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SUPPORTING INFORMATION

Design of Chiral Urea-Quaternary Ammonium Salt Hybrid Catalysts for Asymmetric Reactions of Glycine Schiff Bases

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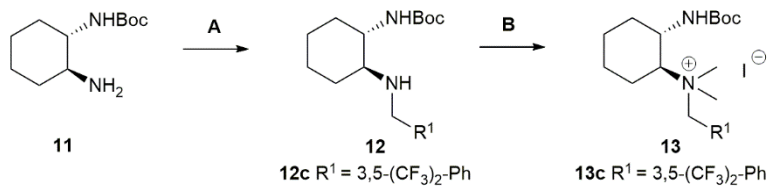
1. General Information:

^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance III 300 MHz spectrometer, on a Bruker Avance III 700 MHz spectrometer with TCI cryoprobe or on Bruker DRX 400, 300, 250 MHz spectrometers. All NMR spectra were referenced on the solvent peak. High resolution mass spectra were obtained using an Agilent 6520 Q-TOF mass spectrometer with an ESI source and an Agilent G1607A coaxial sprayer or using a Thermo Fisher Scientific LTQ Orbitrap XL with an Ion Max API Source. Additional mass spectral analyses were carried out using an electrospray spectrometer, Waters 4 micro quadrupole. Elemental analyses were performed with a FLASHEA 1112 series-Thermo Scientific for CHNS-O apparatus. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer with ATR unit. HPLC analysis were performed either by using a Waters instrument or using a Dionex Summit HPLC system with a Chiralcel OD-H (250 x 4.6 mm, 5 µm), a Chiralcel OD-R (250 x 4.6 mm, 10 µm), a Chiralpak AD-H (250 x 4.6 mm, 5 µm), or a Chiralpak IA-3 (250 x 4.6 mm, 3 µm) chiral stationary phase. Optical rotations were recorded on a Perkin Elmer Polarimeter Model 241 MC and on a Schmidt + Haensch Polarimeter Model UniPol L 1000. All chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. All reactions were performed under an Ar-atmosphere.

2. Optimized Protocol for the Synthesis of Bifunctional Ammonium Salts:

Optimized protocol for quaternization with electron-withdrawing substituents:



11 **12** **13**

12c R^1 = 3,5-$(CF_3)_2$-Ph **13c** R^1 = 3,5-$(CF_3)_2$-Ph

General Syntheses of 13 (via Steps A,B as depicted in Scheme 2 of the manuscript):

Step 1 (A): The corresponding benzaldehyde (2 mmol) was added to a solution of **11** (428 mg, 2 mmol, 1 eq) (prepared from (*S*,*S*)-cyclohexanediamine-**5**-dihydrochloride[1] according to literature[2]) in THF/methanol = 1/1 (10 mL) and the solution was stirred at r.t. overnight. After the addition of $NaBH_4$ (114 mg, 3 mmol, 1.5 eq) stirring was continued for another 2 h at r.t.. The reaction was quenched by addition of water and extracted with water/diethyl ether. The organic phase was washed with brine, dried over Na_2SO_4, and evaporated to dryness to obtain the crude product **12** in quantitative yield which could be directly used without any purification.

Compound 12c (R^1 = 3,5-$(CF_3)_2$-Ph): Obtained in 95% yield (824 mg, 1.9 mmol). ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.08-1.35 (m, 4H), 1.42 (s, 9H), 1.61-1.85 (m, 2H), 1.96 (s (b), 1H), 1.99-2.15 (m, 2H), 3.31-3.47 (m, 1H), 3.83 (d, 1H, *J* = 14.1 Hz), 4.00 (d, 1H, *J* = 14.1 Hz), 4.48 (d, 1H, *J* = 7.3 Hz), 7.73 (s, 1H), 7.82 (s, 2H) ppm.

Step 2 (B): The corresponding amine **12** (1.7 mmol) was dissolved in 3 ml DMF. After the addition of K_2CO_3 (287 mg, 2.1 mmol, 1.2 eq) and methyl iodide (646 µl, 10.4 mmol, 6 eq) the suspension was stirred for 20-30 h at 60 °C. After removal of excess methyl iodide under reduced pressure, the suspension was extracted with dichloromethane/brine. The organic phase was dried over Na_2SO_4 and removal of the solvent under reduced pressure gives **13**, which was used without further purification.

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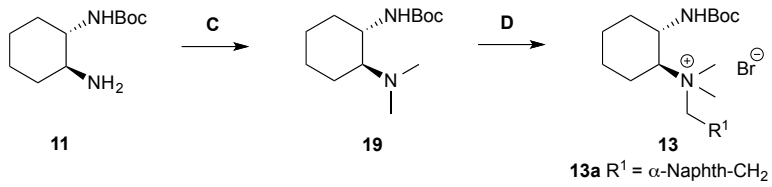
1) H.-J. Schanz, M. Linseis, D. Gilheany, *Tetrahedron: Asymmetry* **2003**, *14*, 2763-2769.

2) D. W: Lee, H.-J. Ha, W. K. Lee, *Synth. Commun.* **2007**, *37*, 737-742.

Compound 13c (R^1 = 3,5-$(CF_3)_2$-Ph): Obtained in 70% yield (1.13 g, 1.2 mmol). $[\alpha]_D^{21}$ (c = 1.8, dichloromethane) = -7.4°; ^{1}H NMR (700 MHz, δ, $CDCl_3$, 298 K): 1.32-1.40 (m, 1H), 1.46 (s, 9H), 1.58-1.66 (m, 1H), 1.66-1.74 (m, 1H), 1.77-1.84 (m, 1H), 1.95-2.06 (m, 3H), 2.59-2.64 (m, 1H), 3.22 (s, 3H), 3.28 (s, 3H), 4.11-4.18 (m, 1H), 4.93-5.00 (m, 1H), 5.16 (d, 1H, J = 12.8 Hz), 5.36 (d, 1H, J = 12.8 Hz), 5.87 (d, 1H, J = 9.9 Hz), 8.01 (s, 1H), 8.13 (s, 2H) ppm; ^{13}C NMR (125 MHz, δ, $CDCl_3$, 298 K): 24.8, 24.8, 27.7, 28.5, 35.7, 49.7, 51.1, 51.7, 63.1, 77.8, 81.5, 122.8 (q, J = 273 Hz), 124.9, 130.3, 133.0 (q, J = 34 Hz), 133.6, 155.9 ppm; ^{19}F NMR (282 MHz, δ, $CDCl_3$, 298 K): -62.8 ppm; IR (film): $\tilde{\nu}$ = 3431, 3270, 3011, 2980, 2939, 2867, 1695, 1625, 1516, 1467, 1455, 1393, 1370, 1323, 1281, 1242, 1176, 1138, 1048, 1024, 904, 870, 844, 737, 709, 683 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{31}F_6N_2O_2^+$: 469.2284 [M^+], found: 469.2281.

Optimized protocol for quaternization with sterically demanding substituents:



11 **19** **13**

13a R^1 = α-Naphth-CH_2

General Syntheses of 13 (via C,D as depicted in Scheme 2 of the manuscript):

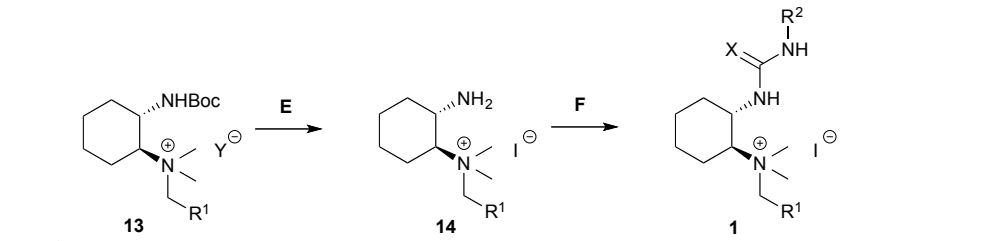
Step 1 (C): Amine **11** was prepared acoording to literature[3]. **11** (535 mg, 2.5 mmol) was dissolved in 40 ml 1,2-dichloroethane. After addition of formaldehyde (37w% aq. solution, 394 µl, 5 mmol, 2 eq) the solution was stirred at r.t. for 15 min. Then $NaBH(OAc)_3$ (1.25 g, 5.8 mmol, 2.3 eq) was added and the solution was stirred at r.t. overnight. The reaction was quenched with 50 ml saturated sodium bicarbonate solution and extracted with dichloromethane. The organic phase was dried over Na_2SO_4 and removal of the solvent under reduced pressure gave **19** (581 mg, 2.4 mmol, 96%) which was directly used without further purification. Analytical data were in accordance with those reported in literature[3]. ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 0.96-1.34 (m, 4H), 1.44 (s, 9H), 1.60-1.70 (m, 1H), 1.72-1.86 (m, 2H), 2.11-2.28 (m, 1H), 2.21 (s, 6H), 2.40-2.52 (m, 1H), 3.12-3.24 (m, 1H), 5.28 (s, 1H) ppm.

3) N. R. Amarasinghe, P. Turner, M. H. Todd, *Adv. Synth. Catal.* **2012**, *354*, 2954-2958.

Step 2 (D): A solution of **19** (50 mg, 0.2 mmol) and the corresponding benzyl bromide derivative (0.6 mmol, 1.5 eq) in 0.5 mL DMF was stirred at 60 °C overnight. Evaporation of the solvent under reduced pressure gave crude **13** which was used without further purification.

Compound 13a (R^1 = α-Naphthyl): Analytical data were found to be in accordance with literature[4]. $[\alpha]_D^{23}$ (c = 1.0, dichloromethane) = -5.2°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.25-1.38 (m, 1H), 1.45 (s, 9H), 1.58-1.77 (m, 3H), 1.85-2.08 (m, 3H), 2.52-2.64 (m, 1H), 2.99 (s, 3H), 3.14 (s, 3H), 4.14-4.28 (m, 1H), 5.07-5.20 (m, 1H), 5.30 (d, 1H, *J* = 13.4 Hz), 5.47 (d, 1H, *J* = 13.4 Hz), 6.16 (d, 1H, *J* = 10.1 Hz), 7.40-7.53 (m, 2H), 7.54-7.63 (m, 1H), 7.67 (d, 1H, *J* = 7.0 Hz), 7.86 (d, 1H, *J* = 8.0 Hz), 7.94 (d, 1H, *J* = 8.3 Hz), 8.22 (d, 1H, *J* = 8.2 Hz) ppm; ^{13}C NMR (75MHz, δ, $CDCl_3$, 298 K): 24.5, 24.6, 27.6, 28.4, 35.6, 48.8, 50.6, 51.6, 62.3, 76.5, 80.7, 123.3, 123.6, 125.0, 126.6, 128.1, 129.3, 132.0, 133.1, 134.0, 134.1, 155.6 ppm; IR (film): $\tilde{\nu}$ = 3439, 3244, 3005, 2976, 2936, 2864, 1697, 1508, 1489, 1456, 1393, 1366, 1321, 1273, 1242, 1159, 1047, 1024, 870, 808, 783, 733 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{35}N_2O_2^+$: 383.2699 [M^+], found: 383.2693.

Optimized protocol for deprotection and coupling with iso(thio)cyanates:



13
13a R^1 = α-Naphth-CH_2, Y = Br
13c R^1 = 3,5-$(CF_3)_2$-Ph, Y = I

14
14a R^1 = α-Naphth-CH_2
14c R^1 = 3,5-$(CF_3)_2$-Ph

1
1a R^1 = α-Naphth-CH_2, R^2 = 3,5-$(COOMe)_2$-Ph
1c R^1 = 3,5-$(CF_3)_2$-Ph, R^2 = Et
1d R^1 = 3,5-$(CF_3)_2$-Ph, R^2 = 3-NO_2-Ph
1e R^1 = 3,5-$(CF_3)_2$-Ph, R^2 = 3,5-$(CF_3)_2$-Ph

General Syntheses of 1 (E,F):

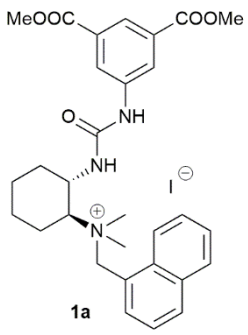
Step 1 (E): The corresponding ammonium salt **13** (1.1 mmol) was dissolved in 12 ml dichloromethane and hydroiodic acid (57w% aq. solution, 1.45 ml, 11 mmol, 10 eq) was added. After stirring for 2 h at r.t. the reaction was basified with saturated sodium carbonate solution and extracted with dichloromethane. The organic phase was dried over Na_2SO_4 and removal of the solvent under reduced pressure gave crude **14** in quantitative yield.

4) J. Novacek, M. Waser, *Eur. J. Org. Chem.* **2014**, 802-809.

Compound 14c (R^1 = 3,5-$(CF_3)_2$-Ph): Obtained in quantitative yield (689 mg, 1.1 mmol). ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.31-1.76 (m, 5H), 1.84-1.95 (m, 1H), 1.96-2.07 (m, 1H), 2.27-2.37 (m, 1H), 3.06 (s, 3H), 3.17 (s, 3H), 3.46 (s (b), 2H), 3.56-3.68 (m, 1H), 4.06-4.17 (m, 1H), 5.12 (d, 1H, *J* = 12.7 Hz), 5.48 (d, 1H, *J* = 12.7 Hz), 7.96 (s, 1H), 8.16 (s, 2H) ppm.

Step 2 (F): A solution of **14** (1 mmol) and the corresponding iso(thio)cyanate (1.2 mmol, 1.2 eq) in 20 ml dichloromethane was stirred for 2-6 h at r.t.. Evaporation of the solvent under reduced pressure gave crude **1**, which was further purified by column chromatography (dichloromethane/methanol = 50/1 to 10/1) to obtain pure catalysts **1**.

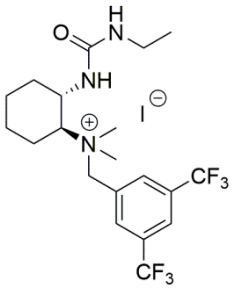
Compound 1a: Obtained in 61% (over 4 steps, starting from 0.2 mmol **11**) as a yellowish oil.



1a

Analytical data were found to be in accordance with literature[4]. $[\alpha]_D^{23}$ (c = 0.75, dichloromethane) = -49.1°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.25-1.48 (m, 2H), 1.62-1.90 (m, 2H), 1.91-2.08 (m, 2H), 2.15-2.28 (m, 1H), 2.58-2.70 (m, 1H), 2.90 (s, 3H), 3.17 (s, 3H), 3.94 (s, 6H), 4.45-4.70 (m, 2H), 5.42 (d, 1H, *J* = 13.1 Hz), 5.70 (d, 1H, *J* = 13.1 Hz), 7.15 (t, 2H, *J* = 7.6 Hz), 7.24 (d, 1H, *J* = 7.8 Hz), 7.45 (d, 1H, *J* = 7.1 Hz), 7.66 (t, 2H, *J* = 8.6 Hz), 7.97 (d, 1H, *J* = 9.7 Hz), 8.08 (d, 1H, *J* = 8.6 Hz), 8.42 (t, 1H, *J* = 1.4 Hz), 8.56 (d, 2H, *J* = 1.4 Hz), 9.05 (s, 1H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 24.5, 25.0, 27.4, 36.1, 48.0, 50.6, 51.4, 52.4, 63.5, 77.3, 122.9, 123.2, 123.8, 124.6, 125.0, 126.4, 127.8, 129.0, 131.2, 131.7, 132.8, 133.6, 133.9, 139.9, 155.2, 166.3 ppm; IR (film): $\tilde{\nu}$ = 3244, 3028, 2943, 2866, 1717, 1684, 1558, 1541, 1508, 1437, 1346, 1317, 1242, 1123, 1047, 997, 876, 808, 783, 754 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{30}H_{36}N_3O_5^+$: 518.2655 [M^+]; found: 518.2662.

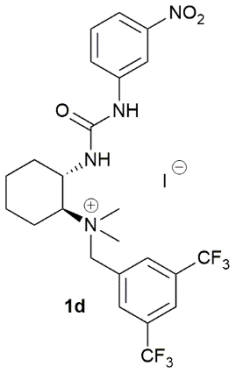
Compound 1c: Obtained in 65% (123.2 mg, 0.217 mmol) as a colourless oil. $[\alpha]_D^{21}$ (c = 1.3, $CHCl_3$) = 13.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.16 (t, *J* = 7.2 Hz 3H), 1.24-1.41 (m, 1H), 1.43-1.66 (m, 2H), 1.67-1.87 (m, 2H), 1.90-2.12 (m, 2H), 1.49-1.61 (m, 1H), 3.06 (s, 3H), 3.18-3.34 (m, 5H), 4.22-4.38 (m, 1H), 4.59-4.52 (m, 1H), 5.32-5.47 (m, 2H), 5.99 (s, 1H), 6.92 (d, *J* = 9.7 Hz, 1H), 7.97 (s, 1H), 8.00 (s, 2H), ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 15.5, 24.7, 25.1, 27.4, 35.2, 35.9, 48.1, 50.9, 51.0, 65.3, 78.0, 122.7 (q, *J* = 273Hz), 124.8, 130.5, 133.0 (q, *J* = 34 Hz), 133.4, 157.7 ppm; ^{19}F NMR (282 MHz, δ, $CDCl_3$, 298 K):



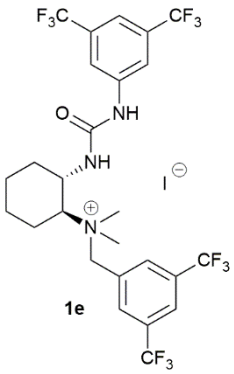
1c

-62.9 ppm IR (film): $\bar{\nu}$ = 3295, 3021, 2988, 2936, 2864, 2349, 2288, 1656, 1546, 1449, 1373, 1278, 1174, 1130, 904, 843, 751, 719, 682, 663, 593, 463, cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{20}H_{28}F_6N_3O^+$: 440.2131 [M^+]; found: 440.2118.

Compound 1d: Obtained in 67% (96 mg, 0.14 mmol) as an orange oil. $[\alpha]_D^{21}$ (c = 0.75, dichloromethane) = -29.3°; ^1H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.29-1.46 (m, 1H), 1.56-2.06 (m, 5H), 2.11-2.23 (m, 1H), 2.55-2.67 (m, 1H), 3.19 (s, 3H), 3.28 (s, 3H), 4.40-4.62 (m, 2H), 5.37 (s, 2H), 7.39 (t, 1H, *J* = 8.2 Hz), 7.47 (d, 1H, *J* = 9.2 Hz), 7.73 (dd, 2H, J_1 = 8.1 Hz, J_2 = 1.5 Hz), 7.84 (dd, 1H, J_1 = 8.1 Hz, J_2 = 1.8 Hz), 7.94 (s, 1H), 8.03 (s, 2H), 8.69 (t, 1H, *J* = 2.1 Hz), 9.11 (s, 1H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 24.5, 25.0, 27.3, 36.0, 49.1, 50.6, 50.9, 65.0, 78.4, 113.0, 117.5, 122.5 (q, *J* = 275 Hz), 124.3, 124.9, 129.6, 130.2, 133.1 (q, *J* = 34 Hz), 133.3, 140.4, 148.6, 155.1 ppm; ^{19}F NMR (282 MHz, δ, $CDCl_3$, 298 K): -63.0 ppm; IR (film): $\bar{\nu}$ = 3462, 3254, 3031, 2944, 2866, 1692, 1600, 1548, 1529, 1485, 1451, 1434, 1372, 1352, 1325, 1280, 1206, 1178, 1137, 904, 843, 830, 798, 737, 709, 683 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{24}H_{27}F_6N_4O_3^+$: 533.1982 [M^+]; found: 533.1998.



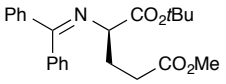
Compound 1e: Obtained in 79% over 2 steps (1.15 g, 1.53 mmol) as an orange oil. $[\alpha]_D^{21}$ (c = 0.75, dichloromethane) = -51.2°; ^1H NMR (700 MHz, δ, $CDCl_3$, 298 K): 1.36-1.44 (m, 1H), 1.55 (qd, 1H, J_1 = 12.1 Hz, J_2 = 2.9 Hz), 1.68-1.77 (m, 1H), 1.80-1.85 (m, 1H), 1.85-1.92 (m, 1H), 2.00-2.07 (m, 1H), 2.17-2.23 (m, 1H), 2.59-2.65 (m, 1H), 3.13 (s, 3H), 3.25 (s, 3H), 4.39 (qd, 1H, J_1 = 10.5 Hz, J_2 = 3.4 Hz), 4.67 (td, 1H, J_1 = 10.8 Hz, J_2 = 2.7 Hz), 5.36 (d, 1H, *J* = 13.5 Hz), 5.38 (d, 1H, *J* = 13.5 Hz), 7.50 (s, 1H), 7.58 (d, 1H, *J* = 9.8 Hz), 7.95 (s, 1H), 8.00 (s, 2H), 8.08 (s, 2H), 9.15 (s, 1H) ppm; ^{13}C NMR (175 MHz, δ, $CDCl_3$, 298 K): 24.7, 25.1, 27.4, 36.0, 48.5, 50.6, 50.9, 65.6, 78.0, 116.1, 118.3, 122.5 (q, *J* = 273 Hz), 123.4 (q, *J* = 273 Hz), 125.1, 130.1, 132.2 (q, *J* = 33 Hz), 133.2, 133.2 (q, *J* = 34 Hz), 140.6, 155.1 ppm; ^{19}F NMR (282 MHz, δ, $CDCl_3$, 298 K): -63.1, -63.1 ppm; IR (film): $\bar{\nu}$ = 3462, 3273, 3091, 3048, 2945, 2867, 1696, 1624, 1567, 1474, 1443, 1387, 1318, 1278, 1176, 1131, 1042, 945, 904, 884, 845, 737, 704, 683, 648 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{26}H_{26}F_{12}N_3O^+$: 624.1879 [M^+]; found: 624.1880.



3. Asymmetric Michael Addition Reactions:

General Procedure: Degased toluene (5 mL) was added to a mixture of the Schiff base **5** (0.1 mmol), catalyst **1c** (10 mol%), and Cs_2CO_3 (1.5 eq) in the Schlenk tube. Stirring rate was set to 1000 rpm and the corresponding electrophile **15** (1.5 eq.) was added. After 24 h at 25 °C the reaction mixture was filtrated over a plug of Na_2SO_4. The solvents were removed under reduced pressure. The crude products were purified by column chromatography (silica gel, heptanes:EtOAc = 20:1 to 2:1) giving the products **16** in the reported yields.

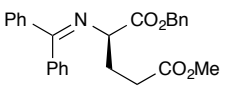
***R*-(+)-16a**. Obtained as a colourless oil in 85% yield and with e.r. = 95:5 upon reacting Schiff base **5a** with acrylate **15a** in the presence of 10 mol% catalyst at 25 °C under the general reaction conditions.



16a

Analytical data are in full accordance with those reported in literature[5,6].$[\alpha]_D^{21}$ (c = 0.70, $CHCl_3$) = 74.9°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.44 (s, 9H), 2.16-2.27 (m, 2H), 2.33-2.41 (m, 2H), 3.59 (s, 3H), 3.93-3.99 (m, 1H), 7.14-7.21 (m, 2H), 7.28-7.47 (m, 6H), 7.60-7.68 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.2, 28.8, 30.5, 51.7, 64.9, 81.3, 127.9, 128.1, 128.6, 128.7, 128.9, 130.5, 136.6, 139.6, 170.8, 170.9, 173.7 ppm; IR (film): $\tilde{\nu}$ = 2978, 2926, 1738, 1707, 1661, 1599, 1578, 1449, 1369, 1319, 1279, 1260, 1234, 1153, 943, 920, 849, 812 cm^{-1}; The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 95:5, 0.5 mL/min, 10 °C, retention times: 10.9 min (major; *R*-enantiomer), 12.3 min (minor; *S*-enantiomer)); Absolute configuration was determined by comparison of the retention times and the $[\alpha]_D$-value with reported data[5,6]. HRMS (ESI): *m/z* calcd for $C_{23}H_{27}NO_4$: 382.2013 $[M+H]^+$; found: 382.2013.

***R*-(+)-16b**. Obtained as a colourless oil in 74% yield and with e.r. = 92:8 upon reacting Schiff base **5b**



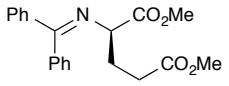
16b

with acrylate **15b** in the presence of 10 mol% catalyst at 25 °C under the general conditions. Analytical data are in full accordance with those reported in literature[7,8]. $[\alpha]_D^{21}$ (c = 0.85, $CHCl_3$) = 17.9°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 2.23-2.32 (m, 2H), 2.33-2.40 (m, 2H), 3.57 (s, 3H), 4.11-4.17 (m, 1H), 5.16 (dd, *J* = 7.0 Hz, 12.5 Hz, 2H), 7.08-7.14 (m, 2H), 7.28-7.42 (m, 11H), 7.59-7.67 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.5, 30.4, 51.5, 64.1, 66.6, 127.8, 128.0, 128.1, 128.2, 128.5, 128.7, 128.9, 130.5, 135.8, 136.1, 171.4, 173.4 ppm; IR (film): $\tilde{\nu}$ = 3063, 2959, 2928, 2853, 1742, 1705, 1659, 1599, 1578, 1499, 1449, 1420, 1389, 1377, 1317, 1279, 1209, 1192, 1177, 1157, 922, 754, 706 cm^{-1}; The

5) B. Lygo, C. Beynon, C. Lumley, M. C. McLeod, C. E. Wade; *Tetrahedron Lett.*, **2009**, *50*, 3363–3365.
6) J. S. Bandar, A. Barthelme, A. Y. Mazoria, T. H. Lambert; *Chem. Sci.,* **2015**, *6*, 1537-1547.
7) T. Shibuguchi, H. Mihara, A. Kuramochi, T.Ohshima, M. Shibasaki, *Chem. Asian J*, **2007**, 794–801.
8) T. Shibuguchi, H. Mihara, A. Kuramochi, T.Ohshima, M. Shibasaki, *Angew. Chem. Int. Ed.* **2006**, *45*, 4635–4637.

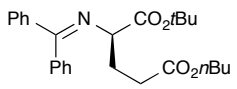
enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 95:5, 0.5 mL/min, 10 °C, retention times: 29.6 min (major; (R)-enantiomer), 36.1 min (minor; (S)-enantiomer)); Absolute configuration was determined by comparison of the retention times and the $[\alpha]_D$-value with reported data[7,8]. HRMS (ESI): *m/z* calcd for $C_{26}H_{25}NO_4$: 416.1856 $[M+H]^+$; found: 416.1858.

(+)-16c. Obtained as a colourless oil in 90% yield and with e.r. = 92:8 upon reacting Schiff base **4c** with acrylate **15c** using 10 mol% catalyst at 25 °C under the general reaction conditions. Analytical data are in full accordance with those reported in literature.[7] $[\alpha]_D^{21}$ (c = 0.9, $CHCl_3$) = 63.1°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 2.20-2.29 (m, 2H), 2.32-2.40 (m, 2H), 3.58 (s, 3H), 3.71 (s, 3H), 4.13 (t, *J* = 6.2 Hz, 1H), 7.14-7.21 (m, 2H), 7.29-7.48 (m, 6H), 7.60-7.67 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.6, 30.4, 51.6, 52.2, 64.1, 127.8, 128.1, 128.6, 128.8, 128.9, 130.6, 172.0, 172.2, 173.4 ppm; IR (film): $\tilde{\nu}$ = 3057, 3051, 2992, 2955, 1736, 1624, 1576, 1445, 1437, 1316, 1265, 1204, 1172, 1074, 1028, 1001, 781, 731, 702 cm^{-1}; The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 95:5, 0.5 mL/min, 10 °C, retention times: 19.2 min (major; (+)-enantiomer), 21.6 min (minor; (-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{23}H_{21}NO_4$: 340.1543 $[M+H]^+$; found: 340.1543.



16c

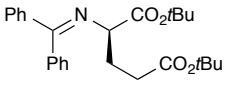
***R*-(+)-16d**. Obtained as a colourless oil in 63% yield and with e.r. = 95:5 upon reacting Schiff base **4c** with acrylate (**15d**) using 10 mol% catalyst at 25 °C under the standard conditions. Analytical data are in full accordance with those reported in literature[9]. $[\alpha]_D^{21}$ (c = 0.3, $CHCl_3$) = 21.7°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 0.90 (t, *J* = 7.3 Hz, 3H), 1.28-1.40 (m, 2H), 1.44 (s, 9H), 1.48-1.60 (m, 2H), 2.17-2.27 (m, 2H), 2.31-2.40 (m, 2H), 3.93-4.03 (m, 3H), 7.13-7.20 (m, 2H), 7.29-7.47 (m, 6H), 7.61-7.68 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 13.8, 19.2, 28.2, 28.8, 30.7, 30.9, 64.4, 67.0, 81.3, 127.9, 128.1, 128.4, 128.6, 128.9, 130.2, 136.6, 139.6, 170.8, 170.9, 173.4 ppm; IR (film): $\tilde{\nu}$ = 2957, 2929, 2855, 2361, 2341, 1734, 1703, 1660, 1448, 1368, 1277, 1151, 920, 845, 764, 702, 639, 464 cm^{-1}; The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane: *i*-PrOH = 95:5, 0.5 mL/min, 10 °C, retention times: 9.8 min (major, *R*-(+)-enantiomer), 10.5 min (minor; *S*-(-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{26}H_{33}NO_4$: 424.2488 $[M+H]^+$; found: 424.2475.



16d

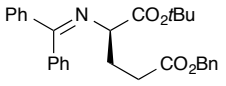
9) J. S. Bandar, T. H. Lambert, *J. Am. Chem. Soc.*, **2012**, *134*, 5552–5555.

***R*-(+)-16e**. Obtained as a colourless oil in <10% yield and with e.r. = 83:17 upon reacting Schiff base **4c** with acrylate (**15e**) using 10 mol% catalyst at 25 °C under the standard conditions and in 52% yield and with e.r. = 83:17 upon reacting Schiff base **4c** with acrylate (**15**) using 10 mol% catalyst at 25 °C using 5 eq. of Cs_2CO_3. Analytical data are in full accordance with those reported in literature[9]. $[\alpha]_D^{21}$ (c = 0.87, $CHCl_3$) = 14.4°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.38 (s, 9H), 1.44 (s, 9H), 2.13-2.30 (m, 4H), 3.91-3.67 (m, 1H), 7.14-7.21 (m, 2H), 7.28-7.52 (m, 6H), 7.56-7.68 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.2, 29.0, 32.2, 80.3, 81.2, 128.0, 128.1, 128.6, 128.7, 129.0, 130.4, 136.7, 139.7, 170.8, 171.1, 172.6 ppm; IR (film): $\bar{\nu}$ = 3061, 2977, 2932, 2873, 2349, 1724, 1625, 1448, 1367, 1252, 1148, 845, 753, 697, 523 468 cm-1; The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 100:1, 0.5 mL/min, 10 °C, retention times: 15.3 min (major, *R*-(+)-enantiomer), 16.3. min (minor; *S*-(-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{26}H_{33}NO_4$: 424.2488 $[M+H]^+$; found: 424.2473.



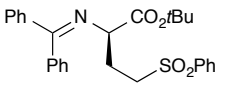
16e

***R*-(+)-16f**. Obtained as a colourless oil in 96% yield and with e.r. = 91:9 upon reacting Schiff base **4c** with acrylate (**15f**) using 10 mol% catalyst at 25 °C under the standard conditions. Analytical data are in full accordance with those reported in literature[9]. $[\alpha]_D^{21}$ (c = 1.44, $CHCl_3$) = 41.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.44 (s, 9H), 2.20-2.30 (m, 2H), 2.38-2.47 (m, 2H), 3.95-4.01 (m, 1H), 5.04 (s, 2H), 7.12-7.19 (m, 2H), 7.27-7.45 (m, 11H), 7.61-7.67 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.2, 28.7, 30.9, 65.0, 66.3, 81.3, 127.9, 128.1, 128.3, 128.6, 128.6, 128.7, 128.9, 130.5, 136.1, 136.6, 139.6, 170.8, 170.9, 173.1 ppm; IR (film): $\bar{\nu}$ = 3062, 3025, 2978, 2932, 1732, 1668, 1456, 1368, 1276, 1254, 1147, 1073, 1028, 919, 846, 751, 696, 638, 459 cm^{-1}; The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 100:1, 1 mL/min, 10 °C, retention times: 17.7 min (major, *R*-(+)-enantiomer), 20.9. min (minor; *S*-(-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{29}H_{31}NO_4$: 458.2331 $[M+H]^+$; found: 458.2311.



