7.89).

(*E*)-Dimethyl 2-(6-(1-phenylpropoxy)-4-hexenyl)malonate (10b). Colorless oil, 85%. TLC (hexanes–EtOAc = 5:1): R_f = 0.36. ^1H NMR: δ 7.32-7.21 (m, 5 H), 5.56 (td, *J* = 5.2, 15.2 Hz, 1 H), 5.51 (td, *J* = 5.2, 15.6 Hz, 1 H), 4.13 (t, *J* = 6.6 Hz, 1 H), 3.82-3.65 (m, 2 H), 3.70 (s, 6 H), 3.33 (t, *J* = 7.6 Hz,

1 H), 2.06-2.01 (m, 2 H), 1.90-1.58 (m, 4 H), 1.41-1.33 (m, 2 H), 0.84 (t, *J* = 7.4 Hz, 3 H). $^{13}C\{^1H\}$ NMR: δ 170.0, 142.8, 133.2, 128.4, 127.6, 127.5, 127.0, 83.0, 69.4, 52.7, 51.7, 32.0, 31.2, 28.6, 26.9, 10.5. IR (neat, cm^{-1}): 2952, 2856, 1737, 1439, 1344, 1203, 1152, 1056, 972, 908, 758, 702. Anal. calcd (found) for $C_{20}H_{28}O_5$: C, 68.94 (68.69); H, 8.10 (8.05).

(*E*)-Dimethyl 2-(6-(cyclohexyloxy)-4-hexenyl)malonate (10c). Colorless oil, 75%. TLC (hexanes–EtOAc = 5:1): R_f = 0.43. ^1H NMR: δ 5.60 (td, *J* = 6.0, 15.2 Hz, 1 H), 5.52 (td, *J* = 5.6, 15.6 Hz, 1 H), 3.89 (d, *J* = 5.6 Hz, 2 H), 3.69 (s, 6 H), 3.31 (t, *J* = 7.4 Hz, 1 H), 3.23-3.17 (m, 1 H), 2.03 (q, *J* = 7.0 Hz, 2 H), 1.89-1.83 (m, 4 H), 1.72-1.64 (m, 2 H), 1.50-1.11 (m, 8 H). $^{13}C\{^1H\}$ NMR: δ 170.0, 132.7, 128.1, 77.0, 68.6, 52.6, 51.7, 32.5, 32.0, 28.6, 26.9, 26.9, 24.4. IR (neat, cm^{-1}): 2931, 2855, 1737, 1440, 1345, 1206, 1152, 1096, 1025, 971. Anal. calcd (found) for $C_{17}H_{28}O_5$: C, 65.36 (65.32); H, 9.03 (8.92).

(*E*)-Dimethyl 2-(6-phenoxy-4-hexenyl)malonate (10d). Colorless oil, 55%. TLC (CH_2Cl_2): R_f = 0.58. ^1H NMR: δ 7.28-7.23 (m, 2 H), 6.93-6.86 (m, 3 H), 5.79 (td, *J* = 6.4, 15.6 Hz, 1 H), 5.70 (td, *J* = 5.6, 15.6 Hz, 1 H), 4.45 (d, *J* = 5.6 Hz, 2 H), 3.72 (s, 6 H), 3.34 (t, *J* = 7.4 Hz, 1 H), 2.11 (q, *J* = 7.0 Hz, 2 H), 1.93-1.87 (m, 2 H), 1.46-1.38 (m, 2 H). $^{13}C\{^1H\}$ NMR: δ 170.0, 158.8, 134.4, 129.6, 125.9, 120.9, 114.9, 68.7, 52.7, 51.7, 32.0, 28.5, 26.8. IR (neat, cm^{-1}): 2951, 1735, 1596, 1494, 1437, 1233, 1153, 1079, 1009, 973, 755, 693. Anal. calcd (found) for $C_{17}H_{22}O_5$: C, 66.65 (66.71); H, 7.24 (7.16). HRMS calcd (found) for $C_{17}H_{22}O_5$ (M^+): 306.1467 (306.1465).

(*E*)-Ethyl 4-phenethoxy-2-butenoate (11a). Colorless oil, 73%. TLC (hexanes–EtOAc = 5:1): R_f = 0.53. ^1H NMR (Figure S6): δ 7.30-7.18 (m, 5 H), 6.92 (td, *J* = 4.4, 15.6 Hz, 1 H), 6.02 (td, *J* = 2.0, 15.6 Hz, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 4.12 (dd, *J* = 2.0, 4.4 Hz, 2 H), 3.67 (t, *J* = 7.0 Hz, 2 H), 2.90 (t, *J* = 7.0 Hz, 2 H), 1.27 (t, *J* = 7.2 Hz, 3 H). $^{13}C\{^1H\}$ NMR (Figure S7): δ 166.5, 144.5, 138.9, 129.1, 128.6, 126.5, 121.5, 72.1, 69.7, 60.6, 36.5, 14.4. IR (neat, cm^{-1}): 2863, 1718, 1661, 1450, 1365, 1296, 1270, 1172, 1127, 1039, 967, 841, 747, 699. HRMS calcd (found) for $C_{14}H_{18}O_3$ (M^+): 234.1256 (234.1254).

(*E*)-Ethyl 4-(1-phenylpropoxy)-2-butenoate (11b). Colorless oil, 77%. TLC (hexanes–EtOAc = 5:1): R_f = 0.62. ^{1}H NMR: δ 7.36-7.23 (m, 5 H), 6.91 (td, *J* = 4.2, 15.6 Hz, 1 H), 6.10 (td, *J* = 2.0, 16.0 Hz, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 4.17 (t, *J* = 7.2 Hz, 1 H), 4.01 (ddd, *J* = 2.0, 4.0, 16.0 Hz, 1 H), 3.91 (ddd, *J* = 2.0, 4.4, 16.0 Hz, 1 H), 1.90-1.63 (m, 2 H), 1.27 (t, *J* = 7.0 Hz, 3 H), 0.88 (t, *J* = 7.4 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 166.7, 145.0, 142.1, 128.6, 127.8, 126.9, 121.1, 83.9, 67.3, 60.5, 31.2, 14.5, 10.4. IR (neat, cm^{-1}): 2973, 1720, 1661, 1451, 1365, 1296, 1270, 1172, 1117, 1038, 969, 838, 757, 701. Anal. calcd (found) for $C_{15}H_{20}O_3$: C, 72.55 (72.57); H, 8.12 (8.12).

(*E*)-(3-Phenethoxy-1-butenyl)benzene (14a). Colorless oil, 96%. TLC (CH_2Cl_2–hexanes = 2:1): R_f = 0.67. ^{1}H NMR: δ 7.38-7.19 (m, 10 H), 6.48 (d, *J* = 16.0 Hz, 1 H), 6.11 (ddd, *J* = 1.2, 7.6, 16.0 Hz, 1 H), 4.05-3.99 (m, 1 H), 3.77-3.55 (m, 2 H), 2.97-2.86 (m, 2 H), 1.35 (d, *J* = 6.4 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 139.3, 136.8, 132.0, 131.1, 129.2, 128.7, 128.5, 127.8, 126.6, 126.3, 76.9, 69.6, 36.8, 21.9. IR (neat, cm^{-1}): 3060, 3027, 2974, 2928, 2861, 1600, 1495, 1450, 1364, 1320, 1144, 1088, 968, 748, 695. Anal. calcd (found) for $C_{18}H_{20}O$: C, 85.67 (85.53); H, 7.99 (8.18). HRMS calcd (found) for $C_{18}H_{20}O$ $(M)^+$): 252.1514 (252.1518).

(*E*)-(1-(4-Phenyl-3-buten-2-yloxy)propyl)benzene (14b). Colorless oil, 90%. TLC (CH_2Cl_2–hexanes = 2:1): R_f = 0.75. dr = 2.7:1, ^{1}H NMR (major diastereomer): δ 7.42-7.19 (m, 10 H), 6.39 (d, *J* = 15.6 Hz, 1 H), 6.12 (dd, *J* = 7.6, 15.6 Hz, 1 H), 4.31 (t, *J* = 6.8 Hz, 1 H), 3.87 (qd, *J* = 6.4, 7.6 Hz, 1 H), 1.91-1.61 (m, 2 H), 1.29 (d, *J* = 6.4 Hz, 3 H), 0.89 (t, *J* = 7.2 Hz, 3 H). ^{1}H NMR (minor diastereomer): δ 7.42-7.19 (m, 10 H), 6.43 (d, *J* = 15.6 Hz, 1 H), 6.08 (dd, *J* = 6.8, 15.6 Hz, 1 H), 4.34 (t, *J* = 6.4 Hz, 1 H), 4.08 (quintet, *J* = 6.4 Hz, 1 H), 1.91-1.61 (m, 2 H), 1.35 (d, *J* = 6.4 Hz, 3 H), 0.92 (t, *J* = 7.6 Hz, 3 H). ^{13}C{^{1}H} NMR (both diastereomers): δ 143.6, 143.3, 137.2, 137.0, 132.9, 132.2, 131.5, 129.7, 128.8, 128.6, 128.5, 128.3, 127.8, 127.5, 127.4, 127.3, 127.1, 127.0, 126.6, 126.5, 81.1, 80.2, 74.1, 73.5, 31.6, 31.1, 22.5, 20.7, 10.6, 10.4. IR (neat, cm^{-1}): 3063, 2930, 2861, 1601, 1495, 1449, 1365, 1140, 1090, 968, 749, 699. Anal. calcd (found) for $C_{19}H_{22}O$: C, 85.67 (85.39); H, 8.32 (8.24).

(*E*)-(3-Methoxy-1-butenyl)benzene (14c).[10] A mixture of (**5**)AuCl (6.2 mg, 0.010 mmol) and AgOTf (2.6 mg, 0.010 mmol) in toluene-d_8 (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **12** (26.0 mg, 0.20 mmol) and methanol (9.6 mg, 0.30 mmol) in toluene-d_8 (0.3 mL) and the resulting suspension was stirred at room temperature for 1 h. The crude reaction mixture was filtered through a pad of Celite (~3 cm) in a pipet and washed with toluene-d_8 (0.5 mL) to give **14c** in 90% ^{1}H NMR yield versus CH_2Cl_2 internal standard. TLC (CH_2Cl_2–hexanes = 1:1): R_f = 0.24. ^{1}H NMR (toluene-d_8): δ 7.29-7.02 (m, 5 H), 6.41 (d, *J* = 16.0 Hz, 1 H), 6.03 (ddd, *J* = 0.8, 7.6, 16.0 Hz, 1 H), 3.73-3.66 (m, 1 H), 3.20 (d, *J* = 0.8 Hz, 3 H), 1.30 (dd, *J* = 0.8, 6.4 Hz, 3 H). ^{13}C{^{1}H} NMR (toluene-d_8): δ 136.8, 131.6, 131.1, 128.3, 127.3, 126.4, 77.9, 55.4, 21.3.

