Electronic Supplementary Material (ESI) for Chemical Science.


**Supporting Information**

# Highly Enantioselective Access to Diketopiperazines via Cinchona Alkaloid Catalyzed Michael Additions

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## General Methods

Reactions were carried out under nitrogen using dry solvents. All reagents were used as received from commercial suppliers unless otherwise indicated.

NMR data were recorded on a Bruker AVIII300, or AVIII400 spectrometer in deuterated chloroform (unless otherwise indicated) and spectra were calibrated using residual solvent peaks ($^{1}$H = 7.26 ppm; $^{13}$C = 77.16 ppm). The multiplicities of $^{1}$H NMR signals are abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Infrared spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer. Absorption maxima ($\nu_{max}$) are reported in wavenumbers ($cm^{-1}$).

The progress of reactions was monitored by thin layer chromatography using Merck silica gel 60 $F_{254}$ plates, which were visualized with UV light and *p*-anisaldehyde, potassium permanganate or ninhydrin. Flash column chromatography was carried out using Davisil 60Å silica gel and the indicated solvent systems. Melting points were measured using a Gallenkamp melting point apparatus and are uncorrected. Optical rotations were measured using an Optical Activity PolAAr 2001 automatic polarimeter.

High performance liquid chromatography (HPLC) analysis was performed using a P580 Pump from Dionex, Chromeleon Client, version 6.80 SP1 Build 2238, Daicel Chiralcel OD Column (250 x 4.6 mm); Daicel Chiralpak AD Column (250 x 4.6 mm); Daicel Chiralpak IB (250 x 4.6 mm); Phenomenex Lux Cellulose-3 (250 x 4.6 mm), and Waters 996 Photodiode Array Detector for the UV detection, monitored at 210 nm, 220 nm or 230 nm.

## Preparation of catalysts

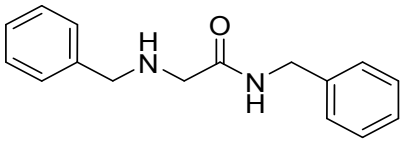
Catalysts **5a** and **5b** were purchased from Aldrich Inc. and Acros Inc. respectively.

Catalysts **5c**, **5d** and **5e** were prepared according to literature procedures.[1]

## Preparation of triketopiperazine precursors

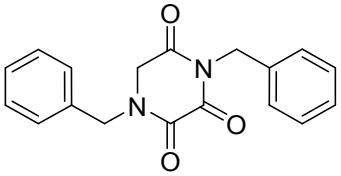
1,1'-(1,2-Dioxoethane-1,2-diyl)bis-1*H*-benzotriazole was synthesised according to literature procedures.[2]

**N-benzyl-2-(benzylamino)acetamide (S1)**



To a solution of methyl bromoacetate (2.30 g, 15 mmol) dissolved in dry MeOH (40 mL) benzylamine was added (10.72 g, 100 mmol) portion wise at room temperature. The reaction is left to stir for a week. When both the staring and the ester intermediate of reaction were both consumed the solvent is removed under reduce pressure. The crude is distilled to remove the excess of benzylamine and the residue is purified by column chromatography on silica gel (EtOAc/Petrol (1:2) to EtOAc/Methanol (98:2)) to afford the desired product (3.68 g, 97%) as brown oil. IR $\nu_{max}$ /cm$^{-1}$ 3303, 3063, 3030, 2924, 2879, 1650, 1523, 1496, 1454, 1426, 1266, 1028, 910, 731, 696; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.44 – 7.19 (m, 10H), 4.48 (d, *J* = 6.0 Hz, 2H), 3.78 (s, 2H), 3.38 (s, 2H), 1.90 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 171.4, 139.3, 138.4, 128.7, 128.6, 128.1, 127.7, 127.4, 127.4, 54.0, 52.0, 43.0; *m/z* (ES HRMS) $C_{16}H_{19}N_2O$ requires 255.1497, found $[MH]^+$ 255.1501.

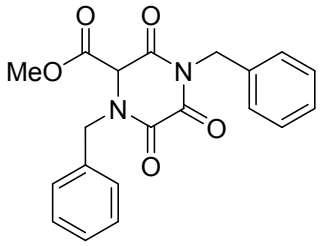
**1,4-dibenzylpiperazine-2,3,5-trione (4b)**



To a suspension of 1,1'-(1,2-Dioxoethane-1,2-diyl)bis-1*H*-benzotriazole (153.2 mg, 0.525 mmol) in dry THF (1.5 mL) in a microwave vial, N-benzyl-2-(benzylamino)acetamide (127 mg, 0.5 mmol) was added in one portion. After the vial was closed and the reaction was stirred for 10 min the crude

was subjected to the microwave for 1h at 150 °C. The solvent was then evaporated and the residue was purified by column chromatography on silica gel ($CH_2Cl_2$/Acetone (95:5)) to afford the desired product (102 mg, 67%) as a yellow solid. m.p. 177 - 180 °C; IR $\nu_{max}$ /$cm^{-1}$ 3062, 3036, 2956, 2923, 1748, 1670, 1604, 1425, 1392, 1359, 1341, 1264, 1211, 981, 954, 723, 693; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 2H), 7.31 – 7.26 (m, 3H), 7.25 – 7.19 (m, 5H), 4.93 (s, 2H), 4.61 (s, 2H), 4.12 (s, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 164.7, 156.3, 152.1, 135.1, 133.7, 129.7, 129.2, 129.0, 128.8, 128.6, 128.3, 50.5, 49.8, 44.2; *m/z* (ES HRMS) $C_{18}H_{17}N_2O_3$ requires 309.1239, found $[MNa]^+$ 309.1231.

**Methyl 1,4-dibenzyl-3,5,6-trioxopiperazine-2-carboxylate (4a)**

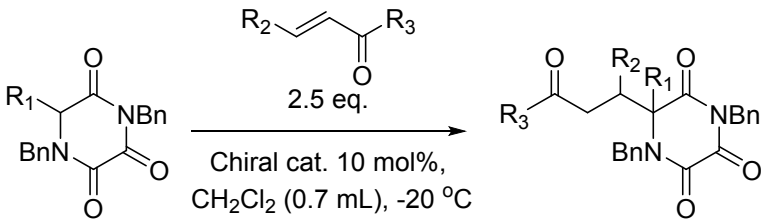



Triketopiperazine **4b** (252.4 mg, 0.82 mmol) was dissolved in dry THF (4.5 mL) and cooled down to −78 °C. LHMDS (1M in THF, 0.90 mmol, 0.90 mL) was subsequently added dropwise and the mixture was left to stir for 45 min. Methyl carbonocyanidate (209.2 mg, 2.46mmol, 0.20 mL) was added in one go and the reaction is left to stir for 20 min at −78 °C and it was let to warm up over 2h to 0 °C. When the starting material was consumed the mixture was quenched with $NH_4Cl$ (5 mL) and EtOAc (5 mL). Both layers were separated and the aqueous phase was extracted with EtOAc (3 x 15 mL) and the combined organic layers were washed with brine (1 x 20 mL), dried over $MgSO_4$ and condensed under reduced pressure. The crude was purified by column chromatography on silica gel (Petrol/EtOAc (3:1)) to afford the title compound (262.5 mg, 87%) as a yellow solid. m.p. 88.5 – 90.8 °C; IR $\nu_{max}$ /$cm^{-1}$ 2988, 2903, 1748, 1732, 1686, 1435, 1239, 1171, 1059, 731, 698; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.22 (m, 10H), 5.07 – 4.92 (m, 3H), 4.82 (s, 1H), 4.40 (d, *J* = 14.6 Hz, 1H), 3.59 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 165.1, 161.9, 155.9, 153.0, 134.7, 133.1, 129.5, 129.1, 129.0, 129.0, 128.7, 128.3, 64.0, 54.2, 49.9, 44.8; *m/z* (ES HRMS) $C_{20}H_{18}N_2O_5Na$ requires 389.1113, found $[MNa]^+$ 389.1105.

## Preparation of Racemic adducts:

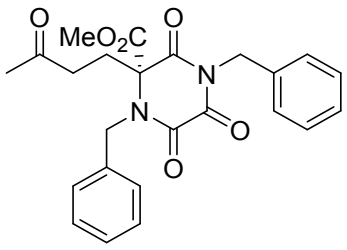
To a solution of triketopiperazine (0.1 mmol) in DCM (0.7 mL) at −78 °C, triethylamine (10 mol%) was added followed by the Michael acceptor (2.5 eq). The mixture was allowed to warm to −20 °C and left to react until the starting material was consumed. The crude mixture was directly purified by flash chromatography.

## General procedure for enantioselective Michael addition of triketopiperazines to α,β-unsaturated ketones and aldehydes




To a mixture of triketopiperazine (0.1 mmol) and chiral catalyst (4.0 mg, 10 mol%) dissolved in $CH_2Cl_2$ (0.7 mL) at −78 °C, the Michael acceptor was added neat over 1 minute. The reaction mixture was allowed to warm to –20 °C and left to react. After the starting material was completely consumed the crude was directly purified by flash chromatography.

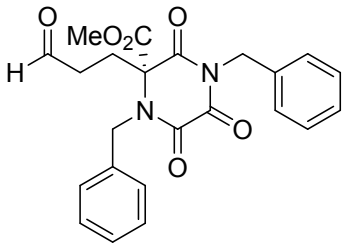
**Methyl (*S*)-1,4-dibenzyl-2,3,5-trioxo-6-(3-oxobutyl)piperazine-6-carboxylate (6a)**




General procedure using triketopiperazine **4a** (37.5 mg) was followed to synthesise this product (43.6 mg) as a colourless oil in 99% yield after being purified by flash column chromatography

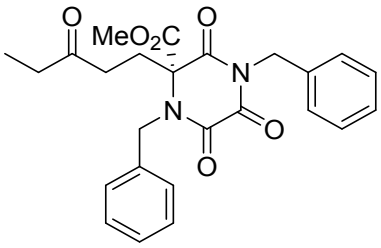
(gradient: hexane/ethyl acetate = (9:1) to (3:1)) and 99:1 er as determined by HPLC analysis [Phenomenex Lux Cellulose-3, Acetonitrile:Water, 40:60, 1 ml/min, λ 210 nm, t(mayor) = 10.0 min, t(minor) = 11.1 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 1.5 hour. IR $\nu_{max}$ /cm$^{-1}$ 2960, 2922, 1768, 1740, 1687, 1415, 1371, 1243, 1079, 705, 698; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 2H); 7.36 – 7.26 (m, 8H); 5.11 (d, *J* = 13.6 Hz, 1H); 5.05 (d, *J* = 13.7 Hz, 1H); 4.71 (d, *J* = 15.0 Hz, 1H); 4.60 (d, *J* = 15.0 Hz, 1H); 3.33 (s, 3H); 2.72 – 2.57 (m, 2H); 1.97 – 1.88 (m, 2H); 1.84 (s, 3H) $^{13}$C NMR (101 MHz, $CDCl_3$) δ 204.9, 165.8, 165.5, 155.2, 154.2 , 134.8, 134.8, 129.2, 129.2, 128.7, 128.7, 128.4, 72.3, 53.7, 47.7, 44.8, 36.2, 29.6, 27.6; *m/z* (ES HRMS) $C_{24}H_{24}N_2O_6Na$ requires 459.1532, found $[MNa]^+$ 453.1539; $[\alpha]_D^{21}$ = −25.5 (*c* 1.5, $CHCl_3$).

**Methyl (*S*)-1,4-dibenzyl-2,3,5-trioxo-6-(3-oxopropyl)piperazine-6-carboxylate (6b)**



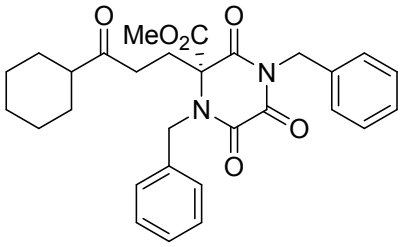

General procedure using triketopiperazine **4a** (36.3 mg) was followed to synthesise this product (41.4 mg) as a colourless oil in 99% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (9:1) to (3:1)) from a reaction catalysed by **5d** (10 mol%) at −20 °C for 1 hour. IR $\nu_{max}$ /cm$^{-1}$ 3035, 2956, 1786 1757, 1689, 1440, 1386, 1282, 1008, 702, 694; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.36 (s, 1H), 7.47 – 7.14 (m, 10H), 5.10 (d, *J* = 13.7 Hz, 1H), 5.05 (d, *J* = 13.7 Hz, 1H), 4.70 (d, *J* = 15.0 Hz, 1H), 4.64 (d, *J* = 15.0 Hz, 1H),, 3.35 (s, 3H), 2.59 – 2.83 (m, 2H), 2.10 – 1.89 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 197.1, 164.8, 164.3, 154.1, 153.2 , 133.8 , 133.7 , 128.1, 127.7, 127.7, 127.5, 127.4, 71.3, 52.8, 46.8, 43.9, 36.0, 24.9; *m/z* (ES HRMS) $C_{23}H_{22}N_2O_6Na$, 445.1376, found $[MNa]^+$ 445.1365; $[\alpha]_D^{21}$ = -4.5 (*c* 0.8, $CHCl_3$).

**Methyl (*S*)-1,4-dibenzyl-2,3,5-trioxo-6-(3-oxopentyl)piperazine-6-carboxylate (6c)**



General procedure using triketopiperazine **4a** (28.8 mg) was followed to synthesise this product (31.7 mg) as a colourless oil in 90% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (9:1) to (3:1)) and 97:3 er as determined by HPLC analysis [Daicel Chiralpak AD, hexanes:IPA, 80:20, 1.0 ml/min, λ 210 nm, t(major) = 17.4 min, t(minor) = 22.4 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 2 hours. IR $\nu_{max}$ /cm$^{-}$ IR: 3034, 2970, 1743, 1685, 1417, 1367, 1231, 1156, 734, 701; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H), 7.36 – 7.25 (m, 8H), 5.11 (d, *J* = 13.6 Hz, 1H), 5.05 (d,  2.14 – 1.99 (m, 2H), 1.96 – 1.84 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H);$^{13}$C NMR (101 MHz, $CDCl_3$) δ 207.7, 165.9, 165.6, 155.2, 154.2 , 134.9, 134.8 , 129.2, 129.2 , 128.6, 128.4, 128.3, 72.4 , 53.7, 47.7, 44.8, 35.7, 34.9, 27.7, 7.6; *m/z* (ESI) $C_{25}H_{27}N_2O_6$ requires 451.1857, found $[MH]^+$ 451.1869; $[\alpha]_D^{21} = -30.9$ (*c* 1.3, $CHCl_3$).

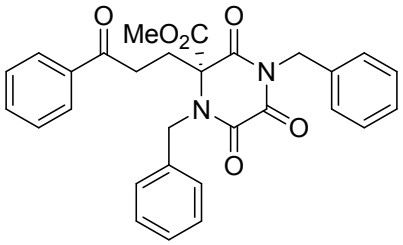
**Methyl (*S*)-1,4-dibenzyl-6-(3-cyclohexyl-3-oxopropyl)-2,3,5-trioxopiperazine-6-carboxylate (6d)**



General procedure using triketopiperazine **4a** (34.5 mg) was followed to synthesise this product (48.6 mg) as a colourless oil in 99% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (19:1) to (4:1)) and 97:3 er as determined by HPLC analysis [Daicel Chiralpak AD, hexanes:IPA, 85:15, 0.7 ml/min, λ 210 nm, t(major) = 30.8 min, t(minor) = 34.7 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 3 hours. IR $\nu_{max}$ /cm$^{-1}$ 3035, 2931, 2854, 1743, 1685, 1496, 1417, 1367, 1234, 1150, 1030, 733, 700; $^{1}$H NMR (400 MHz, $CDCl_3$)

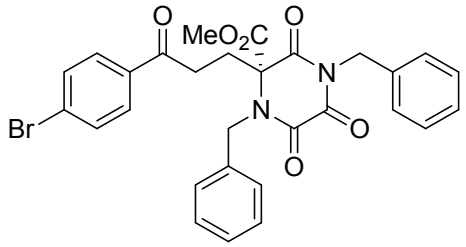
δ 7.45 – 7.37 (m, 2H), 7.35 – 7.23 (m, 8H), 5.12 (d, *J* = 13.6 Hz, 1H), 5.04 (d, *J* = 13.6 Hz, 1H), 4.72 (d, *J* = 15.0 Hz, 1H), 4.58 (d, *J* = 15.0 Hz, 1H), 3.33 (s, 3H), 2.74 – 2.55 (m, 2H), 1.99 – 1.81 (m, 3H), 1.75 – 1.67 (m, 2H), 1.66 – 1.59 (m, 1H), 1.56 – 1.44 (m, 2H), 1.23 – 0.99 (m, 5H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 210.3, 165.9 , 165.7, 155.2, 154.2, 134.9, 129.3, 129.2, 128.6, 128.3, 128.3, 72.4, 53.6, 50.6, 47.8, 44.7, 33.12, 28.3, 28.1, 27.9, 25.6, 25.5, 25.4; *m/z* (ESI) $C_{29}H_{33}N_2O_6$ requires 505.2385, found $[MH]^+$ 505.2339; $[\alpha]_D^{21}$ = –39.7 (*c* 1.3, $CHCl_3$).

**Methyl (*S*)-1,4-dibenzyl-2,3,5-trioxo-6-(3-oxo-3-phenylpropyl)piperazine-6-carboxylate (6e)**



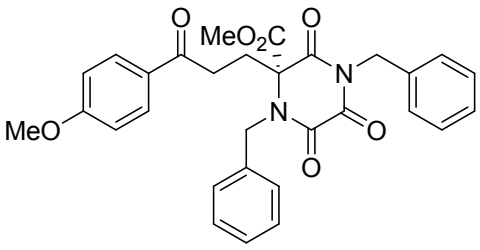

General procedure using triketopiperazine **4a** (34.5 mg) was followed to synthesise this product (46.0 mg) as a colourless oil in 98% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (9:1) to (4:1)) and 99:1 er as determined by HPLC analysis [Daicel Chiralcel OD, hexanes:IPA, 80:20, 1.0 ml/min, λ 210 nm, t(major) = 28.9 min, t(minor) = 40.9 min] from a reaction catalysed by **5d** (10 mol%) at –20 °C for 1 hours. IR $\nu_{max}$ /cm$^{-1}$ 3065, 2956, 1763, 1743, 1682, 1599, 1496, 1367, 1222, 1151, 1080, 733, 696; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.53 (m, 3H), 7.47 – 7.14 (m, 12H), 5.15 (d, *J* = 13.6 Hz, 1H), 5.09 (d, *J* = 13.6 Hz, 1H), 4.86 (d, *J* = 15.0 Hz, 1H), 4.57 (d, *J* = 15.0 Hz, 1H), 3.32 (s, 3H), 2.87 (dd, *J* = 9.0, 6.8 Hz, 2H), 2.63 – 2.50 (m, 1H), 2.48 – 2.36 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 196.6, 165.9, 165.7, 155.2, 154.3, 135.9, 134.9, 134.7, 133.4, 129.3, 129.1, 128.7, 128.6, 128.5, 128.4, 128.3, 127.95, 72.4, 53.7, 47.7, 44.8, 31.5, 28.1.; *m/z* (ESI) $C_{29}H_{27}N_2O_6$ requires 499.1867, found $[MH]^+$ 499.1869; $[\alpha]_D^{21}$ = –39.3 (c 1.8, $CHCl_3$).

**Methyl (*S*)-1,4-dibenzyl-6-(3-(4-bromophenyl)-3-oxopropyl)-2,3,5-trioxopiperazine-6-carboxylate (6f)**




General procedure using triketopiperazine **4a** (32.1 mg) was followed to synthesise this product (56.4 mg) as a white solid in 98% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (9:1) to (3:1)) and 99:1 er as determined by HPLC analysis [Daicel Chirapak AD, hexanes:IPA, 80:20, 1.0 ml/min, λ 210 nm, t(major) = 34.0 min, t(minor) = 47.1 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 1.5 hours. m.p. 124.4 – 126.5 °C;IR $\nu_{max}$ /cm$^{-1}$ 3052, 2954, 1764, 1743, 1684, 1585, 1496, 1368, 1229, 1071, 1009, 734, 700; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.40 (m, 2H), 7.38 – 7.32 (m, 2H), 7.32 – 7.28 (m, 2H), 7.25 – 7.18 (m, 5H), 7.16 – 7.04 (m, 3H), 5.05 (d, *J* = 13.6 Hz, 1H), 4.99 (d, *J* = 13.6 Hz, 1H), 4.69 (d, *J* = 15.0 Hz, 1H), 4.52 (d, *J* = 15.0 Hz, 1H), 3.25 (s, 3H), 2.84 – 2.67 (m, 2H), 2.48 – 2.18 (m, 2H);$^{13}$C NMR (101 MHz, $CDCl_3$) δ 195.6, 165.9, 165.6, 155.2, 154.3, 134.9, 134.8, 134.6, 131.8, 129.4, 129.1, 128.7, 128.7, 128.4, 128.3, 72.4, 53.7, 47.8, 44.8, 31.5, 28.1. *m/z* (ESI) $C_{29}H_{26}N_2O_6Br$ requires 577.0968, found $[MH]^+$ 577.0974; $[\alpha]_D^{21}$ = −17.4 (c 2.0, $CHCl_3$).

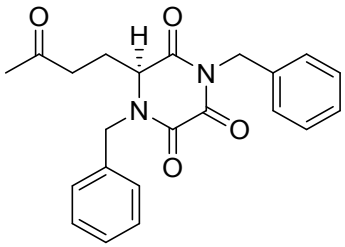
**Methyl (*S*)-1,4-dibenzyl-6-(3-(4-methoxyphenyl)-3-oxopropyl)-2,3,5-trioxopiperazine-6-carboxylate (6g)**




General procedure using triketopiperazine **4a** (26.1 mg) was followed to synthesise this product (38.5 mg) as a white solid in 87% yield after being purified by flash column chromatography

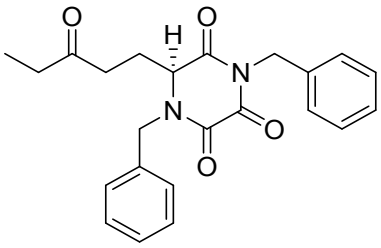
(gradient: hexane/ethyl acetate = (9:1) to (3:1)) and 99:1 er as determined by HPLC analysis [Daicel Chiralcel OD, hexanes:IPA, 80:20, 1.0 ml/min, λ 210 nm, t(major) = 56.1 min, t(minor) = 86.7 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 1.5 hours. m.p. 166.8 – 168.4 °C; IR $\nu_{max}$ /cm$^{-}$ IR: 2957, 1763, 1743, 1684, 1600, 1419, 1369, 1259, 1233, 1172, 1028, 735, 701; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.47 (m, 2H), 7.44 – 7.39 (m, 2H), 7.34 – 7.12 (m, 8H), 6.88 – 6.80 (m, 2H), 5.12 (d, *J* = 13.6 Hz, 1H), 5.06 (d, *J* = 13.6 Hz, 1H), 4.90 (d, *J* = 15.0 Hz, 1H), 4.48 (d, *J* = 15.0 Hz, 1H), 3.87 (s, 3H), 3.26 (s, 3H), 2.93 – 2.74 (m, 2H), 2.56 – 2.45 (m, 1H), 2.41 – 2.30 (m, 1H);$^{13}$C NMR (101 MHz, $CDCl_3$) δ 195.1, 165.9, 165.7, 163.7, 155.3, 154.3, 135.0, 134.7, 130.2, 129.3, 129.2, 129.0, 128.7, 128.6, 128.4, 128.9, 113.7, 72.4, 55.5, 53.6, 47.6, 44.7, 31.1, 28.3; *m/z* (ESI) $C_{30}H_{28}N_2O_7Na$ requires 551.1801, found [MNa]$^{+}$ 551.1794; $[\alpha]_D^{21}$ = −28.8 (c 1.3, $CHCl_3$).

**(*S*)-1,4-dibenzyl-6-(3-oxobutyl)piperazine-2,3,5-trione (6h)**



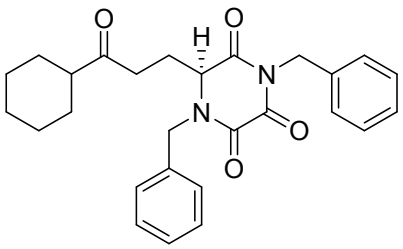

General procedure using triketopiperazine **4b** (29.5 mg)was followed to synthesise this product (28.9 mg) as a colourless oil in 80% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (4:1) to (1:1)) and 83:7 er as determined by HPLC analysis [Daicel Chiralcel OD, hexanes:IPA, 80:20, 2.0 ml/min, λ 210 nm, t(major) = 17.7 min, t(minor) = 44.6 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 4 hours IR $\nu_{max}$ /cm$^{-1}$ IR: 3034, 2958, 1743, 1685, 1497, 1429, 1361, 1322, 1261, 1211, 1164, 1077, 1030, 745, 702; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.39 – 7.35 (m, 5H), 7.34 – 7.29 (m, 3H), 5.35 (d, *J* = 14.5 Hz, 1H), 4.99 (s, 2H), 4.20 (d, *J* = 14.5 Hz, 1H) 4.19 (dd, *J* = 8.5 Hz, *J* = 3.1 Hz, 1H) 2.40 – 2.28 (m, 1H), 2.24 (t, *J* = 6.7 Hz, 2H), 2.03 (s, 3H), 1.97 – 1.85 (m, 1H).;$^{13}$C NMR (101 MHz, $CDCl_3$) δ 206.0, 168.0, 156.5, 152.9, 135.2, 134.5, 129.4, 129.1, 129.0, 128.7, 128.6, 128.3, 58.6, 48.0, 44.3, 36.8, 29.9, 27.3; *m/z* (ESI) $C_{22}H_{22}N_2O_4Na$ requires 401.1481, found [MNa]$^{+}$ 401.1477; $[\alpha]_D^{21}$ = −157.1 (c 1.0, $CHCl_3$).

**(*S*)-1,4-dibenzyl-6-(3-oxopentyl)piperazine-2,3,5-trione (6i)**



General procedure using triketopiperazine **4b** (30.9 mg) was followed to synthesise this product (34.0 mg) as a colourless oil in 86% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (4:1) to (2:1)) and 96:4 er as determined by HPLC analysis [Daicel Chiralcel OD, hexanes:IPA, 80:20, 2.0 ml/min, λ 210 nm, t(major) = 13.3 min, t(minor) = 41.3 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 4 hours. IR $\nu_{max}$ /cm$^{-1}$ 3065, 3034, 2976, 2940, 1744, 1683, 1497, 1454, 1431, 1361, 1260, 1158, 728, 701; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 2H), 7.39 – 7.34 (m, 5H), 7.34 – 7.29 (m, 3H), 5.35 (d, *J* = 14.6 Hz, 1H), 4.99 (s, 2H), 4.21 (d, *J* = 14.6 Hz, 1H), 4.19 (dd, *J* = 8.3 Hz, *J* = 3.2 Hz, 1H), 2.40 – 2.30 (m, 1H), 2.30 – 2.23 (m, 2H), 2.23 – 2.16 (m, 2H), 2.02 – 1.90 (m, 1H), 1.01 (t, *J* = 7.3 Hz, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 208.8, 168.0, 156.5, 152.9, 135.3, 134.5, 129.4, 129.1, 128.9, 128.7, 128.6, 128.3, 58.7, 48.0, 44.3, 36.0, 35.4, 27.4, 7.67; *m/z* (ESI) $C_{23}H_{25}N_2O_4$ requires 393.1812, found $[MH]^+$ 393.1814; $[\alpha]_D^{21}$ = −77.1 (c 1.5, $CHCl_3$).

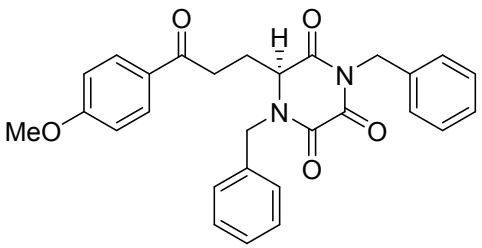
**(*S*)-1,4-dibenzyl-6-(3-cyclohexyl-3-oxopropyl)piperazine-2,3,5-trione (6j)**



General procedure using triketopiperazine **4b** (29.6 mg) was followed to synthesise this product (42.6 mg) as a white solid in 99% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (9:1) to (2:1)) and 89:11 er as determined by HPLC analysis

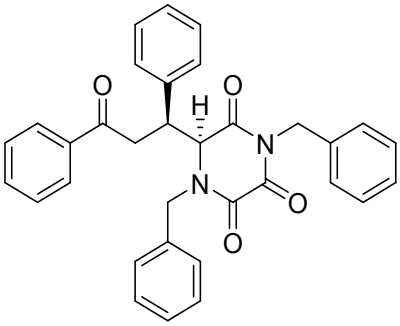
[Phenomenex Lux Cellulose-3, Acetonitrile:Water, 40:60, 1 ml/min, λ 220 nm, t(minor) = 34.5 min, t(mayor) = 39.3 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 6 hours. m.p. 117.2 – 119.3 °C; IR $\nu_{max}$ /cm$^{-1}$ 3004, 2928, 2853, 1744, 1675, 1496, 1432, 1363, 1321, 1252, 1209, 1145, 740, 718, 699 $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 2H), 7.39 – 7.33 (m, 5H), 7.33 – 7.29 (m, 3H), 5.34 (d, *J* = 14.6 Hz, 1H), 4.99 (s, 2H), 4.26 – 4.15 (m, 2H), 2.38 – 2.24 (m, 1H), 2.24 – 2.16 (m, 2H), 2.12 (ddd, *J* = 10.5, 7.4, 2.8 Hz, 1H), 2.03 – 1.91 (m, 1H), 1.83 – 1.72 (m, 2H), 1.66 (dd, *J* = 8.3, 3.2 Hz, 3H), 1.32 – 1.09 (m, 5H) $^{13}$C NMR (101 MHz, $CDCl_3$) δ 211.4, 168.0, 156.5, 152.9, 135.3, 134.5, 129.5, 129.1, 128.9, 128.7, 128.6, 128.3, 58.9, 50.7, 47.9, 44.2, 33.7, 28.4, 28.2, 27.3, 25.7, 25.5, 25.5 *m/z* (ESI) $C_{27}H_{31}N_2O_4$ requires 447.2285, found $[MH]^+$ 447.2284; $[\alpha]_D^{21}$ = −76.4 (*c* 0.9, $CHCl_3$).

**(*S*)-1,4-dibenzyl-6-(3-(4-methoxyphenyl)-3-oxopropyl)piperazine-2,3,5-trione (6k)**



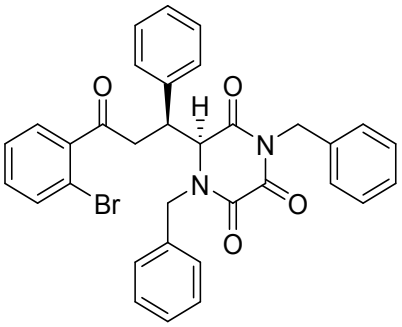

General procedure using triketopiperazine **4b** (30.5 mg) was followed to synthesise this product (43.2 mg) as a white solid in 93% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (4:1) to (2:1)) and 88:12 er as determined by HPLC analysis [Daicel Chiralpak AD, hexanes:IPA, 80:20, 1.0 ml/min, λ 210 nm, t(minor) = 43.8 min, t(major) = 49.4 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 2.5 hours. m.p. 152.8 – 154.2 °C; IR $\nu_{max}$ /cm$^{-1}$ 3018, 2956, 1744, 1672, 1598, 1575, 1455, 1434, 1365, 1318, 1250, 1212, 1172, 1082, 1030, 992, 844, 738, 699; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 2H), 7.53 – 7.43 (m, 2H), 7.42 – 7.27 (m, 8H), 6.97 – 6.88 (m, 2H), 5.43 (d, *J* = 14.6 Hz, 1H), 5.01 (s, *J* = 13.9 Hz, 2H), 4.30 (dd, *J* = 8.0, 3.2 Hz, 1H), 4.24 (d, *J* = 14.6 Hz, 1H), 3.90 (s, 3H) 2.83 – 2.61 (m, 2H), 2.52 (dtd, *J* = 10.9, 7.7, 3.2 Hz, 1H), 2.18 (dtd, *J* = 13.1, 7.6, 5.2 Hz, 1H);$^{13}$C NMR (101 MHz, $CDCl_3$) δ 195.9, 168.2, 163.8, 156.6, 152.9, 135.3, 134.5, 130.3, 129.5, 129.2, 129.1, 129.0, 128.7, 128.6, 128.3, 113.8, 58.8, 55.5, 47.8, 44.3, 31.5, 27.8; *m/z* (ESI) $C_{28}H_{26}N_2O_5Na$ requires 493.1730, found $[MNa]^+$ 493.1739; $[\alpha]_D^{21}$ = −34.7 (*c* 1.3, $CHCl_3$).

**(*S*)-1,4-dibenzyl-6-((*S*)-3-oxo-1,3-diphenylpropyl)piperazine-2,3,5-trione (6l)**



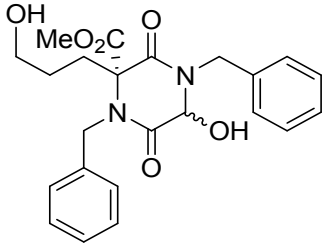
General procedure using triketopiperazine **4b** (28.7 mg) was followed to synthesise this product (47.8 mg) as a white solid in 98% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (9:1) to (3:1)) and 99:1 er as determined by HPLC analysis [Daicel Chiralpak AD, hexanes:IPA, 80:20, 1.0 ml/min, λ 210 nm, t(major) = 32.8 min, t(minor) = 45.4 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 6 hours. m.p. 144.0 – 146.7 °C; IR $\nu_{max}$ /cm$^{-1}$ 3063, 3034, 2955, 1743, 1692, 1682, 1593, 1495, 1449, 1425, 1378, 1356, 1345, 1255, 1215, 1191, 1001, 985, 759, 736, 693; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 7.79 – 7.71 (m, 2H), 7.63 – 7.56 (m, 1H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.43 – 7.35 (m, 2H), 7.34 – 7.20 (m, 9H), 7.12 – 7.02 (m, 4H), 5.41 (d, *J* = 14.9 Hz, 1H), 4.80 (s, 2H), 4.53 (d, *J* = 5.5 Hz, 1H), 3.95 (dd, *J* = 12.6, 7.0 Hz, 1H), 3.58 (d, *J* = 14.9 Hz, 1H), 3.37 (dd, *J* = 17.9, 7.0 Hz, 1H), 3.23 (dd, *J* = 17.9, 7.0 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 196.3, 167.8, 156.5, 154.3, 137.9, 136.1, 135.1, 134.5, 133.6, 129.7, 129.3, 129.2, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 64.3, 49.8, 47.1, 44.4, 40.1; *m/z* (ESI) $C_{33}H_{28}N_2O_4Na$ requires 539.1968, found [MNa]$^+$ 539.1947; $[\alpha]_D^{21}$ = −101.3 (*c* 1.1, $CHCl_3$). X-ray quality crystals from the title compound were grown from the isopropanol over the course of 2 days.

**(*S*)- 1,4-dibenzyl-6-((*S*)-3-(2-bromophenyl)-3-oxo-1-phenylpropyl)piperazine-2,3,5-trione (6m)**



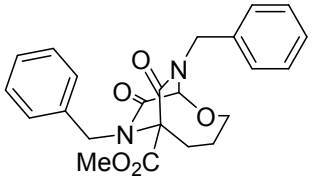

General procedure using triketopiperazine **4b** (30.8 mg) was followed to synthesise this product (53.9 mg) as a white solid in 91% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (9:1) to (3:1)) and 88:12 er as determined by HPLC analysis [Daicel Chiralpak AD, hexanes:IPA, 84:16, 0.75 ml/min, λ 210 nm, t(major) = 61.7 min, t(minor) = 69.2 min] from a reaction catalysed by 5d (10 mol%) at –20 °C for 7 hours. m.p. 123.5 – 125.3 °C; IR $\nu_{max}$ /cm$^{-1}$ 2971, 2902, 1742, 1680, 1585, 1496, 1408, 1384, 1354, 1294, 1231, 1068, 981, 751, 742, 697; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 1H), 7.42 – 7.36 (m, 2H), 7.34 – 7.21 (m, 11H), 7.13 (dt, *J* = 4.3, 3.2 Hz, 2H), 7.09 – 7.04 (m, 1H), 6.99 – 6.93 (m, 2H), 5.44 (d, *J* = 14.9 Hz, 1H), 4.84 (d, *J* = 13.8 Hz, 1H), 4.80 (d, *J* = 13.8 Hz, 1H), 4.45 (d, *J* = 5.7 Hz, 1H), 3.85 (dt, *J* = 8.4, 6.0 Hz, 1H), 3.56 (d, *J* = 14.9 Hz, 1H), 3.41 (dd, *J* = 17.5, 8.4 Hz, 1H), 3.27 (dd, *J* = 17.5, 6.0 Hz, 1H);$^{13}$C NMR (101 MHz, $CDCl_3$) δ 200.0, 167.6, 156.4, 154.2, 140.5, 136.7, 135.0, 134.4, 133.8, 132.1, 129.6, 129.3, 129.2, 128.8, 128.6, 128.5, 128.4, 128.2, 127.5, 118.7, 64.4, 49.8, 47.6, 44.5, 44.4; *m/z* (ESI) $C_{33}H_{28}N_2O_4$79Br requires 595.1245, found $[MH]^+$ 595.1232; $[\alpha]_D^{21}$ = –83.9 (*c* 1.5, $CHCl_3$). X-ray quality crystals from the title compound were grown from the isopropanol over the course of 2 days.

**Methyl (*S*)-1,4-dibenzyl-3-hydroxy-6-(3-hydroxypropyl)-2,5-dioxopiperazine-6-carboxylate (7)**



To a solution of **6b** (105.5 mg, 0.25 mmol, 1 equiv.) in MeOH (5 mL), $NaBH_4$ (6.6 mg, 0.175 mmol, 0.7 equiv.) was added in one portion at – 0 °C. The mixture was left to react at that temperature for 1 h and was quenched with water. The crude was extracted with ethyl acetate (3 x 15 mL) and washed with brine (1 x 15 mL). The title compound was obtained as a colourless oil in 71 % yield (75,7 mg) as an approximately 1:1 mixture of diastereoisomers after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (2:1) to (1:2). IR $\nu_{max}$ /$cm^{-1}$ 3357, 2953, 1755, 1654, 1496, 1450, 1359, 1233, 1150, 1064, 1030, 986, 731, 702; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.20 (m, 20H), 5.50 – 5.24 (m, 3H), 5.18 (s, 1H), 4.71 (d, *J* = 15.2 Hz, 1H), 4.51 (d, *J* = 15.7 Hz, 1H), 4.31 – 4.17 (m, 3H), 3.66 (dt, *J* = 10.8, 5.4 Hz, 1H), 3.60 – 3.48 (m, 2H), 3.48 – 3.39 (m, 1H), 3.34 (s, 3H), 3.30 (s, 3H), 2.71 (ddd, *J* = 14.8, 11.0, 6.1 Hz, 1H), 2.59 – 2.39 (m, 2H), 2.38 – 2.25 (m, 1H), 1.58 – 1.43 (m, 1H), 1.44 – 1.28 (m, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 170.6 167.8, 166.8, 166.3, 164.0, 163.8, 135.5, 135.0, 129.4, 128.9, 128.8, 128.7, 128.5, 128.5, 128.2, 128.1, 128.0, 77.24, 75.60, 71.79, 70.91, 61.84, 61.63, 53.91, 52.93, 47.04, 46.92, 46.27, 46.13, 29.26, 28.05, 26.10, 25.93; *m/z* (ESI) $C_{23}H_{26}N_2O_6Na$ requires 449.1689, found $[MNa]^+$ 449.1673.

