Supporting Information

Powerful Amino Diol Catalyst for Effecting the Direct Asymmetric Conjugate Addition of Aldehydes to Acrylates

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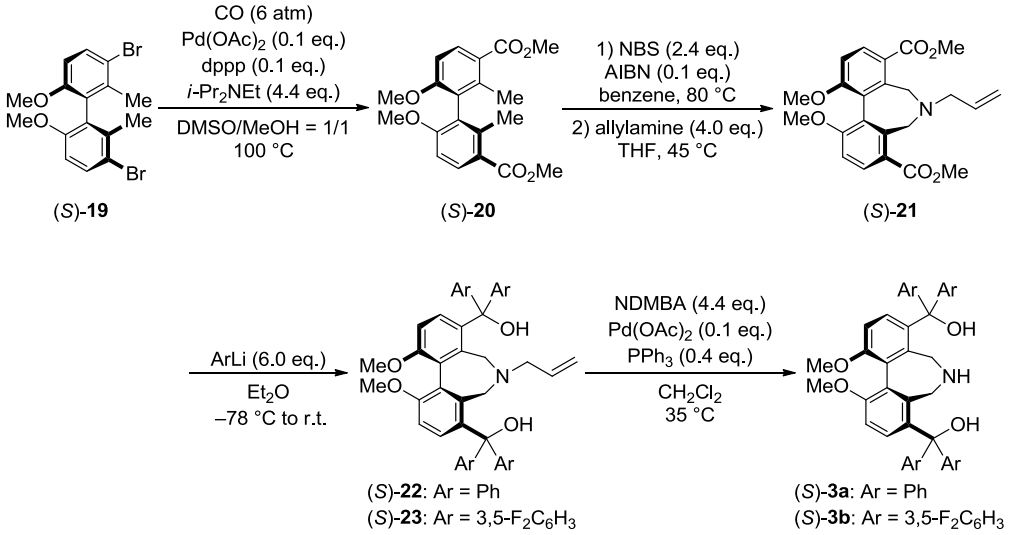
General Information. Infrared (IR) spectra were recorded on a Shimadzu IRPrestige-21 spectrometer. ^{1}H NMR spectra were measured on a JEOL JNM-FX400 (400 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane or the residual solvent as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, dd = double-doublet, ddd = double double doublet, m = multiplet, br = broad, and app = apparent), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured on a JEOL JNM-FX400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. High performance liquid chromatography (HPLC) was performed on Shimadzu 20A instruments using Daicel Chiralpak AD-H, AS-H, AY-H, IC, ID, AD-3, IC-3 and Chiralcel OD-H, OJ-H, OZ-H, OD-3 4.6 mm x 25 cm column. High-resolution mass spectra (HRMS) were performed on Brucker microTOF. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by flash column chromatography on neutral silica gel 60N (Kanto Chemical Co. Inc., 40-50μm). For purification with preparative thin layer chromatography (PLC), Merck precoated PLC plates (silica gel 60 GF_{254}, 0.5 mm) were used.

Dichloromethane and toluene were purchased from Kanto Chemical Co. Inc. as "Dehydrated" and further purified by passing through neutral alumina under nitrogen atmosphere. Diethyl ether and tetrahydrofuran were purchased from Kanto Chemical Co. Inc. as "Dehydrated". The commercially available aldehydes were distilled and stored under argon atmosphere at –17 °C. The commercially available secondary amines, acrylates and vinyltriphenylphosphonium bromide were purchased and used without further purification. Biphenyl-based dibromide (*S*)-**26**,[1] 3-cyclohexylpropanal,[2] 3-benzyloxypropanal,[3] 5-benzyloxypentanal,[4] 3-(pyridin-3-yl)propional,[5] cyclohexylacetaldehyde[6] and di-*t*-butyl 2-methylenemalonate[7] were synthesized according to literature procedure and used after purification by column chromatography. (*S*)-3,3'-Dibromo-6,6'-dimethoxy-2,2'-dimethyl-1,1'-biphenyl (*S*)-**19** was provided from Nippon Soda Co, Ltd.[8]

Synthesis and characterization of amino diol catalysts

Synthesis of (*S*)-3a and (*S*)-3b



Diester (*S*)-20: Dibromide (*S*)-**19**[8] (636 mg, 1.6 mmol), $Pd(OAc)_2$ (54 mg, 0.24 mmol), bis(diphenylphosphino)propane (dppp) (98 mg, 0.24 mmol) and *i*Pr_2NEt (1.2 mL, 6.9 mmol) in DMSO (15 mL) and MeOH (15 mL) were charged into autoclave under argon atmosphere. After pressurized with CO (6 atm), the mixture was heated to 100 °C with stirring for 72 h. After cooling to room temperature, the reaction mixture was poured into H_2O and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 4/1) to give (*S*)-**20**. [54% yield (306 mg)]. $[\alpha]_D^{27}$ –37.7 (*c* = 1.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (2H, d, *J* = 8.8 Hz, Ar-H), 6.83 (2H, d, *J* = 8.8 Hz, Ar-H), 3.87 (6H, s, CO_2CH_3), 3.72 (6H, s, OCH_3), 2.16 (6H, s, $ArCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 159.7, 141.0, 132.0, 127.0, 122.7, 107.6, 55.7, 51.6, 17.5; IR (neat) 2949, 1713, 1585, 1431, 1250, 1211, 1186, 1078, 783 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{20}H_{23}O_6$: 359.1489 ($[M + H]^+$), Found: 359.1491 ($[M + H]^+$).

Allylamine (*S*)-21: To a solution of diester (*S*)-**20** (306 mg, 0.85 mmol) in benzene (8.0 mL) were added *N*-bromosuccinimide (NBS) (365 mg, 2.1 mmol) and azobisisobutylonitrile (AIBN) (20 mg, 0.12 mmol) at room temperature. After 8 h of reflux, the mixture was cooled to room temperature. H_2O was added and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue containing the bromination product was used for the next step without further purifications.

To the mixture obtained above in tetrahydrofuran (9.0 mL) was added allylamine (260 μL, 3.5 mmol) at room temperature. After stirring for 20 h at 45 °C, the mixture was cooled to room temperature. H_2O was added and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and

then concentrated. The residue was purificated by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 5/3) to give (*S*)-**21**. [82% yield (287 mg)]. $[\alpha]_D^{29}$ 260.8 (*c* = 0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (2H, d, *J* = 8.8 Hz Ar-H), 6.96 (2H, d, *J* = 8.8 Hz, Ar-H), 6.02-5.92 (1H, m, CH=CH_2), 5.14 (1H, d, *J* = 3.2 Hz, CH=CHH), 5.10 (1H, s, CH=CHH), 4.84 (2H, d, *J* = 12.8 Hz, CHHN), 3.88 (6H, s, CO_2CH_3), 3.83 (6H, s, OCH_3), 3.38 (1H, dd, *J* = 13.6, 5.6 Hz, NCHHCH), 2.90 (1H, dd, *J* = 13.6, 7.2 Hz, NCHHCH), 2.83 (2H, d, *J* = 12.8 Hz, CHHN); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 159.0, 137.4, 136.5, 132.6, 126.6, 122.2, 116.9, 109.3, 58.9, 55.8, 51.9, 49.5; IR (neat) 2947, 1713, 1582, 1485, 1433, 1252, 1186, 1157, 1076, 920, 826, 787, 754 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{23}H_{26}NO_6$: 412.1755 ($[M + H]^+$), Found: 412.1751 ($[M + H]^+$).

Aminoalcohol (*S*)-22: To a solution of (*S*)-**21** (151 mg, 0.37 mmol) in diethyl ether (4.0 mL) was added a 1.9 M dibutyl ether solution of phenyllithium (1.2 mL, 2.3 mmol) at –78 °C. The mixture was stirred for 10 h at room temperature, and saturated aqueous NH_4Cl was then carefully added. After extraction with ethyl acetate, the organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 1/1) to give (*S*)-**22**. [88% yield (214 mg)]. $[\alpha]_D^{28}$ –131.7 (*c* = 0.98, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.15 (20H, m, Ar-H), 6.69 (2H, d, *J* = 8.4 Hz, Ar-H), 6.60 (2H, d, *J* = 8.8 Hz, Ar-H), 5.77-5.65 (1H, m, CH=CH_2), 4.84 (1H, d, *J* = 9.2 Hz, CH=CHH), 4.78 (1H, d, *J* = 16.8 Hz, CH=CHH), 3.87 (2H, d, *J* = 13.6 Hz, CHHN), 3.76 (6H, s, OCH_3), 3.19 (1H, dd, *J* = 13.6, 4.8 Hz, NCHHCH), 2.68 (2H, d, *J* = 13.2 Hz, CHHN), 2.51 (1H, dd, *J* = 13.4, 8.6 Hz, NCHHCH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 148.6, 147.3, 138.1, 136.2, 135.3, 130.5, 128.22, 128.20, 127.8, 127.7, 127.4, 126.9, 126.7, 117.1, 108.3, 82.7, 59.1, 55.7, 51.1; IR (neat) 1578, 1483, 1447, 1281, 1269, 1076, 1013, 910, 812, 758, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{45}H_{42}NO_4$: 660.3108 ($[M + H]^+$), Found: 660.3121 ($[M + H]^+$).

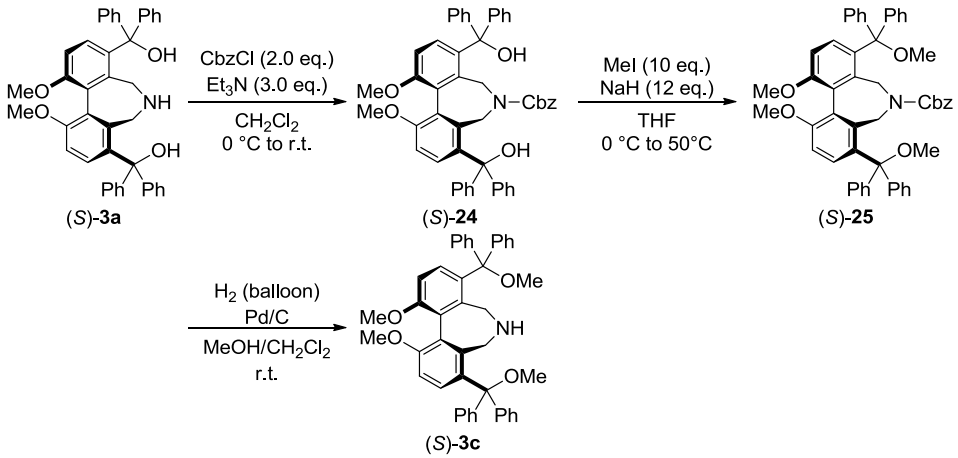
Aminoalcohol (*S*)-23: To a solution of (*S*)-**21** (90 mg, 0.22 mmol) in diethyl ether (4.0 mL) was added a 0.67 M ether/pentane solution of 3,5-difluorophenyllithium (4.5 mL, 3.0 mmol) at –78 °C. The mixture was stirred for 3 h at 0 °C, and saturated aqueous NH_4Cl was then carefully added. After extraction with ethyl acetate, the organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 4/1) to give (*S*)-**12**. [82% yield (144.2 mg)]. $[\alpha]_D^{18}$ –115.5 (*c* 1.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94-6.79 (8H, m, Ar-H), 6.79-6.65 (4H, m, Ar-H), 6.76 (2H, d, *J* = 8.8 Hz, Ar-H), 6.64 (2H, d, *J* = 8.8 Hz, Ar-H), 5.80-5.67 (1H, m, CH=CH_2), 5.00 (1H, d, *J* = 10.0 Hz, CH=CHH), 4.87 (1H, d, *J* = 17.6 Hz, CH=CHH), 3.80 (6H, s, OCH_3), 3.66 (2H, d, *J* = 13.6 Hz, CHHN), 3.32 (1H, dd, *J* = 12.8, 4.4 Hz, NCHHCH), 2.67 (2H, d, *J* = 13.2 Hz, CHHN), 2.61 (1H, dd, *J* = 13.0, 8.6 Hz, NCHHCH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.81 (dd, $J_{C\text{-}F}$ = 250.3, 9.9 Hz), 162.79 (dd, $J_{C\text{-}F}$ = 250.3, 9.9 Hz), 156.6, 151.8 (t, $J_{C\text{-}F}$ = 7.4 Hz), 150.0 (t, $J_{C\text{-}F}$ = 8.3 Hz), 135.48, 135.45, 134.6, 130.3, 128.4, 118.0, 111.2 (d, $J_{C\text{-}F}$ = 26.4 Hz), 110.3 (d, $J_{C\text{-}F}$ = 26.3

Hz), 108.9, 102.9 (t, $J_{C\text{-}F}$ = 25.5 Hz, two peaks overlap), 81.7, 59.6, 55.7, 51.0; IR (neat) 1620, 1597, 1435, 1302, 1119, 1078, 982, 847, 735 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{45}H_{34}F_8NO_4$: 804.2355 ($[M + H]^+$), Found: 804.2357 ($[M + H]^+$).

Aminoalcohol (*S*)-3a: A mixture of (*S*)-**22** (240 mg, 0.36 mmol), *N*,*N*-dimethylbarbituric acid (NDMBA) (256 mg, 1.6 mmol), $Pd(OAc)_2$ (9.5 mg, 0.042 mmol), and triphenylphosphine (43 mg, 0.16 mmol) in CH_2Cl_2 (4.0 mL) was stirred at 35 °C for 15 h under argon atmosphere. After addition of saturated aqueous $NaHCO_3$, the mixture was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 1/2) to give (*S*)-**5**. [90% yield (200 mg)]. $[\alpha]_D^{29}$ –71.6 (*c* = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.20 (20H, m, Ar-H), 6.72 (2H, d, *J* = 8.8 Hz, Ar-H), 6.64 (2H, d, *J* = 8.8 Hz, Ar-H), 3.88 (2H, d, *J* = 12.8 Hz, CHHN), 3.79, (6H, s, OCH_3), 2.77 (2H, d, *J* = 12.8 Hz, CHHN); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 148.2, 147.4, 137.6, 136.2, 130.5, 128.0, 127.9, 127.82, 127.80, 127.7, 127.0, 126.9, 108.4, 82.7, 55.7, 44.6; IR (neat) 1580, 1485, 1447, 1273, 1084, 908, 812, 758, 732, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{42}H_{38}NO_4$: 620.2795 ($[M + H]^+$), Found: 620.2792 ($[M + H]^+$).

Aminoalcohol (*S*)-3b: (*S*)-**3b** was prepared in a similar manner as described above using (*S*)-**23** instead of (*S*)-**22** [89% yield]. $[\alpha]_D^{18}$ –100.8 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93-6.68 (12H, m, Ar-H), 6.77 (2H, d, *J* = 9.2 Hz, Ar-H), 6.63 (2H, d, *J* = 8.8 Hz, Ar-H), 3.81 (6H, s, OCH_3), 3.79 (2H, d, *J* = 13.2 Hz, CHHN), 2.83 (2H, d, *J* = 13.2 Hz, CHHN); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (dd, $J_{C\text{-}F}$ = 250.2, 12.3 Hz), 162.7 (dd, $J_{C\text{-}F}$ = 250.2, 12.3 Hz), 156.5, 151.3 (t, $J_{C\text{-}F}$ = 7.4 Hz), 150.5 (t, $J_{C\text{-}F}$ = 7.8 Hz), 135.6, 135.1, 130.4, 128.0, 111.0 (d, $J_{C\text{-}F}$ = 26.3 Hz), 110.6 (d, $J_{C\text{-}F}$ = 25.5 Hz), 109.0, 103.1 (t, $J_{C\text{-}F}$ = 25.5 Hz), 103.0 (t, $J_{C\text{-}F}$ = 25.5 Hz), 81.9, 55.7, 44.5; IR (neat) 1620, 1597, 1435, 1302, 1277, 1119, 1088, 980, 847 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{42}H_{30}F_8NO_4$: 764.2042 ($[M + H]^+$), Found: 764.2031 ($[M + H]^+$).

Synthesis of (*S*)-3c



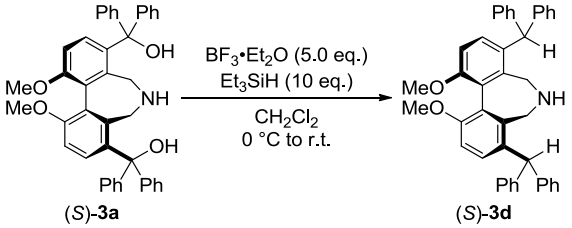
Aminoalcohol (*S*)-24: To a solution of (*S*)-**3a** (50 mg, 0.081 mmol) and triethylamine (35 μL, 0.25 mmol) in CH_2Cl_2 (2.0 mL) was added benzyl chloroformate (24 μL, 0.17 mmol) at 0 °C. After stirring for 3 h at room temperature, saturated aqueous $NaHCO_3$ was then carefully added. After extraction with ethyl acetate, the organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 3/1) to give (*S*)-**24**. [78% yield (48 mg)]. $[\alpha]_D^{31}$ –219.8 (*c* 0.80, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.05 (25H, m, Ar-H), 6.78-6.62 (4H, m, Ar-H), 5.41 (1H, s, OH), 5.27 (1H, d, *J* = 13.2 Hz, CHHN), 4.94 (1H, d, *J* = 12.8 Hz, CHHPh), 4.92 (1H, d, *J* = 14.8 Hz, CHHN), 4.70 (1H, d, *J* = 12.4 Hz, CHHPh), 3.77 (3H, s, OCH_3), 3.74 (3H, s, OCH_3), 3.25 (1H, d, *J* = 13.6 Hz, CHHN), 3.09 (1H, d, *J* = 14.8 Hz, CHHN), 3.07 (1H, s, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 156.3, 155.4, 149.3, 147.3, 146.9, 146.7, 137.7, 137.3, 136.1, 134.2, 133.4, 131.4, 130.8, 129.1, 128.30, 128.27, 127.91, 127.87, 127.76, 127.6, 127.53, 127.51, 127.2, 127.13, 127.11, 127.0, 126.4, 108.9, 108.7, 82.4, 81.0, 67.4, 55.7, 55.6, 43.8, 43.5 (Three peaks are overlapped); IR (neat) 3416, 1663, 1582, 1483, 1431, 1269, 1219, 1082, 908, 733, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{50}H_{43}NNaO_6$: 776.2983 ($[M + Na]^+$), Found: 776.2968 ($[M + Na]^+$).

Amine (*S*)-25: To a suspension of sodium hydride (60% w/w in oil, 40 mg, 1.0 mmol) in tetrahydrofuran (4.0 mL) was added amino alcohol (*S*)-**24** (75 mg, 0.10 mmol) at 0 °C. The mixture was stirred for 2 h at 50 °C. Iodomethane (65 μL, 1.0 mmol) was then added to the mixture at 50 °C. After 5 h of sttiring at 50 °C, the mixtue was diluted with ether at 0 °C, and saturated aqueous NH_4Cl was added carefully. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 4/1) to give (*S*)-**25**. [99% yield (78 mg)]. $[\alpha]_D^{32}$ –168.5 (*c* 1.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.27 (13H, m, Ar-H), 7.24-6.96 (14H, m, Ar-H), 6.83 (2H, d, *J* = 8.8 Hz, Ar-H), 5.28 (1H, d, *J* = 13.6 Hz, CHHN), 5.06 (1H, d, *J* = 14.0 Hz, CHHN), 4.96 (1H, d, *J* = 12.8 Hz, CHHPh), 4.68 (1H, d, *J* = 12.4 Hz, CHHPh), 3.79 (6H, s, OCH_3), 3.02 (3H, s, OCH_3), 3.01 (3H, s, OCH_3), 3.07-2.95 (2H, m, CHHNCHH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 156.4, 153.5, 144.8, 144.5, 137.3, 135.5, 135.4, 132.5, 132.2, 131,9, 131.5, 128.5, 128.2, 128.10, 128.06, 128.01, 127.8, 127.72, 127.67, 127.63, 127.5, 126.8, 126.3, 126.2, 126.1, 108.4, 87.7, 87.6, 66.6, 55.71, 55.69, 53.1, 53.0, 43.1, 42.9 (Six peaks are overlapped); IR (neat) 2938, 1692, 1582, 1420, 1267, 1219, 1072, 733, 698 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{52}H_{47}NNaO_6$: 804.3296 ($[M + Na]^+$), Found: 804.3310 ($[M + Na]^+$).

Amine (*S*)-3c: To a solution of (*S*)-**25** (21 mg, 0.027 mmol) in methanol (2 mL) and CH_2Cl_2 (1 mL) was added palladium on carbon (5 mg) at room temperature. Hydrogen gas (balloon) was then charged to the reaction flask and the mixture was stirred for 16 h at room temperature. The reaction mixture was filtered through Celite with ethyl acetate and concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 2/1) to give (*S*)-**3c**. [86% yield (15 mg)].

$[\alpha]_D^{30}$ –56.8 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50-7.28 (10H, m, Ar-H), 7.28-7.00 (12H, m, Ar-H), 6.81 (2H, d, *J* = 9.2 Hz, Ar-H), 3.81 (6H, s, OCH_3), 3.76 (2H, d, *J* = 12.4 Hz, CHHN), 3.20 (6H, s, OCH_3), 2.76 (2H, d, *J* = 12.4 Hz, CHHN); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 147.3, 145.4, 138.4, 131.9, 130.9, 128.2, 127.8 (two peaks overlap), 127.7, 127.0, 126.4, 126.1, 107.7, 88.0, 55.7, 53.6, 44.4; IR (neat) 2934, 1580, 1483, 1449, 1271, 1072, 908, 733, 705 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{44}H_{42}NO_4$: 648.3108 ($[M + H]^+$), Found: 648.3086 ($[M + H]^+$).

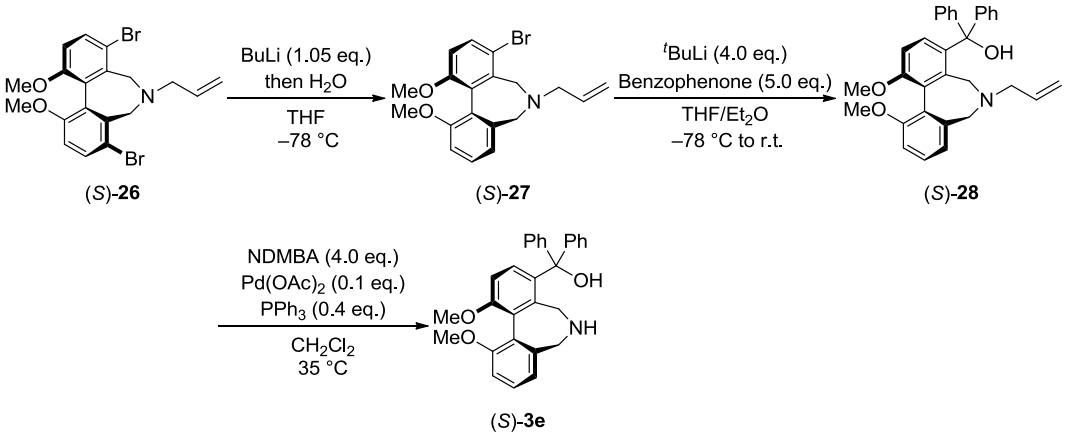
Synthesis of (*S*)-3d



(*S*)-**3a** (*S*)-**3d**

Amine (*S*)-3d: A mixture of (*S*)-**3a** (15 mg, 0.024 mmol), $BF_3 \cdot Et_2O$ (15 μL, 0.12 mmol) triethylsilane (38 μL, 0.24 mmol) in CH_2Cl_2 (0.50 mL) was stirred for 16 h at room temperature under argon atmosphere. After addition of triethylamine (50 μL, 0.36 mmol), the mixture was filtered through a pad of Celite, and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 2/1) to give (*S*)-**3d**. [54% yield (7.5 mg)]. $[\alpha]_D^{32}$ –62.3 (*c* 0.75, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.16 (12H, m, Ar-H), 7.13-7.04 (8H, m, Ar-H), 6.81 (2H, d, *J* = 8.8 Hz, Ar-H), 6.78 (2H, d, *J* = 8.8 Hz, Ar-H), 5.80 (2H, s, Ph_2CH), 3.78 (6H, s, OCH_3), 3.77 (2H, d, *J* = 12.4 Hz, CHHN), 2.91 (2H, d, *J* = 12.4 Hz, CHHN); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 144.6, 143.7, 133.5, 130.32, 130.31, 129.6, 129.5, 128.4, 128.2, 126.7, 126.4, 126.2, 109.5, 55.7, 53.0, 43.4; IR (neat) 2934, 1582, 1483, 1265, 1084, 9.8, 731, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{42}H_{38}NO_2$: 588.2897 ($[M + H]^+$), Found: 588.2878 ($[M + H]^+$).

Synthesis of (*S*)-3e



(*S*)-**26** (*S*)-**27** (*S*)-**28** (*S*)-**3e**

Monobromide (*S*)-27: To a solution of (*S*)-**26**[1] (453 mg, 1.0 mmol) in tetrahydrofuran (8.0 mL) was added a 1.6 M hexane solution of butyllithium (625 μL, 1.0 mmol) at –78 °C. The mixture was stirred for 1 h at –78 °C, and H_2O was then added. After extraction with ethyl acetate, the organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue containing the product was used for the next step without further purifications. [99% yield (374 mg)]. $[\alpha]_D^{33}$ 74.7 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (1H, d, *J* = 9.2 Hz, Ar-H), 7.34 (1H, dd, *J* = 8.4, 7.6 Hz, Ar-H), 6.97 (1H, d, *J* = 8.0 Hz, Ar-H), 6.95 (1H, d, *J* = 7.6 Hz, Ar-H), 6.85 (1H, d, *J* = 8.8 Hz, Ar-H), 6.03-5.92 (1H, m, CH=CH_2), 5.25 (1H, dd, *J* = 13.2, 1.6 Hz, CH=CHH), 5.17 (1H, dd, *J* = 10.2, 1.8 Hz, CH=CHH), 4.13 (1H, d, *J* = 12.8 Hz, CHHN), 3.82 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.61 (1H, d, *J* = 12.0 Hz, CHHN), 3.34 (1H, dd, *J* = 13.6, 6.4 Hz, NCHHCH), 3.09-2.96 (3H, m, $N(CHH)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 155.9, 136.1, 136.0, 135.2, 132.3, 129.1, 127.6, 125.0, 121.6, 117.6, 115.6, 112.0, 110.6, 58.7, 56.0, 55.8, 54.5, 53.8; IR (neat) 2934, 1460, 1263, 1086, 1061, 918, 804, 750 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{19}H_{21}BrNO_2$: 374.0750 ($[M + H]^+$), Found: 374.0756 ($[M + H]^+$).

Aminoalcohol (*S*)-28: To a solution of (*S*)-**27** (113 mg, 0.30 mmol) in diethyl ether (2.0 mL) and tetrahydrofuran (1.0 mL) was added a 1.6 M pentane solution of *tert*-butyllithium (760 μL, 1.2 mmol) at –78 °C. After 2 h of stirring, a solution of benzophenone (278 mg, 1.5 mmol) in tetrahydrofuran (1.0 mL) was added at –78 °C. The mixture was stirred for 16 h at room temperature, and saturated aqueous NH_4Cl was then carefully added. After extraction with ethyl acetate, the organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate = 3/1) to give (*S*)-**28**. [43% yield (62 mg)]. $[\alpha]_D^{32}$ –189.1 (*c* 1.37, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (2H, d, *J* = 7.2 Hz, Ar-H), 7.42-7.16 (9H, m, Ar-H), 7.01 (1H, d, *J* = 8.0 Hz, Ar-H), 6.78 (1H, d, *J* = 6.8 Hz, Ar-H), 6.71 (1H, d, *J* = 8.8 Hz, Ar-H), 6.58 (1H, d, *J* = 8.8 Hz, Ar-H), 5.90-5.77 (1H, m, CH=CH_2), 5.06 (1H, d, *J* = 16.4 Hz, CH=CHH), 5.05 (1H, d, *J* = 11.2 Hz, CH=CHH), 3.88 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 3.53 (1H, d, *J* = 11.6 Hz, CHHN), 3.49 (1H, d, *J* = 14.0 Hz, CHHN), 3.38 (1H, d, *J* = 14.0 Hz, CHHN), 3.01 (1H, dd, *J* = 13.2, 6.8 Hz, NCHHCH), 2.81 (1H, dd, *J* = 13.6, 6.4 Hz, NCHHCH), 2.23 (1H, d, *J* = 11.6 Hz, CHHN); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 155.5, 149.0, 147.2, 139.3, 135.8, 135.4, 133.6, 130.03, 130.01, 128.8, 128.6, 127.7, 127.6, 127.5, 126.7, 126.6, 125.5, 122.1, 118.0, 111.2, 108.8, 82.8, 57.6, 56.0, 55.5, 53.5, 51.8; IR (neat) 3291, 2833, 1576, 1487, 1265, 1084, 754, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{32}H_{32}NO_3$: 478.2377 ($[M + H]^+$), Found: 478.2363 ($[M + H]^+$).

Aminoalcohol (*S*)-3e: (*S*)-**3e** was prepared in a similar manner as described above using (*S*)-**28** instead of (*S*)-**22** [67% yield]. $[\alpha]_D^{30}$ –129.3 (*c* 0.45, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (2H, d, *J* = 7.2 Hz, Ar-H), 7.39-7.19 (9H, m, Ar-H), 7.00 (1H, d, *J* = 8.4 Hz, Ar-H), 6.87 (1H, d, *J* = 7.6 Hz, Ar-H), 6.72 (1H, d, *J* = 8.8 Hz, Ar-H), 6.61 (1H, d, *J* = 8.4 Hz, Ar-H), 3.87 (3H, s, OCH_3), 3.80 (1H, d, *J* = 12.0 Hz, CHHN),

3.76 (3H, s, OC$\underline{H}_3$), 3.64 (1H, d, *J* = 13.6 Hz, C$\underline{H}$HN), 3.30 (1H, d, *J* = 13.6 Hz, CH$\underline{H}$N), 2.94 (1H, d, *J* = 12.0 Hz, CH$\underline{H}$N); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 155.6, 148.8, 147.5, 138.6, 137.3, 135.6, 130.4, 129.4, 128.4, 127.8, 127.7, 127.6, 126.8, 126.7, 125.4, 120.7, 111.1, 108.65, 108.63, 82.7, 56.0, 55.5, 48.3, 44.4; IR (neat) 3308, 2934, 1576, 1474, 1261, 1086, 1015, 908, 756, 731, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{29}H_{28}NO_3$: 438.2064 ([M + H]$^+$), Found: 438.2063 ([M + H]$^+$).

Typical procedure for the organocatalytic conjugate addition to di-*t*-butyl methylenemalonate (1)

A mixture of di-*t*-butyl methylenemalonate (**1**) (30.5 mg, 0.13 mmol) and 3-phenylpropanal (53 μL, 0.40 mmol) in diethyl ether (1.3 mL) was stirred at 0 °C. To the mixture was then added (*S*)-**3a** (8.3 mg, 0.013 mmol). After stirring for 4 h at 0 °C, MeOH (1.0 mL) and sodium borohydride (50 mg) were added successively. After 0.5 h of vigorous stirring at room temperature, saturated aqueous NH_4Cl was added. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 3/1) to give di-*t*-butyl (*R*)-2-(2-benzyl-3-hydroxypropyl)malonate. [94% yield (45.6 mg)].

Di-*t*-butyl (*R*)-2-(2-benzyl-3-hydroxypropyl)malonate (Table1, entry 6): $[\alpha]_D^{23}$ 10.4 (*c* = 1.22, $CHCl_3$; 95% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.24 (2H, m, Ar-$\underline{H}$), 7.22-7.14 (3H, m, Ar-$\underline{H}$), 3.52 (1H, ddd, *J* = 11.2, 4.8, 4.8 Hz, HOC$\underline{H}$HCH), 3.44 (1H, ddd, *J* = 11.2, 5.6, 5.6 Hz, HOCH$\underline{H}$CH), 3.29 (1H, app t, *J* = 7.2 Hz, $CH_2C\underline{H}(CO_2t\text{-}Bu)_2$), 2.67 (1H, dd, *J* = 14.0, 7.6 Hz, C$\underline{H}$HPh), 2.61 (1H, dd, *J* = 14.0, 6.4 Hz, CH$\underline{H}$Ph), 2.01-1.78 (4H, m, $CH_2C\underline{H}C\underline{H}_2CH$, OH), 1.46 (9H, s, C(C$\underline{H}_3$)$_3$), 1.43 (9H, s, C(C$\underline{H}_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 169.1, 140.1, 129.2, 128.3, 126.0, 81.63, 81.56, 63.7, 51.9, 41.0, 37.7, 29.6, 27.9, 27.8; IR (neat) 2978, 1724, 1368, 1254, 1140, 1032, 847, 745, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{21}H_{32}NaO_5$: 387.2142 ([M + Na]$^+$), Found: 387.2127 ([M + Na]$^+$); HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 20/1, flow rate = 0.5 mL/min, λ = 209 nm, retention time; t_R(minor) = 15.8 min, t_R(major) = 20.8 min.

Di-*t*-butyl (*S*)-2-(3-hydroxy-2-methylpropyl)malonate (Table1, entry 9): $[\alpha]_D^{31}$ –6.92 (*c* = 1.12, $CHCl_3$; 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.47 (2H, dd, *J* = 4.4, 4.4 Hz, HOC$\underline{H}_2$CH), 3.27 (1H, dd, *J* = 8.2, 6.2 Hz, $CH_2C\underline{H}(CO_2t\text{-}Bu)_2$), 1.96 (1H, m, $HOCH_2C\underline{H}$), 1.74-1.61 (3H, m, CHC$\underline{H}_2$CH, OH), 1.46 (18H, s, C(C$\underline{H}_3$)$_3$), 0.95 (3H, d, *J* = 6.4 Hz, CHC$\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 169.1, 81.54, 81.51, 67.4, 51.8, 34.1, 31.8, 27.9 (two peaks overlap), 16.6; IR (neat) 2975, 1723, 1456, 1367, 1252, 1141, 1034, 984, 989, 843 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{15}H_{28}NaO_5$: 311.1829 ([M + Na]$^+$), Found: 311.1844 ([M + Na]$^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding benzoate ester. HPLC analysis: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 100/1, flow rate = 0.5 mL/min, λ = 227 nm, retention time; t_R(major) = 14.7 min, t_R(minor) = 17.5 min.

Di-*t*-butyl (*S*)-2-(2-(hydroxymethyl)hexyl)malonate (Table1, entry 11): $[\alpha]_D^{30}$ 4.66 (*c* = 0.98, $CHCl_3$; 94% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (1H, d, *J* = 11.6 Hz, HOC<u>H</u>HCH), 3.47 (1H, d, *J* = 11.2 Hz, HOCH<u>H</u>CH), 3.28 (1H, app t, *J* = 7.0 Hz, $CH_2C\underline{H}(CO_2t\text{-}Bu)_2$), 1.95-1.75 (3H, m, C<u>H</u>C<u>H</u>$_2$CH), 1.46 (18H, s, C(C<u>H</u>$_3$)$_3$), 1.35-1.22 (6H, m, CH_2), 0.90 (3H, t, *J* = 7.0 Hz, $CH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 169.3, 81.6 (two peaks overlap), 64.9, 51.9, 38.9, 30.9, 29.9, 29.1, 27.9 (two peaks overlap), 22.9, 14.0; IR (neat) 3464, 2930, 1726, 1456, 1368, 1254, 1140, 1042, 847 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{18}H_{34}NaO_5$: 353.2298 ([M + Na]$^+$), Found: 353.2284 ([M + Na]$^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding benzoate ester. HPLC analysis: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 200/1, flow rate = 0.2 mL/min, λ = 227 nm, retention time; t_R(major) = 40.0 min, t_R(minor) = 45.1 min.

Di-*t*-butyl (*S*)-2-(2-(hydroxymethyl)octyl)malonate (Table1, entry 12): $[\alpha]_D^{29}$ 5.07 (*c* = 0.76, $CHCl_3$; 94% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (1H, dd, *J* = 11.2, 4.4 Hz, HOC<u>H</u>HCH), 3.46 (1H, dd, *J* = 11.2, 6.0 Hz, HOCH<u>H</u>CH), 3.28 (1H, app t, *J* = 7.2 Hz, $CH_2C\underline{H}(CO_2t\text{-}Bu)_2$), 1.93-1.78 (3H, m, C<u>H</u>C<u>H</u>$_2$CH), 1.46 (18H, s, C(C<u>H</u>$_3$)$_3$), 1.37-1.22 (10H, br, CH_2), 0.88 (3H, t, *J* = 6.0 Hz, $CH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.40, 169.36, 81.58, 81.56, 64.9, 51.9, 38.9, 31.8, 31.2, 29.9, 29.5, 27.9 (two peaks overlap), 26.9, 22.6, 14.1; IR (neat) 2927, 1723, 1457, 1368, 1249, 1134, 1038, 840, 781, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{20}H_{38}NaO_5$: 381.2611 ([M + Na]$^+$), Found: 381.2623 ([M + Na]$^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding benzoate ester. HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 200/1, flow rate = 0.5 mL/min, λ = 227 nm, retention time; t_R(major) = 18.8 min, t_R(minor) = 20.6 min.

Di-*t*-butyl (*R*)-2-(3-cyclohexyl-2-(hydroxymethyl)propyl)malonate (Table1, entry 13): $[\alpha]_D^{30}$ 6.69 (*c* = 0.53, $CHCl_3$; 86% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (1H, dd, *J* = 11.2, 4.4 Hz, HOC<u>H</u>HCH), 3.43 (1H, dd, *J* = 11.6, 5.2 Hz, HOCH<u>H</u>CH), 3.29 (1H, app t, *J* = 7.4 Hz, $CH_2C\underline{H}(CO_2t\text{-}Bu)_2$), 1.91-1.79 (3H, m, $CH_2C\underline{H}C\underline{H}_2CH$), 1.73-1.64 (5H, m, Cy), 1.46 (18H, s, C(C<u>H</u>$_3$)$_3$), 1.27-1.05 (6H, m, Cy), 0.87 (2H, m, CHC<u>H</u>$_2$Cy); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 169.4, 81.58, 81.56, 65.1, 51.8, 39.1, 35.7, 34.8, 33.60, 33.58, 30.2, 27.92, 27.90, 26.6, 26.29, 26.27; IR (neat) 2920, 1722, 1449, 1367, 1254, 1136, 1021, 849, 762, 690 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{21}H_{38}NaO_5$: 393.2611 ([M + Na]$^+$), Found: 393.2606 ([M + Na]$^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding benzoate ester. HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 100/1, flow rate = 0.3 mL/min, λ = 227 nm, retention time; t_R(major) = 16.7 min, t_R(minor) =18.5 min.

Di-*t*-butyl (*S*)-2-(3-(benzyloxy)-2-(hydroxymethyl)propyl)malonate (Table1, entry 14): $[\alpha]_D^{31}$ –7.00 (*c* = 0.97, $CHCl_3$; 93% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (5H, m, Ar-<u>H</u>), 4.51 (2H, s, OC<u>H</u>$_2$Ph), 3.74-3.62 (2H, m, C<u>H</u>$_2$OCH$_2$Ph), 3.60 (1H, dd, *J* = 9.2, 3.6 Hz, HOC<u>H</u>HCH), 3.49 (1H, dd, *J* = 9.2, 6.0 Hz,

HOCHHCH), 3.26 (1H, app t, J = 7.4 Hz, $CH_2CH(CO_2t\text{-}Bu)_2$), 2.48 (1H, t, J = 5.6 Hz, OH), 1.96-1.79 (3H, m, $CHCH_2CH$), 1.45 (18H, s, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.91, 168.88, 138.0, 128.4, 127.7, 127.6, 81.61, 81.57, 73.4, 72.9, 64.7, 51.8, 38.8, 27.9 (two peaks overlap), 27.0; IR (neat) 2978, 1722, 1454, 1368, 1254, 1140, 847, 739, 698 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{22}H_{34}NaO_6$: 417.2248 ([M + Na]$^+$), Found: 417.2254 ([M + Na]$^+$); HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL/min, λ = 208 nm, retention time; t_R(minor) = 30.8 min, t_R(major) = 33.2 min.

Di-*t*-butyl (*S*)-2-(5-(benzyloxy)-2-(hydroxymethyl)pentyl)malonate (Table1, entry 15): $[\alpha]_D^{33}$ –0.67 (*c* = 0.92, $CHCl_3$; 95% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.32 (4H, m, Ar-H), 7.26-7.25 (1H, br, Ar-H), 4.49 (2H, s, OCH_2Ph), 3.54 (1H, dd, J = 11.0, 6.2 Hz, HOCHHCH), 3.51-3.44 (1H, m, HOCHHCH), 3.47 (2H, t, J = 6.4 Hz, CH_2OCH_2Ph), 3.28 (1H, app t, J = 7.4 Hz, $CH_2CH(CO_2t\text{-}Bu)_2$), 1.96-1.79 (3H, m, $CHCH_2CH$), 1.70-1.61 (2H, m, CH_2), 1.45 (18H, s, $C(CH_3)_3$), 1.42-1.32 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3 (two peaks overlap), 138.5, 128.4, 127.6, 127.5, 81.61, 81.58, 73.0, 70.5, 64.6, 51.8, 38.8, 29.8, 27.9 (two peaks overlap), 27.7, 27.0; IR (neat) 2868, 1723, 1455, 1367, 1254, 1140, 900, 838, 731 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{24}H_{38}NaO_6$: 445.2561 ([M + Na]$^+$), Found: 445.2565 ([M + Na]$^+$); HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 20/1, flow rate = 0.5 mL/min, λ = 208 nm, retention time; t_R(minor) = 20.6 min, t_R(major) = 22.6 min.

1,1-Di-*t*-butyl 4-methyl (*R*)-3-(hydroxymethyl)butane-1,1,4-tricarboxylate (Table1, entry 16): $[\alpha]_D^{31}$ –0.68 (*c* = 0.93, $CHCl_3$; 86% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (3H, s, CO_2CH_3), 3.64-3.48 (2H, m, $HOCH_2CH$), 3.26 (1H, app t, J = 7.4 Hz, $CH_2CH(CO_2t\text{-}Bu)_2$), 2.46 (1H, dd, J = 15.6, 7.6 Hz, $CHHCO_2CH_3$), 2.36 (1H, dd, J = 16.0, 5.6 Hz, $CHHCO_2CH_3$), 2.18 (1H, t, J = 6.2 Hz, OH), 2.10-2.01 (1H, m, $HOCH_2CHCH_2$), 2.00-1.87 (1H, m, CHCHHCH), 1.85-1.76 (1H, m, CHCHHCH), 1.46 (18H, s, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 169.0, 168.8, 81.85, 81.78, 64.4, 51.8, 51.7, 36.4, 36.0, 29.6, 27.9 (two peaks overlap); IR (neat) 3539, 2978, 1724, 1439, 1369, 1254, 1140, 847, 745 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{17}H_{30}NaO_7$: 369.1884 ([M + Na]$^+$), Found: 369.1872 ([M + Na]$^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding 4-benzoate ester. HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 254 nm, retention time; t_R(minor) = 18.4 min, t_R(major) =20.5 min.

