ORGANIC CHEMISTRY
FRONTIERS

Supporting Information

A Novel Chiral DMAP-Thiourea Bifunctional Catalyst Catalyzed Enantioselective Steglich and Black Rearrangement Reaction

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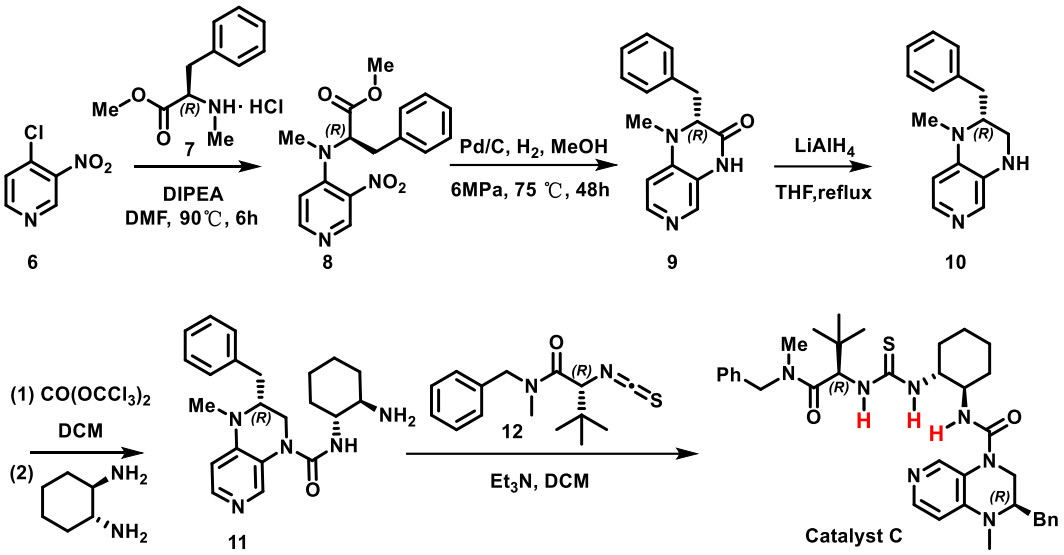
1. GENERAL INFORMATION

Unless otherwise indicated, all starting materials purchased from commercial suppliers were used without further purification. All solvents were dried before use following the standard procedures. Nuclear Magnetic Resonance (NMR) spectras were acquired on a Bruker 400 or Bruker 600 instrument for ^{1}H, ^{13}C, ^{19}F. Chemical shifts are reported in ppm downfield from $CHCl_3$ (δ = 7.26 ppm), DMSO (δ = 2.54 ppm) or Acetone (δ = 2.05 ppm) for ^{1}H NMR and chemical shifts for ^{13}C NMR spectra are reported in ppm relative to the central $CHCl_3$ (δ = 77.0 ppm), DMSO (δ = 39.6 ppm) or Acetone (δ = 29.8 ppm). Coupling constants are given in Hz. Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, quintet = quint, heptet = hept, m = multiplet, br = broad resonance. Optical rotations were measured on JASCO P-1030 or Anton Paar MCP 5500 polarimeter at 589 nm. High resolution mass spectrums were acquired by Agilent 6545 Accurate-Mass Q-TOF LC/MS System.

2. CATALYST PREPARATION

Reaction scheme for preparation catalyst C

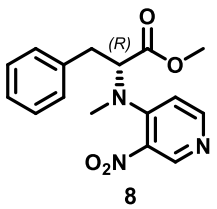


General procedures for the preparation of catalyst C

The starting material, methyl methyl-*D*-phenylalaninate hydrochloride salt (**7**), was prepared according to the literature.[1]

Methyl *N*-methyl-*N*-(3-nitropyridin-4-yl)-*D*-phenylalaninate (8)

To a well-stirred solution of **7** (12.3 g, 1.1 eq, 53.71 mmol) in DMF (150 ml) was added DIPEA (17.8 ml, 107.43 mmol, 2.2 equiv) and **6** (4-chloro-3-nitropyridine, 7.7 g, 1eq，48.83 mmol). The resulting mixture was heated to 90°C and stirred for 6 h, then diluted with 150 mL H_2O, extracted with EtOAc (250 mL × 3). Then, the combined organic phases were washed with brine (200 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give pure products **8**.

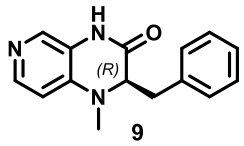


Yellow oil, 6.5 g, 42.2% yield. $[\alpha]_D^{29.9}$= -197.73 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.76 (s, 1H), 8.24 (d, J = 6.1 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.25 – 7.15 (m, 4H), 6.67 (d, J = 6.1 Hz, 1H), 4.39 (dd, J = 9.0, 6.1 Hz, 1H), 3.78 (s, 3H), 3.39 (ABd, J_1 = 14.0 Hz, J_2 = 4.0 Hz, 1H), 3.17 (ABd, J_1 = 14.0 Hz, J_2 = 12.0 Hz, 1H), 2.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.57, 151.98, 149.91, 148.09, 135.97, 135.93, 128.76, 128.68, 127.24, 112.14, 65.09, 52.61, 35.93, 35.80. ESI-HRMS: $[M+H]^{\oplus}$calcd for $C_{16}H_{18}N_3O_4$ 316.1297, found 316.1294.

[1] A. G. Wenzel and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2002, **124**, 12964.

(*R*)-2-benzyl-1-methyl-1, 4-dihydropyrido[3,4-*b*]pyrazin-3(2H)-one (9)

To a well-stirred solution of **8** (3.00 g, 1.0 eq, 9.51 mmol) in MeOH (34 ml) was added 10% Pd/C (w/w 20%, 0.60g). The resulting mixture heated at 75 ^{o}C, 6 MPa for 48 h under hydrogen atmosphere. Then the reaction mixture was filtered and concentrated *in vacuo*, then added DCM to give part of the product **9** as off white solid. The filtrate was concentrated *in vacuo* and purified by silica gel column chromatography to give pure products **9.**

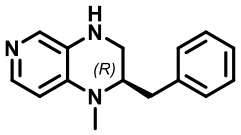


9

Off white solid, 1.28 g, 53% yield. $[\alpha]_D^{29.9}$= +5.07 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 10.52 (s, 1H), 7.81 (d, *J* = 5.5 Hz, 1H), 7.56 (s, 1H), 7.12 – 7.09 (m, 3H), 7.05 – 7.03 (m, 2H), 6.46 (d, *J* = 5.5 Hz, 1H), 4.32 (t, *J* = 5.3 Hz, 1H), 2.97-2.91 (m, 2H), 2.88 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm) 164.98, 144.60, 139.79, 136.25, 133.67, 129.67, 127.89, 126.55, 122.36, 105.21, 63.92, 35.86, 35.09. ESI-HRMS: $[M+H]^{\oplus}$calcd for $C_{15}H_{16}N_3O$ 254.1293, found 254.1290.

(*R*)-2-benzyl-1-methyl-1,2,3,4-tetrahydropyrido[3,4-*b*]pyrazine (10)

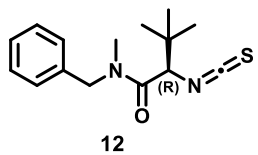
To a well-stirred solution of **9** (0.70 g, 1eq, 2.76 mmol) in THF (20.0 ml) was added $LiAlH_4$ (4.0 eq, 11.04 mmol, 419 mg) under 0 ^{o}C. The resulting mixture heated at 70 ^{o}C for 6 h, then quenched by 10% NaOH solution (2.7 ml). Then the mixture was filtered and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The product was purified by silica gel column chromatography to give pure products **10.**



10

Yellow solid, 0.58 g, 87.7% yield. $[\alpha]_D^{29.9}$= + 28.72 (*c* 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.23 (s, 1H), 7.65 (d, *J* = 6.6 Hz, 1H), 7.32 – 7.28 (m, 2H), 7.26 – 7.14 (m, 3H), 6.85 (s, 1H), 6.41 (d, *J* = 6.6 Hz, 1H), 3.67 – 3.63 (m, 1H), 3.34 (ABd, J_1 = 12.0 Hz, J_2 = 4.0 Hz, 1H), 3.20 (ABd, J_1 = 12.0 Hz, J_2 = 4.0 Hz, 1H), 2.99 – 2.85 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 144.58, 137.36, 132.17, 130.17, 129.42, 128.82, 126.88, 120.02, 103.10, 61.42, 39.88, 38.79, 38.46. ESI-HRMS: $[M+H]^{\oplus}$calcd for $C_{15}H_{18}N_3$ 240.1501, found 240.1498.

(2*R*)-*N*-Benzyl-2-isothiocyanato-*N*,3,3-trimethylbutanamide (12)[2]



12

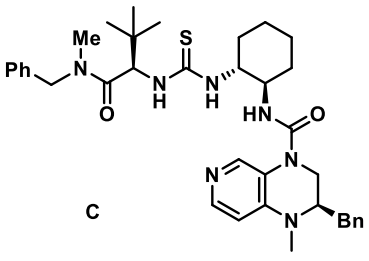
According to a standard literature procedure, the title compound (**12**) was obtained as yellow oil in 48% yield, 267 mg. In the fridge, the compound will slowly turn into off white solid. ^{1}H NMR (600 MHz, $CDCl_3$, compound exists as ~ 2:1 mixture of rotamers, major rotamer identified by *) δ (ppm): 7.41 (t, *J* = 7.4 Hz, 1H, ArH*and ArH), 7.35 - 7.28 (m, 3 H, ArH*and ArH), 7.16 (d, *J* = 7.4 Hz, 1H, ArH*and ArH), 4.75 (d, *J* = 17.0 Hz, 1H, $PhCH_A*H_BN$), 4.48 (d, *J* = 14.4 Hz, 1H, $PhCH_AH_BN$), 4.44 (d, *J* = 16.9 Hz, 1H, $PhCH_AH_B*N$), 4.28 (s, 1H,

[2] (a) A. J. M. Farley, C. Sandford and D. J. Dixon, *J. Am. Chem. Soc*., 2015, **137**, 15992; (b) A. Puglisi, L. Raimondi, M. Benaglia, M. Bonsignore and S. Rossi, *Tetrahedron Lett.*, 2009, **50**, 4340.

CH*(^{t}Bu)), 4.21 (s, 1H, CH(^{t}Bu)), 3.00 (s, 3 H, N(CH_3)), 2.98 (s, 3H, N(CH_3*)), 1.12 (s, 9H, C(CH_3*)$_3$), 1.11 (s, 9H, C(CH_3)$_3$). ^{13}C NMR ($CDCl_3$, 151 MHz, major rotamer identified by *) δ (ppm): 166.87 (C=O), 166.48 (C*=O), 136.52 (ArC*), 135.57 (ArC), 129.18 (one of ArC*H or ArCH), 128.72 (one of ArC*H or ArCH), 128.36 (one of ArC*H or ArCH), 128.08 (one of ArC*H or ArCH), 127.72 (one of ArC*H or ArCH), 126.20 (one of ArC*H or ArCH), 64.19 (C*H(^{t}Bu)), 64.12 (CH(^{t}Bu)), 53.95 (PhCH_2N), 51.72 (PhC*H_2N), 37.67 (CHC*(CH_3)$_3$), 37.51 (C(CH_3)$_3$), 35.64 (N(C*H_3)), 34.86 (N(CH_3)), 26.48 (C(C*H_3)$_3$ and C(CH_3)$_3$).

(*R*)-*N*-((1*R*,2*R*)-2-(3-((*R*)-1-(benzyl(methyl)amino)-3,3-dimethyl-1-oxobutan-2-yl) thioureido)cyclohexyl)-1-methyl-2-phenyl-2,3-dihydropyrido[3,4-*b*]pyrazine-4(1 *H*)-carboxamide (Catalyst C)

A dried round bottom flask was charged with **10** (239.3 mg，1 eq，1.0 mmol) and anhydrous DCM (8 mL) under argon atmosphere. A solution of Triphosgene (0.70 mmol) in anhydrous DCM (2.0 mL) was added. After the mixture was stirred at room temperature for 6 h, a solution of (1*R*, 2*R*)-1, 2-Diaminocyclohexan (3.0 mmol) in anhydrous DCM (2.0 mL) was added. The resulting mixture was stirred at room temperature for overnight. Then the reaction mixture was quenched with 10% NaOH solution, and the pH of the solution was adjusted to about 12. Then extracted with DCM (15 mL × 3), and the combined organic phase was washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude product **11** was used without further purification. To a well-stirred solution of **11** in anhydrous DCM (8.0 ml) was added Et_3N (3 mmol, 0.42ml). Then a solution of **12** (0.62 mmol, 1 eq, 172 mg) in anhydrous DCM (2.0 mL) was added. The resulting mixture was stirred at room temperature overnight. Most solvent was removed under reduced pressure and the crude product was purified by silica gel column chromatography (EA/Acetone=4/1, 1% Et_3N) to afford white solid catalyst **C** (118 mg, 18 % overall yield of the three steps).