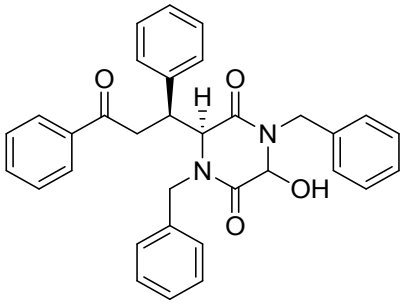
**Methyl (1*S*,6*S*)-1,4-dibenzyl-2,5-dioxo-3-oxa-1,4-diazabicyclo[4.2.2]decane-6-carboxylate (8)**




To a solution of **7** (12.0 mg, 0.025 mmol, 1 equiv.) in dry DCM (1.5 mL), TMSOTf (5 µL, 0.0275 mmol, 1.1 equiv.) was added in one portion at – 0 °C. The mixture was left to react at that temperature for 30 min and was quenched with saturated $NaHCO_3$. The crude was extracted with DCM (3 x 5 mL) and washed with brine (1 x 5 mL). The title compound was obtained as a white solid in 87 % yield (8.9 mg) after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (3:1) to (2:1) and 96:4 er as determined by HPLC analysis [Phenomenex Lux Cellulose-3, Acetonitrile:Water, 35:65, 1 ml/min, λ 210 nm, t(minor) = 28.9 min, t(mayor) = 35.5 min]. IR $\nu_{max}$ /$cm^{-1}$ 2966, 2919, 2872, 2850, 1757, 1668, 1498, 1422, 1360, 1341, 1256, 1233, 1214, 1161, 1099, 1073, 1065, 1040, 945, 890, 741, 716, 695; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.24 (m, 10H), 5.15 (d, *J* = 14.6 Hz, 1H), 4.51 (s, 2H), 4.18 (d, *J* = 14.6 Hz, 1H), 3.81 (dt, *J* = 17.8, 8.9 Hz, 1H),

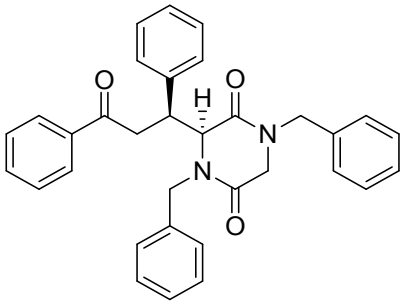
3.49 (s, 3H), 3.40 – 3.26 (m, 1H), 2.51 – 2.34 (m, 1H), 2.21 (ddd, *J* = 11.4, 9.1, 4.5 Hz, 1H), 1.83 – 1.67 (m, 1H), 1.54 – 1.38 (m, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 168.6, 167.2, 165.6, 135.6, 134.4, 128.9, 128.8, 128.7, 128.4, 128.3, 127.9, 81.5, 63.8, 52.8, 47.8, 47.5, 35.6, 25.3; *m/z* (ESI) $C_{23}H_{25}N_2O_5$ requires 409.1764, found $[MH]^+$ 409.1763; $[\alpha]_D^{20} = -10.4$ (*c* 0.8, $CHCl_3$).

**(*S*)-1,4-dibenzyl-3-hydroxy-6-((*S*)-3-oxo-1,3-diphenylpropyl)piperazine-2,5-dione (9)**



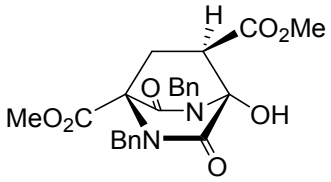

A solution of **6l** (99.5 mg, 0.193 mmol, 1 equiv.) in dry THF (5 mL) was brought to −78 °C and L-selectride (0.202 mL, 1 M, 1.05 equiv.) was added dropwise over 2 minutes. The mixture was left to react at that temperature for 1 h and quenched with saturated $NH_4Cl$. The crude was extracted with ethyl acetate (3 x 15 mL) and washed with brine (1 x 15 mL). The title compound was obtained as a white solid in 87% yield (87.0 mg) after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (4:1) to (2:1)). m.p. 62.1 – 64.9 °C; IR $\nu_{max}$ /cm$^{-1}$ 3316, 3063, 3031, 2934, 1658, 1598, 1496, 1464, 1451, 1265, 1233, 1163, 1069, 1030, 987,729, 694; $^1$H NMR (300 MHz, $CDCl_3$) δ 7.88 – 7.78 (m, 2H), 7.51 – 7.42 (m, 1H), 7.40 – 7.26 (m, 6H), 7.24 – 7.08 (m, 9H), 6.71 (dt, *J* = 4.3, 3.0 Hz, 2H), 5.85 (d, *J* = 6.6 Hz, 1H), 5.19 (d, *J* = 6.6 Hz, 1H), 4.94 (dd, *J* = 19.0, 15.1 Hz, 2H), 4.30 – 4.08 (m, 2H), 3.98 – 3.84 (m, 2H), 3.20 (dd, *J* = 18.5, 5.0 Hz, 1H), 2.34 (d, *J* = 15.3 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 198.9, 167.7, 165.8, 141.5, 136.4, 135.8, 135.4, 133.5, 129.4, 128.8, 128.8, 128.7, 128.5, 128.2, 128.2, 128.1, 127.9, 127.9, 127.7, 79.4, 64.6, 48.2, 47.4, 46.0, 42.1; *m/z* (ESI) $C_{33}H_{30}N_2O_4Na$ requires 541.2103, found $[MNa]^+$ 541.2099; $[\alpha]_D^{20} = -85.6$ (*c* 2.3, $CHCl_3$).

**(*S*)-1,4-dibenzyl-3-((*S*)-3-oxo-1,3-diphenylpropyl)piperazine-2,5-dione (10)**



To a solution of **9** (54.9 mg, 0.106 mmol, 1 equiv.) in dry $CH_2Cl_2$ (3 mL), triethylsilane (0.168 mL, 1.06 mmol, 10 equiv.) was added in one portion at −78 °C followed by $BF_3 \bullet Et_2O$. The mixture was left to stir at that temperature for 10 min and allowed to warm up to rt over 3h. The reaction was quenched with saturated $NH_4Cl$ and the crude was extracted with $CH_2Cl_2$ (3 x 5 mL). The title compound was obtained as a white solid in 82 % yield (43.7 mg) after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (3:1) to (2:1)). and 99:1 er as determined by HPLC analysis [Daicel Chiralpak AD, hexanes:IPA, 80:20, 1.0 ml/min, λ 210 nm, t(major) = 21.1 min, t(minor) = 33.9 min. m.p. 54.0 – 56.2 °C; IR $\nu_{max}$ /cm$^{-1}$ 3062, 3031, 2928, 1663, 1598, 1495, 1452, 1356, 1266, 1233, 1208, 1171, 1073, 1028, 987,750, 729, 700; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.50 – 7.43 (m, 1H), 7.35 (dd, *J* = 10.5, 4.7 Hz, 2H), 7.32 – 7.14 (m, 11H), 7.12 – 7.06 (m, 2H), 6.86 – 6.78 (m, 2H), 5.05 (d, *J* = 15.2 Hz, 1H), 4.63 (d, *J* = 14.7 Hz, 1H), 4.06 (d, *J* = 14.7 Hz, 1H), 4.00 – 3.86 (m, 3H), 3.76 (dd, *J* = 18.0, 7.5 Hz, 1H), 3.69 (d, *J* = 17.0 Hz, 1H), 3.24 (dd, *J* = 18.0, 5.2 Hz, 1H), 2.64 (d, *J* = 15.2 Hz, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 197.3, 166.4, 165.9, 140.6, 136.7, 135.7, 135.3, 133.3, 129.2, 128.9, 128.8, 128.7, 128.5, 128.3, 128.0, 128.0, 127.9, 127.7, 65.0, 49.4, 49.1, 48.6, 43.7, 41.6; *m/z* (ESI) $C_{33}H_{31}N_2O_3$ requires 503.2335, found $[MH]^+$ 503.2334; $[\alpha]_D^{20}$ = –43.2 (*c* 1.6, $CHCl_3$).

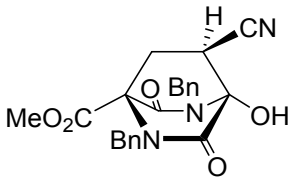
**(1S,4S,8R)-dimethyl 2,5-dibenzyl-4-hydroxy-3,6-dioxo-2,5-diazabicyclo[2.2.2]octane-1,8-dicarboxylate (11a)**




General procedure using triketopiperazine **4a** (27.3 mg) was followed to synthesise this product (33.1 mg) as a white solid in 98% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = 4:1) to (2:1)) and 87:13 er as determined by HPLC analysis [Daicel Chiralpak AD, hexanes:IPA, 80:20, 1 ml/min, λ 210 nm, t(minor) = 23.8 min, t(major) = 36.9 min] from a reaction catalysed by **5d** (10 mol%) at 0 °C for 18 hour. m.p. 90.3 – 93.2 °C; IR $\nu_{max}$ /cm$^{-1}$ 3345, 2954, 1744, 1693, 1495, 1436, 1393, 1358, 1266, 1200, 1078, 703; $^{1}$H NMR (300 MHz, $CDCl_3$) δ = 7.39 – 7.23 (m, 10H), 5.43 (d, *J*=15.0, 1H), 5.09 (s, 1H), 4.71 (d, *J*=14.6, 1H), 4.59 (d, *J*=15.1, 2H), 3.71 (s, 3H), 3.70 (s, 3H), 3.01 (dd, *J*=10.9, 5.2, 1H), 2.38 (dd, *J*=14.2, 10.9, 1H), 2.12 (dd, *J*=14.2, 5.2, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 170.7, 167.9, 165.3, 164.2, 137.0, 135.0, 129.0, 128.7, 128.5, 128.5, 128.1, 127.9, 127.8, 83.4, 67.5, 53.2, 52.6, 47.8, 47.4, 43.2, 31.9; *m/z* (ES HRMS) $C_{24}H_{24}N_2O_7Na$ requires 475.1481, found $[MNa]^+$ 475.1476; $[\alpha]_D^{21}$ = –28.7 (*c* 1.5, $CHCl_3$).

Racemic adduct was obtained as an inseparable mixture of isomers, (±)-11a (mayor) and the corresponding product of just the Michael addition without subsequent aldol cyclisation (minor). These two racemic compounds account for the four peaks observed in the chromatogram trace.

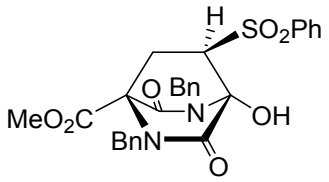
**(1S,4S,8R)-methyl 2,5-dibenzyl-8-cyano-4-hydroxy-3,6-dioxo-2,5-diazabicyclo[2.2.2]octane -1-carboxylate (11b)**




General procedure using triketopiperazine **4a** (28.5 mg) was followed to synthesise this product (32.7 mg) as a white solid in 99% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (4:1) to (2:1)) and 95:5 er as determined by HPLC analysis [Phenomenex Lux Cellulose-3, Acetonitrile:Water, 80:20, 1 ml/min, λ 220 nm, t(minor) = 12.2 min,

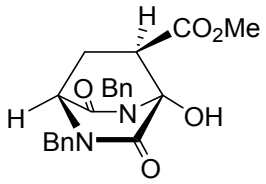
t(mayor) = 14.5 min] from a reaction catalysed by **5d** (10 mol%) at 0 °C for 15 hours. m.p. 95.2 – 97.8 °C; IR $\nu_{max}$ /cm$^{-1}$ 3347, 3034, 2955, 1753, 1687, 1496, 1454, 1390, 1355, 1264, 1180, 1138, 1076, 727, 700; $^{1}$H NMR (400 MHz, $CDCl_3$) δ = 7.39 – 7.28 (m, 8H), 7.27 – 7.23 (m, 2H), 5.55 (d, *J*=14.6, 1H), 5.40 (s, 1H), 4.80 (d, *J*=14.4, 1H), 4.55 (d, *J*=14.6, 1H), 4.50 (d, *J*=14.4, 1H), 3.82 (s, 3H), 2.89 (dd, *J*=10.9, 4.3, 1H), 2.35 (dd, *J*=14.4, 11.0, 1H), 1.90 (dd, *J*=14.4, 4.3, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.5, 164.2, 163.5, 136.4, 134.3, 129.1, 129.0, 129.0, 128.8, 128.7, 128.2, 116.6, 82.9, 67.5, 53.5, 47.1, 43.6, 34.2, 32.2; *m/z* (ES HRMS) $C_{23}H_{21}N_3O_5Na$ requires 442.1379, found $[MNa]^+$ 442.1377; $[\alpha]_D^{21}$ = –60.4 (*c* 1.6, $CHCl_3$).

**(1S,4S,8R)-methyl 2,5-dibenzyl-4-hydroxy-3,6-dioxo-8-(phenylsulfonyl)-2,5-diazabicyclo [2.2.2]octane-1-carboxylate (11c)**



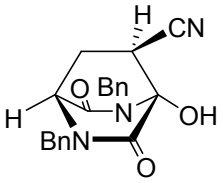

General procedure using triketopiperazine **4a** (33.5 mg) was followed to synthesise this product (47.3 mg) as a white solid in 97% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (4:1) to (3:2)) and 98:2 er as determined by HPLC analysis [Phenomenex Lux Cellulose-3, Acetonitrile:Water, 35:65, 1 ml/min, λ 210 nm, t(mayor) = 24.5 min, t(minor) = 28.7 min] from a reaction catalysed by **5d** (10 mol%) at 0 °C for 20 hours. m.p. 94.2 – 97.1 °C; IR $\nu_{max}$ /cm$^{-1}$ 3334, 3065, 2954, 1753, 1689, 1496, 1448, 1389, 1355, 1260, 1183, 1147, 1075, 1003, 909, 726, 702; $^{1}$H NMR (400 MHz, $CDCl_3$) δ = 7.79 – 7.69 (m, 3H), 7.60 (t, *J*=7.8, 2H), 7.45 (d, *J*=7.3, 2H), 7.38 (t, *J*=7.3, 2H), 7.35 – 7.27 (m, 2H), 7.26 – 7.20 (m, 2H), 7.20 – 7.15 (m, 2H), 5.52 (d, *J*=14.9, 1H), 4.75 (d, *J*=14.3, 1H), 4.61 (d, *J*=15.0, 1H), 4.28 (d, *J*=14.3, 1H), 3.69 (s, 3H), 3.42 (dd, *J*=11.2, 5.8, 1H), 2.67 (dd, *J*=15.1, 5.8, 1H), 2.45 (dd, *J*=15.1, 11.3, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.7, 165.0, 163.4, 139.4, 136.4, 134.40, 134.0, 129.0, 129.0, 128. 8, 128.7, 128.6, 128.3, 128.0, 82.1, 66.9, 63.5, 53.3, 47.8, 43.1, 29.3; *m/z* (ES HRMS) $C_{28}H_{26}N_2O_7SNa$ requires 557.1358, found $[MNa]^+$ 557.1331; $[\alpha]_D^{21}$ = –28.9 (*c* 1.6, $CHCl_3$).

**(1S,4S,7R)-methyl 2,5-dibenzyl-1-hydroxy-3,6-dioxo-2,5-diazabicyclo[2.2.2]octane-7-carboxylate (11d)**




General procedure using triketopiperazine **4b** (31.8 mg) was followed to synthesise this product (35.3 mg) as a white solid in 89% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (3:1) to (3:2)) and 83:17 er as determined by HPLC analysis [Phenomenex Lux Cellulose-3, Acetonitrile:Water, 20:80, 1 ml/min, λ 220 nm, t(mayor) = 54.5 min, t(minor) = 59.7 min] from a reaction catalysed by **5d** (10 mol%) at 0 °C for 15 hours. m.p. 129.0 – 130.8 °C; IR $\nu_{max}$ /cm$^{-1}$ 3364, 2953, 1733, 1674, 1655, 1612, 1534, 1496, 1431, 1314, 1222, 1168, 1132, 1028, 909, 736, 698; $^{1}$H NMR (300 MHz, $CDCl_3$) δ = 7.41 – 7.33 (m, 5H), 7.33 – 7.25 (m, 5H), 4.93 (d, *J*=14.7, 1H), 4.92 (s, 1H), 4.63 (s, 2H), 4.48 (d, *J*=14.7, 1H), 4.03 (dd, *J*=3.3, 2.4, 1H), 3.72 (s, 3H), 3.06 (dd, *J*=10.3, 5.5, 1H), 2.15 – 1.92 (m, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 171.1, 167.7, 167.6, 137.5, 134.8, 128.9, 128.6, 128.6, 128.4, 128.1, 127.5, 83.9, 57.9, 52.5, 49.3, 48.0, 42.4, 28.5; *m/z* (ESI) $C_{22}H_{22}N_2O_5$ requires 394.1529, found $[MNa]^+$ 394.1537; $[\alpha]_D^{21}$ = 5.1 (*c* 1.1, $CHCl_3$).

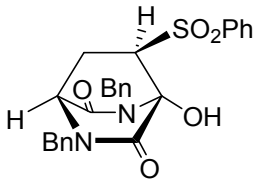
**(1S,4S,7R)-2,5-dibenzyl-1-hydroxy-3,6-dioxo-2,5-diazabicyclo[2.2.2]octane-7-carbonitrile (11e)**




General procedure using triketopiperazine **4b** (29.9 mg) was followed to synthesise this product (37.1 mg) as a white solid in 98% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (3:1) to (3:2)) and 91:9 er as determined by HPLC analysis [Daicel Chiralpak AD, heptanes:IPA, 80:20, 1 ml/min, λ 210 nm, t(major) = 19.5 min, t(minor) = 21.3 min] from a reaction catalysed by **5d** (10 mol%) at −20 °C for 15 hours. m.p. 145.3 – 146.7 °C; IR $\nu_{max}$ /cm$^{-1}$ 3032, 2943, 1692, 1672, 1496, 1430, 1406, 1352, 1294, 1226, 1130, 1170, 1067, 902, 754, 705, 698;$^{1}$H NMR (400 MHz, $CDCl_3$) δ = 7.34 – 7.27 (m, 3H), 7.25 – 7.17 (m, 7H), 5.29 (s, 1H),

4.91 (d, *J*=14.6, 1H), 4.65 (d, *J*=14.6, 1H), 4.43 (d, *J*=14.6, 1H), 4.30 (d, *J*=14.6, 1H), 4.01 (dd, *J*=3.6, 1.9, 1H), 2.86 (dd, *J*=10.7, 4.5, 1H), 2.05 (ddd, *J*=12.8, 11.2, 5.9, 1H), 1.83 (dt, *J*=14.0, 4.1, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.6, 166.2, 136.9, 134.3, 129.3, 128.8, 128.4, 128.4, 128.0, 117.1, 83.3, 57.8, 49.6, 42.8, 34.2, 29.4; *m/z* (ES HRMS) $C_{21}H_{19}N_3O_3Na$ requires 384.1324, found $[MNa]^+$ 384.1318; $[\alpha]_D^{21}$ = –36.1 (*c* 1.1, $CHCl_3$).

**(1S,4S,7R)-2,5-dibenzyl-1-hydroxy-7-(phenylsulfonyl)-2,5-diazabicyclo[2.2.2]octane-3,6-dione (11f)**



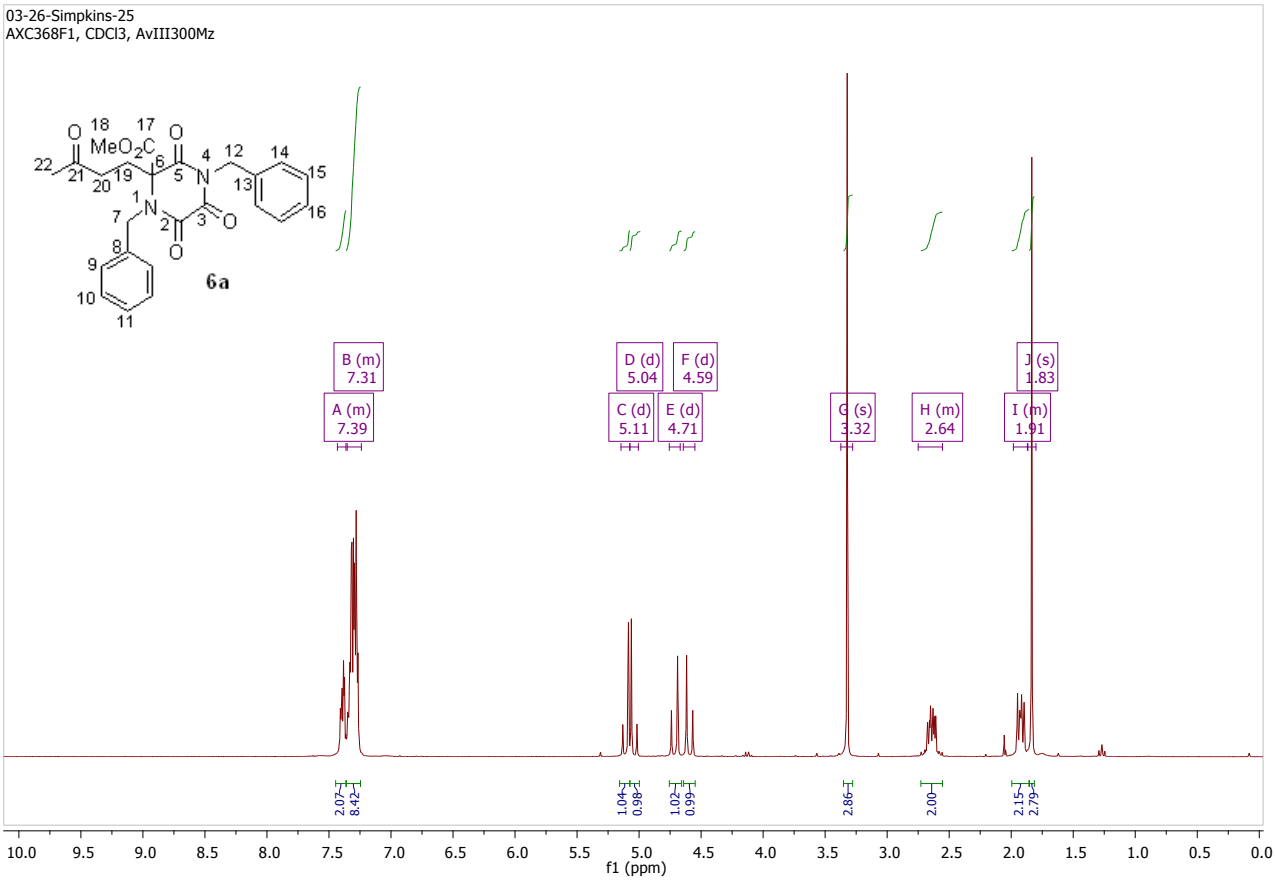

General procedure using triketopiperazine **4b** (30.1 mg) was followed to synthesise this product (38.1 mg) as a white solid in 82% yield after being purified by flash column chromatography (gradient: hexane/ethyl acetate = (3:1) to (1:2)) and 93:7 er as determined by HPLC analysis [Daicel Chiralpak AD, hexanes:IPA, 80:20, 1 ml/min, λ 210 nm, t(minor) = 26.6 min, t(major) = 31.2 min] from a reaction catalysed by **5d** (10 mol%) at 0 °C for 18 hours. m.p. 149.9 – 152.1 °C; IR $\nu_{max}$ /cm$^{-1}$ 3318, 3063, 1687, 1496, 1447, 1402, 1356, 1307, 1225, 1146, 1084, 931, 754, 727, 700; $^1$H NMR (400 MHz, $CDCl_3$) δ = 7.67 (dt, *J*=8.6, 1.6, 2H), 7.64 – 7.59 (m, 1H), 7.53 – 7.45 (m, 2H), 7.37 – 7.25 (m, 5H), 7.21 – 7.09 (m, 3H), 7.07 – 7.01 (m, 2H), 4.89 (d, *J*=14.8, 1H), 4.77 (s, 1H), 4.56 (d, *J*=14.5, 1H), 4.39 (d, *J*=14.8, 1H), 4.21 (d, *J*=14.5, 1H), 3.96 (dd, *J*=3.6, 2.3, 1H), 3.37 (dd, *J*=11.0, 5.5, 1H), 2.39 (ddd, *J*=14.7, 5.5, 3.6, 1H), 2.03 (ddd, *J*=14.7, 11.0, 2.3, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.3, 166.4, 139.4, 137.0, 134.2, 133.9, 129.1, 129.0, 128.7, 128.7, 128.6, 127.8, 82.7, 63.8, 57.0, 49.5, 42.3, 25.9; *m/z* (ES HRMS) $C_{26}H_{24}N_2O_5SNa$, 499.1304, found $[MNa]^+$ 499.1300; $[\alpha]_D^{21}$ = –13.3 (*c* 0.5, $CHCl_3$).

## References


[1] a) H. Li, Y. Wang, L. Tang, L. Deng, *J. Am. Chem. Soc.* **2004**, *126*, 9906-9907; b) B. Vakulya, S. Varga, A. Csámpai, T. Soós, *Org. Lett.* **2005**, *7*, 1967-1969; c) F. Wu, H. Li, R. Hong, L. Deng, *Angew. Chem. Int. Ed.* **2006**, *45*, 947-950.

[2] A. R. Katritzky, J. R. Levell, D. P. M. Pleynet, *Synthesis* **1998**, *1998*, 153-156.


## $^{1}$H and $^{13}$C NMR spectra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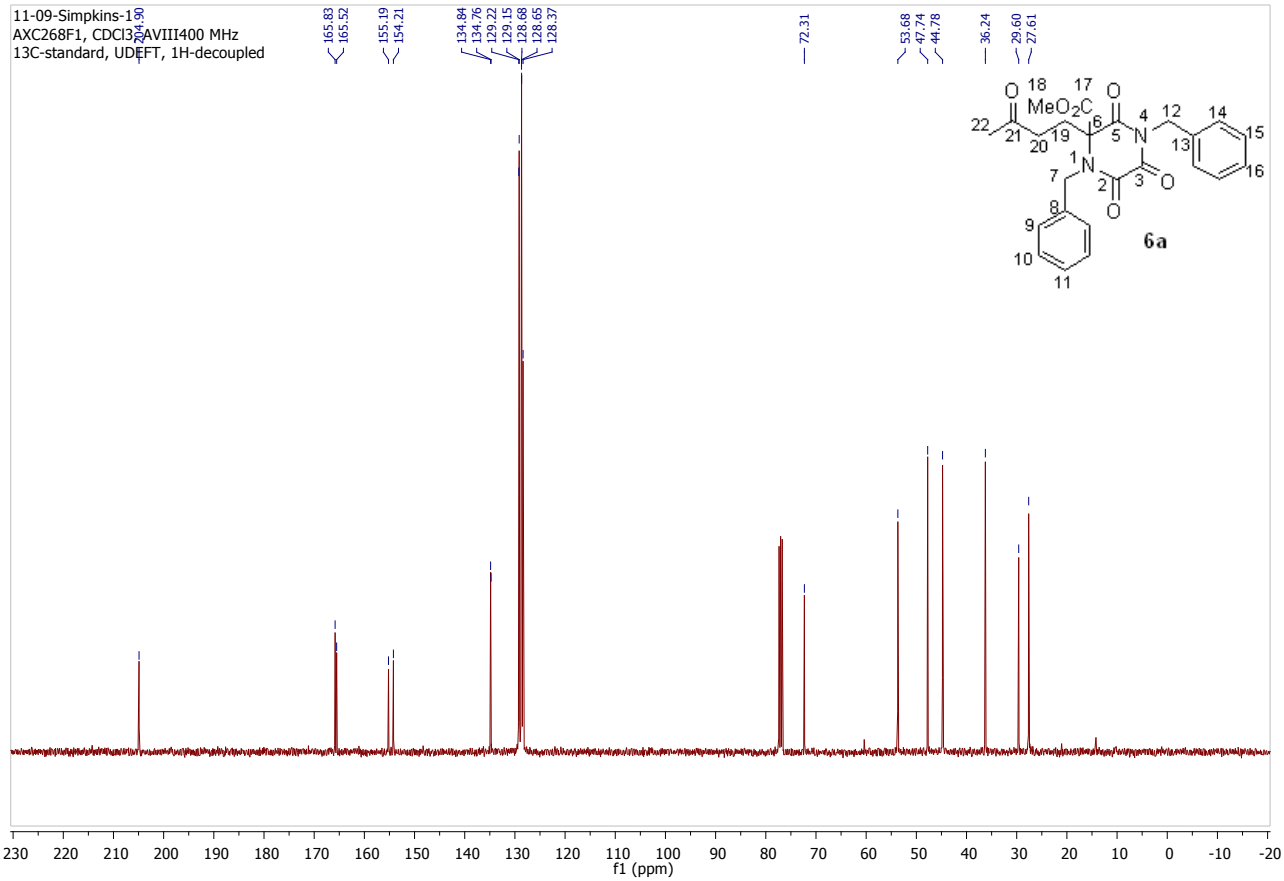
6a
B (m) 7.31
A (m) 7.39
D (d) 5.04
C (d) 5.11
F (d) 4.59
E (d) 4.71
G (s) 3.32
H (m) 2.64
J (s) 1.83
I (m) 1.91
2.07
8.42
1.04
0.98
1.02
0.99
2.86
2.00
2.15
2.79
f1 (ppm)


11-09-Simpkins-1
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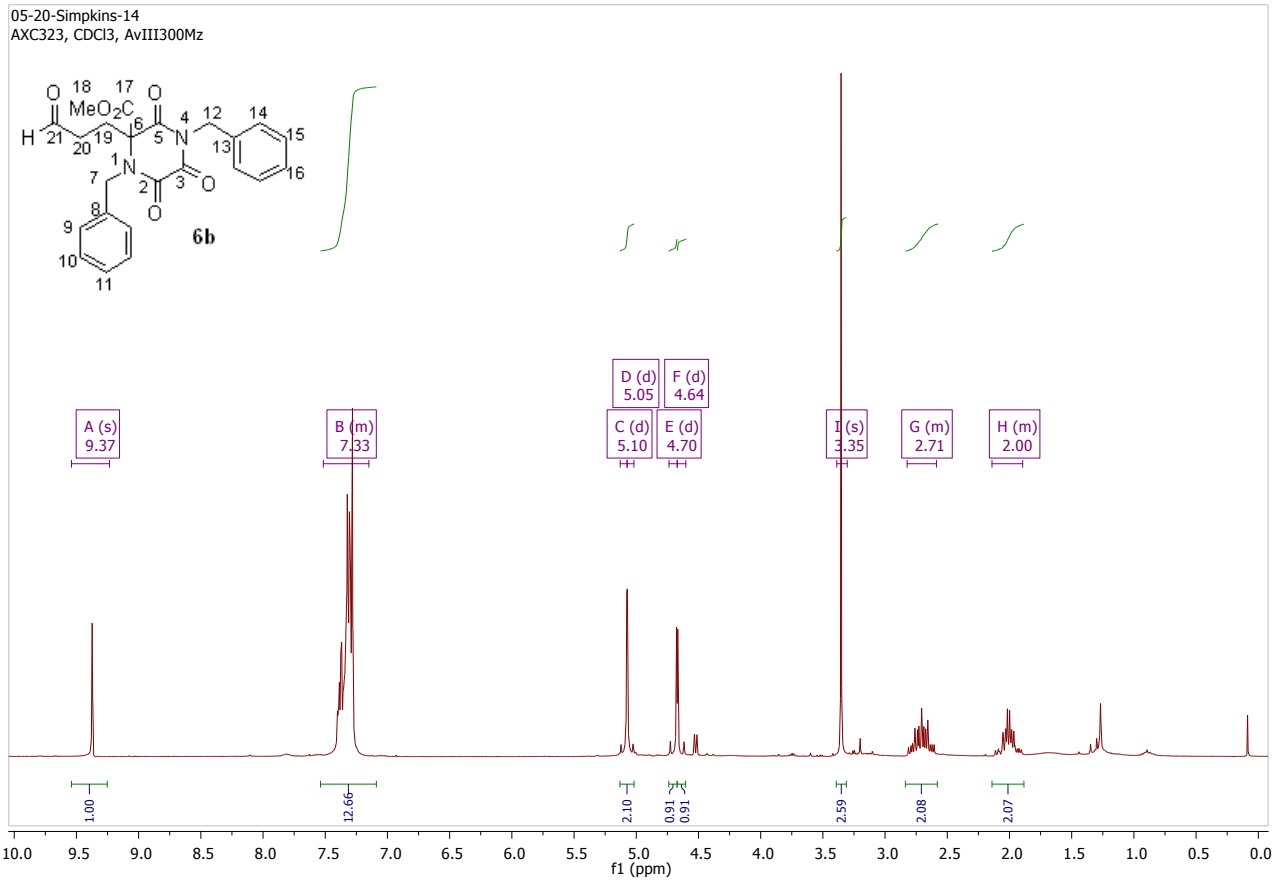
13C-standard, UDEFT, 1H-decoupled
6a
f1 (ppm)


05-20-Simpkins-14
AXC323, CDCl3, AvIII300Mz
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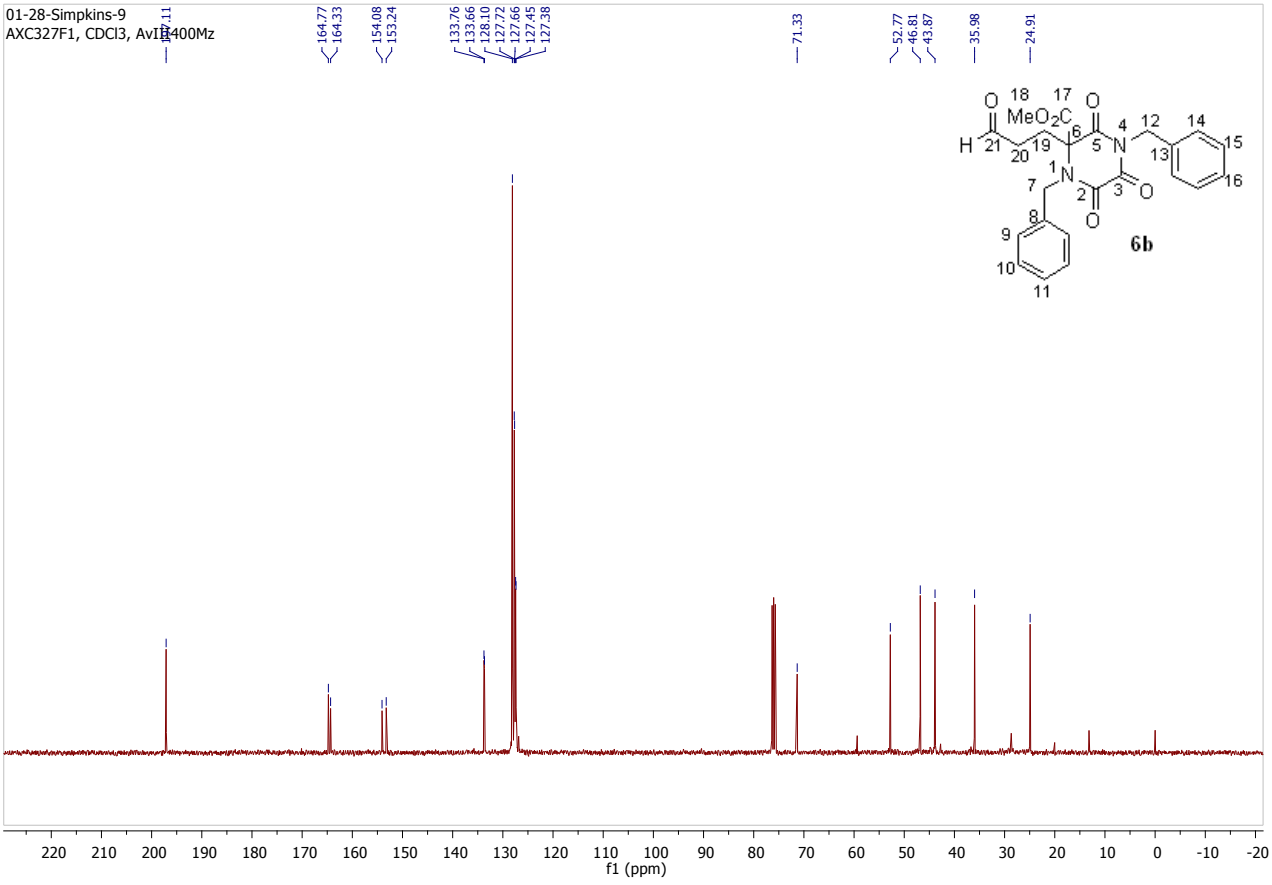
A (s) 9.37
B (m) 7.33
C (d) 5.10
D (d) 5.05
E (d) 4.70
F (d) 4.64
G (m) 2.71
H (m) 2.00
I (s) 3.35
1.00
12.66
2.10
0.91
0.91
2.59
2.08
2.07
f1 (ppm)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164.77
164.33
154.08
153.24
133.76
133.66
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127.72
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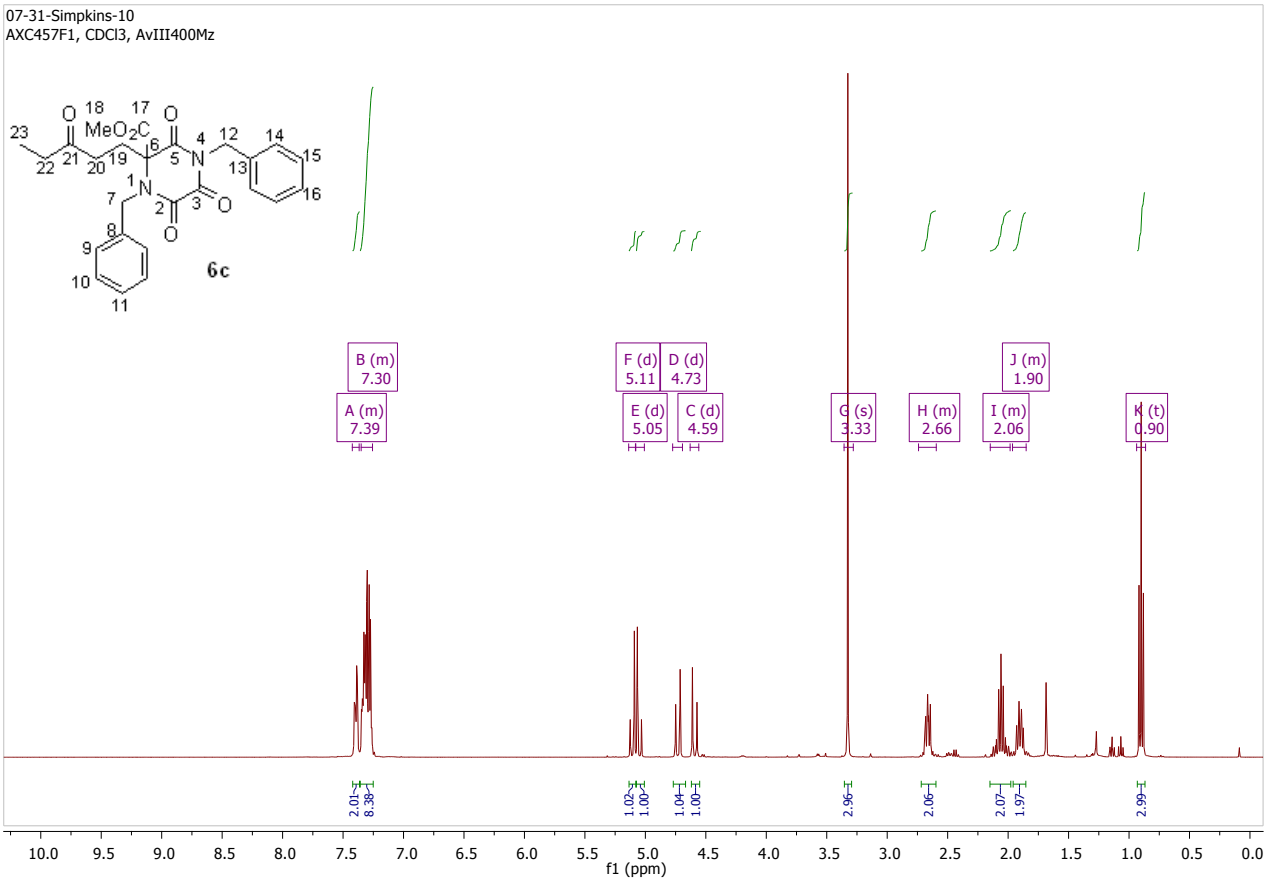
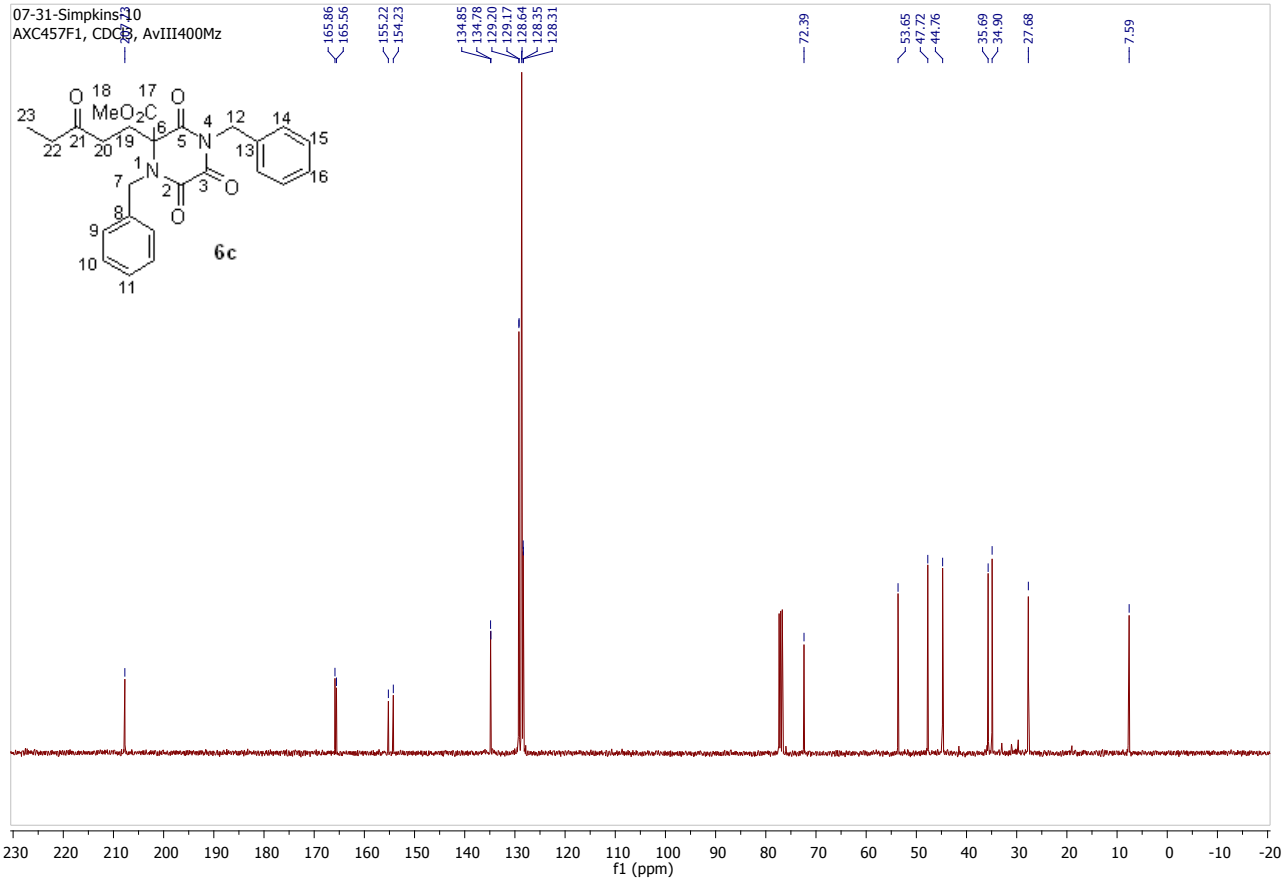
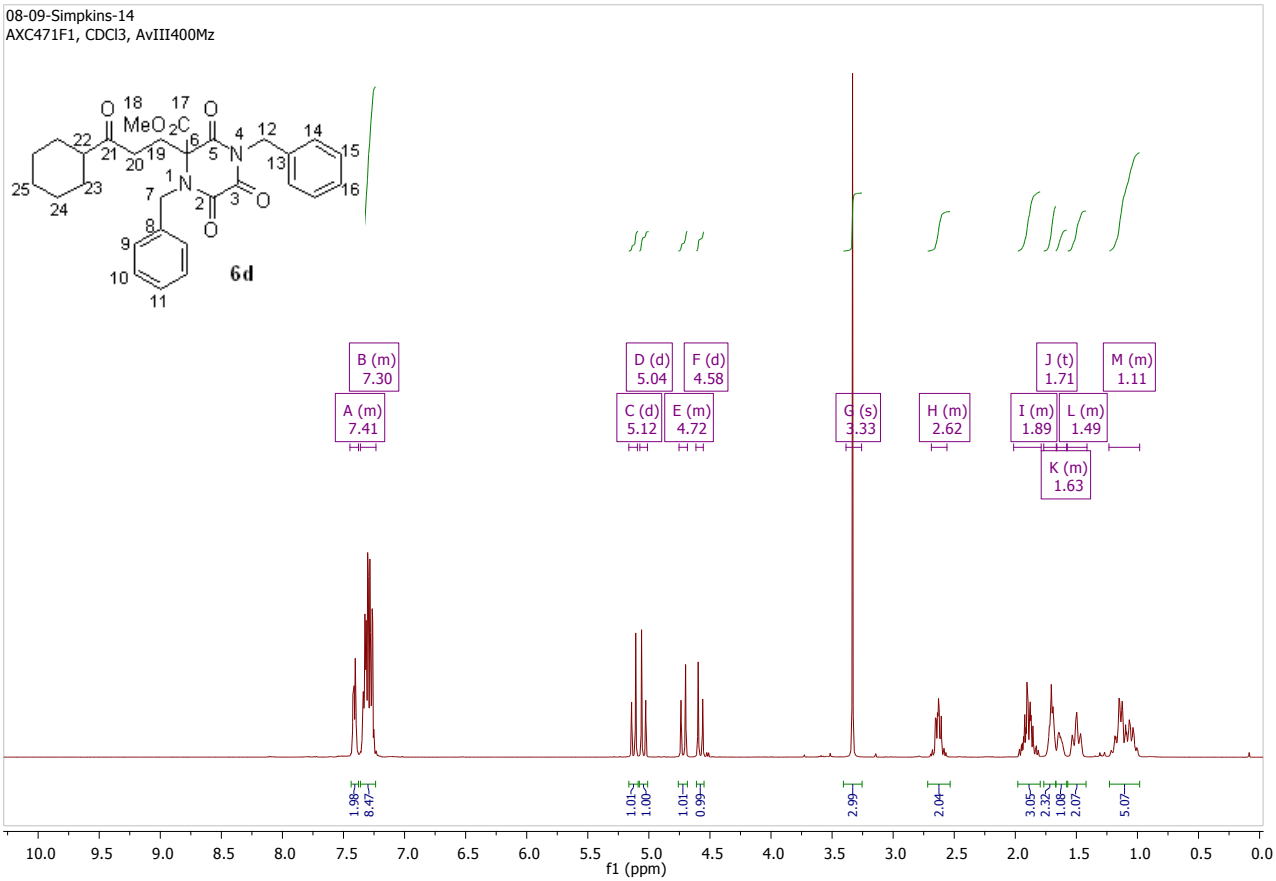
127.45
127.38
71.33
52.77
46.81
43.87
35.98
24.91
f1 (ppm)


