Catalytic Asymmetric [4 + 2] Additions with Aliphatic Nitroalkenes

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Supporting Information

General Information: ^{1}H and ^{13}C NMR spectra were obtained on a Varian spectrometer (400 MHz and 100 MHz, respectively) and internally referenced to the tetramethylsilane signal or to residual protio solvent signals. The data for ^{1}H NMR is presented in the following format: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; sext, sextet; m, multiplet), coupling constant (Hz), and integration. The data for ^{13}C NMR is presented in the following format: chemical shift (δ, ppm). Infrared spectra were recorded on a Nicolet FT-IR spectrometer and the data is reported in frequency of absorption. Low resolution and high resolution mass spectra were recorded on either a Micromass 70-VSE-B instrument (EI, CI), Micromass Q-Tof instrument (ESI) or a Bruker Hct Ultra Ptm Discovery System™. Specific rotations were measured with a Jasco digital polarimeter.

High performance liquid chromatography (HPLC) analysis was performed on a Hewlett-Packard 1100 Series instrument equipped with a quaternary pump, using Daicel Chiralcel OJ or OD columns (250 x 4.6 mm), Chiralpak AD or AS columns (250 x 4.6 mm), or a Regis (R,R)-Whelk-O1 column (250 x 4.6 mm). UV absorption was monitored at 209 nm, 220 nm, 240 nm, or 254 nm.

1. Materials

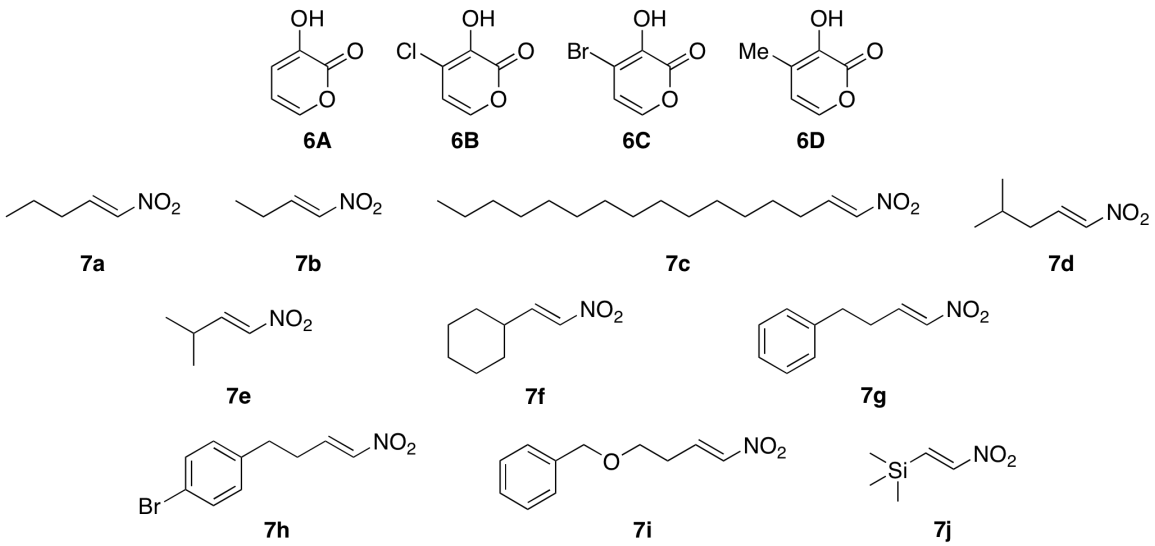

Figure S1. 2-pyrones and nitroalkenes used in this study.

2-pyrones **6A**[1], **6B**[2], and **6C**[2] were prepared according to literature procedures. 2-pyrone **6D** was prepared from 2-pyrone **6C** following a literature procedure.[3] Nitroalkenes **7a**[4], **7e**[4], **7f**[4], **7g**[5], **7i**[6], **7j**[7] and the parent aldehydes of nitroalkenes **7c**[8] and **7h**[9] were prepared according to literature procedures. Nitroalkenes **7b**, **7c**, **7d**, and **7h** were prepared in the same manner as described for **7i** from their corresponding aldehydes.

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[9] Frost, C. G.; Hartley, B. C. *J. Org. Chem.* **2009**, *74* (9), 3599-3602.

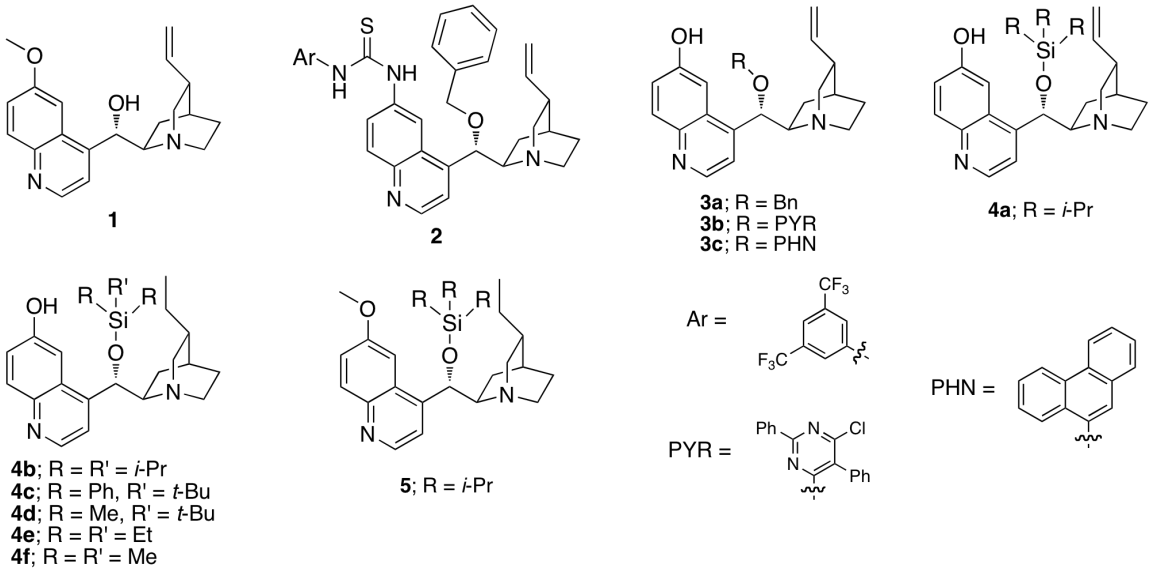


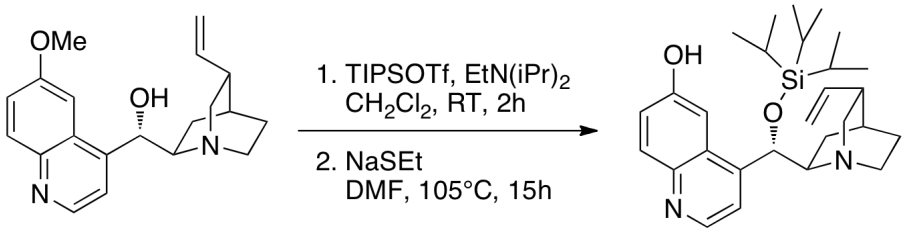
Figure S2. Cinchona alkaloid-derived catalysts screened in this study.

Triethylamine and quinidine (**1**) were purchased from Aldrich and used without further purification. Catalyst **2** was prepared following our method to make analogous catalysts by employing benzyl chloride in the appropriate step.[10] Catalysts **3a**[11], **3b**[12], and **3c**[11] were prepared according to our methods. Preparations of catalysts **4a-4f** and **5** are described below.

[10] Liu, Y.; Sun, B.; Wang, B.; Wakem, M.; Deng, L. *J. Am. Chem. Soc.* **2008**, *131*, 418-419.
[11] Li, H.; Wang, Y.; Tang, L.; Wu, F.; Liu, X.; Guo, C.; Foxman, B. M.; Deng, L. *Angew. Chem. Int. Ed.* **2005,** *44* (1), 105-108.
[12] Wu, F.; Hong, R.; Khan, J.; Liu, X.; Deng, L. *Angew. Chem. Int. Ed.* **2006**, *45*, 4301.

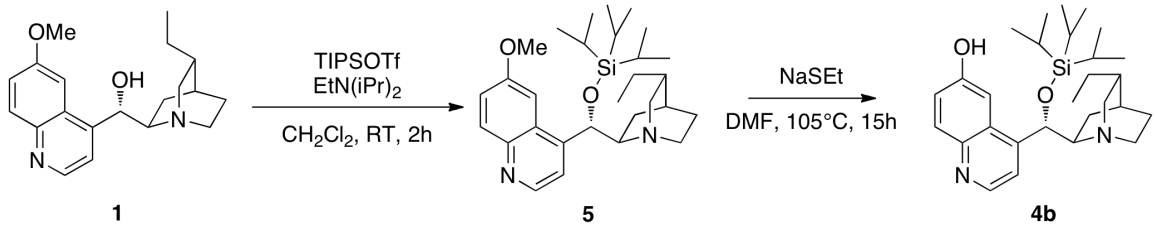
2. Synthesis and Characterization of Silyl Ether Catalysts

4-((*S*)-((triisopropylsilyl)oxy)((1*S*,2*R*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methyl)quinolin-6-ol (4a).



1 **4a**

Catalyst **4a** was prepared in the same manner as described below for catalyst **4b**. Obtained as an 87:13 mixture of rotamers (determined by ^{1}H NMR integration of the set of C2' proton signals {δ_{Major} = 8.71 ppm (d), δ_{Minor} = 8.63 ppm (d)}) as a yellow solid (575 mg, 80%). mp = 115-120 °C (decomp.). $[\alpha]_{20}^{D}$ = +150.7°, (*c* = 0.37, $CHCl_3$). Major rotamer ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.71 (d, *J* = 4.5 Hz, 1H), 8.04 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 9.1 Hz, 1H), 7.55 (d, *J* = 4.5 Hz, 1H), 7.28 (dd, *J* = 9.1 Hz and 2.3 Hz, 1H), 6.10 (s, 1H), 6.08 (ddd, *J* = 16.9 Hz, 10.4 Hz, and 7.6 Hz, 1H), 5.09 (m, 2H), 3.50 (dd, *J* = 13.0 Hz and 9.1 Hz, 1H), 3.08 (dd, *J* = 12.8 Hz and 10.2 Hz, 1H), 2.82-2.72 (m, 4H), 2.38-2.24 (m, 2H), 1.81 (m, 1H), 1.49 (m, 1H), 1.37 (m, 1H), 1.01 (m, 18H), 0.93 (m, 2H), 0.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.9, 148.0, 146.5, 143.6, 139.8, 131.2, 127.1, 123.2, 119.0, 115.3, 106.6, 72.5, 60.7, 50.1, 40.3, 28.1, 25.9, 19.7, 18.4, 18.3, 13.0; IR (film) ν 2942, 2866, 1618, 1465, 1243, 1116, 1009, 882, 754; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{28}H_{43}N_2O_2Si$: 467.3094. Found: 467.3096.

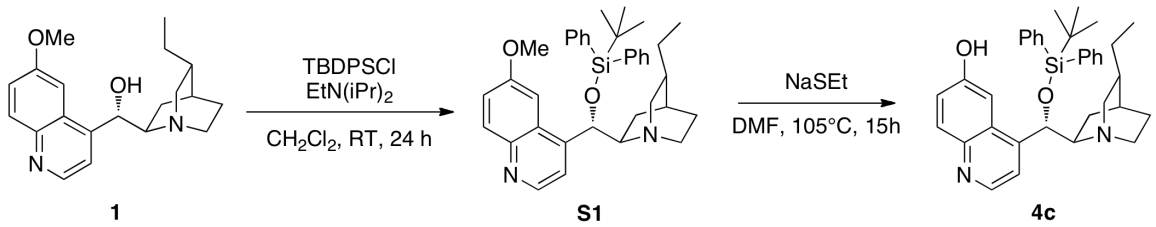


4-((*S*)-((1*S*,2*R*,4*S*,5*S*)-5-ethylquinuclidin-2-yl)((triisopropylsilyl)oxy)methyl)quinolin-6-ol (4b). To a room temperature solution of dihydroquinidine **1** (2.00 g, 6.12 mmol, 1 Eq.) and diisopropylethylamine (3.20 mL, 18.36 mmol, 3 Eq.) in methylene chloride (16 mL) was added triisopropylsilyl trifluoromethanesulfonate (2.46 mL, 9.18 mmol, 1.5 Eq.). The reaction was stirred at room temperature for two hours, at which point the reaction was complete as indicated by TLC analysis. The reaction was quenched with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with methylene chloride (2 x 30 mL). The organic layers were combined, dried over Na_2SO_4, and the solvent was removed *in vacuo*. Purification of the crude residue by flash silica gel chromatography (19:1 Ethyl Acetate/Methanol) afforded **5** as a colorless oil (2.90 g, 98%). Obtained as a 69:31 mixture of rotamers of **5** (determined by ^{1}H NMR integration of the set of C2' proton signals {δ_{Major} = 8.76 ppm (d), δ_{Minor} = 8.64 ppm (d)}). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, *J* = 4.5 Hz, 0.7H), 8.65 (d, *J* = 4.3 Hz, 0.3H), 8.02 (d, *J* = 9.2 Hz, 0.7H), 7.98 (d, *J* = 9.2 Hz, 0.3H), 7.90 (d, *J* = 2.7 Hz, 0.3H), 7.60 (d, *J* = 4.5 Hz, 0.7H), 7.36 (dd, *J* = 9.2 Hz and 1.8 Hz, 0.7H), 7.32 (dd, *J* = 9.2 Hz and 2.9 Hz, 0.3H), 7.16 (s, 0.7H), 7.10 (d, *J* = 4.3 Hz, 0.3H), 5.74 (d, *J* = 3.9 Hz, 0.7H), 4.96 (d, *J* = 9.6 Hz, 0.3H), 3.92 (s, 3H), 3.50 (q, 9.0 Hz, 0.3H), 3.05-2.35 (m, 4.9H), 1.97 (t, *J* = 11.3 Hz, 0.7H), 1.83 (d, *J* = 8.8 Hz, 0.7H), 1.76 (s, 0.7H), 1.67 (s, 0.7H), 1.60-1.30 (m, 5H), 1.19 (m, 1H), 1.10-0.65 (m, 21H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 158.0, 156.6, 147.9, 147.6, 147.5, 145.7, 144.5, 132.1, 131.7, 127.4, 126.9,

121.7, 121.7, 121.5, 119.3, 105.1, 100.8, 80.0, 73.1, 62.4, 61.4, 55.8, 55.6, 51.8, 50.5, 50.0, 49.7, 37.9, 37.8, 27.6, 27.4, 26.9, 26.6, 26.5, 25.7, 25.4, 22.0, 18.3, 18.3, 18.3, 18.1, 13.0, 12.8, 12.3, 12.2.

Catalyst **5** was dissolved in dry N,N-dimethylformamide (60 mL). Then, to a flame-dried round bottom flask under an argon atmosphere was added sodium ethanethiolate (2.02 g, 24.00 mmol, 4 Eq.). The DMF solution was then transferred to the reaction flask via syringe and the reaction was placed into a 105 °C oil bath and stirred for 15 hours. Upon completion, as indicated by TLC analysis, the reaction was removed from the oil bath and allowed to cool to room temperature. After quenching with saturated aqueous NH_4Cl (60 mL) and H_2O (60 mL), the aqueous layer was extracted with methylene chloride (3 x 100 mL). The organic layers were combined, the volume was reduced *in vacuo* to 100 mL, and the residue was washed with H_2O (2 x 50 mL) and brine (1 x 50 mL). After drying over Na_2SO_4, the remaining solvent was removed *in vacuo*, and the crude residue was purified by flash silica gel chromatography (20:1:0.25 EtOAc/MeOH/NH_4OH), affording a 92:8 mixture of rotamers of **4b** (determined by ^{1}H NMR integration of the set of C2' proton signals {δ_{Major} = 8.70 ppm (d), δ_{Minor} = 8.61 ppm (d)}) as a light yellow solid (2.58 g, 92%). mp = 142-145 °C. $[\alpha]_{20}^{D}$ = +109.6°, (*c* = 1.32, $CHCl_3$). Major rotamer ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (d, *J* = 4.5 Hz, 1H), 8.05 (s, 1H), 7.99 (d, *J* = 9.0 Hz, 1H), 7.53 (d, *J* = 4.5 Hz, 1H), 7.31 (dd, *J* = 9.1 Hz and 2.2 Hz, 1H), 6.24 (s, 1H), 3.41 (m, 1H), 3.14 (m, 1H), 2.94-2.75 (m, 3H), 2.30 (t, *J* = 11.5 Hz, 1H), 1.76 (s, 1H), 1.64-1.32 (m, 6H), 1.12-0.98 (m, 21H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.4, 148.1, 146.2, 143.3, 130.9, 127.2, 123.5, 118.9, 106.6, 72.6, 60.7, 51.3, 50.2, 37.5, 26.7, 26.6, 25.1, 19.3, 18.3, 12.9,

12.2; IR (film) ν 2942, 2867, 1618, 1463, 1231, 1118, 1008, 881, 749; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{28}H_{45}N_2O_2Si$: 469.3250. Found: 469.3247.

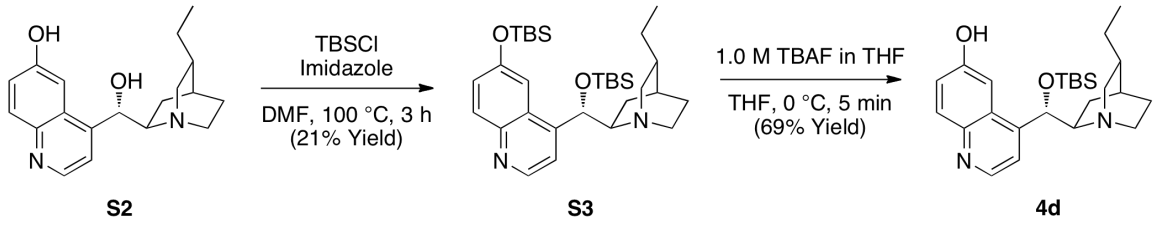


4-((*S*)-((*tert*-butyldiphenylsilyl)oxy)((1*S*,2*R*,4*S*,5*S*)-5-ethylquinuclidin-2-yl)methyl)quinolin-6-ol (4c). To a room temperature solution of dihydroquinidine **1** (500 mg, 1.53 mmol, 1 Eq.) and diisopropylethylamine (0.80 mL, 4.59 mmol, 3 Eq.) in methylene chloride (4 mL) was added *tert*-butyldiphenylsilyl chloride (0.80 mL, 3.06 mmol, 2 Eq.). The reaction was stirred at room temperature for 24 hours, at which point the reaction was complete as indicated by TLC analysis (20:1:0.25 ethyl acetate/methanol/ammonium hydroxide). The reaction was quenched with saturated aqueous $NaHCO_3$ (12 mL) and the aqueous layer was extracted with methylene chloride (2 x 10 mL). The organic layers were combined, dried over Na_2SO_4, and the solvent was removed *in vacuo*. Purification of the crude residue by flash silica gel chromatography (25:1 ethyl acetate/methanol) afforded **S1** as a white foam (759 mg, 88% yield). ^1H NMR (400 MHz, $CDCl_3$): δ 8.64 (d, *J* = 4.6 Hz, 0.6H), 8.51 (d, *J* = 4.3 Hz, 0.4H), 8.06 (d, *J* = 2.7 Hz, 0.4H), 8.00 (d, *J* = 9.2 Hz, 0.4H), 7.88 (d, *J* = 9.2 Hz, 0.6H), 7.76 (dd, *J* = 7.8 Hz and 1.4 Hz, 0.8H), 7.63 (dd, *J* = 7.8 Hz and 1.2 Hz, 1.2H), 7.58 (d, *J* = 4.6 Hz, 0.6H), 7.52-7.40 (m, 1.2H), 7.40-7.32 (m, 2H), 7.32-7.19 (m, 3H), 7.16 (d, *J* = 6.8 Hz, 0.8H), 7.13-7.02 (m, 1.9H), 6.78 (m, 1H), 5.49 (d, *J* = 7.1 Hz, 0.6H), 4.79 (d, *J* = 9.9 Hz, 0.4H), 4.00 (s, 1.2H), 3.76 (s, 1.8H), 3.55 (q, *J* = 9.1 Hz, 0.4H), 2.99 (q, *J* = 8.3 Hz,

0.6H), 2.74 (dd, *J* = 13.2 Hz and 9.5 Hz, 0.6H), 2.68-2.36 (m, 2.8H), 1.98 (dd, *J* = 12.2 Hz and 7.9 Hz, 0.4H), 1.77-1.65 (m, 1.5H), 1.62 (s, 0.6H), 1.58-1.43 (m, 1.8H), 1.43-1.25 (m, 1.8H), 1.25-1.05 (m, 1.5H), 0.98 (s, 5.4H), 0.93 (s, 3.6H), 0.78 (m, 2.6H), 0.67 (m, 1.4H)

Intermediate **S1** (350 mg, 0.620 mmol, 1 Eq.) was dissolved in dry N,N-dimethylformamide (6.2 mL). Then, to a flame-dried round bottom flask under an argon atmosphere was added sodium ethanethiolate (208.6 mg, 2.48 mmol, 4 Eq.). The catalyst solution was then transferred to the reaction flask via syringe and the reaction was placed into a 105 °C oil bath and stirred for 15 hours. Upon completion, as indicated by TLC analysis (20:1:0.25 ethyl acetate/methanol/ammonium hydroxide), the reaction was removed from the oil bath and allowed to cool to room temperature. After quenching with saturated aqueous NH_4Cl (10 mL) and H_2O (10 mL), the aqueous layer was extracted with methylene chloride (3 x 20 mL). The organic layers were combined and the residue was washed with H_2O (2 x 20 mL) and brine (1 x 20 mL). After drying over Na_2SO_4, the remaining solvent was removed *in vacuo*, and the crude residue was purified by preparative TLC (15:1:0.5 EtOAc/MeOH/NH_4OH), affording a 78:22 mixture of rotamers (determined by ^1H NMR integration of the set of C2' proton signals {δ_{Major} = 8.45 ppm (d), δ_{Minor} = 8.42 ppm (d)}) of **4c** as a light yellow solid (31.8 mg, 9%). mp = 135-140 °C $[\alpha]_{20}^{D}$ = +12.4°, (*c* = 0.57). ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, *J* = 4.5 Hz, 0.7H), 8.42 (d, *J* = 4.3 Hz, 0.3H), 8.04 (d, *J* = 1.8 Hz, 0.3H), 7.89 (d, *J* = 9.1 Hz, 0.3H), 7.84 (d, *J* = 9.0 Hz, 0.7H), 7.66 (m, 2H), 7.55 (s, 0.7H), 7.48 (d, *J* = 7.3 Hz, 1.4H), 7.45-7.35 (m, 1.6H), 7.30-7.15 (m, 3.4H), 7.15-6.95 (m, 3.3H), 6.73 (d, *J* = 4.3 Hz, 0.3H), 6.10 (s, 0.7H), 4.71 (d, *J* = 10.0 Hz, 0.3H), 3.64 (m, 0.3H), 3.18 (m, 0.7H), 2.93-

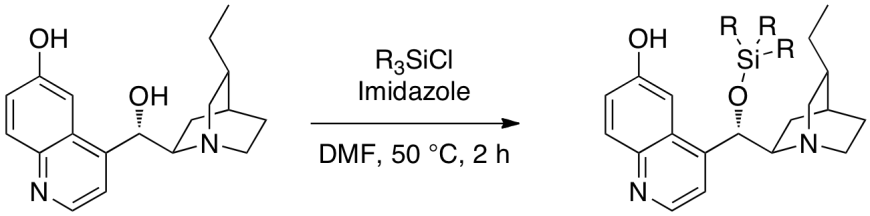
2.43 (m, 4H), 2.27 (m, 0.7H), 2.04 (m, 0.3H), 2.01 (s, 0.3H), 1.71 (s, 0.7H), 1.61 (m, 0.3H), 1.55-1.20 (m, 5.6H), 1.11 (s, 7.5H), 0.92 (m, 0.3H), 0.84 (m, 4H), 0.76 (m, 0.6H), 0.67 (m, 0.7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4, 147.1, 146.1, 146.0, 143.2, 136.1, 136.0, 133.6, 133.0, 130.7, 129.8, 129.7, 127.9, 127.6, 127.5, 122.6, 119.3, 106.3, 72.9, 60.8, 51.1, 50.0, 37.4, 27.5, 27.1, 26.6, 25.2, 20.1, 19.7, 12.2; IR (film) ν 2931, 2858, 1618, 1464, 1216, 1110, 1060, 821, 750, 700; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{35}H_{43}N_2O_2Si$: 551.3096. Found: 551.3101.



S2 **S3** **4d**

4-((*S*)-((*tert*-butyldimethylsilyl)oxy)((1*S*,2*R*,4*S*,5*S*)-5-ethylquinuclidin-2-yl)methyl)quinolin-6-ol (4d). In a reaction vial with a magnetic stirbar 6'-hydroxyhydroquinidine **S2** (100 mg, 0.320 mmol, 1 Eq.) and imidazole (131 mg, 1.92 mmol, 6 Eq.) were dissolved in N,N-dimethylformamide (200 µL) with ultrasonic aid. Next *tert*-butyldimethylsilyl chloride (193 mg, 1.28 mmol, 4 Eq.) was then added and the reaction was heated to 100 °C for 3 hours. After the allotted time the mixture was quenched with 2 mL pH 7.0 buffer and extracted with methylene chloride (2 x 2 mL). The combined organic layer was then washed with pH 7.0 buffer (1 x 5 mL) followed by brine (1 x 5 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude residue was purified by preparative TLC with 20:1:0.25 ethyl acetate/Methanol/Ammonium hydroxide. The resulting di-TBS protected intermediate **S3** (37 mg, 0.068 mmol, 1 Eq.) was then dissolved in THF (0.4 mL), cooled to 0 °C, and

1.0 M TBAF in THF (68 µL, 0.068 mmol, 1 Eq.) was added via syringe. The reaction was stirred at that temperature for 5 minutes, quenched with 2 mL saturated aqueous ammonium chloride, extracted with methylene chloride (2 x 2 mL), and the combined organic layers were dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude residue was purified by preparative TLC (12:1:0.25 ethyl acetate/methanol/ammonium hydroxide), affording **4d** as a light yellow foam (20 mg, 15% over two steps). mp = 198-202 °C (decomp.). $[\alpha]_{20}^{D}$= +162.2°, (*c* = 0.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, *J* = 4.3 Hz, 1H), 8.19 (s, 1H), 8.00 (d, *J* = 9.0 Hz, 1H), 7.48 (d, *J* = 4.3 Hz, 1H), 7.32 (d, *J* = 9.0 Hz, 1H), 6.63 (bs, 1H), 6.02 (s, 1H), 3.30 (m, 1H), 3.10 (m, 1H), 2.88-2.65 (m, 3H), 2.30 (t, *J* = 11.1 Hz, 1H), 1.73 (s, 1H), 1.63-1.30 (m, 6H), 0.96 (s, 9H), 0.92 (t, *J* = 6.7 Hz, 3H), 0.15 (s, 3H), -0.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 147.3, 146.6, 143.8, 131.3, 126.9, 124.0, 118.7, 107.1, 71.7, 60.0, 50.6, 50.1, 37.4, 26.6, 26.5, 26.2, 25.2, 18.7, 18.1, 12.2, -4.5, -4.7 ; IR (film) ν 3077, 2954, 2930, 2858, 1619, 1469, 1255, 1115, 1003, 832, 779, 732; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{25}H_{39}N_2O_2Si$: 427.2781. Found: 427.2775.



S2 R = Et (**4e**) or Me (**4f**)

Catalysts 4e and 4f. In a reaction vial with a magnetic stirbar, 6'-hydroxyhydroquinidine **S2** (100 mg, 0.320 mmol, 1 Eq.) and imidazole (109 mg, 1.60 mL, 5 Eq.) were dissolved in N,N-dimethylformamide (200 µL) with ultrasonic aid. The

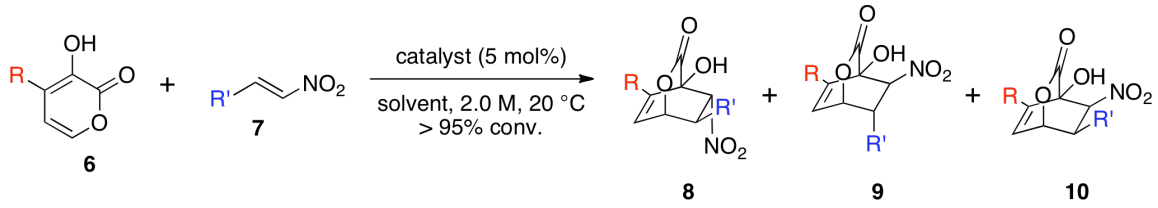
corresponding silyl chloride (1.28 mmol, 4 Eq.) was then added and the reaction was heated to 50 °C for 2 hours. After the allotted time the mixture was quenched with 2 mL pH 7.0 buffer and extracted with methylene chloride (2 x 2 mL). The combined organic layer was then washed with pH 7.0 buffer (1 x 5 mL) followed by brine (1 x 5 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the crude residue was purified by preparative TLC (20:1:0.25 ethyl acetate/methanol/ammonium hydroxide for catalyst **4e** and 10:1:0.25 ethyl acetate/methanol/ammonium hydroxide for catalyst **4f**).

4-((*S*)-((1*S*,2*R*,4*S*,5*S*)-5-ethylquinuclidin-2-yl)((triethylsilyl)oxy)methyl)quinolin-6-ol (4e). Yellow solid (70 mg, 51%). mp = 118-122 °C. $[\alpha]_{20}^{D}$ = +136.5°, (*c* = 1.095, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (d, *J* = 4.4 Hz, 1H), 8.17 (s, 1H), 7.99 (d, *J* = 9.0 Hz, 1H), 7.45 (d, *J* = 4.4 Hz, 1H), 7.31 (dd, *J* = 8.8 Hz and 1.8 Hz, 1H), 6.03 (s, 1H), 5.25 (bs, 1H), 3.38 (dd, *J* = 12.4 Hz and 7.2 Hz, 1H), 3.11 (dd, *J* = 12.3 Hz and 9.4 Hz, 1H), 2.88-2.74 (m, 3H), 2.35 (t, *J* = 11.1 Hz, 1H), 1.74 (s, 1H), 1.66-1.34 (m, 5H), 0.98 (m, 1H), 0.95 (t, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.54 (q, *J* = 7.7 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 147.1, 146.5, 143.7, 131.2, 126.9, 124.0, 118.4, 107.2, 71.6, 60.0, 50.6, 50.2, 37.1, 26.5, 26.3, 25.2, 18.6, 12.1, 7.0, 5.0; IR (film) ν 2953, 2875, 1618, 1465, 1239, 1119, 1005, 860, 819, 746; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{25}H_{39}N_2O_2Si$: 427.2781. Found: 427.2773.