C

$[\alpha]_D^{26.9}$= +28.78 (*c* 1.64, $CHCl_3$); mp: 159.0 ℃. ^{1}H NMR (600 MHz, Acetone-d_6, compound exists as ~3.5:1 mixture of rotamers, major rotamer identified by *) δ 8.57 (s, 1H, ArH), 8.55 (s, 1H, ArH*), 7.96 (d, *J* = 5.6 Hz, 1H, ArH*), 7.94 (d, *J* = 5.6 Hz, 1H, ArH), 7.67 (d, *J* = 8.4 Hz, 1H, NH), 7.64 (d, *J* = 8.6 Hz, 1H, NH*), 7.49 (d, *J* = 7.6 Hz, 1H, ArH*), 7.36 – 7.21 (m, 10H，ArH*), 6.52 (d, *J* = 5.5 Hz, 1H, ArH* and ArH), 6.35 (d, *J* = 8.3 Hz, 1H, ArH*), 6.30 (d, *J* = 8.5 Hz, 1H, ArH), 5.95 (d, *J* = 9.5 Hz, 1H, NH), 5.75 (d, *J* = 9.3 Hz, 1H, NH*), 5.08 (d, *J* = 15.3 Hz, 1H, CHN), 4.82 (d, *J* = 14.6 Hz, 1H,CH_2*N), 4.66 (m, 1H, CH_2*N), 4.51 (s, 1H, CH*N), 4.36 (d, *J* = 14.6 Hz, 1H, CH_2*N), 3.87 (tdd, *J* = 11.3, 7.6, 3.6 Hz, 1H, CH*N), 3.76 – 3.62 (m, 1H, CH*N), 3.22 (s, 3H, CH_3*N), 2.87 (s, 3H, CH_3*N), 2.83 (dd, *J* = 13.4, 5.4 Hz, 1H, CH_2*), 2.72 (dd, *J* = 13.2, 3.2 Hz, 1H, CH_2*), 2.67 – 2.60 (m, 1H, CH_2*), 2.22 (d, *J* = 12.0 Hz, 1H,), 2.02 (m, 1H, CH_2*), 1.74 – 1.71 (m, 1H, CH_2*), 1.48 – 1.32 (m, 4H, CH_2*), 1.02 (s, 9H, C(CH_3*)$_3$), 0.99 (s, 9H, C(CH_3)$_3$). ^{13}C

NMR (151 MHz, Acetone-d_6, major rotamer identified by *) δ183.87 (C*=S) 183.61 (C=S), 172.78 (C*=O) 172.59 (C=O), 156.70 (C*=O), 146.38 (ArC), 146.33 (ArC*), 144.17 (ArC*), 143.91 (ArC), 143.88 (ArC*), 139.25 (ArC*), 138.73 (ArC*), 138.28 (ArC*), 130.59 (ArC*), 129.21 (ArC*), 129.16 (ArC*), 128.96 (ArC*), 128.29 (ArC*), 127.92 (ArC*), 127.14 (ArC*), 122.33 (ArC*), 105.84 (ArC*), 63.77 ($(CH_2)_2$C*HNCH$_3$), 60.06 (C*HN), 59.83 (CHN), 58.98 (C*HN), 55.27 (C*HN), 55.15 (C*HN), 54.54 (CH_2N), 51.36 (C*H_2N), 42.00 (one of ArC*H_2CH or NC*H_2CH), 38.87 (one of ArC*H_2CH or NC*H_2CH), 37.57 (C*H_3N), 37.04 (C$(CH_3)_3$), 36.56 (C*$(CH_3)_3$), 36.33 (C*H_3N), 33.40 (CH_2C*H_2CH), 33.28 (CH_2C*H_2CH), 27.30(C(C$H_3)_3$, 27.15 (C(C*$H_3)_3$), 25.84 (CH_2C*H_2CH_2), 25.61 (CH_2C*H_2CH_2). ESI-HRMS: $[M+H]^{\oplus}$ calcd for $C_{37}H_{50}O_2N_7S$ 656.3752, found 656.37412; IR (KBr) ν (cm^{-1}) 3311, 2928, 1640, 1540, 1327, 1259, 1086, 902, 803, 700, 603.

3. CHARACTERIZATION OF PRODUCTS

GENERAL PROCEDURE: The following starting materials were synthesized according to previously described procedures: 2-phenyl-oxazol-5-yl carbonate **1a-k**[3] and benzofuran-2-yl carbonate **4a-c**.[4] A dried Schlenk flask was charged with **1** or **4** (0.10 mmol), **C** (3.3 mg, 0.005 mmol) and 4Å MS (100 mg) under nitrogen atmosphere, and anhydrous toluene (2.0 mL) was added at -40 ^{o}C. The resulting mixture was stirred at -40 ^{o}C for 24 to 72 hours. Then the reaction mixture was quenched with 1N HCl solution, then extracted with DCM (15 mL × 3), and the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash silica gel (300-400 mesh) chromatography to afford the desired products **3** or **5**. The absolute configuration of products is obtained by comparing known compounds reported in other literature.[3-5]

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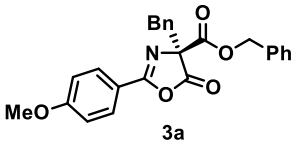
[3] (a) J. C. Ruble and G. C. Fu, *J. Am. Chem. Soc.*, 1998, **120**, 11532; (b) S. A. Shaw, P. Aleman and E. Vedejs, *J. Am. Chem. Soc.*, 2003, **125**, 13368; (c) S. A. Shaw, P. Aleman, J. Christy, J. W. Kampf, P. Va and E. Vedejs, *J. Am. Chem. Soc.*, 2006, **128**, 925.

[4] M. Wang, Z. Zhang, S. Liu, F. Xie and W. Zhang, *Chem. Commun.*, 2014, **50**, 1227.

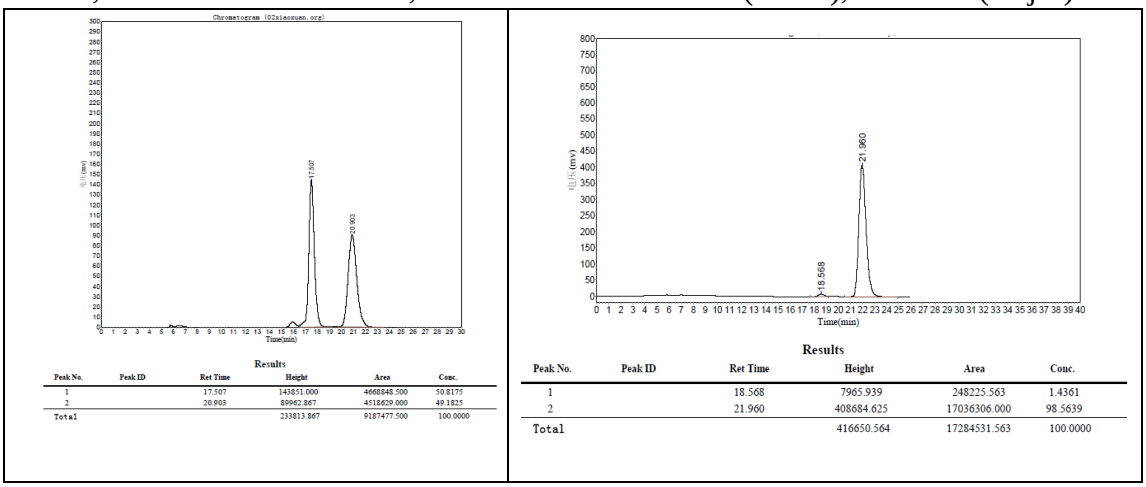
[5] (a) C. Joannesse, C. P. Johnston, C. Concellon, C. Simal, D. Philp and A. D. Smith, *Angew. Chem., Int. Ed.*, 2009, **48**, 8914; (b) Z. Zhang, F. Xie, J. Jia and W. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 15939; (c) J. Zhang, X. Han, X. Wu, Y. Liu and Y. Cui, *ACS Sustainable Chem. Eng.*, 2019, **7**, 5065; (d) M. S. Xie, Y. F. Zhang, M. Shan, X. X. Wu, G. R. Qu and H. M. Guo, *Angew. Chem., Int. Ed.*, 2019, **58**, 2839.

Benzyl (*S*)-4-benzyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate (3a)

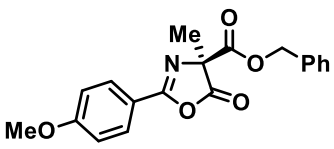


3a

colorless oil, 37.4 mg, 90% yield, 97% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.81 (d, 2H, J = 8.8 Hz), 7.36-7.28 (m, 5H), 7.20-7.12 (m, 5H), 6.92 (d, 2H, J = 8.8 Hz), 5.32-5.21 (m, 2H), 3.84 (s, 3H)， 3.56 (dd, 2H, J = 13.6, 5.6); HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 18.6 min (minor), 22.0 min (major).

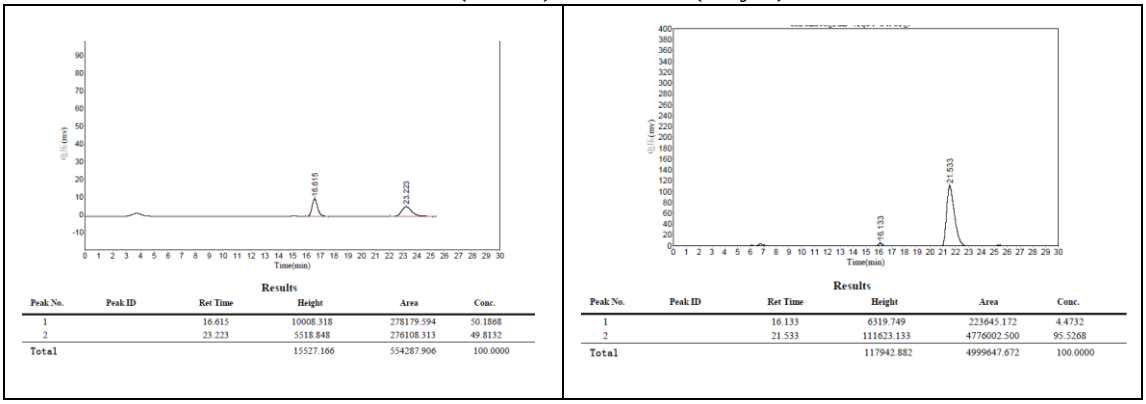


Benzyl (*S*)-2-(4-methoxyphenyl)-4-methyl-5-oxo-4,5-dihydrooxazole-4-carboxylate (3b)

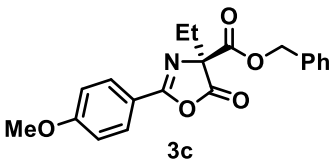


3b

colorless oil, 24.4 mg, 72% yield, 91% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.97 (d, 2H, J = 9.2 Hz), 7.36-7.27 (m, 5H), 6.98 (d, 2H, J = 9.2 Hz), 5.27-5.17 (m, 2H), 3.88 (s, 3H), 1.78 (s, 3H); HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 16.1 min (minor), 21.5 min (major).

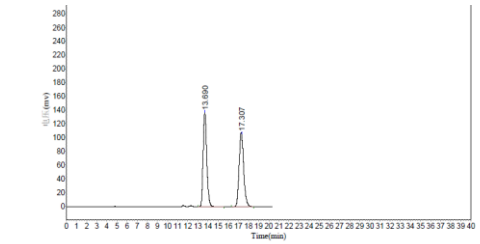


Benzyl(*S*)-4-ethyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate (3c)



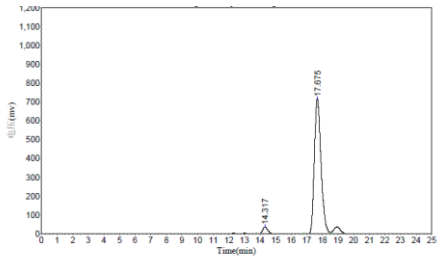
3c

colorless oil, 26.0 mg, 74% yield, 91% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) δ 7.98 (d, 2H, J = 8.8 Hz), 7.35-7.28 (m, 5H), 6.98 (d, 2H, J = 8.8 Hz), 5.28-5.18 (m, 2H), 3.88 (s, 3H), 2.38-2.20 (m, 2H), 0.91 (t, 3H, J = 7.2 Hz); HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 14.3 min (minor), 17.7 min (major).



