Asymmetric Synthesis of Propargylic Alcohols via Aldol Reaction of Aldehydes with Ynals Promoted by Prolinol Ether/Transition Metal/Brønsted Acid Cooperative Catalysis.

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SUPPLEMENTARY INFORMATION

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A) General information

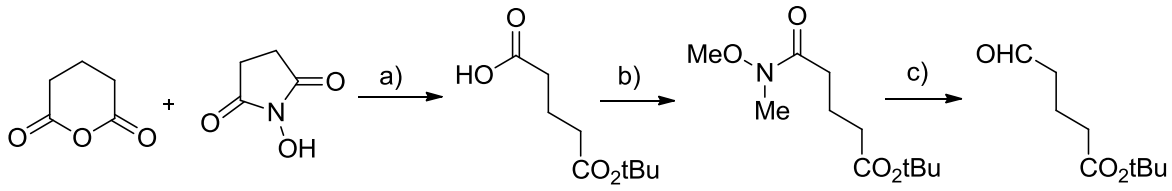
Methylene chloride (CH_2Cl_2) was distilled from CaH_2, THF was dried in a It Pure Solv column. Ethyl acetate and hexane were used as reagent grade. Purification of reaction products was carried out by flash column chromatography using silica gel 60 (0.040-0.063 mm, 230-400 mesh). Analytical thin layer chomatography (TLC) was performed on 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and a solution obtained by admixing ammonium molybdate (21 g), cerium sulphate (1 g) and concentrated sulphuric acid (31 ml) in 470 mL of water, followed by heating. Melting points were measured with a Buchi SMP-20 melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Advance-300 and are reported in ppm from internal tetramethylsilane (TMS). Analytical high performance liquid chromatography (HPLC) was performed on Waters-600E, equipped with 2996 and 2998 photodiode array UV detector, using Daicel Chiralpak AD-H, AS-H, OD-H, AY-H, IB, IC and IA columns. Optical rotations were recorded on a Jasco P-2000 polarimeter. MS spectra were recorded on an ESI-ion trap Mass spectrometer (Agilent 1100 series LC/MSD, SL model). Amine catalyst **4** was prepared according to previously reported procedure.[1]

B) Preparation of aldehydes

Aldehydes **1A-C**, and **1F** were obtained from commercial sources and distilled prior use.

Aldehydes **1D, 1E, 1G** and **1H** were prepared according to reported procedures, as follow.

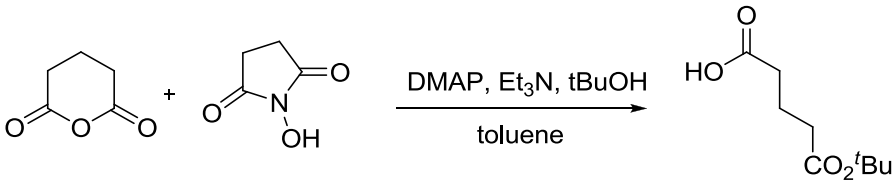
tert-Butyl-5-oxopentanoate (1D)



1D

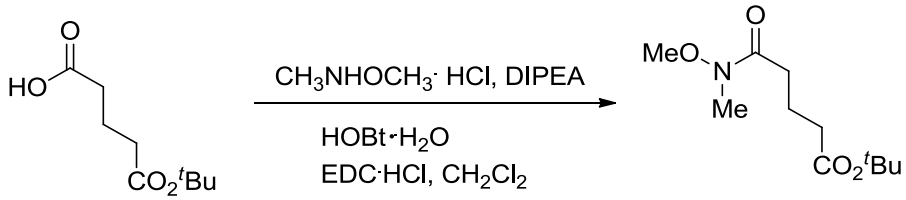
[1] Gómez-Bengoa, E.; Jimenez, J.; Lapuerta, .I; Mielgo, A.; Oiarbide, M.; Otazo, I.; Velilla, I.; Vera, S.; Palomo, C. *Chem. Sci.* **2012**, *3*, 2949-2957.

Procedure for Step a:[2]



Glutaric anhydride (10.0 g, 87.6 mmol) was weighed into a dry flask and purged with N_2. Dry toluene (50 mL) was added followed by *N*-hydroxysuccinimide (3.0 g, 26.1 mmol), 4-dimethylaminopyridine (1.07 g, 8.8 mmol), anhydrous *tert*-butanol (24.3 mL, 262.3 mmol), and triethylamine (3.6 mL, 25.8 mmol). The flask was fitted with a reflux condenser, heated to 115 °C, and allowed to stir for 16 h. The solution was cooled to room temperature, diluted with 300 mL EtOAc, and washed with 5% aqueous $NaHSO_4$ solution (3×, 100 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated. The crude material was purified by column chromatography on silicagel (eluent hexanes/EtOAc 1:1) to yield 8.32 g (50% yield) of a colorless oil. The physical and spectroscopic data were in agreement with those described in the literature. ^{1}H NMR (300MHz, $CDCl_3$): δ 10.83 (bs, 1H), 2.42 (t, *J* = 7.4 Hz, 2H), 2.31 (t, *J* = 2.31 Hz, 2H), 1.92 (m, 2H), 1.45 (s, 9H).

Procedure for Step b:

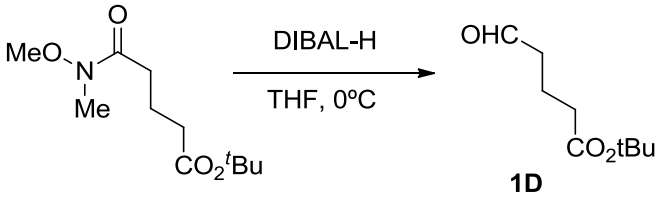


Thus obtained carboxylic acid (8.2 g, 44 mmol) was dissolved in CH_2Cl_2 (200 mL) and to the solution were successively added hydrochloride *N,O*-dimethylhydroxylamine (4.72 g, 48.4 mmol), 1-hydroxybenzotriazole hydrate (6.53 g, 48.4 mmol), diisopropylethylamine (17 mL, 97 mmol), and EDC·HCl (9.28 g, 48.4 mmol). The mixture was stirred at room temperature for 2 h and then concentrated under vacuum to remove most of the CH_2Cl_2. The crude material was diluted with EtOAc (300 mL),

[2] Y. Chi, E. P. English, W. C. Pomerantz, W. S. Horne, L. A. Joyce, L. R. Alexander, W. S. Fleming, E. A. Hopkins, S. H. Gellman *J. Am. Chem. Soc.*. **2007**, *129*, 6050-6055

and washed successively with 5% aqueous $NaHSO_4$ solution (3× 100 mL), 5% aqueous $NaHCO_3$ solution (3× 100 mL), and brine (100 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated to afford 4.8 g (50% yield) of the product as a pale yellow oil which was used without further purification. ^{1}H NMR (300MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.18 (s, 3H), 2.48 (t, *J* = 7.4 Hz, 2H), 2.30 (t, *J* = 7.4 Hz, 2H), 1.92 (m, 2H), 1.45 (s, 9H).

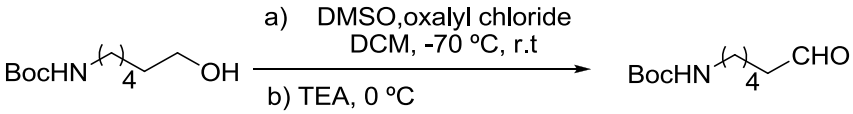
Procedure for Step c:



1D

Weinreb amide (5.0 g, 21.6 mmol) was dissolved in dry THF (100 mL) and the solution was cooled to 0 °C under N_2. Diisobutylaluminum hydride (43 mL of a 1.0 M solution in CH_2Cl_2, 43 mmol) was added dropwise. The reaction mixture was allowed to stir at 0 °C for 30 min and then quenched by slow addition of EtOAc (50 mL). The solution was poured into water (200 mL) and extracted with EtOAc (2 × 400 mL). The combined organic layers were washed successively with sat. aqueous $NaHCO_3$ solution (100 mL) and brine (100 mL), dried over $MgSO_4$, filtered and concentrated. The crude material was purified by silicagel column chromatography (eluent hexanes/EtOAc 3:1) to yield 2.2 g (59% yield) of a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.78 (t, *J* = 1.4 Hz, 1H), 2.51 (td, *J* = 7.3, 1.4 Hz, 2H), 2.28 (t, *J* = 7.3 Hz, 2H), 1.92 (m, 2H), 1.45 (s, 9H).

tert-Butyl 6-oxohexylcarbamate (1E) [3]



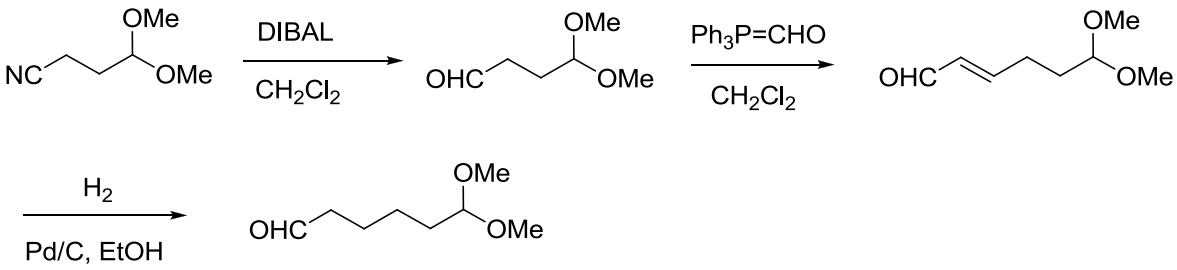
Prepared from *tert*-butyl 6-hydroxyhexylcarbamate (2.0 mL, 10 mmol) by Swern oxidation as follows: A solution of DMSO (2.27 mL, 32.0 mmol) in dichloromethane (16

[3] Adapted from: X. Xiao, S. Antony, G. Kohlhagen, Y. Pommier, M. Cushman, *Bioorg. Med. Chem.* **2004**, *12*, 5147-5160.

mL) was slowly added to a solution of oxalyl chloride (1.4 mL, 16.0 mmol) in dichloromethane (60 mL) previously cooled to –70 ºC. The resulting mixture was stirred at the same temperature for 5 minutes, after which a solution of the precursor alcohol (8.0 mmol) in dichloromethane (16 mL) was added dropwise and stirred for an additional hour at –70 ºC. Triethylamine (6.68 mL, 48 mmol) was subsequently slowly added, the resulting mixture allowed to reach 0 ºC, and stirred at that temperature for one hour. The resulting mixture was poured into water (40 mL) and diluted with Et_2O (400 mL). The organic layer was separated and washed with brine (2 x 75 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silicagel flash column chromatography (eluent hexane:ethyl acetate). The title compound was obtained as a colorless oil: 1.85 g, (85% yield). The physical and spectroscopic data were in agreement with those described in the literature.

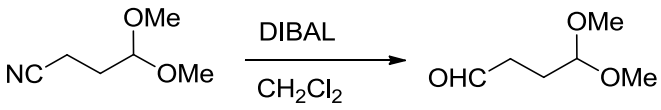
^{1}H-RMN (300 MHz, $CDCl_3$) δ: 9.76 (t, *J*= 1.7 Hz,1H), 3.11 (d, *J*= 6.5 Hz, 2H), 2.43, (dt, *J*= 1.7, 7.2, 7.3 Hz, 2H), 1.70-1.23 (m, 6H), 1.44 (s, 9H).

6,6-Dimethoxyhexanal (1G)[4,5]



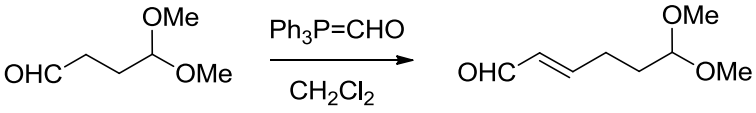
[4] Adapted from: Takeishi, K.; Sugishima, K.; Sasaki, K.; Tanaka, K. *Chem. Eur. J.* **2004**, *10*, 5681-5688.
[5] Adapted from: Lopez, R.; Zalacain, M.; Palomo, C. *Chem. Eur. J.* **2011**, *17*, 2450-2457.

Procedure for Step a:



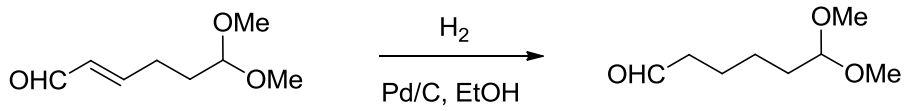
DIBAL (0.95 M in *n*-hexane, 24.4 mL, 23.2 mmol) was added a solution of 3-cianopropionaldehyde dimethyl acetal (3.02 mL, 23.5 mmol) in CH_2Cl_2 (120 mL) at –78 ^oC and the resulting mixture was stirred for 1h. The resulting mixture was warmed slowly to RT, and treated with excess saturated aqueous NH_4Cl. The reaction mixture was then diluted with water and extracted with CH_2Cl_2. The organic layer was washed with water, dried over $MgSO_4$, and concentrated, which afforded crude 4,4-dimethoxybutyraldehyde (2.6 g, 19.6 mmol, 84 %) as a pale yellow oil.

Procedure for Step b:



The aldehyde was added dropwise in CH_2Cl_2 (10 mL) at 0 ^oC to a solution of formylmethylenetriphenylphosphorane (10 g, 34 mmol, 2 equiv) in CH_2Cl_2 (20 mL). The resulting mixture was stirred at the same temperatura for 2 h, warmed up to 50 ^oC, and stirred for 24 h. Upon reaction completion, the solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (eluent mixtures EtOAc / Hexane 80:20) to afford the corresponding pure adehyde (50 % yield) as a pale yellow oil.

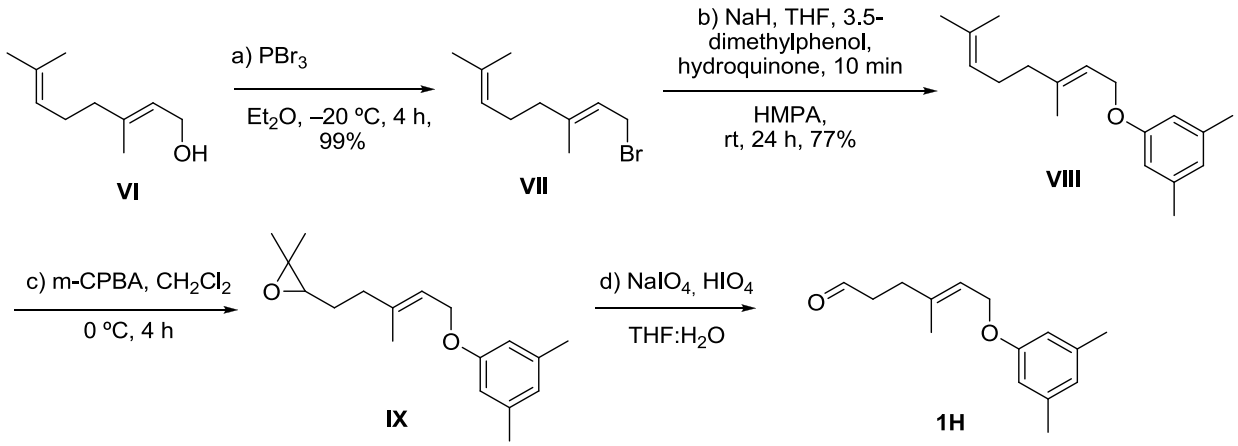
Procedure for Step c:



1G

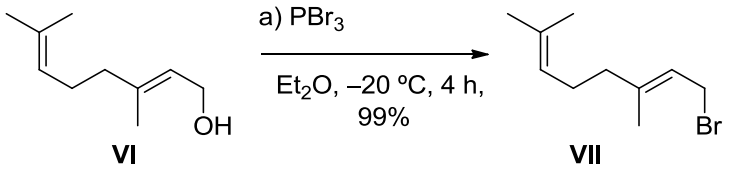
To a 25 mL flash charged with a solution of enal (948 mg, 6 mmol) in ethanol (12 mL) was added Pd/C (10% wt, 180 mg). The flask was filled with hydrogen gas and stirred for 16 h at room temperature under hydrogen balloon. The mixture was filtered over celite pad and the filtrate was concentrated. Purification on a silica gel column (hexane/AcOEt, 80:20) provided 768 mg of the aldehyde **1G** (4.8 mmol, 80% yield) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.80 (t, *J* = 1.7 Hz, 1H), 4.39 (dd, *J* = 7.1 Hz, 4.1, 1H), 3.35 (s, 6H), 2.44 (dd, *J* = 8.2, 6.5 Hz, 3H), 1.97 (td, *J* = 7.3, 5.4 Hz, 4H), 1.43 (tdd, *J* = 10.8, 7.2, 4.0 Hz, 2H).

Synthesis of (E)-6-(3,5-dimethylphenoxy)-4-methylhex-4-enal (1H)



VI **VII** **VIII** **IX** **1H**

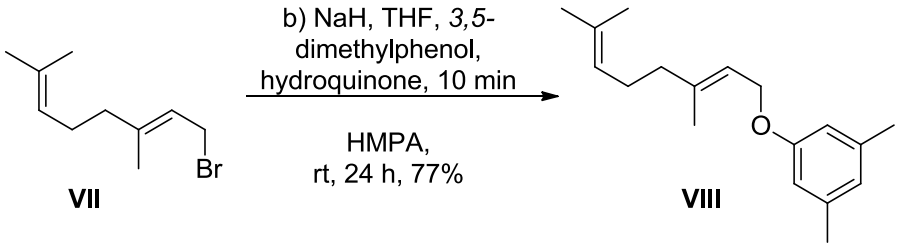
Procedure for step a (VII) [6]



VI **VII**

To a solution of *trans*-geraniol (17.5 mL, 100 mmol) in ether (75 mL) at –20 °C was added a solution of phosphorus tribromide (4.7 mL, 50 mmol) in ether (45 mL) within 10 min, and the reaction mixture was stirred for 4 h. The reaction was quenched with water, extracted with petroleum ether, washed in turn with water, with saturated aqueous $NaHCO_3$, and brine. The organic layer was dried ($MgSO_4$) and evaporated at 30 °C to provide (*E*)-geranyl bromide (**II**) (21.7 g, 99%) of as a labile yellow liquid which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.53 (tq, *J*= 6.5, 1.5 Hz, 1H), 5.08 (m, 1H), 4.02 (d, *J* = 8.4 Hz, 2H), 2.16 – 2.00 (m, 4H), 1.73 (s, 3H), 1.69 (s, 3H), 1.60 (s, 3H).

Procedure for step b (VIII) [7]



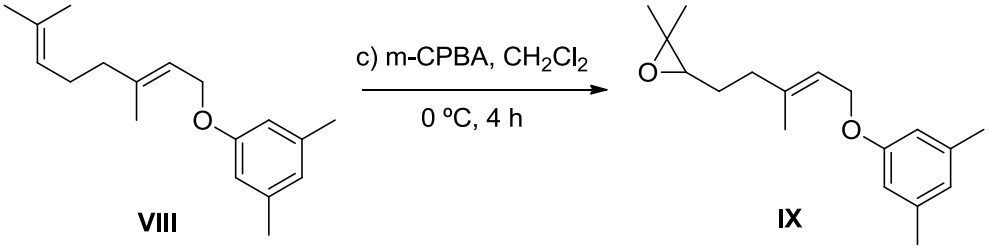
VII **VIII**

To a stirred suspension of sodium hydride (60% in oil, 1050 mg, 25.25 mmol) in THF (75 mL) at room temperature under argon atmosphere was added 3,5-dimethylphenol (25 mmol) portion wise followed by a catalytic amount of hydroquinone (10% mmol). The mixture was stirred for 0.5 h at room temperature. Hexamethylphosphoramide (HMPA, 17.5 mL) and geranyl bromide (**II**) (25 mmol) were successively added. The whole mixture was stirred for 1 day. After decomposition of excess sodium hydride with methanol (2 mL), the mixture was poured into ice-water and extracted with ether. The combined organic layers were dried, concentrated and purified by column chromatography on silica gel (hexane-ethyl acetate 95:5 as eluent) to give geranyl aryl ether (**III**) (70% yield) as a yellow oil. ^{1}H RMN (300 MHz, $CDCl_3$) δ 6.56-6.80 (m, 3H),

[6] Paz, J.L.; Rodroguez, J.A.R.; *J. Braz. Chem. Soc*. **2003**, *14,* 975-981.
[7] Ishihara, K.; Nakamura, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1999,** *121,* 4906-4907.

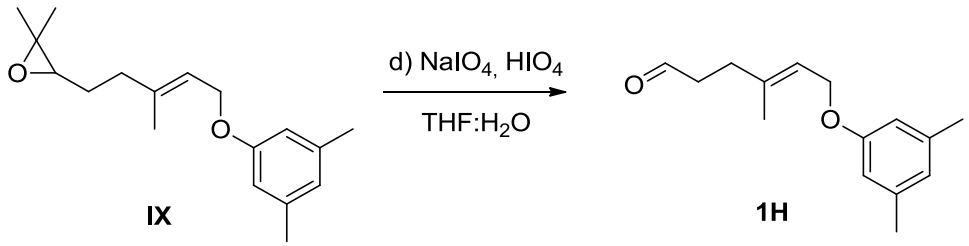
5,50 (tq, *J* = 6.6, 1.5 Hz, 1H), 5,06-5,14 (m, 1H), 4,51 (d, J = 6,6, 2H), 2,29 (s, 6H), 2,10 (m, 4H) 1,74 (s, 3H), 1,69 (s, 3H), 1,62 (s, 3H).

Procedure for step c (IX)[8]



To a solution of geranyl phenyl ether **(VIII)** (17.6 mmol) in CH_2Cl_2 (45 mL) was added dropwise *m*-chloroperbenzoic acid (4.9 g, 70%, 19.4 mmol) in CH_2Cl_2 (50 mL) at 0 ºC. After the addition was complete, the mixture was stirred at 0 ºC for another 4 h. The reaction was quenched by the addition of 50 mL of saturated $NaHCO_3$, the organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuum. The crude product was purified by silica gel chromatography (hexane-ethyl acetate 90:10 as eluent) to give **(IV)** (4.11 g, 87%) as a yellow oil. ^{1}H RMN (300 MHz, $CDCl_3$) δ 6.54-6.60 (m, 3H), 5.50 (tq, *J* = 6.5, 1.3 Hz, 1H), 4.51 (d, *J* = 6.4 Hz, 2H), 2.71 (t, *J* = 6.2, 1H), 2.28 (s, 6H), 2.21 (m, 2H), 1.76 (s, 3H), 1.68 (m, 2H) 1.31 (s, 3H), 1.27 (s, 3H).

Procedure for step d (IH) [9]

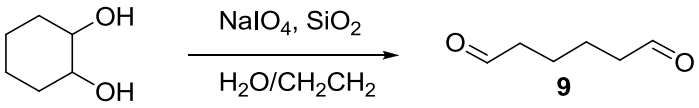


A solution of epoxide (**IX**) (1.0 eq) in $THF:H_2O$ (10:1, 30 mL) was treated sequentially at 0 °C with $NaIO_4$ (0.6 equiv) and $HIO_4{\cdot}2H_2O$ (1.1 equiv). The resultant biphasic mixture was stirred at 0 °C for 10 min and then warmed to room temperature. After 1 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (25 mL), poured into

[8] Surendra. K.; E. J. Corey, *J. Am. Chem. Soc.* **2008**, *130 (27)*, 8865–8869
[9] Surendra, K.; Qiu, W.; E. J. Corey, *J. Am. Chem. Soc.*, **2011**, *133 (25)*, 9724–9726

H_2O (25 mL), and the aqueous layer was extracted with EtOAc (3 x 50 ml). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in *vacuo*. The crude product was purified by silica gel chromatography (hexane-ethyl acetate 95:5 as eluent) to give the desired aldehyde **IH** as orange oil. Yield: 81% (0.8 g). ^{1}H RMN (300 MHz, $CDCl_3$) δ 7.79 (t, *J* = 1.6 Hz, 1H), 6.53-6.60 (m, 3H), 5.51 (tq, *J*: = 6.4, 1.3 Hz, 1H), 4.50 (d, *J* = 5.9 Hz, 2H), 2.59 (m, 2H), 2.41 (m, 2H), 2.29 (s, 6H), 1.75 (s, 3H).

Hexane-1,6-dial (9)[10]

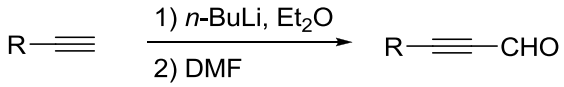


9

To a vigorously stirred suspension of chromatographic grade silica gel (105 g) in CH_2Cl_2 (500mL) was added an aqueous solution of $NaIO_4$ (0.65 M, 68.2 mmol), whence a flaky suspension was formed. 1,2-Cyclohexanediol (6.08 g, 52.3 mmol) in CH_2Cl_2 (200 mL) was then added, and the reaction was stirred for 24 h. The mixture was filtere on a sintered glass, and the silica gel was throughly washed with CH_2Cl_2. Evaporation of the solvent afforded the title compound as a colorleess oil in quantitative yield (5.91 g). No further purification was necessary.

C) Preparation of propargylic aldehydes[11]

All propargylic aldehydes were synthesized as described below, except octynal (**2a**) and phenyl propynal (**2f**) that are commercially available.

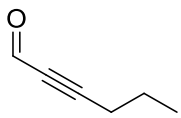


To a round bottomed flask under nitrogen atmosphere filled of dry Et_2O (50 mL) and cooled to -60 ^{o}C, were added dropwise *n*-BuLi (50 mmol, 20 mL, 2.5 M in hexane) and then the corresponding alkyne (50 mmol). The reaction mixture was stirred at this

[10] Lopez, S.; Fernandez-Trillo, F.; Midón, P.; Castedo, L.; Saá, C. *J. Org. Chem.* **2005**, *70*, 6346-6352.
[11] L. Brandsma, *Preparative Acetylenic Chemistry (Studies in Organic Chemistry 34)* Ed. Elsevier, Amsterdam, **1988**, 97-112

temperature for 30 min after which DMF (4.3 mL, 62.5 mmol) was added slowly. The resulting mixture was removed from the bath, warmed slowly to room temperature and stirred at this temperature for 20 minutes. Finally the reaction mixture was poured slowly into a cold solution of water (25 mL) and HCl conc.(4 mL) and a solution of saturated $NaHCO_3$ was added dropwise until pH 6-7. The organic layer was separated and the aqueous phase extracted with Et_2O (3x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduce pressure. The crude product was purified by silica gel chromatography unless otherwise stated.

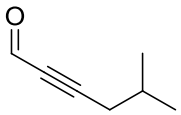
Hex-2-ynal (2b)



Prepared according to general procedure, starting from 1 pentyne (1.9 mL, 20 mmol). Yelow liquid. Yield: 33% (0.6g).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.18 (t, *J* = 0.9 Hz, 1H), 2.39 (td, *J* = 7.0, 0.8 Hz, 2H), 1.64 (dt, *J* = 14.5, 7.3 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H).

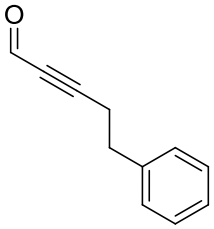
5-Methylhex-2-ynal (2c)



Prepared according to general procedure, starting from 4-methylpent-1-yne (1.4 mL, 10 mmol). Yelow liquid. Yield: 63% (0.7 g).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.19 (t, *J* = 0.8 Hz, 1H), 2.31 (dd, *J* = 6.5, 0.8 Hz, 2H), 1.93 (dt, *J* = 13.3, 6.6 Hz, 1H), 1.02 (d, *J* = 6.7 Hz, 7H).

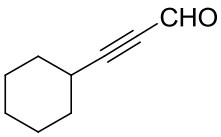
5-Phenylpent-2-ynal (2d)



Prepared according to general procedure, starting from 4-phenyl-1-butyne (1.4 mL, 10 mmol). Yelow liquid. Yield: 89% (1.41 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (t, *J* = 0.8 Hz, 1H), 7.37-7.24 (m, 5H), 2.94 (t, *J* = 7.4 Hz, 2H), 2.74 (dt, *J* = 7.4 Hz, *J* = 0.7 Hz, 2H).

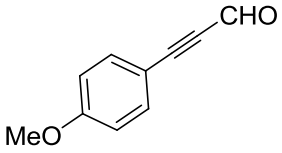
3-Cyclohexylpropiolaldehyde (2e)[12]



Prepared according to general procedure, starting from ethynylcyclohexane (1.3 mL, 10 mmol). Yelow liquid. Yield: 90% (1.22 g). Spectroscopic data were in agreement with those previously reported.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.23 (d, *J* = 0.8 Hz, 1H), 2.70 – 2.55 (m, 1H), 1.96 – 1.83 (m, 2H), 1.83 – 1.67 (m, 2H), 1.56 (m, 3H), 1.48 – 1.23 (m, 3H).

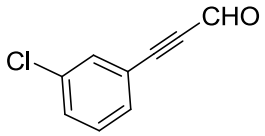
3-(*p*-Methoxyphenyl)propiolaldehyde (2g)[13]



Prepared according to general procedure, starting from 1-ethynyl-4-methoxybenzene (1.30 g, 10 mmol). The crude material was crystallized from hexane. Yield: 52% (0.83 g). Colourless crystals. Spectroscopic data were in agreement with those previously reported.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.39 (s, 1H), 7.59 – 7.52 (m, 2H), 6.95 – 6.88 (m, 2H), 3.85 (s, 3H).

***m*-Clorofenilpropinal (2h)**[14]

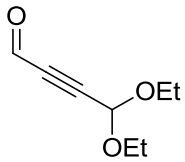


Prepared according to general procedure, starting from 1-chloro-2-etinylbenzene (1.23 g, 10 mmol). The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 98/2) to give the title compound as a yellow oil. Yield: 56% (0.92 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.48 (s, 1H), 7.65 (t, *J* = 1.6 Hz, 1H), 7.46 (m, 1H), 7.42 (m, 1H), 7.30 (dd, *J* = 11.7, 4.0 Hz, 1H).

[12] Y. -L. Shen, W. -T. Wu, Q. Liu, G. -L. Wu, L. -M. Wu. *J. Chem. Res.* **2006**, 545-546.
[13] S. Ma, J. Liu, S. Li, B. Chen, J. Cheng, J. Kuang, Y. Liu, B. Wan, Y. Wang, J. Ye, Q. Yu, W. Yuan, S. Yu, *Adv. Synth. Cat.* **2011**, *353*, 1005-1017.
[14] C.R. Solorio-Alvarado, A. M. Echavarren, *J. Am. Chem. Soc.* **2010**, *132*, 11881-11883.

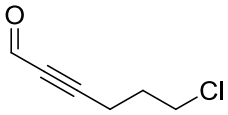
4,4-Diethoxybut-2-ynal (2i)



Prepared according to general procedure, starting from propargyl aldehyde diethyl acetal (1.4 mL, 10 mmol) but the reaction mixture was treated pouring it slowly into a cold solution of 10% citric acid (15 mL) and then a solution of saturated NaHCO3 was added dropwise until pH 6-7. Yield: 50% (0.78 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (d, *J* = 0.5 Hz, 1H), 5.44 (s, 1H), 3.78 (dq, *J* = 7.1 Hz, J = 9.4 Hz, 2H), 3.66 (dq, *J* = 7.1 Hz, *J* = 9.4 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 6H).

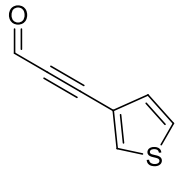
6-Chlorohex-2-ynal (2j)



Prepared according to general procedure, starting from 5 chloro-1-pentyne (0.5mL, 5 mmol). Brown liquid. Yield: 56% (0.3g).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.18 (s, 1H), 3.66 (t, *J* = 6.2, 2H), 2.64 (t, *J* = 6.9, 2H), 2.18 – 1.96 (m, 2H).

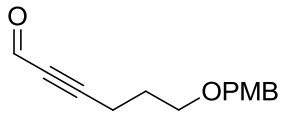
3-(Thiophen-3-yl)propiolaldehyde (2k)



Prepared according to general procedure, starting from 3-ethynylthiophene (0.98mL, 10 mmol). Black oil. Yield: 45% (612.8 mg).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.82 (dd, *J* = 2.9, 1.1, 1H), 7.36 (dd, *J* = 5.0, 3.0, 1H), 7.24 (d, *J* = 1.1, 1H).

6-((4-methoxybenzyl)oxy)hex-2-ynal (2l)

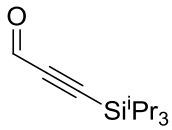


Prepared according to general procedure, starting from 1-methoxy-4-((pent-4-yn-1-yloxy)methyl)benzene[15] (2g,10 mmol). Brown liquid. Yield: 56% (1.2g).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.19 (s, 0H), 7.29 (d, *J* = 8.7, 2H), 6.92 (d, *J* = 8.7, 2H), 4.48 (s, 2H), 3.84 (s, 3H), 3.57 (t, *J* = 5.9, 2H), 2.58 (t, *J* = 7.1, 2H), 1.96 – 1.86 (m, 2H).

[15] K. Frimpong, J. Wzorek, C. Lawlor, K. Spencer, T. Mitzel *J. Org. Chem*. **2009**, *74*, 5861-5870.

3-(triisopropylsilyl)propiolaldehyde (2m)



Prepared according to general procedure, starting from triisopropyl(prop-1-yn-1-yl)silane (2.2mL, 10 mmol). Yellow liquid. Yield: 73% (1.5g).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.23 (s, 0H), 1.13 (d, *J* = 5.5, 18H).

D) General Procedure for the Cross-Aldol reactions

To a solution of the amine catalyst (0.1 mmol, 20 mol %) in THF (0.5 mL) at –60 °C were successively added the corresponding donor aldehyde (0.6 mmol, 1.2 equiv.)[16] the Brønsted acid (0.1 mmol, 20 mol %), CuI (0.05 mmol, 10 mol %) and the ynal (0.5 mmol, 1 equiv.). The resulting solution was stirred at –60 °C for 20 h, and the reaction product was isolated either as alcohol or as acetal following the procedures described below.

The diastereoselectivity of the process was determined by ^{1}H-NMR analysis of an aliquot by integration of the corresponding signals in the aldehyde region before reduction of the intermediate aldehyde adduct.[17] The ratio of isomers does not change after reduction of the adduct at the indicated temperature.[18] Finally this diastereomer ratio was also confirmed by HPLC analysis in the diol compound.

The corresponding racemic compounds were prepared according to this same procedure, but using *rac*-**4** as the catalyst.

A) Isolation of the reaction product as alcohol: To the above mixture, a suspension of $NaBH_4$ (4.5 mmol, 8 equiv.) in EtOH (1 mL) was added drop-wise at -60°C, and after reaction completion (monitored by ^{1}H-NMR), typically (typically 30–60 min), the mixture was quenched with brine (4 mL), and allowed to reach room temperature. After extraction with CH_2Cl_2 (3 x 6 mL), the combined organic phases were washed with brine,

[16] For the reactions with propanal a threefold excess of aldehyde was employed.
[17] In some particular cases because of peak overlapping in the aldehyde region the dr was determined by integration of C*H*OH.
[18] Partial epimerization has been observed when the reduction is performed at higher temperatures.

dried over $MgSO_4$, and concentrated under reduced pressure. The resulting crude was purified over silicagel by flash column chromatography to afford the expected adducts.

B) Isolation of the reaction product as dimethyl acetals: To the above mixture 4.5 mL of MeOH, trimethyl orthoformate (0.16 mL, 1.5 mmol) and *p*-toluenesulfonic acid (20.0 mg, 0.1 mmol, 20 mol%) were successively added at -60°C and the mixture was allowed to reach room temperature. After 2 h of stirring, the reaction was quenched with $NaHCO_3$ sat. (5 mL) and extracted with ethyl acetate (2 x 4 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography on silica gel to afford the expected adducts.[19]

[19] Procedure adapted from, T. Kano, Y. Yamaguchi, Y. Tanaka, K. Maruoka, *Angew. Chem. Int. Ed*. **2007**, *46*, 1738.

E) Reaction Scope

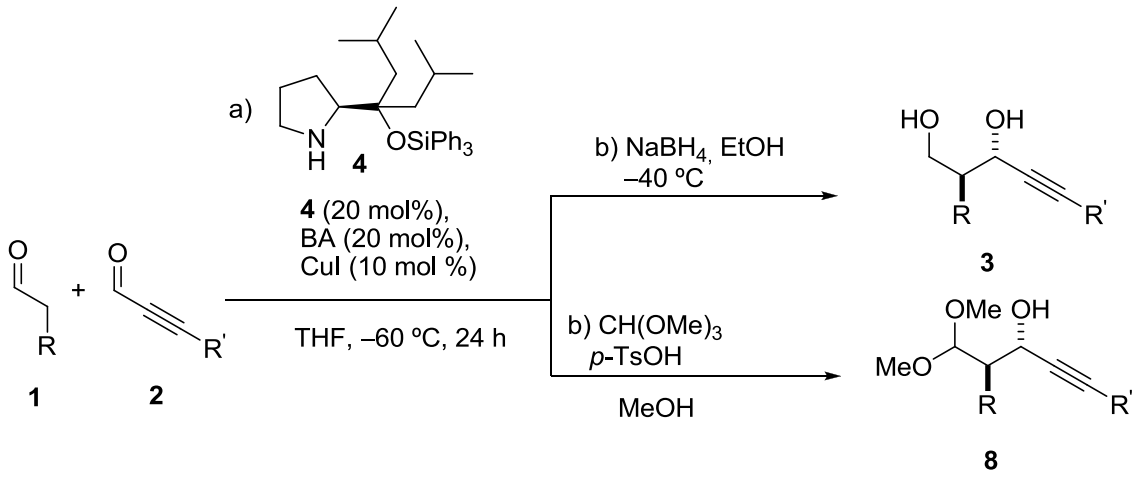
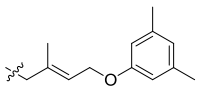
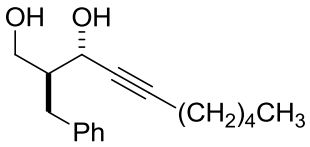


Tabla S1: Functionalized *anti* Propargylic Alcohols[a]

Entry	R	R`	Product	Yield %[b]	*anti:syn*[c]	*ee*%[d]
1	CH_2Ph	$(CH_2)_4CH_3$	**8Aa**	72	>20:1 (7.8:1)	99
2	CH_2Ph	$(CH_2)_2CH_3$	**3Ab**	68	16:1	99
3	CH_2Ph	$(CH_2)_2Ph$	**3Ad**	75	19:1	94
4	CH_2Ph	*c*-C_6H_{11}	**3Ae**	73	>20:1 (5.9:1)[e]	93
5	CH_2Ph	Ph	**3Af**	84	9:1	94
6	CH_2Ph	Ph	**8Af**	64	8.5:1	94
7	CH_2Ph	4-$OMeC_6H_4$	**3Ag**	55	10.2:1	92
8	CH_2Ph	3-Cl C_6H_4	**3Ah**	74	7.2:1	91
8	CH_2Ph	$CH(OEt)_2$	**3Ai**	60	14:1	94
9	CH_2Ph	$(CH_2)_3Cl$	**3Aj**	65	20:1	99
10	CH_3	$(CH_2)_2Ph$	**3Bd**	75	19:1	>99
11	CH_3	Ph	**3Bf**	73	5:1	94
12	CH_3		**3Bk**	50	9:1	99
13	CH_3	$(CH_2)_3OPMB$	**3Cl**	71	9:1	99
14	$CH(CH_3)_2$	$(CH_2)_4CH_3$	**3Ca**	71	20:1	99
15	$CH(CH_3)_2$	Ph	**8Cf**	64	9:1	98
16	$(CH_2)_2CO_2{}^tBu$	*c*-C_6H_{11}	**3De**	69	>20:1(5.4:1)[e]	99
17	$(CH_2)_4NHBoc$	$(CH_2)_2Ph$	**3Ed**	71	13:1	95
18	$CH_2CH{=}CH_2$	$(CH_2)_2CH_3$	**3Fb**	50	>20:1	91
19	$CH_2CH{=}CH_2$	Ph	**8Ff**	84	18:1	94
21	$CH_2CH{=}CH_2$	Si^iPr_3	**8Fm**	70	20:1	99
21	$(CH_2)_3CH(OMe)_2$	Ph	**8Gf**	51	>20:1	99
22		$CH_2CH(CH_3)_2$	**3Hc**	61	>20:1(6:1)[e]	99

[a]Reactions conducted on a 0.5 mmol scale in 0.5 mL of THF (mol ratio **1**/**2**/**4**/BA/CuI, 1.5-1.2:1:0.2: 0.2:0.1.[b] Combined yield of the *anti:syn* cross aldol mixture after chromatography. [c] Determined by ^{1}H-NMR and corroborated by HPLC; data in parentheses refer to reactions carried out with benzoic acid as the sole cocatalyst.[d] Determined by chiral HPLC. [e] NO reactions unsing either CuCl or CuI as the sole calatyst.

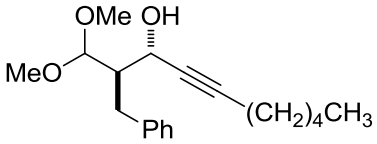
(*2S,3S*)-2-Benzyldec-4-yne-1,3-diol (3Aa)



Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and 2-octynal **2a** (71 μL, 0.5 mmol). The title compound was obtained as a 9.8:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a colorless oil. Yield: 83 % (107 mg). $[\alpha]_D^{22}$= -4.18 (*c*= 0.1, 93 % ee, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.37 (s, 5H), 4.52 (d, *J*=9.1 Hz, 1H), 4.05 (d, *J*=3.2 Hz, 1H), 3.70 (dd, *J*=11.1, 5.6 Hz, 1H), 3.01 (dd, *J*=13.7, 6.2 Hz, 1H), 2.83 – 2.65 (m, 1H), 2.29 (dtd, *J*=9.1, 7.0, 2.0 Hz, 4H), 2.06 (dtd, *J*=14.6, 5.7, 3.2 Hz, 1H), 1.68 – 1.50 (m, 1H), 1.45 – 1.28 (m, 2H), 0.99 – 0.89 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.3, 129.6, 128.8, 126.6, 77.8, 77.4, 77.0, 65.8, 63.7, 48.5, 34.5, 31.5, 30.7, 28.7, 22.6, 19.1, 14.3. MS (ESI, *m/z*): calcd for $C_{17}H_{24}O_2$ (M, H^+), 261.1810; found, 265.1798.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 95/5, flow rate= 1 mL/min, retention times: 35.5 min (min.) and 47.1 min (major)).

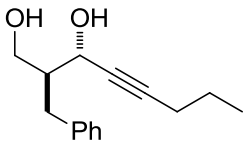
(2*R*,3*S*)-2-benzyl-1,1-dimethoxydec-4-yn-3-ol (8Aa)



Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and 2-octynal **2a** (71 μL, 0.5 mmol). The title compound was obtained as a 20:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate 90:10) to give the title compound as colourless oil. Yield: 72 % (109 mg). $[\alpha]_D^{22}$= 30.7 (*c*= 1, 99 % ee, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.16 (m, 6H), 4.55 (d, *J* = 3.9, 1H), 4.41 (dd, *J* = 7.7, 4.5, 1H), 3.47 – 3.44 (m, 3H), 3.41 (s, 4H), 2.93 – 2.79 (m, 2H), 2.21 (ddd, *J* = 9.4, 7.1, 2.9, 3H), 1.51 (dt, *J* = 14.0, 7.0, 2H), 1.44 – 1.28 (m, 5H), 0.89 (t, *J* = 7.1, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4, 129.5, 128.6, 126.2, 107.1, 86.8, 80.3, 62.3, 56.4, 55.5, 48.6, 31.2, 28.5, 22.4, 18.9, 14.2. MS (ESI, *m/z*): calcd for $C_{19}H_{28}O_3$ (M,H^+),304.4238; found (M-CH_3O),273.185.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 95/5, flow rate= 1 mL/min, retention times: 14.0 min (major.) and 31.6 min (min)).

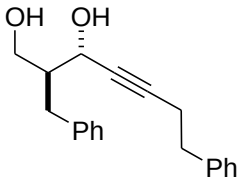
(2S,3S)-2-benzyloct-4-yne-1,3-diol (3Ab)



Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and and 2-hexynal **2b** (48mg, 0.5 mmol). The title compound was obtained as a 20:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ethyl acetate 90:10) to give the title compound as a colorless oil. Yield: 68 % (78 mg). $[\alpha]_D^{22}$= 15.7 (*c*= 1, 99 % ee, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.20 (m, 5H), 4.53 (t, *J* = 5.2 Hz, 1H), 4.10 – 3.98 (m, 1H), 3.71 (dt, *J* = 10.7, 5.3 Hz, 1H), 3.01 (dd, *J* = 13.7, 6.3 Hz, 1H), 2.80 – 2.69 (m, 1H), 2.26 (td, *J* = 7.0, 2.0 Hz, 2H), 2.16 – 2.02 (m, 2H), 1.64 – 1.55 (m, 4H), 1.08 – 0.98 (m, 3H). MS (ESI, *m*/*z*): calcd for $C_{15}H_{21}O_2$ (M,H^+),233.1542; found (M-CH_3O), 233.1541.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 95/5, flow rate= 1 mL/min, retention times: 23.0 min (major.) and 33.8 min (min)).

(*2S,3S*)-2-Benzyl-7-phenylhept-4-yne-1,3-diol (3Ad)

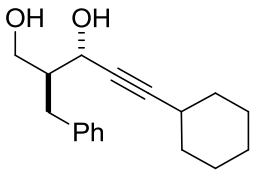


Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (99 μL, 0.75 mmol) and 5-phenylpent-2-ynal **2d** (79 mg, 0.5 mmol). The title compound was obtained as a 19:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a colourless oil. Yield: 75% (111 mg). $[\alpha]_D^{23}$= -4.38 (*c*=1, 94 % ee, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 – 7.22 (m, 5H), 4.48 (m, 1H), 3.94 (dd, *J*=10.8, 3.2 Hz, 1H), 3.61 (dd, *J*=10.8, 5.6 Hz, 1H), 3.12 (brs, 1H), 2.95 (dd, *J*=14.0, 6.0 Hz, 1H), 2.87 (t, *J*=7.4 Hz, 2H), 2.67 (dd, *J*=14.0, 9.0 Hz, 1H), 2.58 (dt, *J*=7.4, 2.0 Hz, 2H), 2.02 – 1.98 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ = 140.5, 139.9, 129.2, 128.5, 128.4, 126.4,

126.2, 86.1, 81.1, 65.2, 63.2, 47.9, 34.9, 34.0, 20.8. MS (ESI, *m/z*): calcd for $C_{20}H_{22}O_2$ (M, H^+), 295.1610; found, 295.1615.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AS-H hexane/isopropanol 90/10, flow rate= 1 mL/min, retention times: 20.7 min (major.) and 28.6 min (min.).

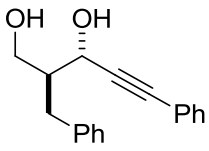
(*2S,3S*)-2-Benzyl-5-cyclohexylpent-4-yne-1,3-diol (3Ae)



Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and 3-cyclohexylpropiolaldehyde **2e** (68 mg, 0.5 mmol). The title compound was obtained as a 20:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 90/10) to give the title compound as a colourless oil. Yield: 73% (100 mg). $[\alpha]_D^{24}$= -4.6 (*c*=0.85, 93 % ee, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.49 – 7.12 (m, 5H), 4.53 (td, *J*=5.0, 1.5 Hz, 1H), 4.10 – 3.97 (m, 1H), 3.70 (dt, *J*=10.8, 5.3 Hz, 1H), 3.01 (dd, *J*=13.7, 6.2 Hz, 1H), 2.74 (dd, *J*=13.7, 8.8 Hz, 1H), 2.60 (d, *J*=5.2 Hz, 1H), 2.47 (ddd, *J*=7.3, 5.3, 2.7 Hz, 1H), 2.30 (d, *J*=5.1 Hz, 1H), 2.06 (ddd, *J*=11.7, 5.8, 2.8 Hz, 1H), 1.89 – 1.25 (m, 10H).^{13}C NMR (75 MHz, $CDCl_3$) δ = 139.9, 129.2, 128.5, 126.2, 91.3, 80.1, 65.3, 63.2, 48.2, 34.1, 32.6, 29.0, 25.8, 24.8. MS (ESI, *m/z*): calcd for $C_{18}H_{24}O_2$ (M, H^+), 273.1810; found, 273.1814.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC hexane/isopropanol 90/10, flow rate= 1 mL/min, retention times: 18.9 min (min.) and 24.3 min (major.)).

(*2S,3S*)-2-Benzyl-5-phenylpent-4-yne-1,3-diol (3Af)

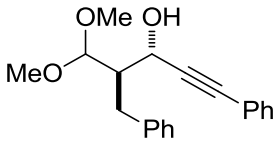


Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and phenylpropiolaldehyde **2f** (61 μL, 0.5 mmol). The title compound was obtained as a 9:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a white solid. Yield: 84 % (112 mg). $[\alpha]_D^{25}$= -

4.3 (*c*= 1, 94 % ee, CH_2Cl_2). M.p.: 82-85 ºC. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.60 – 7.11 (m, 10H), 4.76 (d, *J*=4.2 Hz, 1H), 4.15 (dd, *J*=11.0, 3.1 Hz, 1H), 3.78 (dd, *J*=11.0, 5.3 Hz, 1H), 3.10 (dd, *J*=13.8, 6.4 Hz, 1H), 2.84 (dd, *J*=13.8, 8.7 Hz, 1H), 2.25 – 2.13 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.1, 132.1, 129.6, 128.9, 128.7, 126.7, 122.9, 89.5, 86.7, 65.9, 63.7, 48.3, 34.5. MS (ESI, *m*/*z*): calcd for $C_{18}H_{18}O_2$ (M, H^+), 267.1340; found, 267.1319.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AS-H hexane/isopropanol 90/10, flow rate= 1 mL/min, retention times: 14.1 min (major.) and 17.2 min (min)).

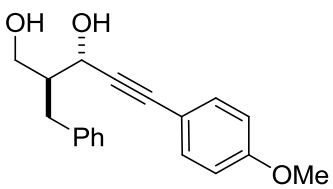
(3S,4R)-4-Benzyl-5,5-dimethoxy-1-phenylpent-1-yn-3-ol (8Af)



Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and phenylpropiolaldehyde **2f** (61 μL, 0.5 mmol). The title compound was obtained as a 8.5:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 90/10) to give the title compound as a yellow oil. Yield: 64 % (591 mg). $[\alpha]_D^{24}$= 1.11 (*c*=1, 94% ee, CH_2Cl_2).). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 6.7, 3.1 Hz, 1H), 7.35 – 7.20 (m, 8H), 4.69 – 4.64 (m, 1H), 4.64 – 4.62 (m, 1H), 3.49 (s, 3H), 3.46 (s, 3H), 2.95 (qd, *J* = 13.9, 7.2 Hz, 2H), 2.39 – 2.29 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1, 131.8, 129.5, 129.2, 128.7, 128.5, 128.4, 126.4, 107.1, 89.4, 85.9, 62.5, 56.5, 55.7, 48.6, 31.2. MS (ESI, *m*/*z*): calcd for $C_{20}H_{22}O_3$ (M,H^+), 310.3869; found 310.1568.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC hexane/isopropanol 98/2, flow rate= 0.5 mL/min, retention times: 30.9 min (min.) and 36.9 min (major)).