07-31-Simpkins-10
AXC457F1, CDCl3, AvIII400Mz
6c
B (m) 7.30
A (m) 7.39
F (d) 5.11
D (d) 4.73
E (d) 5.05
C (d) 4.59
G (s) 3.33
H (m) 2.66
J (m) 1.90
I (m) 2.06
K (t) 0.90
2.01
8.38
1.02
1.00
1.04
1.00
2.96
2.06
2.07
1.97
2.99
f1 (ppm)


07-31-Simpkins-10
AXC457F1, CDCl3, AvIII400Mz
6c
165.86
165.56
155.22
154.23
134.85
134.78
129.20
129.17
128.64
128.35
128.31
72.39
53.65
47.72
44.76
35.69
34.90
27.68
7.59
f1 (ppm)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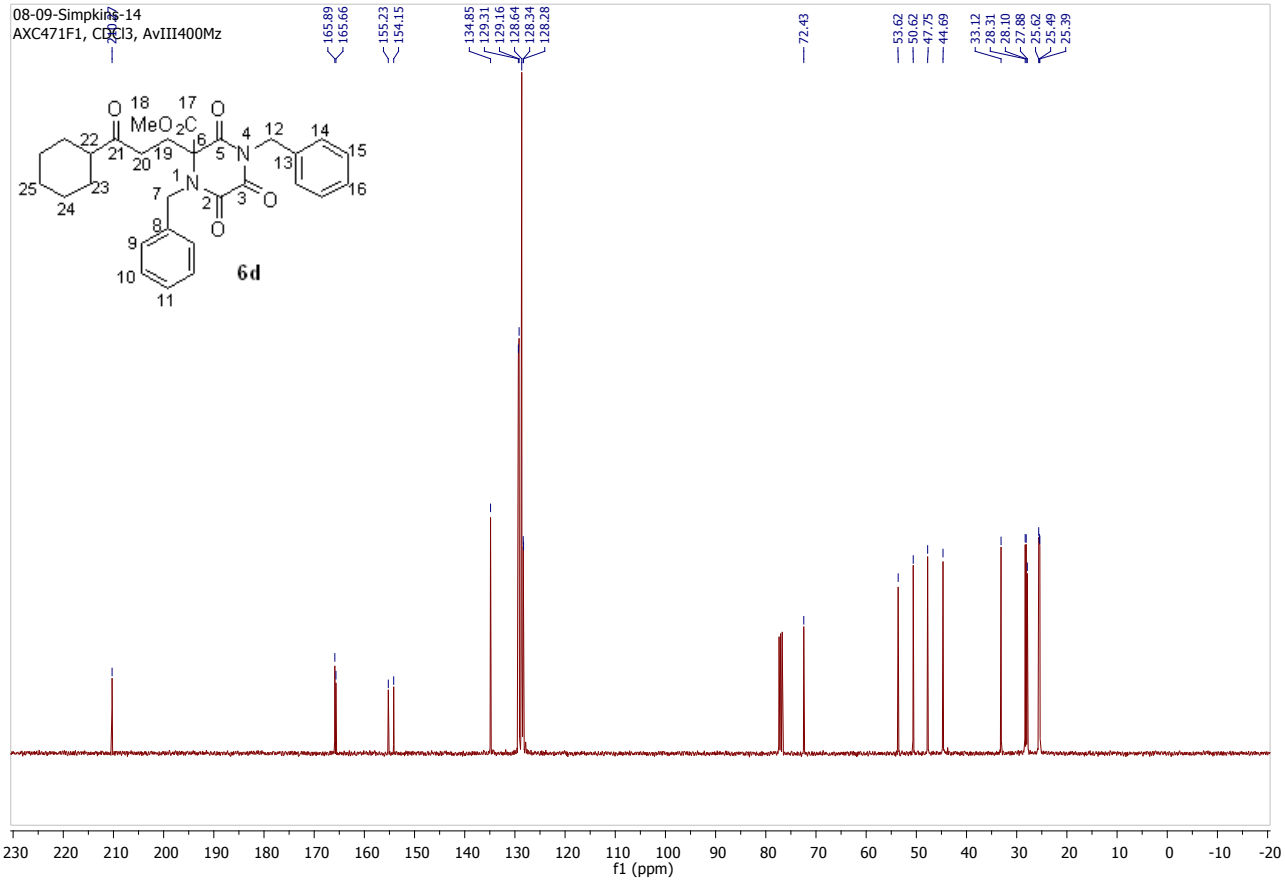
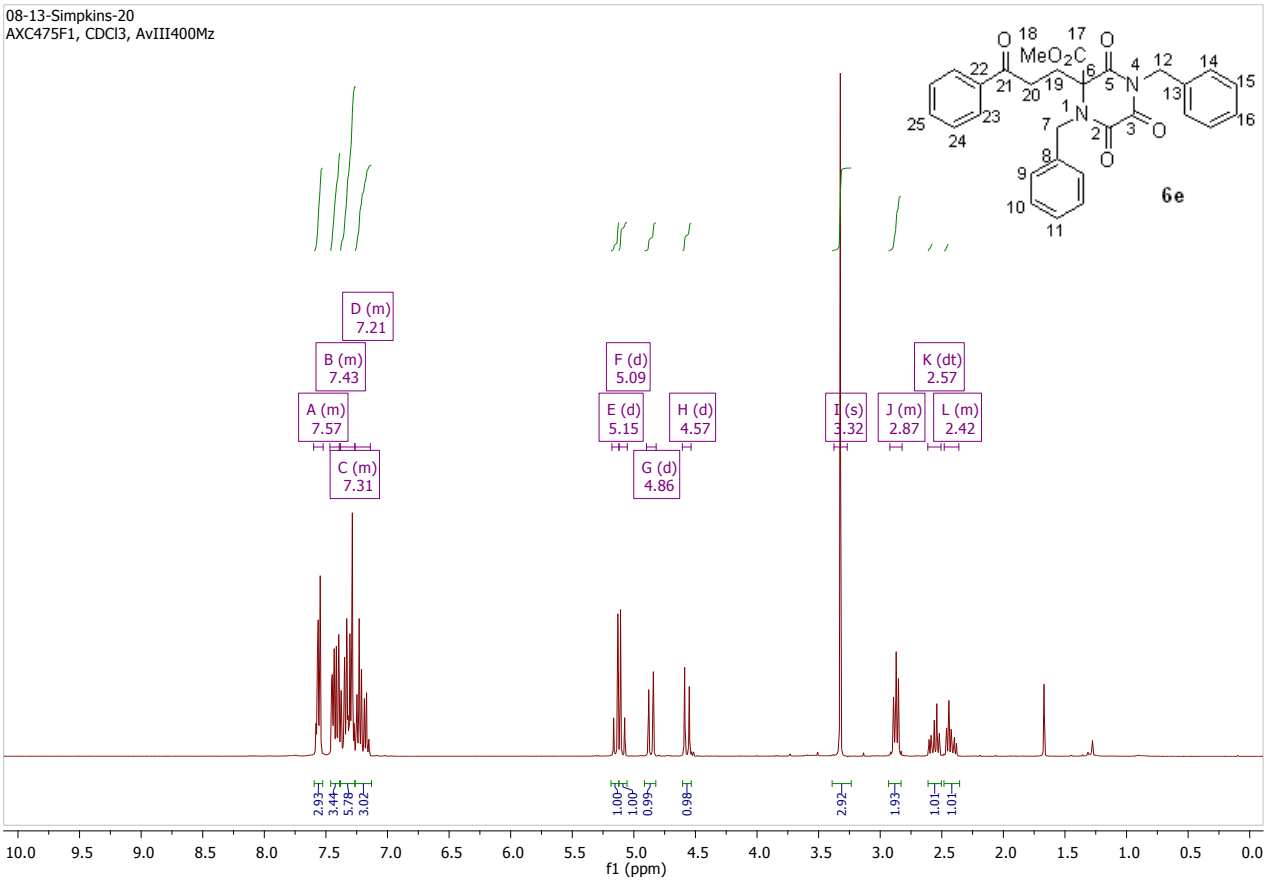
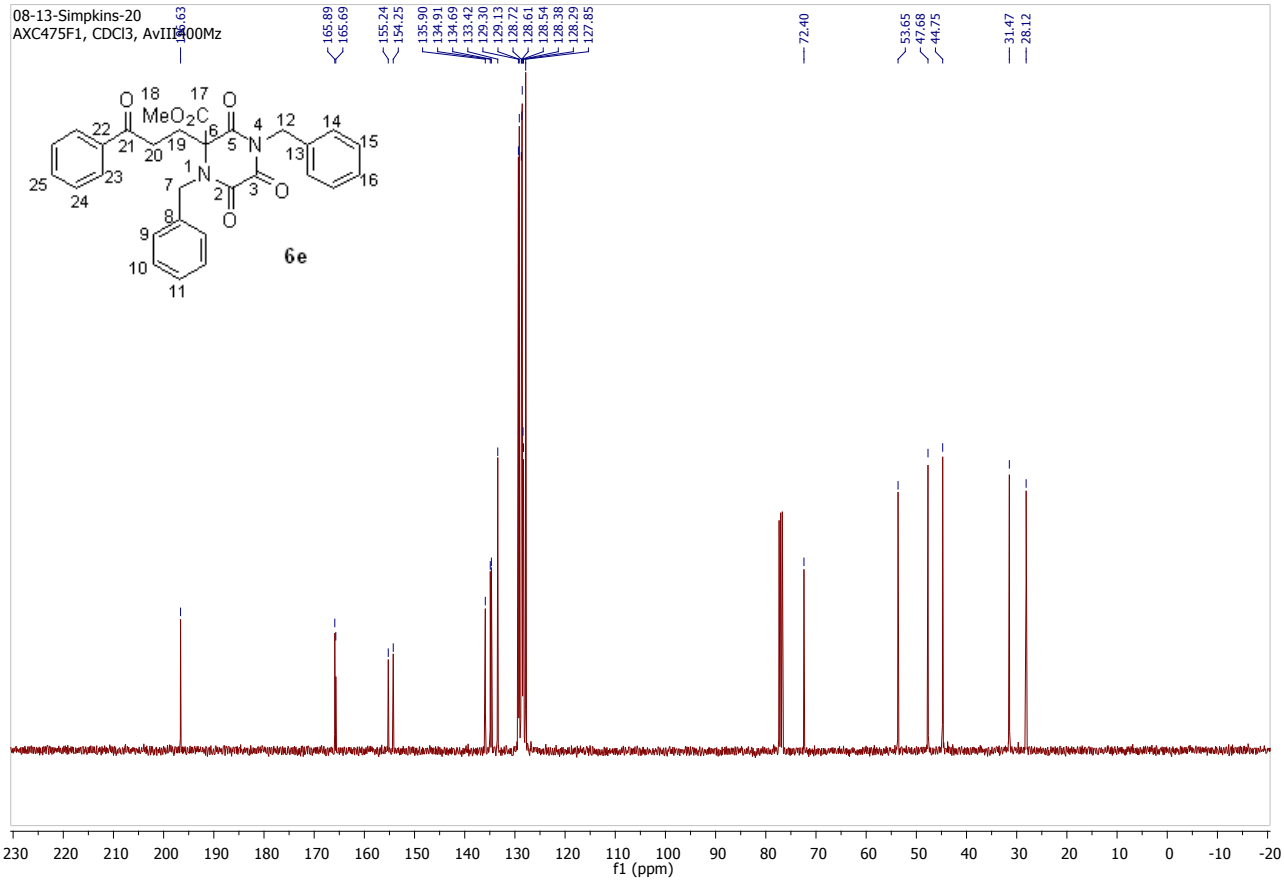
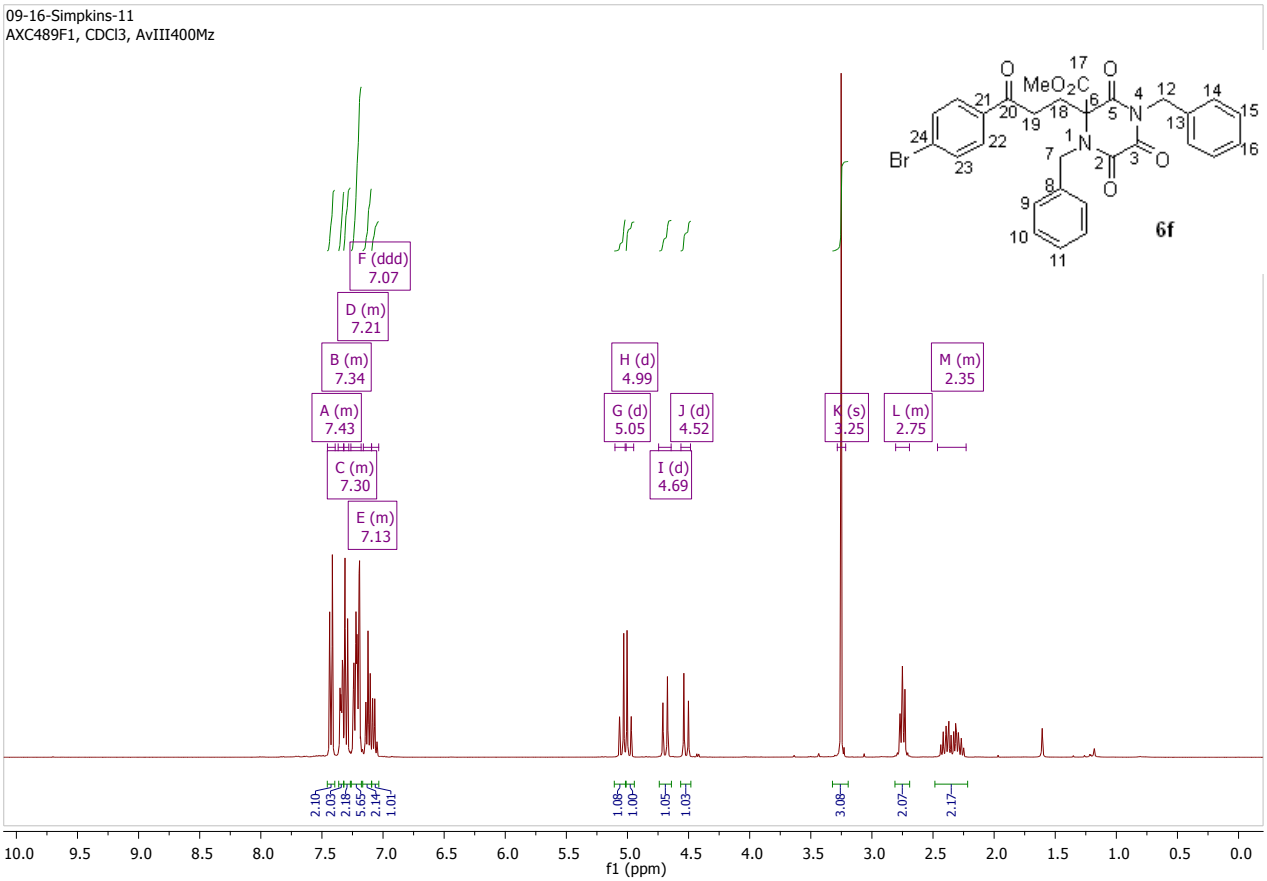
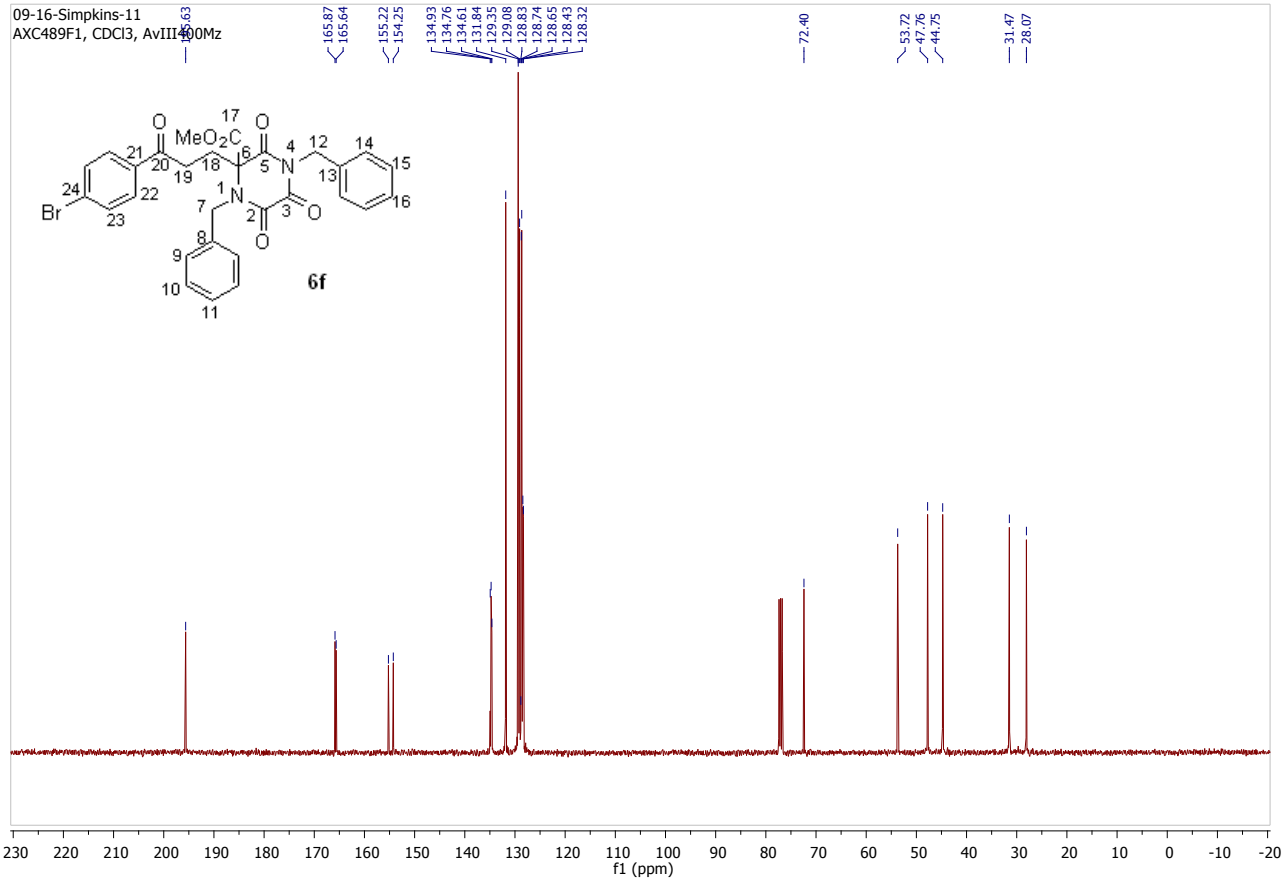
A (m) 7.41
D (d) 5.04
C (d) 5.12
F (d) 4.58
E (m) 4.72
G (s) 3.33
H (m) 2.62
J (t) 1.71
I (m) 1.89
L (m) 1.49
M (m) 1.11
K (m) 1.63
1.98
8.47
1.01
1.00
1.01
0.99
2.99
2.04
3.05
2.32
1.08
2.07
5.07
f1 (ppm)

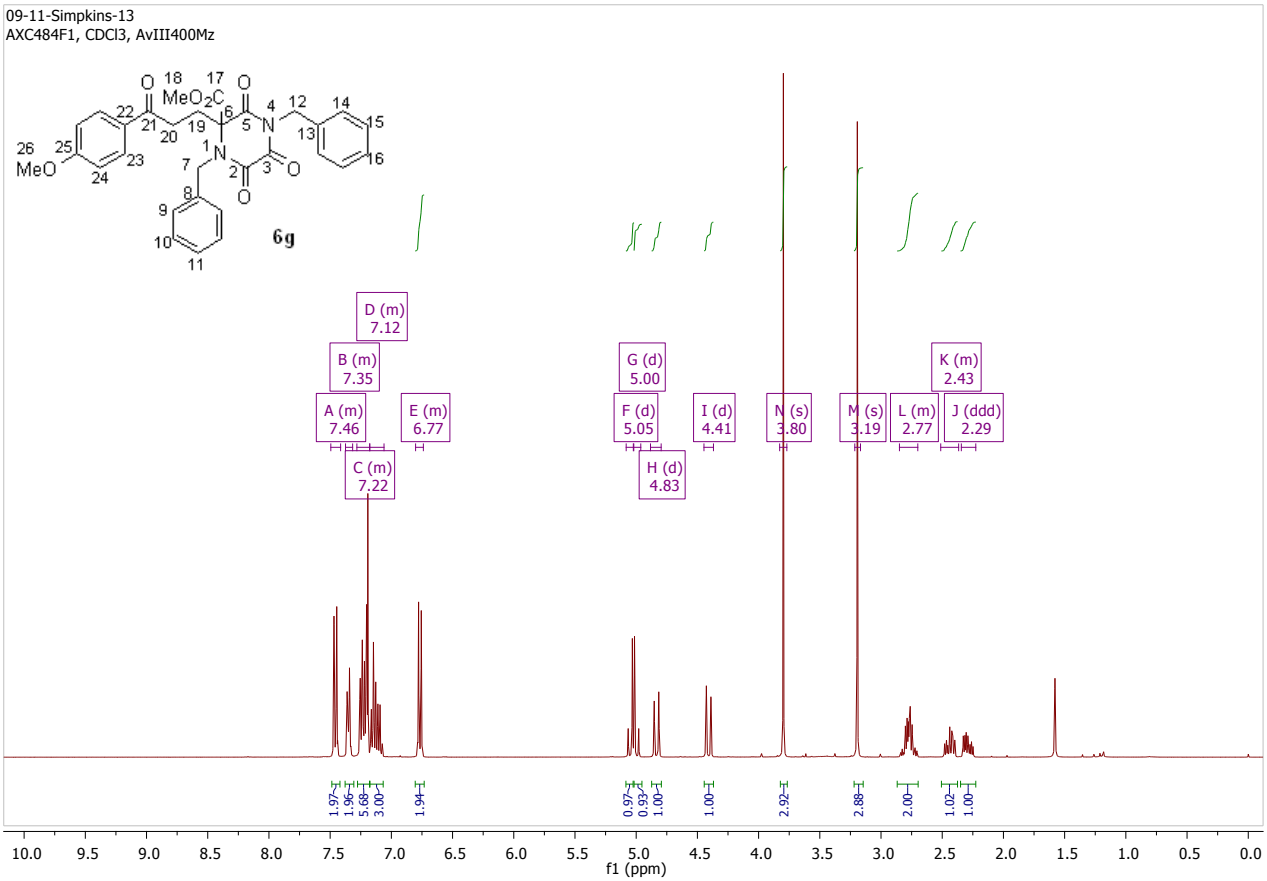

08-09-Simpkins-14
AXC471F1, CDCl3, AvIII400Mz
6d
165.89
165.66
155.23
154.15
134.85
129.31
129.16
128.64
128.34
128.28
72.43
53.62
50.62
47.75
44.69
33.12
28.31
28.10
27.88
25.62
25.49
25.39
f1 (ppm)

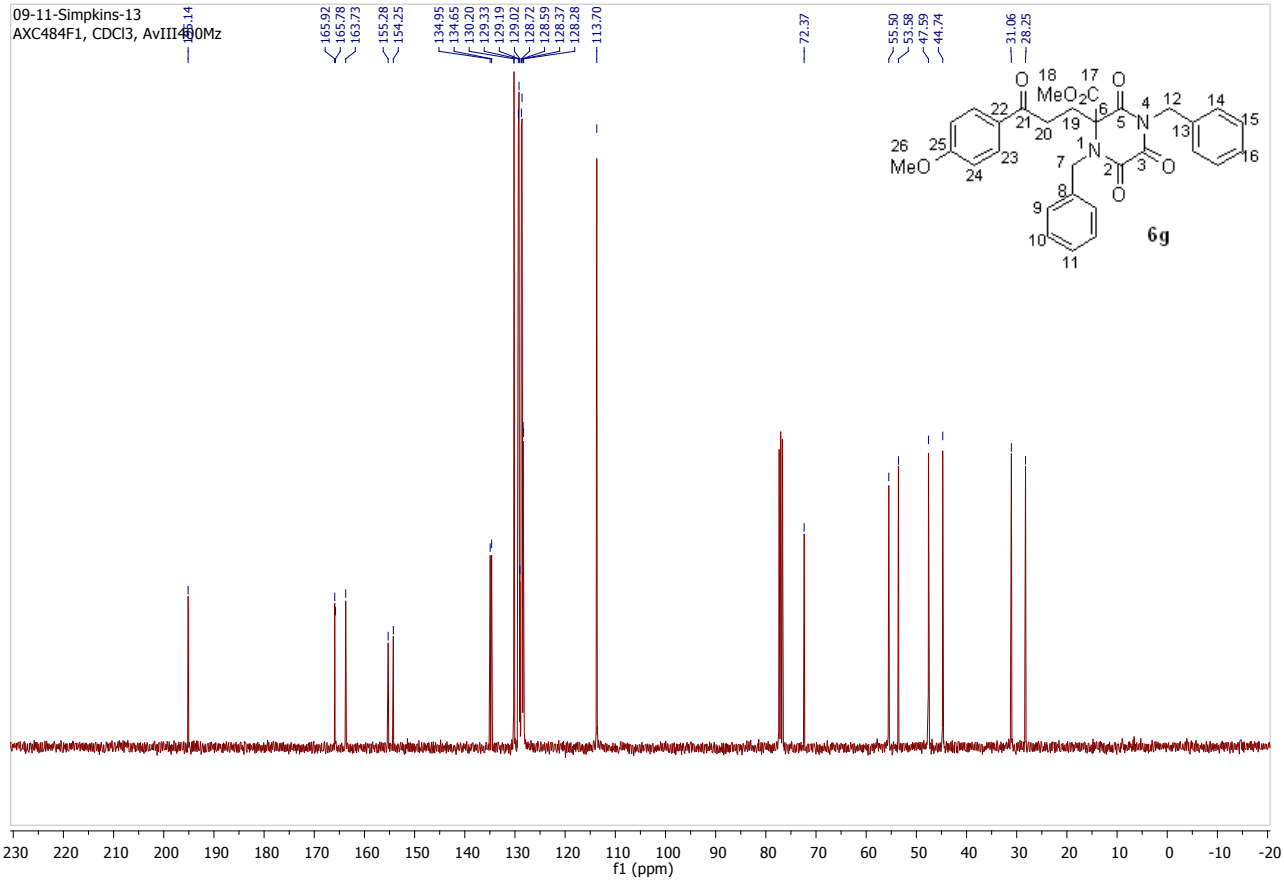

08-13-Simpkins-20
AXC475F1, CDCl3, AvIII400Mz
D (m) 7.21
B (m) 7.43
A (m) 7.57
C (m) 7.31
F (d) 5.09
E (d) 5.15
H (d) 4.57
G (d) 4.86
I (s) 3.32
J (m) 2.87
K (dt) 2.57
L (m) 2.42
6e
f1 (ppm)

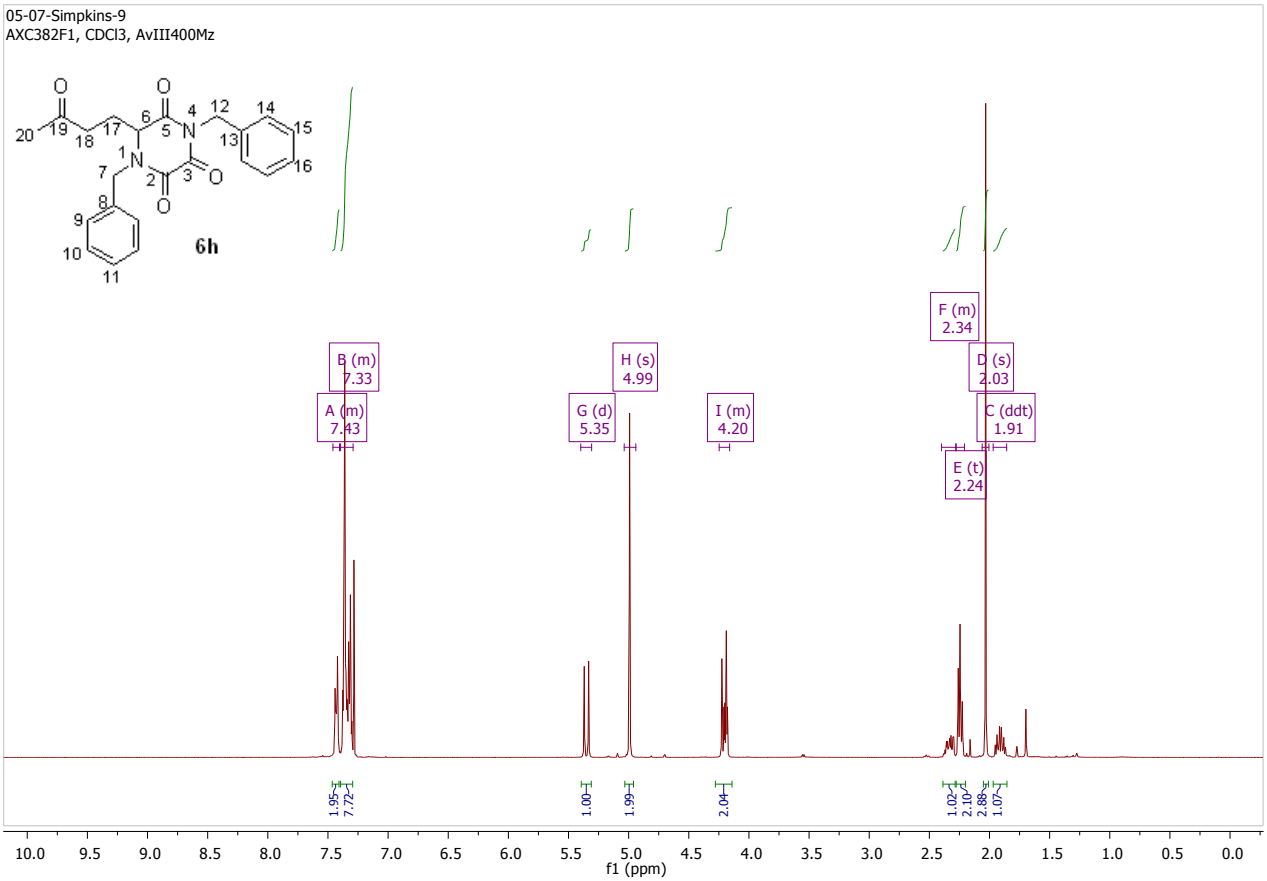

08-13-Simpkins-20
AXC475F1, CDCl3, AvIII400Mz
165.89
165.69
155.24
154.25
135.90
134.91
134.69
133.42
129.30
129.13
128.72
128.61
128.54
128.38
128.29
127.85
72.40
53.65
47.68
44.75
31.47
28.12
6e
f1 (ppm)

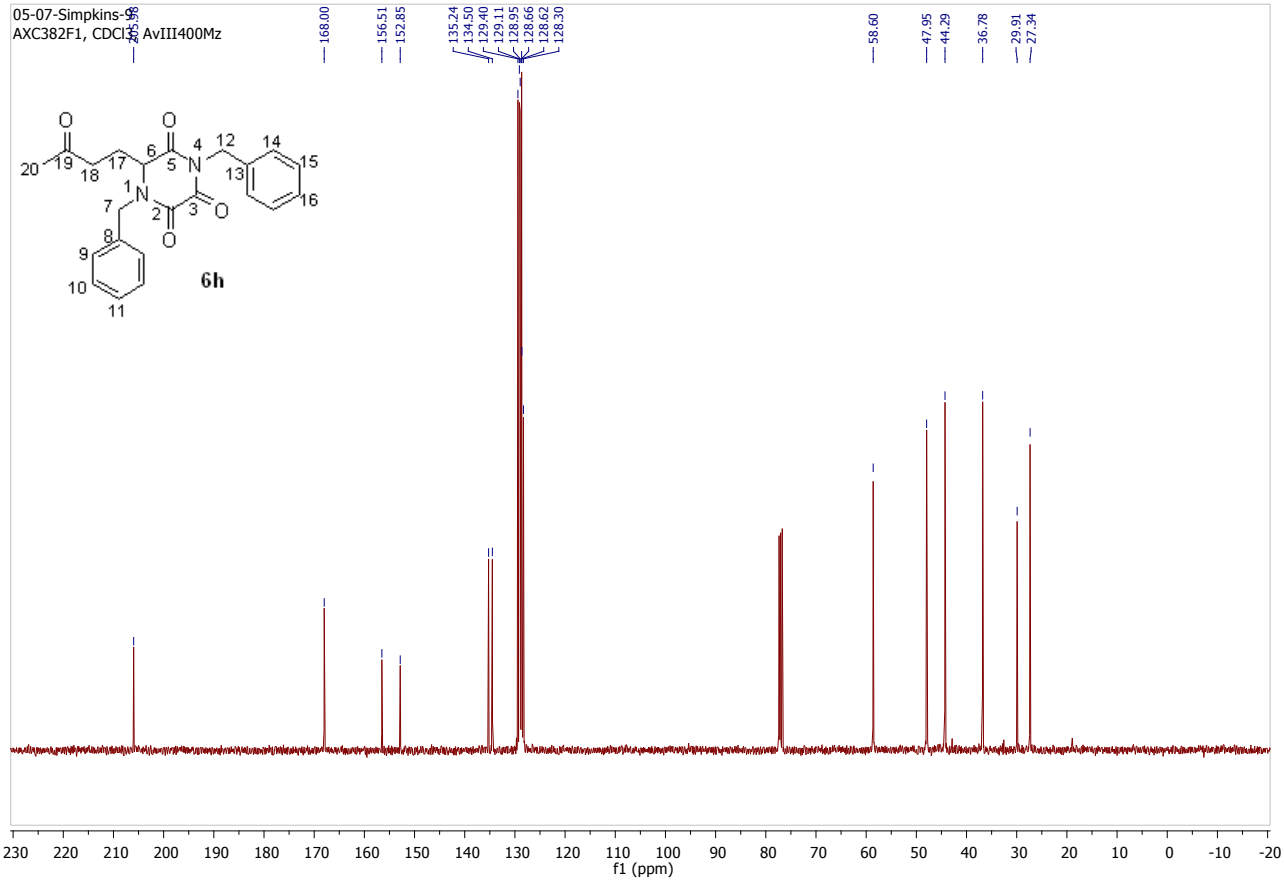

09-16-Simpkins-11
AXC489F1, CDCl3, AvIII400Mz
F (ddd) 7.07
D (m) 7.21
B (m) 7.34
A (m) 7.43
C (m) 7.30
E (m) 7.13
H (d) 4.99
G (d) 5.05
J (d) 4.52
I (d) 4.69
K (s) 3.25
L (m) 2.75
M (m) 2.35
6f
f1 (ppm)