4-((*S*)-((1*S*,2*R*,4*S*,5*S*)-5-ethylquinuclidin-2-yl)((trimethylsilyl)oxy)methyl)quinolin-6-ol (4f). Light yellow solid (53 mg, 43%). mp = 175-177 °C (decomp.). $[\alpha]_{20}^{D}$ = +249.5°, (*c* = 0.74, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, *J* = 4.3 Hz, 1H), 8.27 (s, 1H),

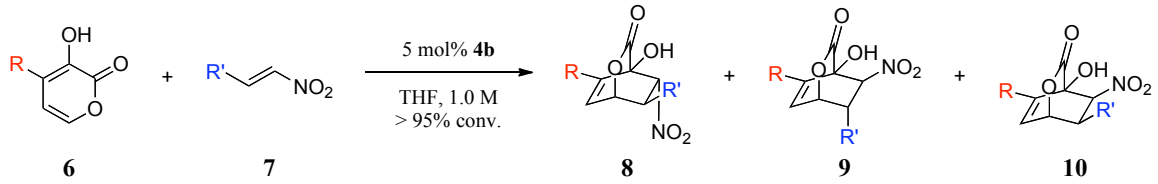
7.98 (d, *J* = 9.0 Hz, 1H), 7.42 (d, *J* = 3.4 Hz, 1H), 7.31 (d, *J* = 8.9 Hz, 1H), 5.93 (s, 1H), 3.33 (m, 1H), 3.14 (t, *J* = 10.8 Hz, 1H), 2.88-2.74 (m, 3H), 2.35 (t, *J* = 10.1 Hz, 1H), 1.74 (s, 1H), 0.98 (m, 1H), 1.68-1.34 (m, 5H), 0.95 (t, *J* = 6.9 Hz, 3H), -0.03 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.6, 146.5, 146.4, 143.6, 131.3, 126.8, 124.0, 118.4, 107.1, 71.4, 59.7, 50.2, 50.0, 36.9, 26.4, 26.2, 25.2, 24.6, 18.5, 12.1, 0.2; IR (film) ν 2954, 2874, 1619, 1467, 1251, 1119, 879, 839, 751; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{22}H_{33}N_2O_2Si$: 385.2311. Found: 385.2316.

3. Preparation of Racemic Cycloadducts



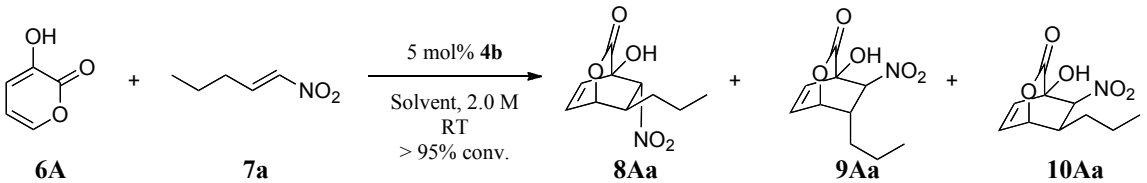
To a room temperature solution of 2-pyrone **6** (0.060 mmol) in THF (60 µL) was added Et_3N (0.009 mmol) followed by nitroolefin **7** (0.120 mmol). Upon completion of the reaction, as indicated by TLC analysis (2:1 Hexanes/Ethyl Acetate), the solvent was removed *in vacuo* without heating. After NMR analysis, the residue was purified by preparative TLC with hexanes/ethyl acetate and **8** was subjected to HPLC analysis.

4. Preparation of Chiral Cycloadducts



2-Pyrone **6** (0.200 mmol, 1 Eq.) and catalyst **4b** (4.7 mg, 0.010 mmol, 0.05 Eq) were dissolved in THF (200 µL). The reaction mixture was then cooled to the appropriate temperature and nitroolefin **7** (0.400 mmol) was then added. The reaction mixture was then stirred at the appropriate temperature for the time indicated and upon completion of the reaction, as indicated by TLC analysis (2:1 Hexanes/Ethyl Acetate), the crude reaction mixture was passed through a short silica gel plug, which was eluted with cold ethyl acetate (3-4 mL). The eluent was then concentrated *in vacuo* without heating. After NMR analysis, the crude residue was purified by silica gel column chromatography (hexanes/ethyl acetate) and subjected to HPLC analysis.

5. Solvent Screen



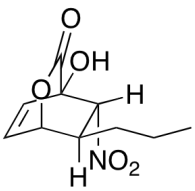
6A **7a** **8Aa** **9Aa** **10Aa**

Entry	Solvent	Time (h)	**8Aa** : **9Aa** : **10Aa**[a]	ee[b] **8** (%)
1	CH_2Cl_2	2	72 : 19 : 9	88
2	THF	1.5	80 : 14 : 6	92
3	$CHCl_3$	4	73 : 23 : 4	84
4	Toluene	4	72 : 21 : 7	88
5	MeOH	17.5	68 : 26 : 6	61
6	Et_2O	1.5	75 : 20 : 5	91
7	EtOAc	1.5	76 : 18 : 6	90

a) Unless noted, reactions were performed with 0.060 mmol **6A** and 0.120 mmol **7a** in 30 μL solvent.
b) Determined by ^{1}H NMR analysis (see Section 6). c) Determined by chiral HPLC analysis (see Section 6).

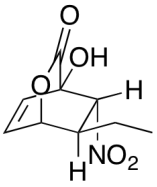
Figure S3. Solvent screen for asymmetric [4+2] addition with aliphatic nitroalkenes.

6. Characterization of Cycloadducts



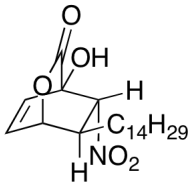
4-hydroxy-8-nitro-7-propyl-2-oxabicyclo[2.2.2]oct-5-en-3-one

***endo*-(8Aa)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-1-nitro-1-pentene **7a** (46.1 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at -20 °C for 20 h to furnish the crude product as a mixture of diastereomers (**8Aa** : **9Aa** : **10Aa** = 82 : 8 : 10, determined by ^{1}H NMR by integration of the C7 and C8 proton signals{δ_{8Aa} = 2.48 ppm (dt), δ_{9Aa} = 2.8 ppm (m), δ_{10Aa} = 5.01 (d)}). The crude product was purified by flash silica gel chromatography (4.5:1 hexanes/ethyl acetate) to afford an inseparable 92:8 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Aa} = 4.36 ppm (d), δ_{10Aa} = 5.01 ppm (d)}) of **8Aa** and **10Aa** as a colorless oil (37.1 mg, 82% yield). Adduct **8Aa** was obtained in 96% ee (determined by chiral HPLC: Chiralcel AD-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 22.1 min, t_R(minor) = 18.0 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.64 (dd, *J* = 7.9 Hz and 5.5 Hz, 1H), 6.42 (d, *J* = 7.9, 1H), 5.16 (d, *J* = 4.9 Hz, 1H), 4.36 (d, *J* = 3.6 Hz, 1H), 4.08 (bs, 1H), 2.48 (dt, *J* = 3.6 Hz and 7.7 Hz, 1H), 1.69 (m, 2H), 1.47 (m, *J* = 7.3 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 133.2, 130.3, 87.3, 76.9, 76.6, 47.3, 34.1, 20.2, 13.8; IR (neat) ν 3442, 2962, 2932, 2874, 1758, 1554, 1358, 1149, 958; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{10}H_{14}NO_5$: 228.0872. Found: 228.0871.



7-ethyl-4-hydroxy-8-nitro-2-oxabicyclo[2.2.2]oct-5-en-3-one

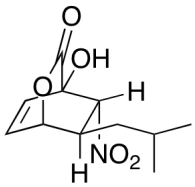
***endo*-(8Ab)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-1-nitro-1-butene **7b** (40.4 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at -20 °C for 28 h to furnish the crude product as a mixture of diastereomers (**8Ab** : **9Ab** : **10Ab** = 81 : 9 : 10, determined by ^{1}H NMR by integration of the C6 and C8 proton signals {δ_{8Ab} = 6.64 ppm (dd), δ_{9Ab} = 6.56 ppm (dd), δ_{10Ab} = 5.01 ppm (d)}). The crude product was purified by flash silica gel chromatography (4.5:1 hexanes/ethyl acetate) to afford an inseparable 91:9 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Ab} = 4.36 ppm (d), δ_{10Ab} = 5.01 ppm (d)}) of **8Ab** and **10Ab** as a white solid (32.8 mg, 77% yield). Adduct **8Ab** was obtained in 95% ee (determined by chiral HPLC: Chiralcel AD-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 16.2 min, t_R(minor) = 38.8 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.64 (dd, *J* = 8.0 Hz and 5.4 Hz, 1H), 6.44 (d, *J* = 8.0, 1H), 5.18 (d, *J* = 5.2 Hz, 1H), 4.32 (d, *J* = 3.7 Hz, 1H), 3.87 (s, 1H), 2.38 (dt, *J* = 3.7 Hz and 7.7 Hz, 1H), 1.71-1.81 (m, *J* = 7.2 Hz, 2H), 1.09 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 133.4, 130.3, 87.2, 76.5, 49.2, 25.2, 11.6; IR (neat) ν 3444, 2970, 2937, 2881, 1756, 1555, 1359, 1148, 960; HRMS (ESI/$[M+H]^+$) Calculated for: $C_9H_{12}NO_5$: 214.0715. Found: 214.0719.



4-hydroxy-8-nitro-7-tetradecyl-2-oxabicyclo[2.2.2]oct-5-en-3-one

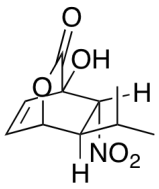
***endo*-(8Ac)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-1-nitro-1-hexadecene **7c** (107.8 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at 0 °C for 21 h to furnish the crude product as a mixture of

diastereomers (**8Ac** : **9Ac** : **10Ac** = 81 : 9 : 10, determined by ^{1}H NMR by integration of the C7 and C8 proton signals{δ_{8Ac} = 2.46 ppm (dt), δ_{9Ac} = 2.77 ppm (m), δ_{10Ac} = 4.99 ppm (d)}). The crude product was purified by flash silica gel chromatography (5.5:1 hexanes/ethyl acetate) to afford an inseparable 94:6 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Ac} = 4.31 ppm (d), δ_{10Ac} = 4.99 ppm (d)}) of **8Ac** and **10Ac** as a white solid (56.7 mg, 75% yield). Adduct **8Ac** was obtained in 95% ee (determined by chiral HPLC: Chiralcel AD-H, Hexanes/Isopropanol = 85:15, 1.0 mL/min, λ = 220 nm, t_R(major) = 9.3 min, t_R(minor) = 11.3 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.64 (dd, *J* = 8.0 Hz and 5.5 Hz, 1H), 6.43 (d, *J* = 7.8, 1H), 5.16 (d, *J* = 4.6 Hz, 1H), 4.31 (d, *J* = 3.7 Hz, 1H), 3.84 (bs, 1H), 2.46 (dt, *J* = 3.8 Hz and 7.8 Hz, 1H), 1.70 (m, 2H), 1.42 (m, 2H), 1.25 (s, 22H), 0.88 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 133.3, 130.3, 87.5, 76.9, 76.6, 47.6, 32.2, 32.1, 29.9, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.5, 29.4, 22.9, 14.3; IR (film) ν 3417, 2917, 2850, 1768, 1553, 1467, 1357, 1146, 959; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{21}H_{36}NO_5$: 382.2593. Found: 382.2592.



4-hydroxy-7-isobutyl-8-nitro-2-oxabicyclo[2.2.2]oct-5-en-3-one *endo*-(8Ad) (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-4-methyl-1-nitro-1-pentene **7d** (51.7 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at -20 °C for 28 h to furnish the crude product as a mixture of diastereomers (**8Ad** : **9Ad** : **10Ad** = 80 : 9 : 11, determined by ^{1}H NMR by integration of the C7 and C8 proton signals {δ_{8Ad} = 2.57 ppm (m), δ_{9Ad} = 2.87 ppm (m), δ_{10Ad} = 4.99

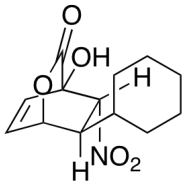
ppm (d)}). The crude product was purified by flash silica gel chromatography (5:1 hexanes/ethyl acetate) to afford an inseparable 92:8 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Ad} = 4.32 ppm (d), δ_{10Ad} = 4.99 ppm (d)}) of **8Ad** and **10Ad** as a colorless oil (38.8 mg, 81% yield). Adduct **8Ad** was obtained in 97% ee (determined by chiral HPLC: Chiralcel OJ-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 12.2 min, t_R(minor) = 9.6 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.66 (dd, *J* = 7.9 Hz and 5.5 Hz, 1H), 6.42 (d, *J* = 7.9 Hz, 1H), 5.12 (d, *J* = 5.5 Hz, 1H), 4.32 (d, *J* = 3.7 Hz, 1H), 3.93 (bs, 1H), 2.57 (m, *J* = 3.6 Hz, 1H), 1.73 (m, *J* = 3.6 Hz, 1H), 1.56 (m, 2H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 133.1, 130.5, 87.5, 77.2, 76.6, 45.4, 41.2, 25.6, 22.8, 22.2; IR (neat) ν 3439, 2960, 2933, 2873, 1759, 1556, 1359, 1151, 958; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{11}H_{16}NO_5$: 242.1028. Found: 242.1033.



4-hydroxy-7-isopropyl-8-nitro-2-oxabicyclo[2.2.2]oct-5-en-3-one

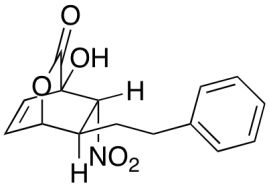
***endo*-(8Ae)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-3-methyl-1-nitro-1-butene **7e** (46.1 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at 0 °C for 46 h to furnish the crude product as a mixture of diastereomers (**8Ae** : **9Ae** : **10Ae** = 77 : 23 : 0, determined by ^{1}H NMR by integration of the set of the C6 proton signals {δ_{8Ae} = 6.66 ppm (dd), δ_{9Ae} = 6.56 ppm (dd)}). The crude product was purified by flash silica gel chromatography (5:1 hexanes/ethyl acetate) to afford pure *endo*-**8Ae** as a colorless oil (33.7 mg, 74% yield) in 96% ee (determined by chiral HPLC: Chiralcel OJ-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 29.5

min, t_R(minor) = 12.5 min). $[\alpha]_{20}^{D}$ = +10.1°, (*c* = 1.40, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.66 (dd, *J* = 7.9 Hz and 5.5 Hz, 1H), 6.38 (d, *J* = 7.9 Hz, 1H), 5.36 (d, *J* = 5.5 Hz, 1H), 4.48 (d, *J* = 3.7 Hz, 1H), 4.10 (s, 1H), 2.19 (dd, *J* = 9.7 Hz and 4.2 Hz, 1H), 1.85 (m, 1H), 1.10 (d, *J* = 6.1 Hz, 3H), 1.06 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 133.0, 130.7, 86.5, 76.9, 75.2, 54.2, 29.9, 20.8, 20.4; IR ($CHCl_3$) ν 3439, 2968, 1758, 1556, 1357, 1151, 951; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{10}H_{14}NO_5$: 228.0872. Found: 228.0869.



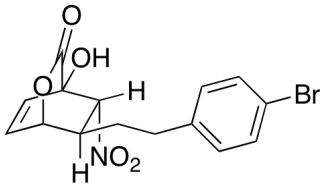
7-cyclohexyl-4-hydroxy-8-nitro-2-oxabicyclo[2.2.2]oct-5-en-3-one *endo*-(8Af) (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-(2-nitrovinyl)cyclohexane **7f** (62.1 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at 0 °C for 54 h to furnish the crude product as a mixture of diastereomers (**8Af** : **9Af** : **10Af** = 78 : 22 : 0, determined by ^{1}H NMR by integration of the set of the C6 proton signals{δ_{8Af} = 6.65 ppm (dd), δ_{10Af} = 6.57 ppm (dd)}). The crude product was purified by flash silica gel chromatography (5:1 hexanes/ethyl acetate) to afford pure *endo*-**8Af** as a white foam (43.0 mg, 81% yield) in 96% ee (determined by chiral HPLC: Chiralcel AD-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 24.2 min, t_R(minor) = 18.6 min). $[\alpha]_{19}^{D}$ = +22.1°, (*c* = 0.92, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.65 (dd, *J* = 7.9 Hz and 5.5 Hz, 1H), 6.38 (d, *J* = 7.9 Hz, 1H), 5.41 (d, *J* = 4.9 Hz, 1H), 4.52 (d, *J* = 3.7 Hz, 1H), 4.17 (bs, 1H), 2.24 (dd, *J* = 9.7 Hz and 3.6 Hz, 1H), 1.63-2.01 (m, 5H), 1.50 (m, 1H), 0.92-1.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 133.0, 130.7, 86.3, 76.9, 74.4, 53.1, 38.9, 31.2, 30.4, 26.0, 25.9, 25.7; IR ($CHCl_3$)

ν 3434, 2929, 2855, 1760, 1556, 1357, 1155, 958; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{13}H_{18}NO_5$: 268.1185. Found: 268.1187.



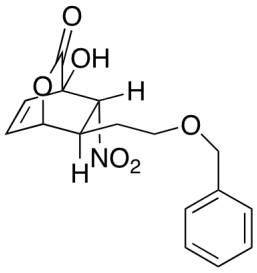
4-hydroxy-8-nitro-7-phenethyl-2-oxabicyclo[2.2.2]oct-5-en-3-one

***endo*-(8Ag)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-(4-nitro-3-butenyl)benzene **7g** (70.9 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at -20 °C for 20 h to furnish the crude product as a mixture of diastereomers (**8Ag** : **9Ag** : **10Ag** = 74 : 15 : 11, determined by ^{1}H NMR by integration of the C8 proton signals {δ_{8Ag} = 4.39 ppm (d), δ_{9Ag} = 4.55 ppm (d), δ_{10Ag} = 5.00 ppm (d)}). The crude product was purified by flash silica gel chromatography (4:1 hexanes/ethyl acetate) to afford an inseparable 90:10 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Ag} = 4.39 ppm (d), δ_{10Ag} = 5.00 ppm (d)}) of **8Ag** and **10Ag** as a white solid (45.5 mg, 79% yield). Adduct **8Ag** was obtained in 96% ee (determined by chiral HPLC: Chiralcel OJ-H, Hexanes/Isopropanol = 65:35, 1.0 mL/min, λ = 220 nm, 67 bar, t_R(major) = 50.0 min, t_R(minor) = 41.0 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (m, 3H), 7.13 (d, *J* = 7.3 Hz, 2H), 6.60 (dd, *J* = 7.9 Hz and 5.5 Hz, 1H), 6.42 (d, *J* = 7.9 Hz, 1H), 5.14 (d, *J* = 5.5 Hz, 1H), 4.40 (d, *J* = 3.6 Hz, 1H), 3.95 (s, 1H), 2.78 (m, 2H), 2.46 (dt, *J* = 3.6 Hz and 7.6 Hz, 1H), 2.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 139.6, 133.0, 130.0, 128.7, 128.3, 128.2, 126.5, 87.0, 76.8, 76.4, 46.5, 33.6, 32.7; IR ($CDCl_3$) ν 3445, 3028, 2930, 1759, 1555, 1358, 1148, 955; HRMS (ESI/$[M+Na]^+$) Calculated for: $C_{15}H_{15}NO_5Na$: 312.0848. Found: 312.0846.



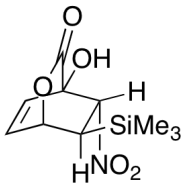
7-(4-bromophenethyl)-4-hydroxy-8-nitro-2-oxabicyclo[2.2.2]oct-5-en-3-one

***endo*-(8Ah)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-1-bromo-4-(4-nitrobut-3-en-1-yl)benzene **7h** (102.4 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at -20 °C for 20 h to furnish the crude product as a mixture of diastereomers (**8Ah** : **9Ah** : **10Ah** = 74 : 18 : 8, determined by ^{1}H NMR by integration of the set of the C8 proton signals {δ_{8Ah} = 4.49 ppm (d), δ_{9Ah} = 4.55 ppm (d), δ_{10Ah} = 4.98 ppm (d)}). The crude product was purified by flash silica gel chromatography (4.5:1 hexanes/ethyl acetate) to afford an inseparable 92:8 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Ah} = 4.38 ppm (d), δ_{10Ah} = 4.98 ppm (d)}) of **8Ah** and **10Ah** as a white foam (50.0 mg, 68% yield). Adduct **8Ah** was obtained in 95% ee (determined by chiral HPLC: Chiralcel AD-H, Hexanes/Isopropanol = 75:25, 1.0 mL/min, λ = 240 nm, 56 bar, t_R(major) = 32.2 min, t_R(minor) = 24.4 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.3 Hz, 2H), 7.02 (d, *J* = 8.3 Hz, 2H), 6.61 (dd, *J* = 8.0 Hz and 5.4 Hz, 1H), 6.44 (d, *J* = 8.0 Hz, 1H), 5.14 (d, *J* = 5.2 Hz, 1H), 4.38 (d, *J* = 3.2 Hz, 1H), 3.87 (s, 1H), 2.85-2.63 (m, 2H), 2.44 (dt, *J* = 3.8 Hz and 7.3 Hz, 1H), 2.11-1.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 138.7, 133.4, 132.1, 130.2, 130.1, 120.6, 87.2, 77.0, 76.9, 76.6, 46.7, 33.7, 32.4; IR (film) ν 3449, 2931, 2867, 1765, 1556, 1359, 1150, 756; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{15}H_{15}BrNO_5$: 368.0134. Found: 368.0124.



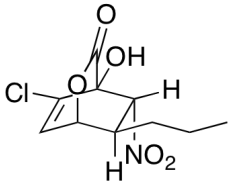
7-(2-(benzyloxy)ethyl)-4-hydroxy-8-nitro-2-oxabicyclo[2.2.2]oct-5-en-3-one

***endo*-(8Ai)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and ((((E)-4-nitro-3-butenyl)oxy)methyl)benzene **7i** (82.9 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at 0 °C for 20 h to furnish the crude product as a mixture of diastereomers (**8Ai** : **9Ai** : **10Ai** = 79 : 11 : 10, determined by ^{1}H NMR by integration of the C7 and C8 proton signals {δ_{8Ai} = 2.78 ppm (dt), δ_{9Ai} = 3.03 ppm (m), δ_{10Ai} = 4.98 ppm (d)}). The crude product was purified by flash silica gel chromatography (4.5:1 hexanes/ethyl acetate) to afford an inseparable 89:11 mixture (determined by ^{1}H NMR by integration of the set of C6 proton signals {δ_{8Ai} = 6.61 ppm (dd), δ_{10Ai} = 6.53 ppm (dd)}) of **8Ai** and **10Ai** as a white solid (49.6 mg, 78% yield). Adduct **7Ai** was obtained in 96% ee (determined by chiral HPLC: Chiralcel AD-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 14.9 min, t_R(minor) = 11.4 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37-7.26 (m, 5H), 6.61 (dd, *J* = 5.5 Hz and 7.9 Hz, 1H), 6.38 (d, *J* = 7.9 Hz, 1H), 5.13 (d, *J* = 4.9 Hz, 1H), 4.51 (d, *J* = 3.7 Hz, 1H), 4.47-4.39 (dd, *J* = 11.6 Hz and 17.1 Hz, 2H), 3.65-3.56 (m, 3H), 2.76 (m, 1H), 2.06-1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 137.6, 132.9, 130.4, 128.7, 128.2, 128.1, 86.7, 77.4, 76.5, 73.5, 70.0, 45.0, 32.0; IR ($CDCl_3$) ν 3445, 3031, 2925, 2864, 1763, 1557, 1359, 1149, 1099, 906; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{16}H_{18}NO_6$: 320.1134. Found: 320.1137.



4-hydroxy-8-nitro-7-(trimethylsilyl)-2-oxabicyclo[2.2.2]oct-5-en-3-one

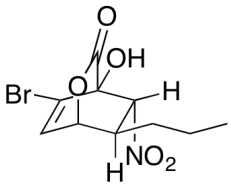
***endo*-(8Aj)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-2-pyrone **6A** (22.4 mg, 0.200 mmol, 1 Eq.) and (E)-trimethyl-(2-nitrovinyl)silane **7j** (58.1 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at -20 °C for 4.5 h to furnish the crude product as a mixture of diastereomers (**8Aj** : **9Aj** : **10Aj** = 90 : 3 : 7, determined by ^{1}H NMR by integration of the set of the C8 proton signals {δ_{8Aj} = 4.59 ppm (d), δ_{9Aj} = 4.75 ppm (d), δ_{10Aj} = 5.05 ppm (d)}). The crude product was purified by flash silica gel chromatography (4.5:1 hexanes/ethyl acetate) to afford an inseparable 93:7 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Aj} = 4.59 ppm (d), δ_{10Aj} = 5.05 ppm (d)}) of **8Aj** and **10Aj** as an off-white solid (39.5 mg, 77% yield). Adduct **8Aj** was obtained in 95% ee (determined by chiral HPLC: Chiralcel AD-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 14.6 min, t_R(minor) = 22.4 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.69 (dd, *J* = 5.5 Hz and 7.9 Hz, 1H), 6.40 (d, *J* = 7.9 Hz, 1H), 5.33 (d, *J* = 4.9 Hz, 1H), 4.59 (d, *J* = 4.3 Hz, 1H), 4.04 (s, 1H), 1.79 (d, *J* = 3.7 Hz, 1H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 132.1, 131.6, 84.8, 77.4, 75.1, 36.6, -2.7; IR ($CHCl_3$) ν 3444, 3092, 2956, 2902, 1757, 1556, 1353, 1256, 1148, 953, 843; HRMS (ESI/$[M+Na]^+$) Calculated for: $C_{10}H_{15}NO_5SiNa$: 280.0617. Found: 280.0607.



5-chloro-4-hydroxy-8-nitro-7-propyl-2-oxabicyclo[2.2.2]oct-5-en-3-one

***endo*-(8Ba)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5

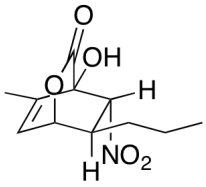
mol %) catalyzed reaction of 4-chloro-3-hydroxy-2-pyrone **6B** (29.3 mg, 0.200 mmol, 1 Eq.) and (E)-1-nitro-1-pentene **7a** (46.1 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at 0 °C for 28 h to furnish the crude product as a mixture of diastereomers (**8Ba** : **9Ba** : **10Ba** = 89 : 1 : 10, determined by ^{1}H NMR by integration of the C7 and C8 proton signals {δ_{8Ba} = 2.56 ppm (dt), δ_{9Ba} = 2.85 ppm (m), δ_{10Ba} = 5.06 ppm (d)}). The crude product was purified by flash silica gel chromatography (5:1 hexanes/ethyl acetate) to afford an inseparable 92:8 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Ba} = 4.42 ppm (d), δ_{10Ba} = 5.06 ppm (d)}) of **8Ba** and **10Ba** as a colorless oil (45.0 mg, 86% yield). Adduct **8Ba** was obtained in 96% ee (determined by chiral HPLC: Chiralcel AD-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 16.6 min, t_R(minor) = 24.3 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.68 (d, *J* = 6.0 Hz, 1H), 5.18 (d, *J* = 5.9 Hz, 1H), 4.42 (d, *J* = 3.7 Hz, 1H), 4.02 (s, 1H), 2.55 (td, *J* = 7.4 Hz and 3.7 Hz, 1H), 1.78-1.65 (m, 2H), 1.54-1.43 (m, *J* = 7.3 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 135.8, 125.8, 86.5, 76.9, 76.0, 47.2, 34.0, 20.2, 13.8; IR (neat) ν 3455, 2963, 2934, 2875, 1767, 1560, 1357, 1152, 966; HRMS (ESI/$[M+Na]^+$) Calculated for: $C_{10}H_{12}ClNO_5Na$: 284.0302. Found: 284.0292.



5-bromo-4-hydroxy-8-nitro-7-propyl-2-oxabicyclo[2.2.2]oct-5-en-3-one

***endo*-(8Ca)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 4-bromo-3-hydroxy-2-pyrone **6C** (38.2 mg, 0.200 mmol, 1 Eq.) and (E)-1-nitro-1-pentene **7a** (46.1 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at 0 °C for 16.5 h to furnish the crude product as a mixture of diastereomers (**8Ca** :

9Ca : **10Ca** = 77 : 13 : 10, determined by ^{1}H NMR by integration of the set of the C6 proton signals {δ_{8Ca} = 6.93 ppm (d), δ_{9Ca} = 6.68 ppm (d), δ_{10Ca} = 6.84 ppm (d)}). The crude product was purified by flash silica gel chromatography (5:1 hexanes/ethyl acetate) to afford an inseparable 80 : 12 : 8 mixture (determined by ^{1}H NMR by integration of the set of C6 proton signals {δ_{8Ca} = 6.93 ppm (d), δ_{9Ca} = 6.68 ppm (d), δ_{10Ca} = 6.84 ppm (d)}) of **8Ca**, **9Ca**, and **10Ca** as a yellow semisolid (34.0 mg, 56% yield). Adduct **8Ca** was obtained in 96% ee (determined by chiral HPLC: Chiralcel OJ-H, Hexanes/Isopropanol = 70:30, 1.0 mL/min, λ = 220 nm, t_R(major) = 25.0 min, t_R(minor) = 20.2 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (d, *J* = 5.9 Hz, 1H), 5.15 (d, *J* = 5.9 Hz, 1H), 4.45 (d, *J* = 3.8 Hz, 1H), 4.15 (s, 1H), 2.57 (td, *J* = 7.5 Hz and 3.8 Hz, 1H), 1.71 (m, 2H), 1.48 (m, 2H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 130.6, 125.9, 86.7, 77.0, 76.0, 46.9, 34.0, 20.2, 13.8; IR (film) ν 3446, 2962, 2933, 2874, 1761, 1556, 1354, 1148, 963; HRMS (ESI/$[M+Na]^+$) Calculated for: $C_{10}H_{12}BrNO_5Na$: 327.9797. Found: 327.9790.



4-hydroxy-5-methyl-8-nitro-7-propyl-2-oxabicyclo[2.2.2]oct-5-en-3-one

***endo*-(8Da)** (Major Diastereomer) The **4b** (4.7 mg, 0.010 mmol, 5 mol %) catalyzed reaction of 3-hydroxy-4-methyl-2-pyrone **6D** (25.2 mg, 0.200 mmol, 1 Eq.) and (E)-1-nitro-1-pentene **7a** (46.1 mg, 0.400 mmol, 2 Eq.) in THF (200 μL) was run at -20 °C for 18 h to furnish the crude product as a mixture of diastereomers (**8Da** : **9Da** : **10Da** = 90 : 0 : 10, determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Da} = 4.30 ppm (d), δ_{10Da} = 4.93 ppm (d)}). The crude product was purified by flash

silica gel chromatography (5:1 hexanes/ethyl acetate) to afford an inseparable 89:11 mixture (determined by ^{1}H NMR by integration of the set of C8 proton signals {δ_{8Da} = 4.30 ppm (d), δ_{10Da} = 4.93 ppm (d)}) of **8Da** and **10Da** as a yellow oil (36.1 mg, 75% yield). Adduct **8Da** was obtained in 98% ee (determined by chiral HPLC: Chiralcel OJ-H, Hexanes/Isopropanol = 85:15, 1.0 mL/min, λ = 220 nm, t_R(major) = 20.1 min, t_R(minor) = 25.5 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.32 (d, *J* = 4.0 Hz, 1H), 5.07 (d, *J* = 5.5 Hz, 1H), 4.30 (d, *J* = 3.7 Hz, 1H), 3.80 (s, 1H), 2.46 (dt, *J* = 3.5 Hz and 7.8 Hz, 1H), 1.94 (s, 3H), 1.65-1.71 (dq, *J* = 3.1 Hz and 7.7 Hz, 2H), 1.42-1.51 (sext, *J* = 7.6 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 141.8, 123.9, 87.6, 77.9, 76.5, 47.3, 34.3, 20.2, 15.6, 13.9; IR ($CDCl_3$) ν 3454, 2962, 2932, 2875, 1755, 1557, 1358, 1147, 960; HRMS (ESI/$[M+Na]^+$) Calculated for: $C_{11}H_{15}NO_5Na$: 264.0848. Found: 264.0855.

