A Unified Synthetic Approach to Polyketides Having Both Skeletal and Stereochemical Diversity

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Supporting Information

A. Materials and Methods

Reagents were obtained from Aldrich Chemical (www.sigma-aldrich.com) or Acros Organics (www.fishersci.com) and used without further purification. Optima grade solvents were obtained from Fisher Scientific (www.fishersci.com), degassed with Ar, and purified on a solvent drying system as described[1] unless otherwise indicated. Triethylamine (Et_3N) and pyridine (pyr) were distilled from CaH under N_2. Trimethylorthoformate (TMOF) was obtained from Aldrich in SureSeal bottles. Dess–Martin periodinane (solid) and (*R*)-(–)-Mosher acid chloride were purchased from Aldrich. Reactions were performed in flame-dried glassware under positive Ar pressure with magnetic stirring. Cold baths were generated as follows: 0 °C,

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996,** *15*, 1518–1520.

wet ice/water; –20 °C, Cryocool® monitored with a thermometer; –44 °C, dry ice/CH_3CN; –78 °C, dry ice/acetone; –100 °C, dry ice/liquid N_2/acetone monitored with a thermometer.

TLC was performed on 0.25 mm E. Merck silica gel 60 F254 plates and visualized under UV light (254 nm) and by staining with potassium permanganate ($KMnO_4$) or cerium ammonium molybdenate (CAM). Silica flash chromatography was performed on E. Merck 230–400 mesh silica gel 60.

Optical rotations were recorded on JASCO model DIP-370 or P-1020 digital polarimeters. IR spectra were recorded on Perkin–Elmer model 1600 or Bruker Optics Tensor 27 standard system FTIR spectrometers with peaks reported in cm^{-1}. NMR spectra were recorded on Bruker DRX500 or AMX400 instruments at 24 °C in $CDCl_3$ unless otherwise indicated. Chemical shifts are expressed in ppm relative to TMS (^1H, 0 ppm) or solvent signals: $CDCl_3$ (^{13}C, 77.0 ppm), C_6D_6 (^1H, 7.16 ppm; ^{13}C, 128.0 ppm), acetone-d_6 (^{13}C, 206.2 ppm); coupling constants are expressed in Hz. Mass spectra were obtained at the MSKCC Analytical Core Facility on a PE Sciex API 100 mass spectrometer with electrospray (ESI) ionization. Diastereomeric and configurational ratios are reported for purified products based on ^1H-NMR analysis.

Atom numbers shown in chemical structures herein correspond to the numbering system used in the text of the article and Supporting Information and do not necessarily correspond to IUPAC nomenclature, which was used solely to name each compound below.

B. COMPLETE LIBRARY SYNTHESIS ROUTE

This figure provides complete details of the synthetic route to 74 polyketide fragments, which is summarized in Scheme 2 of the manuscript.

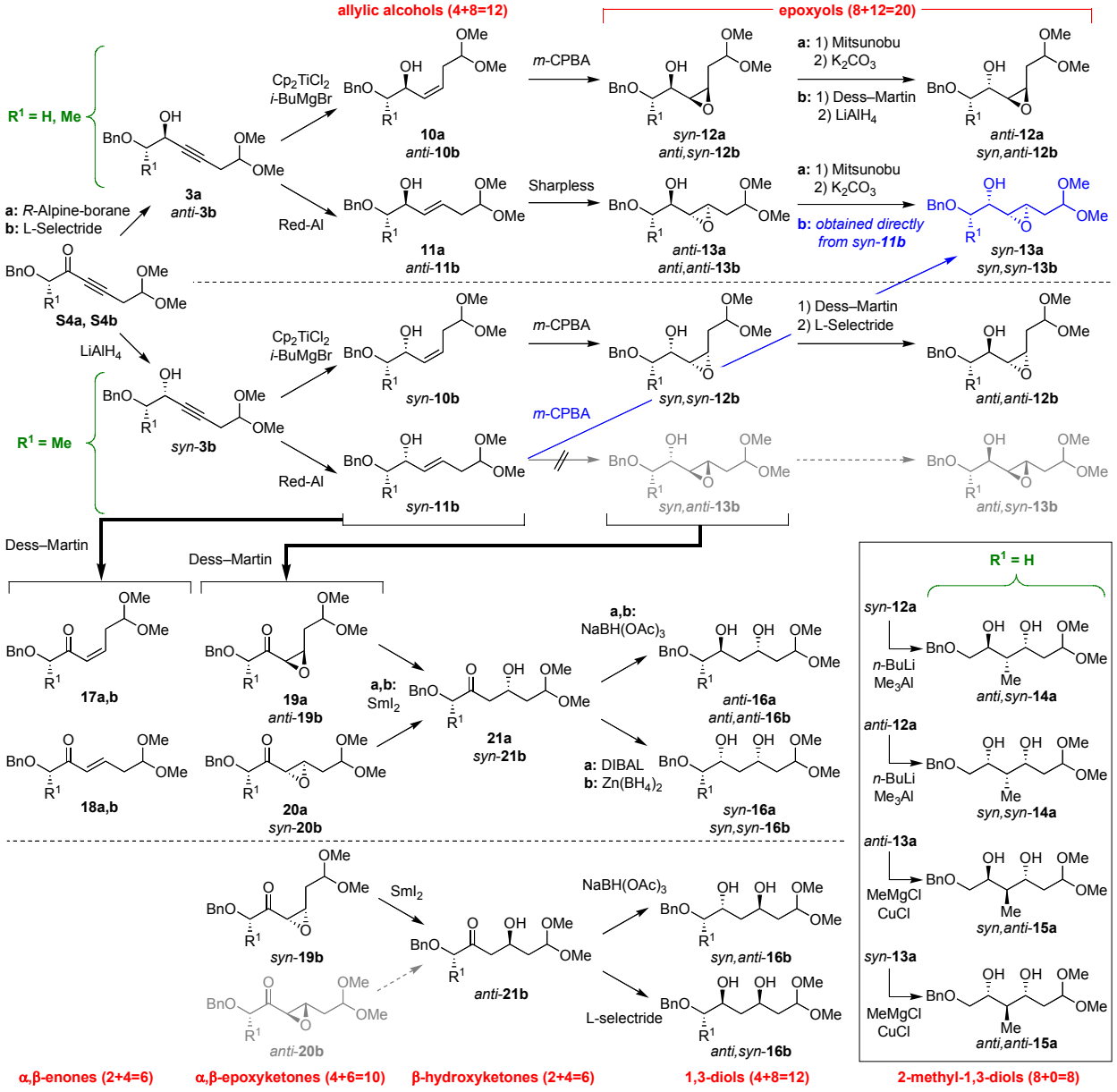


Figure S1. Complete library synthesis route. One enantiomeric series shown for R^1 = H (above dashed line) and R^1 = Me (above and below dashed line). Total library members in each structural class are indicated (red). This route provides comprehensive stereochemical diversification with the exceptions of epoxyols *syn,anti*-**13b** and *anti,syn*-**13b** and epoxyketone *anti,trans*-**18b** (gray). The unusual *syn*-selective epoxidation of *E*-allylic alcohol *syn*-**11b** with *m*-CPBA is highlighted (blue). The 1,3-diols *anti*-**16a** and *syn*-**16a** can also be obtained directly from epoxyols *syn*-**12a** and *anti*-**12a** respectively by treatment with Red-Al (not shown).

C. SYNTHESIS OF PROPARGYLIC ALCOHOLS (3) AND STEREOCHEMICAL ASSIGNMENTS

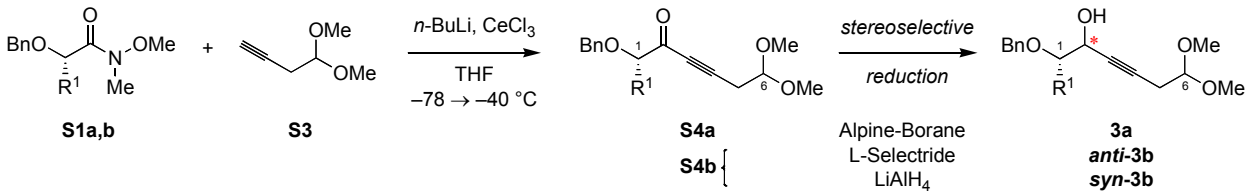
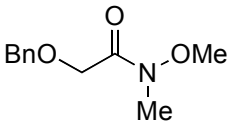


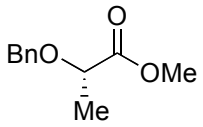
Figure S2. Synthesis of propargylic alcohols 3. Propargylic alcohols **3a** and **3b** (Figure 2) were synthesized by coupling of Weinreb amides **S1** (cf. **1** in Figure 1) and alkyne **S3** (cf. **2** in Figure 1), followed by stereoselective reduction of the resulting α,β-alkynones **S4**. In the R^1 = H series, enantioselective reductions to ***S*-3a** or ***R*-3a** were achieved using Alpine-Borane, with absolute stereochemical assignments made by analogy to literature precedents for alkynone reductions with Alpine-Borane[2] and also with BINAL.[3] In the R^1 = Me series, diastereoselective reductions to ***anti*-3b** or ***syn*-3b** were accomplished using L-Selectride and $LiAlH_4$, respectively. Relative stereochemical assignments were initially made by comparison to products obtained (in lower yields) by alternative asymmetric reduction with *R*- and *S*-BINAL and analogy to literature precedent.[3] These relative stereochemical assignments were subsequently confirmed by NOESY analysis of cyclic carbonates derived from debenzylated ***anti*-3b** and ***syn*-3b** (see below).



2-(Benzyloxy)-*N*-methoxy-*N*-methylacetamide (S1a). Prepared from (benzyloxy)acetyl chloride and *N*,*O*-dimethylhydroxylamine hydrochloride essentially as previously described.[4] Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded Weinreb amide **S1a** (2.72 g, 96%) as a colorless oil.

TLC: R_f 0.34 (2:1 hexanes/EtOAc). **IR** (NaCl, film) 3852, 3744, 2937, 1682 (C=O st), 1558, 1539, 1496, 1455, 1391, 1327, 1267, 1177, 1139, 1087, 1028, 992, 789, 739. **^{1}H-NMR** (400 MHz) δ 7.40–7.27 (m, 5H), 4.67 (s, 2H), 4.28 (s, 2H), 3.63 (s, 3H), 3.19 (s, 3H). **^{13}C-NMR** (125 MHz): δ 171.0, 137.5, 128.4, 128.1, 127.8, 73.2, 67.1, 61.4, 32.3. **ESI-MS** *m/z* (rel int): (pos) 210.1 ($[M+H]^+$, 15), 232.0 ($[M+Na]^+$, 100).

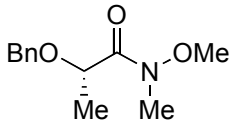
[2] Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.* **1980,** *102*, 867–869.
[3] (a) Nishizawa, M.; Yamada, M.; Noyori, R. *Tetrahedron Lett.* **1981**, *22*, 247–250. (b) Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717–6725.
[4] Williams, R. M.; Ehrlich, P. P.; Zhai, W.; Hendrix, J. *J. Org. Chem.* **1987,** *52*, 2615–2617.



(–)-(*S*)-Methyl 2-(benzyloxy)propanoate (S2).[5] In a 500 mL roundbottom flask, (*S*)-methyl 2-hydroxypropanoate ((*S*)-methyl lactate) (5.20 g, 50.0 mmol, 1.0 equiv) was dissolved in 75 mL 2:1 cyclohexane/anhyd CH_2Cl_2 and cooled to 0 °C. Benzyl 2,2,2-trichloroacetimidate (15.2 g, 60 mmol, 1.2 equiv) was added dropwise via addition funnel, followed by catalytic TfOH (600 mg, 4.0 mmol, 0.08 equiv). The mixture was stirred at 0 °C for 15 min then allowed to warm to rt with stirring for 8 h. Satd aq $NaHCO_3$ was added, the layers were separated, and the aq layer was extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (20:1→15:1→12:1→10:1→8:1 hexanes/EtOAc) yielded benzyl ether **S2** (6.51 g, 67%) as a light yellow oil.

The R-enantiomer was also prepared and used in the synthesis of the enantiomeric series of compounds (not shown below).

TLC: R_f 0.60 (2:1 hexanes/EtOAc). $[\alpha]_D^{21}$: –76.8° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 2931, 1750 (C=O st), 1455, 1206, 1118, 1066, 1026, 976. **^{1}H-NMR** (400 MHz): δ 7.38–7.25 (m, 5H), 4.69 (d, 1H, *J* = 11.7), 4.46 (d, 1H, *J* = 11.7), 4.06 (q, 1H, *J* = 6.8), 3.76 (s, 3H), 1.44 (d, 3H, *J* = 6.8). **^{13}C-NMR** (100 MHz): δ 174.1, 137.9, 128.8, 128.3, 128.2, 74.4, 72.4, 52.3, 19.1. **ESI-MS** *m/z* (rel int): (pos) 217.0 ($[M+Na]^+$, 100); (neg) 193.1 ($[M–H]^–$, 100).

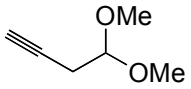


(–)-(*S*)-2-(Benzyloxy)-*N*-methoxy-*N*-methylpropanamide (S1b).[6] In a 500 mL roundbottom flask, methyl ester **S2** (1.94 g, 10.0 mmol, 1.0 equiv) was dissolved in anhyd THF (100 mL) and *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30.1 mmol, 3.0 equiv) was added. The resulting suspension was cooled to –20 °C and *i*-PrMgCl (2.0 M in Et_2O, 30 mL, 60 mmol, 6.0 equiv) was added via syringe over 30 min with stirring. After 15 min, satd aq NH_4Cl was added and the layers were separated. The aq layer was extracted with EtOAc and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1→2:1→1.5:1 hexanes/EtOAc) yielded Weinreb amide **S1b** (1.88 g, 84%) as a clear oil.

TLC: R_f 0.30 (1:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –70.1° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 2937, 1668 (C=O st), 1454, 1387, 1313, 1156, 1106, 1061, 989, 910. **^{1}H-NMR** (400 MHz): δ 7.39–7.22 (m, 5H), 4.67 (d, 1H, *J* = 11.9), 4.42 (d, 1H, *J* = 11.9), 4.39 (q, 1H, *J* = 6.6), 3.57 (s, 3H), 3.21 (s,

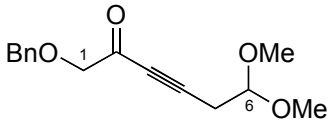
[5] Auge, C.; Serge, D.; Gautheron, C.; Malleron, A.; Cavaye, B. *New J. Chem.* **1988,** *12*, 733–744.
[6] Tomooka, K.; Kikuchi, M.; Igawa, K.; Suzuki, M.; Keong, P.; Nakai, T. *Angew. Chem., Intl. Ed.* **2000,** *39*, 4502–4505.

3H), 1.41 (d, 3H, J = 6.6). **^{13}C-NMR** (125 MHz): δ 173.2, 137.8, 128.4, 128.0, 127.7, 71.4, 71.2, 61.3, 32.4, 18.0. **ESI-MS** *m/z* (rel int): (pos) 224.3 ($[M+H]^+$, 50), 246.0 ($[M+Na]^+$, 100).



4,4-Dimethoxybut-1-yne (S3).[7] To a stirred suspension of Al (6.2 g, 230 mmol, 2.3 equiv) in refluxing anhyd Et_2O (24 mL) was added $HgCl_2$ (352 mg, 1.3 mmol, 0.013 equiv) followed by a solution of propargyl bromide (18.0 g, 151 mmol, 1.5 equiv) in anhyd Et_2O (100 mL). The mixture was stirred at reflux for 1 h. The mixture was then cooled to –78 °C and a solution of trimethyl orthoformate (10.6 g, 100 mmol, 1.0 equiv) in anhyd Et_2O (10 mL) was added with stirring. After 4 h at –78 °C, H_2O (200 mL) and aq 1N NaOH (60 mL) were added and the mixture was warmed to rt and stirred for 15 min. Celite (20 g) was added to the mixture, followed by vacuum filtration over Celite, which was subsequently washed with Et_2O. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (9:1 pentane/Et_2O) provided the volatile alkyne **S3** (7.85 g, 69%) as a clear oil.

TLC: R_f 0.31 (9:1 pentane/Et_2O). **IR** (NaCl, film): 3308 (αC–H st), 2936, 2835, 2252 (CαC st), 1465, 1422, 1362, 1193, 1122, 1067, 993, 908, 734. **^{1}H-NMR** (400 MHz): δ 4.55 (t, 1H, J = 5.6), 3.39 (s, 6H), 2.53 (dd, 2H, J = 5.6, 2.7), 2.04 (t, 1H, J = 2.7). **^{13}C-NMR** (125 MHz): δ 102.3, 79.3, 70.1, 53.4, 23.7.

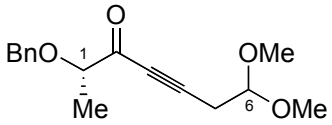


1-(Benzyloxy)-6,6-dimethoxyhex-3-yn-2-one (S4a). Ground $CeCl_3$ beads (15.3 g, 61.9 mmol, 2.25 equiv) was dried by heating to 130 °C *in vacuo* for 15 h with stirring. The resulting off-white solid was allowed to cool to rt, then cooled further to 0 °C. An Ar atmosphere was introduced followed by cool anhyd THF (40 mL) and the resulting chalky suspension was stirred at rt for 1 h. In a separate 500 mL roundbottom flask, a stirred solution of alkyne **S3** (4.72 g, 41.3 mmol, 1.5 equiv) in THF (200 mL) was cooled to –78 °C and a solution of *n*-BuLi (2.5 M in hexanes, 16.52 mL, 41.3 mmol, 1.5 equiv) was added dropwise with stirring. After 1 h, the $CeCl_3$ suspension above was added to the light yellow alkynyl lithium solution. The $CeCl_3$ flask was rinsed with additional THF (2 × 30 mL). After 2.5 h, a solution of azeotropically dried (PhH) Weinreb amide **S1a** (5.76 g, 27.5 mmol, 1.0 equiv) in THF (50 mL) was added to the alkynyl cerium solution at –78 °C. The Weinreb amide flask was rinsed with additional THF (2 × 25 mL). After 1.5 h, the reaction was warmed to –40 °C. After 30 min, the reaction was quenched with satd aq NH_4Cl, filtered through a plug of celite (rinsed with CH_2Cl_2) and

[7] Jung, M. E.; Gardiner, J. M. *Tetrahedron Lett.* **1994,** *35*, 6755–6758.

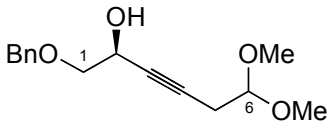
concentrated by rotary evaporation. The crude oil was extracted with CH_2Cl_2, which was then dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1 hexanes/EtOAc) provided alkynone **S4a** (6.13 g, 85%) as a light yellow oil.

TLC: R_f 0.50 (1:1 hexanes/EtOAc). **IR** (NaCl, film): 2936, 2834, 2214 (CαC st), 1691 (C=O st), 1611, 1496, 1453, 1414, 1363, 1189, 1119, 1069, 983, 811, 740. **^{1}H-NMR** (400 MHz): δ 7.38–7.30 (m, 5H), 4.63 (s, 2H), 4.57 (t, 1H, J = 5.6), 4.21 (s, 2H), 3.36 (s, 6H), 2.70 (d, 2H, J = 5.6). **^{13}C-NMR** (125 MHz): δ 184.8, 137.1, 128.5, 128.1, 101.5, 91.7, 79.7, 75.8, 73.4, 53.6, 24.6. **ESI-MS** *m/z* (rel int): (pos) 285.1 ($[M+Na]^+$, 100); (neg) 261.0 ($[M–H]^–$, 53), 297.0 ($[M+Cl]^–$, 100).



(–)-(*S*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-yn-3-one (S4b). Prepared from Weinreb amide **S1b** essentially as above, with stirring at –45 °C for 2 h after the addition of the Weinreb amide. Purification by silica flash chromatography (5:1→4:1→3:1 hexanes/EtOAc) provided alkynone **S4b** (2.05 g, 93%) as a clear oil.

TLC: R_f 0.40 (2:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –43.1° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 2934, 1675 (C=O st), 1454, 1367, 1276, 1260, 1116, 1063, 976. **^{1}H-NMR** (400 MHz): δ 7.40–7.24 (m, 5H), 4.73 (d, 1H, J = 11.7), 4.59 (t, 1H, J = 5.7), 4.46 (d, 1H, J = 11.7), 4.03 (q, 1H, J = 6.8), 3.37 (s, 6H), 2.73 (d, 2H. J = 5.7), 1.43 (d, 3H, J = 6.8). **^{13}C-NMR** (100 MHz): δ 189.5, 137.6, 128.5, 127.9, 127.8, 101.6, 92.2, 80.8, 80.0, 72.1, 53.7, 53.6, 24.7, 17.8. **ESI-MS** *m/z* (rel int): (pos) 277.0 ($[M+H]^+$, 50), 299.1 ($[M+Na]^+$, 100); (neg) 311.2 ($[M+Cl]^–$, 90).

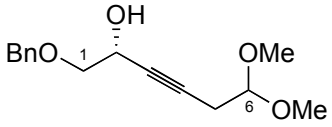


(+)-(*S*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-yn-2-ol (*S*-3a). In a 250mL roundbottom flask, neat alkynone **S4a** (3.0 g, 11.4 mmol, 1.0 equiv) was treated with (*R*)-Alpine-Borane (0.5 M in THF, 100 mL, 50.0 mmol, 4.4 equiv) at rt. The solution was sealed and stirred for 2–4 d at rt until complete conversion had occurred as judged by TLC. The mixture was cooled to 0 °C, then a solution of acetaldehyde (1 mL) in THF (10 mL) was added and the mixture was warmed to rt and stirred for 30 min. The solvent was removed by rotary evaporation. The mixture was then dissolved in THF (70 mL) and treated with ethanolamine (3 mL) at 0 °C. A white precipitate formed and the mixture was stirred for 30 min at rt. Et_2O was added and the mixture was filtered under reduced pressure. The solid was rinsed with additional Et_2O. The combined filtrates were then washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded propargylic alcohol ***S*-3a** (2.93 g, 97%, 86% ee) as a light yellow oil.

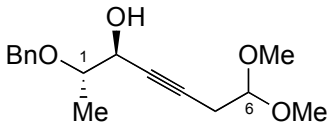
TLC: R_f 0.31 (1:1 hexanes/EtOAc). $[\alpha]_D^{25}$: +4.1° (*c* 1.1, $CHCl_3$). **IR** (NaCl, film): 3433 (O–H st), 2913, 2240, 1451, 1365, 1192, 1118, 1063, 823, 738. **^{1}H-NMR** (400 MHz): δ 7.37–7.28 (m, 5H), 4.64–4.54 (m, 3H), 4.50 (t, 1H, *J* = 5.7), 3.63 (dd, 1H, *J* = 9.8, 3.6), 3.55 (dd, 1H, *J* = 9.8, 7.5), 3.35 (s, 6H), 2.59 (d, 1H, *J* = 4.6), 2.55 (dd, 2H, *J* = 5.6, 1.9). **^{13}C-NMR** (125 MHz): δ 137.7, 128.5, 128.1, 128.0, 102.4, 81.1, 79.5, 73.8, 73.4, 61.8, 53.4, 24.0. **ESI-MS** *m/z* (rel int): (pos) 287.1 ($[M+Na]^+$, 100); (neg) 299.0 ($[M+Cl]^-$, 100).

Analysis (^{1}H-NMR and ^{19}F-NMR) of the derived Mosher ester[8] indicated that propargylic alcohol ***S*-3a** was formed in 86% *ee*: In a 5 mL roundbottom flask, 4 Å molecular sieves, propargylic alcohol ***S*-3a** (5 mg, 18.9 μmol, 1.0 equiv) in anhyd CH_2Cl_2 (0.75 mL), Et_3N (15.9 μL, 114 μmol, 6.0 equiv), and DMAP (2.3 mg, 18.9 μmol, 1.0 equiv) were added and cooled to 0 °C. (*R*)-(–)-Mosher acid chloride (Aldrich, 5.31 μL, 28.4 μmol, 1.5 equiv) was added dropwise via syringe. The mixture was stirred at 0 °C for 5 min then warmed to rt and stirred until complete conversion had occurred as judged by TLC (approx 30 min). Satd aq NH_4Cl was then added at 0 °C and the mixture was warmed to rt and stirred for 15 min. The layers were separated and the aq layer was extracted with CH_2Cl_2. The combined organic extracts were washed with satd aq $NaHCO_3$, and H_2O, dried (Na_2SO_4), filtered, and concentrated by rotary evaporation to afford the crude Mosher ester product, which was analyzed without further purification.

TLC: R_f 0.60 (1:1 hexanes/EtOAc). Ratio of diastereomers determined by analysis of crude product by ^{1}H-NMR and ^{19}F-NMR. Observed diagnostic chemical shifts in the ^{1}H-NMR for the propargyl CH_2 are δ 2.51 (dd, 2H, *J* = 1.9, 5.6) (major diastereomer) and δ 2.53 (dd, 2H, *J* = 2.1, 5.7) (minor diastereomer). Observed diasgnostic chemical shifts in the ^{19}F-NMR are δ 89.9 (major diastereomer) and δ 89.8 (minor diastereomer).



(–)-(*R*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-yn-2-ol (*R*-3a). Prepared from alkynone **S4a** using (*S*)-Alpine-Borane as above. Light yellow oil (2.96 g, 98%, 82% ee based on Mosher ester analysis with the same (*R*)-acid chloride as above). $[\alpha]_D^{26}$: –7.5° (*c* 1.0, $CHCl_3$).

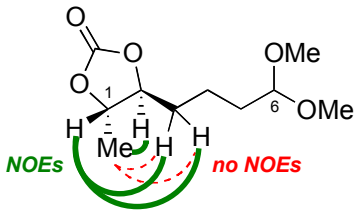


(+)-(2*S*,3*S*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-yn-3-ol (*anti*-3b). In a 200 mL roundbottom flask, alkynone **S4b** (1.00 g, 3.61 mmol, 1.0 equiv) was dissolved in anhyd THF (65 mL) and

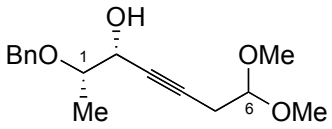
[8] Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969,** *34*, 2543–2549.

cooled to –78 °C. L-selectride (1.0 M in THF, 5.4 mL, 5.4 mmol, 1.5 equiv) was added dropwise via syringe and the mixture was stirred at –78 °C for 2 h. Satd aq NH_4Cl was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (6:1→5:1→4:1 benzene/Et_2O) yielded propargylic alcohol ***anti*-3b** (856 mg, 85%, 89:11 dr) as a clear oil.

TLC: R_f 0.45 (4:1 benzene/Et_2O, double elution). $[\alpha]_D^{21}$: 15.9° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3440 (O–H st), 2920, 1453, 1373, 1192, 1118, 1062, 974, 916. **^{1}H-NMR** (400 MHz): δ 7.41–7.24 (m, 5H), 4.70 (d, 1H, *J* = 11.6), 4.57 (d, 1H, *J* = 11.6), 4.53 (t, 1H, *J* = 6.2), 4.24 (m, 1H), 3.61 (m, 1H), 3.36 (s, 6H), 2.66 (d, 1H. *J* = 4.1), 2.56 (dd, 2H, *J* = 5.7, 1.9), 1.28 (d, 3H, *J* = 6.2). **^{13}C-NMR** (100 MHz): δ 138.5, 128.9, 128.2, 128.1, 102.8, 81.8, 80.5, 78.8, 72.0, 66.9, 53.8, 53.7, 24.4, 16.4. **ESI-MS** *m/z* (rel int): (pos) 301.0 ([M+Na]$^+$, 100); (neg) 313.1 ([M+Cl]$^-$, 90).



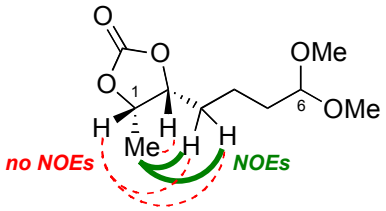
The relative stereochemistry at *C*1 and *C*2 of ***anti*-3b** was determined by NMR analysis of a cyclic carbonate derivative (1. H_2, Pd/C, MeOH/EtOAc (1:1), rt. 5 h, 91%; 2. triphosgene, pyridine, CH_2Cl_2, –78 °C → 0 °C, 1.5 h, 68%). ^{1}H-NMR peaks were assigned by COSY analysis (C_6D_6). NOESY analysis indicated interactions between H^1 (3.55 ppm) and both H^3 protons (1.27–1.12 ppm) and between Me^1 (0.73 ppm) and H^2 (3.41 ppm), but no interactions between Me^1 and either H^3 proton, consistent with an *anti* relationship at *C*1 and *C*2 of ***anti*-3b**.



(+)-(2*S*,3*R*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-yn-3-ol (*syn*-3b). In a 200 mL roundbottom flask, alkynone **S4b** (1.00 g, 3.61 mmol, 1.0 equiv) was dissolved in anhyd CH_2Cl_2 (65 mL) and cooled to –78 °C. $LiAlH_4$ (1.0 M in THF, 1.8 mL, 1.8 mmol, 0.5 equiv) was added dropwise via syringe and the mixture was stirred at –78 °C for 1 h. Satd aq NH_4Cl was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (8:1→6:1→5:1 benzene/Et_2O) yielded propargylic alcohol ***syn*-3b** (887 mg, 88%, 90:10 dr) as a clear oil.

TLC: R_f 0.40 (4:1 benzene/Et_2O, double elution). $[\alpha]_D^{21}$: +2.4° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3434 (O–H st), 2933, 2833, 1496, 1453, 1374, 1241, 1192, 1119, 1064, 976, 917, 813, 738. **^{1}H-NMR** (400 MHz): δ 7.38–7.23 (m, 5H), 4.65 (d, 1H, *J* = 11.9), 4.55 (d, 1H, *J* = 11.9), 4.53 (t,

1H, J = 5.7), 4.47 (m, 1H), 3.66 (ddd, 1H, J = 12.5, 6.2, 3.5), 3.36 (s, 6H), 2.56 (dd, 2H, J = 5.7, 2.0), 2.40 (d, 1H, J = 5.8), 1.28 (d, 3H, J = 6.2). **^{13}C-NMR** (125 MHz): δ 138.2, 128.4, 127.7, 102.4, 81.6, 79.7, 71.0, 65.1, 53.4, 24.1, 14.5. **ESI-MS** *m/z* (rel int): (pos) 279.1 ([M+H]$^+$, 3), 301.0 ([M+Na]$^+$, 100), 317.1 ([M+K]$^+$, 17); (neg) 313.2 ([M+Cl]$^-$, 100).



The relative stereochemistry at *C*1 and *C*2 of ***syn*-3b** was determined by NMR analysis of a cyclic carbonate derivative (1. H_2, Pd/C, MeOH-EtOAc (1:1), rt. 2 h, 88%; 2. triphosgene, pyridine, CH_2Cl_2, –78 °C to 0 °C, 1.5 h, 64%). ^{1}H-NMR peaks were assigned by COSY analysis (C_6D_6). NOESY analysis indicated interactions between Me^1 (0.67 ppm) and both H^3 protons (1.54, 1.21 ppm) (and between the H^1 proton at 3.85 ppm and the H^2 proton at 3.70 ppm), but no interactions between H^1 and either H^3 proton or between Me^1 and H^2 proton, consistent with a *syn* relationship at *C*1 and *C*2 of ***syn*-3b**.

D. SYNTHESIS OF ALLYLIC ALCOHOLS (10,11)

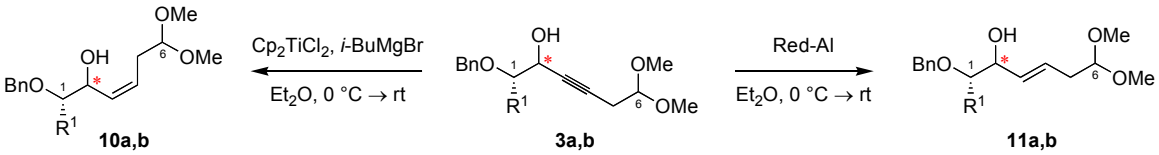
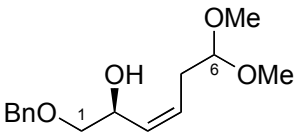


Figure S3. Synthesis of allylic alcohols 10 and 11. Allylic alcohols **10** and **11** were synthesized by stereoselective reduction of the propargylic alcohols **3** using Sato's titanocene-mediated hydromagnesiation[9] and Red-Al[10] respectively.

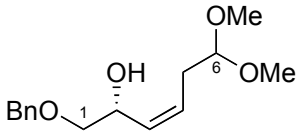


(+)-(*S*,*Z*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-ol (*S*-10a). In a 50 mL roundbottom flask in the dark at 0 °C, Cp_2TiCl_2 (397 mg, 1.6 mmol, 1.0 equiv) was suspended in 4 mL anhyd Et_2O. *i*-BuMgBr (1.8 M in Et_2O, 10.6 mL, 19.1 mmol, 12 equiv) was added gradually, and the mixture was stirred for 30 min. A solution of propargylic alcohol ***S*-3a** (417.7 mg, 1.6 mmol, 1.0 equiv) in anhyd Et_2O (4 mL) was added dropwise via syringe. The reaction was stirred at 0 °C for 30 min, warmed to rt and stirred at rt for 8–48 h until complete conversion had occurred as

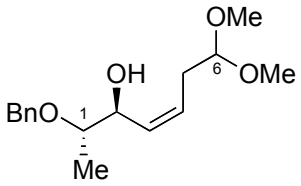
[9] Sato, F.; Ishikawa, H.; Watanabe, H.; Miyake, T.; Sato, M. *J. Chem. Soc., Chem. Commun.* **1981**, 718–720.
[10] Marshall, J. A.; DeHoff, B. S. *J. Org. Chem.* **1986**, *51*, 863–872.

judged by TLC. The mixture was then recooled to 0 °C and quenched with satd aq NH_4Cl. The mixture was extracted with Et_2O, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (2:1 hexanes/EtOAc) yielded the *Z*-allylic alcohol ***S*-10a** (360.9 mg, 86%, 88:12 *Z*/*E*) as a light yellow oil.

TLC: R_f 0.31 (1:1 hexanes/EtOAc). $[\alpha]_D^{26}$: +23.3° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3447 (O–H st), 2904, 1495, 1453, 1362, 1314, 1191, 1121, 1072, 824, 738. **^{1}H-NMR** (400 MHz): δ 7.38–7.28 (m, 5H), 5.60 (m, 2H), 4.63 (m, 1H), 4.58 (s, 2H), 4.36 (t, 1H, *J* = 5.6), 3.49 (dd, 1H, *J* = 9.5, 3.7), 3.44 (dd, 1H, *J* = 9.6, 7.9), 3.34 (s, 3H), 3.32 (s, 3H), 2.68 (d, 1H, *J* = 2.5), 2.52 (m, 1H), 2.38 (m, 1H). **^{13}C-NMR** (125 MHz): δ 137.9, 131.0, 128.5–127.5 (Ar), 103.8, 73.6, 73.4, 66.7, 53.5, 53.2, 31.8. **ESI-MS** *m/z* (rel int): (pos) 289.0 ($[M+Na]^+$, 100); (neg) 301.0 ($[M+Cl]^-$, 100).

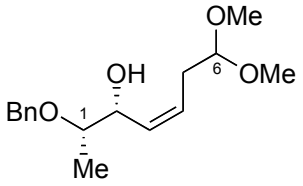


(–)-(*R*,*Z*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-ol (*R*-10a). Prepared from propargylic alcohol ***R*-3a** as above. Light yellow oil (1.17 g, 81%, 88:12 *Z*/*E*). $[\alpha]_D^{26}$: –21.0° (*c* 1.0, $CHCl_3$).



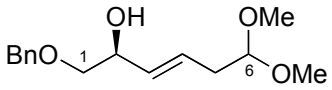
(+)-(2*S*,3*S*,*Z*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-ol (*anti*-10b). Prepared from propargylic alcohol ***anti*-3b** as above. Clear oil (210.6 mg, 86%, ≥98:2 *Z*/*E*).

TLC: R_f 0.40 (2:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +17.8° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3454 (O–H st), 2932, 1453, 1374, 1190, 1121, 1060, 826. **^{1}H-NMR** (400 MHz): δ 7.36–7.27 (m, 5H), 5.60 (m, 1H), 5.52 (m, 1H), 4.69 (d, 1H, *J* = 11.5), 4.52 (d, 1H, *J* = 11.5), 4.38 (t, 1H, *J* = 6.2), 4.27 (t, 1H, *J* = 8.0), 3.46 (m, 1H), 3.34 (m, 1H), 2.85 (br s, 1H), 2.54 (m, 1H), 2.42 (m, 1H), 1.17 (d, 3H, *J* = 6.2). **^{13}C-NMR** (100 MHz): δ 138.3, 130.9, 128.6, 128.5, 127.8, 127.7, 103.8, 78.5, 71.2, 71.1, 53.2, 53.1, 31.9, 15.4. **ESI-MS** *m/z* (rel int): (pos) 303.1 ($[M+Na]^+$, 100); (neg) 315.1 ($[M+Cl]^-$, 90).



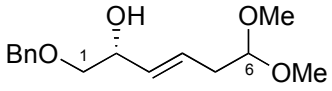
(+)-(2*S*,3*R*,*Z*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-ol (*syn*-10b). Prepared from propargylic alcohol ***syn*-3b** as above. Clear oil (83.2 mg, 86%, ≥98:2 *Z*/*E*).

TLC: R_f 0.38 (1:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +6.8° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3445 (O–H st), 2935, 2834, 1724, 1498, 1454, 1374, 1188, 1121, 1066, 1029, 915, 846, 739, 700. **^{1}H-NMR** (400 MHz): δ 7.38–7.20 (m, 5H), 5.68–5.55 (m, 2H), 4.65 (d, 1H, *J* = 11.8), 4.55 (d, 1H, *J* = 11.8), 4.46 (m, 1H), 4.37 (t, 1H, *J* = 5.6), 3.60 (ddd, 1H, *J* = 12.6, 6.3, 3.9), 3.34 (s, 3H), 3.33 (s, 3H), 2.52 (m, 1H), 2.46 (d, 1H, *J* = 3.9), 2.37 (m, 1H), 1.17 (d, 3H, *J* = 6.0). **^{13}C-NMR** (125 MHz): δ 138.6, 131.4, 128.4, 127.6, 127.3, 103.8, 71.0, 69.7, 53.5, 53.2, 31.8, 14.6. **ESI-MS** *m/z* (rel int): (pos) 302.9 ($[M+Na]^+$, 100), 319.1 ($[M+K]^+$, 32); (neg) 279.2 ($[M–H]^-$, 100).

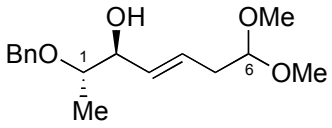


(+)-(*S*,*E*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-ol (*S*-11a). In a 50 mL roundbottom flask at 0 °C, Red-Al (3.33 M in toluene, 11.1 mL, 37.1 mmol, 14 equiv) was dissolved in 8 mL anhyd Et_2O. A solution of propargylic alcohol ***S*-3a** (700 mg, 2.6 mmol, 1.0 equiv) in anhyd Et_2O (7 mL) was added gradually via syringe down the side of the flask. The reaction was stirred at 0 °C for 5 min, warmed to rt and stirred for 3 h, then recooled to 0 °C and quenched with water followed by satd aq NH_4Cl. The mixture was extracted with Et_2O and the combined organic extracts were washed with satd aq NH_4Cl and water, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product, which was configurationally pure by ^{1}H-NMR analysis. Purification by silica flash chromatography (2:1→1:1 hexanes/EtOAc) yielded *E*-allylic alcohol ***S*-11a** (694.5 mg, 99%, ≥98:2 *E*/*Z*) as a light yellow oil.

TLC: R_f 0.31 (1:1 hexanes/EtOAc). $[\alpha]_D^{26}$: +7.5° (*c* 1.2, $CHCl_3$). **IR** (NaCl, film): 3436 (O–H st), 2901, 1452, 1361, 1191, 1120, 1058, 968, 737. **^{1}H-NMR** (400 MHz): δ 7.38–7.28 (m, 5H), 5.74 (dt, 1H, *J* = 15.6, 7.0), 5.56 (dd, 1H, *J* = 15.6, 6.3), 4.57 (s, 2H), 4.39 (t, 1H, *J* = 5.7), 4.33 (m, 1H), 3.51 (dd, 1H, *J* = 9.6, 3.3), 3.37 (dd, 1H, *J* = 9.4, 8.2), 3.32 (s, 6H), 2.41 (d, 1H, *J* = 3.0), 2.35 (m, 2H). **^{13}C-NMR** (125 MHz): δ 137.9, 131.1, 128.5–127.7 (Ar), 103.8, 74.2, 73.4, 71.2, 53.0, 52.9, 35.9. **ESI-MS** *m/z* (rel int): (pos) 289.1 ($[M+Na]^+$, 100); (neg) 301.0 ($[M+Cl]^-$, 100), 265.1 ($[M–H]^-$, 24).

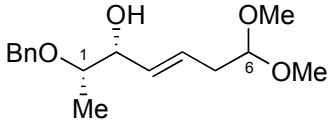


(–)-(*R*,*E*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-ol (*R*-11a). Prepared from propargylic alcohol ***R*-3a** as above. Light yellow oil (1.14 g, 79% yield not optimized due to material losses, ≥98:2 *E*/*Z*). $[\alpha]_D^{26}$: –7.6° (*c* 1.0, $CHCl_3$).



(+)-(2*S*,3*S*,*E*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-ol (*anti*-11b). Prepared from propargylic alcohol ***anti*-3b** essentially as above with stirring at rt for 8 h after the propargylic alcohol was added. Clear oil (99.7 mg, 99%, ≥98:2 *E*/*Z*).

TLC: R_f 0.45 (2:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +42.5° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3437 (O–H st), 2932, 1453, 1374, 1191, 1119, 1058, 969. **^{1}H-NMR** (400 MHz): δ 7.38–7.25 (m, 5H), 5.74 (m, 1H), 5.53 (m, 1H), 4.67 (d, 1H, *J* = 11.5), 4.47 (d, 1H, *J* = 11.5), 4.39 (t, 1H, *J* = 5.8), 3.92 (m, 1H), 3.40 (m, 1H), 3.32 (s, 6H), 2.76 (br s, 1H), 2.39 (br t, 2H, *J* = 5.8), 1.15 (d, 3H, *J* = 6.6). **^{13}C-NMR** (100 MHz): δ 138.6, 132.0, 129.1, 128.9, 128.3, 128.2, 104.2, 78.8, 76.7, 71.6, 53.3, 53.2, 36.4, 15.9. **ESI-MS** *m/z* (rel int): (pos) 303.0 ($[M+Na]^+$, 100); (neg) 315.1 ($[M+Cl]^-$, 90), 279.0 ($[M–H]^-$, 100).



(+)-(2*S*,3*R*,*E*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-ol (*syn*-11b). Prepared from propargylic alcohol ***syn*-3b** essentially as above with stirring at rt for 8 h after the propargylic alcohol was added. Clear oil (50 mg, 99%, ≥98:2 *E*/*Z*).

TLC: R_f 0.56 (1:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +5.1° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3423 (O–H st), 2934, 1721, 1496, 1452, 1374, 1272, 1205, 1072, 1026, 970, 750, 714. **^{1}H-NMR** (400 MHz): δ 7.40–7.21 (m, 5H), 5.68 (m, 1H), 5.58 (dd, 1H, *J* = 15.5, 6.6), 4.64 (d, 1H, *J* = 11.8), 4.53 (1H, *J* = 11.8), 4.39 (t, 1H, *J* = 5.8), 4.21 (m, 1H), 3.60 (ddd, 1H, *J* = 12.7, 6.3, 3.4), 3.33 (s, 3H), 3.32 (s, 3H), 2.39 (dd, 2H, *J* = 6.6, 5.8), 1.14 (d, 3H, 6.3). **^{13}C-NMR** (125 MHz): δ 138.5, 131.3, 128.4, 127.7, 103.9, 77.6, 74.3, 70.9, 52.9, 52.8, 36.0, 14.2. **ESI-MS** *m/z* (rel int): (pos) 303.0 ($[M+Na]^+$, 100), 319.1 ($[M+K]^+$, 21); (neg) 315.2 ($[M+Cl]^-$, 75), 279.2 ($[M–H]^-$, 100).

E. SYNTHESIS OF EPOXYOLS (12,13)

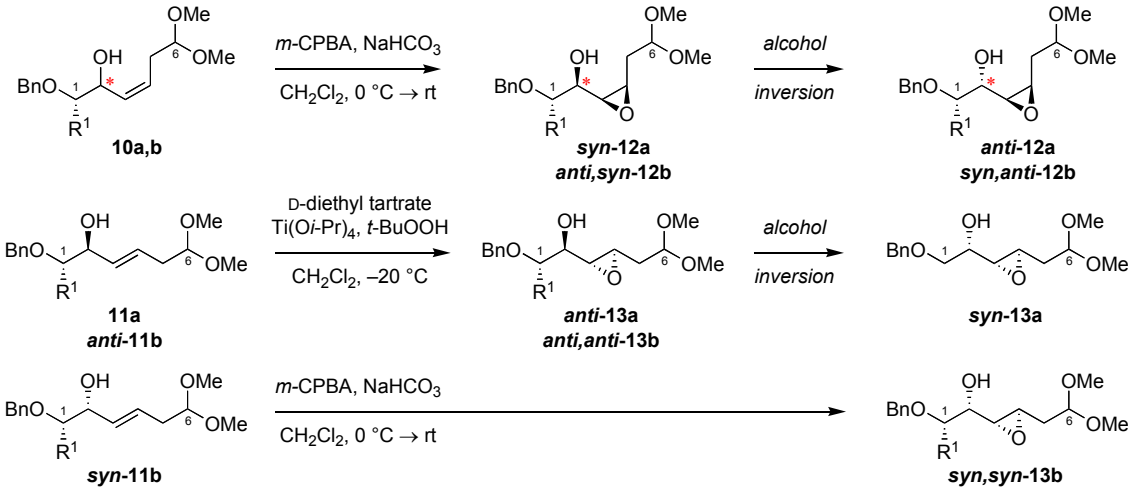
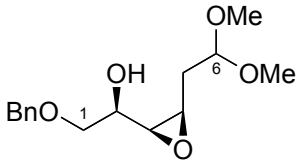


Figure S4. Synthesis of epoxyols 12 and 13. *syn*-Epoxidation of *Z*-allylic alcohols **10** was achieved in all cases using *m*-CPBA to afford *syn*,*cis*-epoxyols ***syn*-12a** and ***anti*,*syn*-12b**.[11] Alcohol inversion was then accomplished via either Mitsunobu protocol[12] (R^1 = H series) or oxidation and re-reduction (R^1 = Me series) to afford the corresponding *anti*,*cis*-epoxyols ***anti*-12a** and ***syn*,*anti*-12b**. *anti*-Epoxidation of *E*-allylic alcohols **11a** and ***anti*-11b** was achieved using matched Sharpless conditions[13] to afford *anti*,*trans*-epoxyols ***anti*-13** and ***anti*,*anti*-13b**. While ***syn*-11b** was unreactive under these conditions, it did undergo an unusual *syn*-epoxidation with *m*-CPBA to form ***syn*,*syn*-13b**. Alcohol inversion was again accomplished using a Mitsunobu protocol in the R^1 = H series to form ***syn*-13b** and was unnecessary in the R^1 = Me series since ***syn*,*syn*-13b** could be accessed directly. Stereochemical assignments were made by analogy to literature precedents[11,14] and by NMR analysis of acetonides and cyclic carbonates derived from these compounds (see SECTIONS I and J below).



(+)-(*R*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*R*-*syn*-12a). In a 25 mL roundbottom flask, *Z*-allylic alcohol ***S*-10a** (327.5 mg, 1.23 mmol, 1.0 equiv) was dissolved in anhyd CH_2Cl_2 (12 mL) and cooled to 0 °C. $NaHCO_3$ (258 mg, 3.08 mmol, 2.5 equiv) was added and stirred at 0 °C for 5 min. To this stirred mixture was added *m*-CPBA (318.4 mg, 1.85 mmol, 1.5 equiv). After 24 h at rt, Et_2O was added. This mixture was washed with water, satd aq $NaHCO_3$, and brine, then dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (2:1 hexanes/EtOAc) yielded epoxyol **2*R*-*syn*-12a** (299.6 mg, 86%, 90:10 dr) as a light yellow oil.

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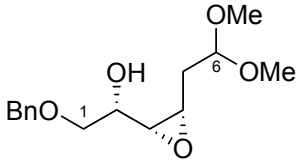
[11] (a) Adam, W.; Wirth, T. *Acc. Chem. Res.* **1999**, *32*, 703–710. (b) Henbest, H. B.; Wilson, R. A. L. *J. Chem. Soc.* **1957**, 1958–1965.

[12] Martin, S. F.; Dodge, J. A. *Tetrahedron Lett.* **1991,** *32*, 3017–3020.

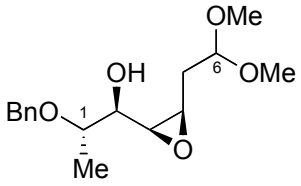
[13] Gao, Y.; Klunder, J. M.; Hanson, R. M.; Masamune, H.; Ko, S. Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987,** *109*, 5765–5780.

[14] (a) Katsuki, T.; Martin, V. S. *Org. React.* **1996**, *48*, 1–299. (b) Pfenninger, A. *Synthesis* **1986**, 89–116.

TLC: R_f 0.33 (1:2 hexanes/EtOAc). $[\alpha]_D^{26}$: +20.7° (*c* 1.1, $CHCl_3$). **IR** (NaCl, film): 3438 (O–H st), 2934, 1717, 1453, 1363, 1269, 1193, 1121, 1060, 837, 741. **^{1}H-NMR** (400 MHz): δ 7.38–7.28 (m, 5H), 4.62 (s, 2H), 4.55 (m, 1H), 3.73 (m, 1H), 3.59 (m, 2H), 3.35 (s, 3H), 3.32 (s, 3H), 3.14 (m, 1H), 3.04 (dd, 1H, *J* = 7.0, 4.4), 2.38 (d, 1H, *J* = 4.3), 1.93 (m, 1H), 1.85 (m, 1H). **^{13}C-NMR** (125 MHz): δ 137.7, 128.5, 127.9, 127.8, 102.7, 73.6, 71.4, 68.9, 57.5, 54.0, 53.5, 53.0, 32.2. **ESI-MS** *m/z* (rel int): (pos) 305.1 ($[M+Na]^+$, 100); (neg) 281.0 ($[M–H]^-$, 17), 316.9 ($[M+Cl]^-$, 100).

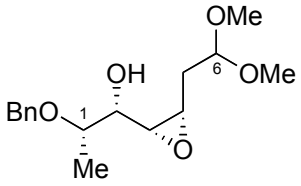


(–)-(*S*)-2-(Benzyloxy)-1-[(2*R*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*S*-*syn*-12a). Prepared from *Z*-allylic alcohol ***R*-10a** as above. Light yellow oil (997 mg, 85%, 90:10 dr). $[\alpha]_D^{26}$: –14.4° (*c* 1.1, $CHCl_3$).



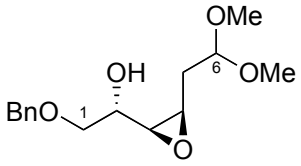
(+)-(1*R*,2*S*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*anti*,*syn*-12b). Prepared from *Z*-allylic alcohol ***anti*-10b** essentially as above with standing in a refrigerator at –4 °C for 20 h after the addition of *m*-CPBA. Clear oil (37 mg, 86%, 92:8 dr).

TLC: R_f 0.30 (2:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +50.9° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3449 (O–H st), 2932, 1720, 1454, 1375, 1192, 1121, 1060, 841. **^{1}H-NMR** (400 MHz): δ 7.38–7.24 (m, 5H), 4.69 (d, 1H, *J* = 11.8), 4.56 (dd, 1H, *J* = 7.0, 4.4), 4.50 (d, 1H, *J* = 11.8), 3.65 (m, 1H), 3.50 (dd, 1H, *J* = 11.0, 5.2), 3.37 (s, 3H), 3.33 (s, 3H), 3.12 (m, 1H), 3.08 (m, 1H), 2.48 (d, 1H, *J* = 5.2), 1.97 (ddd, 1H, *J* = 14.4, 7.0, 3.9), 1.79 (ddd, 1H, *J* = 14.4, 7.9, 4.4), 1.26 (d, 3H, *J* = 6.3). **^{13}C-NMR** (100 MHz): δ 138.1, 128.5, 127.8, 127.7, 102.8, 75.9, 72.0, 71.1, 57.0, 54.0, 53.5, 53.0, 32.3, 15.1. **ESI-MS** *m/z* (rel int): (pos) 319.1 ($[M+Na]^+$, 100); (neg) 331.0 ($[M+Cl]^-$, 90), 295.3 ($[M–H]^-$, 100).



(–)-(1*S*,2*S*)-2-(Benzyloxy)-1-[(2*R*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*syn*,*syn*-12b). Prepared from *Z*-allylic alcohol ***anti*-10b** essentially as above with standing in a refrigerator at –4 °C for 8 h after the addition of *m*-CPBA. Clear oil (55 mg, 93%, ≥98:2 dr).

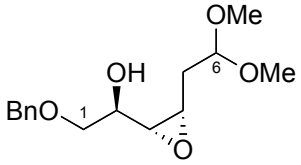
TLC: R_f 0.30 (1:1 hexanes/EtOAc). $[\alpha]_D^{22}$: –5.5° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3446 (O–H st), 2975, 2934, 2832, 1496, 1453, 1372, 1265, 1239, 1192, 1120, 1061, 971, 934, 844, 742. **^{1}H-NMR** (400 MHz): δ 7.39–7.24 (m, 5H), 4.65 (d, 1H, *J* = 11.8), 4.56 (dd, 1H, *J* = 6.8, 4.7), 4.50 (d, 1H, *J* = 11.8), 3.63 (m, 1H), 3.48 (m, 1H), 3.36 (s, 3H), 3.31 (s, 3H), 3.17 (m, 1H), 3.06 (dd, 1H, *J* = 7.0, 4.4), 2.35 (d, 1H, *J* = 4.4), 1.97 (ddd, 1H, *J* = 14.4, 6.8, 4.0), 1.76 (ddd, 1H, *J* = 14.4, 8.1, 4.7), 1.28 (d, 3H, *J* = 6.3). **^{13}C-NMR** (125 MHz): δ 138.2, 128.4, 127.7, 102.7, 76.0, 71.9, 71.0, 57.3, 54.1, 53.7, 53.0, 32.4, 15.4. **ESI-MS** *m/z* (rel int): (pos) 318.9 ($[M+Na]^+$, 100), 335.2 ($[M+K]^+$, 29); (neg) 331.2 ($[M+Cl]^-$, 100), 295.5 ($[M–H]^-$, 30).



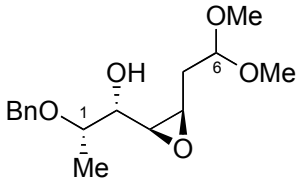
(–)-(*S*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*S*-*anti*-12a). In a 15 mL roundbottom flask, Ph_3P (423 mg, 1.6 mmol, 3.0 equiv) and *p*-nitrobenzoic acid (306 mg, 1.8 mmol, 3.4 equiv) were dissolved in anhyd toluene (1.5 mL). A solution of epoxyol **2*R*-*syn*-12a** (150 mg, 0.53 mmol, 1.0 equiv) in anhyd toluene (3.75 mL) was added and cooled to –78 °C. DIAD (325 μL, 1.7 mmol, 3.2 equiv) was added slowly and the mixture was allowed to warm to 0 °C for 20 min, then warmed rt and stirred for 45 min. Satd aq $NaHCO_3$ was added, the layers were separated, and the aq layer was extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. The resulting mixture was dissolved in MeOH (7.5 mL), followed by addition of K_2CO_3 (221 mg, 1.6 mmol, 3.0 equiv) at rt. After stirring for 30 min, the mixture was diluted with CH_2Cl_2, washed with H_2O, dried (Na_2SO_4), and concentrated by rotary evaporation. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded epoxyol **2*S*-*anti*-12a** (145.3 mg, 97%, 92:8 dr) as a light yellow oil.

