Supporting Information

Nonsilyl bicyclic secondary amine catalyzed Michael addition of nitromethane to *β*,*β*-disubstituted *α*,*β*-unsaturated aldehydes

Rohtash Kumar, Avinash Avinash, Ronak Mehta and Chandrakumar Appayee*

Department of Chemistry, Indian Institute of Technology Gandhinagar, Gandhinagar, Gujarat-382055, India

E-mail: a.chandra@iitgn.ac.in

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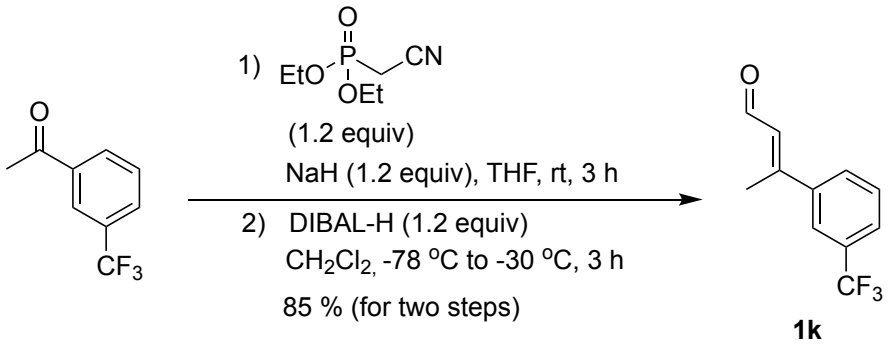
1. General information

All the reagents were purchased from Sigma-Aldrich, TCI and used without further purification unless otherwise mentioned. All the solvents were purchased from Merck or SD Fine and used for the purification of products. Thin-layer chromatography (SiO_2, TLC) was performed on Merck TLC silica gel 60 F_{254} visualized by ultraviolet irradiation, $KMnO_4$ solution. Column chromatography was performed on Merck silica gel 100-200 using standard flash chromatographic methods. The NMR spectra were recorded on Bruker Advance III (500 MHz) spectrometer and were referenced against the residual solvent peaks [$CDCl_3$: δ 7.26 ppm (^{1}H NMR) and 77.16 ppm ($^{13}C\{^1H\}$ NMR). Chemical shifts are reported in parts per million as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet), coupling constant, and integration. Infrared spectra were recorded on Perkin Elmer Spectrum Two FT-IR spectrometer. Selected absorption bands are reported in wave numbers (cm^{-1}). The HRMS data for all the compounds was recorded (in positive ion mode) with Waters Synapt-G2S ESI-Q-TOF Mass instrument. Chiral HPLC analysis was performed on Agilent 1200 series using Daicel Chiralpak IC, IG and IA (Chiral Technologies Eur., 25 cm × 4.6 mm I.D.) were used. Specific rotations were measured with a Rudolph Polarimeter 341 at 589 nm and were reported as $[\alpha]_D^t$ (*c* in g per 100 mL, solvent, *ee*). The compound **1a-1c**[1], **1d**[3], **1e**[1], **1f**[2], **1g-1j**[1], **1l-1n**[1], **1o**[3], **1p**[4],**1q**[5] **1r**[6], and **1s**[7], **1t**[12], were prepared according to the literature procedure.

2. Experimental procedure for the synthesis of (*E*)-3-(3-(trifluoromethyl)phenyl)but-2-enal (1k)

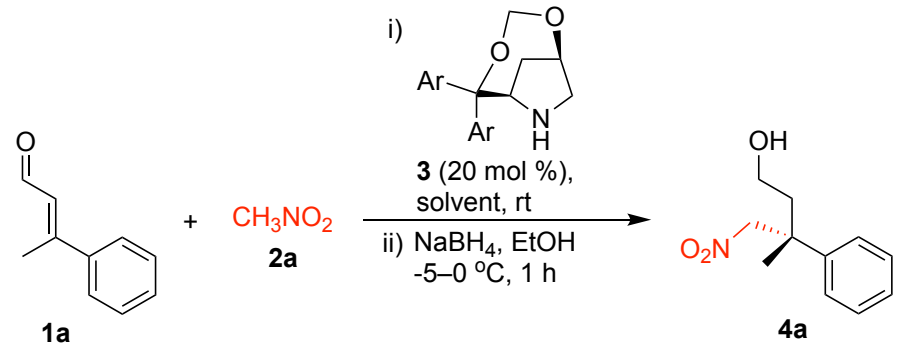


To a solution of NaH (0.96 g, 24.0 mmol, 1.2 equiv, 60% assay) in anhydrous THF (30 mL), diethyl (cyanomethyl)phosphonate (3.9 mL, 24.0 mmol, 1.2 equiv) was added dropwise at rt and stirred for 10 min under argon atmosphere. Then, 1-(3-(trifluoromethyl)phenyl)ethan-1-one (3.76 g, 20 mmol, 1.0 equiv) dissolved in anhydrous THF (30 mL) was added dropwise to the reaction mixture at the same temperature and stirred for 3 h. After completion of the

reaction (monitored by TLC), the crude reaction mixture was diluted with water (40 mL), and extracted with CH_2Cl_2 (3 x 40 mL). The organic layers were combined and dried over anhydrous Na_2SO_4, concentrated over the rotary evaporator. The crude mass was diluted with diethyl ether and passed through a short pad of silica gel. After the removal of solvent, the crude product was used for the next step without further purification.

To a dry 100 ml round bottom flask under argon containing the crude product, was added dry CH_2Cl_2 (20 mL) and cooled to -78 °C. To this solution, DIBAL-H (13.7 mL, 24.0 mmol, 1.2 equiv, concentration 25% by weight in toluene) was added dropwise while maintaining -78 °C temperature and then stirred for 3 h at -30 °C. After completion of the reaction (monitored by TLC), the crude reaction mixture was diluted with EtOAc (100 mL), added to saturated sodium potassium tartrate solution (100 mL), and stirred vigorously for 30 min. The organic layer was separated, and the aqueous layer was again extracted with EtOAc (2 x 40 mL). The organic phases were combined, dried over Na_2SO_4, and concentrated under reduced pressure to get the crude product **1k**, which was further purified as a yellow liquid (3.64 g, 85% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (90:10)]. $\mathbf{R_f}$ = 0.5 [hexane/EtOAc (90:10)]. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.19 (d, J = 7.5 Hz, 1H), 7.76 (s, 1H), 7.71 (d, J = 8 Hz, 1H), 7.66 (d, J = 8 Hz, 1H), 7.54 (t, J = 8 Hz, 1H), 6.38 (dd, J = 7.5, 1.5 Hz, 1H), 2.59 (d, J = 1.0 Hz, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 191.0, 155.7, 141.6, 131.4 (q, J^2 = 32.7 Hz), 129.6, 129.5, 128.4, 126.6 (q, J^3 = 3.8 Hz), 123.9 (q, J^1 = 272.2 Hz), 123.2 (q, J^3 = 3.8 Hz), 16.5. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -62.8. **IR** (neat) ν 2865, 2757, 1663, 1612, 1497, 1439, 1338, 1311, 1245, 1164 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{11}H_{10}F_3O^+$ $[M + H]^+$ 215.0678, found 215.0686.

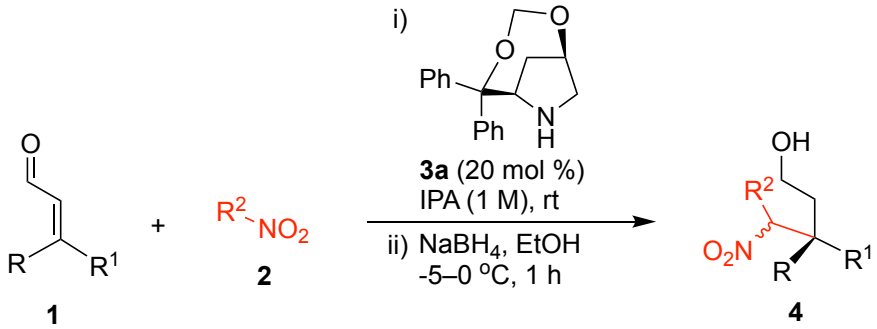
3. Reaction optimization for the synthesis of *β*-substituted *γ*-nitroalcohol 4a



To a solution of bicyclic organocatalyst **3** (0.04 mmol, 0.2 equiv), in solvent (200 µL), (*E*)-3-phenylbut-2-enal **1a** (29 mg, 0.2 mmol, 1 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) were added at rt and stirred under argon atmosphere for the time mention in table 1 (in manuscript). After completion of the reaction (monitored by ^{1}H NMR), to a cooled solution (-5 °C) of $NaBH_4$ (76 mg, 2.0 mmol, 10 equiv) in EtOH (1.6 mL), a solution of the reaction mixture in EtOH (0.8 mL) was added dropwise. The reaction mixture was stirred at -5 °C for 15 min and at 0 °C for 1 h. Then, the reaction mass was quenched with pieces of ice, distilled

the ethanol over the rota evaporator, and diluted with EtOAc (25 mL), washed with a saturated aqueous solution of $NaHCO_3$ (20 mL). The aqueous layer was again extracted with EtOAc (4 × 25 mL). The organic phases were combined, washed with brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure to get the crude product **4a**, which was further purified by flash column chromatography.

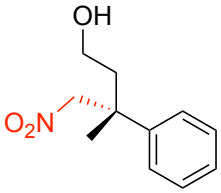
4. Experimental procedure for the synthesis of *β*-substituted *γ*-nitroalcohol 4



1 **2** **4**

To a solution of bicyclic organocatalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), in IPA (200 µL), *β*-substituted *α,β*-unsaturated aldehyde **1** (0.2 mmol, 1.0 equiv) and nitroalkane **2** (2.0 mmol, 10 equiv) were added at rt and stirred under argon atmosphere for the time mention in Scheme 2 (in manuscript). After completion of the reaction (monitored by ^{1}H NMR), to a cooled solution (-5 °C) of $NaBH_4$ (76 mg, 2.0 mmol, 10 equiv) in EtOH (1.6 mL), a solution of the reaction mixture in EtOH (0.8 mL) was added dropwise. The reaction mixture was stirred at -5 °C for 15 min and at 0 °C for 1 h. Then, the reaction mass was quenched with pieces of ice, distilled the ethanol over the rota evaporator, and diluted with EtOAc (25 mL), washed with a saturated aqueous solution of $NaHCO_3$ (20 mL). The aqueous layer was again extracted with EtOAc (4 × 25 mL). The organic phases were combined, washed with brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure to get the crude product **4**, which was further purified by flash column chromatography.

***(R)*-3-methyl-4-nitro-3-phenylbutan-1-ol (4a)**

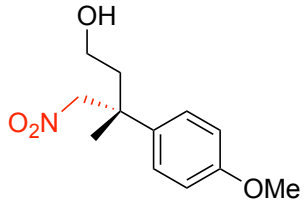


4a

Following the experimental procedure, (*E*)-3-phenylbut-2-enal **1a** (29 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4a** which was purified as a colourless liquid (29 mg, 69% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. $\mathbf{R}_f$ = 0.2 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 75:25, 1.0 mL/min, 210 nm), t_R (major) = 8.2 min, t_R (minor) = 9.7 min, 95% *ee*. $\mathbf{[\alpha]_D^{27}}$ = +24.6 (*c* = 0.2, $CHCl_3$ for 95% *ee*), lit.[9] $\mathbf{[\alpha]_D^{27}}$ = -

11.0 (*c* =0.5, $CHCl_3$ for 96% *ee* of the opposite enantiomer). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39-7.33 (m, 4H), 7.30-7.26 (m, 1H), 4.68 (dd, *J* = 14.2, 11.0 Hz, 2H), 3.63-3.58 (m, 1H), 3.52-3.47 (m, 1H), 2.23-2.17 (m, 1H), 2.06-2.00 (m, 1H), 1.60 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 142.0, 129.0, 127.5, 126.0, 86.1, 59.2, 42.2, 41.5, 23.2. **IR** (neat) *v* 3393, 2956, 2929, 2858, 1596, 1547, 1498, 1454, 1382, 1373 cm^{-1}. *NMR data of **4a** match with that reported in the literature.*[9]

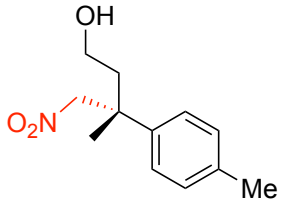
***(R)*-3-(4-methoxyphenyl)-3-methyl-4-nitrobutan-1-ol (4b)**



4b

Following the experimental procedure, *(E)*-3-(4-methoxyphenyl)but-2-enal **1b** (35 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4b** which was purified as a colourless liquid (26 mg, 54% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (65:35)]. **R_f** = 0.2 [hexane/EtOAc (65:35)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 75:25, 1.0 mL/min, 210 nm), t_R (major) = 11.8 min, t_R (minor) = 14.3 min, 94% *ee*. **$[\alpha]_D^{27}$** = +17.6 (*c* = 0.5, $CHCl_3$ for 94% *ee*), lit.[9] **$[\alpha]_D^{27}$** = -32.0 (*c* =0.4, $CHCl_3$ for 95% *ee* of the opposite enantiomer). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26-7.24 (m, 2H), 6.90-6.88 (m, 2H), 4.63 (dd, *J* = 16.2, 11.0 Hz, 2H), 3.80 (s, 3H), 3.64-3.59 (m, 1H), 3.53-3.48 (m, 1H), 2.21-2.15 (m, 1H), 2.03-1.97 (m, 1H), 1.57 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 158.7, 133.8, 127.2, 114.3, 86.4, 59.2, 55.4, 42.2, 41.0, 23.2. **IR** (neat) *v* 3388, 2956, 2924, 2841, 1613, 1544, 1507, 1461, 1374 cm^{-1}. *NMR data of **4b** match with that reported in the literature.*[9]

(*R*)-3-methyl-4-nitro-3-(*p*-tolyl)butan-1-ol (4c)

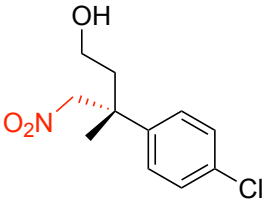


4c

Following the experimental procedure, (*E*)-3-(*p*-tolyl)but-2-enal **1c** (32 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4c** which was purified as a colourless liquid (26 mg, 60% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. **R_f** = 0.4 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 1.0 mL/min, 210 nm), t_R (major) = 20.0 min, t_R (minor) = 24.3 min, 95% *ee*. **$[\alpha]_D^{27}$** = +13.5 (*c* = 1.0, $CHCl_3$ for 95% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 4.65 (dd, *J* = 18.5, 11 Hz,

2H), 3.63-3.58 (m, 1H), 3.53-3.48 (m, 1H), 2.363 (s, 3H), 2.22-2.16 (m, 1H), 2.04-1.98 (m, 1H), 1.57 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 138.9, 137.1, 129.7, 125.9, 86.2, 59.3, 42.2, 41.2, 23.2. 21.0. **IR** (neat) *v* 3364, 3026, 2929, 2862, 1543, 1374, 1053, 1023, 817, 769 cm^{-1}. *NMR data of **4c** match with that reported in the literature.*[10]

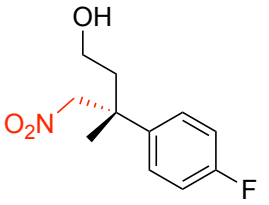
***(R)*-3-(4-chlorophenyl)-3-methyl-4-nitrobutan-1-ol (4d)**



4d

Following the experimental procedure, *(E)*-3-(4-chlorophenyl)but-2-enal **1d** (36 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4d** which was purified as a colourless liquid (23 mg, 48% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. $\mathbf{R}_f$ = 0.2 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 75:25, 1.0 mL/min, 210 nm), t_R (major) = 7.6 min, t_R (minor) = 9.4 min, 93% *ee*. $[\alpha]_D^{27}$ = +15.0 (*c* = 1.0, $CHCl_3$ for 93% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 4.67 (dd, *J* = 18.0, 11.0 Hz, 2H), 3.65-3.60 (m, 1H), 3.52-3.47 (m, 1H), 2.16-2.11 (m, 1H), 2.04-1.98 (m, 1H), 1.58 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 141.2, 132.0, 127.9, 121.5, 85.7, 59.0, 42.2, 41.4, 23.1. **IR** (neat) *v* 3375, 2952, 2925, 1656, 1542, 1487, 1433, 1401, 1378 cm^{-1}. *NMR data of **4d** match with that reported in the literature.*[10]

***(R)*-3-(4-fluorophenyl)-3-methyl-4-nitrobutan-1-ol (4e)**

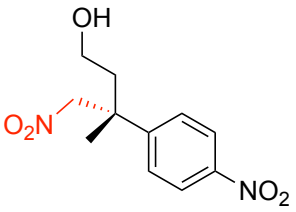


4e

Following the experimental procedure, *(E)*-3-(4-fluorophenyl)but-2-enal **1e** (33 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4e** which was purified as a colourless liquid (27 mg, 61% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (65:35)]. $\mathbf{R}_f$ = 0.2 [hexane/EtOAc (65:35)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 75:25, 0.5 mL/min, 210 nm), t_R (major) = 13.7 min, t_R (minor) = 16.2 min, 91% *ee*. $[\alpha]_D^{27}$ = +7.4 (*c* = 0.4, $CHCl_3$ for 91% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.30 (m, 2H), 7.08-7.04 (m, 2H), 4.67 (dd, *J* = 12.5, 11.5 Hz, 2H), 3.66-3.61 (m, 1H), 3.53-3.48 (m, 1H), 2.19-2.13 (m, 1H), 2.05-1.99 (m, 1H), 1.60 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 161.9 (d, J^1 = 246.9 Hz), 137.8, 127.8 (d, J^3 = 8.8 Hz), 115.8 (d,

J^2 = 21.4 Hz), 86.1, 59.1, 42.3, 41.3, 23.3. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -115.2. **IR** (neat) *v* 3440, 3066, 2957, 2921, 2857, 1706, 1611, 1552, 1492 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{11}H_{14}FNO_3Na^+$ $[M + Na]^+$ 250.0850, found 250.0829.

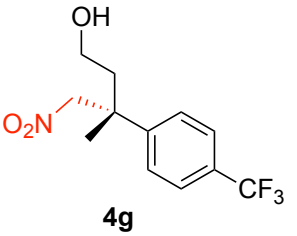
***(R)*-3-methyl-4-nitro-3-(4-nitrophenyl)butan-1-ol (4f)**



4f

Following the experimental procedure, *(E)*-3-(4-nitrophenyl)but-2-enal **1f** (38 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4f** which was purified as a colourless liquid (23 mg, 45% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (60:40)]. $\mathbf{R}_f$ = 0.2 [hexane /EtOAc (60:40)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 75:25, 1.0 mL/min, 210 nm), t_R (major) = 11.3 min, t_R (minor) = 14.4 min, 92% *ee*. **$[\alpha]_D^{27}$** = +37.4 (*c* = 0.1, $CHCl_3$ for 92% *ee*), lit.[9] **$[\alpha]_D^{27}$** = -22.0 (*c* =0.1, $CHCl_3$ for 98% *ee* of the opposite enantiomer). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (t, *J* = 2.0 Hz, 1H), 8.15 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.71(dd, *J* = 8.0, 1.0 Hz, 1H), 7.56 (t, *J* = 8.0 Hz), 4.85 (d, *J* = 11.5 Hz, 1H), 4.73 (d, *J* = 11.5 Hz), 3.70-3.66 (m, 1H), 3.55-3.50 (m, 1H), 2.18-2.12 (m, 1H), 2.10-2.05 (m, 1H), 1.67 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 148.6, 144.8, 132.4, 129.9, 122.5, 121.4, 85.2, 58.8, 42.3, 41.9, 23.1. **IR** (neat) *v* 3376, 2953, 2921, 2854, 1761, 1596, 1542, 1515, 1345 cm^{-1}. *NMR data of **4f** match with that reported in the literature.*[9]

***(R)*-3-methyl-4-nitro-3-(4-(trifluoromethyl)phenyl)butan-1-ol (4g)**

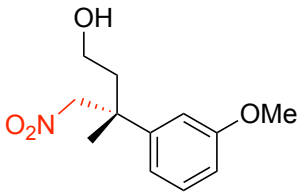


4g

Following the experimental procedure, (4:1, *E/Z* mixture) 3-(4-(trifluoromethyl)phenyl)but-2-enal **1g** (43 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4g** which was purified as a colourless liquid (36 mg, 65% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. $\mathbf{R}_f$ = 0.1 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 1.0 mL/min, 210 nm), t_R (major) = 10.3 min, t_R (minor) = 13.6 min, 92% *ee*. **$[\alpha]_D^{27}$** = +23.8 (*c* = 0.1, $CHCl_3$ for 92% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.5 Hz, 2H),

7.48 (d, J = 8.5 Hz, 2H), 4.78 (d, J = 11.5 Hz, 1H), 4.72 (d, J = 11.5 Hz, 1H), 3.68-3.63 (m, 1H), 3.53-3.48 (m, 1H), 2.19-2.14 (m, 1H), 2.09-2.03 (m, 1H), 1.64 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 146.4, 129.7 (q, J^2 = 32.8 Hz), 126.6, 125.9 (q, J^3 = 3.8 Hz), 124.1 (q, J^1 = 273.4 Hz), 85.4, 59.0, 42.3, 41.8, 23.2. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -62.6. **IR** (neat) ν 3386, 2958, 2921, 2852, 1720, 1618, 1549, 1411, 1374 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{12}H_{15}F_3NO_3^+$ $[M + H]^+$ 278.0999, found 278.1017.

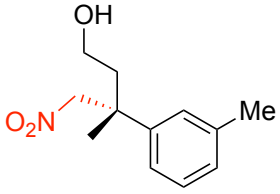
(*R*)-3-methyl-4-nitro-3-(3-methoxyphenyl)butan-1-ol (4h)



4h

Following the experimental procedure, (*E*)-3-(3-methoxyphenyl)but-2-enal **1h** (35 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4h** which was purified as a colourless liquid (19 mg, 40% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (60:40)]. **R_f** = 0.2 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IG, 4.6 mm × 250 mm (hexane/IPA = 80:20, 1.0 mL/min, 210 nm), t_R (major) = 11.9 min, t_R (minor) = 14.9 min, 94% *ee*. **$[\alpha]_D^{27}$** = +18.5 (c = 1.0, $CHCl_3$ for 94% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 (t, J = 8.0 Hz, 1H), 6.93-6.91 (m, 1H), 6.87 (t, J = 2.0 Hz, 1H), 6.82-6.80 (m, 1H), 4.66 (dd, J = 15.5, 11.0 Hz, 2H), 3.81 (s, 3H), 3.63-3.58 (m, 1H), 3.52-3.48 (m, 1H), 2.20-2.15 (m, 1H), 2.04-1.99 (m, 1H), 1.57 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 160.0, 143.8, 130.0, 118.3, 113.1, 111.7, 86.0, 59.2, 55.4, 42.2, 23.1. **IR** (neat) ν 3365, 2929, 2844, 1544, 1429, 1241, 1380, 1295, 1047, 769, 703 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{12}H_{17}NO_4Na^+$ $[M + Na]^+$ 262.1050, found 262.1059.

(*R*)-3-methyl-4-nitro-3-(*m*-tolyl)butan-1-ol (4i)

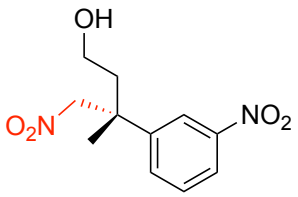


4i

Following the experimental procedure, (*E*)-3-(*m*-tolyl)but-2-enal **1i** (32 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4i** which was purified as a colourless liquid (23 mg, 51% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. **R_f** = 0.4 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 0.7 mL/min, 210 nm), t_R (major) = 32.1 min, t_R (minor) = 37.4 min, 95% *ee*. **$[\alpha]_D^{27}$** = +13.0 (c = 1.0, $CHCl_3$ for 95% *ee*). **^{1}H NMR** (500

MHz, $CDCl_3$) δ 7.27-7.24 (m, 1H), 7.14-7.08 (m, 3H,), 4.67 (dd, *J* = 24.0, 11.0 Hz, 2H), 3.62-3.59 (m, 1H), 3.53-3.48 (m, 1H), 2.36 (s, 3H), 2.22-2.17 (m, 1H), 2.05-2.00 (m, 1H), 1.58 (s, 3H). **$^{13}C\{^1H\}$ NMR** (126 MHz; $CDCl_3$) δ 142.0, 138.6, 128.8, 128.2, 126.7, 123.1, 86.2, 59.3, 42.2, 41.4, 23.2, 21.8. **IR** (neat) *v* 3377, 2923, 2862, 1543, 1374, 1211, 1059, 1029, 769, 702 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{12}H_{18}NO_3^+$ $[M + H]^+$ 224.1281, found 224.1288.

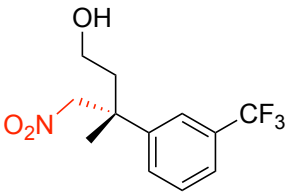
***(R)*-3-methyl-4-nitro-3-(3-nitrophenyl)butan-1-ol (4j)**



4j

Following the experimental procedure, *(E)*-3-(3-nitrophenyl)but-2-enal **1j** (38 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4j** which was purified as a colourless liquid (20 mg, 40% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (60:40)]. $\mathbf{R_f}$ = 0.3 [hexane/EtOAc (60:40)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 75:25, 1.0 mL/min, 210 nm), t_R (major) = 13.9 min, t_R (minor) = 19.4 min, 91% *ee*. $\mathbf{[\alpha]_D^{27}}$ = +8.2 (*c* = 0.3, $CHCl_3$ for 91% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (t, *J* = 2 Hz, 1H), 8.17-8.15 (m, 1H), 7.72-7.70 (m, 1H), 7.57 (t, *J* = 8.0 Hz, 1H), 4.85 (d, *J* = 12.0 Hz, 1H), 4.74 (d, *J* = 11.5 Hz, 1H), 3.72-3.67 (m, 1H), 3.56-3.52 (m, 1H), 2.19-2.13 (m, 1H), 2.11-2.04 (m, 1H), 1.68 (s, 3H). **$^{13}C\{^1H\}$ NMR** (126 MHz; $CDCl_3$) δ 148.7, 144.9, 132.4, 129.9, 122.5, 121.4, 85.2, 58.9, 42.3, 41.9, 23.2. **IR** (neat) *v* 3386, 2955, 2919, 2855, 1723, 1549, 1531, 1467, 1343 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{11}H_{15}N_2O_5^+$ $[M + H]^+$ 255.0975, found 255.0982.

(*R*)-3-methyl-4-nitro-3-(3-(trifluoromethyl)phenyl)butan-1-ol (4k)

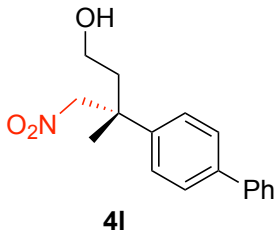


4k

Following the experimental procedure, (*E*)-3-(3-(trifluoromethyl)phenyl)but-2-enal **1k** (43 mg, 0.2 mmol, 1 equiv) and CH_3NO_2 **2a** (107 µL, 2 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4k** which was purified as a colourless liquid (28 mg, 50% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. $\mathbf{R_f}$ = 0.4 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 0.5 mL/min, 210 nm), t_R (major) = 20.6 min, t_R (minor) = 24.6 min, 91% *ee*. $\mathbf{[\alpha]_D^{22}}$ = +13.7 (*c* = 1.0, $CHCl_3$ for 91% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58-7.49 (m, 4H), 4.74 (dd, *J* = 27.0, 11.5 Hz, 2H), 3.67-

3.62 (m, 1H), 3.52-3.47 (m, 1H), 2.19-2.14 (m, 1H), 2.09-2.03 (m, 1H), 1.64 (s, 3H). **$^{13}C\{^1H\}$ NMR** (126 MHz; $CDCl_3$) δ 143.5, 131.3 (q, J^2 = 32.2 Hz), 129.6, 129.4, 124.3 (q, J^3 = 3.7 Hz), 124.1 (q, J^1 = 273.1 Hz), 122.9 (q, J^3 = 3.7 Hz), 85.5, 59.0, 42.2, 41.7, 23.2. **^{19}F NMR** (470 MHz, $CDCl_3$) δ -62.6. **IR** (neat) *v* 3395, 2929, 2856, 1556, 1332, 1162, 1126, 1078, 805, 757, 702 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{12}H_{15}F_3NO_3^+$ $[M + H]^+$ 278.0999, found 278.1021.

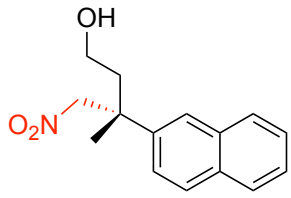
***(R)*-3-([1,1'-biphenyl]-4-yl)-3-methyl-4-nitrobutan-1-ol (4l)**



4l

Following the experimental procedure, *(E)*-3-([1,1'-biphenyl]-4-yl)but-2-enal **1l** (44 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4l** which was purified as a yellow liquid (29 mg, 50% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. $\mathbf{R}_f$ = 0.2 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 85:15, 1.0 mL/min, 210 nm), t_R (major) = 16.1 min, t_R (minor) = 19.1 min, 93% *ee*. $\mathbf{[\alpha]_D^{27}}$ = +6.6 (*c* = 0.4, $CHCl_3$ for 93% *ee*). **^1H NMR** (500 MHz, $CDCl_3$) δ 7.61-7.58 (m, 4H), 7.46-7.36 (m, 5H), 4.73 (dd, *J* = 13.0, 11.0 Hz, 2H), 3.69-3.64 (m, 1H), 3.58-3.55 (m, 1H), 2.27-2.21 (m, 1H), 2.10-2.05 (m, 1H), 1.64 (s, 3H). **$^{13}C\{^1H\}$ NMR** (126 MHz; $CDCl_3$) δ 141.0, 140.4, 140.2, 129.0, 127.63, 127.60, 127.2, 126.5, 86.0, 59.3, 42.2, 41.4, 23.3. **IR** (neat) *v* 3384, 2968, 2929, 2655, 1711, 1542, 1485, 1377, 1329 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{17}H_{19}NO_3Na^+$ $[M + Na]^+$ 308.1257, found 308.1261.

***(R)*-3-methyl-3-(naphthalen-2-yl)-4-nitrobutan-1-ol (4m)**

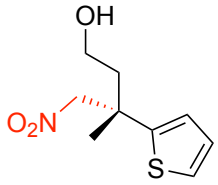


4m

Following the experimental procedure, *(E)*-3-(naphthalen-2-yl)but-2-enal **1m** (39 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4m** which was purified as a colourless liquid (27 mg, 52% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. $\mathbf{R}_f$ = 0.2 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hex/IPA = 85:15, 1.0 mL/min, 210 nm), t_R (major) = 22.5 min, t_R (minor) = 25.8 min, 94% *ee*. $\mathbf{[\alpha]_D^{27}}$ = +25.1 (*c* = 0.3, $CHCl_3$ for 94%

ee). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.87-7.81 (m, 3H), 7.74 (d, *J*= 2.0 Hz, 1H), 7.51-7.48 (m, 3H), 4.86-4.72 (m, 2H), 3.65-3.60 (m, 1H), 3.52-3.47 (m, 1H), 2.33-2.27 (m, 1H), 2.14-2.08 (m, 1H), 1.71 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 139.3, 133.4, 132.4, 128.8, 128.3, 127.6, 126.6, 126.5, 125.3, 123.8, 86.0, 59.2, 42.0, 41.7, 23.2. **IR** (neat) *v* 3353, 3054, 2966, 2926, 2855, 1601, 1548, 1464, 1376 cm^{-1}. *NMR data of **4m** match with that reported in the literature.*[10]

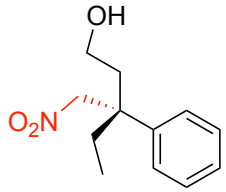
(*S*)-3-methyl-4-nitro-3-(thiophen-2-yl)butan-1-ol (4n)



4n

Following the experimental procedure, (*E*)-3-(thiophen-2-yl)but-2-enal **1n** (30 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4n** which was purified as a colourless liquid (20 mg, 47% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. $\mathbf{R}_f$ = 0.4 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 1.0 mL/min, 210 nm), t_R (major) = 23.1 min, t_R (minor) = 28.3 min, 95% *ee*. $[\alpha]_D^{24}$ = +24.3 (*c* = 0.5, $CHCl_3$ for 95% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26-7.25 (m, 1H), 6.98 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.92 (dd, *J* = 3.5, 1.0 Hz, 1H), 4.69 (dd, *J* = 29.5, 11.0 Hz, 1H), 3.75-3.64 (m, 2H), 2.20-2.09 (m, 2H), 1.64 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 147.6, 127.2, 124.7, 124.5, 86.2, 59.2, 43.0, 41.0, 24.9. **IR** (neat) *v* 3359, 2923, 2856, 1550, 1465, 1435, 1380, 1241, 1217, 1053, 763, 703 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_9H_{13}NO_3SNa^+$ $[M + Na]^+$ 238.0514, found 238.0517.

***(R)*-3-(nitromethyl)-3-phenylpentan-1-ol (4o)**

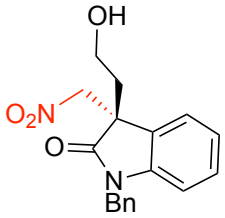


4o

Following the experimental procedure, (*E*)-3-phenylpent-2-enal **1o** (32 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4o** which was purified as a colourless liquid (18 mg, 40% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. $\mathbf{R}_f$ = 0.4 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IA, 4.6 mm × 250 mm (hexane/IPA = 90:10, 0.7 mL/min, 210 nm), t_R (major) = 19.5 min, t_R (minor) = 21.7 min, 88% *ee*. $[\alpha]_D^{27}$ = +25.1 (*c* = 0.5, $CHCl_3$ for 88% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39-7.36 (m, 2H), 7.29-7.23 (m, 3H), 4.91 (dd, *J* = 28.0, 11.0 Hz, 2H), 3.65-

3.60 (m, 2H), 2.14 (t, J = 7.0 Hz, 2H), 1.97-1.92 (m, 1H), 1.87-1.82 (m, 1H), 0.81 (t, J = 7.5 Hz, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 141.3, 129.0, 127.2, 126.1, 81.1, 59.2, 44.8, 38.7, 29.7, 7.9. **IR** (neat) ν 3364, 2921, 2857, 1547, 1454, 1376, 1028, 758, 699 cm^{-1}. *NMR data of **4o** match with that reported in the literature.*[10]

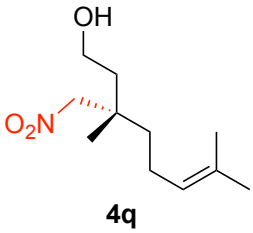
(*S*)-1-benzyl-3-(2-hydroxyethyl)-3-(nitromethyl)indolin-2-one (4p)



4p

Following the experimental procedure, *(Z)*-2-(1-benzyl-2-oxoindolin-3-ylidene)acetaldehyde **1p** (53 mg, 0.2 mmol, 1 equiv) and CH_3NO_2 **2a** (107 µL, 2 mmol, 10 equiv) in the presence of the catalyst **3c** (22 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4p** which was purified as a colourless liquid (33 mg, 51% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (50:50)]. **R_f** = 0.2 [hexane/EtOAc (50:50)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 75:25, 1.0 mL/min, 210 nm), t_R (major) = 10.7 min, t_R (minor) = 19.2 min, 87% *ee*. **$[\alpha]_D^{27}$** = -48.0 (c = 0.3, $CHCl_3$ for 87% *ee*), lit.[8] **$[\alpha]_D^{26}$ =** +28.7 (c = 1.6, $CHCl_3$ for 94% *ee* of the opposite enantiomer). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38-7.31 (m, 4H), 7.29-7.19 (m, 4H), 7.07-7.04 (m, 1H), 6.76 (d, J = 8.0 Hz, 1H), 5.08 (d, J = 13.5 Hz, 1H), 5.01-4.94 (m, 3H), 3.60 (t, J = 6.0 Hz, 1H), 2.17-2.12 (m, 1H), 2.09-2.03 (m, 1H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 177.4, 143.4, 135.5, 129.6, 129.0, 127.9, 127.5, 127.3, 123.2, 110.2, 78.8, 58.4, 50.1, 44.6, 38.2**. IR** (neat) ν 3370, 2958, 2926, 2848, 1604, 1549, 1517, 1462, 1375 cm^{-1}. *NMR data of **4p** match with that reported in the literature.*[8]

(*S*)-3,7-dimethyl-3-(nitromethyl)oct-6-en-1-ol (4q)

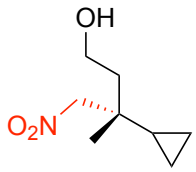


4q

Following the experimental procedure, (1:1, *E/Z* mixture) citral **1q** (30 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4q** which was purified as a colourless liquid (26 mg, 60% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. **R_f** = 0.45 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 0.7 mL/min, 210 nm), t_R (major) = 19.7 min, t_R (minor) = 22.4 min, 58% *ee*. **$[\alpha]_D^{24}$** = -3.6 (c = 1.0, $CHCl_3$ for 58% *ee*), lit.[9] **$[\alpha]_D^{27}$ =**

+7.0 (*c* =0.5, $CHCl_3$ for 90% *ee* of the opposite enantiomer). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.07-5.05 (m, 1H), 4.41 (dd, *J* = 20.5, 10.5 Hz, 2H,), 3.79 (t, *J* = 6.5 Hz, 2H), 2.02-1.97 (m, 2H), 1.72-1.64 (m, 5H), 1.60 (s, 3H), 1.41-1.38 (m, 2H), 1.10 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ132.4, 123.5, 83.9, 59.0, 39.5, 38.0, 37.5, 25.8, 23.2, 22.2, 17.7. **IR** (neat) *v* 3395, 2971, 2917, 2856, 1453, 1550, 1380, 1029, 769 cm^{-1}. *NMR data of **4q** match with that reported in the literature.*[9]

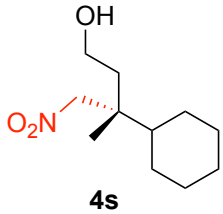
(*R*)-3-cyclopropyl-3-methyl-4-nitrobutan-1-ol (4r)



4r

Following the experimental procedure, (3:1, *E/Z* mixture) 3-cyclopropylbut-2-enal **1r** (22 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4r** which was purified as a colourless liquid (17 mg, 49% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (70:30)]. **R_f** = 0.25 [hexane/EtOAc (70:30)]. **$[\alpha]_D^{27}$** = -3.4 (*c* = 0.5, $CHCl_3$ for 68% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.49-4.40 (m, 2H), 3.92-3.88 (m, 1H), 3.85-3.81 (m, 1H), 1.73 (t, *J* = 6.5 Hz, 2H), 0.87-0.84 (m, 1H), 0.78 (s, 3H), 0.44-0.42 (m, 2H), 0.29-0.27 (m, 2H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 85.5, 59.2, 41.1, 36.8, 18.2, 18.1, 0.44, 0.35. **IR** (neat) *v* 3564, 3371, 3086, 3008, 2929, 2862, 1544, 1465, 1380, 1217, 1047, 1023, 751 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_8H_{15}NO_3Na^+$ $[M + Na]^+$ 196.0944, found 196.0945.

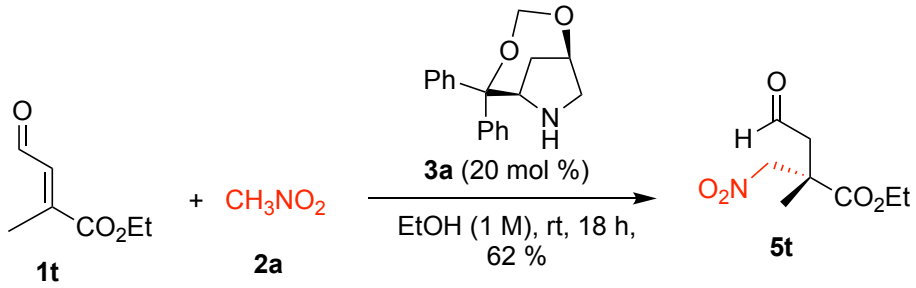
(*R*)-3-cyclohexyl-3-methyl-4-nitrobutan-1-ol (4s)



4s

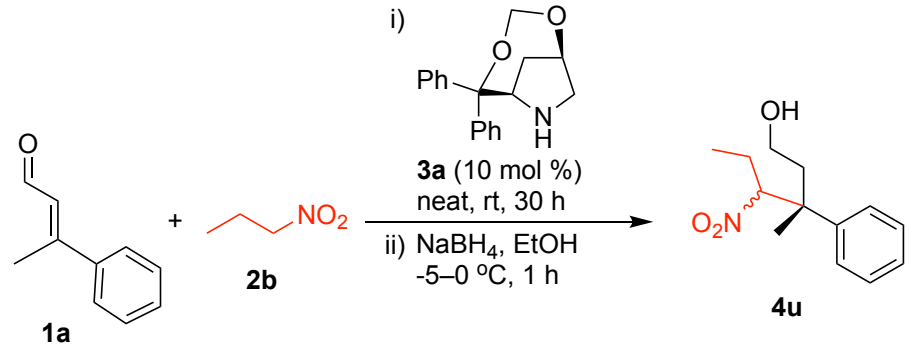
Following the experimental procedure, (5:1, *E/Z* mixture) 3-cyclohexylbut-2-enal **1s** (30 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) in the presence of the catalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), were converted to the product **4s** which was purified as a colourless liquid (26 mg, 61% yield) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (75:25)]. **R_f** = 0.5 [hexane/EtOAc (70:30)]. **$[\alpha]_D^{23}$** = +8.9 (*c* = 0.25, $CHCl_3$ for 83% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.47 (dd, *J* = 22.0, 1.0 Hz, 2H), 3.81-3.74 (m, 2H), 1.82-1.76 (m, 3H), 1.73-1.67 (m, 4H), 1.36-1.30 (m, 1H), 1.27-1.17 (m, 2H), 1.15-1.09 (m, 1H), 1.05 (s, 3H), 1.03-1.00 (m, 2H). **^{13}C{^{1}H} NMR** (126 MHz; $CDCl_3$) δ 82.9, 59.1, 43.7, 40.0, 37.6, 27.1, 26.94, 26.93, 26.5, 20.8. **IR** (neat) *v* 3383, 3080, 2923, 1550, 1459, 1374, 1211, 1023, 763 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{11}H_{21}NO_3Na^+$ $[M + Na]^+$ 238.1414, found 238.1427.

5. Experimental procedure for the synthesis of ethyl (*S*)-2-methyl-2-(nitromethyl)-4-oxobutanoate (5t)



To a solution of bicyclic organocatalyst **3a** (11 mg, 0.04 mmol, 0.2 equiv), in EtOH (200 µL), *β*-substituted *α,β*-unsaturated aldehyde **1t** (28 mg, 0.2 mmol, 1.0 equiv) and CH_3NO_2 **2a** (107 µL, 2.0 mmol, 10 equiv) were added at rt and stirred under argon atmosphere for 18 h. After completion of the reaction (monitored by ^{1}H NMR), the ethanol was removed under reduced pressure to get the crude product **5t**, which was further purified as a yellow liquid (25 mg, 62% yield) using flash column chromatography [Silica gel, hexane/EtOAc (85:15)]. $\mathbf{R_f}$ = 0.5 [hexane/EtOAc (80:20)]. $\mathbf{[\alpha]_D^{23}}$ = -6.2 (*c* = 1.0, $CHCl_3$ for 93% *ee*). lit.[8] $\mathbf{[\alpha]_D^{22}}$ = +1.8 (*c* =1.0, $CHCl_3$ for 91% *ee* of the opposite enantiomer). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 4.80 (dd, *J* = 28.0, 28.0 Hz, 2H), 4.20 (q, *J* = 8.0 Hz, 2H), 2.96 (s, 2H), 1.38 (s, 3H), 1.25 (t, *J* = 8.0 Hz, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 198.7, 172.7, 79.6, 62.2, 47.9, 43.3, 21.9, 14.0. **IR** (neat) *ν* 2976, 2926, 2849, 1724, 1554, 1465, 1380, 1281, 1224, 1129, 1023, 860 cm^{-1}. *NMR data of **5t** match with that reported in the literature.*[8]

6. Experimental procedure for the synthesis of (3*R*)-3-methyl-4-nitro-3-phenylhexan-1-ol (4u)



To a solution of bicyclic organocatalyst **3a** (11 mg, 0.02 mmol, 0.1 equiv), *β*-substituted *α,β*-unsaturated aldehyde **1a** (29 mg, 0.2 mmol, 1.0 equiv) and nitropropane **2b** (178 µL, 2.0 mmol, 10 equiv) were added at rt and stirred under argon atmosphere for 30 h. After completion of the reaction (monitored by ^{1}H NMR), to a cooled solution (-5 °C) of $NaBH_4$ (76 mg, 2.0 mmol, 10 equiv) in EtOH (1.6 mL), a solution of the reaction mixture in EtOH (0.8 mL) was added dropwise. The reaction mixture was stirred at -5 °C for 15 min and 1 h at 0 °C. Then, the reaction mass was quenched with pieces of ice, distilled the ethanol over the rota evaporator, and diluted with EtOAc (25 mL), washed with a saturated aqueous solution of $NaHCO_3$ (20

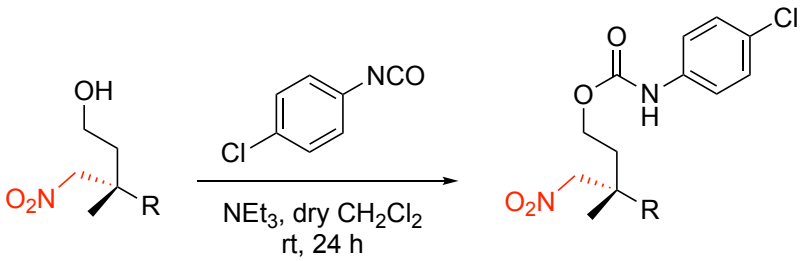
mL). The aqueous layer was again extracted with EtOAc (4 × 25 mL). The organic phases were combined, washed with brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure to get the crude product **4u**, which was purified as a yellow liquid (14 mg, 29% yield, 1.4:1 inseparable mixture of diastereomers) from the crude reaction mixture using flash column chromatography. $\mathbf{R}_f$ = 0.3 [hexane/EtOAc (70:30)].