(*E*)-(3-Methoxy-2-deuterium-1-butenyl)benzene (14c-d_1). A mixture of (**5**)AuCl (6.2 mg, 0.010 mmol) and AgOTf (2.6 mg, 0.010 mmol) in toluene-d_8 (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **12** (26.0 mg, 0.20 mmol) and methanol-d (9.9 mg, 0.30 mmol) in toluene-d_8 (0.3 mL) and the resulting suspension was stirred at room temperature for 1 h. The crude reaction mixture was filtered through a pad of Celite (~3 cm) in a pipet and washed with toluene-d_8 (0.5 mL) to give **14c**-d_1 in 94% ^{1}H NMR yield (CH_2Cl_2 as internal standard, Figure S8 and Figure S9). Integration of the vinyl proton α to the tertiary carbon of **14c**-d_1 [δ 6.03 (ddd, *J* = 0.8, 7.6, 16.0 Hz)] revealed 80% deuterium incorporation. The resonance of the vinyl proton α to the phenyl group appeared as a singlet [δ 6.40, 0.8 H] superimposed on the doublet of residual **14c** [δ 6.41 (d, *J* = 16.0 Hz, 0.2 H)]. In the ^{13}C{^{1}H} NMR of **14c**-d_1, the olefinic carbon atom bonded to the tertiary carbon (δ 131.6) appeared as a small 1:1:1 triplet superimposed on the singlet corresponding to **14c**.

(*E*)-4-Phenyl-3-buten-2-yl propionate (14d).[11] Colorless oil, 80%. TLC (CH_2Cl_2–hexanes = 1:1): R_f = 0.38. ^{1}H NMR: δ 7.38-7.21 (m, 5 H), 6.58 (d, *J* = 16.0 Hz, 1 H), 6.18 (dd, *J* = 6.8, 16.0 Hz, 1 H), 5.53 (quintet, *J* = 6.8 Hz, 1 H), 2.33 (q, *J* = 7.6 Hz, 2 H), 1.39 (d, *J* = 6.4 Hz, 3 H), 1.14 (t, *J* = 7.6 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 174.0, 136.6, 131.6, 129.2, 128.8, 128.1, 126.8, 71.0, 28.1, 20.6, 9.3.

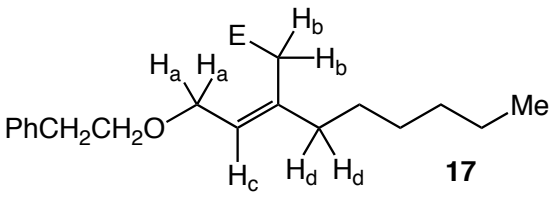
(*E*)-4-Phenethoxy-2-pentenyl benzoate (15a). Colorless oil, 87%. TLC (hexanes–EtOAc = 5:1): R_f = 0.54. ^{1}H NMR: δ 8.05-8.00 (m, 2 H), 7.57-7.16 (m, 8 H), 5.80 (td, *J* = 5.2, 15.6 Hz, 1 H), 5.73 (dd, *J* = 6.4, 15.6 Hz, 1 H), 4.78 (d, *J* = 4.8 Hz, 2 H), 3.88 (quintet, *J* = 6.4 Hz, 1 H), 3.65 (td, *J* = 7.6, 9.2 Hz, 1 H), 3.54 (ddd, *J* = 6.8, 8.0, 9.2 Hz, 1 H), 2.90-2.83 (m, 2 H), 1.24 (d, *J* = 6.4 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 166.5, 139.2, 136.7, 133.2, 130.4, 129.9, 129.2, 128.6, 128.5, 126.4, 125.5, 76.0, 70.0, 64.9, 36.8, 21.4. IR (neat, cm^{-1}): 3028, 2933, 2863, 1719, 1602, 1495, 1450, 1374, 1268, 1098, 1027, 970, 748, 708. Anal. calcd (found) for $C_{20}H_{22}O_3$: C, 77.39 (77.48); H, 7.14 (7.07). HRMS calcd (found) for $C_{20}H_{22}O_3$ (M^+): 310.1569 (310.1565).

(*E*)-4-(Allyloxy)-2-pentenyl benzoate (15b). Colorless oil, 81%. TLC (hexanes–EtOAc = 5:1): R_f = 0.50. ^{1}H NMR: δ 8.06-8.03 (m, 2 H), 7.56-7.52 (m, 1 H), 7.44-7.40 (m, 2 H), 5.94-5.72 (m, 3 H) [5.94-5.84 (m, 1 H), 5.83 (td, *J* = 5.6, 15.6 Hz, 1 H), 5.75 (dd, *J* = 6.4, 15.6 Hz, 1 H)], 5.25 (qd, *J* = 1.6, 17.2 Hz, 1 H), 5.14 (qd, *J* = 1.6, 10.4 Hz, 1 H), 4.81 (d, *J* = 6.0 Hz, 2 H), 4.00 (tdd, *J* = 1.6, 5.2, 12.8 Hz, 1 H), 3.94 (quintet, *J* = 6.4 Hz, 1 H), 3.87 (tdd, *J* = 1.2, 6.0, 12.8 Hz, 1 H), 1.26 (d, *J* = 6.4 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 166.4, 136.5, 135.2, 133.2, 130.3, 129.8, 128.5, 125.7, 116.9, 75.1, 69.4, 64.8, 21.4. IR (neat, cm^{-1}): 2977, 2861, 1720, 1602, 1450, 1374, 1267, 1103, 1073, 1026, 971, 924, 710. Anal. calcd (found) for $C_{15}H_{18}O_3$: C, 73.15 (72.98); H, 7.37 (7.29). HRMS calcd (found) for $C_{15}H_{18}O_3$ (M^+): 246.1256 (246.1255).

(*E*)-4-(Cyclohexyloxy)-2-pentenyl benzoate (15c). Colorless oil, 71%. TLC (hexanes–EtOAc = 5:1): R_f = 0.54. ^{1}H NMR: δ 8.05-8.02 (m, 2 H), 7.56-7.40 (m, 3 H), 5.82 (td, *J* = 5.2, 15.6 Hz, 1 H), 5.77 (td, *J* = 5.6, 16.0 Hz, 1 H), 4.79 (d, *J* = 4.8 Hz, 2 H), 4.04 (dq, *J* = 5.6, 6.4 Hz, 1 H), 3.30-3.24 (m, 1 H), 1.89-1.80 (m, 2 H), 1.75-1.65 (m, 2 H), 1.51-1.48 (m, 1 H), 1.32-1.13 (m, 5 H), 1.22 (d, *J* = 6.4 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 166.5, 137.9, 133.1, 130.4, 129.8, 128.5, 124.4, 75.1, 72.3, 65.0, 33.5, 32.5, 26.0, 24.6, 24.5, 22.0. IR (neat, cm^{-1}): 2930, 2857, 1720, 1602, 1450, 1267, 1074, 1026, 970, 710. Anal. calcd (found) for $C_{18}H_{24}O_3$: C, 74.97 (74.59); H, 8.39 (8.22).

(*E*)-4-(Benzyloxy)-2-pentenyl benzoate (15d). Colorless oil, 87%. TLC (hexanes–EtOAc = 5:1): R_f = 0.48. ^{1}H NMR (Figure S10): δ 8.08-8.06 (m, 2 H), 7.58-7.54 (m, 1 H), 7.46-7.42 (m, 2 H), 7.35-7.23 (m, 5 H), 5.88 (td, *J* = 5.2, 15.6 Hz, 1 H), 5.81 (dd, *J* = 6.4, 15.6 Hz, 1 H), 4.84 (d, *J* = 4.8 Hz, 2 H), 4.57 (d, *J* = 11.6 Hz, 1 H), 4.41 (d, *J* = 11.6 Hz, 1 H), 4.00 (quintet, *J* = 6.4 Hz, 1 H), 1.31 (d, *J* = 6.4 Hz, 3 H). ^{13}C{^{1}H} NMR (Figure S11): δ 166.4, 138.8, 136.5, 133.2, 130.3, 129.8, 128.6, 128.5, 127.8, 127.6, 125.9, 75.1, 70.3, 64.8, 21.5. IR (neat, cm^{-1}): 2865, 1719, 1602, 1451, 1374, 1267, 1100, 1071, 1027, 970, 708. HRMS calcd (found) for $C_{19}H_{20}O_3$ (M^+): 296.1412 (296.1409).

(*Z*)-Ethyl 3-(2-phenethoxyethylidene)nonanoate (17). Colorless oil, 62%. The Z-configuration of 17 was determined by ^{1}H NOE analysis. Irradiation of H_a led to enhancement of H_b, but not H_d, while irradiation of H_c led to enhancement of H_d but not H_b. TLC (CH_2Cl_2): R_f = 0.64. ^{1}H NMR (500 MHz): δ 7.31-7.20 (m, 5 H), 5.54 (t, *J* = 6.5 Hz, 1 H), 4.11 (q, *J* = 7.0 Hz, 2 H), 4.06 (d, *J* = 6.5 Hz, 2 H), 3.65 (t, *J* = 7.5 Hz, 2 H), 3.06 (s, 2 H), 2.90 (t, *J* = 7.5 Hz, 2 H), 2.10 (t, *J* = 7.5 Hz, 2 H), 1.45-1.39 (m, 2 H), 1.34-1.26 (m, 6 H), 1.24 (t, *J* = 7.0 Hz, 3 H), 0.89 (t, *J* = 7.0 Hz, 3 H). ^{13}C{^{1}H} NMR (126 MHz): δ 171.4, 139.1, 136.7, 129.1, 128.5, 126.4, 125.1, 71.4, 67.5, 60.9, 37.9, 36.8, 36.6, 31.9, 29.1, 27.6, 22.8, 14.4, 14.3. IR (neat, cm^{-1}): 2927, 2857, 1735, 1456, 1367, 1255, 1153, 1100, 1033, 946, 747, 699. Anal. calcd (found) for $C_{21}H_{32}O_3$: C, 75.86 (75.85); H, 9.70 (9.79). HRMS calcd (found) for $C_{21}H_{32}O_3$ (M^+): 332.2351 (332.2354).



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1-(Benzyloxy)-2-(5-methyl-3-phenethoxy-4-hexenyl)benzene (20a). Colorless oil, 80%. TLC (CH_2Cl_2–hexanes = 1:1): R_f = 0.49. ^{1}H NMR: δ 7.45-6.86 (m, 14 H), 5.10-5.09 (m, 1 H), 5.07 (s, 2 H), 3.98 (td, *J* = 6.8, 8.8 Hz, 1 H), 3.69-3.63 (m, 1 H), 3.47-3.38 (m, 1 H), 2.92-2.80 (m, 2 H), 2.78-2.64

(m, 2 H), 1.97-1.88 (m, 1 H), 1.79-1.70 (m, 1 H), 1.71 (d, *J* = 1.2 Hz, 3 H), 1.58 (d, *J* = 1.2 Hz, 3 H). $^{13}C\{^{1}H\}$ NMR: δ 156.8, 139.6, 137.7, 135.6, 131.3, 130.2, 129.2, 128.7, 128.4, 127.8, 127.2, 127.1, 126.8, 126.2, 120.8, 111.7, 76.0, 69.9, 69.1, 36.9, 35.7, 26.7, 26.1, 18.5. IR (neat, cm^{-1}): 3062, 3029, 2921, 2863, 1597, 1494, 1450, 1379, 1238, 1088, 1028, 797, 746, 697. Anal. calcd (found) for $C_{28}H_{32}O_2$: C, 83.96 (83.94); H, 8.05 (8.12). HRMS calcd (found) for $C_{28}H_{32}O_2$ (M^+): 400.2402 (400.2404).