(2*S*,3*S*)-2-Benzyl-5-(4-methoxyphenyl) pent-4-yne-1,3-diol (3Ag)

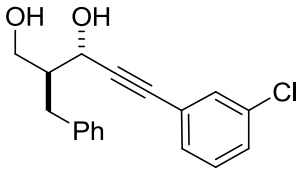


Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and 3-(4-methoxyphenyl) propiolaldehyde **2g** (80 mg, 0.5 mmol). The title compound was obtained as a 10.2:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel

(eluting with hexane/ ethyl acetate 90/10) to give the title compound as a white solid. M.p: 120-123 ºC. Yield: 55 % (81 mg). $[\alpha]_D^{24}$= -3.2 (*c*=0.80, 92 % ee, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.20 (m, 7H), 6.95 – 6.82 (m, 2H), 4.75 (t, *J* = 5.1 Hz, 1H), 4.14 (d, *J* = 10.9 Hz, 1H), 3.85 (s, 3H), 3.82 – 3.72 (m, 1H), 3.08 (dd, *J* = 13.8, 6.4 Hz, 1H), 2.83 (dd, *J* = 13.7, 8.7 Hz, 2H), 2.23 – 2.15 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.8, 133.2, 129.2, 128.5, 126.2, 114.5, 114.0, 87.7, 86.3, 65.6, 63.3, 55.3, 48.0, 34.1. MS (ESI, *m*/*z*): calcd for $C_{19}H_{20}O_2$ (M, H^+), 297.1446; found, 297.1429.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AS-H hexane/isopropanol 90/10, flow rate= 1 mL/min, retention times: 28.0 min (major.) and 31.1 min (min.)).

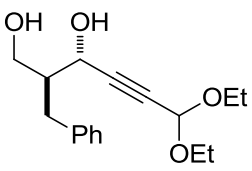
(2*S*,3*S*)-2-Benzyl-5-(4-chlorophenyl)pent-4-yne-1,3-diol (3Ah)



Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and m-chlorophenylpropynal **2h** (72 mg, 0.5 mmol). The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ EtOAc 90/10) to give the title compound as a colourless oil. Yield: 74% (111 mg). $[\alpha]_D^{24}$= -5.7 (c=0.82, 91% ee, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.20 (m, 9H), 4.75 (d, *J* = 5.2 Hz, 1H), 4.22 – 4.12 (m, 1H), 3.78 (dd, *J* = 11.0, 5.3 Hz, 1H), 3.08 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.84 (dd, *J* = 14.0, 8.5 Hz, 1H), 2.23 – 2.13 (m, 1H).^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6, 134.1, 131.5, 129.8, 129.5, 129.1, 128.7, 128.5, 126.3, 124.2, 90.4, 84.7, 65.3, 63.2, 47.7, 34.1. MS (ESI, *m*/*z*): calcd for $C_{18}H_{17}ClO_2$ (M, H^+), 302.0888; found, 302.0898.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AS-H hexane/isopropanol 90/10, flow rate= 1 mL/min, retention times: 11.7min (mayor.) and 14.0min (min.)).

(2S,3S)-2-Benzyl-6,6-diethoxyhex-4-yne-1,3-diol (3Ai)

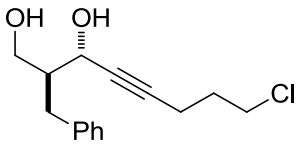


Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (99 µl, 0.75 mmol) and 4,4-diethoxybut-2-ynal **2i** (78 mg, 0.5 mmol). The title compound was obtained as a 14:1 mixture of *anti:syn* isomers. The crude material was purified by flash column

chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a yellow oil. Yield: 60% (88 mg). $[\alpha]_D^{25}$= -1,7 (*c*=1, 94 % ee, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32 – 7.20 (m, 5H), 5.33 (d, *J*=1.2 Hz, 1H), 4.57 (d, *J*=4.9, 1H), 4.03 (dd, *J*=3.1, 11.0 Hz, 1H), 3.81-3.72 (m, 3H), 3.69-3.57 (m, 3H), 2.99 (dd, *J*=6.3, 13.7 Hz, 1H), 2.74 (dd, *J*=8.7, 13.7 Hz, 1H), 2.09 – 2.02 (m, 1H), 1.25 (t, *J*=7.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 139.6, 129.1, 128.4, 126.1, 91.2, 85.6, 81.1, 64.5, 62.7, 61.0, 47.4, 33.9, 14.9. MS (ESI, *m*/*z*): calcd for $C_{17}H_{24}O_4$ (M, H^+), 293,1712; found, 293,1716.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Phenomenex Lux 3µ Cellulose-4 hexane/isopropanol 93/7, flow rate= 1 mL/min, retention times: 35.8 min (min.) and 48.8 min (major.)).

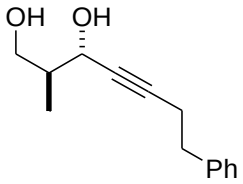
(2S,3S)-2-Benzyl-8-chlorooct-4-yne-1,3-diol (3Aj)



Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.13 mL, 1 mmol) and 6-chlorohex-2-ynal **2j** (65.3 mg, 0.5 mmol). The title compound was obtained as a 20:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a colourless oil. Yield: 65% (85 mg). $[\alpha]_D^{25}$= +-0.25 (*c*=1, 99 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.19 (m, 6H), 4.51 (s, 1H), 4.04 (d, *J* = 10.8, 1H), 3.67 (t, *J* = 6.3, 3H), 2.99 (dd, *J* = 13.7, 6.2, 2H), 2.73 (dd, *J* = 13.7, 8.7, 1H), 2.46 (td, *J* = 6.8, 1.9, 2H), 2.11 – 1.94 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9, 129.3, 128.6, 126.4, 85.0, 81.5, 65.4, 63.4, 48.0, 43.8, 34.2, 31.4, 16.3.MS (ESI, *m*/*z*): calcd for $C_{15}H_{19}ClO_2$ (M, H^+), 266,76; found 266.75.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AD-H hexane/isopropanol 98/2, flow rate= 1 mL/min, retention times: 100 min (mayor.) and 115 min (min.).

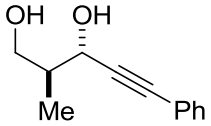
(*2S,3S*)-2-Methyl-7-phenylhept-4-yne-1,3-diol (3Bd)



Prepared according to the General Procedure starting from propionaldehyde **1B** (0.11 ml, 1.5 mmol) and 5-phenylpent-2-ynal **2d** (79 mg, 0.5 mmol). The title compound was obtained as a 19:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a colourless oil. Yield: 75% (82 mg). $[\alpha]_D^{25}$= +3.7 (*c*=0.2, 99.8 % ee, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34 – 7.21 (m, 5H), 4.36 (dt, *J*=6.9, 1.9 Hz, 1H), 3.76 (dd, *J*=11.0, 3.9 Hz, 1H), 3.60 (dd, *J*=11.0, 7.2 Hz, 1H), 2.86 (t, *J*=7.4 Hz, 2H), 2.56 (td, *J*=7.4, 1.9 Hz, 2H), 1.98 – 1.88 (m, 1H), 0.97 (d, *J*=7.0 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ = 140.5, 128.5, 128.4, 126.3, 85.7, 80.8, 67.1, 66.5, 41.4, 35.0, 20.8, 13.0. MS (ESI, *m*/*z*): calcd for $C_{14}H_{18}O_2$ (M, H^+), 219,1311; found, 219,1315.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AY-H hexane/isopropanol 95/5, flow rate= 1 mL/min, retention times: 26.5 min (major.) and 35.4 min (minor.)).

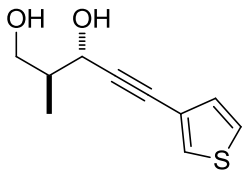
(*2S,3S*)-2-Methyl-5-phenylpent-4-yne-1,3-diol (3Bf)



Prepared according to the General Procedure starting from propanal **1B** (0.11 mL, 1.5 mmol) and phenylpropiolaldehyde **2f** (61 μL, 0.5 mmol). The title compound was obtained as a 5:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a yellow oil. Yield: 73% (69 mg). $[\alpha]_D^{22}$= +4.09 (*c*= 0.25, 94 % ee, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.54 – 7.28 (m, 5H), 4.67 (d, *J*=6.8 Hz, 1H), 3.94 (dd, *J*=10.9, 4.0 Hz, 1H), 3.76 (dd, *J*=10.9, 7.0 Hz, 1H), 2.20 – 2.07 (m, 1H), 1.14 (d, *J*=7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 131.7, 128.4, 122.5, 88.0, 86.2, 66.9, 65.8, 40.4, 12.3. MS (ESI, *m*/*z*): calcd for $C_{12}H_{14}O_2$ (M, H^+), 191.0994; found, 191.0986.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 90/10, flow rate= 1 mL/min, retention times: 13.7 min (min.) and 15.6 min (major)).

(2S,3S)-2-Methyl-5-(thiophen-3-yl)pent-4-yne-1,3-diol (3Bk)

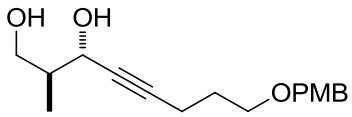


Prepared according to the General Procedure starting from propanal **1B** (0.11 mL, 1.5 mmol) and 3-(thiophen-3-yl)propiolaldehyde **2k** (52 mg , 0.5 mmol). The title compound was obtained as a 9:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 70/30) to give the title compound as a yellow oil. Yield: 50% (49mg). $[\alpha]_D^{25}$= +6.5 (*c*=1, 99 % ee, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 2.9, 1.0 Hz, 1H), 7.39 – 7.23 (m, 1H), 7.14 (dd, *J* = 5.0, 1.1 Hz, 1H), 4.65 (s, 1H), 3.96 – 3.91 (m, 1H), 3.80 – 3.70 (m, 1H), 2.72 (d, *J* = 3.9 Hz, 1H), 2.24 (m, 1H), 2.12 (ddd, *J* = 12.8, 6.4, 3.4 Hz, 1H), 1.12 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.8, 127.9, 124.3, 87.4, 66.4, 65.4, 63.4, 40.37, 24.2, 12.1. . MS (ESI, *m*/*z*): calcd for $C_{10}H_{12}O_2S$ (M, H^+), 196.27; found 196.27.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 93/7, flow rate= 1.2 mL/min, retention times: 31.9 min (min.) and 41.8 min (major)).

(2S,3S)-8-((4-Methoxybenzyl)oxy)-2-methyloct-4-yne-1,3-diol (3Bl)

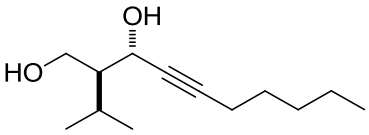
Prepared according to the General Procedure starting from propanal **1B** (0.11 mL, 1.5 mmol) and 6-((4-methoxybenzyl)oxy)hex-2-ynal **2l** (116 mg, 0.5 mmol). The title compound was obtained as a 9:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 70/30) to give the title compound as a yellow oil. Yield: 71% (101.1mg). $[\alpha]_D^{25}$= +3.5 (*c*=1, 99 % ee, CH_2Cl_2).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.7, 2H), 6.88 (d, *J* =



8.7, 2H), 4.44 (s, 2H), 4.34 (d, *J* = 6.8, 1H), 3.80 (s, 3H), 3.75 (d, *J* = 3.8, 1H), 3.67 – 3.58 (m, 1H), 3.52 (t, *J* = 6.2, 2H), 2.34 (dd, *J* = 7.1, 5.1, 2H), 1.97 – 1.88 (m, 1H), 1.80 (t, *J* = 6.6, 2H), 0.98 (d, *J* = 7.0, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 130.6, 129.4, 113.9, 85.9, 80.5, 72.7, 68.5, 67.2, 66.6, 55.4, 41.6, 28.9, 15.7, 13.2. . MS (ESI, *m*/*z*): calcd for $C_{17}H_{24}O_4$ (M, H^+), 292.37; found 292.34.

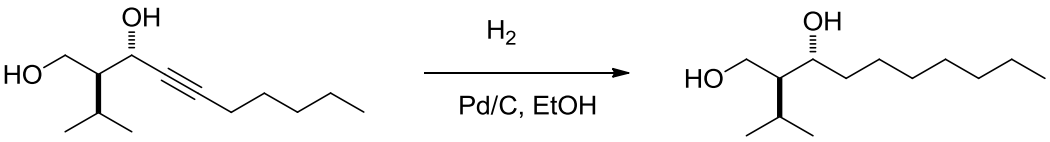
The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak OD-H, hexane/isopropanol 95/5, flow rate= 0.75 mL/min, retention times: 46.3 min (min.) and 51.3 min (major)).

(2*S*,3*S*)-2-Isopropyldec-4-yne-1,3-diol (3Ca)



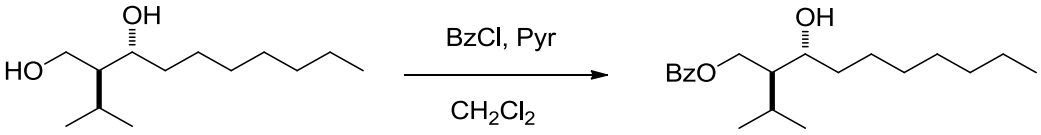
Prepared according to the General Procedure starting from isovaleraldehyde **1C** (0.2 mL, 1.5 mmol) and 2-octynal **2a** (48 mg, 0.5 mmol). The title compound was obtained as a 16:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a colorless oil. Yield: 71% (82 mg). $[\alpha]_D^{22}$= -4.18 (*c*= 0.1, 99 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.69 (t, *J* = 5.2 Hz, 1H), 4.15 (dt, *J* = 19.5, 8.8 Hz, 1H), 3.94 – 3.82 (m, 1H), 2.71 (d, *J* = 5.0 Hz, 1H), 2.43 (s, 1H), 2.26 (td, *J* = 7.1, 2.0 Hz, 2H), 1.49 – 1.32 (m, 6H), 1.07 (d, *J* = 6.8 Hz, 4H), 0.95 (dd, *J* = 14.8, 7.1 Hz, 6H). MS (ESI, *m*/*z*): calcd for $C_{13}H_{25}O_2$ (M,H^+),213.1843; found (M-CH_3O), 213.1855.

For determination of the ee, this adduct was derivatized to the saturated monobenzoate ester as follow.



To a 5 mL flask charged with a solution of diol (51 mg, 0.24 mmol) in ethanol (2 mL) was added Pd/C (10% wt, 10 mg). The flask was filled with hydrogen gas and stirred for 16h at rt under hydrogen balloon. The mixture was filtered over celite pad and the filtrate was concentrated. Purification on a silica gel column (hexane/AcOEt, 80:20) provided 31mg of the corresponding saturated diol (31 mg, 0.15 mmol, 62% yield) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.02 – 3.81 (m, 3H), 3.81 – 3.69 (m, 1H),

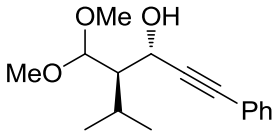
2.01 (dq, *J* = 13.6, 6.8 Hz, 1H), 1.63 – 1.57 (m, 2H), 1.42 – 1.23 (m, 10H), 1.04 (d, *J* = 6.8 Hz Hz, 3H), 0.94 (qd, *J* = 6.8, 2.7 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 77.00, 64.41, 52.98, 39.07, 34.60, 32.43, 32.07, 28.79, 28.59, 25.42, 24.11, 22.22, 16.85.



To a solution of the saturated diol (31 mg, 0.15 mmol) in 1.5 mL of CH_2Cl_2 – 40 °C was added pyridine (59 µL, 0.732 mmol) and benzoyl chloride (30 µL, 0.30 mmol) at. After stirring for 2 h, this solution was diluted with 10 mL of ethyl acetate, washed with 2 × 10 mL of 0.5 M HCl aqueous solution, dried over $MgSO_4$ and concentrated. Purification on a silica gel column (Hexanes/AcOEt, 10/1) provided 32 mg of the ester product (0.1 mmol, 67% yield).

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC, hexaneethanol 98/2, flow rate= 1 mL/min, retention times: 15.6 min (major) and 17.6 min (min.)).

(3*S*,4*R*)-4-(Dimethoxymethyl)-5-methyl-1-phenylhex-1-yn-3-ol (8Cf)

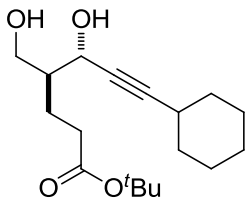


Prepared according to the General Procedure starting from isovaleraldehyde **1C** (0.16 mL, 1.5 mmol) and phenylpropargyl aldehyde **2f** (0.61 mL, 0.5 mmol). The title compound was obtained as a 9:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 90/10) to give the title compound as a yellow oil. Yield: 58%. (133 mg) $[\alpha]_D^{24}$= -100.3 (*c*=1, 98 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.34 – 7.27 (m, 3H), 4.91 – 4.85 (m, 1H), 4.60 (d, *J* = 4.2 Hz, 1H), 3.61 (d, *J* = 4.5 Hz, 1H), 3.46 (d, *J* = 10.4 Hz, 6H), 2.55 – 2.53 (m, 0H), 2.30 – 2.18 (m, 1H), 1.96 (dt, *J* =

6.7, 4.2 Hz, 1H), 1.06 (dd, *J* = 11.3, 7.0 Hz, 7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.8, 128.4, 106.9, 62.7, 55.9, 55.0, 51.3, 26.8, 21.4, 20.0. MS (ESI, *m*/*z*): calcd for $C_{16}H_{22}O_3$ (M, H^+), 262.3441; found, 262.1578.

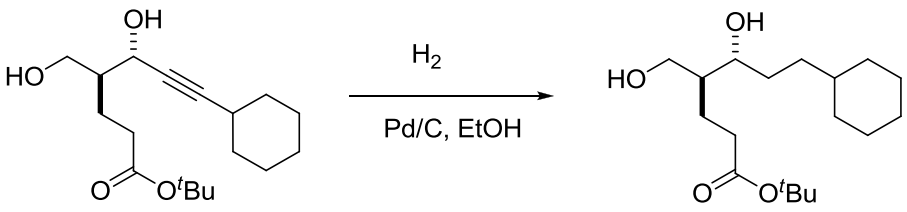
The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IB, hexane/ethanol 95/5, flow rate= 1 mL/min, retention times: 6 min (min) and 7.2 min (major.)).

(4*S*,5*S*)-tert-Butyl-7-cyclohexyl-5-hydroxy-4-(hydroxymethyl)hept-6-ynoate (3De)



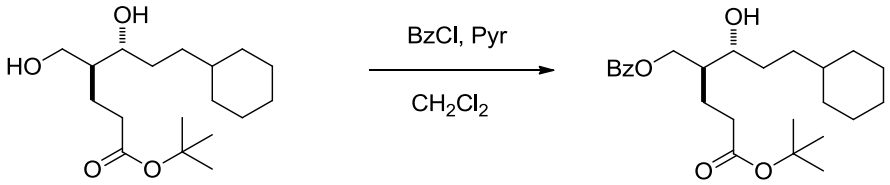
Prepared according to the General Procedure starting from *tert*-Butyl-5-oxopentanoate **1D** (258.3 mg, 1.5 mmol) and 3-cyclohexylpropiolaldehyde **2e** (136, 1 mmol). The title compound was obtained as a 20:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a yellow oil. Yield: 52% (160 mg). $[\alpha]_D^{22}$=-7.83 (*c*= 1,99% *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.45 (d, *J* = 3.3, 1H), 4.00 – 3.94 (m, 1H), 3.72 – 3.60 (m, 2H), 3.53 – 3.43 (m, 1H), 2.33 (t, *J* = 7.2, 3H), 1.86 – 1.63 (m, 9H), 1.42 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 90.9, 80.7, 80.1, 65.5, 63.1, 45.9, 33.4, 32.7, 29.1, 28.2, 25.9, 24.9, 22.8.MS (ESI, *m*/*z*): calcd for $C_{18}H_{30}O_4$ (M,H^+), 310.4284; found (M-$C_4H_{10}O$), 237.1491

For determination of the ee, this adduct was derivatized to the saturated monobenzoate ester as for adduct **3Ac.**



(4S,5R)-tert-Butyl 7-cyclohexyl-5-hydroxy-4-(hydroxymethyl)heptanoate.

Yield: Yellow oil. 85 % (63.9 mg) ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.95 (dd, *J* = 11.4, 3.0, 1H), 3.66 – 3.58 (m, 2H), 2.33 (td, *J* = 7.1, 2.1, 2H), 1.81 (q, *J* = 7.2, 2H), 1.69 (s, 7H), 1.58 (d, *J* = 6.8, 3H), 1.45 (s, 9H), 1.24 (t, *J* = 7.0, 4H).

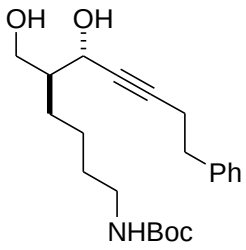


(S)-2-((R)-3-Cyclohexyl-1-hydroxypropyl)-7,7-dimethyl-5-oxooctyl benzoate

Purification on a silica gel column (Hexane/AcOEt 90:10) provided 57.2 mg of the product (0.15 mmol, 50% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.1, 2H), 7.49 (dt, *J* = 15.1, 7.4, 3H), 4.45 (dd, *J* = 9.7, 4.7, 2H), 3.61 (dt, *J* = 8.5, 4.3, 1H), 2.47 – 2.29 (m, 2H), 1.95 – 1.76 (m, 3H), 1.76 – 1.48 (m, 12H), 1.45 (s, 9H), 1.29 – 1.12 (m, 6H), 0.97 – 0.77 (m, 3H).

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/ethanol 99/1, flow rate= 1 mL/min, retention times: 34.7 min (min.) and 40.6 min (major)).

(*2S,3S*)-2-(4-Boc-aminobutyl)-7-phenylhept-4-yne-1,3-diol (3Ed)

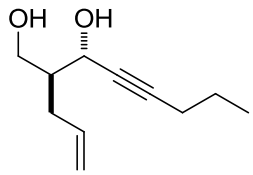


Prepared according to the General Procedure starting from 6-Boc-aminohexanal **1E** (140 mg, 0.65 mmol) and 5-phenylpent-2-ynal **2d** (79 mg, 0.5 mmol). The title compound was obtained as a 13:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a colourless oil. Yield: 71% (134 mg). $[\alpha]_D^{23}$= -1.45 (*c*=0.94, 95 % ee, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34 – 7.21 (m, 5H), 4.57 (brs, 1H), 4.45 (m, 1H), 3.98 (m, 1H), 3.68 – 3.62 (m, 1H), 3.22 – 3.08 (m, 2H), 2.95 (br, 1H), 2.86 (t, *J*= 7.6 Hz, 2H), 2.56 (dt, *J*=7.6, 2.0 Hz, 2H), 1.66 – 1.28 (m, 8H), 1.46 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.4, 140.6, 128.4, 128.3, 126.3, 85.4,

81.3, 79.3, 65.8, 63.3, 45.9, 39.9, 35.0, 30.3, 28.4, 26.9, 24.0, 20.8. MS (ESI, *m*/*z*): calcd for $C_{22}H_{33}NO_4$ (M, H^+), 376.2410; found, 376.2414.

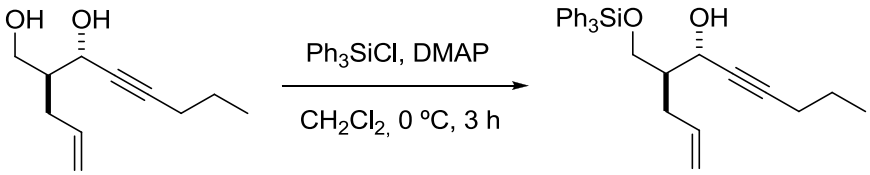
The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Phenomenex Lux 3µ Cellulose-4, hexane/isopropanol 90/10, flow rate= 1.5 mL/min, retention times 33.6 min (min.) and 49.23min (mayor.).

(2*S*,3*S*)-2-Allyloct-4-yne-1,3-diol (3Fb)



Prepared according to the General Procedure starting from 4-pentenal **1F** (0.6 mL, 0.6 mmol) and hex-2-ynal **2b** (96.1 mg, 0.5 mmol). The title compound was obtained as a 20:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a yellow oil. Yield: 50% (44.8 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83 (d, *J* = 7.5 Hz, 1H), 5.09 (t, *J* = 13.4 Hz, 2H), 4.49 (s, 1H), 3.97 (s, 1H), 3.71 (s, 1H), 2.45 (d, *J* = 5.4 Hz, 1H), 2.37 (s, 1H), 2.27 – 2.12 (m, 7H), 1.85 (s, 1H), 1.54 (dd, *J* = 14.4, 7.1 Hz, 4H), 1.30 (s, 2H), 1.05 – 0.95 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 136.2, 124.6, 117.0, 65.7, 63.9, 46.1, 32.6, 22.2, 20.8, 13.6. MS (ESI, *m*/*z*): calcd for $C_{11}H_{18}O_2$ (M,H^+),183.1400; found,183.1385.

The enantiomeric purity of the major diastereoisomer was determined by chiral HPLC analysis of (4*S*,5*S*)-4-[((triphenylsilyl)oxy)methyl]dec-1-en-6-yn-5-ol prepared from **3Fb**.

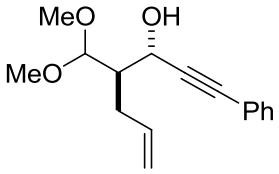


Aduct **3Fb** (47.9 mg; 0.26 mmol) was solved in 1.3 mL of anhydrous CH_2Cl_2 and DMAP (0.31 mmol, 38.1 mg) and Ph_3ClSi (0.26 mmol, 76.7 mg) was added at 0 ºC. The reaction mixture was allowed to stir at 0 °C for 3 h and then quenched by addition of H_2O (5 mL). The combined organic layers were washed successively with 0.1 M aqueous solution of HCl (10 mL) and sat. aqueous $NaHCO_3$ solution (10 mL), dried over $MgSO_4$, filtered and concentrated. Purification on a silica gel column (hexane/AcOEt, 90/10) provided 114 mg of the product (0.2 mmol, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 7.8,

1.5 Hz, 6H), 7.46 (dq, *J* = 17.7, 7.0 Hz, 9H), 5.73 (d, *J* = 7.2 Hz, 1H), 5.00 (t, *J* = 12.5 Hz, 2H), 4.61 (s, 1H), 4.23 (d, *J* = 3.9 Hz, 1H), 3.84 (dd, *J* = 10.1, 5.3 Hz, 1H), 2.24 – 2.16 (m, 4H), 1.52 (dd, *J* = 14.5, 7.2 Hz, 2H), 0.98 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.7, 135.6, 133.8, 130.4, 128.1, 116.9, 86.9, 80.2, 65.1, 64.4, 46.1, 32.2, 29.9, 22.3, 20.9. $[\alpha]_D^{24}$= + 34.5(*c*=0.1, 91 % *ee*, CH_2Cl_2).

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 99/1, flow rate= 1 mL/min, retention times: 7min (min.) and 16.9 min (major.)).

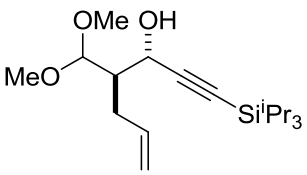
(3*S*, 4*R*)-4-(Dimethoxymethyl)-1-phenylhept-6-en-1-yn-3-ol (8Ff)



Prepared according to the General Procedure starting from 4-pentenal **1F** (0.15 mL, 1.5 mmol) and phenyl propargyl aldehyde **2f** (0.61 mL, 0.5 mmol). The title compound was obtained as a 8:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 90/10) to give the title compound as a yellow oil. Yield: 84% (109 mg). $[\alpha]_D^{24}$= -8.2 (*c*=1.05, 94 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 – 7.31 (m, 5H), 5.94 (ddt, *J* = 17.2, 10.1, 7.2 Hz, 1H), 5.27 – 5.07 (m, 2H), 4.80 (d, *J* = 5.9 Hz, 1H), 4.64 (d, *J* = 4.9 Hz, 1H), 3.50 (s, 3H), 3.49 (s, 3H), 2.55 – 2.37 (m, 2H), 2.20 (ddd, *J* = 10.7, 7.4, 5.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 131.6, 128.3, 128.2, 122.4, 117.0, 106.7, 88.9, 85.7, 63.0, 55.9, 54.8, 46.3, 30.3. MS (ESI, *m*/*z*): calcd for $C_{16}H_{20}O_3$ (M, H^+), 261.1446; found, 261.1440.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AD-H hexane/isopropanol 95/5, flow rate= 1 mL/min, retention times: 19.8 min (min.) and 22.0 min (major.)).

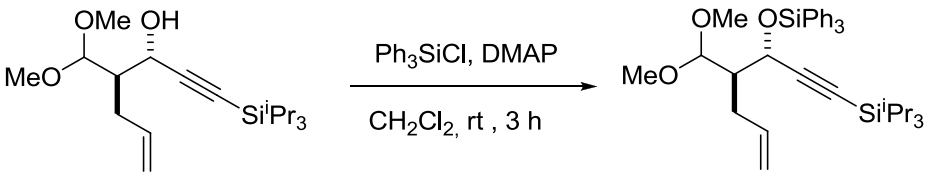
(3S,4R)-4-(dimethoxymethyl)-1-(triisopropylsilyl)hept-6-en-1-yn-3-ol (8Fm)



Prepared according to the General Procedure starting from 4-pentenal **1F** (74 µL, 0.75 mmol) and 3-(triisopropylsilyl)propiolaldehyde **2m** (105.6 mg, 0.5 mmol).

The title compound was obtained as a 20:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 95/5) to give the title compound as a yellow oil. Yellow oil. Yield:55% (53.4mg). $[\alpha]_D^{25}$= +11.9 (*c*=11, 99 % ee, CH_2Cl_2).^{1}H NMR (500 MHz, $CDCl_3$) δ 5.90 (d, *J* = 7.6, 1H), 5.17 (d, *J* = 17.0, 1H), 5.08 (d, *J* = 10.0, 1H), 4.64 (d, *J* = 4.8, 1H), 4.62 – 4.55 (m, 1H), 3.45 (d, *J* = 1.4, 6H), 2.41 (d, *J* = 7.4, 2H), 2.07 (s, 1H), 1.11 (s, 18H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.9, 117.2, 107.6, 106.8, 63.1, 56.2, 54.9, 46.3, 29.7, 18.8, 11.4. MS (ESI, *m/z*): calcd for $C_{19}H_{28}O_3$ (M,H^+),340.57; found (M-2CH_3O),177.1306.

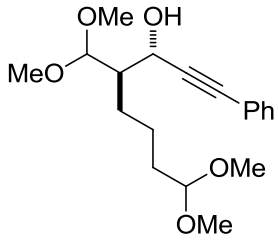
The enantiomeric purity of the major diastereoisomer was determined by chiral HPLC analysis of (((3S,4R)-4-(dimethoxymethyl)-1-(triisopropylsilyl)hept-6-en-1-yn-3-yl)oxy)triphenylsilane prepared from **8Fm**.



Adduct **8Fm** (121 mg; 0.3 mmol) was solved in 1.5 mL of anhydrous CH_2Cl_2 and DMAP (0.45 mmol, 55 mg) and Ph_3ClSi (0.45 mmol, 132.7 mg) was added at rt. The reaction mixture was allowed to stir at rt for 3 h and then quenched by addition of H_2O (5 mL). The combined organic layers were washed successively with 0.1 M aqueous solution of HCl (10 mL) and sat. aqueous $NaHCO_3$ solution (10 mL), dried over $MgSO_4$, filtered and concentrated. Purification triturated with ethanol provided 134 mg of the product (0.22 mmol, 75% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.59 (m, 5H), 7.38 (dt, *J* = 13.9, 6.8, 10H), 6.16 – 5.95 (m, 1H), 5.11 – 4.88 (m, 2H), 4.75 (d, *J* = 4.5, 1H), 4.35 (d, *J* = 7.5, 1H), 3.21 (s, 3H), 3.10 (s, 3H), 2.64 (dd, *J* = 14.0, 7.4, 1H), 2.35 (dd, *J* = 13.6, 7.0, 1H), 2.10 – 1.98 (m, 1H), 1.15 – 1.08 (m, 3H), 1.09 – 0.99 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7, 135.8, 134.3, 130.1, 127.9, 115.0, 106.7, 105.9, 64.8, 53.8, 47.7, 30.7, 18.8, 11.4.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AY-H, hexane/isopropanol 98/2, flow rate= 0.5 mL/min, retention times: 4.9 min (major.) and 15 min (min.)).

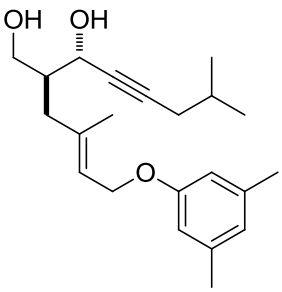
(3*S*,4*R*)-4-(Dimethoxymethyl)-8,8-dimethoxy-1-phenyloct-1-yn-3-ol (8Gf)



Prepared according to the General Procedure starting from 6,6-dimethoxyhexanal **1G** (0.17 mL, 1.5 mmol) and phenyl propargyl aldehyde **2f** (0.61 mL, 0.5 mmol). The title compound was obtained as a 16:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a colorless oil. Yield: 51% (82 mg). $[\alpha]_D^{22}$= -6.18 (*c*= 0.1, 99 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 – 7.32 (m, 4H), 4.78 (t, *J* = 5.9 Hz, 1H), 4.67 (d, *J* = 4.5 Hz, 1H), 4.41 (t, *J* = 5.4 Hz, 1H), 3.54 (t, *J* = 3.0 Hz, 1H), 3.50 (d, *J* = 1.4 Hz, 1H), 3.40 – 3.30 (m, 6H), 2.07 (dd, *J* = 7.4, 3.0 Hz, 1H), 1.80 – 1.46 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.6, 128.3, 122.7, 107.2, 104.4, 89.3, 85.3, 63.0, 56.3, 55.2, 52.7, 46.2, 32.7, 24.9, 22.5.

The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 90/10, flow rate= 1 mL/min, retention times: 23.1 min (min.) and 25.7 min (major)).

(E)-2-(4-(3,5-Dimethylphenoxy)-2-methylbut-2-en-1-yl)-7-methyloct-4-yne-1,3-diol (3Hc)

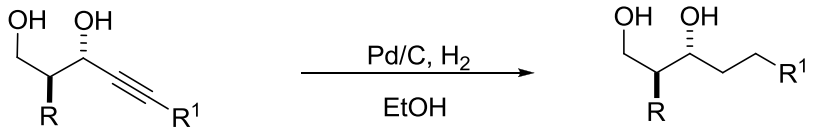


Prepared according to the General Procedure starting from (*E*)-6-(3,5-dimethylphenoxy)-4-methylhex-4-enal **1H** (139.4 mg, 0.6 mmol) and 5-methylhex-2-ynal **2c** (55 mg, 0.5 mmol). The title compound was obtained as a 20:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 80/20) to give the title compound as a yellow oil. Yield: 61% (103.3 mg) $[\alpha]_D^{24}$= 6.5 (*c*=1, 99% *ee*, CH_2Cl_2) ^{1}H- NMR (300 MHz, CDCl3) δ 6.60 (s, 1H), 6.53 (s, 2H), 5.58 (s, 1H), 4.51 (d, *J* = 6.4 Hz, 3H), 3.93 (s, 1H), 3.67 (d, *J* = 5.6 Hz, 1H), 2.42 (s, 2H), 2.28 (s, 5H), 2.13 (dd, *J* = 6.5, 2.0 Hz, 3H), 1.97 (s, 1H), 1.88 – 1.79 (m, 1H), 1.76 (s, 2H), 0.98 (d, *J* = 6.6 Hz, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 139.3, 138.8, 136.2, 122.7, 112.6, 86.0, 81.1, 65.7, 64.6,

63.7, 44.2, 38.1, 28.1, 28.0, 22.1, 21., 16.6. MS (ESI, *m/z*): calcd for $C_{22}H_{32}O_3$ (M,H^+), 344.4877; found ($M-H_2O$), 327.2324

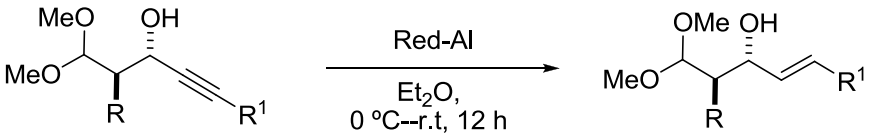
The enantiomeric purity of the major diastereoisomer was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/isopropanol 97/3, flow rate= 1 mL/min, retention times: 31.1 min (min.) and 36.6 min (major)).

F) Reduction of propargylic aldol adducts



3Ae R: CH_2Ph, R^1:*c*-C_6H_{11}
3Bf R: Me, R^1:Ph
3Ca R: $CH(CH_3)_2$, R^1:$(CH_2)_4CH_3$
3De R:$(CH_2)_2CO_2{}^tBu$, R`:c-C_6H_{11}

12 R: CH_2Ph R^1: *c*-C_6H_{11}; 83%
13 R: Me R^1: Ph **;** 83%
14 R: $CH(CH_3)_2$ R': $(CH_2)_4CH_3$; 62%
15R:$(CH_2)_2CO_2{}^tBu$, R`:c-C_6H_{11}**:**85%



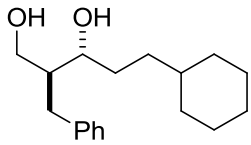
8Aa R: CH_2Ph R': $(CH_2)_4CH_3$
8Af R: CH_2Ph R': Ph
8Ff R: $CH_2CH{=}CH_2$ R: Ph

16 R: CH_2Ph R^1:$(CH_2)_4CH_3$; 88%
17 R: CH_2Ph R^1: Ph **;** 98%
18 R: $CH_2CH{=}CH_2$ R': Ph; 82%

F.1) Hydrogenation of aldol adducts 3Ae, 3Bf, 3Ca and 4De

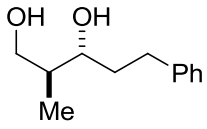
To a solution of **3Ae, 3Bf, 3Ca** or **3De** in EtOH (2 mL) was added 20 wt% Pd/C (60 mg). The reaction mixture was stirred at room temperature under H_2 atmosphere overnight, then filtered through Celite® and concentrated under vacuum.

(*2S,3R*)-2-Benzyl-5-cyclohexylpentane-1,3-diol (12)



Prepared according to the General Procedure starting from **3Ae**. The title compound was obtained as white solid. Yield: 83% (0.41 mmol, 114 mg). $[\alpha]_D^{20}$ = +13.1 (*c*=1, 93 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.68 – 7.39 (m, 5H), 4.19 (dd, *J*=11.0, 2.9 Hz, 1H), 4.04-3.91 (m, 1H), 3.86 (dd, *J*=11.0, 4.6 Hz, 1H), 3.21 – 2.85 (m, 4H), 2.07 – 1.00 (m, 14H).^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.4, 129.1, 129.0, 128.4, 126.0, 75.3, 62.8, 45.9, 37.7, 35.2, 33.5, 33.4, 33.3, 33.0, 30.3, 26.6, 26.3.

(*2S,3R*)-2-Methyl-5-phenylpentane-1,3-diol (13)



Prepared according to the General Procedure starting from **3Bf**. The title compound was obtained as a colorless oil. Yield: 83% (0.41 mmol, 80.5 mg). $[\alpha]_D^{20}$ = +4.15 (*c*=0.25, CH_2Cl_2)^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.51 – 7.05 (m, 4H), 3.84 (dd, *J*=10.8, 3.8 Hz, 1H), 3.67 (dd, *J*=10.8, 7.1 Hz, 1H), 3.00 – 2.82 (m, 1H), 2.82 – 2.70 (m, 1H), 2.02 – 1.71 (m, 3H), 0.94 (d, *J*=7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 142.5, 128.8, 126.3, 77.0, 68.0, 40.4, 37.5, 32.1, 14.2.

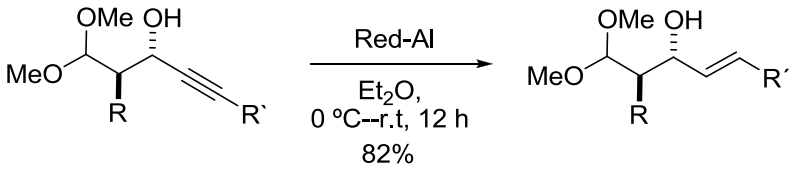
(2*S*,3*R*)-2-isopropyldecane-1,3-diol (14)

For the detailed experimental procedure and characterization data of **14**, see page S25.

(4S,5R)-tert-butyl 7-cyclohexyl-5-hydroxy-4-(hydroxymethyl)heptanoate (15)

For the detailed experimental procedure and characterization data of **15**, see page S27.

F.2) Partial reduction of 8Aa, 8Af, 8Ff.

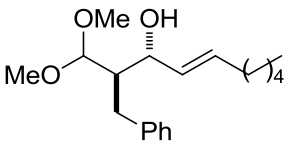


8Aa, 8Af,8Ff

16 R: CH_2Ph R^1:$(CH_2)_4CH_3$; 88%
17 R: CH_2Ph R^1: Ph; 98%
18 R: $CH_2CH{=}CH_2$ R': Ph; 82%

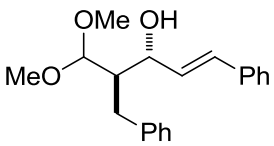
A solution of sodium bis(2-methoxyethoxy)aluminium hydride (Red-Al) (3.60 mL, 1.2 mmol, 65% in toluene) was added dropwise to a solution of **8Aa, 8Af** or **8Ff** (0.8 mmol) in diethyl ether (2 mL) at 0 ºC. The reaction mixture was allowed to stir for 12 h at room temperature. An aqueous solution of saturated potassium sodium tartrate (4 mL) was slowly added at 0 ºC to quench the reaction and then the whole mixture was extracted twice with diethyl ether (2 x 2mL). The combined organic extracts were washed with brine (5 mL) and dried over $MgSO_4$ and evaporated under reduced pressure to give the desired compound, which was not further purified.

(2*R*,3*R*,*E*)-2-Benzyl-1,1-dimethoxydec-4-en-3-ol (16)



Prepared according to the General Procedure starting from **8Aa** (1 mmol). The title compound was obtained as yellow oil. Yield: 88% (0.88 mmol, 270.7 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 – 7.15 (m, 6H), 5.74 – 5.63 (m, 1H), 5.44 (dd, *J* = 15.3, 6.8 Hz, 1H), 4.28 (d, *J* = 3.4 Hz, 1H), 4.16 (dd, *J* = 11.6, 6.1 Hz, 1H), 3.46 (d, *J* = 4.7 Hz, 1H), 3.44 (s, 3H), 3.35 (s, 3H), 2.71 (qd, *J* = 13.9, 7.2 Hz, 2H), 2.12 – 1.98 (m, 3H), 1.41 – 1.24 (m, 7H), 0.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8, 133.0, 131.6, 129.4, 128.5, 126.1, 107.6, 72.3, 56.6, 55.6, 48.1, 32.4, 32.3, 31.6, 29.0, 22.7, 14.2.

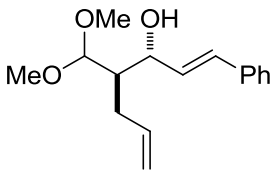
(3*R*,4*R*,*E*)-4-Benzyl-5,5-dimethoxy-1-phenylpent-1-en-3-ol (17)



Prepared according to the General Procedure starting from **8Af** (1.5 mmol). The title compound was obtained as yellow oil. Yield: 98 % (1.4 mmol, 464 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 – 7.16 (m, 12H), 6.63 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.9, 6.2 Hz, 1H), 4.37 (d, *J* = 6.3 Hz, 1H),

4.34 (d, *J* = 3.4 Hz, 1H), 3.59 (d, *J* = 5.3 Hz, 1H), 3.46 (s, 3H), 3.39 (s, 3H), 2.83 – 2.77 (m, 2H), 2.20 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7, 130.7, 129.4, 128.71, 127.6, 126.6, 126.2, 107.5, 72.0, 56.8, 55.8, 48.5, 32.1.

(3*R*,4*R*,*E*)-4-(Dimethoxymethyl)-1-phenylhepta-1,6-dien-3-ol (18)



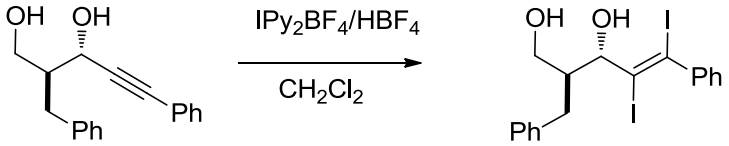
Prepared according to the General Procedure starting from **8Ff** (0.8 mmol). The title compound was obtained as yellow oil. Yield: 98 % (1.4 mmol, 464 mg). Yield: 82% (172mg) ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.51 – 7.19 (m, 6H), 6.64 (s, 1H), 6.30 (d, *J*=6.7 Hz, 1H), 5.95 – 5.78 (m, 1H), 5.20 – 5.05 (m, 3H), 4.49 (d, *J*=4.5 Hz, 1H), 3.50 (s, 2H), 3.46 (s, 3H), 2.33 – 2.22 (m, 2H), 2.07 – 1.97 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 136.5, 131.1, 130.9, 128.5, 127.5, 126.5, 116.8, 107.3, 72.6, 56.2, 54.8, 54.8, 46.2, 30.9.

G) Elaboration of Propargylic Alcohols

The present direct cross aldol approach also enables rapid acces to a variety of optically active structural motifs with at least two contigous stereogenic centers, thereby complementing previous catalyst-controlled asymmetric entries to propargylic alcohols, such as the reduction of ynones, te alkynylation of carbonyls or the 1,2-addition of organometallic reagents,[20] methods that generally provide a sole new stereocenter.

[20] a) Cozzi, P. G.; Hilgraf, R.; Zimmermann, N. *Eur. J. Org. Chem* **2004**, 4095-4105. b) Pu, L. *Tetrahedron* **2003**, *59*, 9873-9886. c) Lu, G; Li, Y.M, X. S. Li, A.S. C. Chan *Coord. Chem. Rev.* **2005**, *249*, 1736-1744.

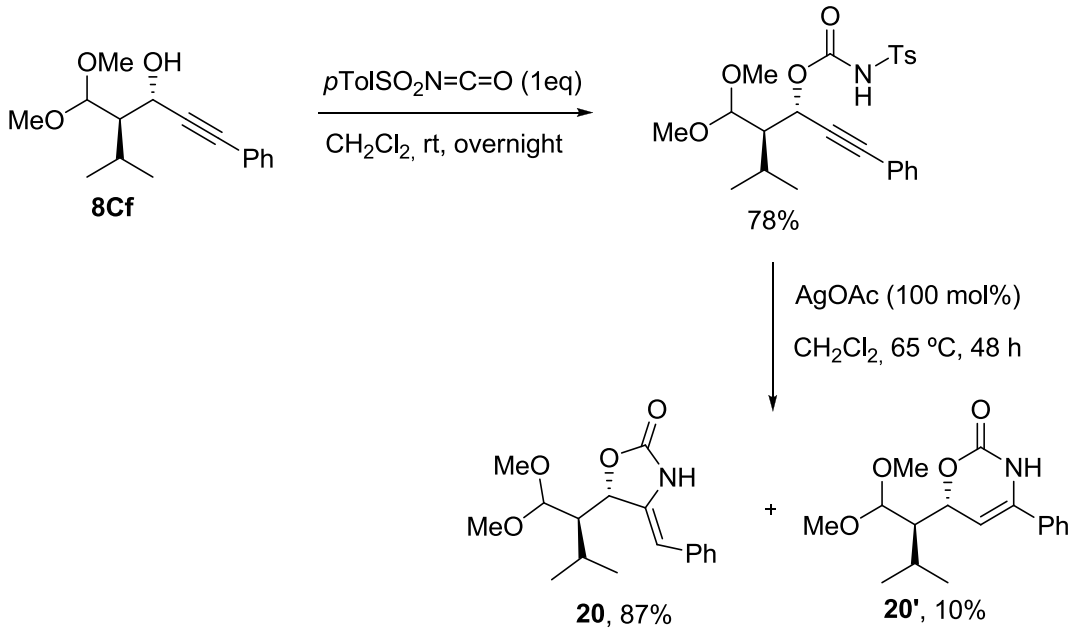
G.1) Diiodination of adduct 3Af



3Af **19**

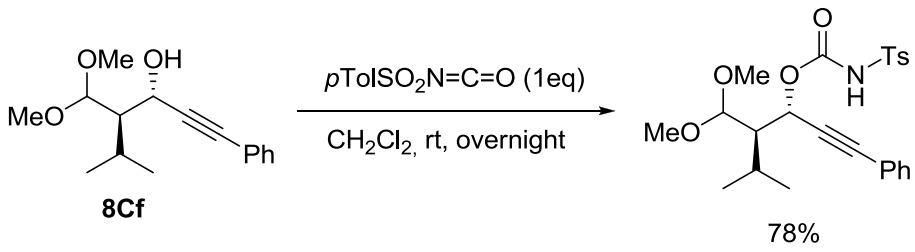
To a solution of **3Af** (1 mmol, 266 mg) in CH_2Cl_2 (3 mL) were added HBF_4 (2 mmol, 0.56 ml, 48 wt % solution in H_2O) and commercially available IPy_2BF_4 (1 mmol, 372 mg) at room temperature. After stirring for 3 h, the solution was quenched with water (6 mL), extracted with CH_2Cl_2 (2 x 3mL), washed with sodium thiosulfate (5 % aqueous solution, 5 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The crude material revealed the presence of two compounds. The first one was the starting material (43%) and the second one was identified as compound **19** by ^{1}H-NMR spectroscopy and X-Ray analysis. The substances were separated by flash column chromatography on silica gel (eluting with hexane/Ethyl acetate, 80:20) and compound **19** was finally crystallized from hexane/CH_2Cl_2. Yield: 53% .^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 – 7.04 (m, 9H), 4.49 (d, *J* = 8.4 Hz, 1H), 3.98 (dd, *J* = 11.0, 2.8 Hz, 1H), 3.79 (dd, *J* = 11.0, 5.9 Hz, 1H), 2.84 (d, *J* = 4.0 Hz, 1H), 2.64 (dd, *J* = 13.6, 11.1 Hz, 1H), 2.44 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 139.3, 129.2, 128.5, 128.0, 126.4, 112.5, 96.8, 83.6, 62.3, 48.2, 33.7. M.p.:170-179ºC

G.2) Intramolecular hydroamination of aldol adduct 8Cf.



General procedure for the synthesis of adducts 20a and 20b[21]

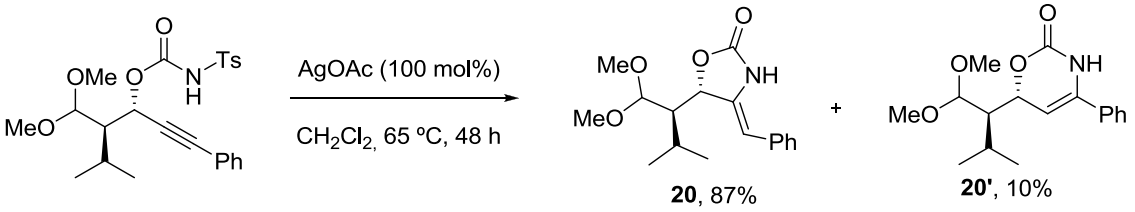
Step 1:



To a solution of **8Cf** (1.7 mmol) in CH_2Cl_2 (1.9mL) toluenesulfonyl isocyanate (1.7 mmol) was added. After stirring the resulting solution for 20 h at room temperature the solvent was removed. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 70:30) to give compound N-tosyl carbamate product as a white solid. Yield: 78 % ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.53 (s, 1H), 7.41 – 7.18 (m, 8H), 5.78 (d, *J* = 5.2 Hz, 1H), 4.46 (d, *J* = 6.6 Hz, 1H), 3.34 (d, *J* = 2.7 Hz, 7H), 2.39 (s, 3H), 2.22 – 2.09 (m, 1H), 2.10 – 2.02 (m, 1H), 1.05 (dd, *J* = 10.1, 7.0 Hz, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.3, 145.0, 131.7, 129.5, 128.7, 128.4, 128.2, 104.1, 84.6, 67.2, 54.1, 54.0, 49.0, 26.0, 21.7, 21.5, 19.8.

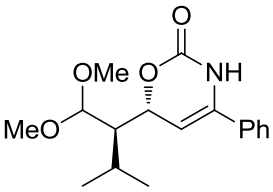
[21] Adapted from: a) Tamaru, Y; Kimura, M; Tanaka, S; Kura, S. Yoshida, Z. *Bull. Chem. Soc. Jpn.* 1994, *67,* 2838-2849 b) Ohe, K.; Ishihara, T.; Chatani, Y. K.; Murai, S. *J. Org. Chem.* **1991**, *56*, 2267-2268.