TLC: R_f 0.33 (1:2 hexanes/EtOAc). $[\alpha]_D^{24}$: –6.7° (*c* 1.1, $CHCl_3$). **IR** (NaCl, film): 3445 (O–H st), 2934, 1733, 1453, 1362, 1192, 1121, 1058, 831, 739. **^{1}H-NMR** (400 MHz): δ 7.35–7.27 (m, 5H), 4.62 (s, 2H), 4.59 (m, 1H), 3.74 (dd, 1H, *J* = 9.7, 3.0), 3.65 (dd, 1H, *J* = 9.7, 6.2), 3.59 (m, 1H), 3.42 (s, 3H), 3.36 (s, 3H), 3.12 (m, 1H), 3.02 (dd, 1H, *J* = 8.5, 4.1), 2.14 (dt, 1H, *J* = 13.8, 3.8), 1.85 (dt, 1H, *J* = 14.0, 7.2). **^{13}C-NMR** (125 MHz): δ 138.3, 128.8, 128.2, 128.1, 102.9,

74.1, 72.5, 69.0, 56.1, 55.2, 53.2, 53.1, 32.1. **ESI-MS** *m/z* (rel int): (pos) 304.9 ($[M+Na]^+$, 100); (neg) 316.9 ($[M+Cl]^-$, 100).



(+)-(*R*)-2-(Benzyloxy)-1-[(2*R*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*R*-*anti*-12a). Prepared from epoxyol **2*S*-*syn*-12a** as above. Light yellow oil (134.2 mg, 90%, 91:9 dr). $[\alpha]_D^{24}$: +7.7° (*c* 1.2, $CHCl_3$).

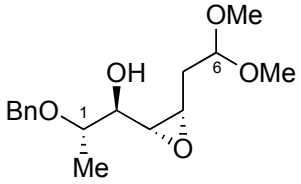


(+)-(1*S*,2*S*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*syn*,*anti*-12b). In a 10 mL roundbottom flask, ***anti*,*syn*-12b** (48.3 mg, 163 μmol, 1.0 equiv) was dissolved in anhyd CH_2Cl_2 (4.0 mL) and cooled to 0 °C. Dess–Martin periodinane (Aldrich, 138.2 mg, 326 μmol, 2.0 equiv) was added in one portion. The mixture was stirred at 0 °C for 30 min, then rt for 8 h. Satd aq $NaHCO_3$ was added with Et_2O (5.0 mL) at 0 °C and the mixture was warmed to rt and stirred for 15 min. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded epoxyketone ***anti*-19b** (47.2 mg, 98%) as a clear oil.

In a 25 mL roundbottom flask, epoxyketone ***anti*-19b** (15 mg, 50 μmol, 1.0 equiv) was dissolved in anhyd CH_2Cl_2 (3.0 mL) and cooled to –78 °C. $LiAlH_4$ (1.0 M in THF, 0.04 mL, 0.04 mmol, 0.8 equiv) was added dropwise via syringe and the mixture was stirred at –78 °C for 1 h. Satd aq NH_4Cl was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1→3:1→2:1→1.5:1 hexanes/EtOAc) yielded epoxyol ***syn*,*anti*-12b** (14.3 mg, 97%, ≥98:2 dr) as a clear oil.

TLC: R_f 0.30 (2:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +9.2° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3448 (O–H st), 2933, 1453, 1378, 1191, 1121, 1059, 844. **^{1}H-NMR** (400 MHz): δ 7.42–7.21 (m, 5H), 4.69 (d, 1H, *J* = 11.9), 4.59 (m, 1H), 4.58 (d, 1H, *J* = 11.9), 3.77 (ddd, 1H, *J* = 12.7, 6.4, 3.9), 3.44 (m, 1H), 3.43 (s, 3H), 3.37 (s, 3H), 3.32 (d, 1H, *J* = 3.2), 3.13–3.04 (m, 2H), 2.13 (m, 1H), 1.85 (m, 1H), 1.31 (d, 3H, *J* = 6.4). **^{13}C-NMR** (125 MHz): δ 138.6, 128.4, 127.7, 127.6, 102.6, 76.5,

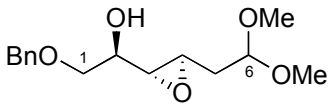
71.8, 71.2, 55.5, 54.8, 52.8, 51.9, 31.8, 14.9. **ESI-MS** *m/z* (rel int): (pos) 319.0 ([M+Na]$^+$, 100); (neg) 331.2 ([M+Cl]$^-$, 90).



(+)-(1*R*,2*S*)-2-(Benzyloxy)-1-[(2*R*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*anti*,*anti*-12b). In a 10 mL roundbottom flask, ***syn*,*syn*-12b** (50.8 mg, 171 μmol, 1.0 equiv) was dissolved in anhyd CH_2Cl_2 (4.0 mL) and cooled to 0 °C. Dess–Martin periodinane (Aldrich, 145.4 mg, 340 μmol, 2.0 equiv) was added in one portion. The mixture was stirred at 0 °C for 30 min, then rt for 8 h. Satd aq $NaHCO_3$ was added with Et_2O (5.0 mL) at 0 °C and the mixture was warmed to rt and stirred for 15 min. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded epoxyketone ***syn*-19b** (46.7 mg, 92%) as a clear oil.

In a 10 mL roundbottom flask, epoxyketone ***syn*-19b** (30.0 mg, 0.102 mmol, 1.0 equiv) was dissolved in anhyd THF (5 mL) and cooled to –78 °C. L-selectride (1.0 M in THF, 0.204 mL, 0.204 mmol, 2.0 equiv) was added dropwise via syringe and the mixture was stirred at –78 °C for 1 h. Satd aq NH_4Cl was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1→3:1→2:1 hexanes/EtOAc) yielded epoxyol ***anti*,*anti*-12b** (30.8 mg, 100%, ≥98:2 dr) as a clear oil.

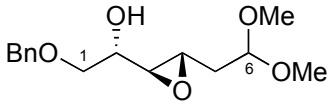
TLC: R_f 0.30 (2:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +8.4° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3441 (O–H st), 2976, 2934, 2833, 1721, 1496, 1453, 1376, 1267, 1235, 1191, 1122, 1063, 917, 846, 748. **^{1}H-NMR** (400 MHz): δ 7.41–7.22 (m, 5H), 4.72 (d, 1H, *J* = 11.6), 4.61 (dd, 1H, *J* = 6.6, 4.1), 4.56 (d, 1H, *J* = 11.6), 3.74 (qd, 1H, 6.4, 5.9), 3.41 (s, 3H), 3.36 (s, 3H), 3.26 (m, 1H), 3.21 (d, 1H, *J* = 3.2), 3.11 (m, 1H), 3.01 (dd, 1H, *J* = 8.4, 4.2), 2.05 (ddd, 1H, *J* = 14.3, 5.7, 4.1), 1.90 (ddd, 1H, *J* = 14.3, 7.5, 6.6), 1.31 (d, 3H, *J* = 6.4). **^{13}C-NMR** (125 MHz): δ 138.3, 128.4, 127.8, 127.7, 102.5, 72.9, 71.3, 55.8, 54.4, 52.8, 52.7, 31.7, 15.6. **ESI-MS** *m/z* (rel int): (pos) 318.9 ([M+Na]$^+$, 100), 335.1 ([M+K]$^+$, 10); (neg) 331.0 ([M+Cl]$^-$, 100), 295.2 ([M–H]$^-$, 70).



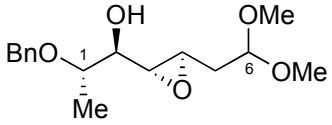
(+)-(*R*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*R*-*anti*-13a). In a 100 mL roundbottom flask with 4 Å molecular sieves, CH_2Cl_2 (20 mL), D-diethyl tartrate (968 mg, 4.7 mmol, 1.0 equiv), and Ti(O*i*-Pr)$_4$ (1.38 mL, 4.7 mmol, 1.0 equiv) were added and

cooled to –20 ˚C. The resulting mixture was stirred for 15 min at –20 ˚C, then *tert*-butyl hydroperoxide (5.5 M in decane, 1.71 mL, 9.4 mmol, 2.0 equiv) was added dropwise. The mixture was stirred for 15 min, then a solution of *E*-allylic alcohol ***S*-11a** (1.27 g, 4.7 mmol) in CH_2Cl_2 (30 mL) was added slowly. The resulting mixture was stirred for 1 h at –20 °C, then stored in a –20 ˚C freezer for 2 d. After this period, a mixture of 3 N NaOH (15 mL) and brine (15 mL) was added and the resulting mixture was stirred at 0 ˚C for 1 h. The layers were separated and the aq layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated by rotary evaporation. Purification by silica flash chromatography (2:1 hexanes/EtOAc) yielded epoxyol **2*R*-*anti*-13a** as a light yellow oil (1.33 g, 99%, 94:6 dr).

TLC: R_f 0.63 (1:2 × 2 hexanes/EtOAc). $[\alpha]_D^{24}$: +14.8° (*c* 1.1, $CHCl_3$). **IR** (NaCl, film): 3447 (O–H st), 2933, 2832, 1496, 1453, 1364, 1243, 1193, 1122, 1059, 887, 819, 740. **^{1}H-NMR** (400 MHz): δ 7.38–7.28 (m, 5H), 4.58 (s, 2H), 4.54 (m, 1H), 3.80 (m, 1H), 3.64 (dd, 1H, *J* = 9.7, 3.9), 3.58 (dd, 1H, *J* = 9.7, 6.0), 3.36 (s, 3H), 3.33 (s, 3H), 3.08 (m, 1H), 2.88 (dd, 1H, *J* = 4.8, 2.2), 2.29 (br s, 1H), 1.95 (m, 1H), 1.78 (m, 1H). **^{13}C-NMR** (125 MHz): δ 137.7, 128.5–127.8 (Ar), 102.3, 73.6, 71.3, 69.4, 57.8, 53.5, 53.0, 52.6, 35.4. **ESI-MS** *m/z* (rel int): (pos) 304.9 ($[M+Na]^+$, 100); (neg) 281.1 ($[M–H]^–$, 18), 317.0 ($[M+Cl]^–$, 100).

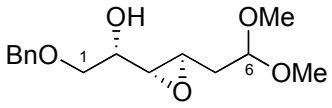


(–)-(*S*)-2-(Benzyloxy)-1-[(2*S*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*S*-*anti*-13a). Prepared from *E*-allylic alcohol ***R*-11a** using L-diethyl tartrate as above. Light yellow oil (1.07 g, 91%, 94:6 dr). $[\alpha]_D^{24}$: –13.4° (*c* 1.1, $CHCl_3$).



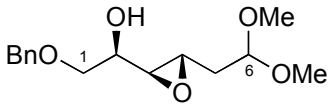
(+)-(1*R*,2*S*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*anti*,*anti*-13b). Prepared from *E*-allylic alcohol ***anti*-11b** essentially as above with storage in a –4 ˚C refrigerator for 3 d. Clear oil (73 mg, 99%, 94:6 dr).

TLC: R_f 0.40 (2:1 hexanes/EtOAc twice). $[\alpha]_D^{21}$: +31.1° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3437 (O–H st), 2934, 1745, 1453, 1376, 1193, 1122, 1064, 893. **^{1}H-NMR** (400 MHz): δ 7.40–7.22 (m, 5H), 4.69 (d, 1H, *J* = 11.5), 4.55 (t, 1H, *J* = 6.3), 4.51 (d, 1H, *J* = 11.5), 3.68 (m, 1H), 3.39 (m, 1H), 3.37 (s, 3H), 3.34 (s, 3H), 3.08 (m, 1H), 2.83 (dd, 1H, *J* = 5.5, 2.2), 2.38 (d, 1H, *J* = 4.4), 2.01 (m, 1H), 1.74 (m, 1H), 1.28 (d, 3H, *J* = 6.3). **^{13}C-NMR** (100 MHz): δ 138.2, 128.5, 128.6, 127.8, 102.4, 72.3, 71.2, 57.9, 53.5, 53.1, 53.0, 35.5, 15.5. **ESI-MS** *m/z* (rel int): (pos) 319.2 ($[M+Na]^+$, 100); (neg) 331.3 ($[M+Cl]^–$, 90).

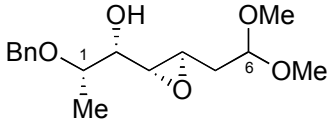


(+)-(*S*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*S*-*syn*-13a). Prepared by Mitsunobu inversion of epoxyol **2*R*-*anti*-13a** as described for epoxyol **2*S*-*anti*-12a** above. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded epoxyol **2*S*-*syn*-13a** (153.5 mg, 100%, 92:8 dr) as a light yellow oil.

TLC: R_f 0.63 (1:2 hexanes/EtOAc, double elution). $[\alpha]_D^{26}$: +28.5° (*c* 1.2, $CHCl_3$). **IR** (NaCl, film): 3436 (O–H st), 2932, 1729, 1453, 1364, 1193, 1122, 1071, 889, 740. **^{1}H-NMR** (400 MHz): δ 7.38–7.28 (m, 5H), 4.58 (s, 2H), 4.54 (m, 1H), 3.79 (m, 1H), 3.58 (m, 2H), 3.36 (s, 3H), 3.33 (s, 3H), 3.07 (m, 1H), 2.92 (m, 1H), 2.23 (d, 1H, *J* = 6.3), 1.92 (m, 1H), 1.79 (m, 1H). **^{13}C-NMR** (125 MHz): δ 138.2, 128.8, 128.2, 128.1, 102.7, 73.9, 72.0, 69.6, 58.9, 53.9, 53.4, 52.3, 35.7. **ESI-MS** *m/z* (rel int): (pos) 283.1 ($[M+H]^+$, 6), 305.1 ($[M+Na]^+$, 100), 321.1 ($[M+K]^+$, 29); (neg) 280.9 ($[M–H]^-$, 4), 316.8 ($[M+Cl]^-$, 100).



(–)-(*R*)-2-(Benzyloxy)-1-[(2*S*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*R*-*syn*-13a). Prepared by Mitsunobu inversion of epoxyol **2*S*-*anti*-13a** as described for epoxyol **2*S*-*anti*-12a** above. Light yellow oil (147.4 mg, 98%, 93:7 dr). $[\alpha]_D^{26}$: –27.4° (*c* 1.1, $CHCl_3$).



(+)-(1*S*,2*S*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*syn*,*syn*-13b). Prepared by *m*-CPBA epoxidation of ***syn*-11b** as described for epoxyol **2*R*-*syn*-12a** above. Clear oil (72.6 mg, 87%, 77:23 dr).

TLC: R_f 0.30 (1:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +40.0° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3435 (O–H st), 2933, 2832, 1718, 1496, 1453, 1373, 1244, 1192, 1121, 1070, 892, 819, 739. **^{1}H-NMR** (400 MHz): δ 7.37–7.21 (m, 5H), 4.67 (d, 1H, *J* = 11.7), 4.55 (dd, 1H, *J* = 6.5, 4.9), 4.52 (d, 1H, *J* = 11.7), 3.63 (m, 1H), 3.52 (m, 1H), 3.36 (s, 3H), 3.33 (s, 3H), 3.07 (m, 1H), 3.03 (m 1H), 1.96 (ddd, 1H, *J* = 14.2, 6.5, 4.3), 1.78 (ddd, 1H, *J* = 14.2, 6.9, 4.9), 1.29 (d, 1H, *J* = 6.3). **^{13}C-NMR** (125 MHz): δ 138.3, 128.4, 127.7, 102.3, 76.5, 73.0, 71.1, 58.1, 53.5, 52.9, 52.5, 35.3, 15.6. **ESI-MS** *m/z* (rel int): (pos) 318.9 ($[M+Na]^+$, 100), 335.2 ($[M+K]^+$, 24); (neg) 331.3 ($[M+Cl]^-$, 100), 295.3 ($[M–H]^-$, 48).

F. SYNTHESIS OF α,β-ENONES (17,18)

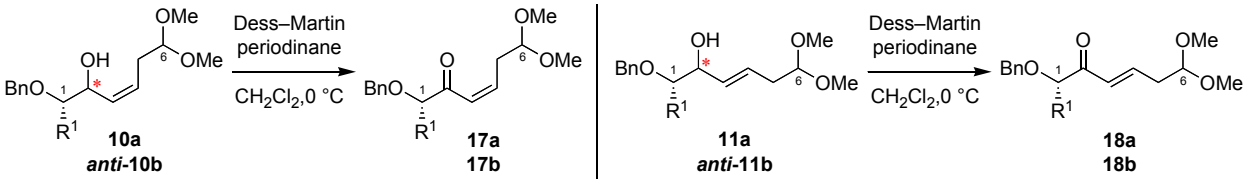
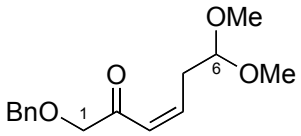
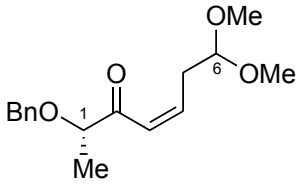


Figure S5. Synthesis of enones 17 and 18. Enones **17** and **18** were prepared by oxidation of 2*S*-allylic alcohols **10a**, ***anti*-10b**, **11a**, and ***anti*-11b** using Dess–Martin periodinane.[15]



(*Z*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-one (17a). In a 10 mL roundbottom flask, Dess–Martin periodinane (Aldrich, 39.7 mg, 93.5 μmmol, 1.5 equiv) was dissolved in anhyd CH_2Cl_2 (0.6 mL) and cooled to 0 °C. A solution of *Z*-allylic alcohol ***S*-10a** (16.6 mg, 62.3 μmol, 1.0 equiv) in anhyd CH_2Cl_2 (2 mL) was added dropwise via syringe. The mixture was stirred at 0 °C for 30 min, then rt for 1 h. Satd aq $NaHCO_3$ and 10% aq $Na_2S_2O_3$ were added at 0 °C and the mixture was warmed to rt and stirred for 15 min. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded *cis*-enone **17a** (15.3 mg, 93%) as a light yellow oil.

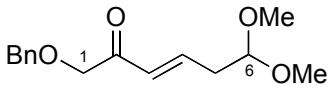
TLC: R_f 0.59 (1:2 hexanes/EtOAc). **IR** (NaCl, film): 2932, 2832, 1695 (C=O st), 1618, 1451, 1424, 1363, 1189, 1121, 1065, 967, 826, 742. **^{1}H-NMR** (400 MHz): δ 7.37–7.27 (m, 5H), 6.41 (dt, 1H, J = 11.5, 1.5), 6.26 (dt, 1H, J = 11.5, 7.1), 4.60 (s, 2H), 4.47 (t, 1H, J = 5.5), 4.12 (s, 2H), 3.35 (s, 6H), 3.03 (ddd, 2H, J = 7.0, 5.5, 1.6). **^{13}C-NMR** (100 MHz): δ 198.8, 144.6, 137.7, 128.9, 128.4, 128.3, 124.4, 104.1, 76.1, 73.7, 53.7, 33.8. **ESI-MS** *m/z* (rel int): (pos) 287.0 ($[M+Na]^+$, 100).



(–)-(*S*,*Z*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-one (17b). Prepared from *Z*-allylic alcohol ***anti*-10b** as above. Clear oil (22 mg, 100%).

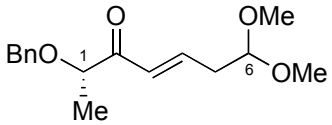
[15] (a) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991,** *113*, 7277–7287. (b) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.

TLC: R_f 0.60 (2:1 hexanes/EtOAc). $[\alpha]_D^{21}$: –19.3° (*c* 0.7, $CHCl_3$). **IR** (ZnSe, film): 2934, 1692 (C=O st), 1615, 1453, 1368, 1191, 1120, 1059, 968, 829. **^{1}H-NMR** (400 MHz): δ 7.38–7.25 (m, 5H), 6.62 (td, 1H, *J* = 11.6, 1.9), 6.32 (td, 1H, *J* = 11.6, 7.1), 4.58 (d, 1H, *J* = 11.6), 4.48 (t, 1H. *J* = 5.6), 4.44 (d, 1H, *J* = 11.6), 3.95 (q, 1H, *J* = 6.9), 3.35 (s, 3H), 3.34 (s, 3H), 3.06–3.01 (m, 2H), 1.35 (d, 3H, *J* = 6.9). **^{13}C-NMR** (125 MHz): δ 203.0, 144.9, 137.6, 128.5, 127.9, 127.8, 123.4, 103.6, 81.0, 71.8, 53.3, 53.2, 33.3, 17.7. **ESI-MS** *m/z* (rel int): (pos) 301.0 ($[M+Na]^+$, 100).



(*E*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-one (18a). Prepared from *E*-allylic alcohol ***S*-11a** as above. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded *trans*-enone **18a** (32.0 mg, 100%) as a light yellow oil.

TLC: R_f 0.61 (1:2 hexanes/EtOAc). **IR** (NaCl, film): 3030, 2916, 2832, 1710, 1693 (C=O st), 1626, 1496, 1454, 1364, 1326, 1262, 1192, 1119, 1062, 972, 738. **^{1}H-NMR** (400 MHz): δ 7.37–7.28 (m, 5H), 6.90 (dt, 1H, *J* = 16.0, 7.2), 6.37 (d, 1H, *J* = 16.0), 4.61 (s, 2H), 4.47 (t, 1H, *J* = 5.6), 4.23 (s, 2H), 3.34 (s, 6H), 2.54 (m, 2H). **^{13}C-NMR** (100 MHz): δ 197.0, 142.9, 137.7, 128.9, 128.8, 128.4, 103.2, 74.4, 73.7, 53.6, 36.7. **ESI-MS** *m/z* (rel int): (pos) 287.2 ($[M+Na]^+$, 100); (neg) 263.1 ($[M–H]^-$, 4), 299.2 ($[M+Cl]^-$, 87).



(–)-(*S*,*E*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-one (18b). Prepared from *E*-allylic alcohol ***syn*-11b** as above. Clear oil (24 mg, 96%).

TLC: R_f 0.65 (2:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –29.8° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 2927, 1696 (C=O st), 1627, 1454, 1368, 1326, 1263, 1120, 1062, 972. **^{1}H-NMR** (400 MHz): δ 7.41–7.24 (m, 5H), 6.99 (td, 1H, *J* = 15.7, 7.2), 6.60 (td, 1H, *J* = 15.7, 1.3), 4.57 (d, 1H, *J* = 11.6), 4.48 (t, 1H, *J* = 5.6), 4.43 (d, 1H, *J* = 11.6), 4.07 (q, 1H, *J* = 6.9), 3.34 (s, 6H), 2.59–2.53 (m, 2H), 1.37 (d, 3H, *J* = 6.9). **^{13}C-NMR** (100 MHz): δ 201.0, 143.2, 137.6, 128.5, 127.9, 127.8, 126.8, 102.9, 80.0, 71.8, 53.1, 53.1, 36.4, 17.9. **ESI-MS** *m/z* (rel int): (pos) 279.1 ($[M+H]^+$, 50), 301.1 ($[M+Na]^+$, 100).

G. SYNTHESIS OF α,β-EPOXYKETONES (19,20)

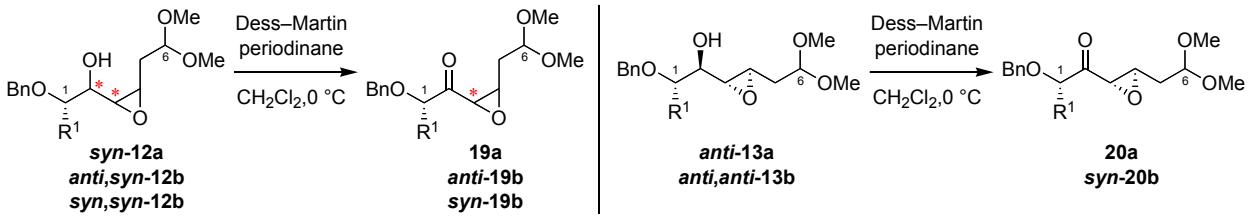
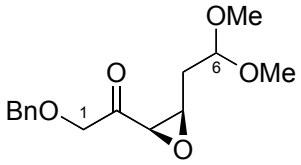
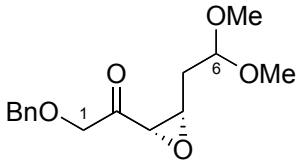


Figure S6. Synthesis of enones 19 and 20. Enones **19** and **20** were synthesized by Dess–Martin oxidation[15] of 2*R*-epoxyols **2*R*-*syn*-12a** and **2*R*-*anti*-13a** in the R^1 = H series and 2*R*-epoxyols ***anti*,*syn*-12b** and ***anti*,*anti*-13b** and 2*S*-epoxyol ***syn*,*syn*-12b** in the R^1 = Me series.

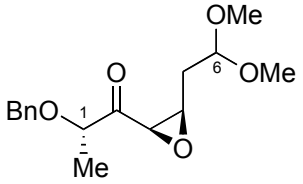


(+)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanone (3*R*-19a). In a 10 mL roundbottom flask, **2*R*-*syn*-12a** (20.0 mg, 70.8 μmol, 1.0 equiv) was dissolved in anhyd CH_2Cl_2 (2.5 mL) and cooled to 0 °C. Dess–Martin periodinane (Aldrich, 45.1 mg, 106 μmol, 1.5 equiv) was added in one portion. The mixture was stirred at 0 °C for 30 min, then rt for 8 h. Satd aq $NaHCO_3$ and 10% aq $Na_2S_2O_3$ were added with Et_2O (2.5 mL) at 0 °C and the mixture was warmed to rt and stirred for 15 min. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded epoxyketone **3*R*-19a** (16.8 mg, 85%, 90:10 *cis*/*trans*) as a light yellow oil.

TLC: R_f 0.59 (1:2 hexanes/EtOAc, triple elution). $[\alpha]_D^{25}$: +16.8° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3436, 2934, 2834, 2252, 1729 (C=O st), 1449, 1368, 1247, 1193, 1121, 1068, 911, 740. **^{1}H-NMR** (400 MHz): δ 7.41–7.30 (m, 5H), 4.63 (d, 2H, *J* = 2.4), 4.48 (dd, 1H, *J* = 6.4, 4.1), 4.27 (d, 1H, *J* = 17.2), 4.20 (d, 1H, *J* = 17.2), 3.87 (d, 1H, *J* = 4.8), 3.38 (m, 2H), 3.33 (s, 3H), 3.28 (s, 3H), 1.93 (m, 1H), 1.76 (m, 1H). **^{13}C-NMR** (100 MHz): δ 203.2, 137.3, 129.0, 128.6, 128.4, 102.8, 74.9, 74.0, 56.3, 55.7, 54.7, 53.6, 31.3. **ESI-MS** *m/z* (rel int): (pos) 303.2 ($[M+Na]^+$, 100); (neg) 279.2 ($[M–H]^-$, 100).

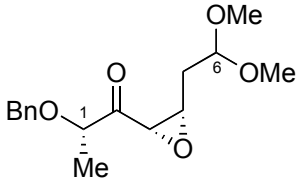


(–)-2-(Benzyloxy)-1-((2*S*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl)ethanone (3*S*-19a). Prepared from epoxyol **2*S*-*syn*-12a** as above. Light yellow oil (25.5 mg, 98%, 88:12 *cis*/*trans*). $[\alpha]_D^{25}$: –16.6° (*c* 1.0, $CHCl_3$).



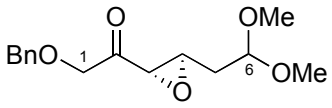
(+)-(*S*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-one (*anti*-19b). Prepared from epoxyol ***anti*,*syn*-12b** as above. Clear oil (47 mg, 98%).

TLC: R_f 0.50 (2:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +37.7° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 2936, 1725 (C=O st), 1453, 1370, 1191, 1119, 1067. **^{1}H-NMR** (400 MHz): δ 7.39–7.24 (m, 5H), 4.62 (d, 1H, *J* = 11.7), 4.55 (d, 1H, *J* = 11.7), 4.51 (dd, 1H, *J* = 6.5, 4.3), 4.12 (q, 1H, *J* = 6.9), 4.07 (m, 1H), 3.42 (m, 1H), 3.35 (s, 3H), 3.30 (s, 3H), 1.85 (ddd, 1H, *J* = 14.4, 6.8, 4.3), 1.77 (ddd, 1H, *J* = 14.4, 6.5, 5.3), 1.45 (d, 3H, *J* = 6.9). **^{13}C-NMR** (125 MHz): δ 206.5, 137.4, 128.6, 128.1, 127.7, 102.5, 80.0, 71.9, 55.6, 55.2, 54.2, 53.2, 30.8, 17.1. **ESI-MS** *m/z* (rel int): (pos) 317.1 ($[M+Na]^+$, 100); (neg) 329.2 ($[M+Cl]^-$, 90), 293.2 ($[M–H]^-$, 100).



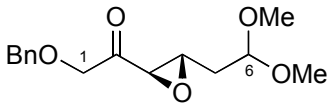
(–)-(*S*)-2-(Benzyloxy)-1-[(2*S*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-one (*syn*-19b). Prepared from epoxyol ***syn*,*syn*-12b** as above. Clear oil (46 mg, 92%).

TLC: R_f 0.50 (2:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –22.6° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 2935, 2833, 1725 (C=O st), 1496, 1452, 1370, 1192, 1120, 1069, 975, 886, 749. **^{1}H-NMR** (400 MHz): δ 7.40–7.24 (m, 5H), 4.64 (d, 1H, *J* = 11.8), 4.60 (d, 1H, *J* = 11.8), 4.52 (dd, 1H, 6.3, 5.1), 4.12 (q, 1H, *J* = 6.9), 4.06 (m, 1H), 3.41 (m, 1H), 3.35 (s, 3H), 3.31 (s, 3H), 1.87–1.72 (m, 2H), 1.37 (d, 3H, *J* = 6.9). **^{13}C-NMR** (125 MHz): δ 206.7, 137.1, 128.6, 128.1, 127.9, 102.0, 79.5, 72.1, 56.6, 55.4, 53.9, 53.0, 35.6, 16.8. **ESI-MS** *m/z* (rel int): (pos) 317.0 ($[M+Na]^+$, 100); (neg) 329.0 ($[M+Cl]^-$, 90).

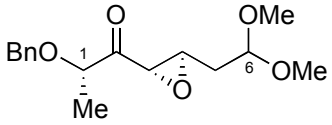


(–)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanone (3*S*-20a). Prepared from epoxyol **2*R*-*anti*-13a** as above. Light yellow oil (174.5 mg, 88%, ≥98:2 *trans*/*cis*).

TLC: R_f 0.59 (1:2 hexanes/EtOAc, triple elution). $[\alpha]_D^{25}$: –4.2° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 2930, 2838, 2252, 1728 (C=O st), 1447, 1369, 1193, 1121, 1069, 909, 733. **^{1}H-NMR** (400 MHz): δ 7.40–7.30 (m, 5H), 4.60 (s, 2H), 4.54 (m, 1H), 4.24 (d, 1H, *J* = 17.9), 4.12 (d, 1H, *J* = 17.9), 3.45 (d, 1H, *J* = 2.0), 3.36 (s, 3H), 3.33 (s, 3H), 3.16 (m, 1H), 1.99 (m, 1H), 1.82 (m, 1H). **^{13}C-NMR** (100 MHz): δ 203.8, 137.3, 129.0, 128.6, 128.4, 102.3, 73.9, 72.6, 58.0, 56.1, 54.2, 53.5, 36.0. **ESI-MS** *m/z* (rel int): (pos) 303.2 ($[M+Na]^+$, 100); (neg) 279.2 ($[M–H]^–$, 100).



(+)-2-(Benzyloxy)-1-[(2*R*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanone (3*R*-20a). Prepared from epoxyol **2*S*-*anti*-13a** as above. Light yellow oil (219.3 mg, 89%, ≥98:2 *trans*/*cis*). $[\alpha]_D^{24}$: +4.8° (*c* 1.0, $CHCl_3$).



(–)-(*S*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-one (*syn*-20b). Prepared from epoxyol ***anti*,*anti*-13b** as above. Clear oil (24 mg, 95%).

TLC: R_f 0.50 (2:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –31.7° (*c* 1.1, $CHCl_3$). **IR** (ZnSe, film): 2927, 1725 (C=O st), 1453, 1370, 1191, 1118, 1061, 885. **^{1}H-NMR** (400 MHz): δ 7.42–7.27 (m, 5H), 4.61 (d, 1H, *J* = 11.6), 4.57 (d, 1H, *J* = 11.6), 4.54 (t, 1H, *J* = 5.8), 4.14 (q, 1H, *J* = 6.8), 3.77 (d, 1H, *J* = 1.9), 3.35 (s, 3H), 3.32 (s, 3H), 3.12 (dd, 1H, *J* = 5.7, 1.9), 1.96–1.89 (m, 2H), 1.39 (d, 3H, *J* = 6.8). **^{13}C-NMR** (100 MHz): δ 206.7, 137.1, 128.6, 128.2, 128.0, 102.0, 79.5, 72.1, 56.6, 55.4, 53.8, 53.0, 35.6, 16.8. **ESI-MS** *m/z* (rel int): (pos) 317.1 ($[M+Na]^+$, 100); (neg) 329.2 ($[M+Cl]^–$, 90), 293.1 ($[M–H]^–$, 100).

H. SYNTHESIS OF β-HYDROXYKETONES (21)

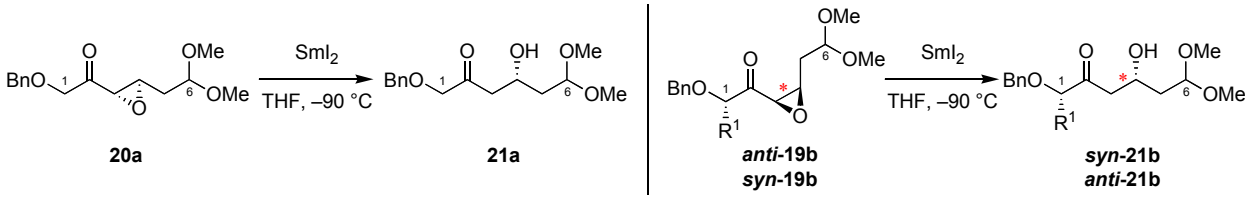
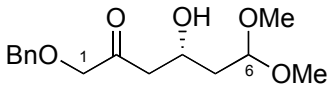
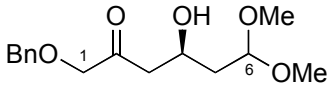


Figure S7. Synthesis of β-hydroxyketones 21. β-Hydroxyketones **21** were synthesized by SmI_2-mediated reductive epoxide opening [16] of *trans*-epoxyketones **20a** in the R^1 = H series and *cis*-epoxyketones ***anti*-19b** and ***syn*-19b** in the R^2 = Me series. The other available epoxyketone starting materials provide degenerate products.



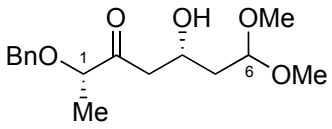
(–)-(*R*)-1-(Benzyloxy)-4-hydroxy-6,6-dimethoxyhexan-2-one (*R*-21a). In a 10 mL round-bottom flask, epoxyketone **3*S*-20a** (30.0 mg, 107 μmol, 1.0 equiv) was dissolved in anhyd THF (2 mL) and cooled to –90 °C. Freshly prepared[17] SmI_2 (0.1 M in THF, 4.0 mL, 400 μmol, 3.7 equiv) was added dropwise via syringe. The mixture was stirred at –90 °C for 20 min, and –78 °C for 1 h. Satd aq NH_4Cl_4 was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (2:1→1.5:1→1:1 hexanes/EtOAc) yielded β-hydroxyketone ***R*-21a** (25.9 mg, 86%) as a light yellow oil.

TLC: R_f 0.36 (1:2 hexanes/EtOAc). $[\alpha]_D^{25}$: –13.2° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film/KBr, pellet): 3479 (O–H st), 2932, 2834, 2249, 1722 (C=O st), 1495, 1452, 1387, 1327, 1260, 1192, 1122, 1059, 962, 911, 818, 736. **^{1}H-NMR** (400 MHz): δ 7.40–7.29 (m, 5H), 4.60 (m, 3H), 4.26 (m, 1H), 4.09 (s, 2H), 3.36 (s, 3H), 3.35 (s, 3H), 3.27 (d, 1H, *J* = 2.8), 2.63 (m, 2H), 1.77 (m, 2H). **^{13}C-NMR** (100 MHz): δ 208.9, 137.5, 128.9, 128.5, 128.3, 103.5, 75.8, 73.8, 64.8, 54.1, 53.8, 46.3, 39.6. **ESI-MS** *m/z* (rel int): (pos) 305.2 ($[M+Na]^+$, 100); (neg) 317.1 ($[M+Cl]^-$, 21), 281.3 ($[M–H]^-$, 100).



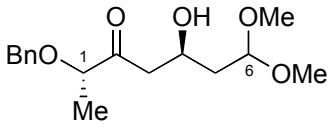
(+)-(*S*)-1-(Benzyloxy)-4-hydroxy-6,6-dimethoxyhexan-2-one (*S*-21a). Prepared from epoxy-ketone **3*R*-20a** essentially as above. Light yellow oil (107.9 mg, 54% yield not optimized). $[\alpha]_D^{25}$: +13.0° (*c* 1.0, $CHCl_3$).

[16] Molander, G. A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 2596–2599.
[17] Girard P.; Namy J. L.; Kagan H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693–2698.



(–)-(2*S*,5*R*)-2-(Benzyloxy)-5-hydroxy-7,7-dimethoxyheptan-3-one (*syn*-21b). Prepared from epoxyketone ***anti*-19b** as above. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded β-hydroxyketone ***syn*-21b** (29 mg, 65%; 25% of starting material was recovered) as a clear oil. (Alternatively, ***syn*-21b** could be prepared from epoxyketone ***syn*-20b** as above (11 mg, 54%).)

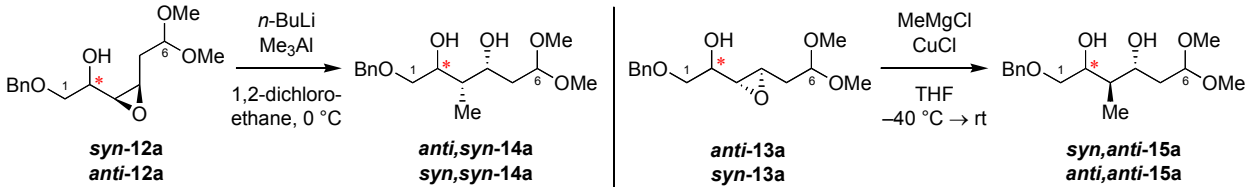
TLC: R_f 0.40 (1:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –37.1° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3431 (O–H st), 2938, 1717 (C=O st), 1455, 1373, 1315, 1193, 1124, 1053, 913. **^{1}H-NMR** (400 MHz): δ 7.41–7.26 (m, 5H), 4.60 (m, 1H), 4.59 (d, 1H, *J* = 11.7), 4.51 (d, 1H, *J* = 11.7), 4.25 (m, 1H), 3.95 (q, 1H, *J* = 6.7), 3.36 (s, 6H), 3.25 (d, 1H, *J* = 4.2), 2.78–2.74 (m, 2H), 1.81 (ddd, 1H, *J* = 14.1, 8.8, 5.2), 1.77 (ddd, 1H, *J* = 14.1, 5.9, 3.6), 1.34 (d, 3H, *J* = 6.7). **^{13}C-NMR** (125 MHz): δ 213.0, 137.4, 128.5, 128.0, 127.8, 103.1, 80.6, 71.9, 64.4, 53.6, 53.5, 44.3, 39.2, 17.1. **ESI-MS** *m/z* (rel int): (pos) 319.1 ($[M+Na]^+$, 100); (neg) 331.0 ($[M+Cl]^-$, 90).



(–)-(2*S*,5*S*)-2-(Benzyloxy)-5-hydroxy-7,7-dimethoxyheptan-3-one (*anti*-21b). Prepared from epoxyketone ***syn*-19b** as above. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded β-hydroxyketone ***anti*-21b** (67 mg, 93%) as a clear oil.

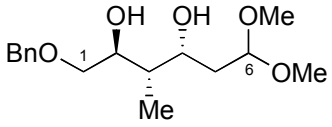
TLC: R_f 0.40 (1:1 hexanes/EtOAc). $[\alpha]_D^{20}$: –14.7° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3478 (O–H st), 2934, 2832, 1716 (C=O st), 1469, 1453, 1371, 1309, 1192, 1124, 1058, 965, 910, 820, 750. **^{1}H-NMR** (400 MHz): δ 7.38–7.22 (m, 5H), 4.59 (m, 1H), 4.55 (d, 1H, *J* = 11.7), 4.51 (d, 1H. *J* = 11.7), 4.23 (m, 1H), 3.95 (q, 1H, *J* = 6.9), 3.36 (s, 6H), 3.24 (d, 1H, *J* = 3.0), 2.79 (dd, 1H, *J* = 17.7, 8.4), 2.66 (dd, 1H, *J* = 17.7, 3.9), 1.81 (ddd, 1H, *J* = 14.1, 8.8, 5.2), 1.73 (ddd, 1H, *J* = 14.1, 5.8, 3.6), 1.34 (d, 3H, *J* = 6.9). **^{13}C-NMR** (125 MHz): δ 213.0, 137.5, 128.5, 128.0, 127.8, 103.1, 80.7, 71.9, 64.5, 64.4, 53.6, 53.5, 44.3, 39.2, 17.1. **ESI-MS** *m/z* (rel int): (pos) 318.9 ($[M+Na]^+$, 100); (neg) 331.0 ($[M+Cl]^-$, 90).

I. SYNTHESIS OF 2-METHYL 1,3-DIOLS (14a,15a) AND STEREOCHEMICAL ASSIGNMENTS



***syn*-12a** ***anti*-12a** ***anti,syn*-14a** ***syn,syn*-14a** ***anti*-13a** ***syn*-13a** ***syn,anti*-15a** ***anti,anti*-15a**

Figure S8. Synthesis of 2-methyl-1,3-diols 14a and 15a. In the R^1 = H series, 1,3-diols **14a** and **15a** could be obtained directly from epoxyols **12a** and **13a** in good yields using *n*-BuLi/Me_3Al [18] or MeMgCl/CuCl[19] respectively. Importantly, access to both enantiomeric series provided access to all eight stereoisomeric products **14a** and **15a**. Analogous epoxide openings in the R^1 = Me series afforded only 1,2-diol products. Stereochemical assignments were confirmed by conversion of the 1,3-diols to the corresponding acetonides, determination of *syn* and *anti* diol relationships using Rychnovsky's ^{13}C-NMR method, [20] and determination of *C*3-methyl stereochemistry via NOESY analysis. The resulting stereochemical assignments were consistent with the *syn* and *anti* epoxyol assignments made for **12a** and **13a** in SECTION E above by analogy to literature precedents.

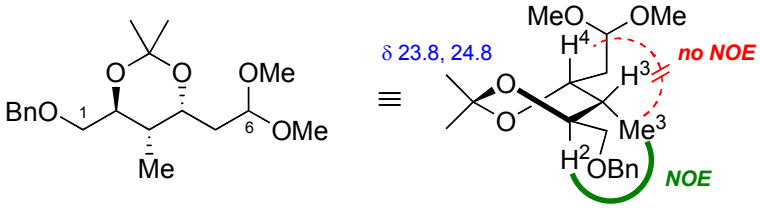


(+)-(2*S*,3*S*,4*R*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*S*-*anti*,*syn*-14a). *Note: For best results, new bottles of n-BuLi, Me_3Al, and 1,2-dichloroethane should be used. In the example below, the addition reaction was carried out in four smaller batches that were combined prior to oxidative cleavage and purification. However, we have not yet assessed whether or not this protocol is necessary for optimal yields compared to carrying out the addition reaction in a single larger batch.* In 4 × 5 mL roundbottom flasks, *cis*-epoxyol **2*R*-*syn*-12a** (4 × 4 mg, 14.2 μmol, 1.0 equiv) was azeotropically dried twice with toluene then dissolved in anhyd 1,2-dichloroethane (4 × 0.5 mL) (Aldrich SureSeal bottle) and cooled to 0 °C. *n*-BuLi (1.6 M in hexanes, 4 × 44.3 μL, 70.8 μmol, 5.0 equiv) was added dropwise via syringe. The mixture was stirred at 0 °C for 30 min, then Me_3Al (2 M in hexanes, 4 × 56.7 μL, 113 μmol, 8.0 equiv) was added dropwise and the mixture was stirred at 0 °C for 30 min, then warmed to rt for 2 h. Satd aq NH_4Cl was added at 0 °C and the mixture was warmed to rt. The four reaction mixtures were combined, the layers were separated, and the aq layer was extracted with Et_2O. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. The residue was dissolved in 60% aq MeCN (2 mL) followed by slow addition of $NaIO_4$ (20 mg, 93.5 μmol, 1.6 equiv) at 0 °C. After stirring for 1 h at rt, the MeCN was removed by rotary evaporation and the aq layer was extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and concentrated by rotary evaporation. Purification by silica flash

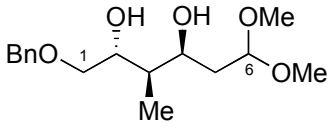
[18] Sasaki, M.; Tanino, K.; Miyashita, M. *Org. Lett.* **2001**, *3*, 1765–1767.
[19] Tius, M. A.; Fauq, A. H. *J. Org. Chem.* **1983**, *48*, 4131–4132.
[20] (a) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990,** *31*, 945–948. (b) Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993,** *58*, 3511–3515.

chromatography (3:1→2.5:1 hexanes/EtOAc) yielded pure 1,3-diol **2*S*-*anti*,*syn*-14a** (12.3 mg, 73%, ≥98:2 dr) as a light yellow oil.

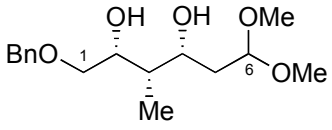
TLC: R_f 0.46 (1:2 hexanes/EtOAc, double elution). $[\alpha]_D^{24}$: +1.7° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3440 (O–H st), 2929, 2246, 1454, 1383, 1192, 1116, 1053, 912, 818, 735. **^{1}H-NMR** (400 MHz): δ 7.39–7.27 (m, 5H), 4.59 (t, 1H, *J* = 5.5), 4.57 (s, 2H), 4.07 (m, 1H), 3.81 (m, 1H), 3.60 (dd, 1H, *J* = 9.6, 3.8), 3.49 (dd, 1H, *J* = 9.6, 7.0), 3.38 (s, 3H), 3.36 (s, 3H), 3.24 (d, 1H, *J* = 3.9), 1.88 (m, 1H), 1.76 (m, 1H), 1.62 (m, 1H), 0.90 (d, 1H, *J* = 7.1). **^{13}C-NMR** (100 MHz): δ 138.4, 128.8, 128.2, 104.6, 73.9, 73.8, 73.2, 69.8, 54.4, 53.5, 39.9, 36.8, 11.6. **ESI-MS** *m/z* (rel int): (pos) 321.3 ($[M+Na]^+$, 100); (neg) 297.4 ($[M–H]^-$, 100).



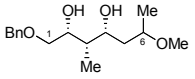
The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of **2*S*-*anti*,*syn*-14a** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, PPTS, CH_2Cl_2, rt, 30 min; 68%). ^{13}C-NMR resonances were observed at 23.8 and 24.8 ppm (and 100.8 ppm), indicative of an *anti*-diol-derived acetonide in a twist-boat conformation.[20] ^{1}H-NMR peaks were then assigned by COSY analysis. NOESY analysis indicated interactions between Me^3 (0.84 ppm) and H^2 (3.51 ppm), but no interaction between Me^3 and H^4 (4.01 ppm), consistent with the assigned relative configurations at *C*2, *C*3, and *C*4 of **2*S*-*anti*,*syn*-14a**.



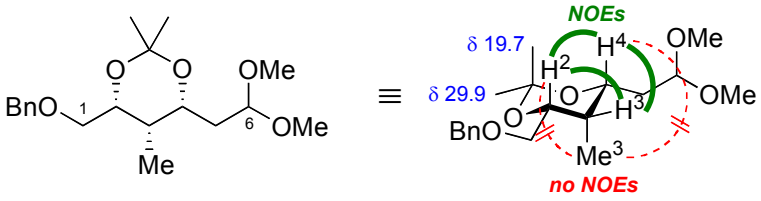
(–)-(2*R*,3*R*,4*S*)-1-(benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*R*-*anti*,*syn*-14a). Prepared from *cis*-epoxyol **2*S*-*syn*-12a** essentially as above. Light yellow oil (34.2 mg, 47% yield not optimized, ≥98:2 dr). $[\alpha]_D^{24}$: –2.1° (*c* 1.0, $CHCl_3$).



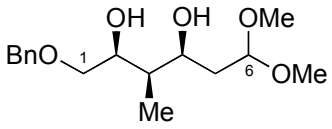
(–)-(2*R*,3*S*,4*R*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*R*-*syn*,*syn*-14a). Prepared from *cis*-epoxyol **2*S*-*anti*-12a** as above. Purification by silica flash chromatography (3:1→5:2 hexanes/EtOAc) yielded the 1,3-diol **2*R*-*syn*,*syn*-14a** (9.2 mg, 68%, ≥98:2 dr) as a light yellow oil containing an inseparable methyl ether impurity (8% by NMR):



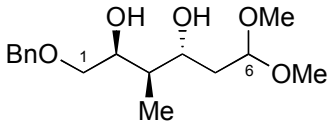
TLC: R_f 0.49 (1:2 hexanes/EtOAc, double elution). $[\alpha]_D^{25}$: –8.8° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3444 (O–H st), 2921, 1454, 1375, 1312, 1237, 1191, 1117, 1054, 913, 820, 738. **^{1}H-NMR** (400 MHz): δ 7.37–7.27 (m, 5H), 4.56 (m, 3H), 4.07 (m, 2H), 3.49 (m, 2H), 3.38 (s, 3H), 3.36 (s, 3H), 3.08 (d, 1H, *J* = 1.8), 1.90 (m, 1H), 1.64 (m, 2H), 0.93 (d, 3H, *J* = 7.1). **^{13}C-NMR** (100 MHz): δ 138.4, 128.9, 128.2, 104.7, 74.7, 73.8, 72.8, 72.4, 54.5, 53.6, 39.9, 37.9, 6.6. **ESI-MS** *m/z* (rel int): (pos) 321.4 ($[M+Na]^+$, 100), 337.2 ($[M+K]^+$, 5); (neg) 297.4 ($[M–H]^-$, 100).



The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of **2*R*-*syn*,*syn*-14a** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, PPTS, CH_2Cl_2, rt, 30 min; 65%). ^{13}C-NMR resonances were observed at 19.7 and 29.9 ppm (and 99.0 ppm), indicative of a *syn*-diol-derived acetonide in a chair conformation.[20] ^{1}H-NMR peaks were then assigned by COSY analysis. This allowed assignment of a small 2.3 Hz H^2–H^3 coupling constant (4.19, 1.48 ppm), consistent with an axial methyl substituent at *C*3 (the H^3–H^4 coupling constant could not be determined due to overlap). NOESY analysis indicated interactions between H^2 (4.19 ppm) and H^4 (4.06 ppm) (and also between H^3 and both H^2 and H^4) but no interactions between Me^3 (0.83 ppm) and either H^2 or H^4, consistent with the assigned relative configurations at *C*2, *C*3, and *C*4 of **2*R*-*syn*,*syn*-14a**.



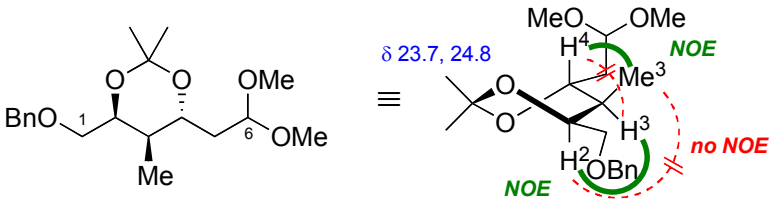
(+)-(2*S*,3*R*,4*S*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*S*-*syn*,*syn*-14a). Prepared from *cis*-epoxyol **2*R*-*anti*-12a** essentially as above. Light yellow oil (16.3 mg, 58% yield not optimized, ≥98:2 dr). $[\alpha]_D^{25}$: +7.8° (*c* 1.0, $CHCl_3$).



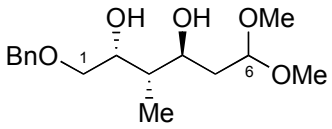
(–)-(2*S*,3*R*,4*R*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*S*-*syn*,*anti*-15a). In a 10 mL roundbottom flask, CuCl (157.8 mg, 1.59 mmol, 6.0 equiv) was suspended in anhyd 1:1 THF/Et_2O (4 mL) and cooled to –20 °C. MeMgCl (3 M in THF, 1.06 mL, 3.19 mmol, 12.0 equiv) was added dropwise via syringe. The mixture was stirred at –20 °C for 30 min, then cooled to –40 °C. A solution of *trans*-epoxyol **2*R*-*anti*-13a** (75 mg, 0.266 mmol, 1.0 equiv) in

anhyd Et_2O (2 mL) was added dropwise via syringe. The mixture was stirred at –40 °C for 1.5 h, warmed to –20 °C for 1.5 h, 0 °C for 1 h, and rt for 20 min. A mixture of 2:1 satd aq NH_4Cl/30% aq NH_4OH was added at –40 °C and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. The residue was dissolved in 60% aq MeCN (7 mL) followed by slow addition of $NaIO_4$ (113.4 mg, 0.53 mmol, 2.0 equiv) at 0 °C. After stirring for 1 h at rt, the MeCN was removed by rotary evaporation and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4) and concentrated by rotary evaporation. Purification by silica flash chromatography (2:1→1:1→1:2 hexanes/EtOAc) yielded 1,3-diol **2*S*-*syn*,*anti*-15a** (53.6 mg, 68%, ≥98:2 dr) as a light yellow oil.

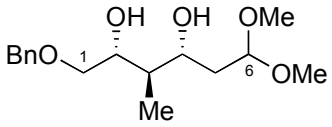
TLC: R_f 0.44 (1:2 hexanes/EtOAc, triple elution). $[\alpha]_D^{25}$: –2.1° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3444 (O–H st), 2927, 1495, 1454, 1385, 1247, 1192, 1112, 1055, 991, 912, 820, 738. **^{1}H-NMR** (400 MHz): δ 7.37–7.27 (m, 5H), 4.56 (m, 3H), 4.18 (m, 1H), 3.82 (m, 1H), 3.59 (d, 1H, *J* = 2.9), 3.54 (dd, 1H, *J* = 9.4, 7.6), 3.48 (dd, 1H, *J* = 9.5, 4.6), 3.39 (s, 3H), 3.36 (s, 3H), 3.17 (d, 1H, *J* = 2.9), 1.88 (m, 1H), 1.80 (m, 1H), 1.68 (m, 1H). **^{13}C-NMR** (100 MHz): δ 138.5, 128.8, 128.1, 104.6, 73.8, 72.9, 72.6, 71.4, 54.4, 53.5, 40.3, 38.2, 11.7. **ESI-MS** *m/z* (rel int): (pos) 321.4 ($[M+Na]^+$, 100); (neg) 297.2 ($[M–H]^-$, 100), 333.2 ($[M+Cl]^-$, 86).



The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of **2*S*-*syn*,*anti*-15a** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, PPTS, CH_2Cl_2, rt, 30 min; 85%). ^{13}C-NMR resonances were observed at 23.7 and 24.8 ppm (and 100.8 ppm), indicative of an *anti*-diol-derived acetonide in a twist-boat conformation.[20] ^{1}H-NMR peaks were then assigned by COSY analysis. This allowed assignment of a small 5.6 Hz H^2–H^3 coupling constant and a large 9.2 Hz H^3–H^4 coupling constant (1.72, 3.40 ppm), consistent with a *syn*-H^2,H^3 relationship and an *anti*-H^3,H^4 relationship. NOESY analysis indicated interactions between Me^3 (0.82 ppm) and H^4 (3.40 ppm) (and between H^2 at 4.12 ppm and H^3), but no interactions between Me^3 and H^2 (or between H^3 and H^4), consistent with the assigned relative configurations at *C*2, *C*3, and *C*4 of **2*S*-*syn*,*anti*-15a**.