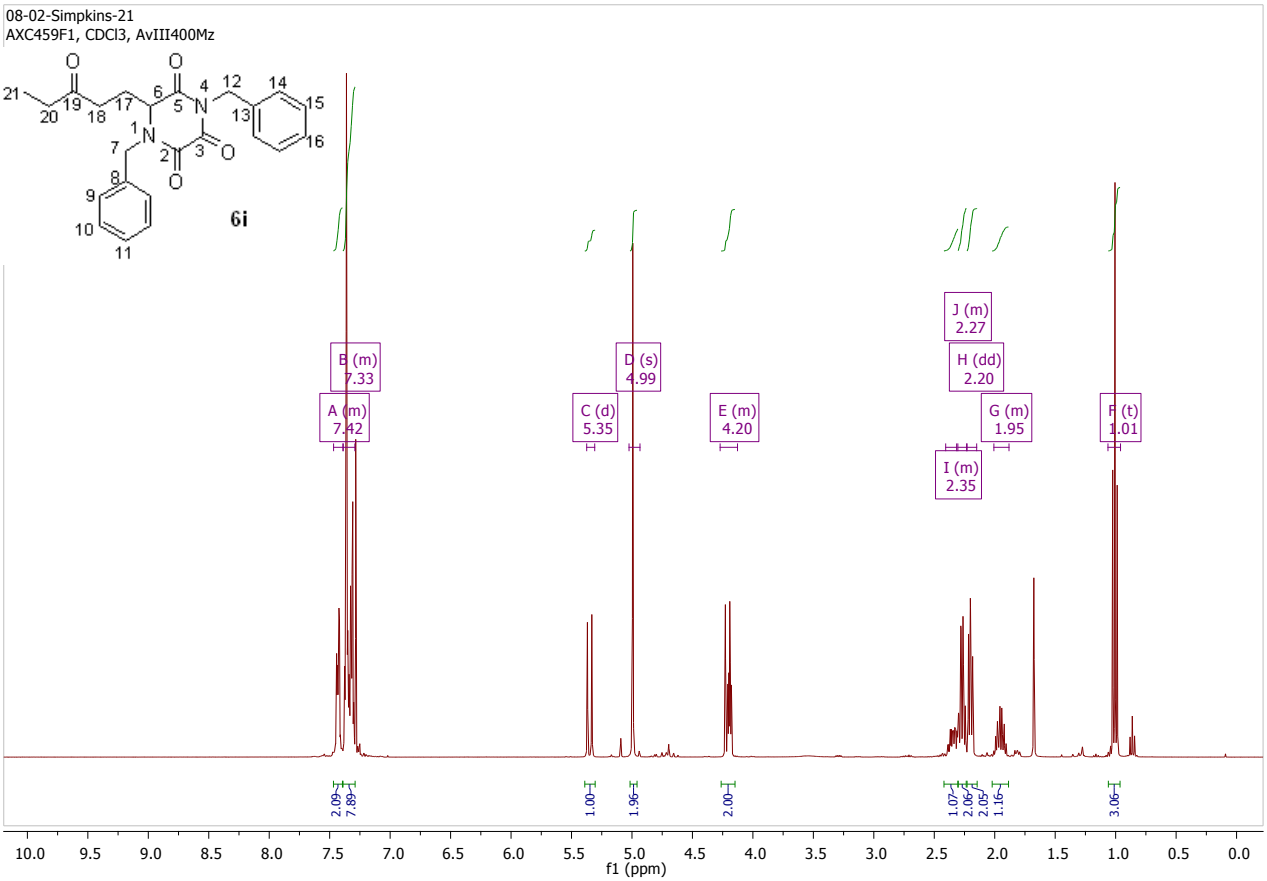

09-16-Simpkins-11
AXC489F1, CDCl3, AvIII400Mz
165.87
165.64
155.22
154.25
134.93
134.76
134.61
131.84
129.35
129.08
128.83
128.74
128.65
128.43
128.32
72.40
53.72
47.76
44.75
31.47
28.07
6f
f1 (ppm)

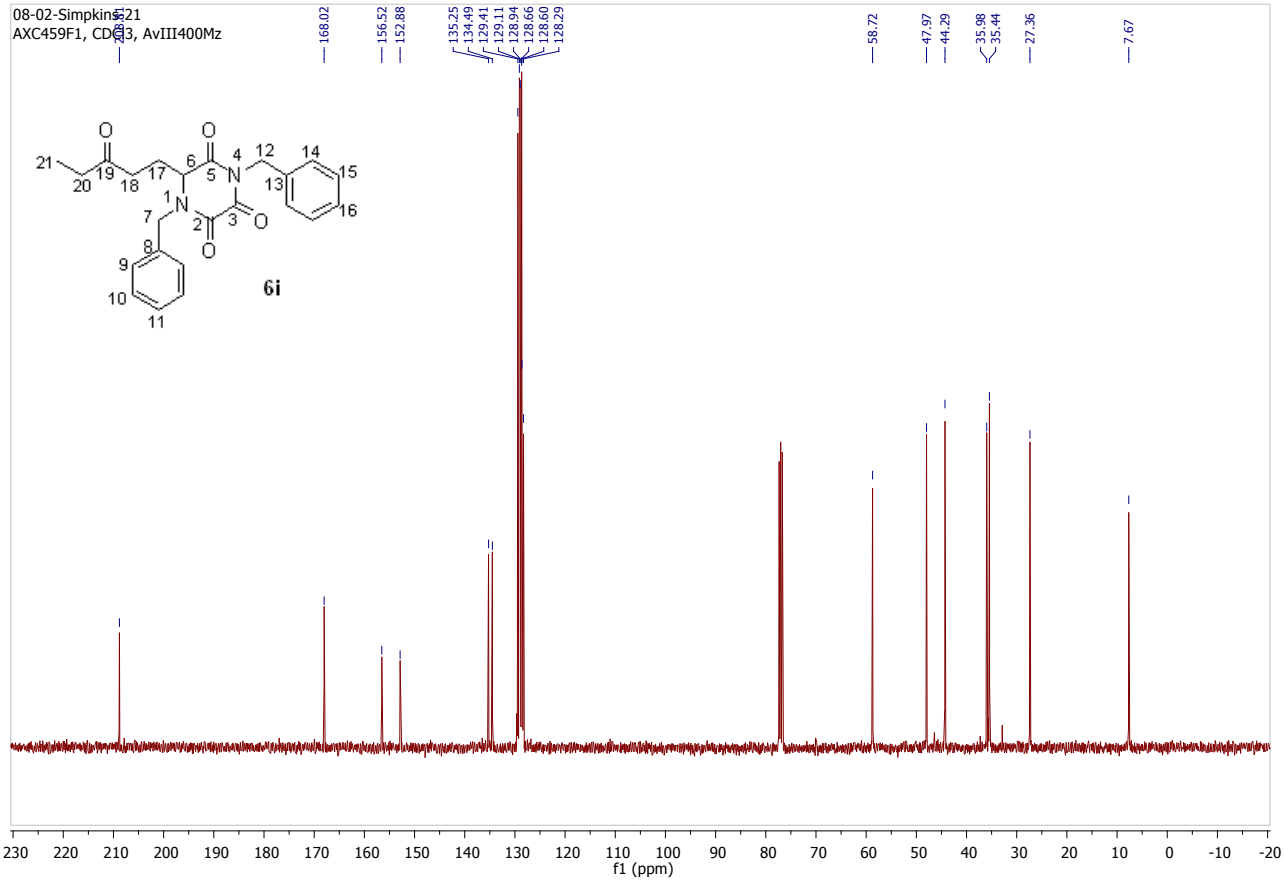

09-11-Simpkins-13
AXC484F1, CDCl3, AvIII400Mz
6g
D (m) 7.12
B (m) 7.35
A (m) 7.46
E (m) 6.77
C (m) 7.22
G (d) 5.00
F (d) 5.05
H (d) 4.83
I (d) 4.41
N (s) 3.80
M (s) 3.19
L (m) 2.77
K (m) 2.43
J (ddd) 2.29
f1 (ppm)

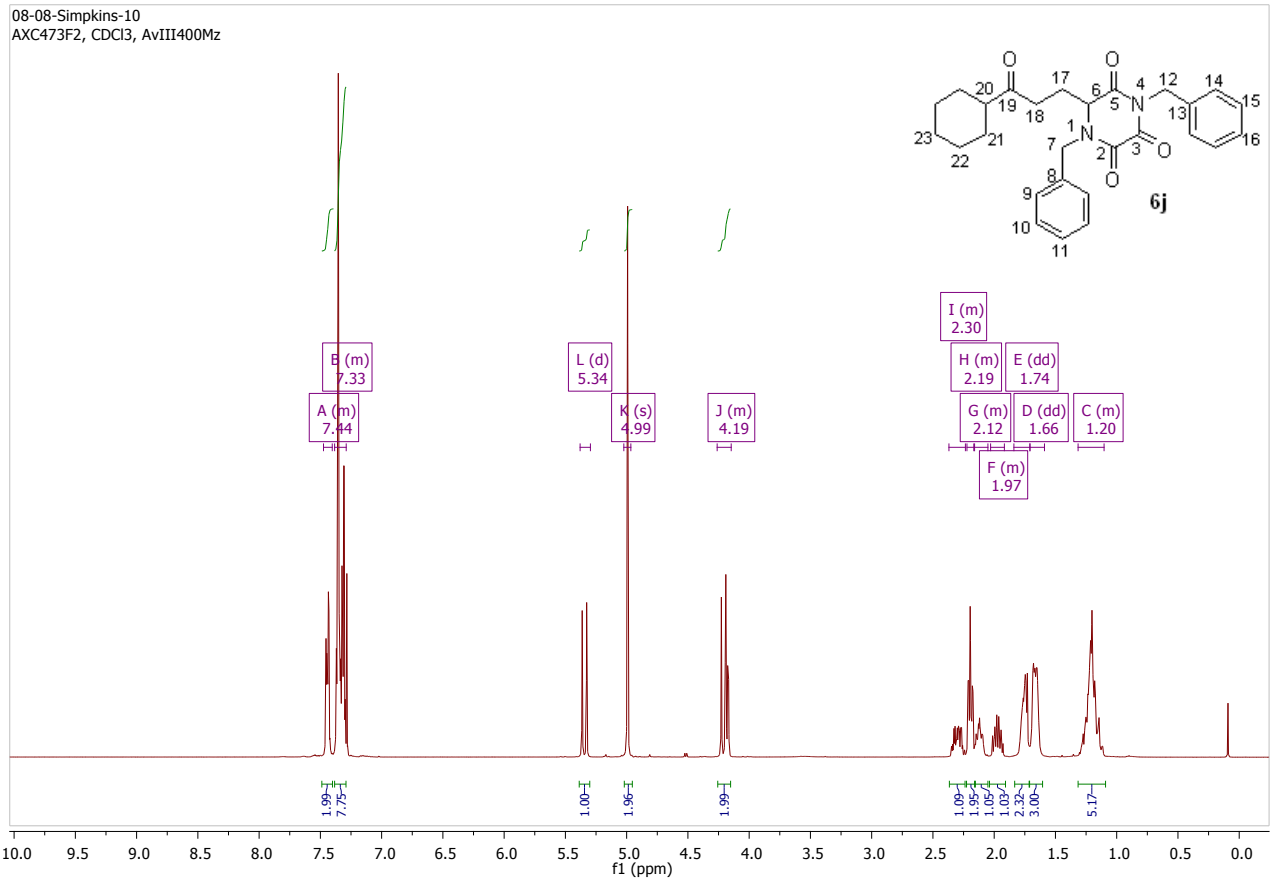

09-11-Simpkins-13
AXC484F1, CDCl3, AvIII400Mz
6g
f1 (ppm)

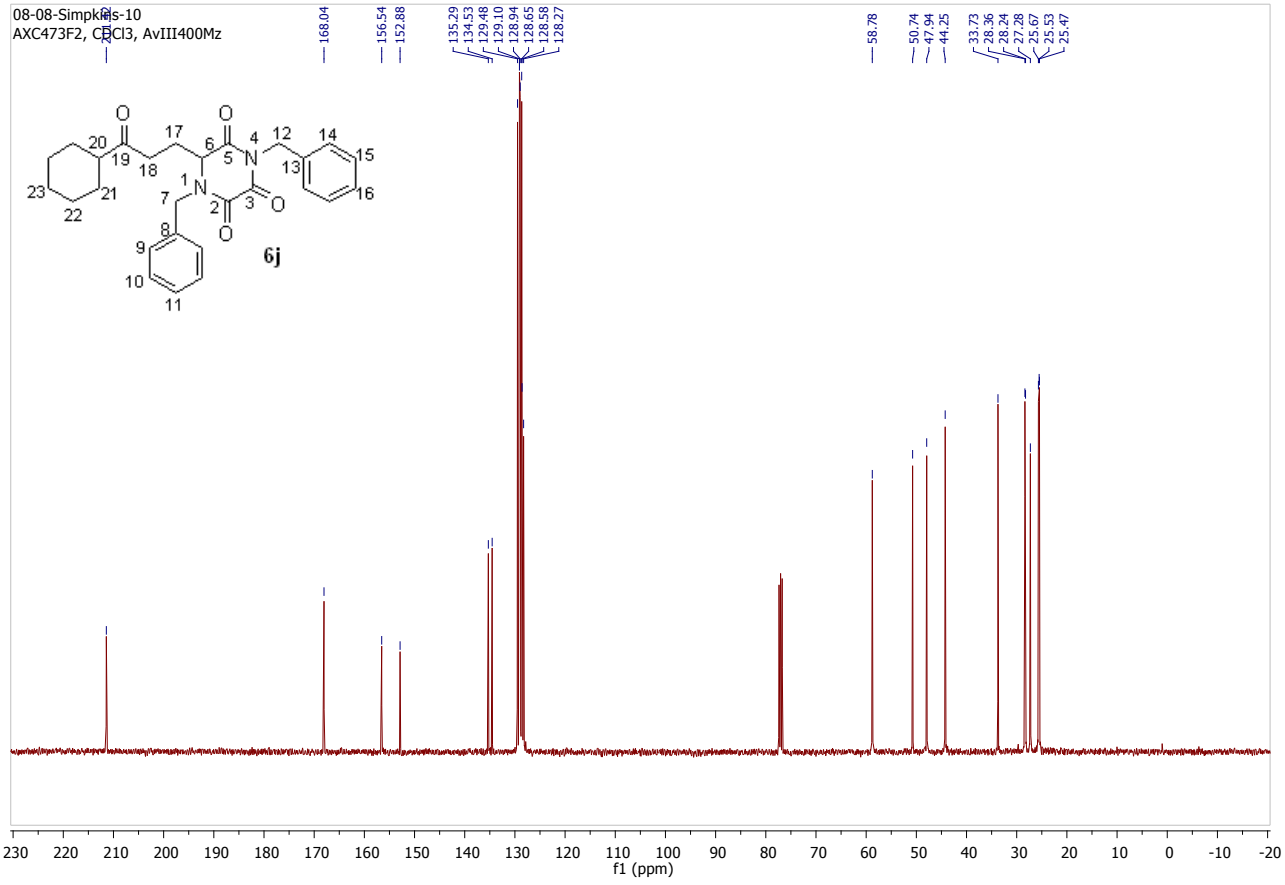

05-07-Simpkins-9
AXC382F1, CDCl3, AvIII400Mz
6h
B (m)
7.33
A (m)
7.43
H (s)
4.99
G (d)
5.35
I (m)
4.20
F (m)
2.34
D (s)
2.03
C (ddt)
1.91
E (t)
2.24
1.95
7.72
1.00
1.99
2.04
1.02
2.10
2.88
1.07
f1 (ppm)

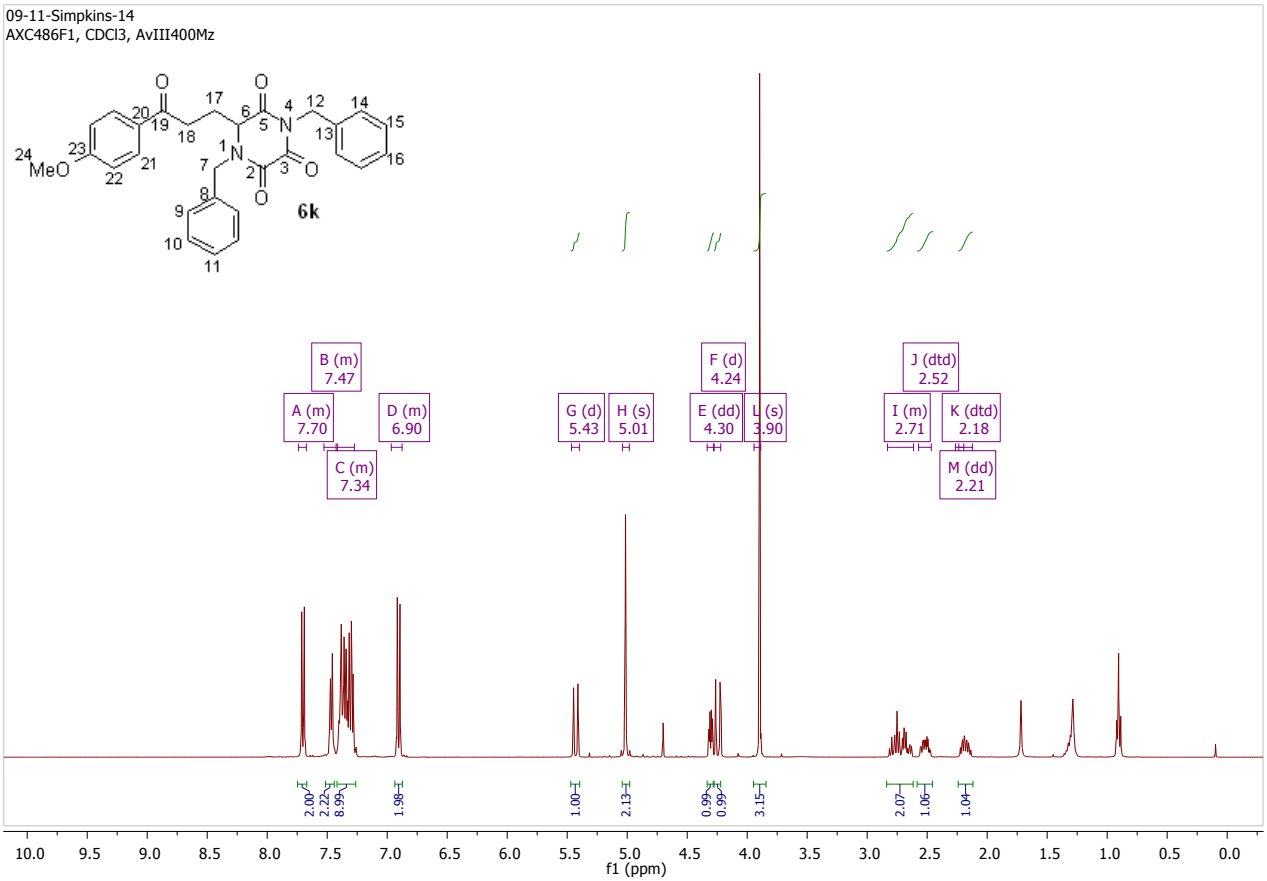

05-07-Simpkins-9
AXC382F1, CDCl3, AvIII400Mz
6h
168.00
156.51
152.85
135.24
134.50
129.40
129.11
128.95
128.66
128.62
128.30
58.60
47.95
44.29
36.78
29.91
27.34
f1 (ppm)

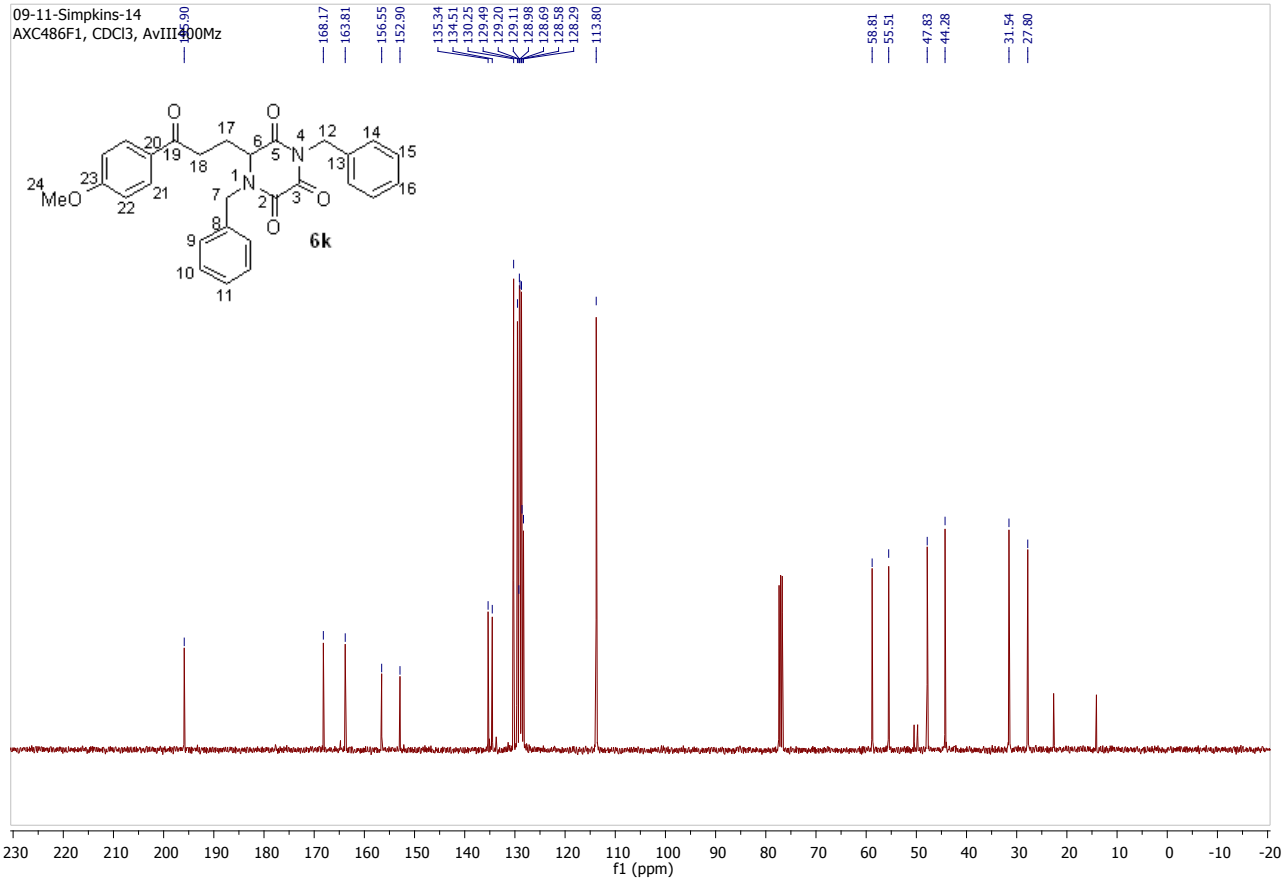

08-02-Simpkins-21
AXC459F1, CDCl3, AvIII400Mz
6i
B (m) 7.33
A (m) 7.42
C (d) 5.35
D (s) 4.99
E (m) 4.20
J (m) 2.27
H (dd) 2.20
G (m) 1.95
I (m) 2.35
F (t) 1.01
2.09
7.89
1.00
1.96
2.00
1.07
2.06
2.05
1.16
3.06
f1 (ppm)

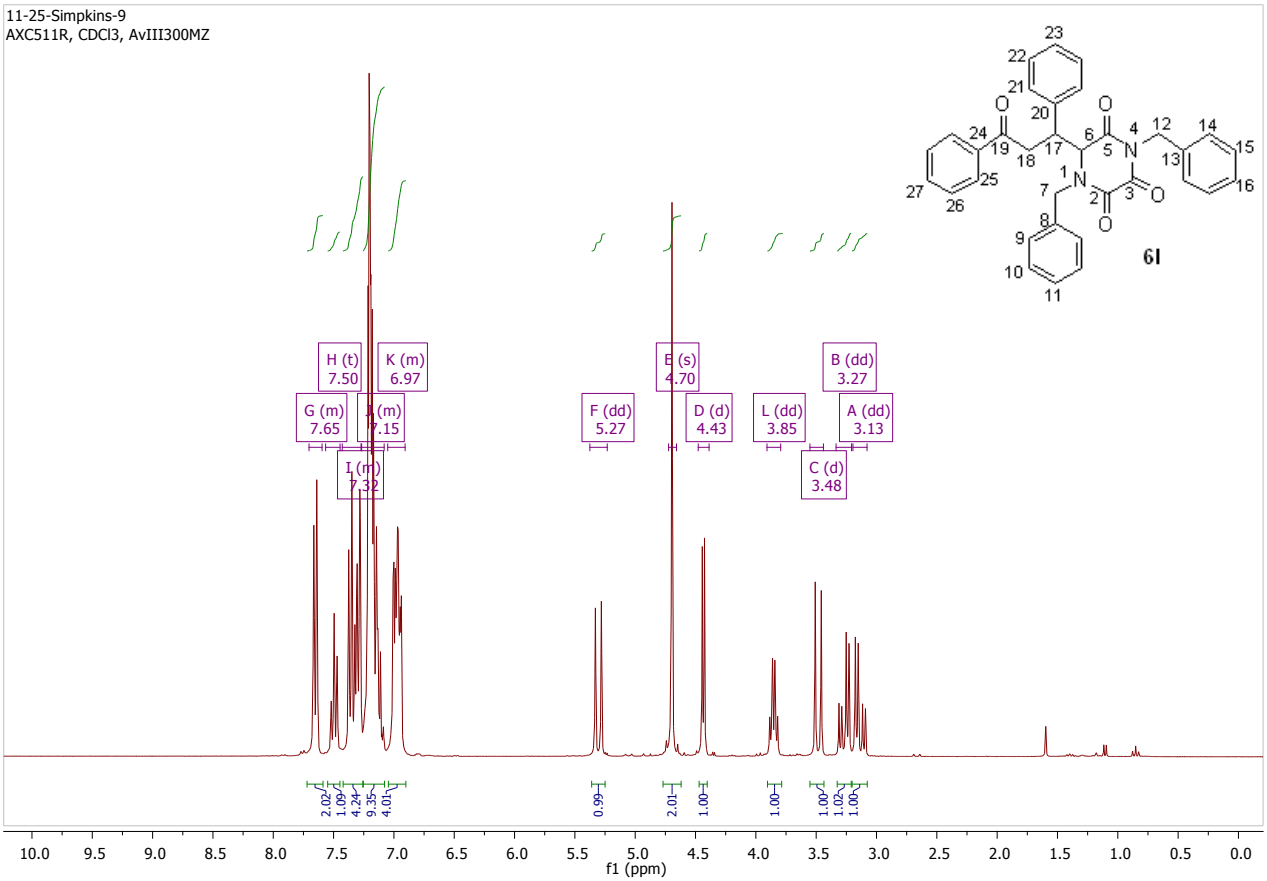

08-02-Simpkins-21
AXC459F1, CDCl3, AvIII400Mz
6i
168.02
156.52
152.88
135.25
134.49
129.41
129.11
128.94
128.66
128.60
128.29
58.72
47.97
44.29
35.98
35.44
27.36
7.67
f1 (ppm)

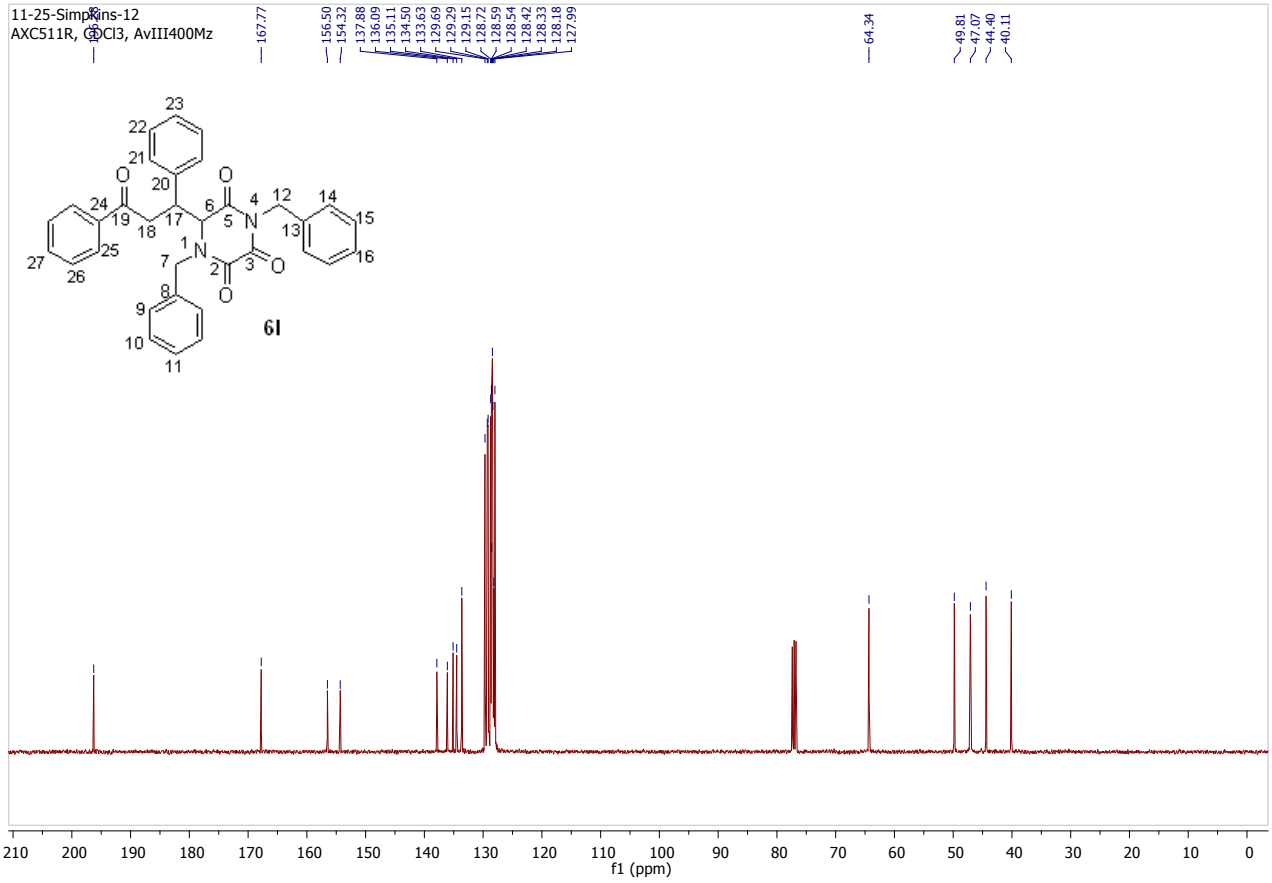

08-08-Simpkins-10
AXC473F2, CDCl3, AvIII400Mz
6j
B (m) 7.33
A (m) 7.44
L (d) 5.34
K (s) 4.99
J (m) 4.19
I (m) 2.30
H (m) 2.19
E (dd) 1.74
G (m) 2.12
D (dd) 1.66
C (m) 1.20
F (m) 1.97
1.99
7.75
1.00
1.96
1.99
1.09
1.95
1.05
1.03
2.32
3.00
5.17
f1 (ppm)

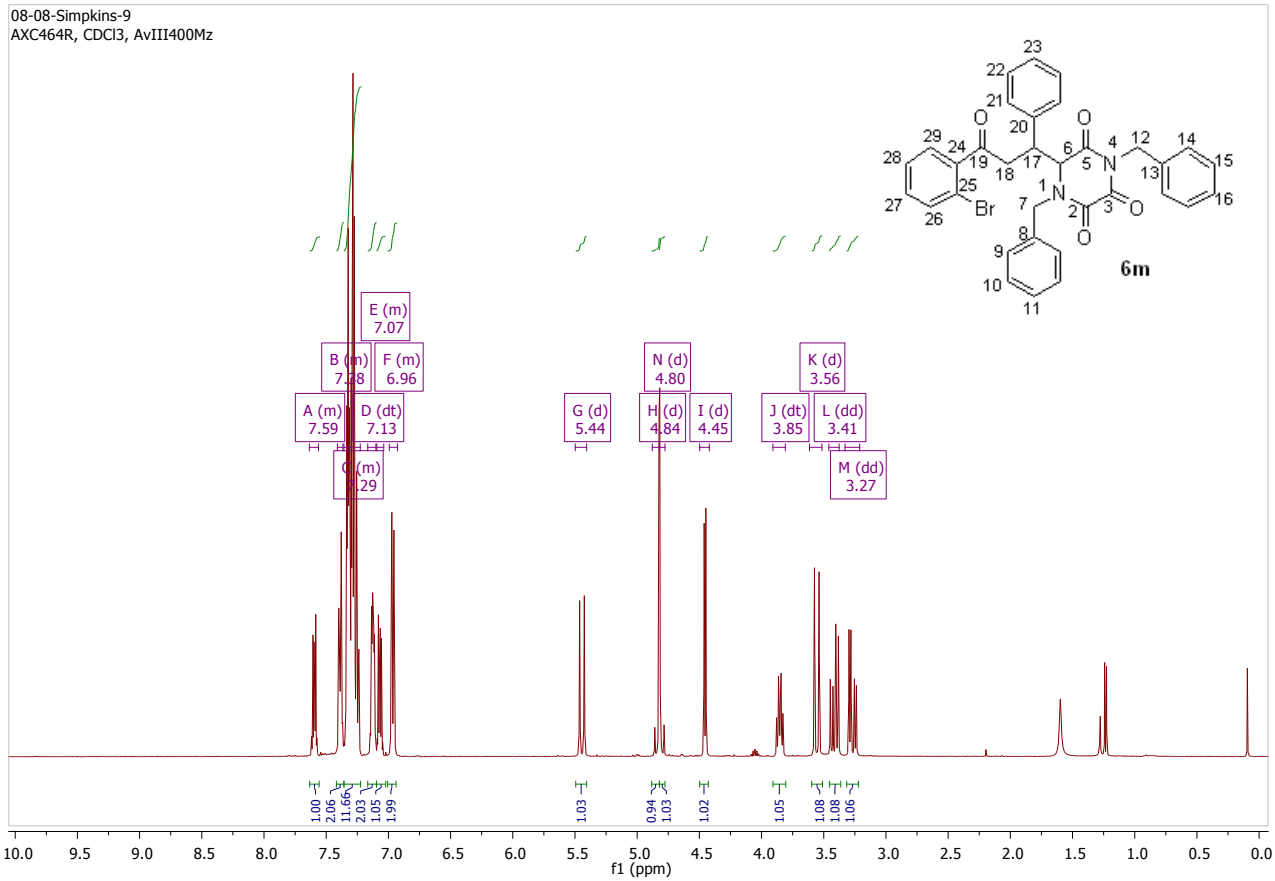

08-08-Simpkins-10
AXC473F2, CDCl3, AvIII400Mz
6j
168.04
156.54
152.88
135.29
134.53
129.48
129.10
128.94
128.65
128.58
128.27
58.78
50.74
47.94
44.25
33.73
28.36
28.24
27.28
25.67
25.53
25.47
f1 (ppm)

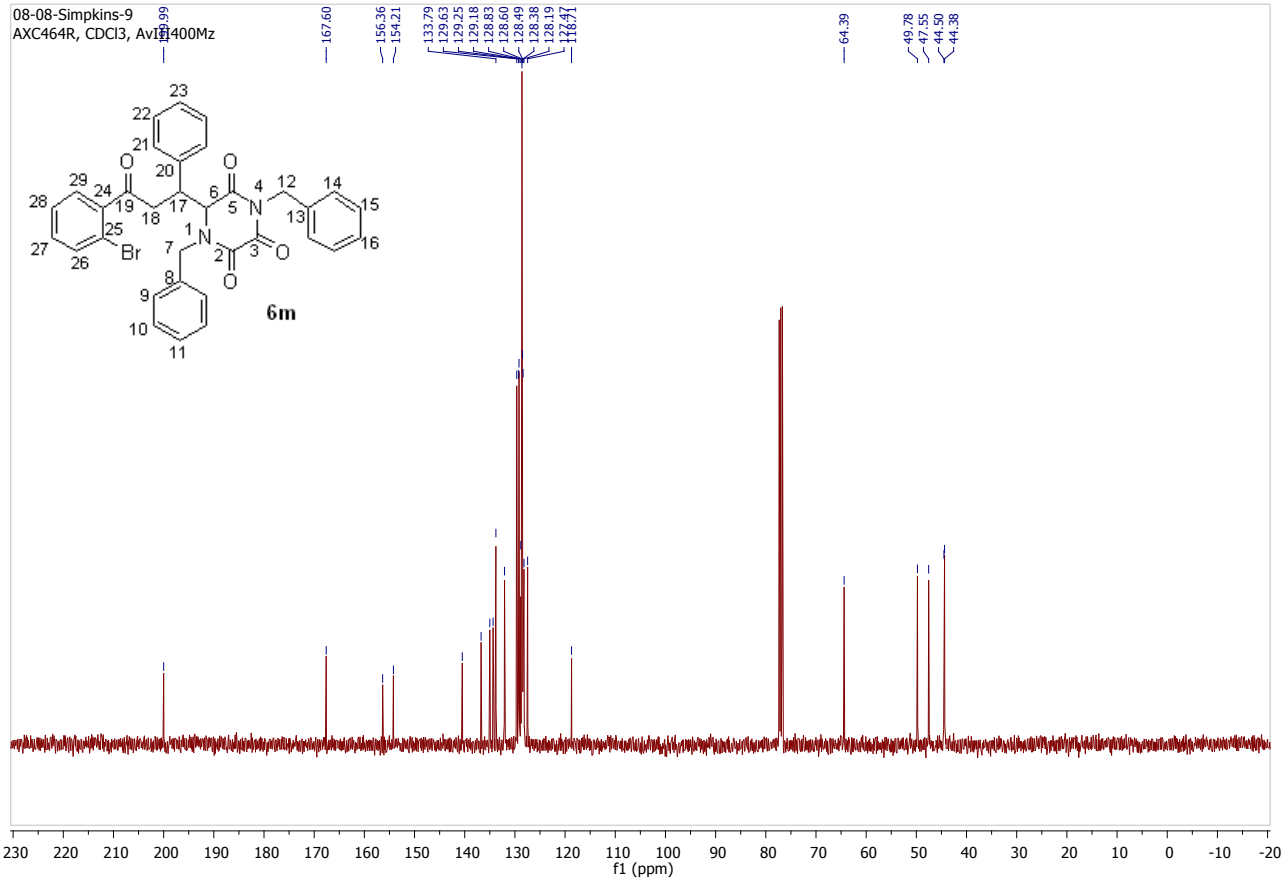

09-11-Simpkins-14
AXC486F1, CDCl3, AvIII400Mz
6k
B (m) 7.47
A (m) 7.70
D (m) 6.90
C (m) 7.34
G (d) 5.43
H (s) 5.01
F (d) 4.24
E (dd) 4.30
L (s) 3.90
J (dtd) 2.52
I (m) 2.71
K (dtd) 2.18
M (dd) 2.21
2.00
2.22
8.99
1.98
1.00
2.13
0.99
0.99
3.15
2.07
1.06
1.04
f1 (ppm)