Di-*t*-butyl (*R*)-2-(3-(((benzyloxy)carbonyl)amino)-2-(hydroxymethyl)propyl)malonate (Table1, entry 17): $[\alpha]_D^{30}$ –15.2 (*c* = 1.19, $CHCl_3$; 84% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.28 (5H, m, Ar-H), 5.28 (1H, br, $CONHCH_2$), 5.11 (2H, s, CO_2CH_2Ph), 3.61-3.50 (1H, m, CONHCHHCH), 3.48-3.28 (3H, m, $CONHCHHCHCH_2OH$), 3.23 (1H, app t, J = 7.2 Hz, $CH_2CH(CO_2t\text{-}Bu)_2$), 3.17-3.07 (1H, m, $HOCH_2CHCH_2$), 1.75 (1H, dd, J = 7.2, 7.2 Hz, $CHCH_2CH$), 1.454 (9H, s, $C(CH_3)_3$), 1.451 (9H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 168.9, 157.8, 136.3, 128.5, 128.2, 128.1, 81.90, 81.87, 67.0, 62.0,

51.9, 40.7, 39.9, 27.9 (two peaks over lap), 26.8; IR (neat) 3391, 2976, 1719, 1524, 1368, 1252, 1140, 847, 741 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{23}H_{35}NNaO_7$: 460.2306 ([M + Na]$^+$), Found: 460.2291 ([M + Na]$^+$); HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 208 nm, retention time; t_R(minor) = 20.8 min, t_R(major) = 23.7 min.

Di-*t*-butyl (*R*)-2-(3-hydroxy-2-(pyridine-3-ylmethyl)propyl)malonate (Table1, entry 18): $[\alpha]_D^{32}$ 1.57 (*c* = 0.93, $CHCl_3$; 93% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (1H, s, Ar-H), 8.46 (1H, d, *J* = 5.8 Hz, Ar-H), 7.78 (1H, d, *J* = 8.0 Hz, Ar-H), 7.42 (1H, dd, *J* = 7.8, 5.8 Hz, Ar-H), 3.52-3.38 (2H, m, HOCH_2CH), 3.27 (1H, app t, *J* = 7.0 Hz, $CH_2CH(CO_2t\text{-Bu})_2$), 2.82 (1H, dd, *J* = 14.0, 8.4 Hz, CHHAr), 2.69 (1H, dd, *J* = 14.0, 6.0 Hz, CHHAr), 2.02-1.92 (2H, m, CH_2CHCH_2, OH), 1.87-1.77 (2H, m, CHCH_2CH), 1.47 (9H, s, C(CH_3)$_3$), 1.45 (9H, s, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 168.7, 148.0, 145.3, 139.8, 138.3, 124.9, 82.2, 82.0, 62.2, 51.8, 40.4, 34.5, 29.3, 27.9 (two peaks overlap); IR (neat) 3522, 2978, 2371, 1721, 1369, 1254, 1161, 1140, 845, 745 cm^{-1}; HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 208 nm, retention time; t_R(minor) = 16.1 min, t_R(major) =19.0 min.

Di-*t*-butyl (*R*)-2-(2-(hydroxymethyl)-3-methylbutyl)malonate (Table1, entry 19): $[\alpha]_D^{30}$ 12.3 (*c* = 1.12, $CHCl_3$; 97% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (1H, ddd, *J* = 11.6, 5.8, 5.8 Hz, HOCHHCH), 3.54 (1H, ddd, *J* = 11.6, 5.8, 5.8 Hz, HOCHHCH), 3.30 (1H, dd, *J* = 8.6, 6.6 Hz, $CH_2CH(CO_2t\text{-Bu})_2$), 1.95-1.72 (4H, m, $(CH_3)_2CHCHCH_2$), 1.46 (18H, s, C(CH_3)$_3$), 0.93 (3H, d, *J* = 3.2 Hz, CHCH_3), 0.91 (3H, d, *J* = 3.2 Hz, CHCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 169.3, 81.6, 81.5, 63.6, 52.5, 44.7, 28.7, 27.9 (two peaks overlap), 27.2, 19.9, 19.3; IR (neat) 2957, 1721, 1457, 1367, 1253, 1137, 842, 781 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{17}H_{32}NaO_5$: 339.2142 ([M + Na]$^+$), Found: 339.2140 ([M + Na]$^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding 4-nitrobenzoate ester. HPLC analysis: Daicel Chiralpak AS-H, hexane/*i*-PrOH = 40/1, flow rate = 0.2 mL/min, λ = 254 nm, retention time; t_R(minor) = 25.3 min, t_R(major) =26.4 min.

Di-*t*-butyl (*R*)-2-(2-cyclohexyl-3-hydroxypropyl)malonate (Table1, entry 20): $[\alpha]_D^{30}$ 9.73 (*c* = 1.32, $CHCl_3$; 94% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 (1H, ddd, *J* = 10.8, 5.4, 5.4 Hz, HOCHHCH), 3.54 (1H, ddd, *J* = 10.8, 5.4, 5.4 Hz, HOCHHCH), 3.29 (1H, dd, *J* = 8.4, 6.8 Hz, $CH_2CH(CO_2t\text{-Bu})_2$), 1.97-1.88 (1H, m, $HOCH_2CH$), 1.86-1.78 (2H, m, CHCH_2CH), 1.77-1.61 (5H, m, Cy), 1.464 (9H, s, C(CH_3)$_3$), 1.461 (9H, s, C(CH_3)$_3$), 1.35-1.00 (6H, m, Cy); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 169.3, 81.6, 81.5, 63.4, 52.5, 44.3, 39.2, 30.2, 29.9, 27.9 (two peaks overlap), 27.5, 26.7, 26.7, 26.6; IR (neat) 2924, 1726, 1368, 1254, 1140, 1040, 847, 745 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{20}H_{36}NaO_5$: 379.2455 ([M + Na]$^+$), Found: 379.2448 ([M + Na]$^+$); HPLC analysis: Daicel Chiralpak IC, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 217 nm, retention time; t_R(major) = 17.0 min, t_R(minor) = 27.6 min.

Typical procedure for organocatalytic conjugate addition to 1,1,1,3,3,3-hexafluoropropan-2-yl acrylate(2)

A mixture of 1,1,1,3,3,3-hexafluoropropan-2-yl acrylate (**2**) (83 μL, 0.50 mmol) and 3-phenylpropanal (6.5 μL, 0.049 mmol) in diethyl ether (2.0 mL) was stirred at 15 °C. To the mixture was then added (*S*)-**3b** (3.8 mg, 5.0 μmol). After stirring for 24 h at 15 °C, MeOH (1.0 mL) and sodium borohydride (20 mg, 0.53 mmol) were added successively. After 0.5 h of vigorous stirring at room temperature, saturated NH_4Cl was added. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 1/1) to give (*R*)-2-benzylpentane-1,5-diol. [86% yield (8.2 mg)].

(*R*)-2-Benzylpentane-1,5-diol (Table 3, entry 7, Table 4, entry 3): $[\alpha]_D^{24}$ 4.02 (*c* 0.68, $CHCl_3$; 97% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.22 (2H, m, Ar-H), 7.22-7.11 (3H, m, Ar-H), 3.63 (2H, t, *J* = 6.4 Hz, CH_2CH_2OH), 3.61-3.46 (2H, m, $HOCH_2CH$), 2.71-2.57 (2H, m, CH_2Ph), 1.90-1.77 (1H, m, $HOCH_2CH$), 1.77-1.32 (6H, m, $CHCH_2CH_2CH_2$, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 129.1, 128.3, 125.9, 64.6, 63.0, 42.3, 37.8, 29.8, 26.8; IR (neat) 3340, 2928, 1452, 1051, 739, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{12}H_{18}NaO_2$: 217.1199 ($[M + Na]^+$), Found: 217.1204 ($[M + Na]^+$); HPLC analysis: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 209 nm, retention time; t_R(major) = 23.5 min, t_R(minor) = 25.2 min.

(*S*)-2-Methylpentane-1,5-diol (Table 4, entry 1): ^{1}H NMR, ^{13}C NMR and IR match those reported in the literature.[9] $[\alpha]_D^{29}$ –18.0 (*c* 0.80, $CHCl_3$; 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (2H, t, *J* = 6.6 Hz, CH_2CH_2OH), 3.52 (1H, dd, *J* = 10.6, 6.2 Hz, $HOCHHCH$), 3.47 (1H, dd, *J* = 10.4, 6.4 Hz, $HOCHHCH$) 1.72-1.45 (5H, m, $CHCHHCH_2$, OH), 1.36 (1H, br, OH), 1.26-1.15 (1H, m, $CHCHHCH_2$), 0.94 (3H, d, *J* = 6.8 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.1, 63.2, 35.5, 30.0, 29.2, 16.6; IR (neat) 3277, 2934, 2872, 1458, 1045, 912, 743 cm^{-1}; The enantiomeric excess was determined by HPLC after conversion to the corresponding dibenzoate ester. HPLC analysis: Daicel Chiralcel OD-3, hexane/*i*-PrOH = 19/1, flow rate = 0.5 mL/min, λ = 227 nm, retention time; t_R(minor) = 19.5 min, t_R(major) = 21.1 min.

(*S*)-2-Butylpentane-1,5-diol (Table 4, entry 2): $[\alpha]_D^{25}$ –8.68 (*c* 0.91, $CHCl_3$; 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (2H, t, *J* = 6.6 Hz, CH_2CH_2OH), 3.59 (1H, dd, *J* = 10.6, 5.0 Hz, $HOCHHCH$), 3.53 (1H, dd, *J* = 10.6, 5.8 Hz, $HOCHHCH$), 1.74-1.21 (13H, m, CH, CH_2, OH), 0.90 (3H, t, *J* = 6.4 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.5, 63.2, 40.2, 30.7, 29.8, 29.1, 27.0, 23.0, 14.0; IR (neat) 3335, 2926, 2859, 1456, 1053, 748 cm^{-1}; The enantiomeric excess was determined by HPLC after conversion to the corresponding dibenzoate ester. HPLC analysis: Daicel Chiralpak AY-H, hexane/EtOH = 30/1, flow rate = 0.3 mL/min, λ = 227 nm, retention time; t_R(majorr) = 31.5 min, t_R(minor) = 33.4 min.

(*R*)-2-(Cyclohexylmethyl)pentane-1,5-diol (Table 4, entry 4): $[\alpha]_D^{24}$ –8.27 (*c* 0.66, $CHCl_3$; 92% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 3.66 (2H, t, *J* = 6.6 Hz, $CH_2C\underline{H}_2OH$), 3.58 (1H, dd, *J* = 11.0, 4.6 Hz, $HOC\underline{H}HCH$), 3.50 (1H, ddd, *J* = 10.9, 5.9, 0.9 Hz, $HOCH\underline{H}CH$), 1.80-1.04 (18H, m, CH, CH_2, OH), 0.86 (2H, app dd, *J* = 21.6, 11.6 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.8, 63.3, 39.1, 37.0, 35.0, 33.8, 33.7, 29.7, 27.4, 26.7, 26.4(two peaks overlap); IR (neat) 3331, 2920, 2849, 1449, 1040, 912, 743 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{12}H_{24}NaO_2$: 223.1669 ($[M + Na]^+$), Found: 223.1661 ($[M + Na]^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding dibenzoate ester. HPLC analysis: Daicel Chiralpak ID, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 227 nm, retention time; t_R(major) = 13.9 min, t_R(minor) = 14.7 min.

(*S*)-2-(Benzyloxy)methyl)pentane-1,5-diol (Table 4, entry 5): $[\alpha]_D^{25}$ –19.6 (*c* 0.67, $CHCl_3$; 88% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.24 (5H, m, Ar-$\underline{H}$), 4.54 (1H, d, *J* = 6.2 Hz, $OC\underline{H}HPh$), 4.50 (1H, d, *J* = 6.0 Hz, $OCH\underline{H}Ph$), 3.73 (1H, dd, *J* = 10.6, 3.8 Hz, $C\underline{H}HOCH_2Ph$), 3.68-3.59 (4H, m, $HOC\underline{H}HCH$, $CH_2C\underline{H}_2OH$, $CH\underline{H}OCH_2Ph$), 3.49 (1H, dd, *J* = 9.2, 7.2 Hz, $HOCH\underline{H}CH$), 1.94-1.82 (1H, m, $HOCH_2C\underline{H}$), 1.66-1.52 (2H, m, $CH_2C\underline{H}_2CH_2$), 1.46-1.30 (2H, m, $CHC\underline{H}_2CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 128.5, 127.8, 127.6, 73.8, 73.5, 65.8, 62.9, 40.4, 30.2, 24.2; IR (neat) 3397, 2930, 2864, 1734, 1364, 1051, 748 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{13}H_{20}NaO_3$: 247.1305 ($[M + Na]^+$), Found: 247.1306 ($[M + Na]^+$); HPLC analysis: Daicel Chiralpak IC, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 205 nm, retention time; t_R(minor) = 46.7 min, t_R(major) = 50.2 min.

(*R*)-2-(3-(Benzyloxy)propyl)pentane-1,5-diol (Table 4, entry 6): $[\alpha]_D^{26}$ –4.81 (*c* 0.84, $CHCl_3$; 94% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.31 (4H, m, Ar-$\underline{H}$), 7.30-7.27 (1H, m, Ar-$\underline{H}$), 4.50 (2H, s, $OC\underline{H}_2Ph$), 3.63 (1H, dt, *J* = 6.4, 2.1 Hz, $CH_2C\underline{H}_2OH$), 3.59-3.50 (2H, m, $HOC\underline{H}_2CH$), 3.47 (2H, t, *J* = 6.6 Hz, $C\underline{H}_2OCH_2Ph$), 1.77 (1H, br, OH), 1.71-1.30 (10H, m, CH, CH_2, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 128.4, 127.7, 127.6, 73.0, 70.7, 65.2, 63.1, 40.0, 29.8, 27.5, 27.0, 26.9; IR (neat) 3366, 2938, 2864, 1454, 1055, 912, 738, 698 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{15}H_{25}O_3$: 253.1798 ($[M + H]^+$), Found: 253.1802 ($[M + H]^+$); HPLC analysis: Daicel Chiralpak AS-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 205 nm, retention time; t_R(minor) = 21.5 min, t_R(major) = 27.6 min.

(*R*)-2-Isopropylpentane-1,5-diol (Table 4, entry 7): $[\alpha]_D^{23}$ –7.11 (*c* 0.60, $CHCl_3$; 94% ee); ^1H NMR (400 MHz, $CDCl_3$) δ 3.67 (2H, t, *J* = 10.0 Hz, $CH_2C\underline{H}_2OH$), 3.70-3.63 (1H, m, $HOC\underline{H}HCH$), 3.57 (1H, dd, *J* = 10.8, 5.6 Hz, $HOCH\underline{H}CH$), 1.85-1.73 (1H, m, $HOCH_2C\underline{H}$), 1.70-1.54 (4H, m, $CH_2C\underline{H}_2CH_2$, OH), 1.50-1.30 (3H, m, $CHC\underline{H}_2CH_2$, $C\underline{H}(CH_3)_2$), 0.92 (3H, d, *J* = 1.6 Hz, $C\underline{H}_3$), 0.90 (3H, d, *J* = 1.6 Hz, $C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.8, 63.1, 46.2, 30.7, 28.3, 24.0, 19.8, 19.4; IR (neat) 3327, 2955, 1738, 1466, 1038, 741 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_8H_{19}O_2$: 147.1380 ($[M + H]^+$), Found: 147.1382 ($[M + H]^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding

dibenzoate ester. HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 20/1, flow rate = 0.5 mL/min, λ = 227 nm, retention time; t_R(major) = 44.8 min, t_R(minor) = 47.5 min.

(*R*)-2-Cyclohexylpentane-1,5-diol (Table 4, entry 8): $[\alpha]_D^{27}$ –27.8 (*c* 0.50, $CHCl_3$; 95% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71-3.63 (3H, m, HOC<u>H</u>HCH, $CH_2C\underline{H}_2OH$), 3.57 (1H, dd, *J* = 10.6, 5.8 Hz, HOCH<u>H</u>CH), 1.79-0.99 (16H, m, CH, CH_2, OH), 0.92-0.82 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.7, 63.2, 45.8, 38.9, 30.8, 30.2, 30.1, 26.85, 26.81, 26.7, 24.3; IR (neat) 3333, 2922, 2853, 1449, 1051, 912, 743 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{11}H_{22}NaO_2$: 209.1512 ($[M + Na]^+$), Found: 209.1514 ($[M + Na]^+$); The enantiomeric excess was determined by HPLC after conversion to the corresponding dibenzoate ester. HPLC analysis: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 19/1, flow rate = 0.5 mL/min, λ = 227 nm, retention time; t_R(major) = 18.4 min, t_R(minor) = 19.7 min.

Synthesis and characterization of (*R*)-5-benzyltetrahydro-2*H*-pyran-2-one (7)

To a solution of (*R*)-di-*t*-butyl 2-(3-hydroxy-2-benzylpropyl)malonate (14.4 mg, 0.040 mmol) in toluene (1.0 mL) was added trifluoroacetic acid (13 μL, 0.16 mmol) at room temperature. After stirring for 48 h at 80 °C, the mixture was cooled to room temperature. H_2O was added and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 3/1) to give (*R*)-5-benzyltetrahydro-2*H*-pyran-2-one (**7**). [99% yield (7.6 mg)]. ^{1}H NMR, ^{13}C NMR and IR match those reported in the literature.[10] $[\alpha]_D^{30}$ –1.06 (*c* = 0.83, $CHCl_3$; 95% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (2H, m, Ar-<u>H</u>), 7.25-7.21 (1H, m, Ar-<u>H</u>), 7.18-7.13 (2H, m, Ar-<u>H</u>), 4.31 (1H, ddd, *J* = 11.2, 4.4, 1.8 Hz, $CO_2C\underline{H}H$), 4.02 (1H, dd, *J* = 11.2, 9.6 Hz, $CO_2CH\underline{H}$), 2.70-2.56 (3H, m, $O_2C\underline{C}H$, $C\underline{H}_2Ph$), 2.49 (1H, ddd, *J* = 18.0, 9.6, 7.6 Hz, $O_2CCH\underline{H}$), 2.28-2.16 (1H, m, $C\underline{H}CH_2Ph$), 2.03-1.98 (1H, m, $O_2CCH_2C\underline{H}H$), 1.67-1.56 (1H, m, $O_2CCH_2CH\underline{H}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 138.4, 128.8, 128.7, 126.7, 73.1, 37.9, 34.7, 29.0, 25.3; IR (neat) 2924, 1734, 1456, 1246, 1182, 1053, 914, 746, 702 cm^{-1}; HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 207 nm, retention time; t_R(minor) = 47.3 min, t_R(major) = 54.6 min.

Synthesis and characterization of di-*t*-butyl (*S*)-4-benzyldihydrofuran-2,2(3*H*)-dicarboxylate (8)[11]

To a solution of di-*t*-butyl (*R*)-2-(3-hydroxy-2-benzylpropyl)malonate (16.3 mg, 0.045 mmol) in chloroform (5.0 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (68 μL, 0.46 mmol), and the mixture was stirred for 0.5 h at 0 °C. One equivalent of trifluoromethanesulfonyl chloride (4.8 μL, 0.045 mmol) was added five times in every 3 h at 0 °C (total 0.23 mmol of trifluoromethanesulfonyl chloride). The mixture was then stirred for 8 h at room temperature. The reaction mixture was quenched and washed with H_2O. The organic layer was dried over Na_2SO_4 and then concentrated. The resulting residue was purified

by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 3/1) to give di-*t*-butyl (*S*)-4-benzyldihydrofuran-2,2(3*H*)-dicarboxylate (**8**). [70% yield (11.4 mg)]. $[\alpha]_D^{27}$ –17.2 (*c* = 0.76, $CHCl_3$; 95% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (2H, m, Ar-H), 7.23-7.19 (1H, m, Ar-H), 7.19-7.13 (2H, m, Ar-H), 4.08 (1H, dd, *J* = 8.2, 6.6 Hz, OCHHCH), 3.71 (1H, dd, *J* = 8.4, 3.6 Hz, OCHHCH), 2.73-2.59 (3H, m, CHHCHCH$_2$Ph), 2.52 (1H, dd, *J* = 13.2, 7.6 Hz, CHHCH), 2.06 (1H, dd, *J* = 13.2, 8.0 Hz, CHCH$_2$Ph), 1.49 (9H, s, C(CH$_3$)$_3$), 1.46 (9H, s, C(CH$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 168.6, 140.1, 128.6, 128.5, 126.2, 87.2, 82.23, 82.15, 75.0, 40.8, 38.6, 38.3, 27.9, 27.8; IR (neat) 2978, 1732, 1369, 1300, 1252, 1146, 1113, 845, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{21}H_{30}NaO_5$: 385.1985 ([M + Na]$^+$), Found: 385.1987 ([M + Na]$^+$); HPLC analysis: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL/min, λ = 208 nm, retention time; t_R(minor) = 14.9 min, t_R(major) = 18.4 min.

Synthesis and characterization of di-*t*-butyl (*R*)-2-(2-benzyl-3-(benzylamino)propyl)malonate (9)

A mixture of di-*t*-butyl methylenemalonate (34.0 mg, 0.15 mmol) and 3-phenylpropanal (61 μL, 0.46 mmol) in diethyl ether (1.5 mL) was stirred at 0 °C. To the mixture was then added (*S*)-**3a** (8.6 mg, 0.014 mmol). After stirring for 4 h at 0 °C, benzylamine (52 μL, 0.48 mmol) was added. After stirring for 3 h at 0 °C, MeOH (1.0 mL) and sodium borohydride (30 mg) were added successively, and the mixture was vigorously stirred for 0.5 h at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 3/1) to give di-*t*-butyl (*R*)-2-(2-benzyl-3-(benzylamino)propyl)malonate (**9**). [99% yield (66.9 mg)]. $[\alpha]_D^{31}$ 10.4 (*c* = 1.61, $CHCl_3$; 93% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.10 (10H, m, Ar-H), 3.72 (1H, d, *J* = 13.2 Hz, PhCHHNH), 3.69 (1H, d, *J* = 13.2 Hz, PhCHHNH), 3.32 (1H, app t, *J* = 7.6 Hz, CH$_2$CH(CO$_2$*t*-Bu)$_2$), 2.70-2.58 (2H, m, CHCH$_2$Ph), 2.58-2.48 (2H, m, NHCH$_2$CH), 1.96-1.76 (3H, m, CHCH$_2$CH), 1.45 (9H, s, C(CH$_3$)$_3$), 1.34 (9H, s, C(CH$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0 (two peaks overlap), 140.7, 140.5, 129.2, 128.3 (two peaks overlap), 128.1, 126.8, 125.9, 81.3, 81.2, 54.0, 52.0, 51.9, 39.0, 38.3, 31.4, 27.94, 27.86; IR (neat) 2976, 2930, 1722, 1452, 1367, 1254, 1138, 847, 741, 698 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{28}H_{40}NO_4$: 454.2952 ([M + H]$^+$), Found: 454.2955 ([M + H]$^+$); HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 40/1, flow rate = 0.5 mL/min, λ = 206 nm, retention time; t_R(minor) = 13.9 min, t_R(major) = 16.4 min.

Synthesis and characterization of (*R*)-1,5-dibenzylpiperidin-2-one (10)

To a solution of di-*t*-butyl (*R*)-2-(2-benzyl-3-(benzylamino)propyl)malonate (**9**) (36.5 mg, 0.081 mmol) in toluene (1.0 mL) was added trifluoroacetic acid (25 μL, 0.33 mmol) at room temperature. After stirring for 48 h at 100 °C, the mixture was cooled to room temperature. H_2O was added and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The residue

was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 2/1) to give (*R*)-1,5-dibenzylpiperidin-2-one (**10**). [91% yield (20.3 mg)]. ^{1}H NMR, ^{13}C NMR and IR match those reported in the literature.[12] $[\alpha]_D^{33}$ –39.0 (*c* = 1.00, $CHCl_3$; 93% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.17 (8H, m, Ar-H), 7.05 (2H, d, *J* = 7.6 Hz, Ar-H), 4.63 (1H, d, *J* = 14.8 Hz, PhCHHN), 4.49 (1H, d, *J* = 14.8 Hz, PhCHHN), 3.19 (1H, ddd, *J* = 12.4, 5.2, 1.6 Hz, NCHHCH), 2.95 (1H, dd, *J* = 12.2, 9.8 Hz, NCHHCH), 2.62-2.47 (3H, m, NCOCHH, CHCH_2Ph), 2.39 (1H, ddd, *J* = 18.6, 11.2, 6.6 Hz, NCOCHH), 2.13-2.02 (1H, br, CHCH_2Ph), 1.92-1.83 (1H, br, CHCHHCH_2), 1.66-1.44 (1H, m, CHCHHCH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 139.1, 137.2, 128.9, 128.6, 128.5, 128.1, 127.4, 126.3, 52.3, 50.3, 39.4, 35.7, 31.3, 26.9; IR (neat) 2924, 2853, 1721, 1454, 1260, 739, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{19}H_{22}NO$: 280.1696 ($[M + H]^+$), Found: 280.1694 ($[M + H]^+$); HPLC analysis: Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 9/1, flow rate = 0.3 mL/min, λ = 208 nm, retention time; t_R(minor) = 60.8 min, t_R(major) = 63.2 min.

Synthesis and characterization of di-*t*-butyl (*S*)-1,4-dibenzylpyrrolidine-2,2-dicarboxylate (11)[13]

To a solution of di-*t*-butyl (*R*)-2-(2-benzyl-3-(benzylamino)propyl)malonate (**9**) (30.0 mg, 0.066 mmol) and (diacetoxyiodo)benzene (33.0 mg, 0.10 mmol) in THF (2.0 mL) was added tetrabutylammonium iodide (38.0 mg, 0.10 mmol). After stirring for 15 h at room temperature, the mixture was concentrated under reduced pressure. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 20/1) to give di-*t*-butyl (*S*)-1,4-dibenzylpyrrolidine-2,2-dicarboxylate (**11**). [61% yield (18.3 mg)]. $[\alpha]_D^{28}$ –4.24 (*c* = 1.18, $CHCl_3$; 93% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (2H, d, *J* = 7.6 Hz, Ar-H), 7.32-7.28 (2H, t, *J* = 7.6 Hz, Ar-H), 7.24-7.18 (3H, m, Ar-H), 7.16-7.08 (3H, m, Ar-H), 3.98 (2H, s, PhCH_2N), 2.84 (1H, dd, *J* = 8.2, 6.6 Hz, CHCHHN), 2.68 (2H, d, *J* = 6.8 Hz, CHCH_2Ph), 2.61-2.45 (3H, m, CH_2CHCHHN), 2.12-2.02 (1H, m, CHCH_2Ph), 1.50 (9H, s, C(CH_3)$_3$), 1.46 (9H, s, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 169.9, 140.9, 140.6, 128.7, 128.3, 128.11, 128.09, 126.6, 125.8, 81.7, 81.5, 75.5, 57.1, 54.7, 40.6, 40.5, 37.5, 28.11, 28.06; IR (neat) 2976, 1724, 1454, 1368, 1254, 1144, 847, 737, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{28}H_{38}NO_4$: 452.2795 ($[M + H]^+$), Found: 452.2776 ($[M + H]^+$); HPLC analysis: Daicel Chiralcel OZ-H, hexane/*i*-PrOH = 400/1, flow rate = 0.5 mL/min, λ = 204 nm, retention time; t_R(major) = 10.5 min, t_R(minor) = 11.7 min.

Synthesis and characterization of di-*t*-butyl (*S*)-5-benzylcyclohex-3-ene-1,1-dicarboxylate (12)[14]

A mixture of di-*t*-butyl methylenemalonate (16.7 mg, 0.073 mmol) and 3-phenylpropanal (13.1 μL, 0.099 mmol) in diethyl ether (0.8 mL) was stirred at 0 °C. To the mixture was then added (*S*)-**3a** (5.0 mg, 7.4 μmol). The mixture was stirred for 4 h at 0 °C, and diluted with THF (0.8 mL). To the mixture were added vinyltriphenylphosphonium bromide (92.0 mg, 0.25 mmol) and sodium hydride (20.0 mg, 0.50 mmol) were added at –78 °C. The whole mixture was stirred for 2 h at –78 °C, and quenched with saturated aqueous NH_4Cl was added. The resulting mixture was extracted with ethyl acetate. The organic layer was washed

with brine, dried over Na_2SO_4 and then concentrated. The residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 8/1) to give di-*t*-butyl (*S*)-5-benzylcyclohex-3-ene-1,1-dicarboxylate (**12**). [61% yield (31.0 mg)]. $[\alpha]_D^{31}$ 21.1 (*c* = 1.20, $CHCl_3$; 92% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.28 (2H, m, Ar-H), 7.22-7.13 (3H, m, Ar-H), 5.69-5.63 (1H, m, CH_2CH=CHCH), 5.55 (1H, d, *J* = 10.0 Hz, CH_2CH=C*H*CH), 2.72-2.55 (3H, m, C*H*HCH=CH, CH_2Ph), 2.48-2.36 (1H, br, CH), 2.26-2.13 (2H, m, CH*H*CH=CHCHC*H*H), 1.55-1.43 (1H, m, CHCH*H*CCH_2), 1.42 (9H, s, C(CH_3)$_3$), 1.39 (9H, s, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 170.0, 140.0, 130.2, 129.0, 128.2, 126.0, 124.4, 81.2, 80.7, 54.5, 42.3, 34.8, 34.0, 27.84, 27.77; IR (neat) 2976, 2928, 1726, 1368, 1256, 1167, 1142, 1082, 847, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{23}H_{32}NaO_4$: 395.2193 ($[M + Na]^+$), Found: 395.2199 ($[M + Na]^+$); HPLC analysis: Daicel Chiralcel OD-3, hexane/*i*-PrOH = 400/1, flow rate = 0.5 mL/min, λ = 210 nm, retention time; t_R(minor) = 17.2 min, t_R(major) = 18.2 min.

Synthesis and characterization of 1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (13)

A mixture of 1,1,1,3,3,3-hexafluoropropan-2-yl acrylate (**2**) (95 μL, 0.57 mmol) and 3-phenylpropanal (7.5 μL, 0.057 mmol) in diethyl ether (2.5 mL) was stirred at 15 °C. To the mixture was then added (*S*)-**3b** (4.4 mg, 5.8 μmol). After stirring for 24 h at 15 °C, ethylene glycol (32 μL, 0.57 mmol) and *p*-toluenesulfonic acid monohydrate (11 mg, 0.058 mmol) were added successively. After 12 h of vigorous stirring at room temperature, saturated aqueous NH_4Cl was added. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/dichloromethane = 1/1) to give 1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-4-(1,3-dioxolan- 2-yl)-5-phenylpentanoate (**13**). [62% yield (14.2 mg)]. $[\alpha]_D^{27}$ 6.49 (*c* 1.40, $CHCl_3$; 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.24 (2H, m, Ar-H), 7.23-7.16 (3H, m, Ar-H), 5.73 (1H, sep, $J_{H\text{-}F}$ = 6.2 Hz, $CO_2CH(CF_3)_2$), 4.75 (1H, d, *J* = 3.6 Hz, $(CH_2O)_2CH$), 4.02-3.92 (2H, m, OCHHCHHO), 3.91-3.81 (2H, m, OCHHCHHO), 2.90 (1H, dd, *J* = 14.0, 6.0 Hz, CHHPh), 2.64-2.47 (3H, m, CHHPh, CH_2CO_2CH), 2.09-1.99 (1H, m, $CHCH_2Ph$), 1.89-1.78 (1H, m, $CHHCH_2CO_2$), 1.77-1.66 (1H, m, $CHHCH_2CO_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 139.6, 129.1, 128.4, 126.2, 120.44 (q, $J_{C\text{-}F}$ = 283.1 Hz), 120.41 (q, $J_{C\text{-}F}$ = 283.1 Hz), 105.6, 66.3 (sep, $J_{C\text{-}F}$ = 34.8 Hz), 65.1, 64.9, 42.3, 36.0, 31.2, 23.3; IR (neat) 2924, 1780, 1738, 1385, 1288, 1229, 1202, 1111, 907, 746, 698 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{17}H_{18}F_6NaO_4$: 423.1001 ($[M + Na]^+$), Found: 423.0997 ($[M + Na]^+$); HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 205 nm, retention time; t_R(minor) = 13.6 min, t_R(major) = 24.4 min.

Synthesis and characterization of (*R*)-*N*-benzyl-4-(1,3-dioxolan-2-yl)-5-phenylpentanamide (14)

To a solution of 1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (**13**) (8.4 mg, 0.021 mmol) in dichloromethane (1.0 mL) was added benzylamine (15 μL, 0.14 mmol). After stirring

for 15 h at room temperature, the mixture was added H_2O and extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 1/1) to give (*R*)-*N*-benzyl-4-(1,3-dioxolan-2-yl)-5-phenylpentanamide (**14**). [99% yield (7.3 mg)]. $[\alpha]_D^{22}$ 2.60 (*c* 0.87, $CHCl_3$; 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.21 (7H, m, Ar-H), 7.20-7.11 (3H, m, Ar-H), 5.74 (1H, br, CONHCH$_2$Ph), 4.74 (1H, d, *J* = 3.6 Hz, (CH$_2$O)$_2$CH), 4.40 (1H, dd, *J* = 14.8, 5.6 Hz, NHCHHPh), 4.35 (1H, dd, *J* = 14.4, 5.6 Hz, NHCHHPh), 3.98-3.89 (2H, m, OCHHCHHO), 3.87-3.76 (2H, m, OCHHCHHO), 2.87 (1H, dd, *J* = 14.0, 6.4 Hz, CHHPh), 2.55 (1H, dd, *J* = 13.8, 8.6 Hz, CHHPh), 2.24 (2H, t, *J* = 8.0 Hz, CH$_2$CONH), 2.06-1.96 (1H, m, CHCH$_2$Ph), 1.90-1.78 (1H, m, CHCHHCH$_2$), 1.73-1.61 (1H, m, CHCHHCH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 140.1, 138.4, 129.2, 128.6, 128.3, 127.9, 127.4, 126.0, 105.8, 65.0, 64.8, 43.5, 42.6, 36.1, 34.6, 24.8; IR (neat) 3291, 2884, 1643, 1547, 1136, 1030, 743, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{21}H_{26}NO_3$: 340.1907 ([M + H]$^+$), Found: 340.1912 ([M + H]$^+$); HPLC analysis: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 207 nm, retention time; t_R(minor) = 37.6 min, t_R(major) = 41.6 min.

Synthesis and characterization of methyl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (15)

To a solution of 1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (**13**) (9.5 mg, 0.024 mmol) in MeOH (1.0 mL) was added triethylamine (10 μL, 0.075 mmol). After stirring for 5 h at room temperature, the mixture was added H_2O. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 3/1) to give methyl (*R*)-4-(1,3-dioxolan- 2-yl)-5-phenylpentanoate (**15**). [80% yield (5.0 mg)]. $[\alpha]_D^{21}$ 4.66 (*c* 0.87, $CHCl_3$; 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (2H, m, Ar-H), 7.21-7.15 (3H, m, Ar-H), 4.76 (1H, d, *J* = 4.0 Hz, (CH$_2$O)$_2$CH), 4.02-3.93 (2H, m, OCHHCHHO), 3.90-3.79 (2H, m, OCHHCHHO), 3.61 (3H, s, CH$_3$), 2.86 (1H, dd, *J* = 13.8, 6.2 Hz, CHHPh), 2.55 (1H, dd, J = 13.8, 8.6 Hz, CHHPh), 2.45-2.28 (2H, m, CH$_2$CO$_2$CH$_3$), 2.06-1.96 (1H, m, CHCH$_2$Ph), 1.86-1.75 (1H, m, CHCHHCH$_2$), 1.71-1.60 (1H, m, CHCHHCH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0 140.1, 129.2, 128.3, 126.0, 105.7, 65.1, 64.9, 51.4, 42.7, 35.7, 32.1, 23.8; IR (neat) 2924, 1738, 1452, 1368, 1215, 748, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{15}H_{20}NaO_4$: 287.1254 ([M + Na]$^+$), Found: 287.1261 ([M + Na]$^+$); HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 209 nm, retention time; t_R(minor) = 24.8 min, t_R(major) = 42.5 min.

Synthesis and characterization of phenyl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (16)

To a solution of 1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (**13**) (12 mg, 0.030 mmol) and phenol (5.0 mg, 0.053 mmol) in dichloromethane (1.0 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (7.0 μL, 0.047 mmol). After stirring for 15 h at room

temperature, the mixture was acidified with 1N HCl (1.0 mL). The resulting mixture was extracted with dichloromethane. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/dichloromethane = 1/1) to give phenyl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (**16**). [70% yield (6.8 mg)]. $[\alpha]_D^{26}$ 13.3 (*c* 0.63, $CHCl_3$; 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.16 (8H, m, Ar-H), 7.02 (2H, d, *J* = 8.0 Hz, Ar-H), 4.82 (1H, d, *J* = 3.2 Hz, $(CH_2O)_2CH$), 4.05-3.95 (2H, m, OCHHCHHO), 3.93-3.82 (2H, m, OCHHCHHO), 2.91 (1H, dd, *J* = 14.0, 6.0 Hz, CHHPh), 2.69-2.53 (3H, m, CHHPh, CH_2CO_2Ph), 2.18-2.07 (1H, m, CHCH$_2$Ph), 1.98-1.87 (1H, m, CHCHHCH$_2$), 1.84-1.73 (1H, m, CHCHHCH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 150.7, 140.0, 129.3, 129.2, 128.4, 126.1, 125.6, 121.6, 105.7, 65.1, 64.9, 42.6, 35.8, 32.4, 23.8; IR (neat) 2926, 1751, 1368, 1200, 1132, 912, 746, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{20}H_{22}NaO_4$: 349.1410 ([M + Na]$^+$), Found: 349.1423 ([M + Na]$^+$); HPLC analysis: Daicel Chiralpak IC, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 205 nm, retention time; t_R(major) = 17.9 min, t_R(minor) = 26.4 min.

Synthesis and characterization of *S*-ethyl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanethioate (17)

To a solution of 1,1,1,3,3,3-hexafluoropropan-2-yl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (**13**) (13 mg, 0.030 mmol) in ethanethiol (0.50 mL) was added sodium ethanethiolate (13 mg, 0.15 mmol). After stirring for 15 h at room temperature, the mixture was added H_2O. The resulting mixture was extracted with dichloromethane. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 5/1) to give *S*-ethyl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanethioate (**17**). [76% yield (7.5 mg)]. $[\alpha]_D^{25}$ 13.0 (*c* 0.68, $CHCl_3$; 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.24 (2H, m, Ar-H), 7.23-7.15 (3H, m, Ar-H), 4.75 (1H, d, *J* = 3.2 Hz, $(CH_2O)_2CH$), 4.02-3.92 (2H, m, OCHHCHHO), 3.90-3.79 (2H, m, OCHHCHHO), 2.84 (2H, q, *J* = 7.5 Hz, $COSCH_2CH_3$), 2.88-2.80 (1H, m, CHHPh), 2.68-2.50 (3H, m, CHHPh, CH_2COSEt), 2.06-1.96 (1H, m, CHCH$_2$Ph), 1.90-1.79 (1H, m, CHCHHCH$_2$), 1.73-1.62 (1H, m, CHCHHCH$_2$), 1.22 (3H, t, *J* = 7.6 Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 140.0, 129.2, 128.3, 126.0, 105.5, 65.1, 65.0, 42.5, 42.1, 35.7, 24.3, 23.2, 14.8; IR (neat) 2928, 1738, 1686, 1371, 1215, 1032, 972, 746, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{16}H_{22}NaO_3S$: 317.1182 ([M + Na]$^+$), Found: 317.1191 ([M + Na]$^+$); HPLC analysis: Daicel Chiralpak IC, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 209 nm, retention time; t_R(major) = 12.1 min, t_R(minor) = 21.7 min.

Synthesis and characterization of methyl (*R*)-4-benzyl-5-hydroxypentanoate (18)

A mixture of 1,1,1,3,3,3-hexafluoropropan-2-yl acrylate (**1**) (125 μL, 0.75 mmol) and 3-phenylpropanal (10 μL, 0.076 mmol) in diethyl ether (3.0 mL) was stirred at 15 °C. To the mixture was then added (*S*)-**3b** (5.8 mg, 7.6 μmol). After stirring for 24 h at 15 °C, MeOH (2.0mL) and triethylamine (102 μL, 0.77 mmol) were added successively. After 3 h of stirring at room temperature, sodium borohydride (30 mg, 0.79

mmol) was added. After 0.5 h of vigorous stirring at room temperature, saturated aqueous NH_4Cl was added. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/dichloromethane = 2/1) to give methyl (*R*)-4-benzyl-5-hydroxypentanoate (**18**). [67% yield (11.3 mg)]. $[\alpha]_D^{25}$ 1.15 (*c* 0.88, $CHCl_3$; 97% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.24 (2H, m, Ar-H), 7.23-7.13 (3H, m, Ar-H), 3.67 (3H, s, CH_3), 3.54 (1H, dd, *J* = 11.2, 4.4 Hz, HOCHHCH), 3.48 (1H, dd, *J* = 11.4, 5.0 Hz, HOCHHCH), 2.68 (1H, dd, *J* = 13.8, 7.4 Hz, CHHPh), 2.61 (1H, dd, *J* = 14.0, 6.4 Hz, CHHPh), 2.42-2.34 (2H, m, $CH_2CO_2CH_3$), 1.88-1.57 (4H, m, $CH_2CHCH_2CH_2$, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 140.2, 129.1, 128.4, 126.0, 64.0, 51.7, 42.2, 37.6, 31.6, 25.6; IR (neat) 3416, 2926, 1736, 1452, 1202, 1034, 743, 702 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{13}H_{18}NaO_3$: 245.1148 ($[M + Na]^+$), Found: 245.1148 ($[M + Na]^+$); HPLC analysis: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 209 nm, retention time; t_R(minor) = 17.8 min, t_R(major) = 18.6 min.

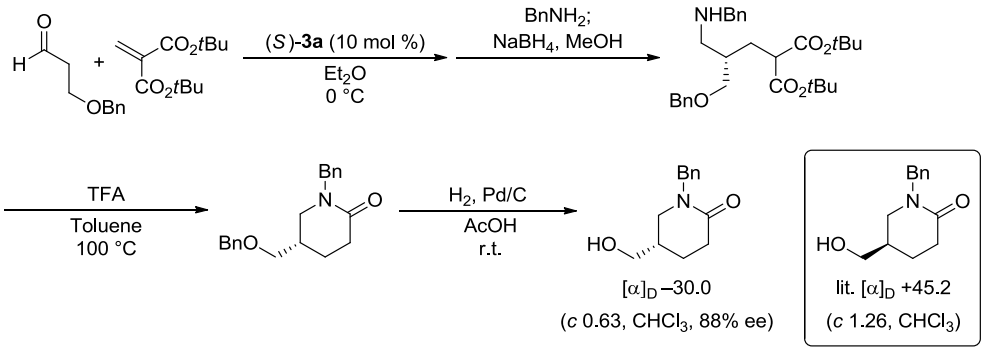
Comparison of the reaction rate: Monitoring of conjugate adduct formation using ^{1}H NMR

To a solution of 1,1,1,3,3,3-hexafluoropropan-2-yl acrylate (**2**) (19 μL, 0.11 mmol) and 3-phenylpropanal (3.0 μL, 0.023 mmol) in THF-d_8 (0.75 mL) was added (*S*)-**3a** (1.4 mg, 2.3 μmol) or (*S*)-**4b** (0.74 mg, 2.3 μmol) at room temperature. By using ^{1}H NMR, the mixtures were monitored and conversion values were calculated. The results were summarized in Table S1.

Table S1. Conversion (%) of 3-phenylpropanal over time.

