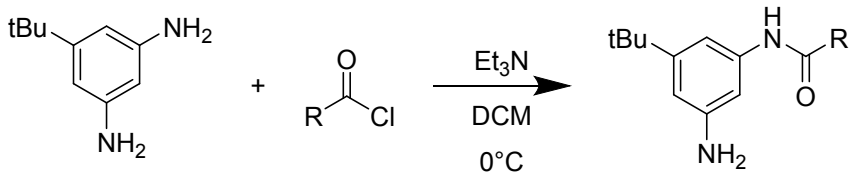
Table of Contents

General Information:

Unless otherwise noted, all commercial reagents were used without further purification. Dichloromethane, toluene, ether, THF were purified by passage through an activated alumina column under argon. Thin-layer chromatography (TLC) analysis of reaction mixtures were performed using Huanghai silica gel HSGF254 TLC plates, and visualized under UV or by staining with ceric ammonium molybdate or potassium permanganate. Flash column chromatography was carried out on Huanghai Silica Gel HHGJ-300, 300-400 mesh. Nuclear magnetic resonance (NMR) spectra were recorded using Bruker Avance III HD spectrometer (FT, 400 MHz for ^{1}H, 101 MHz for ^{13}C). ^{1}H and ^{13}C chemical shifts are reported in ppm downfield of tetramethylsilane and referenced to residual solvent peak ($CHCl_3$; δH = 7.26 and δC = 77.16, CD_3OD, δH = 3.31 and δC = 49.00, $(CD_3)_2CO$, δH = 2.05 and δC = 29.84). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad resonance. FT-IR spectras were recorded on PerkinElmer Frontier FT-IR Spectrometer, and absorption frequencies are reported in reciprocal centimeters (cm^{-1}). Mass spectral data were obtained from the Agilent Technologies 6230 TOF LC/MS spectrometer in electrospray ionization (ESI^{+}) mode. Optical rotations were measured with an Autopol V Plus/VI digital polarimeter. X-Ray structure analyses were performed using a Bruker D8 Venture X-ray single crystal diffractometer. Enantiomeric excesses were determined on an Agilent 1260 Chiral HPLC using IA, IB, IC and ID columns under the detective wavelength of 254 nm. The racemic products were synthesized by using (±)-**A3** or (±)-**A8** as catalyst.

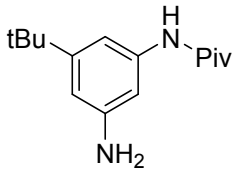
Synthesis of substrates:

Method A for synthesis of substrate 3a-3f,3h-3j



General procedure of method A for synthesis of substrate 3a-3f, 3h-3j: To a solution of 5-(tert-butyl)benzene-1,3-diamine **S1**[1] (246 mg, 1.5 mmol) in DCM (8 mL) was added trimethylamine (0.19 mL, 1.35 mmol, 0.9 equiv.). Then acyl chloride (1.35 mmol, 0.9 equiv.) was added slowly at 0 ℃. After stirring overnight at room temperature, the reaction mixture was quenched by adding water (15mL). The mixture was extracted with DCM for 3 times and the combined organic layer was dried over Na_2SO_4 and concentrated under vacuum, which was purified by flash column chromatography to give the substrate **3**.

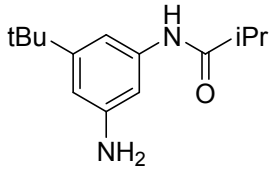
N-(3-amino-5-(tert-butyl)phenyl)pivalamide (**3a**)



This reaction was performed on 1.5 mmol scale of **S1** with pivaloyl chloride according to **method A**. Purification by flash column chromatography (petroleum ether/EtOAc = 6: 1) gave the product **3a** (260 mg, 70%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (s, 1H), 7.06 (t, *J* = 2.1 Hz, 1H), 6.70 (d, *J* = 1.8 Hz, 1H), 6.46 (t, *J* = 1.9 Hz, 1H), 3.65 (s, 2H), 1.30 (s, 9H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.5, 153.2, 146.9, 138.7, 108.4, 107.2, 104.3, 39.6, 34.6, 31.2, 27.7. IR (cm^{-1}): *f* = 3382, 3173, 2960, 2862, 1640, 1599, 1487, 848, 700. m/z HRMS (ESI) found $[M+H]^+$ 249.1955, $C_{15}H_{25}N_2O^+$ requires 249.1961.

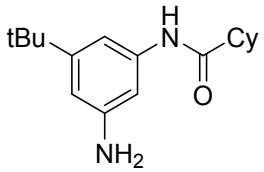
N-(3-amino-5-(tert-butyl)phenyl)isobutyramide (**3b**)



This reaction was performed on 1.5 mmol scale of **S1** with isobutyryl chloride according to **method A**. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3b** (195 mg, 56%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (s, 1H), 7.01 (t, *J* = 2.1 Hz, 1H), 6.79 (t, *J* = 1.8 Hz, 1H), 6.43 (t, *J* = 1.9 Hz, 1H), 3.51 (s, 2H), 2.48 (hept, *J* = 6.8 Hz, 1H), 1.23 (s, 9H), 1.20 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 153.2, 146.8, 138.9, 108.4, 107.4, 104.3, 36.7, 34.6, 31.2, 19.7. IR (cm^{-1}): *f* = 3306, 2963, 2870, 1661, 1611, 1548, 1427, 1220, 844, 733, 699. m/z HRMS (ESI) found $[M+H]^+$ 235.1800, $C_{14}H_{23}N_2O^+$ requires 235.1805.

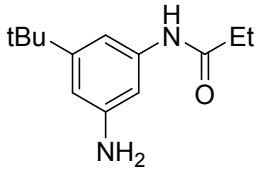
N-(3-amino-5-(tert-butyl)phenyl)cyclohexanecarboxamide (**3c**)



This reaction was performed on 1.5 mmol scale of **S1** with cyclohexanecarbonyl chloride according to **method A**. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3c** (227 mg, 55%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 (s, 1H), 7.07 (t, *J* = 2.0 Hz, 1H), 6.70 (t, *J* = 1.7 Hz, 1H), 6.45 (t, *J* = 1.9 Hz, 1H), 3.44 (s, 2H), 2.19 (tt, *J* = 11.7, 3.5 Hz, 1H), 1.99 – 1.44 (m, 8H), 1.29 (d, 2H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 153.3, 146.9, 138.9, 108.4, 107.2, 104.2, 46.8, 34.7, 31.3, 29.8, 25.8. IR (cm^{-1}): *f* = 3296, 2926, 2853, 1657, 1611, 1549, 1427, 1202, 843, 698. m/z HRMS (ESI) found $[M+H]^+$ 275.2110, $C_{17}H_{27}N_2O^+$ requires 275.2118.

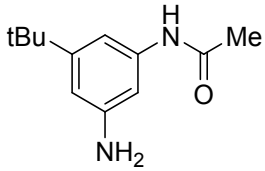
N-(3-amino-5-(tert-butyl)phenyl)propionamide (**3d**)



This reaction was performed on 1.5 mmol scale of **S1** with propionyl chloride according to **method A**. Purification by flash column chromatography (petroleum ether/EtOAc = 3: 2) gave the product **3d** (198 mg, 60%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (s, 1H), 7.01 (s, 1H), 6.73 (s, 1H), 6.44 (s, 1H), 3.37 (s, 2H), 2.34 (q, *J* = 7.5 Hz, 2H), 1.22 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 152.1, 145.7, 137.7, 107.4, 106.3, 103.3, 33.6, 30.2, 29.7, 8.7. IR (cm^{-1}): *f* = 3303, 2962, 1569, 1613, 1551, 1430, 1222, 844, 698. m/z HRMS (ESI) found $[M+H]^+$ 221.1645, $C_{13}H_{21}N_2O^+$ requires 221.1648.

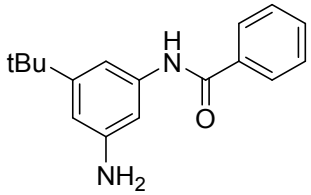
N-(3-amino-5-(tert-butyl)phenyl)acetamide (**3e**)



This reaction was performed on 1.5 mmol scale of **S1** with acetyl chloride according to **method A**. Purification by flash column chromatography (petroleum ether/EtOAc = 2: 3) gave the product **3e** (105 mg, 34%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (s, 1H), 7.03 (d, *J* = 2.1 Hz, 1H), 6.65 (t, *J* = 1.8 Hz, 1H), 6.45 (t, *J* = 1.8 Hz, 1H), 3.65 (s, 2H), 2.12 (s, 3H), 1.24 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 153.2, 146.9, 138.7, 108.6, 107.4, 104.4, 34.7, 31.3, 24.8. IR (cm^{-1}): *f* = 3419, 3314, 2958, 1667, 1596, 1556, 1471, 1417, 1362, 1261, 856, 842, 698. m/z HRMS (ESI) found $[M+H]^+$ 207.1488, $C_{12}H_{19}N_2O^+$ requires 207.1492.

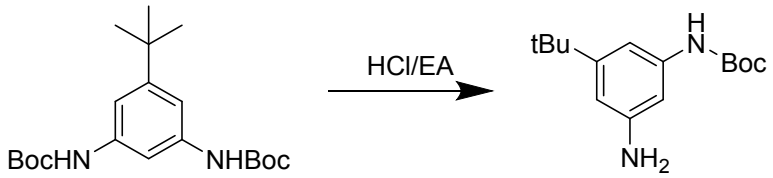
N-(3-amino-5-(tert-butyl)phenyl)benzamide (**3f**)



This reaction was performed on 1.5 mmol scale of **S1** with benzoyl chloride according to **method A**. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3f** (267 mg, 66%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89 (s, 1H), 7.85 (dd, *J* = 7.2, 1.8 Hz, 2H), 7.56 – 7.48 (m, 1H), 7.48 – 7.40 (m, 2H), 7.19 (t, *J* = 2.1 Hz, 1H), 6.82 (t, *J* = 1.8 Hz, 1H), 6.51 (t, *J* = 1.9 Hz, 1H), 3.69 (s, 2H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 153.3, 147.0, 138.7, 135.3, 131.7, 128.7, 127.0, 108.8, 107.6, 104.6, 34.7, 31.2. IR (cm^{-1}): *f* = 3426, 3314, 3218, 2954, 2899, 1647, 1610, 1550, 1421, 1294, 846, 701. m/z HRMS (ESI) found $[M+H]^+$ 269.1641, $C_{17}H_{21}N_2O^+$ requires 269.1648.

tert-butyl (3-amino-5-(tert-butyl)phenyl)carbamate (**3g**)

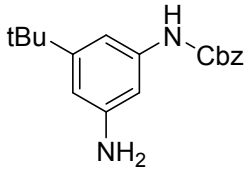


S2 **3g**

Procedure for synthesis **3g**: To a residue of **S2**[1] (546 mg, 1.5 mmol) was added a solution of HCl/EA (10 mL, 2.0 M). After stirring for 1h, an aqueous solution of 1M NaOH was added until the pH of reaction mixture reached 7. The mixture was extracted with EA for 3 times and the combined organic layer was dried over Na_2SO_4 and concentrated under vacuum, which was purified by flash column chromatography (petroleum ether/EtOAc = 4: 1) to give the product **3g** (158 mg, 40%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.83 (s, 1H), 6.55 (t, *J* = 1.9 Hz, 1H), 6.48 (s, 1H), 6.40 (t, *J* = 1.9 Hz, 1H), 3.61 (s, 2H), 1.51 (s, 9H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 152.9, 146.9, 139.1, 107.5, 106.3, 102.9, 80.3, 34.7, 31.3, 28.5. IR (cm^{-1}): *f* = 3426, 3348, 2955, 1726, 1603, 1549, 1495, 1233, 1153, 1065, 880, 858, 700. m/z HRMS (ESI) found $[M+H]^+$ 265.1905, $C_{15}H_{25}N_2O_2^+$ requires 265.1911.

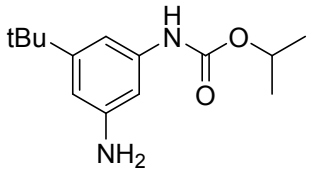
benzyl (3-amino-5-(tert-butyl)phenyl)carbamate (**3h**)



This reaction was performed on 1.22 mmol scale of **S1** with benzyl carbonochloridate according to **method A** (using DIEPA instead of Et_3N). Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3h** (202 mg, 56%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.30 (m, 5H), 6.82 (s, 1H), 6.68 – 6.54 (m, 2H), 6.43 (t, *J* = 1.9 Hz, 1H), 5.19 (s, 2H), 3.66 (s, 2H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.5, 147.0, 138.5, 136.3, 128.7, 128.4, 128.4, 108.0, 106.5, 103.0, 67.0, 34.7, 31.3, 1.2. IR (cm^{-1}): *f* = 3673, 3411, 3341, 2965, 2900, 1727, 1601, 1565, 1491, 1227, 1070, 835, 761, 693. m/z HRMS (ESI) found $[M+H]^+$ 299.1746, $C_{18}H_{23}N_2O_2^+$ requires 299.1754.

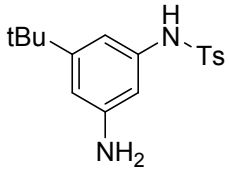
isopropyl (3-amino-5-(tert-butyl)phenyl)carbamate (**3i**)



This reaction was performed on 1.5 mmol scale of **S1** with isopropyl carbonochloridate according to **method A**. Purification by flash column chromatography (petroleum ether/EtOAc = 5: 1) gave the product **3i** (57 mg, 15%).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.80 (s, 1H), 6.62 (t, *J* = 1.8 Hz, 1H), 6.56 – 6.46 (m, 1H), 6.42 (t, *J* = 1.8 Hz, 1H), 5.00 (hept, *J* = 6.2 Hz, 1H), 3.65 (s, 2H), 1.28 (d, *J* = 6.2 Hz, 6H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.4, 153.3, 146.9, 138.9, 107.7, 106.4, 102.9, 68.6, 34.7, 31.3, 22.2. IR (cm^{-1}): *f* = 3428, 2968, 2900, 1725, 1602, 1533, 1264, 1219, 736, 704. m/z HRMS (ESI) found $[M+H]^+$ 251.1750, $C_{14}H_{23}N_2O_2^+$ requires 251.1754.

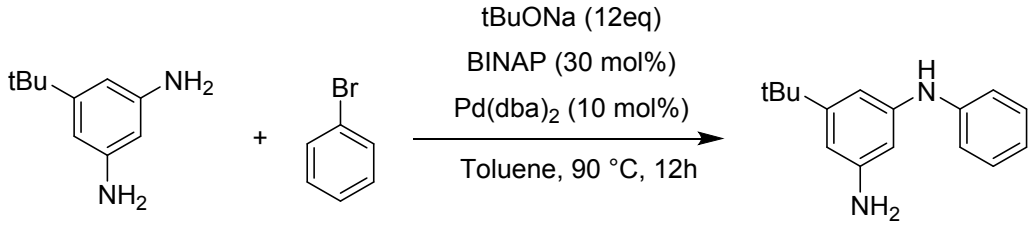
N-(3-amino-5-(tert-butyl)phenyl)-4-methylbenzenesulfonamide (**3j**)



This reaction was performed on 1.6 mmol scale of **S1** with 4-methylbenzenesulfonyl chloride according to **method A**. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3j** (305 mg, 60%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 – 7.61 (m, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 6.99 (s, 1H), 6.42 (t, *J* = 1.8 Hz, 1H), 6.37 (t, *J* = 1.7 Hz, 1H), 6.33 (t, *J* = 2.0 Hz, 1H), 3.65 (s, 2H), 2.35 (s, 3H), 1.14 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.7, 147.0, 143.7, 137.4, 136.2, 129.6, 127.5, 109.5, 109.2, 105.5, 34.7, 31.1, 21.6. IR (cm^{-1}): *ƒ* = 3385, 3254, 2964, 1598, 1315, 1153, 1090, 883. m/z HRMS (ESI) found $[M+H]^+$ 319.1469, $C_{17}H_{23}N_2O_2S^+$ requires 319.1475.

5-(tert-butyl)-N1-phenylbenzene-1,3-diamine (**3k**)

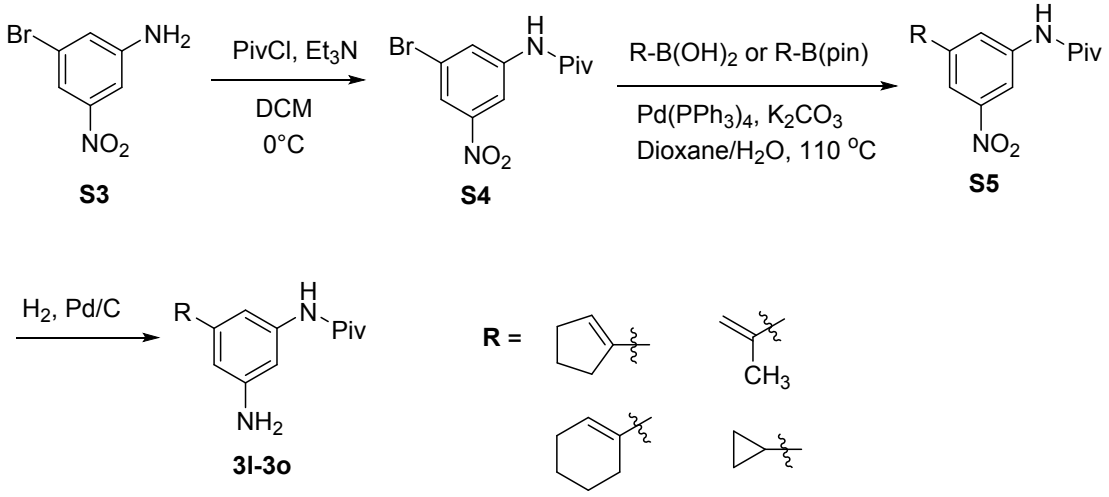


Procedure for synthesis of **3k**: To a 50 mL Schlenk tube, **S1** (1.5 mmol), Pd(dba)2 (86 mg, 0.15 mmol), BINAP (280 mg, 0.45 mmol), tBuONa (1.7 g, 18 mmol), bromobenzene (236 mg, 1.5 mmol), and toluene (15 mL) were added. The tube was charged with N_2 for three times and the mixture was then heated at 90℃ for 12 h. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a short pad of silica. The filtrate was concentrated under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc = 10: 1) to give the substrate **3k** (90 mg, 25%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 – 7.21 (m, 2H), 7.11 – 6.99 (m, 2H), 6.94 – 6.84 (m, 1H), 6.49 (t, *J* = 1.8 Hz, 1H), 6.31 (t, *J* = 1.8 Hz, 1H), 6.28 (t, *J* = 2.0 Hz, 1H), 5.62 (s, 1H), 3.56 (s, 2H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 147.1, 143.9, 143.5, 129.4, 120.7,

118.0, 106.5, 105.9, 101.8, 34.7, 31.4. IR (cm^{-1}): f = 3335, 3275, 2949, 1584, 1487, 1452, 1175, 837, 752, 694. m/z HRMS (ESI) found $[M+H]^+$ 241.1695, $C_{16}H_{21}N_2^+$ requires 241.1699.

General procedure of method B for synthesis of substrate 3l-3o:

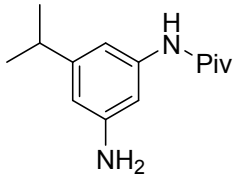


S5: To a solution of 3-bromo-5-nitroaniline **S3** (810 mg, 3.7 mmol) in DCM (15 mL) was added trimethylamine (0.55 mL, 3.9 mmol, 1.05 equiv.). Then pivaloyl chloride (0.51 mL, 4.1 mmol, 1.1 equiv.) was added slowly at 0℃. After stirring at rt overnight, the reaction mixture was quenched by adding water (20 mL). The mixture was extracted with DCM for 3 times and the combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to afford a residue, which was purified by column chromatography (petroleum ether/EtOAc = 10:1) as eluent to give the product **S4** (1.08 g, 96%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (t, J = 2.0 Hz, 1H), 8.24 (t, J = 1.9 Hz, 1H), 8.06 (t, J = 1.9 Hz, 1H), 7.62 (s, 1H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.3, 149.0, 140.2, 128.5, 123.2, 121.9, 113.5, 40.1, 27.6. IR (cm^{-1}): f = 3307, 2969, 1663, 1584, 1518, 1339, 1170, 742.

A mixture of **S4** (322 mg, 1.5 mmol), R-B(OH)$_2$ or R-B(pin) (1.95 mmol), tetrakis(triphenylphosphine) palladium (86 mg, 0.075 mmol) and K_2CO_3 (496 mg, 3.6 mmol) were dissolved in 1,4-dioxane (16 mL) and H_2O (8 mL). The mixture was purged with N_2 for 3 times, and then heated to reflux overnight. The reaction mixture was then cooled to room temperature and filtered through celite to give the filtrate, which was extracted with EtOAc for 3 times. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to give a residue, which was purified by flash column chromatography to give the product **S5**.

To a solution of **S5** (1.0 equiv.) in MeOH (5 mL) was add Pd/C (10 mol%). After stirring under H_2 atmosphere (1 atm) overnight, the reaction mixture was filtered through celite and concentrated under vacuum to give a residue, which was purified by flash column chromatography to give the product **3l-3o**.

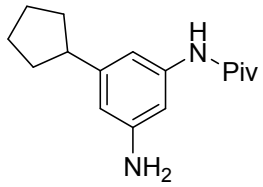
N-(3-amino-5-isopropylphenyl)pivalamide (**3l**)



This reaction was performed on 0.67 mmol scale of **S4** with 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane according to **method B**. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3l** (152 mg, 97%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (s, 1H), 6.98 (t, *J* = 2.1 Hz, 1H), 6.63 (t, *J* = 1.8 Hz, 1H), 6.29 (t, *J* = 1.8 Hz, 1H), 3.63 (s, 2H), 2.74 (hept, *J* = 6.9 Hz, 1H), 1.28 (s, 9H), 1.18 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 150.8, 147.2, 139.0, 109.3, 108.2, 104.5, 39.6, 34.2, 27.6, 23.8. IR (cm^{-1}): *ƒ* = 3307, 2954, 2869, 1650, 1600, 1549, 1429, 1200, 844, 696. m/z HRMS (ESI) found $[M+H]^+$ 235.1800, $C_{14}H_{23}N_2O^+$ requires 235.1805.

N-(3-amino-5-cyclopentylphenyl)pivalamide (**3m**)

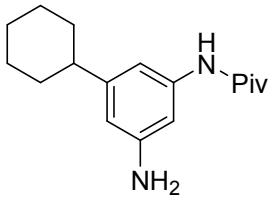


This reaction was performed on 1 mmol scale of **S4** with 2-(cyclopent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane according to **method B**. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3m** (213 mg, 82%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (s, 1H), 7.01 (t, *J* = 2.0 Hz, 1H), 6.62 (t, *J* = 1.8 Hz, 1H), 6.32 (t, *J* = 1.8 Hz, 1H), 3.61 (s, 2H), 3.04 – 2.73 (m, 1H), 2.12 – 1.92 (m, 2H), 1.76 (qt, *J* = 6.5, 3.8 Hz, 2H), 1.70 – 1.48 (m, 4H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 148.6, 147.1, 139.0, 110.0, 108.8, 104.4, 46.0, 39.7, 34.4, 27.7, 25.6. IR (cm^{-1}): *ƒ* = 3435, 3354, 3303,

2953, 2864, 1639, 1599, 1532, 1480, 1433, 1205, 928, 843, 678. m/z HRMS (ESI) found $[M+H]^+$ 261.1955, $C_{16}H_{25}N_2O^+$ requires 261.1961.

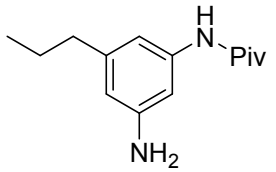
N-(3-amino-5-cyclohexylphenyl)pivalamide (**3n**)



This reaction was performed on 1 mmol scale of **S4** with cyclohex-1-en-1-ylboronic acid according to **method B**. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3n** (213 mg, 71%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 (s, 1H), 6.96 (t, *J* = 2.0 Hz, 1H), 6.65 (t, *J* = 1.8 Hz, 1H), 6.28 (t, *J* = 1.8 Hz, 1H), 3.69 (s, 2H), 2.34 (ddd, *J* = 11.5, 8.1, 3.4 Hz, 1H), 1.80 (dq, *J* = 10.3, 6.8, 5.5 Hz, 4H), 1.35 (ddd, *J* = 17.6, 14.4, 10.6 Hz, 4H), 1.27 (s, 9H), 1.25 – 1.06 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 150.1, 146.8, 138.9, 109.9, 108.8, 104.7, 44.7, 39.6, 34.3, 27.6, 26.9, 26.2. IR (cm^{-1}): *f* = 3419, 3357, 3333, 2967, 2922, 2849, 1653, 1611, 1598, 1538, 1432, 1201, 840, 690. m/z HRMS (ESI) found $[M+H]^+$ 275.2111, $C_{17}H_{27}N_2O^+$ requires 275.2118.

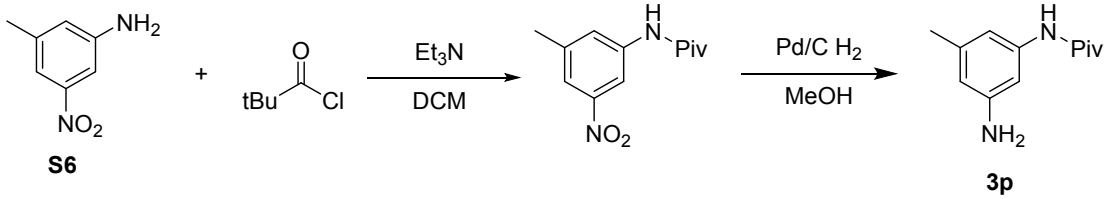
N-(3-amino-5-propylphenyl)pivalamide (**3o**)



This reaction was performed on 0.86 mmol scale of **S4** with cyclopropylboronic acid according to **method B**. Purification by flash column chromatography (petroleum ether/EtOAc = 4: 1) gave the product **3o** (183 mg, 91%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (s, 1H), 7.00 (t, *J* = 2.1 Hz, 1H), 6.56 (d, *J* = 1.8 Hz, 1H), 6.26 (t, *J* = 1.8 Hz, 1H), 3.63 (s, 2H), 2.44 (dd, *J* = 8.6, 6.7 Hz, 2H), 1.60 (q, *J* = 7.5 Hz, 2H), 1.29 (s, 9H), 0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 147.2, 144.7, 139.0, 111.3, 110.2, 104.3, 39.7, 38.2, 27.7, 24.4, 14.0. IR (cm^{-1}): *f* = 3420, 3290, 2961, 2927, 2869, 1649, 1606, 1528, 1477, 1432, 1201, 814, 694. m/z HRMS (ESI) found $[M+H]^+$ 235.1800, $C_{14}H_{23}N_2O^+$ requires 235.1805.

N-(3-amino-5-methylphenyl)pivalamide (**3p**)



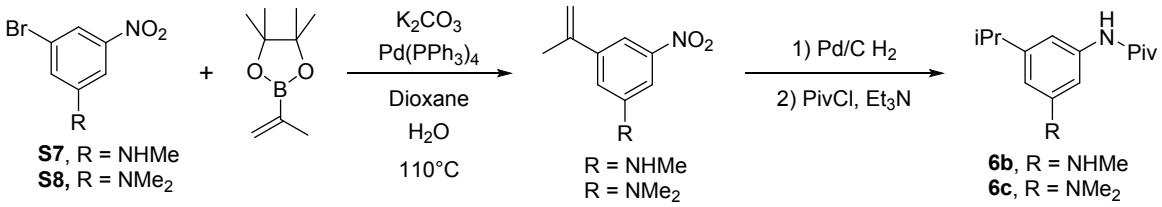
Procedure for synthesis **3p**: To a solution of 3-methyl-5-nitroaniline (**S6**, 304 mg, 2 mmol) in DCM (15mL) was added trimethylamine (0.3 mL, 2.1 mmol, 1.05 equiv.). Then pivaloyl chloride (0.27 mL, 2.2 mmol, 1.1 equiv.) was added slowly at 0℃. The mixture was stirred at rt overnight. After the completion of reaction, water (20 mL) was added. The mixture was extracted with DCM for 3 times. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to afford a residue.

To the solution of the abovementioned residue in MeOH (5 ml) was add Pd/C (10 mol%). After stirring under H_2 atmosphere (1 atm) overnight, the reaction mixture was filtered through celite and concentrated under vacuum to give a residue, which was purified by flash column chromatography (petroleum ether/EtOAc = 4: 1) to give the product **3p** (370 mg, 90%).

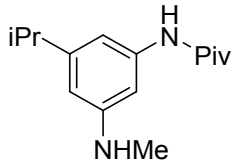
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 (s, 1H), 6.97 (d, *J* = 2.2 Hz, 1H), 6.57 (d, *J* = 1.9 Hz, 1H), 6.25 (t, *J* = 1.7 Hz, 1H), 3.62 (s, 2H), 2.21 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 147.2, 139.8, 139.0, 111.8, 110.7, 104.0, 39.7, 27.7, 21.5. IR (cm^{-1}): *ƒ* = 3482, 3389, 3275, 2964, 1644, 1606, 1434, 1203, 836, 690. m/z HRMS (ESI) found $[M+H]^+$ 207.1488, $C_{12}H_{19}N_2O^+$ requires 207.1492.

Substrates 6b and 6c were synthesized from S7 and S8 by adopting general method B:

General procedure of method B:

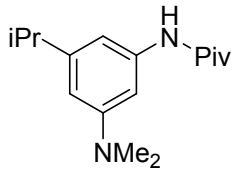


N-(3-isopropyl-5-(methylamino)phenyl)pivalamide (**6b**)



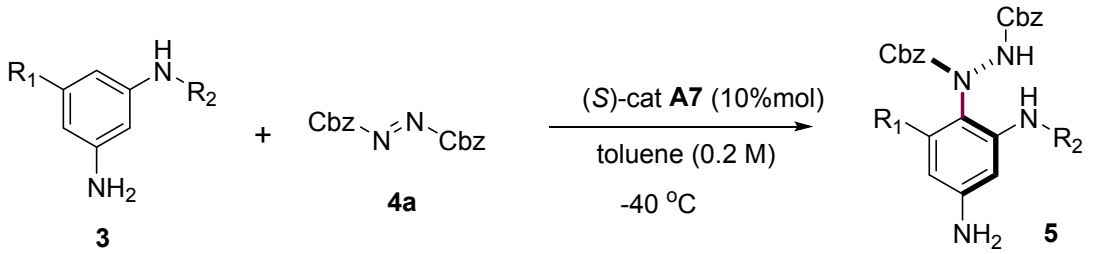
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.23 (s, 1H), 6.94 (t, *J* = 2.2 Hz, 1H), 6.57 (d, *J* = 2.6 Hz, 1H), 6.24 (d, *J* = 2.9 Hz, 1H), 3.72 (s, 1H), 2.83 (s, 3H), 2.79 (hept, *J* = 7.0 Hz, 1H), 1.31 (s, 9H), 1.22 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 150.8, 150.2, 139.2, 107.0, 106.9, 101.5, 39.8, 34.5, 30.9, 27.8, 24.0. IR (cm^{-1}): *f* = 3329, 2957, 2871, 1653, 1615, 1602, 1440, 1399, 1209, 837, 701. m/z HRMS (ESI) found $[M+H]^+$ 249.1954, $C_{15}H_{25}N_2O^+$ requires 249.1961.

N-(3-(dimethylamino)-5-isopropylphenyl)pivalamide (**6c**)



^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.26 (s, 1H), 7.01 (t, *J* = 2.3 Hz, 1H), 6.63 (s, 1H), 6.34 (s, 1H), 2.93 (s, 6H), 2.80 (hept, *J* = 7.0 Hz, 1H), 1.30 (s, 9H), 1.22 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 151.4, 150.5, 139.0, 107.1, 106.2, 102.0, 40.8, 39.8, 34.8, 27.8, 24.1. IR (cm^{-1}): *f* = 3334, 2956, 2925, 1650, 1610, 1550, 1426, 825, 697. m/z HRMS (ESI) found $[M+H]^+$ 263.2110, $C_{16}H_{27}N_2O^+$ requires 263.2118.

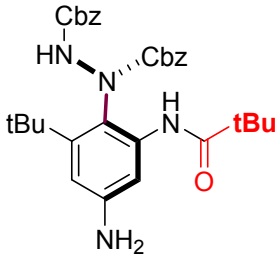
Asymmetric synthesis of products:



General procedure for the asymmetric synthesis of products 5a to 5p: To a solution of **3** (0.2 mmol), **2** (0.24 mmol) in Toluene (1 mL) was added (*s*)-cat **A7** (0.02 mmol) at -40 °C. After

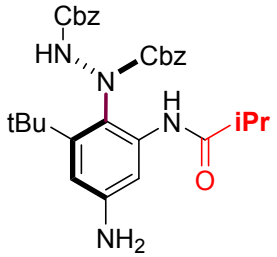
stirring at -40 °C for 3 h, the reaction was directly purified by flash column chromatography to give the product **5**. (Noting: The product **5b, 5f, 5p** were synthesized by using (*R*)-cat **A1** catalyst)

(*R*)-Dibenzyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5a**)



106 mg, 97% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.77 (m, 1H), 7.39 – 7.06 (m, 11), 6.84 (d, *J* = 7.2 Hz, 1H), 6.43 (t, *J* = 3.0 Hz, 1H), 5.25 – 4.80 (m, 4H), 3.67 (s, 2H), 1.22 – 1.09 (m, 18). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 156.7, 155.0, 147.0, 145.7, 137.3, 134.2, 133.9, 127.6, 127.6, 127.5, 127.5, 127.4, 127.3, 119.5, 109.4, 108.3, 67.7, 67.7, 38.8, 34.7, 30.7, 26.3. $[\alpha]_D^{25}$ = -51.50 (c = 1.0, DCM). IR (cm^{-1}): *f* = 3673, 3289, 2968, 2900, 1706, 1524, 1455, 1230, 1056, 740, 694. m/z HRMS (ESI) found $[M+H]^+$ 547.2907, $C_{31}H_{39}N_4O_5^+$ requires 547.2915. HPLC: Chiralpak ID column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 10.9 min (major), 13.2 min (minor); 98:1.5 er.

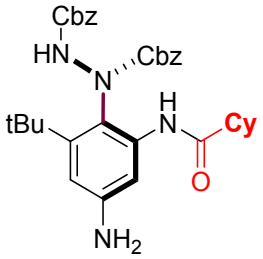
(*S*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-isobutyramidophenyl)hydrazine-1,2-dicarboxylate (**5b**)



100 mg, 94% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.04 (m, 1H), 8.05 – 7.50 (m, 1H), 7.34 (d, *J* = 6.4 Hz, 5H), 7.30 – 7.12 (m, 5H), 6.90 (d, *J* = 10.7 Hz, 1H), 6.45 (d, *J* = 2.7 Hz, 1H), 5.58 – 4.86 (m, 4H), 3.41 (s, 2H), 2.62 (hept, *J* = 6.9 Hz, 1H), 1.22 – 1.03 (m, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.5, 158.4, 156.1, 148.5, 147.3, 138.8, 135.4, 134.9, 128.8, 128.8, 128.6, 128.5, 128.4, 128.3, 119.1, 109.7, 107.1, 68.9, 68.8, 36.3, 32.0, 19.9, 19.4. $[\alpha]_D^{25}$ = 10.30 (c = 1.0, DCM). IR (cm^{-1}): *f* = 3673, 3274, 2964, 1706, 1683, 1614, 1225, 1056, 734, 695. m/z HRMS

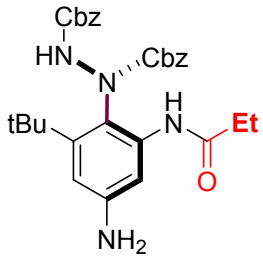
(ESI) found $[M+H]^+$ 533.2753, $C_{30}H_{37}N_4O_5^+$ requires 533.2758. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 10.0 min (major), 13.5 min (minor); 93.5:6.5 er.

(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-(cyclohexanecarboxamido)phenyl)hydrazine-1,2-dicarboxylate (**5c**)



109 mg, 95% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.93 (m, 1H), 7.64 (dd, *J* = 43.7, 2.6 Hz, 1H), 7.32 – 7.23 (m, 5H), 7.21 – 7.07 (m, 5H), 6.85 (m, 1H), 6.37 (d, *J* = 2.7 Hz, 1H), 5.21 – 4.90 (m, 4H), 3.68 (s, 2H), 2.26 (m, 1H), 1.90 – 1.21 (m, 10H), 1.15 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.7, 158.3, 156.1, 148.4, 147.3, 138.8, 135.4, 135.0, 128.8, 128.7, 128.6, 128.5, 128.3, 128.3, 119.0, 109.6, 107.0, 68.8, 68.7, 46.2, 35.8, 32.0, 29.6, 29.4, 25.8. $[\alpha]_D^{25}$ = -20.30 (c = 1.0, DCM). IR (cm^{-1}): *f* = 3673, 3273, 2966, 2924, 1707, 1454, 1231, 1057, 733, 694. m/z HRMS (ESI) found $[M+H]^+$ 573.3064, $C_{33}H_{41}N_4O_5^+$ requires 573.3071. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 15.1 min (minor), 18.5 min (major); 93:7 er.

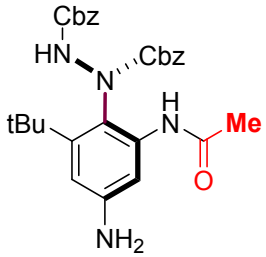
(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-propionamidophenyl)hydrazine-1,2-dicarboxylate (**5d**)



93 mg, 90% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.96 (m, 1H), 7.64 (m, 1H), 7.41 – 7.06 (m, 10H), 6.91 (m, 1H), 6.37 (d, *J* = 2.8 Hz, 1H), 5.42 – 4.77 (m, 4H), 3.74 (s, 2H), 2.63 – 1.98 (m, 2H), 1.15 (s, 9H), 1.03 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 158.4, 156.0, 148.5, 147.4, 138.6, 135.5, 134.9, 128.7, 128.7, 128.5, 128.5, 128.3, 128.3, 118.9, 109.6, 106.8, 68.8, 68.6, 35.8, 31.9, 30.6, 9.9. $[\alpha]_D^{25}$ = -11.90 (c = 1.0, DCM). IR (cm^{-1}): *f* = 3673, 3270, 2967, 1705, 1682, 1455, 1225, 1056, 733, 694. m/z HRMS (ESI) found $[M+H]^+$ 519.2595, $C_{29}H_{35}N_4O_5^+$

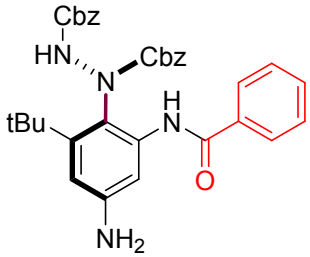
requires 519.2602. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 12.5 min (minor), 15.0 min (major); 91:9 er.

(*R*)-dibenzyl-1-(2-acetamido-4-amino-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5e**)



73 mg, 72% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.03 (m, 1H), 7.62 (m, 1H), 7.37 – 7.05 (m, 10H), 6.84 (mm, 1H), 6.40 (d, *J* = 2.8 Hz, 1H), 5.39 – 4.81 (m, 4H), 3.71 (s, 2H), 1.97 (m, 3H), 1.17 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 158.5, 156.0, 148.6, 147.4, 138.6, 135.6, 134.9, 128.8, 128.8, 128.6, 128.6, 128.4, 128.4, 118.9, 109.7, 106.7, 68.9, 68.7, 35.8, 32.0, 24.5. $[\alpha]_D^{25}$ = -10.50 (c = 1.0, DCM). IR (cm^{-1}): *f* = 3673, 3270, 2967, 2900, 1705, 1615, 1455, 1232, 1057, 733, 695. m/z HRMS (ESI) found $[M+H]^+$ 505.2440, $C_{28}H_{33}N_4O_5^+$ requires 505.2445. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 13.7 min (minor), 15.1 min (major); 93.5:6.5 er.

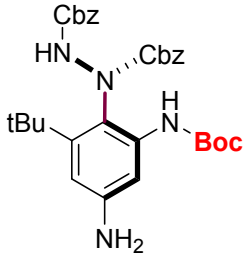
(*S*)-dibenzyl-1-(4-amino-2-benzamido-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5f**)



110 mg, 97%yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.59 (m, 1H), 7.87 (m, 2H), 7.67 – 6.72 (m, 15H), 6.48 (p, *J* = 2.8 Hz, 1H), 4.99 (m, 4H), 3.84 – 3.18 (m, 2H), 1.30 – 0.93 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 158.1, 156.2, 148.4, 147.1, 138.1, 135.2, 135.1, 134.9, 131.4, 128.7, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 120.9, 111.0, 109.5, 68.9, 68.8, 35.8, 31.8. $[\alpha]_D^{25}$ = 33.90 (c = 1.0, DCM). IR (cm^{-1}): *f* = 3673, 3245, 2968, 2900, 1705, 1661, 1533, 1455, 1240, 1056, 692. m/z HRMS (ESI) found $[M+H]^+$ 567.2594, $C_{33}H_{35}N_4O_5^+$ requires 567.2602.

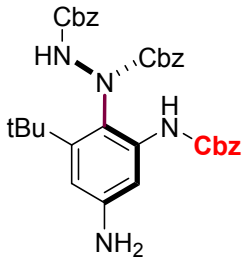
HPLC: Chiralpak ID column, 70:30 hexanes/isopropanol, 1 ml/min; t_R = 23.4 min (minor), 26.1 min (major); 88:12 er.

(*R*)-dibenzyl-1-(4-amino-2-((tert-butoxycarbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5g**)



111 mg, 99% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.39 (m, 1H), 7.54 – 7.12 (m, 11H), 6.87 (m, 1H), 6.39 (dd, *J* = 5.7, 2.7 Hz, 1H), 5.35 – 4.80 (m, 4H), 3.60 (s, 2H), 1.49 (d, *J* = 7.6 Hz, 9H), 1.20 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.0, 156.1, 153.9, 148.5, 147.2, 139.2, 135.5, 135.1, 128.7, 128.6, 128.4, 128.1, 127.8, 127.8, 118.9, 108.9, 105.8, 79.6, 68.6, 68.6, 35.7, 31.9, 28.4. $[\alpha]_D^{25}$ = -21.30 (c = 1.0, DCM). IR (cm^{-1}): *f* = 3673, 3272, 2968, 2900, 1703, 1538, 1454, 1231, 1154, 1056, 734, 694. m/z HRMS (ESI) found $[M+H]^+$ 563.2854, $C_{31}H_{39}N_4O_6^+$ requires 563.2864. HPLC: Chiralpak ID column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 10.2 min (major), 12.8 min (minor); 92:8 er.

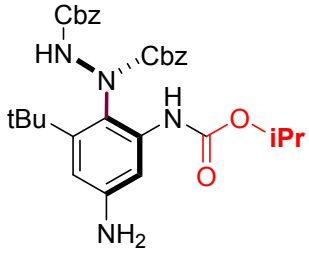
(*R*)-dibenzyl-1-(4-amino-2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5h**)



118mg, 99%yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.12 – 9.49 (m, 1H), 7.40 – 7.18 (m, 10H), 7.18 – 6.97 (m, 6H), 6.83 (m, 1H), 6.34 (t, *J* = 2.7 Hz, 1H), 5.38 – 4.60 (m, 6H), 3.68 (s, 2H), 1.14 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 156.0, 154.3, 148.7, 147.3, 138.8, 137.1, 135.5, 135.0, 128.7, 128.6, 128.5, 128.4, 128.4, 128.1, 128.0, 127.8, 127.7, 119.2, 109.4, 106.0,

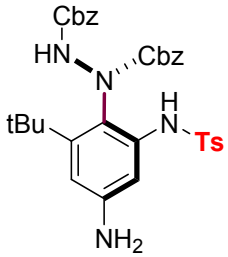
68.8, 68.6, 66.2, 35.8, 31.9. $[\alpha]_D^{25}$ = -30.80 (c = 1.0, DCM). IR (cm^{-1}): *f* = 3673, 3251, 2968, 2900, 1701, 1224, 1056, 732, 693. m/z HRMS (ESI) found $[M+H]^+$ 597.2696, $C_{34}H_{37}N_4O_6^+$ requires 597.2708. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 23.0 min (major), 27.6 min (minor); 94.5:5.5 er.

(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-((isopropoxycarbonyl)amino)phenyl)hydrazine-1,2-dicarboxylate (**5i**)



108 mg, 99% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.52 (s, 1H), 7.34 – 7.06 (m, 11H), 6.81 (m, 1H), 6.34 (t, *J* = 2.5 Hz, 1H), 5.29 – 4.94 (m, 4H), 4.94 – 4.72 (m, 1H), 3.56 (s, 2H), 1.38 – 1.00 (m, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 156.1, 154.3, 148.5, 147.2, 139.0, 135.5, 135.1, 128.7, 128.6, 128.4, 128.2, 127.9, 119.1, 109.2, 109.1, 106.1, 68.7, 68.6, 68.2, 35.8, 31.9, 22.1. $[\alpha]_D^{25}$ = -30.80 (c = 0.5, DCM). IR (cm^{-1}): *f* = 3673, 3265, 2969, 2900, 1700, 1609, 1539, 1227, 1056, 733, 694. m/z HRMS (ESI) found $[M+H]^+$ 549.2703, $C_{30}H_{37}N_4O_6^+$ requires 549.2708. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 12.6 min (major), 14.2 min (minor); 93.5:6.5 er.

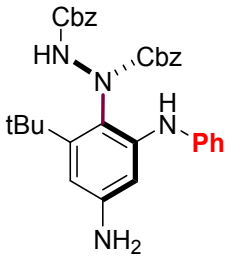
(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-((4-methylphenyl)sulfonamido)phenyl)hydrazine-1,2-dicarboxylate (**5j**)



122 mg, 99% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.18 (m, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.42 – 7.10 (m, 9H), 7.08 – 6.91 (m, 3H), 6.89 – 6.63 (m, 2H), 6.25 (dd, *J* = 6.9, 2.6 Hz, 1H), 5.34

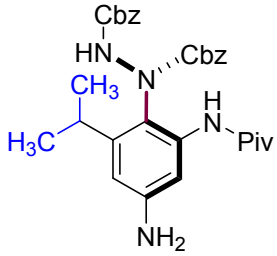
– 4.62 (m, 4H), 3.28 (s, 2H), 2.19 (m, 3H), 1.06 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 155.9, 149.4, 147.5, 143.2, 138.3, 137.8, 135.2, 134.9, 129.5, 128.8, 128.6, 128.6, 128.4, 128.1, 127.8, 127.2, 118.0, 109.2, 102.7, 69.1, 68.7, 35.8, 31.8, 21.5. $[\alpha]_D^{25}$ = 3.60 (c = 0.5, DCM). IR (cm^{-1}): *f* = 3673, 3379, 2968, 2900, 1705, 1454, 1240, 1056, 797, 695. m/z HRMS (ESI) found $[M+H]^+$ 617.2421, $C_{33}H_{37}N_4O_6S^+$ requires 617.2428. HPLC: Chiralpak IB column, 60:40 hexanes/isopropanol, 1 ml/min; t_R = 11.7 min (major), 16.3 min (minor); 96:4 er.

(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-(phenylamino)phenyl)hydrazine-1,2-dicarboxylate (**5k**)



45 mg, 42% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.54 (m, 1H), 7.43 – 6.96 (m, 14H), 6.93 – 6.68 (m, 2H), 6.63 – 6.43 (m, 1H), 6.18 (d, *J* = 2.6 Hz, 1H), 5.46 – 4.81 (m, 4H), 3.51 (s, 2H), 1.21 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.2, 156.3, 149.5, 147.1, 144.4, 143.5, 135.8, 135.2, 129.2, 128.8, 128.7, 128.7, 128.3, 127.9, 127.7, 120.7, 120.1, 119.2, 106.3, 101.1, 68.7, 68.5, 35.8, 32.1. $[\alpha]_D^{25}$ = -35.30 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3294, 2966, 2900, 1697, 1590, 1496, 1258, 1065, 1014, 795, 695. m/z HRMS (ESI) found $[M+H]^+$ 539.2647, $C_{32}H_{35}N_4O_4^+$ requires 539.2653. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 11.3 min (major), 15.1 min (minor); 93.5:6.5 er.

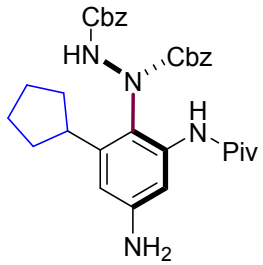
(*R*)-dibenzyl-1-(4-amino-2-isopropyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5l**)



102 mg, 96% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.59 (s, 1H), 7.41 – 7.35 (m, 1H), 7.33 – 7.02 (m, 11H), 6.19 (d, *J* = 2.7 Hz, 1H), 5.17 – 4.85 (m, 4H), 3.70 (s, 2H), 2.49 (hept, *J* = 6.9 Hz,

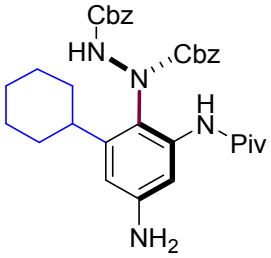
1H), 1.16 (s, 9H), 0.98 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 157.8, 156.4, 147.7, 147.1, 137.1, 135.5, 135.1, 128.7, 128.7, 128.6, 128.6, 128.4, 128.2, 119.8, 107.6, 107.6, 68.6, 68.6, 40.0, 29.0, 27.3, 23.8. $[\alpha]_D^{25}$ = -42.60 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3224, 2966, 2900, 1703, 1522, 1453, 1393, 1241, 1057, 797, 693. m/z HRMS (ESI) found $[M+H]^+$ 533.2748, $C_{30}H_{37}N_4O_5^+$ requires 533.2758. HPLC: Chiralpak IC column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 9.2 min (major), 13.6 min (minor); 97.5:2.5 er.

(*R*)-dibenzyl1-(4-amino-2-cyclopentyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5m**)



110 mg, 99% yield%. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.57 (s, 1H), 7.50 – 7.34 (m, 1H), 7.31 – 6.99 (m, 11H), 6.19 (d, *J* = 2.6 Hz, 1H), 5.14 – 4.56 (m, 4H), 3.69 (s, 2H), 2.74 – 2.34 (m, 1H), 1.91 – 1.22 (m, 8H), 1.15 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 157.7, 156.4, 147.6, 145.1, 137.1, 135.6, 135.1, 128.7, 128.6, 128.5, 128.5, 128.3, 128.1, 120.6, 108.0, 107.4, 68.5, 40.6, 39.9, 34.7, 27.3, 25.8, 25.7. $[\alpha]_D^{25}$ = -37.20 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3226, 2968, 2900, 1706, 1533, 1452, 1241, 1056, 734, 694. m/z HRMS (ESI) found $[M+H]^+$ 559.2909, $C_{32}H_{39}N_4O_5^+$ requires 559.2915. HPLC: Chiralpak IC column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 10.5 min (major), 13.6 min (minor); 97.5:2.5 er.

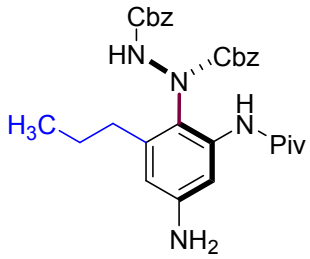
(*R*)-dibenzyl-1-(4-amino-2-cyclohexyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5n**)



113 mg, 99% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.59 (s, 1H), 7.42 – 7.32 (m, 1H), 7.31 – 6.89 (m, 11H), 6.15 (d, *J* = 2.6 Hz, 1H), 5.28 – 4.71 (m, 4H), 3.68 (s, 2H), 2.00 (t, *J* = 11.7 Hz,

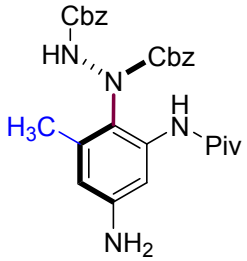
1H), 1.75 – 1.39 (m, 4H), 1.29 – 1.17 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 157.7, 156.4, 147.6, 146.1, 137.0, 135.6, 135.0, 128.7, 128.7, 128.6, 128.5, 128.3, 128.2, 119.8, 108.6, 107.6, 68.6, 68.6, 39.9, 34.2, 33.9, 27.3, 26.9, 26.0. $[\alpha]_D^{25}$ = -47.50 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3227, 2968, 2921, 1715, 1448, 1393, 1241, 1056, 797, 694. m/z HRMS (ESI) found $[M+H]^+$ 573.3602, $C_{33}H_{41}N_4O_5^+$ requires 573.3071. HPLC: Chiralpak IA column, 75:25 hexanes/isopropanol, 1 ml/min; t_R = 5.8 min (minor), 6.4 min (major); 97:3 er.

(*R*)-dibenzyl-1-(4-amino-2-pivalamido-6-propylphenyl)hydrazine-1,2-dicarboxylate (**5o**)



105 mg, 99% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.59 (s, 1H), 7.37 (d, *J* = 7.9 Hz, 2H), 7.33 – 6.98 (m, 10H), 6.12 (d, *J* = 2.6 Hz, 1H), 5.34 – 4.68 (m, 4H), 3.71 (s, 2H), 2.14 (t, *J* = 7.8 Hz, 2H), 1.53 – 1.23 (m, 2H), 1.15 (s, 9H), 0.89 – 0.63 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 157.8, 156.3, 147.4, 140.7, 137.2, 135.5, 135.1, 128.6, 128.6, 128.5, 128.5, 128.3, 128.1, 120.7, 110.7, 107.5, 68.6, 68.5, 39.9, 33.5, 27.3, 22.8, 14.1. $[\alpha]_D^{25}$ = -43.00 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3227, 2967, 2900, 1705, 1533, 1453, 1241, 1056, 735, 694. m/z HRMS (ESI) found $[M+H]^+$ 533.2753, $C_{30}H_{37}N_4O_5^+$ requires 533.2758. HPLC: Chiralpak IC column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 9.7 min (major), 17.5 min (minor); 96.5:3.5 er.

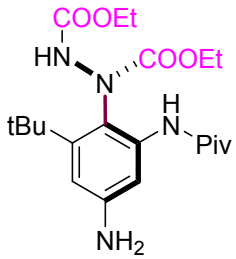
(*S*)-dibenzyl-1-(4-amino-2-methyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5p**)



100 mg, 99% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.57 (s, 1H), 7.84 – 7.53 (m, 1H), 7.38 (d, *J* = 2.6 Hz, 1H), 7.31 – 7.00 (m, 10H), 6.06 (d, *J* = 2.6 Hz, 1H), 5.30 – 4.82 (m, 4H), 3.35 (s,

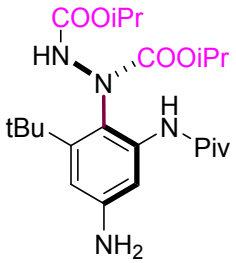
2H), 1.87 (s, 3H), 1.13 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 157.8, 156.2, 147.4, 137.2, 136.4, 135.6, 135.1, 128.6, 128.6, 128.5, 128.5, 128.2, 127.8, 120.9, 111.8, 107.1, 68.5, 68.4, 39.9, 27.3, 17.9. $[\alpha]_D^{25}$ = 28.50 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3227, 2968, 2900, 1705, 1455, 1393, 1241, 1057, 734, 694. m/z HRMS (ESI) found $[M+H]^+$ 505.2438, $C_{28}H_{33}N_4O_5^+$ requires 505.2445. HPLC: Chiralpak IA column, 70:30 hexanes/isopropanol, 1 ml/min; t_R = 8.5 min (major), 9.3 min (minor); 96.5:3.5 er.

(*R*)-diethyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5q**)



84 mg, 99% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.92 (s, 1H), 7.13 (d, *J* = 2.6 Hz, 1H), 6.90 (s, 1H), 6.47 (d, *J* = 2.7 Hz, 1H), 4.32 – 3.82 (m, 4H), 3.58 (s, 2H), 1.24 (s, 9H), 1.21 (m, 12H), 1.06 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.7, 157.9, 156.1, 148.1, 146.7, 138.3, 121.1, 110.7, 109.9, 63.3, 62.9, 39.8, 35.8, 31.8, 27.5, 14.6, 14.4. $[\alpha]_D^{25}$ = -73.30 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3273, 2968, 2900, 1700, 1522, 1249, 1065, 1026, 795. m/z HRMS (ESI) found $[M+H]^+$ 423.2593, $C_{21}H_{35}N_4O_5^+$ requires 423.2602. HPLC: Chiralpak IA column, 85:15 hexanes/isopropanol, 1 ml/min; t_R = 7.4 min (minor), 9.1 min (major); 97.5:2.5 er.

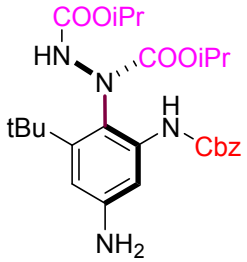
(*R*)-Diisopropyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5r**)



89 mg, 99% yield. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.93 (m, 1H), 7.54 – 7.11 (m, 1H), 6.71 (m, 1H), 6.50 (dd, *J* = 8.4, 2.7 Hz, 1H), 4.99 (hept, *J* = 6.2 Hz, 1H), 4.82 (hept, *J* = 6.2 Hz, 1H), 3.74 (s, 2H), 1.29 (s, 9H), 1.27 (d, *J* = 3.3 Hz, 9H), 1.22 (t, *J* = 5.5 Hz, 6H), 1.10 (m, 6H). ^{13}C

NMR (126 MHz, $CDCl_3$) δ 177.6, 157.7, 155.7, 148.0, 146.6, 138.5, 121.0, 110.5, 109.5, 71.4, 71.0, 39.9, 35.8, 31.9, 27.5, 22.0, 21.9. $[\alpha]_D^{25}$ = -63.40 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3281, 2969, 2900, 1699, 1669, 1455, 1372, 1249, 1103, 1052, 797. m/z HRMS (ESI) found $[M+H]^+$ 451.2905, $C_{23}H_{39}N_4O_5^+$ requires 451.2915. HPLC: Chiralpak IA column, 90:10 hexanes/isopropanol, 1 ml/min; t_R = 7.1 min (minor), 11.6 min (major); 97.5:2.5 er.

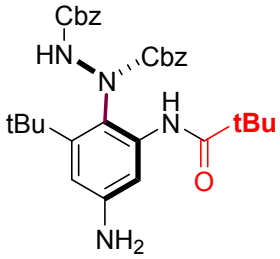
(*R*)-diisopropyl-1-(4-amino-2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5s**)



96 mg, 96% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.85 (m, 1H), 7.40 – 7.29 (m, 2H), 7.30 – 7.10 (m, 4H), 6.59 (m, 1H), 6.39 (dd, *J* = 6.0, 2.7 Hz, 1H), 5.21 – 5.06 (m, 2H), 5.05 – 4.92 (m, 1H), 4.81 (p, *J* = 6.3 Hz, 1H), 3.67 (s, 2H), 1.40 – 0.77 (m, 21H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 155.6, 154.5, 148.6, 147.0, 138.8, 137.1, 128.4, 128.0, 127.8, 120.1, 109.5, 106.6, 71.3, 66.3, 35.8, 32.1, 32.0, 22.0, 21.7. $[\alpha]_D^{25}$ = -36.80 (c = 0.5, DCM). IR (cm^{-1}): *f* = 3673, 3240, 2970, 2900, 1698, 1454, 1373, 1228, 1073, 1050, 795, 696. m/z HRMS (ESI) found $[M+H]^+$ 501.2700, $C_{26}H_{37}N_4O_6^+$ requires 501.2708. HPLC: Chiralpak IA column, 80:20 hexanes/isopropanol, 1 ml/min; t_R = 10.7 min (minor), 13.9 min (major); 97.5:2.5 er.

