Supporting Information for

Brønsted Acid-Catalyzed Stereoselective [4+3] Cycloadditions of *ortho*-Hydroxybenzyl Alcohols with *N*,*N*'-Cyclic Azomethine Imines

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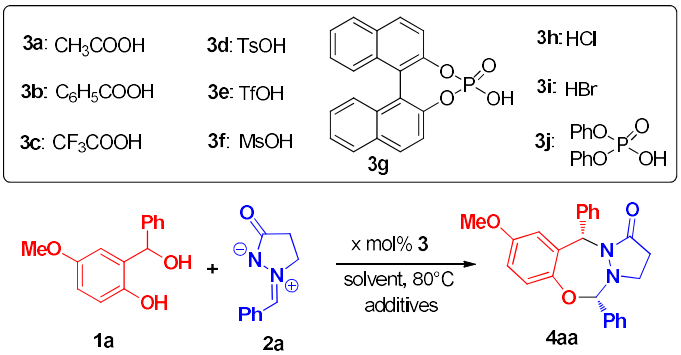
Contents:

1. General information

^{1}H and ^{13}C NMR spectra were measured respectively at 400 and 100 MHz, respectively. The solvent used for NMR spectroscopy was $CDCl_3$, using tetramethylsilane as the internal reference. HRMS (ESI) was determined by a HRMS/MS instrument. Analytical grade solvents for the column chromatography were used after distillation. All starting materials commercially available were used directly.

2. Screening of catalysts and optimization of reaction conditions

Table 1. Screening of catalysts and optimization of reaction conditions[a]

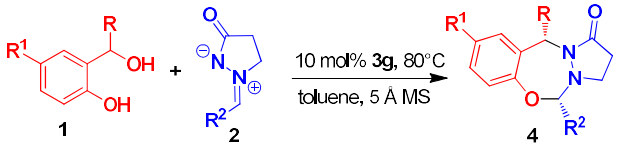


entry	**Cat.**	x	solvent	T (°C)	**1a**:**2a**	additives	yield (%)[b]
1	**3a**	10	toluene (1 mL)	80	1:1.2	3 Å MS	trace
2	**3b**	10	toluene (1 mL)	80	1:1.2	3 Å MS	trace
3	**3c**	10	toluene (1 mL)	80	1:1.2	3 Å MS	34
4	**3d**	10	toluene (1 mL)	80	1:1.2	3 Å MS	trace
5	**3e**	10	toluene (1 mL)	80	1:1.2	3 Å MS	trace
6	**3f**	10	toluene (1 mL)	80	1:1.2	3 Å MS	trace
7	**3g**	10	toluene (1 mL)	80	1:1.2	3 Å MS	40
8	**3h**	10	toluene (1 mL)	80	1:1.2	3 Å MS	trace
9	**3i**	10	toluene (1 mL)	80	1:1.2	3 Å MS	trace
10	**3g**	10	toluene (1 mL)	80	1:1	3 Å MS	36
11	**3g**	10	toluene (1 mL)	80	1:1.5	3 Å MS	52
12	**3g**	10	toluene (1 mL)	80	1:2	3 Å MS	39
13	**3g**	10	toluene (1 mL)	80	1:3	3 Å MS	36
14	**3g**	10	toluene (1 mL)	80	1.2:1	3 Å MS	38
15	**3g**	10	toluene (1 mL)	80	1.5:1	3 Å MS	40
16	**3g**	10	toluene (1 mL)	80	2:1	3 Å MS	46
17	**3g**	10	toluene (1 mL)	80	3:1	3 Å MS	48
18	**3g**	10	toluene (1 mL)	80	1:1.5	-	13
19	**3g**	10	toluene (1 mL)	80	1:1.5	4 Å MS	trace

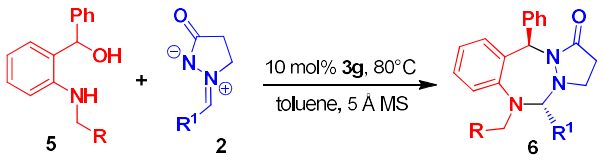
20	**3g**	10	toluene (1 mL)	80	1:1.5	5 Å MS	70
21	**3g**	10	toluene (1 mL)	80	1:1.5	$MgSO_4$	16
22	**3g**	10	toluene (1 mL)	80	1:1.5	Na_2SO_4	17
23	**3g**	10	CH_2ClCH_2Cl (1 mL)	80	1:1.5	5 Å MS	53
24	**3g**	10	1,4-dioxane (1 mL)	80	1:1.5	5 Å MS	trace
25	**3g**	10	EtOAc (1 mL)	80	1:1.5	5 Å MS	trace
26	**3g**	10	CH_3CN (1 mL)	80	1:1.5	5 Å MS	trace
27	**3g**	10	*o*-xylene (1 ml)	80	1:1.5	5 Å MS	58
28	**3g**	10	*m*-xylene (1 mL)	80	1:1.5	5 Å MS	59
29	**3g**	10	*p*-xylene (1 mL)	80	1:1.5	5 Å MS	60
30	**3g**	10	F-Ph (1 mL)	80	1:1.5	5 Å MS	51
31 32	**3g**	10	Cl-Ph (1 mL)	80	1:1.5	5 Å MS	50
33	**3g**	10	Br-Ph (1 mL)	80	1:1.5	5 Å MS	49
34	**3g**	10	toluene (0.5 mL)	80	1:1.5	5 Å MS	56
	3g	10	toluene (2 mL)	80	1:1.5	5 Å MS	58
35	**3g**	10	toluene (4 mL)	80	1:1.5	5 Å MS	29
36	**3g**	10	toluene (1 mL)	100	1:1.5	5 Å MS	49
37	**3g**	5	toluene (1 mL)	80	1:1.5	5 Å MS	63
38	**3g**	20	toluene (1 mL)	80	1:1.5	5 Å MS	63
39	**3g**	30	toluene (1 mL)	80	1:1.5	5 Å MS	60
40	**3g**	50	toluene (1 mL)	80	1:1.5	5 Å MS	66
41	**3j**	10	toluene (1 mL)	80	1:1.5	5 Å MS	66

[a]Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale catalyzed by x mol% **3** in a solvent with additives (100 mg) at T°C for 15 h. [b]Isolated yield.

3. General procedure for the synthesis of products 4 and 6



To the mixture of *ortho*-hydroxybenzyl alcohols **1** (0.1 mmol), *N,N'*-cyclic azomethine imines **2** (0.15 mmol), 5 Å molecular sieves (100 mg) and the catalyst **3g** (0.01 mmol), was added toluene (1 mL). After being stirred at 80 °C for 15 h, the reaction mixture was filtered to remove molecular sieves and the solid powder was washed with ethyl acetate. The resultant solution was concentrated under the reduced pressure to give the residue, which was purified through preparative thin layer chromatography to afford pure products **4**.



To the mixture of *ortho*-aminobenzyl alcohols **5** (0.1 mmol), *N,N'*-cyclic azomethine imines **2** (0.15 mmol), 5 Å molecular sieves (100 mg) and the catalyst **3g** (0.01 mmol), was added toluene (1 mL). After being stirred at 80 °C for 15 h, the reaction mixture was filtered to remove molecular sieves and the solid powder was washed with ethyl acetate. The resultant solution was concentrated under the reduced pressure to give the residue, which was purified through preparative thin layer chromatography to afford pure products **6**.

4. Characterization data of products 4 and 6

9-methoxy-5,11-diphenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4] oxadiazepin-1-one (4aa): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 70% (27.1 mg); >95:5 dr; white solid; m.p. 146–147°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.27 (m, 10H), 6.93 (d, *J* = 8.7 Hz, 1H), 6.88 (d, *J* = 2.8 Hz, 1H), 6.78 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.60 (s, 1H), 5.11 (s, 1H), 3.78 (s, 3H), 3.08 (dd, *J* = 20.4, 9.2 Hz, 1H), 2.83 – 2.74 (m, 1H), 2.73 – 2.63 (m, 1H), 2.44 – 2.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 156.3, 150.6, 138.1, 137.6, 133.3, 129.6, 128.8, 128.3, 128.2, 127.6, 127.5, 123.6, 114.8, 114.5, 101.1, 60.4, 55.6, 46.5, 30.1; IR (KBr): 3333, 2999, 2920, 2849, 1960, 1678, 1584, 1496, 1380, 1206, 1043, 857, 736 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{22}N_2O_3+Na)^+$ requires m/z 409.1523, found m/z 409.1520.

9-methoxy-5-phenyl-11-(*o*-tolyl)-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ba): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 63% (25.2 mg); >95:5 dr; white solid; m.p. 159–160°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.32 (m, 5H), 7.27 – 7.22 (m, 3H), 7.19 – 7.14 (m, 1H), 6.89 (d, *J* = 8.8 Hz, 1H), 6.77 – 6.69 (m, 2H), 6.61 (s, 1H), 5.26 (s, 1H), 3.73 (s, 3H), 3.25 – 3.13 (m, 1H), 2.88 (dd, *J* = 12.5, 8.6 Hz, 1H), 2.78 – 2.67 (m, 1H), 2.44 (s, 3H), 2.28 (dd, *J* = 16.8, 8.2 Hz, 1H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 170.5, 156.5, 149.7, 137.7, 136.7, 135.6, 134.3, 130.5, 130.2, 129.6, 128.8, 127.8, 127.6, 125.9, 123.8, 114.2, 99.5, 57.7, 55.6, 46.6, 29.6, 19.7; IR (KBr): 3327, 2920, 2849, 1936, 1678, 1499, 1399, 1213, 1038, 1006, 852, 823, 748, 690 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_3+Na)^+$ requires m/z 423.1680, found m/z 423.1685.

9-methoxy-11-(2-methoxyphenyl)-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ca): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 68% (28.4 mg); >95:5 dr; yellow solid; m.p. 166–167°C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 5H), 7.30 (t, *J* = 7.3 Hz, 2H), 6.95 – 6.89 (m, 3H), 6.86 (d, *J* = 2.8 Hz, 1H), 6.82 (s, 1H), 6.74 (dd, *J* = 8.7, 2.9 Hz, 1H), 5.17 (s, 1H), 3.88 (s, 3H), 3.72 (s, 3H), 3.10 – 3.01 (m, 1H), 2.80 – 2.72 (m, 1H), 2.70 – 2.60 (m, 1H), 2.32 – 2.23 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 157.3, 156.3, 150.5, 137.8, 134.2, 131.0, 129.5, 129.0, 128.8, 127.6, 125.7, 123.6, 120.2, 114.3, 114.0, 110.2, 100.7, 55.6, 55.4, 46.4, 29.9;IR (KBr): 3378, 3030, 2924, 2832, 1960, 1812, 1697, 1492, 1395, 1307, 1206, 1114, 935, 862, 764 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_4+Na)^+$ requires m/z 439.1629, found m/z 439.1624.

9-methoxy-5-phenyl-11-(*m*-tolyl)-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4da): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 73% (29.2 mg); >95:5 dr; yellow sticky oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 7.25 – 7.20 (m, 1H), 7.15 – 7.08 (m, 3H), 6.93 (d, *J* = 8.7 Hz, 1H), 6.86 (d, *J* = 3.0 Hz, 1H), 6.77 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.56 (s, 1H), 5.12 (s, 1H), 3.77 (s, 3H), 3.13 – 3.04 (m, 1H), 2.82 – 2.74 (m, 1H), 2.73 – 2.63 (m, 1H), 2.42 – 2.35 (m, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 156.3, 150.5, 138.1, 137.8, 137.6, 133.4, 129.6, 128.9, 128.7, 128.32, 128.1, 127.5, 125.4, 123.6, 114.7, 114.5, 101.0, 60.4, 55.6, 46.5, 30.1, 21.6; IR (KBr): 3627, 2922, 2850, 1771, 1698, 1684, 1496, 1394, 1205, 1039, 820, 749, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_3+Na)^+$ requires m/z 423.1680, found m/z 423.1685.

9-methoxy-11-(3-methoxyphenyl)-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyr

azolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ea): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 72% (30.1 mg); >95:5 dr; white sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 7.26 – 7.22 (m, 1H), 6.93 – 6.88 (m, 3H), 6.87 – 6.82 (m, 2H), 6.76 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.55 (s, 1H), 5.11 (s, 1H), 3.78-3.77 (m, 6H), 3.14 – 3.05 (m, 1H), 2.82 – 2.75 (m, 1H), 2.73 – 2.63 (m, 1H), 2.43 – 2.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 159.5, 156.3, 150.5, 139.7, 137.5, 133.2, 129.6, 129.2, 128.8, 127.6, 123.6, 120.7, 114.7, 114.5, 114.3, 112.7, 101.0, 60.3, 55.6, 55.2, 46.5, 30.1;IR (KBr): 2924, 2835, 1694, 1600, 1497, 1393, 1212, 1069, 1041, 821, 760, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_4+Na)^+$ requires m/z 439.1629, found m/z 439.1624.

11-(3-fluorophenyl)-9-methoxy-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4fa): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 68% (27.6 mg); >95:5 dr; pale yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.34 (m, 5H), 7.33 – 7.27 (m, 1H), 7.06 – 6.96 (m, 3H), 6.94 (d, *J* = 8.7 Hz, 1H), 6.88 (d, *J* = 3.0 Hz, 1H), 6.79 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.56 (s, 1H), 5.09 (s, 1H), 3.79 (s, 3H), 3.14 – 3.05 (m, 1H), 2.83 – 2.76 (m, 1H), 2.73 – 2.63 (m, 1H), 2.44 – 2.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 162.8 (*J* = 243.8 Hz), 156.4, 150.6, 137.4, 132.8, 129.7, 129.6 (*J* = 8.2 Hz), 128.8, 127.5, 123.8, 123.7, 115.3 (*J* = 22.5 Hz), 114.7 (*J* = 24.9 Hz), 114.4 (*J* = 21.1 Hz), 101.1, 59.8, 55.7, 46.5, 30.0; IR (KBr): 3063, 2921, 2850, 1697, 1589, 1498, 1456, 1389, 1210, 1038, 1002, 873, 820, 762, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{21}FN_2O_3+Na)^+$ requires m/z 427.1429, found m/z 427.1421.

9-methoxy-5-phenyl-11-(*p*-tolyl)-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ga): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 75% (30.1 mg); >95:5 dr; white solid; m.p. 130–131°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 1H), 6.86 (d, *J* = 3.0 Hz, 1H), 6.76 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.57 (s, 1H), 5.10 (s, 1H), 3.77 (s, 3H), 3.11 – 3.01 (m, 1H), 2.80 – 2.62 (m, 2H), 2.41 – 2.32 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 171.3, 156.3, 150.5, 137.6, 137.1, 135.2, 133.5, 129.6, 128.9, 128.7, 128.2, 127.6, 123.6, 114.6, 114.4, 101.1, 60.3, 55.6, 46.5, 30.1, 21.2; IR (KBr): 3002, 2920, 2849, 1675, 1501, 1403, 1315, 1217, 1044, 1004, 938, 830, 718, 688 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_3+Na)^+$ requires m/z 423.1680, found m/z 423.1685.

9-methoxy-11-(4-methoxyphenyl)-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ha): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 69% (28.9 mg); >95:5 dr; white solid; m.p. 78–79°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 7.27 – 7.24 (m, 2H), 6.92 (d, *J* = 8.7 Hz, 1H), 6.88 – 6.84 (m, 3H), 6.76 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.55 (s, 1H), 5.10 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.09 – 3.01 (m, 1H), 2.79 – 2.62 (m, 2H), 2.40 – 2.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 158.9, 156.3, 150.4, 137.6, 133.6, 130.3, 129.6, 128.8, 127.6, 123.6, 114.6, 114.5, 113.6, 101.1, 60.1, 55.6, 55.2, 46.5, 30.2; IR (KBr): 2923, 2835, 1690, 1609, 1510, 1393, 1249, 1212, 1036, 893, 829, 767, 700 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_4\text{-}H)^-$ requires m/z 415.1653, found m/z 415.1649.

11-(4-fluorophenyl)-9-methoxy-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ia): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 73% (29.3 mg); >95:5 dr; pale yellow solid; m.p. 96–97°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.34 (m, 5H), 7.33 – 7.26 (m, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 1H), 6.87 (d, *J* = 3.0 Hz, 1H), 6.78 (dd, *J* = 8.8, 3.0 Hz, 1H), 6.56 (s, 1H), 5.09 (s, 1H), 3.78 (s, 3H), 3.12 – 2.99 (m, 1H), 2.81 – 2.74 (m, 1H), 2.72 – 2.62 (m, 1H), 2.41 – 2.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 162.2 (*J* = 244.5 Hz), 156.4, 150.5, 137.4, 133.9(*J* = 3.1 Hz), 133.2, 130.0 (*J* = 8.0 Hz), 128.8, 127.5, 123.7, 115.1 (*J* = 21.3 Hz), 114.7, 101.1, 59.8, 55.7, 46.5, 30.1; IR (KBr): 3033, 2922, 2849, 1683, 1506, 1399, 1215, 1066, 1004, 849, 766 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{21}FN_2O_3\text{-}H)^-$ requires m/z 403.1453, found m/z 403.1455.

11-(4-chlorophenyl)-9-methoxy-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ja): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 72% (30.3

mg); >95:5 dr; white solid; m.p. 133–134 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.32 (m, 5H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 1H), 6.87 (d, *J* = 3.0 Hz, 1H), 6.78 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.55 (s, 1H), 5.09 (s, 1H), 3.78 (s, 3H), 3.12 – 2.99 (m, 1H), 2.82 – 2.73 (m, 1H), 2.72 – 2.62 (m, 1H), 2.42 – 2.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.4, 150.5, 137.4, 136.7, 133.4, 132.9, 129.7, 128.8, 128.4, 127.5, 123.7, 114.7, 101.1, 59.8, 55.7, 46.5, 30.0; IR (KBr): 3031, 2921, 2840, 1682, 1500, 1402, 1310, 1215, 1043, 1013, 938, 846, 765 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{21}ClN_2O_3\text{-}H)^-$ requires m/z 419.1158, found m/z 419.1150.

4-(9-methoxy-1-oxo-5-phenyl-2,3-dihydro-1*H*,5*H*,11*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-11-yl)benzonitrile (4ka): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 88% (36.2 mg); dr = 75:25 (inseparable diastereomers); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.64 (m, 2H), 7.51 – 7.29 (m, 7H), 7.07 – 6.56 (m, 4H), 5.70 (s, 0.25H), 5.10 (s, 0.75H), 3.82 (s, 3H), 3.29 – 3.05 (m, 1H), 2.91 – 2.38 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.5, 150.6, 143.5, 137.2, 132.4, 132.2, 132.1, 129.8, 128.9, 128.5, 128.1, 127.4, 126.6, 123.9, 122.1, 118.8, 115.4, 114.9, 114.9, 111.4, 101.2, 93.1, 59.8, 55.7, 46.4, 29.9; IR (KBr): 2998, 2915, 1680, 1496, 1380, 1206, 1043, 880 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{21}N_3O_3\text{+}Na)^+$ requires m/z 434.1475, found m/z 434.1477.

9-methoxy-5-phenyl-11-(thiophen-2-yl)-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4la): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 66% (25.9 mg); >95:5 dr; yellow solid; m.p. 109–110ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.47 (m, 2H), 7.45 – 7.37 (m, 3H), 7.27 (d, *J* = 4.5 Hz, 1H), 7.00 (d, *J* = 3.2 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 3H), 6.78 (s, 1H), 6.75 (dd, *J* = 8.8, 2.9 Hz, 1H), 5.07 (s, 1H), 3.76 (s, 3H), 3.09 – 2.96 (m, 1H), 2.79 – 2.67 (m, 1H), 2.66 – 2.55 (m, 1H), 2.40 – 2.27 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 156.3, 150.4, 140.9, 137.4, 133.8, 129.7, 128.9, 127.7, 127.3, 126.1, 123.7, 114.7, 114.1, 101.8, 57.1, 55.7, 46.4, 30.2;IR (KBr): 3062, 2926, 2850, 1697, 1608, 1500, 1457, 1373, 1216, 1031, 892, 755, 715

cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{20}N_2O_3S\text{-}H)^-$ requires m/z 391.1112, found m/z 391.1110.

9-methoxy-11-methyl-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ma): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 67% (21.6 mg); >95:5 dr; yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.50 (m, 2H), 7.48 – 7.39 (m, 3H), 6.91 – 6.80 (m, 2H), 6.68 (dd, *J* = 8.7, 2.7 Hz, 1H), 5.41 (q, *J* = 6.9 Hz, 1H), 4.92 (s, 1H), 3.78 (s, 3H), 3.15 – 3.01 (m, 1H), 2.89 – 2.70 (m, 1H), 2.62 – 2.51 (m, 1H), 2.42 – 2.26 (m, 1H), 1.73 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 156.3, 150.8, 137.7, 136.0, 129.7, 128.9, 128.6, 127.5, 126.8, 123.1, 113.6, 113.2, 102.2, 55.6, 53.8, 46.3, 30.4, 18.3;IR (KBr): 2924, 2850, 1771, 1669, 1497, 1456, 1397, 1225, 1210, 1037, 812, 736, 700 cm^{-1}; ESI FTMS exact mass calcd for $(C_{19}H_{20}N_2O_3\text{+}H)^+$ requires m/z 325.1547, found m/z 325.1544.

11-ethyl-9-methoxy-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4na): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 76% (25.7 mg); >95:5 dr; white solid; m.p. 123–124 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.48 (m, 2H), 7.47 – 7.37 (m, 3H), 6.87 (d, *J* = 8.7 Hz, 1H), 6.82 (d, *J* = 2.8 Hz, 1H), 6.68 (dd, *J* = 8.7, 2.8 Hz, 1H), 5.11 (dd, *J* = 8.9, 6.8 Hz, 1H), 4.94 (s, 1H), 3.77 (s, 3H), 3.10 (dd, *J* = 20.3, 8.9 Hz, 1H), 2.83 – 2.68 (m, 1H), 2.64 – 2.52 (m, 1H), 2.49 – 2.32 (m, 2H), 2.07 – 1.97 (m, 1H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 156.1, 150.8, 137.9, 135.2, 129.6, 128.9, 127.5, 123.1, 113.9, 113.6, 101.9, 59.7, 55.6, 46.4, 30.3, 25.0, 11.2;IR (KBr): 3056, 2967, 2919, 2856, 1771, 1682, 1586, 1498, 1357, 1273, 1211, 1055, 903, 874, 773, 703 cm^{-1}; ESI FTMS exact mass calcd for $(C_{20}H_{22}N_2O_3\text{+}H)^+$ requires m/z 339.1703, found m/z 339.1700.

11-isobutyl-9-methoxy-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4oa): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 64% (23.5 mg);>95:5 dr; white solid; m.p. 128–129ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.50 (m, 2H), 7.48 – 7.40 (m, 3H), 6.87 (d, *J* = 8.7 Hz, 1H), 6.83 (d, *J* = 2.7 Hz, 1H), 6.67 (dd, *J* =

8.7, 2.7 Hz, 1H), 5.30 (dd, *J* = 9.3, 6.2 Hz, 1H), 4.96 (s, 1H), 3.77 (s, 3H), 3.12 (dd, *J* = 20.9, 9.4 Hz, 1H), 2.83 – 2.74 (m, 1H), 2.65 – 2.53 (m, 1H), 2.49 – 2.41 (m, 1H), 2.37 – 2.27 (m, 1H), 1.79 – 1.70 (m, 1H), 1.59 – 1.49 (m, 1H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 156.2, 150.9, 137.9, 135.7, 129.6, 128.9, 127.4, 123.2, 113.6, 113.5, 101.7, 55.9, 55.7, 46.3, 40.6, 30.3, 24.9, 23.1, 22.1; IR (KBr): 3045, 2953, 2923, 2869, 1867, 1682, 1586, 1496, 1273, 1171, 1038, 921, 853, 701 cm^{-1}; ESI FTMS exact mass calcd for $(C_{22}H_{26}N_2O_3+H)^+$ requires m/z 367.2016, found m/z 367.2010.

9-methoxy-11-pentyl-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4pa): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 74% (28.0 mg); >95:5 dr; white solid; m.p. 117–118ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.49 (m, 2H), 7.48 – 7.38 (m, 3H), 6.87 (d, *J* = 8.7 Hz, 1H), 6.82 (d, *J* = 2.8 Hz, 1H), 6.68 (dd, *J* = 8.7, 2.8 Hz, 1H), 5.25 – 5.14 (m, 1H), 4.94 (s, 1H), 3.77 (s, 3H), 3.15 – 3.04 (m, 1H), 2.83 – 2.69 (m, 1H), 2.64 – 2.52 (m, 1H), 2.49 – 2.31 (m, 2H), 2.01 – 1.89 (m, 1H), 1.45 – 1.27 (m, 6H), 0.89 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 156.1, 150.8, 137.9, 135.5, 129.6, 128.9, 127.5, 123.1, 113.8, 113.6, 101.9, 58.2, 55.6, 46.4, 31.6, 31.4, 30.3, 26.1, 22.5, 14.0;IR (KBr): 3002, 2923, 2855, 1678, 1585, 1500, 1406, 1213, 1039, 1003, 919, 870, 821, 755, 702 cm^{-1}; ESI FTMS exact mass calcd for $(C_{23}H_{28}N_2O_3+H)^+$ requires m/z 381.2173, found m/z 381.2168.

11-cyclopentyl-9-methoxy-5-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4qa): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 71% (26.9 mg); >95:5 dr; white solid; m.p. 163–164 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.49 (m, 2H), 7.47 – 7.40 (m, 3H), 6.87 (d, *J* = 8.7 Hz, 1H), 6.82 (d, *J* = 2.7 Hz, 1H), 6.67 (dd, *J* = 8.7, 2.7 Hz, 1H), 4.94 (s, 1H), 4.89 (d, *J* = 10.9 Hz, 1H), 3.76 (s, 3H), 3.28 – 3.17 (m, 1H), 3.11 (dd, *J* = 20.4, 9.2 Hz, 1H), 2.79 – 2.71 (m, 1H), 2.62 – 2.53 (m, 1H), 2.39 – 2.29 (m, 1H), 1.96 – 1.87 (m, 1H), 1.74 – 1.53 (m, 4H), 1.34 – 1.18 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 155.9, 150.8, 137.9, 135.2, 129.6, 128.9, 127.5, 123.0, 114.4, 113.4, 101.8, 63.2, 55.6, 46.4, 41.0, 30.7, 30.2, 30.2, 25.4,

24.9; IR (KBr): 3064, 2954, 2867, 1686, 1588, 1502, 1395, 1336, 1274, 1211, 1071, 1034, 930, 890, 815, 764 cm^{-1}; ESI FTMS exact mass calcd for $(C_{23}H_{26}N_2O_3+H)^+$ requires m/z 379.2016, found m/z 379.2015.

9-methyl-5,11-diphenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ra): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 61% (22.6 mg); >95:5 dr; white solid; m.p. 151–152°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 5H), 7.34 – 7.28 (m, 5H), 7.18 (s, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 6.61 (s, 1H), 5.12 (s, 1H), 3.13 – 3.02 (m, 1H), 2.81 – 2.74 (m, 1H), 2.71 – 2.62 (m, 1H), 2.42 – 2.33 (m, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 154.8, 138.3, 137.6, 134.5, 132.1, 130.6, 129.9, 129.6, 128.8, 128.3, 128.2, 127.5, 127.4, 122.6, 101.1, 60.3, 46.5, 30.1, 20.7;IR (KBr): 3030, 2920, 2850, 1686, 1599, 1500, 1455, 1309, 1256, 1222, 1048, 1001, 941, 864, 792, 744 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{22}N_2O_2+H)^+$ requires m/z 371.1754, found m/z 371.1759.

5,11-diphenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4sa): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 51% (18.1 mg); >95:5 dr; white solid; m.p. 114–115°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 6H), 7.35 – 7.26 (m, 6H), 7.17 (d, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 7.9 Hz, 1H), 6.67 (s, 1H), 5.17 (s, 1H), 3.14 – 3.04 (m, 1H), 2.82 – 2.74 (m, 1H), 2.73 – 2.63 (m, 1H), 2.45 – 2.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 156.9, 138.3, 137.5, 132.5, 130.2, 129.7, 129.4, 128.8, 128.2, 128.2, 127.6, 127.4, 124.9, 122.9, 101.0, 60.3, 46.5, 30.1; IR (KBr): 3027, 2919, 2850, 1682, 1605, 1582, 1492, 1456, 1396, 1255, 1208, 1048, 1001, 905, 807, 767, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{23}H_{20}N_2O_2+H)^+$ requires m/z 357.1598, found m/z 357.1601.

9-methoxy-5-(2-methoxyphenyl)-11-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ab): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 72% (30.0 mg); >95:5 dr; yellow solid; m.p. 144–145°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.5 Hz, 1H), 7.38 – 7.27 (m, 6H), 6.99 – 6.94 (m, 2H), 6.93 – 6.88 (m, 2H), 6.80 –

6.76 (m, 1H), 6.61 (s, 1H), 5.73 (s, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 3.11 (dd, *J* = 19.8, 11.0 Hz, 1H), 2.91 – 2.84 (m, 1H), 2.82 – 2.72 (m, 1H), 2.42 – 2.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 156.5, 156.2, 151.1, 138.2, 133.2, 130.3, 128.4, 128.3, 128.2, 127.4, 126.0, 123.7, 121.2, 114.7, 114.5, 110.4, 93.5, 60.0, 55.7, 55.6, 46.3, 30.7; IR (KBr): 3061, 3013, 2923, 2839, 2040, 1888, 1686, 1591, 1358, 1287, 1108, 1051, 959, 887, 784 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_4+Na)^+$ requires m/z 439.1629, found m/z 439.1630.

5-(2-chlorophenyl)-9-methoxy-11-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ac): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 66% (27.8 mg); >95:5 dr; white solid; m.p. 136–137°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.34 – 7.30 (m, 3H), 7.29 – 7.25 (m, 4H), 6.99 (d, *J* = 8.7 Hz, 1H), 6.91 (d, *J* = 3.0 Hz, 1H), 6.80 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.61 (s, 1H), 5.71 (s, 1H), 3.79 (s, 3H), 3.19 – 3.09 (m, 1H), 2.86 – 2.74 (m, 2H), 2.48 – 2.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.5, 150.6, 137.9, 135.2, 133.4, 133.1, 130.4, 129.4, 129.2, 128.2, 127.8, 127.6, 127.4, 123.7, 114.9, 114.6, 95.9, 60.0, 55.7, 46.1, 30.6; IR (KBr): 3735, 3628, 1868, 1749, 1697, 1558, 1507, 1436, 1395, 1225, 907, 668 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{21}ClN_2O_3+Na)^+$ requires m/z 443.1134, found m/z 443.1130.