16f

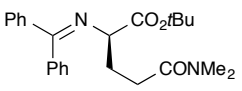
***R*-(+)-16g**. Obtained as a colourless oil in 81% yield and with e.r. = 65:35 upon reacting Schiff base **4c** with acrylate (**15g**) using 10 mol% catalyst at 25 °C under the general reaction conditions. Analytical data are in full accordance with those reported in literature[9]. $[\alpha]_D^{21}$ (c = 0.92, $CHCl_3$) = 17.0°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.38 (s, 9H), 2.08-2.32 (m, 2H), 3.14-3.37 (m, 2H), 3.97–4.04 (m, 1H), 7.08-7.16 (m, 2H), 7.28-7.47 (m, 6H), 7.51-7.60 (m, 4H), 7.61-7.69 (m, 1H), 7.86-7.93 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 27.2, 28.1, 53.0, 63.7, 81.9, 127.8, 128.2, 128.3, 128.8, 129.0, 129.4, 130.8, 133.8, 136.2, 139.0, 139.2, 170.0, 171.6 ppm; IR (film): $\bar{\nu}$ = 3060, 2977, 2932, 1768, 1622, 1446, 1393,



16g

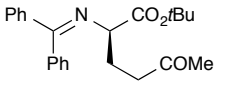
1368, 1306, 1291, 1230, 1142, 1086, 845, 750, 691, 532, 440 cm^{-1};The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 95:5, 1 mL/min, 10 °C, retention times: 18.6 min (major, *R*-(+)-enantiomer), 26.6 min (minor; *S*-(-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{27}H_{29}NO_4S$: 464.1896 $[M+H]^+$; found: 464.1884.

(+)-16h. Obtained as a colourless oil in around 10% yield and with e.r. = 88:12 upon reacting Schiff base **4c** with acrylamide (**15h**) using 10 mol% catalyst at 25 °C under the standard conditions. Analytical data are in accordance with those reported in literature[10]. $[\alpha]_D^{21}$ (c = 0.26, $CHCl_3$) = 42.3°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.43 (s, 9H), 2.15-2.25 (m, 2H), 2.27-2.47 (m, 2H), 2.90 (s, 3H), 3.00 (s, 3H), 3.98-4.04 (m, 1H), 7.12-7.19 (m, 2H), 7.28-7.46 (m, 6H), 7.61-7.66 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.2, 29.4, 29.7, 35.5, 37.5, 65.1, 81.2, 127.9, 128.2, 128.6, 128.7, 128.9, 130.4, 136.6, 139.7, 170.6, 171.3, 172.7 ppm; IR (film): $\bar{\nu}$ = 3080, 3055, 2953, 2930, 2173, 1736, 1714, 1659, 1622, 1599, 1578, 1491, 1447, 1437, 1358, 1317, 1275, 1265, 1204, 1177, 1161, 1094, 1074, 1042, 1028, 1001, 941, 920, 810, 783, 766, 733, 698 cm^{-1}; The enantioselectivity was determined by HPLC (Chiralcel OD-R, eluent: AcN:H_2O = 55:45, 0.7 mL/min, 10 °C, retention times: 11.1 min (major, *R*-(+)-enantiomer), 12.9 min (minor; *S*-(-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{24}H_{30}N_2O_3$: 395.2329 $[M+H]^+$; found: 395.2325.



16h

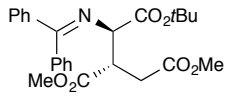
***S*-(+)-16i**. Obtained as a colourless oil in 95% yield and with e.r. = 92:8 upon reacting Schiff base **4c** with MVK (**15i**) using 10 mol% catalyst at 25 °C under the standard conditions. Analytical data are in full accordance with those reported in literature[9]. $[\alpha]_D^{21}$ (c = 0.3, $CHCl_3$) = 29.7°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.43 (s, 9H), 2.08-2.19 (m, 5H), 2.41-2.61 (m, 2H), 3.95 (t, *J* = 6.1 Hz, 1H), 7.13-7.19 (m, 2H), 7.29-7.47 (m, 6H), 7.60-7.66 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 27.8, 28.2, 30.0, 40.0, 64.8, 81.3, 127.8, 128.2, 128.6, 128.7, 128.9, 130.4, 136.6, 139.6, 170.6, 171.1, 208.4 ppm; IR (film): $\bar{\nu}$ = 3061, 2926, 2853, 2348, 1728, 1658, 1598, 1447, 1367, 1317, 1276, 1153, 941, 919, 763, 699, 638 cm^{-1}. The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 100:1, 1.0 mL/min, 10 °C, retention times: 14.8 min (major, *R*-(+)-enantiomer), 17.0. min (minor; *S*-(-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{23}H_{27}NO_3$: 366.2069 $[M+H]^+$; found: 324.2057.



16i

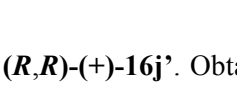
10) G.N Gururaja, R. Herchl; A. Pichler; K. Gratzer; M. Waser; *Molecules* **2013**, *18*, 4357-4372.

(*R*,*S*)-(+)-16j. Obtained as a colourless oil in 85% yield and with d.r. = 20:1 and e.r. = 95:5 (major diastereomer) upon reacting Schiff base **4c** with dimethylmaleat (**15j**) using 10 mol% catalyst at 25 °C under standard conditions. $[\alpha]_D^{21}$ (c = 0.59, $CHCl_3$) = 92.2°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.43 (s, 9H), 2.58 (dd, *J* = 5.2, 16.9 Hz, 1H), 2.84 (dd, *J* = 9.3, 16.8 Hz, 1H), 3.51-3.59 (m, 1H), 3.64 (s, 3H), 3.70 (s, 3H), 4.20 (d, *J* = 3.7 Hz, 1H), 7.13-7.20 (m, 2H), 7.27- 7.46 (m, 6H), 7.57-7.63 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.0, 32.7, 45.1, 51.9, 52.0, 66.3, 81.9, 127.7, 128.1, 128.6, 128.9, 129.1, 130.7, 136.2, 139.2, 169.1, 172.0, 172.4, 172.7 ppm; IR (film): $\bar{\nu}$ = 2979, 2952, 1732, 1626, 1437, 1368, 1228, 1148, 1001, 845, 782, 752, 696, 513 cm^{-1}; E.r. was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 98:2, 1.0 mL/min, 10 °C, retention times of the major diastereomer: 14.3 min (minor; (-)-enantiomer)), 17.6 min (major, (+)-enantiomer); HRMS (ESI): *m/z* calcd for $C_{25}H_{29}NO_6$: 440.2073 $[M+H]^+$; found: 440.2057.



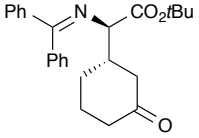
16j

(*R*,*R*)-(+)-16j'. Obtained as a colourless oil in 96% yield and with d.r. > 20:1 and e.r. = 88:12 (major diastereomer) upon reacting Schiff base **5a** with dimethylfumarat (**15j'**) using 10 mol% catalyst at 25 °C under the general conditions. Analytical data are in full accordance with those reported in literature[9]. $[\alpha]_D^{21}$ (c = 0.82, $CHCl_3$) = 73.7°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.43 (s, 9H), 2.69 (dd, *J* = 3.9, 17.0 Hz, 1H), 3.10 (dd, *J* = 9.6, 17.0 Hz, 1H), 3.60 (s, 3H), 3.61-3.69 (s, 4H), 4.20 (d, *J* = 3.7 Hz, 1H, characteristic signal of the minor diastereomer), 4.42 (d, *J* = 5.0 Hz, 1H), 7.12-7.20 (m, 2H), 7.27- 7.47 (m, 6H), 7.57-7.63 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.1, 32.4, 44.7, 51.9, 52.1, 66.2, 82.1, 128.0, 128.1, 128.5, 128.9, 129.1, 130.6, 136.2, 139.4, 169.3, 172.2, 172.7, 172.9 ppm; IR (film): $\bar{\nu}$ = 2979, 2952, 1732, 1626, 1437, 1368, 1228, 1148, 1001, 845, 782, 752, 696, 513 cm^{-1}; E.r. was determined by HPLC (Chiralcel AD-H, eluent: *n*-hexane:*i*-PrOH = 98:2, 1.0 mL/min, 10 °C, retention times of the major diastereomer: 16.7 min (major, (+)-enantiomer), 39.4 min (minor; (-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{25}H_{29}NO_6$: 440.2073 $[M+H]^+$; found: 440.2062.



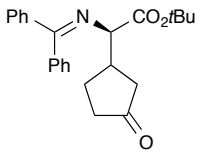
16j'

(2*R*,3*S*)-(+)-16k. Obtained as white solid in 25% yield and with d.r. = 3:1 and e.r. = 86:14 (major diastereomer) upon reacting Schiff base **4c** with cyclohexenone (**15k**) using 10 mol% catalyst at 25 °C under standard conditions and in 36% yield and with d.r. = 3:1 and e.r. = 86:14 upon reacting Schiff base **4c** with 5 eq. of cyclohexenone (**15k**) using 10 mol% catalyst. $[\alpha]_D^{21}$ (c = 0.86, $CHCl_3$) = 39.9°; ^{1}H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.43 (s, 9H), 1.55-1.74 (m, 3H), 1.95-2.56 (m, 5H), 2.60-2.44 (m, 1H), 3.79 (d, *J* = 5.0 Hz, 1H, minor), 3.90 (d, *J* = *4*.3 Hz, 1H, major), 7.08-7.18 (m, 2H), 7.28-7.48 (m, 6H), 7.63-7.70 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 25.5*, 26.3, 28.2, 38.3, 40.1*,



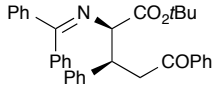
40.3, 41.0, 42.2*, 68.0, 69.1*, 81.6, 127.9, 127.9*, 128.2, 128.4*, 128.7, 128.8, 128.8*, 128.9, 130.6, 136.5*, 136.7, 139.3, 139.4*, 170.3, 170.4*, 171.1, 171.5* ppm (*denotes minor diastereomer where observable); IR (film): $\tilde{\nu}$ = 3059, 2976, 2931, 2864, 2349, 1709, 1624, 1446, 1422, 1367, 1282, 1224, 1146, 1107, 965, 846, 781, 752, 696, 637, 504 cm^{-1}; The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent *n*-hexane:*i*-PrOH = 98:2, 0.5 mL/min, 10 °C, retention times of the major diastereomer: 26.5 min (major, (+)-enantiomer), 44.8 min (minor; (-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{25}H_{29}NO_3$: 392.2226 $[M+H]^+$; found: 392.2229.

(+)-16l. Obtained as a colourless oil in 82% yield and with d.r. = 4:1 and with e.r. = 95:5 (major



diastereomer) upon reacting Schiff base **4c** with cyclopentenone (**15l**) using 10 mol% catalyst at 25 °C under standard conditions. $[\alpha]_D^{21}$ (c = 1.15, $CHCl_3$) = 86.8°; ^1H NMR (300 MHz, δ, $CDCl_3$, 298 K) of the major diastereomer: 1.44 (s, 9H), 1.55-1.69 (m, 1H), 1.96-2.08 (m, 1H), 2.08-2.56 (m, 4H), 2.85-3.00 (m, 1H), 4.00 (d, *J* = 5.0 Hz, 1H, major), 7.12-7.20 (m, 2H), 7.29-7.50 (m, 6H), 7.59-7.66 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 25.5*, 26.4, 28.2, 38.3, 40.1*, 40.3, 41.0, 42.2*, 68.5, 69.1*, 81.6, 127.9, 128.2, 128.4*, 128.7, 128.8*, 128.8, 128.9, 130.6, 136.7, 139.3, 170.3, 170.4*, 171.1, 171.5* ppm (*denotes the minor diastereomer where observable).; IR (film): $\tilde{\nu}$ = 3059, 2975, 2872, 2372, 1732, 1623, 1446, 1367, 1277, 1253, 1142, 910, 845, 781, 754, 695, 563, 485, cm^{-1}; The enantioselectivity was determined by HPLC (Chiralcel AD-H, eluent *n*-hexane : *i*-PrOH = 100:3.5, 1.0 mL/min, 10 °C, retention times (major diastereomer): 7.1 min (major, (+)-enantiomer), 10.1 min (minor, (-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{24}H_{28}NO_3$: 378.2069 $[M+H]^+$; found: 378.2057.

(2*R*, 3*S*)-(+)-16m. Obtained as a colourless oil in 90% yield and with d.r. > 20:1 and e.r. = 93:7 (major



diastereomer) upon reacting Schiff base **4c** with chalcone (**15m**) using 10 mol% catalyst at 25 °C under standard conditions. Analytical data are in full accordance with those reported in literature[11]. $[\alpha]_D^{21}$ (c = 0.65, $CHCl_3$) = 53.1°; ^1H NMR (300 MHz, δ, $CDCl_3$, 298 K): 1.32 (s, 9H), 3.56-3.82 (m, 2H), 4.14-4.24 (m, 2H), 6.67-6.75 (m, 2H), 7.10-7.20 (m, 5H), 7.30-7.58 (m, 9H), 7.65-7.72 (m, 2H), 7.94-8.00 (m, 2H) ppm; ^{13}C NMR (75 MHz, δ, $CDCl_3$, 298 K): 28.0, 40.2, 44.9, 71.1, 81.4, 126.7, 127.7, 128.2, 128.3, 128.5, 128.6, 128.7, 128.9, 129.0, 130.5, 133.0, 136.4, 137.3, 139.5, 141.5, 170.2, 171.3, 198.8 ppm; IR (film): $\tilde{\nu}$ = 3060, 3027, 2979, 2931, 1727, 1685, 1597, 1447, 1367, 1147, 1002, 845, 750, 694, 546, 531 cm^{-1}; The enantioselectivity of the major diastereomer was determined by HPLC (Chiralcel AD-

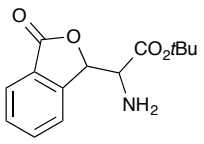
11) T. Ma, X. Fu, C. W. Kee, L. Zong, Y. Pan, K.-W. Huang, C.-H. Tan, *J. Am. Chem. Soc.* **2011**, *133*, 2828–2831.

H, eluent: *n*-hexane:*i*-PrOH = 95:5, 1.0 mL/min, 10 °C, retention times: 12.1 min (major, (+)-enantiomer), 16.6 min (minor, (-)-enantiomer)); HRMS (ESI): *m/z* calcd for $C_{35}H_{35}NO_4$: 504.2587 $[M+H]^+$; found: 504.2565.

4. Asymmetric Aldol-Initiated Cascade Reactions:

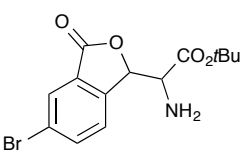
General Procedure: In a round-bottom flask, 2-cyanbenzaldehydes **6** (0.10 mmol) were added at room temperature to a stirred solution of glycine Schiff base **5** (1.1 eq., 0.11 mmol), K_2CO_3 (1 eq.) and catalyst **1d** (5% mol) in CH_2Cl_2 (3 mL). The mixture was stirred at r.t. for 24 h (1000 rpm). After, the mixture was purified directly by flash chromatography on silica gel with hexane:ethyl acetate = 8:2 to give the intermediates **7** as a mixture of diastereoisomers. The products **7** were dissolved in a cooled solution of 0.5 M HCl (1 mL) and THF (3 mL) (0 °C). The mixtures were stirred at the same temperature for 2 h and then concentrated under vacuum. The resulting residue was treated with saturated $NaHCO_3$ (20 mL), extracted with CH_2Cl_2 (4 x 30 mL) and purified by flash chromatography (silica gel, hexanes:EtOAc = 2:1).

(-)-8a. Obtained according to the general procedure in 83% (22 mg, 0.083 mmol) as an amorphous solid. (dr = 4:1; e.r. (major) = 95:5). $[\alpha]_D^{20}$ = - 2.5 (c 0.5 in $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 6.48 Hz, 1H), 7.58 (t, *J* = 7.42 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 5.77 (d, *J* = 3.5 Hz, 1H), 4.04 (d, *J* = 3.6 Hz, 1H), 1.61 (br s, 2H), 1.40 (s, 9H) ppm. ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 171.5, 171.3, 147.5, 135.2, 130.8, 128.3, 126.9, 123.8, 83.9, 83.3, 58.7, 29.1 ppm. MS (ESI): m/z = 264.1 $(M+H)^+$. Anal. calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.97; H, 6.41; N, 5.37%. HPLC separation of the major diastereomer: Chiralcel OD-H, hexane:i-PrOH = 9:1, 25 °C, 0.7 mL/min, (retention times: 25.3 min (minor); 34.3 min (major)).



8a

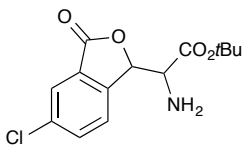
(-)-8b. Obtained according to the general procedure in 80% (27 mg, 0.08 mmol) as an amorphous solid. (dr = 2.5:1; e.r. (major) = 91:9). $[\alpha]_D^{20}$ = - 4 (c 0.5 in $CHCl_3$). 1H-NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, *J* =1.7 Hz, 1H), 7.78 (dd, J_1 = 8.1 Hz, J_2 = 1.7 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 5.70 (d, *J* = 3.8 Hz, 1H), 3.99 (d, *J* = 3.7 Hz, 1H,) 1.44 (s, 9H) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 170.1, 168.3, 144.8, 136.9, 129.1, 128.5, 124.1, 123.4, 82.9, 81.7, 57.2, 27.8 ppm. MS (ESI): m/z = 343.2 $(M+H)^+$. Anal. calcd for $C_{14}H_{16}BrNO_4$:C, 43.14; H, 4.71; N, 4.09. Found: C, 43.39; H, 4.62; N, 4.23%. HPLC



8b

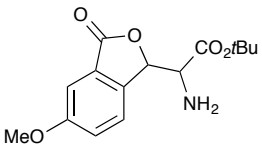
separation of the major diastereomer: Chiralcel OD-H, hexane:i-PrOH = 9:1, 25 °C, 0.7 mL/min, (retention times: 27.1 min (minor); 35.0 min (major)).

(-)-8c. Obtained according to the general procedure in 78% (23 mg, 0.078 mmol) as an amorphous solid. (dr = 3.5:1; e.r. (major) = 88:12). $[\alpha]_D^{20}$ = -11.8 (c 0.43 in $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 1.8 Hz, 1H), 7.62 (dd, J_1 = 8.1 Hz, J_2 = 1.8 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 5.71 (d, *J* = 3.6 Hz, 1H), 3.99 (d, *J* = 3.6 Hz, 1H) 1.43 (s, 9H) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 170.2, 168.6, 145.1, 135.8, 134.4, 128.6, 125.5, 123.2, 82.8, 81.5, 56.7, 27.8 ppm. MS (ESI): m/z = 298.1 $(M+H)^+$. Anal. calcd for $C_{14}H_{16}ClNO_4$: C, 56.48, H, 5.42; N, 4.70. Found: C, 56.40; H, 5.62; N, 4.63%. HPLC separation of the major diastereomer: Chiralcel OD-H, hexane:i-PrOH = 9:1, 25 °C, 0.7 mL/min, (retention times: 11.7 min (minor); 14.6 min (major)).



8c

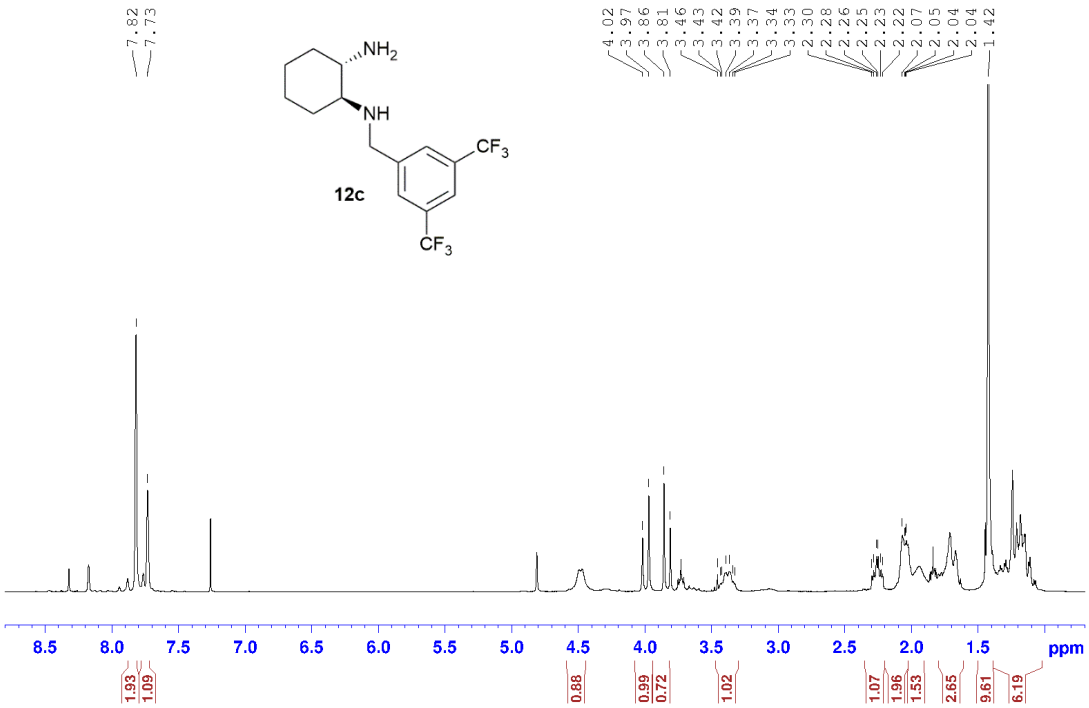
(-)-8d. Obtained according to the general procedure in 75% (22 mg, 0.075 mmol) as an amorphous solid. (dr = 3:1; e.r. (major) = 87:13). $[\alpha]_D^{20}$ = - 1.5 (c 0.35 in $CHCl_3$). ^{1}H-NMR (250 MHz, $CDCl_3$): δ = 7.34-7.29 (m, 2H), 7.23-7.22 (m, 1H), 5.71 (d, *J* = 3.3 Hz, 1H), 4.00 (d, *J* = 3.3 Hz, 1H,) 3.86 (s, 3H), 1.42 (s, 9H) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 170.3, 170.0, 138.2, 128.5, 123.3, 123.0, 122.7, 107.5, 82.5, 81.6, 57.4, 55.7, 27.8 ppm. MS (ESI): m/z = 294.1 $(M+H)^+$. Anal. calcd for $C_{15}H_{19}NO_5$: C, 61.42; H, 6.53; N, 4.78. Found: C, 61.35; H, 6.63; N, 4.56%. HPLC separation of the major diastereomer: IA3 column, hexane:i-PrOH = 9:1, 25 °C, 0.6 mL/min, (retention times: 30.2 min (major); 33.4 min (minor)).