Results

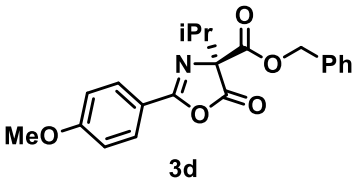
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.690	137700.000	3393377.500	49.9744
2		17.307	107242.719	3396858.000	50.0256
Total			244942.719	6790235.500	100.0000



Results

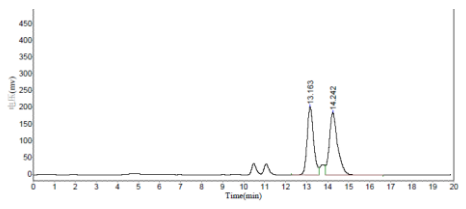
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		14.317	38599.852	966187.000	4.3047
2		17.675	718233.750	21478504.000	95.6953
Total			756833.602	22444691.000	100.0000

Benzyl (*S*)-4-isopropyl-2-(4-methoxyphenyl)-5-oxo-4, 5-dihydrooxazole-4-carboxylate (3d)



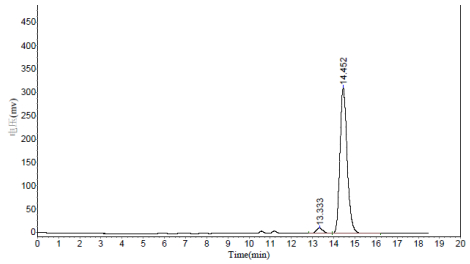
3d

colorless oil, 24.0 mg, 67% yield, 94% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.99 (d, 2H, J = 9.2 Hz), 7.36-7.30 (m, 5H), 6.98 (d, 2H, J = 9.2 Hz), 5.30-5.21 (m, 2H), 3.88 (s, 3H), 2.83-2.75 (m, 1H), 1.02 (d, 3H, J = 6.8 Hz), 0.96 (d, 3H, J = 6.8 Hz); HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 13.3 min (minor), 14.4 min (major).



Results

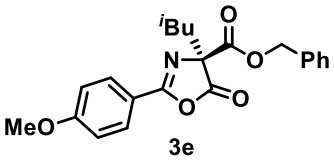
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.163	203699.688	4343904.000	45.9653
2		14.242	187478.469	5106489.500	54.0347
Total			391178.156	9450393.500	100.0000



Results

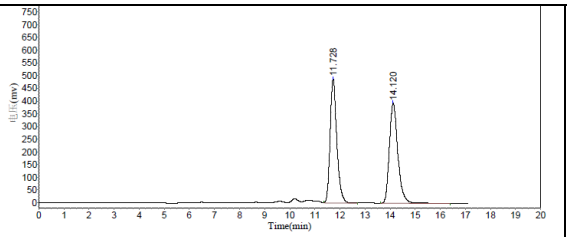
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.333	11466.816	246345.547	3.2445
2		14.452	312227.406	7346372.000	96.7555
Total			323694.223	7592717.547	100.0000

Benzyl (*S*)-4-isobutyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate (3e)



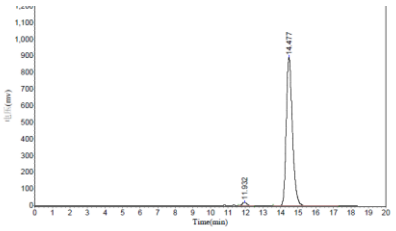
3e

colorless oil, 29.4 mg, 74% yield, 96% *ee*. ^{1}H NMR (400 MHz, CDC1$_3$) δ (ppm) 7.98 (d, 2H, J = 8.8 Hz), 7.35-7.27 (m, 5H), 6.98 (d, 2H, J = 8.8 Hz), 5.21 (dd, 2H, J = 18.0, 12.4 Hz), 3.88 (s, 3H), 2.38 (dd, 1H, J = 14.4, 6.0 Hz), 2.06 (dd, 1H, J = 14.4, 7.2 Hz), 1.76-1.65 (m, 1H), 0.92 (d, 3H, J = 6.8 Hz), 0.88 (d, 3H, J = 6.4 Hz); HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 11.9 min (minor), 14.5 min (major).



Results

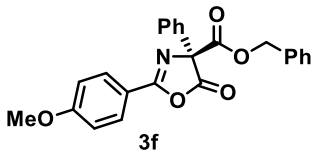
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		11.728	488473.406	9105648.000	49.7435
2		14.120	393265.344	9199550.000	50.2565
Total			881738.750	18305198.000	100.0000



Results

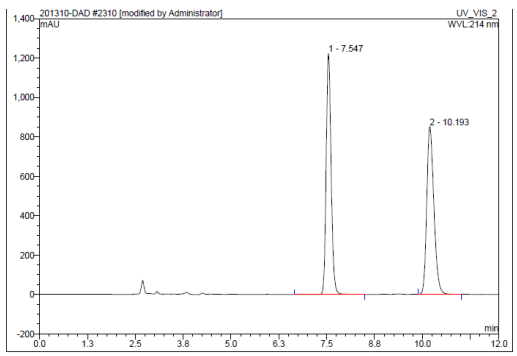
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		11.932	21393.012	402111.656	1.8271
2		14.477	892471.750	21606630.000	98.1729
Total			913864.762	22008741.656	100.0000

Benzyl(S)-2-(4-methoxyphenyl)-5-oxo-4-phenyl-4, 5-dihydrooxazole-4-carboxylate (3f)

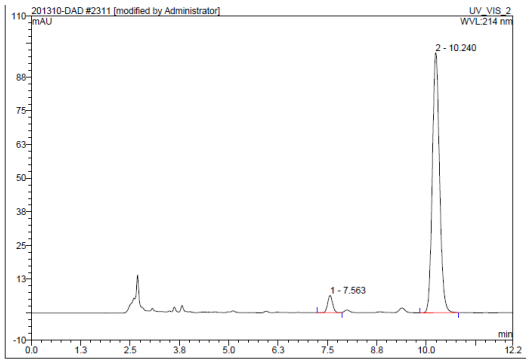


3f

colorless oil, 30.0 mg, 75% yield, 92% *ee*. ^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.99 (d, 2H, J = 8.8 Hz), 7.67-7.62 (m, 2H), 7.36-7.12 (m, 8H), 6.98 (d, 2H, J = 8.8 Hz), 5.17 (s, 2H), 3.82 (s, 3H); HPLC: ID-H Column; detected at 214 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.7 mL/min; retention time: 7.6 min (minor), 10.2 min (major).

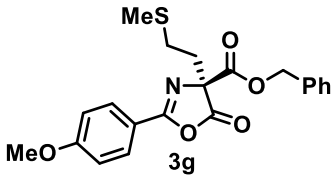


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.55	n.a.	1223.009	182.625	50.01	n.a.	BMB*
2	10.19	n.a.	849.881	182.587	49.99	n.a.	BMB
Total:			2072.890	365.212	100.00	0.000	



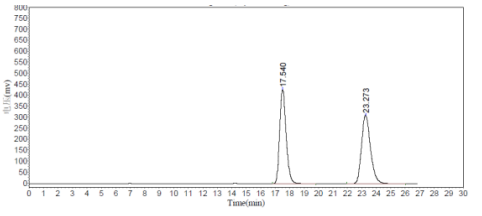
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	7.56	n.a.	6.350	0.906	4.25	n.a.	BMB*
2	10.24	n.a.	96.469	20.410	95.75	n.a.	BMB
Total:			102.820	21.316	100.00	0.000	

Benzyl (*S*)-2-(4-methoxyphenyl)-4-(2-(methylthio)ethyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate (3g)



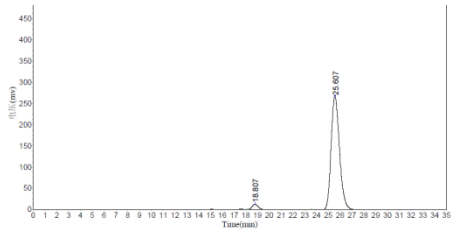
3g

colorless oil, 31.2 mg, 78% yield, 93% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.97 (d, 2H, J = 9.2 Hz), 7.36-7.27 (m, 5H), 6.98 (d, 2H, J = 9.2 Hz), 5.26 (d, 1H, J = 12.4 Hz), 5.21 (d, 1H, J = 12.4 Hz), 3.87 (s, 3H), 2.68-2.42 (m, 4H), 2.04 (s, 3H); HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 18.8 min (minor), 25.6 min (major).



Results

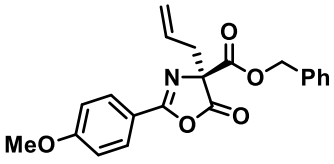
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		17.540	430094.594	13385680.000	49.9227
2		23.273	311248.375	13427144.000	50.0773
Total			741342.969	26812824.000	100.0000



Results

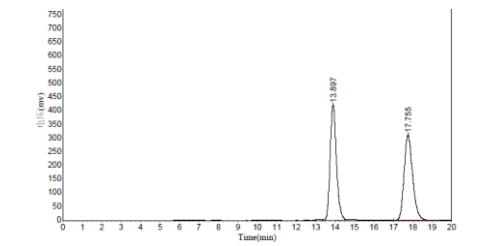
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		18.807	12643.538	490713.813	3.5622
2		25.607	268682.500	13285045.000	96.4378
Total			281326.038	13775758.812	100.0000

Benzyl (*S*)-4-allyl-2-(4-methoxyphenyl)-5-oxo-4, 5-dihydrooxazole-4-carboxylate (3h)



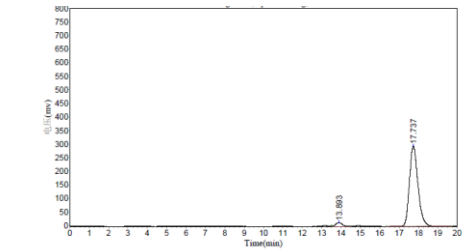
3h

colorless oil, 22.1 mg, 60% yield, 93% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.74 (d, 2H, J = 8.4 Hz), 7.38-7.28 (m, 5H), 6.91 (d, 2H, J = 8.4 Hz), 5.70-5.54 (m, 1H), 5.30-5.04 (m, 4H), 3.84 (s, 3H), 3.26-3.03 (m, 2H); HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 13.9 min (minor), 17.7 min (major).



Results

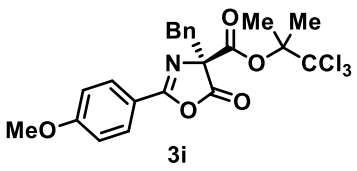
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.897	421774.250	9465621.000	49.7940
2		17.755	311921.813	9543927.000	50.2060
Total			733696.063	19009548.000	100.0000



Results

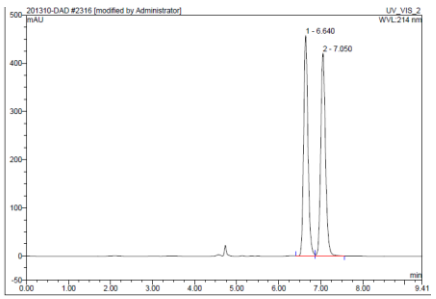
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		13.893	13790.803	306862.188	3.2964
2		17.737	295108.094	9002197.000	96.7036
Total			308898.896	9309059.188	100.0000

1,1,1-trichloro-2-methylpropan-2-yl (*S*)-4-benzyl-2-(4-methoxyphenyl)-5-oxo-4,5-dihydrooxazole-4-carboxylate (3i)

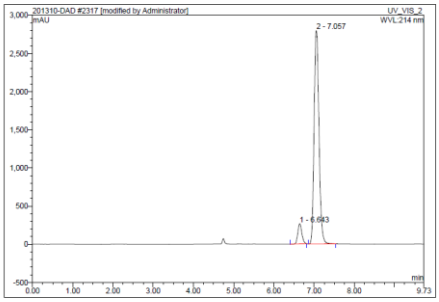


3i

colorless oil, 41.4 mg, 86% yield, 85% *ee*. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.80 (d, 2H, J = 8.8 Hz), 7.22-7.14 (m, 5H), 6.90 (d, 2H, J = 8.8 Hz), 3.85 (s, 3H), 3.54 (dd, 2H, J = 41.2, 14.0 Hz), 1.94 (s, 3H), 1.92 (s, 3H); HPLC: IC Column; detected at 214 nm; *n*-hexane / *i*-propanol = 95/5; flow rate = 0.7 mL/min; retention time: 6.6 min (minor), 7.0 min (major).

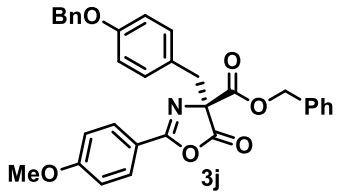


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.64	n.a.	457.751	54.338	49.72	n.a.	BM *
2	7.05	n.a.	421.043	54.951	50.28	n.a.	MB*
Total:			878.794	109.289	100.00	0.000	



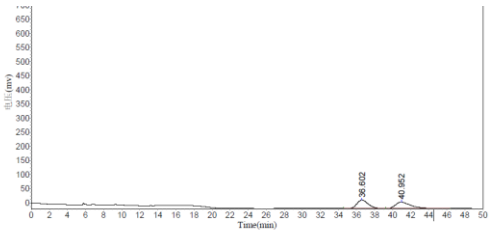
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	6.64	n.a.	266.675	30.705	7.27	n.a.	BMB*
2	7.06	n.a.	2795.749	391.679	92.73	n.a.	BMB*
Total:			3062.425	422.384	100.00	0.000	

Benzyl (*S*)-4-(4-(benzyloxy) benzyl)-2-(4-methoxyphenyl)-5-oxo-4, 5-dihydrooxazole-4-carboxylate (3j)



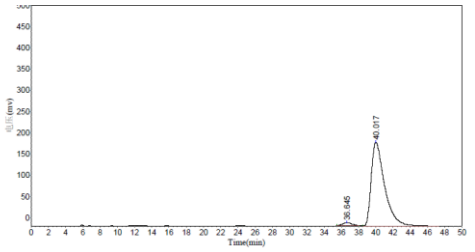
3j

pale yellow oil, 38.2 mg, 73% yield, 95% *ee*. $[\alpha]_D^{26.6}$= -104.77 (*c* 0.63, $CHCl_3$) for 95% *ee*; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.83 (d, 2H, J = 8.8 Hz), 7.40-7.27 (m, 10H), 7.10 (d, 2H, J = 8.8 Hz), 6.92 (d, 2H, J = 8.8 Hz), 6.76 (d, 2H, J = 8.8 Hz), 5.28 (d, 1H, J = 12.8 Hz), 5.23 (d, 1H, J = 12.4 Hz), 4.94 (s, 2H), 3.85 (s, 3H), 3.50 (dd, 2H, J = 50.0, 13.6 Hz); ^{13}C NMR (100 MHz, $CDC1_3$) δ (ppm) 173.78, 165.80, 163.52, 162.68, 158.11, 136.81, 134.76, 131.50, 130.13, 128.61, 128.51, 128.48, 127.98, 127.91, 127.43, 125.09, 117.24, 114.55, 114.17, 77.67, 69.82, 68.19, 55.49, 39.44; IR (KBr) v (cm^{-1}) 3342, 2924, 1647, 1457, 1376, 1071, 751, 701; HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 36.6 min (minor), 40.0 min (major).