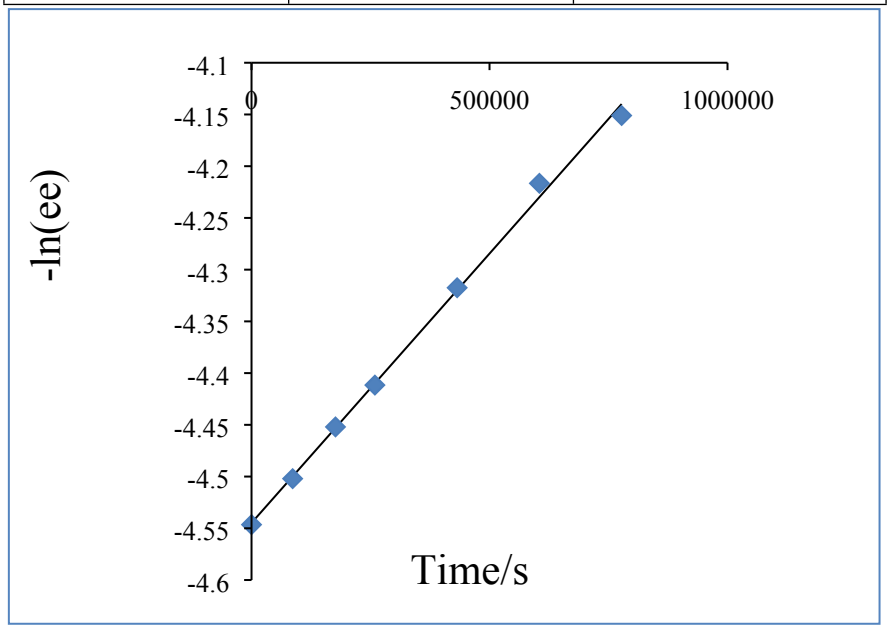
Determination of $t_{1/2}$ rac and Rotation Barrier

(*R*)-Dibenzyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5a**)



Barriers to racemization of **5a** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	94.3	-4.54648
86400	90.2	-4.50203
176400	85.8	-4.45202
259200	82.4	-4.41159
432000	75	-4.31749
604800	67.8	-4.21656
777600	63.5	-4.15104



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=2.605*10^{-7}s^{-1}$

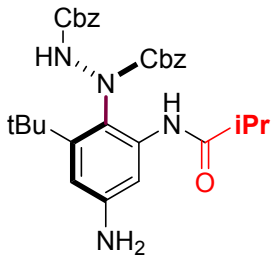
$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=369.6$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{2.605\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

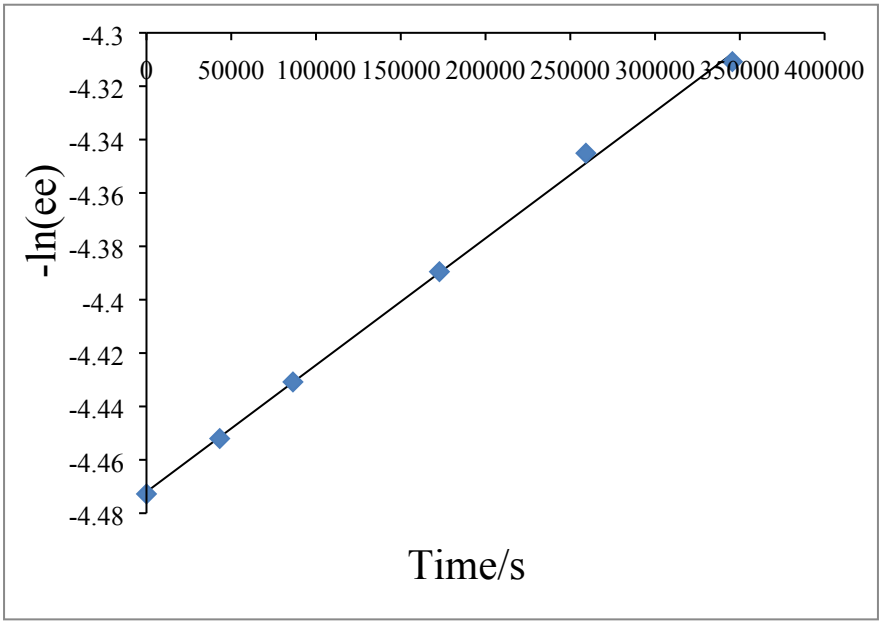
=139.12 kJ/mol (33.2 kcal/mol)

(*S*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-isobutyramidophenyl)hydrazine-1,2-dicarboxylate (**5b**)



Barriers to racemization of **5b** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	87.6	-4.47278
43200	85.8	-4.45202
86400	84	-4.43082
172800	80.6	-4.3895
259200	77.1	-4.3451
345600	74.5	-4.3108



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=2.375*10^{-7}s^{-1}$

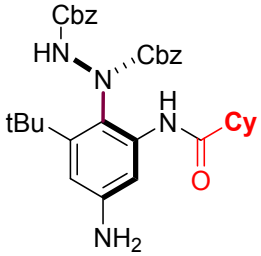
$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=405.4$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent} \times h}{k_B \times T}\right) = -8.314 \times 373.15 \times \ln\left(\frac{2.375 \times 10^{-7} \times 6.626 \times 10^{-34}}{1.381 \times 10^{-23} \times 373.15}\right)$$

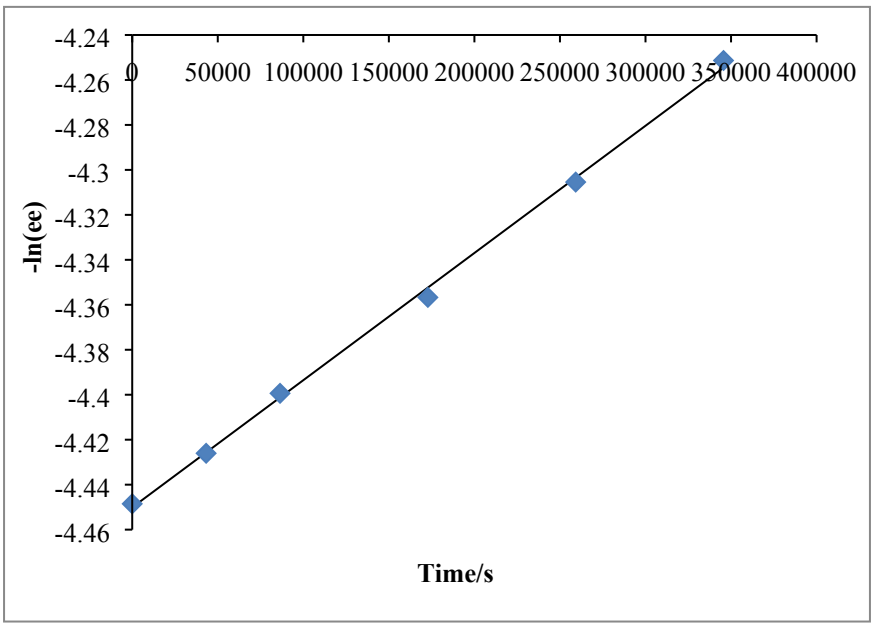
=139.41 kJ/mol (33.3 kcal/mol)

(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-(cyclohexanecarboxamido)phenyl)hydrazine-1,2-dicarboxylate (**5c**)



Barriers to racemization of **5c** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	85.5	-4.44852
43200	83.6	-4.42604
86400	81.4	-4.39938
172800	78	-4.35671
259200	74.1	-4.30542
345600	70.2	-4.25135



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=2.83*10^{-7}s^{-1}$

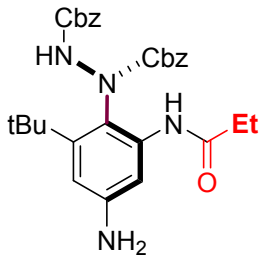
$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=340.2$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{2.83\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

=138.86 kJ/mol (33.2 kcal/mol)

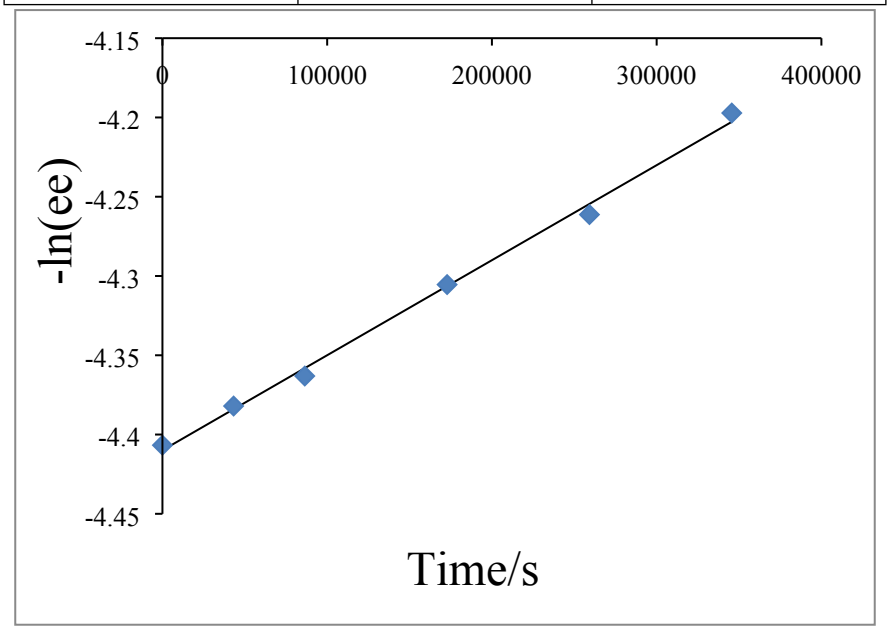
(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-propionamidophenyl)hydrazine-1,2-dicarboxylate (**5d**)



Barriers to racemization of **5d** at 100°C in toluene

Time/s	ee(%)	-ln(ee)
0	82	-4.40672
43200	80	-4.38203

86400	78.5	-4.3631
172800	74.1	-4.30542
259200	70.9	-4.26127
345600	66.5	-4.1972



-ln(ee)=2k_{ent}t+C

Therefore, k_{ent}=2.995*$10^{-7}s^{-1}$

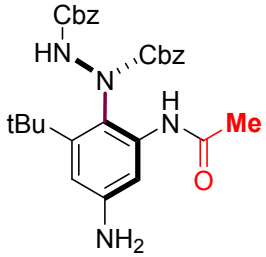
$t_{1/2}{}^{100}{}_{rac}$=ln(2)/2k_{ent}=321.4 h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{2.995\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

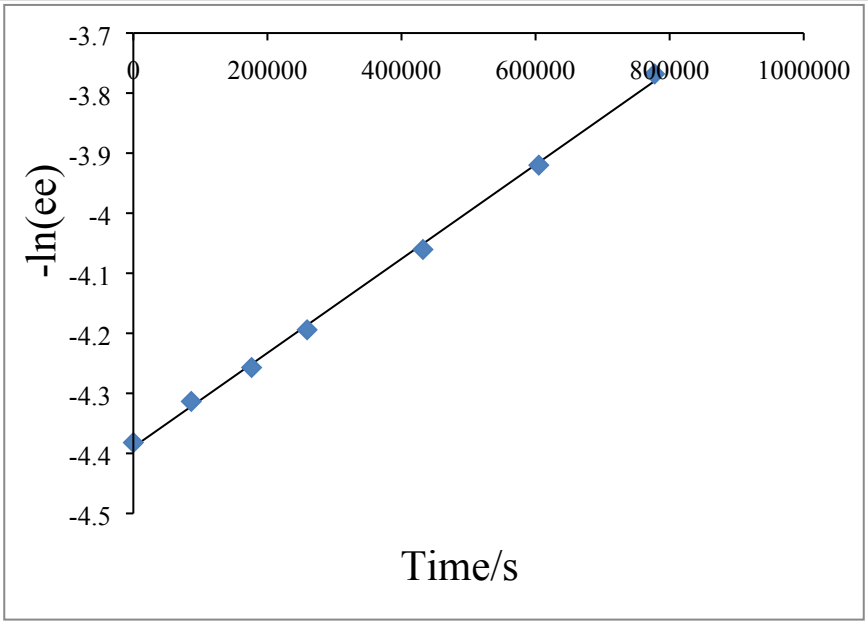
=138.69 kJ/mol (33.1 kcal/mol)

(*R*)-dibenzyl-1-(2-acetamido-4-amino-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5e**)



Barriers to racemization of **5e** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	80	-4.38203
86400	74.7	-4.31348
176400	70.6	-4.25703
259200	66.3	-4.19419
432000	58	-4.06044
604800	50.4	-3.91999
777600	43.3	-3.76815



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=3.92*10^{-7}s^{-1}$

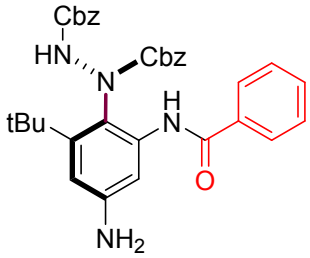
$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=245.6$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{3.92\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

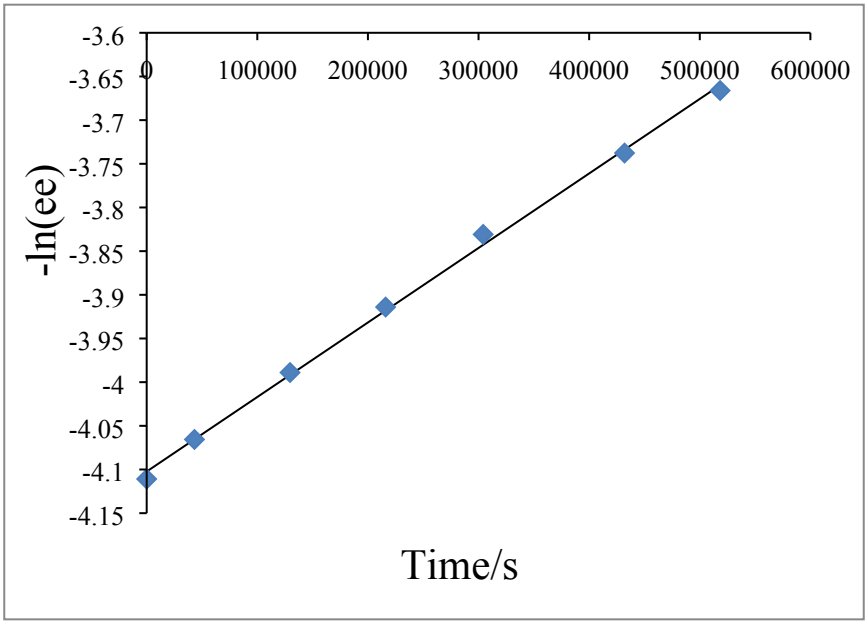
=137.85 kJ/mol (32.9 kcal/mol)

(*S*)-dibenzyl-1-(4-amino-2-benzamido-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5f**)



Barriers to racemization of **5f** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	61	-4.11087
43200	58.3	-4.0656
129600	54	-3.98898
216000	50.1	-3.91402
304200	46.1	-3.83081
432000	42	-3.73767
518400	39.1	-3.66612



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=4.265*10^{-7}s^{-1}$

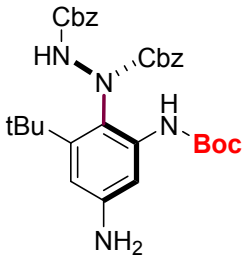
$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=225.7$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent} \times h}{k_B \times T}\right) = -8.314 \times 373.15 \times \ln\left(\frac{4.265 \times 10^{-7} \times 6.626 \times 10^{-34}}{1.381 \times 10^{-23} \times 373.15}\right)$$

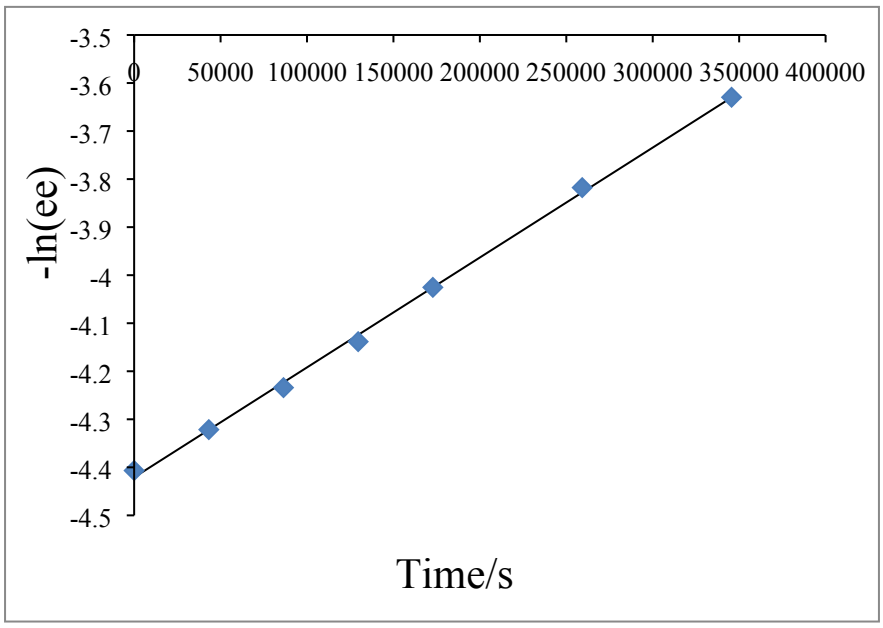
=137.59 kJ/mol (32.8 kcal/mol)

(*R*)-dibenzyl-1-(4-amino-2-((tert-butoxycarbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5g**)



Barriers to racemization of **5g** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	82	-4.40672
43200	75.3	-4.32148
86400	69	-4.23411
129600	62.7	-4.13836
172800	56	-4.02535
259200	45.5	-3.81771
345600	37.7	-3.62966



-ln(ee)=2k_{ent}t+C

Therefore, k_{ent}=1.145*$10^{-6}s^{-1}$

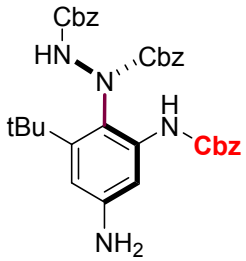
$t_{1/2}{}^{100}{}_{rac}$=ln(2)/2k_{ent}=84.1 h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{1.145\times 10^{-6}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

=134.53 kJ/mol (32.1 kcal/mol)

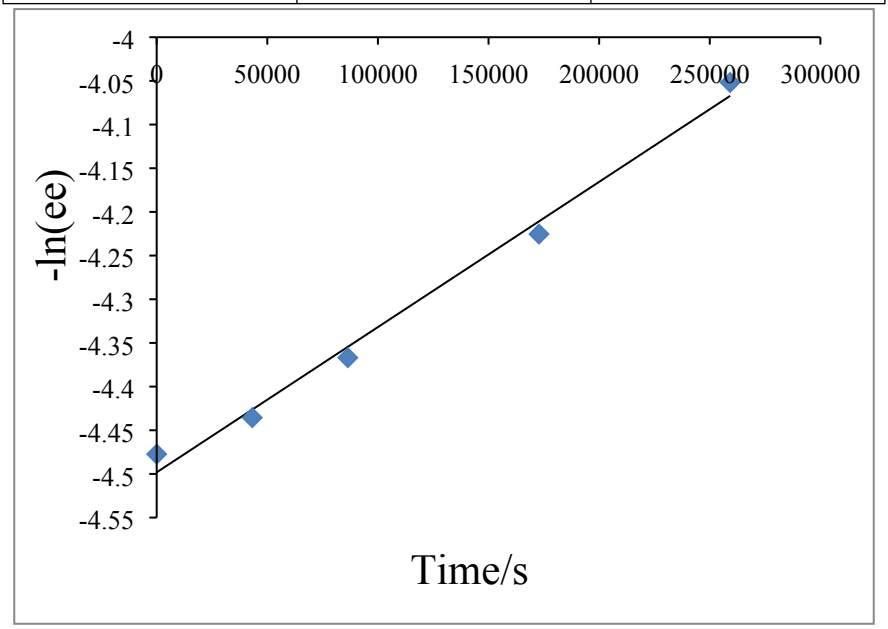
(*R*)-dibenzyl-1-(4-amino-2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5h**)



Barriers to racemization of **5h** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	88	-4.47734
43200	84.4	-4.43557

86400	78.8	-4.36691
172800	68.4	-4.22537
259200	57.5	-4.05178



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=0.83*10^{-6}s^{-1}$

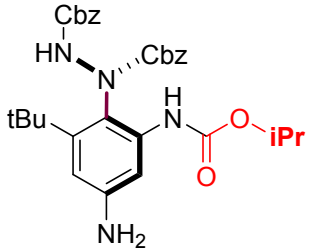
$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=116$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{0.83\times 10^{-6}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

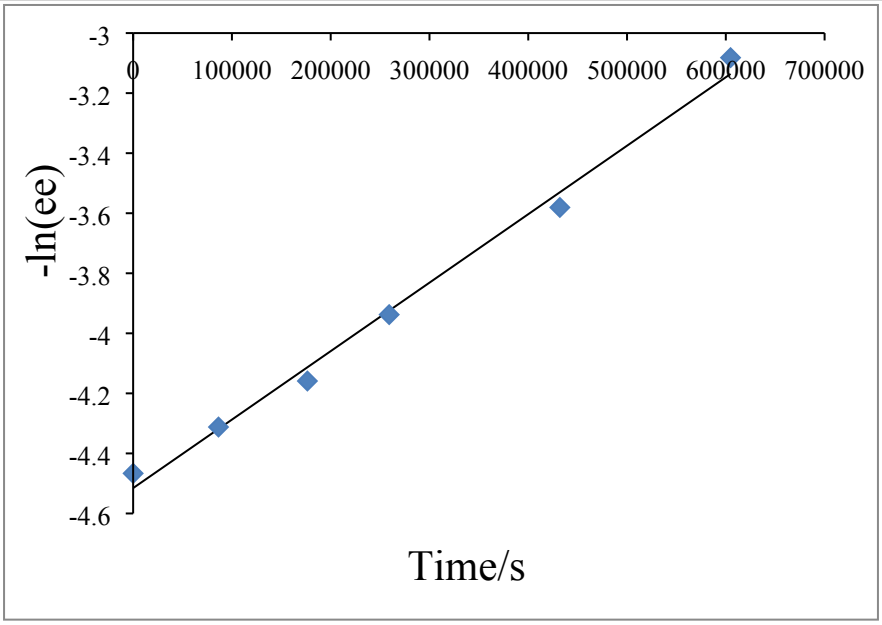
=135.52 kJ/mol (32.3 kcal/mol)

(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-((isopropoxycarbonyl)amino)phenyl)hydrazine-1,2-dicarboxylate (**5i**)



Barriers to racemization of **5i** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	87.05	-4.46648
86400	74.6	-4.31214
176400	64	-4.15888
259200	51.3	-3.93769
432000	35.9	-3.58074
604800	21.8	-3.08191



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=1.14*10^{-6}s^{-1}$

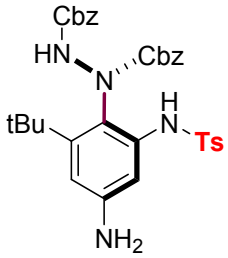
Employing the Eyring equation:

$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=84.5$ h

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{1.14\times 10^{-6}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

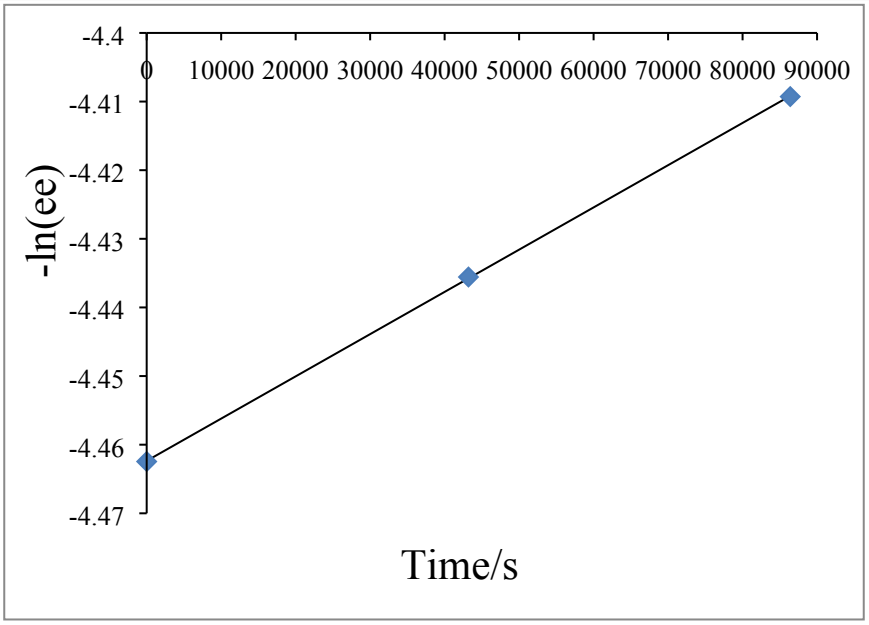
=134.54 kJ/mol (32.1 kcal/mol)

(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-((4-methylphenyl)sulfonamido)phenyl)hydrazine-1,2-dicarboxylate (**5j**)



Barriers to racemization of **5j** at 70℃ in Dioxane

Time/s	ee(%)	-ln(ee)
0	86.7	-4.46245
43200	84.4	-4.43557
86400	82.21	-4.40928



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=3.075*10^{-7}s^{-1}$

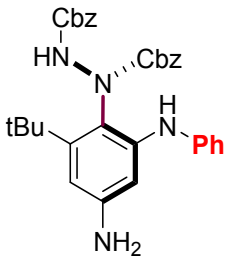
$t_{1/2}{}^{70}{}_{rac}=\ln(2)/2k_{ent}=313.1$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 343.15\times \ln\left(\frac{3.075\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 343.15}\right)$$

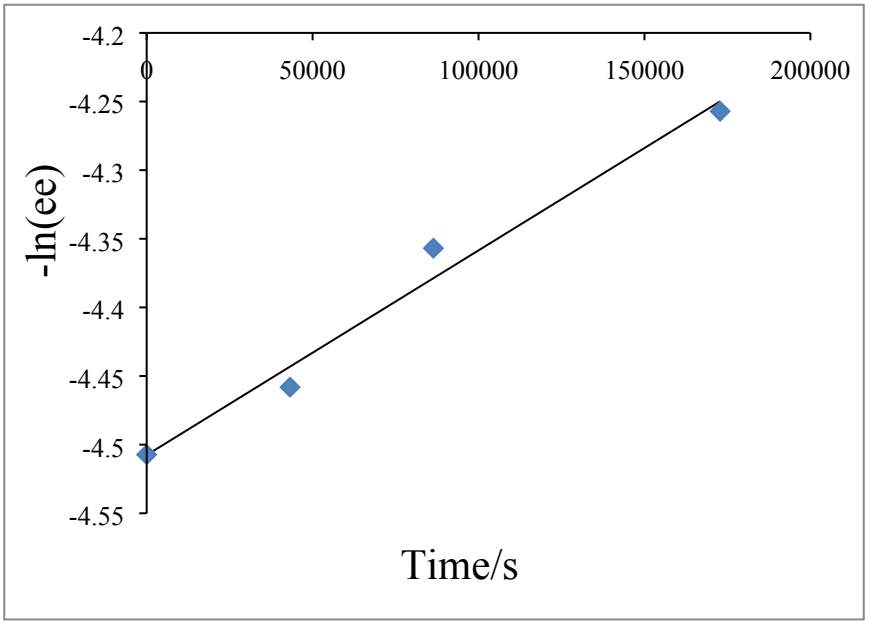
=127.22 kJ/mol (30.4 kcal/mol)

(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-(phenylamino)phenyl)hydrazine-1,2-dicarboxylate (**5k**)



Barriers to racemization of **5k** at 70°C in Dioxane

Time/s	ee(%)	-ln(ee)
0	90.674	-4.50727
43200	86.326	-4.45813
86400	78.012	-4.35686
172800	70.604	-4.25709



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=7.45*10^{-7}s^{-1}$

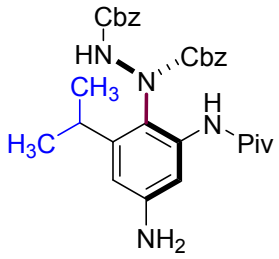
$t_{1/2}{}^{70}{}_{rac}=\ln(2)/2k_{ent}=129.2$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 343.15\times \ln\left(\frac{7.45\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 343.15}\right)$$

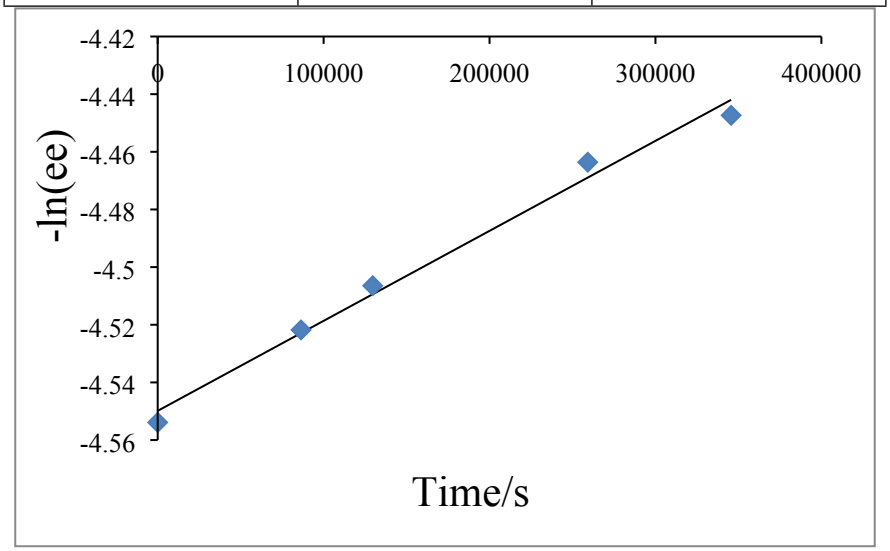
=125.70 kJ/mol (30 kcal/mol)

(*R*)-dibenzyl-1-(4-amino-2-isopropyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5l**)



Barriers to racemization of **5l** at 50℃ in toluene

Time/s	ee(%)	-ln(ee)
0	95	-4.55388
86400	92	-4.52179
129600	90.6	-4.50645
259200	86.8	-4.46361
345600	85.4	-4.44735



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=1.56*10^{-7}s^{-1}$

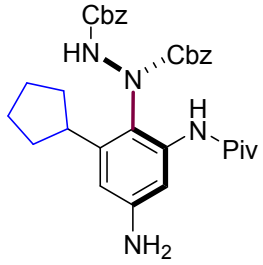
$t_{1/2}{}^{50}{}_{rac}=\ln(2)/2k_{ent}=617.1$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 323.15\times \ln\left(\frac{1.56\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 323.15}\right)$$

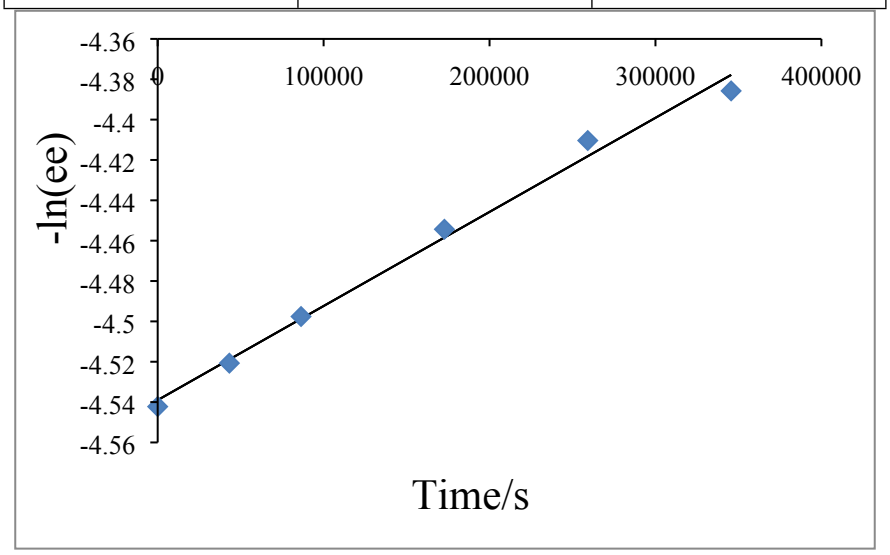
=121.47 kJ/mol (29 kcal/mol)

(*R*)-dibenzyl1-(4-amino-2-cyclopentyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5m**)



Barriers to racemization of **5m** at 50℃ in toluene

Time/s	ee(%)	-ln(ee)
0	93.9	-4.54223
43200	91.9	-4.5207
86400	89.8	-4.49758
172800	86	-4.45435
259200	82.3	-4.41037
345600	80.3	-4.38577



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=2.33*10^{-7}s^{-1}$

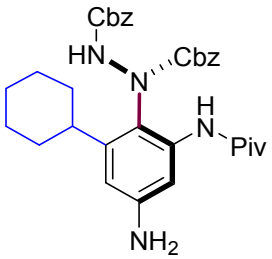
$t_{1/2}{}^{50}{}_{rac}=\ln(2)/2k_{ent}=413.2$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent} \times h}{k_B \times T}\right) = -8.314 \times 323.15 \times \ln\left(\frac{2.33 \times 10^{-7} \times 6.626 \times 10^{-34}}{1.381 \times 10^{-23} \times 323.15}\right)$$

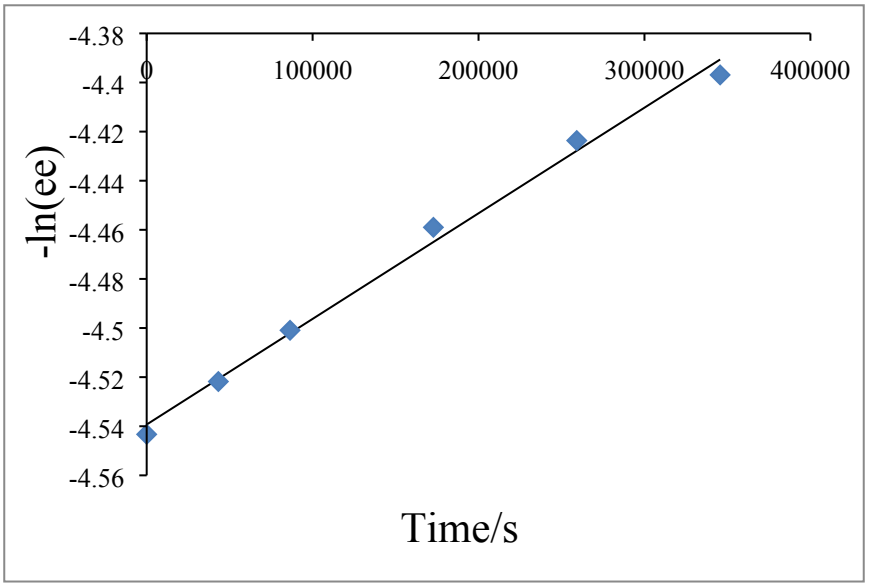
=120.39 kJ/mol (28.7 kcal/mol)

(*R*)-dibenzyl-1-(4-amino-2-cyclohexyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5n**)



Barriers to racemization of **5n** at 50℃ in toluene

Time/s	ee(%)	-ln(ee)
0	94	-4.54329
43200	92	-4.52179
86400	90.1	-4.50092
172800	86.4	-4.45899
259200	83.4	-4.42365
345600	81.2	-4.39692



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=2.15*10^{-7}s^{-1}$

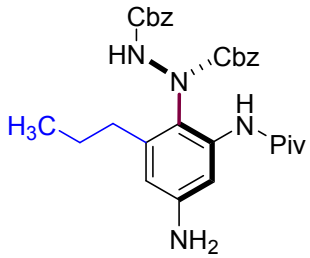
$t_{1/2}{}^{50}{}_{rac}=\ln(2)/2k_{ent}=447.8$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 323.15\times \ln\left(\frac{2.15\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 323.15}\right)$$

=120.61 kJ/mol (28.8 kcal/mol)

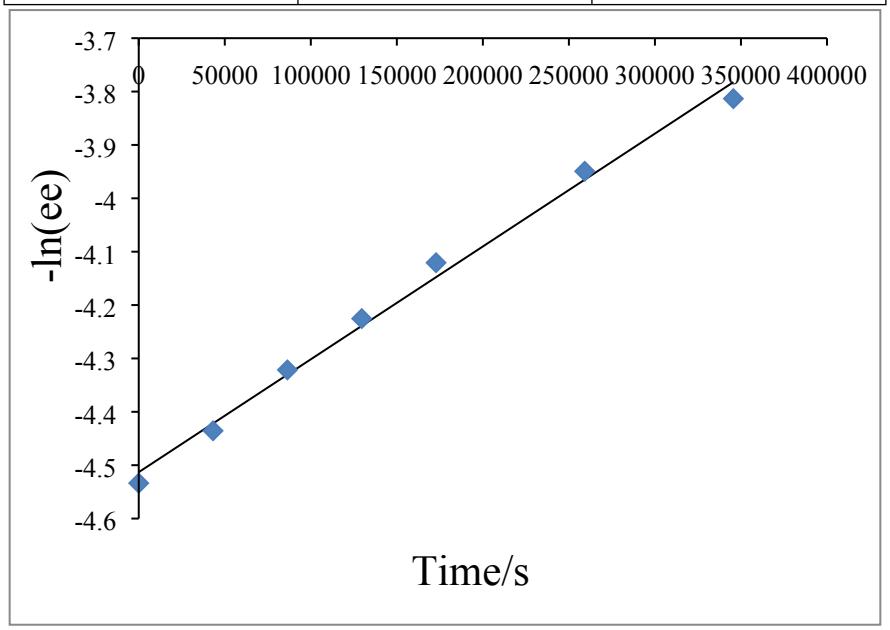
(*R*)-dibenzyl-1-(4-amino-2-pivalamido-6-propylphenyl)hydrazine-1,2-dicarboxylate (**5o**)



Barriers to racemization of **5o** at 50℃ in toluene

Time/s	ee(%)	-ln(ee)
0	93.1	-4.53367
43200	84.4	-4.43557
86400	75.3	-4.32148

129600	68.4	-4.22537
172800	61.6	-4.12066
259200	51.9	-3.94932
345600	45.3	-3.81331



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=1.055*10^{-6}s^{-1}$

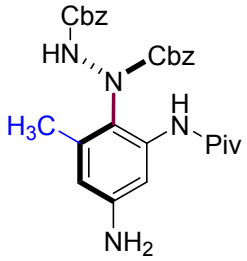
$t_{1/2}{}^{50}{}_{rac}=\ln(2)/2k_{ent}=91.3$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 323.15\times \ln\left(\frac{1.055\times 10^{-6}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 323.15}\right)$$

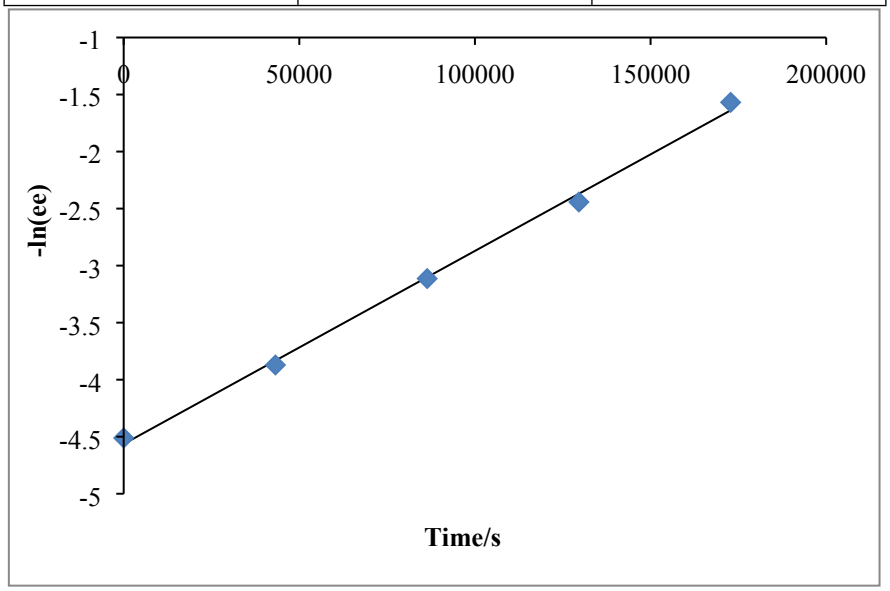
=116.33 kJ/mol (27.8 kcal/mol)

(*S*)-dibenzyl-1-(4-amino-2-methyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5p**)



Barriers to racemization of **5p** at 50°C in toluene

Time/s	ee(%)	-ln(ee)
0	91	-4.51086
43200	48	-3.8712
86400	22.5	-3.11352
129600	11.5	-2.44235
172800	4.8	-1.56862



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=8.45*10^{-6}s^{-1}$

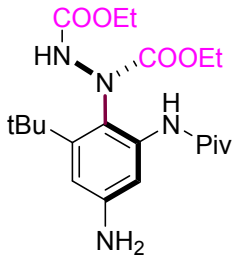
$t_{1/2}{}^{50}{}_{rac}=\ln(2)/2k_{ent}=11.4$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 323.15\times \ln\left(\frac{8.45\times 10^{-6}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 323.15}\right)$$

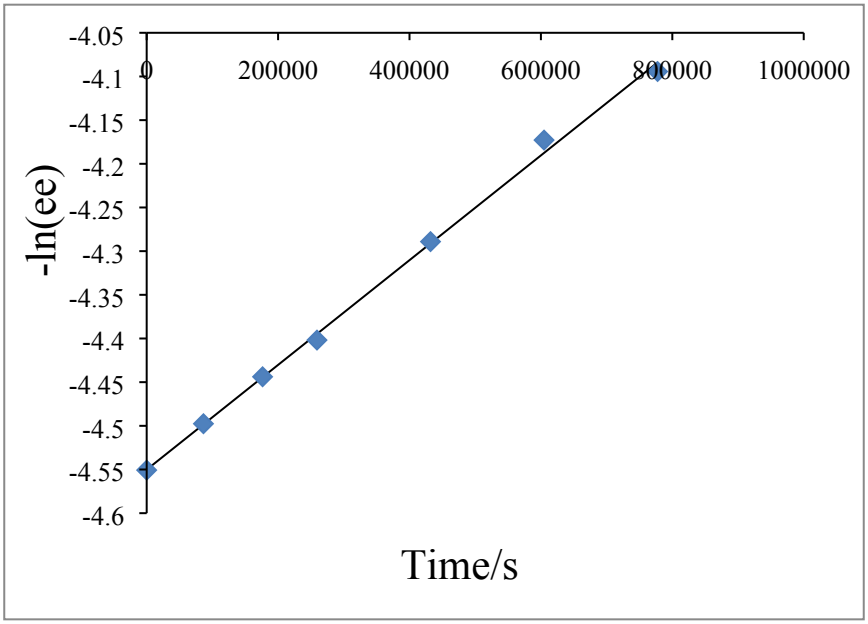
=110.74 kJ/mol (26.4 kcal/mol)

(*R*)-diethyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5q**)



Barriers to racemization of **5q** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	94.7	-4.55071
86400	89.8	-4.49758
176400	85.1	-4.44383
259200	81.6	-4.40183
432000	72.9	-4.28909
604800	64.9	-4.17285
777600	60	-4.09434



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=3.00*10^{-7}s^{-1}$

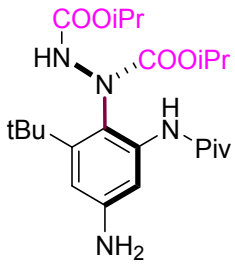
$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=320.9$ h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent} \times h}{k_B \times T}\right) = -8.314 \times 373.15 \times \ln\left(\frac{3.00 \times 10^{-7} \times 6.626 \times 10^{-34}}{1.381 \times 10^{-23} \times 373.15}\right)$$

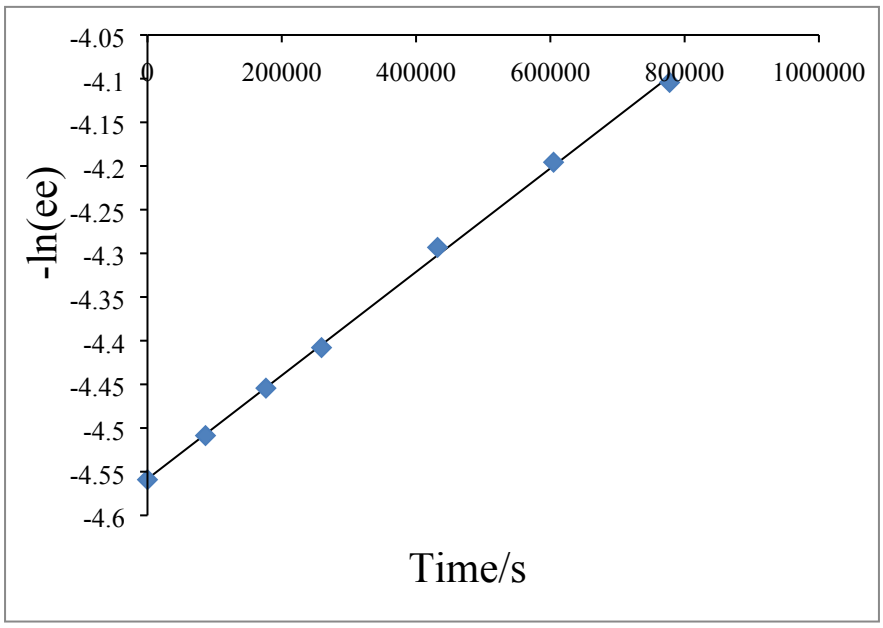
=138.68 kJ/mol (33.1 kcal/mol)

(*R*)-Diisopropyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5r**)



Barriers to racemization of **5r** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	95.5	-4.55913
86400	90.8	-4.50866
176400	86	-4.45435
259200	82.1	-4.40794
432000	73.2	-4.2932
604800	66.4	-4.1957
777600	60.6	-4.10429



-ln(ee)=2k_{ent}t+C

Therefore, k_{ent}=2.965*$10^{-7}s^{-1}$

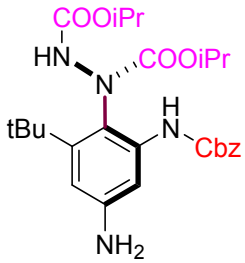
$t_{1/2}{}^{100}{}_{rac}$=ln(2)/2k_{ent}=324.7 h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{2.965\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

138.72 kJ/mol (33.1 kcal/mol)

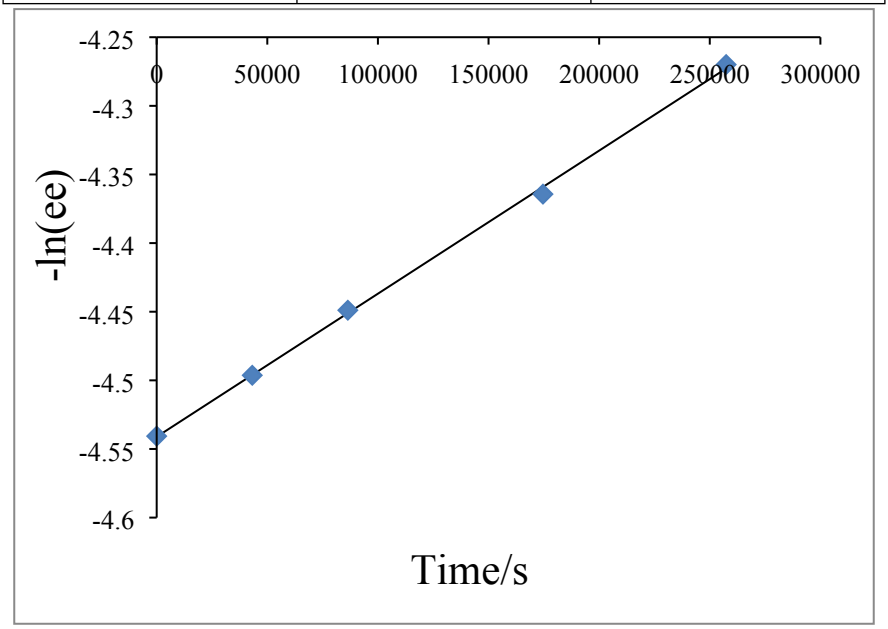
(*R*)-diisopropyl-1-(4-amino-2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5s**)



Barriers to racemization of **5s** at 100℃ in toluene

Time/s	ee(%)	-ln(ee)
0	93.752	-4.54065
43200	89.686	-4.49631

86400	85.534	-4.44891
174600	78.596	-4.36432
257400	71.516	-4.26992



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=5.2*10^{-7}s^{-1}$

$t_{1/2}{}^{100}{}_{rac}=\ln(2)/2k_{ent}=185.1$ h

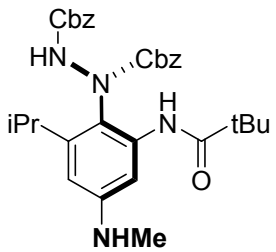
Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 373.15\times \ln\left(\frac{5.2\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 373.15}\right)$$

=136.97 kJ/mol (32.7 kcal/mol)

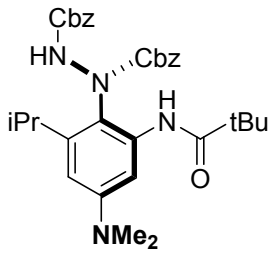
Mechanistic studies:

(*R*)-dibenzyl-1-(2-isopropyl-4-(methylamino)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**7b**)



95 mg, 87% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.58 (s, 1H), 7.42 – 7.32 (m, 1H), 7.29 – 7.08 (m, 10H), 7.06 (d, *J* = 6.5 Hz, 1H), 6.11 (d, *J* = 2.7 Hz, 1H), 5.23 – 4.78 (m, 4H), 3.81 (s, 1H), 2.75 (s, 3H), 2.61 – 2.30 (m, 1H), 1.17 (s, 9H), 1.00 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 157.7, 156.6, 150.2, 146.9, 137.2, 135.6, 135.1, 128.7, 128.7, 128.6, 128.6, 128.4, 128.2, 118.7, 104.8, 104.6, 68.6, 68.6, 40.1, 30.7, 29.1, 27.4, 23.9. $[\alpha]_D^{25}$ = -14.50 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3226, 2968, 2900, 1705, 1613, 1454, 1241, 1055, 734, 694. m/z HRMS (ESI) found $[M+H]^+$ 547.2907, $C_{31}H_{39}N_4O_5^+$ requires 547.2915. HPLC: Chiralpak IA column, 85:15 hexanes/isopropanol, 1 ml/min; t_R = 10.5 min (major), 11.8 min (minor); 72:28 er.

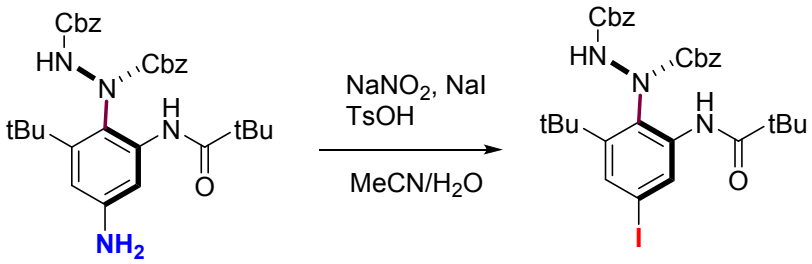
(*R*)-dibenzyl-1-(4-(dimethylamino)-2-isopropyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**7c**)



105 mg, 94% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.56 (s, 1H), 7.63 – 7.37 (m, 1H), 7.33 – 7.07 (m, 10H), 6.99 (s, 1H), 6.21 (d, *J* = 2.9 Hz, 1H), 5.31 – 4.72 (m, 4H), 2.90 (s, 6H), 2.51 (hept, *J* = 6.8 Hz, 1H), 1.18 (s, 9H), 1.03 (m, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 157.7, 156.6, 151.1, 146.4, 136.9, 135.7, 135.1, 128.7, 128.7, 128.6, 128.6, 128.4, 128.3, 118.1, 104.9, 104.8, 68.7, 68.6, 40.6, 40.1, 29.3, 27.4, 24.0, 23.9. $[\alpha]_D^{25}$ = 21.10 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3224, 2967, 2900, 1716, 1610, 1539, 1393, 1255, 1056, 794, 694. m/z HRMS (ESI) found $[M+H]^+$ 561.3064, $C_{32}H_{41}N_4O_5^+$ requires 561.3071. HPLC: Chiralpak IA column, 85:15 hexanes/isopropanol, 1 ml/min; t_R = 4.7 min (major), 5.0 min (minor); 81:19 er.

Derivatizations of chiral products:

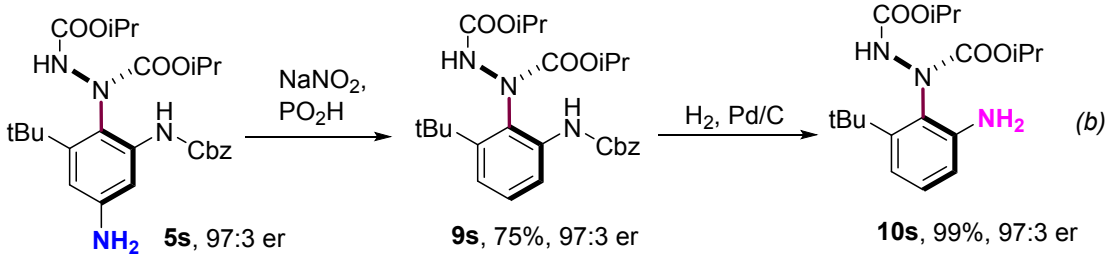
(*R*)-dibenzyl-1-(2-(tert-butyl)-4-iodo-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**8a**)



5a, 98.5:1.5 er

8a, 79%, 96.5:3.5 er

To a solution of *p*-TsOH.H_2O (114 mg, 0.6 mmol) in MeCN (3 mL) was added **5a** (109 mg, 0.2 mmol). The resulting suspension of amine salt was cooled to 5-10 °C and to this was gradually added a solution of $NaNO_2$ (28 mg, 0.4 mmol) and NaI (75 mg, 0.5 mmol) in H_2O (0.4 mL). The reaction mixture was stirred for 10 min then allowed to warm to 20 °C. After stirring for 30 min, the reaction mixture was then added H_2O (2 mL), $NaHCO_3$ (1 M; until pH = 9-10) and $Na_2S_2O_3$ (2 M, 1 mL). The mixture was extracted with EtOAc for 3 times. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to afford a residue, which was purified by column chromatography (petroleum ether/EtOAc = 10:1) as eluent to give the product **8a** (104 mg, 79% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.85 (m, 1H), 8.27 (m, 1H), 7.46 (dd, *J* = 4.5, 2.1 Hz, 1H), 7.38 – 7.02 (m, 10H), 6.82 (d, *J* = 2.5 Hz, 1H), 5.66 – 4.74 (m, 4H), 1.61 – 0.82 (m, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.6, 157.9, 155.3, 149.1, 138.7, 134.9, 134.7, 133.4, 132.3, 128.9, 128.8, 128.7, 128.7, 128.6, 128.6, 128.5, 95.6, 69.2, 69.1, 39.9, 35.9, 31.7, 27.3. $[\alpha]_D^{25}$ = -31.70 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3281, 2968, 2900, 1717, 1516, 1393, 1256, 1055, 796, 735, 694. m/z HRMS (ESI) found $[M+H]^+$ 658.1765, $C_{31}H_{37}IN_3O_5^+$ requires 658.1772. HPLC: Chiralpak IA column, 90:10 hexanes/isopropanol, 1 ml/min; t_R = 5.9 min (major), 6.8 min (minor); 96.5:3.5 er.



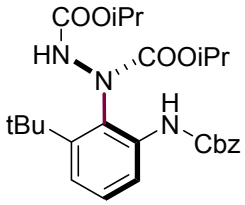
5s, 97:3 er

9s, 75%, 97:3 er

10s, 99%, 97:3 er

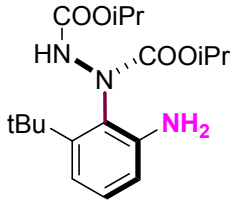
($t_{1/2}^{70}{}_{rac}$ = 198 h)

(*R*)-diisopropyl-1-(2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**9s**)



To a solution of **5s** (100 mg, 0.2 mmol) in THF (8 mL) was added hypophosphorous acid (50% solution in water, 4 mmol) at 0℃.Then sodium nitrite (41.4 mg, 0.6 mmol) was added and the reaction mixture was stirred at 0℃ for 4 h and at rt for 12 h. Afterwards saturated $NaHCO_3$ was added until the pH of aqueous phase was about 8. The mixture was extracted with EtOAc for 3 times. The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude was purified by column chromatography (petroleum ether/EtOAc = 10:1) as eluent to give the product **9s** (104 mg, 75% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.87 (m, 1H), 8.04 – 7.62 (m, 1H), 7.41 – 7.30 (m, 2H), 7.30 – 7.05 (m, 5H), 6.58 (d, *J* = 9.7 Hz, 1H), 5.14 (q, *J* = 12.6 Hz, 2H), 5.06 – 4.94 (m, 1H), 4.84 (tt, *J* = 12.6, 6.4 Hz, 1H), 1.28 (s, 9H), 1.21 – 0.83 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 155.1, 154.6, 147.7, 138.0, 137.0, 129.4, 128.5, 128.2, 127.9, 127.6, 123.2, 121.0, 71.6, 66.4, 36.0, 32.2, 32.1, 21.9, 21.6. $[\alpha]_D^{25}$ = -64.10 (c = 1, DCM). IR (cm^{-1}): *f* = 3673, 3218, 2970, 2900, 1734, 1700, 1522, 1368, 1240, 1051, 795, 696. m/z HRMS (ESI) found $[M+H]^+$ 486.2592, $C_{26}H_{36}N_3O_6^+$ requires 486.2599. HPLC: Chiralpak IA column, 90:10 hexanes/isopropanol, 1 ml/min; t_R = 7.1 min (minor), 12.8 min (major); 97:3 er.

(*R*)-diisopropyl 1-(2-amino-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**10s**)

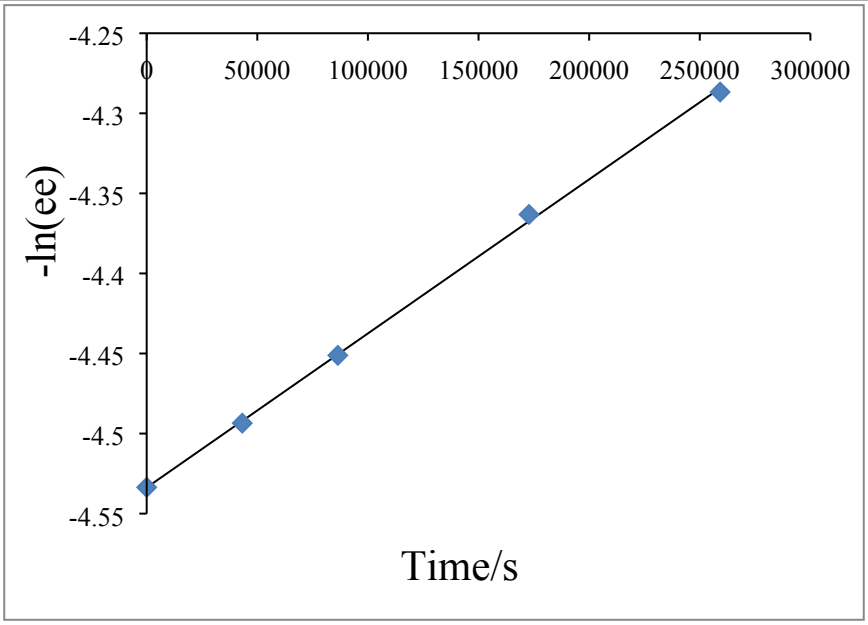


To a solution of **9s** (50 mg, 0.1 mmol) in MeOH (3 mL) was add Pd/C (5 mg, 10 % Pd, 55% w/w water). After stirring under H_2 atmosphere (1 atm) overnight, the reaction mixture was filtered through celite and concentrated under vacuum to give a residue, which was purified by flash column chromatography (Petroleum ether/EtOAc = 9:1) to give the product **10s** (36.1 mg, 99% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.05 (t, *J* = 7.9 Hz, 1H), 6.77 (dt, *J* = 8.0, 2.5 Hz, 1H), 6.72 – 6.49 (m, 2H), 5.05 (s, 2H), 5.03 – 4.93 (m, 2H), 1.35 (s, 9H), 1.33 – 1.09 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 148.4, 147.1, 129.8, 129.5, 116.6, 114.9, 114.5, 71.1, 70.8,

35.8, 32.3, 32.2, 22.0. $[\alpha]_D^{25}$ = 34.80 (c = 1, DCM). IR (cm^{-1}): f = 3673, 3469, 3375, 3338, 2969, 2900, 1740, 1716, 1623, 1370, 1232, 1103, 1051, 795, 757. m/z HRMS (ESI) found $[M+H]^+$ 352.2223, $C_{18}H_{30}N_3O_4^+$ requires 352.2231. HPLC: Chiralpak IA column, 90:10 hexanes/isopropanol, 1 ml/min; t_R = 6.6 min (minor), 10.5 min (major); 97:3 er.

Barriers to racemization of **10s** at 70 ℃ in toluene

Time/s	ee(%)	-ln(ee)
0	93.092	-4.53359
43200	89.434	-4.4935
86400	85.726	-4.45116
172800	78.504	-4.36315
259200	72.728	-4.28673



$-\ln(ee)=2k_{ent}t+C$

Therefore, $k_{ent}=4.81*10^{-7}s^{-1}$

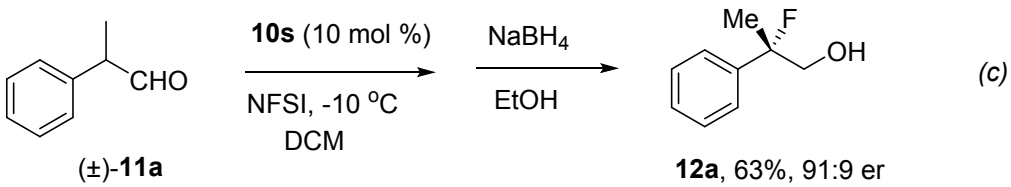
$t_{1/2}^{70}{}_{rac}=\ln(2)/2k_{ent}$=200.2 h

Employing the Eyring equation:

$$\Delta G = -RT\ln\left(\frac{k_{ent}\times h}{k_B\times T}\right) = -8.314\times 343.15\times \ln\left(\frac{4.81\times 10^{-7}\times 6.626\times 10^{-34}}{1.381\times 10^{-23}\times 343.15}\right)$$

=125.95kJ/mol (30.1 kcal/mol)

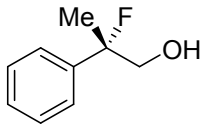
Application of chiral aniline catalyst 10s:



(±)-**11a** **12a**, 63%, 91:9 er (c)

The catalyst **10s** (7 mg, 0.02 mmol, 97:3 er), DCM (1mL) were added to the a-branched aldehyde **11a** (26.8 mg, 0.2 mmol) in a 4 mL vial. After 30 min stirring at -10℃, NFSI (75.6 mg, 0.24 mmol) was added and the reaction mixture stirred at -10℃ overnight. After full conversion was detected by GC-MS, the mixture was diluted with EtOH (1mL) and $NaBH_4$ (3.0 equiv.) was added. Then the reaction was stirred at 0℃ until full conversion was detected by GC-MS. Then $NaHSO_4$ solution (1M) and CH_2Cl_2 were added and the aqueous phase was extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered and the solvent evaporated. The crude product was purified by flash column chromatography (Petroleum ether/EtOAc = 8:1) to give the product **12a** (19 mg, 63% yield).