Time (h)	(*S*)-**3a**	(*S*)-**4b**	Time (h)	(*S*)-**3a**	(*S*)-**4b**
1	16.7	-	48	66.3	19.1
2	28.1	-	60	66.6	27.8
3	37.9	-	72	66.4	36.2
4	46.5	1.2	96	66.4	46.5
5	50.5	2.0	120	66.4	52.2
7	56.3	2.5	144	66.7	54.2
10	63.4	3.7	168	66.4	55.0
15	64.9	5.4	192	66.6	55.2
24	65.4	8.8	216	66.4	55.2
36	66.1	14.2	240	66.4	55.0

Determination of absolute configuration of the conjugate addition product



The optical rotaion of (*R*)-1-benzyl-5-(hydroxymethyl)piperidin-2-one was reported.[15] Based on this information, the absolute configuration of the product obtained in the (*S*)-**3a** catalyzed conjugate addition between 3-benzyloxypropanal and di-*t*-butyl 2-methylenemalonate was determined to be *S* by converting to 1-benzyl-5-(hydroxymethyl)piperidin-2-one and by comparison of the sign of the optical rotation.

Determination of absolute configuration of methyl 4-benzyl-5-hydroxypentanoate (18)

The absolute configuration of the title compound was determined to be *R* by converting to 5-benzyltetrahydro-2*H*-pyran-2-one (**7**)[10] and by comparing the sign of optical rotation: To a solution of methyl 4-benzyl-5-hydroxypentanoate (**18**) (8.3 mg, 0.037 mmol) in toluene (1.0 mL) was added trifluoroacetic acid (25 μL, 0.34 mmol) at room temperature. After stirring for 12 h at 100 °C, the mixture was added H_2O. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and then concentrated. The resulting residue was purified by preparative thin layer chromatography (eluting with hexane/ethyl acetate = 3/1) to give 5-benzyltetrahydro-2*H*-pyran-2-one (**7**). [93% yield (6.6 mg)]. ^{1}H NMR, ^{13}C NMR and IR match those reported in the literature.[10] HPLC analysis: Daicel Chiralcel OD-H, hexane/*i*-PrOH = 9/1, flow rate = 0.5 mL/min, λ = 207 nm, retention time; t_R(minor) = 47.3 min, t_R(major) = 54.6 min; $[\alpha]_D^{23}$ –3.65 (*c* 0.46, $CHCl_3$; 97% ee): $[\alpha]_D^{30}$ –1.06 (*c* 0.83, $CHCl_3$; 95% ee, *R* isomer; See page S14 of this supporting information).

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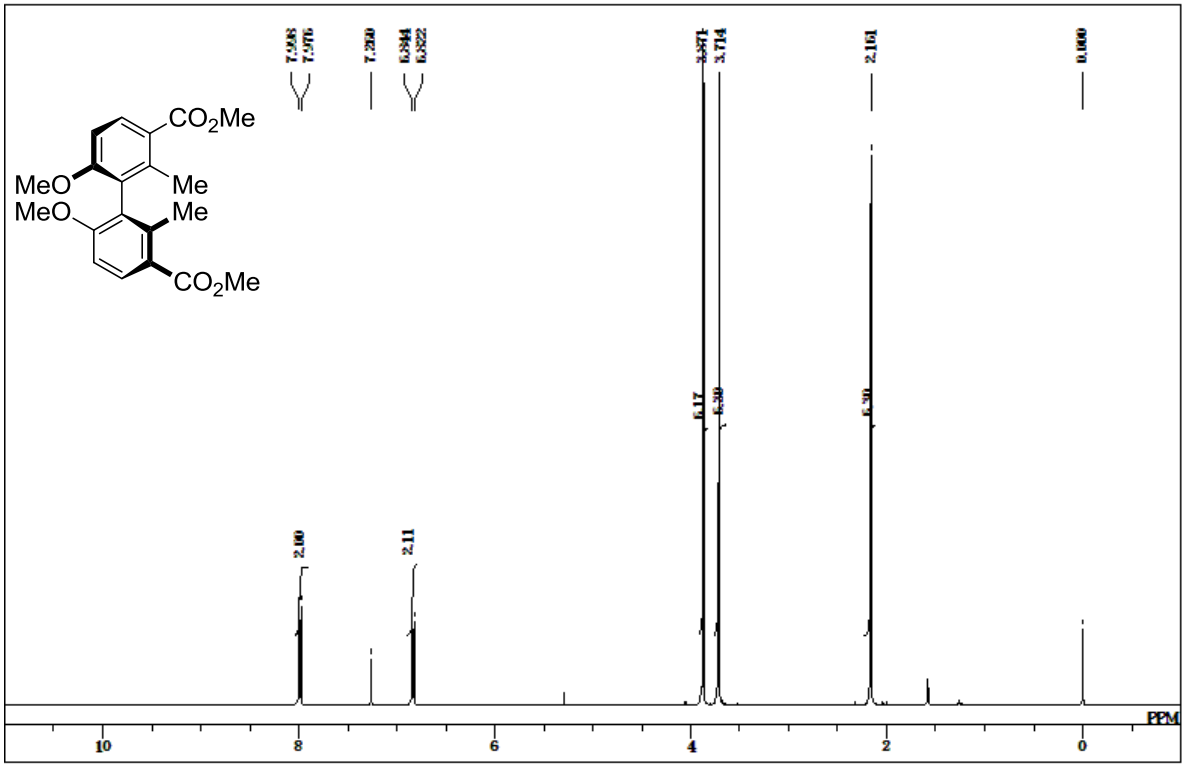
Diester (*S*)-20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MeO
Me
Me
CO2Me
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7.250
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6.322
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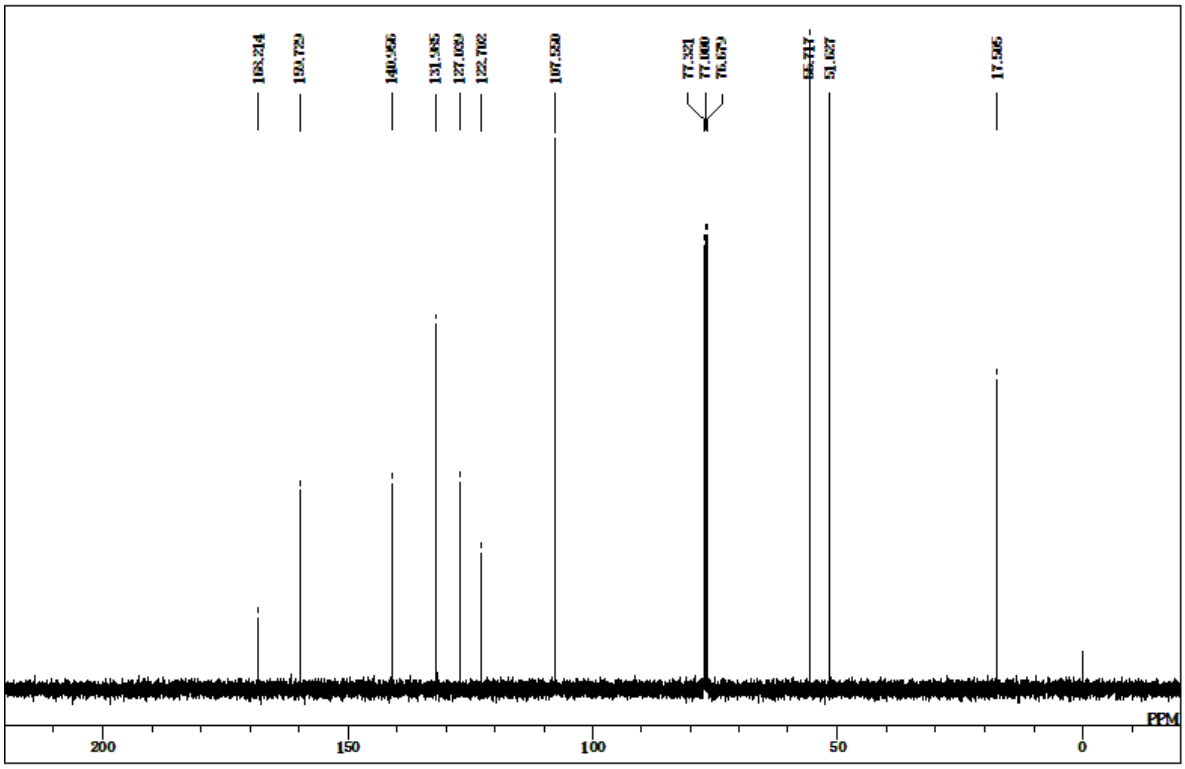
2.11
PPM
10
8
6
4
2
0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PPM
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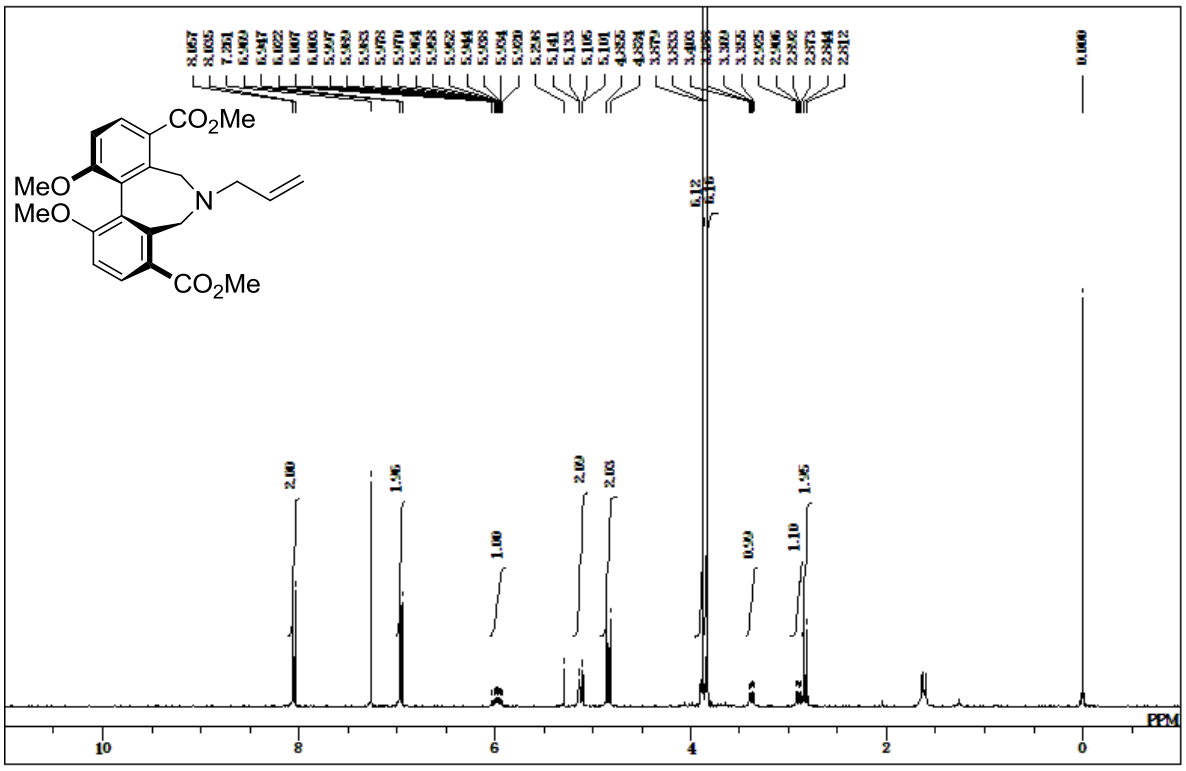
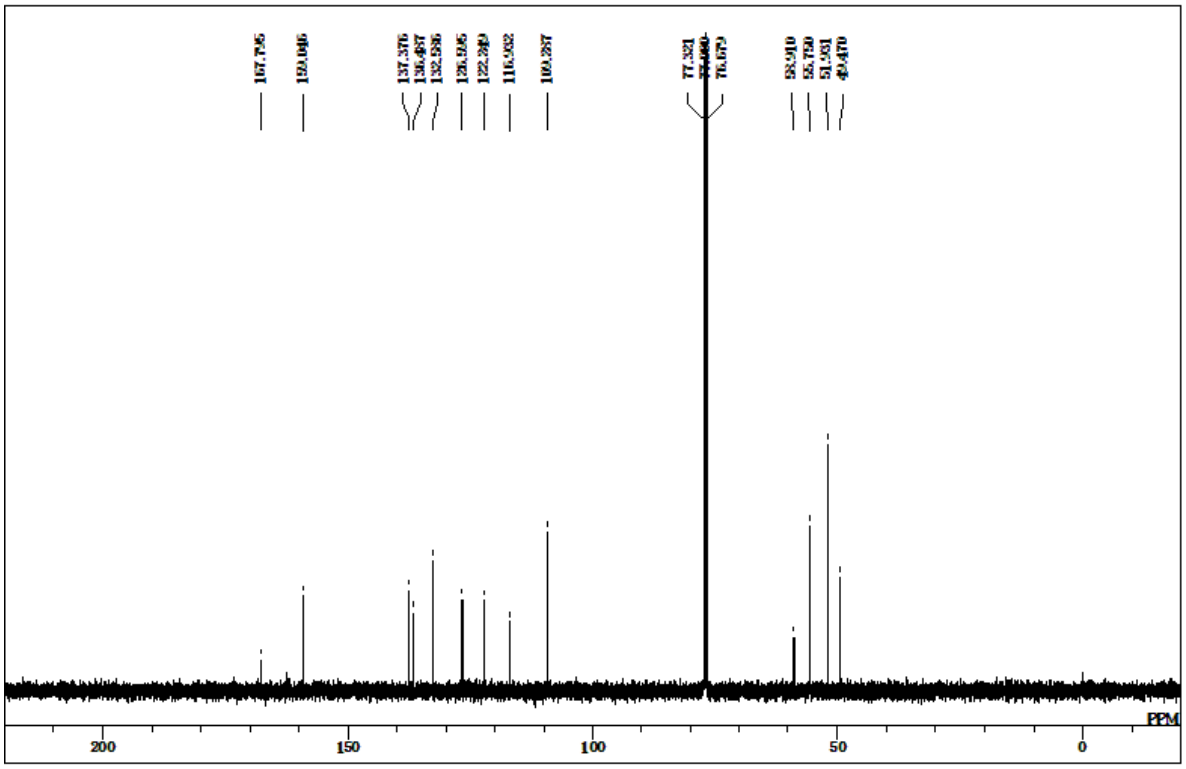
50
0

Allylamine (*S*)-21





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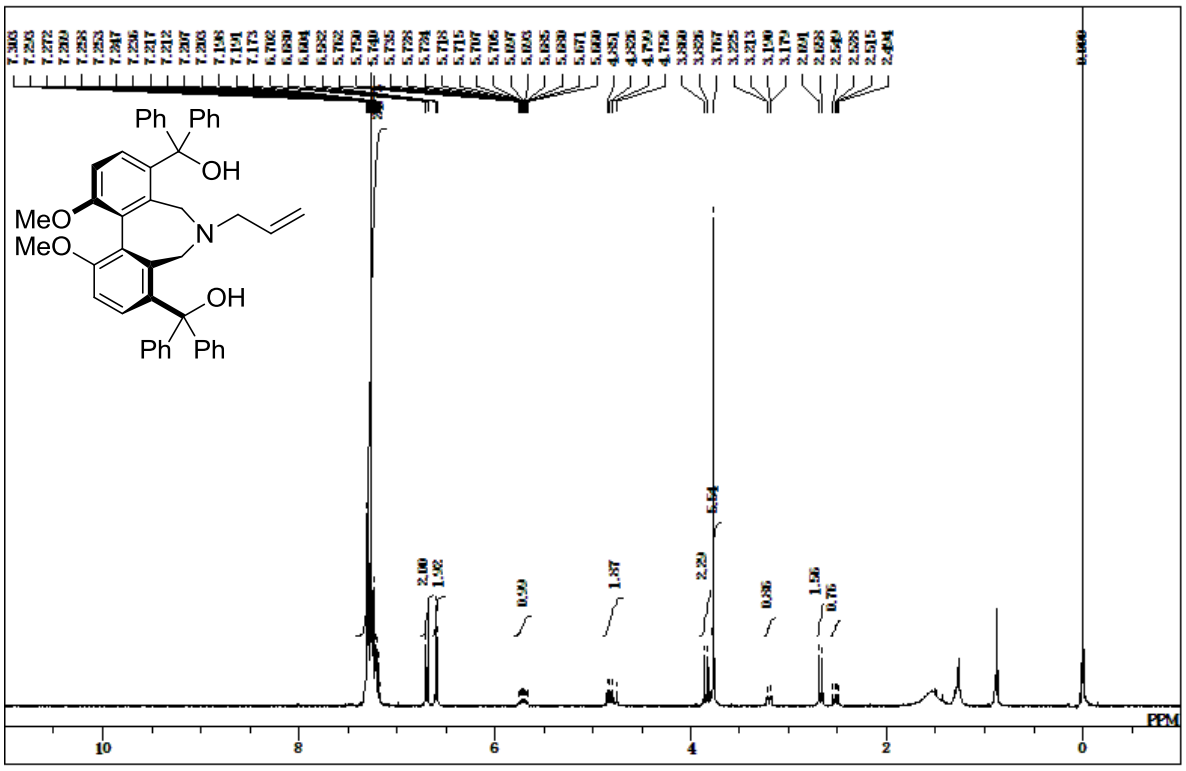

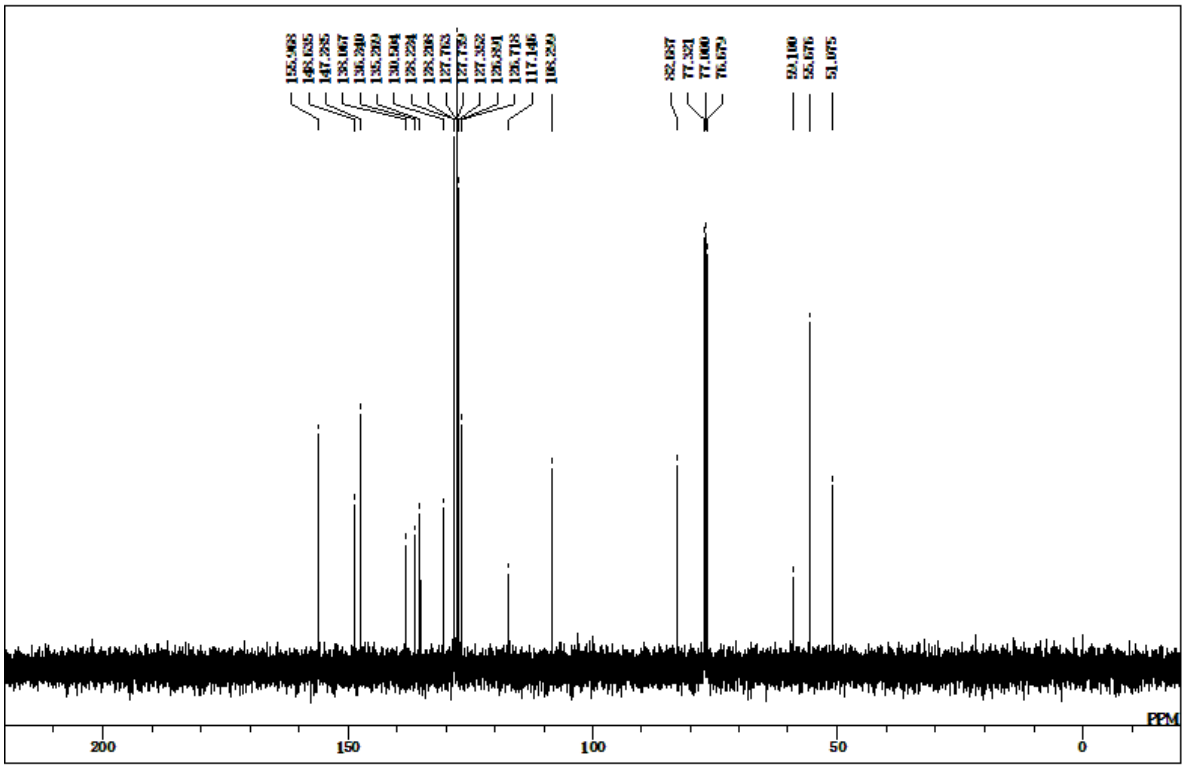

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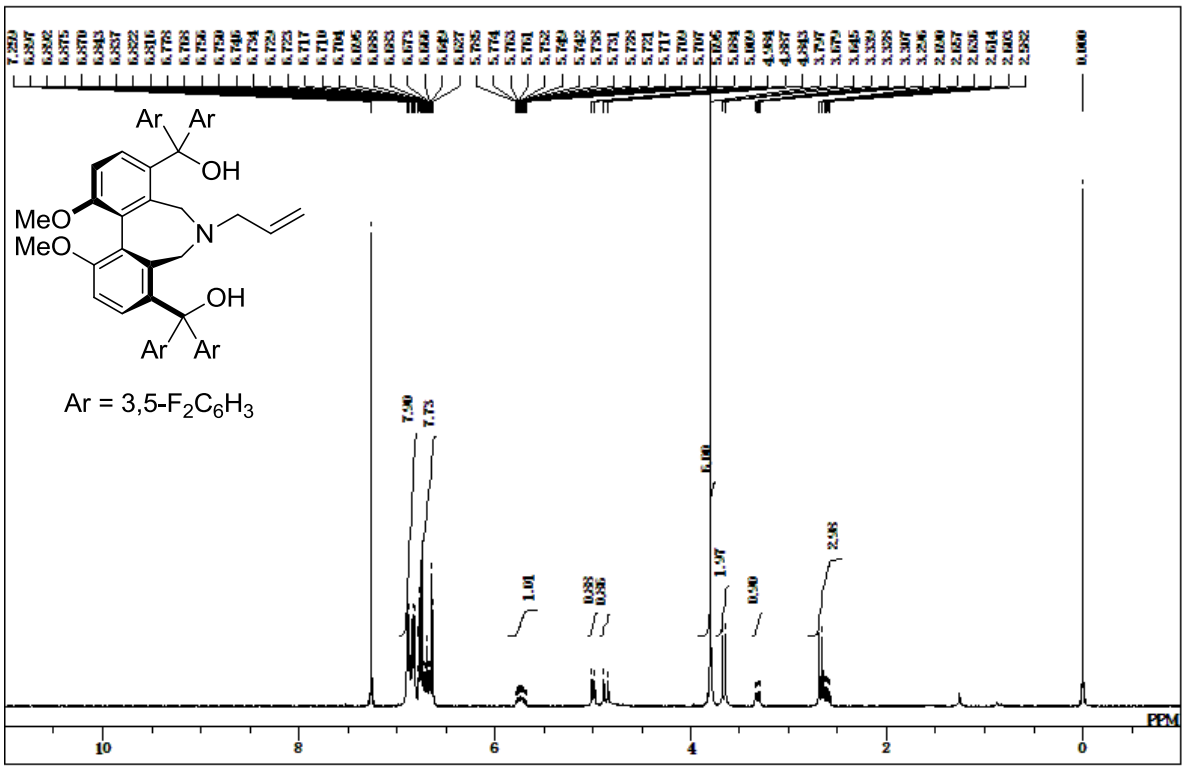

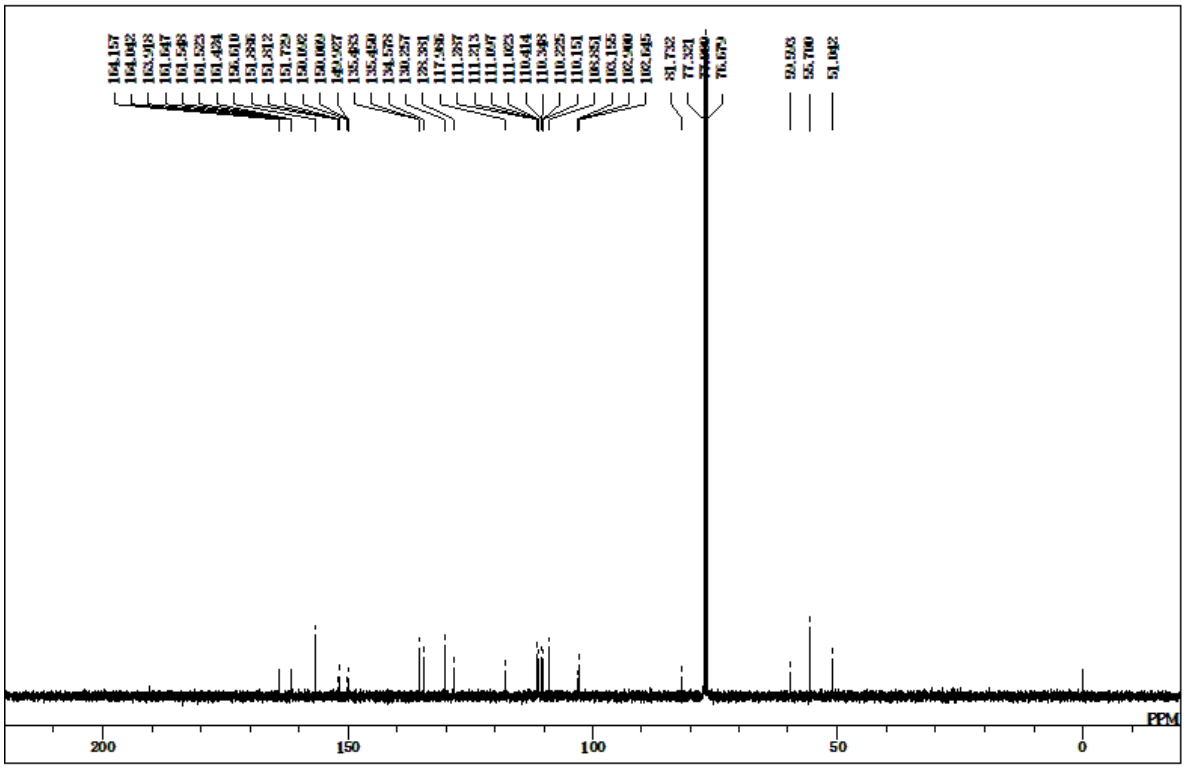

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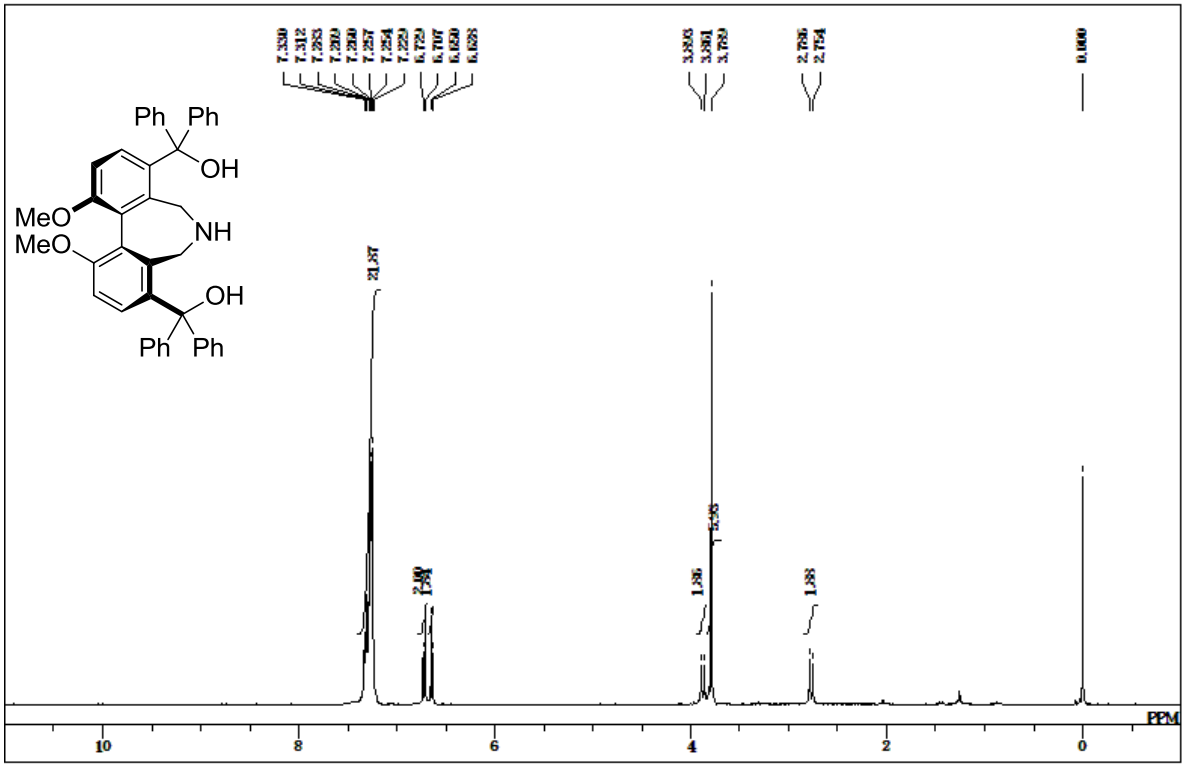

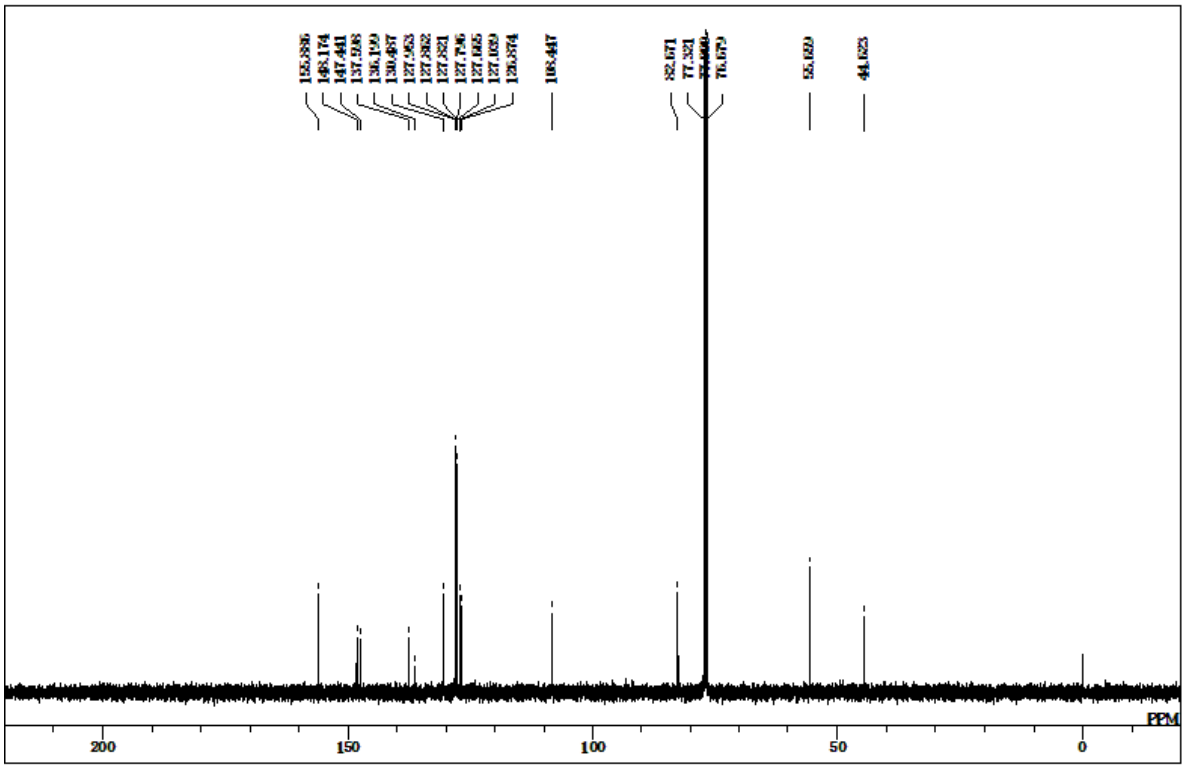

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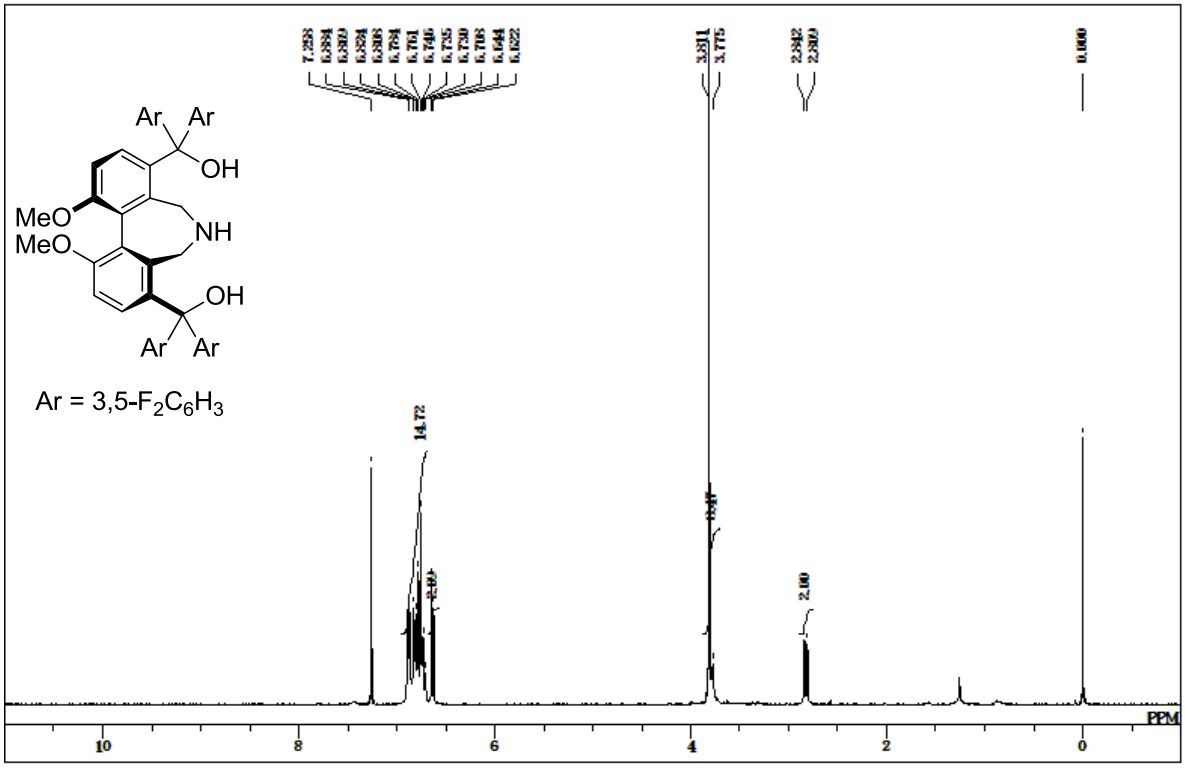
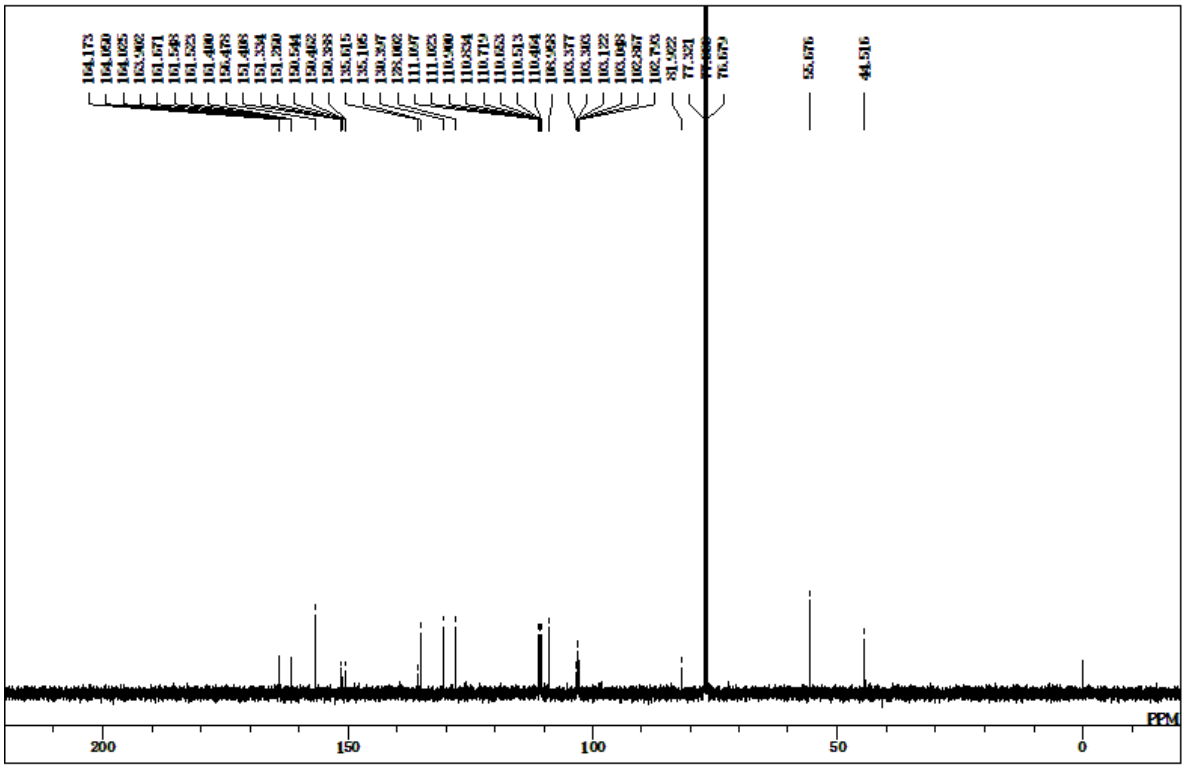
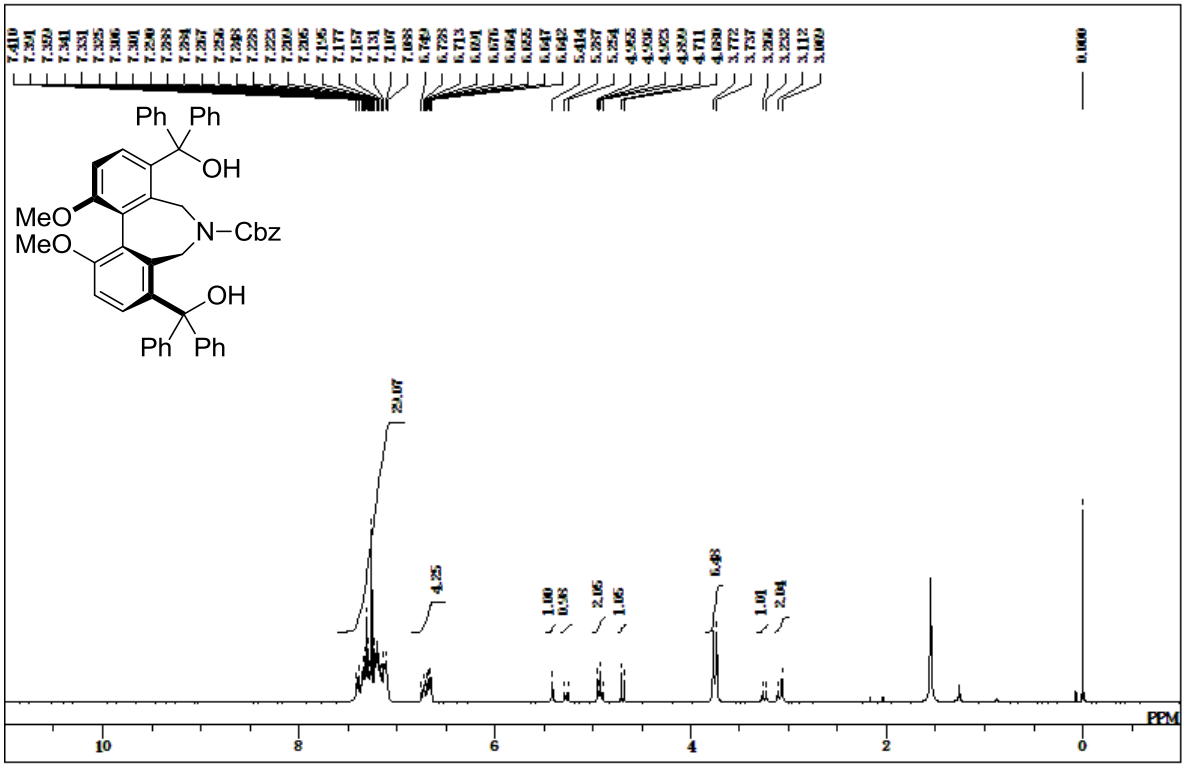
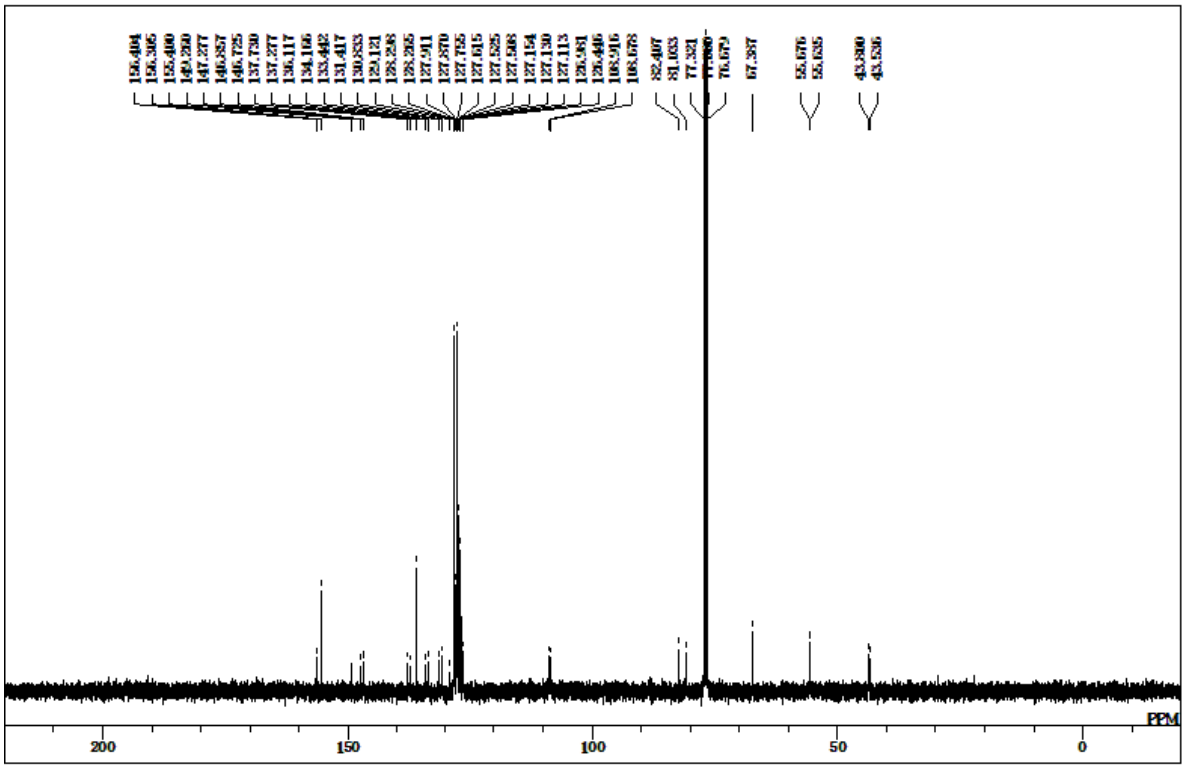