Results

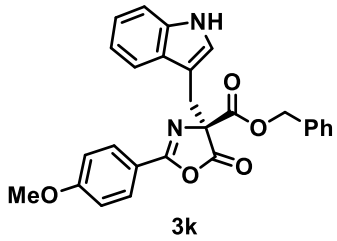
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		36.602	29588.443	2572317.750	49.4804
2		40.952	22480.010	2626343.250	50.5196
Total			52068.453	5198661.000	100.0000



Results

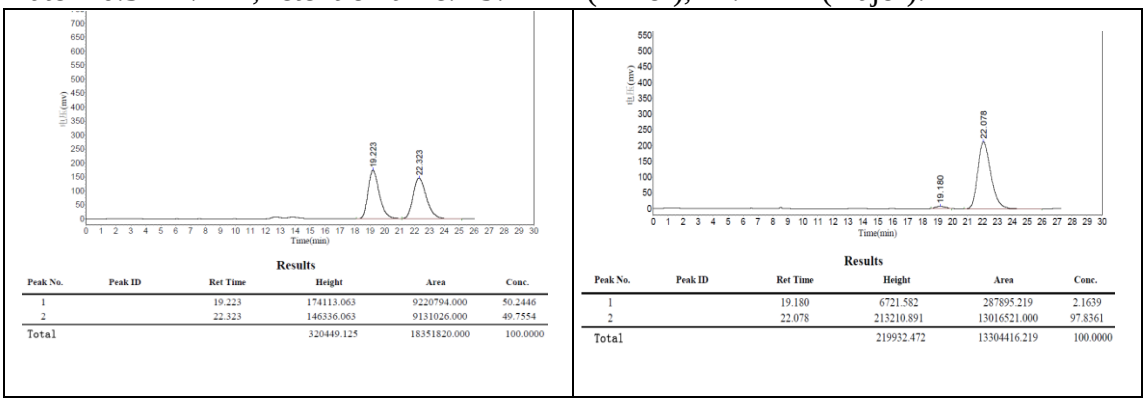
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		36.645	7068.438	543420.625	2.5212
2		40.017	196600.172	21011018.000	97.4789
Total			203668.610	21554438.625	100.0000

Benzyl (*S*)-4-((1H-indol-3-yl)methyl)-2-(4-methoxyphenyl)-5-oxo-4, 5-dihydrooxazole-4-carboxylate (3k)

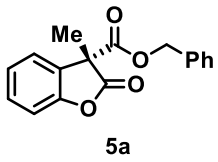


3k

pale yellow oil, 38.6 mg, 85% yield, 96% *ee*. $[\alpha]_D^{26.7}$= -16.2 (*c* 1.65, $CHCl_3$) for 96% *ee*; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.00 (s, 1H), 7.77-7.68 (m, 3H), 7.38-7.17 (m, 6H), 7.12-6.98 (m, 3H), 6.84 (d, 2H, *J* = 8.8 Hz), 5.33 (d, 1H, *J* = 12.4 Hz), 5.23 (d, 1H, *J* = 12.8 Hz), 3.84-3.66 (m, 5H); ^{13}C NMR (100 MHz, $CDC1_3$) δ (ppm) 174.17 166.04, 163.37, 162.83, 135.69, 134.84, 130.12, 128.61, 128.44, 127.98, 127.54, 124.19, 121.98, 119.59, 119.56, 117.26, 114.02, 110.86, 107.33, 78.01, 68.13, 55.43, 30.52; IR (KBr) *v* (cm^{-1}) 3404, 2923, 1735, 1606, 1491, 1256, 1209, 1027, 843, 740, 579; HPLC: OD-H Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 19.2 min (minor), 22.1 min (major).

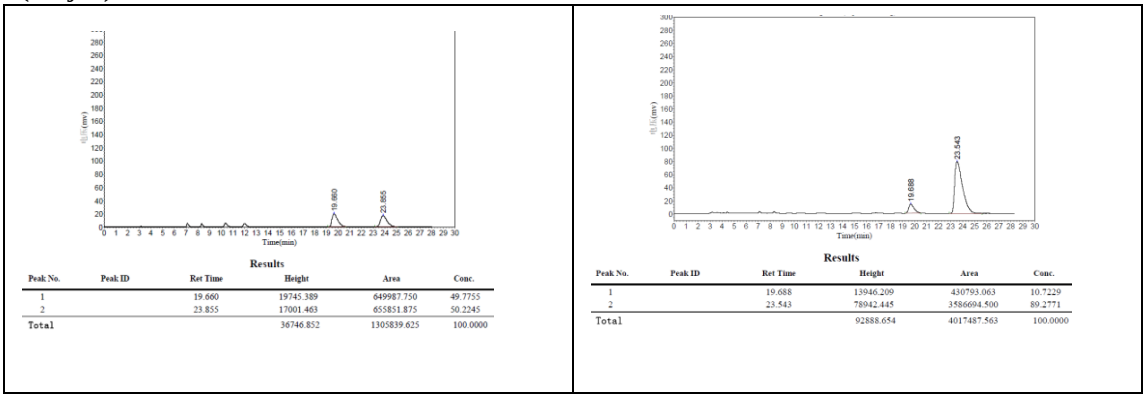


Benzyl (*R*)-3-methyl-2-oxo-2, 3-dihydrobenzofuran-3-carboxylate (5a)

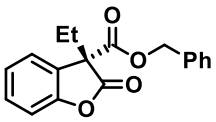


5a

colorless oil, 21.4 mg, 75% yield, 79% *ee*. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.37-7.21 (m, 5H), 7.17-7.11 (m, 4H), 5.16 (d, 1H, *J* = 12.4 Hz), 5.11 (d, 1H, *J* = 12.4 Hz), 1.78 (s, 3H); HPLC: OJ-H Column; detected at 210 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 1.0 mL/min; retention time: 19.7 min (minor), 23.5 min (major).

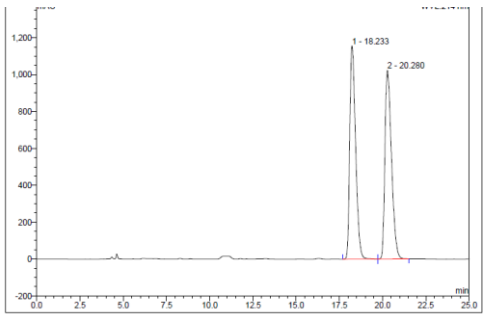


Benzyl (*R*)-3-ethyl-2-oxo-2, 3-dihydrobenzofuran-3-carboxylate (5b)

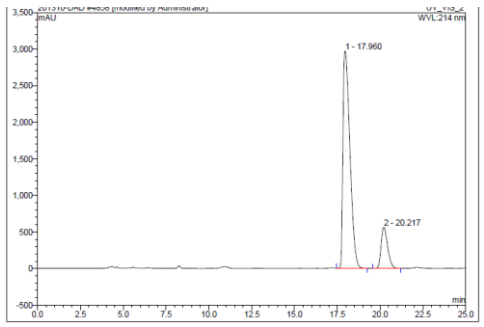


5b

colorless oil, 18.4 mg, 62% yield, 70% *ee*. $[\alpha]_D^{28.0}$= -28.37 (*c* 0.60, $CHCl_3$) for 70% *ee*; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.39-7.22 (m, 5H), 7.21-7.08 (m, 4H), 5.17 (d, 1H, *J* = 12.8 Hz), 5.13 (d, 1H, *J* = 12.4 Hz), 2.43-2.23 (m, 2H), 0.775 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, CDC1$_3$) δ (ppm) 173.16, 167.66, 153.65, 129.94, 128.54, 128.31, 127.53, 126.20, 124.57, 123.82, 110.98, 67.71, 59.17, 28.05, 8.32. IR (KBr) *v* (cm^{-1}) 2970, 1783, 1655, 1456, 1378, 1221, 1177, 1135, 960, 742, 697; HPLC: OD-H Column; detected at 214 nm; *n*-hexane / *i*-propanol = 99/1; flow rate = 0.7 mL/min; retention time: 18.2 min (major), 20.3 min (minor).

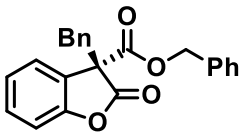


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	18.23	n.a.	1156.959	453.389	50.22	n.a.	BM
2	20.28	n.a.	1022.781	449.434	49.78	n.a.	MB
Total:			2179.741	902.823	100.00	0.000	



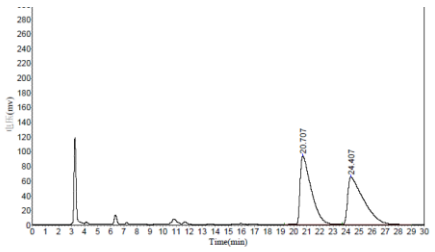
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	17.96	n.a.	2969.517	1395.244	84.99	n.a.	BMB*
2	20.22	n.a.	562.589	246.464	15.01	n.a.	BMB*
Total:			3532.106	1641.708	100.00	0.000	

Benzyl (*R*) - 3-benzyl-2-oxo-2, 3-dihydrobenzofuran-3-carboxylate (5c)



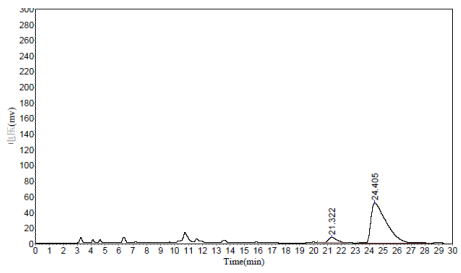
5c

wax solid, 32.8 mg, 92% yield, 87% *ee*. $[\alpha]_D^{27.8}$= -67.42 *c* 0.68, $CHCl_3$) for 87% *ee*; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.34-6.98 (m, 11H), 6.95-6.85 (m, 3H), 5.21 (d, 1H, *J* = 12.4 Hz), 5.17 (d, 1H, *J* = 12.4 Hz), 3.62 (d, 1H, *J* = 14 Hz), 3.58 (d, 1H, *J* = 13.6 Hz); ^{13}C NMR (100 MHz, CDC1$_3$) δ (ppm) 172.57, 167.39, 153.36, 134.79, 133.41, 130.03, 129.98, 128.56, 128.38, 128.15, 127.62, 127.34, 125.71, 124.33, 124.24, 110.92, 67.96, 60.12, 40.23. IR (KBr) *v* (cm^{-1}) 3030, 1780, 1743, 1596, 1463, 1373, 1227, 1125, 1021, 888, 762, 583, 495; HPLC: OJ-H Column; detected at 210 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 1 mL/min; retention time: 21.3 min (minor), 24.4 min (major).



Results

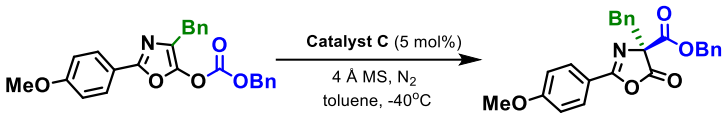
Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		20.707	92845.094	5457772.500	50.1601
2		24.407	64446.848	5422928.500	49.8399
Total			157291.941	10880701.000	100.0000



Results

Peak No.	Peak ID	Ret Time	Height	Area	Conc.
1		21.322	6444.900	256742.750	6.2504
2		24.405	51024.930	3850862.750	93.7496
Total			57469.830	4107605.500	100.0000

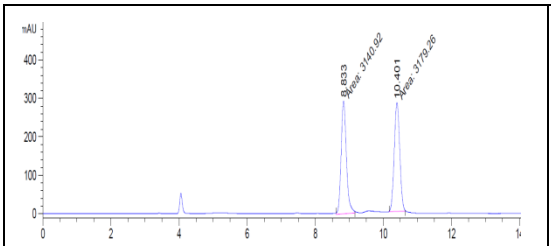
4. GRAM-SCALE EXPERIMENT



1a
1.000 G

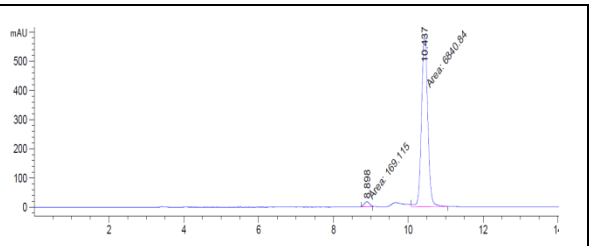
3a
0.928 G
93% yield, 95% ee

A dried Schlenk flask (100mL) was charged with **1a** (2.4 mmol, 1.0 g), catalyst **C** (79.0 mg, 0.12 mmol) and 4Å MS (2.4 g) under nitrogen atmosphere. Then, anhydrous toluene (48 mL) was added at -40 ºC by syringe and the resulting mixture was stirred at -40 ºC for 24 hours. The reaction mixture was quenched with 1N HCl solution at the same temperature and slowly warmed to 0 ºC, then filtered to remove solid and washed with DCM. The filtration was washed with water and the aqueous layer was re-extracted with DCM (30 mL × 3), then the combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash silica gel (300-400 mesh) chromatography to afford colorless oil **3a** (0.928g, 93% yield, 95% *ee*). HPLC: OD-3 Column; detected at 254 nm; *n*-hexane / *i*-propanol = 90/10; flow rate = 0.5 mL/min; retention time: 8.9 min (minor), 10.4 min (major).