9-methoxy-5-(3-methoxyphenyl)-11-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ad): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 69% (28.5 mg); >95:5 dr; pale yellow solid; m.p. 128–129°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 6H), 6.96 – 6.87 (m, 5H), 6.78 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.59 (s, 1H), 5.08 (s, 1H), 3.77 (s, 6H), 3.10 (dd, *J* = 20.8, 9.3 Hz, 1H), 2.84 – 2.76 (m, 1H), 2.73 – 2.62 (m, 1H), 2.44 – 2.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 159.8, 156.3, 150.5, 138.9, 138.1, 133.3, 129.8, 128.3, 128.2, 127.5, 123.7, 119.8, 114.9, 114.7, 114.5, 113.0, 100.8, 60.3, 55.7, 55.3, 46.4, 30.1; IR (KBr): 2998, 2921, 2849, 1693, 1589, 1497, 1393, 1264, 1078, 888, 775 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_4+Na)^+$ requires m/z 439.1629, found m/z 439.1630.

5-(3-fluorophenyl)-9-methoxy-11-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ae): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 66% (26.5 mg); >95:5 dr; white solid; m.p. 143–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 4H), 7.27 (d, *J* = 7.0 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.11 – 7.04 (m, 2H), 6.92 (d, *J* = 8.7 Hz, 1H), 6.87 (d, *J* = 3.0 Hz, 1H), 6.80 – 6.75 (m, 1H), 6.59 (s, 1H), 5.10 (s, 1H), 3.78 (s, 3H), 3.17 – 3.06 (m, 1H), 2.81 – 2.64 (m, 2H), 2.46 – 2.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 162.9 (*J* = 245.9 Hz), 156.5, 150.3, 139.8, 139.7, 137.9, 133.3, 130.4(*J* = 8.1 Hz), 128.3, 128.2, 127.6, 123.6, 123.3, 116.7(*J* = 21.1 Hz), 114.8, 114.5(*J* = 22.1 Hz), 100.0, 60.4, 55.7, 46.4, 30.0;IR (KBr): 3059, 2919, 2848, 1682, 1592, 1500, 1339, 1219, 1041, 966, 870, 788 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{21}FN_2O_3+Na)^+$ requires m/z 427.1429, found m/z 427.1434.

9-methoxy-11-phenyl-5-(p-tolyl)-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4af): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 72% (28.7 mg); >95:5 dr; white solid; m.p. 105–106°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 1H), 6.88 (d, *J* = 2.9 Hz, 1H), 6.80 – 6.75 (m, 1H), 6.60 (s, 1H), 5.08 (s, 1H), 3.78 (s, 3H), 3.13 – 3.01 (m, 1H), 2.83 – 2.75 (m, 1H), 2.72 – 2.62 (m, 1H), 2.41 – 2.32 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.3, 150.6, 139.6, 138.2, 134.7, 133.3, 129.4, 128.3, 128.2, 127.4, 123.7, 114.7, 114.5, 100.9, 60.4, 55.6, 46.5, 30.1, 21.3; IR (KBr): 3029, 2918, 2841, 1686, 1609, 1501, 1391, 1215, 1145, 1009, 916, 897, 762 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{24}N_2O_3+Na)^+$ requires m/z 423.1680, found m/z 423.1682.

5-(4-fluorophenyl)-9-methoxy-11-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ag): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 70% (28.3 mg); >95:5 dr; pale white sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.26 (m, 7H), 7.06 (t, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 1H), 6.87 (d, *J* = 2.9 Hz, 1H), 6.77 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.59 (s, 1H), 5.10 (s, 1H), 3.77 (s, 3H), 3.08 (dd, *J* = 18.8,

9.1 Hz, 1H), 2.78 – 2.63 (m, 2H), 2.44 – 2.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 163.3 (*J* = 247.2 Hz), 156.4, 150.3, 138.0, 133.6, 133.3, 129.4(*J* = 8.3 Hz), 128.6, 128.3, 128.2, 127.5, 123.6, 115.8(*J* = 21.5 Hz), 114.6 (*J* = 26.3 Hz), 100.0, 60.4, 55.7, 46.5, 30.0; IR (KBr): 3060, 2922, 2849, 1694, 1607, 1498, 1393, 1216, 1040, 940, 895, 848, 741, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{21}FN_2O_3+H)^+$ requires m/z 405.1609, found m/z 405.1614.

3,5,11-triphenyl-2,3-dihydro-1*H*,5*H*,11*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ah): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 92% (41.8 mg); dr = 58:42; yellow oil; **major diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.51 – 7.31 (m, 7H), 7.10 (d, *J* = 8.8 Hz, 1H), 6.94 (d, *J* = 14.8 Hz, 1H), 6.91 – 6.79 (m, 2H), 5.97 (s, 1H), 3.81 (s, 3H), 3.19 (dd, *J* = 20.7, 9.0 Hz, 1H), 2.80 (t, *J* = 8.6 Hz, 1H), 2.76 – 2.63 (m, 1H), 2.57 (dd, *J* = 15.7, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 155.0, 150.7, 138.9, 138.3, 130.9 (d, *J* = 32.3), 128.6, 128.0, 127.4, 127.0, 125.8, 125.4, 123.9 (d, *J* = 284.2), 121.2, 115.5, 114.9, 91.6, 56.8, 55.8, 42.7, 30.7; IR (KBr): 2925, 2850, 1647, 1405, 1197, 825, 701 cm^{-1}; **minor diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.41 – 7.28 (m, 5H), 6.92 (dd, *J* = 10.8, 5.8 Hz, 2H), 6.81 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.63 (s, 1H), 5.18 (s, 1H), 3.81 (s, 3H), 3.11 (dd, *J* = 21.6, 10.8 Hz, 1H), 2.81 – 2.63 (m, 2H), 2.44 (dt, *J* = 16.1, 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 156.5, 150.2, 141.1, 137.9, 133.3, 131.9 (d, *J* = 36.0), 128.3, 128.2, 128.1, 127.6, 125.8, 125.8, 123.5, 114.8, 114.6, 100.0, 60.4, 55.7, 46.4, 30.0; IR (KBr): 2956, 2846, 1650, 1447, 1396, 1038, 860, 700 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{21}F_3N_2O_3+Na)^+$ requires m/z 477.1396, found m/z 477.1394.

4-(9-methoxy-1-oxo-11-phenyl-2,3-dihydro-1*H*,5*H*,11*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-5-yl)benzonitrile (4ai): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 85% (35.0 mg); dr = 55:45; yellow oil; **major diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.38 (dd, *J* = 11.6, 7.1 Hz, 3H), 7.32 (d, *J* = 7.3 Hz, 2H), 7.09 (d, *J* = 8.9 Hz, 1H), 6.95 (s, 1H), 6.90 – 6.83 (m, 1H), 6.81 (d, *J*

= 2.9 Hz, 1H), 5.96 (s, 1H), 3.81 (s, 3H), 3.22 – 3.11 (m, 1H), 2.83 – 2.73 (m, 1H), 2.67 (dd, *J* = 11.9, 9.0 Hz, 1H), 2.63 – 2.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 155.1, 150.5, 139.5, 138.7, 132.2, 128.7, 128.0, 127.4, 127.4, 125.7, 121.2, 118.3, 115.6, 115.0, 112.6, 91.3, 56.7, 55.8, 42.7, 30.7; IR (KBr): 2918, 1650, 1400, 1185, 700 cm^{-1}; **minor diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.9 Hz, 2H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.35 (t, *J* = 8.1 Hz, 3H), 7.27 (d, *J* = 7.5 Hz, 2H), 6.90 (dd, *J* = 8.1, 5.9 Hz, 2H), 6.84 – 6.78 (m, 1H), 6.62 (s, 1H), 5.16 (s, 1H), 3.80 (s, 3H), 3.10 (t, J = 7.2 Hz, 1H), 2.80 – 2.62 (m, 2H), 2.45 (dd, J = 12.0, 9.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 156.6, 150.0, 142.0, 137.8, 133.3, 132.6, 128.5, 128.3, 128.1, 127.6, 123.5, 118.3, 114.8, 114.6, 113.6, 99.7, 60.4, 55.7, 46.3, 29.9; IR (KBr): 2940, 2833, 1645, 1450, 1400, 1025, 890, 701 cm^{-1}; ESI FTMS exact mass calcd for $(C_{25}H_{21}N_3O_3+Na)^+$ requires m/z 434.1475, found m/z 434.1475.

5-([1,1'-biphenyl]-4-yl)-9-methoxy-11-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4aj): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 63% (29.1 mg); >95:5 dr; pale white sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.56 (m, 4H), 7.48 – 7.42 (m, 4H), 7.39 – 7.31 (m, 6H), 6.97 (d, *J* = 8.7 Hz, 1H), 6.90 (d, *J* = 2.9 Hz, 1H), 6.79 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.63 (s, 1H), 5.17 (s, 1H), 3.79 (s, 3H), 3.18 – 3.09 (m, 1H), 2.89 – 2.81 (m, 1H), 2.76 – 2.66 (m, 1H), 2.46 – 2.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.4, 150.6, 142.6, 140.5, 138.1, 136.5, 133.3, 128.9, 128.3, 127.9, 127.7, 127.5, 127.2, 123.8, 114.8, 114.5, 100.8, 60.4, 55.7, 46.6, 30.1; IR (KBr): 3030, 2921, 2849, 1694, 1540, 1497, 1418, 1393, 1266, 1213, 1076, 1039, 1007, 895, 829, 765, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{26}N_2O_3+Na)^+$ requires m/z 485.1836, found m/z 485.1833.

9-methoxy-5-(naphthalen-2-yl)-11-phenyl-2,3,5,11-tetrahydro-1*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4ak): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 61% (26.6 mg); >95:5 dr; pale yellow solid; m.p. 119–120^{o}C;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.79 (m, 4H), 7.55 – 7.46 (m, 3H), 7.41 – 7.31 (m, 5H), 6.98 – 6.89 (m, 2H), 6.78 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.65 (s, 1H), 5.28 (s, 1H), 3.79 (s, 3H), 3.14 – 3.03 (m, 1H),

2.86 – 2.78 (m, 1H), 2.76 – 2.66 (m, 1H), 2.46 – 2.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.4, 150.6, 138.2, 134.9, 133.9, 133.3, 132.9, 128.9, 128.3, 128.2, 127.8, 127.5, 127.2, 126.8, 126.5, 124.6, 123.7, 114.8, 114.6, 101.3, 60.4, 55.7, 46.5, 30.1; IR (KBr): 3346, 3056, 2921, 2849, 1948, 1751, 1685, 1600, 1582, 1495, 1448, 1348, 1211, 1181, 1041, 912, 885, 729, 699 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{24}N_2O_3+Na)^+$ requires m/z 459.1680, found m/z 459.1685.

3,5,11-triphenyl-2,3-dihydro-1*H*,5*H*,11*H*-benzo[*f*]pyrazolo[1,2-*c*][1,3,4]oxadiazepin-1-one (4sl): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 72% (31.1 mg); dr = 68:32; yellow oil; **major diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 12H), 7.22 – 7.00 (m, 5H), 6.80 – 6.62 (m, 3H), 5.46 (s, 1H), 4.14 (d, *J* = 8.7 Hz, 1H), 3.23 (dd, *J* = 17.0, 9.3 Hz, 1H), 2.62 (dd, *J* = 17.0, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 156.9, 140.5, 137.5, 132.5, 130.1, 129.7, 129.4, 129.4, 128.8, 128.1, 127.7, 127.4, 127.0, 126.2, 125.0, 123.0, 101.1, 60.1, 58.2, 37.1; IR (KBr): 2920, 2849, 1670, 1399, 1200, 1038, 823, 690 cm^{-1}; **minor diastereomer**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.37 (m, 5H), 7.36 – 7.29 (m, 2H), 7.22 – 6.98 (m, 11H), 6.98 – 6.92 (m, 2H), 6.09 (s, 1H), 4.65 – 4.51 (m, 1H), 3.14 (dd, *J* = 17.1, 10.1 Hz, 1H), 2.68 (dd, *J* = 17.0, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 157.6, 142.2, 138.6, 133.6, 131.7, 128.6, 128.5, 128.3, 128.0, 127.9, 127.8, 126.7, 126.6, 126.5, 125.8, 122.8, 120.5, 93.7, 57.1, 56.7, 40.8; IR (KBr): 3327, 2921, 2850, 1678, 1500, 1399, 1213, 1038, 852, 690 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{24}N_2O_2+Na)^+$ requires m/z 455.1730, found m/z 455.1731.

6-(4-methoxybenzyl)-5,11-diphenyl-2,3,5,6-tetrahydrobenzo[*e*]pyrazolo[1,2-*a*][1,2,4]triazepin-1(11*H*)-one (6aa): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 50% (23.7 mg); >95:5 dr; yellow solid; m.p. 138–139°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.3 Hz, 2H), 7.49 – 7.41 (m, 3H), 7.40 – 7.35 (m, 3H), 7.31 (t, *J* = 7.3 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.98 – 6.90 (m, 5H), 6.55 (d, *J* = 7.8 Hz, 1H), 6.49 (d, *J* = 7.7 Hz, 1H), 6.38 (s, 1H), 4.77 (s, 1H), 4.14 (d, *J* = 13.8 Hz, 1H), 3.90 (d, *J* = 13.8 Hz, 1H), 3.83 (s, 3H), 3.43 – 3.33 (m, 1H), 2.91 (dd, *J* = 12.2, 7.8 Hz, 1H), 2.81 – 2.70 (m, 1H), 2.14 (dd, *J*

= 16.6, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 158.9, 144.9, 141.2, 136.2, 135.2, 129.8, 129.4, 128.8, 128.7, 128.2, 127.9, 127.7, 123.9, 123.5, 114.2, 81.7, 62.2, 55.3, 53.7, 47.9, 29.9; IR (KBr): 3060, 3029, 2933, 2835, 2544, 2244, 1953, 1887, 1693, 1610, 1510, 1489, 1453, 1385, 1171, 1031, 957, 881, 822, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{29}N_3O_2+H)^+$ requires m/z 476.2333, found m/z 476.2338.

6-(3-methoxybenzyl)-5,11-diphenyl-2,3,5,6-tetrahydrobenzo[*e*]pyrazolo[1,2-*a*][1,2,4]triazepin-1(11*H*)-one (6ba): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 61% (29.1 mg); >95:5 dr; yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.3 Hz, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.39 – 7.30 (m, 6H), 7.21 – 7.12 (m, 2H), 6.98 – 6.89 (m, 4H), 6.55 (d, *J* = 7.8 Hz, 1H), 6.50 (d, *J* = 7.7 Hz, 1H), 6.39 (s, 1H), 4.77 (s, 1H), 4.18 (d, *J* = 14.1 Hz, 1H), 3.92 (d, *J* = 14.1 Hz, 1H), 3.86 (s, 3H), 3.45 – 3.30 (m, 1H), 2.91 (dd, *J* = 12.2, 7.9 Hz, 1H), 2.81 – 2.70 (m, 1H), 2.14 (dd, *J* = 16.6, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 160.1, 144.8, 141.1, 139.6, 136.1, 135.0, 129.8, 128.9, 128.8, 128.3, 128.2, 127.9, 127.7, 124.0, 123.3, 120.5, 113.7, 112.8, 81.9, 62.1, 55.3, 55.1, 54.3, 48.0, 29.9; IR (KBr): 3028, 2837, 2359, 1693, 1596, 1489, 1453, 1386, 1264, 1153, 1048, 879, 737, 703 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{29}N_3O_2+H)^+$ requires m/z 476.2333, found m/z 476.2338.

6-(3-methoxybenzyl)-5-(2-methoxyphenyl)-11-phenyl-2,3,5,6-tetrahydrobenzo[*e*]pyrazolo[1,2-*a*][1,2,4]triazepin-1(11*H*)-one (6bb): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 65% (32.6 mg); >95:5 dr; yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.6 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.39 – 7.28 (m, 4H), 7.22 (d, *J* = 7.9 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.98 (s, 1H), 6.95 – 6.91 (m, 2H), 6.80 – 6.75 (m, 2H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.47 (d, *J* = 7.7 Hz, 1H), 6.35 (s, 1H), 5.58 (s, 1H), 4.14 (d, *J* = 14.5 Hz, 1H), 4.07 (d, *J* = 14.5 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 3.40 – 3.29 (m, 1H), 2.95 – 2.84 (m, 2H), 2.23 – 2.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 159.7, 158.2, 144.7, 141.2, 140.4, 136.1, 129.7, 129.5, 129.2, 128.9, 128.7, 128.3, 128.2, 127.7, 127.6, 124.3, 123.7, 123.6, 120.4, 120.1, 112.9, 109.8, 74.6, 62.2, 55.3, 55.2, 55.0, 54.0, 47.8, 30.3; IR (KBr): 3058, 2934, 2837, 1944, 1801, 1686, 1596,

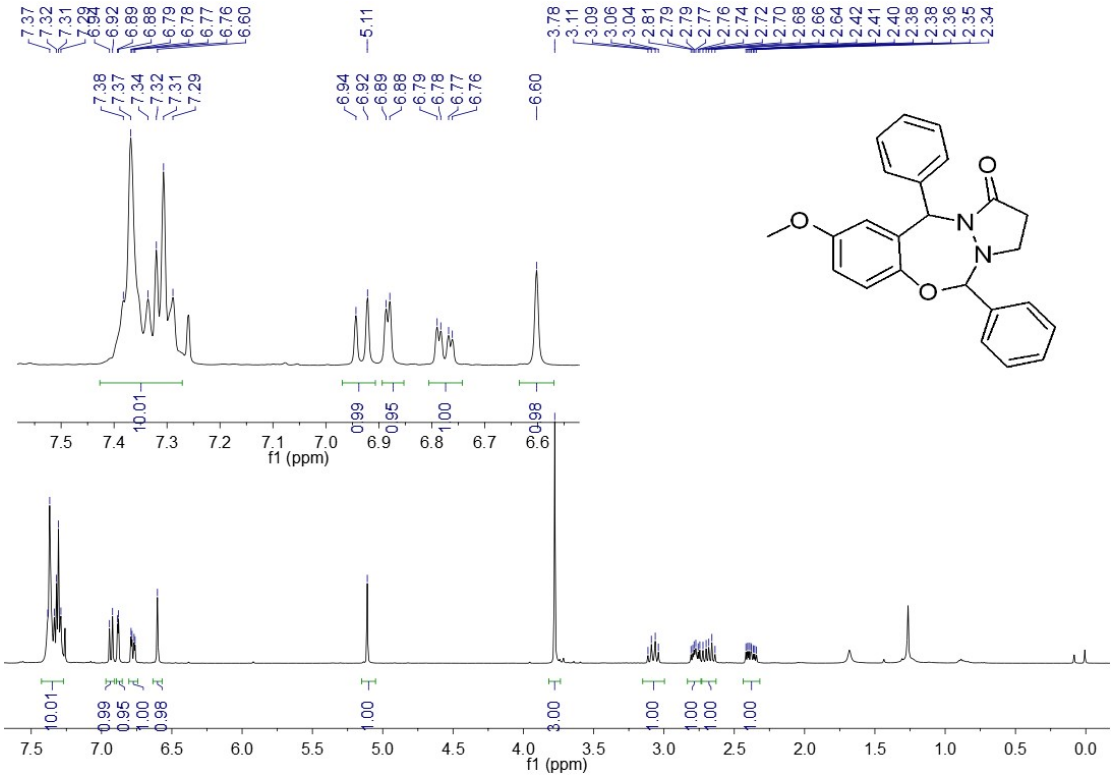
1489, 1454, 1375, 1265, 1153, 1066, 961, 879, 783, 734, 700 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{31}N_3O_3+H)^+$ requires m/z 506.2438, found m/z 506.2435.

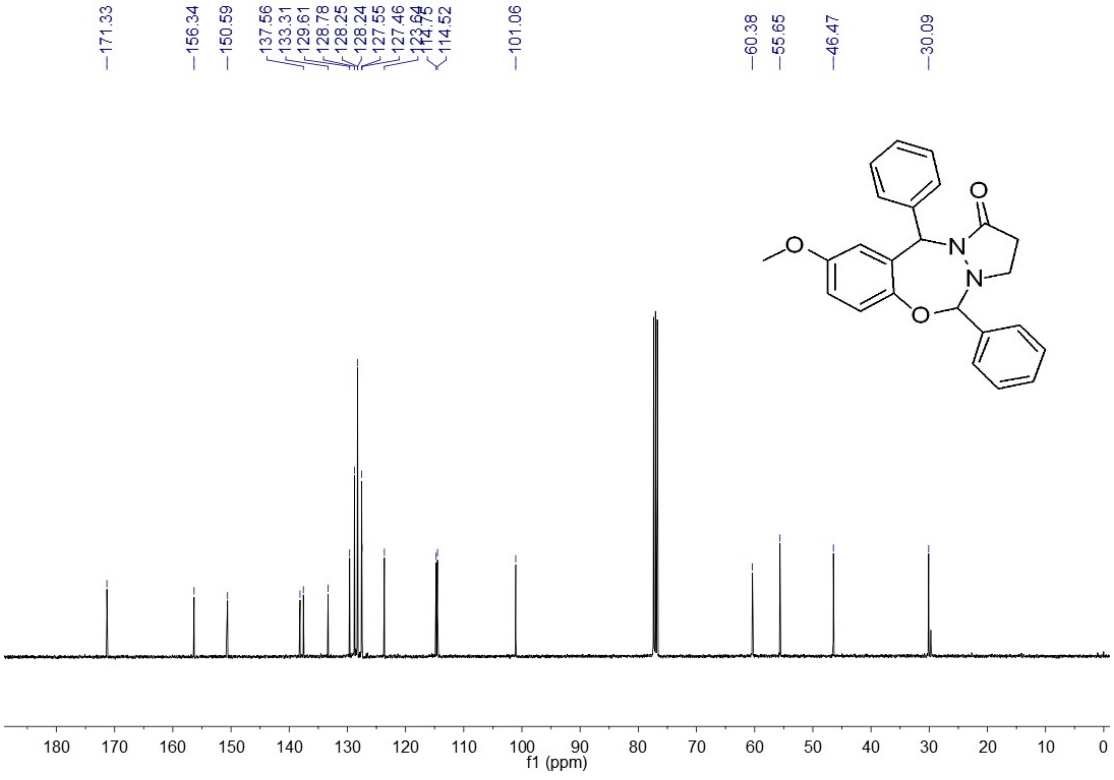
6-(3-methoxybenzyl)-5-(3-methoxyphenyl)-11-phenyl-2,3,5,6-tetrahydrobenzo[*e*]pyrazolo[1,2-*a*][1,2,4]triazepin-1(11*H*)-one (6bd): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 66% (33.2 mg); >95:5 dr; yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 2H), 7.38 (d, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.22 – 7.13 (m, 3H), 6.95 – 6.83 (m, 3H), 6.62 – 6.55 (m, 2H), 6.48 (d, *J* = 7.7 Hz, 1H), 6.41 (s, 1H), 6.38 (s, 1H), 4.74 (s, 1H), 4.19 (d, *J* = 14.1 Hz, 1H), 3.94 (d, *J* = 14.1 Hz, 1H), 3.85 (s, 3H), 3.65 (s, 3H), 3.43 – 3.34 (m, 1H), 2.93 (dd, *J* = 12.2, 7.9 Hz, 1H), 2.80 – 2.70 (m, 1H), 2.14 (dd, *J* = 16.6, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 160.1, 159.2, 144.9, 141.1, 139.6, 136.6, 136.0, 129.7, 128.8, 128.7, 128.3, 127.7, 124.0, 123.4, 121.2, 120.5, 114.9, 113.7, 113.4, 112.7, 81.8, 62.1, 55.3, 55.1, 54.3, 48.0, 29.9; IR (KBr): 3058, 2836, 1942, 1693, 1596, 1489, 1453, 1385, 1262, 1154, 1046, 872, 789, 738, 701 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{31}N_3O_3+H)^+$ requires m/z 506.2438, found m/z 506.2435.

6-(3-methoxybenzyl)-11-phenyl-5-(*m*-tolyl)-2,3,5,6-tetrahydrobenzo[*e*]pyrazolo[1,2-*a*][1,2,4]triazepin-1(11*H*)-one (6bf): Preparative thin layer chromatography, petroleum ether/ methylene dichloride = 3/1; Reaction time = 15 h; yield: 64% (31.5 mg); >95:5 dr; yellow sticky oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.3 Hz, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 7.1 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.21 – 7.09 (m, 4H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.86 – 6.80 (m, 3H), 6.57 (d, *J* = 7.8 Hz, 1H), 6.49 (d, *J* = 7.7 Hz, 1H), 6.38 (s, 1H), 4.74 (s, 1H), 4.17 (d, *J* = 14.1 Hz, 1H), 3.92 (d, *J* = 14.1 Hz, 1H), 3.86 (s, 3H), 3.43 – 3.31 (m, 1H), 2.92 (dd, *J* = 12.3, 7.7 Hz, 1H), 2.80 – 2.69 (m, 1H), 2.38 (s, 3H), 2.13 (dd, *J* = 16.6, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 160.1, 144.9, 141.1, 139.7, 138.6, 136.1, 132.0, 129.8, 128.7, 128.6, 128.2, 128.2, 127.7, 123.9, 123.2, 120.5, 113.6, 112.8, 81.8, 62.1, 55.3, 54.2, 47.9, 29.9, 21.3; IR (KBr): 3028, 2837, 2244, 1909, 1802, 1686, 1596, 1489, 1453, 1385, 1264, 1153, 1048, 933, 880, 822, 785, 701 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{31}N_3O_2+H)^+$ requires m/z 490.2489, found m/z 490.2492.