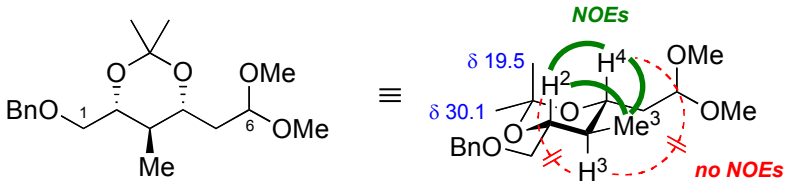


(+)-(2*R*,3*S*,4*S*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*R*-*syn*,*anti*-15a). Prepared from *trans*-epoxyol **2*S*-*anti*-13a** as above. Light yellow oil (54.2 mg, 69%, 98:2 dr). $[\alpha]_D^{25}$: +1.2° (*c* 1.0, $CHCl_3$).

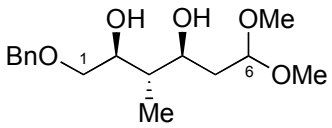


(–)-(2*R*,3*R*,4*R*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*R*-*anti*,*anti*-15a). Prepared from *trans*-epoxyol **2*S*-*syn*-13a** as above. Light yellow oil (54.2 mg, 69%, 94:6 dr).

TLC: R_f 0.38 (1:2 hexanes/EtOAc, triple elution). $[\alpha]_D^{25}$: –5.8° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3436 (O–H st), 2929, 1495, 1453, 1365, 1314, 1245, 1192, 1120, 1052, 967, 913, 814, 738. **^{1}H-NMR** (400 MHz): δ 7.37–7.28 (m, 5H), 4.57 (m, 3H), 3.86 (t, 1H, *J* = 8.3), 3.79 (m, 1H), 3.75 (s, 1H), 3.63 (dd, 1H, *J* = 9.6, 2.9), 3.47 (dd, 1H, *J* = 9.6, 7.0), 3.39 (s, 3H), 3.37 (s, 3H), 3.30 (s, 1H), 1.87 (m, 1H), 1.74 (m, 2H), 0.83 (d, 3H, *J* = 6.9). **^{13}C-NMR** (100 MHz): δ 138.4, 128.9, 128.2, 104.5, 74.5, 73.8, 73.2, 72.1, 54.4, 53.5, 41.6, 37.1, 12.8. **ESI-MS** *m/z* (rel int): (pos) 321.2 ($[M+Na]^+$, 100), 337.3 ($[M+K]^+$, 34); (neg) 297.4 ($[M–H]^-$, 100), 333.2 ($[M+Cl]^-$, 84).



The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of **2*R*-*anti*,*anti*-15a** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, PPTS, CH_2Cl_2, rt, 30 min; 82%). ^{13}C-NMR resonances were observed at 19.5 and 30.1 ppm (and 98.0 ppm), indicative of a *syn*-diol-derived acetonide in a chair conformation.[20] ^{1}H-NMR peaks were then assigned by COSY analysis. This allowed assignment of a large 10.4 Hz H^3–H^4 coupling constant (1.47, 3.59 ppm), consistent with a *trans*-diaxial relationship and an equatorial methyl substituent at *C*3 (the H^2–H^3 coupling constant could not be determined due to overlap). NOESY analysis indicated interactions between Me^3 (0.77 ppm) and H^2 (3.66 ppm), between Me^3 and H^4, and between H^2 and H^4 (but no interactions between H^3 and either H^2 or H^4), consistent with the assigned relative configurations at *C*2, *C*3, and *C*4 of **2*R*-*anti*,*anti*-15a**.



(+)-(2*S*,3*S*,4*S*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*S*-*anti*,*anti*-15a). Prepared from *trans*-epoxyol **2*R*-*syn*-13a** as above. Light yellow oil (41.1 mg, 52% yield not optimized due to material losses, 91:9 dr). $[\alpha]_D^{25}$: +3.3° (*c* 1.0, $CHCl_3$).

J. SYNTHESIS OF 1,3-DIOLS (16) AND STEREOCHEMICAL ASSIGNMENTS

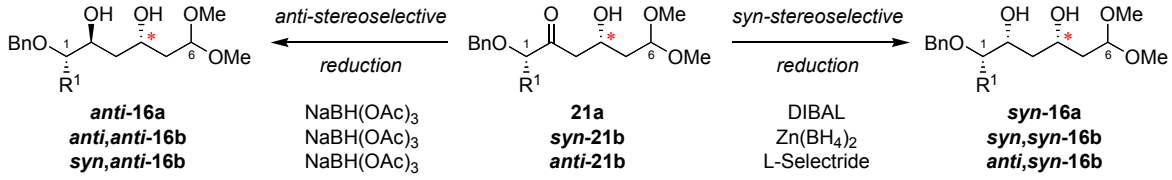
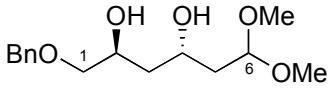


Figure S9. Synthesis of 1,3-diols 16. Stereoselective reductions of β-hydroxyketones **21** provided both *anti*- and *syn*-1,3-diol products in both the R^1 = H and R^1 = Me series.[21] In the R^1 = H series, these 1,3-diols can also be obtained in high yields by direct epoxide opening of epoxyols ***syn*-12a** and ***anti*-12a** using Red-Al (not shown).[22] Relative stereochemical assignments at *C*2 and *C*4 were made by conversion of the 1,3-diols to the corresponding acetonides and ^{13}C-NMR analysis using Rychnovsky's method.[20] The resulting stereochemical assignments were consistent with the *syn* and *anti* epoxyol assignments made for **12** and **13** in SECTION E above by analogy to literature precedents. Furthermore, conversion of ***syn*-21b** to two different cyclic carbonate derivatives and NOESY analysis provided direct confirmation of relative stereochemical assignments at *C*1 and *C*2 (and hence *C*4), also consistent with relative stereochemical assignments made for the epoxyol precursors **12b** and **13b** in SECTION E above.



(–)-(2*S*,4*S*)-1-(Benzyloxy)-6,6-dimethoxyhexane-2,4-diol (2*S*-*anti*-16a).

β-Hydroxyketone Method: In a 15 mL roundbottom flask, $NaBH(OAc)_3$ (112.5 mg, 531 μmol, 5.7 equiv) was dissolved in anhyd CH_3CN (2.6 mL) and cooled to –20 °C. AcOH (0.4 mL) was added and the mixture was stirred at –20 °C for 20 min. The above solution was added dropwise via syringe to a solution of β-hydroxyketone ***R*-21a** (26.4 mg, 93.5 μmol, 1.0 equiv) in anhyd CH_3CN (4.5 mL). The mixture was stirred at –20 °C for 1 h, then satd aq $NaHCO_3$ was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded 1,3-diol **2*S*-*anti*-16a** (25.3 mg, 95%, 98:2 dr) as a light yellow oil.

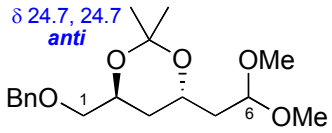
Epoxyol Method: To a stirred –40 °C solution of *syn*,*cis*-epoxyol **2*R*-*anti*-13a** (75 mg, 266 μmol, 1.0 equiv) in THF (7.5 mL) was added Red-Al (3.3 M in toluene, 1.49 mL, 4.92 mmol, 18.5 equiv) in THF (3.5 mL) dropwise. The mixture was stirred at –40 °C for 3 h, then warmed slowly to rt and stirred for 2 d. The reaction was recooled to –40 °C, then H_2O and satd aq NH_4Cl were added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were washed with satd aq NH_4Cl and H_2O, dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. The residue was dissolved in 60% aq MeCN (7 mL) followed by slow addition of $NaIO_4$ (113.4 mg, 0.53 mmol, 2.0 equiv) at 0 °C. After stirring for 1 h at rt, the MeCN was removed by rotary evaporation and the aq layer was extracted with CH_2Cl_2. The combined organic layers were

[21] (a) Evans, D. A.; Clark, J. S.; Metternich, R.; Novack, V. J.; Sheppard, G. S. *J. Am. Chem. Soc.* **1990**, *112*, 866–868. (b) Kiyooka, S.; Kuroda, H.; Shimasaki, Y. *Tetrahedron Lett.* **1986,** *27*, 3009–3012.

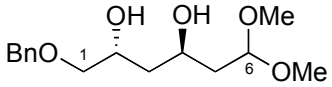
[22] Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982,** *23*, 2719–2722.

dried (Na_2SO_4) and concentrated by rotary evaporation. Purification by silica flash chromatography (2:1→1:1→1:2 hexanes/EtOAc) yielded 1,3-diol **2*S*-*anti*-16a** (62.8 mg, 83%, 94:6 dr) as a light yellow oil.

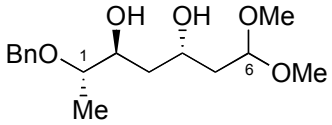
TLC: R_f 0.34 (1:2 hexanes/EtOAc, double elution). $[\alpha]_D^{25}$: –14.0° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3431 (O–H st), 2933, 1495, 1452, 1388, 1364, 1310, 1248, 1192, 1121, 1073, 1052, 960, 908, 839, 814, 738. **^{1}H-NMR** (400 MHz): δ 7.37–7.27 (m, 5H), 4.58 (t, 1H, *J* = 5.5), 4.53 (s, 2H), 4.12 (m, 2H), 3.50 (dd, 1H, *J* = 9.5, 4.0), 3.41 (m, 2H), 3.37 (s, 3H), 3.34 (s, 3H), 3.02 (d, 1H, *J* = 3.2), 1.84 (m, 1H), 1.73 (m, 1H), 1.60 (m, 2H). **^{13}C-NMR** (100 MHz): δ 138.4, 128.8, 128.2, 128.1, 104.3, 74.8, 73.7, 68.1, 66.1, 54.2, 53.4, 39.9. **ESI-MS** *m/z* (rel int): (pos) 307.3 ($[M+Na]^+$, 100), 323.3 ($[M+K]^+$, 5); (neg) 283.1 ($[M–H]^-$, 100), 319.2 ($[M+Cl]^-$, 22).



The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of **2*S*-*anti*-16a** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, PPTS, CH_2Cl_2, rt, 30 min; 80%). ^{13}C-NMR resonances were observed at 24.7 and 24.7 ppm (peak overlap confirmed by HMQC analysis) (and 100.5 ppm), indicative of an *anti*-diol-derived acetonide in a twist-boat conformation.[20]



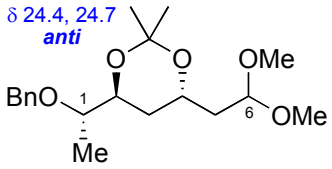
(+)-(2*R*,4*R*)-1-(Benzyloxy)-6,6-dimethoxyhexane-2,4-diol (2*R*-*anti*-16a). **Epoxyol Method:** Prepared directly from *syn*,*cis*-epoxyol **2*S*-*anti*-13a** using Red-Al as described above. Light yellow oil (65.2 mg, 87%, 96:4 dr). $[\alpha]_D^{25}$: +11.2° (*c* 1.0, $CHCl_3$).



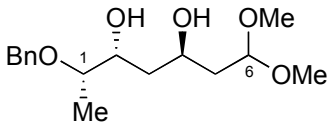
(–)-(3*S*,5*S*,6*S*)-6-(Benzyloxy)-1,1-dimethoxyheptane-3,5-diol (*anti*,*anti*-16b). **β-Hydroxyketone Method:** Prepared from β-hydroxyketone ***syn*-21b** as above. Clear oil (14 mg, 93%, 93:7 dr).

TLC: R_f 0.15 (1:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +17.1° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3435 (O–H st), 2925, 1453, 1375, 1192, 1068, 893, 814. **^{1}H-NMR** (400 MHz): δ 7.41–7.22 (m, 5H), 4.68 (d, 1H, *J* = 11.5), 4.59 (dd, 1H, *J* = 5.8, 5.3), 4.45 (d, 1H, *J* = 11.5), 4.10 (m, 1H), 3.78 (m, 1H), 3.45 (m, 1H), 3.37 (s, 3H), 3.35 (s, 3H), 3.34 (d, 1H, *J* = 3.2), 2.88 (d, 1H, *J* = 3.2), 1.85 (ddd, 1H, *J* = 14.1, 9.3, 5.8), 1.75 (ddd, 1H, *J* = 14.1, 5.3, 3.9), 1.64 (m, 1H), 1.58 (m, 1H), 1.19 (d,

3H, *J* = 6.2). **^{13}C-NMR** (125 MHz): δ 138.3, 128.5, 127.8, 127.7, 103.8, 78.4, 72.1, 71.1, 65.7, 53.7, 53.1, 39.7, 39.2, 15.4. **ESI-MS** *m/z* (rel int): (pos) 321.1 ([M+Na]$^+$, 100); (neg) 333.5 ([M+Cl]$^-$, 90), 297.4 ([M–H]$^-$, 100).

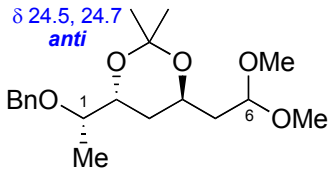


The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of ***anti*,*anti*-16b** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, TsOH, acetone, rt, 2 h; 79%). ^{13}C-NMR resonances were observed at 24.4 and 24.7 ppm (and 101.9 ppm), indicative of an *anti*-diol-derived acetonide in a twist-boat conformation.[20]



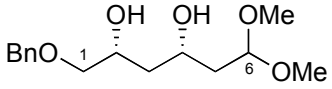
(+)-(3*R*,5*R*,6*S*)-6-(Benzyloxy)-1,1-dimethoxyheptane-3,5-diol (*syn*,*anti*-16b). <u>β-Hydroxyketone Method:</u> Prepared from β-hydroxyketone ***anti*-21b** as above. Purification by silica flash chromatography (1:1→2:3 hexanes/EtOAc) yielded *anti*-1,3-diol ***syn*,*anti*-16b** (26.6 mg, 88%, 95:5 dr) as a light yellow oil.

TLC: R_f 0.20 (1:1 hexanes/EtOAc). $[\alpha]_D^{20}$: +32.9° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3441 (O–H st), 3063, 3030, 2932, 2832, 2356, 1604, 1496, 1453, 1385, 1329, 1252, 1192, 1125, 1068, 966, 909, 817, 739. **^{1}H-NMR** (400 MHz): δ 7.40–7.21 (m, 5H), 4.63 (d, 1H, *J* = 11.8), 4.57 (dd, 1H, *J* = 6.3, 4.5), 4.51 (d, 1H, *J* = 11.8), 4.11 (m, 1H), 3.99 (ddd, 1H, *J* = 12.0, 7.6, 4.4), 3.54 (ddd, 1H, *J* = 12.5, 9.5, 4.6), 3.39 (s, 3H), 3.35 (s, 3H), 3.31 (d, 1H, *J* = 2.6), 2.72 (d, 1H, *J* = 4.3), 1.86 (ddd, 1H, *J* = 14.3, 9.5, 6.3), 1.75 (ddd, 1H, *J* = 14.3, 4.6, 4.5), 1.66 (m, 1H), 1.61 (m, 1H), 1.19 (d, 1H, *J* = 6.4). **^{13}C-NMR** (125 MHz): δ 138.6, 128.4, 127.7, 127.6, 104.2, 77.7, 70.7, 70.5, 66.0, 54.0, 52.9, 39.4, 38.4, 14.3. **ESI-MS** *m/z* (rel int): 321.0 ([M+Na]$^+$, 100); (neg) 333.4 ([M+Cl]$^-$, 90), 297.4 ([M–H]$^-$, 100).



The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of ***syn*,*anti*-16b** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, TsOH,

acetone, rt, 8 h; 57%). ^{13}C-NMR resonances were observed at 24.5 and 24.7 ppm (and 101.9 ppm), indicative of an *anti*-diol-derived acetonide in a twist-boat conformation.[20]

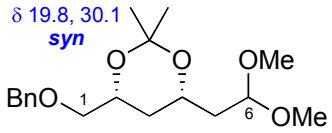


(–)-(2*R*,4*S*)-1-(Benzyloxy)-6,6-dimethoxyhexane-2,4-diol (2*R*-*syn*-16a).

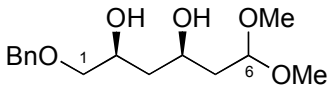
β-Hydroxyketone Method: In a 15 mL roundbottom flask, β-hydroxyketone ***R*-21a** (26.4 mg, 93.5 μmol, 1.0 equiv) was dissolved in anhyd THF (7.5 mL) and cooled to –78 °C. DIBAL (1 M in toluene, 319 μL, 319 μmol, 3.4 equiv) was added dropwise via syringe. The mixture was stirred at –78 °C for 1 h, then satd aq sodium potassium tartrate was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded *syn*-1,3-diol **2*R*-*syn*-16a** (24.0 mg, 90%, 98:2 dr) as a clear oil.

Epoxyol Method: Prepared directly from *anti*,*cis*-epoxyol **2*S*-*syn*-13a** using Red-Al as described above. Light yellow oil (45.4 mg, 61%, 98:2 dr).

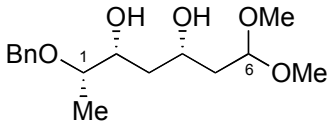
TLC: R_f 0.42 (1:2 hexanes/EtOAc, double elution). $[\alpha]_D^{25}$: –0.4° (*c* 1.0, $CHCl_3$). **IR** (NaCl, film): 3422 (O–H st), 2929, 1748, 1495, 1452, 1387, 1364, 1312, 1239, 1193, 1121, 1073, 1052, 959, 910, 847, 814, 738. **^{1}H-NMR** (400 MHz): δ 7.39–7.27 (m, 5H), 4.58 (t, 1H, *J* = 5.5), 4.55 (s, 2H), 4.07 (m, 2H), 3.71 (s, 1H), 3.43 (m, 3H), 3.37 (s, 3H), 3.36 (s, 3H), 1.81 (m, 1H), 1.73 (m, 1H), 1.60 (m, 2H). **^{13}C-NMR** (100 MHz): δ 138.4, 128.8, 128.2, 103.9, 74.7, 73.8, 71.2, 69.0, 54.1, 53.7, 40.3, 40.2. **ESI-MS** *m/z* (rel int): (pos) 307.3 ($[M+Na]^+$, 100), 323.3 ($[M+K]^+$, 15); (neg) 283.2 ($[M–H]^–$, 15), 319.1 ($[M+Cl]^–$, 100).



The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of **2*R*-*syn*-16a** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, PPTS, CH_2Cl_2, rt, 30 min; 59%). ^{13}C-NMR resonances were observed at 19.8 and 30.1 ppm (and 98.6 ppm), indicative of a *syn*-diol-derived acetonide in a chair conformation.[20]

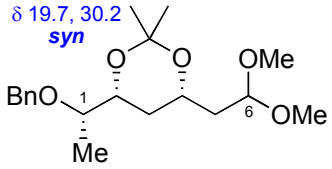


(+)-(2*S*,4*R*)-1-(Benzyloxy)-6,6-dimethoxyhexane-2,4-diol (2*S*-*syn*-16a). **Epoxyol Method:** Prepared directly from *anti*,*cis*-epoxyol **2*R*-*syn*-13a** using Red-Al as described above. Light yellow oil (46.7 mg, 62%, 98:2 dr). $[\alpha]_D^{25}$: +4.8° (*c* 1.0, $CHCl_3$).



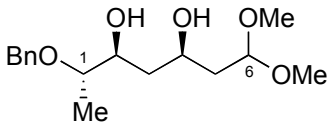
(+)-(3*S*,5*R*,6*S*)-6-(Benzyloxy)-1,1-dimethoxyheptane-3,5-diol (*syn*,*syn*-16b). **β-Hydroxyketone Method:** In a 20 mL roundbottom flask, β-hydroxyketone ***syn*-21b** (15 mg, 0.05 mmol, 1.0 equiv) was dissolved in anhyd CH_2Cl_2 (3.0 mL) and cooled to –45 °C. $Zn(BH_4)_2$ (1.0 M in DME, 0.15 mL, 0.15 mmol, 3.0 equiv) prepared as previously described[23] was added dropwise via syringe and the mixture was stirred at –45 °C for 3 h. Satd aq NH_4Cl was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded *syn*-1,3-diol ***syn*,*syn*-16b** (10.7 mg, 72%, 88:12 dr) as a clear oil.

TLC: R_f 0.20 (1:1 hexanes/EtOAc). $[\alpha]_D^{21}$: +11.5° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3426 (O–H st), 2929, 1453, 1192, 1068, 853, 817. **^{1}H-NMR** (400 MHz): δ 7.41–7.24 (m, 5H), 4.63 (d, 1H, *J* = 11.7), 4.58 (t, 1H, *J* = 5.5), 4.52 (d, 1H, *J* = 11.7), 4.05 (m, 1H), 3.90 (m, 1H), 3.73 (br s, 1H), 3.47 (m, 1H), 3.38 (s, 3H), 3.37 (s, 3H), 3.24 (d, 1H, *J* = 2.3), 1.82 (ddd, 1H, *J* = 14.2, 8.8, 5.5), 1.74 (ddd, 1H, *J* = 14.2, 5.5, 3.0), 1.67 (m, 1H), 1.58 (m, 1H), 1.20 (d, 3H, *J* = 6.4). **^{13}C-NMR** (125 MHz): δ 138.5, 128.4, 127.7, 127.6, 103.6, 77.7, 74.5, 70.9, 69.1, 53.8, 53.4, 40.1, 38.6, 14.6. **ESI-MS** *m/z* (rel int): (pos) 321.0 ($[M+Na]^+$, 100); (neg) 333.4 ($[M+Cl]^-$, 90), 297.4 ($[M–H]^-$, 100).



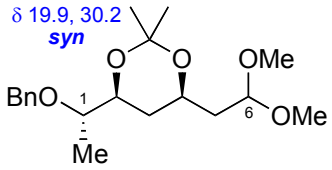
The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of ***syn*,*syn*-16b** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, TsOH, acetone, rt, 8 h; 81%). ^{13}C-NMR resonances were observed at 19.7 and 30.2 ppm (and 98.5 ppm), indicative of a *syn*-diol-derived acetonide in a chair conformation.[20]

[23] Crabbe, P.; Garcia, G. A.; Rius, C. *J. Chem. Soc., Perkin Trans. I*, **1973**, 810–816.



(+)-(3*R*,5*S*,6*S*)-6-(Benzyloxy)-1,1-dimethoxyheptane-3,5-diol (*anti*,*syn*-16b). **β-Hydroxyketone Method:** In a 10 mL roundbottom flask, β-hydroxyketone **anti-21b** (30.0 mg, 0.101 mmol, 1.0 equiv) was dissolved in anhyd THF (5 mL) and cooled to –78 °C. L-selectride (1.0 M in THF, 0.202 mL, 0.202 mmol, 2.0 equiv) was added dropwise via syringe and the mixture was stirred at –78 °C for 2 h. Satd aq NH_4Cl was added and the mixture was warmed to rt. The layers were separated and the aq layer was extracted with Et_2O. The combined organic extracts were washed with 3 N aq NaOH, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation. Purification by silica flash chromatography (1:1→2:3 hexanes/EtOAc) yielded *syn*-1,3-diol ***anti*,*syn*-16b** (28.7 mg, 95%, ≥98:2 dr) as a clear oil.

TLC: R_f 0.20 (1:1 hexanes/EtOAc). $[\alpha]_D^{25}$: +16.0° (*c* 1.0, $CHCl_3$). **IR** (ZnSe, film): 3441 (O–H st), 2932, 2832, 1717, 1496, 1453, 1375, 1309, 1192, 1123, 1069, 960, 912, 851, 817, 748. **^{1}H-NMR** (400 MHz): δ 7.39–7.22 (m, 5H), 4.66 (d, 1H, *J* = 11.6), 4.59 (t, 1H, *J* = 5.5), 4.45 (d, 1H, *J* = 11.6), 4.04 (m, 1H), 3.78 (d, 1H, *J* = 1.3), 3.75 (m, 1H), 3.45 (m, 1H), 3.38 (s, 3H), 3.37 (s, 3H), 3.29 (d, 1H, *J* = 2.4), 1.79 (m, 1H), 1.72 (m, 1H), 1.58 (m, 1H), 1.55 (m, 1H), 1.18 (d, 3H, *J* = 6.2). **^{13}C-NMR** (125 MHz): δ 138.3, 128.5, 127.8, 127.7, 103.4, 78.0, 75.0, 71.1, 68.6, 53.6, 53.5, 40.1, 38.8, 15.0. **ESI-MS** *m/z* (rel int): (pos) 320.9 ($[M+Na]^+$, 100); (neg) 333.4 ($[M+Cl]^-$, 90), 297.4 ($[M–H]^-$, 100).



The relative stereochemistry of the secondary alcohols at *C*2 and *C*4 of ***anti*,*syn*-16b** was determined by ^{13}C-NMR analysis of the corresponding acetonide (2,2-dimethoxypropane, TsOH, acetone, rt, 5 h; 89%). ^{13}C-NMR resonances were observed at 19.9 and 30.2 ppm (and 98.5 ppm), indicative of a *syn*-diol-derived acetonide in a chair conformation.[20]

ASSIGNMENT OF RELATIVE STEREOCHEMISTRY AT *C*1 AND *C*2 (*C*4) IN THE R^1 = Me SERIES

Relative stereochemical assignments at the *C*1 and *C*2 (and hence *C*4) positions of 1,3-diols ***anti*,*anti*-16b** and ***syn*,*syn*-16b** in the R^1 = Me series could not be determined unambiguously by NOESY analysis of the derived acetonides above. This information was required to confirm the relative configurations at *C*1 and *C*4 of β-hydroxyketones **21b**, at *C*1 and *C*3/*C*4 of epoxyketones **19b** and **20b**, and at *C*1 and *C*3/*C*4 of epoxyols **12b** and **13b** (Figure S10).

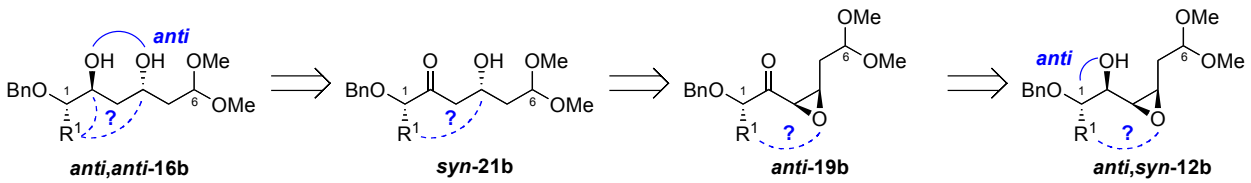


Figure S10. Relative stereochemical relationships in 1,3-diols, β-hydroxyketones, epoxyketones, and epoxyols in the R^1 = Me series.

Thus, the required relative stereochemical relationships were determined as outlined below (Figure S11). Briefly, β-hydroxyketone ***syn*-21b** was silylated at the *C*4 hydroxyl to form **S5**, then reduced in *anti*- and *syn*-stereoselective fashions to **S6** and **S7**. (Relative configurations at *C*2 and *C*4 were confirmed by desilylation of a portion of the material and comparison to authentic samples of 1,3-diols ***anti*,*anti*-16b** and ***syn*,*syn*-16b** synthesized above.) Debenzylation then provided 1,2-diols **S8** and **S9**, which were then converted to cyclic carbonates **S10** and **S11**. Assignment of ^{1}H-NMR peaks by COSY analysis and subsequent NOESY analysis allowed unambiguous assignment of relative stereochemistry at *C*1 and *C*2, and by extension at *C*1 and *C*4. These relative stereochemical assignments were then traced back through ***syn*-21b**, ***anti*-19b**, and ***anti*,*syn*-12b**. By process of elimination, relative stereochemical assignments could also be made for β-hydroxyketone ***anti*-21b** and its precursors.

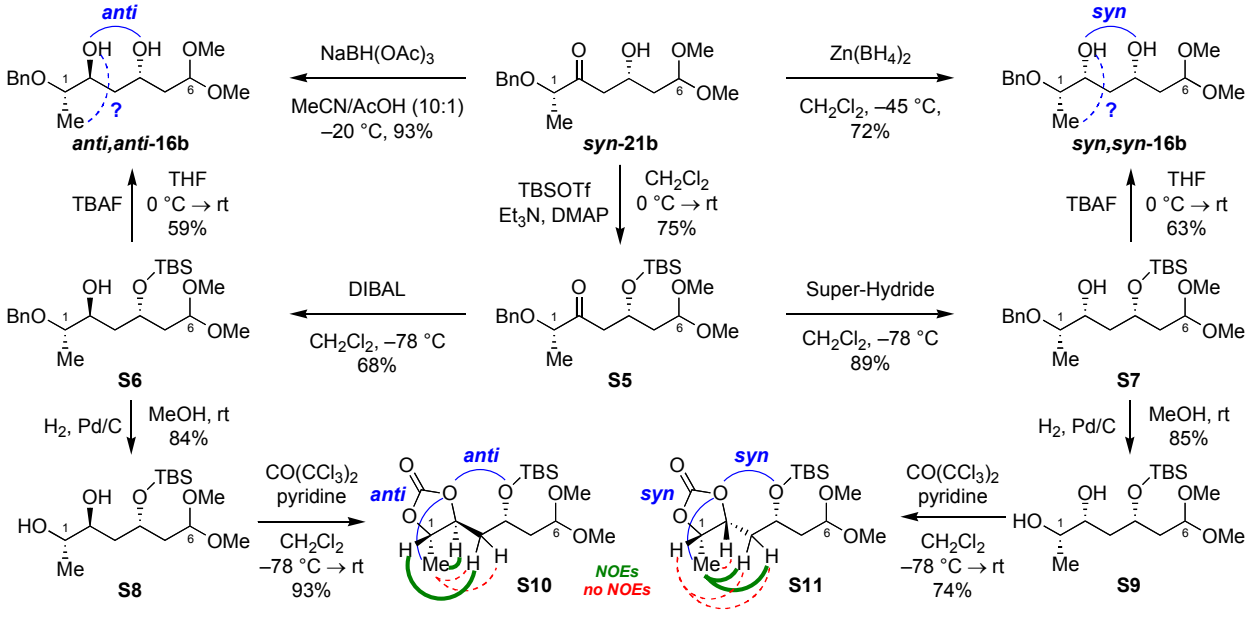
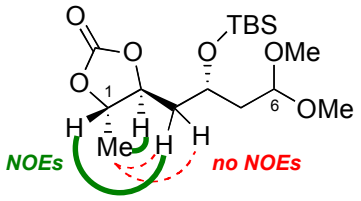


Figure S11. Conversion of β-hydroxyketone *syn*-21b to cyclic carbonate derivatives and assignment of relative stereochemistries at *C*1, *C*2, and *C*4. Relative stereochemistry at *C*2 and *C*4 of hydroxy-silyl ethers **S6** and **S7** were determined by desilylation and comparison to authentic samples of 1,3-diols ***anti*,*anti*-16b** and ***syn*,*syn*-16b** synthesized directly from the β-hydroxyketone ***syn*-21b**. Relative stereochemical assignments at *C*1 and *C*2 of cyclic carbonates **S10** and **S11** were made by NOESY analysis. Observed NOE interactions are shown as green bold lines, absent NOE interactions are shown as red dashed lines.

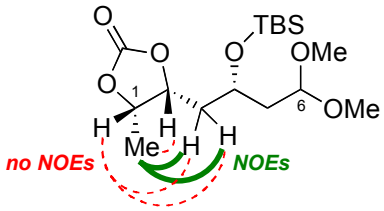
SELECTED SPECTRAL DATA FOR CYCLIC CARBONATES S10 AND S11



(4*S*,5*S*)-4-((*S*)-2-(*tert*-butyldimethylsilyloxy)-4,4-dimethoxybutyl)-5-methyl-1,3-dioxolan-2-one (S10).

TLC: R_f 0.50 (2:1 hexanes/EtOAc). **^{1}H-NMR** (400 MHz, C_6D_6): δ 3.95 (m, 1H), 3.92 (m, 1H), 3.48 (m, 1H), 3.07 (s, 3H), 3.05 (s, 3H), 1.76 (ddd, 1H, *J* = 14.1, 10.9, 5.5), 1.67 (ddd, 1H, *J* = 14.1, 6.0, 5.9), 1.39 (ddd, 1H, *J* = 14.5, 10.2, 3.1), 1.19 (ddd, 1H, *J* = 14.5, 9.2, 2.5), 0.87 (s, 9H), 0.66 (d, 3H, *J* = 6.2), 0.01 (s, 3H), 0.00 (s, 3H). **ESI-MS** *m/z* (rel int): (pos) 370.9 ($[M+Na]^+$, 100); (neg) 383.2 ($[M+Cl]^-$, 90).

^{1}H-NMR peaks were assigned by COSY analysis. NOESY analysis indicated interactions between Me^1 (0.66 ppm) and H^2 (3.95 ppm) and between H^1 (3.48 ppm) and one of H^3 protons (1.39 ppm), but no interactions between Me^1 and either of the H^3 protons, consistent with an *anti* relationship at *C*1 and *C*2 and, hence, a *syn* relationship at *C*1 and *C*4.

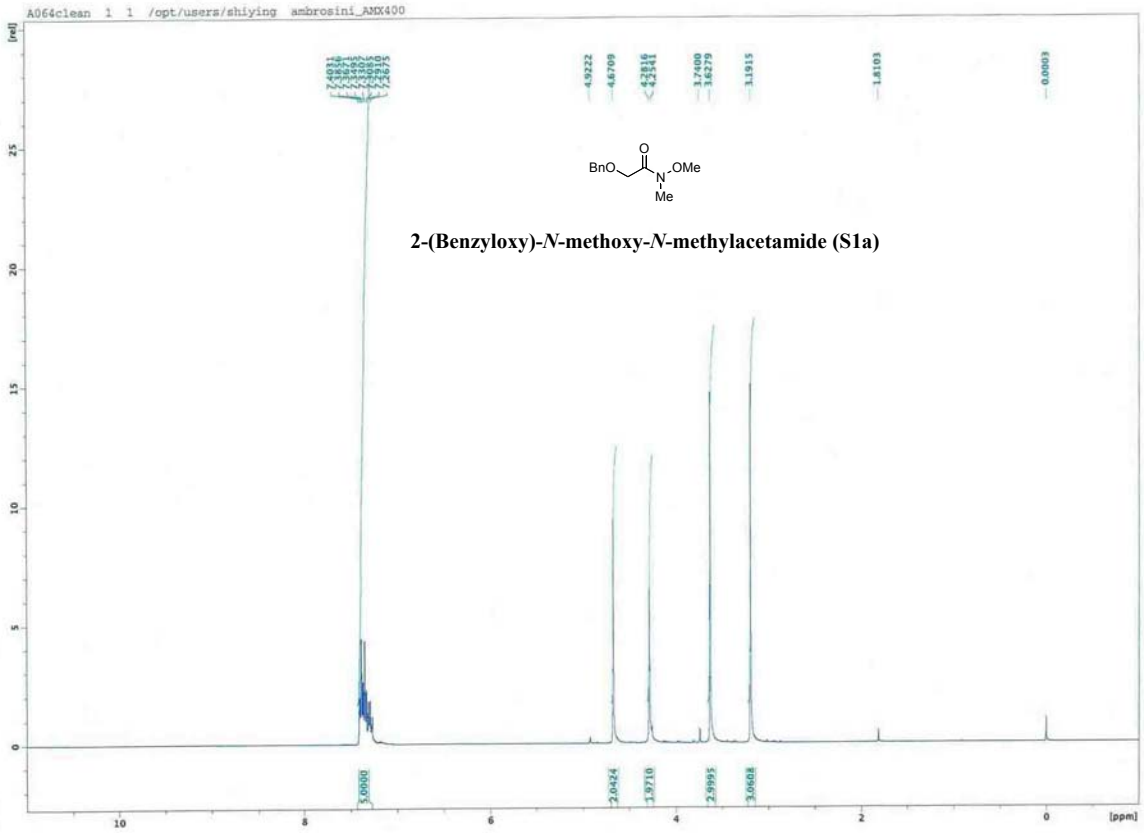


(4*R*,5*S*)-4-((*S*)-2-(*tert*-butyldimethylsilyloxy)-4,4-dimethoxybutyl)-5-methyl-1,3-dioxolan-2-one (S11).

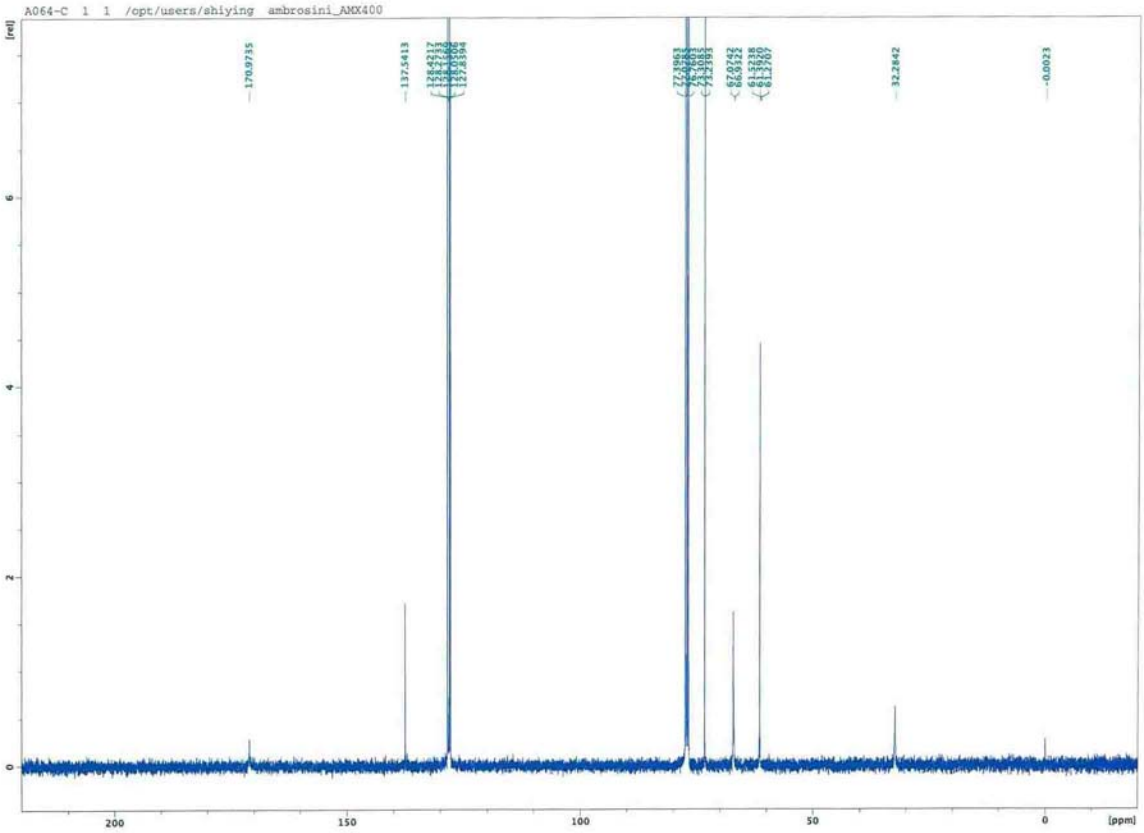
TLC: R_f 0.40 (2:1 hexanes/EtOAc). **^{1}H-NMR** (400 MHz, C_6D_6): δ 4.53 (dd, 1H, *J* = 6.3, 4.9), 4.12 (ddd, 1H, *J* = 10.3, 7.2, 3.0), 3.93 (m, 1H), 3.77 (td, 1H, *J* = 7.2, 6.6), 3.12 (s, 3H), 3.05 (s, 3H), 1.78 (ddd, 1H, *J* = 14.1, 6.3, 4.9), 1.73 (ddd, 1H, *J* = 14.1, 7.4, 4.9), 1.53 (ddd, 1H, *J* = 14.4, 10.3, 3.9), 1.20 (ddd, 1H, 14.4, 7.4, 3.0), 0.87 (s, 9H), 0.58 (d, 3H, *J* = 6.6), 0.01 (s, 3H), –0.08 (s, 3H). **ESI-MS** *m/z* (rel int): (pos) 370.9 ($[M+Na]^+$, 100); (neg) 383.3 ($[M+Cl]^-$, 90).

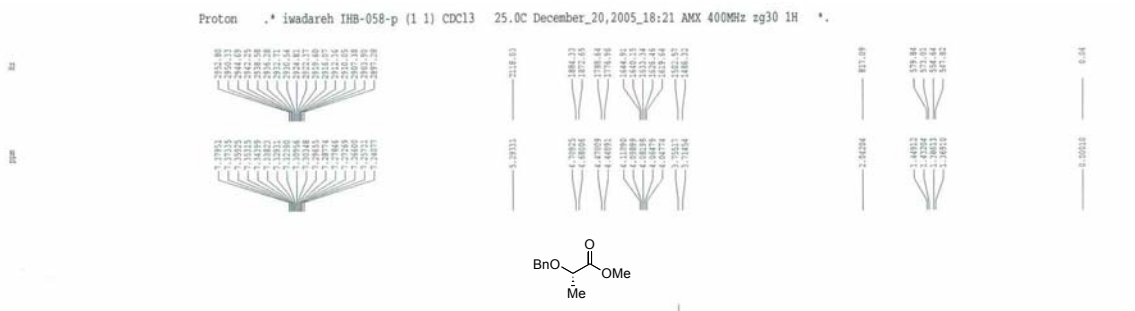
^{1}H-NMR peaks were assigned by COSY analysis. NOESY analysis indicated interactions between Me^1 (0.58 ppm) and both H^3 protons (1.53, 1.20 ppm) but no interactions between Me^1 and H^2 (4.12 ppm) or between H^1 (3.77 ppm) and either H^3 proton, consistent with a *syn* relationship at *C*1 and *C*2 and, hence, a *syn* relationship at *C*1 and *C*4.

K. ^{1}H-NMR AND ^{13}C-NMR SPECTRA

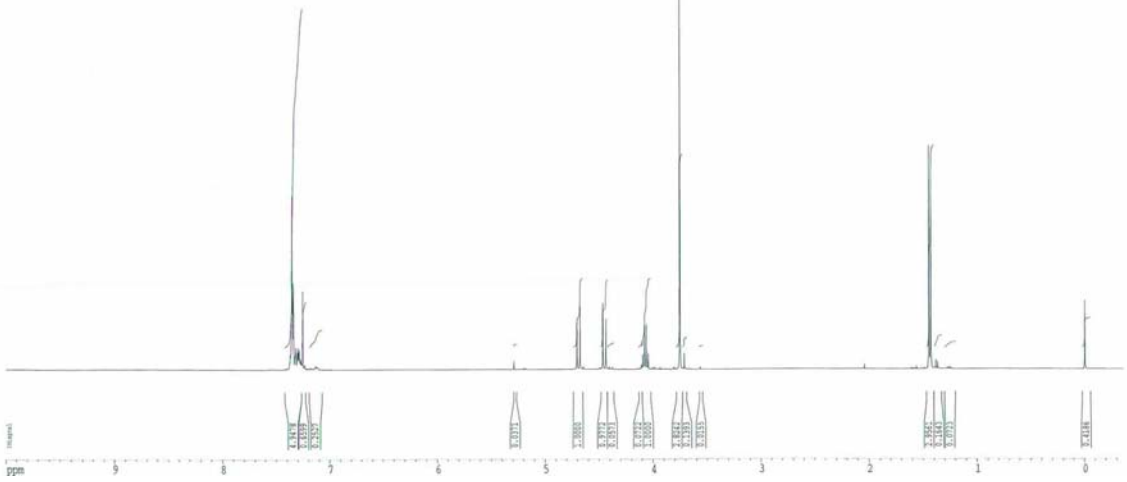


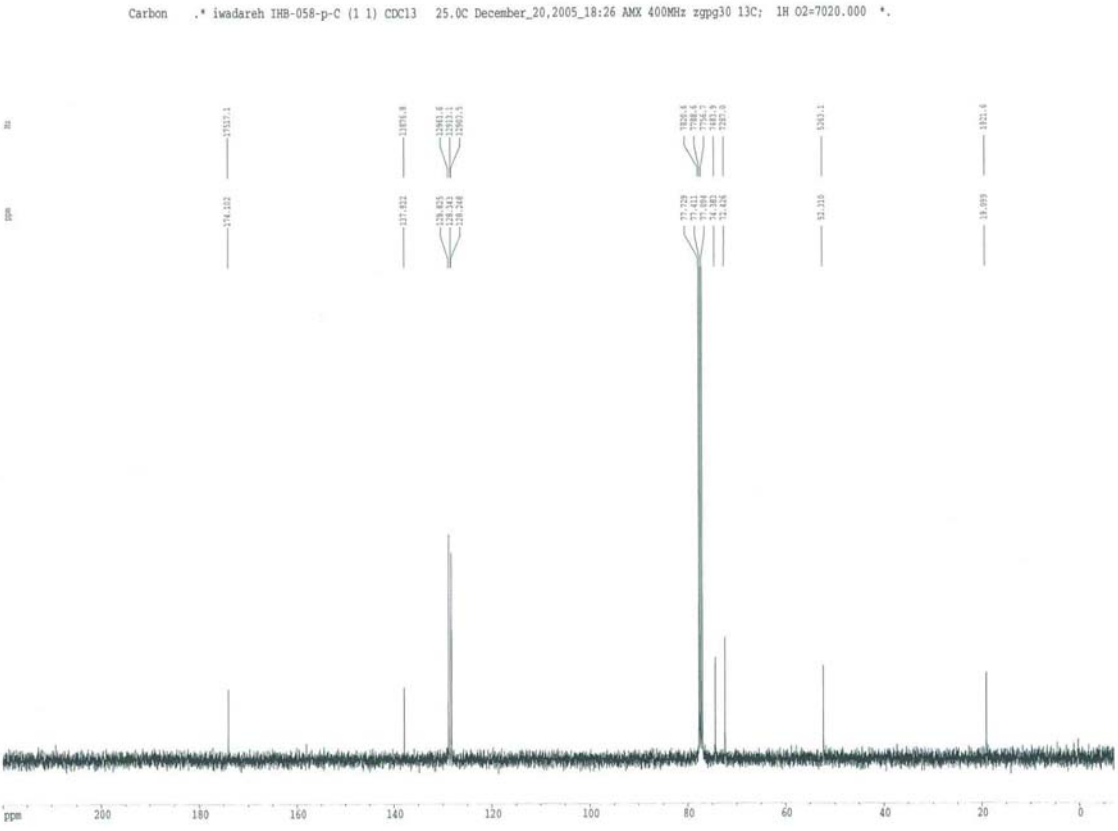
2-(Benzyloxy)-*N*-methoxy-*N*-methylacetamide (S1a)

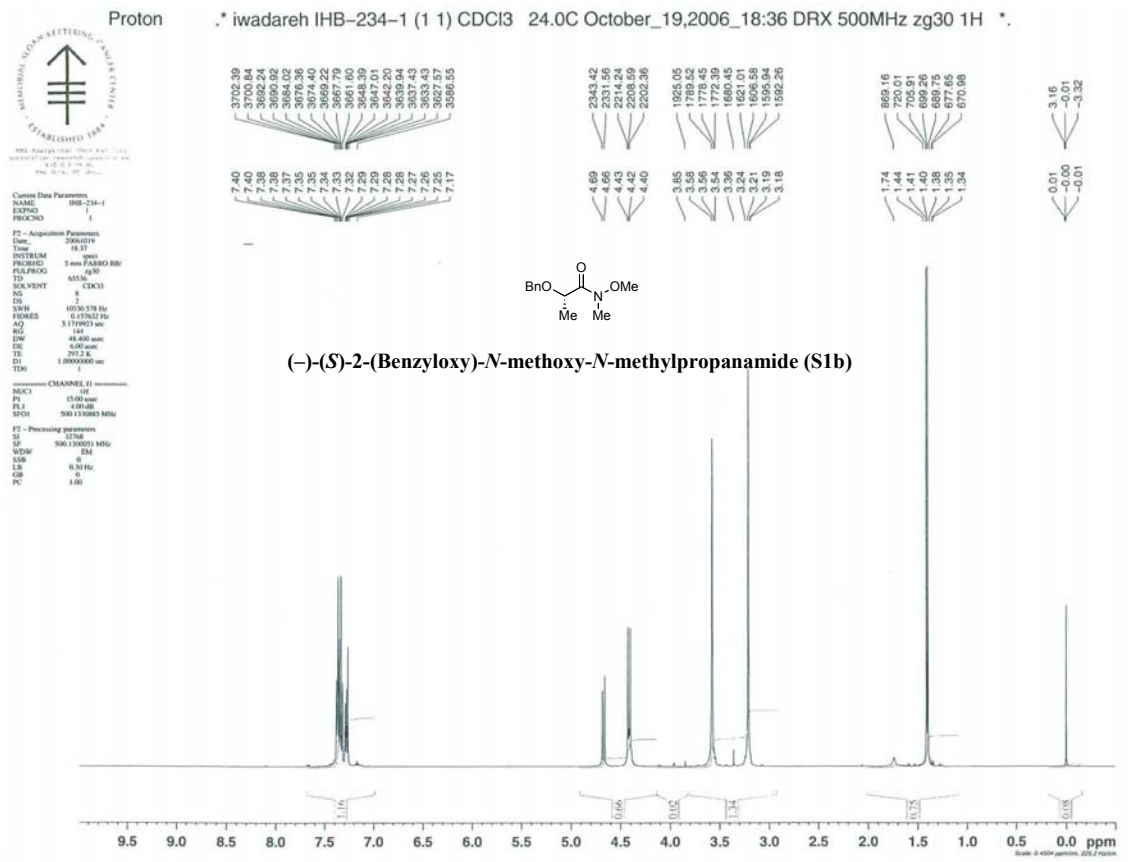




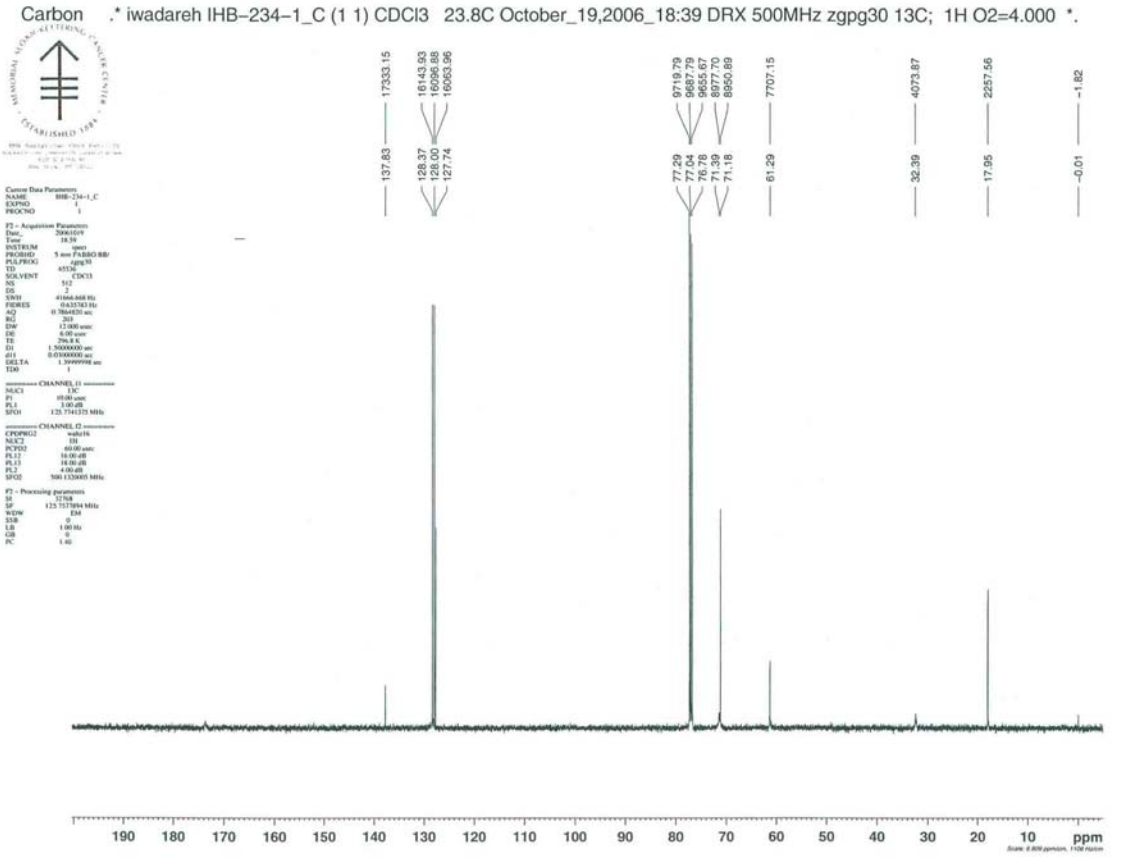
(–)-(*S*)-Methyl 2-(benzyloxy)propanoate (S2)