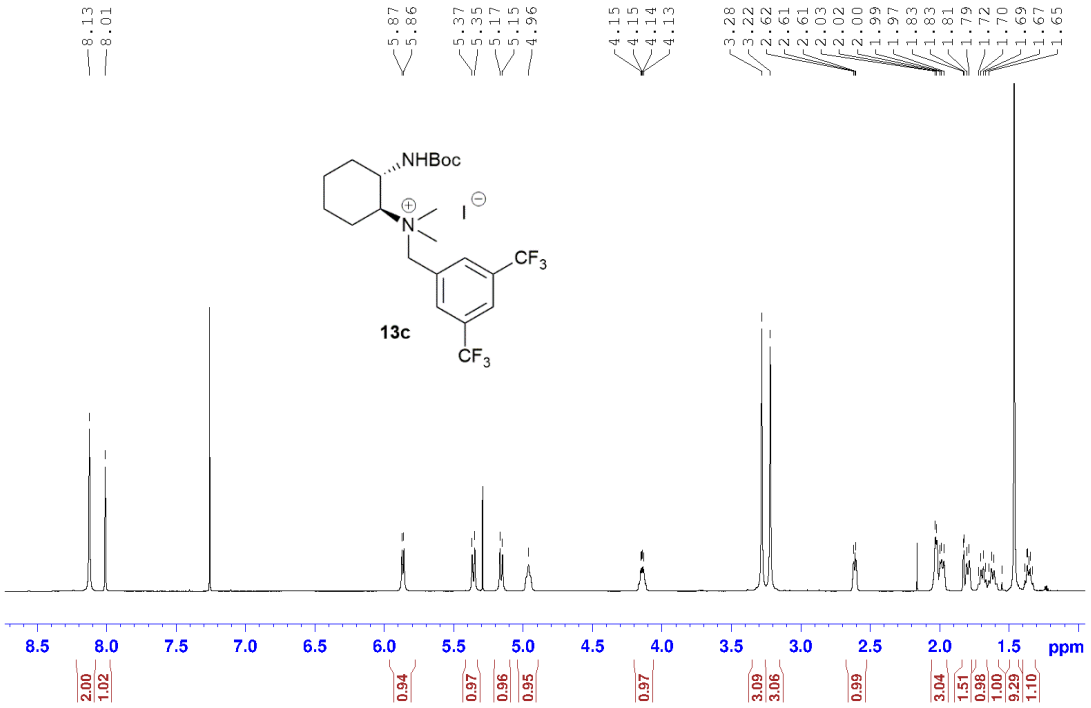


8d

5. Copies of NMR Spectra of Key-Intermediates and Most Relevant Catalysts:

Crude product

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2.03
2.02
2.00
1.99
1.97
1.83
1.81
1.79
1.72
1.70
1.69
1.67
1.65
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I
N
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CF3
13c
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7.5
7.0
6.5
6.0
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4.0
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2.0
1.5
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0.97
0.96
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3.04
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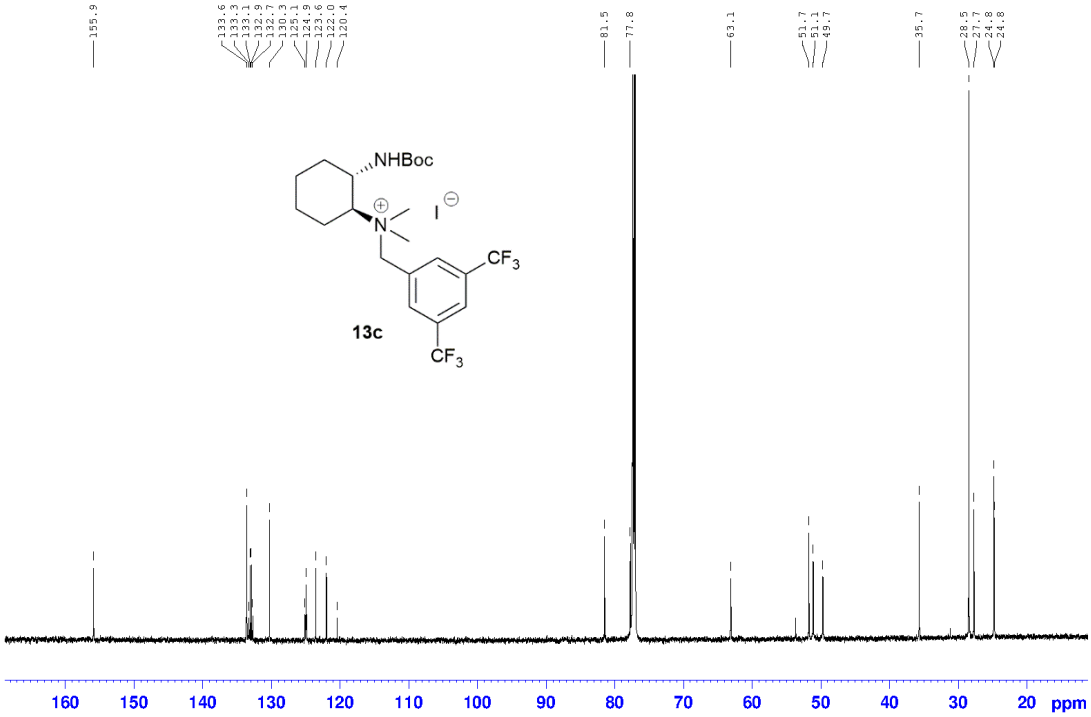
1.10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77.8
63.1
51.7
51.1
49.7
35.7
28.5
27.7
24.8
24.8
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I
N
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CF3
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120
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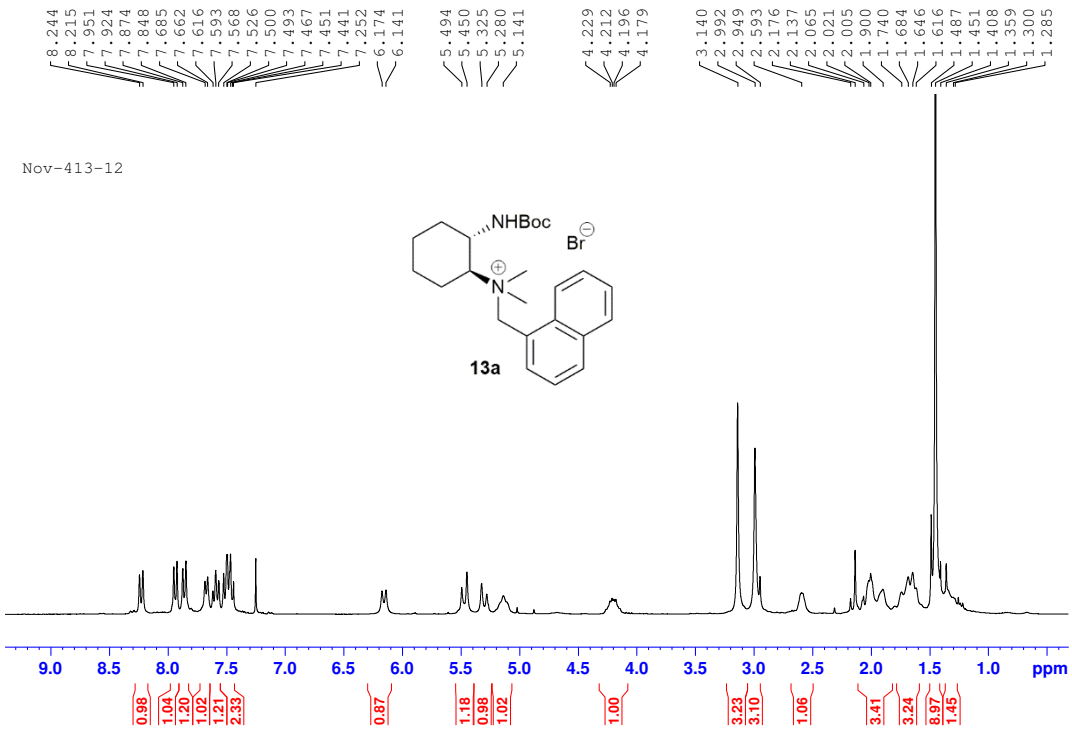
20
ppm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5.141
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4.196
4.179
3.140
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2.005
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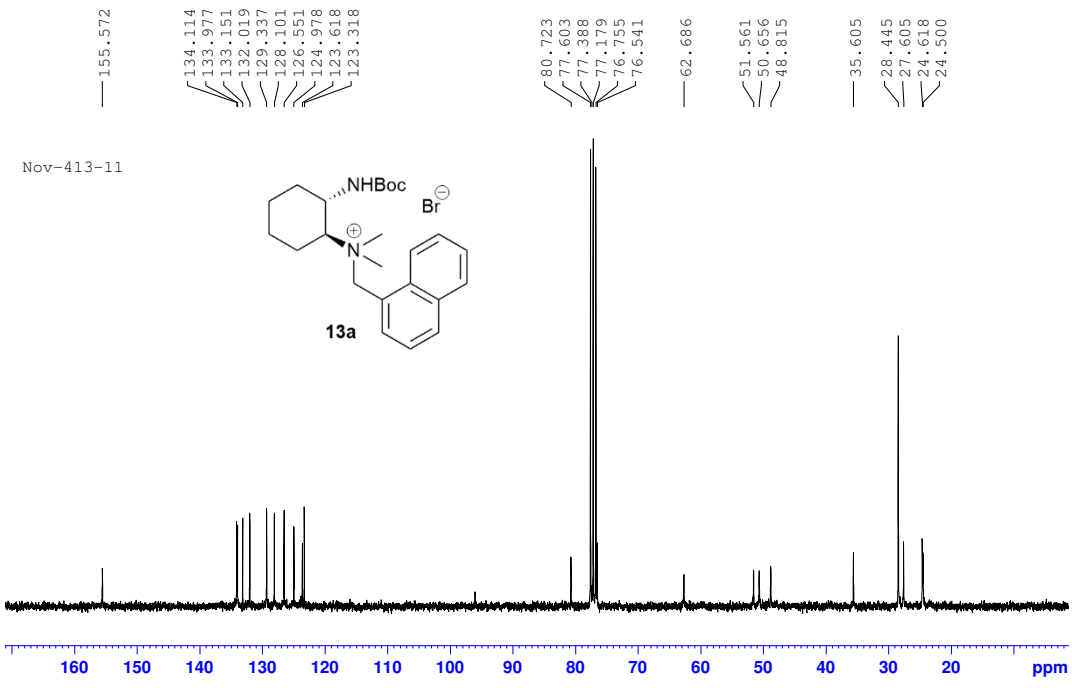
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77.179
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76.541
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50.656
48.815
35.605
28.445
27.605
24.618
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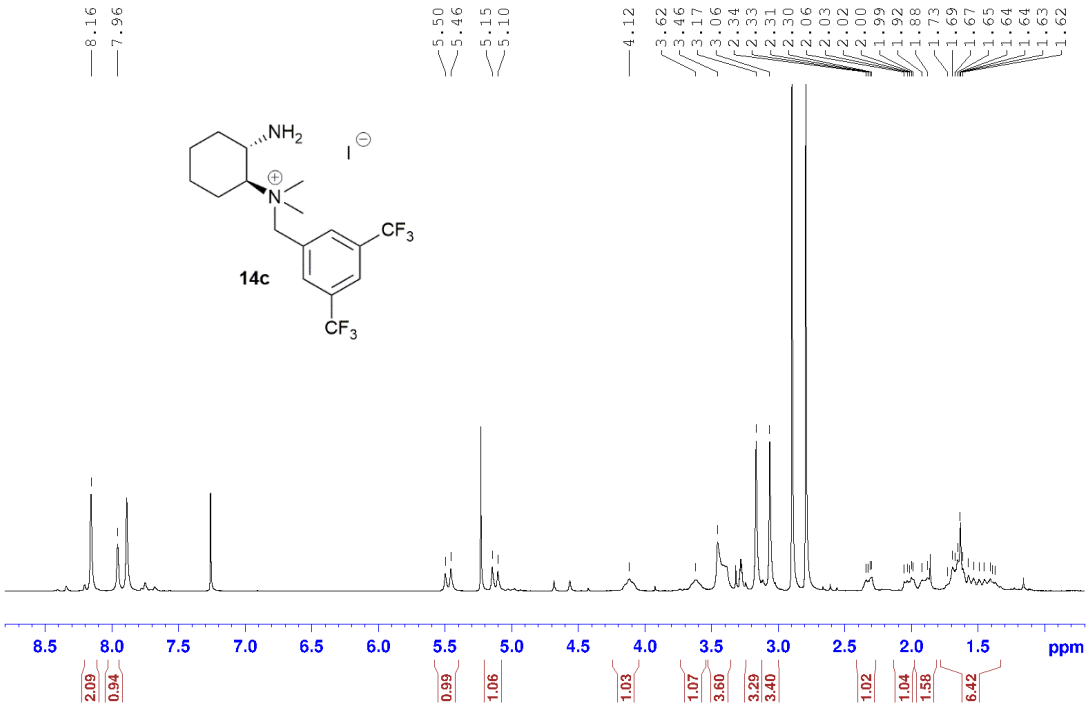
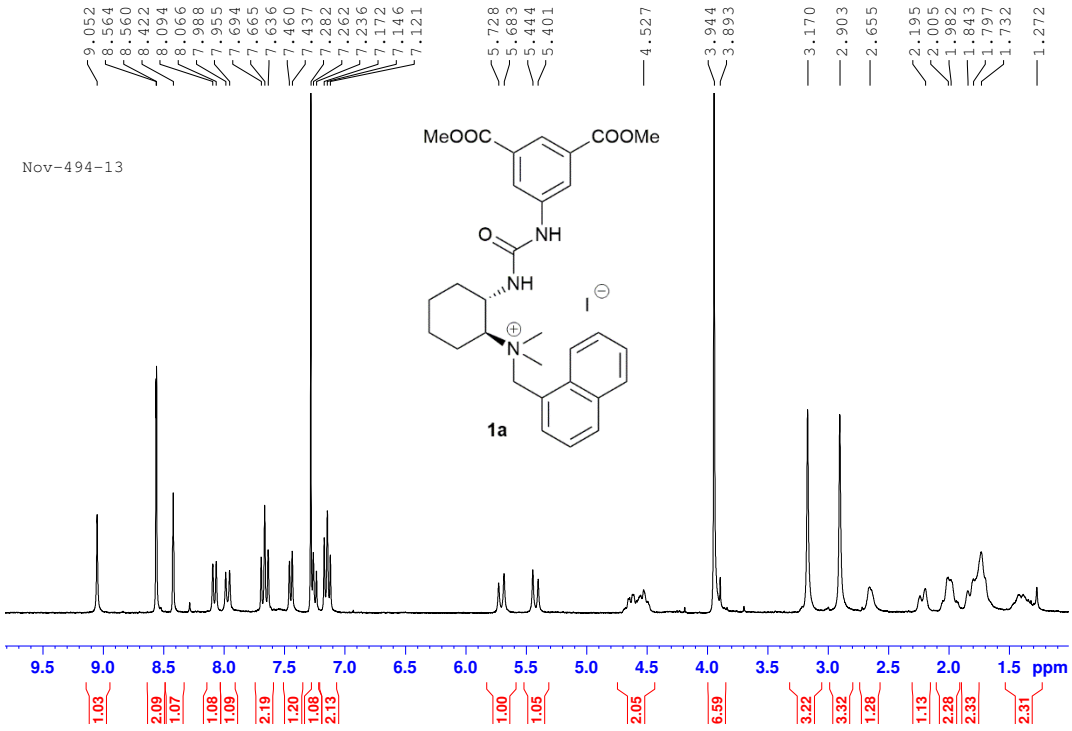
20
ppm

Crude product

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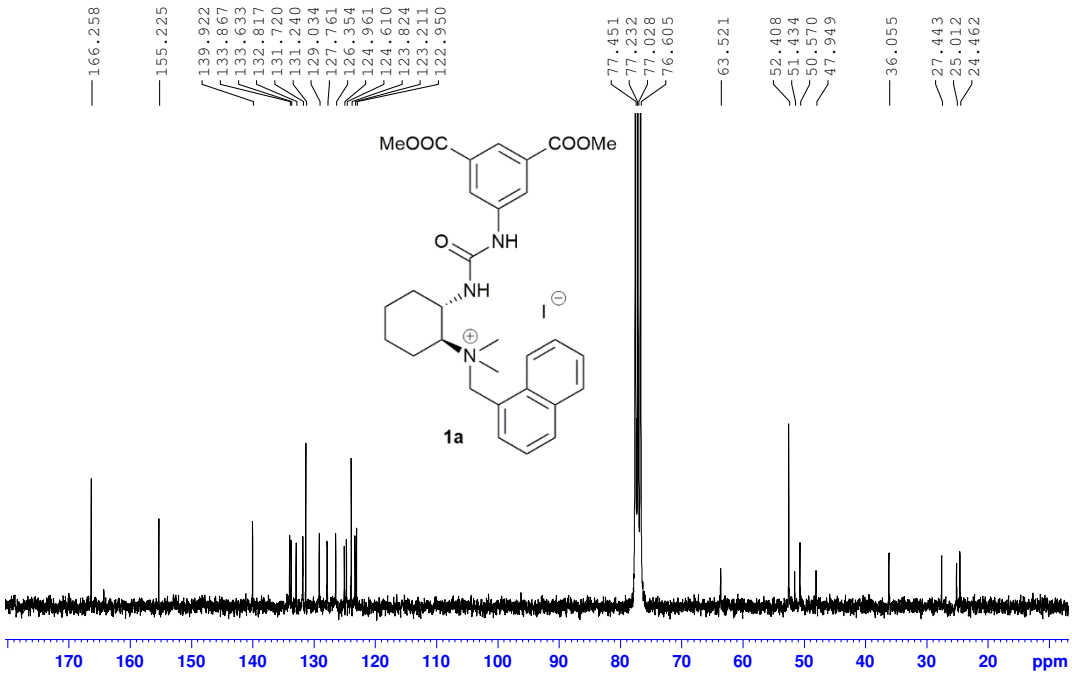
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COOMe
O
NH
NH
I
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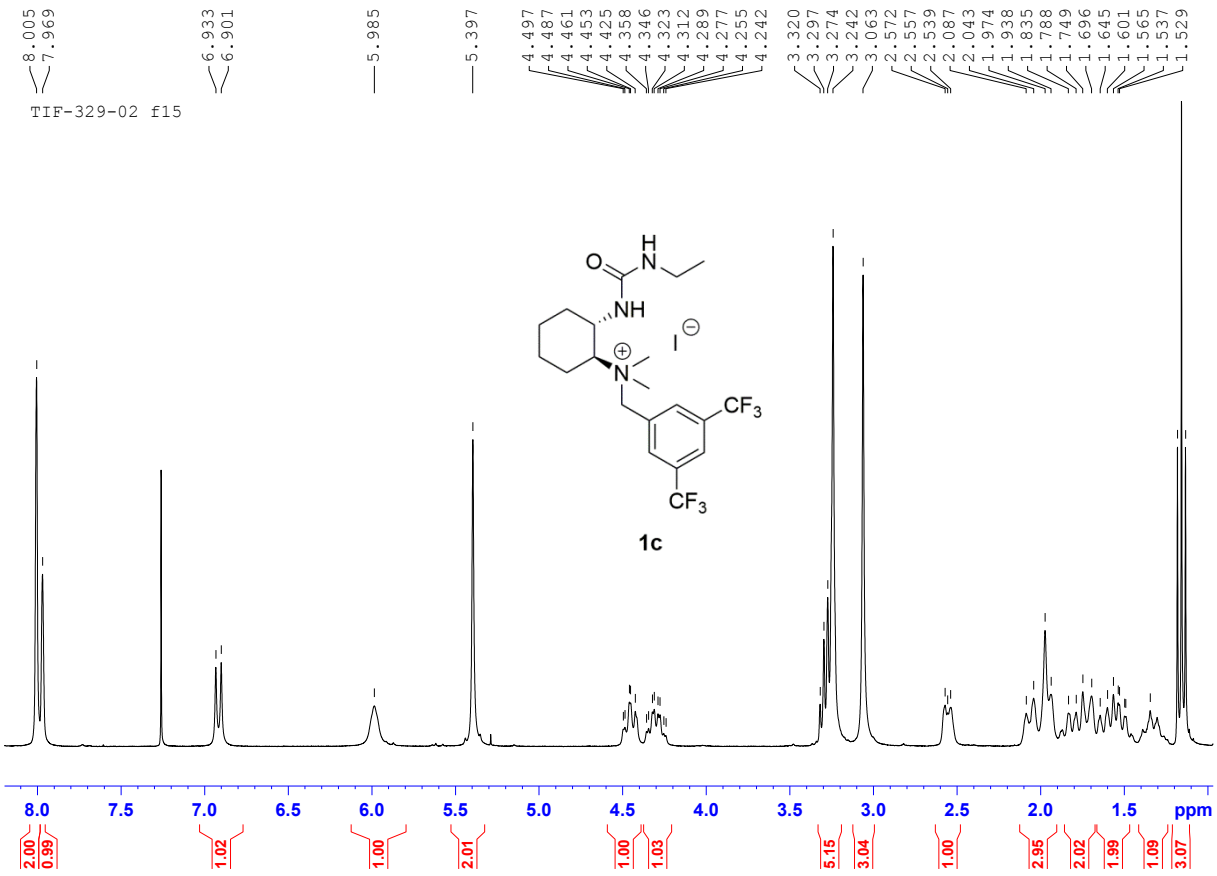
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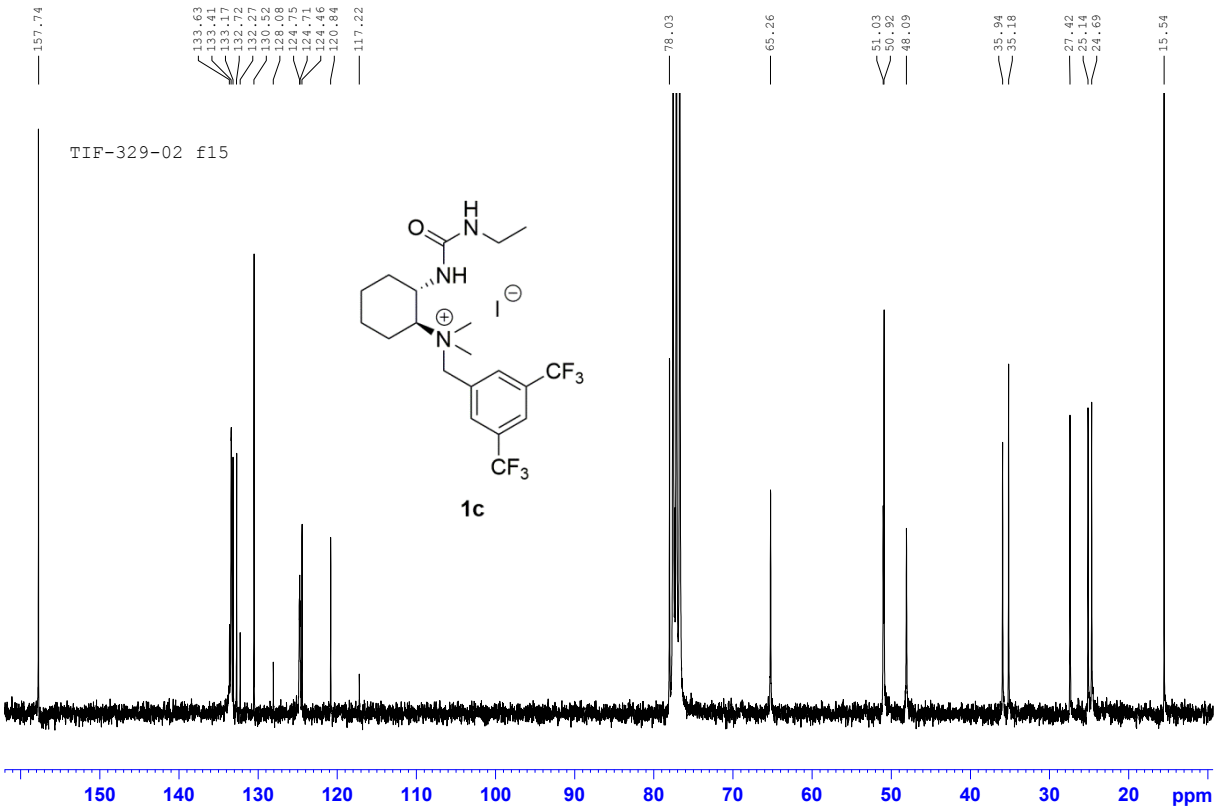
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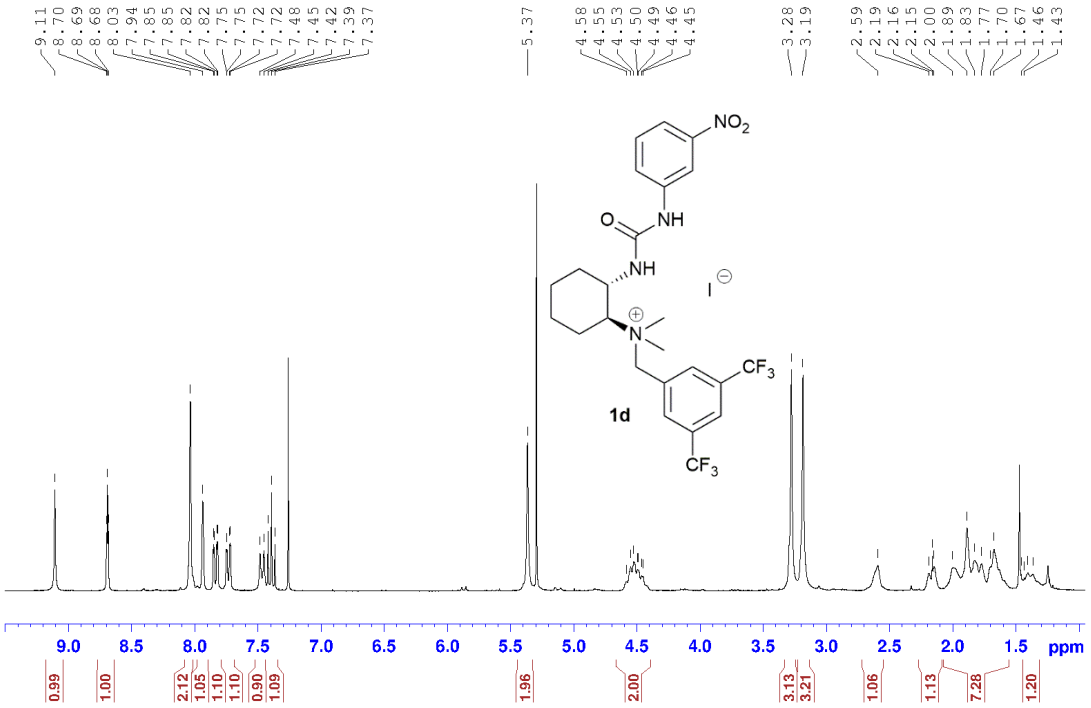
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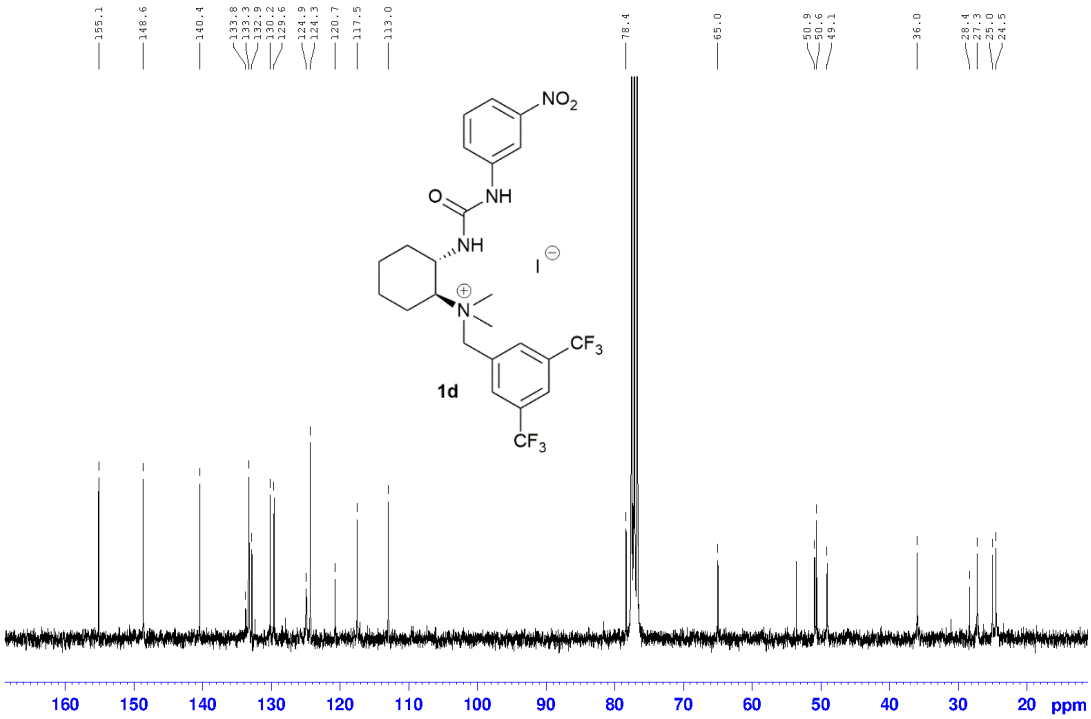
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25.0
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NO2
O
NH
NH
I
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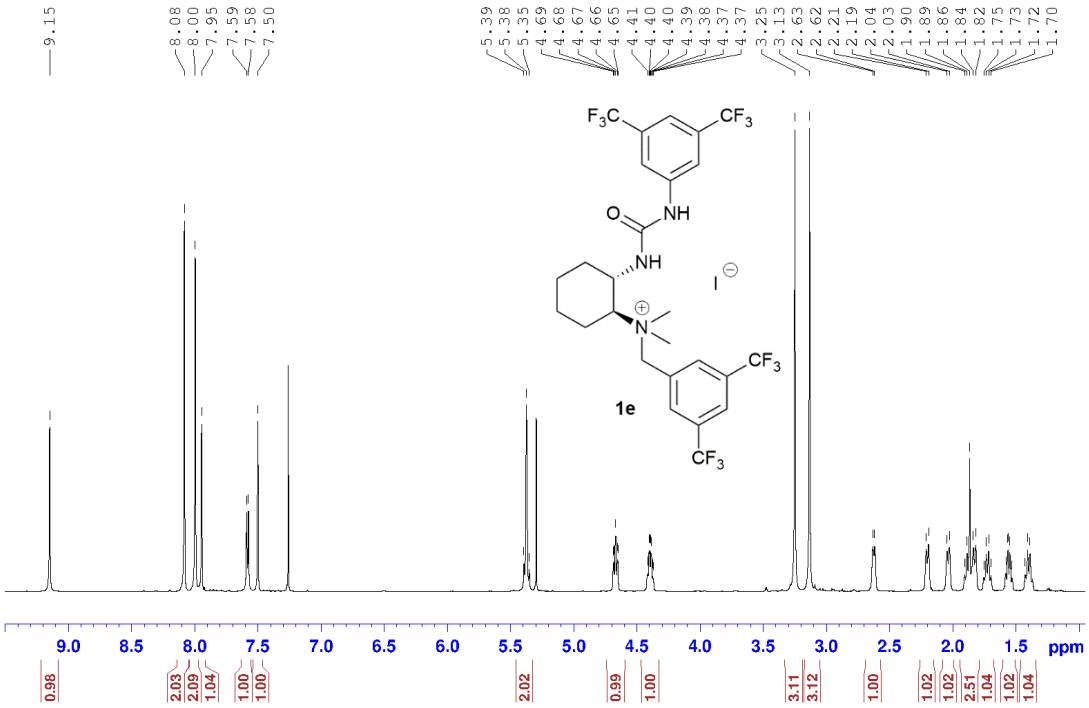
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CF3
O
NH
NH
I
N
CF3
CF3
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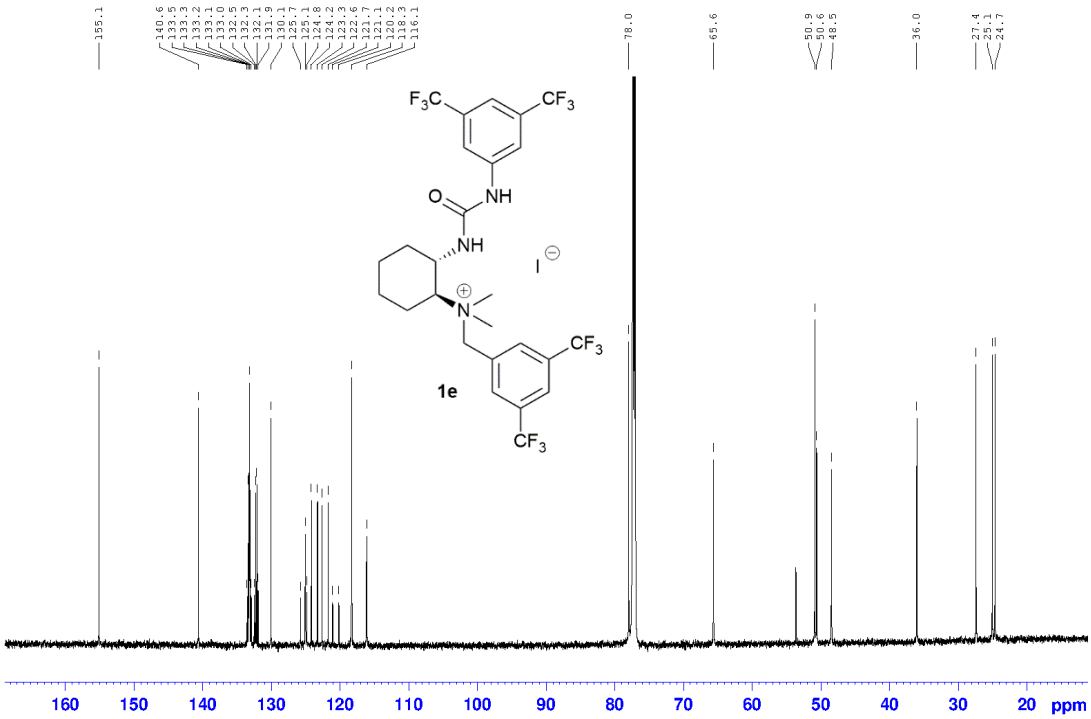
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F3C
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CF3
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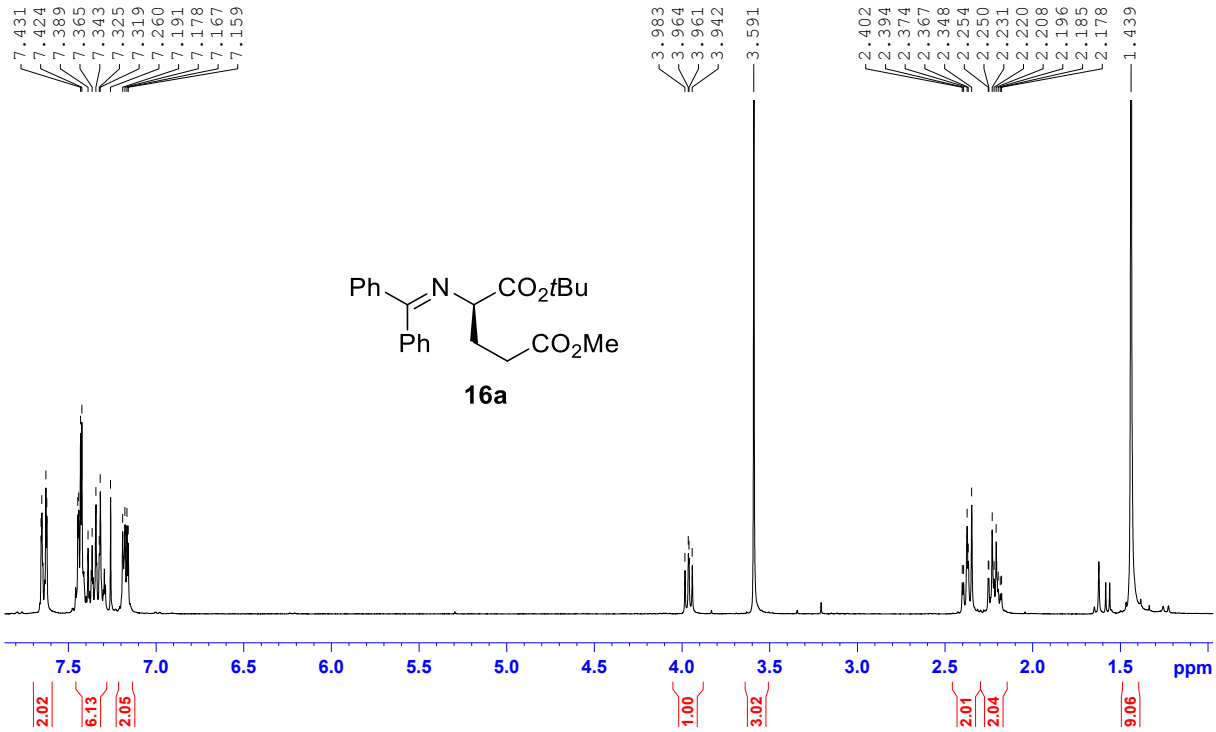
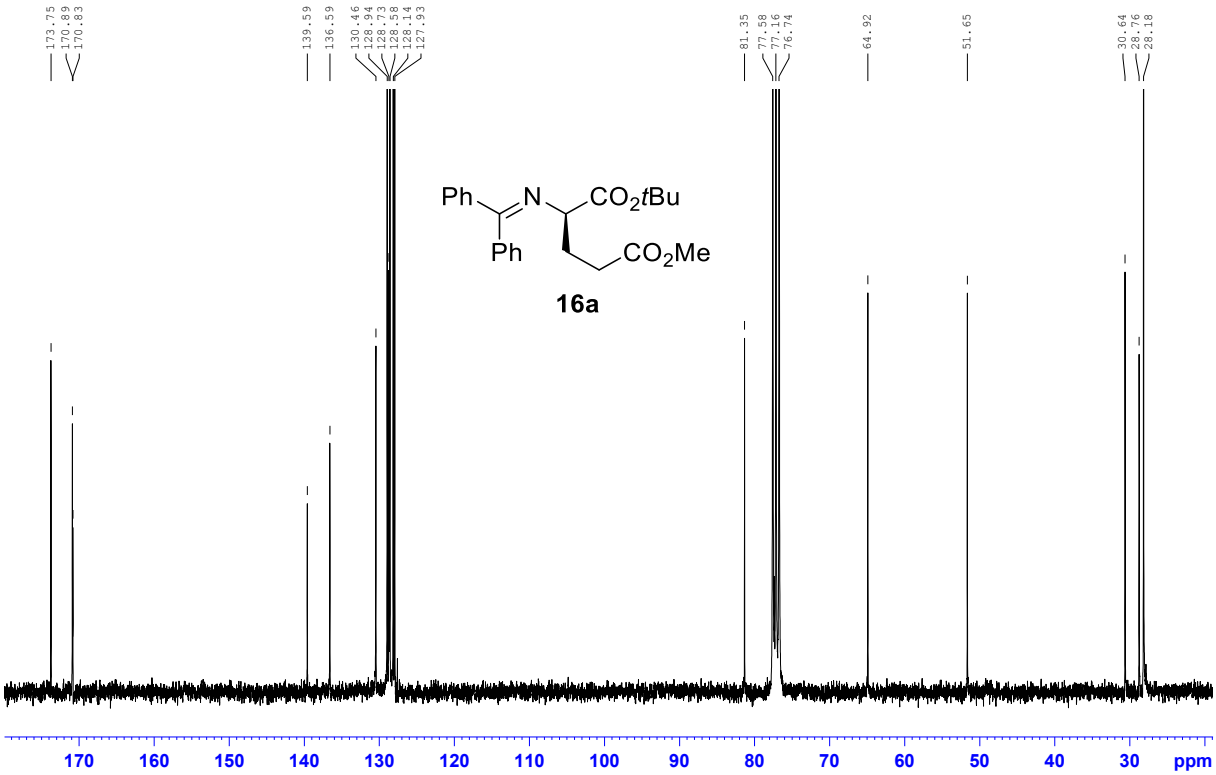
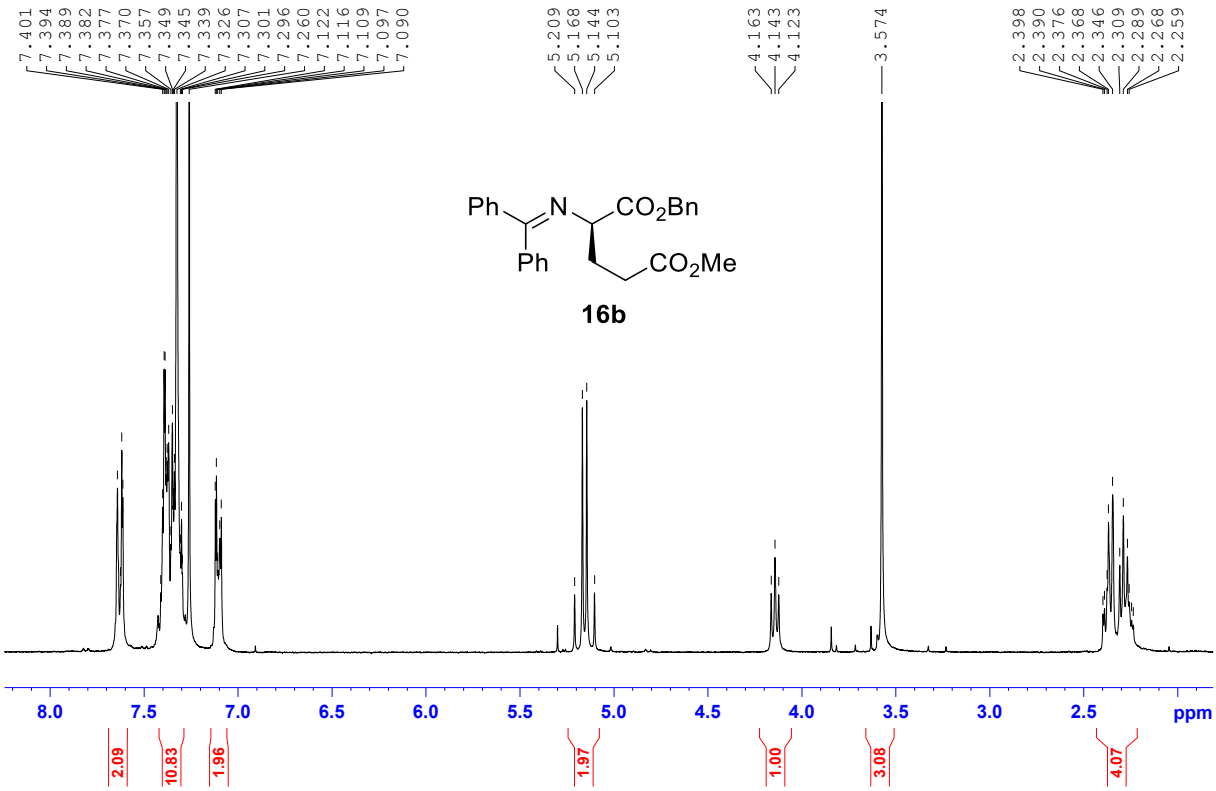
6. Copies of NMR Spectra of Selected Products 16 and Products 8:



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Ph
CO2Me
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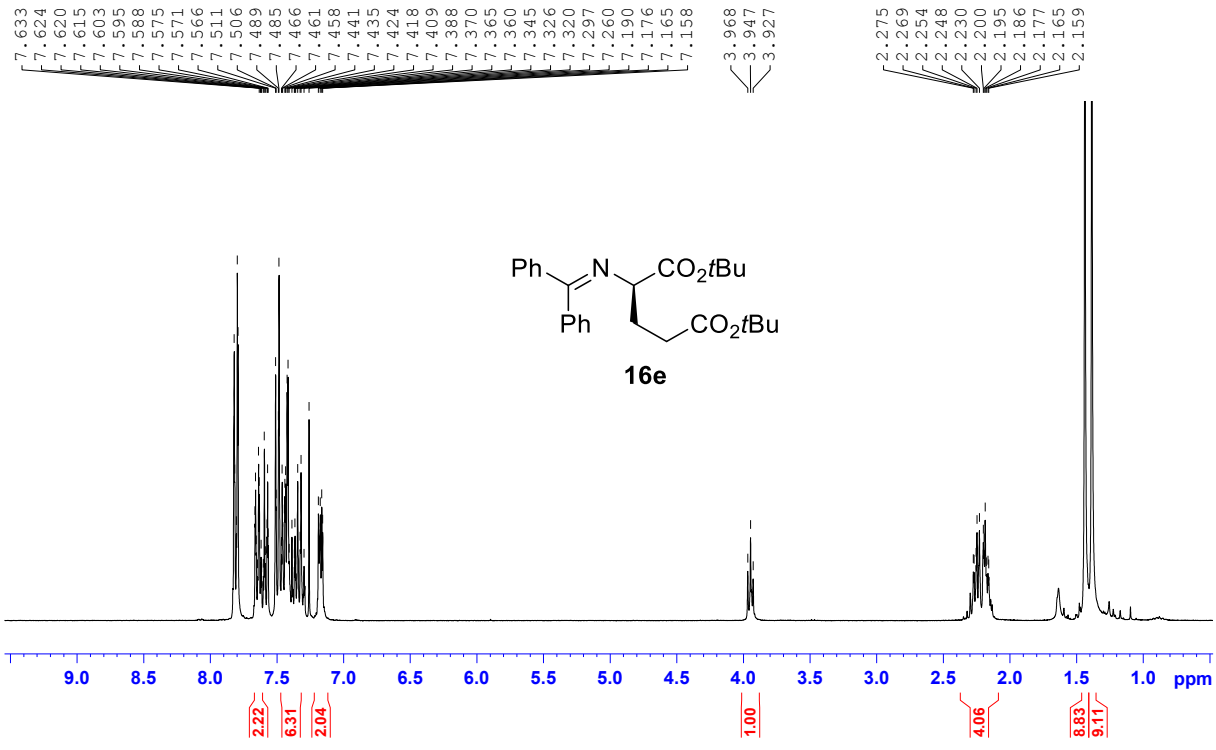
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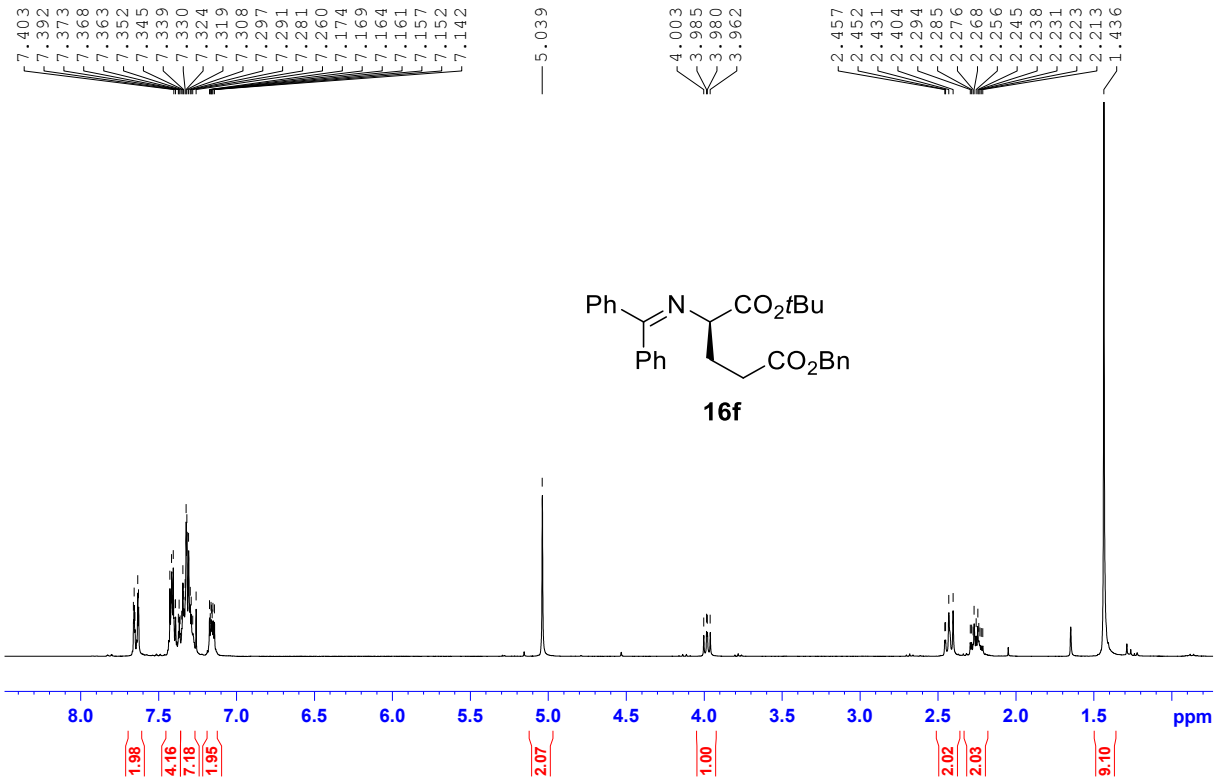
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2.256
2.245
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CO2tBu
Ph
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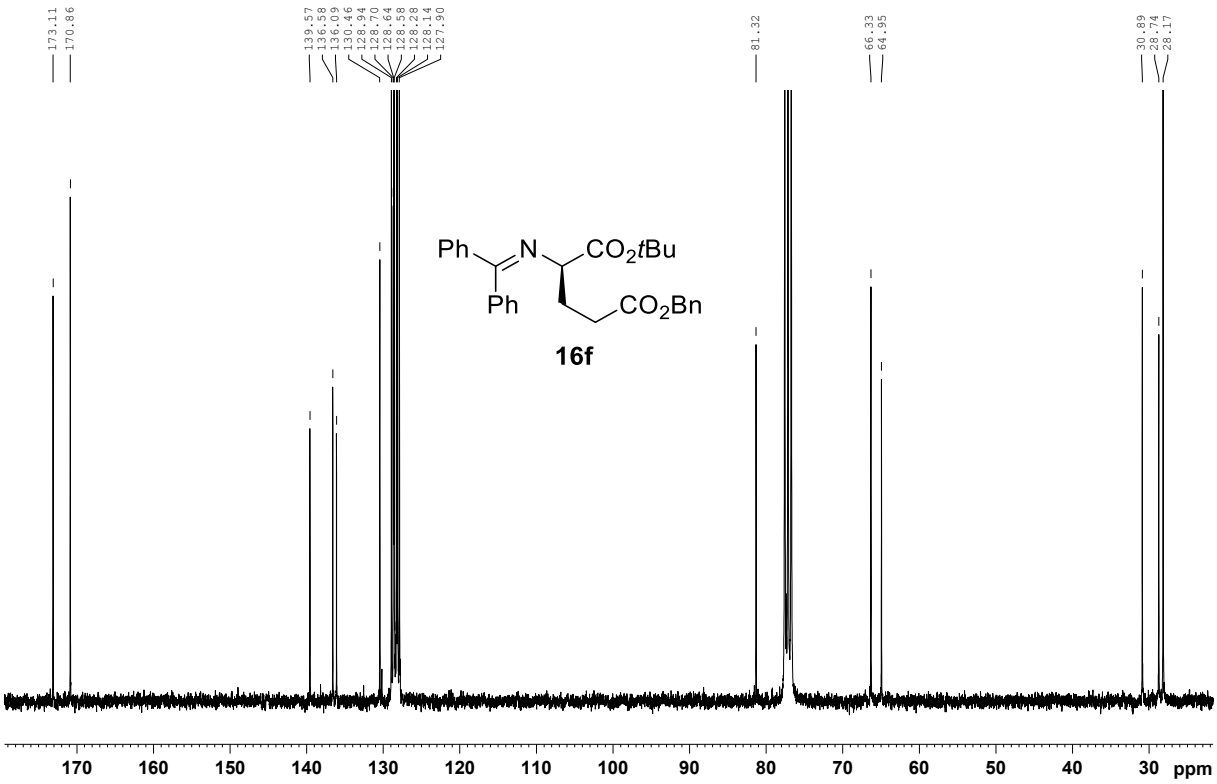
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66.33
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30.89
28.74
28.17
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CO2tBu
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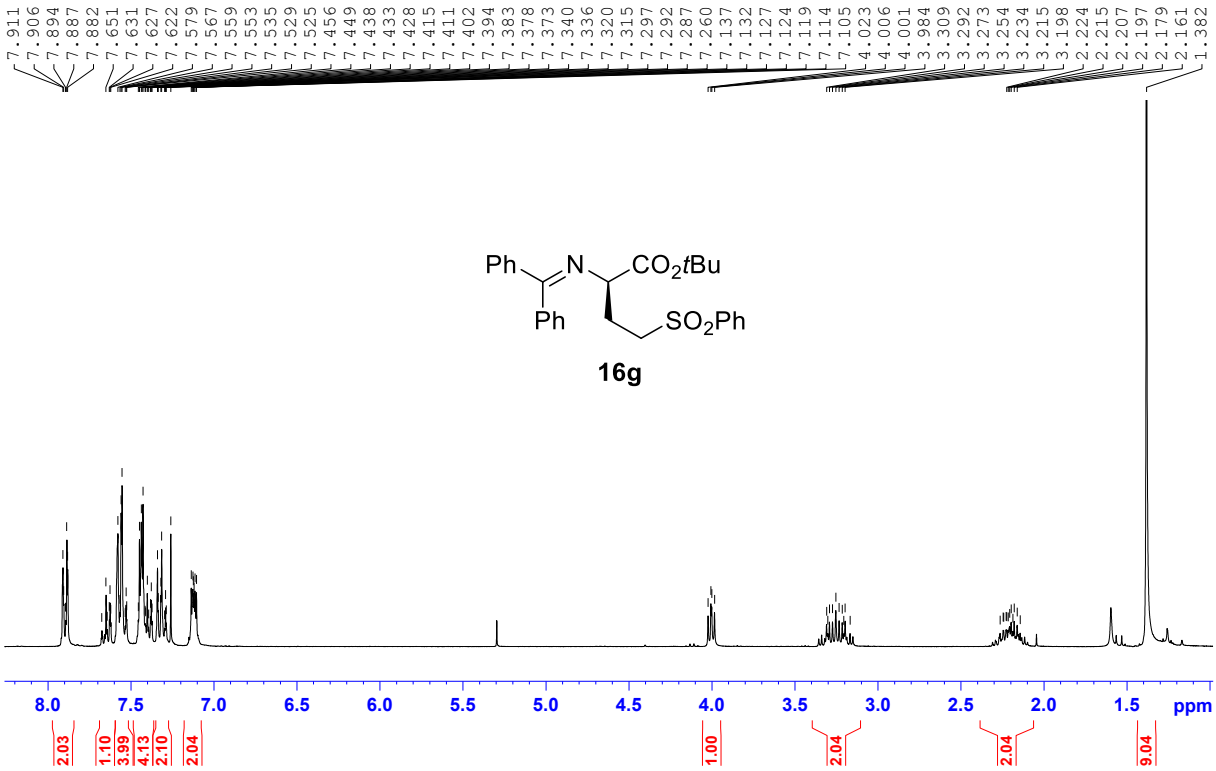
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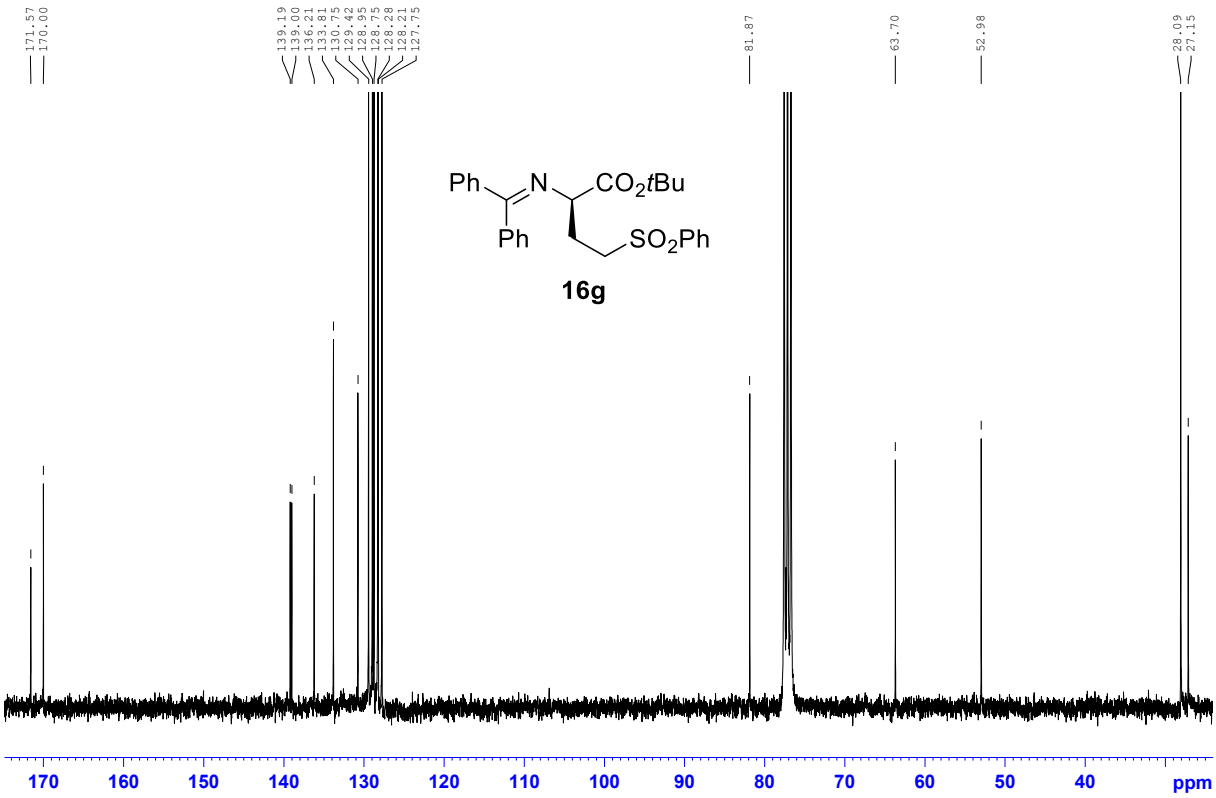
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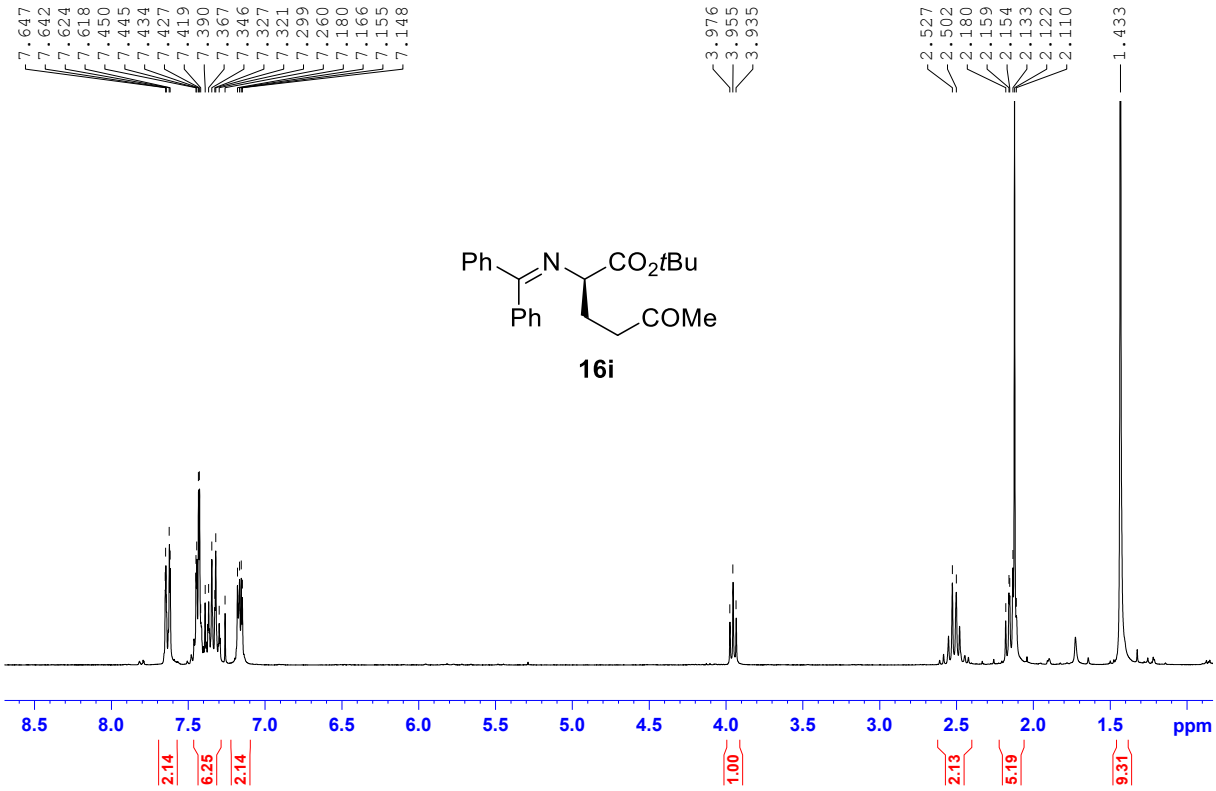
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2.180
2.159
2.154
2.133
2.122
2.110
1.433
Ph
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CO2tBu
Ph
COMe
16i
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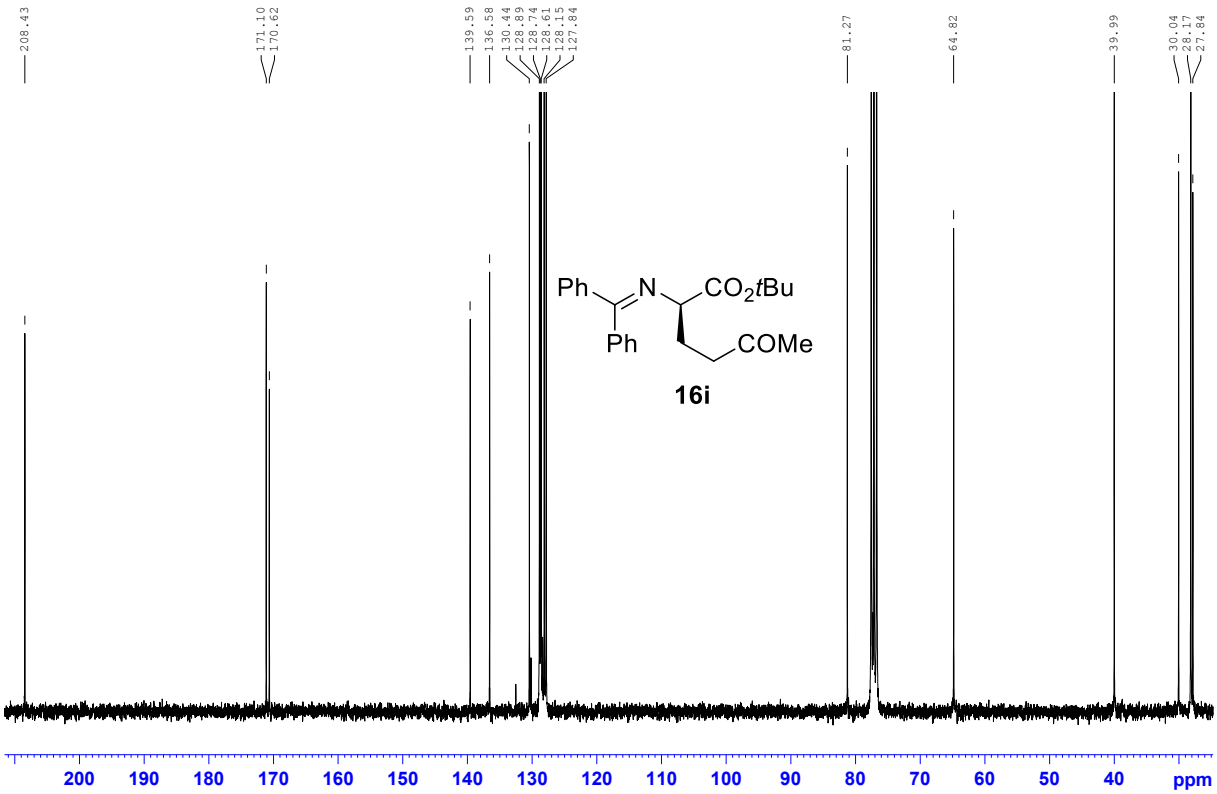
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27.84
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Ph
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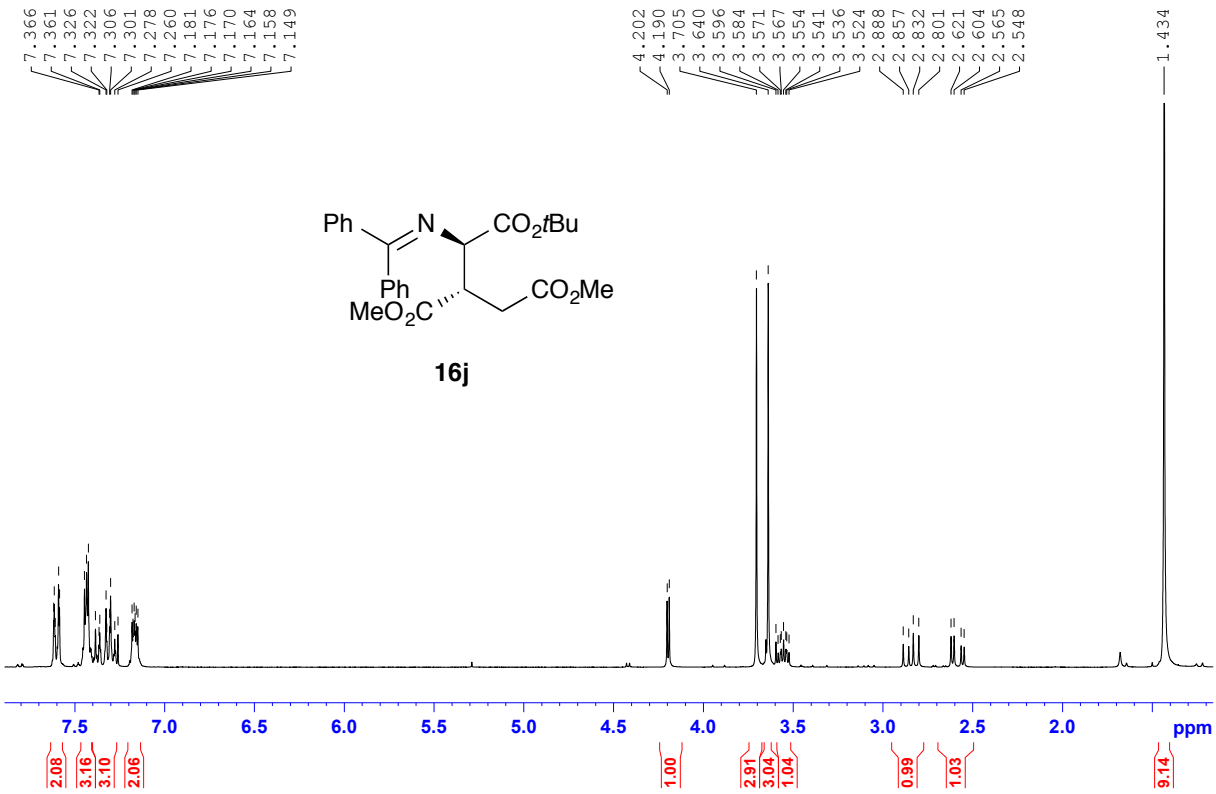
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CO2tBu
Ph
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CO2Me
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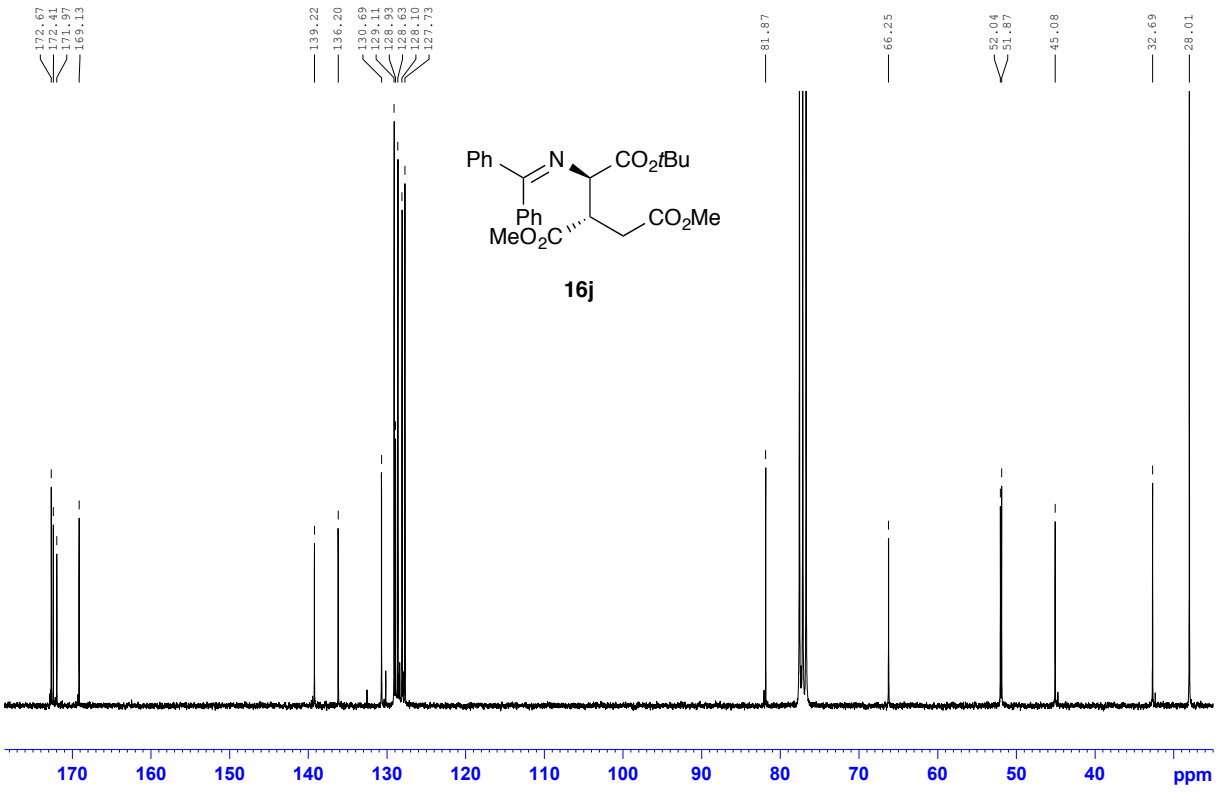
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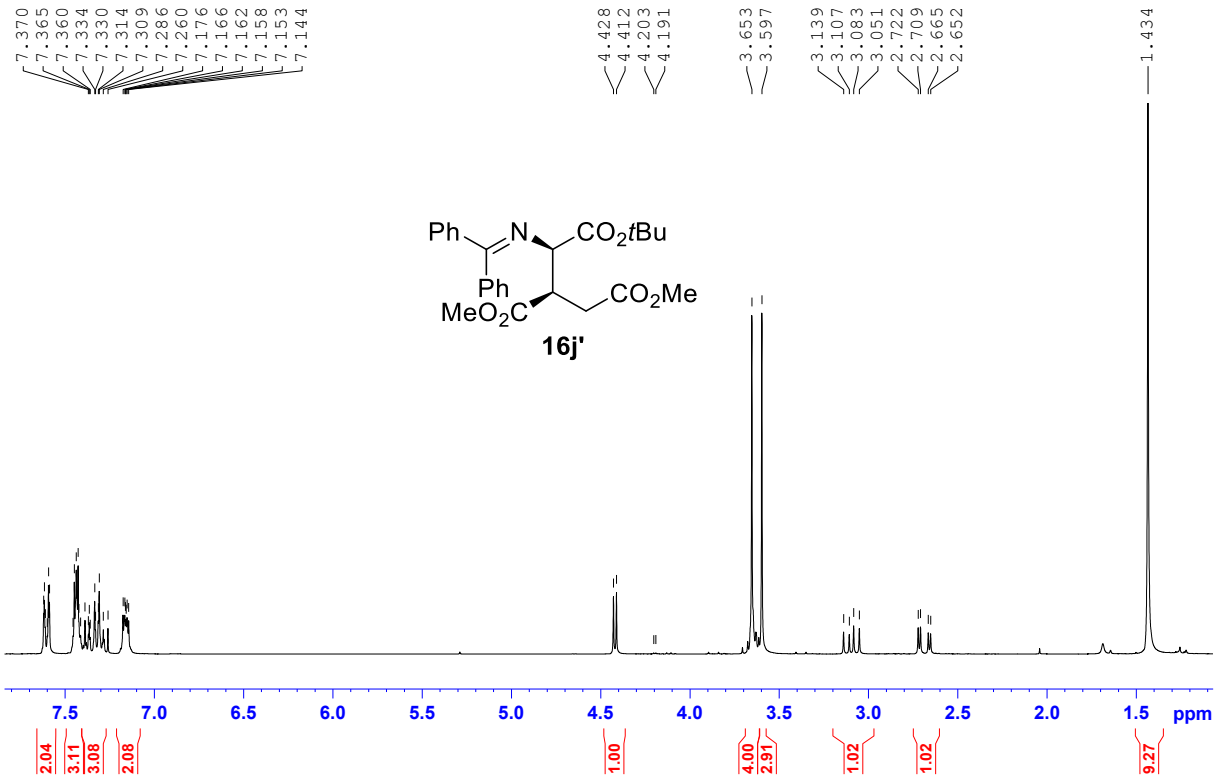
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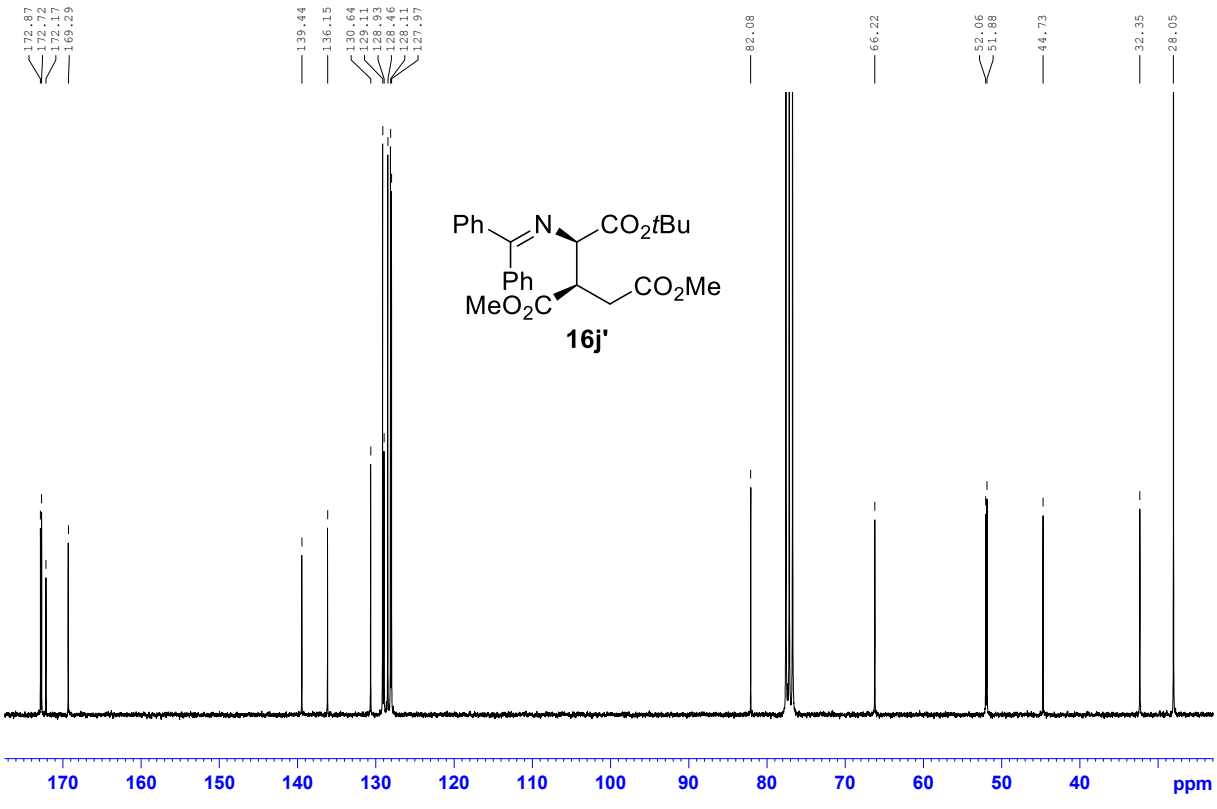
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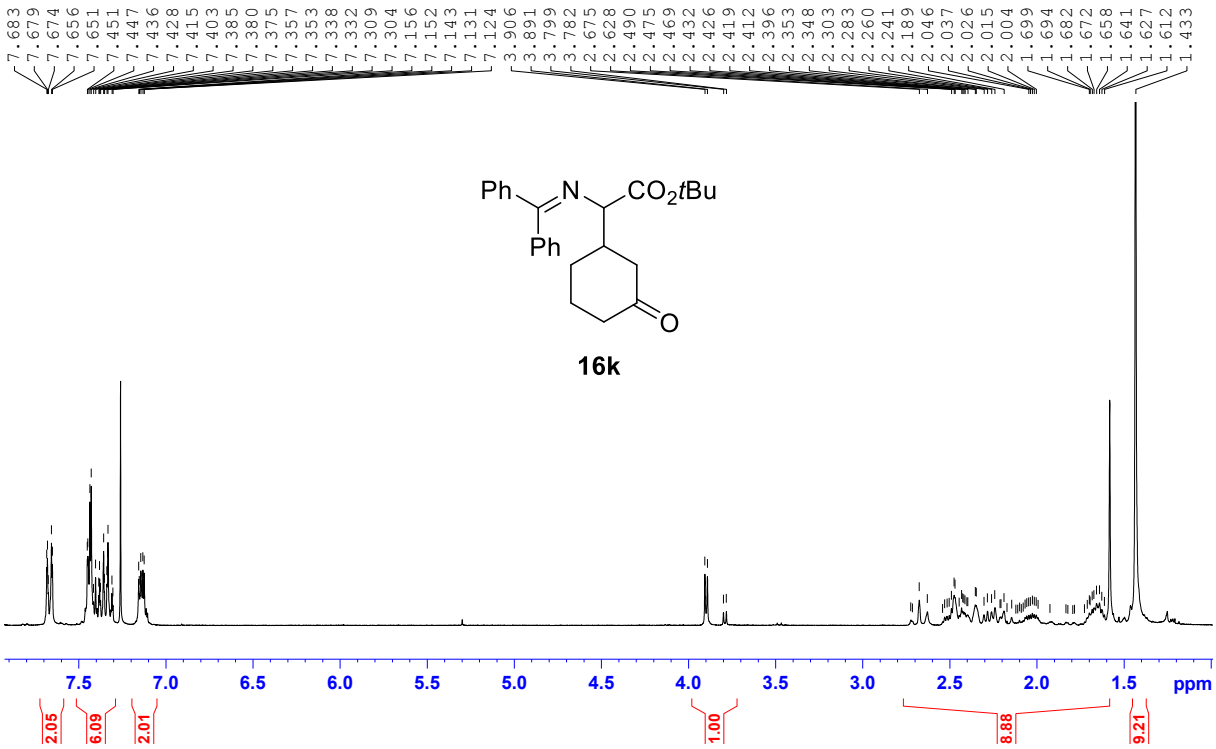
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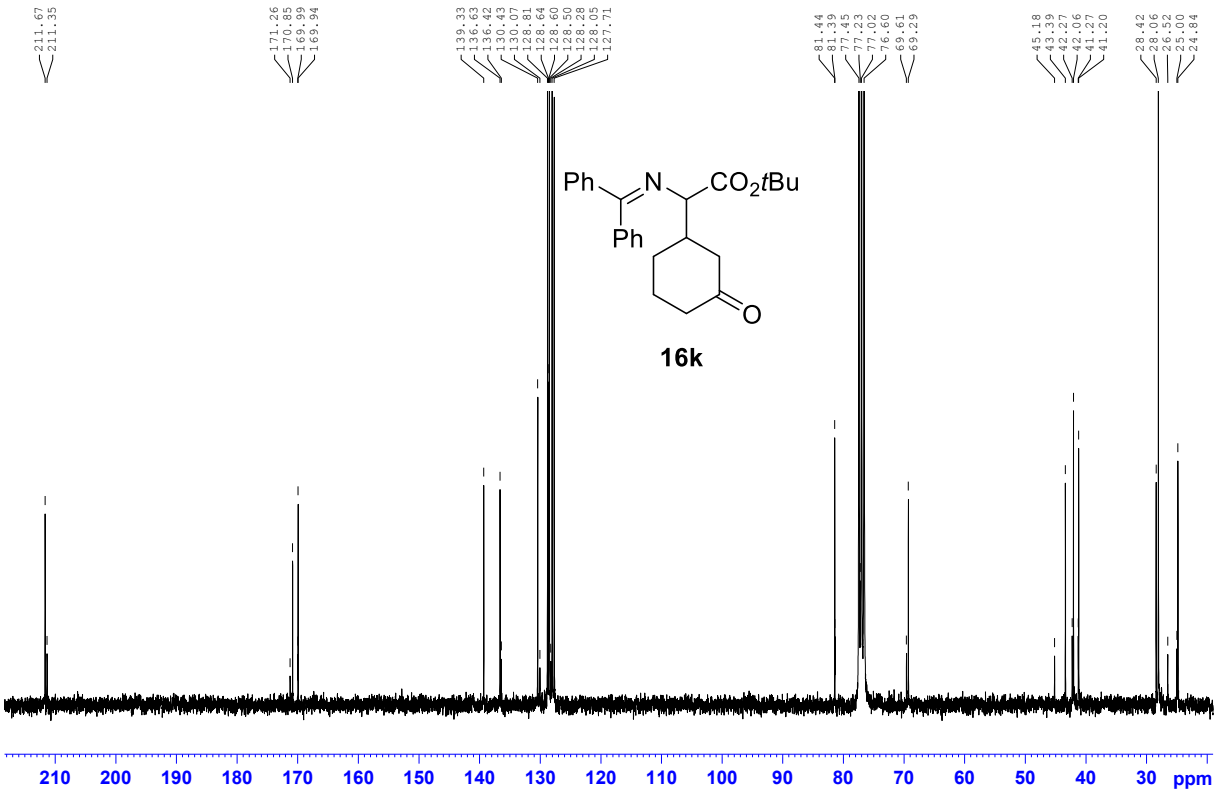
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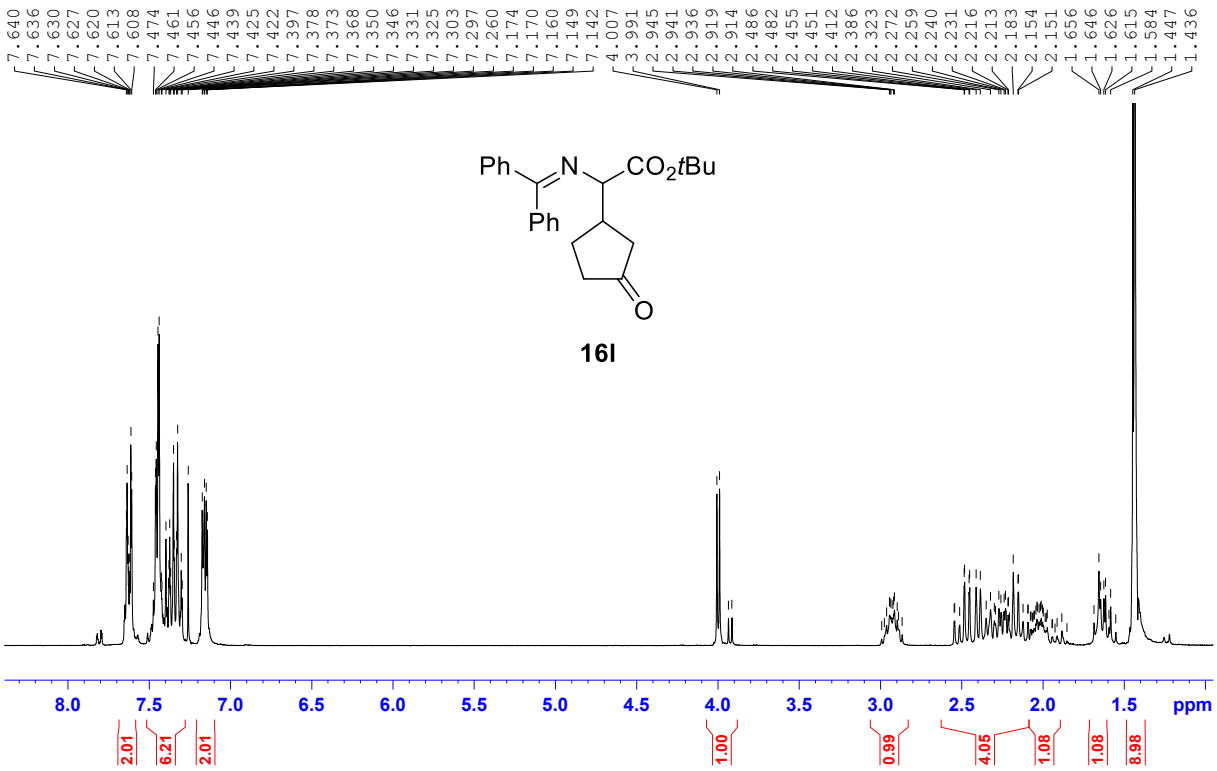
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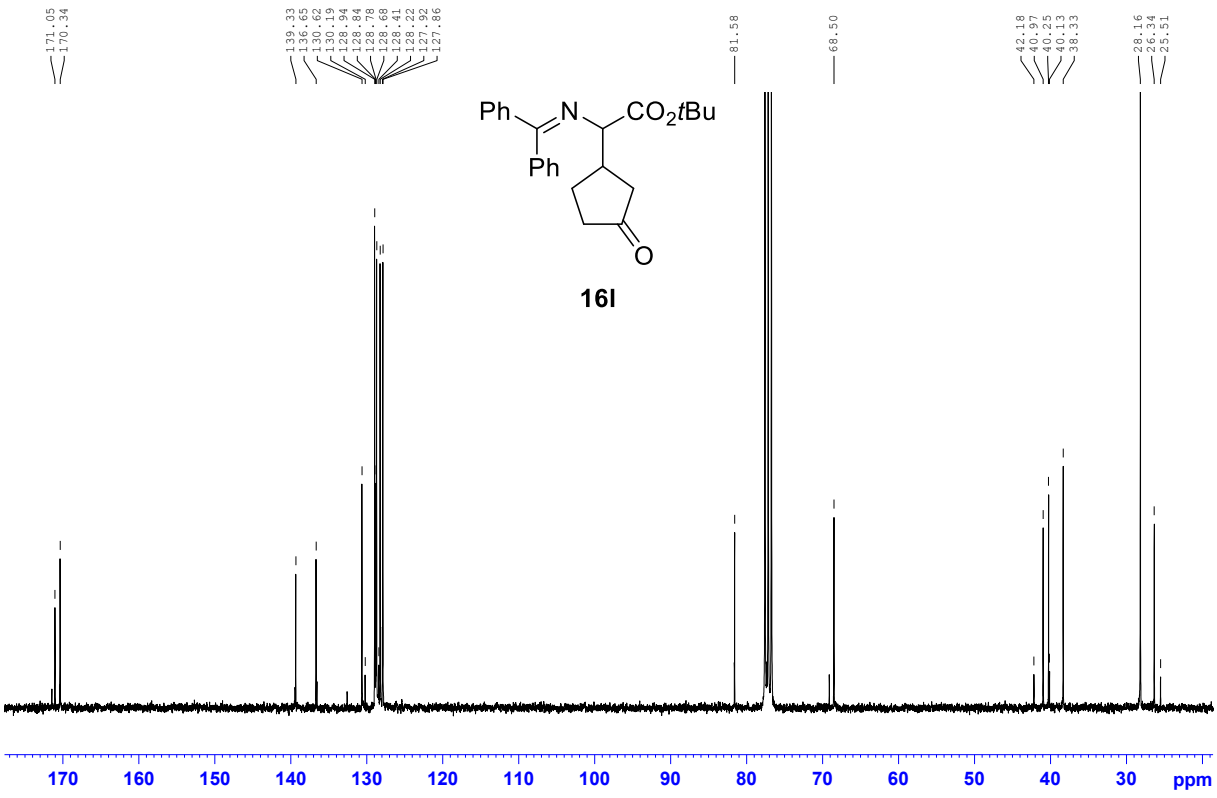
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CO2tBu
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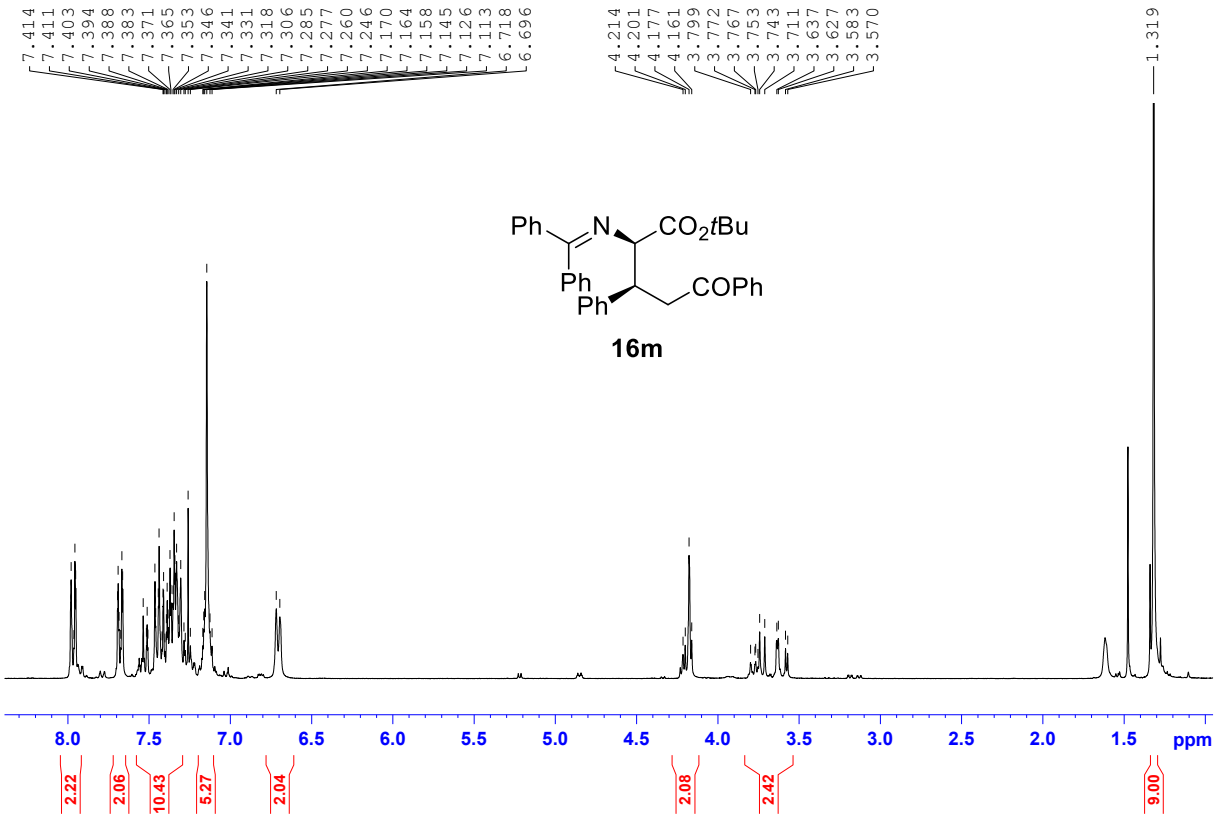
30
ppm