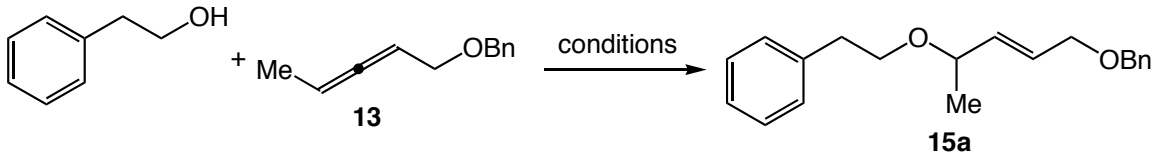
1-(Benzyloxy)-2-(3-(cyclohexyloxy)-5-methylhex-4-enyl)benzene (20b). Colorless oil, 64%. TLC (CH_2Cl_2–hexanes = 1:1): R_f = 0.43. ^{1}H NMR: δ 7.47-6.88 (m, 9 H), 5.13-5.11 (m, 1 H), 5.07 (s, 2 H), 4.14 (td, *J* = 6.4, 9.2 Hz, 1 H), 3.28-3.22 (m, 1 H), 2.79-2.66 (m, 2 H), 1.94-1.45 (m, 7 H), 1.72 (s, 3 H), 1.61 (s, 3 H), 1.34-1.17 (m, 5 H). $^{13}C\{^{1}H\}$ NMR: δ 156.8, 137.8, 134.1, 131.5, 130.0, 128.6, 127.9, 127.8, 127.1, 127.0, 120.8, 111.7, 74.3, 73.0, 69.9, 36.1, 34.0, 32.4, 26.9, 26.2, 26.1, 24.7, 24.6, 18.5. IR (neat, cm^{-1}): 2928, 2856, 1596, 1495, 1450, 1377, 1238, 1082, 1045, 907, 746, 695. Anal. calcd (found) for $C_{26}H_{34}O_2$: C, 82.49 (82.56); H, 9.05 (9.06).

(2-(1-(Benzyloxy)-5-ethyl-4-hepten-3-yloxy)ethyl)benzene (21). Colorless oil, 41%. TLC (CH_2Cl_2–hexanes = 1:1): R_f = 0.14. ^{1}H NMR: δ 7.35-7.16 (m, 10 H), 4.96 (d, *J* = 9.6 Hz, 1 H), 4.47-4.39 (m, 2 H), 4.24-4.18 (m, 1 H), 3.70-3.39 (m, 4 H), 2.88-2.77 (m, 2 H), 2.06 (q, *J* = 7.4 Hz, 2 H), 2.02 (dq, *J* = 1.0, 7.4 Hz, 2 H), 1.95-1.63 (m, 2 H), 0.98 (t, *J* = 7.4 Hz, 3 H), 0.95 (t, *J* = 7.4 Hz, 3 H). $^{13}C\{^{1}H\}$ NMR: δ 147.1, 139.6, 138.9, 129.1, 128.5, 128.4, 127.8, 127.6, 126.2, 124.2, 73.1, 72.9, 69.1, 67.2, 36.8, 36.5, 29.1, 23.8, 13.6, 13.0. IR (neat, cm^{-1}): 3029, 2962, 2866, 1495, 1455, 1364, 1204, 1090, 863, 810, 738, 697. Anal. calcd (found) for $C_{24}H_{32}O_2$: C, 81.77 (81.48); H, 9.15 (9.03).

(2-(2,4-Dimethyl-3-penten-2-yloxy)ethyl)benzene (23). Colorless oil, 55%. TLC (CH_2Cl_2–hexanes = 1:1): R_f = 0.60. ^{1}H NMR (Figure S12): δ 7.30-7.17 (m, 5 H), 5.07 (quintet, *J* = 1.2 Hz, 1 H), 3.49 (t, *J* = 7.6 Hz, 2 H), 2.84 (t, *J* = 7.6 Hz, 2 H), 1.76 (d, *J* = 1.2 Hz, 3 H), 1.69 (d, *J* = 1.2 Hz, 3 H), 1.29 (s, 6 H). $^{13}C\{^{1}H\}$ NMR (Figure S13: **23** decomposed significantly during acquisition): δ 139.7, 135.5, 129.2, 129.0, 128.4, 126.2, 75.1, 63.9, 37.6, 28.5, 27.1, 18.6. IR (neat, cm^{-1}): 2928, 2867, 1665,

1604, 1495, 1450, 1380, 1243, 1171, 1137, 1071, 909, 817, 747, 697. HRMS calcd (found) for $C_{15}H_{22}O$ (M^+): 218.1671 (218.1670).

Control Experiments



(1) Treatment of 2-phenyl-1-ethanol (26.9 mg, 0.22 mmol), **13** (37.6 mg, 0.20 mmol), and *n*-hexadecane (20 μL, as internal standard) with (**5**)AuCl (5 mol %) in toluene (0.5 mL) at 23 °C for 16 h led to no consumption of **13** as determined by GC analysis of the crude reaction mixture.

(2) Treatment of 2-phenyl-1-ethanol (26.9 mg, 0.22 mmol), **13** (37.6 mg, 0.20 mmol), and *n*-hexadecane (20 μL, as internal standard) with **5** (5 mol %) and AgOTf (5 mol%) in toluene (0.5 mL) at 23 °C for 16 h led to no consumption of **13** as determined by GC analysis of the crude reaction mixture.

(3) Treatment of 2-phenyl-1-ethanol (26.9 mg, 0.22 mmol), **13** (37.6 mg, 0.20 mmol), and *n*-hexadecane (20 μL, as internal standard) with **5** (5 mol %) and HOTf (5 mol%) in toluene (0.5 mL) at 23 °C for 16 h led to no consumption of **13** as determined by GC analysis of the crude reaction mixture.

(4) Treatment of 2-phenyl-1-ethanol (26.9 mg, 0.22 mmol), **13** (37.6 mg, 0.20 mmol), and *n*-hexadecane (20 μL, as internal standard) with HOTf (30 mol %) in toluene (0.5 mL) at 23 °C for 20 h led to no consumption of **13** as determined by GC analysis of the crude reaction mixture. Further reaction at 60 °C for 24 h led to 59% conversion but with no detectable formation of **15a**.

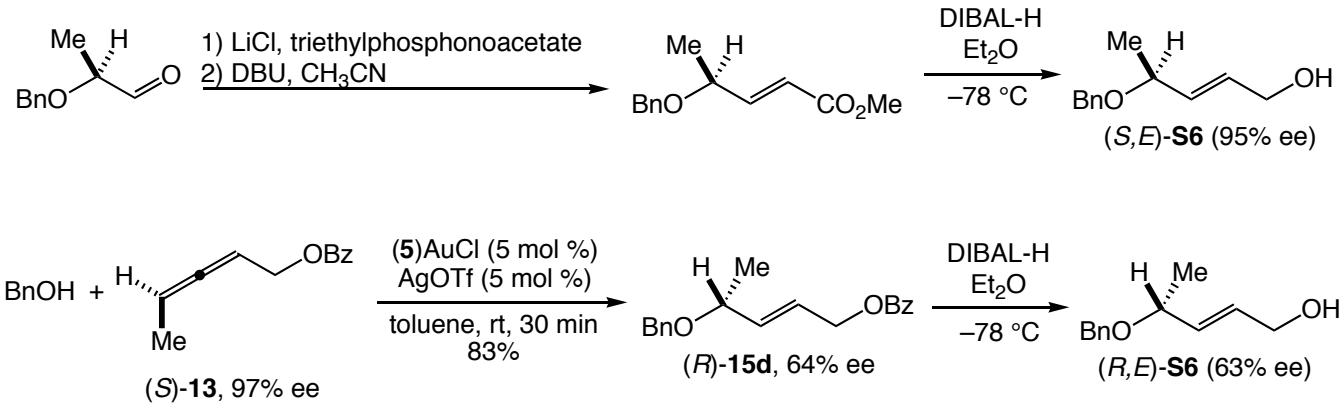
Hydroalkylation with Enantiomerically Enriched Reagents

Reaction of 8 with (*R*)-(+)-1-phenyl-1-propanol. A mixture of (**5**)AuCl (6.2 mg, 0.010 mmol) and AgOTf (2.6 mg, 0.010 mmol) in toluene (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of **8** (28.0 mg, 0.25 mmol) and (*R*)-(+)-1-phenyl-1-propanol (27.2 mg, 0.20 mmol, 99% ee) in toluene (0.3 mL) and the resulting suspension was stirred at room temperature for 10 h. Column

chromatography of the crude reaction mixture (hexanes–EtOAc = 30:1) gave (*R*)-**11b** (37.5 mg, 75%, 99% ee) as a colorless oil. The enantiomeric purity of (*R*)-**11b** was determined by HPLC analysis (Figure S14).

Reaction of (*S*)-13 with benzyl alcohol. A mixture of (**5**)AuCl (6.2 mg, 0.010 mmol) and AgOTf (2.6 mg, 0.010 mmol) in toluene (0.2 mL) was stirred at room temperature for 5 min, treated with a solution of (*S*)-**13** (37.6 mg, 0.20 mmol, 97% ee) and benzyl alcohol (23.8 mg, 0.22 mmol) in toluene (0.3 mL) and the resulting suspension was stirred at room temperature for 30 min. Column chromatography of the crude reaction mixture (hexanes-EtOAc = 30:1 → 20:1) gave (*R*)-**15d** (49.0 mg, 83%, 64% ee) as a colorless oil. The enantiomeric purity of (*R*)-**15d** was determined by HPLC analysis (Figure S15).

Determination of Absolute Configuration of (*R*)-15d. The absolute configuration of (*R*)-**15d** formed in the intermolecular hydroalkoxylation of (*S*)-**13** with benzyl alcohol catalyzed by (**5**)AuCl/AgOTf was assigned on the basis of the experiments described below and outlined in Scheme S8. (*S,E*)-4-(Benzyloxy)-2-penten-1-ol (*S,E*)-**S6** (95% ee; Figure S16, middle trace; Scheme 8) was synthesized from (*S*)-2-(benzyloxy)propional employing a published procedure.[12] (*R*)-**15d** (64% ee; Figure S22, right trace) formed from (*S*)-**13** was converted to (*R,E*)-**S6** (63% ee, Figure S16, right trace; Scheme 8) via DIBAL reduction. Comparison of the HPLC trace of this latter sample of (*R,E*)-**S6** (63% ee, Figure S16, right trace) with the HPLC trace of (*S,E*)-**S6** (Figure S16, middle trace) generated from (*S*)-2-(benzyloxy)propional established that the absolute configuration of (*R*)-**15d** formed in the intermolecular hydroalkoxylation of (*S*)-**13** with benzylalcohol catalyzed by (**5**)AuCl/AgOTf.