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

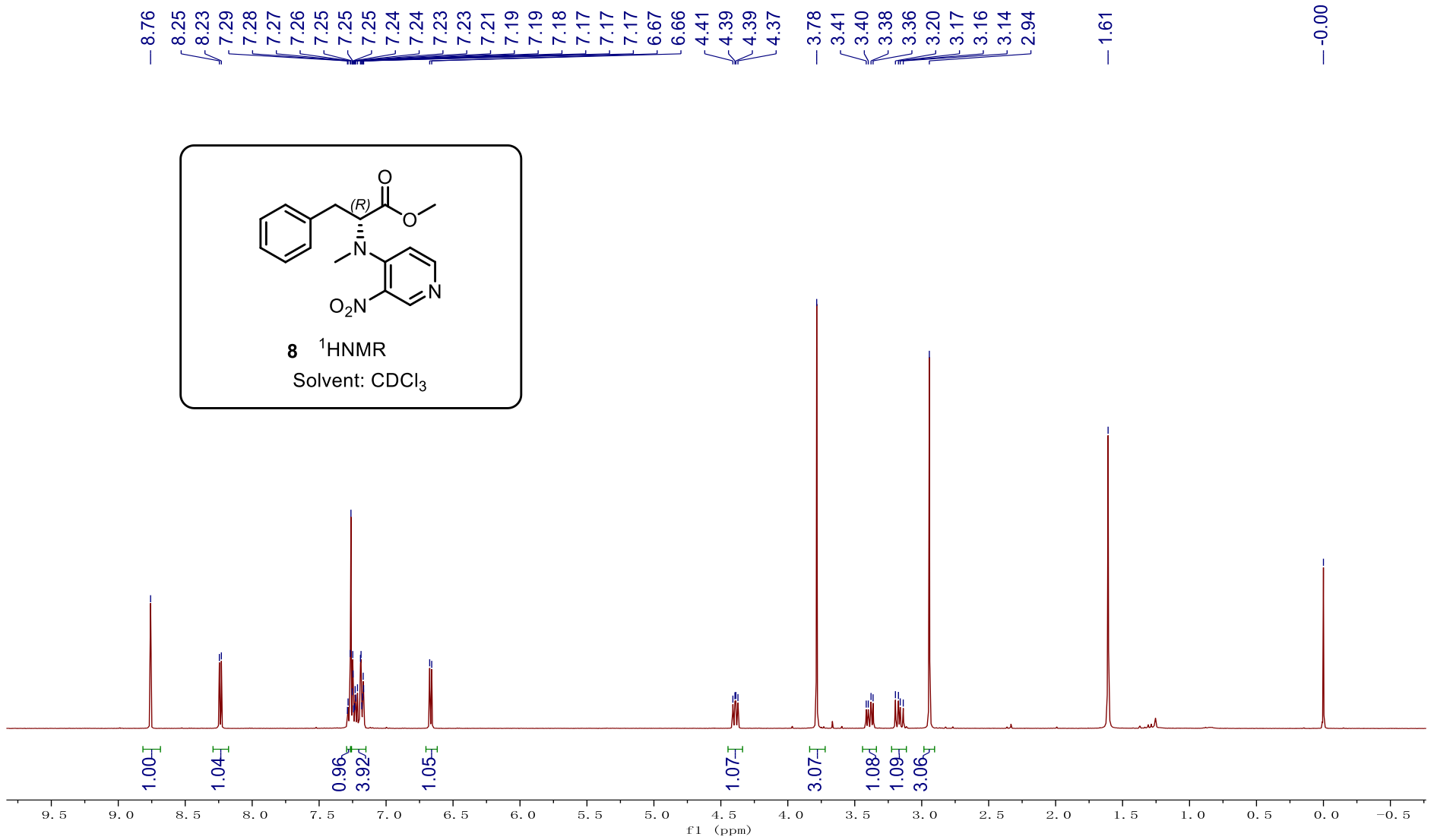
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.833	MM	0.1791	3140.91870	292.35062	49.6967
2	10.401	MM	0.1875	3179.26099	282.65186	50.3033