(*S*)-2-fluoro-2-phenylpropan-1-ol (**12a**)[2]



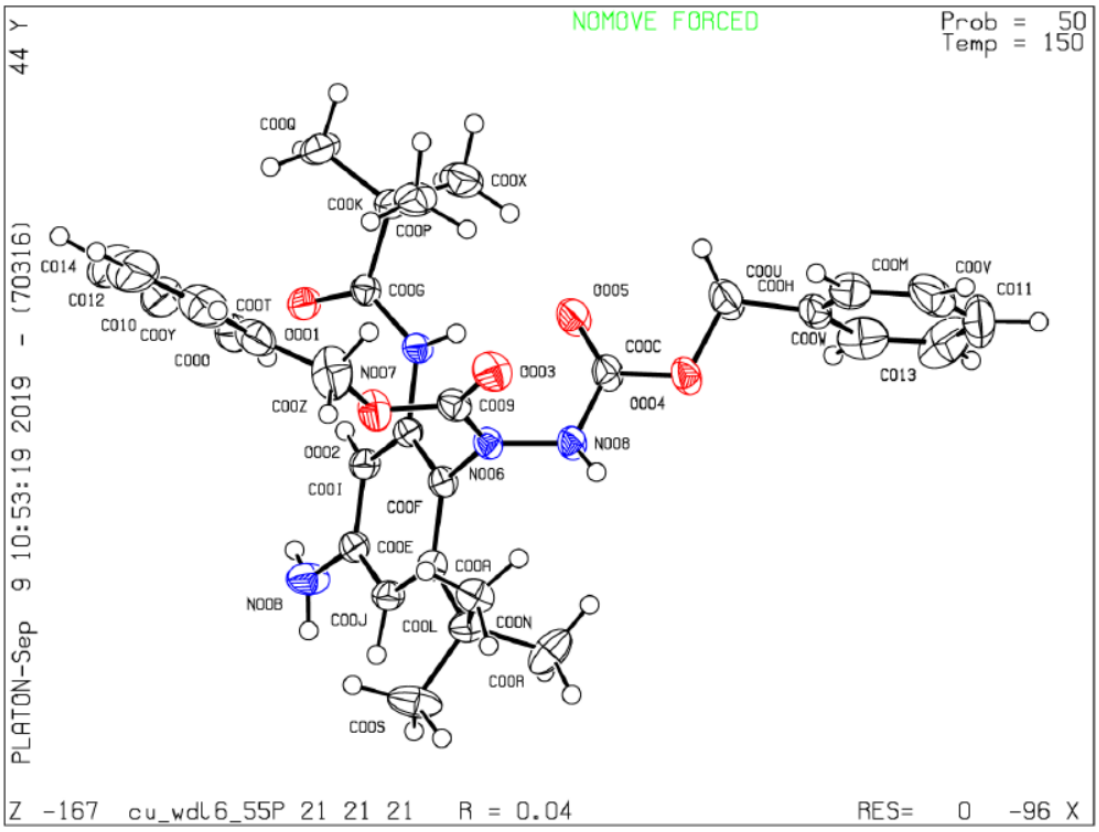
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.47 – 7.28 (m, 5H), 4.19 – 3.48 (m, 2H), 1.86 (s, 1H), 1.71 (d, *J* = 22.7 Hz, 3H). $[\alpha]_D^{25}$ = 9.60 (c = 1, DCM). HPLC: Chiralpak IA column, 95:05 hexanes/isopropanol, 1 ml/min; t_R = 9.9 min (major), 11.5 min (minor); 91:9 er.

References:

[1] T. M. Baker, M. C. T. Fyre, G. W. Harbottle, V. Hasimbegovic, P. Meghani, A. RigbyI, C. Sambrook-Smith, S. M. Thom, *US2014296208 (A1)* **2014**.

[2] L. Cui, Y. e. You, X. Mi, S. Luo, *J. Org. Chem.* **2018**, *83*, 4250-4256.

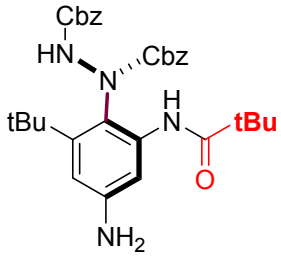
X-Ray structures:

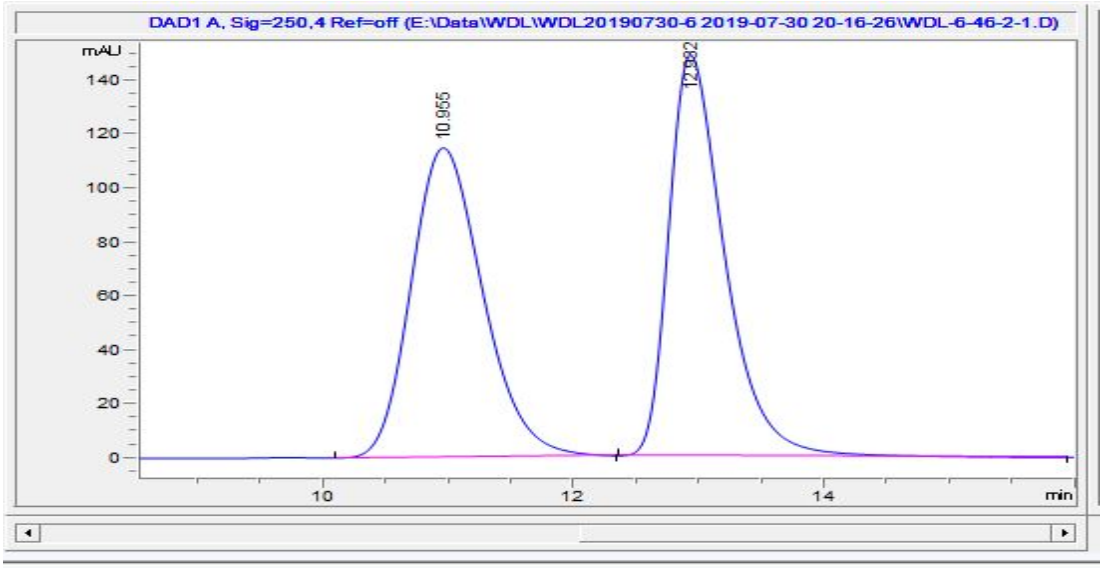


X-Ray structure of (*R*)-**5a**

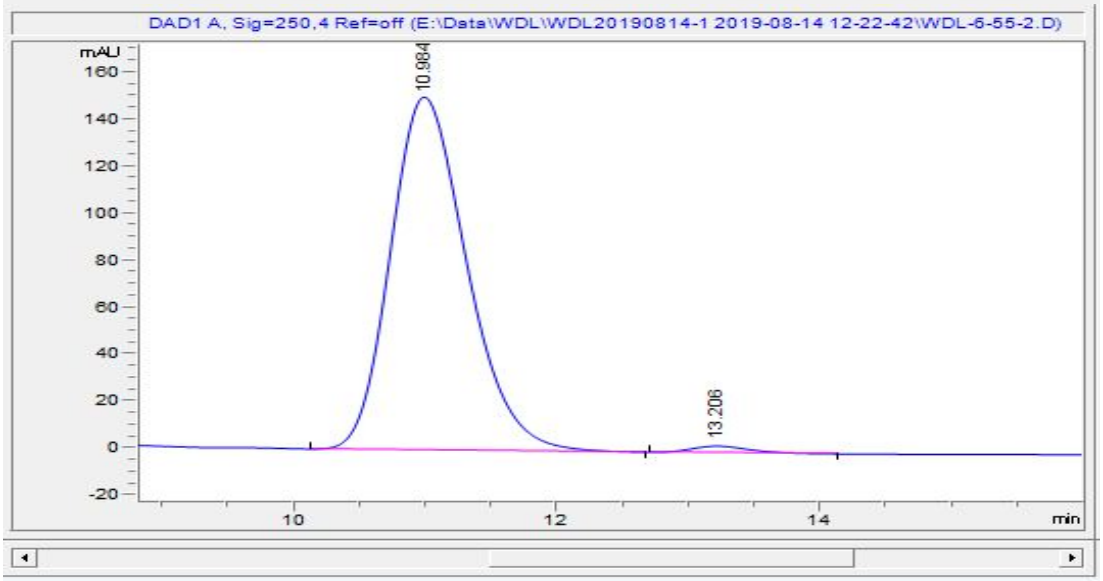
HPLC traces:

(R)-dibenzyl 1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5a**)



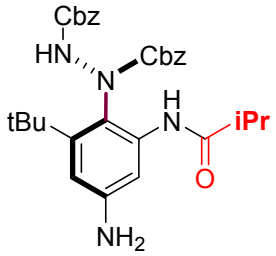


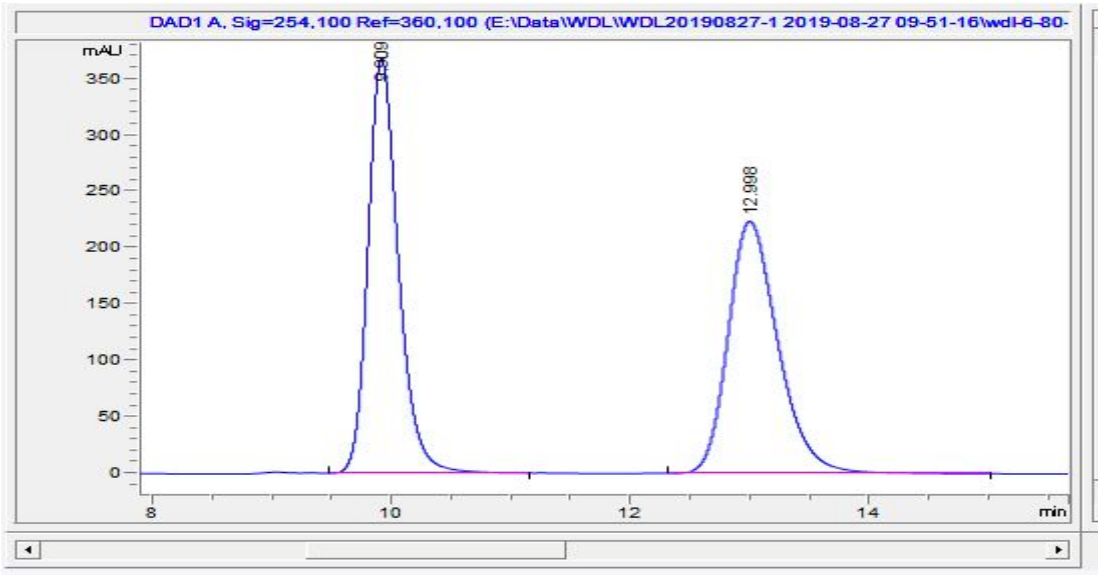
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.955	BB	4576.4	114.9	0.6166	49.631	0.776
2	12.932	BBA	4644.4	149	0.4737	50.369	0.59



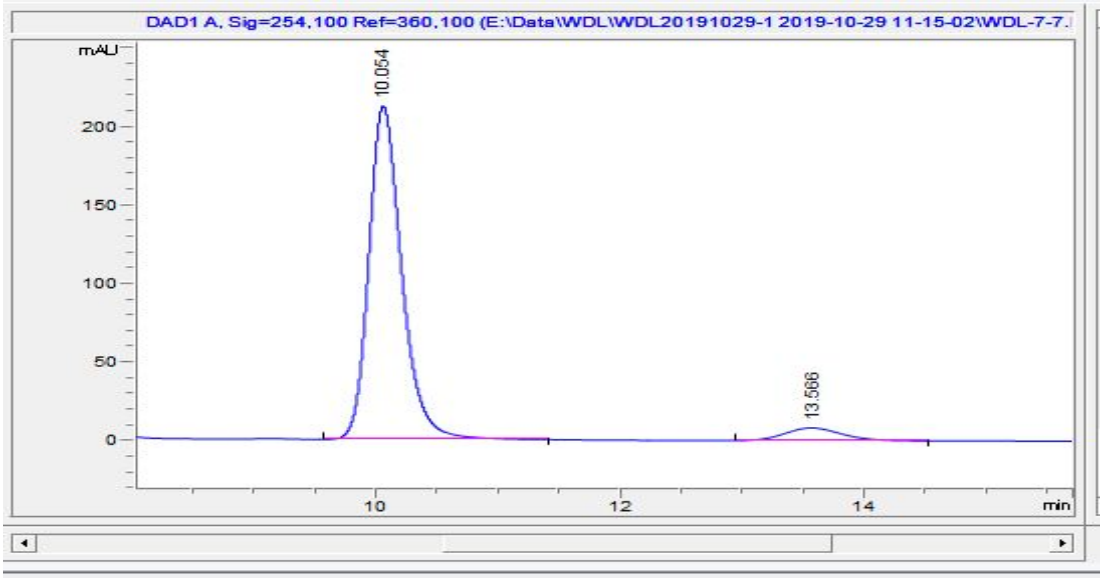
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.984	BB	6027.9	149.7	0.6218	98.576	0.759
2	13.206	BB	87.1	2.9	0.4555	1.424	0.745

(S)-dibenzyl 1-(4-amino-2-(tert-butyl)-6-isobutyramidophenyl)hydrazine-1,2-dicarboxylate (**5b**)



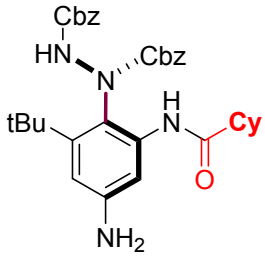


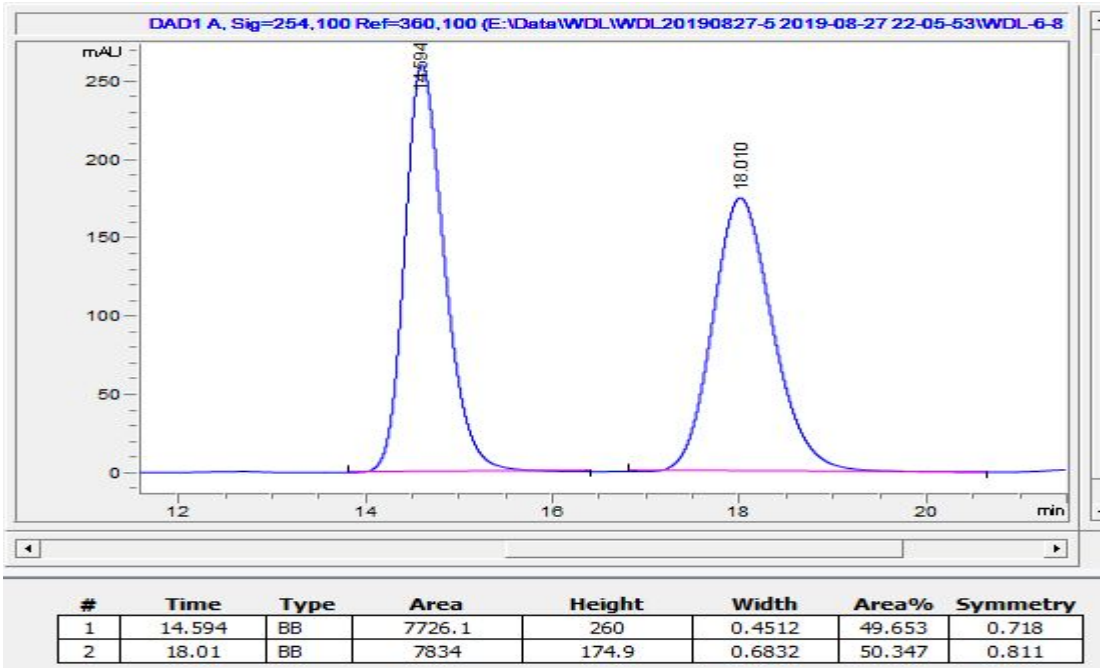
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.909	BB	6492.1	367.2	0.2703	50.009	0.741
2	12.998	BB	6489.6	223.1	0.4383	49.991	0.727



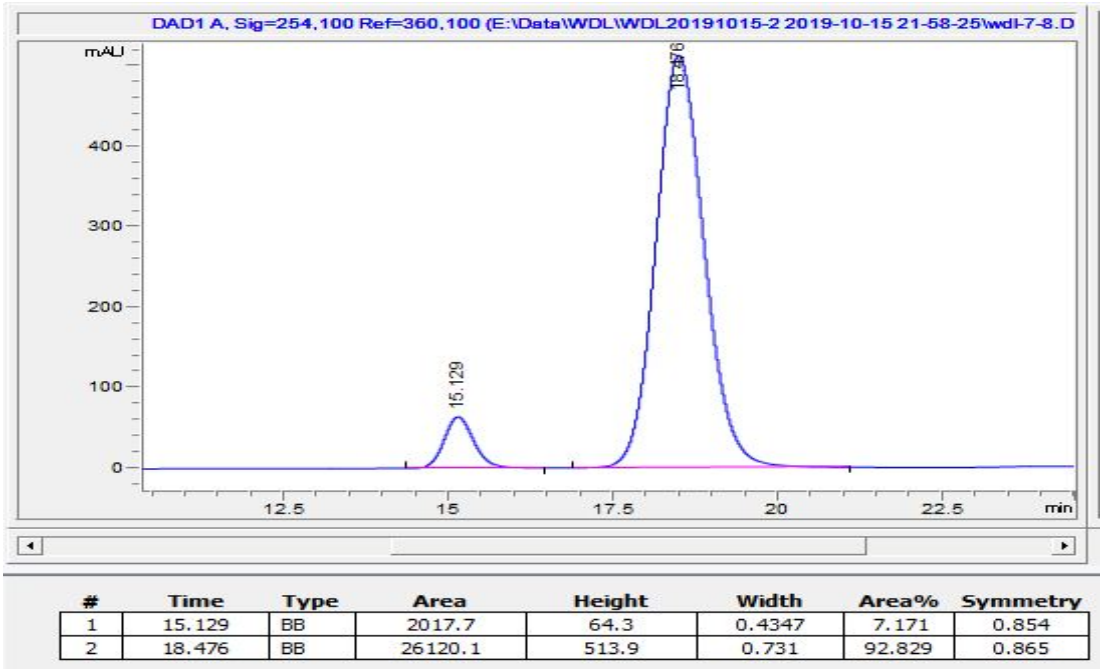
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.054	BB	3976.1	212.2	0.2846	93.789	0.734
2	13.566	BB	263.3	8.1	0.3806	6.211	0.903

(R)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-(cyclohexanecarboxamido)phenyl)hydrazine-1,2-dicarboxylate (**5c**)



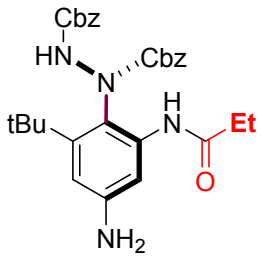


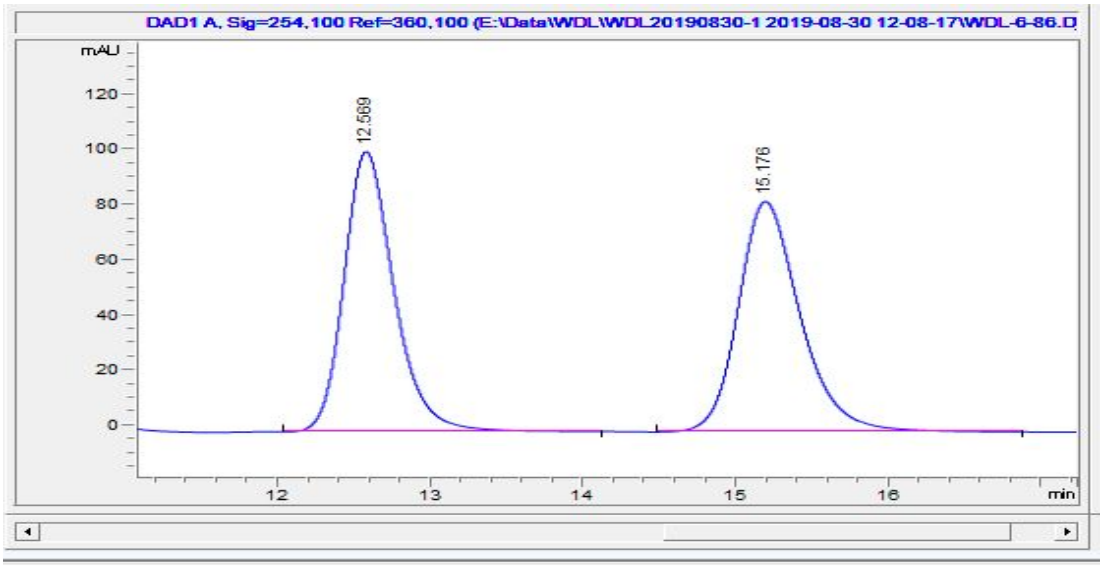
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	14.594	BB	7726.1	260	0.4512	49.653	0.718
2	18.01	BB	7834	174.9	0.6832	50.347	0.811



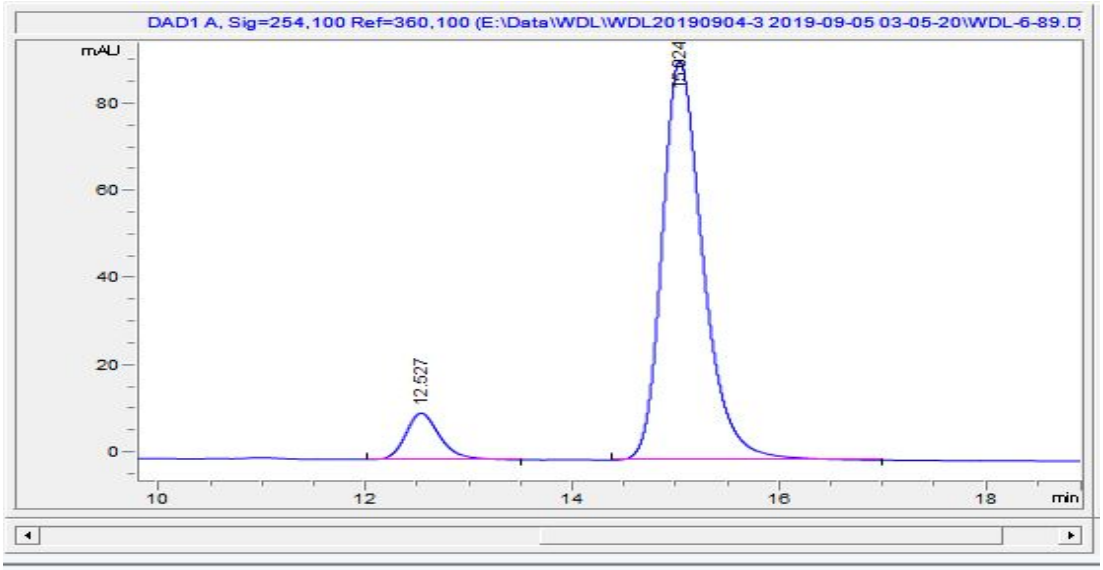
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	15.129	BB	2017.7	64.3	0.4347	7.171	0.854
2	18.476	BB	26120.1	513.9	0.731	92.829	0.865

(R)-dibenzyl 1-(4-amino-2-(tert-butyl)-6-propionamidophenyl)hydrazine-1,2-dicarboxylate (**5d**)



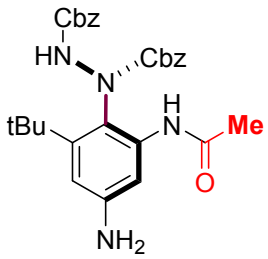


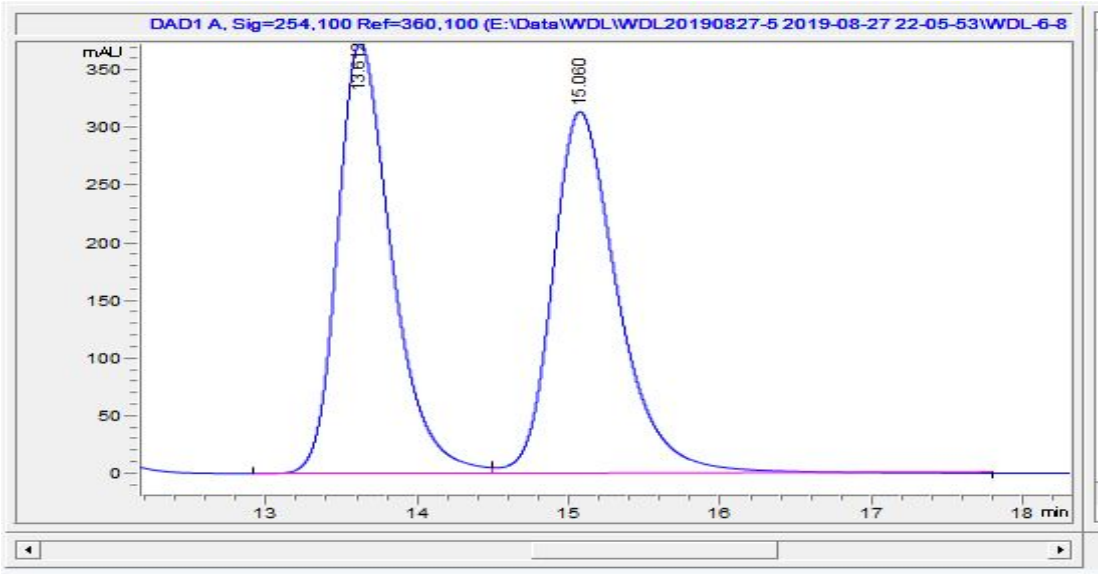
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	12.569	BB	2298.7	101.4	0.3425	49.445	0.745
2	15.176	BB	2350.3	83.4	0.425	50.555	0.741



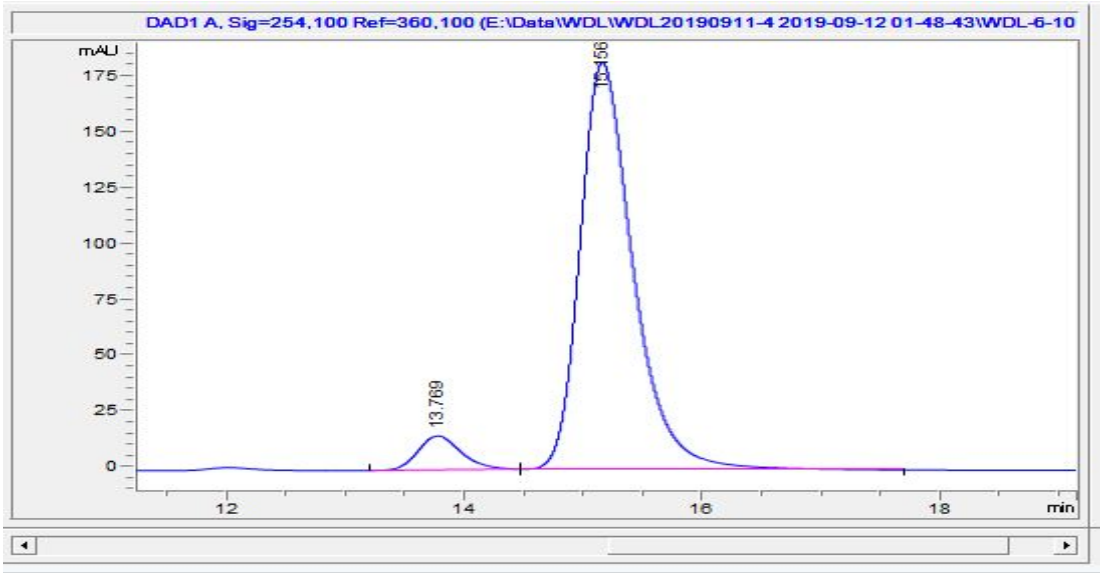
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	12.527	BB	241.8	10.6	0.3134	8.808	0.798
2	15.024	BB	2503.8	91.2	0.4143	91.192	0.708

(R)-dibenzyl 1-(2-acetamido-4-amino-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5e**)



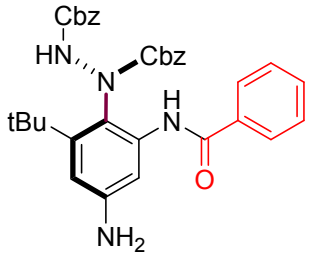


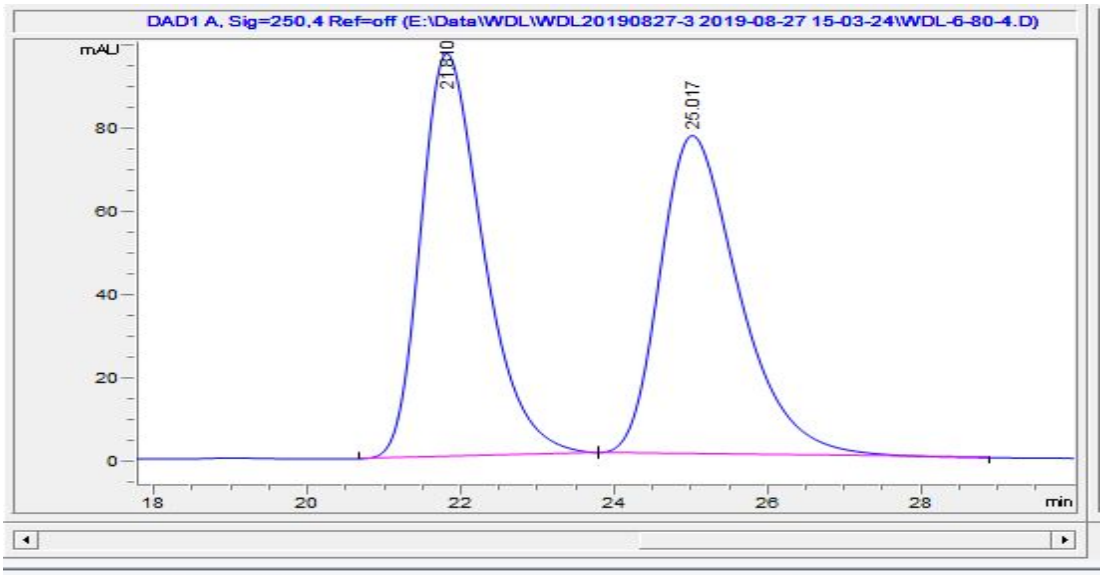
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	13.612	BV	9236.3	372.6	0.3772	49.603	0.676
2	15.06	VB	9384	313.2	0.4531	50.397	0.68



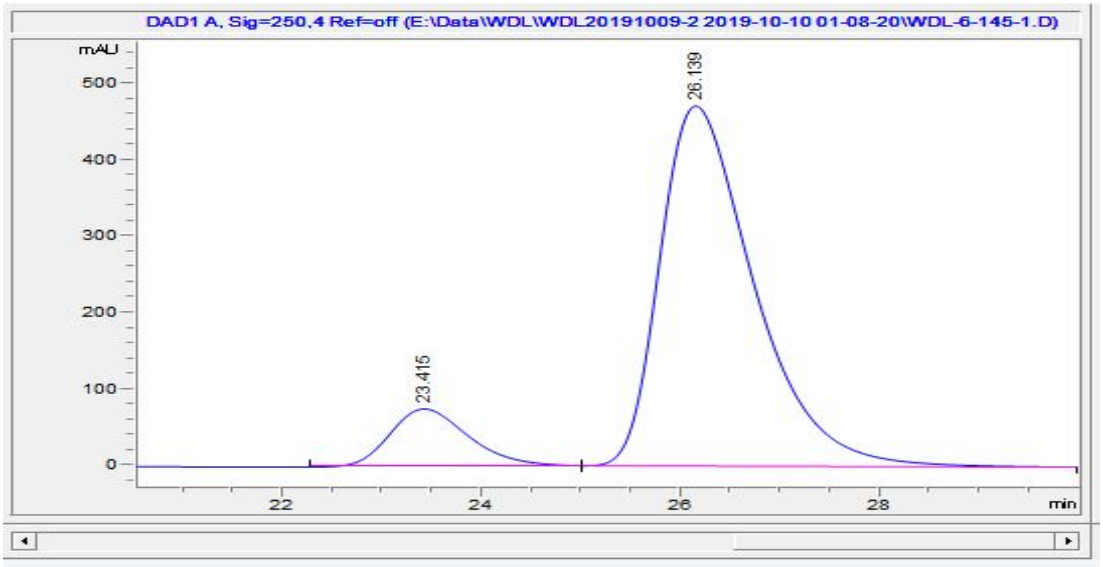
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	13.769	BB	380.6	15.2	0.3376	6.328	0.793
2	15.156	BB	5634.9	181.6	0.4669	93.672	0.675

(S)-dibenzyl-1-(4-amino-2-benzamido-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5f**)





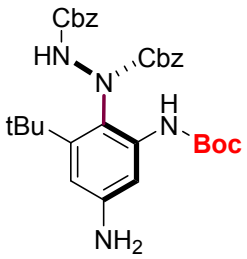
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	21.81	BB	5454.8	96.3	0.8651	49.956	0.674
2	25.017	BB	5464.5	76	1.0828	50.044	0.648

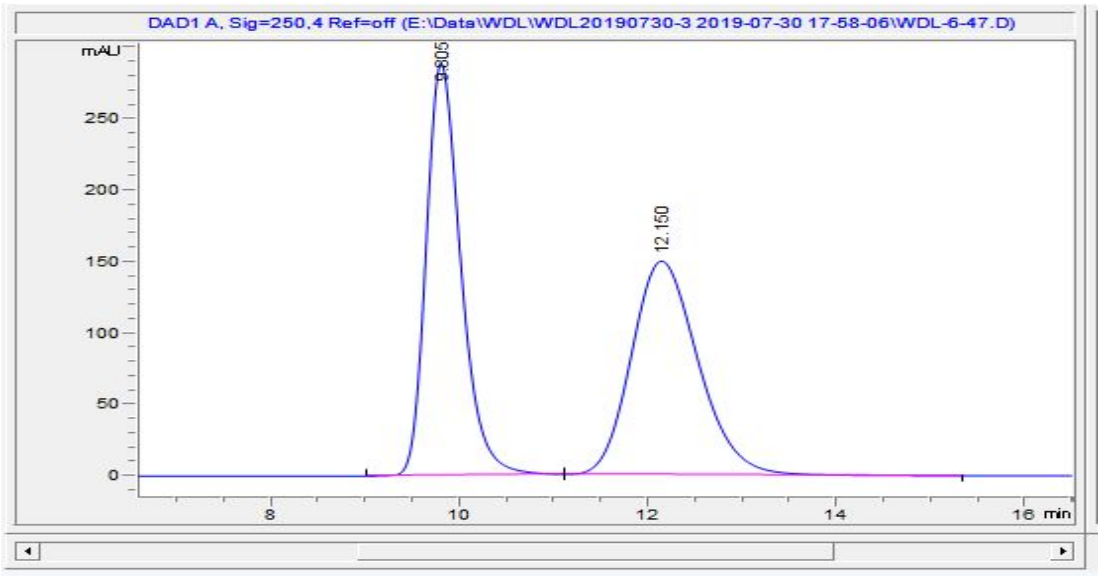


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	23.415	BB	4110.4	75.1	0.8426	11.762	0.745
2	26.139	BBA	30834.7	469.9	1.0055	88.238	0.574

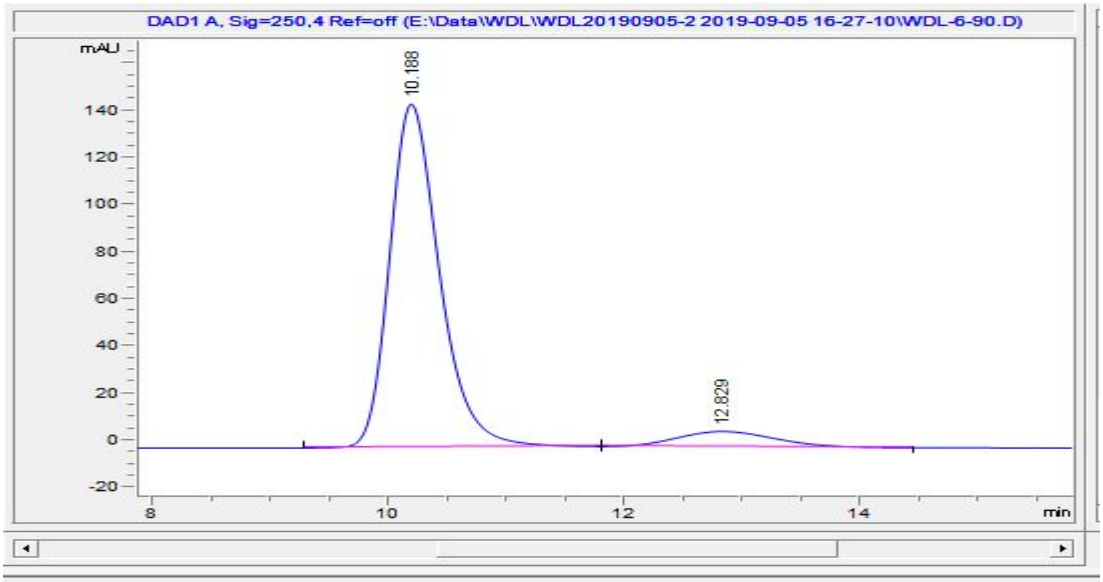
(R)-dibenzyl

1-(4-amino-2-((tert-butoxycarbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5g**)



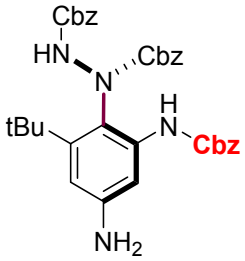


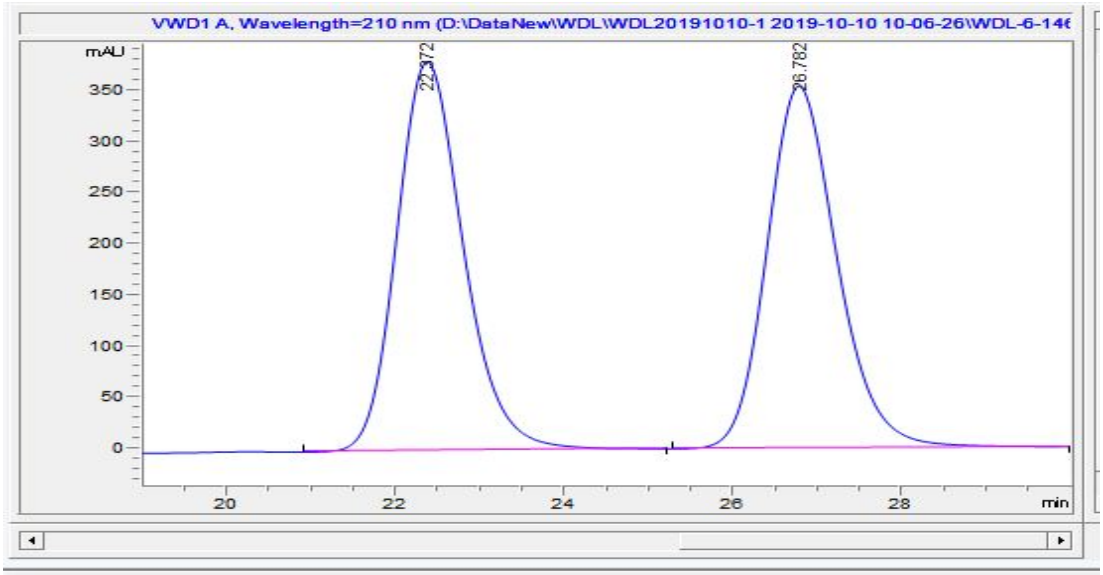
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.805	BB	7379.6	288.3	0.3926	49.987	0.715
2	12.15	BB	7383.6	149.5	0.7661	50.013	0.786



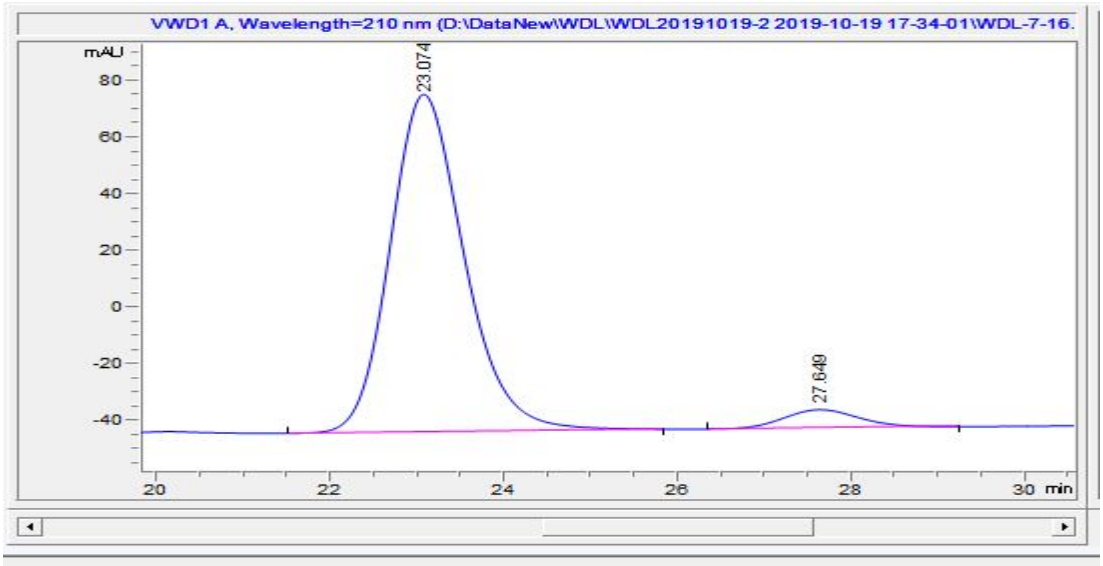
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.188	BB	4299.3	145.9	0.4519	91.764	0.725
2	12.829	BB	385.9	6.6	0.7687	8.236	0.816

(R)-dibenzyl-1-(4-amino-2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5h**)



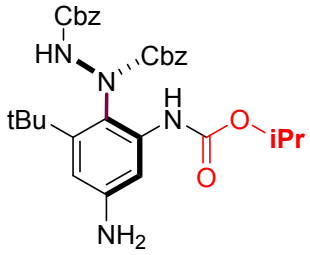


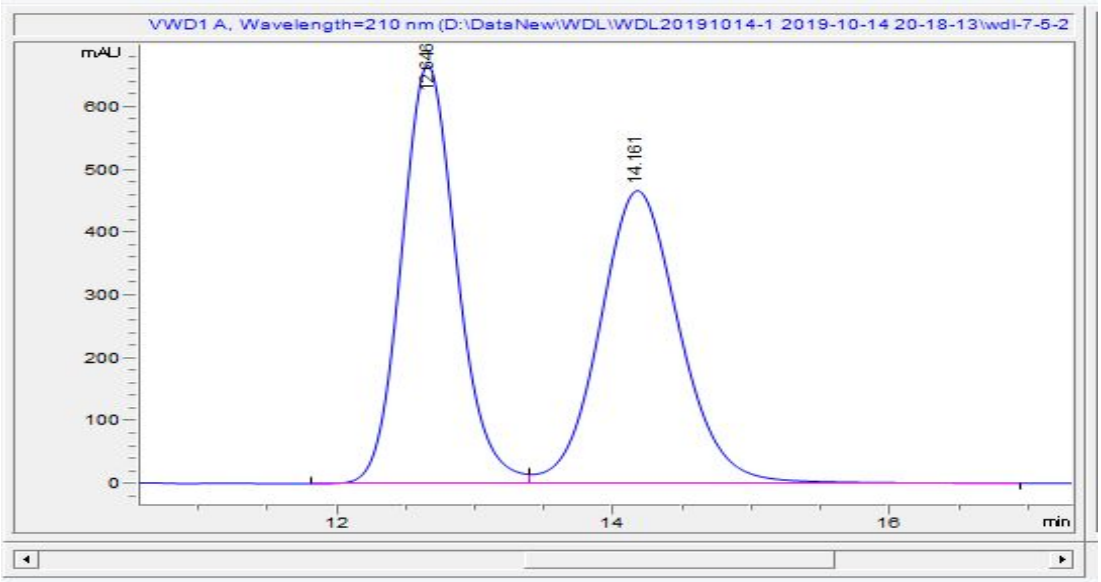
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	22.372	BB	20923.1	379.3	0.8475	50.629	0.794
2	26.782	BBA	20403.5	353	0.8884	49.371	0.795



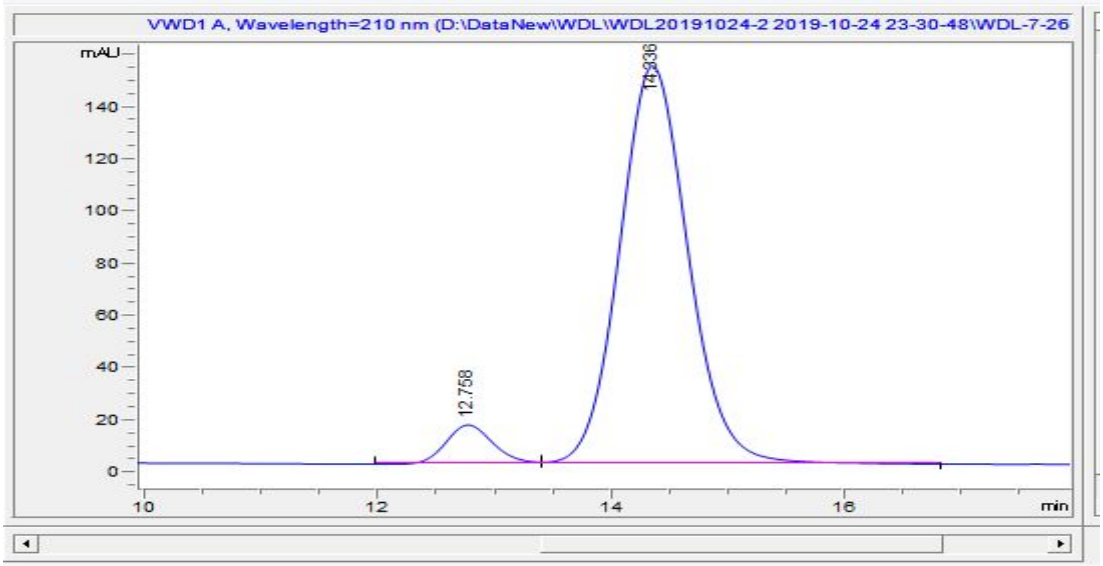
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	23.074	BB	7066.7	119	0.9145	94.735	0.793
2	27.649	BB	392.7	6.5	0.9278	5.265	0.894

(R)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-((isopropoxycarbonyl)amino)phenyl)hydrazine-1,2-dicarboxylate (**5i**)



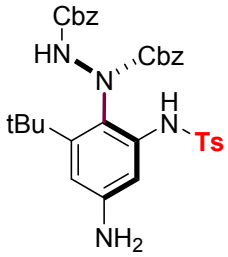


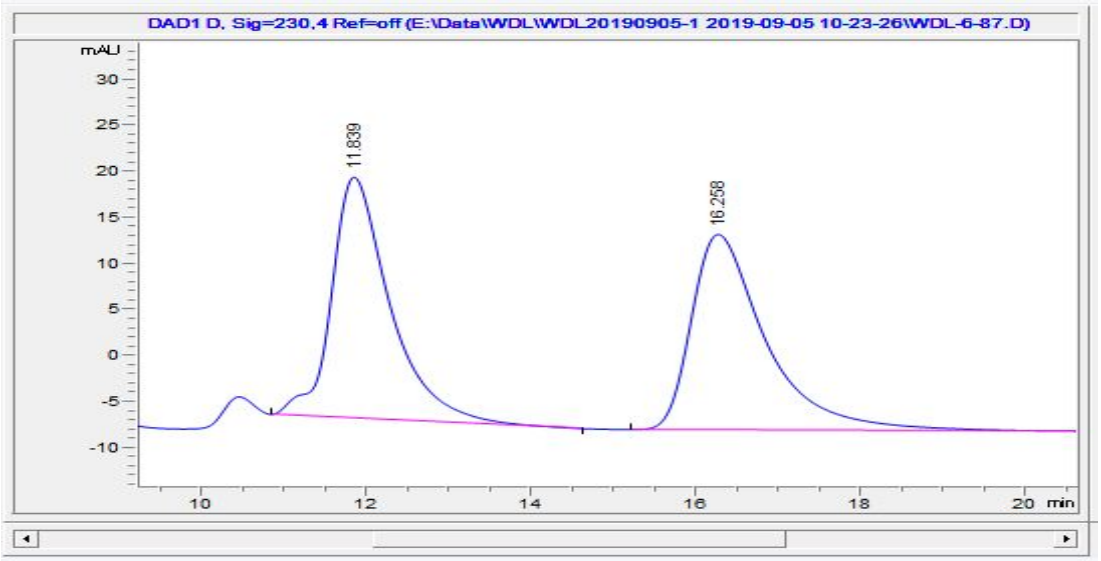
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	12.646	BV	18428.2	664.7	0.4274	49.734	0.86
2	14.161	VB	18625.6	465.3	0.615	50.266	0.864



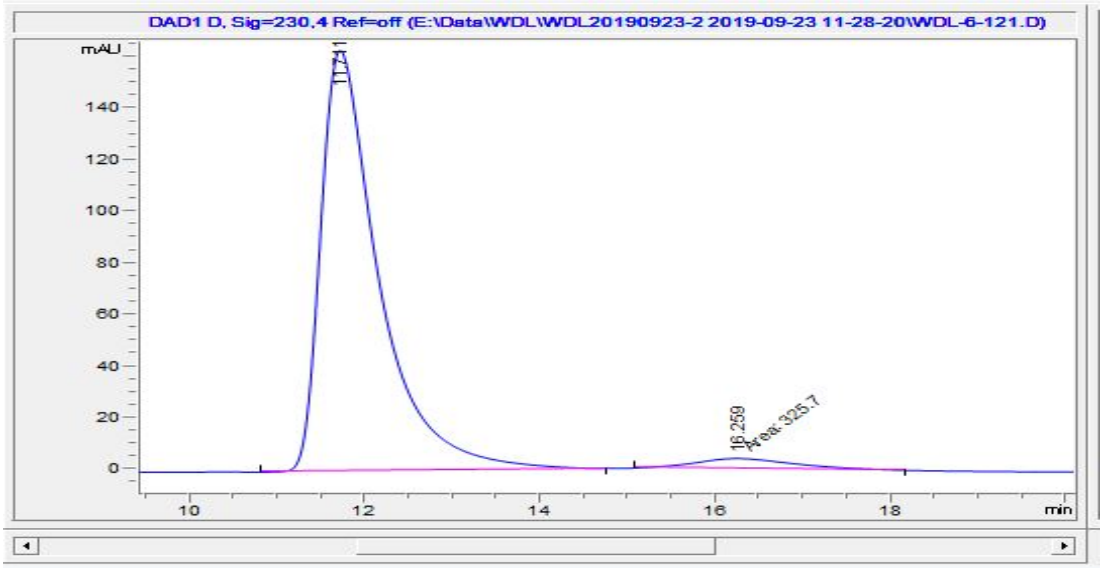
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	12.758	BV	430	15.1	0.4362	6.421	0.841
2	14.336	VB	6267	153.3	0.631	93.579	0.886

(R)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-((4-methylphenyl)sulfonamido)phenyl)hydrazine-1,2-dicarboxylate (**5j**)



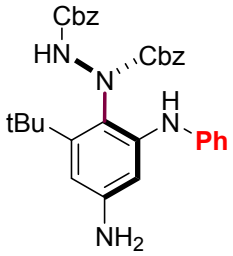


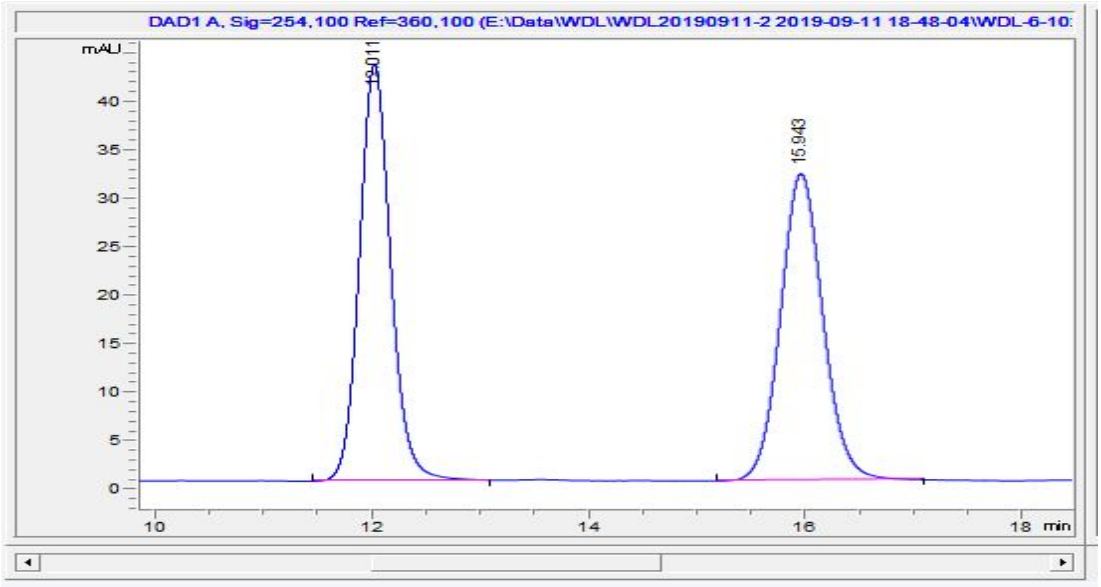
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	11.839	BB	1301.7	26.3	0.7302	49.231	0.604
2	16.258	BB	1342.3	21.3	0.9145	50.769	0.517



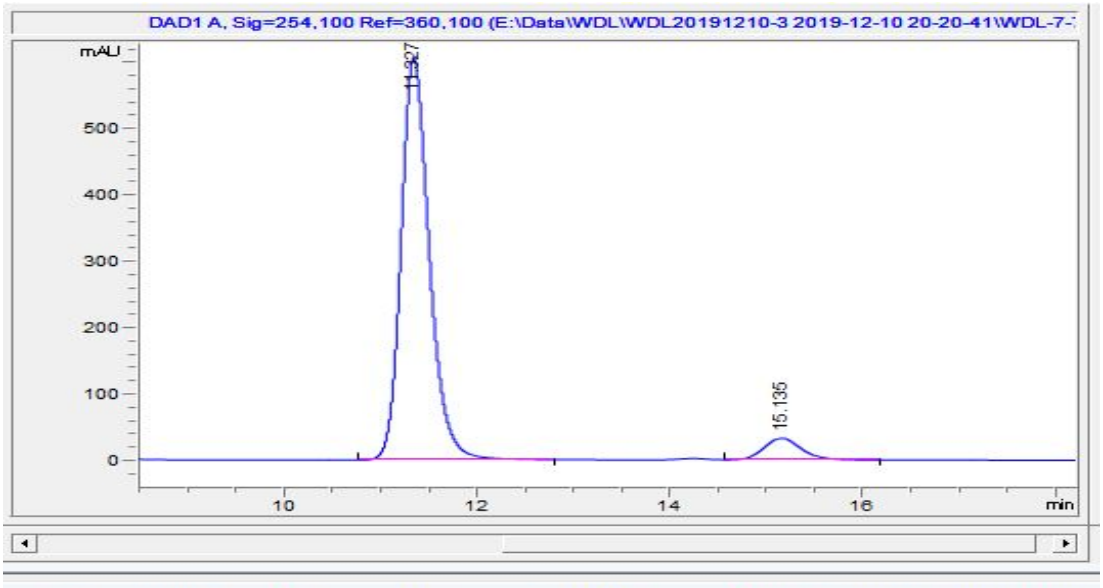
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	11.711	BB	7518.5	162.9	0.6805	95.848	0.458
2	16.259	MM	325.7	4	1.3464	4.152	0.689

(R)-dibenzyl 1-(4-amino-2-(tert-butyl)-6-(phenylamino)phenyl)hydrazine-1,2-dicarboxylate (**5k**)



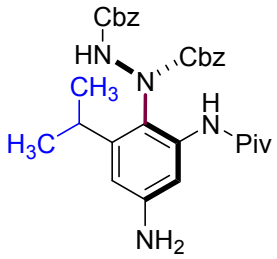


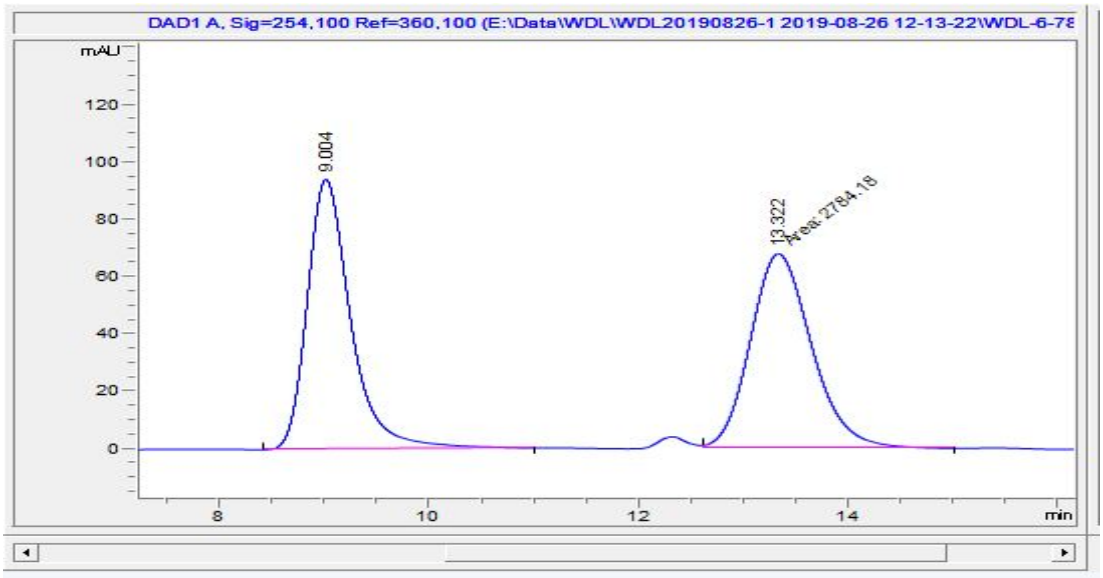
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	12.011	BB	865.7	43.1	0.305	49.976	0.864
2	15.943	BB	866.6	31.8	0.3959	50.024	0.897



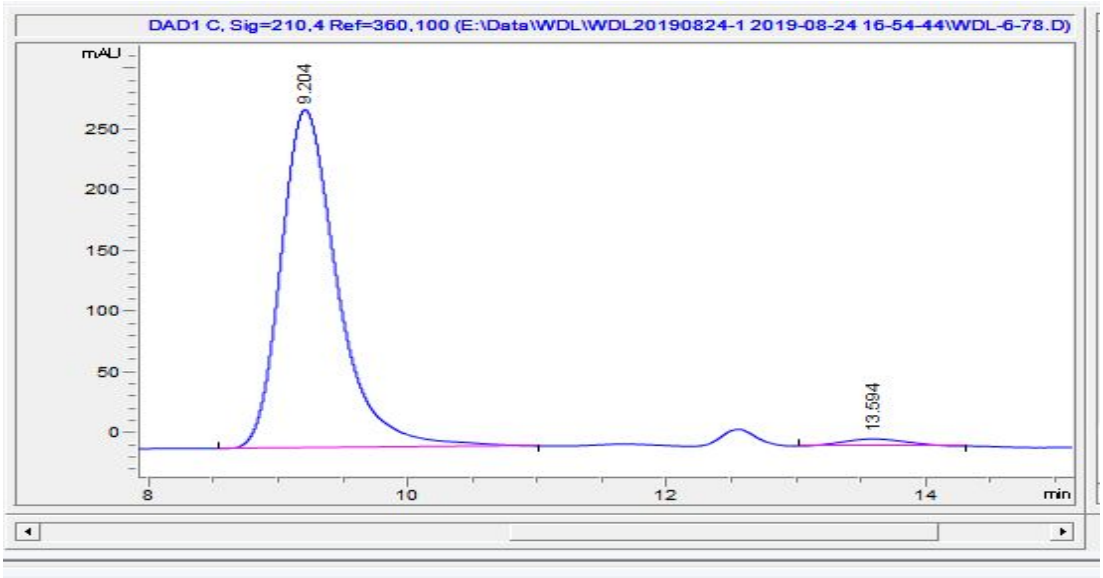
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	11.327	BB	12304.2	605.5	0.2946	93.344	0.767
2	15.135	BB	877.4	32.7	0.3243	6.656	0.845

(R)-dibenzyl 1-(4-amino-2-isopropyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5l**)



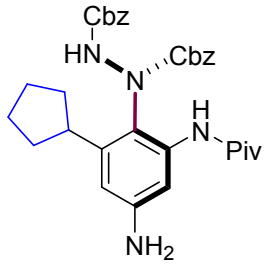


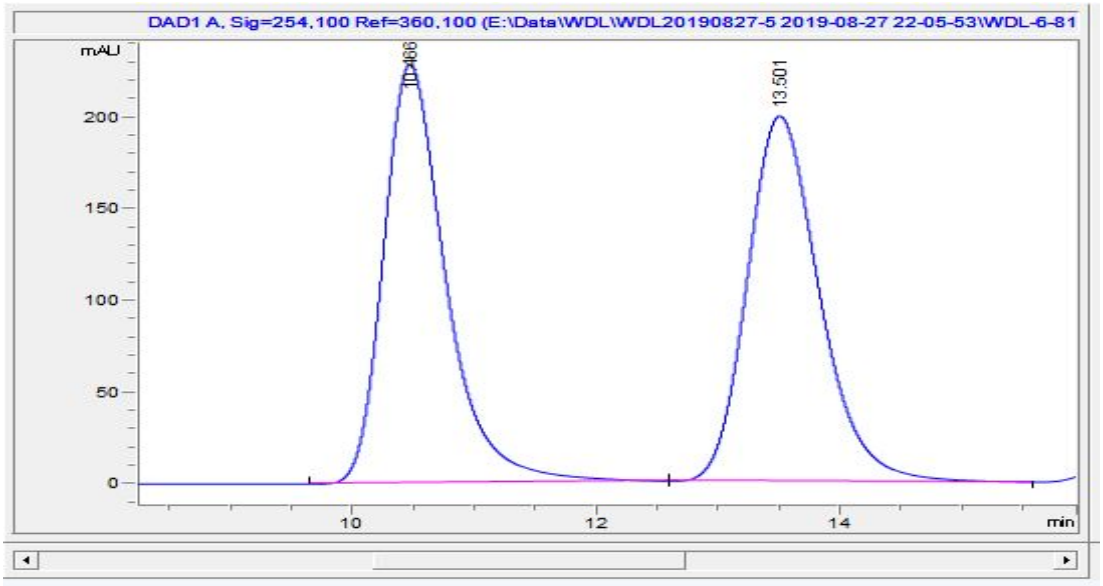
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.004	BB	2726.8	94.5	0.4343	49.479	0.69
2	13.322	FM	2784.2	68.2	0.6807	50.521	0.817