Major diastereomer: **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 1.0 mL/min, 210 nm), t_R (major) = 11.3 min, t_R (minor) = 15.2 min, 83% *ee*, t_{RB} (major) = 17.0 min, t_{RB} (minor) = 65.2 min, 83% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.32-7.17 (m, 5H), 4.48 (dd, *J* = 12.0, 4.0 Hz, 1H), 3.51-3.44 (m, 1H), 3.38-3.31 (m, 1H), 2.20-1.13 (m, 1H), 2.00-1.85 (m, 2H), 1.73-1.63 (m, 2H), 1.46 (s, 3H), 0.82 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR** (100 MHz; $CDCl_3$) δ: 141.4, 128.6, 127.3, 126.8, 100.6, 59.0, 43.6, 39.3, 22.0, 20.5, 11.1.

Minor diastereomer: **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 1.0 mL/min, 210 nm), t_R (major) = 17.0 min, t_R (minor) = 65.2 min, 83% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.32-7.17 (m, 5H), 4.60 (dd, *J* = 12.0, 2.3 Hz, 1H), 3.38-3.32 (m, 1H), 3.21-3.15 (m, 1H), 2.32-2.25 (m, 1H), 2.02-1.85 (m, 1H), 1.73-1.63 (m, 1H), 1.43 (s, 3H), 1.23-1.13 (m, 2H), 0.71 (t, *J* = 8.0 Hz, 3H). **^{13}C{^{1}H} NMR** (100 MHz; $CDCl_3$) δ: 141.8, 129.0, 127.3, 126.6, 100.4, 59.0, 43.5, 42.1, 21.6, 17.9, 11.0.

IR (neat) *v* 3340, 3058, 3027, 2925, 1648, 1601, 1542, 1495, 1444, 1366, 1025, 1010, 758, 696 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{13}H_{20}NO_3^+$ $[M + H]^+$ 238.1438, found 238.1440.

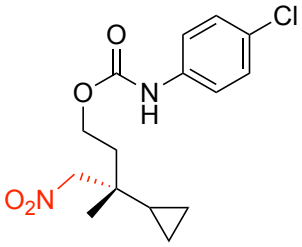
7. Experimental procedure for the synthesis of carbamate 6



4 **6**

To a solution of the **4** (0.10 mmol, 1.0 equiv), NEt_3 (14 µL, 0.10 mmol, 1.0 equiv) in dry CH_2Cl_2 (0.50 mL) was added 4-chlorophenyl isocyanate (17.0 mg, 0.11 mmol, 1.1 equiv) at rt and stirred for 24 h at the same temperature. After completion of the reaction, monitored by crude ^{1}H NMR, the crude reaction mass was quenched with brine (30 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to get the crude product **6**, which was further purified by flash column chromatography.

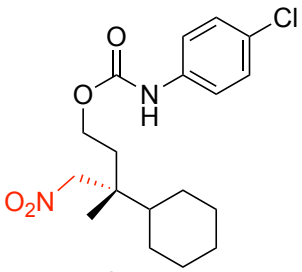
(*R*)-3-cyclopropyl-3-methyl-4-nitrobutyl (4-chlorophenyl)carbamate (6r)



6r

Following the experimental procedure, **4r** (17 mg, 0.10 mmol, 1.0 equiv), was converted to product **6r** which was purified as a clear liquid (28 mg, 85% yield) using flash column chromatography [Silica gel, hexane/EtOAc (80:20)]. $\mathbf{R}_f$ = 0.4 [hexane/EtOAc (80:20)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 1.0 mL/min, 210 nm), t_R (minor) = 15.9 min, t_R (major) = 17.6 min 68% *ee*. $\mathbf{[\alpha]_D^{22}}$ = +6.5 (*c* = 0.5, $CHCl_3$ for 68% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32-7.30 (m, 2H), 7.27-7.24 (m, 2H), 6.60 (bs, 1H), 4.41-4.27 (m, 4H), 1.89-1.85 (m, 2H), 0.86-0.82 (m, 1H), 0.79 (s, 3H), 0.49-0.40 (m, 2H), 0.35-0.30 (m, 1H), 0.28-0.23 (m, 1H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$) δ 153.3, 136.4, 129.2, 128.8, 120.0, 61.8, 37.7, 36.7, 17.9, 17.8, 0.79, 0.24. **IR** (neat) *v* 3322, 2965, 2917, 1707, 1598, 1543, 1308, 1229, 1096, 824, 775 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{15}H_{19}ClN_2O_4Na^+$ $[M + Na]^+$ 349.0926; found 349.0933.

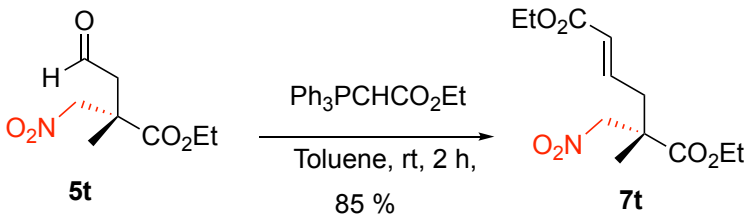
(*R*)-3-cyclohexyl-3-methyl-4-nitrobutyl (4-chlorophenyl)carbamate (6s)



6s

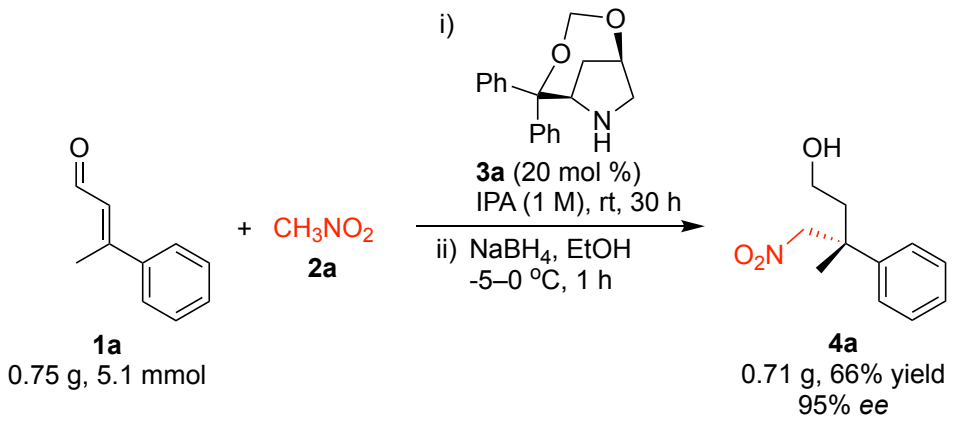
Following the experimental procedure, **4s** (21 mg, 0.10 mmol, 1.0 equiv), was converted to product **6s** which was purified as a clear liquid (33 mg, 90% yield) using flash column chromatography [Silica gel, hexane/EtOAc (80:20)]. $\mathbf{R}_f$ = 0.5 [hexane/EtOAc (80:20)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 0.7 mL/min, 210 nm), t_R (major) = 27.6 min, t_R (minor) = 30.2 min, 83% *ee*. $\mathbf{[\alpha]_D^{23}}$ = -5.8 (*c* = 1.0, $CHCl_3$ for 83% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27-7.25 (m, 2H), 7.20-7.18 (m, 2H), 6.58 (bs, 1H), 4.31 (s, 2H), 4.23-4.13 (m, 2H), 1.82-1.72 (m, 5H), 1.67-1.60 (m, 2H), 1.30-1.25 (m, 1H), 1.20-1.12 (m, 2H), 1.08-1.05 (m, 1H) 1.02 (s, 3H), 0.98-0.9 (m, 2H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$) δ 153.3, 136.4, 129.2, 128.7, 120.0, 82.5, 61.6, 43.9, 39.8, 34.0, 27.1, 27.0, 26.90, 26.89, 26.4, 20.8. **IR** (neat) *v* 3328, 2929, 2856, 1707, 1604, 1556, 1223, 1090, 775 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{18}H_{25}ClN_2O_4Na^+$ $[M + Na]^+$ 391.1395, found 391.1387.

8. Experimental procedure for the synthesis of diethyl (*S,E*)-5-methyl-5-(nitromethyl)hex-2-enedioate (7t)



To a solution of the **5t** (20 mg, 0.10 mmol, 1.0 equiv) in dry toluene, ethyl(triphenylphosphoranylidene)acetate (52 mg, 0.15 mmol, 1.5 equiv) was added at rt and stirred for 2 h at the same temperature. After completion of the reaction, monitored by crude ^{1}H NMR, the toluene was removed under reduced pressure to get the crude product **7t**, which was further purified as a clear liquid (23 mg, 85% yield) using flash column chromatography [Silica gel, hexane/EtOAc (90:10)]. $\mathbf{R}_f$ = 0.5 [hexane/EtOAc (85:15)]. **HPLC** analysis Daicel Chiralcel IC, 4.6 mm × 250 mm (hexane/IPA = 90:10, 1 mL/min, 230 nm), t_R (major) = 18.3 min, t_R (minor) = 28.1 min, 93 % *ee*. $[\alpha]_D^{21}$ = -8.5 (*c* = 1.0, $CHCl_3$ for 93% *ee*). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.80 (q, *J* = 8.0 Hz, 1H), 5.89 (d, *J* = 16.0 Hz, 1H), 4.63 (d, *J* = 16.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.24-4.14 (m, 4H), 2.62-2.48 (m, 2H), 1.31 (s, 3H), 1.26 (t, *J* = 8 Hz, 6H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 172.7, 165.7, 141.0, 126.4, 80.2, 62.0, 60.6, 45.6, 38.4, 20.4, 14.3, 14.1. **IR** (neat) *v* 2994, 2961, 2929, 2857, 1722, 1658, 1557, 1464, 1376, 1274, 1218, 1189, 1133, 1028, 988, 895, 863, 774 cm^{-1}. **HRMS** (ESI) m/z calcd for $C_{12}H_{19}NO_6Na^+$ $[M + Na]^+$ 296.1105, found 296.1108.

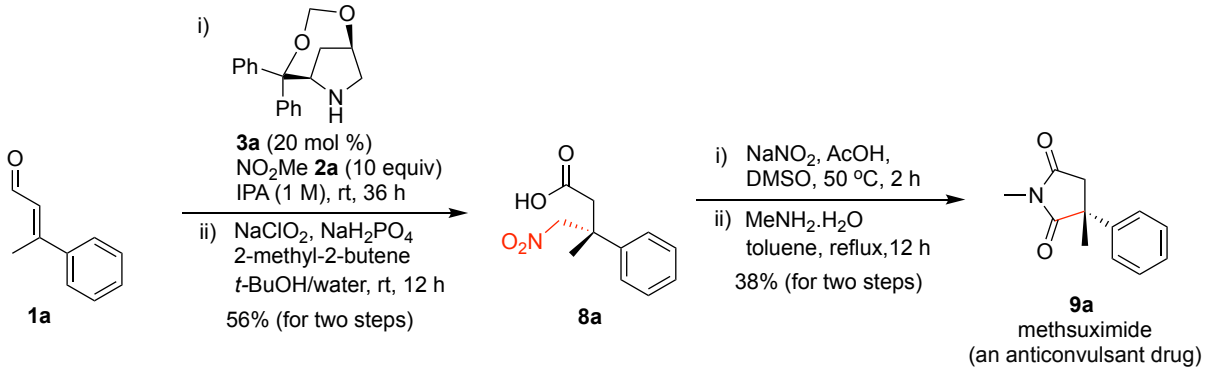
9. Experimental procedure for the scale-up synthesis of alcohol 4a



To a solution of bicyclic organocatalyst **3a** (290 mg, 1.03 mmol, 0.2 equiv), in IPA (5.13 mL), (*E*)-3-phenylbut-2-enal **1a** (0.75 g, 5.13 mmol, 1.0 equiv) and CH_3NO_2 **2a** (2.75 mL, 51.3 mmol, 10 equiv) were added at rt and stirred under argon atmosphere for 30 h. After completion of the reaction (monitored by ^{1}H NMR), to a cooled solution (-5 °C) of $NaBH_4$ (1.95 g, 51.3 mmol, 10 equiv) in EtOH (40 mL), a solution of the reaction mixture in EtOH (20 mL) was added, dropwise. The reaction was stirred at -5 °C for 15 min and at 0 °C for 1 h. Then, the reaction mass was quenched with pieces of ice, distilled the ethanol over the rota evaporator,

washed with a saturated aqueous solution of $NaHCO_3$ (20 mL) and extracted with EtOAc (4 x 50 mL). The organic phases were combined, washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure to get the crude product **4a**, which was further purified as a clear liquid (0.71 g, 66% yield with 95% *ee*) using silica gel column chromatography [Silica gel, hexane/EtOAc (70:30)].

10. Experimental procedure for the synthesis of methsuximide 9a



To a solution of bicyclic organocatalyst **3a** (20 mg, 0.07 mmol, 0.2 equiv), in IPA (360 µL), (*E*)-3-phenylbut-2-enal **1a** (53 mg, 0.36 mmol, 1.0 equiv) and CH_3NO_2 **2a** (193 µL, 3.6 mmol, 10 equiv) were added at rt and stirred under argon atmosphere for 36 h. After the reaction was completed (monitored by ^{1}H NMR), the reaction mass was diluted with water and extracted with EtOAc (4 × 25 mL). The organic phases were combined, washed with brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure to get the crude aldehyde, which was directly used for the next step without further purification.

To a solution of the above crude aldehyde in *t*-BuOH (1.8 mL) and water (0.6 mL) were added $NaClO_2$ (65 mg, 0.72 mmol, 2.0 equiv), $NaH_2PO_4.2H_2O$ (168 mg, 1.08 mmol, 3.0 equiv), and 2-methyl-2-butene (114 µL, 1.08 mmol, 3.0 equiv) and stirred for 12 h at rt. After the reaction was completed (monitored by ^{1}H NMR), the reaction mass was diluted with EtOAc (20 mL) and extracted with a saturated aqueous solution of $NaHCO_3$ (4 × 3 mL). The aqueous layer was then acidified (up to 1–2 pH value) with 20% aqueous HCl solution, and the product was later extracted with EtOAc (4 × 25 mL). The organic phases were combined, washed with brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure to get product **8a** as a clear liquid (45 mg, 56% yield for two steps). $[\alpha]_D^{25}$ = +28.4 (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38-7.35 (m, 2H), 7.32-7.26 (m, 3H), 4.88 (dd, *J* = 26.0, 11.5 Hz, 2H), 3.01 (dd, *J* = 37.5, 16.5 Hz, 2H), 1.64 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$) δ 176.2, 141.7, 129.0, 127.7, 125.6, 83.8, 42.6, 40.7, 24.2. **IR** (neat) *ν* 3483, 3176, 2975, 2922, 2853, 1783, 1703, 1550, 1449, 1221, 1068, 988 cm^{-1}. *NMR data of **8a** match with that reported in the literature.*[10]

To a solution of **8a** (42 mg, 0.19 mmol, 1.0 equiv) in DMSO (0.8 mL) was added AcOH (109 µL, 1.9 mmol, 10.0 equiv) and $NaNO_2$ (39 mg, 0.56 mmol, 3.0 equiv) at rt and stirred for 2 h at 50 °C. After the reaction was completed (monitored by ^{1}H NMR), the reaction mass was diluted with EtOAc (20 mL) extracted with a saturated aqueous solution of $NaHCO_3$ (4 × 3 mL). The basic aqueous layer was then acidified (up to 1–2 pH value) with 20% aqueous HCl solution, and the product was later extracted with EtOAc (4 × 25 mL). The organic phases were combined, washed with brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure to get the crude di-carboxylic acid, which was directly used for the next step without further purification.

To a solution of the above crude di-carboxylic acid in toluene (3 mL), $MeNH_2$ (295 µL, 3.8 mmol, 20 equiv, 40% w/v in water) was added and stirred at 110 °C, for 12 h using Dean-Stark apparatus. After the reaction was completed (monitored by ^{1}H NMR), the solvent was evaporated over the rotary evaporator to get the crude product **9a**, which was further purified as a clear liquid (15 mg, 38% yield for two steps) from the crude reaction mixture using flash column chromatography [Silica gel, hexane/EtOAc (75:25)]. $\mathbf{R_f}$ = 0.5 [hexane/EtOAc (70:30)]. **HPLC** analysis Daicel Chiralcel AD-H, 4.6 mm × 250 mm (hexane/IPA = 90:10, 0.5 mL/min, 210 nm), t_R (major) = 13.7 min, t_R (minor) = 14.7 min, 93% *ee*. $\mathbf{[\alpha]_D^{29}}$ = +27.9 (*c* = 1.0, $CHCl_3$ for 93% *ee*), lit.[11] $\mathbf{[\alpha]_D^{24}}$ = +18.6 (*c* = 1.26, $CHCl_3$ for 75% *ee*). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38-7.34 (m, 4H), 7.31-7.27 (m, 1H), 3.12 (d, *J* = 18.5 Hz, 1H), 3.07 (s, 3H), 2.86 (d, *J* = 18.0 Hz, 1H), 1.72 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$) δ 181.2, 175.8, 141.9, 129.1, 127.7, 125.7, 48.0, 45.3, 25.8, 25.3. **IR** (neat) *v* 2928, 1780, 1697, 1430, 1383, 1282, 1087, 1028, 696 cm^{-1}. *NMR data of **9a** match with that reported in the literature.*[11]

11. References

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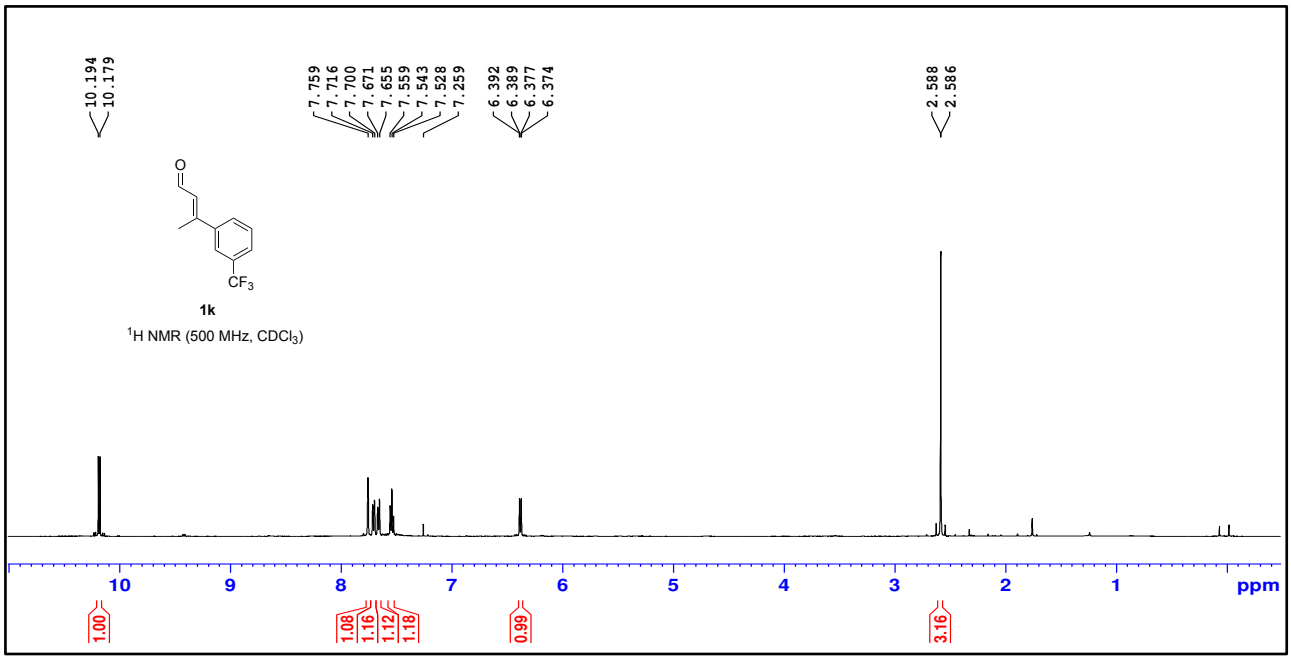
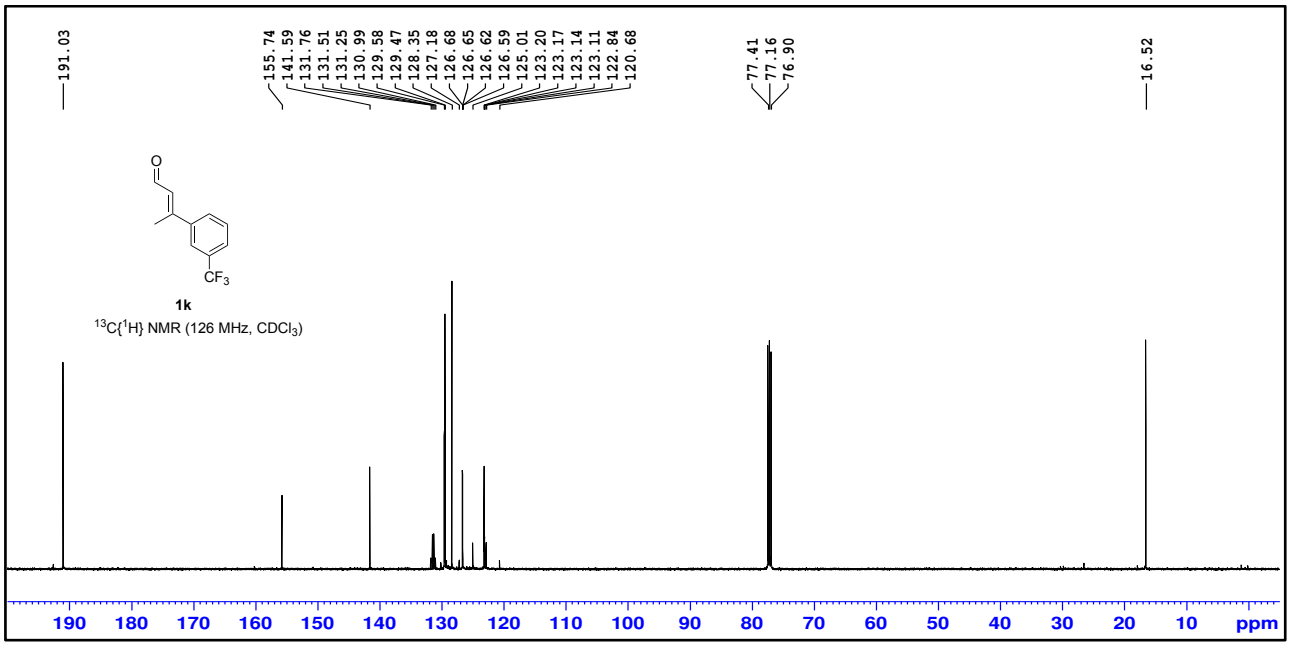
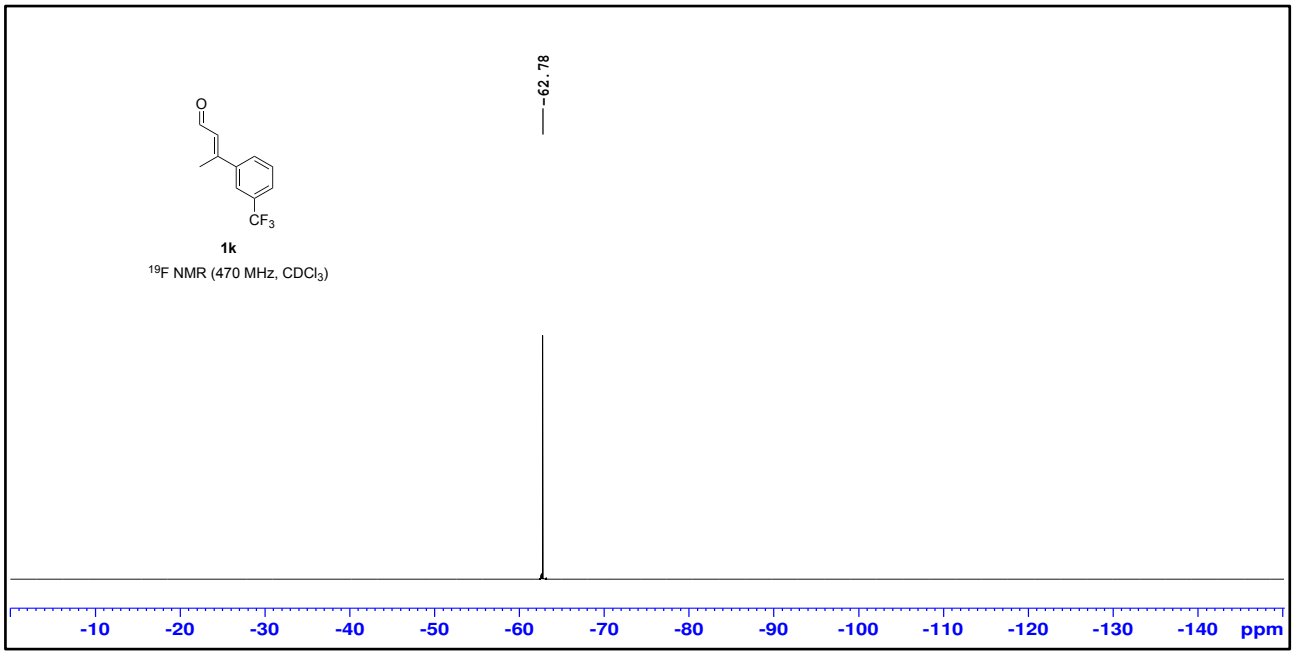
12. NMR and HPLC data

(*E*)-3-(3-(trifluoromethyl)phenyl)but-2-enal (1k)



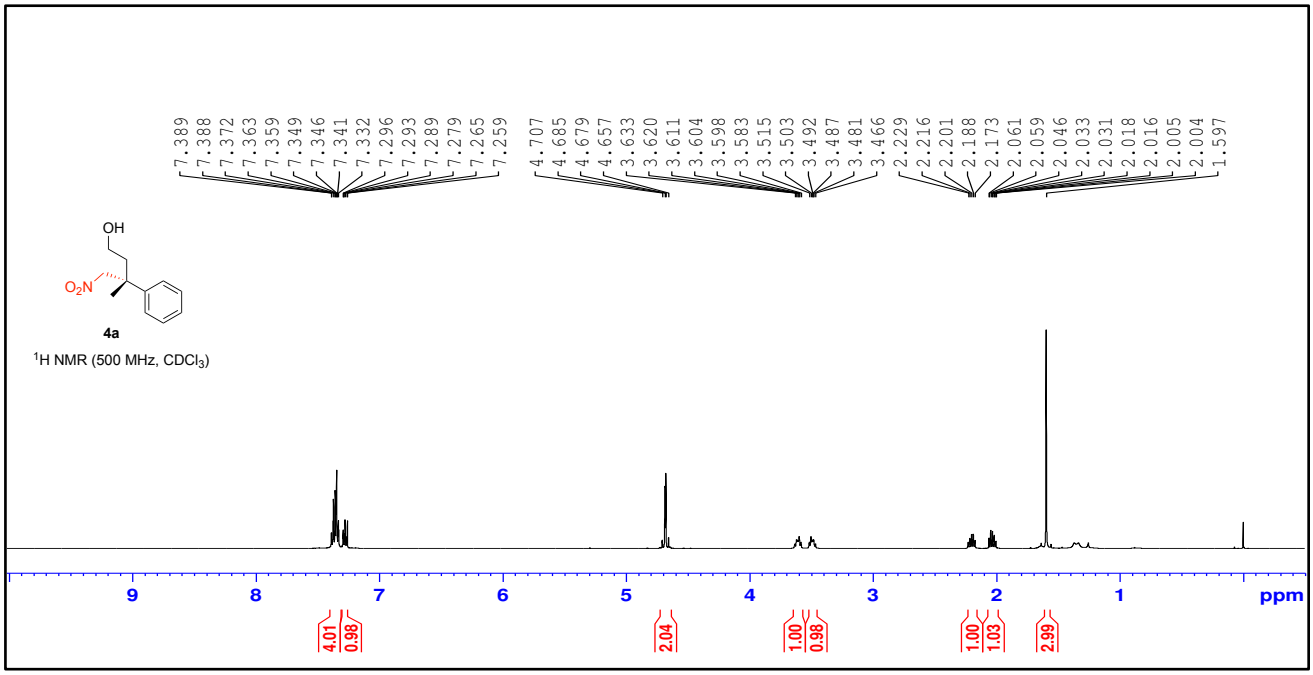


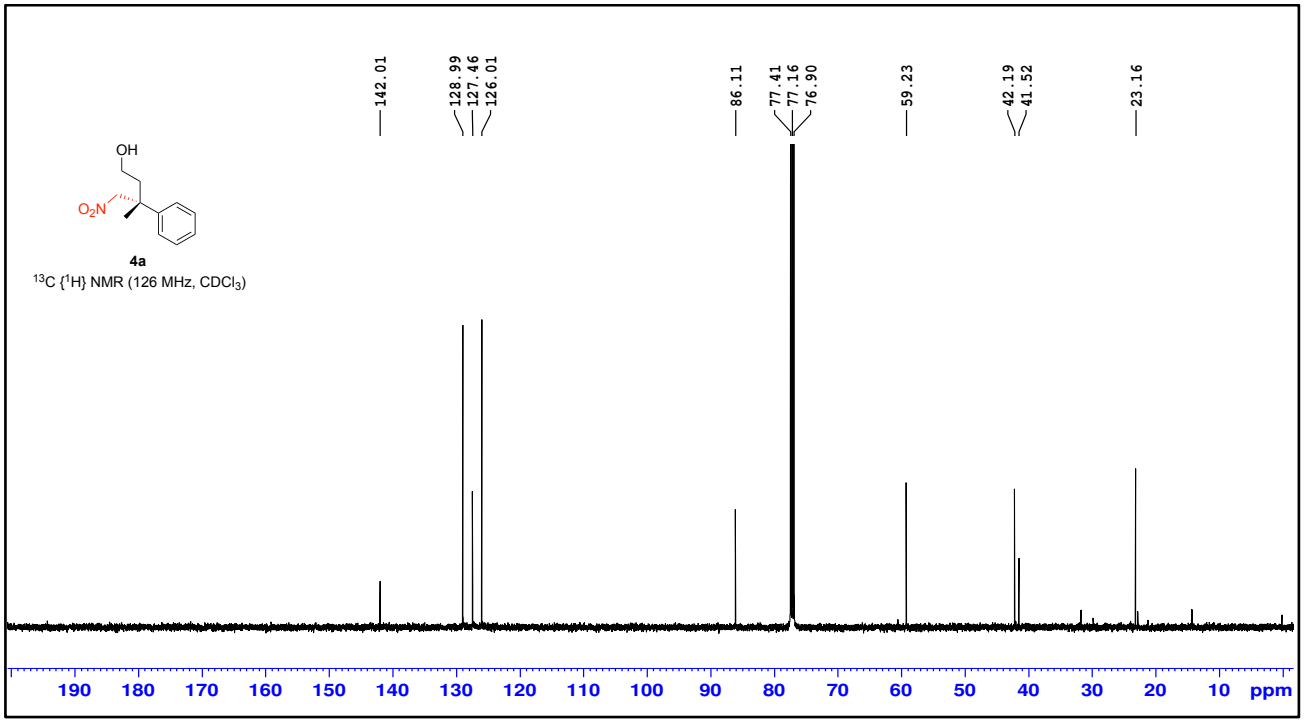


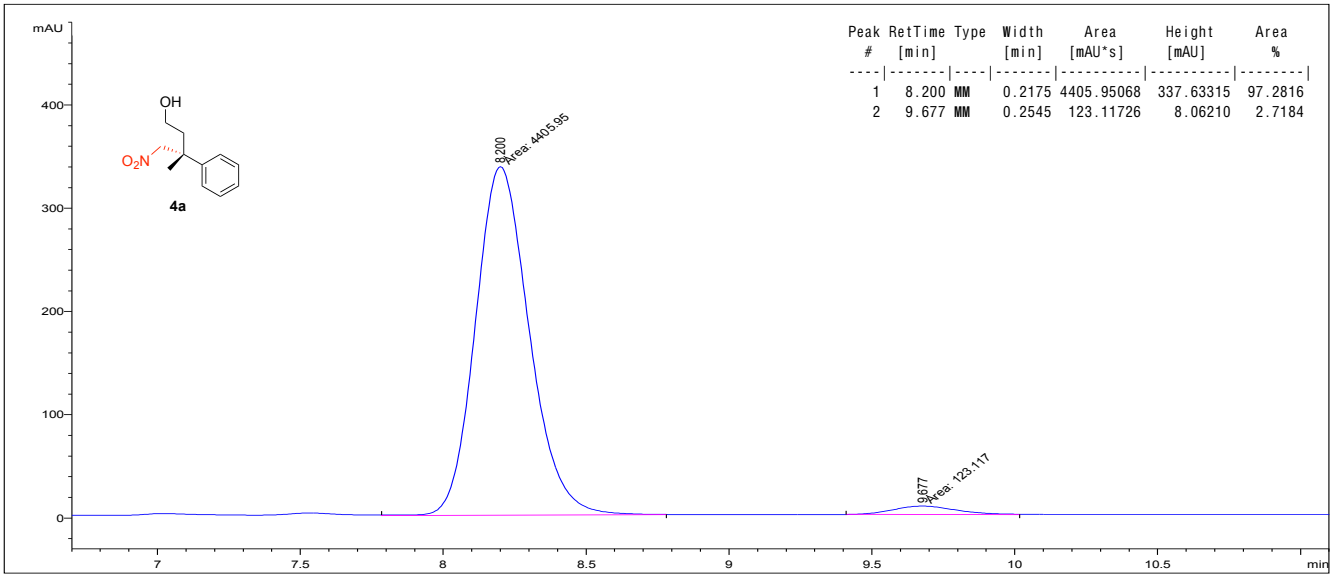
1k

^{19}F NMR (470 MHz, $CDCl_3$)

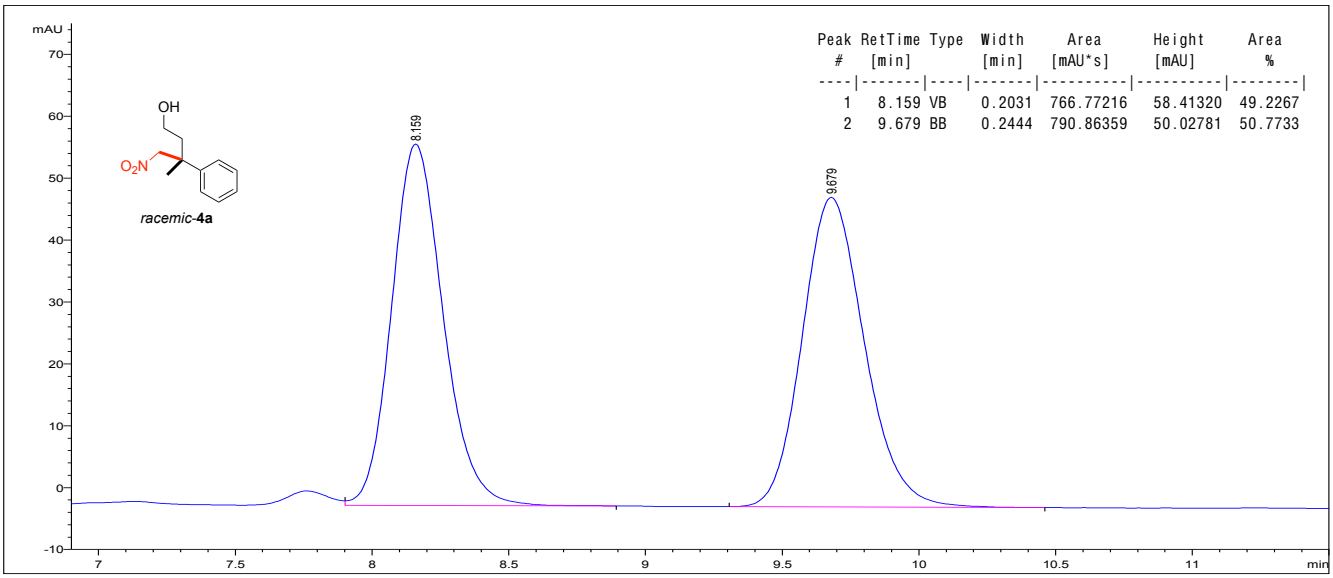
(R)-3-methyl-4-nitro-3-phenylbutan-1-ol (4a)





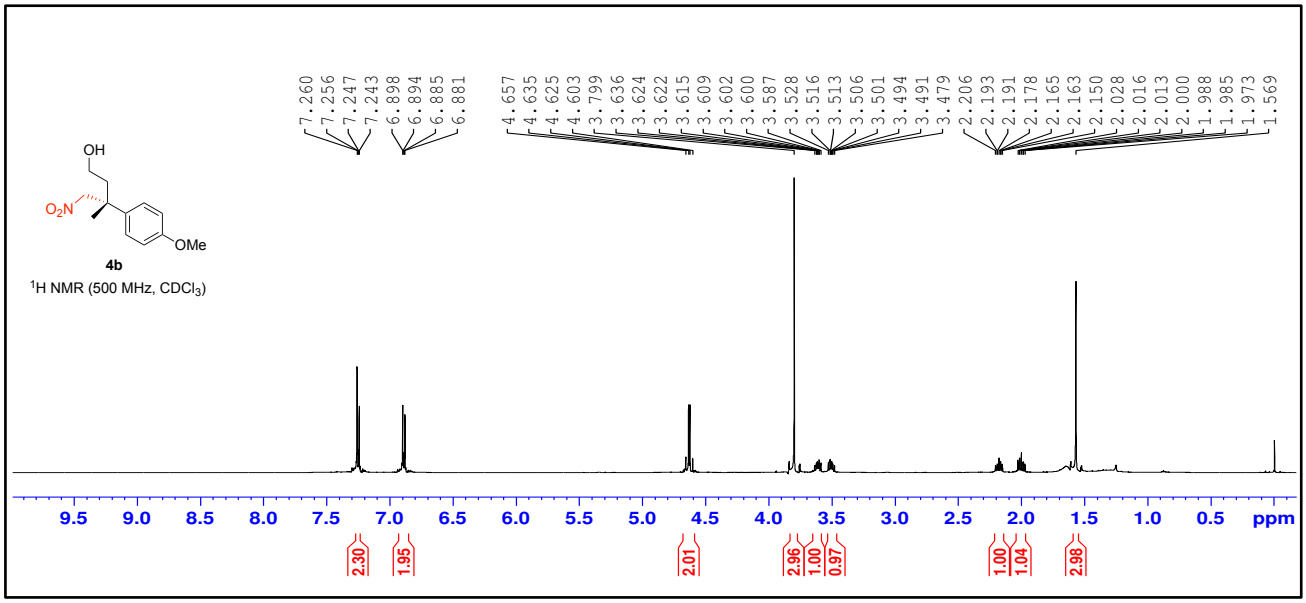


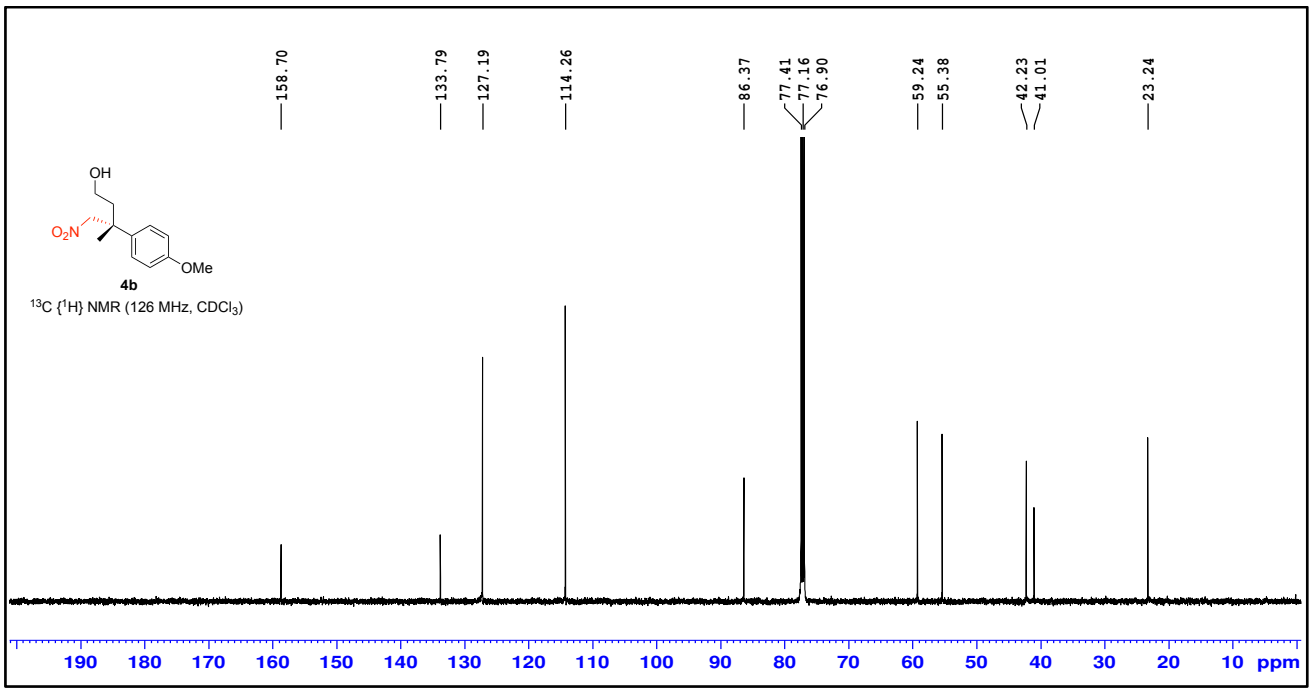
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.200	MM	0.2175	4405.95068	337.63315	97.2816
2	9.677	MM	0.2545	123.11726	8.06210	2.7184

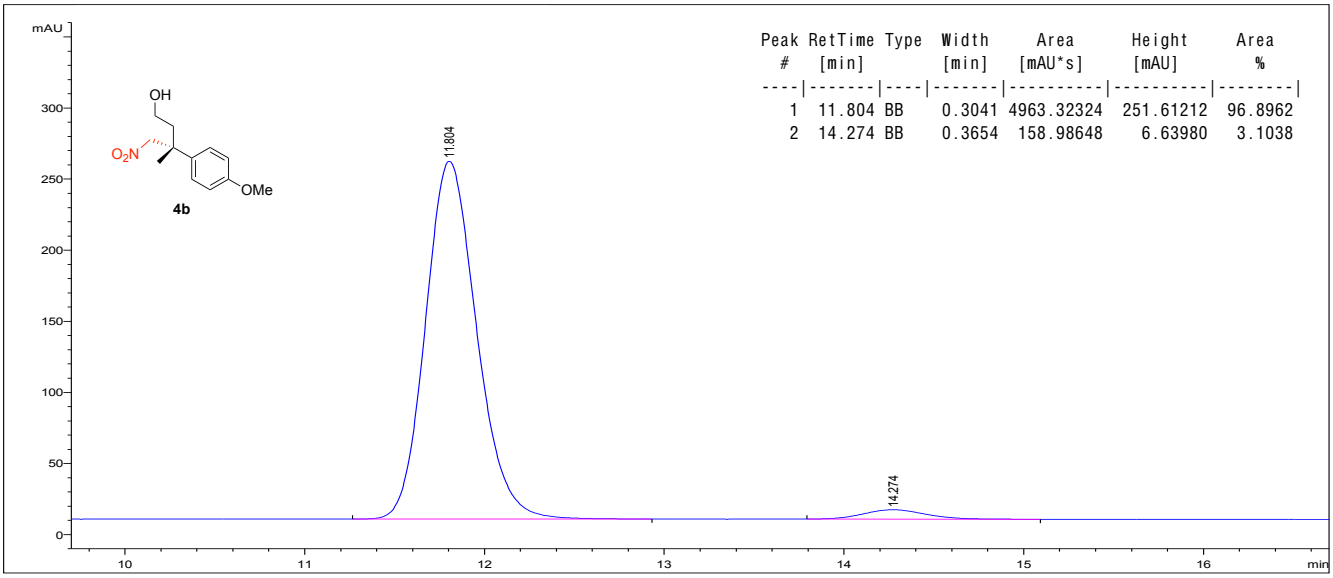


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.159	VB	0.2031	766.77216	58.41320	49.2267
2	9.679	BB	0.2444	790.86359	50.02781	50.7733