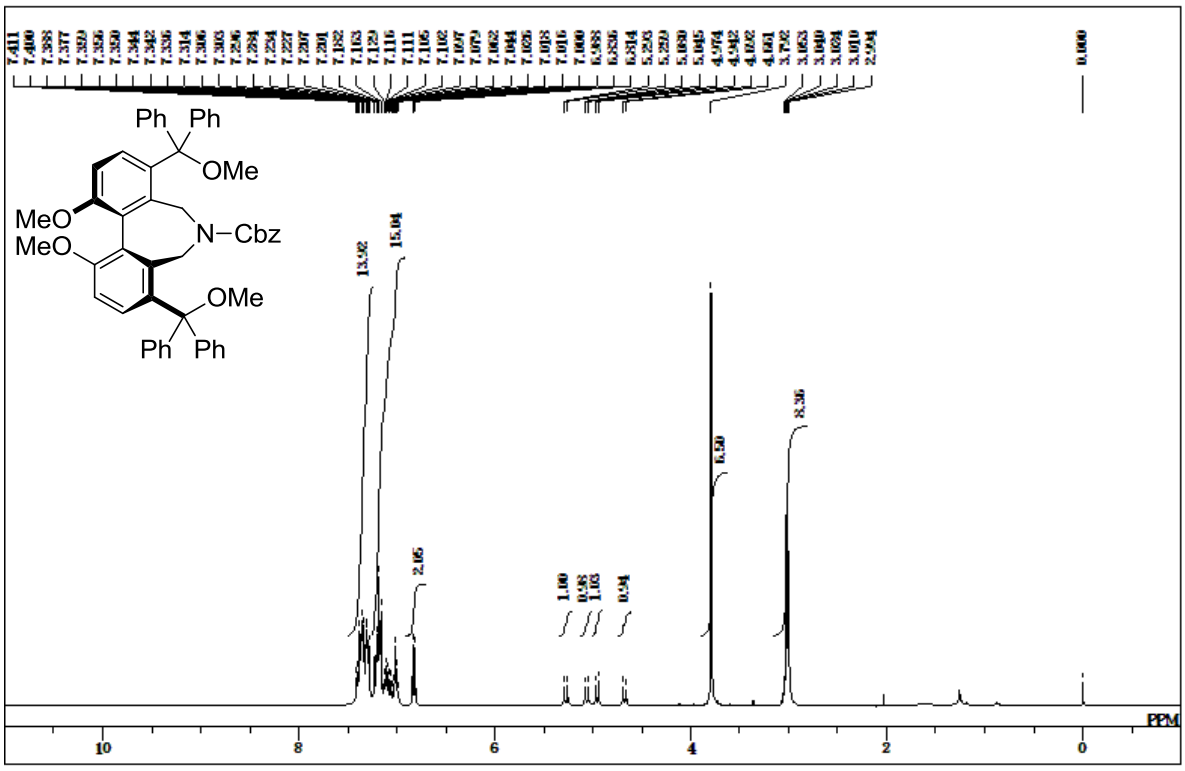


Aminoalcohol (*S*)-24





Amine (*S*)-25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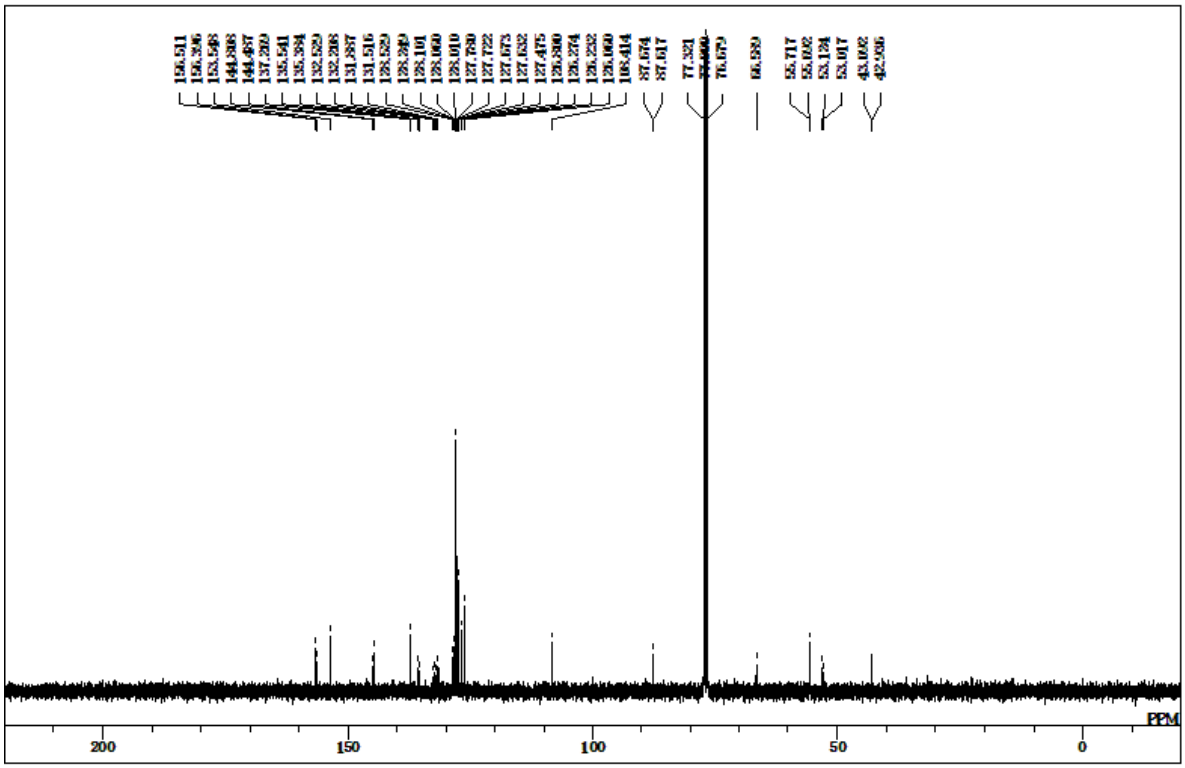
PPM
10
8
6
4
2
0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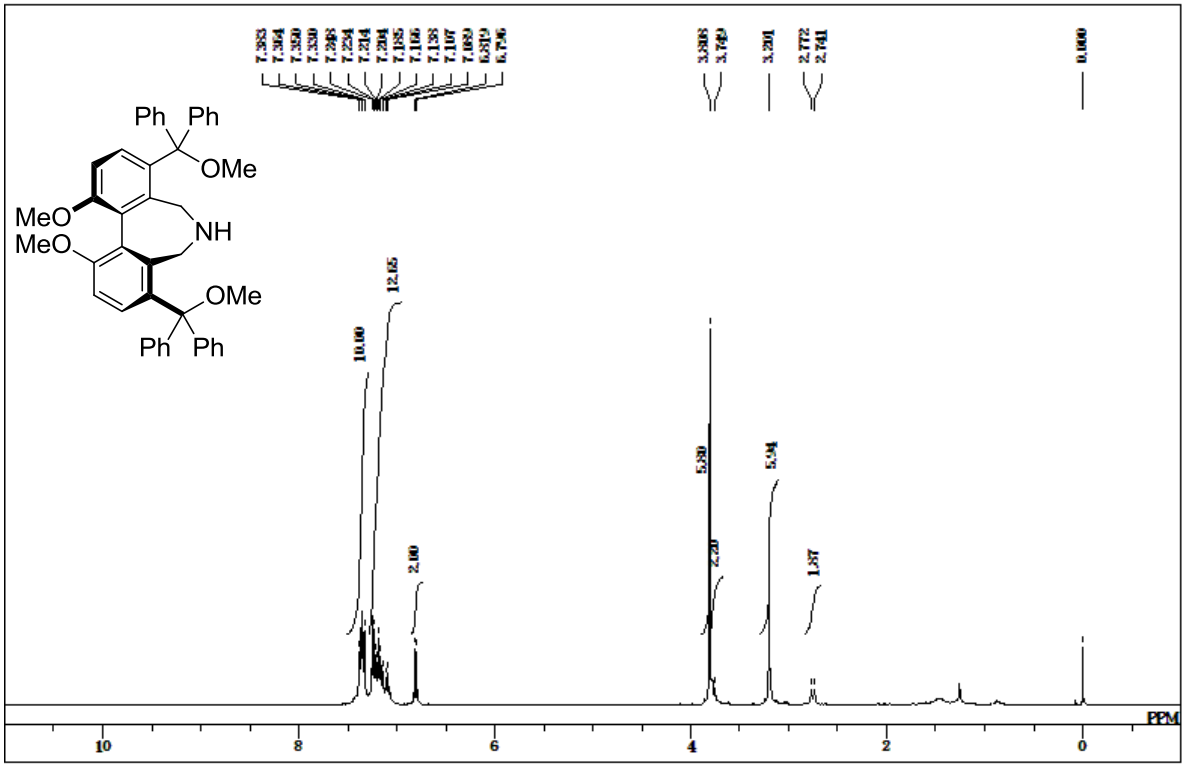

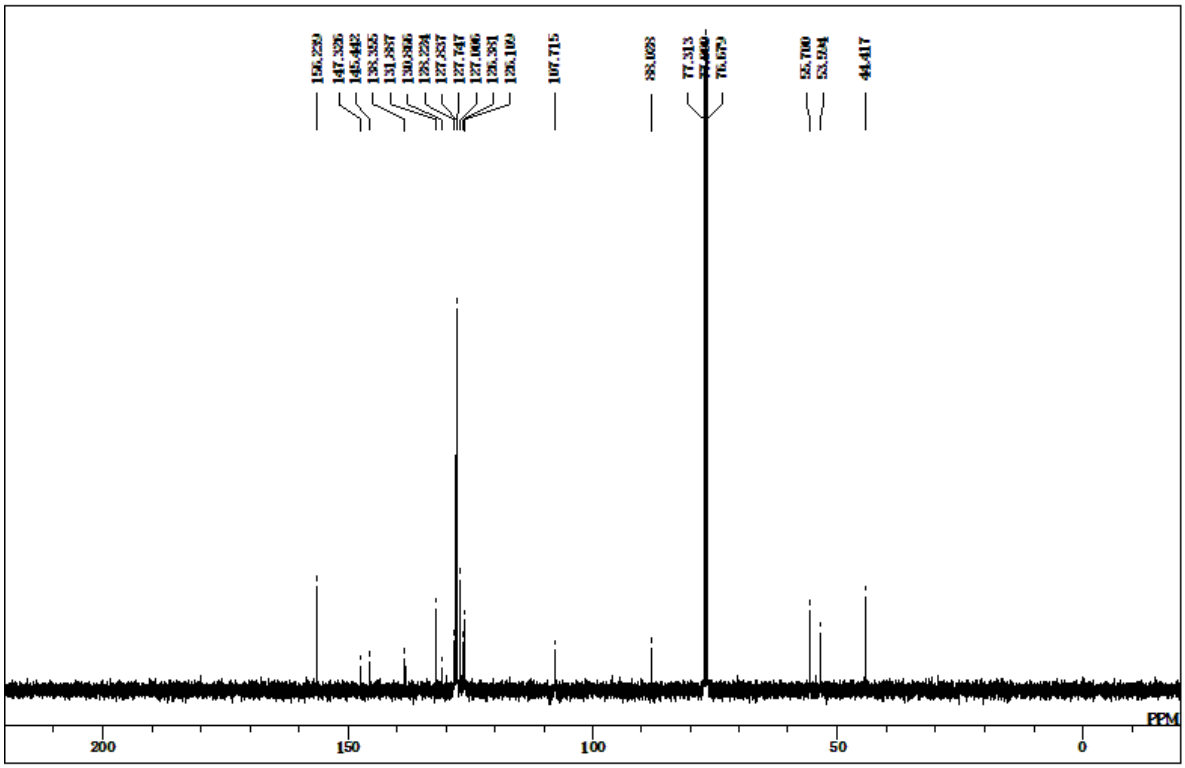

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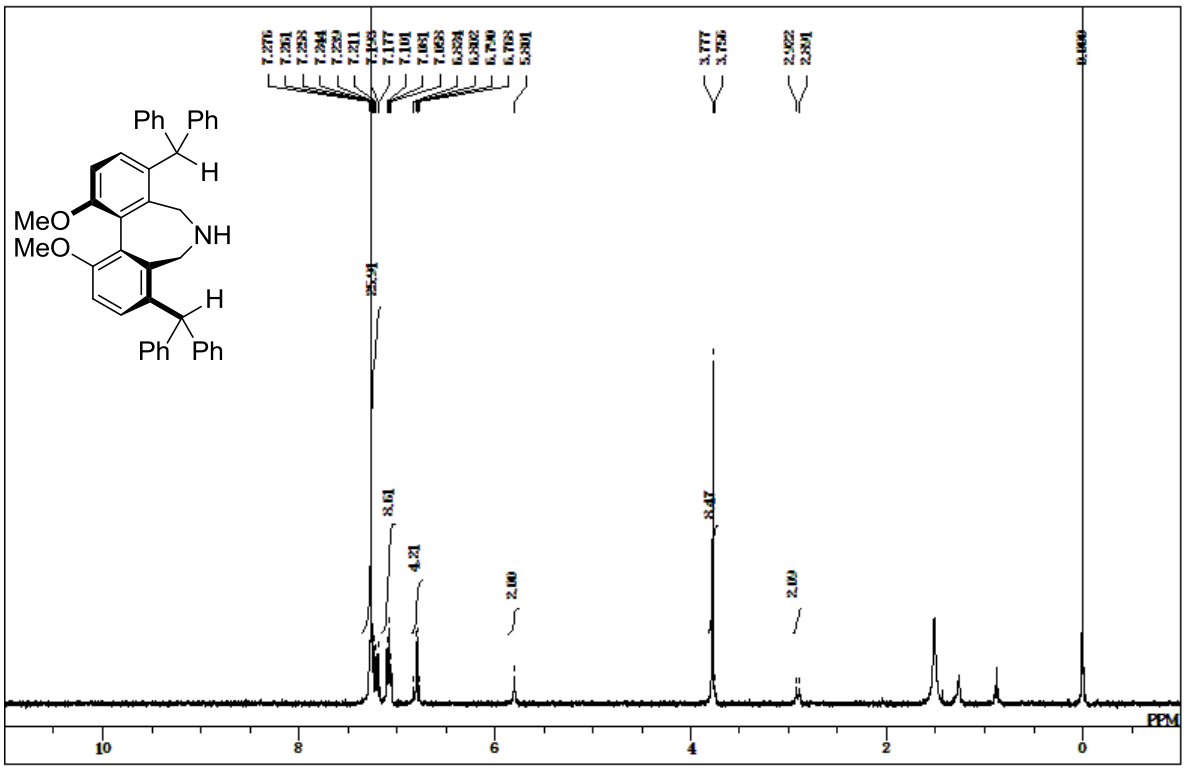
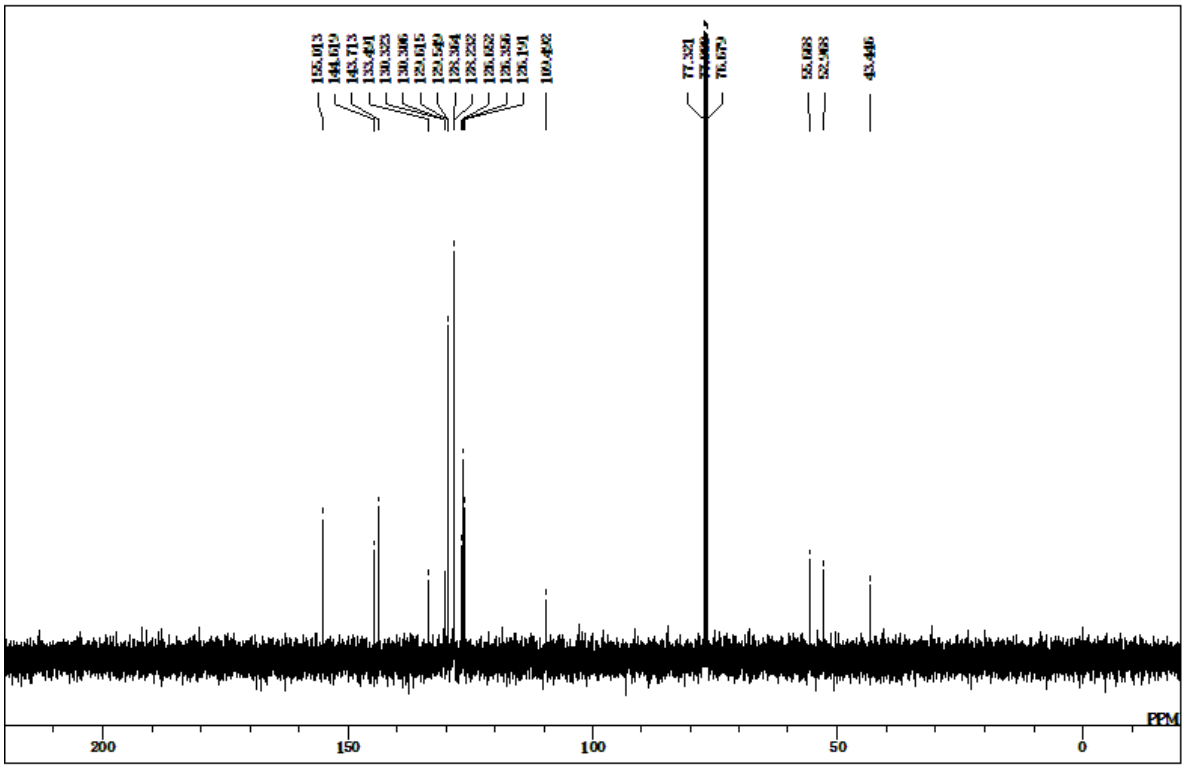
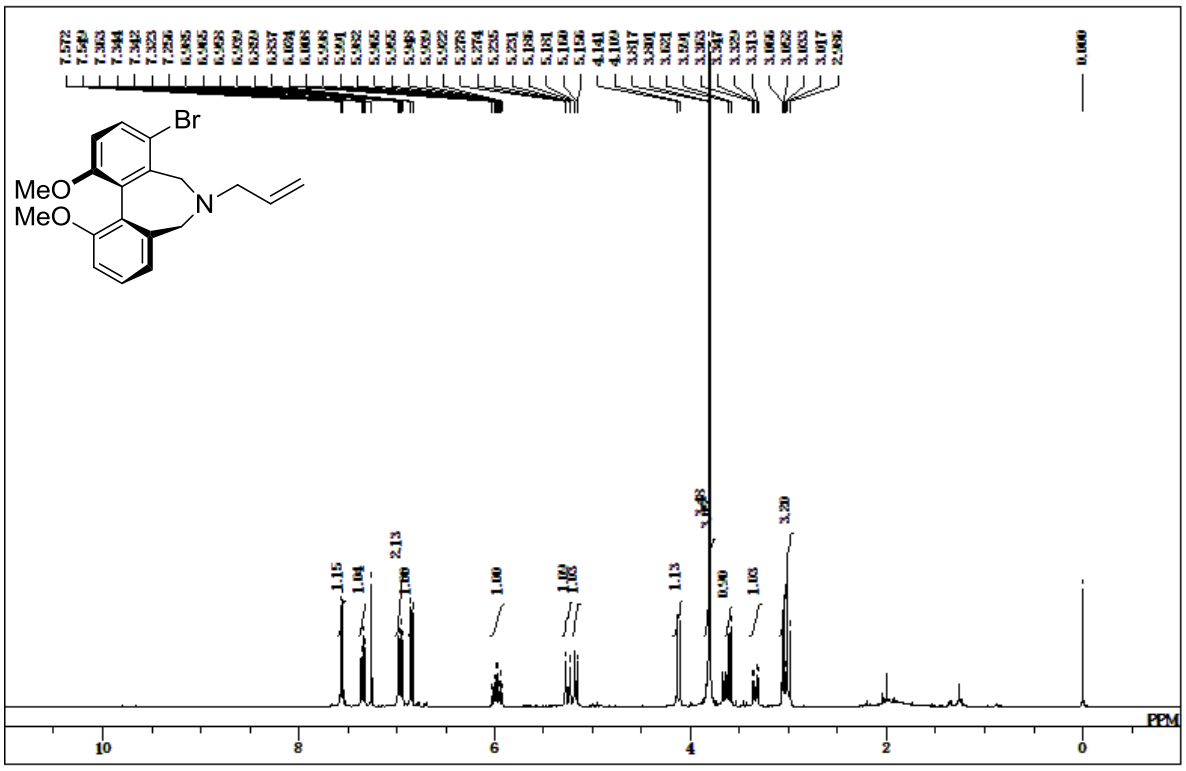
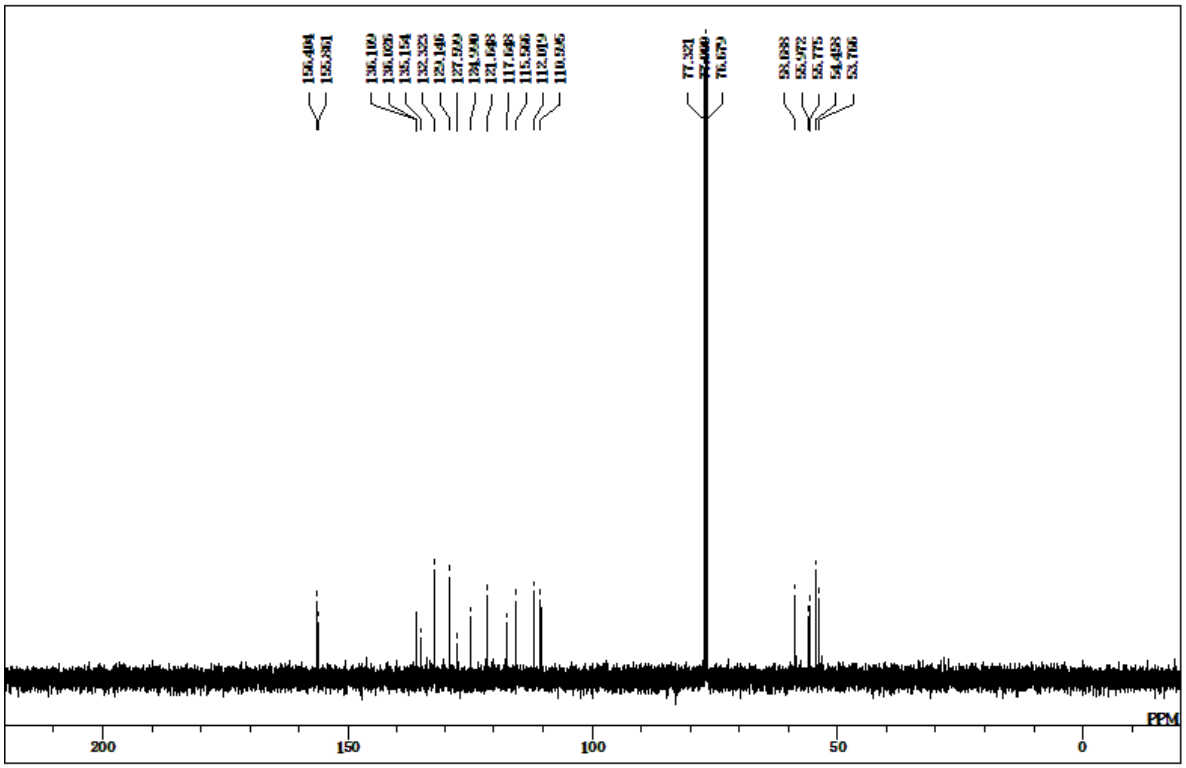


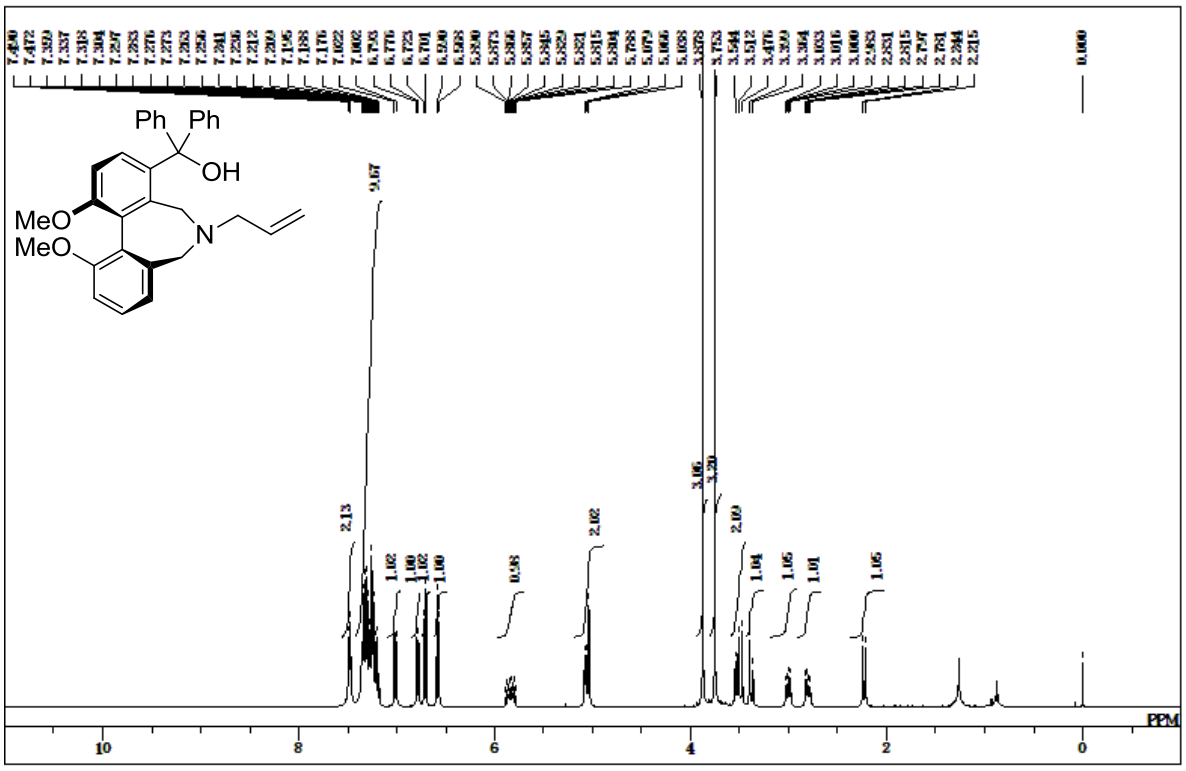


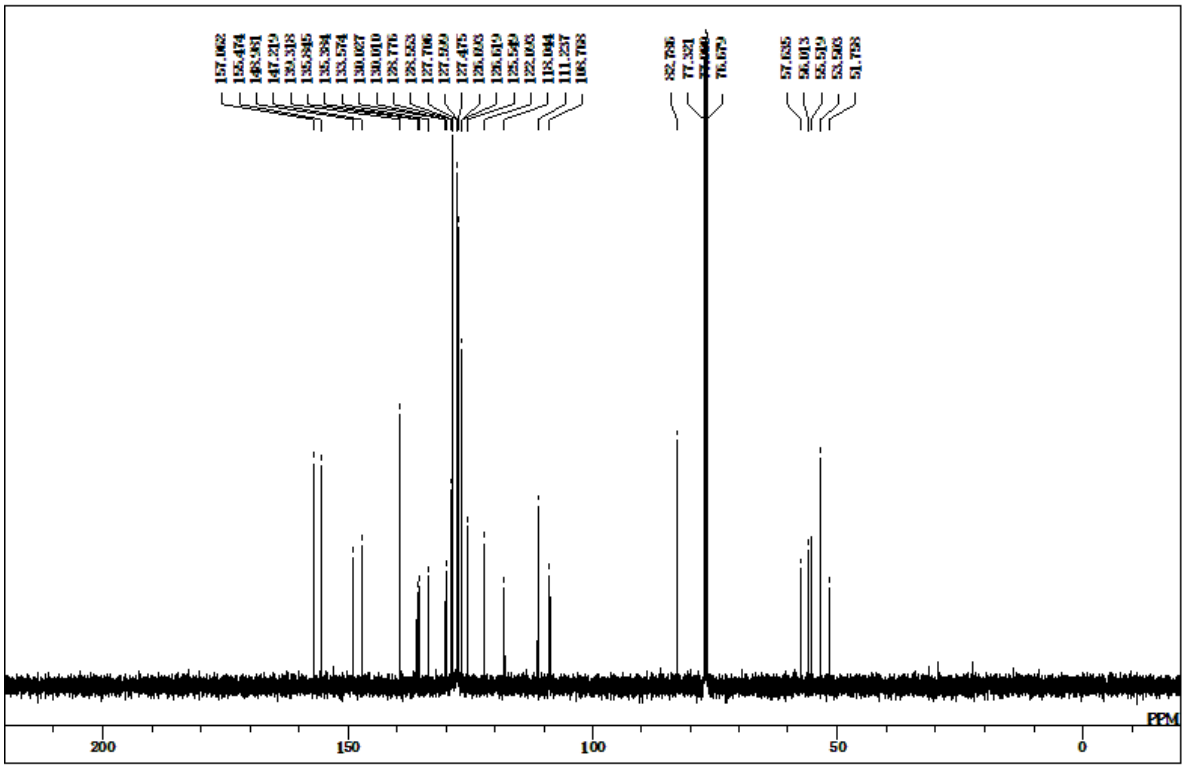
Monobromide (*S*)-27





Aminoalcohol (*S*)-28





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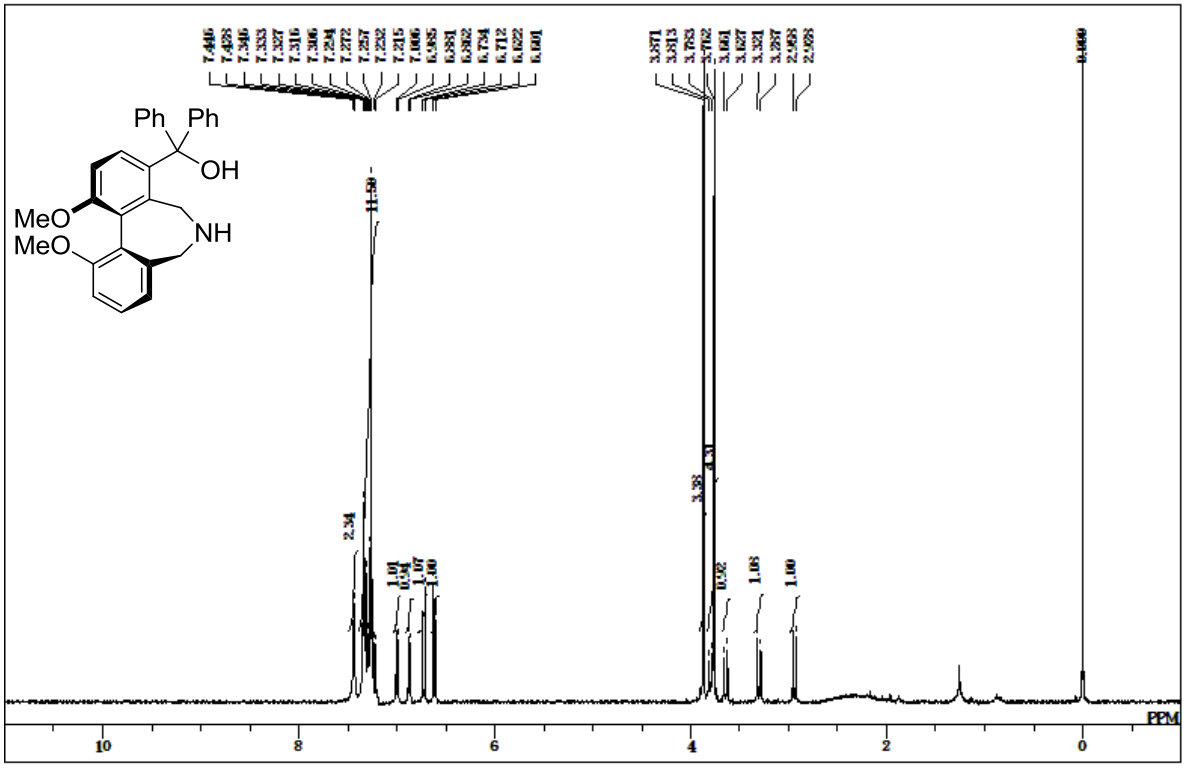
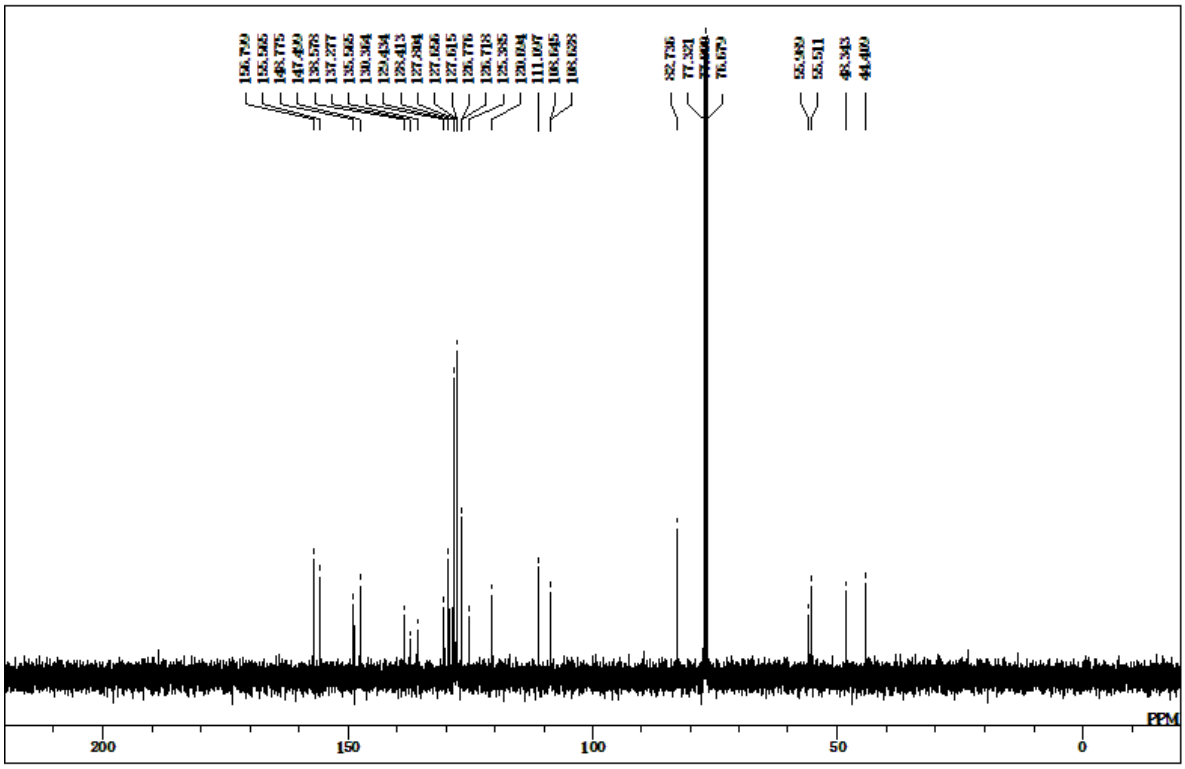
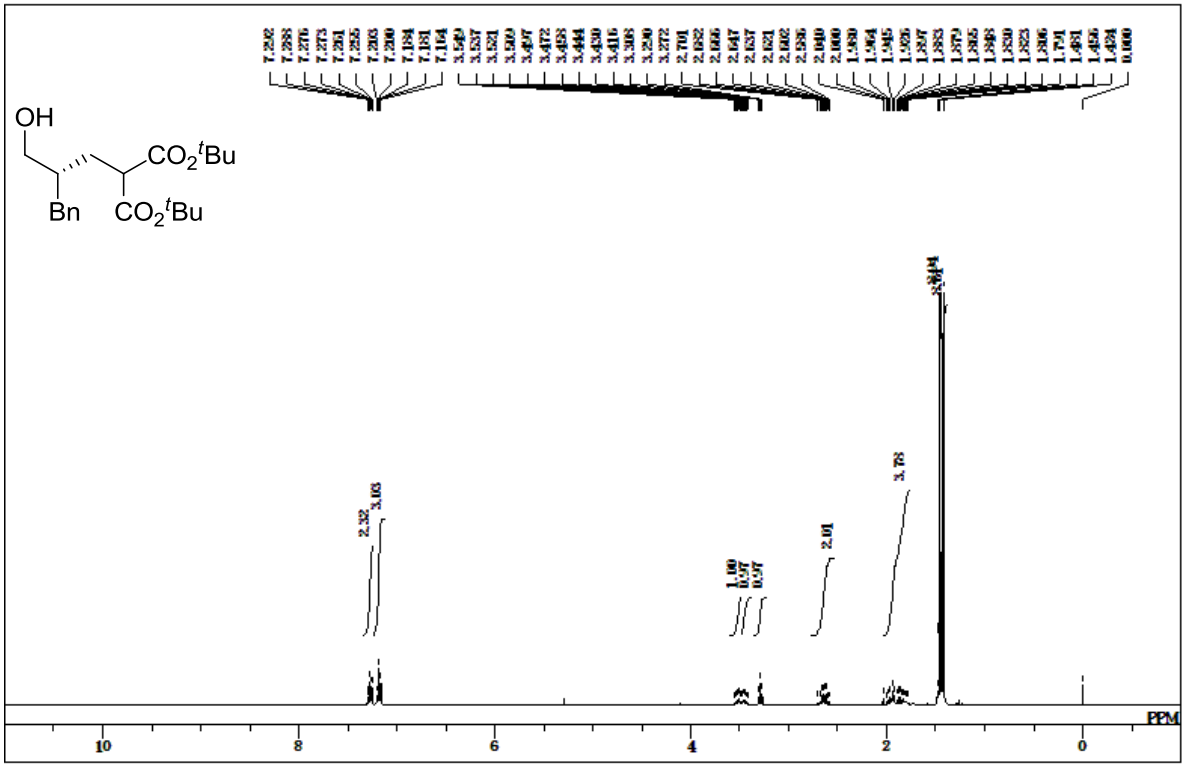
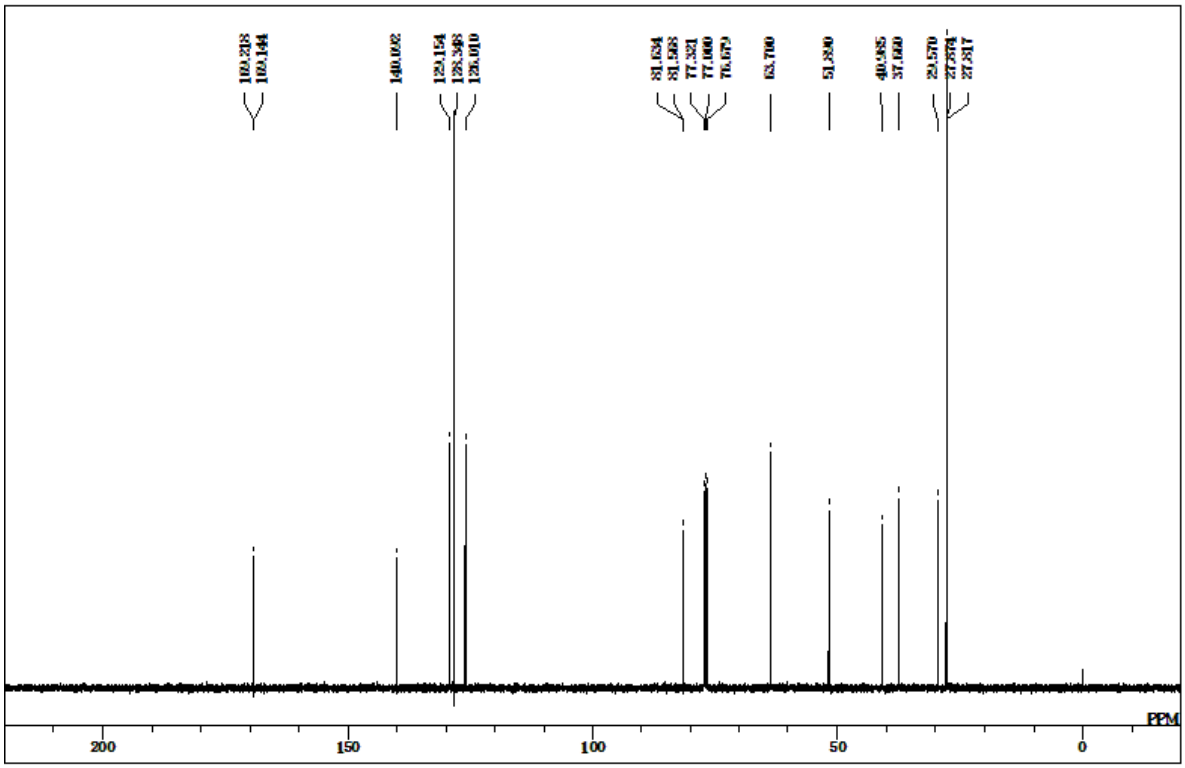




Di-*t*-butyl (*R*)-2-(2-benzyl-3-hydroxypropyl)malonate (Table 1, entry 6)