Step 2[22]**:**



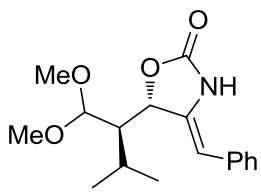
To a stirred solution of (3S,4R)-4-(dimethoxymethyl)-5-methyl-1-phenylhex-1-yn-3-yl tosylcarbamate (0.46 mmol, 212 mg), in CH_2Cl_2 (0.5 ml) was added AgOAc (100 mol%, 76.8 mg). The reaction mixture was stirred for 48h at 65 °C and then filtered through a pad of celite with a washing with 10 ml of CH_2Cl_2. After removal of filtrate solvent in vacuum the residue was purified by silica gel flash column chromatography on silica gel (eluting with hexane/ethyl acetate 95:5) to afford pure compounds **20'** as white oil (10 %) and **20** as white oil (87 %)**.**

(*R*)-6-((*R*)-1,1-Dimethoxy-3-methylbutan-2-yl)-4-phenyl-3,6-dihydro-2H-1,3-oxazin-2-one (20')



Colorless oil. Yield: 10 % $[\alpha]_D^{25}$= +21.7(c=0.98, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 8.4, 1.4, 2H), 7.58 – 7.42 (m, 3H), 6.97 (d, *J* = 11.9, 1H), 6.29 – 6.19 (m, 1H), 4.41 (d, *J* = 5.6, 1H), 3.77 – 3.65 (m, 1H), 3.34 (d, *J* = 9.0, 6H), 1.97 (dd, *J* = 13.2, 6.7, 1H), 0.94 (dd, *J* = 9.7, 6.9, 7H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.0, 145.8 138.7, 132.6, 128.4, 128.3, 126.7, 105.9, 54.1, 53.9, 46.0, 28.9, 21.0, 19.0. MS (ESI, m/z):calcd for $C_{17}H_{23}NO_4$ (M,H^+), 305,3688; found, (M- Ph): 231.1385.

(*S,Z*)-4-Benzylidene-5-((*R*)-1,1-dimethoxy-3-methylbutan-2-yl)oxazolidin-2-one (20)

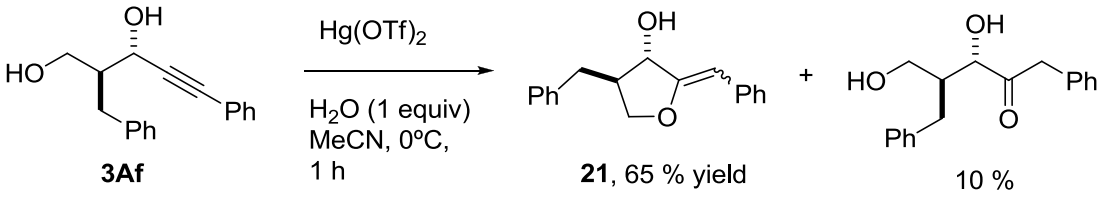


Colorless oil. Yield: 87 %.$[\alpha]_D^{25}$= +38.8(*c*=1.08, CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.51 (dq, *J* = 8.5, 7.1 Hz, 3H), 6.96 – 6.80 (m, 2H), 4.48 (d, *J* = 7.0

[22] Adapted from: Vasudev, R.; Looper, R. E. *J. Am. Chem. Soc*. **2011**, *133*, 20172-20174.

Hz, 1H), 3.37 (d, *J* = 8.5 Hz, 6H), 2.48 (dd, *J* = 12.6, 8.1 Hz, 1H), 2.13 – 2.00 (m, 1H), 0.93 (dd, *J* = 17.6, 6.9 Hz, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5, 146.1, 138.0, 132.5, 128.7, 128.6, 128.4, 104.8, 77.4, 77.0, 76.5, 54.0, 53.5, 52.0, 28.1, 21.5, 18.1. MS (ESI, m/z):calcd for $C_{17}H_{23}NO_4$ (M,H^+), 305,3688; found, (M- Ph): 231.1385.

G.3) Intramolecular hydroalkoxylation of adduct 3Af [23]

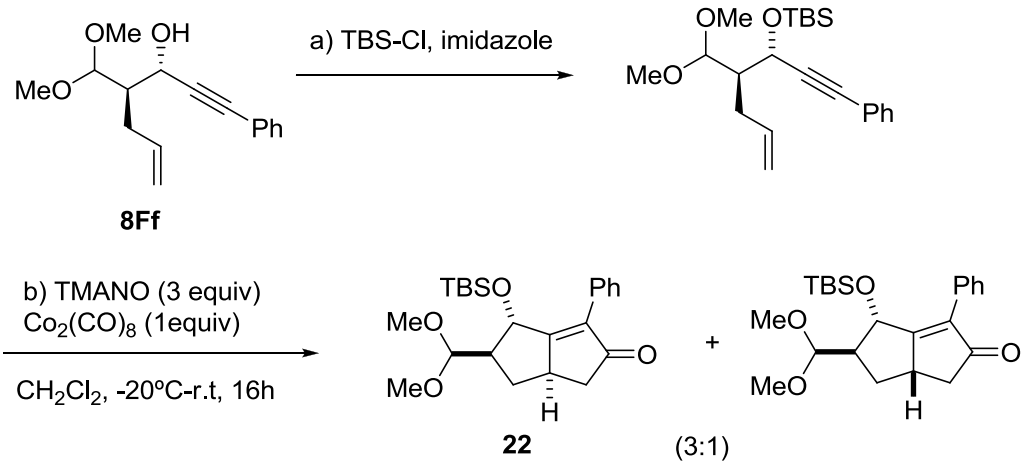


To a stirred mixture of **3Af** (266 mg, 1 mmol) and H_2O (54mg, 3 mmol) in MeCN (3.3 mL), was added a solution of $Hg(OTf)_2$ (0.1M MeCN soln, 0.1 mL, 0.01 mmol) at 0^0C, and the mixture was stirred for 1 hour at the same temperatura. After addition of Et_3N (15 µL) and then brine (3 mL), the organic materials were extrated with Et_2O. Dried and concentrated extract was subjeted to a column chromatography on SiO_2 using hexane and EtOAc (2:1) as an eluent to give the compound **21** (173.1 mg, 65% yield) as a colerless oil. ^{1}H NMR (300 MHz, CDCl3) δ 7.65 – 7.59 (m, 1H), 7.41 – 7.29 (m, 10H), 5.50 (s, 1H), 5.49 – 5.47 (m, 0H), 4.59 (s, 1H), 4.36 (dd, *J* = 8.4, 6.9 Hz, 1H), 4.24 (t, *J* = 8.7 Hz, 1H), 3.07 (dd, *J* = 13.5, 7.4 Hz, 1H), 2.79 – 2.67 (m, 2H), 2.62 (dd, *J* = 8.2, 6.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 140.6, 136.2, 129.1, 128.8, 128.3, 127.8, 126.1, 124.9, 97.0, 74.7, 64.1, 62.6, 59.7, 45.1, 35.1. MS (ESI, m/z):calcd for $C_{18}H_{19}O_2$ (M,H^+), 267.1385; found: 267.1382.

A small amount (28.4 mg, 10% yield) of hydrated side product was also obtained.

[23] Nishizawa, M.; Takemoto, T.; Sasaki, I.; Nakano, M; Ho, E.; Namba, K.; Yamamoto, H.; Imagawa, H. *Synlett* **2009**, 1175-1179.

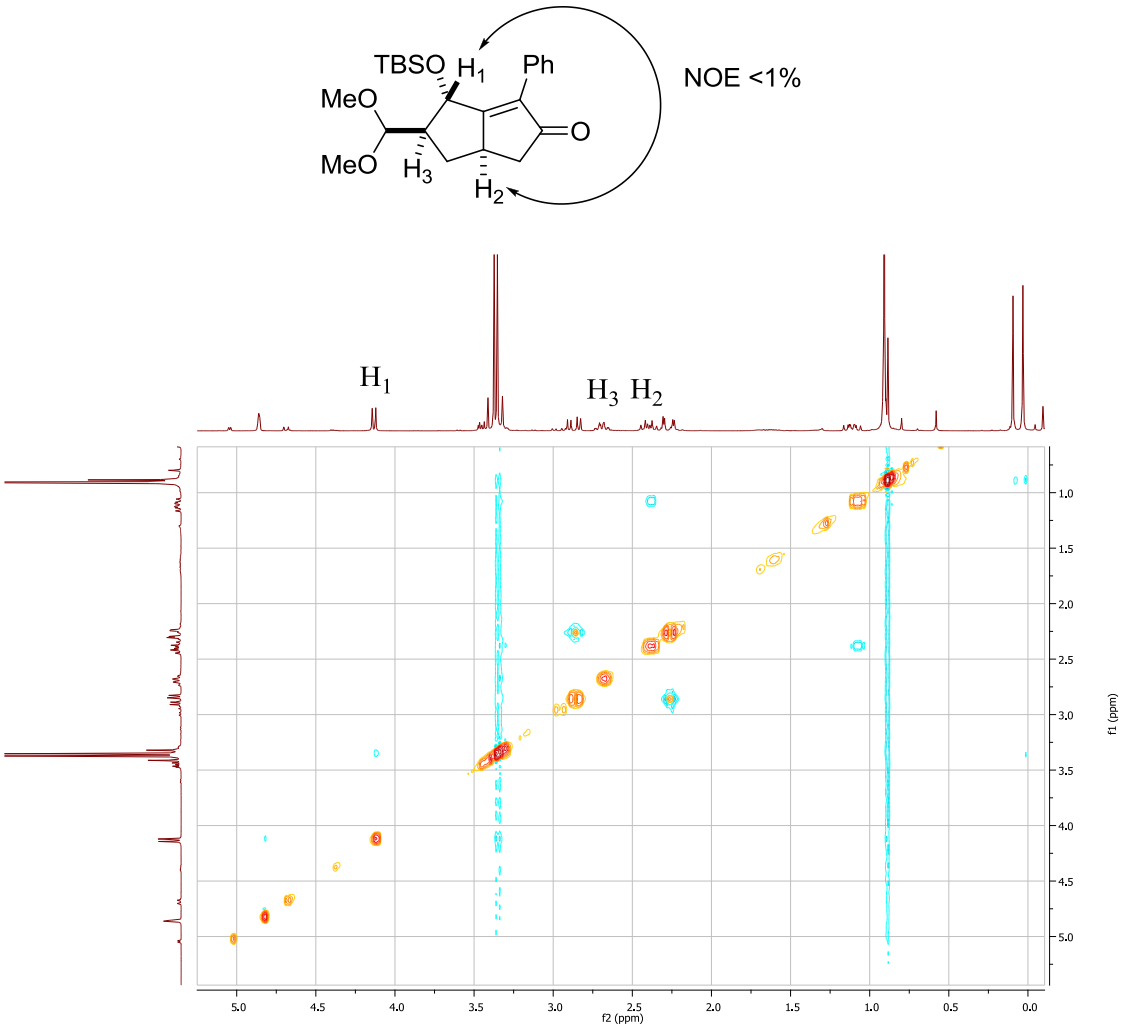
G.4) Intramolecular cycloaddition reaction[24]



TBS= $^{t}BuMe_2SiCl$
TMANO= trimethylamine N-oxide

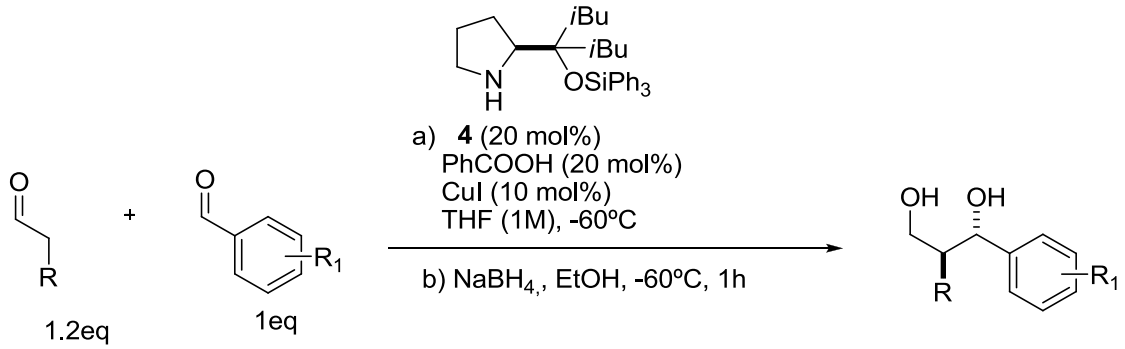
Alter silylation of **8Ff** with TBS-Cl and DMAP system under standard conditions, to a solution of TBS ether (134mg, 0.36 mmol, 1 equiv) in DCM (1 mL) at room temperature was added $Co_2(CO)_8$ (1 equiv) and was stirred for 30 min. Then the TMANO (3 equiv) was added at -10ºC and the mixture was allowed to warm to room temperatura and stirred at room temperature until the starting material disappeared (4-16 hours) at which time usually purple precipitate had formed. The mixture was passed though a small plug of silica gel and the filtrate was concentrated in vacuo and purifield by silica gel chromatography to give the exo product (53 %), and endo product (14 %).^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 – 7.34 (m, 6H), 4.86 (s, 1H), 4.15 (t, *J* = 7.6 Hz, 1H), 3.37 (s, 3H), 3.35 (s, 3H), 2.96 – 2.80 (m, 1H), 2.76 – 2.62 (m, 1H), 2.47 – 2.36 (m, 1H), 2.35 – 2.16 (m, 2H), 1.21 – 1.03 (m, 1H), 0.91 (s, 9H), 0.09 (s, 3H), 0.03 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 208.9, 179.9, 134.6, 131.3, 128.7, 128.4, 106.2, 70.3, 54.9, 53.6, 42.6, 40.3, 30.9, 25.7, -4.0, -5.0. MS (ESI, m/z):calcd for $C_{23}H_{35}O_4Si$ (M,H^+), 403,2289; found: 403.2305.

[24] a) Turlington, M.; Yue, Y.; Yu, X.-Q.; Pu, L. *J. Org. Chem.* **2010**, *75*, 6941-6952. b) Mukai, C.; Sonobe, H.; Kim, J. S. ; Hanaoka, M. *J.Org. Chem.* **2000**, *65*, 6654-6659.



H) Cross-aldol reaction of aliphatic aldehydes with aromatic aldehydes

Table S2

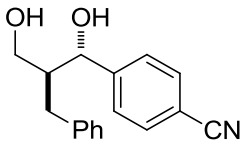


R	R_1	Time(h)	Yield(%)[a]	*anti:syn*[b,c]	ee (%)[d]
CH_2Ph	4-CN	24	60	5:1 (4:1)[d]	97
CH_2Ph	4-NO_2	24	45	4:1 (4:1)[d]	95[e]
$CH_2CH{=}CH_2$	4-CN	48	50	3:1 (3:1)[d]	97

[a]Reactions conducted at 0.5mmol scale, using 1.2 equiv. of aldehyde donor,THF (0.5mL). [b] Determined by ^{1}H-RMN and corroborated by HPLC.[c]Data in parenthesis refer to reactions carried out with benzoic acid as the sole cocatalyst.[d]Determined by chiral HPLC.[e]Reaction carried out at -40 ºC because of the low solubility of p-nitrobenzaldehyde in THF at -60 ºC. Some extent of homoaldolization was observed.

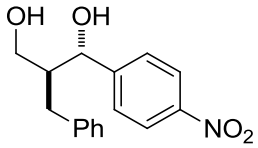
4-((1S,2S)-2-Benzyl-1,3-dihydroxypropyl)benzonitrile (23)

Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (79 μL, 0.6 mmol) and 4-formylbenzonitrile (65.6 mg, 0.5 mmol). The title compound was obtained as a 5:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 50/50) to give the title compound as a yellow oil. Yield: 60 % (80 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (t, *J* = 8.5 Hz, 2H), 7.51 (dd, *J* = 19.8, 8.4 Hz, 3H), 7.24 (ddd, *J* = 28.6, 14.4 Hz, 7.2, 7H), 7.03 (d, *J* = 6.7 Hz, 1H), 5.21 (s, 1H), 4.86 (s, 1H), 3.71 (d, *J* = 11.7 Hz, 2H), 3.61 (s, 1H), 3.50 (d, *J* = 4.6 Hz, 1H), 3.35 (s, 1H), 2.87 (d, *J* = 6.9 Hz, 1H), 2.85 – 2.78 (m, 1H), 2.78 – 2.71 (m, 1H), 2.70 – 2.63 (m, 1H), 2.54 (dd, *J* = 13.8, 4.3 Hz, 1H).



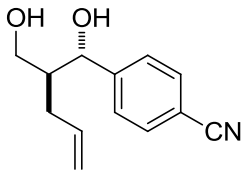
(1S,2S)-2-benzyl-1-(4-nitrophenyl)propane-1,3-diol (24)

Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A**



(79 μL, 0.6 mmol) and 4-nitrobenzaldehyde (75.6 mg, 0.5 mmol). The title compound was obtained as a 4:1 mixture of *anti:syn* isomers.The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 50/50) to give the title compound as a yellow oil. Yield: 45 % (64.6 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 – 8.21 (m, 5H), 7.60 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 5H), 7.33 – 7.14 (m, 7H), 7.03 (d, *J* = 7.5 Hz, 2H), 5.27 (s, 1H), 4.91 (s, 2H), 4.84 (s, 2H), 3.77 (s, 1H), 3.70 (s, 3H), 3.62 (d, *J* = 4.6 Hz, 3H), 2.85 (d, *J* = 6.8 Hz, 2H), 2.82 – 2.75 (m, 2H), 2.67 (s, 2H), 2.55 (s, 1H).

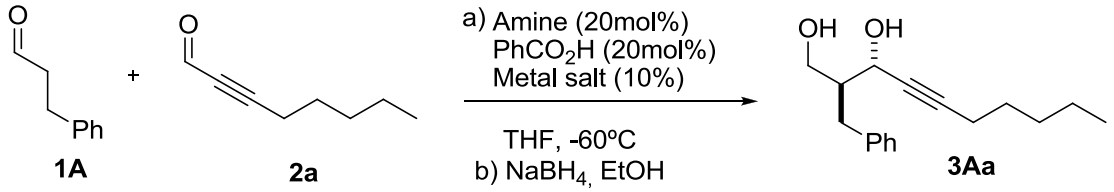
4-((1S,2S)-1-Hydroxy-2-(hydroxymethyl)pent-4-en-1-yl)benzonitrile (25)

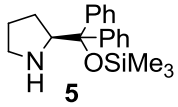
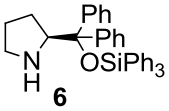
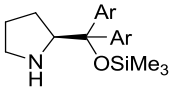


Prepared according to the General Procedure starting from 4-pentenal **1F** (60 μL, 0.6 mmol) and 4-formylbenzonitrile (65.6 mg, 0.5 mmol). The title compound was obtained as a 3:1 mixture of *anti:syn* isomers. The crude material was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 70/30) to give the title compound as a yellow oil. Yield: 50 % (55 mg). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 2.3 Hz, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 5.74 (t, *J* = 15.1 Hz, 1H), 5.17 – 5.00 (m, 2H), 4.86 (t, *J* = 5.3 Hz, 1H), 3.87 – 3.68 (m, 2H), 3.46 (d, *J* = 4.8 Hz, 0H), 3.30 (s, 1H), 2.17 (dd, *J* = 14.3, 8.0 Hz, 3H), 1.96 (d, *J* = 24.6 Hz, 2H).

I) Results from other amine catalysts

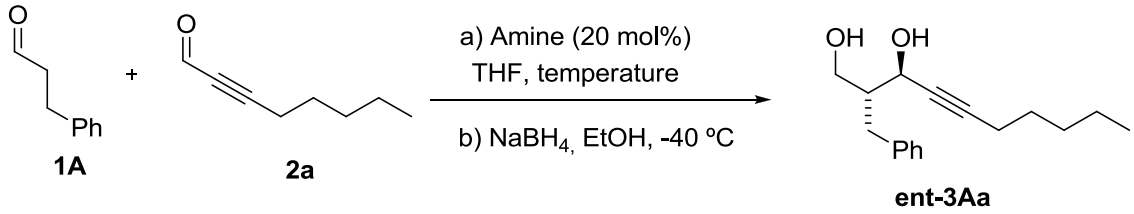
Table S3: Aldol reaction of **1A** with **2a** using α,α-diarylprolinol ethers as catalysts.

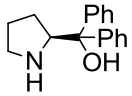
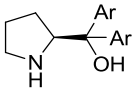


Amine	Metal salt	Time(h)	Conversion (%)[b,c]	*anti:syn*[d]	*ee* (%)[e]
 **5**	--	20	45	3:1	ND
	$Cu(OAc)_2 \cdot H_2O$	20	74(54)	2:1	97
 **6**	--	20	60	1.5:1	97
	CuI	20	73(48)	1.5:1	99
 **7**: Ar: 3,5 $(CF_3)_2C_6H_3$	--	20	30	n.d	ND
	CuI	20	33	2.5:1	98

[a] Reactions conducted on a 0.5 mmol scale in 0.5 mL of THF (mol ratio of **1**/**2**/amine, 1.5:1:0.2); [b] Determined by ^{1}H NMR. [c] Conversions were essentially the same after 48 h of reaction. Numbers in parentheses refer to isolated yields by column chromatography. [d] Determined by ^{1}H NMR of an aliquot in the aldehyde product before reduction, and confirmed in the crude alcohol products. [e] *ee* of major diastereomer determined by chiral HPLC. ND: not determined.

Table S4: Aldol reaction of **1A** with **2a** using representative bifunctional amine catalysts[a]



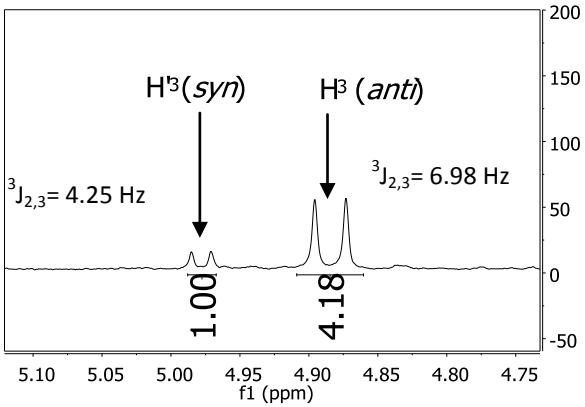
Amine	T (ºC)	t (h)	Yield (%)[b]	*anti:syn*[c]	*ee* (%)[d]
(L)-Proline[e]	0	48	40/30	1:1	ND
	0	72	60	2:1	90
	−20	48	NR	--	--
 Ar: 3,5 $(CF_3)_2C_6H_3$	0	72	52	1:1	97
	−20	48	NR	--	--

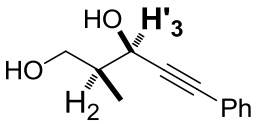
[a] Reactions conducted on a 0.5 mmol scale in 0.5 mL of THF (mol ratio of **1**/**2**/amine, 3:1:0.2). [b] Isolated yield of cross aldol product/self-aldol (dehydration). [c] Determined by ^{1}H NMR. [d] Determined by chiral HPLC. [e] No Brønsted acid added; DMF as solvent; syringe pump was not used. N.R: no reaction; N.D.: not determined.

J) Determination of the relative and absolute configuration of adducts

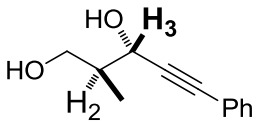
Relative configuration

Assignment the relative *syn* and *anti* configuration to adducts was primarily made on the bases of the $J_{2,3}$ coupling constants and then by NOESY experiments. In general $^{3}J_{2,3}$ (*anti*) › $^{3}J_{2,3}$ (*syn*) for diols [25].





syn-**3Bb**



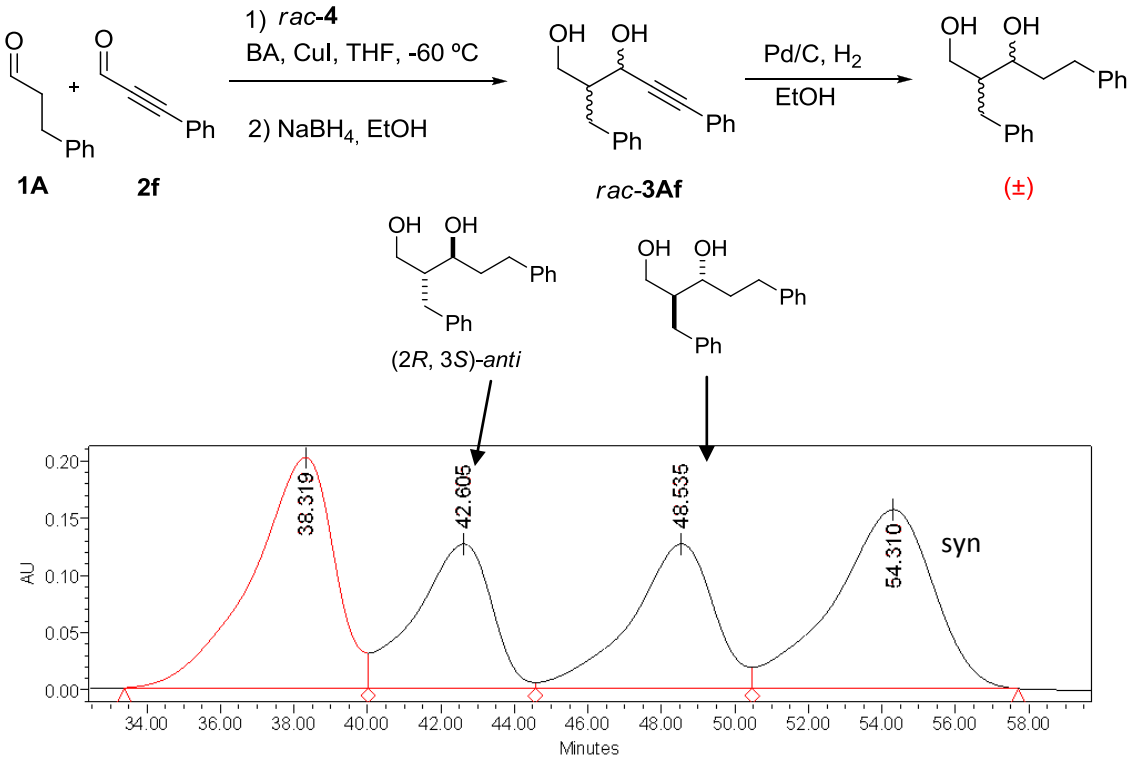
anti-**3Bb**

Absolute configuration

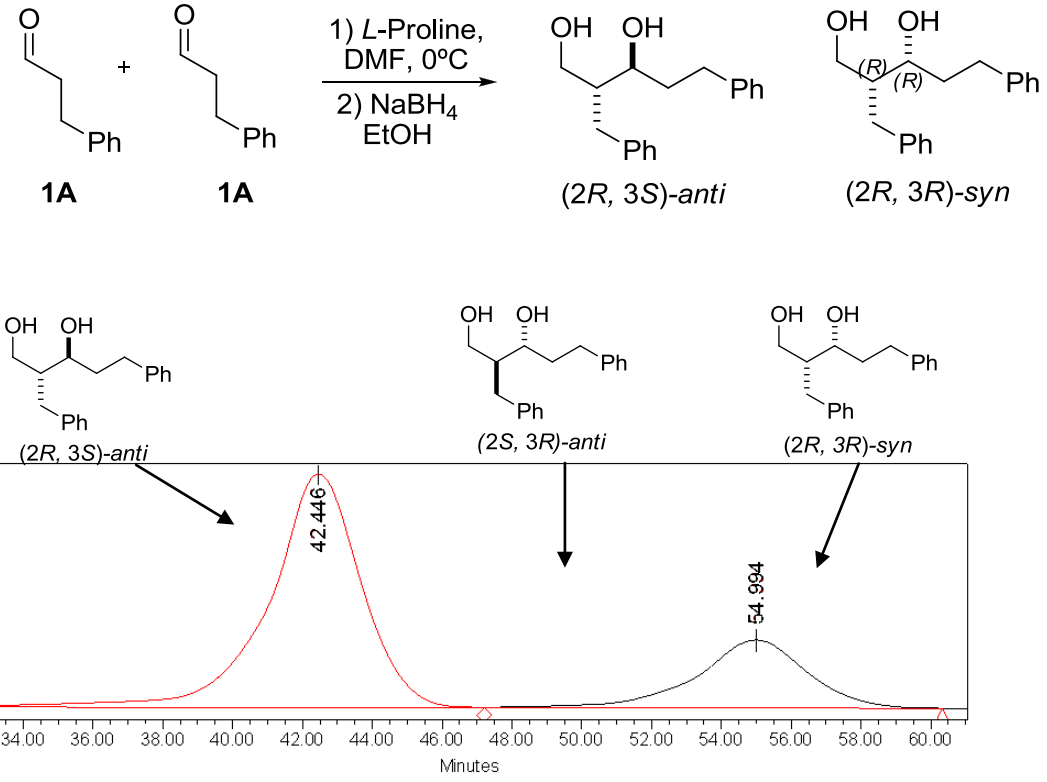
The absolute configuration was determined by correlating HPLC chromatograms with literature values as follow:

1) The non selective reaction between hydrocinnamaldehyde **1A** and phenyl propargyl aldehyde (**2f**) promoted by racemic catalyst **4** followed by reduction and hydrogenation led to the racemic sample of the corresponding adduct containing the two *syn*/*anti* diastereomers.

[25] Heathcock, C.H. "The Aldol Addition Reaction" in "Asymmetric Synthesis"; Morrison J.D., Ed.; Academic Press: New York, 1983; Vol 3, Chapter 2, pp. 111-212.

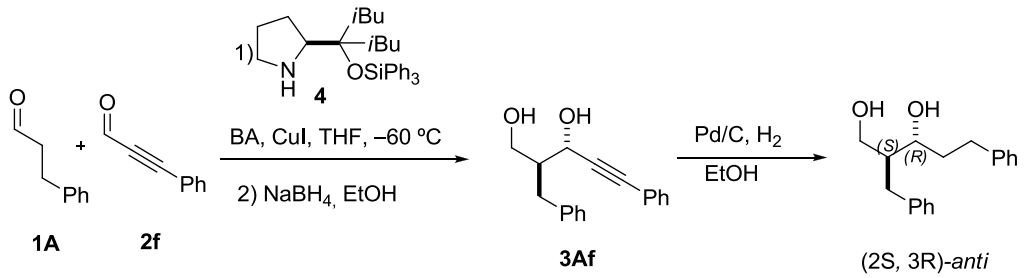


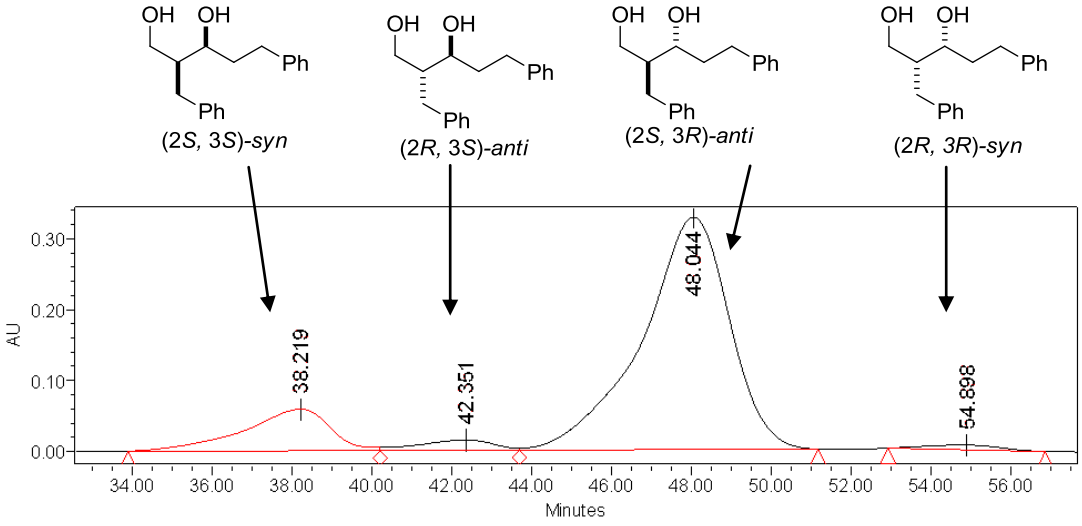
2) Self aldol reaction of hydrocinnamaldehyde **1A** using *L*-Proline as catalyst, provided the corresponding adduct as a 80:20 *anti/syn* mixture of diastereomers.[26]



[26] Experimental procedure adapted from: I.K. Mangion, A. B. Northrup, D. W. C. MacMillan. *Angew. Chem. Int. Ed*. **2004**, *43*, 6722-24

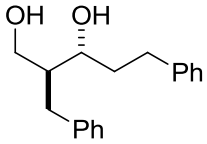
3) The reaction between aldehydes **1A** and **2f** in the presence of catalyst **3**, followed by reduction and subsequent hydrogenation of the resulting **3Af** adduct, provided stereoisomer (2*S*, 3*R*)-*anti*, the opposite enantiomer to obtained using *L*-proline as catalyst.





Configuration of the other adducts was established by assuming a uniform reaction mechanism and by X-ray analysis of compound **19** (see below).

(*2S,3R*)-2-Benzyl-5-phenylpentane-1,3-diol



Prepared according to the General Procedure starting from hydrocinnamaldehyde **1A** (0.2 mL, 1.5 mmol) and phenylpropiolaldehyde **2f** (61 μL, 0.5 mmol). The crude material was purified by flash column chromatography on silica gel (eluent

hexane/ ethyl acetate 80/20) to give compound **3Ab** as a white solid. The solid was then dissolved in EtOH (2 mL) 20 wt% Pd/C (60 mg) was added and the mixture was stirred at room temperature under H_2 atmosphere (1 atm) overnight. The mixture was then filtered trough Celite® and concentrated under vacuum. The title compound was obtained as colourless oil. Mixture of isomers *anti:syn* 85:15. Yield: 70 % (94mg). $[\alpha]_D^{24}$= +15.9 (*c*=1,dr 85:15, 93 % ee CH_2Cl_2).

(*2R,3S*)-2-Benzyl-5-phenylpentane-1,3-diol

Prepared according to the procedure reported in the literature[27] using *L*-proline as catalyst. The physical and spectroscopic data were in agreement with those described in the literature.[28] $[\alpha]_D^{24}$= +7.4 (*c*=1, dr 75:25, 99 % ee, CH_2Cl_2).

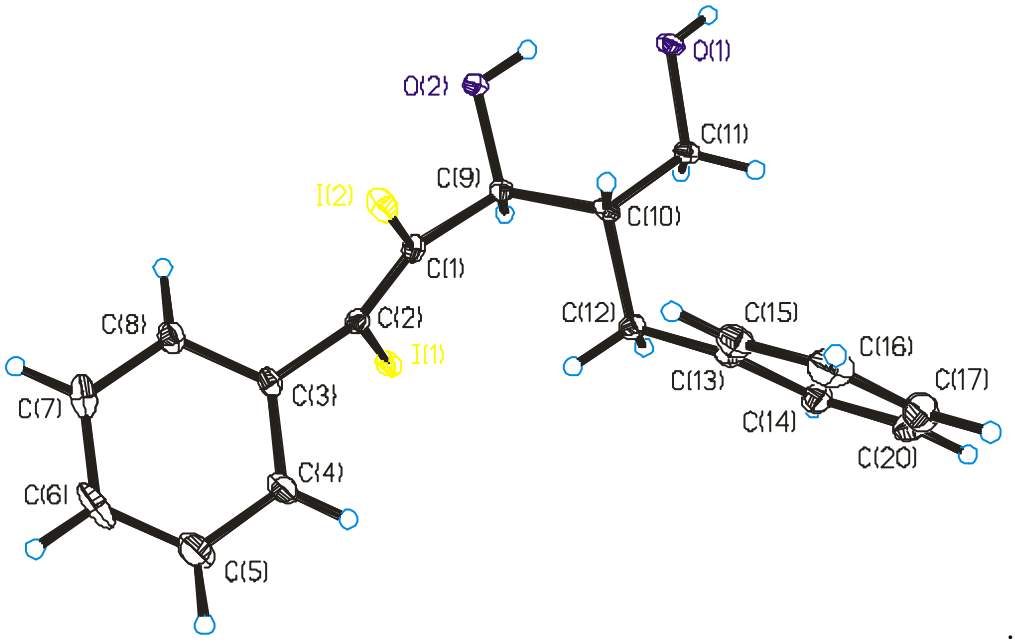
The enantiomeric purity of the major and minor diastereoisomers was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol/EtOH 98/1/1, flow rate= 1 mL/min, retention times: *syn*: 38.3 min (minor) and 54.9min (major); *anti:* 42.3 min (major) and 48.0 min (minor)).

[27] Adapted from the literature (A. B. Northrup, D.W.C MacMillan, *J. Am. Chem. Soc.* **2002**, *124*, 6798-6799.), but without using syringe pump

[28].A. Seifert, U. Scheffler, M. Markert, R Mahrwald; *Org. Lett***, 2010,** *12*.1660.

K) Determination of absolute/relative configuration of19 by X-Ray analysis.

ORTEP diagram of compound **19**



Absolute configuration of **19** (*2S, 3S*) was unequivocally established by a single-crystal X-ray analysis (absolute structure parameter: 0.04(2); Flack, H. D. Acta Cryst. **1983** A39, 876).

Crystallographic Studies Suitable single crystals of the title compound for X-ray study were grown from a solution in dichloromethane/hexane. Crystal data and refinement are summarized in Table S5 for compound **19** A colourless prism (0.15 × 0.09 × 0.02 mm) was selected and mounted on a Bruker X8 APEX area diffractometer. Unit-cell parameters were determined from 1271 frames of intensity data covering 0.3º in ω over a hemisphere of the reciprocal space by combination of three exposure sets, and refined by the least-squares method. Intensities were collected with graphite monochromatized Mo-$K\alpha$ radiation (λ = 0.71073 Å), using the $\omega/2\theta$ scan-technique. A total of 3395 indepent reflections for **19** were measured in the range $2.43 \leq \theta \leq 25.08$. Lorentz-polarization and absorption corrections were made.

The structures were solved by direct methods using the SHELXS computer program[1] and refined by the full-matrix least-squares method with the SHELX97 computer program,[1] using 3395 reflections for **19**. The function minimized were $\Sigma w|\ |Fo|^2 - |Fc|^2|^2$, where $w = [\sigma^2(I) + (0.0382P)^2 + 0.0000P]^{-1}$ for **19** and $P = (|Fo|^2 + 2|Fc|^2)/3$. f, f' and f" were taken from International Tables of X-ray Crystallography.[2] All hydrogen atoms were computed and refined using a riding model. The final R (on F) factor was 0.0235, wR (on $|F|^2$) = 0.0659 and goodness of fit = 1.164 for all observed reflections. The number of refined parameters was 203. Max. shift/esd = 0.001, Mean shift/esd = 0.00. Max. and min. peaks in final difference synthesis was 0.674 and -0.576 eÅ^{-3}, respectively.

Table S5. Crystal data and structure refinement for **19**.

Identification code	Itot7.35	
Empirical formula	C18 H18 I2 O2	
Formula weight	520.12	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 7.7537(2) Å	□= 90°.
	b = 8.7833(3) Å	□= 90°.
	c = 28.0793(10) Å	□ = 90°.
Volume	1912.29(11) Å^3	
Z	4	
Density (calculated)	1.807 Mg/m^3	
Absorption coefficient	3.293 mm^{-1}	
F(000)	992	
Crystal size	0.15 x 0.09 x 0.02 mm^3	
Theta range for data collection	2.43 to 25.08°.	
Index ranges	-9<=h<=9, -10<=k<=10, -33<=l<=33	
Reflections collected	20538	
Independent reflections	3395 [R(int) = 0.0475]	
Completeness to theta = 25.08°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9477 and 0.6379	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	3395 / 0 / 203
Goodness-of-fit on F^2	1.164
Final R indices [I>2sigma(I)]	R1 = 0.0204, wR2 = 0.0485
R indices (all data)	R1 = 0.0235, wR2 = 0.0659
Absolute structure parameter	-0.05(4)
Largest diff. peak and hole	0.674 and -0.576 e.$Å^{-3}$

Table S6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **19**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
I(1)	11818(1)	3963(1)	1938(1)	21(1)
I(2)	6315(1)	6641(1)	1489(1)	24(1)
O(1)	4554(5)	1679(5)	2200(1)	21(1)
O(2)	6423(5)	4094(4)	2369(1)	20(1)
C(1)	8210(7)	5113(6)	1762(2)	18(1)
C(2)	9854(7)	5480(6)	1710(2)	17(1)
C(3)	10576(7)	6887(6)	1492(2)	19(1)
C(4)	11342(8)	6828(7)	1046(2)	34(2)
C(5)	12059(9)	8137(8)	848(2)	44(2)
C(6)	12060(9)	9464(8)	1095(2)	39(2)
C(7)	11341(8)	9525(7)	1553(2)	33(1)
C(8)	10610(8)	8231(6)	1749(2)	25(1)
C(9)	7463(6)	3671(6)	1973(2)	16(1)
C(10)	6476(6)	2706(6)	1613(2)	16(1)
C(11)	5793(6)	1259(6)	1847(2)	20(1)
C(12)	7589(7)	2293(6)	1178(2)	20(1)
C(13)	6552(7)	1652(6)	768(2)	21(1)
C(14)	6835(9)	179(7)	601(2)	29(1)
C(15)	5318(8)	2527(8)	542(2)	29(1)
C(16)	4354(9)	1993(9)	171(2)	41(2)
C(17)	4638(9)	535(9)	12(2)	42(2)
C(20)	5867(10)	-367(8)	223(2)	42(2)

Table S7. Bond lengths [Å] and angles [°] for **19**.

I(1)-C(2)	2.122(5)	C(16)-C(17)	1.374(11)
I(2)-C(1)	2.133(5)	C(16)-H(16A)	0.9300
O(1)-C(11)	1.430(6)	C(17)-C(20)	1.373(10)
O(1)-H(1A)	0.86(5)	C(17)-H(17A)	0.9300
O(2)-C(9)	1.422(6)	C(20)-H(20A)	0.9300
O(2)-H(2A)	0.8200		
C(1)-C(2)	1.323(8)	C(11)-O(1)-H(1A)	108(3)
C(1)-C(9)	1.514(7)	C(9)-O(2)-H(2A)	109.5
C(2)-C(3)	1.490(7)	C(2)-C(1)-C(9)	128.0(5)
C(3)-C(8)	1.384(8)	C(2)-C(1)-I(2)	118.1(4)
C(3)-C(4)	1.387(8)	C(9)-C(1)-I(2)	113.8(4)
C(4)-C(5)	1.394(9)	C(1)-C(2)-C(3)	127.6(5)
C(4)-H(4A)	0.9300	C(1)-C(2)-I(1)	120.4(4)
C(5)-C(6)	1.356(10)	C(3)-C(2)-I(1)	112.1(4)
C(5)-H(5A)	0.9300	C(8)-C(3)-C(4)	119.7(5)
C(6)-C(7)	1.404(9)	C(8)-C(3)-C(2)	120.0(5)
C(6)-H(6A)	0.9300	C(4)-C(3)-C(2)	120.1(5)
C(7)-C(8)	1.383(8)	C(3)-C(4)-C(5)	120.0(6)
C(7)-H(7A)	0.9300	C(3)-C(4)-H(4A)	120.0
C(8)-H(8A)	0.9300	C(5)-C(4)-H(4A)	120.0
C(9)-C(10)	1.526(7)	C(6)-C(5)-C(4)	120.3(6)
C(9)-H(9A)	0.9800	C(6)-C(5)-H(5A)	119.8
C(10)-C(11)	1.526(7)	C(4)-C(5)-H(5A)	119.8
C(10)-C(12)	1.538(7)	C(5)-C(6)-C(7)	120.1(6)
C(10)-H(10A)	0.9800	C(5)-C(6)-H(6A)	120.0
C(11)-H(11A)	0.9700	C(7)-C(6)-H(6A)	120.0
C(11)-H(11B)	0.9700	C(8)-C(7)-C(6)	119.7(6)
C(12)-C(13)	1.512(7)	C(8)-C(7)-H(7A)	120.1
C(12)-H(12A)	0.9700	C(6)-C(7)-H(7A)	120.1
C(12)-H(12B)	0.9700	C(7)-C(8)-C(3)	120.1(5)
C(13)-C(15)	1.382(8)	C(7)-C(8)-H(8A)	120.0
C(13)-C(14)	1.394(8)	C(3)-C(8)-H(8A)	120.0
C(14)-C(20)	1.385(9)	O(2)-C(9)-C(1)	107.7(4)
C(14)-H(14A)	0.9300	O(2)-C(9)-C(10)	112.3(4)
C(15)-C(16)	1.366(9)	C(1)-C(9)-C(10)	113.3(4)
C(15)-H(15A)	0.9300	O(2)-C(9)-H(9A)	107.8

C(1)-C(9)-H(9A)	107.8	H(12A)-C(12)-H(12B)	107.8
C(10)-C(9)-H(9A)	107.8	C(15)-C(13)-C(14)	118.0(5)
C(9)-C(10)-C(11)	110.6(4)	C(15)-C(13)-C(12)	120.7(5)
C(9)-C(10)-C(12)	112.1(4)	C(14)-C(13)-C(12)	121.2(5)
C(11)-C(10)-C(12)	109.9(4)	C(20)-C(14)-C(13)	119.6(6)
C(9)-C(10)-H(10A)	108.1	C(20)-C(14)-H(14A)	120.2
C(11)-C(10)-H(10A)	108.1	C(13)-C(14)-H(14A)	120.2
C(12)-C(10)-H(10A)	108.1	C(16)-C(15)-C(13)	122.6(6)
O(1)-C(11)-C(10)	108.5(4)	C(16)-C(15)-H(15A)	118.7
O(1)-C(11)-H(11A)	110.0	C(13)-C(15)-H(15A)	118.7
C(10)-C(11)-H(11A)	110.0	C(15)-C(16)-C(17)	118.6(7)
O(1)-C(11)-H(11B)	110.0	C(15)-C(16)-H(16A)	120.7
C(10)-C(11)-H(11B)	110.0	C(17)-C(16)-H(16A)	120.7
H(11A)-C(11)-H(11B)	108.4	C(20)-C(17)-C(16)	120.6(6)
C(13)-C(12)-C(10)	113.2(4)	C(20)-C(17)-H(17A)	119.7
C(13)-C(12)-H(12A)	108.9	C(16)-C(17)-H(17A)	119.7
C(10)-C(12)-H(12A)	108.9	C(17)-C(20)-C(14)	120.4(6)
C(13)-C(12)-H(12B)	108.9	C(17)-C(20)-H(20A)	119.8
C(10)-C(12)-H(12B)	108.9	C(14)-C(20)-H(20A)	119.8

Symmetry transformations used to generate equivalent atoms:

Table S8. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **19**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
I(1)	12(1)	22(1)	30(1)	1(1)	1(1)	0(1)
I(2)	18(1)	19(1)	35(1)	8(1)	-2(1)	1(1)
O(1)	20(2)	18(2)	24(2)	5(2)	9(2)	-1(2)
O(2)	20(2)	18(2)	22(2)	-1(2)	7(2)	-2(2)
C(1)	20(3)	14(2)	20(2)	-1(2)	-2(2)	2(2)
C(2)	19(3)	14(3)	18(3)	0(2)	0(2)	1(2)
C(3)	17(3)	20(3)	19(3)	2(2)	-6(2)	-5(2)
C(4)	37(4)	36(3)	28(3)	0(3)	6(3)	-18(3)
C(5)	47(4)	52(4)	33(3)	3(3)	3(3)	-24(4)
C(6)	29(4)	40(4)	48(4)	24(3)	-13(3)	-21(3)
C(7)	36(3)	21(3)	42(4)	3(3)	-13(3)	-7(3)
C(8)	29(3)	22(3)	25(3)	3(3)	-2(2)	-5(3)
C(9)	11(2)	16(3)	20(2)	-2(2)	0(2)	3(2)
C(10)	10(3)	20(3)	18(2)	6(2)	1(2)	1(2)
C(11)	16(3)	22(3)	24(3)	-1(2)	4(2)	0(2)
C(12)	19(3)	20(3)	23(3)	-2(2)	3(2)	2(2)
C(13)	26(3)	25(3)	12(2)	3(2)	5(2)	-6(3)
C(14)	38(3)	24(3)	24(3)	0(2)	7(3)	-4(3)
C(15)	25(3)	37(4)	24(3)	9(3)	-1(3)	-1(3)
C(16)	34(4)	65(5)	24(3)	10(3)	-6(3)	-3(4)
C(17)	43(4)	64(5)	19(3)	0(3)	-6(3)	-21(4)
C(20)	57(5)	45(4)	25(3)	-9(3)	14(3)	-17(4)

Table S9. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **19**.

	x	y	z	U(eq)
H(1A)	4290(70)	880(60)	2363(18)	13(14)
H(2A)	5648	3469	2403	30
H(4A)	11377	5913	879	41
H(5A)	12540	8101	544	53
H(6A)	12537	10335	960	47
H(7A)	11356	10430	1725	40
H(8A)	10141	8265	2053	30
H(9A)	8424	3057	2094	19
H(10A)	5486	3300	1501	19
H(11A)	5259	610	1609	24
H(11B)	6734	701	1993	24
H(12A)	8192	3197	1071	25
H(12B)	8448	1551	1273	25
H(14A)	7669	-434	742	35
H(15A)	5138	3519	646	34
H(16A)	3521	2604	28	49
H(17A)	3992	155	-240	51
H(20A)	6051	-1350	111	51

Table S10. Torsion angles [°] for **19**

C(9)-C(1)-C(2)-C(3)	178.5(5)	I(2)-C(1)-C(9)-C(10)	62.0(5)
I(2)-C(1)-C(2)-C(3)	1.9(7)	O(2)-C(9)-C(10)-C(11)	-58.8(5)
C(9)-C(1)-C(2)-I(1)	0.0(8)	C(1)-C(9)-C(10)-C(11)	178.8(4)
I(2)-C(1)-C(2)-I(1)	-176.6(2)	O(2)-C(9)-C(10)-C(12)	178.2(4)
C(1)-C(2)-C(3)-C(8)	78.7(7)	C(1)-C(9)-C(10)-C(12)	55.8(6)
I(1)-C(2)-C(3)-C(8)	-102.8(5)	C(9)-C(10)-C(11)-O(1)	64.8(5)
C(1)-C(2)-C(3)-C(4)	-106.6(7)	C(12)-C(10)-C(11)-O(1)	-171.0(4)
I(1)-C(2)-C(3)-C(4)	72.0(6)	C(9)-C(10)-C(12)-C(13)	-167.0(4)
C(8)-C(3)-C(4)-C(5)	-3.4(9)	C(11)-C(10)-C(12)-C(13)	69.6(6)
C(2)-C(3)-C(4)-C(5)	-178.2(6)	C(10)-C(12)-C(13)-C(15)	63.3(6)
C(3)-C(4)-C(5)-C(6)	2.0(11)	C(10)-C(12)-C(13)-C(14)	-118.1(5)
C(4)-C(5)-C(6)-C(7)	0.2(11)	C(15)-C(13)-C(14)-C(20)	-1.0(8)
C(5)-C(6)-C(7)-C(8)	-0.9(10)	C(12)-C(13)-C(14)-C(20)	-179.6(5)
C(6)-C(7)-C(8)-C(3)	-0.5(9)	C(14)-C(13)-C(15)-C(16)	1.4(9)
C(4)-C(3)-C(8)-C(7)	2.7(9)	C(12)-C(13)-C(15)-C(16)	180.0(5)
C(2)-C(3)-C(8)-C(7)	177.5(5)	C(13)-C(15)-C(16)-C(17)	-0.9(10)
C(2)-C(1)-C(9)-O(2)	120.4(6)	C(15)-C(16)-C(17)-C(20)	0.0(10)
I(2)-C(1)-C(9)-O(2)	-62.8(4)	C(16)-C(17)-C(20)-C(14)	0.3(10)
C(2)-C(1)-C(9)-C(10)	-114.7(6)	C(13)-C(14)-C(20)-C(17)	0.2(9)

Symmetry transformations used to generate equivalent atoms:

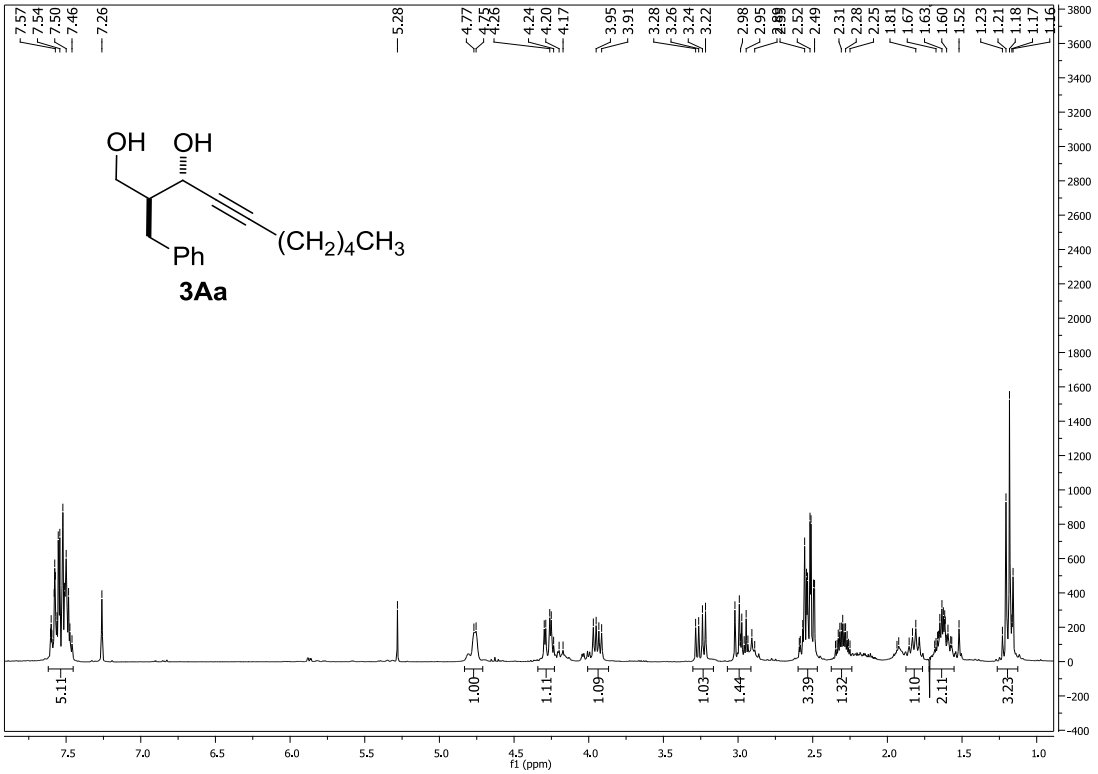
Table S11. Hydrogen bonds for **19** [Å and °].