16l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7.306
7.285
7.277
7.260
7.246
7.170
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7.145
7.126
7.113
6.718
6.696
4.214
4.201
4.177
4.161
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3.772
3.767
3.753
3.743
3.711
3.637
3.627
3.583
3.570
1.319
Ph
N
CO2tBu
Ph
Ph
COPh
16m
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
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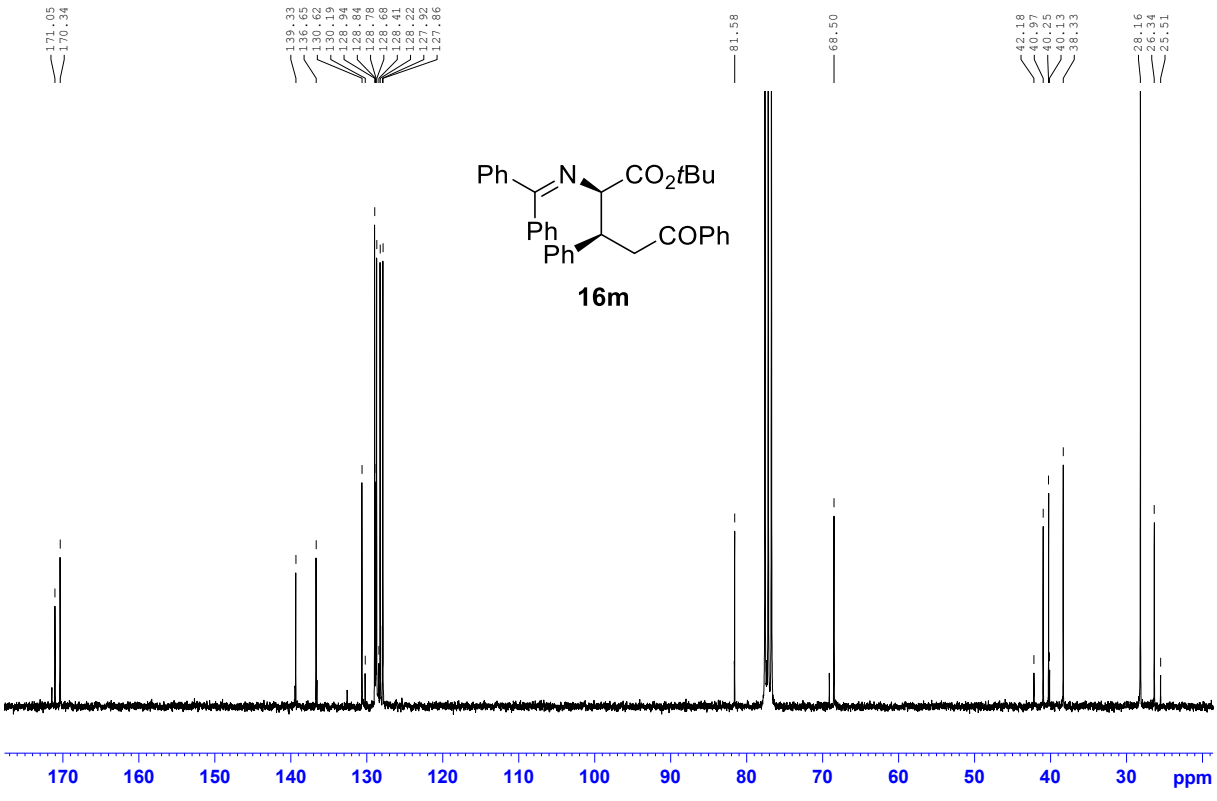
2.06
10.43
5.27
2.04
2.08
2.42
9.00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127.86
81.58
68.50
42.18
40.97
40.25
40.13
38.33
28.16
26.34
25.51
Ph
N
CO2tBu
Ph
Ph
COPh
16m
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160
150
140
130
120
110
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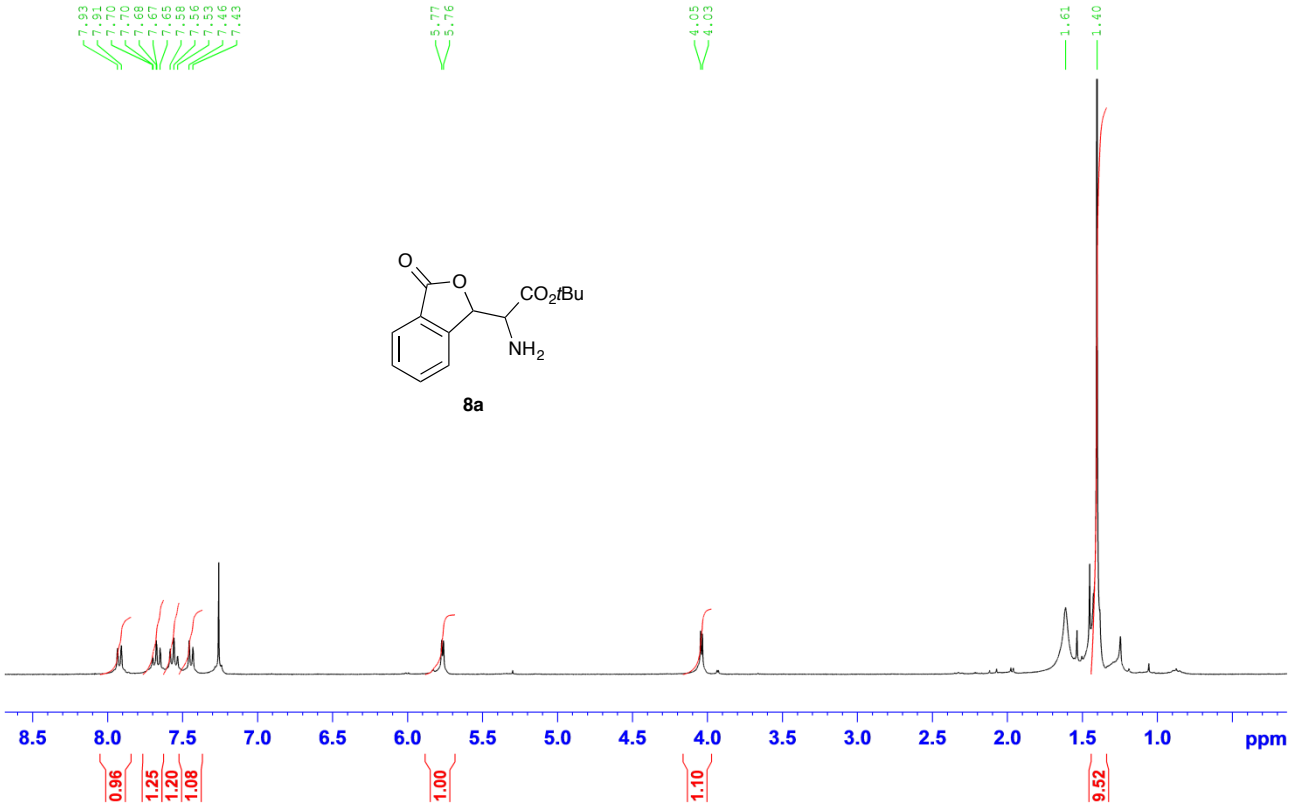
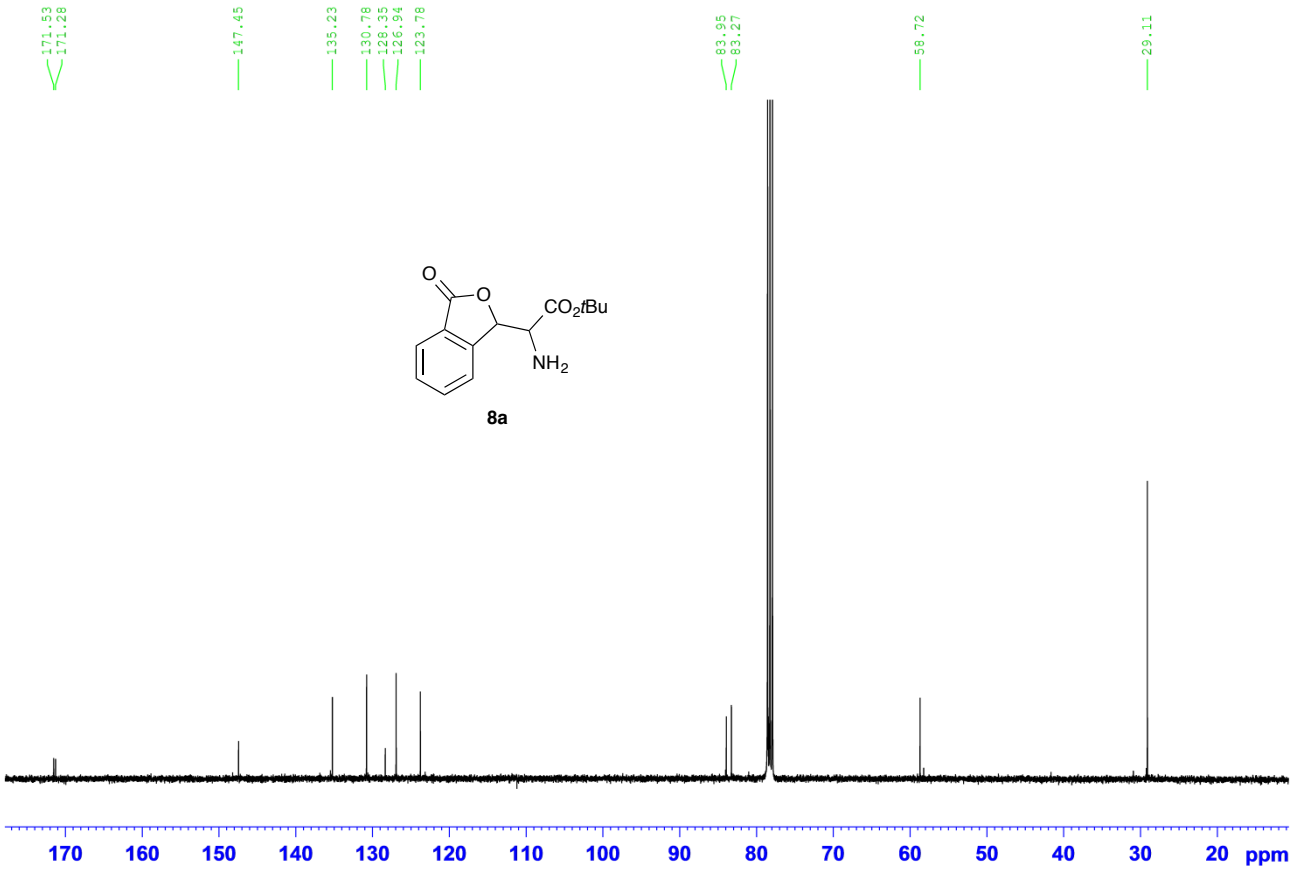
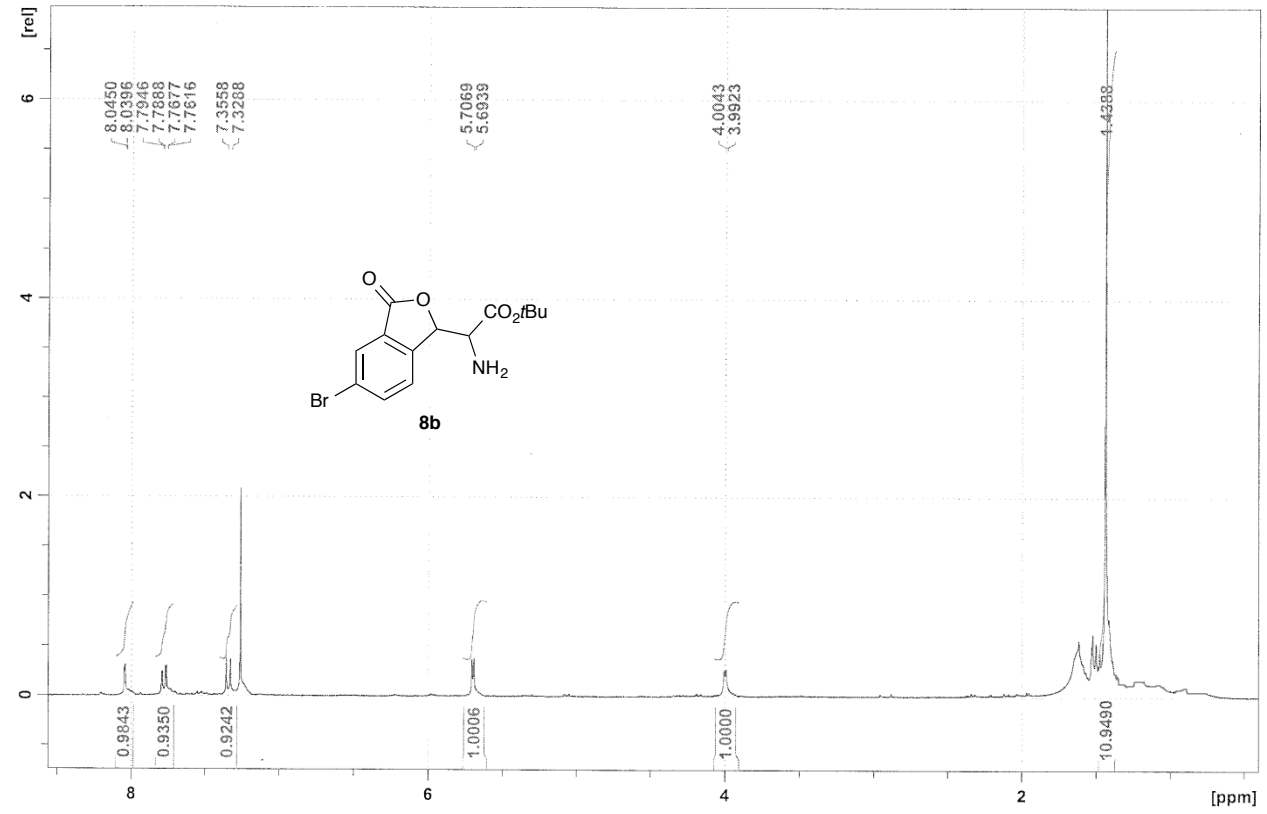
90
80
70
60
50
40
30
ppm