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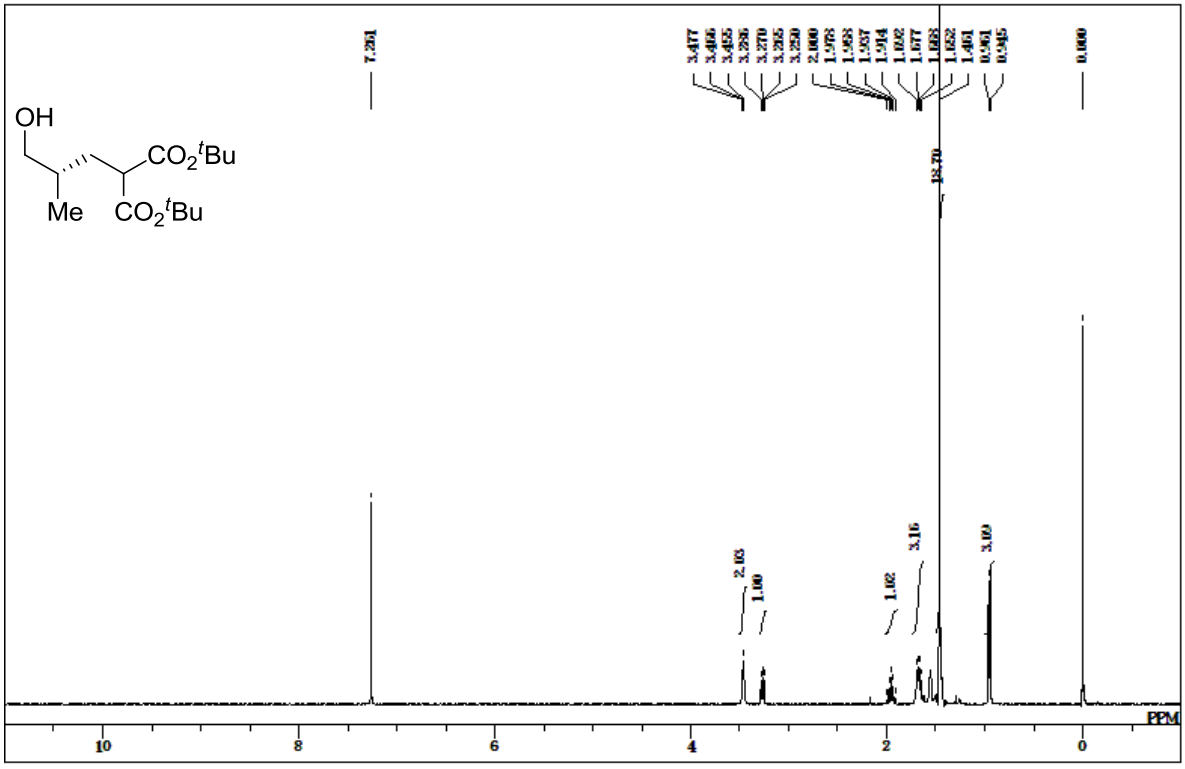
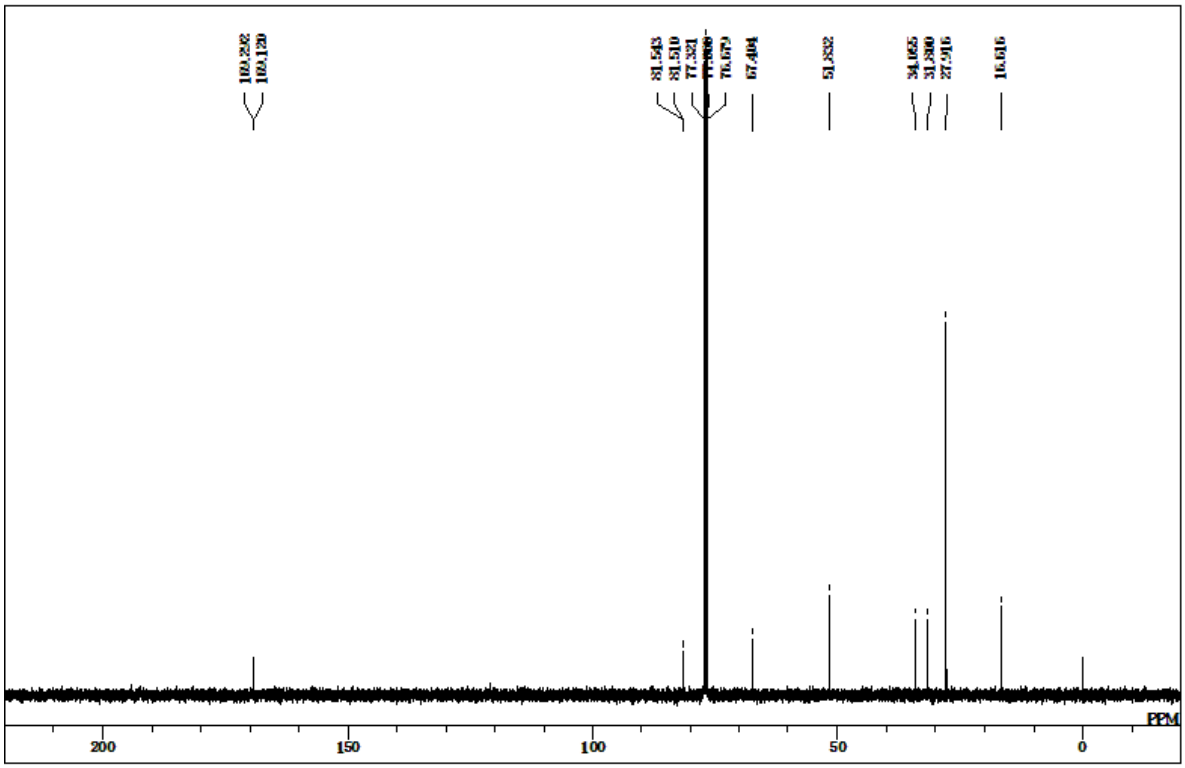
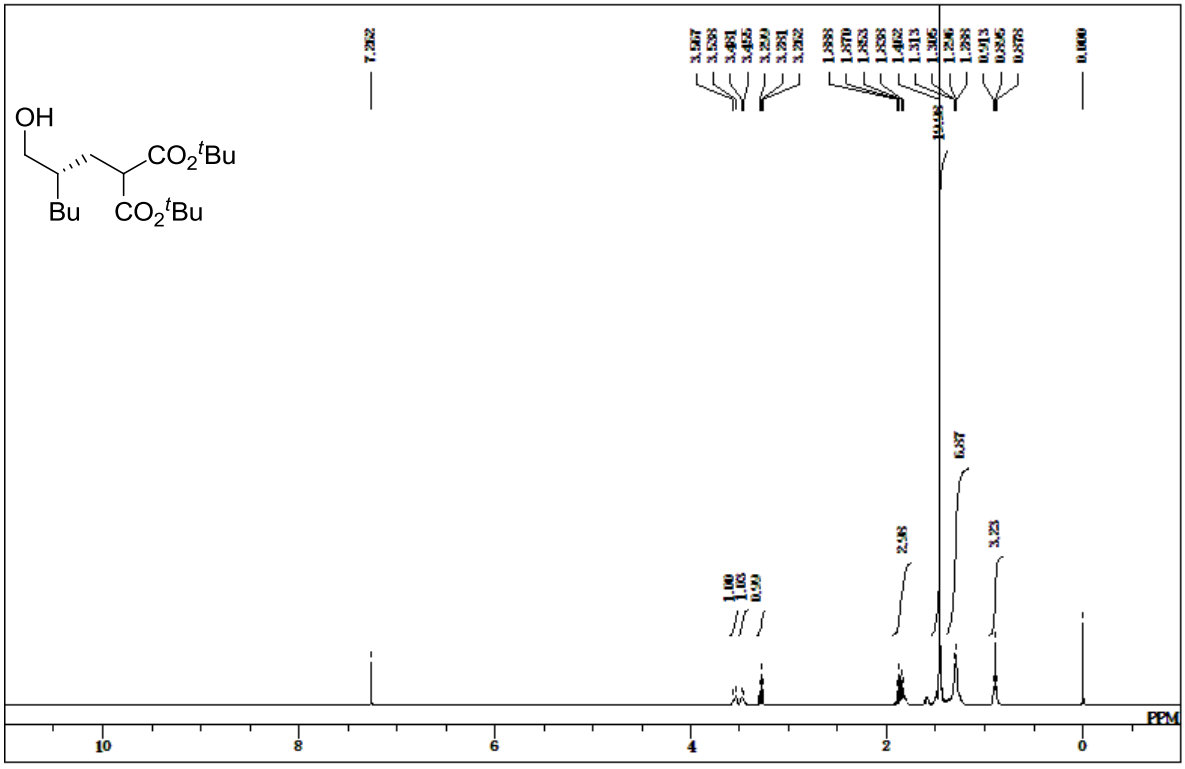
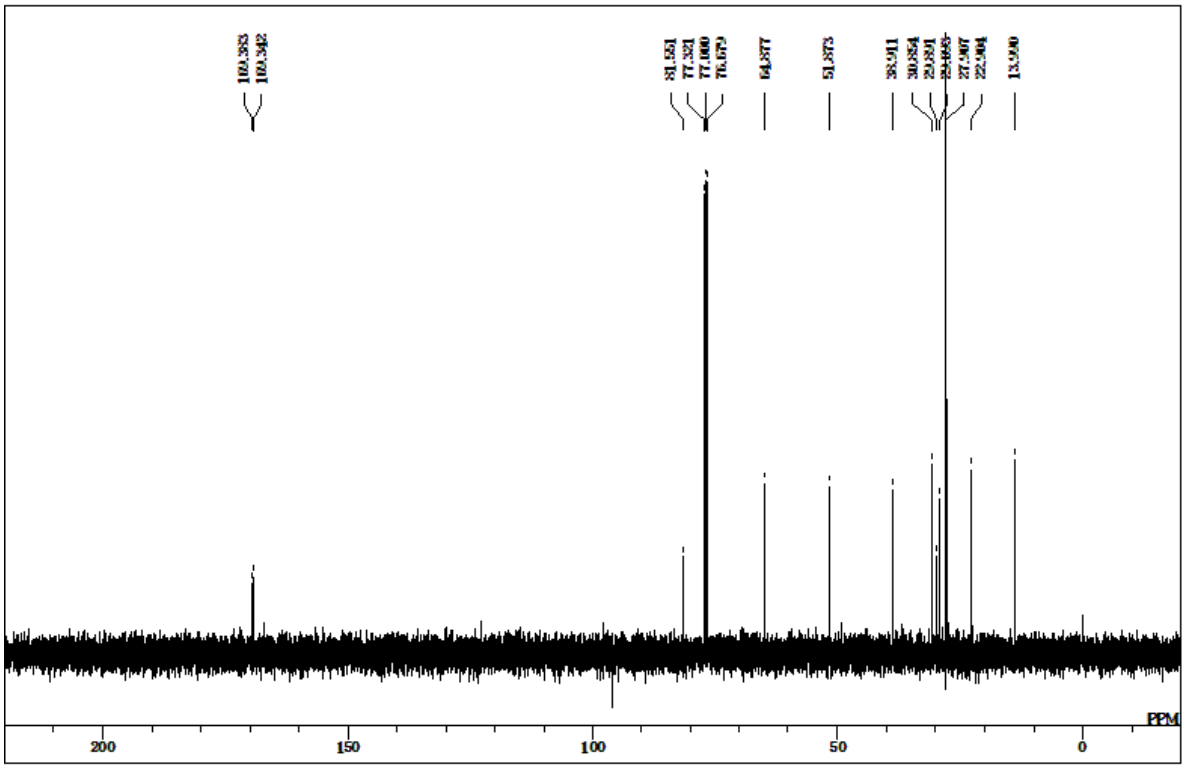




Di-*t*-butyl (*S*)-2-(2-(hydroxymethyl)hexyl)malonate (Table 1, entry 11)





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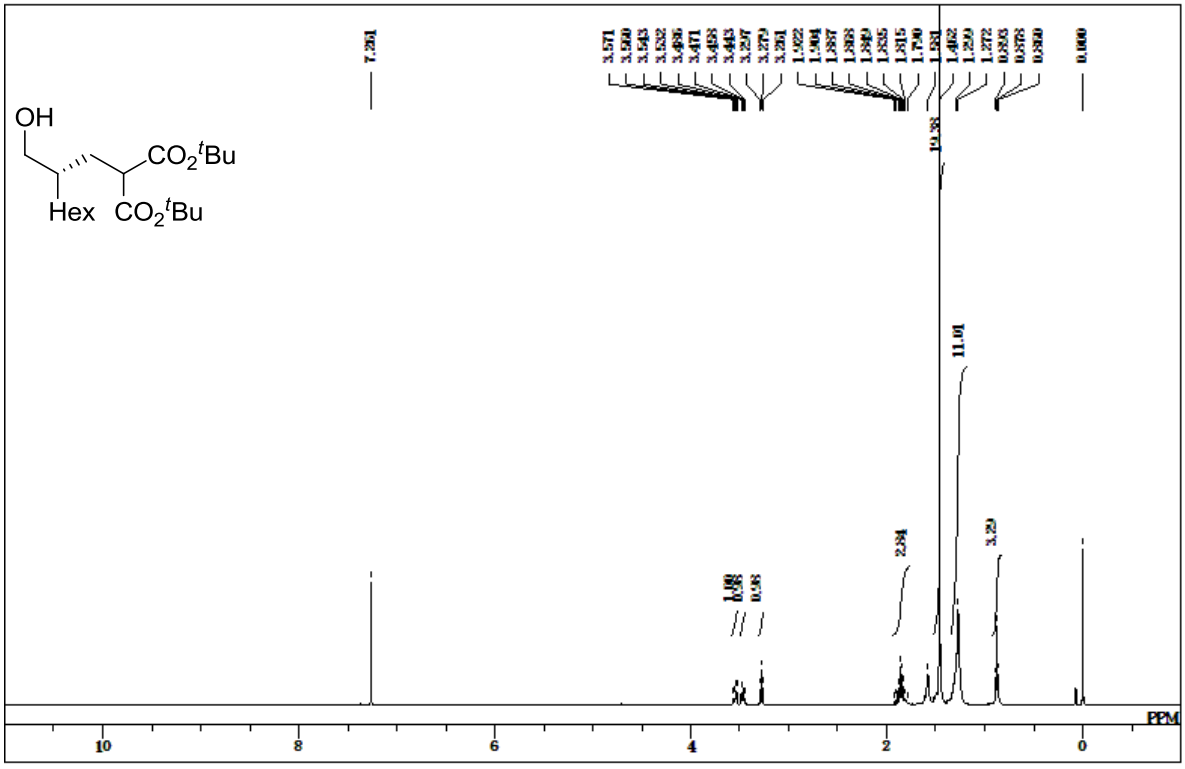
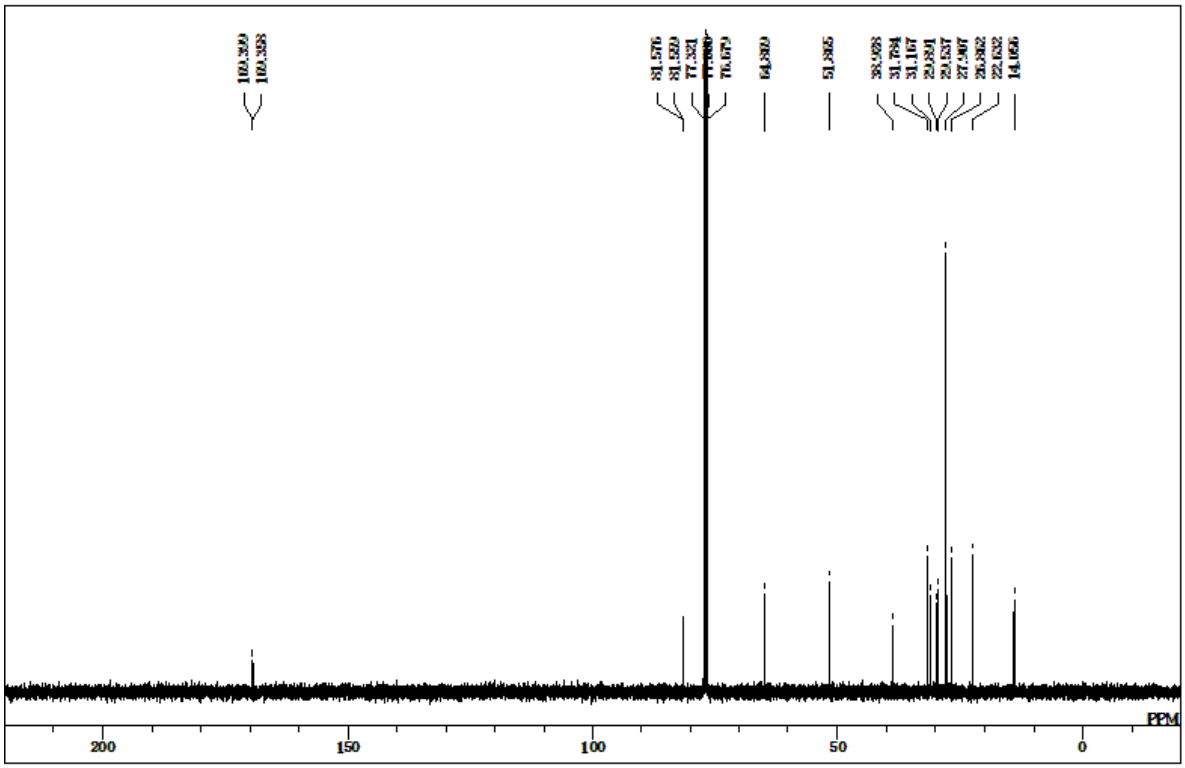
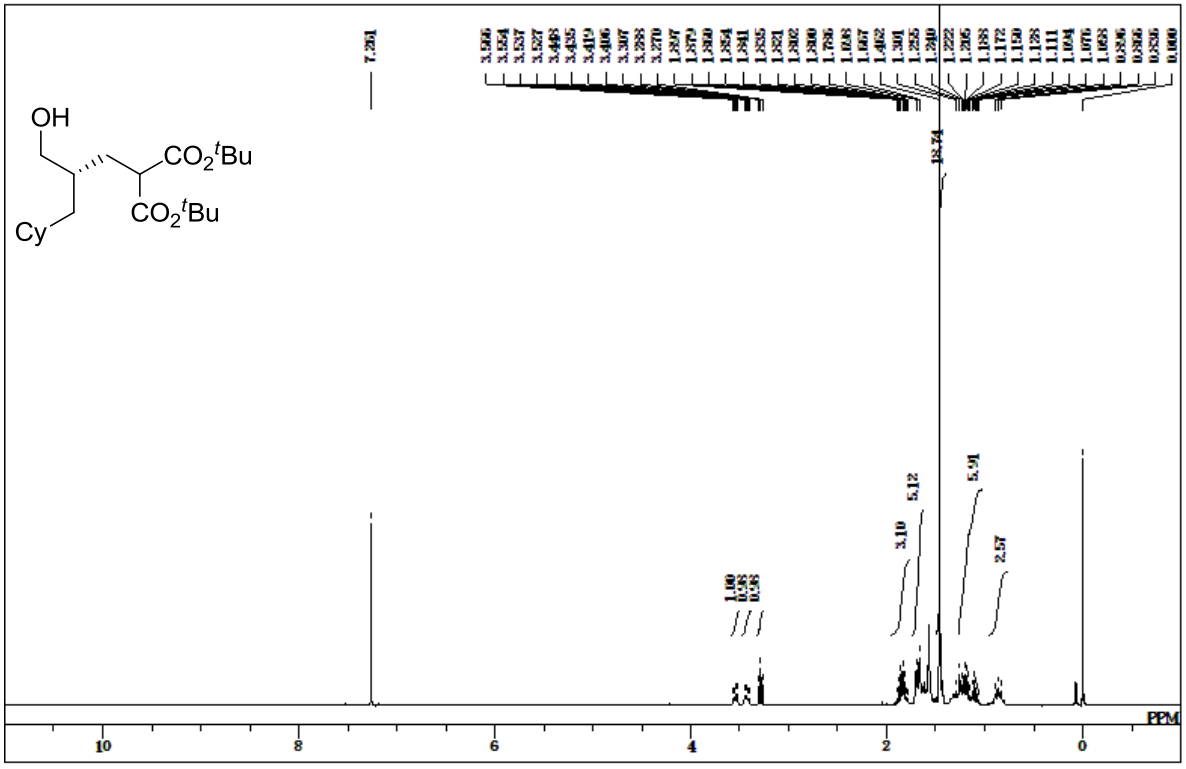
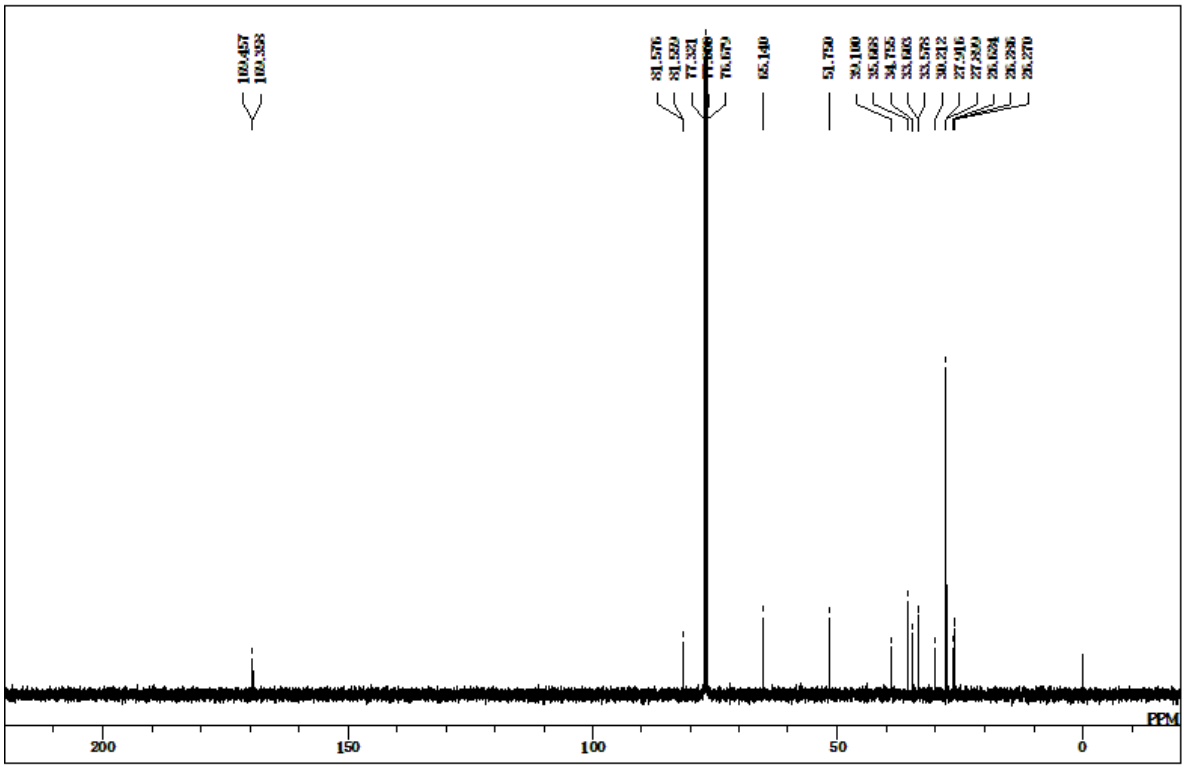


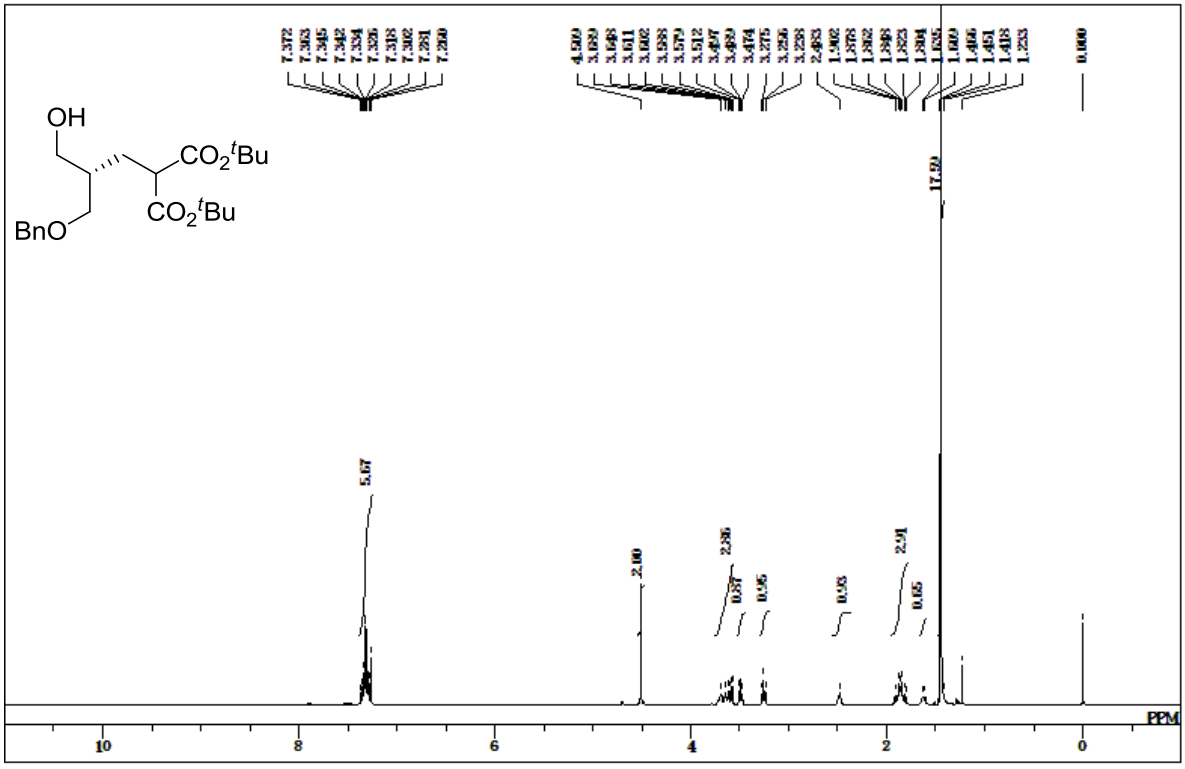


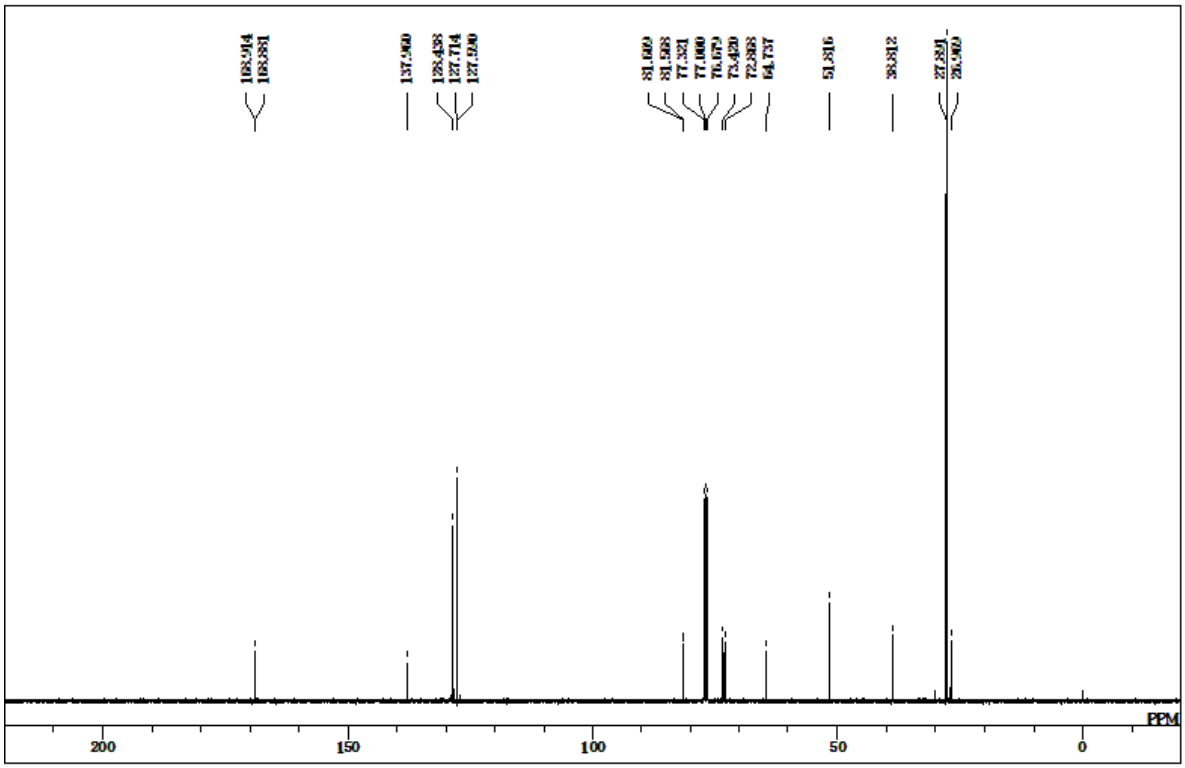
Di-*t*-butyl (*R*)-2-(3-cyclohexyl-2-(hydroxymethyl)propyl)malonate (Table 1, entry 13)



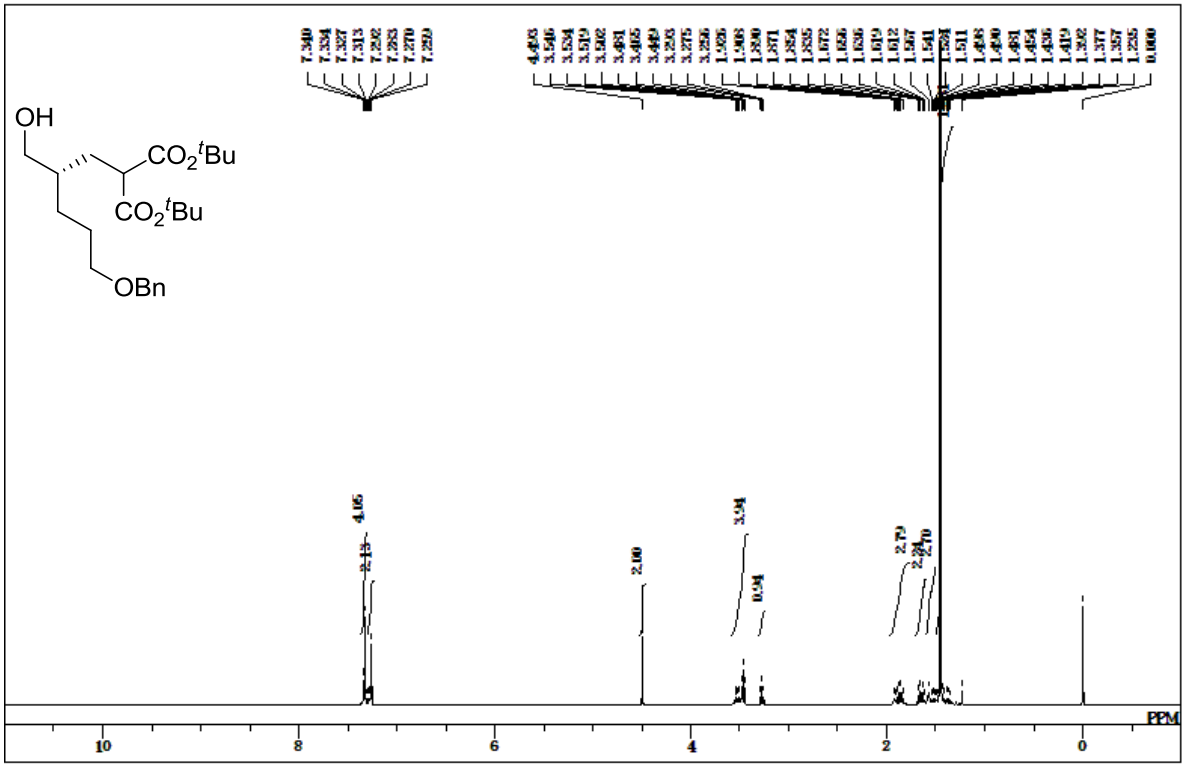


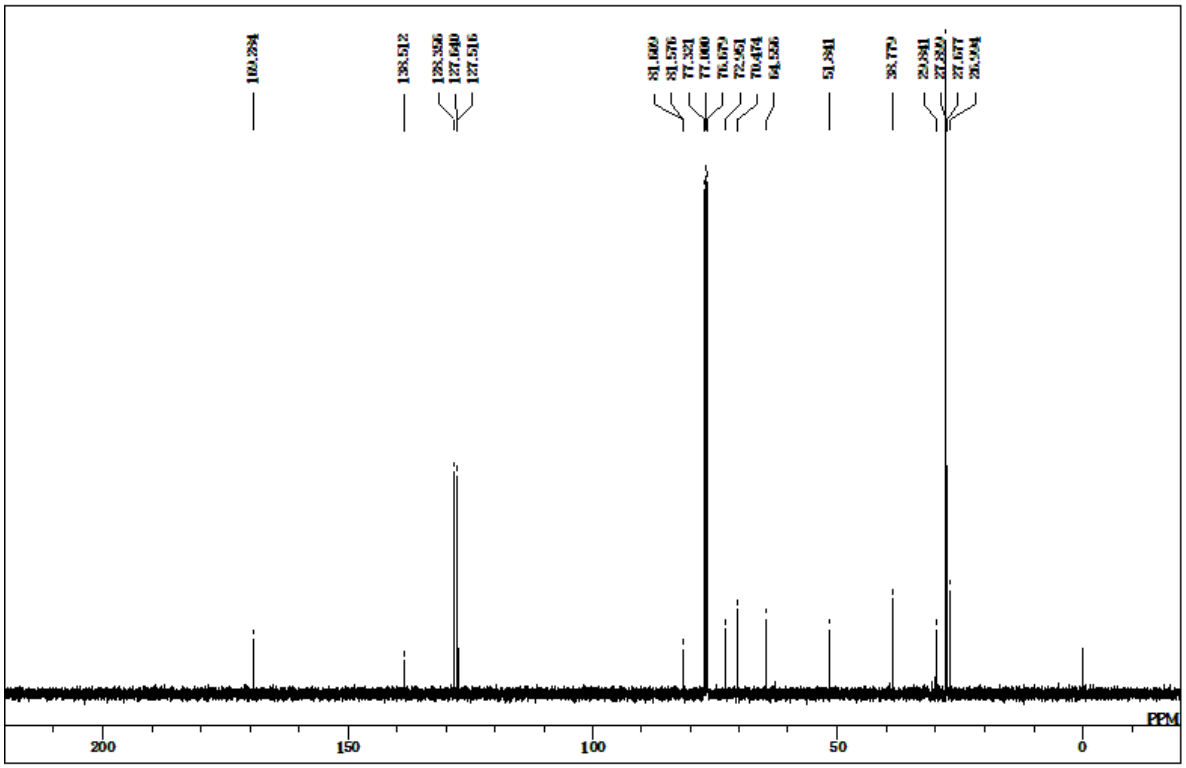
Di-*t*-butyl (*S*)-2-(3-(benzyloxy)-2-(hydroxymethyl)propyl)malonate (Table 1, entry 14)



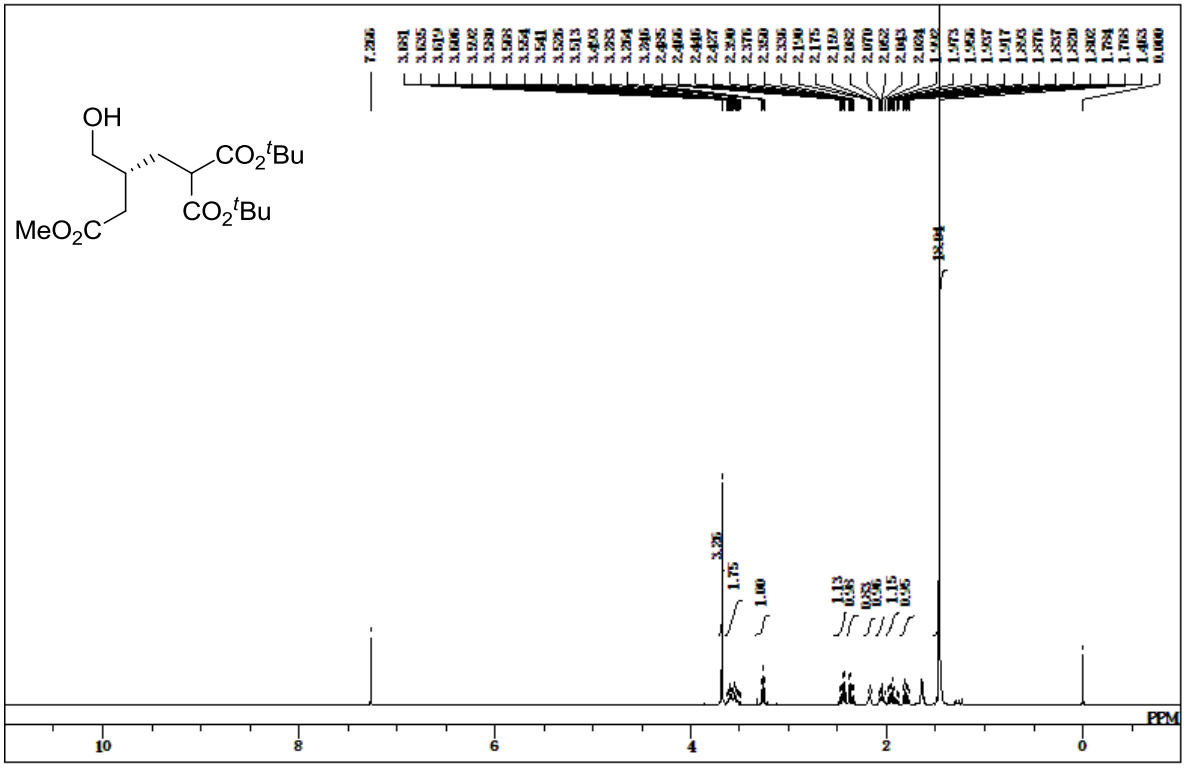


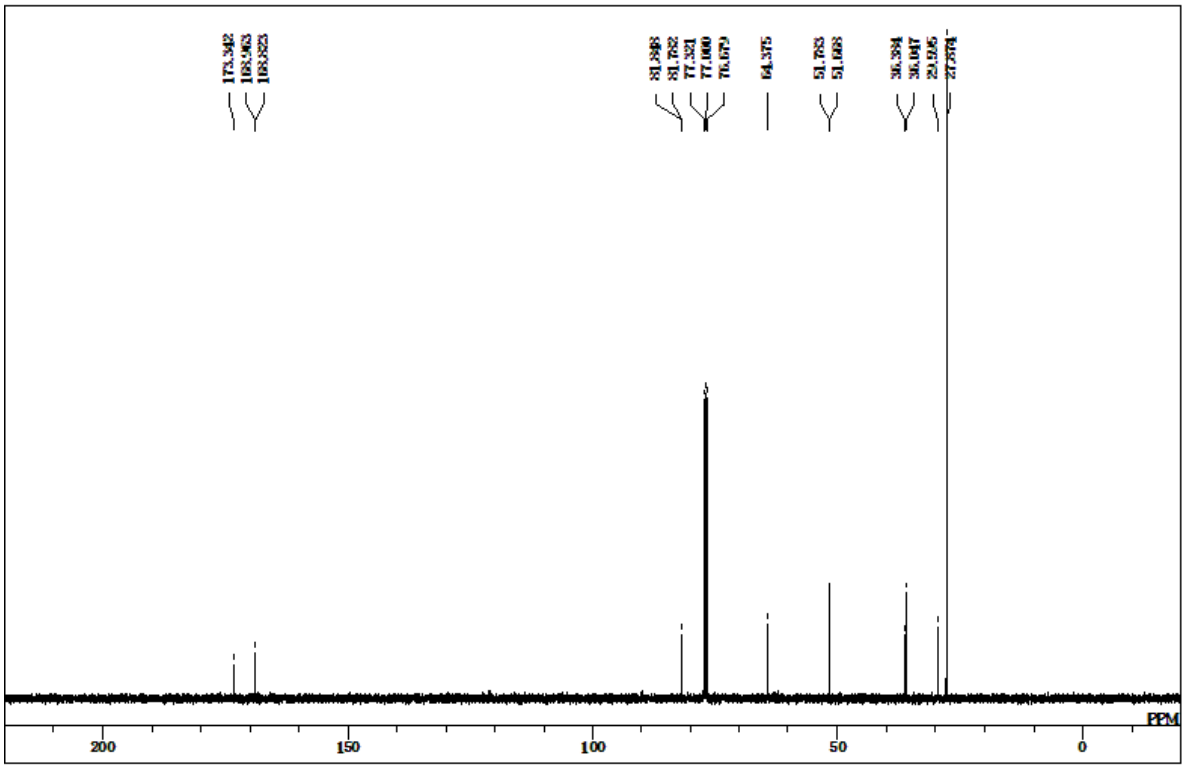
Di-*t*-butyl (*S*)-2-(5-(benzyloxy)-2-(hydroxymethyl)pentyl)malonate (Table 1, entry 15)





1,1-Di-*t*-butyl 4-methyl (*R*)-3-(hydroxymethyl)butane-1,1,4-tricarboxylate (Table 1, entry 16)