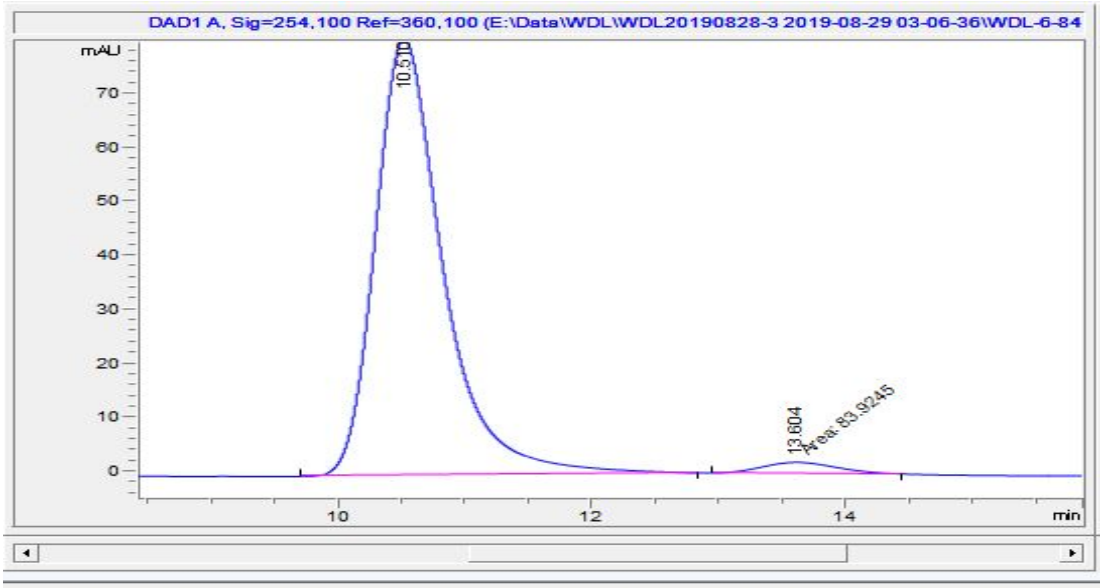
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.204	BB	8438	277.7	0.4015	97.602	0.698
2	13.594	BB	207.3	5.9	0.4143	2.398	0.916

(R)-dibenzyl 1-(4-amino-2-cyclopentyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5m**)



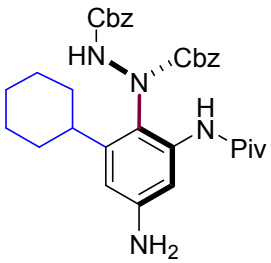


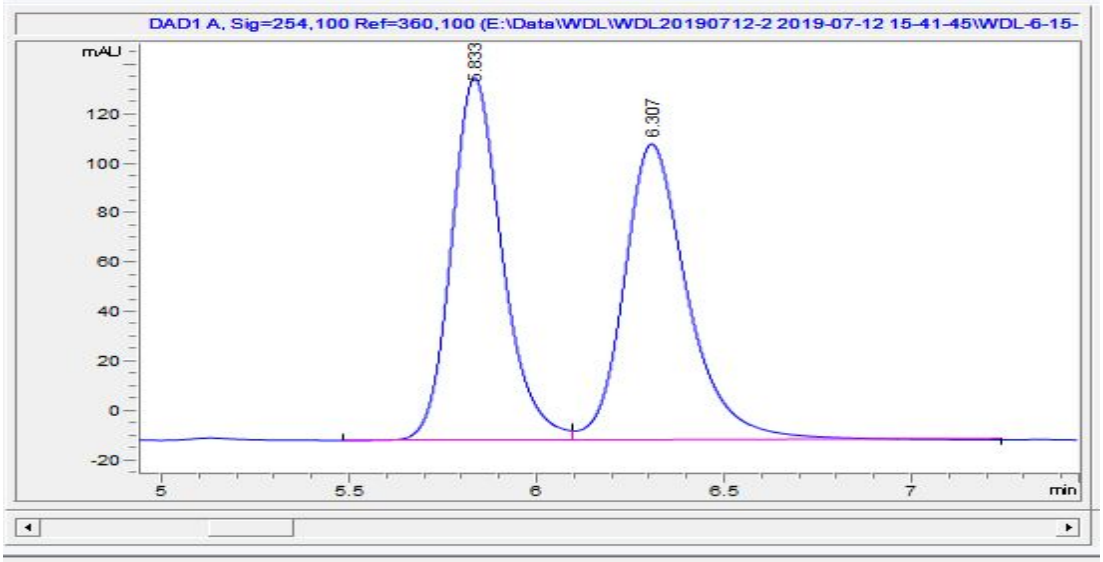
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.466	BB	8139.8	228.6	0.5263	49.801	0.681
2	13.501	BB	8204.7	199.6	0.6116	50.199	0.774



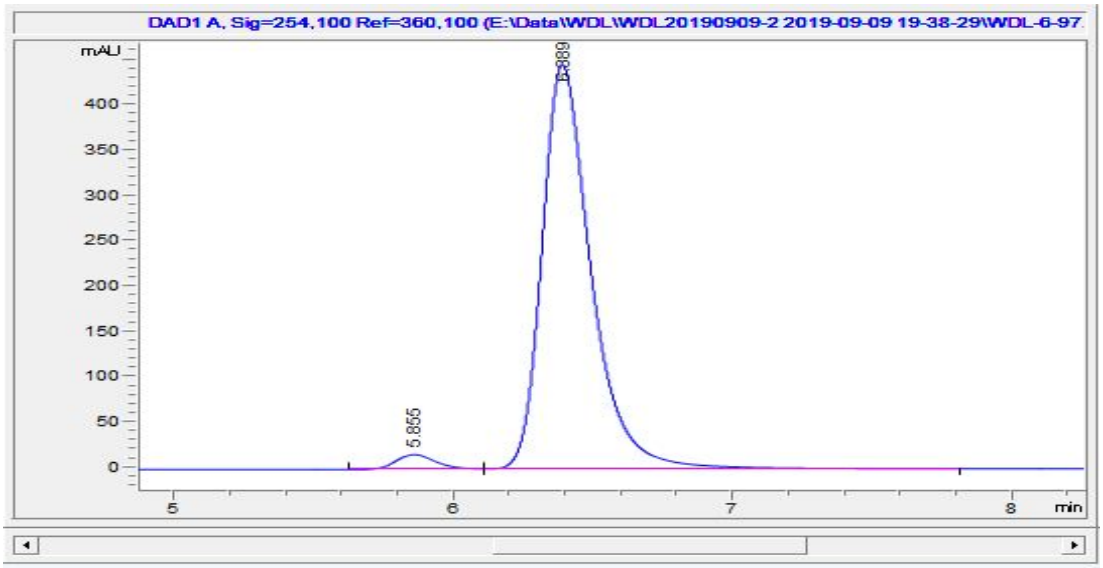
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.51	BB	2999.3	80.7	0.5008	97.278	0.677
2	13.604	MM	83.9	2.1	0.6757	2.722	0.896

(R)-dibenzyl 1-(4-amino-2-cyclohexyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5n**)



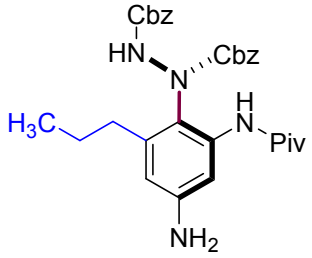


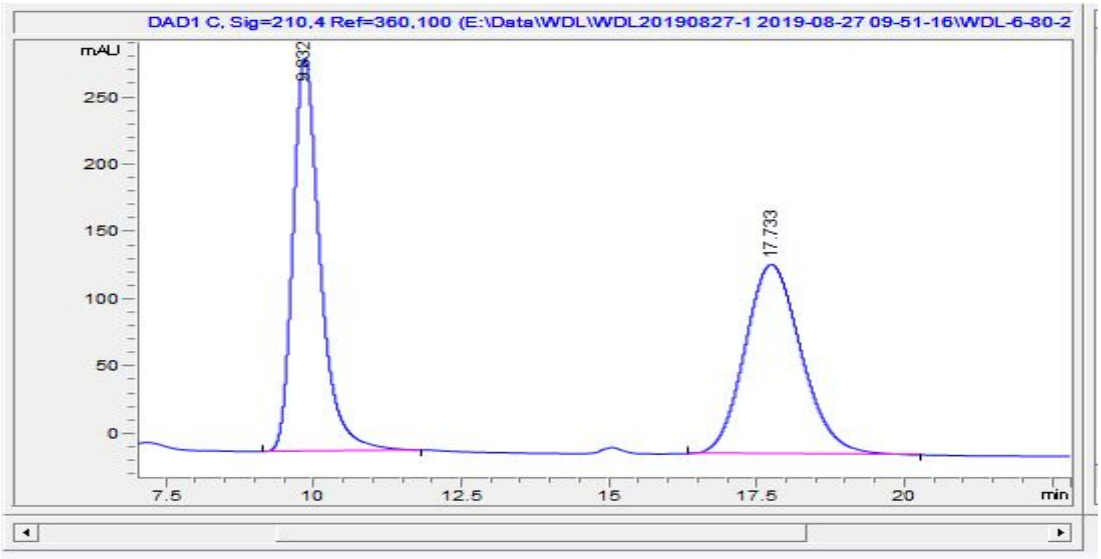
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.833	BV	1386	146.4	0.1445	49.387	0.791
2	6.307	VB	1420.4	119.6	0.1786	50.613	0.717



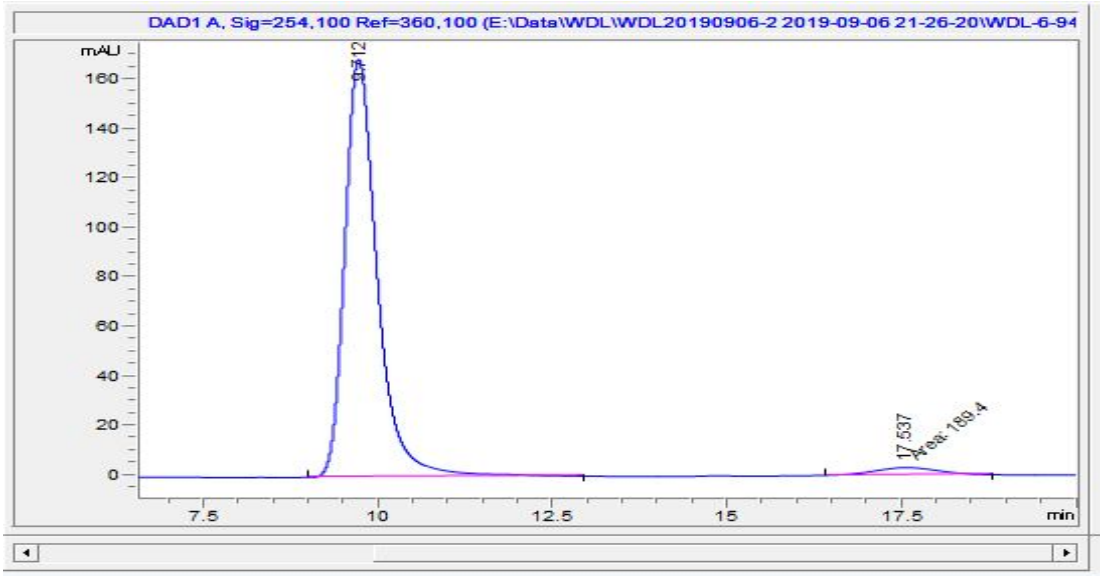
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.855	BV	164	16.5	0.1532	2.892	0.79
2	6.389	VB	5505.7	447.4	0.1851	97.108	0.651

(R)-dibenzyl 1-(4-amino-2-pivalamido-6-propylphenyl)hydrazine-1,2-dicarboxylate (**5o**)



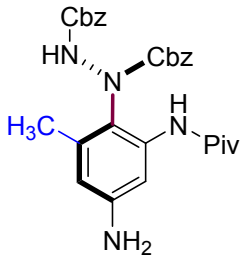


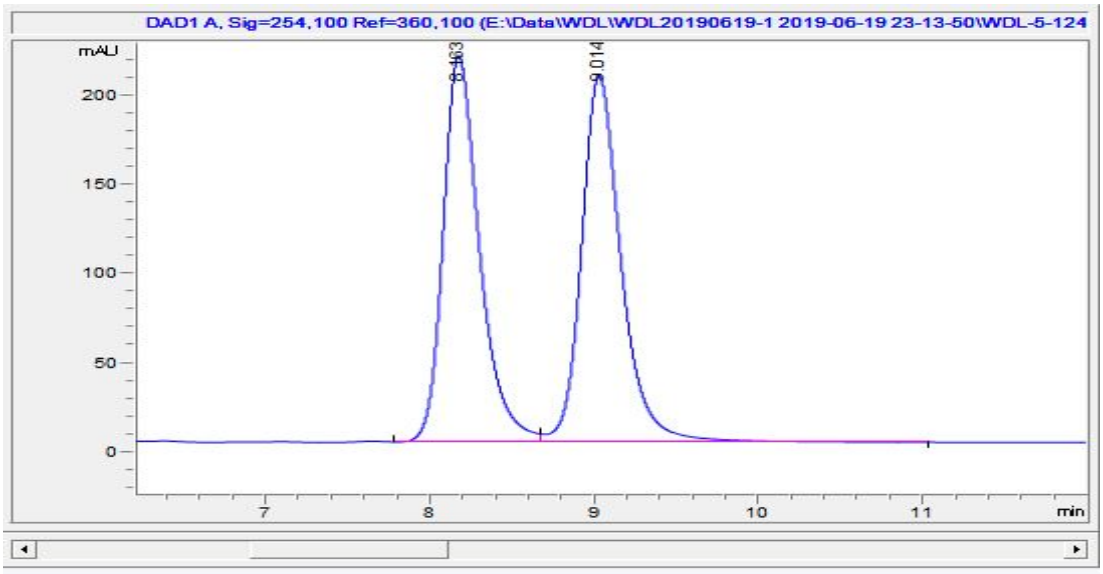
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.832	BB	9343.8	291	0.4712	49.966	0.698
2	17.733	BB	9356.4	140.5	0.7802	50.034	0.842



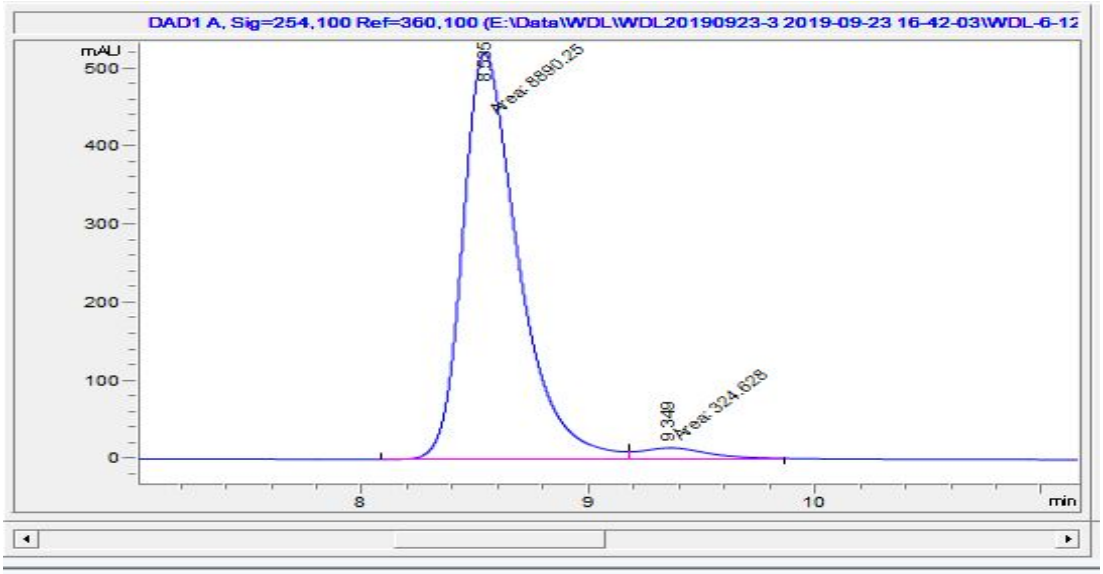
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.712	BB	5489.2	168.8	0.4913	96.665	0.677
2	17.537	MM	189.4	3	1.0592	3.335	0.921

(S)-dibenzyl 1-(4-amino-2-methyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5p**)



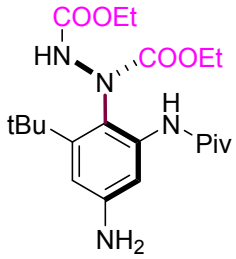


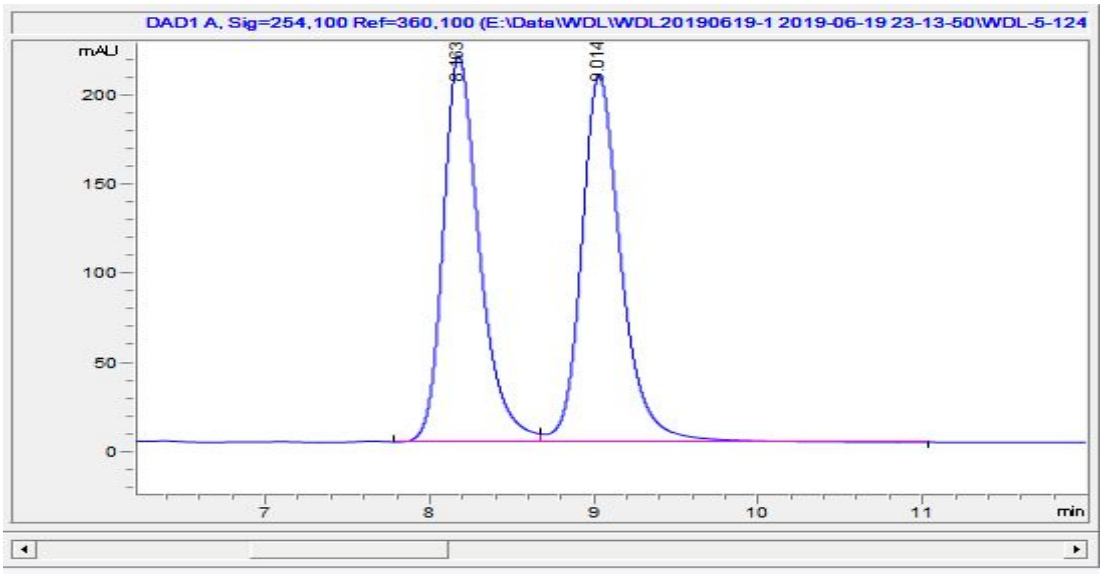
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	8.163	BV	3315.1	216	0.2321	49.116	0.692
2	9.014	VB	3434.5	205.1	0.2509	50.884	0.733



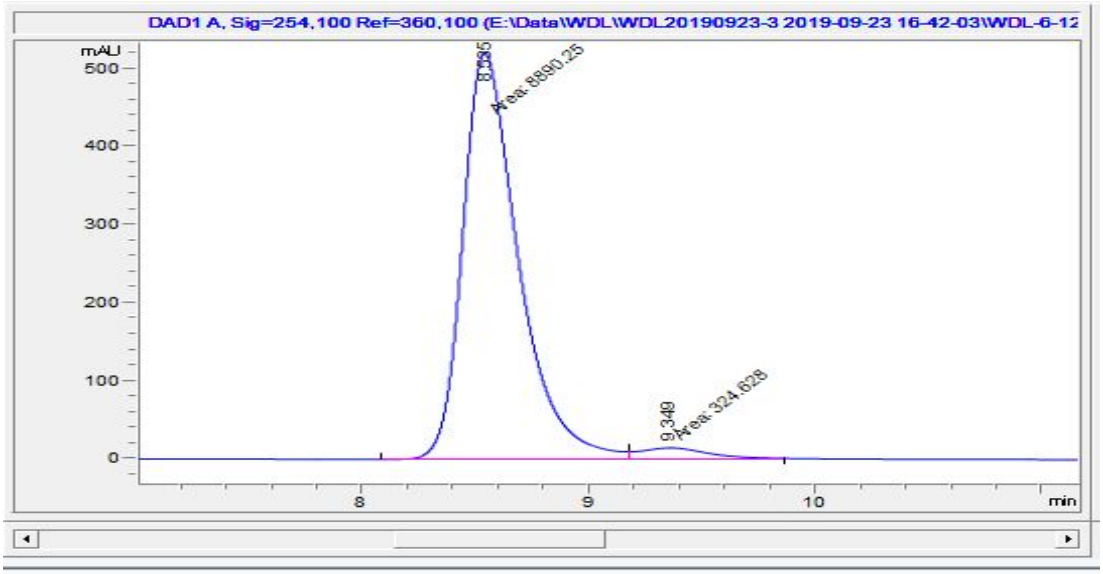
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	8.535	MF	8890.3	520	0.2849	96.477	0
2	9.349	MF	324.6	14.9	0.3626	3.523	0.667

(R)-diethyl 1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5q**)



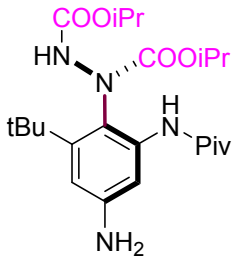


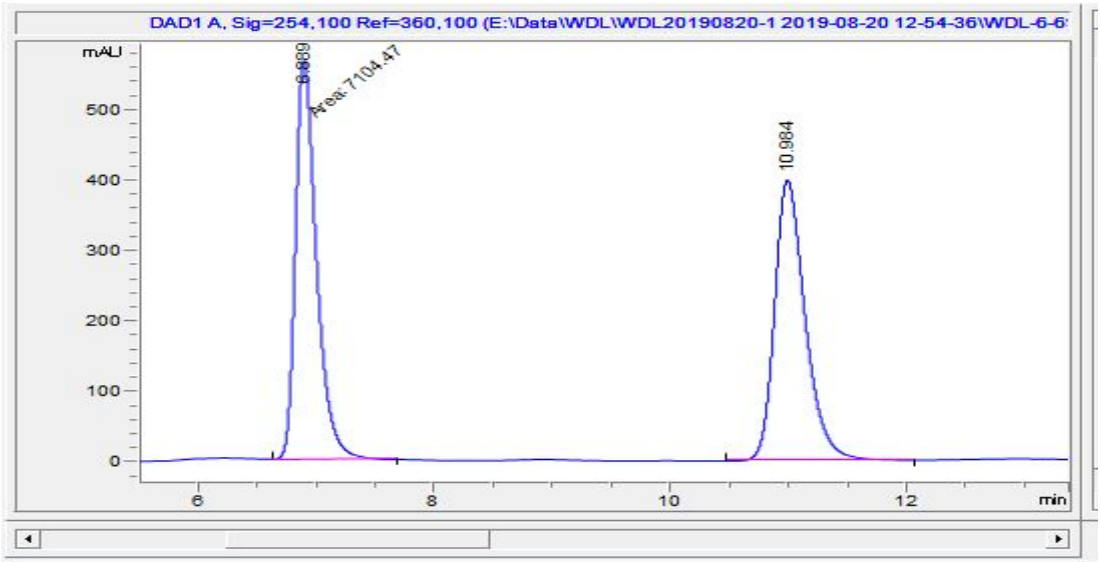
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	8.163	BV	3315.1	216	0.2321	49.116	0.692
2	9.014	VB	3434.5	205.1	0.2509	50.884	0.733



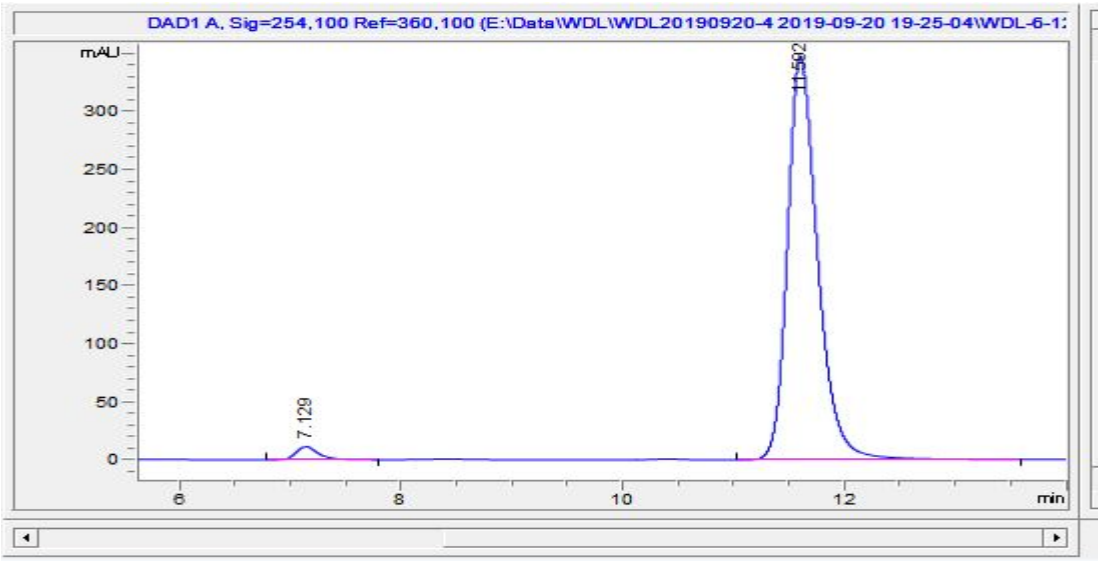
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	8.535	MF	8890.3	520	0.2849	96.477	0
2	9.349	MF	324.6	14.9	0.3626	3.523	0.667

(R)-diisopropyl 1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5r**)



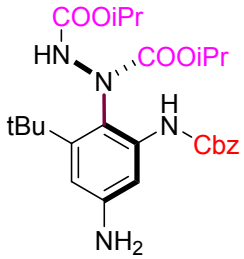


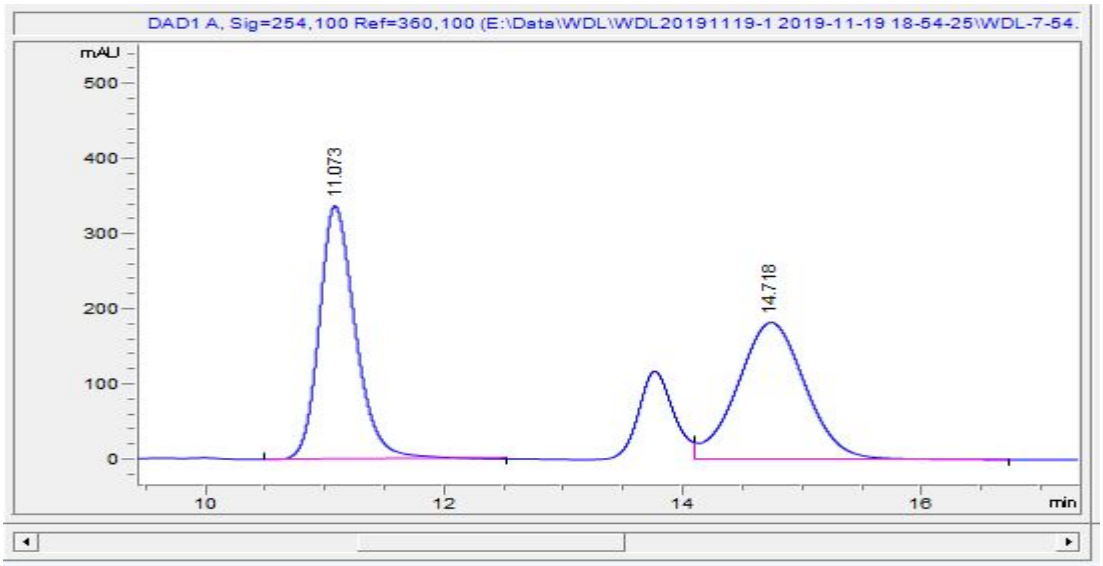
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.889	FM	7104.5	568.7	0.2082	49.757	0.635
2	10.984	BB	7173.8	399.5	0.272	50.243	0.683



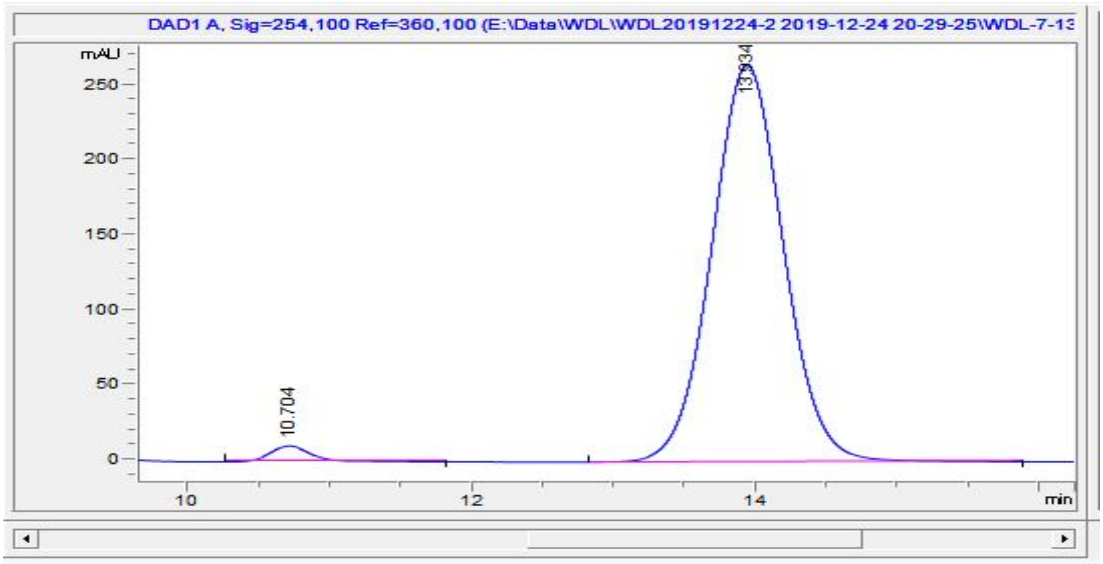
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	7.129	BB	157.4	11.2	0.2123	2.325	0.722
2	11.592	BB	6612	347.9	0.2897	97.675	0.697

(R)-diisopropyl-1-(4-amino-2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5s**)



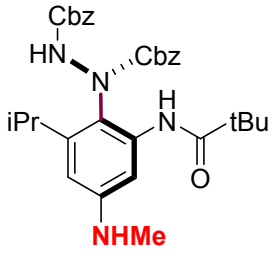


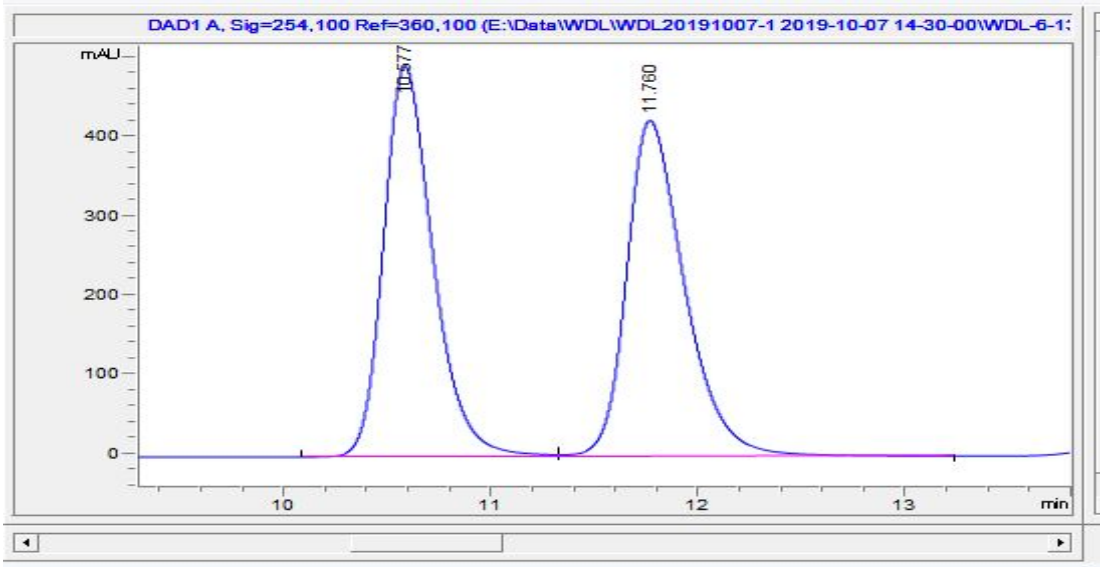
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	11.073	BB	7153.2	338.6	0.3215	49.862	0.73
2	14.718	VB	7192.9	183.2	0.5961	50.138	0.945



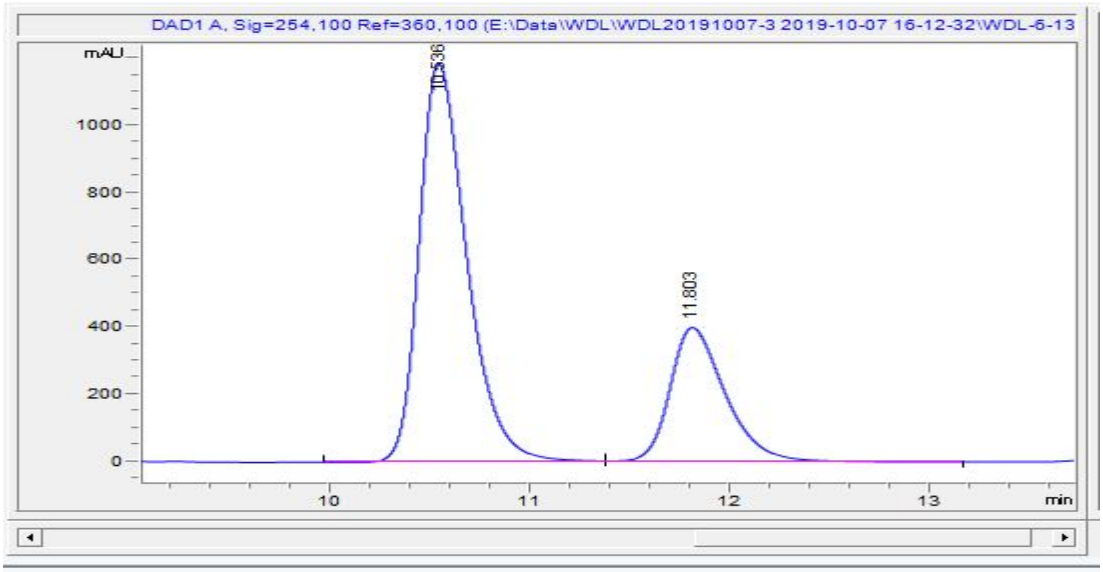
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.704	BB	219	10.7	0.2718	2.300	0.791
2	13.934	BB	9300.3	264.1	0.5409	97.700	0.935

(R)-dibenzyl-1-(2-isopropyl-4-(methylamino)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**7b**)



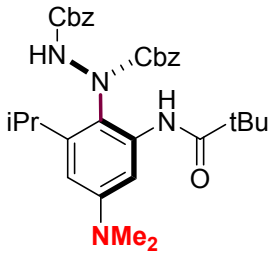


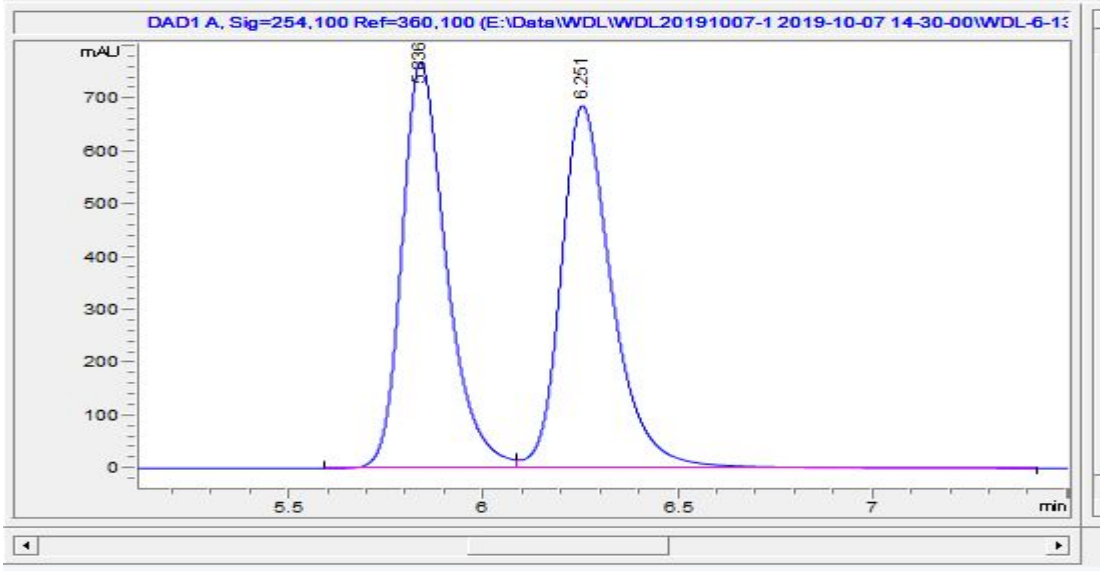
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.577	BV	8214.3	492.9	0.2549	49.865	0.713
2	11.76	VB	8258.8	423.7	0.2959	50.135	0.641



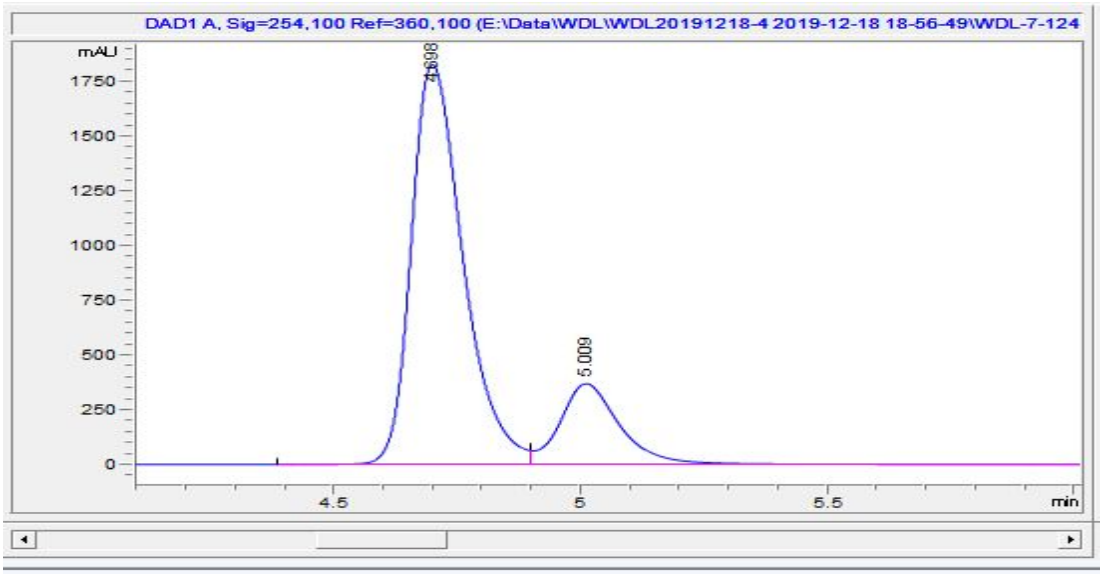
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.536	BV	19779.7	1189.8	0.2539	71.787	0.647
2	11.803	VB	7773.5	401.7	0.2943	28.213	0.649

(R)-dibenzyl-1-(4-(dimethylamino)-2-isopropyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**7c**)



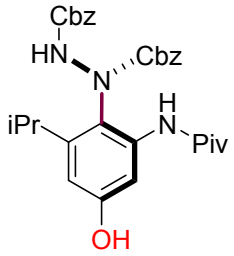


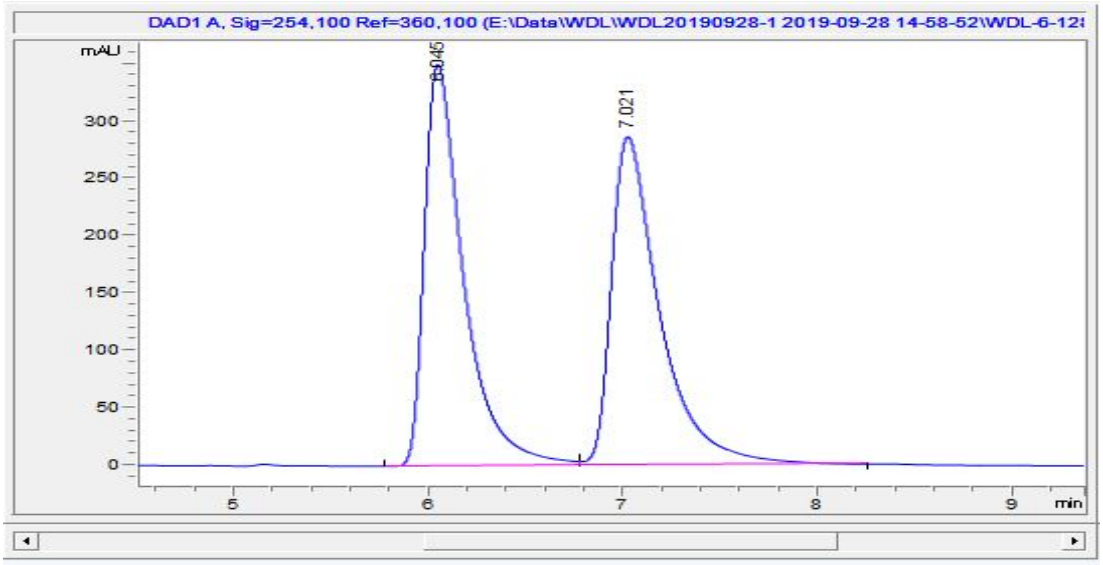
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.836	BV	6109.1	767.9	0.1203	49.354	0.695
2	6.251	VB	6269.2	687	0.1375	50.646	0.68



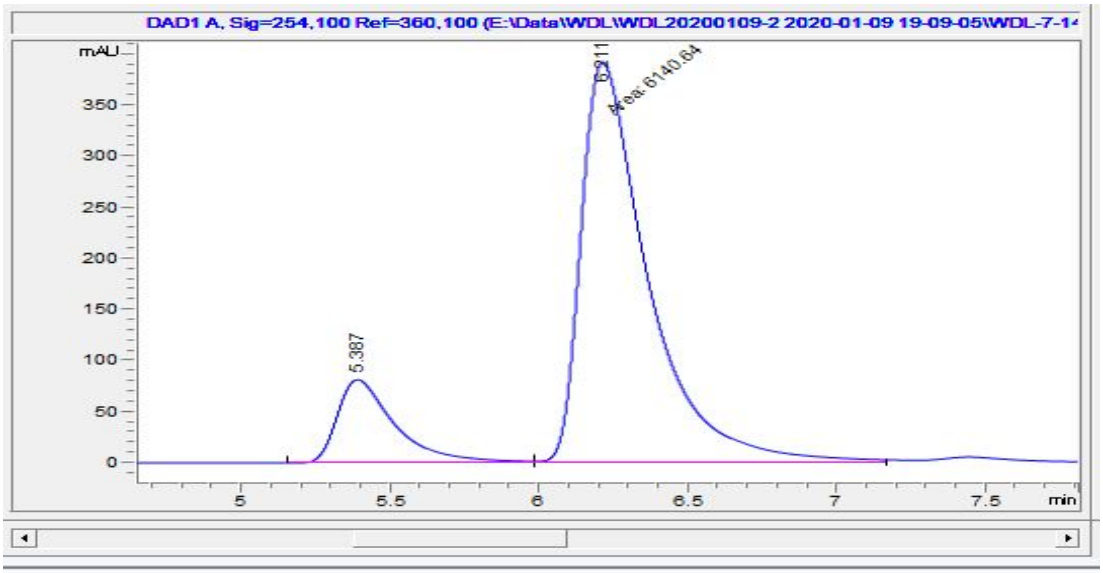
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.698	BV	13373.9	1827.6	0.1119	81.013	0.648
2	5.009	VB	3134.5	369.7	0.1259	18.987	0.699

(R)-dibenzyl 1-(4-hydroxy-2-isopropyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**7d**)





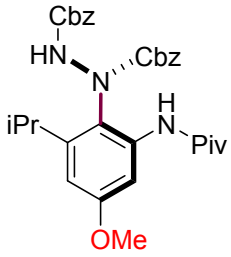
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.045	BV	4922	351.1	0.2081	49.830	0.472
2	7.021	VB	4955.6	287.2	0.2533	50.170	0.469

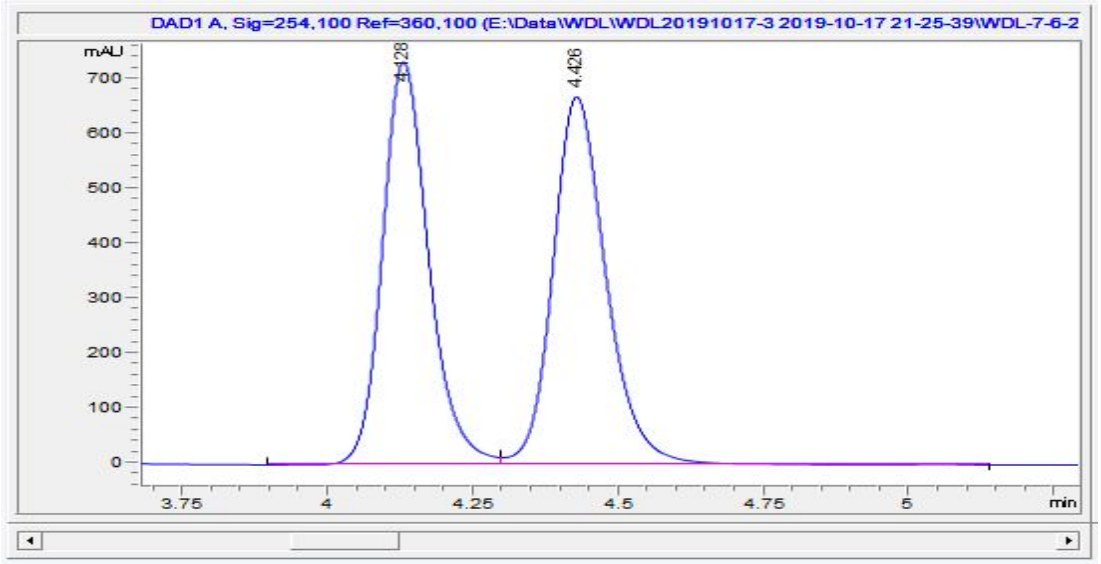


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.387	BV	1097.1	81.1	0.1967	15.158	0.491
2	6.211	MF	6140.6	390.8	0.2619	84.842	0.461

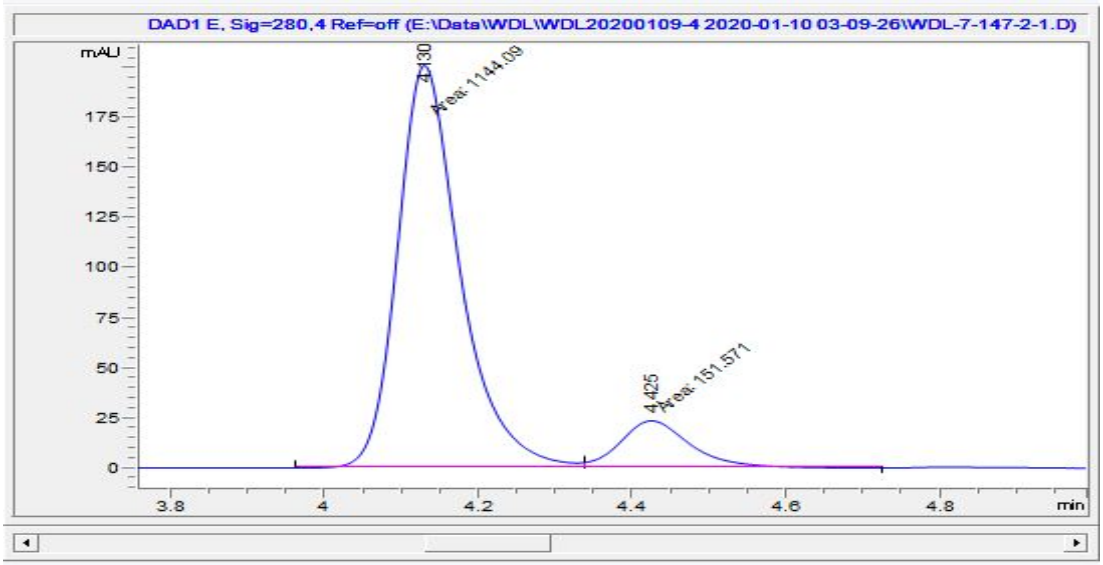
(R)-dibenzyl 1-(2-isopropyl-4-methoxy-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate

Diisopropyl (**7e**)



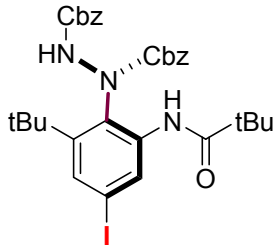


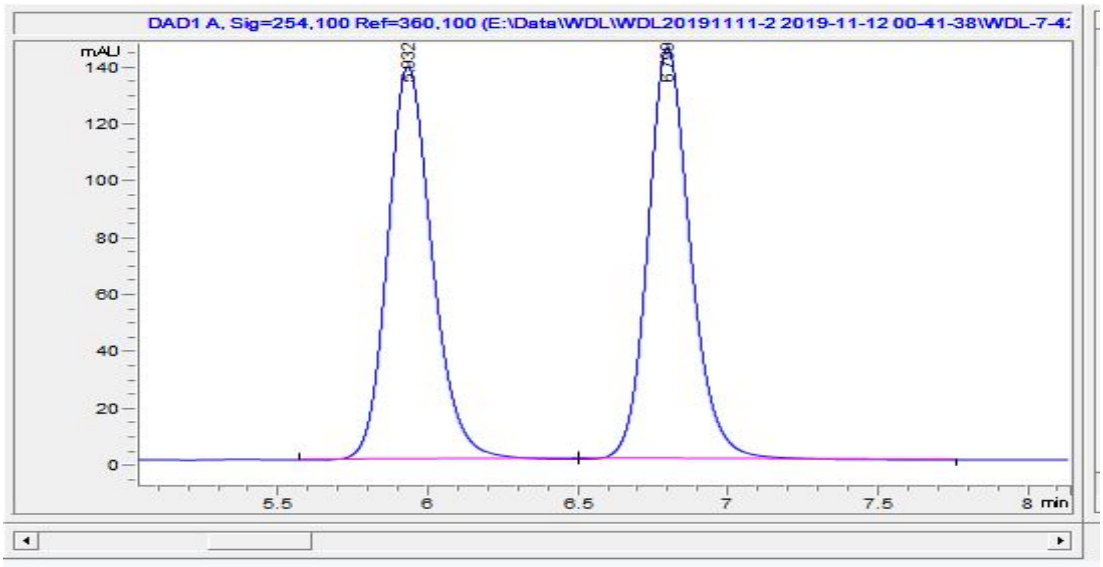
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.128	BV	4096.5	737.9	0.0848	48.742	0.79
2	4.426	VV R	4308.1	674.1	0.0969	51.258	0.764



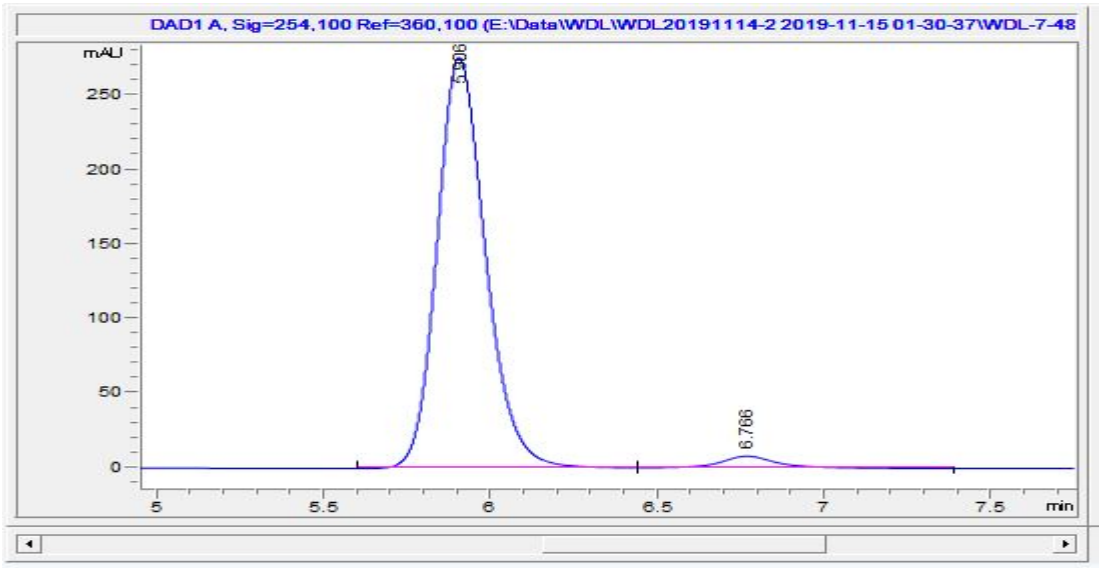
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.13	MF	1144.1	201.5	0.0946	88.302	0
2	4.425	FM	151.6	23.6	0.1069	11.698	0.758

(*R*)-dibenzyl-1-(2-(tert-butyl)-4-iodo-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**8a**)



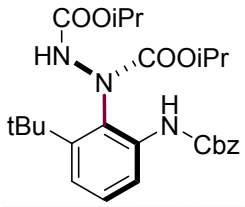


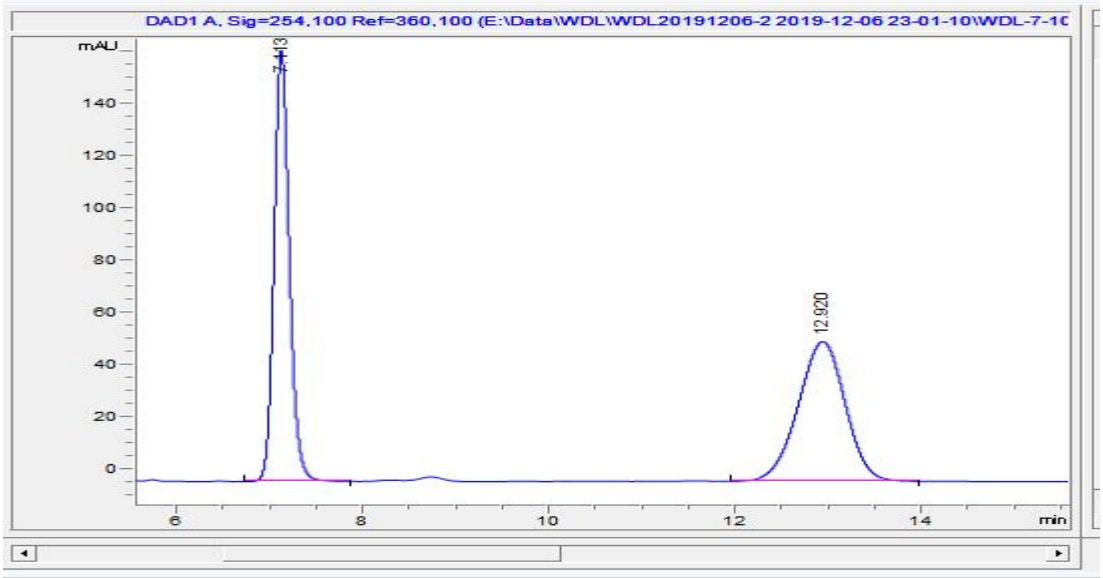
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.932	BB	1427.7	138.1	0.1591	49.917	0.792
2	6.799	BB	1432.5	144.6	0.1501	50.083	0.802



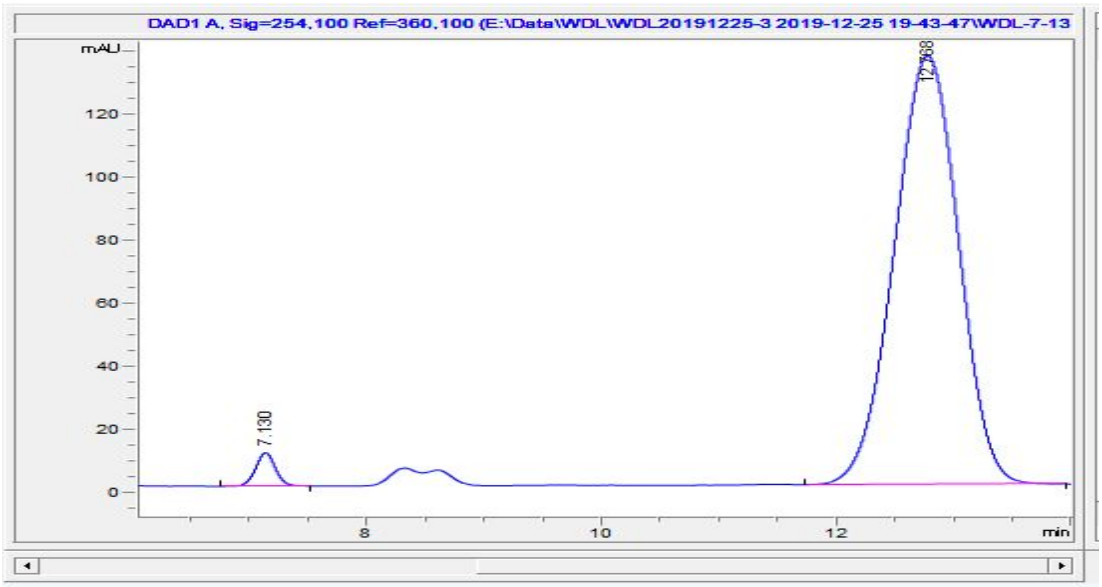
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.906	BB	2785.4	275.3	0.1555	96.718	0.79
2	6.766	BB	94.5	7.9	0.1762	3.282	0.824

(R)-1-(2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**9s**)



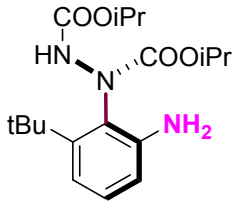


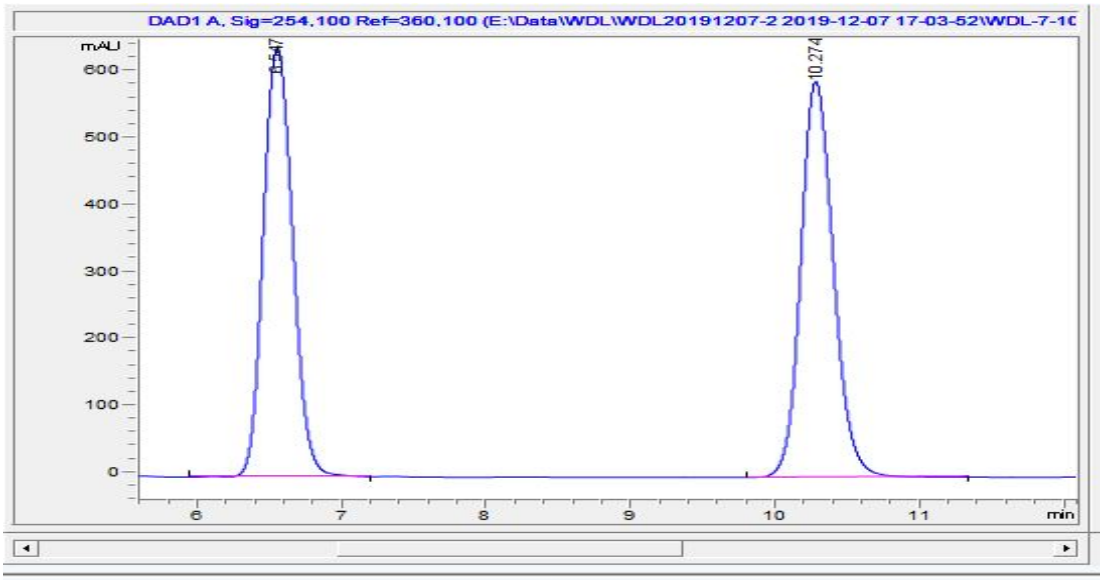
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	7.113	BB	1875.7	165.1	0.1741	49.979	0.831
2	12.92	BB	1877.3	53.5	0.5088	50.021	1.078



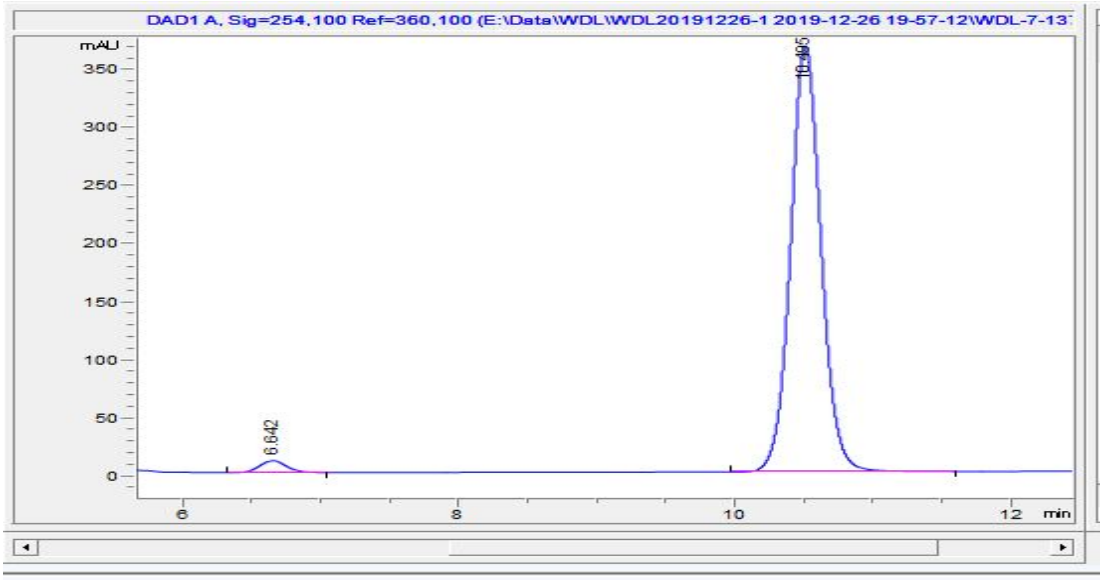
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	7.13	BB	123.6	10.6	0.1743	2.330	1.007
2	12.768	BB	5181.7	136	0.5077	97.670	1.112