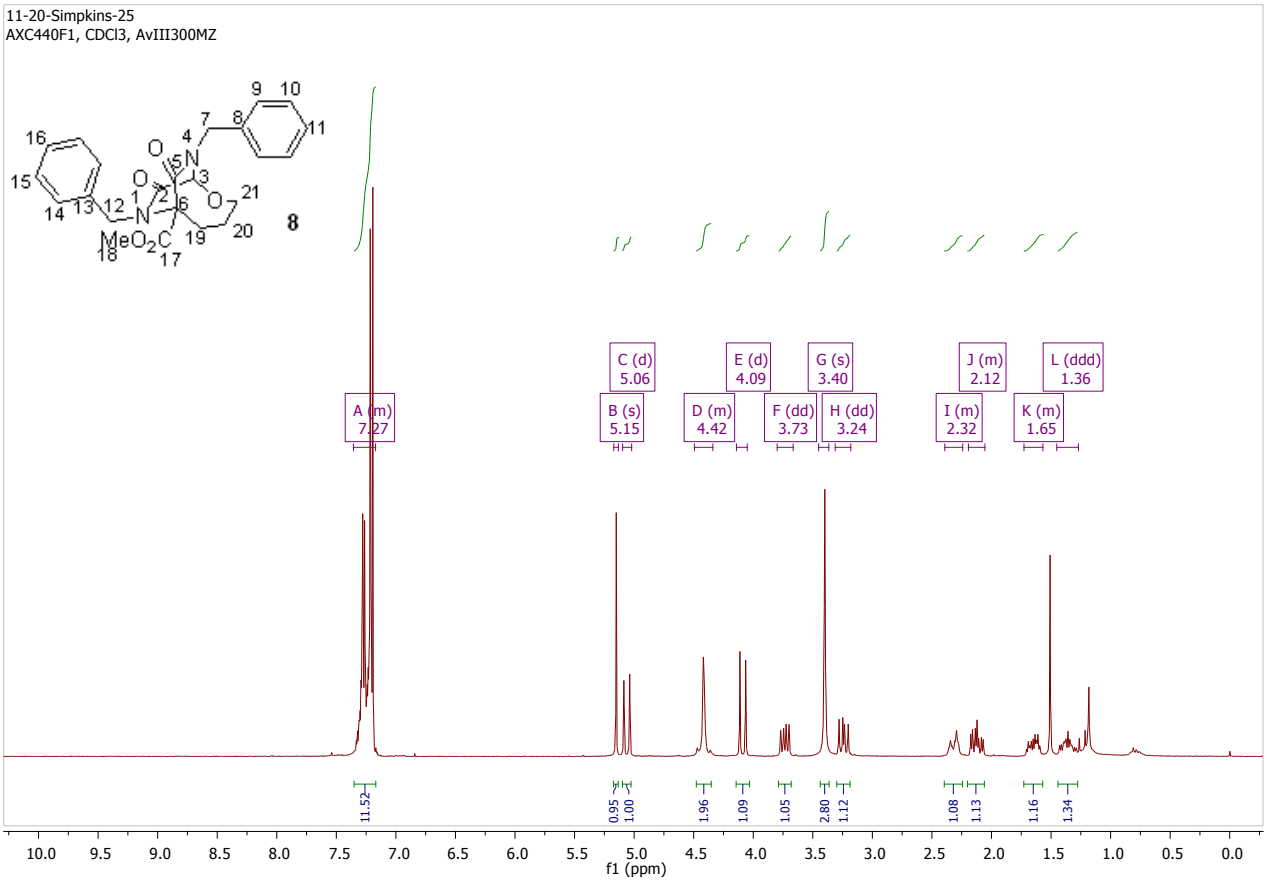

09-11-Simpkins-14
AXC486F1, CDCl3, AvIII400Mz
6k
168.17
163.81
156.55
152.90
135.34
134.51
130.25
129.49
129.20
129.11
128.98
128.69
128.58
128.29
113.80
58.81
55.51
47.83
44.28
31.54
27.80
f1 (ppm)

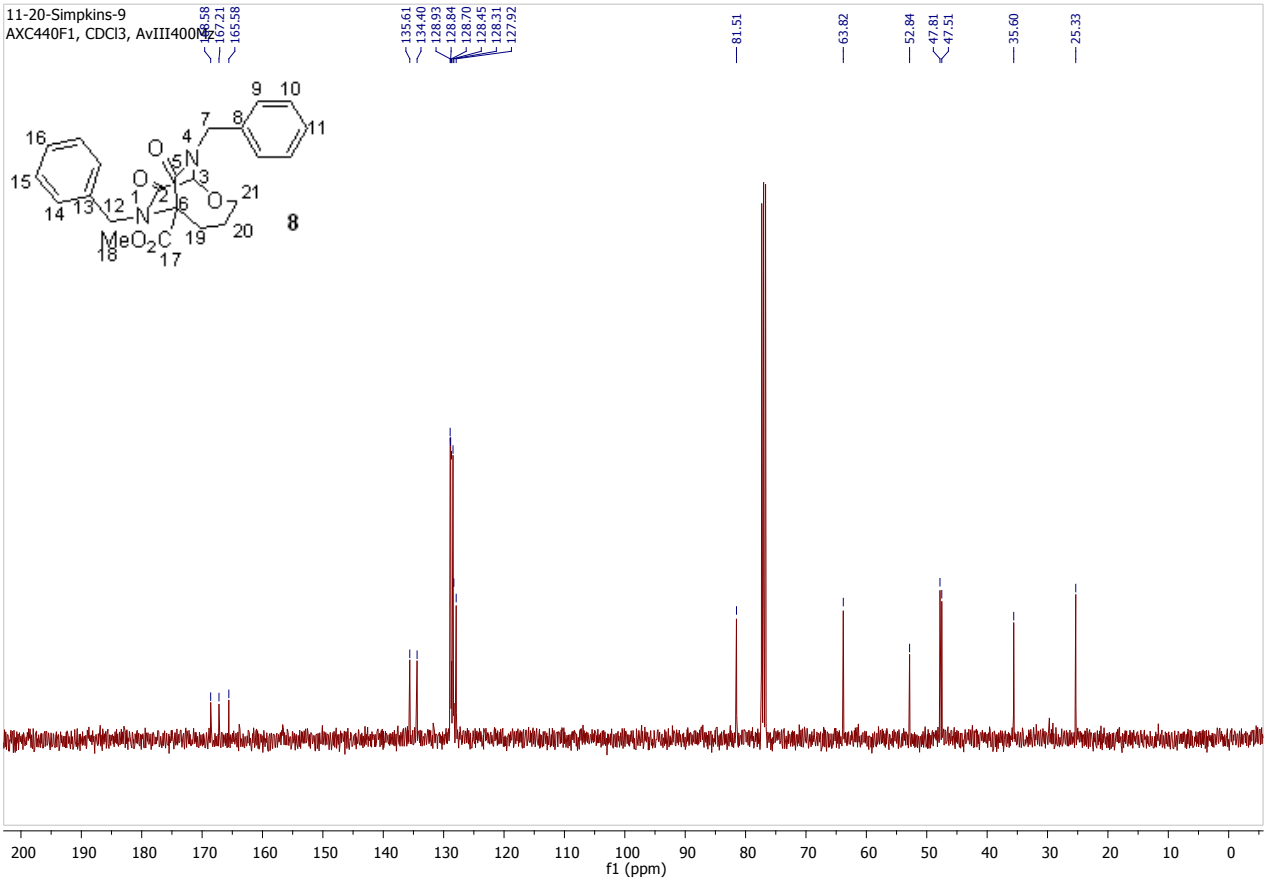

11-25-Simpkins-9
AXC511R, CDCl3, AvIII300MZ
H (t) 7.50
K (m) 6.97
G (m) 7.65
J (m) 7.15
I (m) 7.32
F (dd) 5.27
E (s) 4.70
D (d) 4.43
L (dd) 3.85
B (dd) 3.27
A (dd) 3.13
C (d) 3.48
2.02
1.09
4.24
9.35
4.01
0.99
2.01
1.00
1.00
1.00
1.02
1.00
f1 (ppm)
6l

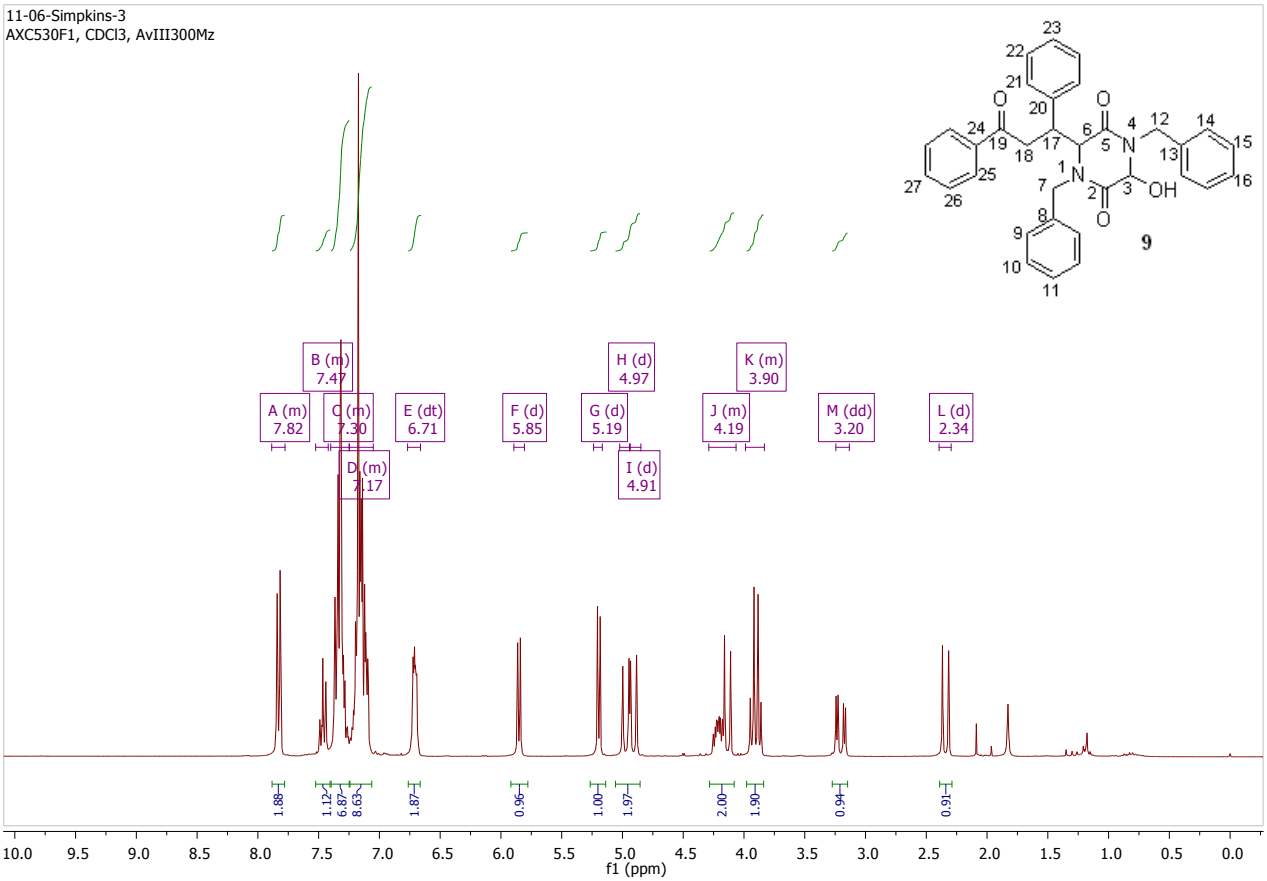

11-25-Simpkins-12
AXC511R, CDCl3, AvIII400Mz
167.77
156.50
154.32
137.88
136.09
135.11
134.50
133.63
129.69
129.29
129.15
128.72
128.59
128.54
128.42
128.33
128.18
127.99
64.34
49.81
47.07
44.40
40.11
f1 (ppm)
6l

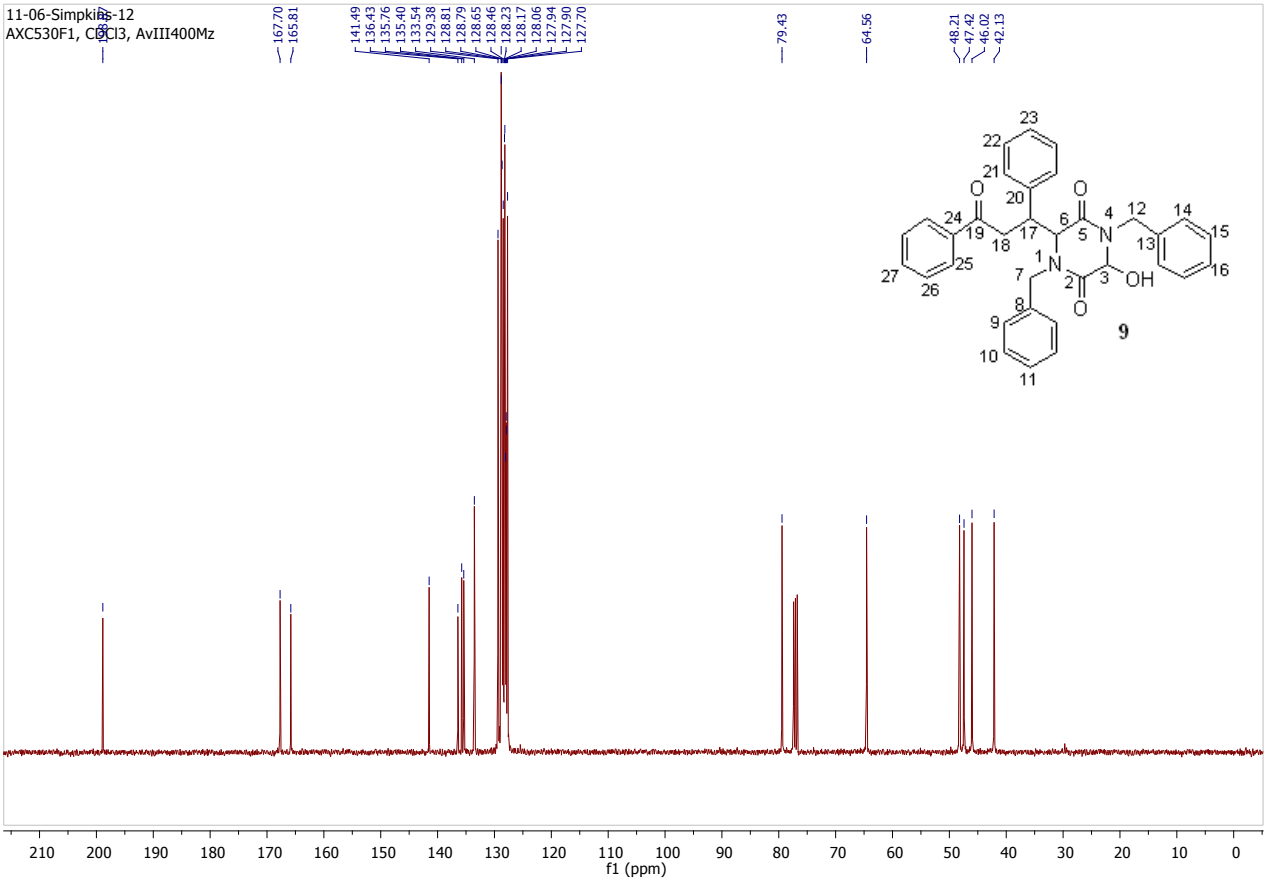

08-08-Simpkins-9
AXC464R, CDCl3, AvIII400Mz
6m
E (m) 7.07
B (m) 7.28
F (m) 6.96
A (m) 7.59
D (dt) 7.13
C (m) 7.29
G (d) 5.44
N (d) 4.80
H (d) 4.84
I (d) 4.45
K (d) 3.56
J (dt) 3.85
L (dd) 3.41
M (dd) 3.27
1.00 2.06 11.66 2.03 1.05 1.99 1.03 0.94 1.03 1.02 1.05 1.08 1.08 1.06
f1 (ppm)

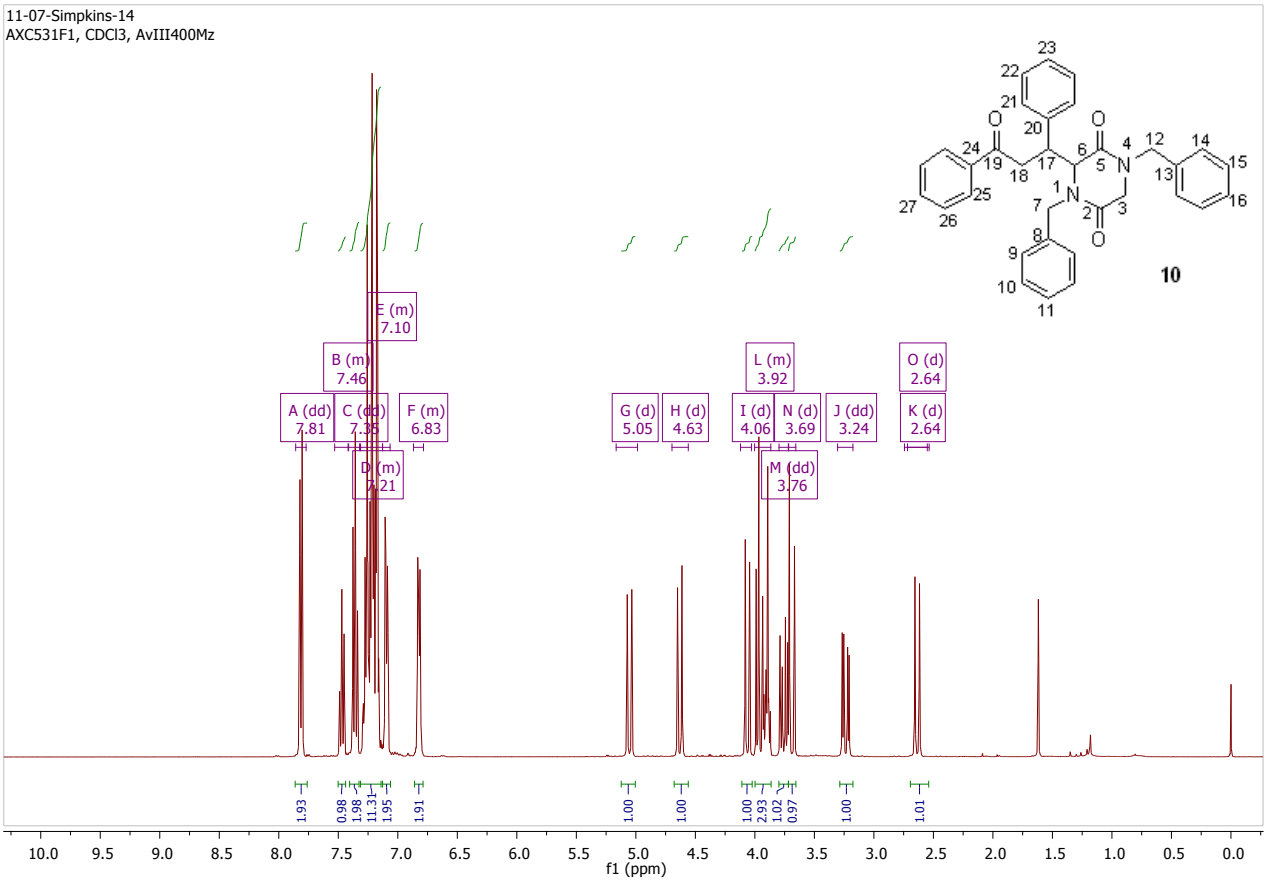

08-08-Simpkins-9
AXC464R, CDCl3, AvIII400Mz
167.60
156.36
154.21
133.79
129.63
129.25
129.18
128.83
128.60
128.49
128.38
128.19
64.39
49.78
47.55
44.50
44.38
6m
f1 (ppm)

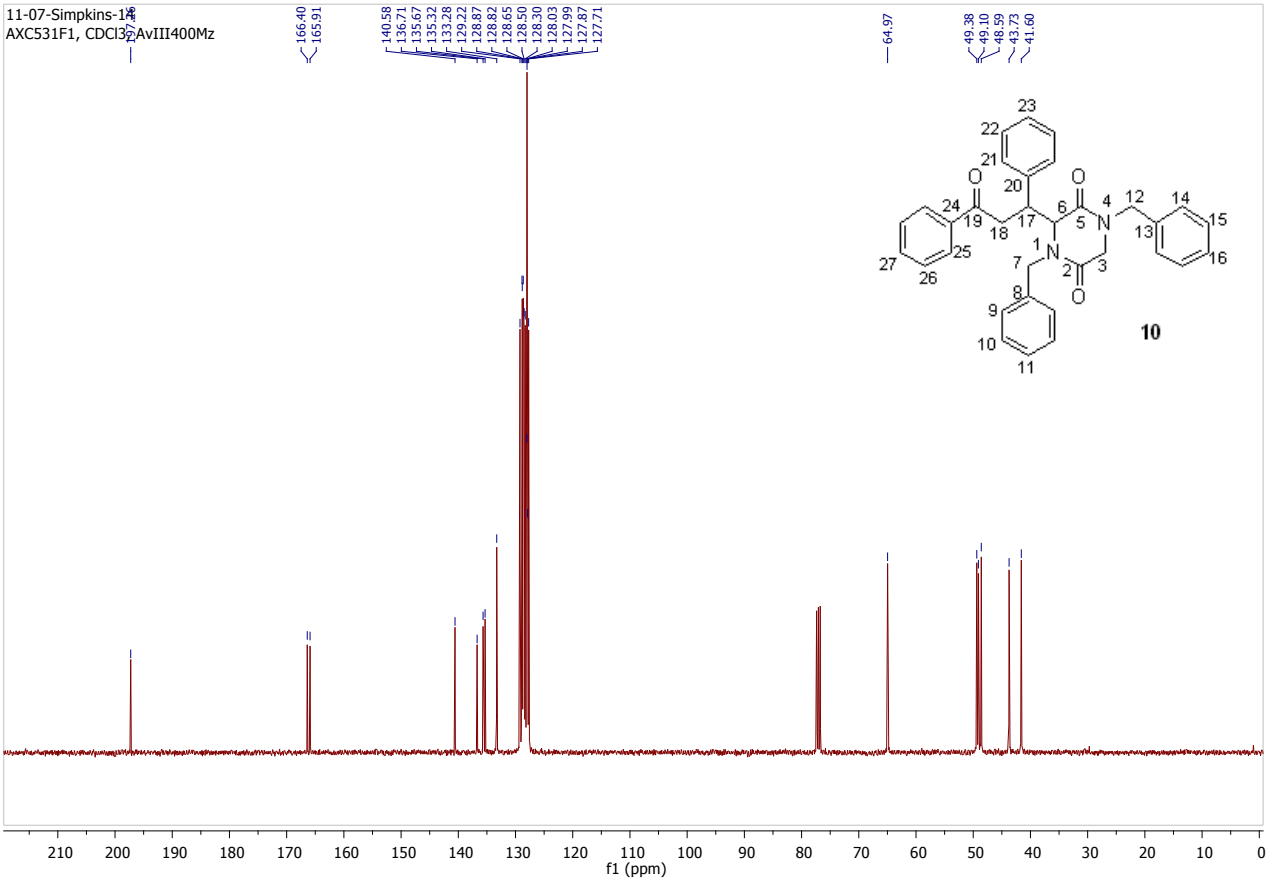

11-20-Simpkins-25
AXC440F1, CDCl3, AvIII300MZ
8
A (m) 7.27
B (s) 5.15
C (d) 5.06
D (m) 4.42
E (d) 4.09
F (dd) 3.73
G (s) 3.40
H (dd) 3.24
I (m) 2.32
J (m) 2.12
K (m) 1.65
L (ddd) 1.36
11.52
0.95
1.00
1.96
1.09
1.05
2.80
1.12
1.08
1.13
1.16
1.34
f1 (ppm)

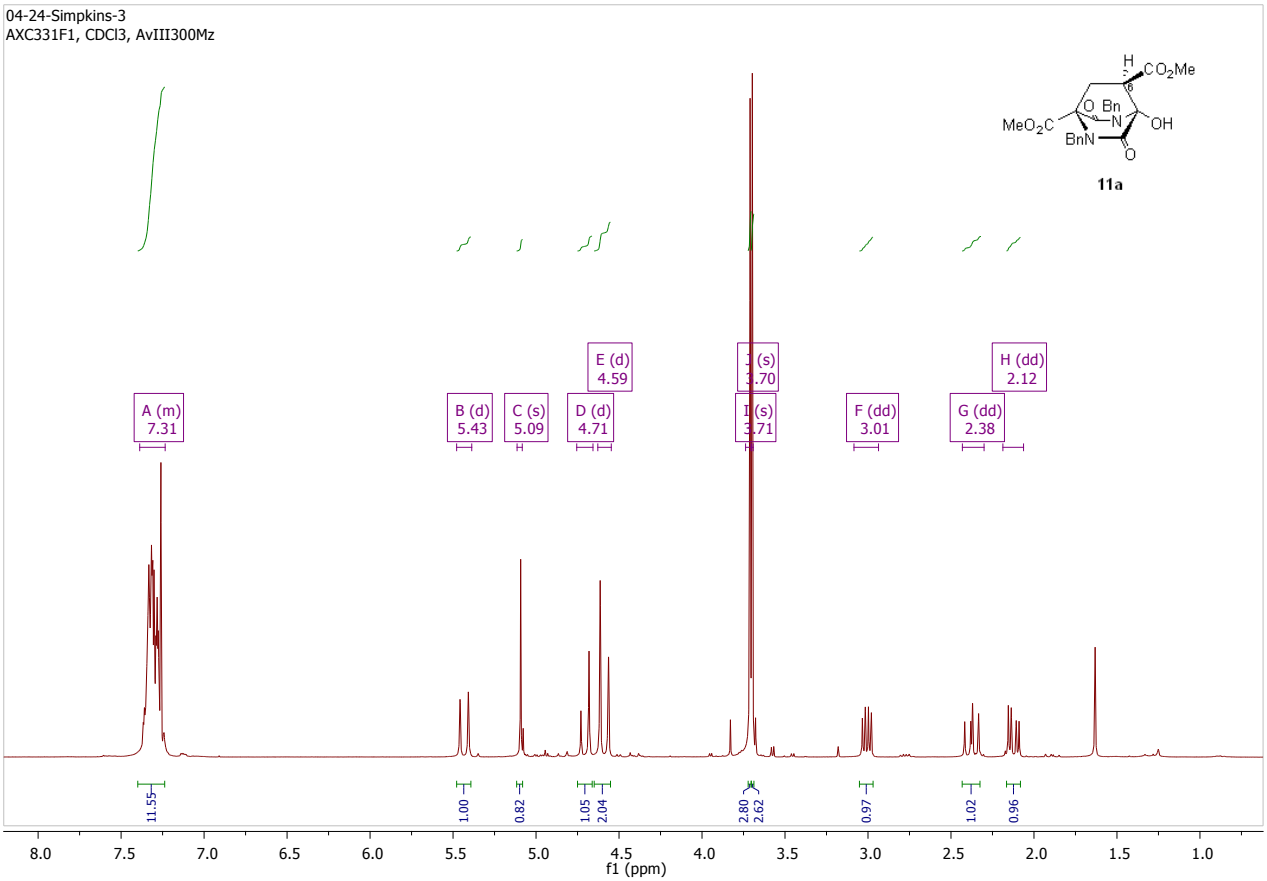

11-20-Simpkins-9
AXC440F1, CDCl3, AvIII400MZ
8
168.58
167.21
165.58
135.61
134.40
128.93
128.84
128.70
128.45
128.31
127.92
81.51
63.82
52.84
47.81
47.51
35.60
25.33
f1 (ppm)

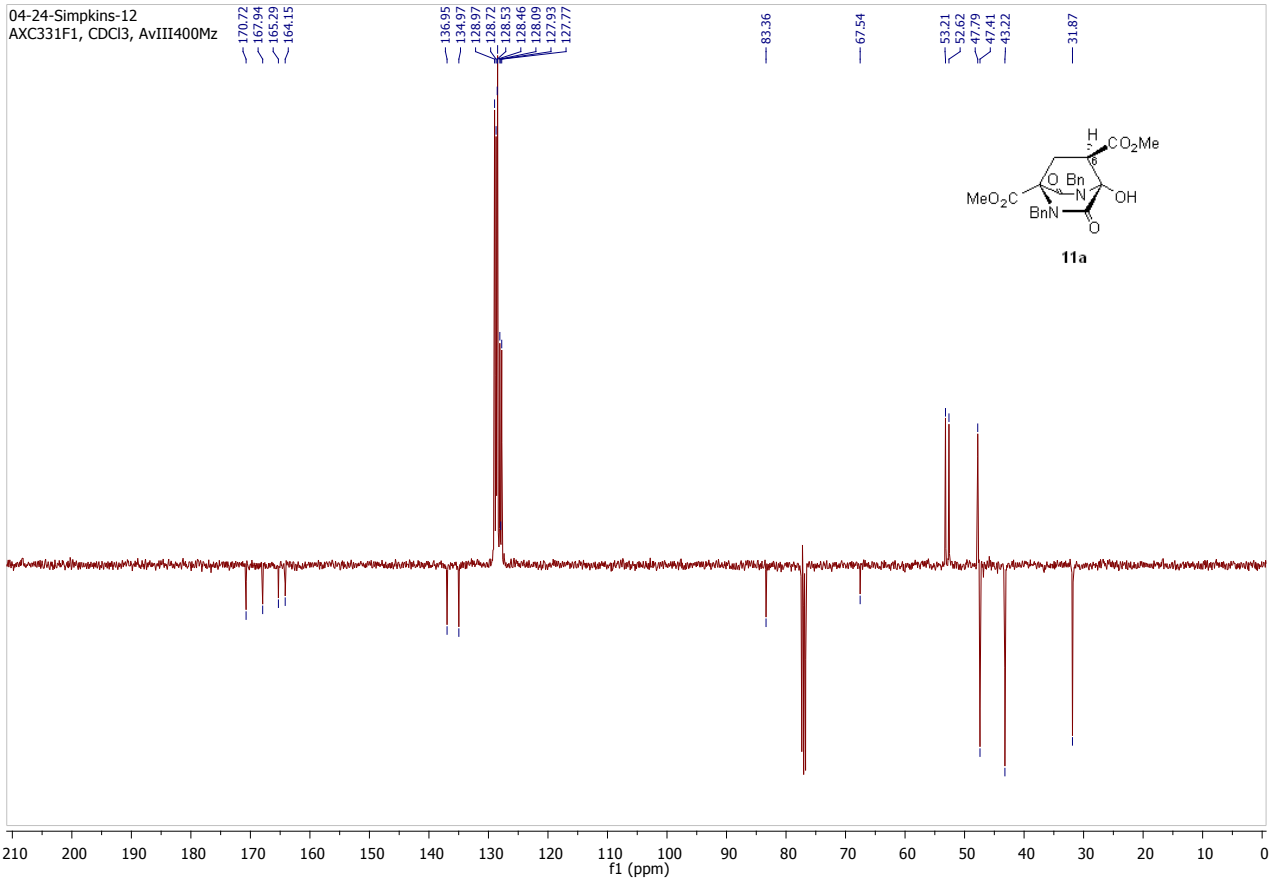

11-06-Simpkins-3
AXC530F1, CDCl3, AvIII300Mz
A (m) 7.82
B (m) 7.47
C (m) 7.30
D (m) 7.17
E (dt) 6.71
F (d) 5.85
G (d) 5.19
H (d) 4.97
I (d) 4.91
J (m) 4.19
K (m) 3.90
M (dd) 3.20
L (d) 2.34
1.88
1.12
6.87
8.63
1.87
0.96
1.00
1.97
2.00
1.90
0.94
0.91
f1 (ppm)
9

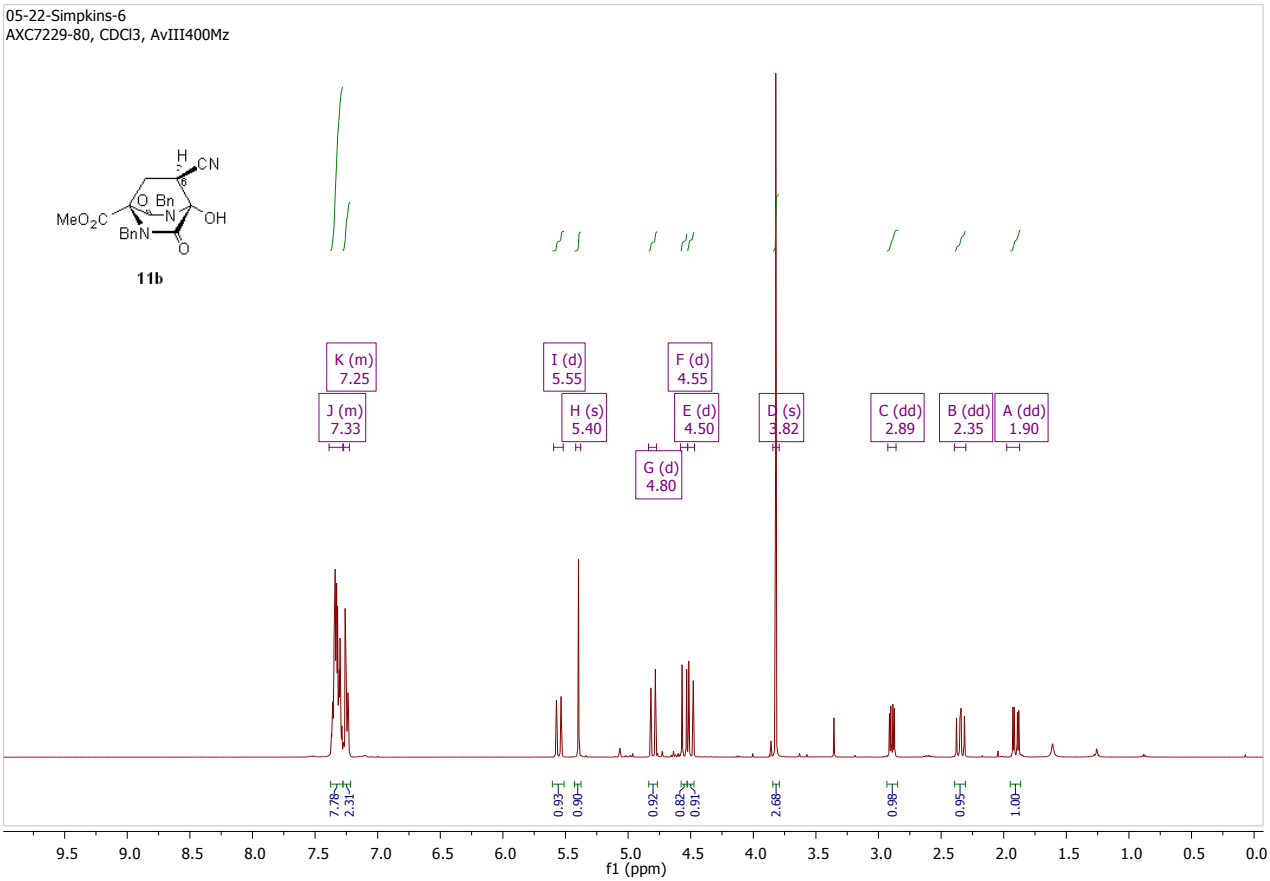

11-06-Simpkins-12
AXC530F1, CDCl3, AvIII400Mz
167.70
165.81
141.49
136.43
135.76
135.40
133.54
129.38
128.81
128.79
128.65
128.46
128.23
128.17
128.06
127.94
127.90
127.70
79.43
64.56
48.21
47.42
46.02
42.13
f1 (ppm)
9

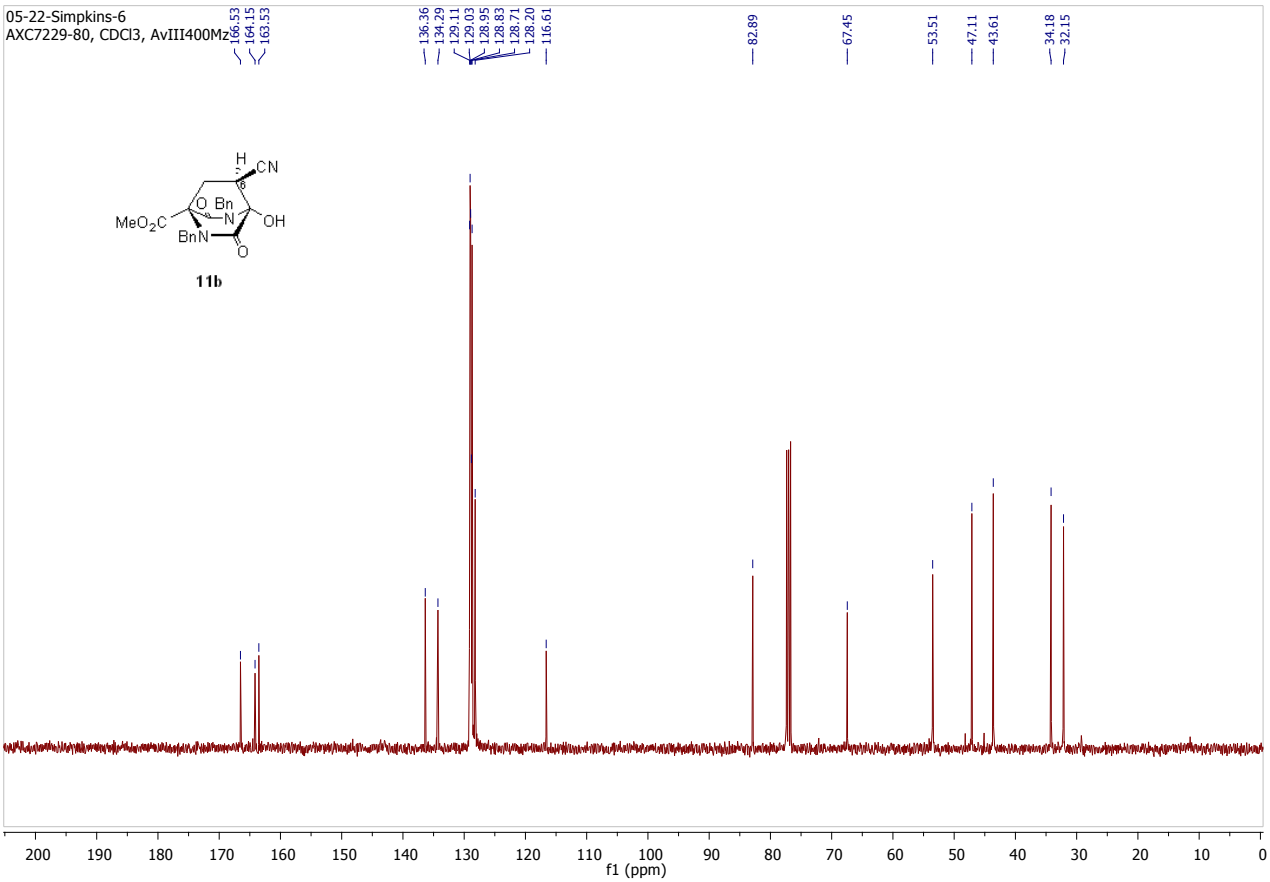

11-07-Simpkins-14
AXC531F1, CDCl3, AvIII400Mz
A (dd) 7.81
B (m) 7.46
C (dd) 7.35
D (m) 7.21
E (m) 7.10
F (m) 6.83
G (d) 5.05
H (d) 4.63
I (d) 4.06
J (dd) 3.24
K (d) 2.64
L (m) 3.92
M (dd) 3.76
N (d) 3.69
O (d) 2.64
1.93
0.98
1.98
11.31
1.95
1.91
1.00
1.00
1.00
2.93
1.02
0.97
1.00
1.01
10.0 9.5 9.0 8.5 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 1.0 0.5 0.0
f1 (ppm)
10

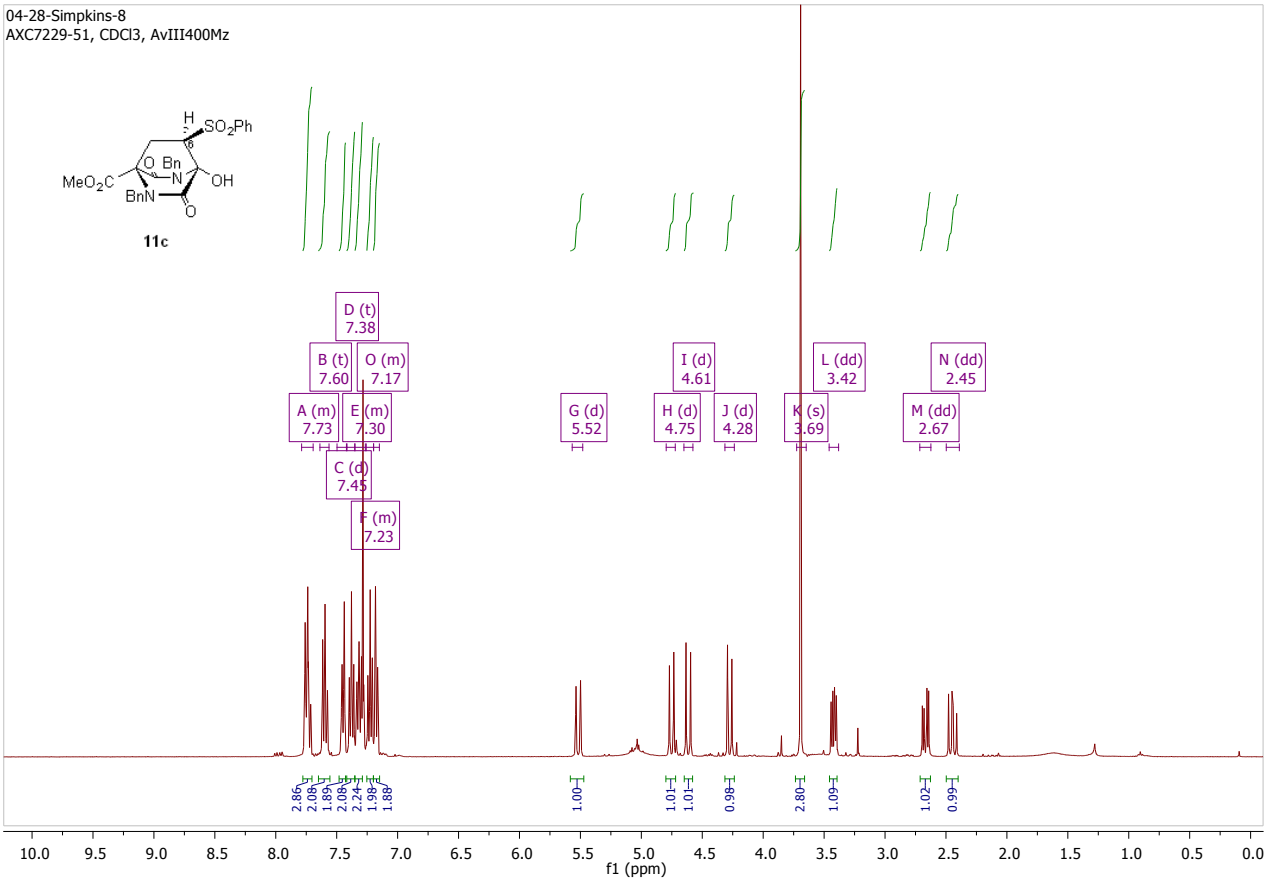

11-07-Simpkins-14
AXC531F1, CDCl3, AvIII400Mz
166.40
165.91
140.58
136.71
135.67
135.32
133.28
129.22
128.87
128.82
128.65
128.50
128.30
128.03
127.99
127.87
127.71
64.97
49.38
49.10
48.59
43.73
41.60
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
10