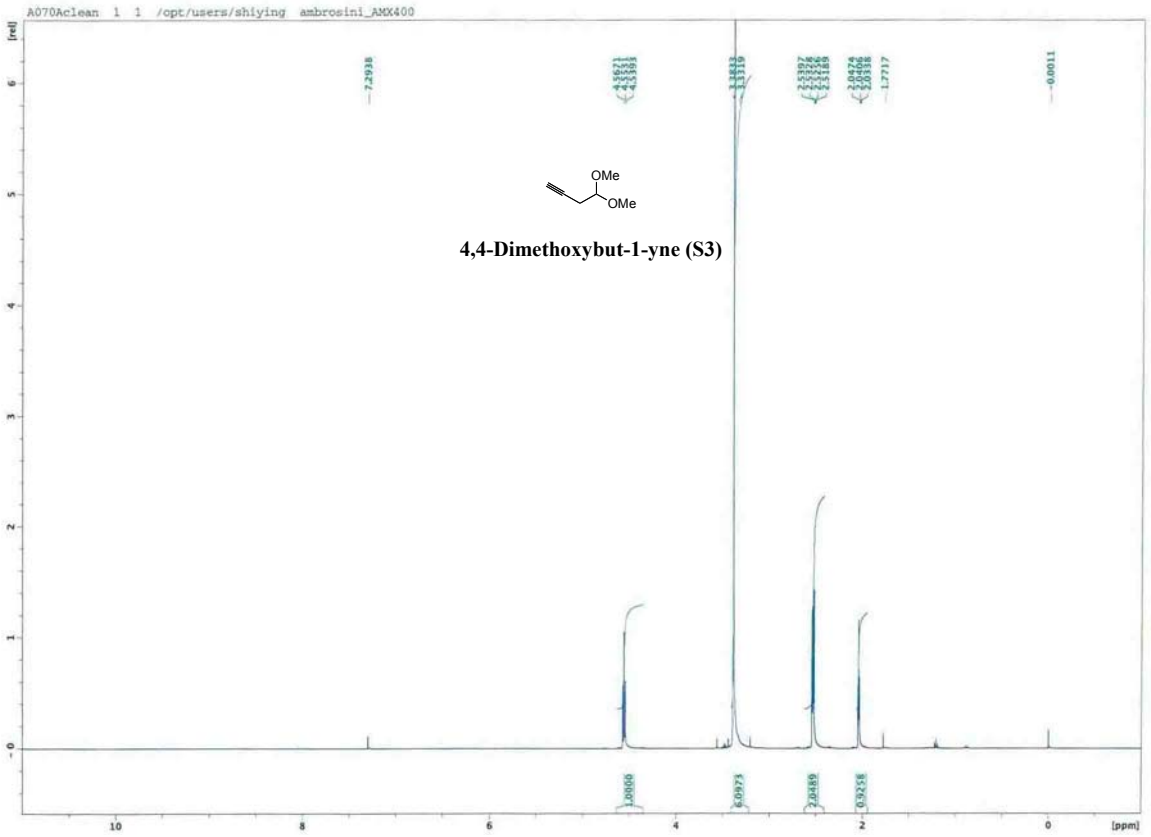




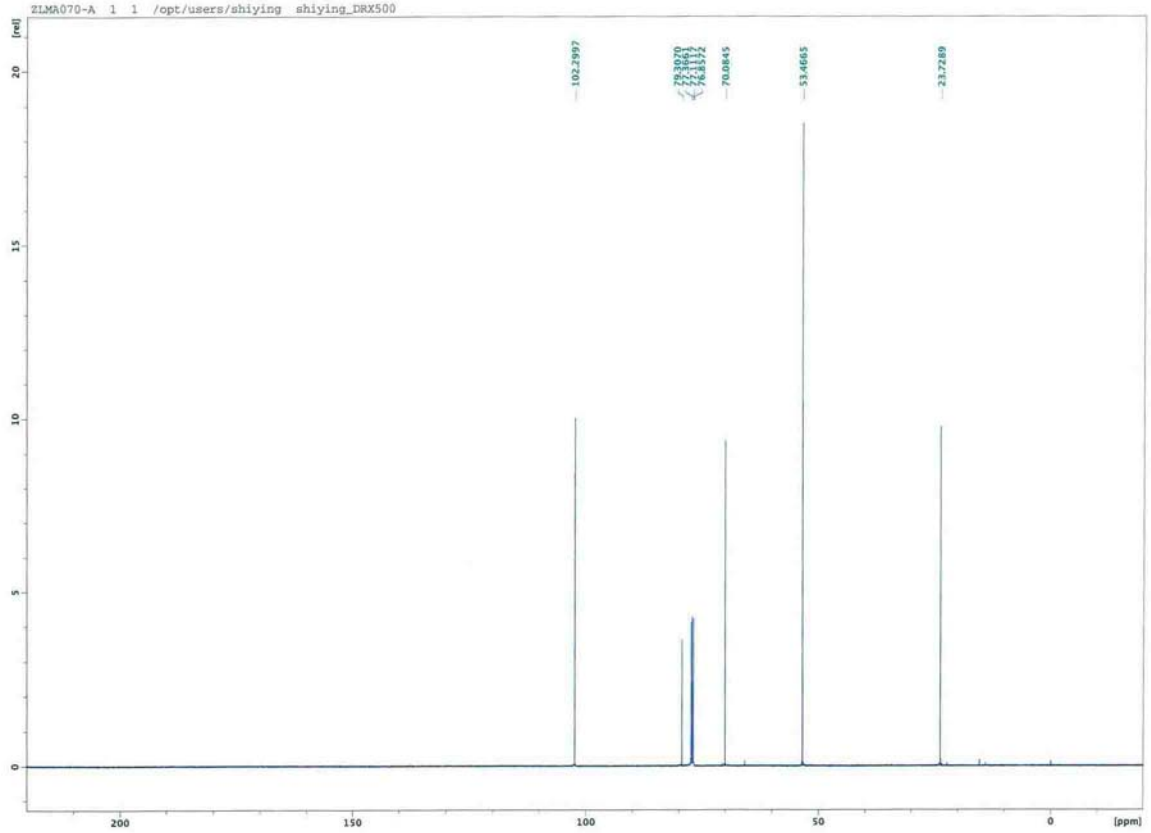


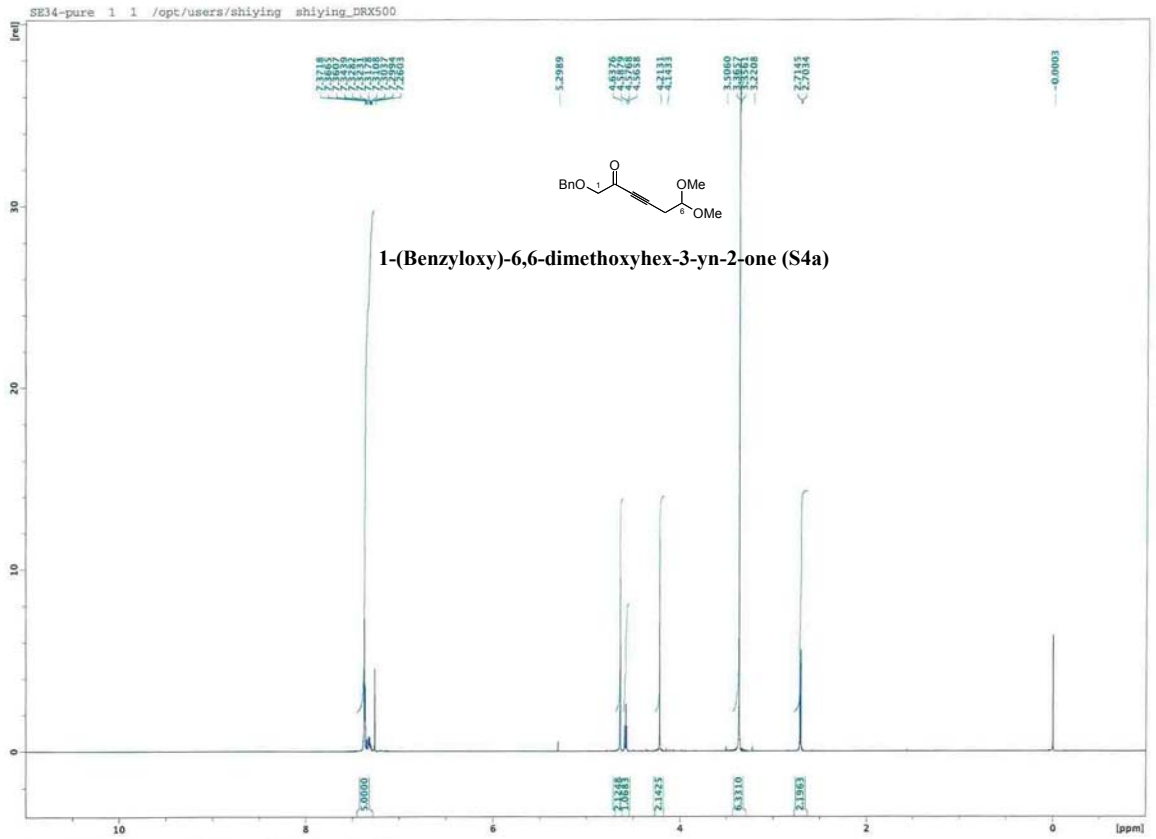
(–)-(*S*)-2-(Benzyloxy)-*N*-methoxy-*N*-methylpropanamide (S1b)



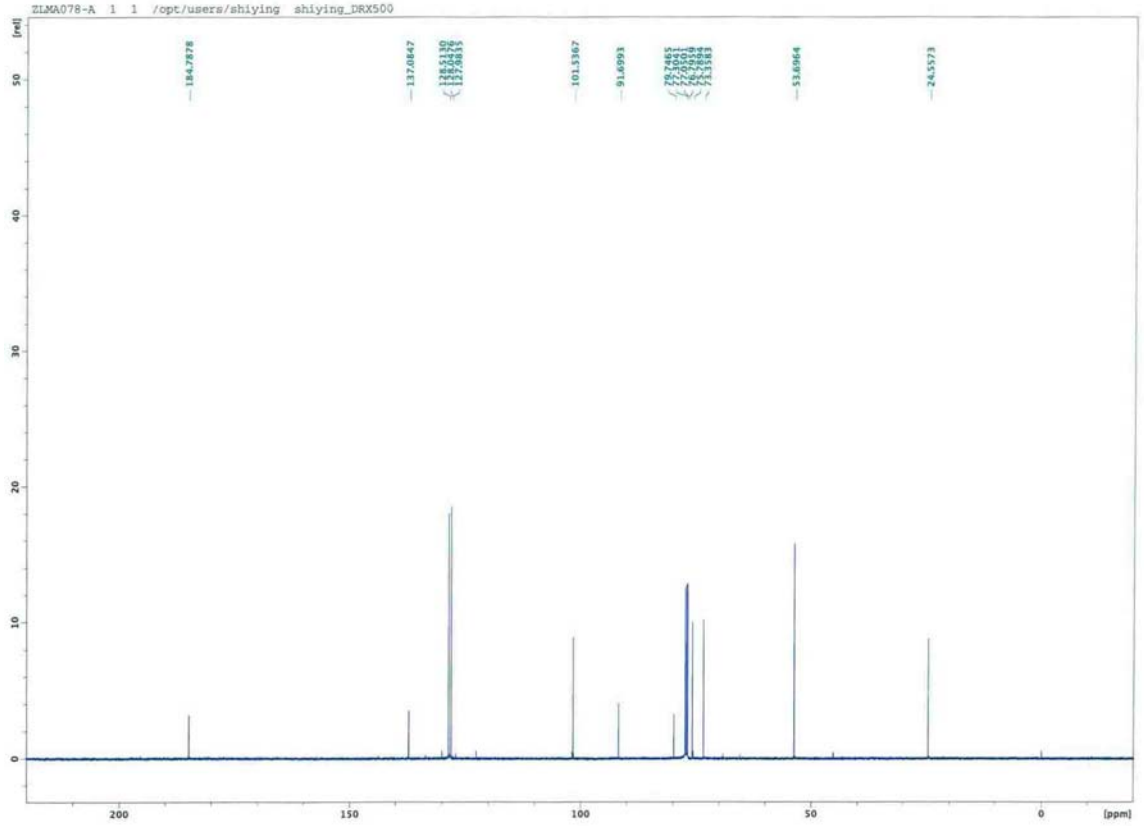


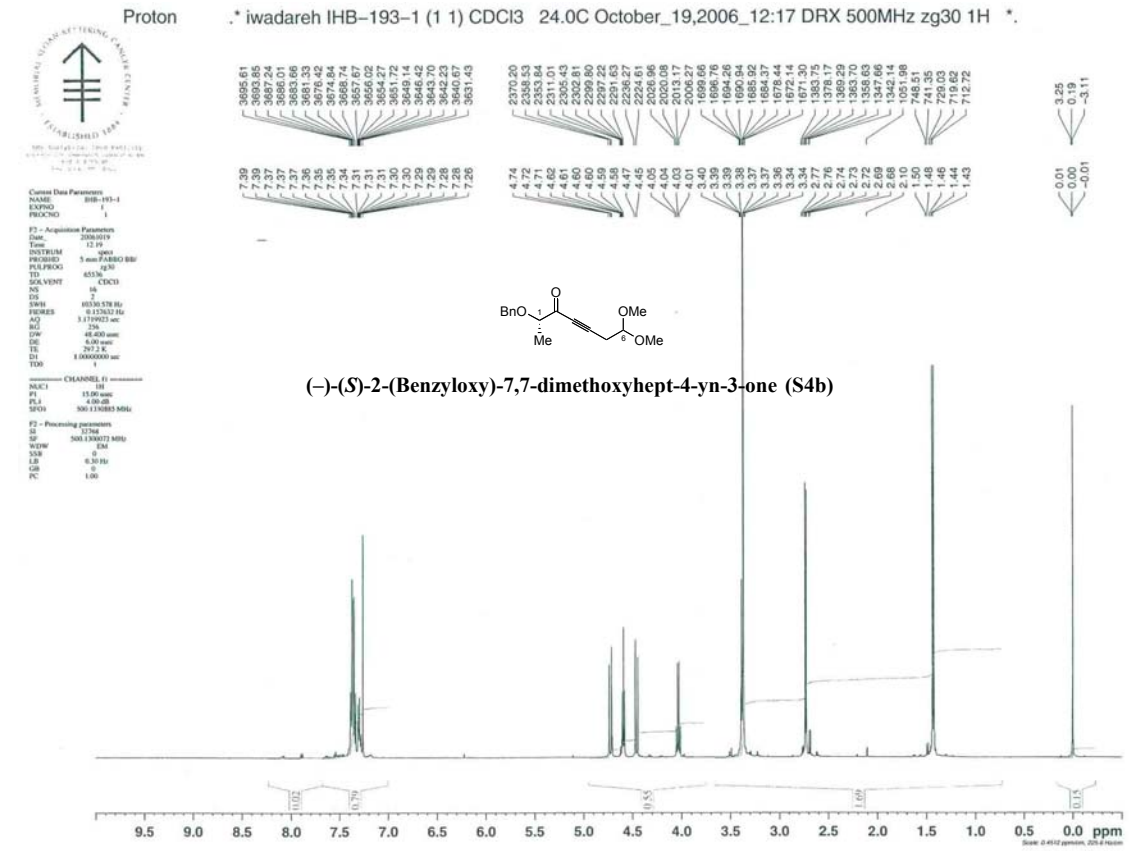
4,4-Dimethoxybut-1-yne (S3)



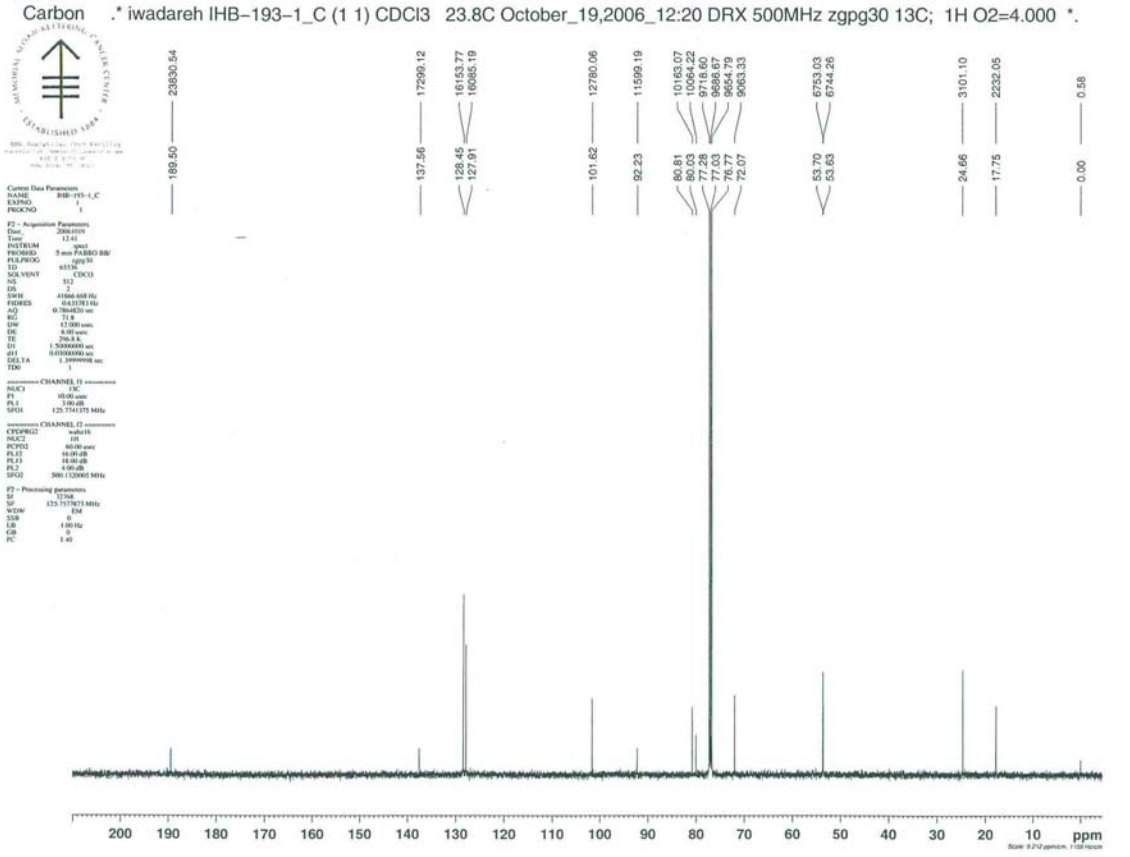


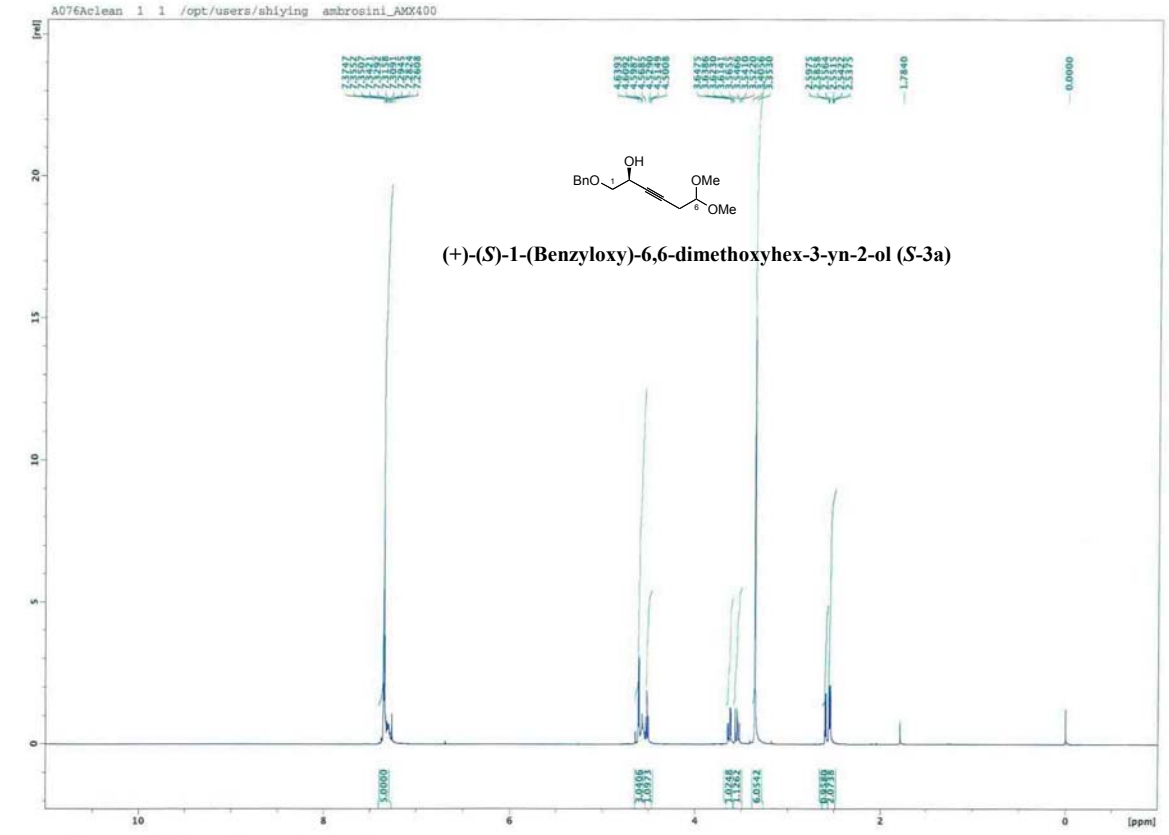
1-(Benzyloxy)-6,6-dimethoxyhex-3-yn-2-one (S4a)



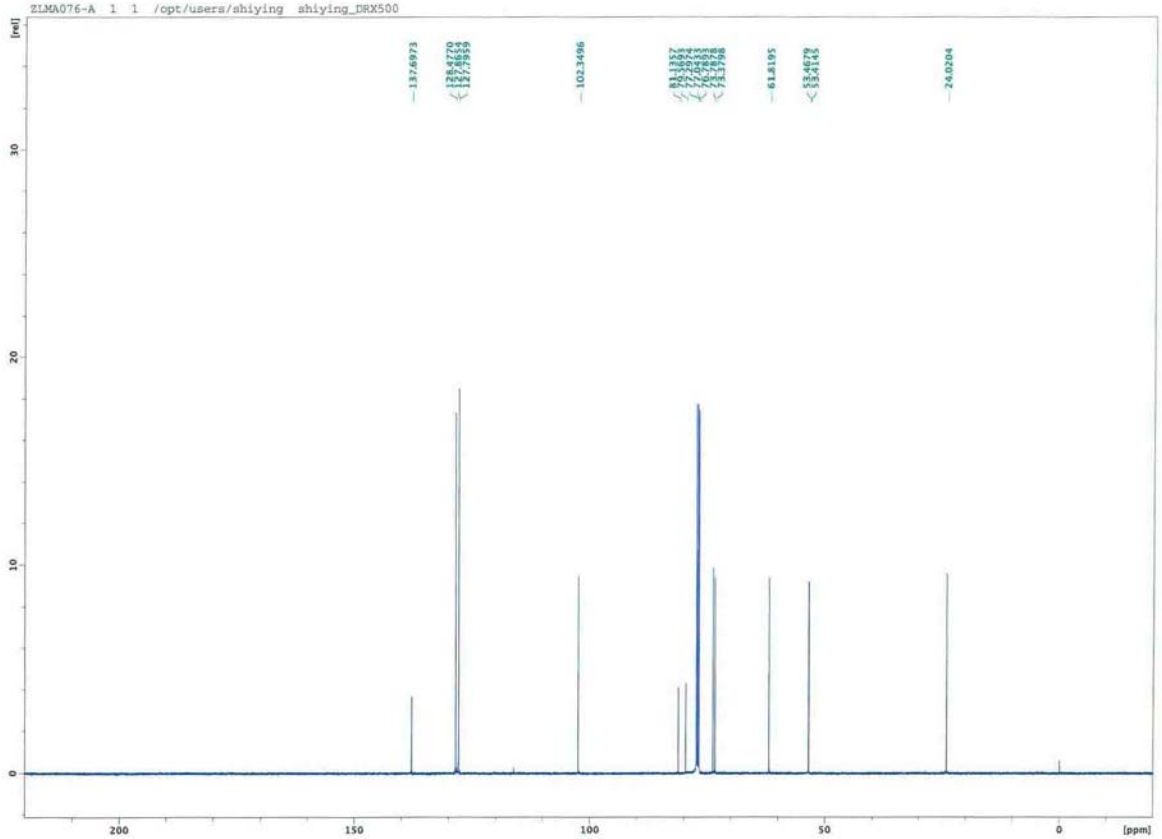


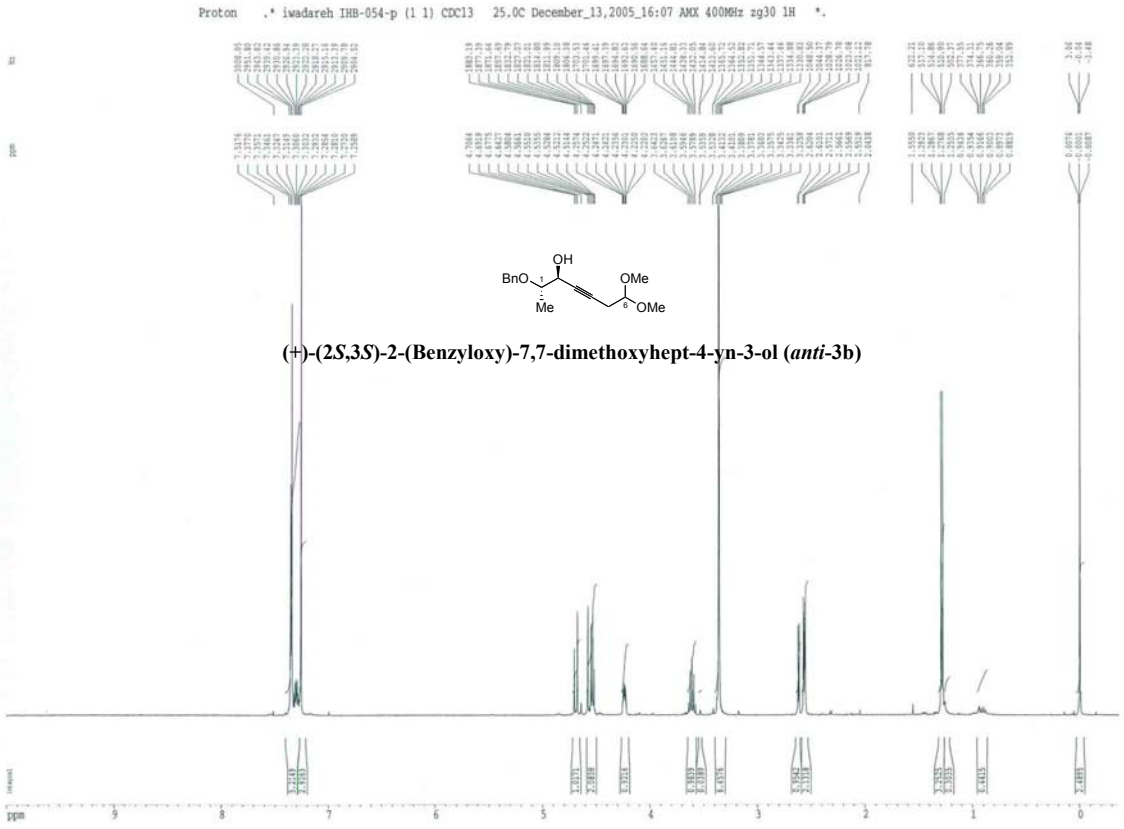
(–)-(*S*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-yn-3-one (S4b)



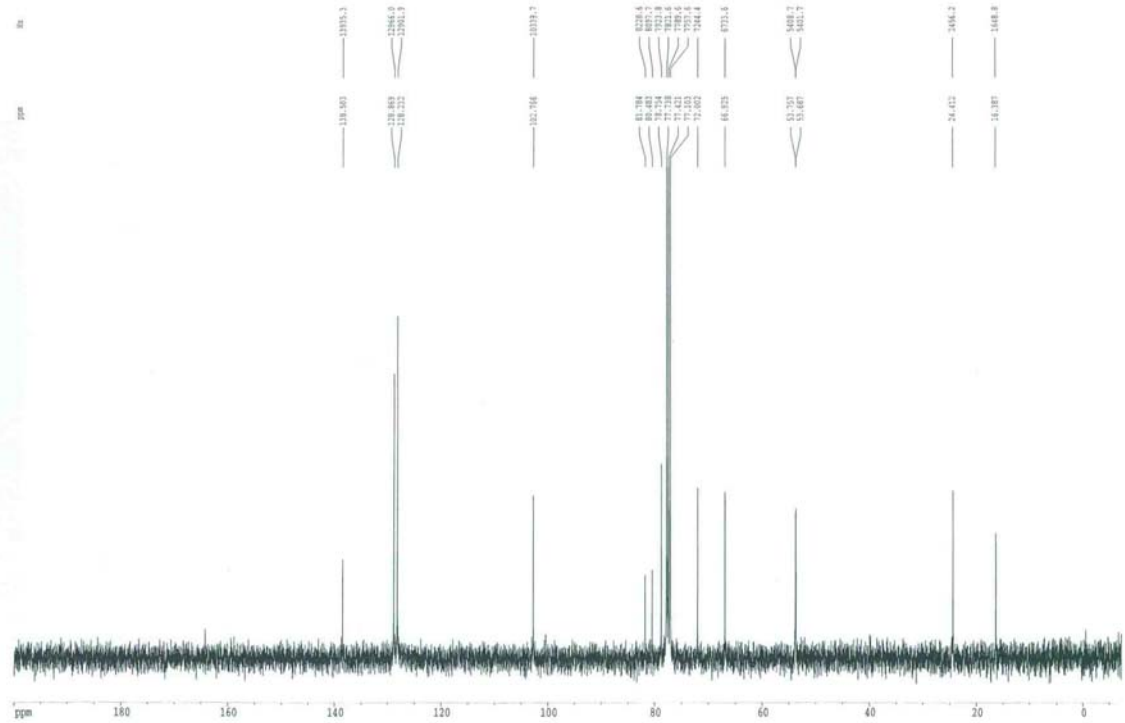


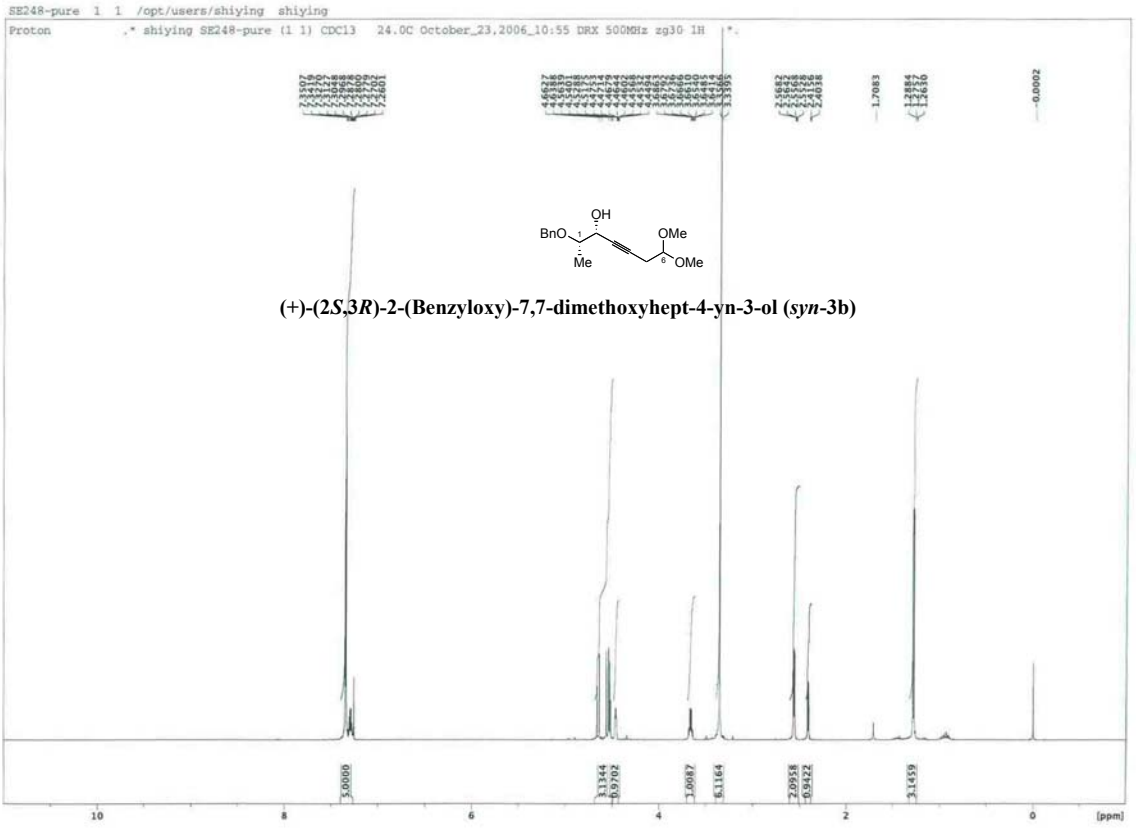
(+)-(*S*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-yn-2-ol (*S*-3a)





(+)-(2*S*,3*S*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-yn-3-ol (*anti*-3b)





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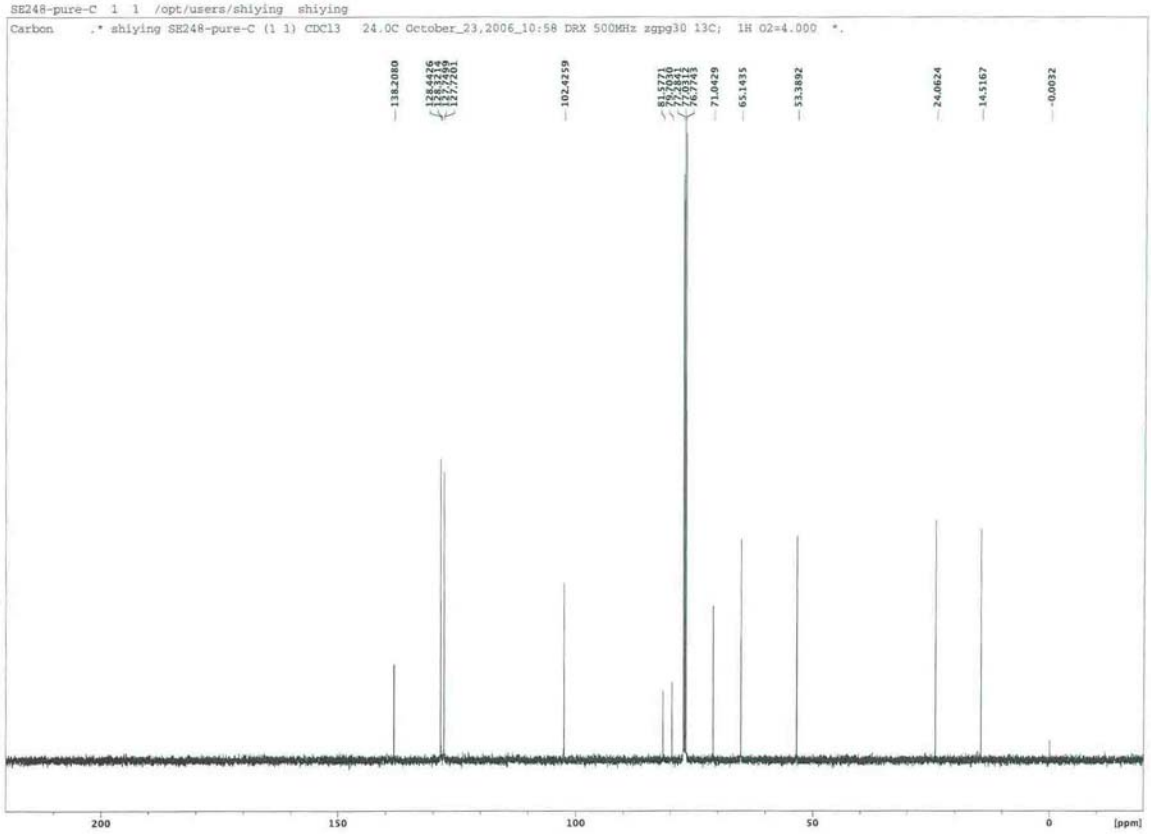
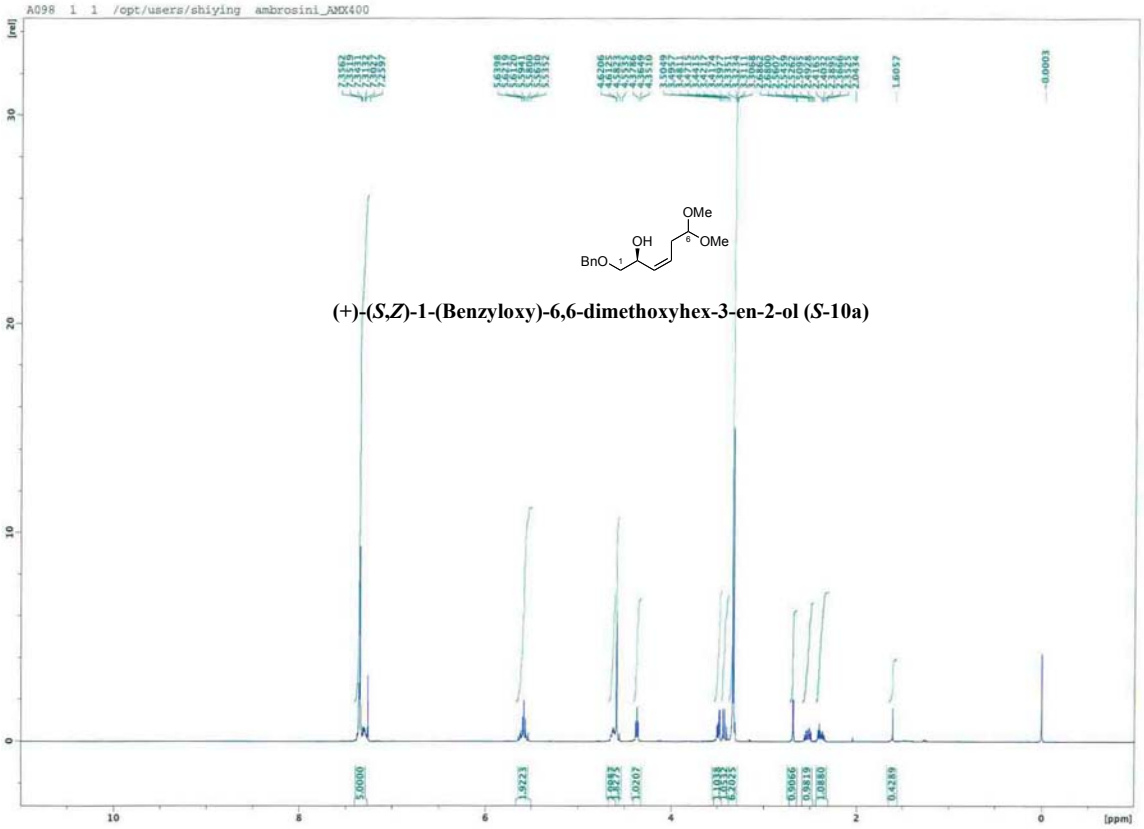
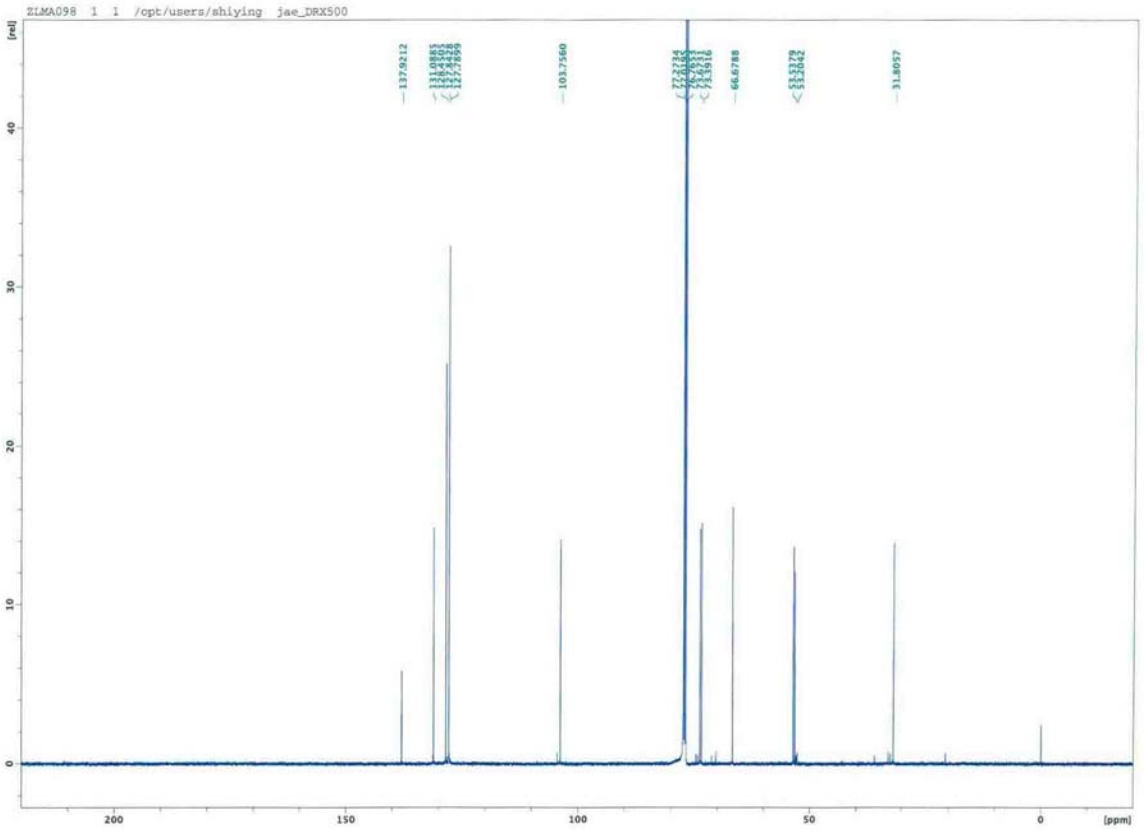
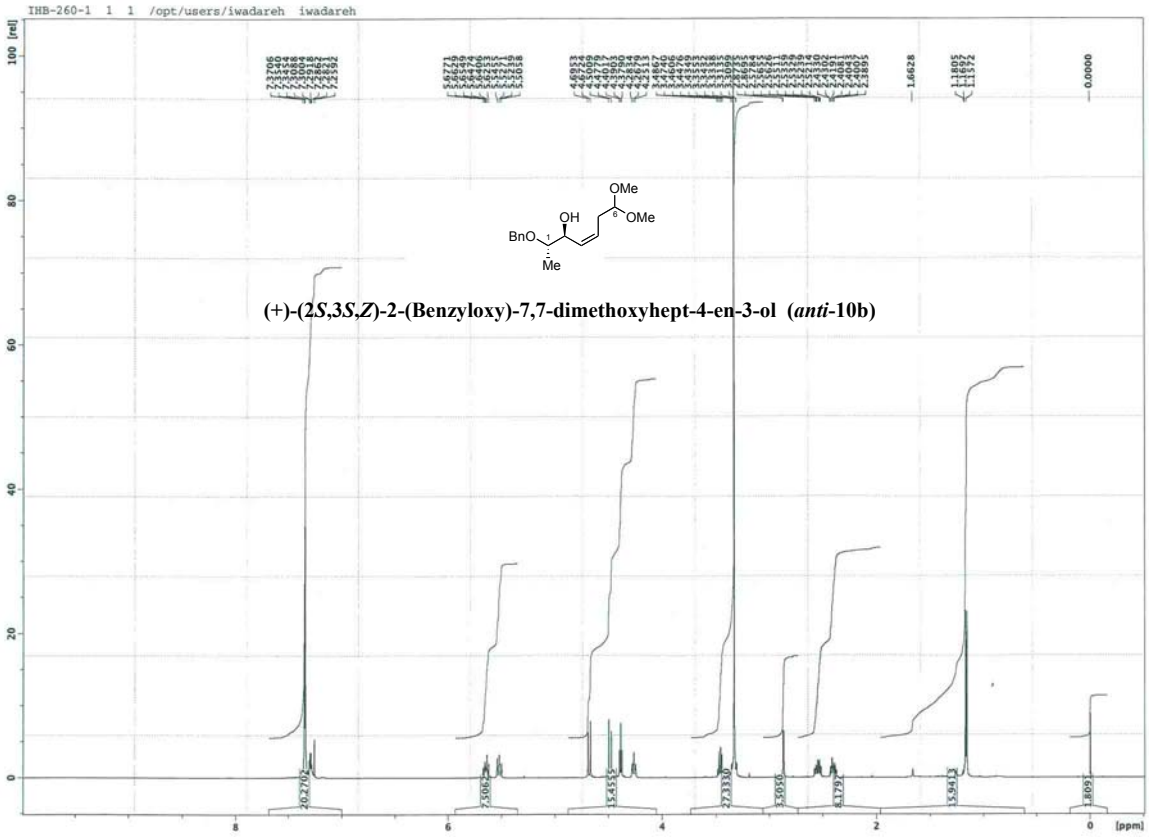


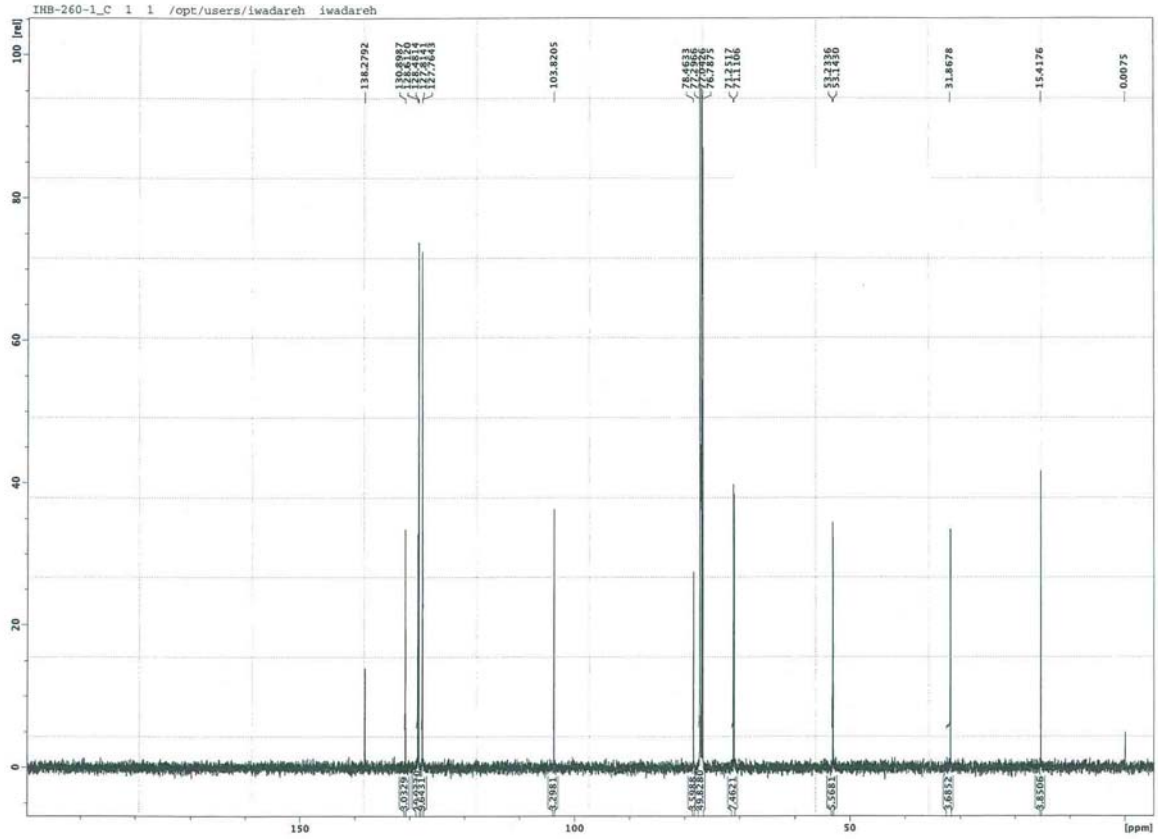


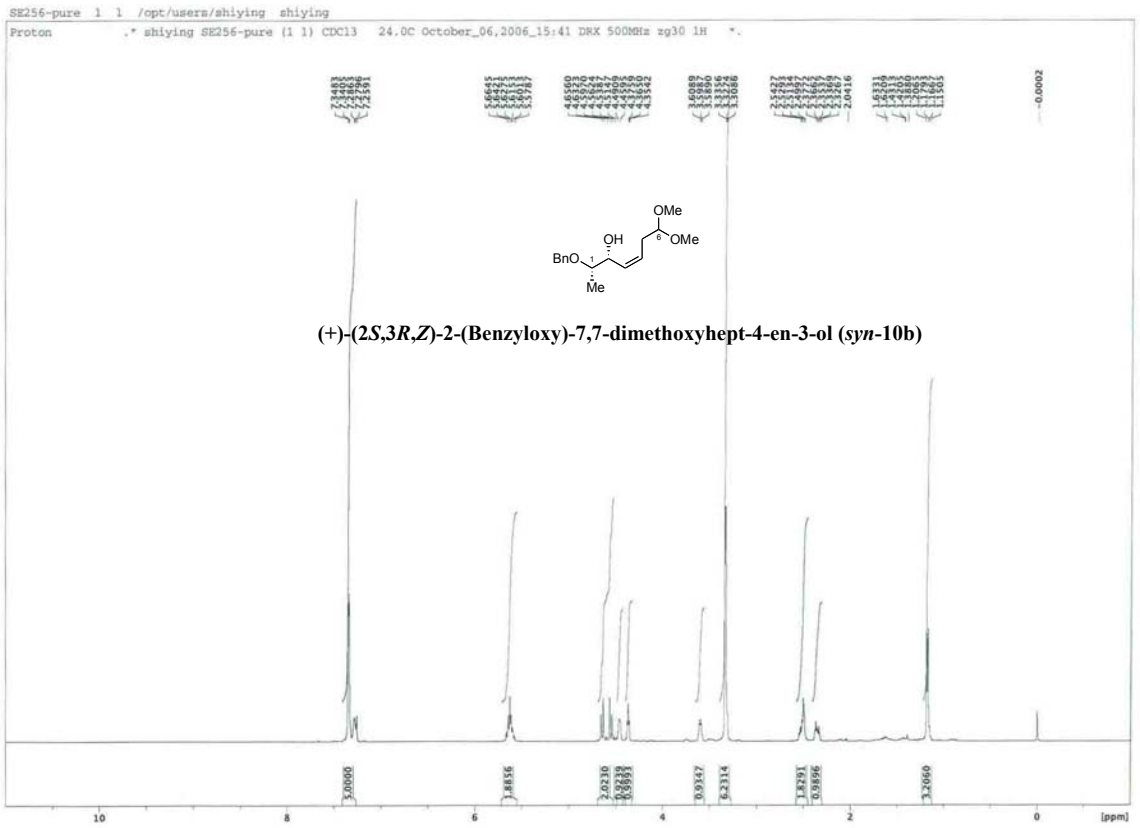
(+)-(*S*,*Z*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-ol (*S*-10a)



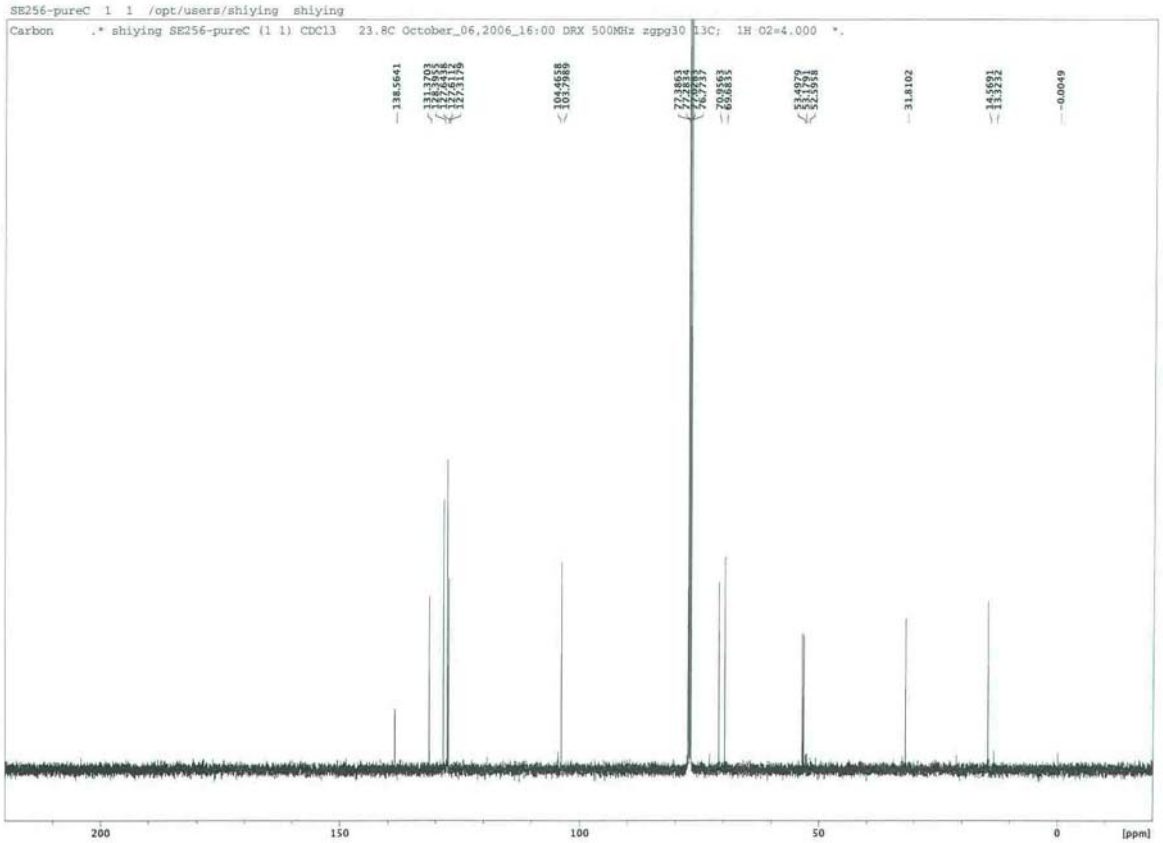


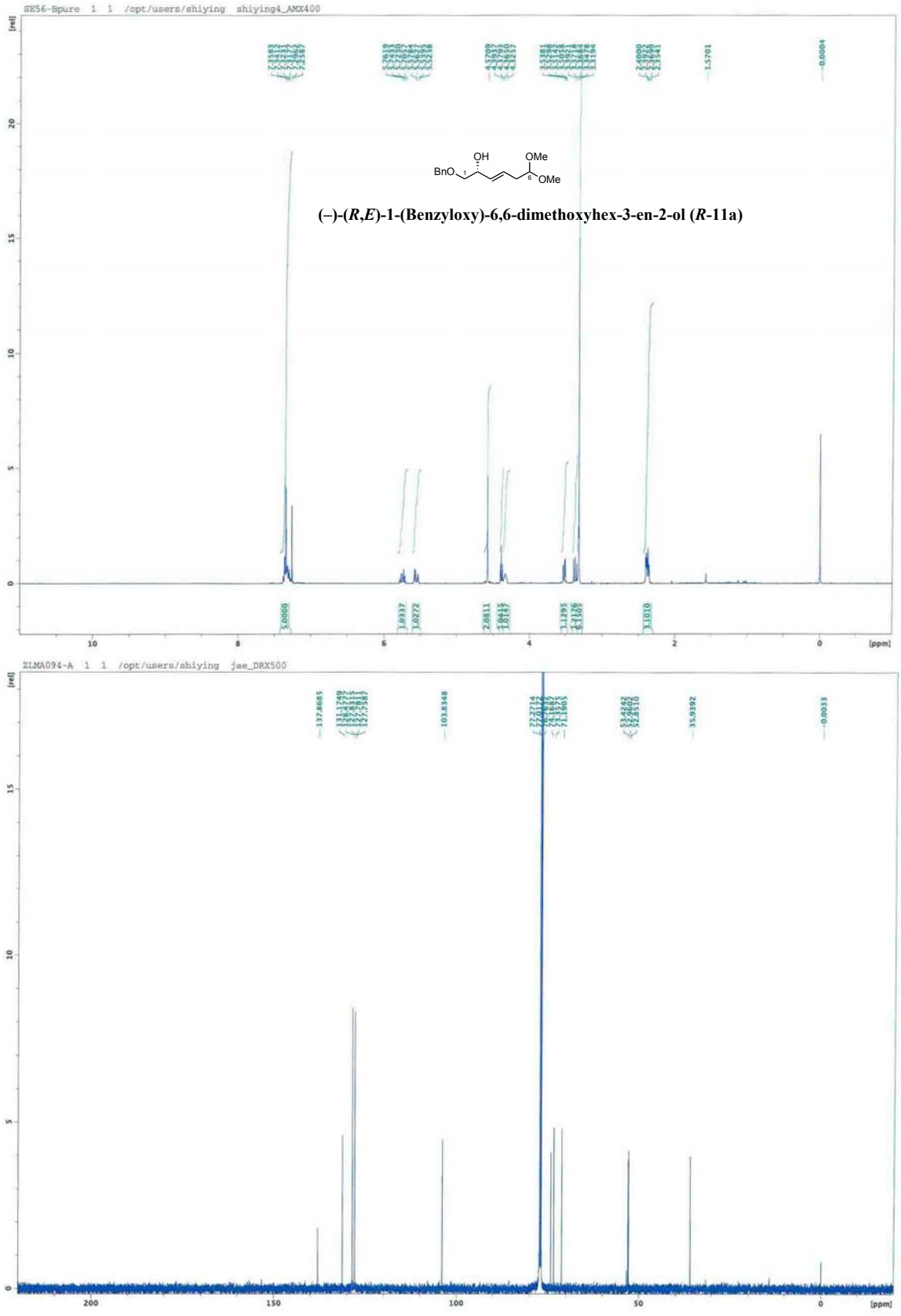
(+)-(2*S*,3*S*,*Z*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-ol (*anti*-10b)