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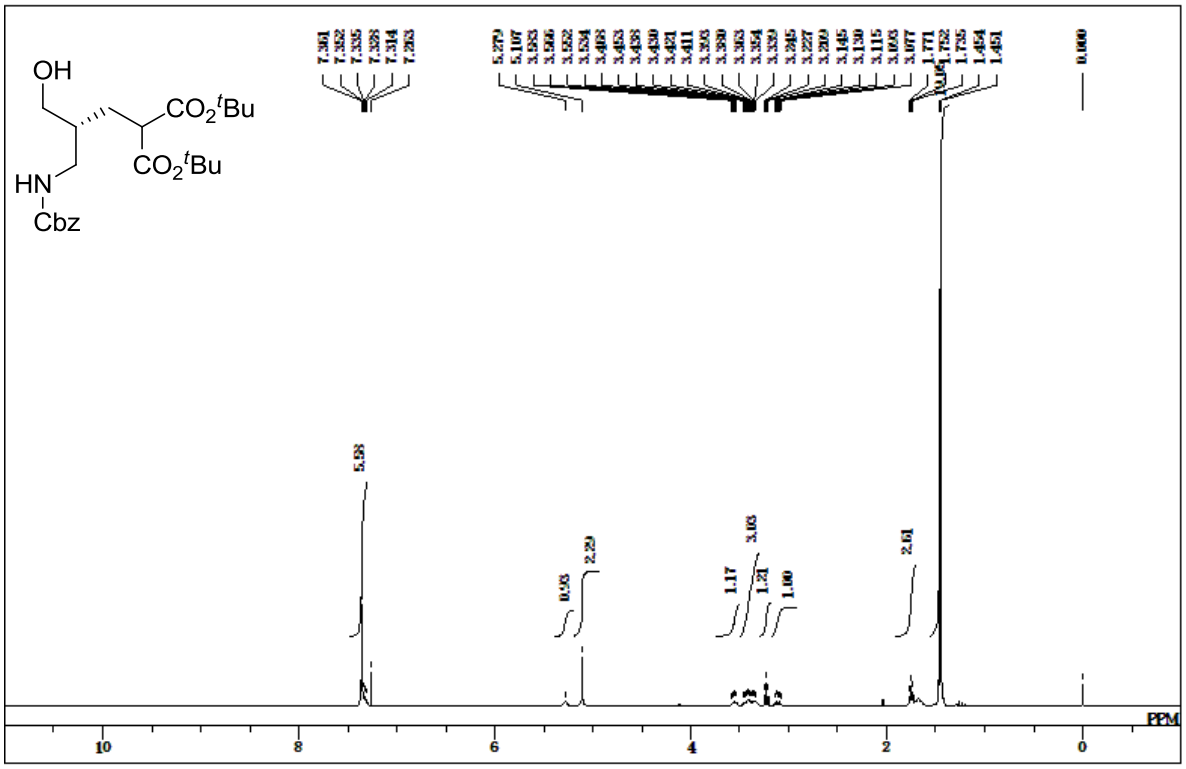
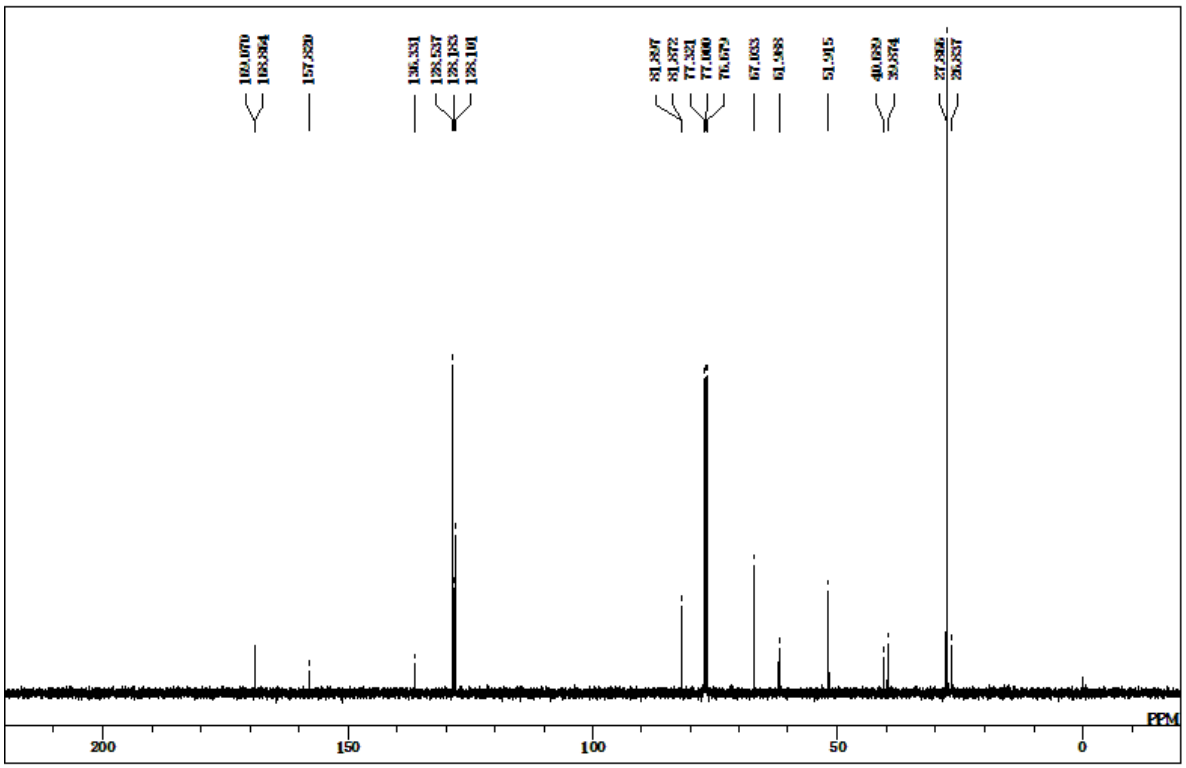
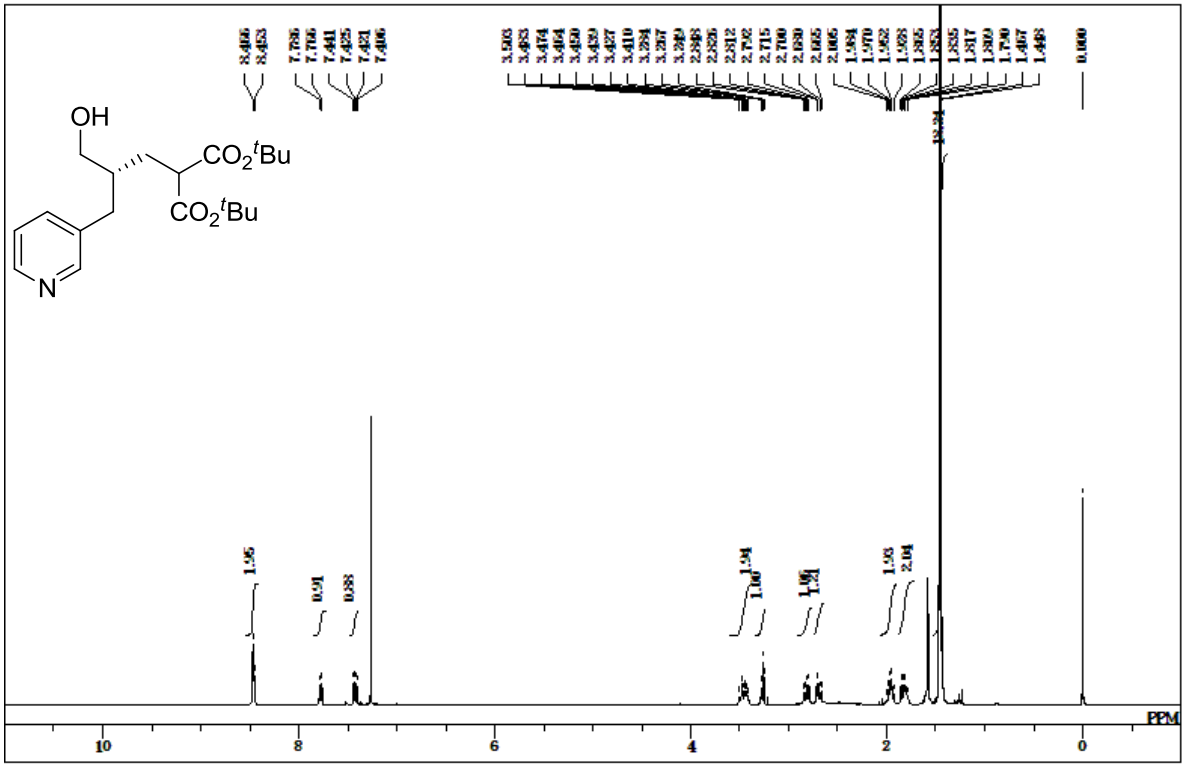
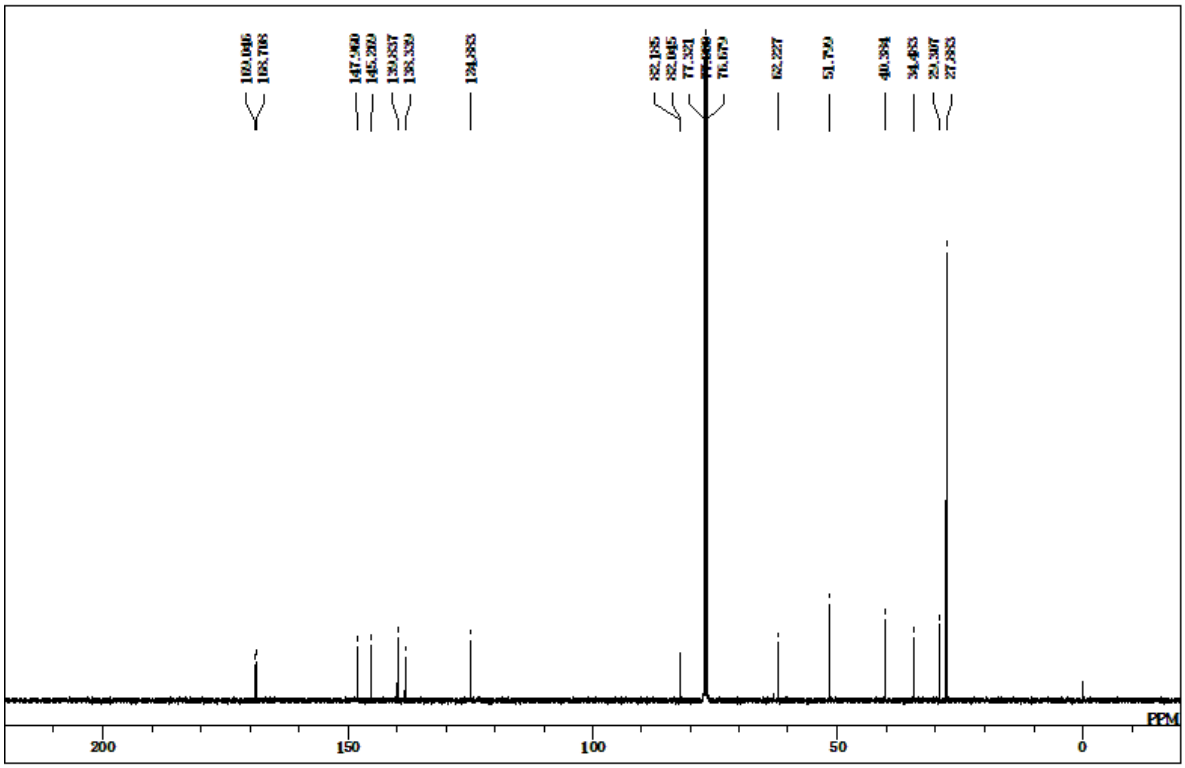


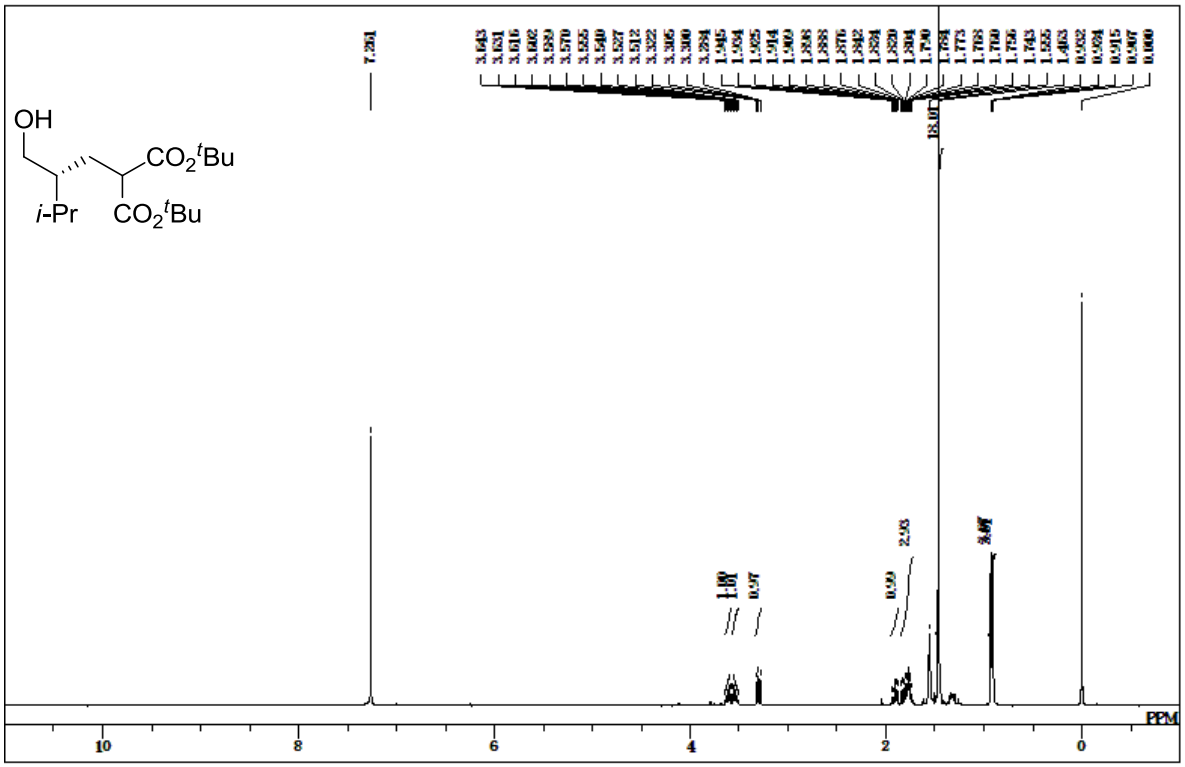


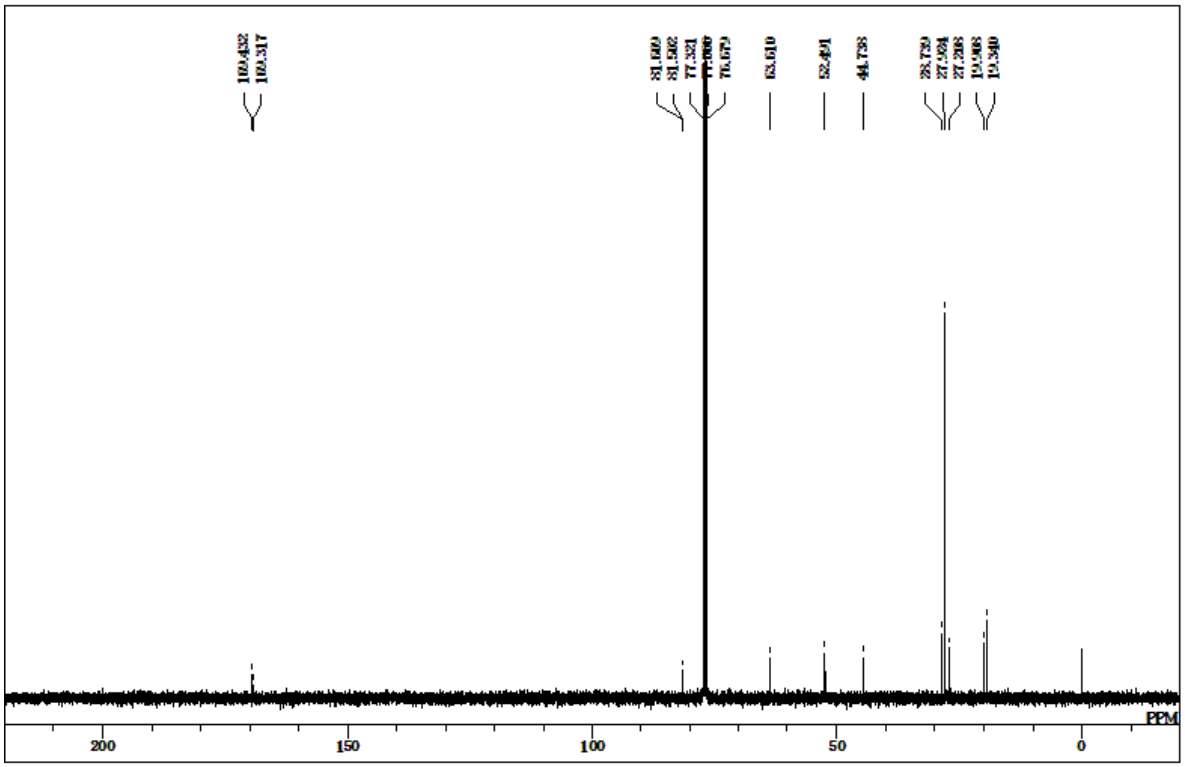
Di-*t*-butyl (*R*)-2-(3-hydroxy-2-(pyridin-3-ylmethyl)propyl)malonate (Table 1, entry 18)



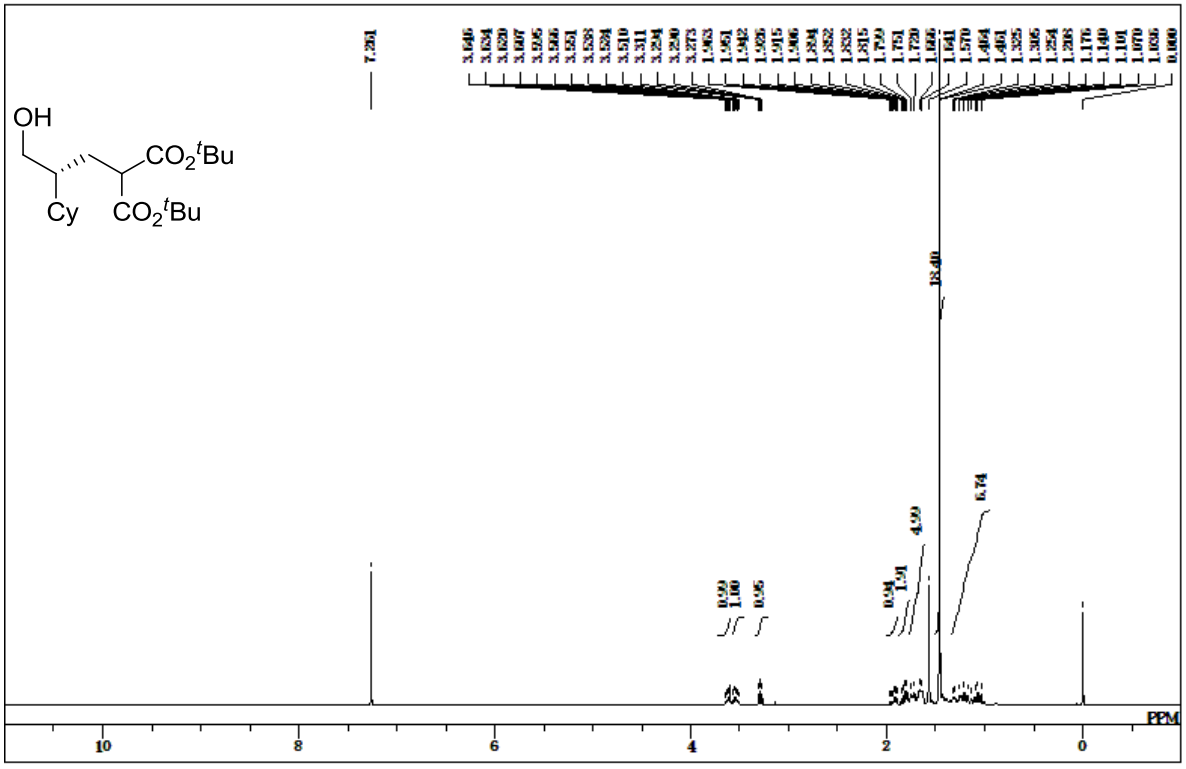


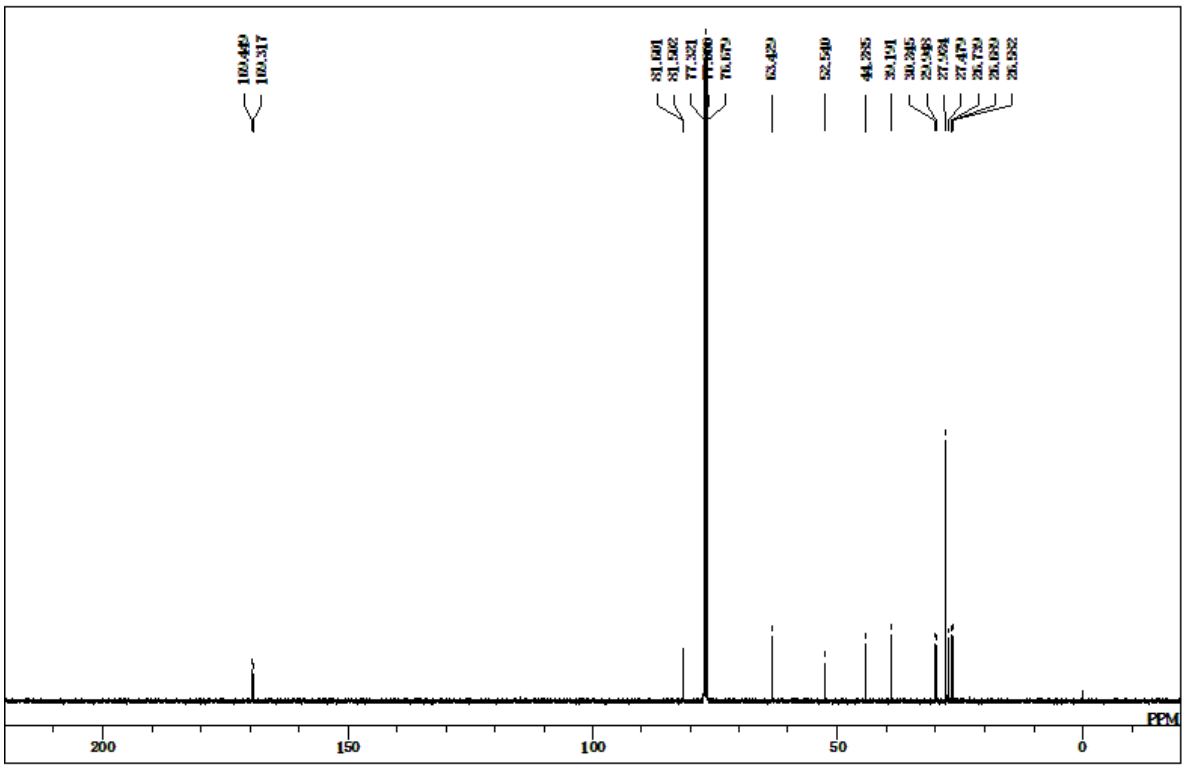
Di-*t*-butyl (*R*)-2-(2-(hydroxymethyl)-3-methylbutyl)malonate (Table 1, entry 19)



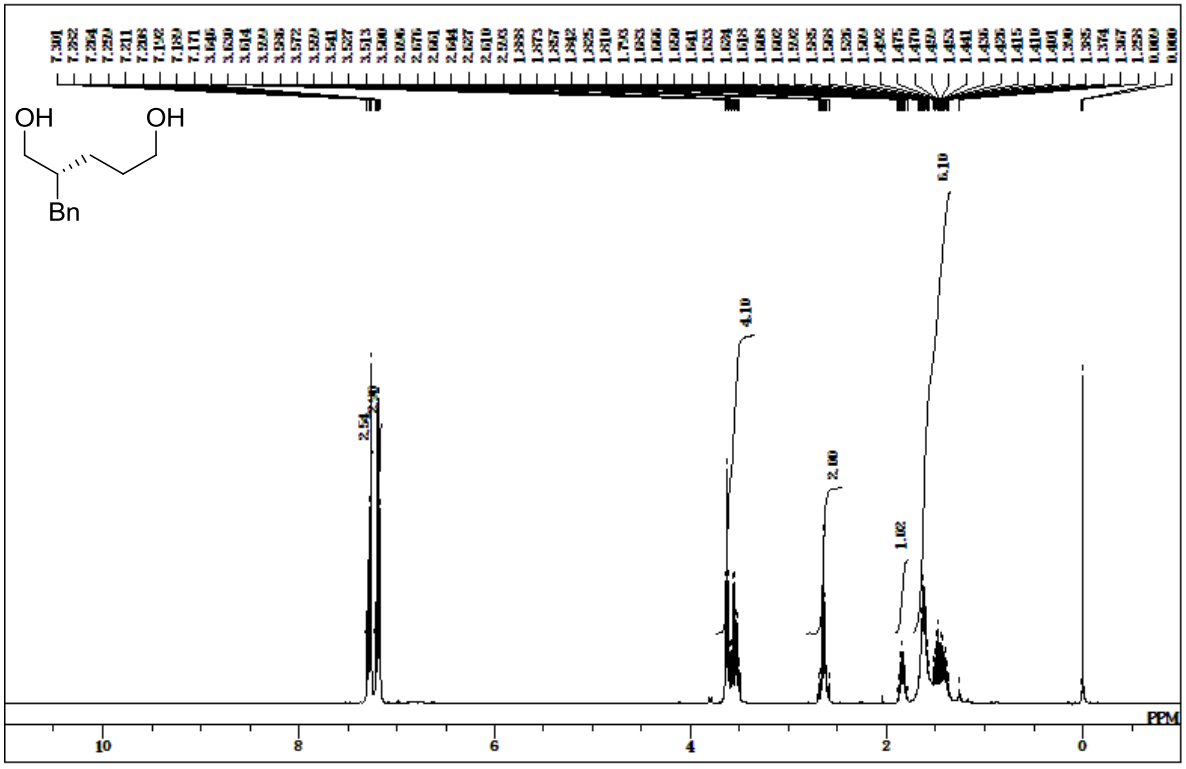


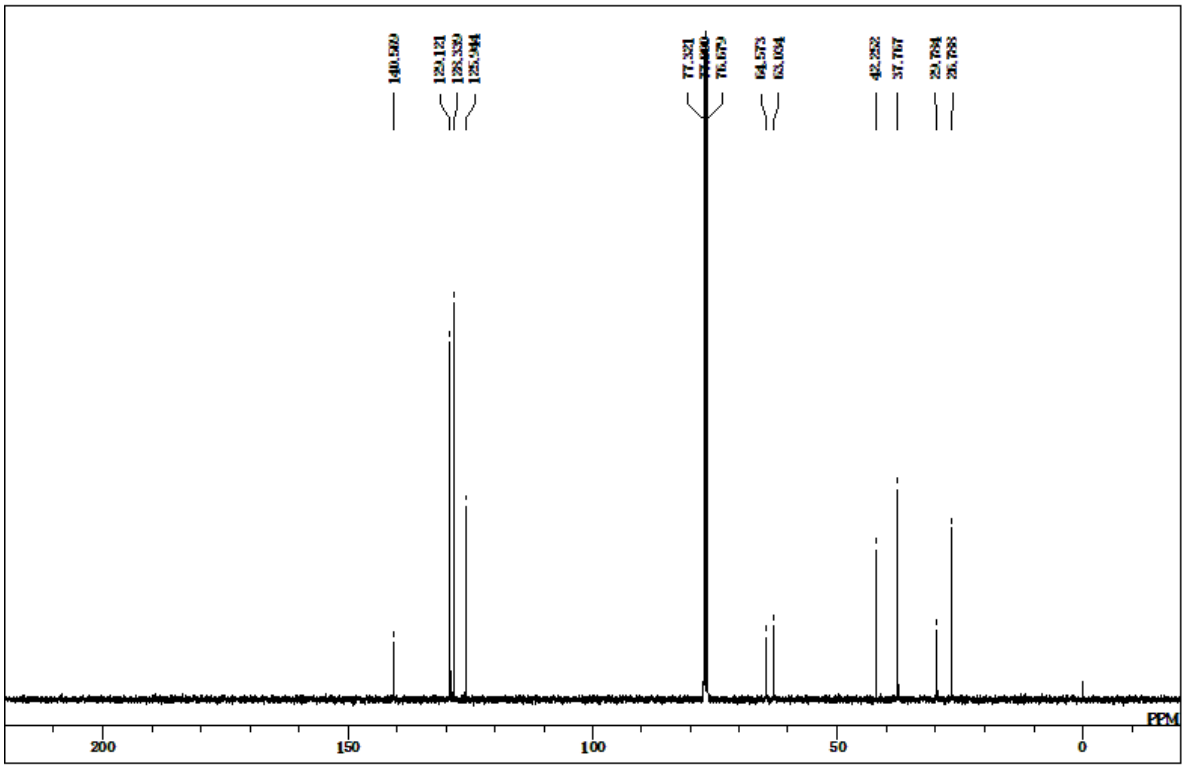
Di-*t*-butyl (*R*)-2-(2-cyclohexyl-3-hydroxypropyl)malonate (Table 1, entry 20)



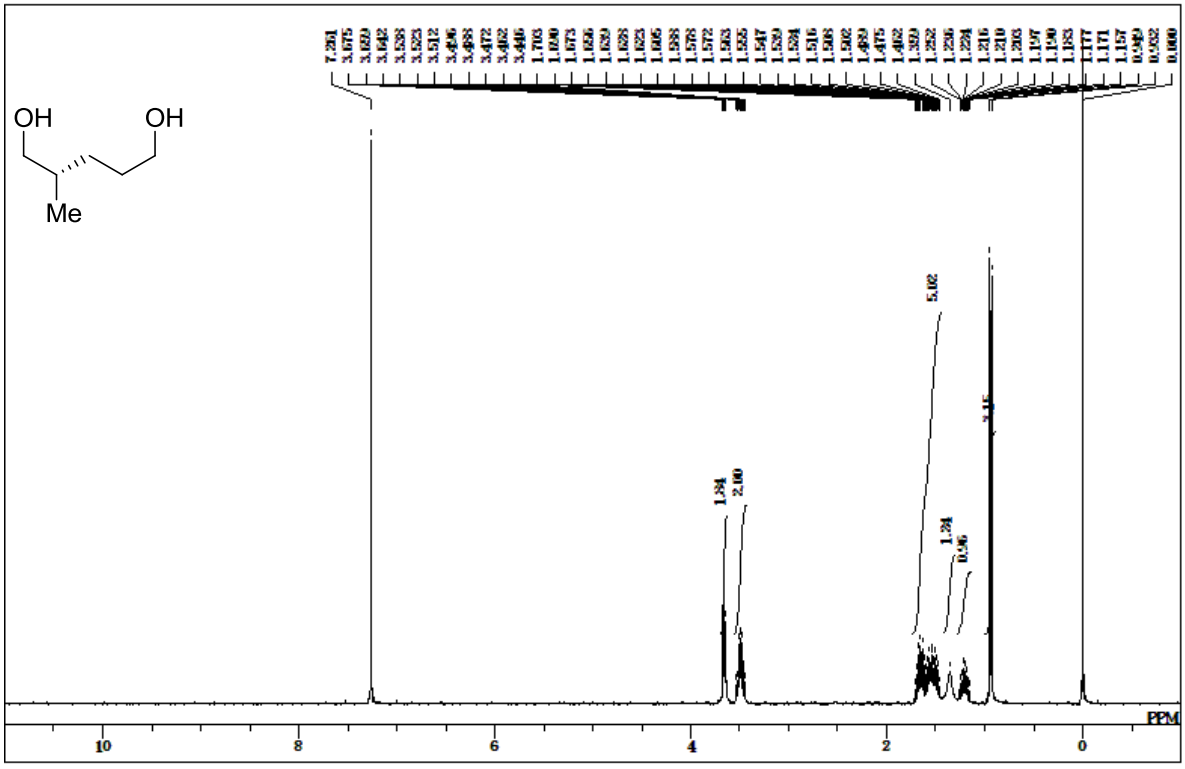


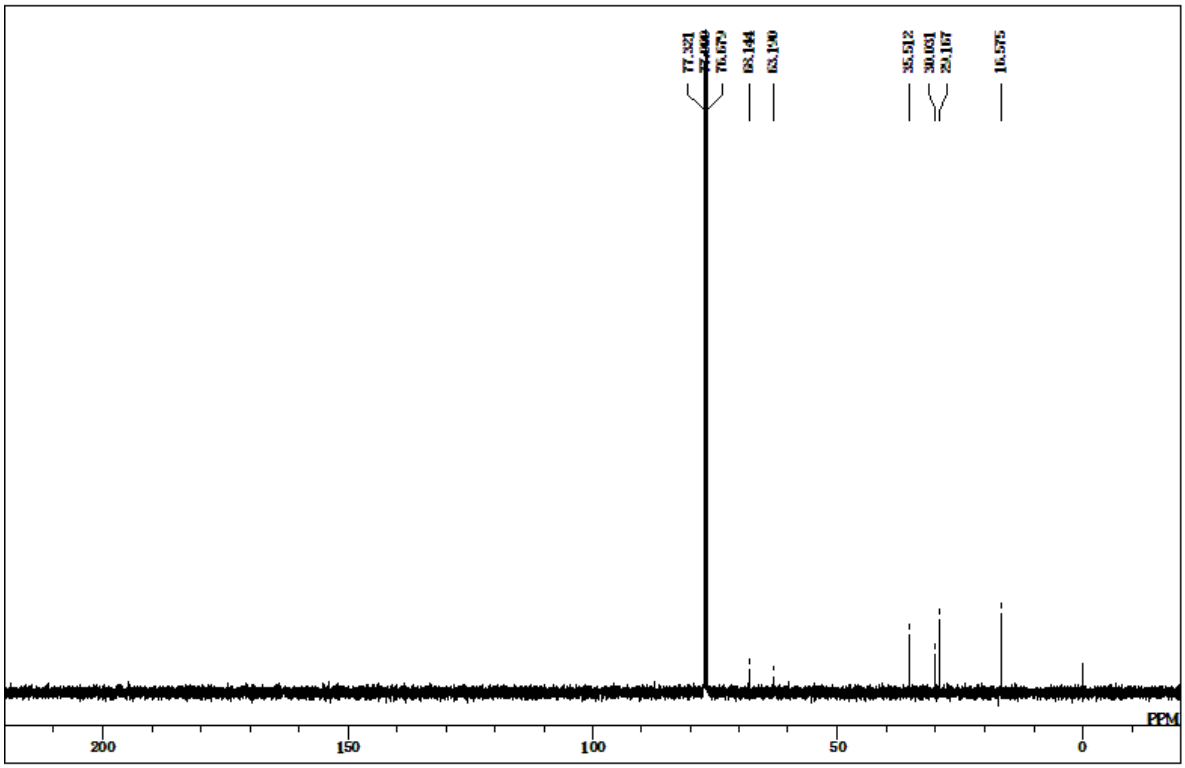
(*R*)-2-Benzylpentane-1,5-diol (Table 3, entry 7, Table 4, entry 3)



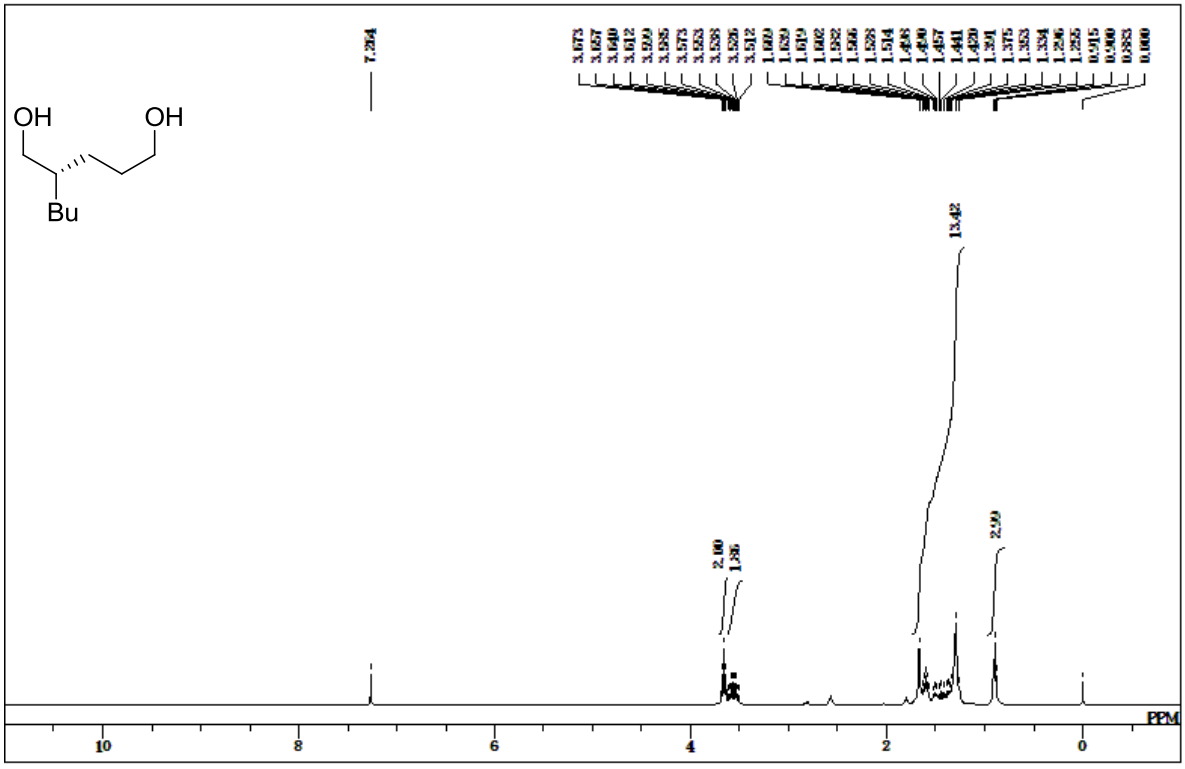


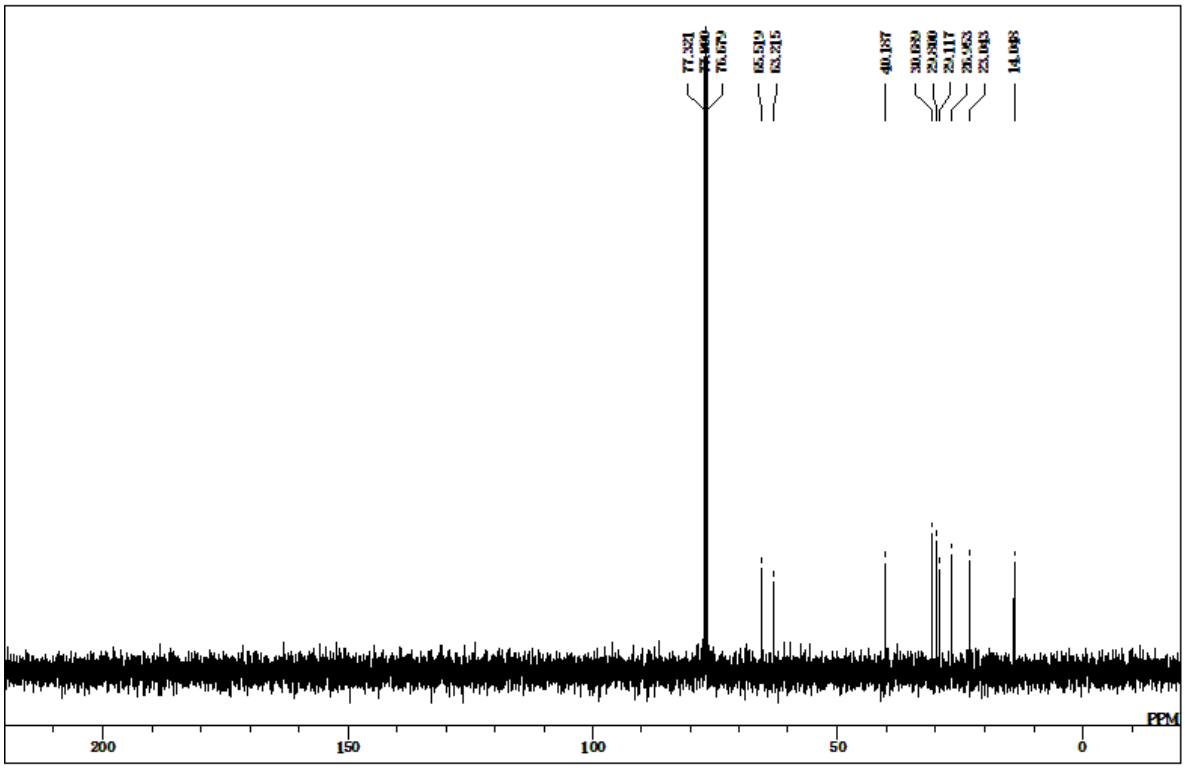
(*S*)-2-Methylpentane-1,5-diol (Table 4, entry 1)



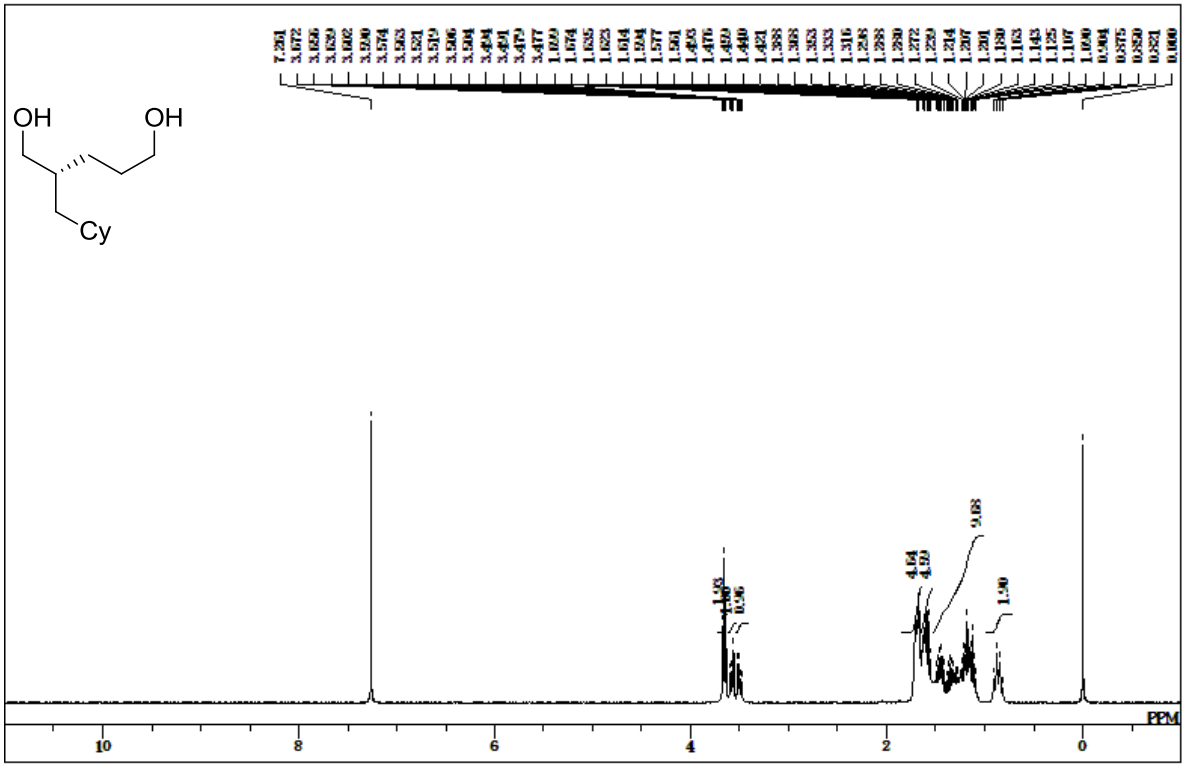


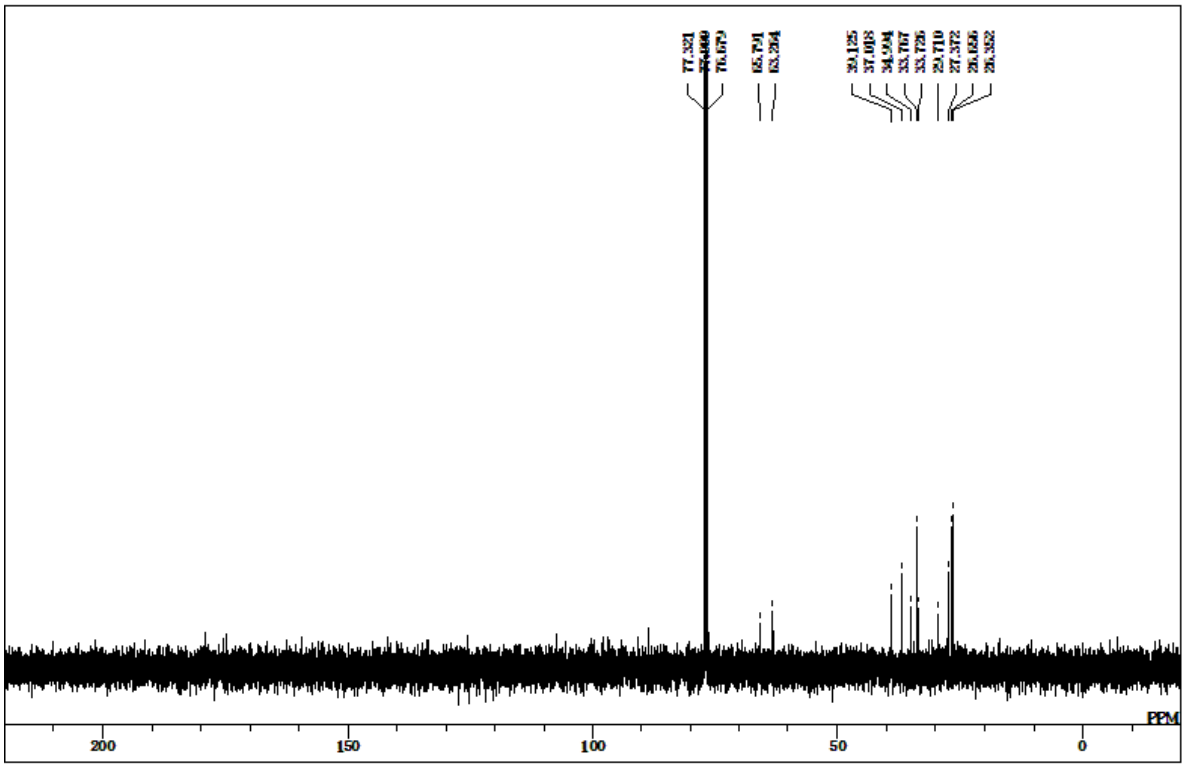
(*S*)-2-Butylpentane-1,5-diol (Table 4, entry 2)