7. Relative and Absolute Configuration Assignment of Cycloadducts

7.1 Assignment of the Relative Configuration of Cycloadducts

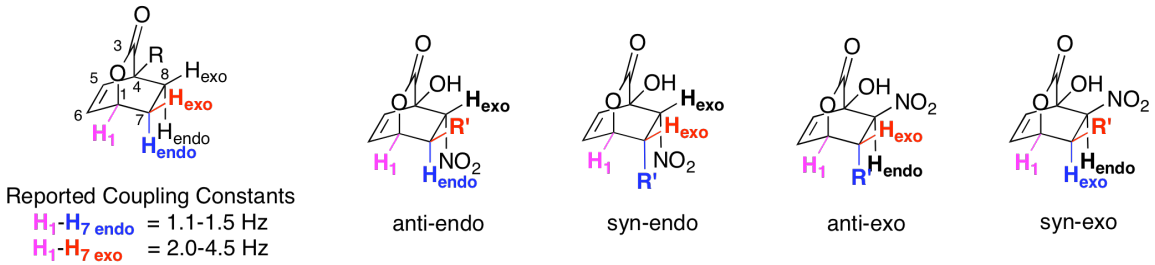


Figure S4. Determination of *endo* and *exo* configuration.

The relative configuration of the Diels-Alder adducts was obtained by ^{1}H NMR analysis. As described by Posner and coworkers[13], $H_{7\ endo}$ and $H_{7\ exo}$ can be assigned based on their respective coupling constants with H_1 (H_1 - $H_{7\ endo}$ = 1.1-1.5 Hz and H_1 - $H_{7\ exo}$ = 2.0-4.5 Hz). Once the configuration at C7 was assigned, the configuration of C8 relative to C7 was assigned based on the H7-H8 coupling constant (*syn*, 9-10 Hz; *anti*, 4-6 Hz). Consequently, the *endo* or *exo* configuration could be assigned for the Diels-Alder adducts.

[13] Afarinkia, K.; Vinader, V.; Nelson, T. D.; Posner, G. H. *Tetrahedron* **1992**, *48*, 9111-9171 and references therein.

7.2 Assignment of Absolute Configuration of *endo*-8Ah by X-ray Analysis

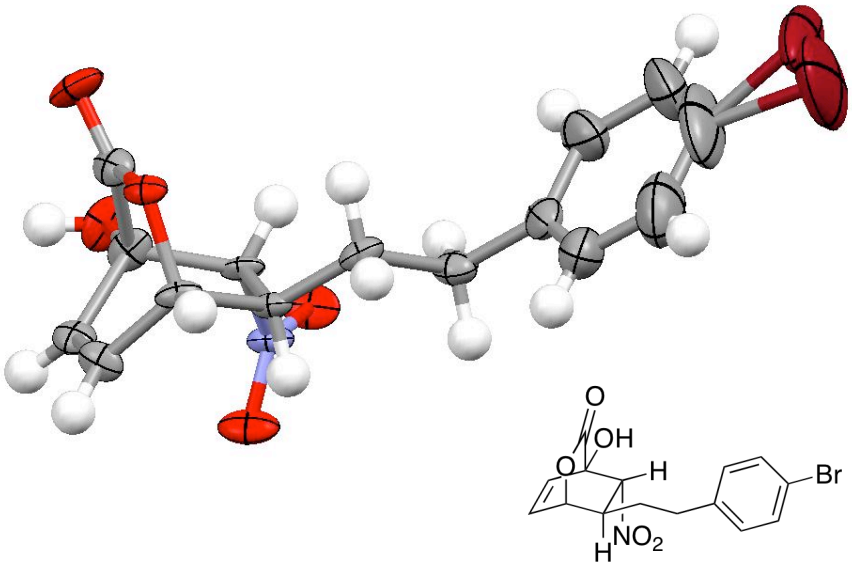


Figure S5. X-ray structure of adduct **8Ah**.

X-Ray data collection, solution, and refinement for 8Ah. All operations were performed on a Bruker-Nonius Kappa Apex2 diffractometer, using graphite-monochromated MoKα radiation. All diffractometer manipulations, including data collection, integration, scaling, and absorption corrections were carried out using the Bruker Apex2 software.[14] Preliminary cell constants were obtained from three sets of 12 frames. Data collection was carried out at 120 K, using a frame time of 20 sec and a detector distance of 60 mm. The optimized strategy used for data collection consisted of six phi and three omega scan sets, with 0.5° steps in phi or omega; completeness was 100.0%. A total of 2877 frames were collected. Final cell constants were obtained from the xyz centroids of 7653 reflections after integration. From the systematic absences and

[14] Apex2, Version 2 User Manual, M86-E01078, Bruker Analytical X-ray Systems, Madison, WI, June 2006.

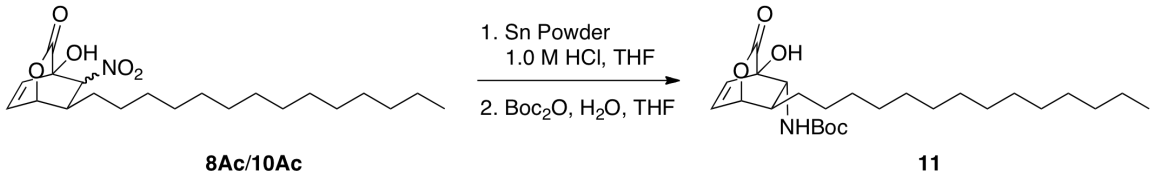
the observed metric constants and intensity statistics, space group $P2_12_12_1$ was chosen initially; subsequent solution and refinement confirmed the correctness of this choice. The structure was solved using *SIR92*[15], and refined (full-matrix-least squares) using the Oxford University *Crystals for Windows* program.[16] Crystals were of low quality, but of sufficient quality to obtain a useful data set. As described below, disorder of part of the main molecule as well as solvate diethyl ether, complicated the analysis. Fortunately, the disorder is distant from the chiral centers, which allowed an unambiguous determination of the absolute configuration. The bromophenyl moiety was disordered, apparently by an in-plane pivot about C(11). Owing to the relatively low resolution of the data, only the (1:1) Br disorder could be resolved by refinement (occupancies of the two constituent Br atoms were fixed at 0.5). All non-hydrogen atoms were refined using anisotropic displacement parameters. The unit cell contained four disordered molecules of diethyl ether. The final model was refined by using anisotropic displacement atoms for the ether C and O atoms and C-C/C-O bond length and C-C-O/C-O-C bond angle restraints, as well as thermal similarity restraints on the ADPs of the diethyl ether. The ether oxygen atom is a hydrogen bond acceptor; alcohol donor atoms O(3) and H(31) complete the hydrogen bond with an O(3)···O(6, *x–1, y, z*) distance of 2.816 Å, and an O(3)–H(31)···O(6) angle of 157º. The constituent atoms are represented by carbon atoms C(34), C(35) and C(36) and the associated H atoms. The absolute configuration of the crystal and molecule was established by Flack parameter refinement; the final value of the Flack parameter was 0.06(4). The final assignment of carbon atom chirality for atoms

[15] Altomare, A; Cascarano, G; Giacovazzo, G.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Cryst*. **1994**, *27*, 435.
[16] Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, K.; Watkin, D. J. *J. Appl. Cryst.* **2003**, *36*, 1487.

C(1), C(4), C(7) and C(8), respectively, is *S*, *S*, *R*, *R*. After location of H atoms on electron-density difference maps, the H atoms were initially refined with soft restraints on the bond lengths and angles to regularise their geometry (C---H in the range 0.93--0.98 Å and U_{iso} (H) in the range 1.2-1.5 times U_{eq} of the parent atom), after which the positions for all H atoms were refined with riding constraints. The final least-squares refinement converged to $R_1 = 0.0826$ ($I > 2\sigma(I)$, 2545 data) and $wR_2 = 0.2147$ (F^2, 2822 data, 255 parameters). CIFcheck reported three Alert B errors, two related to the low resolution, and one related to the disorder issues, both described above. Accordingly, the CIF contains three validation reply form items in response to the Alert B entries. The final CIF is available as supporting material.

8. Synthetic Application

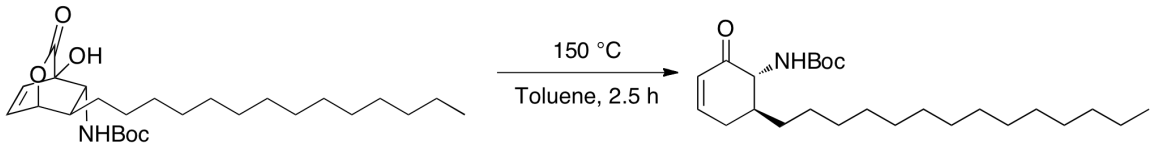
8.1 Synthesis of Cyclic Sphingosine Analogue (15)



8Ac/10Ac **11**

***tert*-butyl ((1*S*,4*S*,7*R*,8*R*)-4-hydroxy-3-oxo-7-tetradecyl-2-oxabicyclo[2.2.2]oct-5-en-8-yl)carbamate (11).** To a rapidly stirring room temperature solution of hexadecyl Diels-Alder adducts **8Ac**/**10Ac** (100 mg, 0.260 mmol, 1 Eq.) in 2.5 mL THF was added 1.0 M aqueous HCl (14.0 mL, 14.0 mmol, 54 Eq.) and 100 mesh Tin powder (164 mg, 1.38 mmol, 5.3 Eq.). The reaction was allowed to stir at room temperature for 1 hour, at which point the starting material was consumed as indicated by TLC analysis (1:1 Hexanes/Ethyl Acetate). The reaction mixture was then heated to 60 °C for 1 hour. After cooling to room temperature, the reaction was neutralized with approximately 6.0 mL saturated aqueous sodium bicarbonate and an additional 5 mL THF was added, along with di-*tert*-butyl dicarbonate (0.310 mmol, 1.2 Eq., 72 μL), and the reaction was stirred at room temperature for sixteen hours. The mixture was then extracted with ethyl acetate (4 x 10 mL), dried over sodium sulfate, and the solvent was removed *in vacuo*. The crude residue was taken up in chloroform and purified by flash column chromatography (3:1 hexanes/ethyl acetate) which afforded product **11** as a colorless oil (69 mg, 59% yield over 2 steps) in 96% ee (determined by chiral HPLC: Chiralcel AD, Hexanes/Isopropanol = 90:10, 1.0 mL/min, λ = 220 nm, t_R(major) = 8.5 min, t_R(minor) = 6.6 min). $[\alpha]_{19}^{D}$ = +5.0°, (*c* = 1.76, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.55 (dd, *J* = 7.9 Hz and 4.9 Hz, 1H), 6.34 (d, *J* = 7.9 Hz, 1H), 4.99 (dd, *J* = 5.5 Hz and 1.8 Hz, 1H),

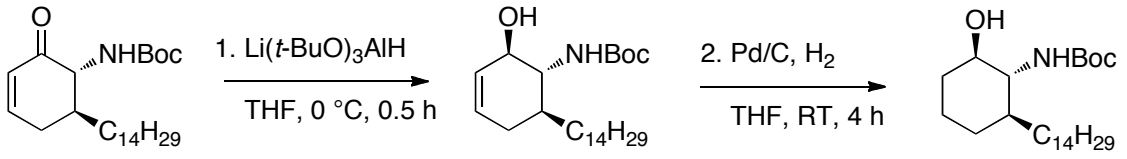
4.52 (d, J = 8.5 Hz, 1H), 3.82 (bs, 1H), 3.58 (d, J = 3.1 Hz, 1H), 1.70 (m, 1H), 1.60-1.56 (m, 2H), 1.45 (s, 9H), 1.39 (m, 2H), 1.25 (s, 22H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 156.2, 134.4, 131.4, 80.6, 78.0, 76.1, 55.1, 48.8, 32.1, 31.9, 29.8, 29.8, 29.8, 29.7, 29.7, 29.6, 29.5, 28.4, 27.2, 22.9, 14.3; IR (film) ν 3347, 2922, 2853, 1756, 1693, 1519, 1366, 1153; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{26}H_{46}NO_5$: 452.3376. Found: 452.3368.



11 **12**

***tert*-butyl ((1*R*,6*S*)-2-oxo-6-tetradecylcyclohex-3-en-1-yl)carbamate (12).** A 0.044 M solution of N-Boc protected Diels-Alder adduct **11** (50 mg, 0.111 mmol, 1 Eq.) in anhydrous toluene (2.52 mL) was prepared and transferred to a 50 mL sealed tube. The mixture was placed in a 150 °C oil bath and stirred for 2.5 hours and then allowed to cool to room temperature. Upon completion of the reaction, as indicated by TLC analysis (2:1 Hexanes/Ethyl Acetate), the crude mixture was directly purified by flash column chromatography (8:1 hexanes/ethyl acetate), affording enone **12** as a white solid (40 mg, 89% yield) in 96% ee (determined by chiral HPLC: (R,R)-Whelk-O1, Hexanes/Isopropanol = 96:4, 1.0 mL/min, λ = 209 nm, t_R(major) = 16.4 min, t_R(minor) = 12.3 min). mp = 45-46 °C. $[\alpha]_{19}^{D}$ = -2.5°, (c = 1.34, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71 (s, 2H), 5.08 (d, J = 8.5 Hz, 1H), 4.37 (t, J = 10.1 Hz, 1H), 3.02 (ABq, $\Delta\nu_{AB}$ = 80.9 Hz, J = 19.8 Hz, 2H), 2.29 (m, 1H), 1.70-1.61 (m, 1H), 1.50 (m, 1H), 1.46 (s, 9H), 1.26 (s, 24H), 0.88 (t, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.7,

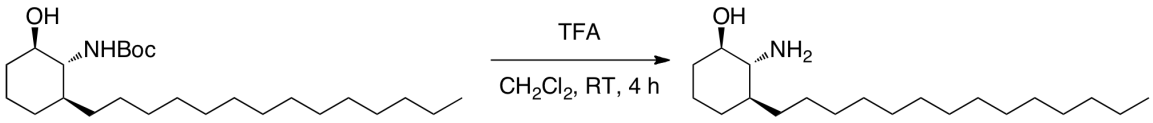
156.3, 130.4, 123.2, 80.0, 60.7, 45.5, 40.5, 32.2, 32.1, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 28.4, 26.1, 22.9, 14.3; IR (film) ν 3344, 2923, 2853, 1714, 1499, 1366, 1248, 1167; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{25}H_{46}NO_3$: 408.3478. Found: 408.3470.



12 **13** **14**

***tert*-butyl ((1*R*,2*R*,6*S*)-2-hydroxy-6-tetradecylcyclohexyl)carbamate (14)**. To a vial (20 mL) with stirbar is added N-Boc enone **12** (39.2 mg, 0.096 mmol, 1 Eq.) and THF (3.9 mL). The mixture was then cooled to 0 °C and solid lithium tri(*tert*-butoxy)aluminum hydride (73.2 mg, 0..288 mmol, 3 Eq.) was added in one portion. The reaction was stirred at 0 °C for 0.5 hours, at which point the reaction was complete as indicated by TLC analysis (3:1 Hexanes/Ethyl Acetate), and quenched with saturated aqueous ammonium chloride (2 mL). The mixture was then filtered through a short pad of Celite on a fine-fritted glass funnel, the insoluble material was washed with diethyl ether (2 x 5 mL), and the filtrate was extracted with diethyl ether (3 x 3 mL). The combined organic layers were dried over sodium sulfate, the solvent was removed *in vacuo*, and the resulting allylic alcohol **13** was taken up in THF (4 mL) and transferred to a 20 mL reaction vial with a stirbar. Then Pd/C (10.4 mg, 0.0096 mmol, 0.1 Eq.) was added and the vial was sealed with a septum and fitted with a hydrogen balloon. After vigorous stirring for 4 hours at room temperature, the reaction was complete as indicated by TLC analysis (3:1 Hexanes/Ethyl Acetate). The crude reaction mixture was filtered through a short plug of Celite, which was rinsed with THF (2 x 2 mL), and the solvent

was removed *in vacuo*. The crude residue was purified by flash chromatography (3:1 hexanes/ethyl acetate), affording alcohol **14** as a single diastereomer. The relative configuration of the diastereomer was confirmed via comparison to *rac*-**14**, which was obtained by Boc-protection of an authentic sample of *rac*-**15** that was prepared following the literature procedure (vide infra). (White solid, 37.2 mg, 94% yield over 2 steps). mp = 81-84 °C. $[\alpha]_{19}^{D}$ = +17.5°, (*c* = 0.87, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.36 (d, *J* = 8.5 Hz, 1H), 3.27 (td, *J* = 9.6 Hz and 3.9 Hz, 1H), 3.09 (q, *J* = 8.7 Hz, 1H), 2.80 (bs, 1H), 2.05 (d, *J* = 11.9 Hz, 1H), 1.78 (d, *J* = 13.0 Hz, 1H), 1.72 (d, *J* = 12.8 Hz, 1H), 1.54 (m, 1H), 1.46 (s, 9H), 1.25 (s, 28H), 0.98 (m, 1H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 80.0, 75.6, 61.2, 41.9, 34.3, 32.4, 32.1, 30.8, 30.1, 29.9, 29.8, 29.5, 28.5, 26.8, 23.4, 22.9, 14.3; IR (film) ν 3352, 2917, 2849, 1685, 1533, 1176, 1016; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{25}H_{50}NO_3$: 412.3791. Found: 412.3793.



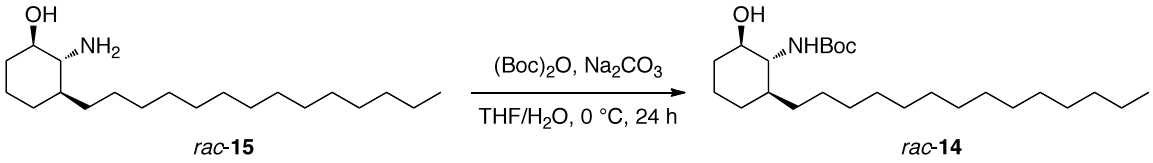
14 **15**

(1*R*,2*R*,3*S*)-2-amino-3-tetradecylcyclohexanol (15). To a vial (4 mL) with a flea stirbar was added N-Boc aminoalcohol **14** (13.0 mg, 0.032 mmol, 1 Eq.) and CH_2Cl_2 (0.30 mL). Trifluoroacetic acid (73 μL, 0.95 mmol, 30 Eq.) was then added and the mixture was stirred at room temperature for 4 hours, at which point the reaction was complete as indicated by TLC analysis (3:1 Hexanes/Ethyl Acetate). The solvent was removed *in vacuo*. The residue was then taken up in diethyl ether (1 mL) and water (1 mL). Two drops of 0.2 N NaOH was added and the mixture was mixed and extracted with diethyl

ether (2 x 1 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed *in vacuo*, affording pure aminoalcohol **15** as a yellow semisolid (9.4 mg, 96% yield). $[\alpha]_{19}^{D}$ = +11.7°, (*c* = 0.65, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.05 (bs, 3H), 3.34 (m, 1H), 2.36 (t, *J* = 9.1 Hz, 1H), 2.03 (bs, 1H), 1.81 (d, *J* = 12.7 Hz, 1H), 1.73 (s, 1H), 1.65 (m, 1H), 1.32 (m, 1H), 1.25 (bs, 26H), 0.95 (m, 1H), 0.88 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 73.7, 61.7, 42.2, 33.7, 32.3, 32.1, 30.4, 30.2, 29.9, 29.8, 29.6, 26.6, 23.5, 22.9, 14.4; IR (film) ν 3361, 3093, 2922, 2853, 1674, 1523, 1463, 1202, 1138, 1054, 839, 722; HRMS (ESI/$[M+H]^+$) Calculated for: $C_{20}H_{42}NO_5$: 312.3266. Found: 312.3257.

8.2 Confirmation of Relative Configuration of 15

To confirm the relative configuration of our synthetic sample **15**, we prepared authentic *rac*-**15** according to the literature procedure reported by del Olmo.[17] *Rac*-**15** and **15** were then both converted to the N-Boc aminoalcohols *rac*-**14** and **14** following the representative below and the NMR spectra of *rac*-**14** and **14** were found to be identical (See Figure S6).



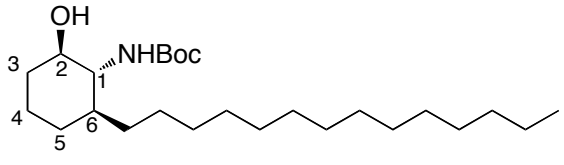
rac-**15** *rac*-**14**

***tert*-butyl (2-hydroxy-6-tetradecylcyclohexyl)carbamate (*rac*-14).**

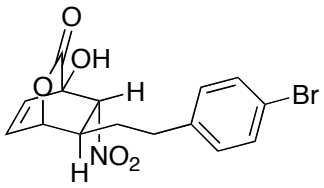
[17] Rebollo, O.; del Olmo, E.; Ruiz, G.; López-Pérez, J. L.; Giménez, A.; San Feliciano, A., *Bioorg. Med. Chem. Lett.* **2008,** *18*, 184-187.

To a vial (8 mL) with a flea stirbar is added aminoalcohol *rac*-**15** (15 mg, 0.048 mmol, 1 Eq.), sodium carbonate (11.7 mg, 0.110 mmol, 2.3 Eq.), and a mixture of THF/H_2O (2:1, 0.2 M, 0.24 mL). The reaction was cooled to 0 °C and a 1.15 M solution of Boc_2O in THF (12.2 μL, 0.053 mmol, 1.1 Eq., in 46 μL THF) was added in one portion. The reaction was stirred at that temperature for one hour and then allowed to warm to room temperature overnight. Upon completion of the reaction, as indicated by TLC analysis (20:1:0.25 Ethyl Acetate/Methanol/Ammonium Hydroxide), the mixture was diluted with water (2 mL) and extracted with dichloromethane (2 x 2 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The crude residue was then purified by column chromatography (3:1-2:1 hexanes/ethyl acetate), affording alcohol *rac*-**14** as a white solid (16.3 mg, 83%). The spectroscopic data matched that reported for compound **14**, confirming the relative configuration of aminoalcohol **15**.

8.3 Determination of the Absolute Configuration of 15



14



8Ah

The absolute configurations of *C*1 and *C*6 in compound **14** are known from the data obtained in the X-ray structure of compound **8Ah** (see Section 7.2). The determination of the relative configuration of *C2* as *trans* to *C*1 was determined through the above experiment (see Section 8.1). As a result, it is possible to assign *C*2 center as *R*.

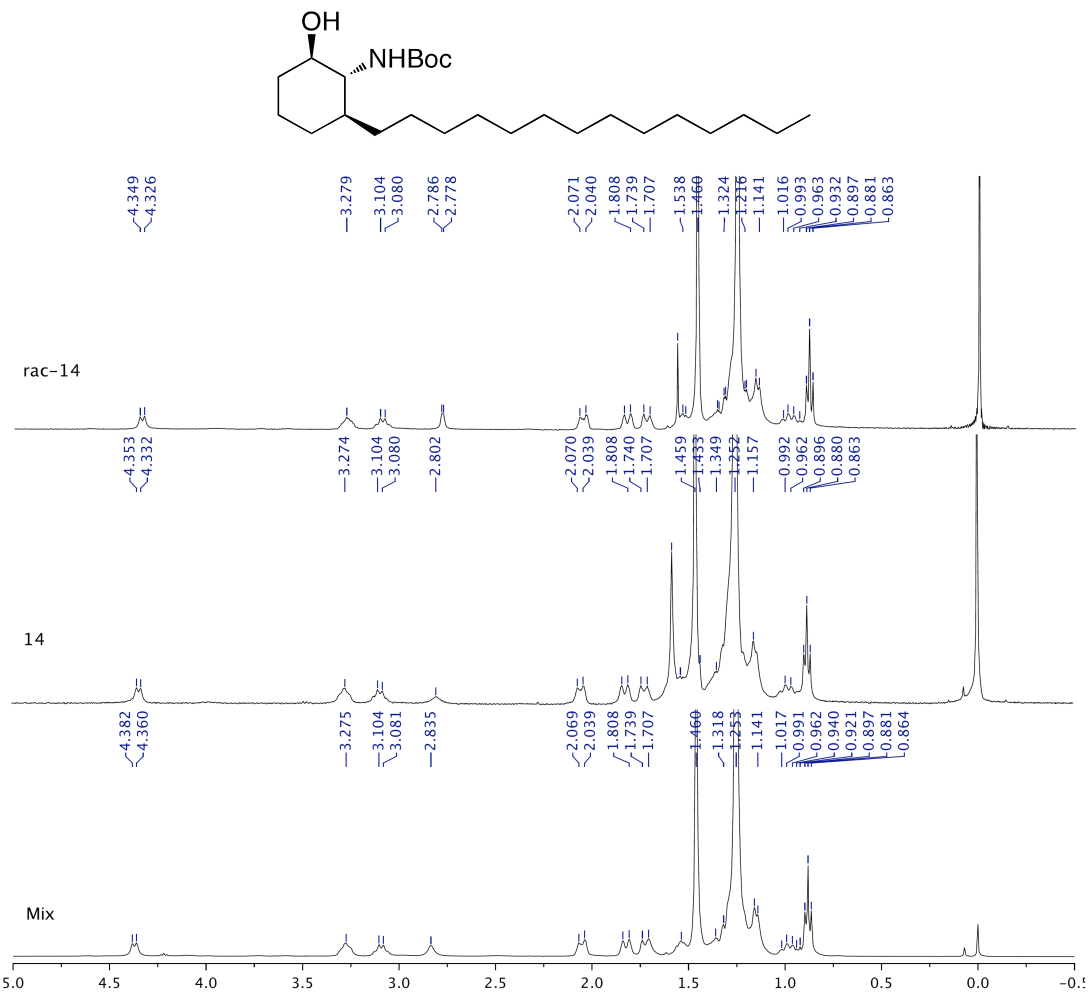


Figure S6. ^{1}H NMR comparison of *rac*-**14** and **14**.

9. Carbon Isotope Effect Study

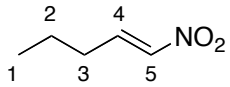
9.1 Reaction Procedure

To a 5 mL volumetric flask at 20 °C was added catalyst **4b** (93.8 mg, 0.200 mmol, 0.05 Eq.). In a separate vial 3-hydroxy-2-pyrone (**6A**) (896.7 mg, 8.0 mmol, 2 Eq.) was dissolved in 3.5 mL THF, transferred to the flask containing catalyst, and then the solution was mixed with the syringe used to transfer the pyrone solution. (E)-1-nitro-1-pentene (**7a**) (460.5 mg, 4.0 mmol, 1 Eq.) was weighed out in a syringe, added to the reaction mixture, and the solution was mixed again with the syringe used to transfer the nitroalkene. The mixture was then diluted to 5 mL with THF and allowed to react at 20 °C for 35 minutes, at which point 100 μL was removed, quickly diluted to 2 mL with acetonitrile in a volumetric flask, and immediately analyzed by HPLC to determine the conversion (PrincetonSPHER 60A Cyano-silica (5 micron), Water : Acetonitrile, 1.0 mL/min, 254 nm, 126 bar; 0-3 min = 90:10, 3-30 min = 90:10 to 60:40, 30-60 min = 60:40). At the same time, the remaining reaction mixture was quenched by loading it onto a pre-cooled Combiflash cartridge and then applying vacuum to dry the silica. Unreacted (E)-1-nitro-1-pentene was then isolated by column chromatography on a Combiflash system with Redisep Gold R_f column (diethyl ether : pentane; 1% for 5 column volumes, 1% to 15% over 10 column volumes, 15% for 5 column volumes). This was repeated three times at 73%, 74%, and 75% conversion. The isolated (E)-1-nitro-1-pentene was then subjected to the following NMR analysis.

9.2 NMR Analysis

The ^{13}C analysis of the virgin and recovered samples of (E)-1-nitro-1-pentene (**7a**) was performed following Singleton's method at natural abundance.[18] The NMR samples were prepared in an identical fashion by weighing out 90 mg of (E)-1-nitro-1-pentene in a 5 mm high precision NMR tube and adding 0.5 mL $CDCl_3$, resulting in a sample height of 4.40 cm. A T1 determination by the inversion-recovery method was performed on each sample before analysis and any sample that showed significantly different T1 values was omitted. The ^{13}C NMR spectra were recorded with inverse gated decoupling and calibrated 45° pulses. A 60 s delay time between pulses was used to minimize any T1 variations (d1 = 60 s, at = 5.0 s, np = 255170, nt = 720). All NMR data is summarized below in Table S1. Only a zero-order baseline correction was applied to each spectrum and the integration region for each peak was five times the peak width at half height.

[18] a) Singleton, D. A.; Thomas, A. A., *J. Am. Chem. Soc.* **1995,** *117* (36), 9357-9358.
b) Kwon, K.-H.; Lee, D. W.; Yi, C. S., *Organometallics* **2010,** *29* (22), 5748-5750.



Run 1

C#	Virgin	Recovered (73%)	R/R_0	% Change
1	**1.000**	**1.000**	**1.000**	**0.00**
2	0.994	0.992	0.998	-0.20
3	0.985	0.985	1.000	0.00
4	1.001	1.037	1.036	3.60
5	1.006	1.011	1.005	0.50

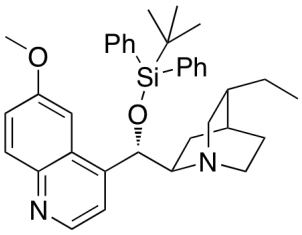
Run 2

C#	Virgin	Recovered (74%)	R/R_0	% Change
1	**1.000**	**1.000**	**1.000**	**0.00**
2	0.994	0.987	0.993	-0.70
3	0.985	0.988	1.003	0.30
4	1.001	1.039	1.038	3.80
5	1.006	1.010	1.004	0.40

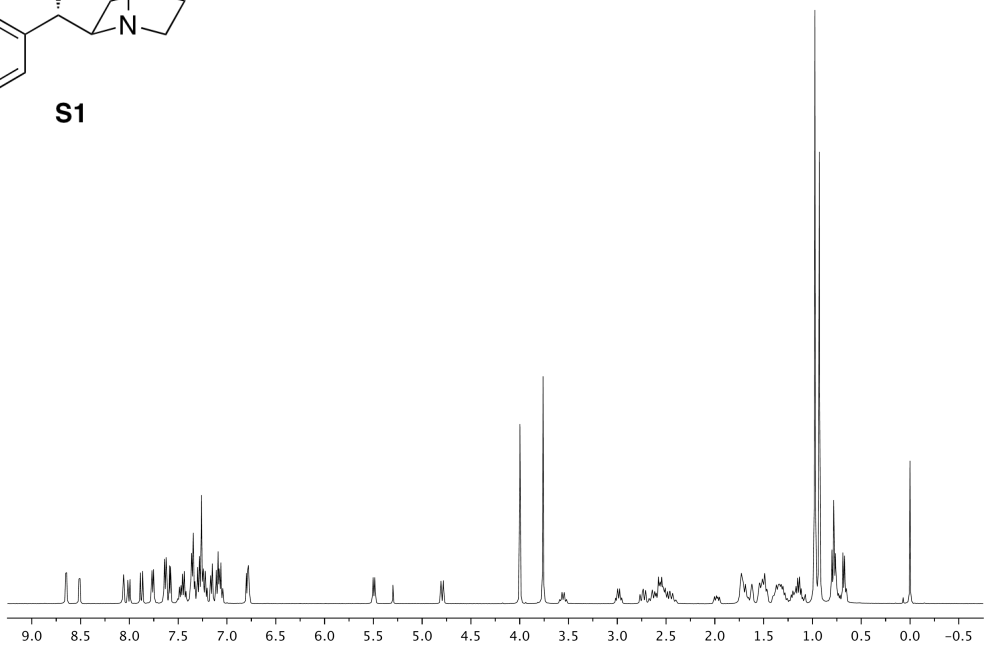
Run 3

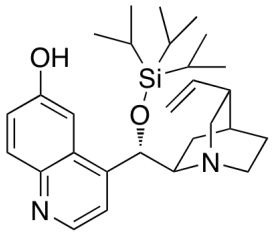
C#	Virgin	Recovered (75%)	R/R_0	% Change
1	**1.000**	**1.000**	**1.000**	**0.00**
2	0.994	0.992	0.998	-0.20
3	0.985	0.987	1.002	0.20
4	1.001	1.055	1.054	5.40
5	1.006	1.012	1.006	0.60

Table S1. ^{13}C integrations of recovered and virgin samples of nitroalkene **7a**.

