Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.


# Enantioselective Friedel-Crafts Reaction of Hydoxyarenes with Nitroenynes to Access Chiral Heterocycles *via* Sequential Catalysis

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## General Experimental Methods

Commercial reagents were used as purchased. Dichloromethane, 1,2-dichloroethane and toluene were distilled from $CaH_2$. Tetrahydrofuran was distilled from sodium benzophenone ketyl. Reactions were monitored by TLC (thin layer chromatography) analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040–0.063 mm.

NMR spectra were run in a Bruker DPX300 spectrometer (Bruker, Billerica, MA, USA) at 300 MHz for $^{1}H$ and at 75 MHz for $^{13}C$ using residual non-deuterated solvent as internal standard ($CHCl_3$: $\delta$ 7.26 for $^{1}H$ and 77.0 ppm for $^{13}C$). Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments.

High-resolution mass spectra (ESI) were recorded on a TRIPLETOFT5600 spectrometer LC/MS/MS System, (AB SCIEX) equipped with Ion Spray Voltage (ISVF): 5500. The MS was using method with infusion experiment. Data was evaluated using the PeakView™. Specific optical rotations were measured using sodium light (D line 589 nm). Chiral HPLC (High performance liquid chromatography) analyses were performed in a chromatograph equipped with a UV diode-array detector using chiral stationary columns from Daicel. Typically, enantiomeric ratios were measure using their absorbance in the 230-250 nm range. Melting points were determined in capillary tubes.

Organocatalysts **I**, **II** and **III** derived from cinchona alkaloids[1], differently substituted 2-naphtols **1**[2], (*E*)-nitrobut-1-en-3-ynes **2**[3] were prepared according to known procedures.

[1] For squaramides **I** and **III** see Yang, W. *et al. Org. Lett.* **2010**, *12*, 5450-5453. For thiourea **II** see Vakulya, B. *et al. Org. Lett*. **2010**, *7*, 1967-1969.

[2] For 3-methoxynaphthalen-2-ol (**1h**) see Sivapackiam, J. *et al. Dalton Trans*. **2010**, *39*, 5842-5850. For methyl 6-hydroxy-1-naphthoate (**1i**) see Harmange, J.-C. *et al. J. Med. Chem*. **2008**, *51*, 1649-1667.

[3] Frimpong, K. *et al. J.* Org. Chem. **2009**, *74*, 5861-5870. Tissot, M. *et al. Chem. Eur. J.* **2013**, *19*, 11352-11363.

## Typical procedures and characterization data for compounds 3

### General procedure for the enantioselective Friedel-Crafts reaction

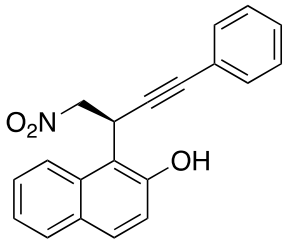
A vial containing 2-naphthol **1** (0.1 mmol) and chiral Rawal's squaramide **IV** (0.002 mmol, 0.8 mg) was purged with a stream of $N_2$ during 10 minutes. Then, the mixture was dissolved in 0.5 mL of $CHCl_3$ and a solution of nitroalkenyne **2** (0.12 mmol) in 0.5 mL of $CHCl_3$ was added at -20 °C. The mixture was stirred at this temperature until TLC analysis indicated full conversion of the starting material. Finally, purification by flash chromatography on silica gel with mixtures hexane:AcOEt afforded compounds **3** in an enantiomerically enriched fashion.

### General procedure for the non-enantioselective Friedel-Crafts reaction

2-Naphthol **1** (0.1 mmol), nitroalkenyne **2** (0.12 mmol) and non-chiral 3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-((3-dimethylamino)propyl)amino)cyclobu-3-en-1,2-dione (0.01 mmol, 4.1 mg) were weighted in a reaction flask. Then 1 mL of $CH_2Cl_2$ was added and the mixture was stirred at room temperature until TLC analysis indicated full conversion of the starting material. Finally, purification by flash chromatography on silica gel with mixtures hexane:AcOEt afforded compounds **3** in a racemic fashion.

### (*S*)-1-(1-Nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3a)

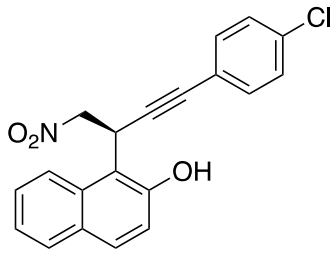
The enantiomeric excess (96% ee) was determined by chiral HPLC (Phenomenex, Amylose 1), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 5.7 min, minor enantiomer $t_r$ = 6.8 min. After purification with flash chromatography (hexane/AcOEt 80:20) the product was obtained as a brown oil in 88% yield (27.9 mg, 0.088 mmol). $[\alpha]^{20}_D$= -9.9 (c 0.46, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.11 (d, *J* = 8.6 Hz, 1H), 7.76 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.70 (d, *J* = 8.9 Hz, 1H), 7.53 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.41 – 7.31 (m, 3H), 7.30 – 7.18 (m, 3H), 7.06 (d, *J* = 8.9 Hz, 1H), 6.51 (s, 1H), 5.71 (dd, *J* = 9.8, 5.8 Hz, 1H), 4.95 (dd, *J* = 12.3, 9.9 Hz, 1H), 4.65 (dd, *J* = 12.3, 5.8, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 152.7 (C, $sp^2$), 131.89 (2·CH), 131.6 (C, $sp^2$), 130.8 (CH), 129.7 (C, $sp^2$), 129.2 (CH), 129.0 (CH), 128.4 (2·CH), 127.6 (CH), 123.9 (CH), 121.6 (CH), 121.5 (C, $sp^2$), 119.0 (CH), 112.1 (C, $sp^2$), 86.8 (C, *sp*), 84.4 (C, *sp*), 77.1 ($CH_2$), 28.7 (CH). **HRMS** (ESI) m/z 318.1119 [M+H]+, $[C_{20}H_{16}NO_3]^+$ requires 318.1125.

### (*S*)-1-(4-(4-Chlorophenyl)-1-nitrobut-3-yn-2-yl)naphthalen-2-ol (3b)

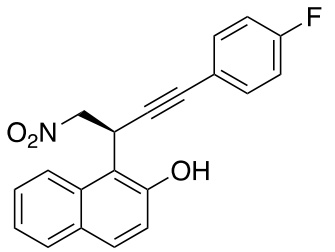
The enantiomeric excess (98% ee) was determined by chiral HPLC (Phenomenex, Amylose-1), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 7.6 min, minor enantiomer $t_r$ = 6.2 min. After purification with flash chromatography (hexane/AcOEt 70:30) the product was obtained as a brown oil in 94% yield (33 mg, 0.094 mmol). $[[\alpha]^{20}_D$ = -62.5 (c 0.55, $CHCl_3$).




**$^{1}$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.10 (d, *J* = 8.6 Hz, 1H), 7.73 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.50 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.31 (ddd, *J* = 8.0, 6.8, 1.0 Hz, 1H), 7.25 – 7.17 (m, 3H), 7.16 (d, *J* = 2.6 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.27 (s, 1H), 5.69 (dd, *J* = 9.7, 5.8 Hz, 1H), 4.96 (dd, *J* = 12.4, 9.7 Hz, 1H), 4.64 (dd, *J* = 12.3, 5.9 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 152.4 (C), 134.9 (C), 133.0 (2·CH), 131.6 (C, *sp*$^2$), 130.85 (CH), 129.67 (C, *sp*$^2$), 129.21 (CH), 128.68 (2·CH), 127.57 (CH), 123.85 (CH), 121.8 (CH), 120.2 (C, *sp*$^2$), 118.7 (CH), 112.2 (C, *sp*$^2$), 85.8 (C, *sp*), 85.1 (C, *sp*), 77.2 ($CH_2$), 28.6 (CH). **HRMS** (ESI) m/z: 369.1006 $[M+NH_4]^+$, $[C_{20}H_{18}ClN_2O_3]^+$ requires 369.1000.

**(*S*)-1-(4-(4-Fluorophenyl)-1-nitrobut-3-yn-2-yl)naphthalen-2-ol (3c)**

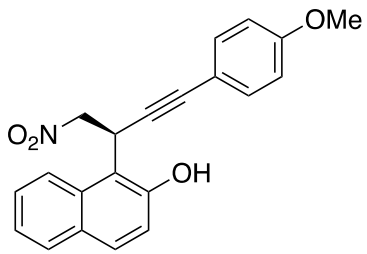
The enantiomeric excess (94% ee) was determined by chiral HPLC (Chiralcel, OD-H), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 12.9 min, minor enantiomer $t_r$ = 7.9 min. After purification with flash chromatography (hexane/AcOEt 90:10) the product was obtained as a brown oil in 94% yield (31 mg, 0.094 mmol). $[\alpha]^{20}_D$= -39.5 (c 0.6, $CHCl_3$).




**$^{1}$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.20 (d, *J* = 8.6 Hz, 1H), 7.83 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.60 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.48 – 7.34 (m, 3H), 7.13 (d, *J* = 8.9 Hz, 1H), 7.07 – 6.84 (m, 2H), 6.49 (s, 1H), 5.78 (dd, *J* = 9.8, 5.8 Hz, 1H), 5.04 (dd, *J* = 12.3, 9.8 Hz, 1H), 4.73 (dd, *J* = 12.3, 5.8 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 162.8 (d, $J_{C\text{-}F}$ = 250.5 Hz, C), 152.5 (C), 133.8 (d, $J_{C\text{-}F}$ = 8.5 Hz, 2·CH), 131.6 (C, *sp*$^2$), 130.8 (CH), 129.7 (C, *sp*$^2$), 129.2 (CH), 127.6 (CH), 123.9 (CH), 121.7 (CH), 118.8 (CH), 117.7 (d, $J_{C\text{-}F}$ = 3.5 Hz, C, *sp*$^2$), 115.7 (d, $J_{C\text{-}F}$ = 22.2 Hz, 2·CH), 112.2 (C, *sp*$^2$), 85.4 (C, *sp*), 84.4 (C, *sp*) ,77.1 ($CH_2$) , 28.6 (CH). **$^{19}$F NMR** (282 MHz, $CDCl_3$) $\delta$ -109.65. **HRMS** (ESI) m/z: 336.1038 $[M+H]^+$, $[C_{20}H_{15}FNO_3]^+$ requires 336.1030.

**(*S*)-1-(4-(4-Methoxyphenyl)-1-nitrobut-3-yn-2-yl)naphthalen-2-ol (3d)**

The enantiomeric excess (91% ee) was determined by chiral HPLC (Phenomenex, i-Amylose-1), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 8.3 min, minor enantiomer $t_r$ = 7.4 min. After purification with flash chromatography ($CH_2Cl_2$) the product was obtained as a brown oil in 75% yield (26.1 mg, 0.075 mmol). $[\alpha]^{20}_D$= -27.2 (c 0.4, $CHCl_3$).

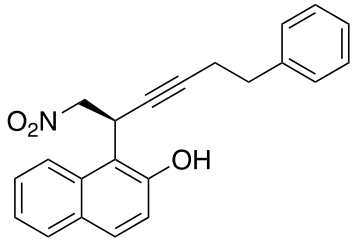



**$^{1}$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.16 (d, *J* = 8.6 Hz, 1H), 7.82 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.59 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.47 – 7.33 (m, 3H), 7.13 (d, *J* = 8.9 Hz, 1H), 6.89 – 6.75 (m, 3H), 5.76 (dd, *J* = 9.9, 5.7 Hz, 1H), 4.98 (dd, *J* = 12.3, 10 Hz, 1H), 4.70 (dd, *J* = 12.3, 5.7 Hz, 1H), 3.80 (s, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 160.2 (C, *sp*$^2$), 153.0 (C, *sp*$^2$), 133.4 (2·CH), 131.6 (C, *sp*$^2$), 130.8 (CH), 129.7 (C, *sp*$^2$), 129.3 (CH), 12.6 (CH), 123.9 (CH), 121.6 (CH), 119.2 (CH), 114.1 (2·CH),

113.4 (C, *sp²*), 112.2 (C, *sp²*), 87.2 (C, *sp*), 82.9 (C, *sp*), 77.2 ($CH_2$), 55.4 ($CH_3$), 28.9 (CH). **HRMS** (ESI) m/z: 348.1228 $[M+H]^+$, $[C_{21}H_{18}NO_4]^+$ requires 348.1230.

**(*S*)-1-(1-Nitro-6-phenylhex-3-yn-2-yl)naphthalen-2-ol (3e)**

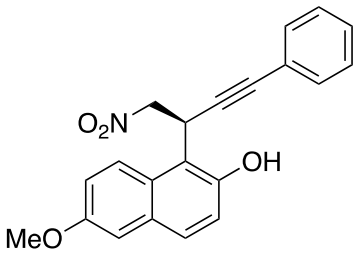
The enantiomeric excess (95% ee) was determined by chiral HPLC (Chiralpak, AS-H), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 8.3 min, minor enantiomer $t_r$ = 7.4 min. After purification with flash chromatography ($CH_2Cl_2$) the product was obtained as a brown oil in 96% yield (33 mg, 0.096 mmol). $[\alpha]^{20}_D$= -49.7 (c 0.66, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 7.98 (d, *J* = 8.6 Hz, 1H), 7.78 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.53 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.37 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 7.31 – 7.15 (m, 5H), 7.08 (d, *J* = 8.9 Hz, 1H), 6.71 (s, 1H), 5.53 – 5.36 (m, 1H), 4.76 (dd, *J* = 12.4, 10.3 Hz, 1H), 4.50 (dd, *J* = 12.4, 5.4 Hz, 1H), 2.82 (t, *J* = 7.4 Hz, 2H), 2.57 – 2.52 (m, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 153.1 (C, *sp²*), 139.9 (C, *sp²*), 131.3 (C, *sp²*), 130.6 (CH), 129.5 (C, *sp²*), 129.1 (CH), 128.5 (2·CH), 128.4 (2·CH), 127.5 (CH), 126.5 (CH), 123.7 (CH), 121.3 (CH), 119.4 (CH), 111.9 (C, *sp²*), 87.6 (C, *sp*), 77.1 ($CH_2$), 76.3 (C, *sp*), 34.5 ($CH_2$), 28.3 (CH), 20.9 ($CH_2$). **HRMS** (ESI) m/z: 346.1425 $[M+H]^+$, $[C_{22}H_{20}NO_3]^+$ requires 346.1438.

**(*S*)-6-Methoxy-1-(1-nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3f)**

The enantiomeric excess (94% ee) was determined by chiral HPLC (Phenomenex, i-Amylose 1), hexane-*i*PrOH 80:20, 1 mL/min, minor enantiomer $t_r$ = 6.8 min, major enantiomer $t_r$ = 7.7 min. After purification with flash chromatography (hexane/AcOEt 90:10) the product was obtained as a brown oil in 85% yield (29.5 mg, 0.085 mmol). $[\alpha]^{20}_D$= -1.9 (c 0.59, $CHCl_3$).

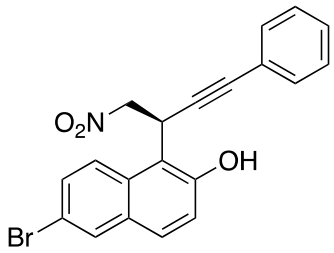



**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.06 (d, *J* = 9.3 Hz, 1H), 7.59 (d, *J* = 8.9 Hz, 1H), 7.39 – 7.36 (m, *J* = 2H), 7.29 – 7.19 (m, 4H), 7.09 (d, *J* = 2.7 Hz, 1H), 7.04 (d, *J* = 8.9 Hz, 1H), 6.31 (s, 1H), 5.68 (dd, *J* = 9.7, 5.9 Hz, 1H), 4.96 (dd, *J* = 12.3, 9.7 Hz, 1H), 4.66 (dd, *J* = 12.3, 5.9 Hz, 1H), 3.86 (s, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 156.0 (C, *sp²*), 150.9 (C, *sp²*), 131.8 (2·CH), 130.8 (C, *sp²*), 129.4 (CH), 128.9 (CH), 128.3 (2·CH), 126.7 (C, *sp²*), 123.3 (CH), 121.6 (C, *sp²*), 119.8 (CH), 119.4 (CH), 112.8 (C, *sp²*), 107.6 (CH), 86.5 (C, *sp*), 84.7 (C, *sp*), 77.2 ($CH_2$), 55.3 ($CH_3$), 28.8 (CH). **HRMS** (ESI) m/z: 348.1236 $[M+H]^+$, $[C_{21}H_{18}NO_4]^+$ requires 348.1230.

**(*S*)-6-Bromo-1-(1-nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3g)**

The enantiomeric excess (98% ee) was determined by chiral HPLC (Chiralcel, OD-H), hexane-iPrOH 90:10, 1 mL/min, major enantiomer $t_r$ = 15.8 min, minor enantiomer $t_r$ = 19.0 min. After purification with flash chromatography (hexane/AcOEt 90:10) the

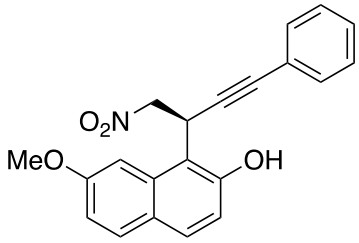
product was obtained as a brown oil in 82% yield (32 mg, 0.082 mmol). $[\alpha]^{20}_D$= -17.5 (c 0.55, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.01 (d, *J* = 9.2 Hz, 1H), 7.89 (d, *J* = 2.1 Hz, 1H), 7.69 – 7.50 (m, 2H), 7.36 (dd, *J* = 7.7, 1.9 Hz, 2H), 7.29 – 7.18 (m, 3H), 7.06 (d, *J* = 8.9 Hz, 1H), 6.42 (s, 1H), 5.66 (dd, *J* = 9.4, 6.1 Hz, 1H), 4.93 (dd, *J* = 12.4, 9.4 Hz, 1H), 4.66 (dd, *J* = 12.4, 6.2 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 152.9 (C, $sp^2$), 131.9 (2·CH), 131.1 (CH), 130.9 (C, $sp^2$), 130.8 (CH), 130.3 (C, $sp^2$), 129.9 (CH), 129.1 (CH), 128.5 (2·CH), 123.7 (CH), 121.4 (C, $sp^2$), 120.1 (CH), 117.6 (C, $sp^2$), 112.8 (C, $sp^2$), 86.9 (C, *sp*), 84.2 (C, *sp*), 77.1 ($CH_2$), 28.7 (CH). **HRMS** (ESI) m/z: 396.0221 $[M+H]^+$, $[C_{20}H_{15}BrNO_3]^+$ requires 396.0230.

**(*S*)-7-Methoxy-1-(1-nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3h)**

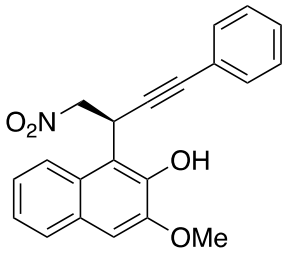
The enantiomeric excess (96% ee) was determined by chiral HPLC (Phenomenex, Cellulose-4), hexane-*i*PrOH 90:10, 1 mL/min, major enantiomer $t_r$ = 16.8 min, minor enantiomer $t_r$ = 11.7 min. After purification with flash chromatography (hexane/AcOEt 80:20) the product was obtained as a brown oil in 99% yield (34.2 mg, 0.099 mmol). $[\alpha]^{20}_D$= -1.8 (c 0.68, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 7.64 (d, *J* = 8.9 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.48 (d, *J* = 1.8 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.28 – 7.18 (m, 3H), 7.00 (dd, *J* = 8.9, 2.4 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 1H), 6.36 (s, 1H), 5.67 (dd, *J* = 9.7, 5.8 Hz, 1H), 4.96 (dd, *J* = 12.2, 9.7 Hz, 1H), 4.66 (dd, *J* = 12.2, 5.8 Hz, 1H), 3.89 (s, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 159.0 (C, $sp^2$), 153.1 (C, $sp^2$), 133.1 (C, $sp^2$), 131.8 (2·CH), 130.7 (CH), 130.5 (CH), 128.9 (CH), 128.4 (2·CH), 125.0 (C, $sp^2$), 121.6 (C, $sp^2$), 116.2 (CH), 115.9 (CH), 111.3 (C, $sp^2$), 101.3 (CH), 86.7 (C, *sp*), 84.7 (C, *sp*), 77.1 ($CH_2$), 55.4 ($CH_3$), 28.9 (CH). **HRMS** (ESI) m/z: 365.1499 $[M+NH_4]^+$, $C_{21}H_{21}N_2O_4^+$ requires 365.1496.

**(S)-3-Methoxy-1-(1-nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3i)**

The enantiomeric excess (95% ee) was determined by chiral HPLC (Chiralcel, OD-H), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 13.5 min, minor enantiomer $t_r$ = 16.5 min. After purification with flash chromatography (hexane/AcOEt 90:10) the product was obtained as a brown oil in 95% yield (33 mg, 0.095 mmol). $[\alpha]^{20}_D$= -16.3 (c 0.69, $CHCl_3$).

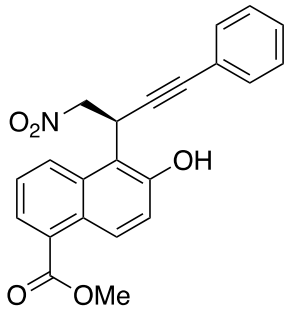



**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.21 (d, *J* = 8.5 Hz, 1H), 7.61 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.35 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.30 – 7.24 (m, 3H), 7.16 - 7.14 (m, 3H), 7.01 (s, 1H), 6.32 (s, 1H), 5.70 (dd, *J* = 9.0, 6.6 Hz, 1H), 5.09 (dd, *J* = 12.3, 9.0 Hz, 1H), 4.74 (dd, *J* = 12.3, 6.6 Hz, 1H), 3.90 (s, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 146.4

(C, *sp²*), 144.0 (C, *sp²*), 131.7 (2·CH), 129.2 (C, *sp²*), 128.3 (CH), 128.1 (2·CH), 127.8 (CH), 127.1 (C, *sp²*), 124.9 (CH), 124.1 (CH), 122.7 (C, *sp²*), 122.6 (CH), 112.8 (C, *sp²*), 106.5 (CH), 85.7 (C, *sp*), 84.2 (C, *sp*), 77.2 ($CH_2$), 56.0 ($CH_3$), 28.3 (CH). **HRMS** (ESI) m/z: 348.1236 $[M+H]^+$, $[C_{21}H_{18}NO_4]^+$ requires 348.1230. **HRMS** (ESI) m/z: 348.1232 $[M+H]^+$, $[C_{21}H_{18}NO_4]^+$ requires 348.1230.

**Methyl (*S*)-3-hydroxy-4-(1-nitro-4-phenylbut-3-yn-2-yl)-1-naphthoate (3j)**

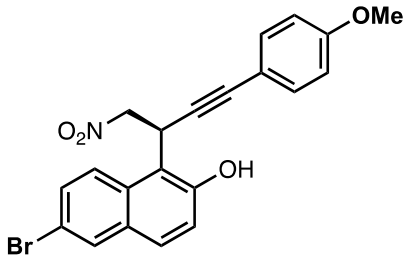
The enantiomeric excess (95% ee) was determined by chiral HPLC (Phenomenex, i-Amylose-1), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 11.8 min, minor enantiomer $t_r$ = 9.2 min. After purification with flash chromatography (hexane/AcOEt 90:10) the product was obtained as a brown oil in 75% yield (28 mg, 0.075 mmol). $[\alpha]^{20}_D$= -35.6 (c 0.47, $CHCl_3$).




**$^1$H NMR** (300 MHz, CDCl3) *δ* 8.76 (d, *J* = 9.4 Hz, 1H), 8.42 (d, *J* = 8.7 Hz, 1H), 8.00 (dd, *J* = 7.3, 1.0 Hz, 1H), 7.55 (dd, *J* = 8.7, 7.3 Hz, 1H), 7.38 – 7.34 (m, 2H), 7.32 – 7.22 (m, 3H), 7.17 (d, *J* = 9.4 Hz, 1H), 6.72 (s, 1H), 5.77 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.99 (dd, *J* = 12.3, 9.5 Hz, 1H), 4.69 (dd, *J* = 12.4, 6.0 Hz, 1H), 3.95 (s, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) *δ* 168.3 (C, *sp²*), 152.6 (C, *sp²*), 132.4 (C, *sp²*), 131.8 (2·CH), 128.9 (CH), 128.5 (C, *sp²*), 128.4 (CH), 128.3 (2·CH), 127.6 (CH), 127.4 (C, *sp²*), 126.7(CH), 126.1 (CH), 121.6 (C), 120.3 (CH), 112.8 (C, *sp²*), 86.4 (C, *sp*), 84.7 (C, *sp*), 77.2 ($CH_2$), 52.4 ($CH_3$), 28.7 (CH). **HRMS** (ESI) m/z: 376.1172 $[M+H]^+$, $[C_{22}H_{18}NO_5]^+$ requires 376.1179.

**(*S*)-6-bromo-1-(4-(4-methoxyphenyl)-1-nitrobut-3-yn-2-yl)naphthalen-2-ol (3k)**

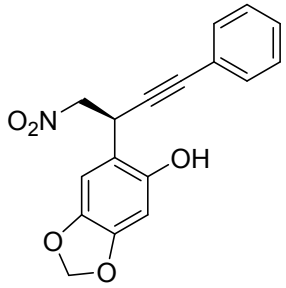
The enantiomeric excess (94% ee) was determined by chiral HPLC (Phenomenex, i-Amylose-1), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 11.9 min, minor enantiomer $t_r$ = 9.2 min. After purification with flash chromatography (hexane/AcOEt 90:10) the product was obtained as a brown oil in 92% yield (23 mg, 0.092 mmol). $[\alpha]^{20}_D$= -28.9 (c 0.35, $CHCl_3$).




**$^1$H NMR** (300 MHz, CDCl3) *δ* 8.05 (d, *J* = 9.1 Hz, 1H), 7.96 (d, *J* = 2.1 Hz, 1H), 7.71 – 7.61 (m, 2H), 7.40 – 7.32 (m, 2H), 7.19 – 7.10 (m, 1H), 6.88 – 6.78 (m, 2H), 6.74 (s, 1H), 5.69 (dd, *J* = 9.6, 6.0 Hz, 1H), 4.96 (dd, *J* = 12.3, 9.6 Hz, 1H), 4.70 (dd, *J* = 12.3, 6.0 Hz, 1H), 3.81 (s, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) *δ* 160.4 (C, *sp²*), 153.2 (C, *sp²*), 133.5 (CH), 131.2 (CH), 131.0 (C, *sp²*), 130.8 (CH), 130.3 (C, *sp²*), 130.0 (CH), 123.7 (CH), 120.4 (CH), 117.7 (C, *sp²*), 114.2 (CH), 113.4 (C, *sp²*), 112.8 (C, *sp²*), 87.5 (C, *sp*), 82.7 (C, *sp*), 77.3 ($CH_2$), 55.5 ($CH_3$), 29.0 ($CH_3$). **HRMS** (ESI) m/z: 426.0338 $[M+H]^+$, $[C_{21}H_{17}BrNO_4]^+$ requires 426.0335.

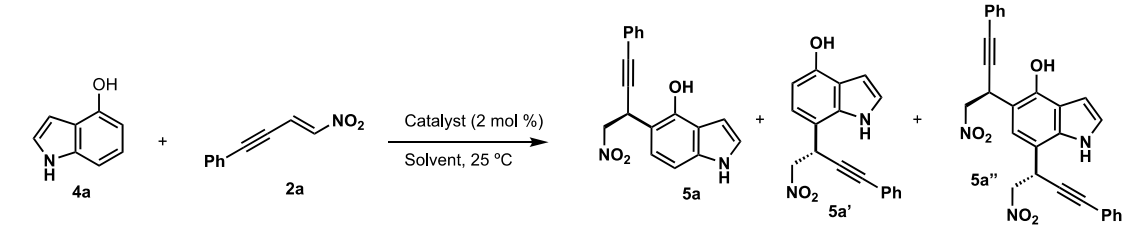
**(*S*)-6-(1-Nitro-4-phenylbut-3-yn-2-yl)benzo[*d*][1,3]dioxol-5-ol (3l)**

The enantiomeric excess (95% ee) was determined by chiral HPLC (Chiralcel, AD-H), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 14.5 min, minor enantiomer $t_r$ = 9.9 min. After purification with flash chromatography ($CH_2Cl_2$) the product was obtained as a brown oil in 81% yield (25 mg, 0.081 mmol). $[\alpha]^{20}_D$=-27.6

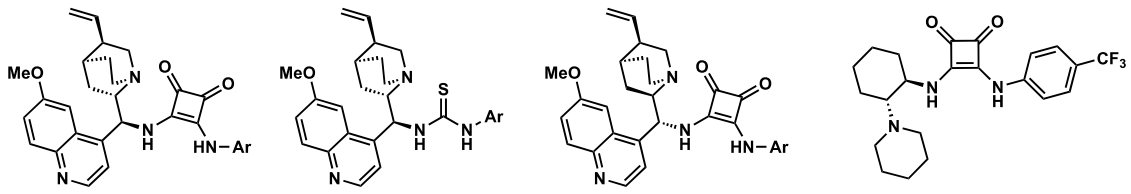


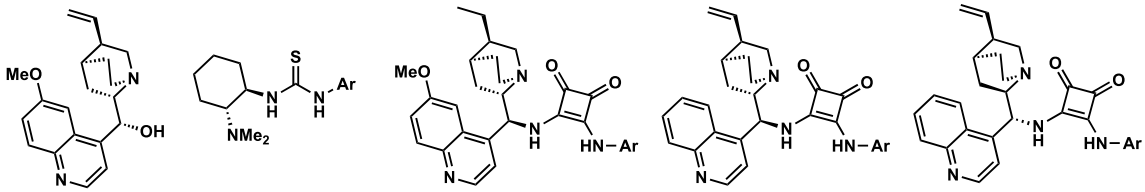

**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 7.50 – 7.40 (m, 2H), 7.40 – 7.27 (m, 3H), 7.03 (s, 1H), 6.41 (s, 1H), 5.92 (s, 2H), 5.40 (s, 1H), 4.97 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.75 (dd, *J* = 12.0, 5.7 Hz, 1H), 4.61 (dd, *J* = 12.0, 9.0 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 148.0 (C, $sp^2$), 147.6 (C, $sp^2$), 142.0 (C, $sp^2$), 131.8 (2·CH), 128.6 (CH), 128.3 (2·CH), 122.1 (C, $sp^2$), 113.7 (C, $sp^2$), 108.6 (CH), 101.4 ($CH_2$), 98.6 (CH), 85.9 (C, *sp*), 85.0 (C, *sp*), 78.4 ($CH_2$), 32.1 (CH). **HRMS** (ESI) m/z: 312.0870 $[M+H]^+$, $[C_{17}H_{14}NO_5]^+$ requires 312.0866.