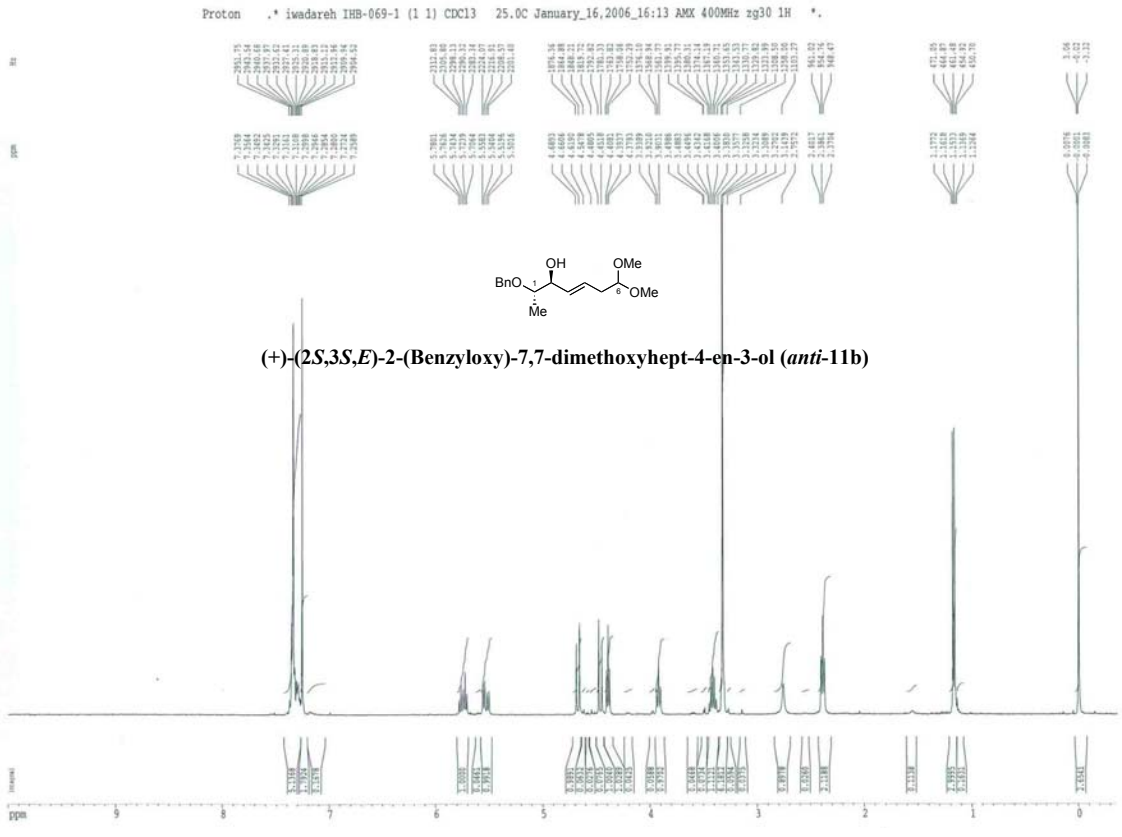




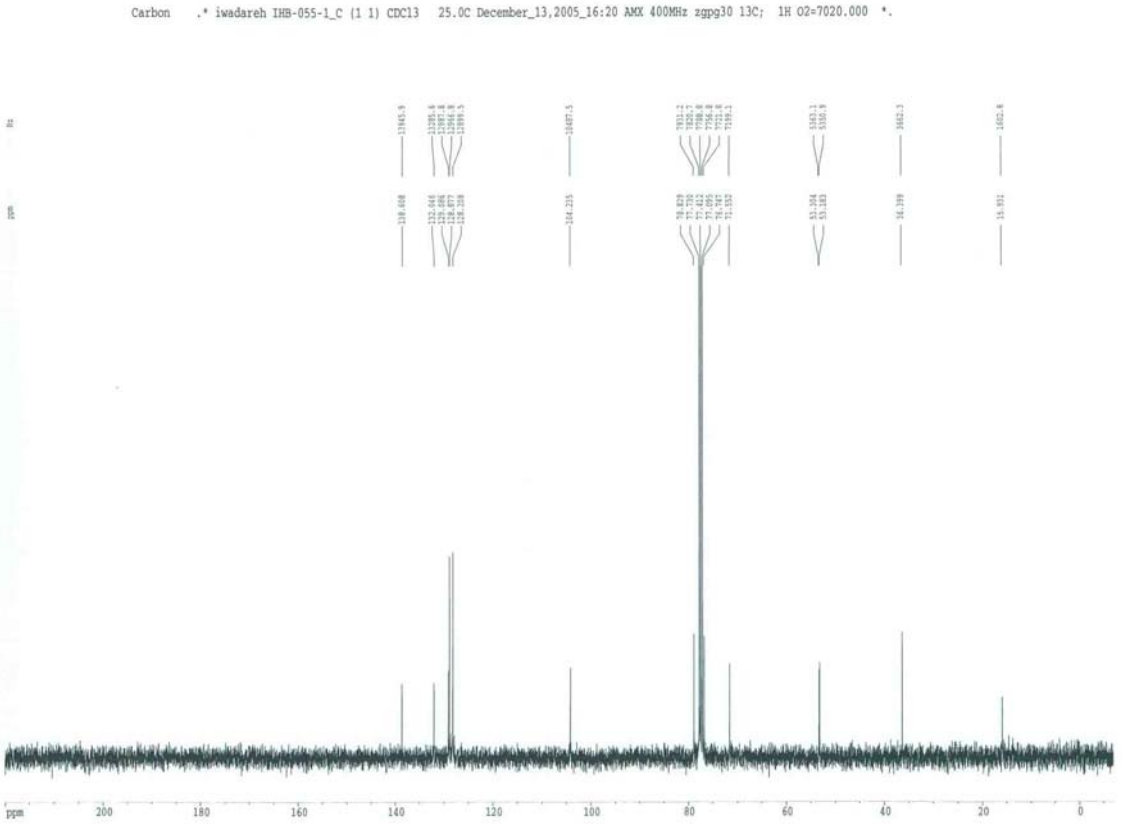
(+)-(2*S*,3*R*,*Z*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-ol (*syn*-10b)

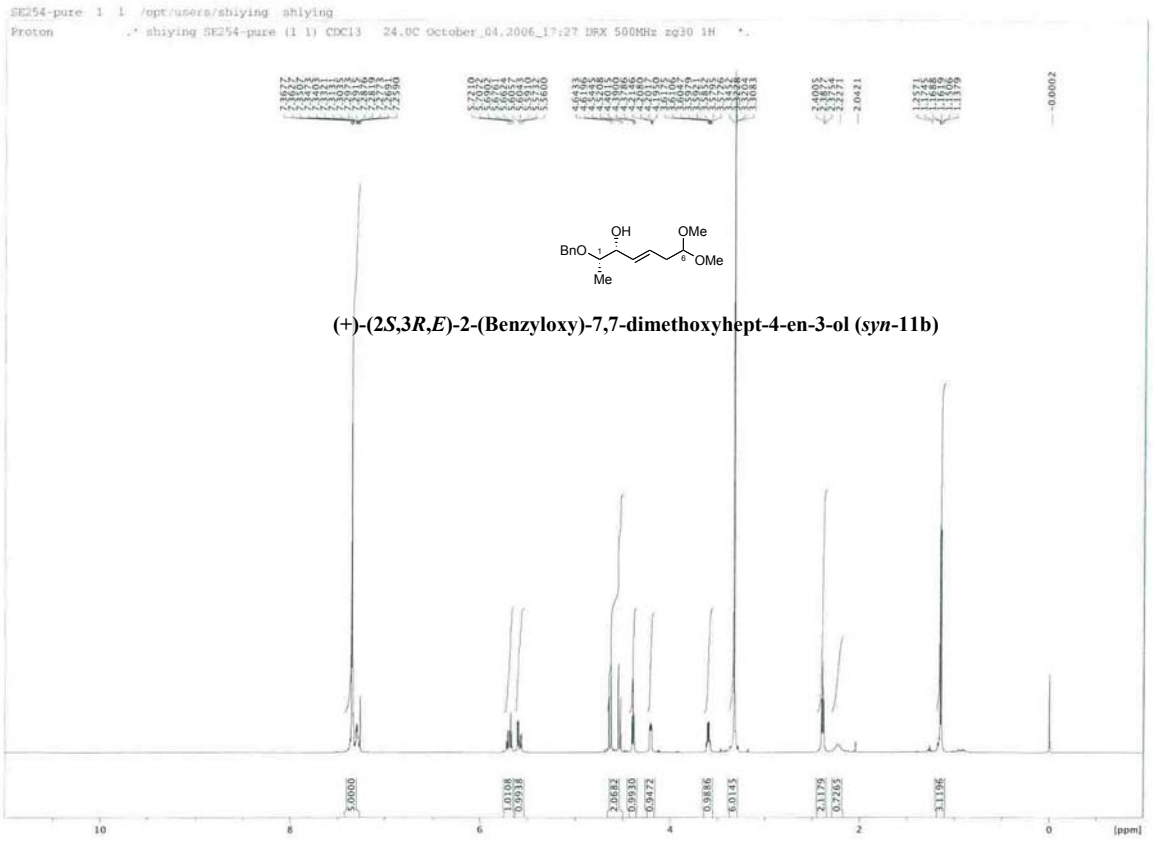



SE56-Bpure 1 1 /opt/users/shiying shiying4_AMX400
OH
OMe
BnO
OMe
(–)-(R,E)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-ol (R-11a)
ZLMA094-A 1 1 /opt/users/shiying jae_DRX500
[ppm]

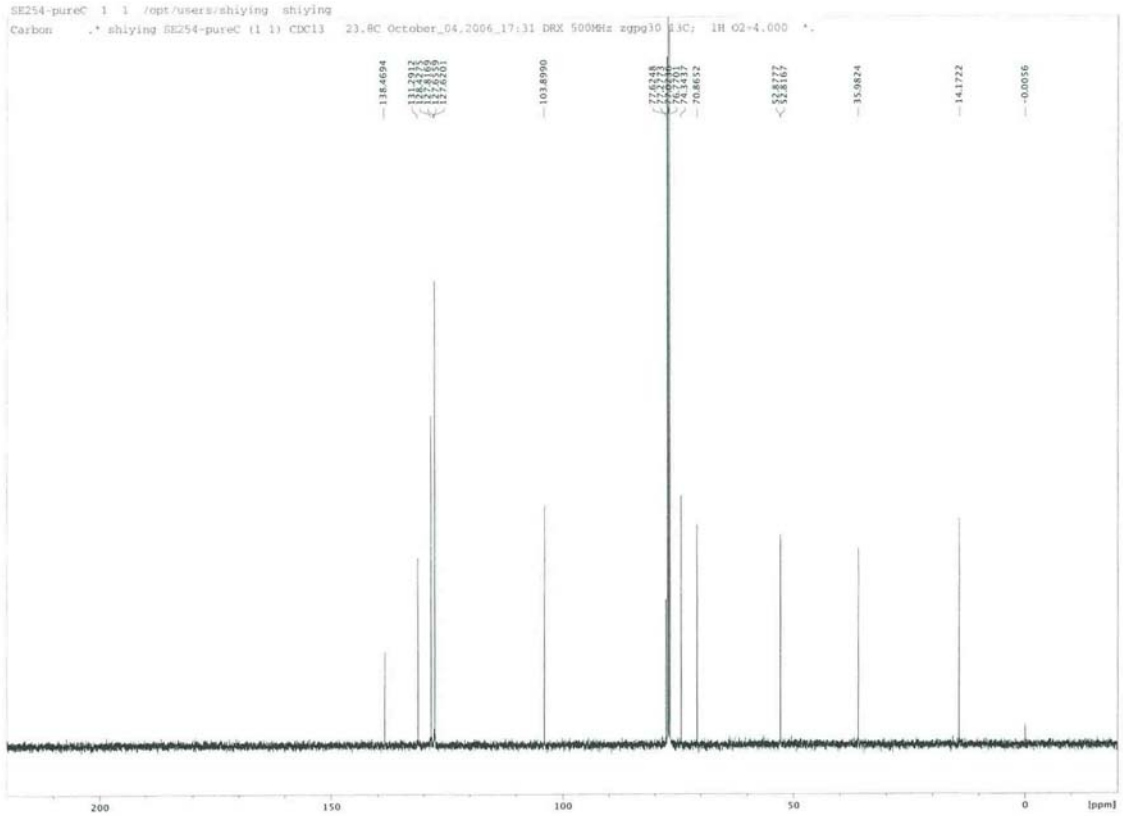


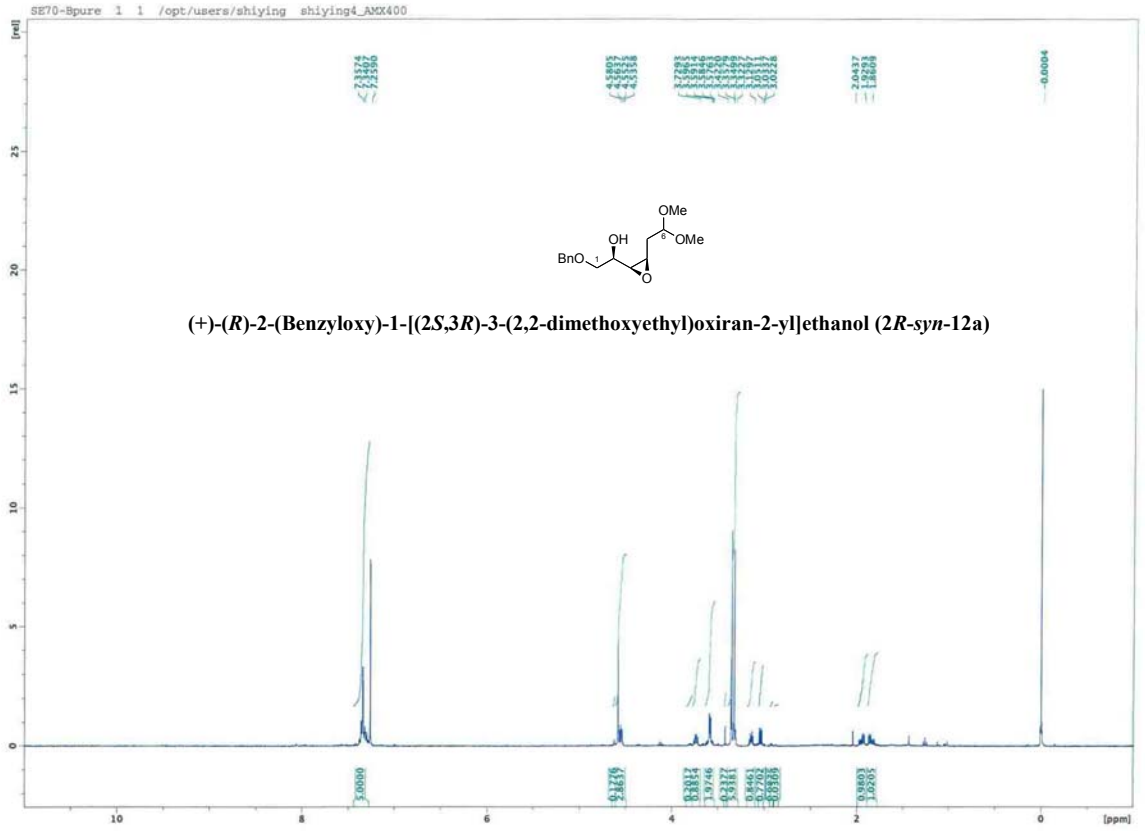
(+)-(2*S*,3*S*,*E*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-ol (*anti*-11b)



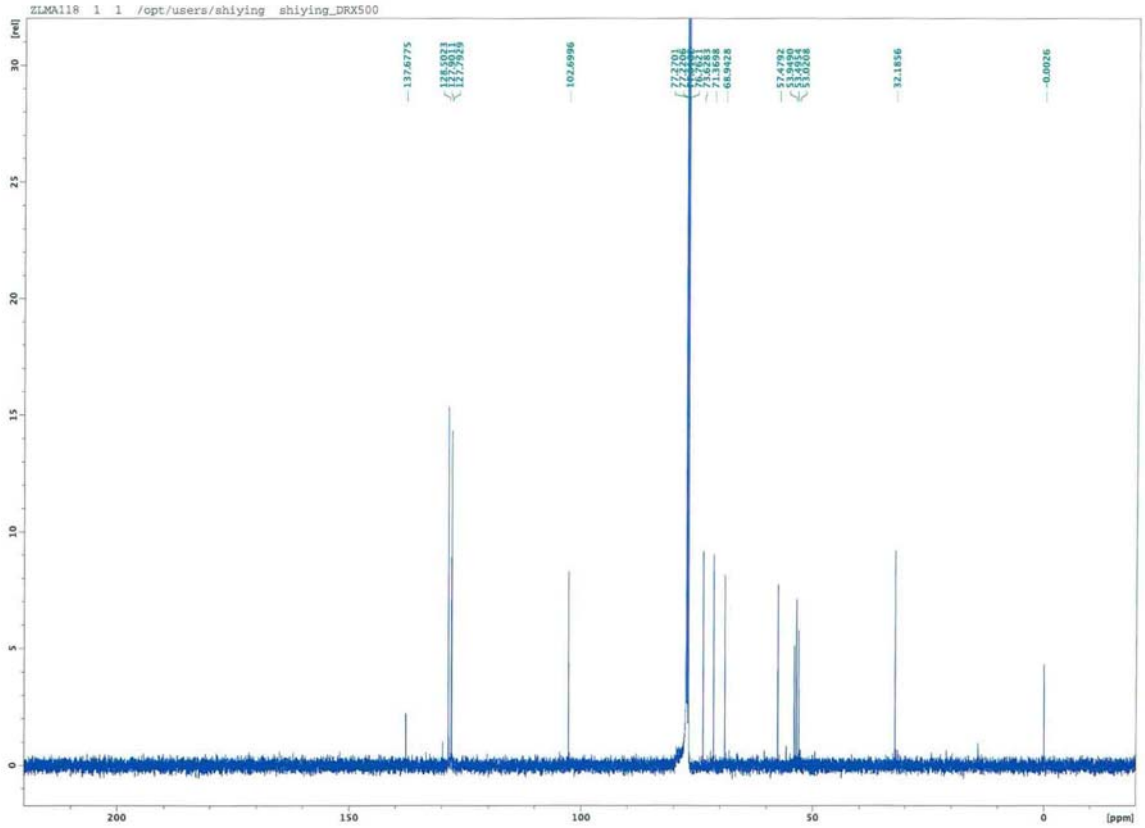


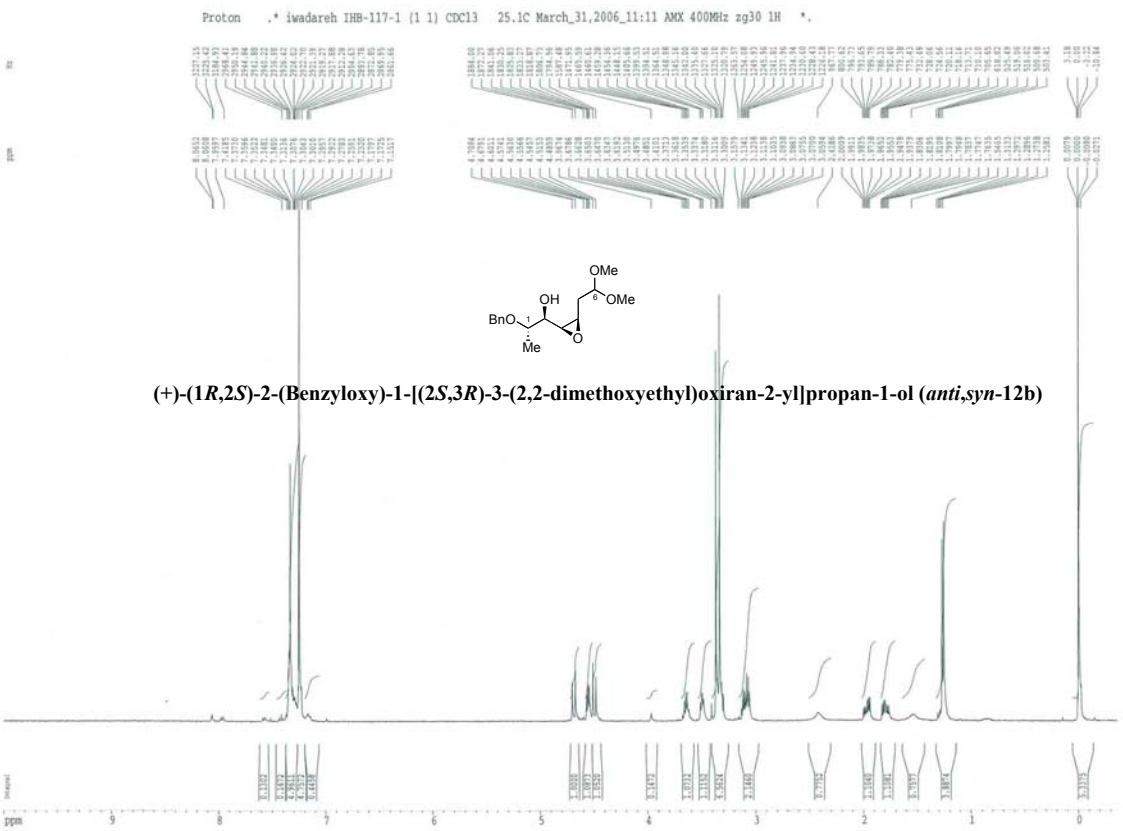
(+)-(2*S*,3*R*,*E*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-ol (*syn*-11b)



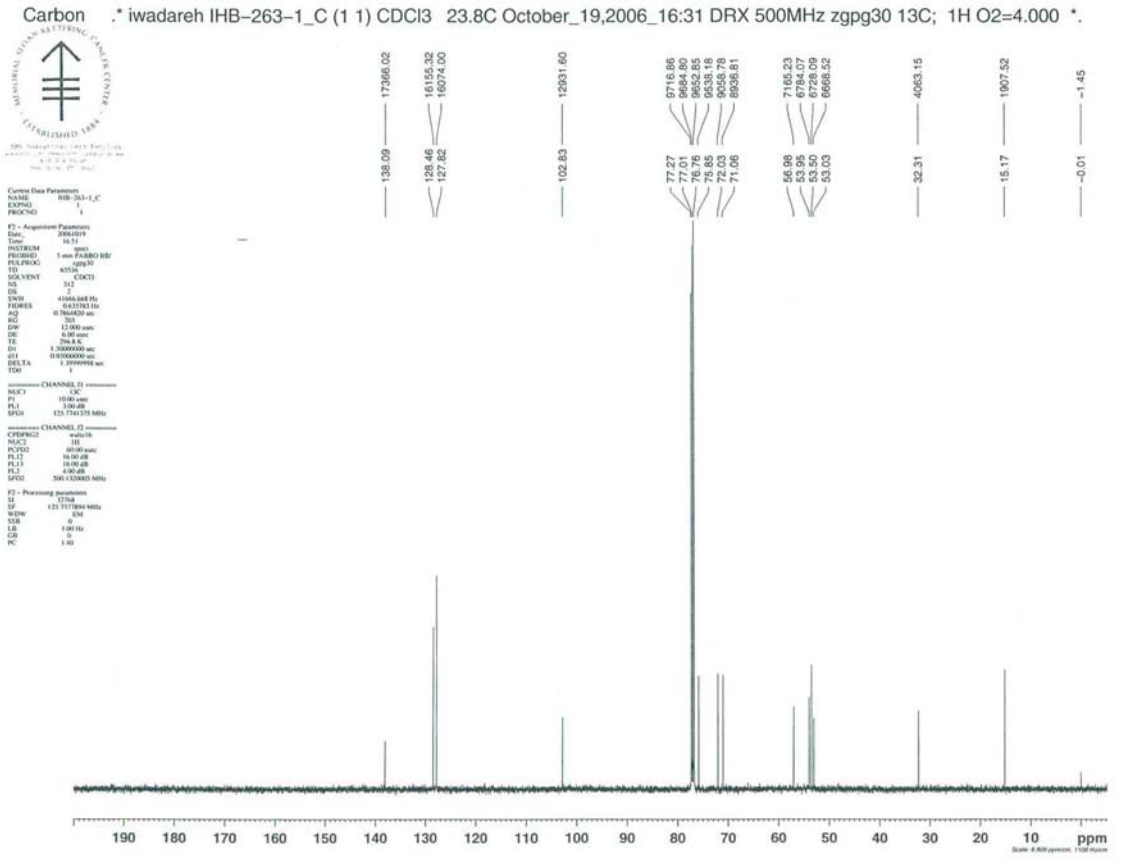


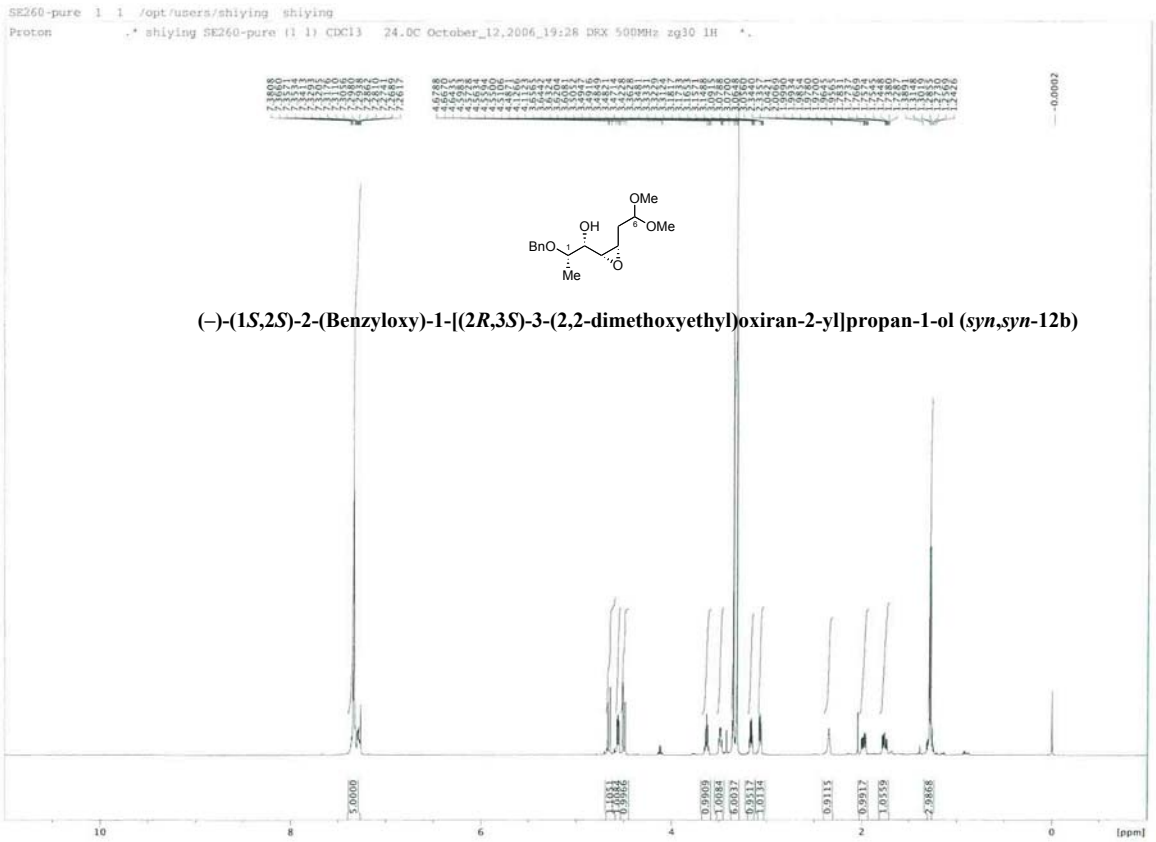
(+)-(*R*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*R*-*syn*-12a)



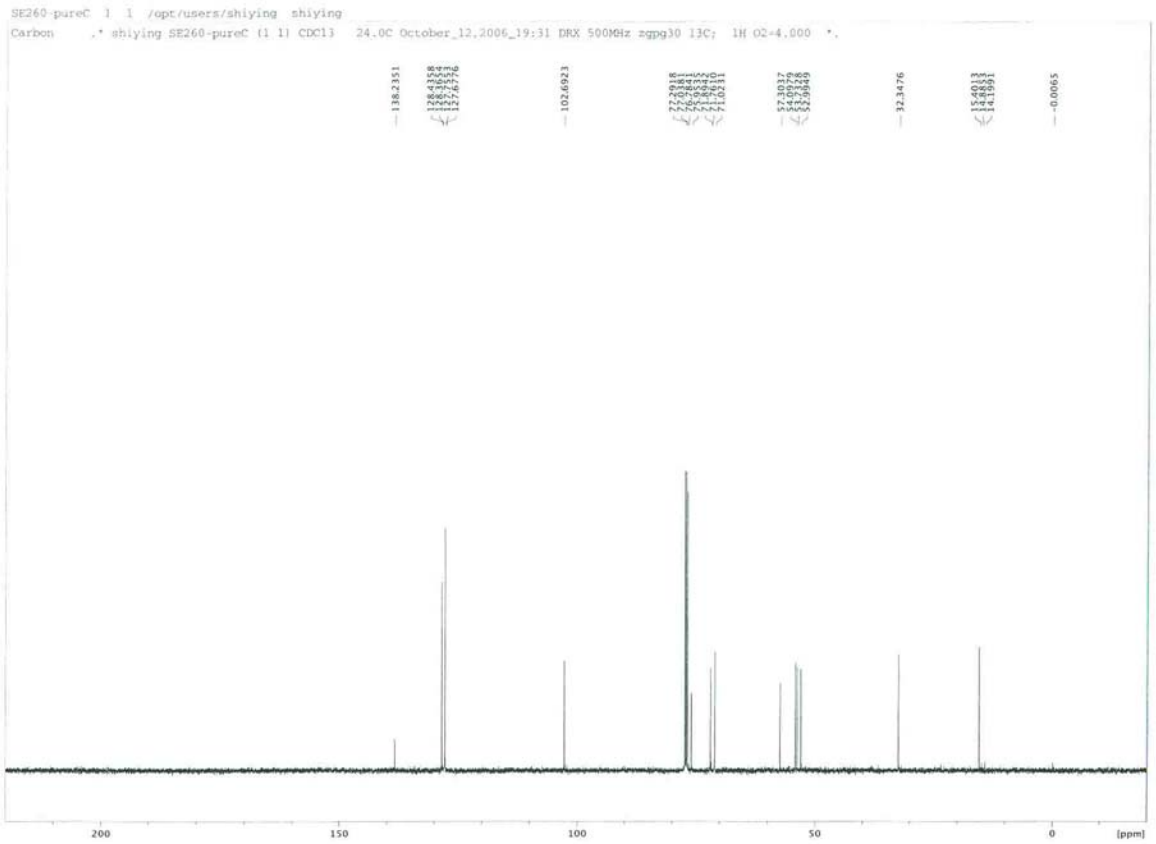


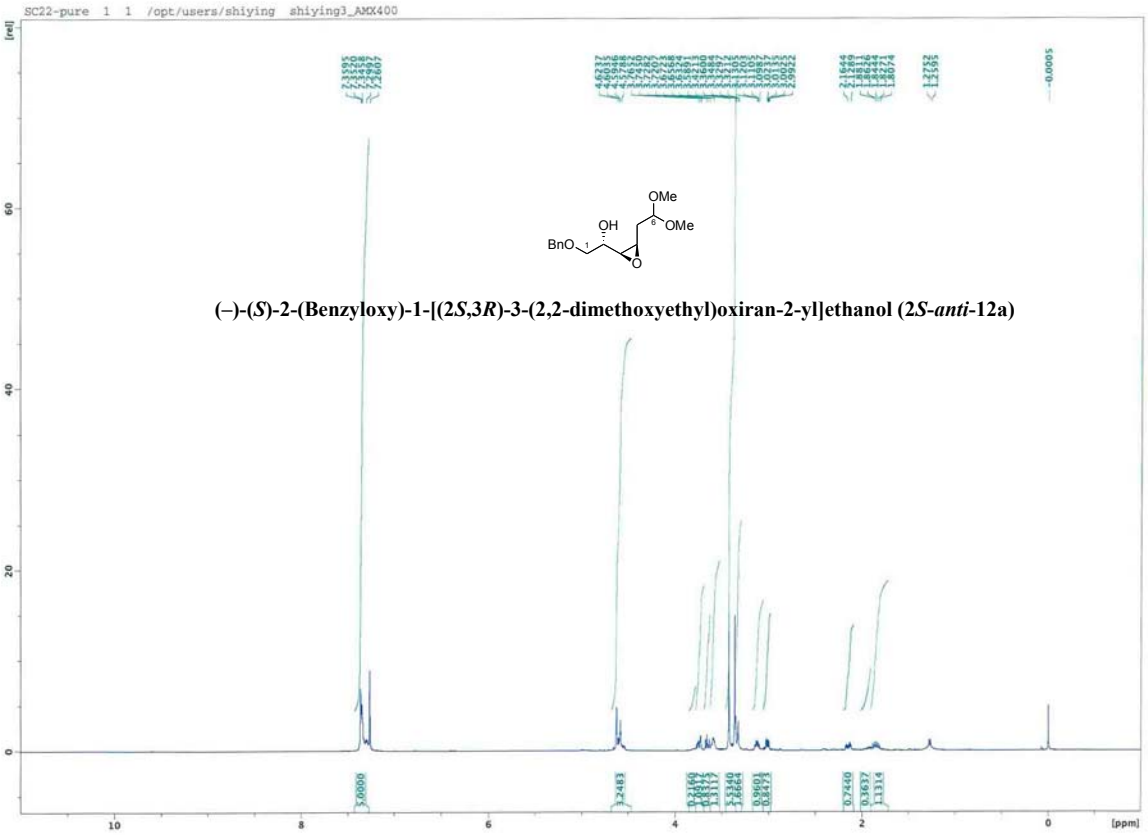
(+)-(1*R*,2*S*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*anti*,*syn*-12b)



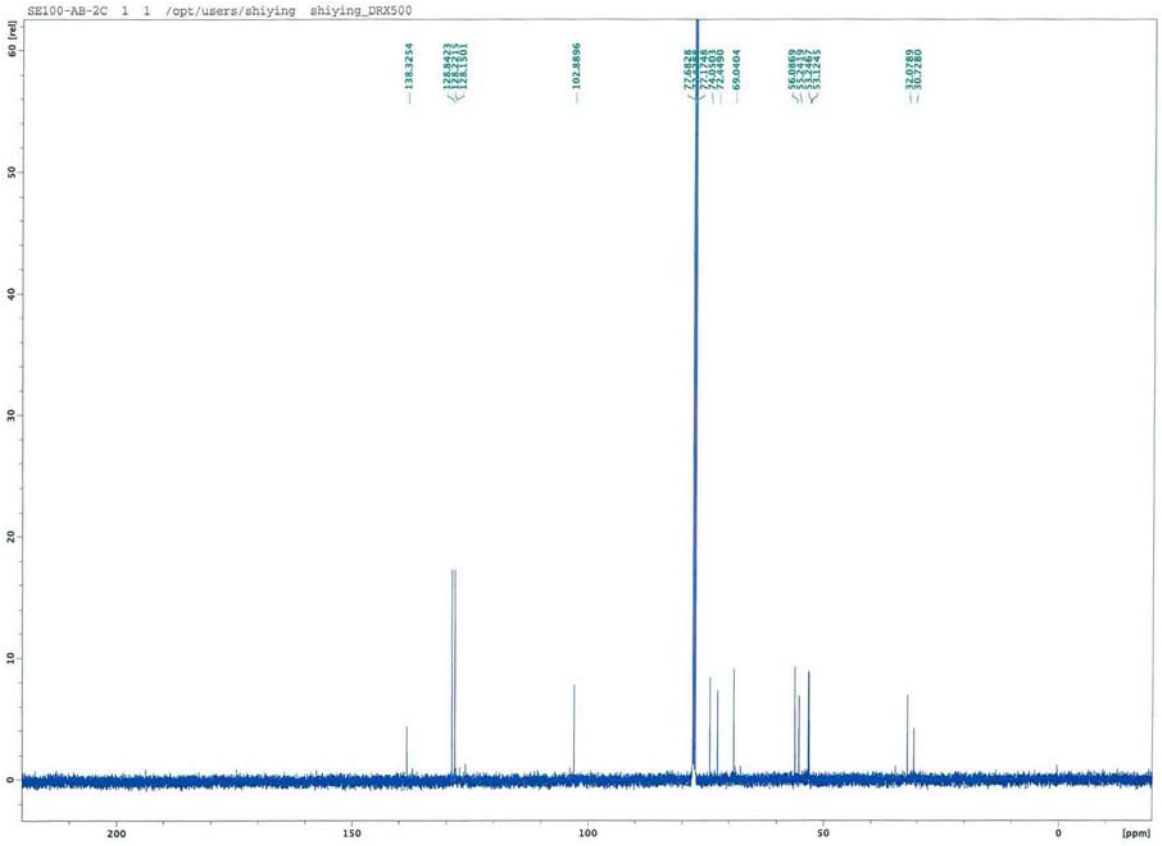


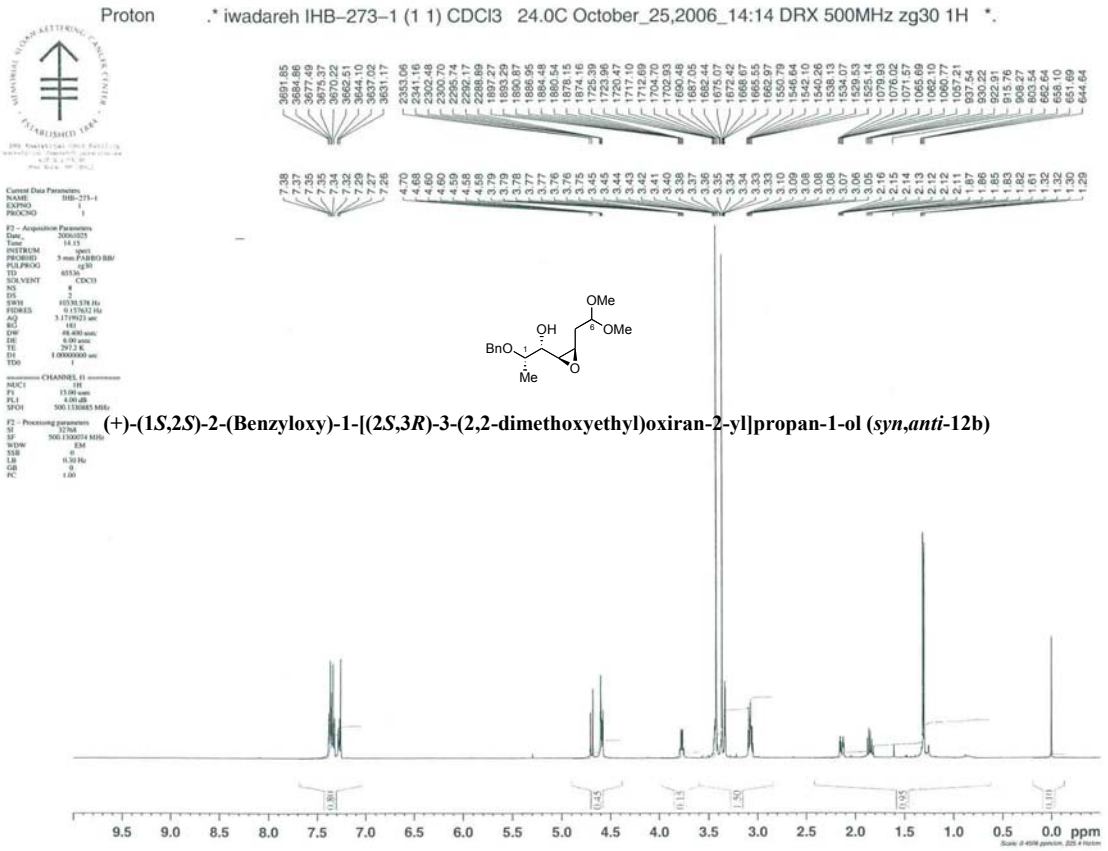
(–)-(1*S*,2*S*)-2-(Benzyloxy)-1-[(2*R*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*syn*,*syn*-12b)



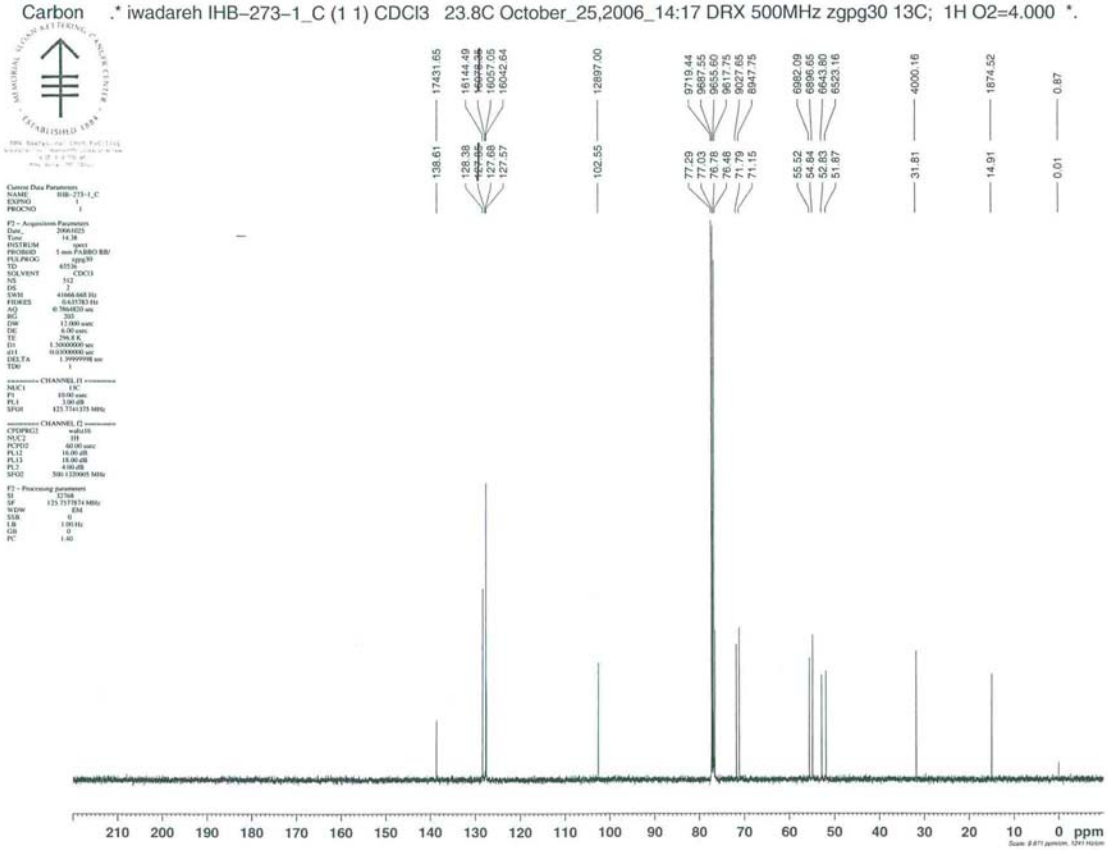


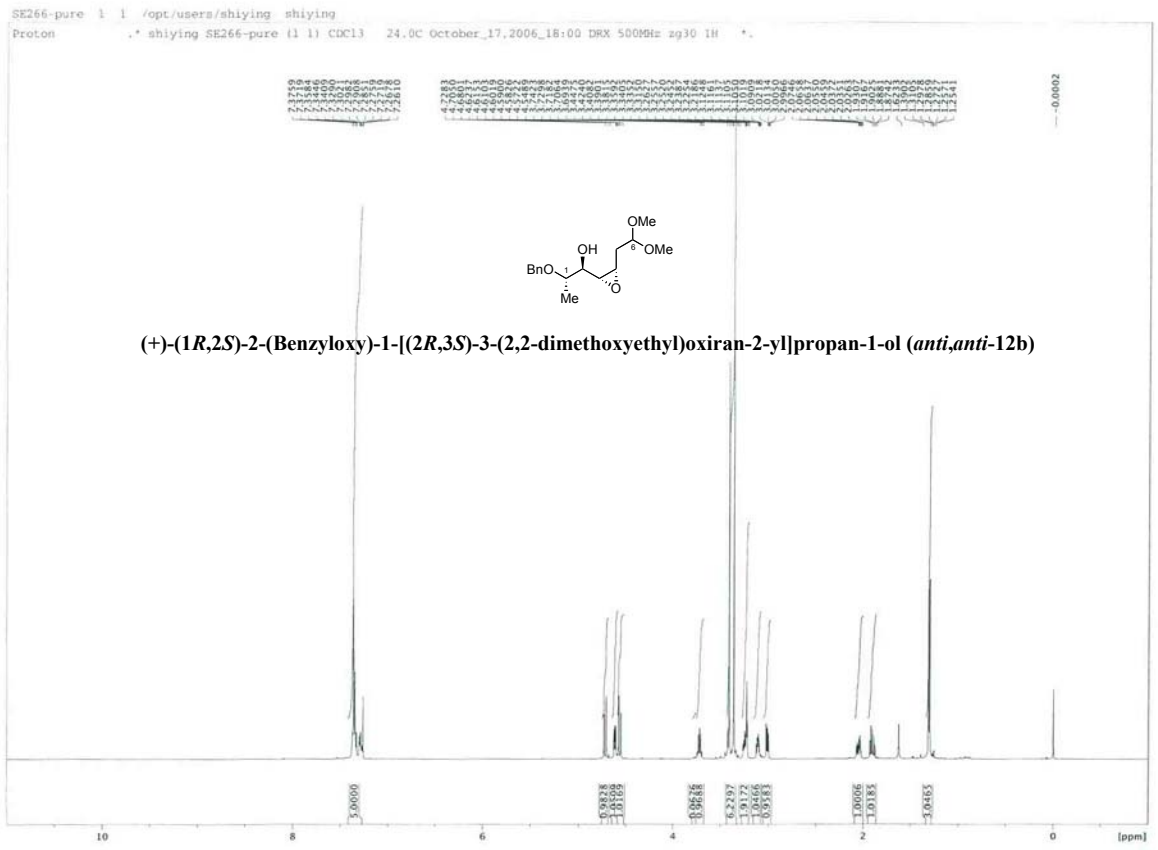
(–)-(*S*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*S*-*anti*-12a)



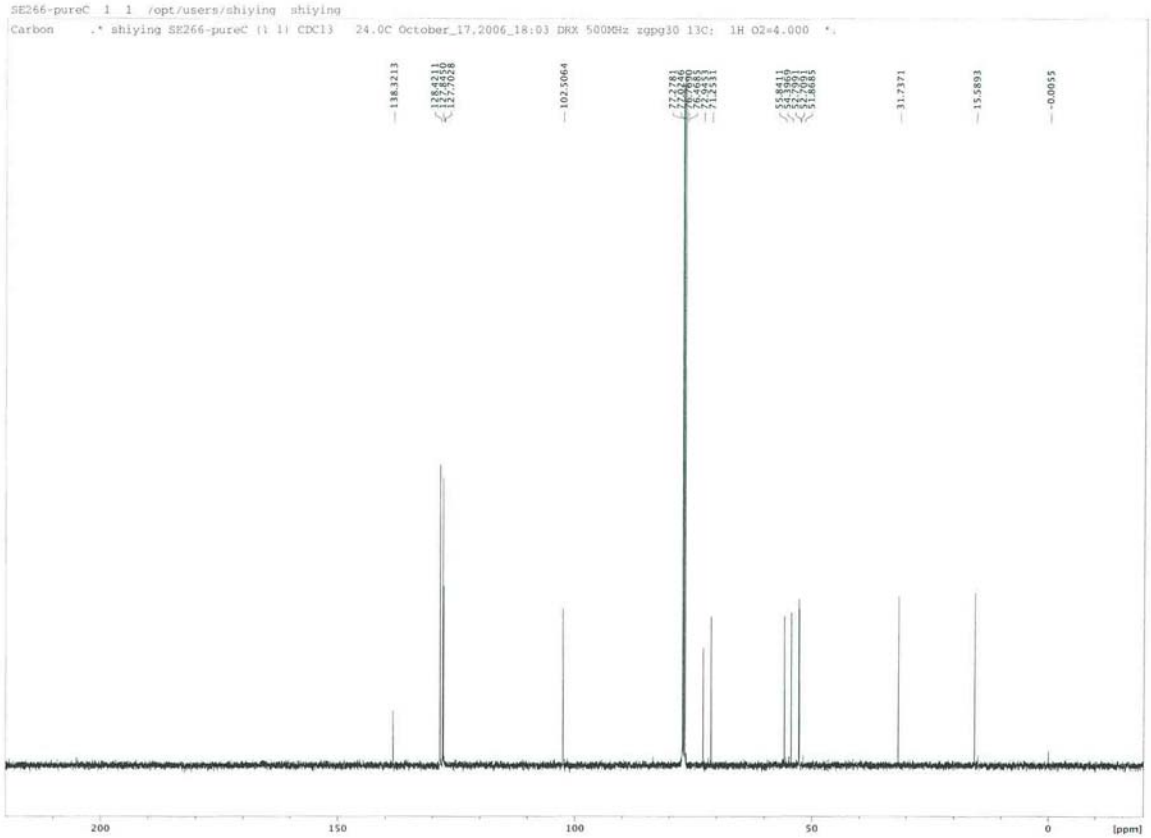


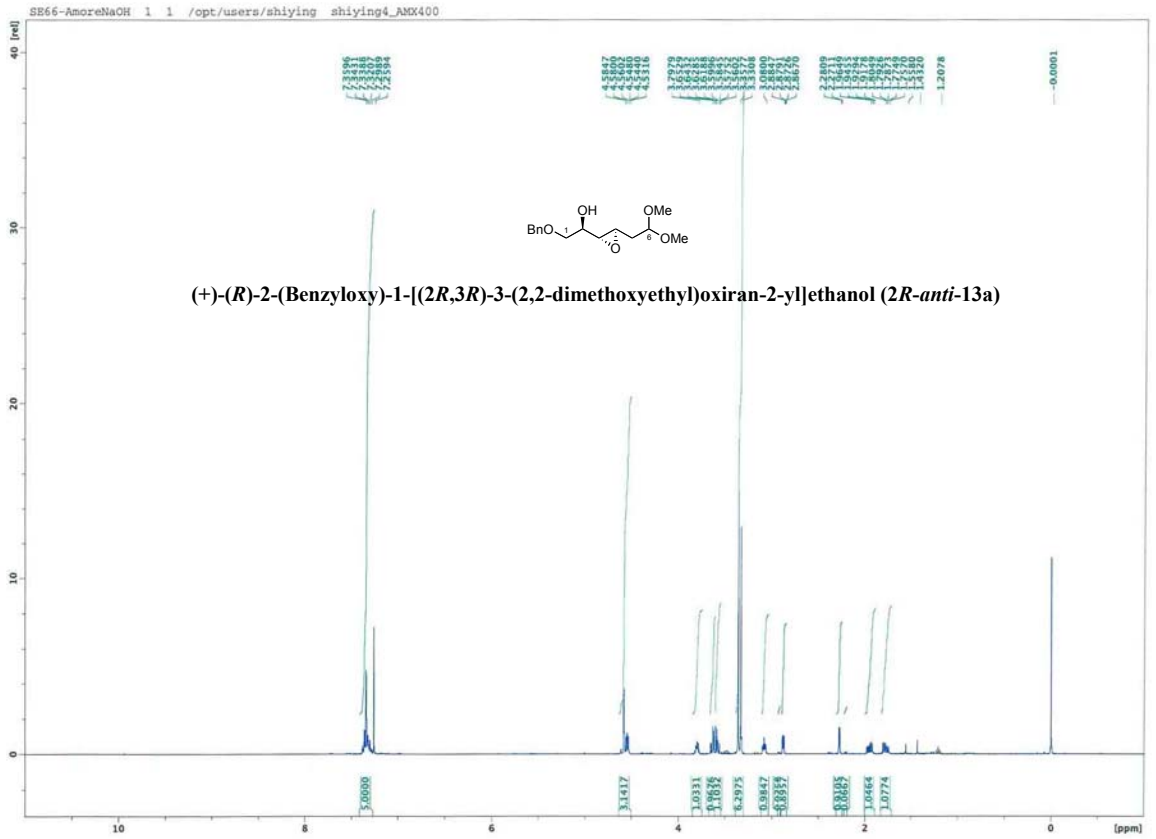
(+)-(1*S*,2*S*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*syn*,*anti*-12b)



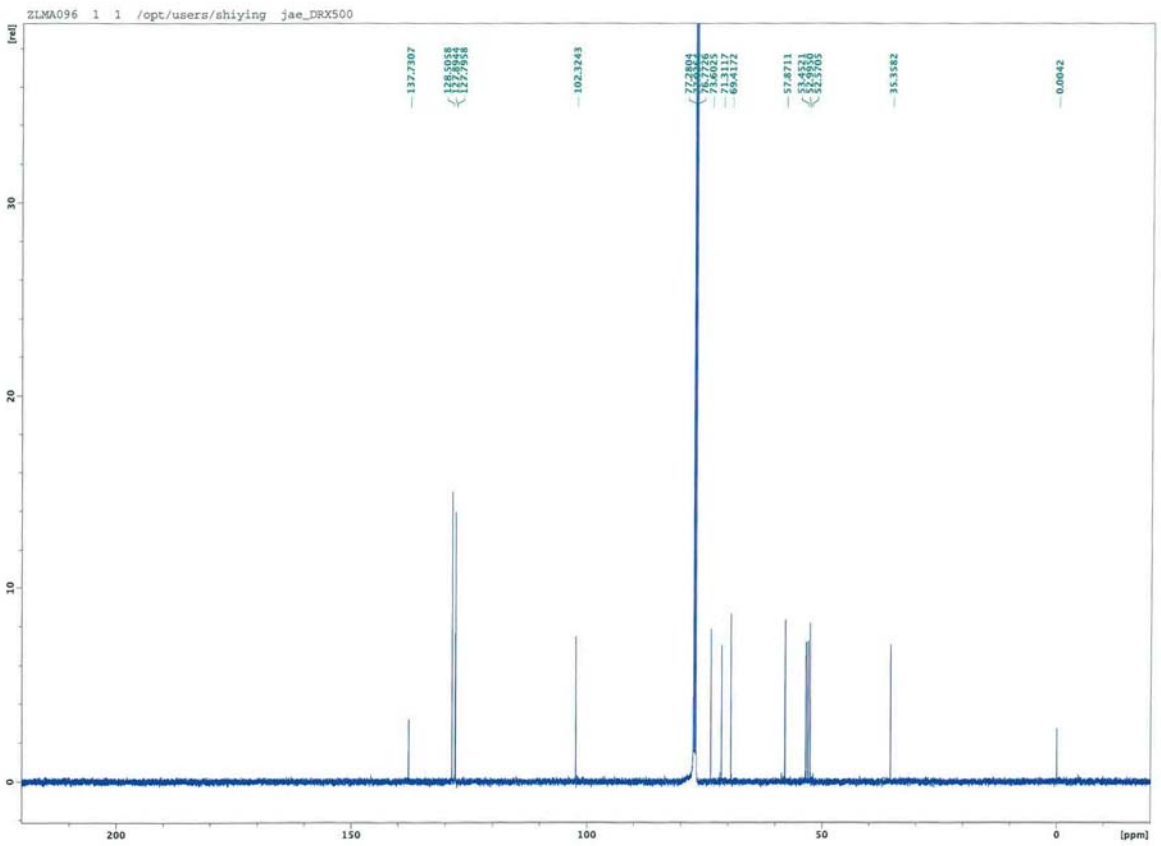


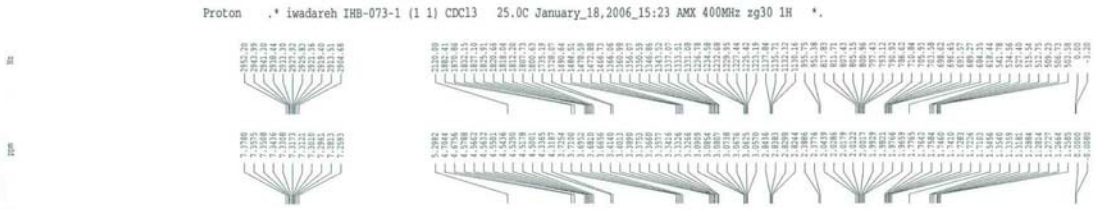
(+)-(1*R*,2*S*)-2-(Benzyloxy)-1-[(2*R*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*anti*,*anti*-12b)