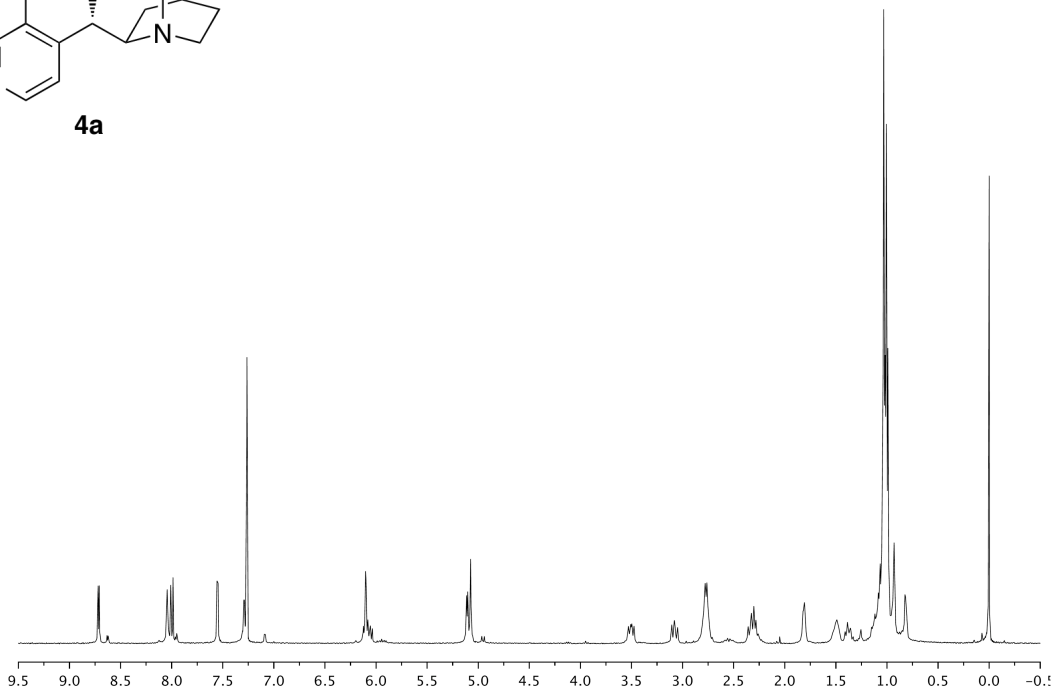


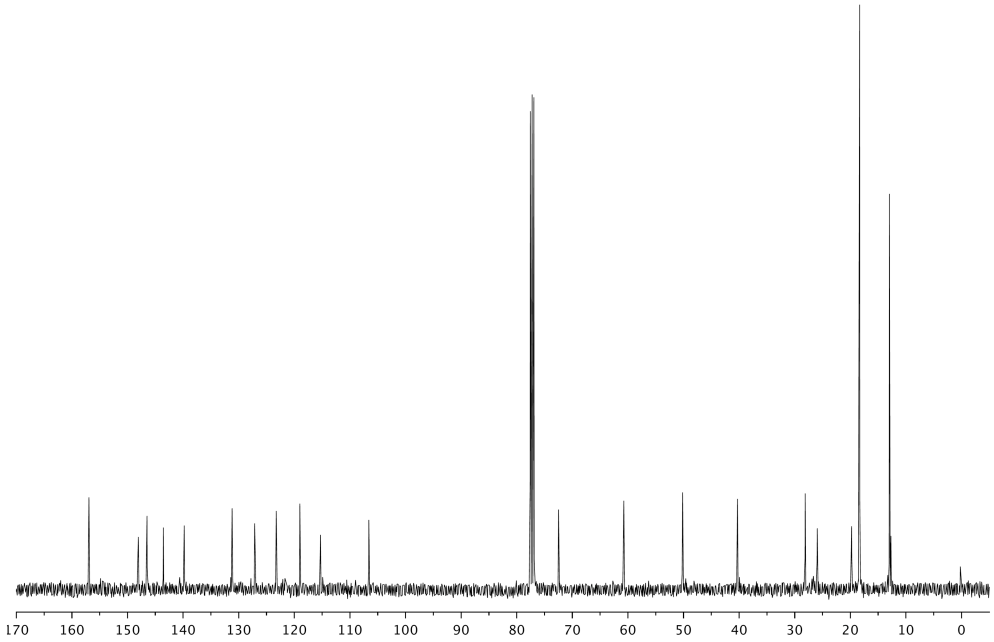
S1

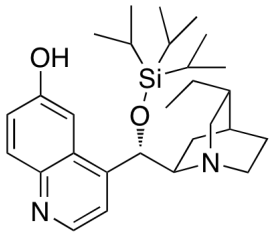




4a







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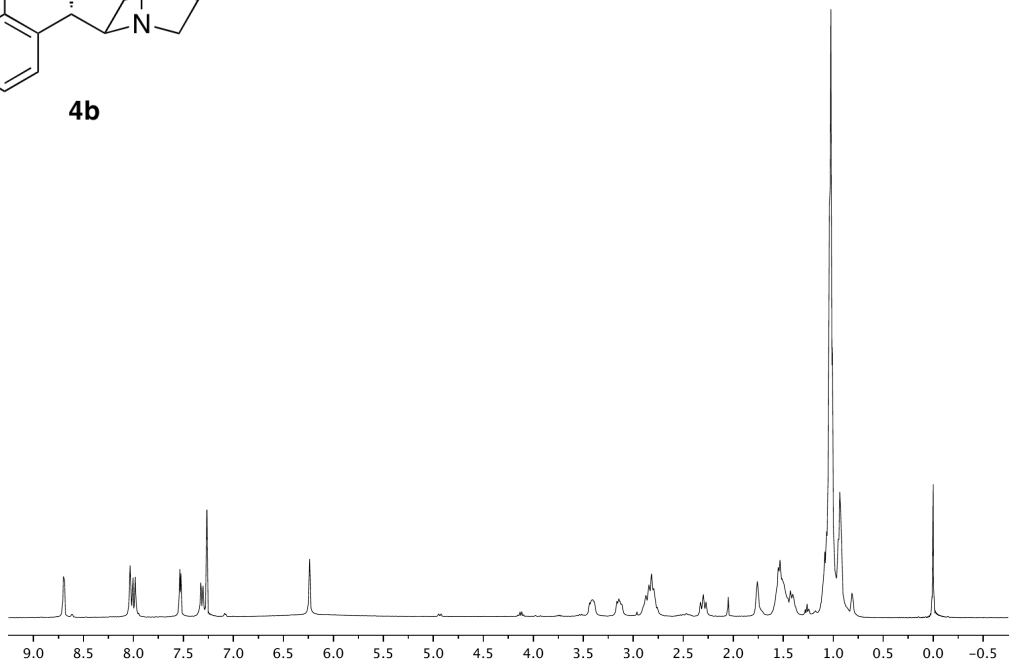
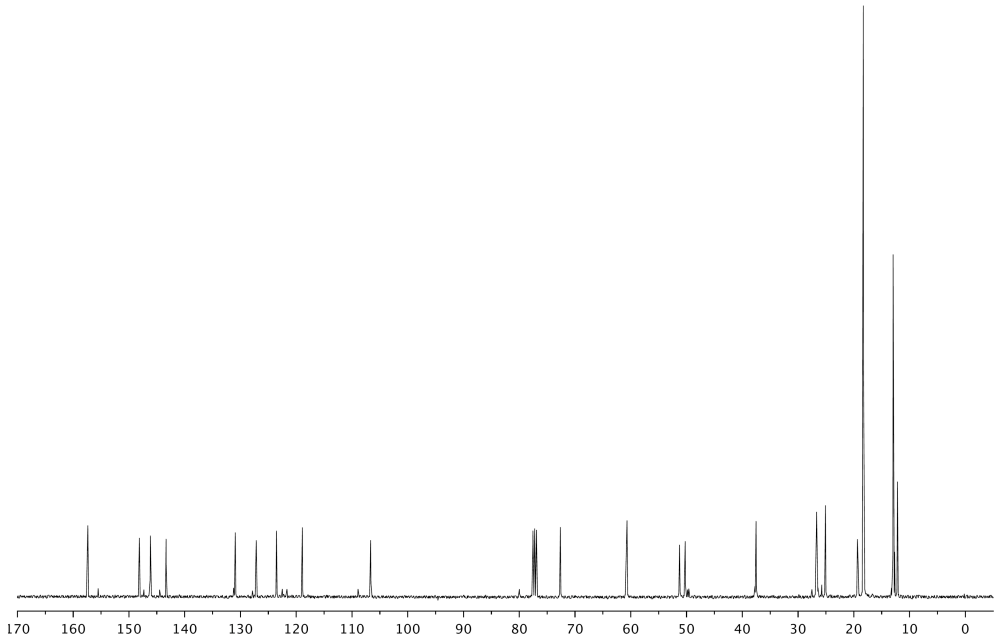
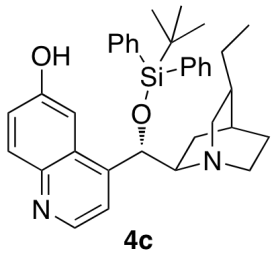
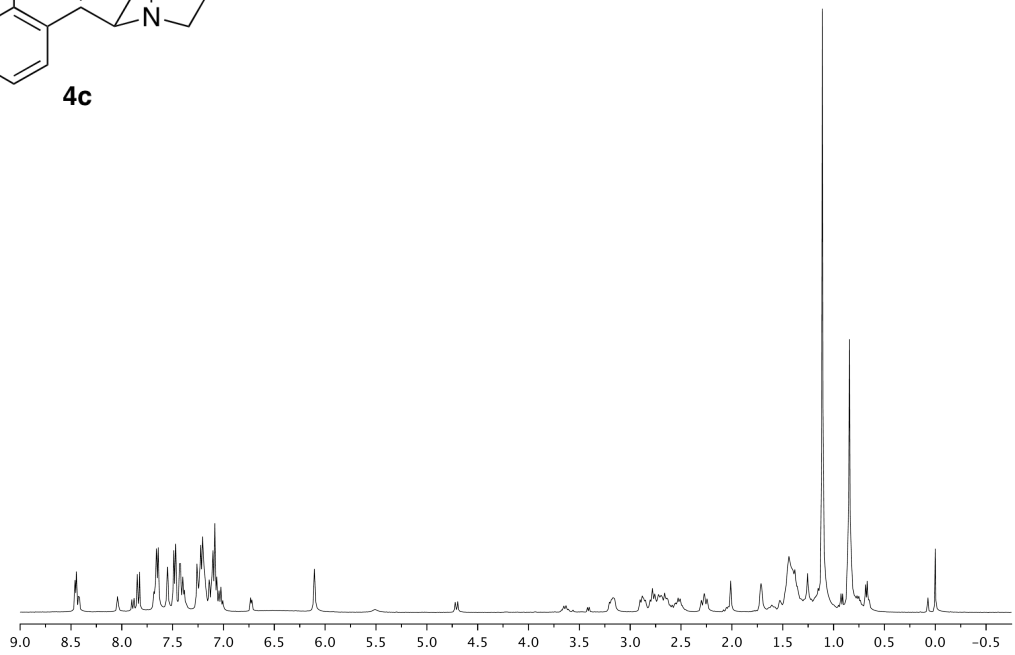
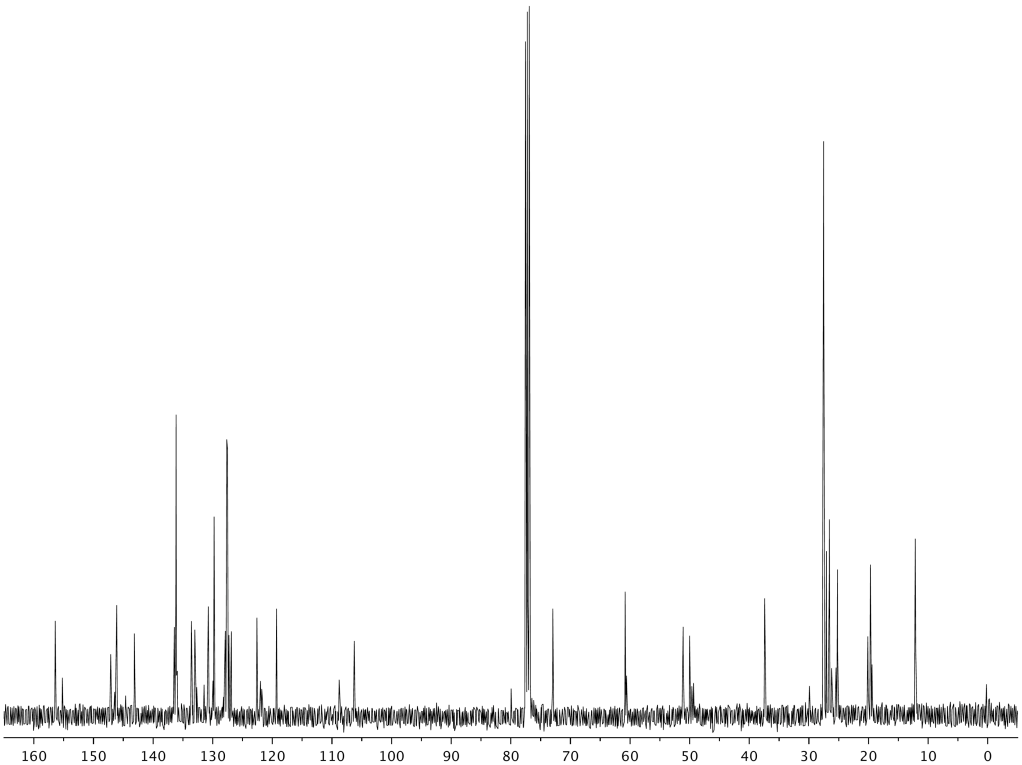


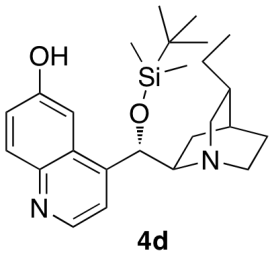




4c







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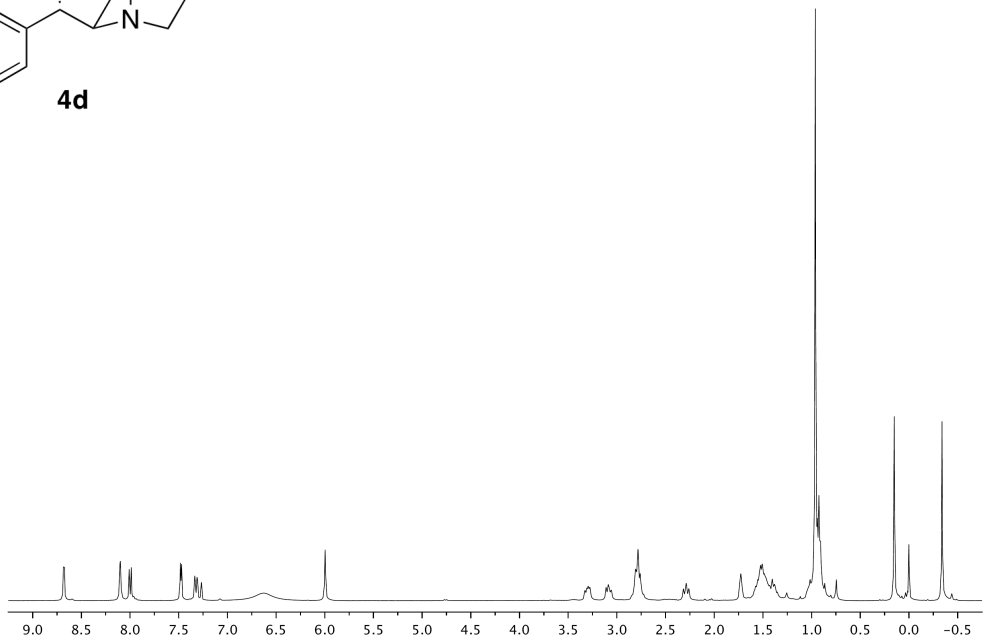

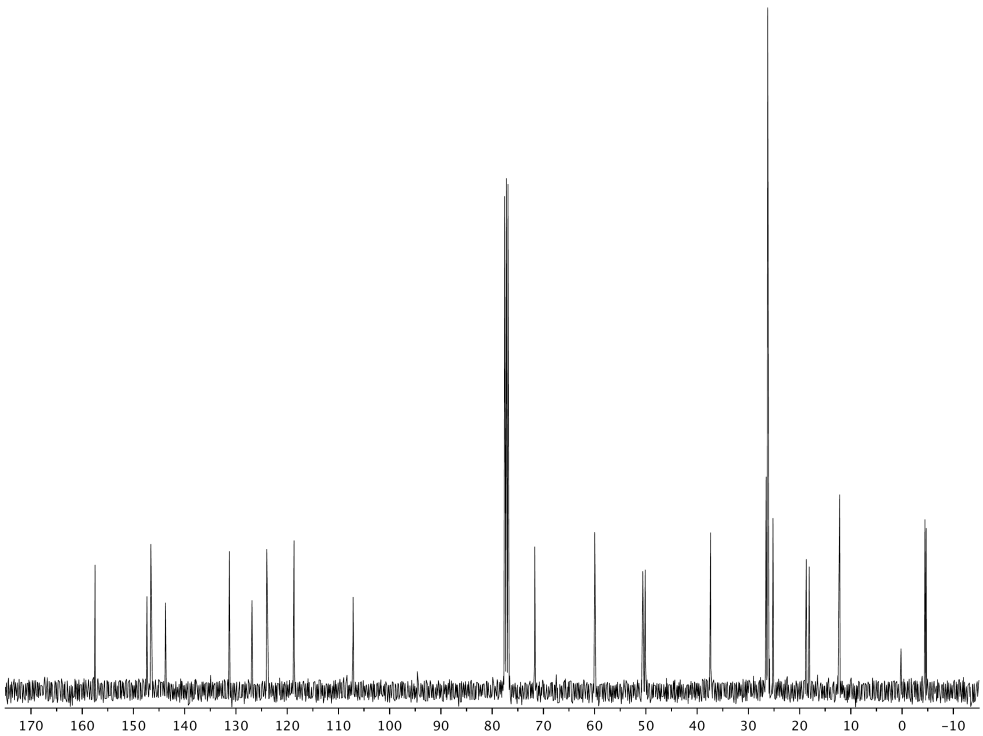

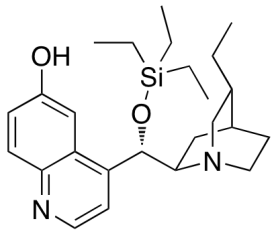

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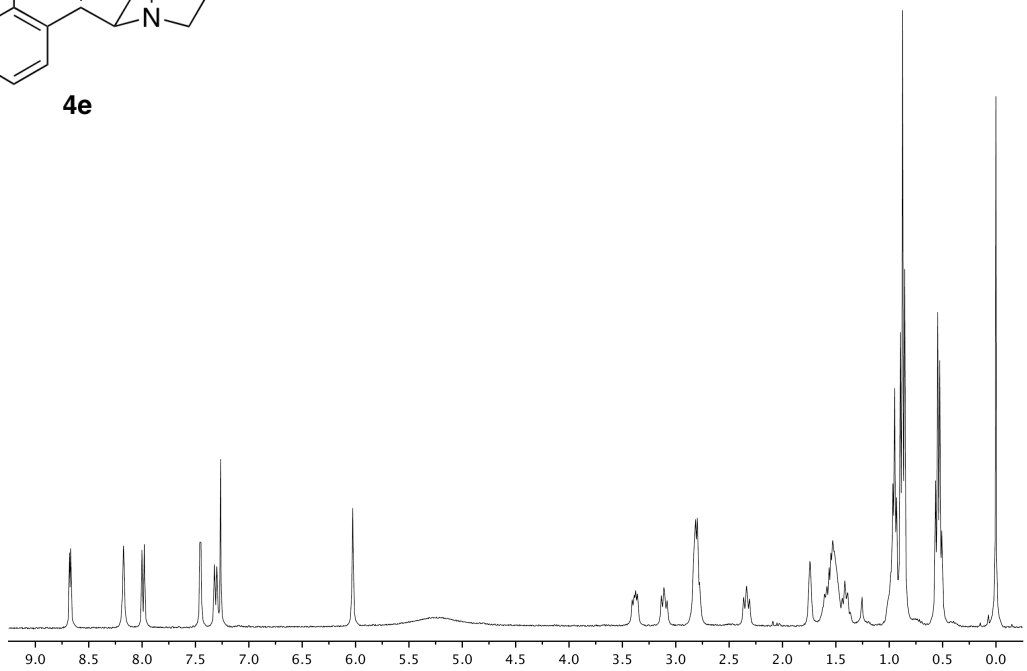

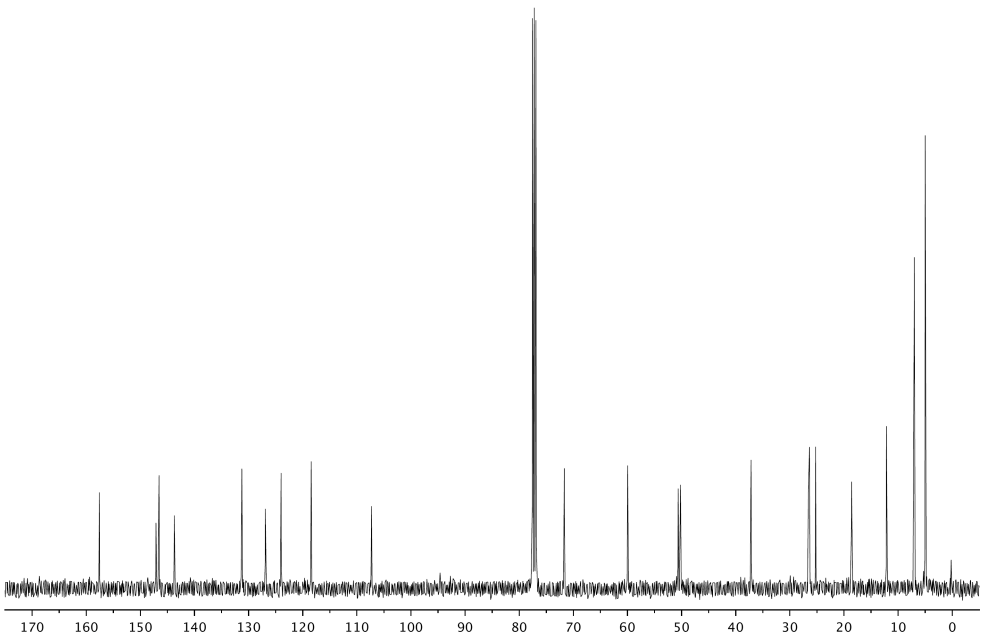

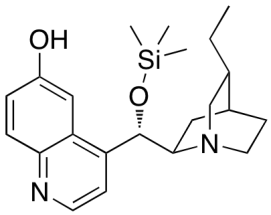

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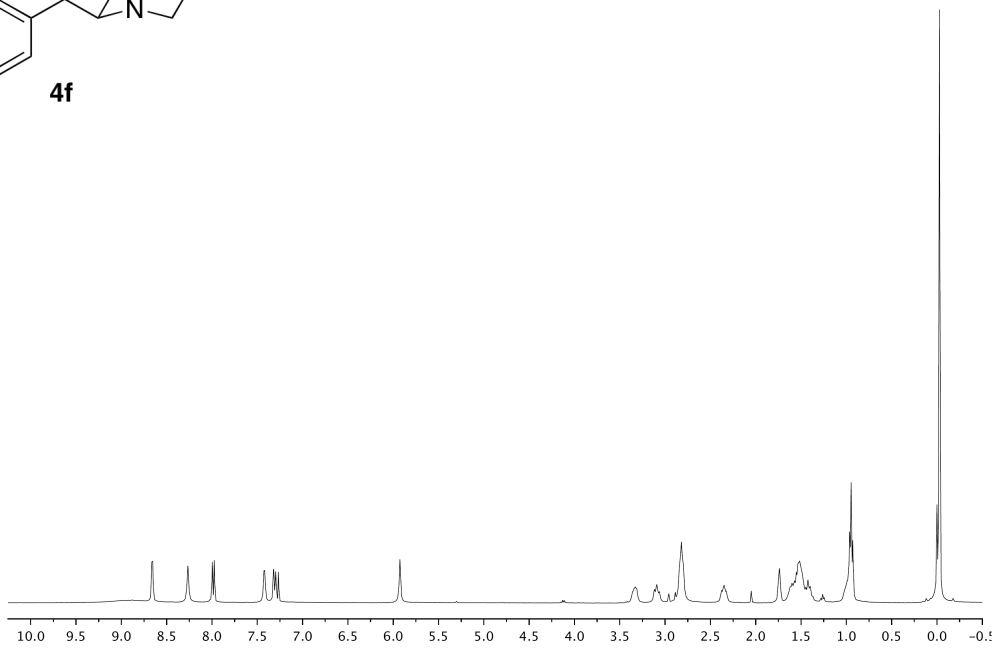

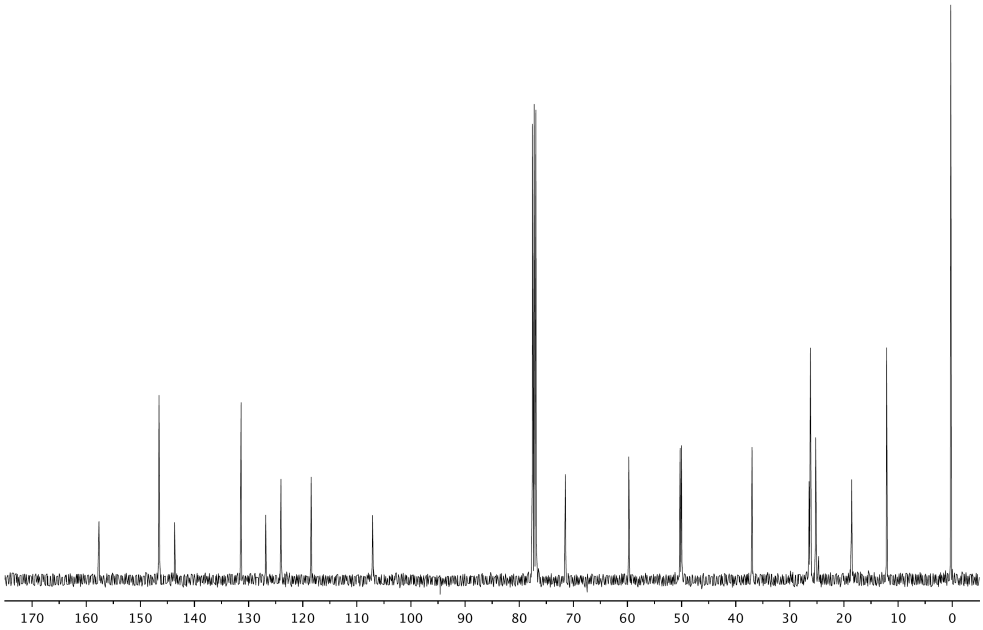

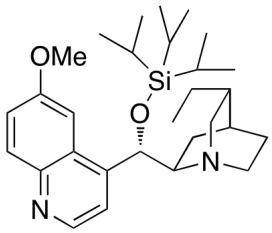

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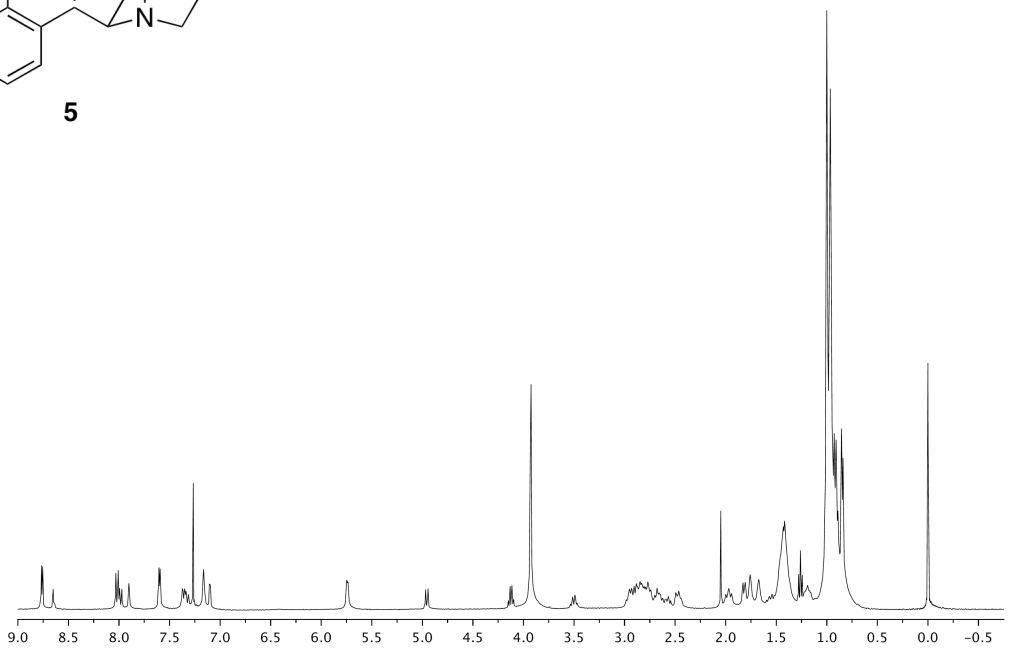