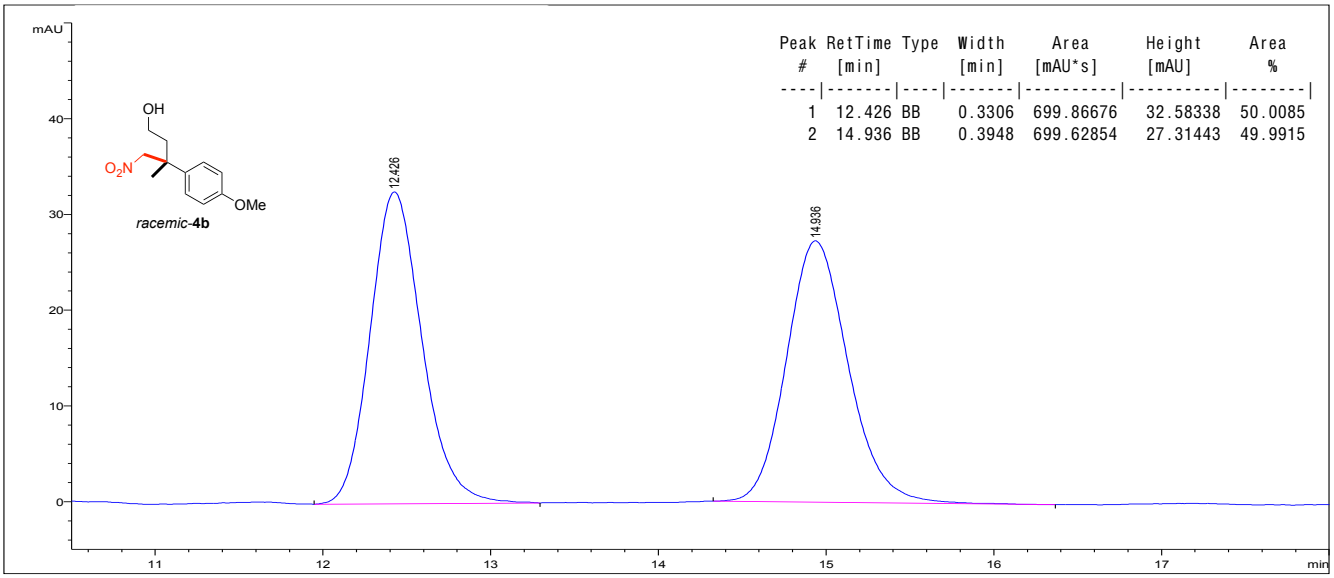
(R)-3-(4-methoxyphenyl)-3-methyl-4-nitrobutan-1-ol (4b)





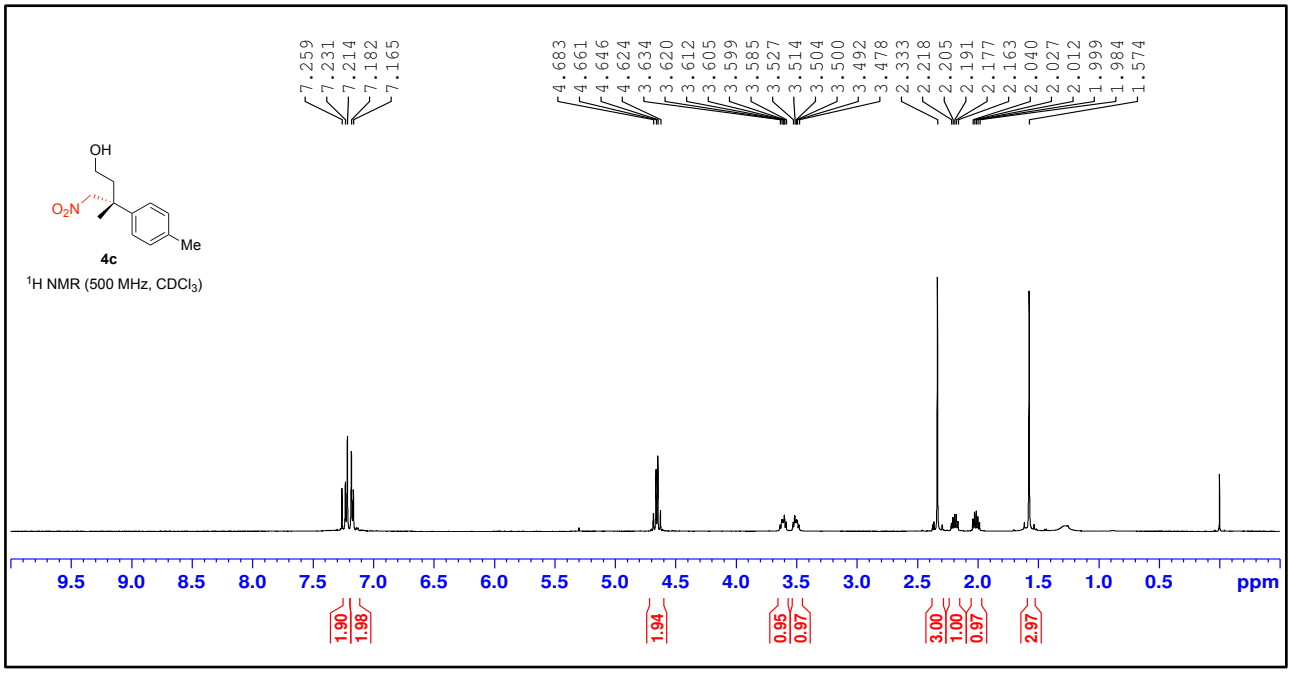


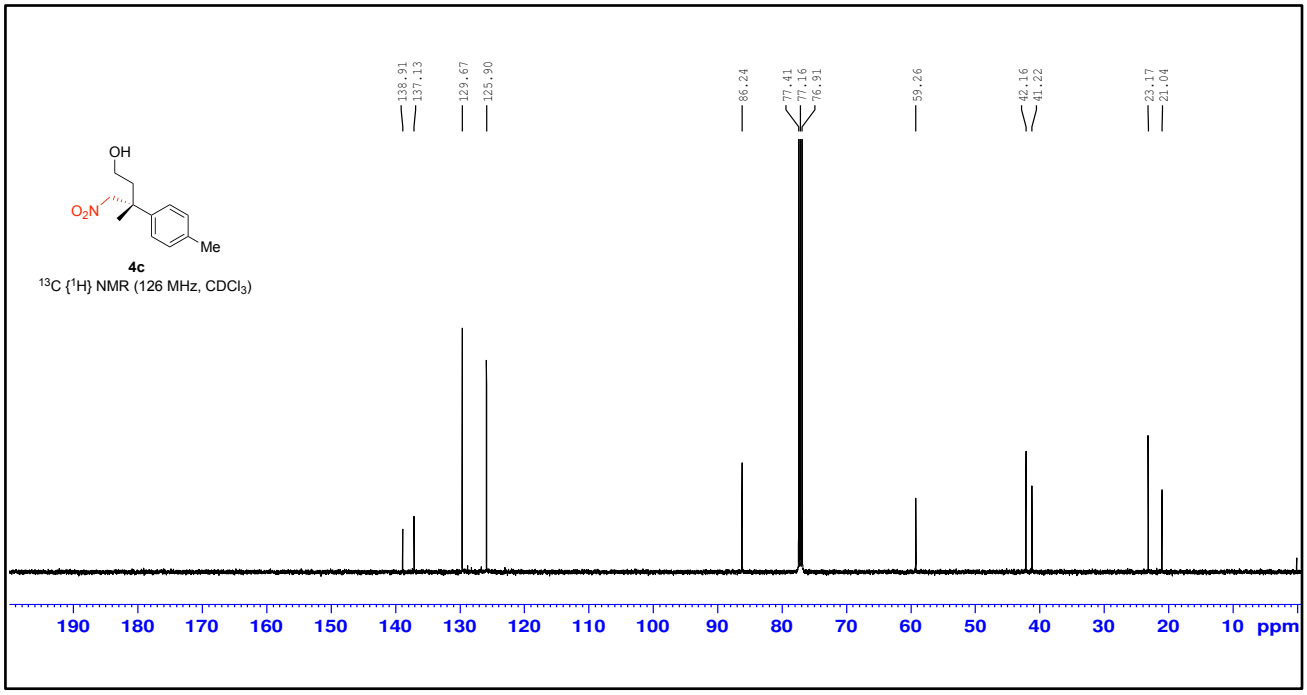
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.804	BB	0.3041	4963.32324	251.61212	96.8962
2	14.274	BB	0.3654	158.98648	6.63980	3.1038

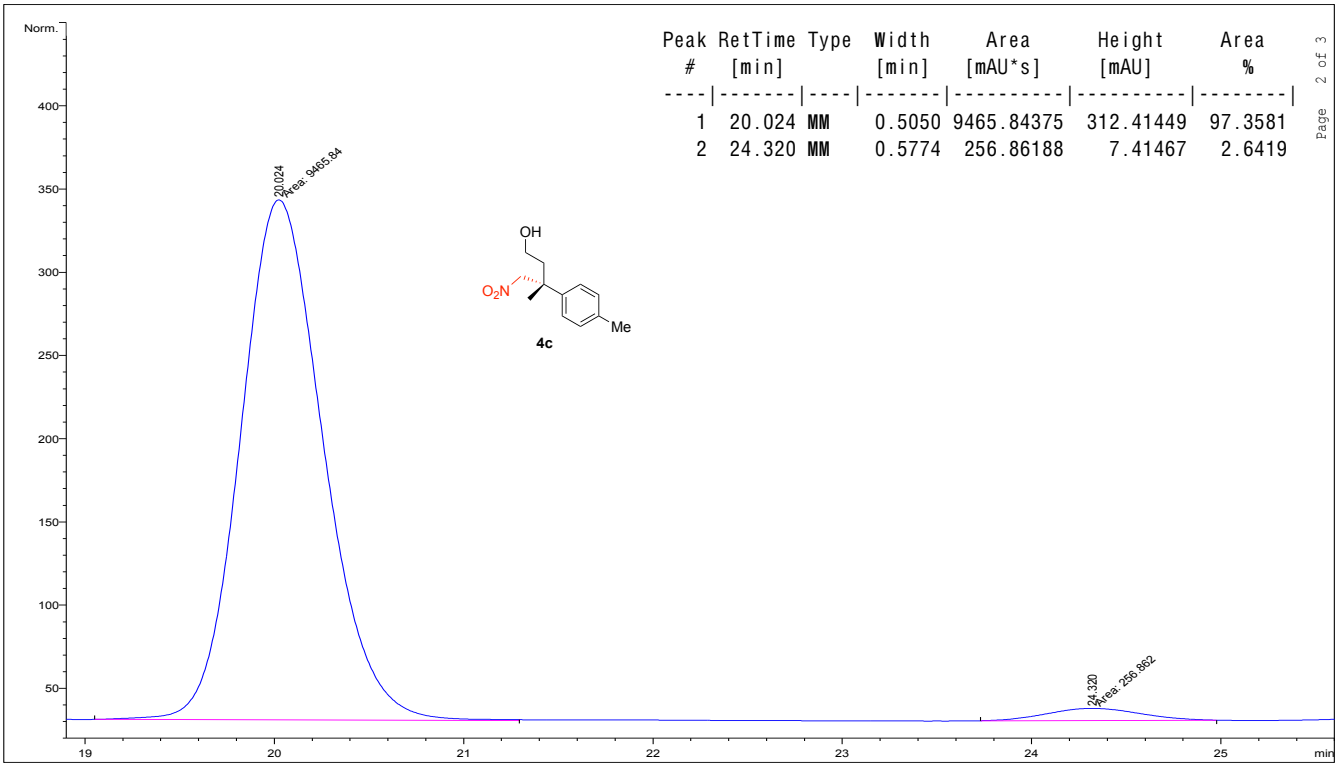


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.426	BB	0.3306	699.86676	32.58338	50.0085
2	14.936	BB	0.3948	699.62854	27.31443	49.9915

(*R*)-3-methyl-4-nitro-3-(*p*-tolyl)butan-1-ol (4c)







Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.024	MM	0.5050	9465.84375	312.41449	97.3581
2	24.320	MM	0.5774	256.86188	7.41467	2.6419

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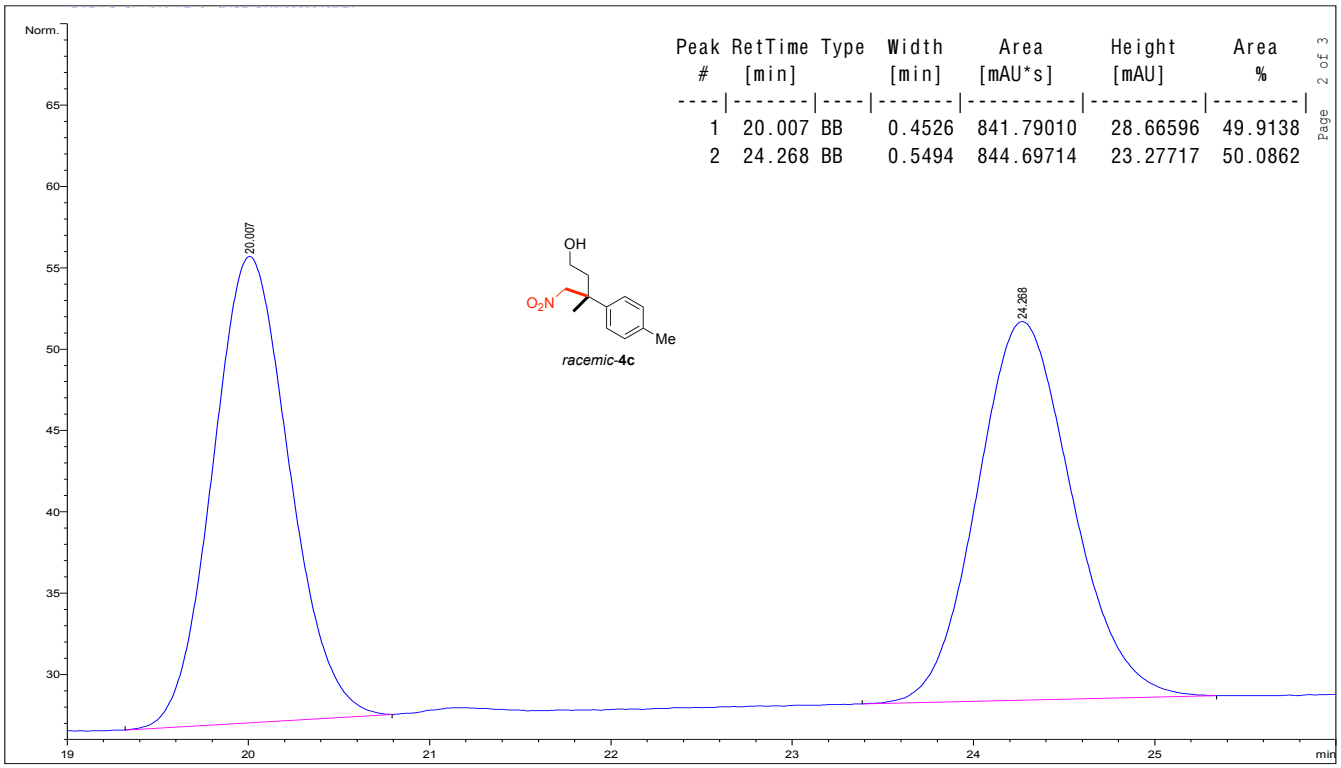

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.007	BB	0.4526	841.79010	28.66596	49.9138
2	24.268	BB	0.5494	844.69714	23.27717	50.0862

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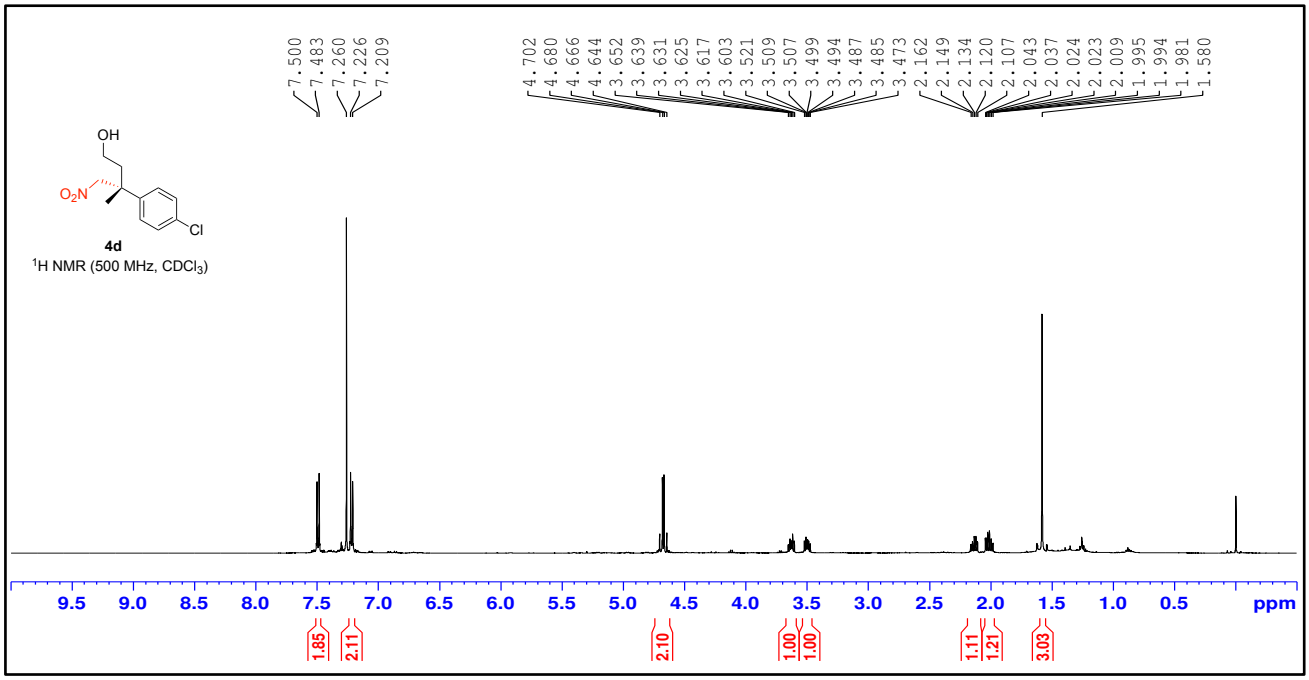
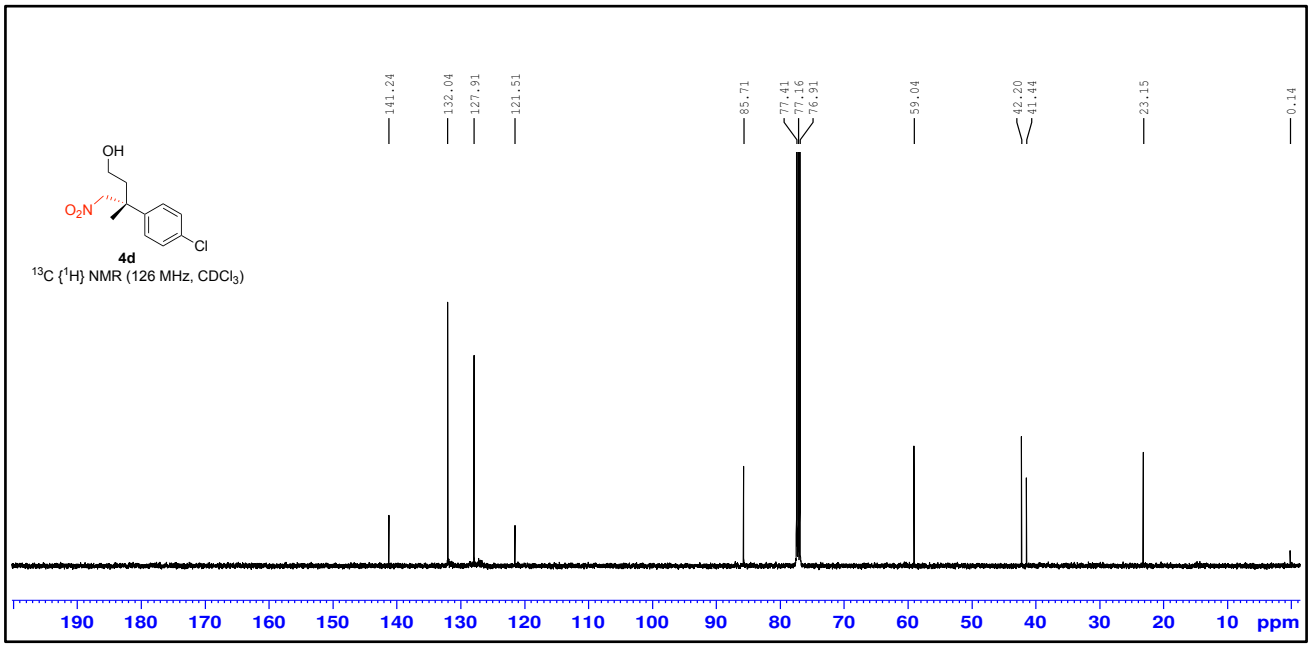
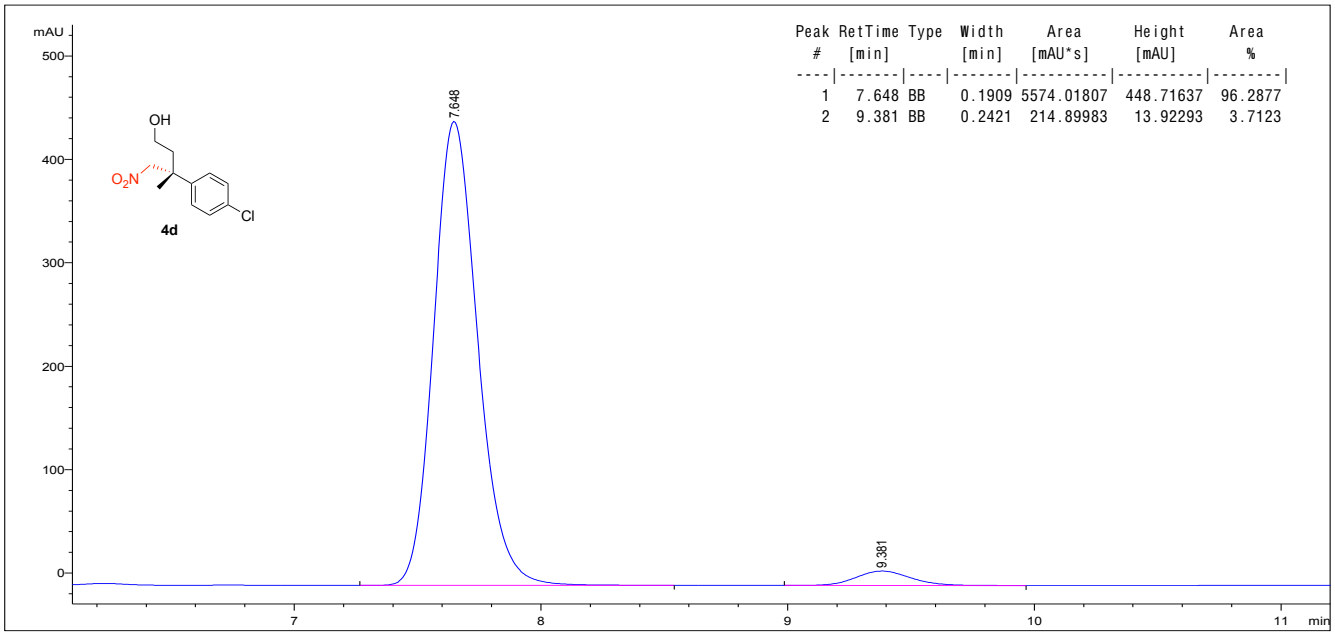
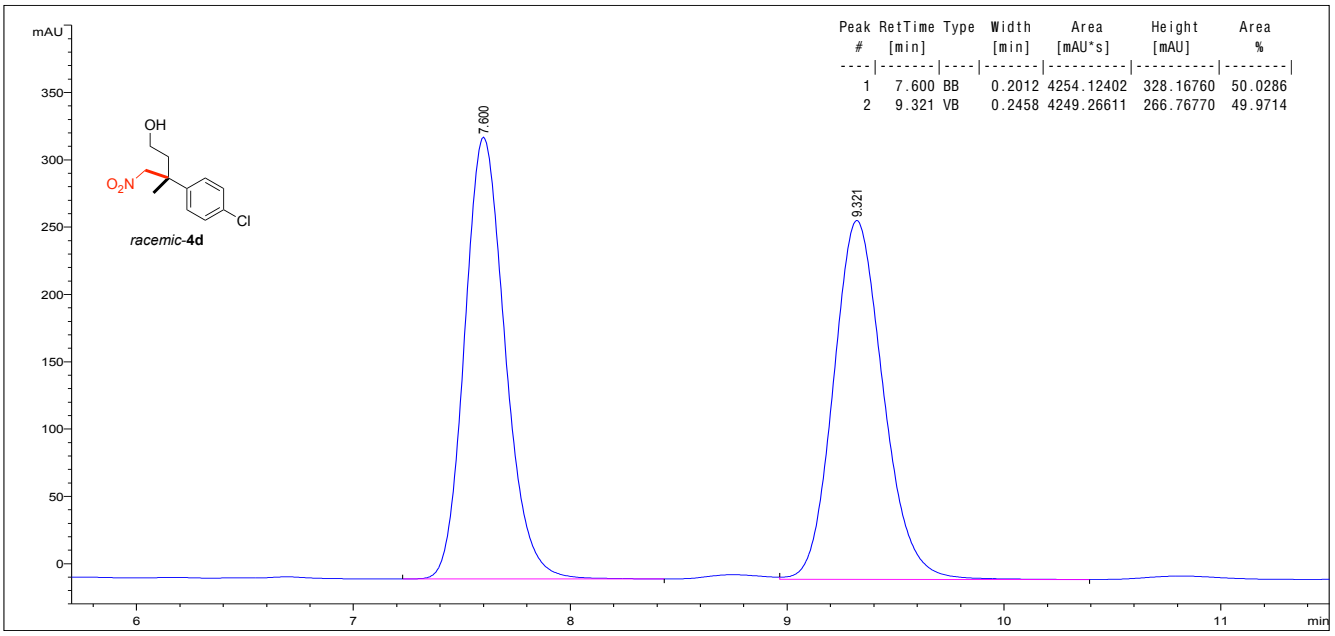
(R)-3-(4-chlorophenyl)-3-methyl-4-nitrobutan-1-ol (4d)





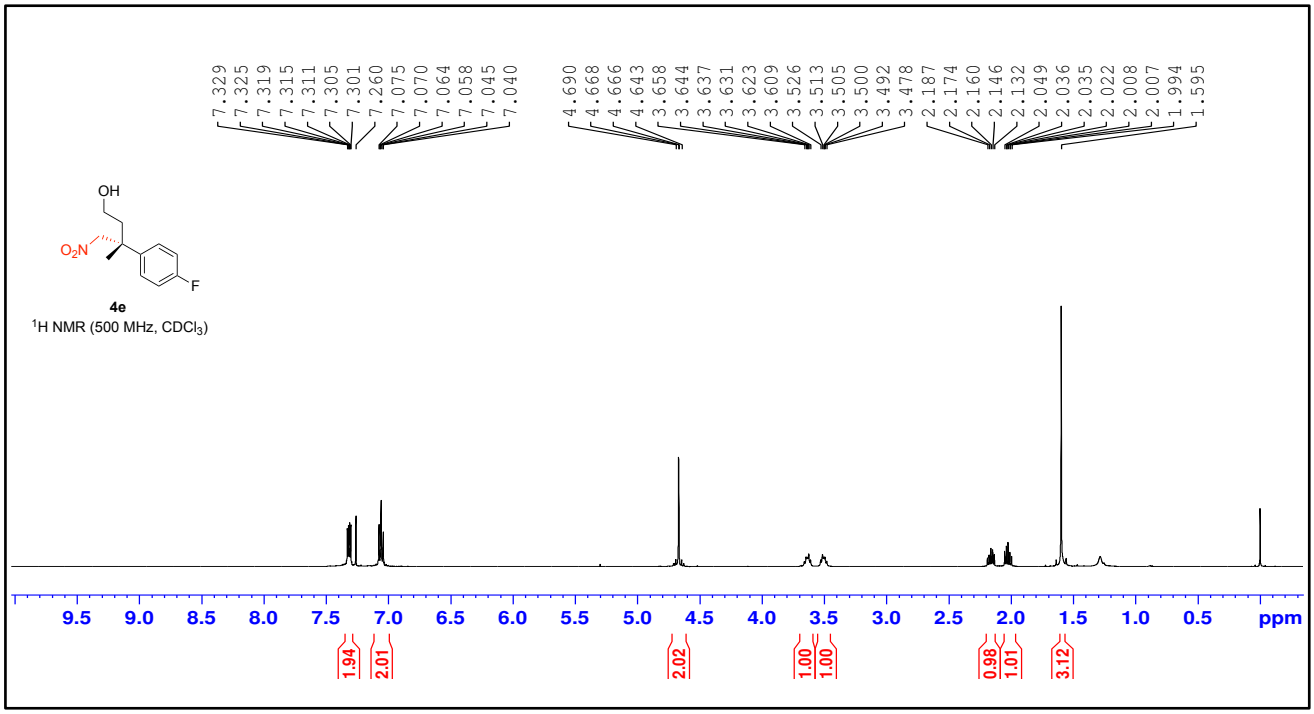


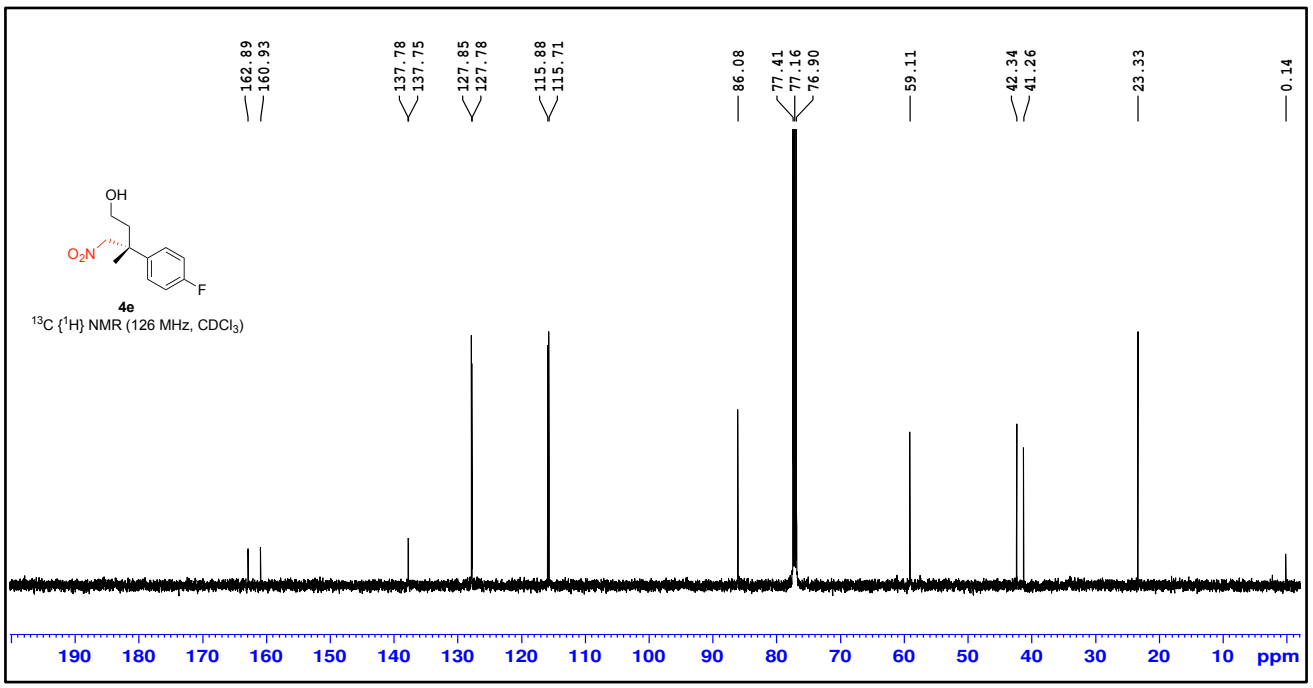
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.648	BB	0.1909	5574.01807	448.71637	96.2877
2	9.381	BB	0.2421	214.89983	13.92293	3.7123

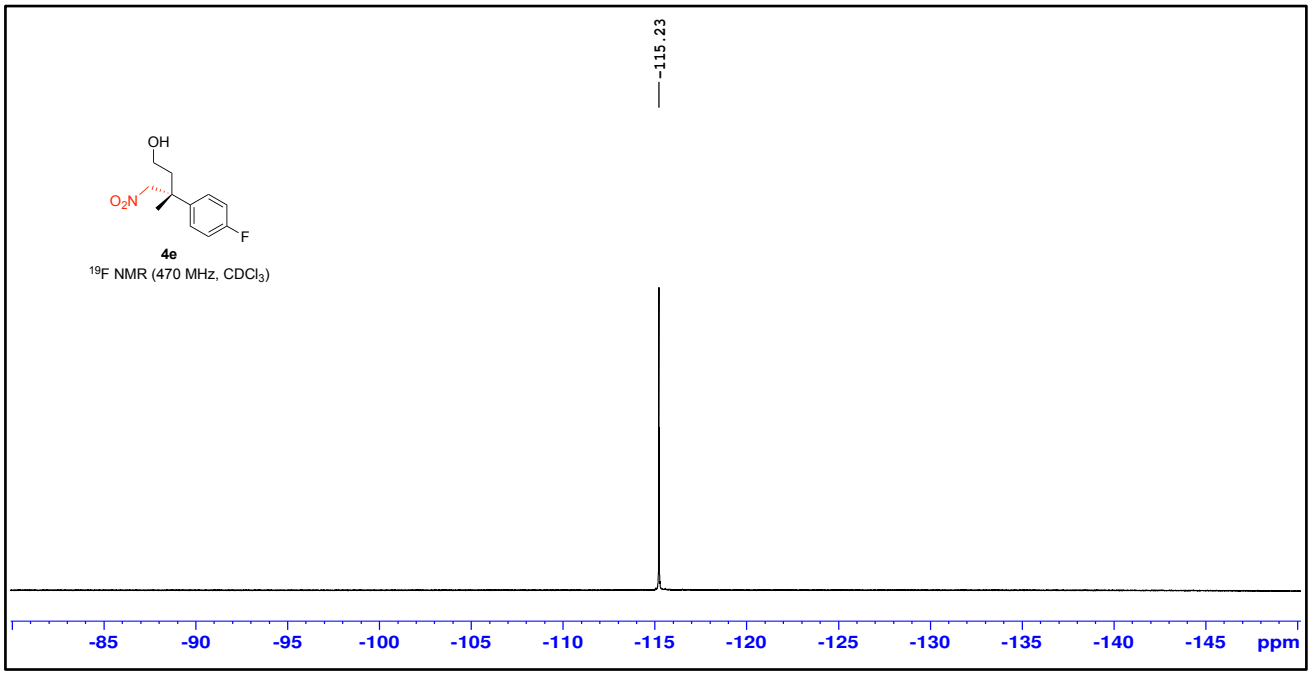


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.600	BB	0.2012	4254.12402	328.16760	50.0286
2	9.321	VB	0.2458	4249.26611	266.76770	49.9714

(R)-3-(4-fluorophenyl)-3-methyl-4-nitrobutan-1-ol (4e)

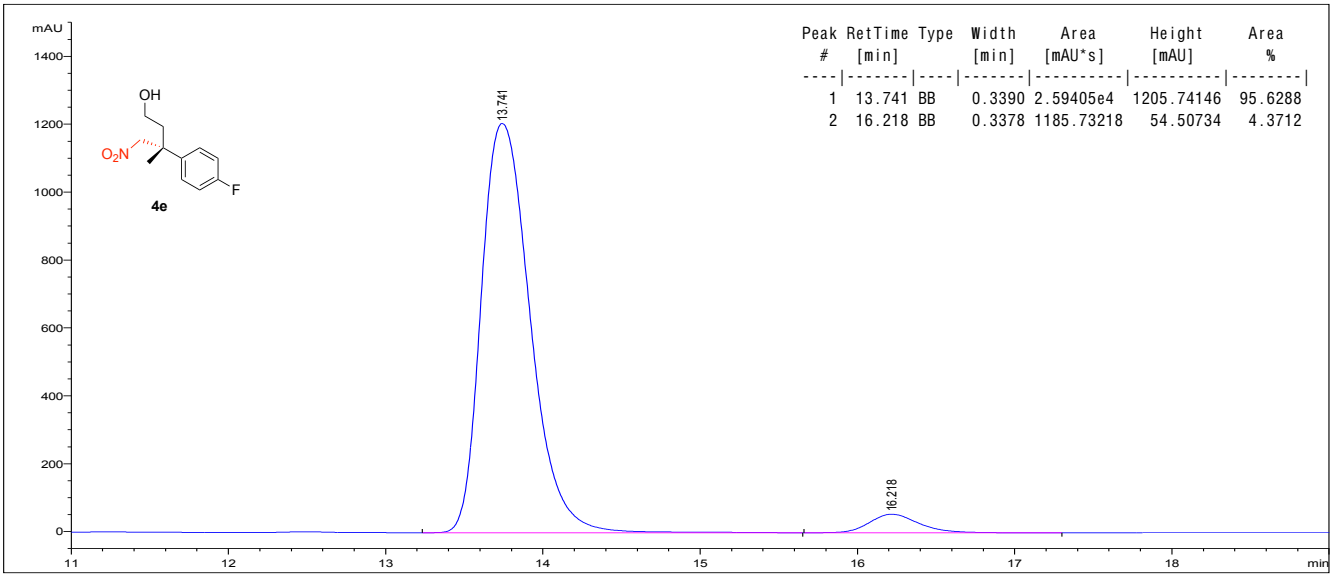




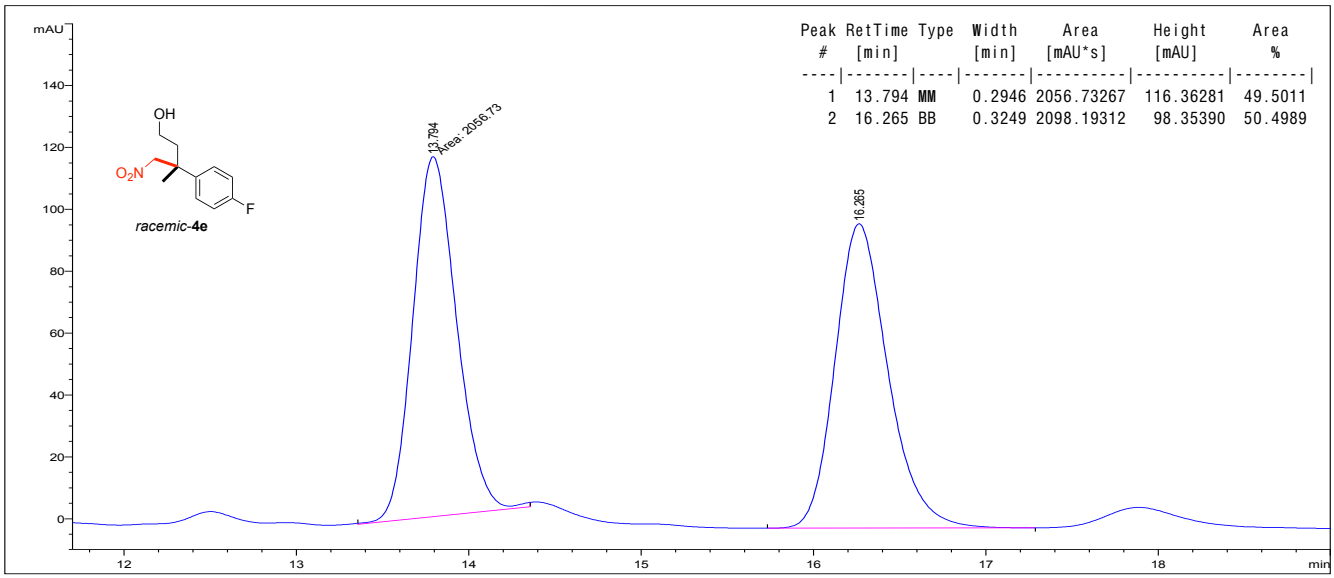


4e

^{19}F NMR (470 MHz, $CDCl_3$)

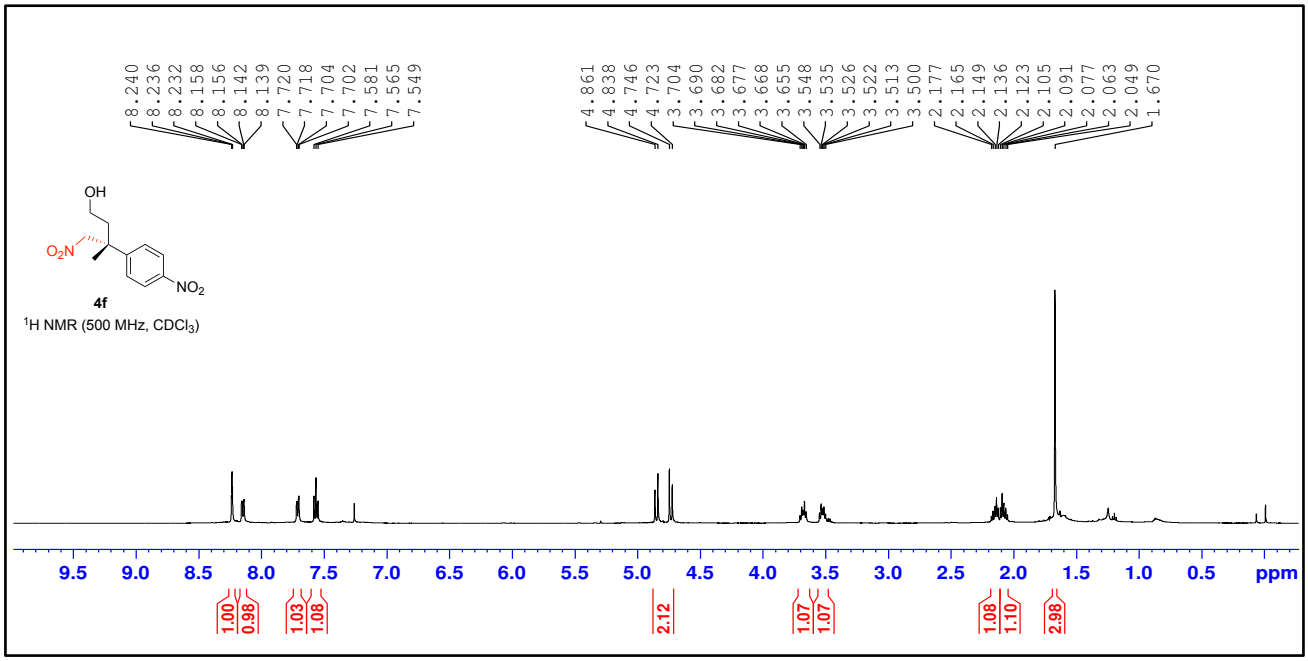


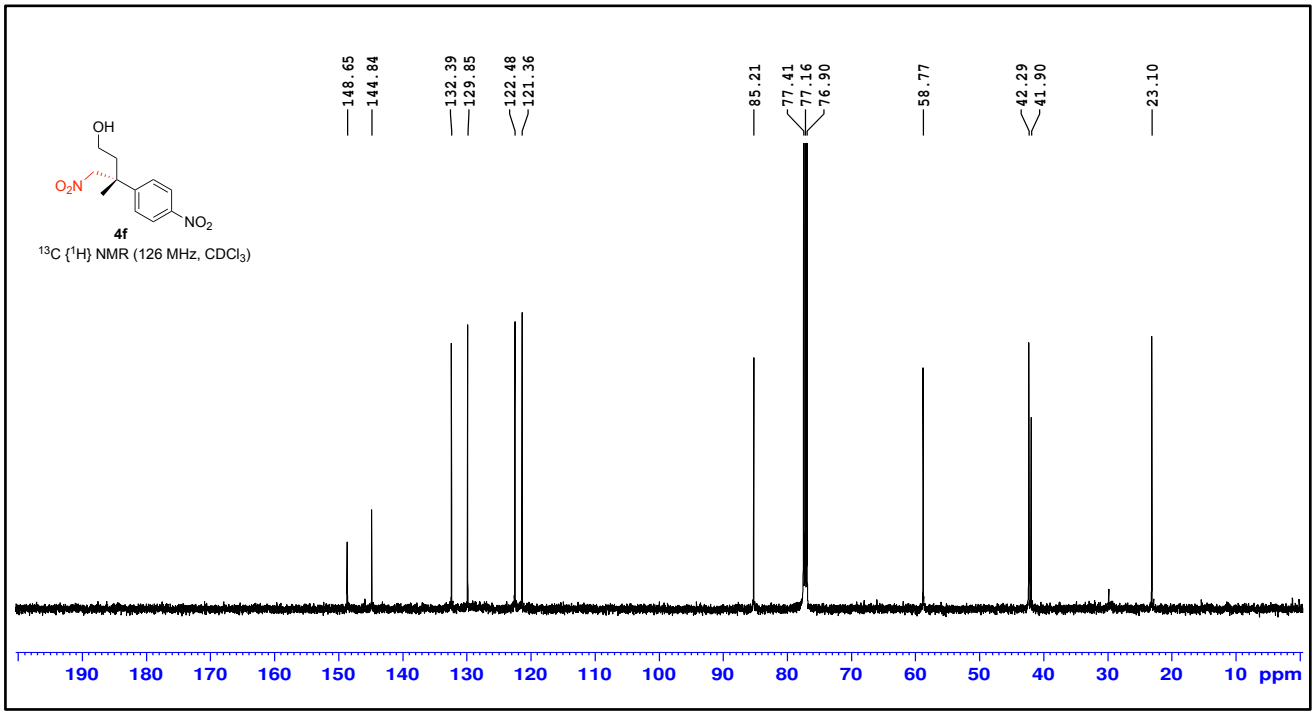
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.741	BB	0.3390	2.59405e4	1205.74146	95.6288
2	16.218	BB	0.3378	1185.73218	54.50734	4.3712