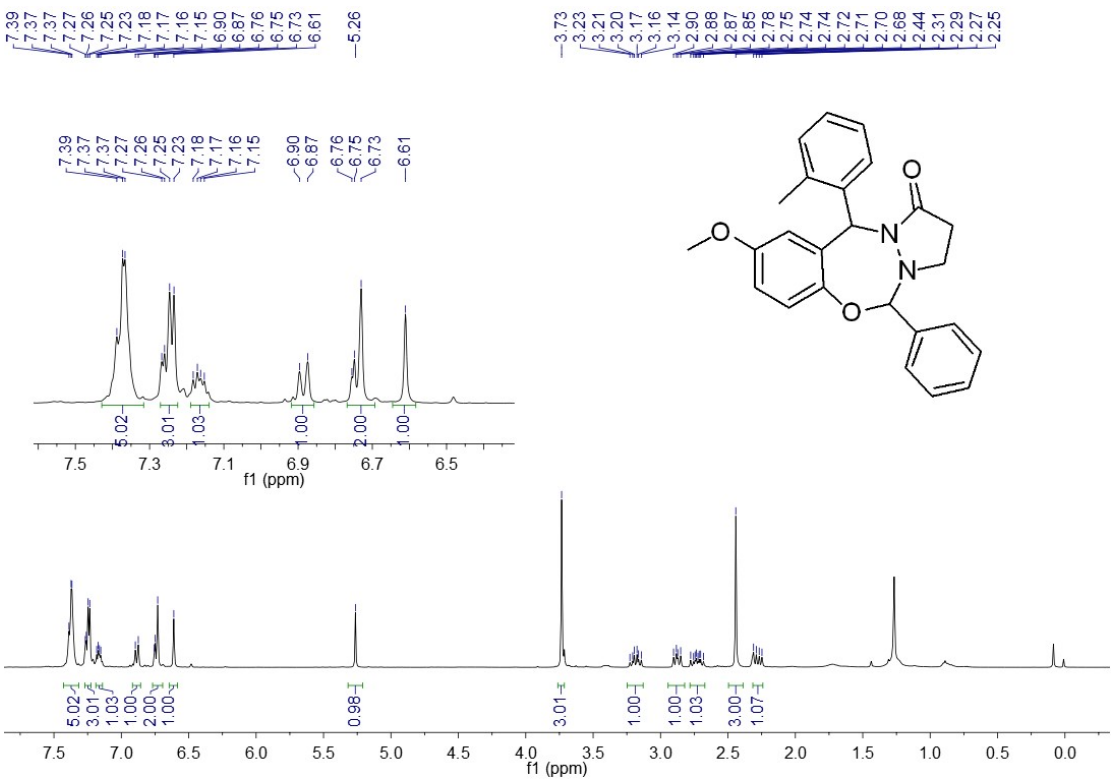
5. NMR Spectra of products 4 and 6

4aa





4ba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2.68
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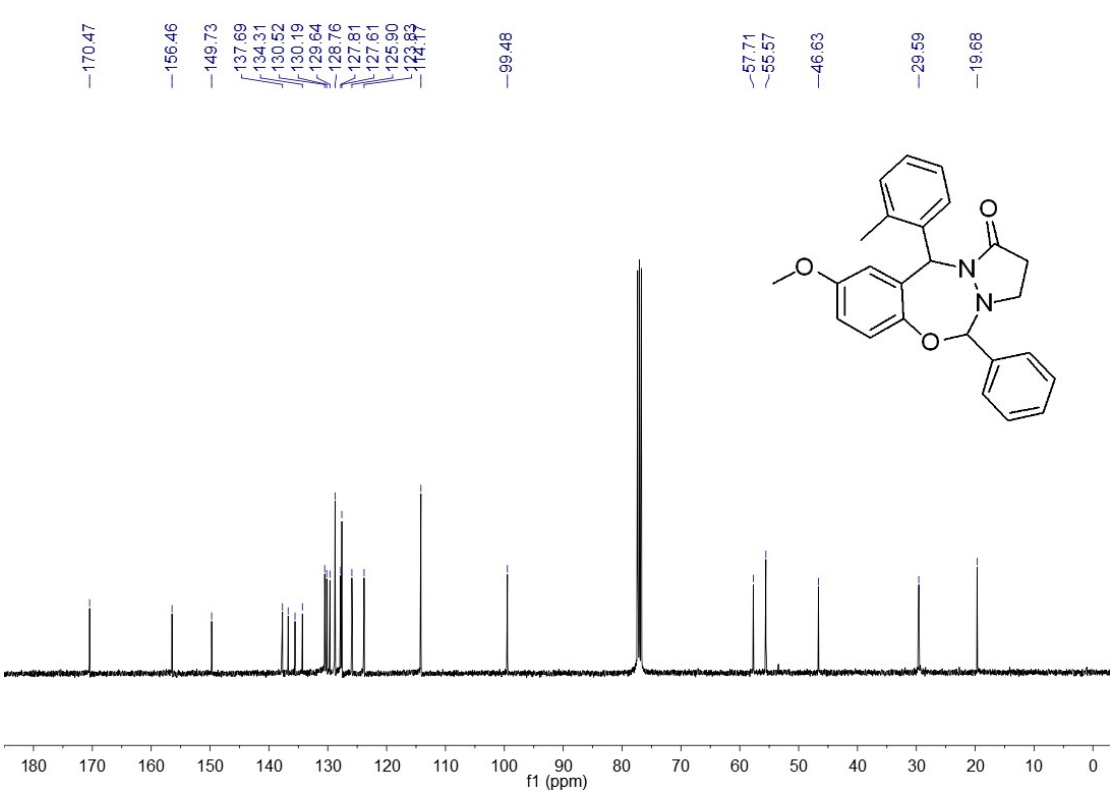
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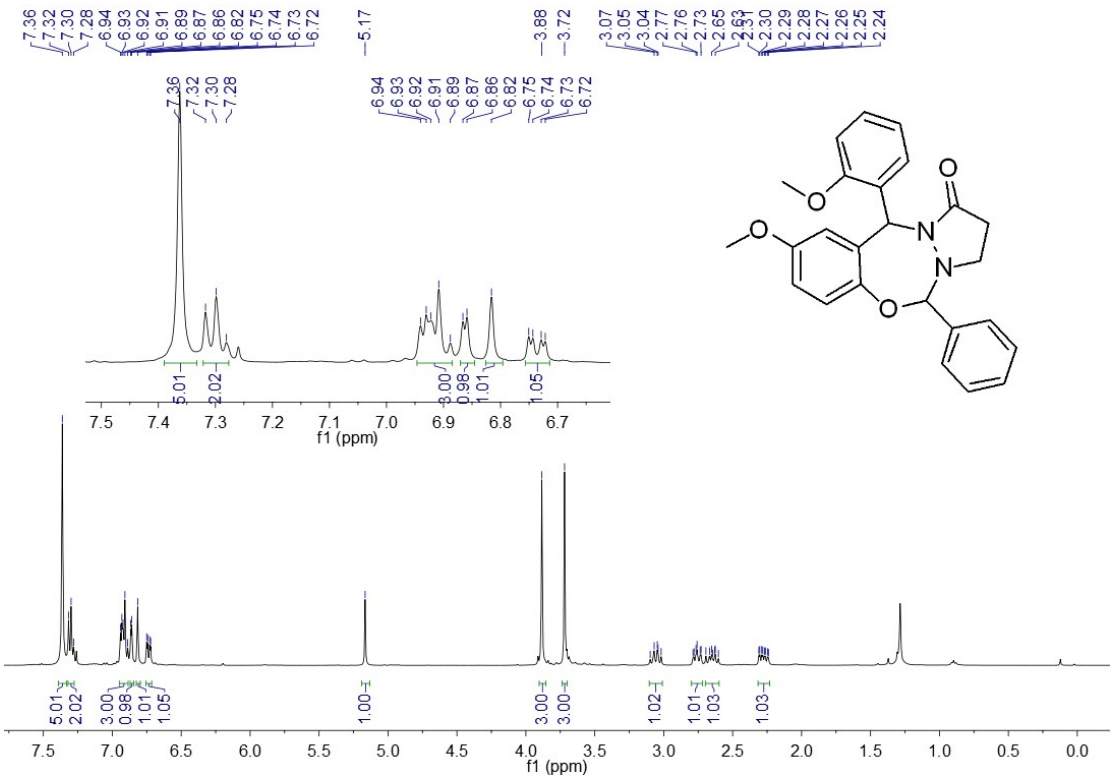
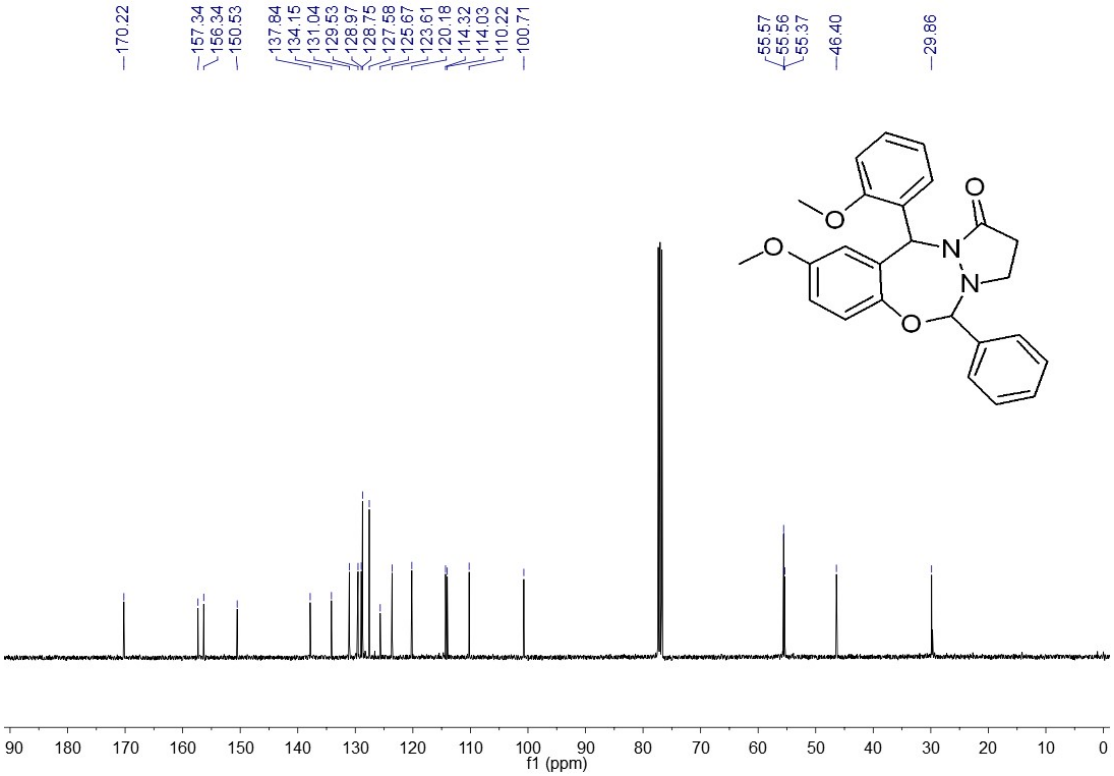
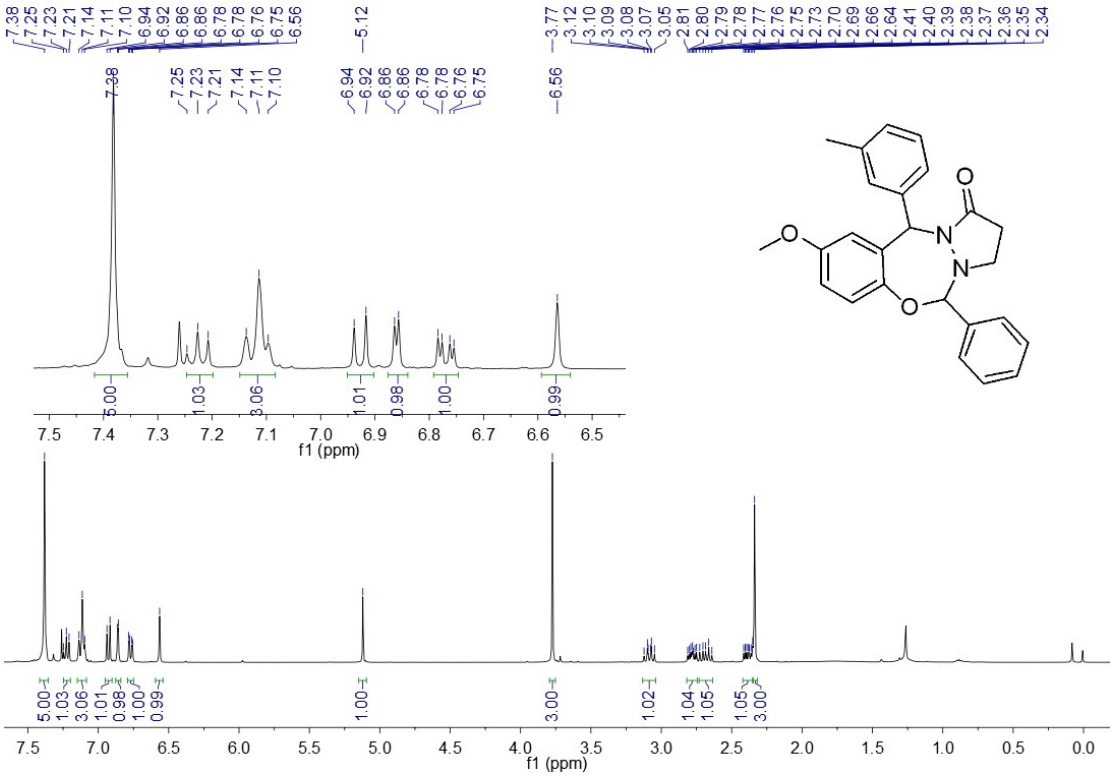
57.71
55.57
46.63
29.59
19.68
f1 (ppm)

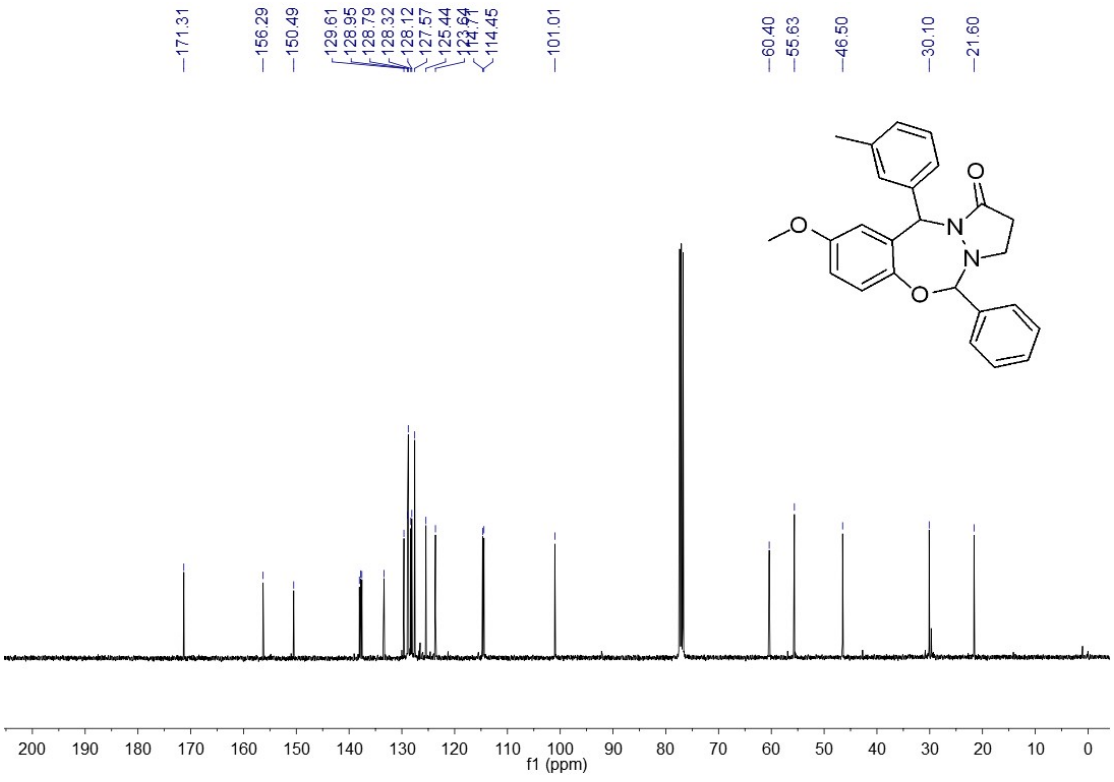
4ca


7.36 7.32 7.30 7.28 6.94 6.93 6.92 6.91 6.89 6.87 6.86 6.82 6.75 6.74 6.73 6.72 5.17 3.88 3.72 3.07 3.05 3.04 2.77 2.76 2.73 2.65 2.63 2.31 2.30 2.29 2.28 2.27 2.26 2.25 2.24
5.01 2.02 3.00 0.98 1.01 1.05 1.00 3.00 3.00 1.02 1.01 1.03 1.03
f1 (ppm)

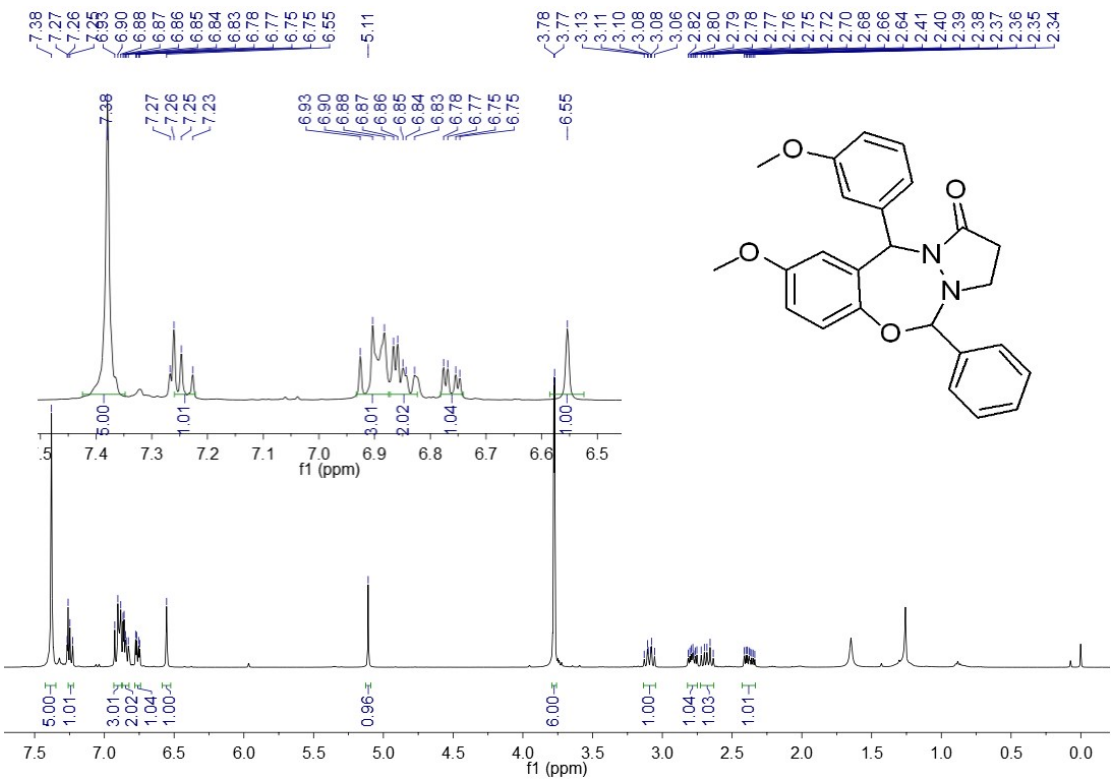

170.22 157.34 156.34 150.53 137.84 134.15 131.04 129.53 128.97 128.75 127.58 125.67 123.61 120.18 114.32 114.03 110.22 100.71 55.57 55.56 55.37 46.40 29.86
f1 (ppm)

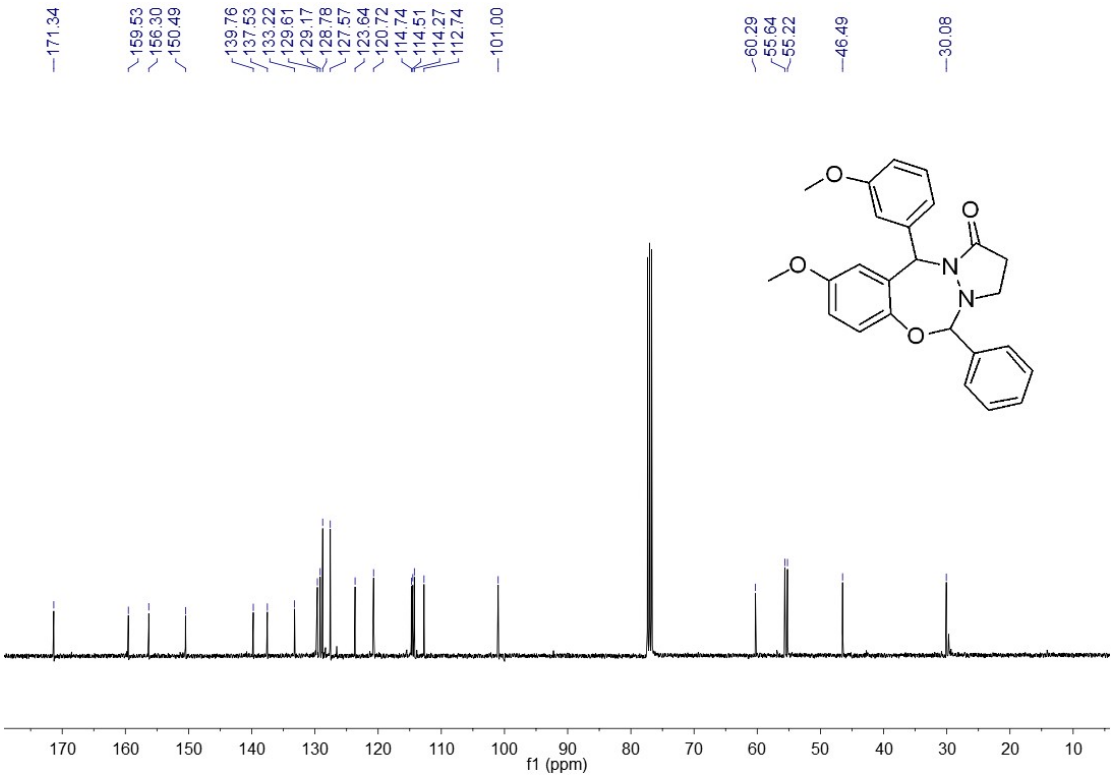
4da



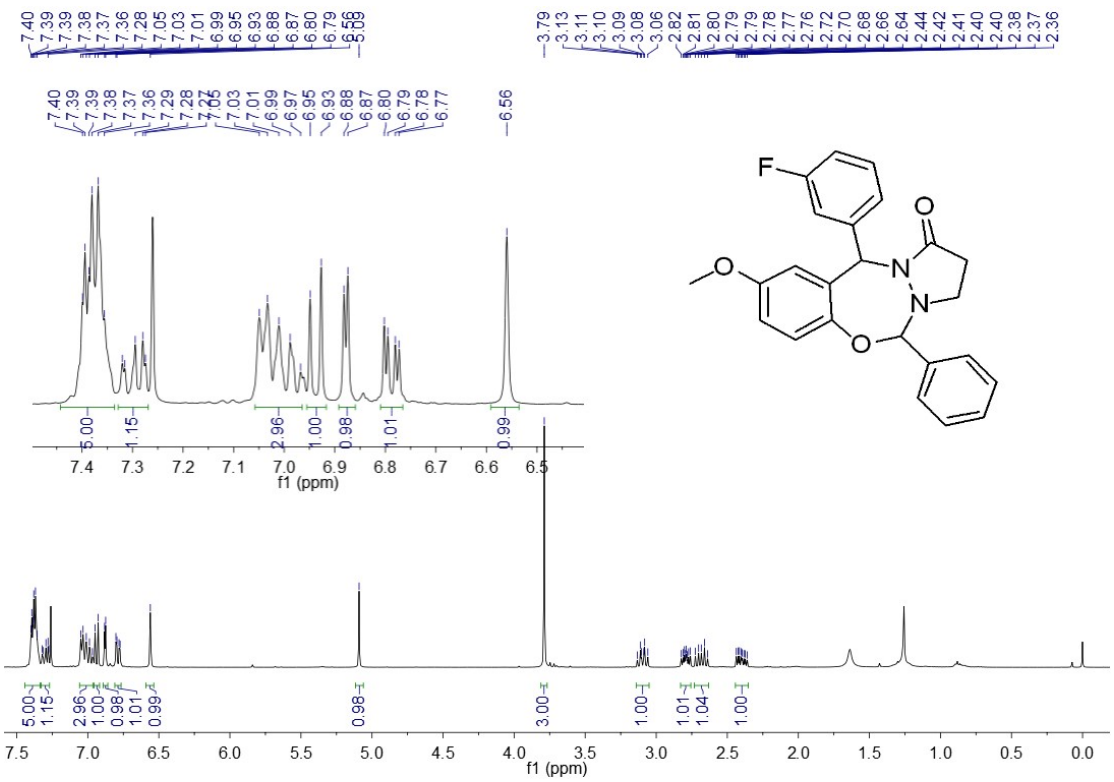


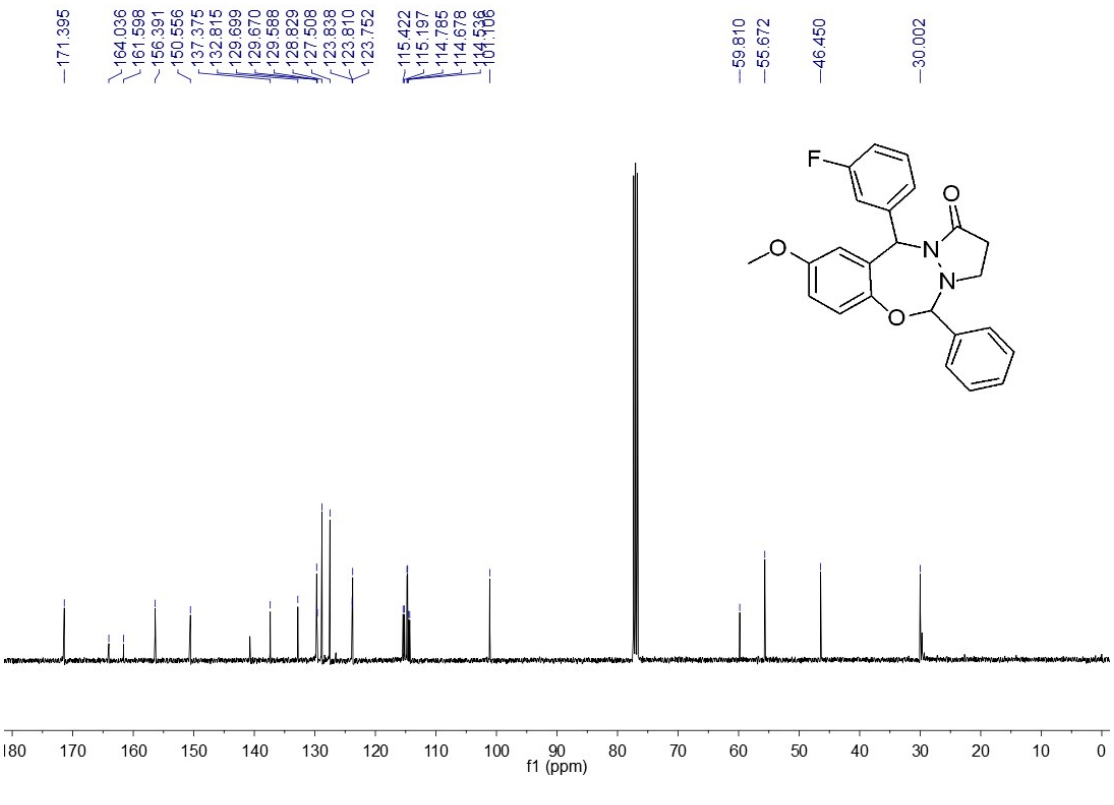
4ea



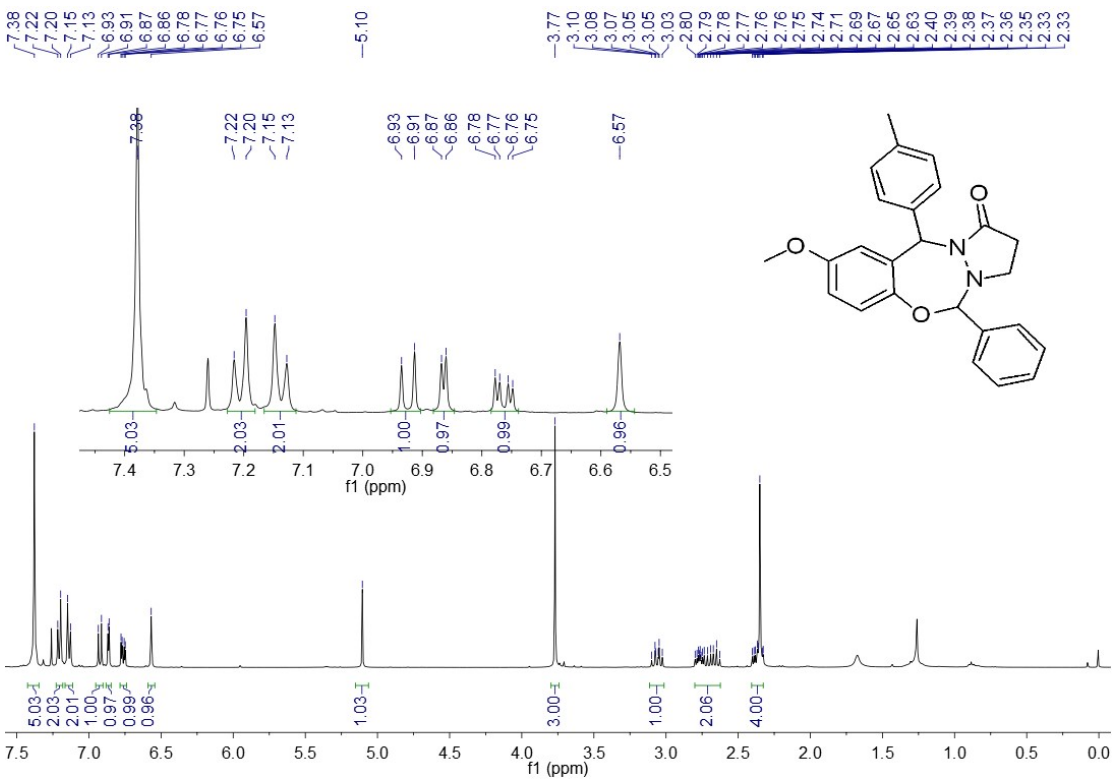


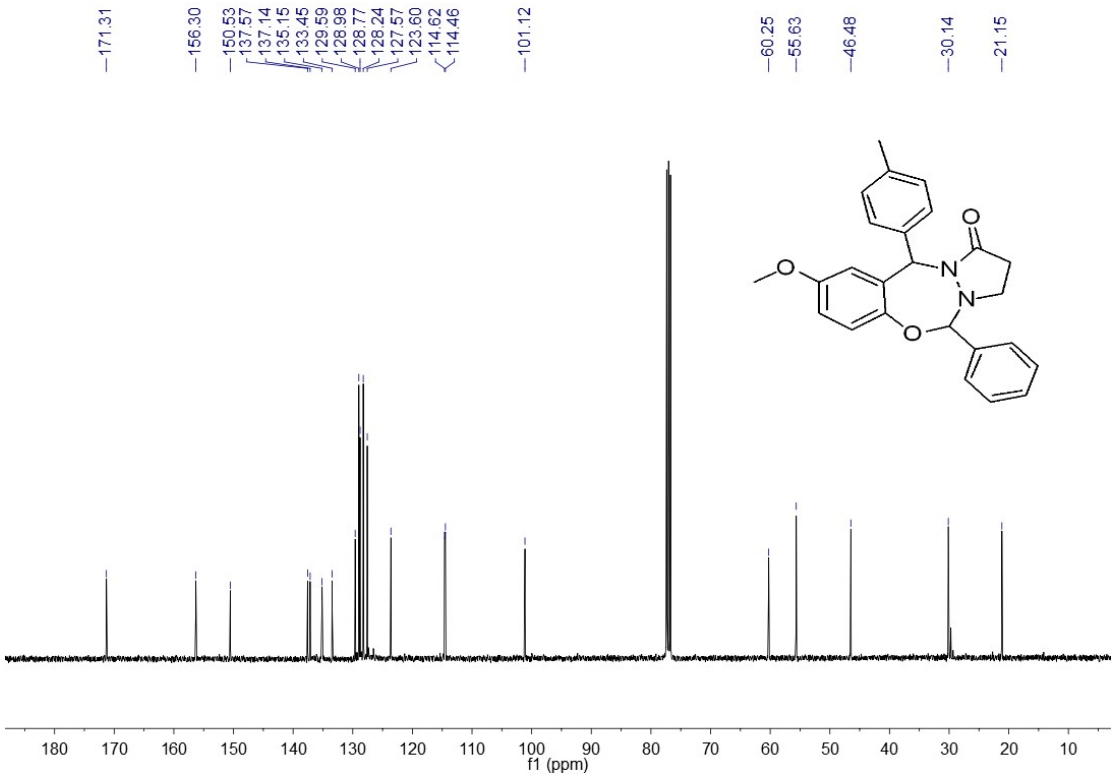
4fa


7.40 7.39 7.39 7.38 7.37 7.36 7.28 7.05 7.03 7.01 6.99 6.95 6.93 6.88 6.87 6.80 6.79 6.56
3.79 3.13 3.11 3.10 3.09 3.08 3.06 2.82 2.81 2.80 2.79 2.79 2.78 2.77 2.76 2.72 2.70 2.68 2.66 2.64 2.44 2.42 2.41 2.40 2.40 2.38 2.37 2.36
5.00 1.15 2.96 1.00 0.98 1.01 0.99 0.98 3.00 1.00 1.01 1.04 1.00
f1 (ppm)

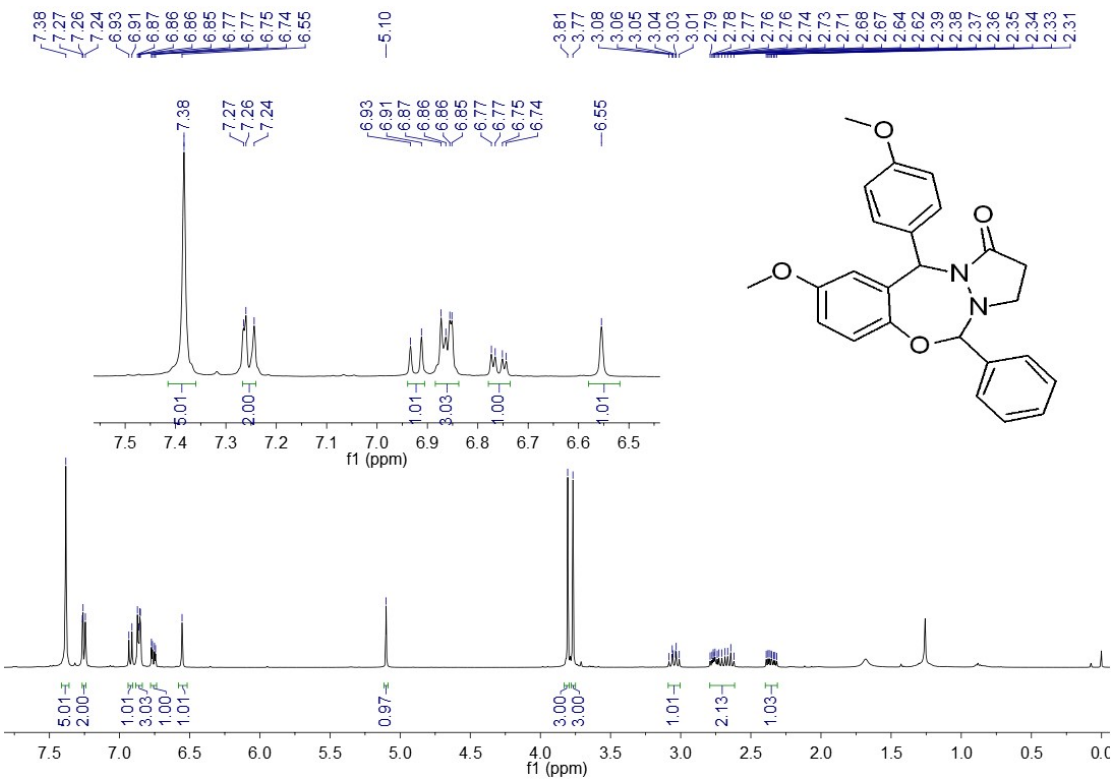

171.395 164.036 161.598 156.391 150.556 137.375 132.815 129.699 129.670 129.588 128.829 127.508 123.838 123.810 123.752 115.422 115.197 114.785 114.678 59.810 55.672 46.450 30.002
f1 (ppm)