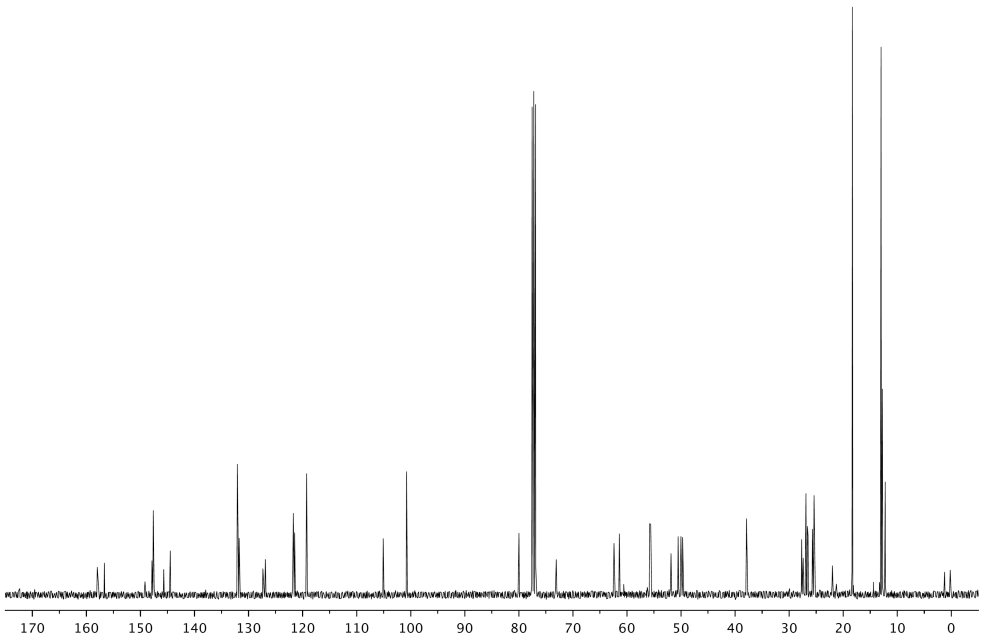

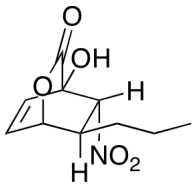

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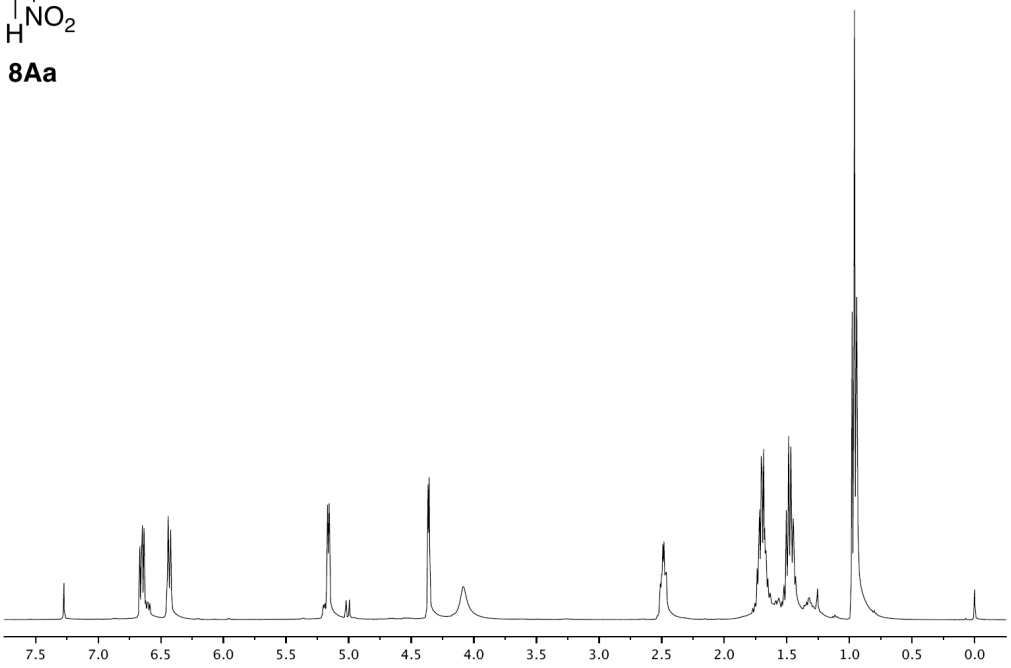

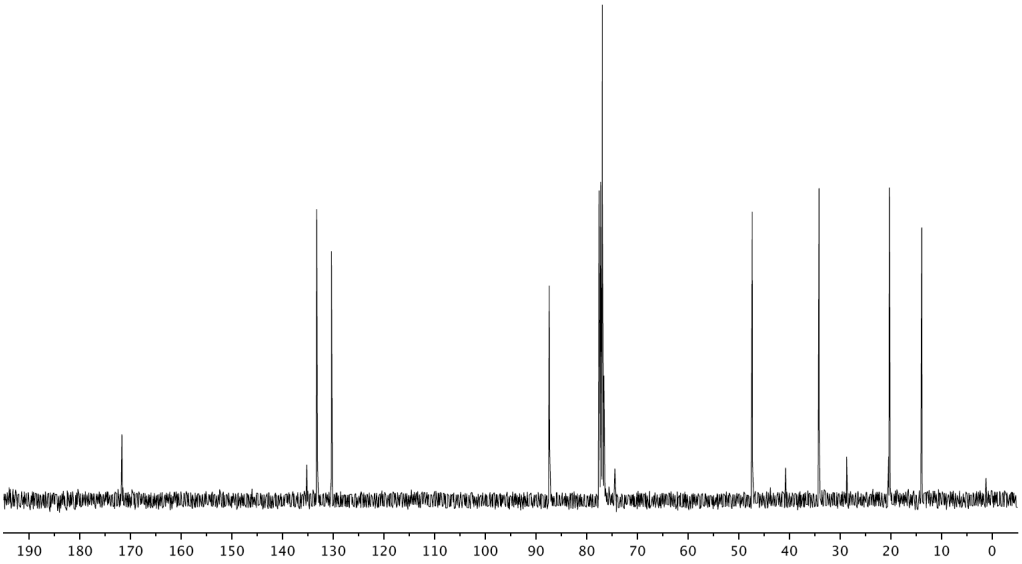

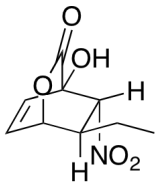
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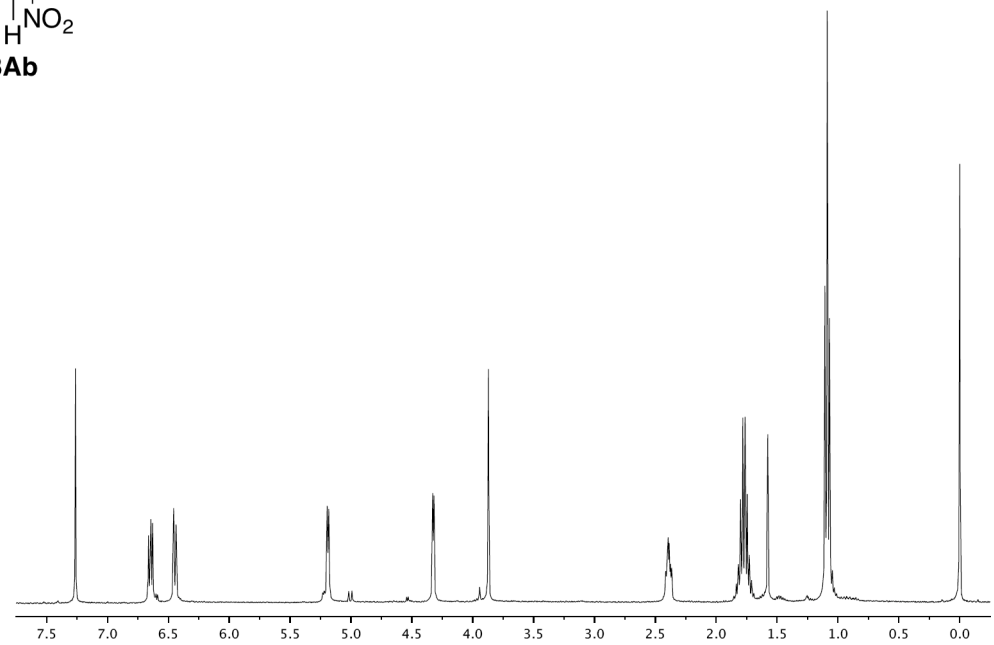
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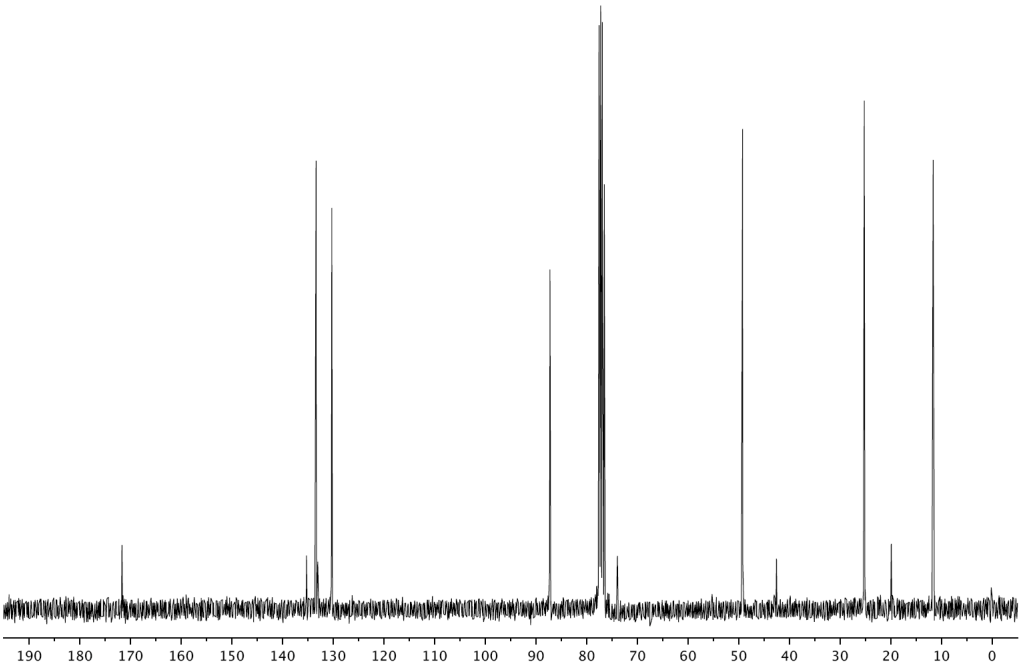
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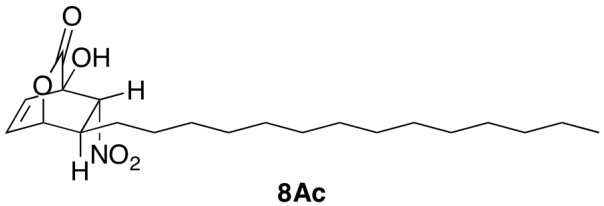
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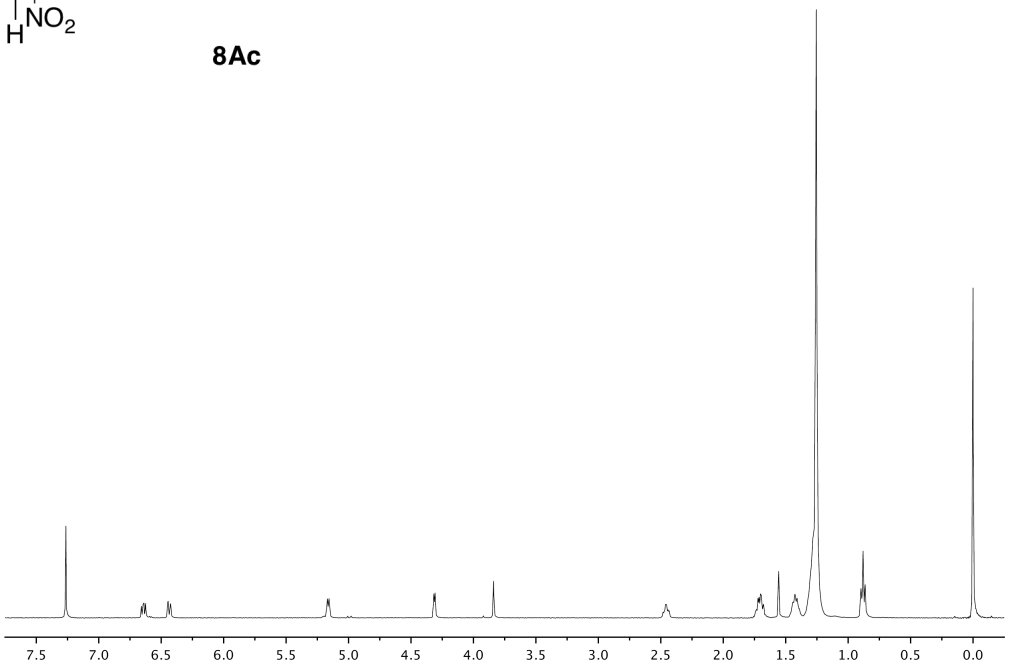
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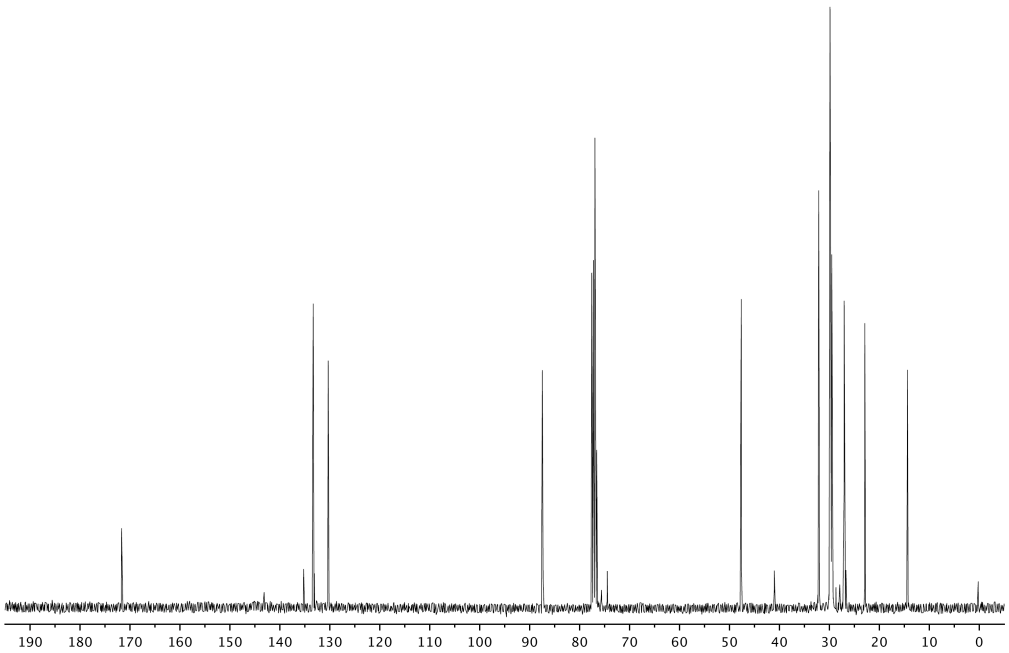
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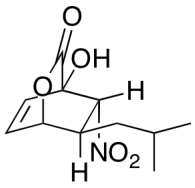

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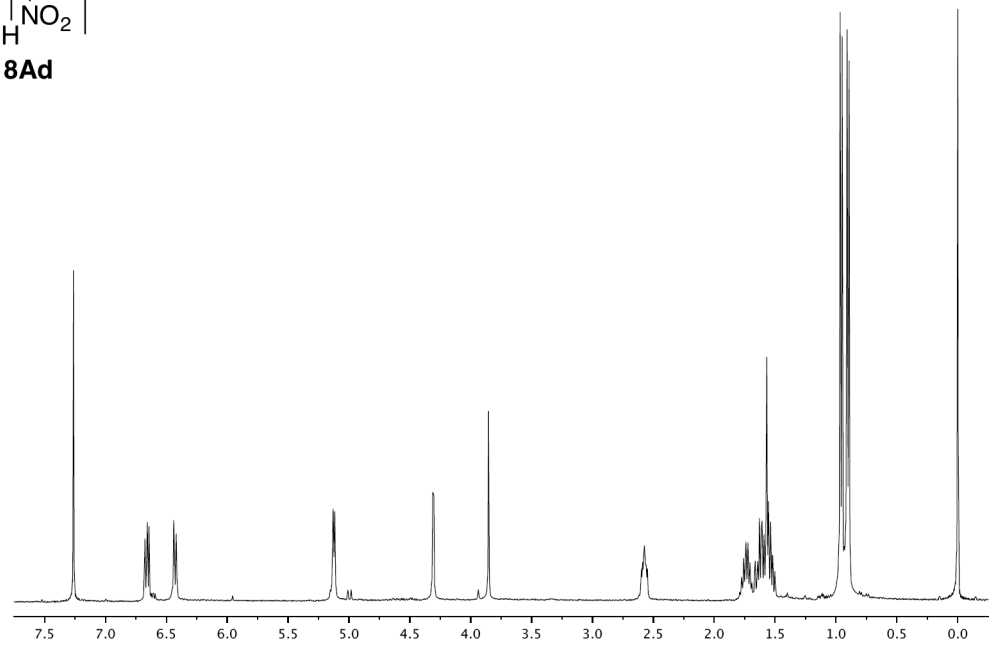

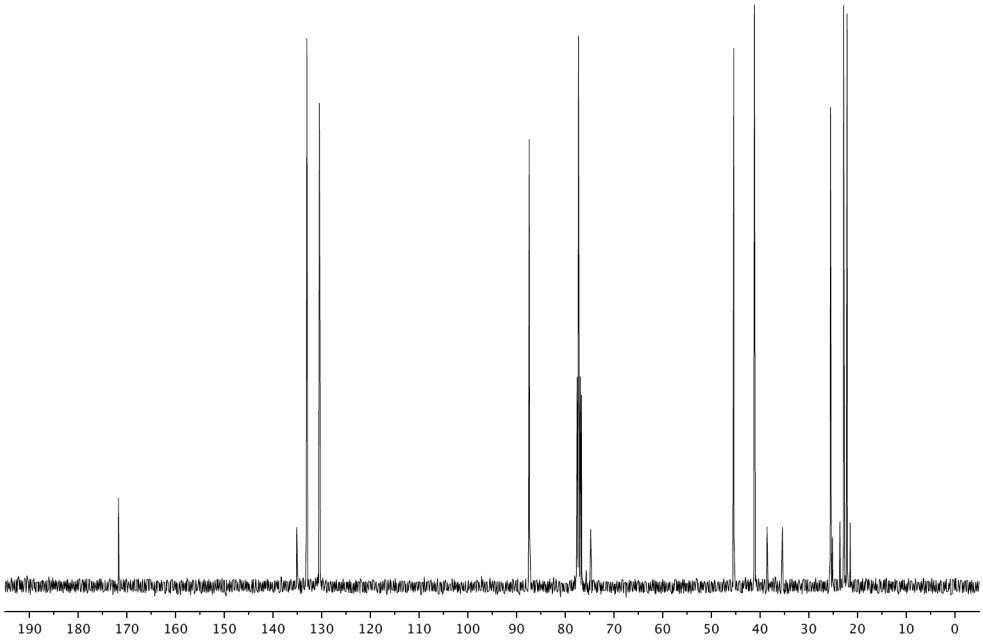

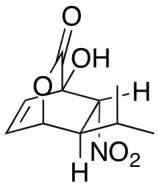

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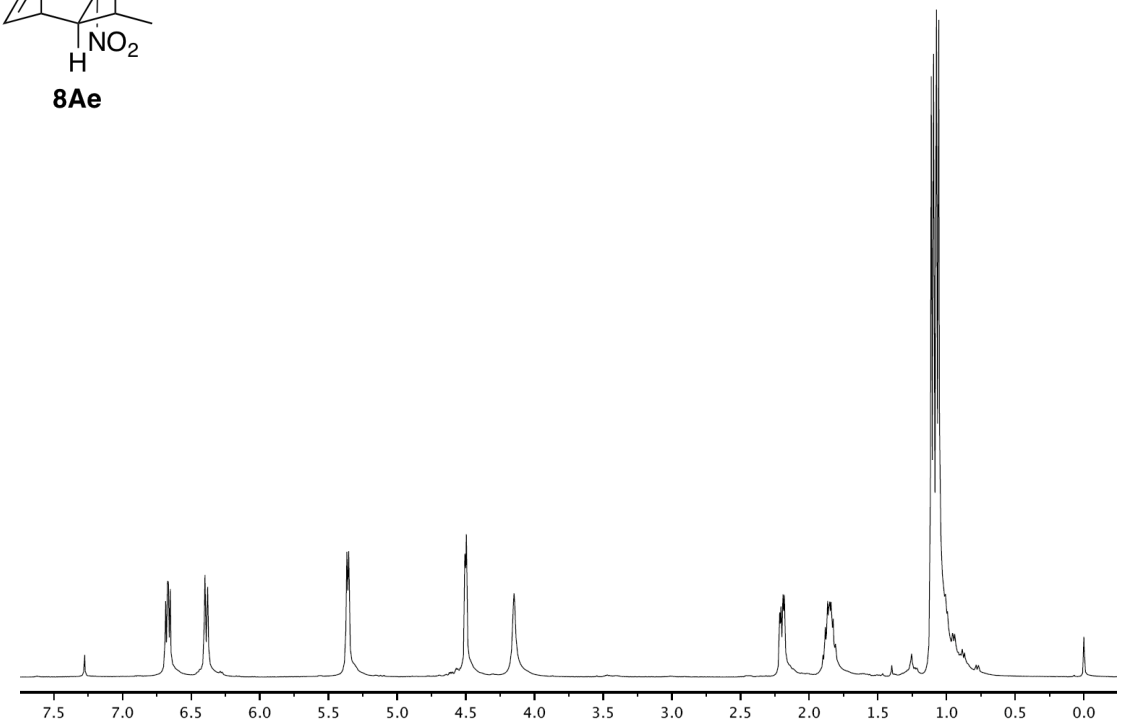

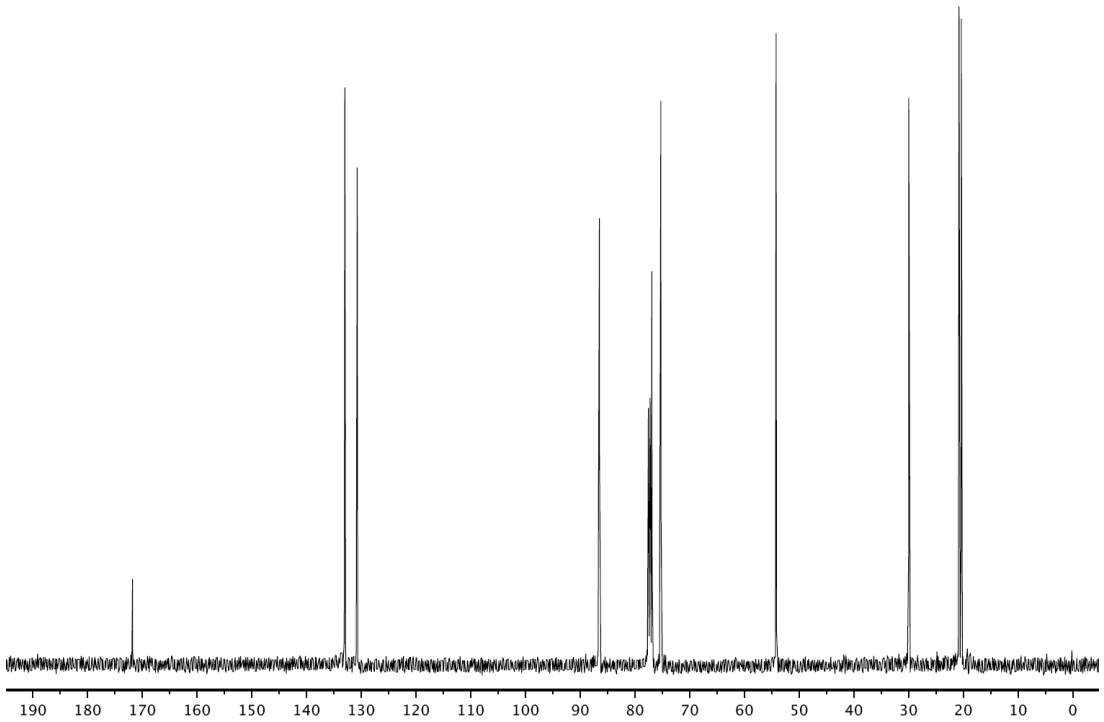

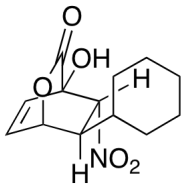

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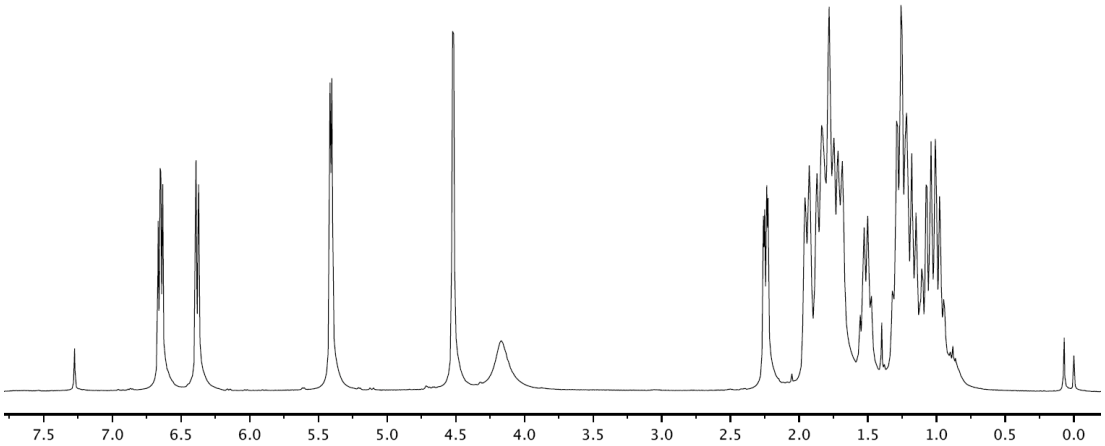

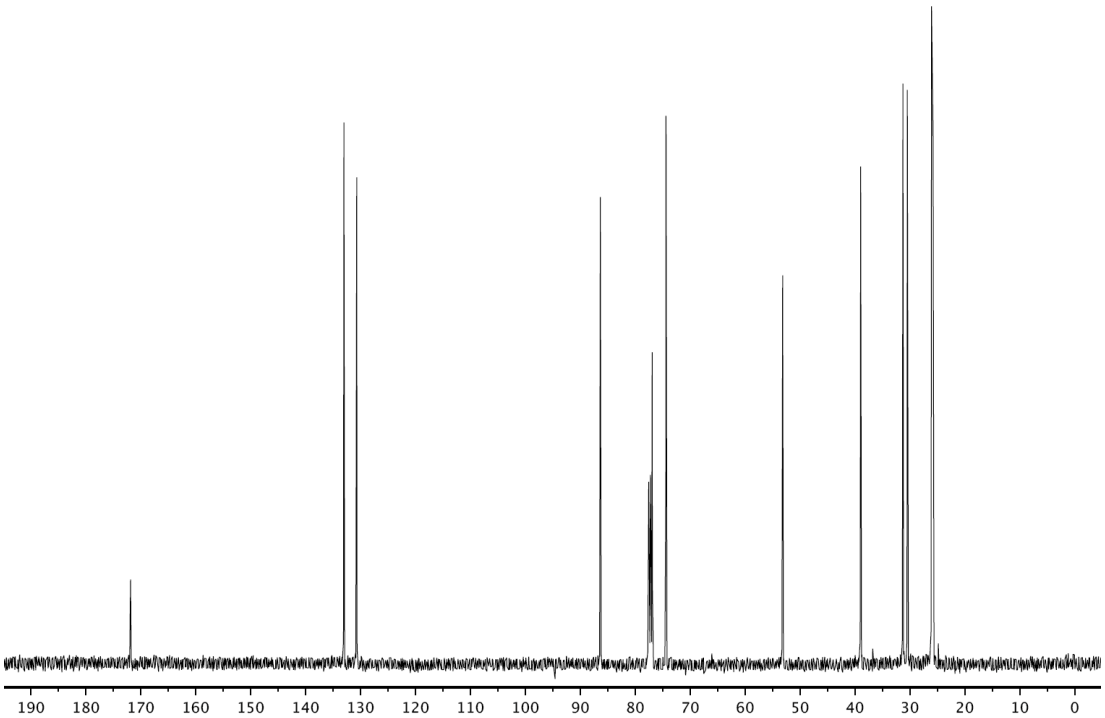

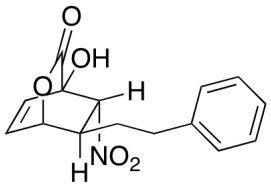

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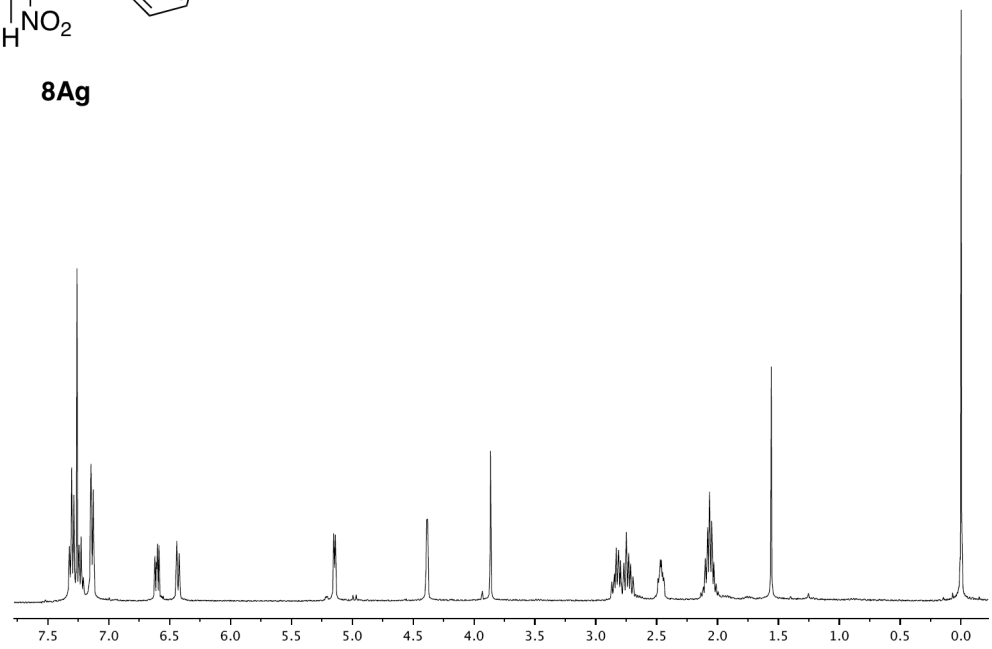