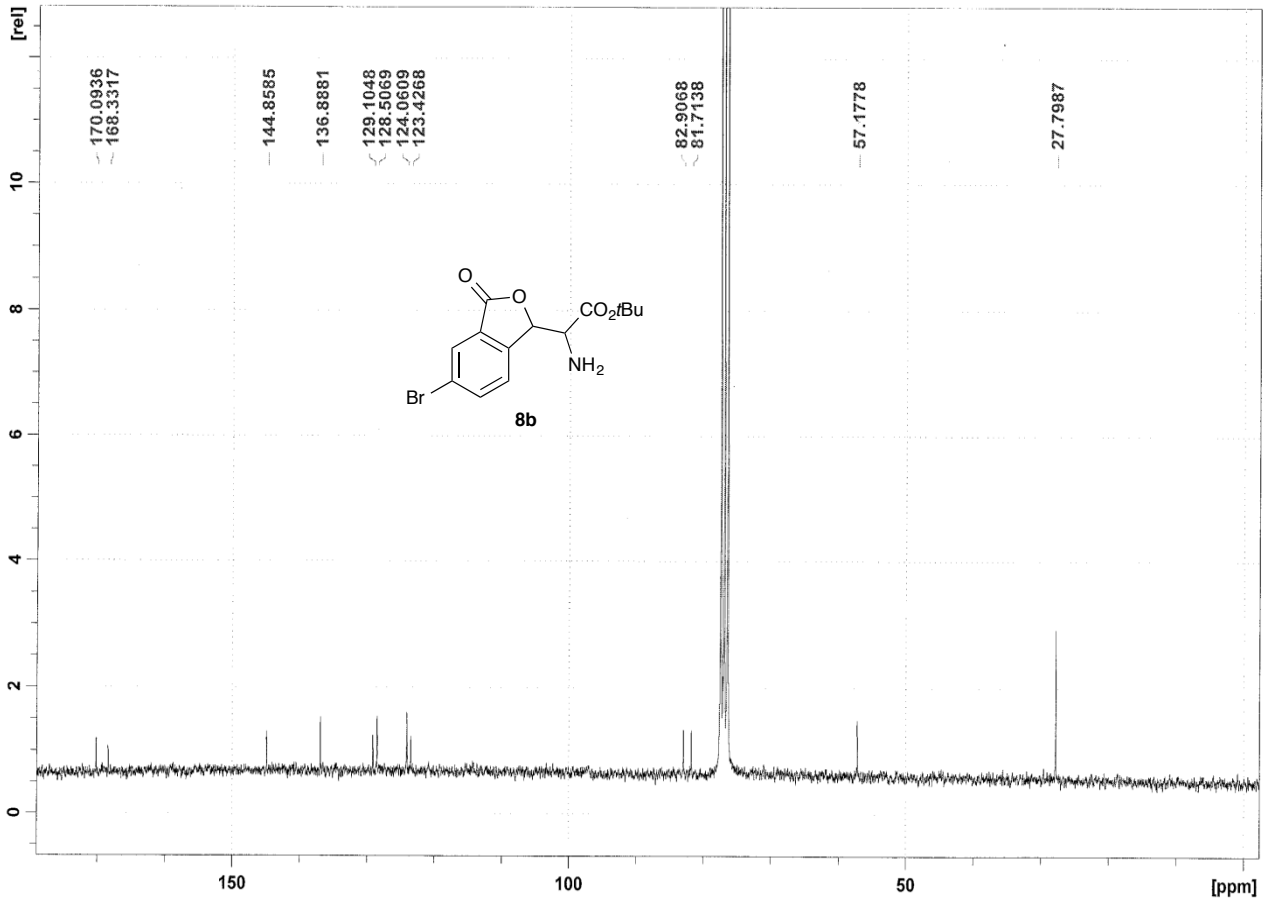
Major diastereomer



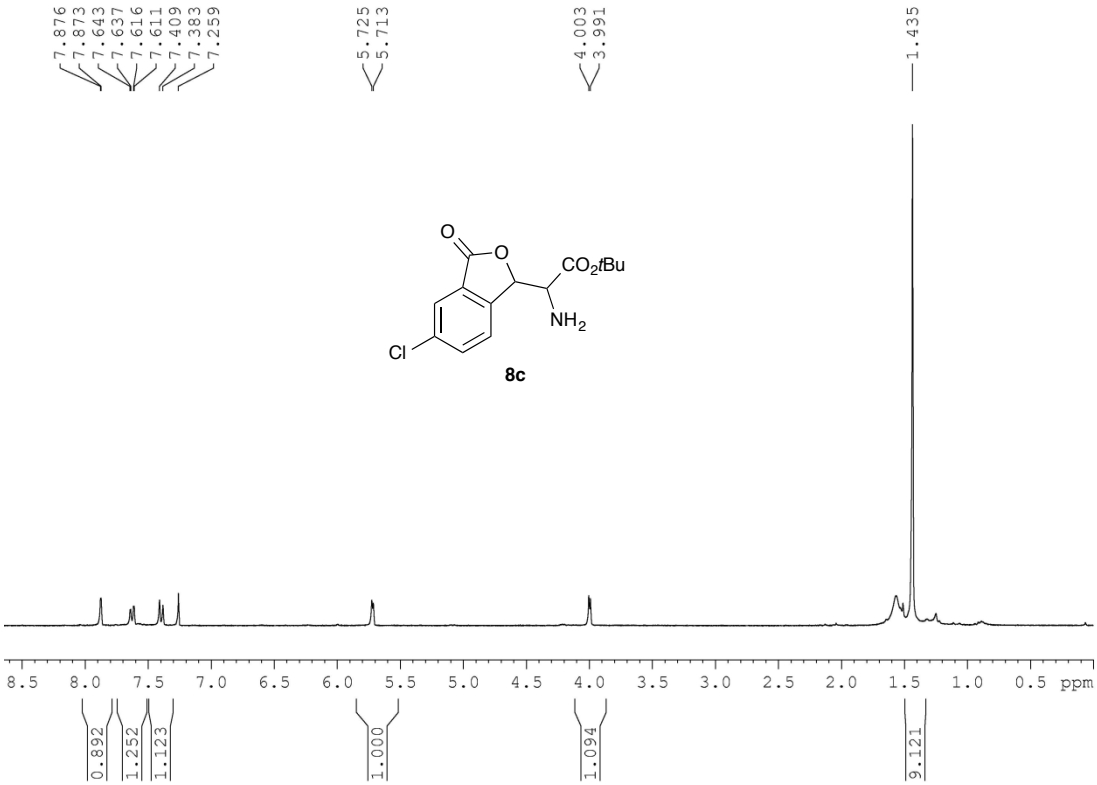


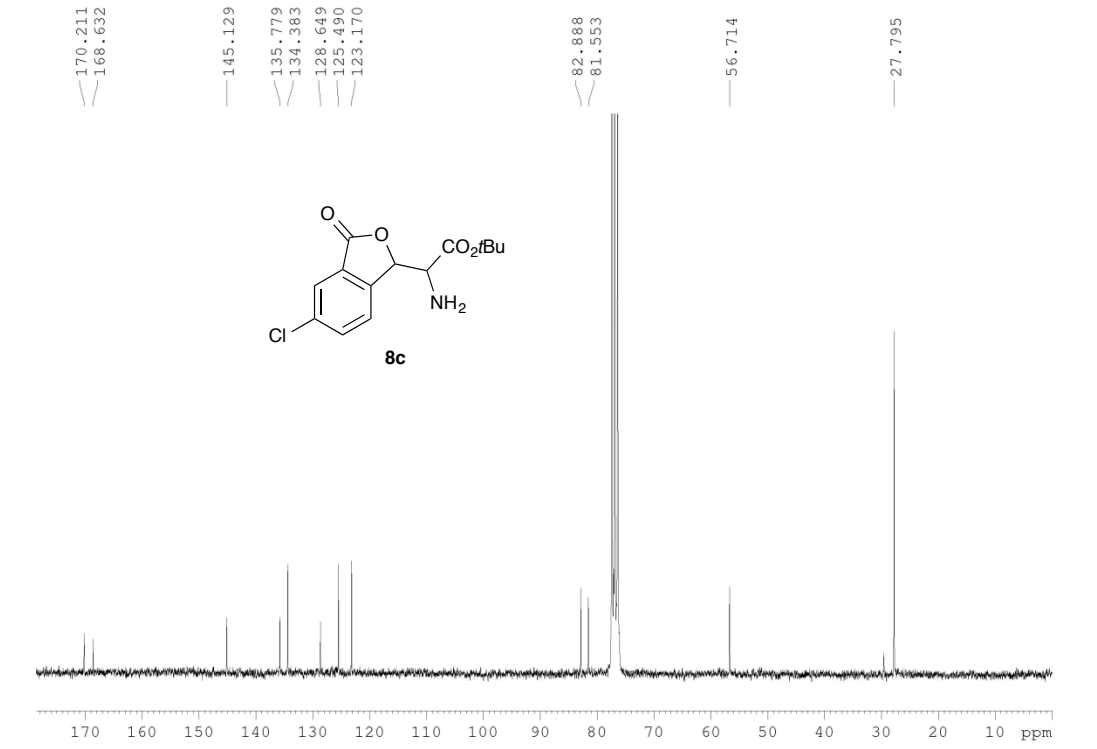
Major diastereomer



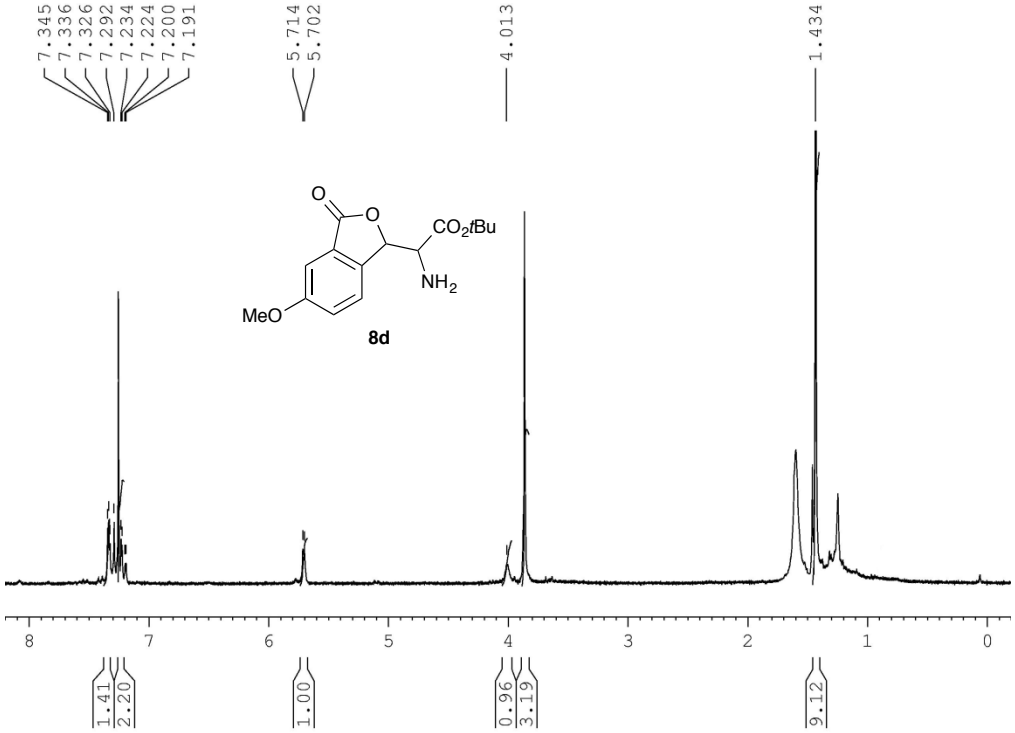


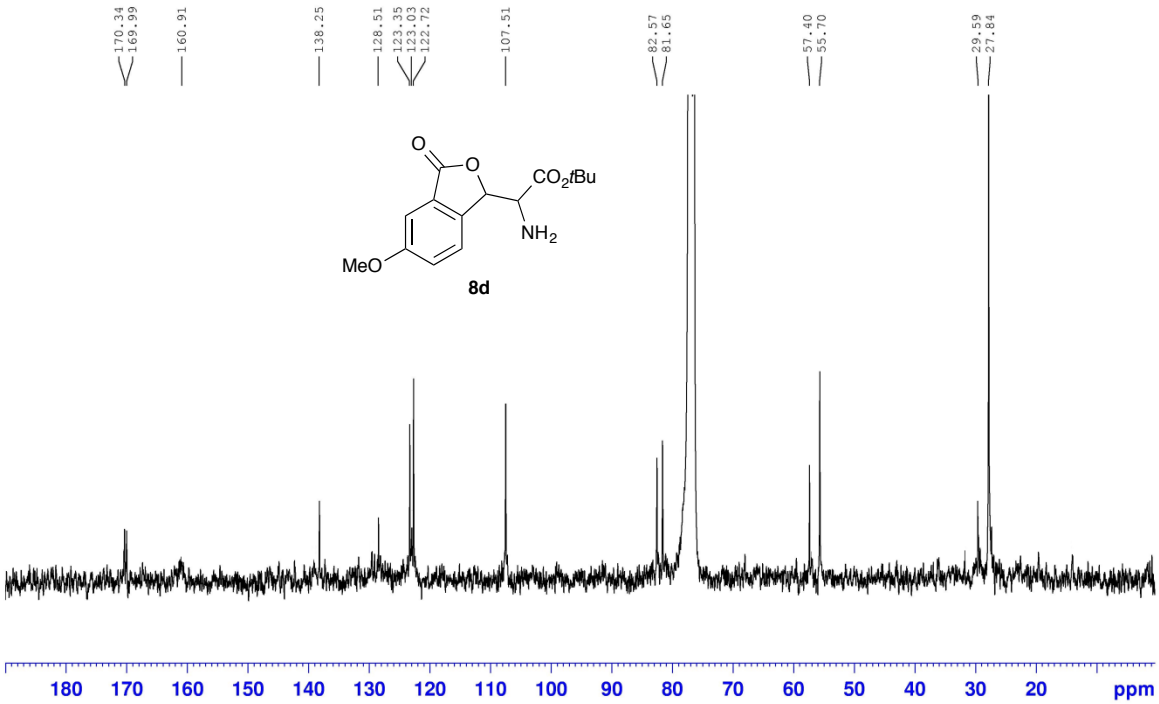
Major diastereomer





Major diastereomer

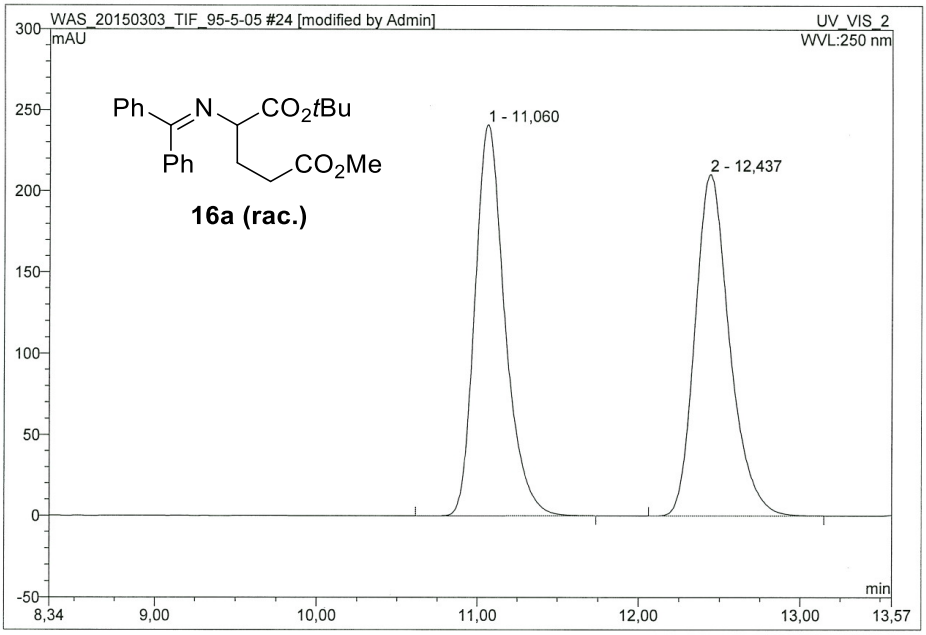




7. Copies of HPLC Chromatograms of Products 16 and 8:

24 TIF-269-02

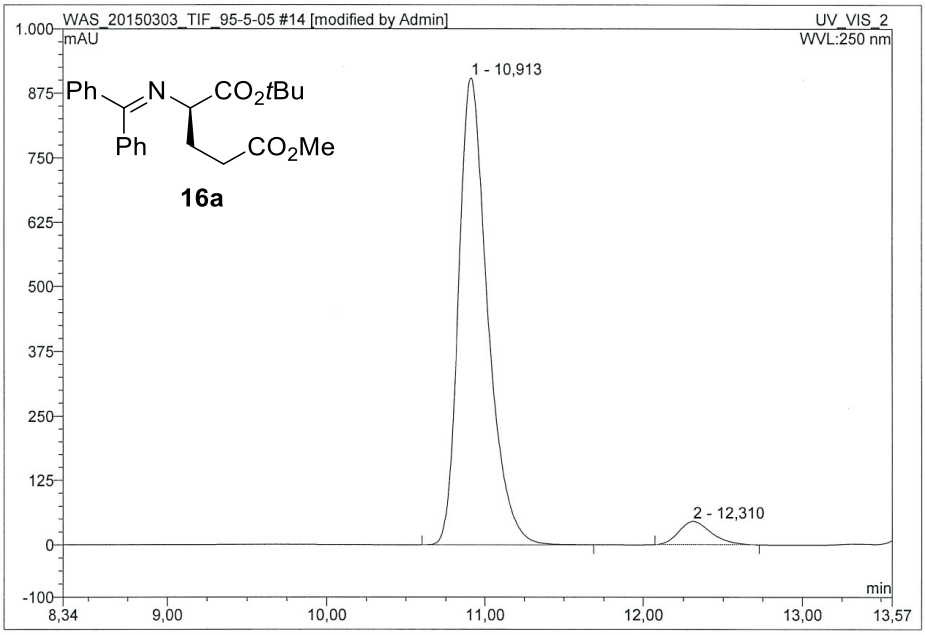
Sample Name:	**TIF-269-02**	*Injection Volume:*	**5,0**
Vial Number:	**RE4**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**26.3.2015 16:43**	*Flow ml/min:*	**0,500**
Run Time (min):	**25,00**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11,06	n.a.	241,158	52,295	50,09	n.a.	BMB*
2	12,44	n.a.	210,807	52,110	49,91	n.a.	BMB*
Total:			451,964	104,405	100,00	0,000	

14 TIF-256-02

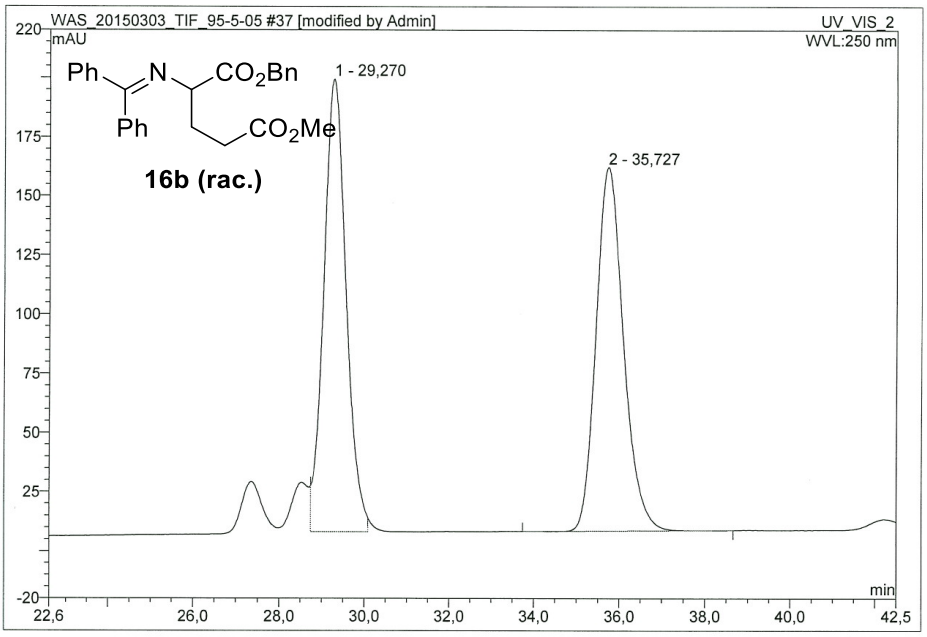
Sample Name:	**TIF-256-02**	*Injection Volume:*	**5,0**
Vial Number:	**RA1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**13.3.2015 14:34**	*Flow ml/min:*	**0,500**
Run Time (min):	**17,88**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	10,91	n.a.	903,789	192,805	94,81	n.a.	BM *
2	12,31	n.a.	44,727	10,545	5,19	n.a.	BM *
Total:			948,516	203,350	100,00	0,000	

37 TIF-282-02

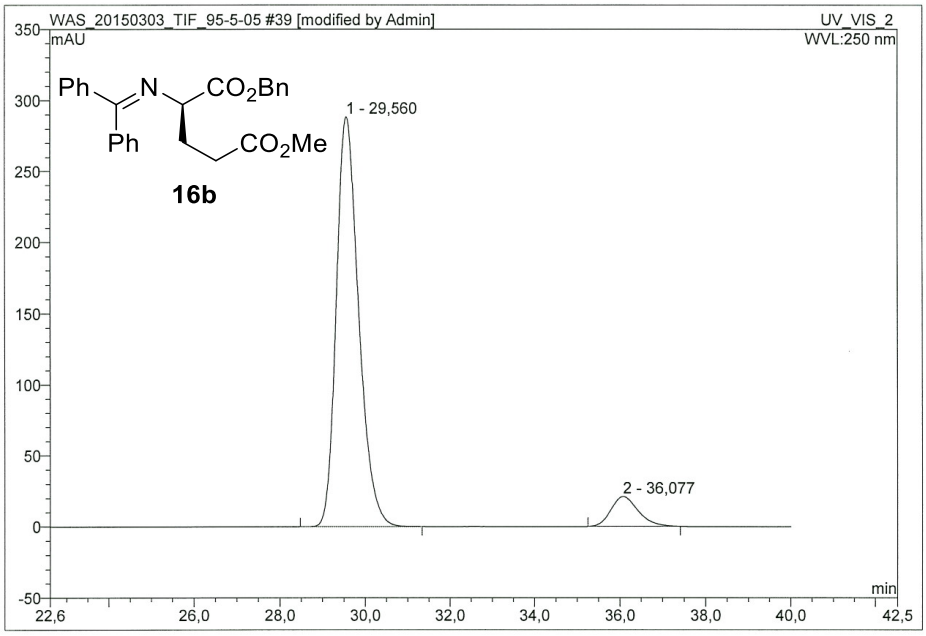
Sample Name:	**TIF-282-02**	*Injection Volume:*	**5,0**
Vial Number:	**RA1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**8.4.2015 16:33**	*Flow ml/min:*	**0,500**
Run Time (min):	**66,12**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	29,27	n.a.	191,252	115,654	50,18	n.a.	M *
2	35,73	n.a.	153,953	114,842	49,82	n.a.	BMB*
Total:			345,205	230,496	100,00	0,000	

39 TIF-281-02

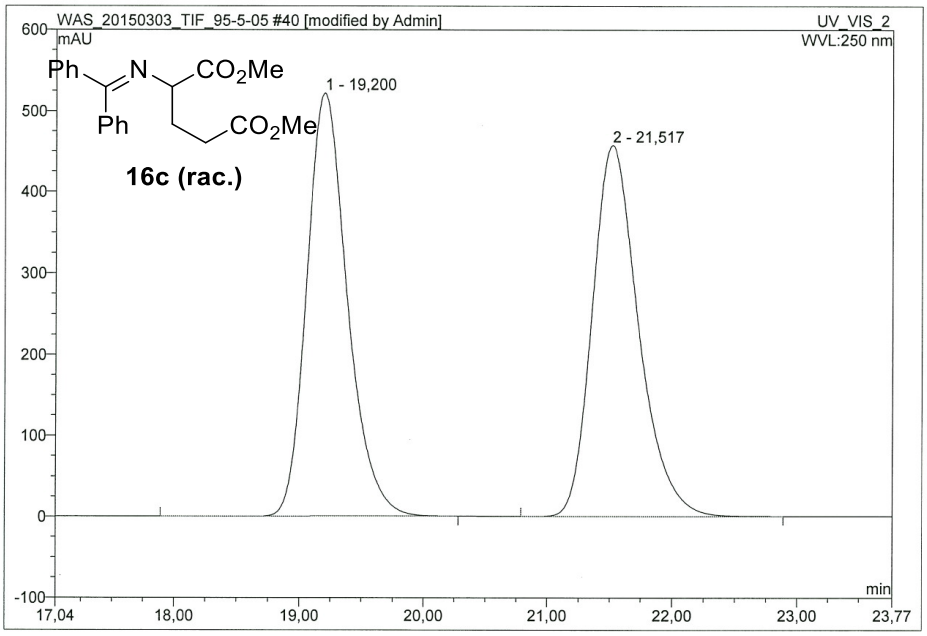
Sample Name:	**TIF-281-02**	*Injection Volume:*	**5,0**
Vial Number:	**RA3**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**9.4.2015 11:08**	*Flow ml/min:*	**0,500**
Run Time (min):	**40,00**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	29,56	n.a.	288,527	175,217	91,73	n.a.	BMB*
2	36,08	n.a.	21,300	15,791	8,27	n.a.	BMB*
Total:			309,827	191,008	100,00	0,000	

40 TIF-287-02

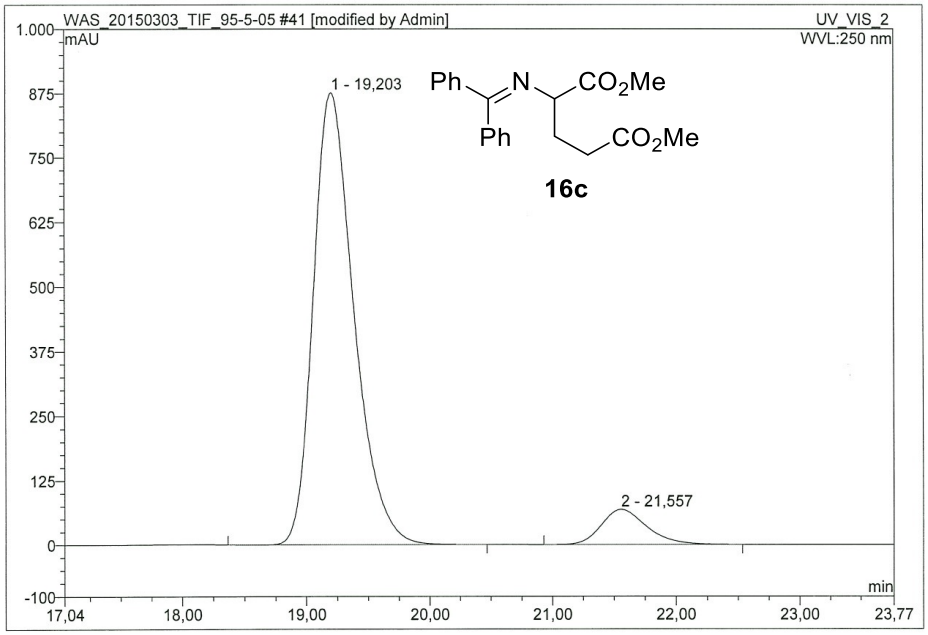
Sample Name:	**TIF-287-02**	*Injection Volume:*	**5,0**
Vial Number:	**RB4**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**9.4.2015 16:20**	*Flow ml/min:*	**0,500**
Run Time (min):	**26,65**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	19,20	n.a.	521,987	197,204	50,00	n.a.	BMB*
2	21,52	n.a.	457,950	197,195	50,00	n.a.	BMB*
Total:			979,937	394,398	100,00	0,000	

41 TIF-285-02

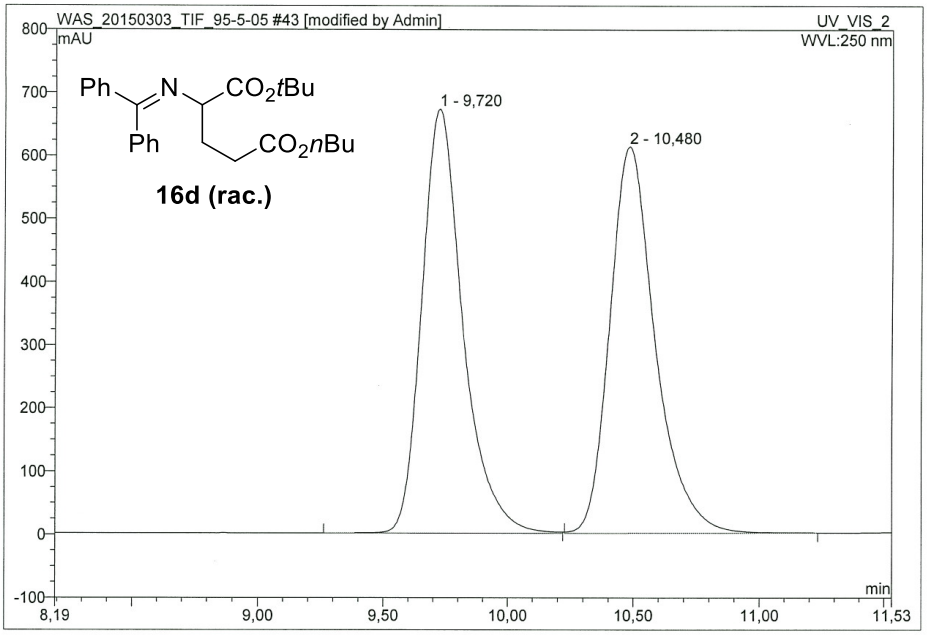
Sample Name:	**TIF-285-02**	*Injection Volume:*	**5,0**
Vial Number:	**RB1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**9.4.2015 17:16**	*Flow ml/min:*	**0,500**
Run Time (min):	**25,00**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	19,20	n.a.	875,758	332,098	91,99	n.a.	BMB*
2	21,56	n.a.	67,865	28,932	8,01	n.a.	BMB*
Total:			943,623	361,031	100,00	0,000	