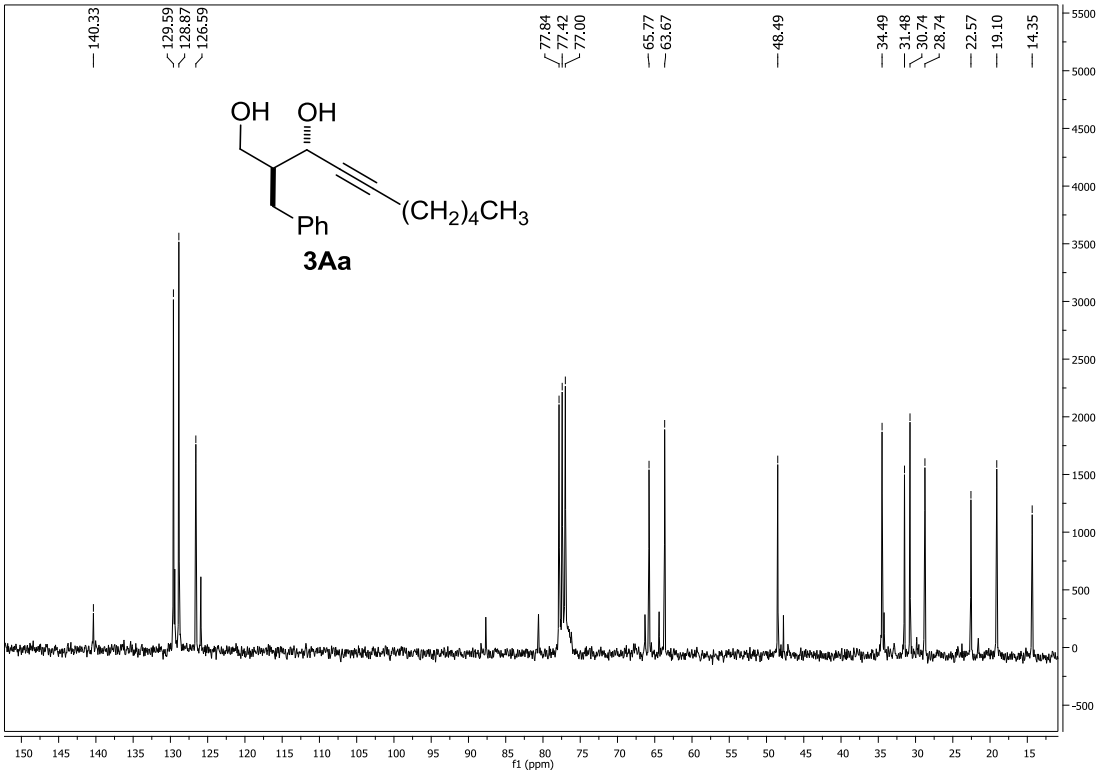
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1A)...O(2)#1	0.86(5)	1.82(6)	2.682(5)	172(5)
O(1)-H(1A)...I(2)#1	0.86(5)	3.32(5)	3.741(4)	113(4)
O(2)-H(2A)...O(1)	0.82	1.88	2.613(5)	149.0
O(2)-H(2A)...I(1)#2	0.82	3.27	3.772(4)	121.9

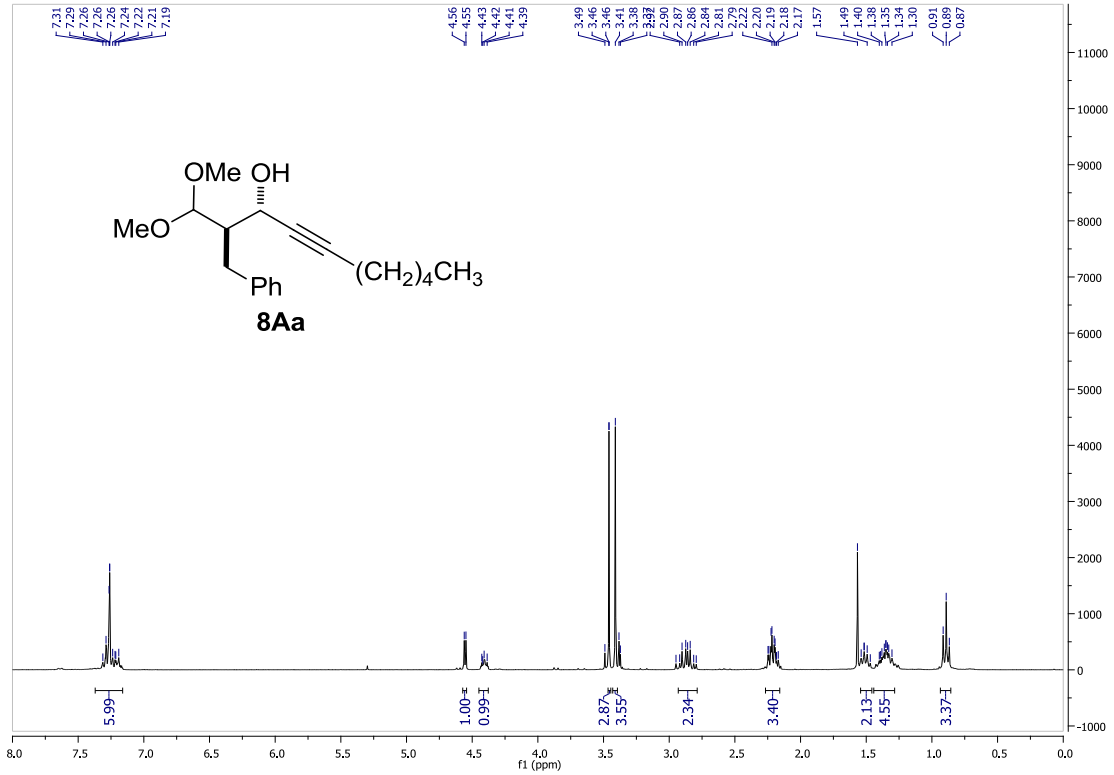
Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y-1/2,-z+1/2 #2 x-1,y,z

L) ^{1}H and ^{13}C RMN of compounds.



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Ph
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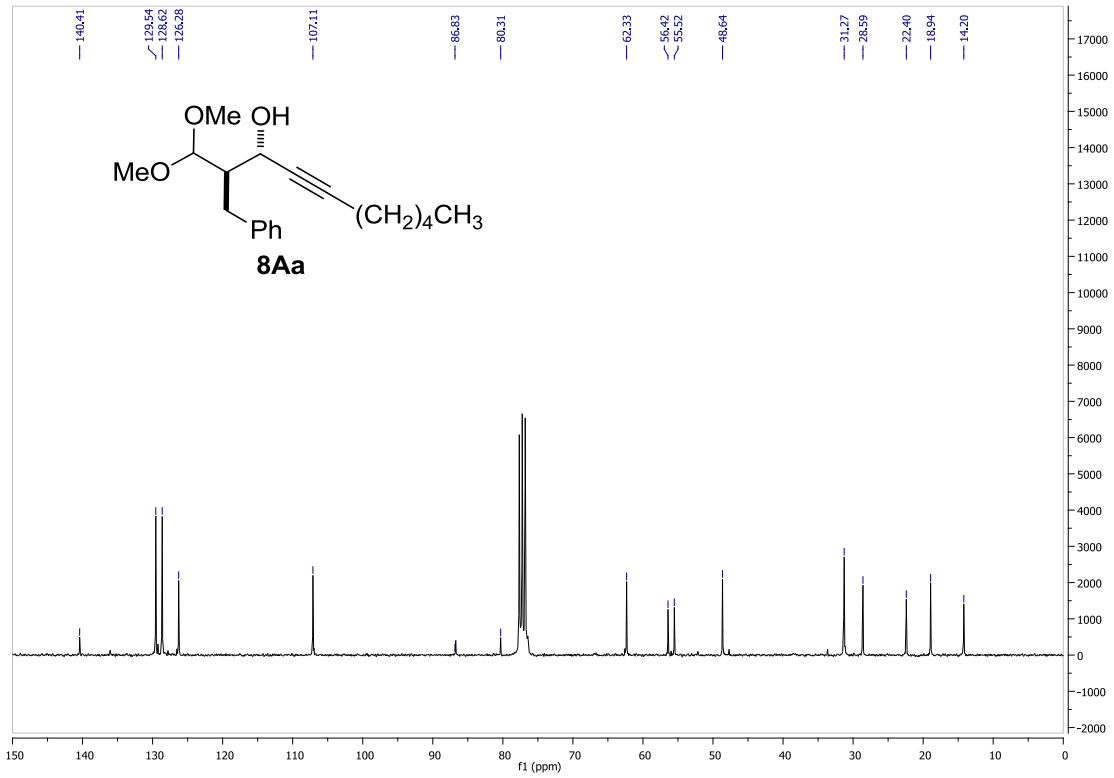
f1 (ppm)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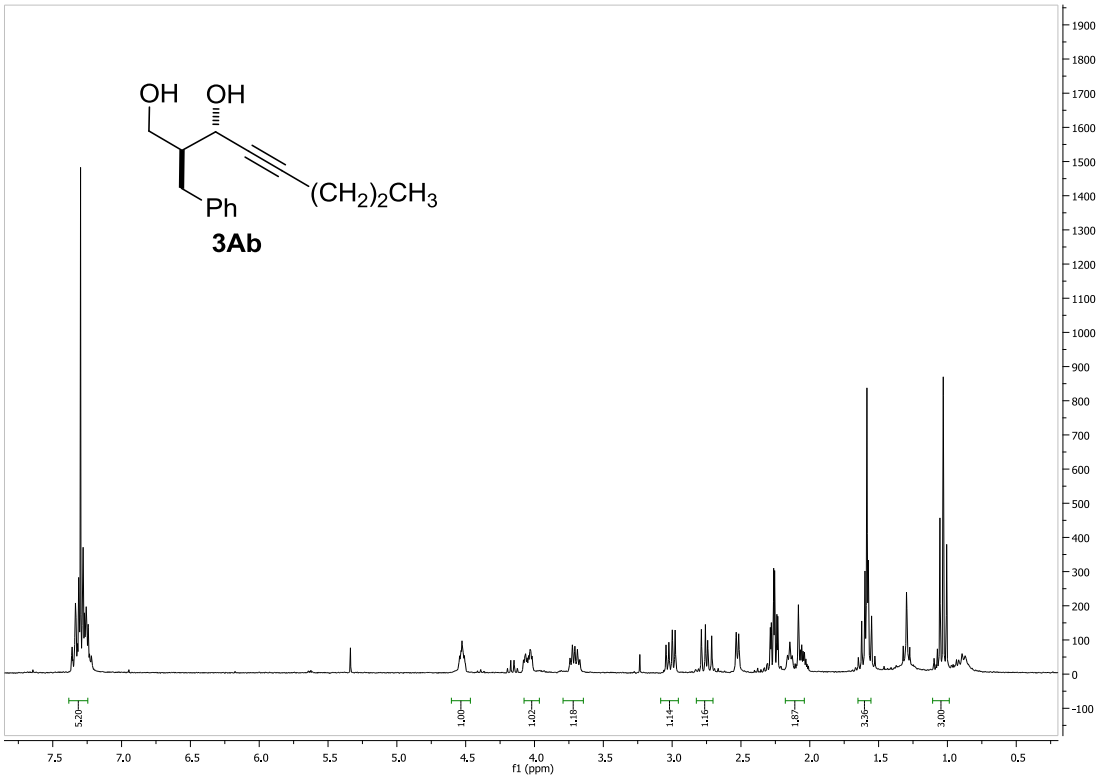
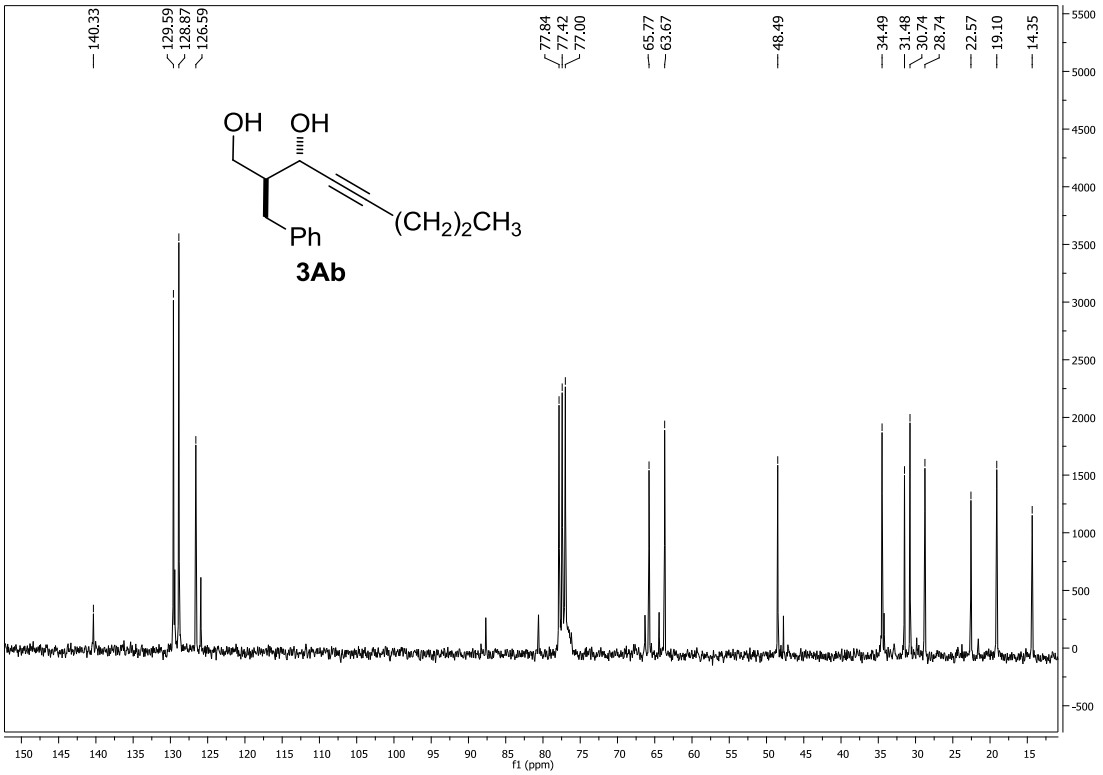
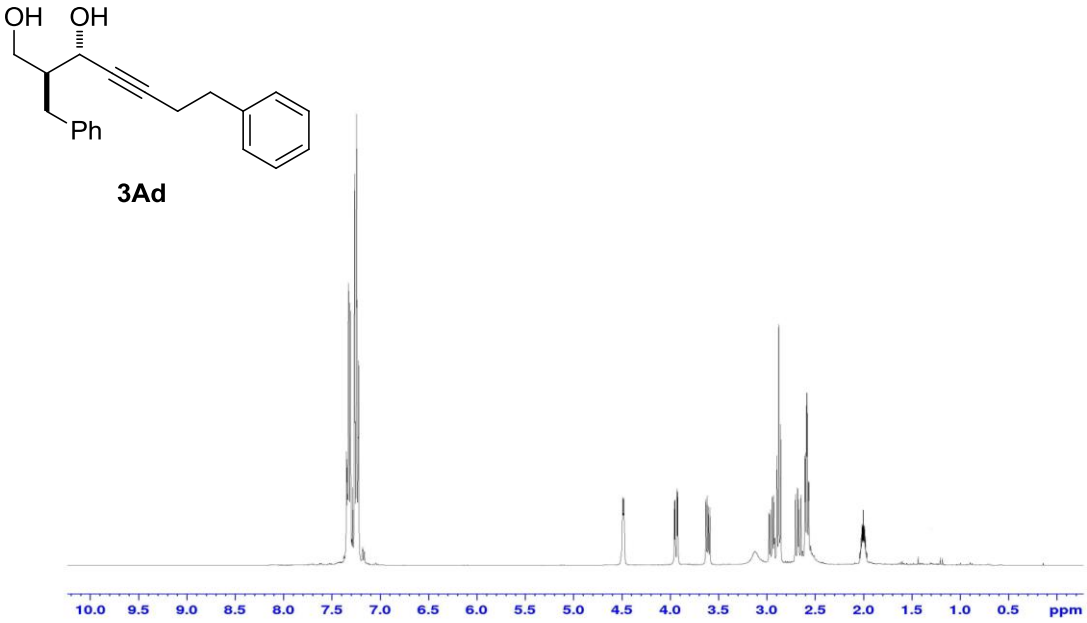
Ph
(CH2)4CH3
8Aa
f1 (ppm)



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OH
Ph
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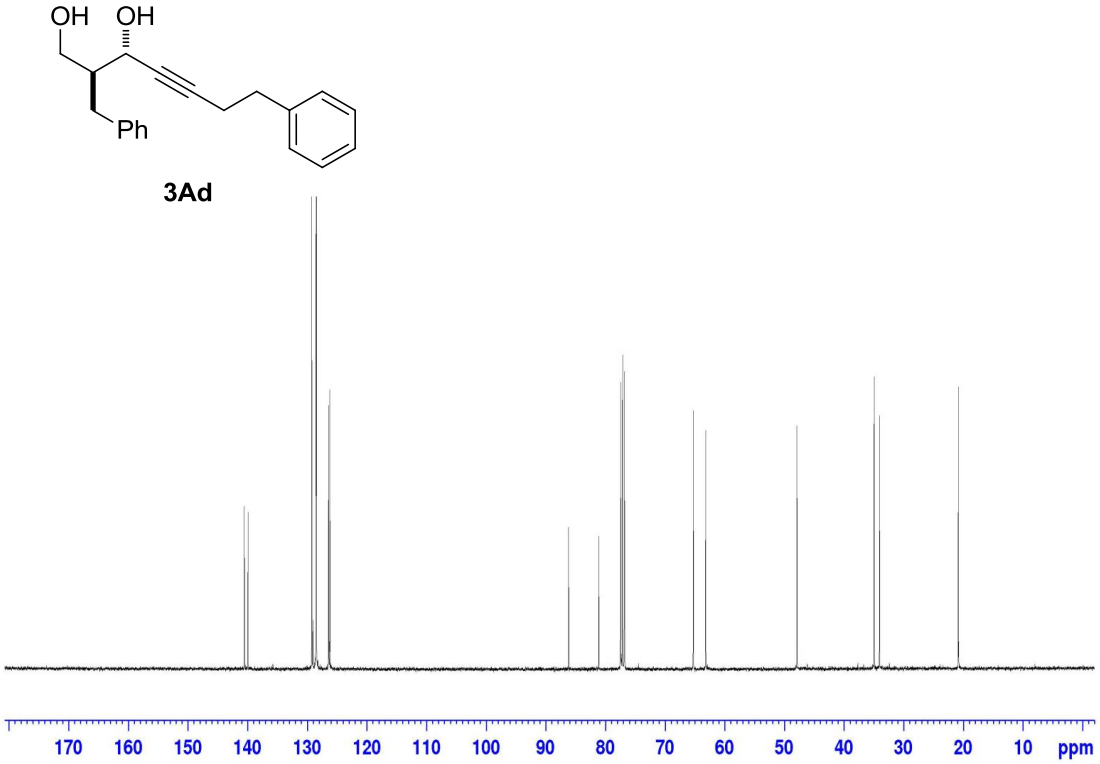
3Ad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OH
Ph
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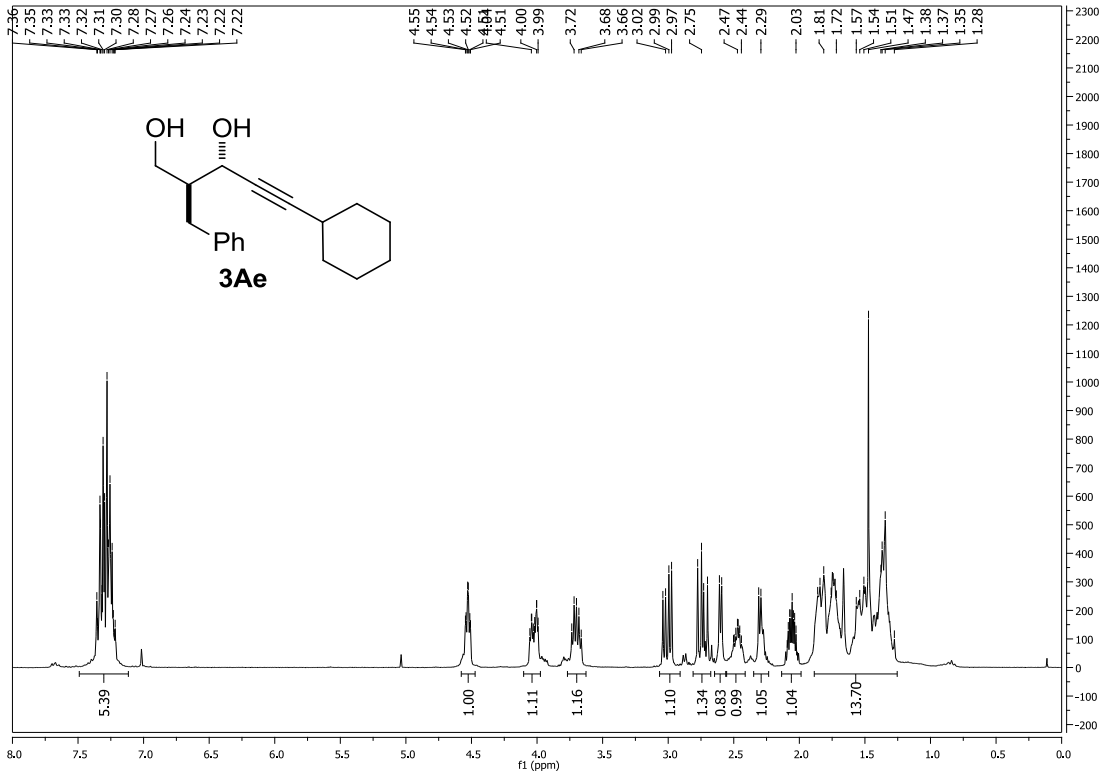
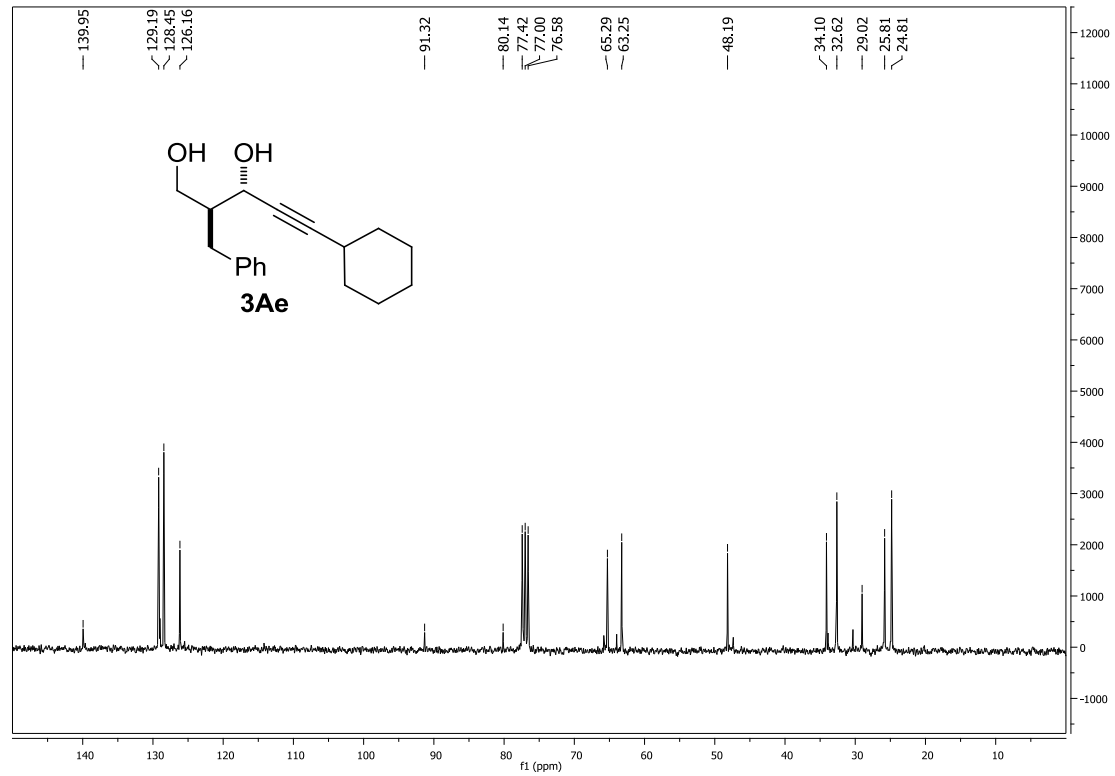
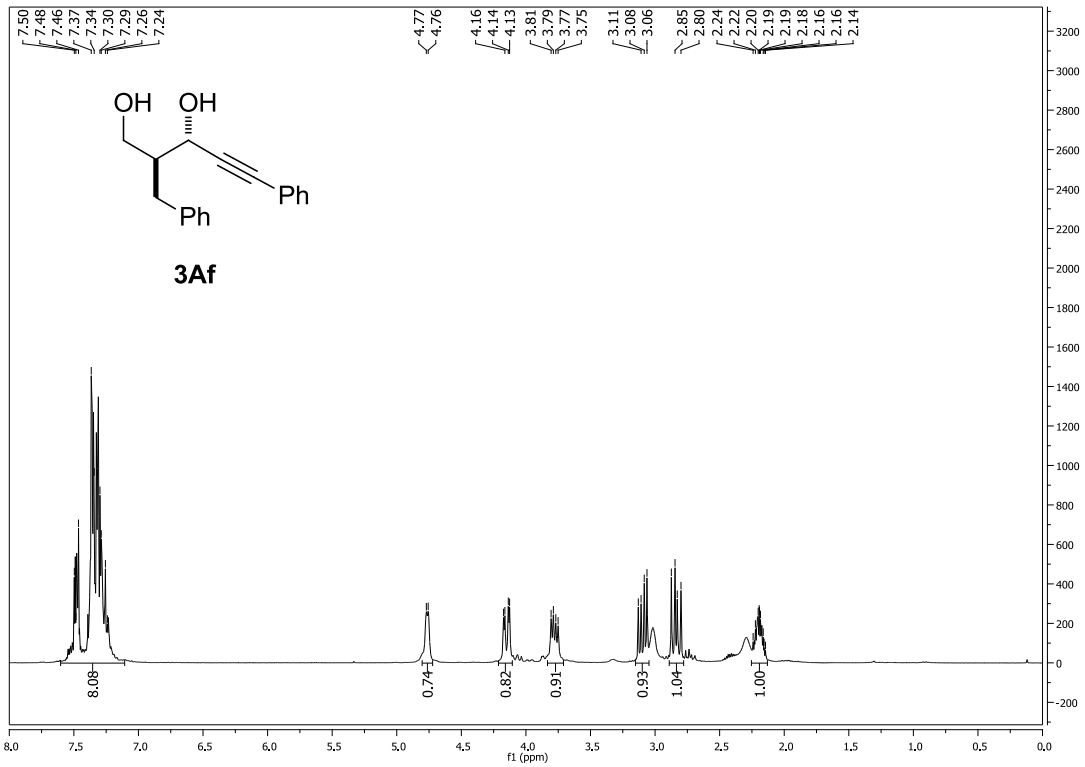
3Ad



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3.08
3.06
2.85
2.80
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2.22
2.20
2.19
2.18
2.16
2.16
2.14
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OH
Ph
Ph
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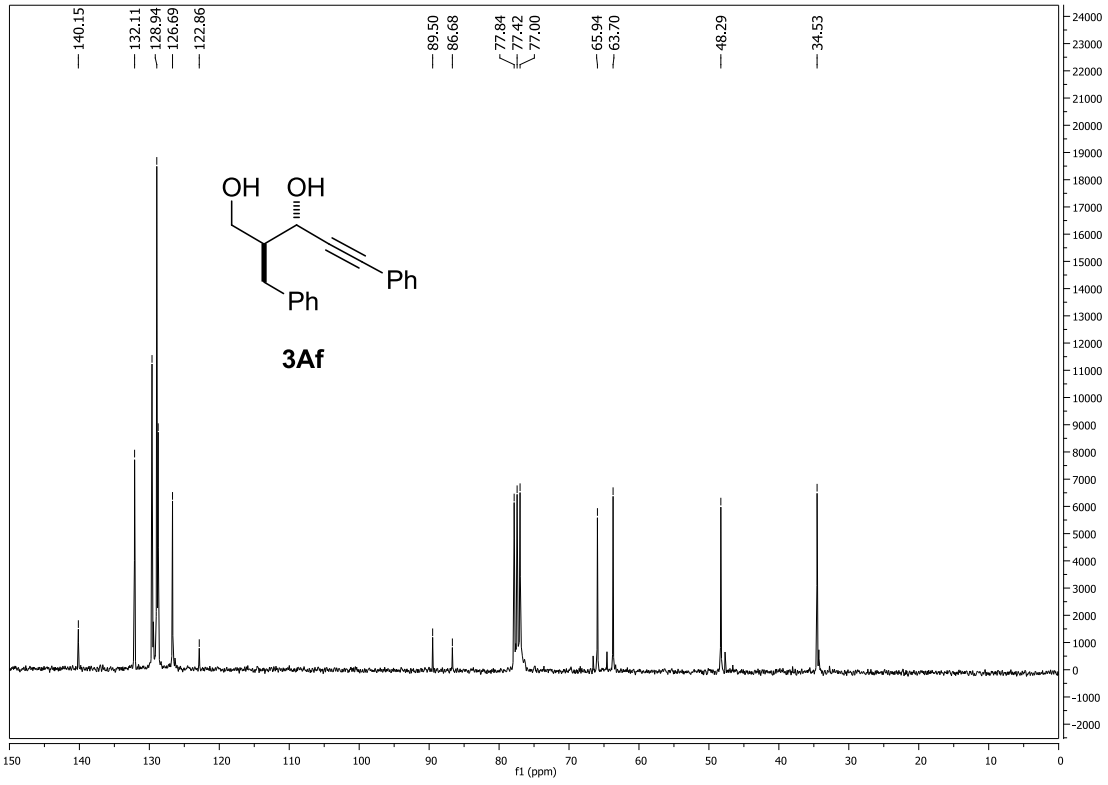
1.00
f1 (ppm)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65.94
63.70
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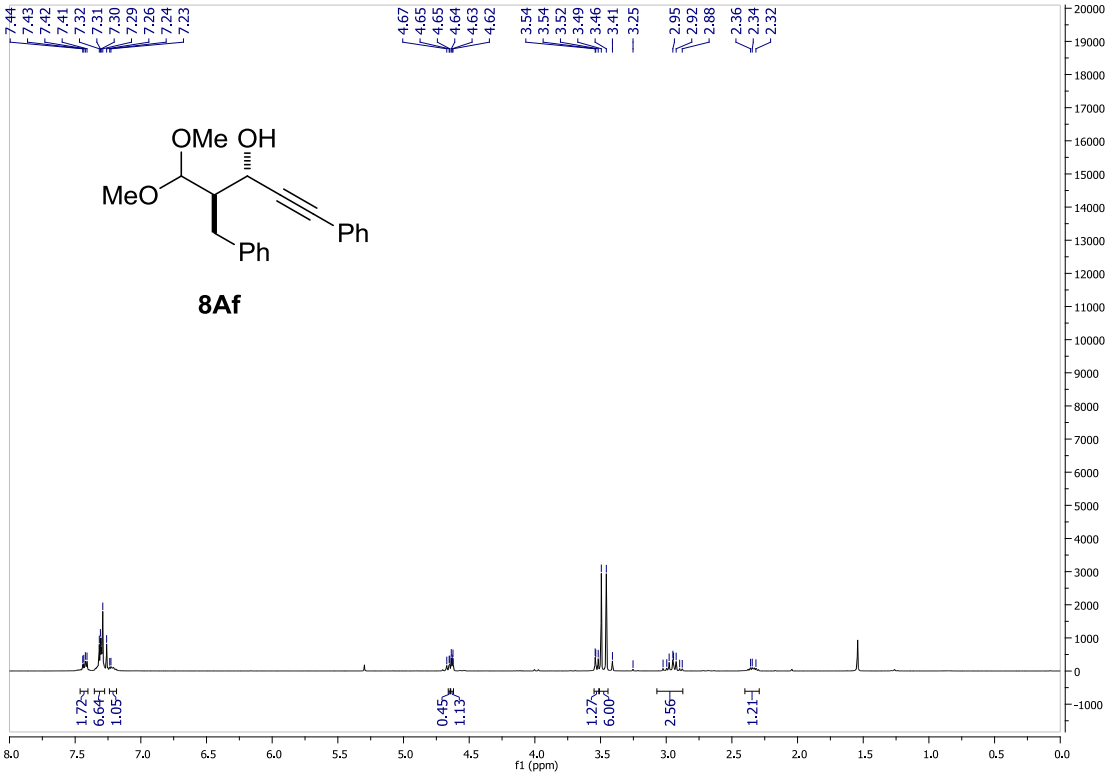
OH
OH
Ph
Ph
3Af
f1 (ppm)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4.63
4.62
3.54
3.54
3.52
3.49
3.46
3.41
3.25
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2.92
2.88
2.36
2.34
2.32
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MeO
Ph
Ph
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6.00
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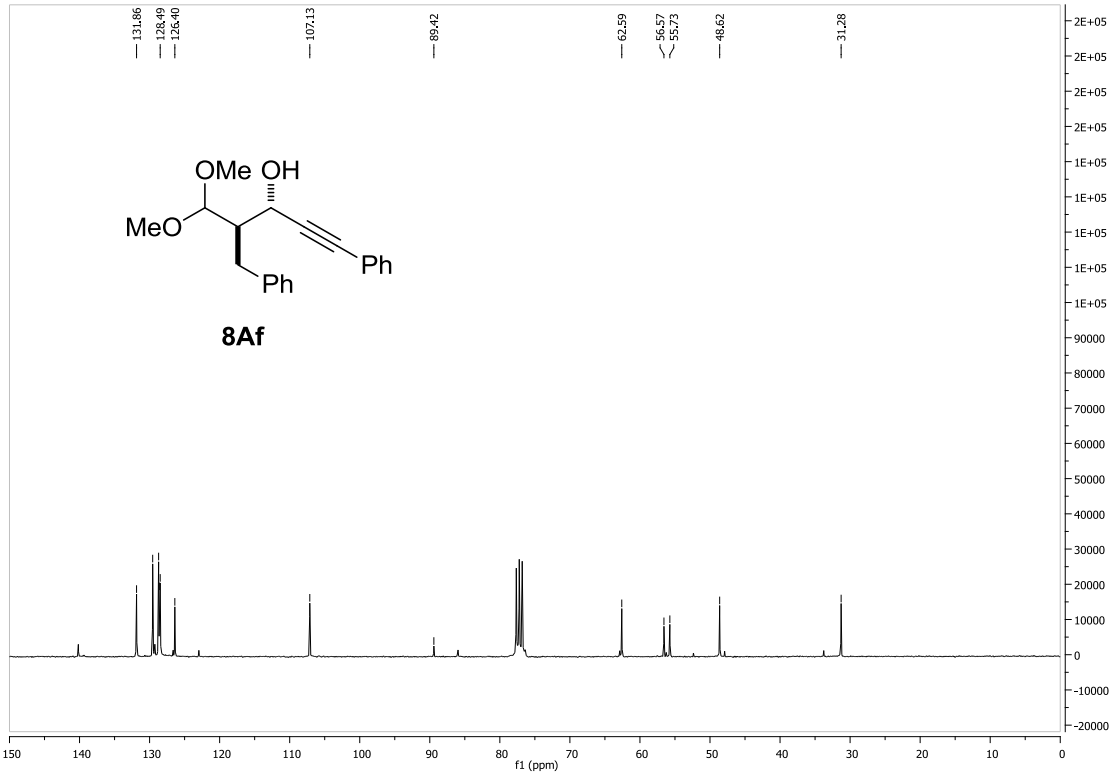
1.21
f1 (ppm)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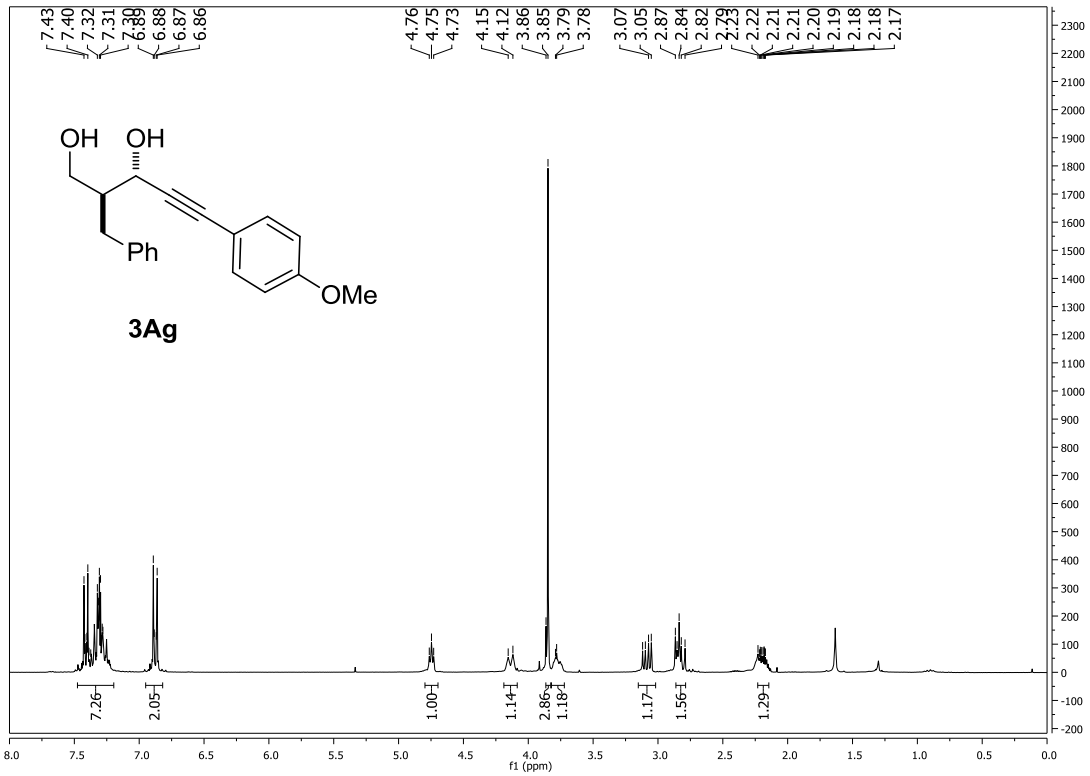
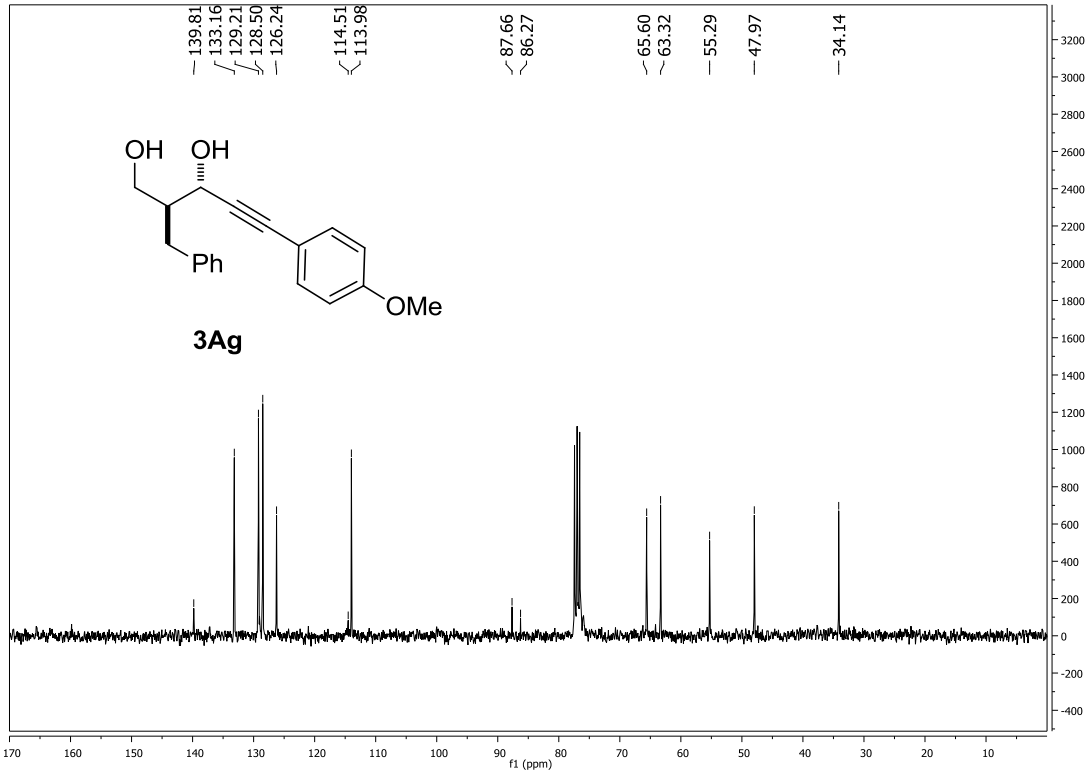
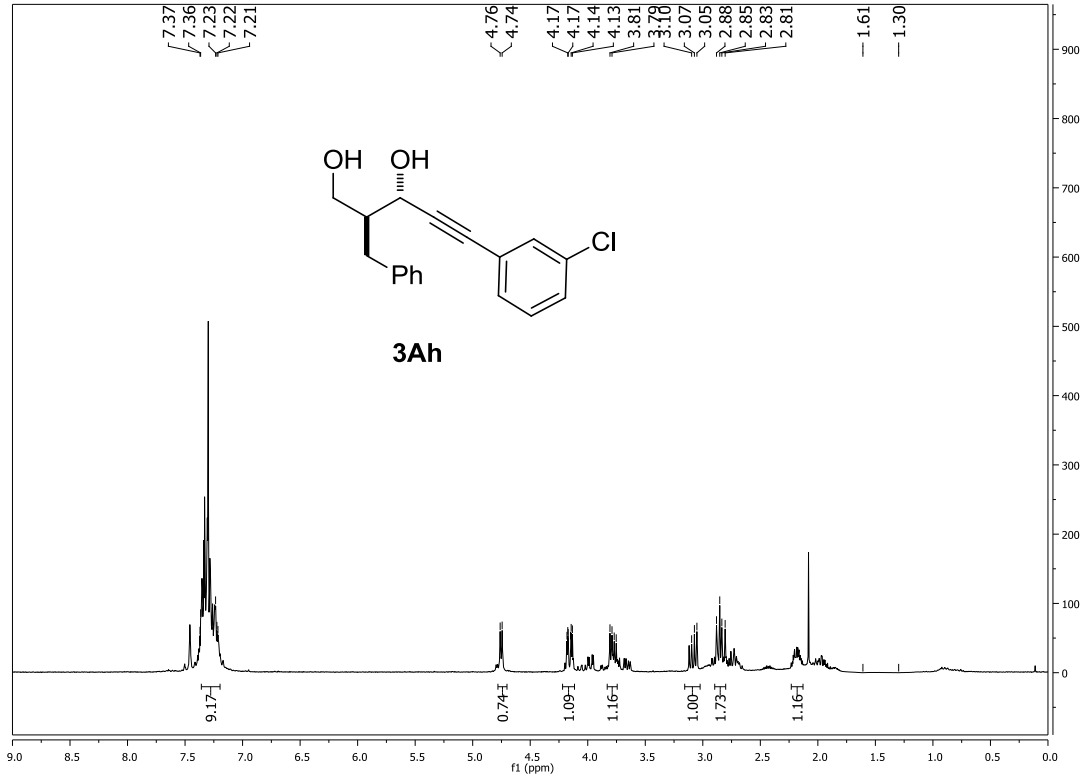
Ph
Ph
8Af
f1 (ppm)