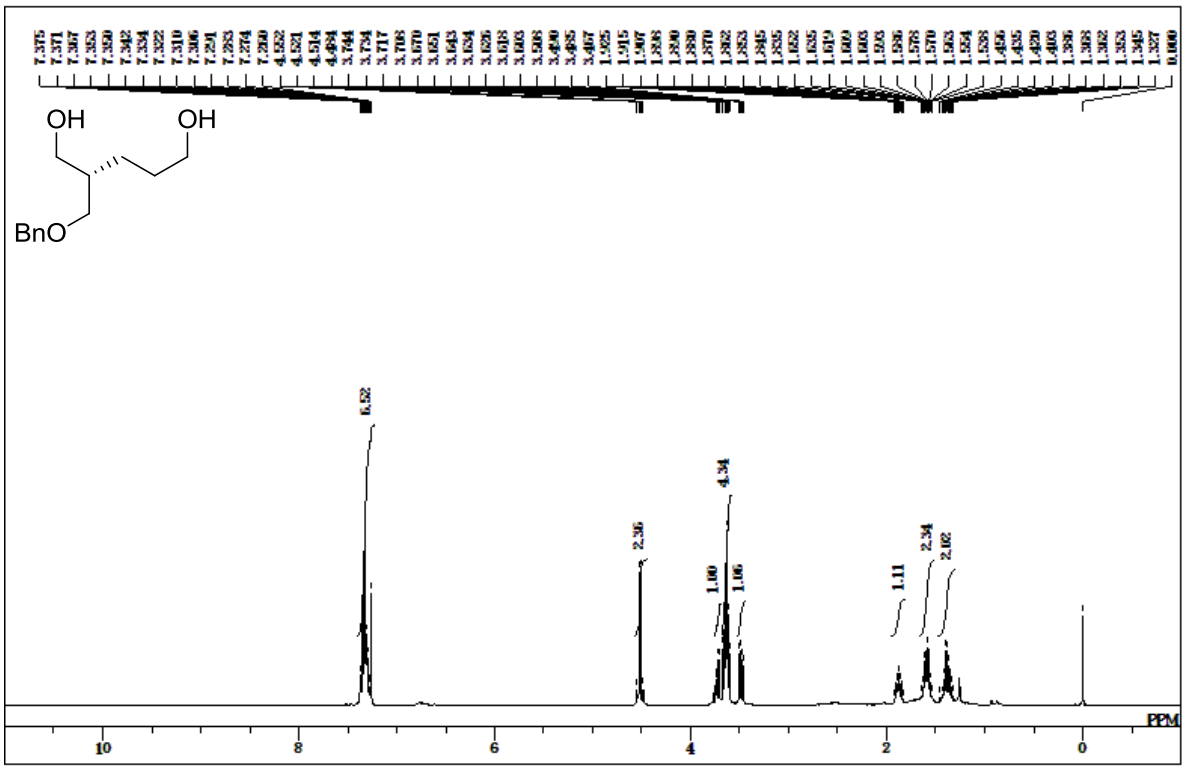


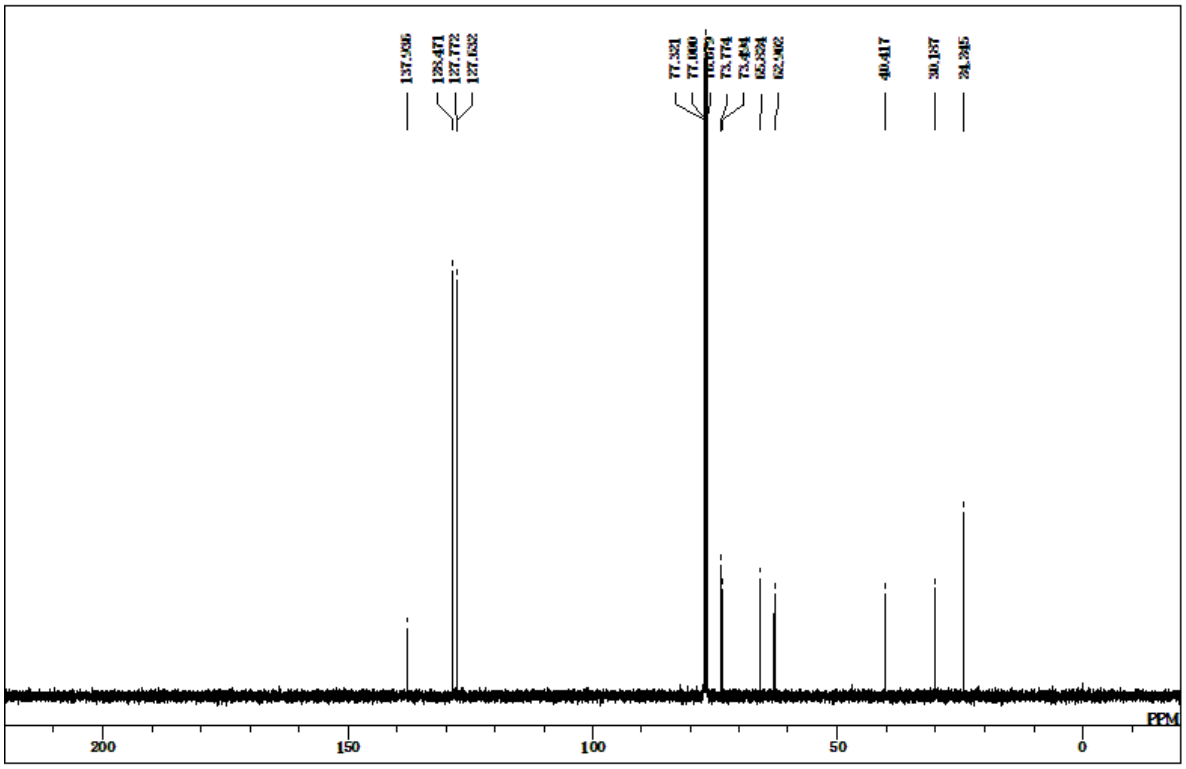
(*R*)-2-(Cyclohexylmethyl)pentane-1,5-diol (Table 4, entry 4)



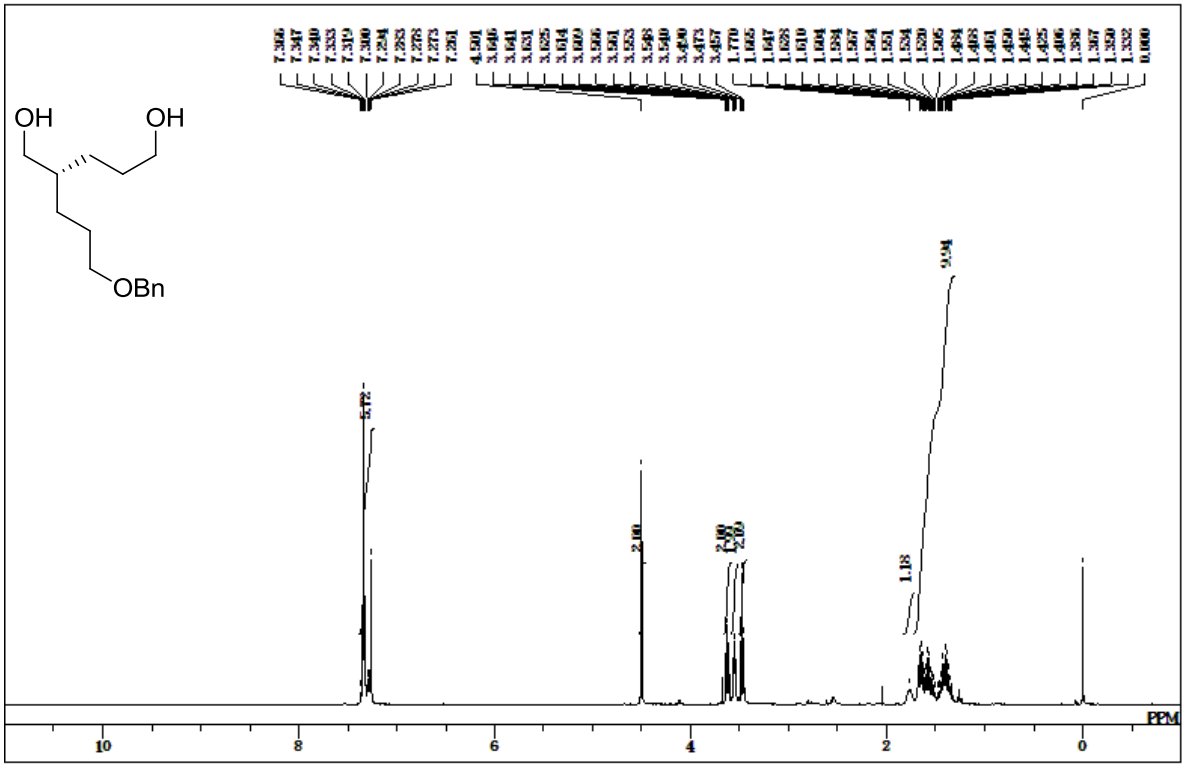


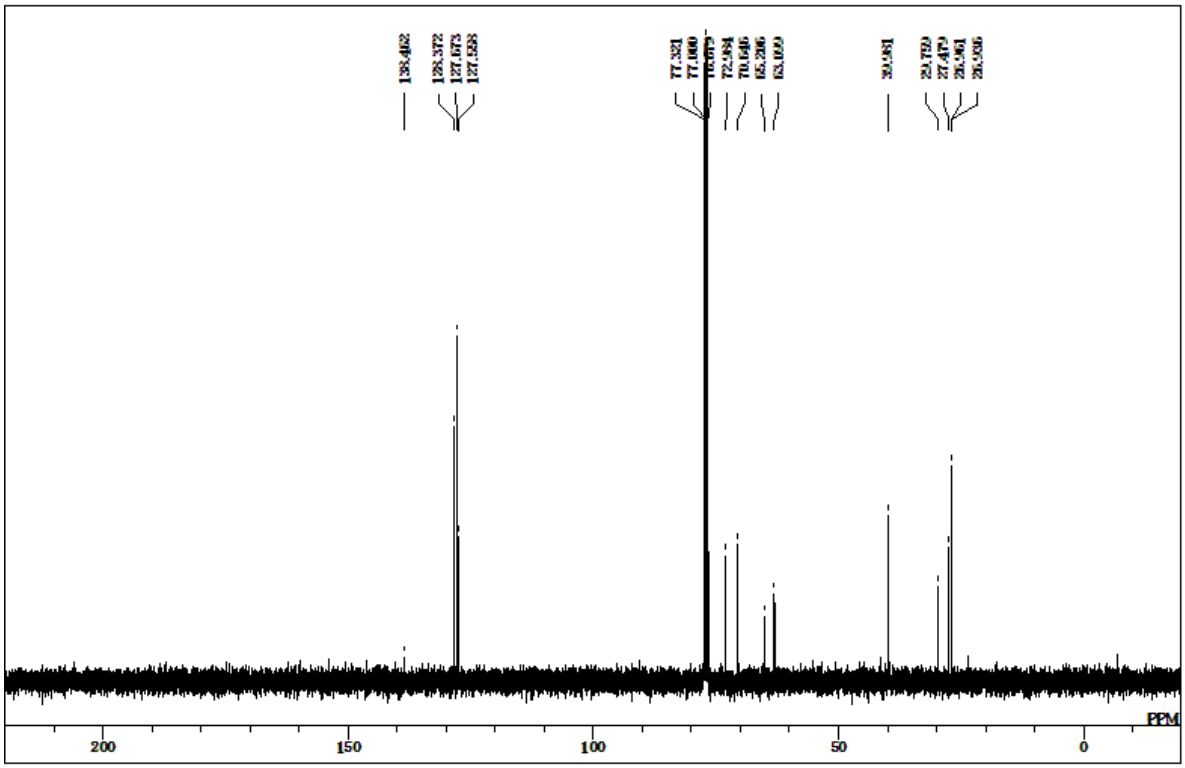
(*S*)-2-(Benzyloxy)methyl)pentane-1,5-diol (Table 4, entry 5)



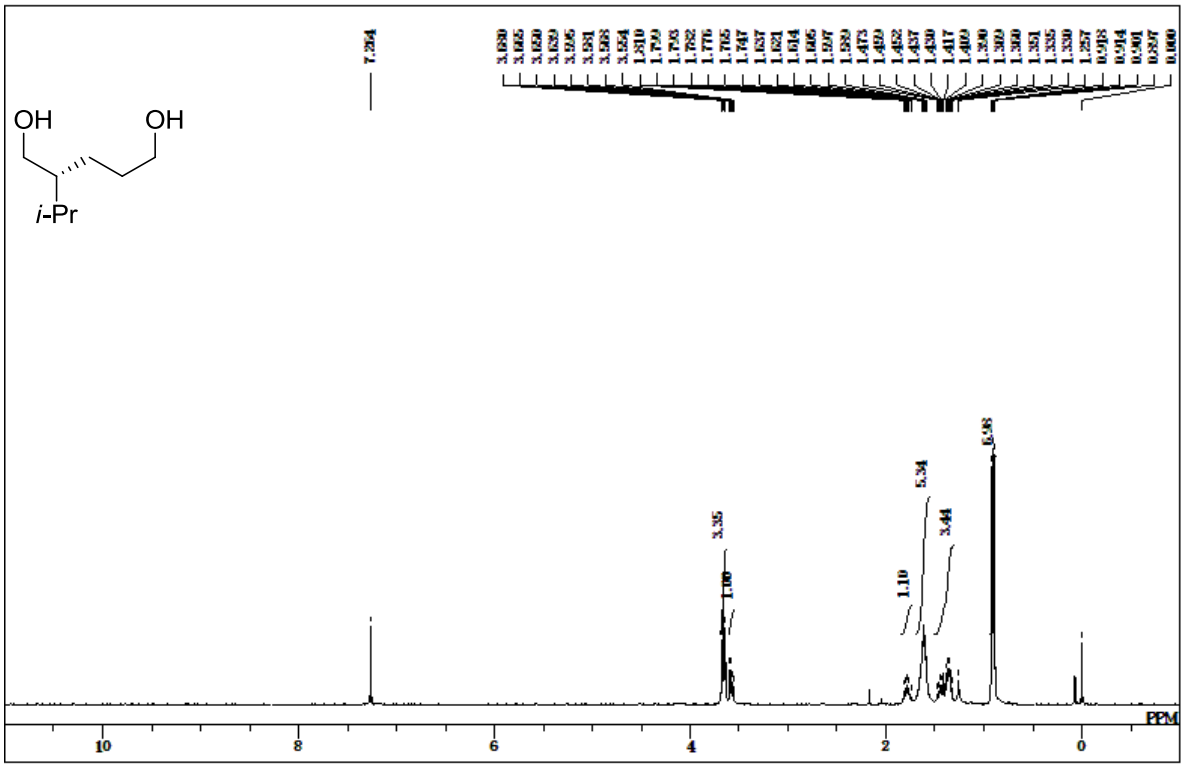


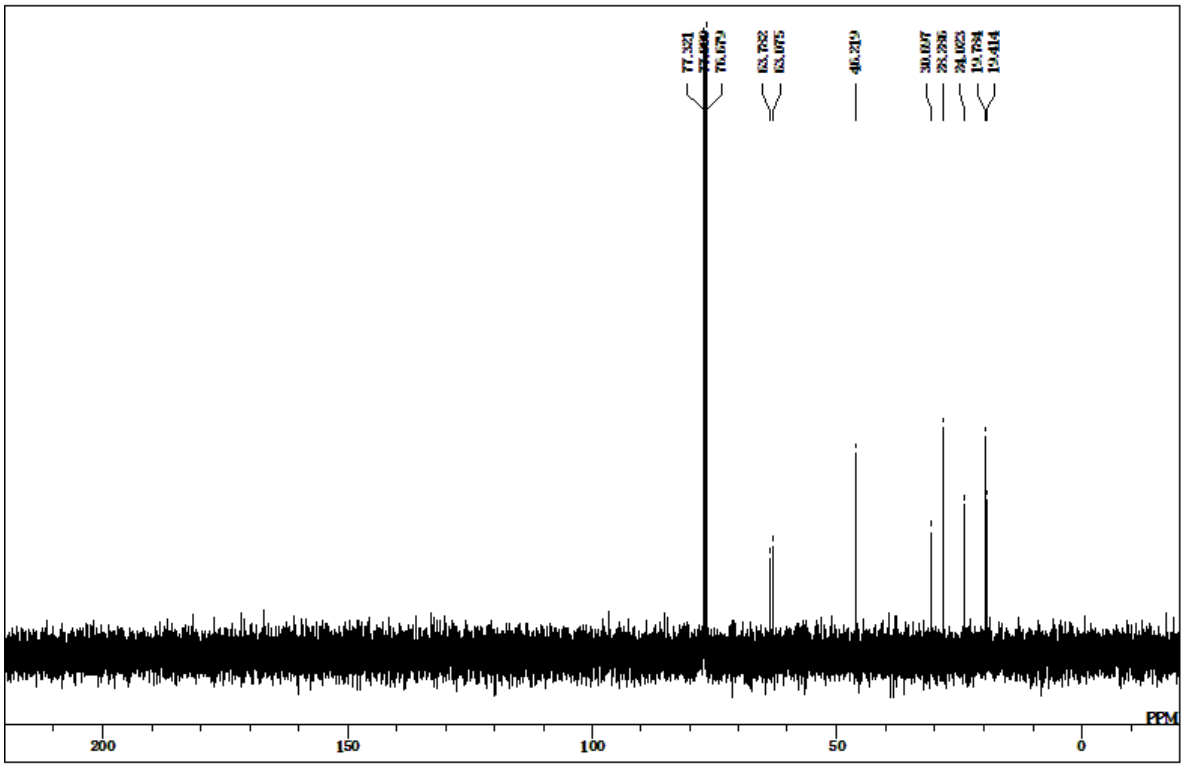
(*R*)-2-(3-(Benzyloxy)propyl)pentane-1,5-diol (Table 4, entry 6)



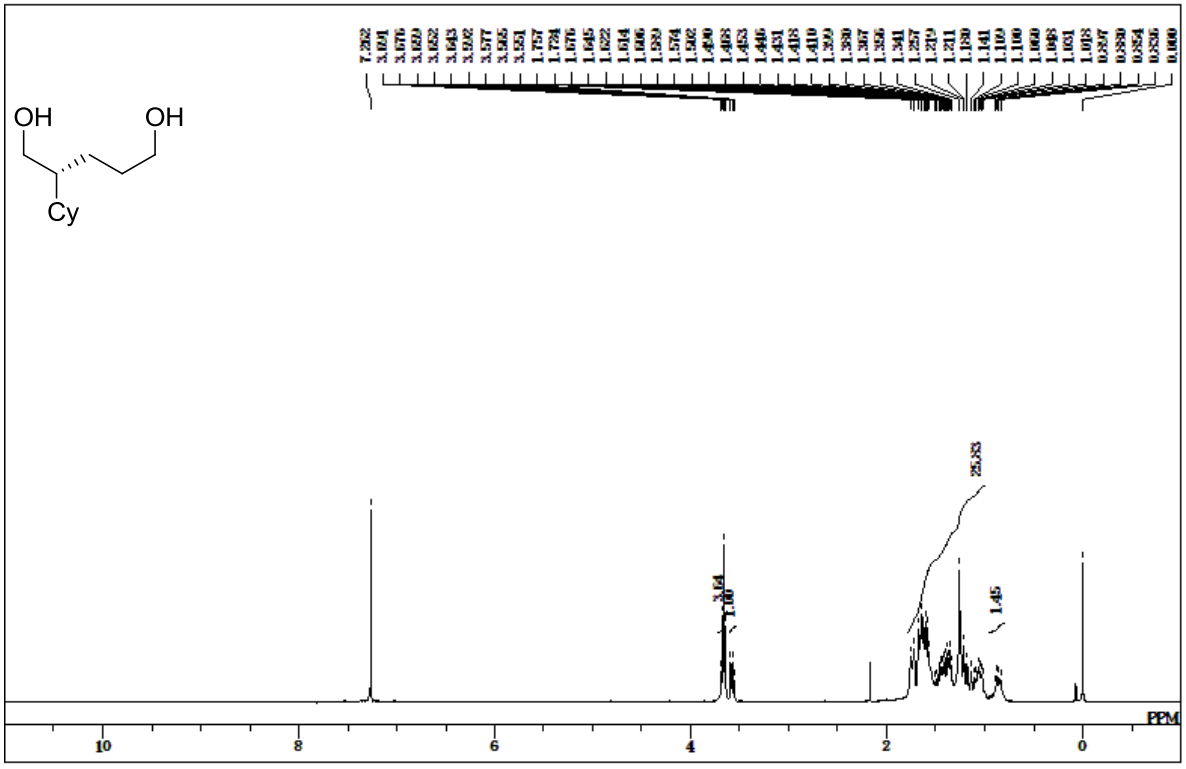


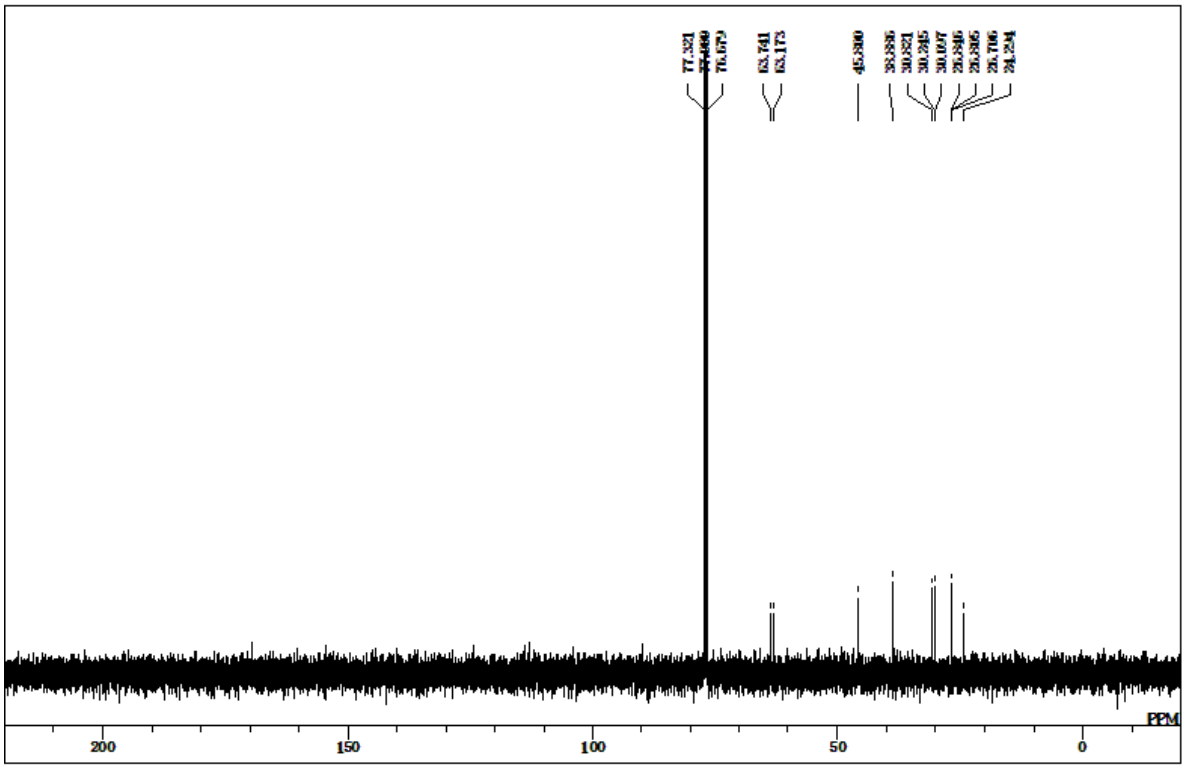
(*R*)-2-Isopropylpentane-1,5-diol (Table 4, entry 7)



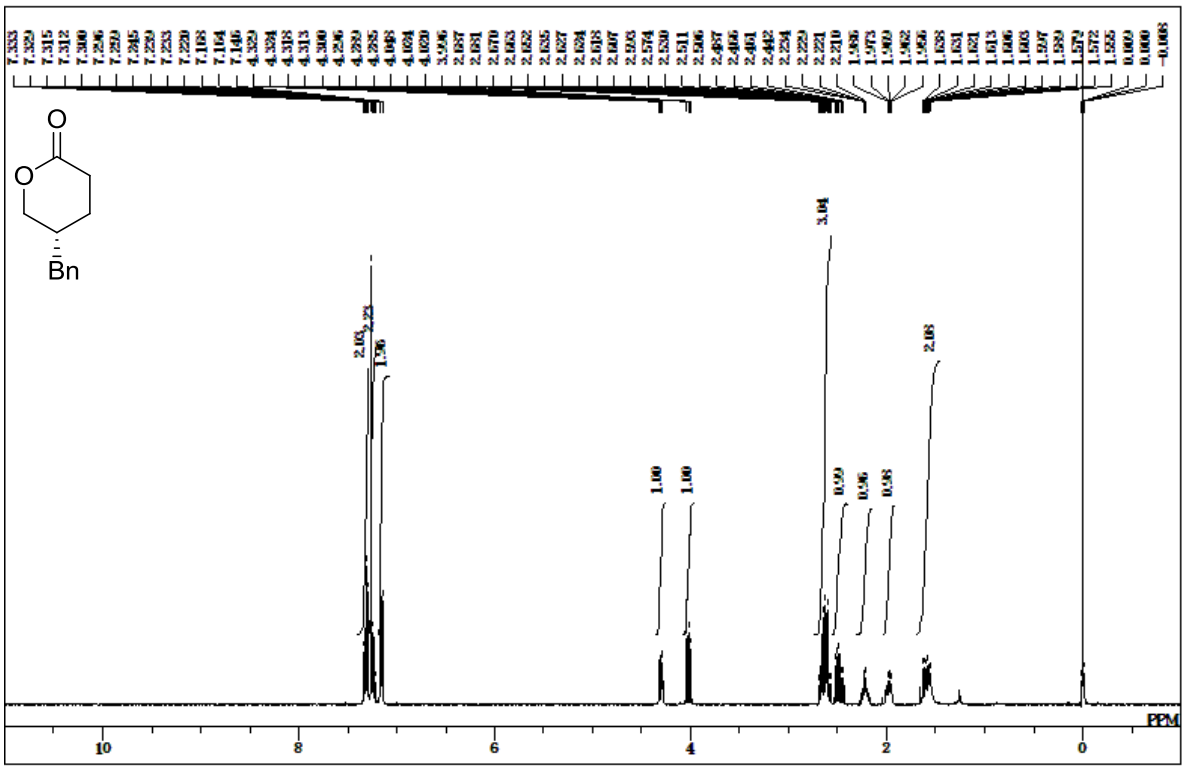


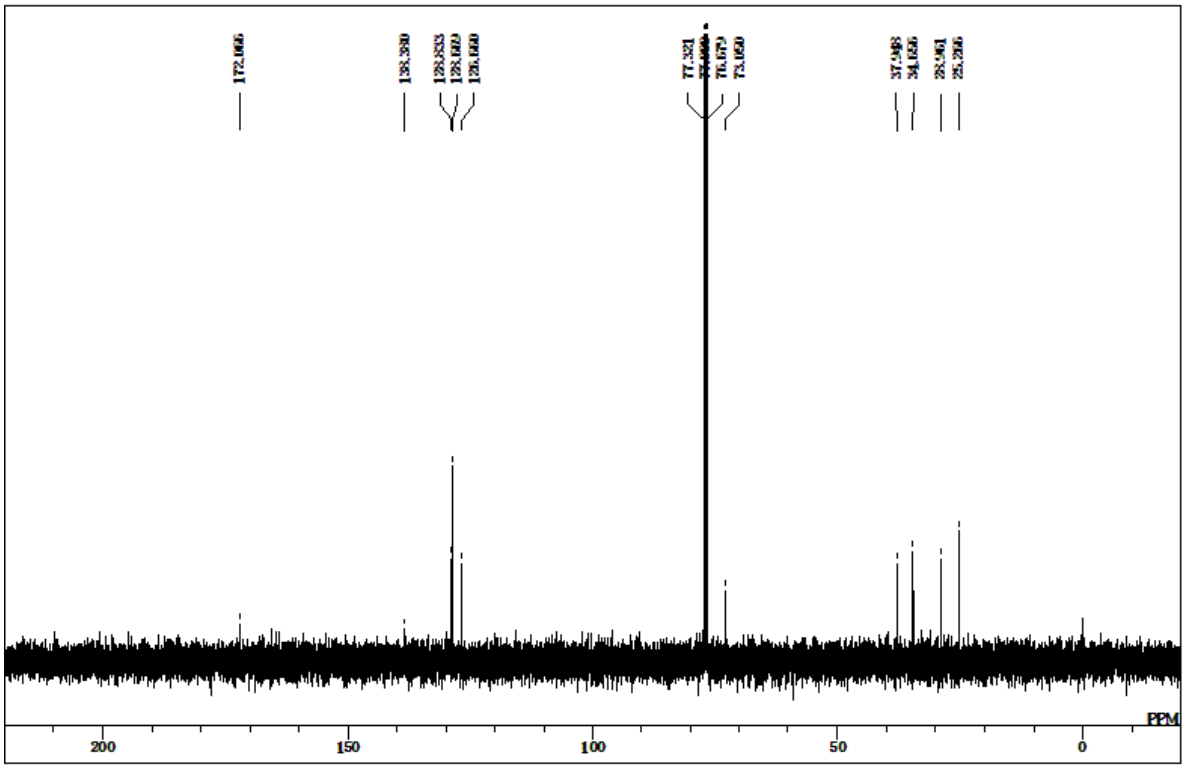
(*R*)-2-Cyclohexylpentane-1,5-diol (Table 4, entry 8)



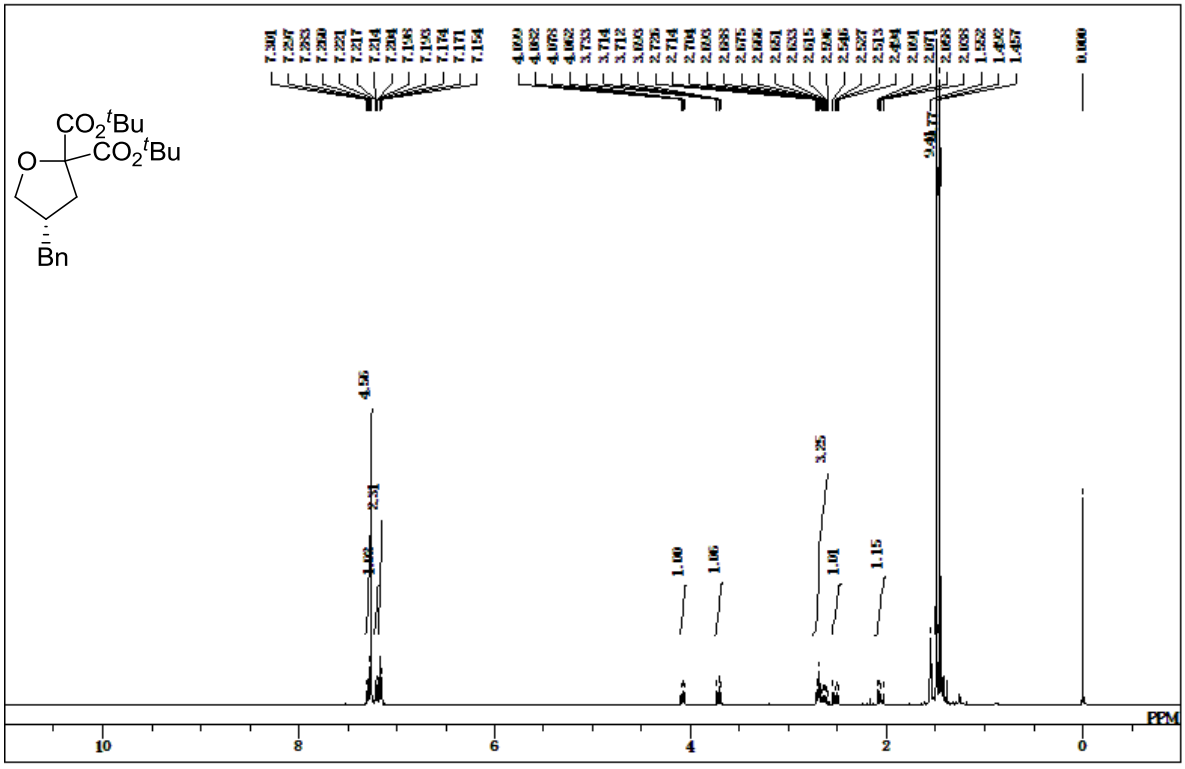


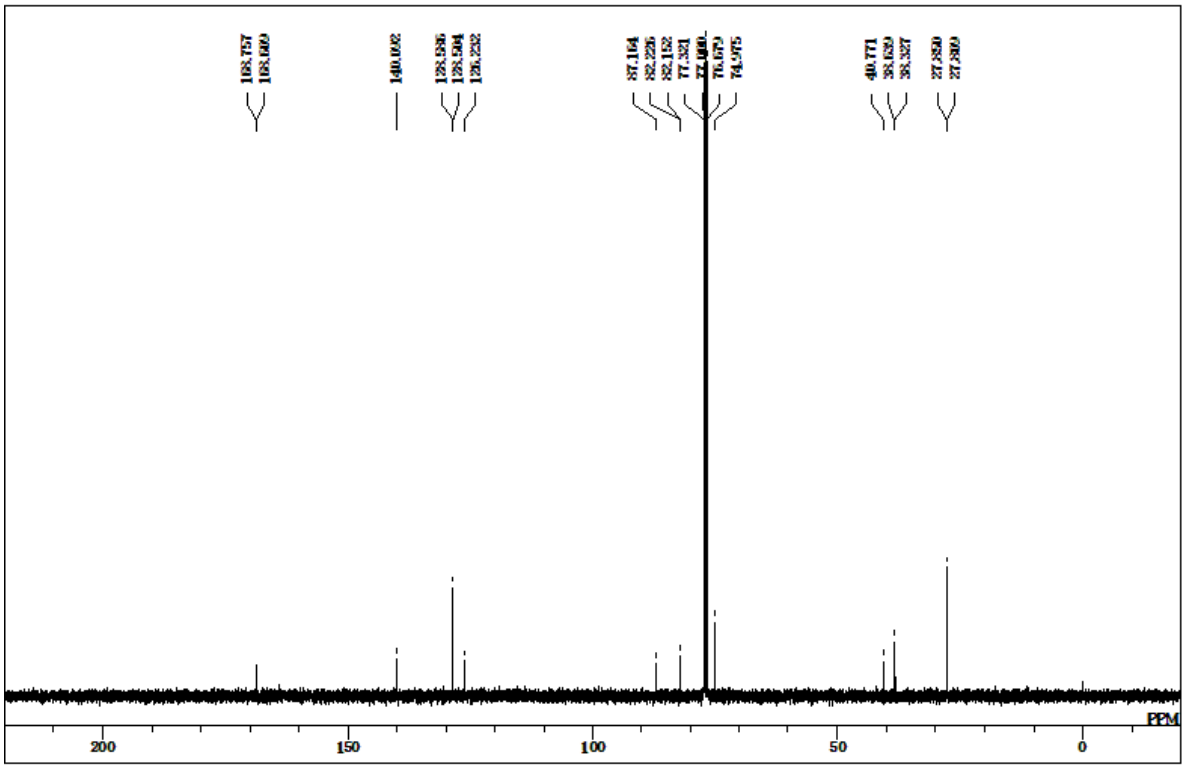
(*R*)-5-Benzyltetrahydro-2*H*-pyran-2-one (7)



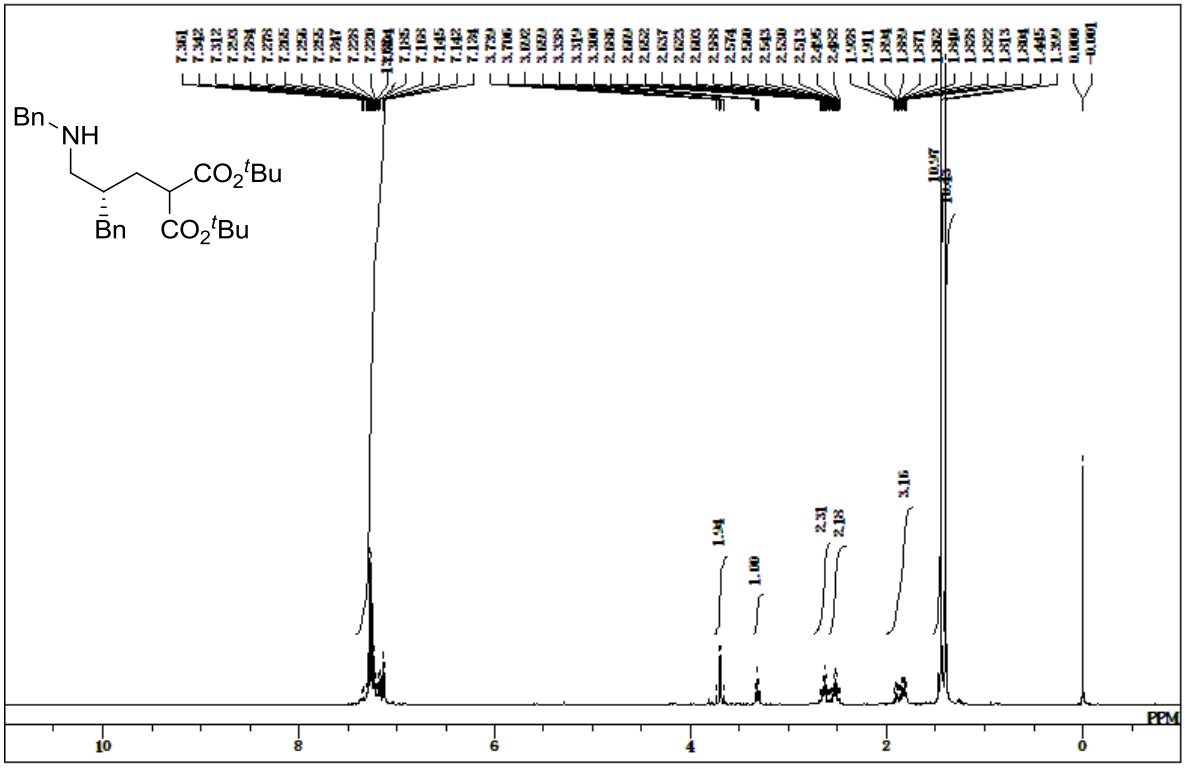


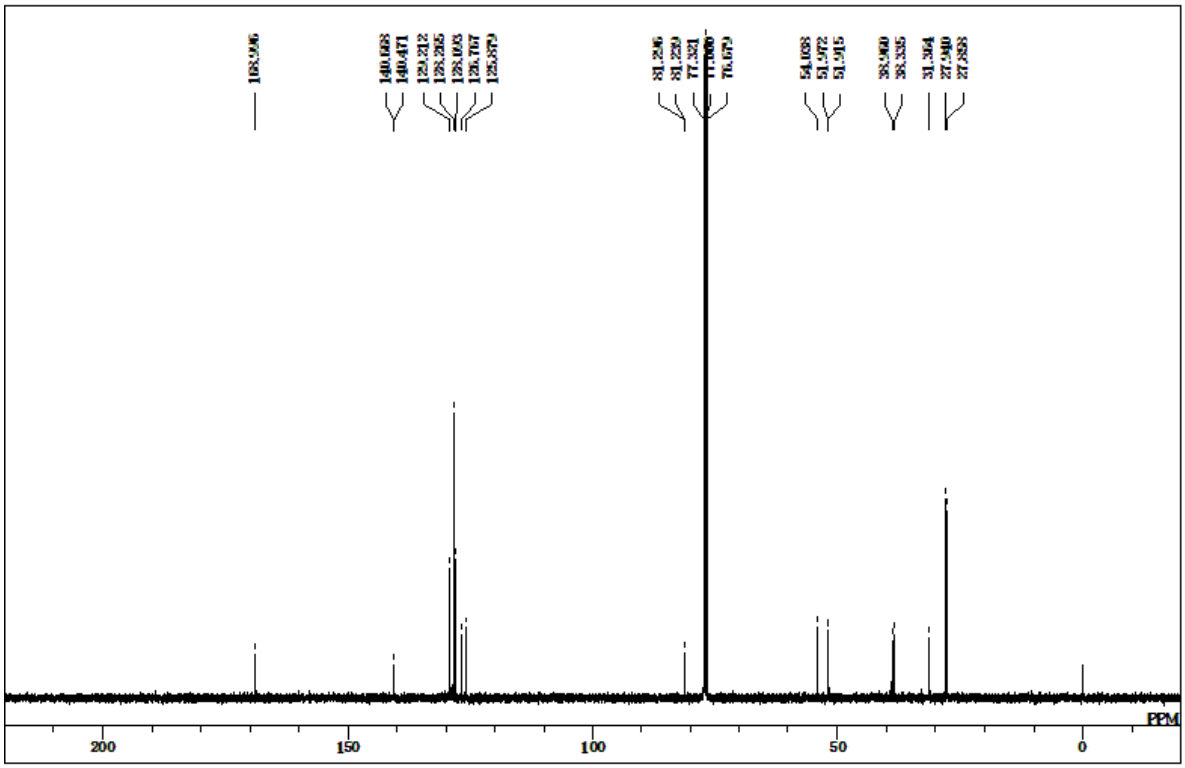
Di-*t*-butyl (*S*)-4-benzyldihydrofuran-2,2(3*H*)-dicarboxylate (8)



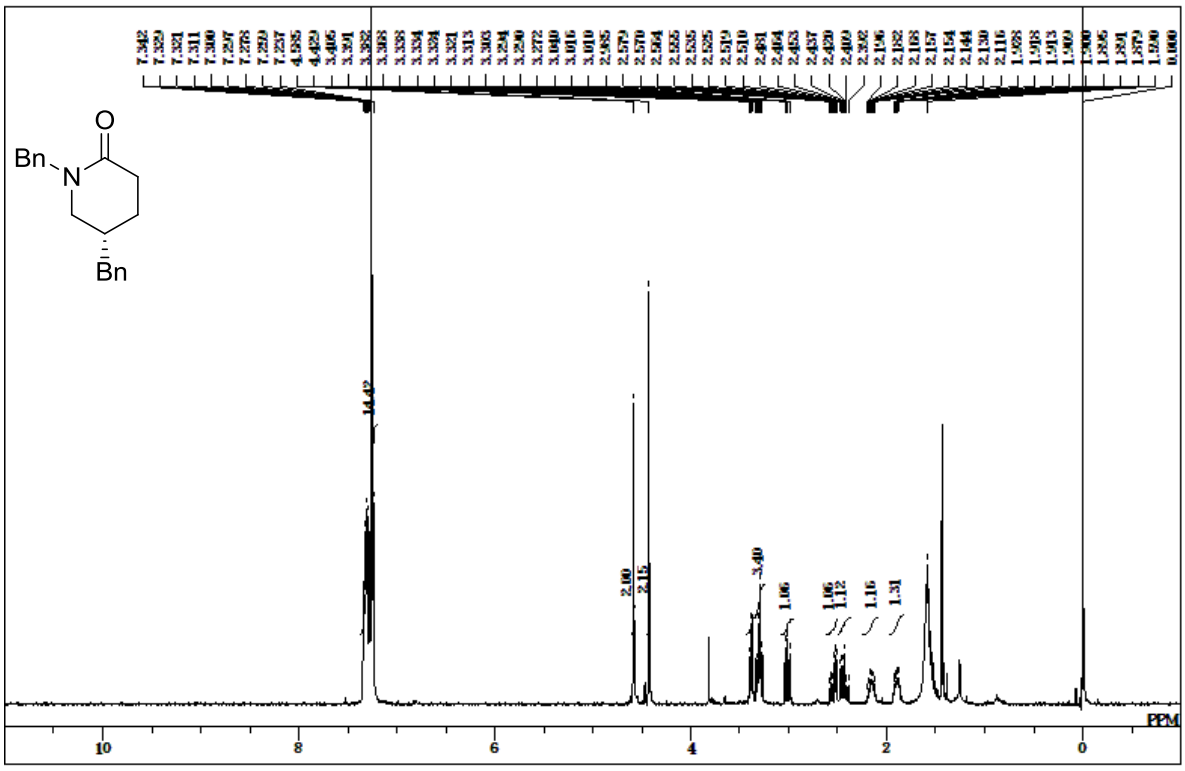


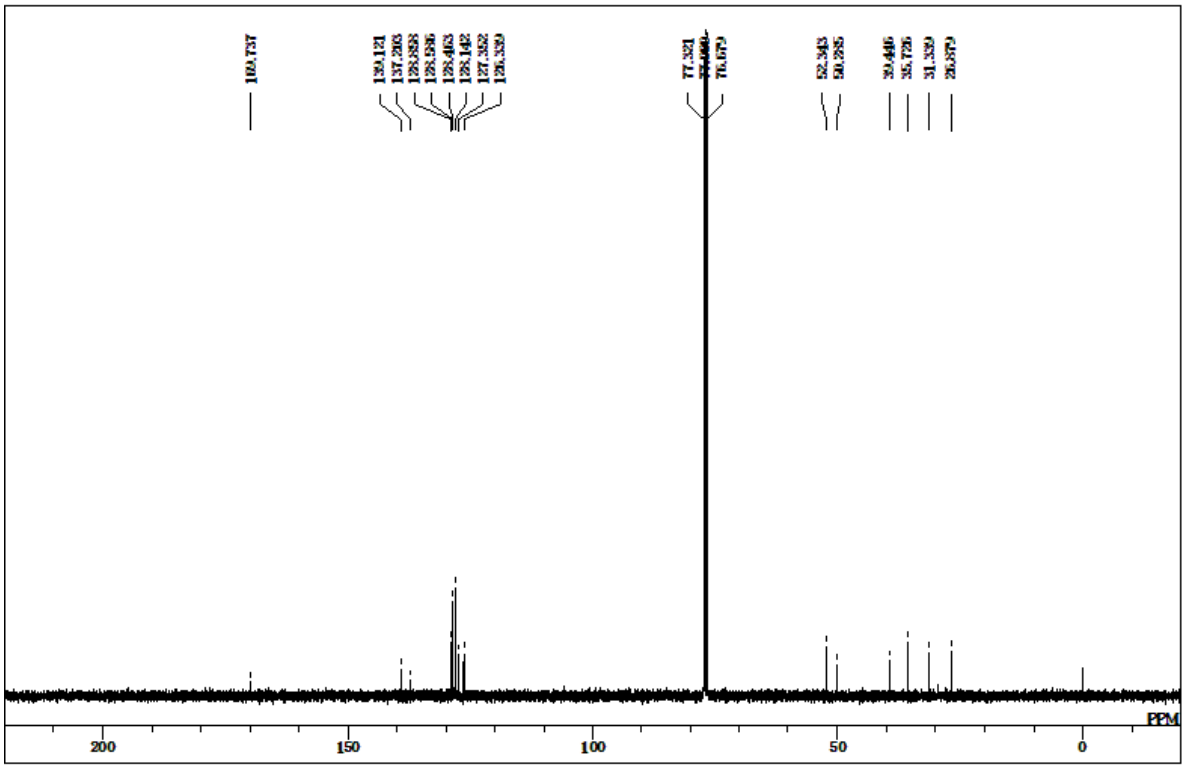
Di-*t*-butyl (*R*)-2-(2-benzyl-3-(benzylamino)propyl)malonate (9)