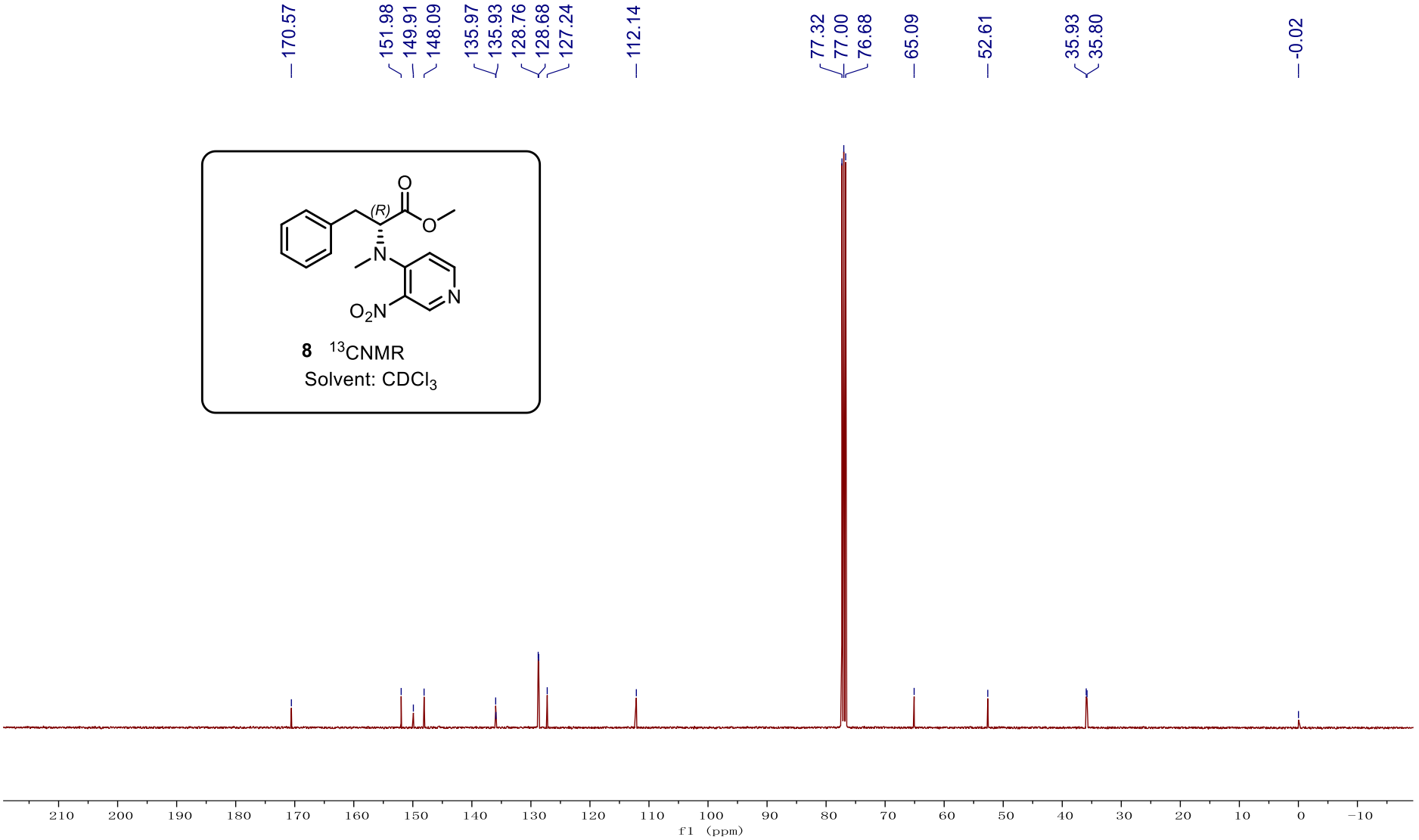


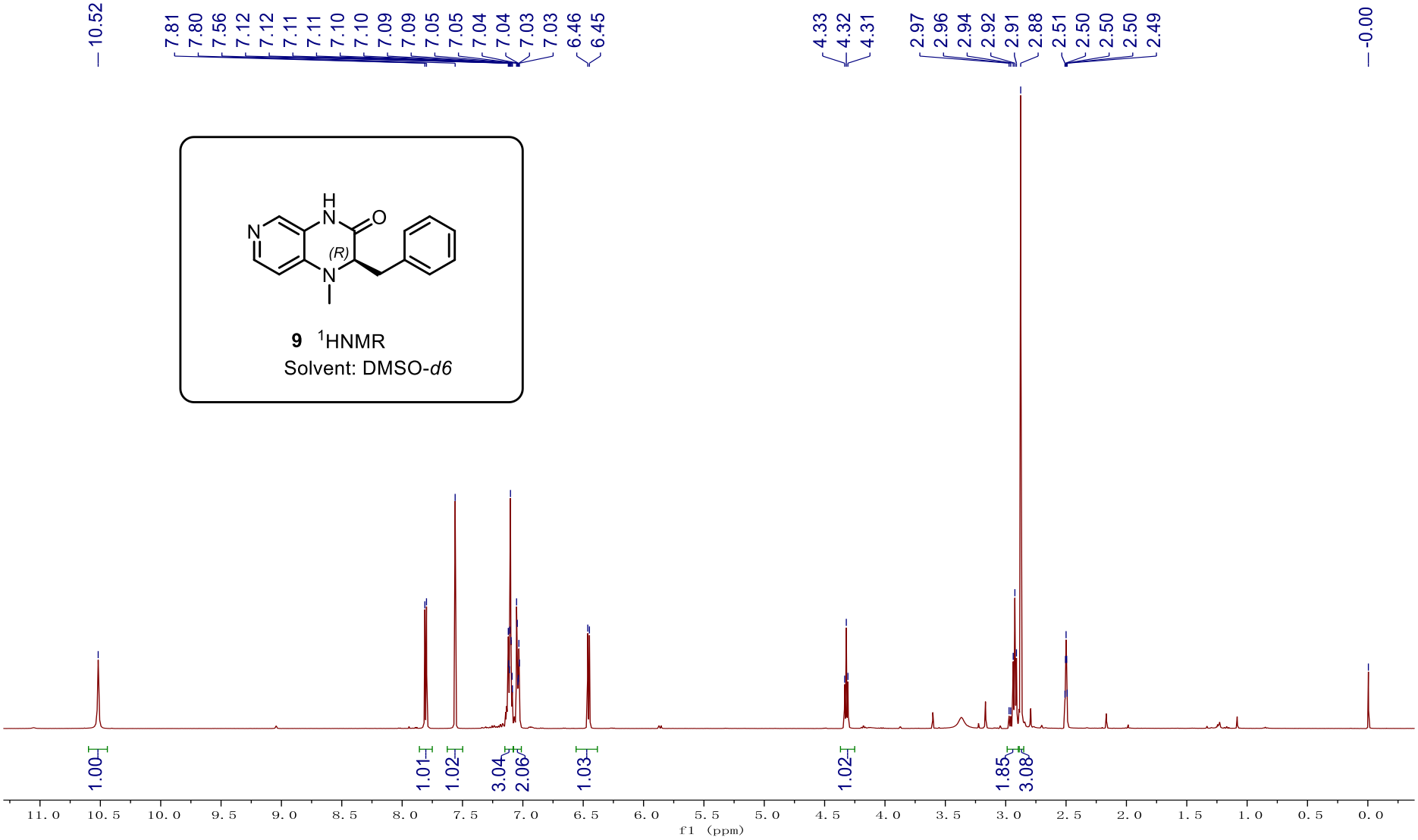
Signal 1: DAD1 A, Sig=254,4 Ref=360,100

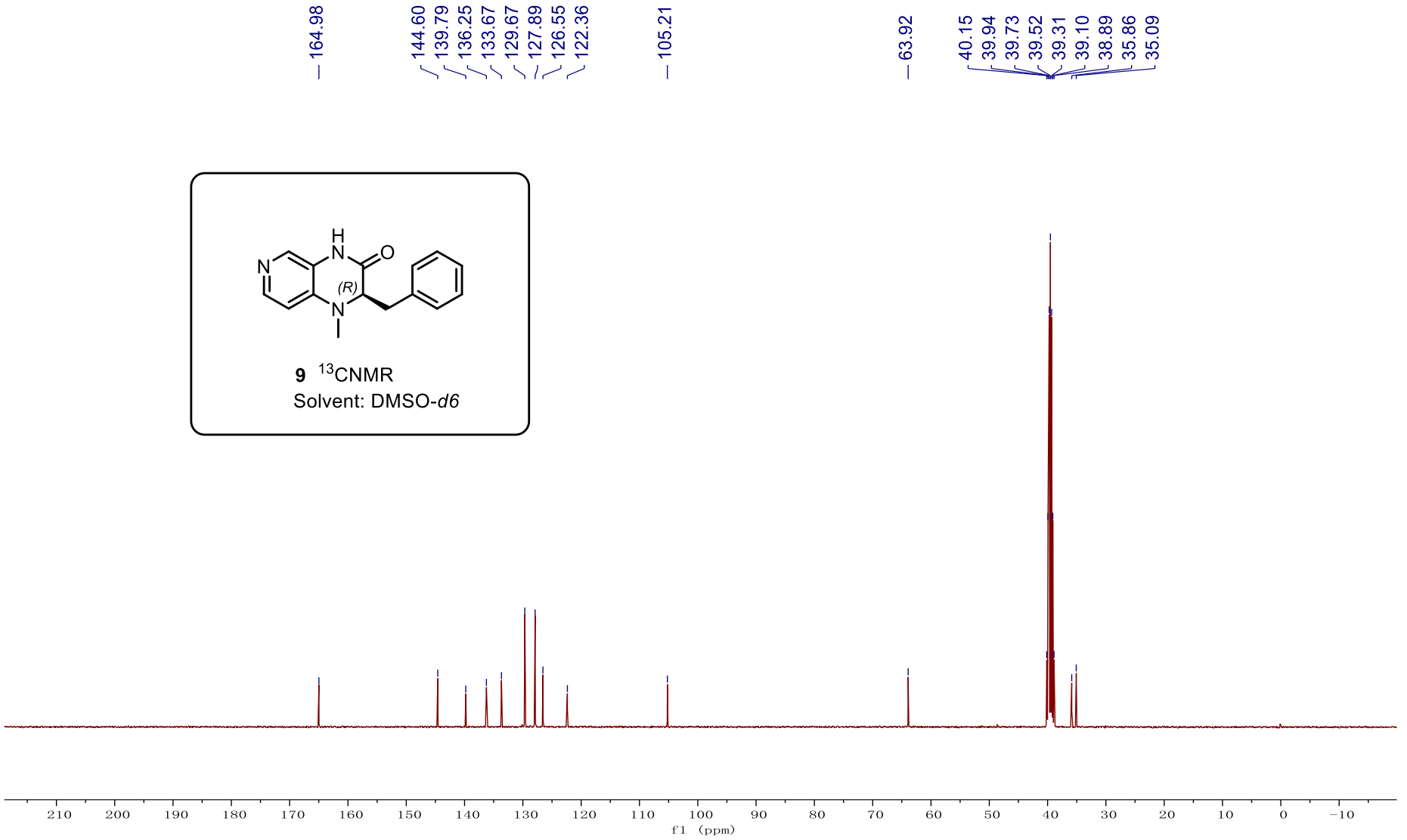
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.898	MM	0.1627	169.11537	17.32306	2.4125
2	10.437	FM	0.1939	6840.83594	588.14178	97.5875

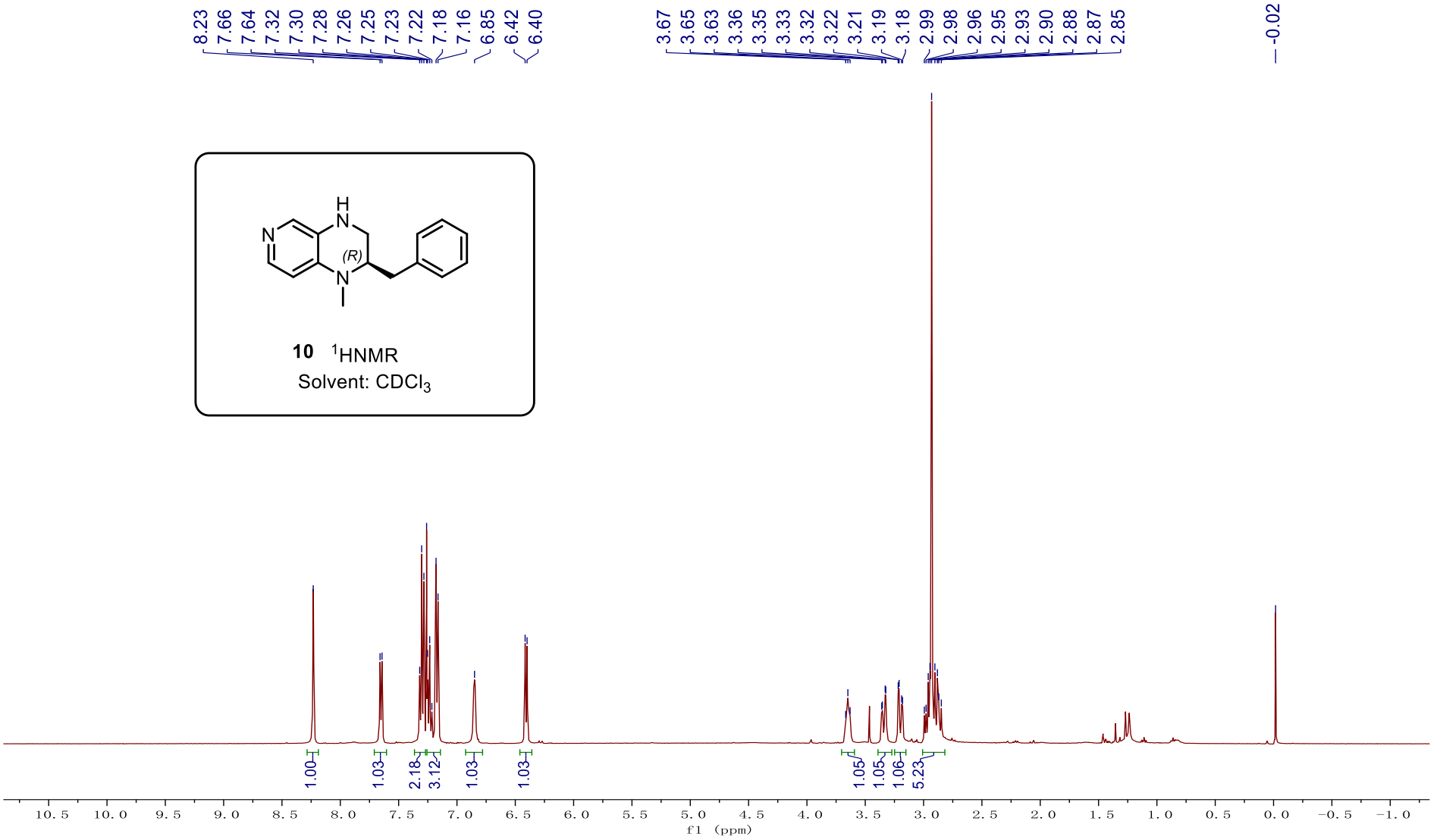
5. ^{1}H NMR, ^{13}C NMR, DEPT135 & HSQC

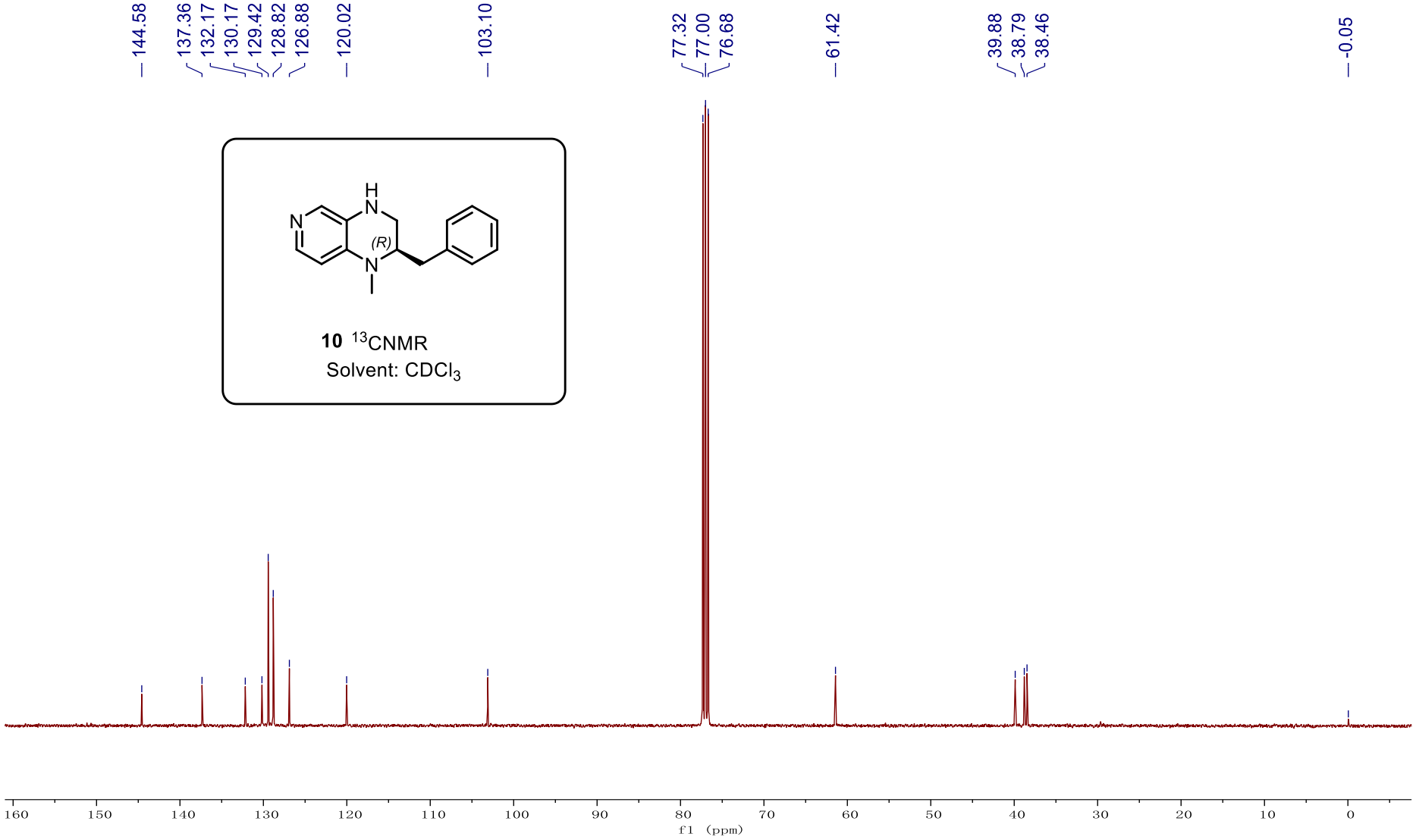

8.76
8.25
8.23
7.29
7.28
7.27
7.26
7.25
7.25
7.25
7.24
7.24
7.23
7.23
7.21
7.19
7.19
7.18
7.17
7.17
7.17
6.67
6.66
4.41
4.39
4.39
4.37
3.78
3.41
3.40
3.38
3.36
3.20
3.17
3.16
3.14
2.94
1.61
-0.00
(R)
O
O
N
N
O2N
8 1HNMR
Solvent: CDCl3
1.00
1.04
0.96
3.92
1.05
1.07
3.07
1.08
1.09
3.06
9.5
9.0
8.5
8.0
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
-0.5
f1 (ppm)