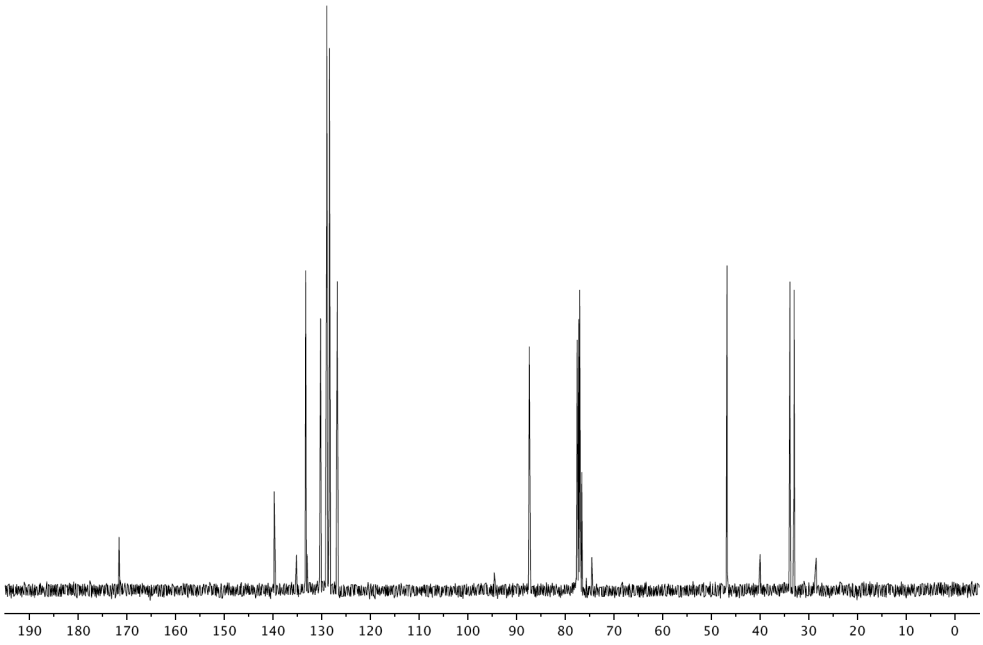

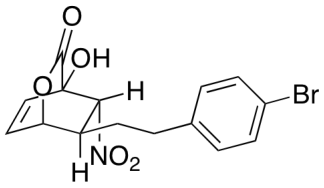

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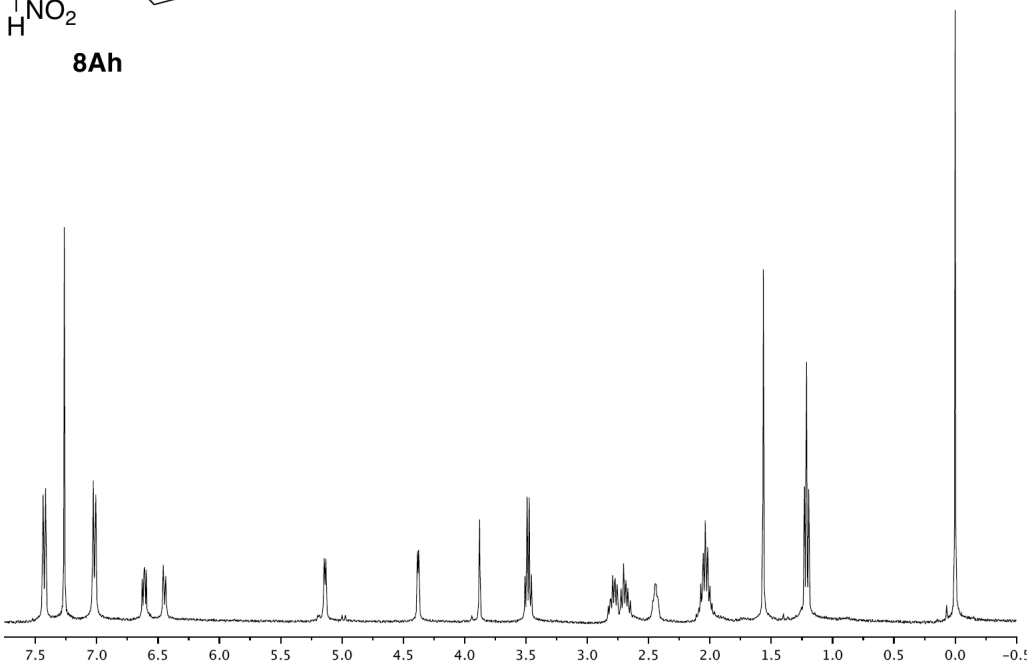

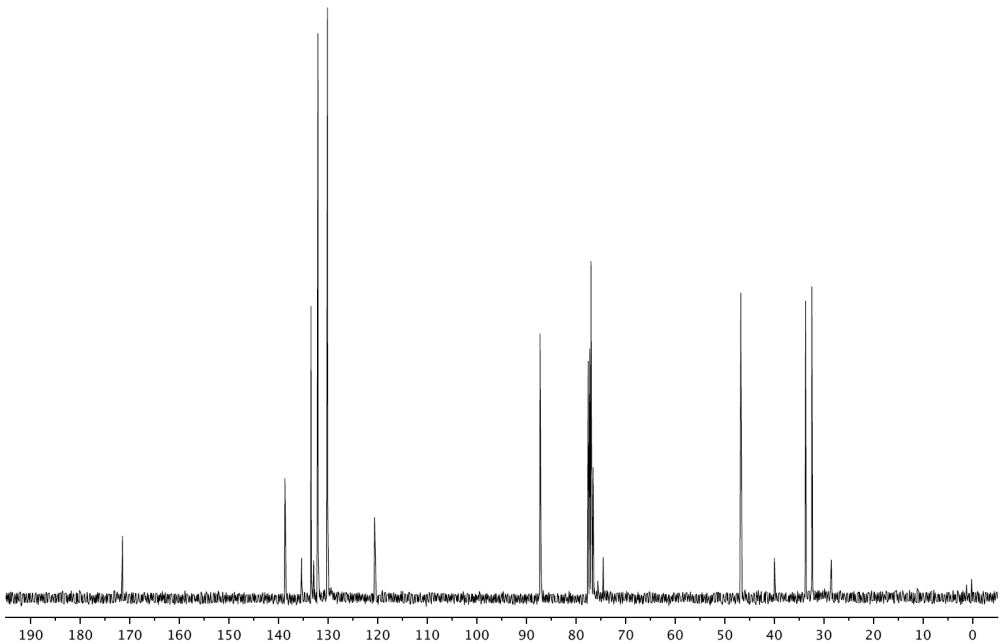

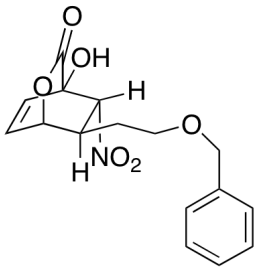

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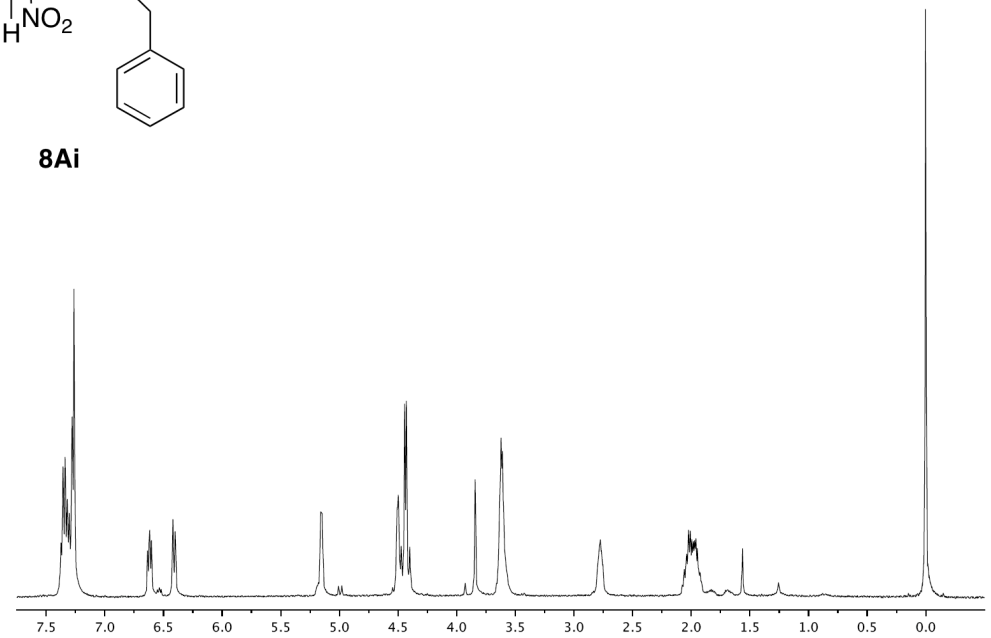

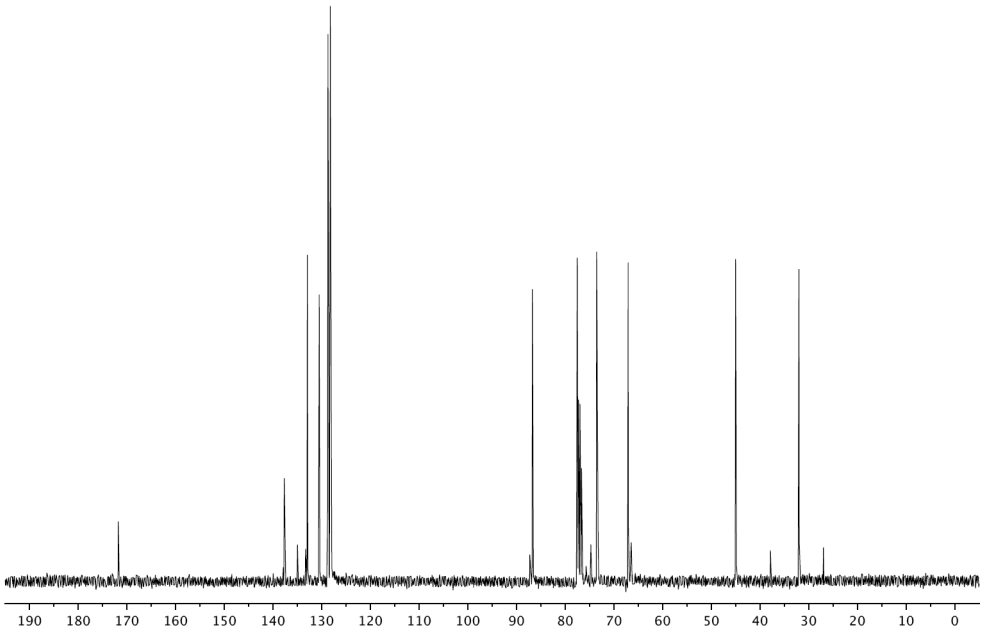

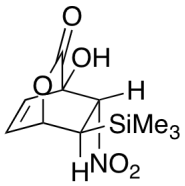
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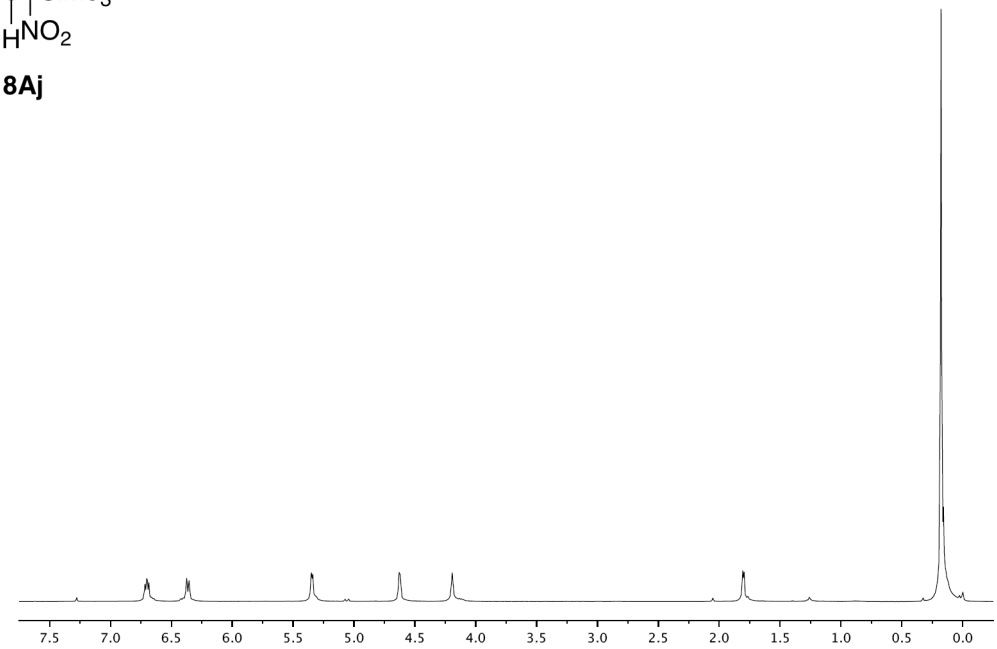
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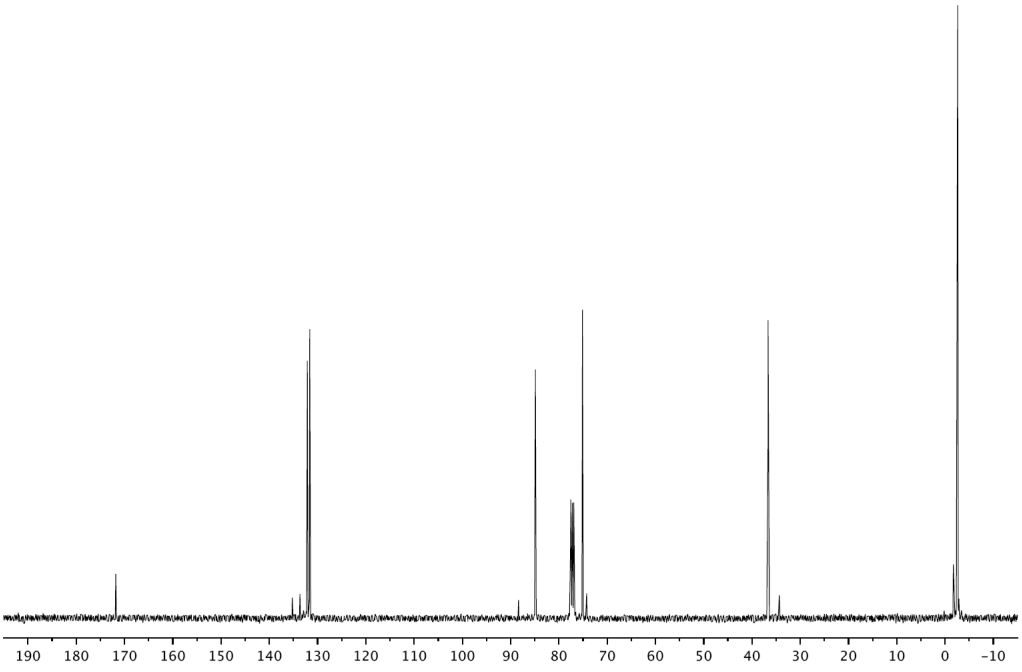
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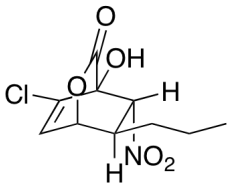

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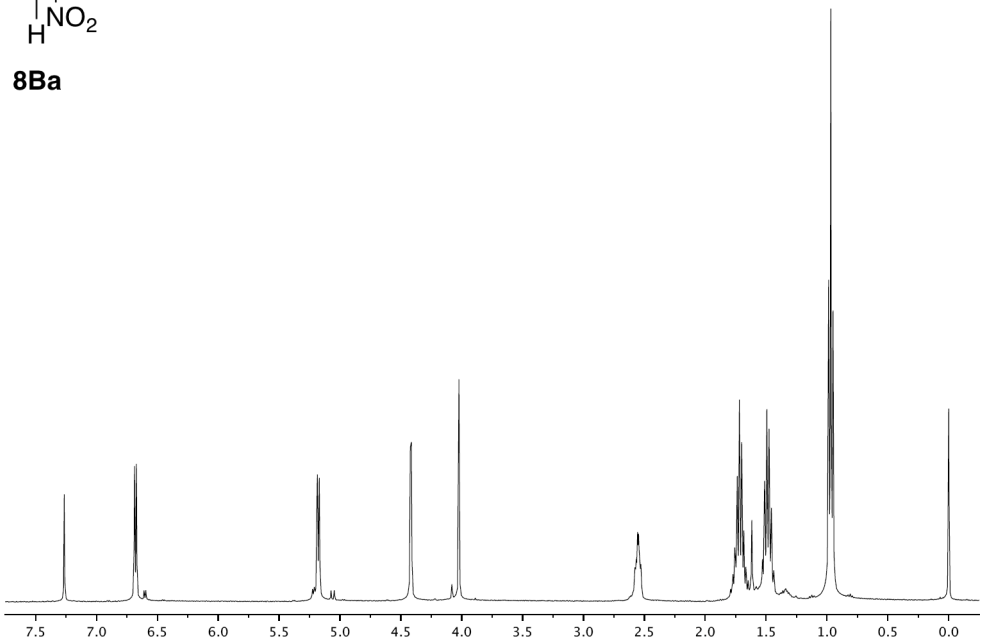

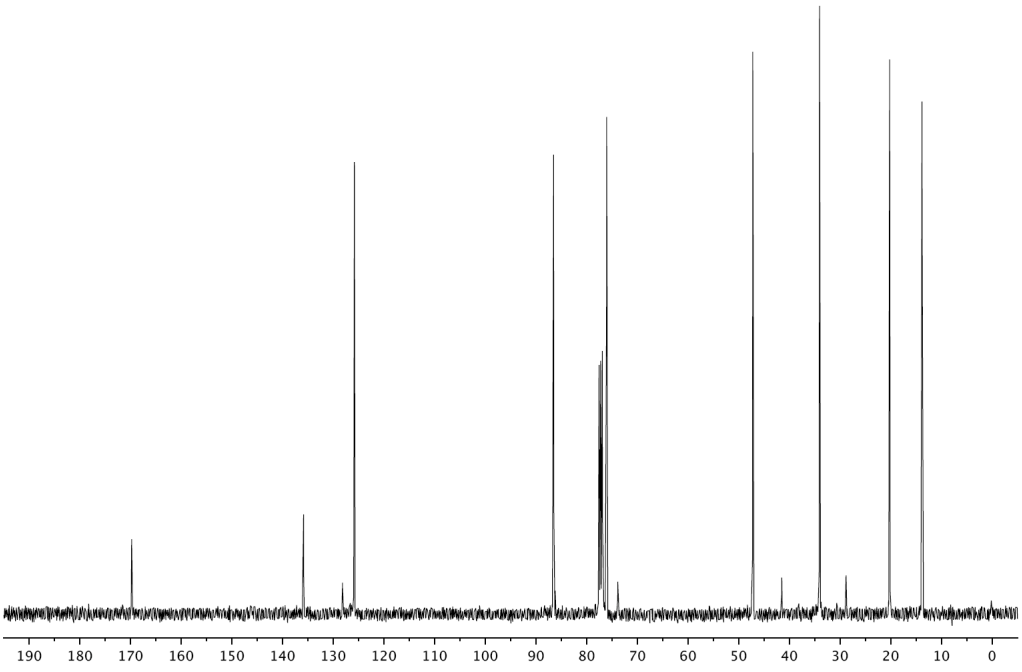

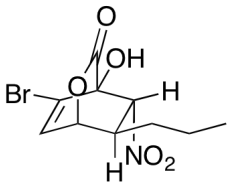

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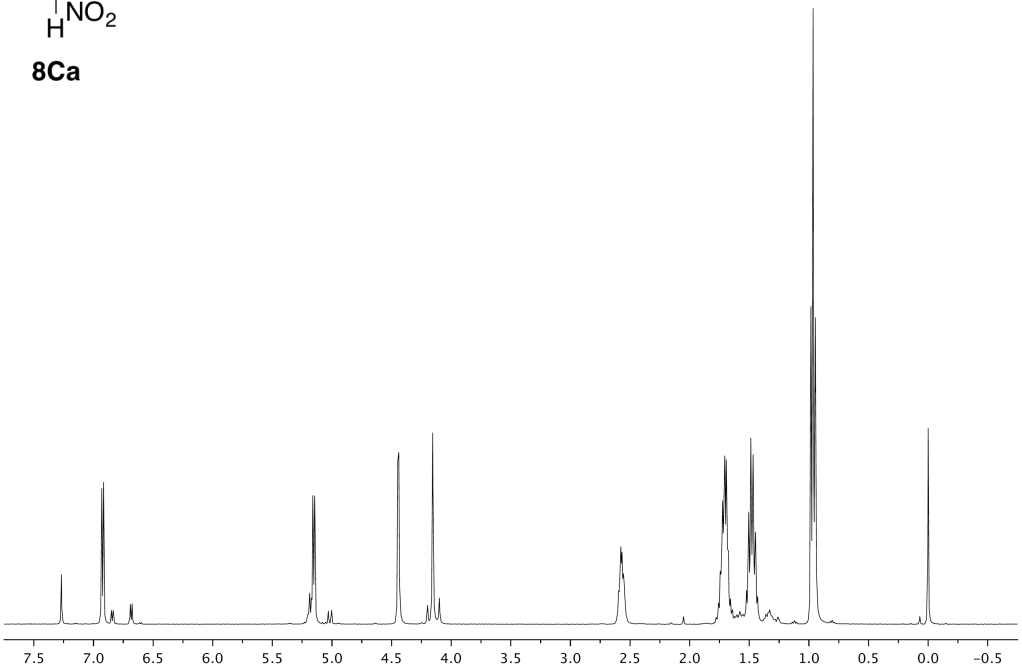

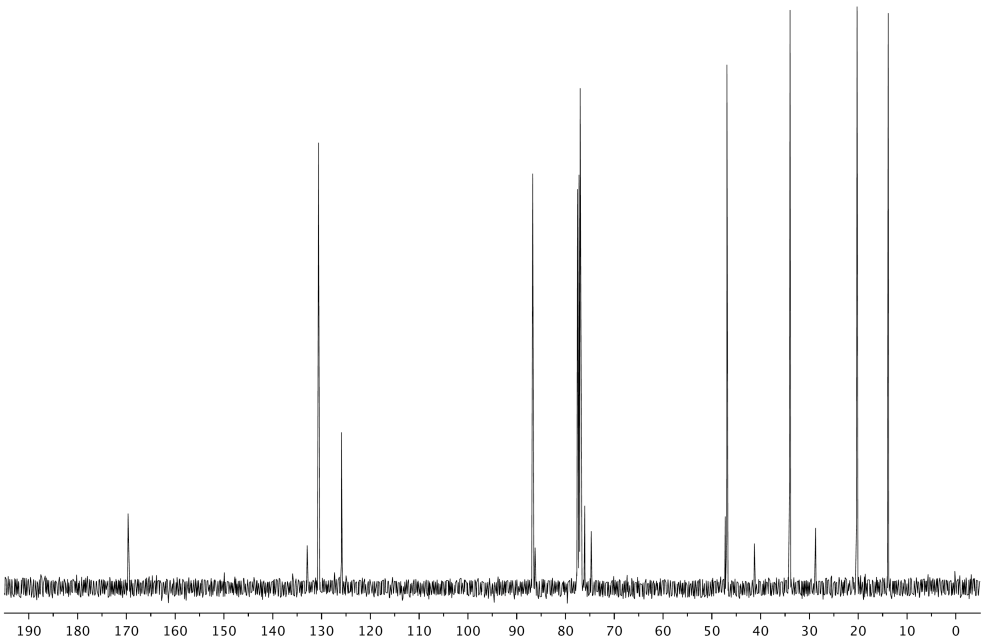

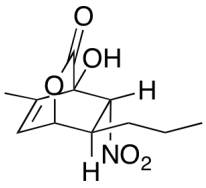

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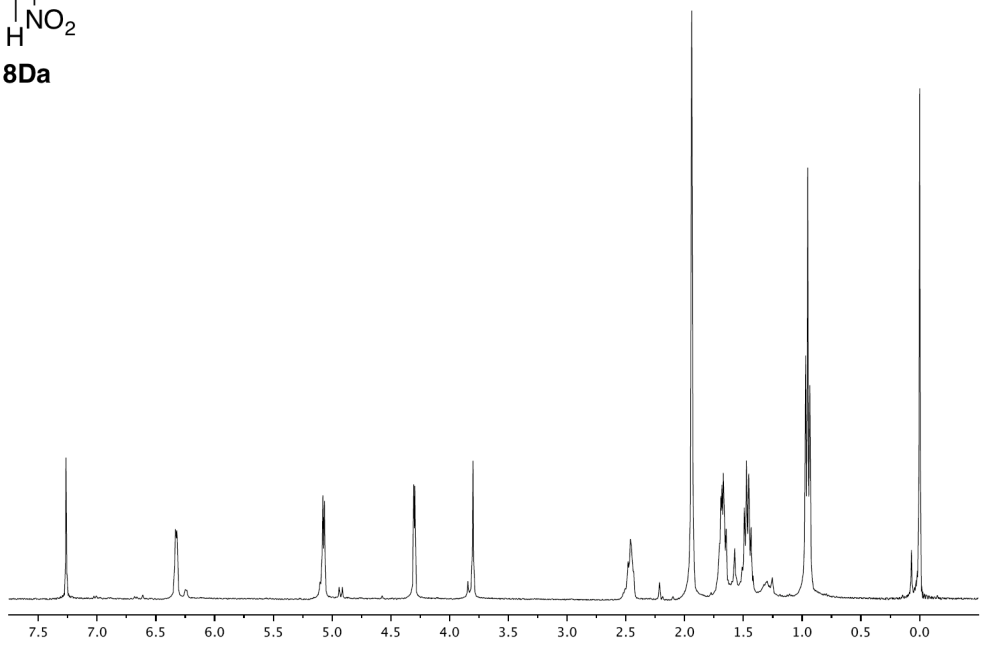

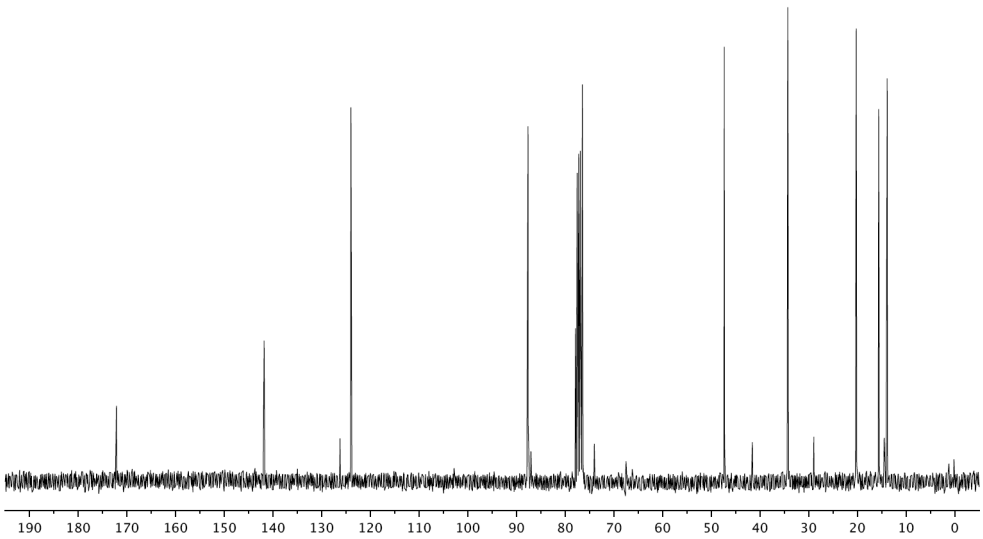

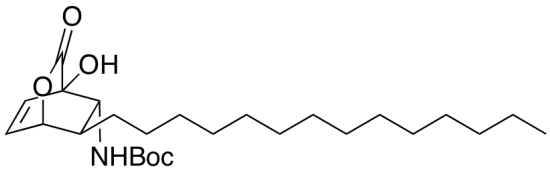

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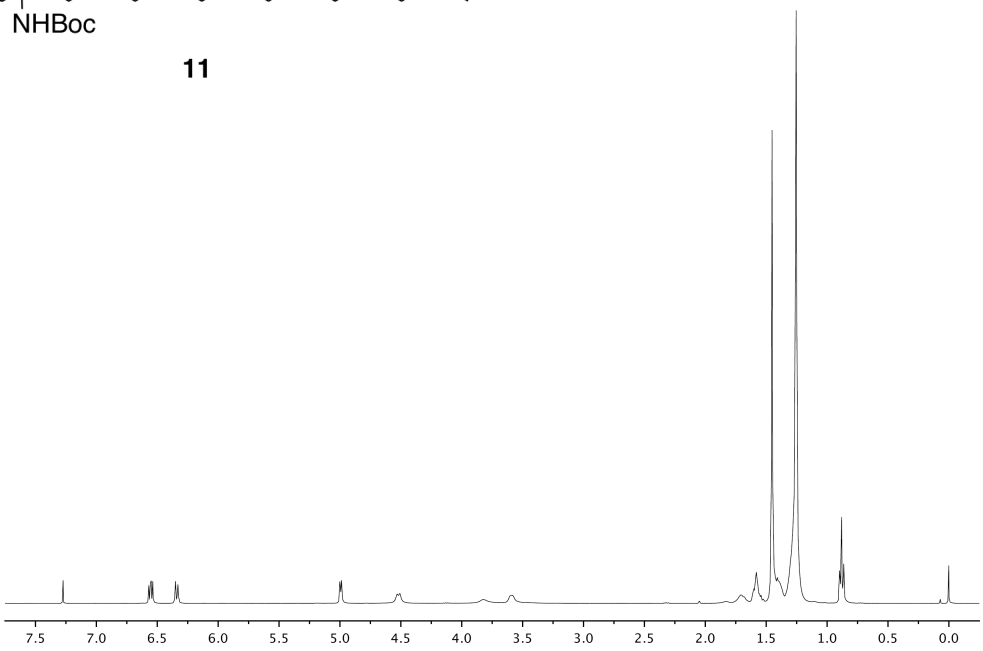

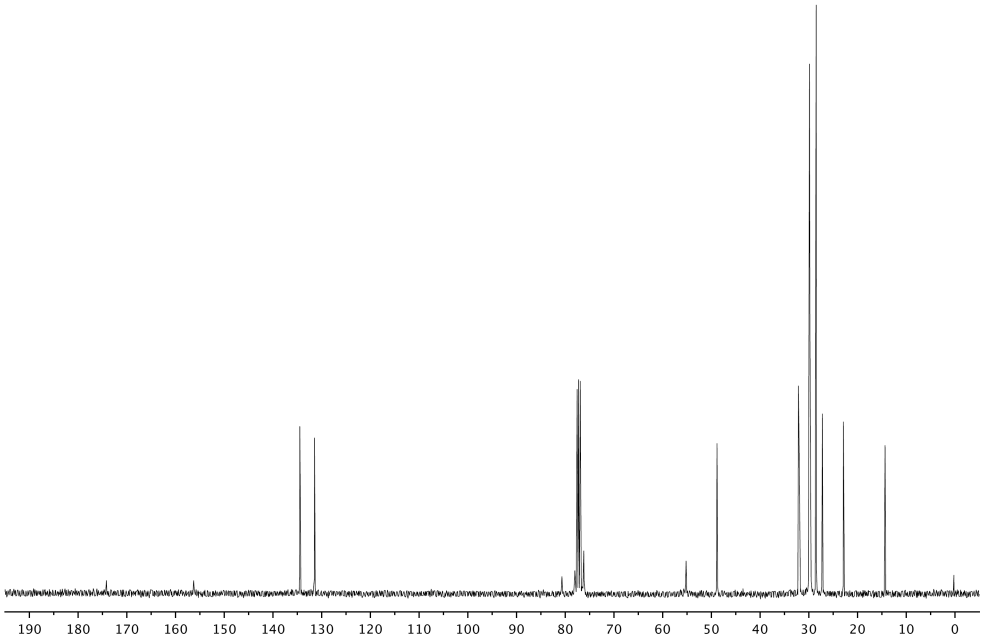

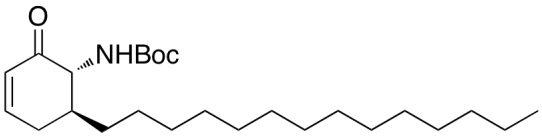

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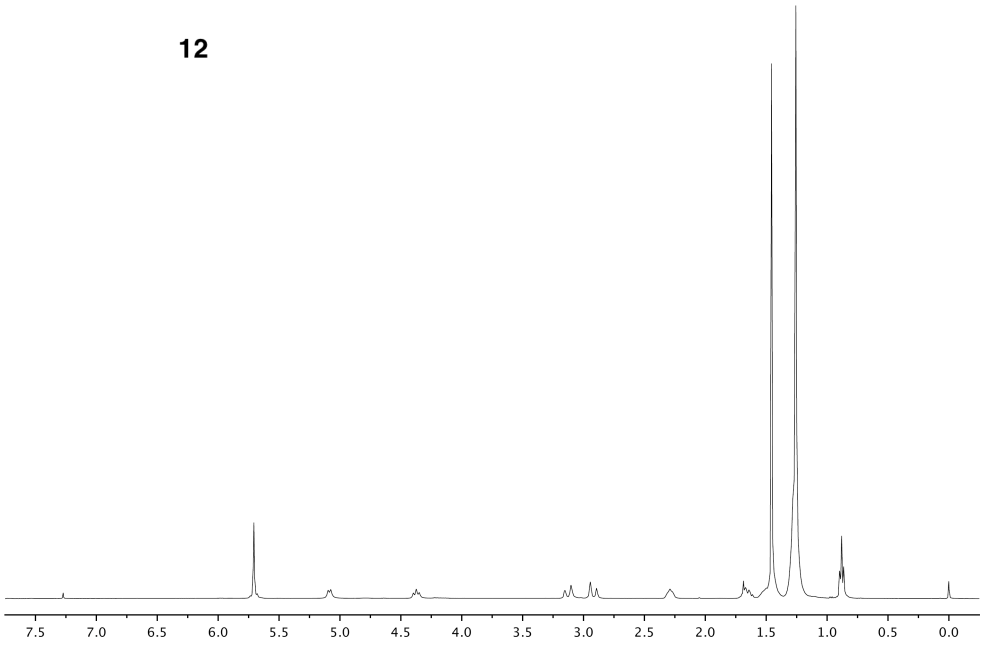