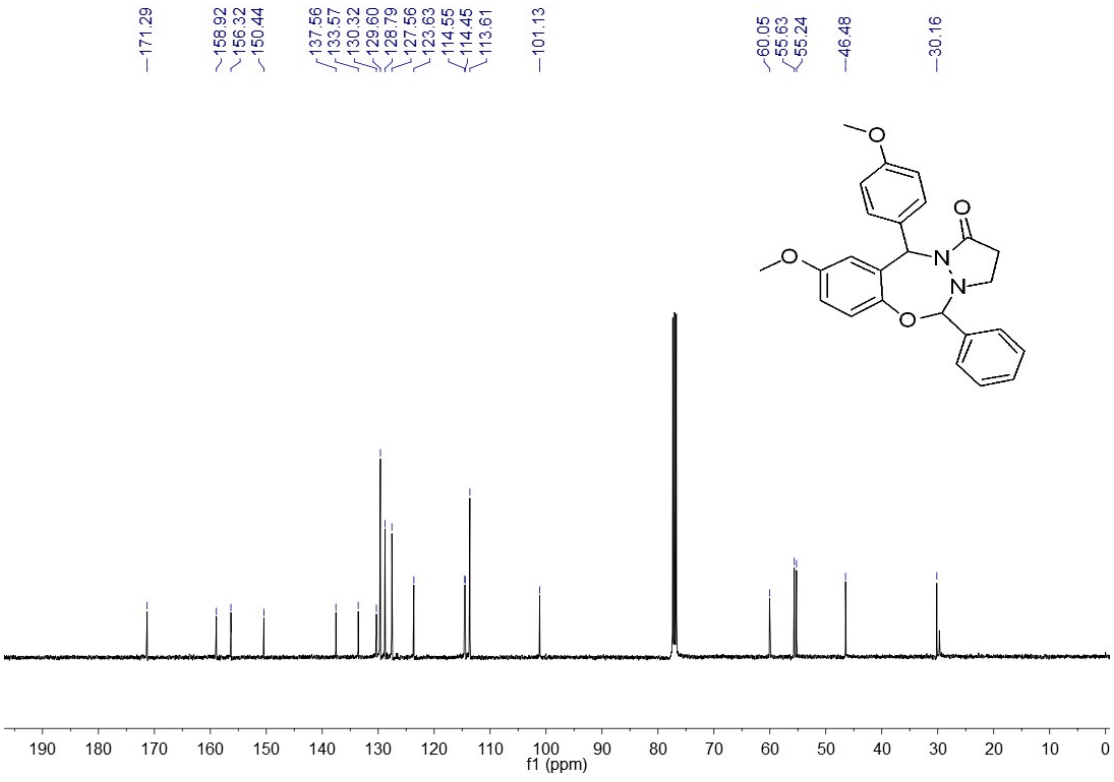
4ga


7.38
7.22
7.20
7.15
7.13
6.93
6.91
6.87
6.86
6.78
6.77
6.76
6.75
6.57
5.10
3.77
3.10
3.08
3.07
3.05
3.05
3.03
2.80
2.79
2.78
2.77
2.76
2.76
2.75
2.74
2.71
2.69
2.67
2.65
2.63
2.40
2.39
2.38
2.37
2.36
2.35
2.33
2.33
5.03
2.03
2.01
1.00
0.97
0.99
0.96
1.03
3.00
1.00
2.06
4.00
f1 (ppm)

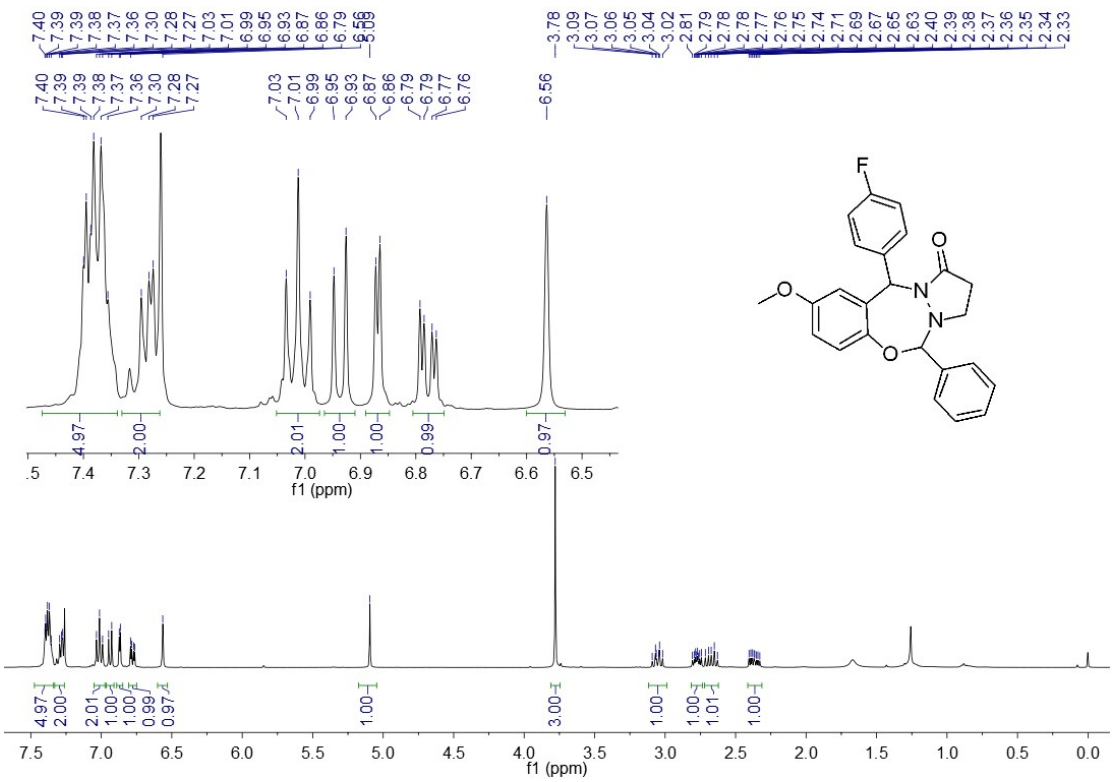

171.31
156.30
150.53
137.57
137.14
135.15
133.45
129.59
128.98
128.77
128.24
127.57
123.60
114.62
114.46
101.12
60.25
55.63
46.48
30.14
21.15
f1 (ppm)

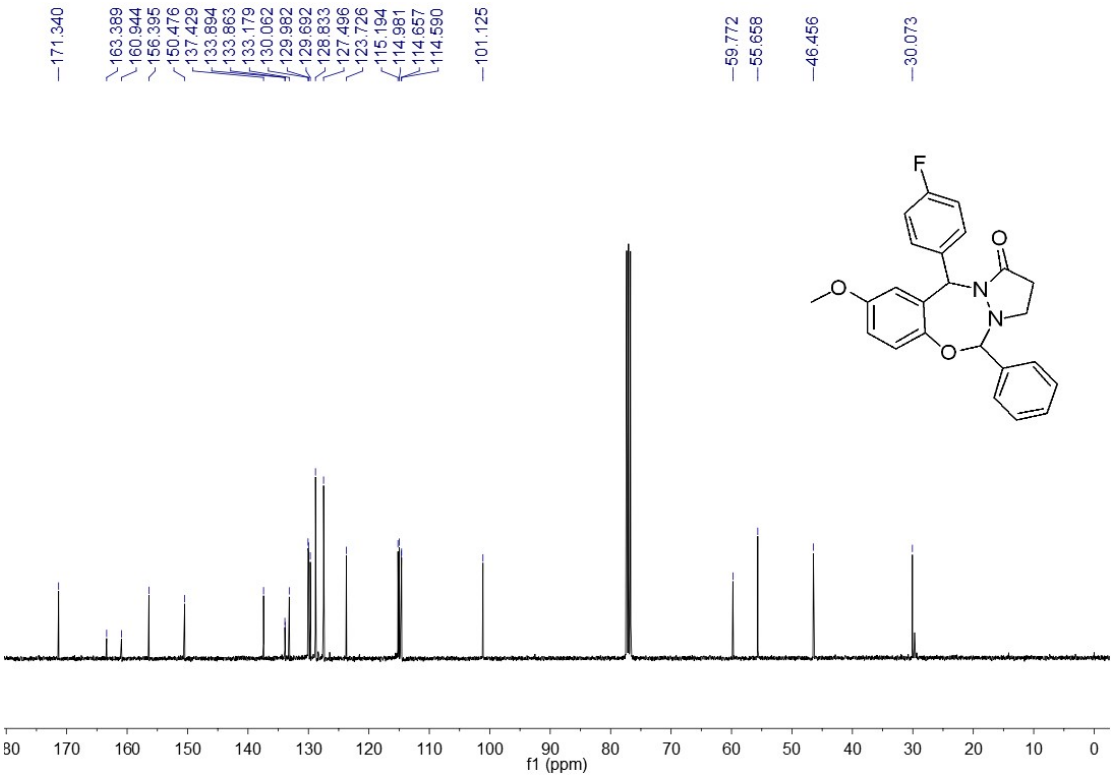
4ha


7.38
7.27
7.26
7.24
6.93
6.91
6.87
6.86
6.86
6.85
6.77
6.77
6.75
6.74
6.55
5.10
3.81
3.77
3.08
3.06
3.05
3.04
3.03
3.01
2.79
2.78
2.77
2.76
2.76
2.74
2.73
2.71
2.68
2.67
2.64
2.62
2.39
2.38
2.37
2.36
2.35
2.34
2.33
2.31
5.01
2.00
1.01
3.03
1.00
1.01
0.97
3.00
3.00
1.01
2.13
1.03
f1 (ppm)

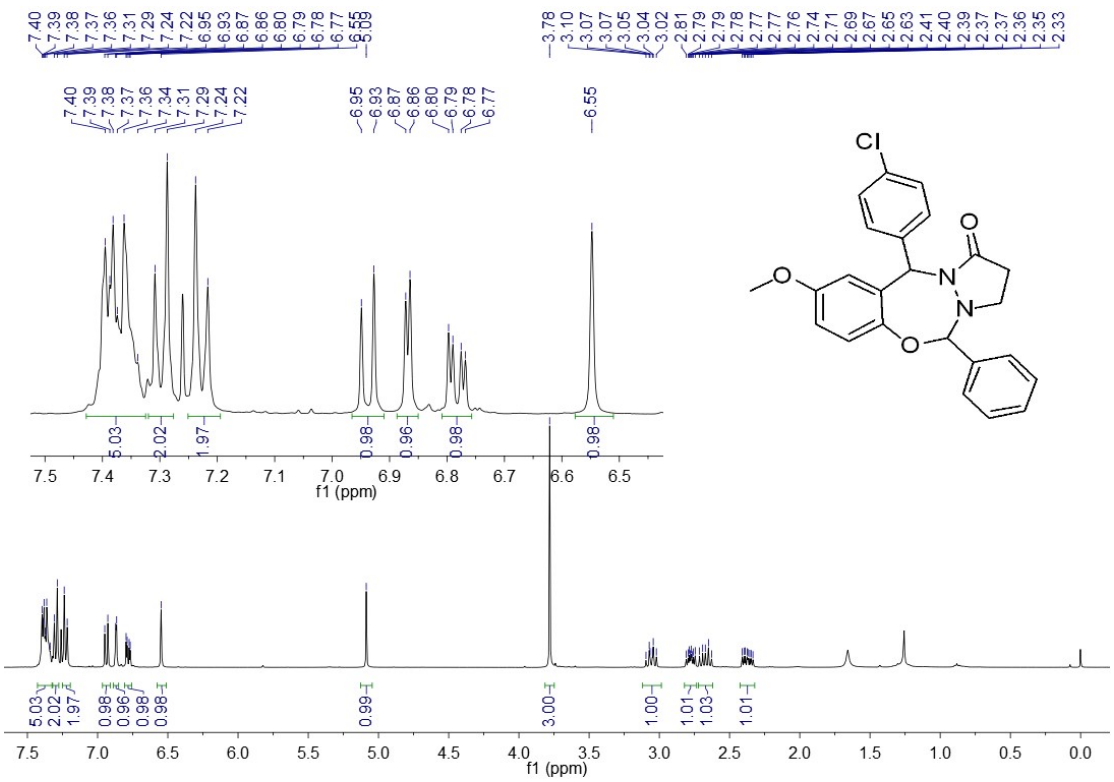

171.29
158.92
156.32
150.44
137.56
133.57
130.32
129.60
128.79
127.56
123.63
114.55
114.45
113.61
101.13
60.05
55.63
55.24
46.48
30.16
f1 (ppm)

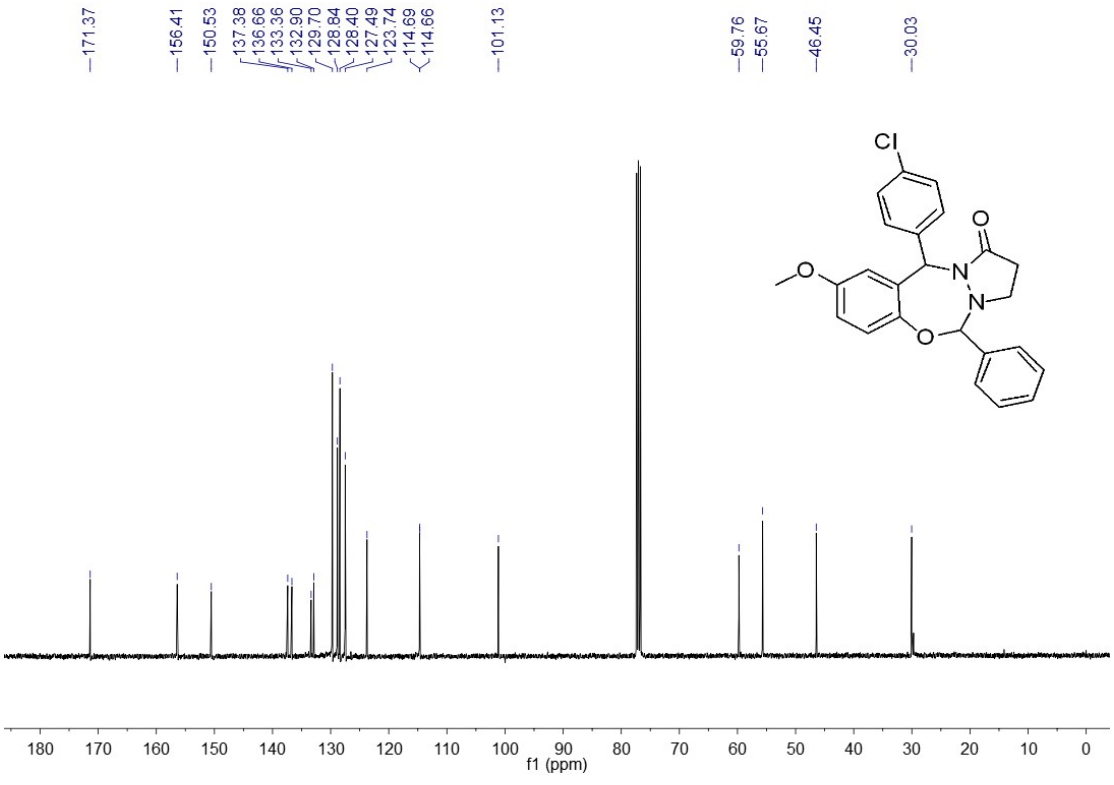
4ia



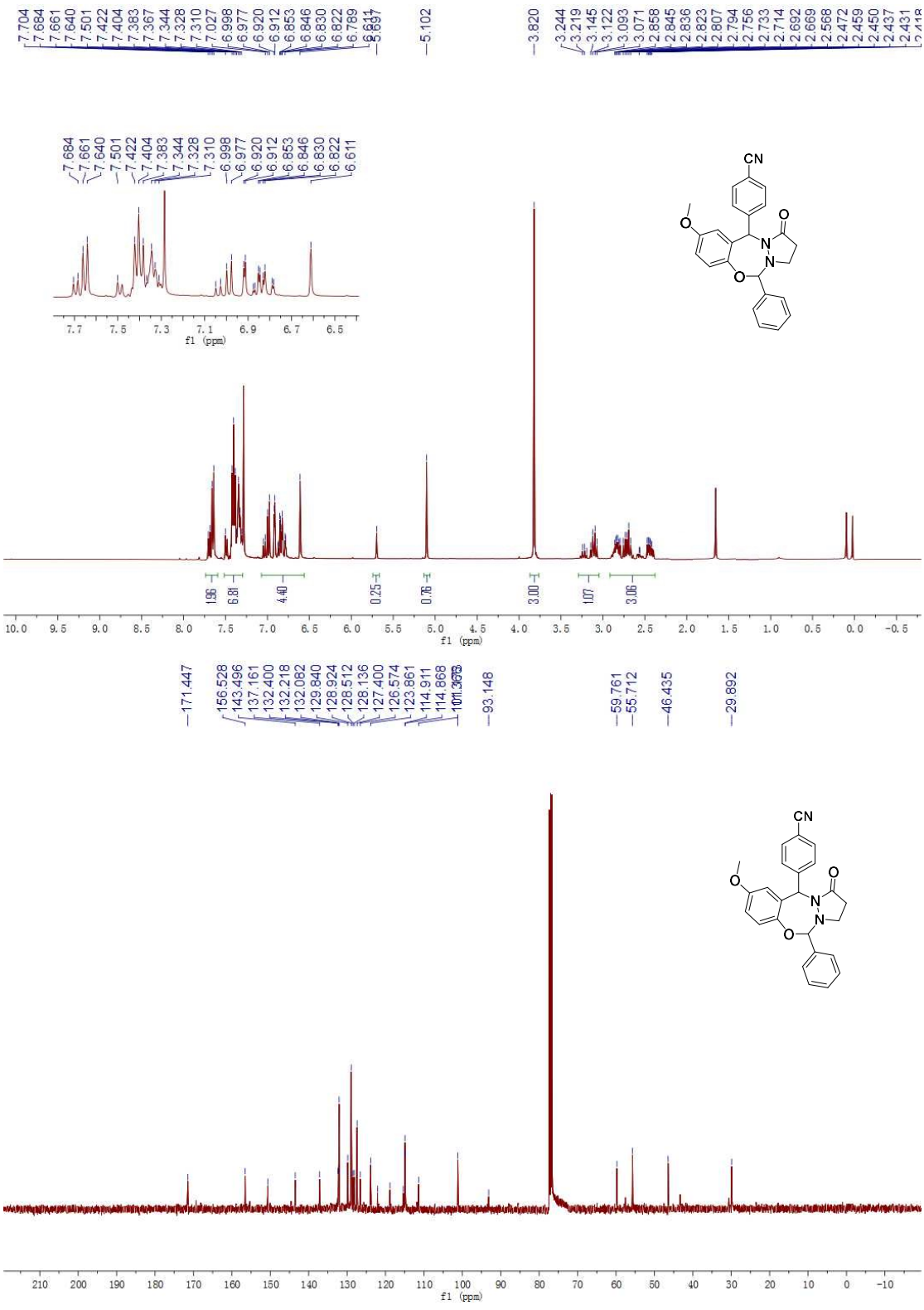


4ja

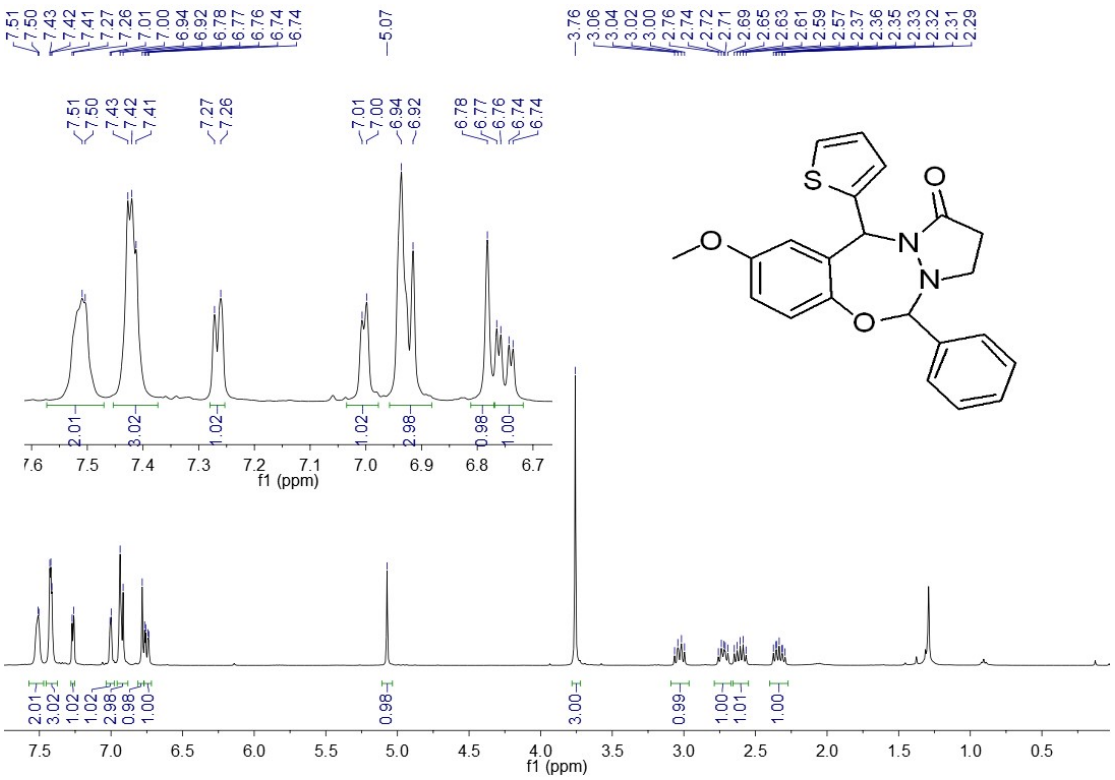

7.40
7.39
7.38
7.37
7.36
7.31
7.29
7.24
7.22
6.95
6.93
6.87
6.86
6.80
6.79
6.78
6.77
6.55
5.09
3.78
3.10
3.07
3.05
3.04
3.02
2.81
2.79
2.78
2.77
2.76
2.74
2.71
2.69
2.67
2.65
2.63
2.41
2.40
2.39
2.37
2.36
2.35
2.33
5.03
2.02
1.97
0.98
0.96
0.98
0.98
0.99
3.00
1.00
1.01
1.03
1.01
f1 (ppm)
Cl
O
N
N
O
O

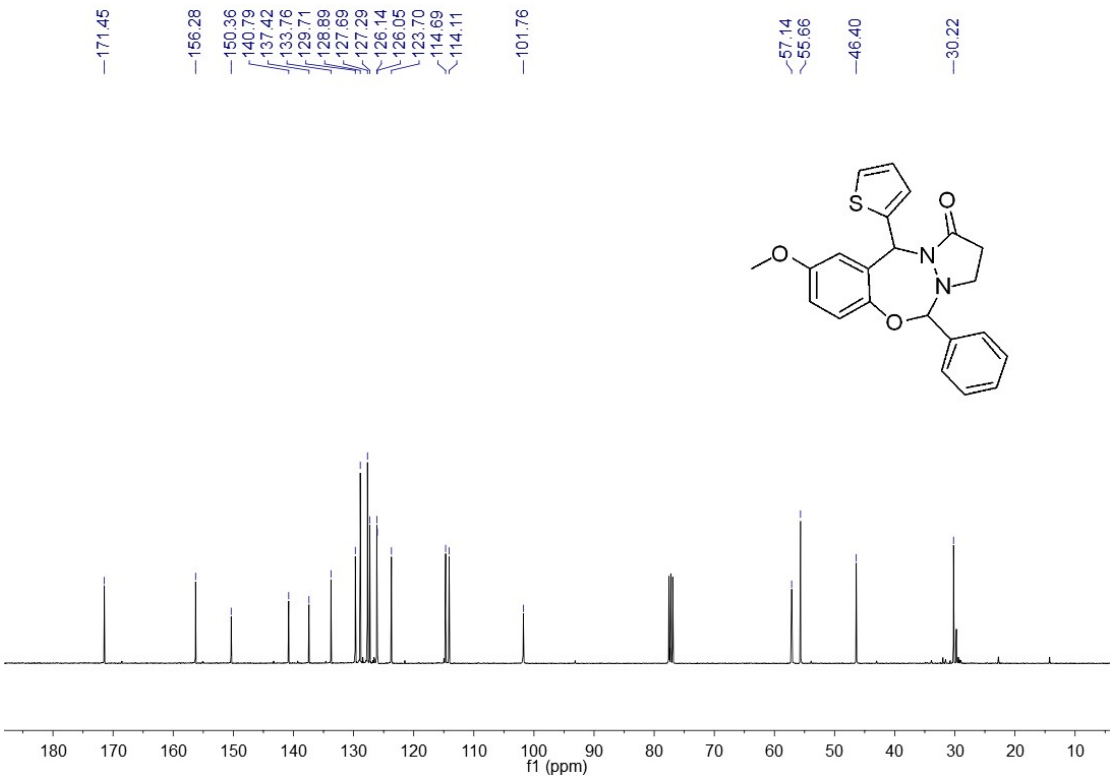

171.37
156.41
150.53
137.38
136.66
133.36
132.90
129.70
128.84
128.40
127.49
123.74
114.69
114.66
101.13
59.76
55.67
46.45
30.03
f1 (ppm)
Cl
O
N
N
O
O

4ka (inseparable diastereomers)

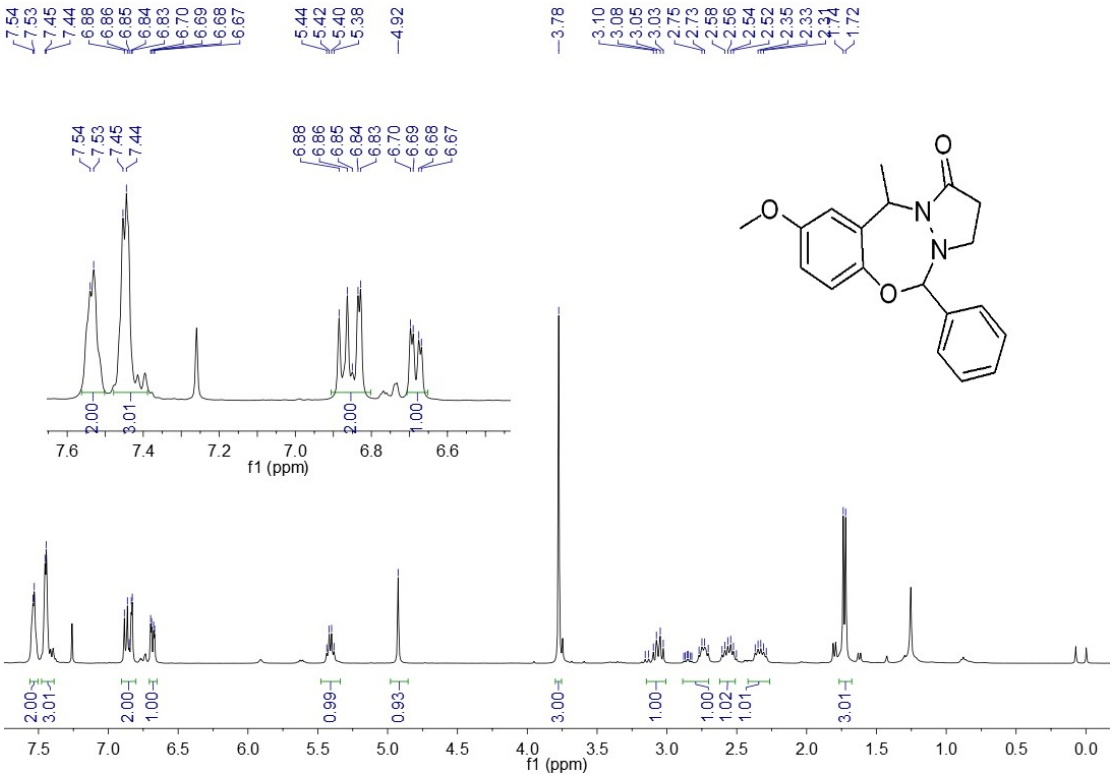


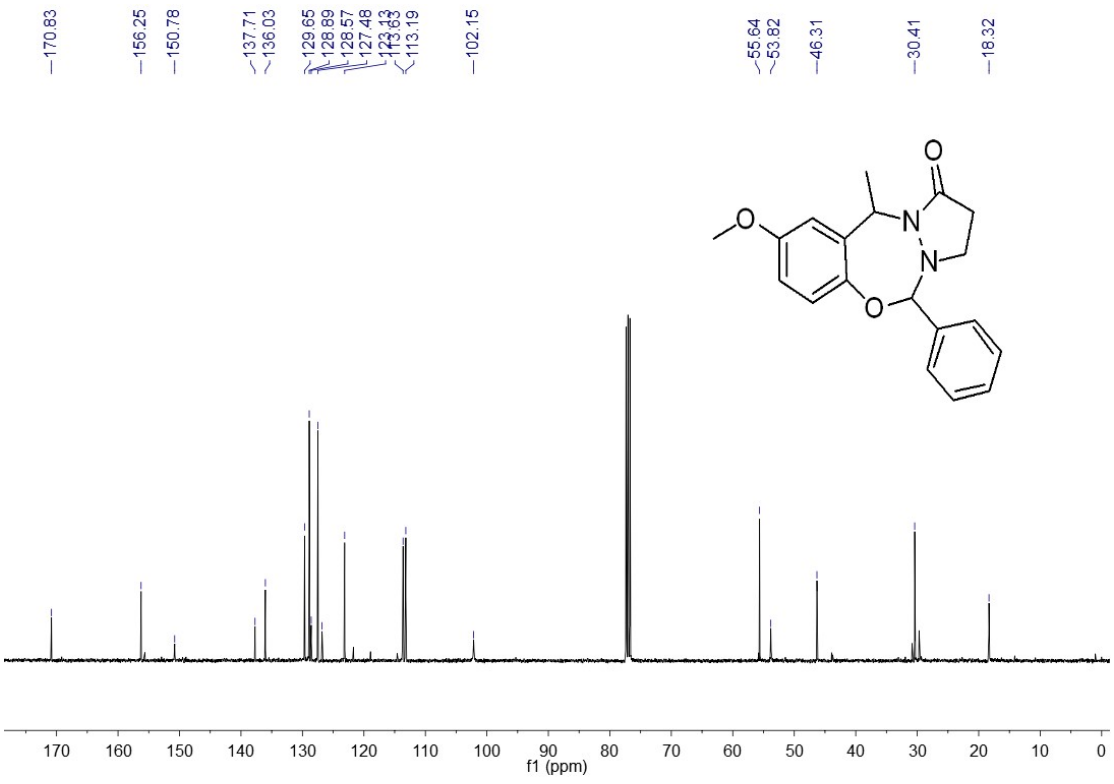
4la


7.51
7.50
7.43
7.42
7.41
7.27
7.26
7.01
7.00
6.94
6.92
6.78
6.77
6.76
6.74
6.74
5.07
3.76
3.06
3.04
3.02
3.00
2.76
2.74
2.72
2.71
2.69
2.65
2.63
2.61
2.59
2.57
2.37
2.36
2.35
2.33
2.32
2.31
2.29
S
O
N
N
O
2.01
3.02
1.02
1.02
2.98
0.98
1.00
0.98
3.00
0.99
1.00
1.01
1.00
f1 (ppm)