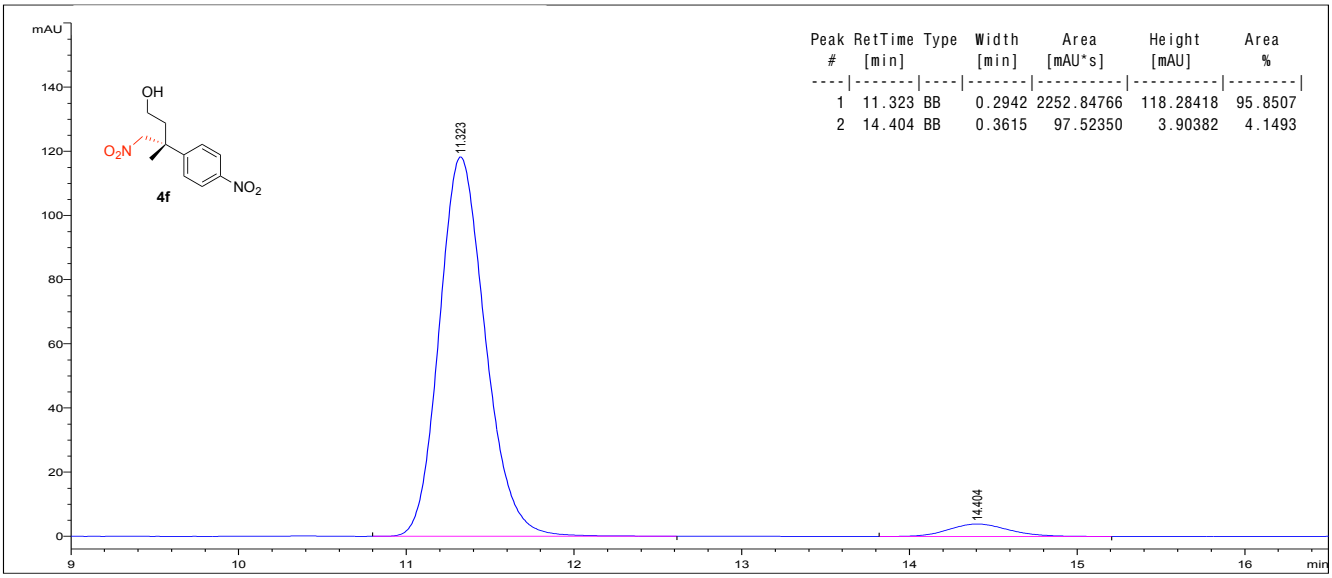


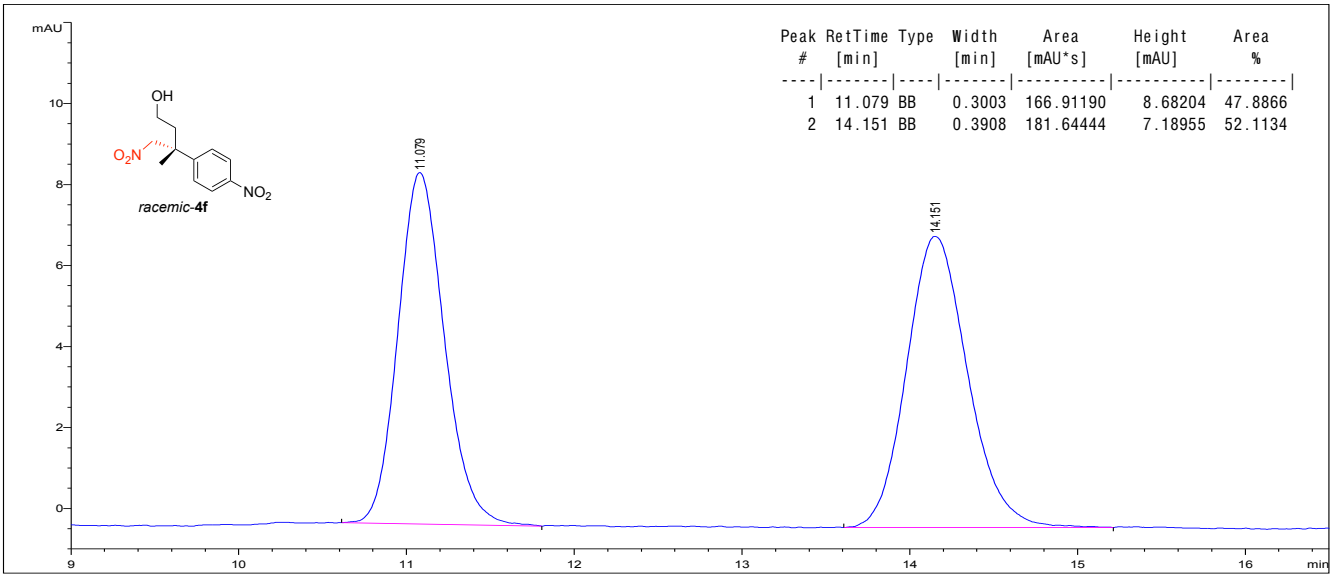
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.794	MM	0.2946	2056.73267	116.36281	49.5011
2	16.265	BB	0.3249	2098.19312	98.35390	50.4989

(R)-3-methyl-4-nitro-3-(4-nitrophenyl)butan-1-ol (4f)

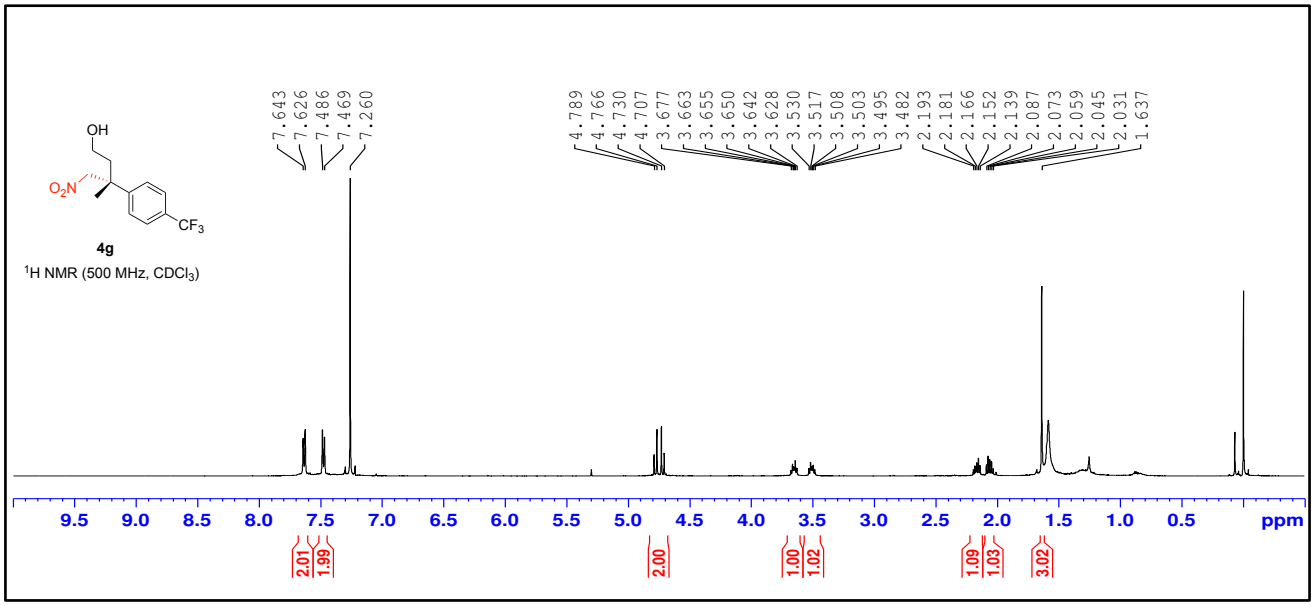


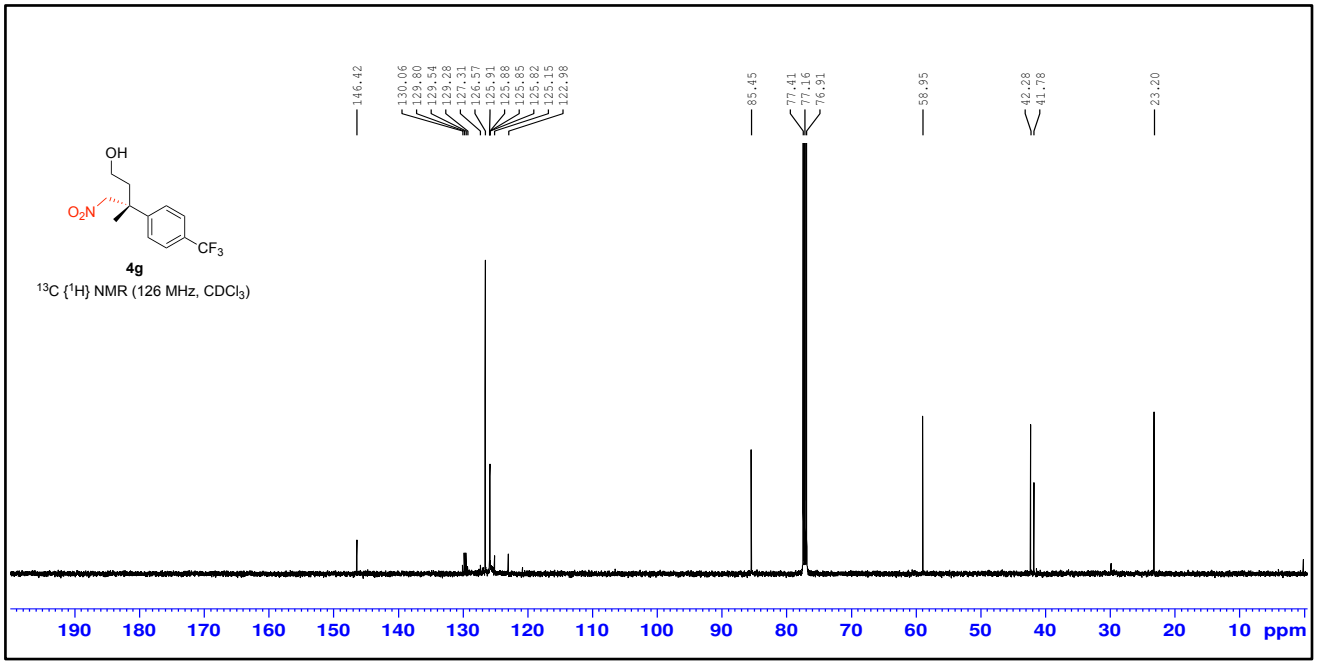


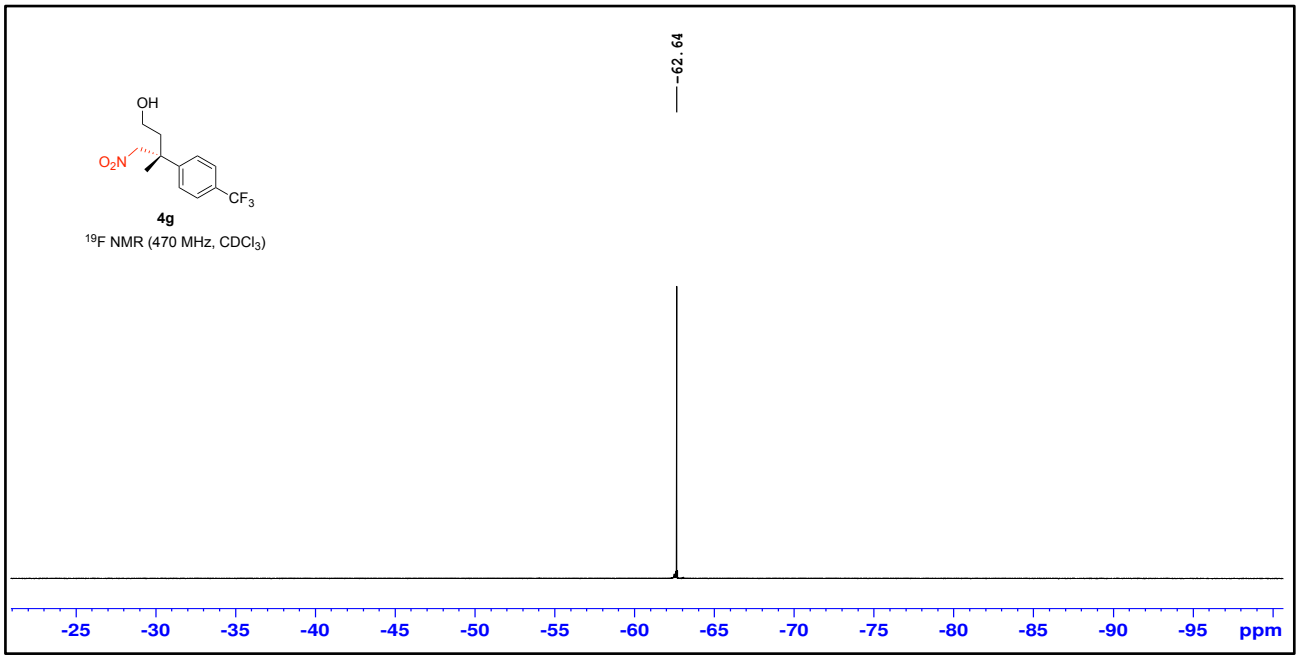

mAU
140
120
100
80
60
40
20
0
9
10
11
12
13
14
15
16
min
OH
O_2N
NO_2
4f
11.323
14.404
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 11.323 | BB | 0.2942 | 2252.84766 | 118.28418 | 95.8507
2 | 14.404 | BB | 0.3615 | 97.52350 | 3.90382 | 4.1493


mAU
10
8
6
4
2
0
9
10
11
12
13
14
15
16
min
OH
O_2N
NO_2
racemic-4f
11.079
14.151
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 11.079 | BB | 0.3003 | 166.91190 | 8.68204 | 47.8866
2 | 14.151 | BB | 0.3908 | 181.64444 | 7.18955 | 52.1134

(R)-3-methyl-4-nitro-3-(4-(trifluoromethyl)phenyl)butan-1-ol (4g)

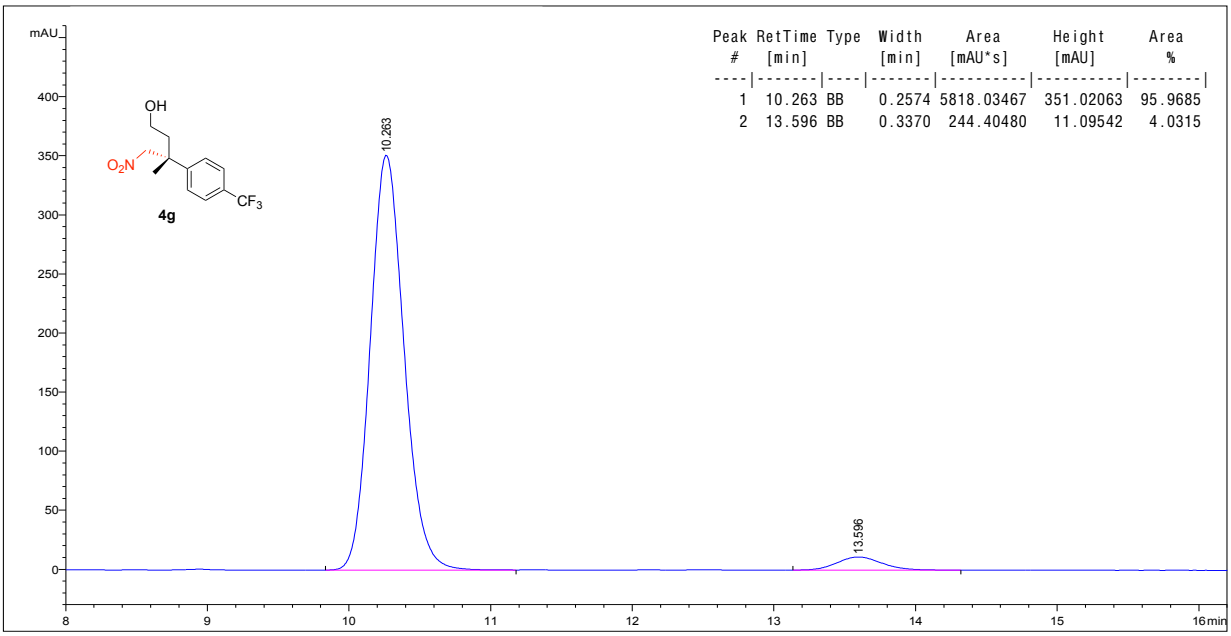




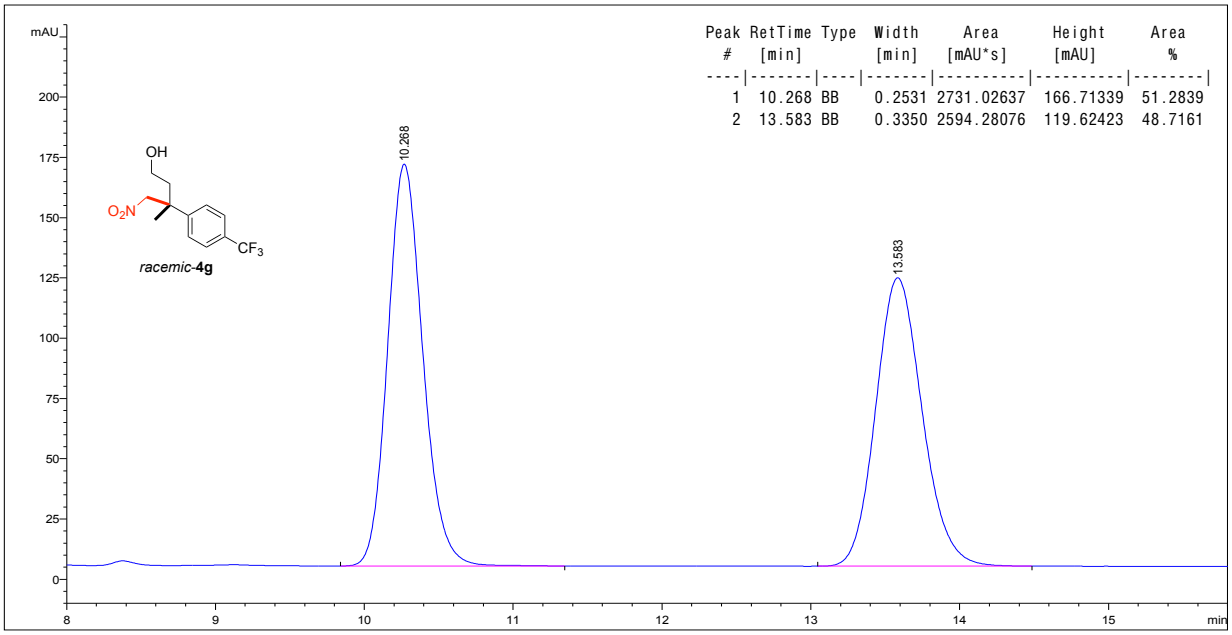


4g

^{19}F NMR (470 MHz, $CDCl_3$)

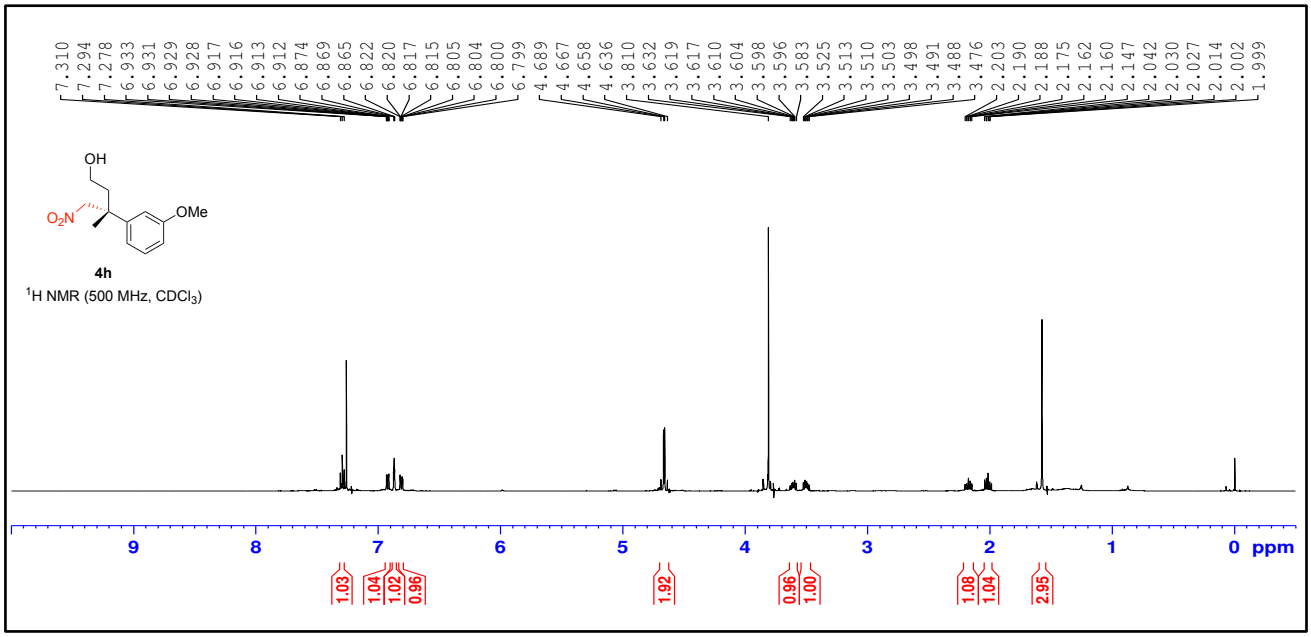


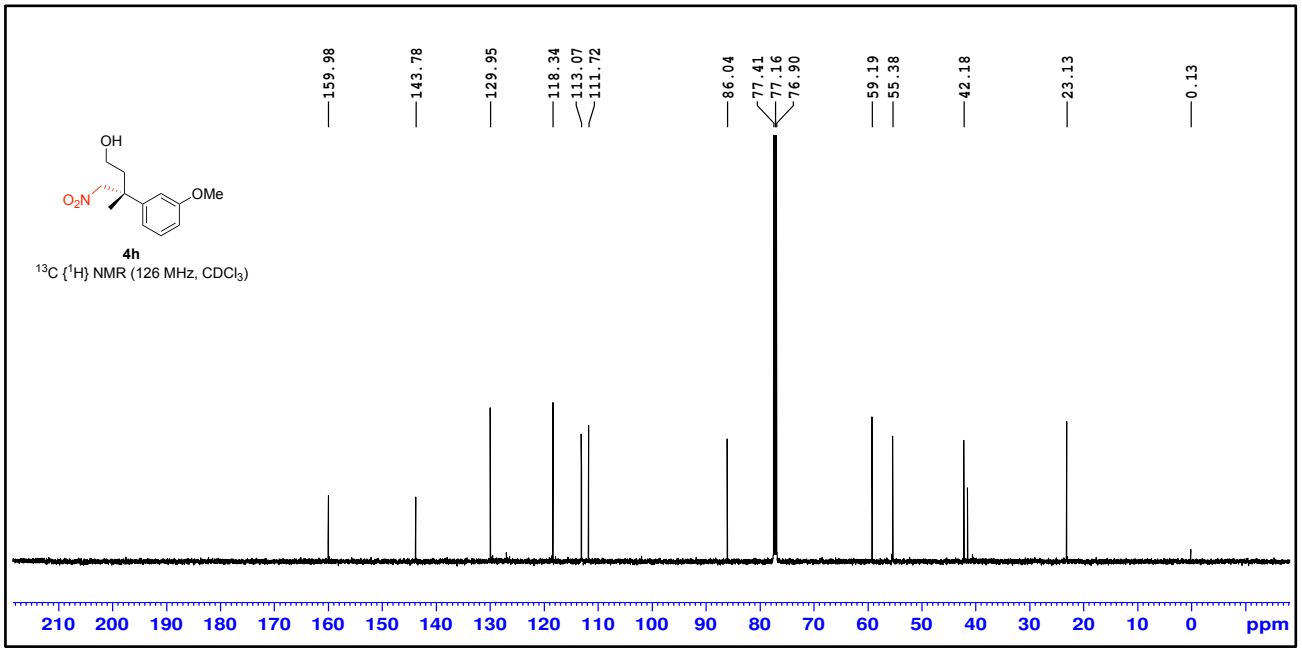
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.263	BB	0.2574	5818.03467	351.02063	95.9685
2	13.596	BB	0.3370	244.40480	11.09542	4.0315

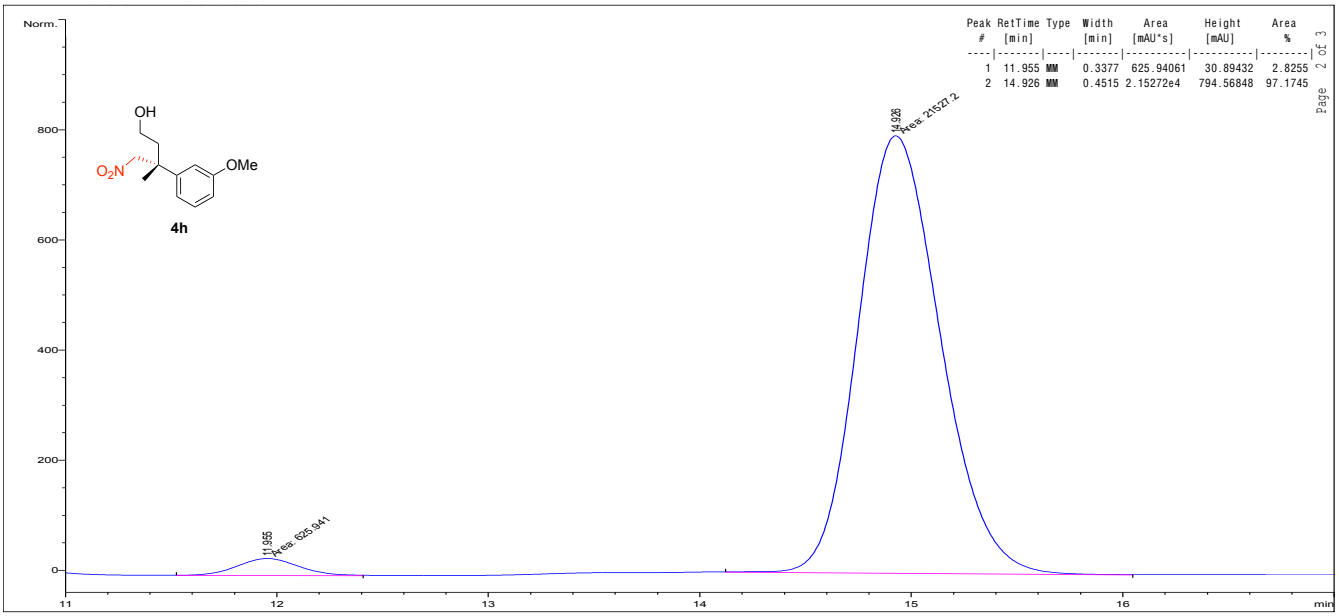


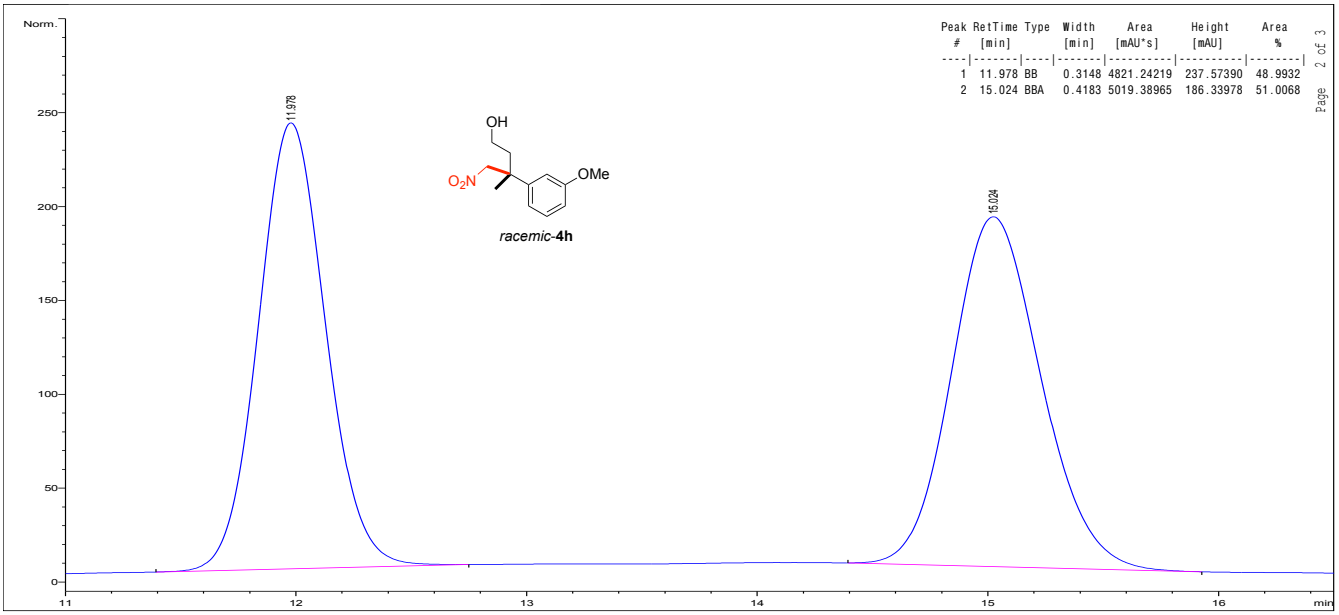
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.268	BB	0.2531	2731.02637	166.71339	51.2839
2	13.583	BB	0.3350	2594.28076	119.62423	48.7161

(*R*)-3-methyl-4-nitro-3-(3-methoxyphenyl)butan-1-ol (4h)

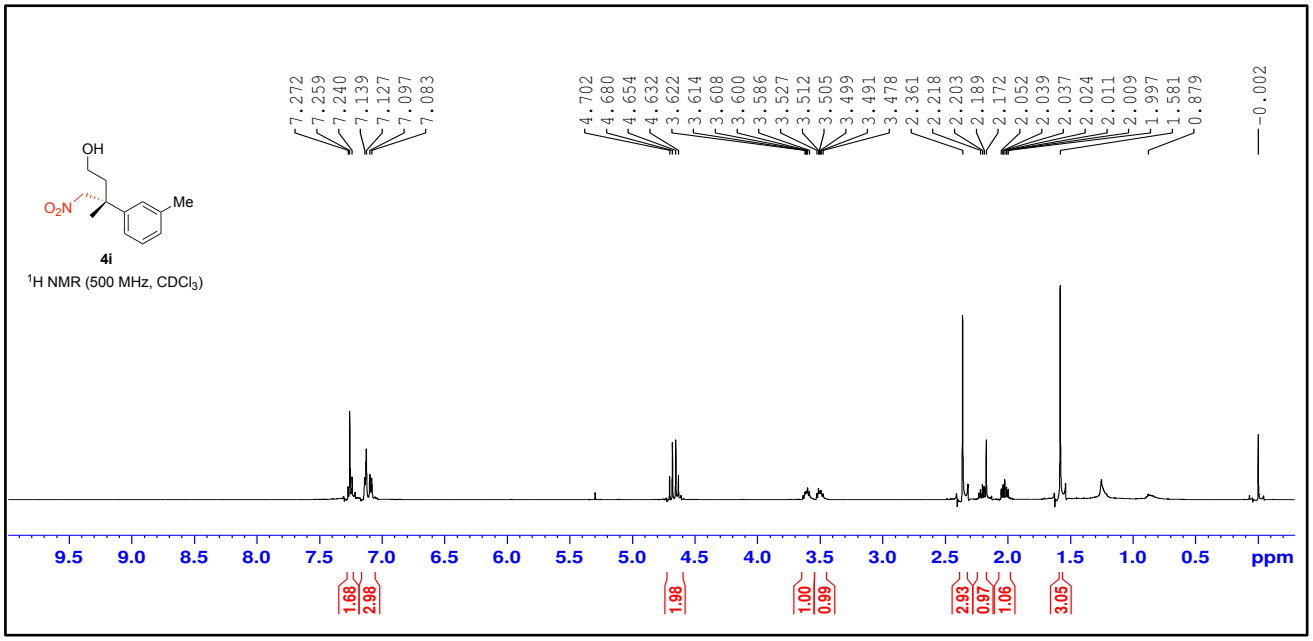


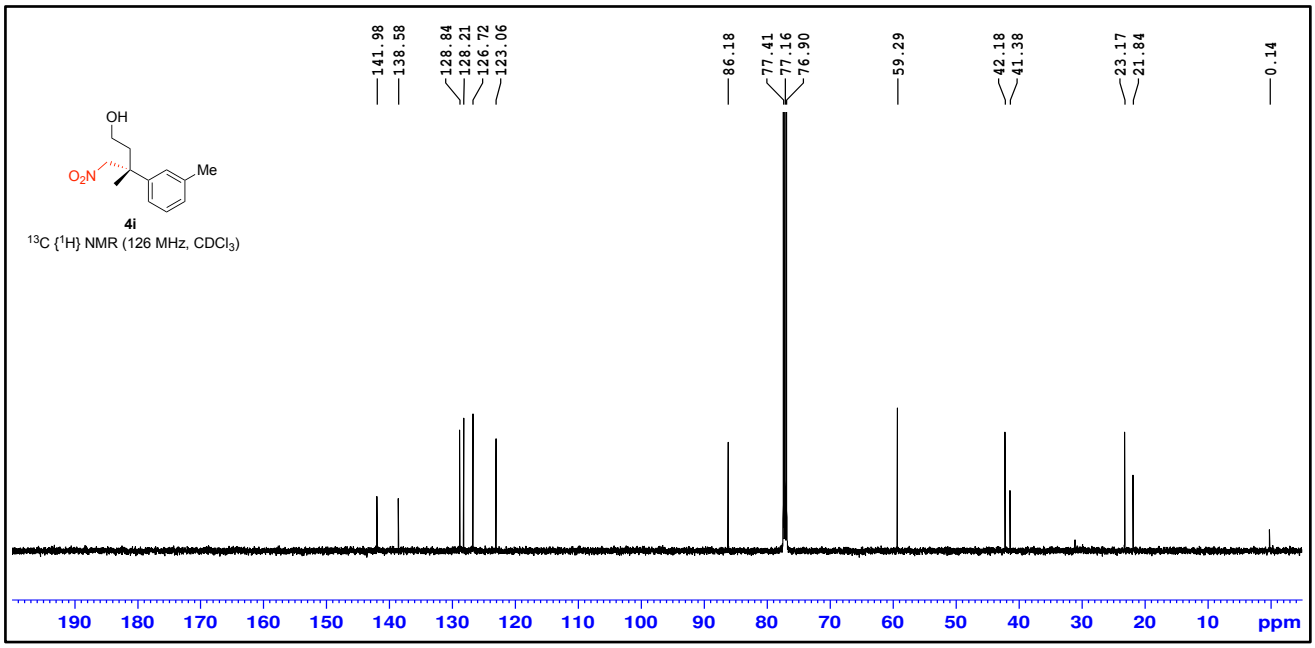


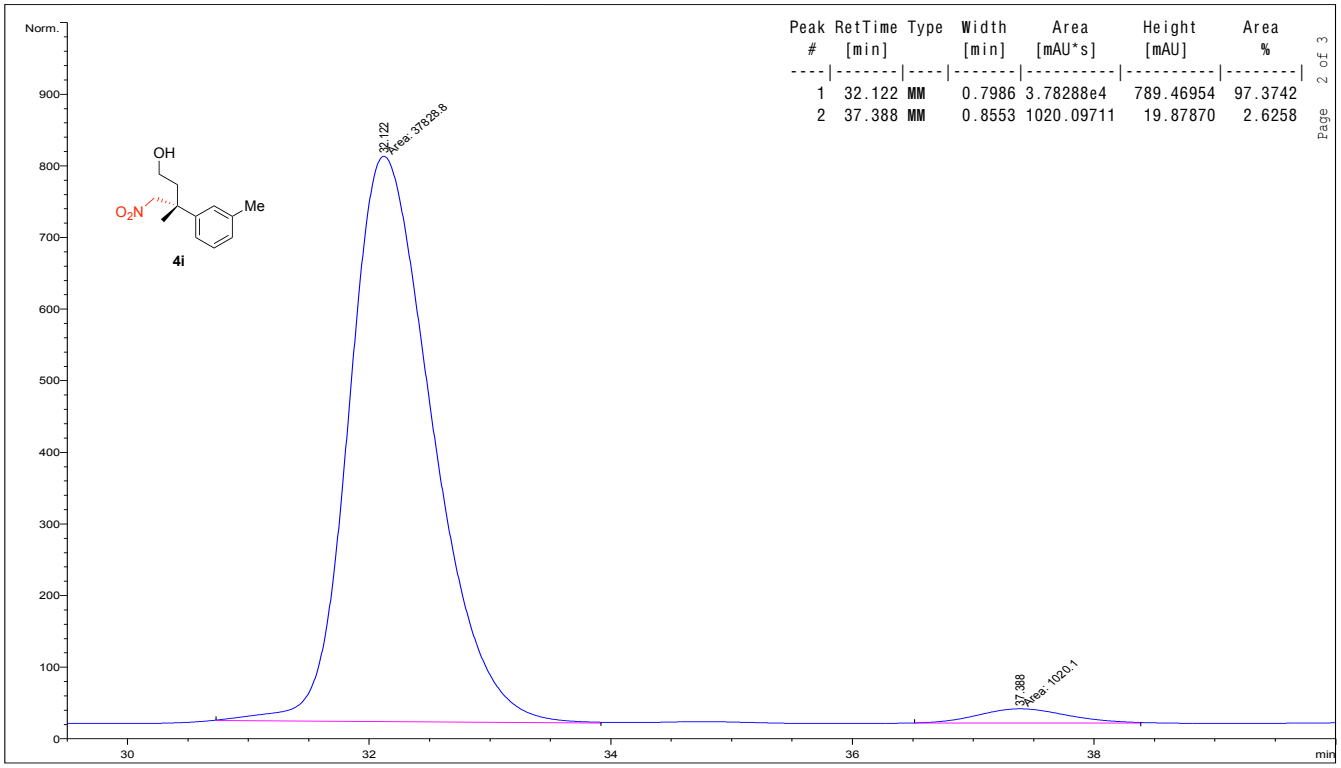

Norm.
OH
O2N
OMe
4h
11.955
Area: 625.941
14.926
Area: 21527.2
Peak RetTime Type Width Area Height Area
[min] [min] [mAU*s] [mAU] %
1 11.955 MM 0.3377 625.94061 30.89432 2.8255
2 14.926 MM 0.4515 2.15272e4 794.56848 97.1745
Page 2 of 3
min

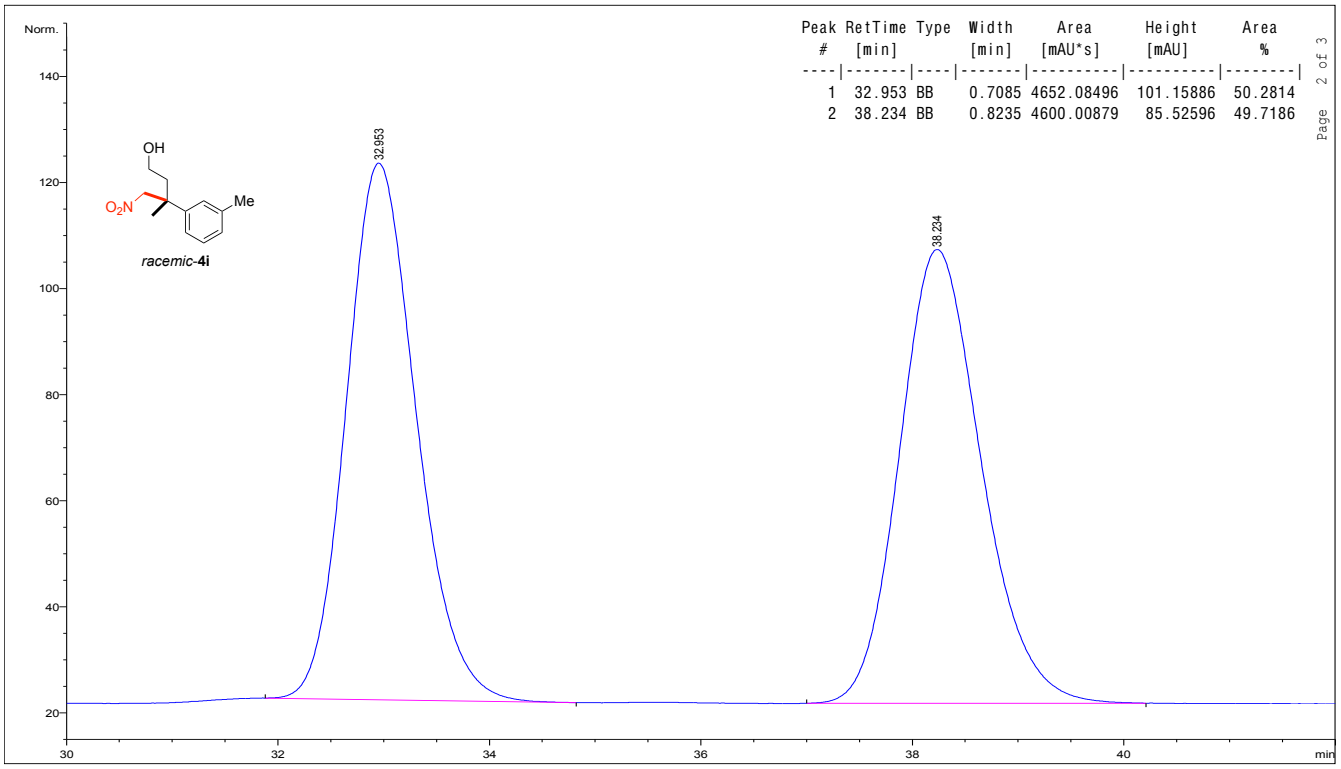

Norm.
OH
O2N
OMe
racemic-4h
11.978
15.024
Peak RetTime Type Width Area Height Area
[min] [min] [mAU*s] [mAU] %
1 11.978 BB 0.3148 4821.24219 237.57390 48.9932
2 15.024 BBA 0.4183 5019.38965 186.33978 51.0068
Page 2 of 3
min

(*R*)-3-methyl-4-nitro-3-(*m*-tolyl)butan-1-ol (4i)