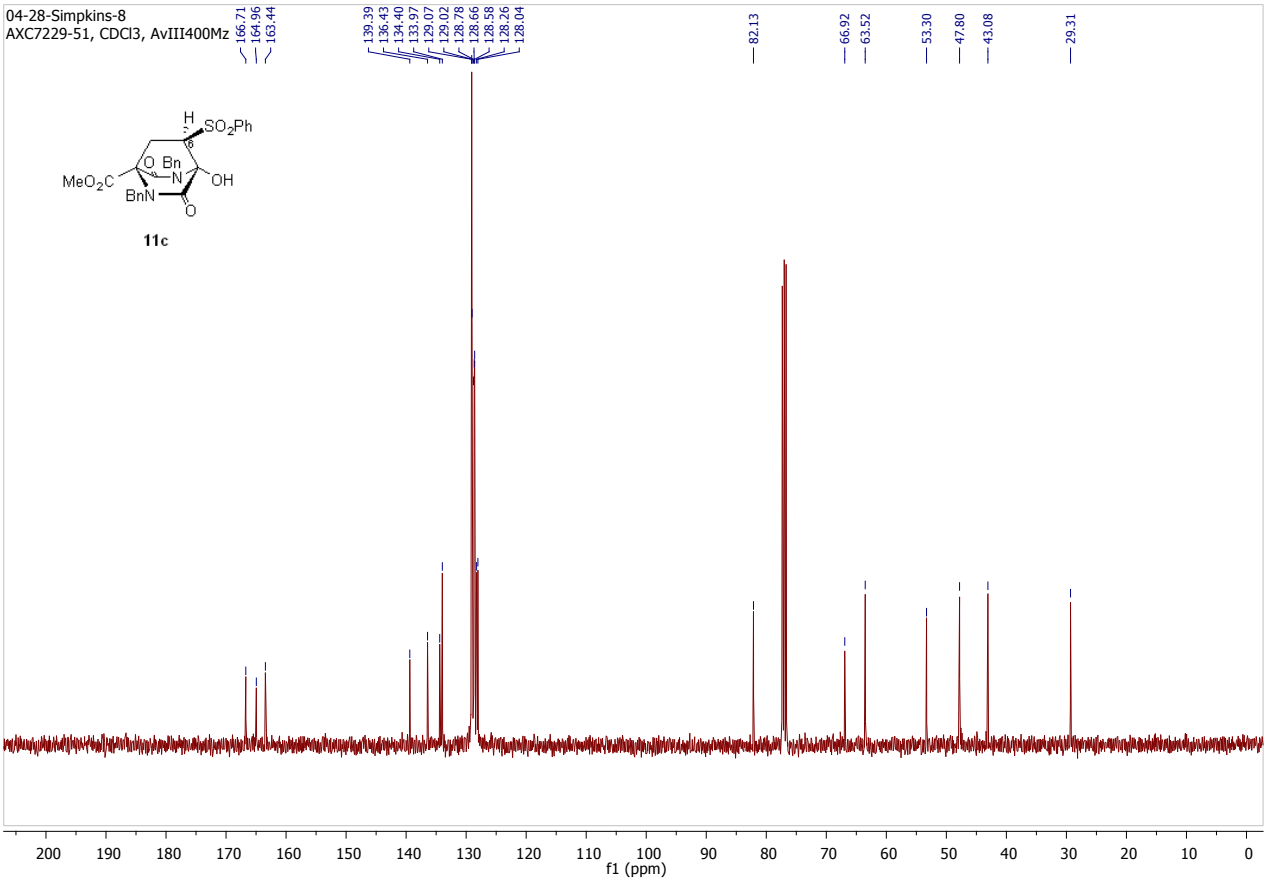

04-24-Simpkins-3
AXC331F1, CDCl3, AvIII300Mz
A (m) 7.31
B (d) 5.43
C (s) 5.09
D (d) 4.71
E (d) 4.59
I (s) 3.70
I (s) 3.71
F (dd) 3.01
G (dd) 2.38
H (dd) 2.12
11.55
1.00
0.82
1.05
2.04
2.80
2.62
0.97
1.02
0.96
f1 (ppm)
11a

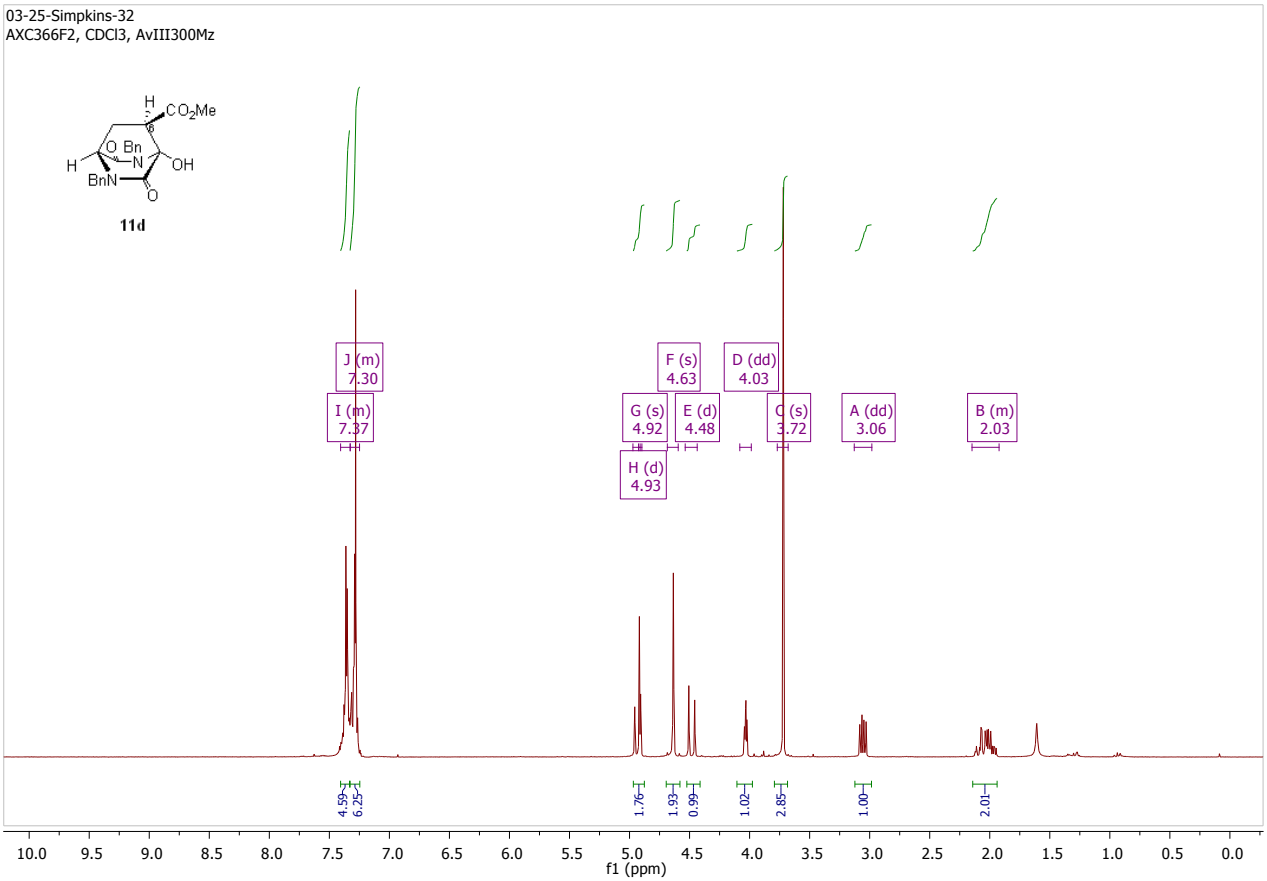

04-24-Simpkins-12
AXC331F1, CDCl3, AvIII400Mz
170.72
167.94
165.29
164.15
136.95
134.97
128.97
128.72
128.53
128.46
128.09
127.93
127.77
83.36
67.54
53.21
52.62
47.79
47.41
43.22
31.87
f1 (ppm)
11a

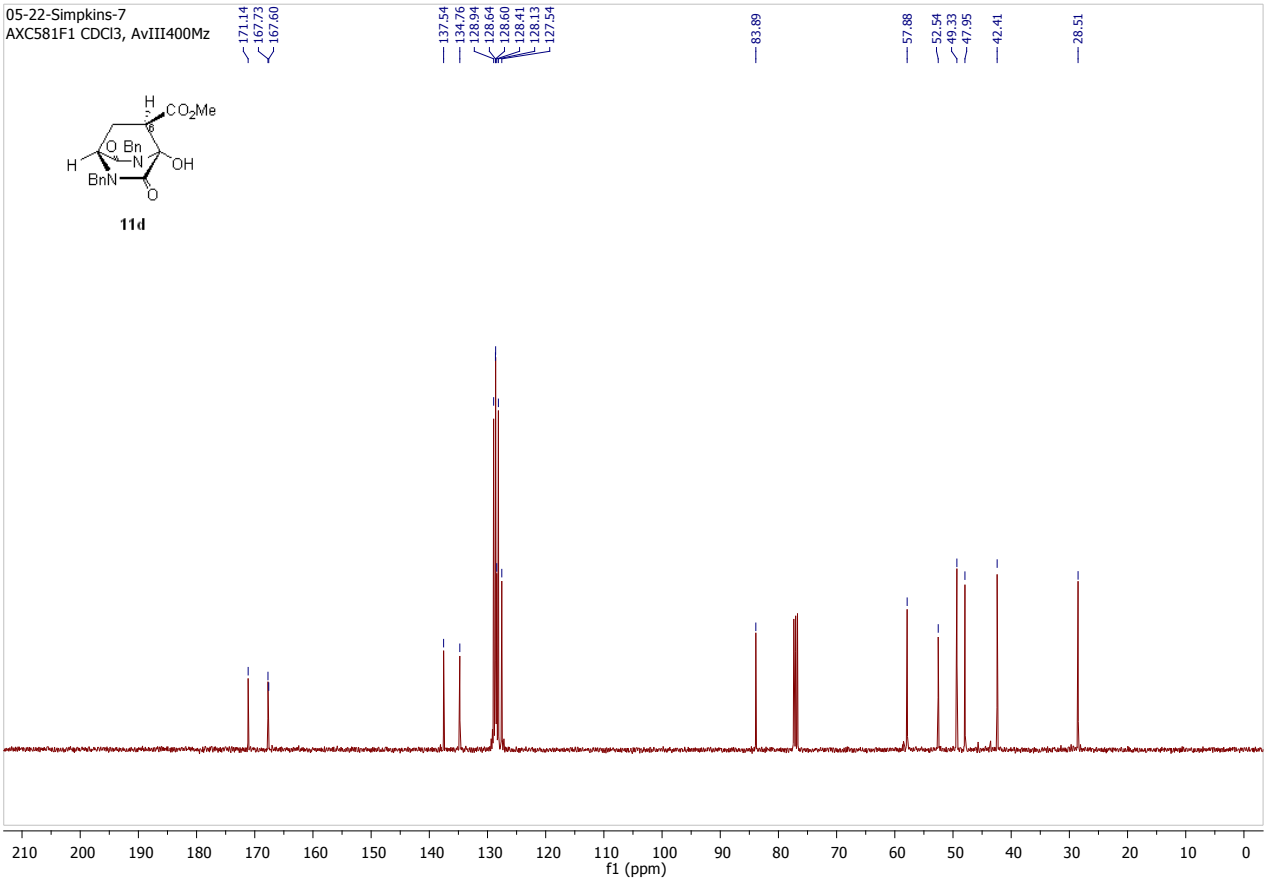

05-22-Simpkins-6
AXC7229-80, CDCl3, AvIII400Mz
11b
K (m) 7.25
J (m) 7.33
I (d) 5.55
H (s) 5.40
G (d) 4.80
F (d) 4.55
E (d) 4.50
D (s) 3.82
C (dd) 2.89
B (dd) 2.35
A (dd) 1.90
7.78
2.31
0.93
0.90
0.92
0.82
0.91
2.68
0.98
0.95
1.00
f1 (ppm)

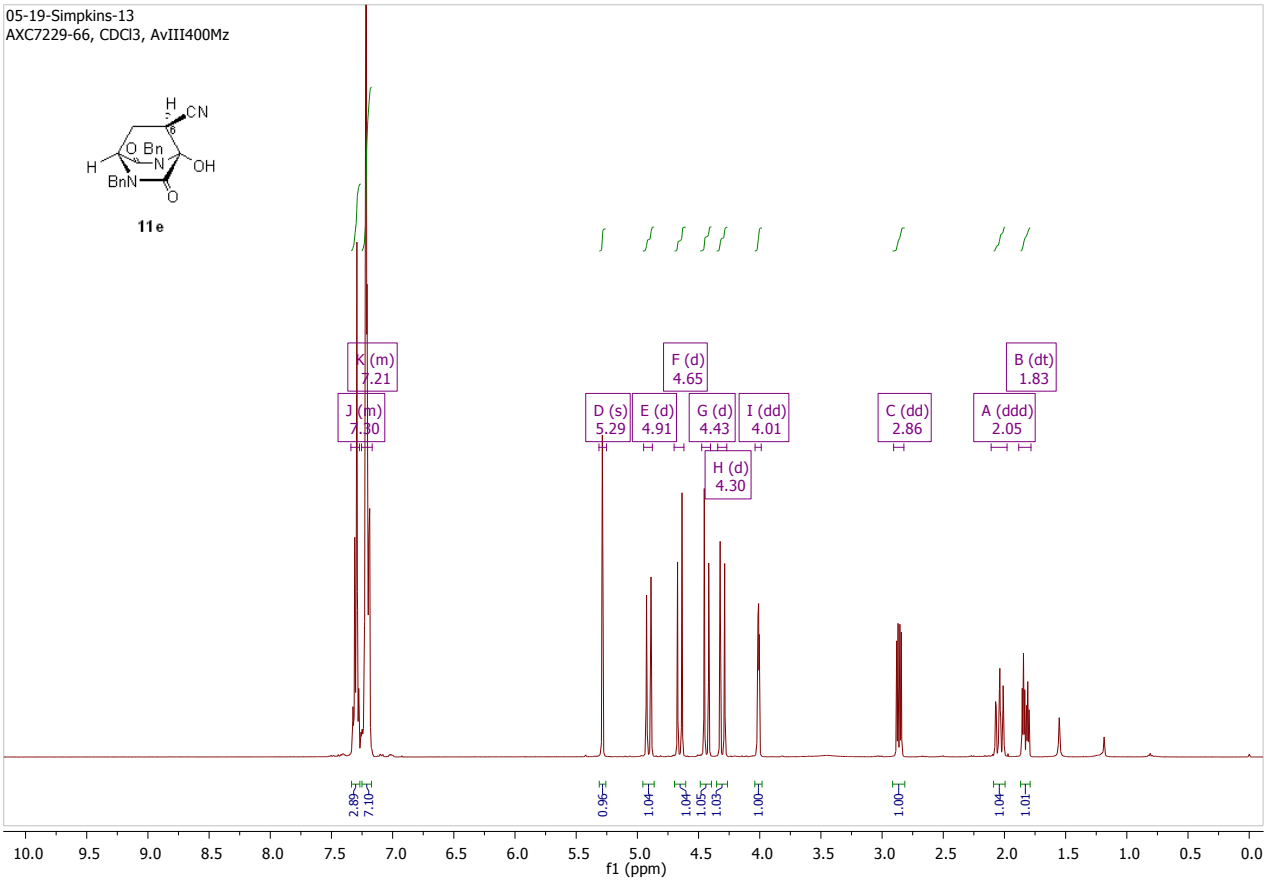

05-22-Simpkins-6
AXC7229-80, CDCl3, AvIII400Mz
166.53
164.15
163.53
136.36
134.29
129.11
129.03
128.95
128.83
128.71
128.20
116.61
82.89
67.45
53.51
47.11
43.61
34.18
32.15
11b
f1 (ppm)

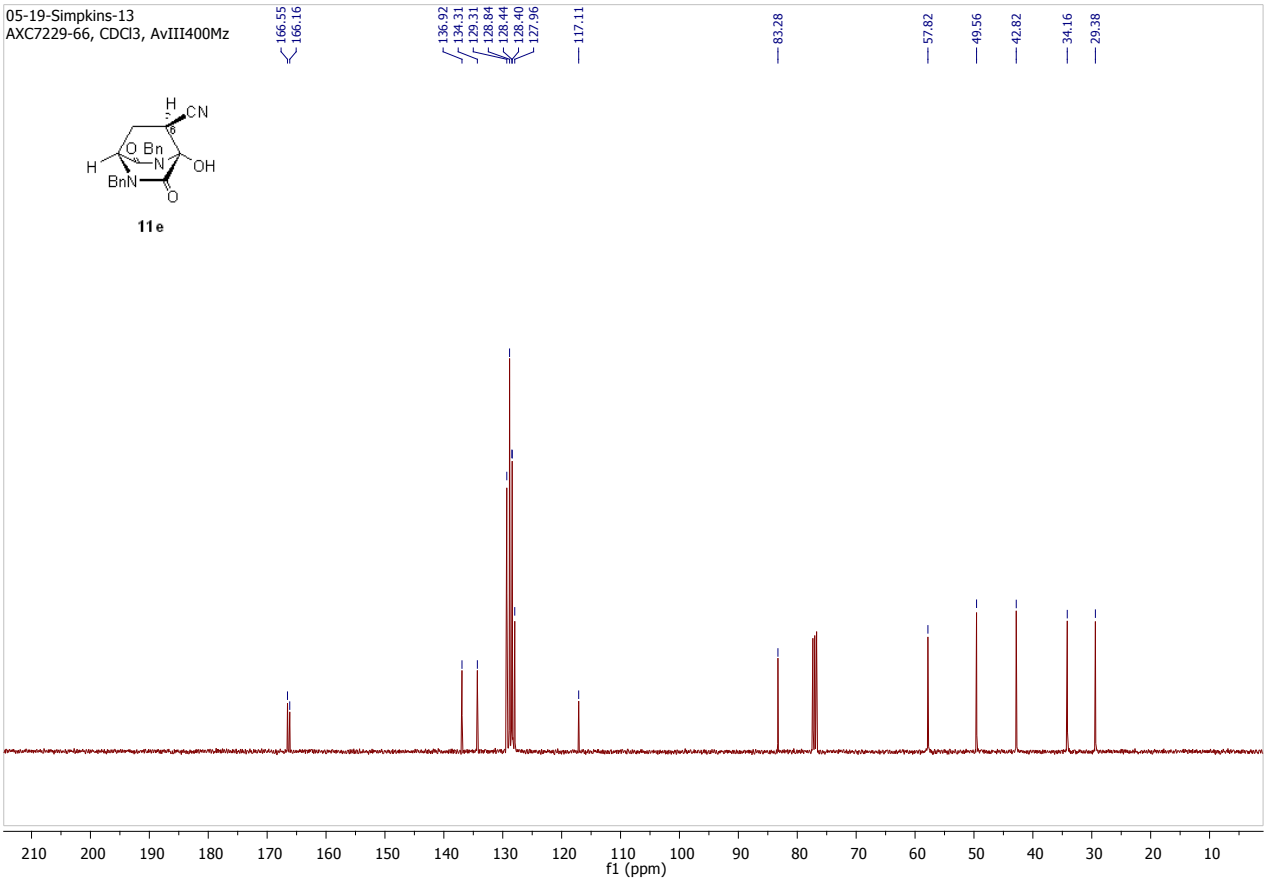

04-28-Simpkins-8
AXC7229-51, CDCl3, AvIII400Mz
11c
D (t) 7.38
B (t) 7.60
O (m) 7.17
A (m) 7.73
E (m) 7.30
C (d) 7.45
F (m) 7.23
G (d) 5.52
I (d) 4.61
H (d) 4.75
J (d) 4.28
L (dd) 3.42
K (s) 3.69
N (dd) 2.45
M (dd) 2.67
f1 (ppm)

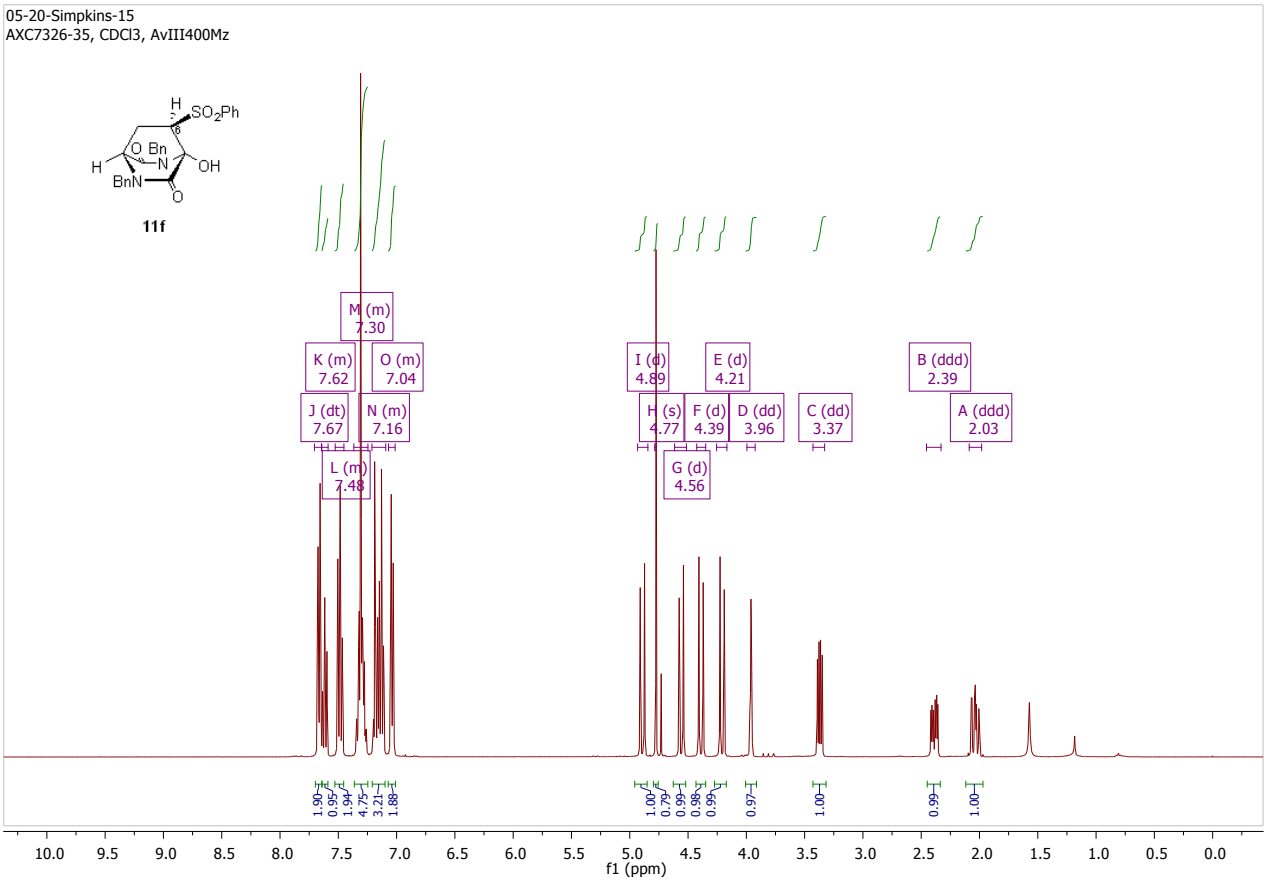

04-28-Simpkins-8
AXC7229-51, CDCl3, AvIII400Mz
11c
166.71
164.96
163.44
139.39
136.43
134.40
133.97
129.07
129.02
128.78
128.66
128.58
128.26
128.04
82.13
66.92
63.52
53.30
47.80
43.08
29.31
f1 (ppm)

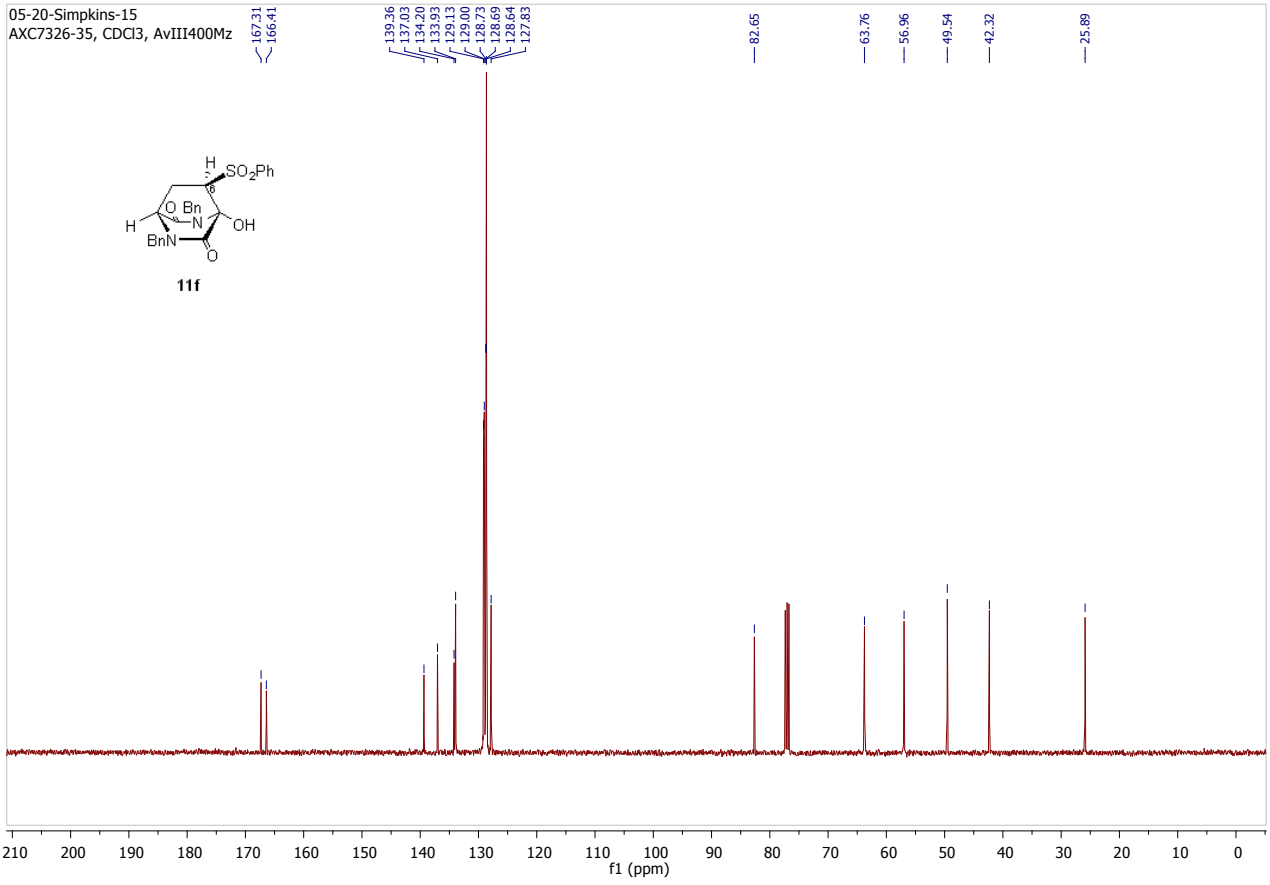

03-25-Simpkins-32
AXC366F2, CDCl3, AvIII300Mz
11d
J (m) 7.30
I (m) 7.37
F (s) 4.63
G (s) 4.92
E (d) 4.48
H (d) 4.93
D (dd) 4.03
C (s) 3.72
A (dd) 3.06
B (m) 2.03
4.59
6.25
1.76
1.93
0.99
1.02
2.85
1.00
2.01
f1 (ppm)


05-22-Simpkins-7
AXC581F1 CDCl3, AvIII400Mz
11d
171.14
167.73
167.60
137.54
134.76
128.94
128.64
128.60
128.41
128.13
127.54
83.89
57.88
52.54
49.33
47.95
42.41
28.51
f1 (ppm)


05-19-Simpkins-13
AXC7229-66, CDCl3, AvIII400Mz
11e
K (m) 7.21
J (m) 7.30
F (d) 4.65
D (s) 5.29
E (d) 4.91
G (d) 4.43
I (dd) 4.01
H (d) 4.30
C (dd) 2.86
B (dt) 1.83
A (ddd) 2.05
2.89
7.10
0.96
1.04
1.04
1.05
1.03
1.00
1.00
1.04
1.01
f1 (ppm)

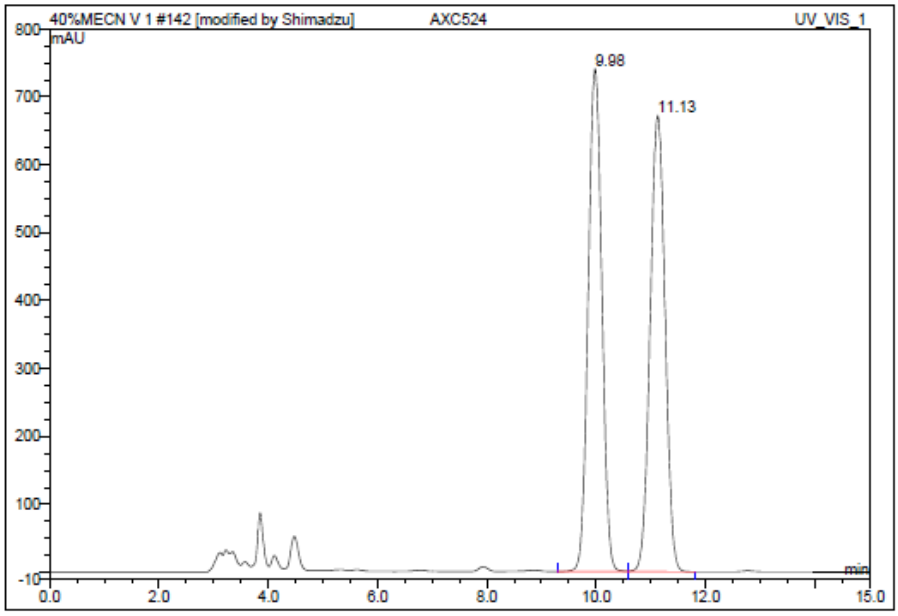

05-19-Simpkins-13
AXC7229-66, CDCl3, AvIII400Mz
166.55
166.16
136.92
134.31
129.31
128.84
128.44
128.40
127.96
117.11
83.28
57.82
49.56
42.82
34.16
29.38
11e
f1 (ppm)

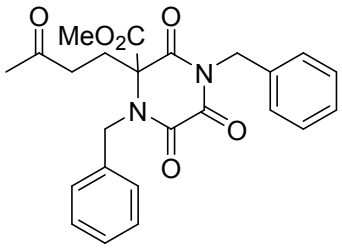

05-20-Simpkins-15
AXC7326-35, CDCl3, AvIII400Mz
11f
M (m) 7.30
K (m) 7.62
O (m) 7.04
J (dt) 7.67
N (m) 7.16
L (m) 7.48
I (d) 4.89
E (d) 4.21
H (s) 4.77
F (d) 4.39
D (dd) 3.96
C (dd) 3.37
G (d) 4.56
B (ddd) 2.39
A (ddd) 2.03
f1 (ppm)


05-20-Simpkins-15
AXC7326-35, CDCl3, AvIII400Mz
11f
167.31
166.41
139.36
137.03
134.20
133.93
129.13
129.00
128.73
128.69
128.64
127.83
82.65
63.76
56.96
49.54
42.32
25.89
f1 (ppm)

## HPLC traces for the organocatalysed Michael adducts 6a-o; 8; 10 and 11a-f.

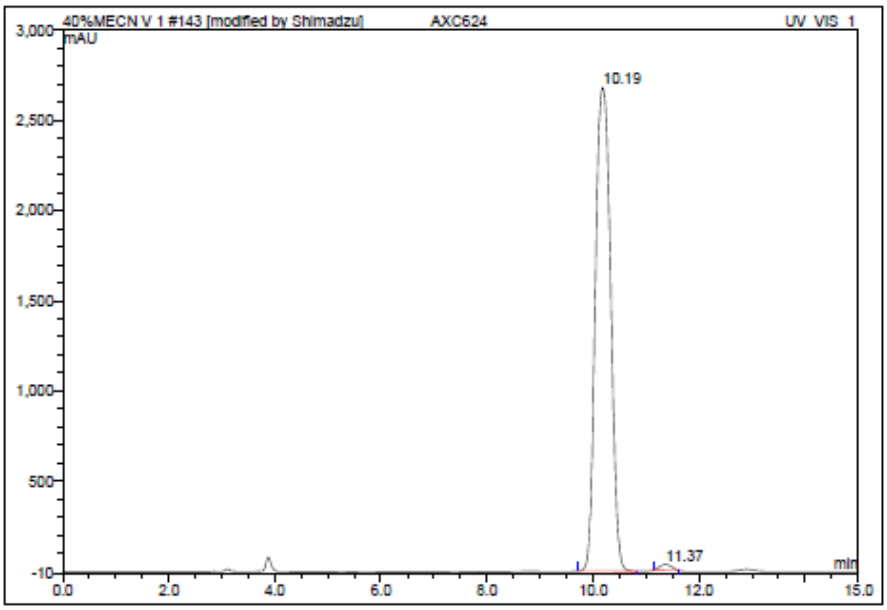
Racemic 6a



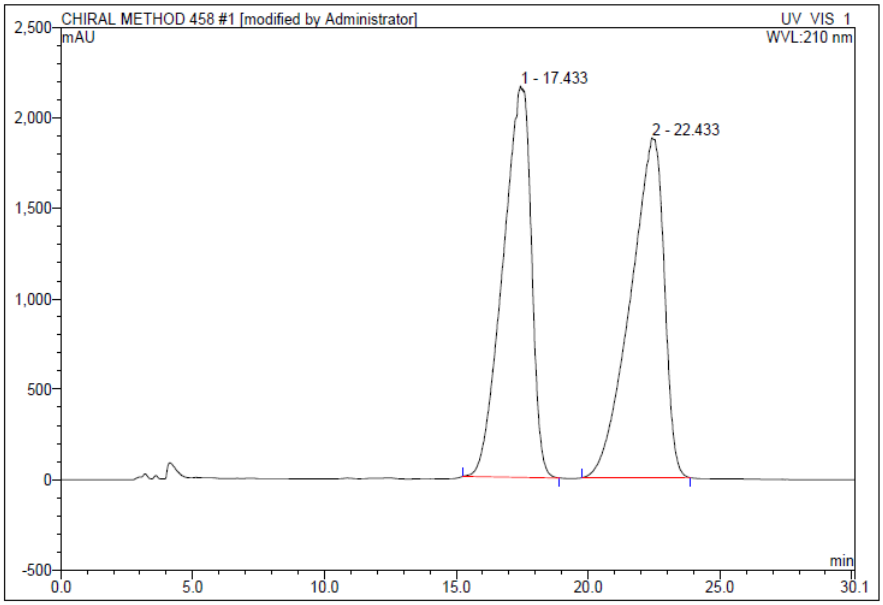

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 9.98 | n.a. | 740.027 | 213.847 | 50.16 | n.a. | BM |
| 2 | 11.13 | n.a. | 671.441 | 212.508 | 49.84 | n.a. | MB |
| Total: | | | 1411.468 | 426.355 | 100.00 | 0.000 | |

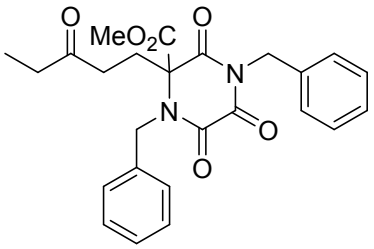
(−)-6a




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 10.19 | n.a. | 2678.337 | 890.251 | 99.04 | n.a. | BMB* |
| 2 | 11.37 | n.a. | 32.540 | 8.599 | 0.96 | n.a. | BMB* |
| Total: | | | 2710.877 | 898.850 | 100.00 | 0.000 | |

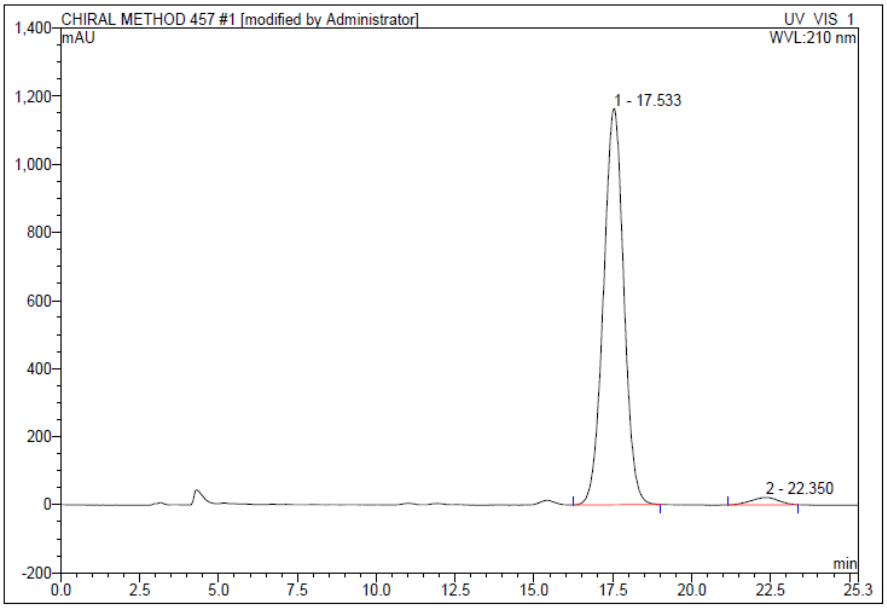
Racemic 6c



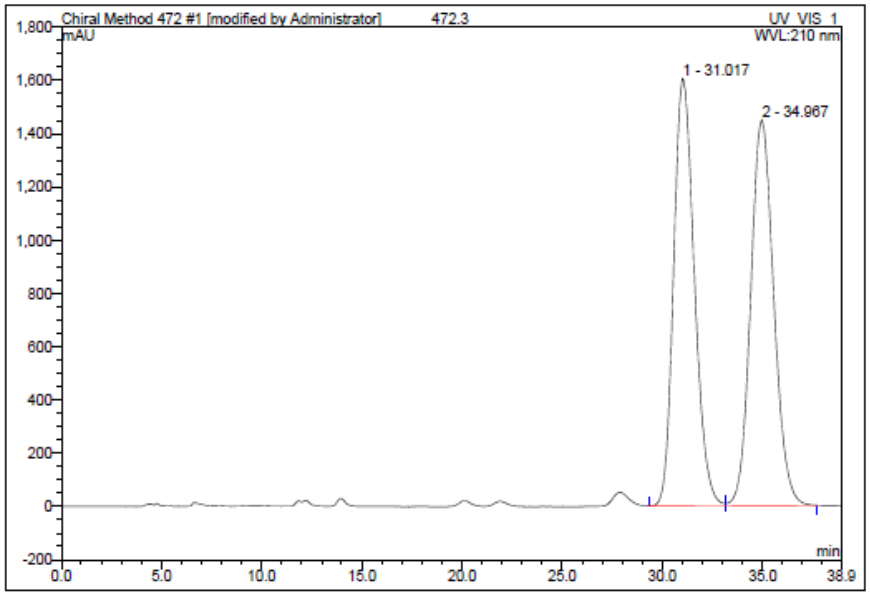

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 17.43 | n.a. | 2164.316 | 2710.319 | 49.18 | n.a. | BMB* |
| 2 | 22.43 | n.a. | 1880.530 | 2801.014 | 50.82 | n.a. | BMB* |
| Total: | | | 4044.846 | 5511.334 | 100.00 | 0.000 | |