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3.07
3.05
2.88
2.85
2.83
2.81
1.61
1.30
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OH
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Ph
3Ah
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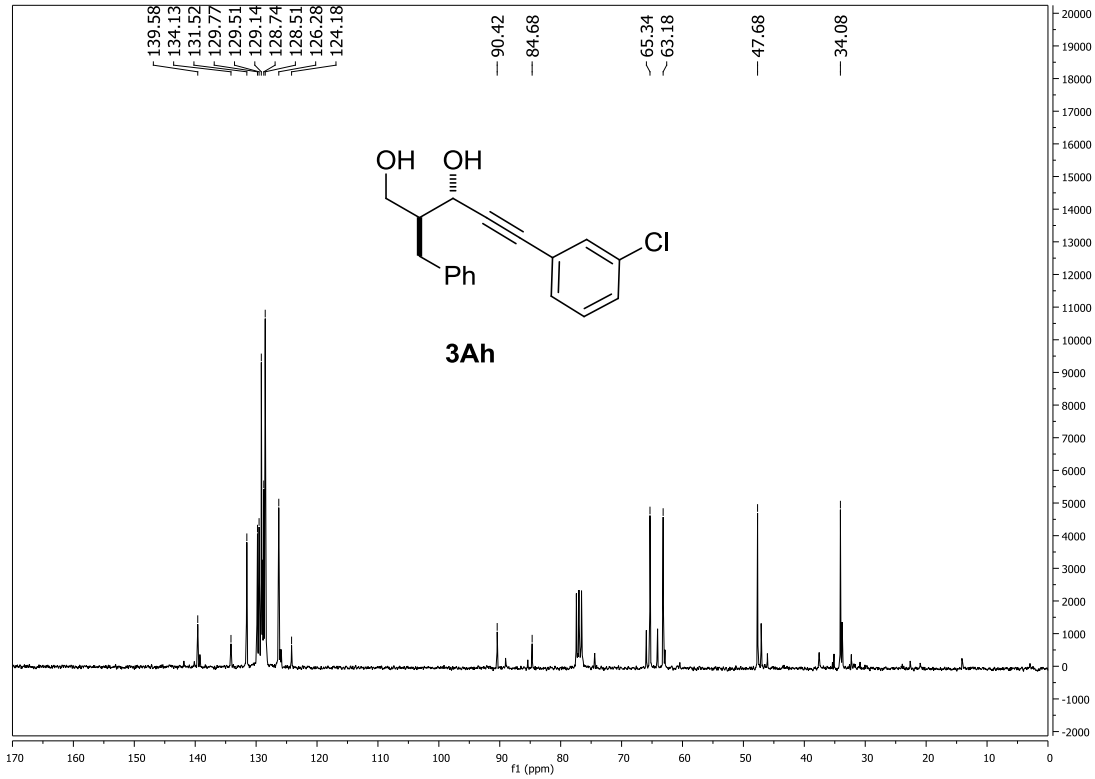
1.16
1.00
1.73
1.16
f1 (ppm)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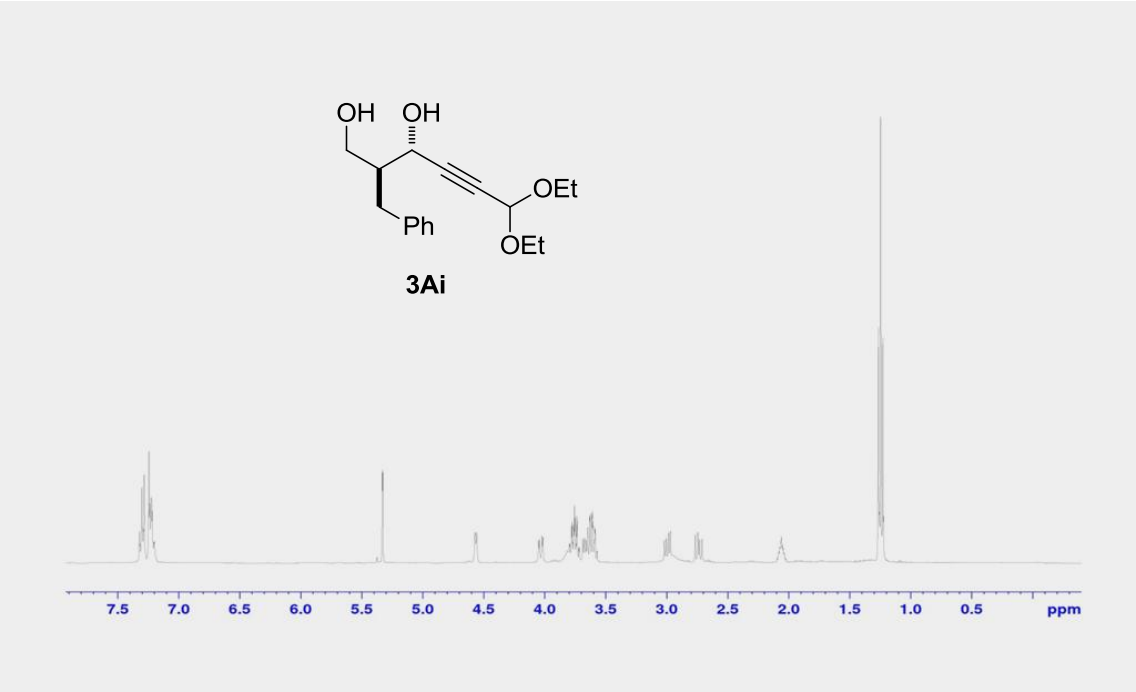
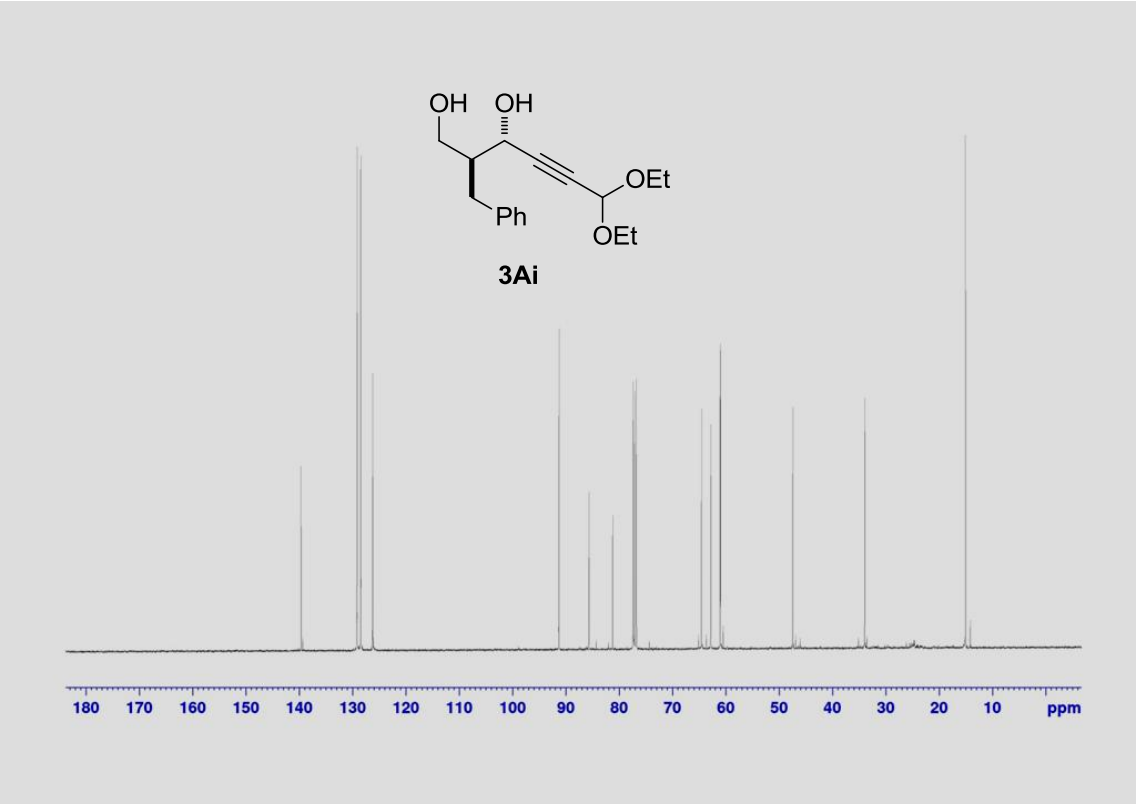
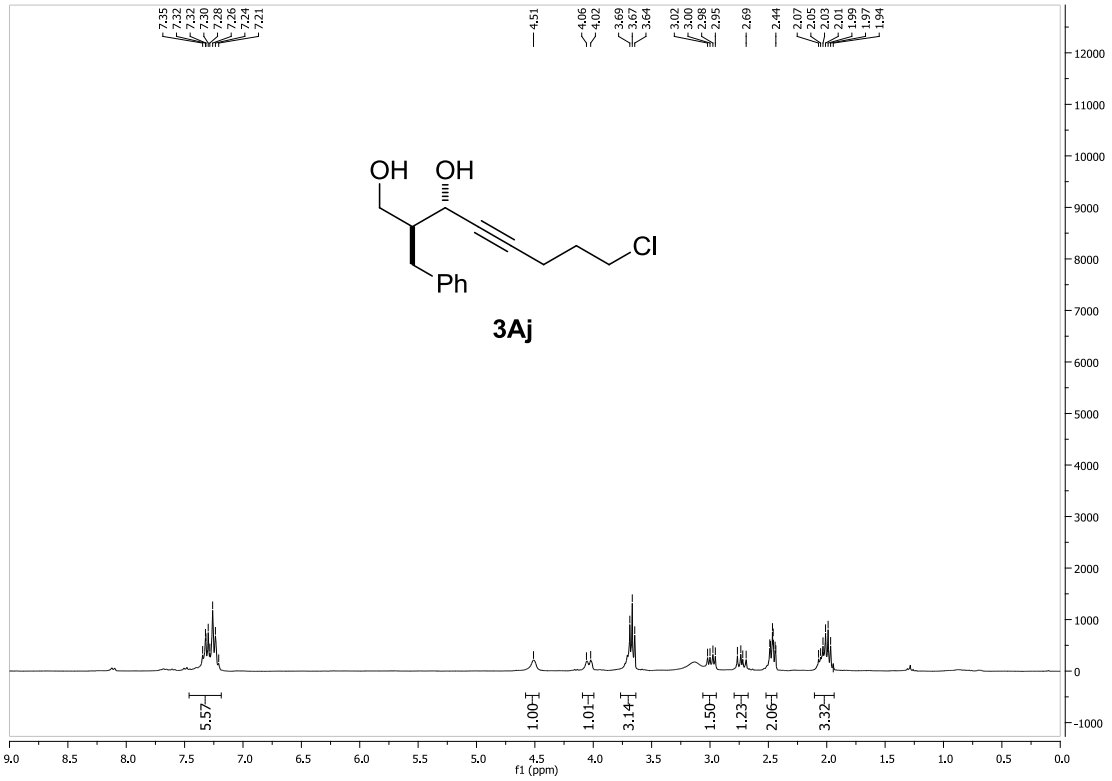
OH
OH
Cl
Ph
3Ah
f1 (ppm)



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3.00
2.98
2.95
2.69
2.44
2.07
2.05
2.03
2.01
1.99
1.97
1.94
OH
OH
Cl
Ph
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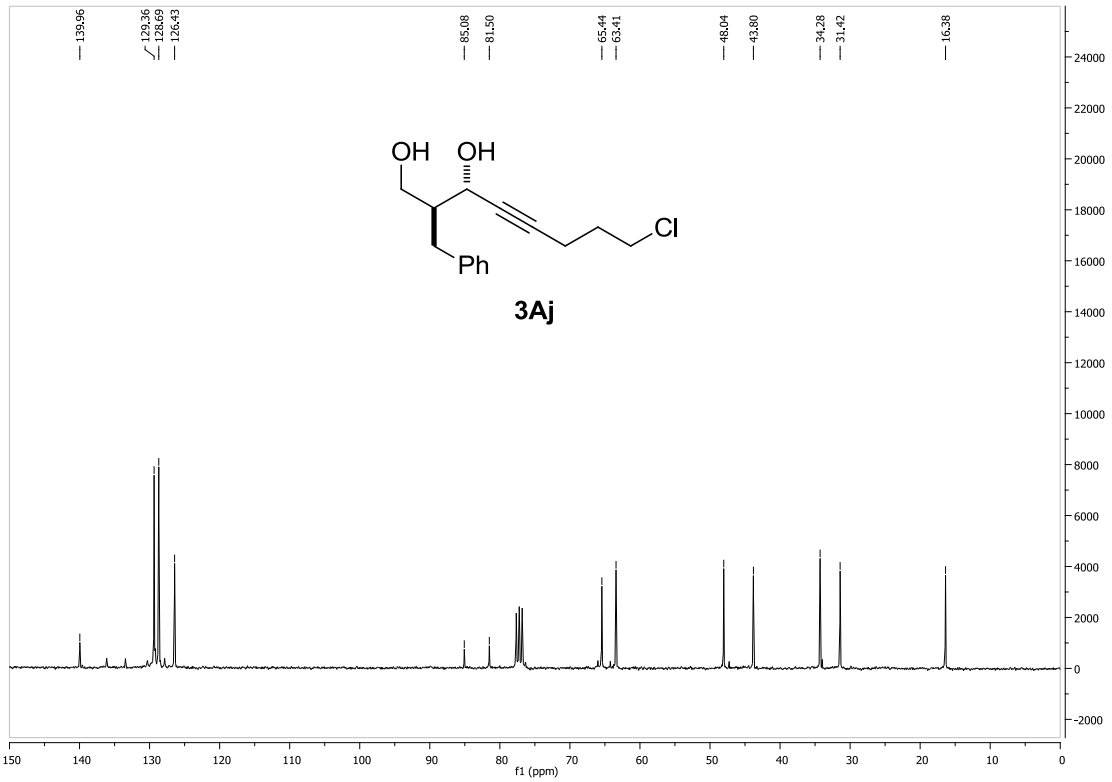
1.01
3.14
1.50
1.23
2.06
3.32
f1 (ppm)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34.28
31.42
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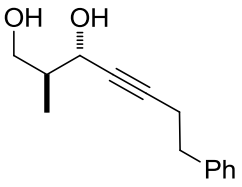
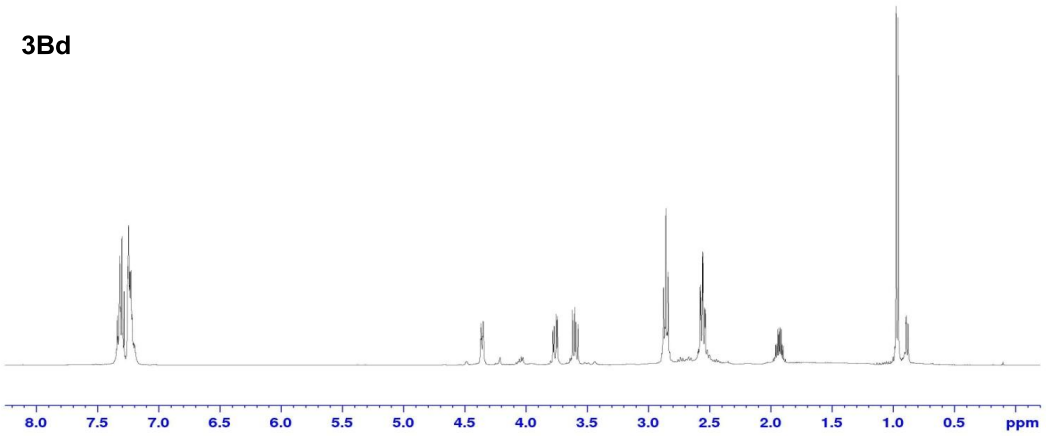
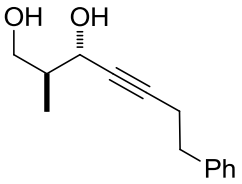
OH
OH
Cl
Ph
3Aj
f1 (ppm)

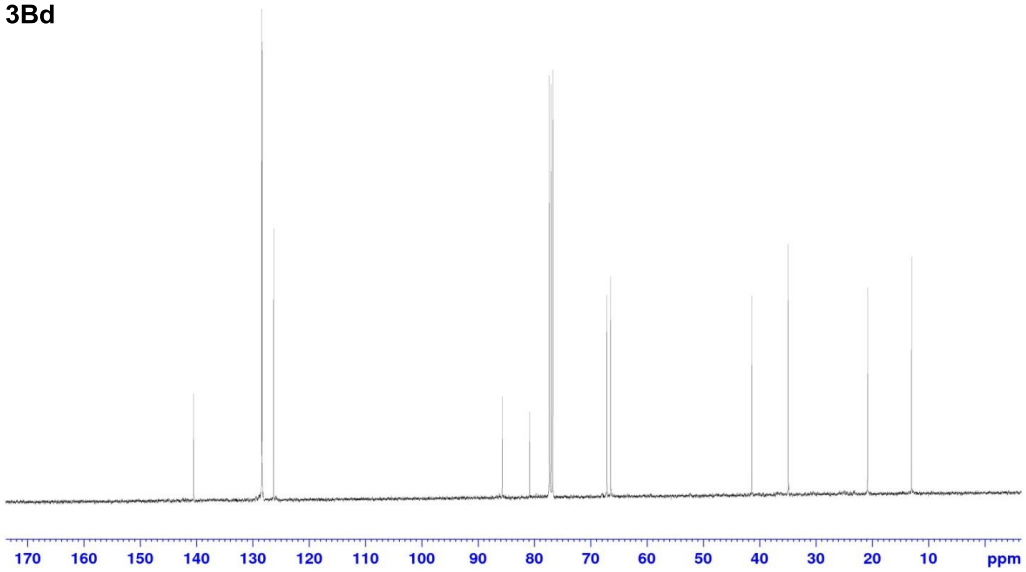


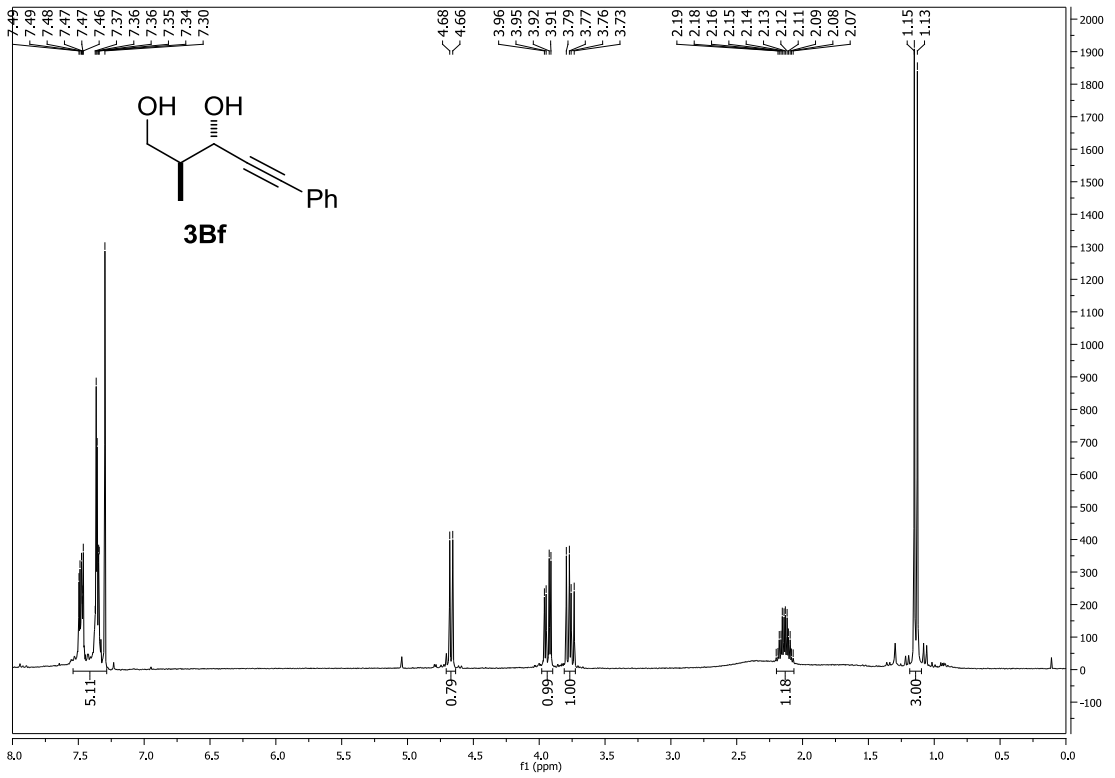
3Bd

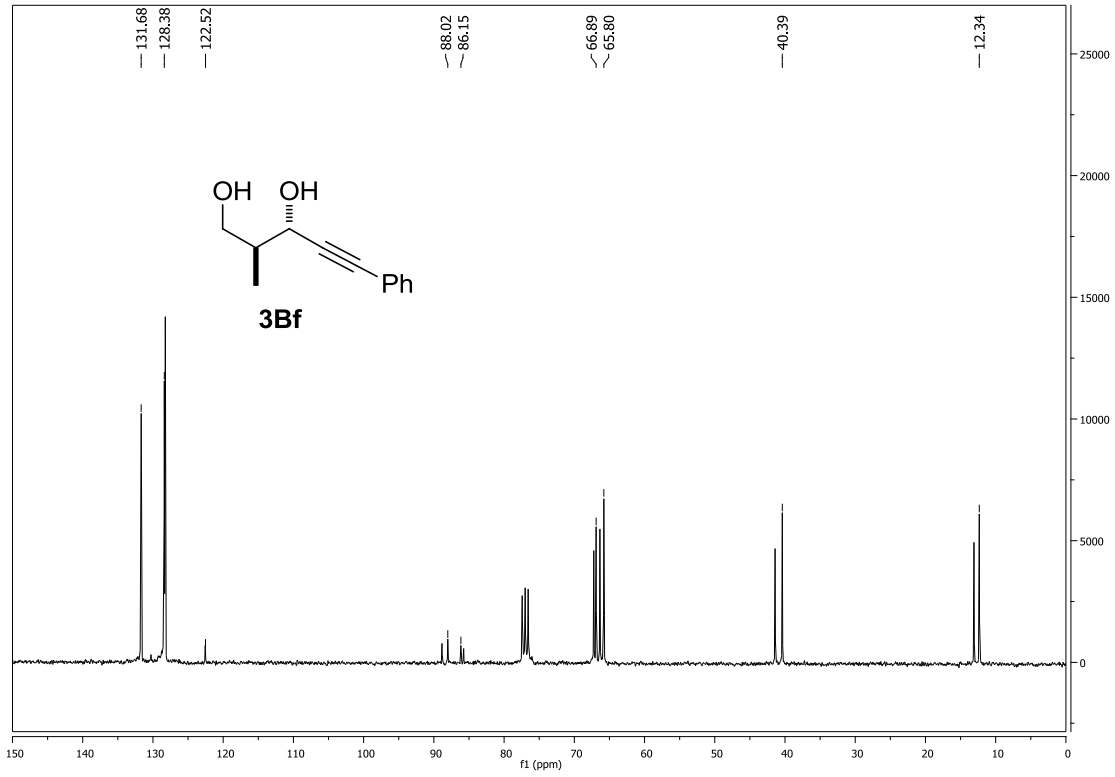


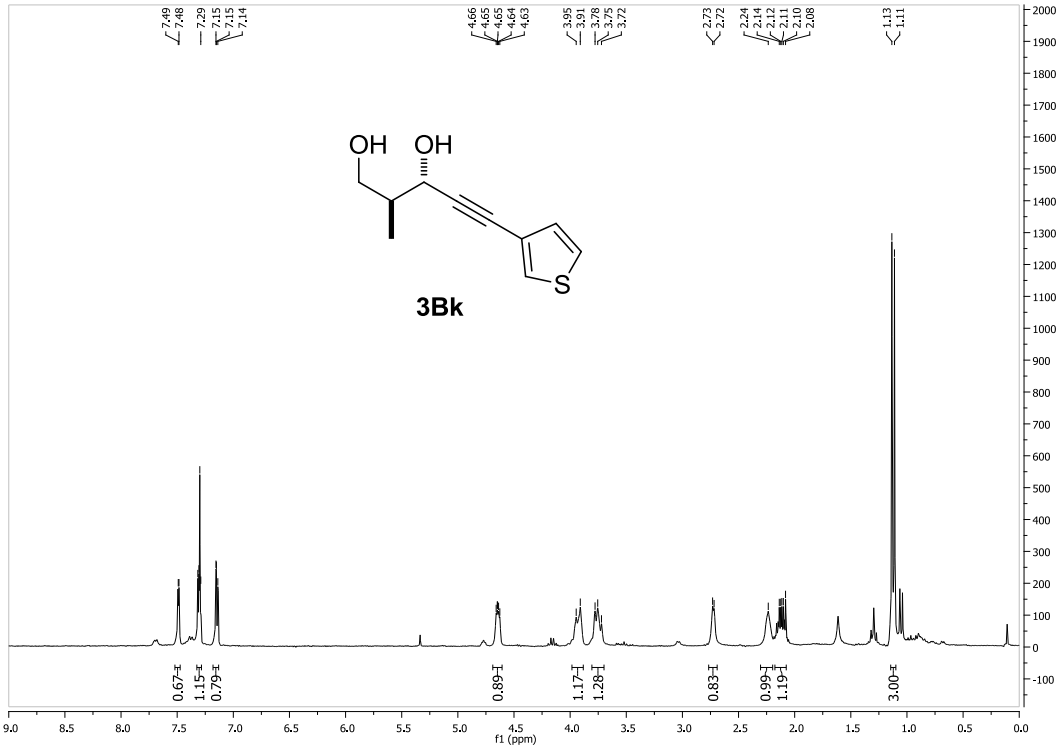


3Bd





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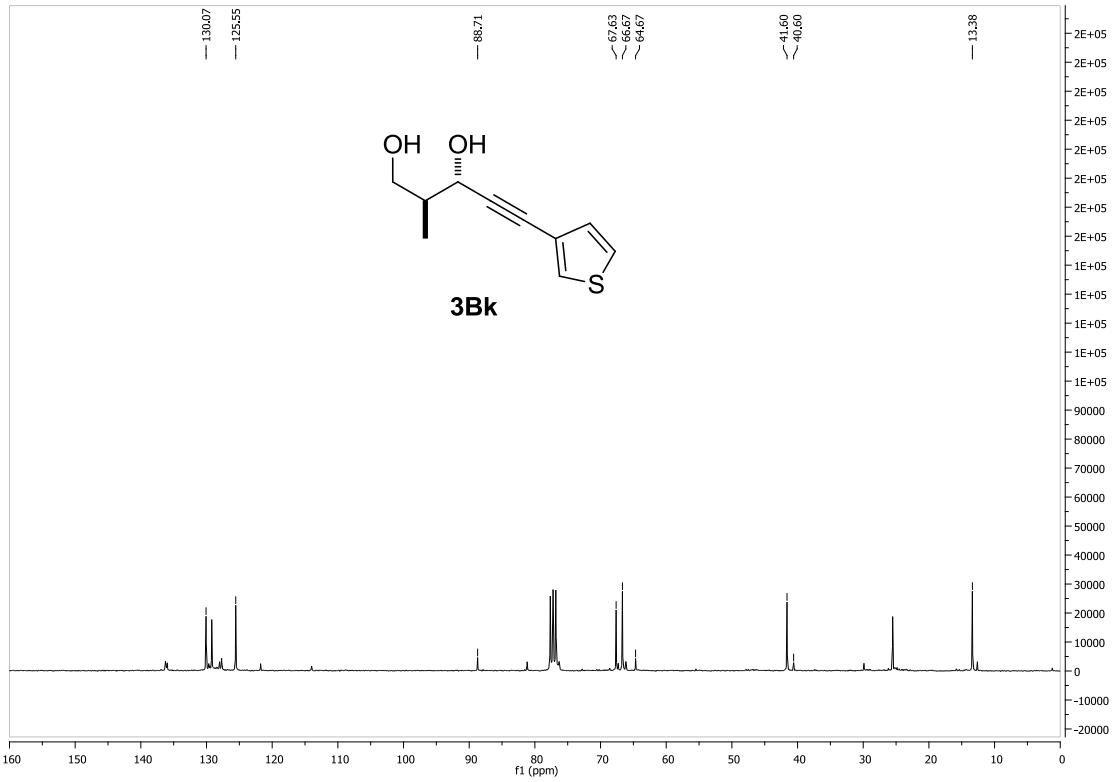
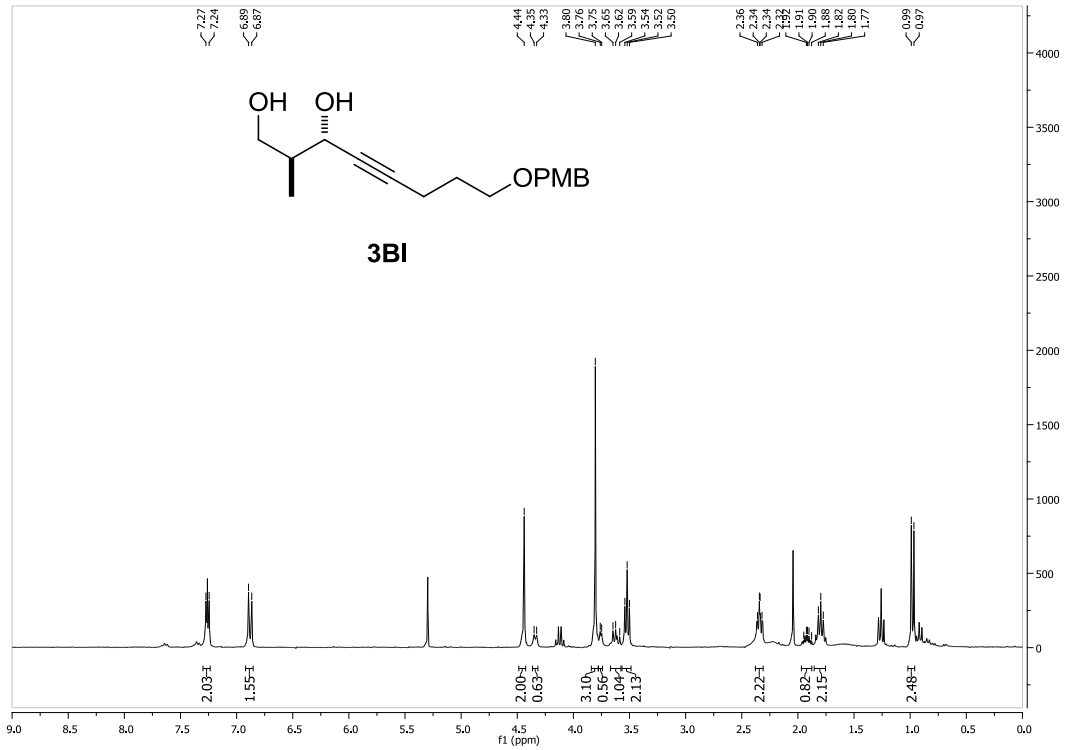
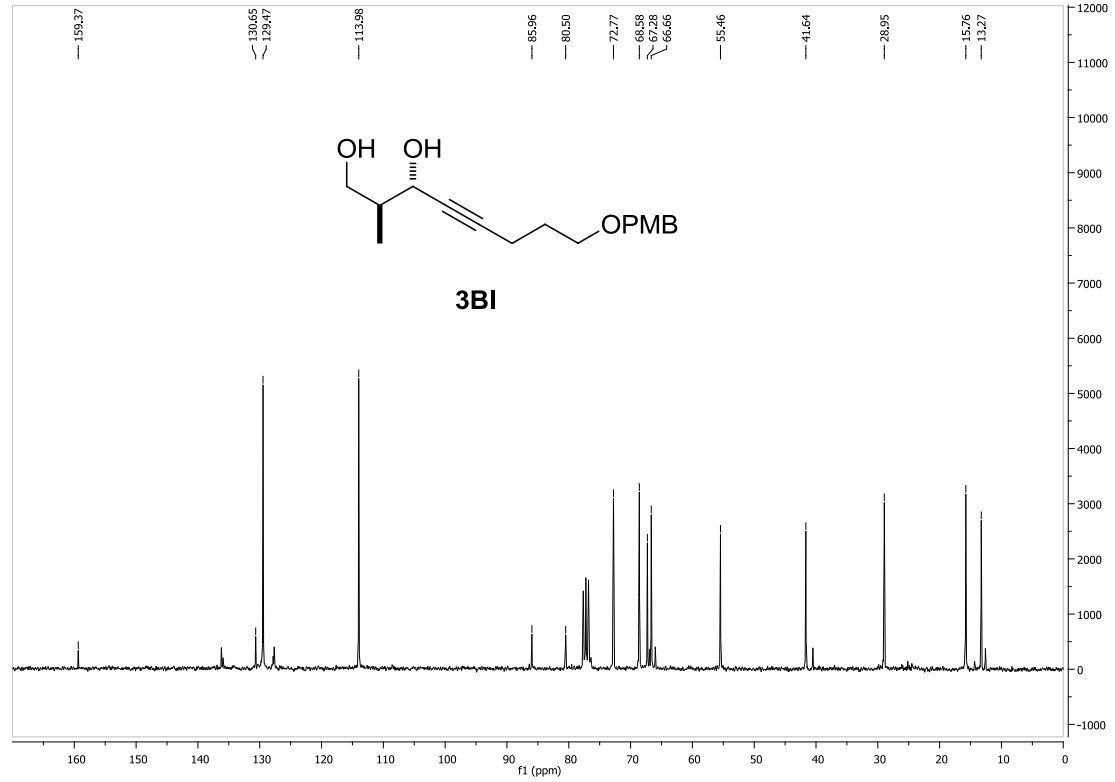
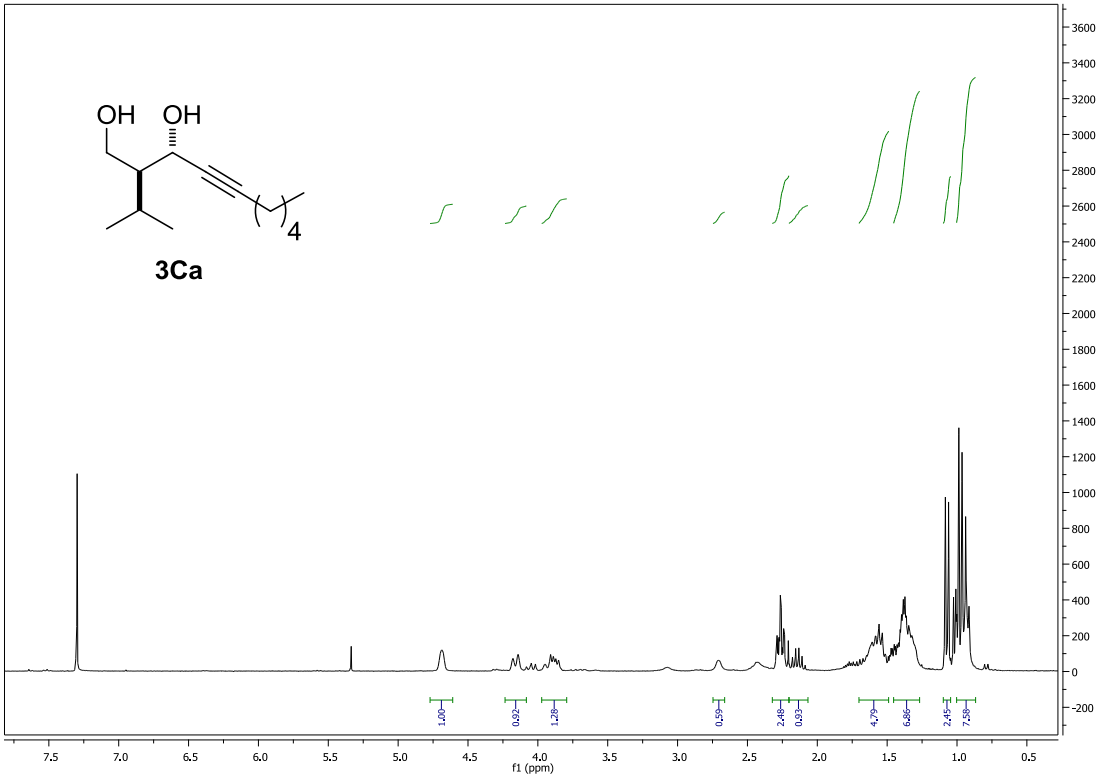
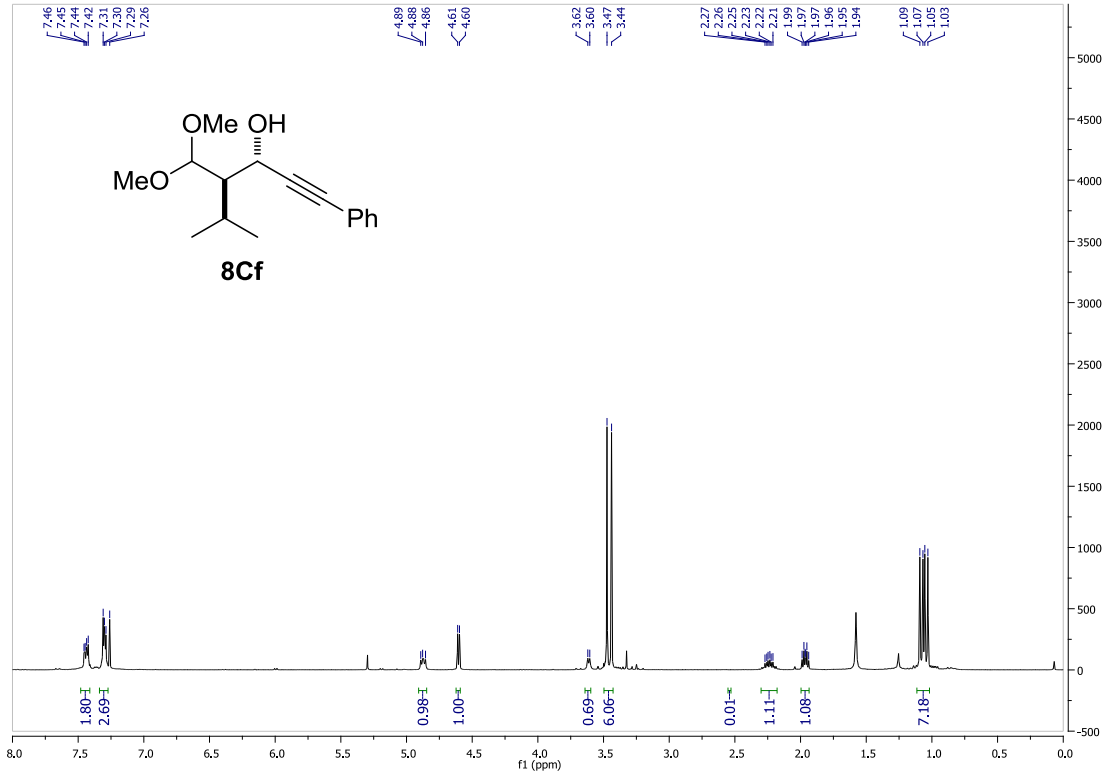
7.48
7.29
7.15
7.15
7.14
4.66
4.65
4.65
4.64
4.63
3.95
3.91
3.78
3.75
3.72
2.73
2.72
2.24
2.14
2.12
2.11
2.10
2.08
1.13
1.11
OH
OH
S
3Bk
0.67
1.15
0.79
0.89
1.17
1.28
0.83
0.99
1.19
3.00
f1 (ppm)

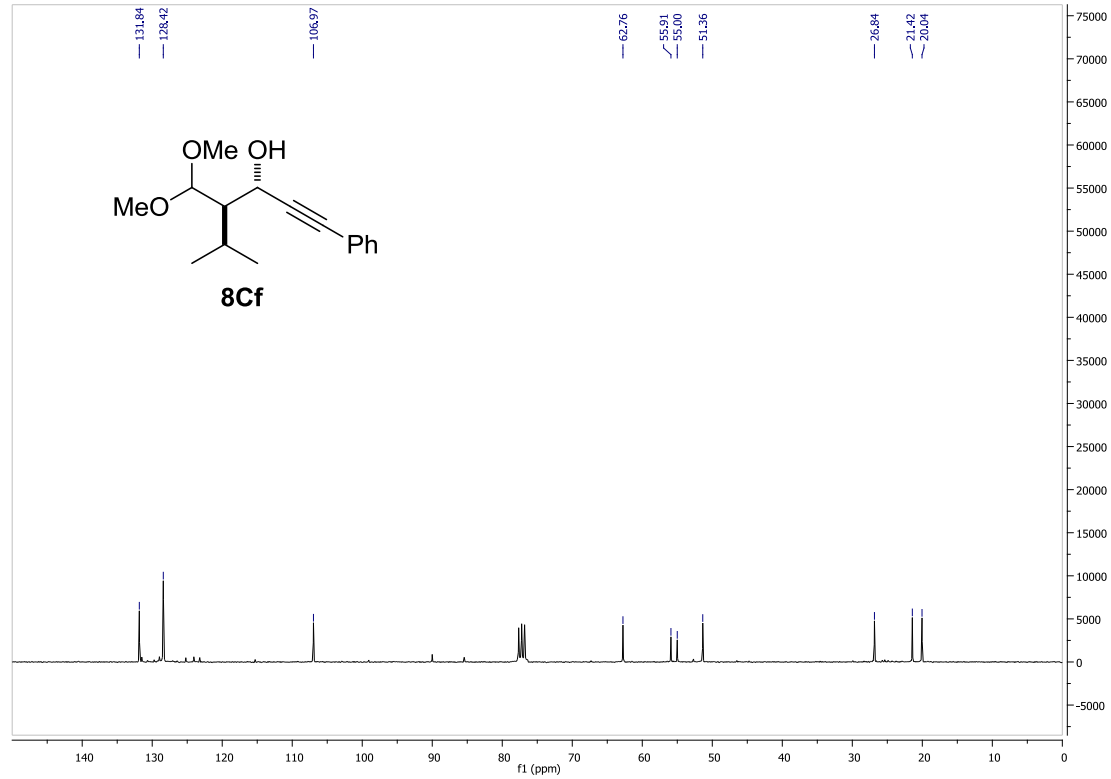

130.07
125.55
88.71
67.63
66.67
64.67
41.60
40.60
13.38
OH
OH
S
3Bk
f1 (ppm)

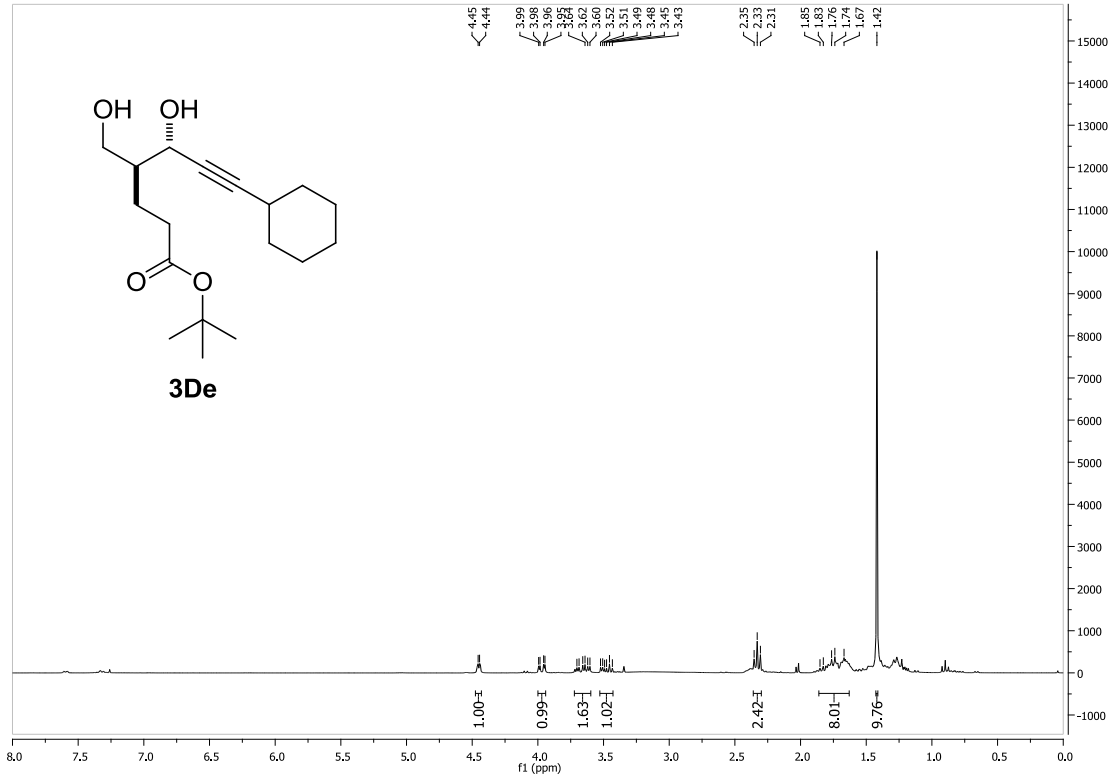

OH
OH
OPMB
3BI
f1 (ppm)

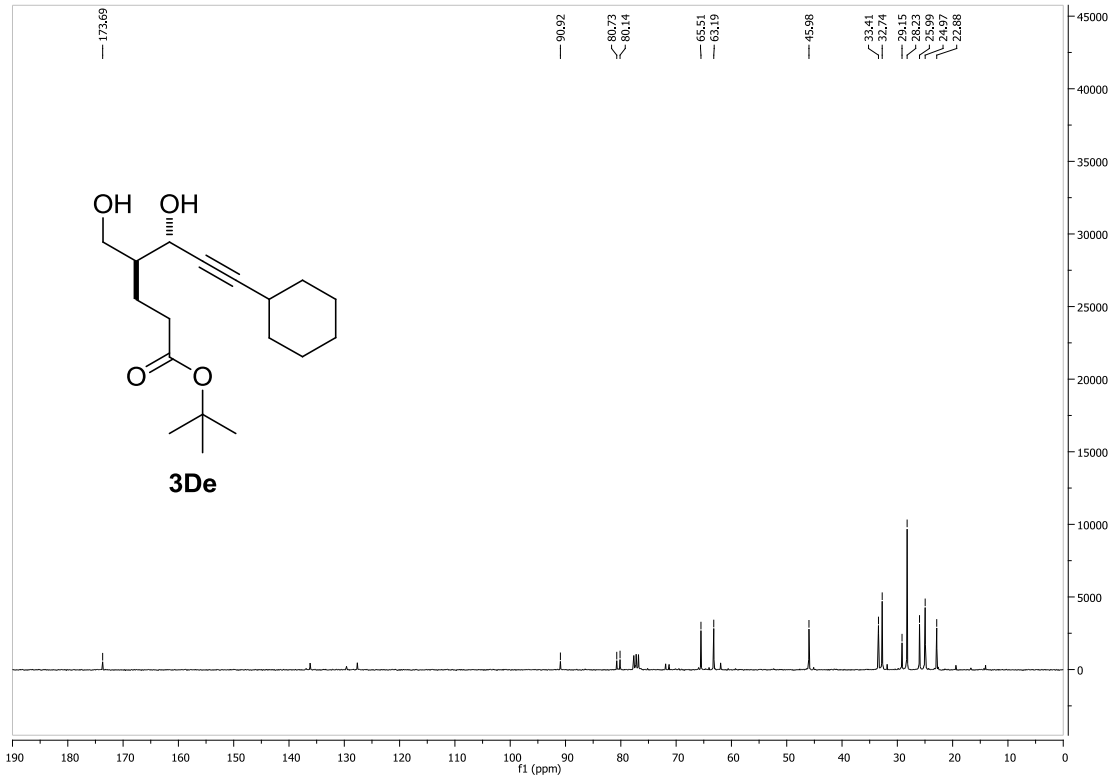

OH
OH
OPMB
3BI
f1 (ppm)

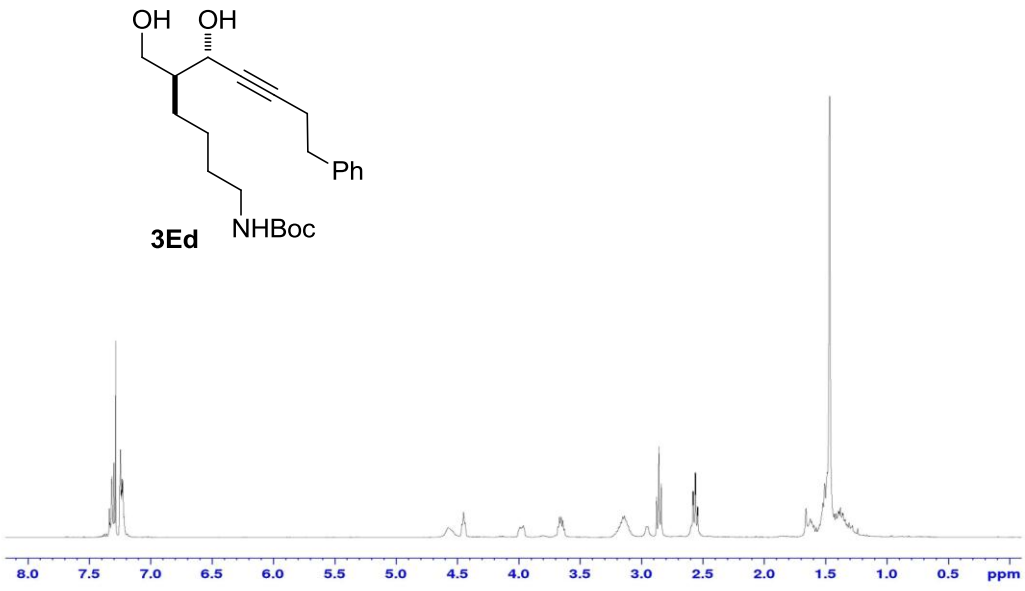


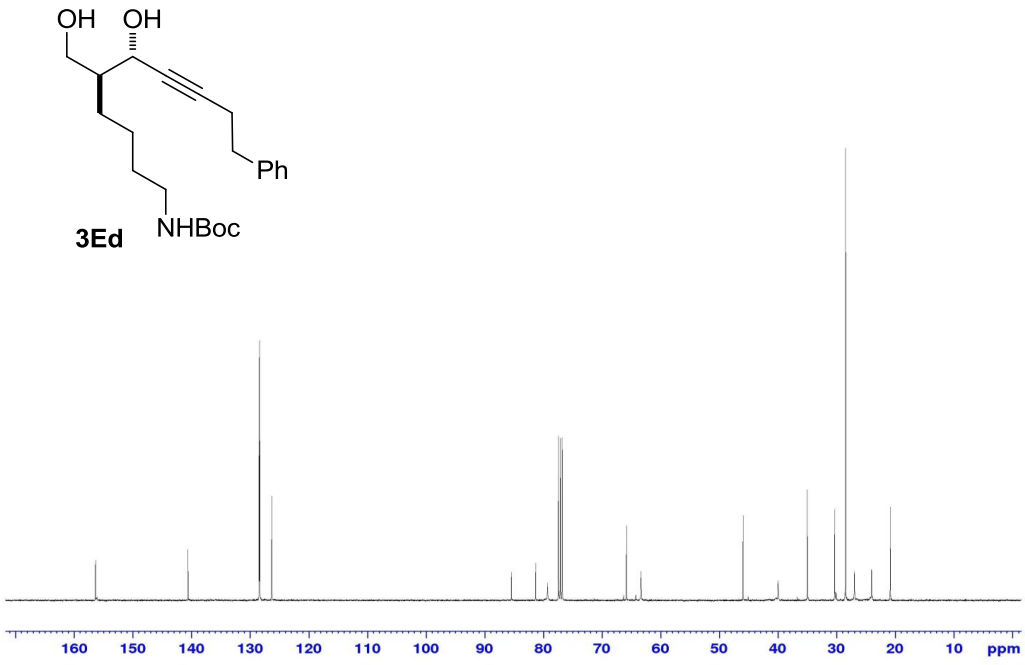

7.46
7.45
7.44
7.42
7.31
7.30
7.29
7.26
4.89
4.88
4.86
4.61
4.60
3.62
3.60
3.47
3.44
2.27
2.26
2.25
2.23
2.22
2.21
1.99
1.97
1.97
1.96
1.95
1.94
1.09
1.07
1.05
1.03
OMe OH
MeO
Ph
8Cf
1.80
2.69
0.98
1.00
0.69
6.06
0.01
1.11
1.08
7.18
f1 (ppm)

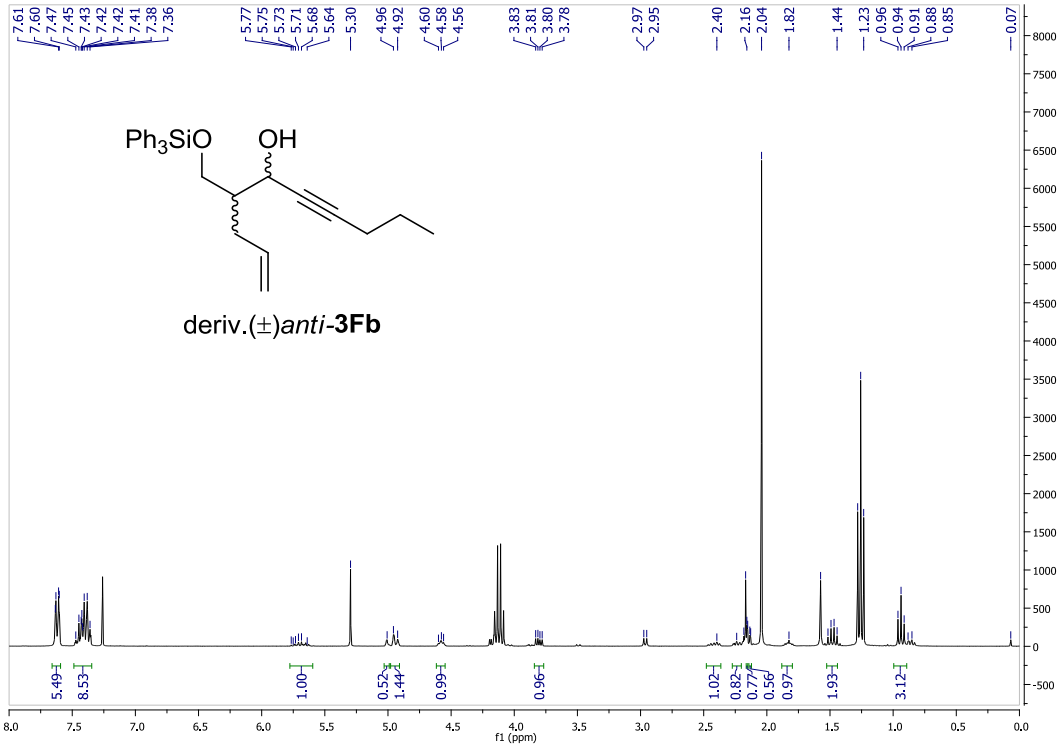

131.84
128.42
106.97
62.76
55.91
55.00
51.36
26.84
21.42
20.04
OMe OH
MeO
Ph
8Cf
f1 (ppm)

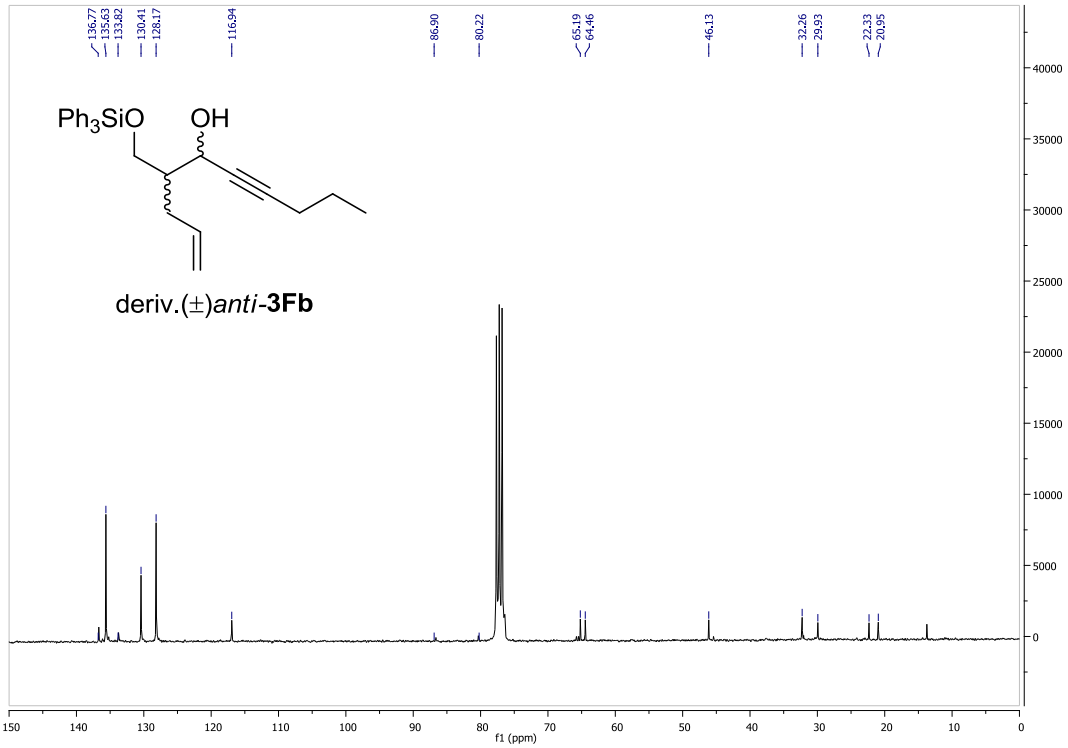

OH
OH
O
O
3De
4.45
4.44
3.99
3.98
3.96
3.62
3.60
3.52
3.51
3.49
3.48
3.45
3.43
2.35
2.33
2.31
1.85
1.83
1.76
1.74
1.67
1.42
1.00
0.99
1.63
1.02
2.42
8.01
9.76
f1 (ppm)