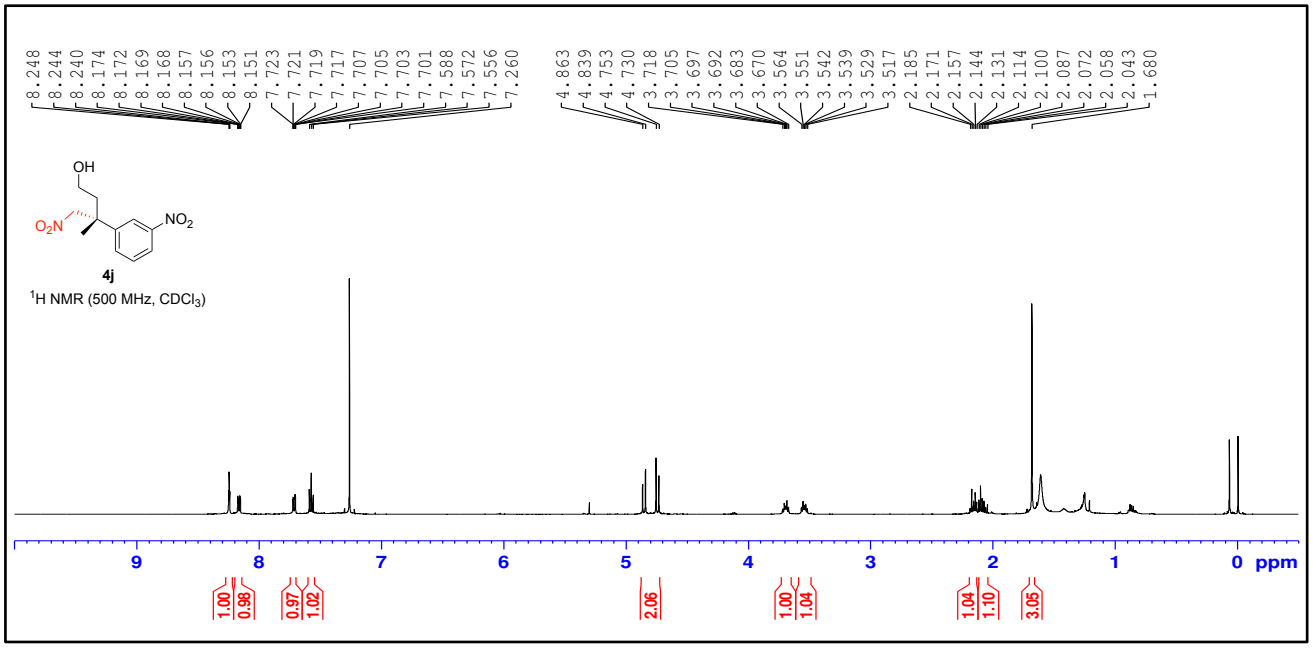


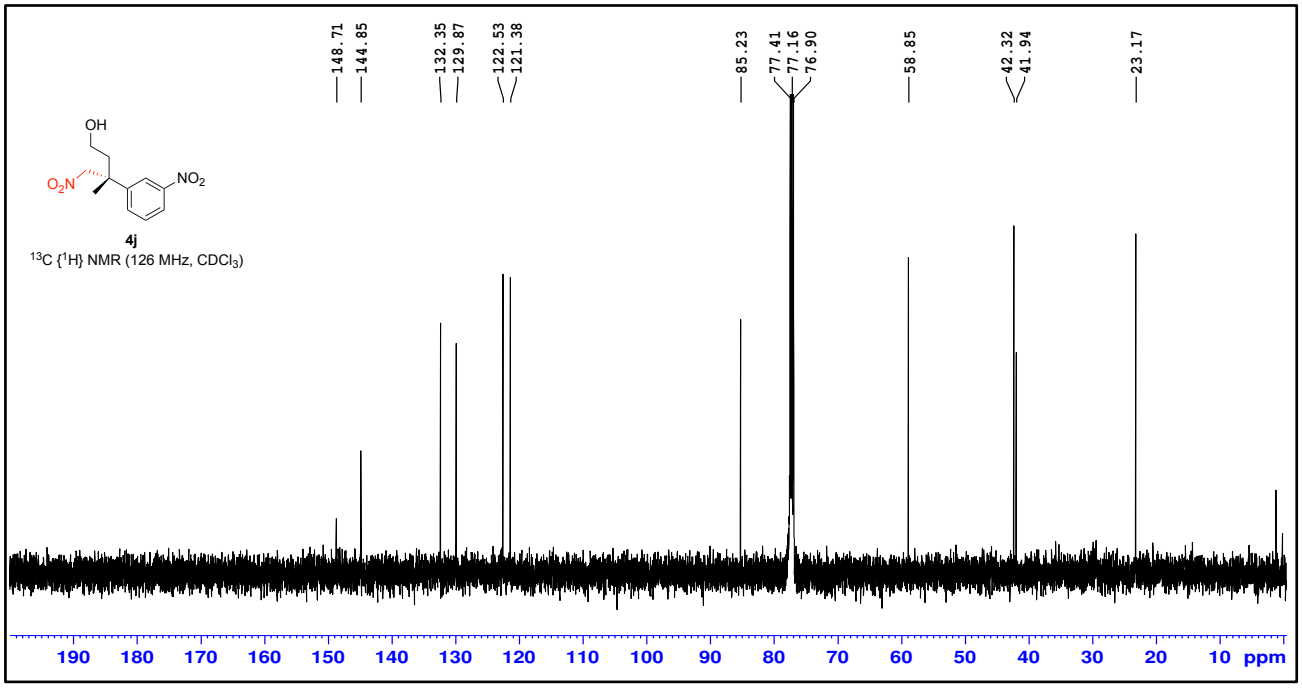


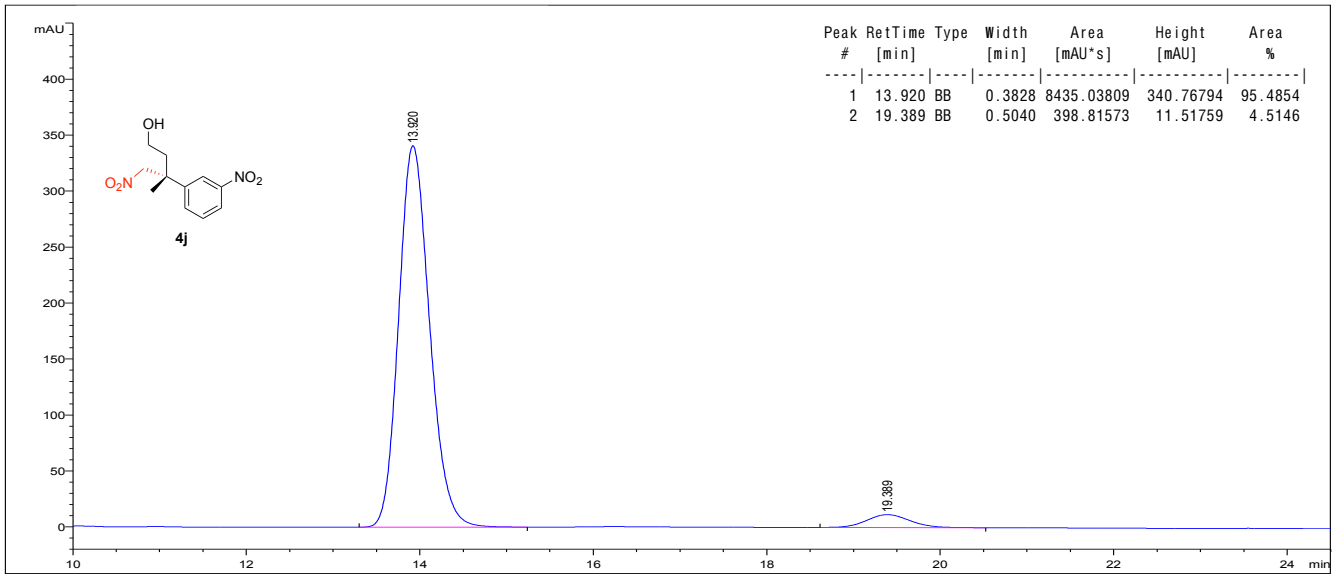

Norm.
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 32.122 | MM | 0.7986 | 3.78288e4 | 789.46954 | 97.3742
2 | 37.388 | MM | 0.8553 | 1020.09711 | 19.87870 | 2.6258
Page 2 of 3
32.122
Area: 37828.8
37.388
Area: 1020.1
OH
O2N
Me
4i
min


Norm.
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 32.953 | BB | 0.7085 | 4652.08496 | 101.15886 | 50.2814
2 | 38.234 | BB | 0.8235 | 4600.00879 | 85.52596 | 49.7186
Page 2 of 3
32.953
38.234
OH
O2N
Me
racemic-4i
min

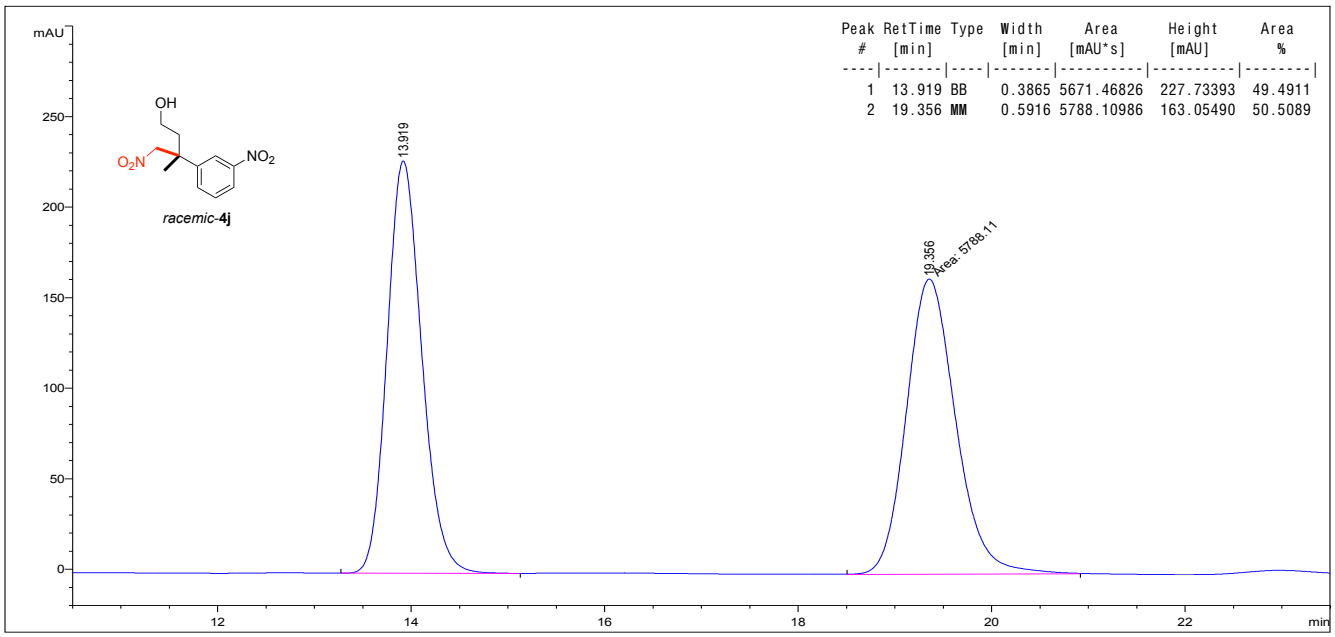
(R)-3-methyl-4-nitro-3-(3-nitrophenyl)butan-1-ol (4j)





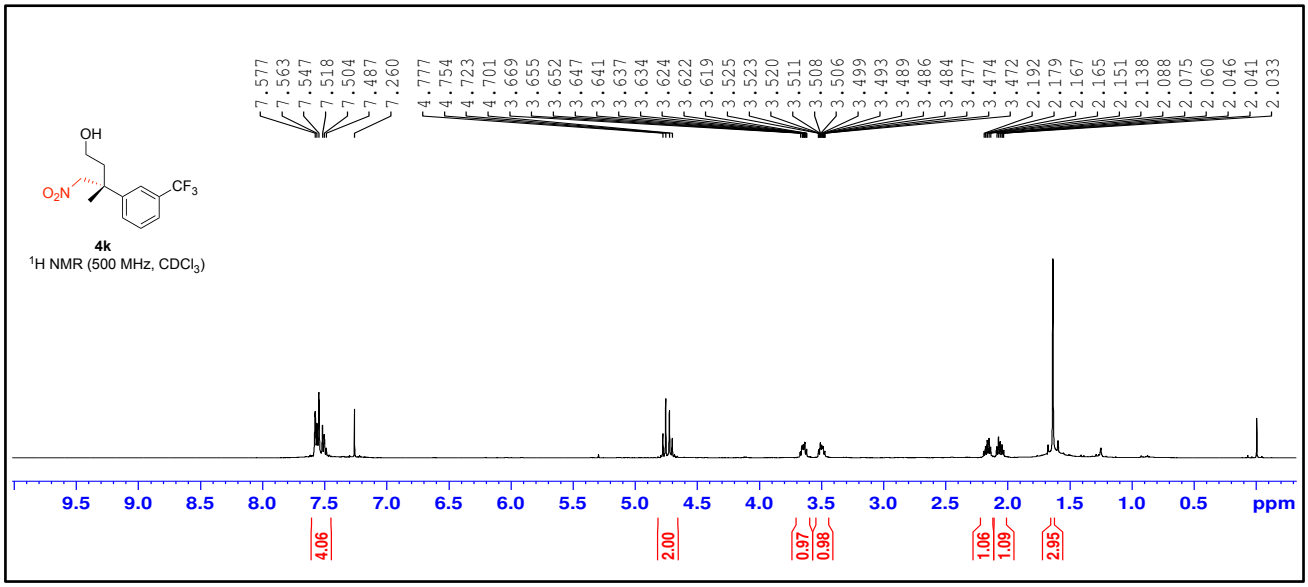


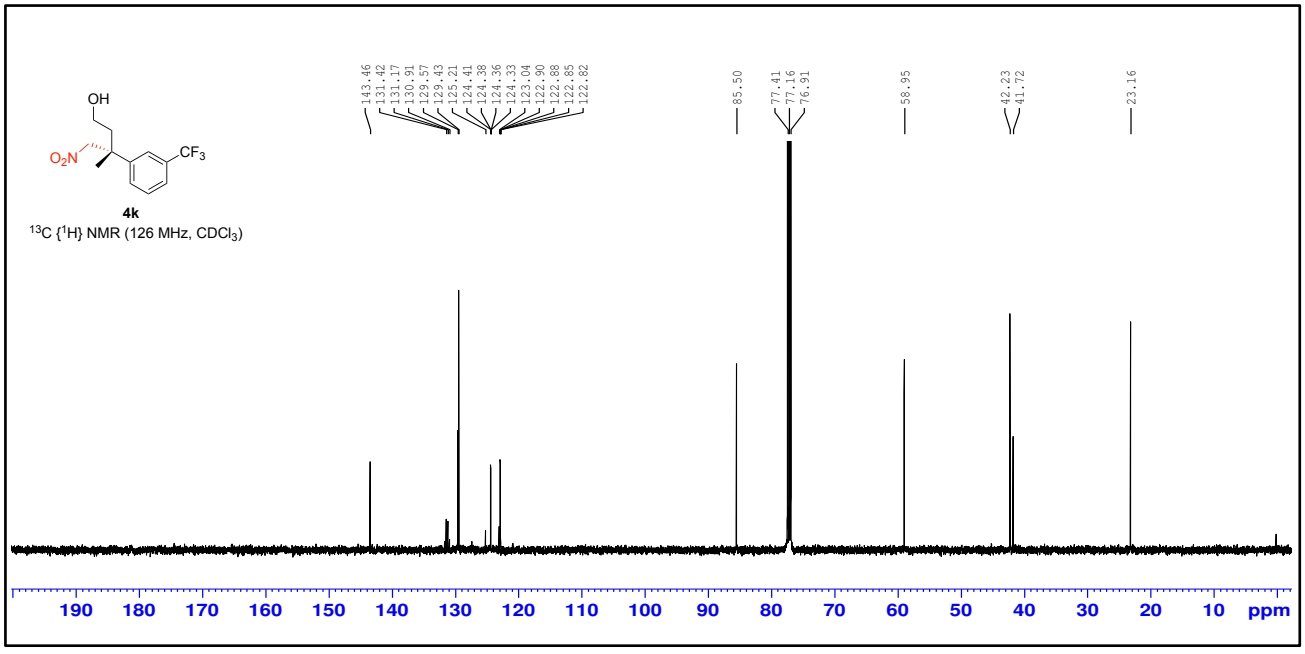
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.920	BB	0.3828	8435.03809	340.76794	95.4854
2	19.389	BB	0.5040	398.81573	11.51759	4.5146

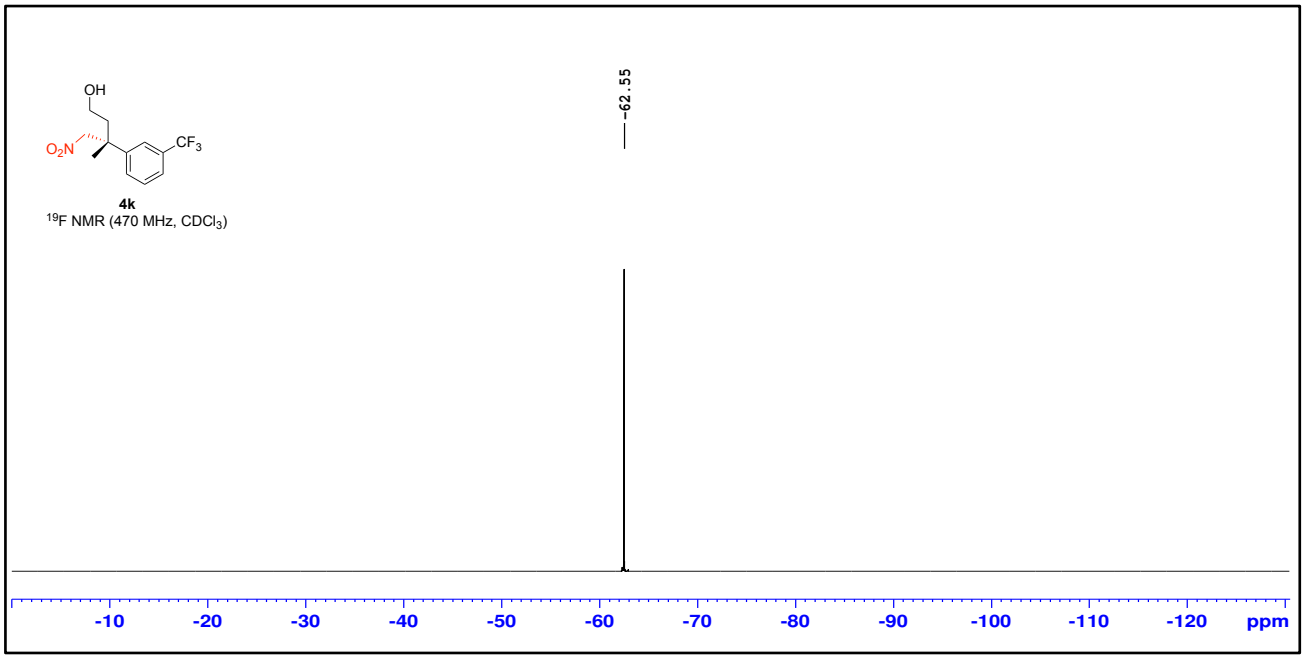


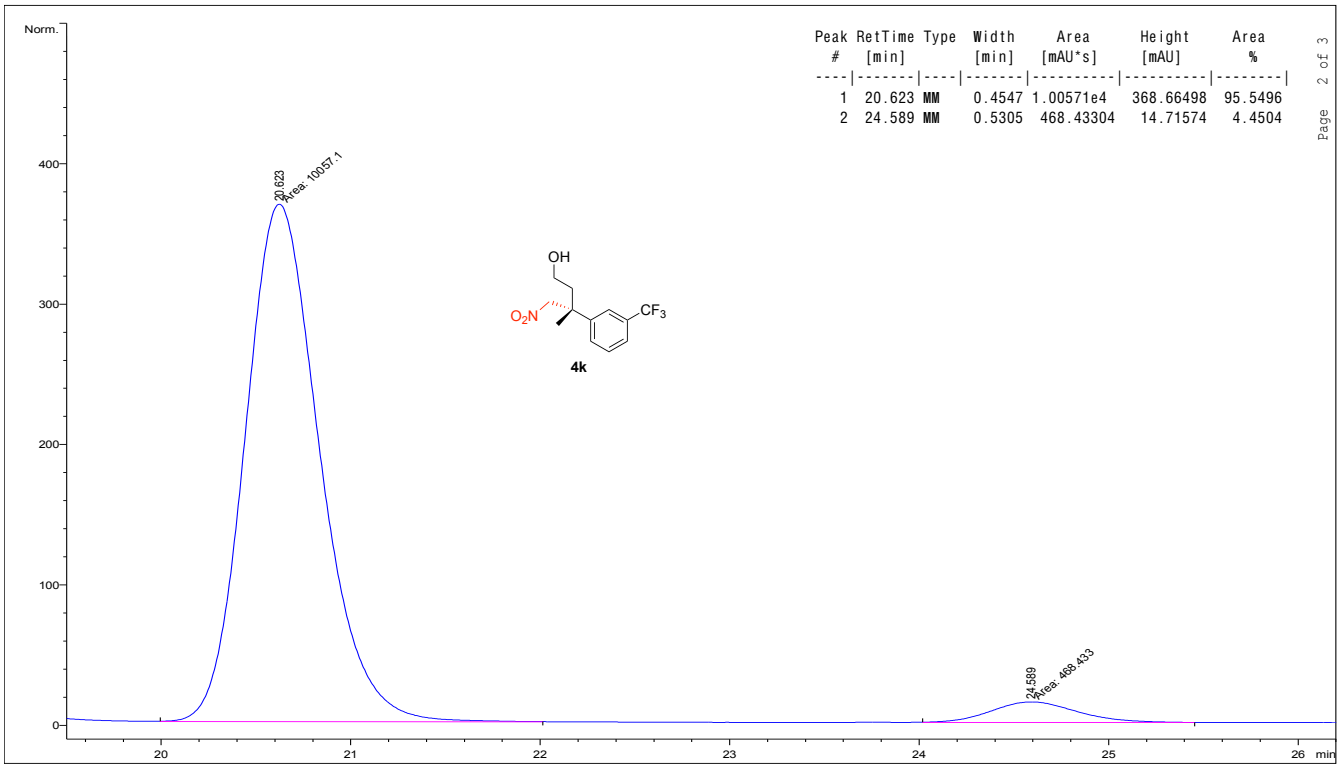
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.919	BB	0.3865	5671.46826	227.73393	49.4911
2	19.356	MM	0.5916	5788.10986	163.05490	50.5089

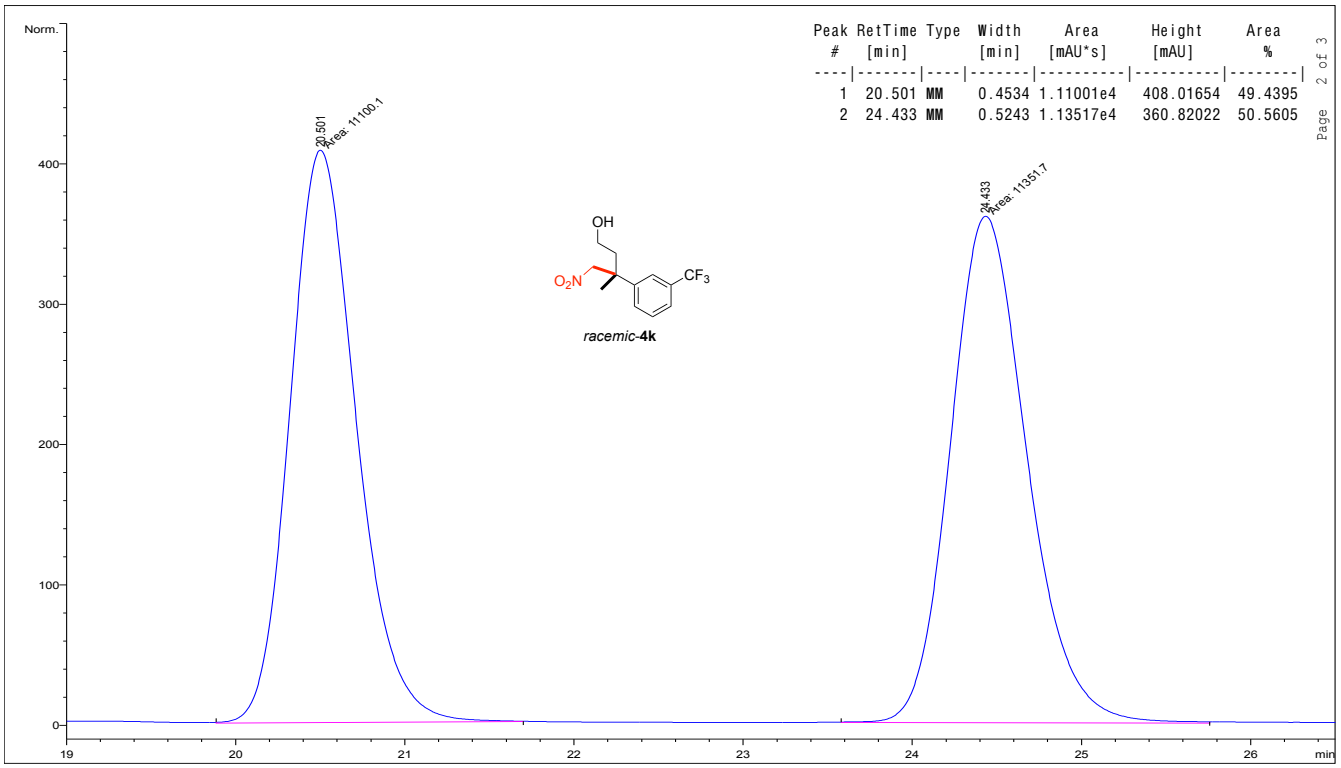
(*R*)-3-methyl-4-nitro-3-(3-(trifluoromethyl)phenyl)butan-1-ol (4k)



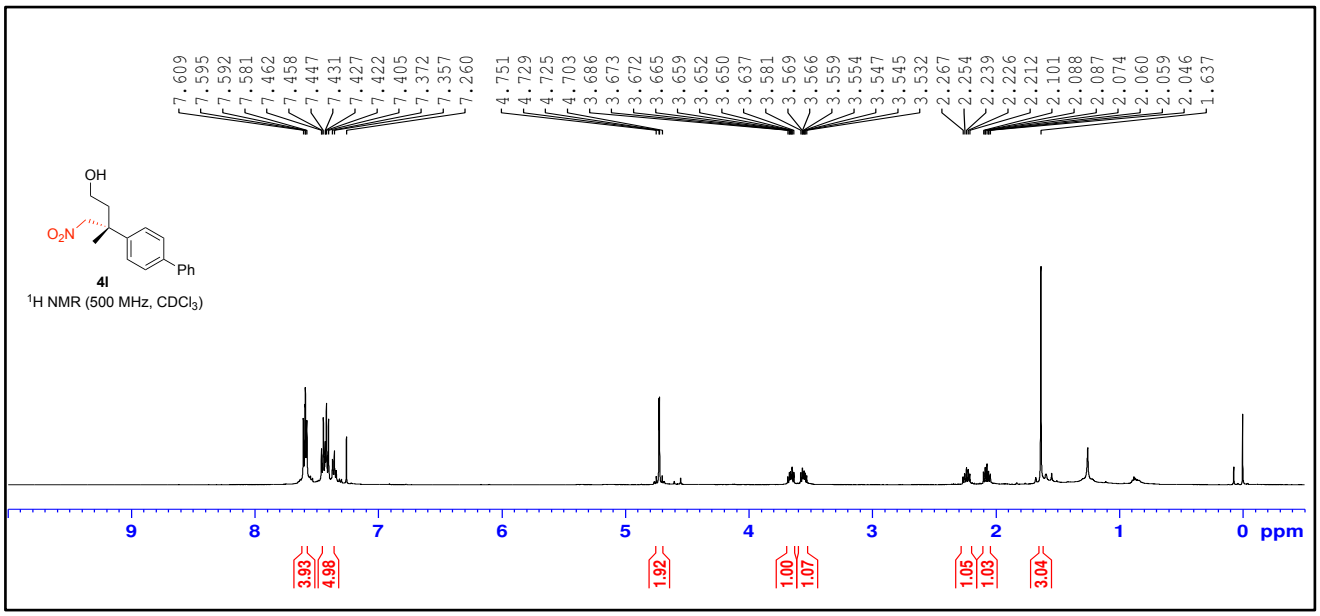


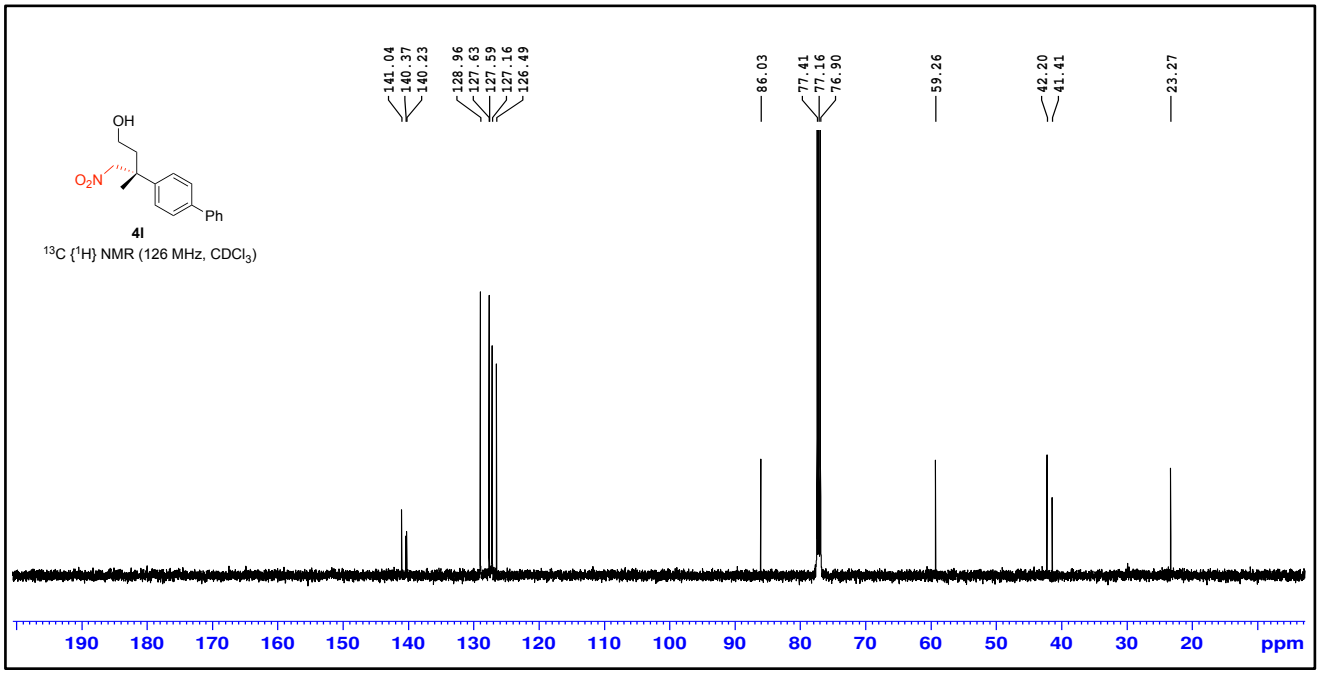

OH
O2N
CF3
4k
19F NMR (470 MHz, CDCl3)
-62.55
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
ppm

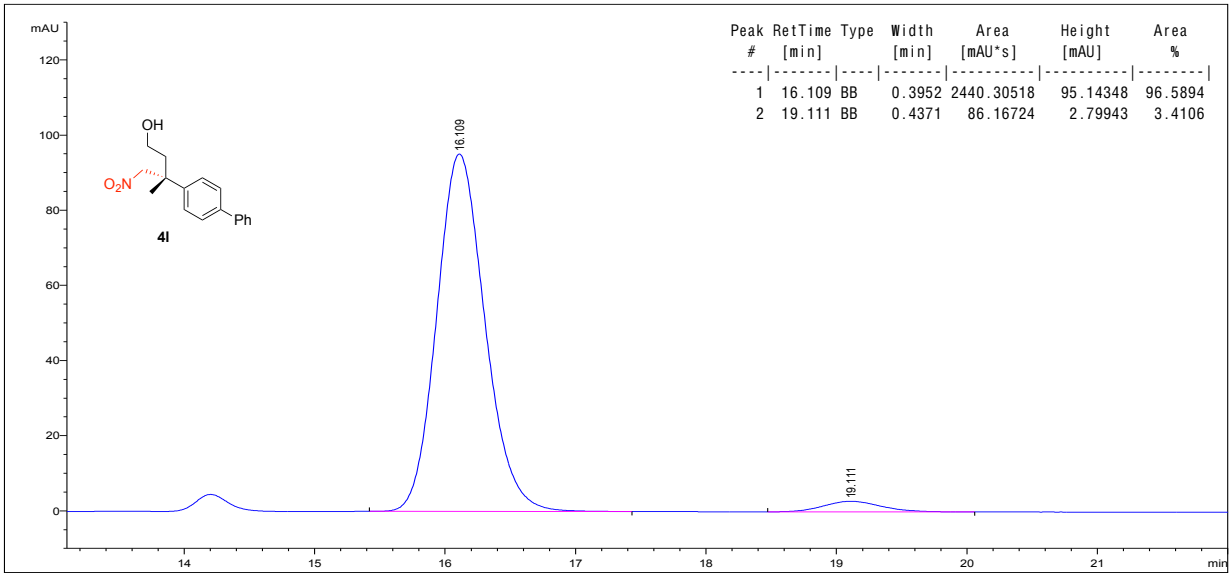

Norm.
Peak RetTime Type Width Area Height Area
[min] [min] [mAU*s] [mAU] %
1 20.623 MM 0.4547 1.00571e4 368.66498 95.5496
2 24.589 MM 0.5305 468.43304 14.71574 4.4504
Page 2 of 3
20.623
Area: 10057.1
24.589
Area: 468.433
OH
O_2N
CF_3
4k
min


Norm.
Peak RetTime Type Width Area Height Area
[min] [min] [mAU*s] [mAU] %
1 20.501 MM 0.4534 1.11001e4 408.01654 49.4395
2 24.433 MM 0.5243 1.13517e4 360.82022 50.5605
Page 2 of 3
20.501
Area: 11100.1
24.433
Area: 11351.7
OH
O_2N
CF_3
racemic-4k
min

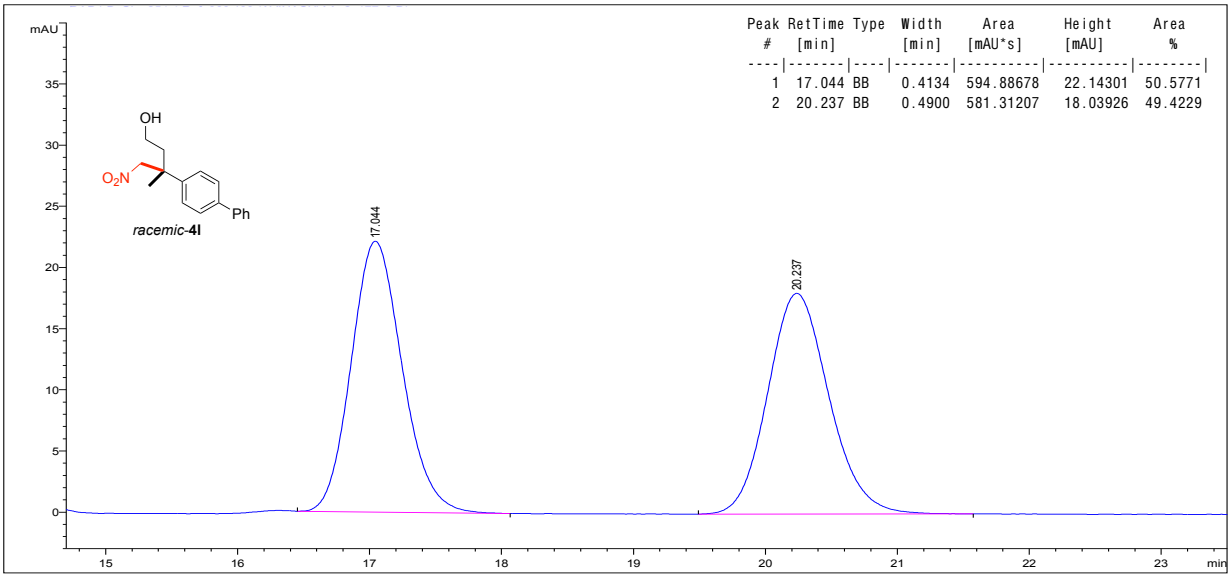
***(R)*-3-([1,1'-biphenyl]-4-yl)-3-methyl-4-nitrobutan-1-ol (4l)**





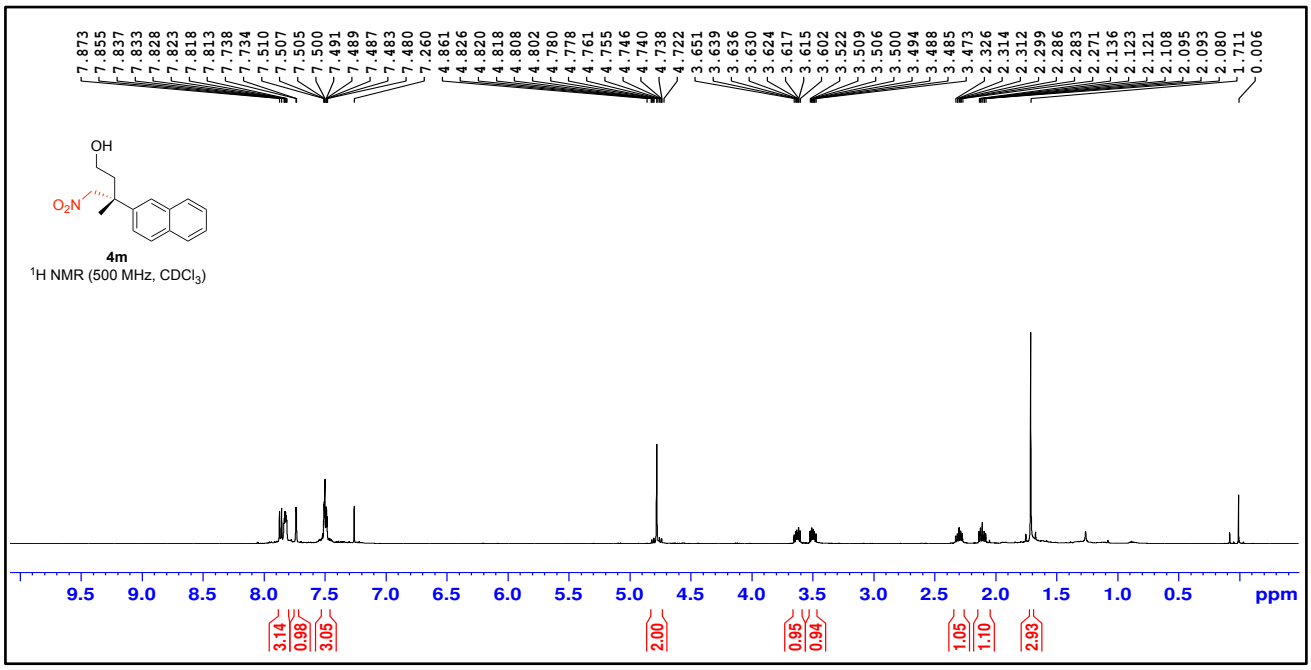


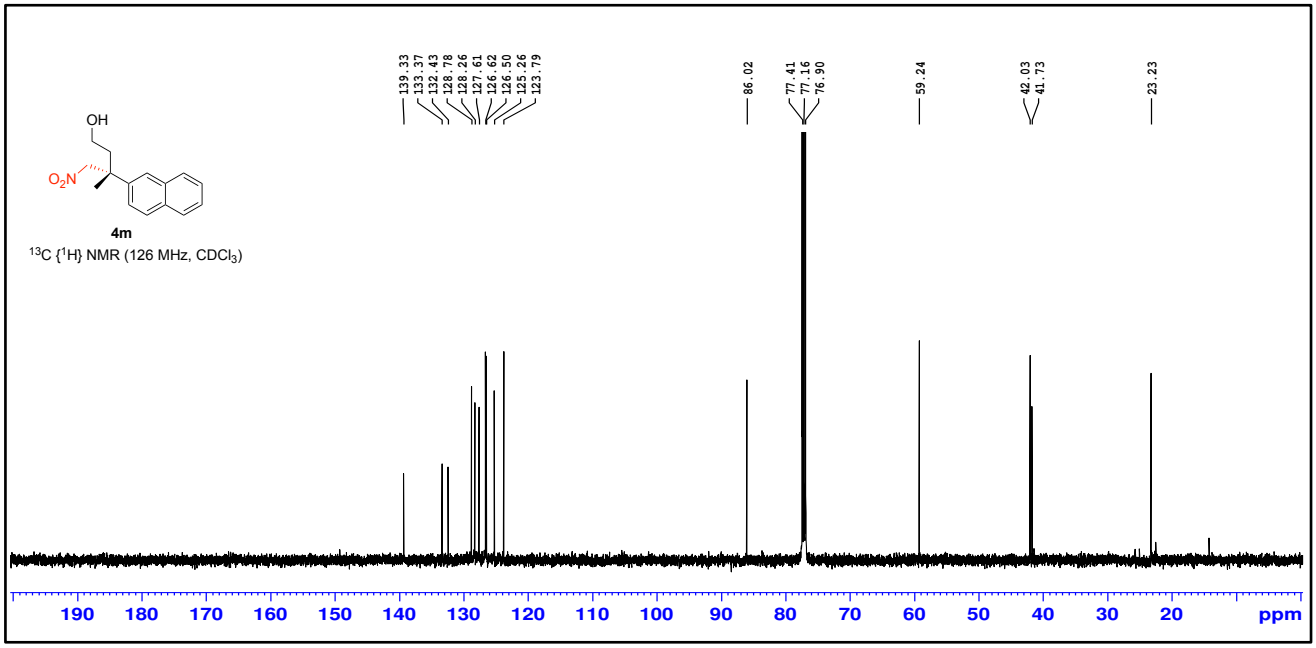
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.109	BB	0.3952	2440.30518	95.14348	96.5894
2	19.111	BB	0.4371	86.16724	2.79943	3.4106

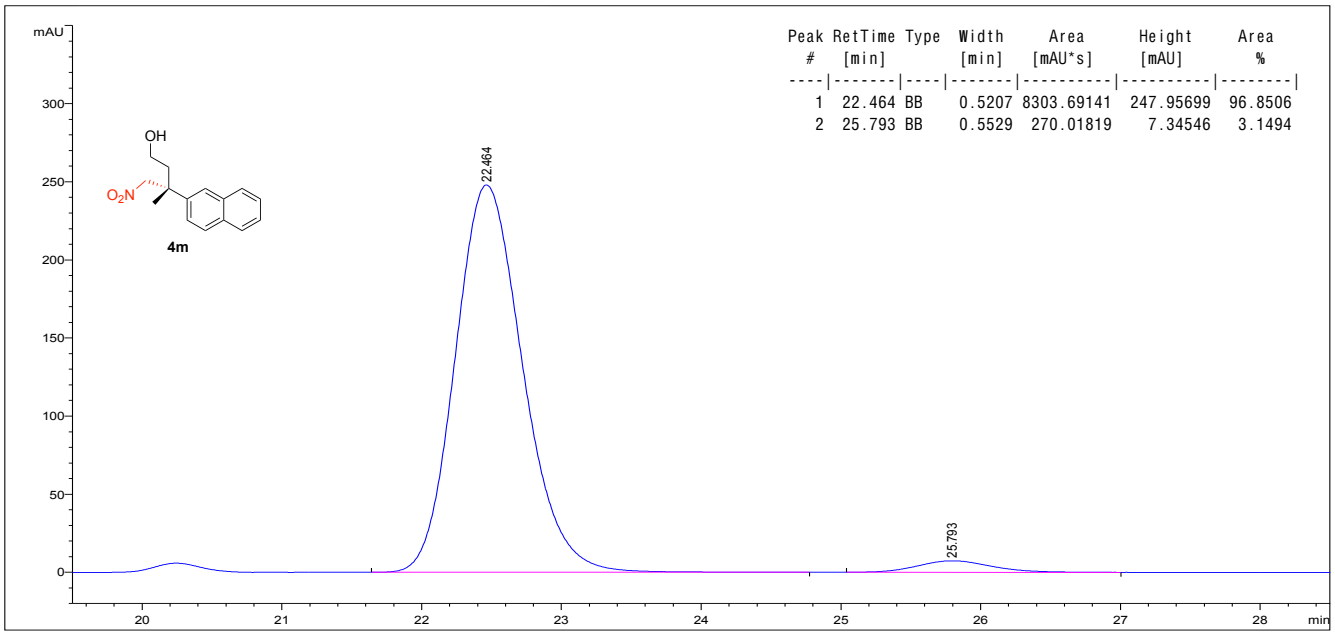


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.044	BB	0.4134	594.88678	22.14301	50.5771
2	20.237	BB	0.4900	581.31207	18.03926	49.4229

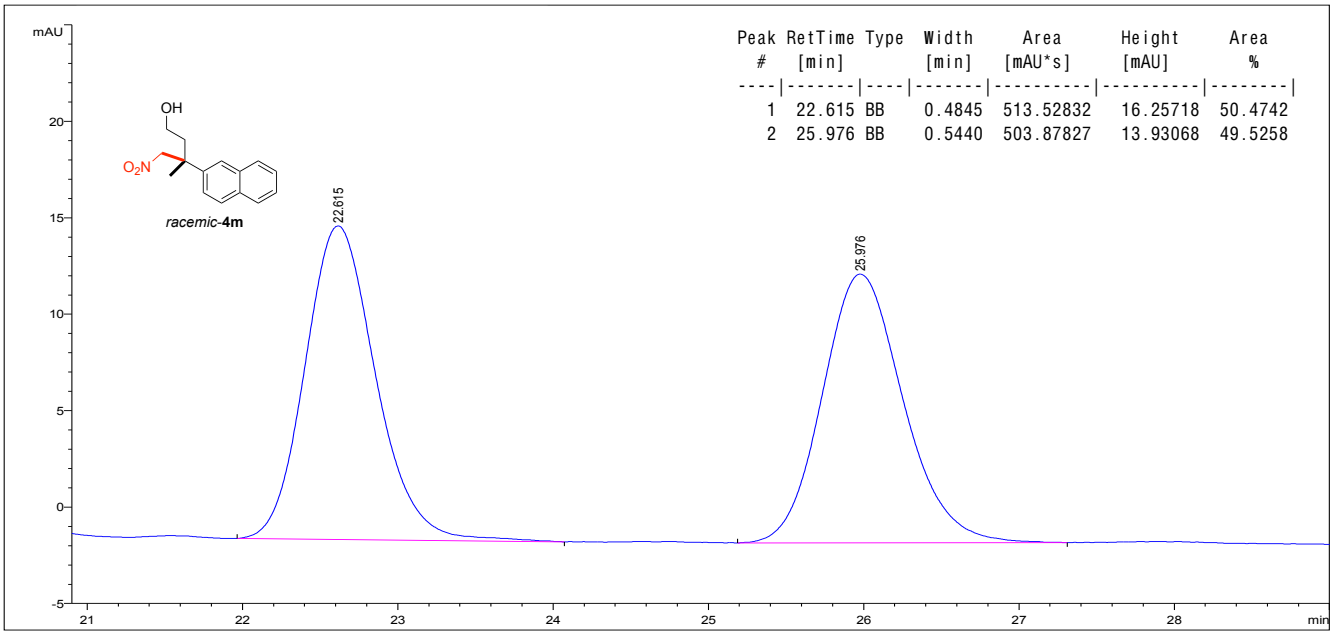
(R)-3-methyl-3-(naphthalen-2-yl)-4-nitrobutan-1-ol (4m)