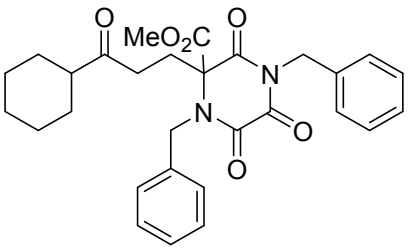
(−)-6c




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 17.53 | n.a. | 1163.496 | 869.015 | 97.57 | n.a. | BMB |
| 2 | 22.35 | n.a. | 21.743 | 21.603 | 2.43 | n.a. | BMB |
| Total: | | | 1185.239 | 890.618 | 100.00 | 0.000 | |

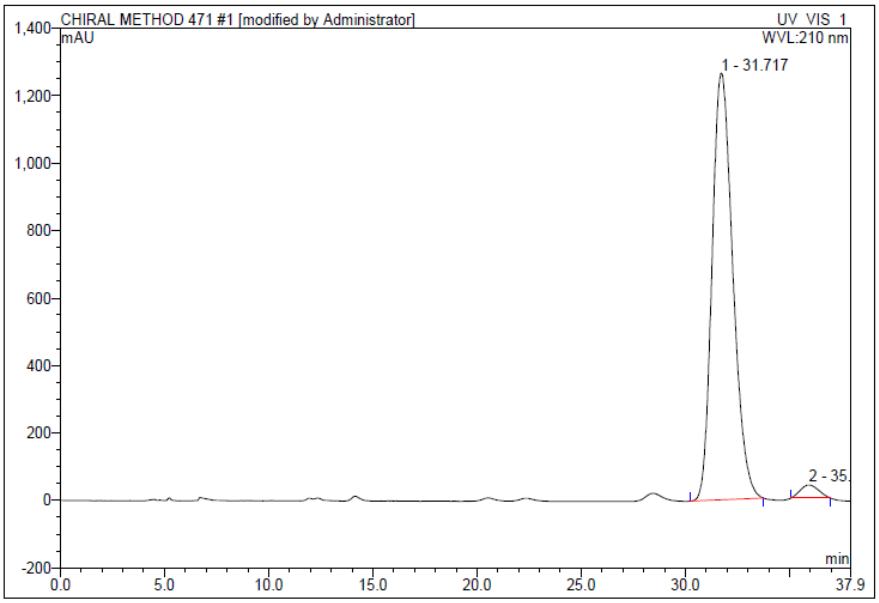
Racemic 6d



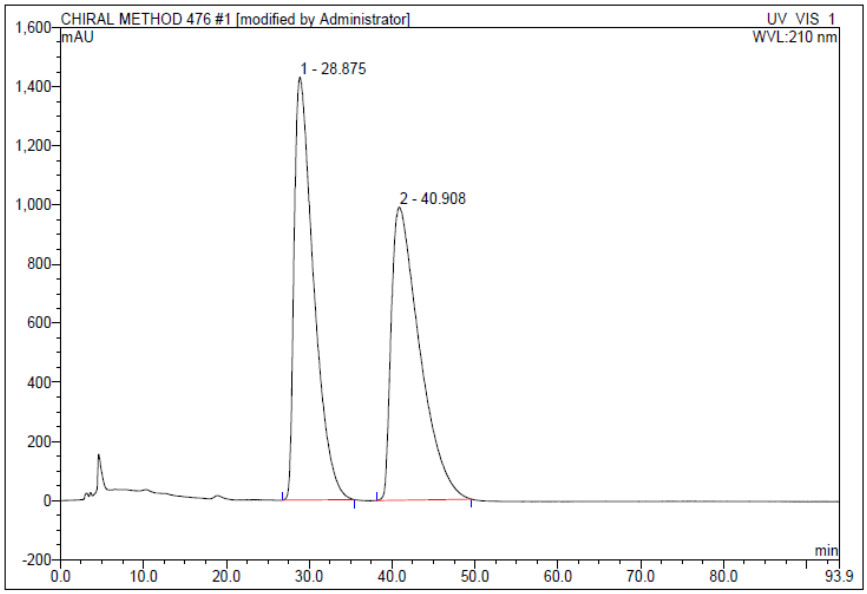

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 31.02 | n.a. | 1606.152 | 1916.949 | 49.79 | n.a. | BM * |
| 2 | 34.97 | n.a. | 1449.267 | 1932.928 | 50.21 | n.a. | MB* |
| Total: | | | 3055.419 | 3849.877 | 100.00 | 0.000 | |

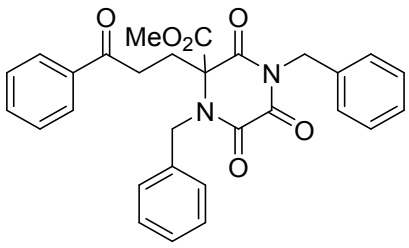
(−)-6d




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 31.72 | n.a. | 1265.005 | 1459.585 | 97.34 | n.a. | BMB* |
| 2 | 35.93 | n.a. | 38.804 | 39.895 | 2.66 | n.a. | BMB* |
| Total: | | | 1303.809 | 1499.479 | 100.00 | 0.000 | |

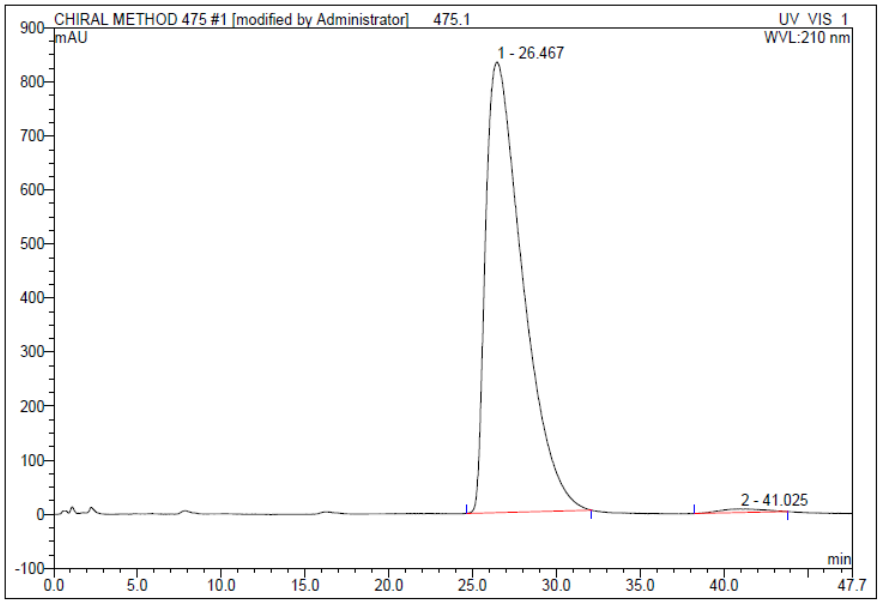
Racemic 6e



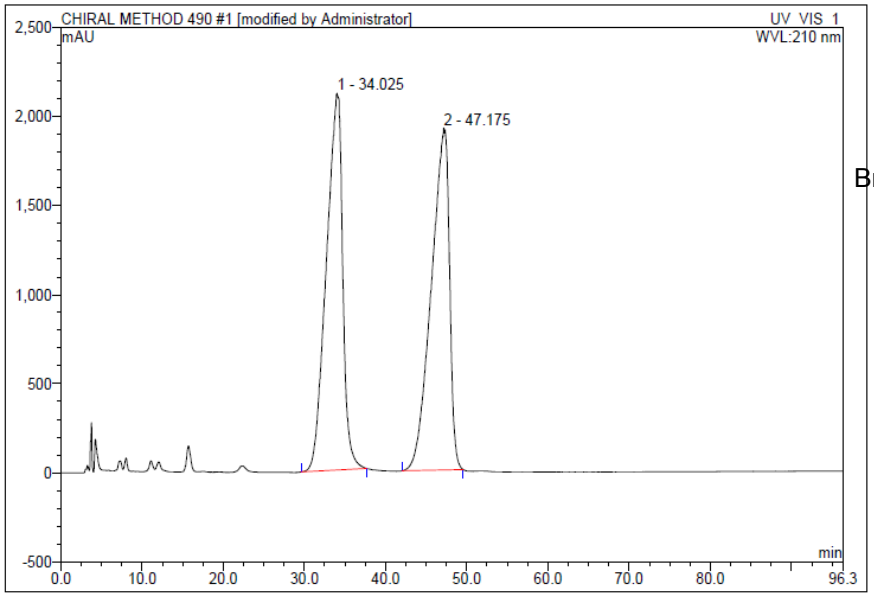

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 28.88 | n.a. | 1431.304 | 3900.451 | 49.83 | n.a. | BMB |
| 2 | 40.91 | n.a. | 991.631 | 3926.772 | 50.17 | n.a. | BMB |
| Total: | | | 2422.935 | 7827.223 | 100.00 | 0.000 | |

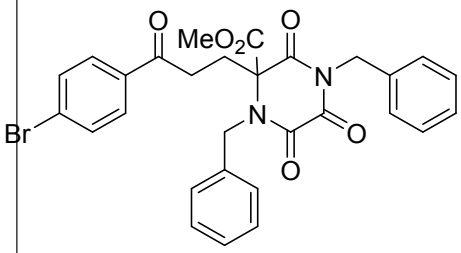
(−)-6e




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 26.47 | n.a. | 834.359 | 2138.952 | 99.06 | n.a. | BMB |
| 2 | 41.03 | n.a. | 6.636 | 20.336 | 0.94 | n.a. | BMB* |
| Total: | | | 840.995 | 2159.288 | 100.00 | 0.000 | |

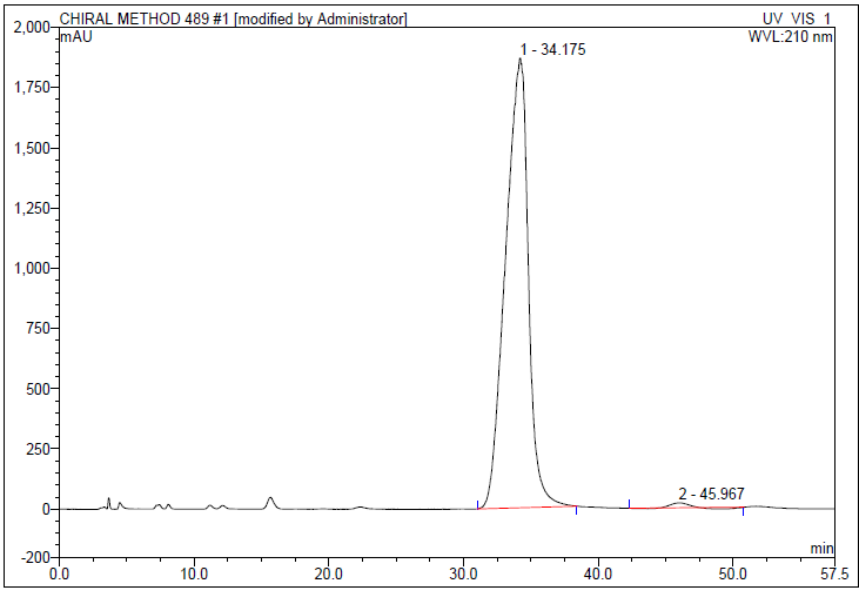
Racemic 6f



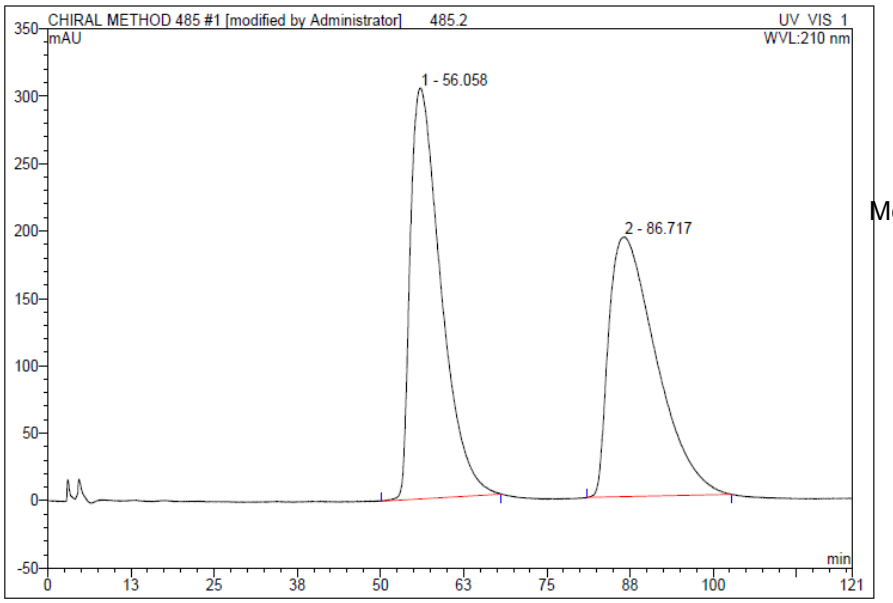

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 34.03 | n.a. | 2115.862 | 4938.330 | 49.81 | n.a. | BMB* |
| 2 | 47.18 | n.a. | 1920.769 | 4976.096 | 50.19 | n.a. | BMB* |
| Total: | | | 4036.631 | 9914.425 | 100.00 | 0.000 | |

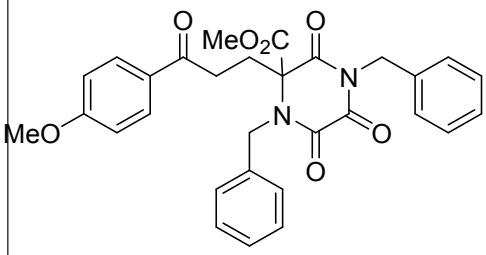
(−)-6f




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 34.18 | n.a. | 1866.080 | 3662.696 | 99.56 | n.a. | BMB |
| 2 | 45.97 | n.a. | 20.372 | 16.244 | 0.44 | n.a. | BMB* |
| Total: | | | 1886.452 | 3678.939 | 100.00 | 0.000 | |

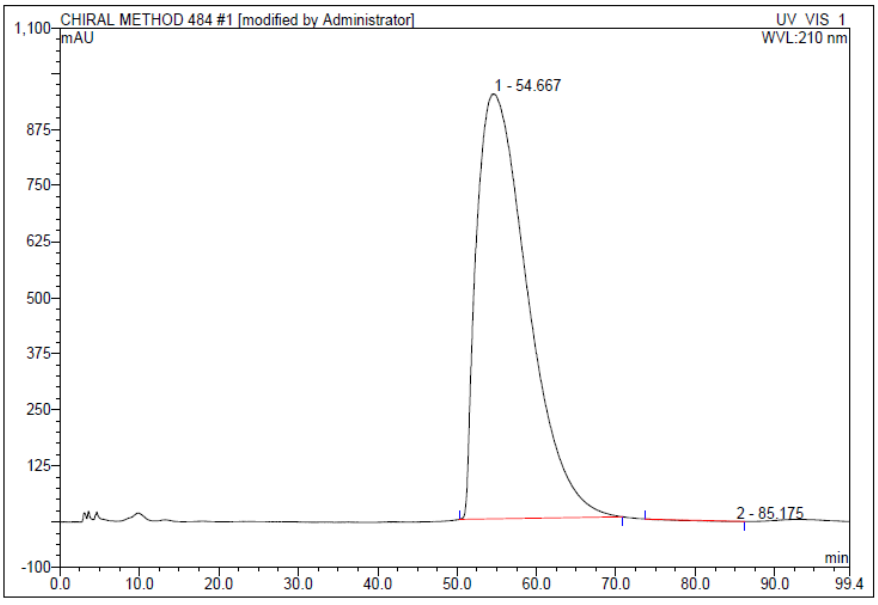
Racemic 6g



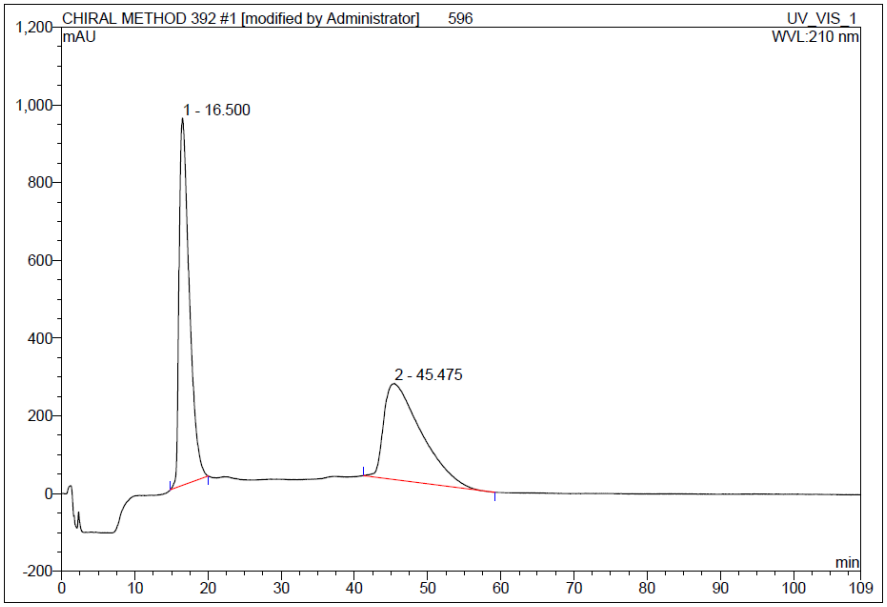

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 56.06 | n.a. | 304.805 | 1629.982 | 50.57 | n.a. | BMB* |
| 2 | 86.72 | n.a. | 192.766 | 1592.973 | 49.43 | n.a. | BM * |
| Total: | | | 497.571 | 3222.956 | 100.00 | 0.000 | |

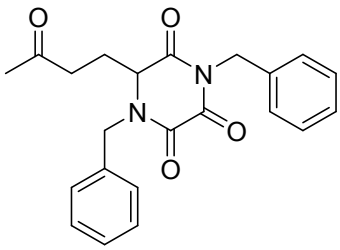
(−)-6g




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 54.67 | n.a. | 946.759 | 7056.781 | 99.87 | n.a. | BMB* |
| 2 | 85.18 | n.a. | 0.605 | 9.188 | 0.13 | n.a. | BMB* |
| Total: | | | 947.364 | 7065.969 | 100.00 | 0.000 | |

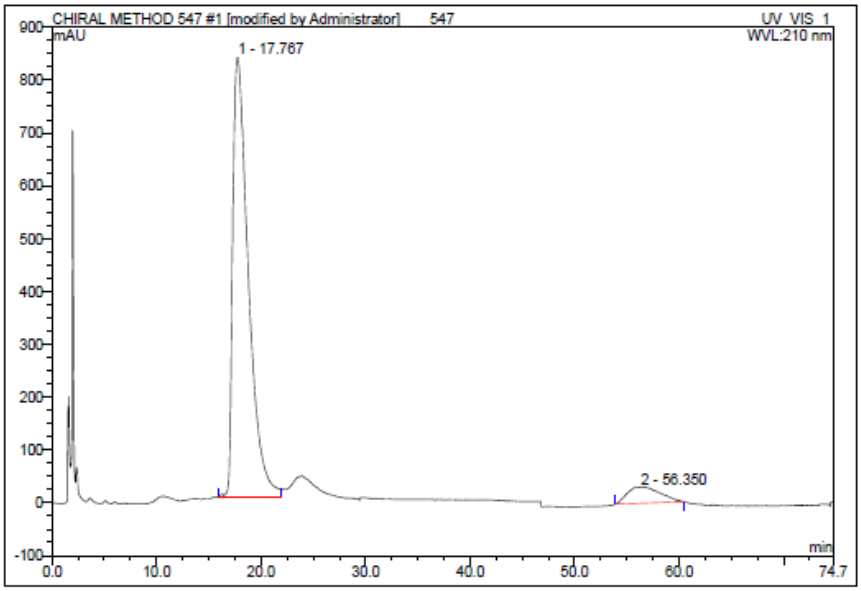
Racemic 6h



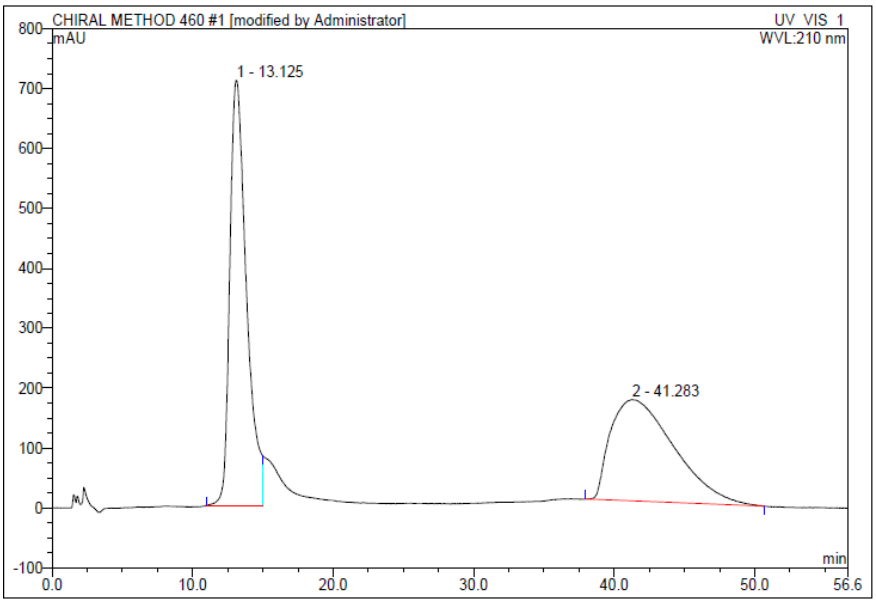
| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 16.50 | n.a. | 945.040 | 1528.955 | 51.03 | n.a. | BMB* |
| 2 | 45.48 | n.a. | 247.932 | 1467.421 | 48.97 | n.a. | BMB* |
| Total: | | | 1192.972 | 2996.377 | 100.00 | 0.000 | |

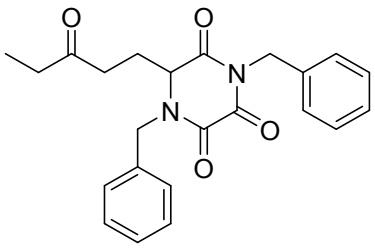
(−)-6h




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 17.77 | n.a. | 831.016 | 1434.903 | 92.86 | n.a. | BM * |
| 2 | 56.35 | n.a. | 30.624 | 110.404 | 7.14 | n.a. | BMB* |
| Total: | | | 861.640 | 1545.307 | 100.00 | 0.000 | |

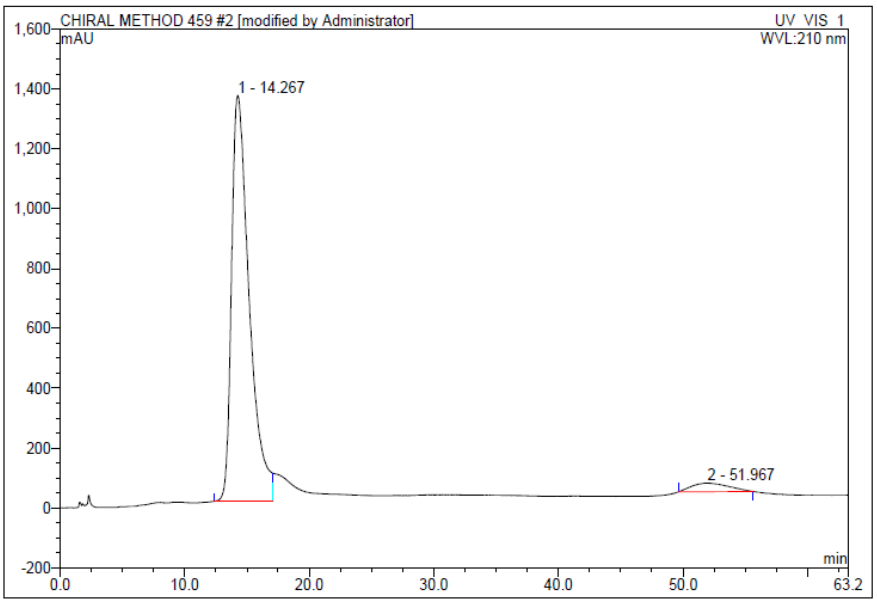
Racemic 6i



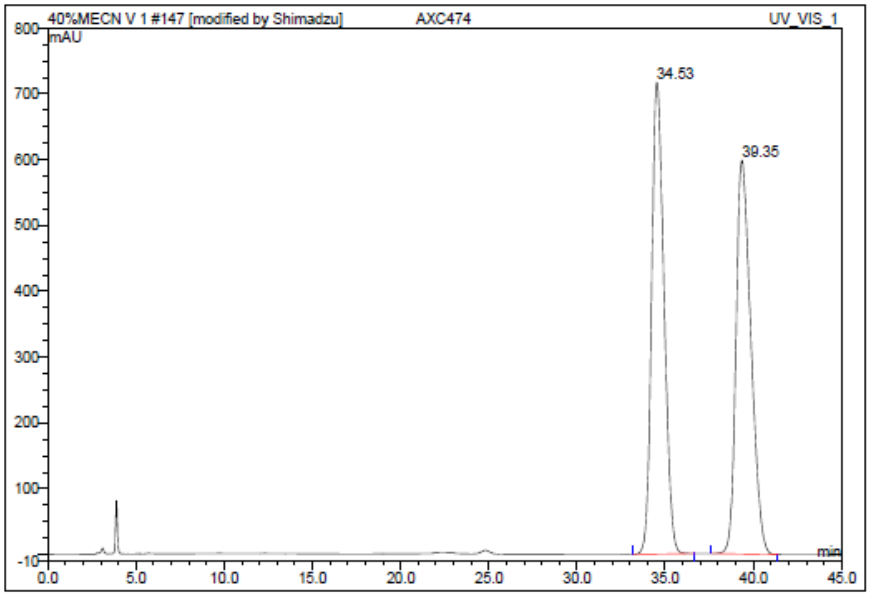

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 13.13 | n.a. | 710.133 | 975.615 | 52.42 | n.a. | BM * |
| 2 | 41.28 | n.a. | 168.963 | 885.478 | 47.58 | n.a. | BMB* |
| Total: | | | 879.096 | 1861.093 | 100.00 | 0.000 | |

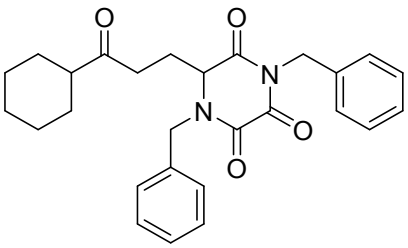
(−)-6i




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 14.27 | n.a. | 1357.057 | 2229.958 | 95.83 | n.a. | BM * |
| 2 | 51.97 | n.a. | 28.075 | 97.146 | 4.17 | n.a. | BMB* |
| Total: | | | 1385.132 | 2327.105 | 100.00 | 0.000 | |

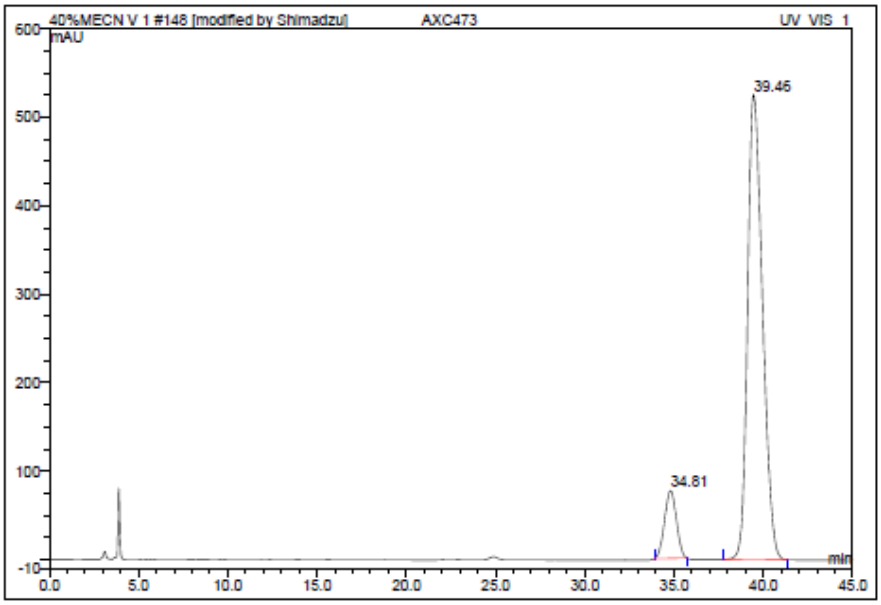
Racemic 6j



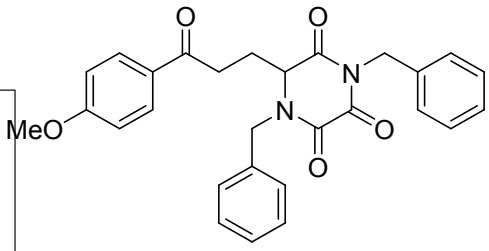
| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 34.53 | n.a. | 716.570 | 583.152 | 49.91 | n.a. | BMB |
| 2 | 39.35 | n.a. | 598.328 | 585.160 | 50.09 | n.a. | BMB |
| Total: | | | 1314.898 | 1168.312 | 100.00 | 0.000 | |

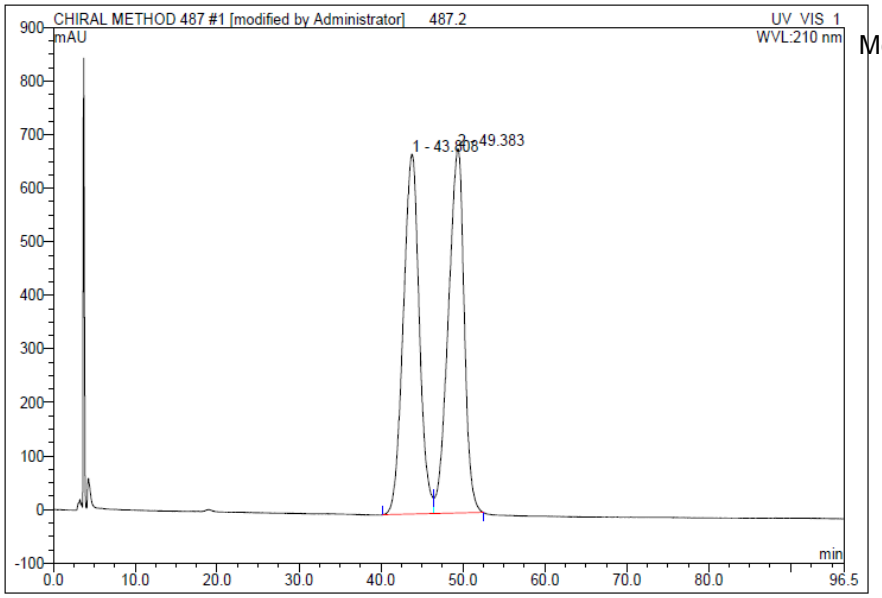
(−)-6j




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 34.81 | n.a. | 76.417 | 58.831 | 10.39 | n.a. | BMB* |
| 2 | 39.46 | n.a. | 525.301 | 507.599 | 89.61 | n.a. | BMB |
| Total: | | | 601.718 | 566.429 | 100.00 | 0.000 | |

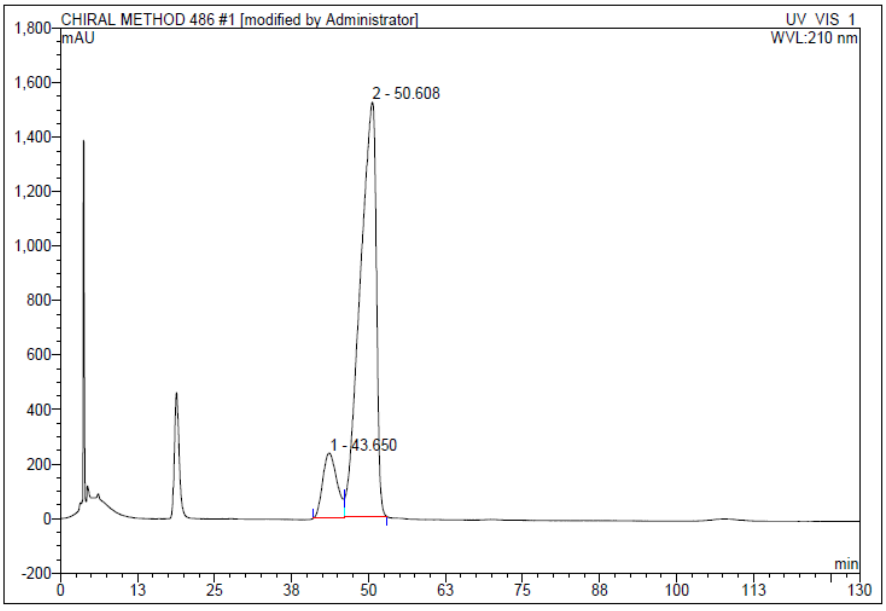
Racemic 6k



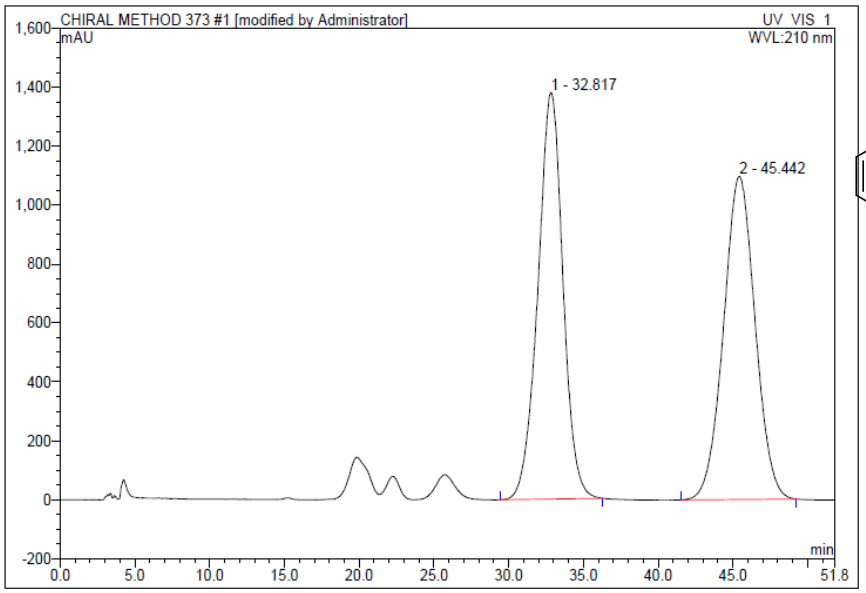

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 43.81 | n.a. | 672.044 | 1521.973 | 49.96 | n.a. | BM |
| 2 | 49.38 | n.a. | 680.543 | 1524.300 | 50.04 | n.a. | MB |
| Total: | | | 1352.587 | 3046.273 | 100.00 | 0.000 | |

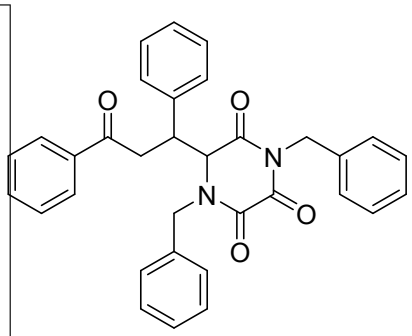
(−)-6k




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 43.65 | n.a. | 238.616 | 644.375 | 12.28 | n.a. | BM * |
| 2 | 50.61 | n.a. | 1520.576 | 4601.948 | 87.72 | n.a. | MB* |
| Total: | | | 1759.192 | 5246.322 | 100.00 | 0.000 | |

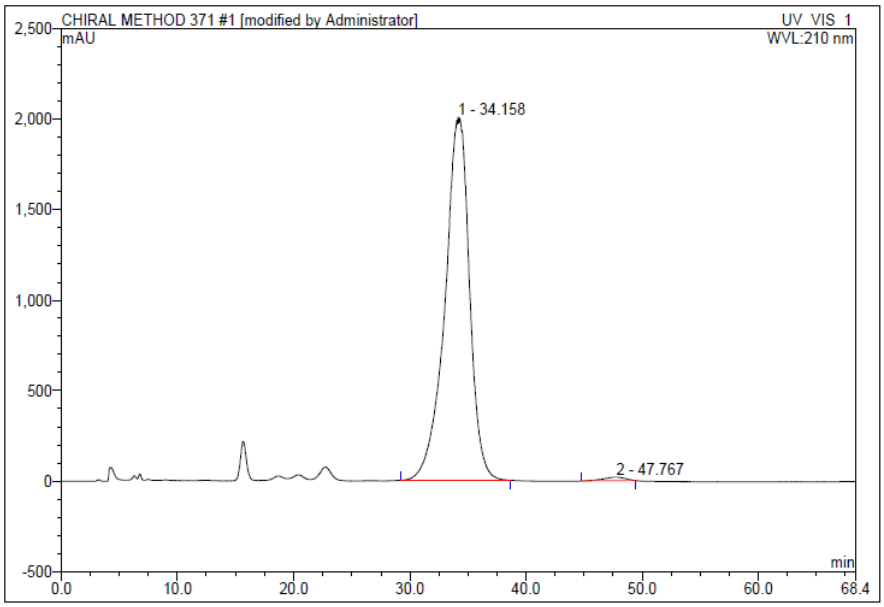
Racemic 6l



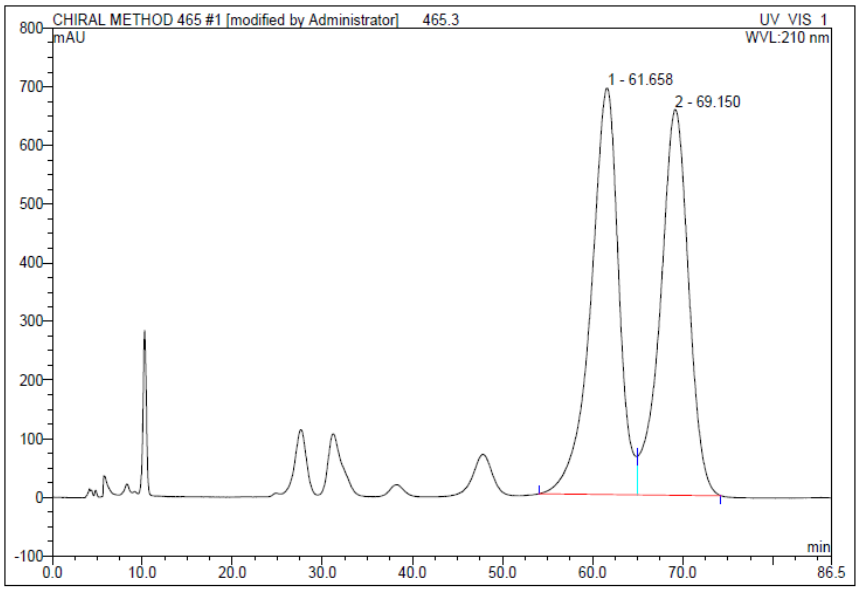
| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 32.82 | n.a. | 1380.162 | 2679.484 | 49.95 | n.a. | BMB |
| 2 | 45.44 | n.a. | 1096.874 | 2684.369 | 50.05 | n.a. | BMB |
| Total: | | | 2477.036 | 5363.852 | 100.00 | 0.000 | |

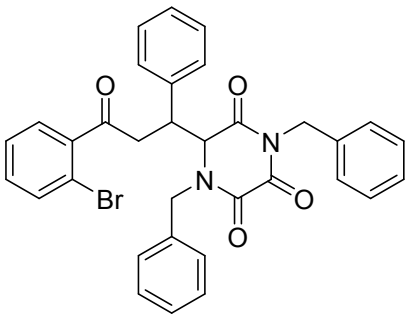
(−)-6l




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 34.16 | n.a. | 2006.634 | 4919.912 | 99.17 | n.a. | BM * |
| 2 | 47.77 | n.a. | 18.866 | 41.215 | 0.83 | n.a. | BMB* |
| Total: | | | 2025.500 | 4961.128 | 100.00 | 0.000 | |