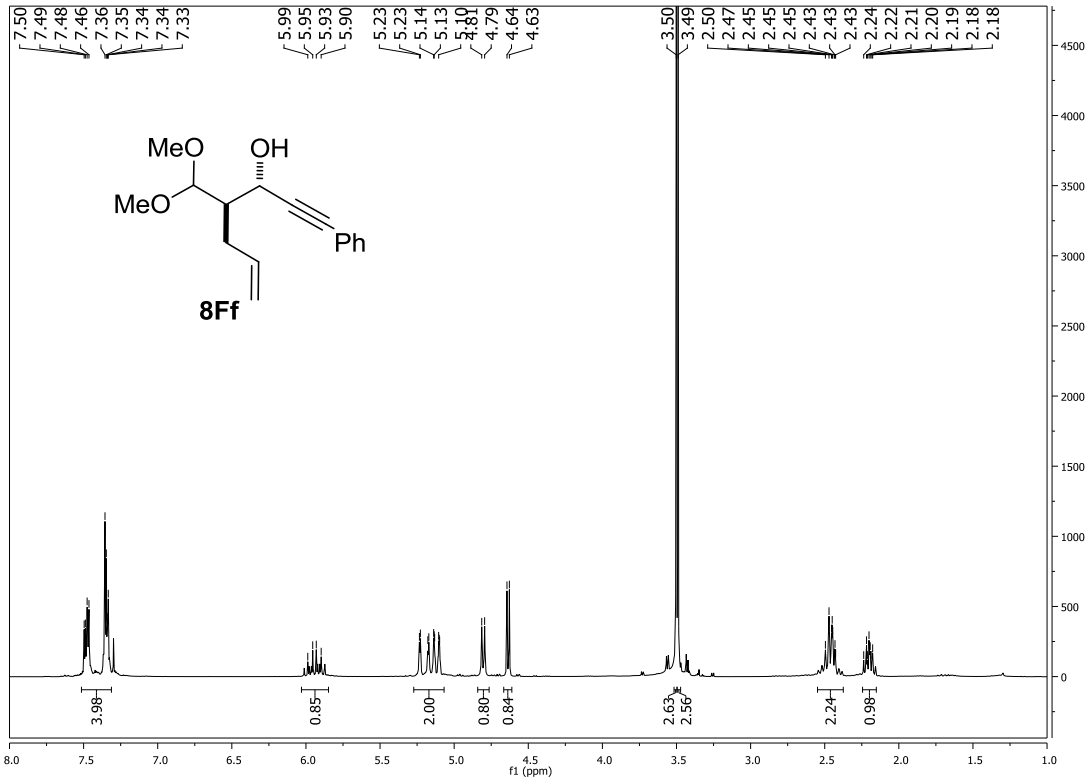

OH
OH
O
O
3De
173.69
90.92
80.73
80.14
65.51
63.19
45.98
33.41
32.74
29.15
28.23
25.99
24.97
22.88
f1 (ppm)







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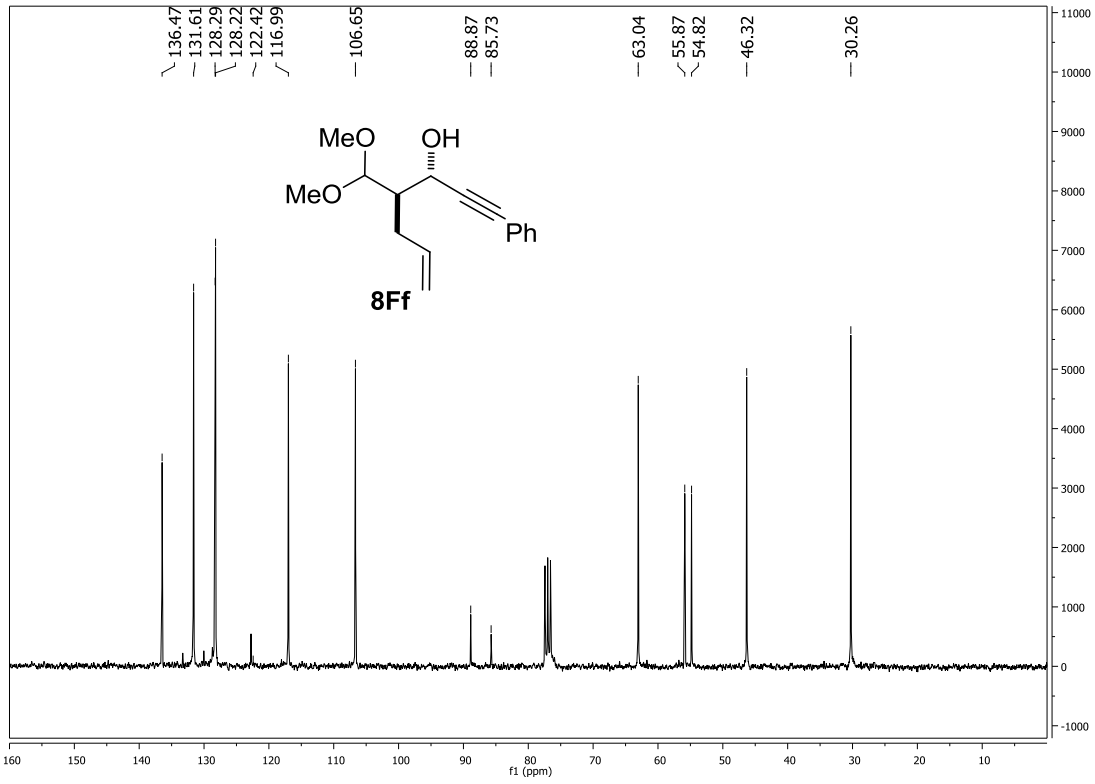
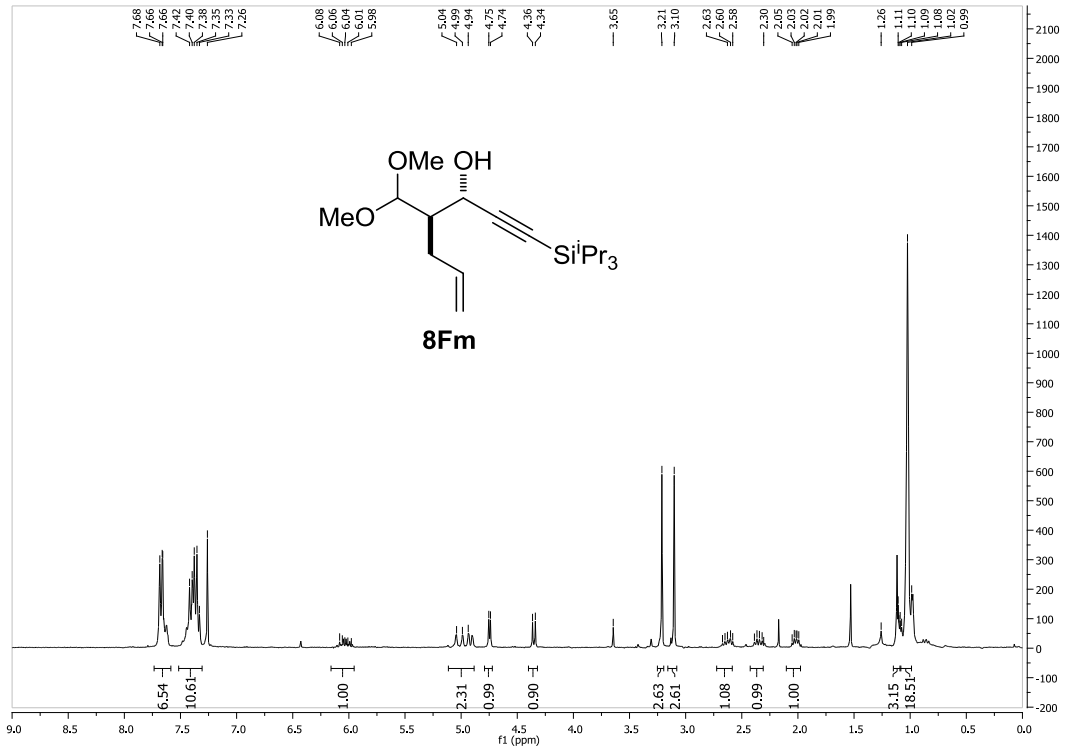
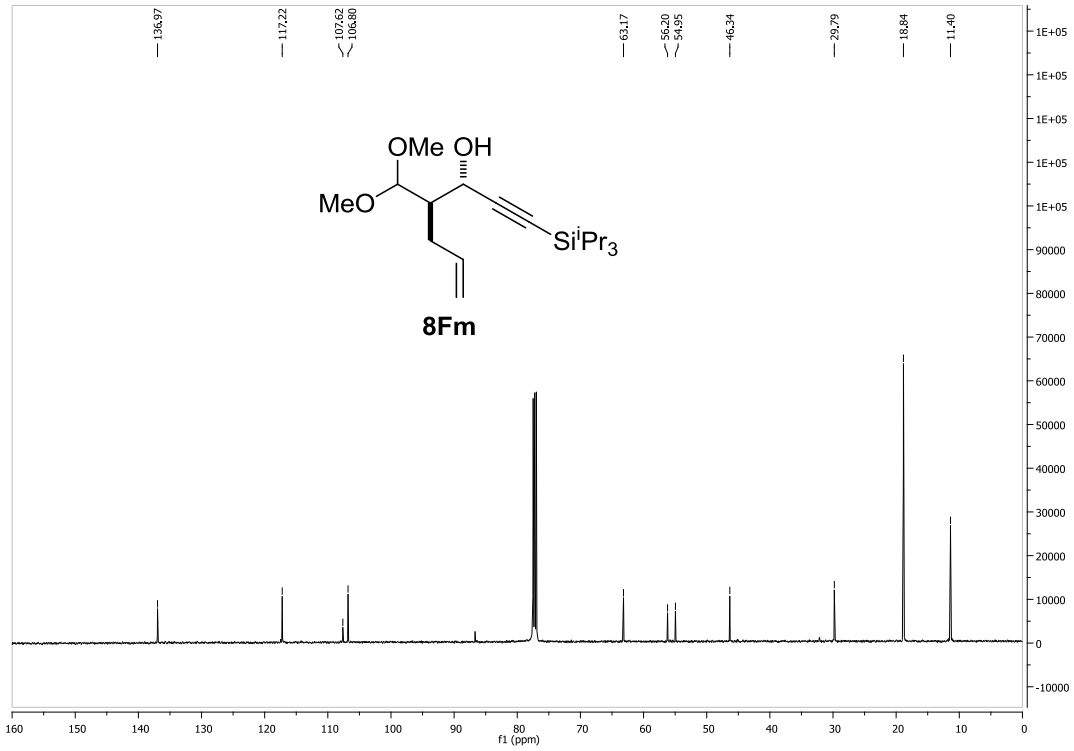
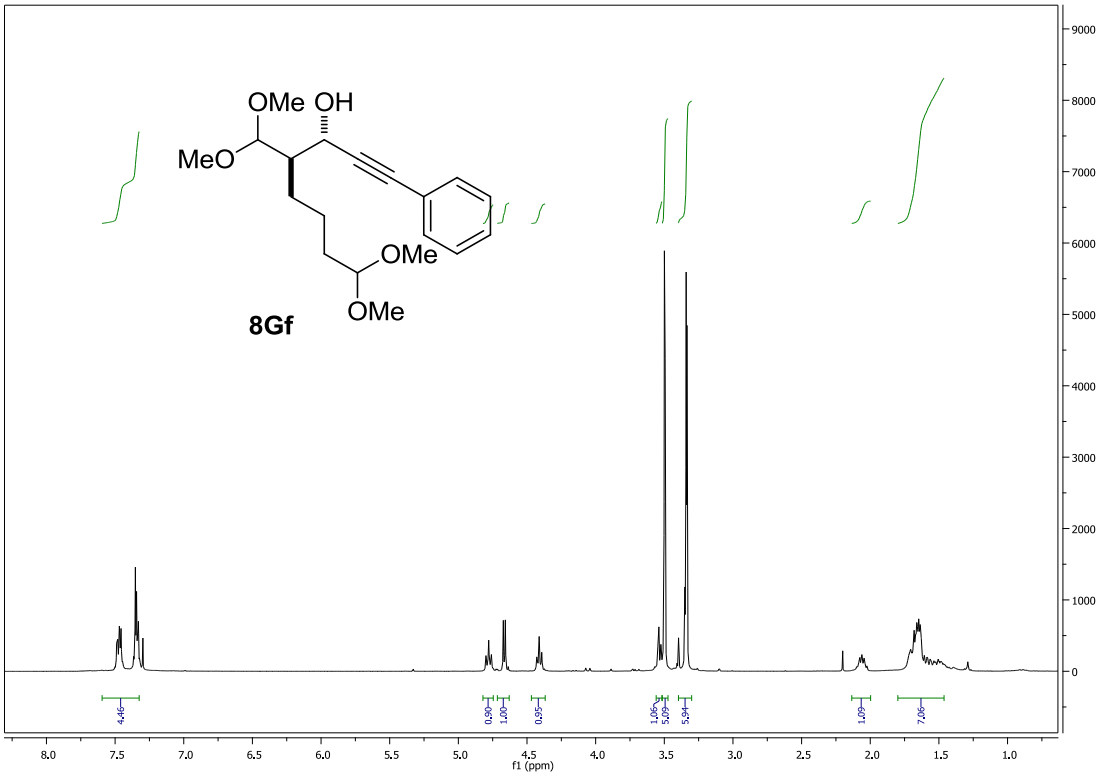
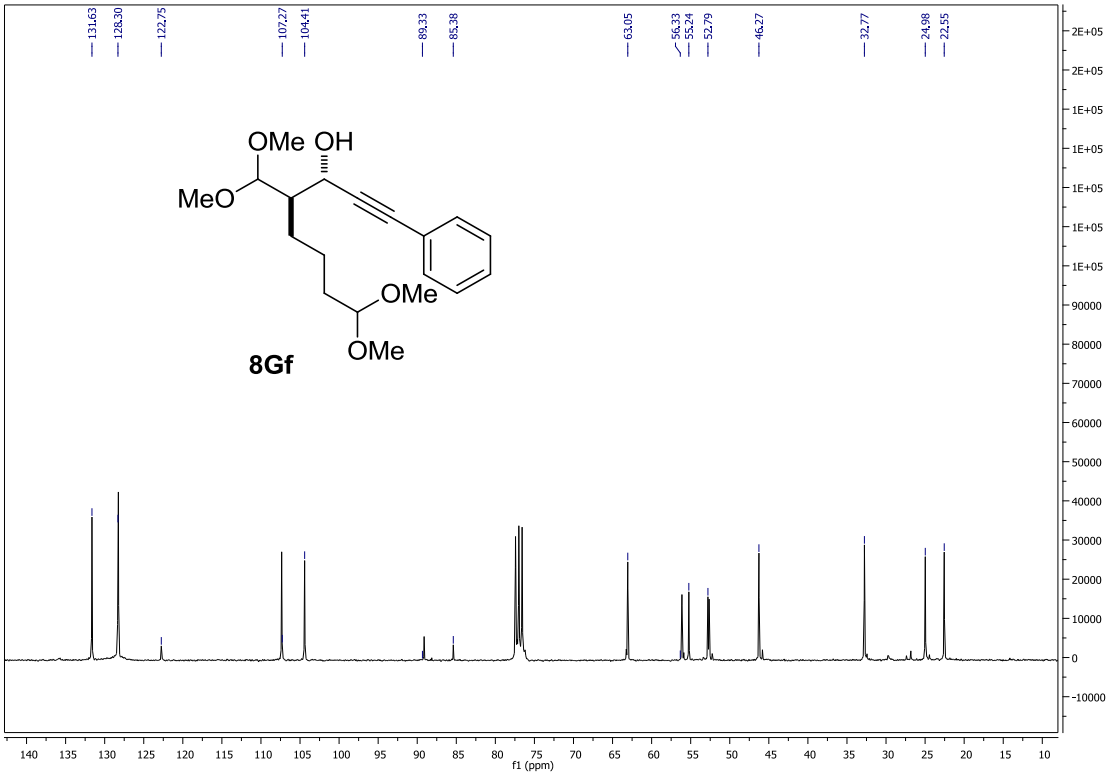
7.49
7.48
7.46
7.36
7.35
7.34
7.34
7.33
5.99
5.95
5.93
5.90
5.23
5.23
5.14
5.13
4.81
4.79
4.64
4.63
3.50
3.49
2.50
2.47
2.45
2.45
2.45
2.43
2.43
2.43
2.24
2.22
2.21
2.20
2.19
2.18
2.18
MeO
OH
MeO
Ph
8Ff
3.98
0.85
2.00
0.80
0.84
2.63
2.56
2.24
0.98
f1 (ppm)

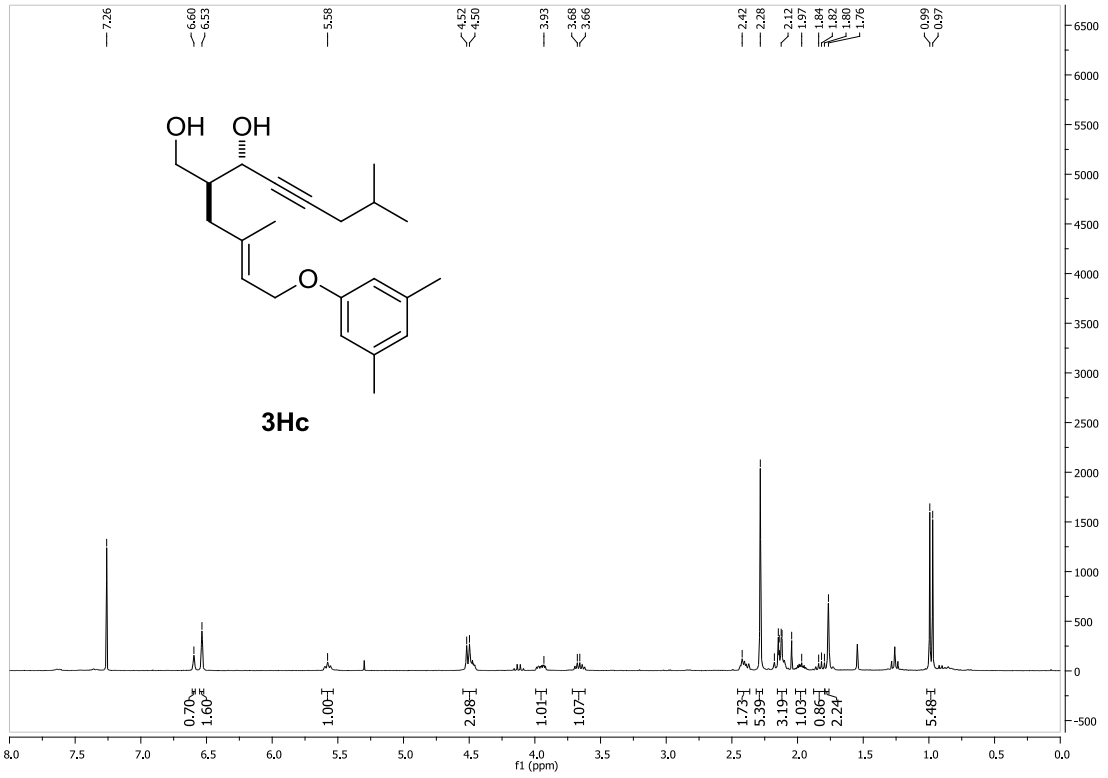

136.47
131.61
128.29
128.22
122.42
116.99
106.65
88.87
85.73
63.04
55.87
54.82
46.32
30.26
MeO
OH
MeO
Ph
8Ff
f1 (ppm)

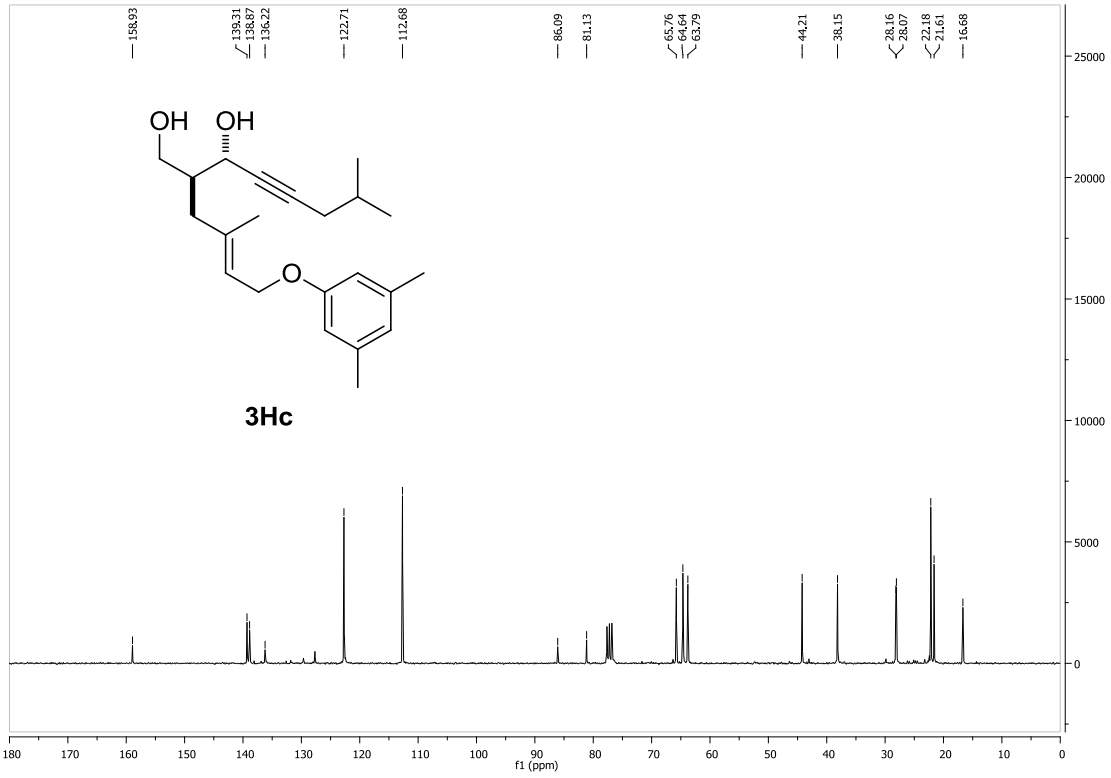

OMe OH
MeO
SiiPr3
8Fm
f1 (ppm)


OMe OH
MeO
SiiPr3
8Fm
f1 (ppm)


OMe OH
MeO
OMe
OMe
8Gf
f1 (ppm)


131.63
128.30
122.75
107.27
104.41
89.33
85.38
63.05
56.33
55.24
52.79
46.27
32.77
24.98
22.55
OMe OH
MeO
OMe
OMe
8Gf
f1 (ppm)


7.26
6.60
6.53
5.58
4.52
4.50
3.93
3.68
3.66
2.42
2.28
2.12
1.97
1.84
1.82
1.80
1.76
0.99
0.97
OH
OH
O
3Hc
0.70
1.60
1.00
2.98
1.01
1.07
1.73
5.39
3.19
1.03
0.86
2.24
5.48
f1 (ppm)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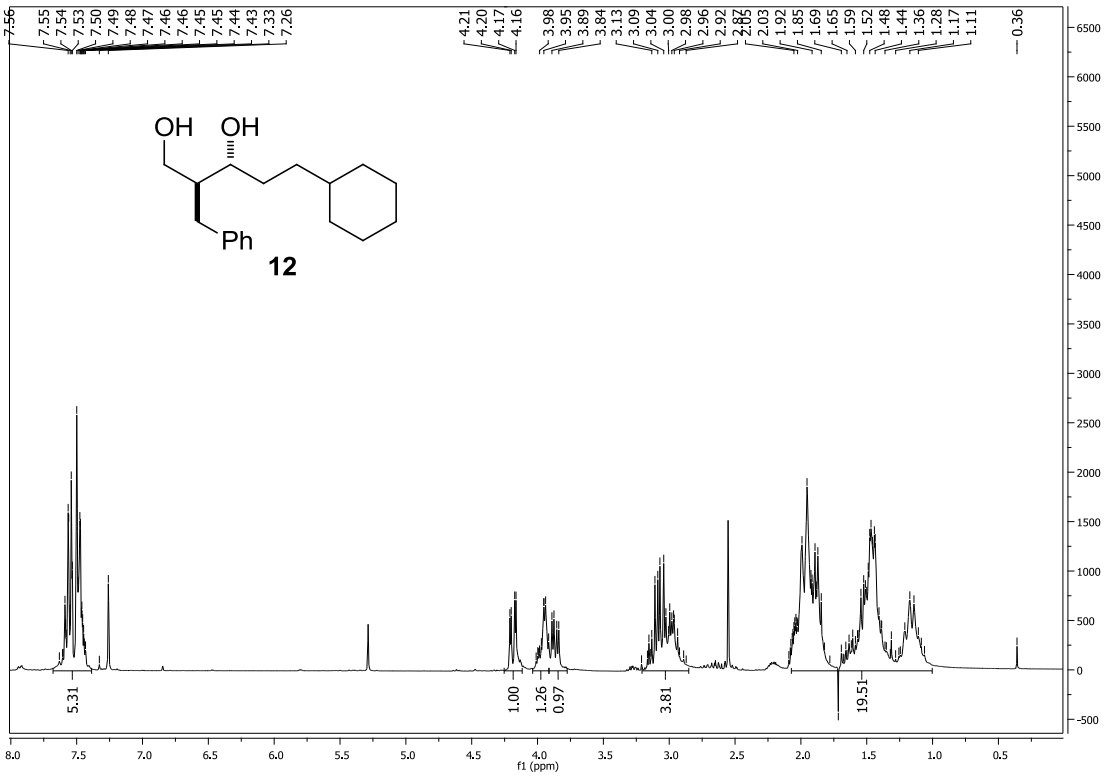
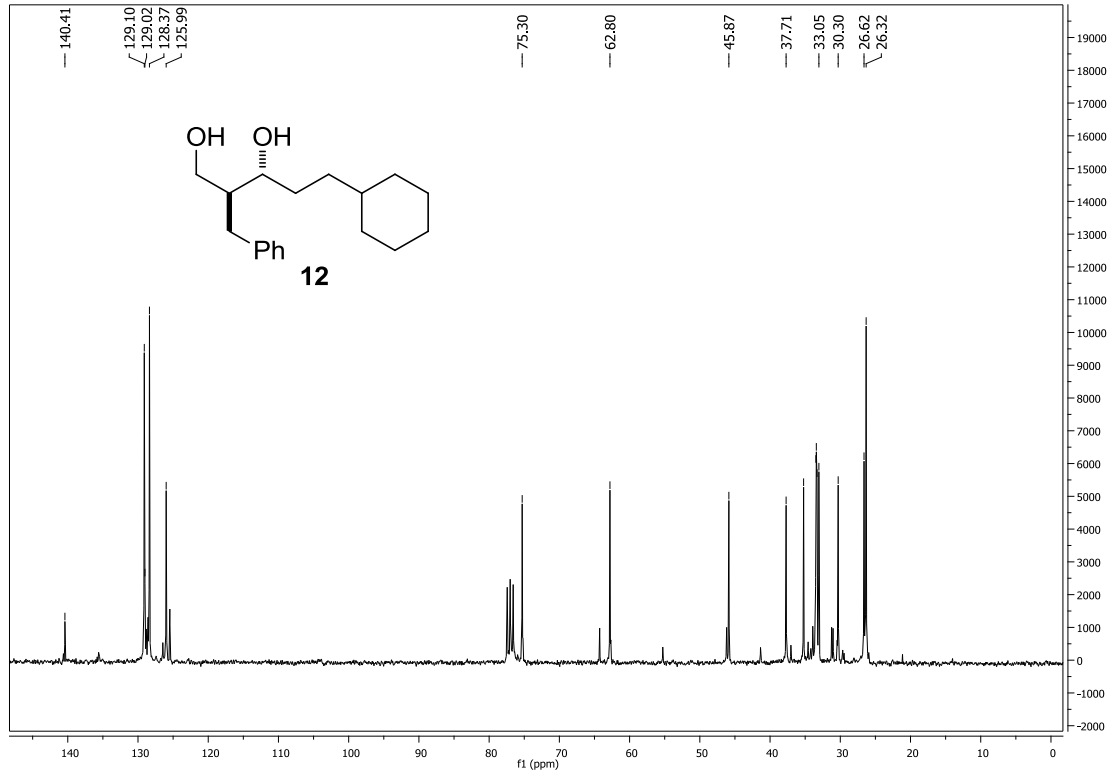
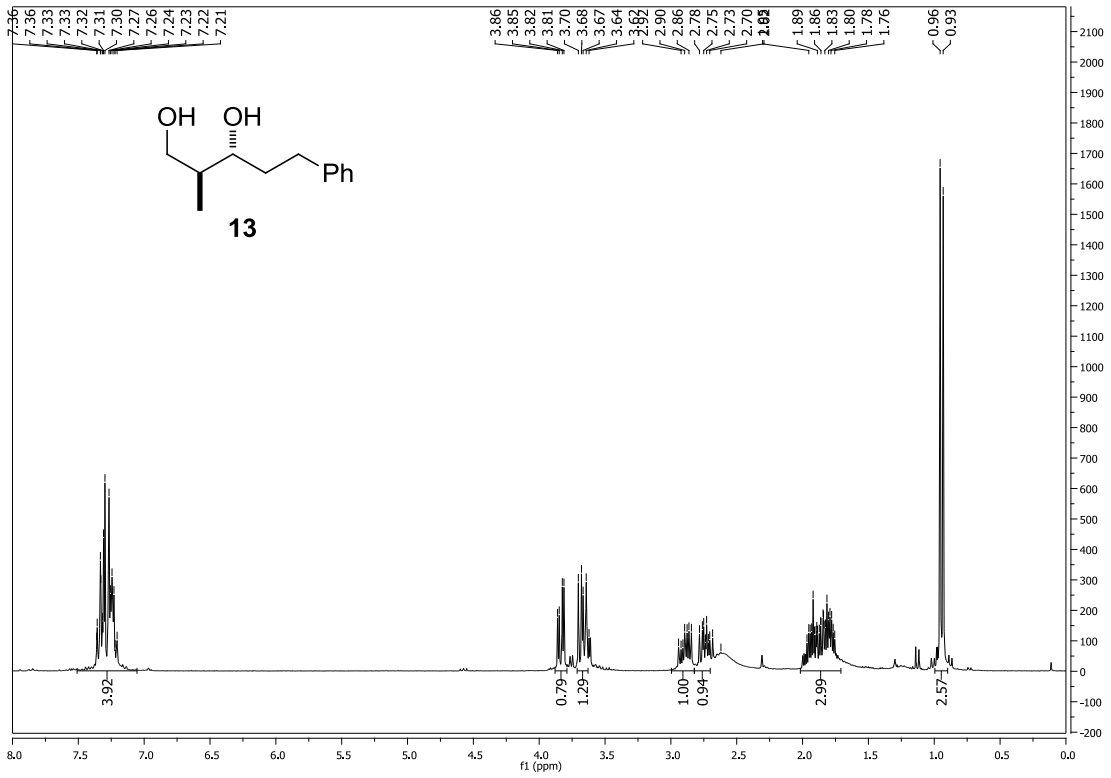
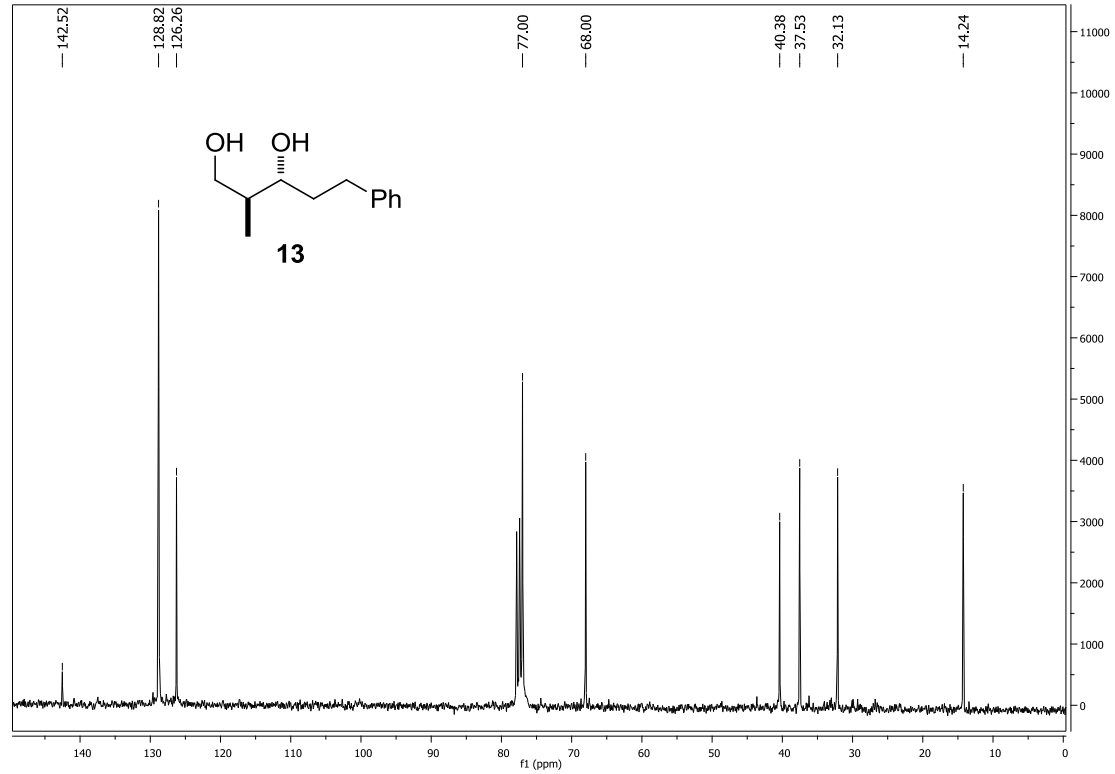
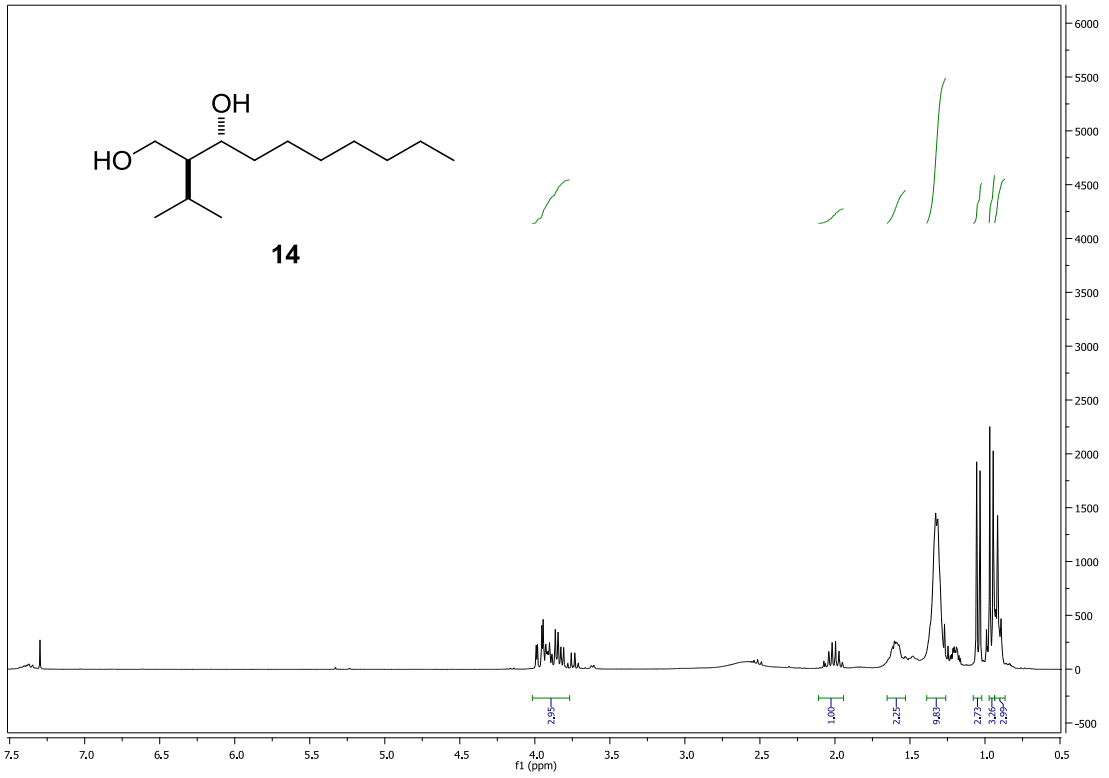
139.31
138.87
136.22
122.71
112.68
86.09
81.13
65.76
64.64
63.79
44.21
38.15
28.16
28.07
22.18
21.61
16.68
OH
OH
O
3Hc
f1 (ppm)

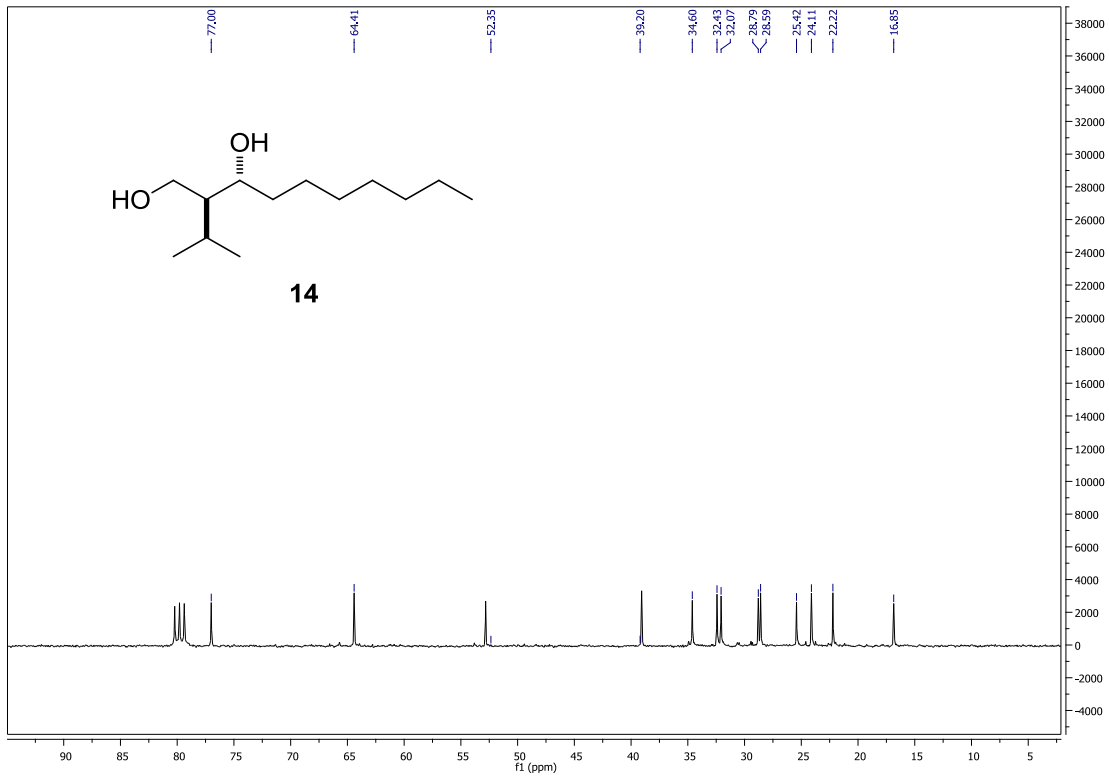

OH
OH
Ph
12
f1 (ppm)

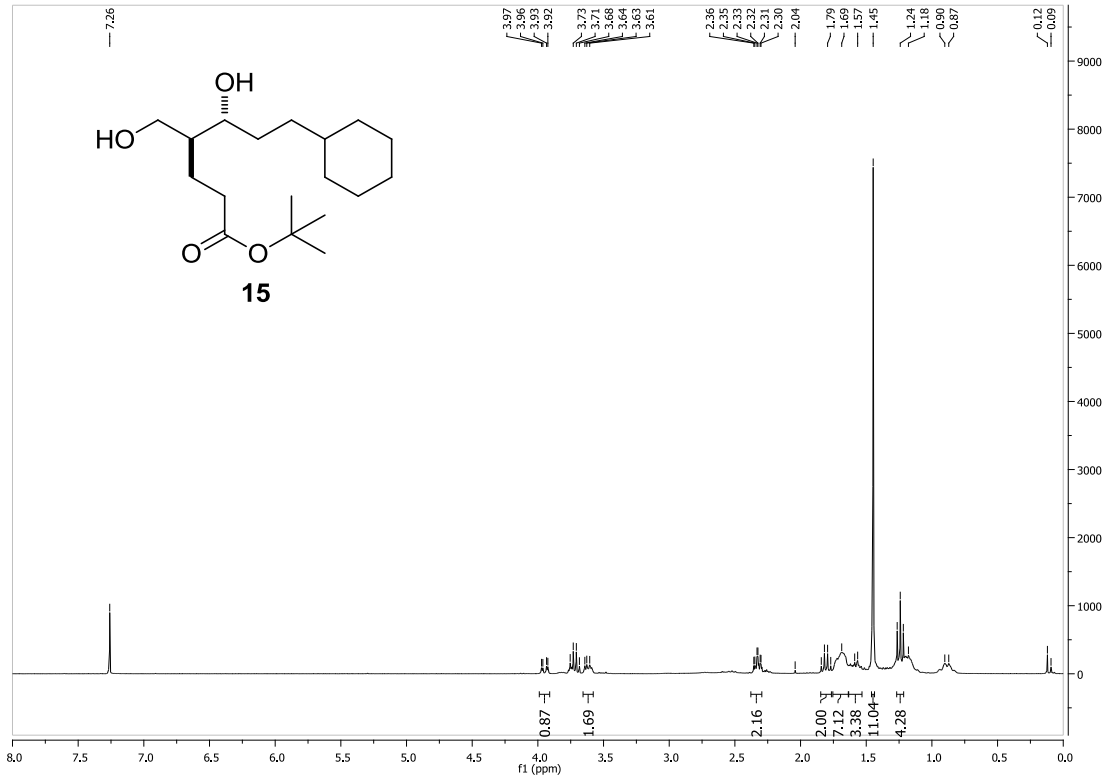

OH
OH
Ph
12
f1 (ppm)