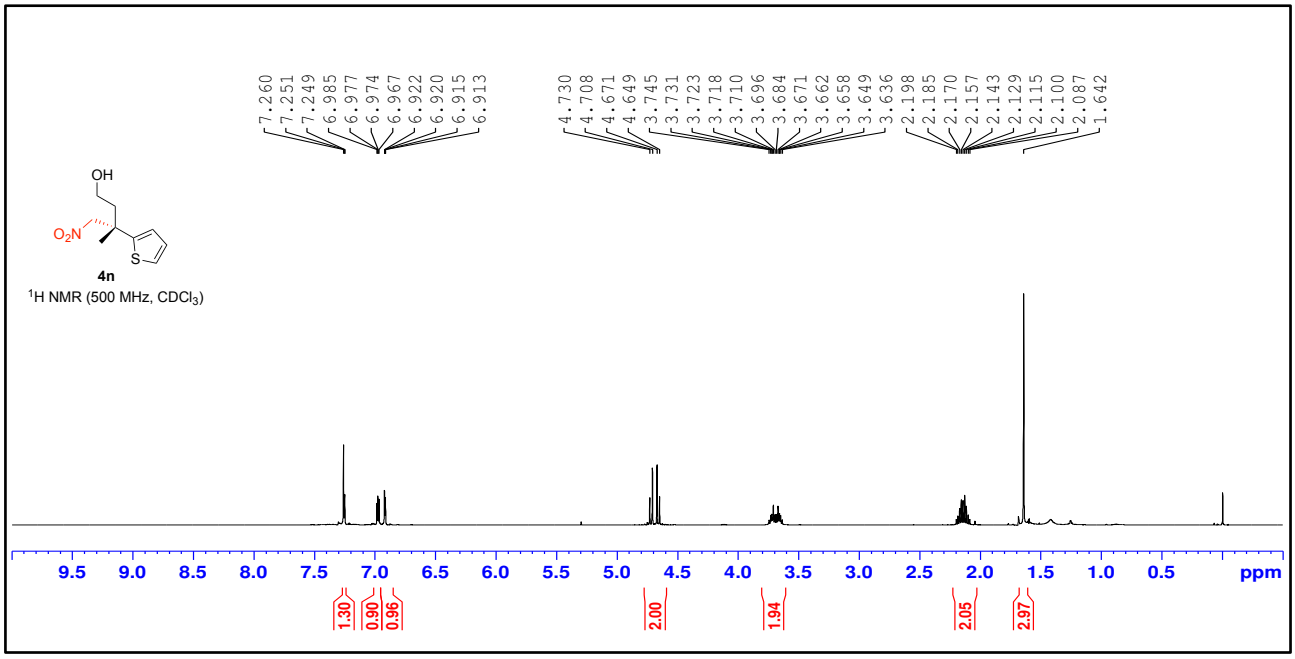


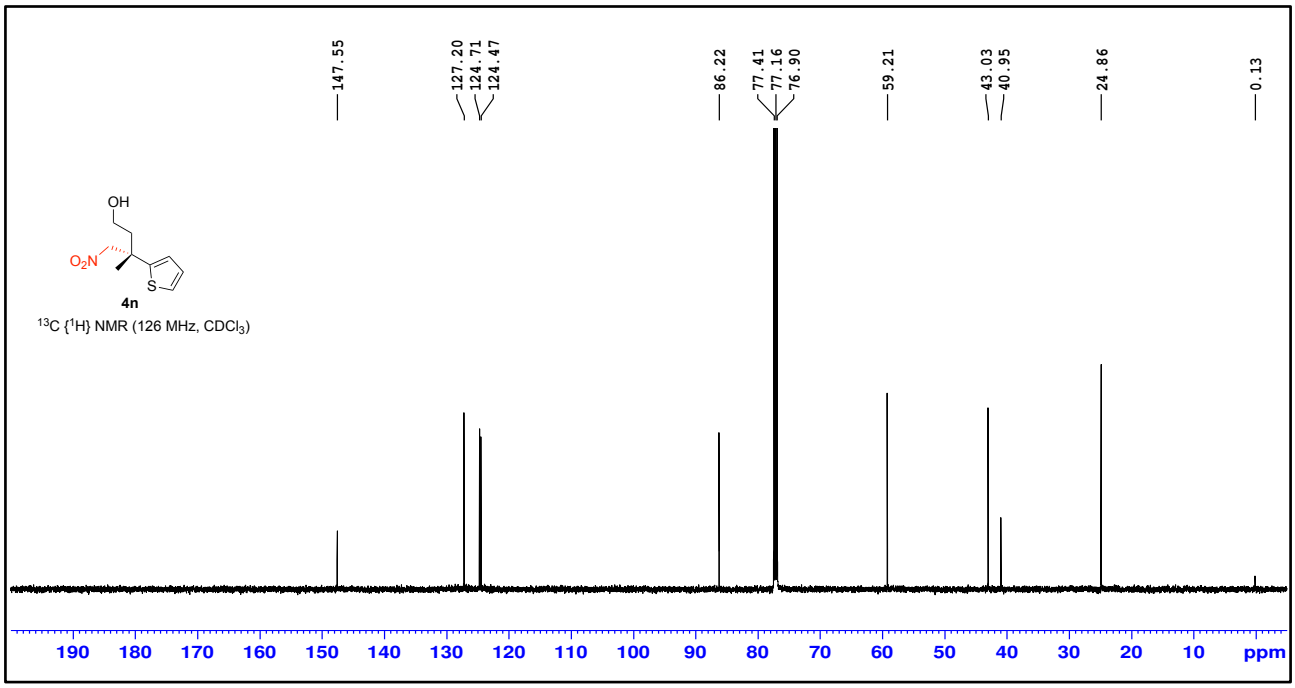
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.464	BB	0.5207	8303.69141	247.95699	96.8506
2	25.793	BB	0.5529	270.01819	7.34546	3.1494

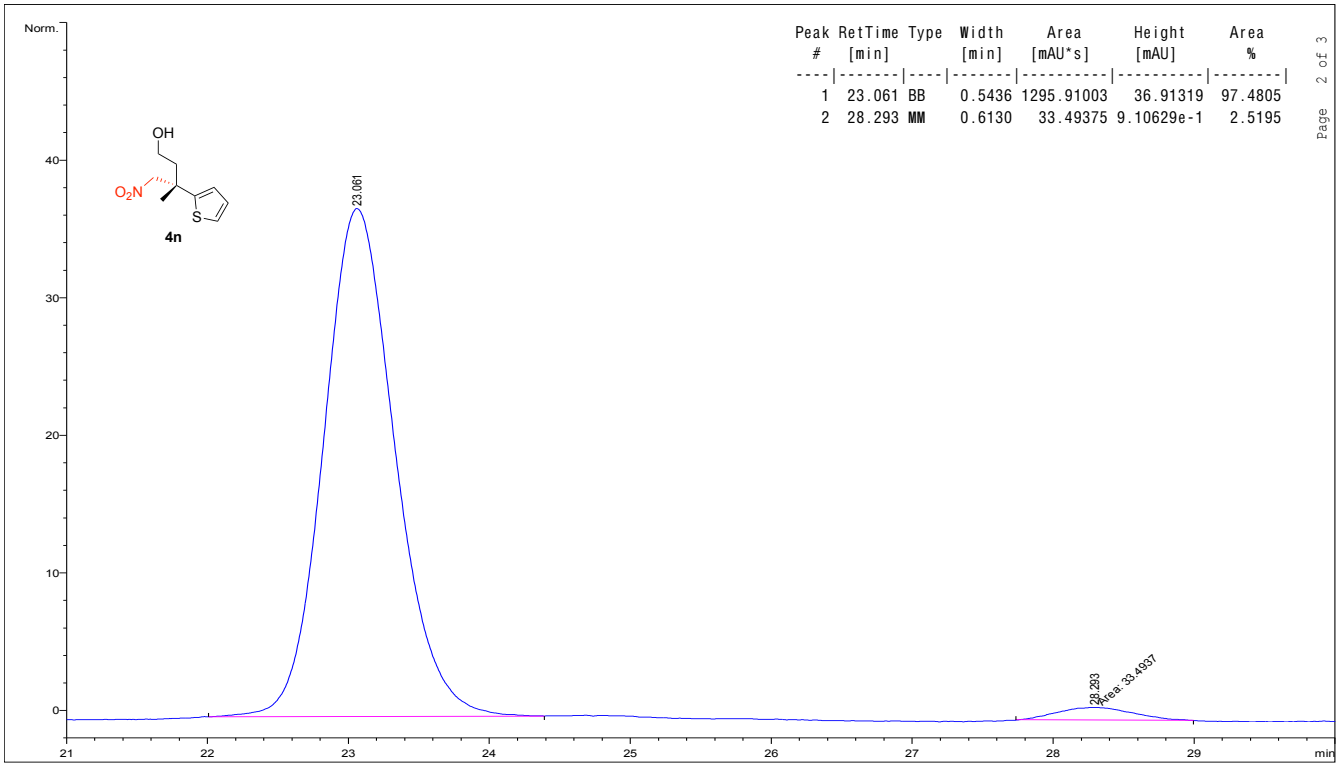


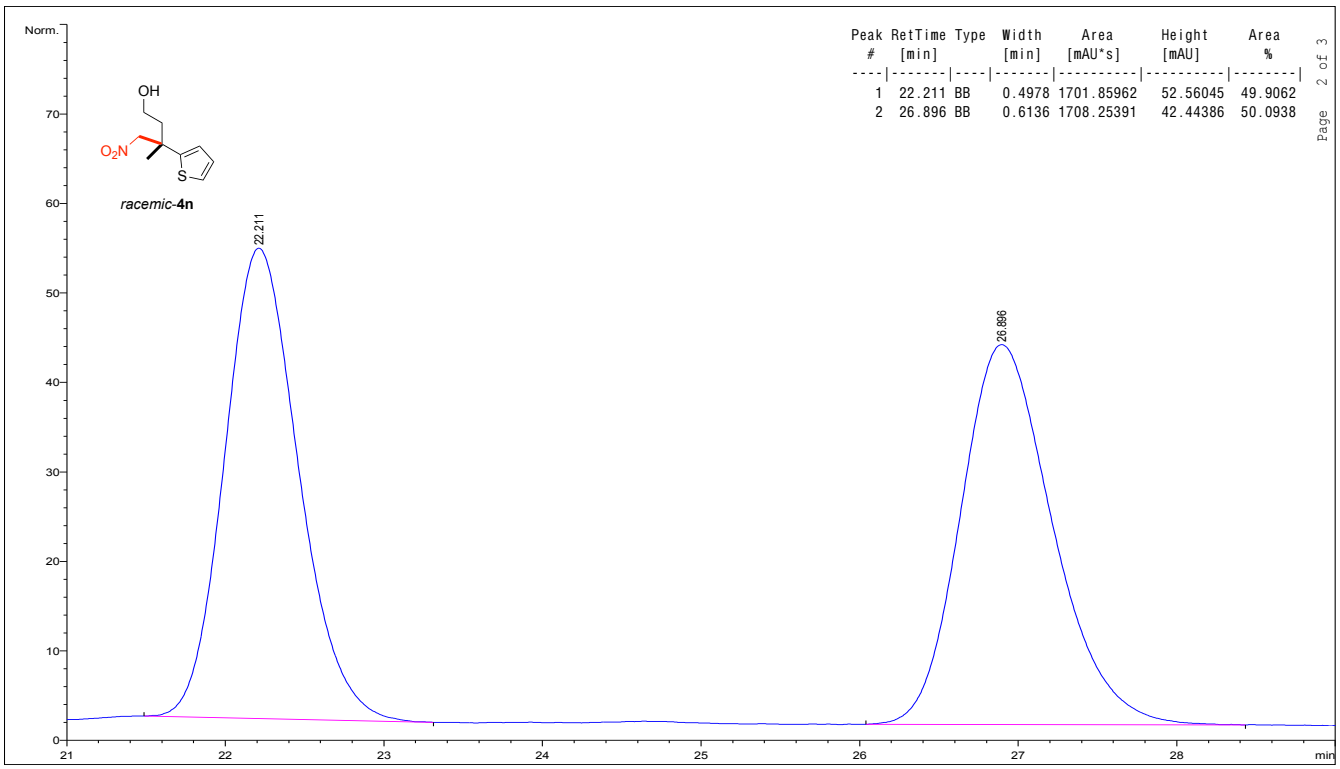
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.615	BB	0.4845	513.52832	16.25718	50.4742
2	25.976	BB	0.5440	503.87827	13.93068	49.5258

(*S*)-3-methyl-4-nitro-3-(thiophen-2-yl)butan-1-ol (4n)

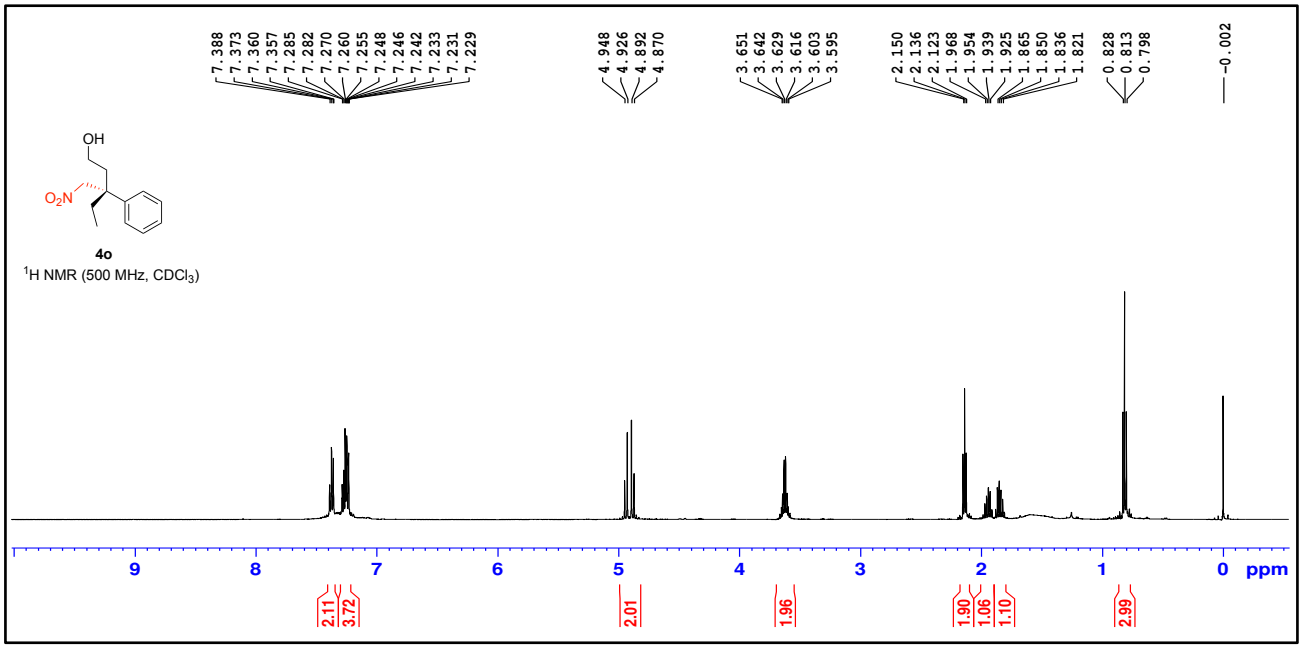


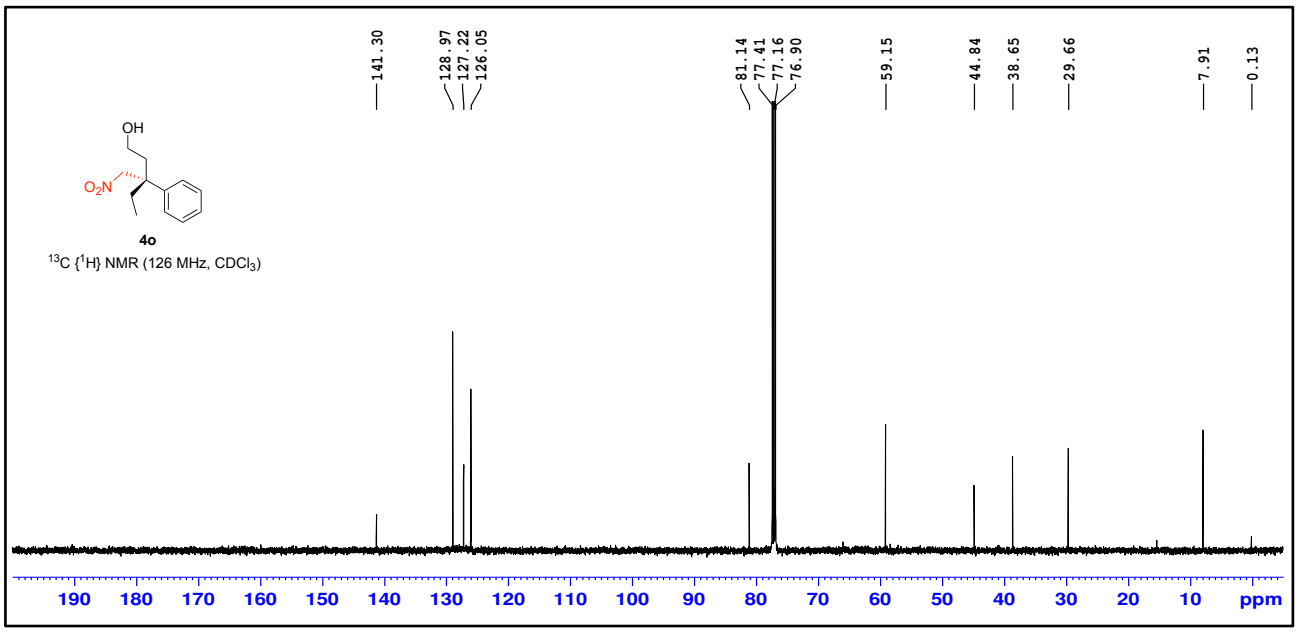


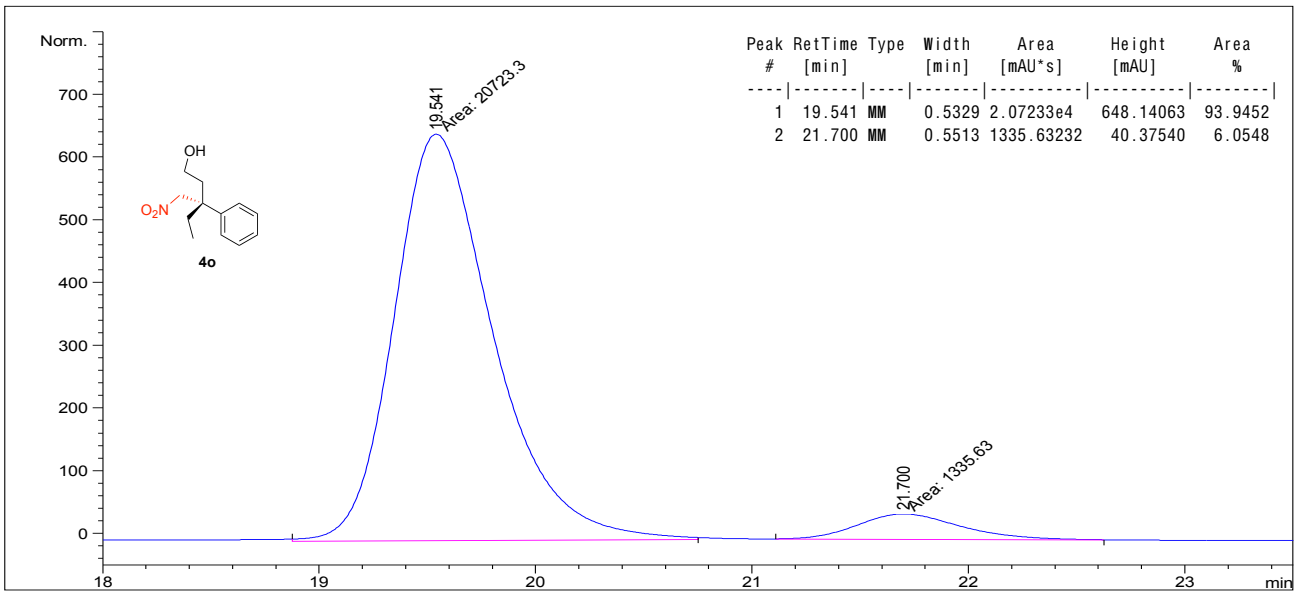

Norm.
OH
O_2N
S
4n
23.061
28.293
Area: 33.4937
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 23.061 | BB | 0.5436 | 1295.91003 | 36.91319 | 97.4805
2 | 28.293 | MM | 0.6130 | 33.49375 | 9.10629e-1 | 2.5195
Page 2 of 3
min


Norm.
OH
O_2N
S
racemic-4n
22.211
26.896
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 22.211 | BB | 0.4978 | 1701.85962 | 52.56045 | 49.9062
2 | 26.896 | BB | 0.6136 | 1708.25391 | 42.44386 | 50.0938
Page 2 of 3
min

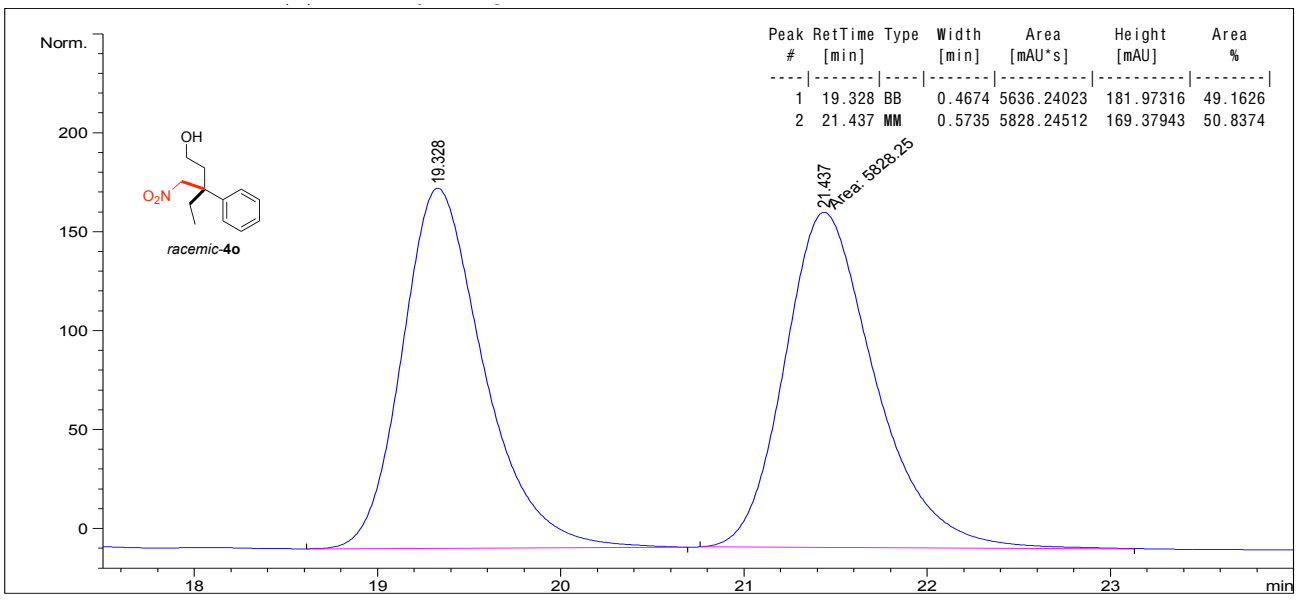
(R)-3-(nitromethyl)-3-phenylpentan-1-ol (4o)





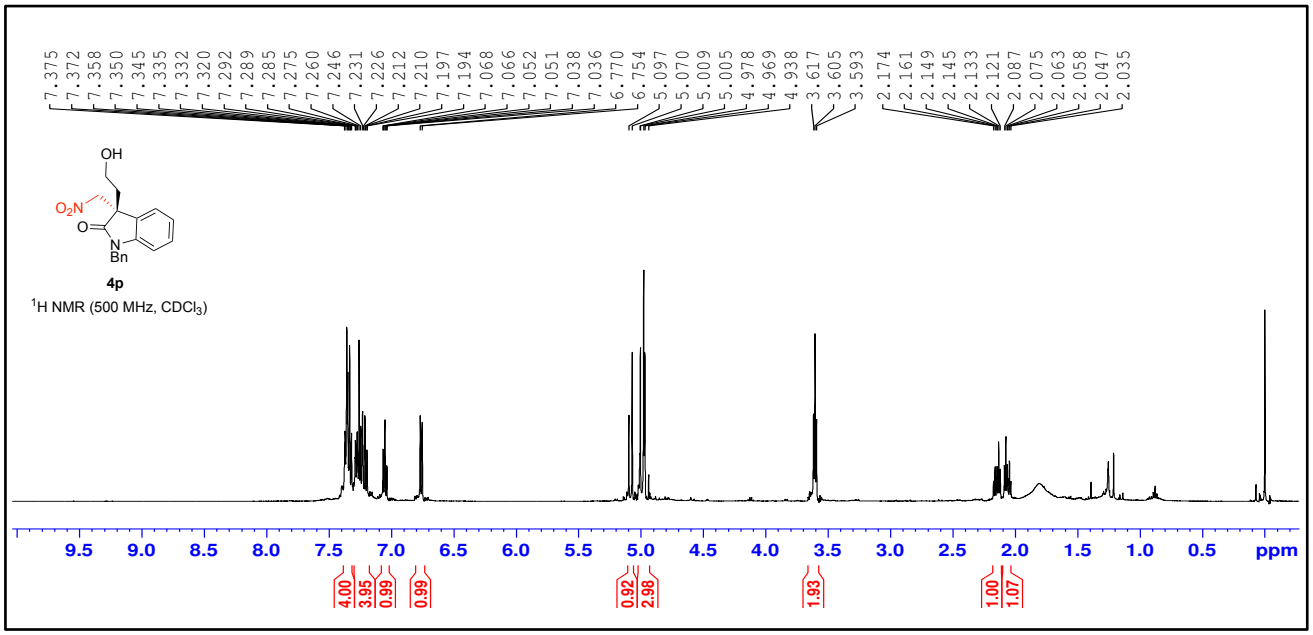


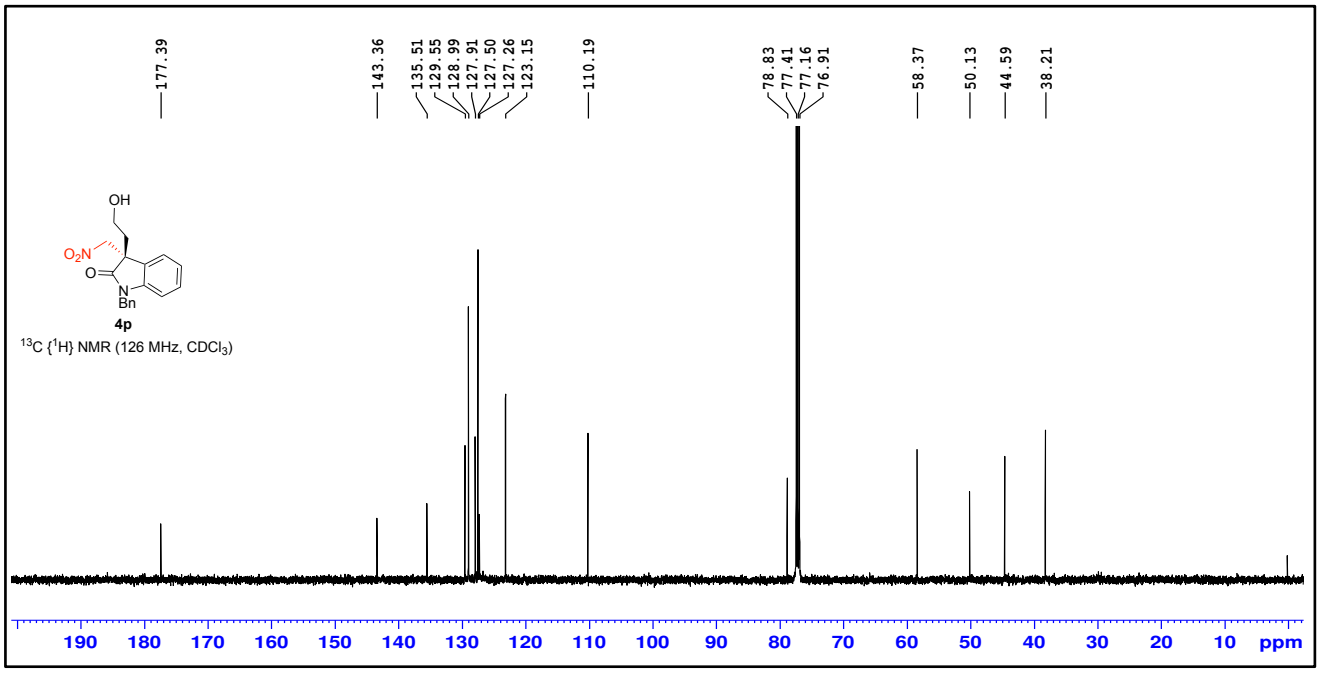
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.541	MM	0.5329	2.07233e4	648.14063	93.9452
2	21.700	MM	0.5513	1335.63232	40.37540	6.0548

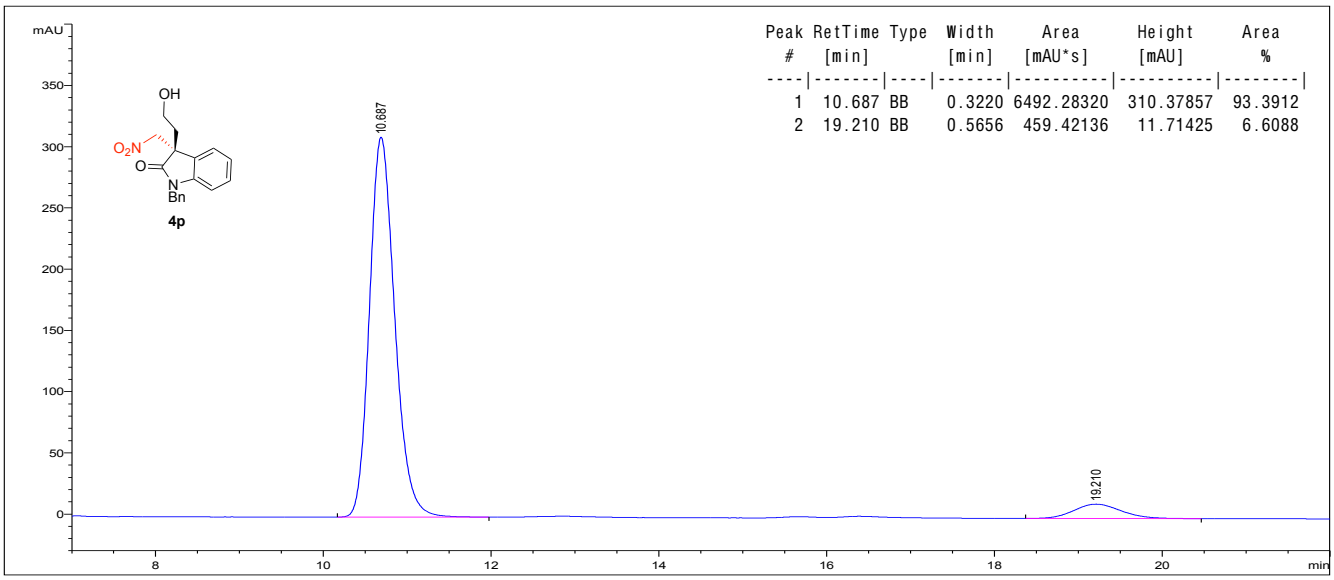


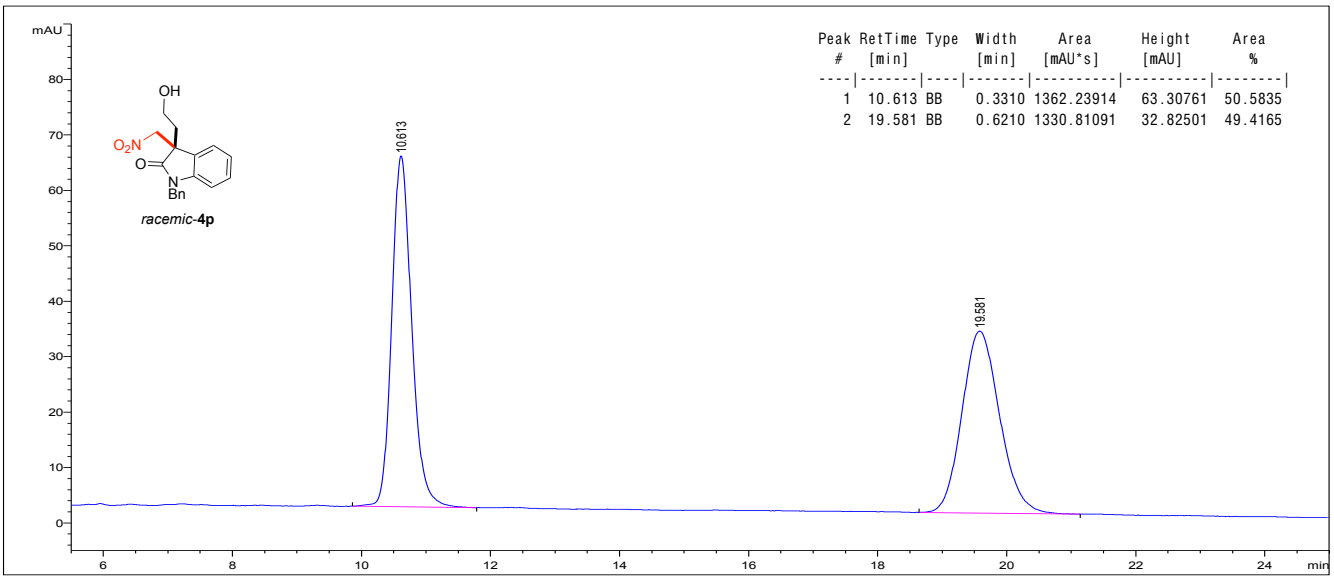
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.328	BB	0.4674	5636.24023	181.97316	49.1626
2	21.437	MM	0.5735	5828.24512	169.37943	50.8374

(S)-1-benzyl-3-(2-hydroxyethyl)-3-(nitromethyl)indolin-2-one (4p)

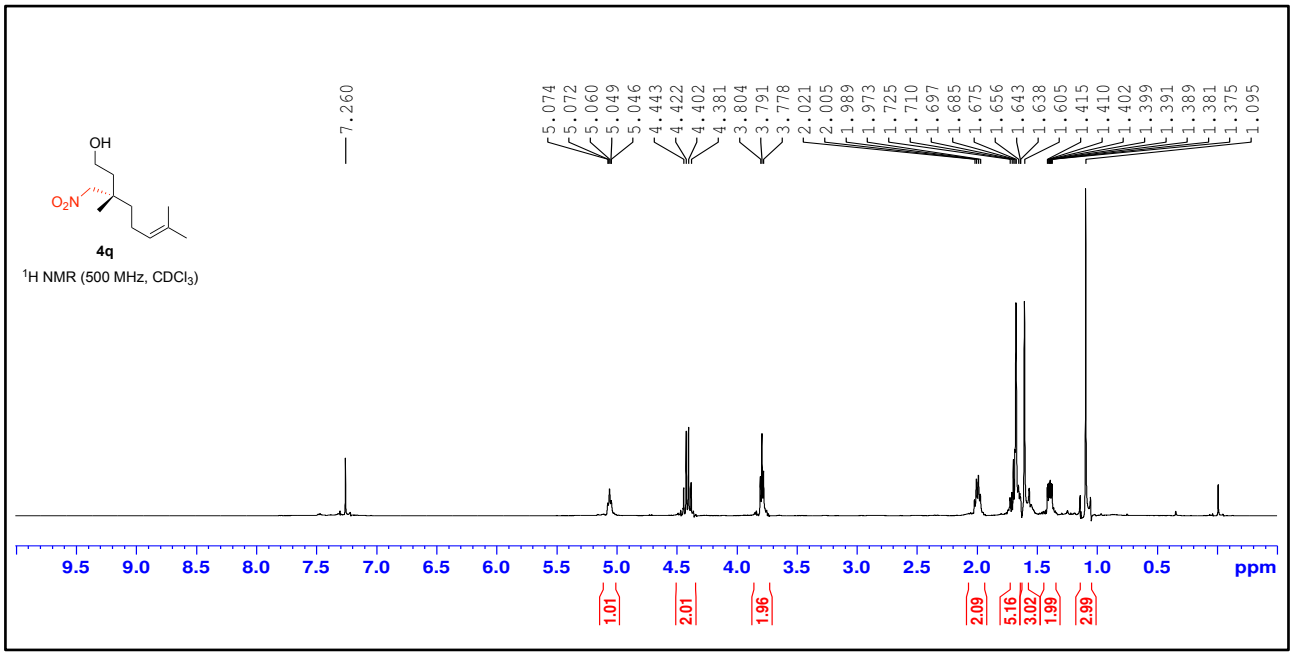


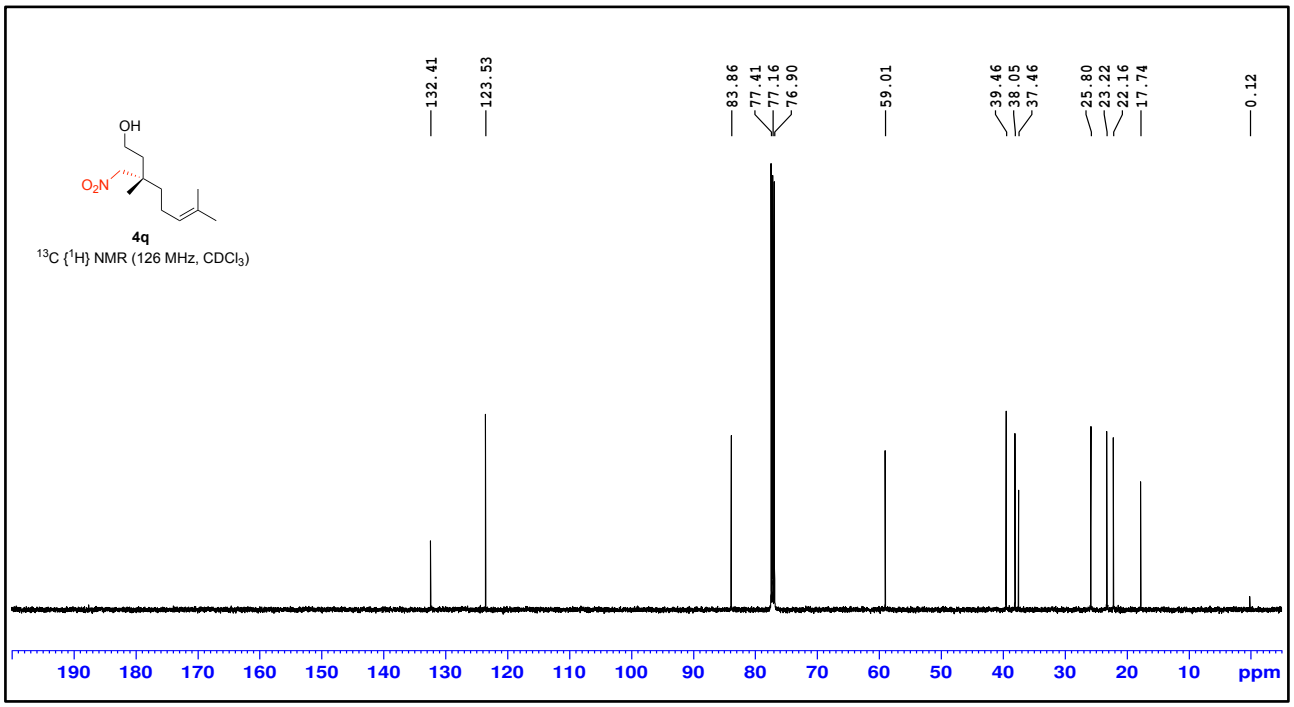


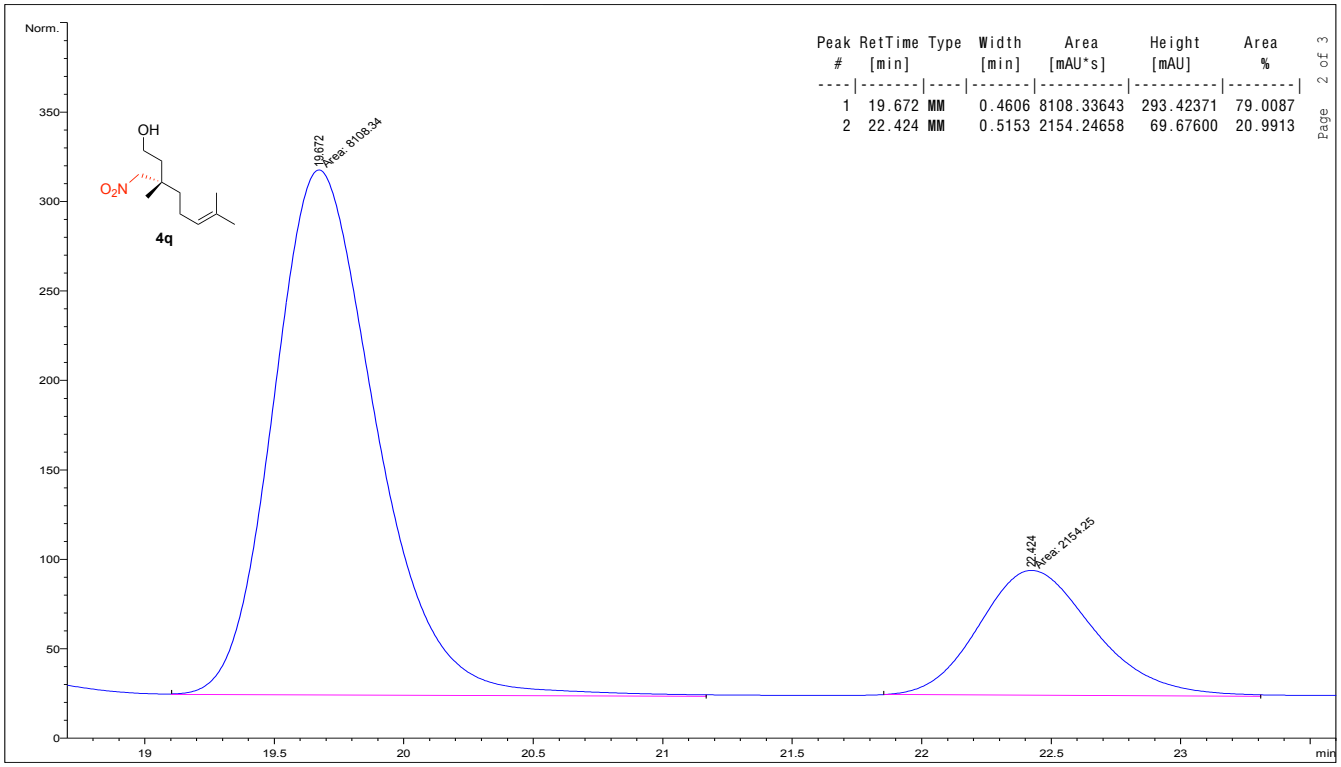

mAU
350
300
250
200
150
100
50
0
8
10
12
14
16
18
20
min
10.687
19.210
OH
O2N
O
N
Bn
4p
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 10.687 | BB | 0.3220 | 6492.28320 | 310.37857 | 93.3912
2 | 19.210 | BB | 0.5656 | 459.42136 | 11.71425 | 6.6088