## Optimization for the enantioselective Friedel-Crafts reaction with hydroxyindoles




Ar = 3,5-$(CF_3)_2C_6H_3$-




| Entry | Catalyst | Solvent | 4a : 2a (equiv.) | Time (h) | Yield (%) | 5a:5a':5a'' | ee 5a (%) |
|---|---|---|---|---|---|---|---|
| **1** | V | $CHCl_3$ | 1.5 : 1.0 | 48 | 14 | 1:1:1 | 35 |
| **2** | II | $CHCl_3$ | 1.5 : 1.0 | 18 | 45 | 5:1:2 | -82 |
| **3** | VI | $CHCl_3$ | 1.5 : 1.0 | 18 | 32 | 3:1:2 | 35 |
| **4** | III | $CHCl_3$ | 1.5 : 1.0 | 18 | 57 | 9:1:2 | 62 |
| **5** | IX | $CHCl_3$ | 1.5 : 1.0 | 18 | 54 | 9:1:2 | 57 |
| **6** | I | $CHCl_3$ | 1.5 : 1.0 | 18 | 66 | 15:1:3 | -83 |
| **7** | VIII | $CHCl_3$ | 1.5 : 1.0 | 18 | 73 | 8:1:2 | -85 |
| **8** | VII | $CHCl_3$ | 1.5 : 1.0 | 18 | 72 | 11:1:1 | -85 |
| **9** | IV | $CHCl_3$ | 1.5 : 1.0 | 18 | 78 | 13:1:3 | 96 |
| **10** | IV | $CH_2Cl_2$ | 1.5 : 1.0 | 2 | 66 | 18:1:5 | 96 |
| **11** | IV | DCE | 1.5 : 1.0 | 2 | 64 | 24:1:4 | 96 |
| **12** | IV | THF | 1.5 : 1.0 | 48 | 56 | 9:1:1 | 93 |
| **13** | IV | Toluene | 1.5 : 1.0 | 2 | 56 | 11:1:4 | 91 |
| **14** | IV | $CHCl_3$ | 1.1 : 1.0 | 15 | 61 | 39:1:5 | 96 |
| **15** | IV | $CHCl_3$ | 1.0 : 1.2 | 3 | 56 | 46:1:8 | 98 |
| **16** | IV | $CHCl_3$ (0 °C) | 1.1 : 1.0 | 15 | 66 | 20:1:4 | 96 |
| **17** | IV | $CHCl_3$ (0 °C) | 1.5 : 1.0 | 15 | 63 | 10:1:3 | 96 |

## Typical procedures and characterization data for compounds 5

### General procedure for the enantioselective Friedel-Crafts reaction

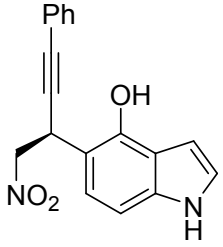
Hydroxyindole **4** (0.15 mmol), nitroalkenyne **2** (0.10 mmol) and Rawal's squaramide **IV** (0.84 mg, 0.002 mmol) were weighted in a reaction flask, which was purged then with a stream of $N_2$ during 10 minutes. Then, 1 mL of $CHCl_3$ was added and the reaction mixture was stirred at room temperature until TLC analysis indicated full conversion of the starting material. Finally, purification by flash chromatography on silica-gel with afforded compounds **5** in an enantiomerically enriched fashion.

### General procedure for the non-enantioselective Friedel-Crafts reaction

Hydroxyindole **4** (0.15 mmol), nitroalkenyne **2** (0.10 mmol) and non-chiral 3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-((2-(2-(dimethylamino)ethyl)amino)cyclobut-3-ene-1,2-dione (0.8 mg, 0.002 mmol) were weighted in a reaction flask. Then 1 mL of $CHCl_3$ was added and the reaction mixture was stirred at room temperature until TLC analysis indicated full conversion of the starting material. Finally, purification by flash chromatography on silica-gel with afforded compounds **5** in a racemic fashion.

### (*S*)-5-(1-Nitro-4-phenylbut-3-yn-2-yl)-1*H*-indol-4-ol (5a)

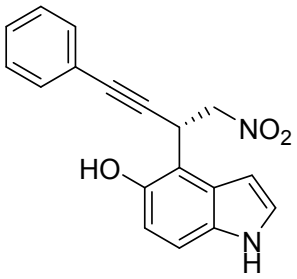
The enantiomeric excess (96% ee) was determined by Chiral HPLC (ChiralPak AS-H), hexane: *i*PrOH 80:20, 1 mL/min, major enantiomer $t_R$ = 22.2 min, minor enantiomer $t_R$ = 26.3 min. After purification with flash chromatography ($CH_2Cl_2$/AcOEt 98:2) the product was obtained as a yellow solid in 78% yield (24 mg, 0.078 mmol); m.p. 156-157 $^oC$. $[\alpha]^{20}_D$=-8.5 (c 0.19, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.24 (s, 1H), 7.51 – 7.42 (m, 2H), 7.36 – 7.28 (m, 4H), 7.19 (dd, *J* = 3.4, 2.4 Hz, 1H), 7.05 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.56 (ddd, *J* = 3.2, 2.1, 1.0 Hz, 1H), 5.60 (s, 1H), 5.17 (dd, *J* = 9.3, 5.9 Hz, 1H), 4.87 – 4.66 (m, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 146.2 (C, $sp^2$), 137.3 (C, $sp^2$), 131.9 (CH), 128.5 (CH), 128.3 (CH), 124.0 (CH), 123.3 (CH), 122.4 (C, $sp^2$), 118.0 (C, $sp^2$), 110.7 (C, $sp^2$), 104.8 (CH), 98.3 (CH), 85.9 (C, *sp*), 85.7 (C, *sp*), 78.9 ($CH_2$), 32.2 (CH). **HRMS** (ESI) m/z: 307.1075 $[M+H]^+$, $C_{18}H_{15}N_2O_3^+$ requires 307.1077.

**(*S*)-4-(1-Nitro-4-phenylbut-3-yn-2-yl)-1*H*-indol-5-ol (5b)**

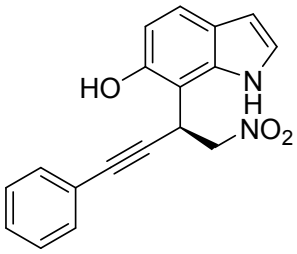
The enantiomeric excess (96% ee) was determined by Chiral HPLC (ChiralPak AS-H), hexane: *i*PrOH 80:20, 1 mL/min, major enantiomer $t_R$ = 16.1 min, minor enantiomer $t_R$ = 22.6 min. After purification with flash chromatography (hexane/AcOEt 70:30) the product was obtained as a green oil in 94% yield (29 mg, 0.094 mmol); $[\alpha]^{20}_D$=-19.1 (c 0.20, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 77.93 (s, 1H), 77.22 – 77.14 (m, 2H), 77.09 – 77.01 (m, 3H), 77.00 – 76.96 (m, 2H), 76.53 (dd, *J* = 8.6, 0.5 Hz, 1H), 76.51 (ddd, *J* = 3.1, 2.1, 1.0 Hz, 1H), 75.27 (s, 1H), 75.15 (dd, *J* = 9.4, 6.3 Hz, 1H), 74.70 (dd, *J* = 12.2, 9.4 Hz, 1H), 74.49 (dd, *J* = 12.2, 6.3 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 147.5 (C, $sp^2$), 131.8 (CH), 131.4 (C), 128.7 (CH), 128.3 (CH), 127.1 (C, $sp^2$), 125.6 (CH), 122.0 (C, $sp^2$), 113.3 (CH), 112.1 (CH), 110.8 (C, $sp^2$), 100.5 (CH), 85.6 (C, *sp*), 85.2 (C, *sp*), 77.2 ($CH_2$), 30.5 (CH). **HRMS** (ESI) m/z: 307.1080 $[M+H]^+$, $C_{18}H_{15}N_2O_3^+$ requires 307.1077.

**(*S*)-7-(1-Nitro-4-phenylbut-3-in-2-il)-1H-indol-6-ol (5c)**

The enantiomeric excess (96% ee) was determined by Chiral HPLC (Lux® 5 µm Amylose-1), hexane: *i*PrOH 80:20, 1 mL/min, major enantiomer $t_R$ = 9.6 min, minor enantiomer $t_R$ = 7.5 min. After purification with flash chromatography (hexane/AcOEt 70:30) the product was obtained as a yellow oil in 74% yield (23 mg, 0.075 mmol); $[\alpha]^{20}_D$ +15.6 (c 0.99, $CHCl_3$).

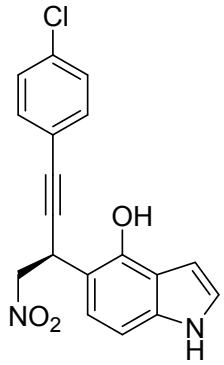



**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 9.03 (s, 1H), 7.51 – 7.42 (m, 3H), 7.40 – 7.29 (m, 3H), 7.14 (dd, *J* = 3.3, 2.4 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.50 (dd, *J* = 3.3, 2.1 Hz, 1H), 5.49 (dd, *J* = 8.6, 6.4 Hz, 1H), 5.09 (s, 1H), 4.86 – 4.70 (m, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 148.3 (C, $sp^2$), 135.3 (C, $sp^2$), 131.8 (CH), 129.0 (CH), 128.5 (CH), 123.9 (CH), 123.7 (C, $sp^2$), 121.7 (C, $sp^2$), 121.5 (CH), 110.0 (CH), 103.0 (C, $sp^2$), 102.8 (CH), 86.0 (C, *sp*), 85.3 (C, *sp*), 77.2 ($CH_2$), 28.9 (CH). **HRMS** (ESI) m/z: 307.1072 $[M+H]^+$, $C_{18}H_{15}N_2O_3^+$ requires 307.1077.

**(*S*)-5-(4-(4-Chlorophenyl)-1-nitrobut-3-in-2-il)-1H-indol-4-ol (5d)**

The enantiomeric excess (94% ee) was determined by Chiral HPLC (Lux® 5 µm Amylose-1), hexane: *i*PrOH 80:20, 1 mL/min, major enantiomer $t_R$ = 20.4 min, minor enantiomer $t_R$ = 11.6 min. After purification with flash chromatography ($CH_2Cl_2$/AcOEt 98:2) the product was obtained as a green solid in 69% yield (24 mg, 0.070 mmol); m.p. 118-120 $^o$C. $[\alpha]^{20}_D$ -25.28 (c 1.01, $CHCl_3$).

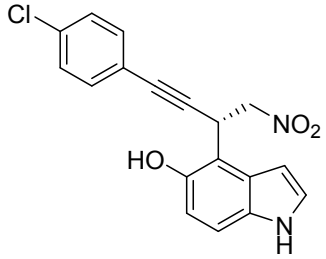
**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.20 (s, 1H), 7.33 (d, *J* = 2.0 Hz, 1H), 7.31 (d, *J* = 2.1 Hz, 1H), 7.23 (d, *J* = 1.3 Hz, 2H), 7.20 (d, *J* = 2.0 Hz, 1H), 7.12 (dd, *J* = 3.4, 2.4 Hz, 1H), 6.98 (dd, *J* = 8.5, 1.0 Hz, 1H), 6.48 (ddd, *J* = 3.3, 2.1, 1.0 Hz, 1H), 5.50 (s, 1H), 5.13 (dd, *J* = 9.4, 5.8 Hz, 1H), 4.79 – 4.58 (m, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 146.0 (C, $sp^2$), 137.3 (C, $sp^2$), 134.5



(C, *sp²*), 133.1 (CH), 128.6 (CH), 124.1 (CH), 123.1 (CH), 120.9 (C, *sp²*), 117.9 (C, *sp²*), 110.5 (C, *sp²*), 104.9 (CH), 98.1 (CH), 87.1 (C, *sp*), 84.4 (C, *sp*), 78.8 ($CH_2$), 32.1 (CH). **HRMS** (ESI) m/z: 341.0691 $[M+H]^+$, $C_{18}H_{14}ClN_2O_3^+$ requires 341.0687.

**(*S*)-4-(4-(4-Chlorophenyl)-1-nitrobut-3-in-2-il)-1H-indol-5-ol (5e)**

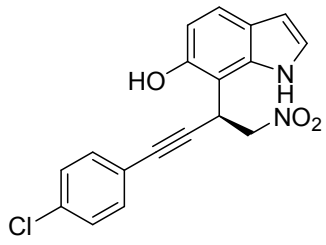
The enantiomeric excess (97% ee) was determined by Chiral HPLC (ChiralPak OD-H), hexane: *i*PrOH 80:20, 1 mL/min, major enantiomer $t_R$ = 14.8 min, minor enantiomer $t_R$ = 11.5 min. After purification with flash chromatography (hexane/AcOEt 70:30) the product was obtained as a yellow oil in 96% yield (32mg, 0.094 mmol); $[\alpha]_D^{20}$ -19.9 (c 1.00, $CHCl_3$).



**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.09 (s, 1H), 7.27 – 7.21 (m, 2H), 7.19 – 7.09 (m, 4H), 6.71 – 6.62 (m, 2H), 5.31 (dd, *J* = 9.4, 6.3 Hz, 1H), 5.25 (s, 1H), 4.86 (dd, *J* = 12.2, 9.4 Hz, 1H), 4.64 (dd, *J* = 12.2, 6.3 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 147.2 (C, *sp²*), 134.7 (C, *sp²*), 133.0 (CH), 131.4 (C, *sp²*), 128.2 (CH), 127.1 (C, *sp²*), 125.7 (CH), 120.7 (C, *sp²*), 113.1 (CH), 112.1 (CH), 110.7 (C, *sp²*), 100.5 (CH), 86.4 (C, *sp*), 84.2 (C, *sp²*), 77.3 ($CH_2$), 30.3 (CH). **HRMS** (ESI) m/z: 341.0684 $[M+H]^+$, $C_{18}H_{14}ClN_2O_3^+$ requies 341.0687.

**(*S*)-7-(4-(4-Chlorophenyl)-1-nitrobut-3-in-2-il)-*1H*-indol-6-ol (5f)**

The enantiomeric excess (95% ee) was determined by Chiral HPLC (ChiralPak AS-H), hexane: *i*PrOH 80:20, 1 mL/min, major enantiomer $t_R$ = 19.3 min, minor enantiomer $t_R$ = 13.3 min. After purification with flash chromatography (hexane/AcOEt 80:20) the product was obtained as a yellow oil in 97% yield (33 mg, 0.097 mmol); $[\alpha]_D^{20}$ +2.7 (c 0.98, $CHCl_3$).



**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.94 (s, 1H), 7.46 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.14 (dd, *J* = 3.3, 2.4 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.51 (dd, *J* = 3.3, 2.1 Hz, 1H), 5.47 (dd, *J* = 8.8, 6.2 Hz, 1H), 5.19 (s, 1H), 4.86 – 4.69 (m, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 148.3 (C, *sp²*), 135.2 (C, *sp²*), 135.1 (C, *sp²*), 133.1 (CH), 128.8 (CH), 123.9 (CH), 123.7 (C, *sp²*), 121.5 (CH), 120.2 (C, *sp²*), 110.0 (CH), 102.9 (CH), 102.8 (C, *sp²*), 86.3 (C, *sp*), 84.8 (C, *sp*), 77.3 ($CH_2$), 28.9 (CH). **HRMS** (ESI) m/z: 341.0681 $[M+H]^+$, $C_{18}H_{14}ClN_2O_3^+$ requires 341.0687.

## Typical procedures and characterization data for compounds 6

### General procedure for the enantioselective tandem Friedel-Crafts/hydroalkoxylation reaction

A vial containing 2-naphthol **1** (0.1 mmol) and chiral Rawal's squaramide **IV** (0.002 mmol, 0.8 mg) was purged with a stream of $N_2$ during 10 minutes. Then, the mixture was dissolved in 0.5 mL of $CHCl_3$ and a solution of nitroalkenyne **2** (0.12 mmol) in 0.5 mL of $CHCl_3$ was added at -20 °C.

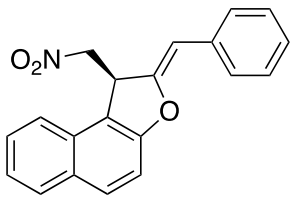
The mixture was stirred at this temperature until TLC analysis indicated full conversion of the starting material. Then, both AgOTf (5 mol%, 1.3 mg) and $K_2CO_3$ (0.2 mmol, 28 mg) were added. Finally, purification by flash chromatography on silica gel with mixtures hexane:$CH_2Cl_2$ afforded compounds **6** in an enantiomerically enriched fashion.

### General procedure for the non-enantioselective tandem Friedel-Crafts/hydroalkoxylation reaction

2-Naphtol **1** (0.1 mmol), nitroalkenyne **2** (0.12 mmol) and non-chiral 3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-((3-dimethylamino)propyl)amino)cyclobu-3-en-1,2-dione (0.01 mmol, 4.1 mg) were weighted in a reaction flask. Then 1 mL of $CH_2Cl_2$ was added and the mixture was stirred at room temperature until TLC analysis indicated full conversion of the starting material. Then, both AgOTf (5 mol%, 1.3 mg) and $K_2CO_3$ (0.2 mmol, 28 mg) were added. Finally, purification by flash chromatography on silica gel with mixtures hexane:$CH_2Cl_2$ afforded compounds **6** in a racemic fashion.

### (*S*,*Z*)-2-Benzylidene-1-(nitromethyl)-1,2-dihydronaphtho[2,1-*b*]furan (6a)

The enantiomeric excess (97% ee) was determined by chiral HPLC (Chiralcel, OD-H), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 22.1 min, minor enantiomer $t_r$ = 41.5 min. After purification with flash chromatography ($CH_2Cl_2$) the product was obtained as a reddish oil in 63% yield (22 mg, 90% purity, 0.063 mmol). $[\alpha]^{20}_D$= -49.7 (c 0.35, $CHCl_3$).

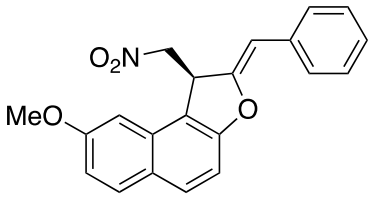



**$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 7.90 (d, *J* = 8.3 Hz, 1H), 7.87 (d, *J* = 9.1 Hz, 1H), 7.73 – 7.70 (m, 3H), 7.59 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.46 – 7.34 (m, 4H), 7.28 – 7.22 (m, 1H), 5.75 (d, *J* = 1.6 Hz, 1H), 5.30 (dd, *J* = 9.2, 2.4 Hz, 1H), 5.04 (dd, *J* = 13.1, 3.7 Hz, 1H), 4.64 (dd, *J* = 13.1, 9.2 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 156.0 (C), 154.5 (C), 134.3 (C), 131.4 (CH), 130.4 (C), 129.7 (CH), 129.3 (C), 128.6 (2·CH), 128.5 (2·CH), 128.1 (CH), 126.9 (CH), 124.3 (CH), 121.4 (CH), 115.1 (C), 111.9 (CH), 105.4 (CH), 78.3 ($CH_2$), 44.0 (CH). **HRMS** (ESI) m/z: 318.1120 $[M+H]^+$, $C_{20}H_{16}NO_3^+$ requires 318.1125.

### (*S*,*Z*)-2-Benzylidene-8-methoxy-1-(nitromethyl)-1,2-dihydronaphtho[2,1-*b*]furan (6b)

The enantiomeric excess (93% ee) was determined by chiral HPLC (Chiralcel, OD-H), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 28.9 min, minor enantiomer $t_r$ =

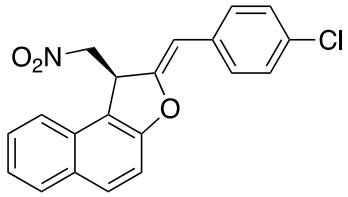
20.9 min. After purification with flash chromatography ($CH_2Cl_2$) the product was obtained as a brown oil in 67% yield (23 mg, 0.067 mmol). $[\alpha]^{20}_D$= -2.0 (c 0.45, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 7.80 – 7.66 (m, 4H), 7.43 – 7.36 (m, 2H), 7.28 – 7.24 (m, 1H), 7.19 (d, *J* = 8.8 Hz, 1H), 7.07 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.92 (d, *J* = 2.4 Hz, 1H), 5.76 (d, *J* = 1.6 Hz, 1H), 5.24 (dd, *J* = 8.2, 4.1 Hz, 1H), 4.99 (dd, *J* = 13.0, 4.3 Hz, 1H), 4.63 (dd, *J* = 12.9, 8.4 Hz, 1H), 3.95 (s, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 159.4 (C, $sp^2$), 156.5 (C, $sp^2$), 154.6 (C, $sp^2$), 134.3 (C, $sp^2$), 131.1 (CH), 131.1 (CH), 130.7 (C, $sp^2$), 128.5 (2·CH), 128.4 (2·CH), 126.8 (CH), 125.7 (C, $sp^2$), 116.7 (CH), 114.5 (C, $sp^2$), 109.1 (CH), 105.2 (CH), 100.2 (CH), 78.5 ($CH_2$), 55.5 ($CH_3$), 44.2 (CH). **HRMS** (ESI) m/z: 348.1238 $[M+H]^+$, $C_{21}H_{18}NO_4^+$ requires 348.1230.

**(*S*,*Z*)-2-(4-Chlorobenzylidene)-1-(nitromethyl)-1,2-dihydronaphtho[2,1-*b*]furan (6c)**

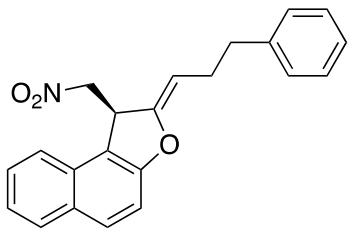
The enantiomeric excess (93% ee) was determined by chiral HPLC (Chiralcel, AD-H), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 11.4 min, minor enantiomer $t_r$ = 10.6 min. After purification with flash chromatography ($CH_2Cl_2$) the product was obtained as a brown oil in 45% yield (16 mg, 0.045 mmol). $[\alpha]^{20}_D$= -4.1 (c 0.25, $CHCl_3$).




**$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 7.91 (d, J = 8.3 Hz, 1H), 7.88 (d, J = 9.0 Hz, 1H), 7.72 (dd, J = 8.3, 0.7 Hz, 1H), 7.66 – 7.62 (m, 2H), 7.59 (ddd, J = 8.3, 6.9, 1.2 Hz, 1H), 7.44 (ddd, J = 8.1, 6.9, 1.1 Hz, 1H), 7.38 – 7.32 (m, 3H), 5.71 (d, J = 1.5 Hz, 1H), 5.30 (dd, J = 9.2, 2.3 Hz, 1H), 5.05 (dd, J = 13.1, 3.7 Hz, 1H), 4.64 (dd, J = 13.1, 9.3 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 155.8 (C, $sp^2$), 154.9 (C, $sp^2$), 132.7 (C, $sp^2$), 132.3 (C, $sp^2$), 131.5 (CH), 130.4 (C, $sp^2$), 129.8 (2·CH), 129.7 (CH), 129.2 (C, $sp^2$), 128.6 (2·CH), 128.2 (CH), 124.4 (CH), 121.4 (CH), 115.0 (C, $sp^2$), 111.8 (CH), 104.2 (C, $sp^2$), 78.1 ($CH_2$), 44.0 (CH). **HRMS** (ESI) m/z: 352.0731 $[M+H]^+$, $C_{20}H_{15}ClNO_3^+$ requires 352.0735.

**(*S*,*Z*)-1-(Nitromethyl)-2-(3-phenylpropylidene)-1,2-dihydronaphtho[2,1-*b*]furan (6d)**

The enantiomeric excess (92% ee) was determined by chiral HPLC (Chiralcel, AD-H), hexane-*i*PrOH 80:20, 1 mL/min, major enantiomer $t_r$ = 18.5 min, minor enantiomer $t_r$ = 28.4 min. After purification with flash chromatography ($CH_2Cl_2$) the product was obtained as a reddish oil in 68% yield (24 mg, 0.068 mmol). $[\alpha]^{20}_D$= -75.6 (c 0.38, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 7.85 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.53 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.31 – 7.14 (m, 6H), 5.06 (dd, *J* = 9.5, 2.0 Hz, 1H), 4.91 (dd, *J* = 12.8, 3.8 Hz, 1H), 4.81 (td, *J* = 7.3, 1.6 Hz, 1H), 4.43 (dd, *J* = 12.8, 9.6 Hz, 1H), 2.85 – 2.69 (m, 2H), 2.67 – 2.52 (m, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 155.9 (C, $sp^2$), 153.9 (C, $sp^2$), 141.6 (C, $sp^2$), 131.1 (CH), 120.0 (C, $sp^2$), 129.5 (CH), 129.5 (C, $sp^2$), 128.5 (2·CH), 128.3 (CH), 127.9 (CH), 125.9

(CH), 123.9 (CH), 121.3 (CH), 115.4 (C, *sp²*), 111.7 (CH), 104.9 (CH), 78.3 ($CH_2$), 42.2 (CH), 35.6 ($CH_2$), 27.1 ($CH_2$). **HRMS** (ESI) m/z: 346.1431 $[M+H]^+$, $C_{22}H_{20}NO_3^+$ requires 346.1438.

## Typical procedures and characterization data for compound 7

### General procedure for the enantioselective tandem Friedel-Crafts/hydroalkoxylation reaction

A vial containing 2-naphthol **1** (0.1 mmol) and chiral Rawal's squaramide **IV** (0.002 mmol, 0.8 mg) was purged with a stream of $N_2$ during 10 minutes. Then, the mixture was dissolved in 0.5 mL of $CHCl_3$ and a solution of nitroalkenyne **2** (0.12 mmol) in 0.5 mL of $CHCl_3$ was added at -20 °C.

Once finished the addition reaction; *p*-toluensulfonic acid (2 mg, 0.01 mmol), $Ph_3PAuCl$ (2.5 mg, 0.005 mmol) and AgOTf (1.4 mg, 0.0005 mmol) were added. The tube was coated with aluminium foil and purged with $N_2$ for 10 min. The reaction mixture was stirred at room temperature. Finally, the product was purified by flash chromatography using a mixture of hexane:$CH_2Cl_2$ as the mobile phase.

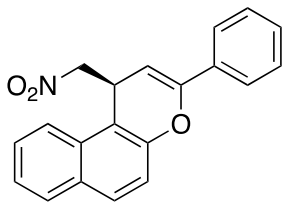
### General procedure for the non-enantioselective tandem Friedel-Crafts/hydroalkoxylation reaction

2-Naphtol **1a** (14.4 mg, 0.10 mmol, 1.0 eq.), nitroalkenyne **2a** (20.8 mg, 0.12 mmol, 1.2 eq.) and (non-chiral 3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-((3-dimethylamino)propyl)amino)cyclobu-3-en-1,2-dione (4.1 mg, 0.01 mmol) were weighted in a reaction flask. Then, 1 mL of $CHCl_3$ was added and the reaction mixture was stirred at -20 °C until TLC analysis indicated full conversion of the starting material.

Once finished the addition reaction; *p*-toluensulfonic acid (2 mg, 0.01 mmol), $Ph_3PAuCl$ (2.5 mg, 0.005 mmol) and AgOTf (1.4 mg, 0.0005 mmol) were added. The tube was coated with aluminium foil and purged with $N_2$ for 10 min. The reaction mixture was stirred at room temperature. Finally, the product was purified by flash chromatography using a mixture of hexane:$CH_2Cl_2$ as the mobile phase.

### (*S*)-1-(Nitromethyl)-3-phenyl-1H-benzo[*f*]chromene (7)

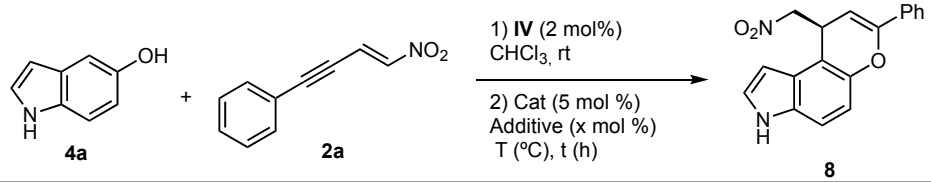
The enantiomeric excess (68% ee) was determined by chiral HPLC (Chiralcel, AD-H), hexane-*i*PrOH 90:10, 1 mL/min, major enantiomer $t_r$ = 8.2 min, minor enantiomer $t_r$ = 8.8 min. After purification with flash chromatography ($CH_2Cl_2$) the product was obtained as a brown oil in 81% yield (25.7 mg, 0.081 mmol). $[\alpha]_D^{25}$ +29.3 (c 0.10, $CHCl_3$).




**$^1$H NMR** (300 MHz, $CDCl_3$) $\delta$ 7.99 (d, *J* = 8.1 Hz, 1H), 7.92 – 7.86 (m, 1H), 7.83 (d, *J* = 8.9 Hz, 1H), 7.79 – 7.74 (m, 2H), 7.64 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.52 – 7.39 (m, 4H), 7.35 (d, *J* = 8.9 Hz, 1H), 5.78 (d, *J* = 5.5 Hz, 1H), 5.10 (ddd, *J* = 9.6, 5.6, 3.5 Hz, 1H), 4.85 (dd, *J* = 11.9, 3.5 Hz, 1H), 4.49 (dd, *J* = 12.0, 10.1 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 151.3 (C, *sp²*), 150.4 (C, *sp²*), 133.1

(C, *sp²*), 131.0 (C, *sp²*), 130.6 (C, *sp²*), 129.9 (CH), 129.3 (CH), 129.1 (CH), 128.5 (2·CH), 127.7 (CH), 125.1 (2·CH), 124.8 (CH), 121.2 (CH), 118.00 (CH), 110.0 (C, *sp²*), 95.5 (CH), 80.3 ($CH_2$), 31.7 (CH). **HRMS** (ESI) m/z: 318.1123 $[M+H]^+$, $C_{20}H_{16}NO_3^+$ requires 318.1125.

## Optimization for the enantioselective Friedel-Crafts reaction / Au-catalyzed cyclization




| Entry | Catalyst | Additive | T (ºC) | Time (h) | Yield (%) | ee (%) |
|---|---|---|---|---|---|---|
| **1** | AgOTf | $K_2CO_3$ (1 eq.) | rt | 24 | nr | nd |
| **2** | $Ph_3PAuCl$ | $K_2CO_3$ (1 eq.) | rt | 24 | nr | nd |
| **3** | $Ph_3PAuCl$/AgOTf | $K_2CO_3$ (1 eq.) | ta | 72 | 12 | nd |
| **4** | $Ph_3PAuCl$/AgOTf | $K_2CO_3$ (1 eq.) | 50 | 72 | nr | nd |
| **5** | $Ph_3PAuCl$/AgOTf | PTSA (0.1 eq.) | rt | 24 | 78 | 83 |

## Typical procedures and characterization data for compound 8

### General procedure for the enantioselective tandem Friedel-Crafts/hydroalkoxylation reaction

Hydroxyindole **4a** (20 mg, 0.15 mmol, 1.5 eq.), nitroalkenyne **2a** (17.3 mg, 0.10 mmol, 1.0 eq.) and Rawal's squaramide **IV** (0.84 mg, 0.002 mmol) were weighted in a reaction flask. After purging with a stream of $N_2$ for 10 minutes, 1 mL of $CHCl_3$ was added and the reaction mixture was stirred at room temperature until TLC analysis indicated full conversion of the starting material.

Then, *p*-toluensulfonic acid (2 mg, 0.01 mmol), $Ph_3PAuCl$ (2.5 mg, 0.005 mmol) and AgOTf (1.4 mg, 0.0005 mmol) were added. The tube was coated with aluminium foil and purged with $N_2$ for 10 minutes and the reaction was kept at room temperature. The product was purified by flash chromatography using a mixture of hexane:AcOEt as the mobile phase.

### General procedure for the non-enantioselective tandem Friedel-Crafts/hydroalkoxylation reaction

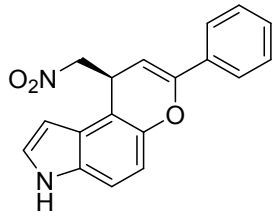
Hydroxyindole **4a** (20 mg, 0.15 mmol, 1.5 eq.), nitroalkenyne **2a** (17.3 mg, 0.10 mmol, 1.0 eq.) and non-chiral organocatalyst 3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-((2-(2-(dimethylamino)ethyl)amino)cyclobut-3-ene-1,2-dione (0.8 mg, 0.002 mmol) were weighted in a reaction flask. Then, 1 mL of $CHCl_3$ was added and the reaction mixture was stirred at room temperature until TLC analysis indicated full conversion of the starting material.

Once finished the addition reaction, the solvent was concentrated. Then, *p*-toluensulphonic acid (2 mg, 0.01 mmol), $Ph_3PAuCl$ (2.5 mg, 0.005 mmol) and AgOTf (1.4

mg, 0.0005 mmol) were added. The tube was coated with aluminium foil and purged with $N_2$ for 10 min. Finally, 1 mL of dry $CH_2Cl_2$ was added and the reaction was kept at room temperature. The product was purified by flash chromatography using a mixture of hexane:AcOEt as the mobile phase.