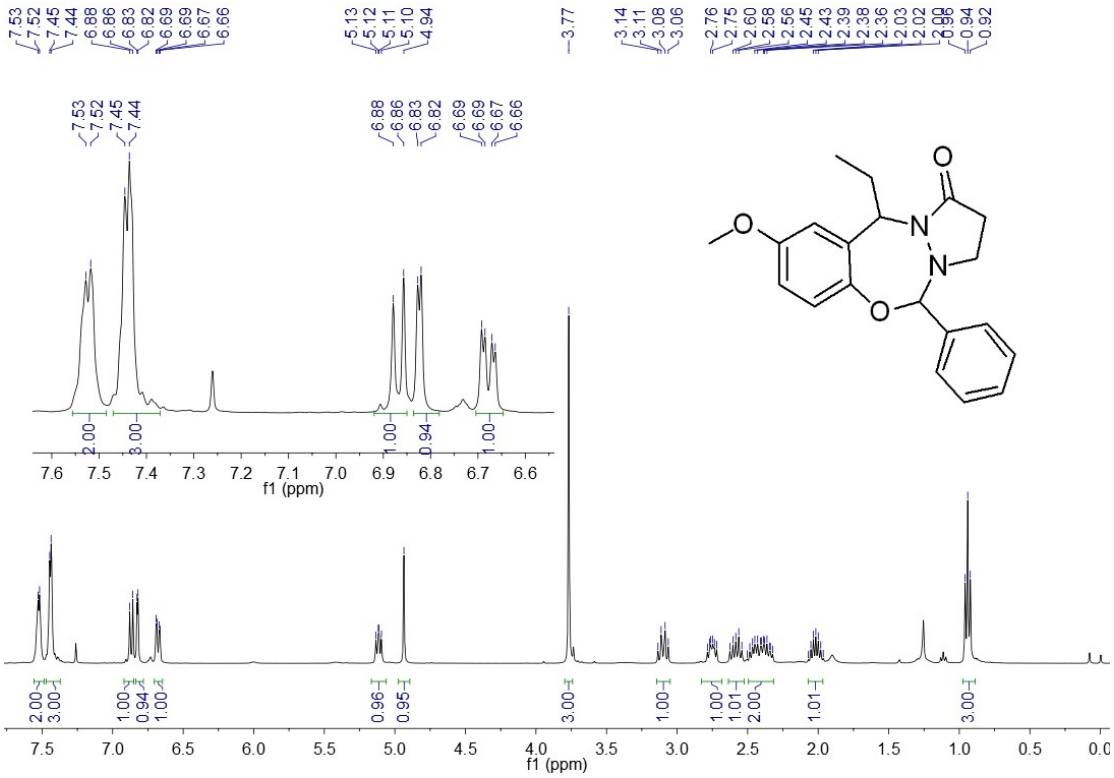

171.45
156.28
150.36
140.79
137.42
133.76
129.71
128.89
127.69
127.29
126.14
126.05
123.70
114.69
114.11
101.76
57.14
55.66
46.40
30.22
S
O
N
N
O
O
f1 (ppm)

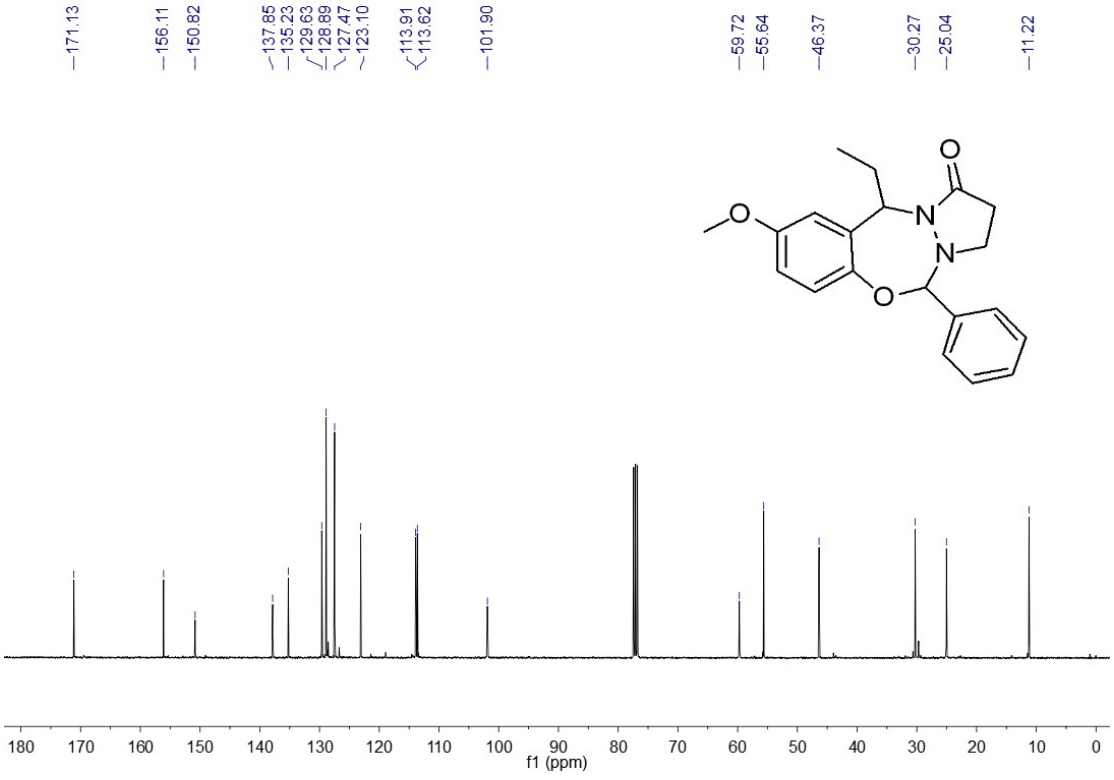
4ma


7.54
7.53
7.45
7.44
6.88
6.86
6.85
6.84
6.83
6.70
6.69
6.68
6.67
5.44
5.42
5.40
5.38
4.92
3.78
3.10
3.08
3.05
3.03
2.75
2.73
2.58
2.56
2.54
2.52
2.35
2.33
2.31
1.74
1.72
O
N
N
O
O
2.00
3.01
2.00
1.00
7.6
7.4
7.2
7.0
6.8
6.6
f1 (ppm)
2.00
3.01
2.00
1.00
0.99
0.93
3.00
1.00
1.00
1.02
1.01
3.01
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

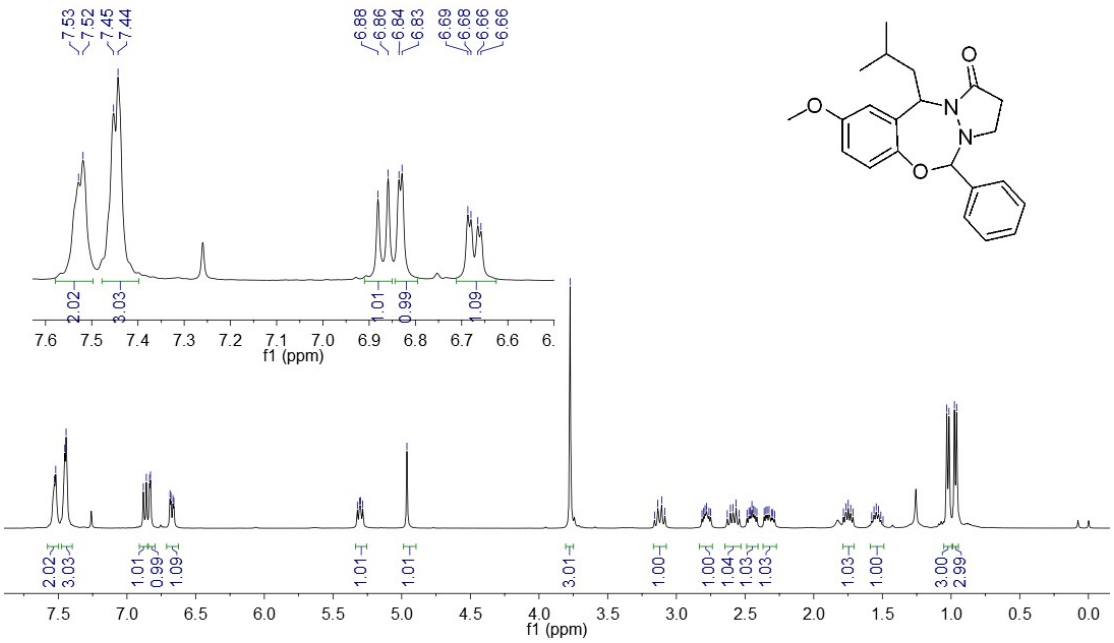

170.83
156.25
150.78
137.71
136.03
129.65
128.89
128.57
127.48
113.19
102.15
55.64
53.82
46.31
30.41
18.32
O
N
N
O
O
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

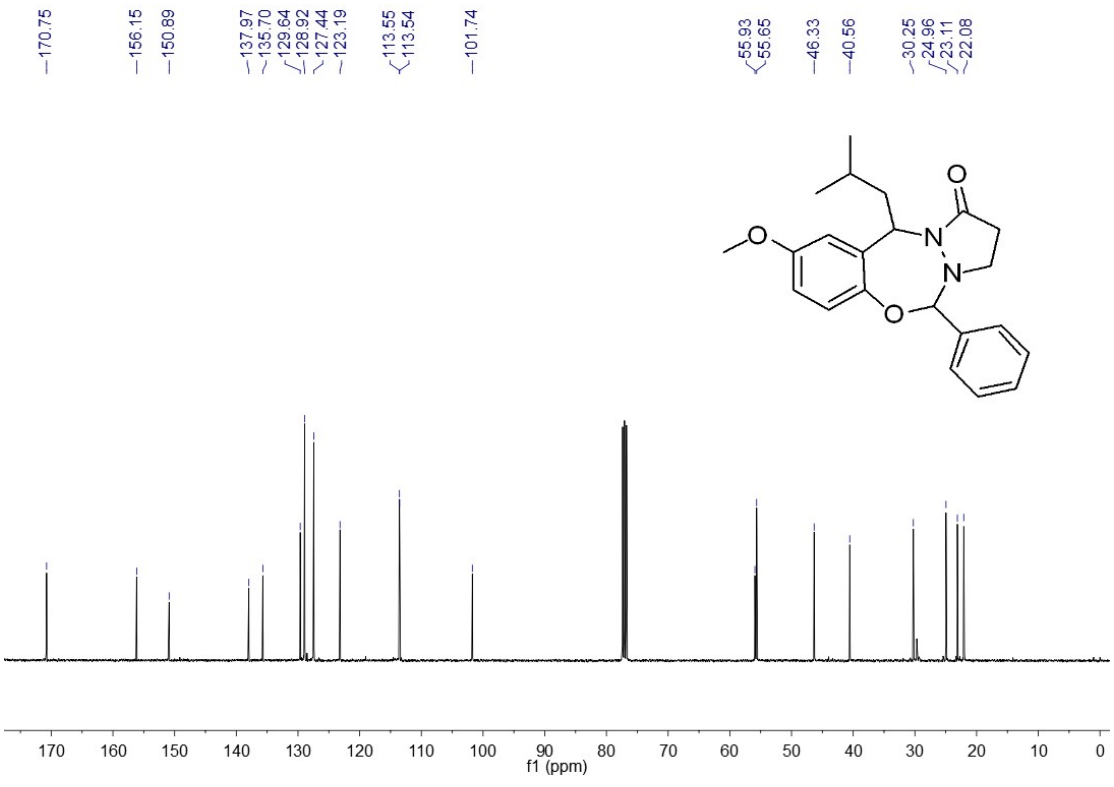
4na


7.53
7.52
7.45
7.44
6.88
6.86
6.83
6.82
6.69
6.69
6.67
6.66
5.13
5.12
5.11
5.10
4.94
3.77
3.14
3.11
3.08
3.06
2.76
2.75
2.60
2.58
2.56
2.45
2.43
2.39
2.38
2.36
2.03
2.02
0.94
0.92
2.00
3.00
1.00
0.94
1.00
f1 (ppm)
O
N
N
O
O
2.00
3.00
1.00
0.94
1.00
0.96
0.95
3.00
1.00
1.00
1.01
2.00
1.01
3.00
f1 (ppm)

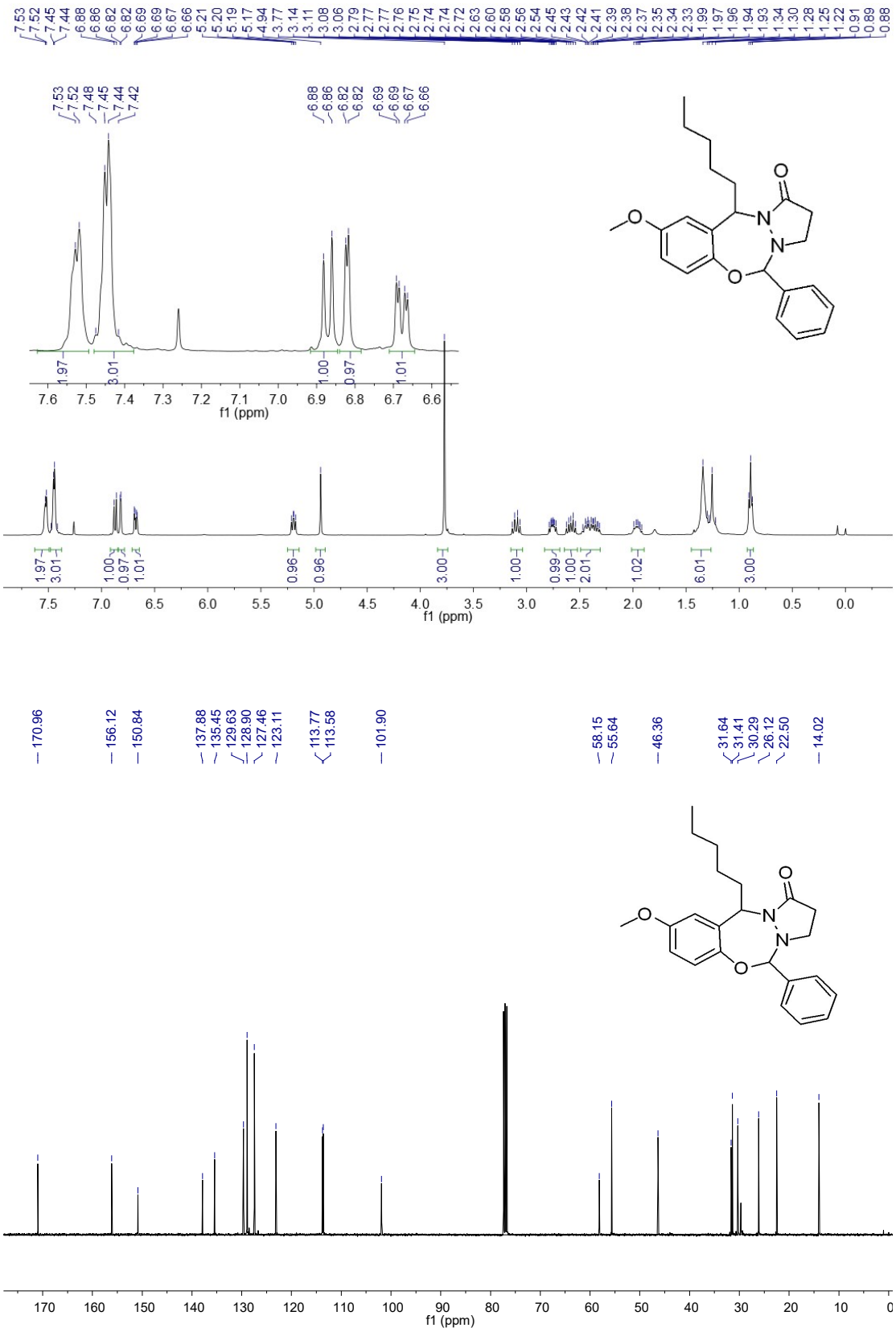

171.13
156.11
150.82
137.85
135.23
129.63
128.89
127.47
123.10
113.91
113.62
101.90
59.72
55.64
46.37
30.27
25.04
11.22
O
N
N
O
O
f1 (ppm)

4oa

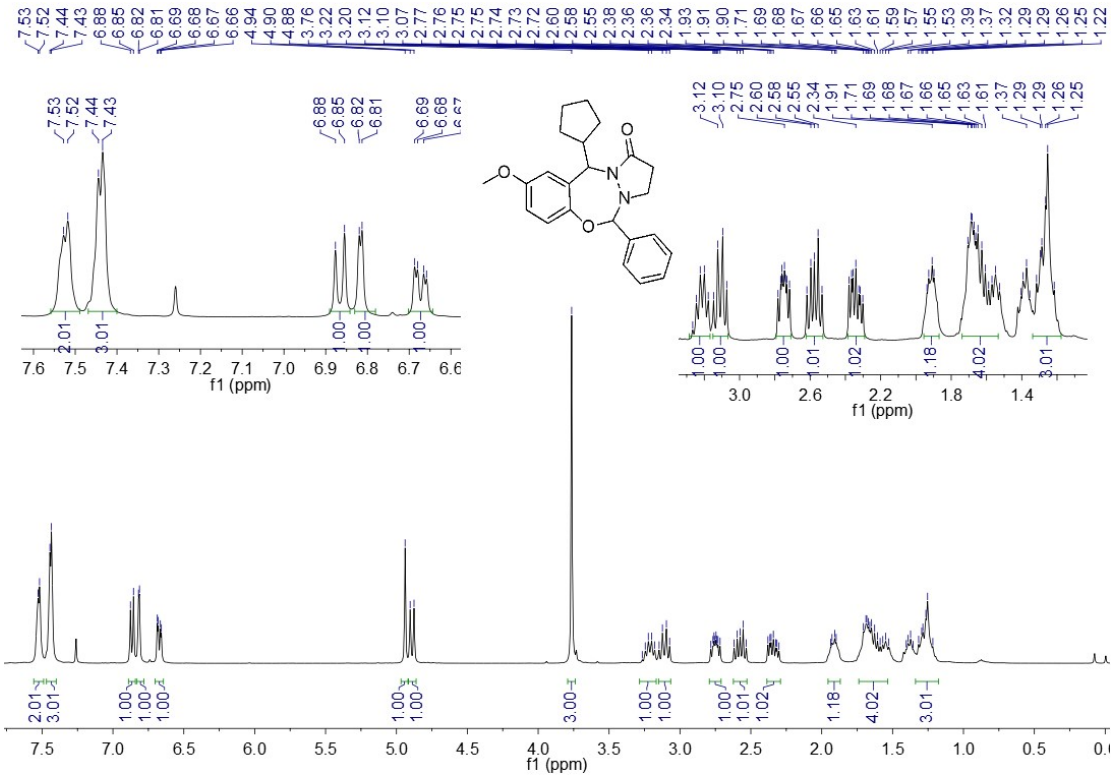


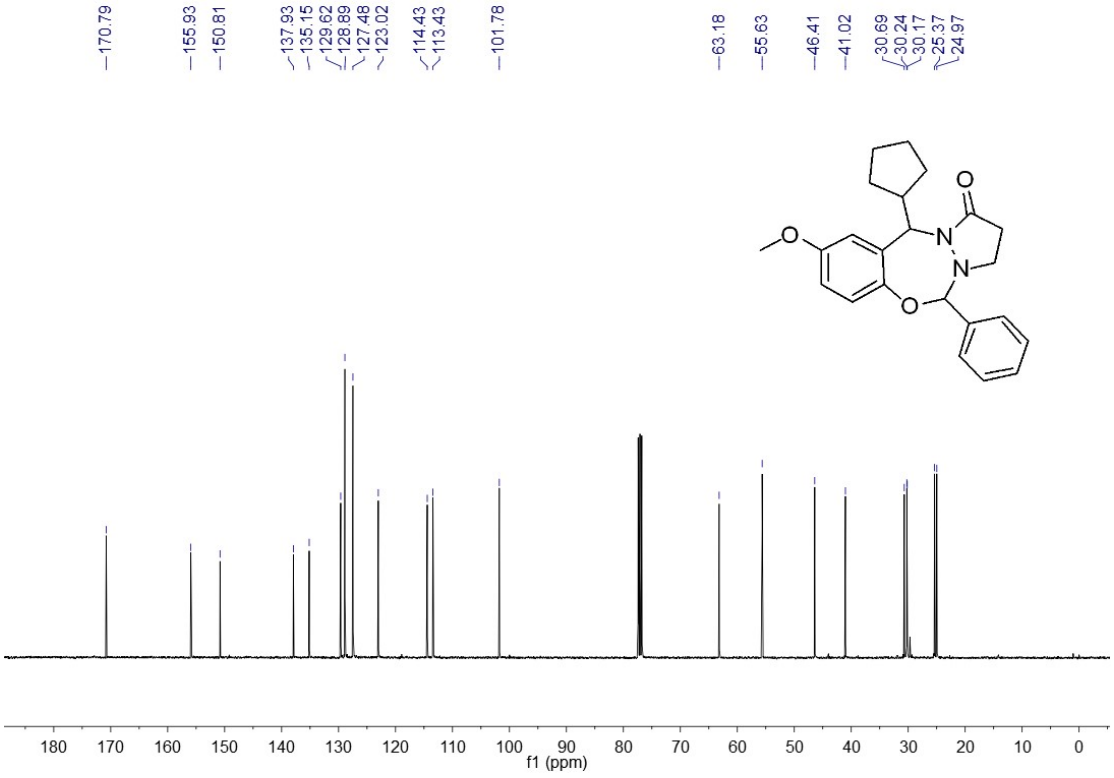


4pa

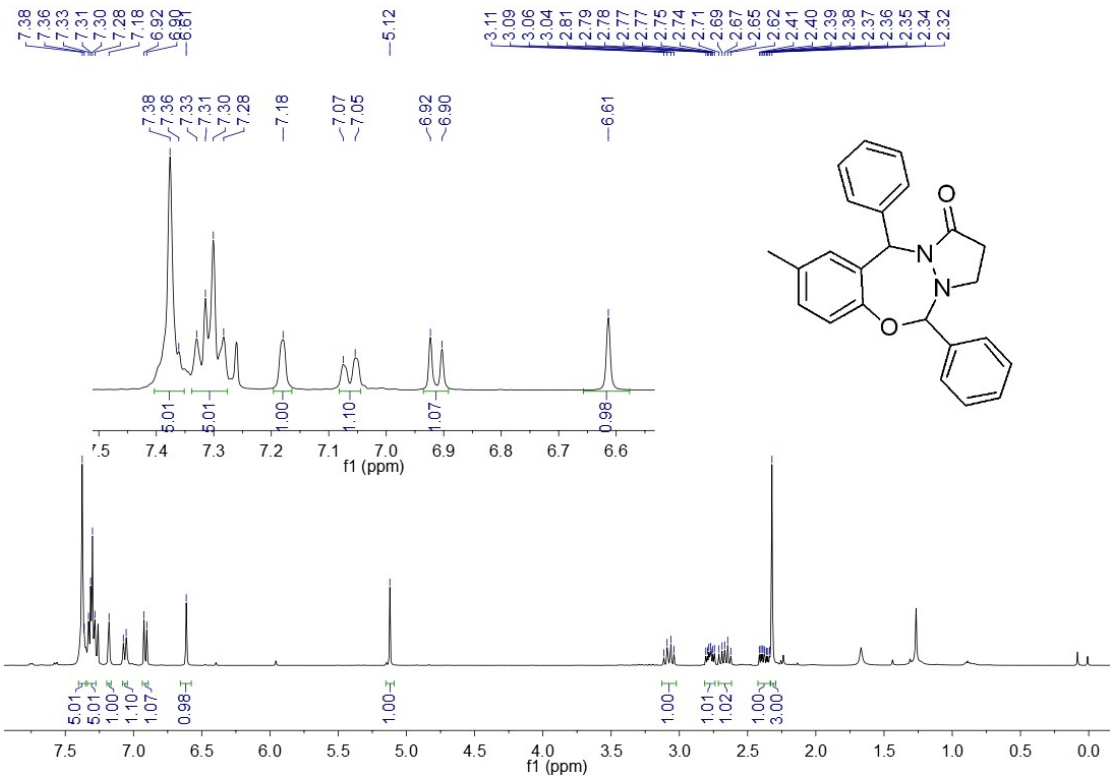

7.53 7.52 7.45 7.44 6.88 6.86 6.82 6.82 6.69 6.69 6.67 6.66 5.21 5.20 5.19 5.17 4.94 3.77 3.14 3.11 3.08 3.06 2.79 2.77 2.77 2.76 2.75 2.74 2.74 2.72 2.63 2.60 2.58 2.56 2.54 2.45 2.43 2.42 2.41 2.39 2.38 2.37 2.35 2.34 2.33 1.99 1.97 1.96 1.94 1.93 1.34 1.30 1.28 1.25 1.22 0.91 0.89 0.88
7.53 7.52 7.48 7.45 7.44 7.42 6.88 6.86 6.82 6.82 6.69 6.69 6.67 6.66
1.97 3.01 1.00 0.97 1.01 0.96 0.96 3.00 1.00 0.99 1.00 2.01 1.02 6.01 3.00
f1 (ppm)
O N N O O
170.96 156.12 150.84 137.88 135.45 129.63 128.90 127.46 123.11 113.77 113.58 101.90 58.15 55.64 46.36 31.64 31.41 30.29 26.12 22.50 14.02
f1 (ppm)

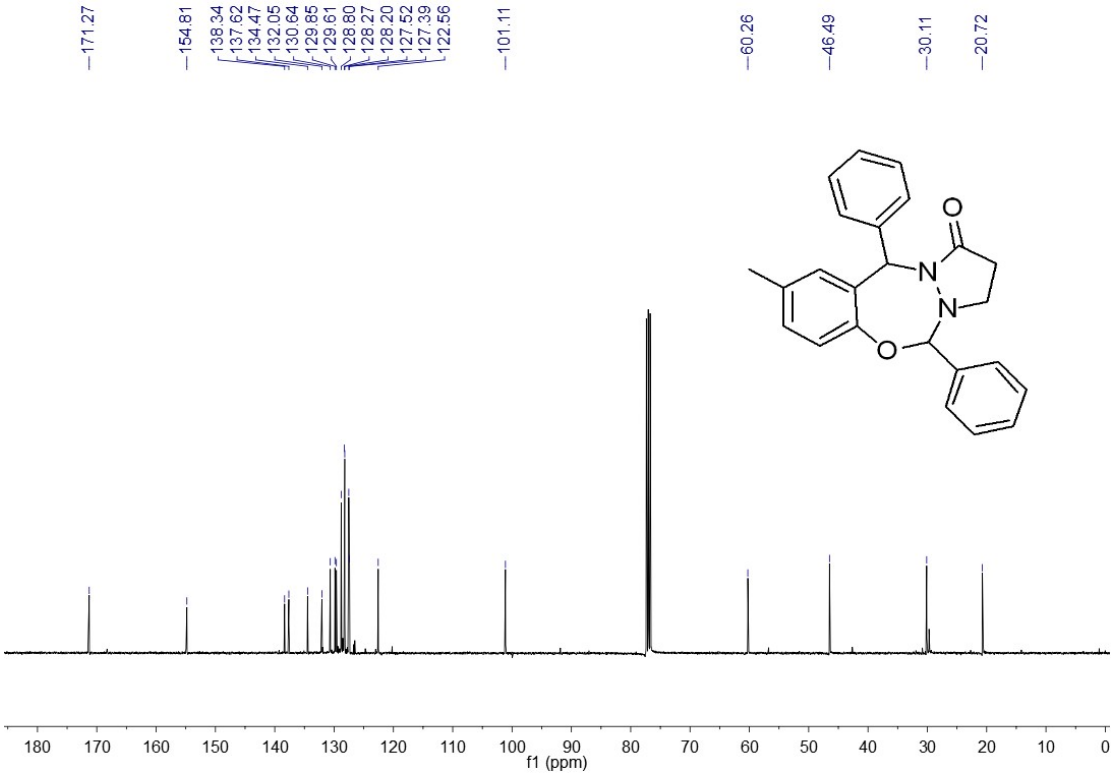
4qa



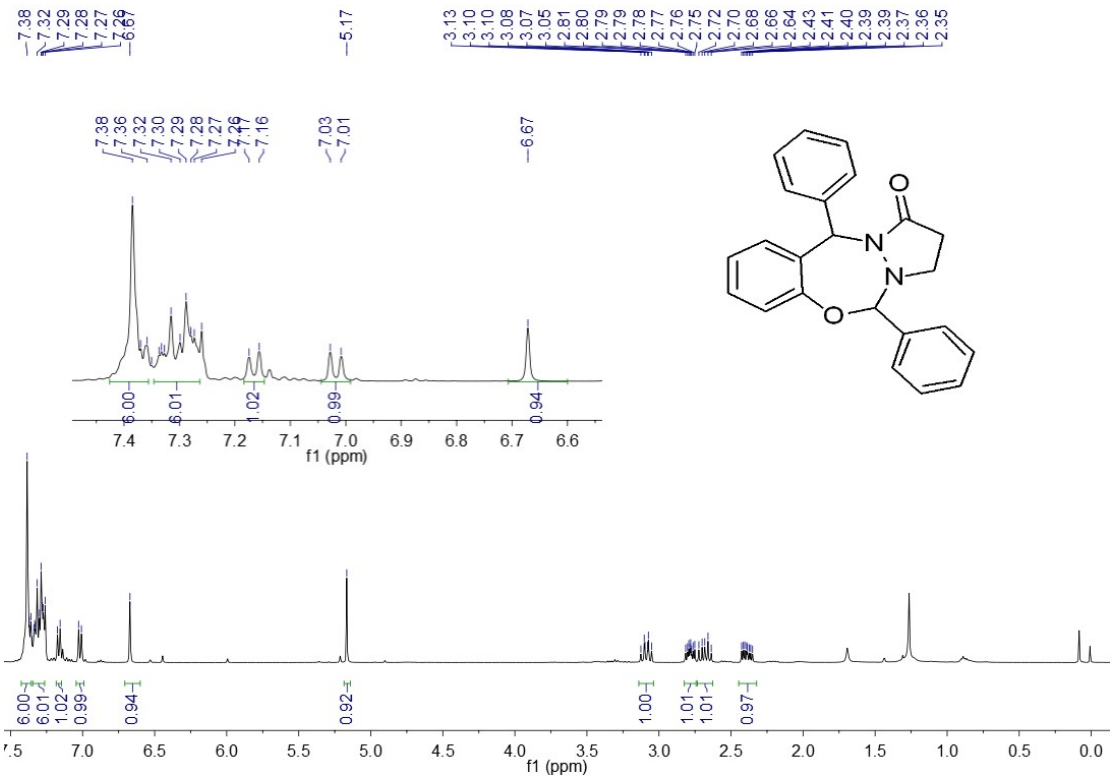


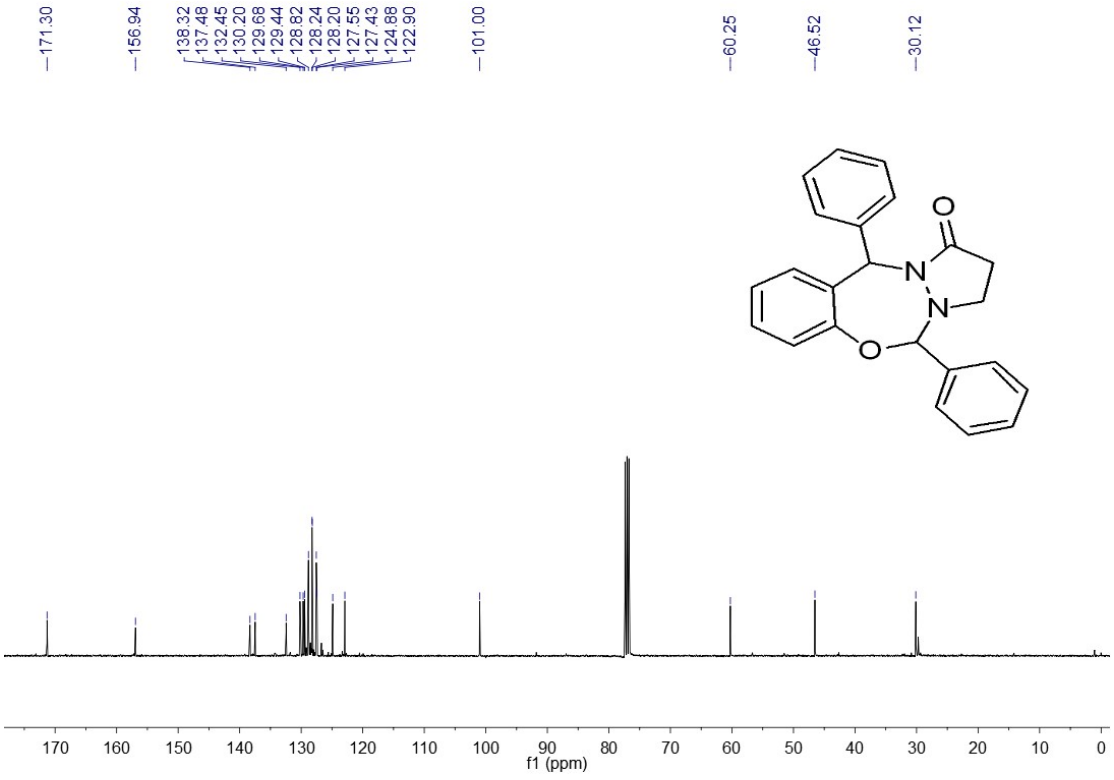
4ra


7.38
7.36
7.33
7.31
7.30
7.28
7.18
6.92
6.90
6.81
5.12
3.11
3.09
3.06
3.04
2.81
2.79
2.78
2.77
2.77
2.75
2.74
2.71
2.69
2.67
2.65
2.62
2.41
2.40
2.39
2.38
2.37
2.36
2.35
2.34
2.32
7.38
7.36
7.33
7.31
7.30
7.28
7.18
7.07
7.05
6.92
6.90
6.61
5.01
5.01
1.00
1.10
1.07
0.98
f1 (ppm)
O
N
N
O
5.01
5.01
1.00
1.10
1.07
0.98
1.00
1.00
1.01
1.02
1.00
3.00
f1 (ppm)