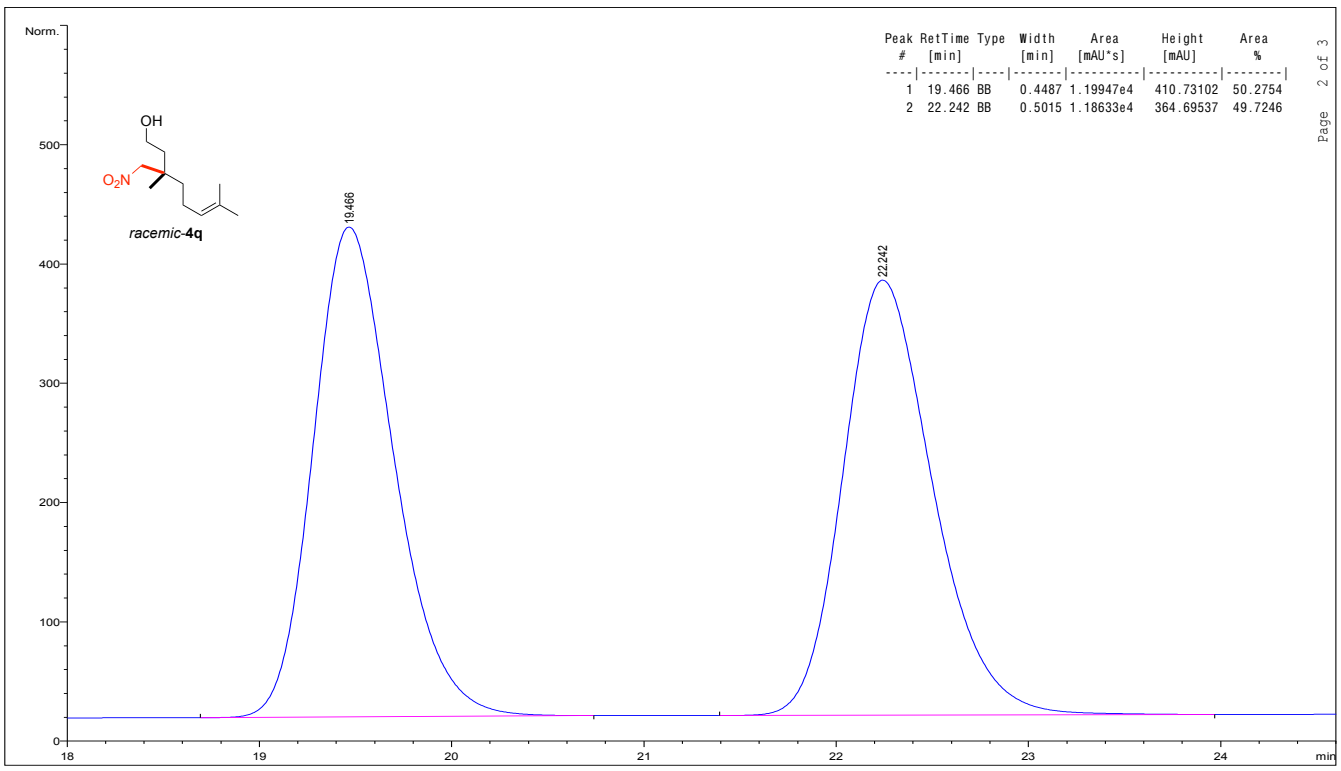

mAU
80
70
60
50
40
30
20
10
0
6
8
10
12
14
16
18
20
22
24
min
10.613
19.581
OH
O2N
O
N
Bn
racemic-4p
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 10.613 | BB | 0.3310 | 1362.23914 | 63.30761 | 50.5835
2 | 19.581 | BB | 0.6210 | 1330.81091 | 32.82501 | 49.4165

(S)-3,7-dimethyl-3-(nitromethyl)oct-6-en-1-ol (4q)

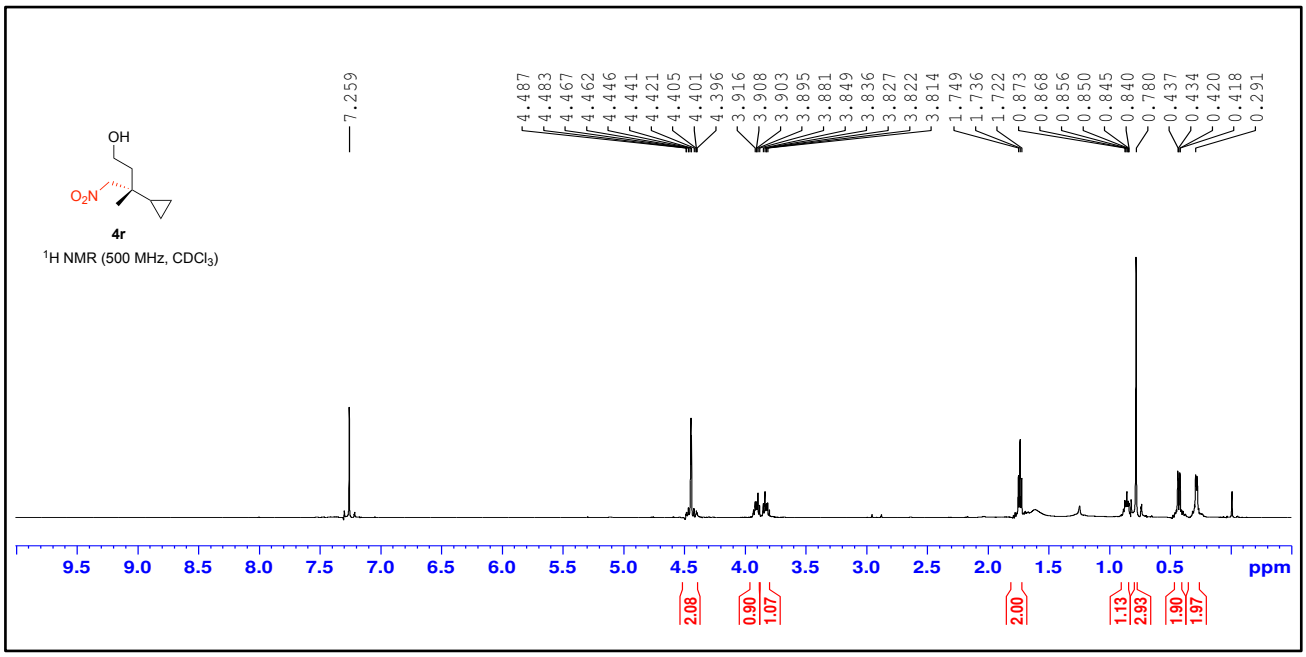


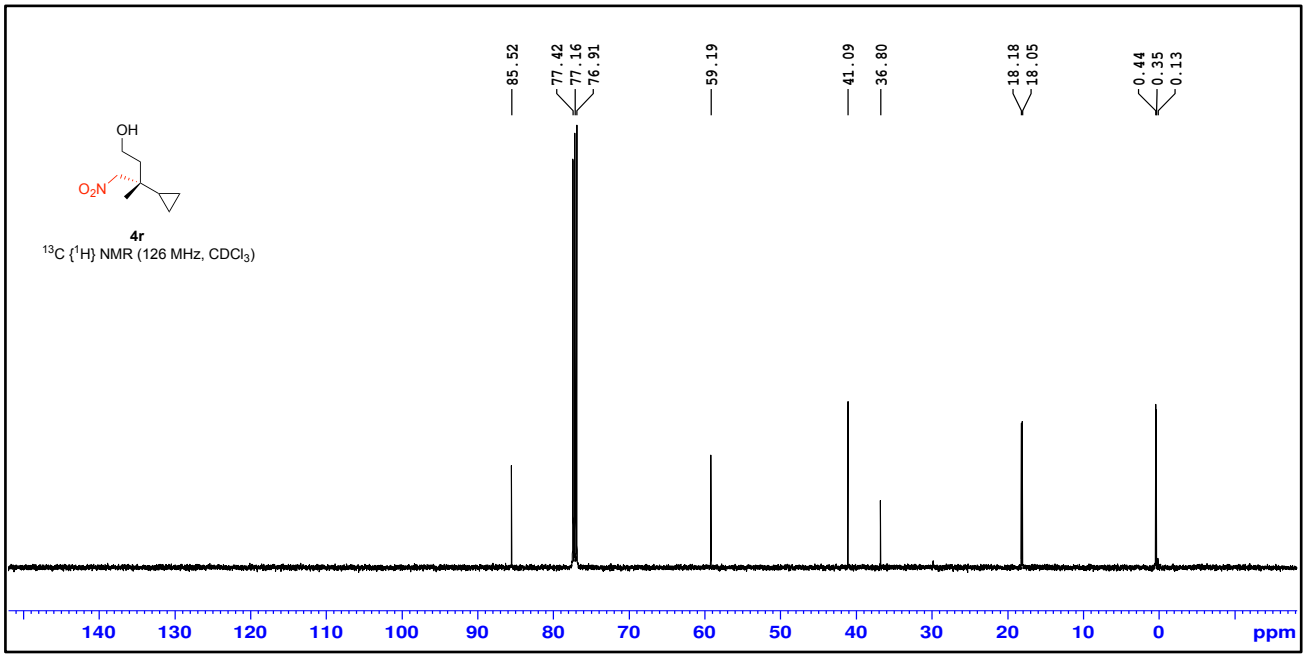



Norm.
OH
O2N
4q
19.672
Area: 8108.34
22.424
Area: 2154.25
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 19.672 | MM | 0.4606 | 8108.33643 | 293.42371 | 79.0087
2 | 22.424 | MM | 0.5153 | 2154.24658 | 69.67600 | 20.9913
Page 2 of 3
min

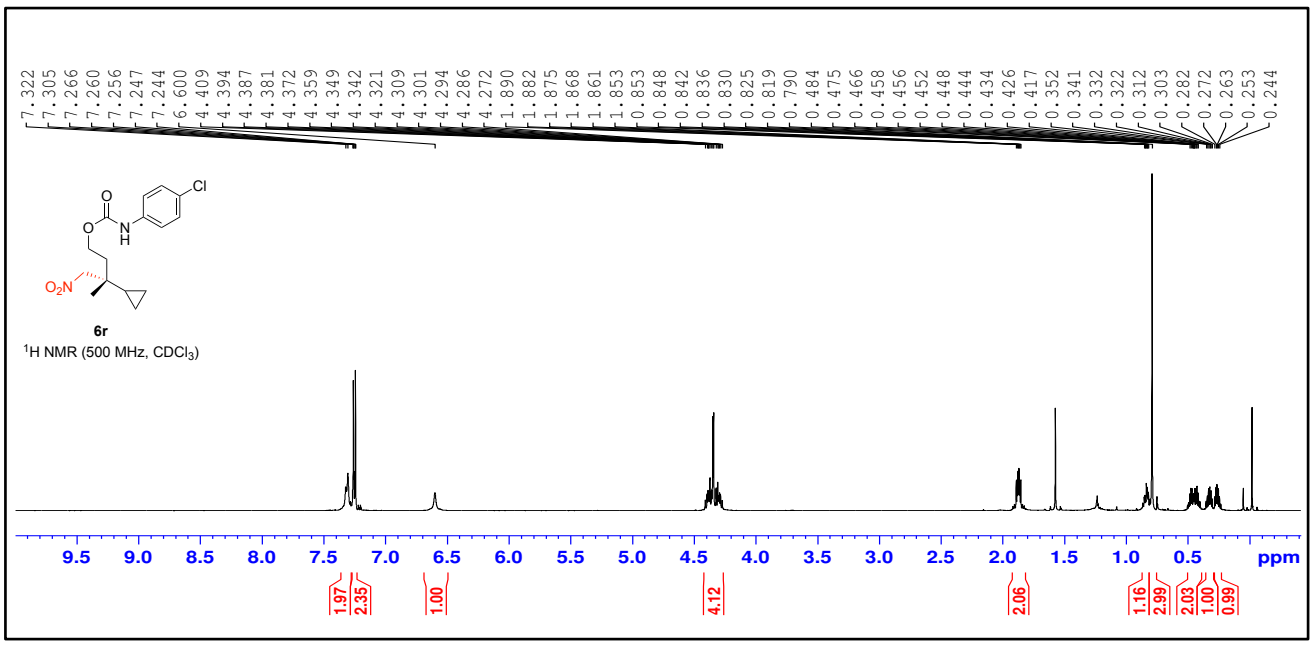

Norm.
OH
O2N
racemic-4q
19.466
22.242
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 19.466 | BB | 0.4487 | 1.19947e4 | 410.73102 | 50.2754
2 | 22.242 | BB | 0.5015 | 1.18633e4 | 364.69537 | 49.7246
Page 2 of 3
min

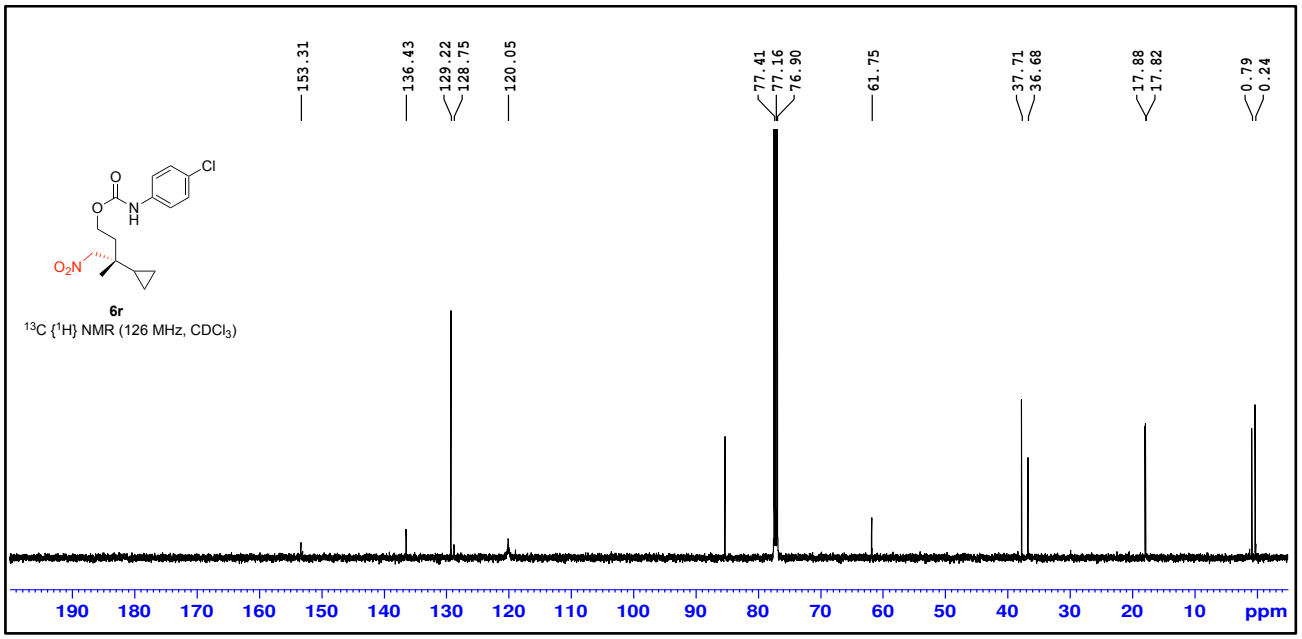
(*R*)-3-cyclopropyl-3-methyl-4-nitrobutan-1-ol (4r)

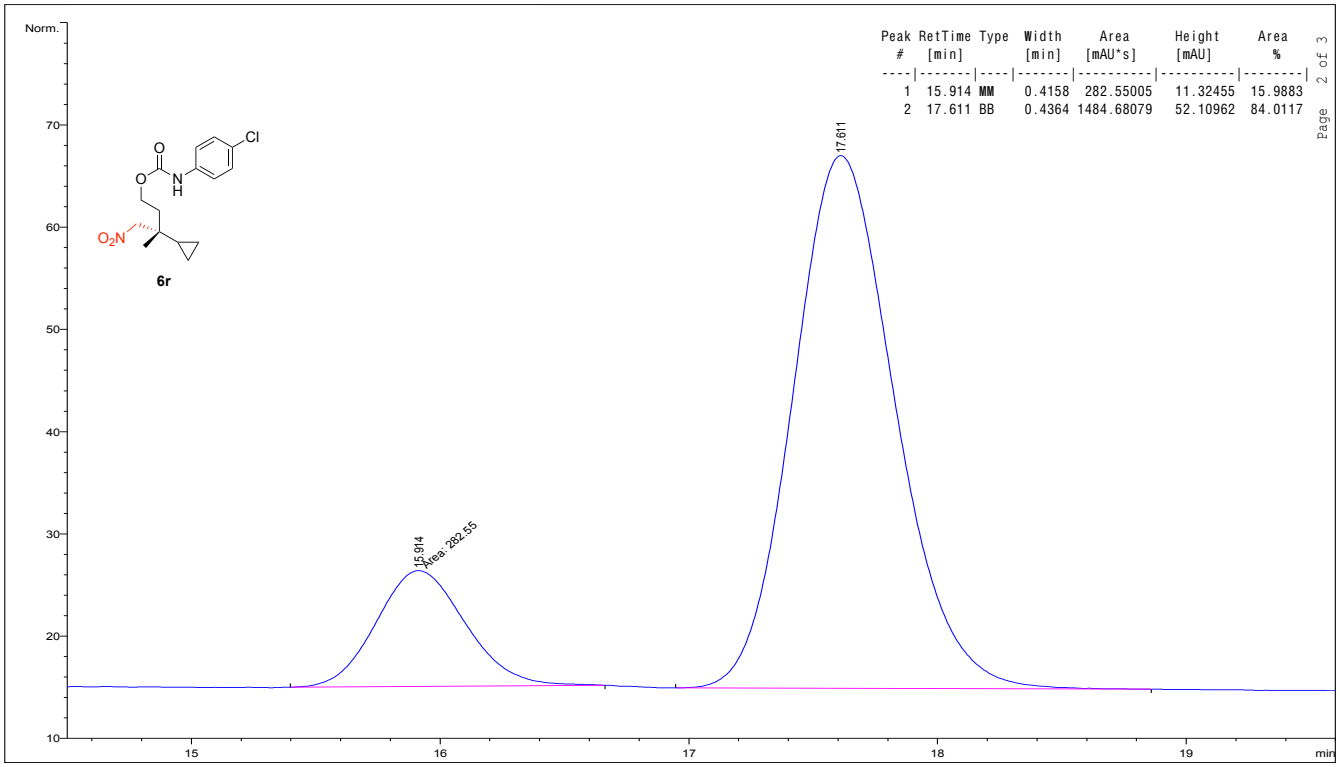


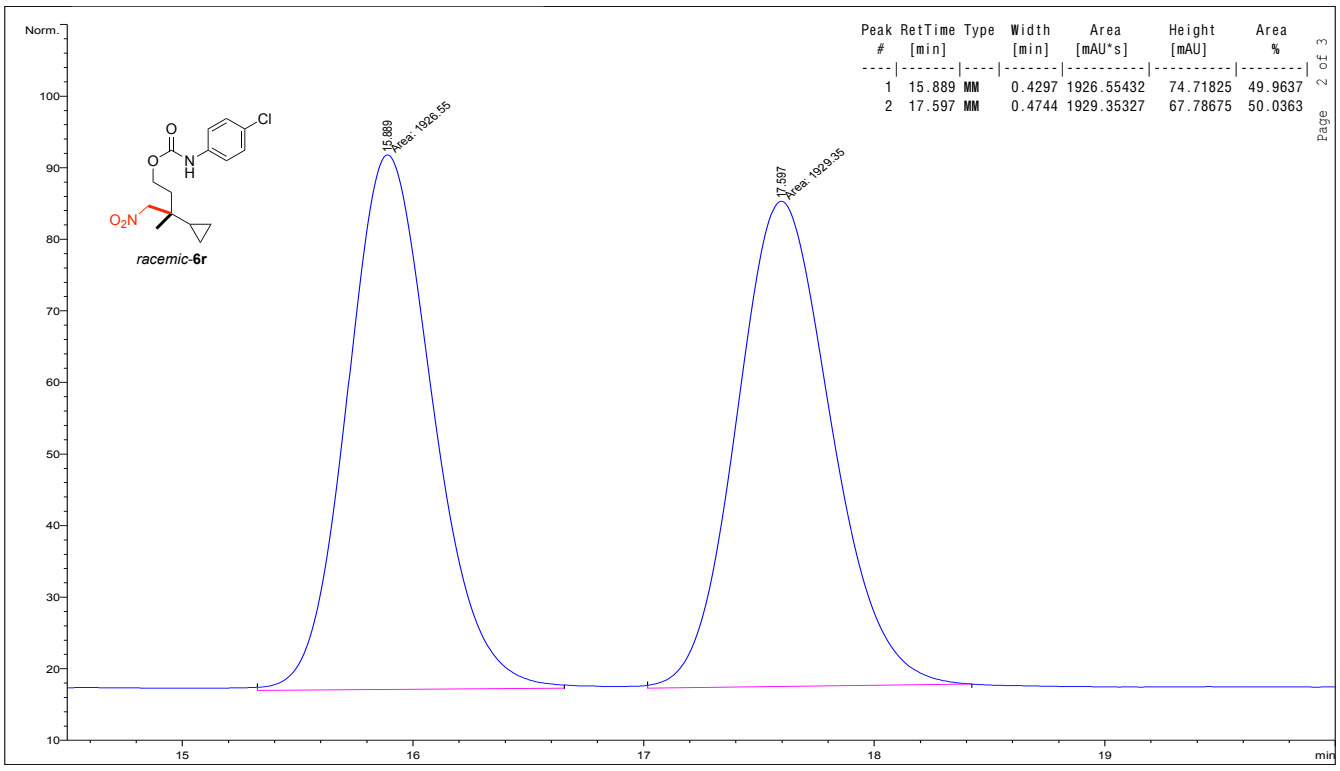


(*R*)-3-cyclopropyl-3-methyl-4-nitrobutyl (4-chlorophenyl)carbamate (6r)

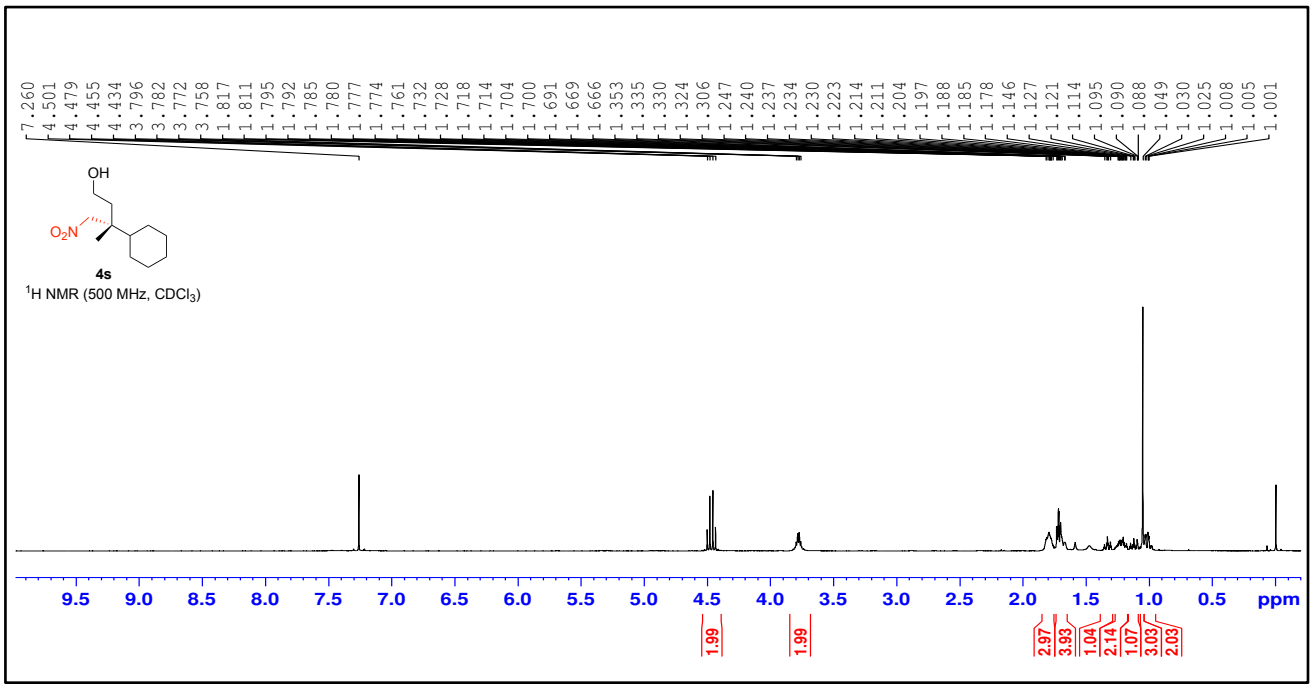


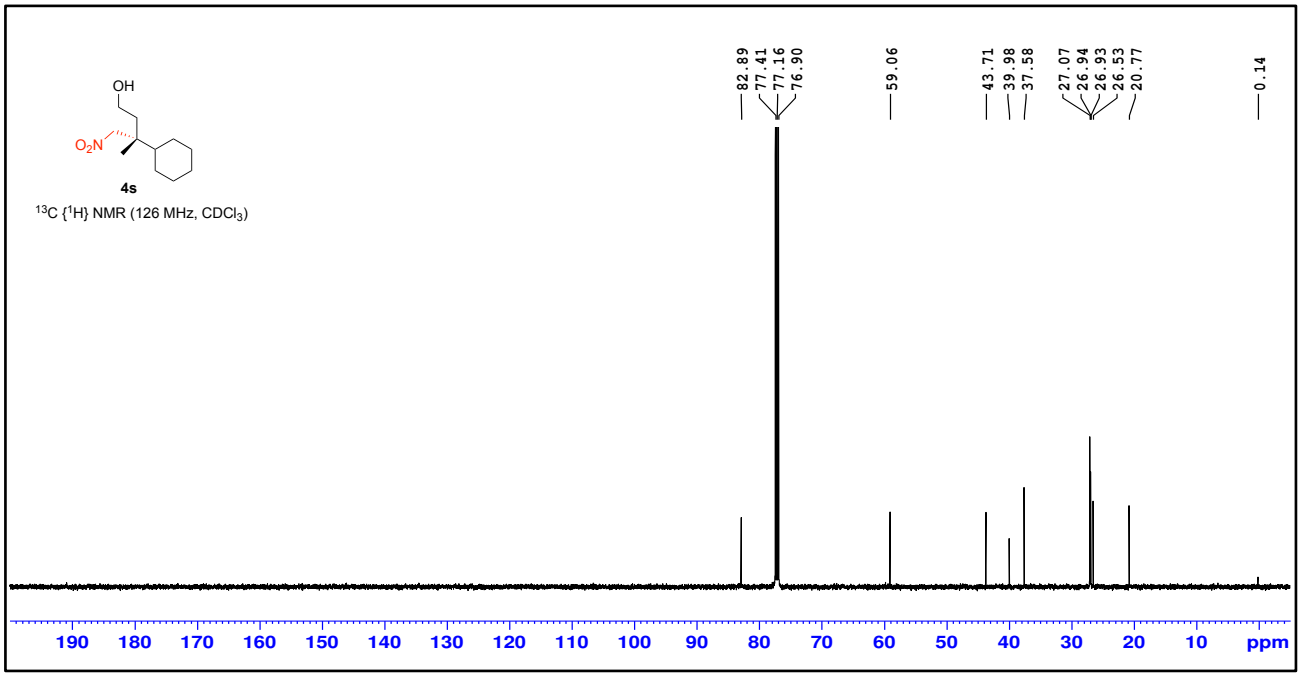



Norm.
Cl
O
N
H
O
O2N
6r
17.611
15.914
Area: 282.55
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 15.914 | MM | 0.4158 | 282.55005 | 11.32455 | 15.9883
2 | 17.611 | BB | 0.4364 | 1484.68079 | 52.10962 | 84.0117
Page 2 of 3
min

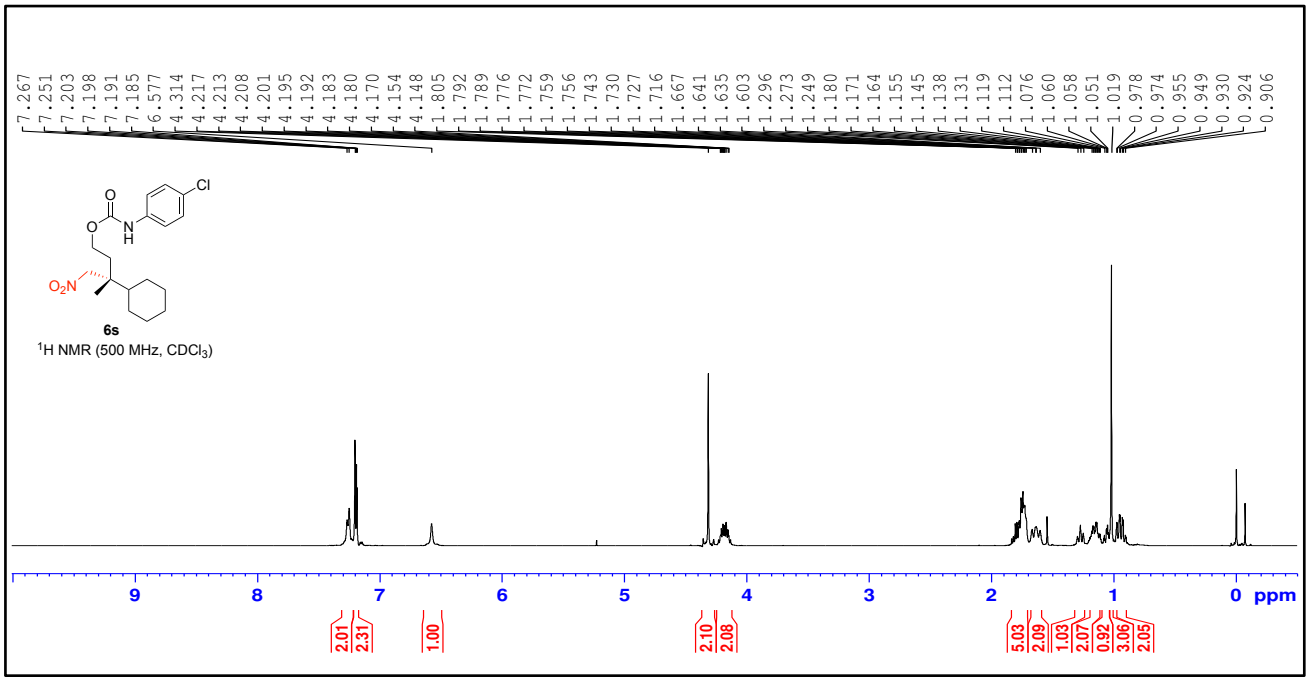

Norm.
Cl
O
N
H
O
O2N
racemic-6r
15.889
Area: 1926.55
17.597
Area: 1929.35
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 15.889 | MM | 0.4297 | 1926.55432 | 74.71825 | 49.9637
2 | 17.597 | MM | 0.4744 | 1929.35327 | 67.78675 | 50.0363
Page 2 of 3
min

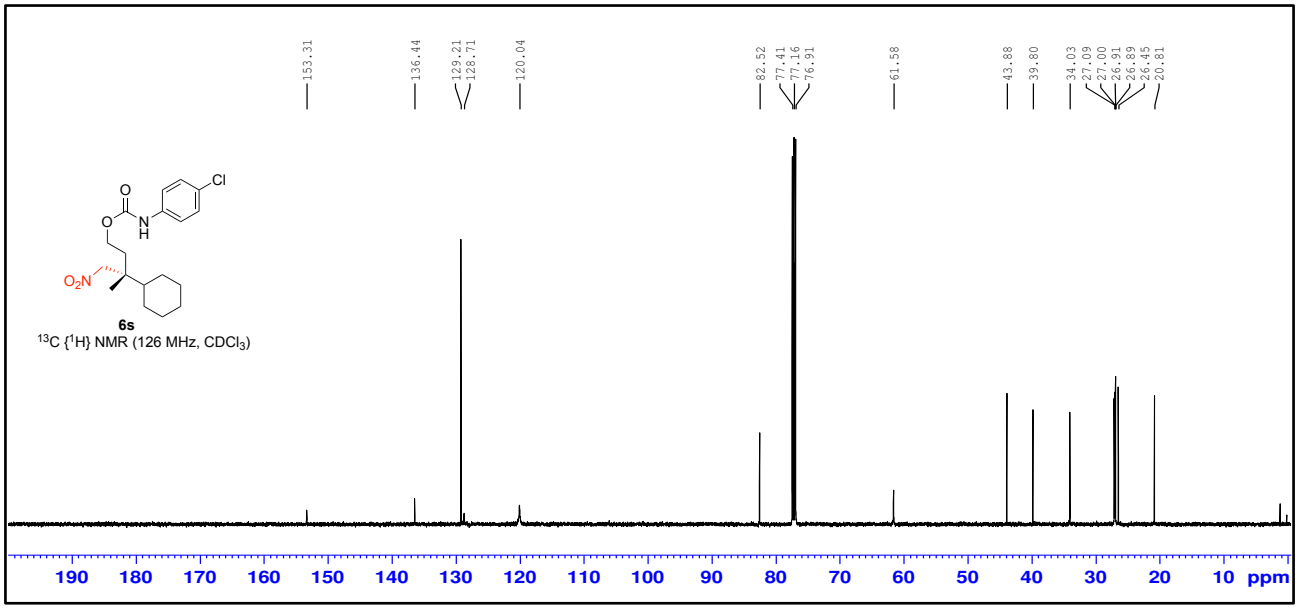
(*R*)-3-cyclohexyl-3-methyl-4-nitrobutan-1-ol (4s)

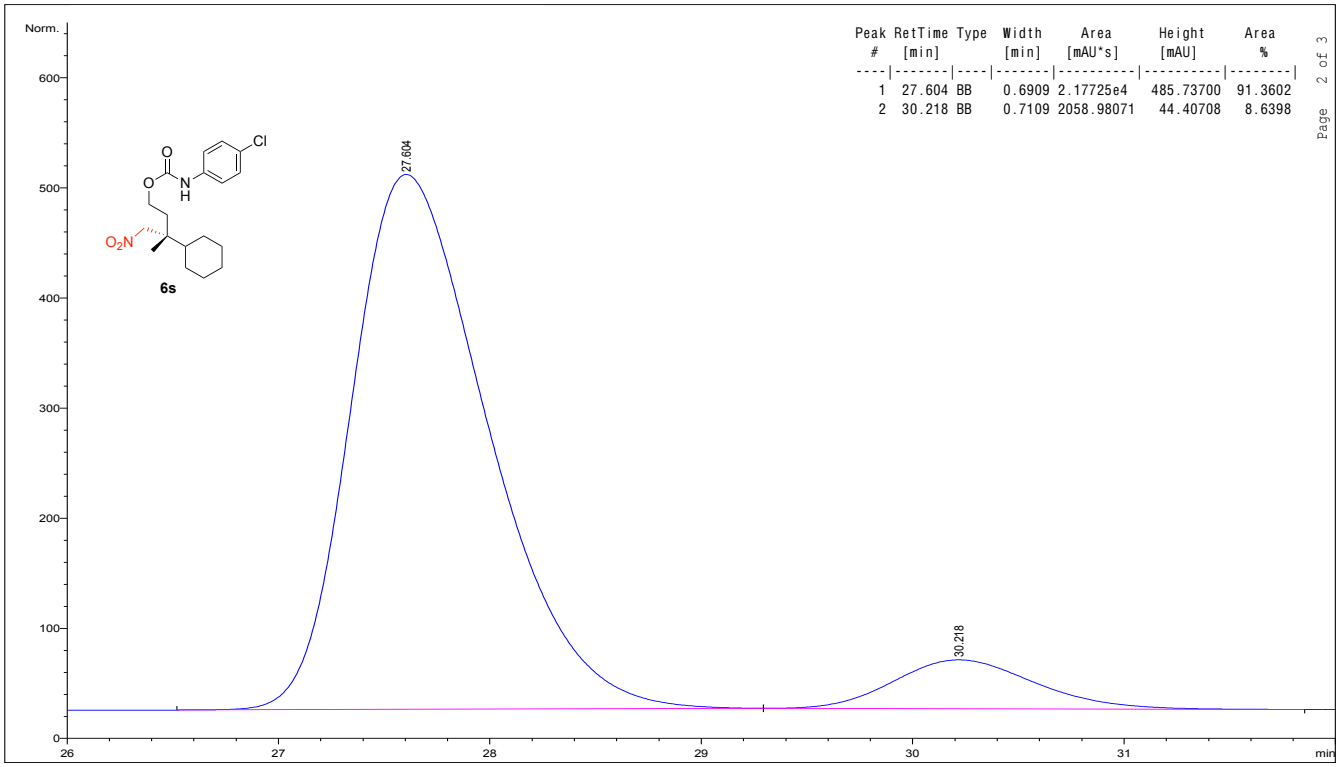


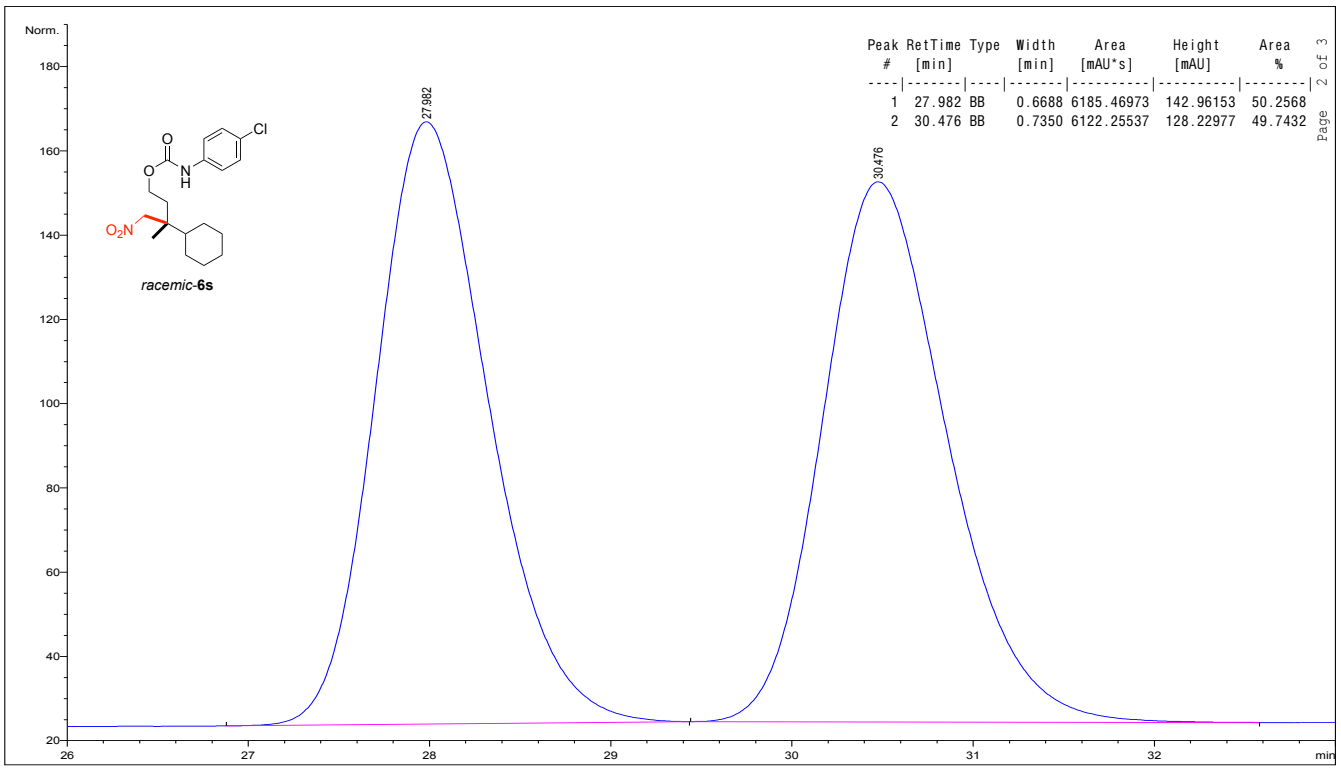


(R)-3-cyclohexyl-3-methyl-4-nitrobutyl (4-chlorophenyl)carbamate (6s)

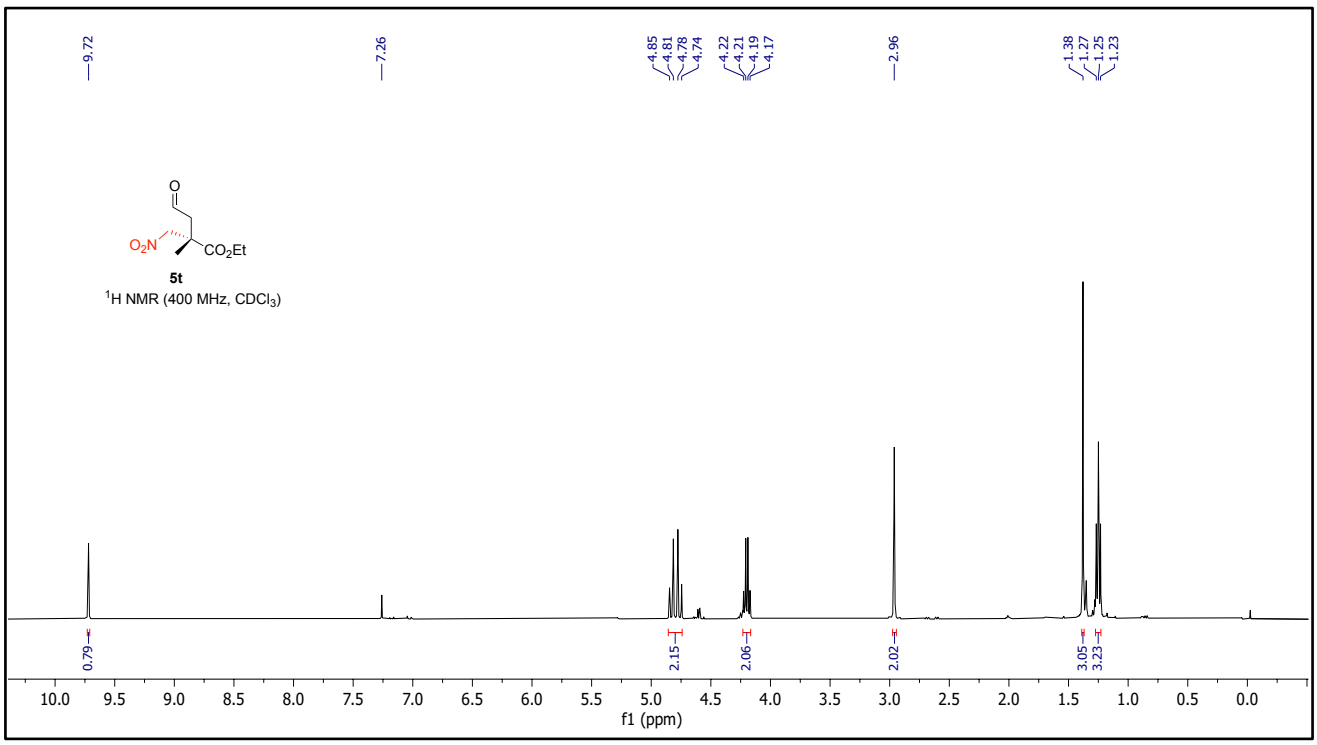


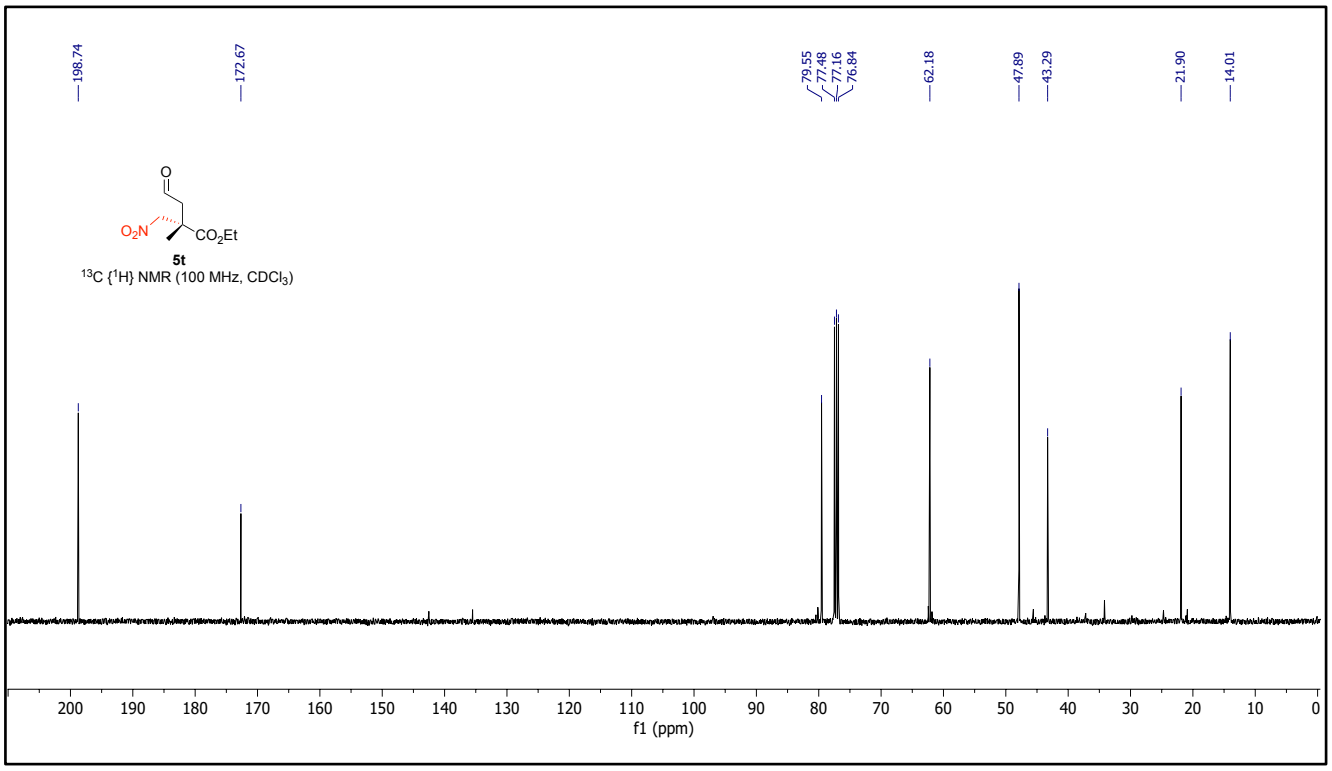



Norm.
600
500
400
300
200
100
0
26
27
28
29
30
31
min
27.604
30.218
Cl
O
N
H
O2N
6s
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 27.604 | BB | 0.6909 | 2.17725e4 | 485.73700 | 91.3602
2 | 30.218 | BB | 0.7109 | 2058.98071 | 44.40708 | 8.6398
Page 2 of 3