(R)-diisopropyl 1-(2-amino-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**10s**)



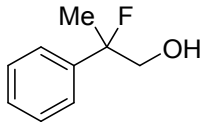


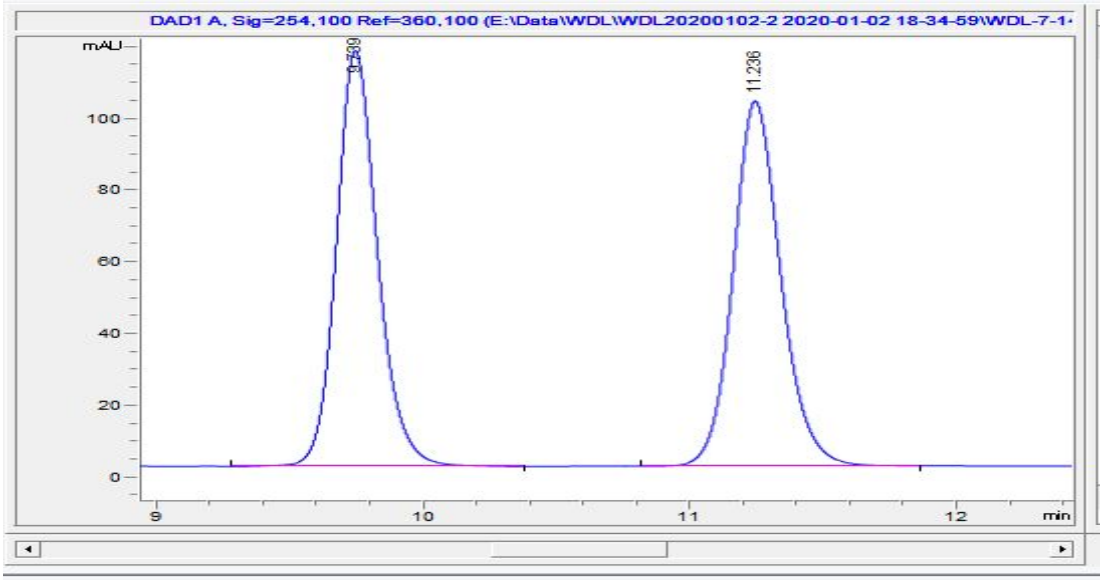
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.547	VB R	9037.8	640.1	0.1776	49.335	0.901
2	10.274	BB	9281.5	590.5	0.2034	50.665	0.794



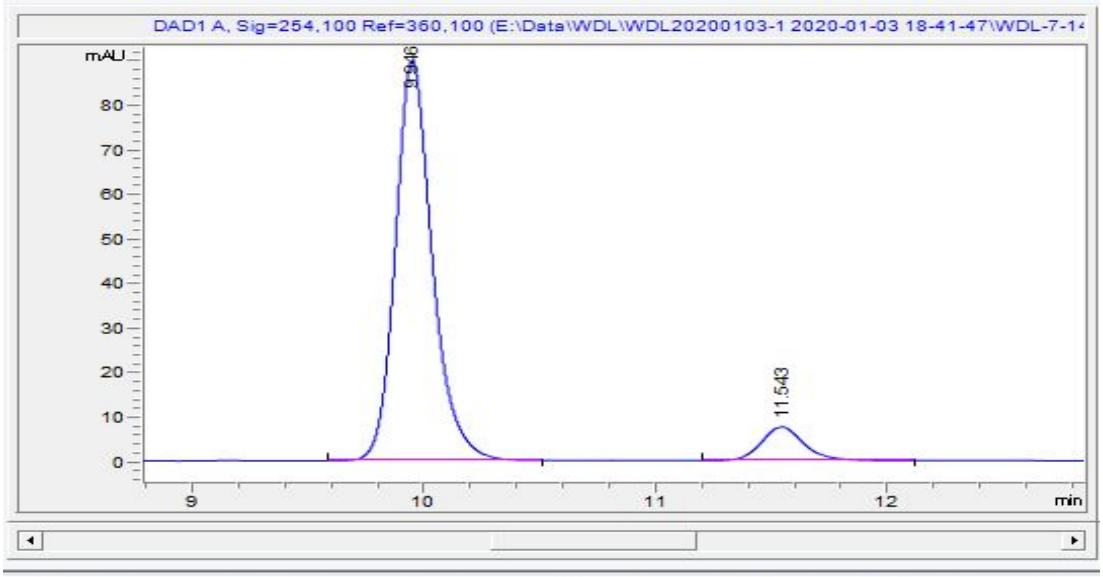
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.642	BB	136.4	10.2	0.198	2.358	0.925
2	10.495	BB	5647.9	367.2	0.239	97.642	0.889

2-fluoro-2-phenylpropan-1-ol (**12a**)





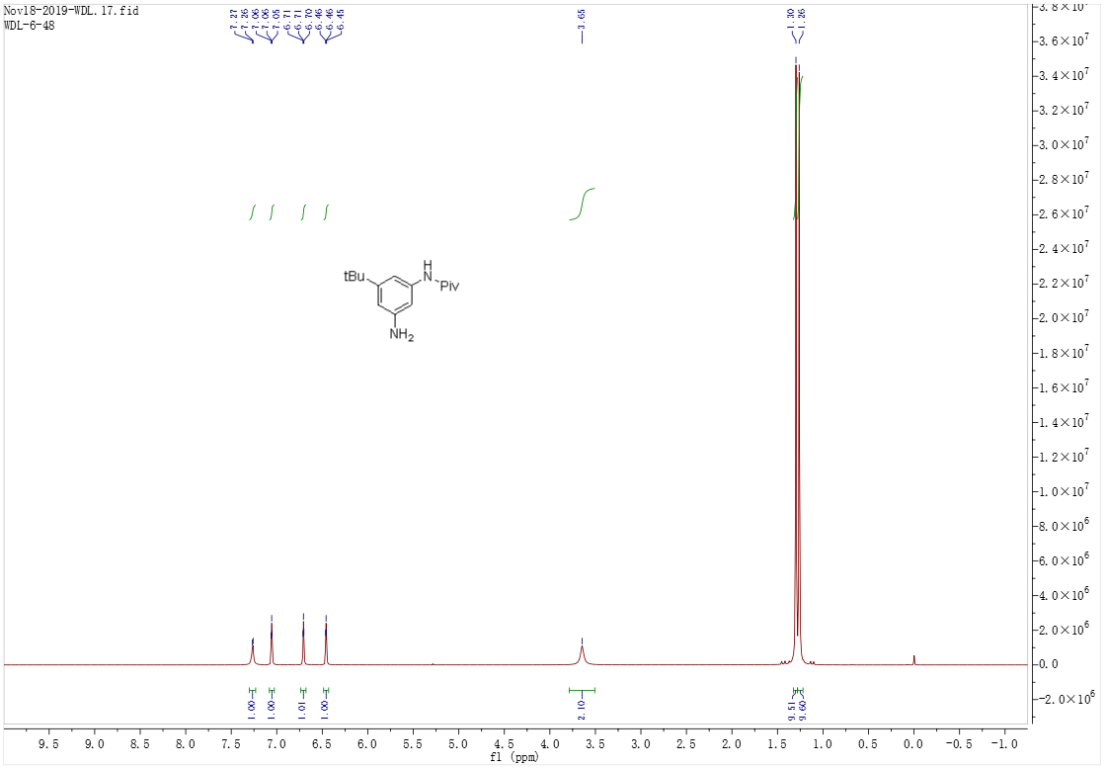
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.739	BB	1248.5	116.1	0.1639	49.593	0.821
2	11.236	BB	1269	102	0.1897	50.407	0.832

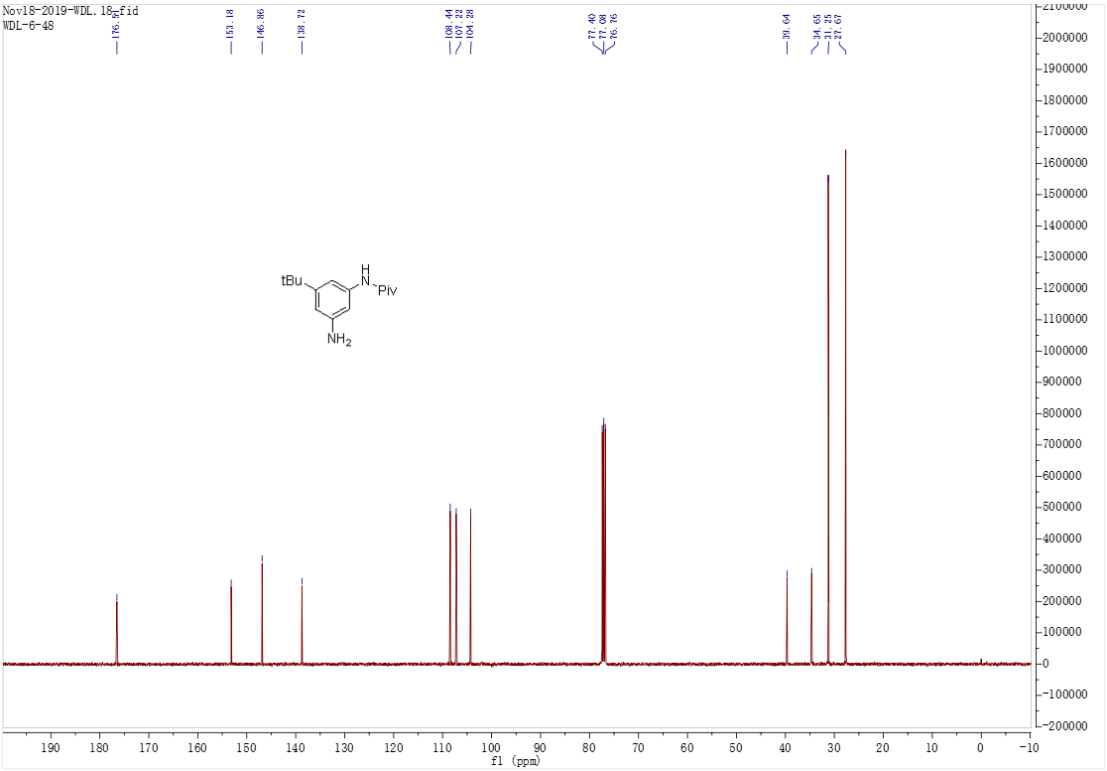


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.946	BB	1000.1	90	0.1677	91.122	0.792
2	11.543	BB	97.4	7.6	0.1793	8.878	0.858

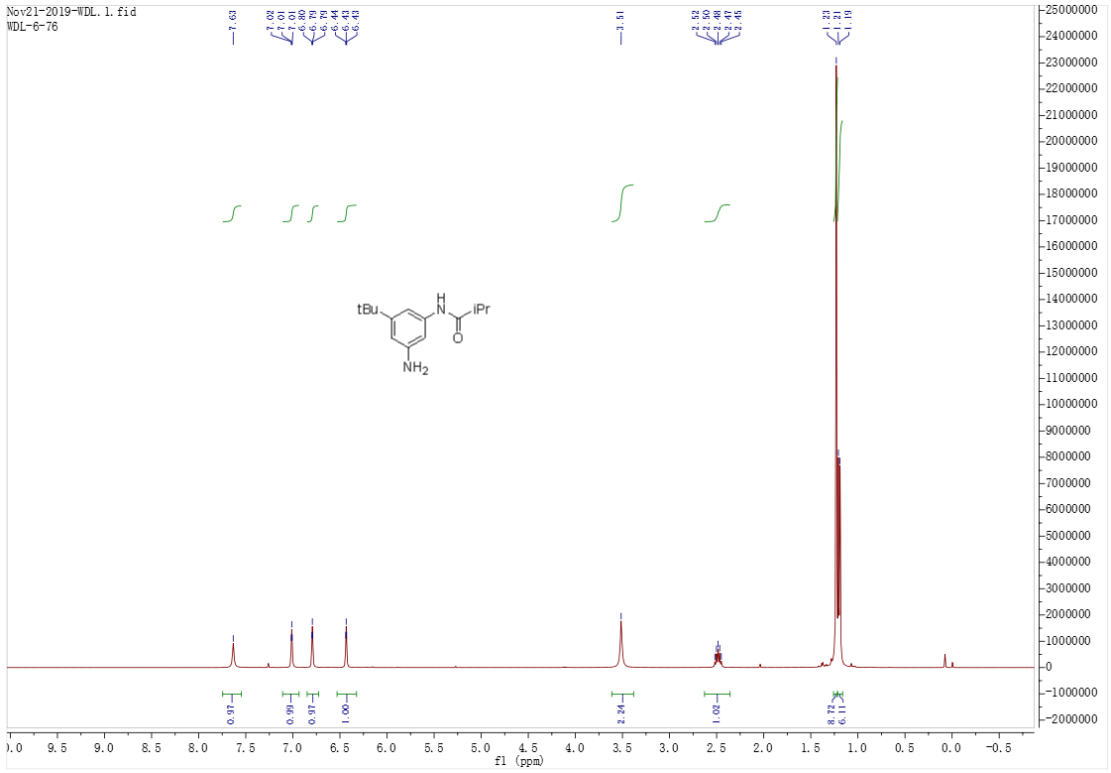
NMR spectrums:

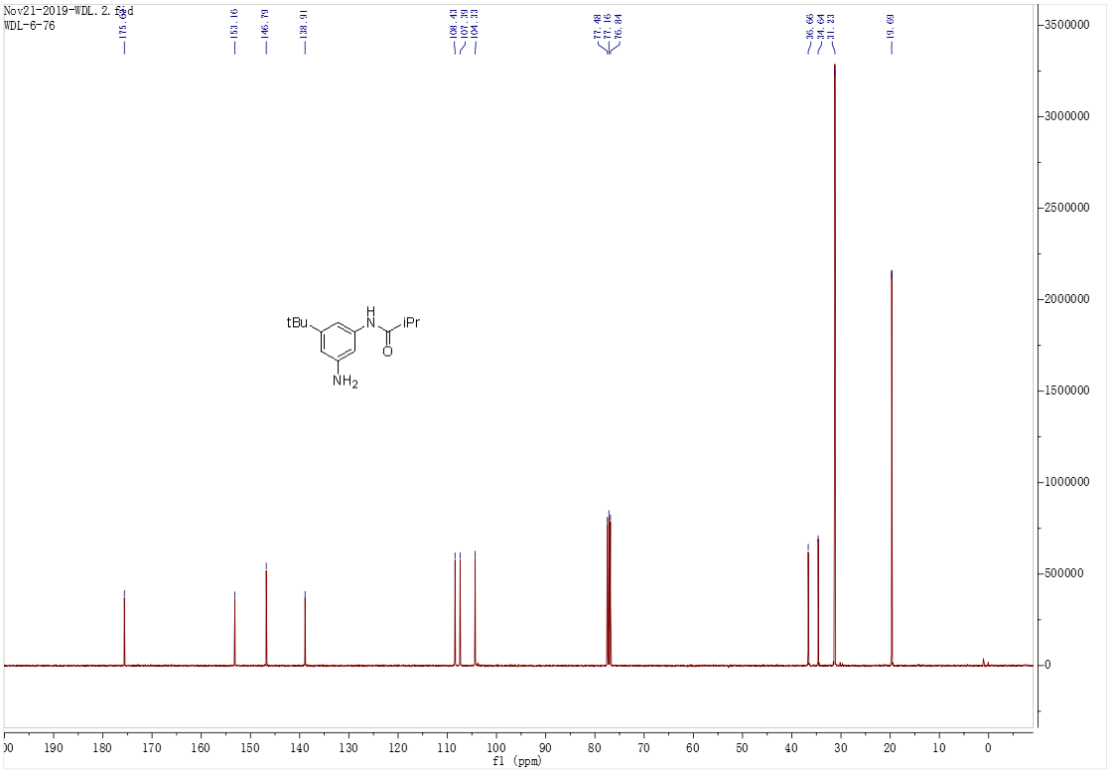
N-(3-amino-5-(tert-butyl)phenyl)pivalamide (**3a**)



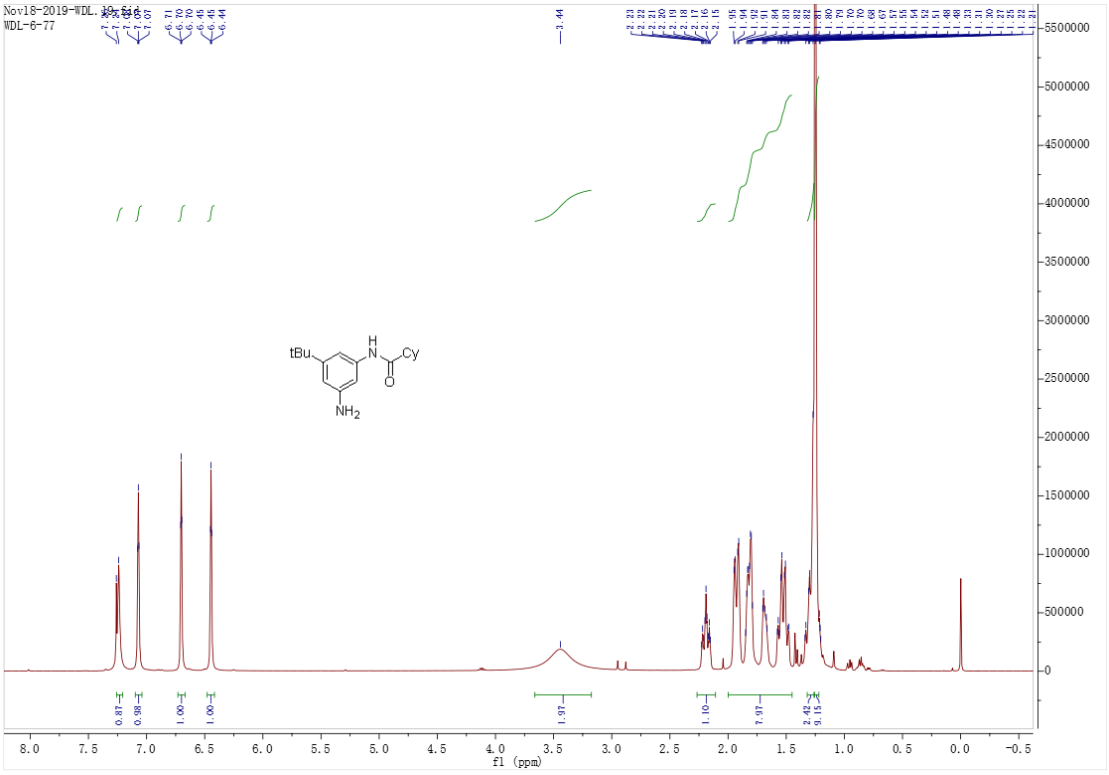


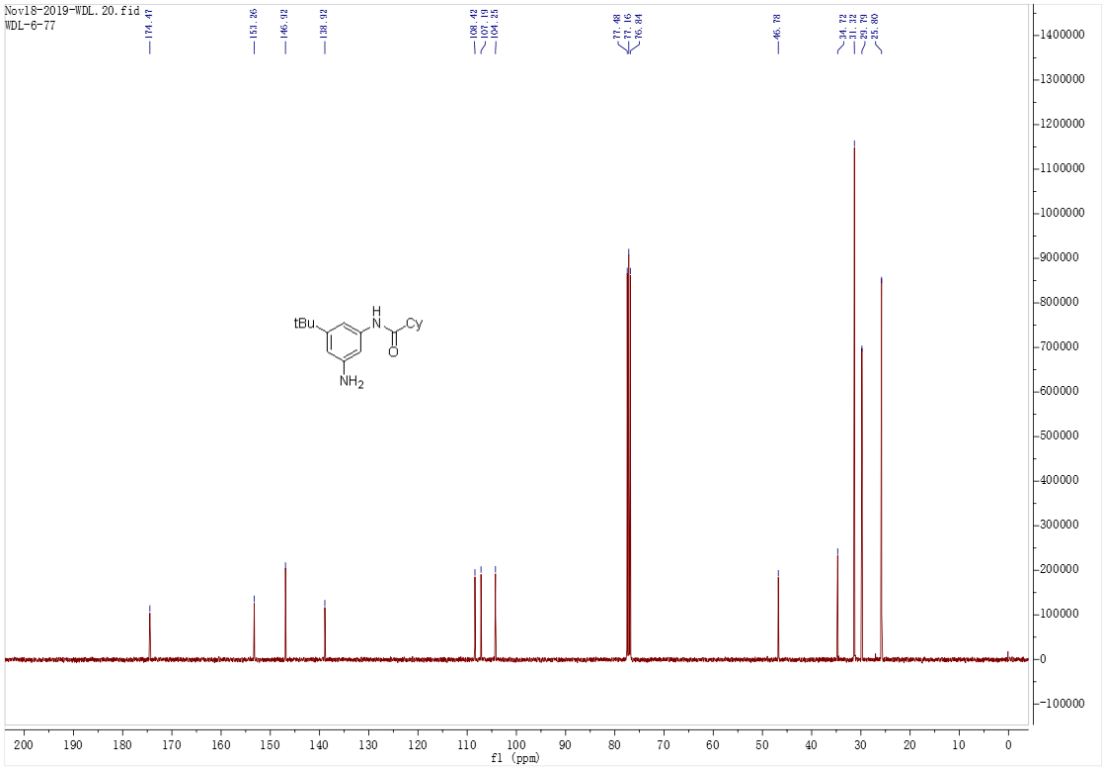
N-(3-amino-5-(tert-butyl)phenyl)isobutyramide (**3b**)



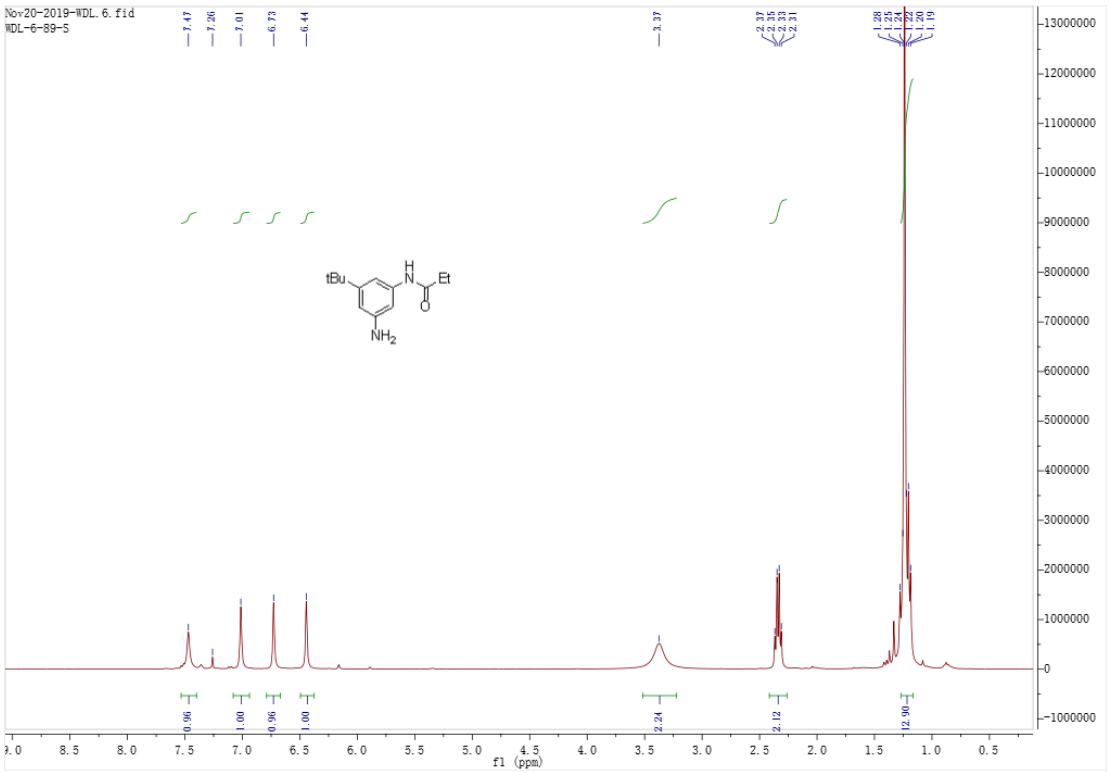


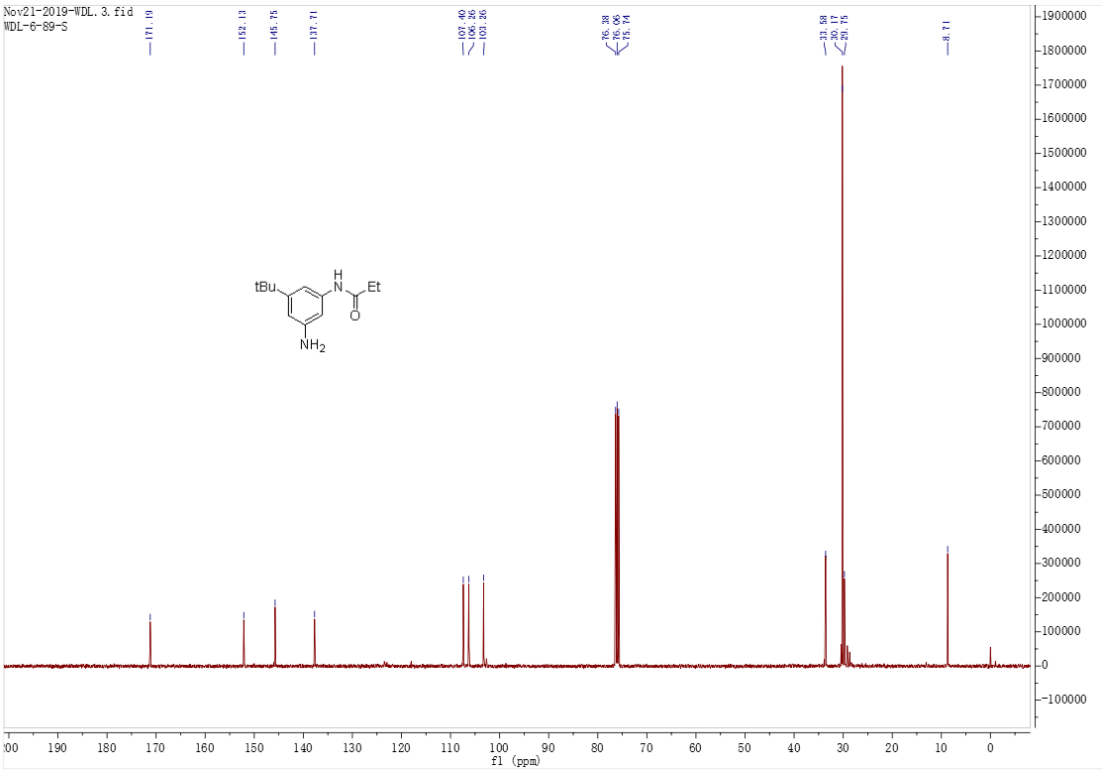
N-(3-amino-5-(tert-butyl)phenyl)cyclohexanecarboxamide (**3c**)



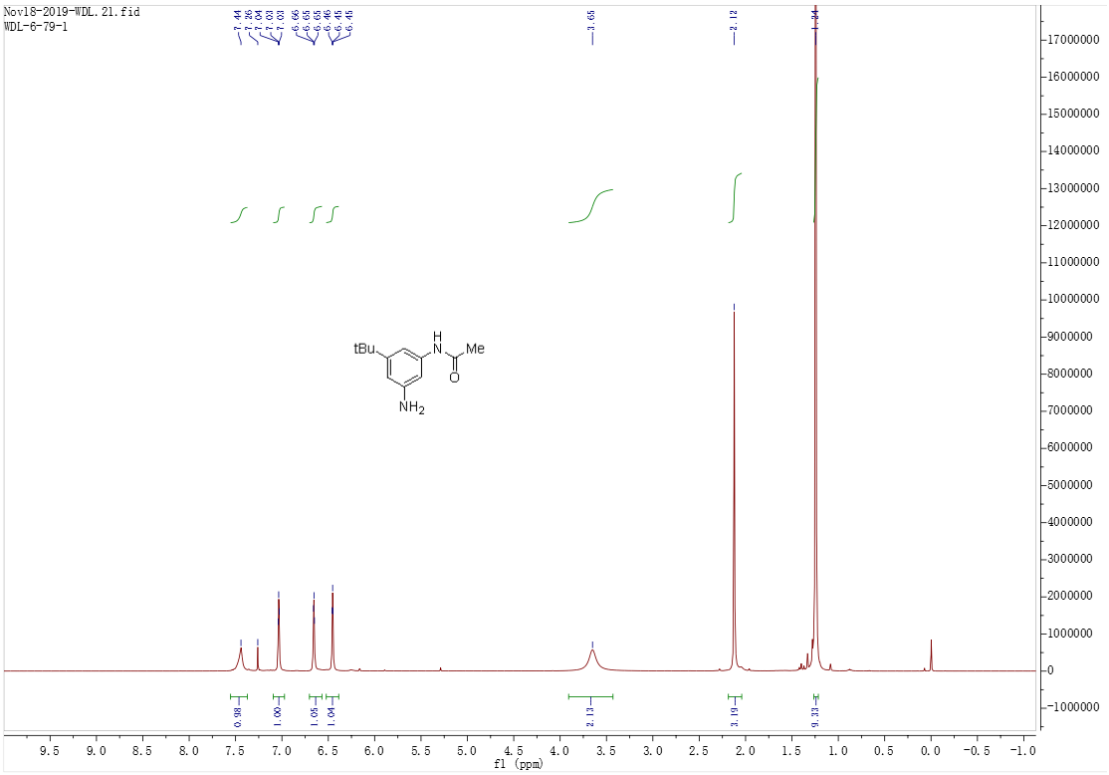


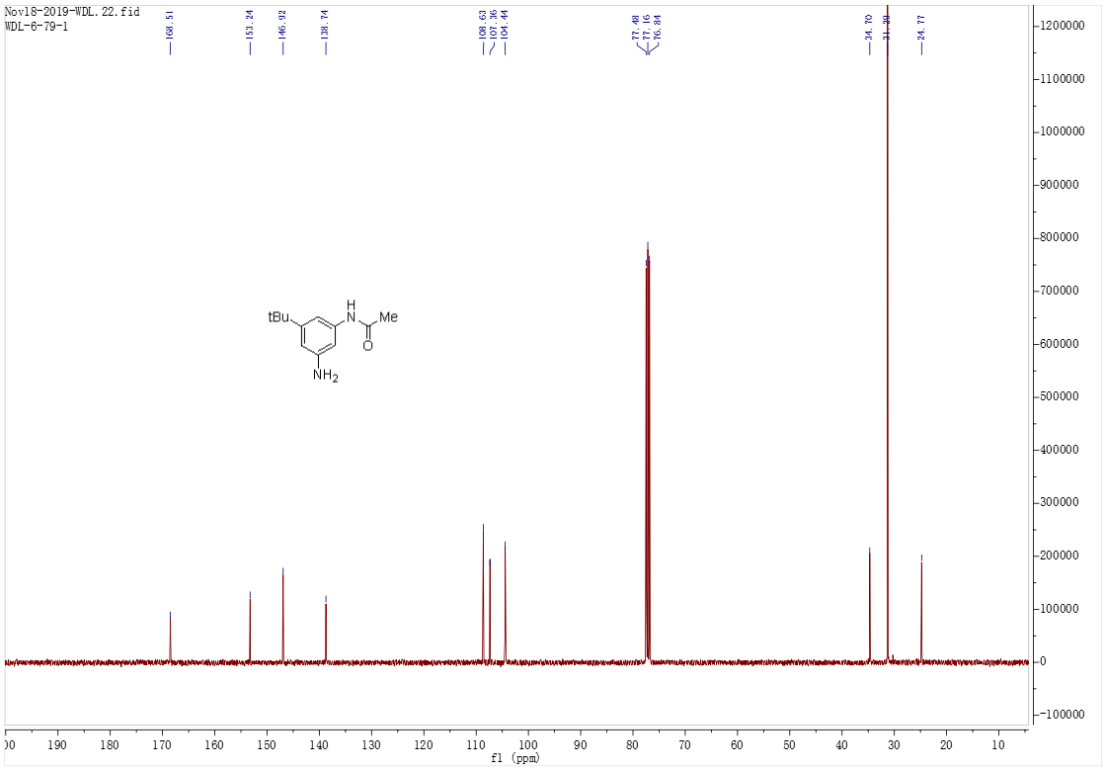
N-(3-amino-5-(tert-butyl)phenyl)propionamide (**3d**)



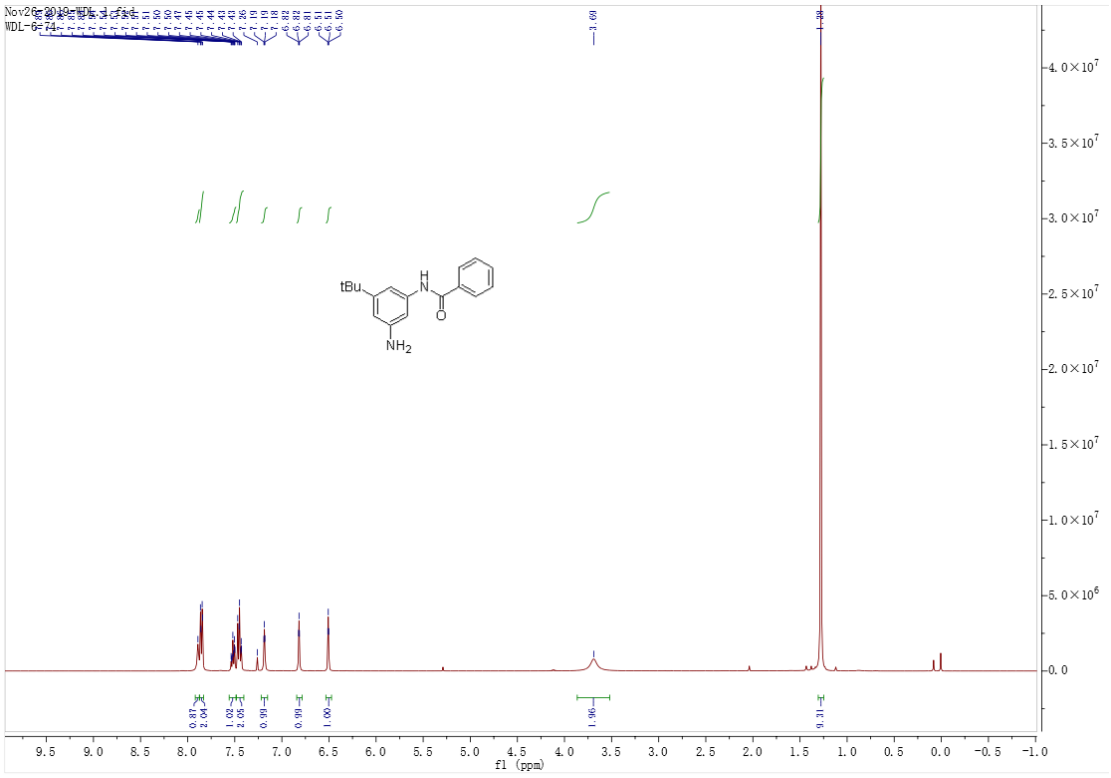


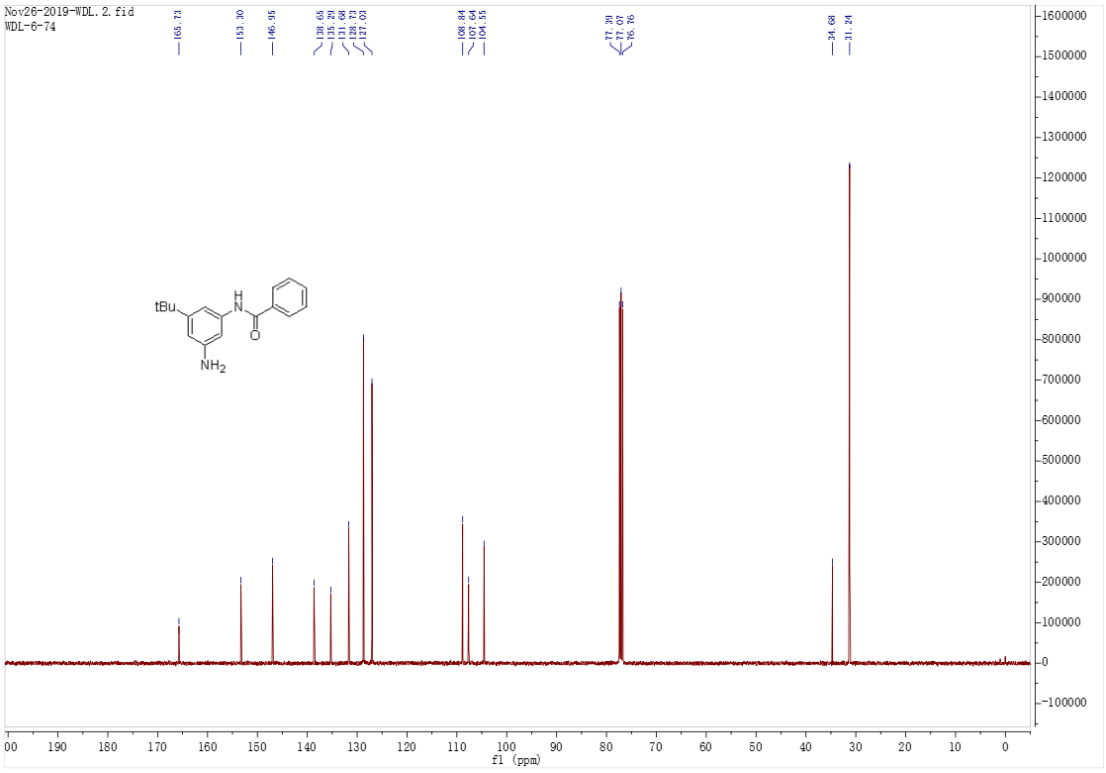
N-(3-amino-5-(tert-butyl)phenyl)acetamide (**3e**)



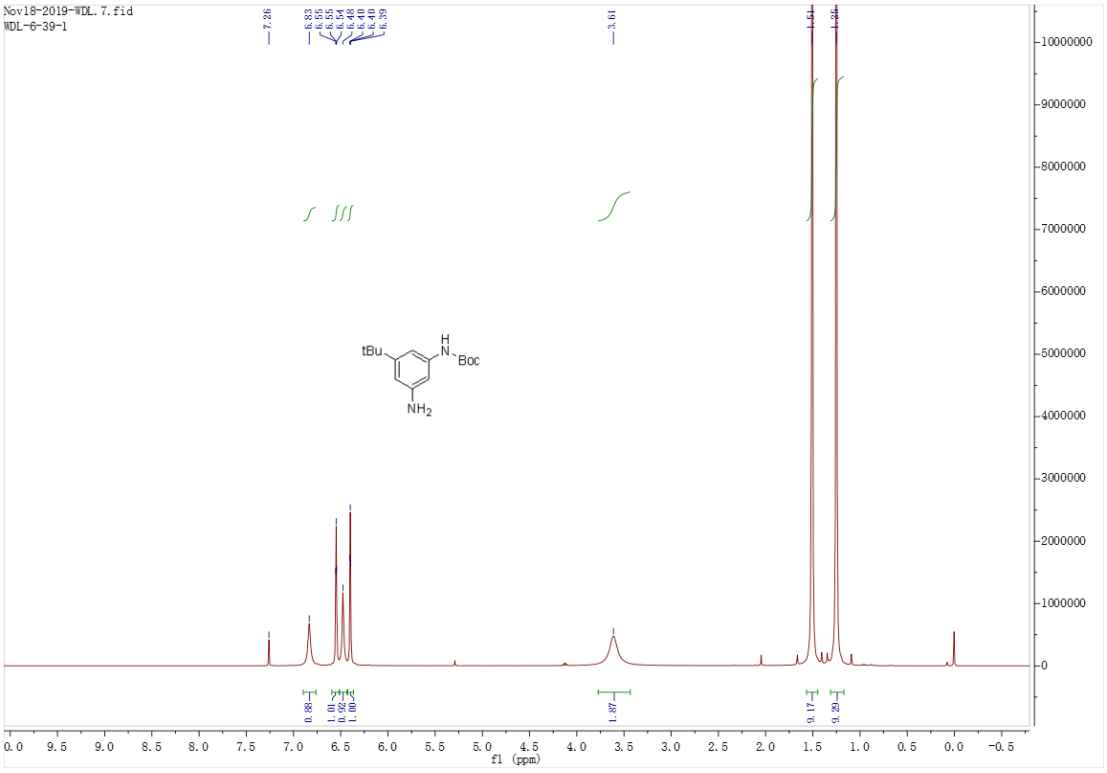


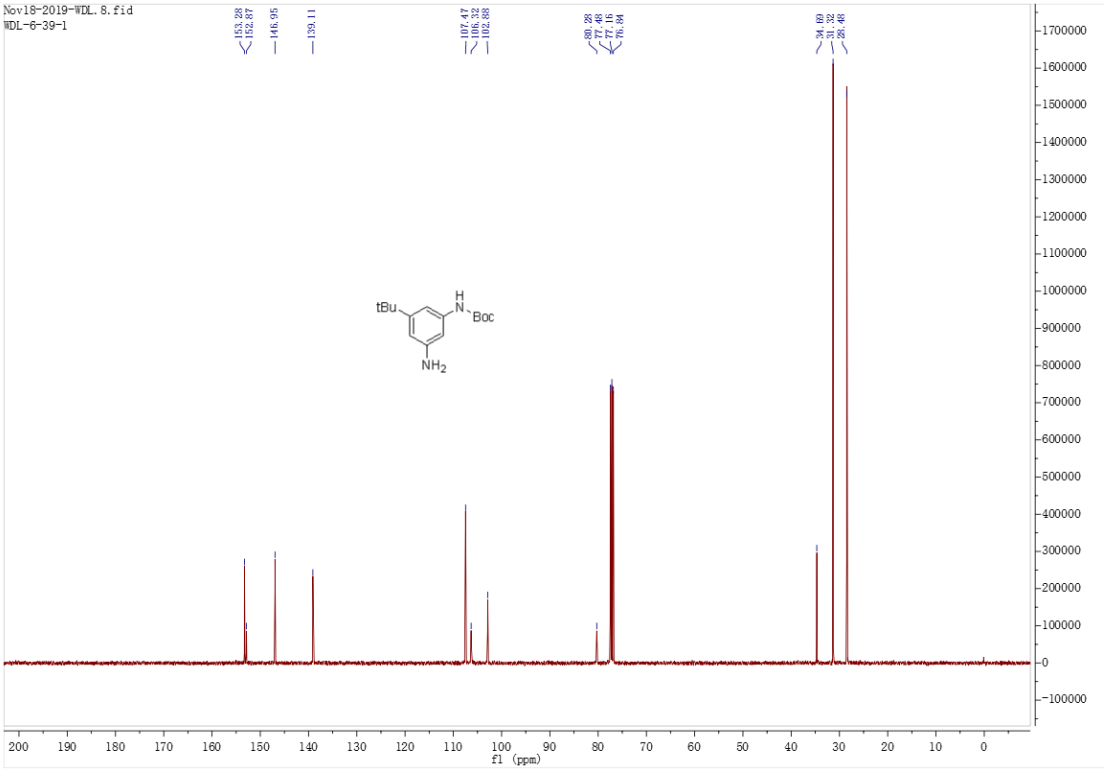
N-(3-amino-5-(tert-butyl)phenyl)benzamide (**3f**)



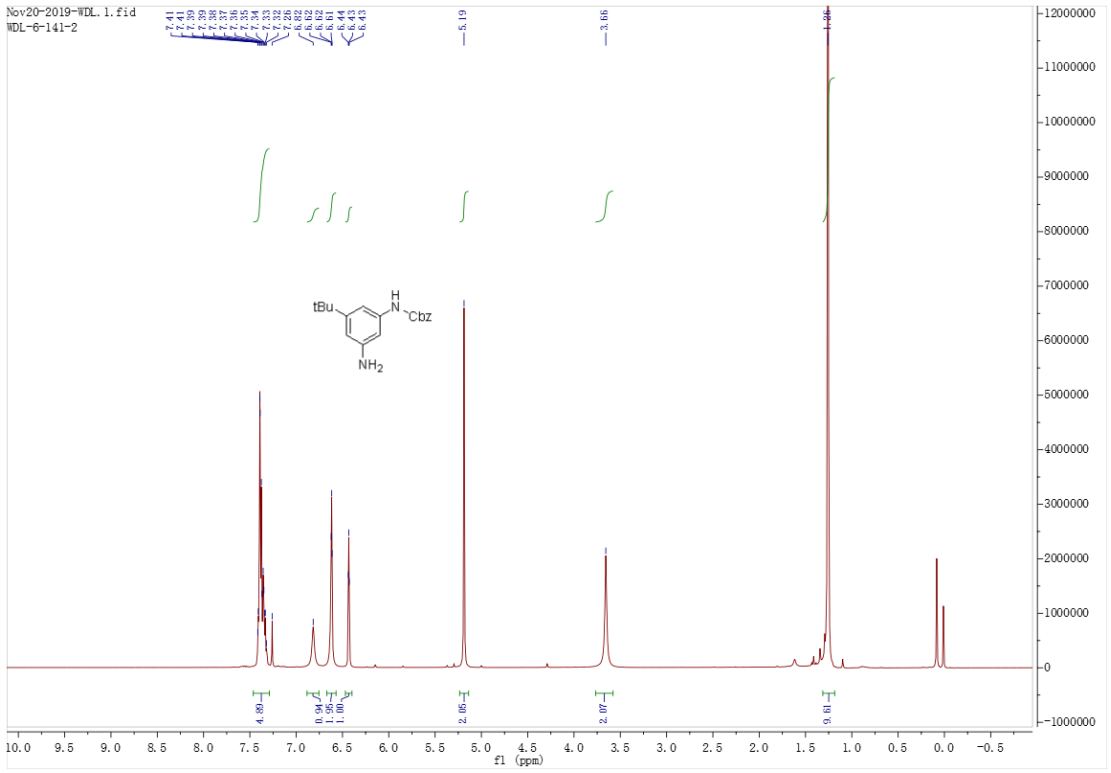


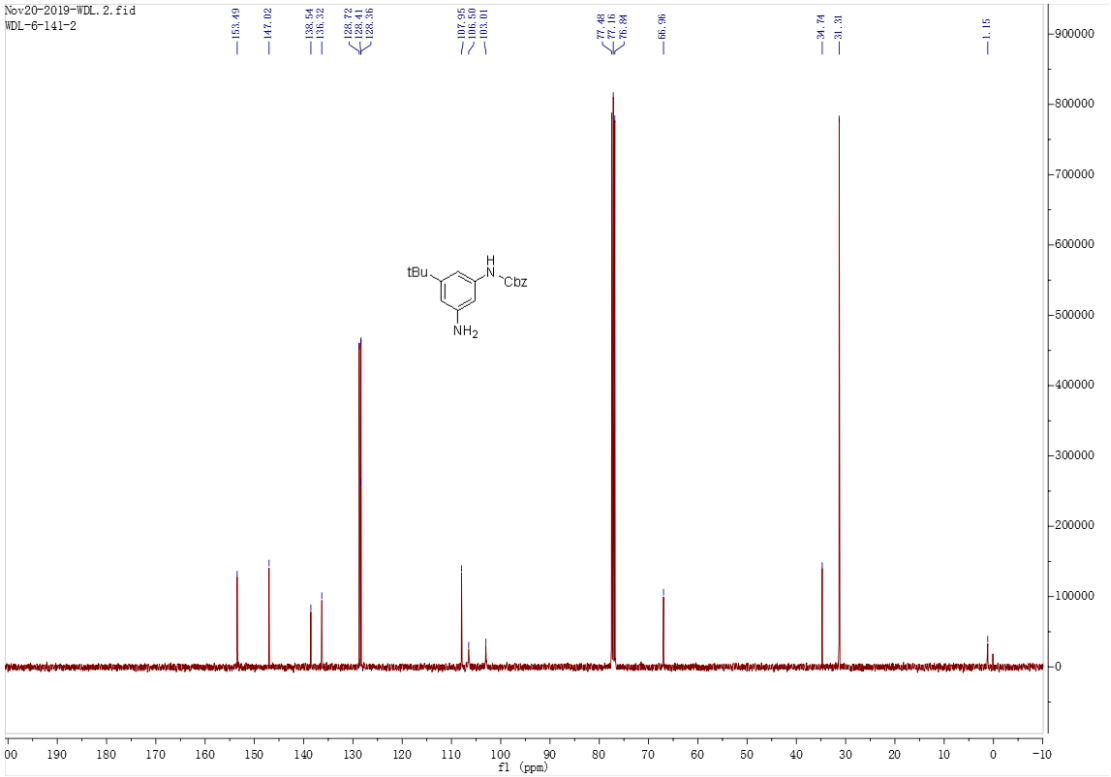
tert-butyl (3-amino-5-(tert-butyl)phenyl)carbamate (**3g**)



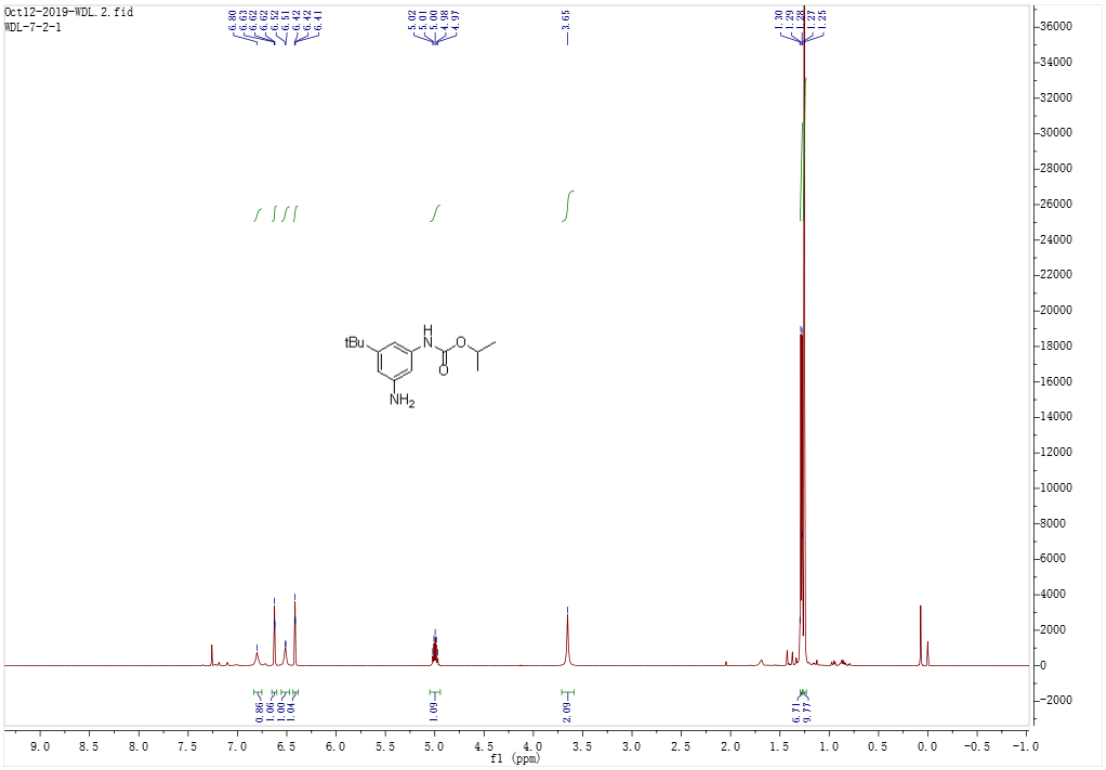


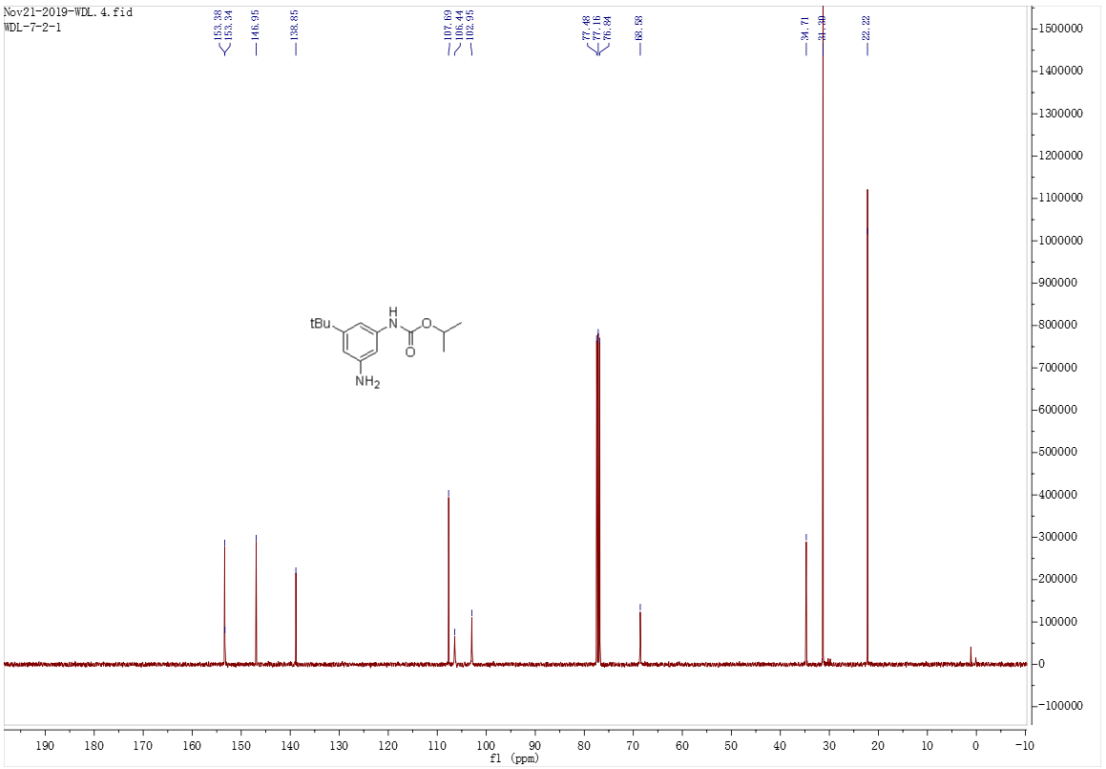
benzyl (3-amino-5-(tert-butyl)phenyl)carbamate (**3h**)



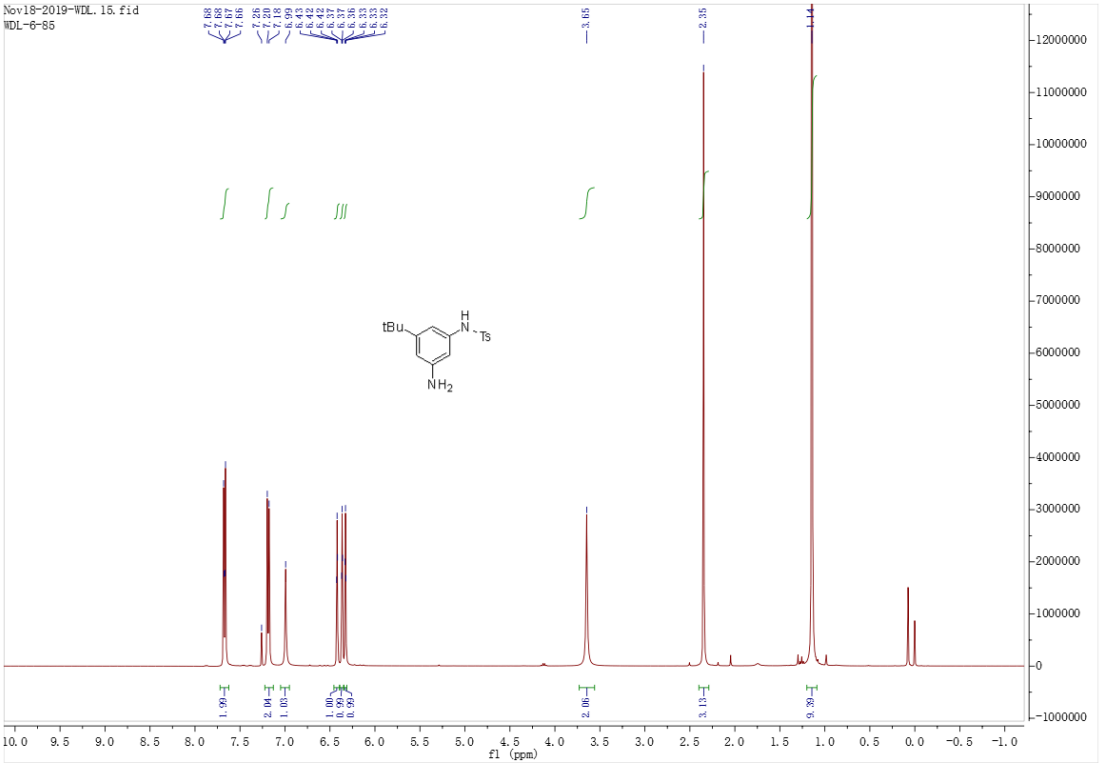


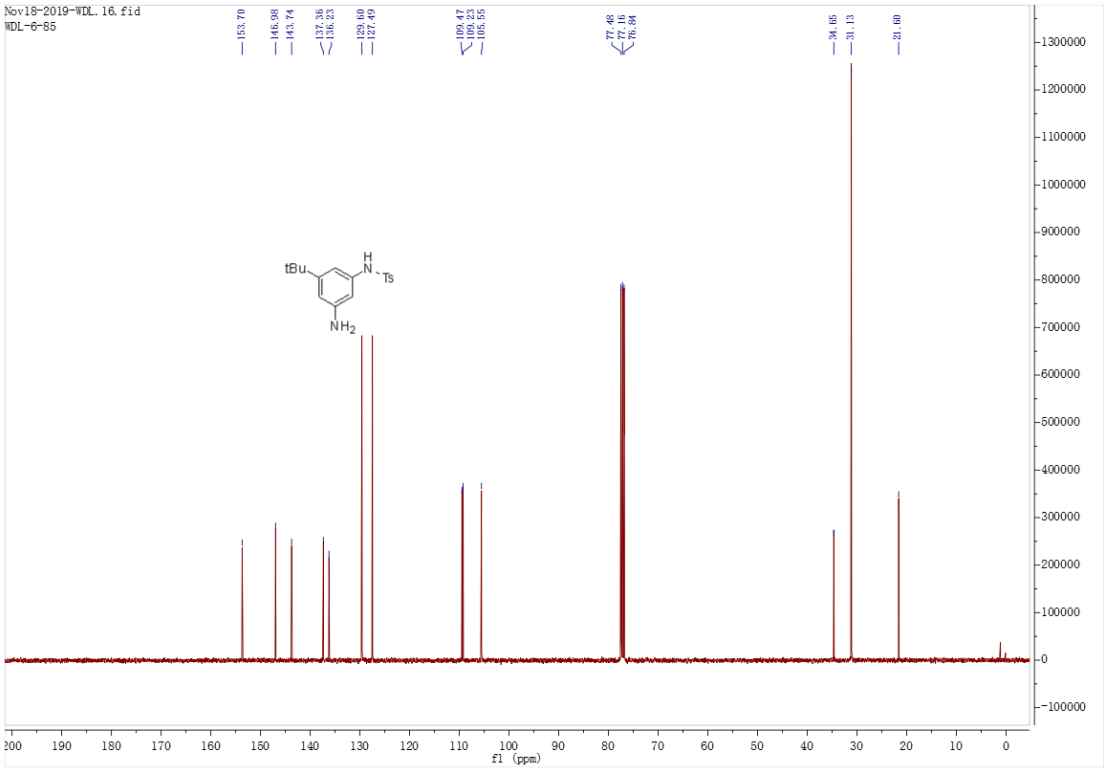
isopropyl (3-amino-5-(tert-butyl)phenyl)carbamate (**3i**)