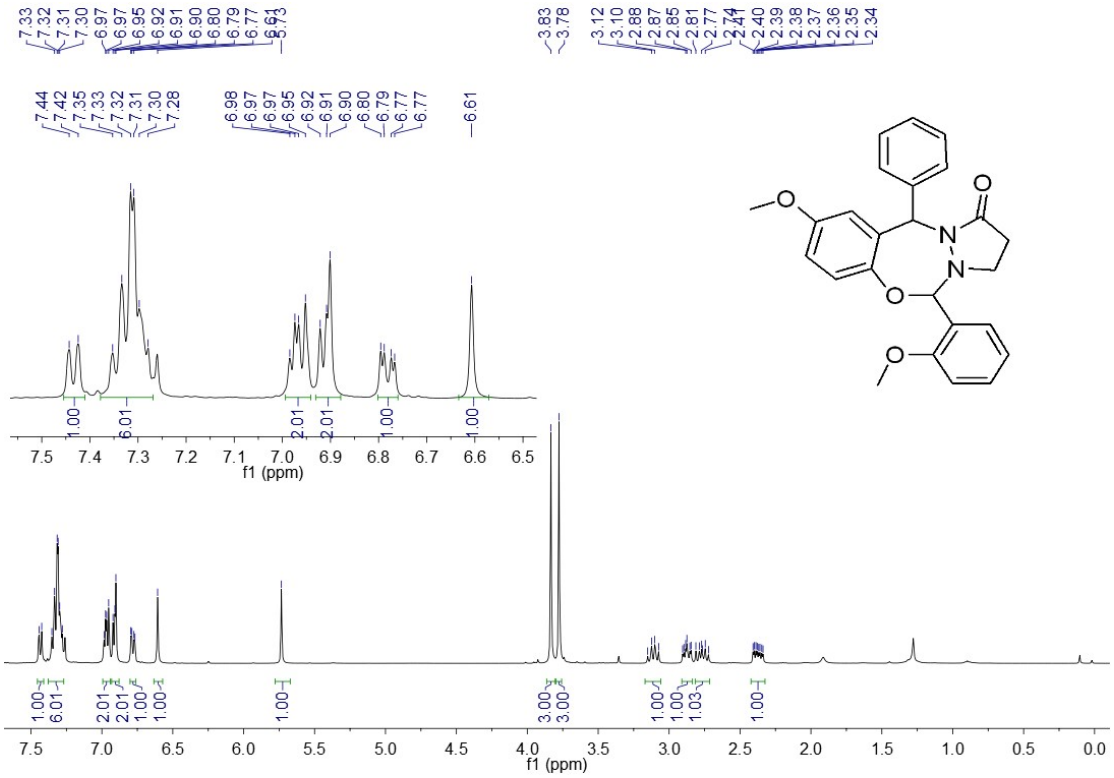

171.27
154.81
138.34
137.62
134.47
132.05
130.64
129.85
129.61
128.80
128.27
128.20
127.52
127.39
122.56
101.11
60.26
46.49
30.11
20.72
O
N
N
O
f1 (ppm)

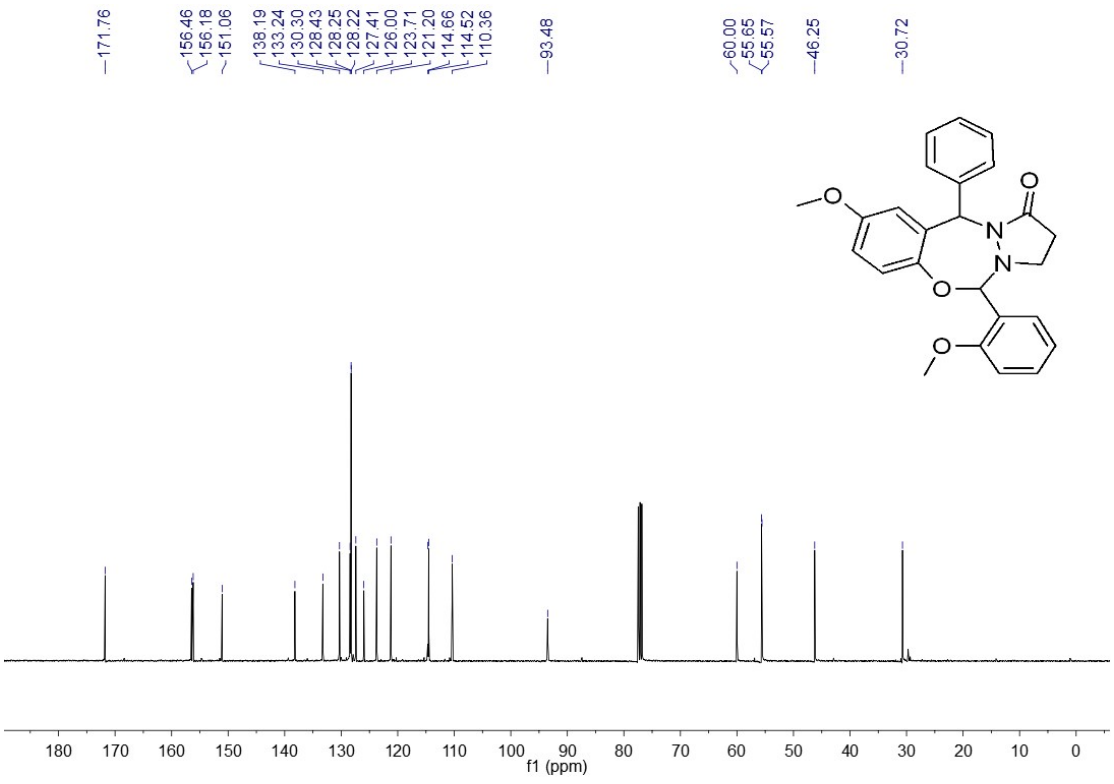
4sa


7.38
7.32
7.29
7.28
7.27
6.67
5.17
3.13
3.10
3.10
3.08
3.07
3.05
2.81
2.80
2.79
2.79
2.78
2.77
2.76
2.75
2.72
2.70
2.68
2.66
2.64
2.43
2.41
2.40
2.39
2.39
2.37
2.36
2.35
7.38
7.36
7.32
7.30
7.29
7.28
7.27
7.26
7.17
7.16
7.03
7.01
6.67
6.00
6.01
1.02
0.99
0.94
f1 (ppm)
O
N
N
O
6.00
6.01
1.02
0.99
0.94
0.92
1.00
1.01
1.01
0.97
f1 (ppm)

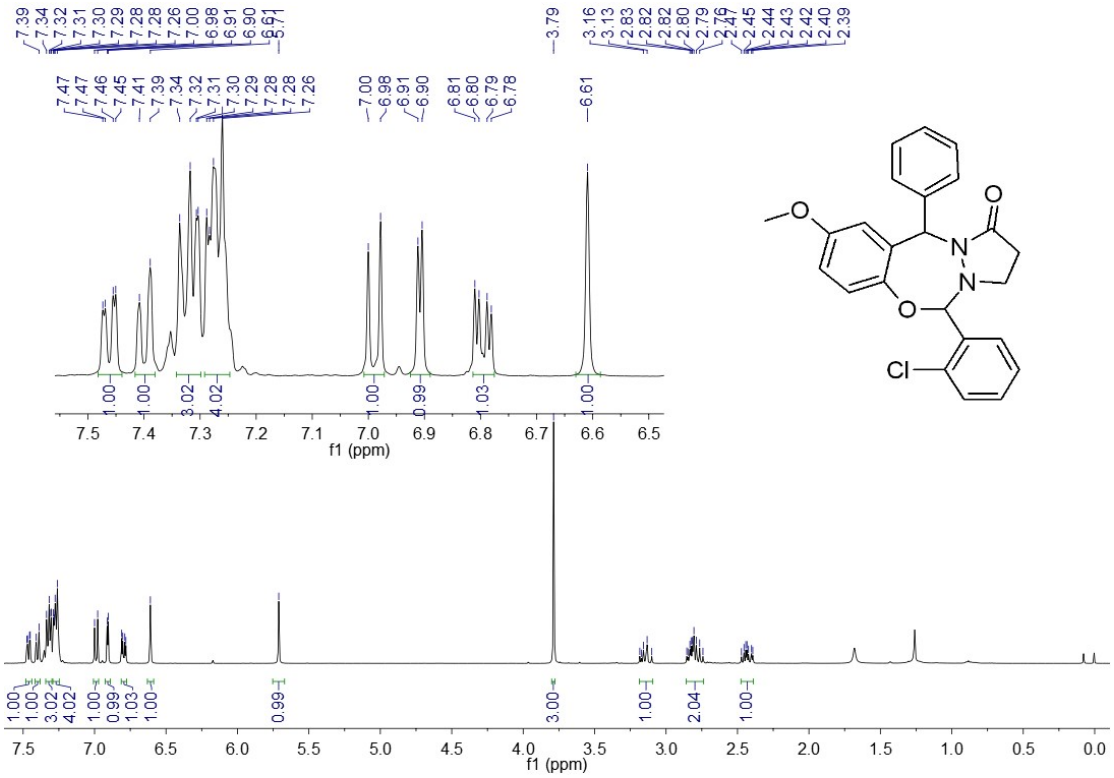

171.30
156.94
138.32
137.48
132.45
130.20
129.68
129.44
128.82
128.24
128.20
127.55
127.43
124.88
122.90
101.00
60.25
46.52
30.12
O
N
N
O
f1 (ppm)

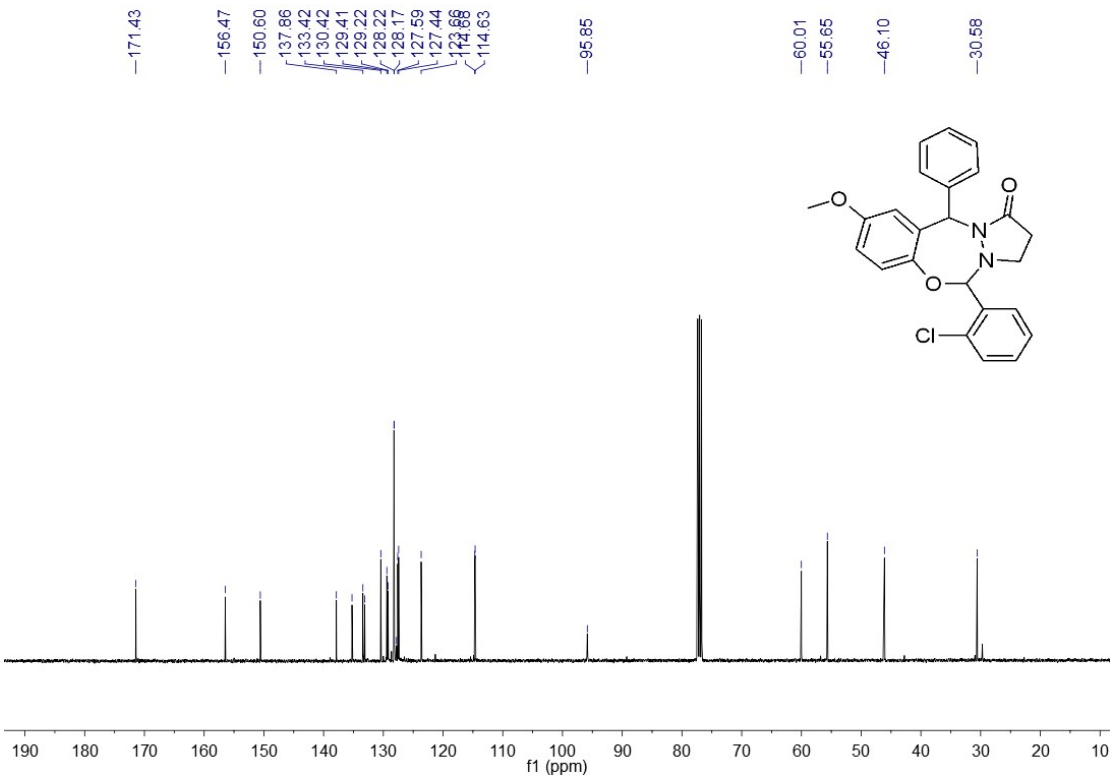
4ab


7.33
7.32
7.31
7.30
6.97
6.95
6.92
6.91
6.90
6.80
6.79
6.77
3.83
3.78
3.12
3.10
2.88
2.87
2.85
2.81
2.77
2.74
2.41
2.40
2.39
2.38
2.37
2.36
2.35
2.34
7.44
7.42
7.35
7.33
7.32
7.31
7.30
7.28
6.98
6.97
6.95
6.92
6.91
6.90
6.80
6.79
6.77
6.77
6.61
1.00
6.01
2.01
2.01
1.00
1.00
7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5
f1 (ppm)
1.00
6.01
2.01
2.01
1.00
1.00
1.00
3.00
3.00
1.00
1.00
1.03
1.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

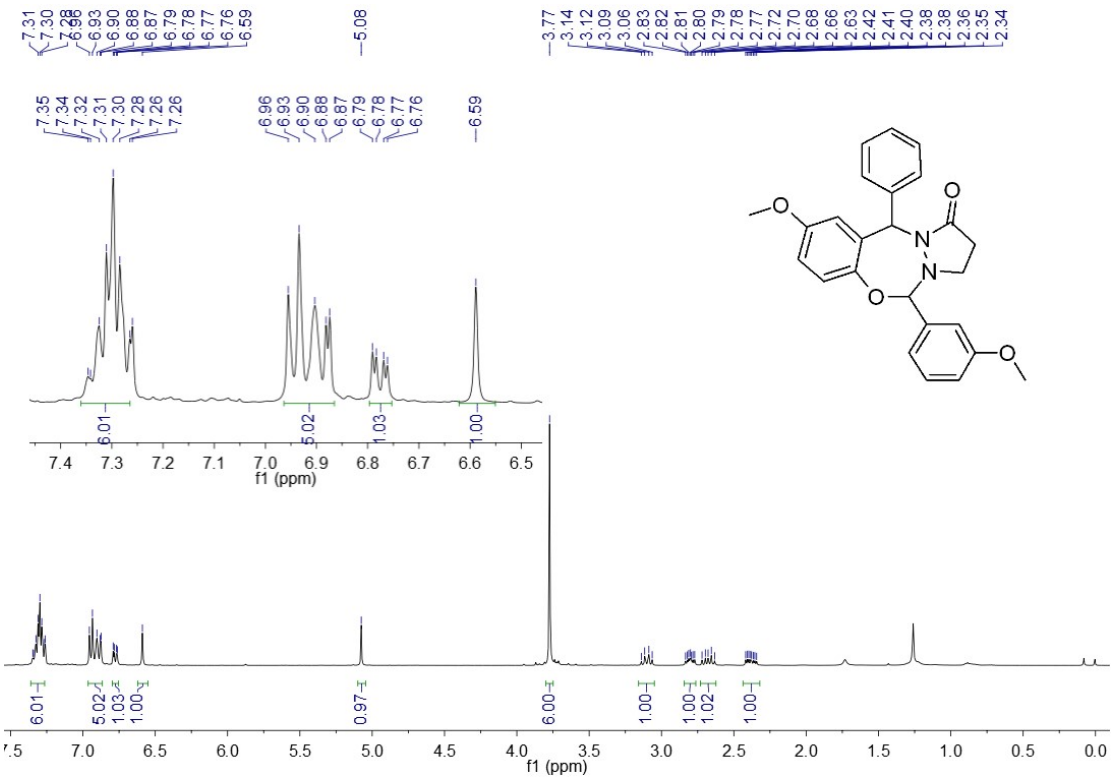

171.76
156.46
156.18
151.06
138.19
133.24
130.30
128.43
128.25
128.22
127.41
126.00
123.71
121.20
114.66
114.52
110.36
93.48
60.00
55.65
55.57
46.25
30.72
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

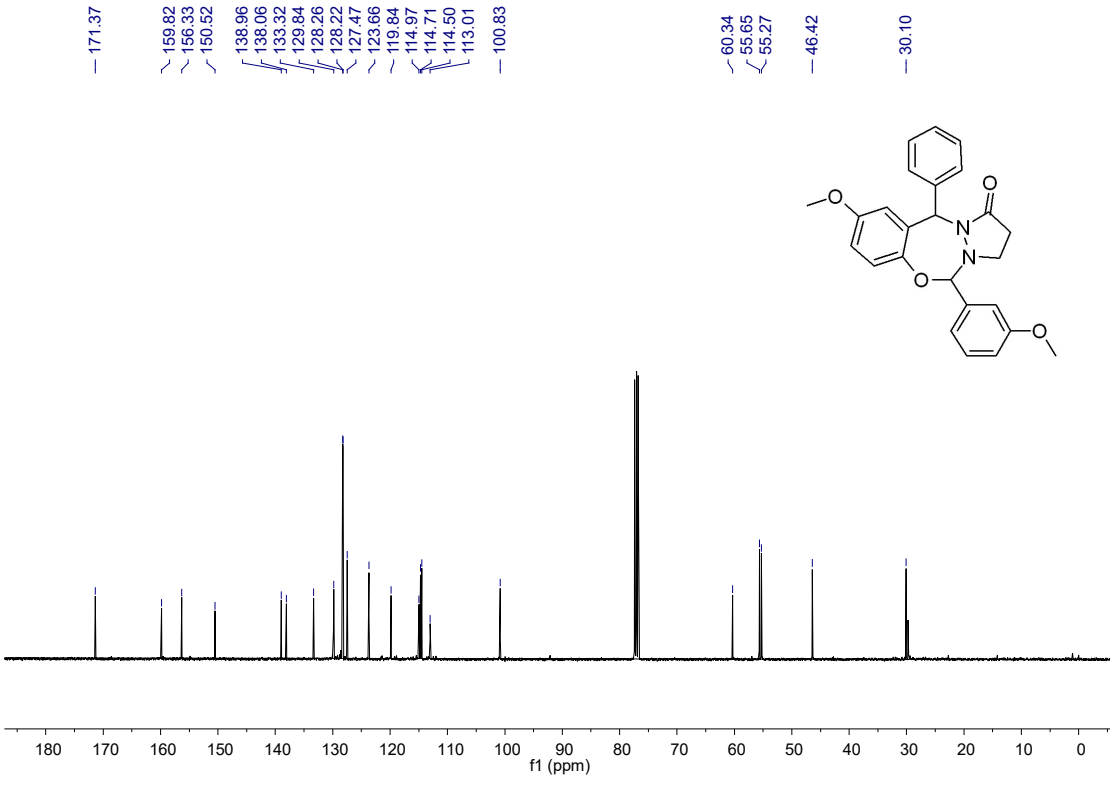
4ac


7.39
7.34
7.32
7.31
7.30
7.29
7.28
7.28
7.26
7.00
6.98
6.91
6.90
6.91
3.79
3.16
3.13
2.83
2.82
2.82
2.80
2.79
2.47
2.45
2.44
2.43
2.42
2.40
2.39
7.47
7.47
7.46
7.45
7.41
7.39
7.34
7.32
7.31
7.30
7.29
7.28
7.28
7.26
7.00
6.98
6.91
6.90
6.81
6.80
6.79
6.78
6.61
1.00
1.00
3.02
4.02
1.00
1.00
1.03
1.00
7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5
f1 (ppm)
O
N
N
O
O
Cl
1.00
1.00
3.02
4.02
1.00
0.99
1.03
1.00
0.99
3.00
1.00
2.04
1.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

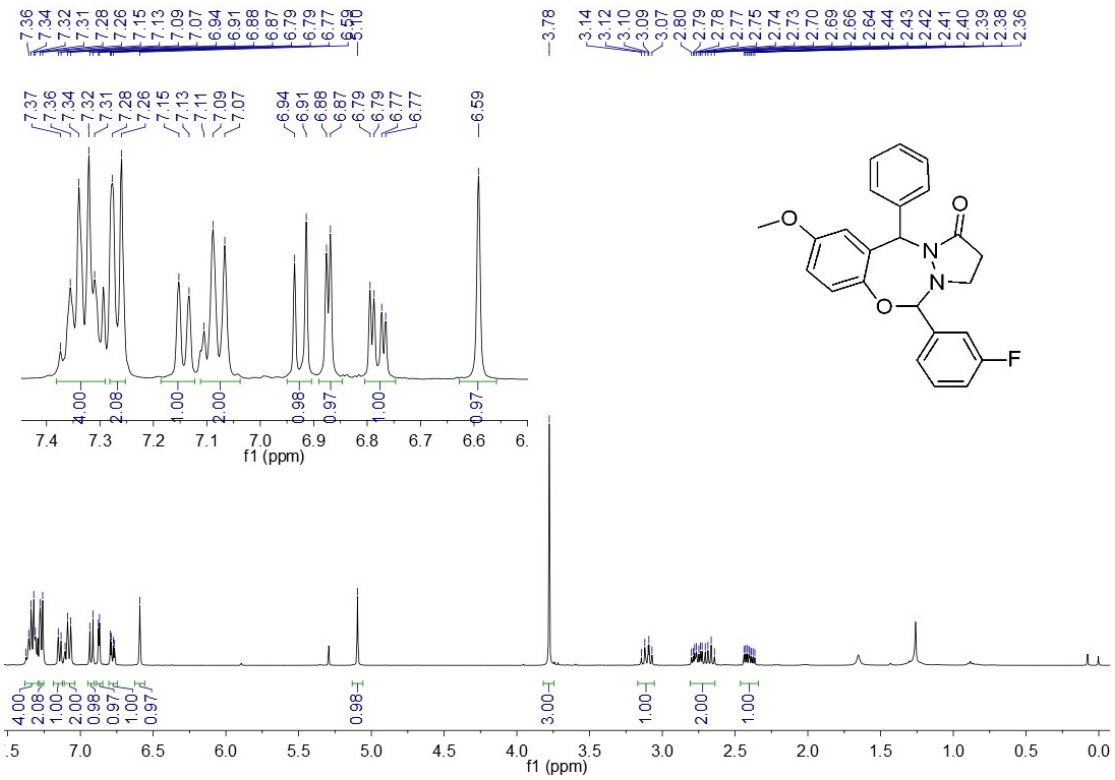

171.43
156.47
150.60
137.86
133.42
130.42
129.41
129.22
128.22
128.17
127.59
127.44
114.63
95.85
60.01
55.65
46.10
30.58
O
N
N
O
O
Cl
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

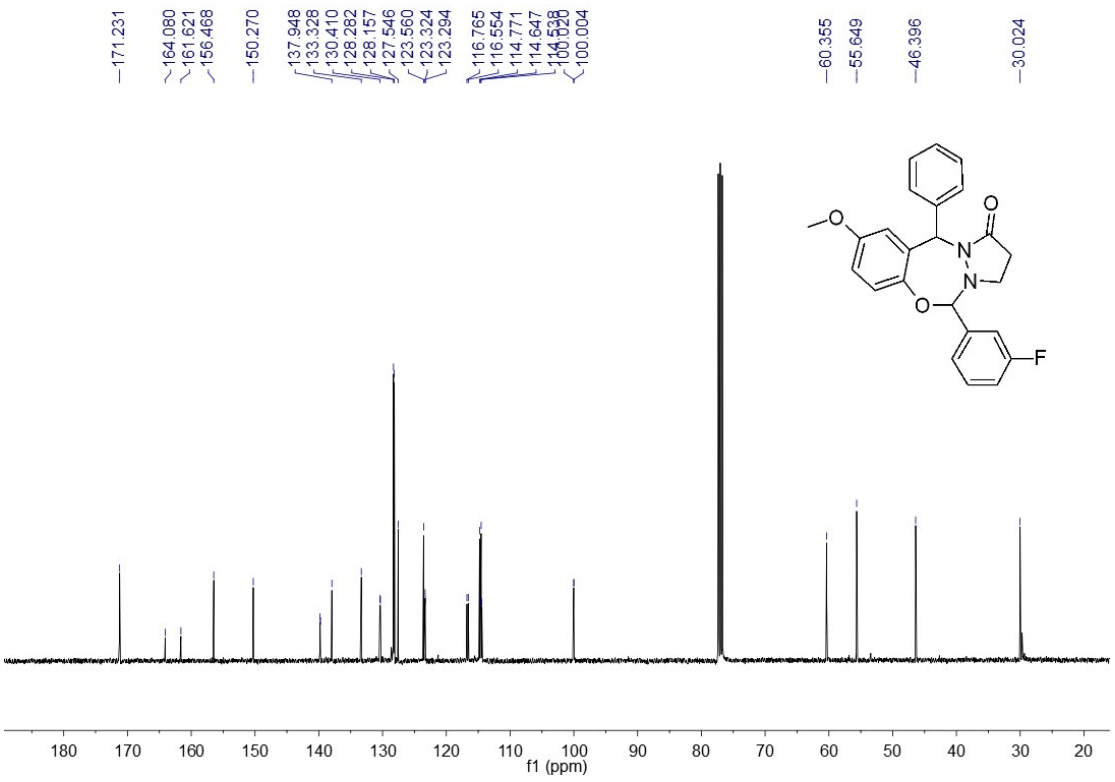
4ad


7.31
7.30
6.93
6.90
6.88
6.87
6.79
6.78
6.77
6.76
6.59
5.08
3.77
3.14
3.12
3.09
3.06
2.83
2.82
2.81
2.80
2.79
2.78
2.77
2.72
2.70
2.68
2.66
2.63
2.42
2.41
2.40
2.38
2.36
2.35
2.34
6.01
5.02
1.03
1.00
f1 (ppm)
0.97
6.00
1.02