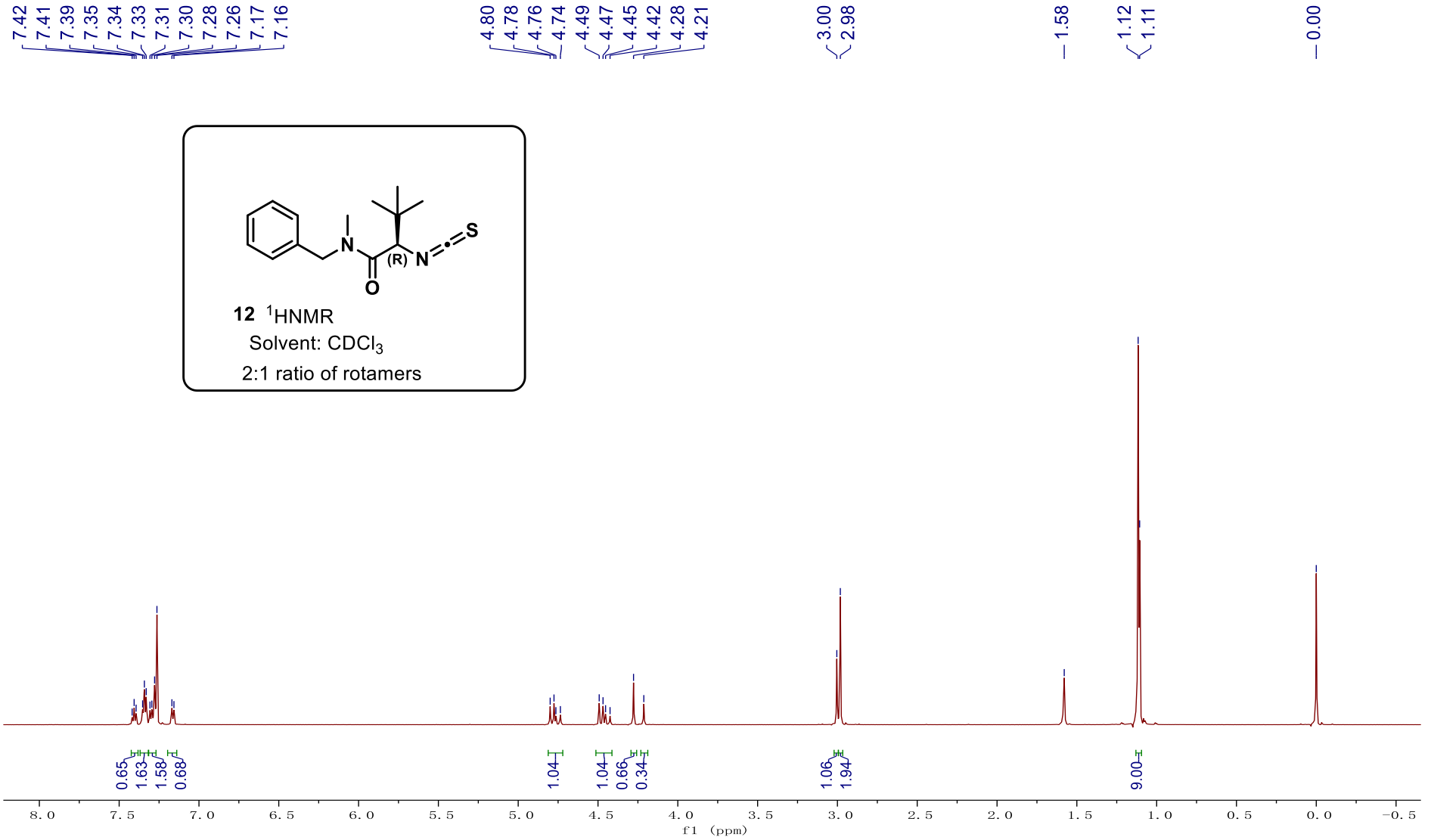

170.57
151.98
149.91
148.09
135.97
135.93
128.76
128.68
127.24
112.14
77.32
77.00
76.68
65.09
52.61
35.93
35.80
-0.02
(R)
O
O
N
N
O2N
8 13CNMR
Solvent: CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

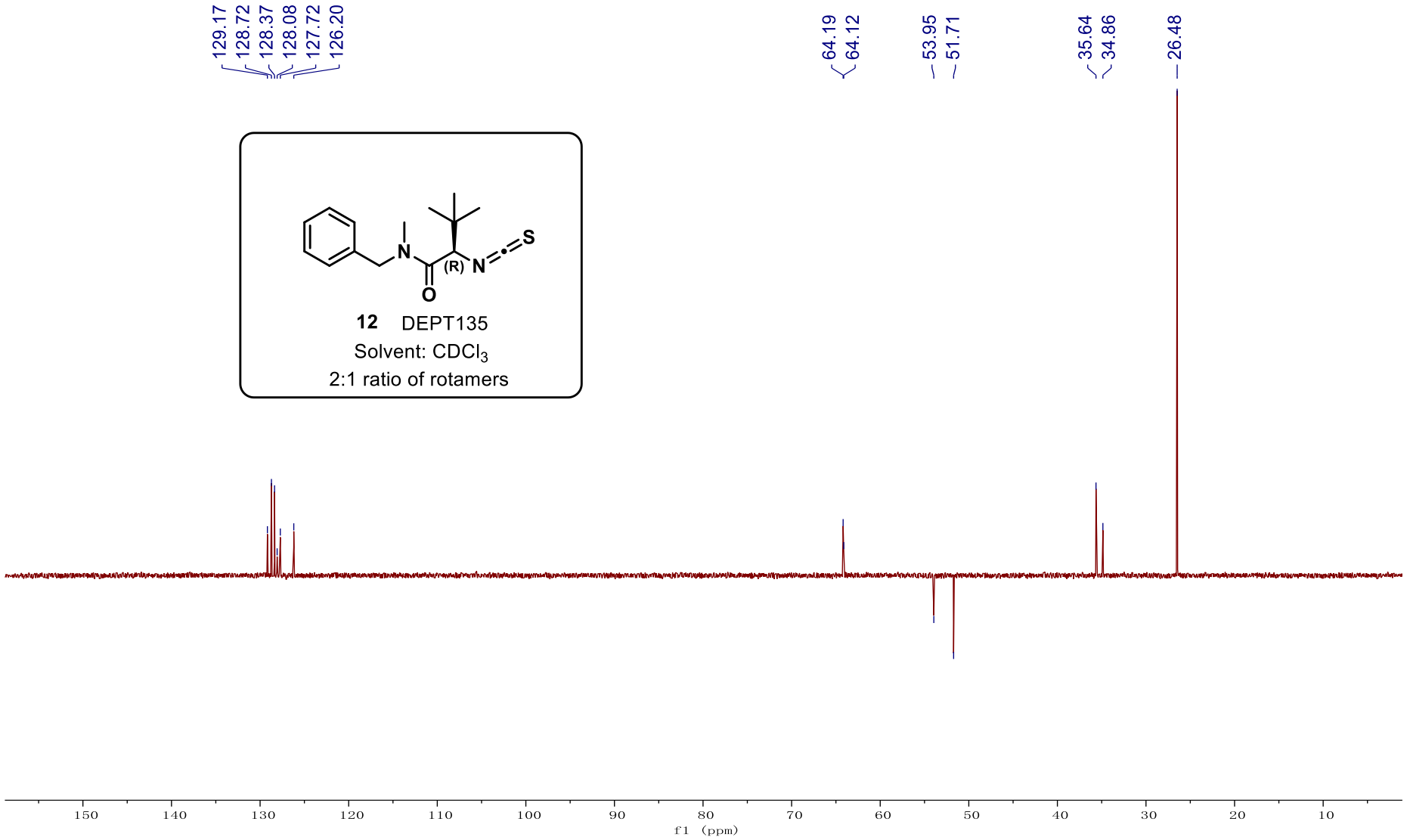

10.52
7.81
7.80
7.56
7.12
7.12
7.11
7.11
7.10
7.10
7.09
7.09
7.05
7.05
7.04
7.04
7.03
7.03
6.46
6.45
4.33
4.32
4.31
2.97
2.96
2.94
2.92
2.91
2.88
2.51
2.50
2.50
2.50
2.49
0.00
(R)
9 1HNMR
Solvent: DMSO-d6
1.00
1.01
1.02
3.04
2.06
1.03
1.02
1.85
3.08
f1 (ppm)

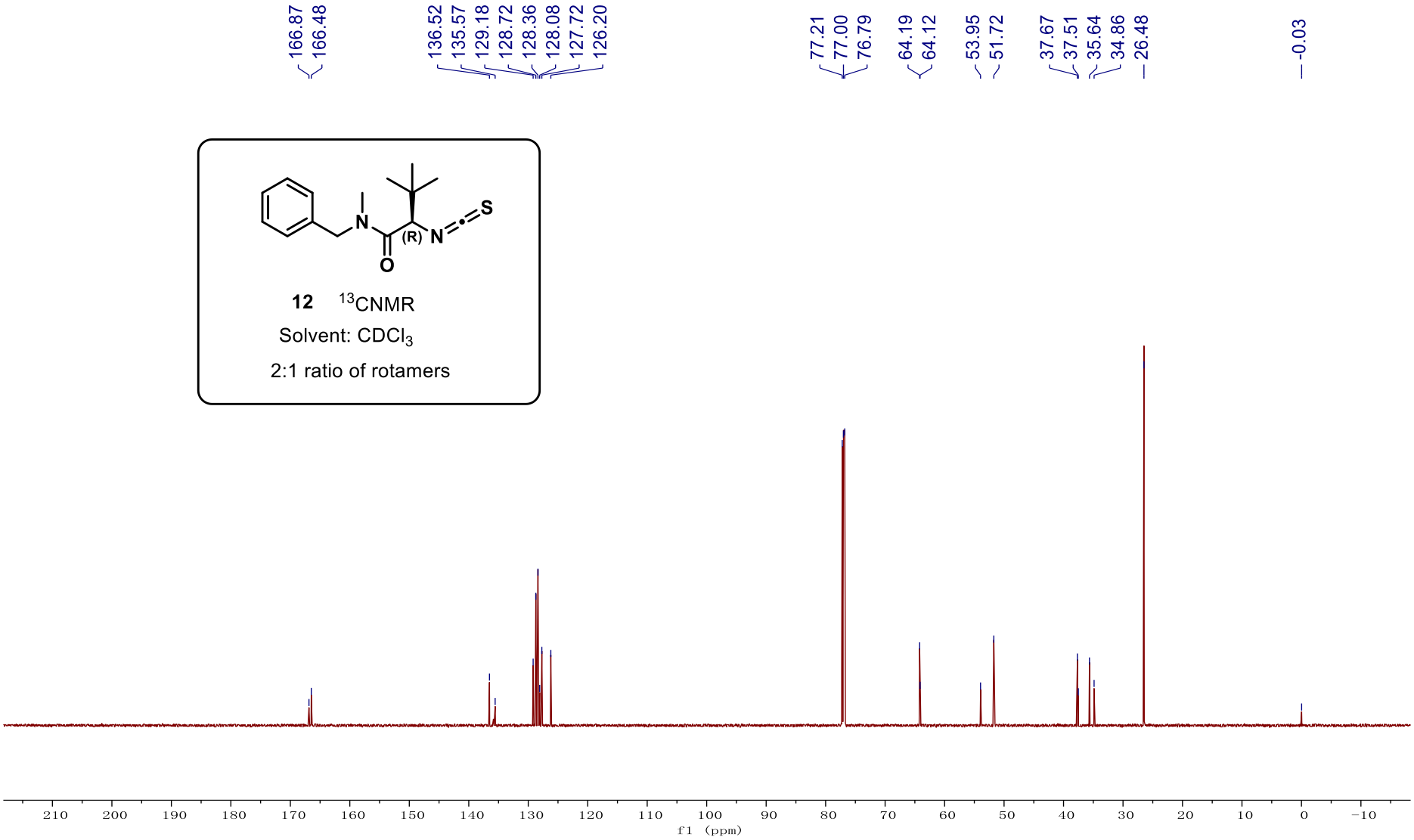

164.98
144.60
139.79
136.25
133.67
129.67
127.89
126.55
122.36
105.21
63.92
40.15
39.94
39.73
39.52
39.31
39.10
38.89
35.86
35.09
H
N
O
N
(R)
N
9 13CNMR
Solvent: DMSO-d6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