43 TIF-291-02

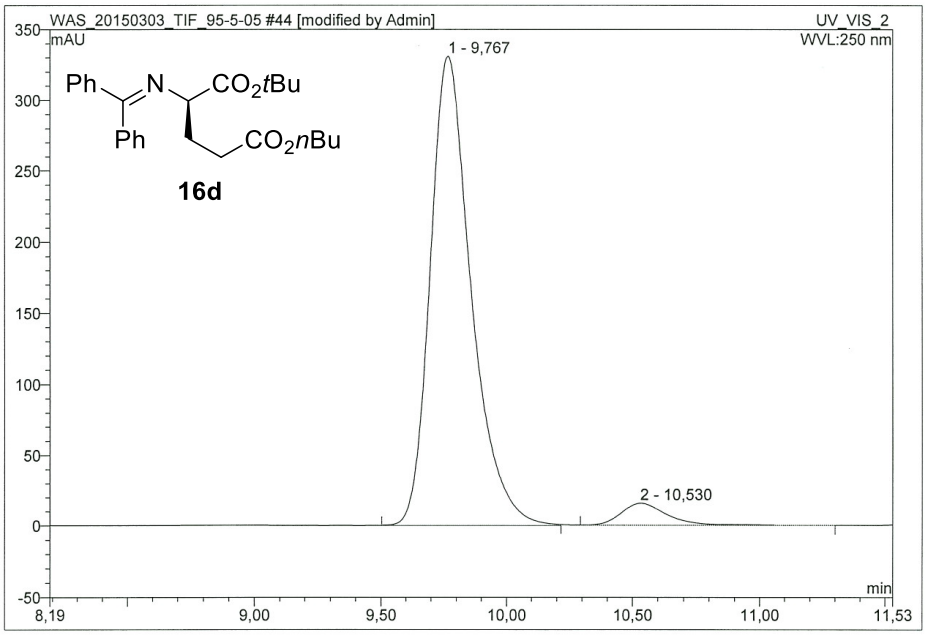
Sample Name:	**TIF-291-02**	*Injection Volume:*	**5,0**
Vial Number:	**RC1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**13.4.2015 14:03**	*Flow ml/min:*	**0,500**
Run Time (min):	**63,33**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9,72	n.a.	672,386	128,319	50,05	n.a.	BM *
2	10,48	n.a.	612,855	128,060	49,95	n.a.	MB*
Total:			1285,241	256,379	100,00	0,000	

44 TIF-289-02

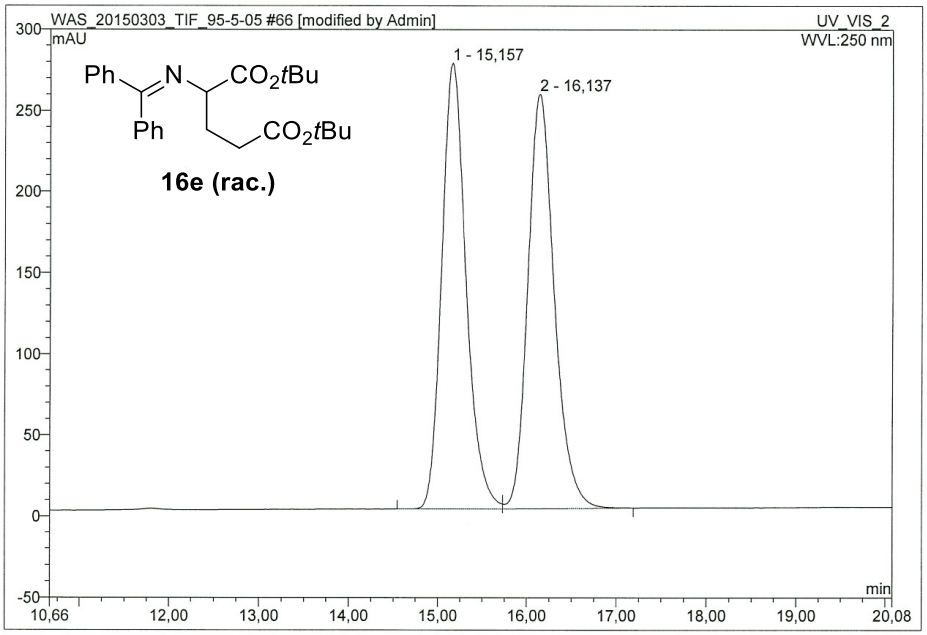
Sample Name:	**TIF-289-02**	*Injection Volume:*	**5,0**
Vial Number:	**RC2**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**13.4.2015 15:07**	*Flow ml/min:*	**0,500**
Run Time (min):	**22,46**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	9,77	n.a.	330,788	62,823	94,90	n.a.	BM *
2	10,53	n.a.	15,837	3,374	5,10	n.a.	M *
Total:			346,626	66,197	100,00	0,000	

66 TIF-303-02

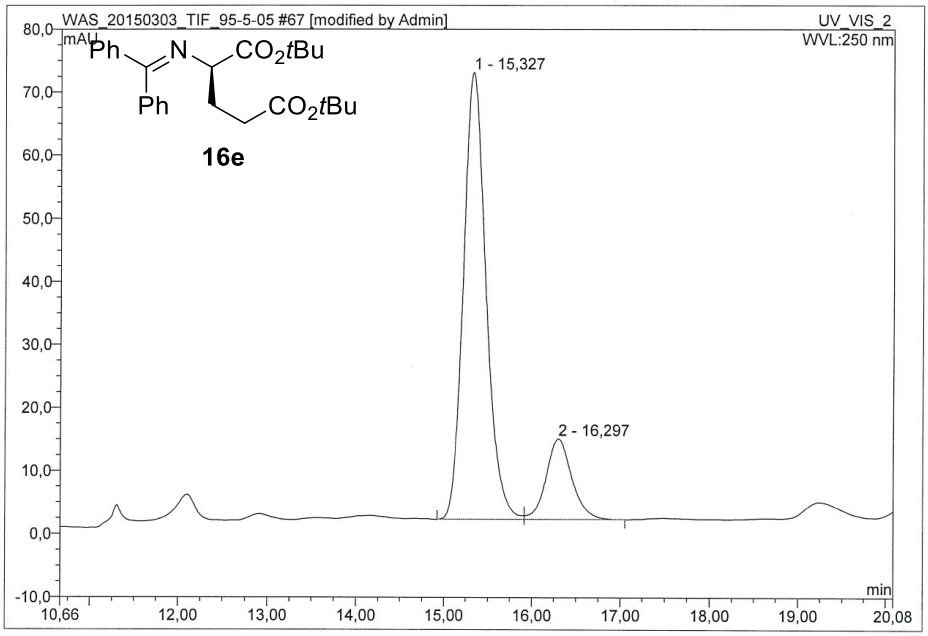
Sample Name:	**TIF-303-02**	*Injection Volume:*	**5,0**
Vial Number:	**RB3**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_80min_100-1_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**24.4.2015 9:23**	*Flow ml/min:*	**0,500**
Run Time (min):	**25,38**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	15,16	n.a.	274,994	87,626	49,87	n.a.	BM *
2	16,14	n.a.	255,833	88,098	50,13	n.a.	MB*
Total:			530,827	175,724	100,00	0,000	

67 TIF-301-02

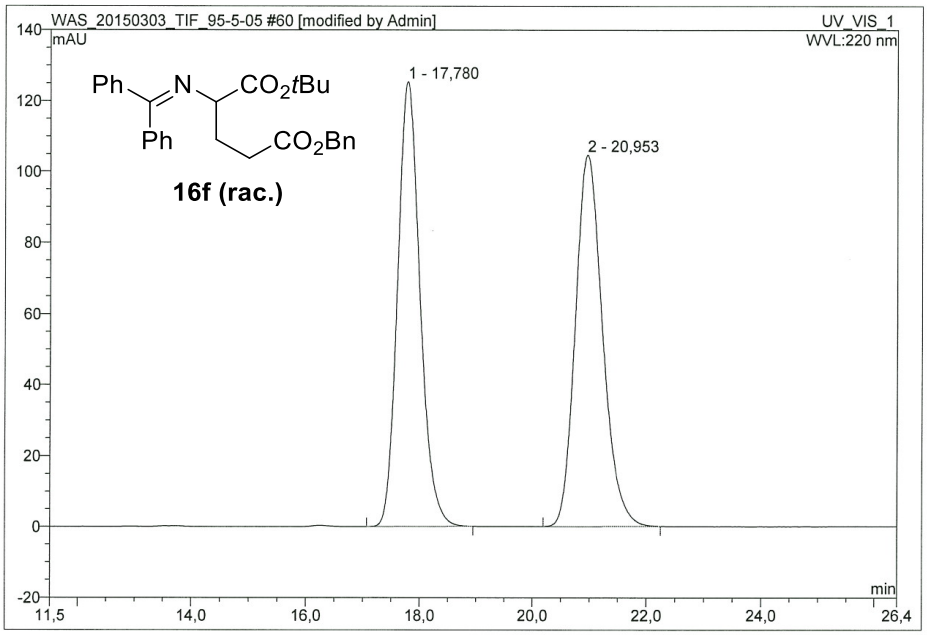
Sample Name:	**TIF-301-02**	*Injection Volume:*	**5,0**
Vial Number:	**RA4**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_80min_100-1_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**24.4.2015 9:50**	*Flow ml/min:*	**0,500**
Run Time (min):	**80,00**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	15,33	n.a.	70,872	21,150	82,94	n.a.	BM *
2	16,30	n.a.	12,818	4,351	17,06	n.a.	MB*
Total:			83,690	25,501	100,00	0,000	

60 TIF-292-02

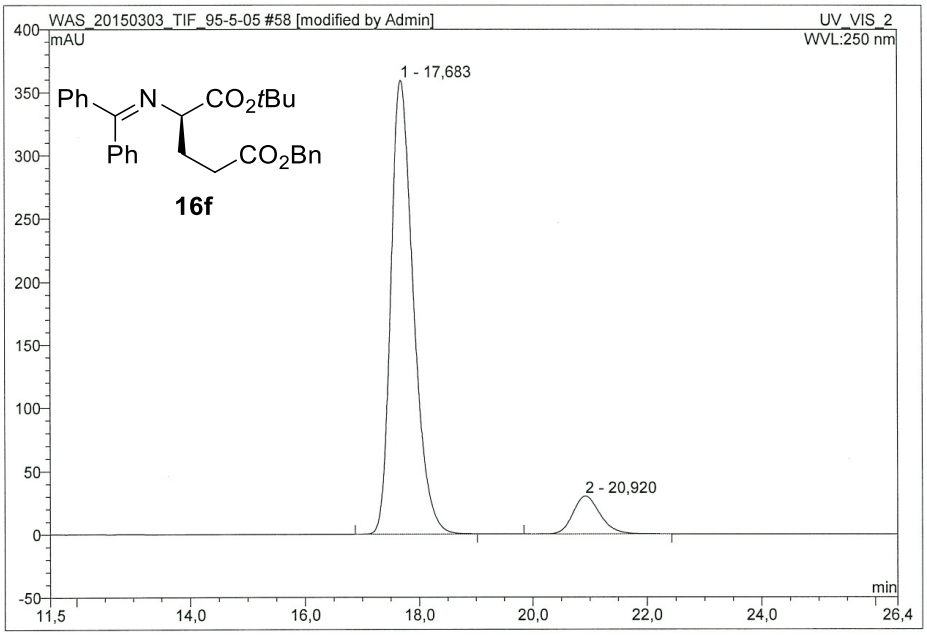
Sample Name:	**TIF-292-02**	*Injection Volume:*	**5,0**
Vial Number:	**RD1**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**220**
Control Program:	**AD_H_80min_100-1_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**17.4.2015 16:29**	*Flow ml/min:*	**1,000**
Run Time (min):	**32,16**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17,78	n.a.	125,380	57,801	49,97	n.a.	BMB
2	20,95	n.a.	104,763	57,872	50,03	n.a.	BMB
Total:			230,144	115,673	100,00	0,000	

58 TIF-294-02

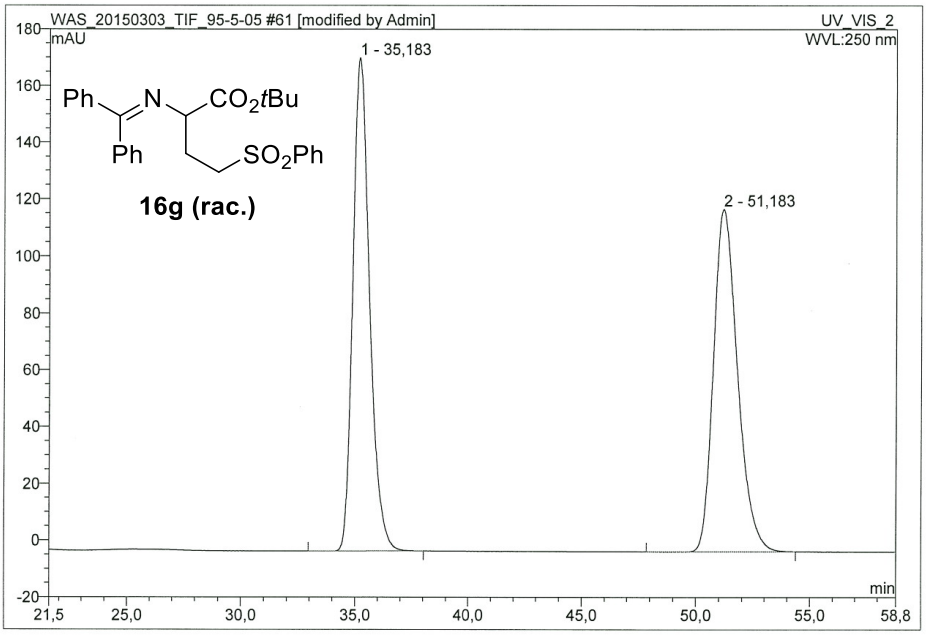
Sample Name:	**TIF-294-02**	*Injection Volume:*	**5,0**
Vial Number:	**RD3**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_80min_100-1_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**17.4.2015 15:23**	*Flow ml/min:*	**1,000**
Run Time (min):	**30,09**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17,68	n.a.	359,414	165,197	90,92	n.a.	BM *
2	20,92	n.a.	30,151	16,500	9,08	n.a.	MB*
Total:			389,565	181,697	100,00	0,000	

61 TIF-298-02

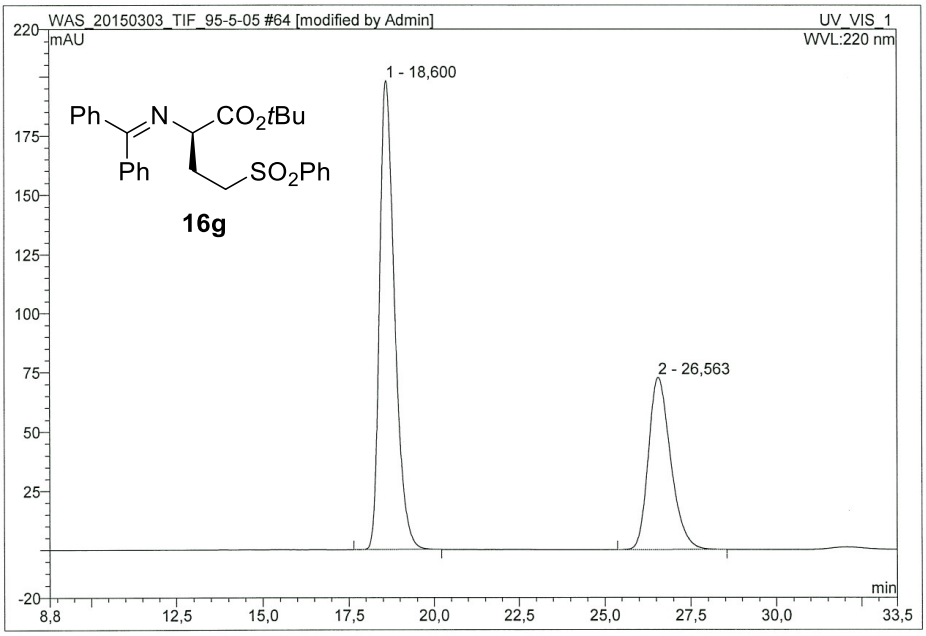
Sample Name:	**TIF-298-02**	*Injection Volume:*	**5,0**
Vial Number:	**RD4**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_100min_95-5_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**23.4.2015 12:24**	*Flow ml/min:*	**0,500**
Run Time (min):	**58,76**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	35,18	n.a.	173,671	147,978	50,13	n.a.	BMB*
2	51,18	n.a.	120,671	147,209	49,87	n.a.	BMB*
Total:			294,342	295,188	100,00	0,000	

64 TIF-299-03

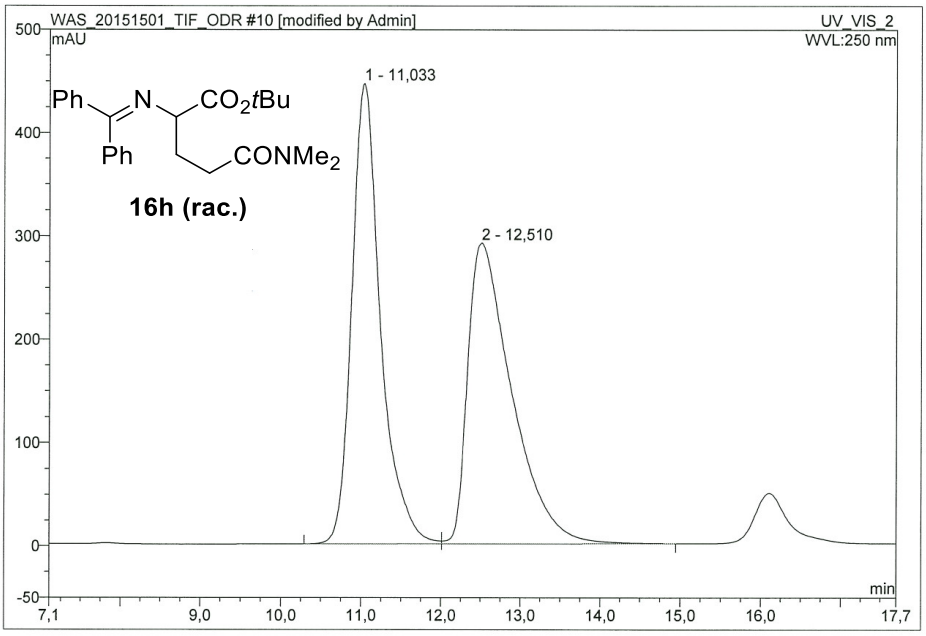
Sample Name:	**TIF-299-03**	*Injection Volume:*	**5,0**
Vial Number:	**RC4**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**220**
Control Program:	**AD_H_80min_100-1_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**23.4.2015 16:14**	*Flow ml/min:*	**1,000**
Run Time (min):	**44,07**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	18,60	n.a.	198,293	101,521	65,01	n.a.	BMB*
2	26,56	n.a.	72,672	54,653	34,99	n.a.	BMB*
Total:			270,965	156,174	100,00	0,000	

10 TIF-304-03

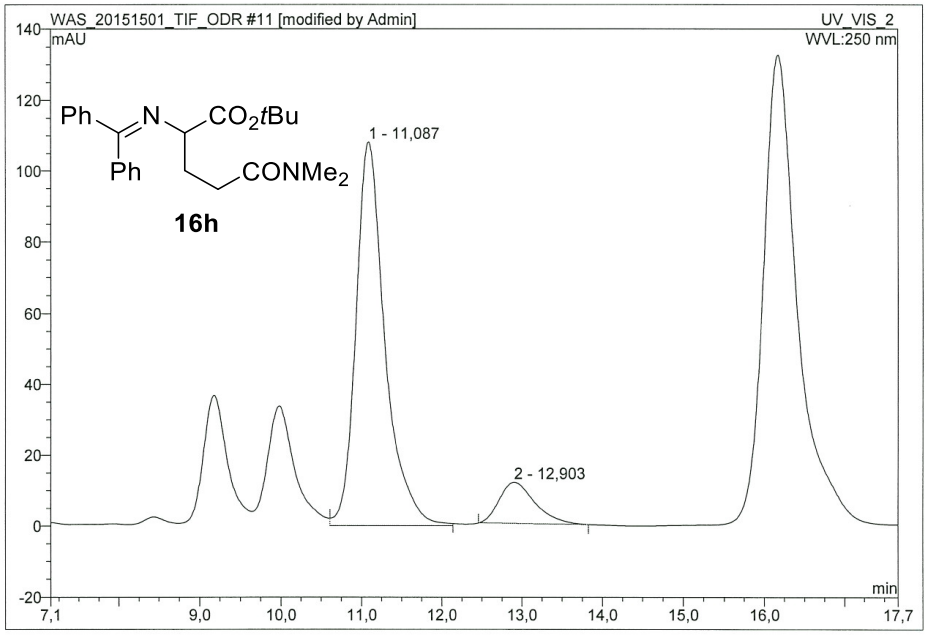
Sample Name:	**TIF-304-03**	*Injection Volume:*	**10,0**
Vial Number:	**RA1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**OD_R_80Min_45_55_flow07**	*Bandwidth:*	**4**
Quantif. Method:	**OD_R**	*Temperature/Column:*	**10**
Recording Time:	**4.5.2015 14:35**	*Flow ml/min:*	**0,700**
Run Time (min):	**55,96**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11,03	n.a.	446,048	185,719	49,83	n.a.	BM
2	12,51	n.a.	291,605	186,975	50,17	n.a.	MB
Total:			737,653	372,694	100,00	0,000	

11 TIF-305-03

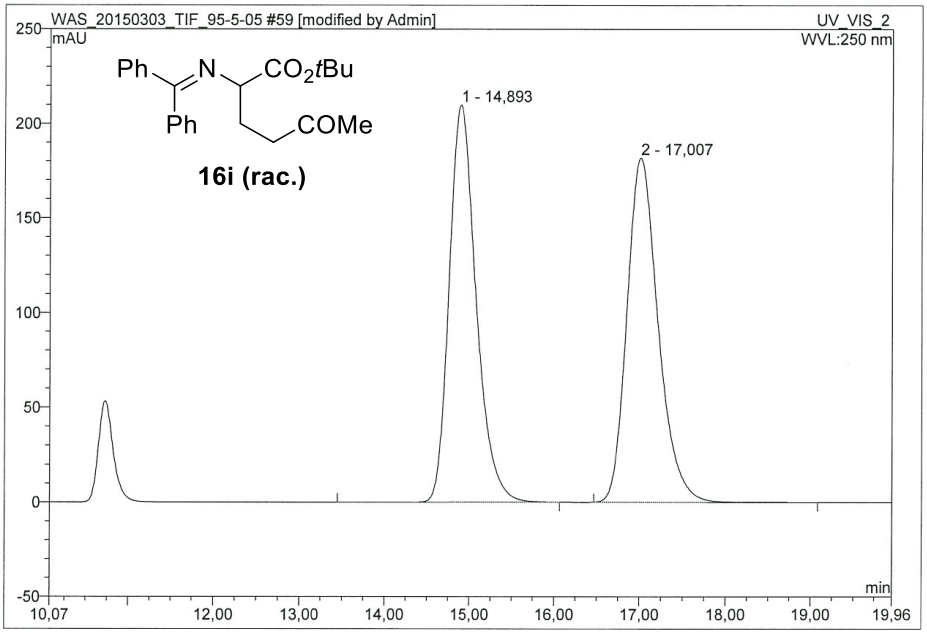
Sample Name:	**TIF-305-03**	*Injection Volume:*	**10,0**
Vial Number:	**RA2**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**OD_R_80Min_45_55_flow07**	*Bandwidth:*	**4**
Quantif. Method:	**OD_R**	*Temperature/Column:*	**10**
Recording Time:	**4.5.2015 15:32**	*Flow ml/min:*	**0,700**
Run Time (min):	**41,41**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11,09	n.a.	108,191	45,189	88,27	n.a.	M *
2	12,90	n.a.	11,641	6,006	11,73	n.a.	BMB*
Total:			119,832	51,195	100,00	0,000	

59 TIF-297-02

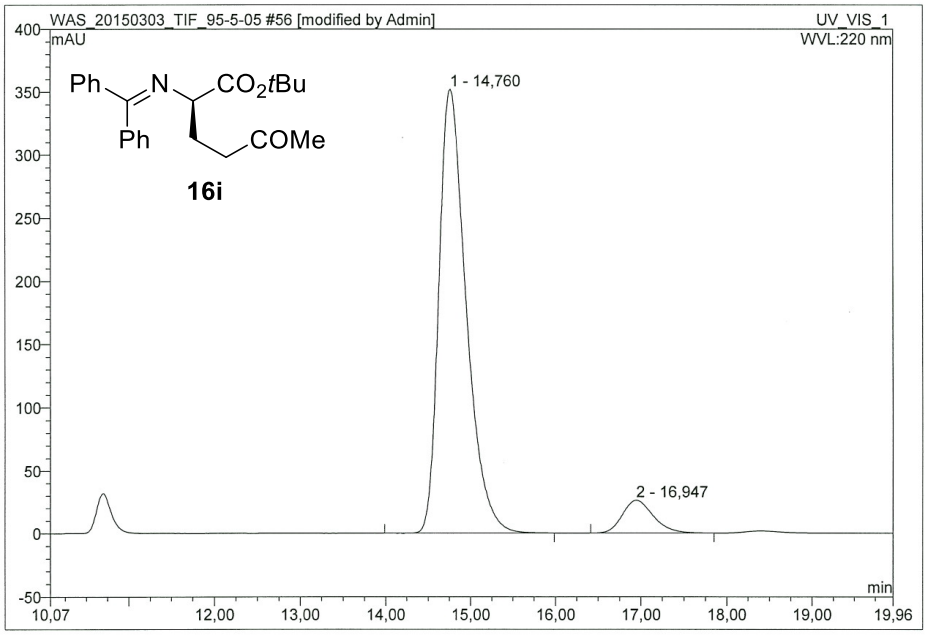
Sample Name:	**TIF-297-02**	*Injection Volume:*	**5,0**
Vial Number:	**RE1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_80min_100-1_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**17.4.2015 15:55**	*Flow ml/min:*	**1,000**
Run Time (min):	**32,46**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14,89	n.a.	209,925	77,705	50,19	n.a.	BMB*
2	17,01	n.a.	181,888	77,104	49,81	n.a.	BMB*
Total:			391,813	154,810	100,00	0,000	

56 TIF-296-02

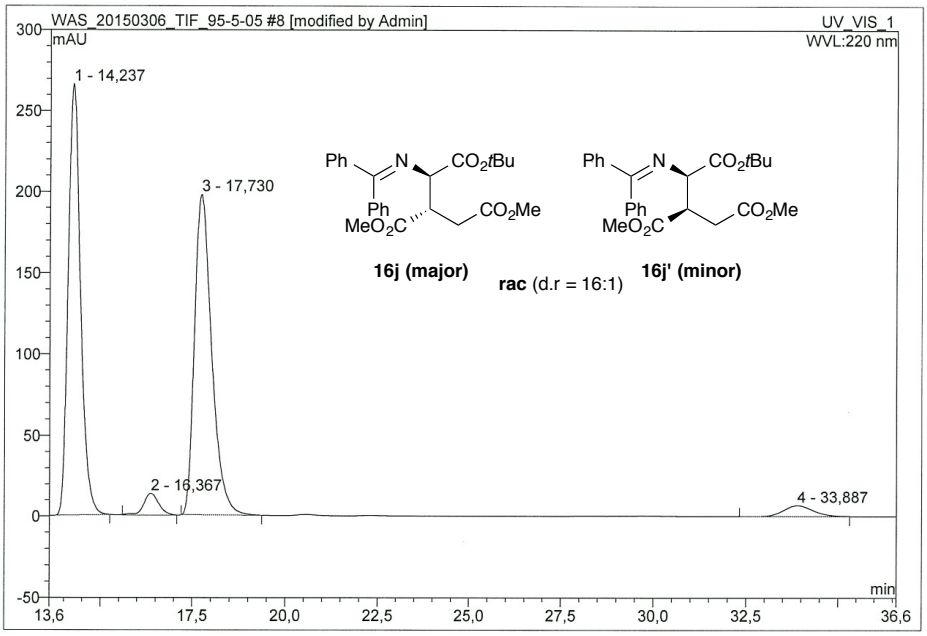
Sample Name:	**TIF-296-02**	*Injection Volume:*	**5,0**
Vial Number:	**RE3**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**220**
Control Program:	**AD_H_80min_100-1_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**17.4.2015 14:27**	*Flow ml/min:*	**1,000**
Run Time (min):	**25,43**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14,76	n.a.	352,084	131,976	92,35	n.a.	BM *
2	16,95	n.a.	26,215	10,937	7,65	n.a.	BMB*
Total:			378,298	142,913	100,00	0,000	

8 TIF-342-02

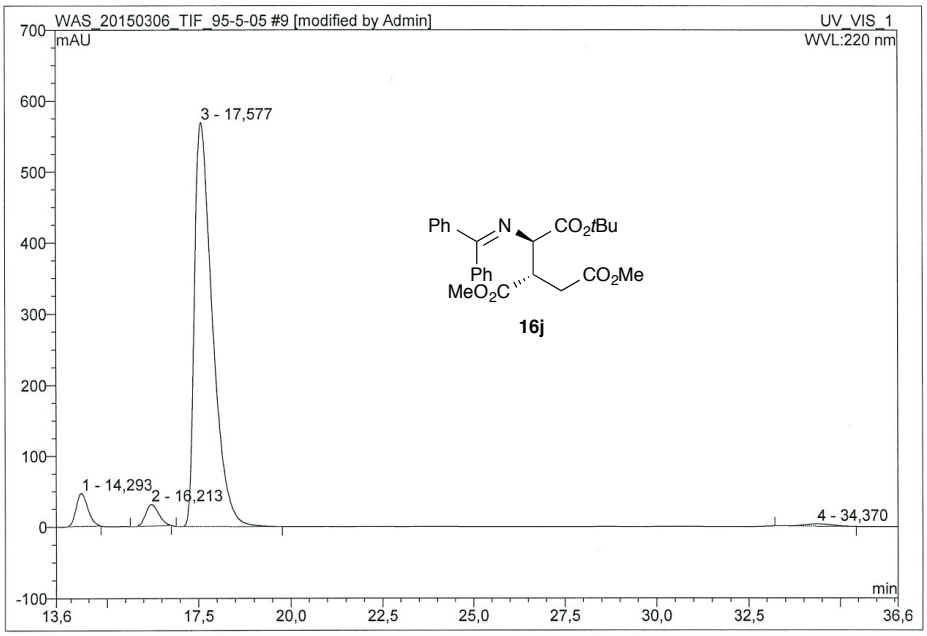
Sample Name:	**TIF-342-02**	*Injection Volume:*	**10,0**
Vial Number:	**RC1**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**220**
Control Program:	**AD_H_120min_98-2_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**5.6.2015 15:28**	*Flow ml/min:*	**1,000**
Run Time (min):	**49,49**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14,24	n.a.	266,031	105,264	46,89	n.a.	BMB*
2	16,37	n.a.	13,653	6,488	2,89	n.a.	MB*
3	17,73	n.a.	197,516	106,457	47,42	n.a.	BMB*
4	33,89	n.a.	6,733	6,266	2,79	n.a.	BMB*
Total:			483,933	224,476	100,00	0,000	