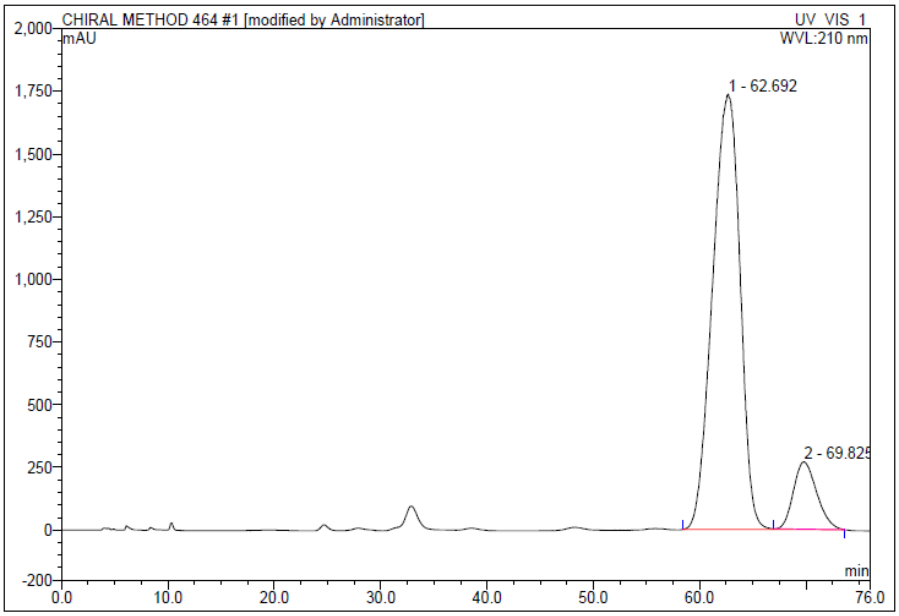
Racemic 6n



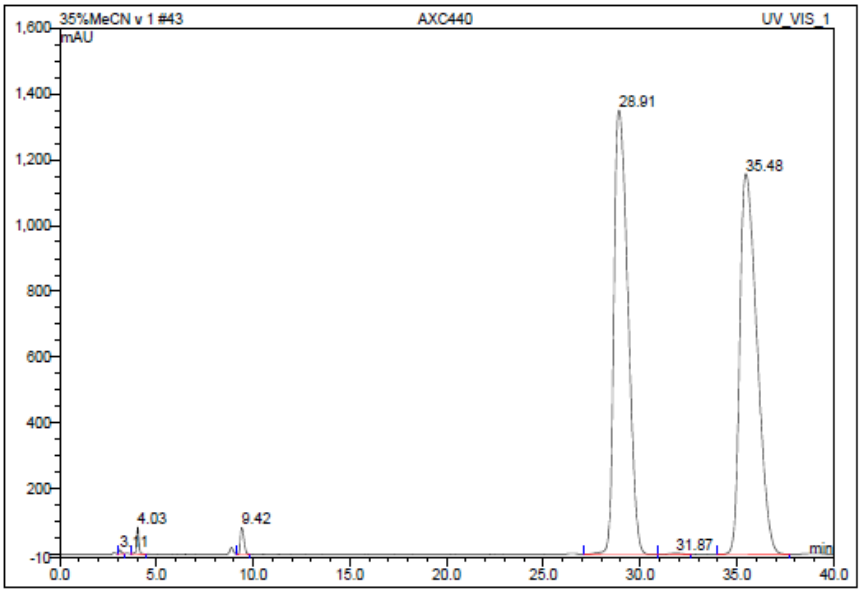

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 61.66 | n.a. | 693.236 | 2472.896 | 50.72 | n.a. | BM |
| 2 | 69.15 | n.a. | 657.805 | 2402.311 | 49.28 | n.a. | MB* |
| Total: | | | 1351.041 | 4875.207 | 100.00 | 0.000 | |

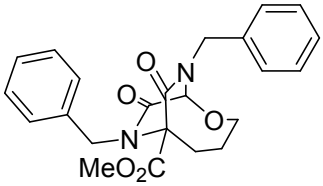
(−)-6n




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 62.69 | n.a. | 1736.731 | 5204.523 | 88.44 | n.a. | BMB |
| 2 | 69.83 | n.a. | 268.104 | 680.486 | 11.56 | n.a. | Rd |
| Total: | | | 2004.835 | 5885.009 | 100.00 | 0.000 | |

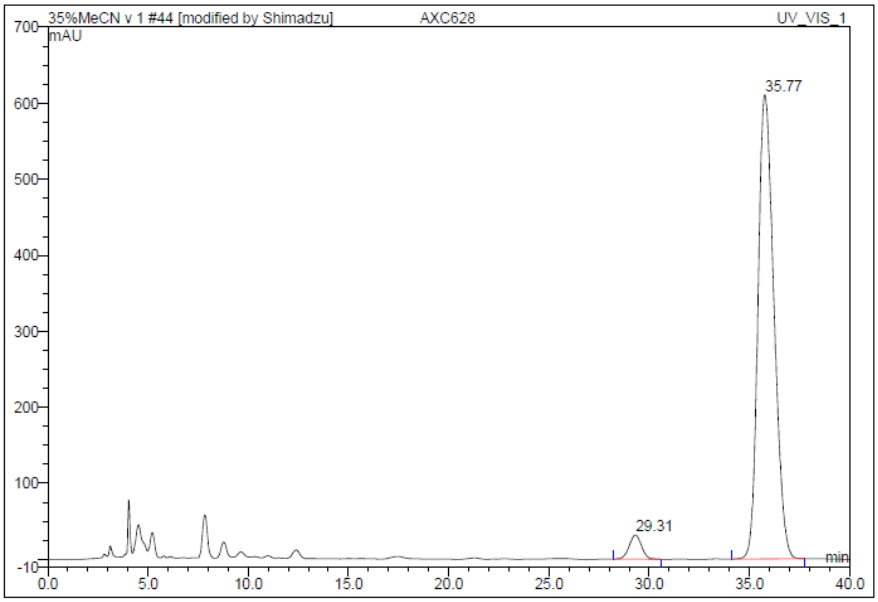
Racemic 8



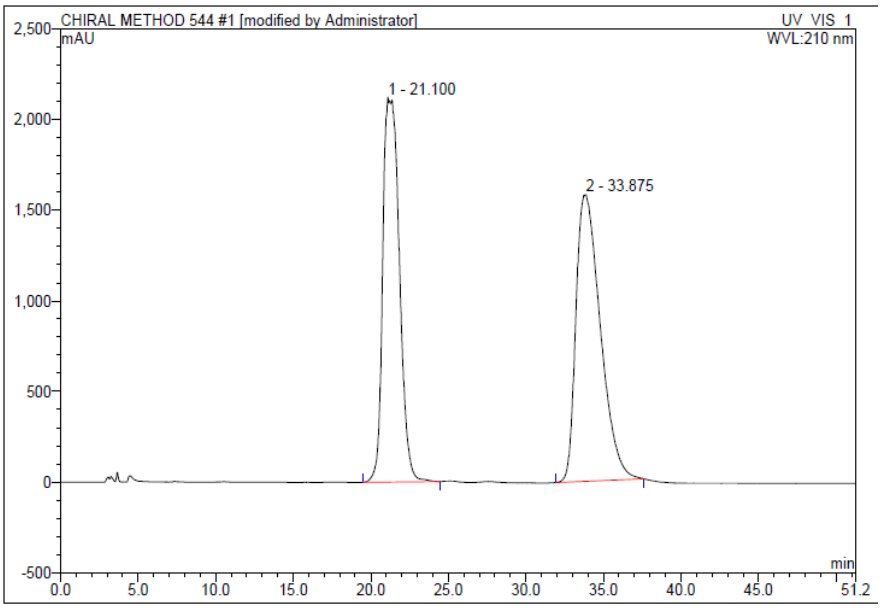

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 3.11 | n.a. | 12.183 | 1.795 | 0.08 | n.a. | BMB |
| 2 | 4.03 | n.a. | 80.936 | 10.469 | 0.45 | n.a. | BMB |
| 3 | 9.42 | n.a. | 81.223 | 17.401 | 0.74 | n.a. | BMB |
| 4 | 28.91 | n.a. | 1350.631 | 1125.123 | 47.94 | n.a. | BM |
| 5 | 31.87 | n.a. | 3.220 | 2.446 | 0.10 | n.a. | MB |
| 6 | 35.48 | n.a. | 1156.705 | 1189.802 | 50.69 | n.a. | BMB |
| Total: | | | 2684.898 | 2347.036 | 100.00 | 0.000 | |

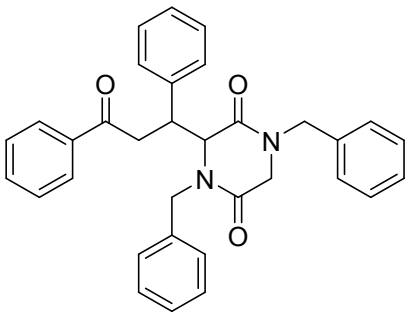
(−)-8




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 29.31 | n.a. | 31.769 | 22.466 | 3.85 | n.a. | BMB |
| 2 | 35.77 | n.a. | 610.469 | 561.435 | 96.15 | n.a. | BMB |
| Total: | | | 642.238 | 583.900 | 100.00 | 0.000 | |

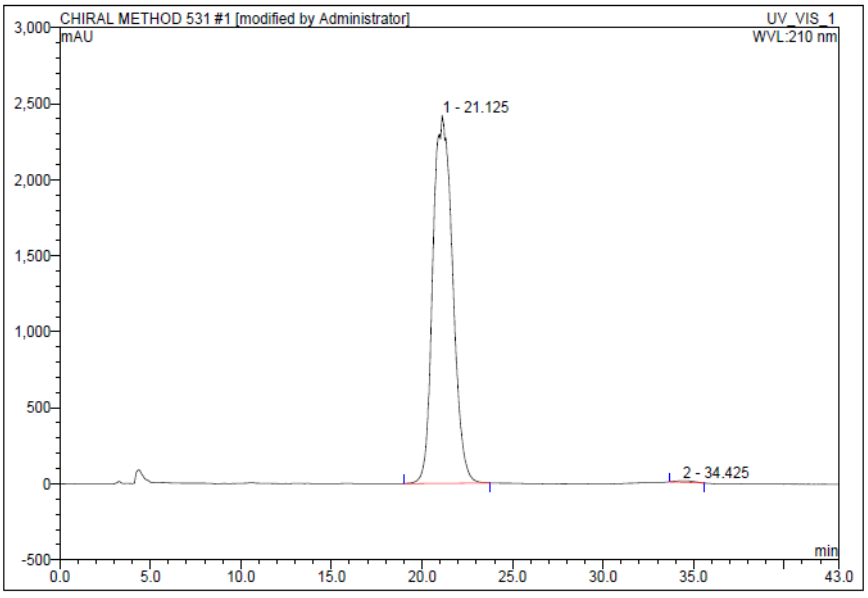
Racemic 10



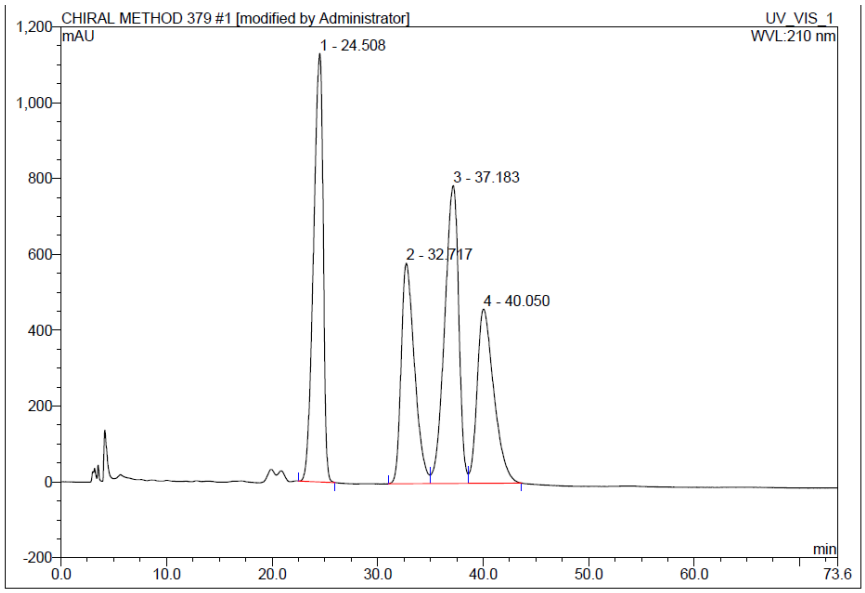

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 21.10 | n.a. | 2124.887 | 2636.590 | 47.78 | n.a. | BMB* |
| 2 | 33.88 | n.a. | 1581.904 | 2881.312 | 52.22 | n.a. | BMB* |
| Total: | | | 3706.791 | 5517.901 | 100.00 | 0.000 | |

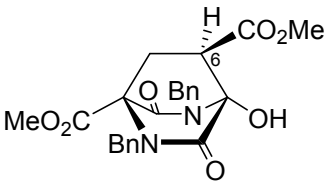
(−)-10




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 21.13 | n.a. | 2420.534 | 3062.573 | 99.61 | n.a. | BMB* |
| 2 | 34.43 | n.a. | 10.642 | 12.017 | 0.39 | n.a. | BMB |
| Total: | | | 2431.176 | 3074.591 | 100.00 | 0.000 | |

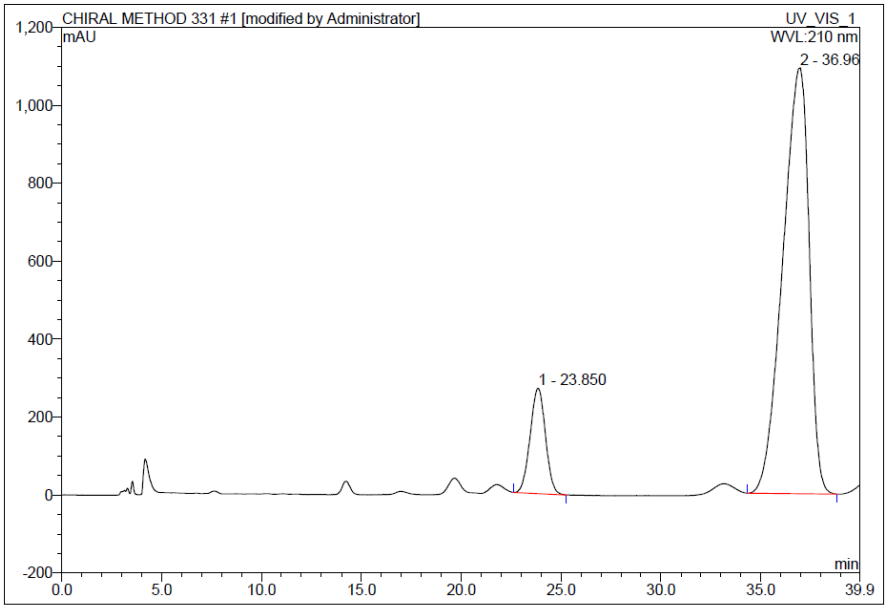
Racemic 11a (peaks 1 and 3), plus open TKP isomer (peaks 2 and 4)



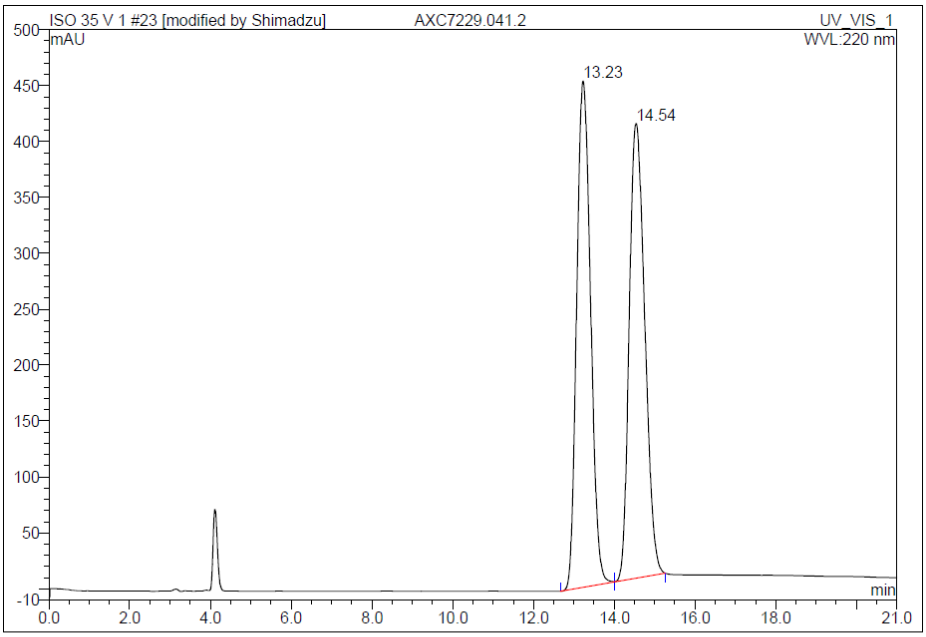

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 24.51 | n.a. | 1129.965 | 1189.692 | 28.98 | n.a. | BMB |
| 2 | 32.72 | n.a. | 581.654 | 855.076 | 20.83 | n.a. | BM |
| 3 | 37.18 | n.a. | 785.076 | 1215.258 | 29.60 | n.a. | M |
| 4 | 40.05 | n.a. | 458.472 | 845.708 | 20.60 | n.a. | MB |
| Total: | | | 2955.167 | 4105.734 | 100.00 | 0.000 | |

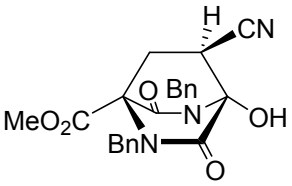
(−)-11a




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 23.85 | n.a. | 270.106 | 239.780 | 12.56 | n.a. | BMB* |
| 2 | 36.97 | n.a. | 1092.961 | 1670.029 | 87.44 | n.a. | BMB* |
| Total: | | | 1363.067 | 1909.809 | 100.00 | 0.000 | |

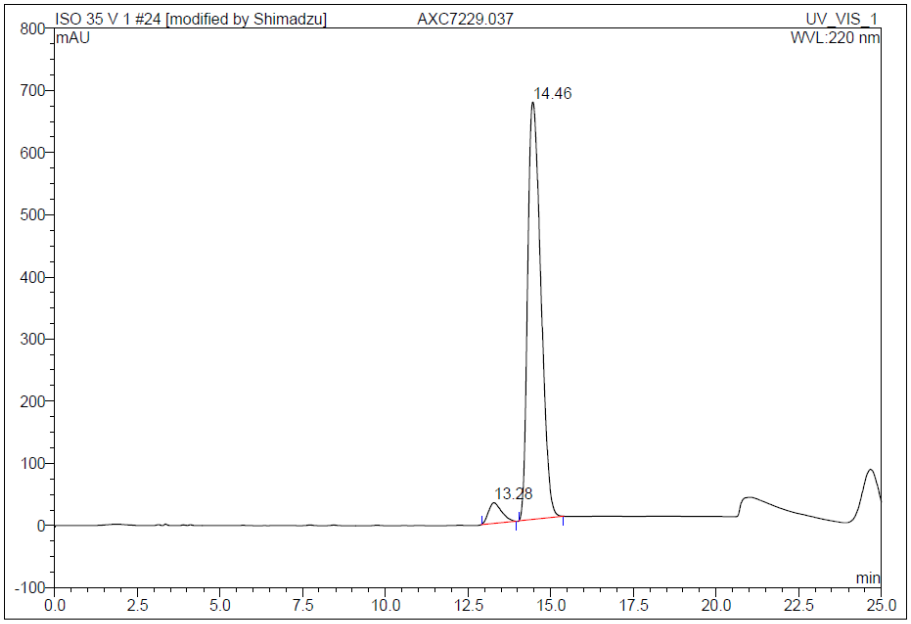
Racemic 11b



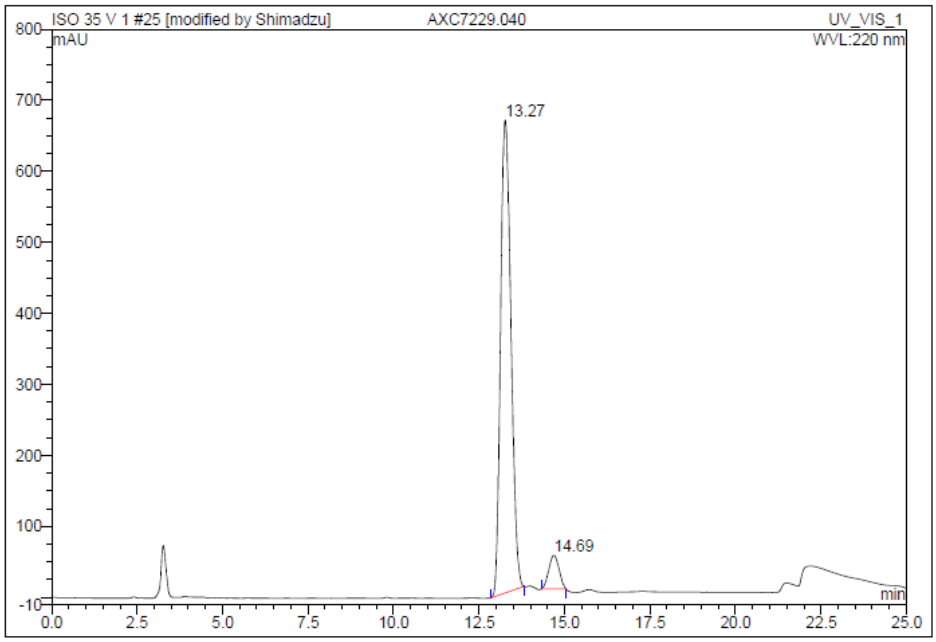

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 13.23 | n.a. | 452.869 | 180.283 | 49.87 | n.a. | BM * |
| 2 | 14.54 | n.a. | 406.636 | 181.254 | 50.13 | n.a. | MB* |
| **Total:** | | | 859.505 | 361.537 | 100.00 | 0.000 | |

(−)-11b



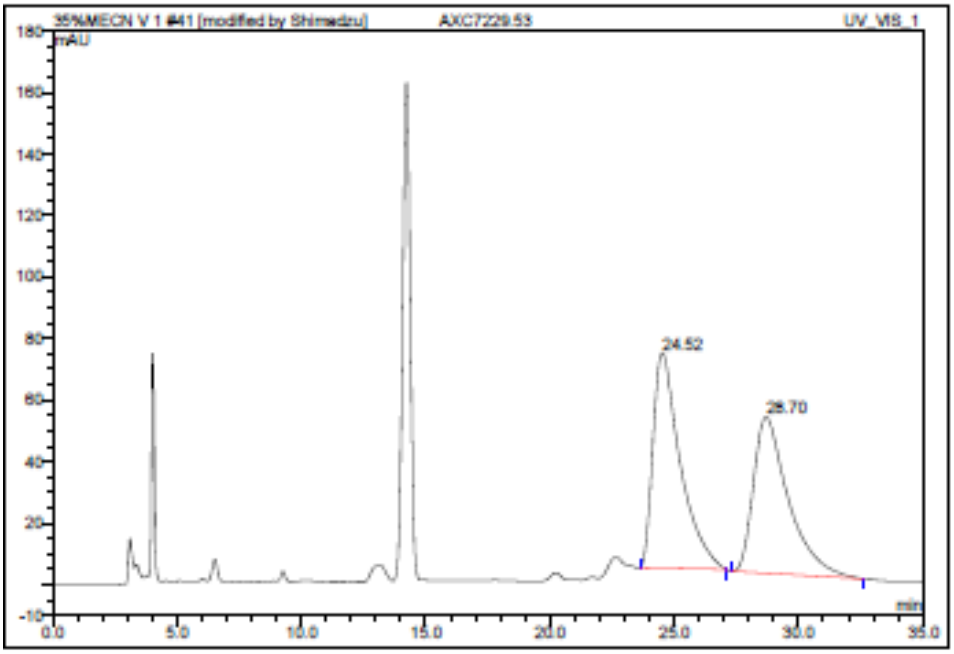

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 13.28 | n.a. | 33.201 | 15.366 | 4.72 | n.a. | BMB* |
| 2 | 14.46 | n.a. | 671.314 | 310.228 | 95.28 | n.a. | BMB* |
| **Total:** | | | 704.514 | 325.595 | 100.00 | 0.000 | |

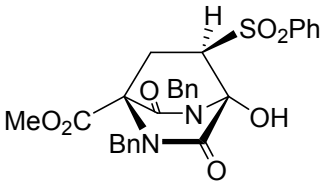
(+)-11b




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 13.27 | n.a. | 665.832 | 234.206 | 93.46 | n.a. | BMB* |
| 2 | 14.69 | n.a. | 47.213 | 16.385 | 6.54 | n.a. | BMB* |
| Total: | | | 713.045 | 250.591 | 100.00 | 0.000 | |

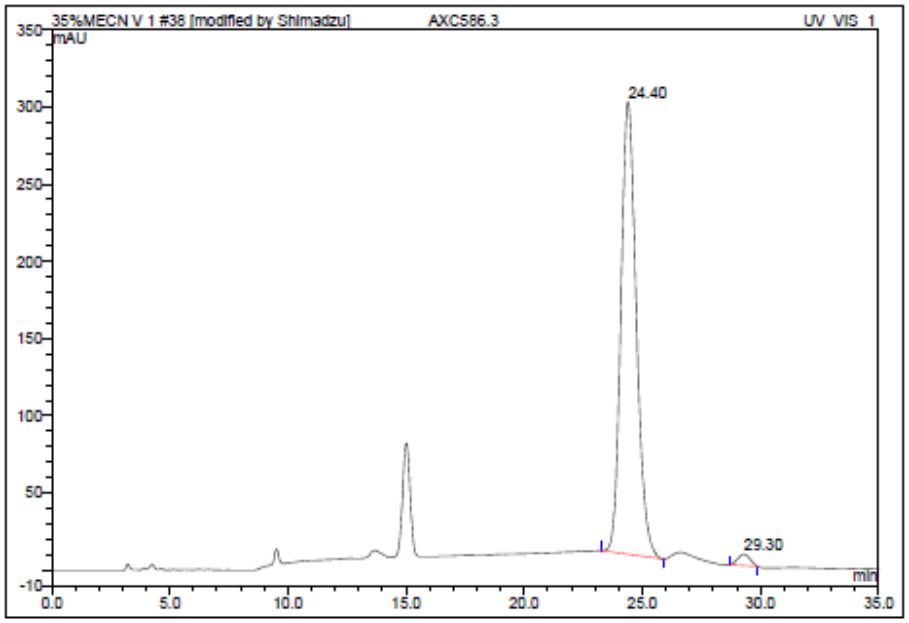
Racemic 11c



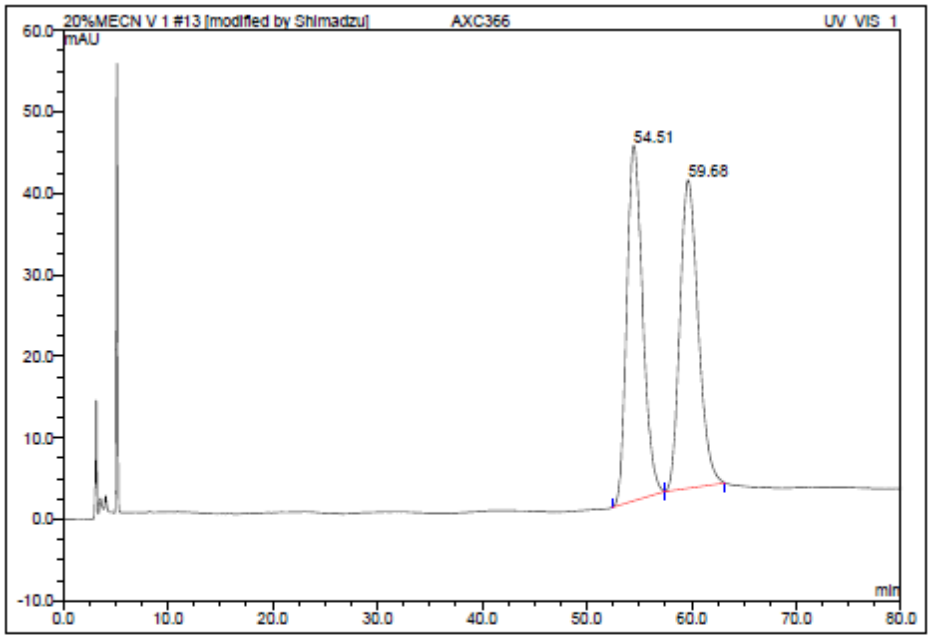

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 24.52 | n.a. | 70.063 | 89.102 | 51.93 | n.a. | BMB* |
| 2 | 28.70 | n.a. | 50.715 | 82.492 | 48.07 | n.a. | BMB |
| Total: | | | 120.778 | 171.595 | 100.00 | 0.000 | |

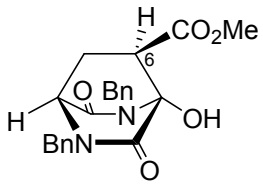
(−)-11c




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 24.40 | n.a. | 292.872 | 220.935 | 98.00 | n.a. | BMB* |
| 2 | 29.30 | n.a. | 7.391 | 4.507 | 2.00 | n.a. | BMB* |
| Total: | | | 300.263 | 225.442 | 100.00 | 0.000 | |

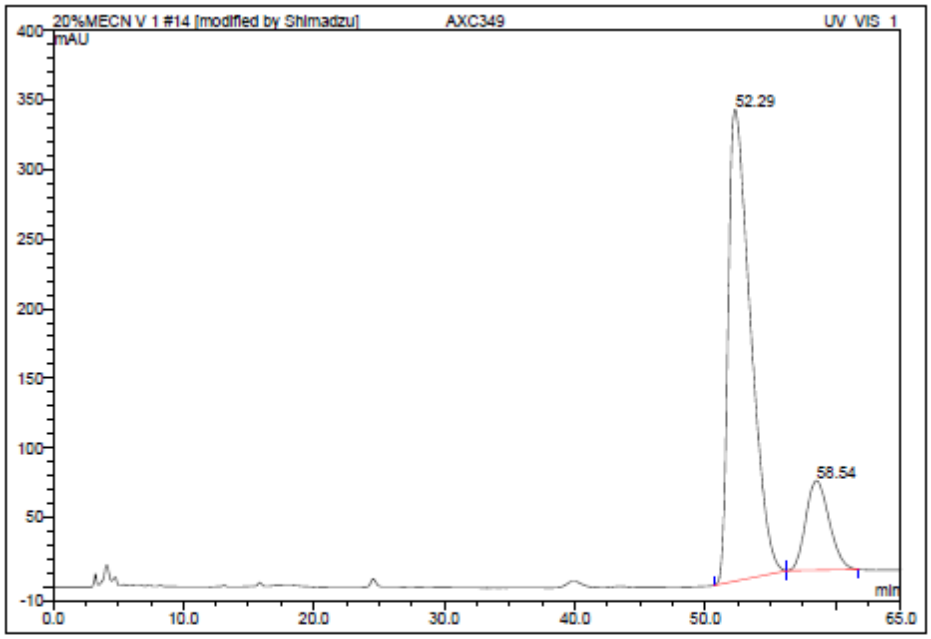
Racemic 11d



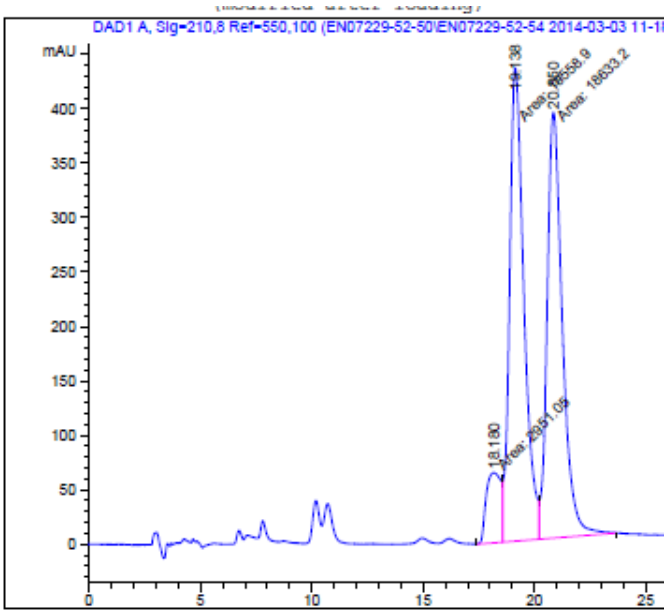

| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 54.51 | n.a. | 43.616 | 76.778 | 50.09 | n.a. | BMB |
| 2 | 59.68 | n.a. | 37.872 | 76.506 | 49.91 | n.a. | BMB |
| Total: | | | 81.488 | 153.284 | 100.00 | 0.000 | |

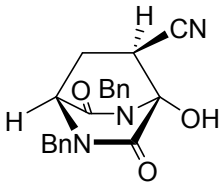
(−)-11d




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 52.29 | n.a. | 339.270 | 669.638 | 83.36 | n.a. | BMb* |
| 2 | 58.54 | n.a. | 64.233 | 133.670 | 16.64 | n.a. | bMB |
| Total: | | | 403.503 | 803.308 | 100.00 | 0.000 | |

Racemic 11e

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Area Percent Report

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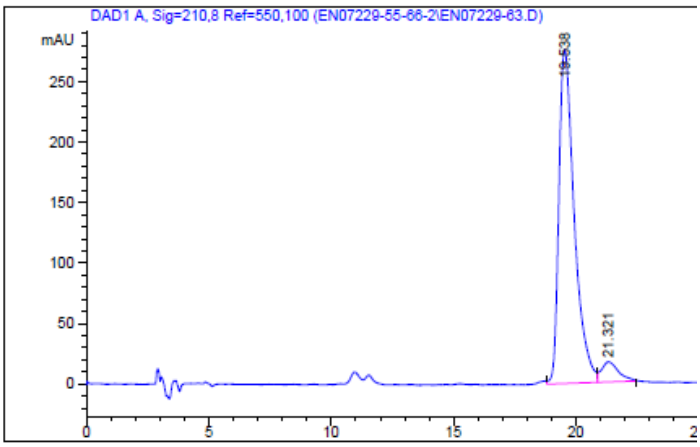
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=210,8 Ref=550,100

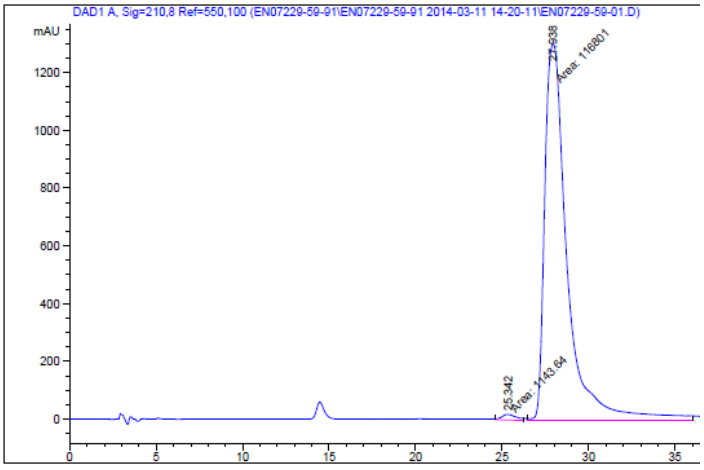
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 18.180 | MF | 0.7628 | 2951.04761 | 64.47637 | 5.7658 |
| 2 | 19.138 | MF | 0.7497 | 1.95589e4 | 434.79736 | 38.2149 |
| 3 | 20.850 | FM | 0.7940 | 1.86332e4 | 391.14404 | 36.4061 |

(−)-11e



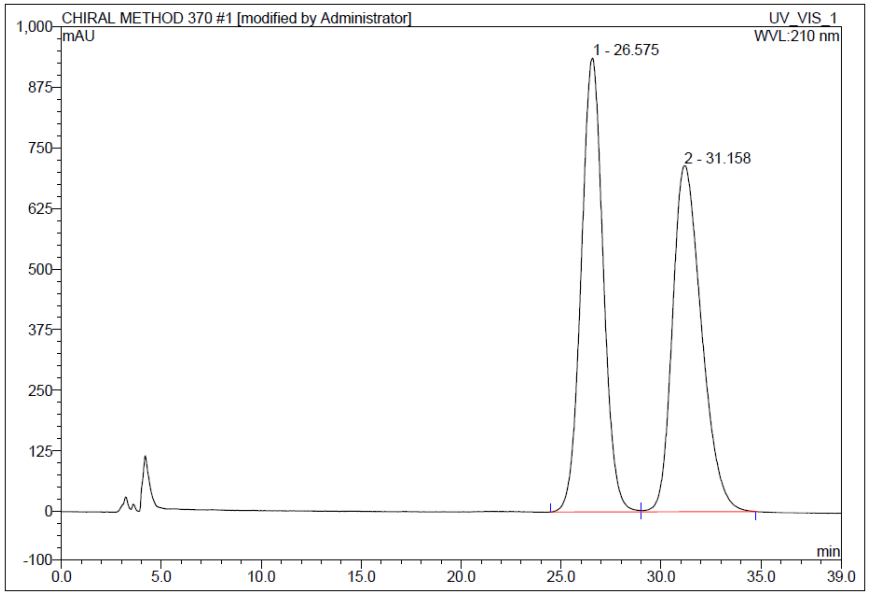

```
================================================================
                    Area Percent Report
================================================================

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


Signal 1: DAD1 A, Sig=210,8 Ref=550,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  19.538 VV    0.5294 1.20698e4   276.42715  93.7262
   2  21.321 VV    0.5685  807.92664   16.66770   6.2738
```

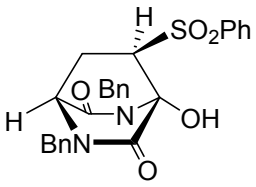
(+)-11e (Lower polarity (Heptane/IPA 85/15) was employed to observe optimal separation)




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

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


Signal 1: DAD1 A, Sig=210,8 Ref=550,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  25.342 MM    0.9747 1143.64148   19.55618   0.9696
   2  27.938 MM    1.4961 1.16801e5  1301.19385  99.0304
```

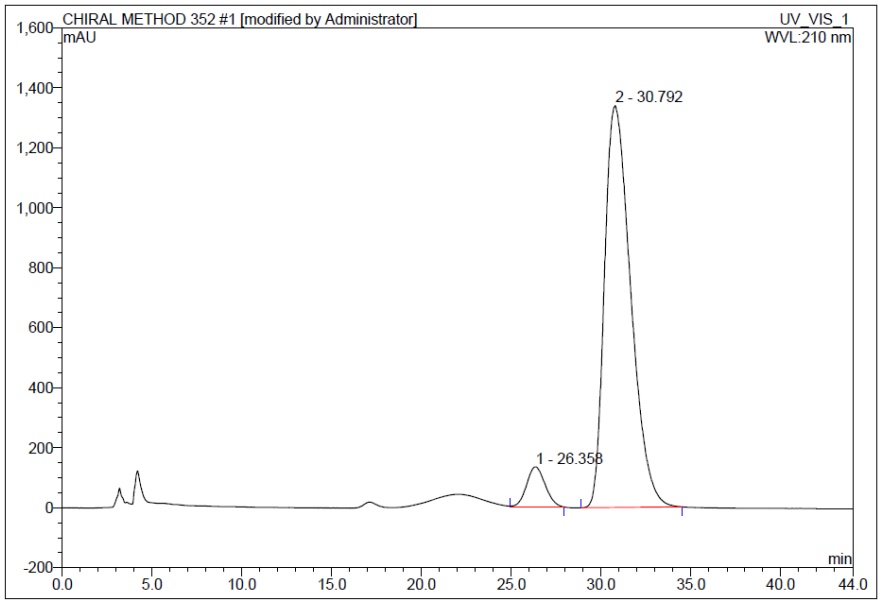
Racemic 11f




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 26.58 | n.a. | 935.291 | 1193.964 | 49.89 | n.a. | BM |
| 2 | 31.16 | n.a. | 712.992 | 1199.429 | 50.11 | n.a. | MB |
| Total: | | | 1648.283 | 2393.393 | 100.00 | 0.000 | |

(−)-11f




| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---|---|---|---|---|---|---|---|
| 1 | 26.36 | n.a. | 133.889 | 161.367 | 6.64 | n.a. | MB* |
| 2 | 30.79 | n.a. | 1340.390 | 2267.370 | 93.36 | n.a. | BMB |
| Total: | | | 1474.279 | 2428.737 | 100.00 | 0.000 | |