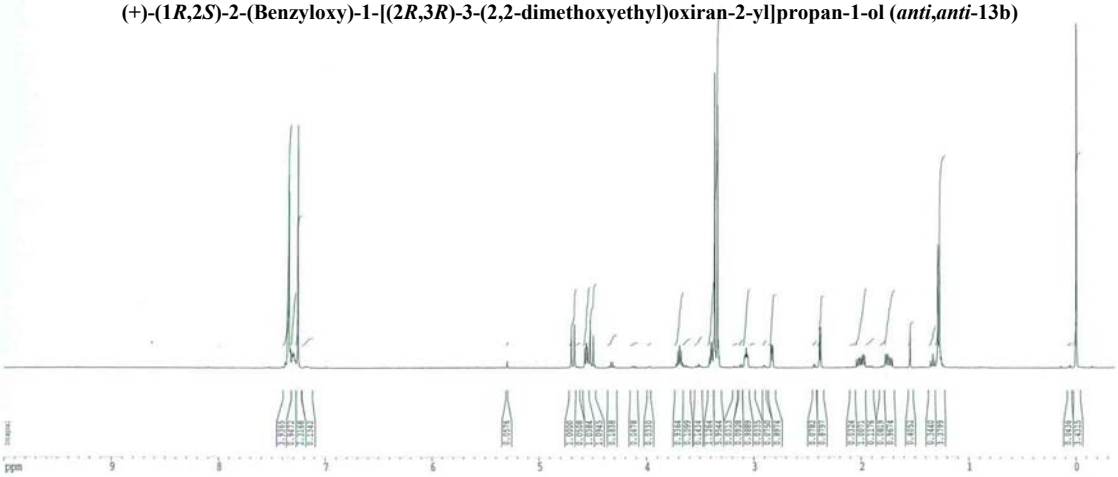


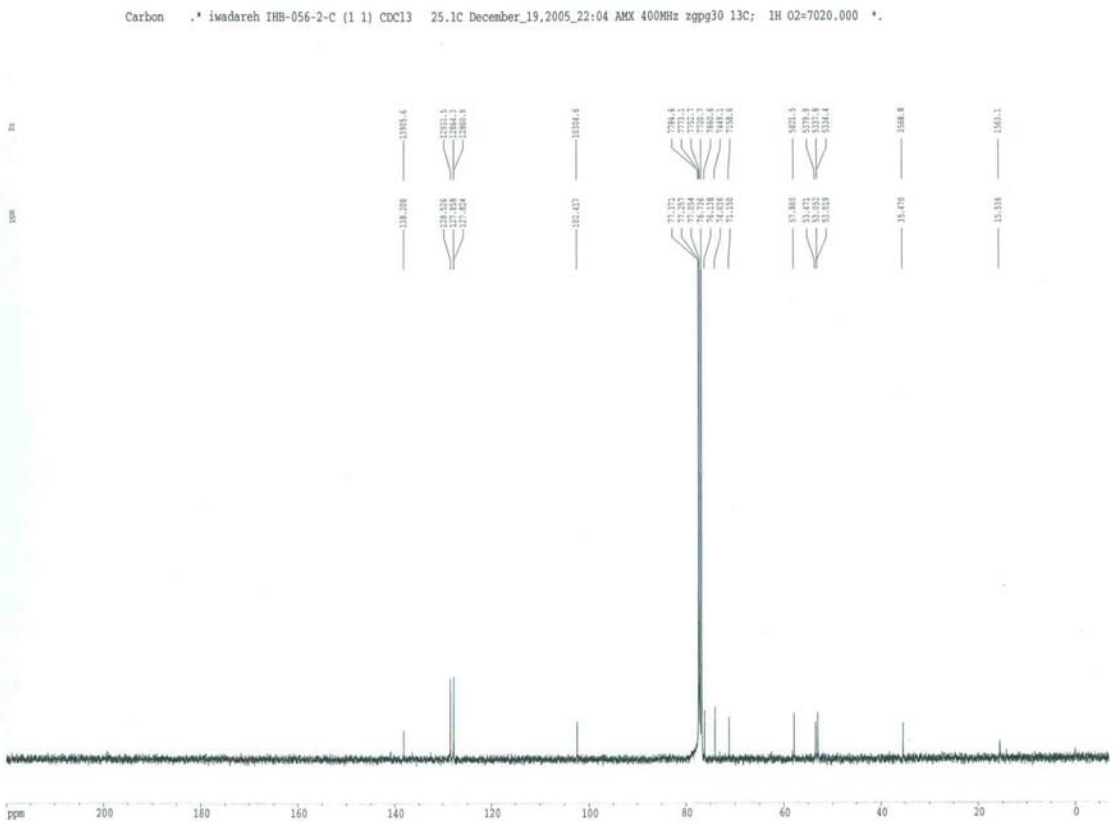
(+)-(*R*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*R*-*anti*-13a)

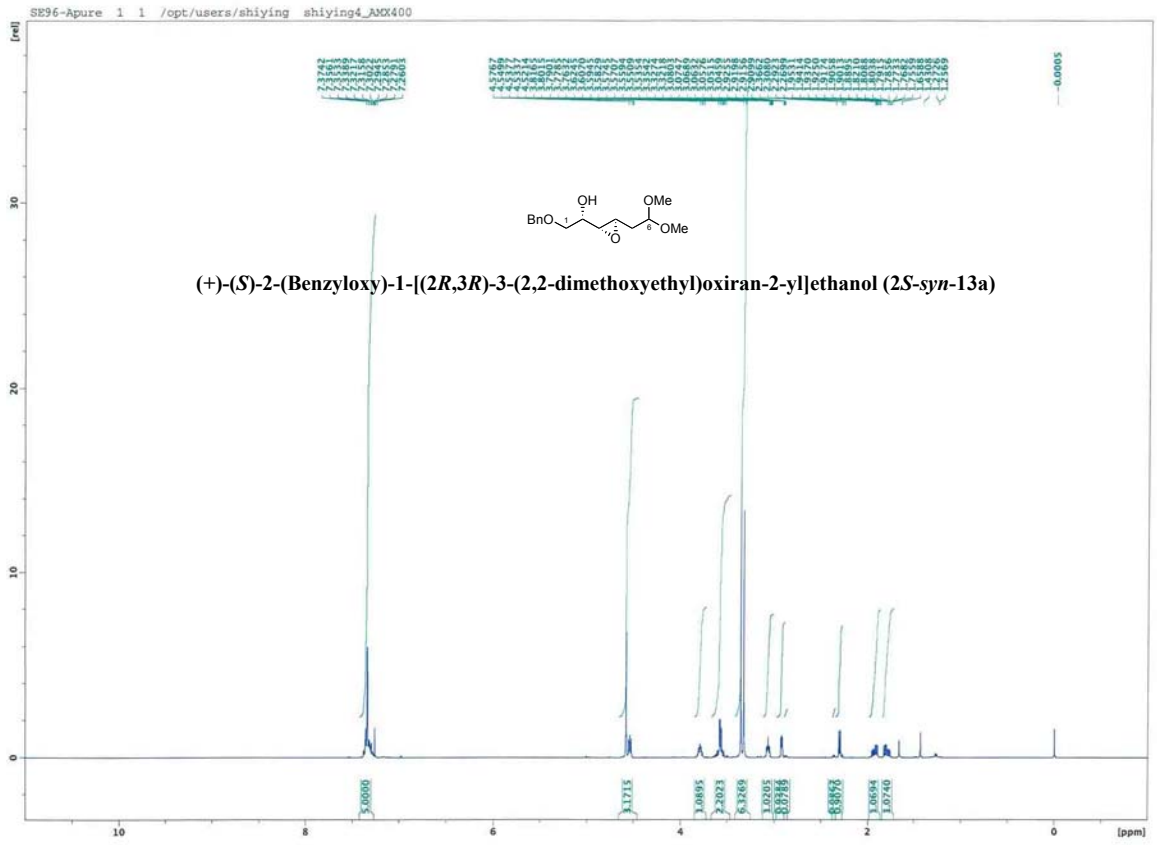




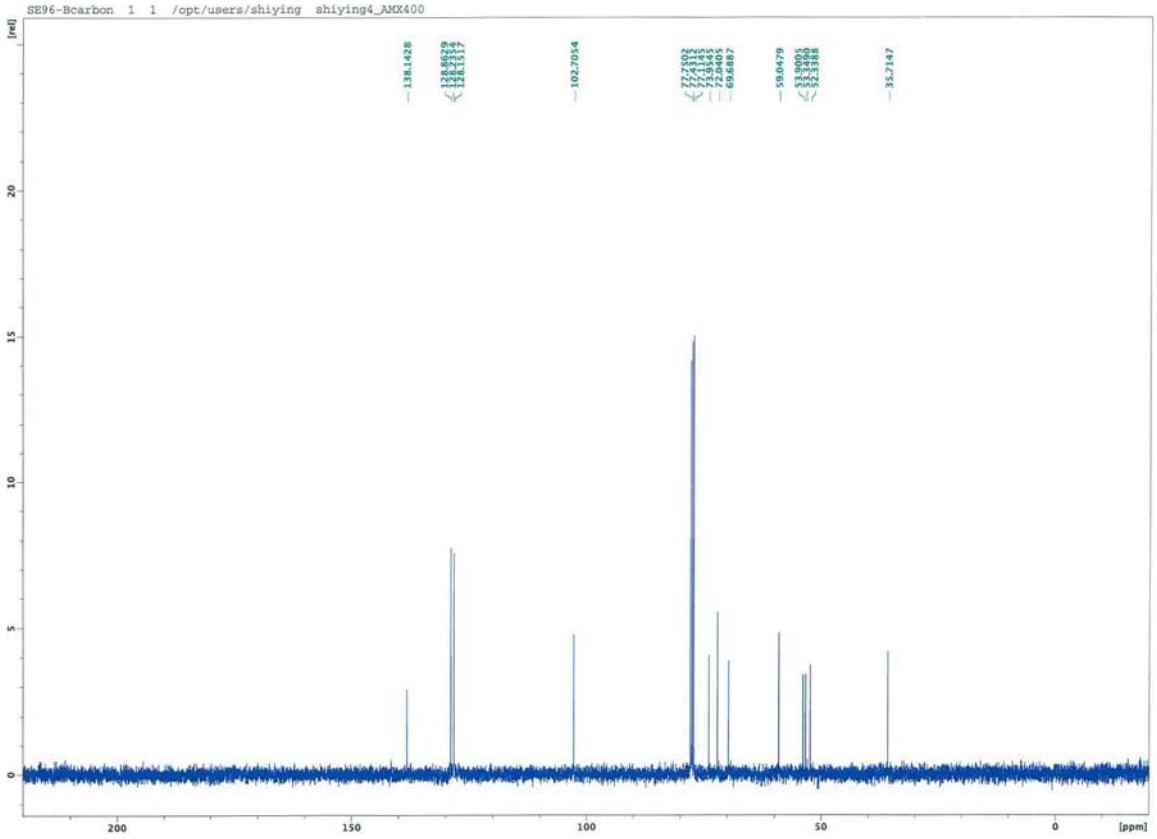
(+)-(1*R*,2*S*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*anti*,*anti*-13b)

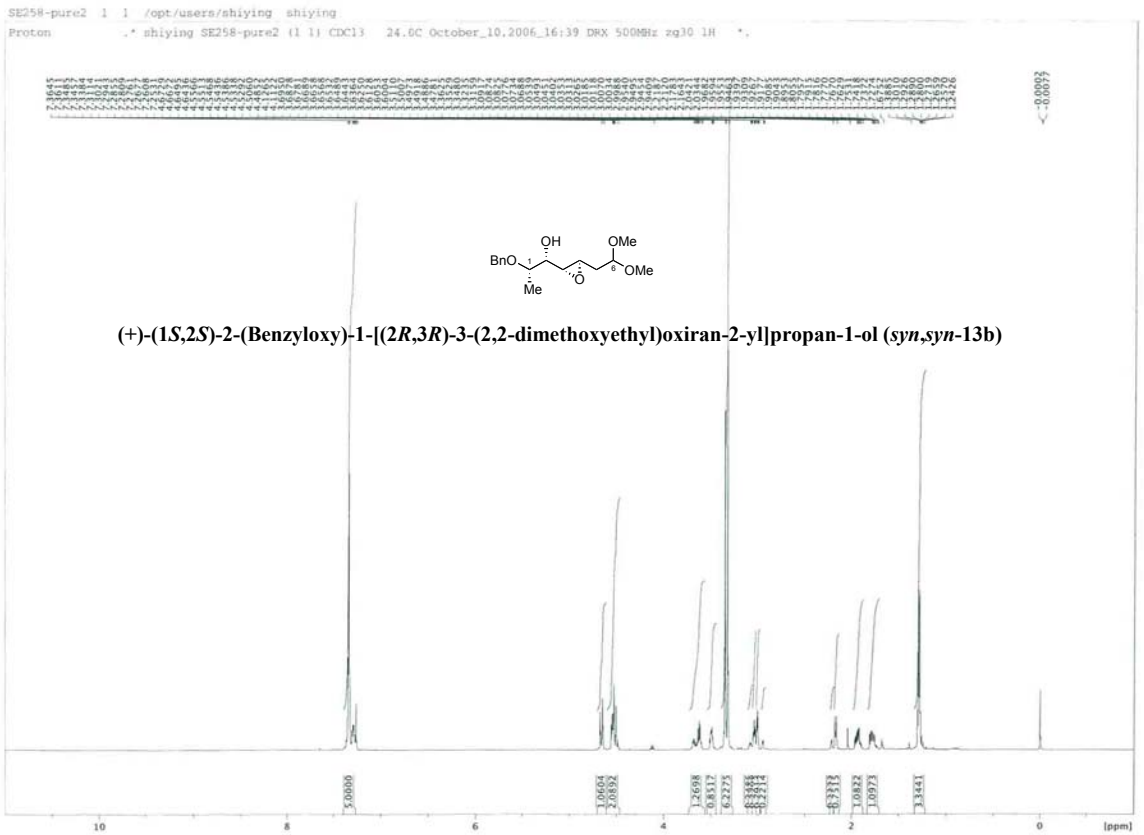




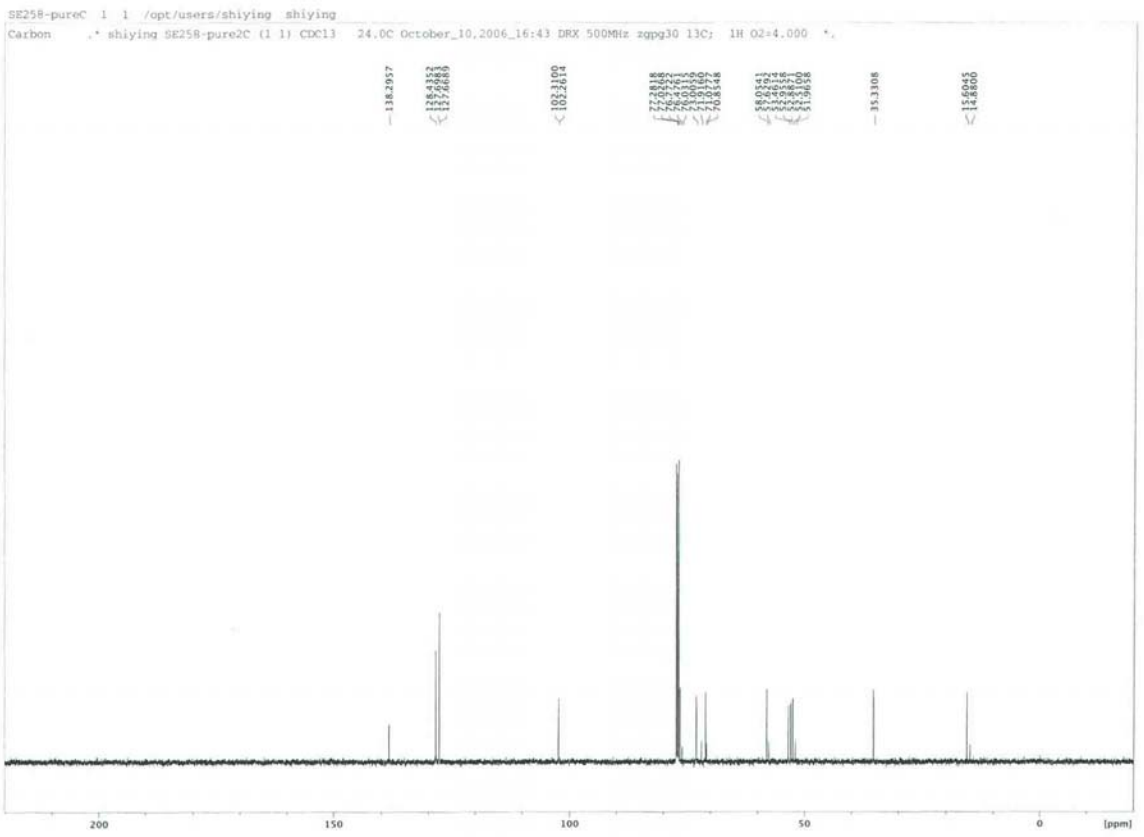


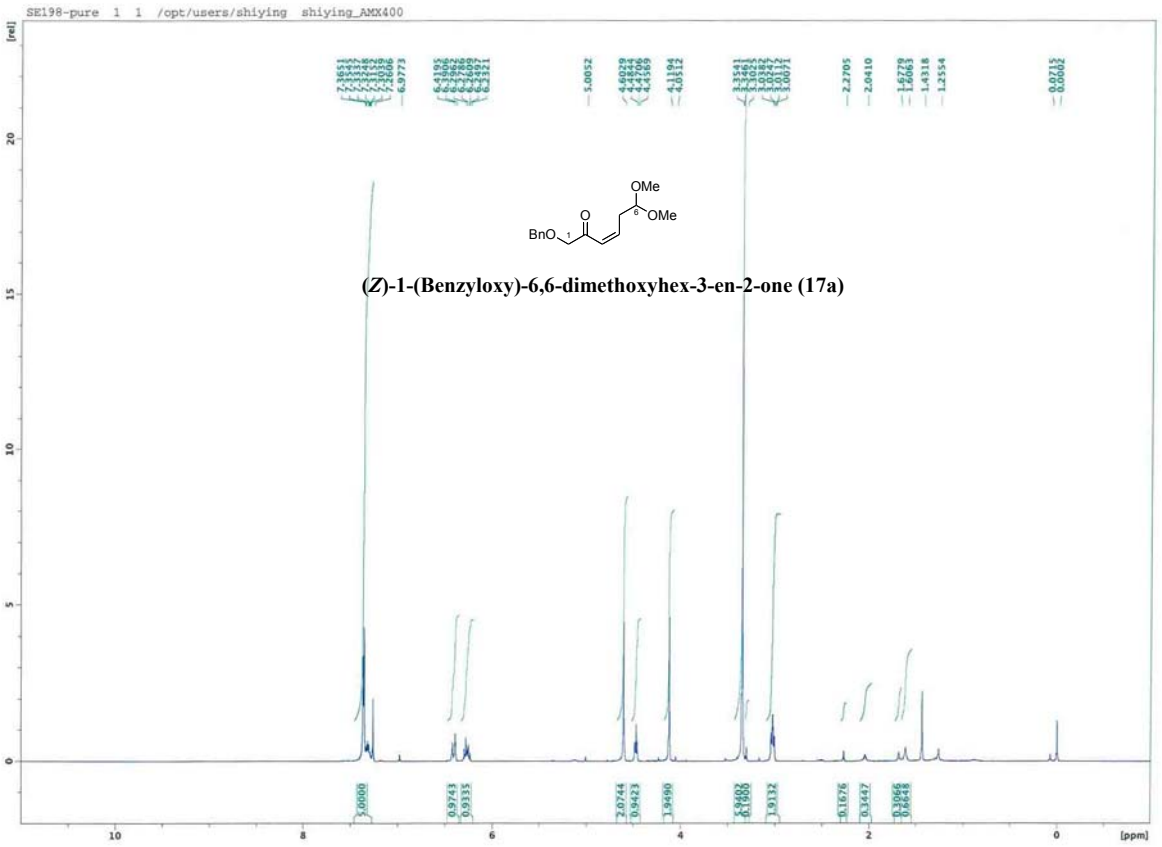
(+)-(*S*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanol (2*S*-*syn*-13a)



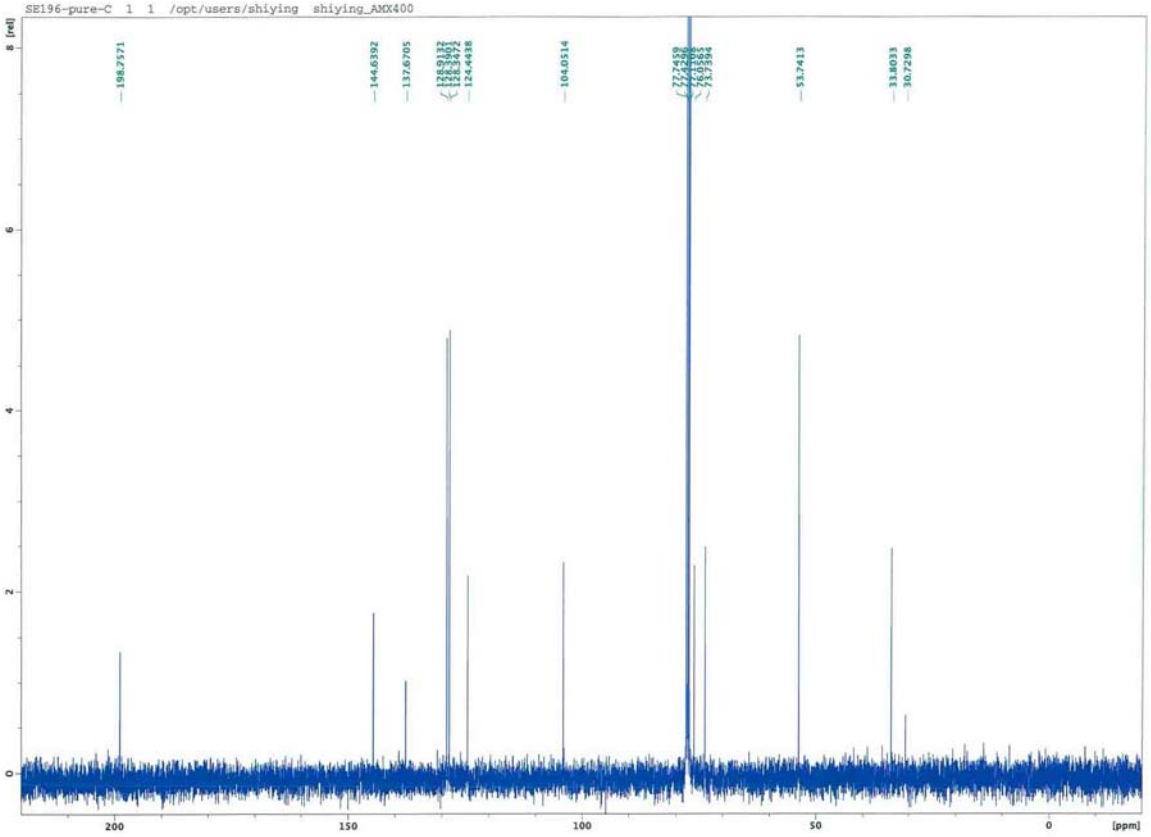


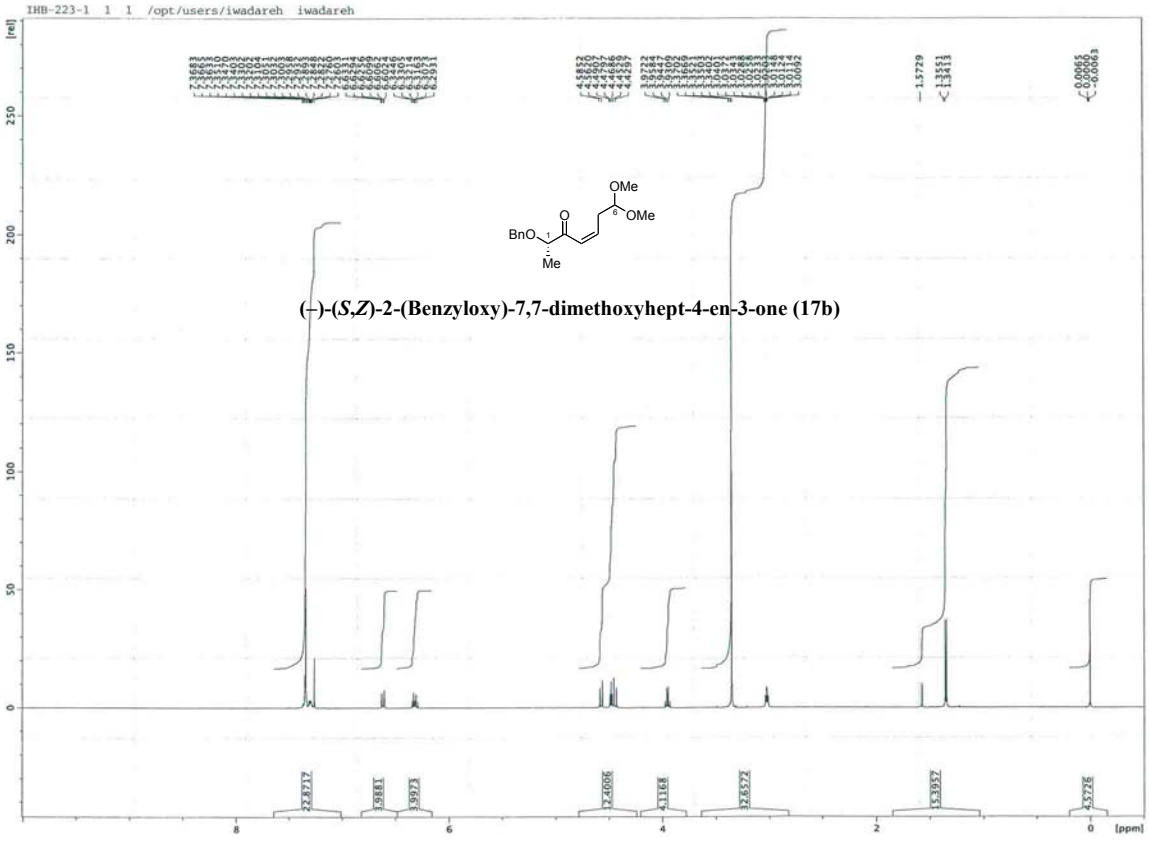
(+)-(1*S*,2*S*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-ol (*syn*,*syn*-13b)



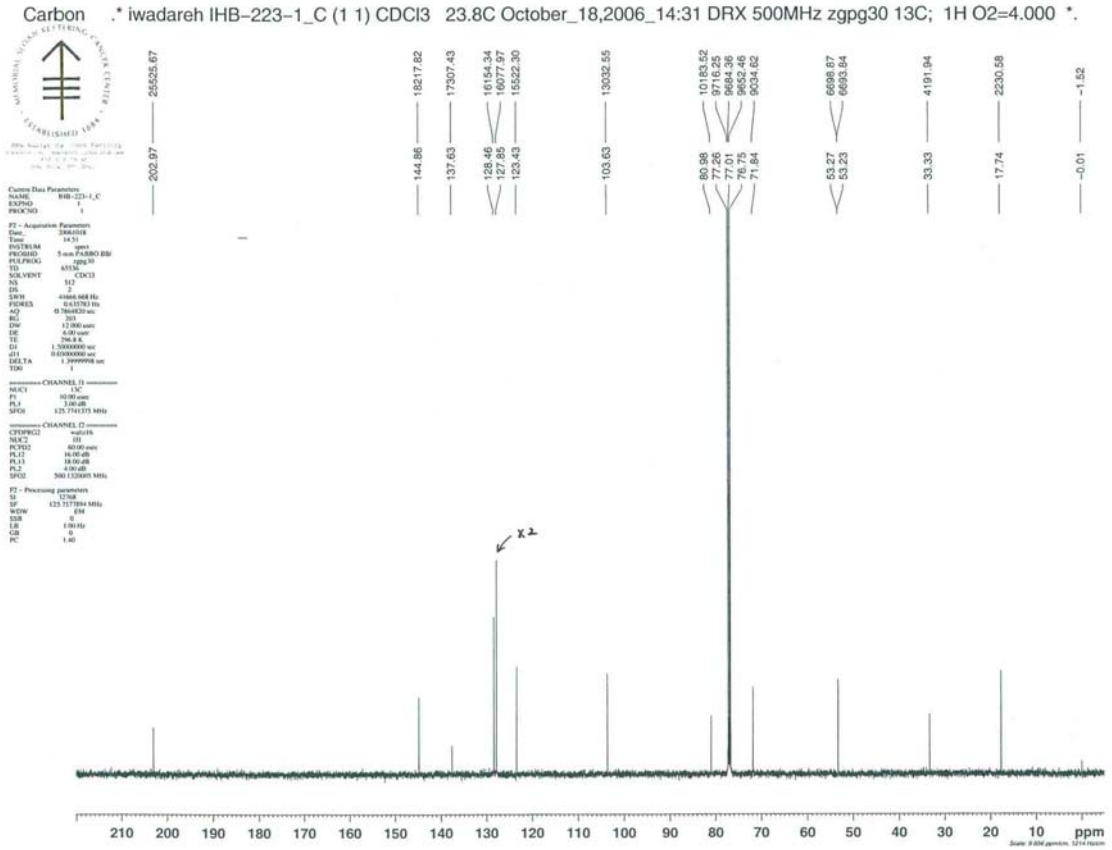


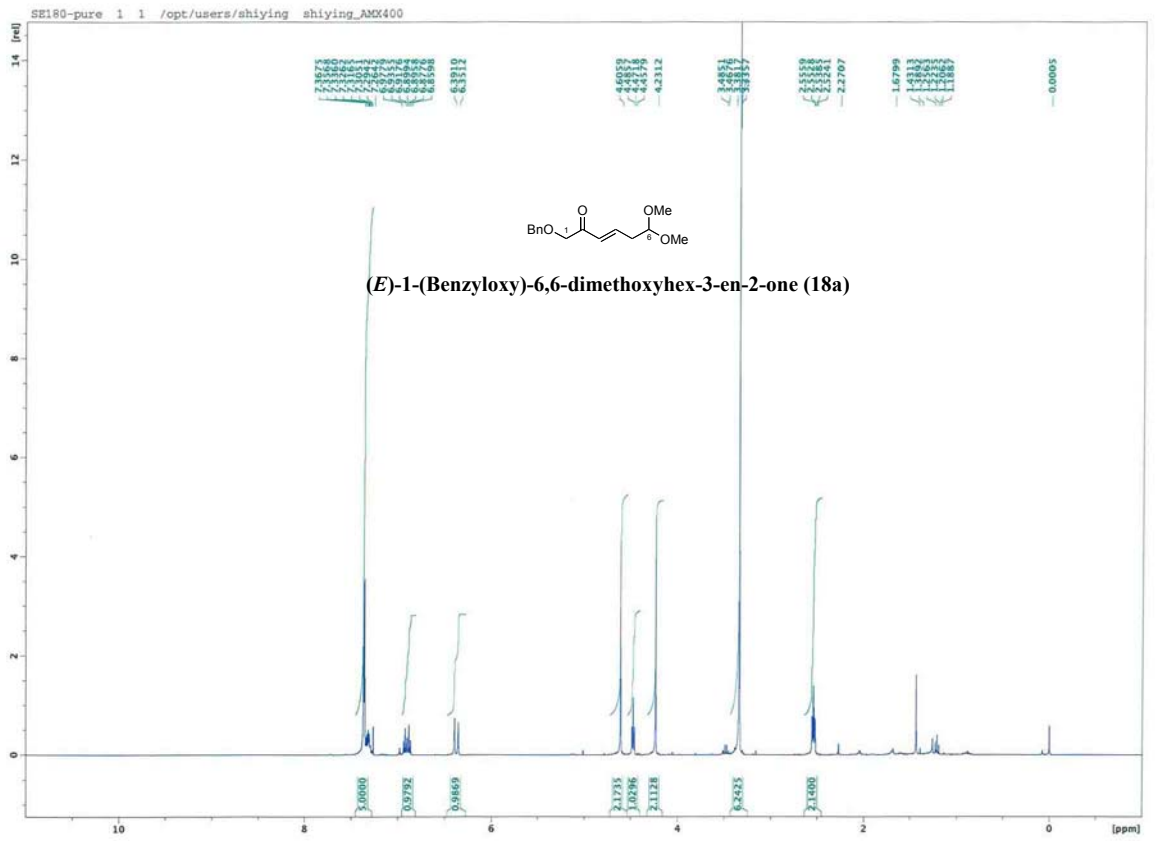
(*Z*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-one (17a)



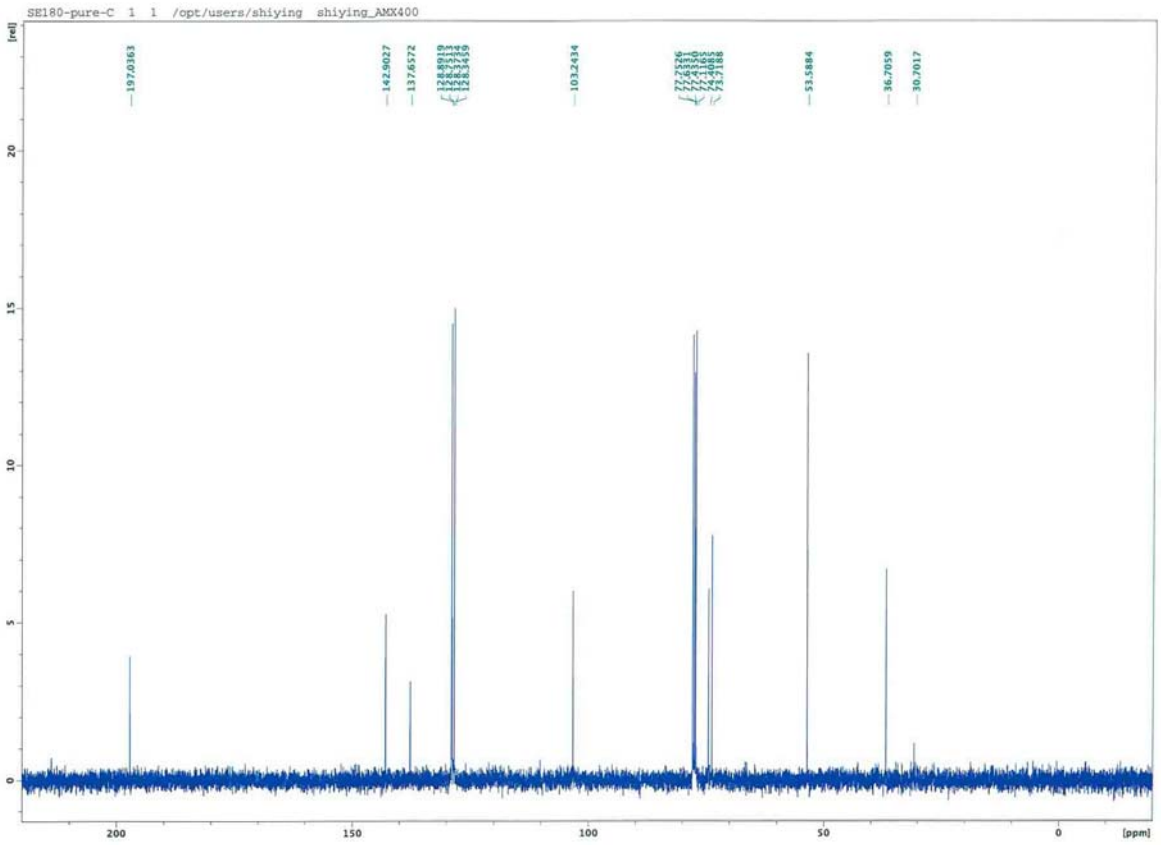


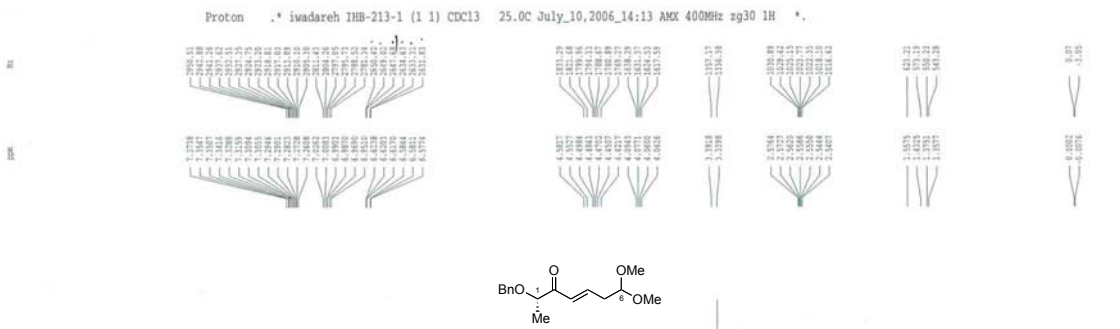
(–)-(*S*,*Z*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-one (17b)



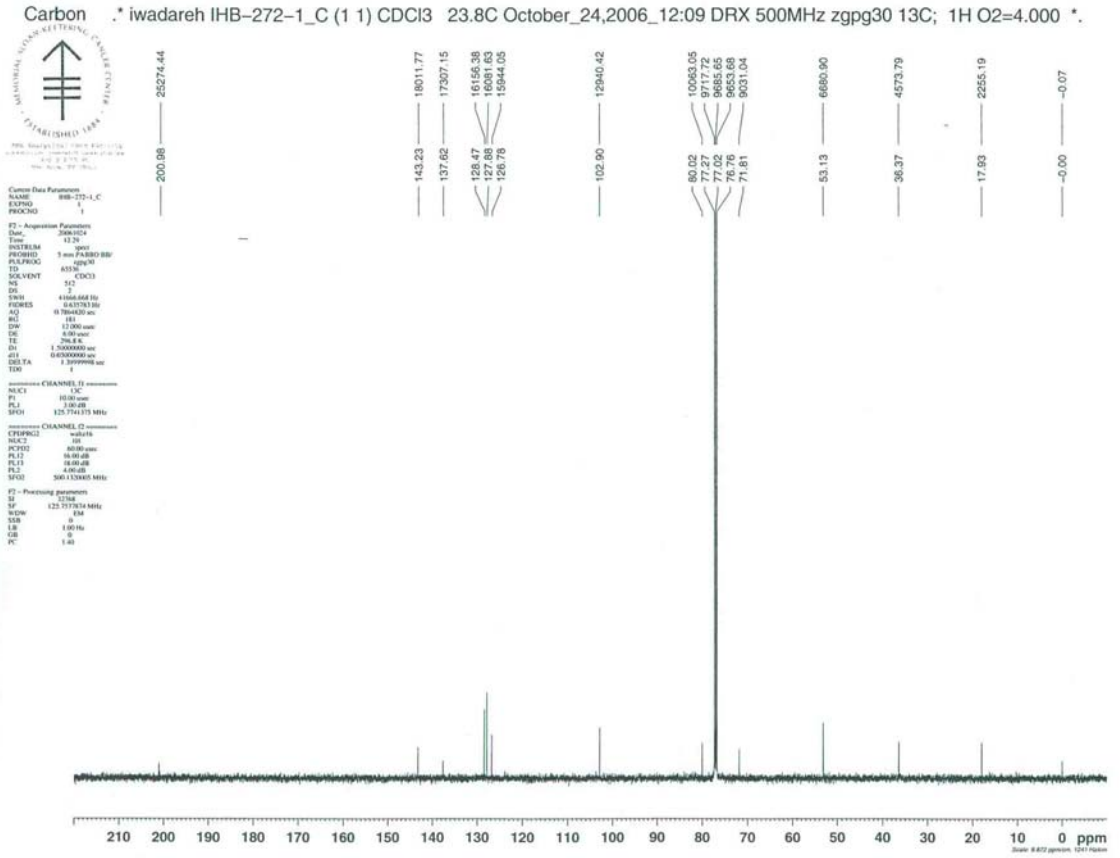


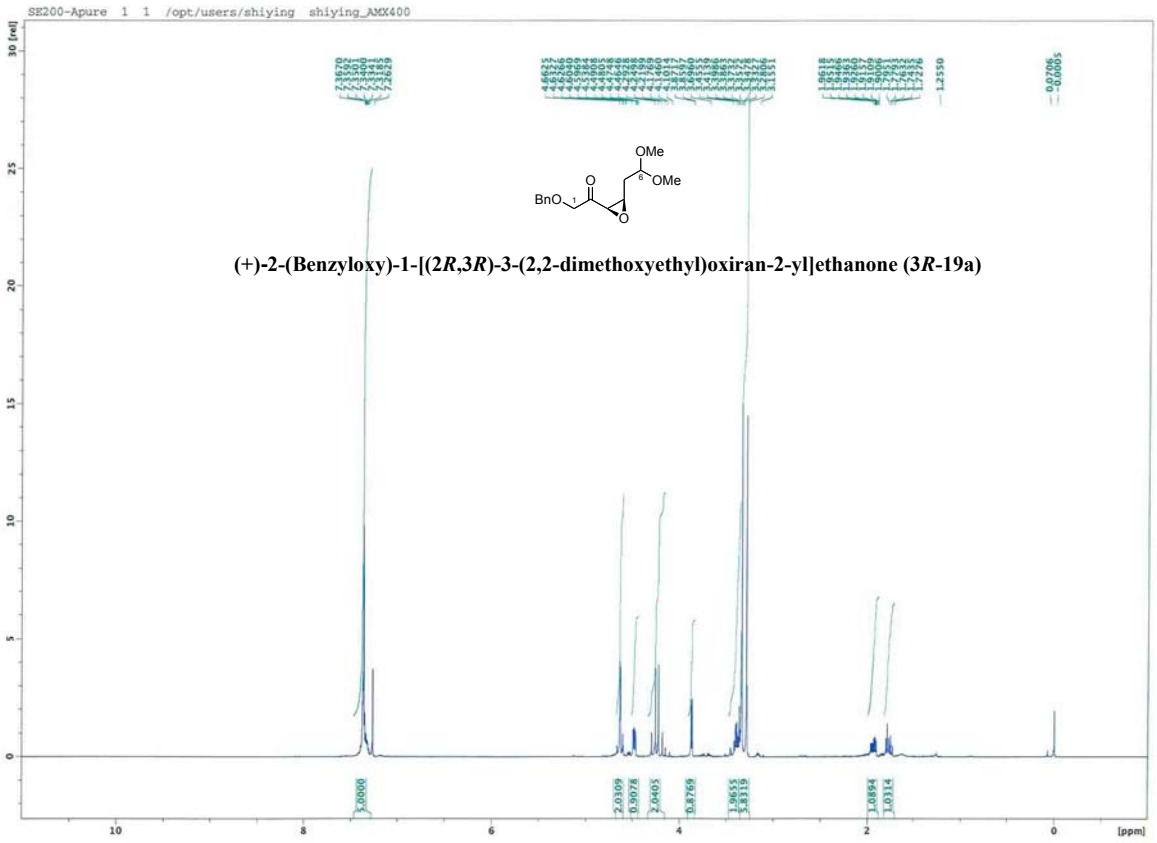
(*E*)-1-(Benzyloxy)-6,6-dimethoxyhex-3-en-2-one (18a)



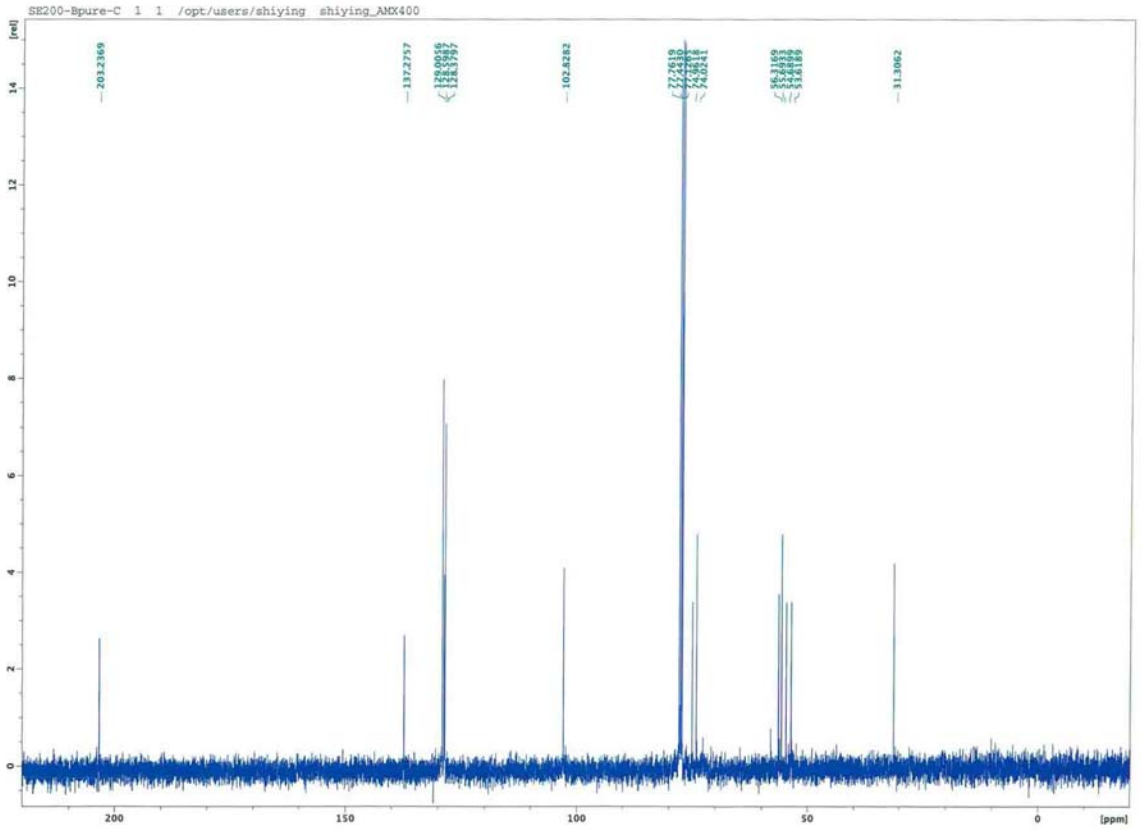


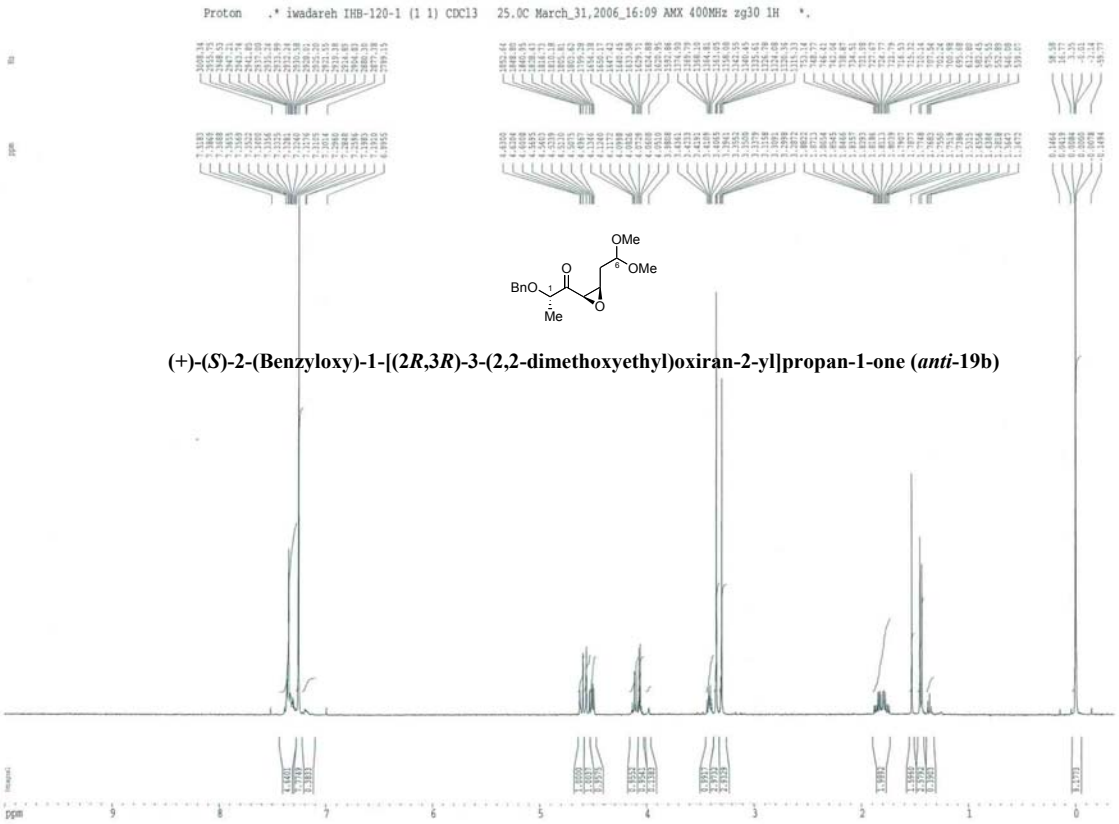
(–)-(*S*,*E*)-2-(Benzyloxy)-7,7-dimethoxyhept-4-en-3-one (18b)



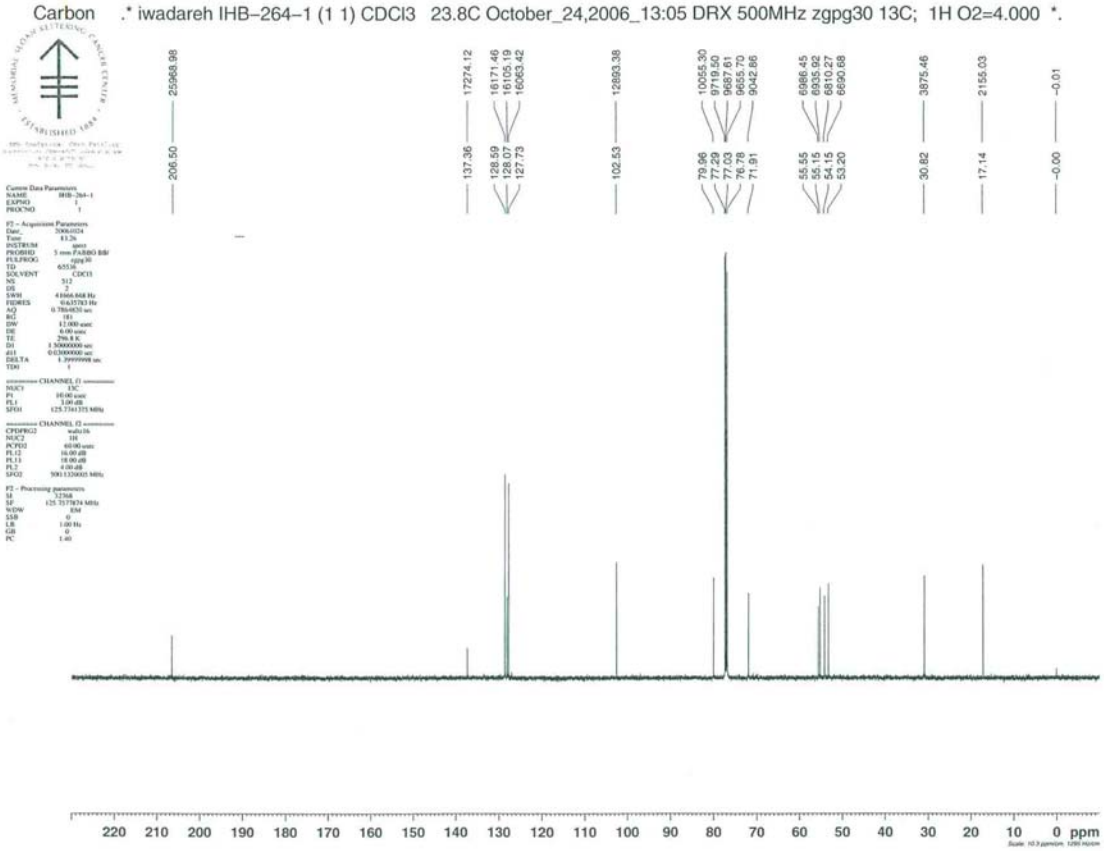


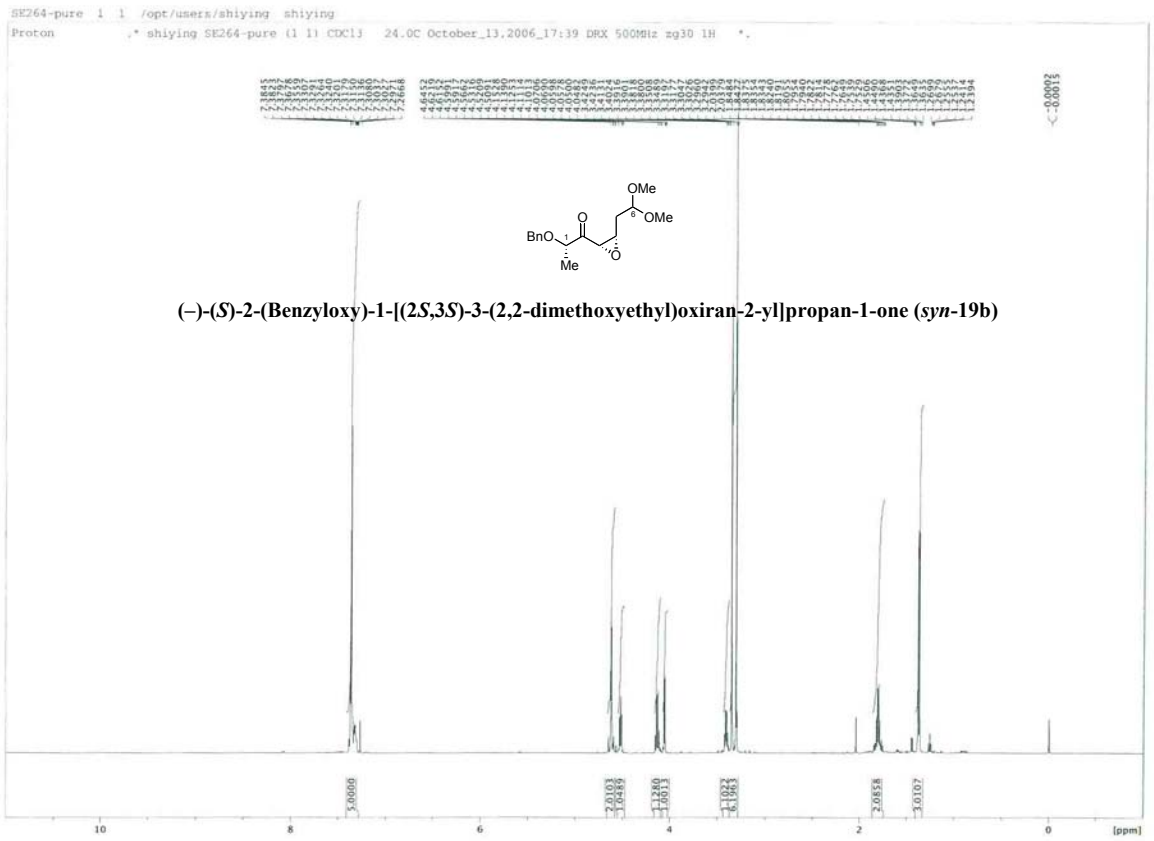
(+)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanone (3*R*-19a)