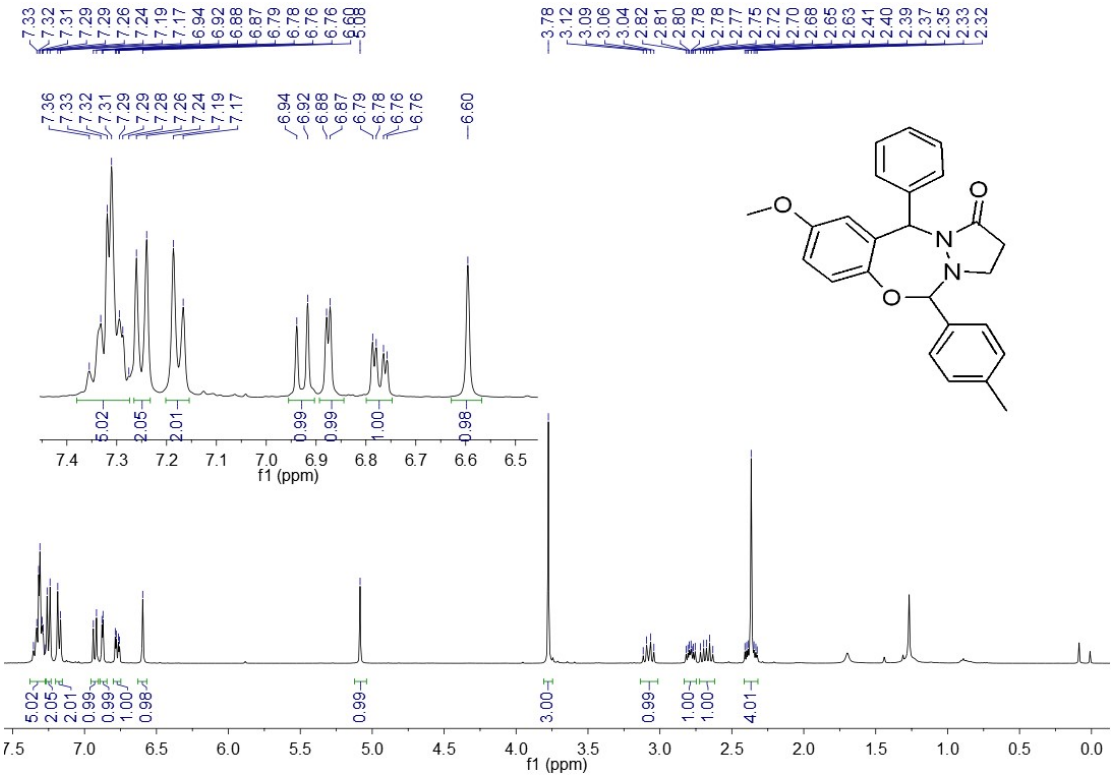

171.37
159.82
156.33
150.52
138.96
138.06
133.32
129.84
128.26
128.22
127.47
123.66
119.84
114.97
114.71
114.50
113.01
100.83
60.34
55.65
55.27
46.42
30.10
f1 (ppm)

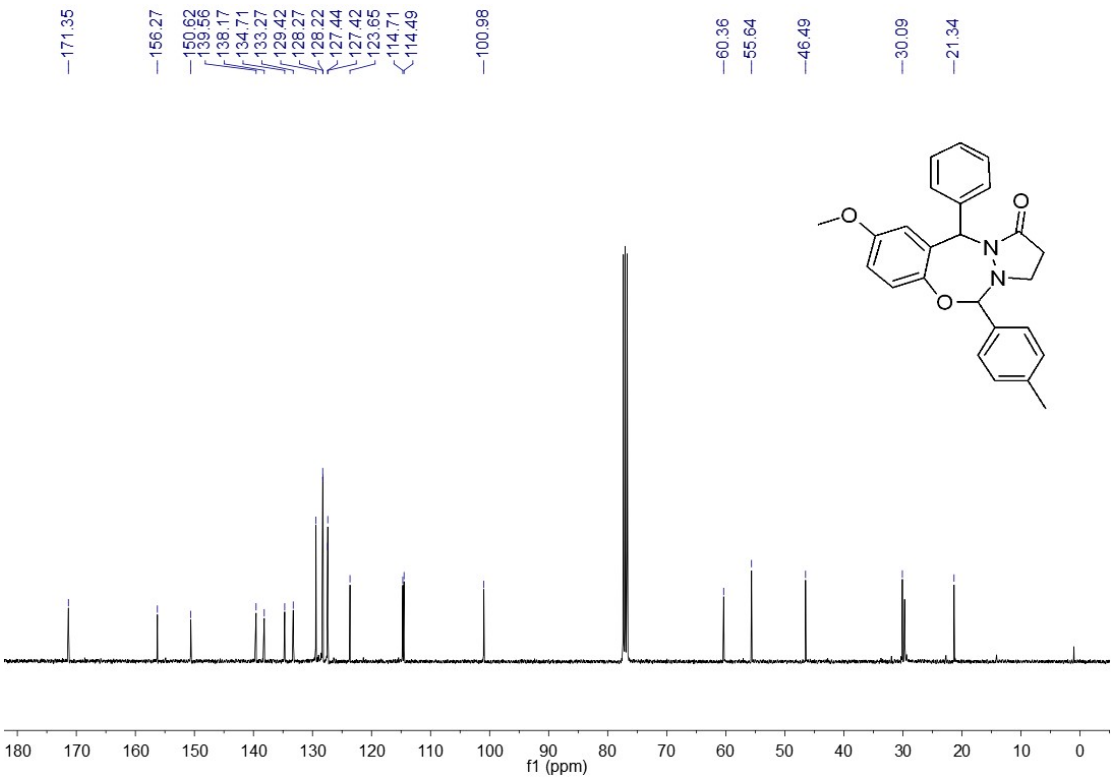
4ae


7.36
7.34
7.32
7.31
7.28
7.26
7.15
7.13
7.09
7.07
6.94
6.91
6.88
6.87
6.79
6.77
6.59
3.78
3.14
3.12
3.10
3.09
3.07
2.80
2.79
2.78
2.77
2.75
2.74
2.73
2.70
2.69
2.66
2.64
2.44
2.43
2.42
2.41
2.40
2.39
2.38
2.36
O
N
N
O
F
f1 (ppm)

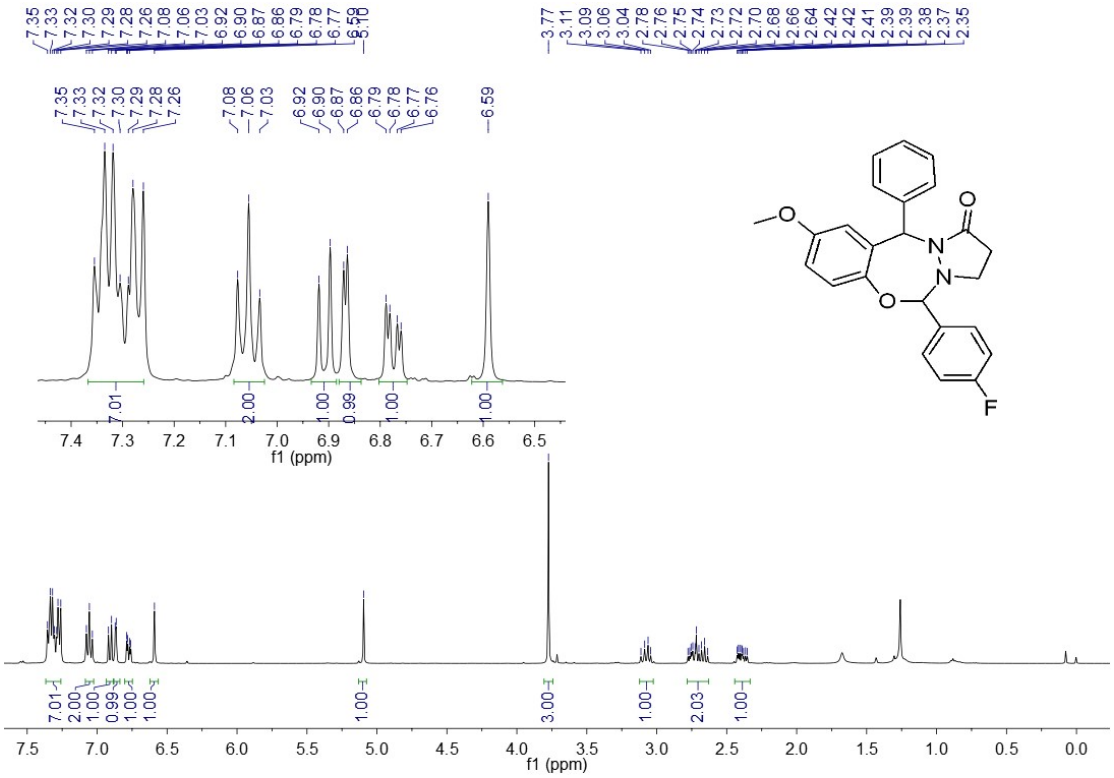

171.231
164.080
161.621
156.468
150.270
137.948
133.328
130.410
128.282
128.157
127.546
123.560
123.324
123.294
116.765
116.554
114.771
114.647
114.538
100.020
100.004
60.355
55.649
46.396
30.024
O
N
N
O
F
f1 (ppm)

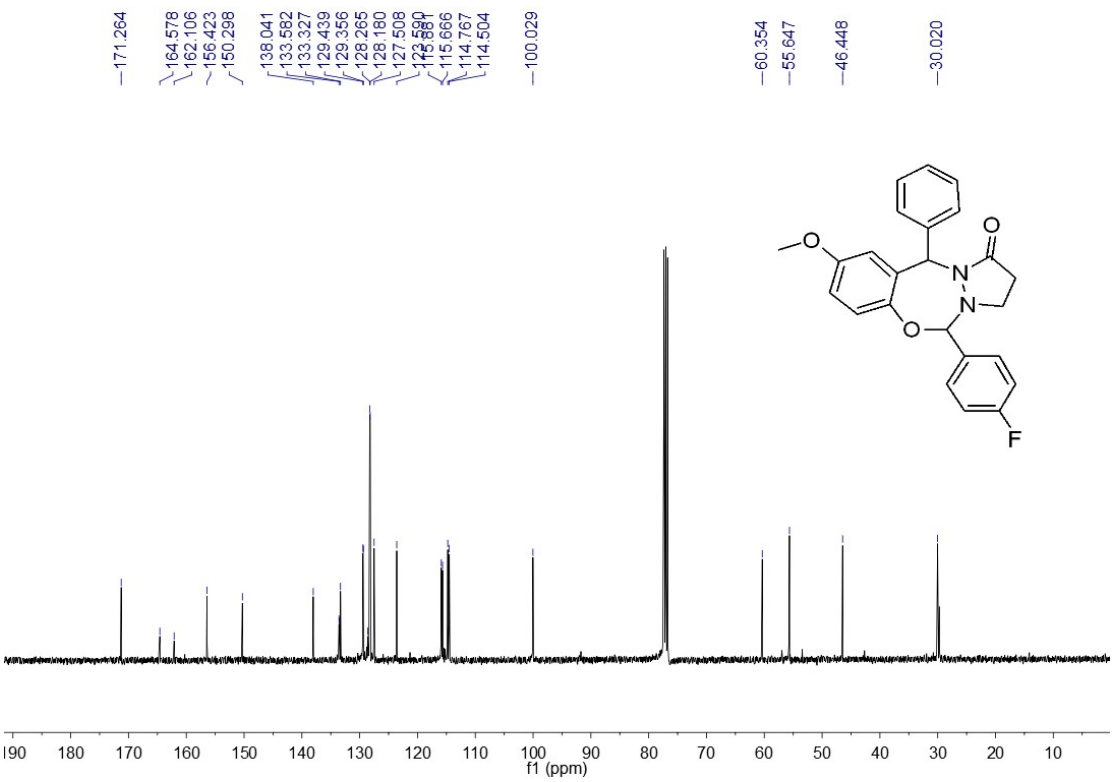
4af


7.33
7.32
7.31
7.29
7.29
7.26
7.24
7.19
7.17
6.94
6.92
6.88
6.87
6.79
6.78
6.76
6.76
6.60
6.60
3.78
3.12
3.09
3.06
3.04
2.82
2.81
2.80
2.78
2.78
2.77
2.75
2.72
2.70
2.68
2.65
2.63
2.41
2.40
2.39
2.37
2.35
2.33
2.32
5.02
2.05
2.01
0.99
0.99
1.00
0.98
f1 (ppm)
5.02
2.05
2.01
0.99
0.99
1.00
0.98
0.99
3.00
0.99
1.00
1.00
4.01
f1 (ppm)

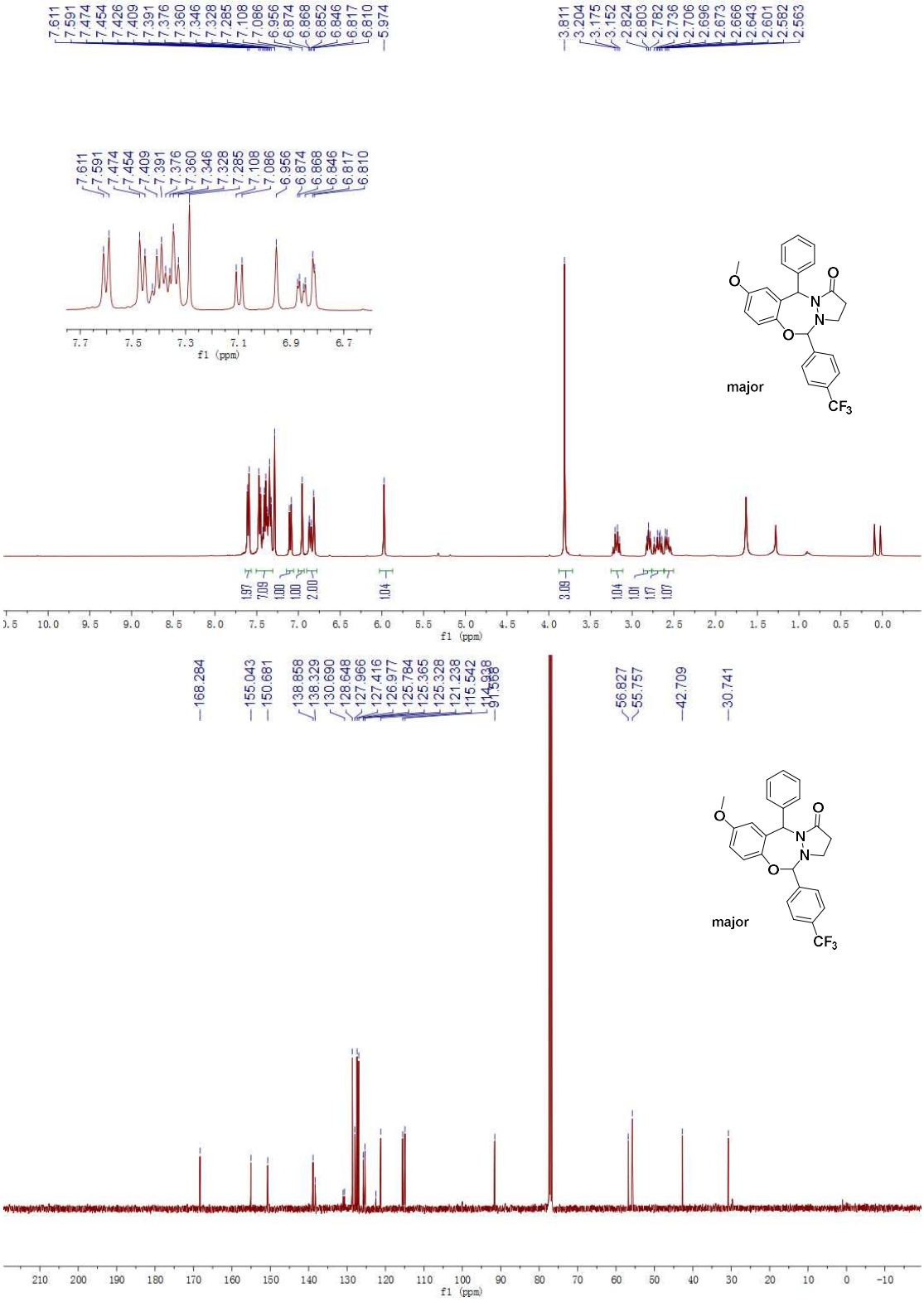

171.35
156.27
150.62
139.56
138.17
134.71
133.27
129.42
128.27
128.22
127.44
127.42
123.65
114.71
114.49
100.98
60.36
55.64
46.49
30.09
21.34
f1 (ppm)

4ag

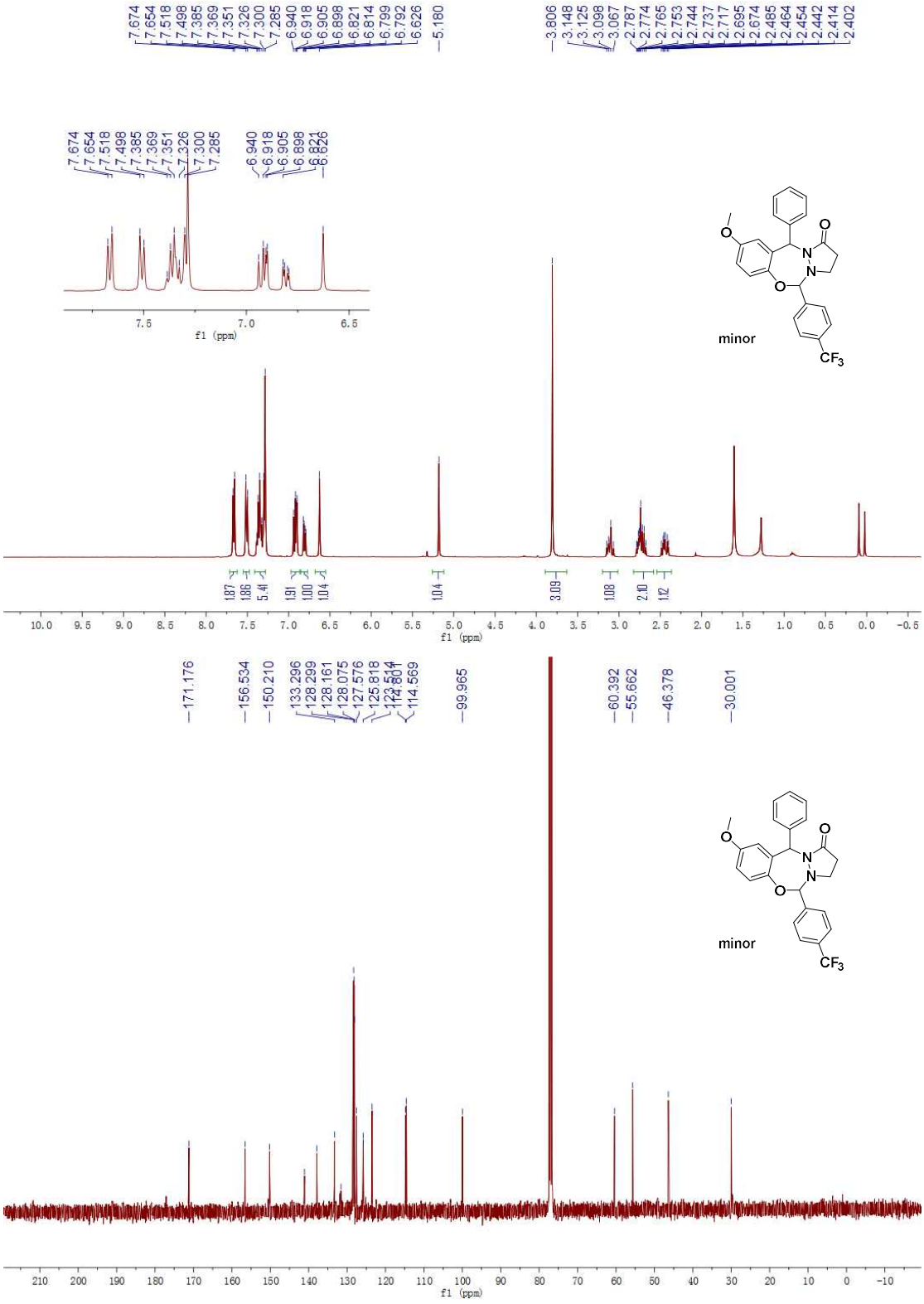

7.35
7.33
7.32
7.30
7.29
7.28
7.26
7.08
7.06
7.03
6.92
6.90
6.87
6.86
6.79
6.78
6.77
6.76
6.59
3.77
3.11
3.09
3.06
3.04
2.78
2.76
2.75
2.74
2.73
2.72
2.70
2.68
2.66
2.64
2.42
2.42
2.41
2.39
2.39
2.38
2.37
2.35
O
N
N
O
F
f1 (ppm)


171.264
164.578
162.106
156.423
150.298
138.041
133.582
133.327
129.439
129.356
128.265
128.180
127.508
115.666
114.767
114.504
100.029
60.354
55.647
46.448
30.020
O
N
N
O
F
f1 (ppm)

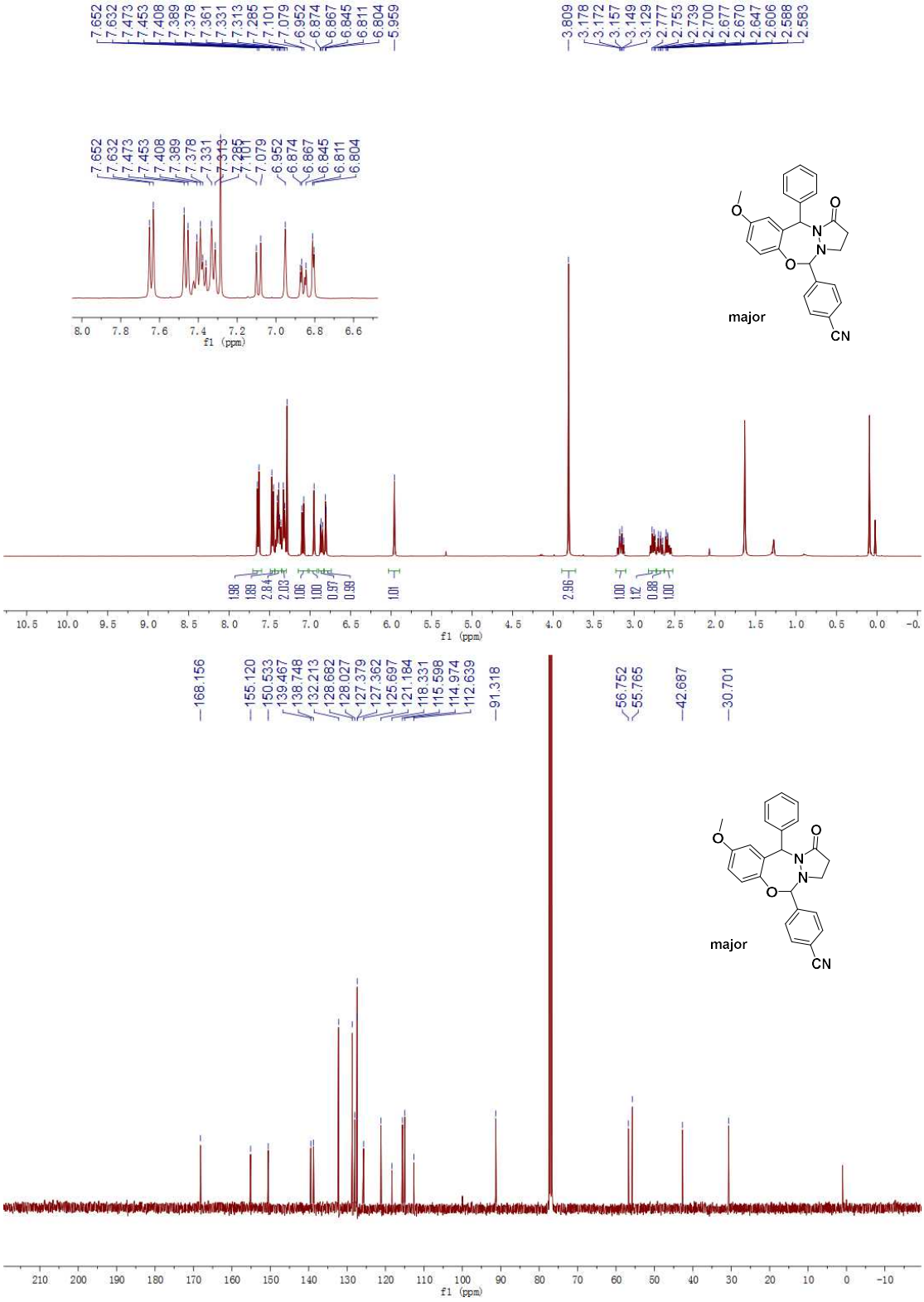
4ah (major diastereomer)



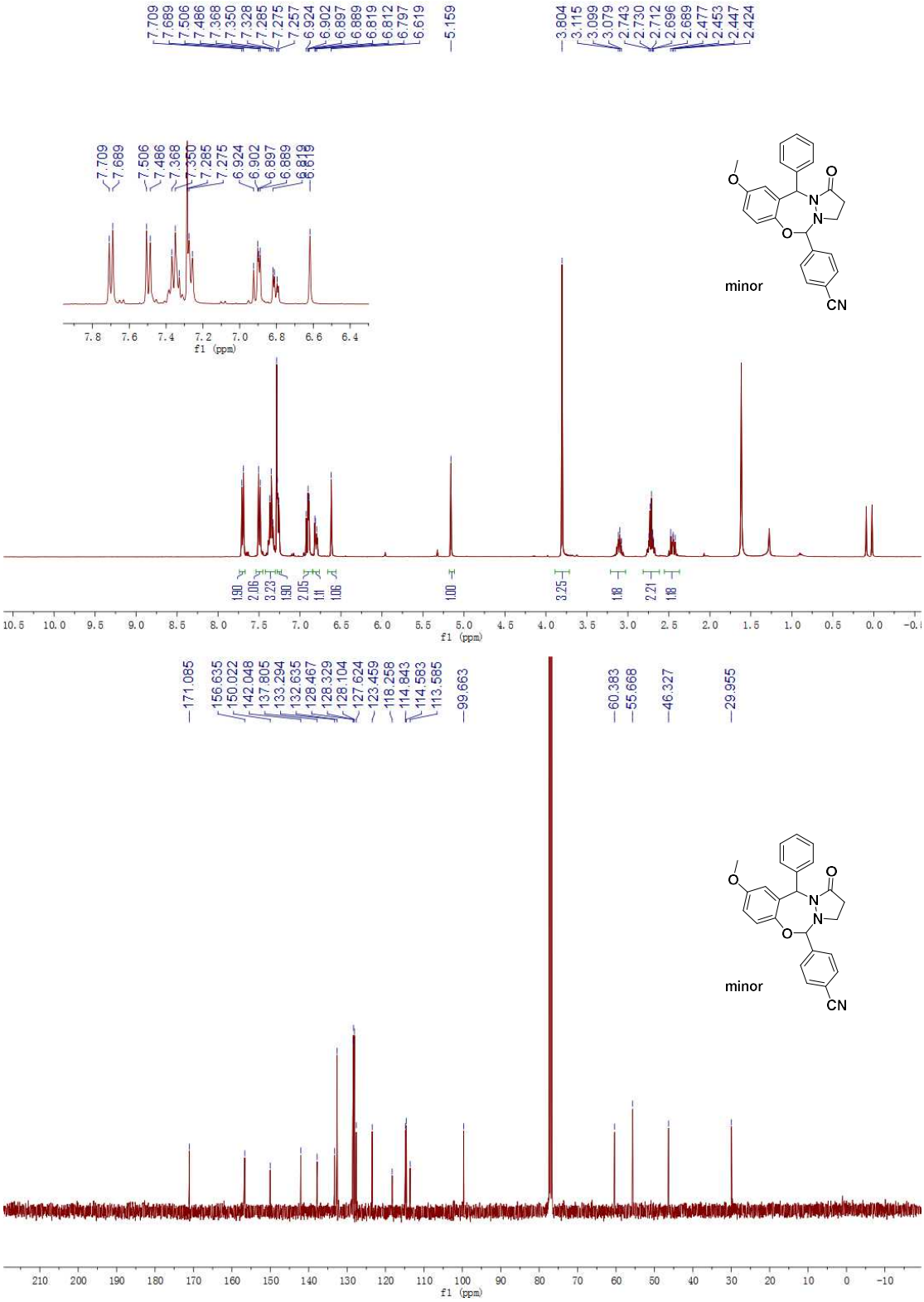
4ah (minor diastereomer)



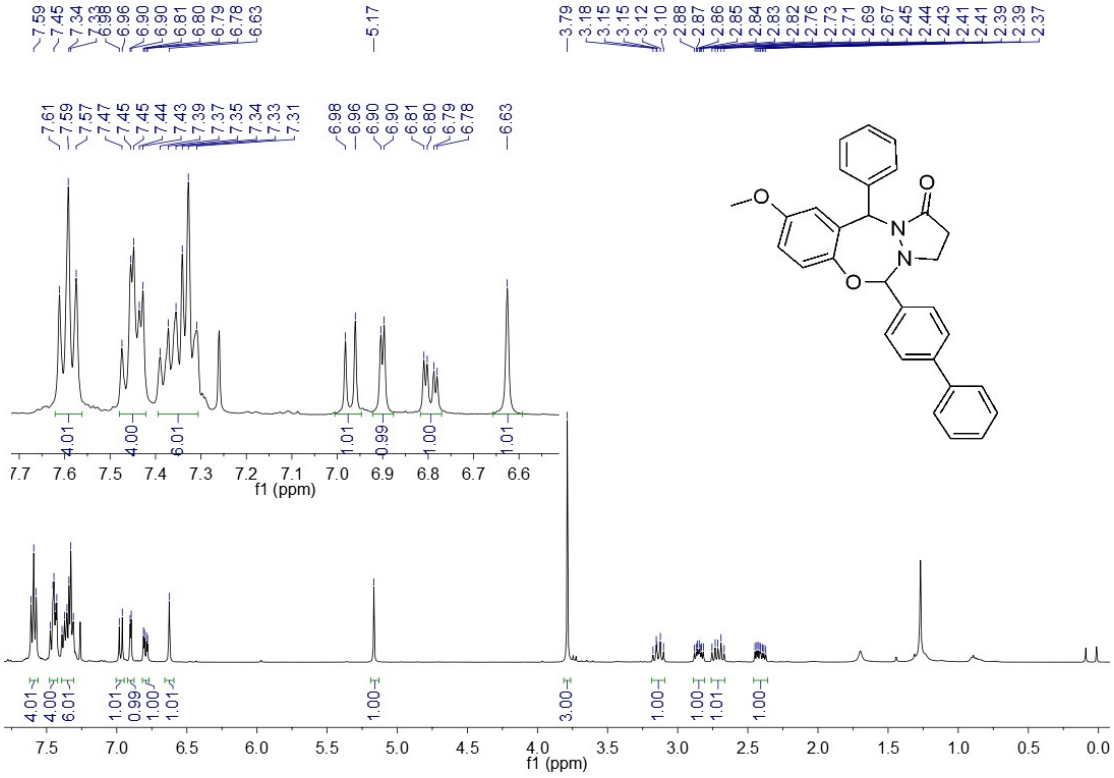
4ai (major diastereomer)