Scheme S8

For (*E*)-S6:[16] DIBAL-H (1.0 M in toluene, 0.22 mL, 0.22 mmol) was added dropwise to a solution of **15d** (29.6 mg, 0.10 mmol) in Et_2O (0.5 mL) at –78 °C. The resulting mixture was stirred for 2 h, quenched with methanol (1 mL), stirred for 30 min at –78 °C, and treated with saturated NH_4Cl (0.5 mL). The resulting white suspension was warmed to room temperature, filtered through a pad of celite, eluted with Et_2O (100 mL), dried ($MgSO_4$), and concentrated. The residue was chromatographed (EtOAc–hexanes = 5:1 → 2:1) to give (*E*)-**S1** (16.9 mg, 88%) as a colorless oil. ^{1}H NMR: δ 7.37-7.19 (m, 5 H), 5.80 (dtd, *J* = 0.8, 5.2, 15.6 Hz, 1 H), 5.66 (tdd, *J* = 1.6, 7.2, 15.6 Hz, 1 H), 4.54 (d, *J* = 12.0 Hz, 1 H), 4.40 (d, *J* = 12.0 Hz, 1 H), 4.16-4.14 (m, 2 H), 3.96 (quintet, *J* = 6.8 Hz, 1 H), 1.53 (s, br, 1 H), 1.28 (d, *J* = 6.4 Hz, 3 H). ^{13}C{^{1}H} NMR: δ 138.9, 133.7, 131.1, 128.6, 127.9, 127.7, 75.3, 70.3, 63.2, 21.6.

Figure S1. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) (*S*)-**13**. HPLC conditions: hexanes–isopropanol = 99.8 : 0.2 @ 0.5 mL/min.

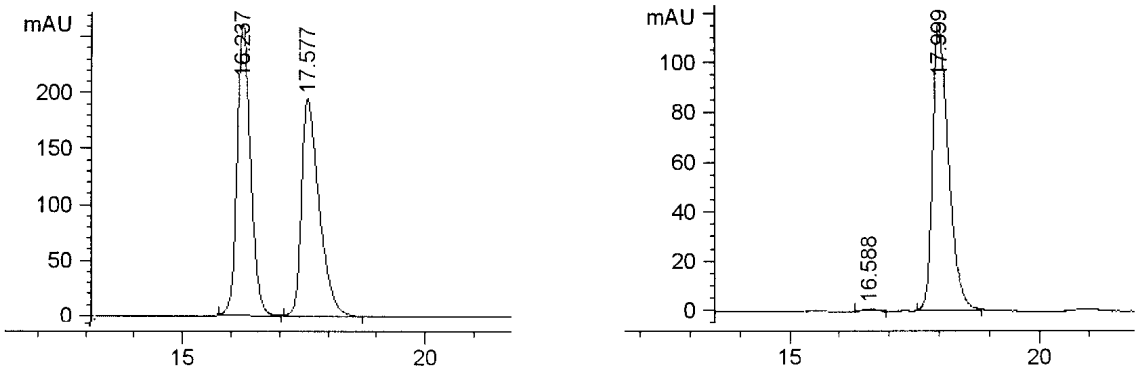


Figure S2. ^{1}H NMR spectra of **19**.

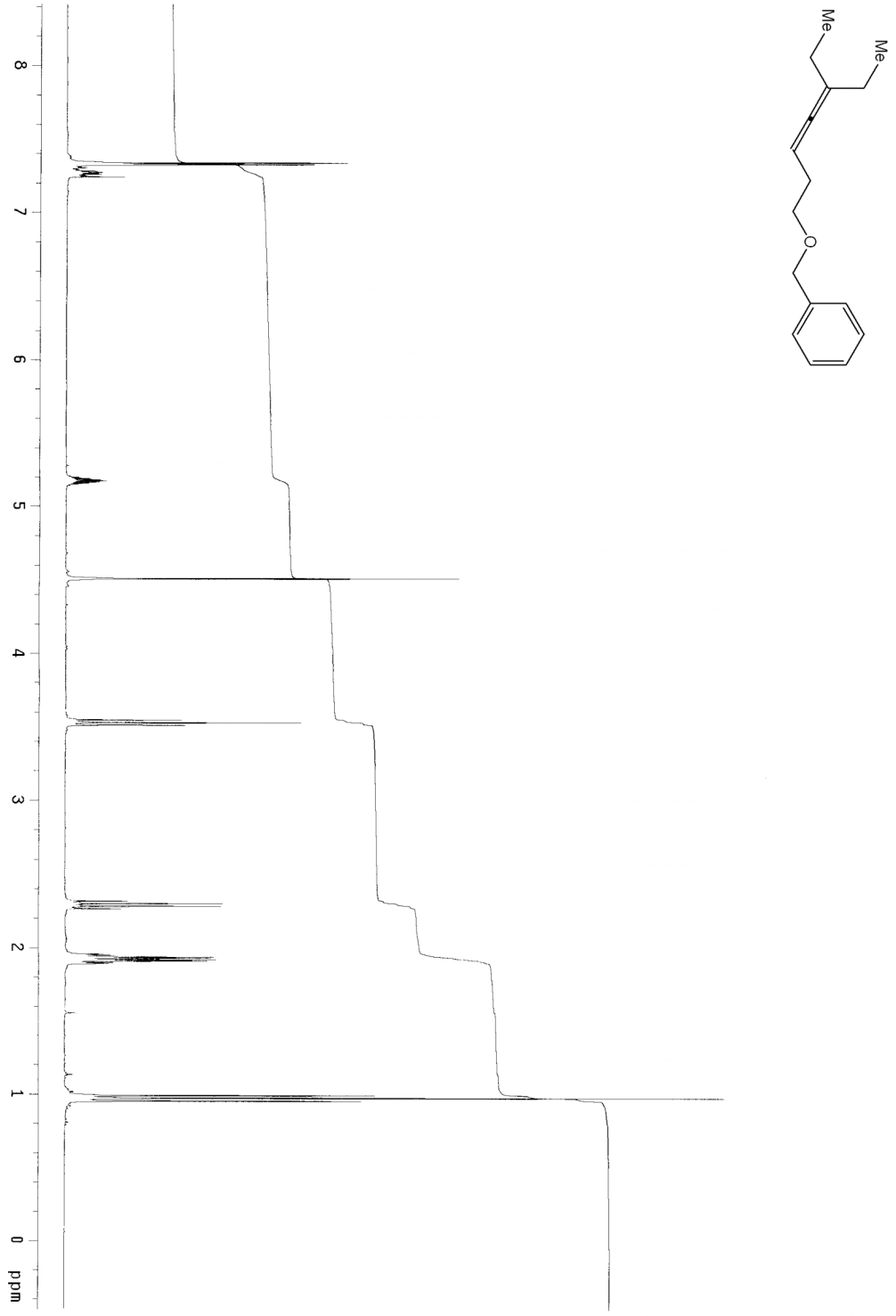


Figure S3. $^{13}C\{^{1}H\}$ NMR spectra of **19**.

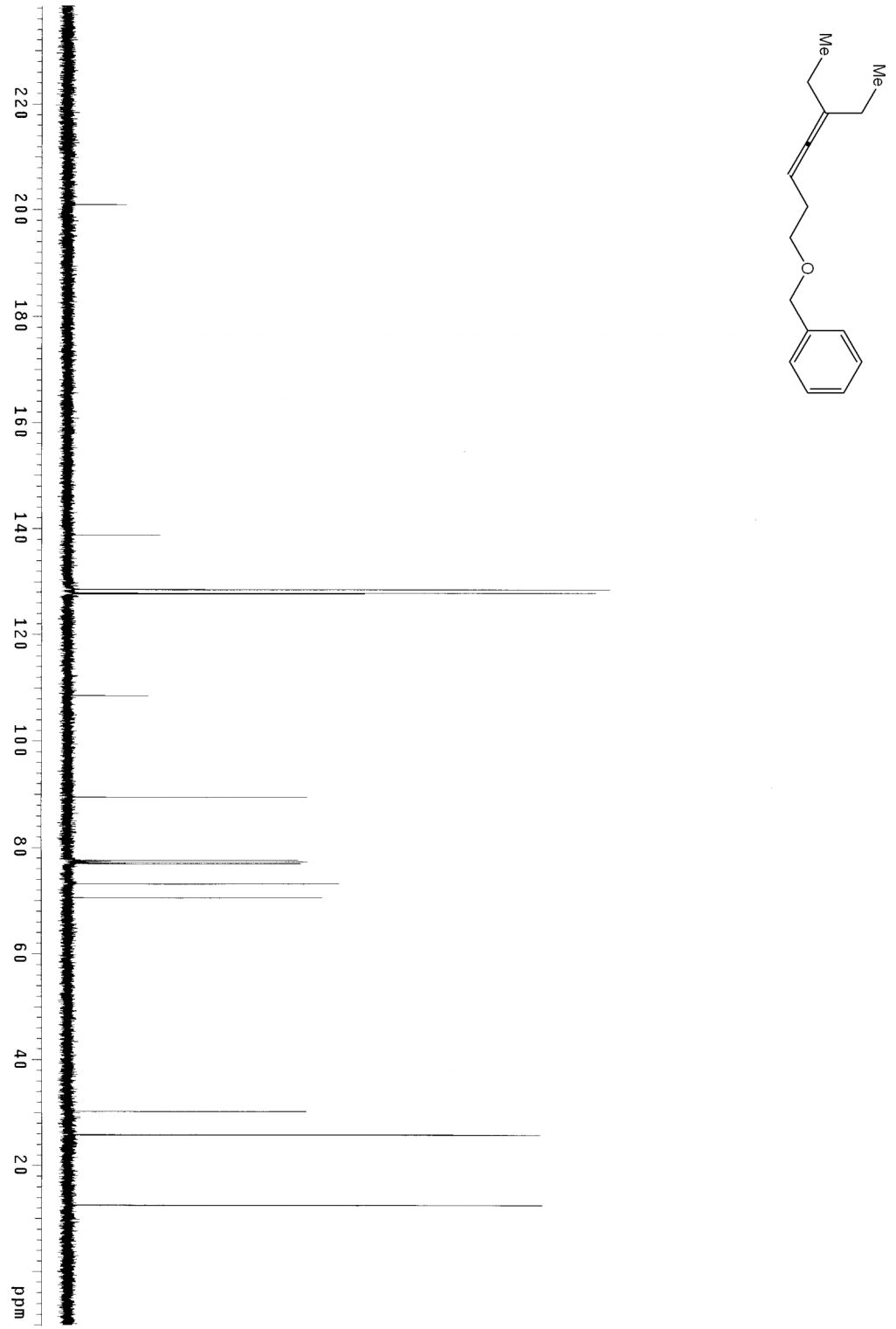


Figure S4. ^{1}H NMR spectra of **4**.