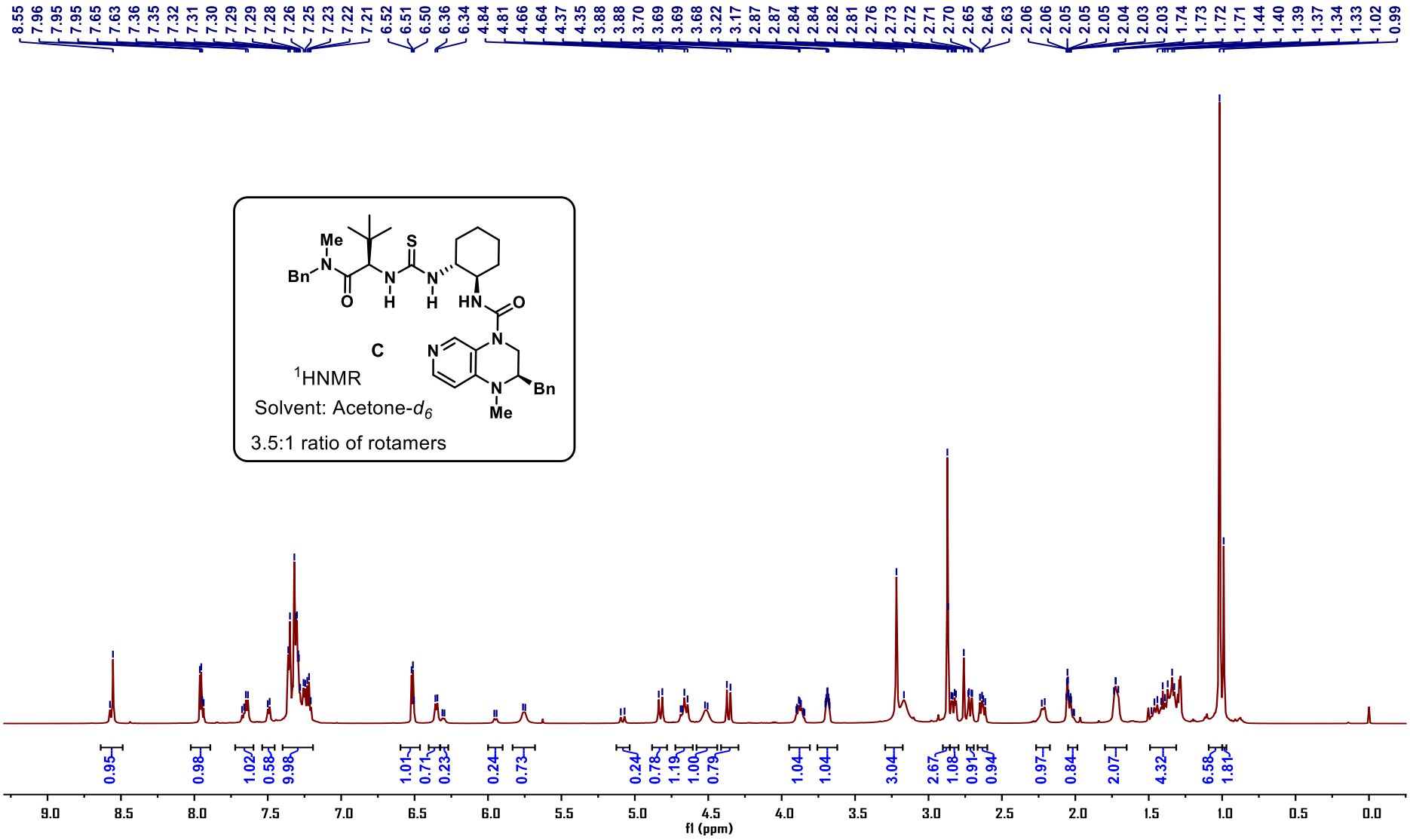

8.23
7.66
7.64
7.32
7.30
7.28
7.26
7.25
7.23
7.22
7.18
7.16
6.85
6.42
6.40
3.67
3.65
3.63
3.36
3.35
3.33
3.32
3.22
3.21
3.19
3.18
2.99
2.98
2.96
2.95
2.93
2.90
2.88
2.87
2.85
-0.02
H
N
N
(R)
N
10 1HNMR
Solvent: CDCl3
1.00
1.03
2.18
3.12
1.03
1.03
1.05
1.05
1.06
5.23
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 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 -0.5 -1.0
f1 (ppm)

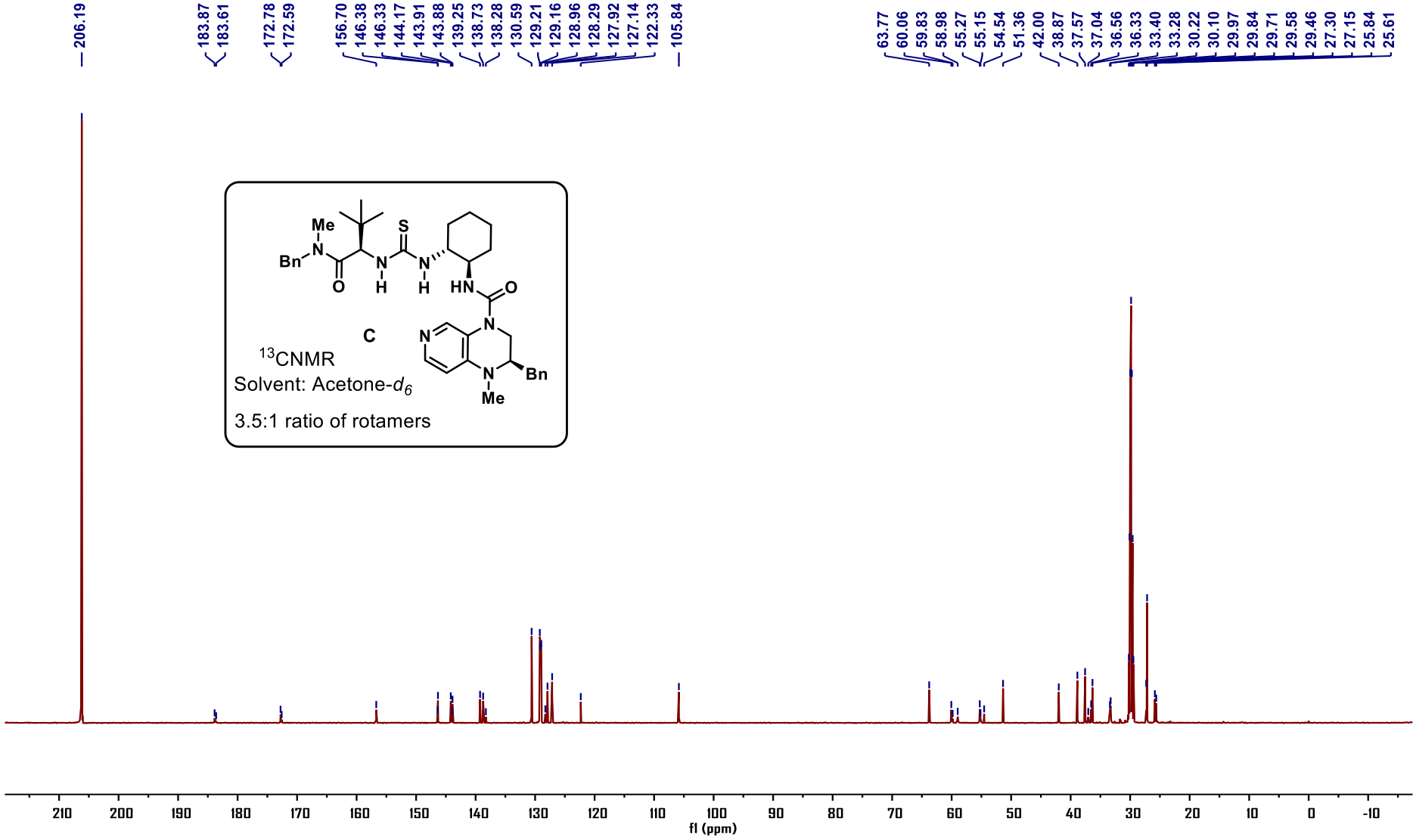

144.58
137.36
132.17
130.17
129.42
128.82
126.88
120.02
103.10
77.32
77.00
76.68
61.42
39.88
38.79
38.46
-0.05
H
N
N
(R)
N
10 13CNMR
Solvent: CDCl3
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

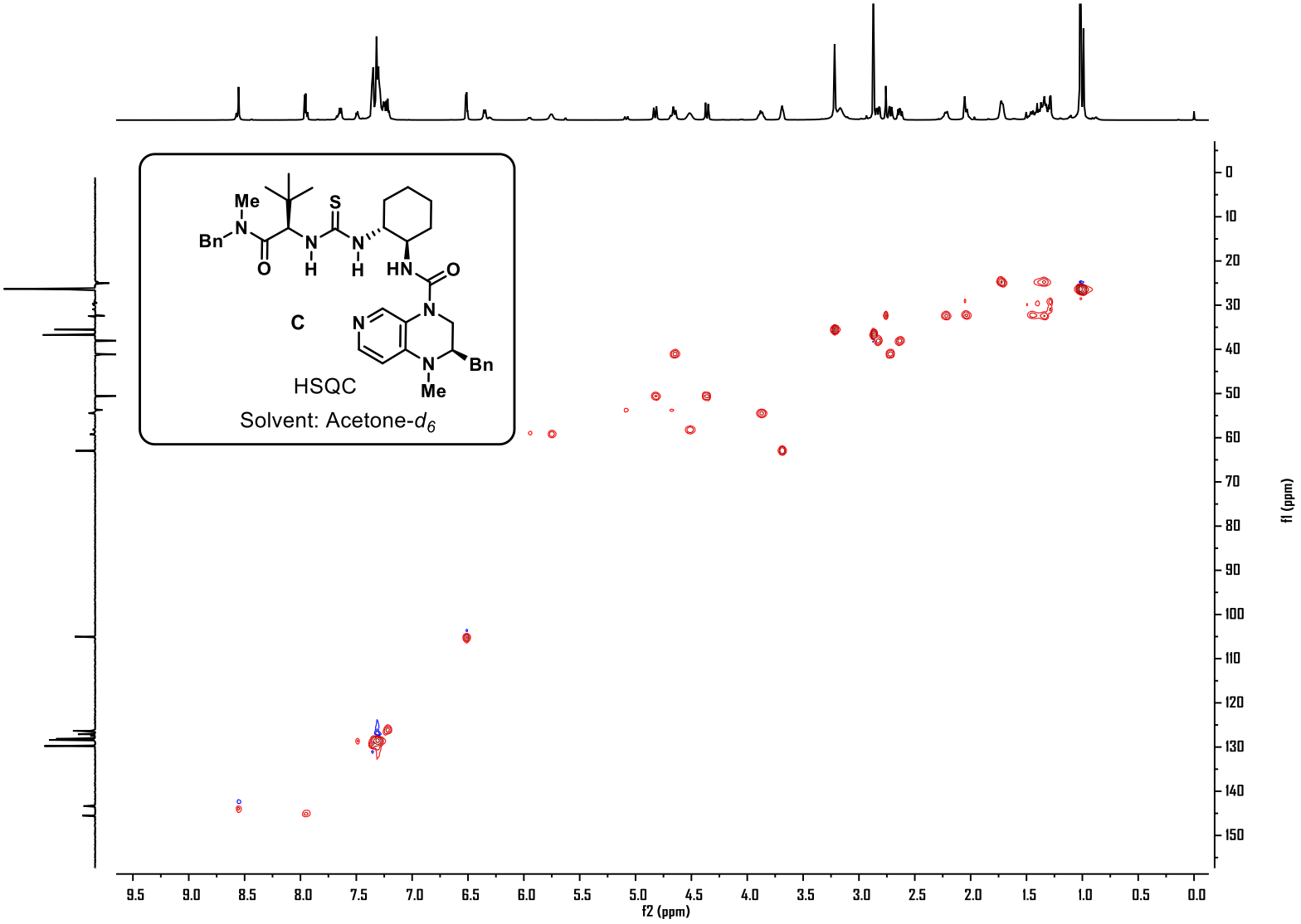

7.42
7.41
7.39
7.35
7.34
7.33
7.31
7.30
7.28
7.26
7.17
7.16
4.80
4.78
4.76
4.74
4.49
4.47
4.45
4.42
4.28
4.21
3.00
2.98
1.58
1.12
1.11
0.00
12 1HNMR
Solvent: CDCl3
2:1 ratio of rotamers
0.65
1.63
1.58
0.68
1.04
1.04
0.66
0.34
1.06
1.94
9.00
f1 (ppm)


129.17
128.72
128.37
128.08
127.72
126.20
64.19
64.12
53.95
51.71
35.64
34.86
26.48
N
(R)
N
S
O
12 DEPT135
Solvent: CDCl3
2:1 ratio of rotamers
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


166.87
166.48
136.52
135.57
129.18
128.72
128.36
128.08
127.72
126.20
77.21
77.00
76.79
64.19
64.12
53.95
51.72
37.67
37.51
35.64
34.86
26.48
-0.03
12 13CNMR
Solvent: CDCl3
2:1 ratio of rotamers
f1 (ppm)


8.55 7.96 7.95 7.95 7.65 7.63 7.36 7.35 7.32 7.31 7.30 7.29 7.29 7.28 7.26 7.25 7.23 7.22 7.21 6.52 6.51 6.50 6.36 6.34 4.84 4.81 4.66 4.64 4.37 4.35 3.88 3.88 3.70 3.69 3.69 3.68 3.22 3.17 2.87 2.87 2.84 2.84 2.82 2.81 2.76 2.73 2.72 2.71 2.70 2.65 2.64 2.63 2.06 2.06 2.05 2.05 2.05 2.04 2.03 2.03 1.74 1.73 1.72 1.71 1.44 1.40 1.39 1.37 1.34 1.33 1.02 0.99
Me
Bn
S
O
H
H
HN
O
C
N
Bn
Me
1HNMR
Solvent: Acetone-d6
3.5:1 ratio of rotamers
0.95 0.98 1.02 0.58 9.98 1.01 0.71 0.23 0.24 0.73 0.24 0.78 1.19 1.00 0.79 1.04 1.04 3.04 2.67 1.08 0.91 0.94 0.97 0.84 2.07 4.32 6.58 1.81
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)


206.19
183.87
183.61
172.78
172.59
156.70
146.38
146.33
144.17
143.91
143.88
139.25
138.73
138.28
130.59
129.21
129.16
128.96
128.29
127.92
127.14
122.33
105.84
63.77
60.06
59.83
58.98
55.27
55.15
54.54
51.36
42.00
38.87
37.57
37.04
36.56
36.33
33.40
33.28
30.22
30.10
29.97
29.84
29.71
29.58
29.46
27.30
27.15
25.84
25.61
C
13CNMR
Solvent: Acetone-d6
3.5:1 ratio of rotamers
f1 (ppm)


Me
N
Bn
O
S
N
H
N
H
HN
O
C
N
N
Bn
N
Me
HSQC
Solvent: Acetone-d_6
f2 (ppm)
f1 (ppm)