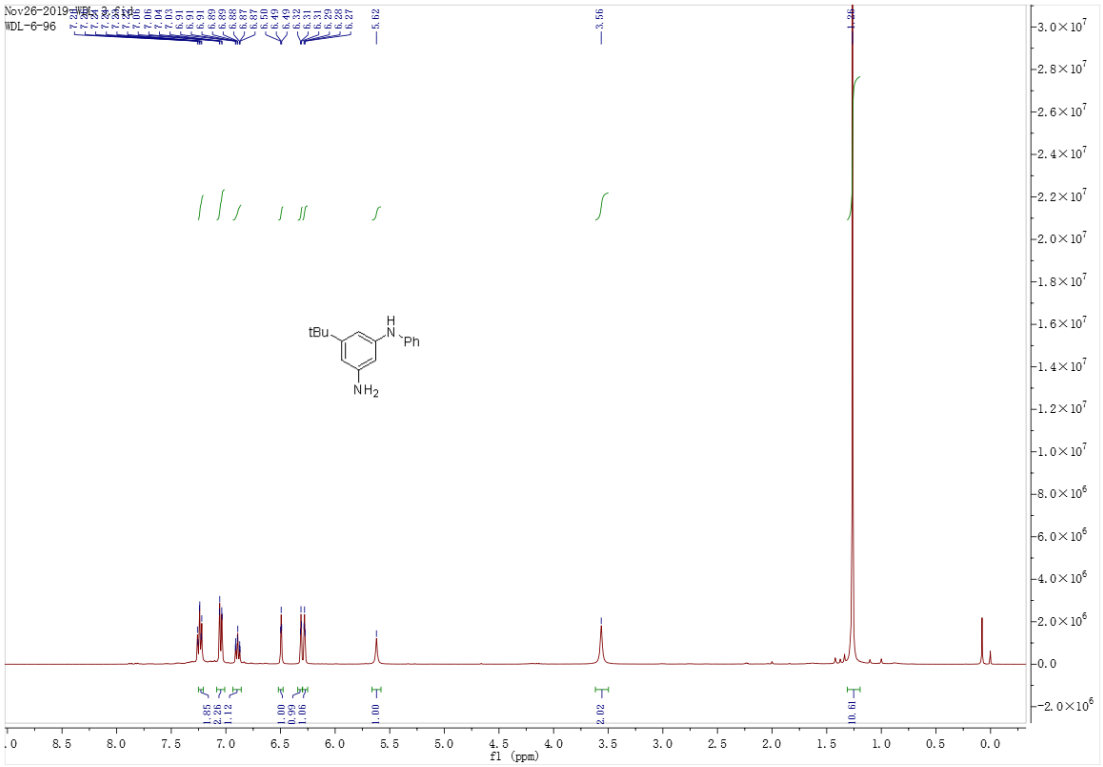


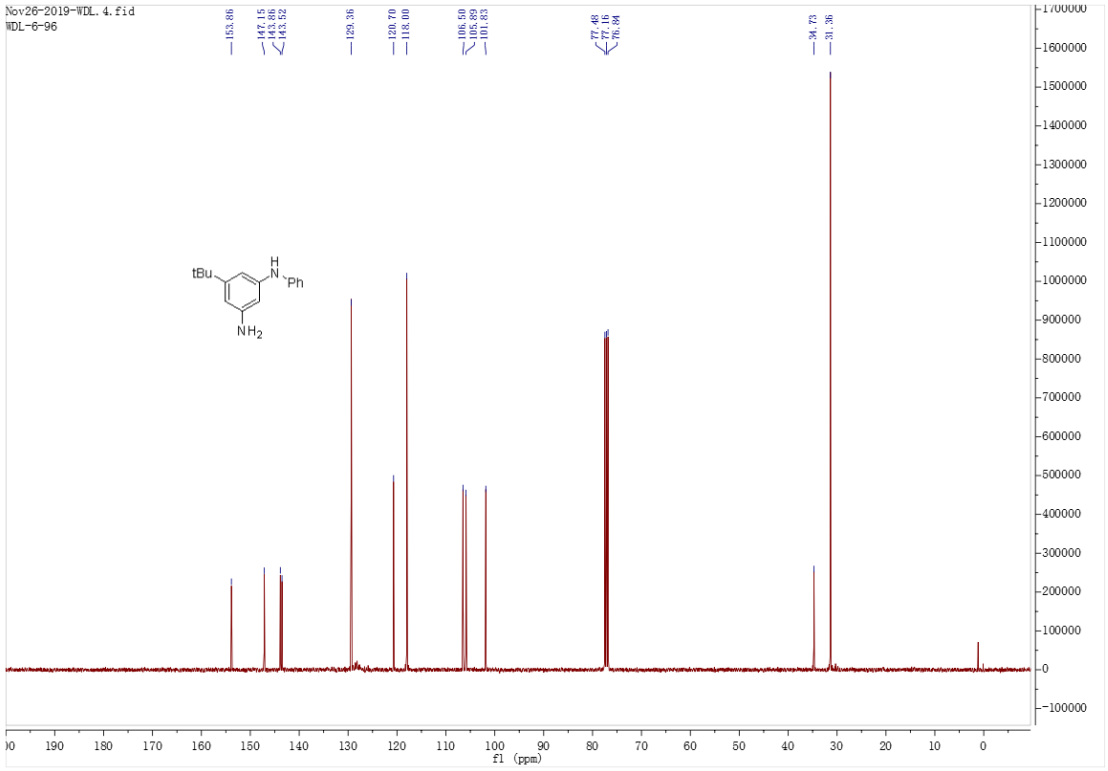
N-(3-amino-5-(tert-butyl)phenyl)-4-methylbenzenesulfonamide (**3j**)



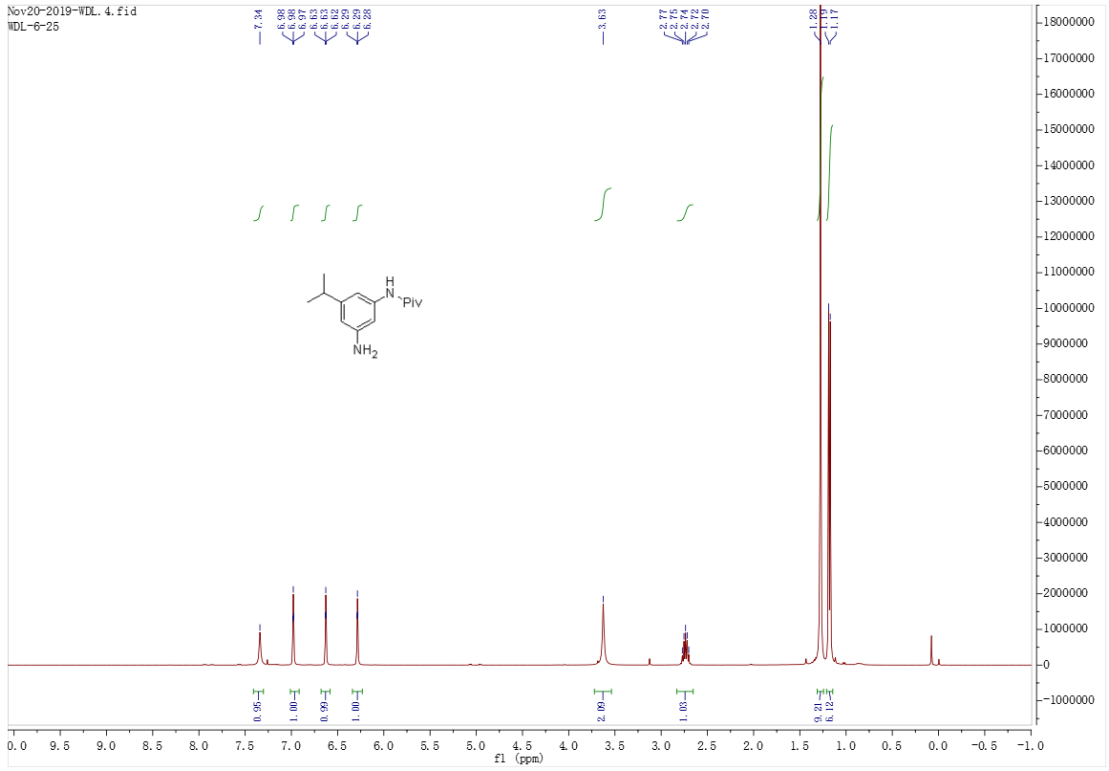


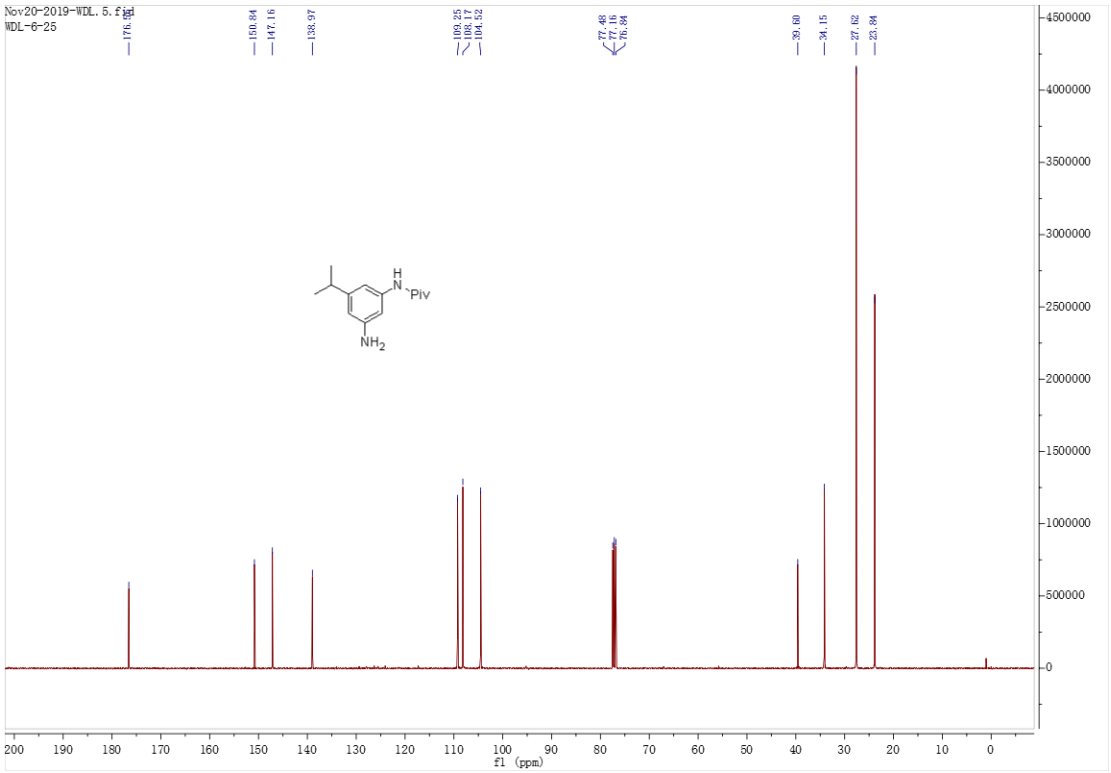
5-(tert-butyl)-N1-phenylbenzene-1,3-diamine (**3k**)



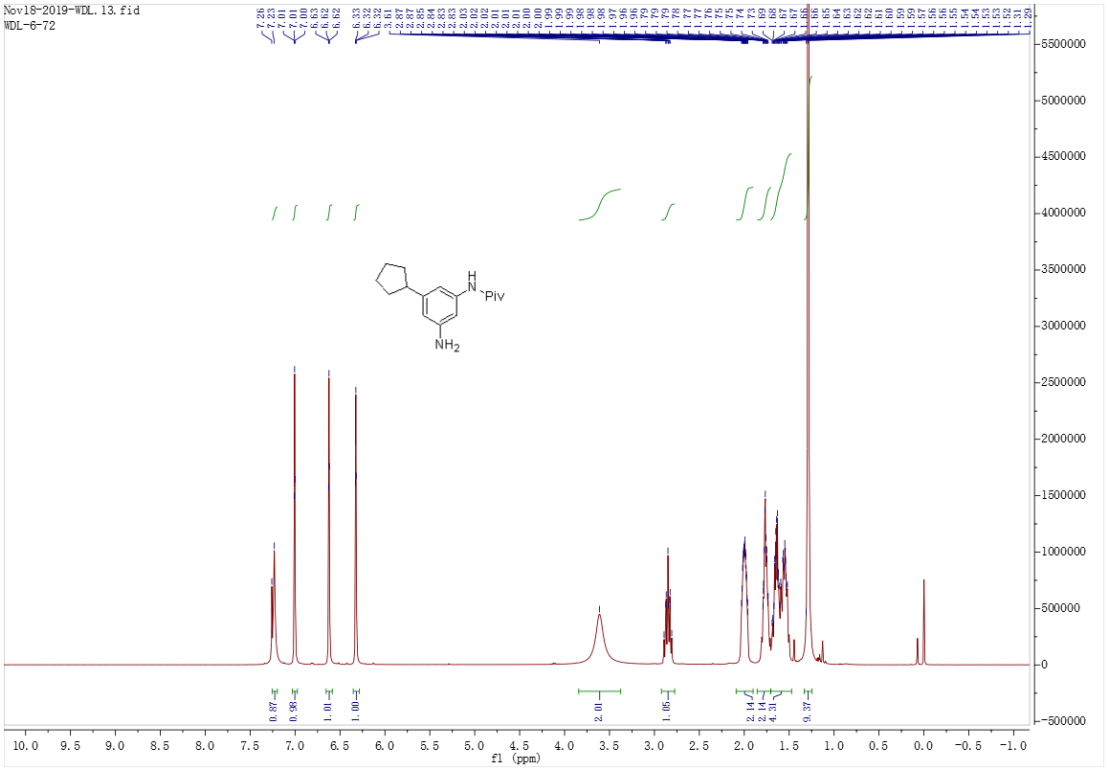


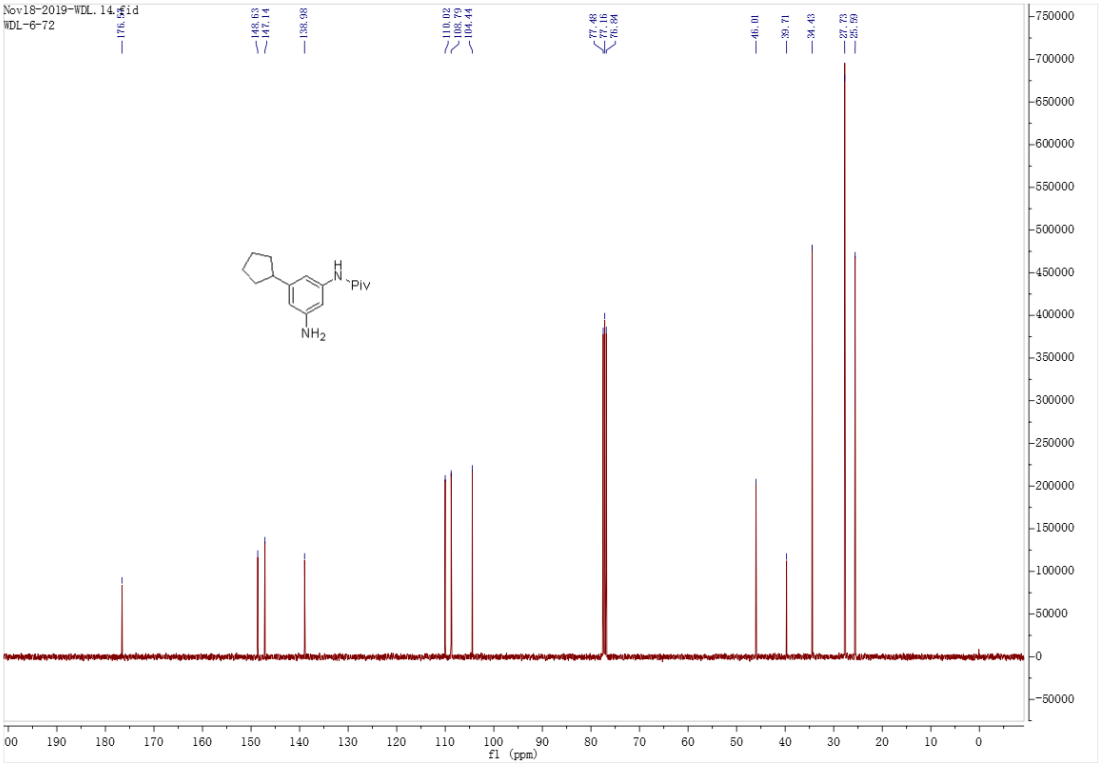
N-(3-amino-5-isopropylphenyl)pivalamide (**3l**)



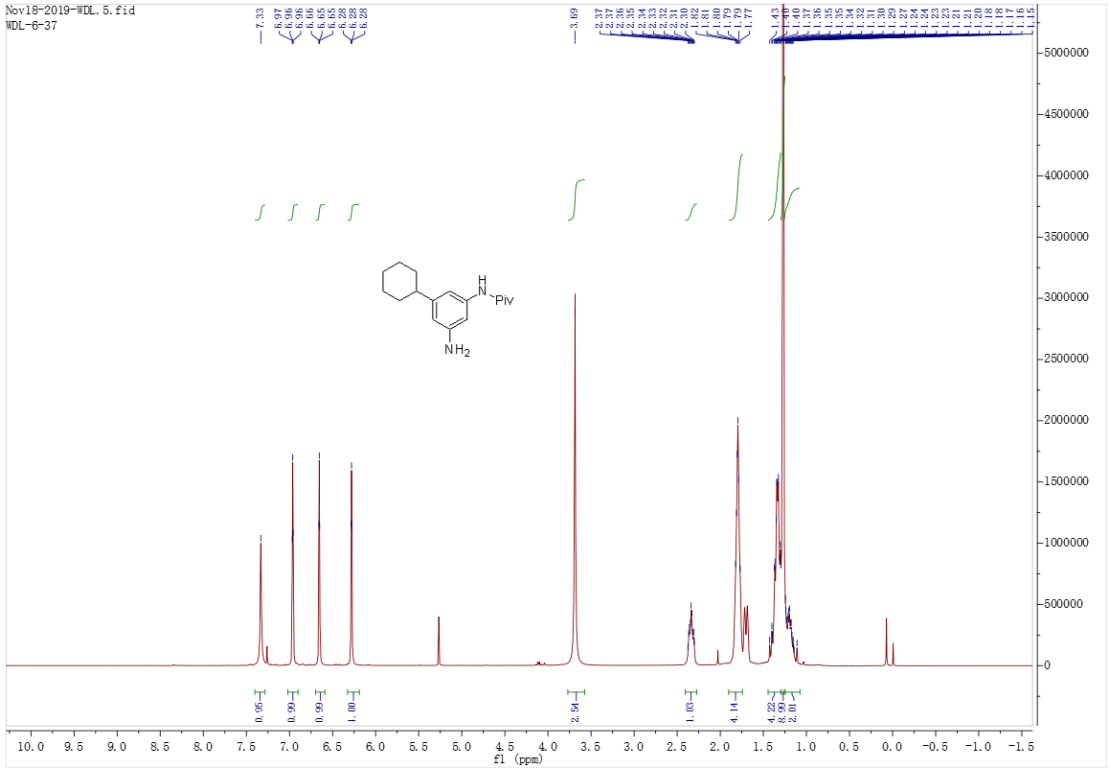


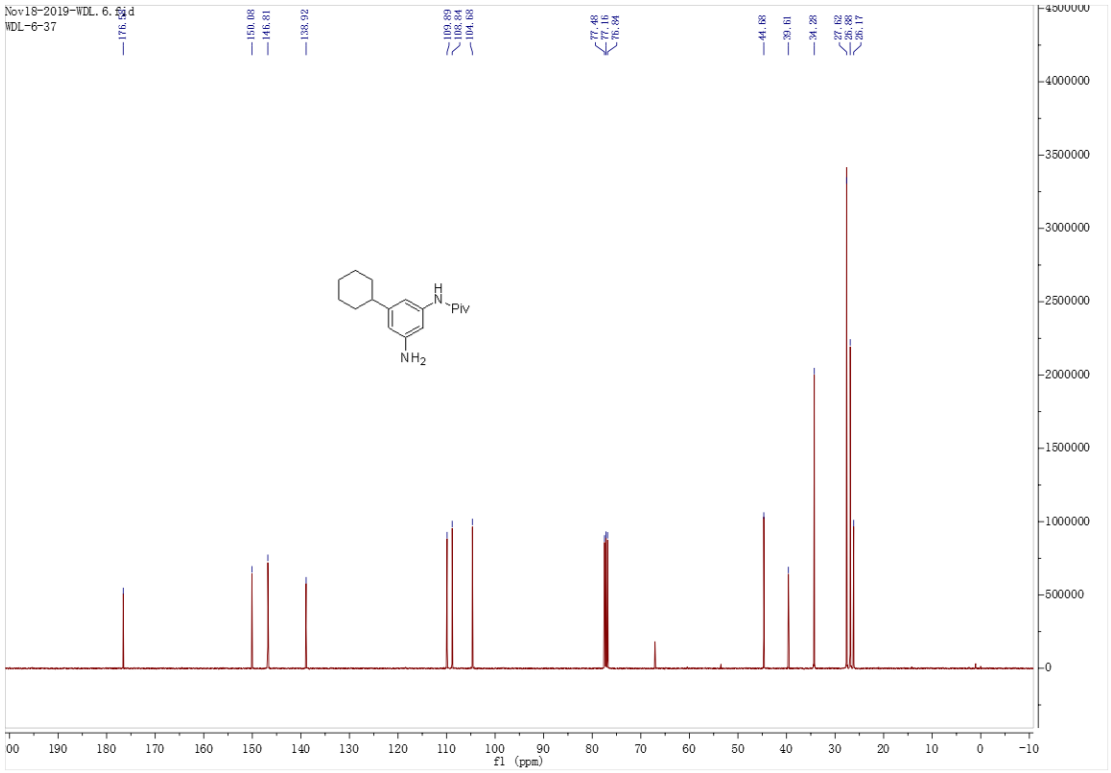
N-(3-amino-5-cyclopentylphenyl)pivalamide (**3m**)



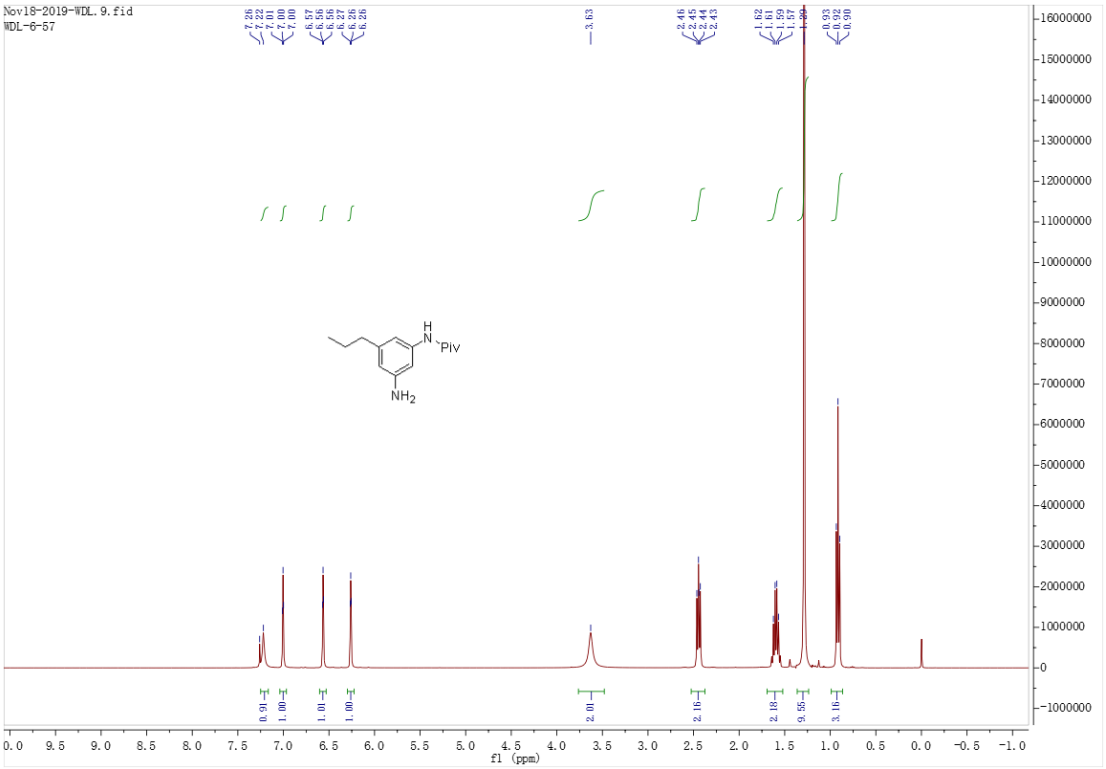


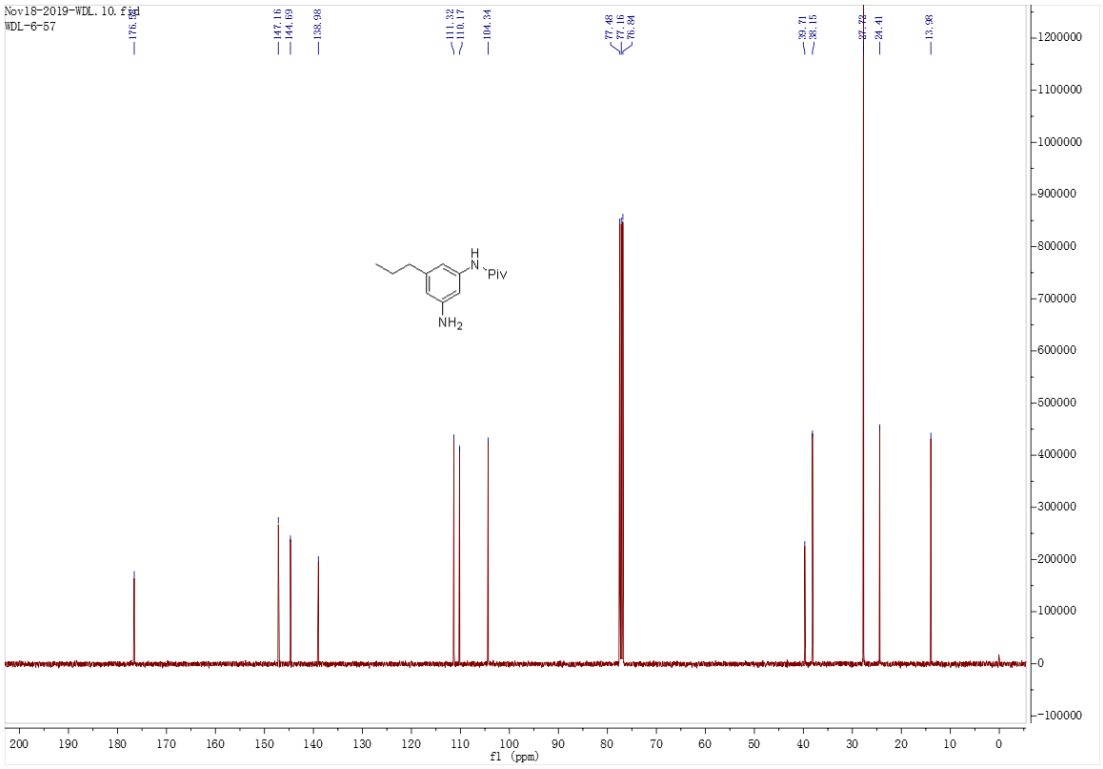
N-(3-amino-5-cyclohexylphenyl)pivalamide (**3n**)



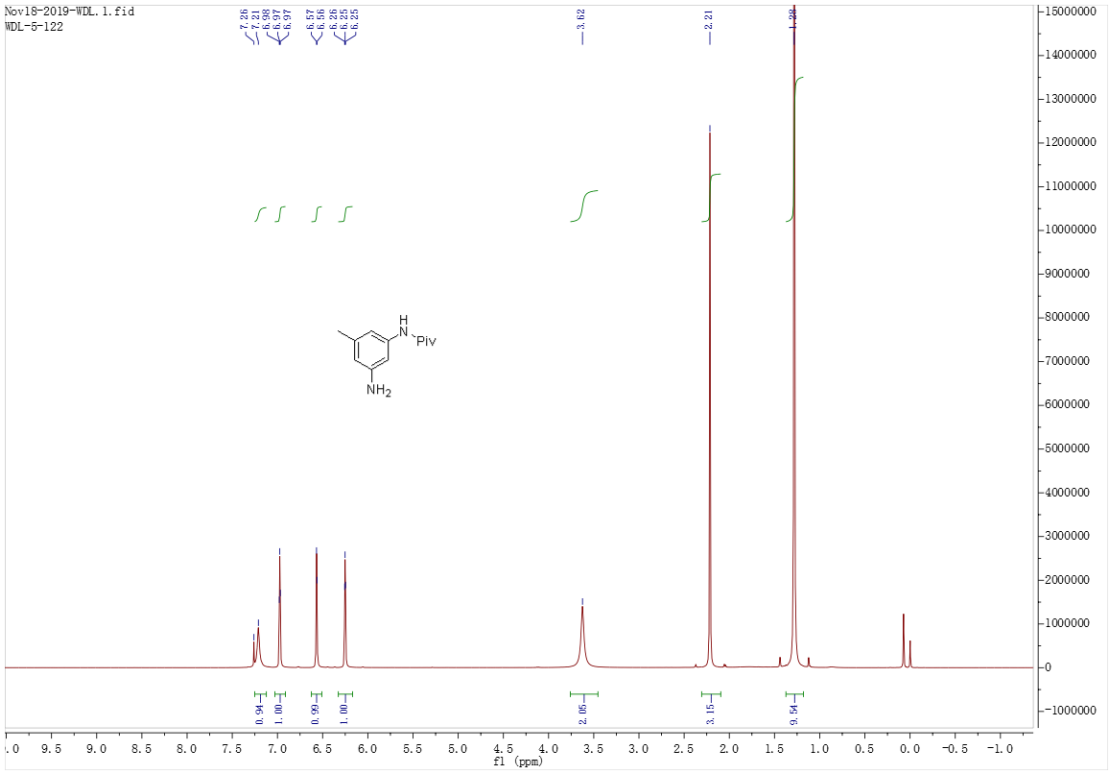


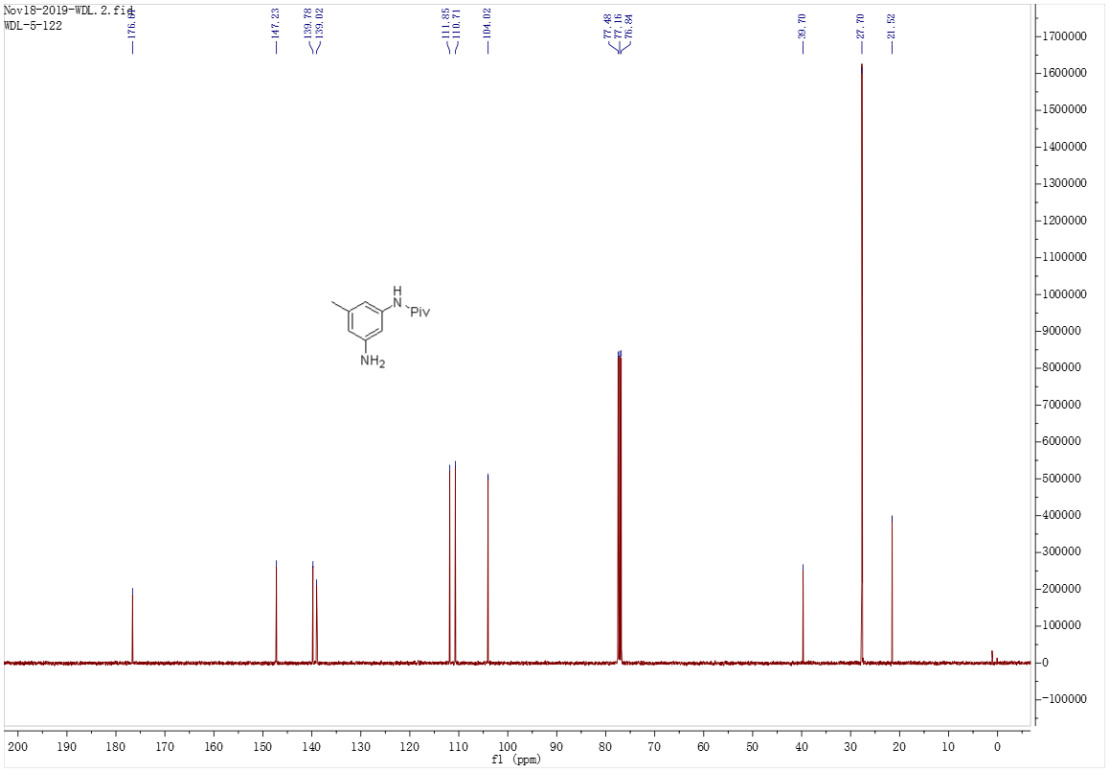
N-(3-amino-5-propylphenyl)pivalamide (**3o**)



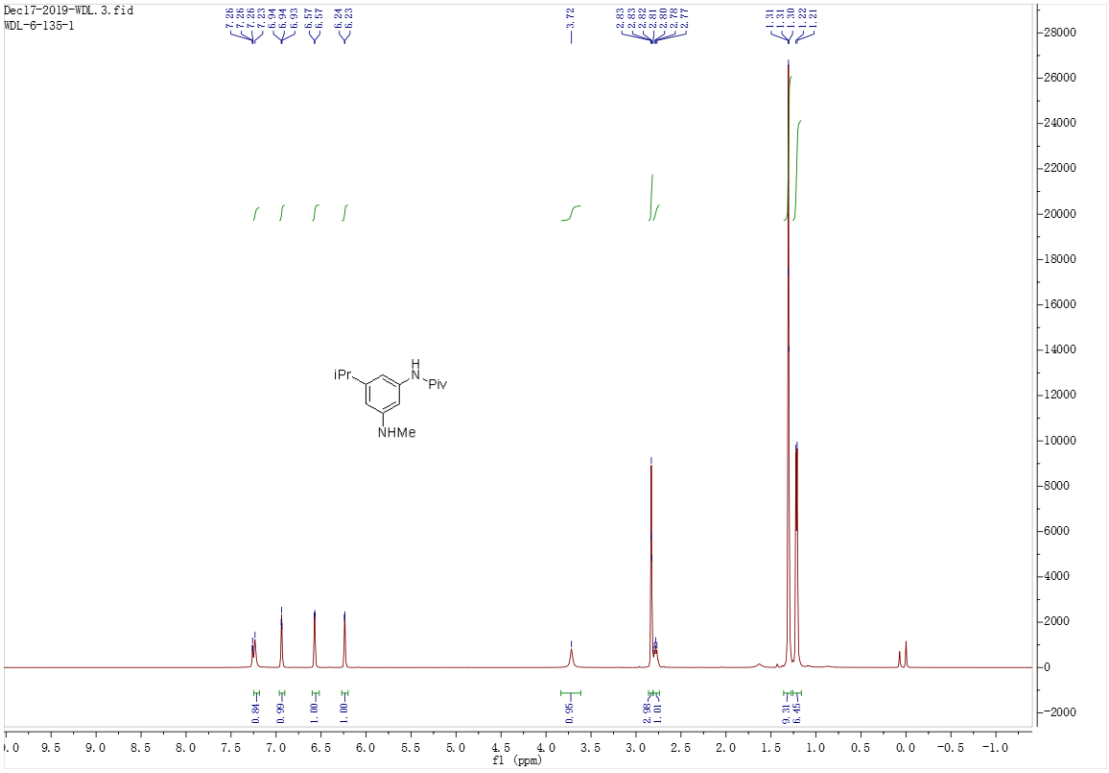


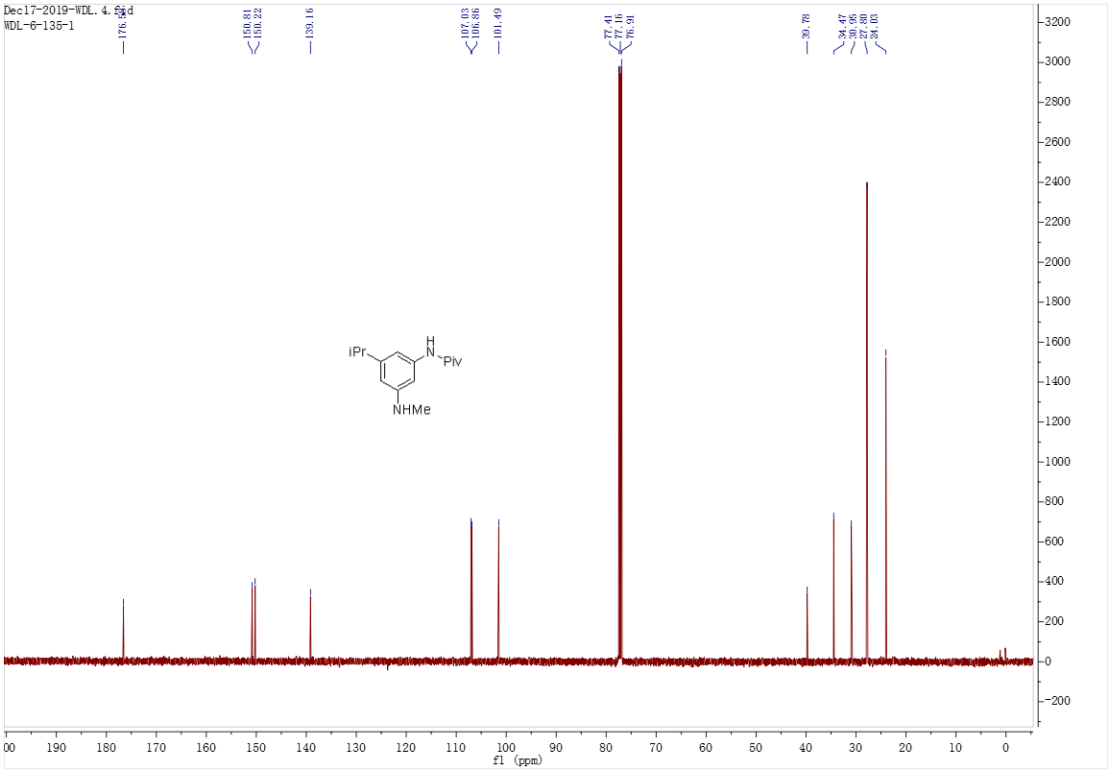
N-(3-amino-5-methylphenyl)pivalamide (**3p**)



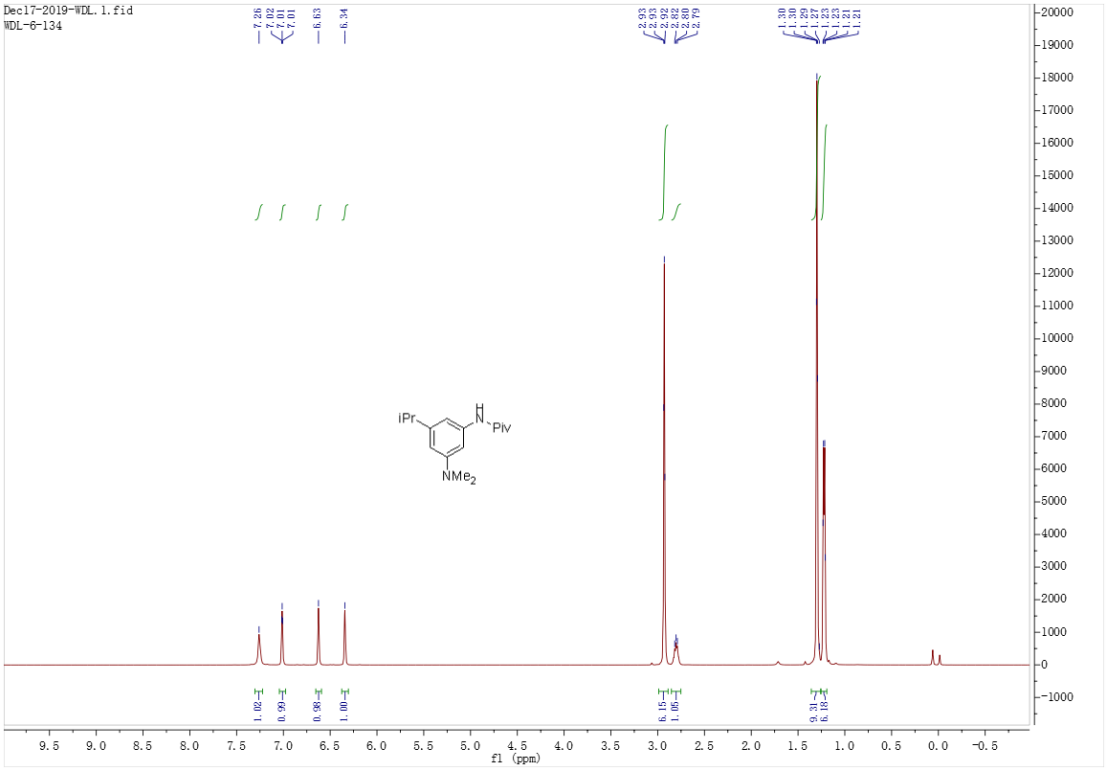


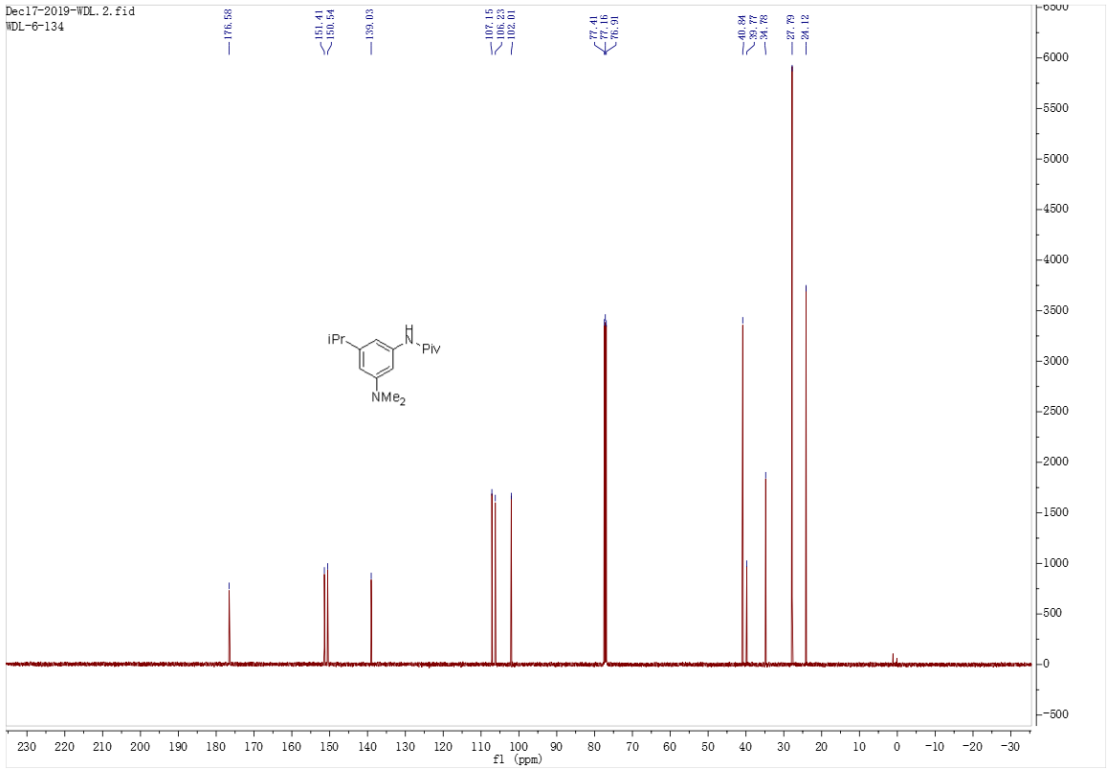
N-(3-isopropyl-5-(methylamino)phenyl)pivalamide (**6b**)



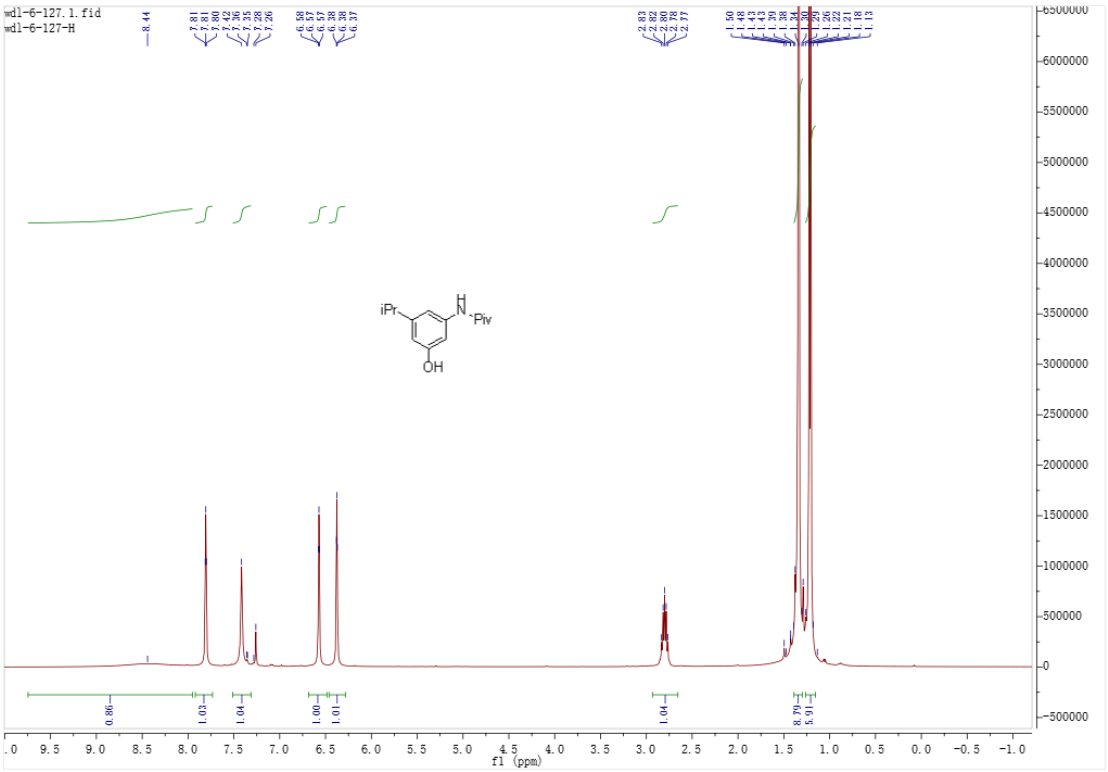


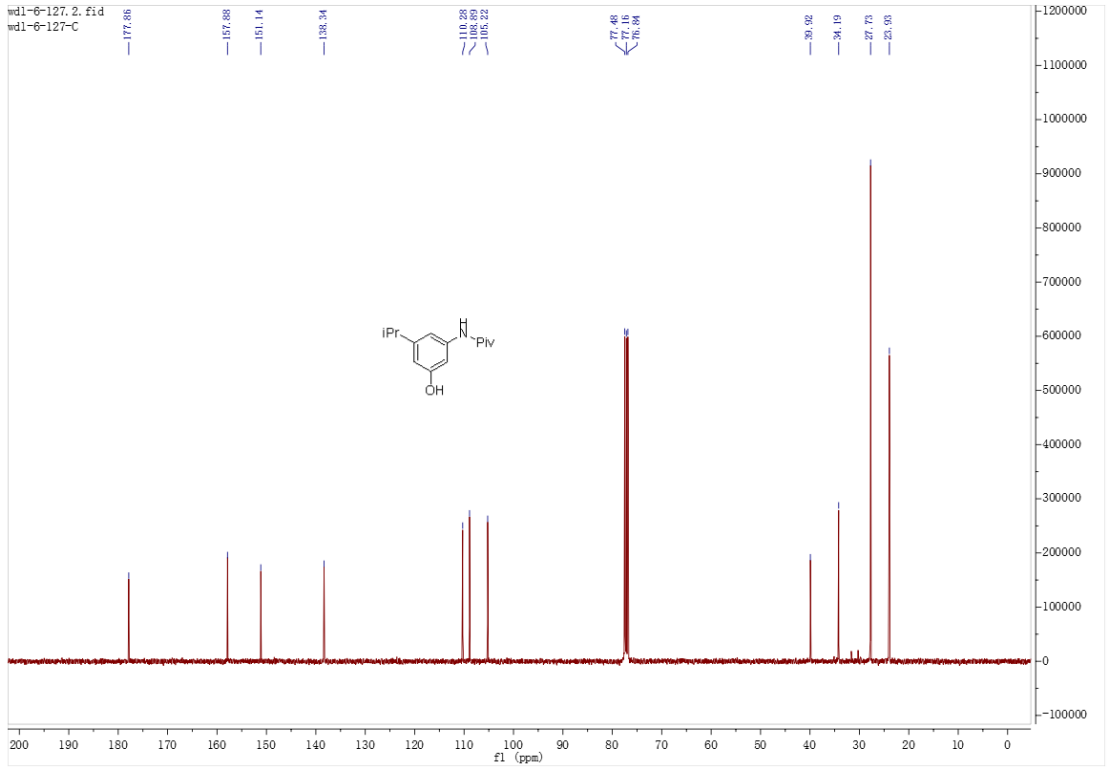
N-(3-(dimethylamino)-5-isopropylphenyl)pivalamide (**6c**)



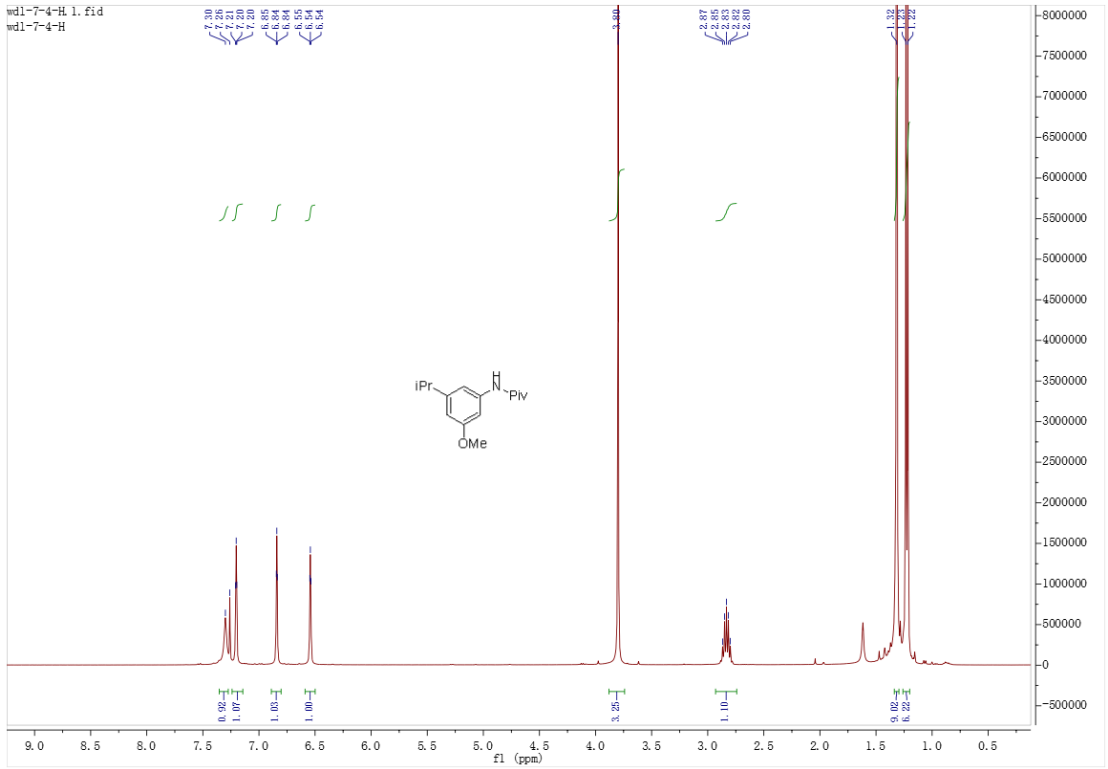


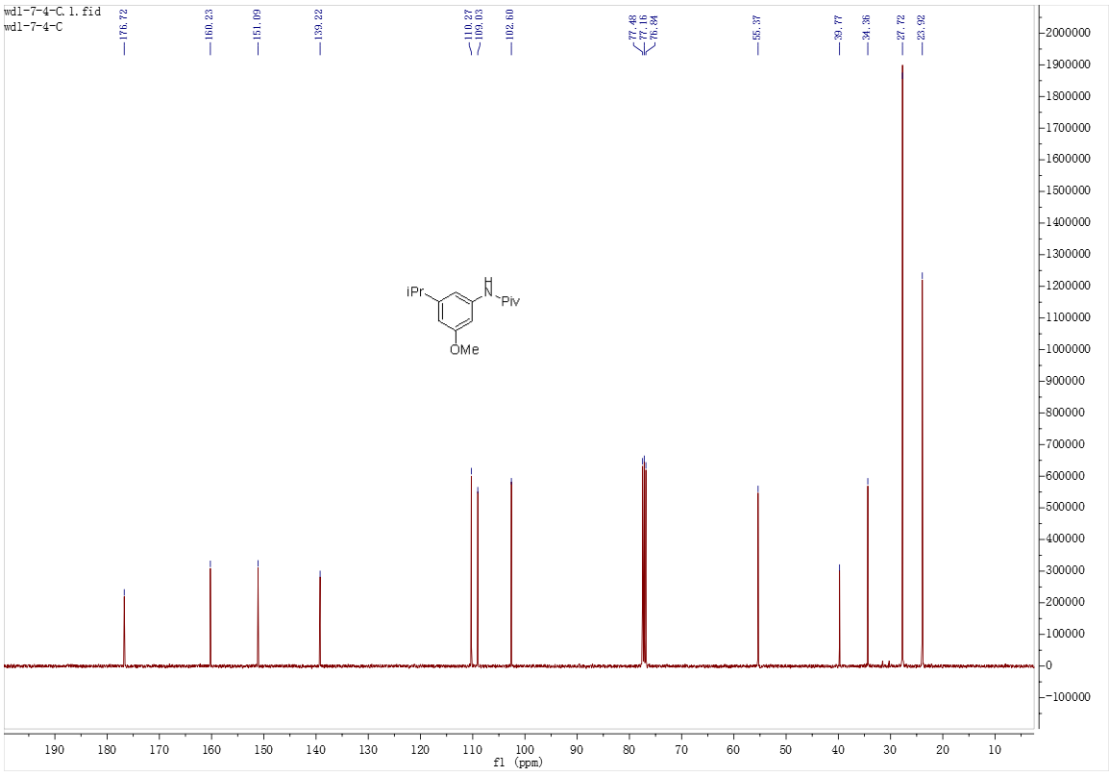
N-(3-hydroxy-5-isopropylphenyl)pivalamide (**6d**)



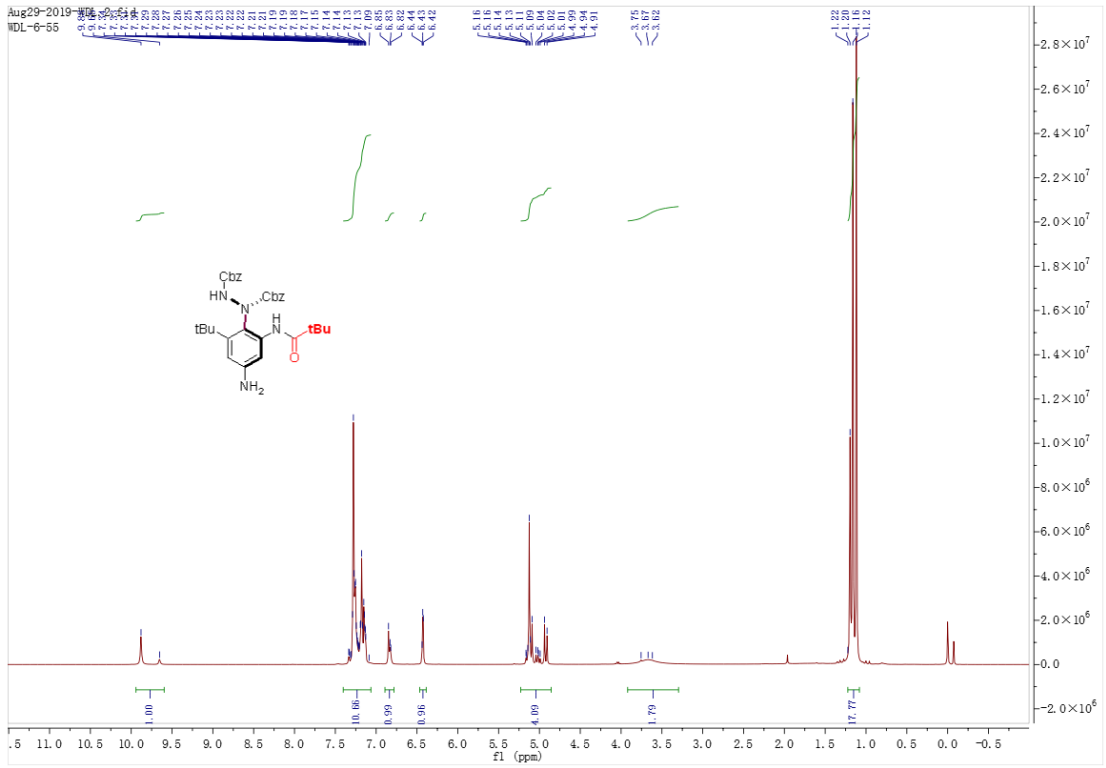


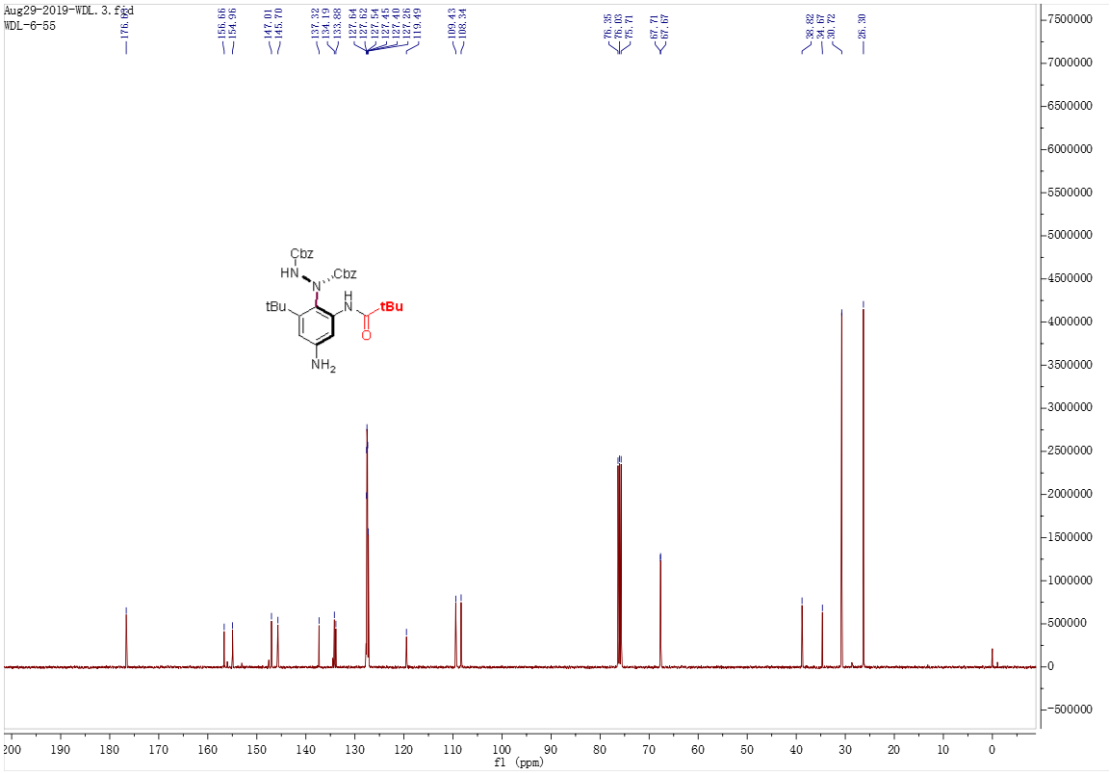
N-(3-isoprop1l-5-methoxyphenyl)pivalamide (**6e**)



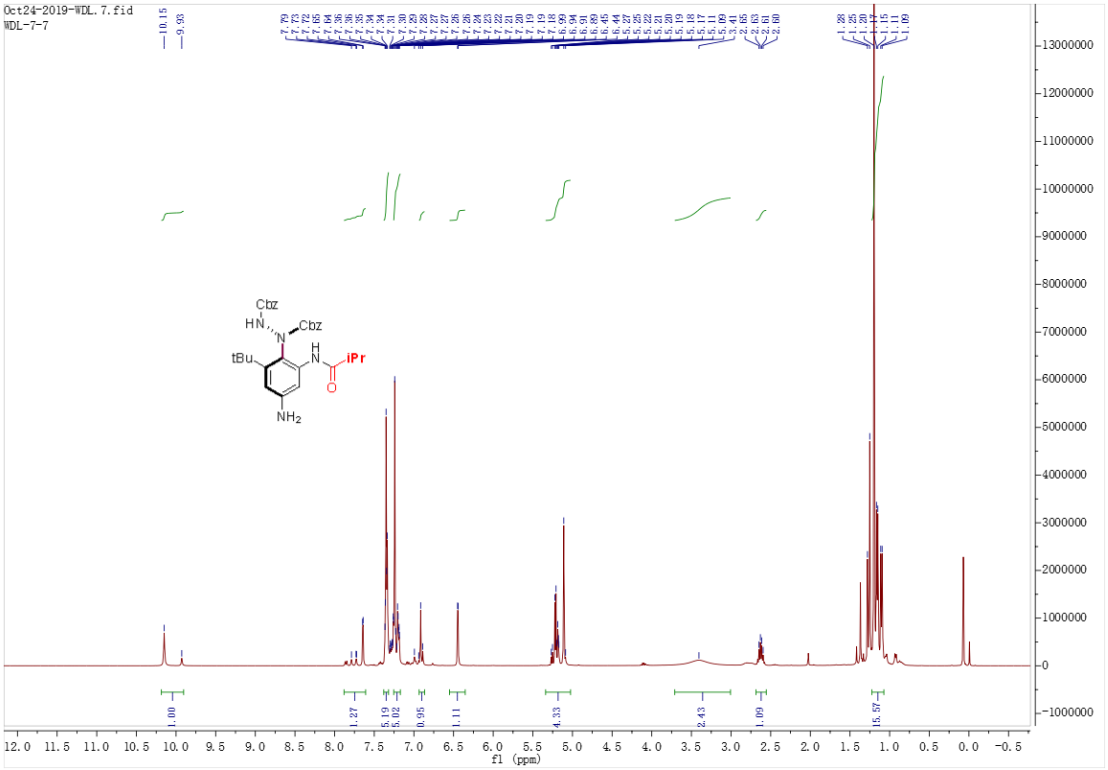


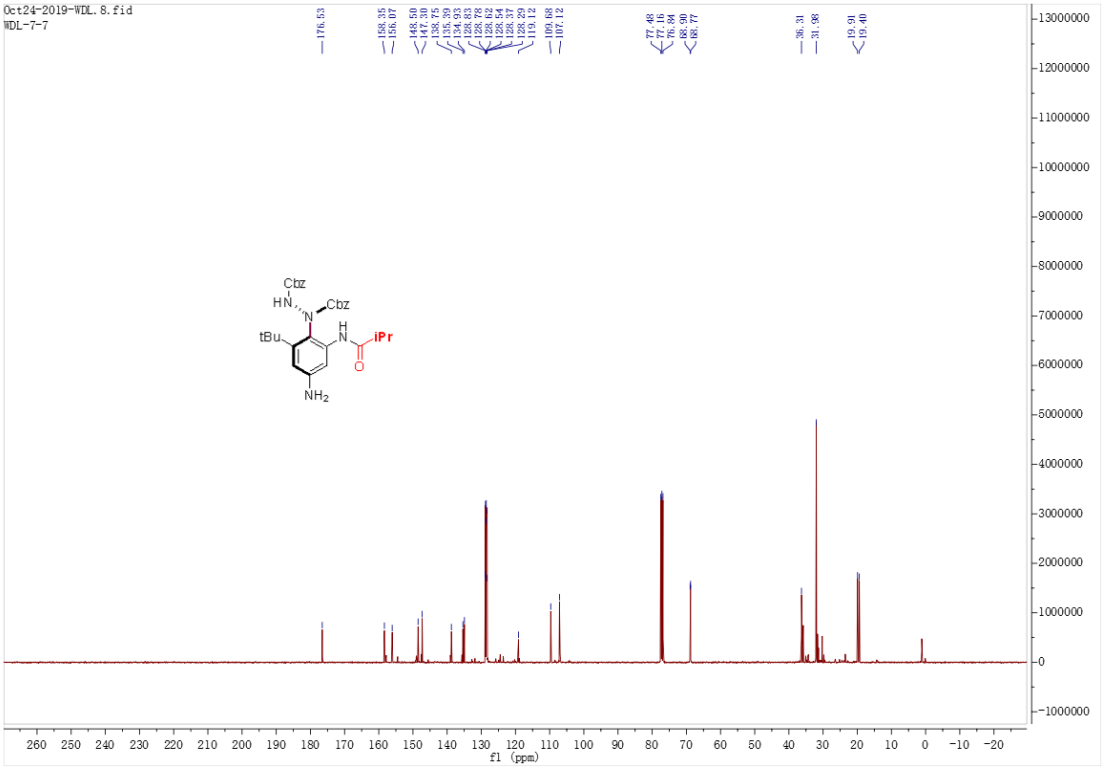
(*R*)-Dibenzyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5a**)