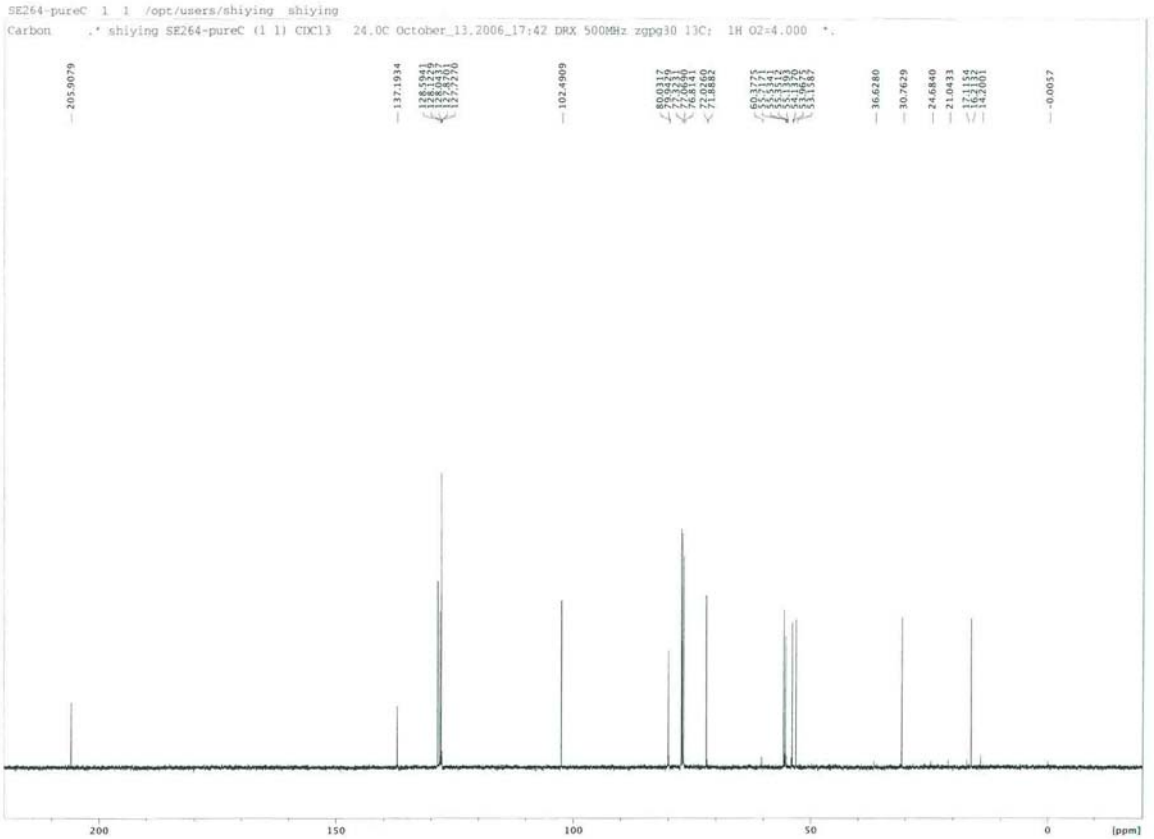


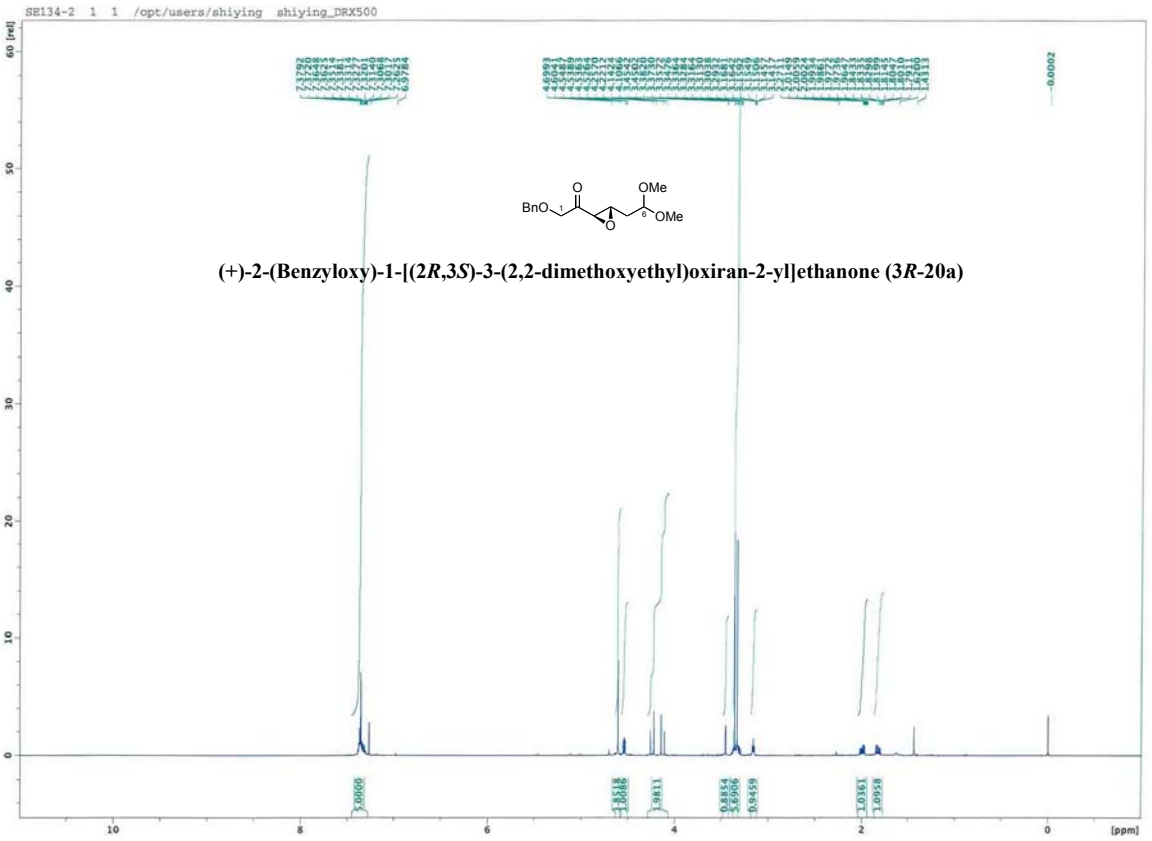
(+)-(*S*)-2-(Benzyloxy)-1-[(2*R*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-one (*anti*-19b)



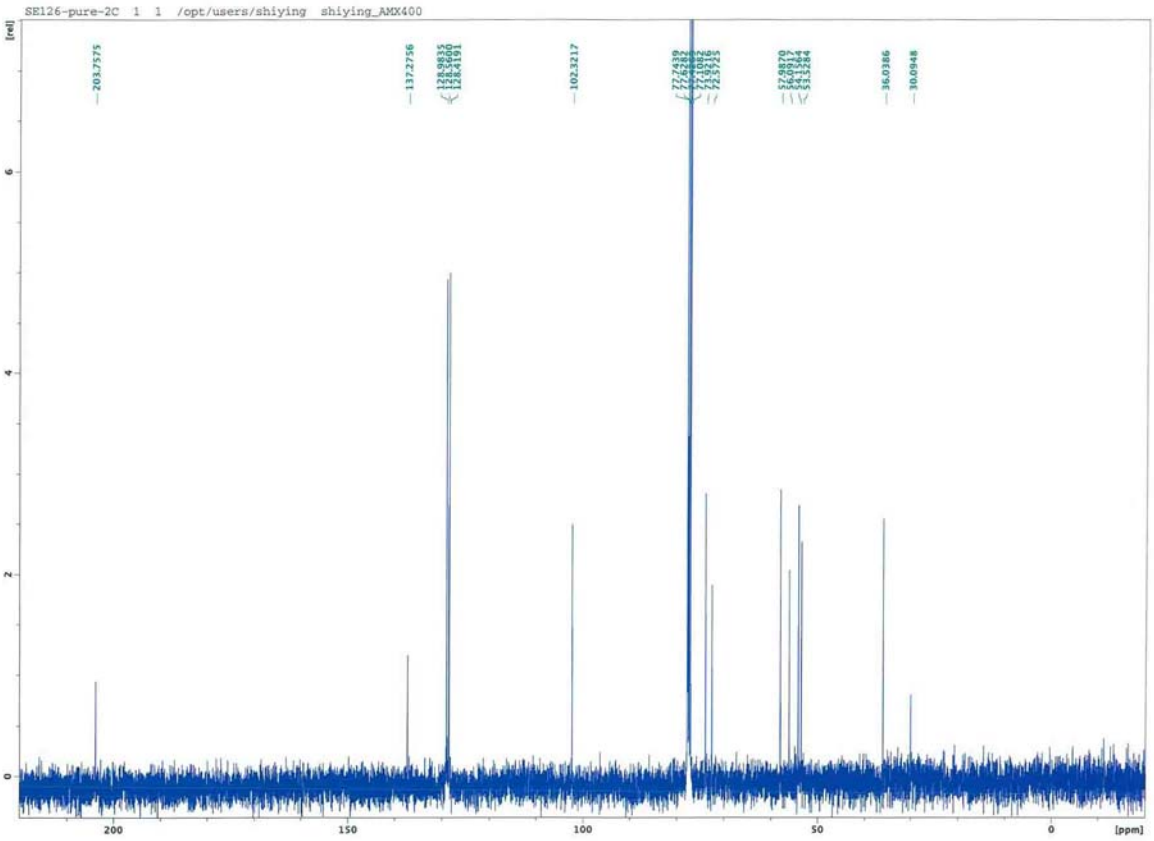


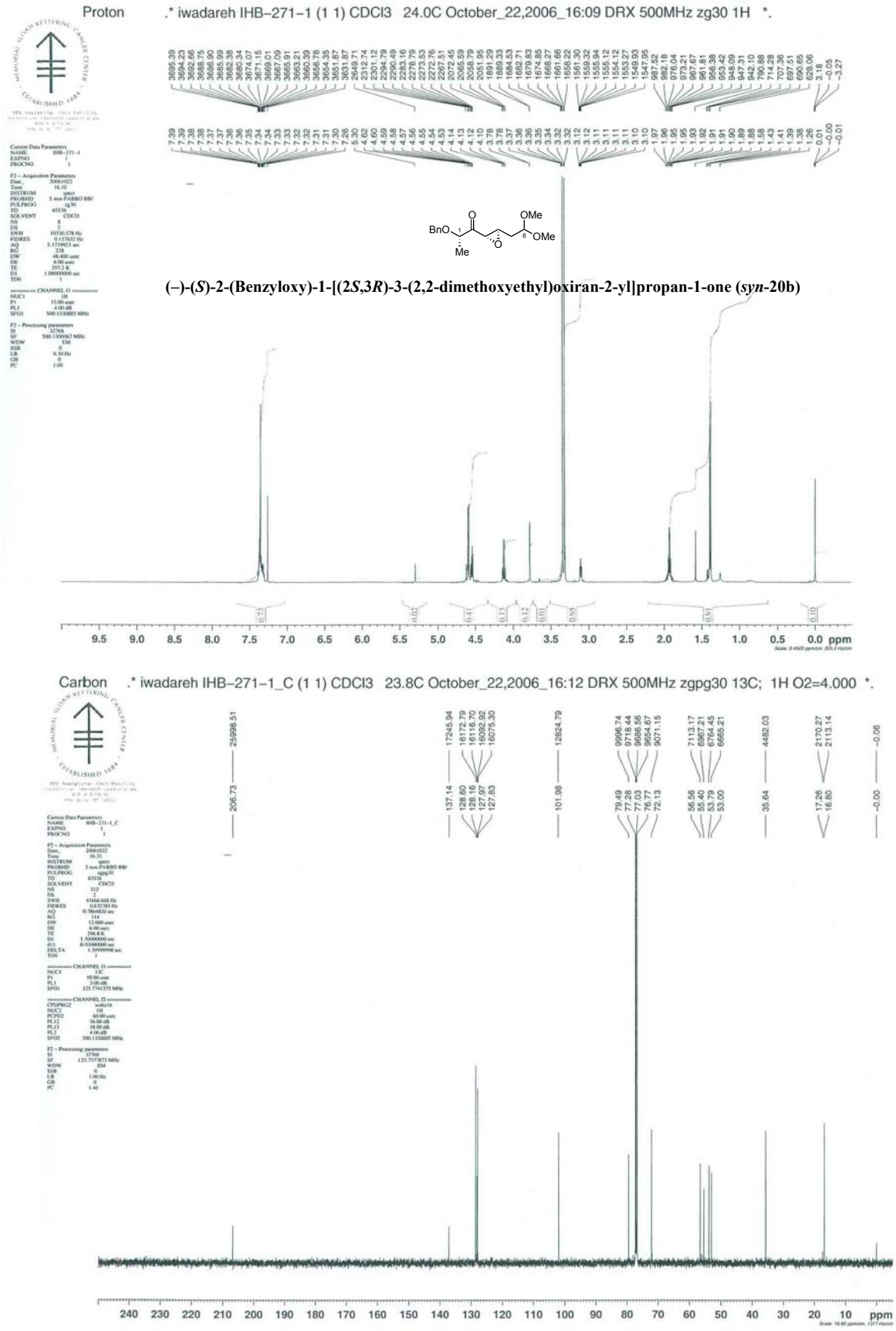
(–)-(*S*)-2-(Benzyloxy)-1-[(2*S*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-one (*syn*-19b)



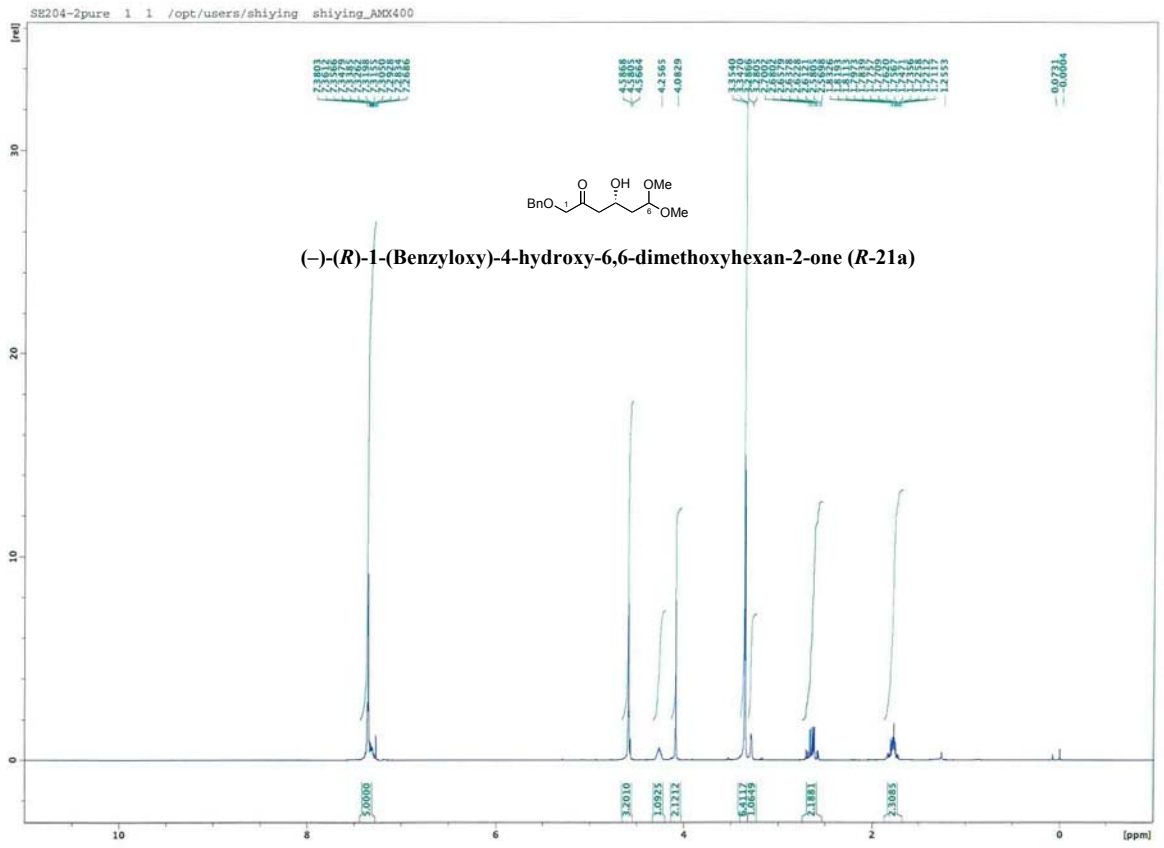


(+)-2-(Benzyloxy)-1-[(2*R*,3*S*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]ethanone (3*R*-20a)

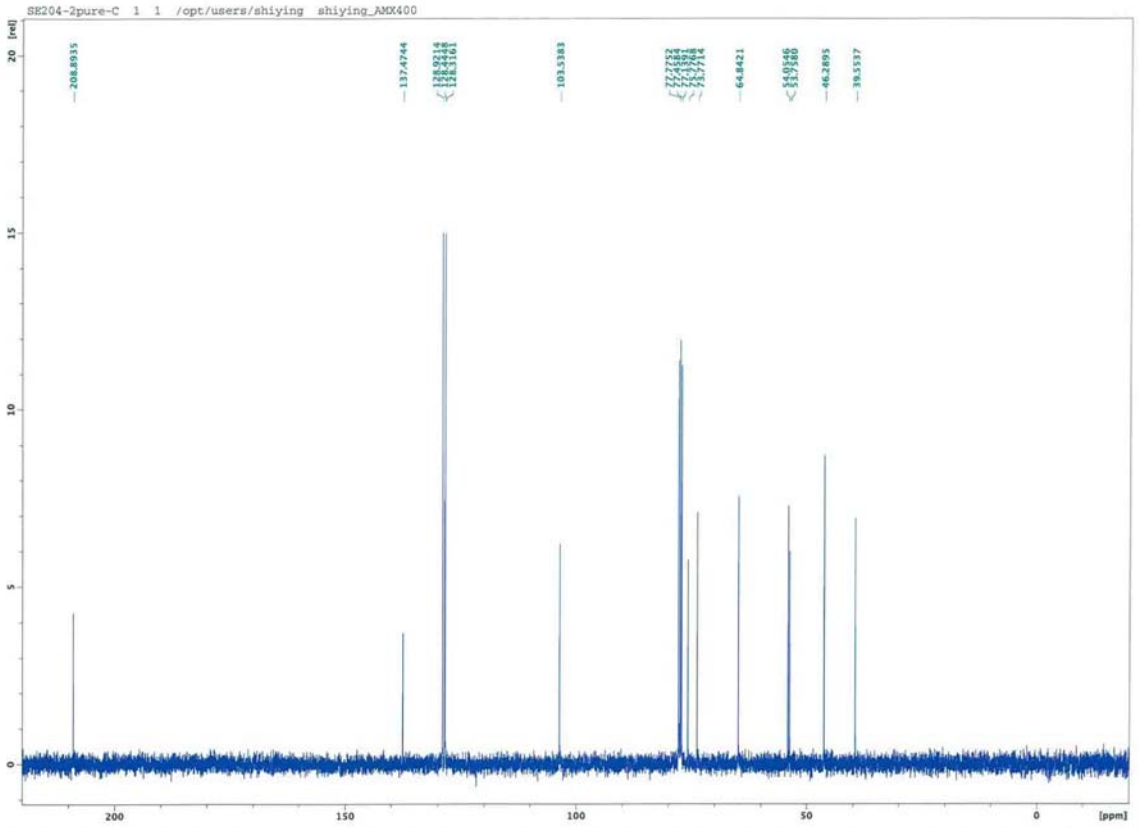


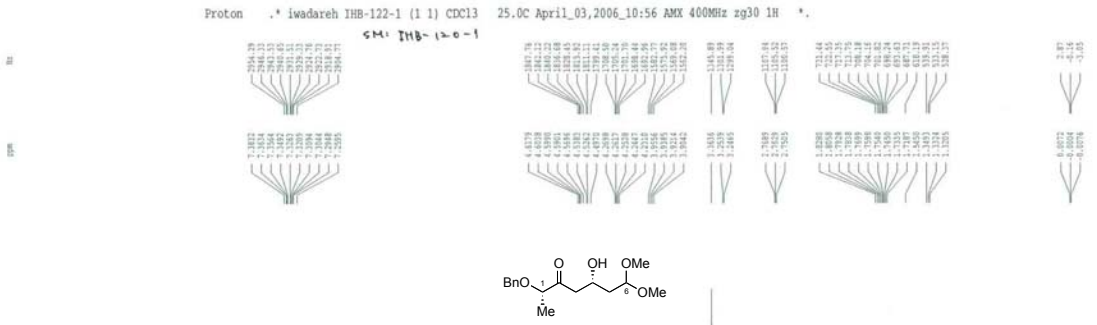


(–)-(*S*)-2-(Benzyloxy)-1-[(2*S*,3*R*)-3-(2,2-dimethoxyethyl)oxiran-2-yl]propan-1-one (*syn*-20b)

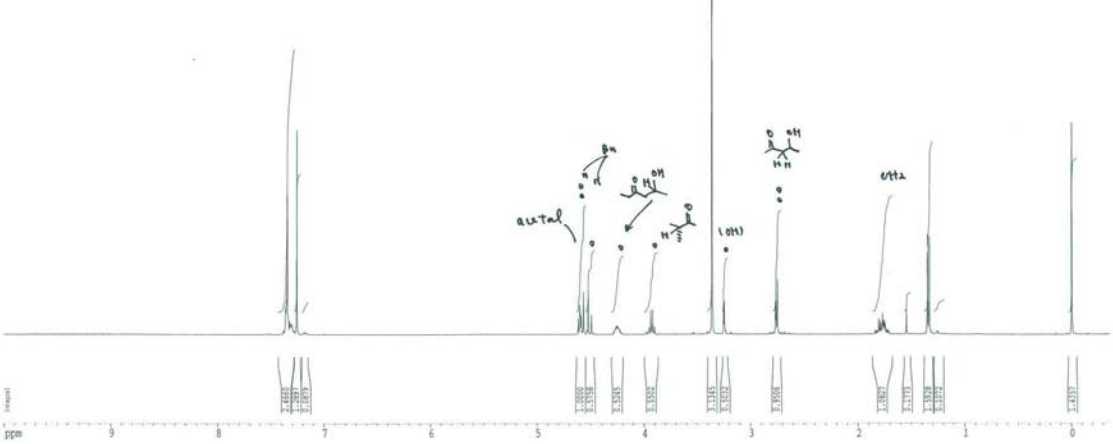


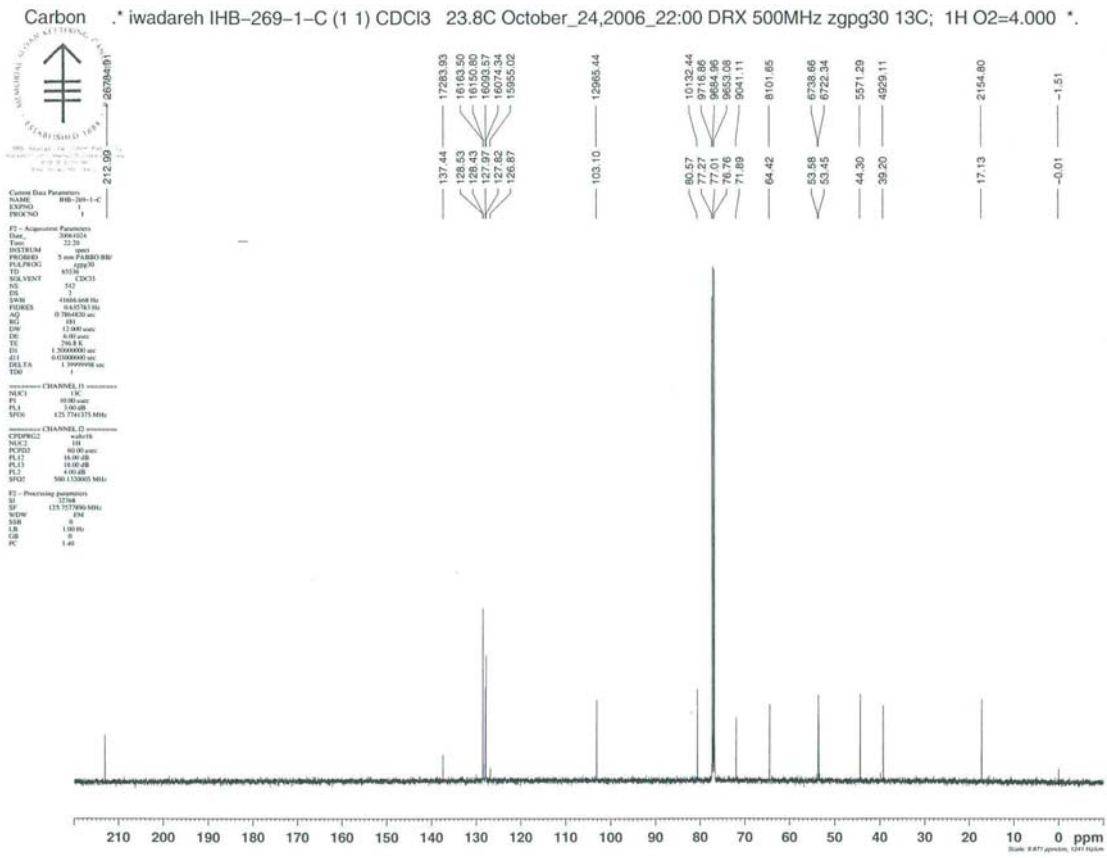
(–)-(*R*)-1-(Benzyloxy)-4-hydroxy-6,6-dimethoxyhexan-2-one (*R*-21a)

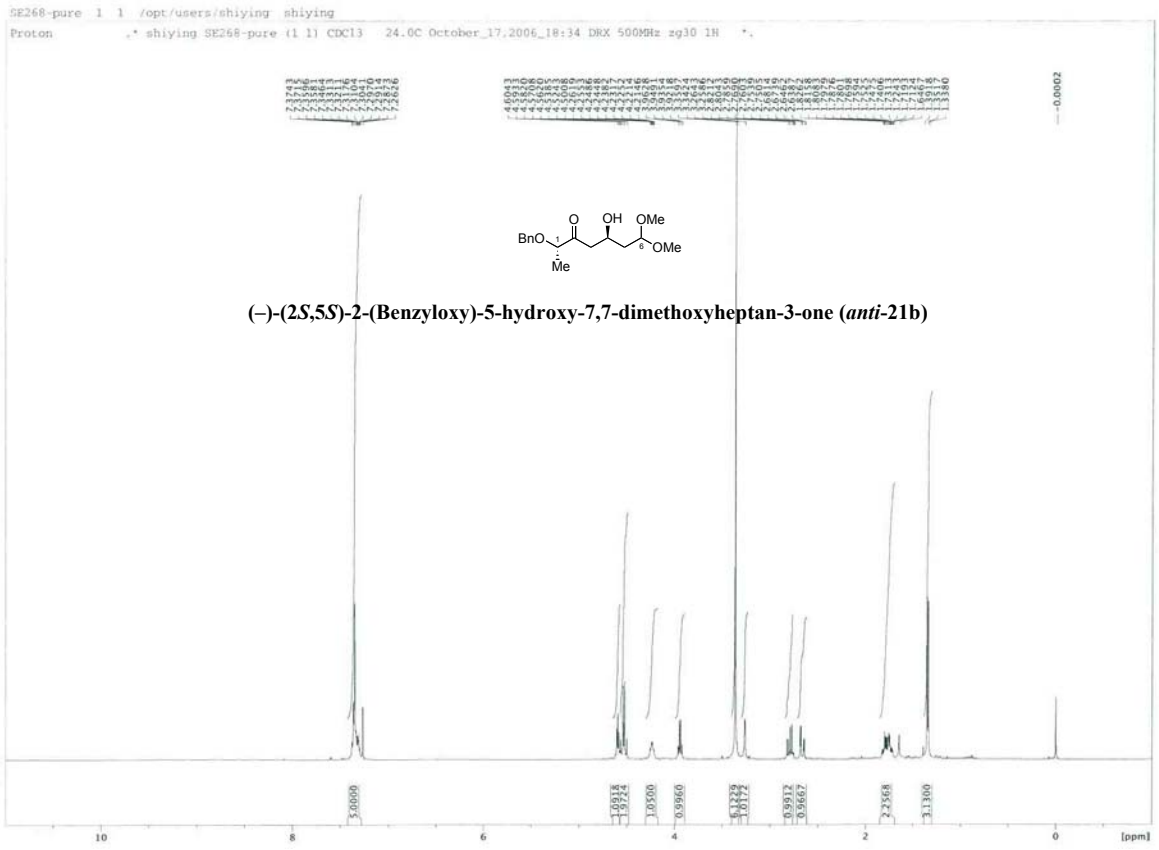




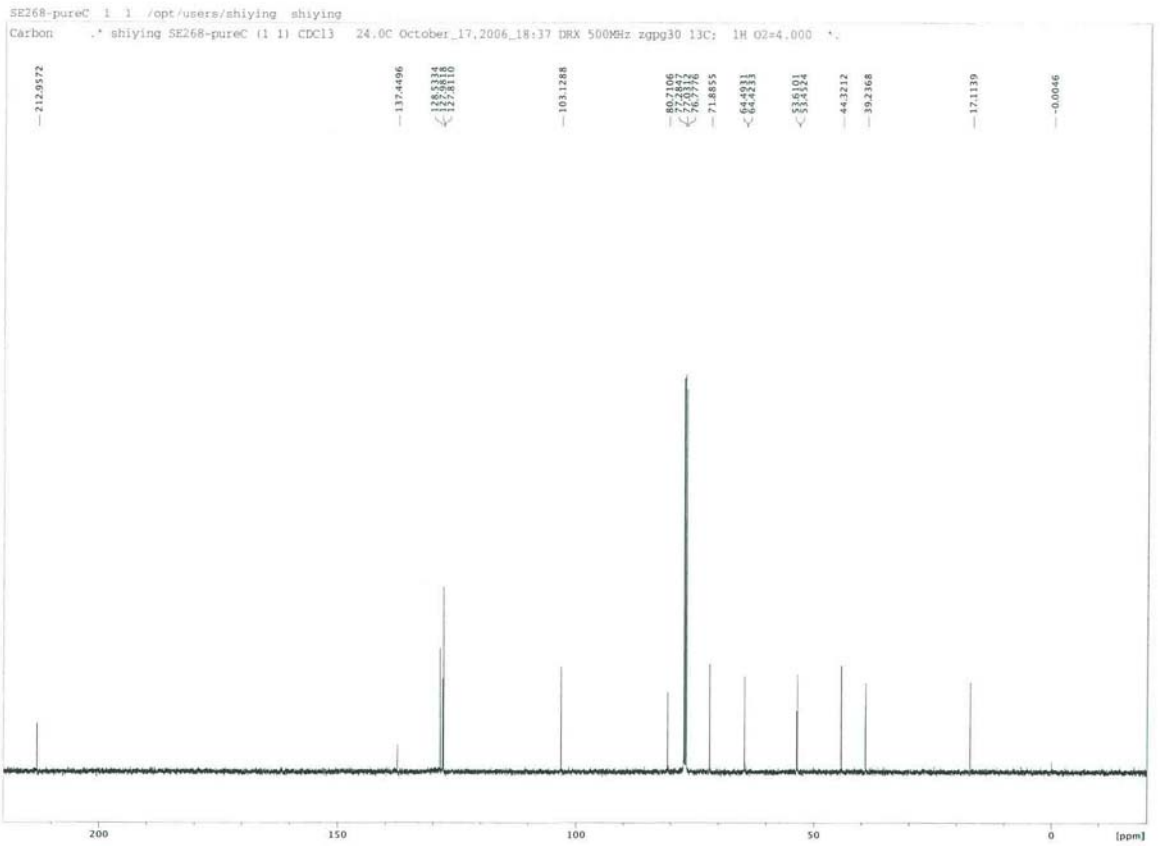
(–)-(2*S*,5*R*)-2-(Benzyloxy)-5-hydroxy-7,7-dimethoxyheptan-3-one (*syn*-21b)

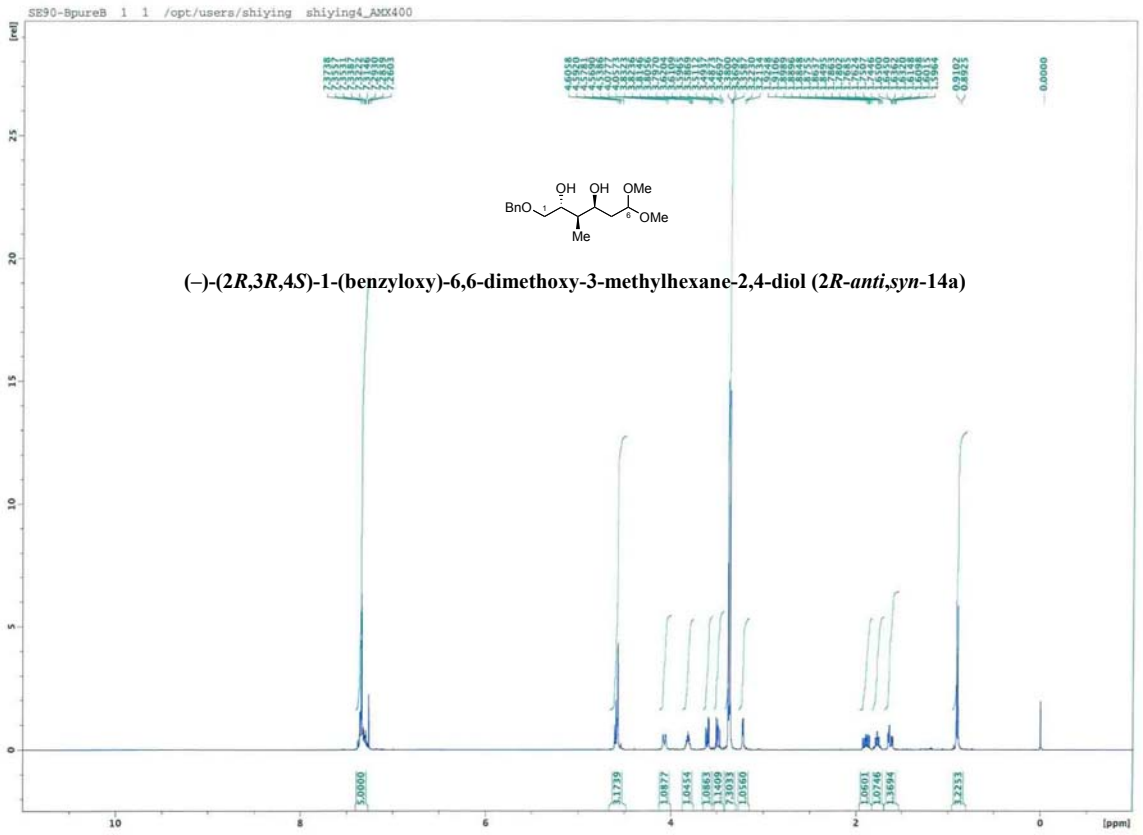




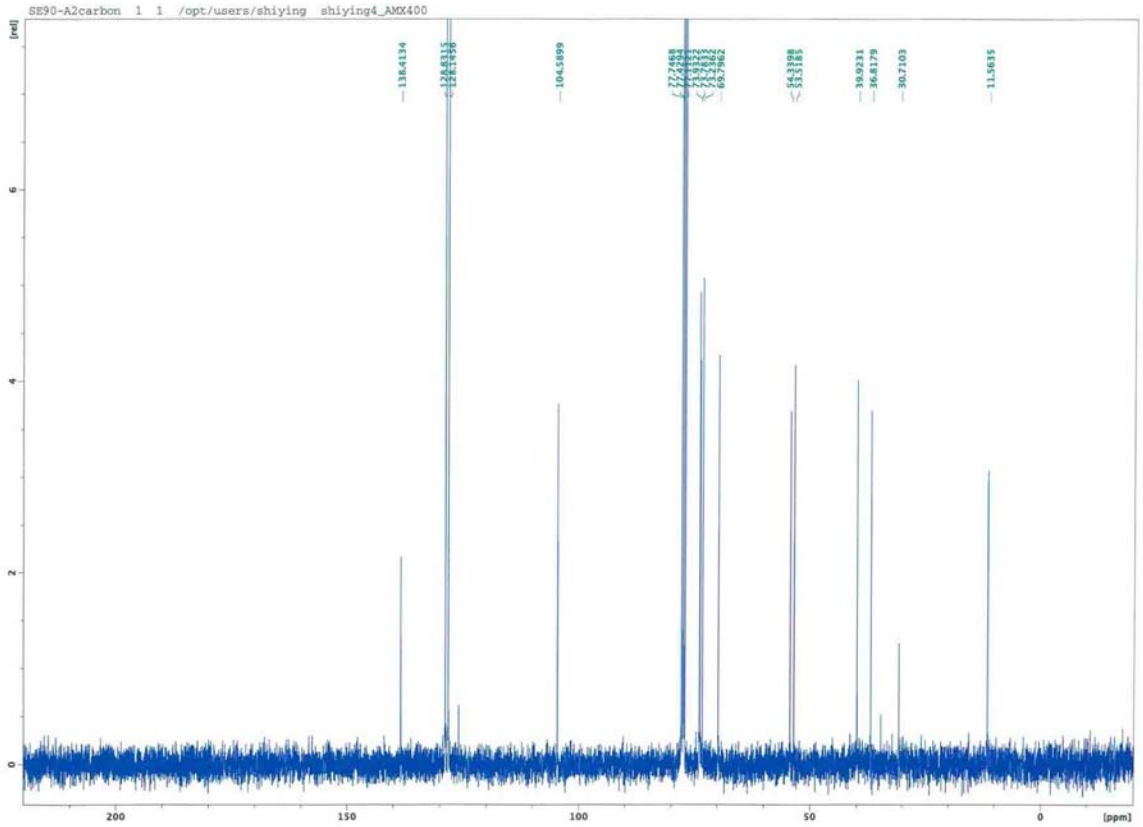


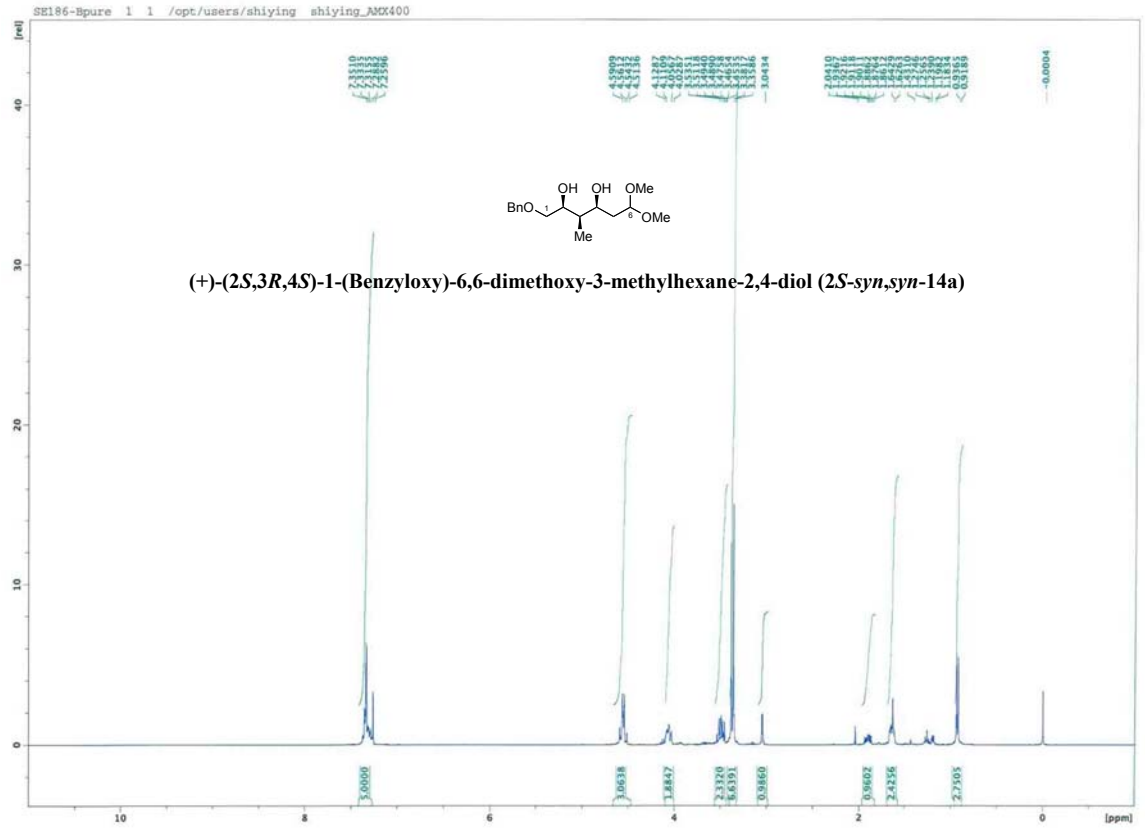
(–)-(2*S*,5*S*)-2-(Benzyloxy)-5-hydroxy-7,7-dimethoxyheptan-3-one (*anti*-21b)



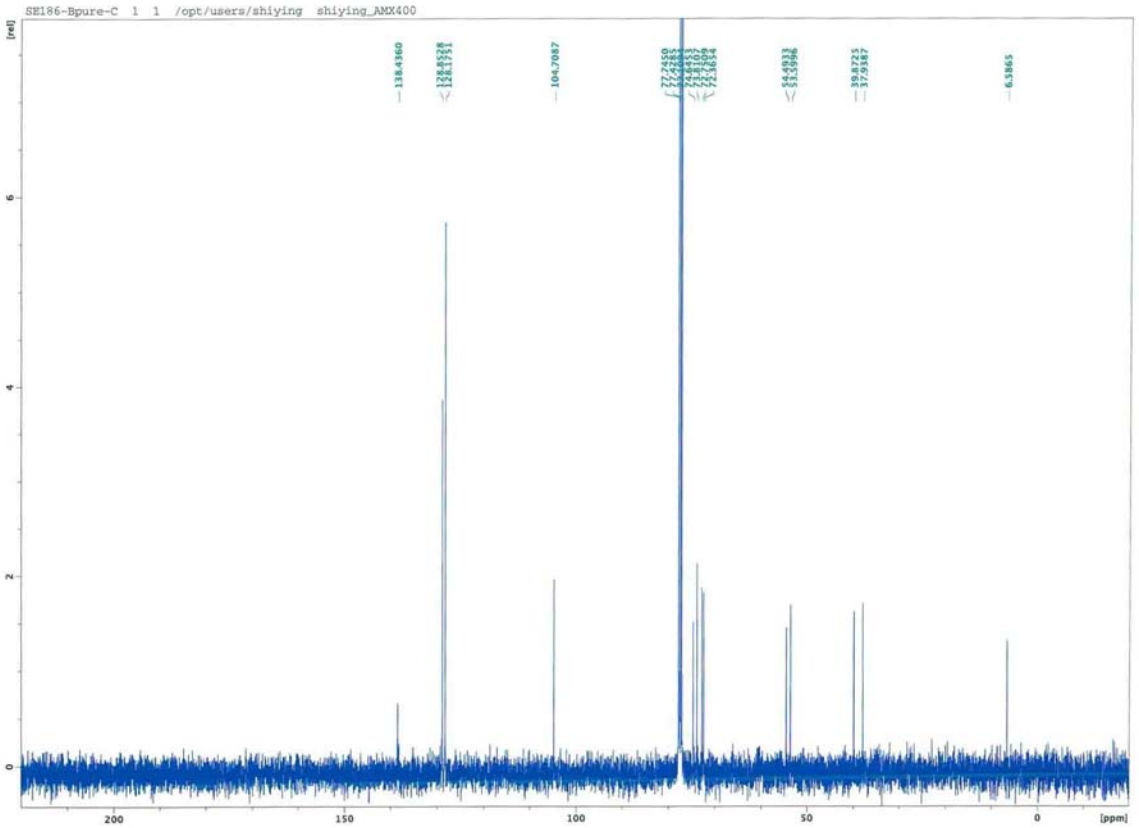


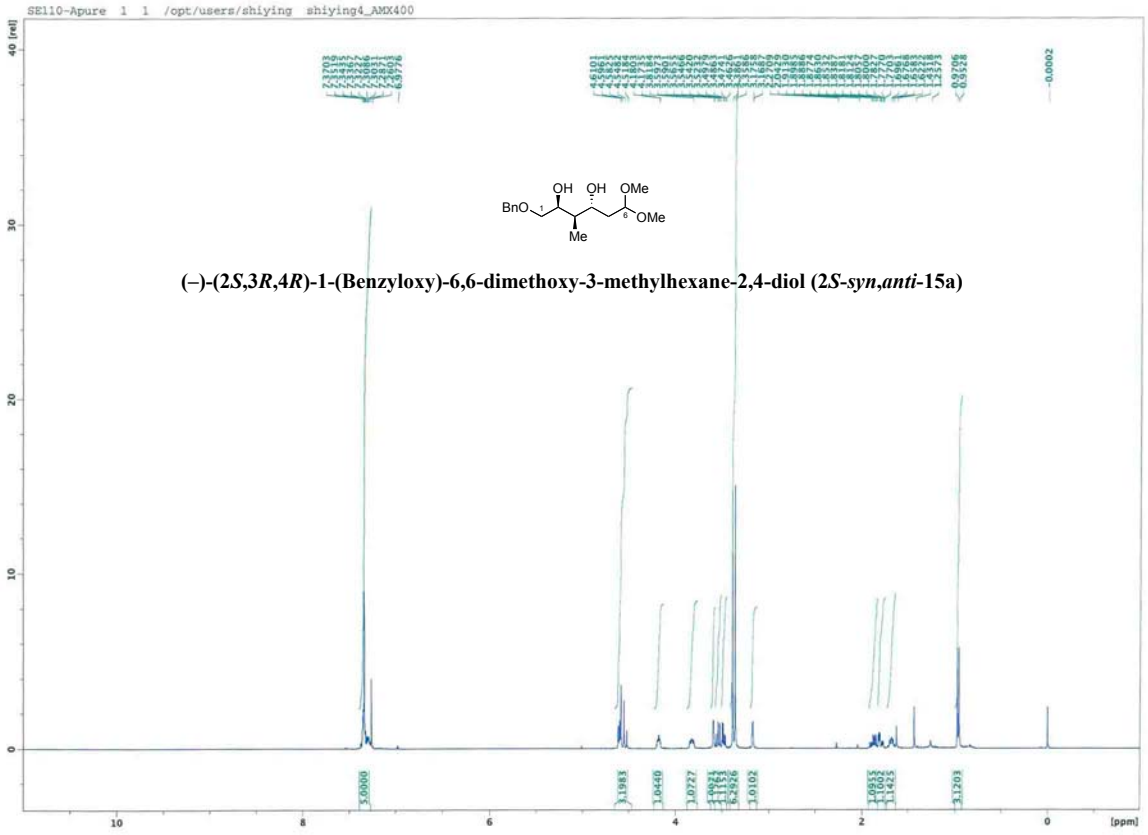
(–)-(2*R*,3*R*,4*S*)-1-(benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*R*-*anti*,*syn*-14a)



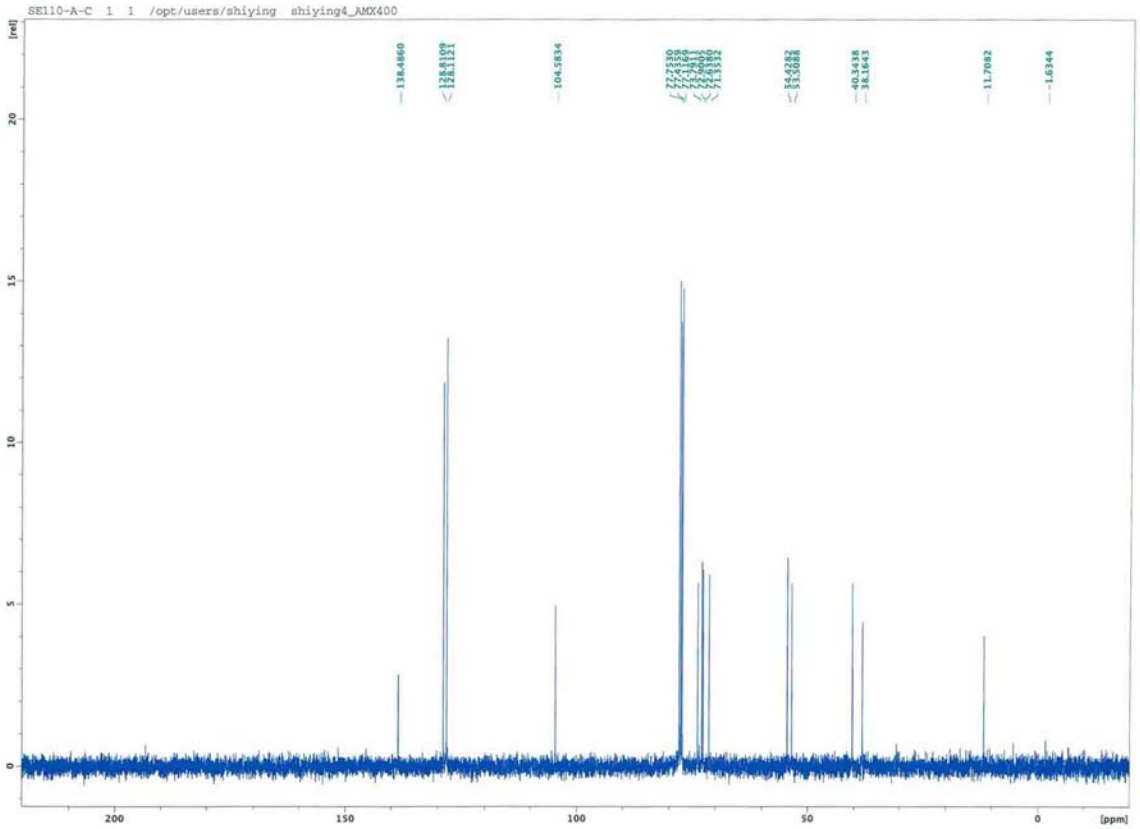


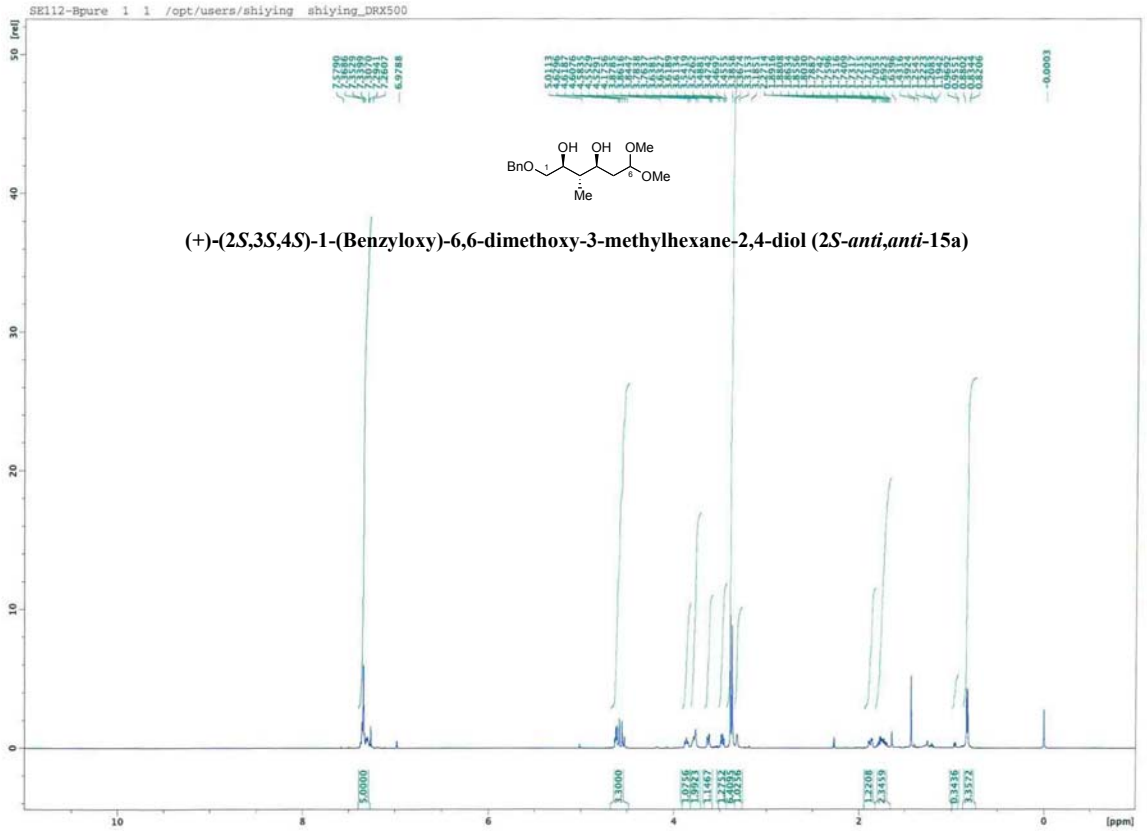
(+)-(2*S*,3*R*,4*S*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*S*-*syn*,*syn*-14a)



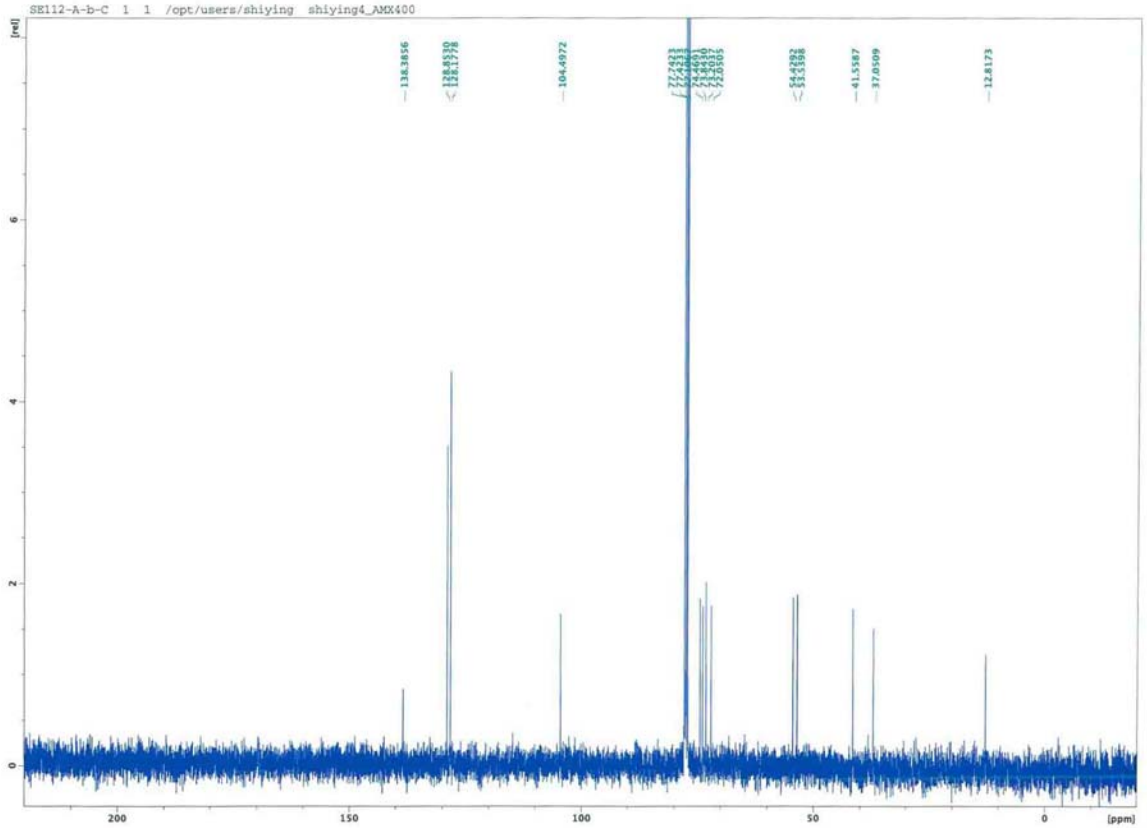


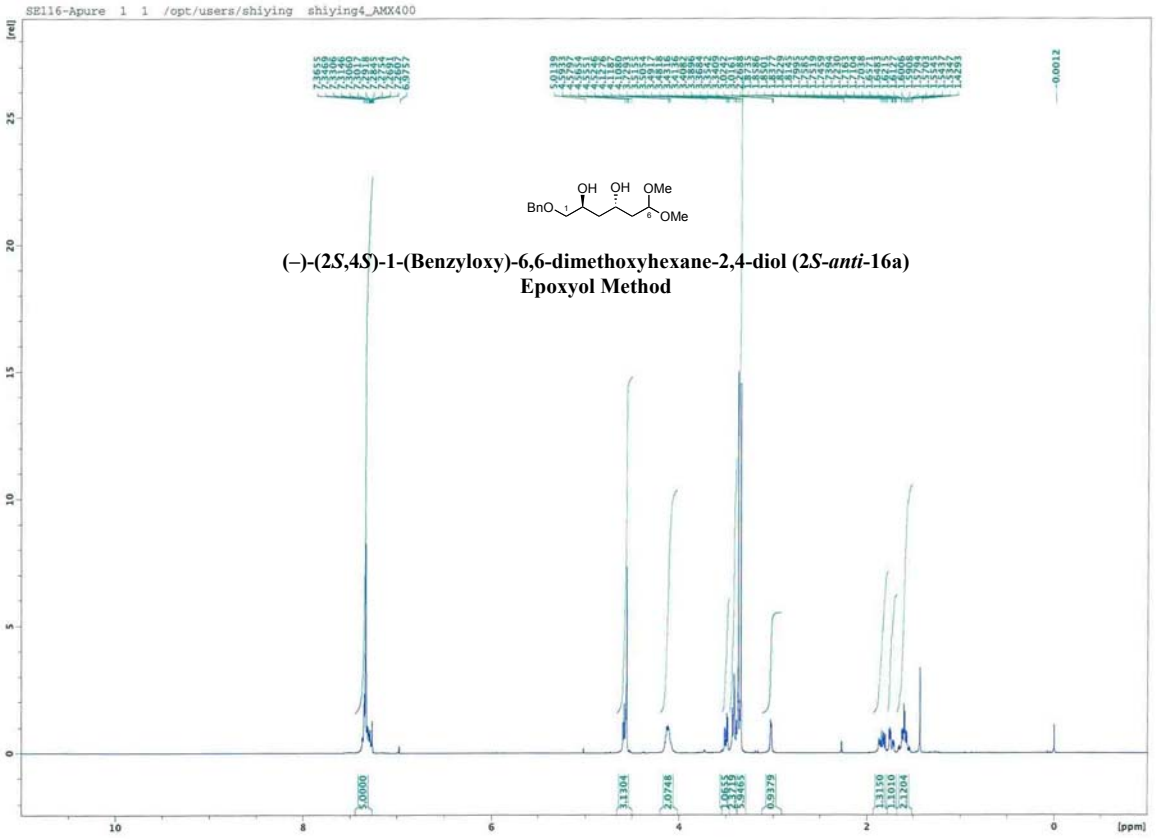
(–)-(2*S*,3*R*,4*R*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*S*-*syn*,*anti*-15a)