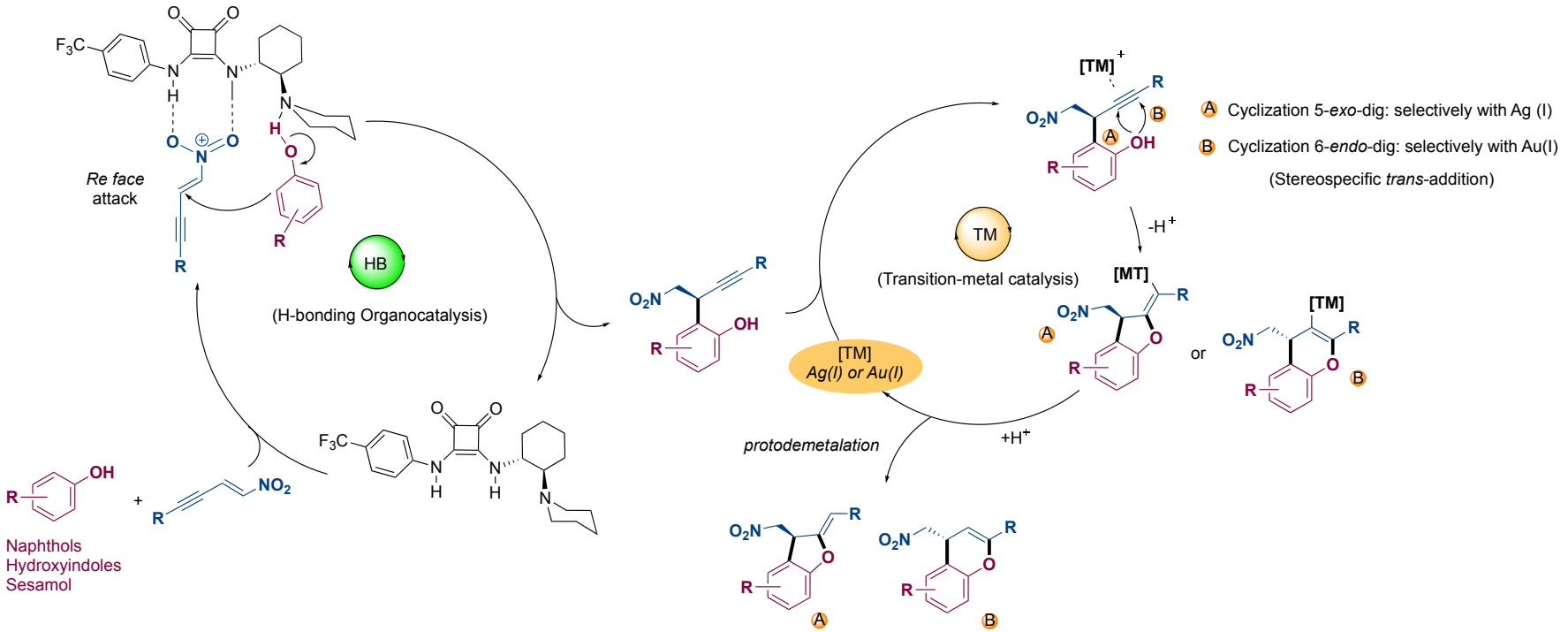
**(*S*)-9-(Nitromethyl)-7-phenyl-3,9-dihydropyrano[3,2-*e*]indole (8)**

The enantiomeric excess (83% ee) was determined by Chiral HPLC (ChiralPak AD-H), hexane: *i*PrOH 80:20, 1 mL/min, major enantiomer $t_R$ = 8.26 min, minor enantiomer $t_R$ = 9.45 min. After purification with flash chromatography (Hexane/AcOEt 70:30) the product was obtained as a yellow solid in 78% yield (24 mg, 0.078 mmol); m.p. 130-135 $^{o}$C. $[\alpha]_D^{20}$ +59.8 (c 0.35, $CHCl_3$).



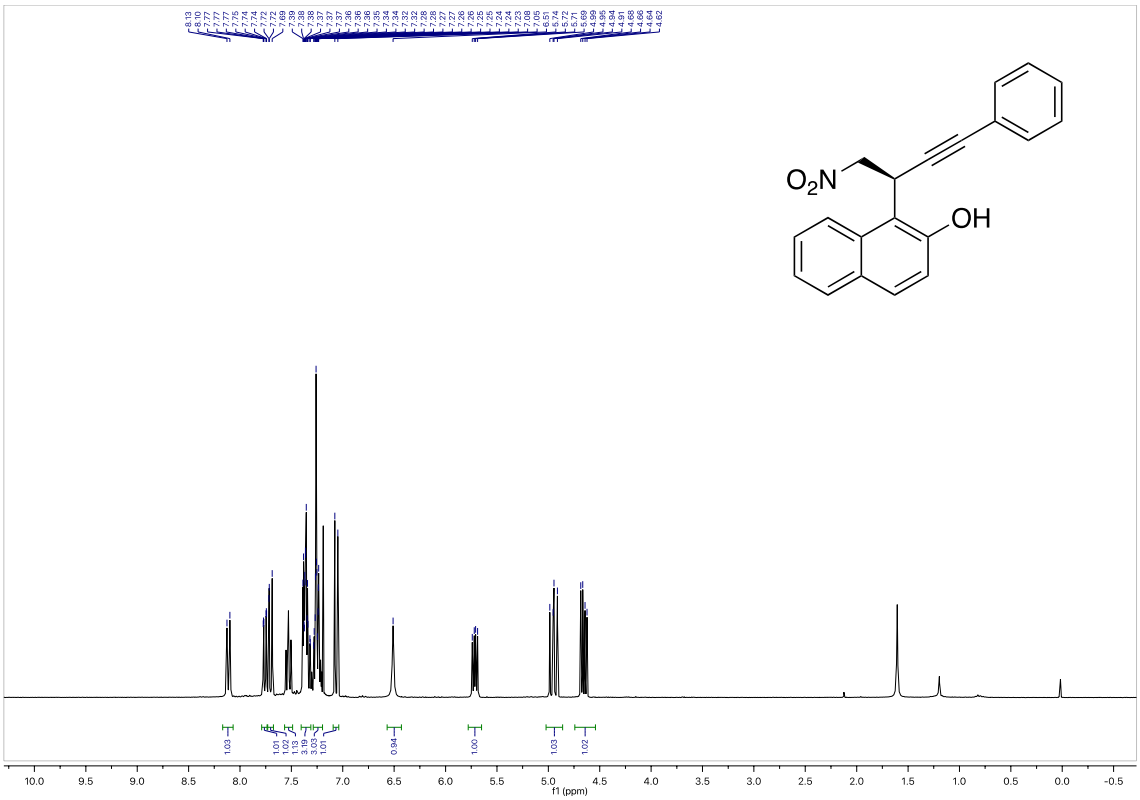

**$^{1}$H NMR** (300 MHz, $CDCl_3$) $\delta$ 8.31 (s, 1H), 7.81 – 7.69 (m, 2H), 7.51 – 7.24 (m, 6H), 7.05 (d, *J* = 8.8 Hz, 1H), 6.59 (ddd, *J* = 3.2, 2.0, 1.0 Hz, 1H), 5.64 (d, *J* = 4.9 Hz, 1H), 4.93 (dd, *J* = 11.4, 4.0 Hz, 1H), 4.89 – 4.80 (m, 1H), 4.53 (dd, *J* = 11.4, 9.4 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) $\delta$ 151.3 (C, $sp^2$), 146.2 (C, $sp^2$), 133.9 (C, $sp^2$), 132.3 (C, $sp^2$), 129.0 (CH), 128.4 (CH), 125.7 (CH), 125.4 (C, $sp^2$), 125.1 (CH), 112.7 (CH), 111.7 (CH), 108.0 (C, $sp^2$), 99.9 (CH), 94.5 (CH), 80.7 ($CH_2$), 33.4 (CH). **HRMS** (ESI) m/z: 307.1079 $[M+H]^+$, $C_{18}H_{15}N_2O_3^+$ requires 307.1077.

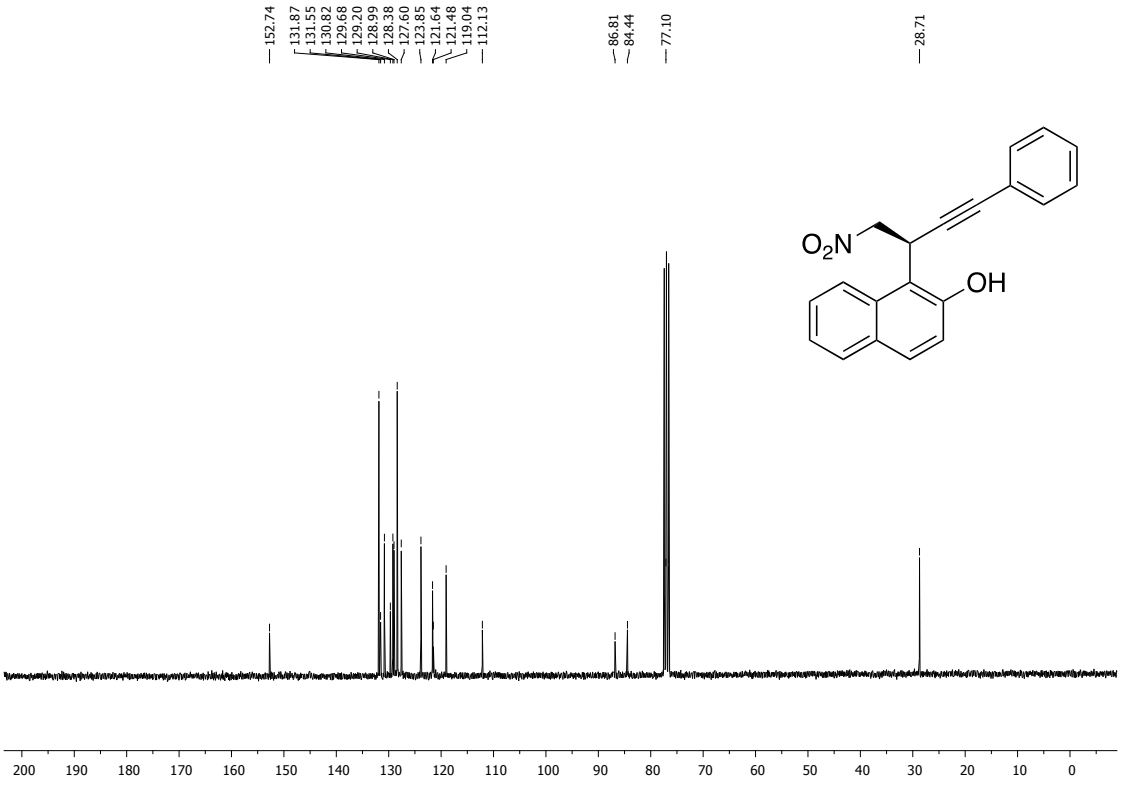
## Stereochemical model and mechanistic proposal



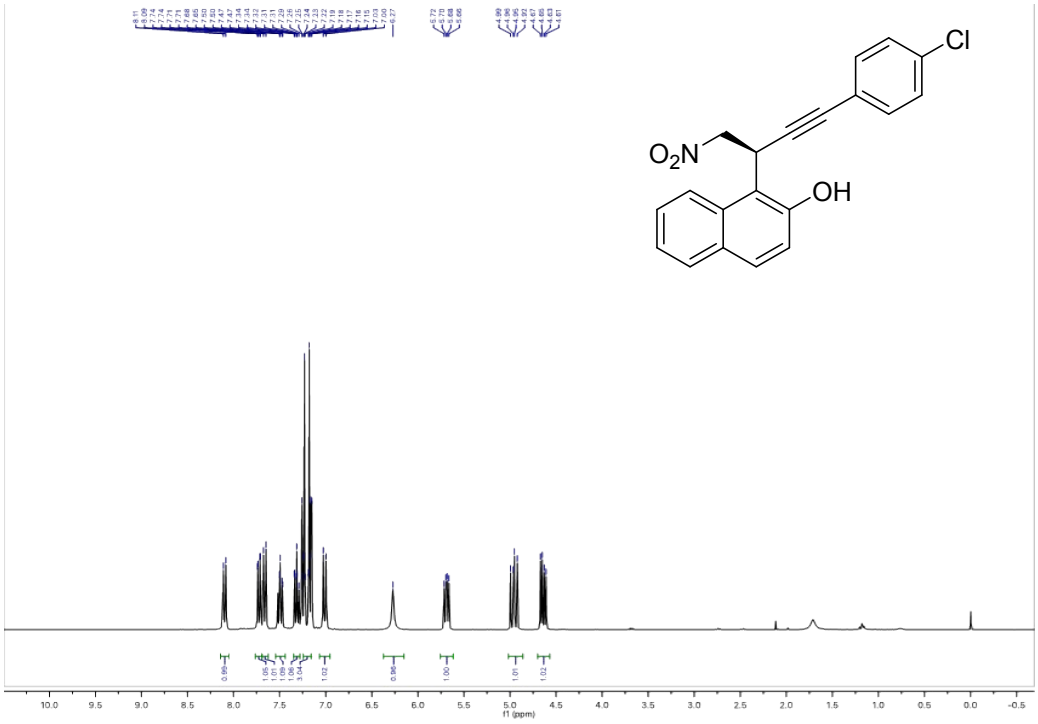
## $^{1}H$ and $^{13}C$ NMR spectra

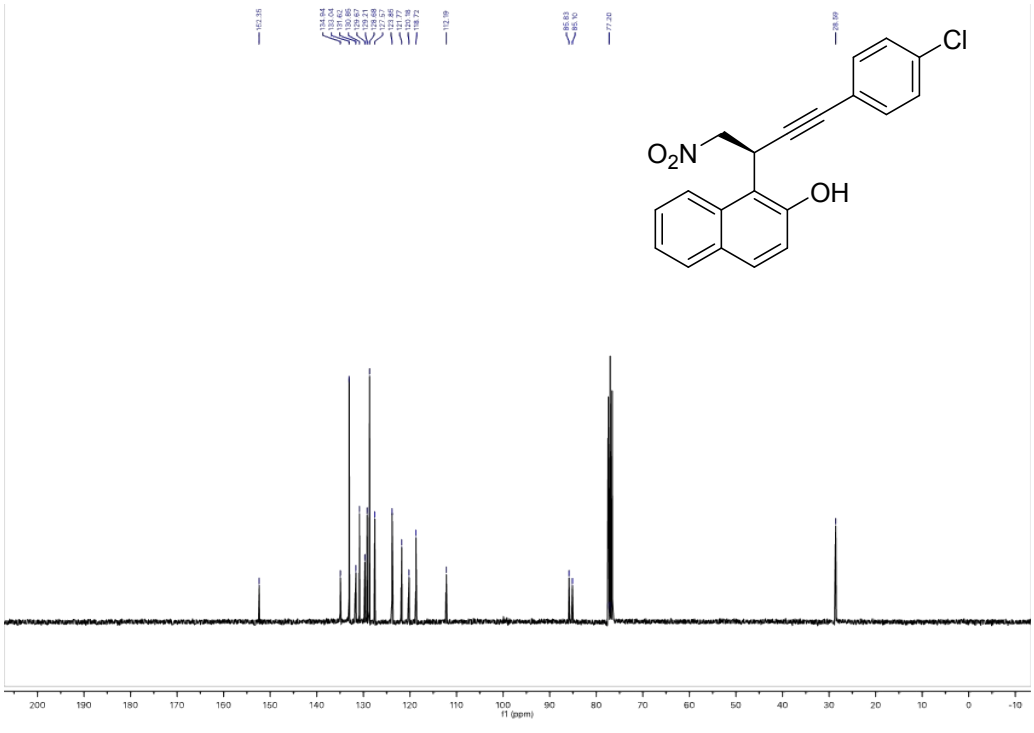
### (*S*)-1-(1-Nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3a)



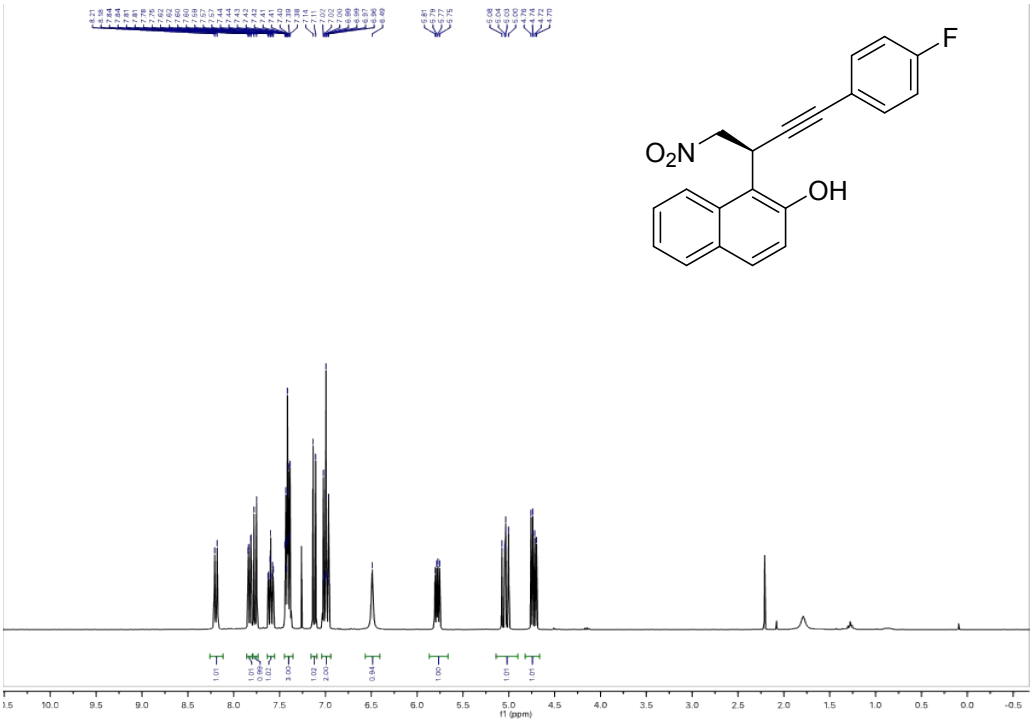



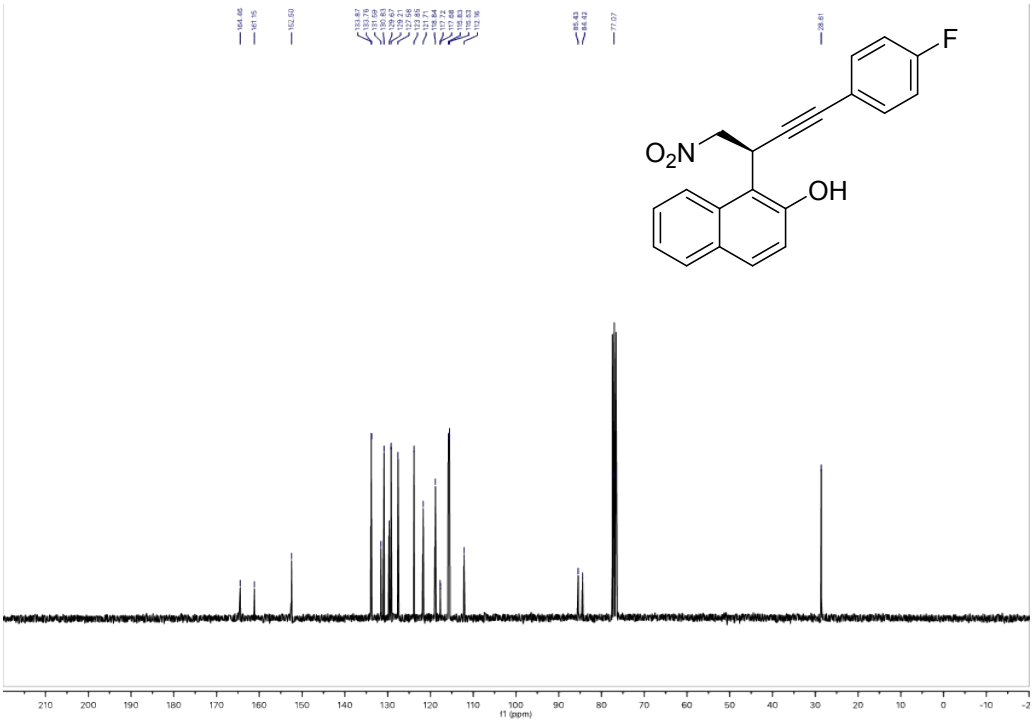
**(*S*)-1-(4-(4-Chlorophenyl)-1-nitrobut-3-yn-2-yl)naphthalen-2-ol (3b)**



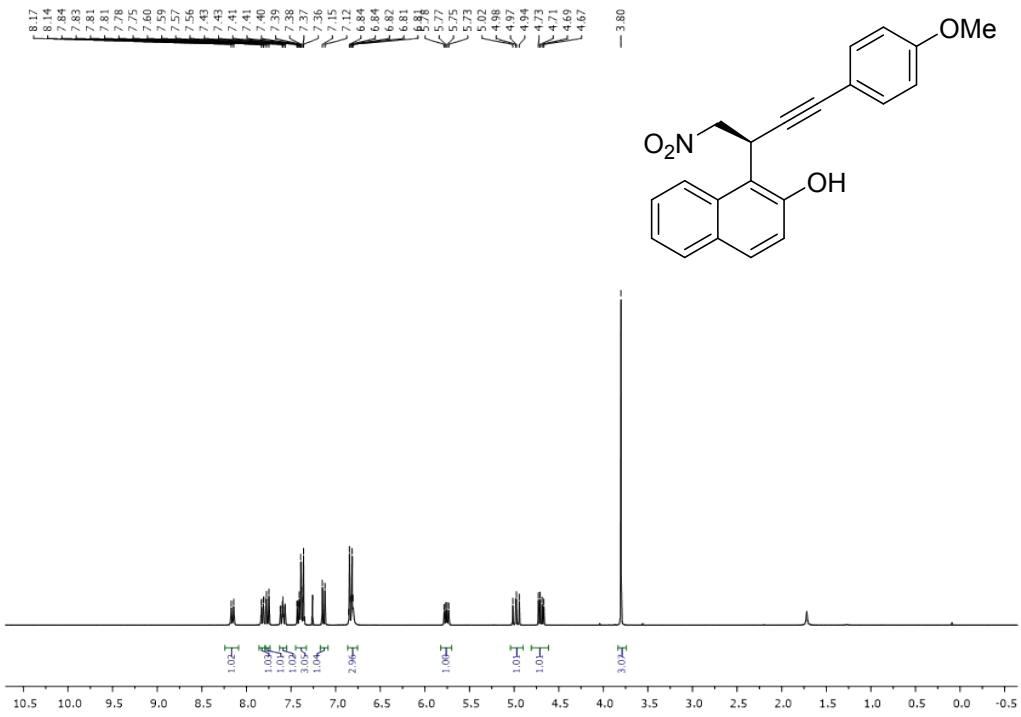



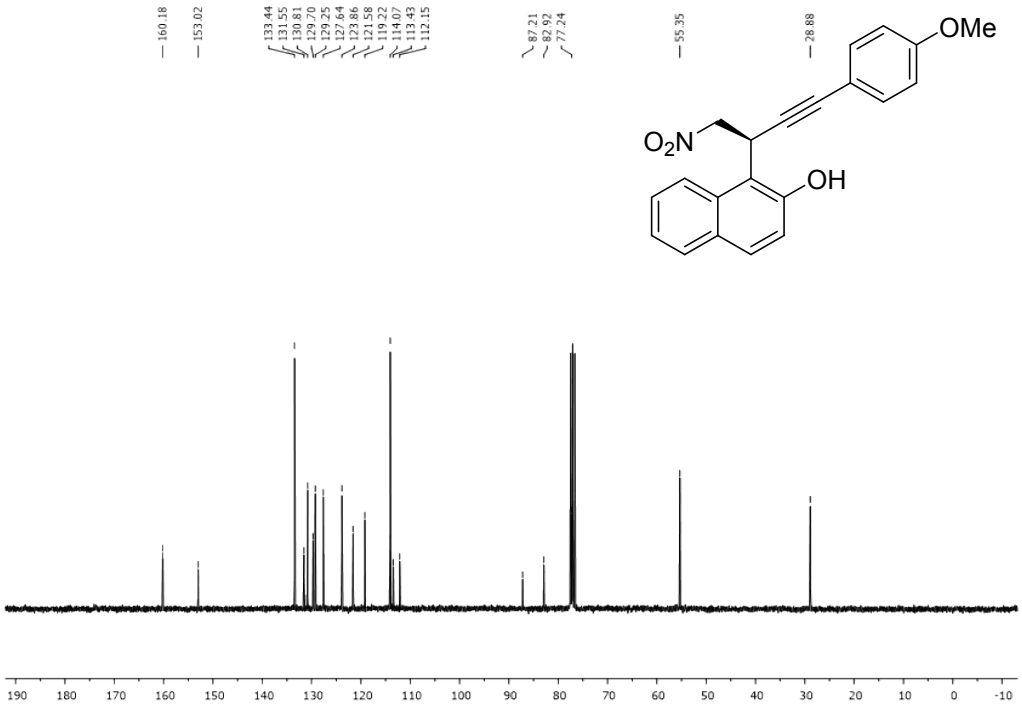
**(*S*)-1-(4-(4-Fluorophenyl)-1-nitrobut-3-yn-2-yl)naphthalen-2-ol (3c)**



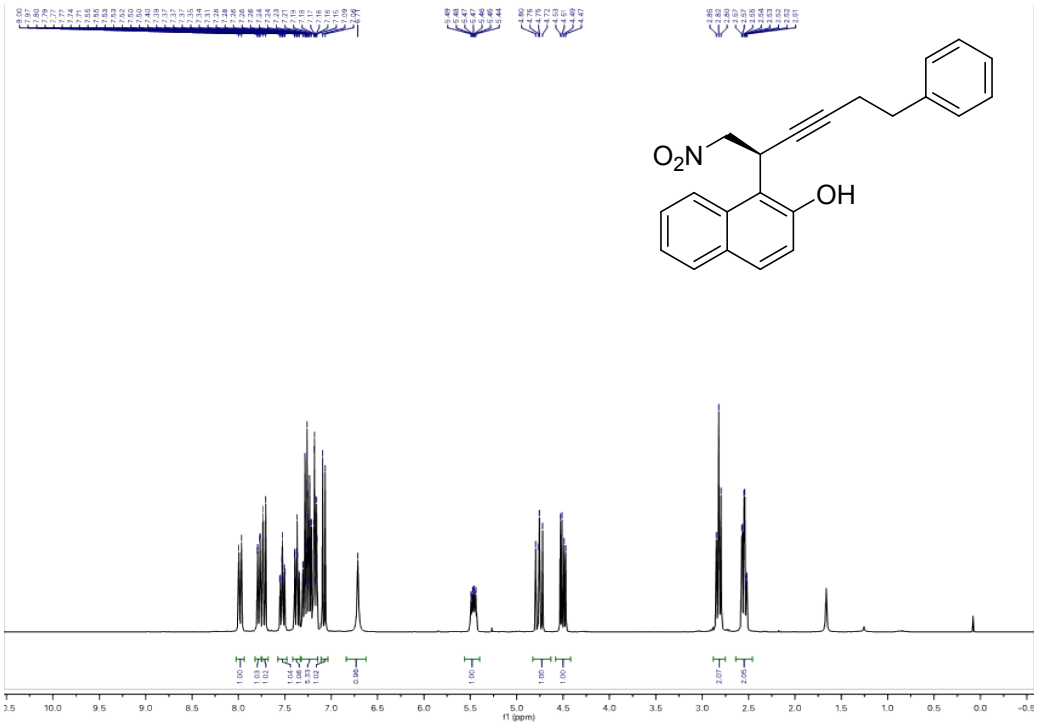



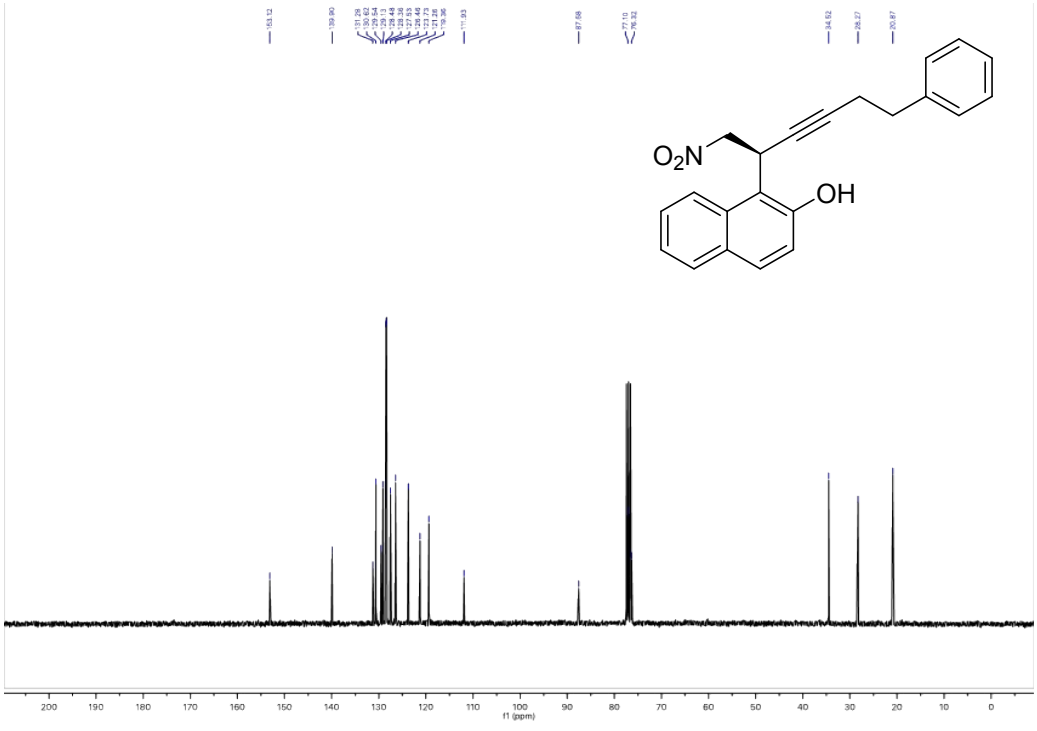
**(*S*)-1-(4-(4-Methoxyphenyl)-1-nitrobut-3-yn-2-yl)naphthalen-2-ol (3d)**



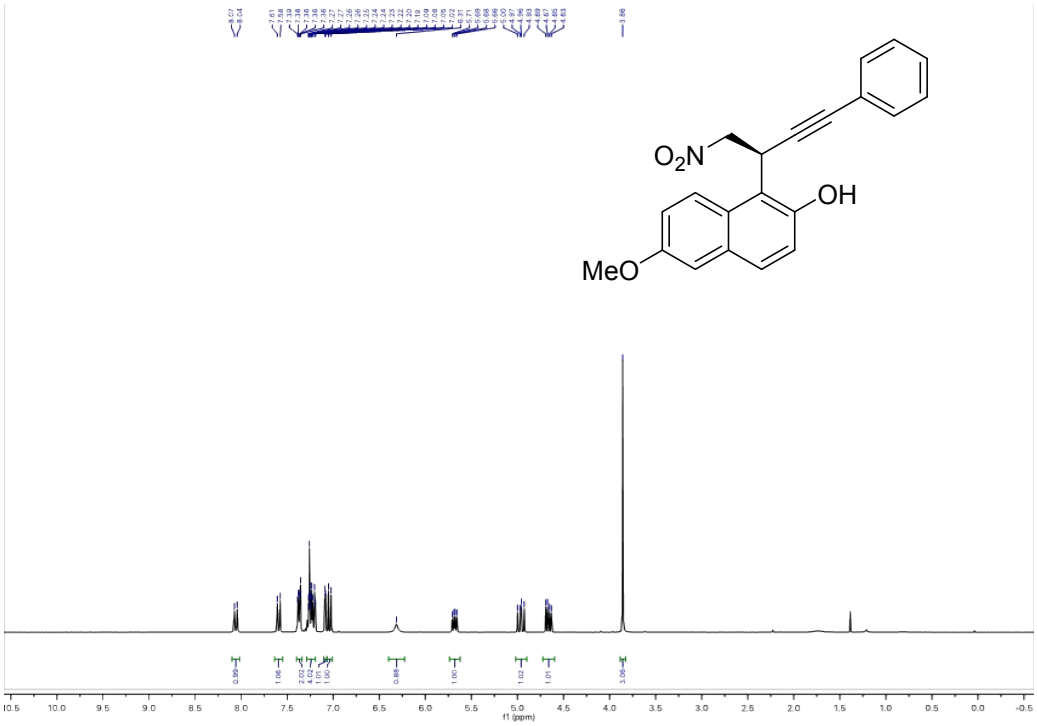



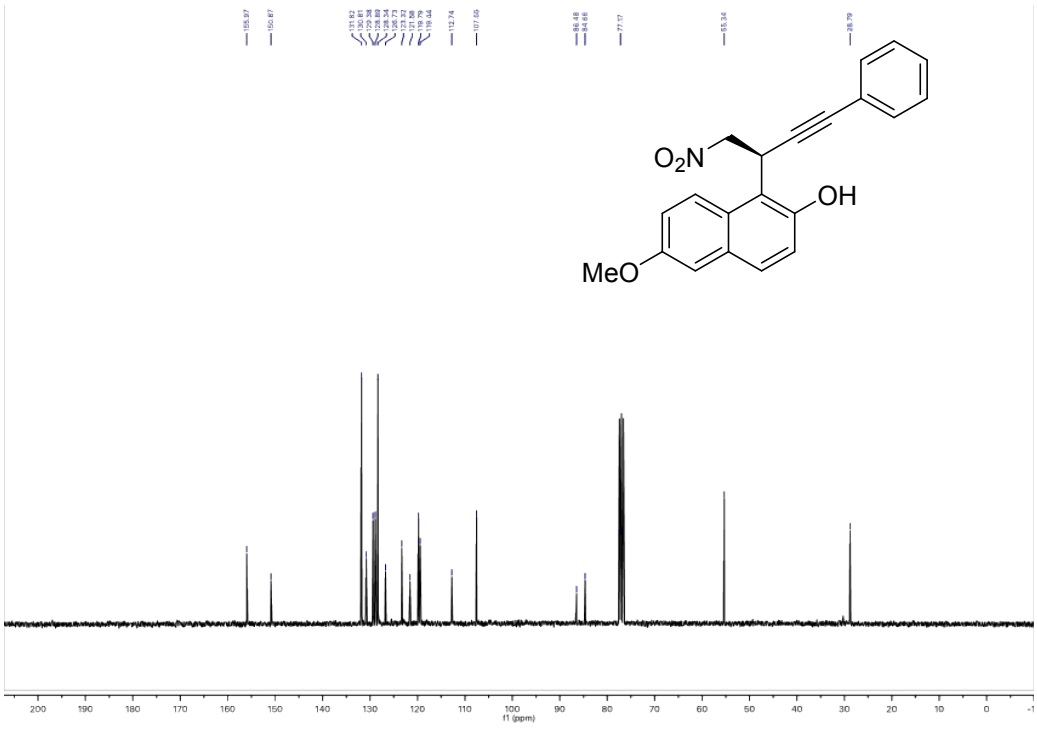
**(*S*)-1-(1-Nitro-6-phenylhex-3-yn-2-yl)naphthalen-2-ol (3e)**