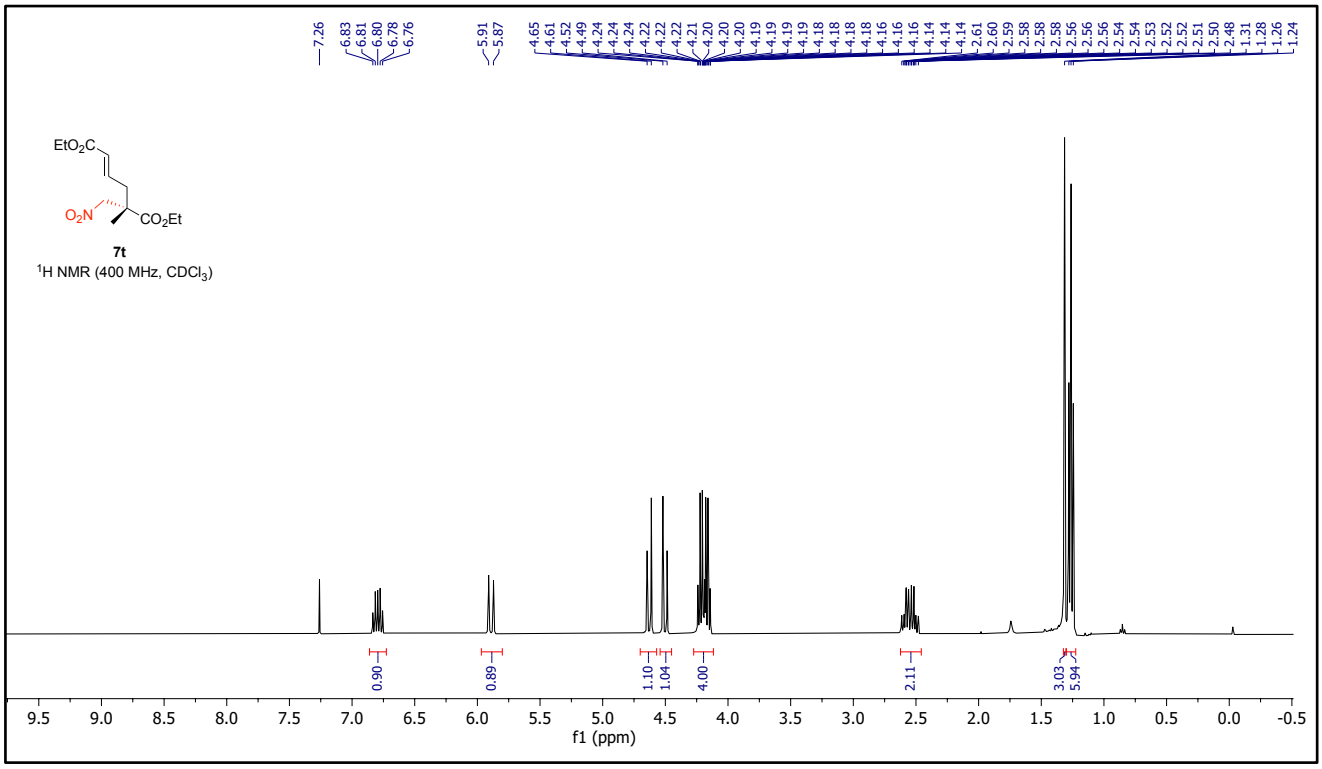

Norm.
180
160
140
120
100
80
60
40
20
26
27
28
29
30
31
32
min
27.982
30.476
Cl
O
N
H
O2N
racemic-6s
Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area %
1 | 27.982 | BB | 0.6688 | 6185.46973 | 142.96153 | 50.2568
2 | 30.476 | BB | 0.7350 | 6122.25537 | 128.22977 | 49.7432
Page 2 of 3

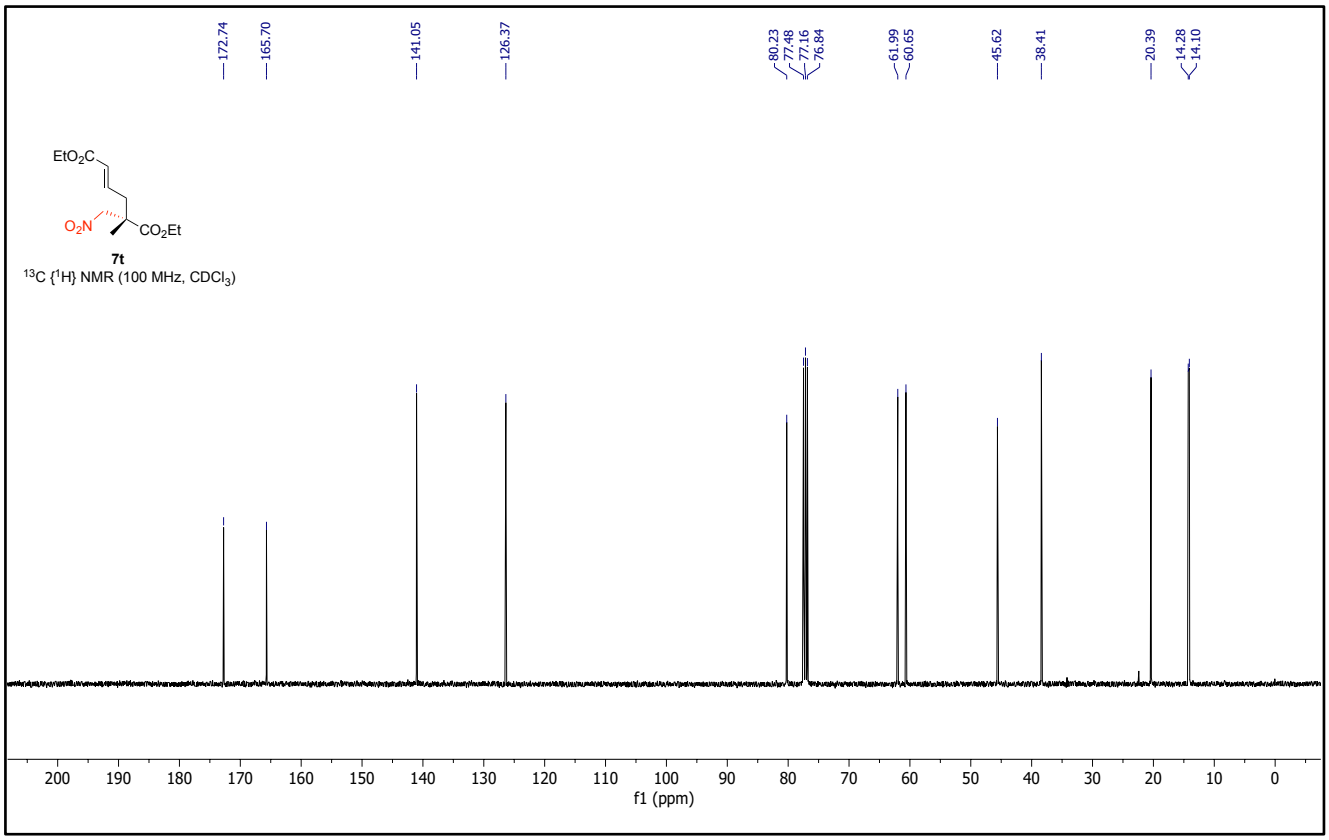
Ethyl (*S*)-2-methyl-2-(nitromethyl)-4-oxobutanoate (5t)

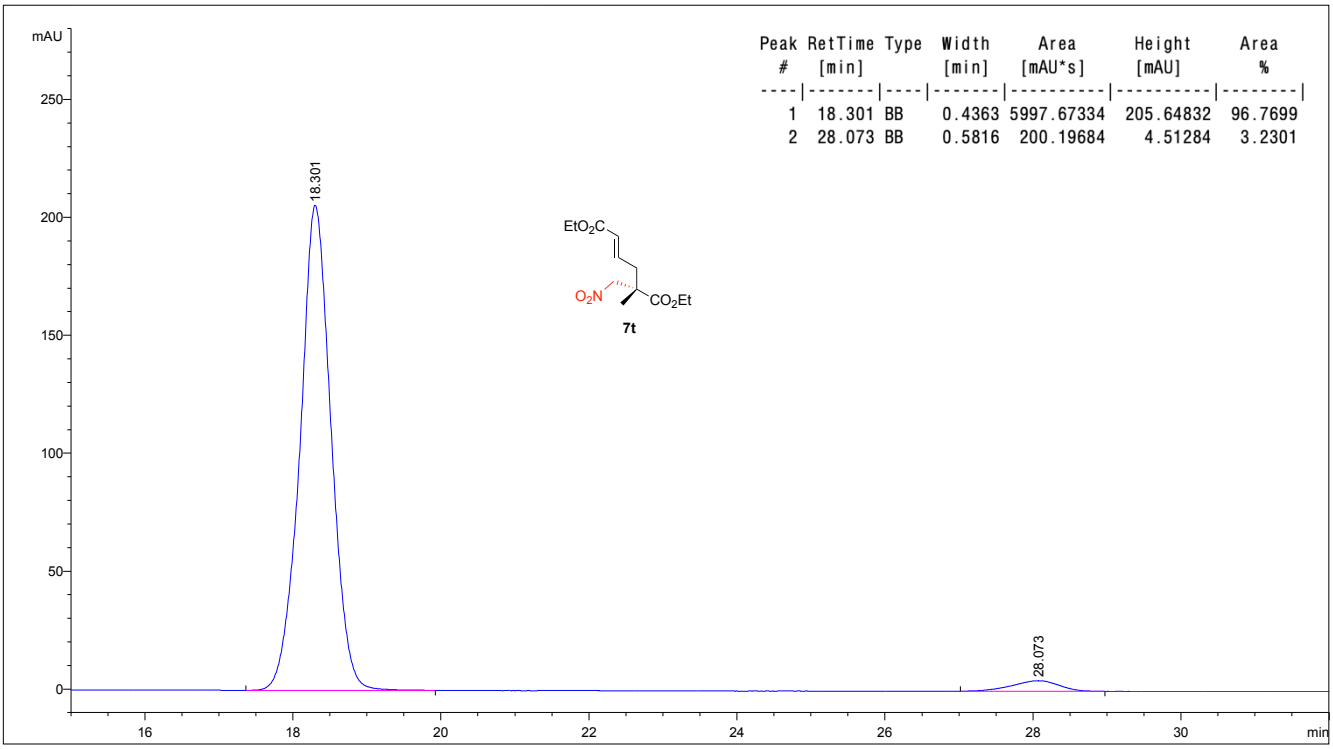




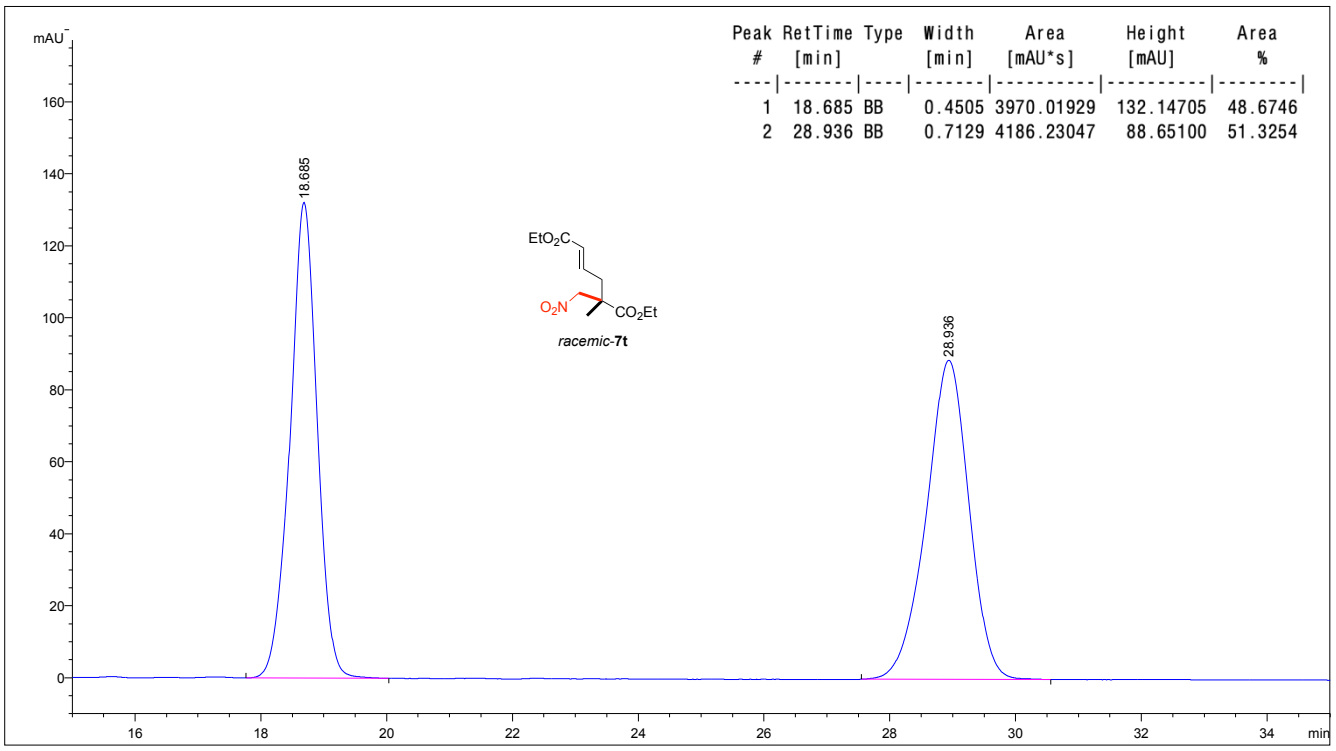
Diethyl (*S*,*E*)-5-methyl-5-(nitromethyl)hex-2-enedioate (7t)





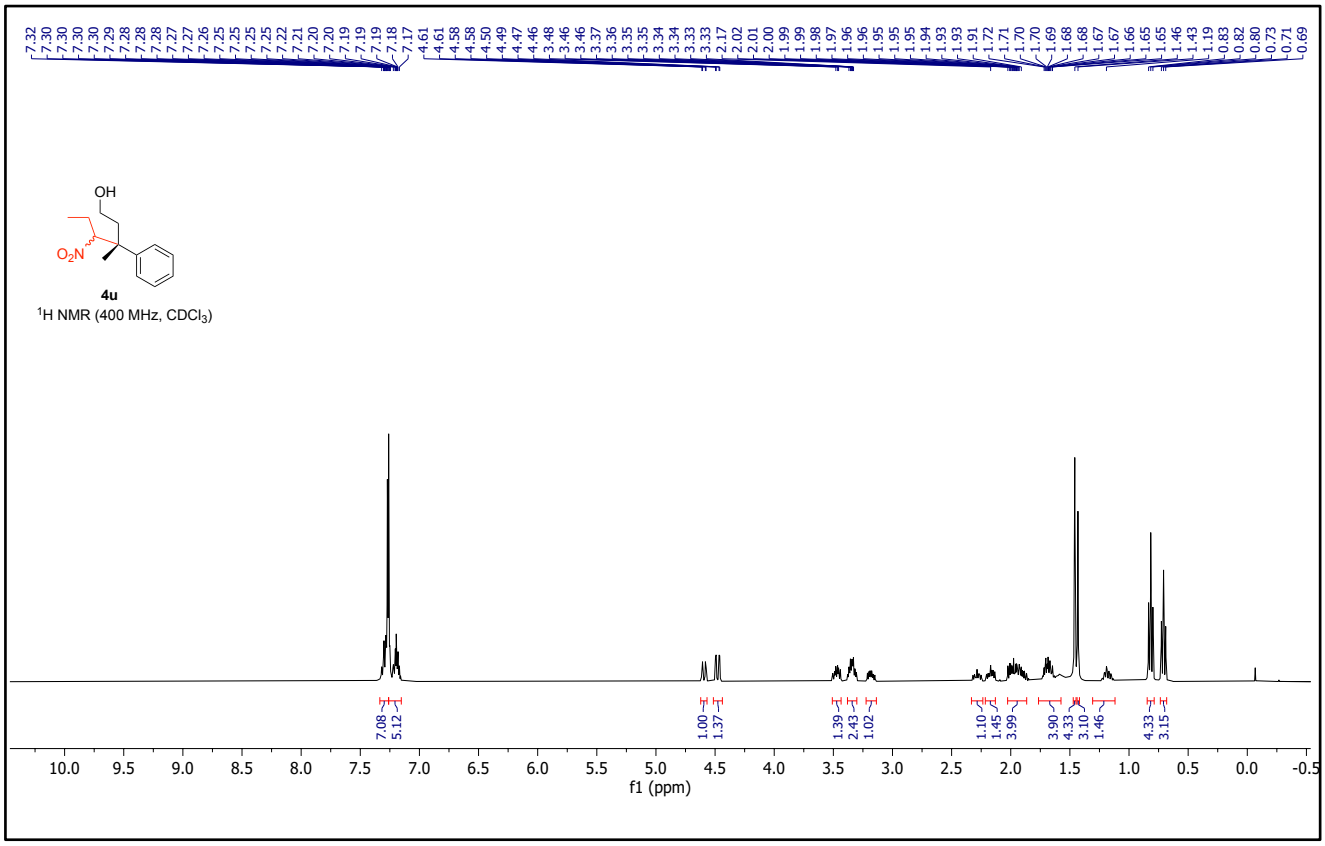


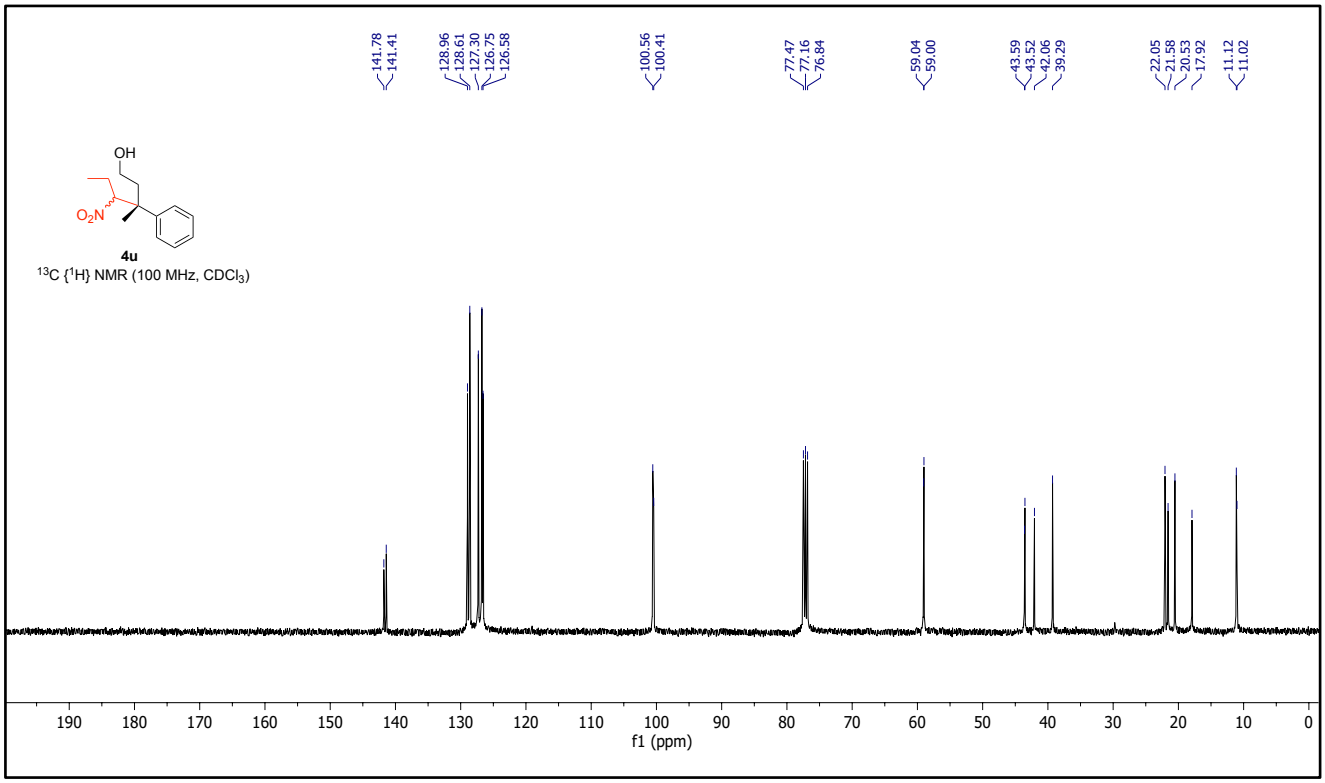
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.301	BB	0.4363	5997.67334	205.64832	96.7699
2	28.073	BB	0.5816	200.19684	4.51284	3.2301

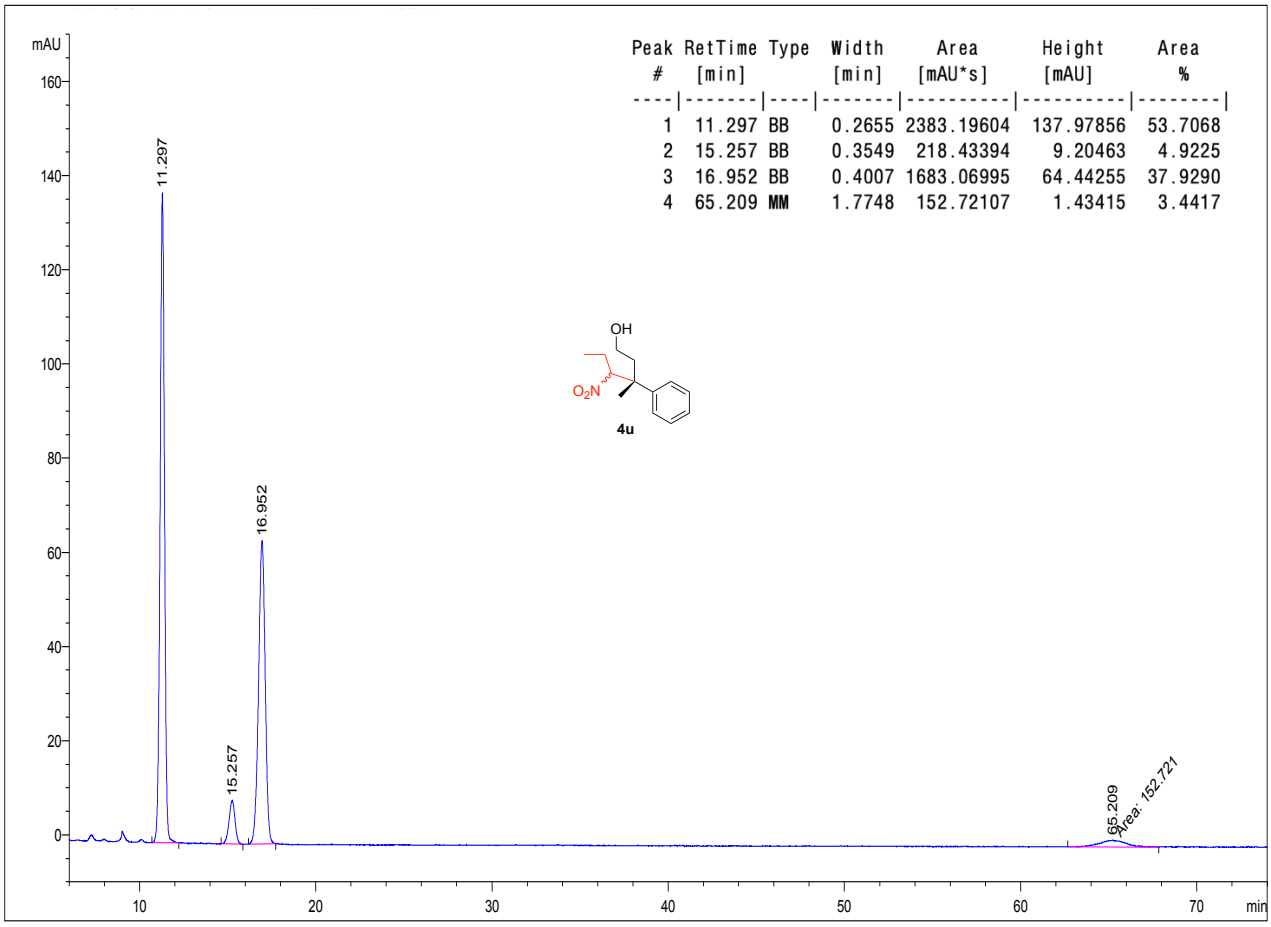


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.685	BB	0.4505	3970.01929	132.14705	48.6746
2	28.936	BB	0.7129	4186.23047	88.65100	51.3254

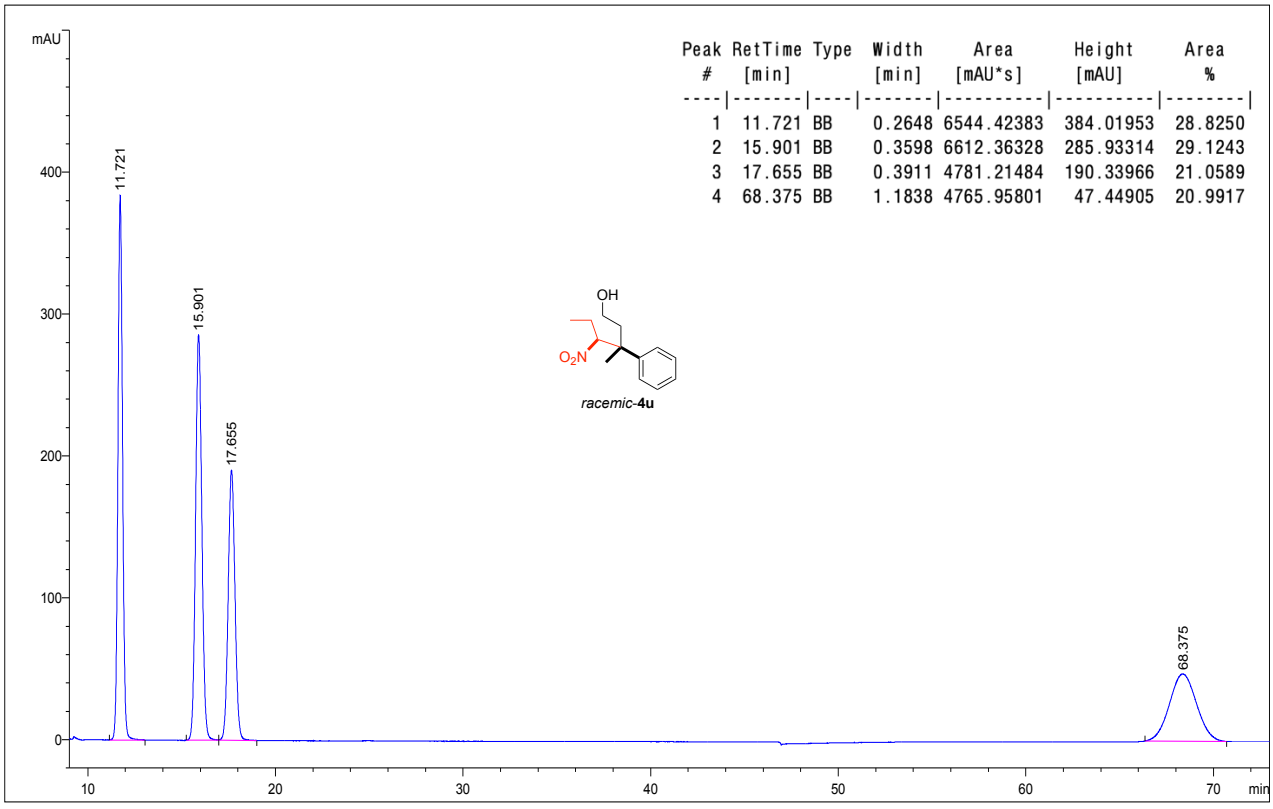
(3*R*)-3-methyl-4-nitro-3-phenylhexan-1-ol (4u)





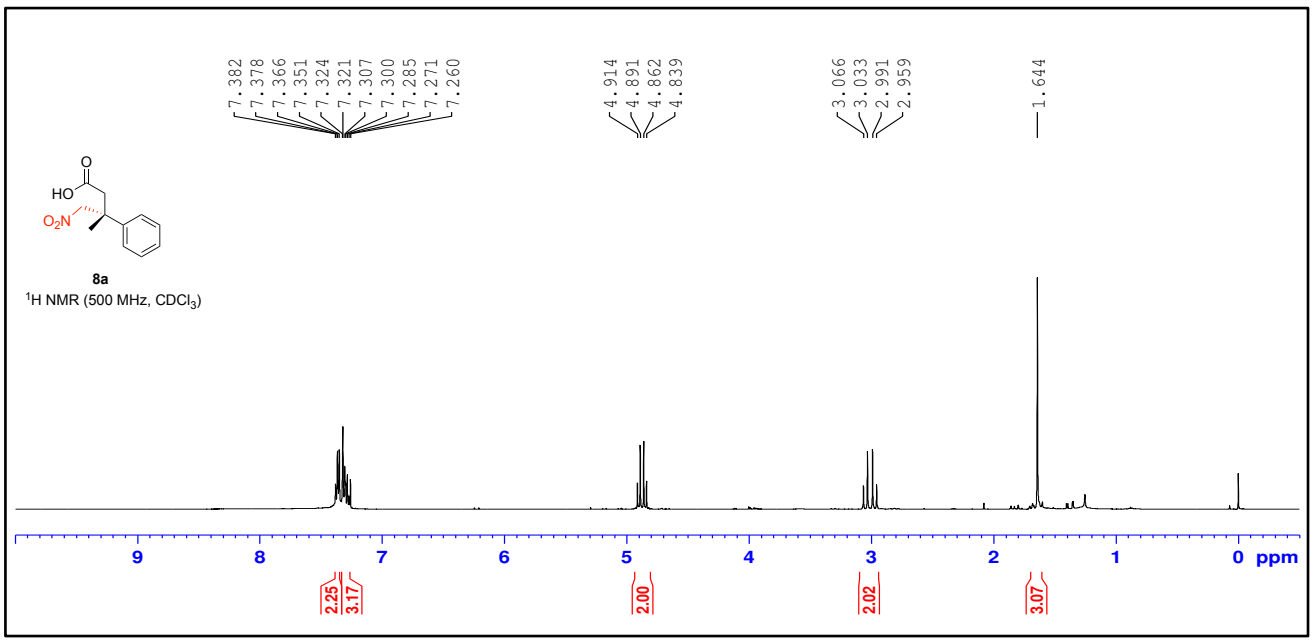


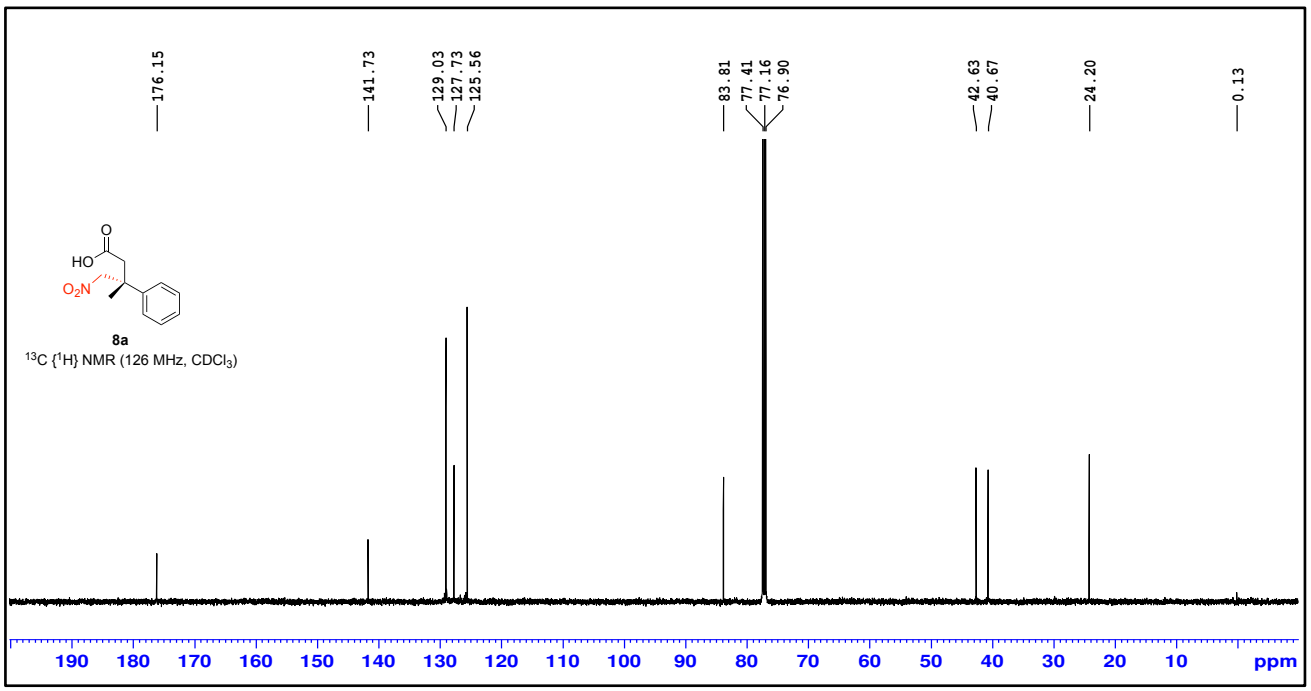
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.297	BB	0.2655	2383.19604	137.97856	53.7068
2	15.257	BB	0.3549	218.43394	9.20463	4.9225
3	16.952	BB	0.4007	1683.06995	64.44255	37.9290
4	65.209	MM	1.7748	152.72107	1.43415	3.4417



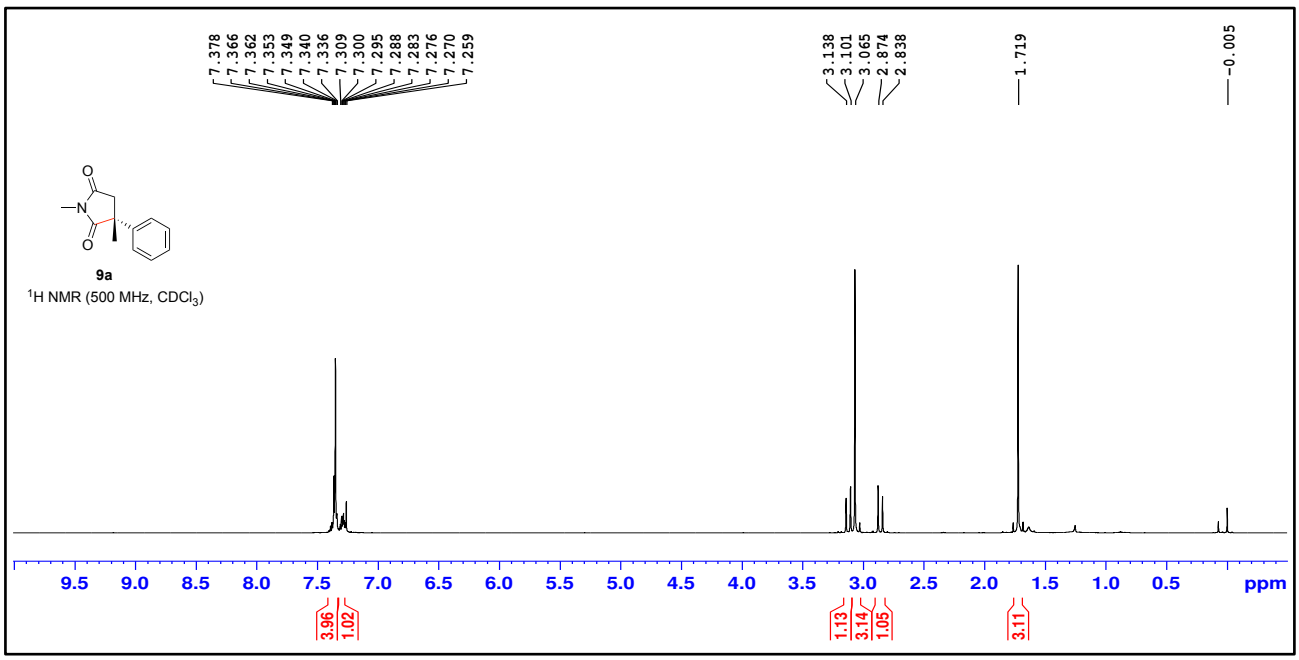
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.721	BB	0.2648	6544.42383	384.01953	28.8250
2	15.901	BB	0.3598	6612.36328	285.93314	29.1243
3	17.655	BB	0.3911	4781.21484	190.33966	21.0589
4	68.375	BB	1.1838	4765.95801	47.44905	20.9917

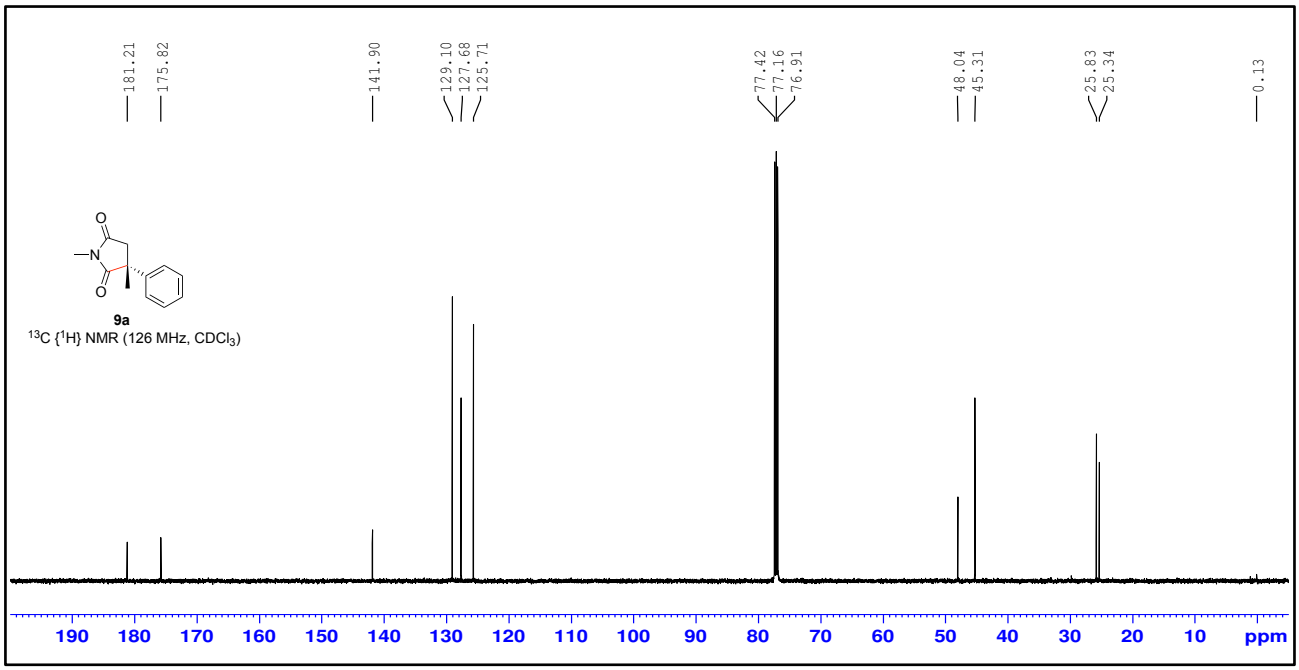
3-methyl-4-nitro-3-phenylbutanoic acid (8a)

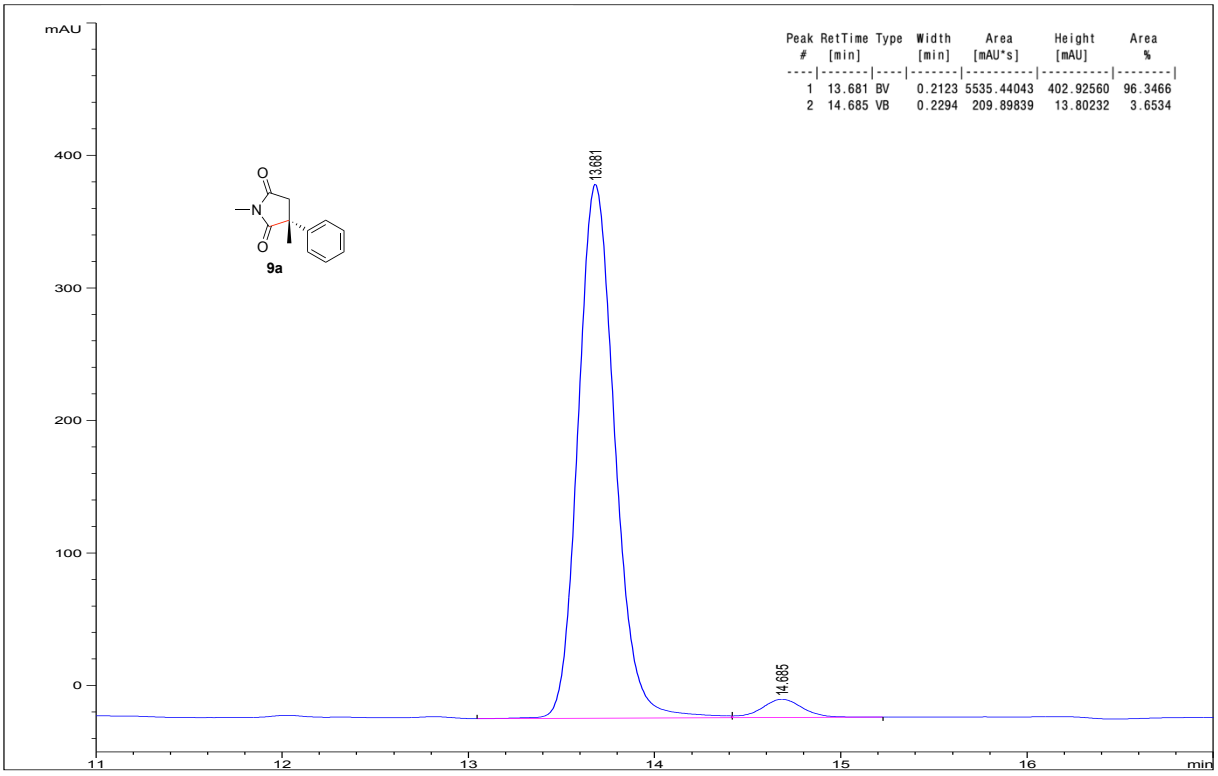




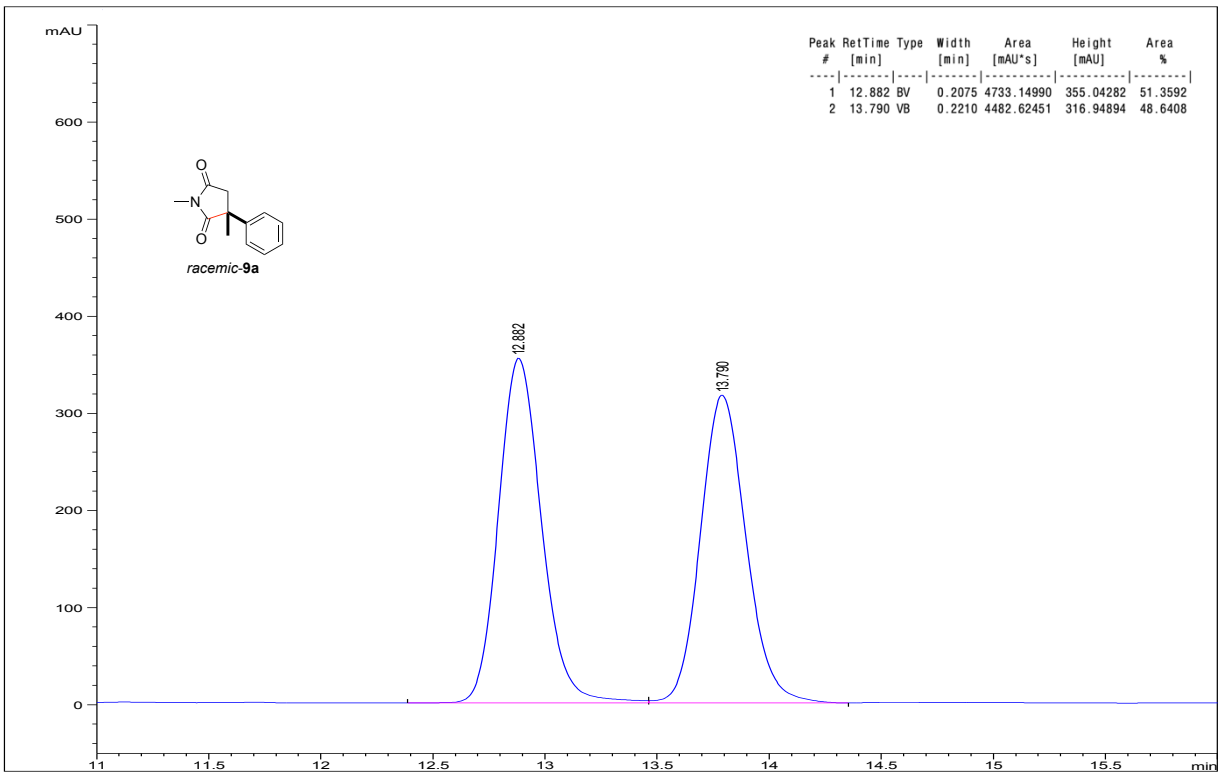
Methsuximide (9a)







Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.681	BV	0.2123	5535.44043	402.92560	96.3466
2	14.685	VB	0.2294	209.89839	13.80232	3.6534



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.882	BV	0.2075	4733.14990	355.04282	51.3592
2	13.790	VB	0.2210	4482.62451	316.94894	48.6408