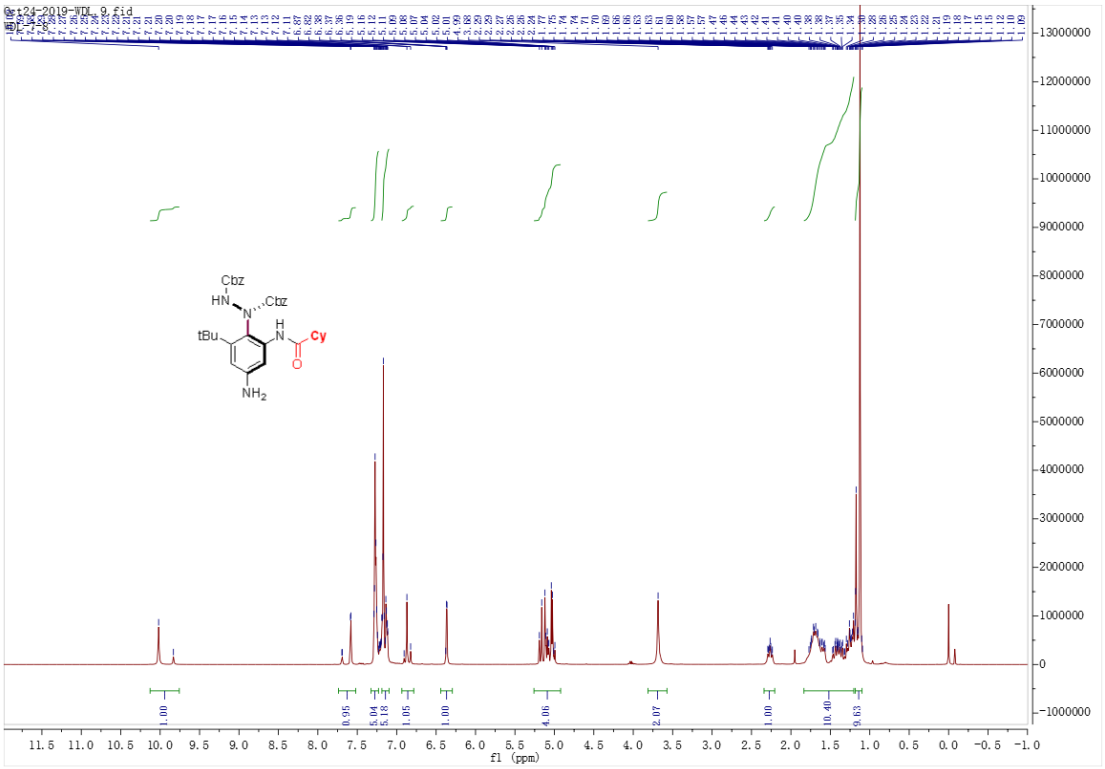


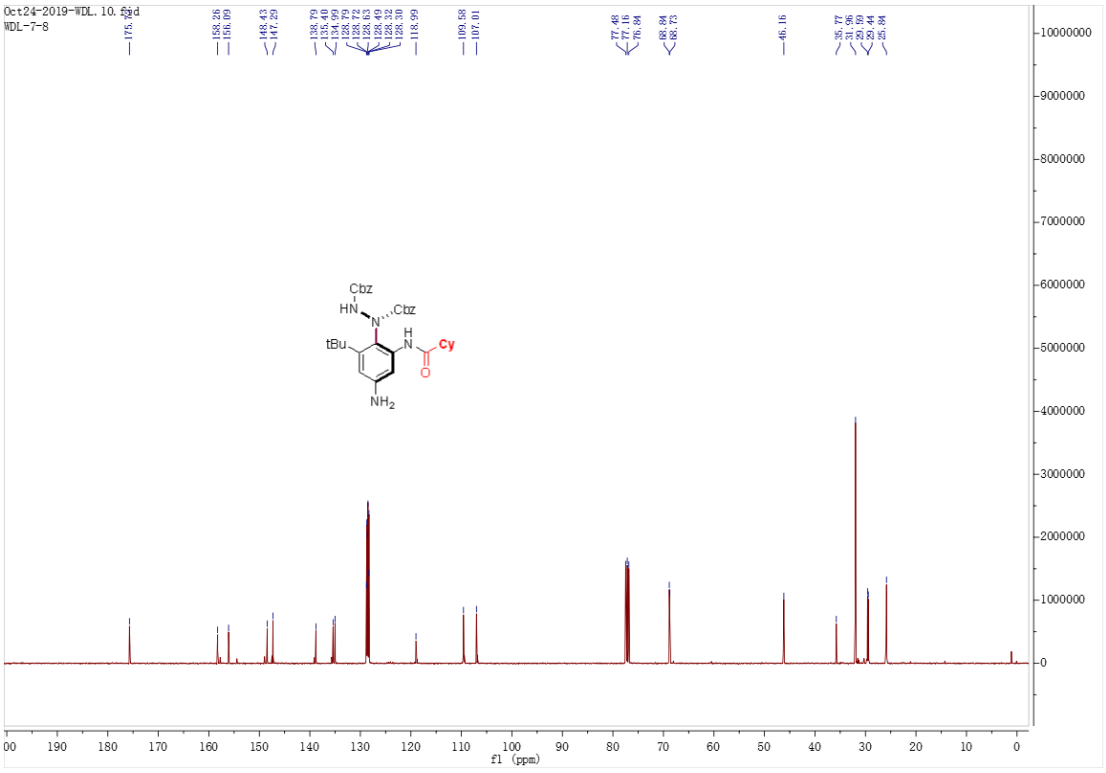
(*S*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-isobutyramidophenyl)hydrazine-1,2-dicarboxylate (**5b**)



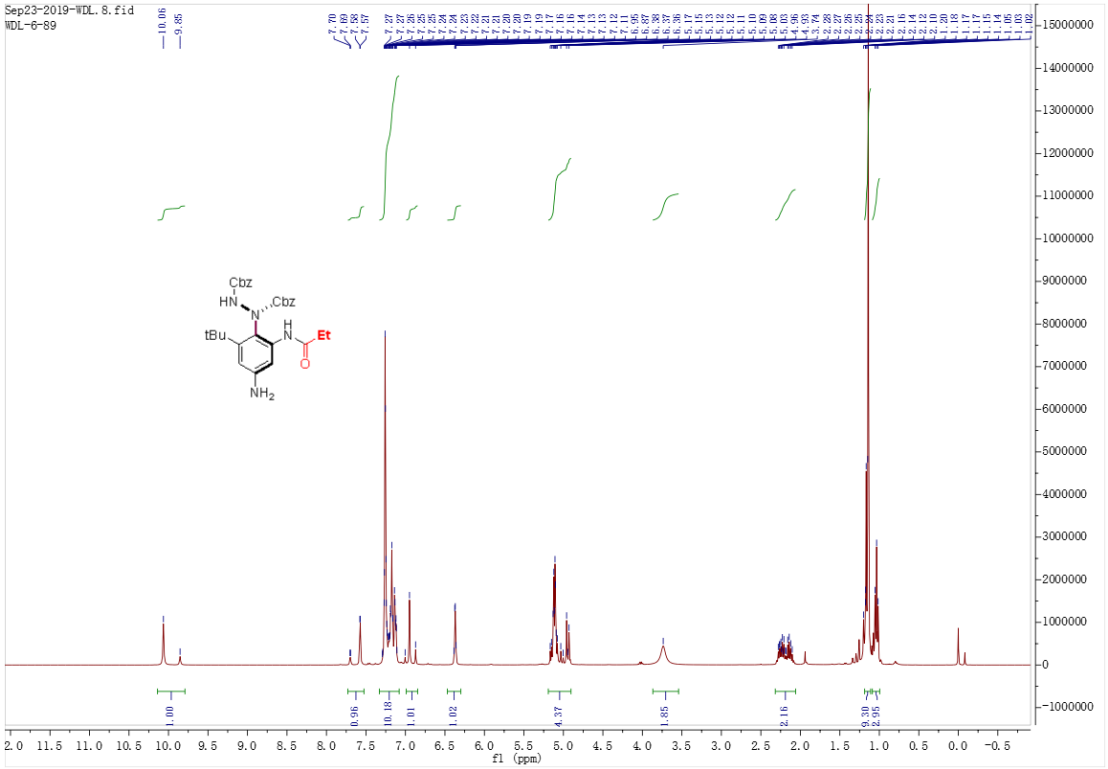


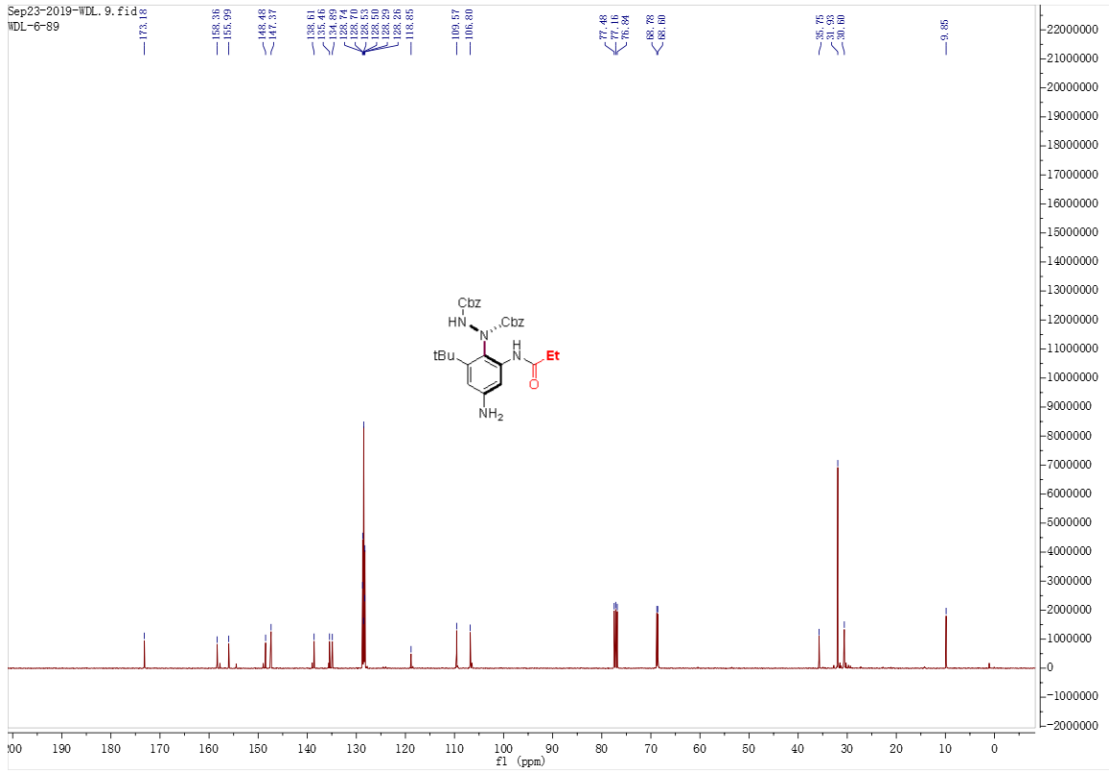
(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-(cyclohexanecarboxamido)phenyl)hydrazine-1,2-dicarboxylate (**5c**)



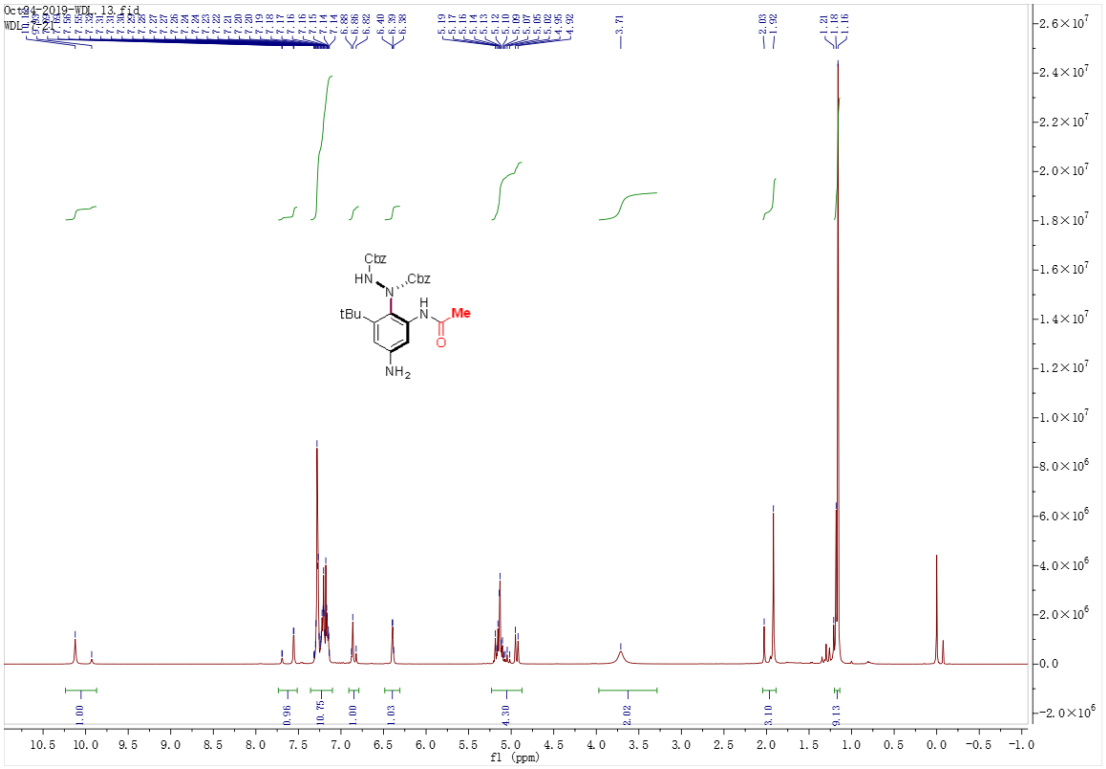


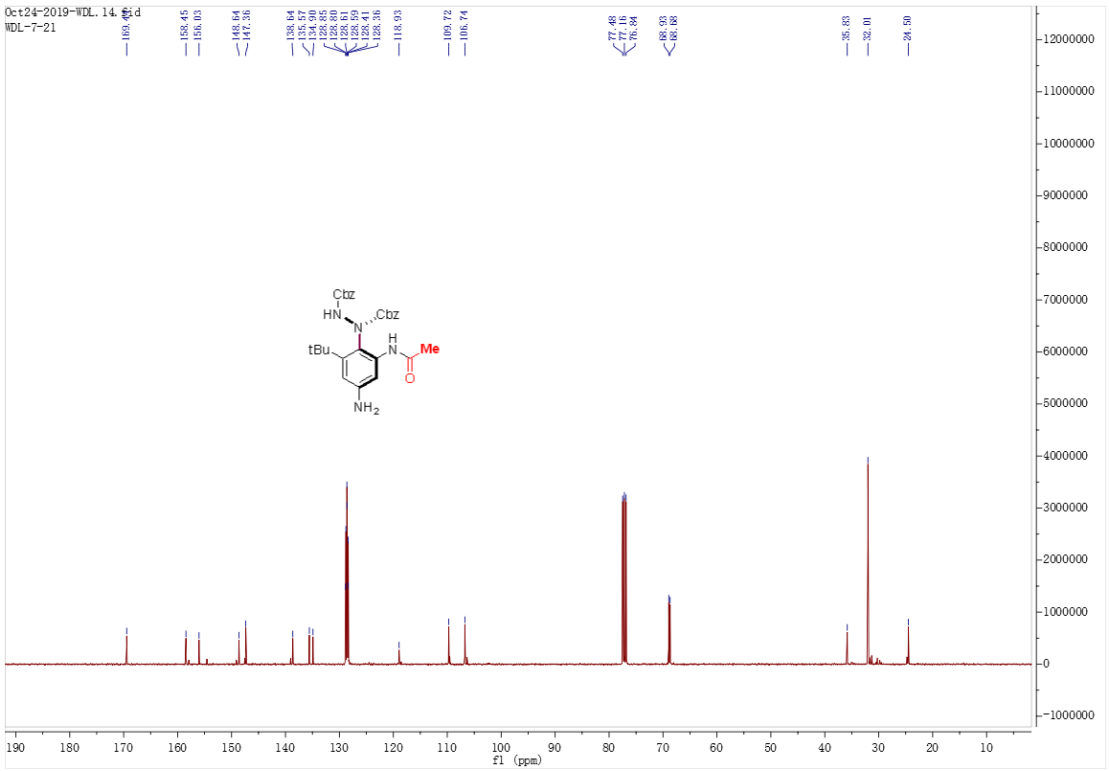
(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-propionamidophenyl)hydrazine-1,2-dicarboxylate (**5d**)



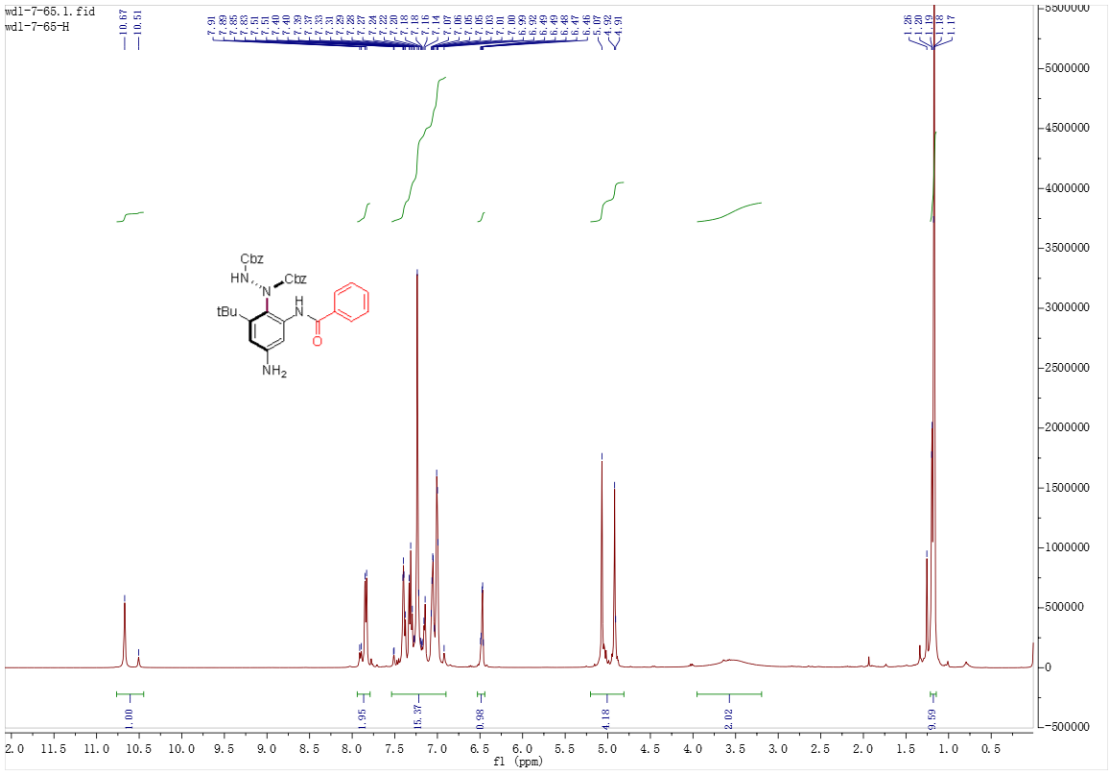


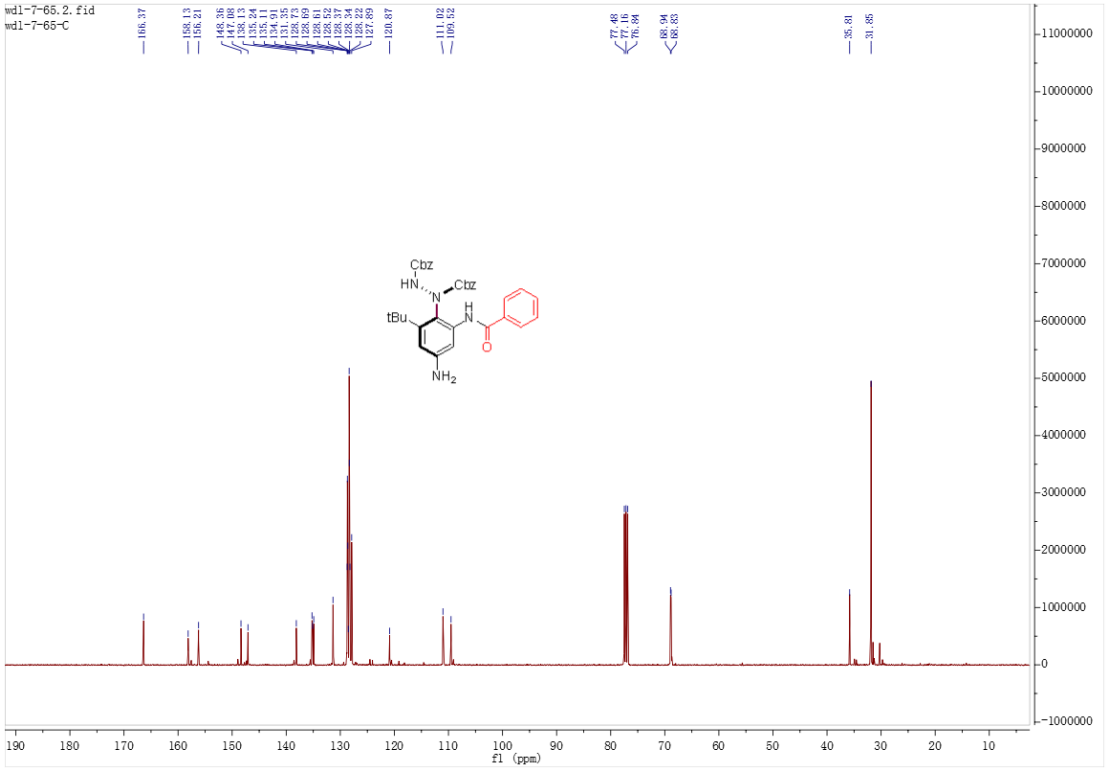
(*R*)-dibenzyl-1-(2-acetamido-4-amino-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5e**)



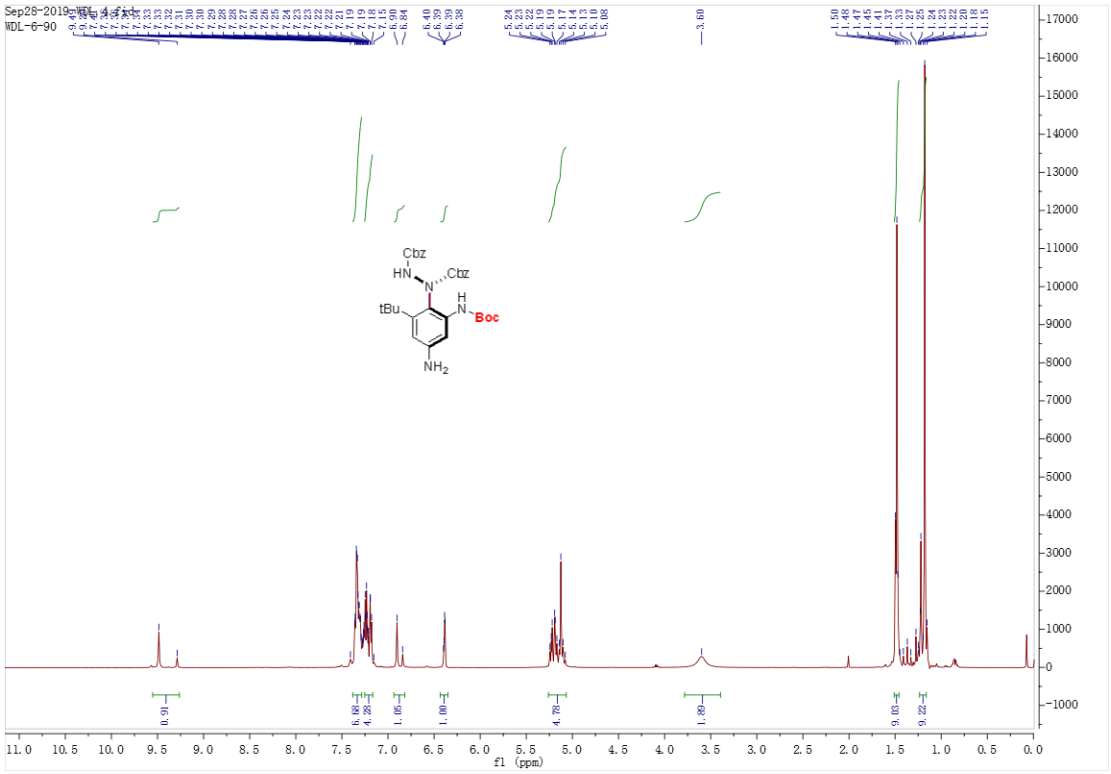


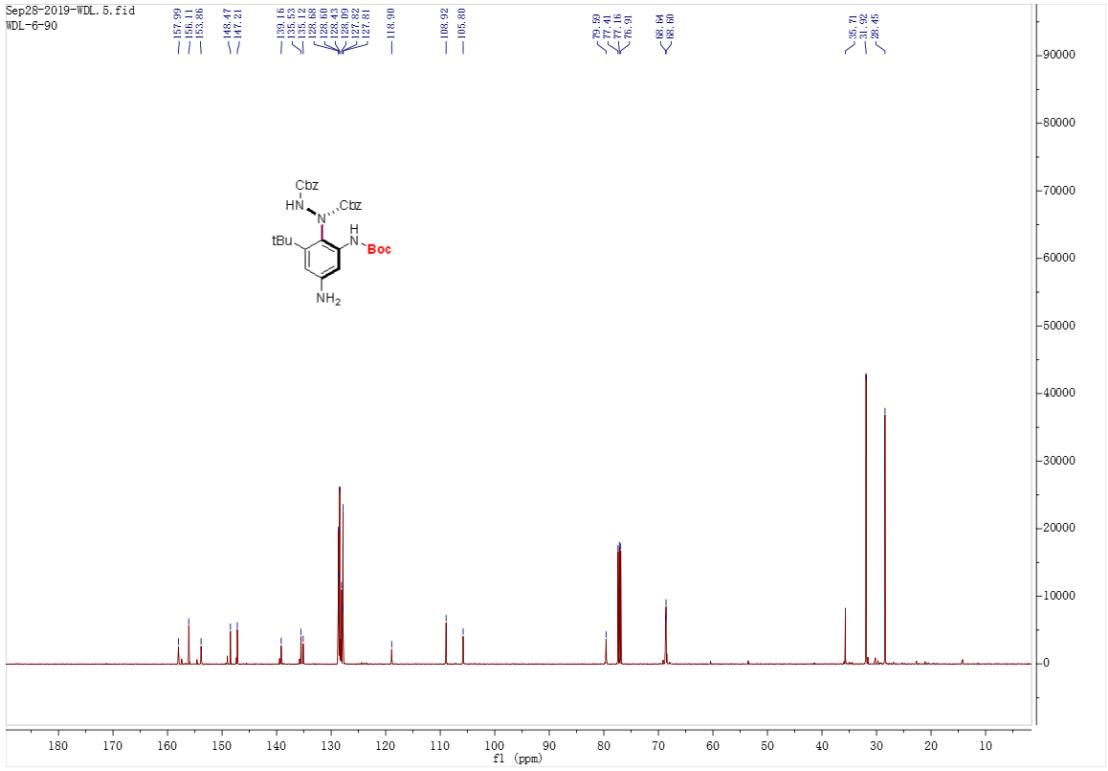
(*S*)-dibenzyl-1-(4-amino-2-benzamido-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5f**)



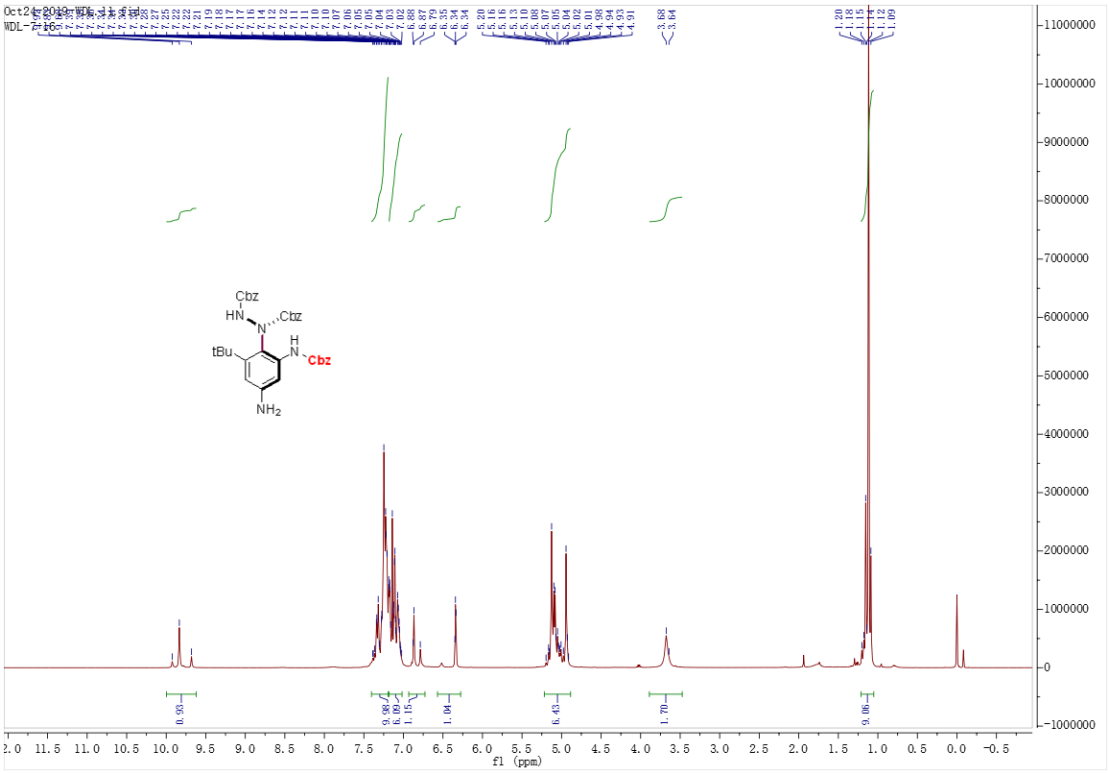


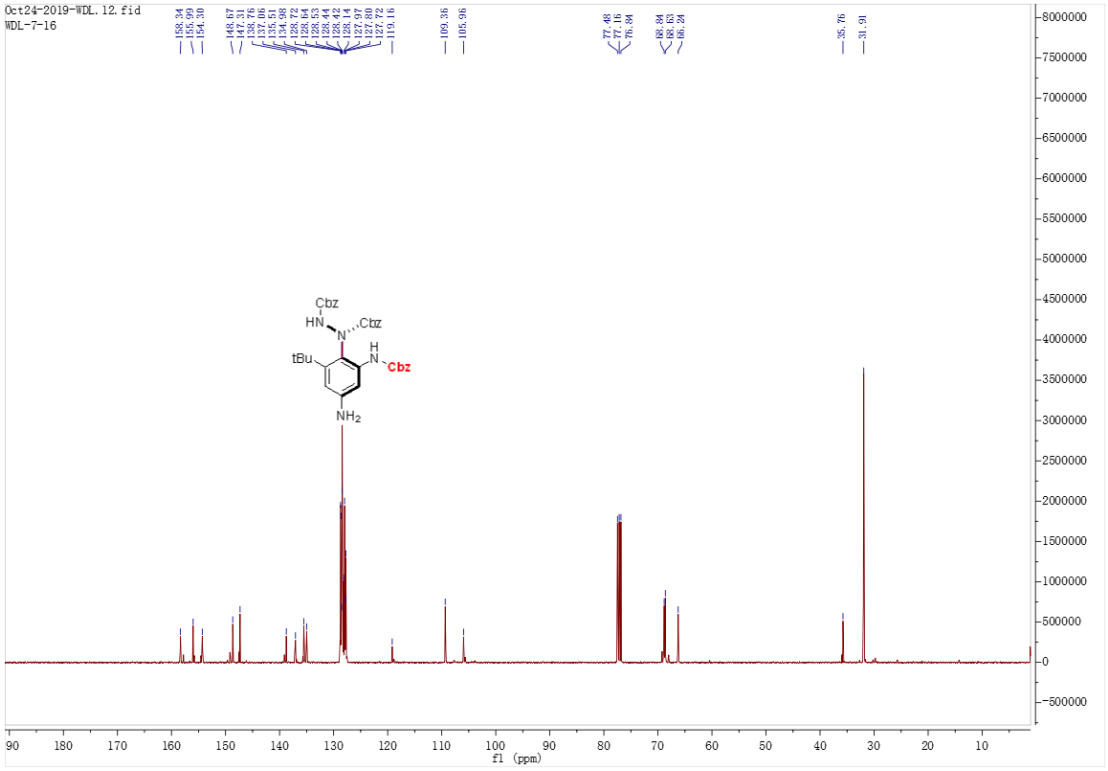
(*R*)-dibenzyl-1-(4-amino-2-((tert-butoxycarbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5g**)



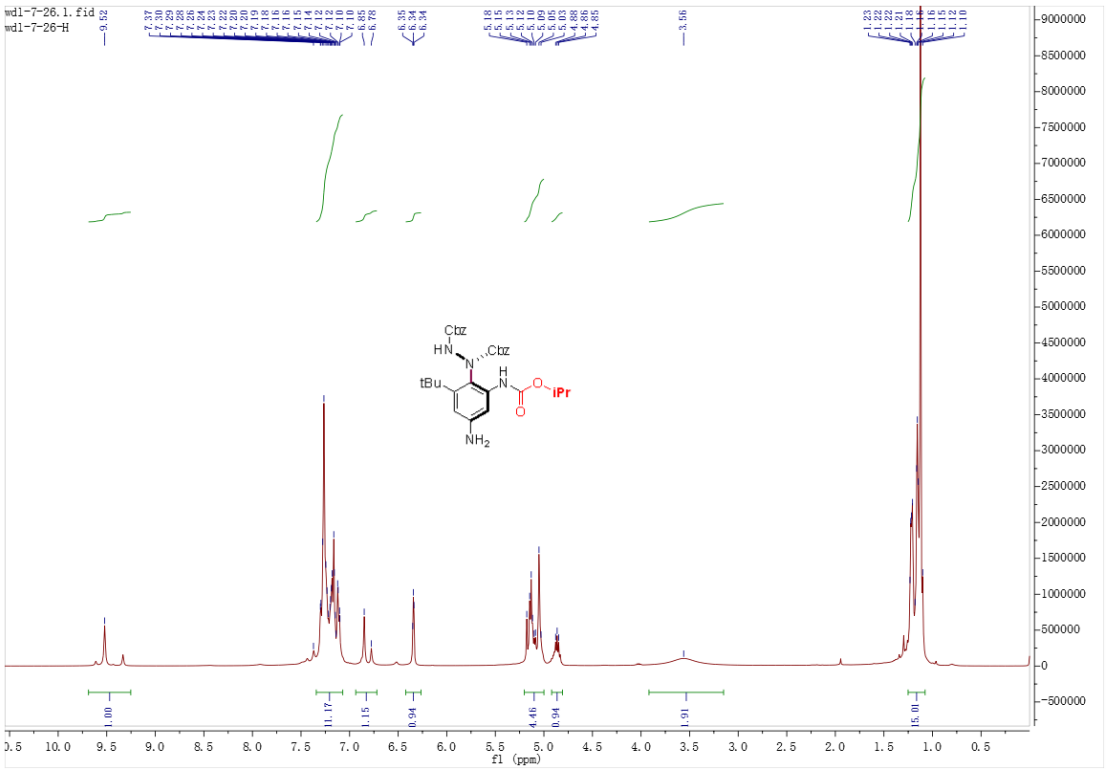


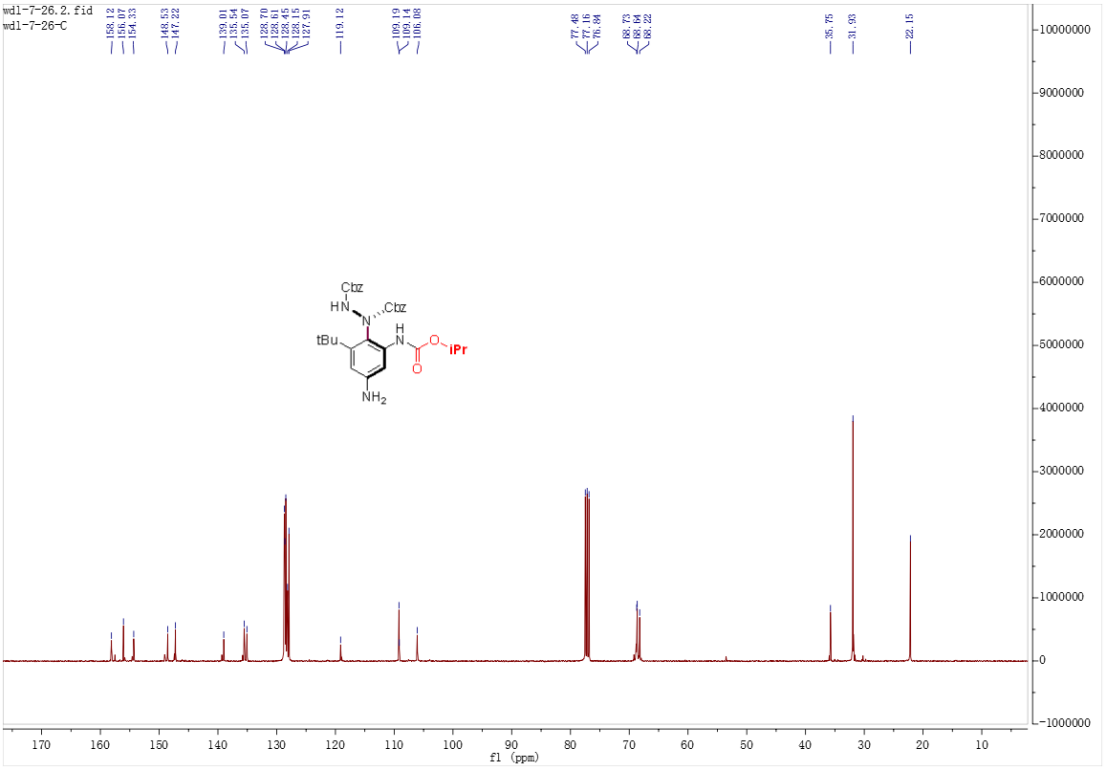
(*R*)-dibenzyl-1-(4-amino-2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5h**)



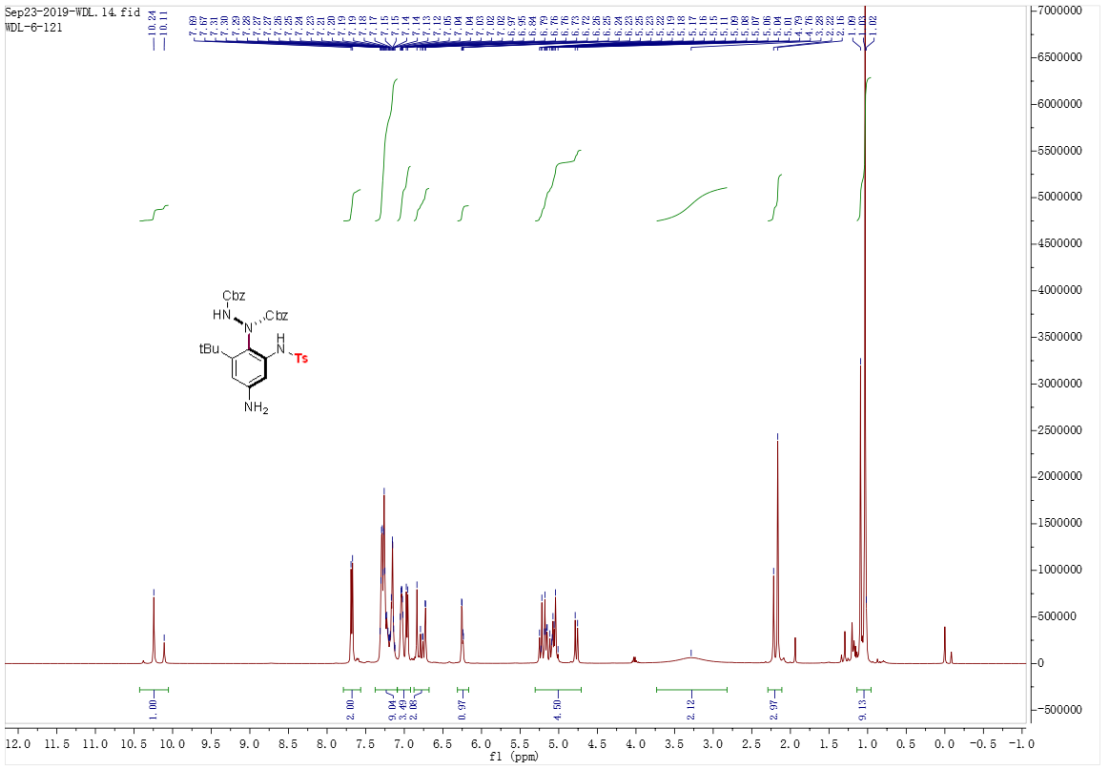


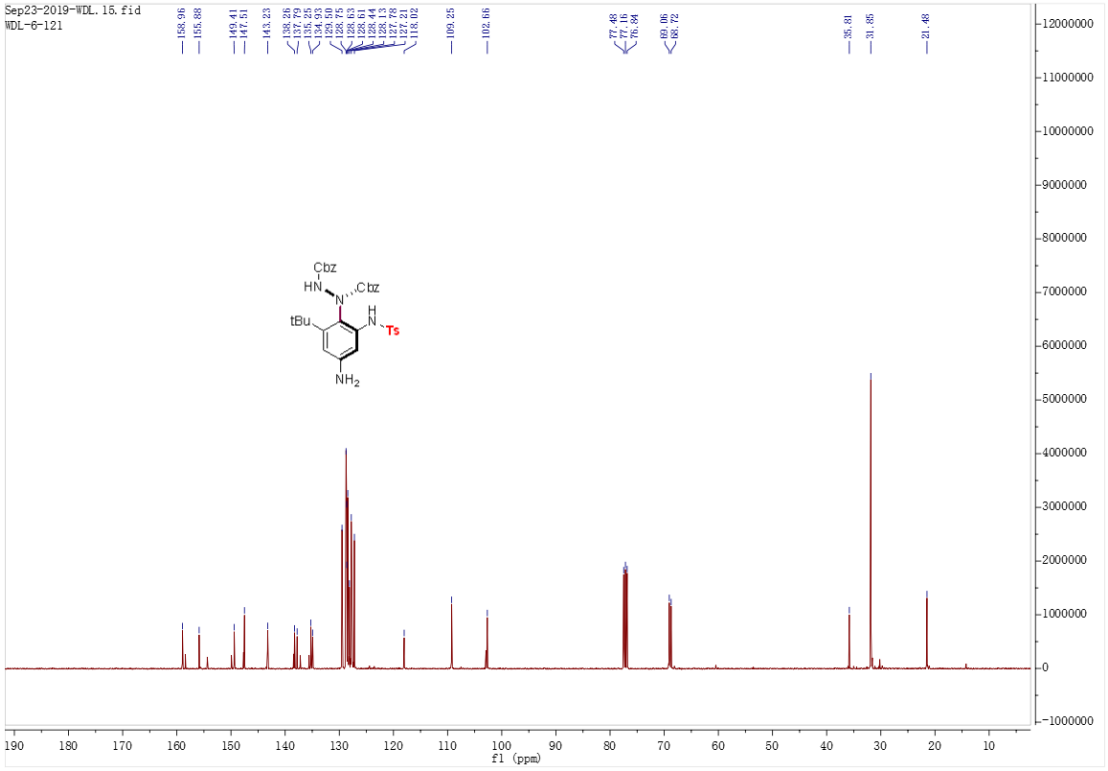
(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-((isopropoxycarbonyl)amino)phenyl)hydrazine-1,2-dicarboxylate (**5i**)



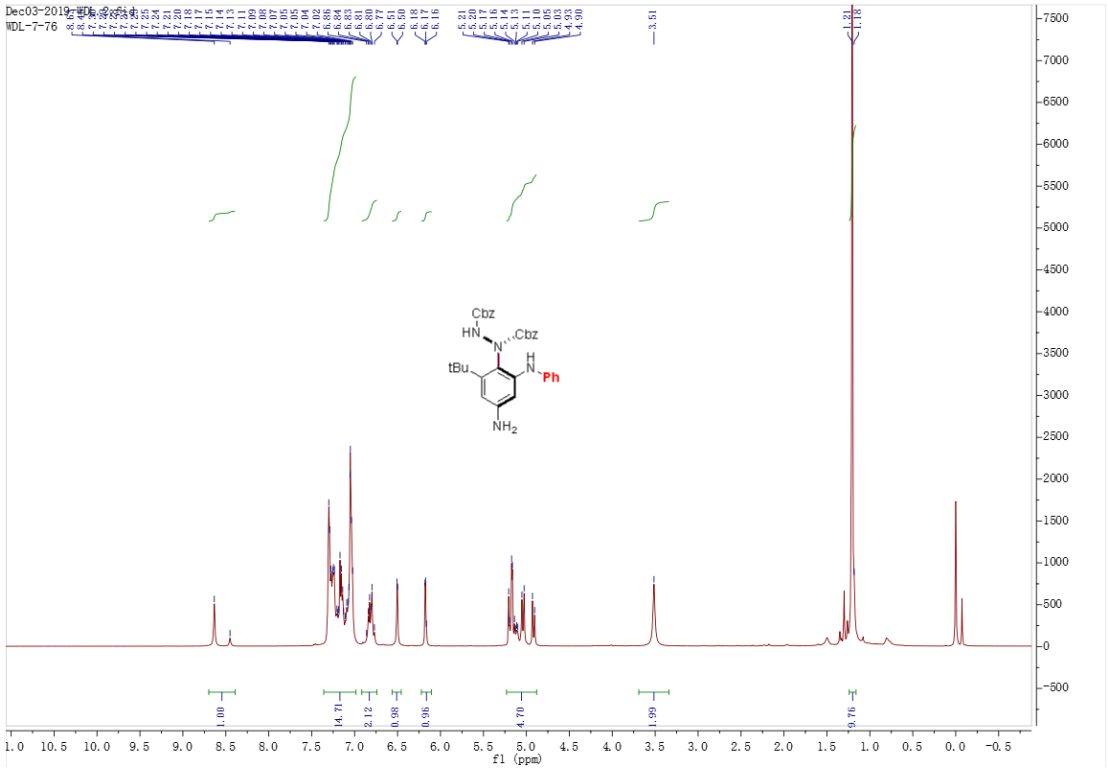


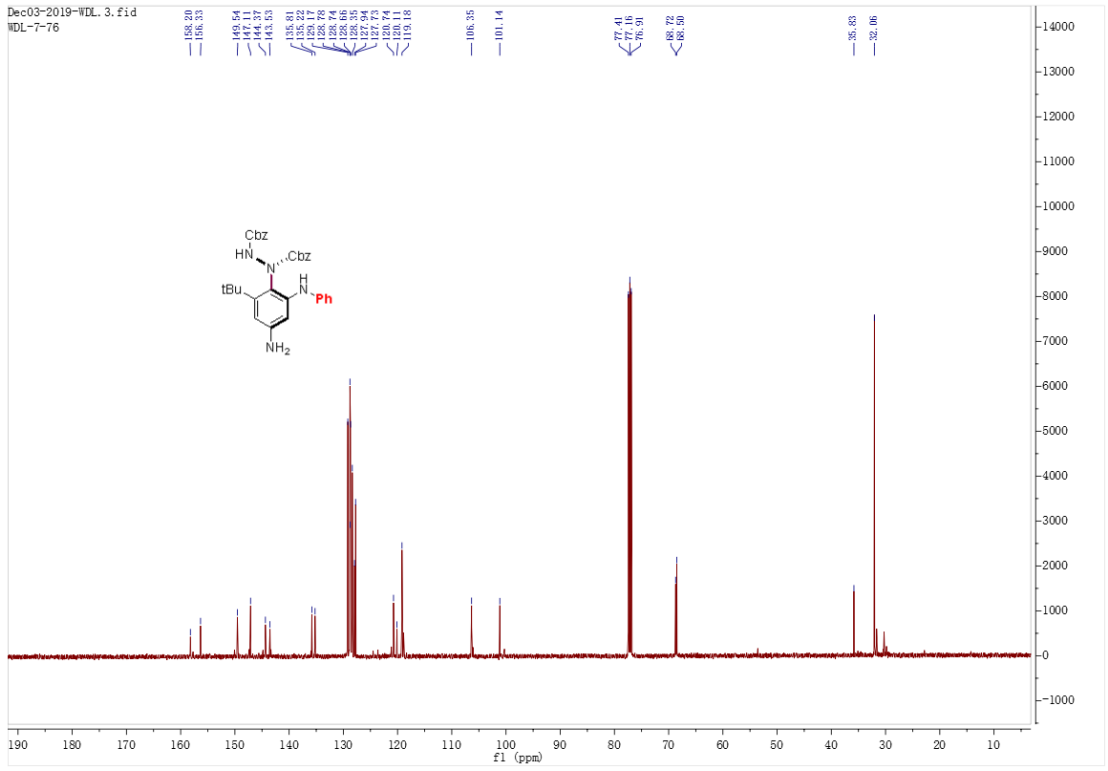
(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-((4-methylphenyl)sulfonamido)phenyl)hydrazine-1,2-dicarboxylate (**5j**)



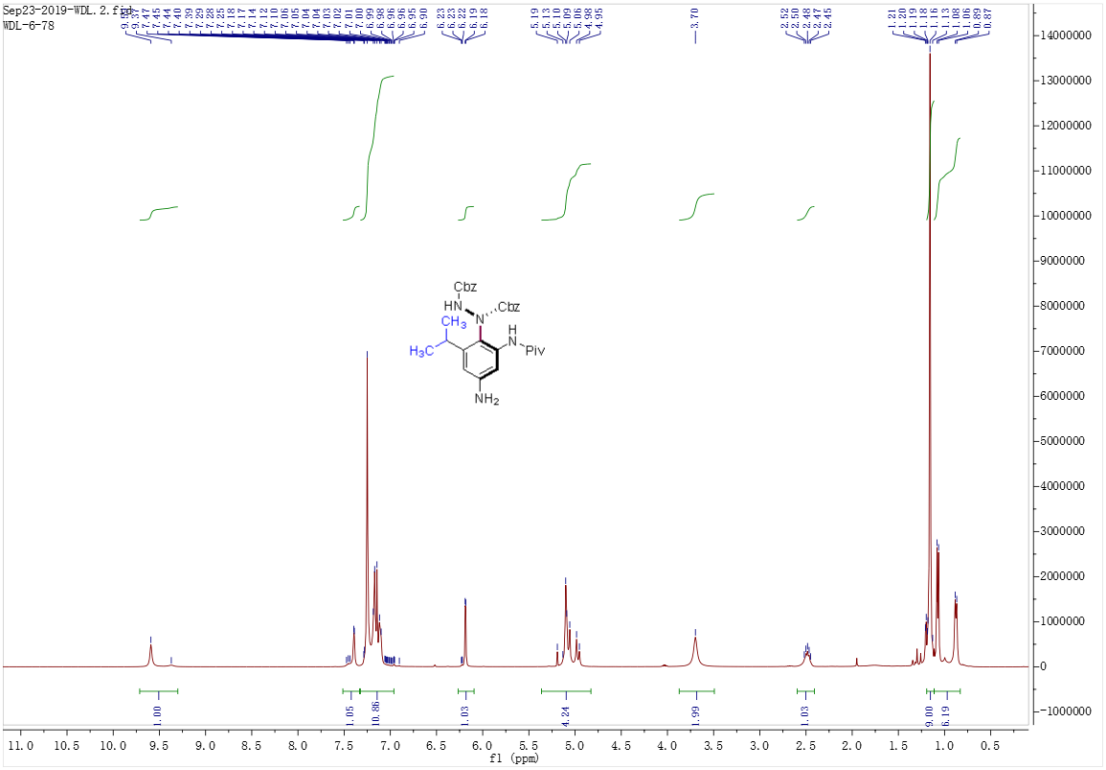


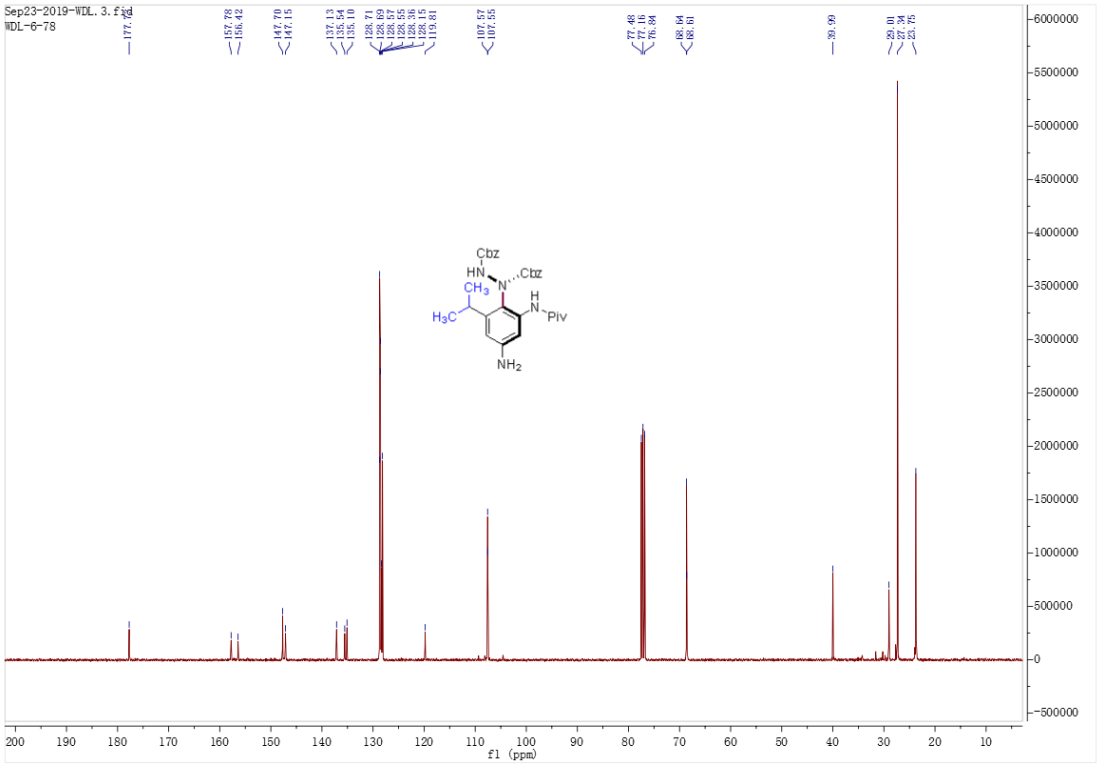
(*R*)-dibenzyl-1-(4-amino-2-(tert-butyl)-6-(phenylamino)phenyl)hydrazine-1,2-dicarboxylate (**5k**)



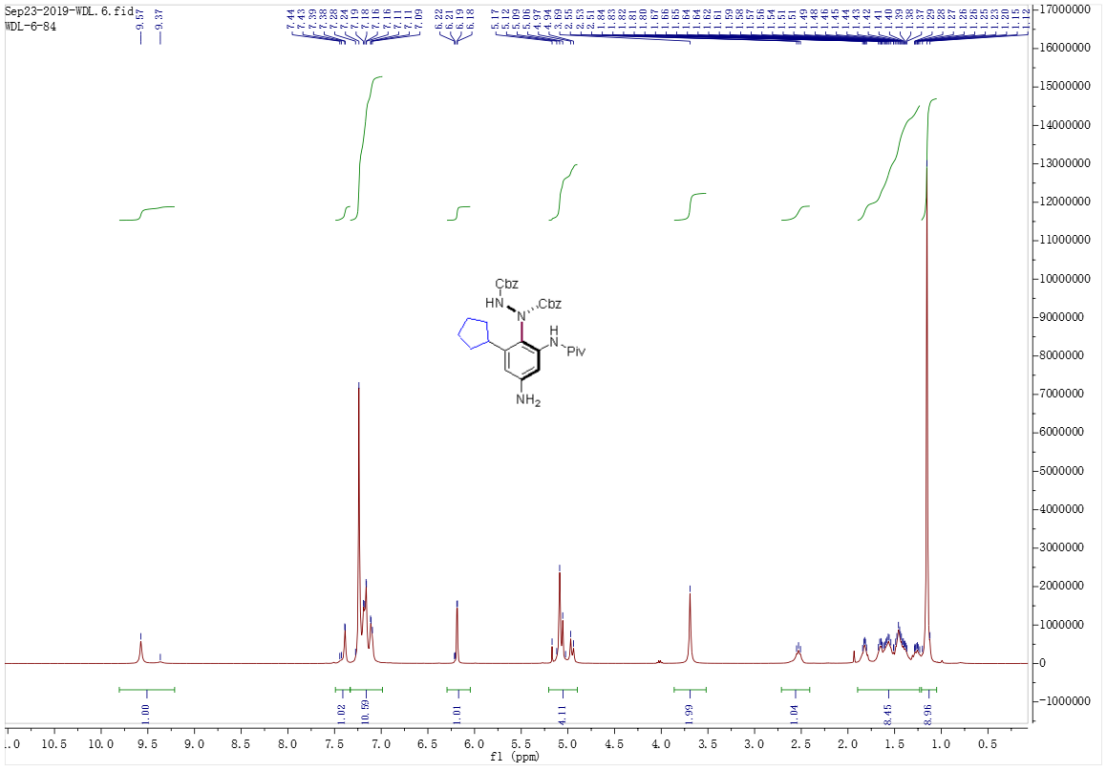


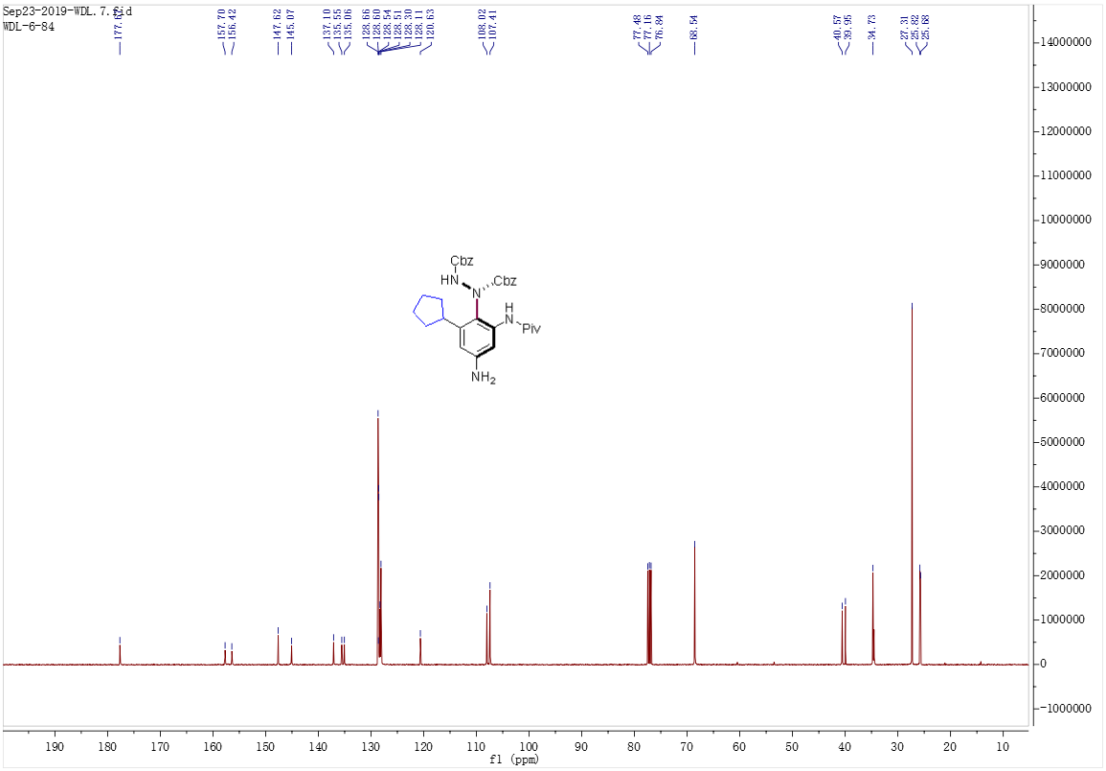
(*R*)-dibenzyl-1-(4-amino-2-isopropyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5l**)