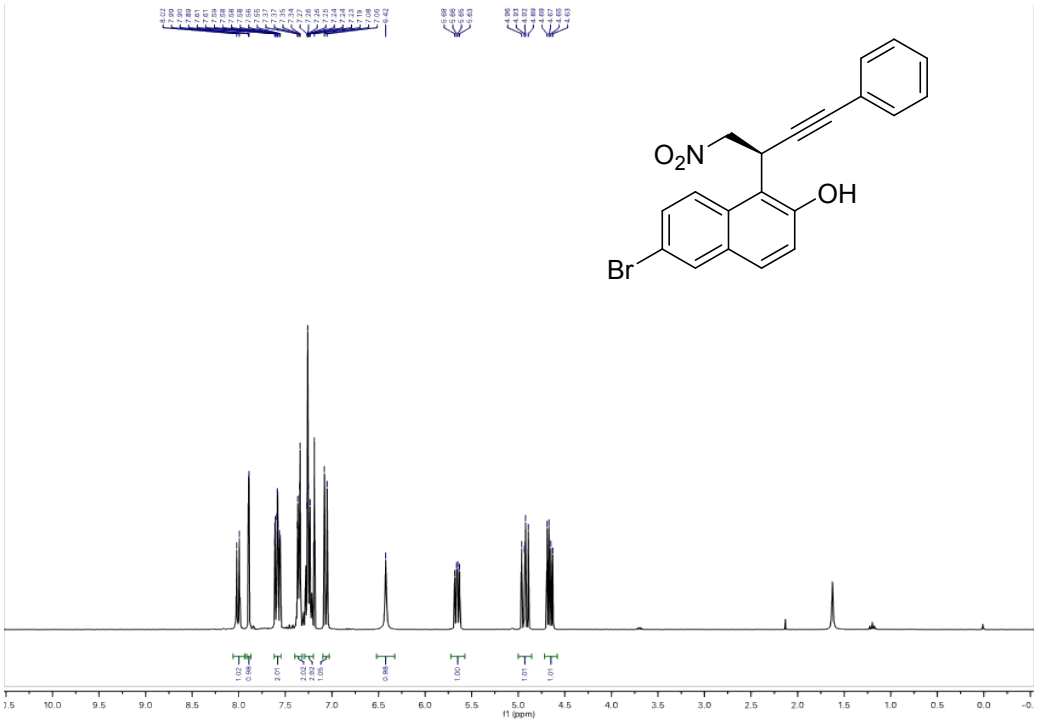



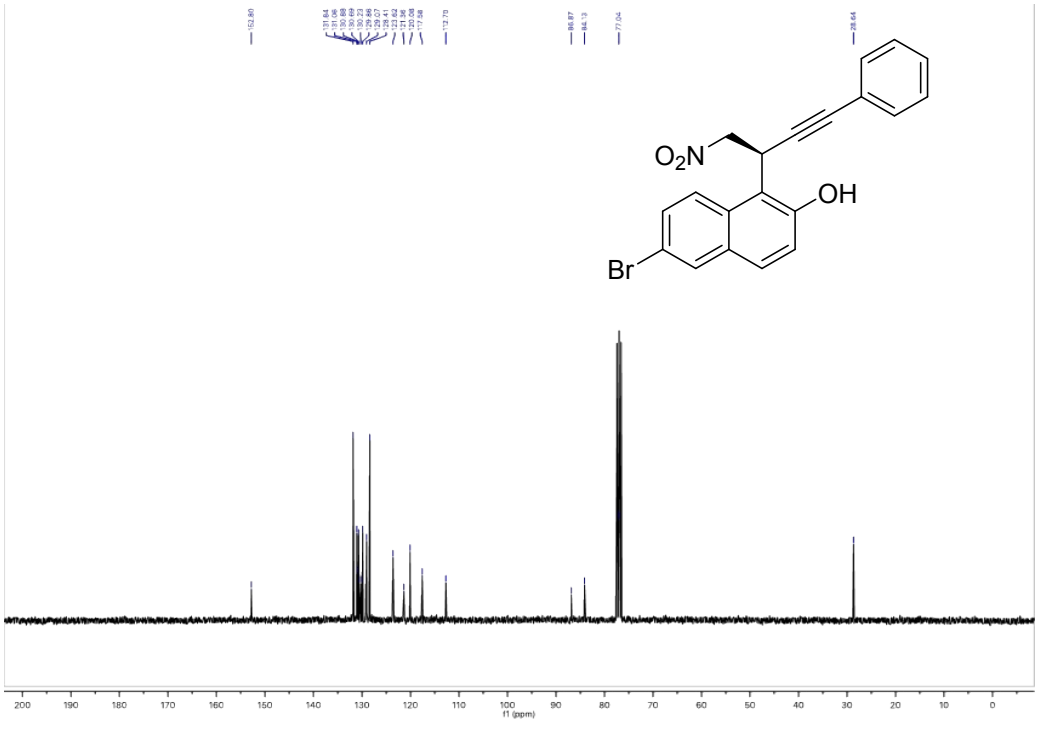
**(*S*)-6-Methoxy-1-(1-nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3f)**



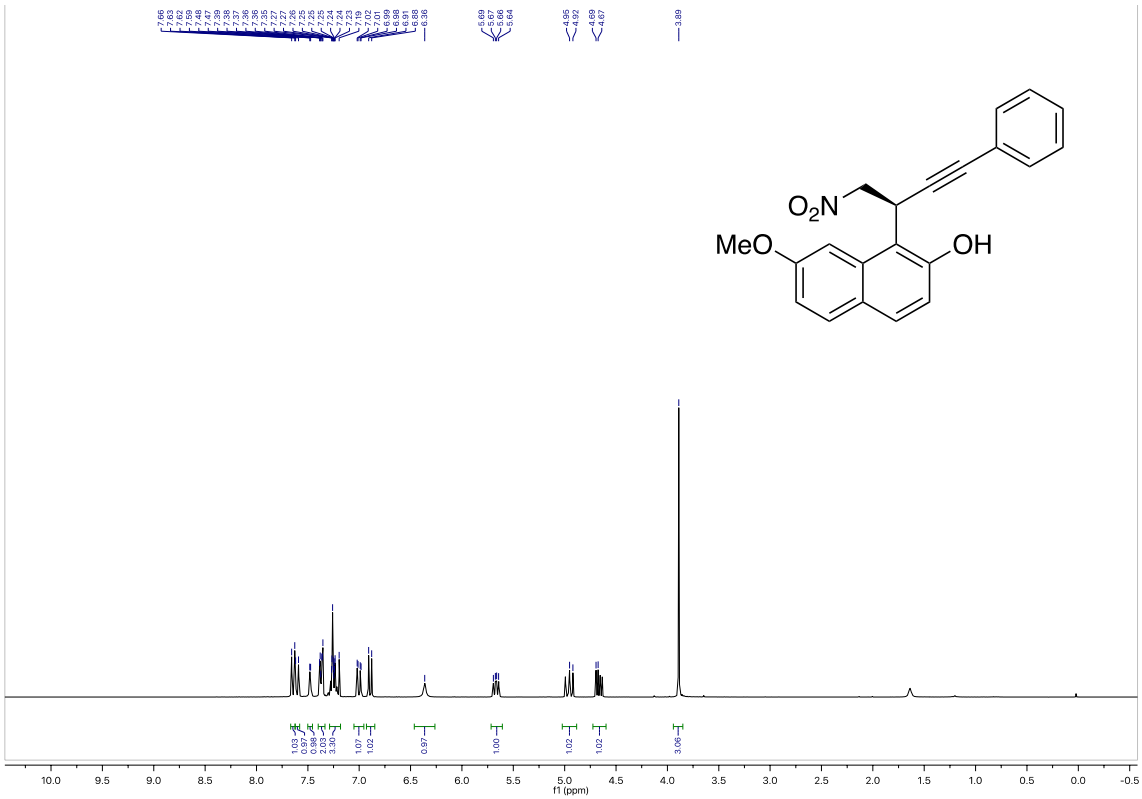



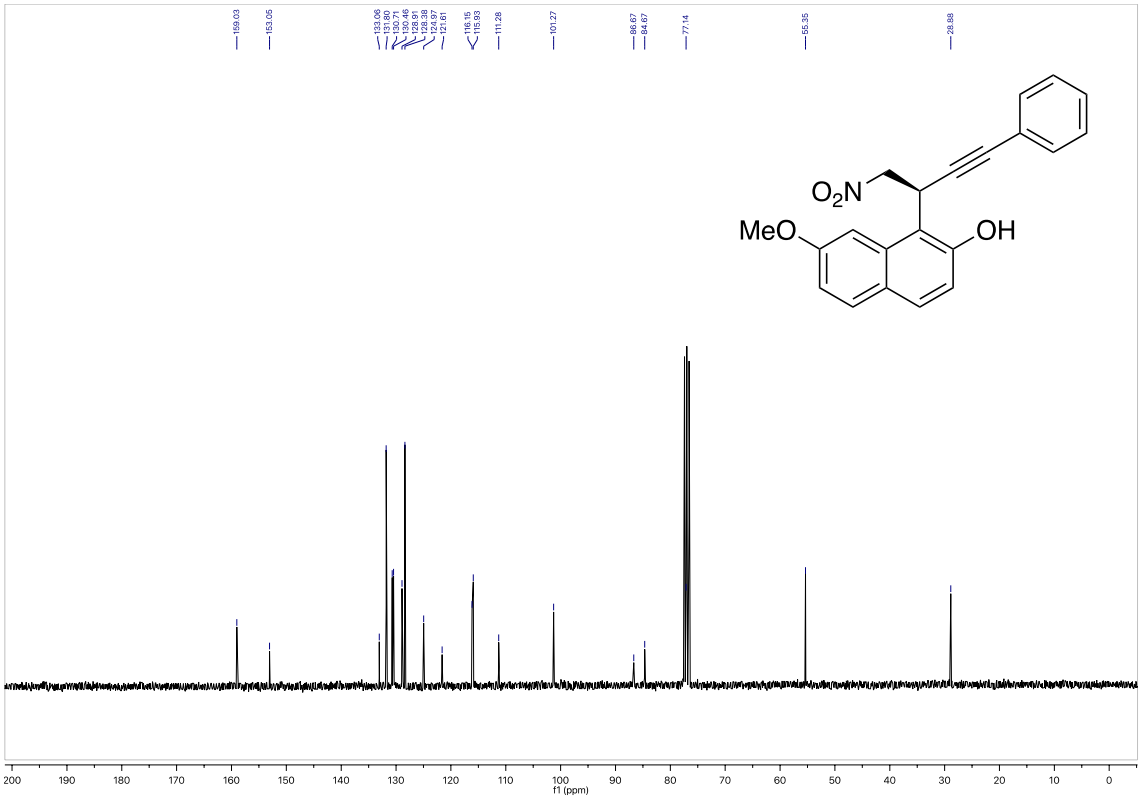
**(*S*)-6-Bromo-1-(1-nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3g)**



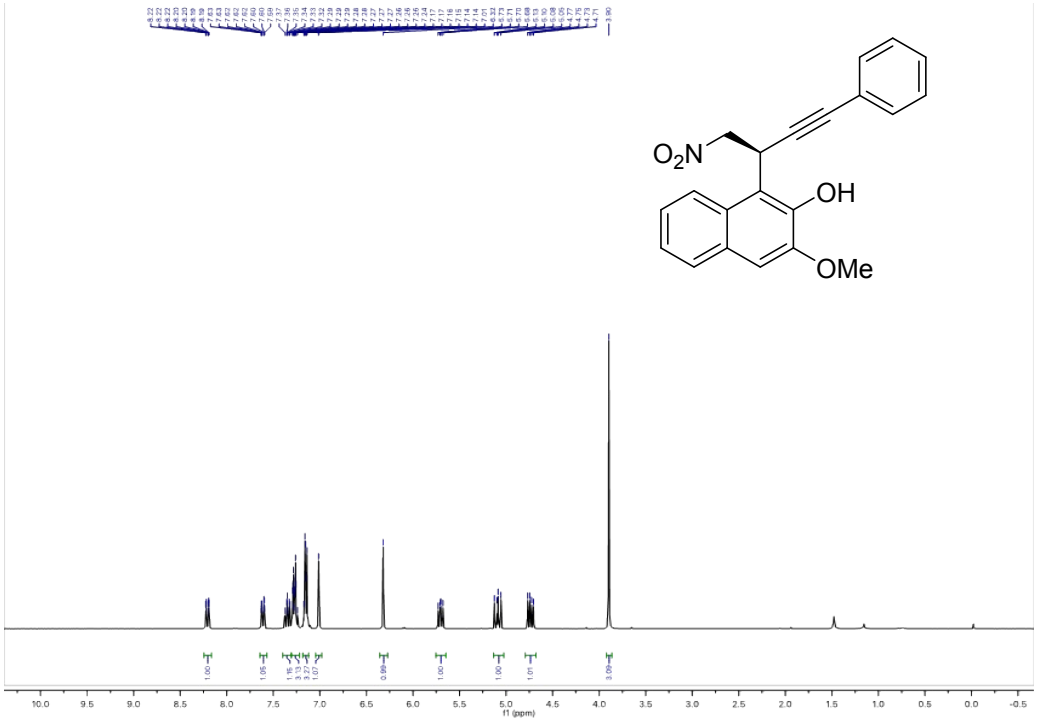



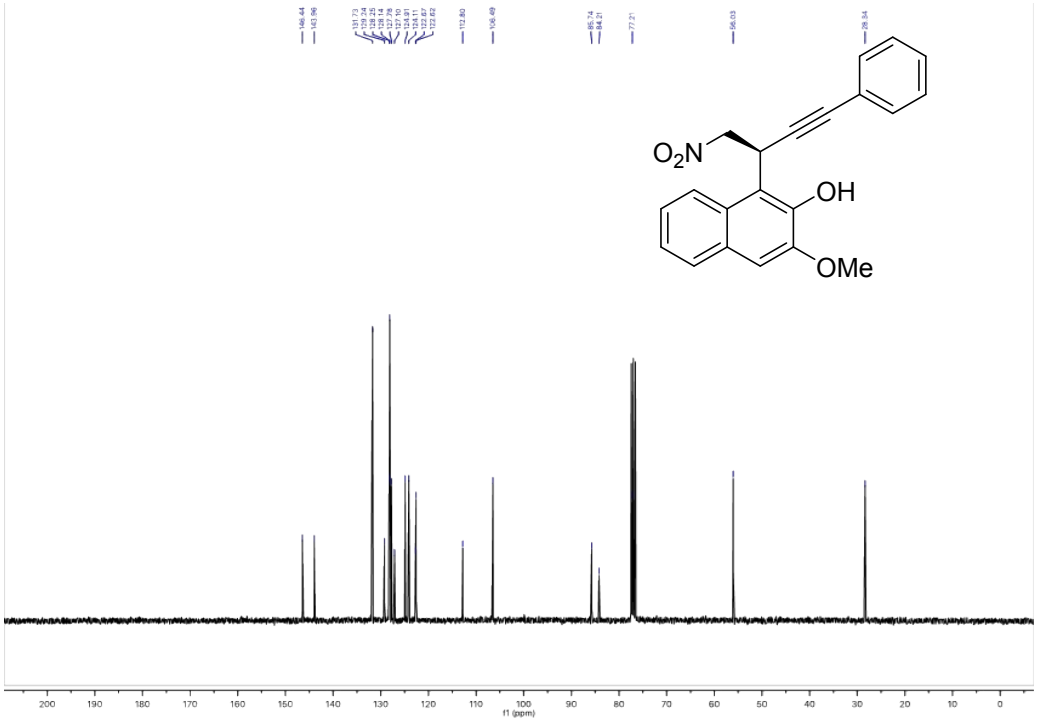
## (*S*)-7-Methoxy-1-(1-nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3h)



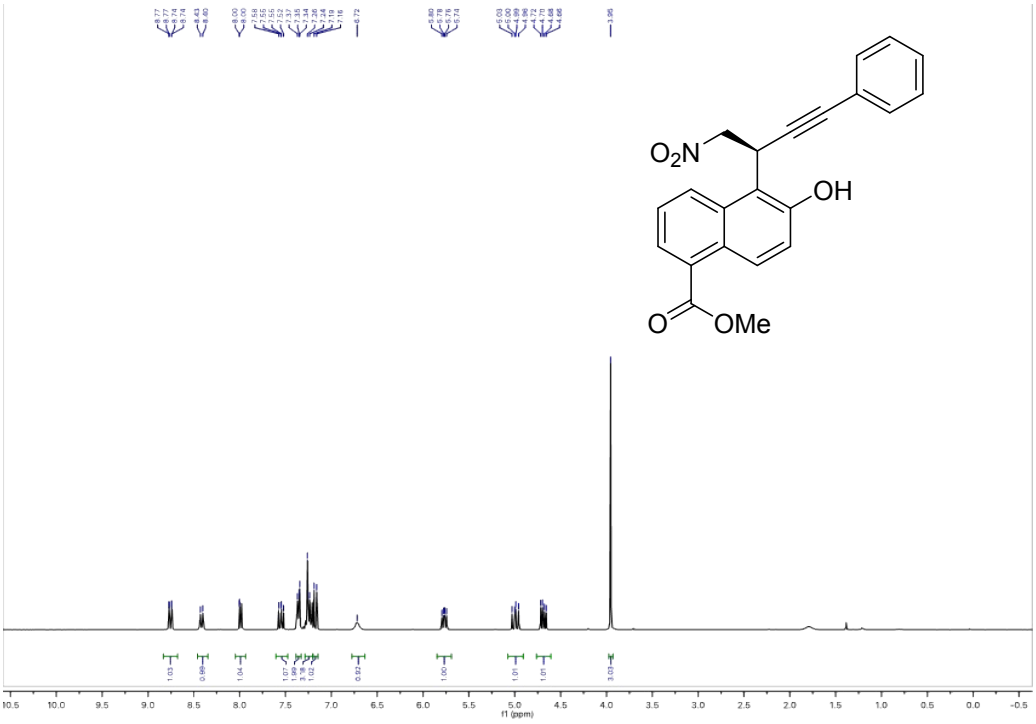



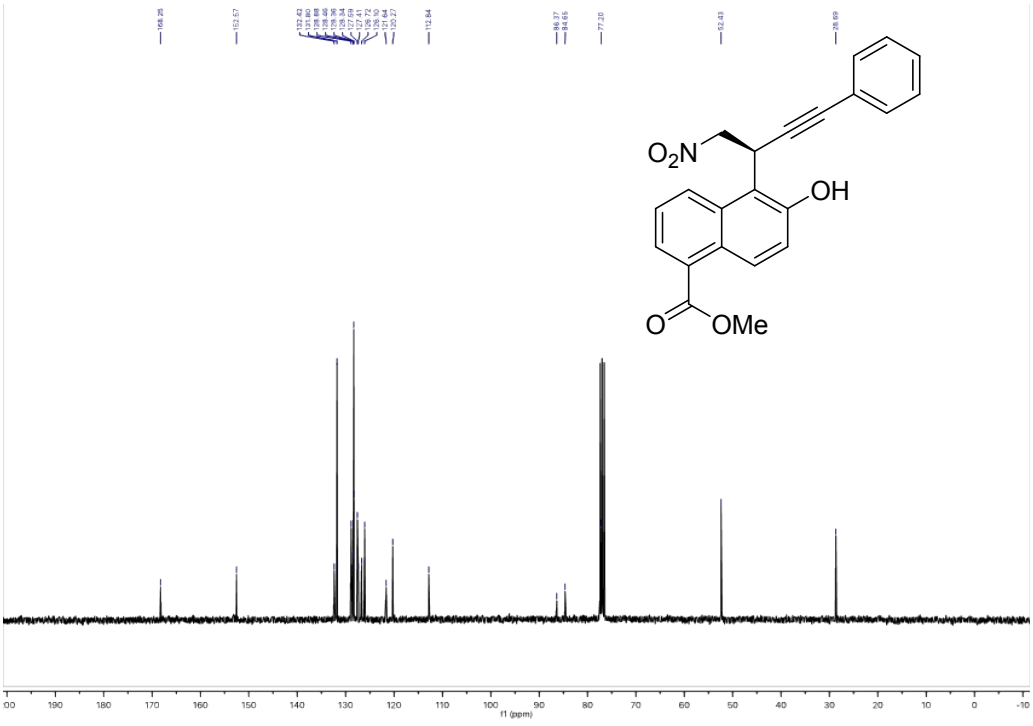
**(S)-3-Methoxy-1-(1-nitro-4-phenylbut-3-yn-2-yl)naphthalen-2-ol (3i)**



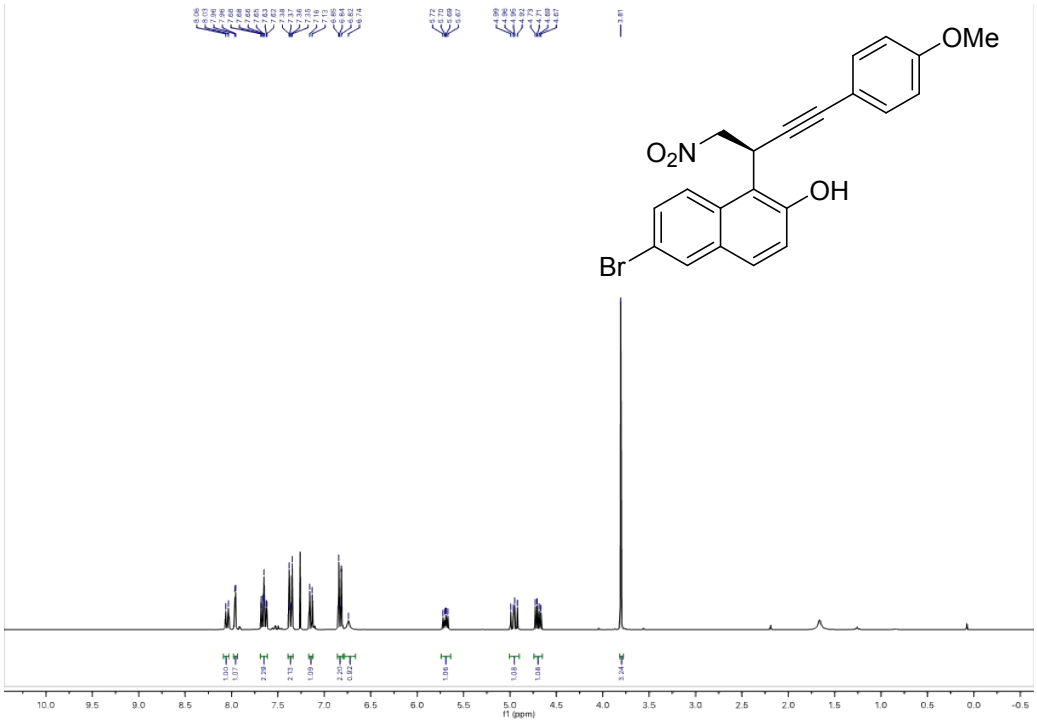



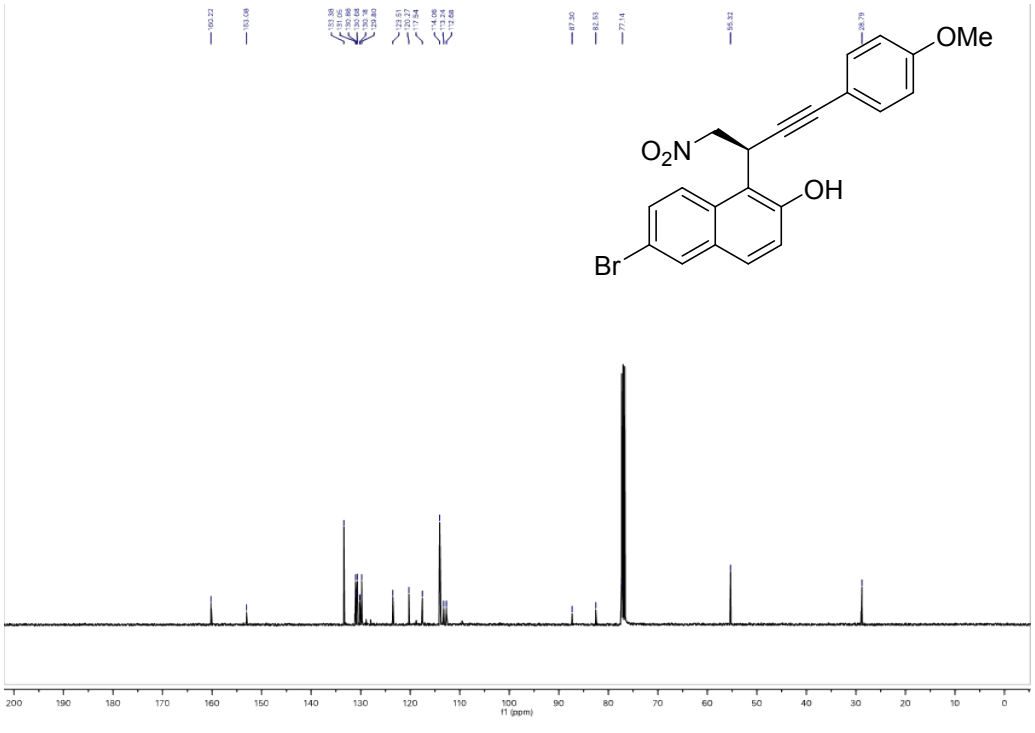
**Methyl (*S*)-3-hydroxy-4-(1-nitro-4-phenylbut-3-yn-2-yl)-1-naphthoate (3j)**



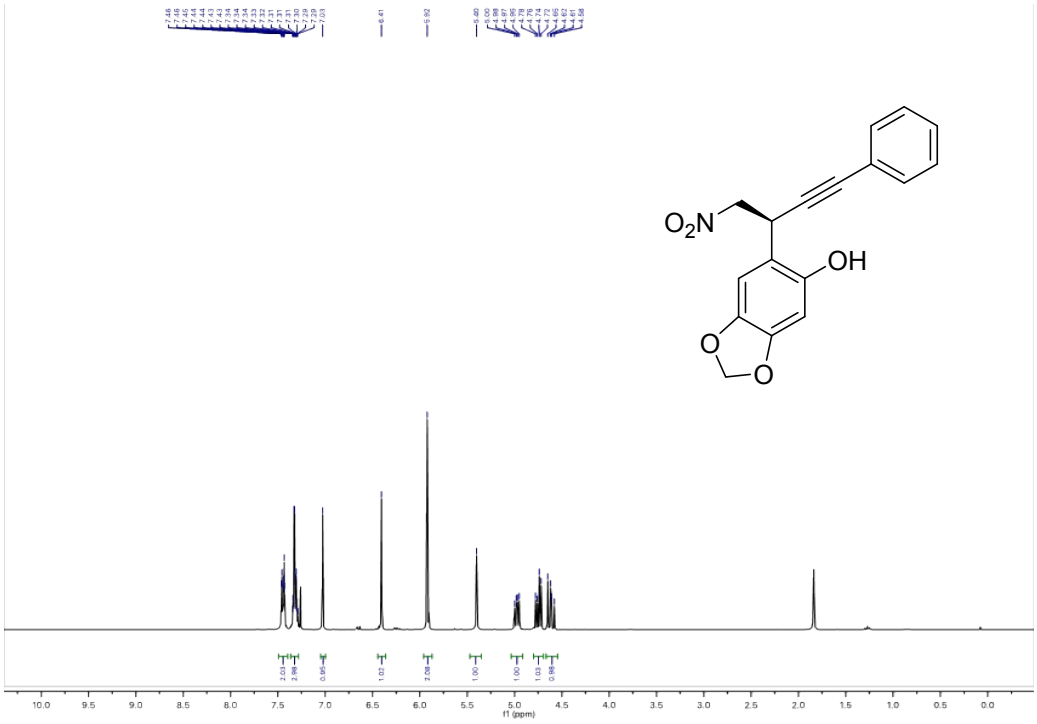



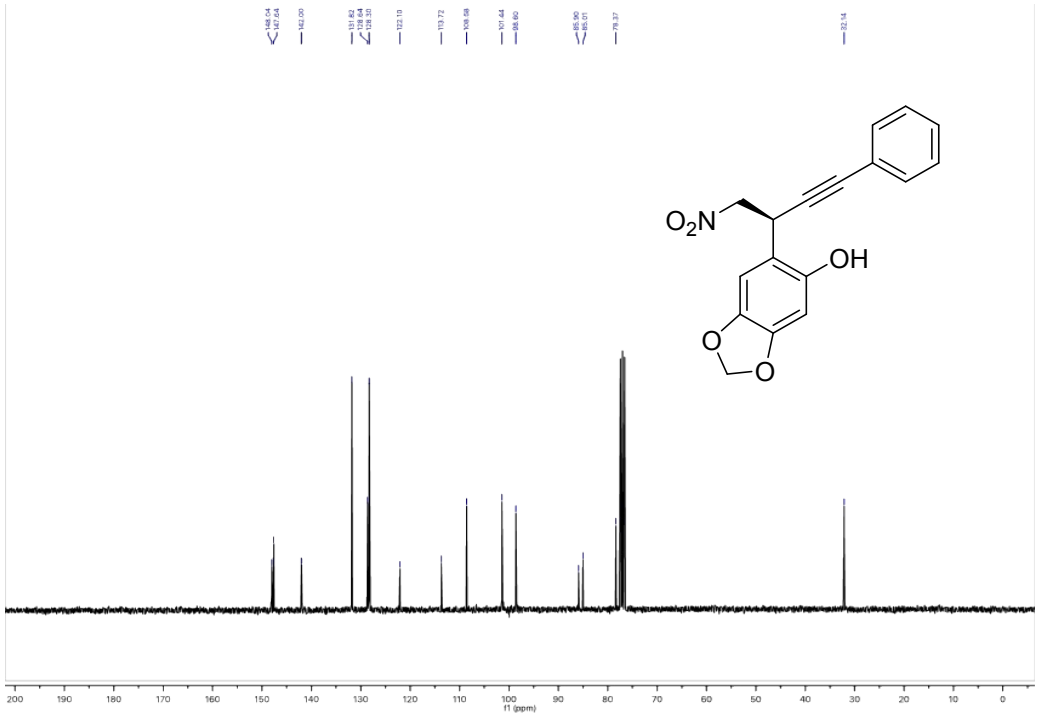
**(*S*)-6-bromo-1-(4-(4-methoxyphenyl)-1-nitrobut-3-yn-2-yl)naphthalen-2-ol (3k)**