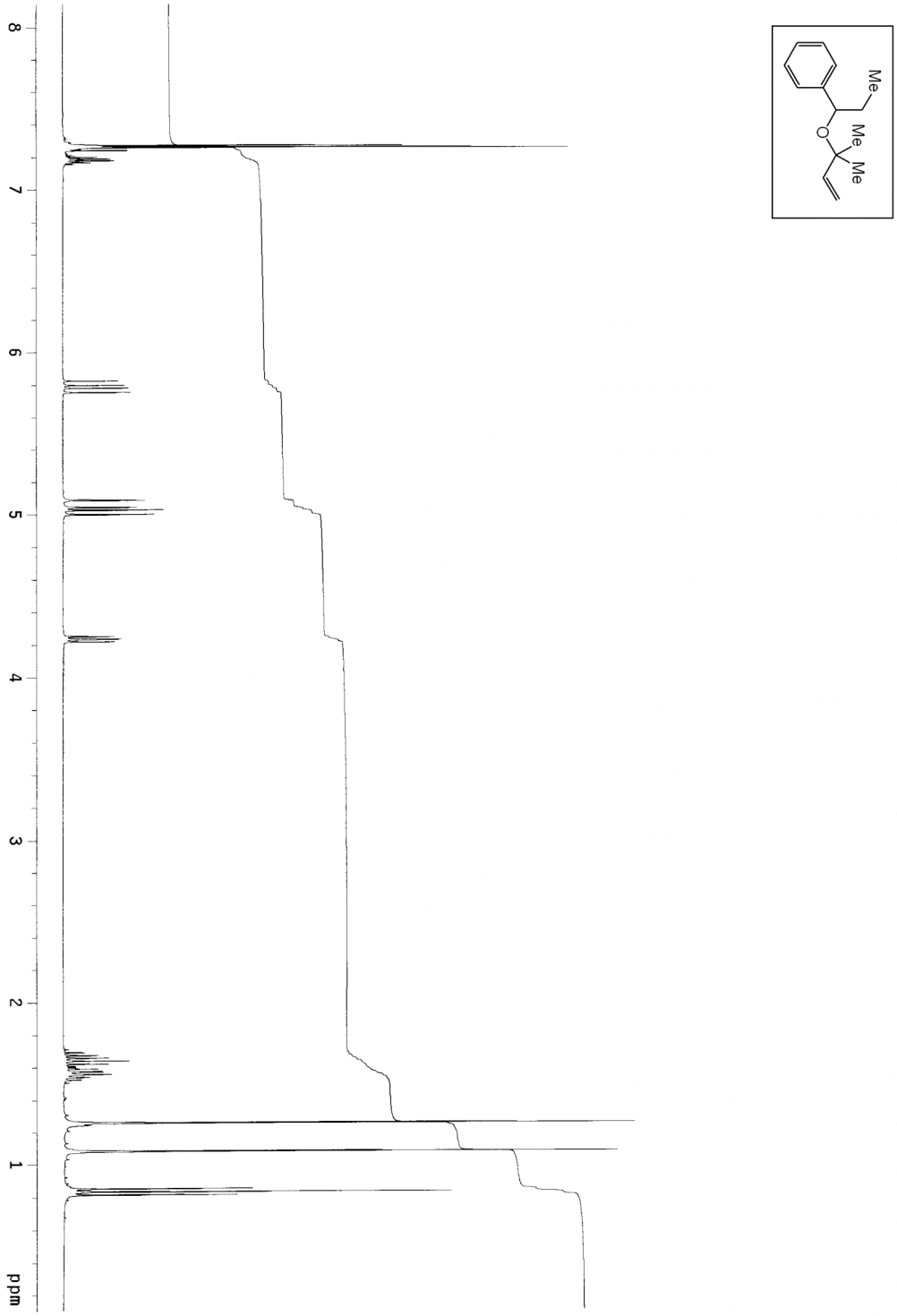


Figure S5. ^{13}C NMR spectra of **4**.

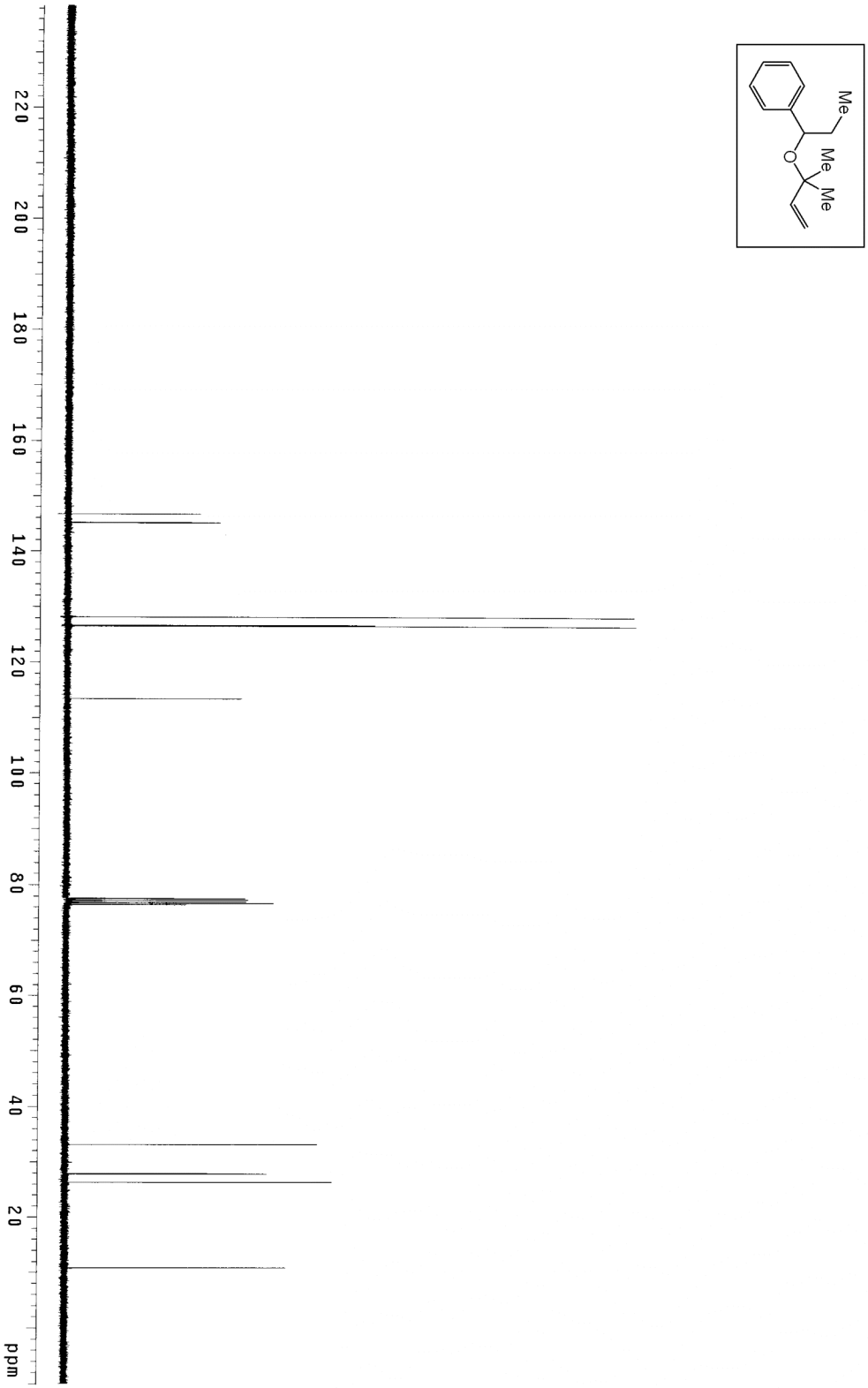


Figure S6. ^{1}H NMR spectra of **11a**.

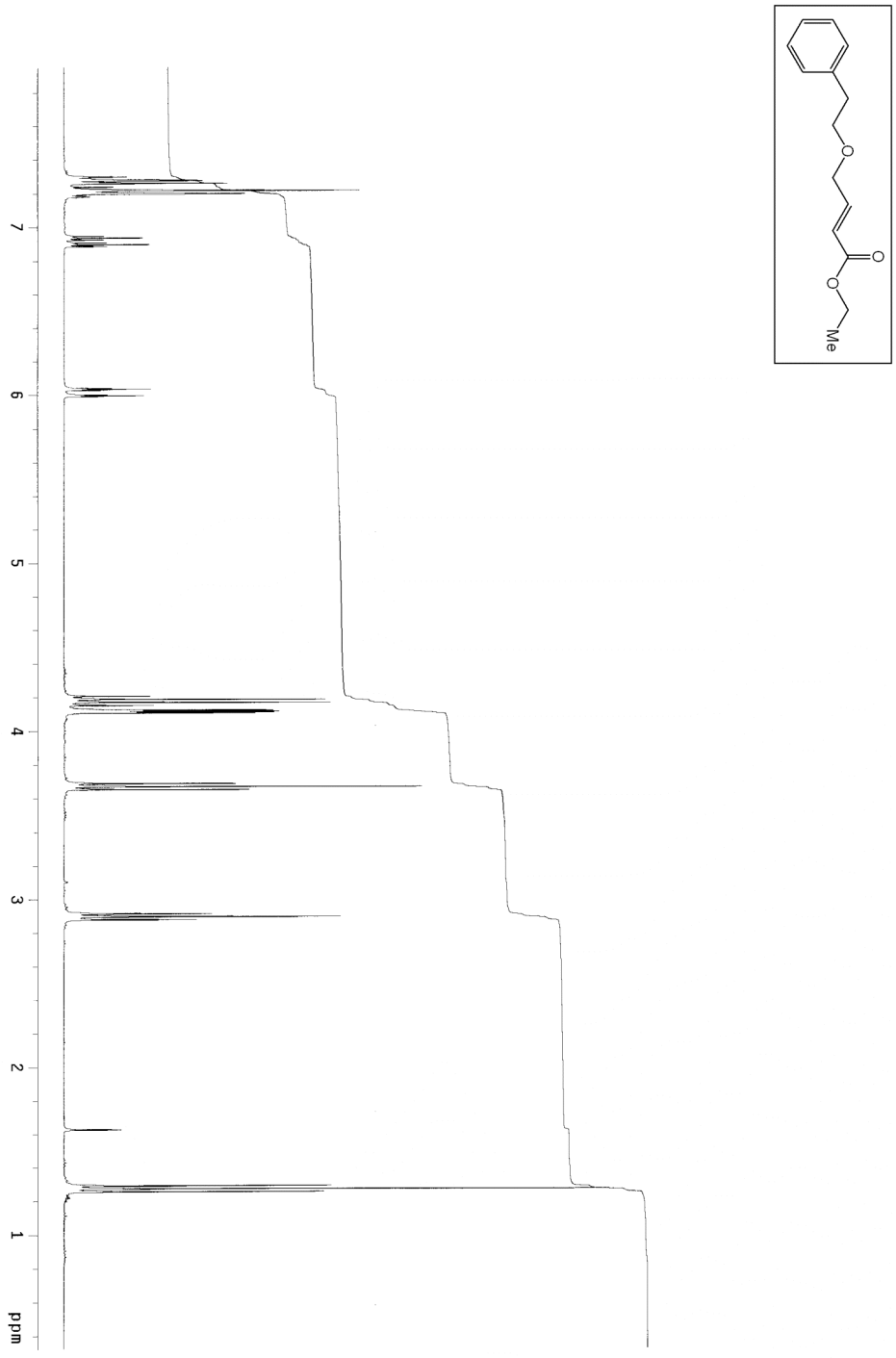


Figure S7. ^{13}C NMR spectra of **11a**.