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3.68
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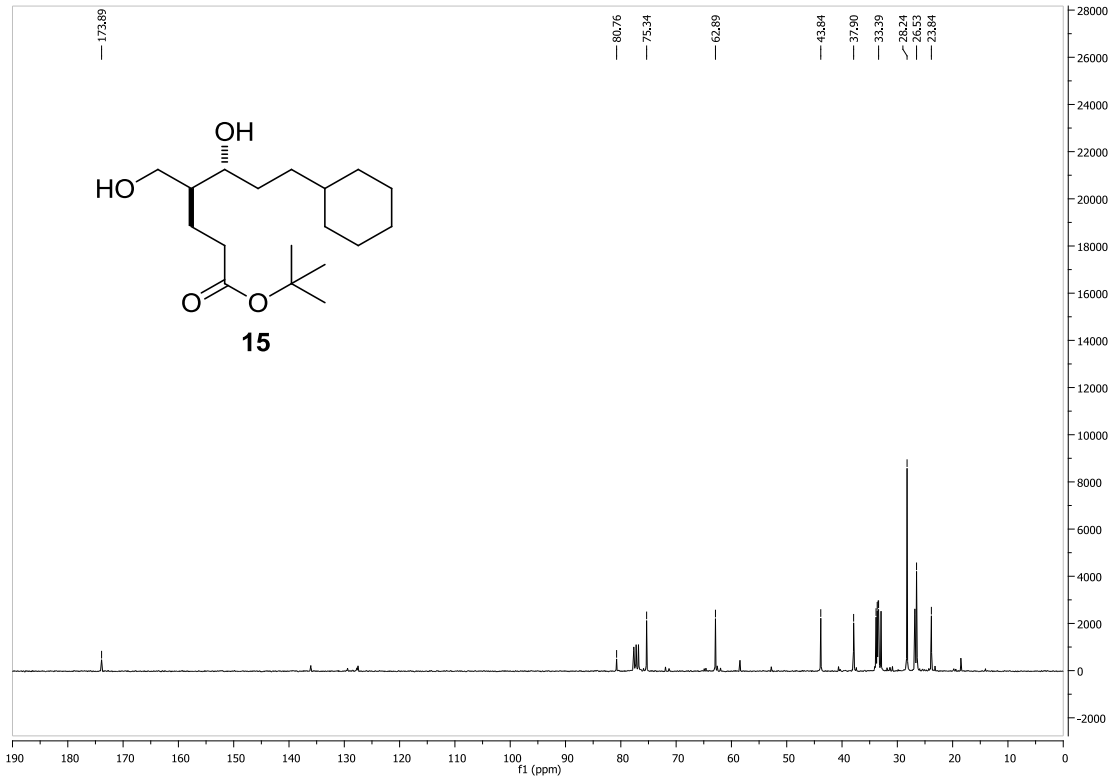
3.63
3.61
2.36
2.35
2.33
2.32
2.31
2.30
2.04
1.79
1.69
1.57
1.45
1.24
1.18
0.90
0.87
0.12
0.09
OH
HO
O
O
15
0.87
1.69
2.16
2.00
7.12
3.38
11.04
4.28
f1 (ppm)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80.76
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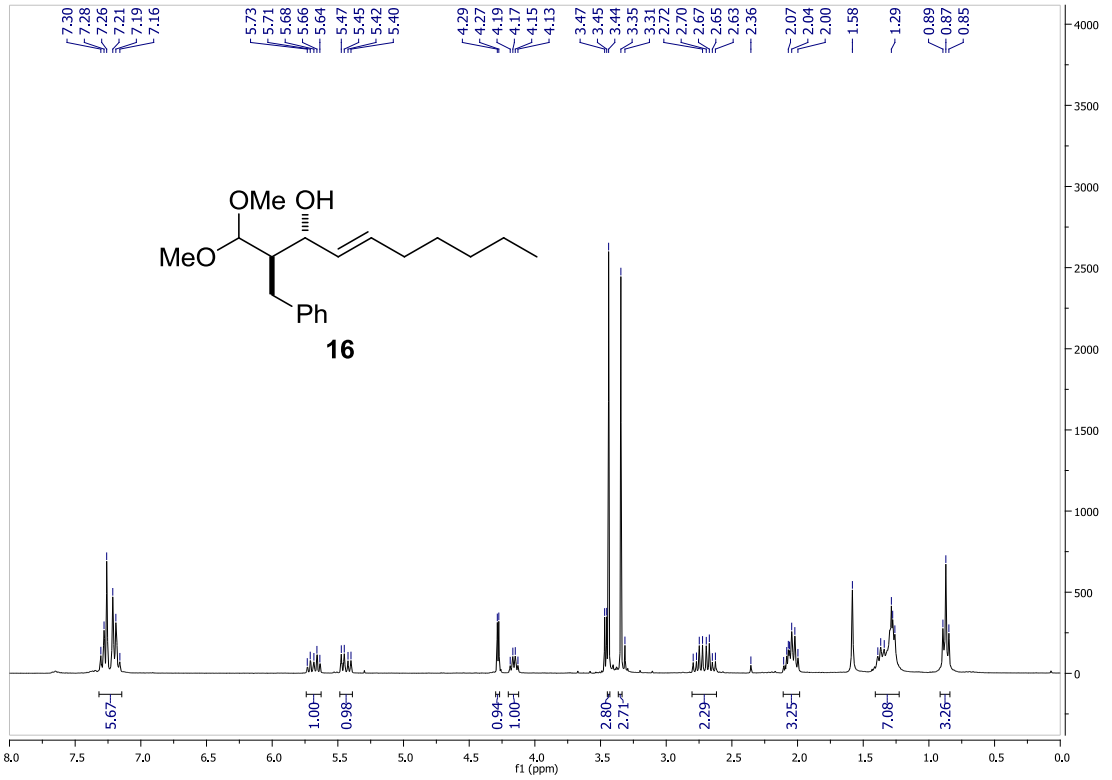
37.90
33.39
28.24
26.53
23.84
OH
HO
O
O
15
f1 (ppm)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7.16
5.73
5.71
5.68
5.66
5.64
5.47
5.45
5.42
5.40
4.29
4.27
4.19
4.17
4.15
4.13
3.47
3.45
3.44
3.35
3.31
2.72
2.70
2.67
2.65
2.63
2.36
2.07
2.04
2.00
1.58
1.29
0.89
0.87
0.85
OMe OH
MeO
Ph
16
5.67
1.00
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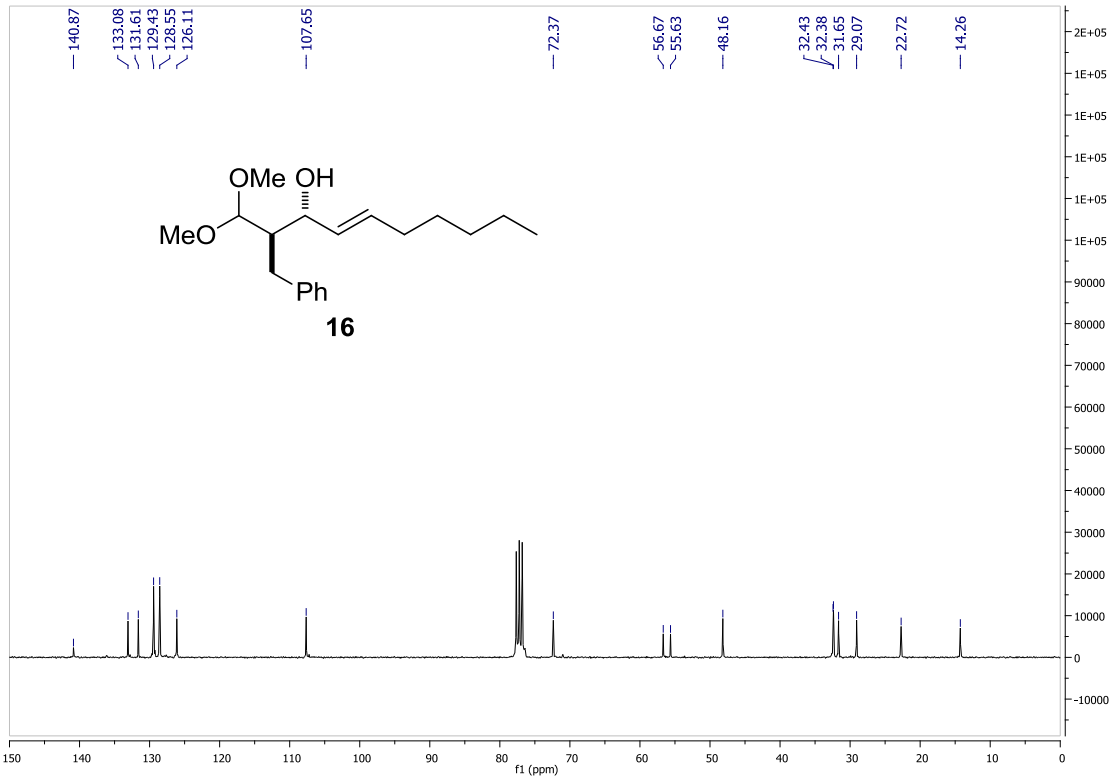
0.94
1.00
2.80
2.71
2.29
3.25
7.08
3.26
f1 (ppm)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128.55
126.11
107.65
72.37
56.67
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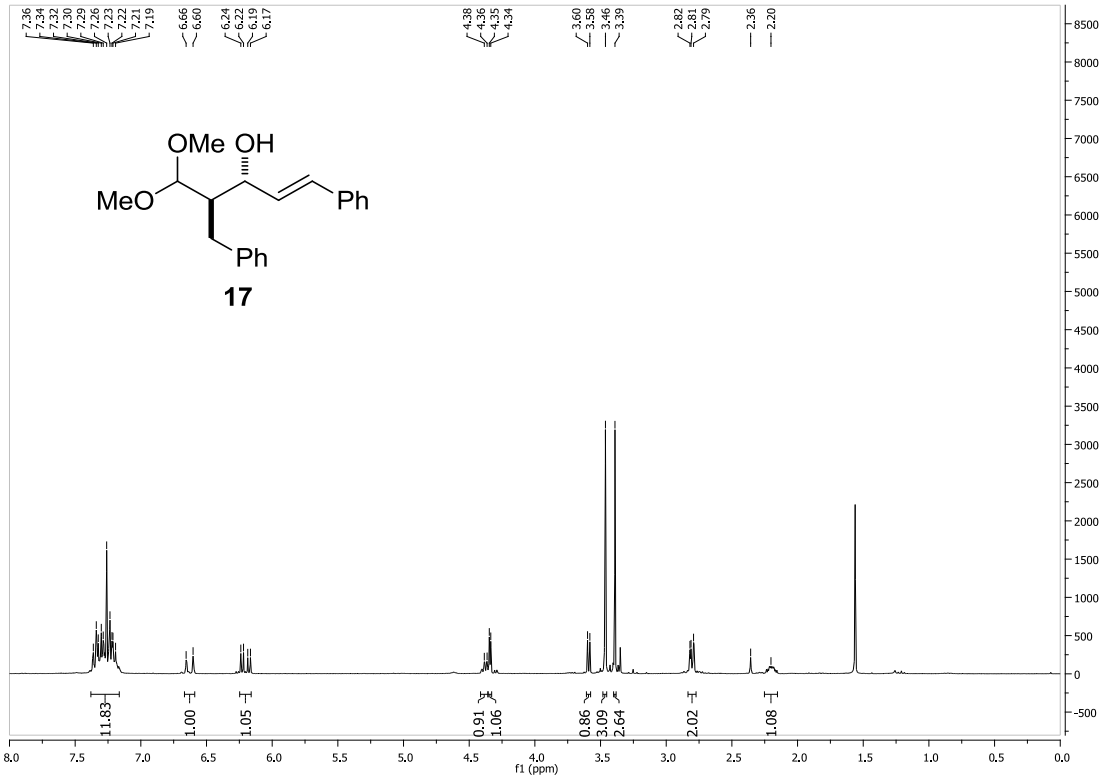
48.16
32.43
32.38
31.65
29.07
22.72
14.26
OMe OH
MeO
Ph
16
f1 (ppm)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7.26
7.23
7.22
7.21
7.19
6.66
6.60
6.24
6.22
6.19
6.17
4.38
4.36
4.35
4.34
3.60
3.58
3.46
3.39
2.82
2.81
2.79
2.36
2.20
OMe OH
MeO
Ph
Ph
17
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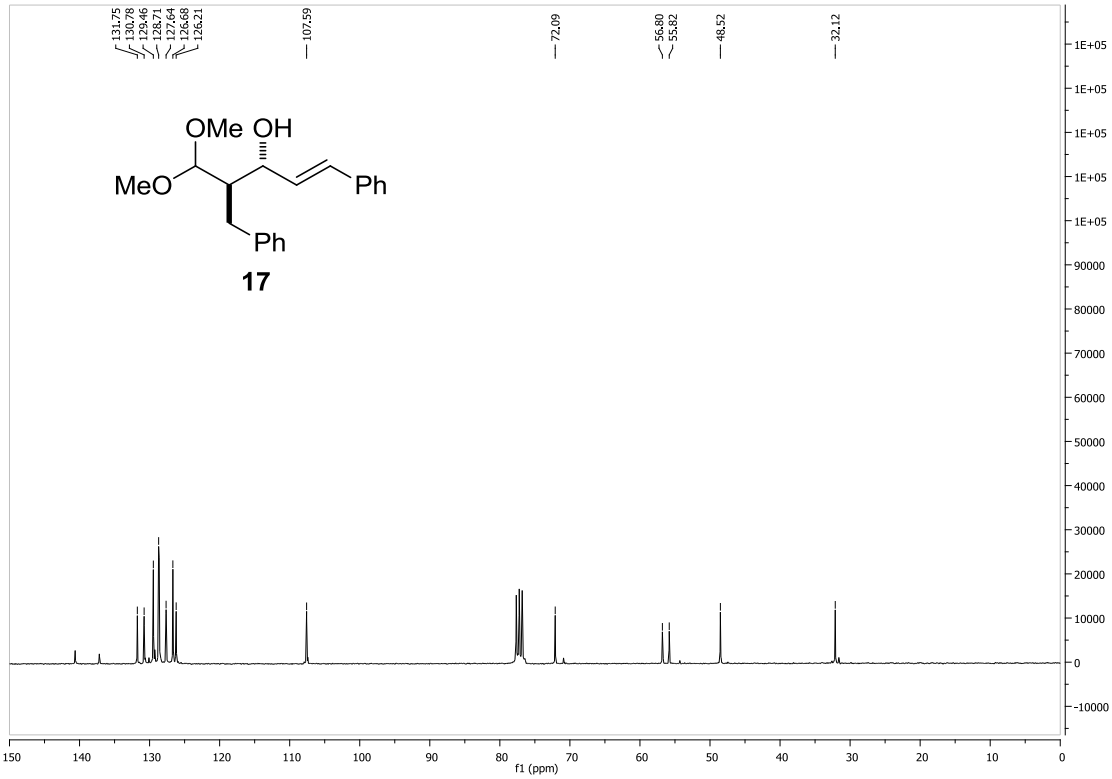
1.05
0.91
1.06
0.86
3.09
2.64
2.02
1.08
f1 (ppm)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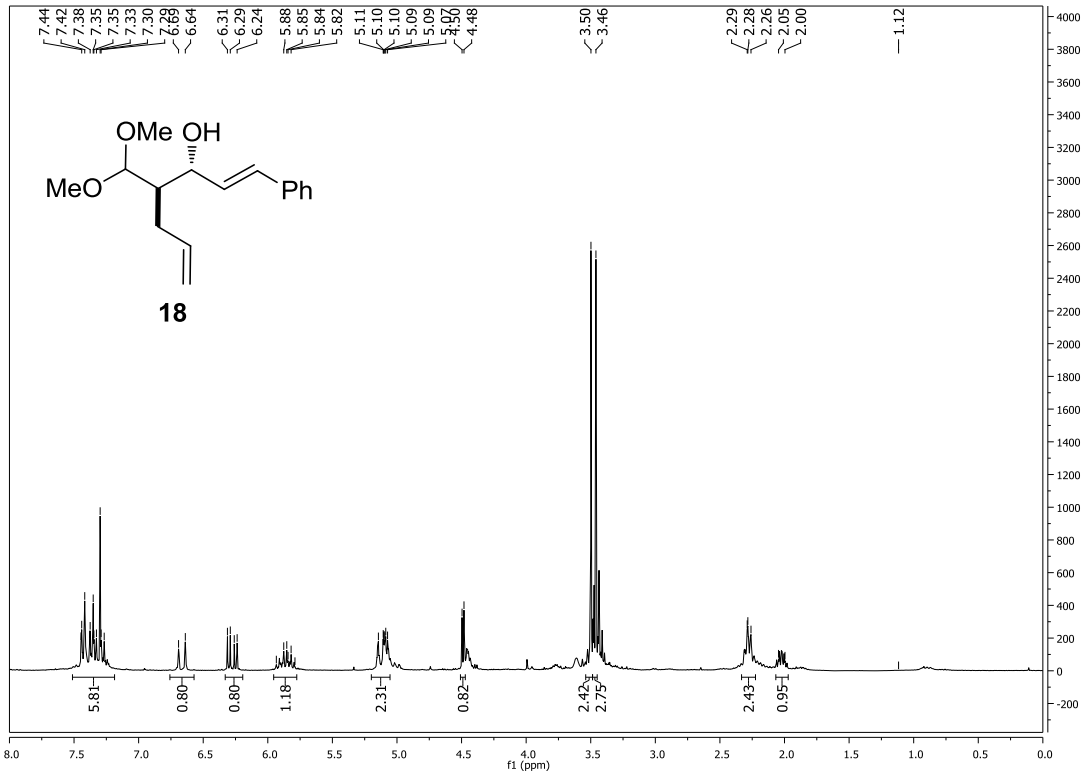
129.46
128.71
127.64
126.68
126.21
107.59
72.09
56.80
55.82
48.52
32.12
OMe OH
MeO
Ph
Ph
17
f1 (ppm)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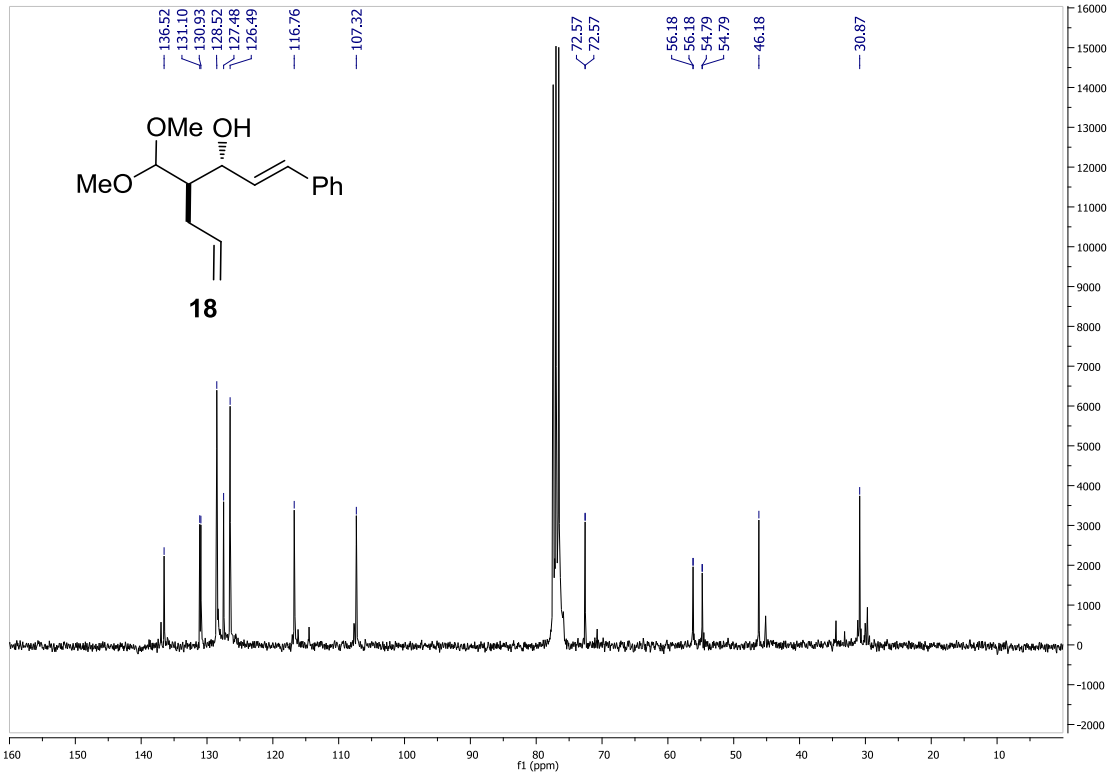
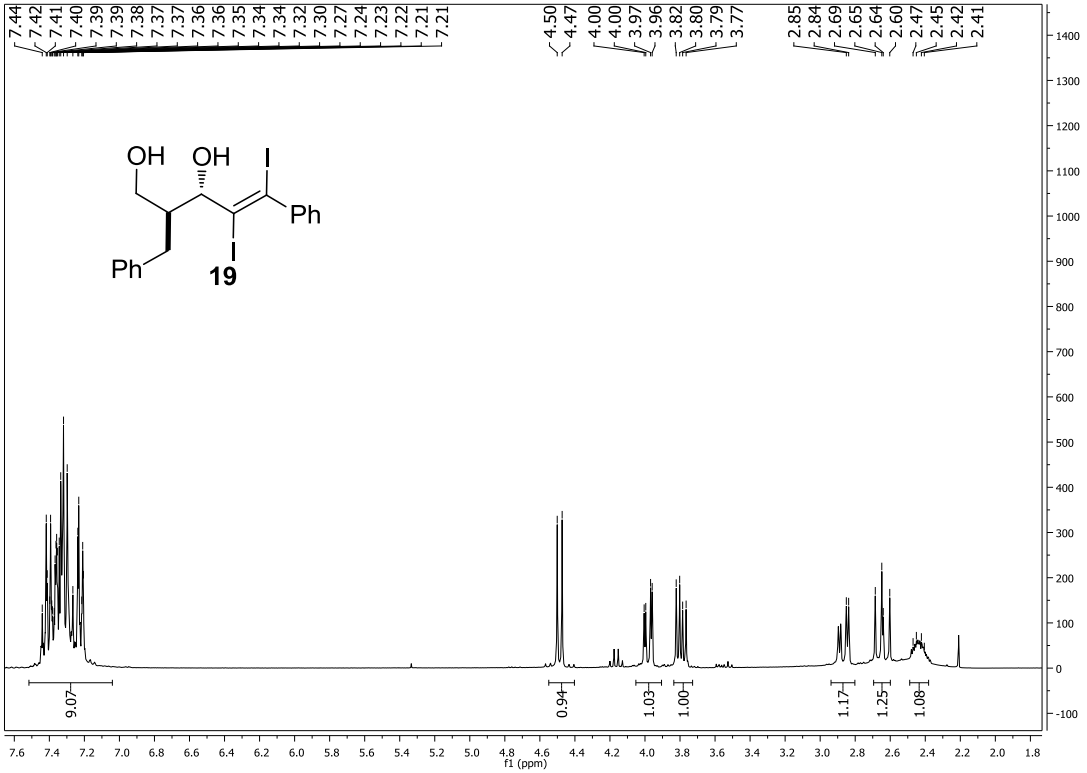
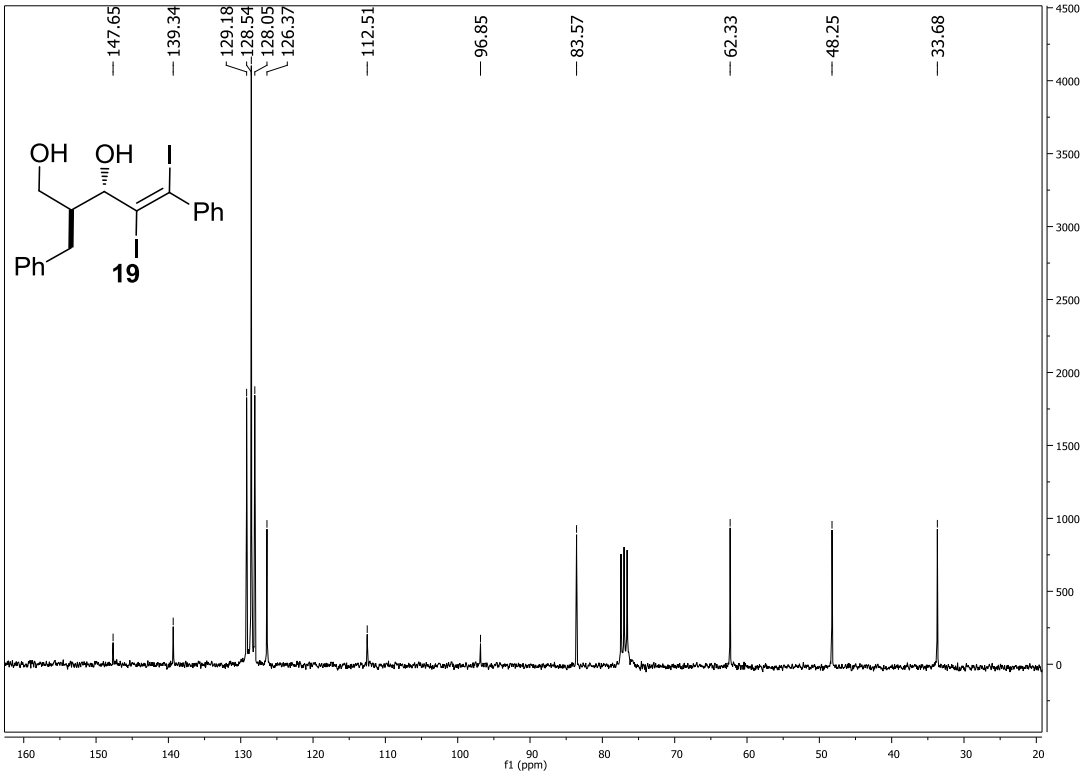
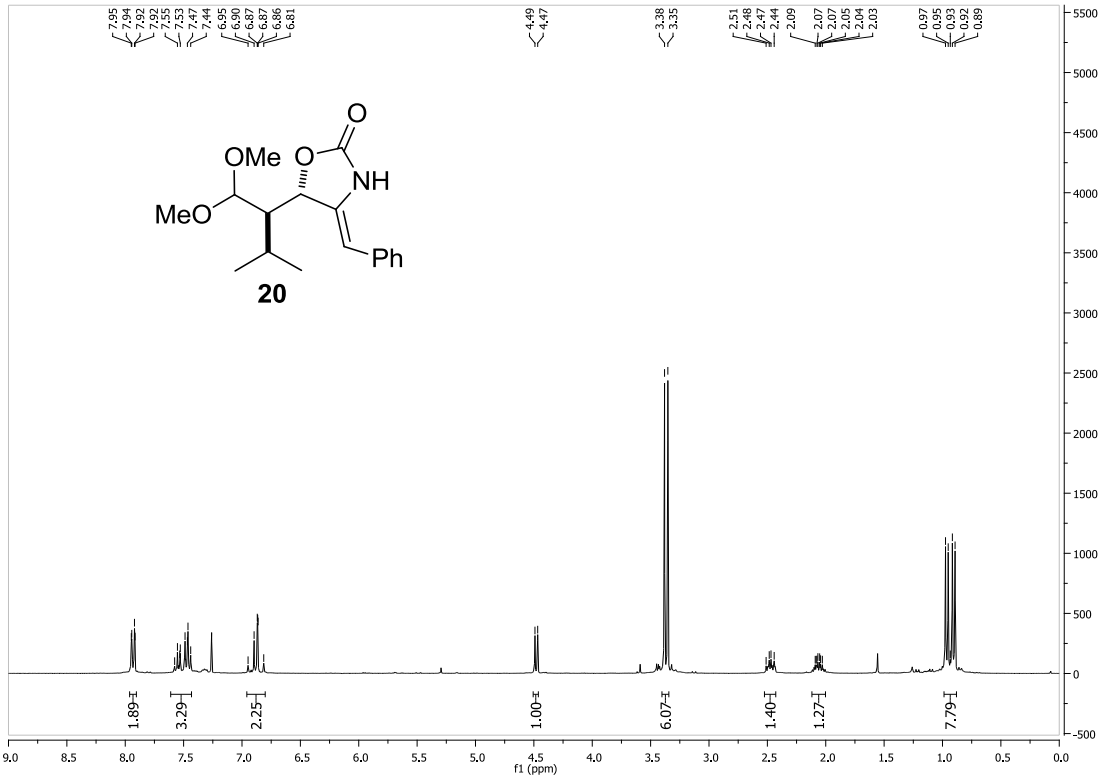
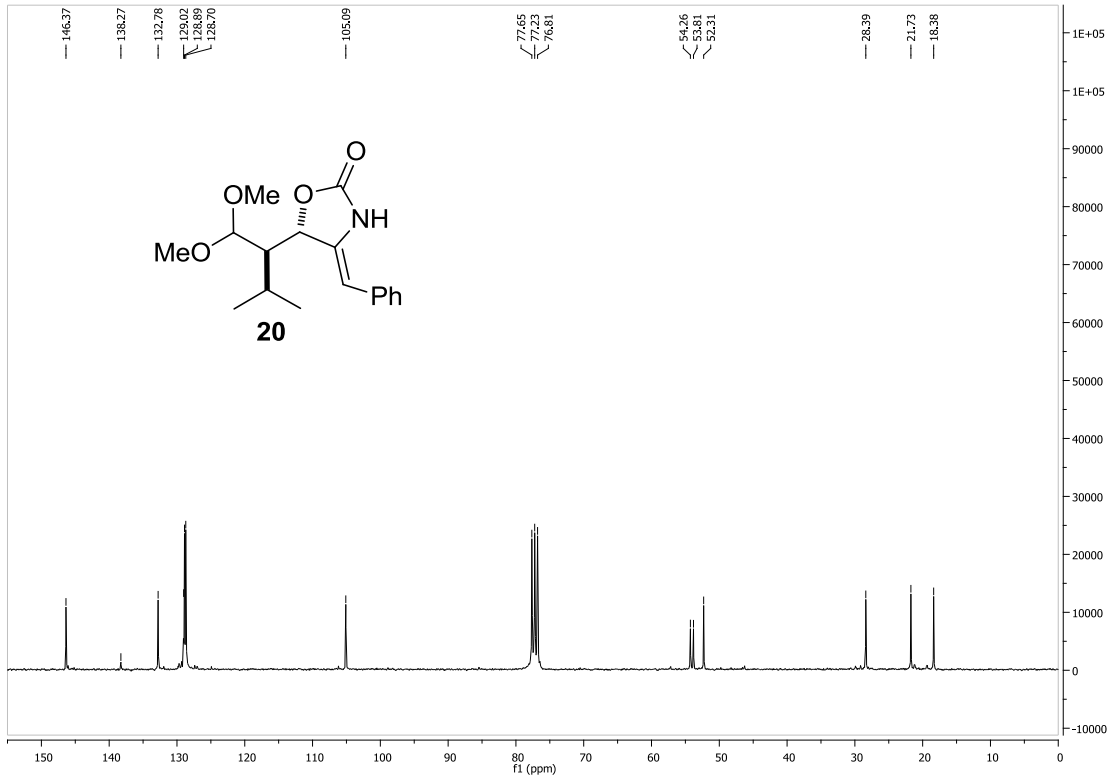
7.42
7.38
7.35
7.35
7.33
7.30
7.29
6.69
6.64
6.31
6.29
6.24
5.88
5.85
5.84
5.82
5.11
5.10
5.09
5.09
5.07
4.48
3.50
3.46
2.29
2.28
2.26
2.05
2.00
1.12
OMe OH
MeO
Ph
18
5.81
0.80
0.80
1.18
2.31
0.82
2.42
2.75
2.43
0.95
f1 (ppm)

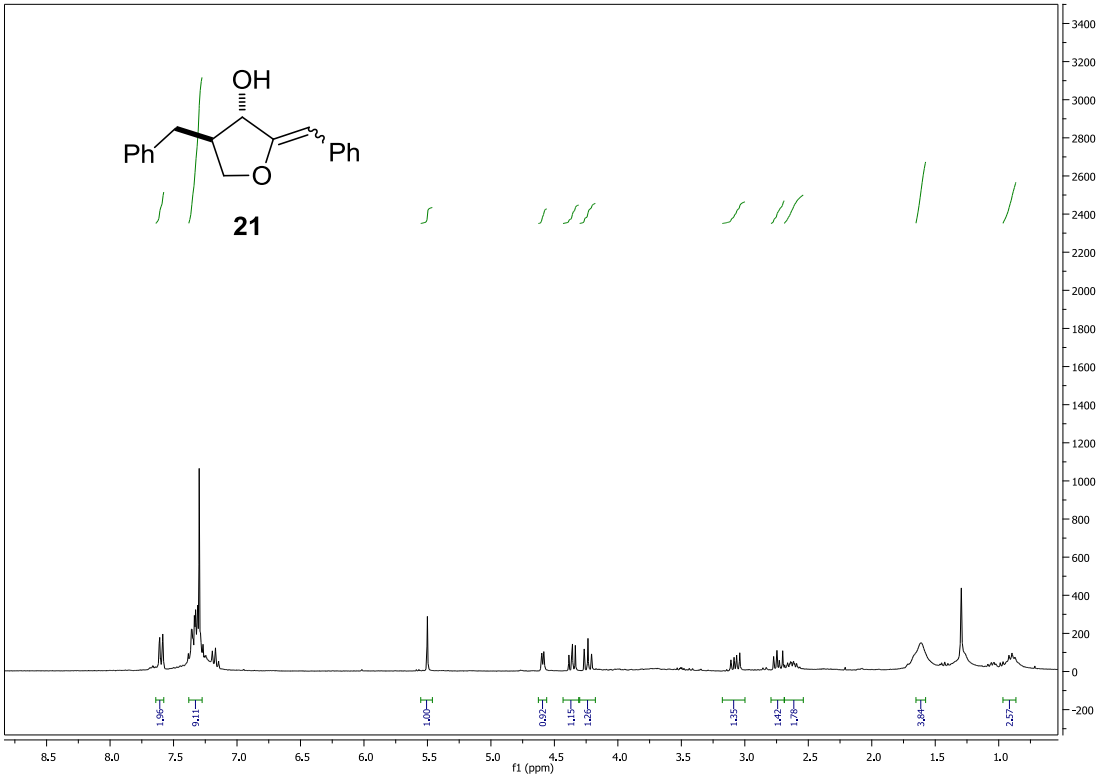

136.52
131.10
130.93
128.52
127.48
126.49
116.76
107.32
72.57
72.57
56.18
56.18
54.79
54.79
46.18
30.87
OMe OH
MeO
Ph
18
f1 (ppm)

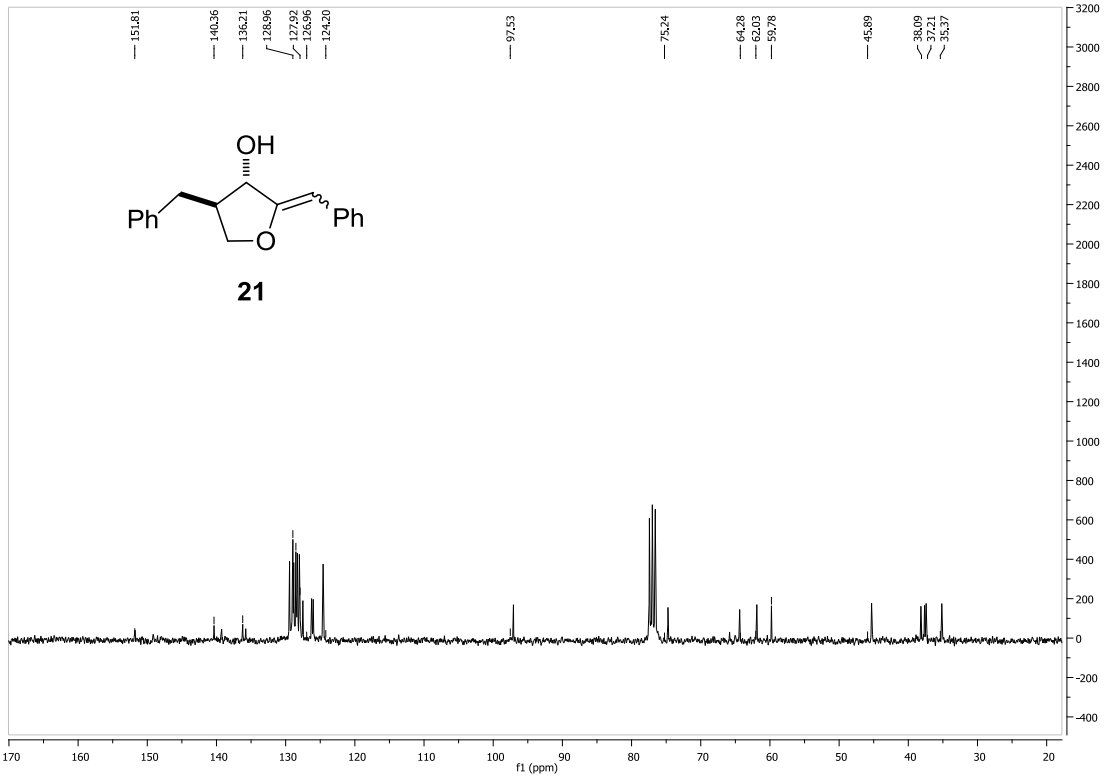


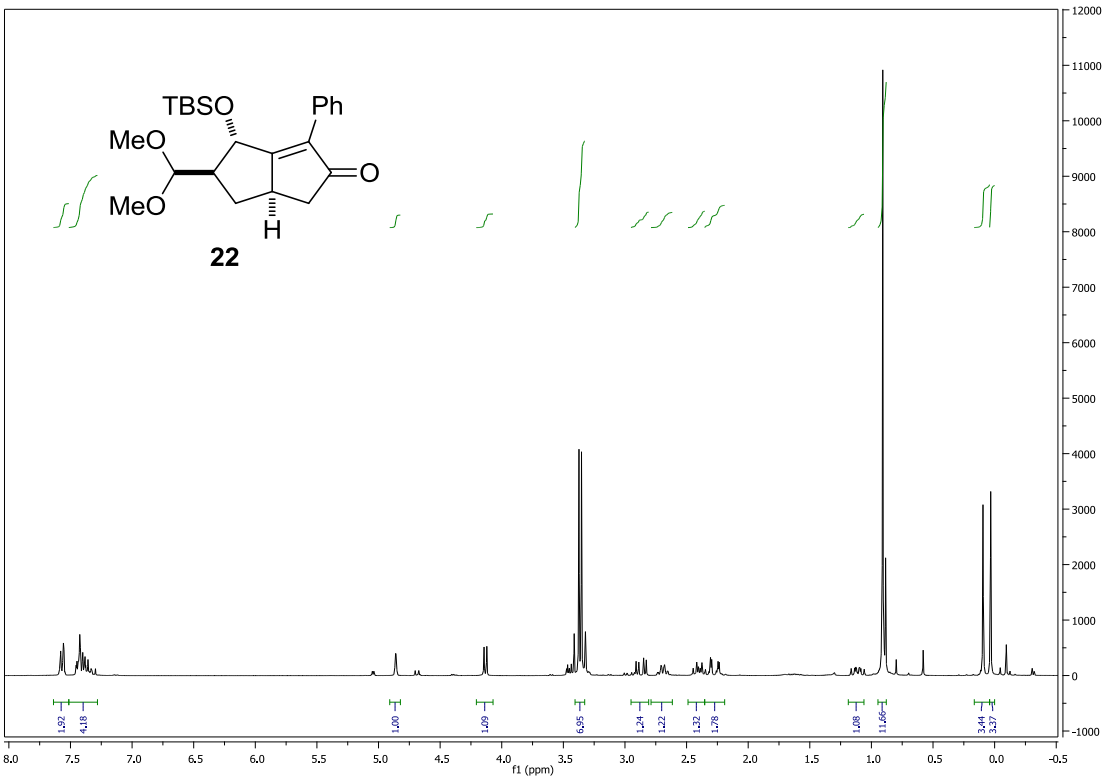


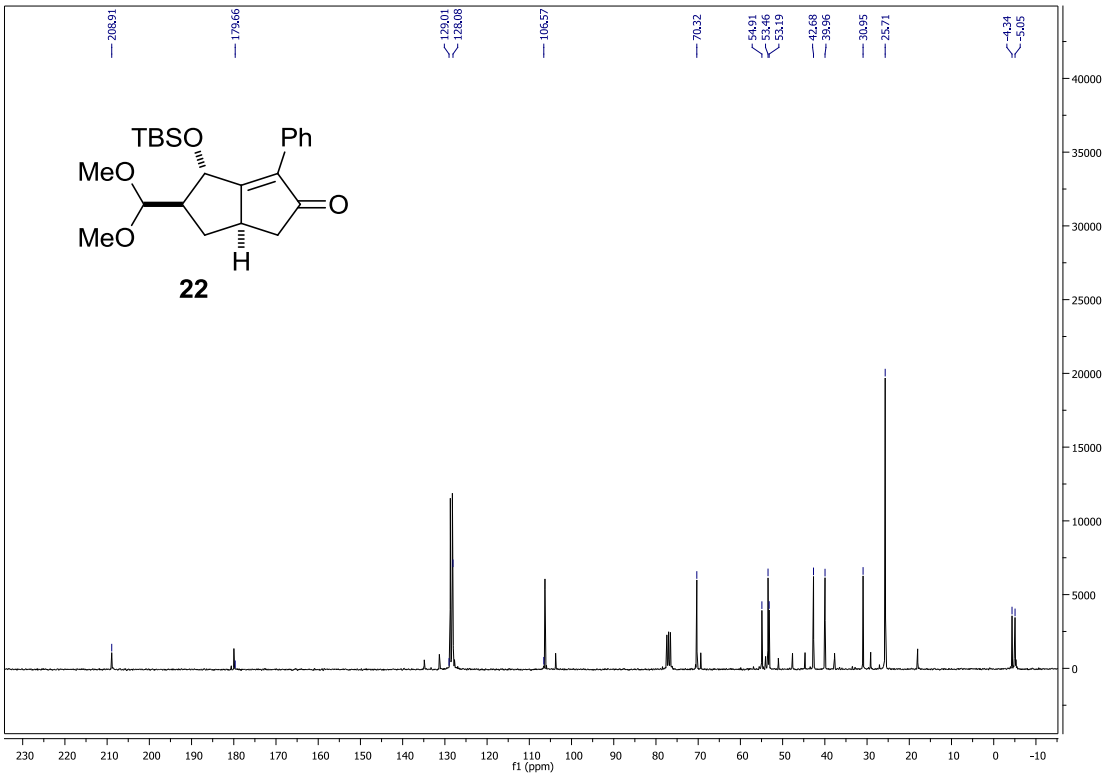

7.95
7.94
7.92
7.92
7.55
7.53
7.47
7.44
6.95
6.90
6.87
6.87
6.86
6.81
4.49
4.47
3.38
3.35
2.51
2.48
2.47
2.44
2.09
2.07
2.07
2.05
2.04
2.03
0.97
0.95
0.93
0.92
0.89
OMe
O
O
NH
MeO
Ph
20
1.89
3.29
2.25
1.00
6.07
1.40
1.27
7.79
f1 (ppm)


146.37
138.27
132.78
129.02
128.89
128.70
105.09
77.65
77.23
76.81
54.26
53.81
52.31
28.39
21.73
18.38
OMe
O
O
NH
MeO
Ph
20
f1 (ppm)


OH
Ph
Ph
O
21
f1 (ppm)

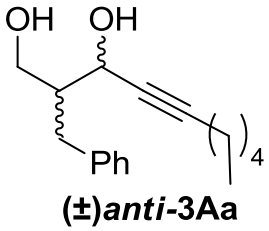

151.81
140.36
136.21
128.96
127.92
126.96
124.20
97.53
75.24
64.28
62.03
59.78
45.89
38.09
37.21
35.57
OH
Ph
Ph
O
21
f1 (ppm)


TBSO
Ph
MeO
MeO
O
H
22
f1 (ppm)


208.91
179.66
129.01
128.08
106.57
70.32
54.91
53.46
53.19
42.68
39.96
30.95
25.71
-4.34
-5.05
TBSO
Ph
MeO
MeO
O
H
22
f1 (ppm)

M) HPLC chromatograms of selected products

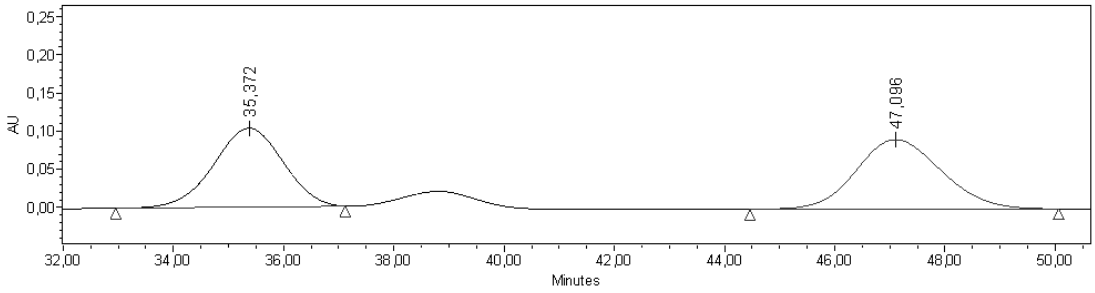
PDA 210nm, Chiralpak IC, 95:5 hex:iPrOH, f:1 mL/min

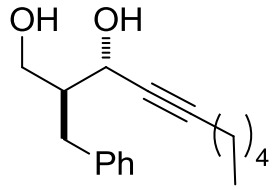


(±)*anti*-3Aa

Processed Channel Descr.: 2998 Ch2 210nm@2.4nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	2998 Ch2 210nm@2.4nm	35,372	9057902	48,06	103362
2	2998 Ch2 210nm@2.4nm	47,096	9790717	51,94	90944

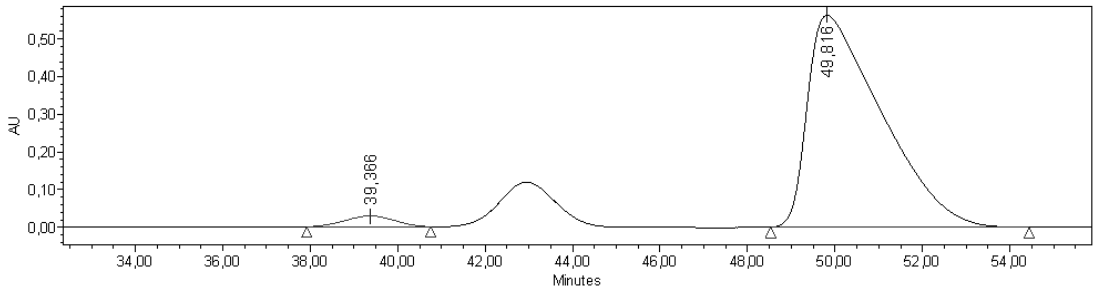




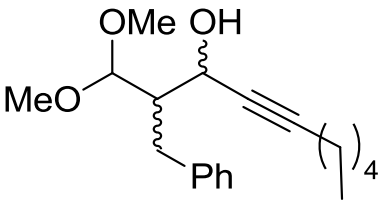
3Aa

Processed Channel Descr.: 2998 Ch2 210nm@2.4nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	2998 Ch2 210nm@2.4nm	39,366	2263704	3,31	28641
2	2998 Ch2 210nm@2.4nm	49,816	66023952	96,69	562380



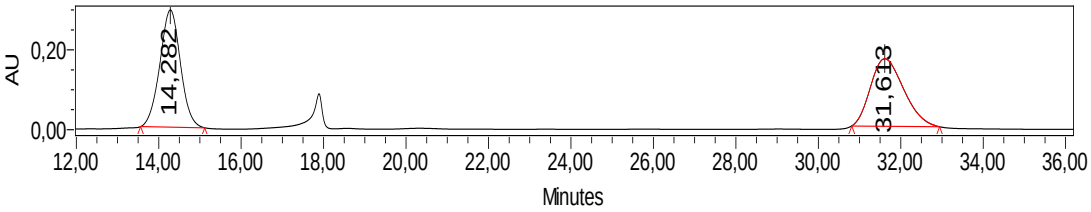
PDA 210nm, Chiralpak IC, 95:5 hex:ipr, f:1mL/min

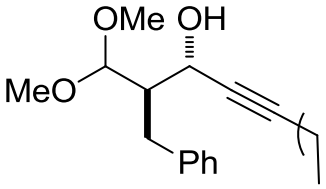


(±)*anti*-8Aa

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	14,282	10185489	51,83	294058
2	PDA 210,0 nm	31,613	9465881	48,17	169419

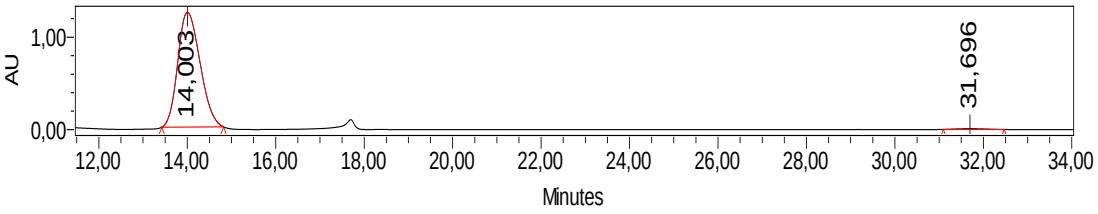




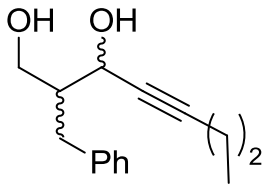
8Aa

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	14,003	43512523	99,20	1244172
2	PDA 210,0 nm	31,696	352587	0,80	7784



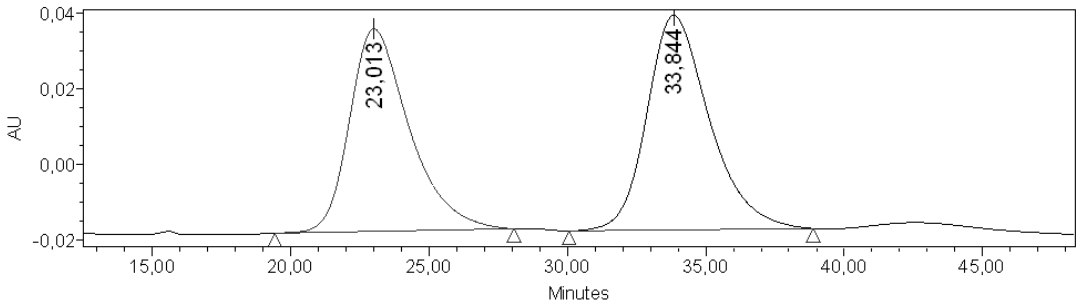
PDA 209nm, Chiralpak IC, 95:5 hex:ipr, f:1 mL/min

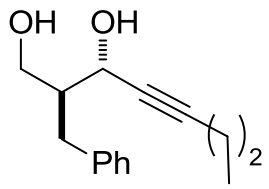


(±)-*anti*-3Ab

Processed Channel Descr.: 2998 Ch1 254nm@2.4nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	2998 Ch1 254nm@2.4nm	23,005	7638919	47,27	50844
2	2998 Ch1 254nm@2.4nm	33,833	8521675	52,73	53980

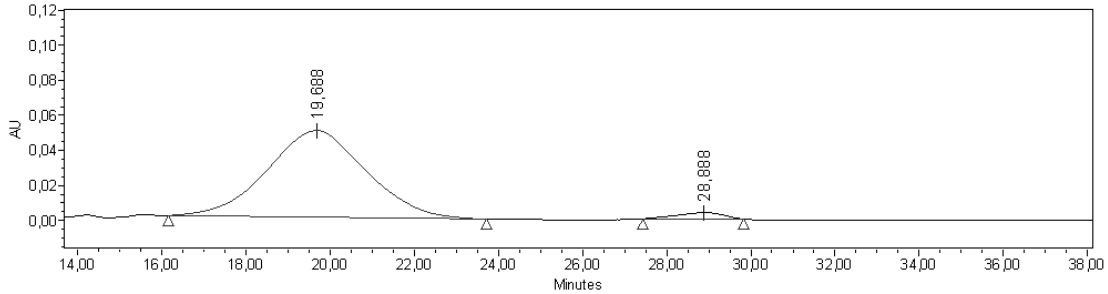




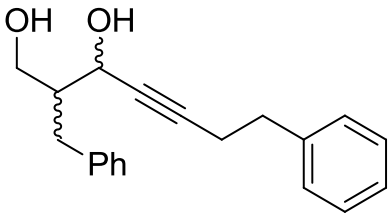
3Ab

Processed Channel Descr.: PDA 209,8 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 209,8 nm	19,688	8030630	96,78	49408
2	PDA 209,8 nm	28,888	267337	3,22	3563



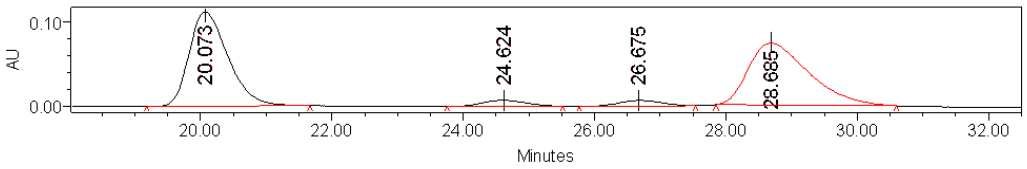
PDA 220nm, Chiralpak AS-H, 90:10 hex:ipr, f:1 mL/min

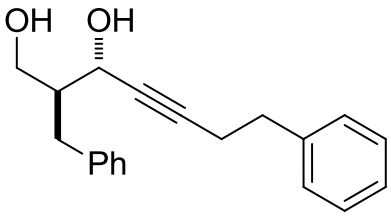


(+)anti 3Ad

Processed Channel Descr.: PDA 221.3 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 221.3 nm	20.073	4586585	46.31	111918
2	PDA 221.3 nm	24.624	329225	3.32	7217
3	PDA 221.3 nm	26.675	303986	3.07	6676
4	PDA 221.3 nm	28.685	4684898	47.30	73517

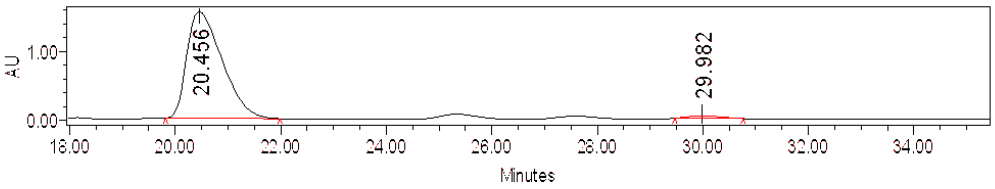




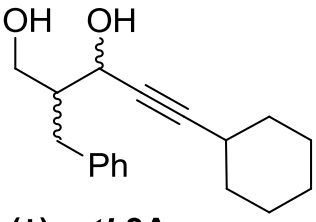
3Ad

Processed Channel Descr.: PDA 217.5 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 217.5 nm	20.456	72215410	97.87	1547174
2	PDA 217.5 nm	29.982	1574188	2.13	35063



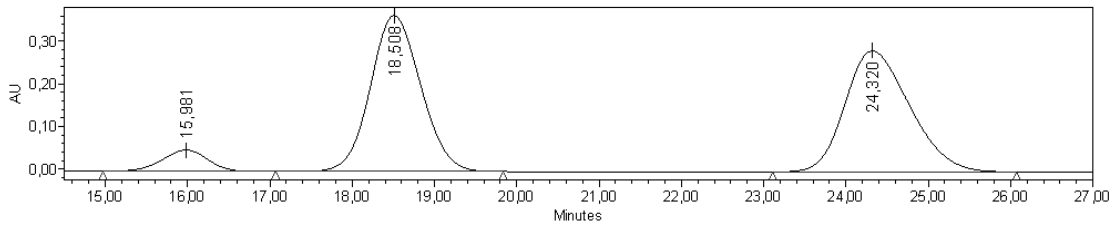
PDA 210nm, Chiralpak IC, 90:10 hex:ipr, f:1mL/min

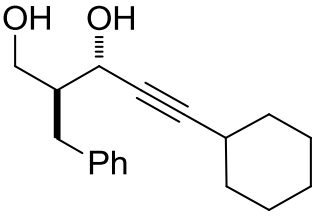


(±)*anti*-3Ae

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	18,508	15563763	50,04	365883
2	PDA 210,0 nm	24,320	15538789	49,96	284030

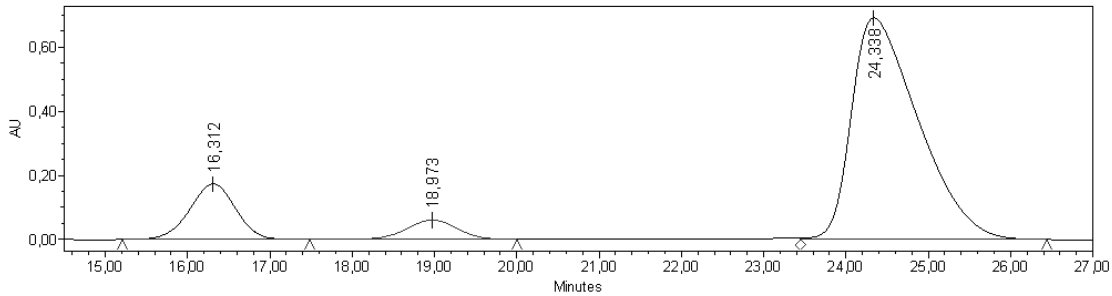




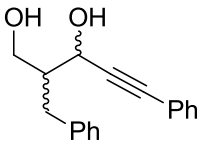
3Ae

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	18,973	1924681	4,69	52776
2	PDA 210,0 nm	24,338	39085502	95,31	691688



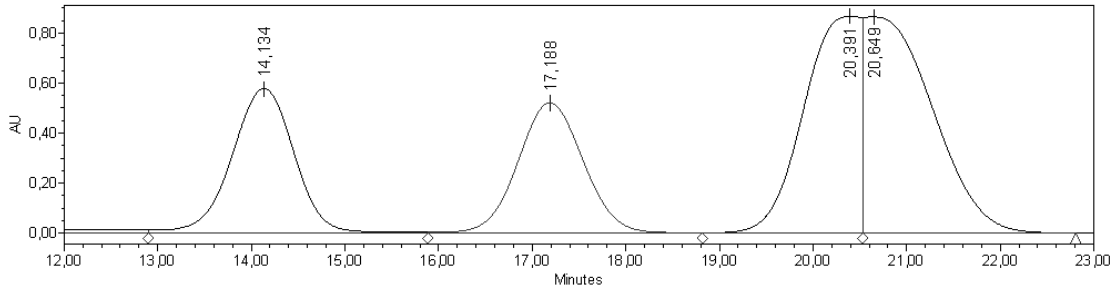
PDA 240nm, Chiralpak AS-H, 90:10 hex:ipr, f:1mL/min

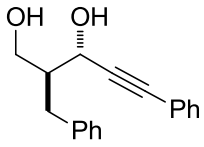


(±)*anti*-3Af

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	14,134	26256755	51,43	567546
2	PDA 240,0 nm	17,188	24795620	48,57	511488

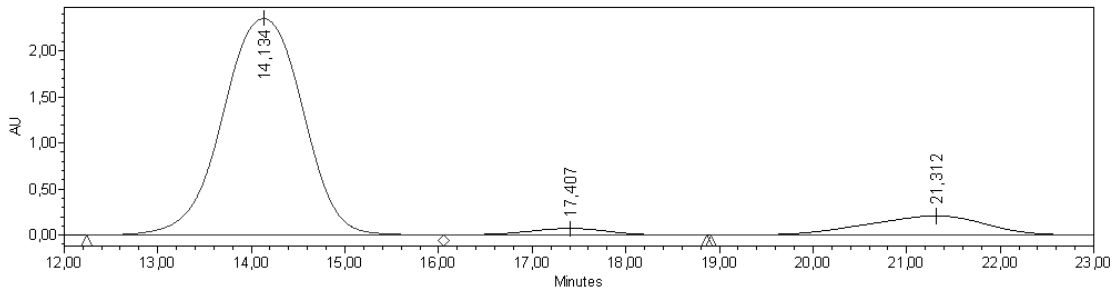




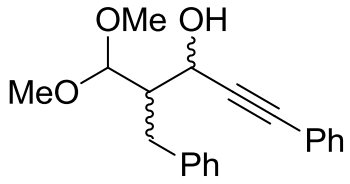
3Af

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	14,131	137379555	97,11	2319140
2	PDA 240,0 nm	17,407	4083750	2,89	69693



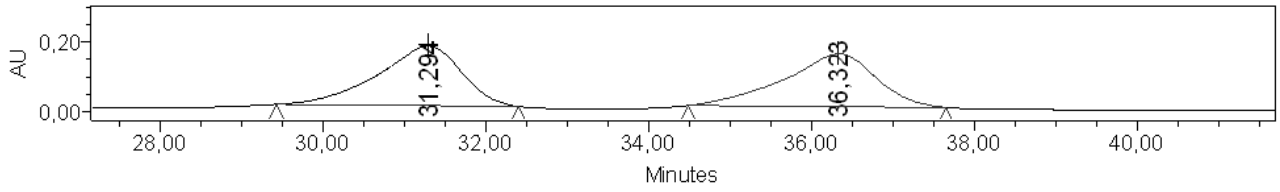
PDA 240nm, Chiralpak IC, 98:2 hex:ipr, f:05mL/min