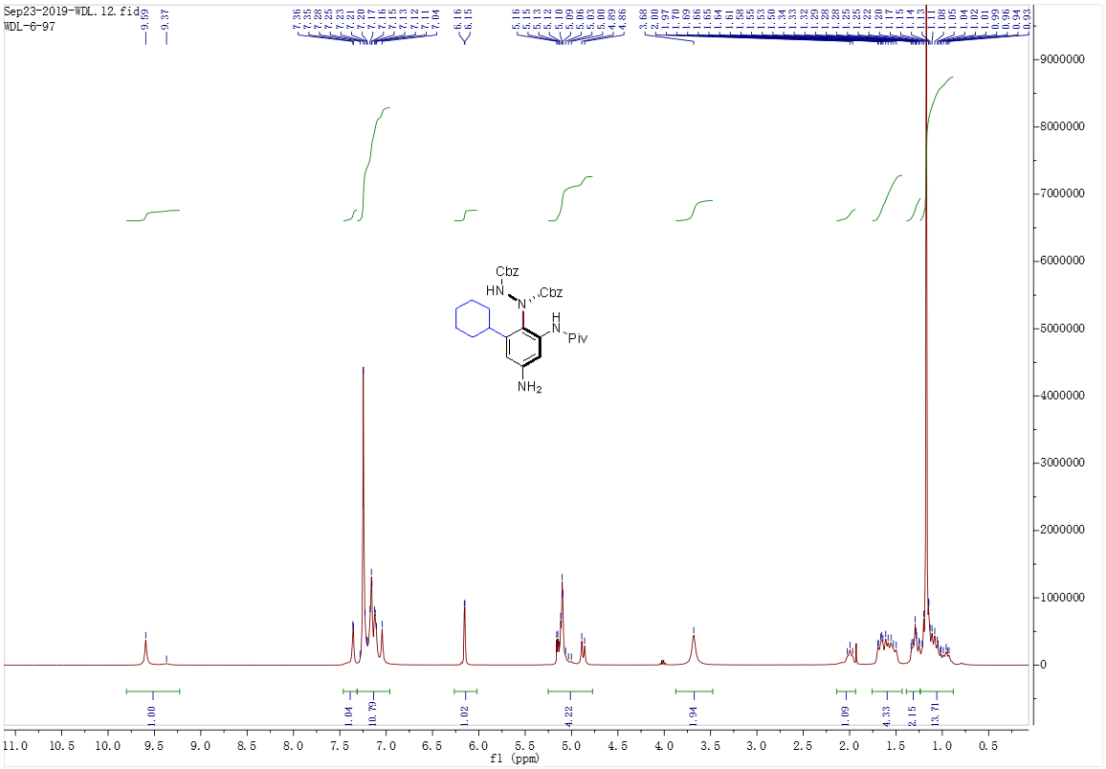


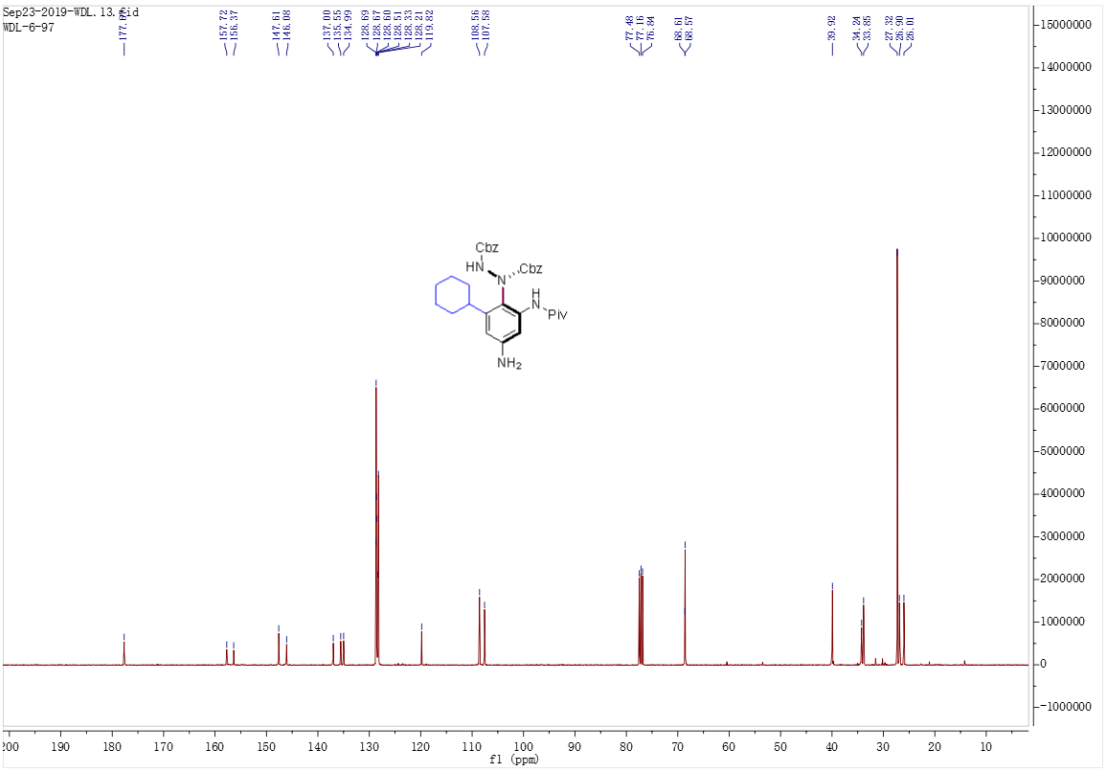
(*R*)-dibenzyl1-(4-amino-2-cyclopentyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5m**)



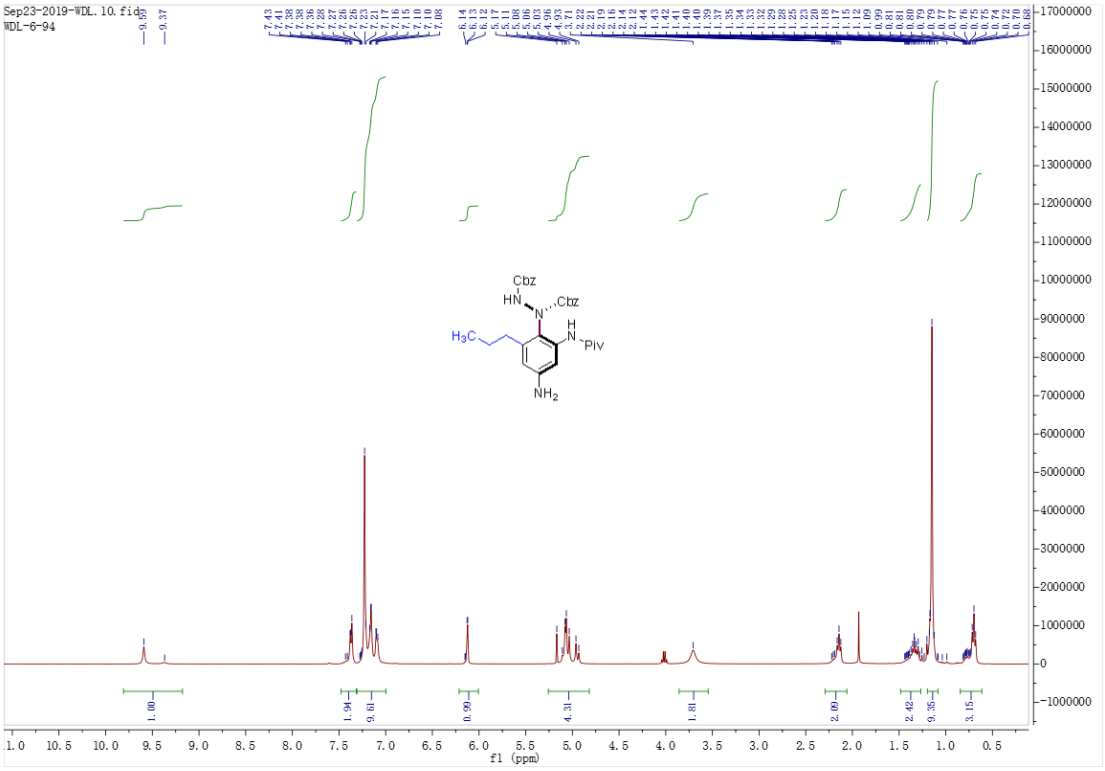


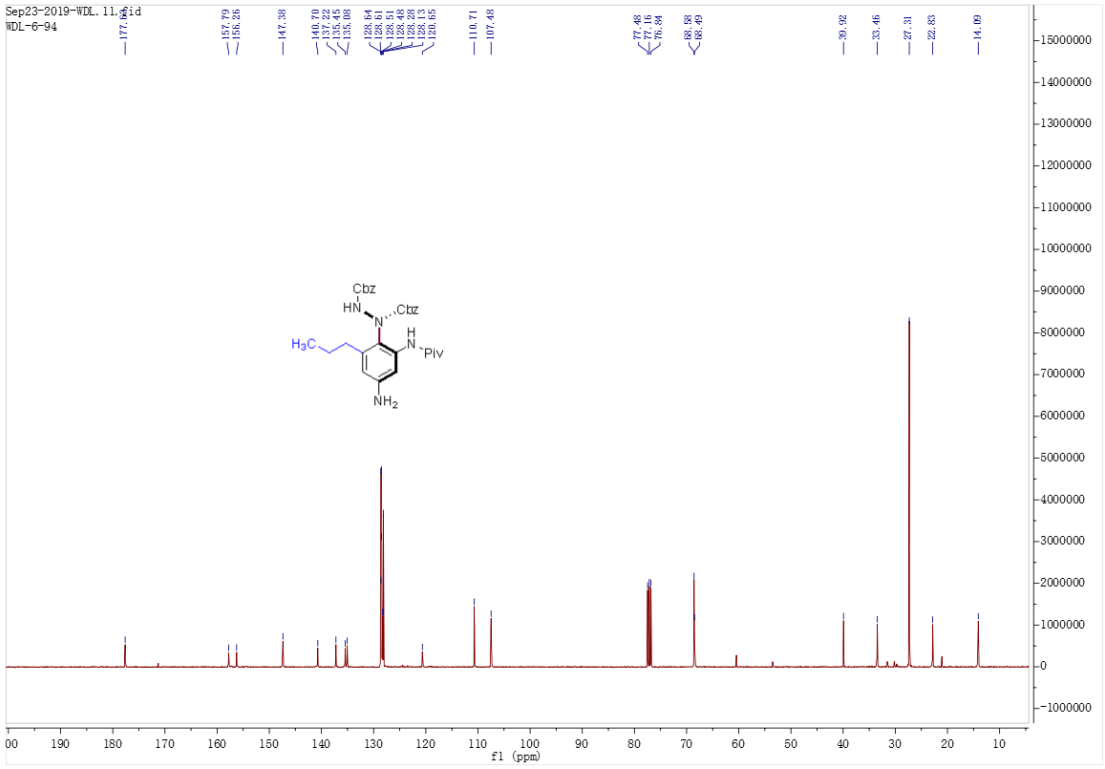
(*R*)-dibenzyl-1-(4-amino-2-cyclohexyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5n**)



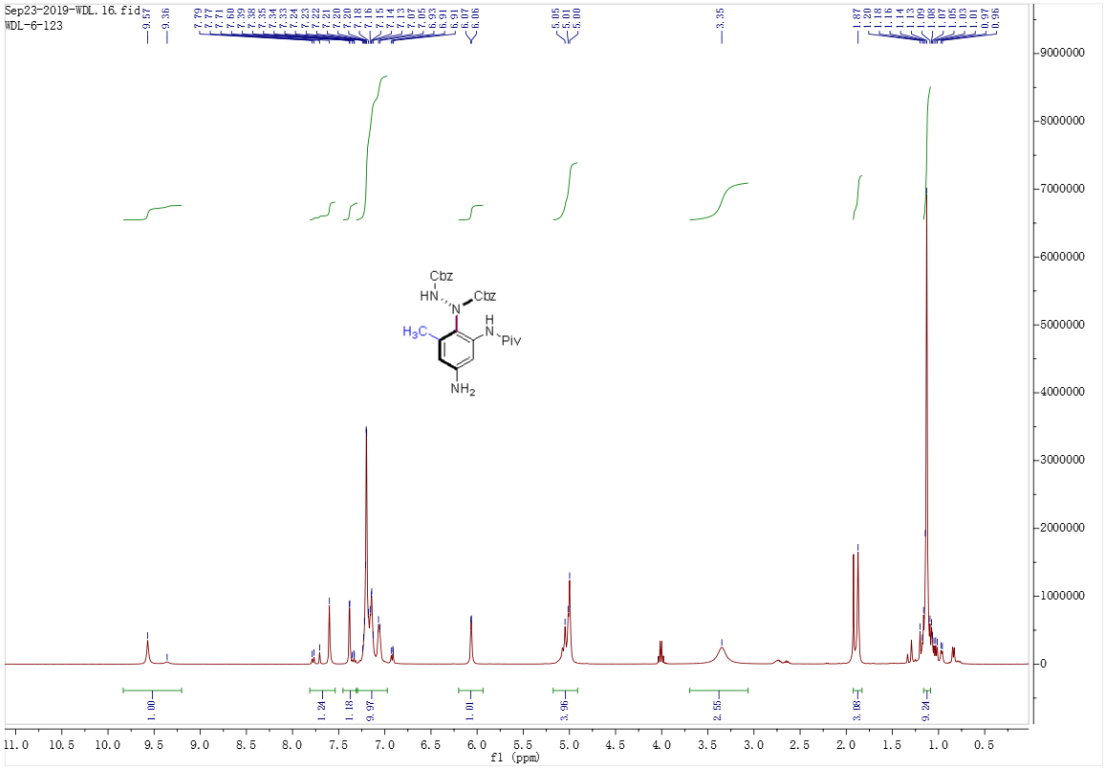


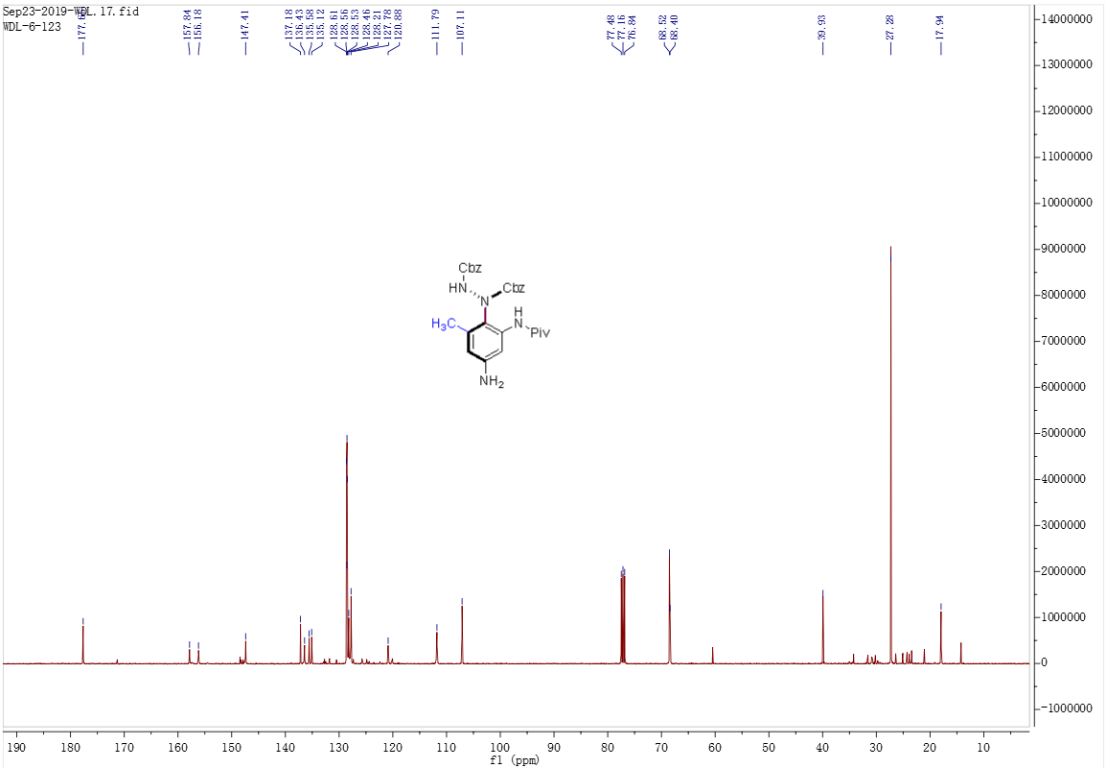
(*R*)-dibenzyl-1-(4-amino-2-pivalamido-6-propylphenyl)hydrazine-1,2-dicarboxylate (**5o**)



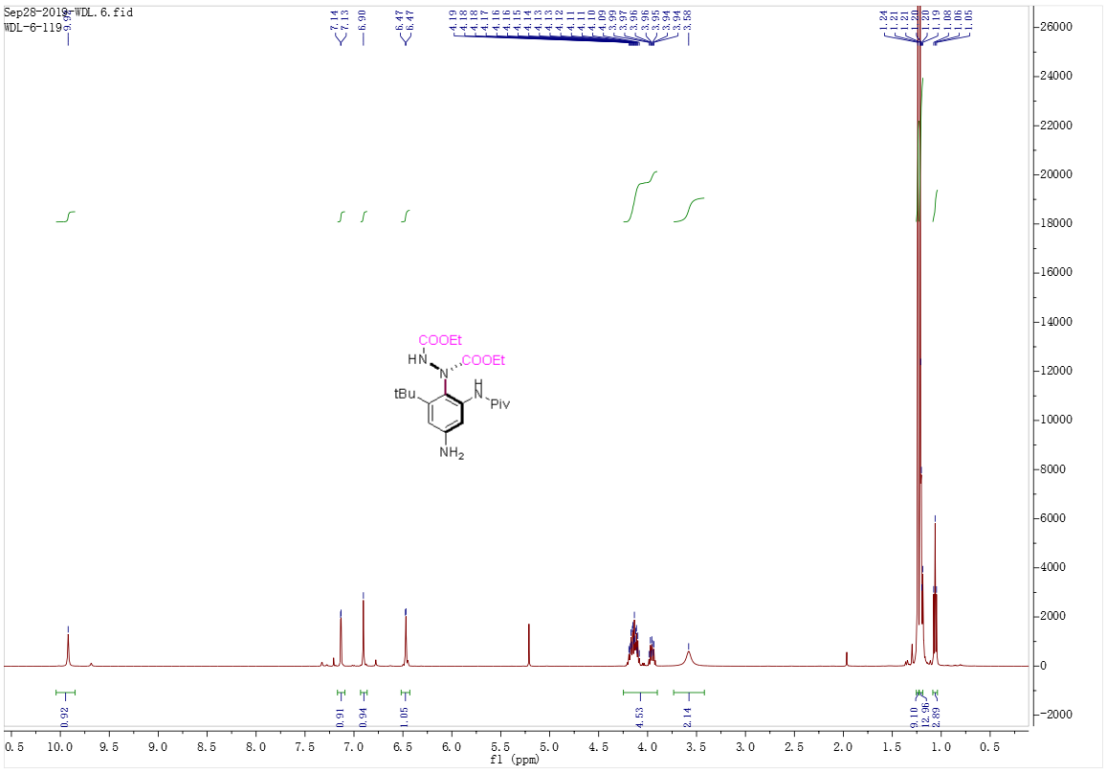


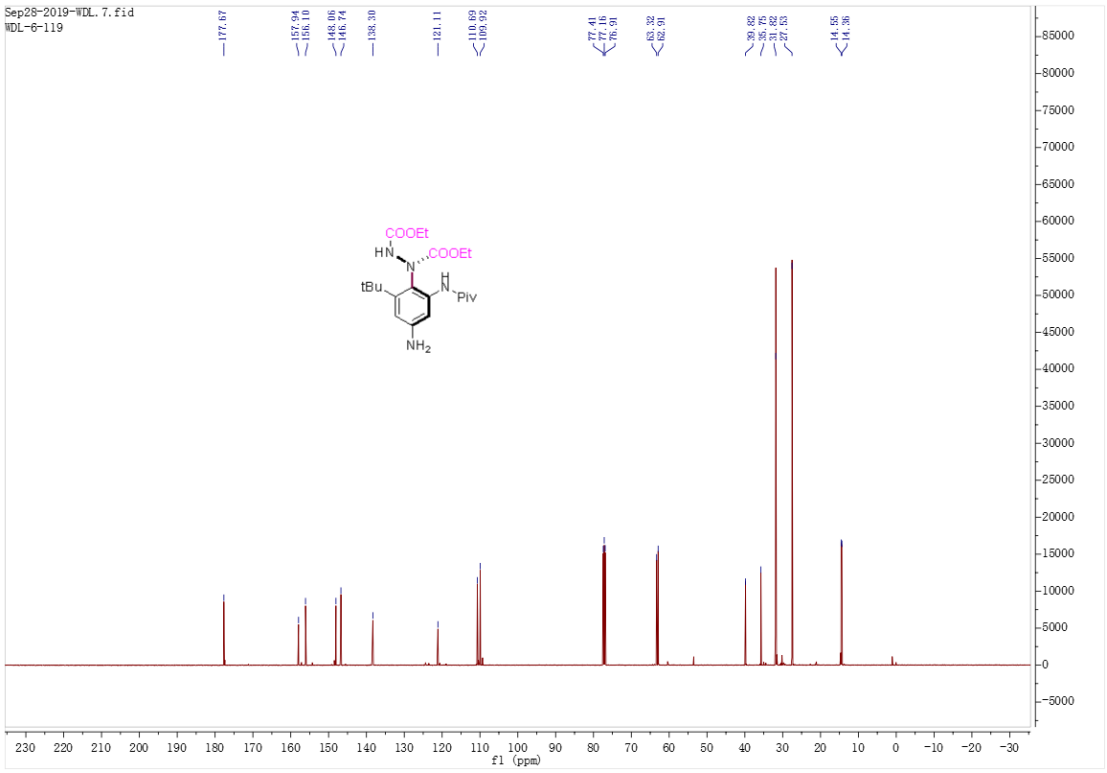
(*S*)-dibenzyl-1-(4-amino-2-methyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5p**)



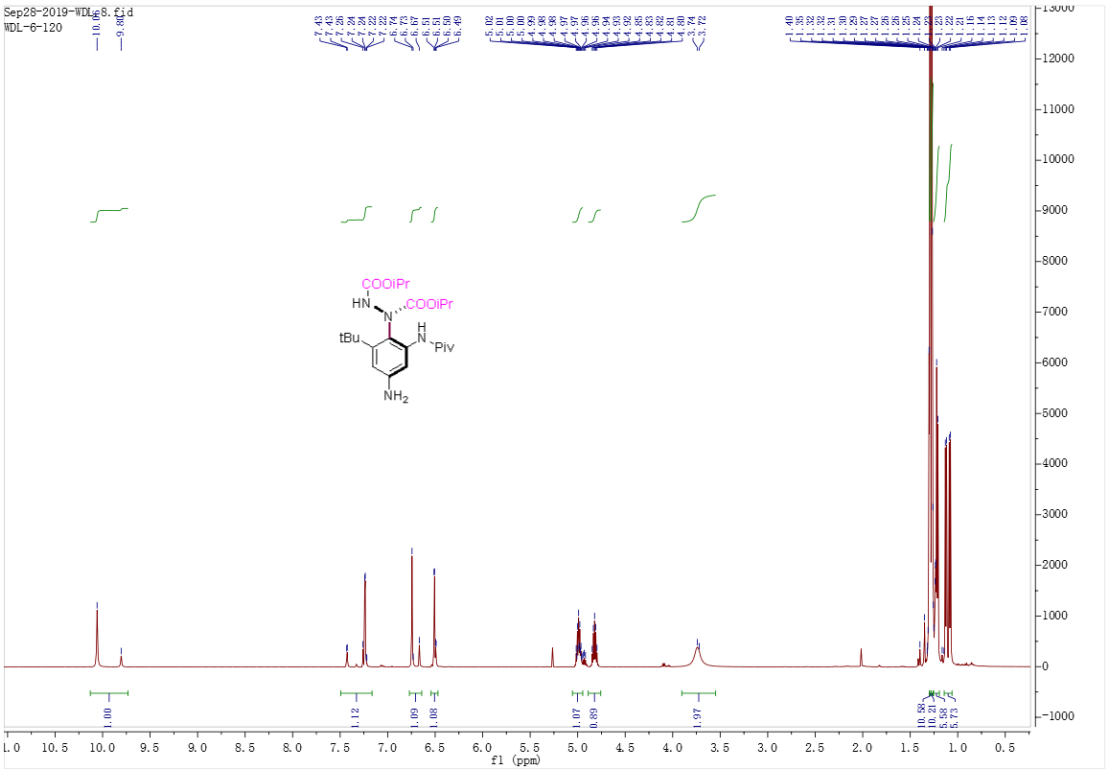


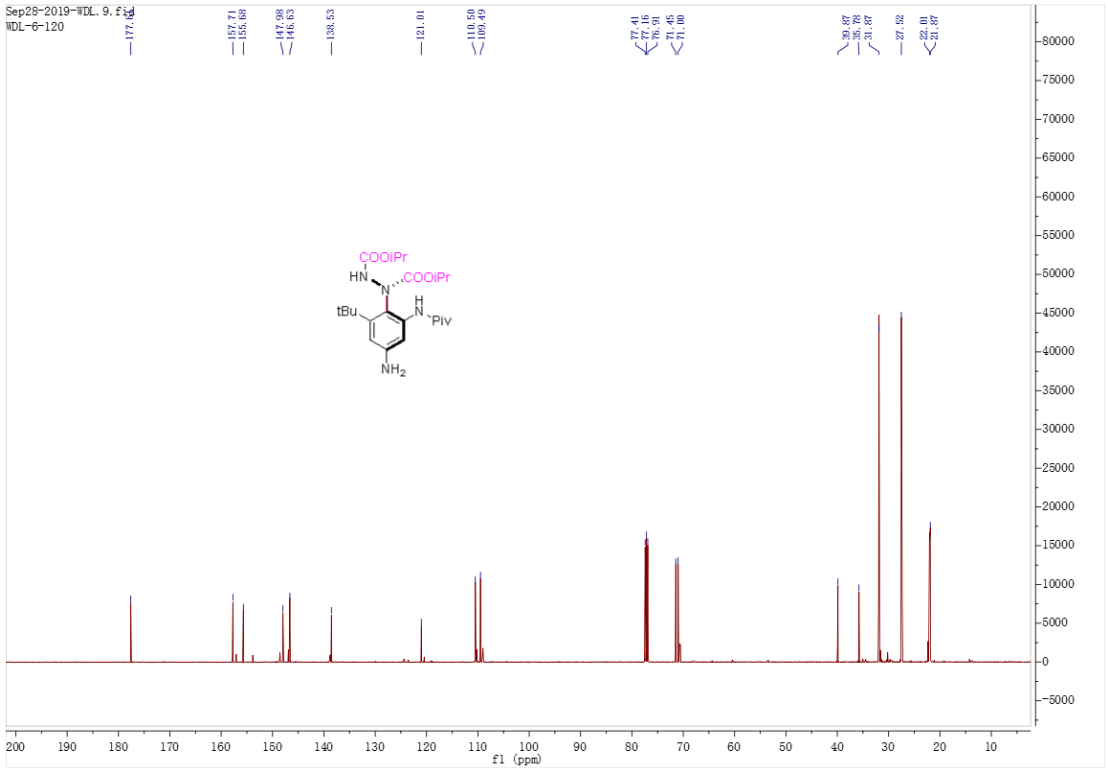
(*R*)-diethyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5q**)



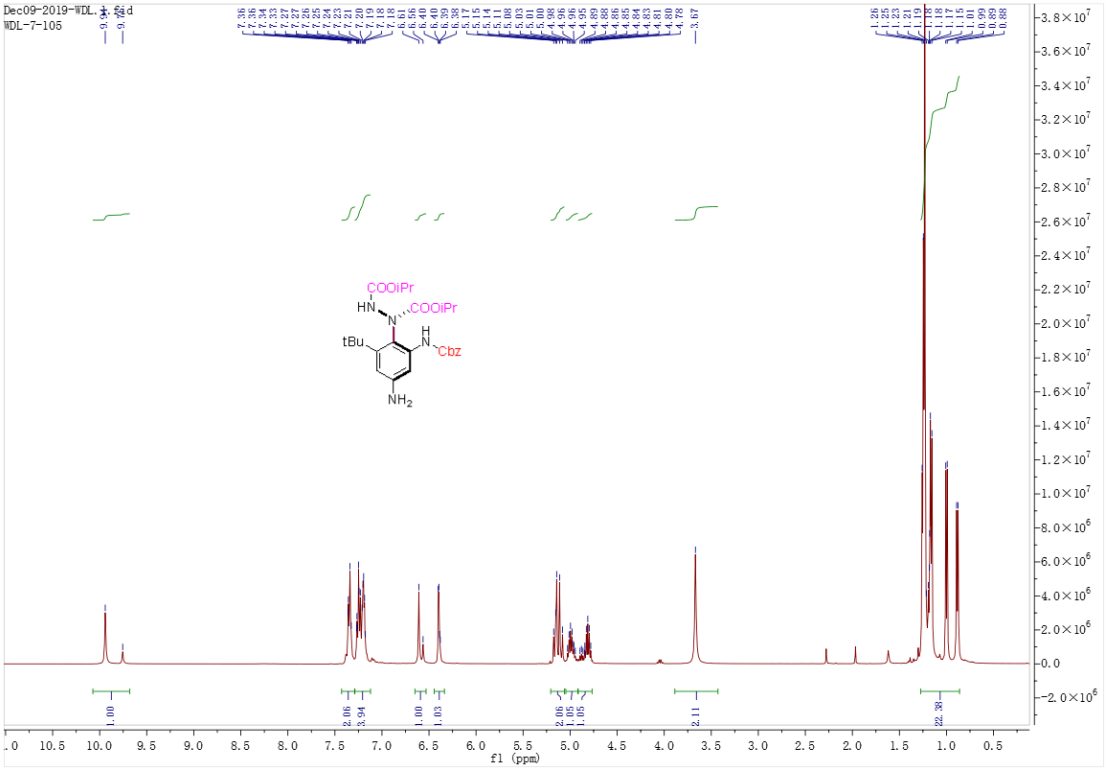


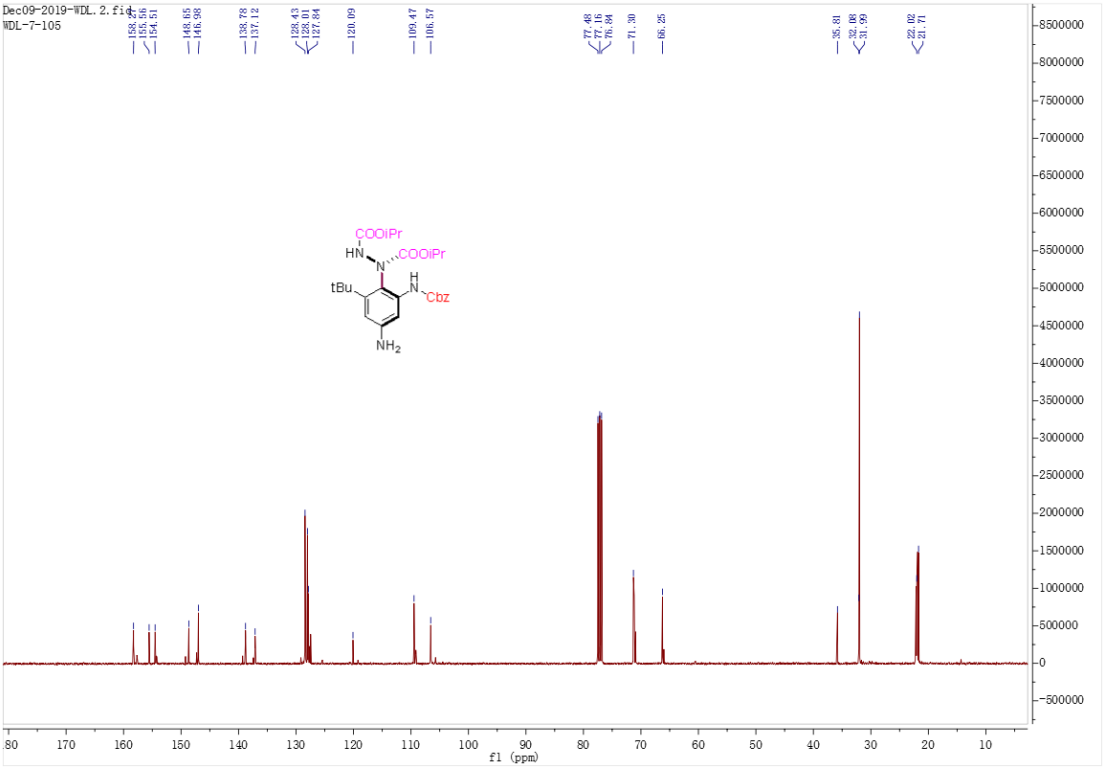
(*R*)-Diisopropyl-1-(4-amino-2-(tert-butyl)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**5r**)





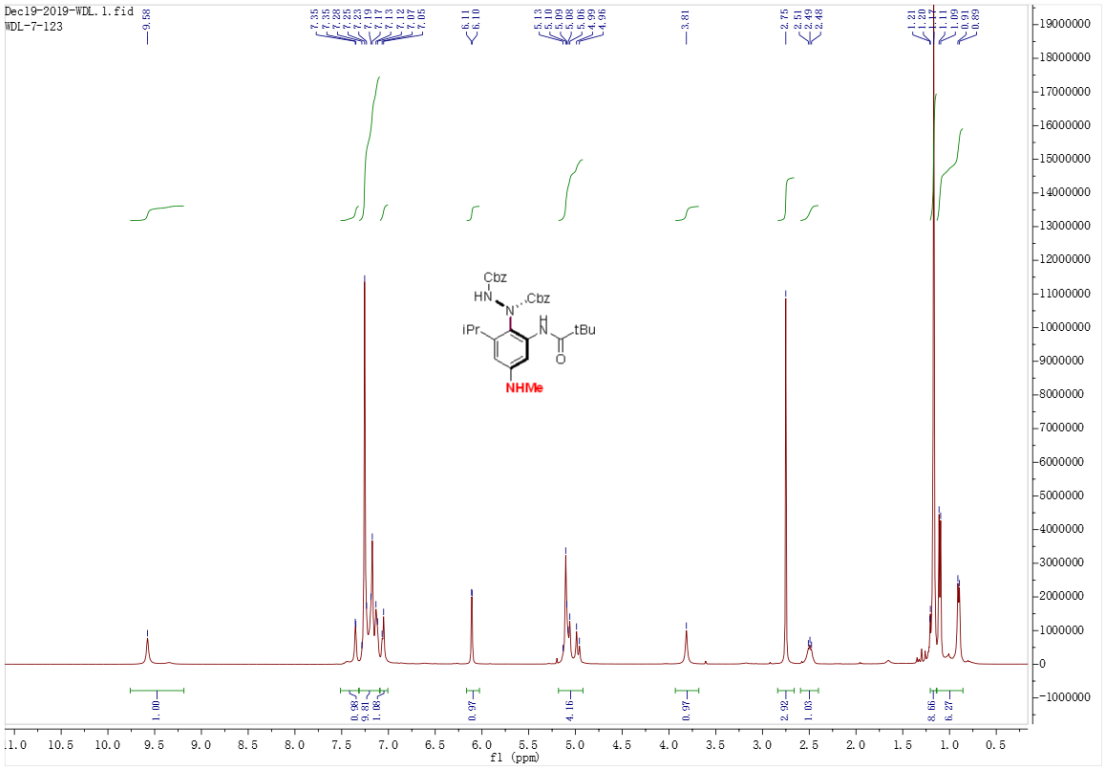
(*R*)-diisopropyl-1-(4-amino-2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**5s**)

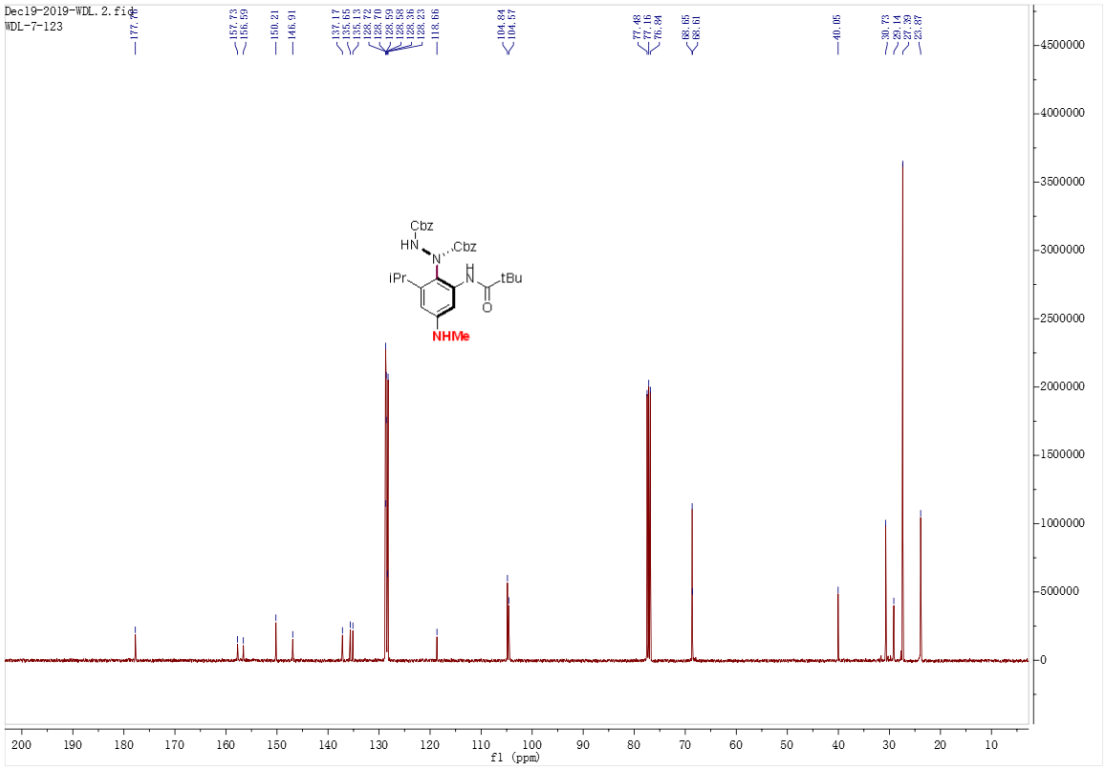




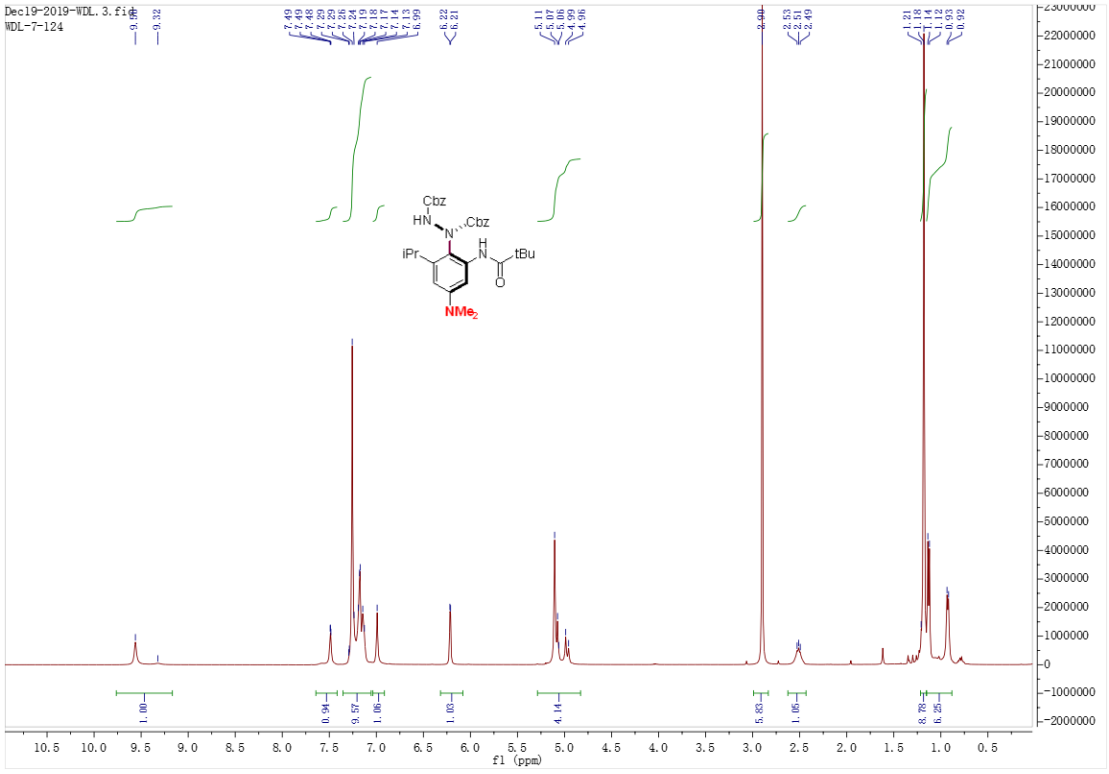
(*R*)-dibenzyl-1-(2-isopropyl-4-(methylamino)-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate

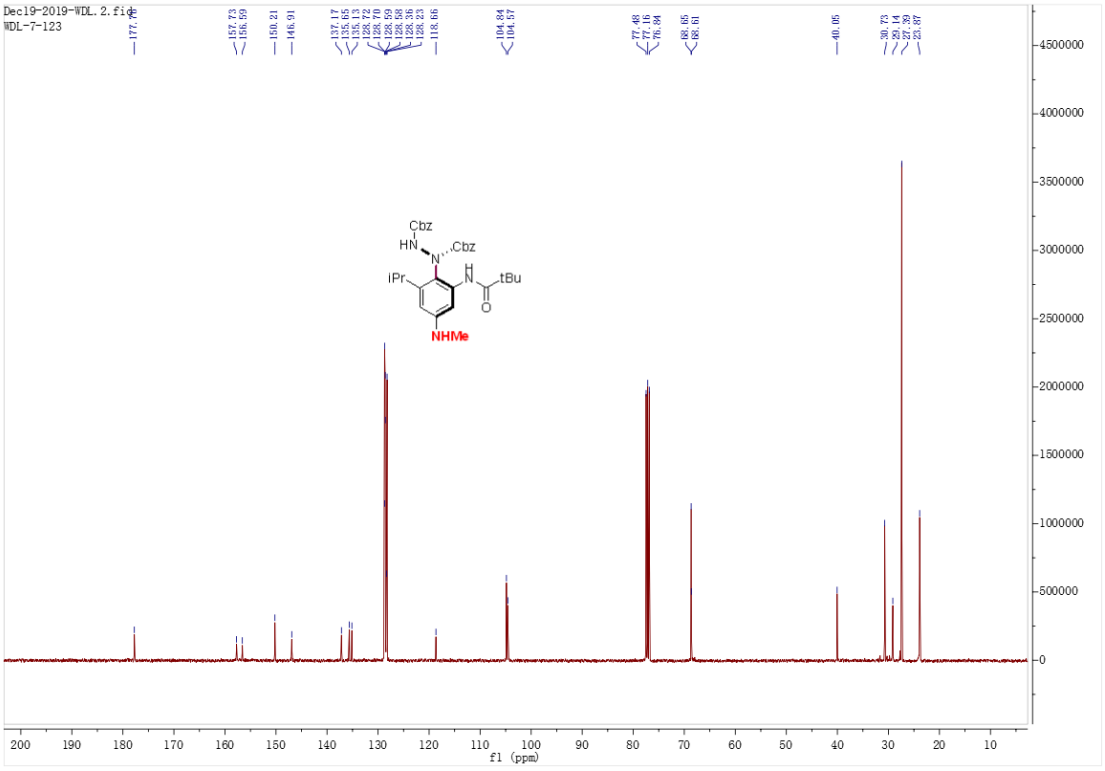
(**7b**)



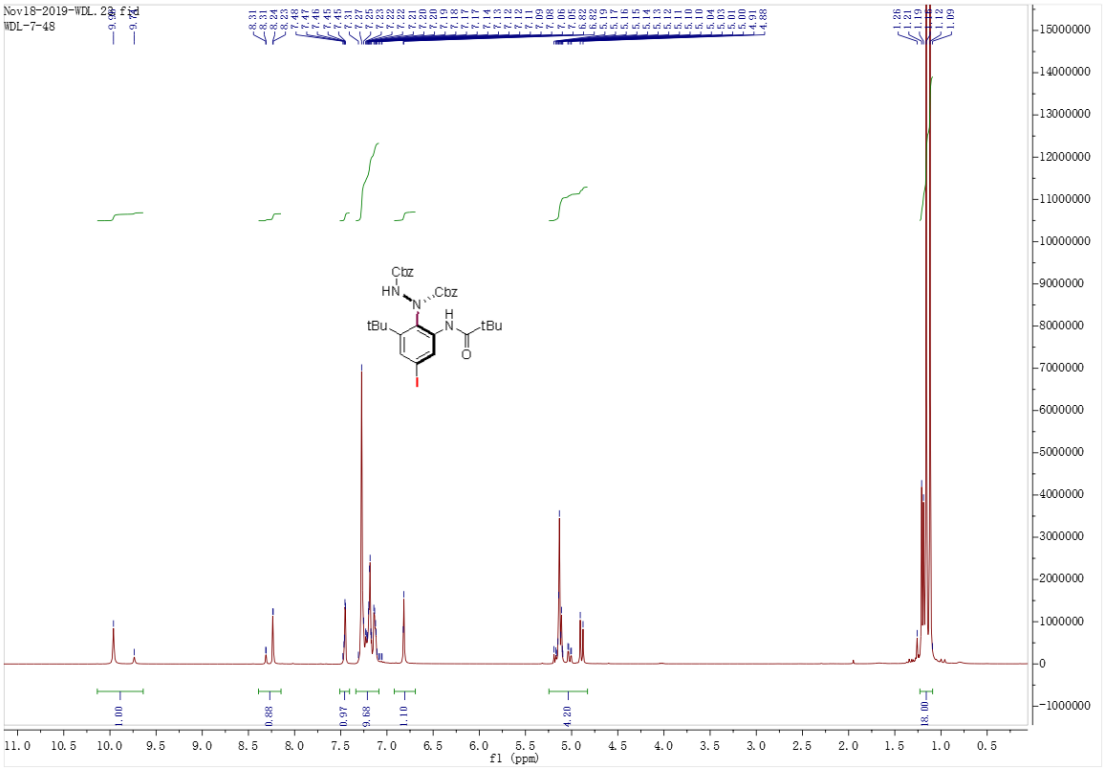


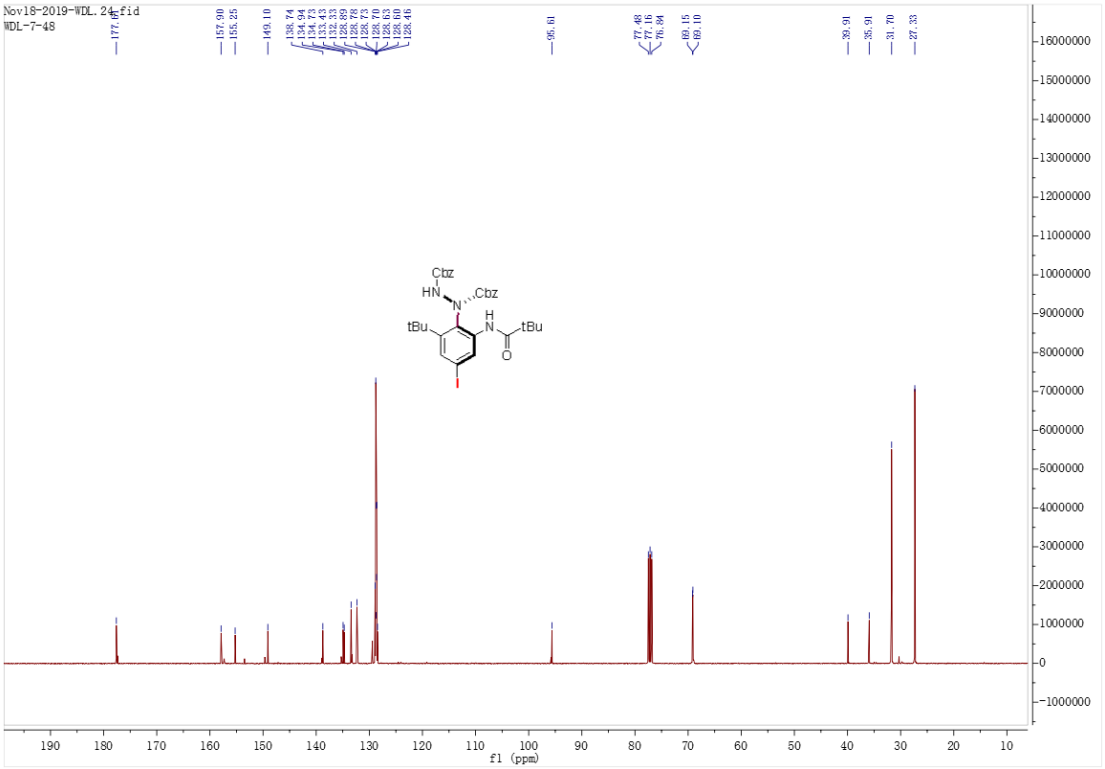
(*R*)-dibenzyl-1-(4-(dimethylamino)-2-isopropyl-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**7c**)



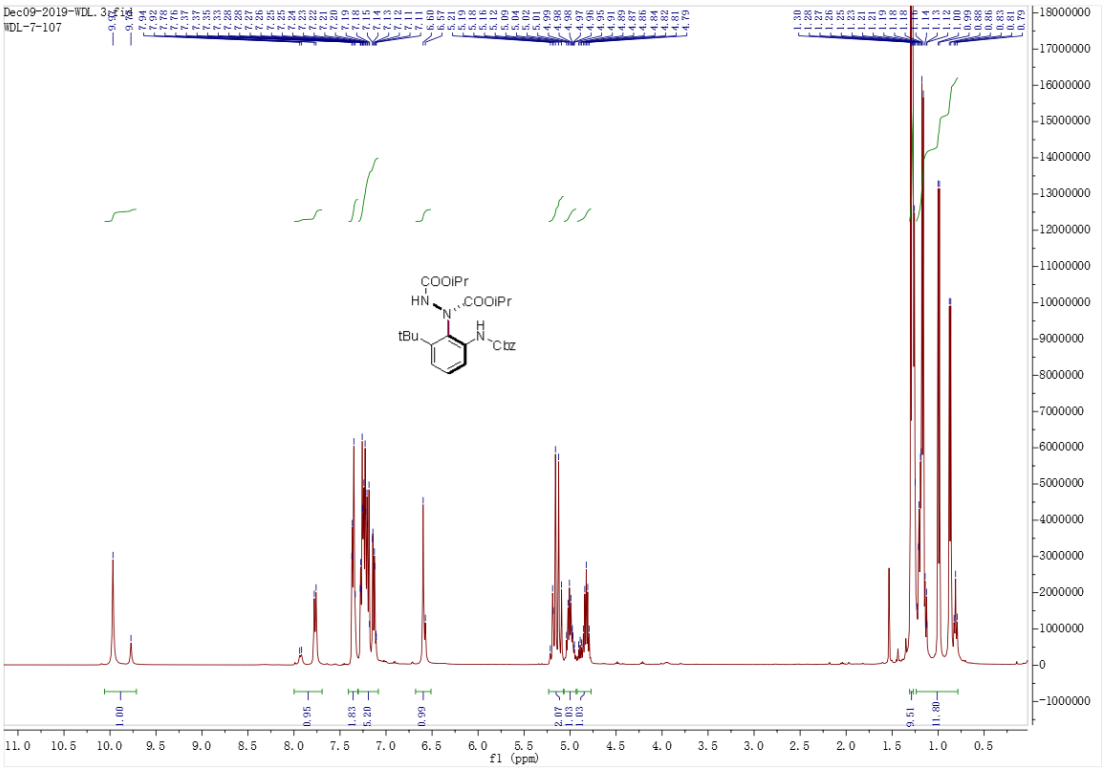


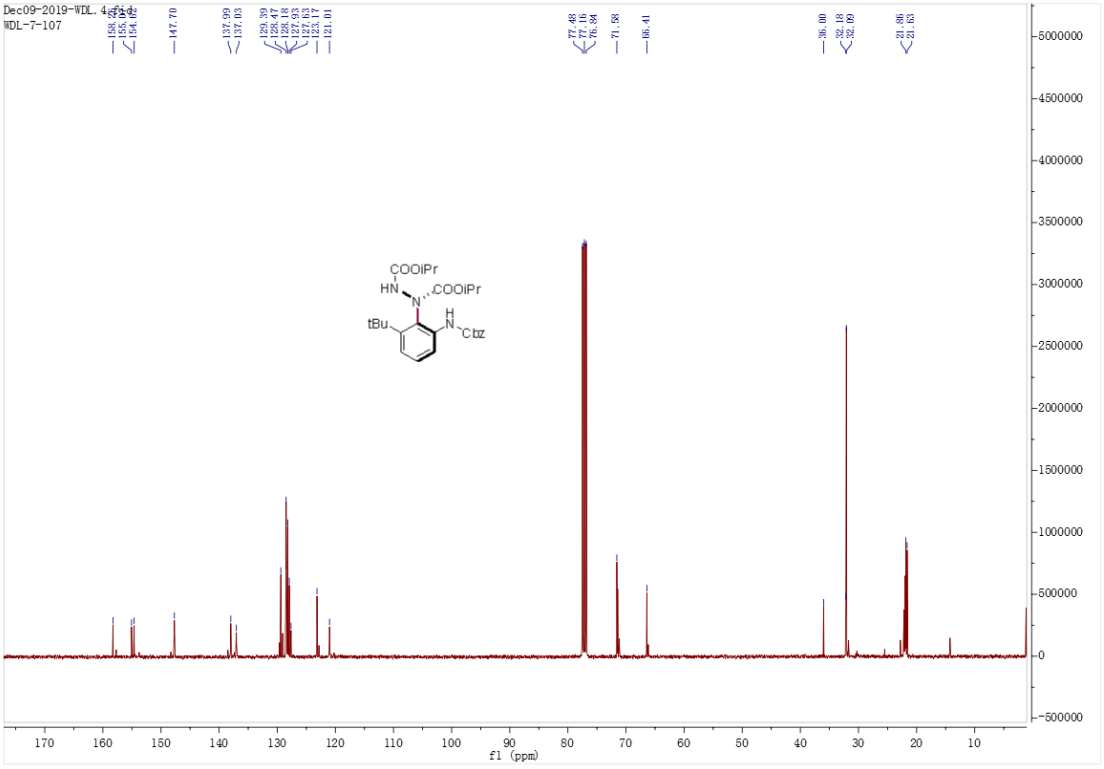
(*R*)-dibenzyl-1-(2-(tert-butyl)-4-iodo-6-pivalamidophenyl)hydrazine-1,2-dicarboxylate (**8a**)



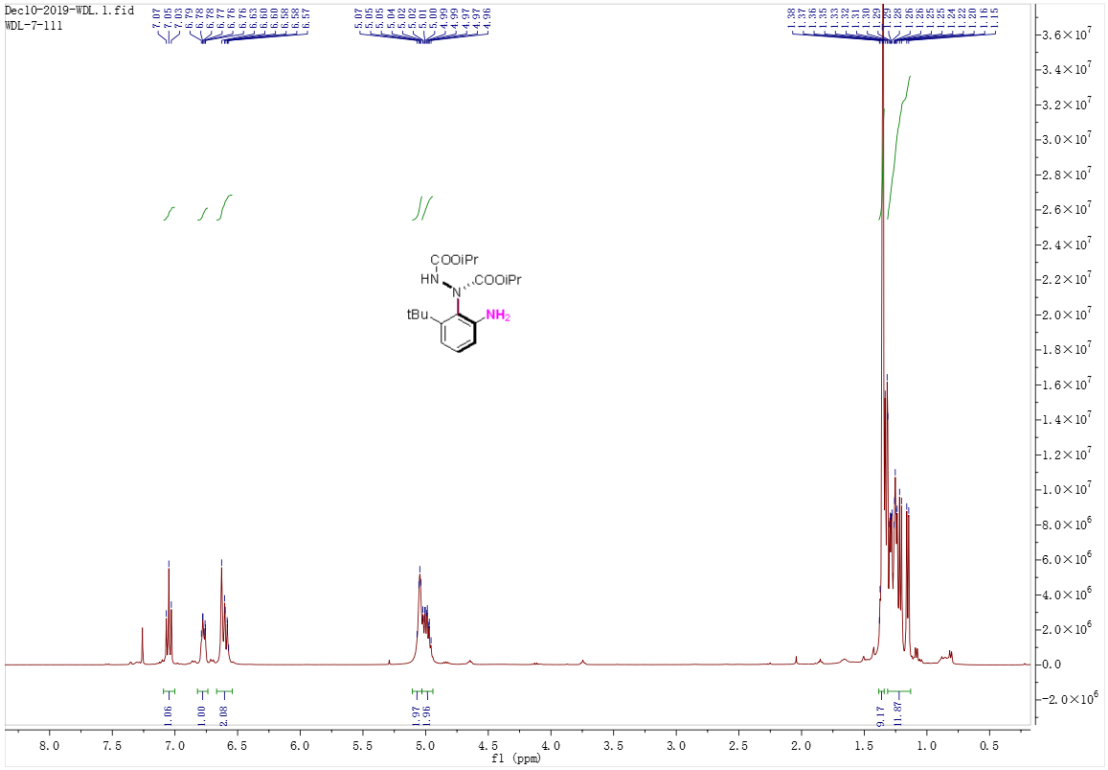


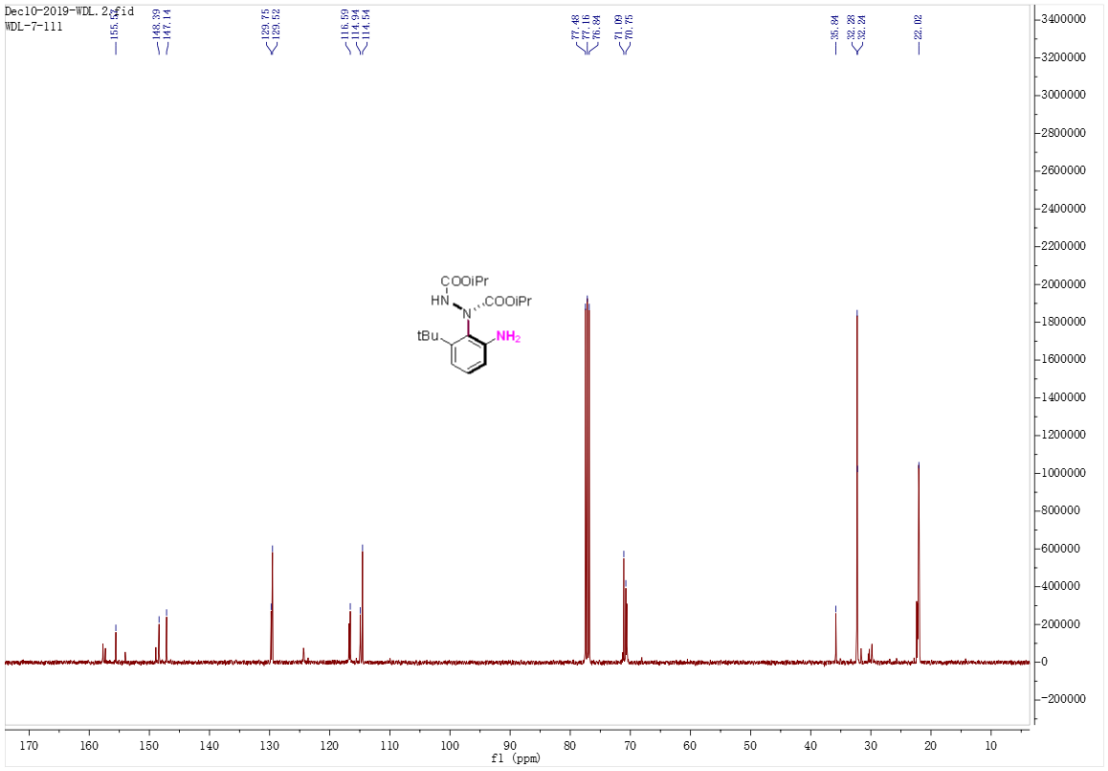
(*R*)-diisopropyl-1-(2-(((benzyloxy)carbonyl)amino)-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**9s**)





(*R*)-diisopropyl 1-(2-amino-6-(tert-butyl)phenyl)hydrazine-1,2-dicarboxylate (**10s**)





(*S*)-2-fluoro-2-phenylpropan-1-ol (**12a**)