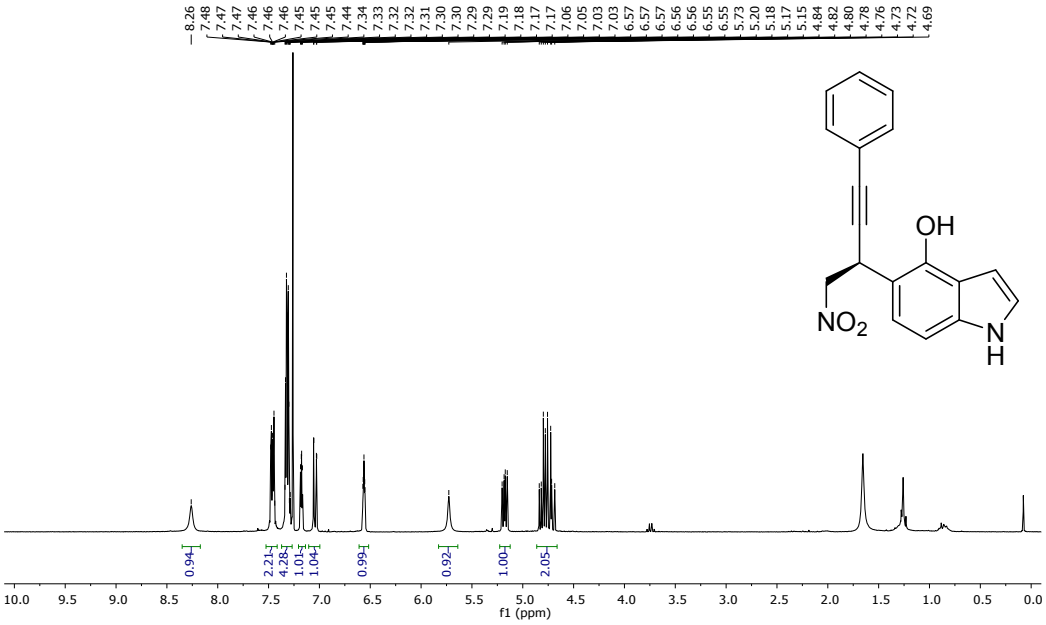



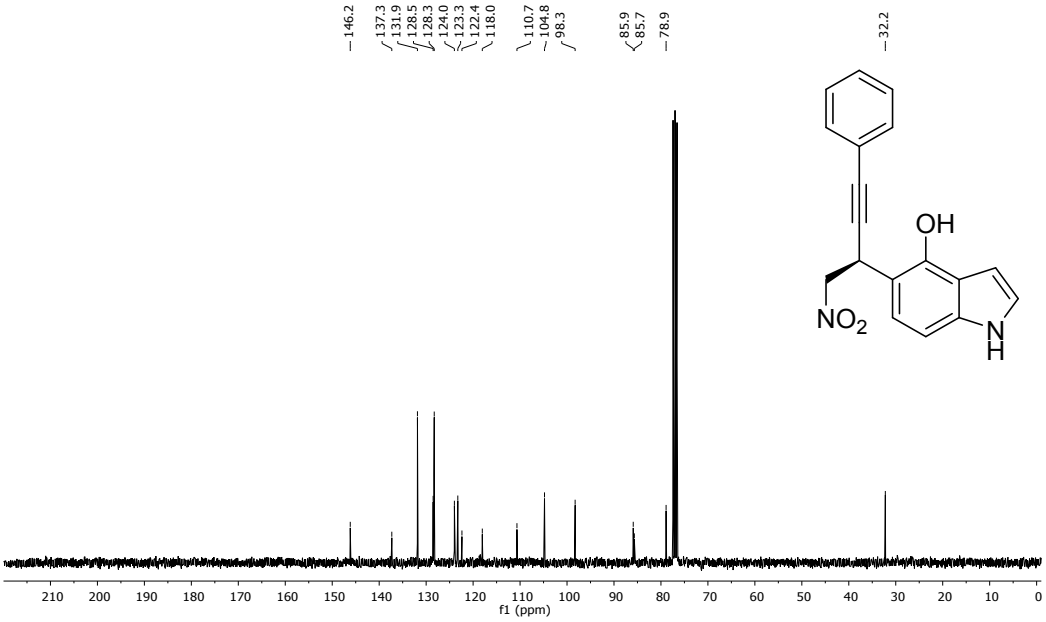
**(*S*)-6-(1-Nitro-4-phenylbut-3-yn-2-yl)benzo[*d*][1,3]dioxol-5-ol (3l)**



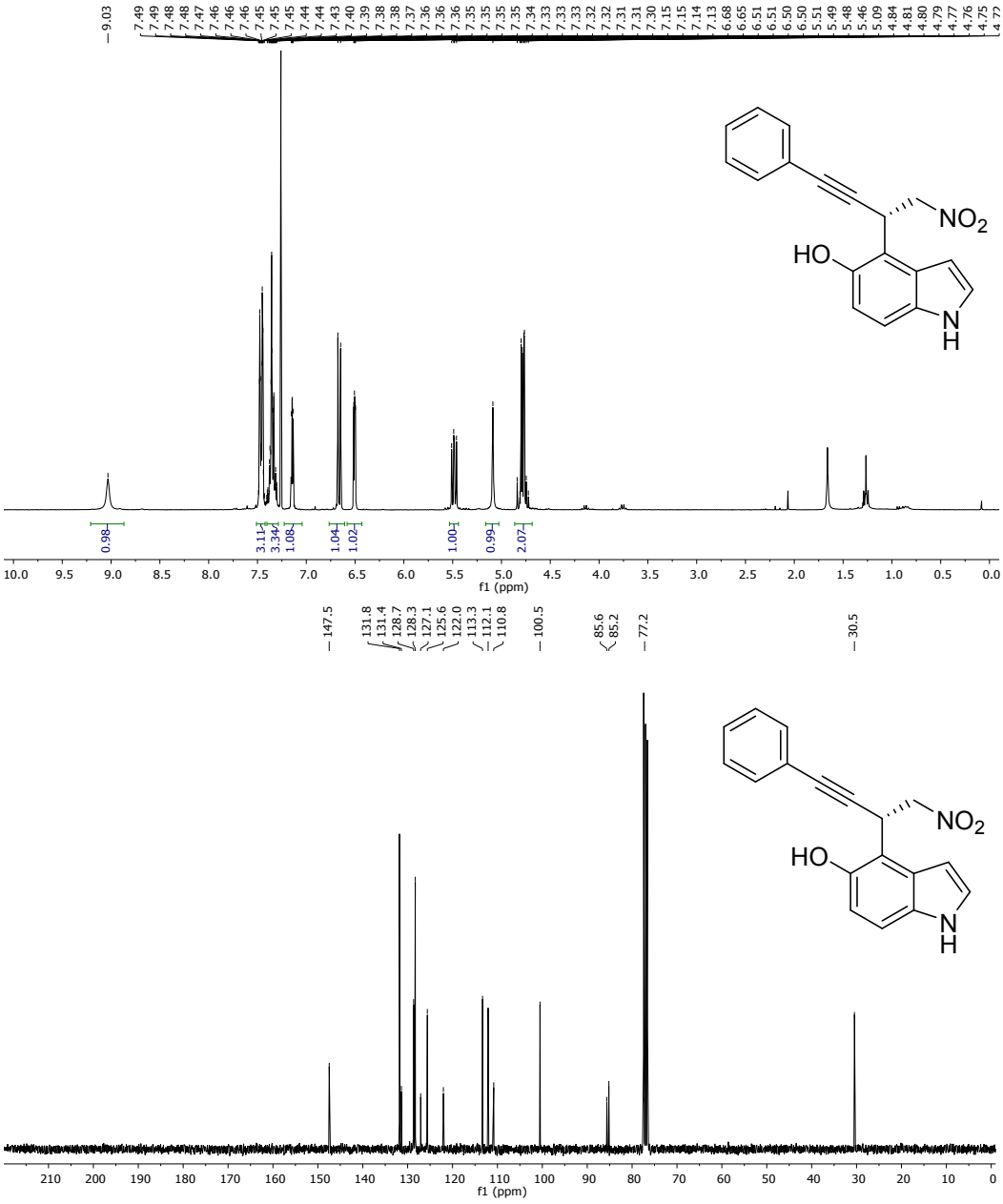



**(*S*)-5-(1-Nitro-4-phenylbut-3-yn-2-yl)-1*H*-indol-4-ol (5a)**

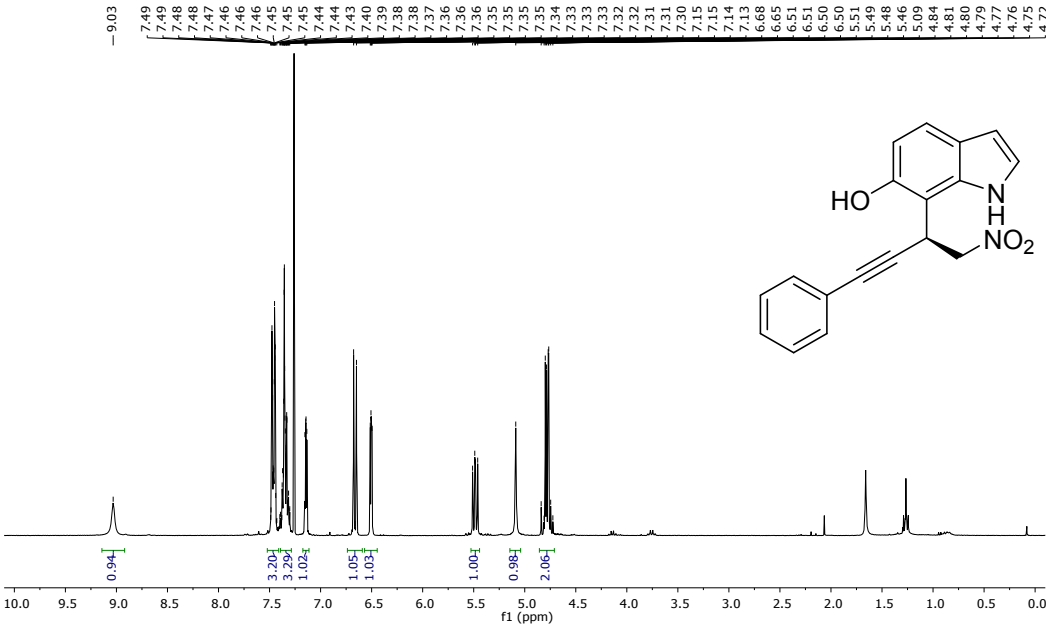


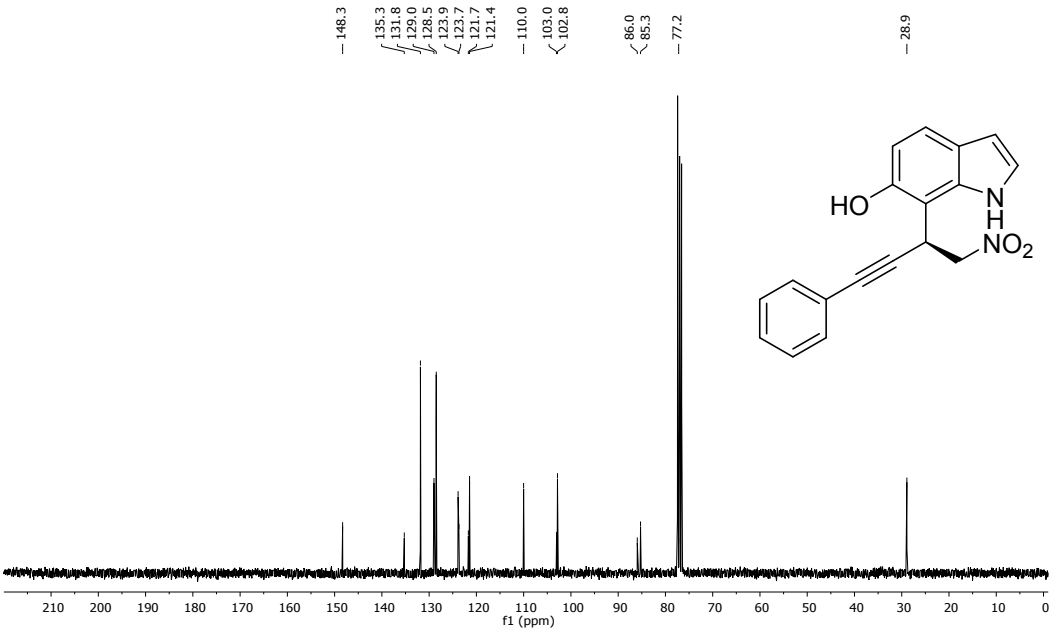



**(*S*)-4-(1-Nitro-4-phenylbut-3-yn-2-yl)-1*H*-indol-5-ol (5b)**

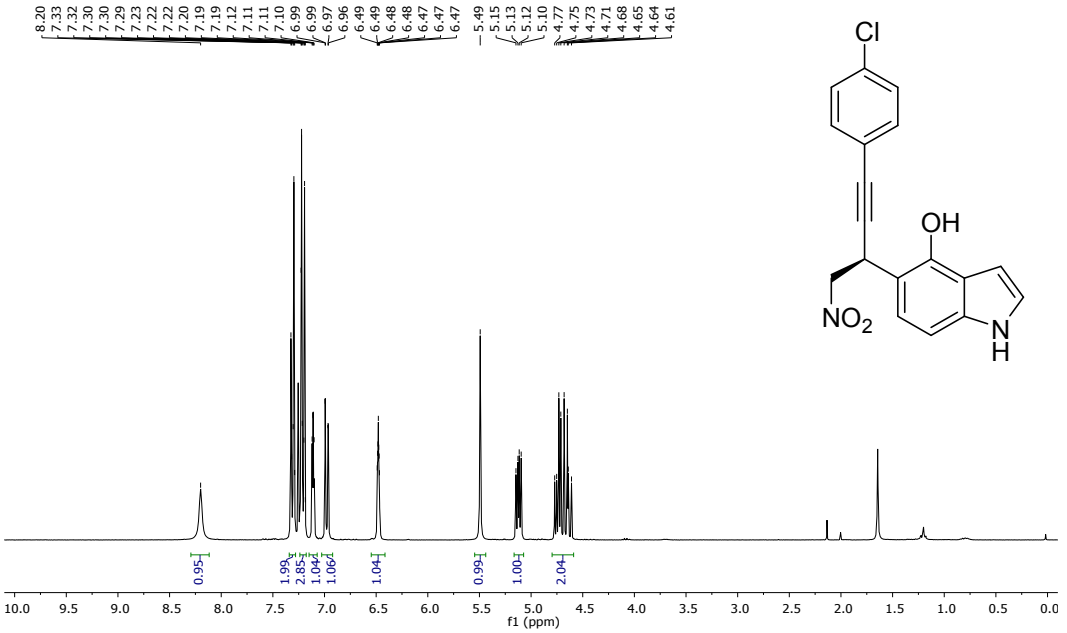


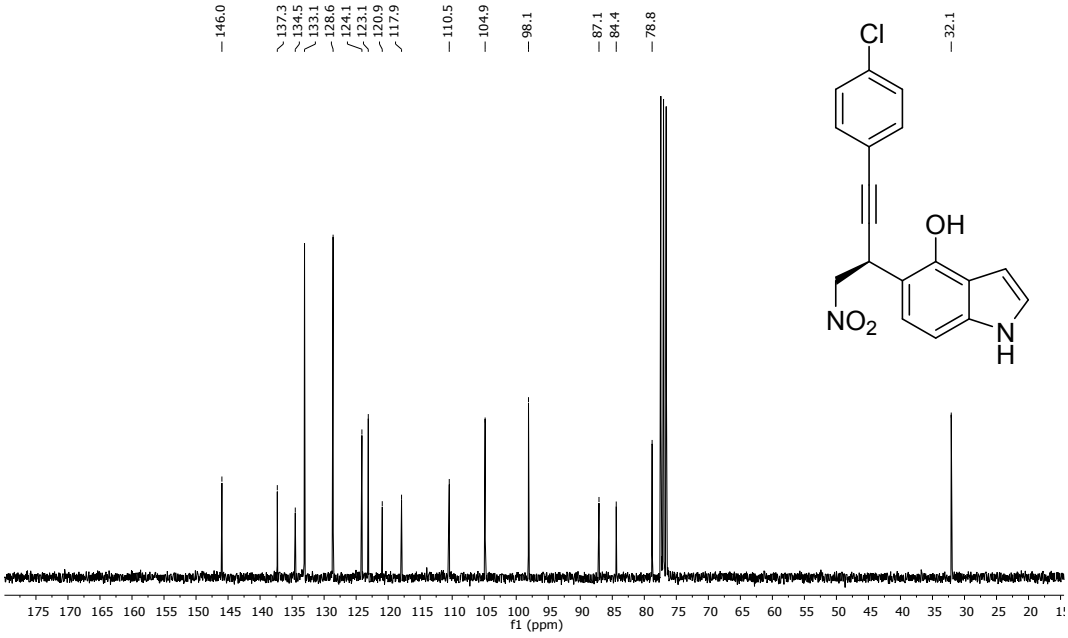
**(*S*)-7-(1-Nitro-4-phenylbut-3-in-2-il)-1H-indol-6-ol (5c)**



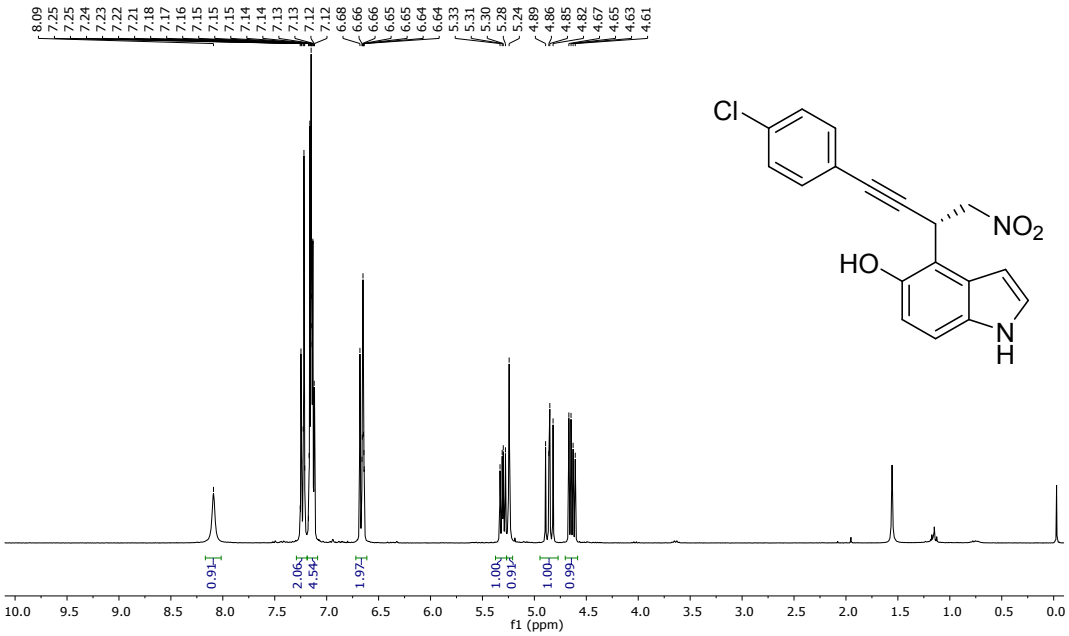



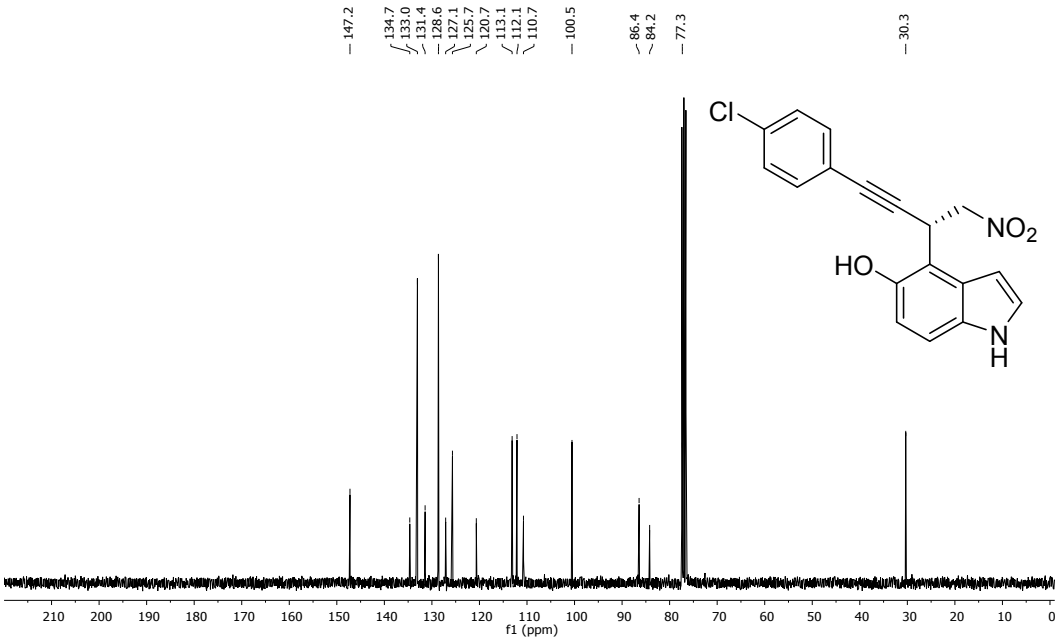
**(*S*)-5-(4-(4-Chlorophenyl)-1-nitrobut-3-in-2-il)-1H-indol-4-ol (5d)**



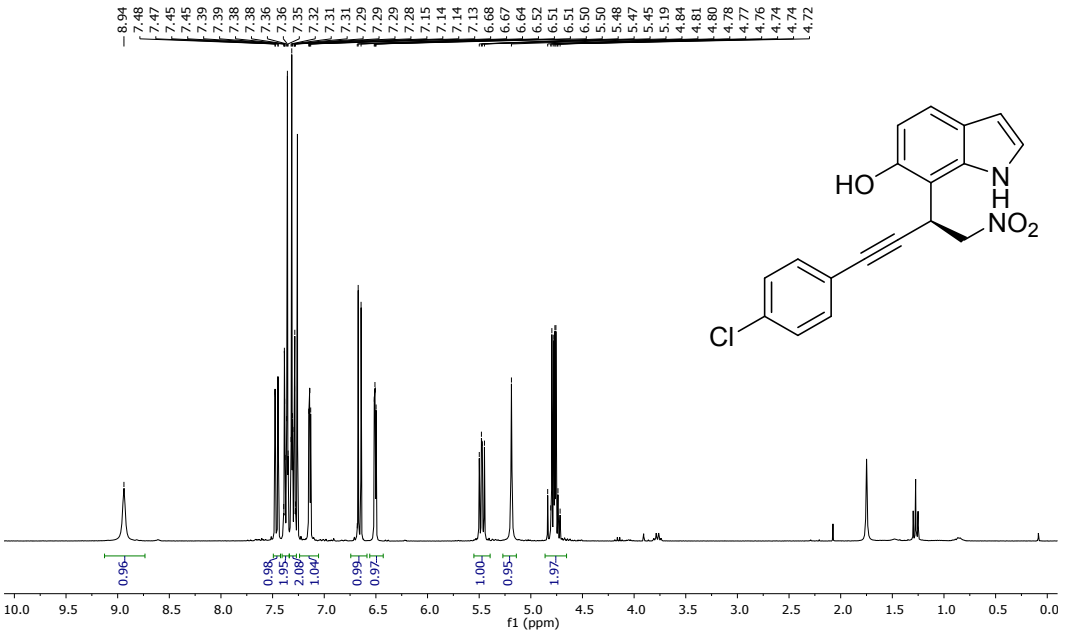



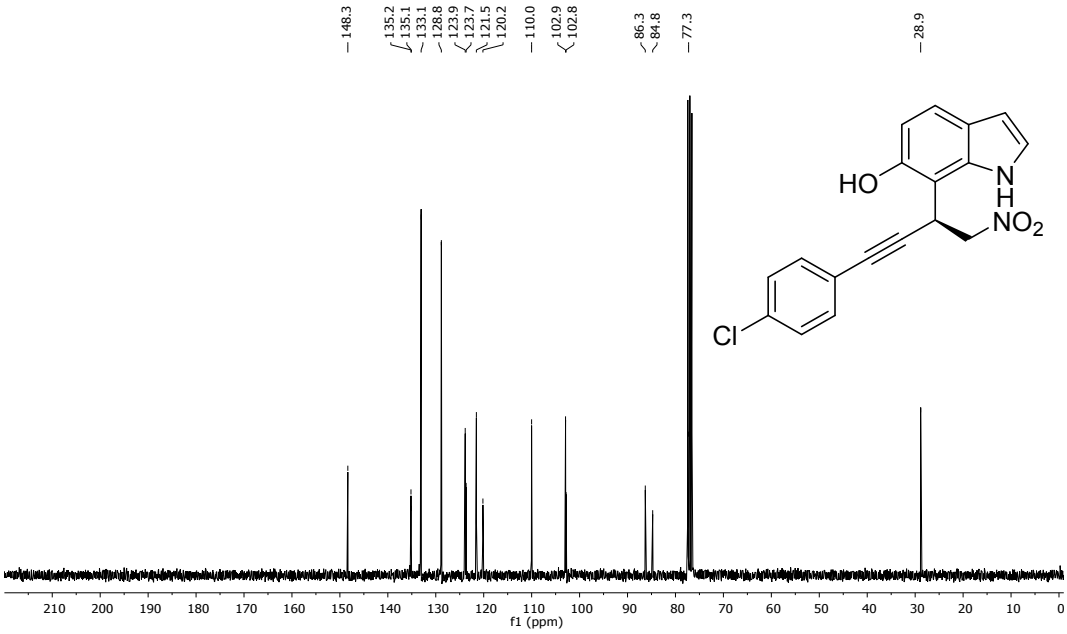
**(*S*)-4-(4-(4-Chlorophenyl)-1-nitrobut-3-in-2-il)-1H-indol-5-ol (5e)**



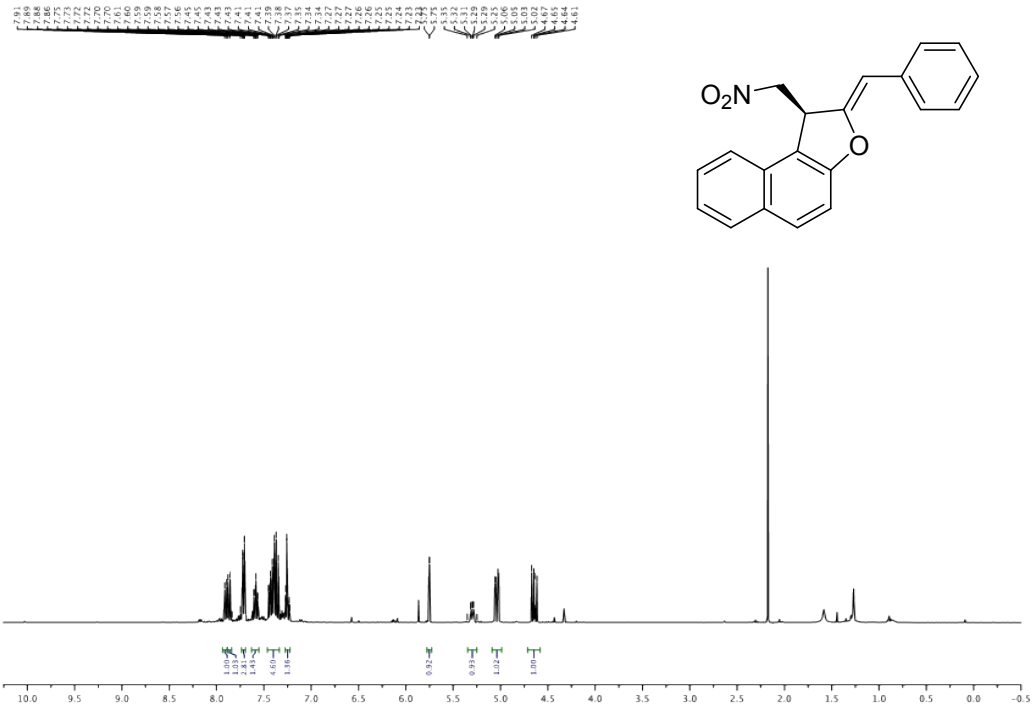



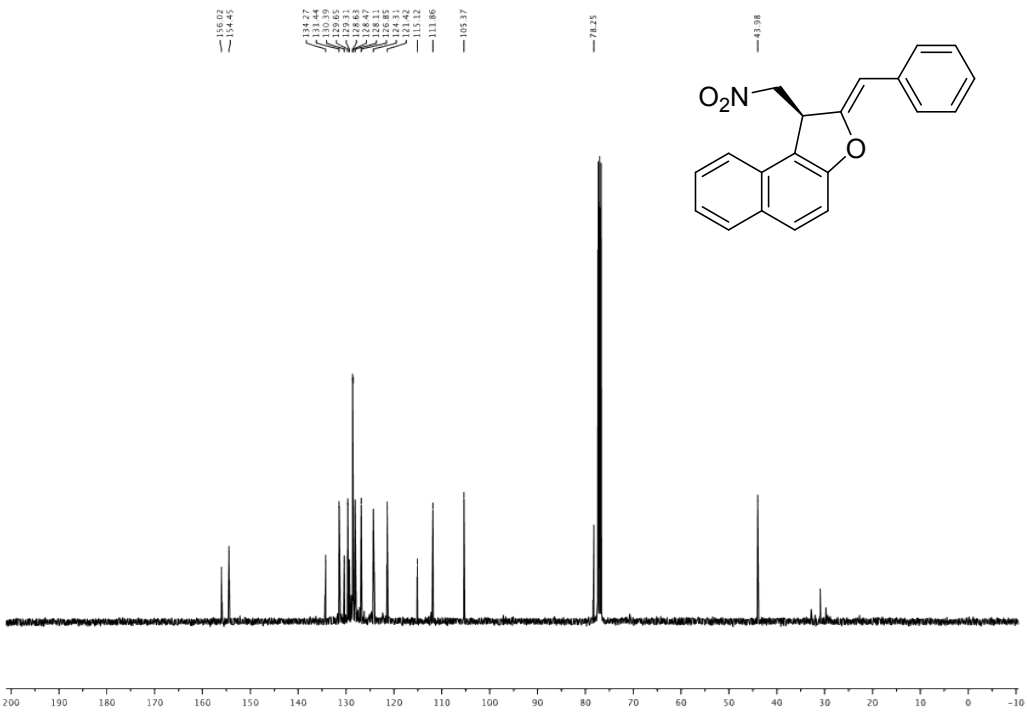
**(*S*)-7-(4-(4-Chlorophenyl)-1-nitrobut-3-in-2-il)-*1H*-indol-6-ol (5f)**