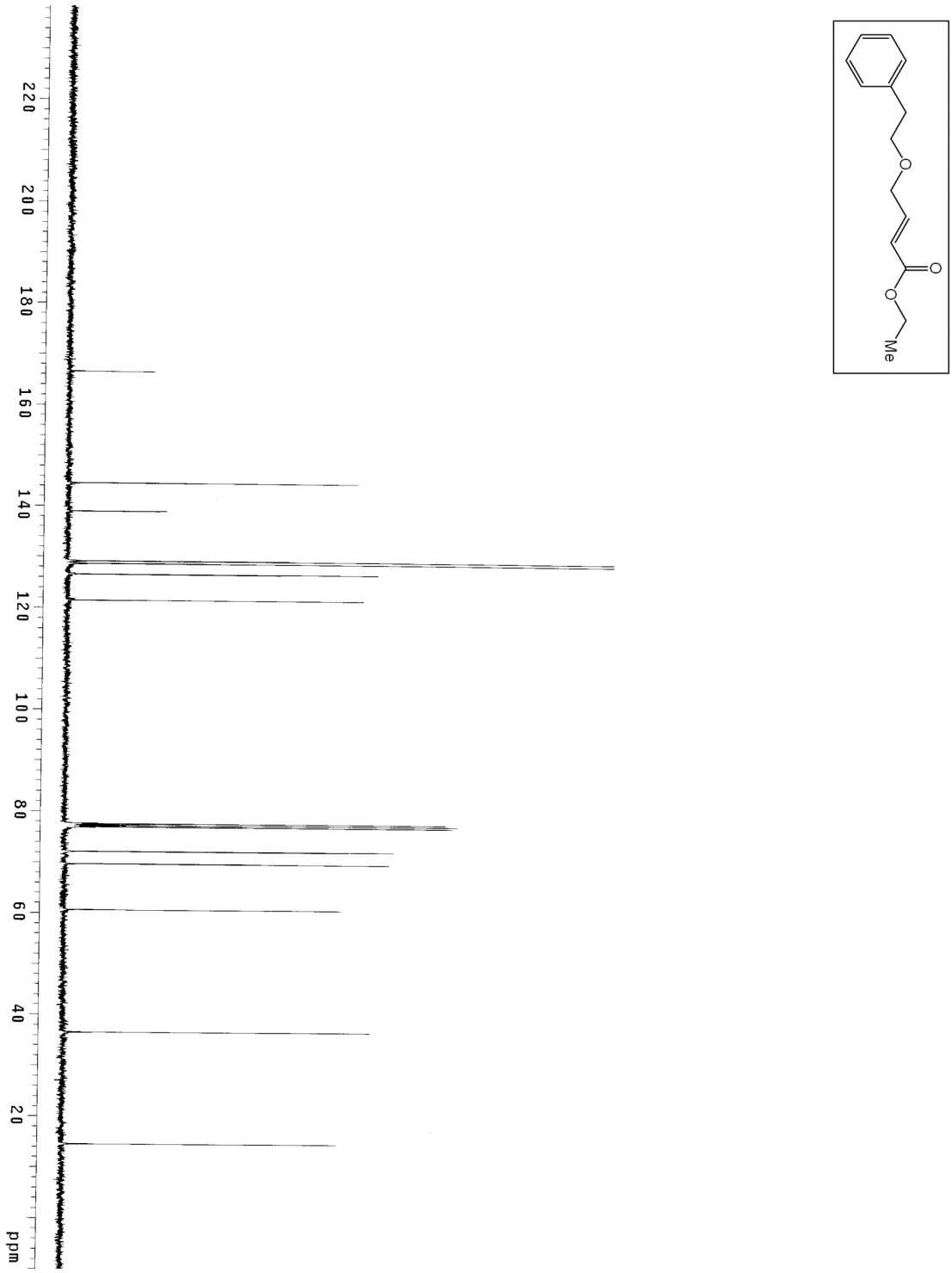


Figure S8. ^{1}H NMR spectra of **14c**-d_1.

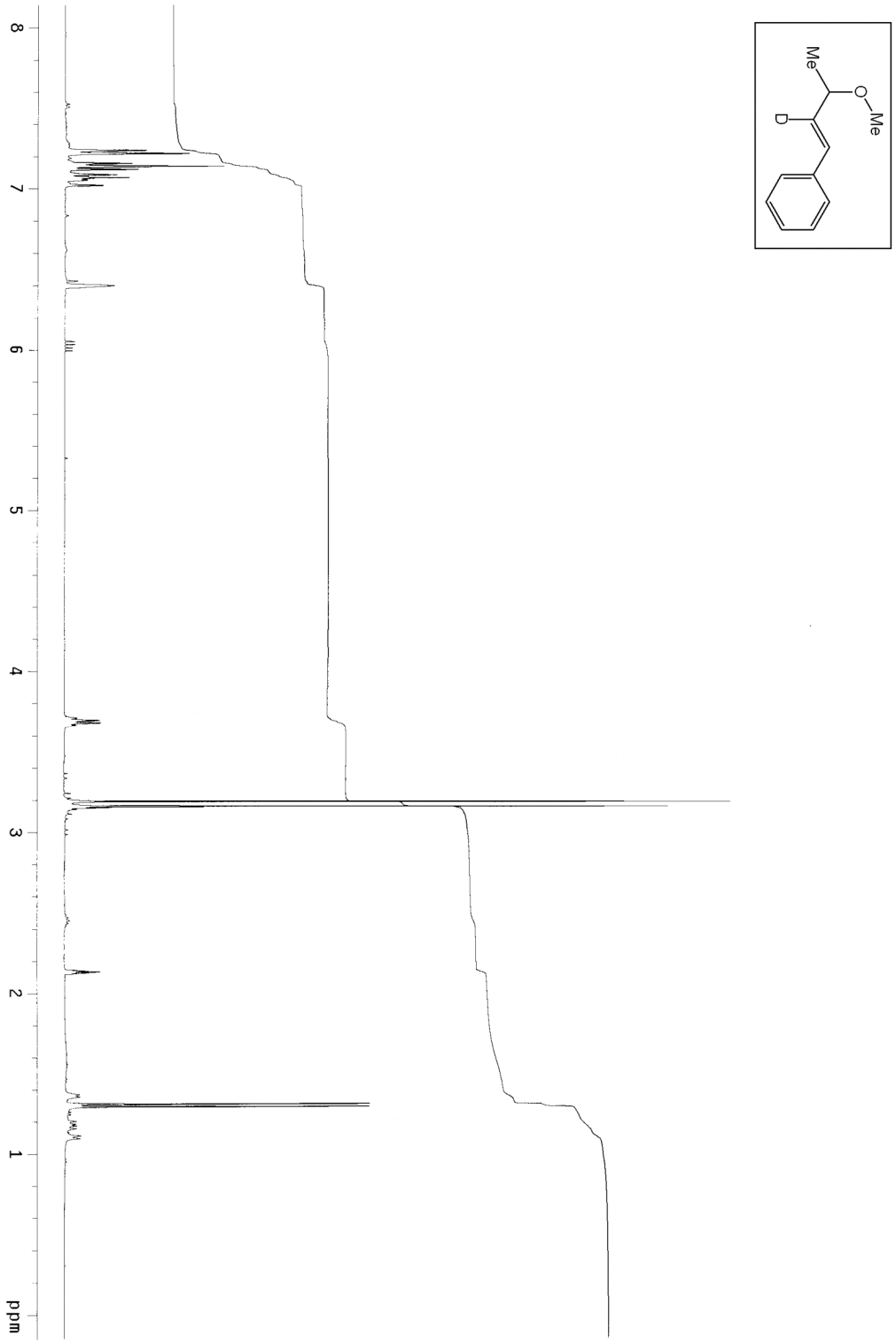


Figure S9. ^{13}C NMR spectra of **14c**-d_1.

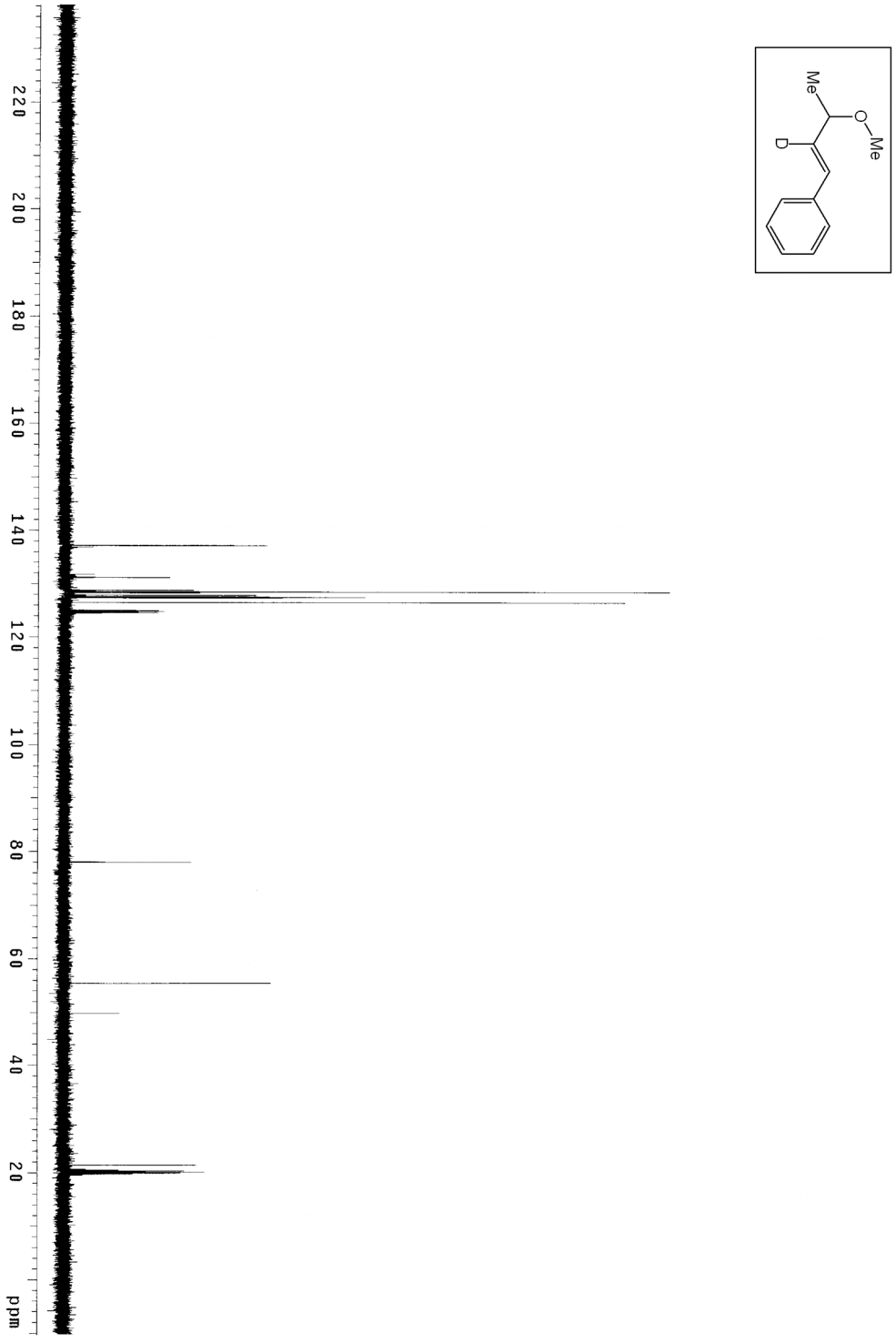


Figure S10. ^{1}H NMR spectra of **15d**.