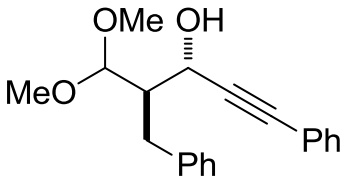


(±)-*anti*-8Af

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	31,294	12131233	50,58	170537
2	PDA 210,0 nm	36,323	11851663	49,42	151805

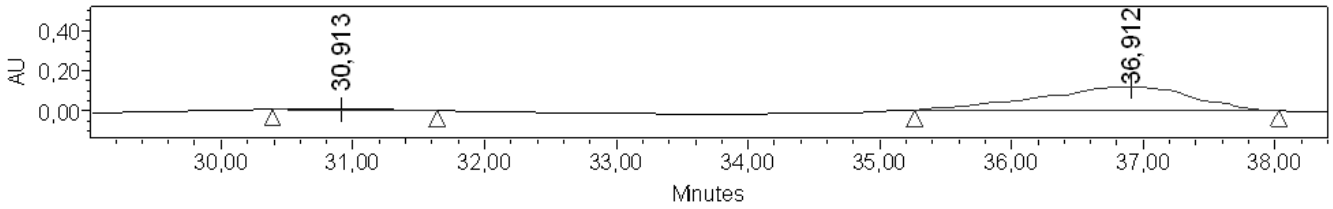




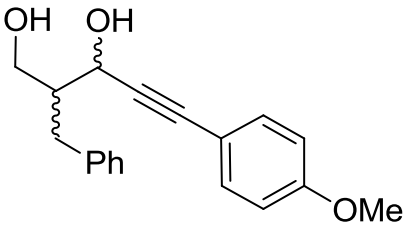
8Af

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	30,913	253398	2,67	5972
2	PDA 210,0 nm	36,912	9243051	97,33	117740



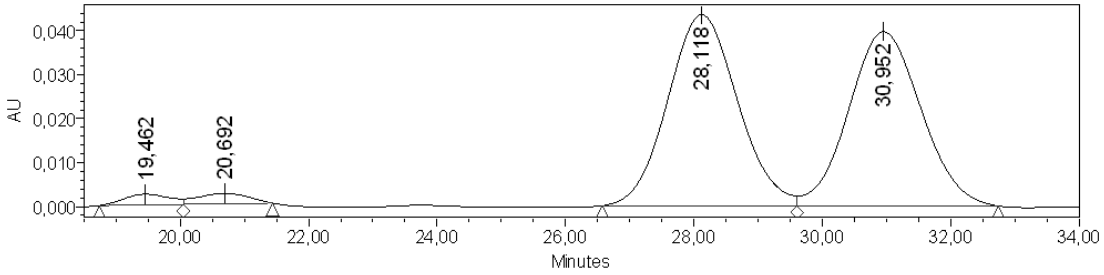
PDA 240nm, Chiralpak AS-H, 90:10 hex:ipr, f:1 mL/min

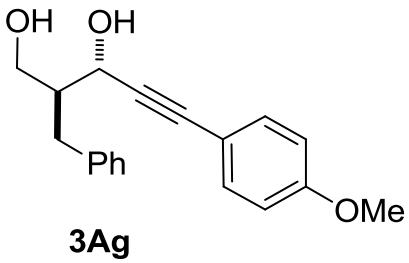


(±)*anti*-3Ag

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	28,118	3287985	51,41	43503
2	PDA 240,0 nm	30,952	3107720	48,59	39630

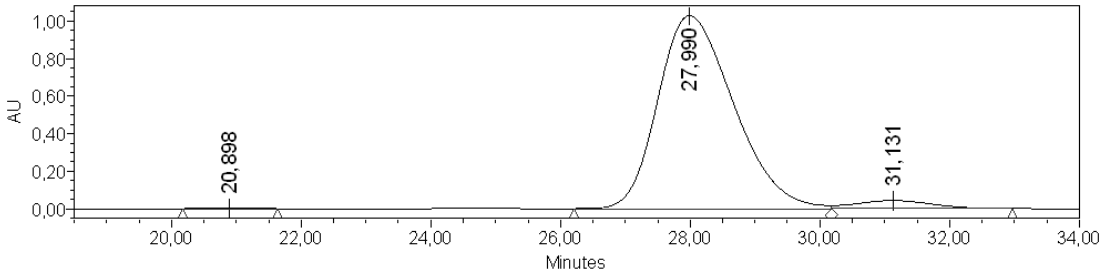




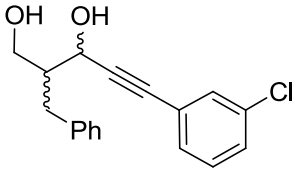
3Ag

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	27,990	83366956	95,97	1028432
2	PDA 240,0 nm	31,131	3500131	4,03	42865



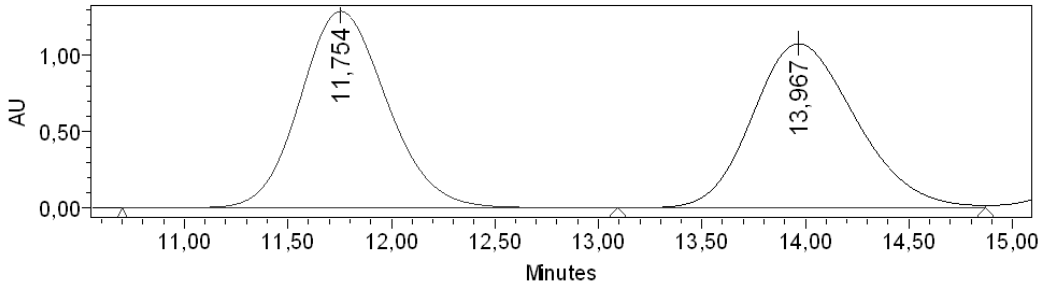
PDA 240nm, Chiralpak AS-H, 90:10 hex:ipr, f:1 mL/min

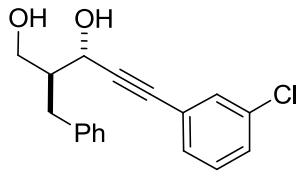


(±)anti-3Ah

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	11,754	37766089	50,20	1288695
2	PDA 240,0 nm	13,967	37468214	49,80	1075921

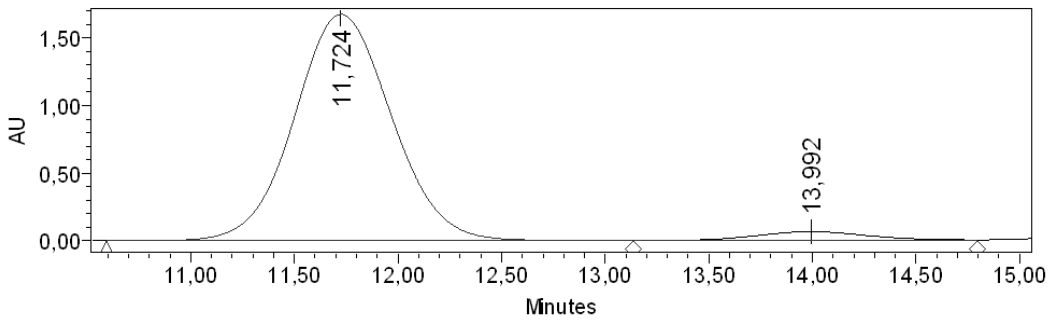




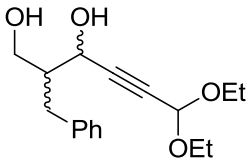
3Ah

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	11,724	54770546	95,42	1674406
2	PDA 240,0 nm	13,992	2628661	4,58	66162

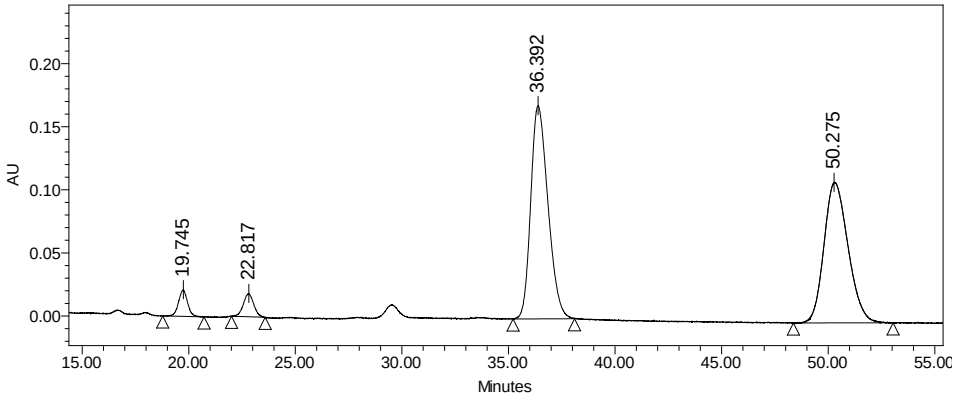


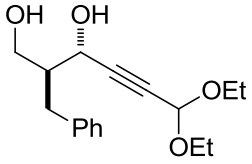
PDA 208.0 nm, Phenomenex Lux 3 Cellulose-4, 93 : 7 hex : ipr, f: 1 mL/min



(±)*anti*-3Ai

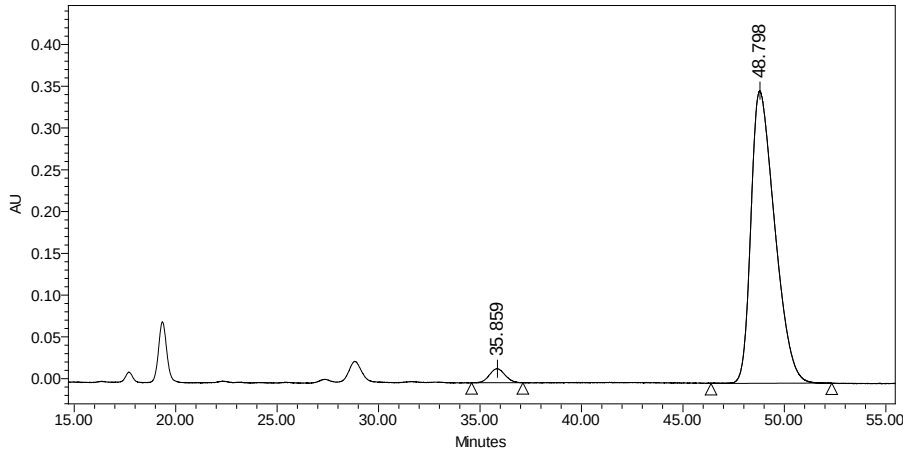
	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 208.0 nm	19.745	616200	3.26	21209
2	PDA 208.0 nm	22.817	620133	3.28	18256
3	PDA 208.0 nm	36.392	8932161	47.19	164853
4	PDA 208.0 nm	50.275	8759745	46.28	111366



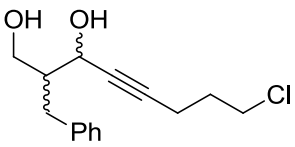


3Ai

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 208.0 nm	35.859	901691	3.07	16652
2	PDA 208.0 nm	48.798	28477495	96.93	350182



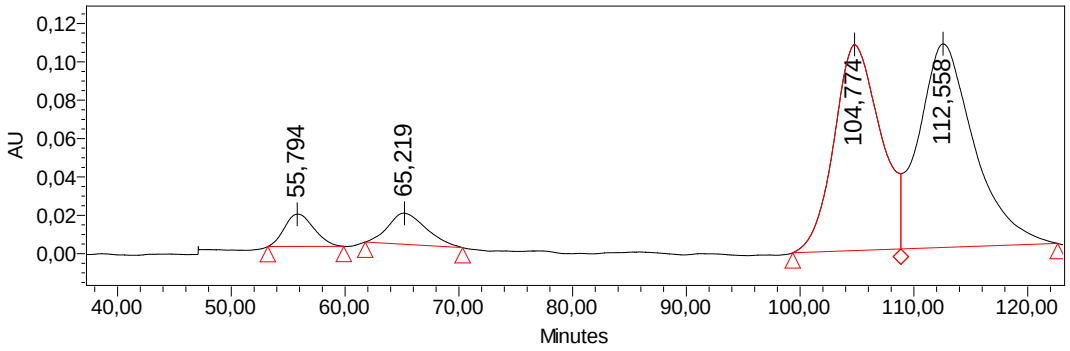
PDA 240nm, Chiralpak AD-H, 98:2 hex:ipr, f:1 mL/min

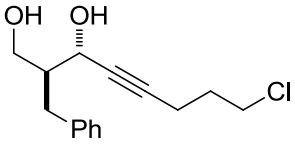


(±)*anti*-3Aj

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	55,794	3016962	6,65	16803
2	PDA 210,0 nm	65,219	3774808	8,32	16200
3	PDA 210,0 nm	104,689	19451537	42,89	85214
4	PDA 210,0 nm	112,681	19108239	42,13	74861

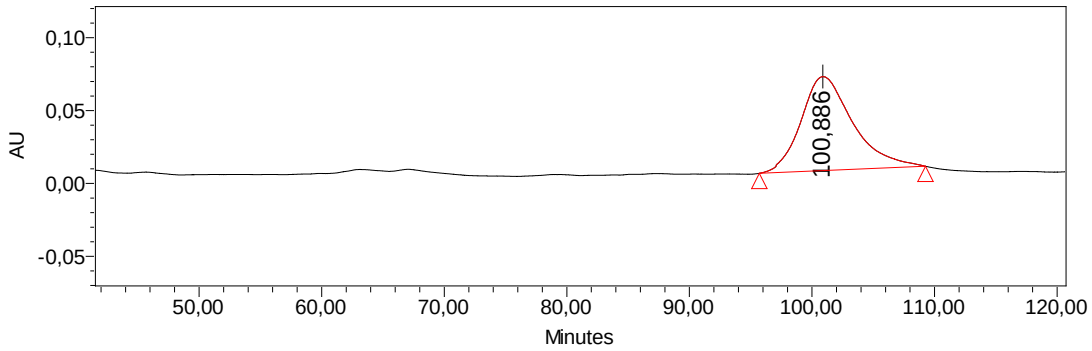




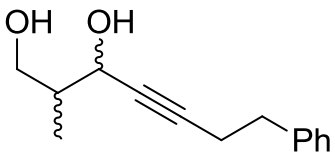
3Aj

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	100,886	18983398	100,00	64457



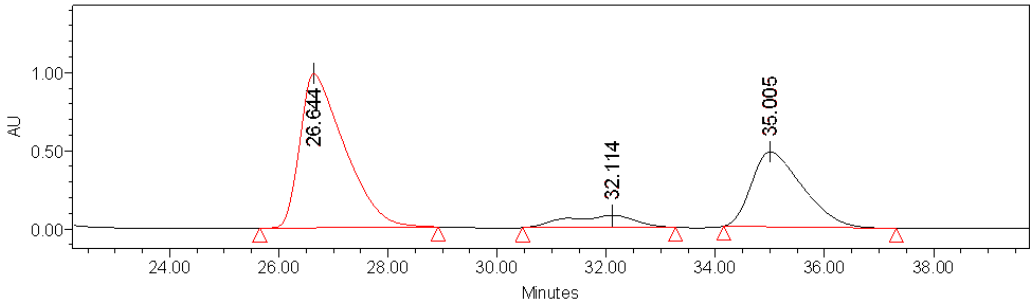
PDA 210nm, Chiralpak AY-H, 95:5 hex:ipr, f:1 mL/min

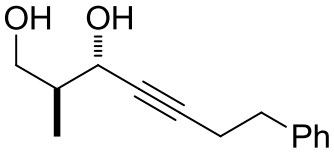


(±)*anti*-3Bd

Processed Channel Descr.: PDA 211.9 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 211.9 nm	26.644	55924034	59.53	985210
2	PDA 211.9 nm	32.114	6866605	7.31	78522
3	PDA 211.9 nm	35.005	31146529	33.16	481322

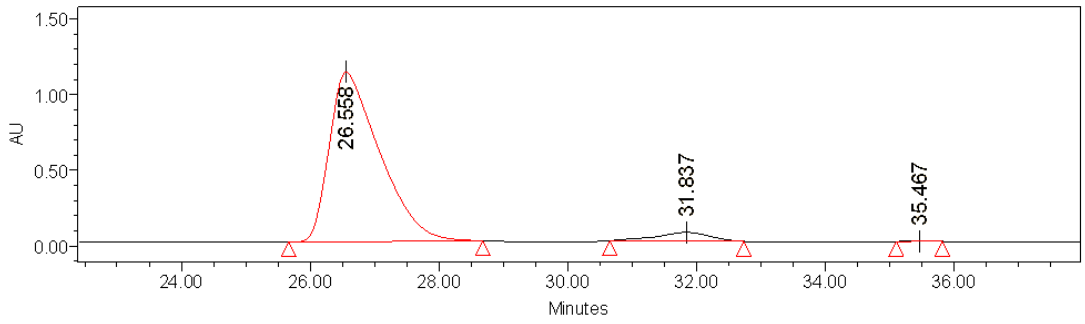




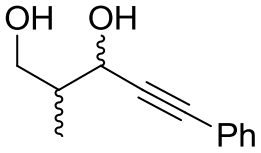
3Bd

Processed Channel Descr.: PDA 208.4 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 208.4 nm	26.558	60759401	94.83	1119080
2	PDA 208.4 nm	31.837	3239118	5.06	56806
3	PDA 208.4 nm	35.467	75713	0.12	2750



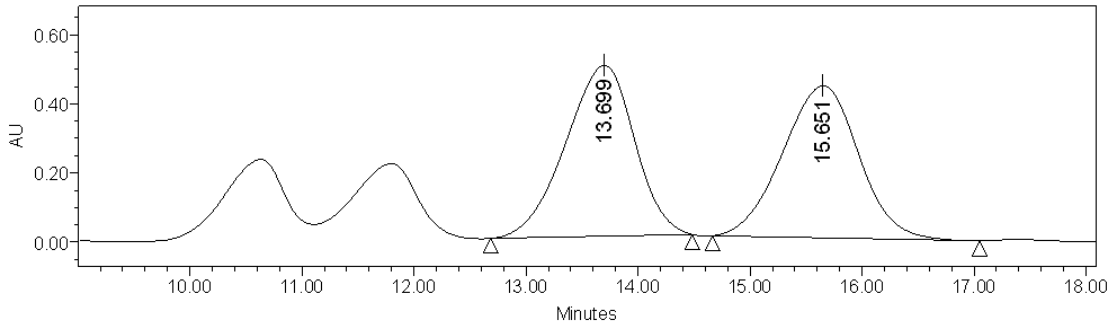
PDA 254.1nm, Chiralpak IC, 90:10 hex:ipr, f:1mL/min

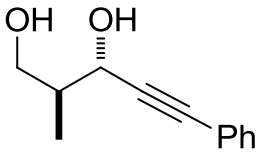


(±)*anti*-3Bf

Processed Channel Descr.: PDA 254.1 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 254.1 nm	13.699	21138223	50.38	494449
2	PDA 254.1 nm	15.651	20821017	49.62	439792

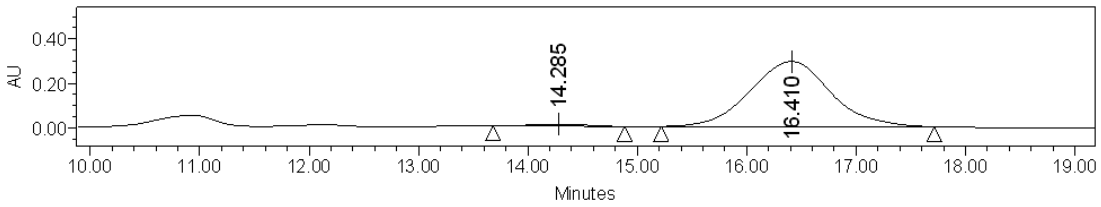




3Bf

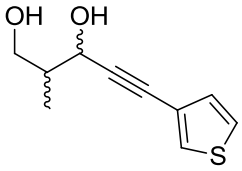
Processed Channel Descr.: PDA 254.3 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 254.3 nm	14.285	322132	2.10	9375
2	PDA 254.3 nm	16.410	15005305	97.90	292813



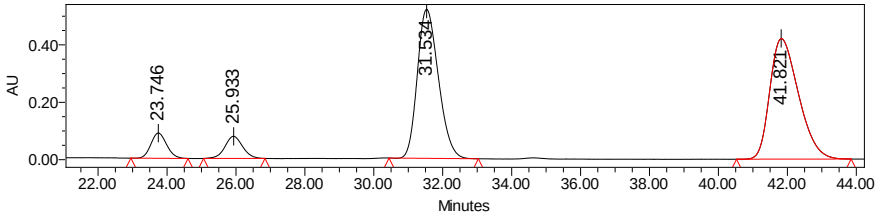
PDA 208.0 nm, Daicel Chiralpak IC-3 93 : 7 hex : ipr, f: 1.2 mL/min

Processed Channel Descr.: PDA 215.0 nm

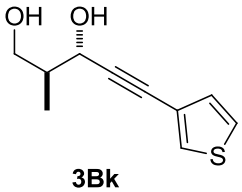


(±)*anti*-3Bk

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 215.0 nm	23.746	3102156	5.40	97838
2	PDA 215.0 nm	25.933	2941034	5.12	84795
3	PDA 215.0 nm	31.534	24562707	42.76	578382
4	PDA 215.0 nm	41.821	26830736	46.71	466338



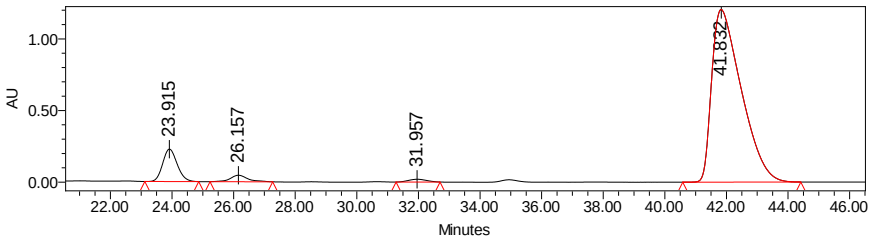
Processed Channel Descr.: PDA 215.0 nm



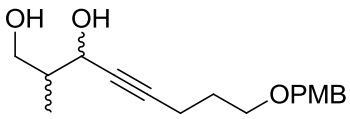
3Bk

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 215.0 nm	23.915	3419753	8.14	104377
2	PDA 215.0 nm	26.157	743910	1.77	21025
3	PDA 215.0 nm	31.957	367740	0.88	8984
4	PDA 215.0 nm	41.832	37486650	89.22	567037

el	RT	Area	% Area	Height
	31.957	331909	0.86	8599
	41.832	38186368	99.14	577829



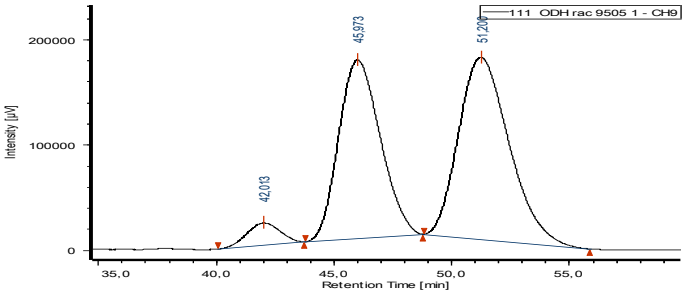
PDA 225.0 nm, Daicel Chiralcel OD-H ,95 : 5 hex : ipr, f: 0.75 mL/min

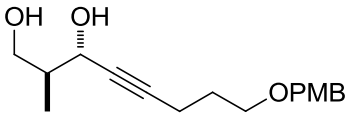


(±)*anti*-3BI

Processed Channel Descr.: PDA 225.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 225.0 nm	42,013	2067904	4,258	21047
2	PDA 225.0 nm	45,973	20761994	42,752	168818
3	PDA 225.0 nm	51,200	25733573	52,990	172220





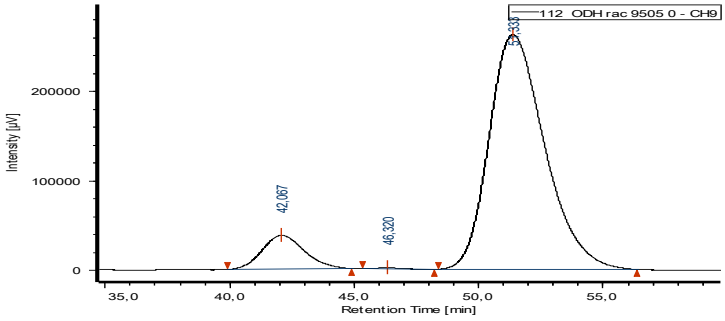
3BI

Processed Channel Descr.: PDA 225.0 nm

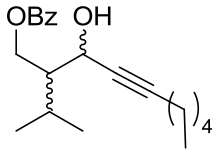
	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 225.0 nm	42,067	4412274	9,802	37511
2	PDA 225.0 nm	46,320	82187	0,183	1107
2	PDA 225.0 nm	51,333	40520603	90,016	261500

Processed Channel Descr.: PDA 225.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 225.0 nm	46,320	100850	0,248	1241
2	PDA 225.0 nm	51,333	40588685	99,752	261661



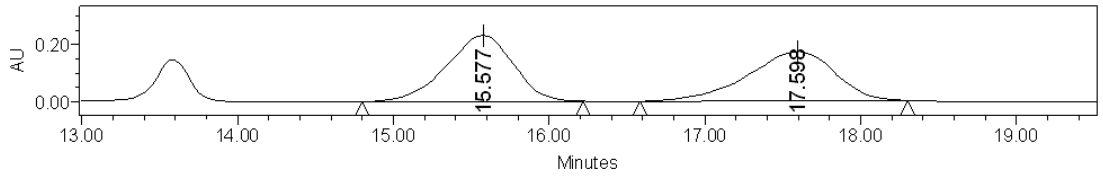
PDA 240nm, Chiralpak IC, 98:2 hex:et, f:1 mL/min

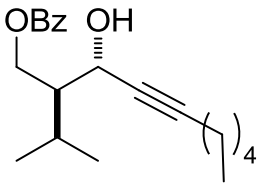


deriv. (±)***anti*-3Ca**

Processed Channel Descr.: PDA 225.5 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 225.5 nm	15.577	6945095	50.99	230890
2	PDA 225.5 nm	17.598	6674108	49.01	172715

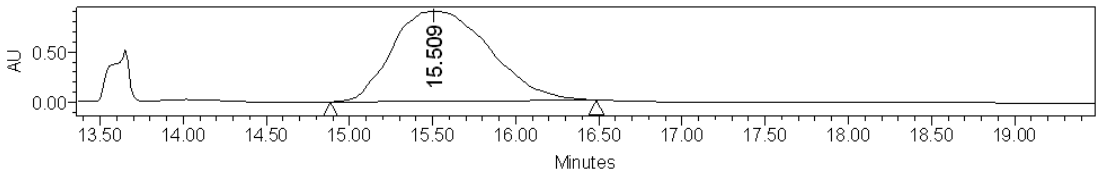




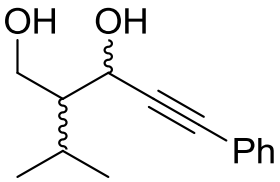
deriv. **3Ca**

Processed Channel Descr.: PDA 209.8 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 209.8 nm	15.509	36180568	100.00	892057



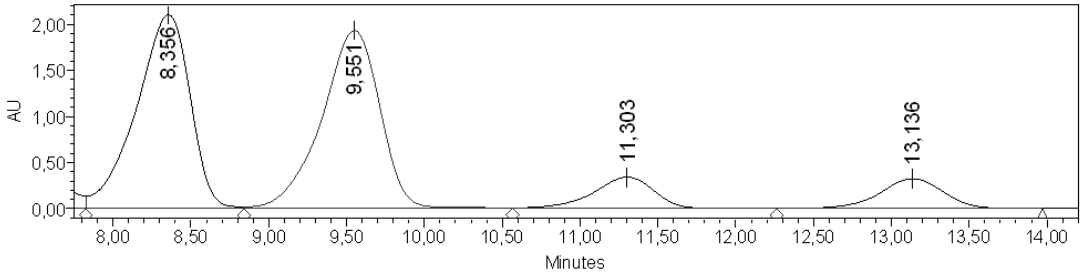
PDA 240nm, Chiralpak AY-H, 90:10 hex:ipr, f:1mL/min

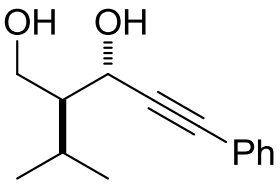


(±)-*anti*-3Cf

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	8,356	50518329	50,10	2103434
2	PDA 240,0 nm	9,551	50315308	49,90	1930338

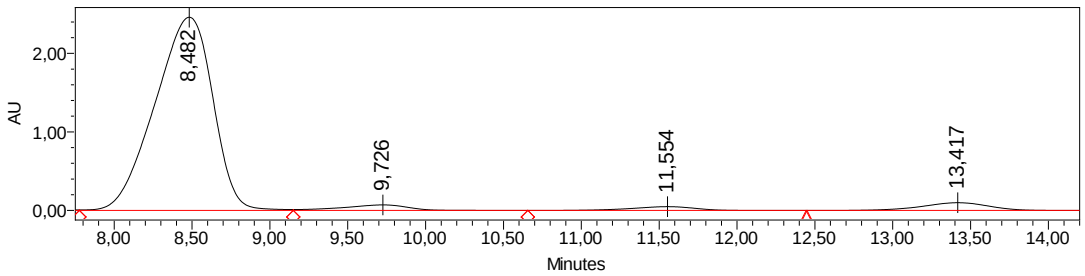




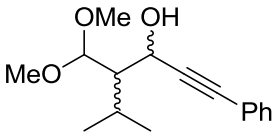
3Cf

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	8,482	63648367	96,92	2458930
2	PDA 240,0 nm	9,726	2021843	3,08	70139



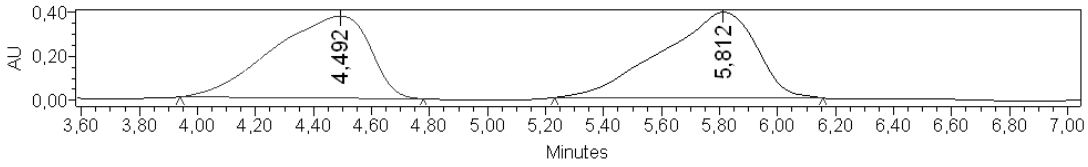
PDA 240nm, Chiralpak IB, 95:5 hex:ipr, f:1mL/min

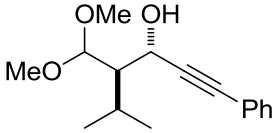


(±)-*anti*-8Cf

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	4,492	8669379	49,61	374339
2	PDA 210,0 nm	5,812	8805884	50,39	389922

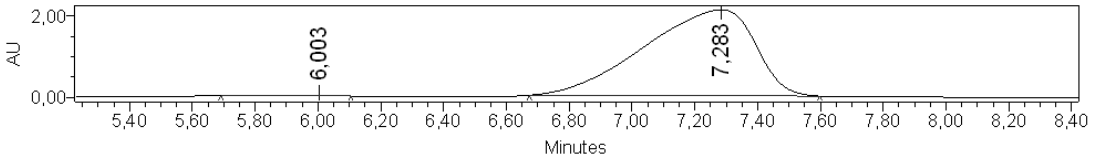




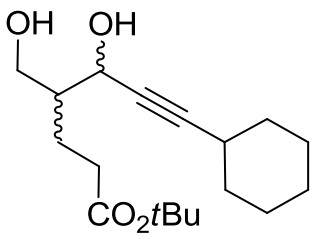
8Cf

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	6,003	324987	0,63	18395
2	PDA 240,0 nm	7,283	51651122	99,37	2115425



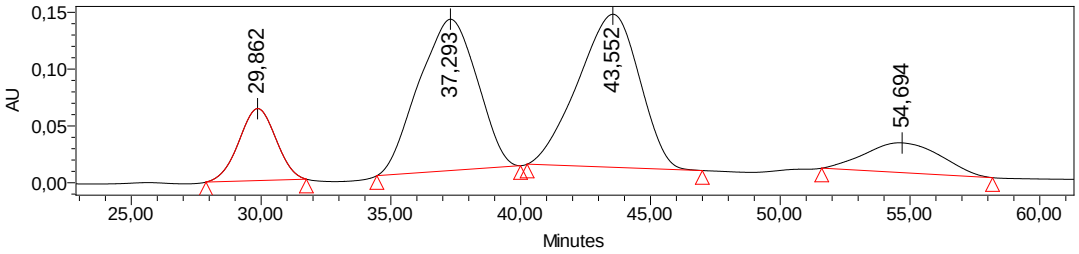
PDA 218nm, Chiralpak IC, 99:1 hex:Et, f:1mL/min

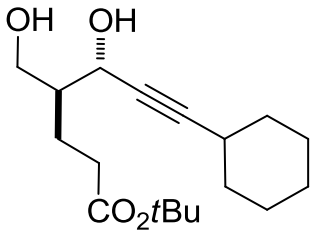


(±)*anti*-3De

Processed Channel Descr.: PDA 218,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 218,0 nm	29,879	5989969	11,26	62019
2	PDA 218,0 nm	37,293	21189331	39,84	134316
3	PDA 218,0 nm	43,556	21594696	40,60	133255
4	PDA 218,0 nm	54,750	4413243	8,30	23553

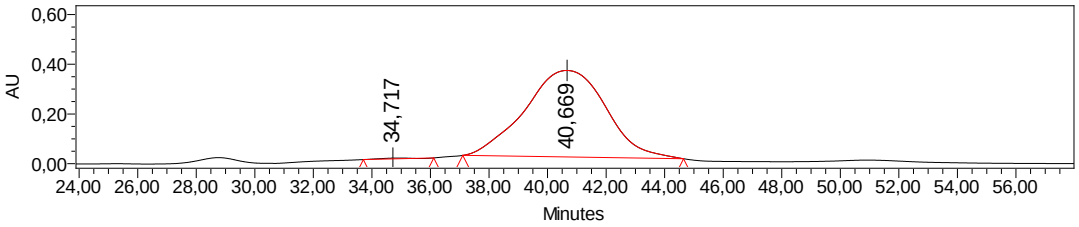




3De

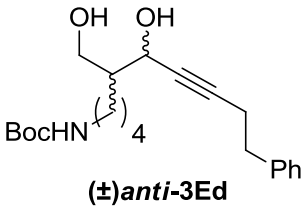
Processed Channel Descr.: PDA 218,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 218,0 nm	34,971	77334	0,13	1823
2	PDA 218,0 nm	40,645	60933758	99,87	333168



PDA 207.0 nm, Phenomenex Lux 3µ Cellulose-4,

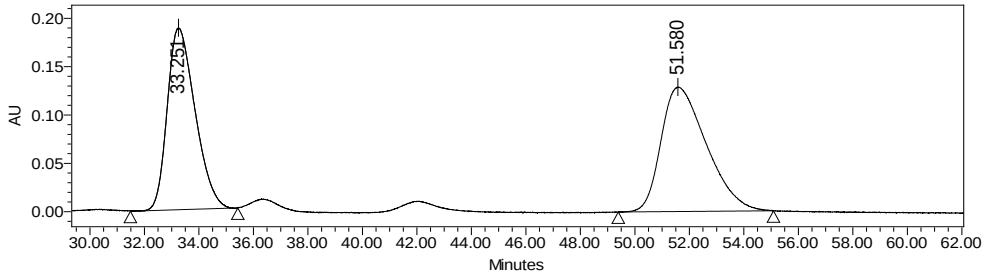
90 :10 hex :ipr, f :1.5 mL/min



(±)*anti*-3Ed

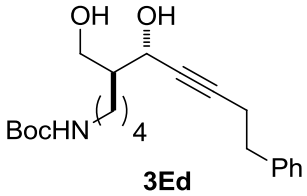
Processed Channel Descr.: PDA 207.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 207.0 nm	33.251	13315513	47.23	188060
2	PDA 207.0 nm	51.580	14878183	52.77	128701



PDA 207.0 nm, Phenomenex Lux 3µ Cellulose-4,

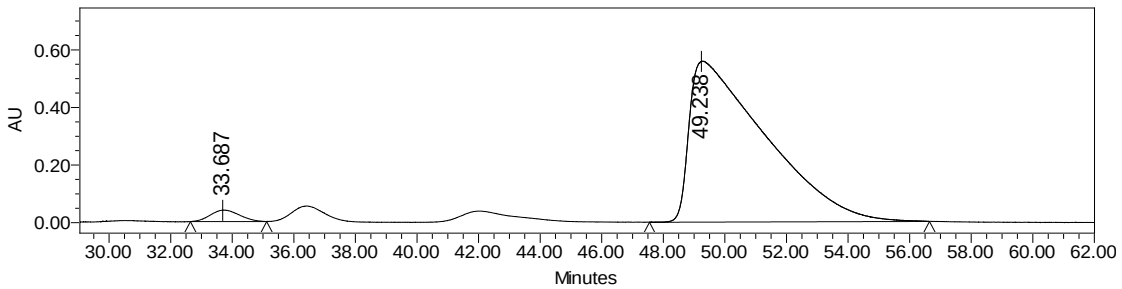
90 :10 hex :ipr, f :1.5 mL/min



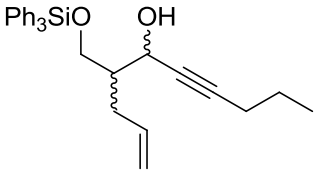
3Ed

Processed Channel Descr.: PDA 207.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 207.0 nm	33.687	2617316	2.64	39337
2	PDA 207.0 nm	49.238	96472644	97.36	557987



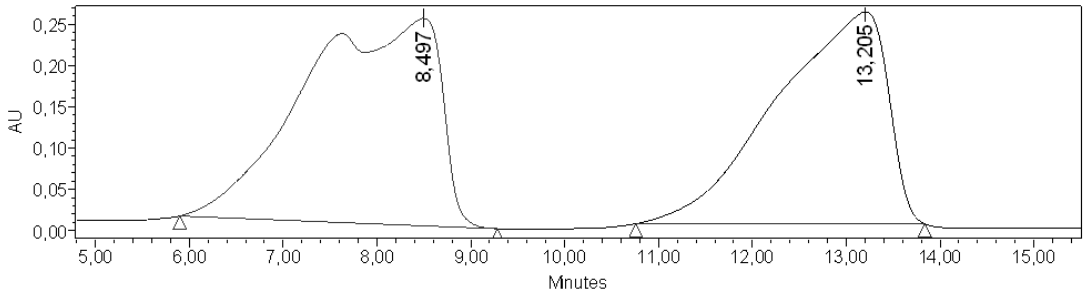
PDA 210nm, Chiralpak IB, 99:1 hex:ipr, f:1mL/min

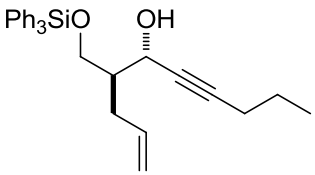


deriv.(±)*anti3***Fb**

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	8,497	25139861	54,26	250911
2	PDA 210,0 nm	13,205	21192560	45,74	256596

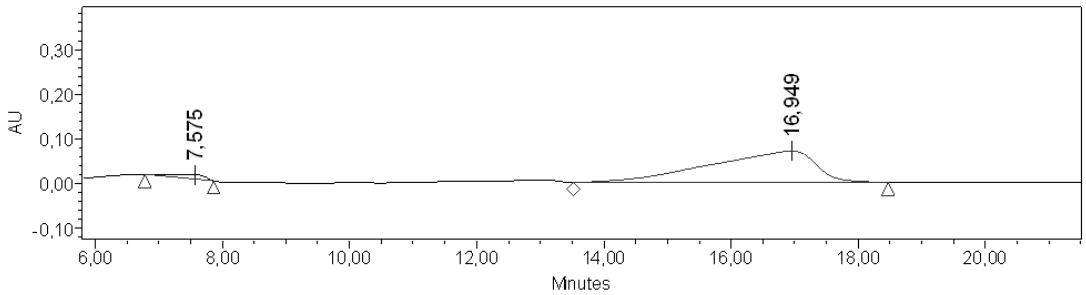




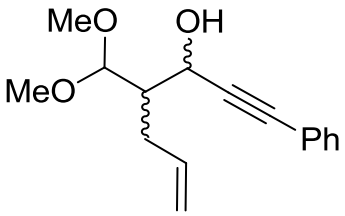
deriv.**3Fb**

Processed Channel Descr.: PDA 209,8 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 209,8 nm	7,575	365534	4,33	10439
2	PDA 209,8 nm	16,949	8080611	95,67	70102



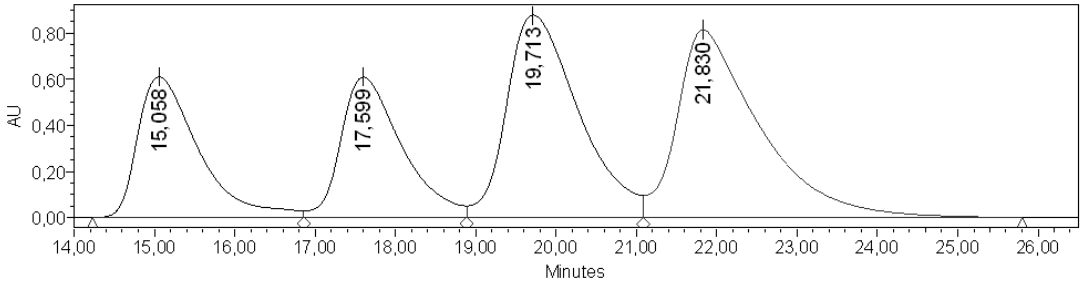
PDA 240nm, Chiralpak AD-H, 95:5 hex:ipr, f:0.5 mL/min

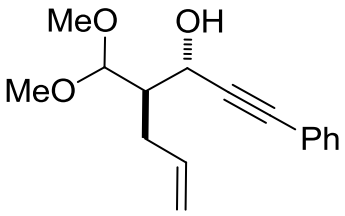


(±)*anti*-8Ff

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	19,713	54485396	48,46	876391
2	PDA 240,0 nm	21,830	57958813	51,54	812794

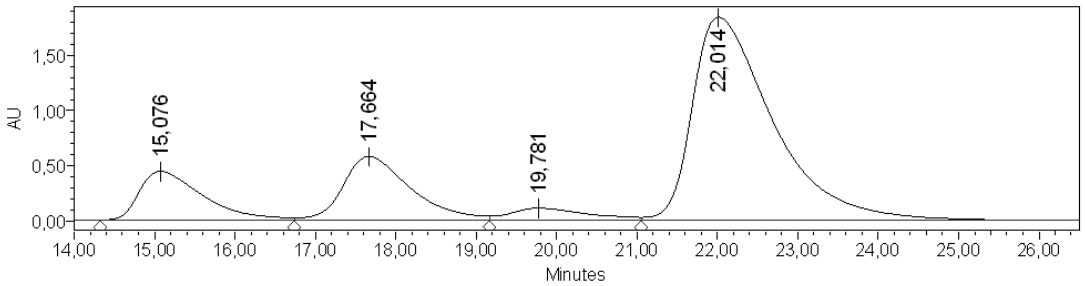




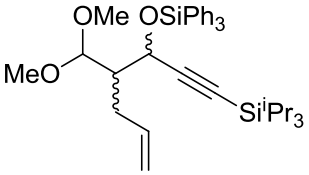
8Ff

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	19,781	2824138	2,24	64368
2	PDA 240,0 nm	22,014	123181399	97,76	1807772



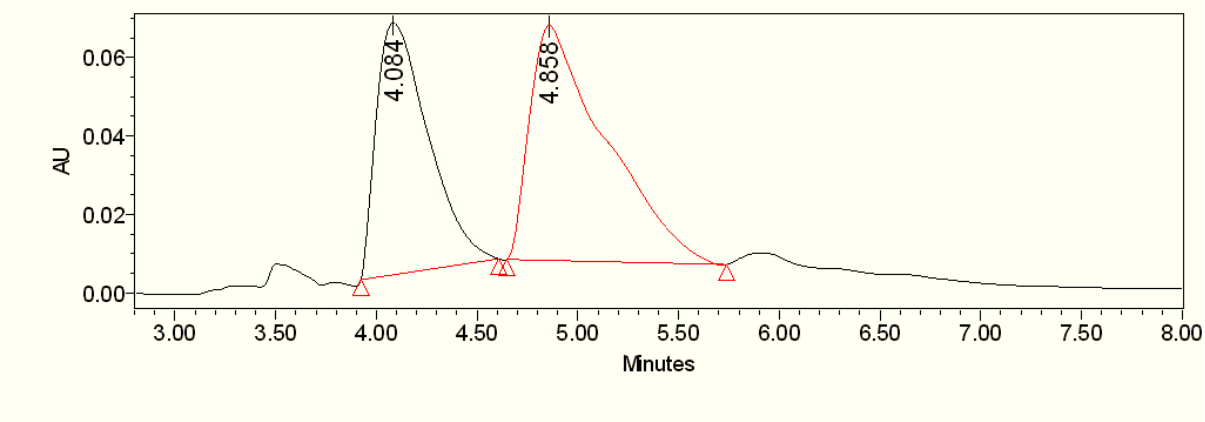
PDA 240nm, Chiralpak AY-H, hex f:1 mL/min

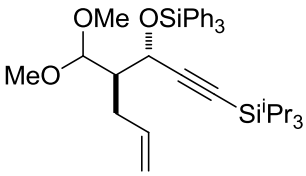


deriv. (±)*anti*-8Fm

Processed Channel Descr.: PDA 240.0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240.0 nm	4.084	1151453	42.36	64124
2	PDA 240.0 nm	4.858	1566586	57.64	59833

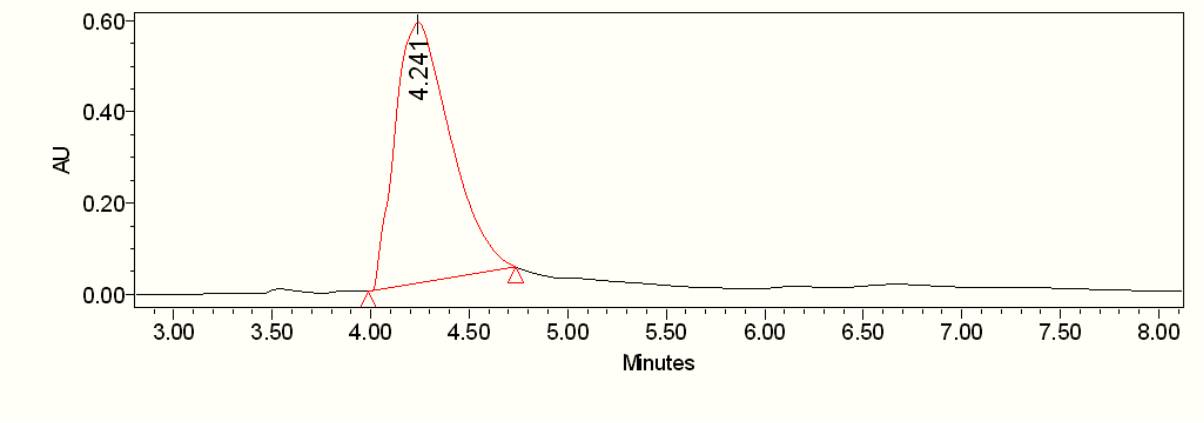




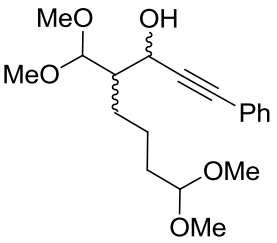
deriv. 8Fm

Processed Channel Descr.: PDA 234.1 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 234.1 nm	4.241	11176393	100.00	571846



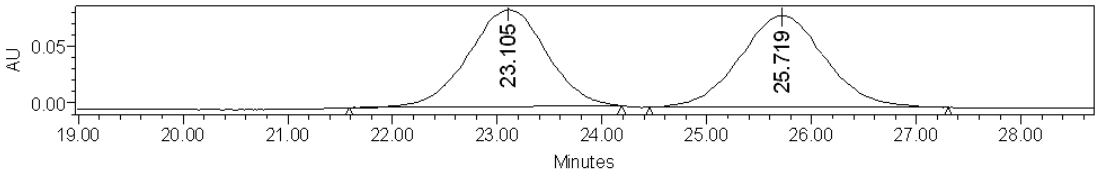
PDA 240nm, Chiralpak IB, 95:5 hex:ipr, f:1mL/min

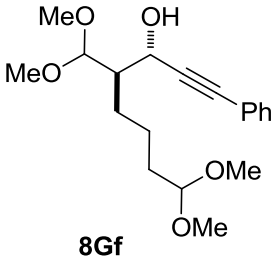


(±)*anti*-**8Gf**

Processed Channel Descr.: PDA 243.4 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 243.4 nm	23.105	4379286	49.27	85241
2	PDA 243.4 nm	25.719	4508588	50.73	80296

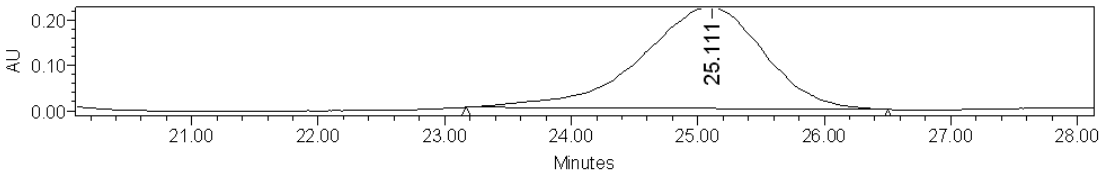




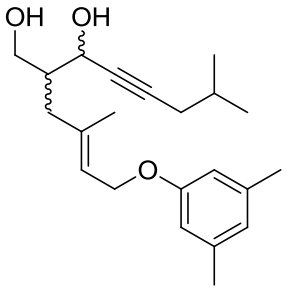
8Gf

Processed Channel Descr.: PDA 243.4 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 243.4 nm	25.111	15052120	100.00	224132



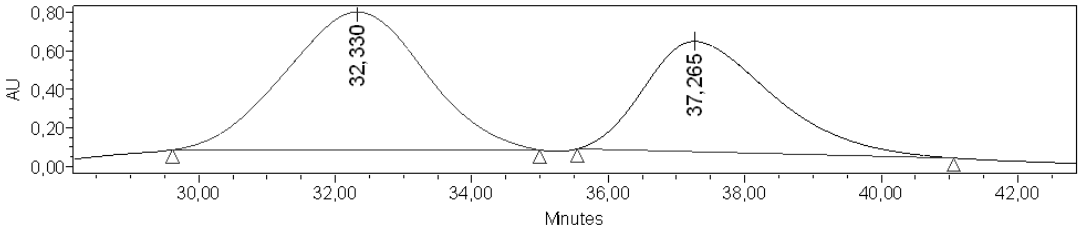
PDA 240nm, Chiralpak AD-H, 97:3 hex:ipr, f:1mL/min

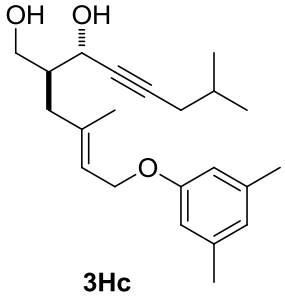


(±)*anti*-**3Hc**

Processed Channel Descr.: PDA 210,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 210,0 nm	32,330	102202564	57,69	717221
2	PDA 210,0 nm	37,265	74965294	42,31	572864





3Hc

Processed Channel Descr.: PDA 240,0 nm

	Processed Channel Descr.	RT	Area	% Area	Height
1	PDA 240,0 nm	31,105	14786	0,37	330
2	PDA 240,0 nm	36,602	3966787	99,63	31375