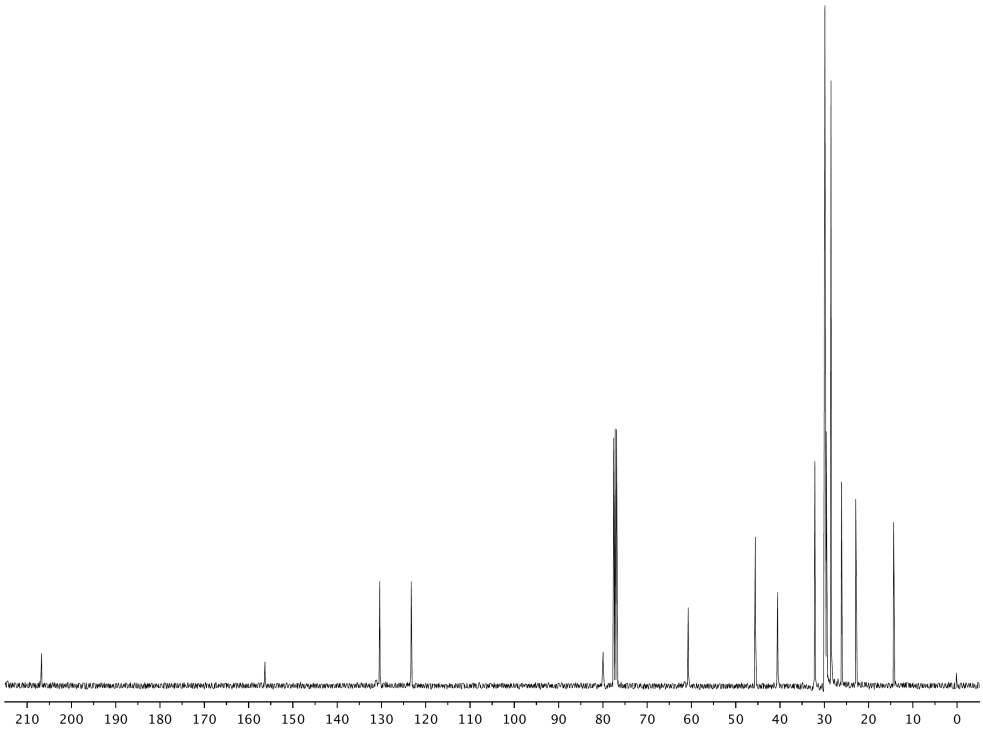

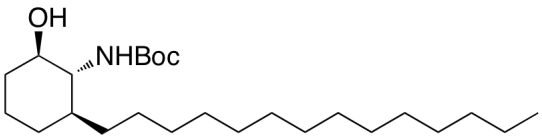

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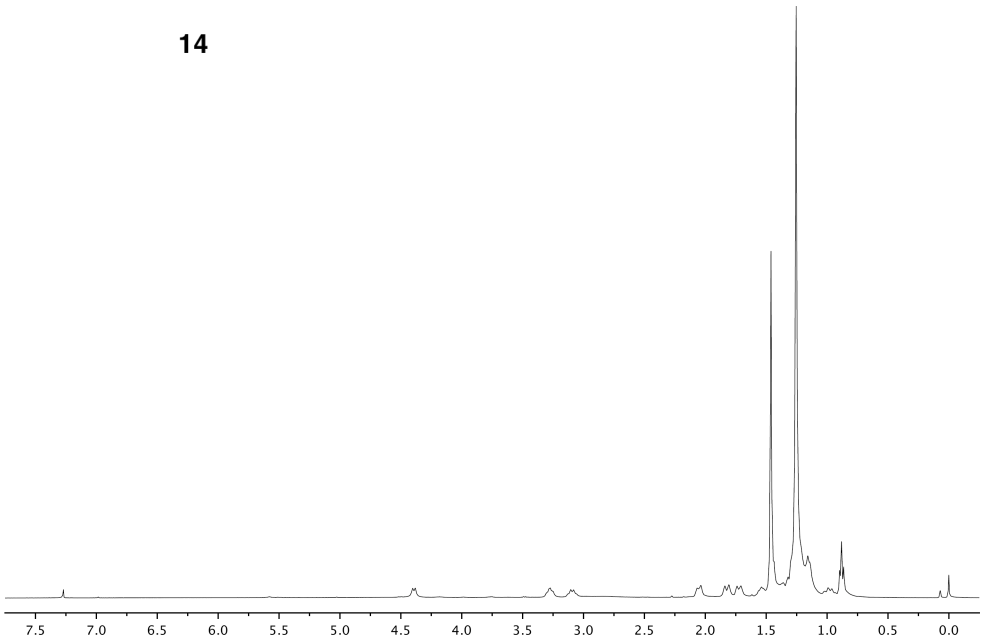
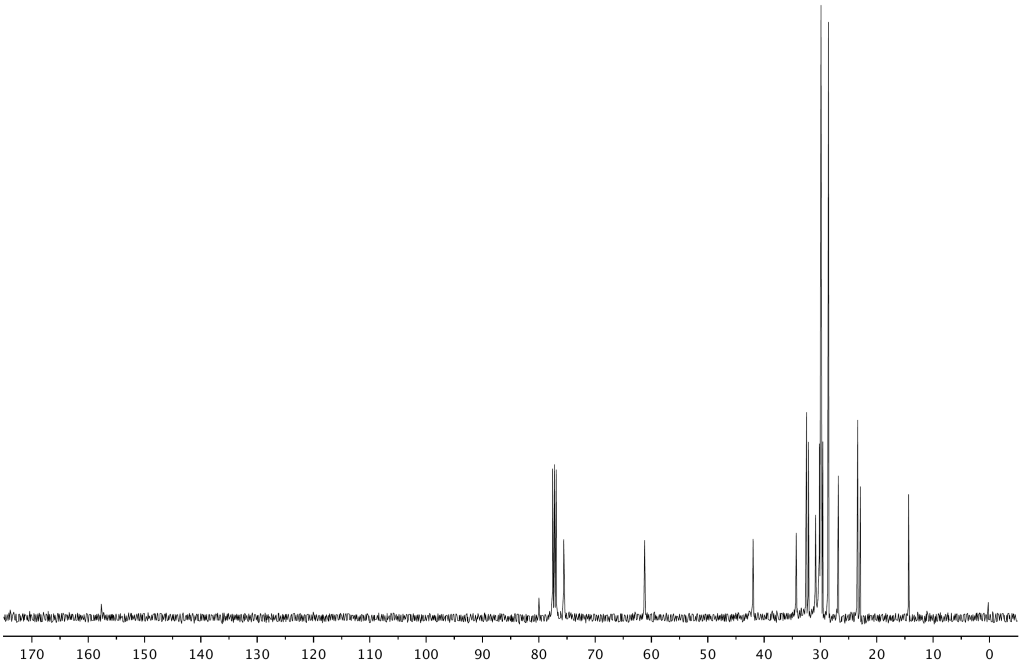
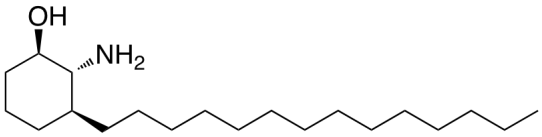
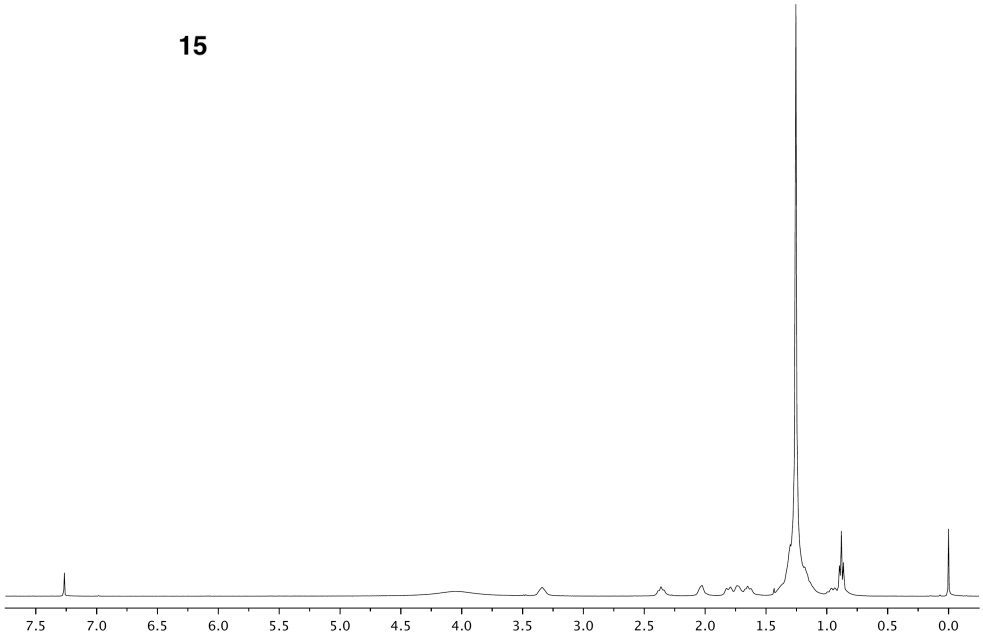





OH
NH2

15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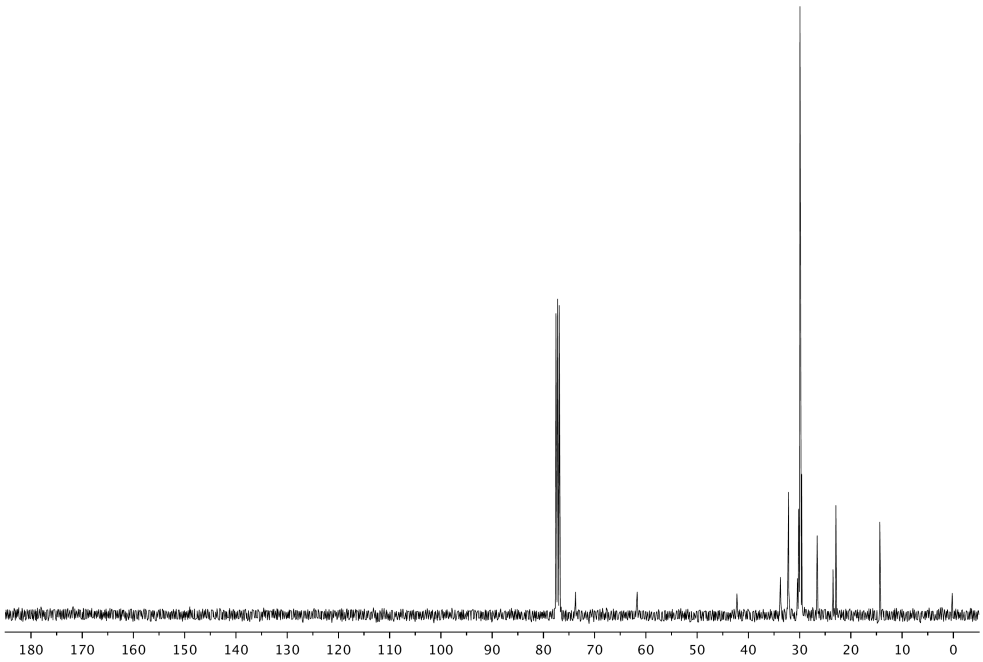
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


180
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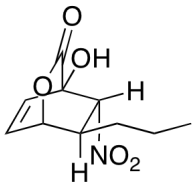
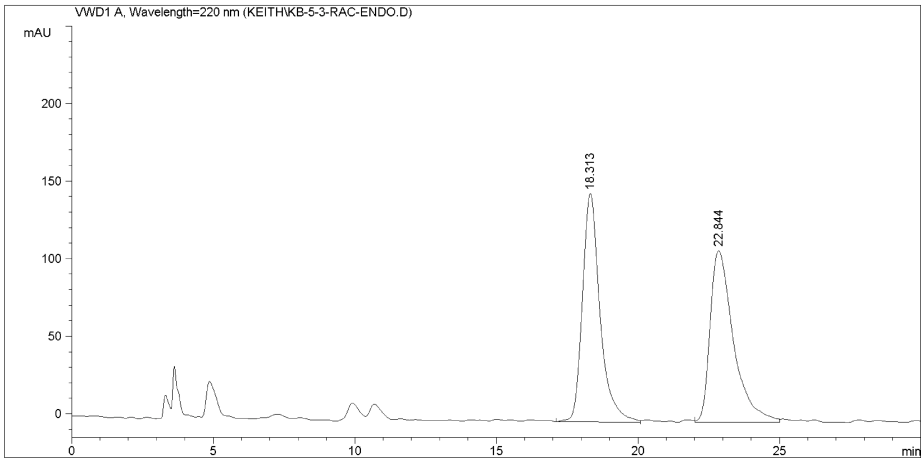
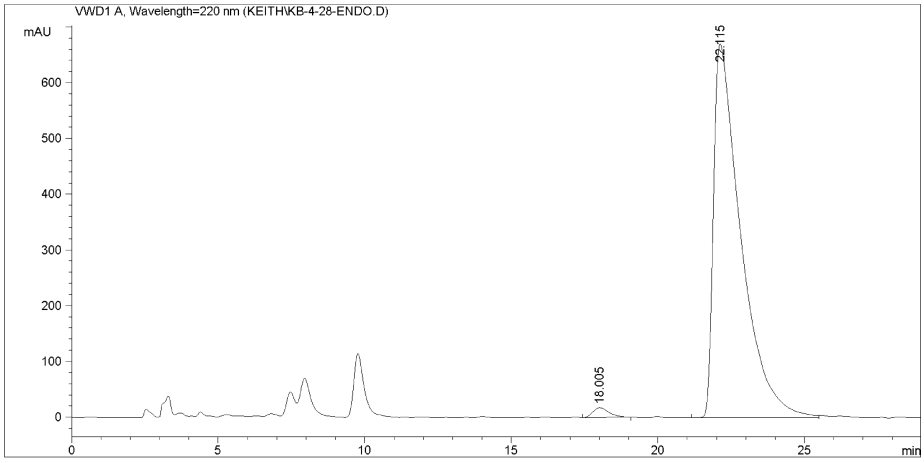
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



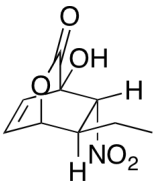
8Aa



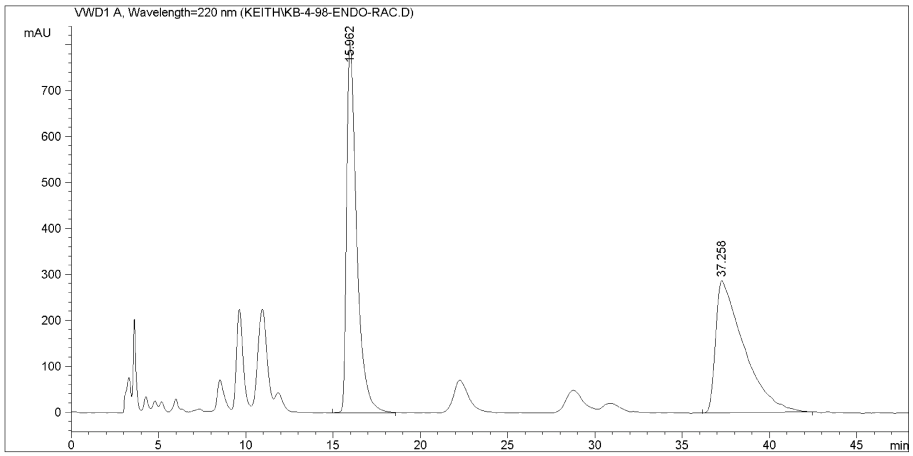

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.313 VB    0.6497 6378.53906  147.18475  49.9830
   2  22.844 VB    0.8851 6382.88721  110.72114  50.0170

Totals :                  1.27614e4   257.90589
```



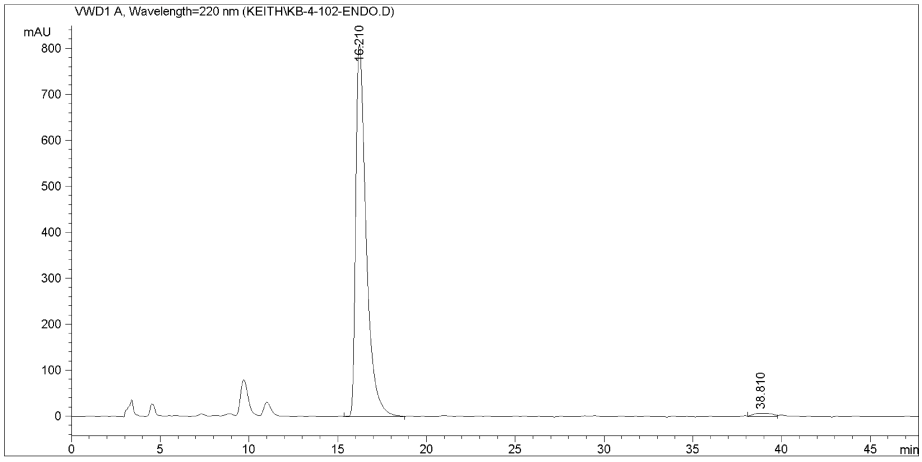

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.005 VB    0.5896  675.29529   17.57116   1.5338
   2  22.115 VV    0.9303 4.33520e4   670.63629  98.4662

Totals :                  4.40273e4   688.20745
```



8Ab




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  15.962 VB    0.6135 3.24463e4   801.56573  50.0533
   2  37.258 VB    1.4547 3.23772e4   287.91083  49.9467

Totals :                 6.48235e4  1089.47656
```

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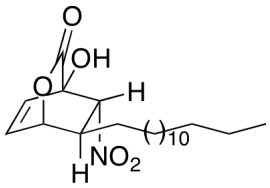
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

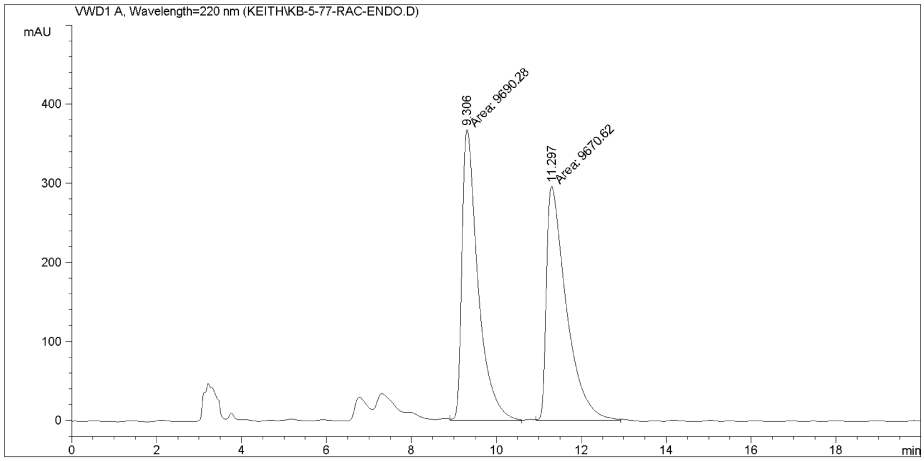

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  16.210 VB    0.6154 3.32698e4   811.17755  98.1058
   2  38.810 VV    1.0425  642.37524    8.24874   1.8942

Totals :                 3.39122e4   819.42629
```



8Ac



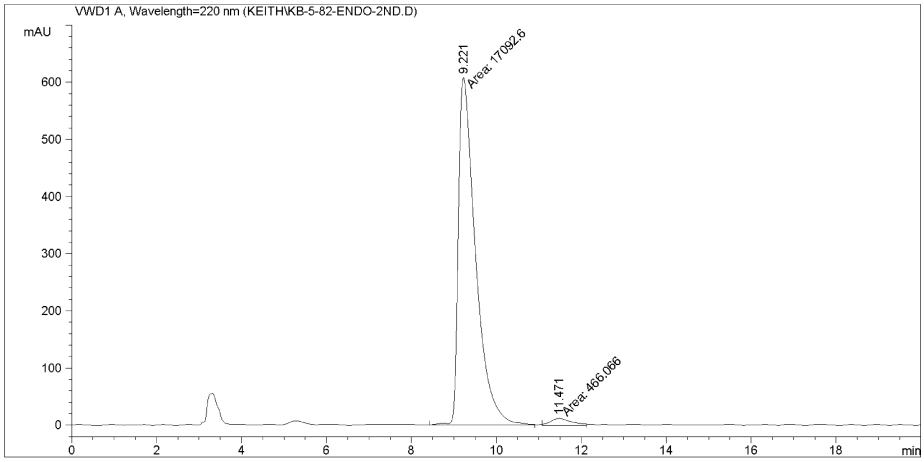

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   9.306 MM    0.4385 9690.28320  368.29663  50.0508
   2  11.297 MM    0.5441 9670.62109  296.25290  49.9492

Totals :                  1.93609e4   664.54953
```

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=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   9.221 MM    0.4687 1.70926e4   607.85791  97.3457
   2  11.471 MM    0.5966  466.06638   13.02071   2.6543

Totals :                  1.75586e4   620.87862
```
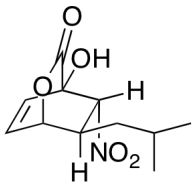
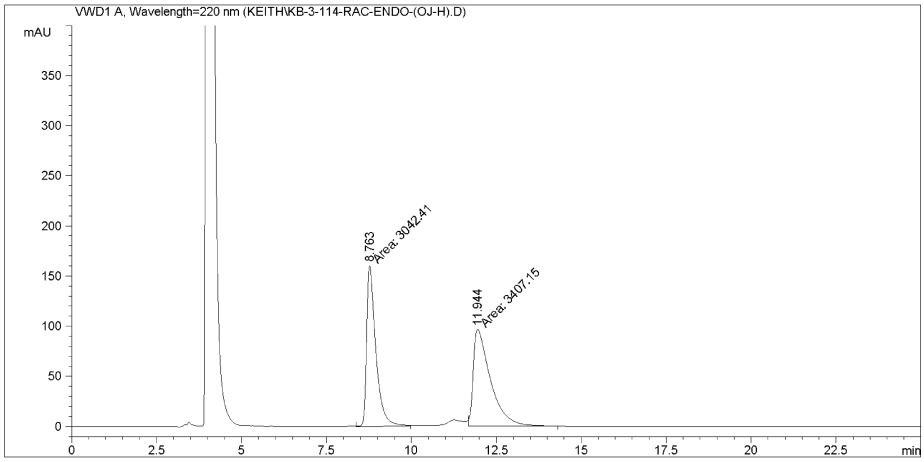



8Ad

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=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   8.763 MM    0.3158 3042.41382  160.56100  47.1724
   2  11.944 FM    0.5882 3407.14771   96.54253  52.8276

Totals :                  6449.56152  257.10353
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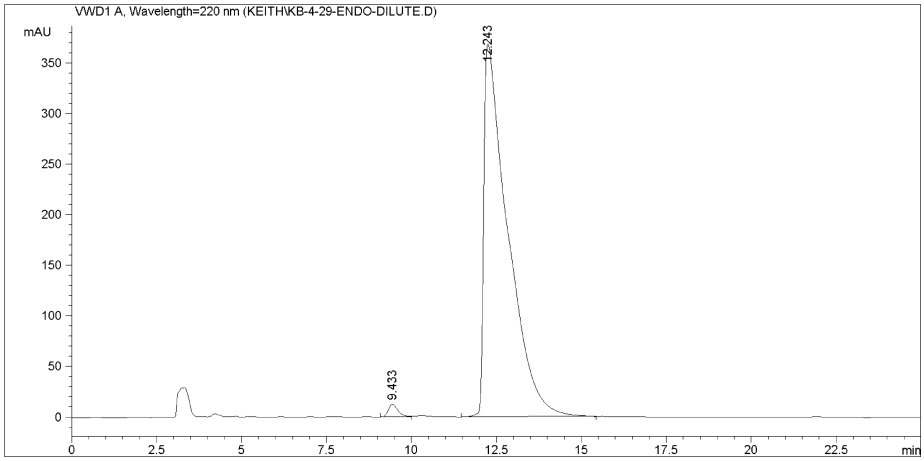


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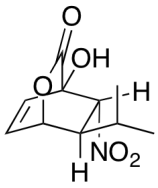
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

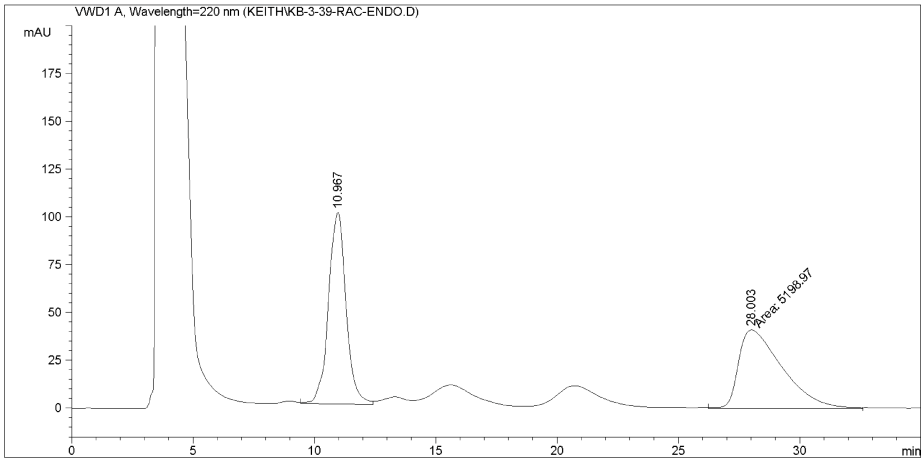

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   9.433 BB    0.3038  253.43420   12.63806   1.3868
   2  12.243 BB    0.6766 1.80214e4   368.68515  98.6132

Totals :                  1.82749e4   381.32321
```



8Ae

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=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  10.967 VB    0.7927 5071.61719  100.22666  49.3800
   2  28.003 MM    2.1042 5198.96680   41.17975  50.6200
```

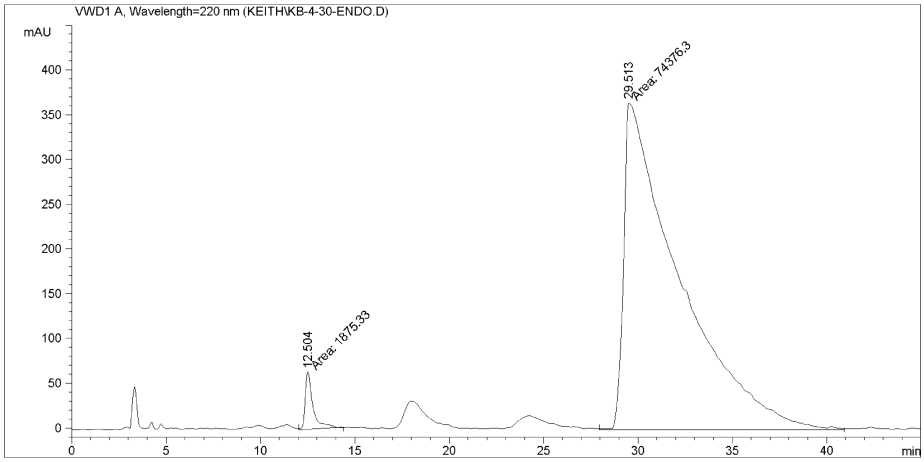


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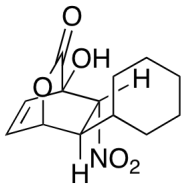
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

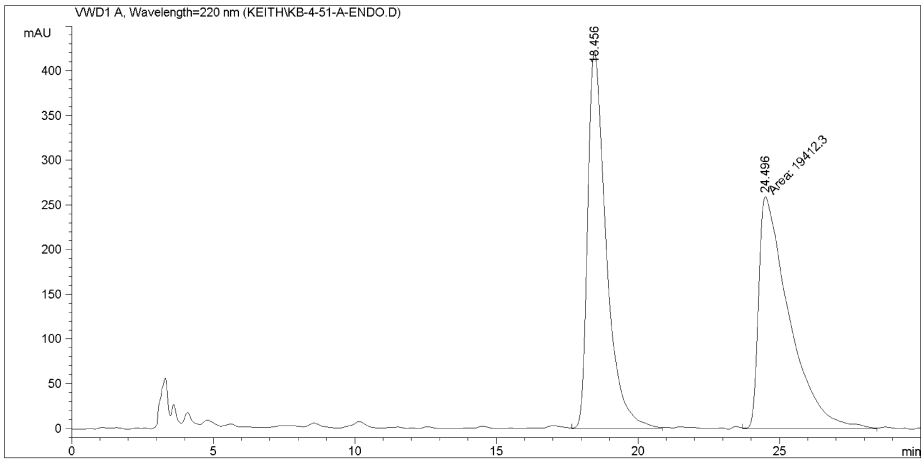

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.504 MM    0.4849 1875.32971   64.46164   2.4594
   2  29.513 MM    3.3905 7.43763e4   365.61545  97.5406

Totals :                  7.62517e4   430.07709
```



8Af

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=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.456 VB    0.6771 1.93031e4   421.39755  49.8591
   2  24.496 MM    1.2459 1.94123e4   259.68967  50.1409

Totals :                  3.87154e4   681.08722
```