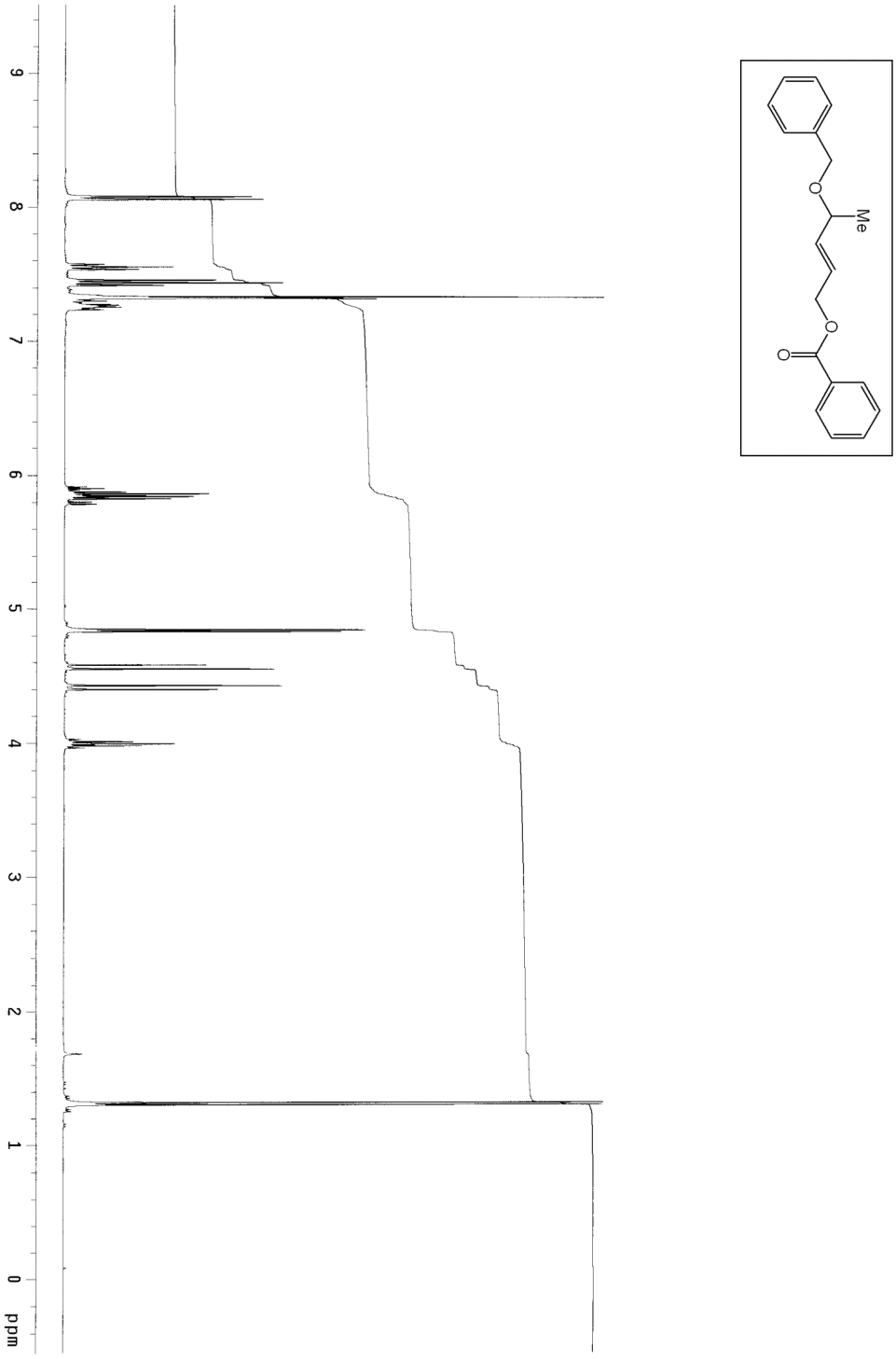


Figure S11. ^{13}C NMR spectra of **15d**.

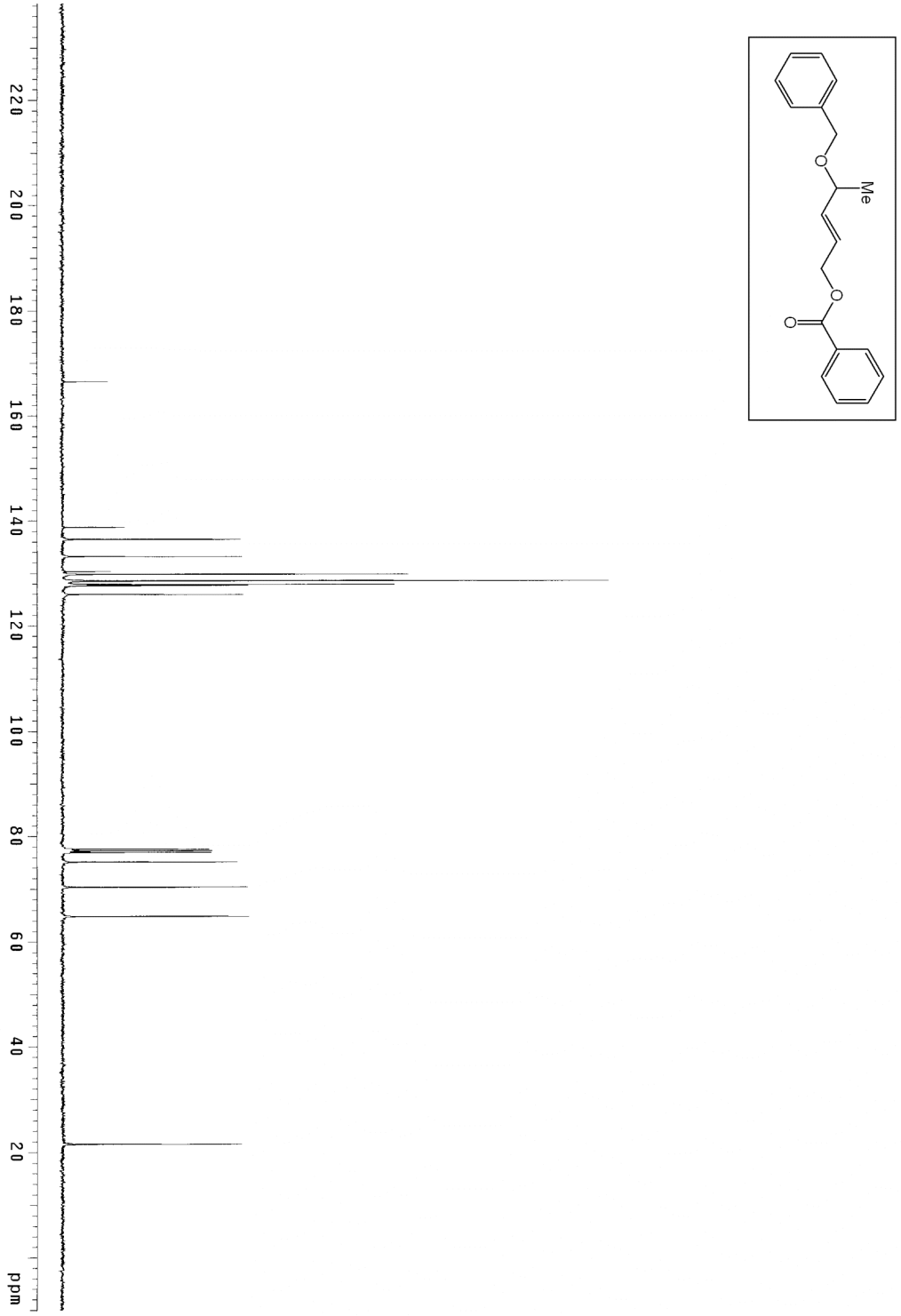


Figure S12. ^{1}H NMR spectra of **23**.

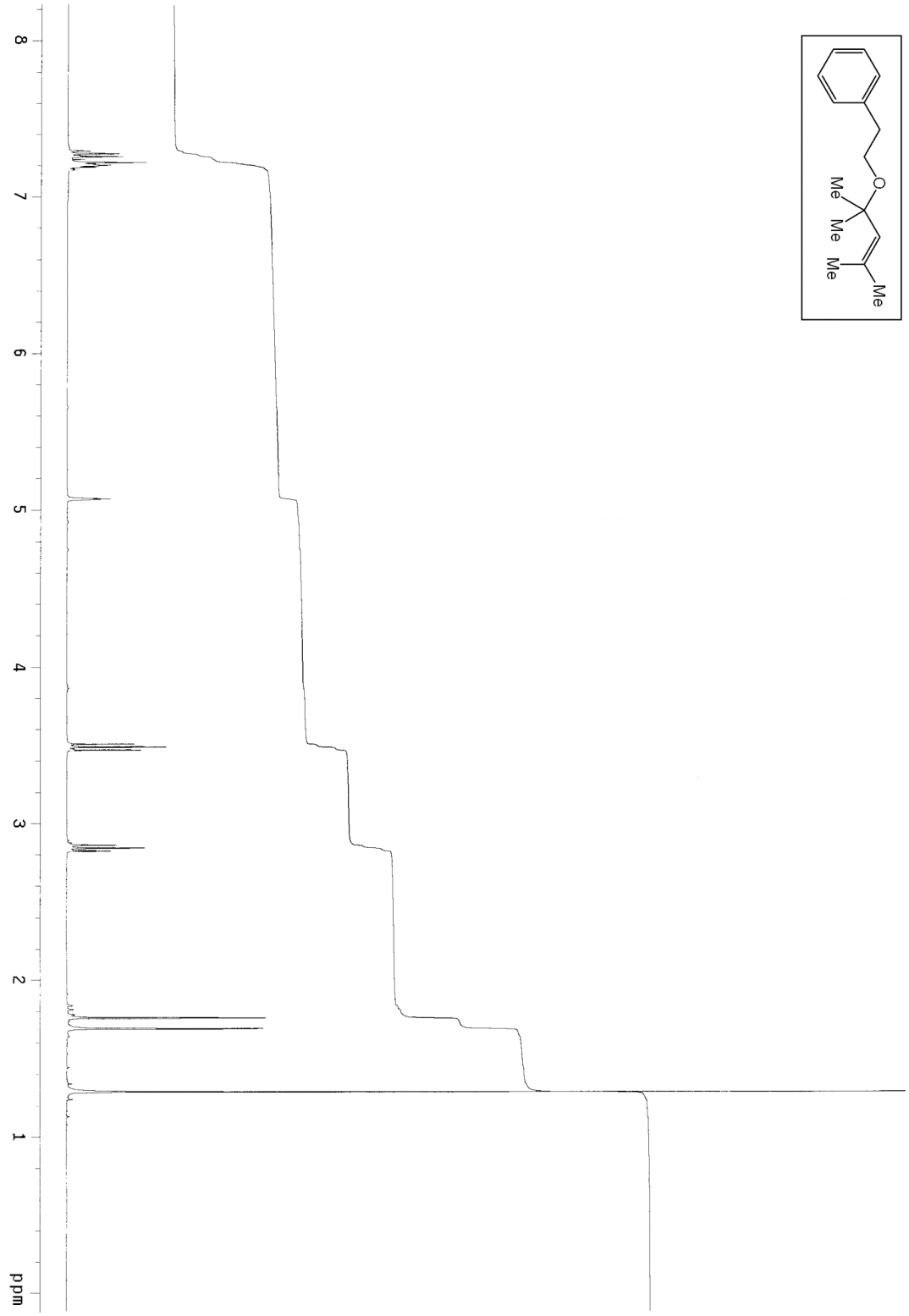


Figure S13. ^{13}C NMR spectra of **23**.