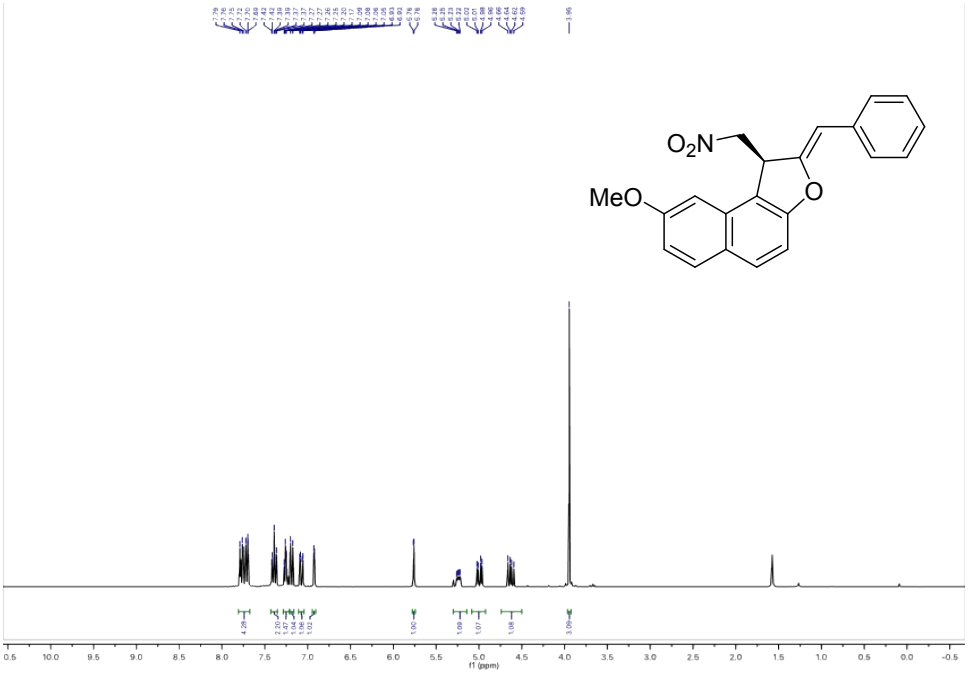



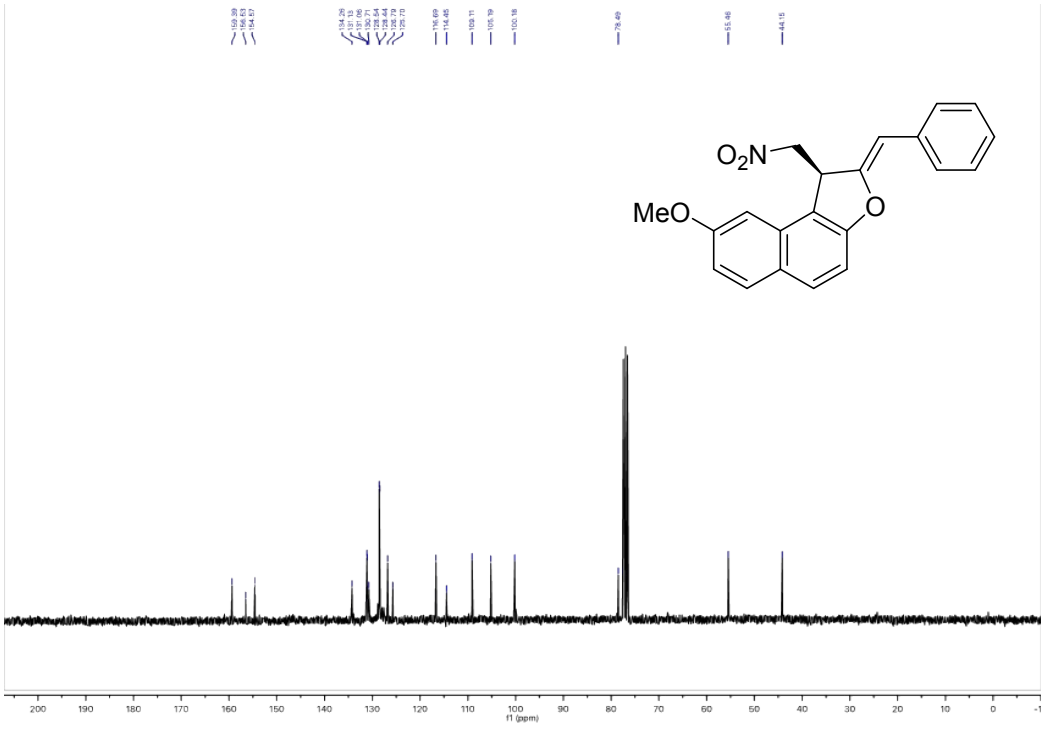
**(*S*,*Z*)-2-Benzylidene-1-(nitromethyl)-1,2-dihydronaphtho[2,1-*b*]furan (6a)**



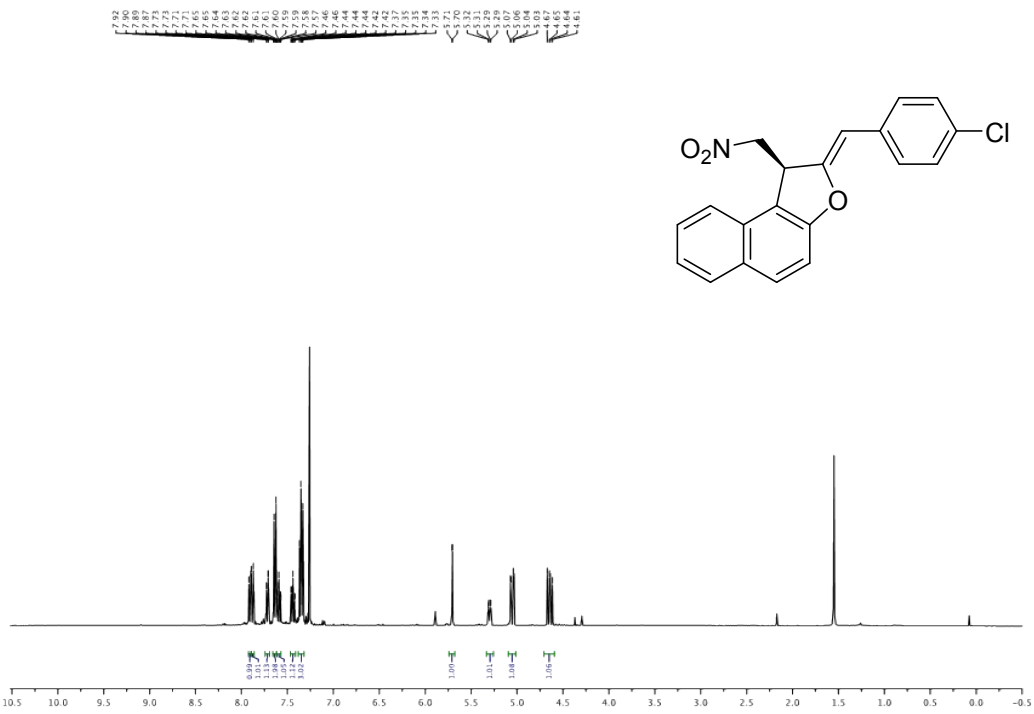



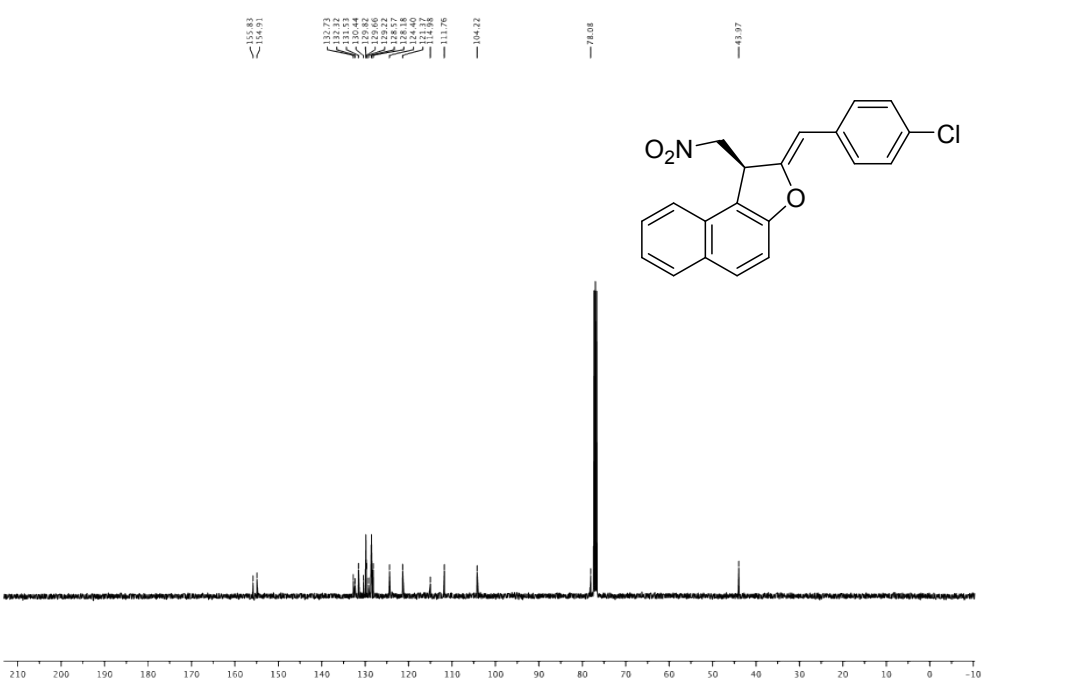
**(*S*,*Z*)-2-Benzylidene-8-methoxy-1-(nitromethyl)-1,2-dihydronaphtho[2,1-*b*]furan (6b)**



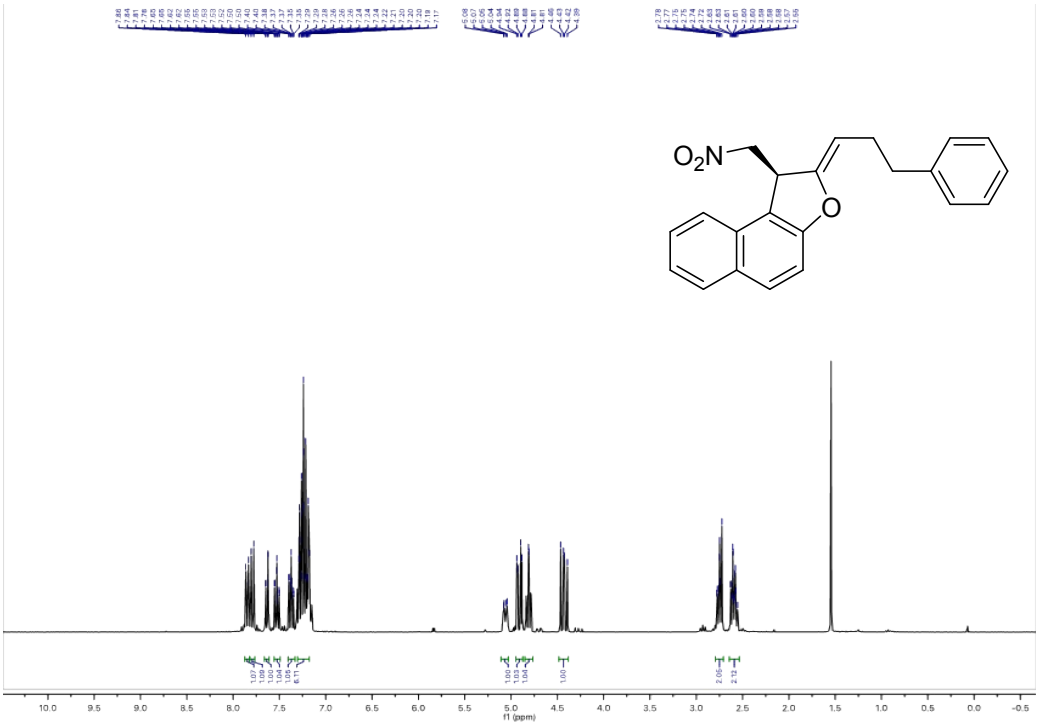



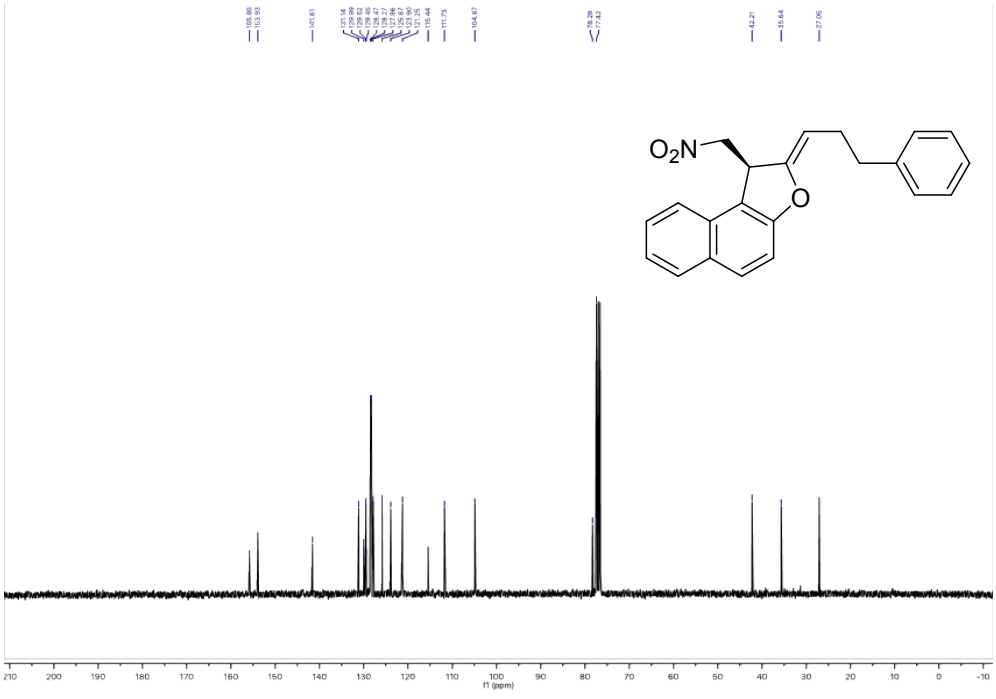
**(*S*,*Z*)-2-(4-Chlorobenzylidene)-1-(nitromethyl)-1,2-dihydronaphtho[2,1-*b*]furan (6c)**



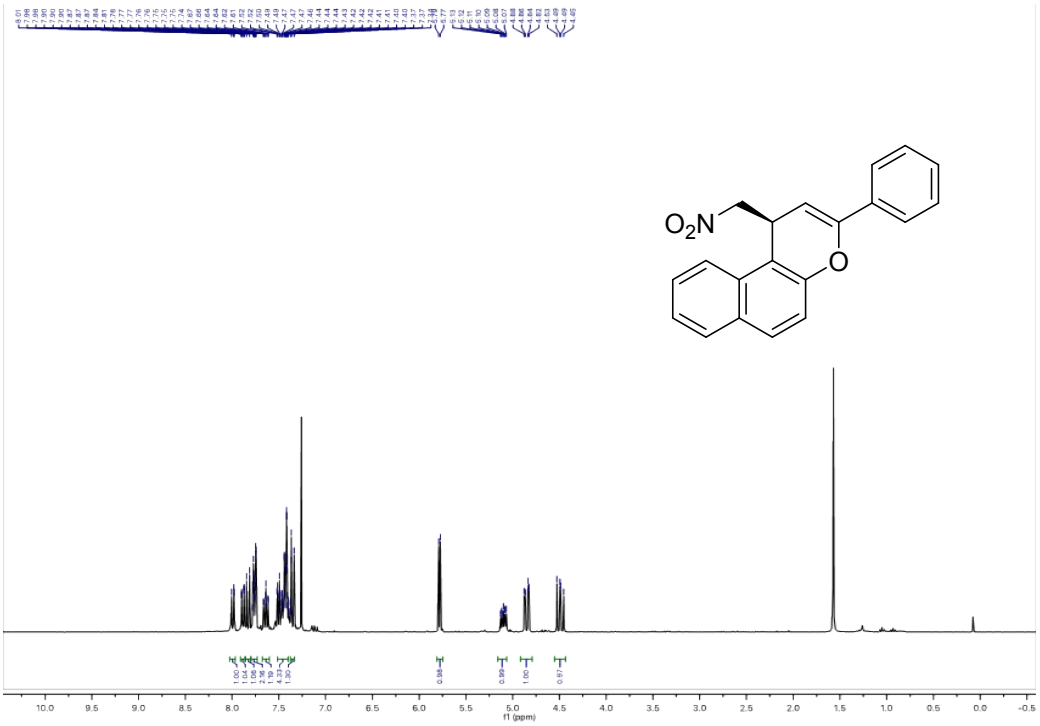



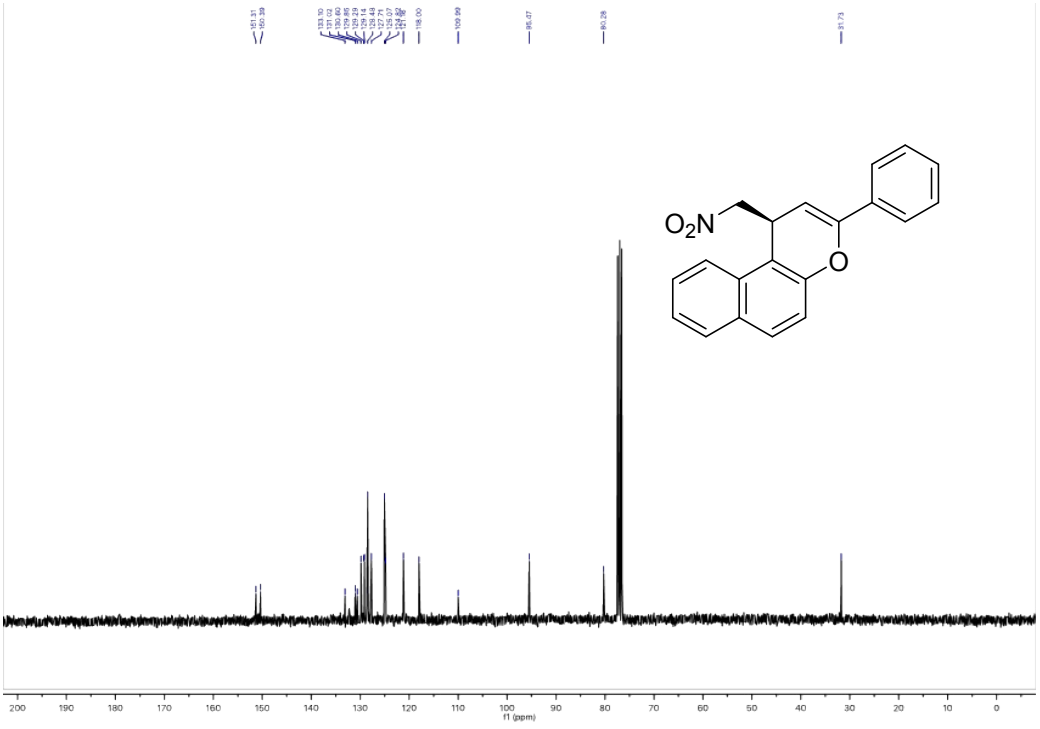
**(*S*,*Z*)-1-(Nitromethyl)-2-(3-phenylpropylidene)-1,2-dihydronaphtho[2,1-*b*]furan (6d)**



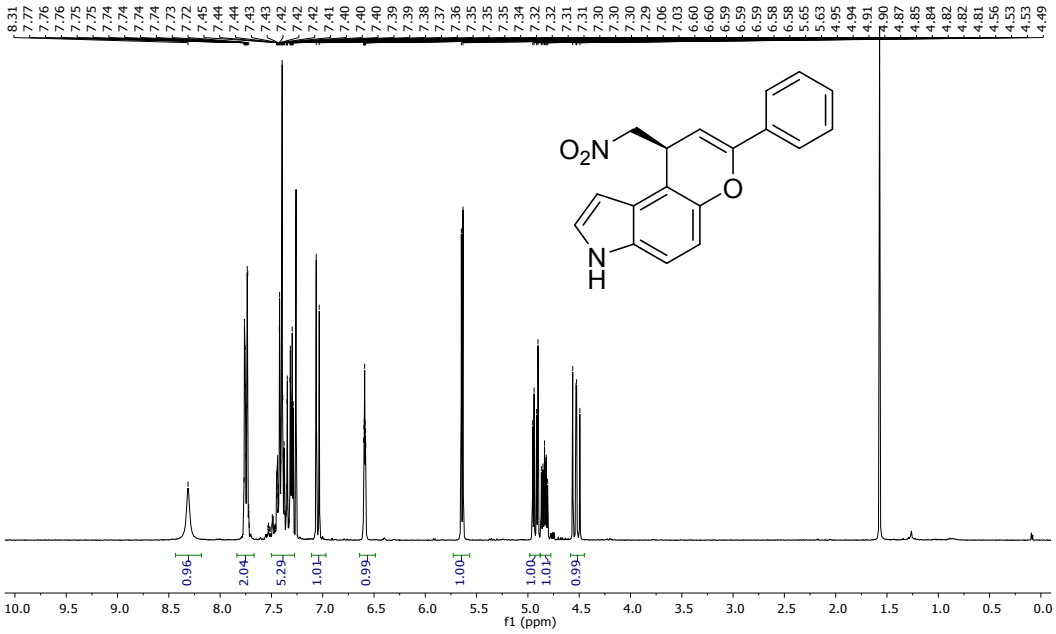



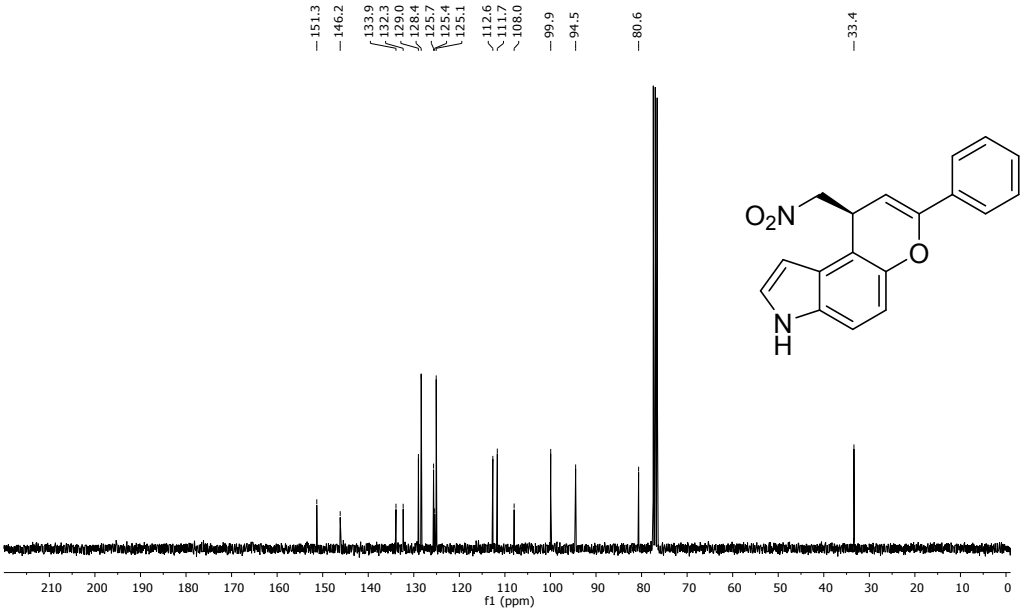
**(*S*)-1-(Nitromethyl)-3-phenyl-1H-benzo[*f*]chromene (7)**



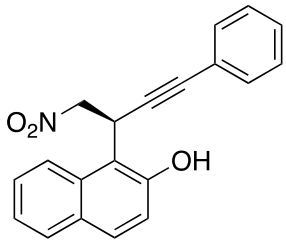



**(*S*)-9-(Nitromethyl)-7-phenyl-3,9-dihydropyrano[3,2-*e*]indole (8)**



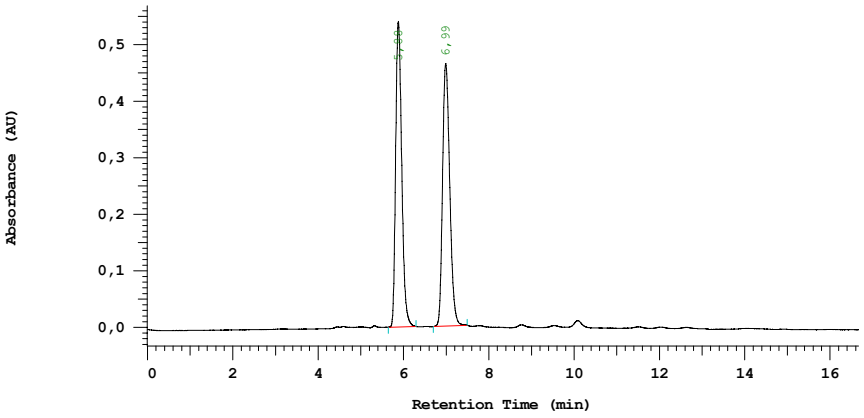



## Chiral analysis chromatograms



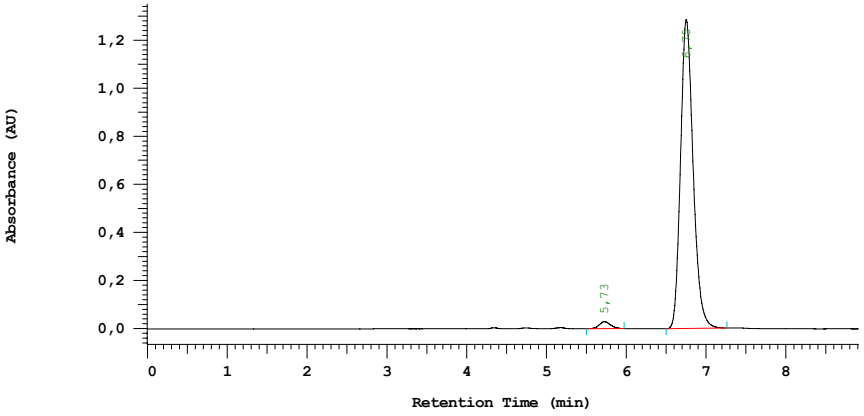

**(3a)**

Non-enantioselective reaction:

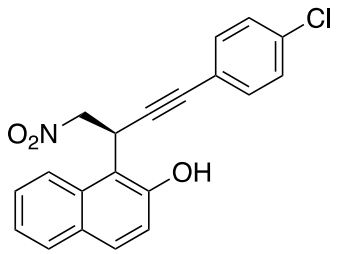



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 5,88 | 2663230 | 49,595 | |
| 2 | 6,99 | 2706760 | 50,405 | |
| | | 5369990 | 100,000 | |

Enantioselective reaction:

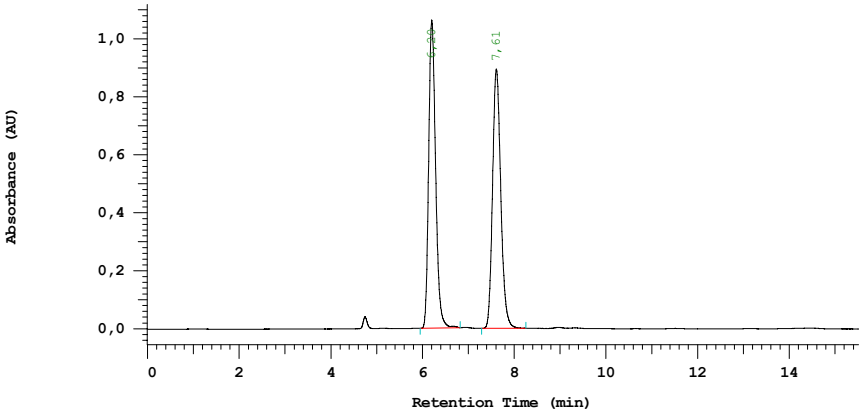



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 5,73 | 141675 | 1,978 | |
| 2 | 6,75 | 7019329 | 98,022 | |
| | | 7161004 | 100,000 | |



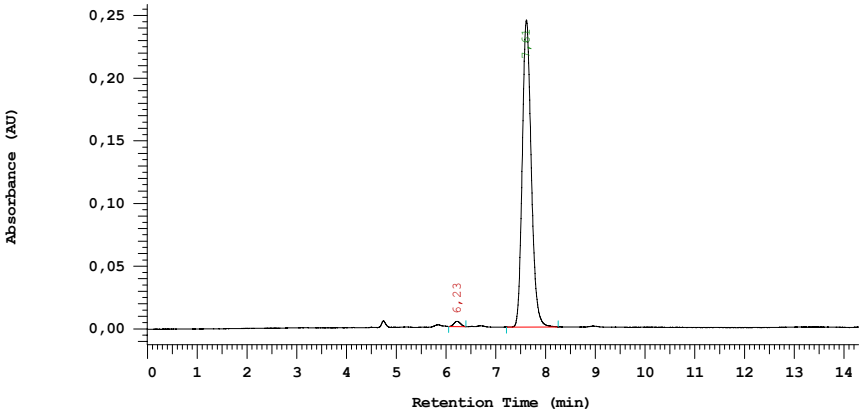

**(3b)**

Non-enantioselective reaction:

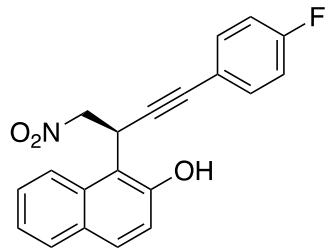



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 6,20 | 5588980 | 49,942 | |
| 2 | 7,61 | 5601930 | 50,058 | |
| | | 11190910 | 100,000 | |

Enantioselective reaction:

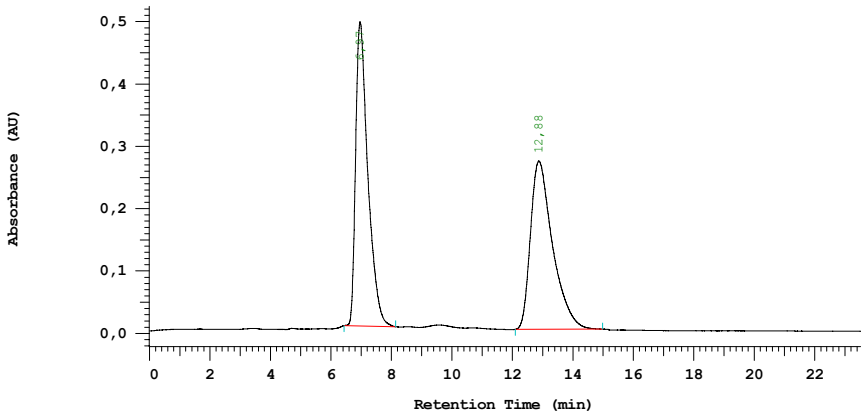



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 6,23 | 19160 | 1,236 | |
| 2 | 7,61 | 1530540 | 98,764 | |
| | | 1549700 | 100,000 | |



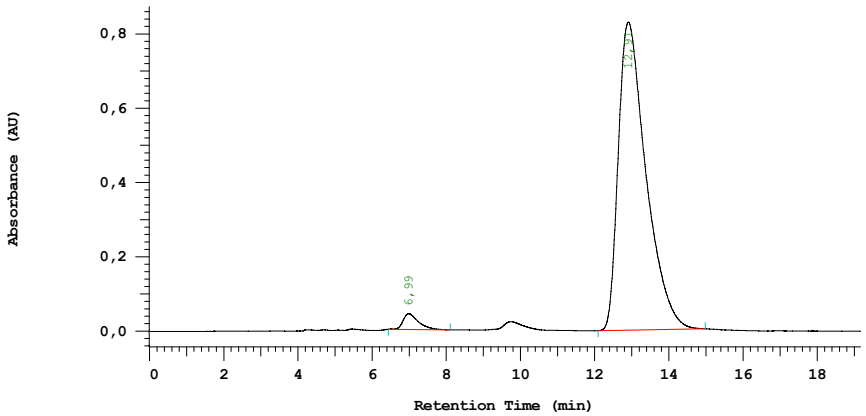

**(3c)**

Non-enantioselective reaction:

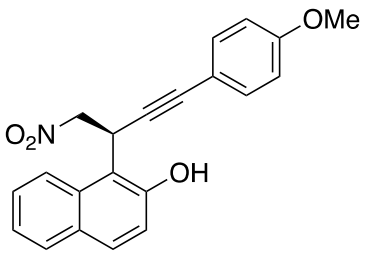



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 6,97 | 6801915 | 49,854 | |
| 2 | 12,88 | 6841809 | 50,146 | |
| | | 13643724 | 100,000 | |

Enantioselective reaction:

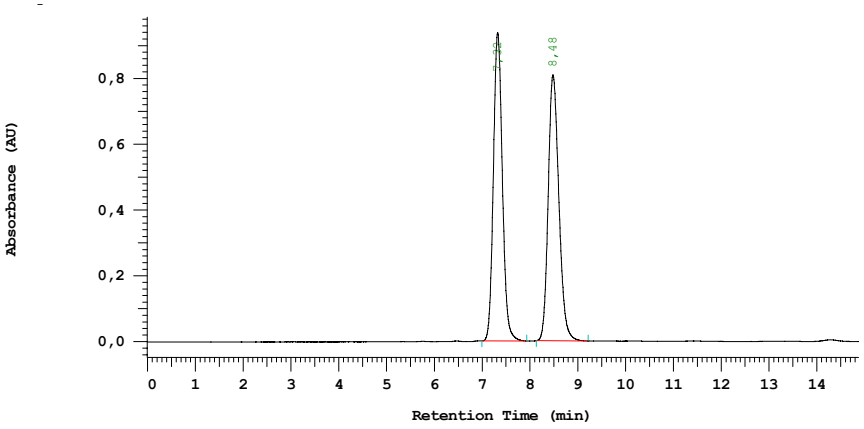



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 6,99 | 611660 | 2,772 | |
| 2 | 12,91 | 21457844 | 97,228 | |
| | | 22069504 | 100,000 | |



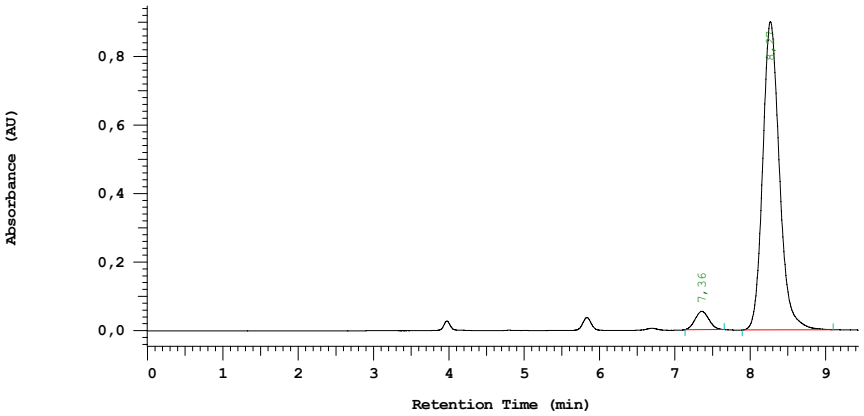

**(3d)**

Non-enantioselective reaction:

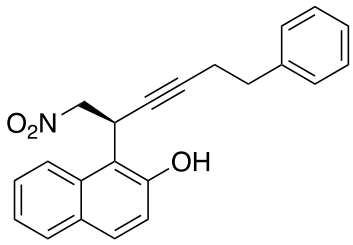



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 7,32 | 6159895 | 49,659 | |
| 2 | 8,48 | 6244475 | 50,341 | |
| | | 12404370 | 100,000 | |

Enantioselective reaction:

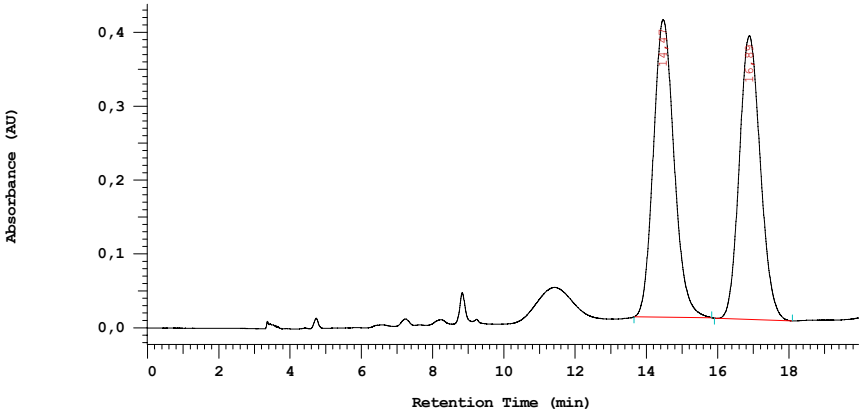



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 7,36 | 339540 | 4,668 | |
| 2 | 8,27 | 6934244 | 95,332 | |
| | | 7273784 | 100,000 | |



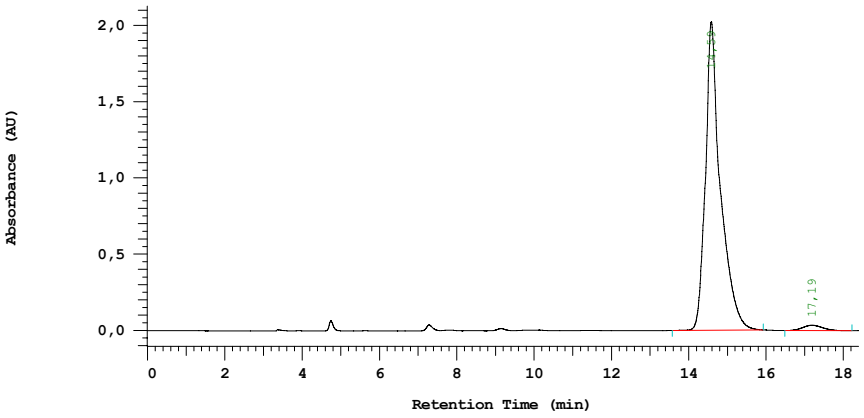

**(3e)**

Non-enantioselective reaction:

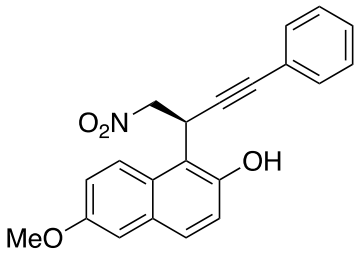



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 14,47 | 8178084 | 50,900 | |
| 2 | 16,89 | 7888769 | 49,100 | |
| | | 16066853 | 100,000 | |

Enantioselective reaction:

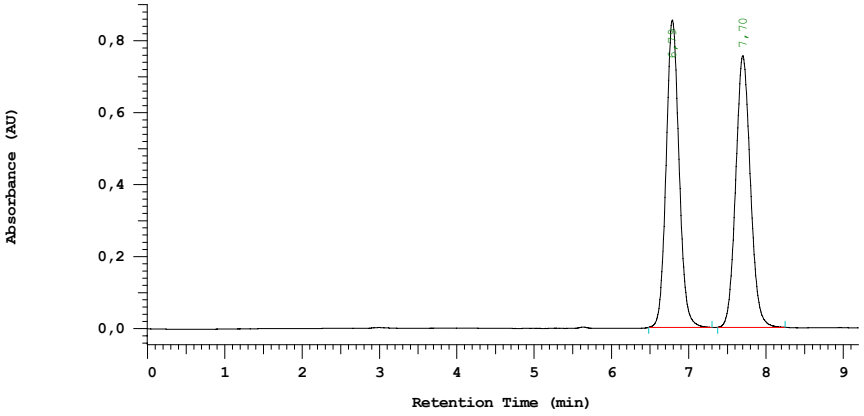



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 14,59 | 27254588 | 97,710 | |
| 2 | 17,19 | 638770 | 2,290 | |
| | | 27893358 | 100,000 | |



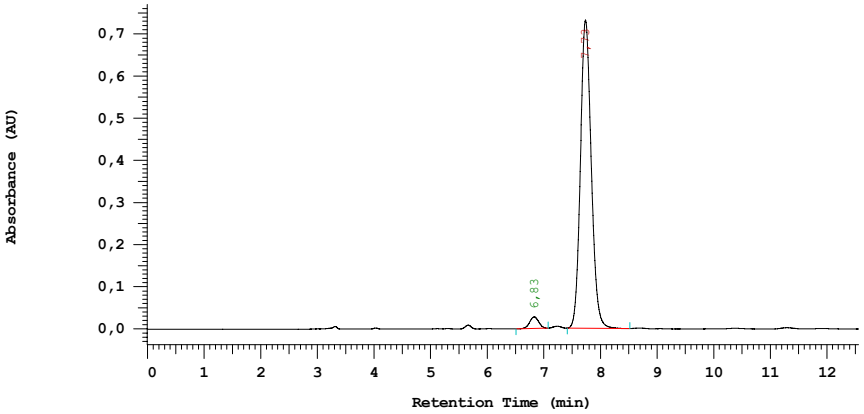

**(3f)**

Non-enantioselective reaction:

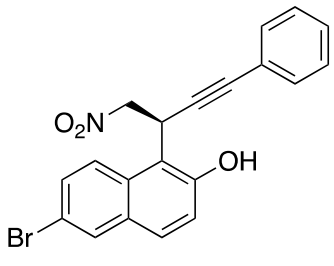



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 6,79 | 4954760 | 49,796 | |
| 2 | 7,70 | 4995340 | 50,204 | |
| | | 9950100 | 100,000 | |

Enantioselective reaction:

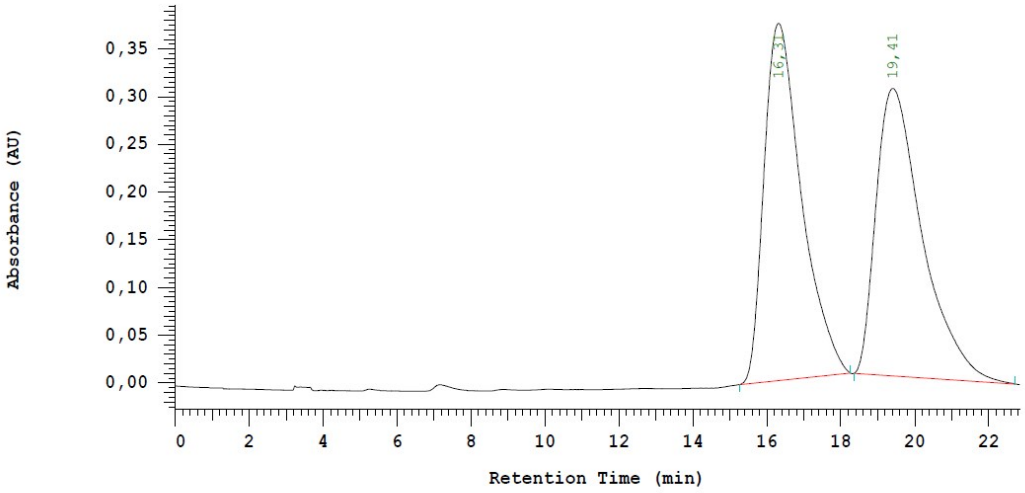



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 6,83 | 151685 | 3,015 | |
| 2 | 7,73 | 4878770 | 96,985 | |
| | | 5030455 | 100,000 | |



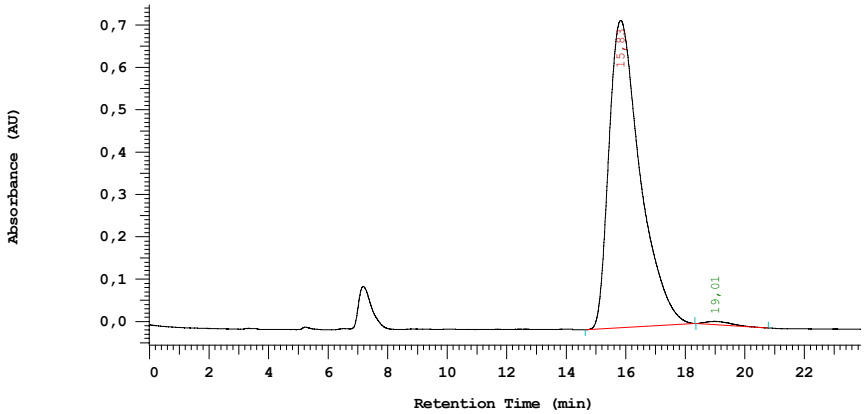

**(3g)**

Non-enantioselective reaction:

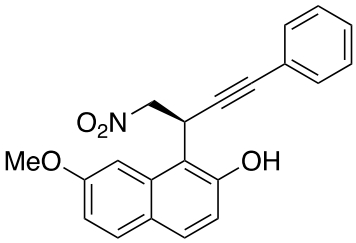



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 16,31 | 13154415 | 50,155 | |
| 2 | 19,41 | 13073140 | 49,845 | |
| | | 26227555 | 100,000 | |

Enantioselective reaction:

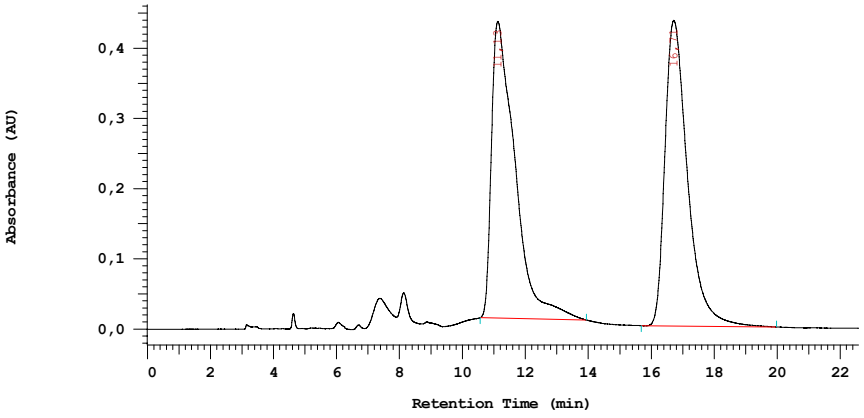



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 15,83 | 26353880 | 99,098 | |
| 2 | 19,01 | 239985 | 0,902 | |
| | | 26593865 | 100,000 | |



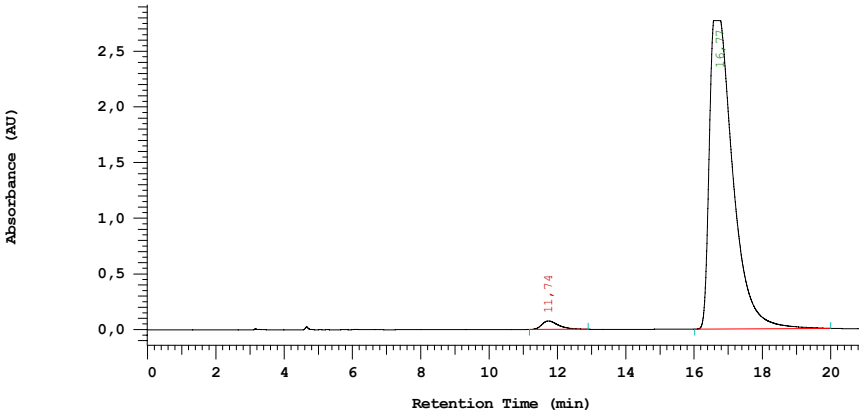

**(3h)**

Non-enantioselective reaction:

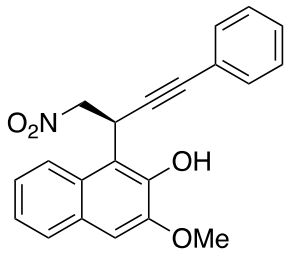



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 11,13 | 10976160 | 50,322 | |
| 2 | 16,71 | 10835840 | 49,678 | |
| | | 21812000 | 100,000 | |

Enantioselective reaction:

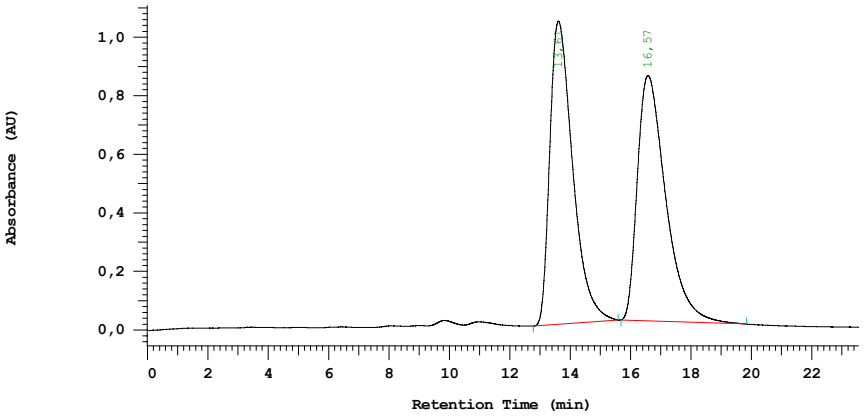



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 11,74 | 1275230 | 1,881 | |
| 2 | 16,77 | 66524288 | 98,119 | |
| | | 67799518 | 100,000 | |



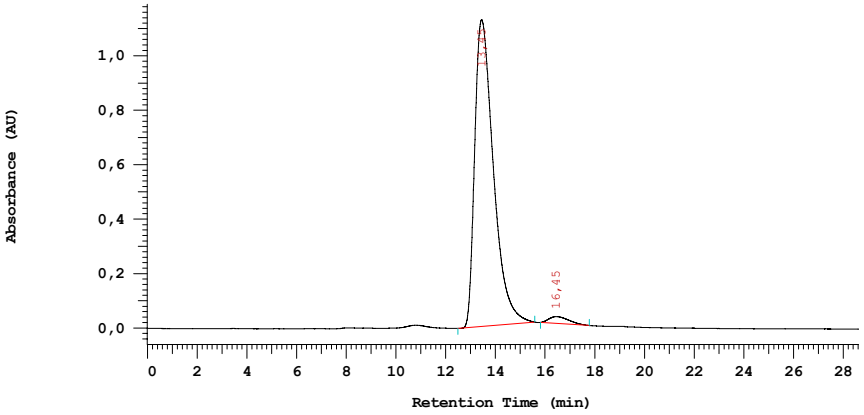

**(3i)**

Non-enantioselective reaction:

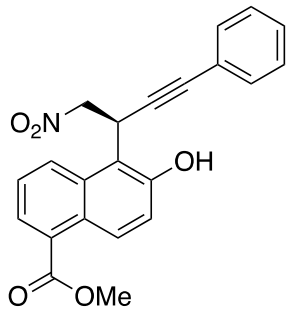



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 13,61 | 27196899 | 49,916 | |
| 2 | 16,57 | 27288611 | 50,084 | |
| | | 54485510 | 100,000 | |

Enantioselective reaction:

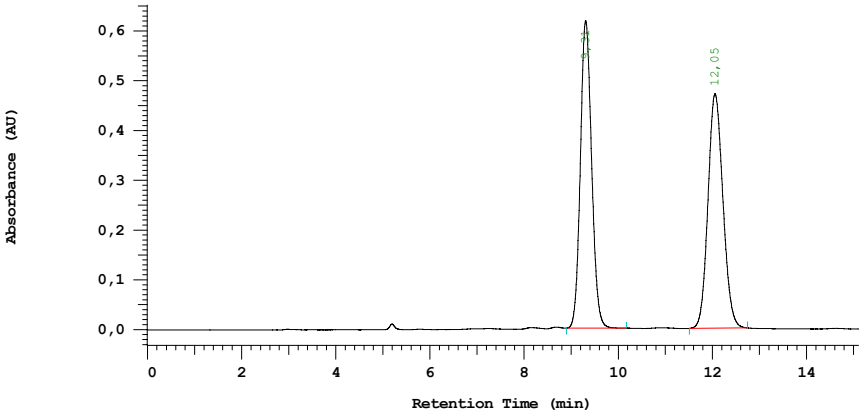



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 13,45 | 29336268 | 97,665 | |
| 2 | 16,45 | 701500 | 2,335 | |
| | | 30037768 | 100,000 | |



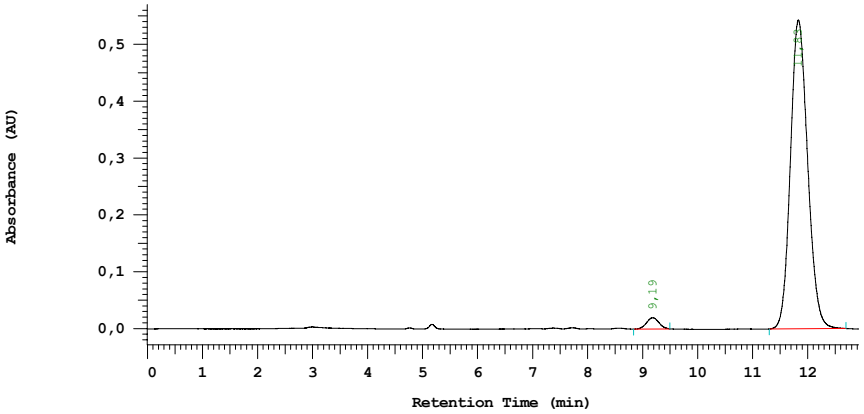

**(3j)**

Non-enantioselective reaction:

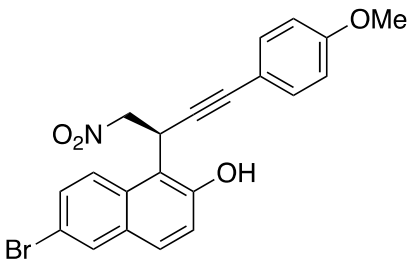



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 9,31 | 5137020 | 49,790 | |
| 2 | 12,05 | 5180340 | 50,210 | |
| | | 10317360 | 100,000 | |

Enantioselective reaction:

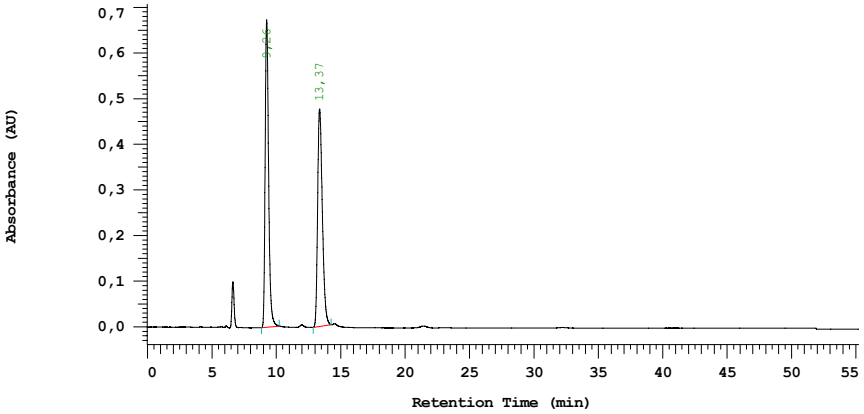



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 9,19 | 153510 | 2,540 | |
| 2 | 11,83 | 5891075 | 97,460 | |
| | | 6044585 | 100,000 | |



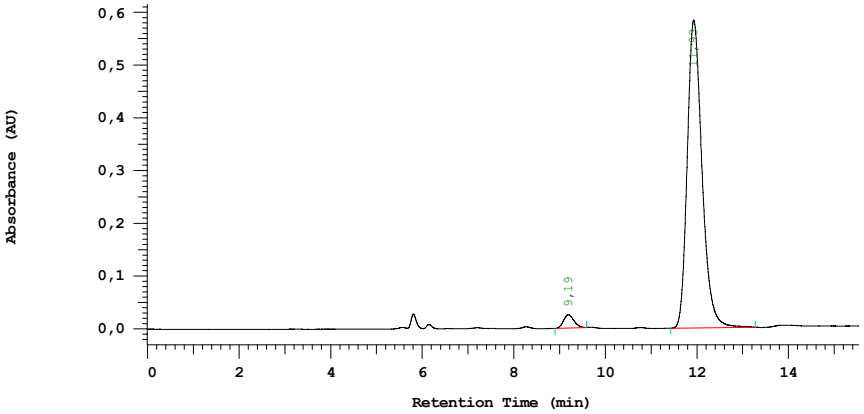

**(3k)**

Non-enantioselective reaction:

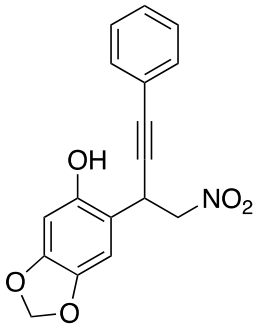



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 9,26 | 6031510 | 50,540 | |
| 2 | 13,37 | 5902550 | 49,460 | |
| | | 11934060 | 100,000 | |

Enantioselective reaction:

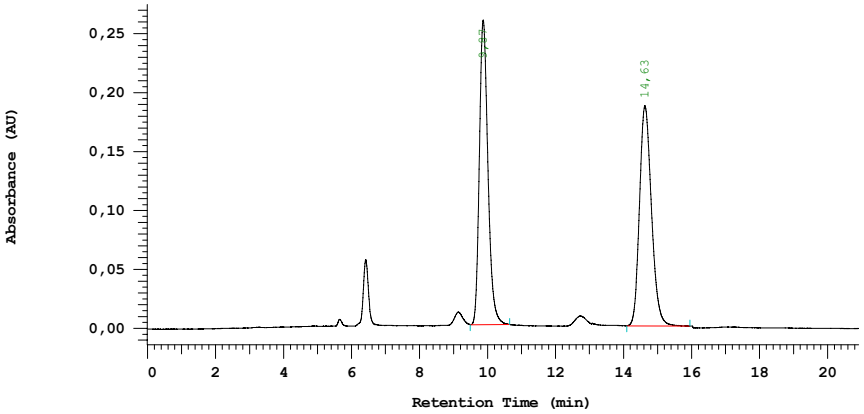



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 9,19 | 199015 | 2,946 | |
| 2 | 11,93 | 6557340 | 97,054 | |
| | | 6756355 | 100,000 | |



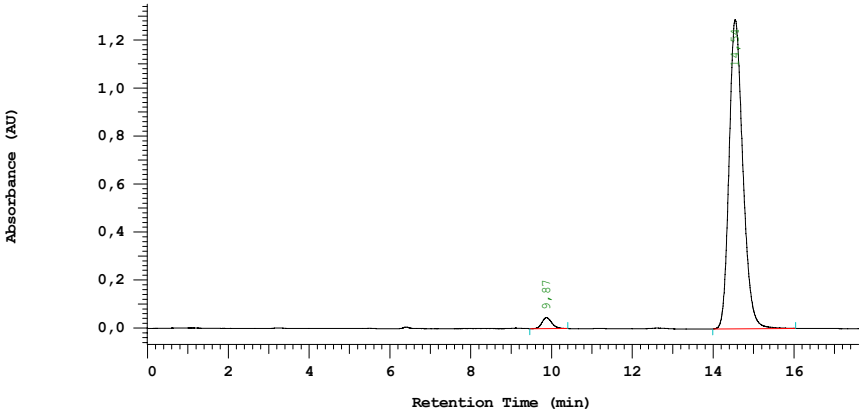

**(3l)**

Non-enantioselective reaction:

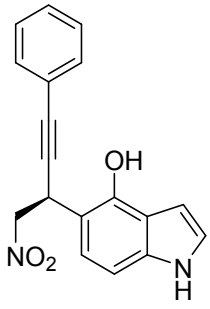



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 9,87 | 2242080 | 49,697 | |
| 2 | 14,63 | 2269455 | 50,303 | |
| | | 4511535 | 100,000 | |

Enantioselective reaction:

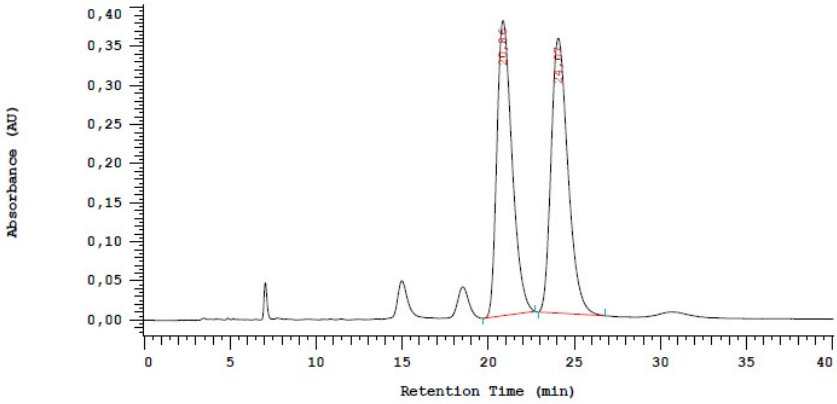



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 9,87 | 387760 | 2,479 | |
| 2 | 14,54 | 15253120 | 97,521 | |
| | | 15640880 | 100,000 | |



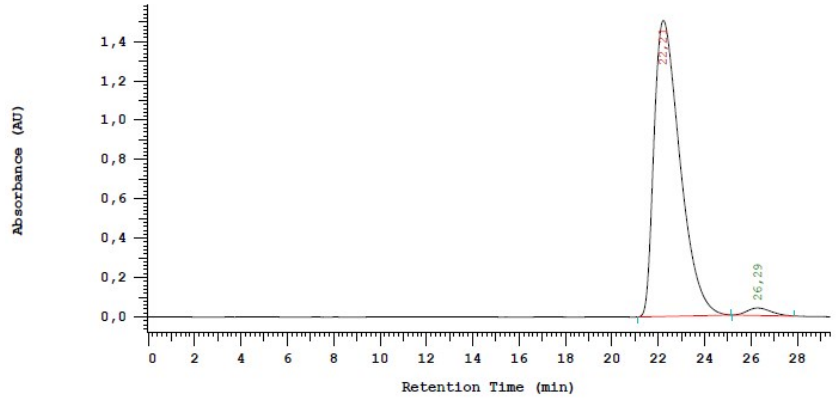

**(5a)**

Non-Enantioselective reaction:

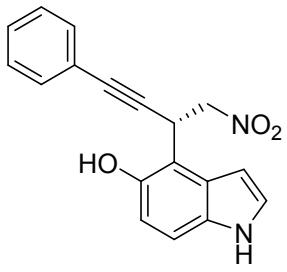



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 20,86 | 11485230 | 48,980 | |
| 2 | 24,07 | 11963729 | 51,020 | enant. (+) |
| | | 23448959 | 100,000 | |

Enantioselective reaction:

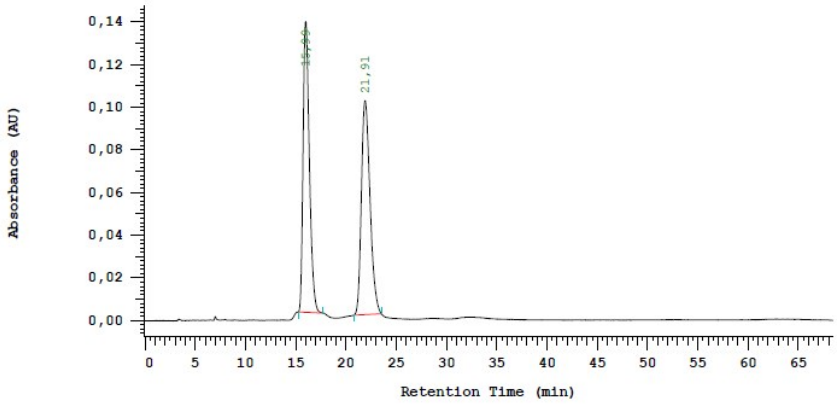



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 22,21 | 58375257 | 97,752 | enant. (+) |
| 2 | 26,29 | 1342410 | 2,248 | enanti (-) |
| | | 59717667 | 100,000 | |



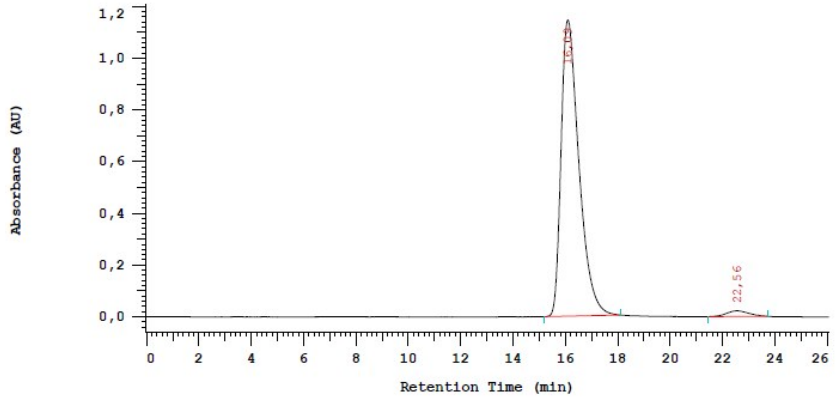

**(5b)**

Non-Enantioselective reaction:

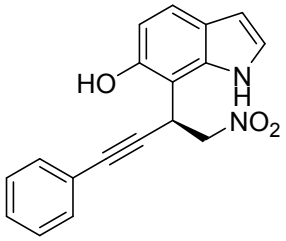



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 15,99 | 2882350 | 49,397 | |
| 2 | 21,91 | 2952680 | 50,603 | enant. (+) |
| | | 5835030 | 100,000 | |

Enantioselective reaction:

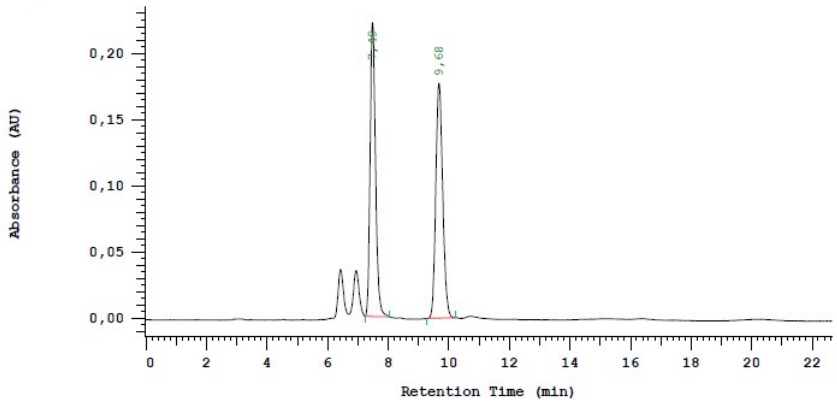



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 16,09 | 27055628 | 97,710 | |
| 2 | 22,56 | 634185 | 2,290 | enant. (+) |
| | | 27689813 | 100,000 | |



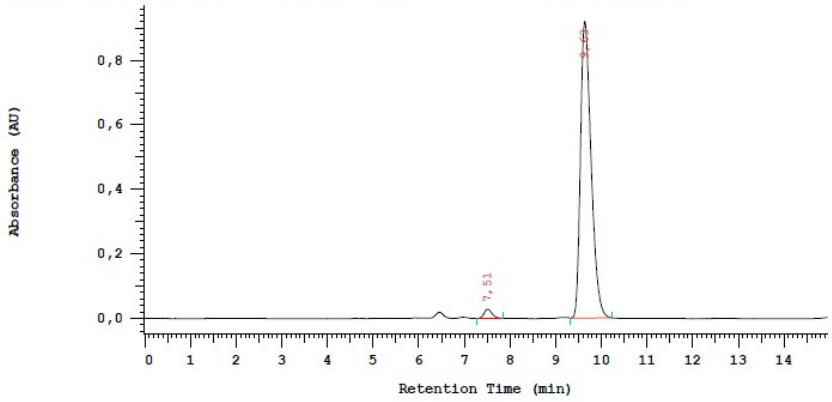

**(5c)**

Non-Enantioselective reaction:

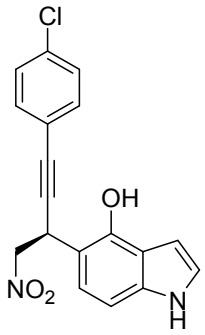



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 7,49 | 1390720 | 49,841 | |
| 2 | 9,68 | 1399605 | 50,159 | |
| | | 2790325 | 100,000 | |

Enantioselective reaction:

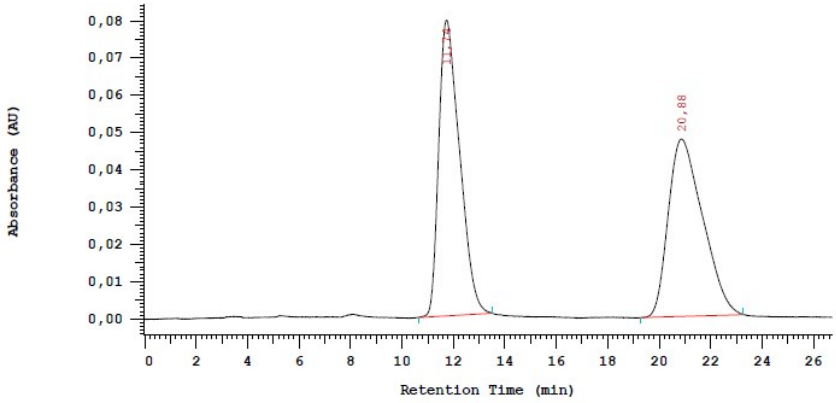



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 7,51 | 173305 | 2,285 | |
| 2 | 9,63 | 7410644 | 97,715 | |
| | | 7583949 | 100,000 | |



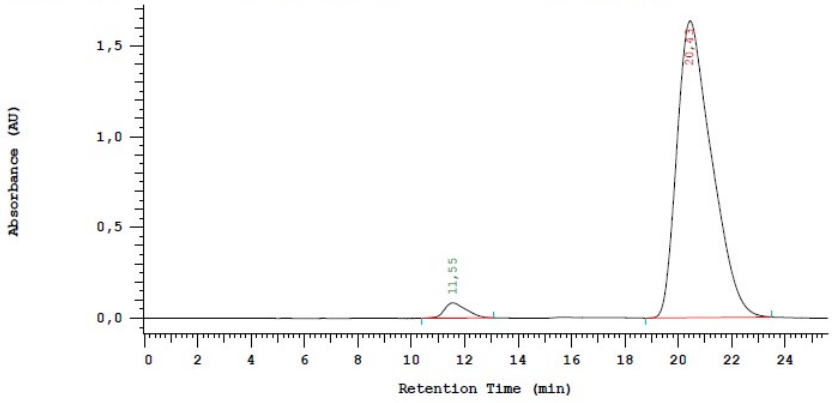

**(5d)**

Non-Enantioselective reaction:

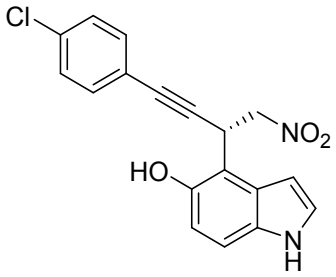



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 11,74 | 2235125 | 50,299 | |
| 2 | 20,88 | 2208590 | 49,701 | |
| | | 4443715 | 100,000 | |

Enantioselective reaction:

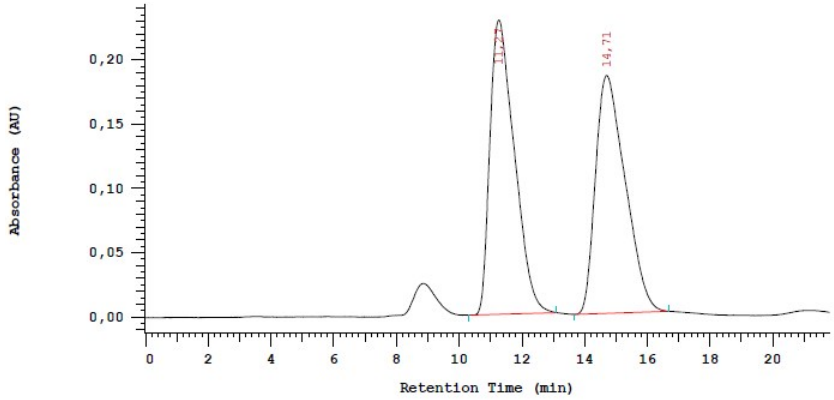



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 11,55 | 2388410 | 3,133 | |
| 2 | 20,43 | 73835769 | 96,867 | |
| | | 76224179 | 100,000 | |



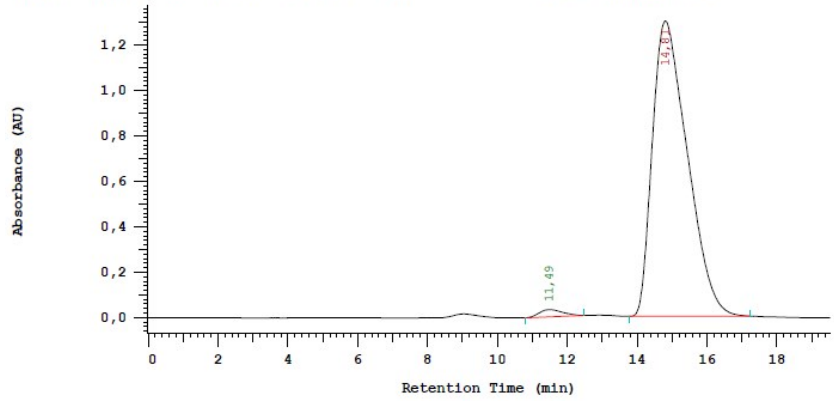

**(5e)**

Non-Enantioselective reaction:

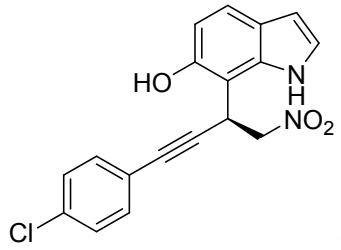



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 11,27 | 6191744 | 50,432 | |
| 2 | 14,71 | 6085550 | 49,568 | |
| | | 12277294 | 100,000 | |

Enantioselective reaction:

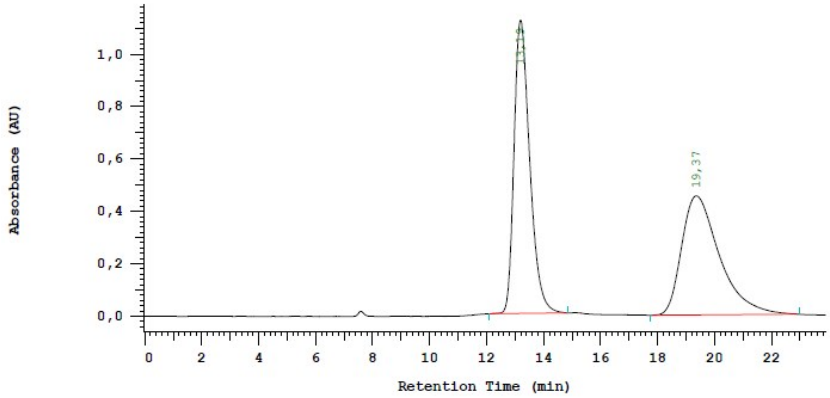



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 11,49 | 743500 | 1,620 | |
| 2 | 14,81 | 45162188 | 98,380 | |
| | | 45905688 | 100,000 | |



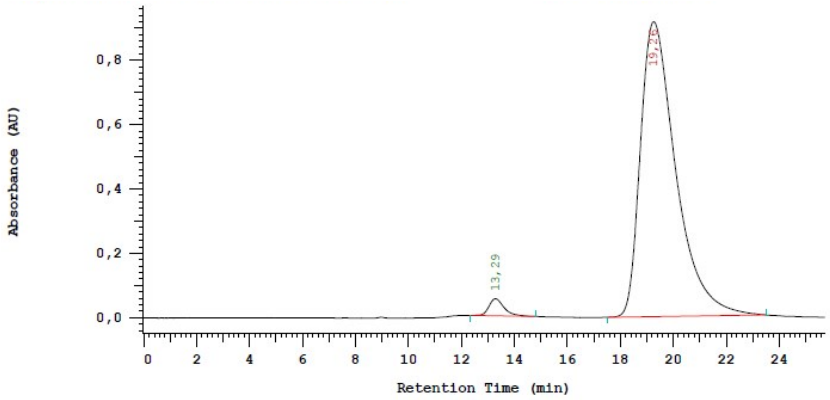

**(5f)**

Non-Enantioselective reaction:

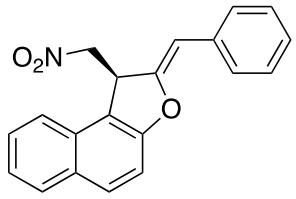



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 13,19 | 21481249 | 50,593 | |
| 2 | 19,37 | 20977814 | 49,407 | |
| | | 42459063 | 100,000 | |

Enantioselective reaction:

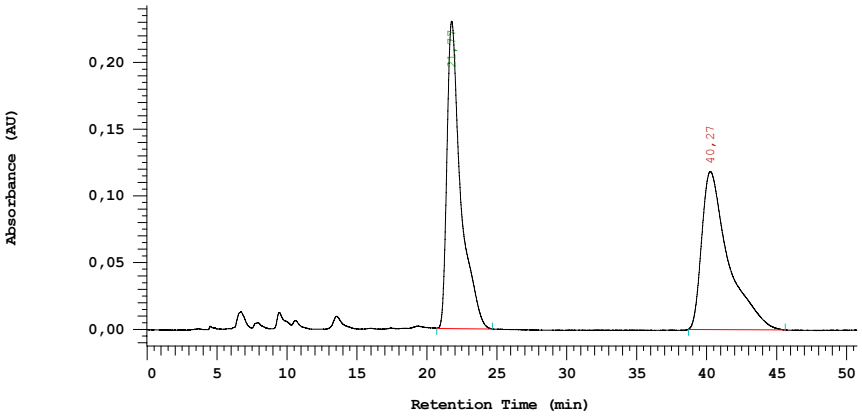



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 13,29 | 1052690 | 2,416 | |
| 2 | 19,26 | 42518099 | 97,584 | |
| | | 43570789 | 100,000 | |



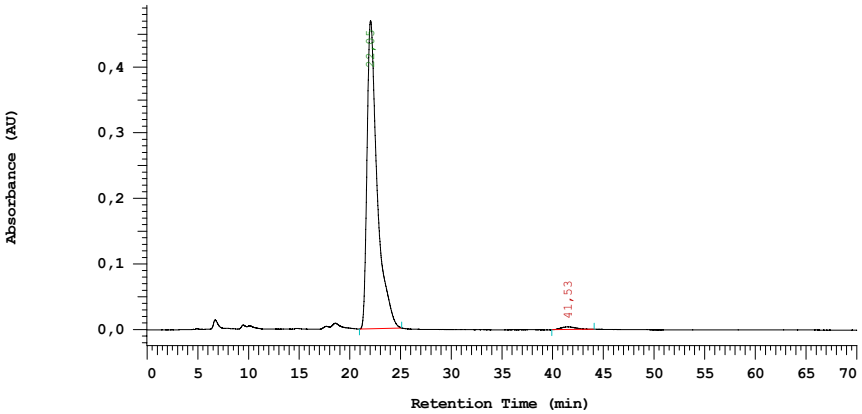

**(6a)**

Non-enantioselective reaction:

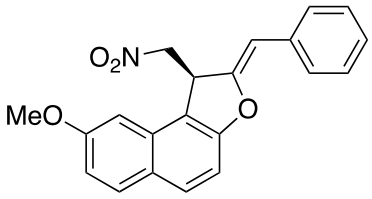



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 21,77 | 7821800 | 50,148 | enant. (+) |
| 2 | 40,27 | 7775564 | 49,852 | |
| | | 15597364 | 100,000 | |

Enantioselective reaction:

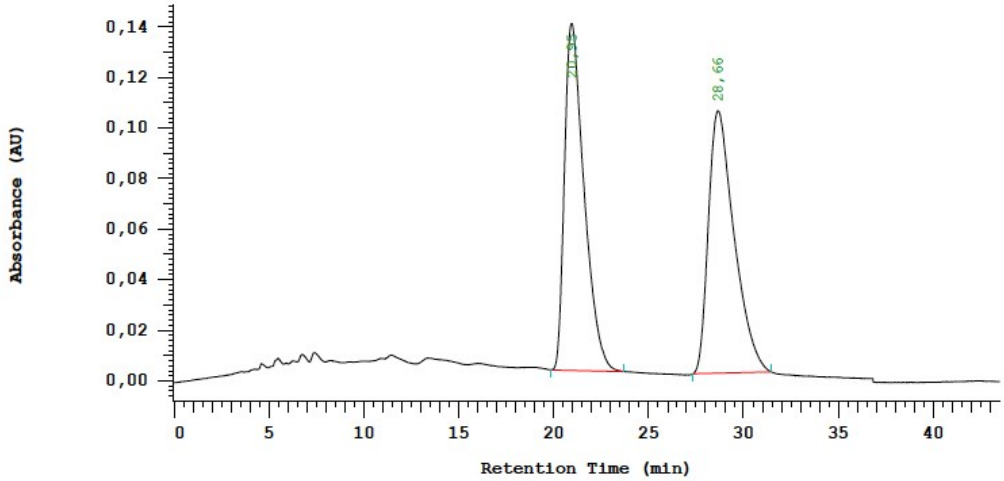



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 22,05 | 16177569 | 98,689 | enant. (+) |
| 2 | 41,53 | 214925 | 1,311 | |
| | | 16392494 | 100,000 | |



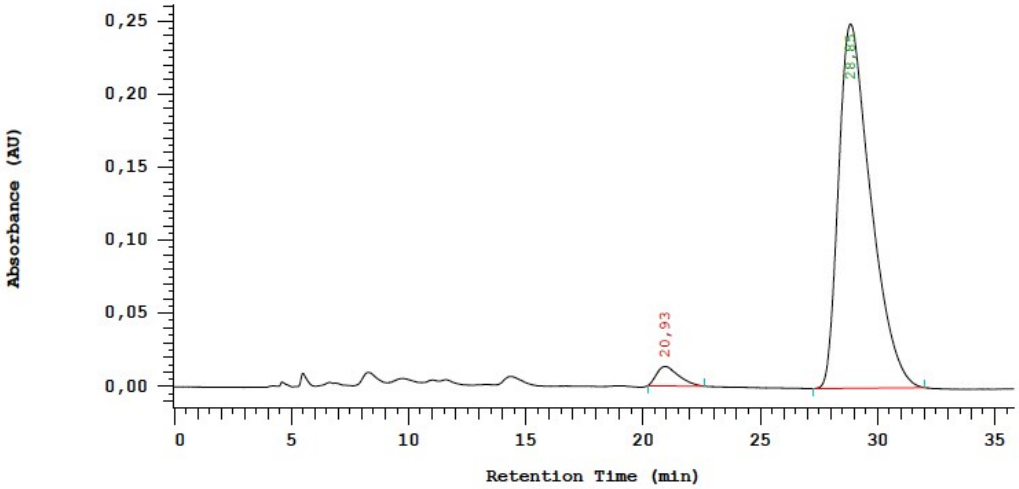

**(6b)**

Non-enantioselective reaction:

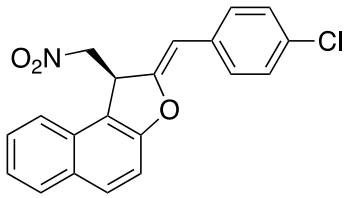



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 20,95 | 4897180 | 50,142 | |
| 2 | 28,66 | 4869390 | 49,858 | enanti (-) |
| | | 9766570 | 100,000 | |

Enantioselective reaction:

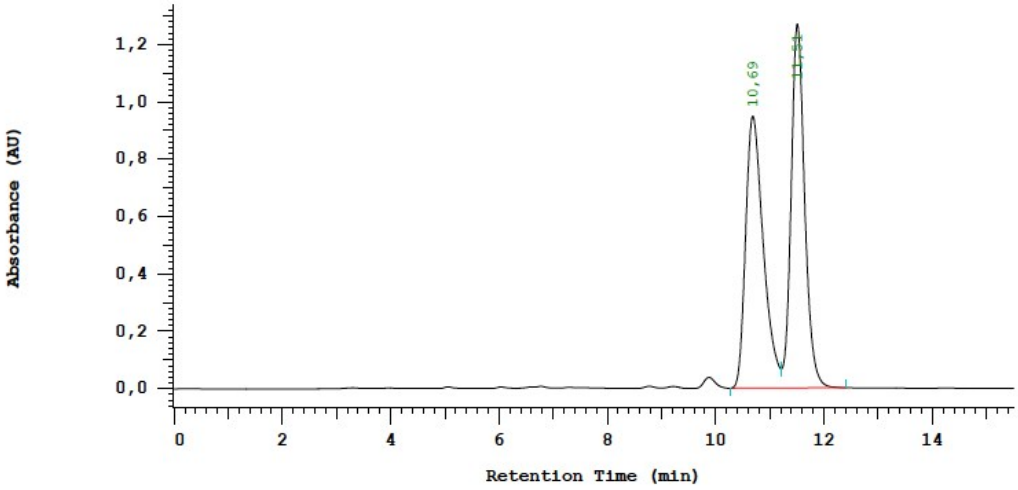



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 20,93 | 429255 | 3,486 | |
| 2 | 28,85 | 11883544 | 96,514 | enanti (-) |
| | | 12312799 | 100,000 | |



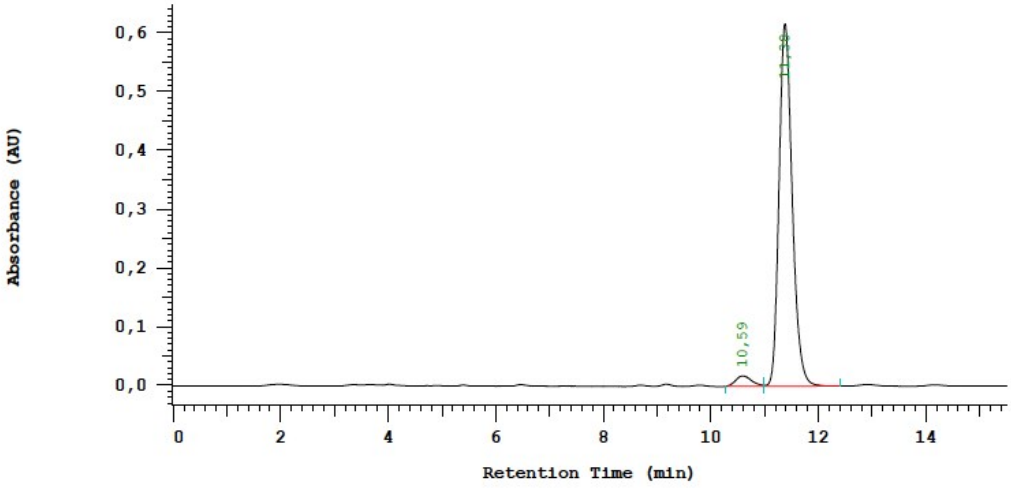

**(6c)**

Non-enantioselective reaction:

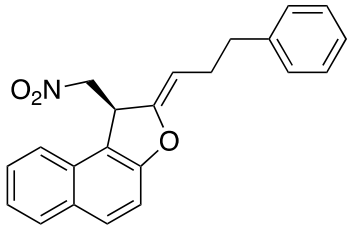



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 10,69 | 10726953 | 49,255 | |
| 2 | 11,51 | 11051256 | 50,745 | |
| | | 21778209 | 100,000 | |

Enantioselective reaction:

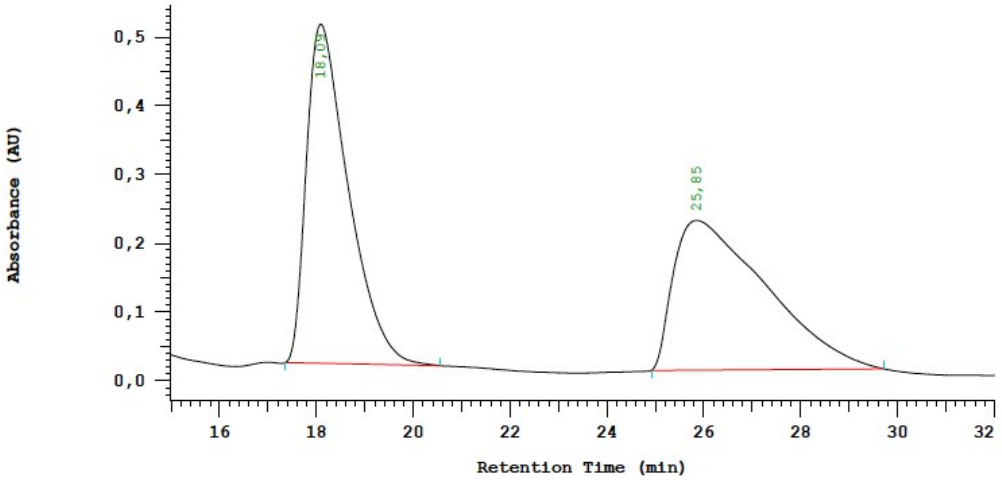



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 10,59 | 180211 | 3,327 | |
| 2 | 11,38 | 5235908 | 96,673 | |
| | | 5416119 | 100,000 | |



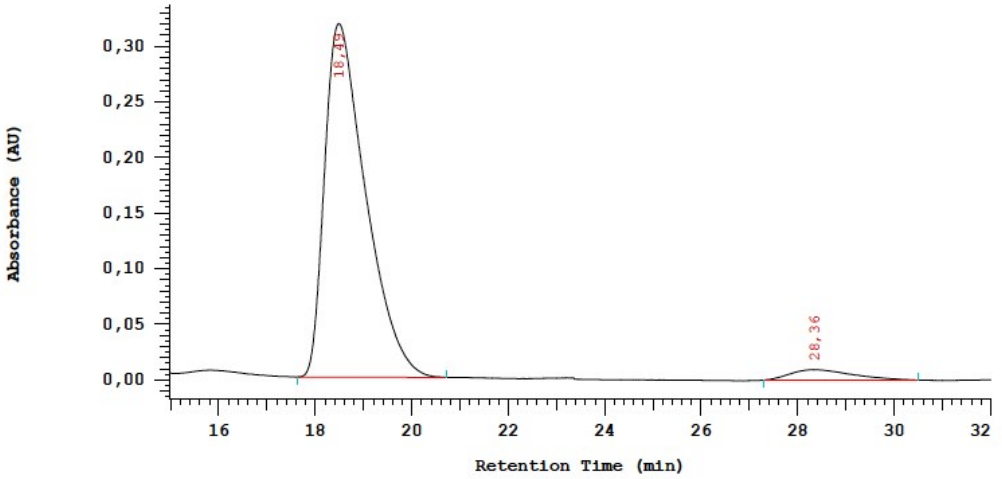

**(6d)**

Non-enantioselective reaction:

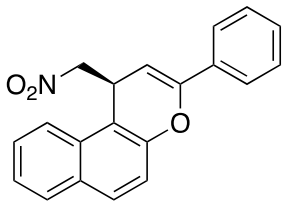



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 18,09 | 14852430 | 50,696 | |
| 2 | 25,85 | 14444460 | 49,304 | enant. (+) |
| | | 29296890 | 100,000 | |

Enantioselective reaction:

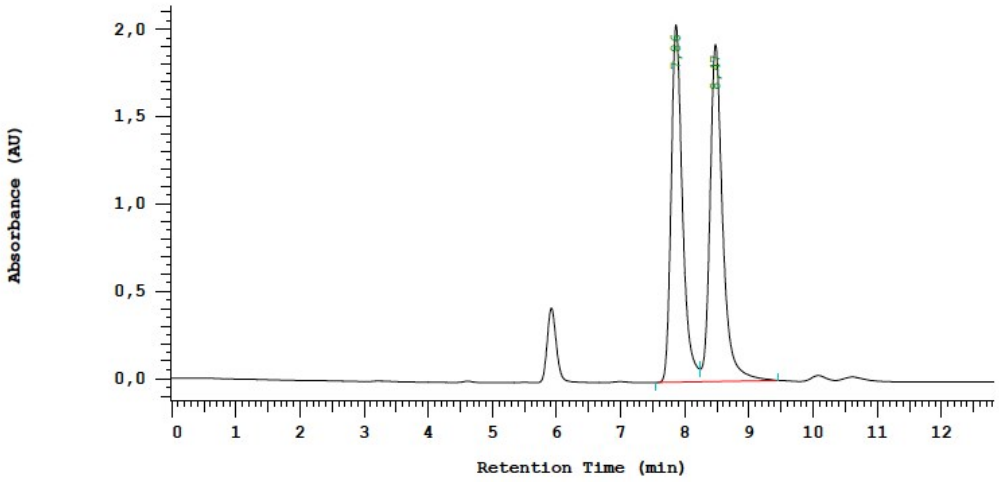



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 18,49 | 9385590 | 95,814 | |
| 2 | 28,36 | 410000 | 4,186 | enanti (-) |
| | | 9795590 | 100,000 | |



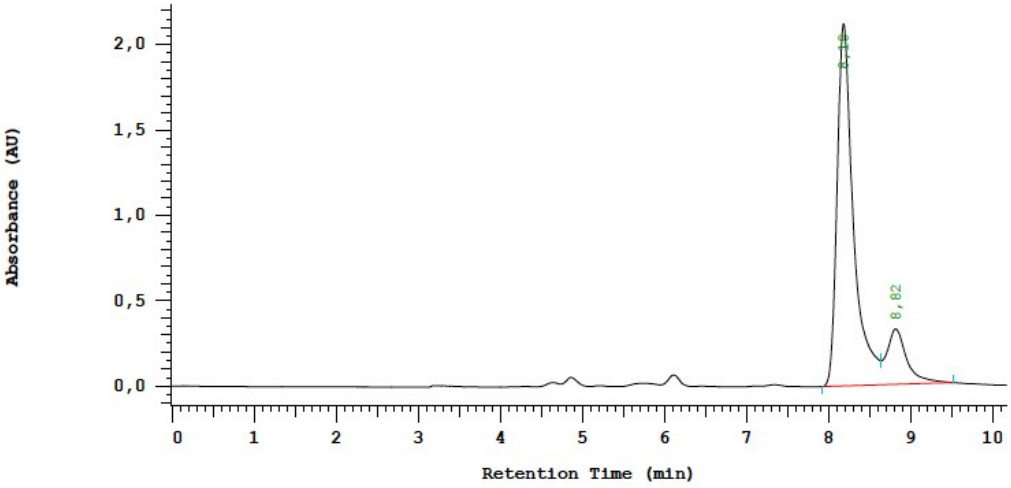

**(7)**

Non-enantioselective reaction:

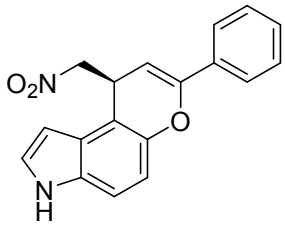



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 7,86 | 12636362 | 48,561 | |
| 2 | 8,47 | 13385523 | 51,439 | |
| | | 26021885 | 100,000 | |

Enantioselective reaction:

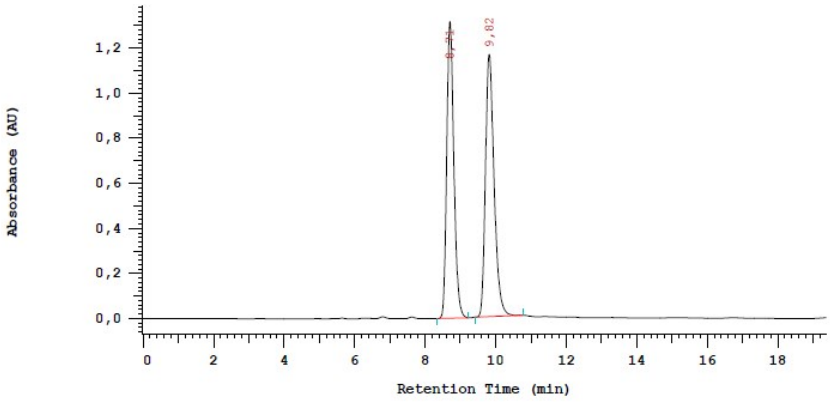



| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 8,18 | 14655996 | 84,092 | |
| 2 | 8,82 | 2772614 | 15,908 | |
| | | 17428610 | 100,000 | |



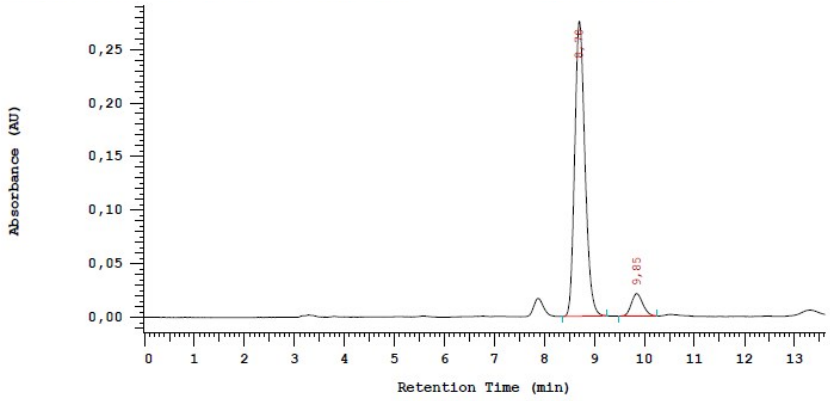

**(8)**

Non-Enantioselective reaction:




| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 8,71 | 9195070 | 48,217 | |
| 2 | 9,82 | 9875169 | 51,783 | |
| | | 19070239 | 100,000 | |

Enantioselective reaction:




| No. | RT | Area | Area % | Name |
|---|---|---|---|---|
| 1 | 8,70 | 1960700 | 92,126 | |
| 2 | 9,85 | 167590 | 7,874 | |
| | | 2128290 | 100,000 | |