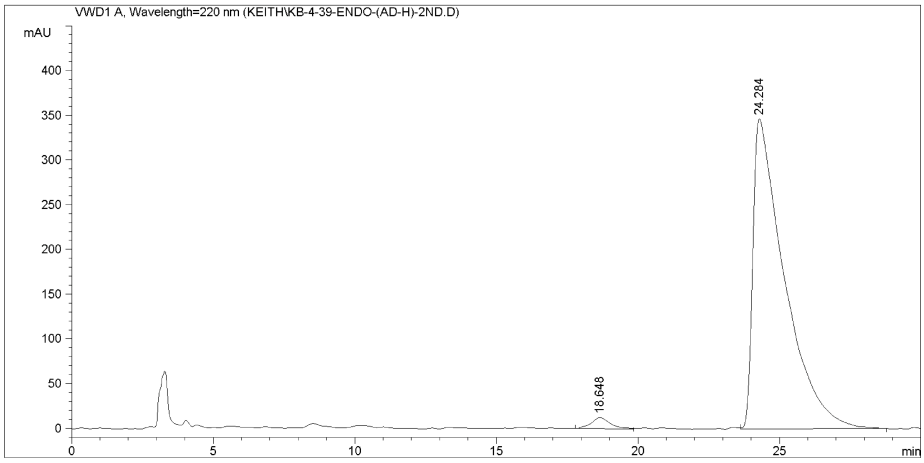


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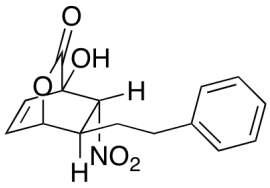
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

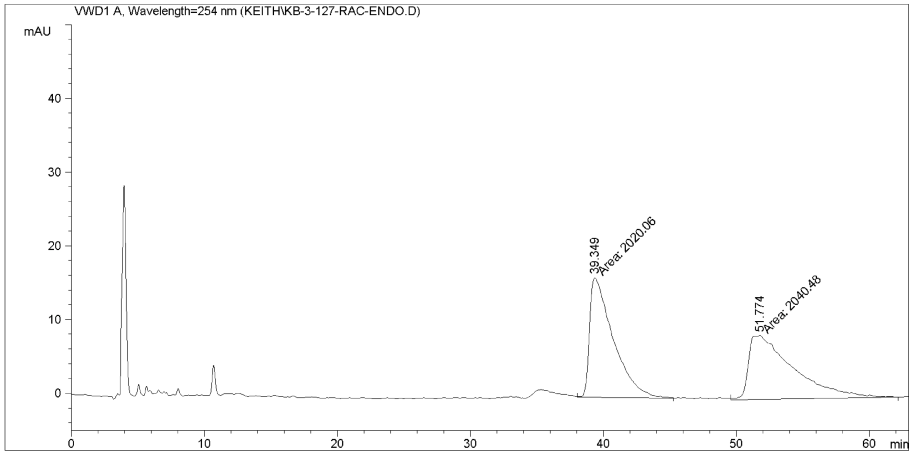

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.648 BB    0.6936  595.74115   12.45227   2.1729
   2  24.284 VB    1.0463 2.68211e4   346.84766  97.8271

Totals :                  2.74169e4   359.29993
```



8Ag

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================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  39.349 MM    2.0705 2020.06006   16.26092  49.7486
   2  51.774 MM    3.9297 2040.47778    8.65400  50.2514

Totals :                  4060.53784   24.91492
```

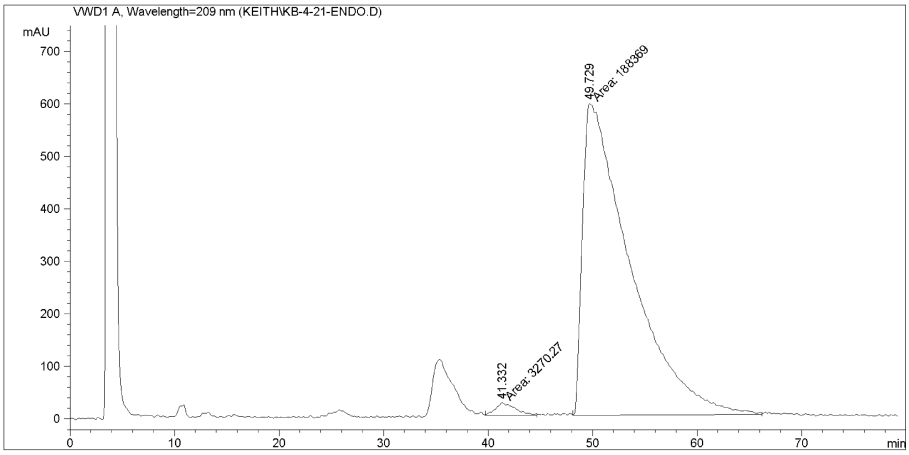


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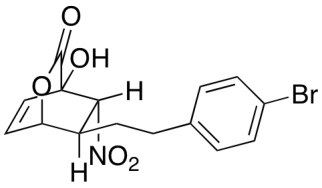
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

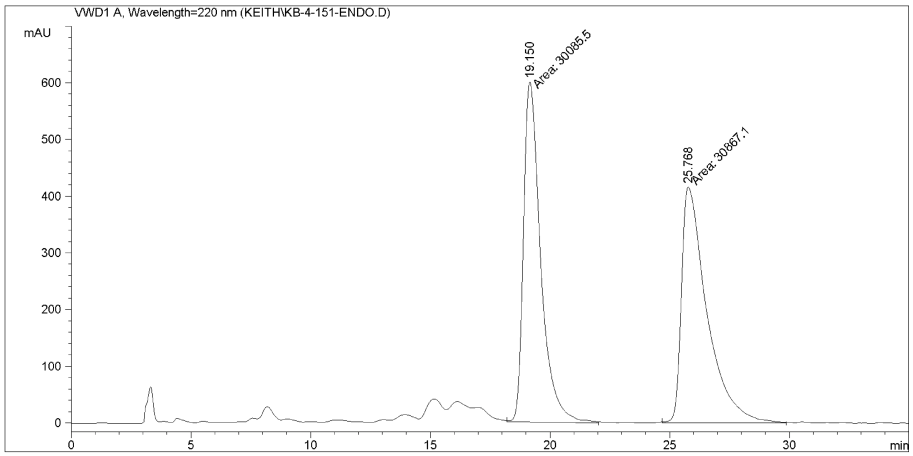

Signal 1: VWD1 A, Wavelength=209 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  41.332 MM    2.2391 3270.27393   24.34267   1.7065
   2  49.729 MM    5.2905 1.88369e5   593.41730  98.2935

Totals :                  1.91639e5   617.75997
```



8Ah



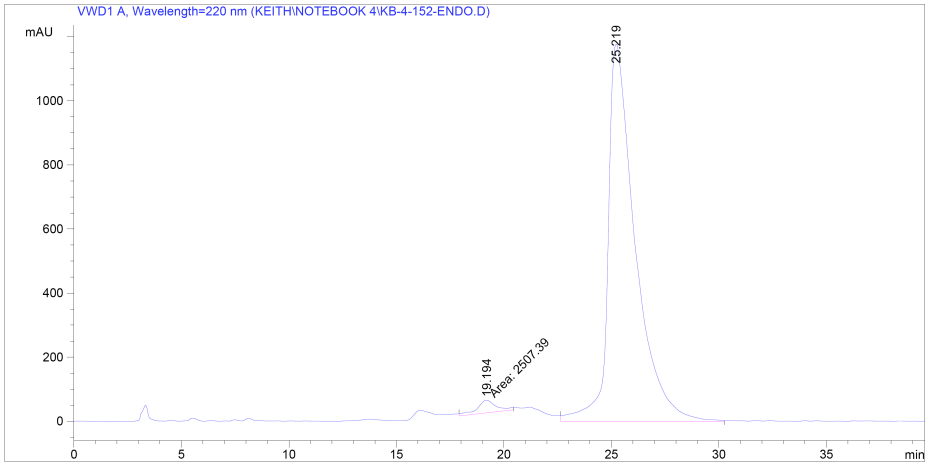

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  19.150 MM    0.8354 3.00855e4   600.23895  49.3588
   2  25.768 MM    1.2351 3.08671e4   416.52316  50.6412

Totals :                  6.09526e4  1016.76212
```



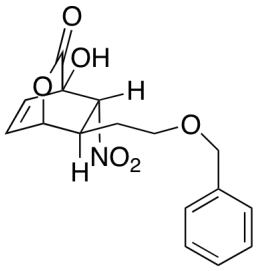

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

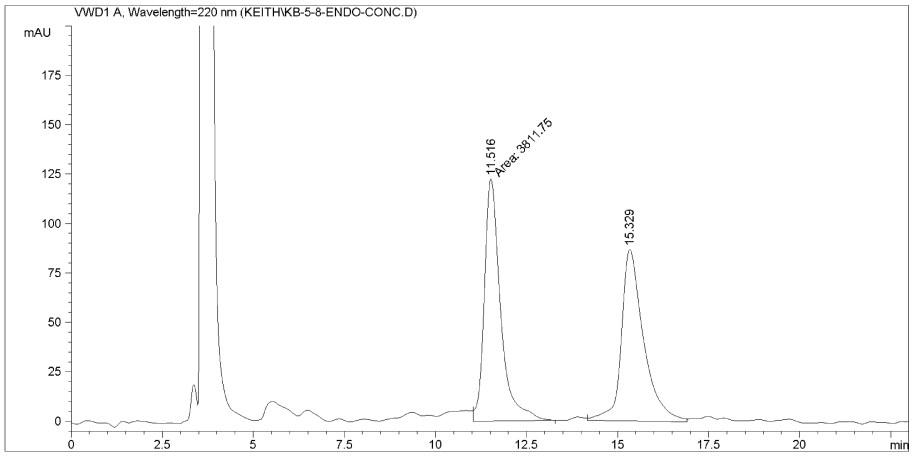

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s   [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  19.194 MM    1.0582 2507.38916   39.49121   2.3606
   2  25.219 VB    1.2184 1.03711e5  1177.33911  97.6394

Totals :                  1.06218e5  1216.83032
```



8Ai



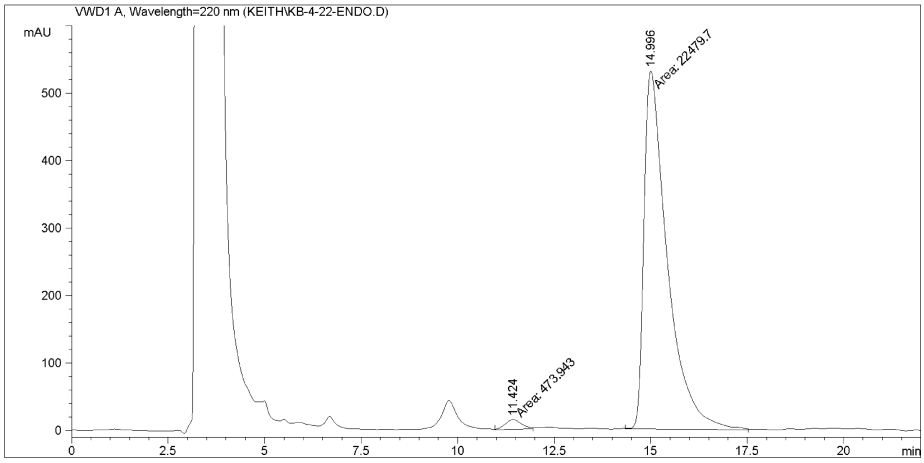

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.516 FM    0.5179 3811.75366  122.67505  50.6730
   2  15.329 VB    0.6192 3710.50806   86.86565  49.3270

Totals :                  7522.26172  209.54070
```



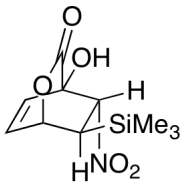

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

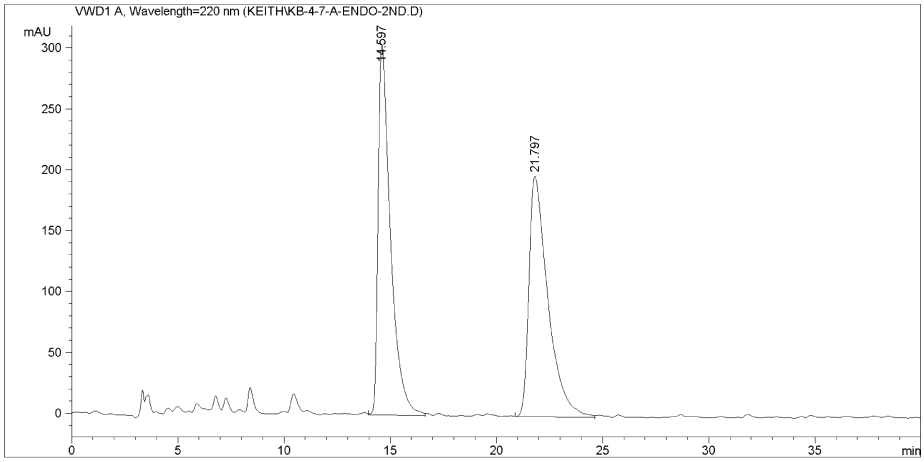

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  11.424 MM    0.5130  473.94315   15.39757   2.0648
   2  14.996 MM    0.7049 2.24797e4   531.50165  97.9352

Totals :                  2.29537e4   546.89921
```



8Aj



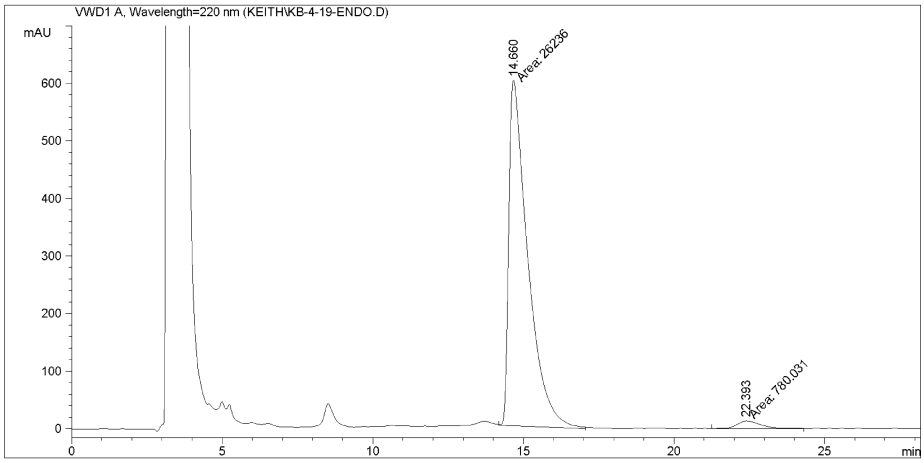

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  14.597 VV    0.5970 1.23719e4   304.98398  50.2445
   2  21.797 VB    0.9013 1.22515e4   197.50153  49.7555

Totals :                  2.46234e4   502.48550
```



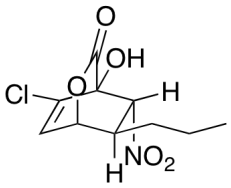

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

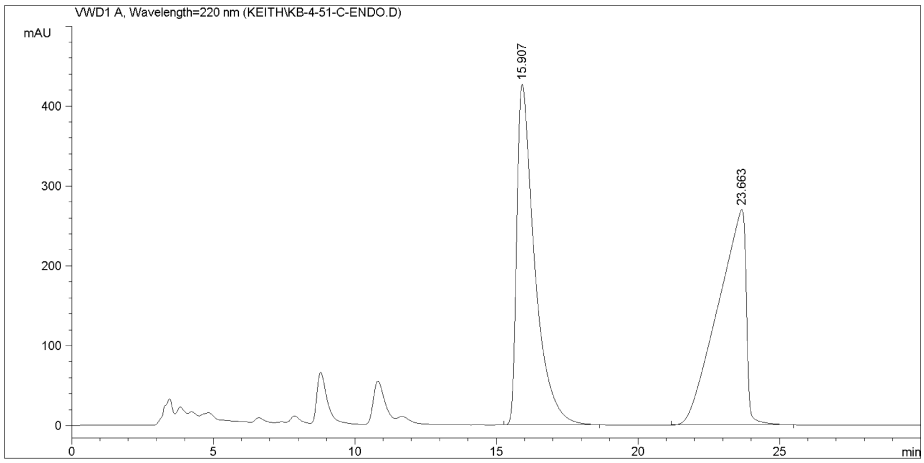

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  14.660 MM    0.7282 2.62360e4   600.43439  97.1127
   2  22.393 MM    0.9688  780.03064   13.41862   2.8873

Totals :                  2.70160e4   613.85301
```



8Ba



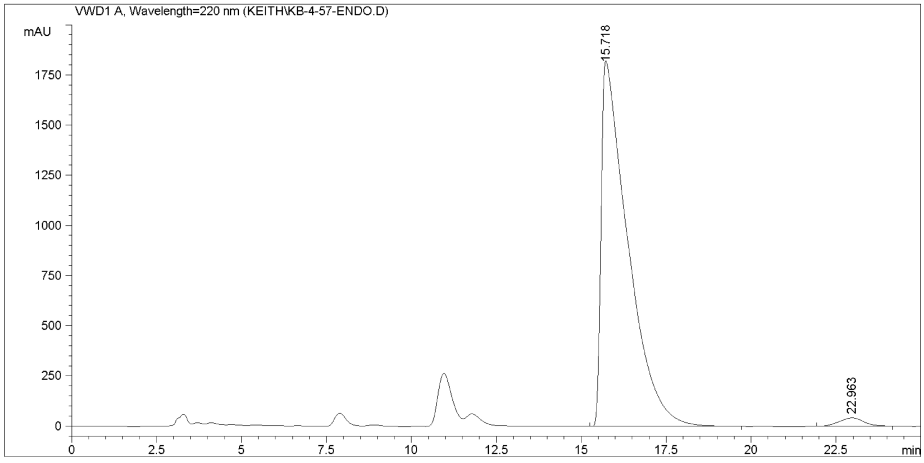

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  15.907 BB    0.6416 1.86442e4   426.00259  49.8587
   2  23.663 BB    0.9635 1.87499e4   269.37775  50.1413

Totals :                  3.73941e4   695.38034
```



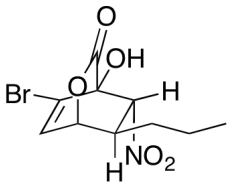

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

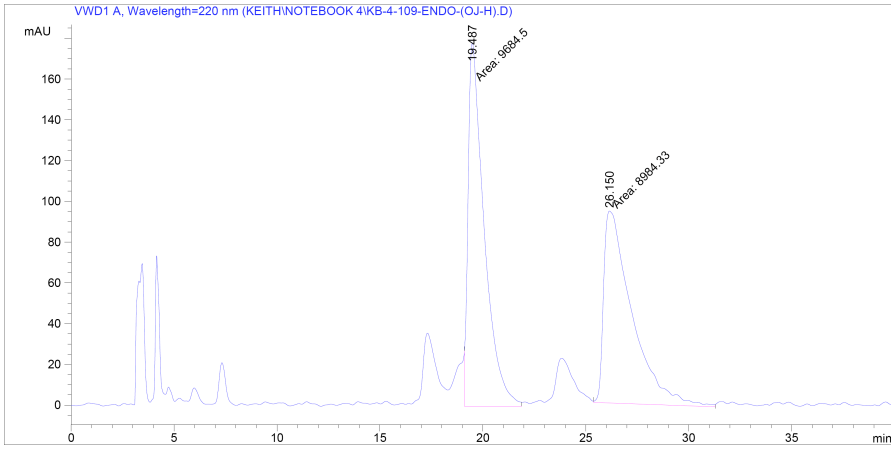

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  15.718 VB    0.7568 9.91531e4  1823.02637  97.6707
   2  22.963 VV    0.8059 2364.68262   43.80975   2.3293

Totals :                  1.01518e5  1866.83611
```



8Ca



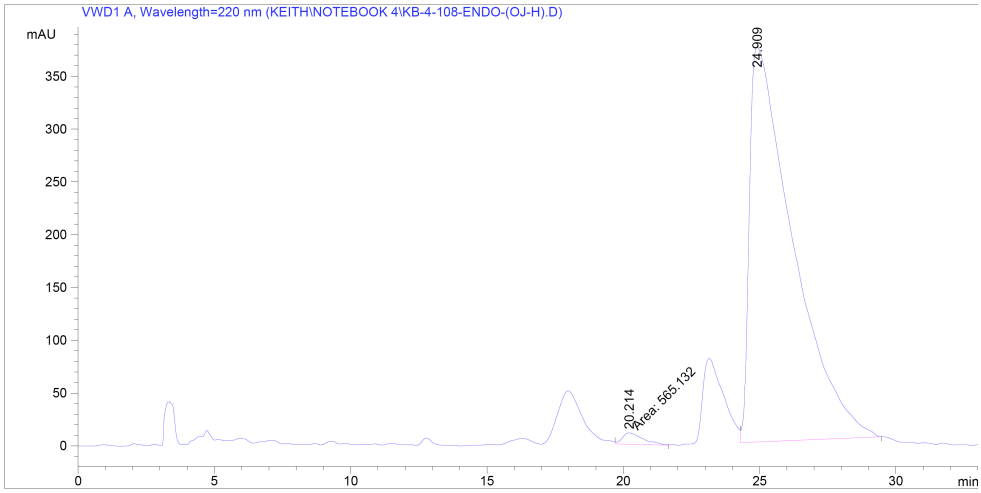

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU    ]      %
----|-------|----|-------|----------|----------|--------|
   1  19.487 FM    0.9046 9684.50293  178.43120  51.8753
   2  26.150 MM    1.5896 8984.32813   94.19874  48.1247

Totals :                 1.86688e4   272.62994
```



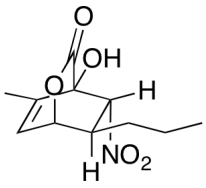

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

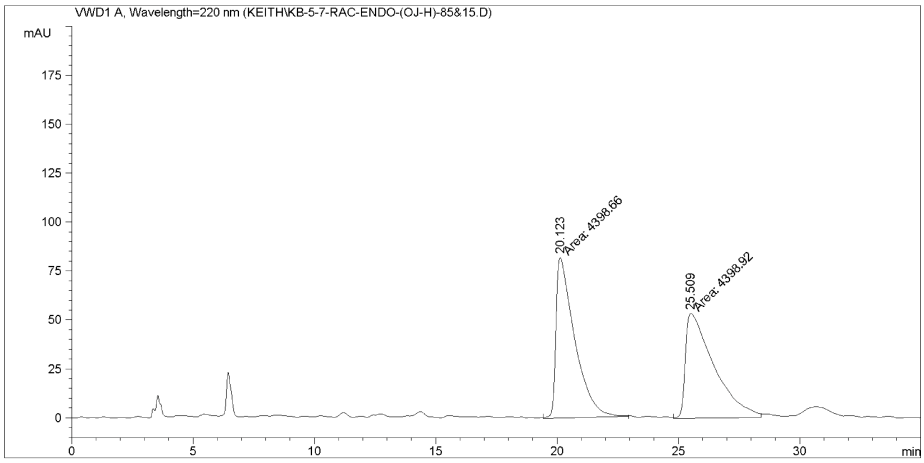

Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s   [mAU    ]      %
----|-------|----|-------|----------|----------|--------|
   1  20.214 MM    0.8737  565.13184   10.78103   1.3486
   2  24.909 VB    1.5189 4.13400e4   374.21497  98.6514

Totals :                 4.19052e4   384.99600
```



8Da

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==================================================================================
                                Area Percent Report
==================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  20.123 MM    0.8945 4398.66406   81.95724  49.9985
   2  25.509 MF    1.3694 4398.92041   53.53854  50.0015

Totals :                  8797.58447  135.49578
```
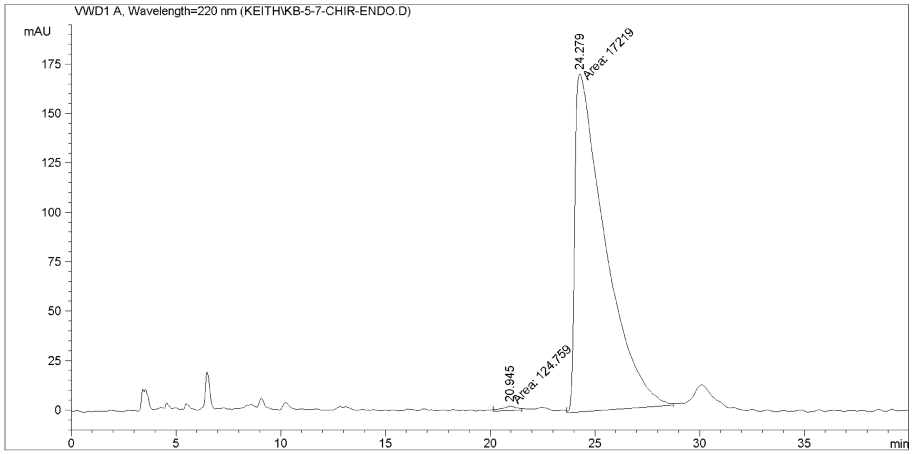
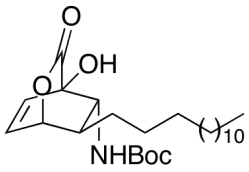
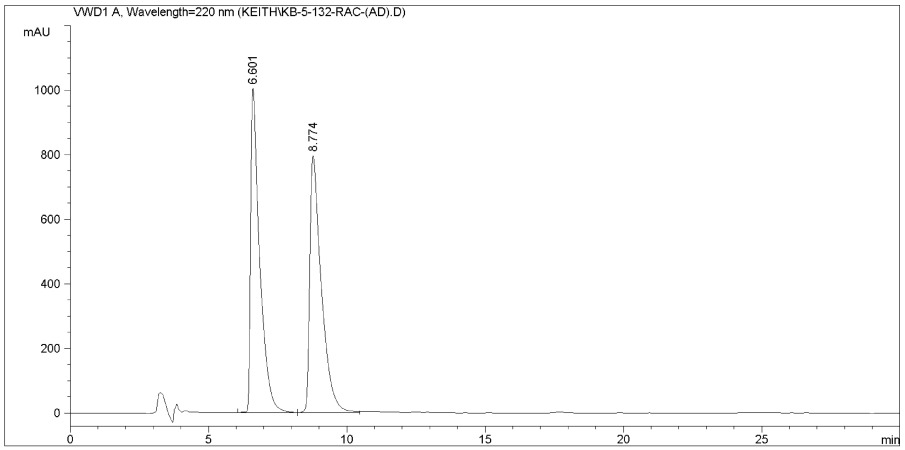



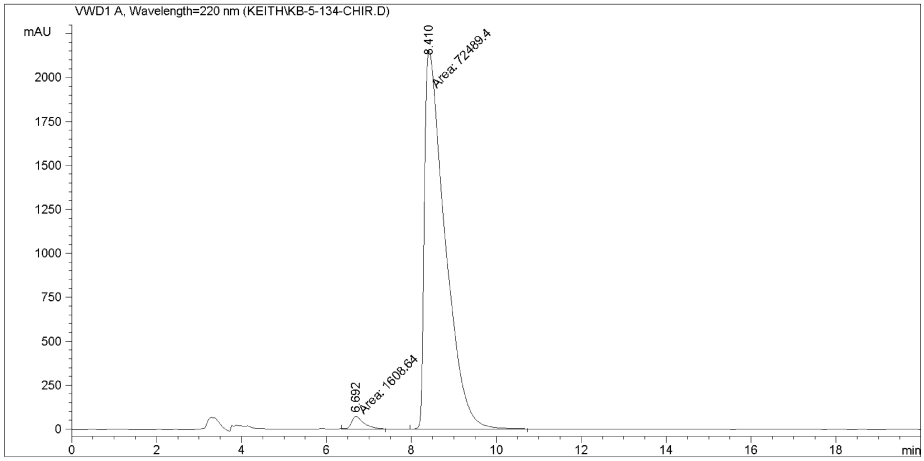

```
==================================================================================
                                Area Percent Report
==================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  20.945 MM    0.8530  124.75947    2.43764   0.7193
   2  24.279 MM    1.6763 1.72190e4   171.19792  99.2807

Totals :                  1.73438e4   173.63556
```



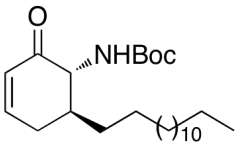
11



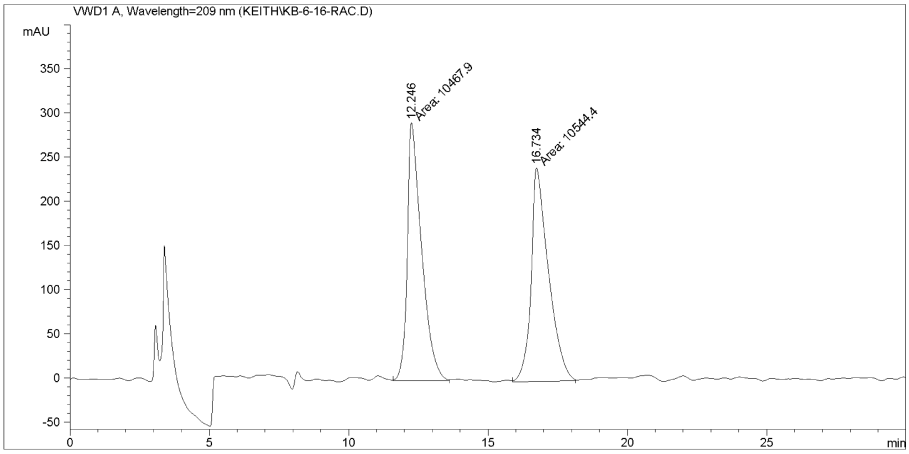

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   6.601 VV     0.3260 2.29081e4  1003.68646  49.6878
   2   8.774 VB     0.4202 2.31960e4   795.71503  50.3122

Totals :                  4.61041e4  1799.40149
```



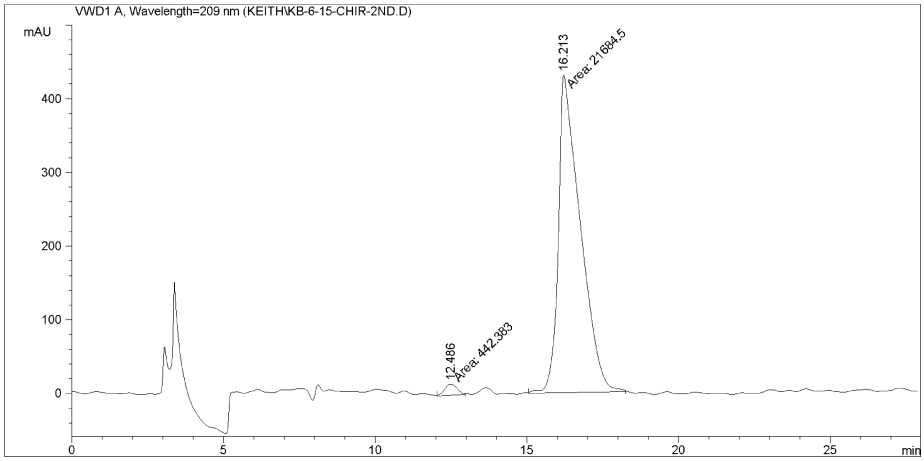

```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   6.692 MM     0.3629 1608.63745   73.87260   2.1710
   2   8.410 MM     0.5606 7.24894e4  2155.15015  97.8290

Totals :                  7.40981e4  2229.02275
```



12




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=209 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.246 MM    0.5967 1.04679e4   292.38962  49.8180
   2  16.734 MM    0.7259 1.05444e4   242.10197  50.1820

Totals :                  2.10123e4   534.49159
```




```
=====================================================================
                        Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=209 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  12.486 MM    0.4780  442.38287   15.42424   1.9993
   2  16.213 MM    0.8378 2.16845e4   431.37070  98.0007

Totals :                  2.21269e4   446.79494
```