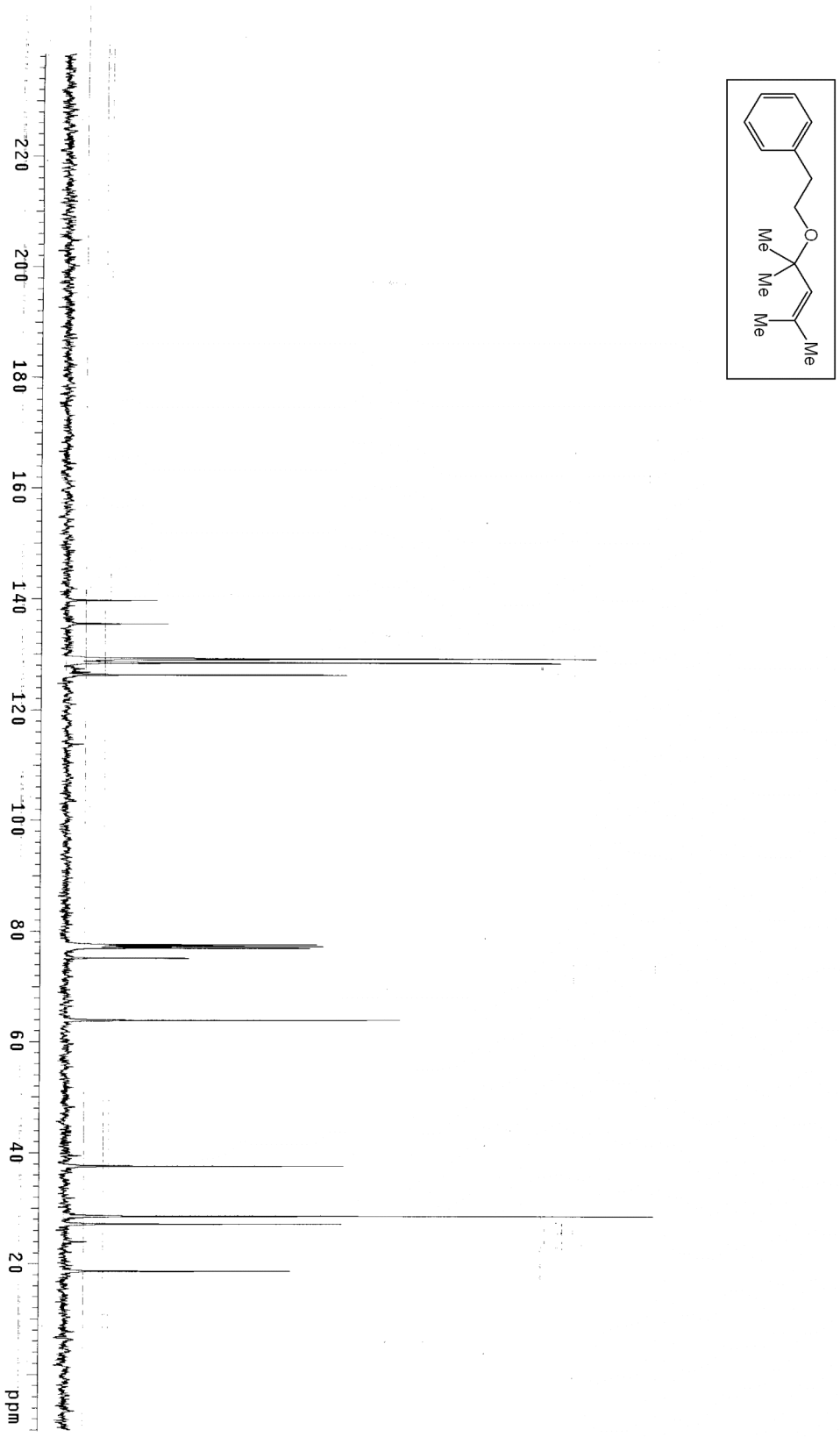


Figure S14. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) (*R*)-**11b**. HPLC conditions: hexanes–isopropanol = 99 : 1 @ 0.5 mL/min.

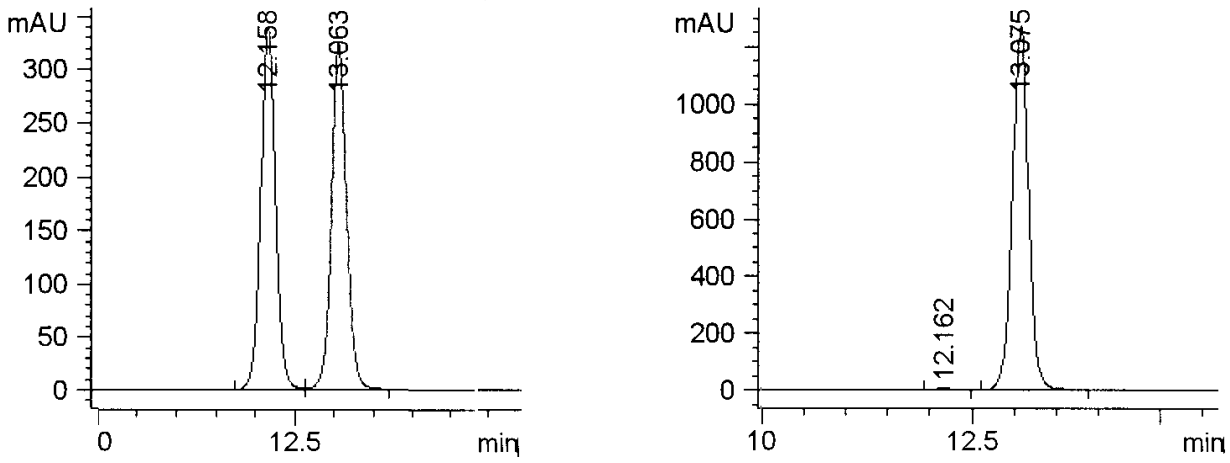


Figure S15. HPLC trace for racemic (left trace) and enantiomerically enriched (right trace) (*R*)-**15d**. HPLC conditions: hexanes–isopropanol = 99.5 : 0.5 @ 0.5 mL/min.

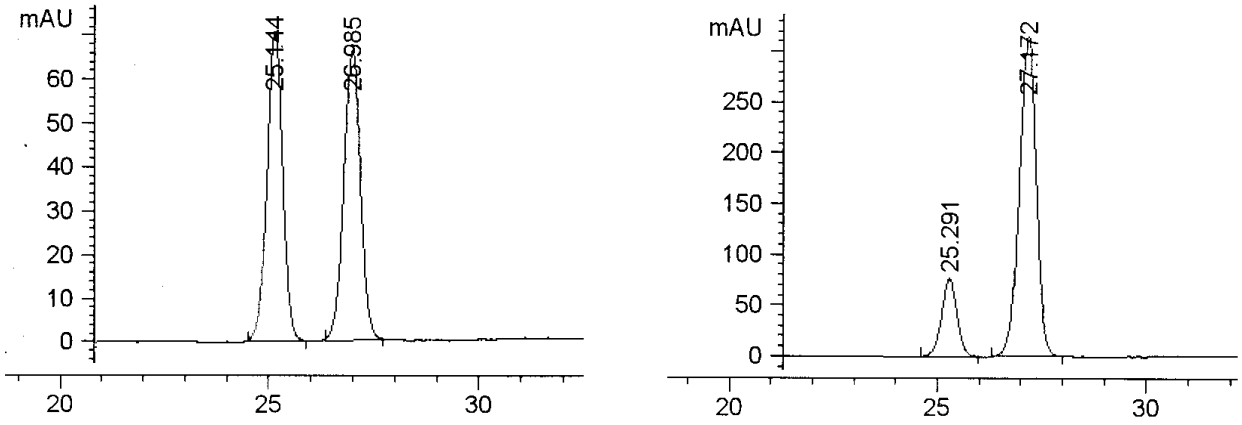
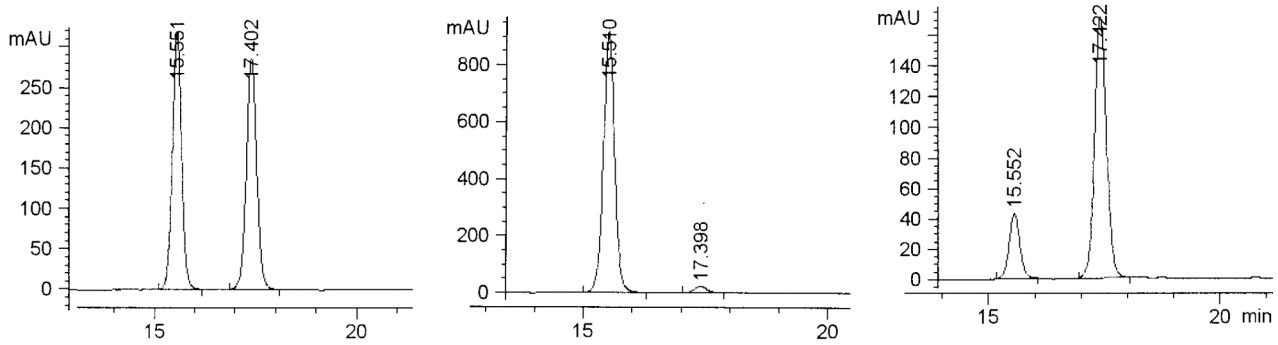


Figure S16. HPLC trace for racemic (*E*)-**S6** (left trace), the authentic sample of (*S,E*)-**S6** (middle trace), and enantiomerically enriched (*R,E*)-**S6** generated from (*R*)-**15d** (right trace), and. HPLC conditions: hexanes–isopropanol = 95:5 @ 0.5 mL/min.



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