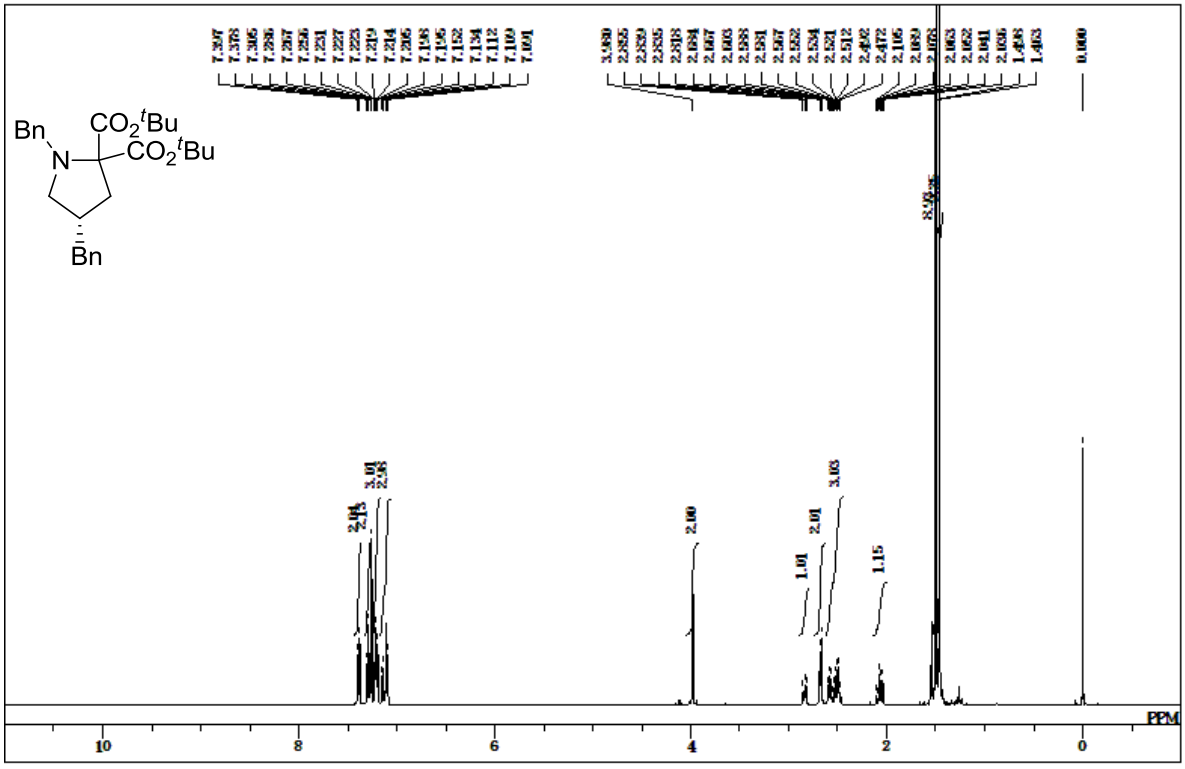


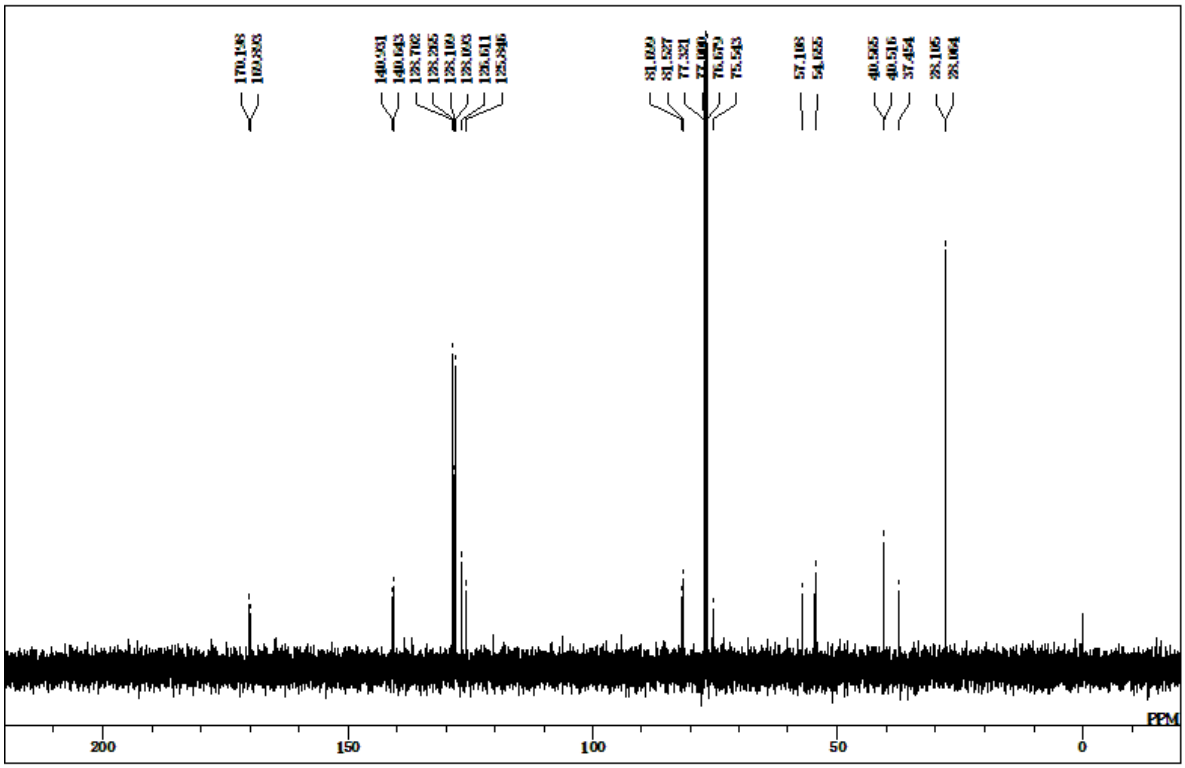
(*R*)-1,5-Dibenzylpiperidin-2-one (10)



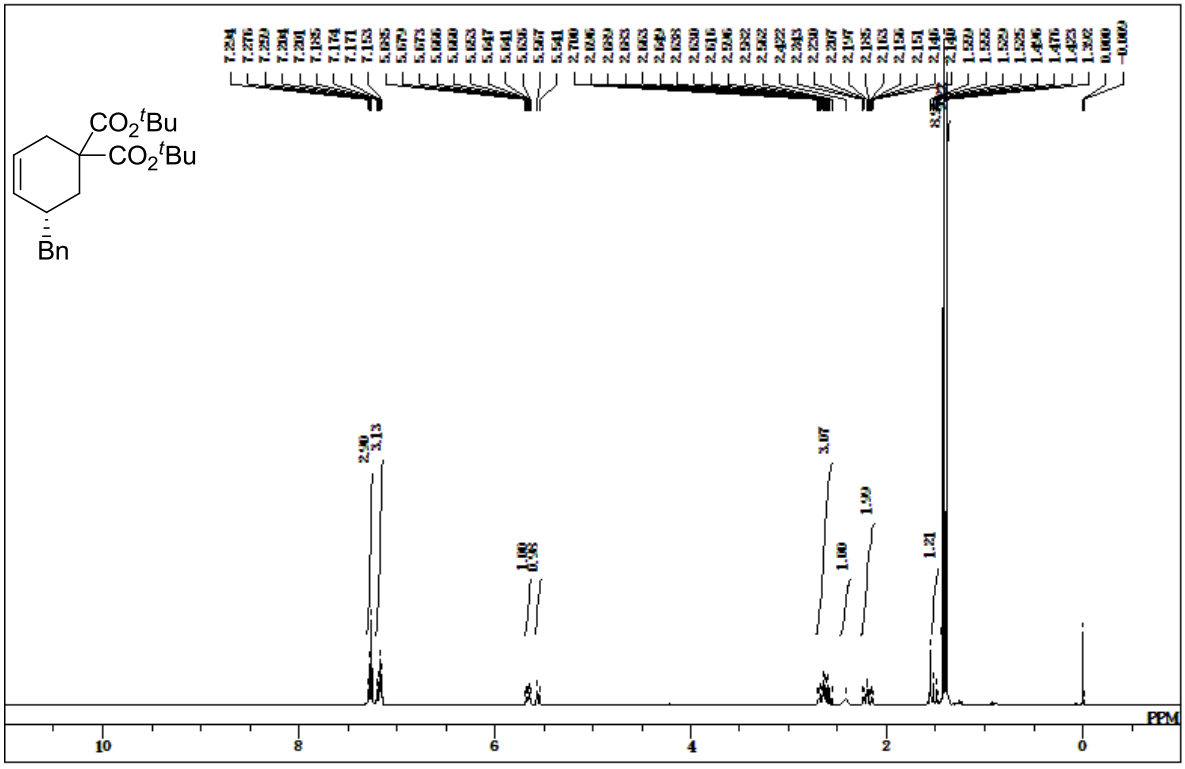


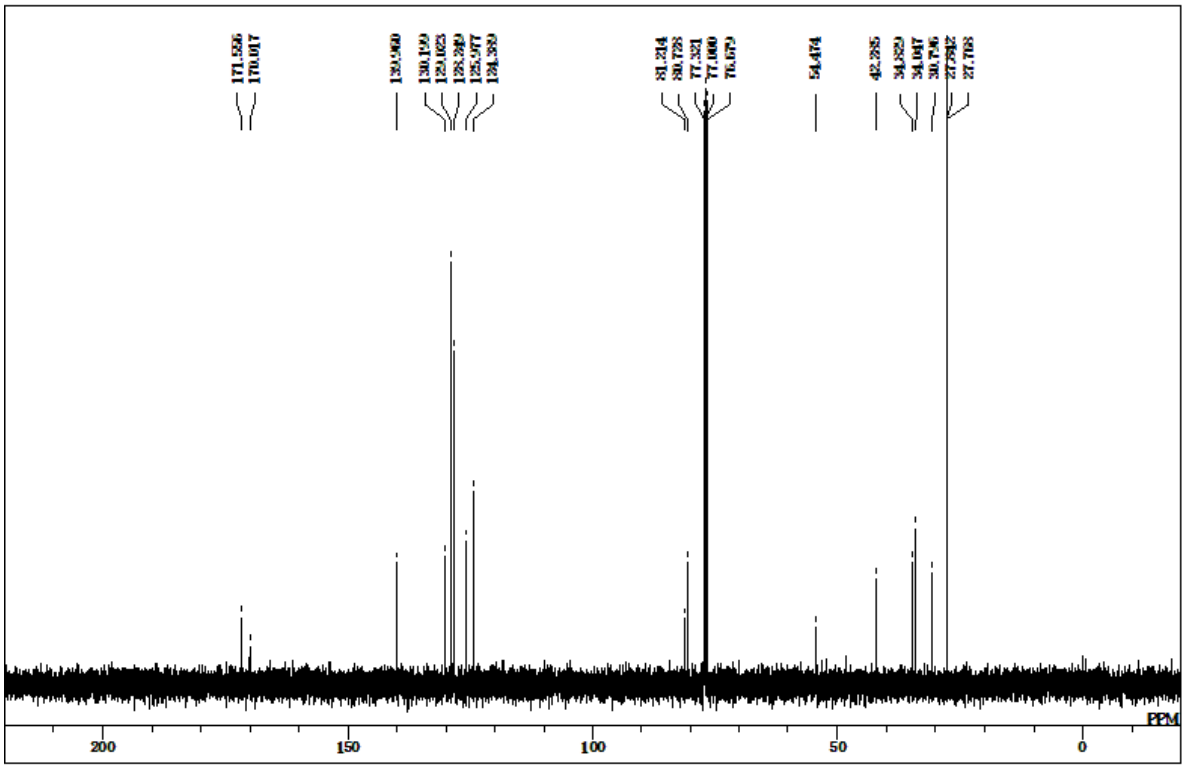
Di-*t*-butyl (*S*)-1,4-dibenzylpyrrolidine-2,2-dicarboxylate (11)



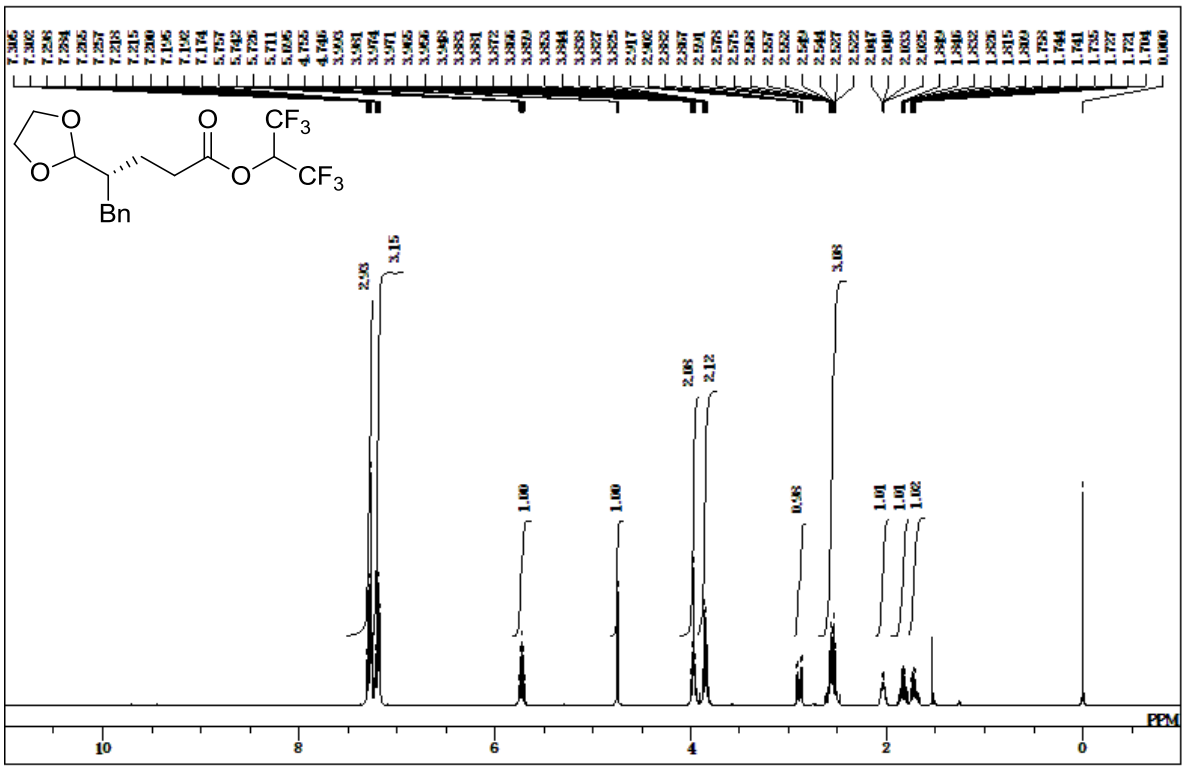


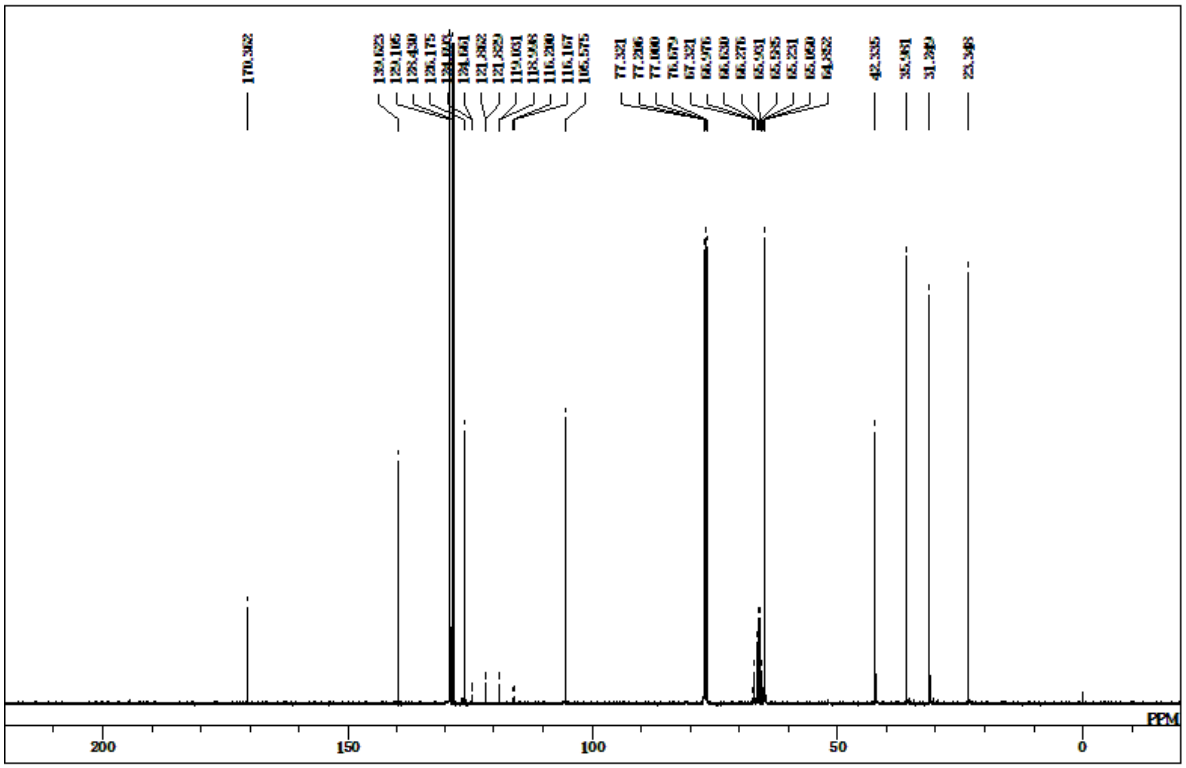
Di-*t*-butyl (*S*)-5-benzylcyclohex-3-ene-1,1-dicarboxylate (12)



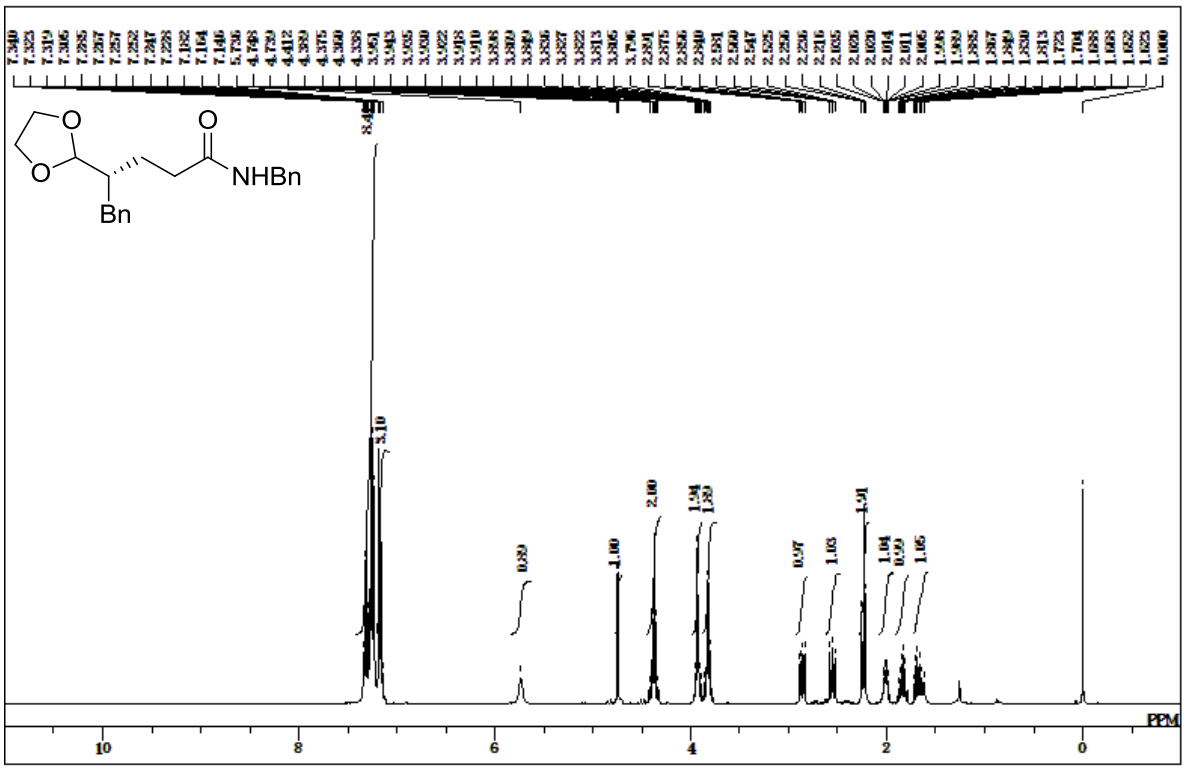


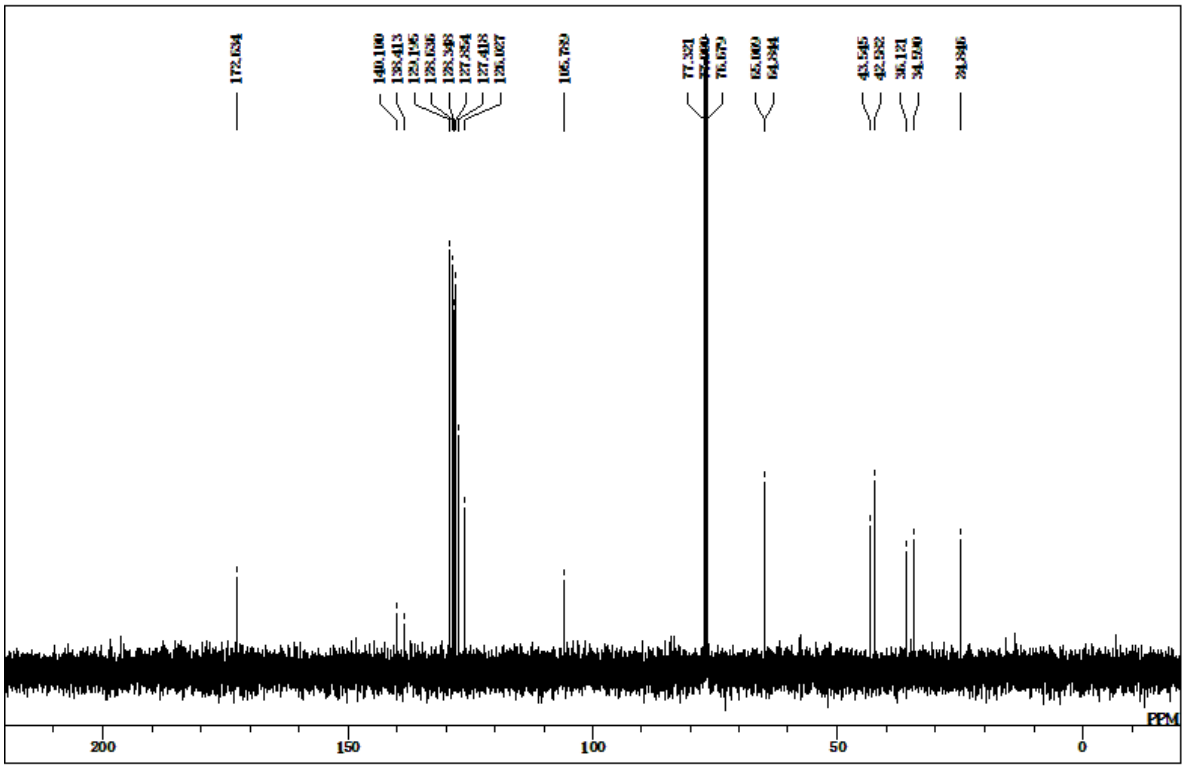
1,1,1,3,3,3-Hexafluoropropan-2-yl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (13)



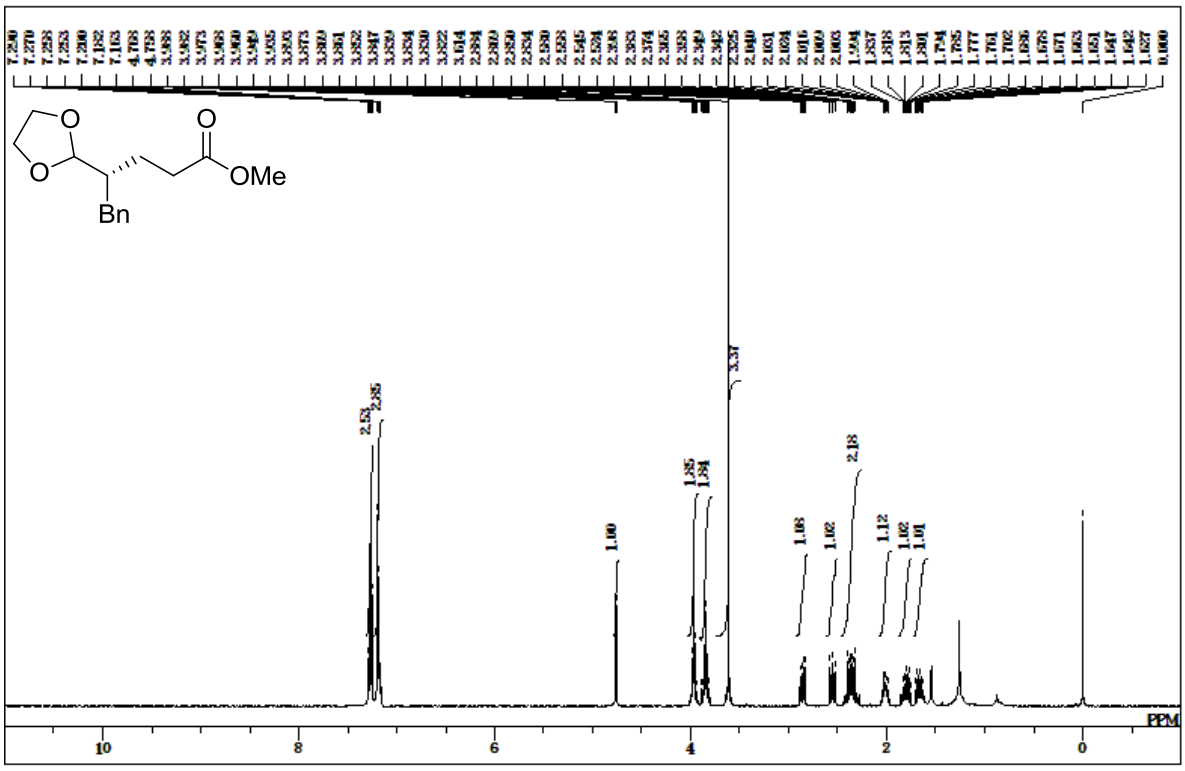


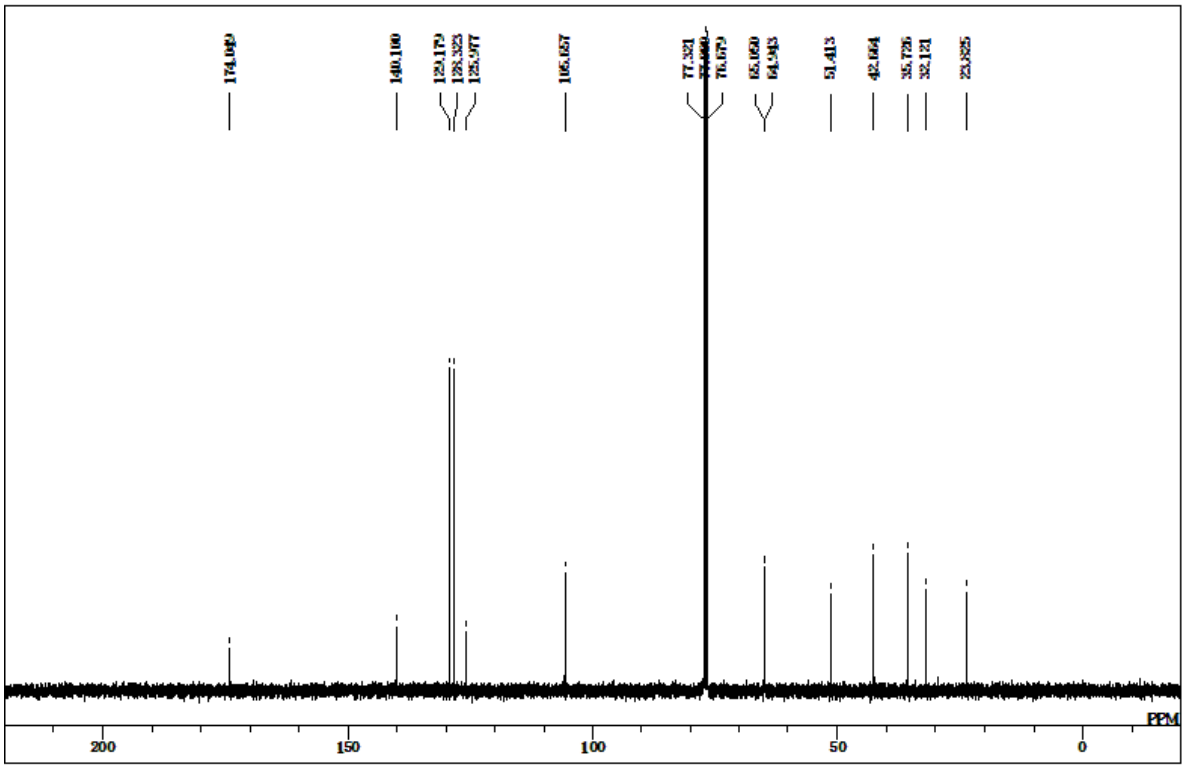
(*R*)-*N*-Benzyl-4-(1,3-dioxolan-2-yl)-5-phenylpentanamide (14)



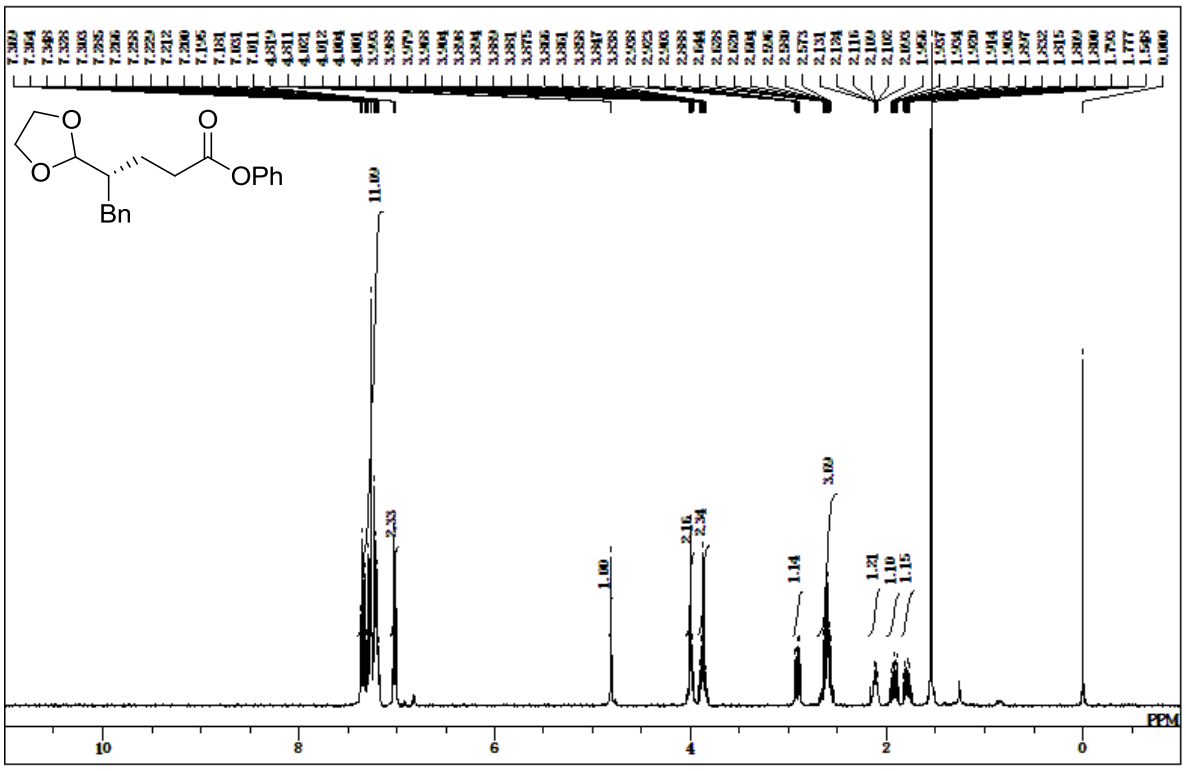


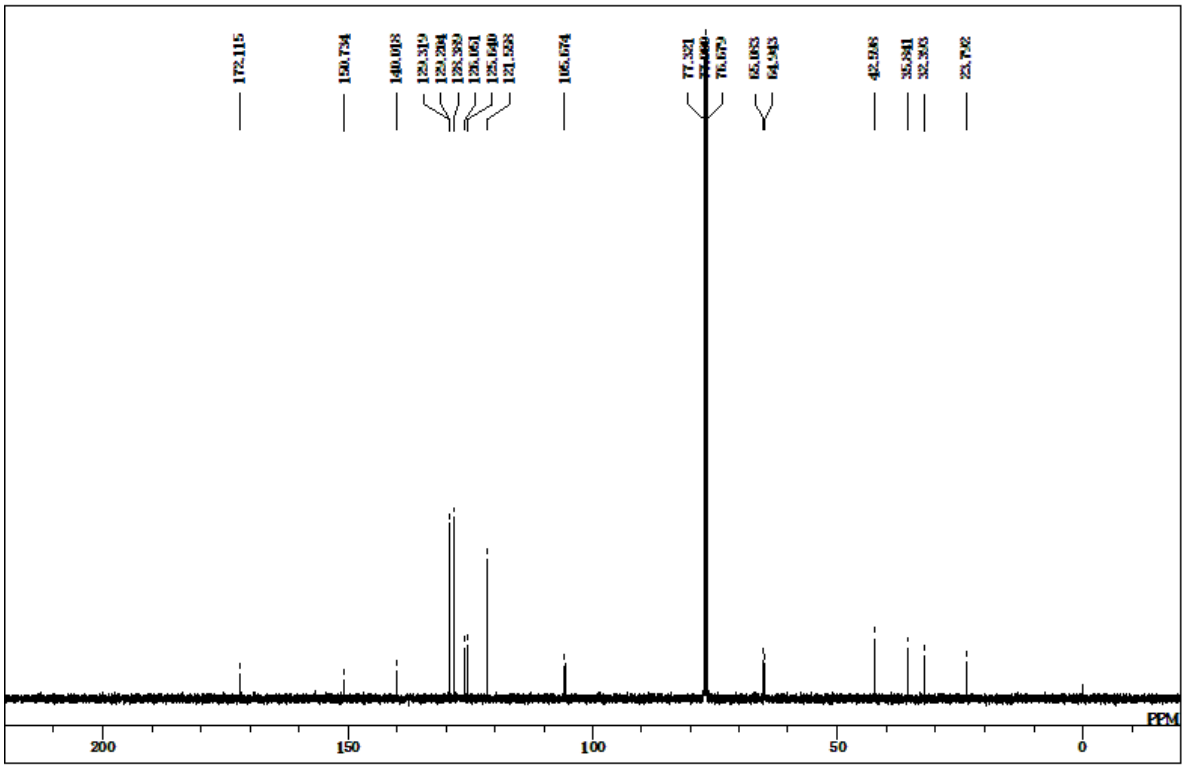
Methyl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (15)



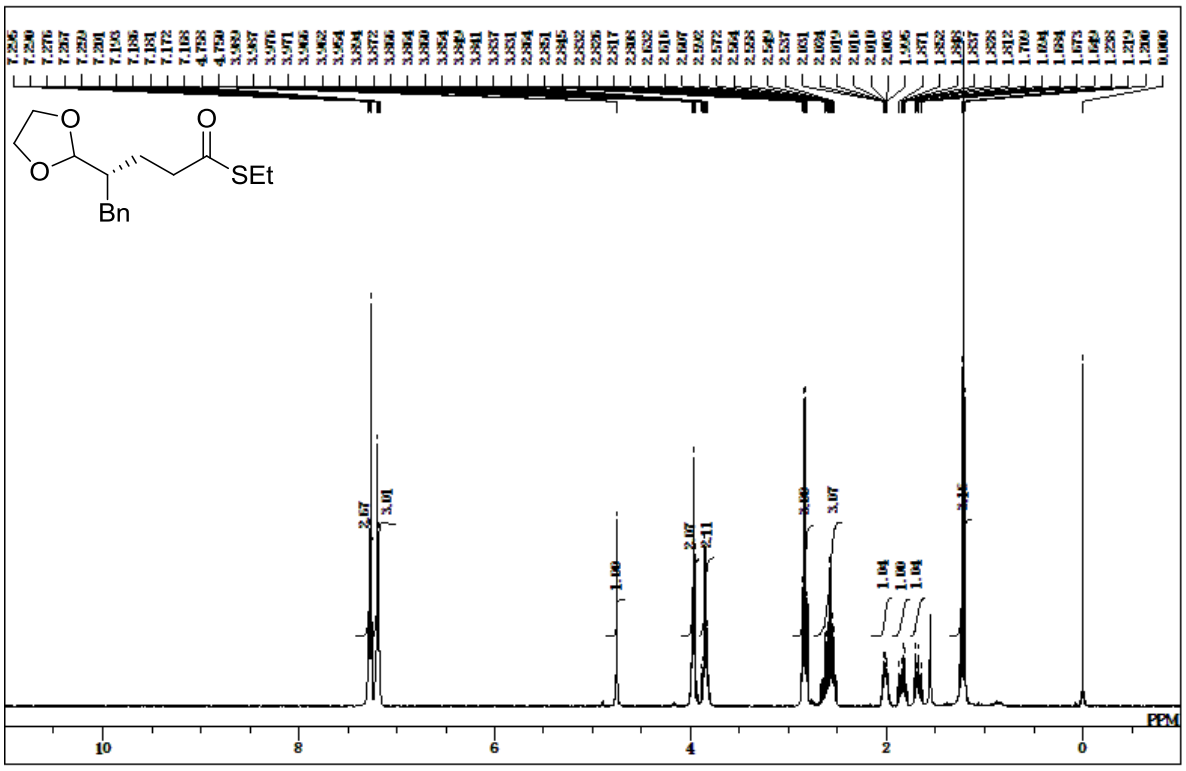


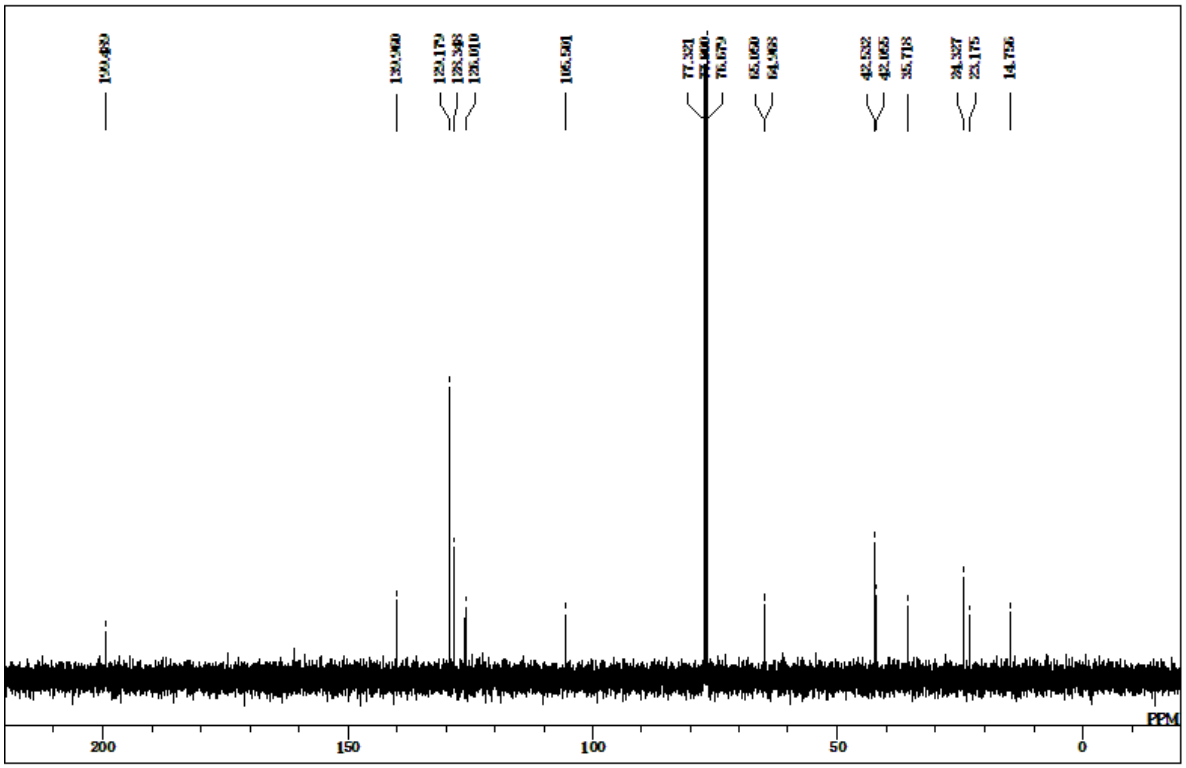
Phenyl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanoate (16)





***S*-Ethyl (*R*)-4-(1,3-dioxolan-2-yl)-5-phenylpentanethioate (17)**





Methyl (*R*)-4-benzyl-5-hydroxypentanoate (18)