9 TIF-344-02

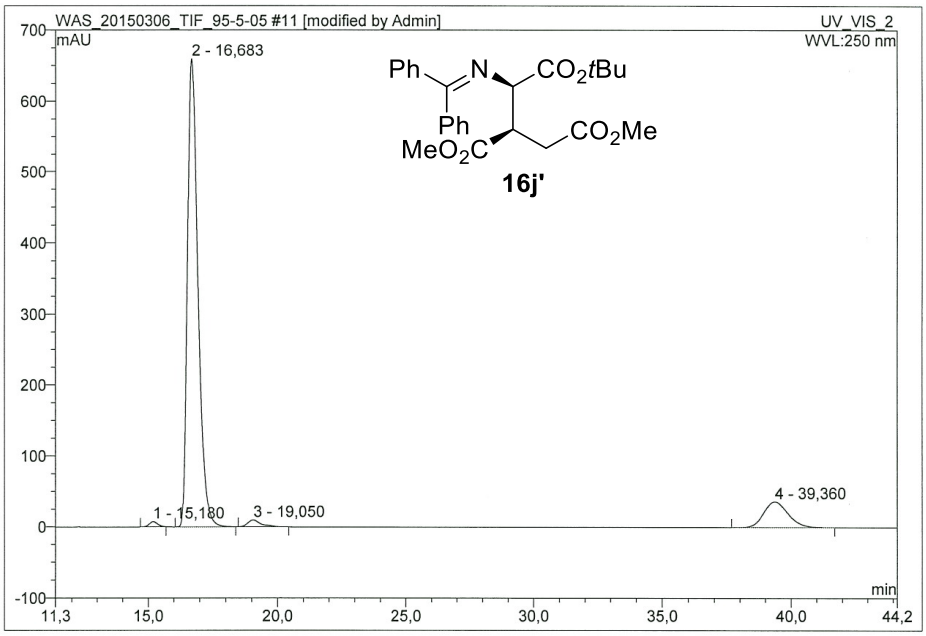
Sample Name:	**TIF-344-02**	*Injection Volume:*	**10,0**
Vial Number:	**RC2**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**220**
Control Program:	**AD_H_120min_98-2_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**5.6.2015 16:18**	*Flow ml/min:*	**1,000**
Run Time (min):	**93,74**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	14,29	n.a.	46,331	16,941	4,81	n.a.	BMB*
2	16,21	n.a.	30,448	12,778	3,63	n.a.	BMB*
3	17,58	n.a.	568,620	319,457	90,78	n.a.	BMB*
4	34,37	n.a.	3,117	2,733	0,78	n.a.	BMB*
Total:			648,516	351,909	100,00	0,000	

11 TIF-346-02

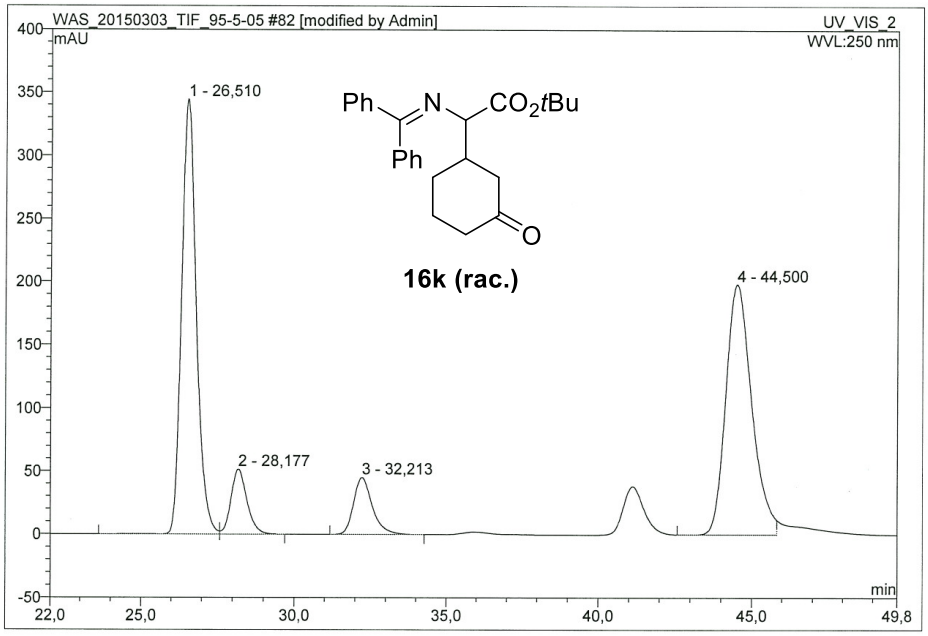
Sample Name:	**TIF-346-02**	*Injection Volume:*	**20,0**
Vial Number:	**RE1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_120min_98-2_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**19.6.2015 15:46**	*Flow ml/min:*	**1,000**
Run Time (min):	**120,00**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	15,18	n.a.	7,382	2,847	0,79	n.a.	BMB*
2	16,68	n.a.	659,226	310,585	86,45	n.a.	BM *
3	19,05	n.a.	9,560	5,668	1,58	n.a.	BMB*
4	39,36	n.a.	36,445	40,176	11,18	n.a.	BM *
Total:			712,612	359,277	100,00	0,000	

82 TIF-310-03

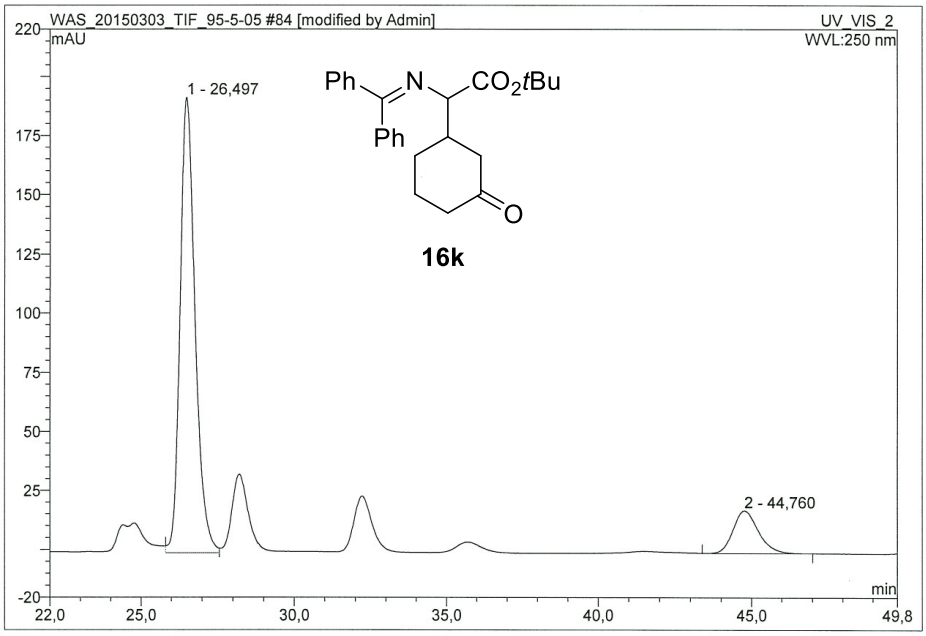
Sample Name:	**TIF-310-03**	*Injection Volume:*	**5,0**
Vial Number:	**RE1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_60min_98-2_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**29.5.2015 10:34**	*Flow ml/min:*	**0,500**
Run Time (min):	**60,00**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	26,51	n.a.	344,715	193,815	42,86	n.a.	BM *
2	28,18	n.a.	51,660	31,015	6,86	n.a.	MB*
3	32,21	n.a.	45,356	32,167	7,11	n.a.	BMB*
4	44,50	n.a.	198,224	195,238	43,17	n.a.	BM *
Total:			639,955	452,235	100,00	0,000	

84 TIF-327-02

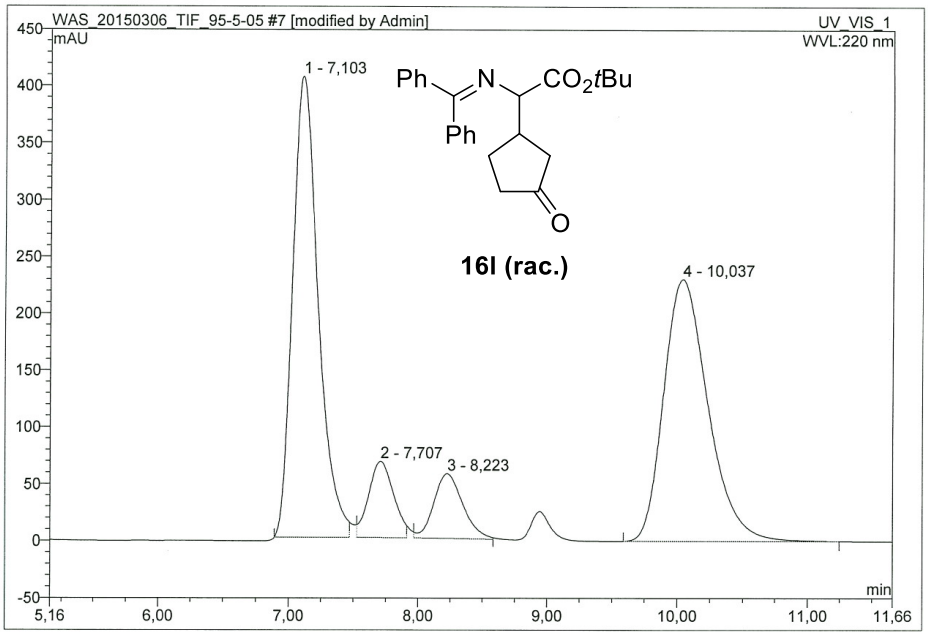
Sample Name:	**TIF-327-02**	*Injection Volume:*	**20,0**
Vial Number:	**RB1**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_60min_98-2_flow05**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**29.5.2015 13:02**	*Flow ml/min:*	**0,500**
Run Time (min):	**58,30**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	26,50	n.a.	192,499	108,767	86,09	n.a.	M *
2	44,76	n.a.	17,948	17,574	13,91	n.a.	MB*
Total:			210,447	126,341	100,00	0,000	

7 TIF-340-02

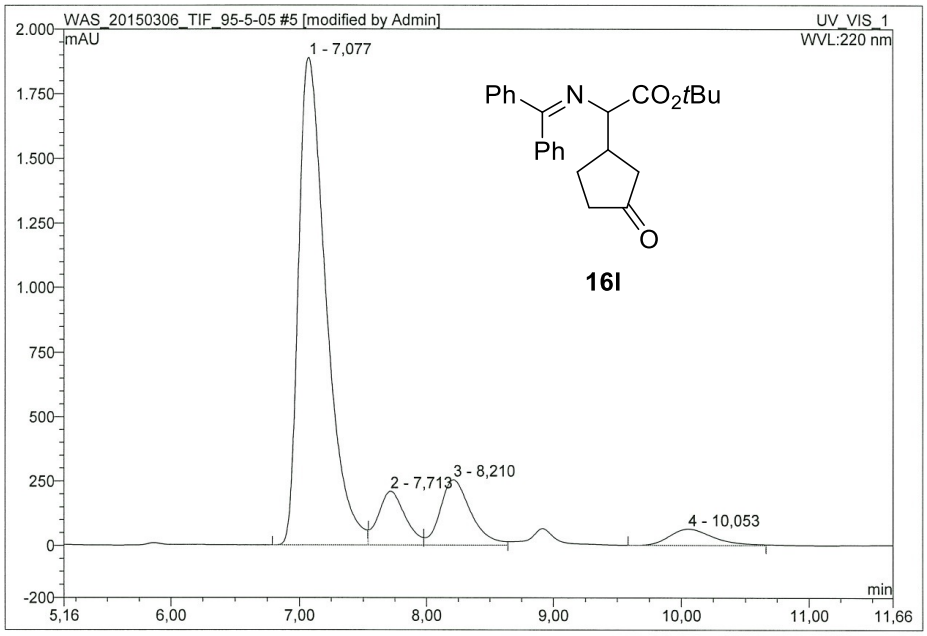
Sample Name:	**TIF-340-02**	*Injection Volume:*	**10,0**
Vial Number:	**RE1**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**220**
Control Program:	**AD_H_40Min_100_3,5_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**5.6.2015 14:16**	*Flow ml/min:*	**1,000**
Run Time (min):	**28,88**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7,10	n.a.	405,634	92,964	43,59	n.a.	BM *
2	7,71	n.a.	67,262	14,964	7,02	n.a.	M *
3	8,22	n.a.	57,090	14,864	6,97	n.a.	M *
4	10,04	n.a.	230,618	90,464	42,42	n.a.	BM *
Total:			760,603	213,256	100,00	0,000	

5 TIF-341-02

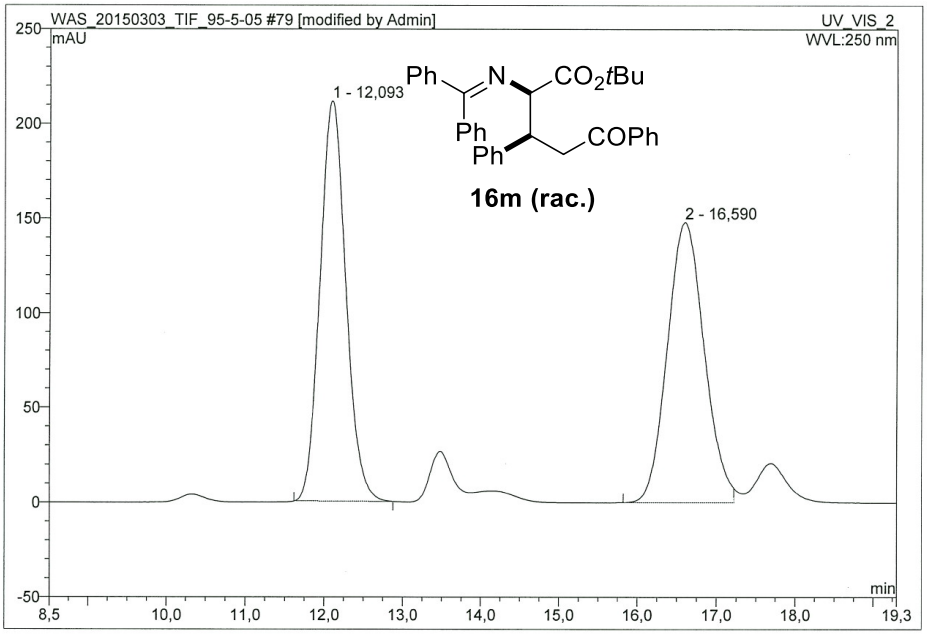
Sample Name:	**TIF-341-02**	*Injection Volume:*	**20,0**
Vial Number:	**RA2**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**220**
Control Program:	**AD_H_40Min_100_3,5_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**5.6.2015 13:40**	*Flow ml/min:*	**1,000**
Run Time (min):	**14,12**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7,08	n.a.	1887,742	471,113	76,17	n.a.	BM *
2	7,71	n.a.	208,414	51,107	8,26	n.a.	M *
3	8,21	n.a.	253,420	71,146	11,50	n.a.	M *
4	10,05	n.a.	63,082	25,111	4,06	n.a.	BM *
Total:			2412,658	618,477	100,00	0,000	

79 TIF-317-02

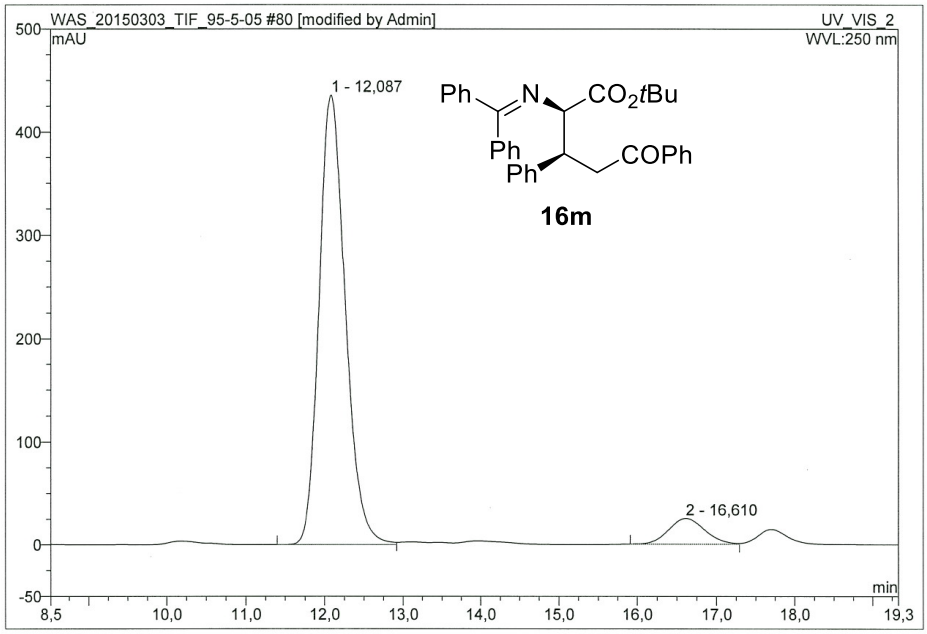
Sample Name:	**TIF-317-02**	*Injection Volume:*	**5,0**
Vial Number:	**RD2**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_60min_95-5_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**15.5.2015 15:46**	*Flow ml/min:*	**1,000**
Run Time (min):	**30,00**	*Sample Amount:*	**1,0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12,09	n.a.	211,544	80,528	50,21	n.a.	BMB*
2	16,59	n.a.	148,099	79,839	49,79	n.a.	BM *
Total:			359,642	160,367	100,00	0,000	

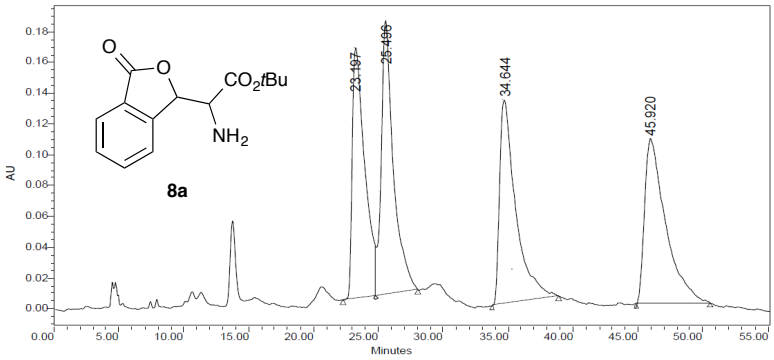
80 TIF-316-02

Sample Name:	**TIF-316-02**	*Injection Volume:*	**5,0**
Vial Number:	**RD3**	*Channel:*	**UV_VIS_2**
Sample Type:	**unknown**	*Wavelength:*	**250**
Control Program:	**AD_H_60min_95-5_flow1**	*Bandwidth:*	**4**
Quantif. Method:	**AD_H**	*Temperature/Column:*	**10**
Recording Time:	**15.5.2015 16:16**	*Flow ml/min:*	**1,000**
Run Time (min):	**24,59**	*Sample Amount:*	**1,0000**



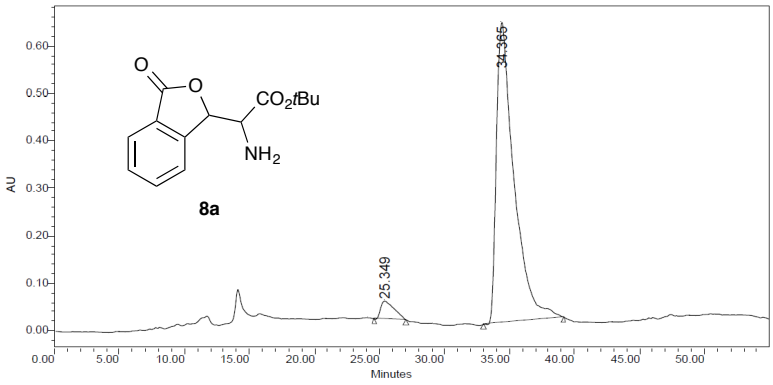
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	12,09	n.a.	435,656	168,067	92,69	n.a.	BM *
2	16,61	n.a.	25,038	13,260	7,31	n.a.	BM *
Total:			460,693	181,326	100,00	0,000	

HPLC trace of the racemic mixture of diastereomers



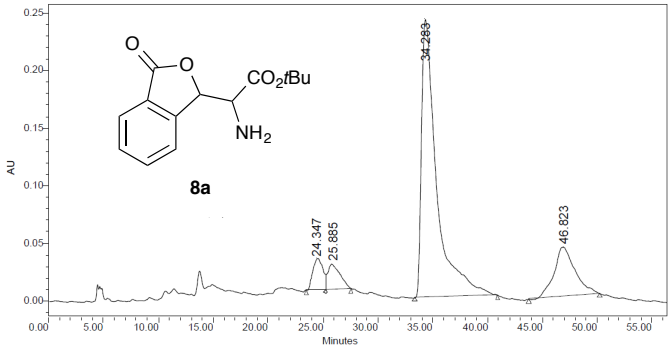
	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	23.197	11093420	24.41	162742	28.23
2	25.496	11540725	25.40	177423	30.78
3	34.644	11548820	25.42	132294	22.95
4	45.920	11254379	24.77	104029	18.05

HPLC trace of enantioenriched major diastereomer



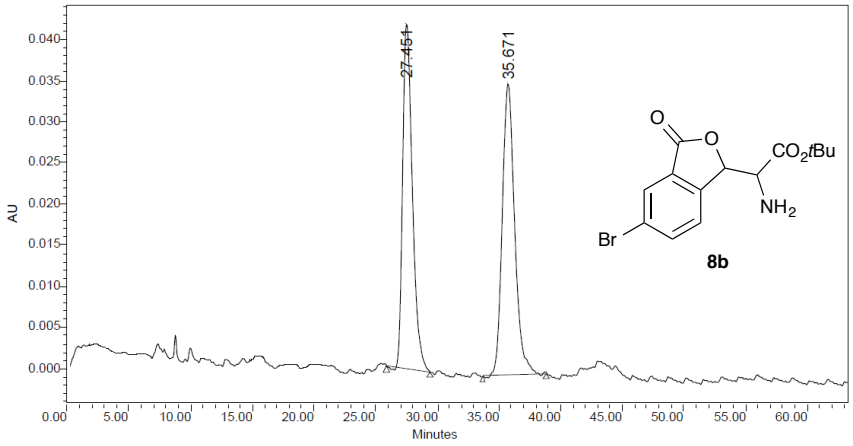
	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	25.349	2846528	4.54	38554	5.74
2	34.365	59793802	95.46	632962	94.26

HPLC trace of enantioenriched mixture of diastereomers



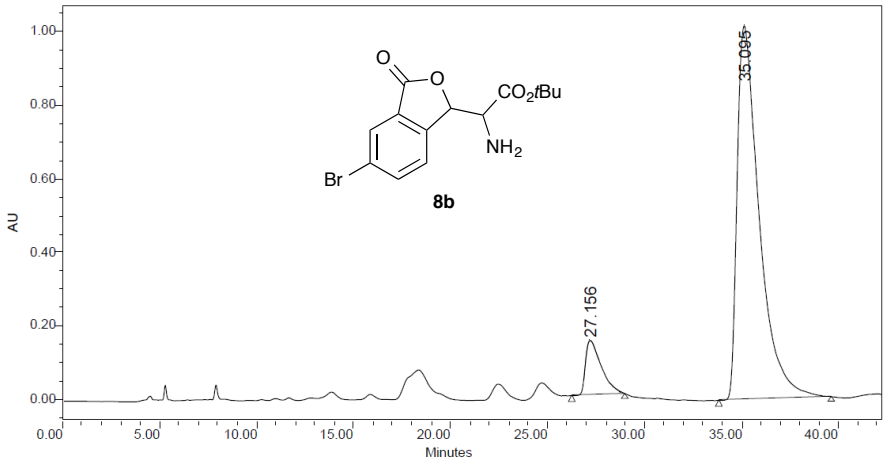
	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	24.347	2081918	6.40	28036	8.37
2	25.885	1517108	4.66	22502	6.72
3	34.283	23124054	71.05	241268	72.04
4	46.823	5822509	17.89	43080	12.86

HPLC trace of *rac*- major diastereomer



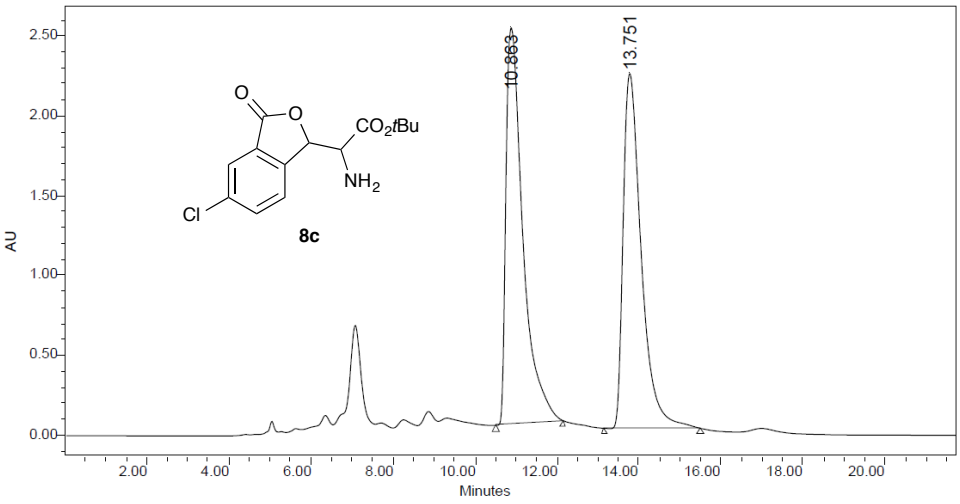
	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	27.451	2319447	48.16	41894	54.18
2	35.671	2496237	51.84	35427	45.82

HPLC trace of enantioenriched major diastereomer

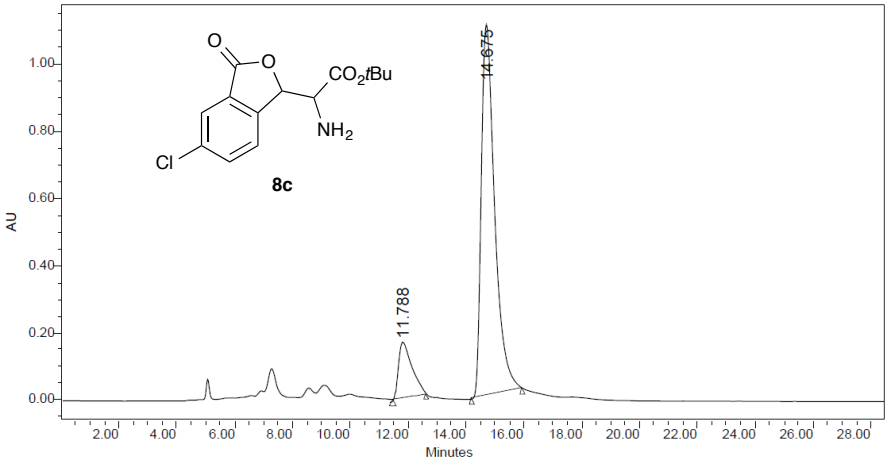


	RT (min)	Area (µV*sec)	% Area	Height (µV)	% Height
1	27.156	7852923	8.93	139989	12.16
2	35.095	80047741	91.07	1011375	87.84

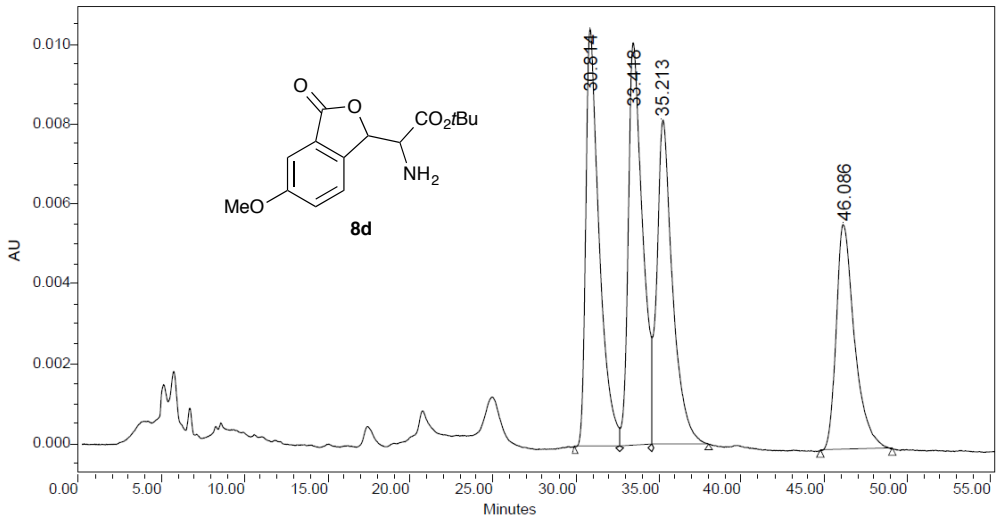
HPLC trace of *rac*- major diastereomer



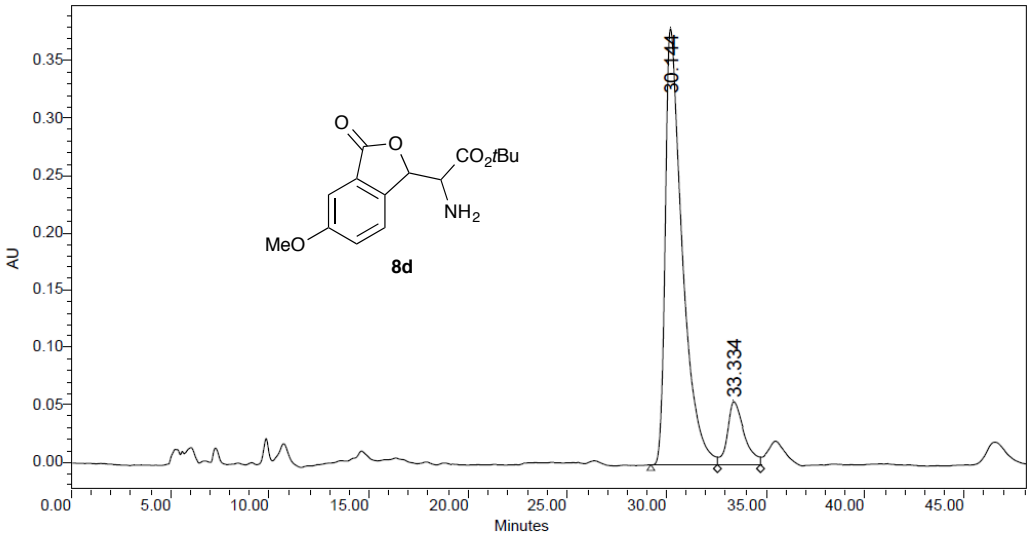
	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	10.863	71330897	51.07	2485891	52.78
2	13.751	68340129	48.93	2223798	47.22



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	11.788	4868466	11.99	158764	12.54
2	14.675	35736984	88.01	1107132	87.46



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	30.814	591827	27.16	10457	30.44
2	33.418	606462	27.83	10092	29.38
3	35.213	541301	24.84	8145	23.71
4	46.086	439213	20.16	5657	16.47



	RT (min)	Area (μV*sec)	% Area	Height (μV)	% Height
1	30.144	22878533	87.23	381032	87.14
2	33.334	3347953	12.77	56218	12.86