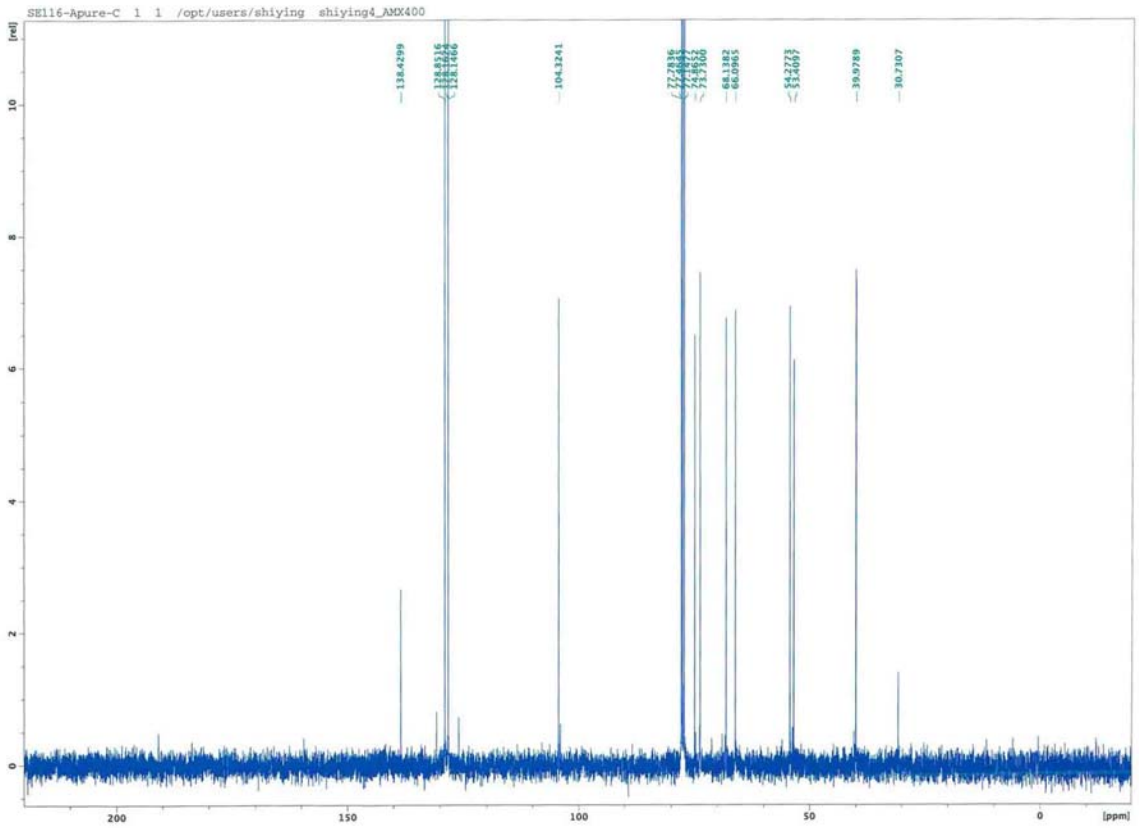


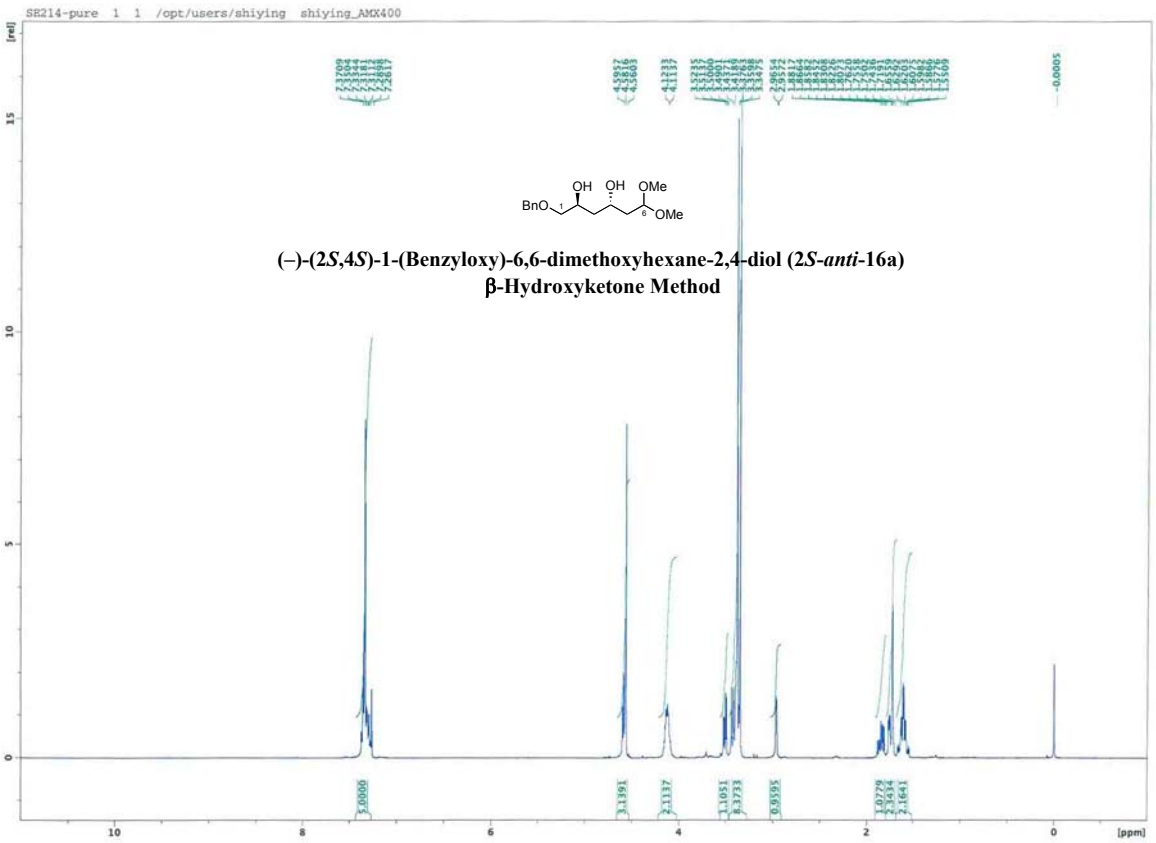
(+)-(2*S*,3*S*,4*S*)-1-(Benzyloxy)-6,6-dimethoxy-3-methylhexane-2,4-diol (2*S*-*anti*,*anti*-15a)



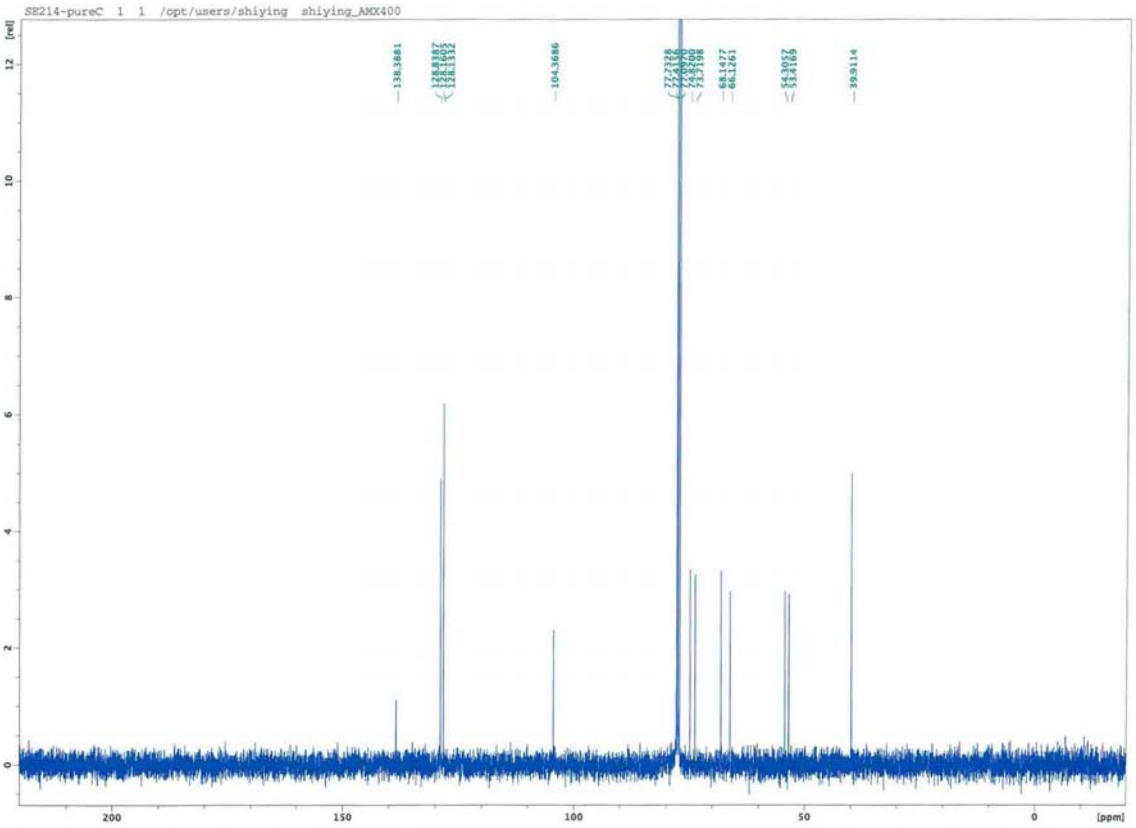


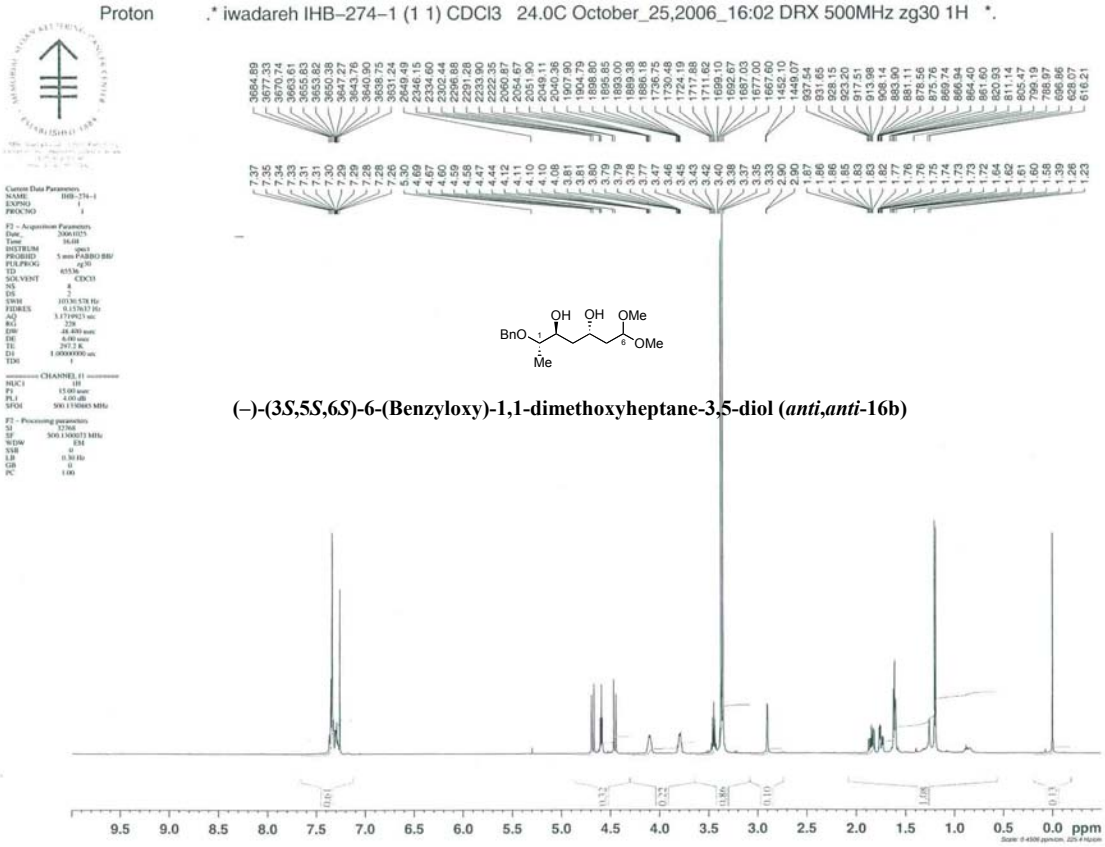
(–)-(2*S*,4*S*)-1-(Benzyloxy)-6,6-dimethoxyhexane-2,4-diol (2*S*-*anti*-16a)
Epoxyol Method



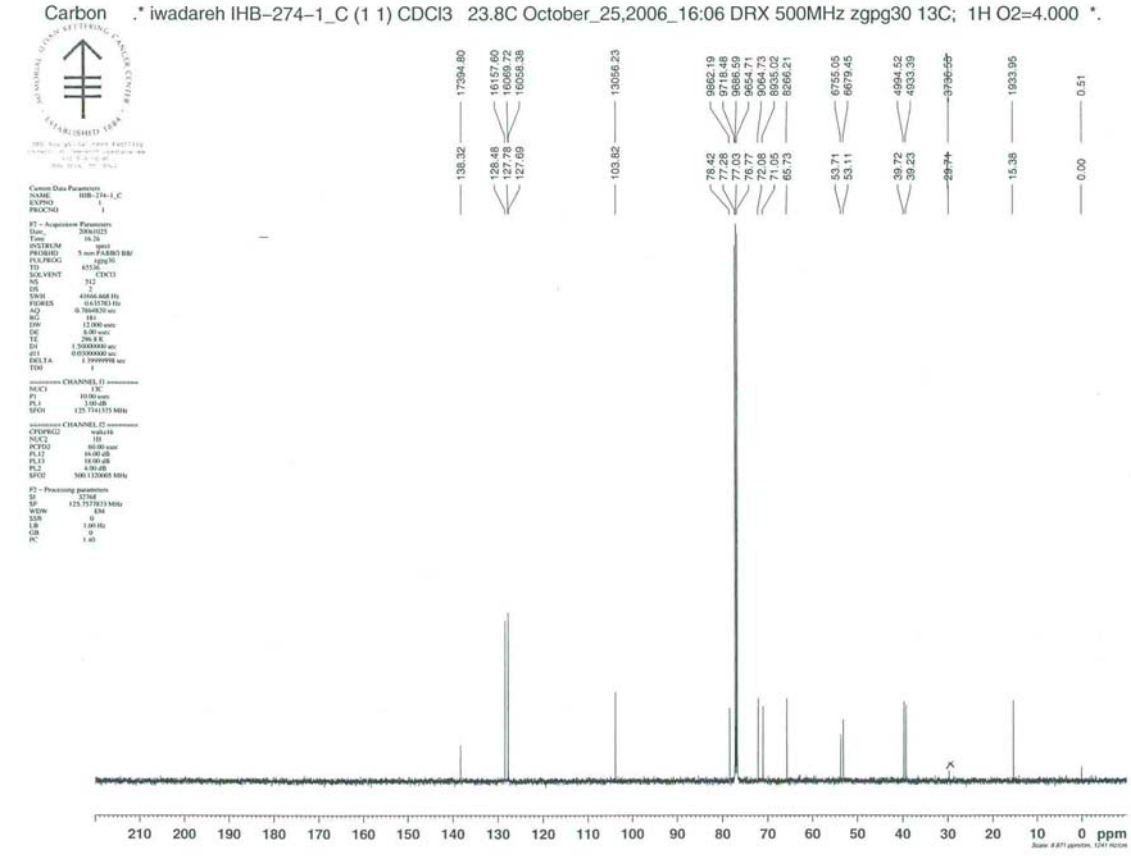


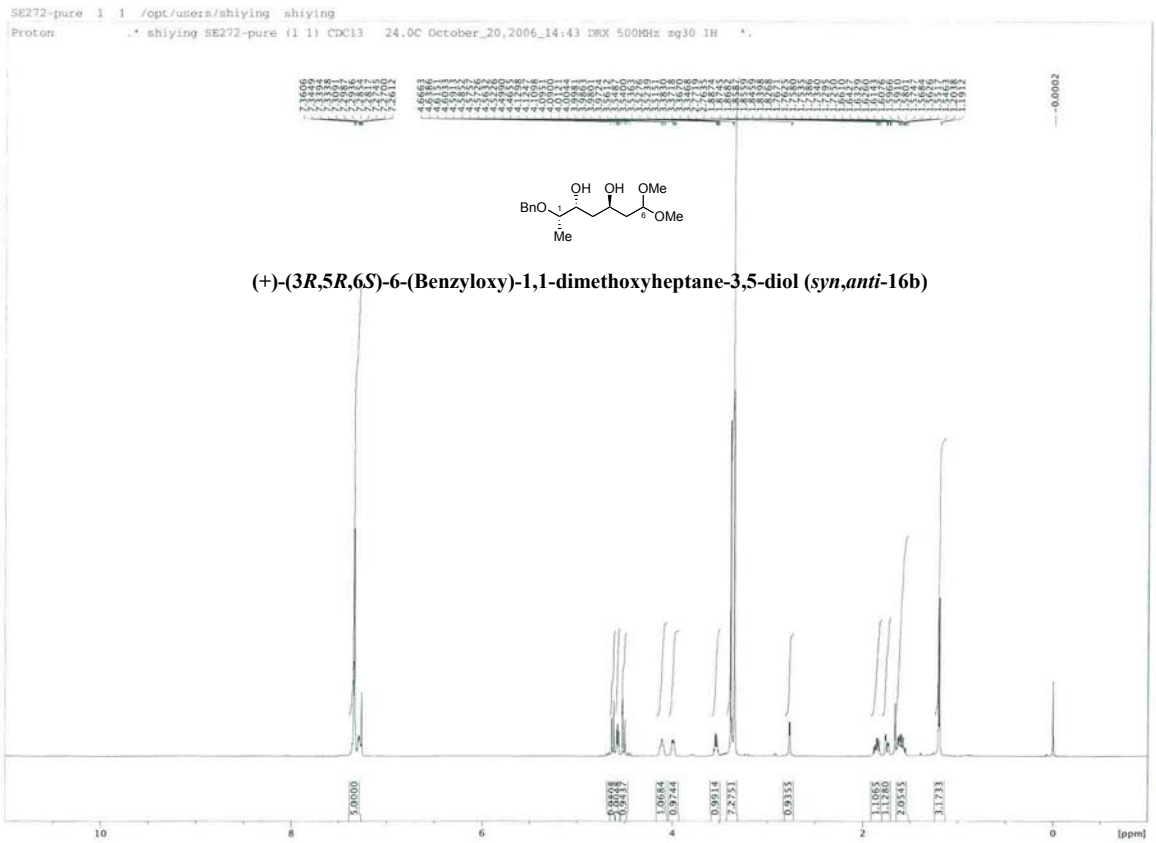
(–)-(2*S*,4*S*)-1-(Benzyloxy)-6,6-dimethoxyhexane-2,4-diol (2*S*-*anti*-16a)
β-Hydroxyketone Method



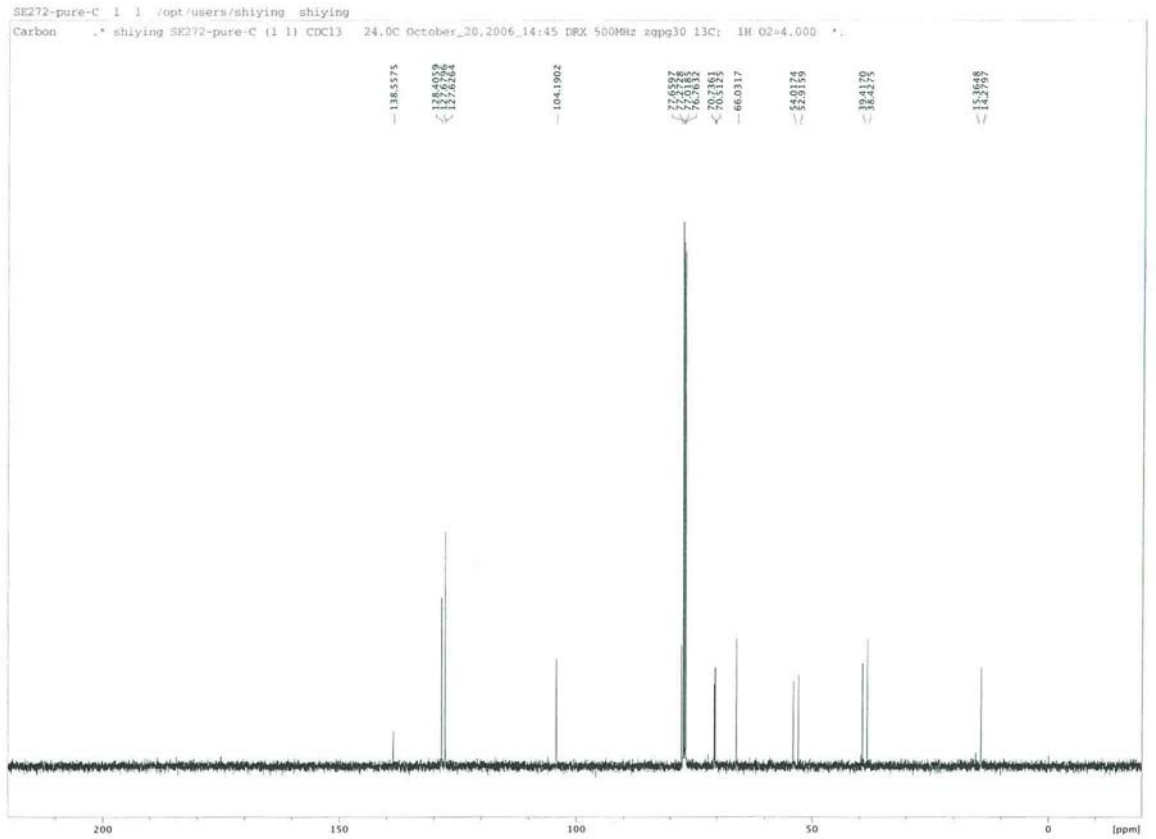


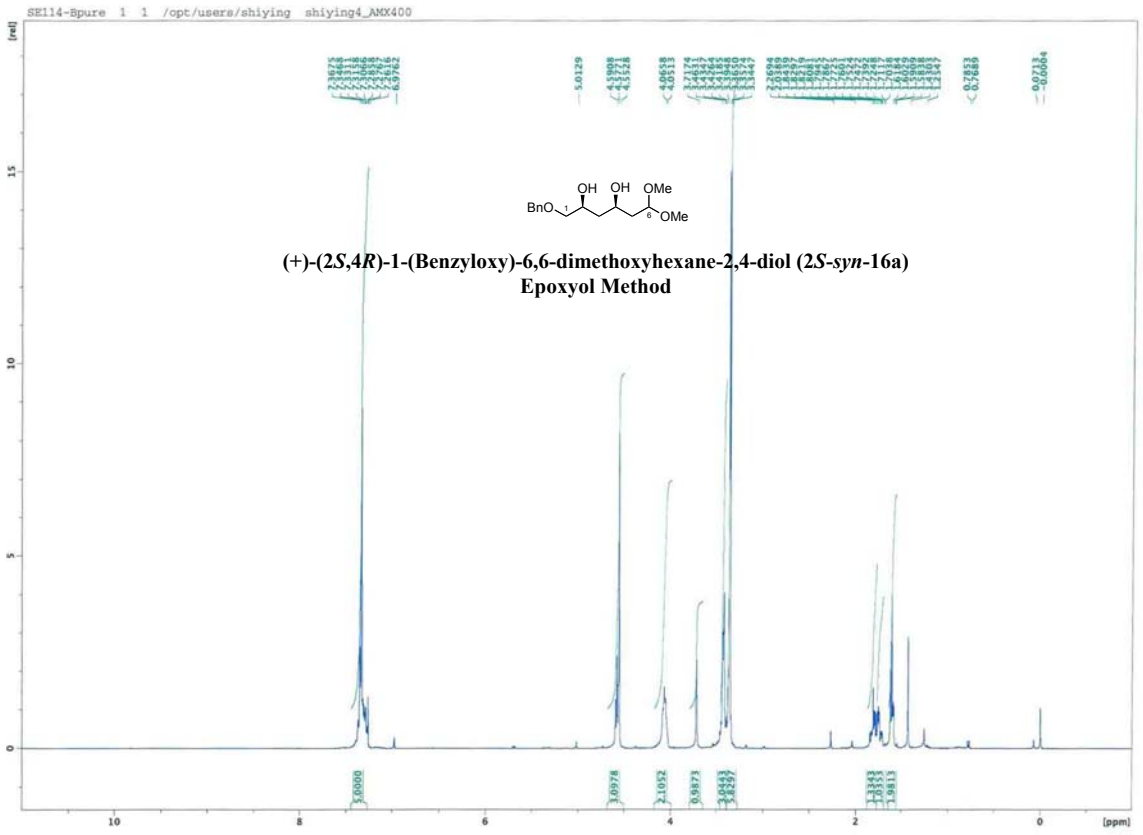
(–)-(3*S*,5*S*,6*S*)-6-(Benzyloxy)-1,1-dimethoxyheptane-3,5-diol (*anti*,*anti*-16b)



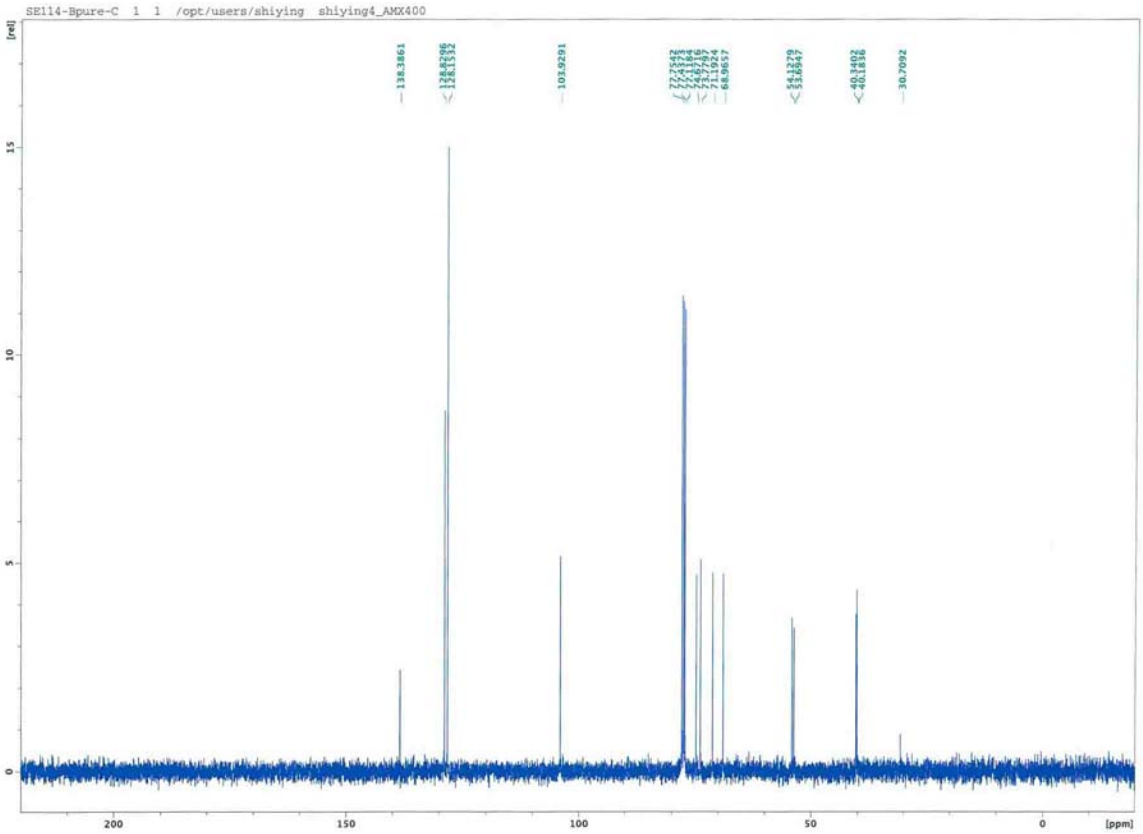


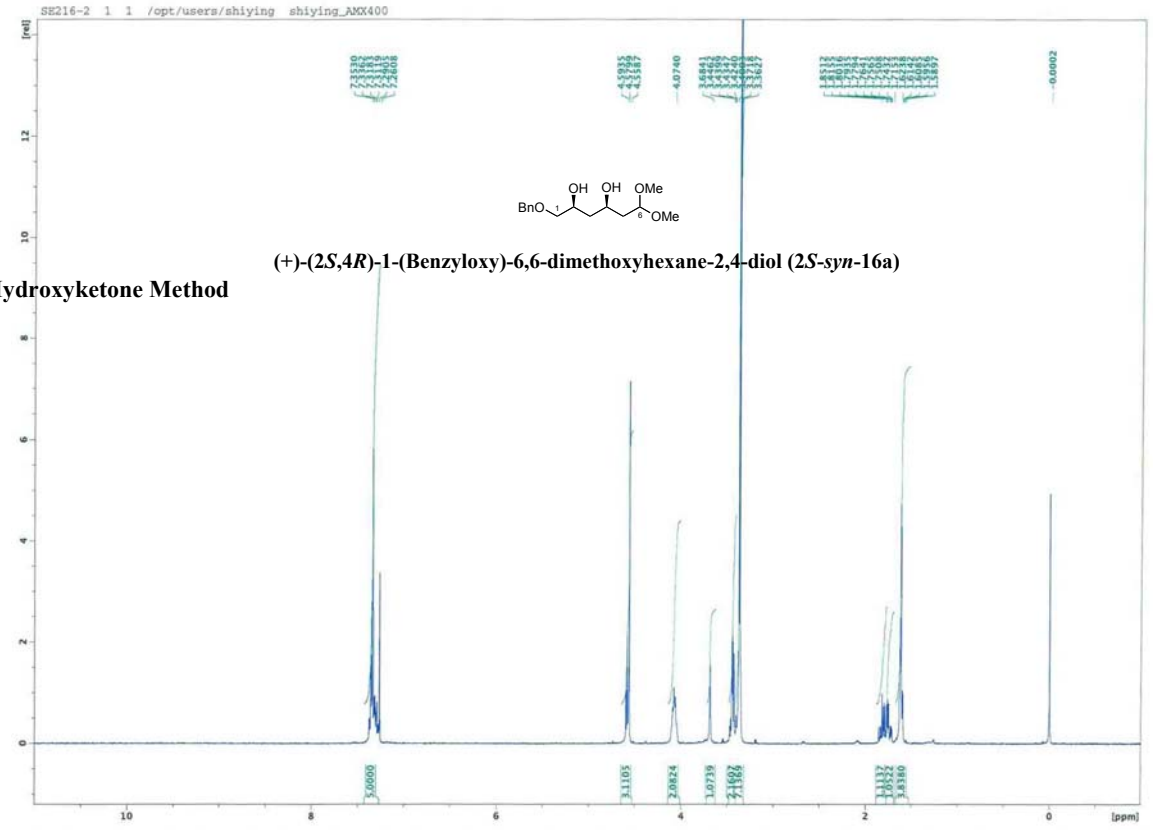
(+)-(3*R*,5*R*,6*S*)-6-(Benzyloxy)-1,1-dimethoxyheptane-3,5-diol (*syn*,*anti*-16b)





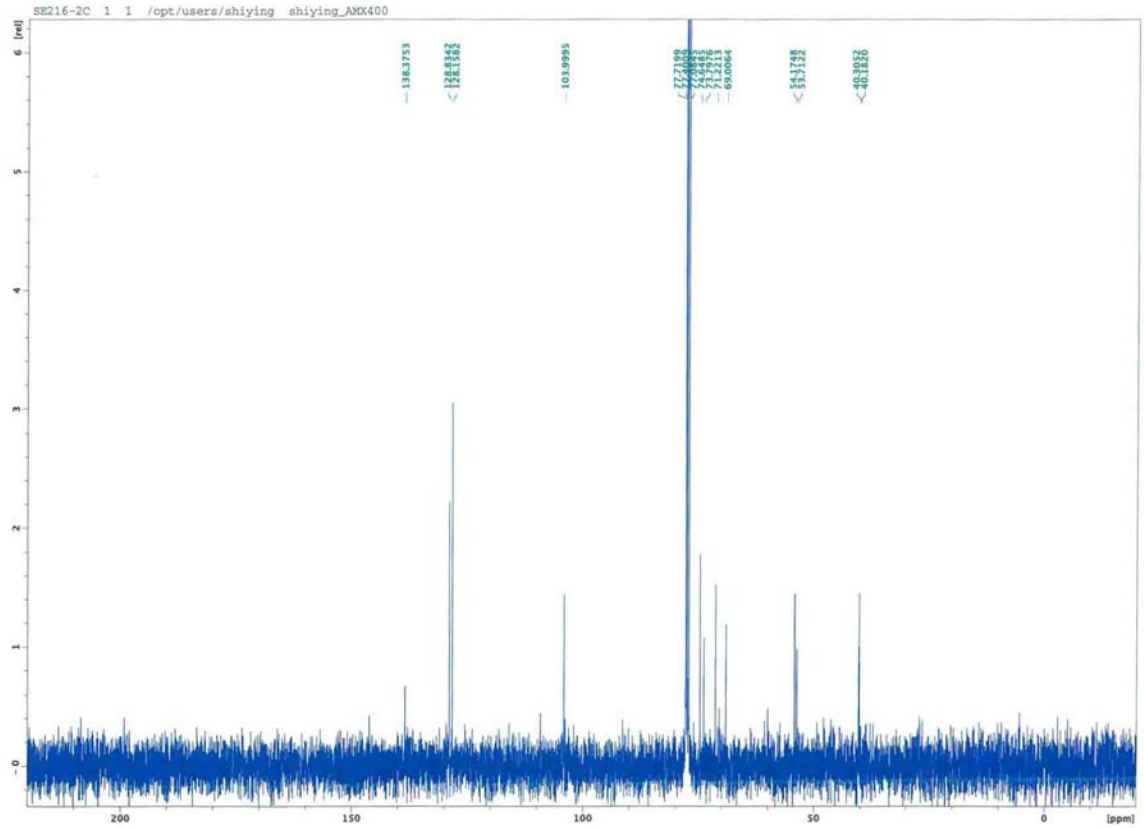
(+)-(2*S*,4*R*)-1-(Benzyloxy)-6,6-dimethoxyhexane-2,4-diol (2*S*-*syn*-16a)
Epoxyol Method

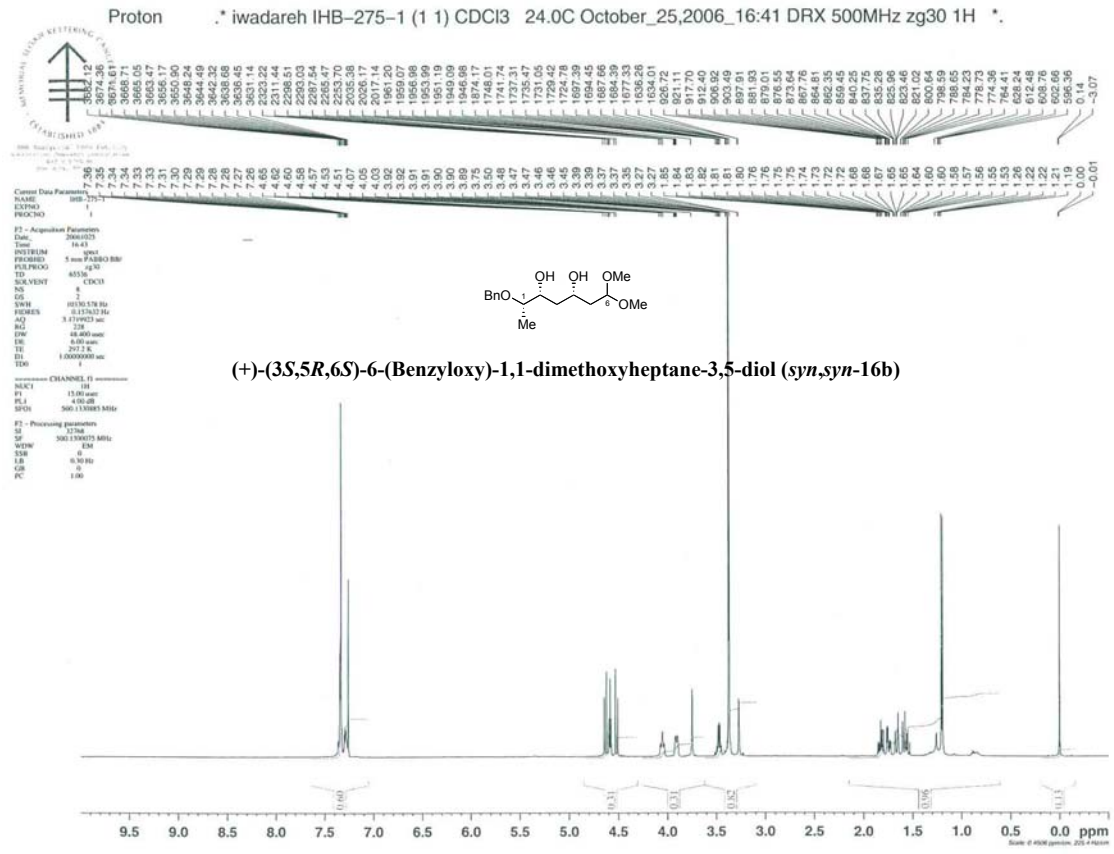




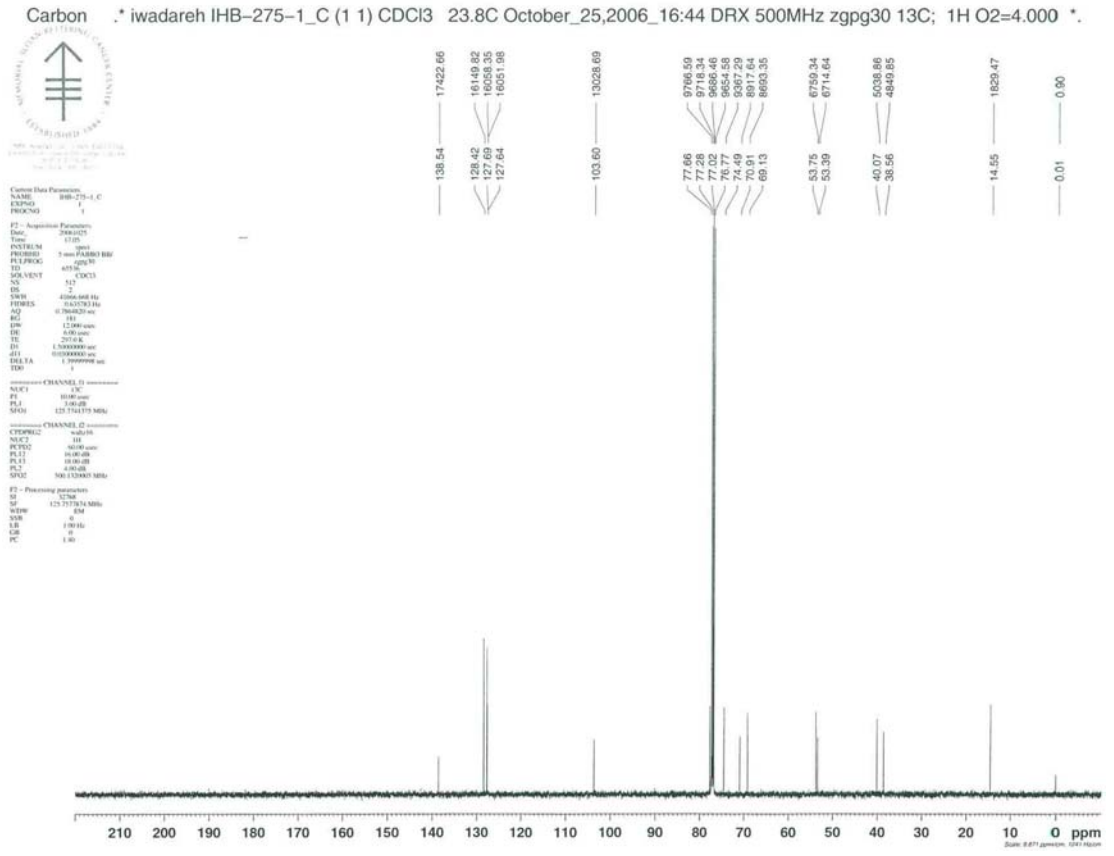
(+)-(2*S*,4*R*)-1-(Benzyloxy)-6,6-dimethoxyhexane-2,4-diol (2*S*-*syn*-16a)

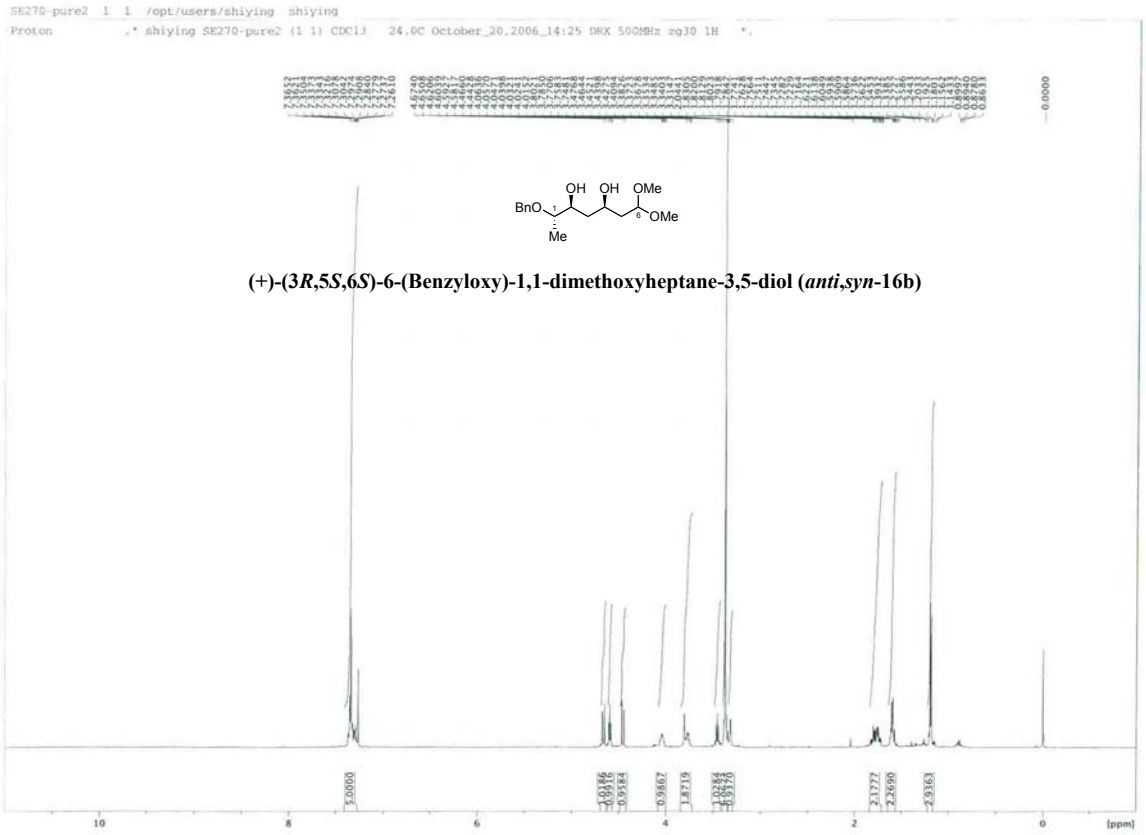
β-Hydroxyketone Method



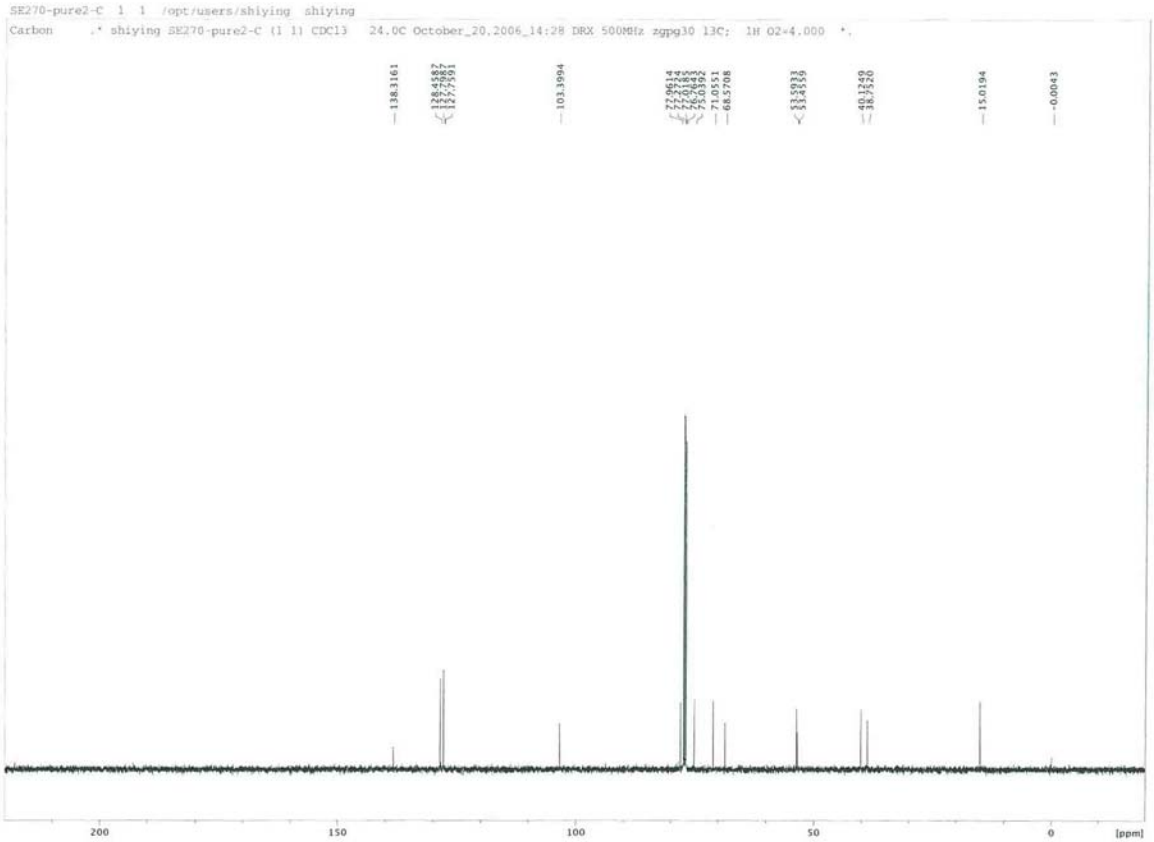


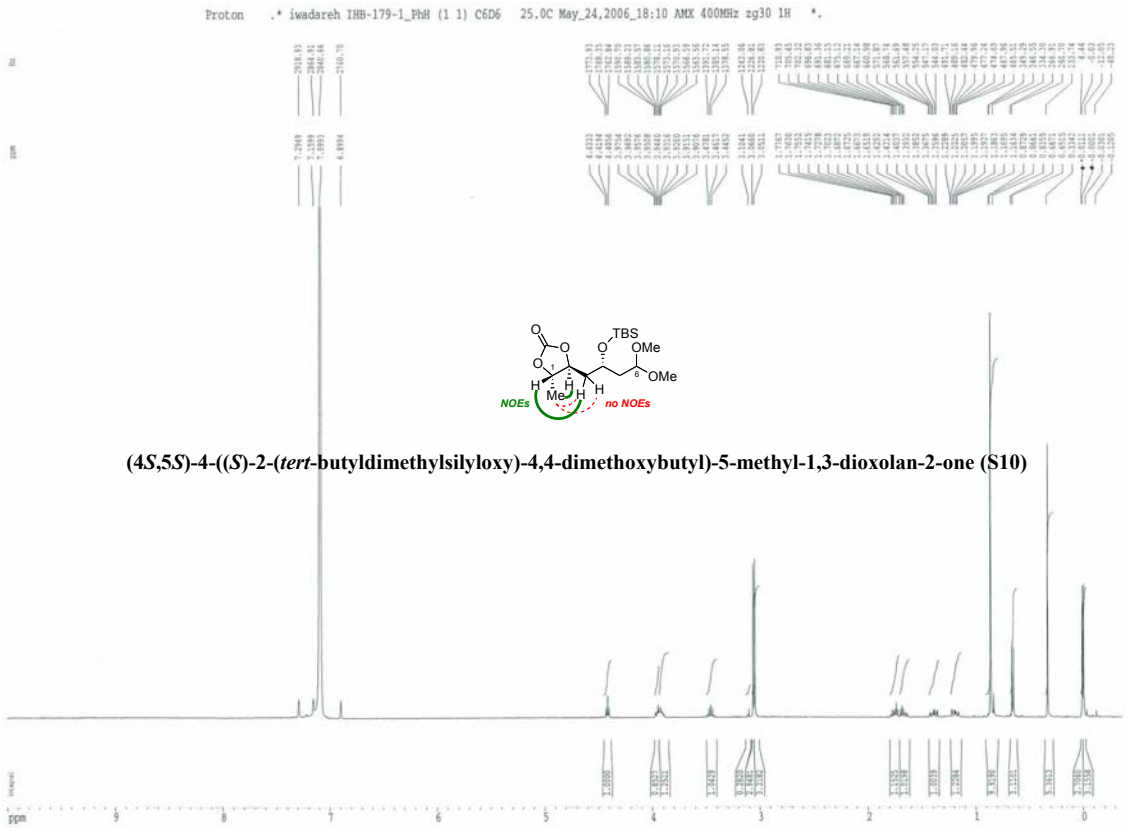
(+)-(3*S*,5*R*,6*S*)-6-(Benzyloxy)-1,1-dimethoxyheptane-3,5-diol (*syn*,*syn*-16b)



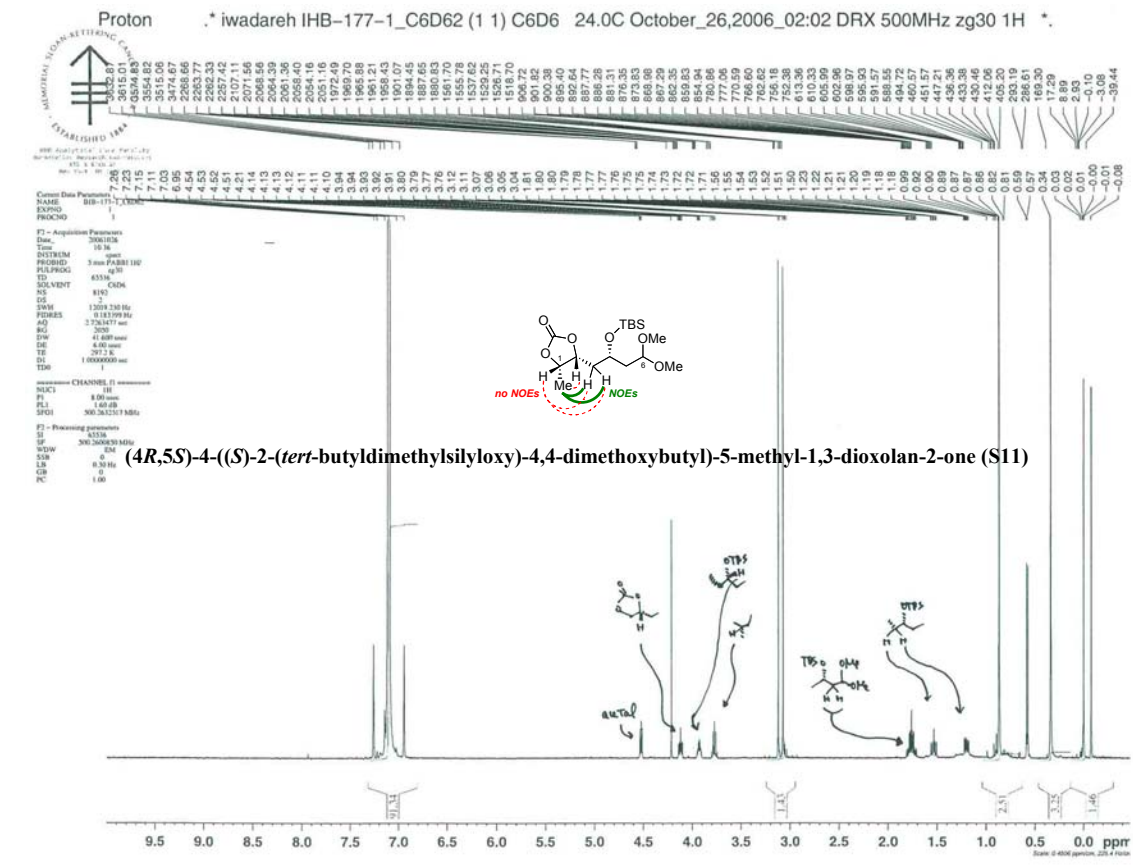


(+)-(3*R*,5*S*,6*S*)-6-(Benzyloxy)-1,1-dimethoxyheptane-3,5-diol (*anti*,*syn*-16b)





(4*S*,5*S*)-4-((*S*)-2-(*tert*-butyldimethylsilyloxy)-4,4-dimethoxybutyl)-5-methyl-1,3-dioxolan-2-one (S10)



(4*R*,5*S*)-4-((*S*)-2-(*tert*-butyldimethylsilyloxy)-4,4-dimethoxybutyl)-5-methyl-1,3-dioxolan-2-one (S11)