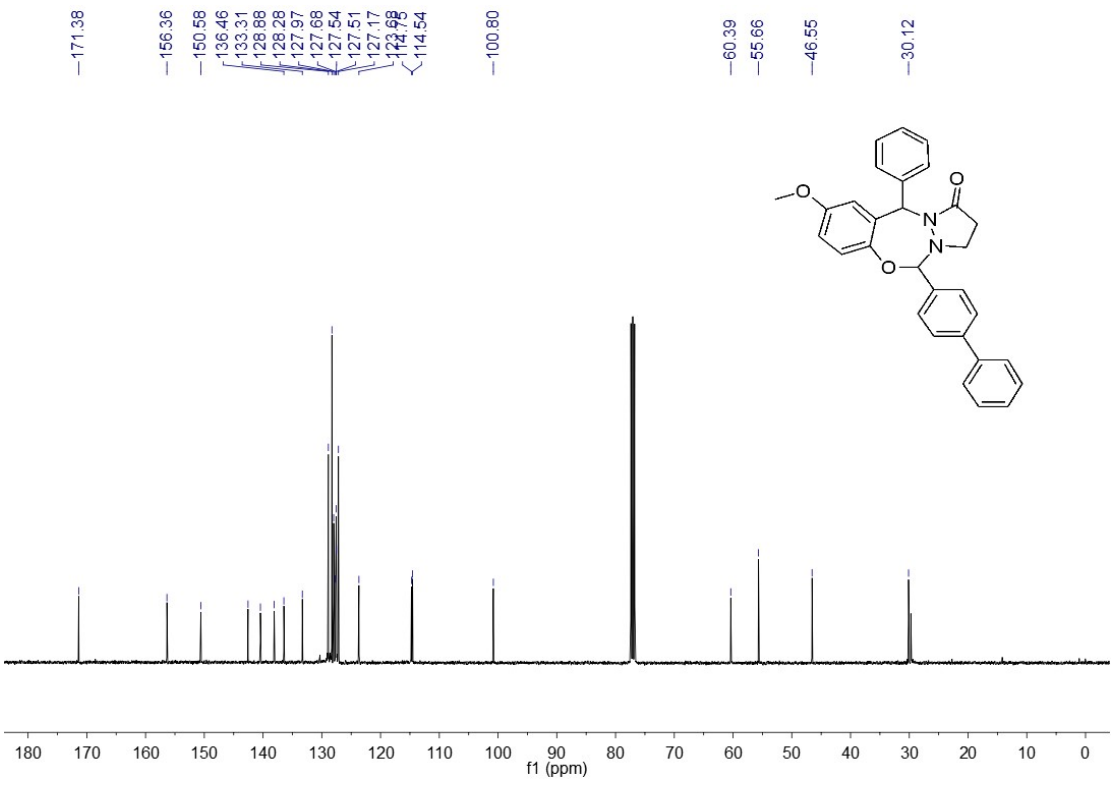


4ai (minor diastereomer)

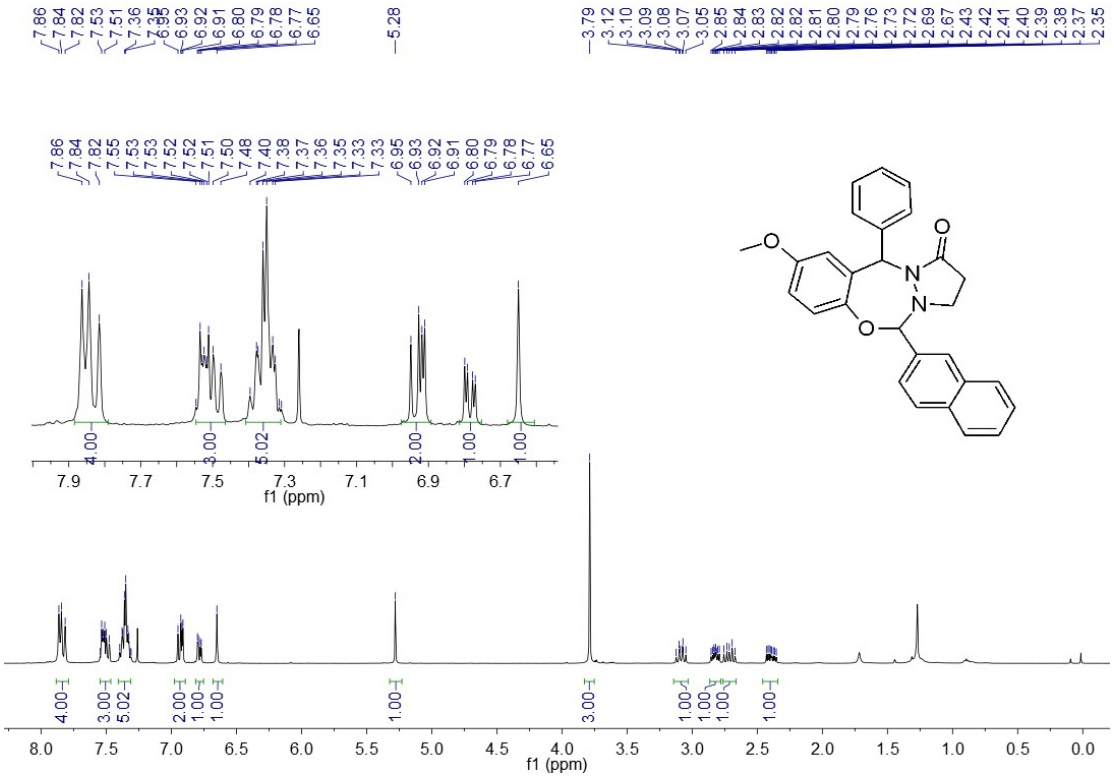


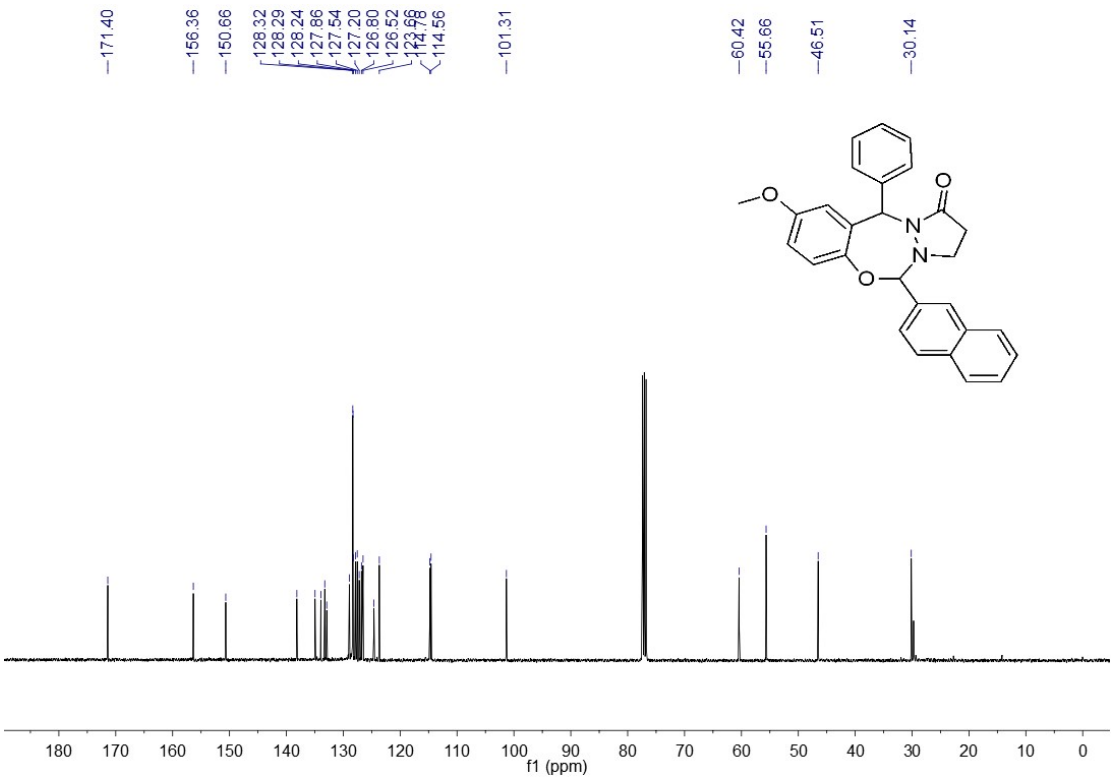
4aj


7.59
7.45
7.34
7.33
6.98
6.96
6.90
6.90
6.81
6.80
6.79
6.78
6.63
5.17
3.79
3.18
3.15
3.15
3.12
3.10
2.88
2.87
2.86
2.85
2.84
2.83
2.82
2.76
2.73
2.71
2.69
2.67
2.45
2.44
2.43
2.41
2.41
2.39
2.39
2.37
4.01
4.00
6.01
1.01
0.99
1.00
1.01
f1 (ppm)
4.01
4.00
6.01
1.01
0.99
1.00
1.01
1.00
3.00
1.00
1.00
1.01
1.00
f1 (ppm)

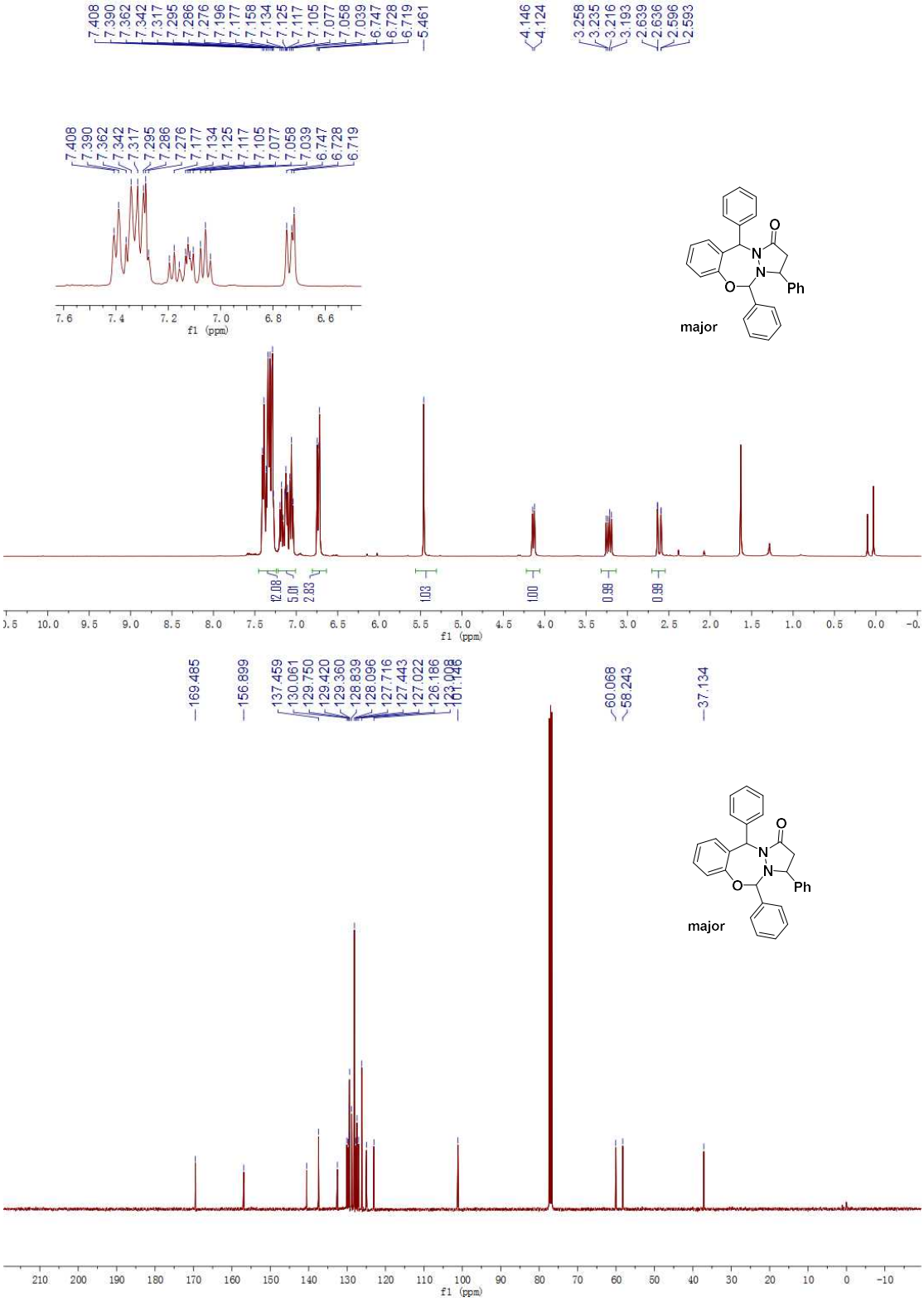

171.38
156.36
150.58
136.46
133.31
128.88
128.28
127.97
127.68
127.54
127.51
127.17
123.68
114.75
114.54
100.80
60.39
55.66
46.55
30.12
f1 (ppm)

4ak

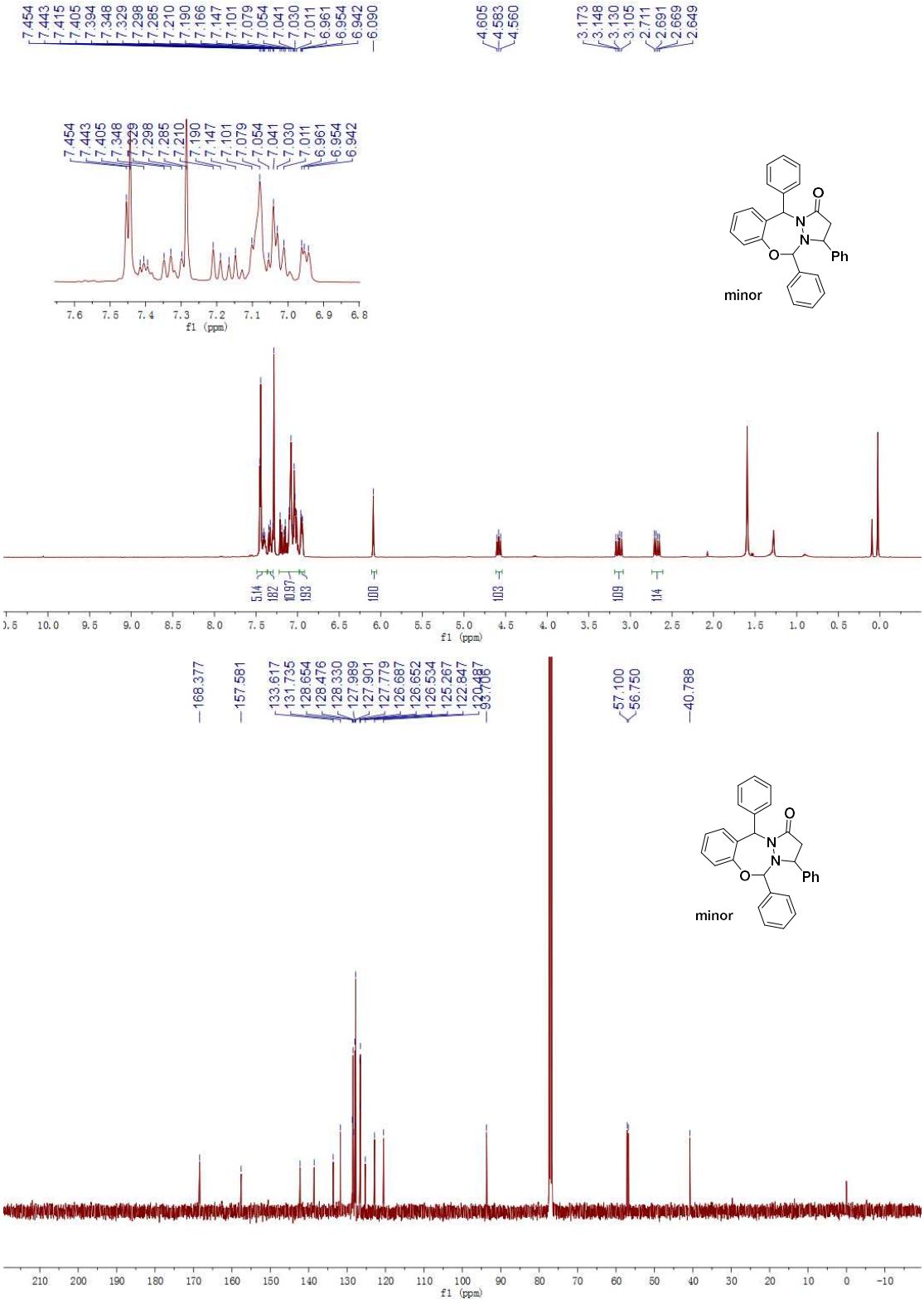

7.86
7.84
7.82
7.53
7.51
7.36
6.93
6.92
6.91
6.80
6.79
6.78
6.77
6.65
5.28
3.79
3.12
3.10
3.09
3.08
3.07
3.05
2.85
2.84
2.83
2.82
2.82
2.81
2.80
2.79
2.76
2.73
2.72
2.69
2.67
2.43
2.42
2.41
2.40
2.39
2.38
2.37
2.35
7.55
7.53
7.52
7.51
7.50
7.48
7.40
7.38
7.37
7.36
7.35
7.33
6.95
6.93
6.92
6.91
6.80
6.79
6.78
6.77
6.65
4.00
3.00
5.02
2.00
1.00
1.00
7.9
7.7
7.5
7.3
7.1
6.9
6.7
f1 (ppm)
O
N
N
O
O
4.00
3.00
5.02
2.00
1.00
1.00
1.00
3.00
1.00
1.00
1.00
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


171.40
156.36
150.66
128.32
128.29
128.24
127.86
127.54
127.20
126.80
126.52
114.78
114.56
101.31
60.42
55.66
46.51
30.14
O
N
N
O
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

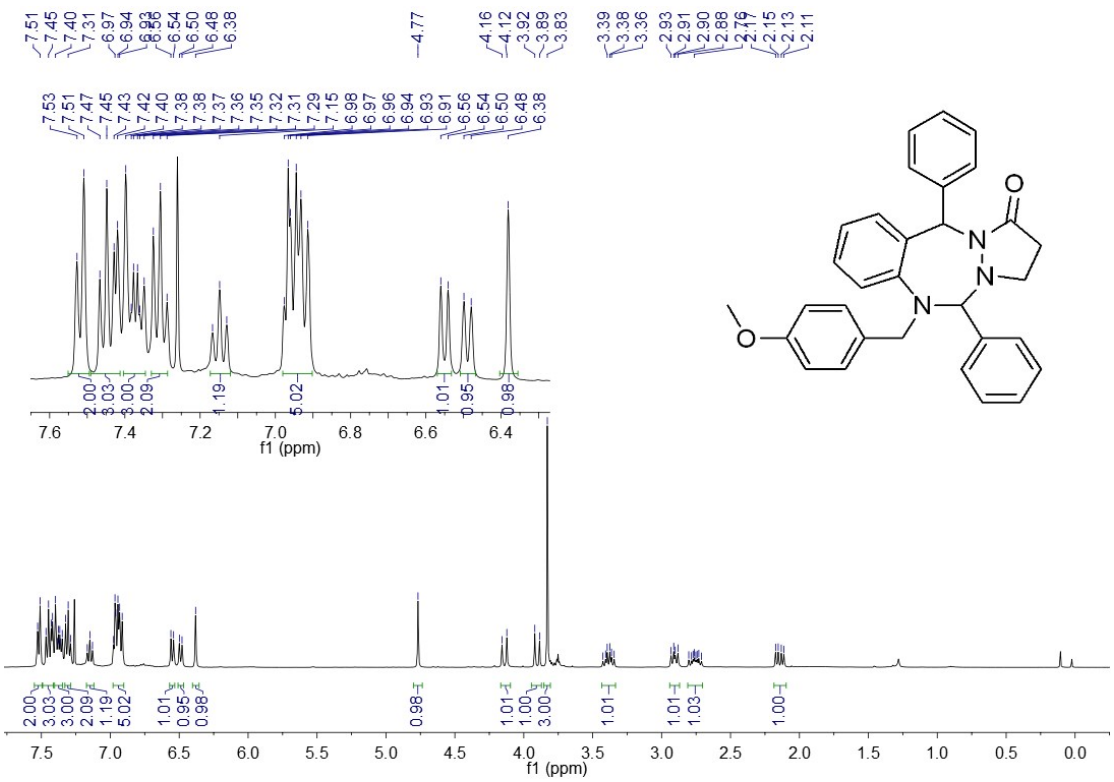
4sl (major diastereomer)

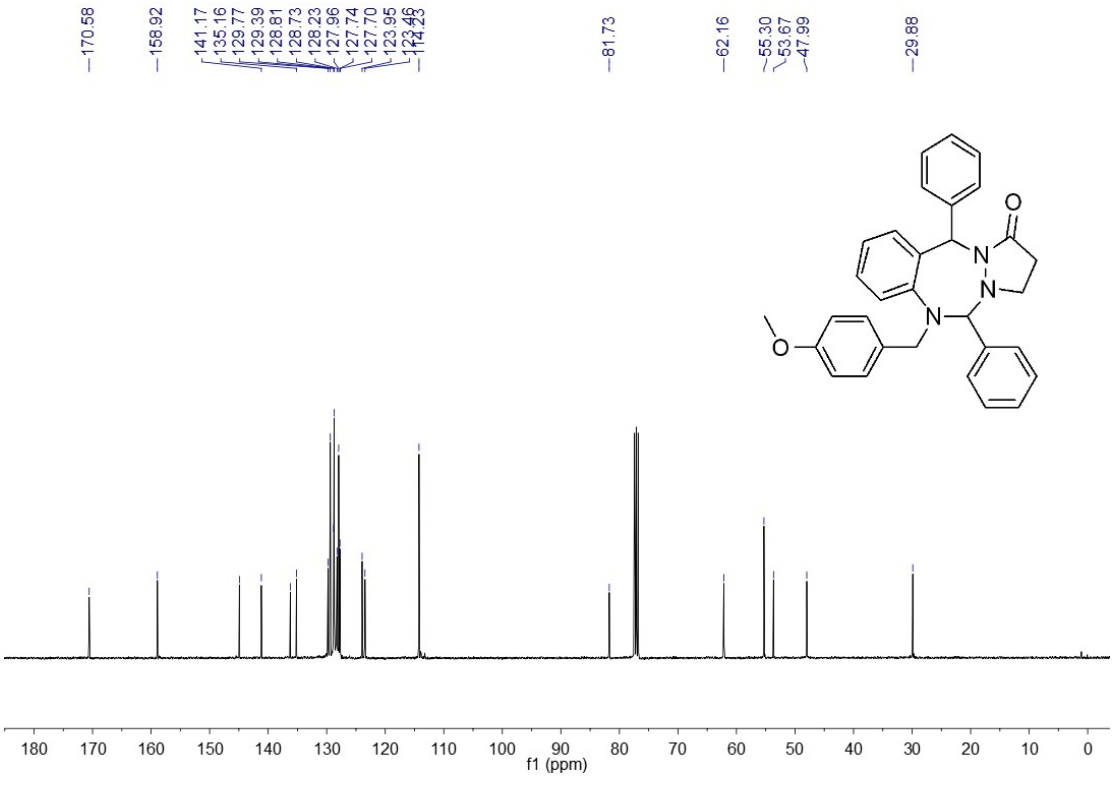


4sl (minor diastereomer)

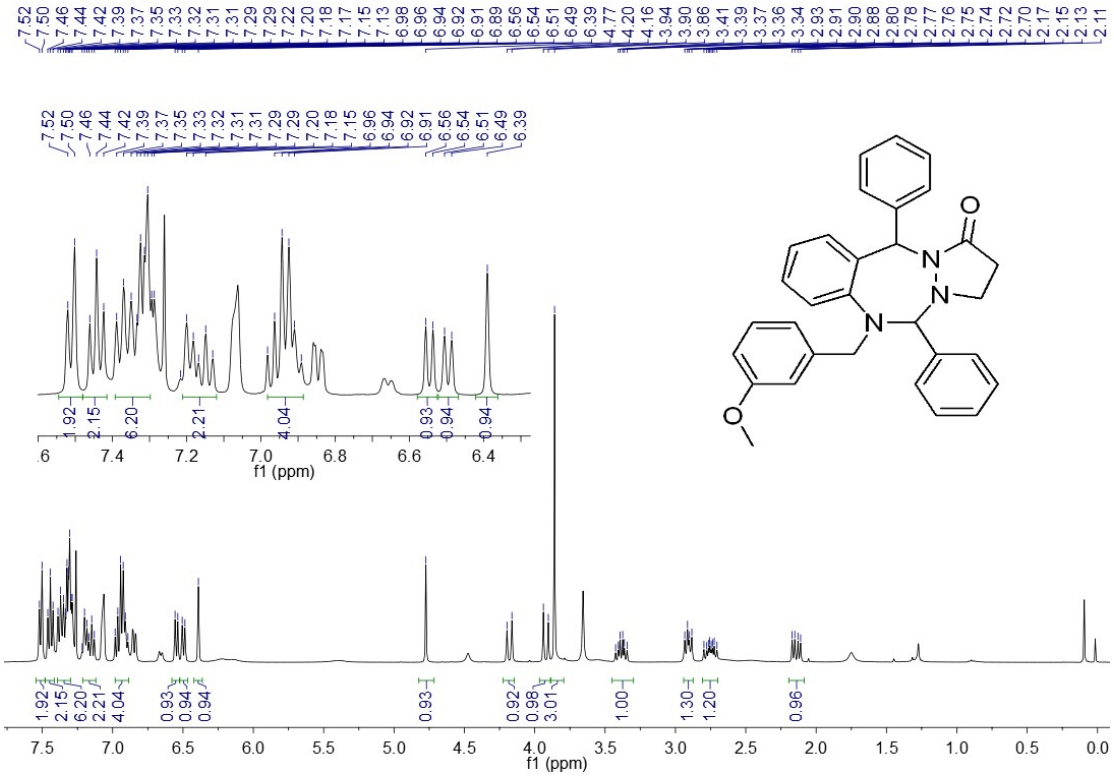


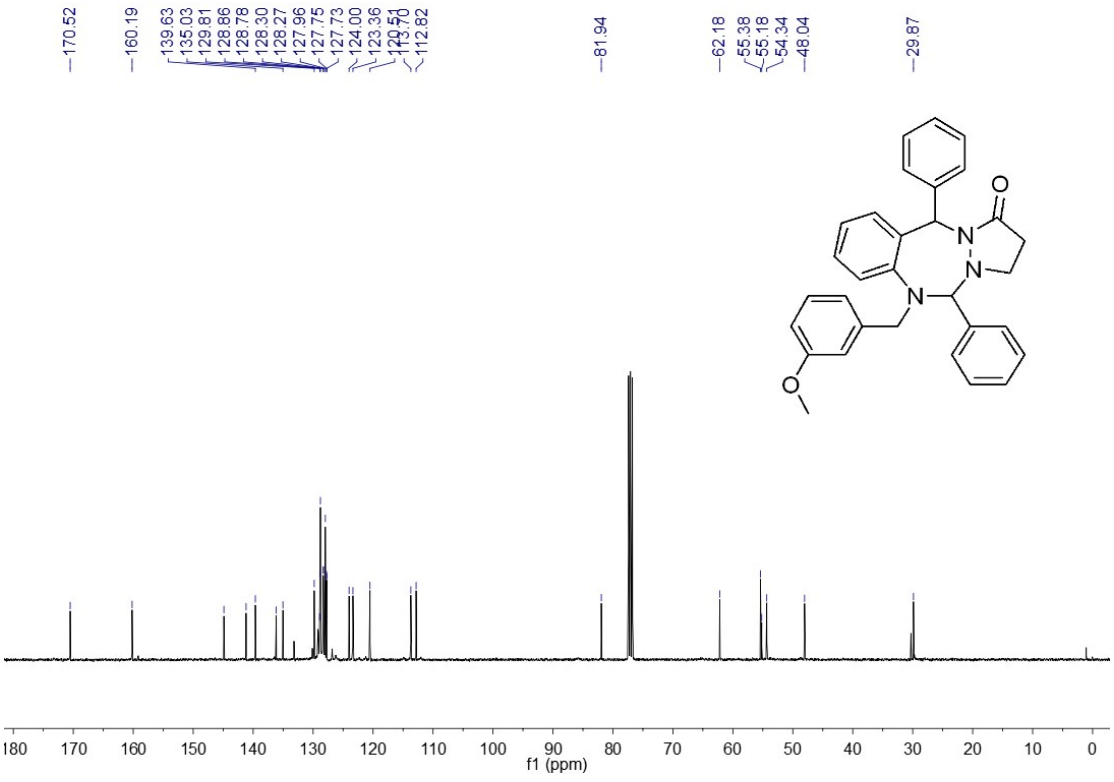
6aa


7.51
7.45
7.40
7.31
6.97
6.94
6.54
6.50
6.48
6.38
4.77
4.16
4.12
3.92
3.89
3.83
3.39
3.38
3.36
2.93
2.91
2.90
2.88
2.15
2.13
2.11
O
N
N
N
O
f1 (ppm)


170.58
158.92
141.17
135.16
129.77
129.39
128.81
128.73
128.23
127.96
127.74
127.70
123.95
81.73
62.16
55.30
53.67
47.99
29.88
O
N
N
N
O
f1 (ppm)

6ba





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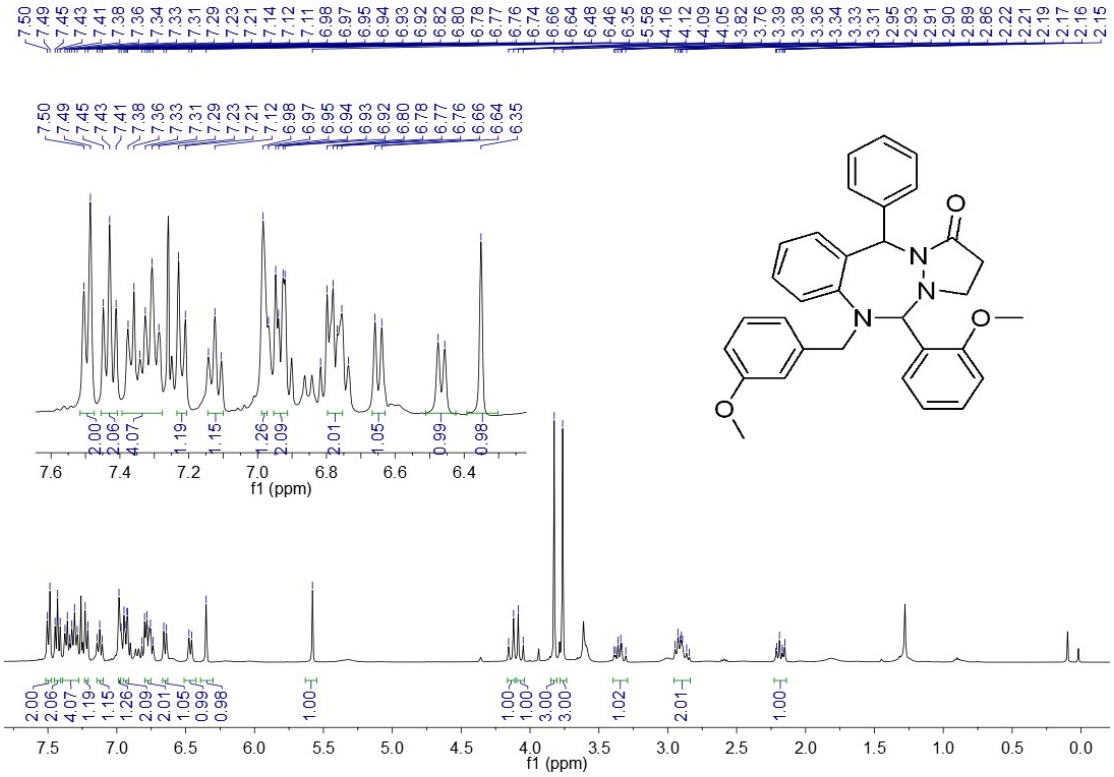

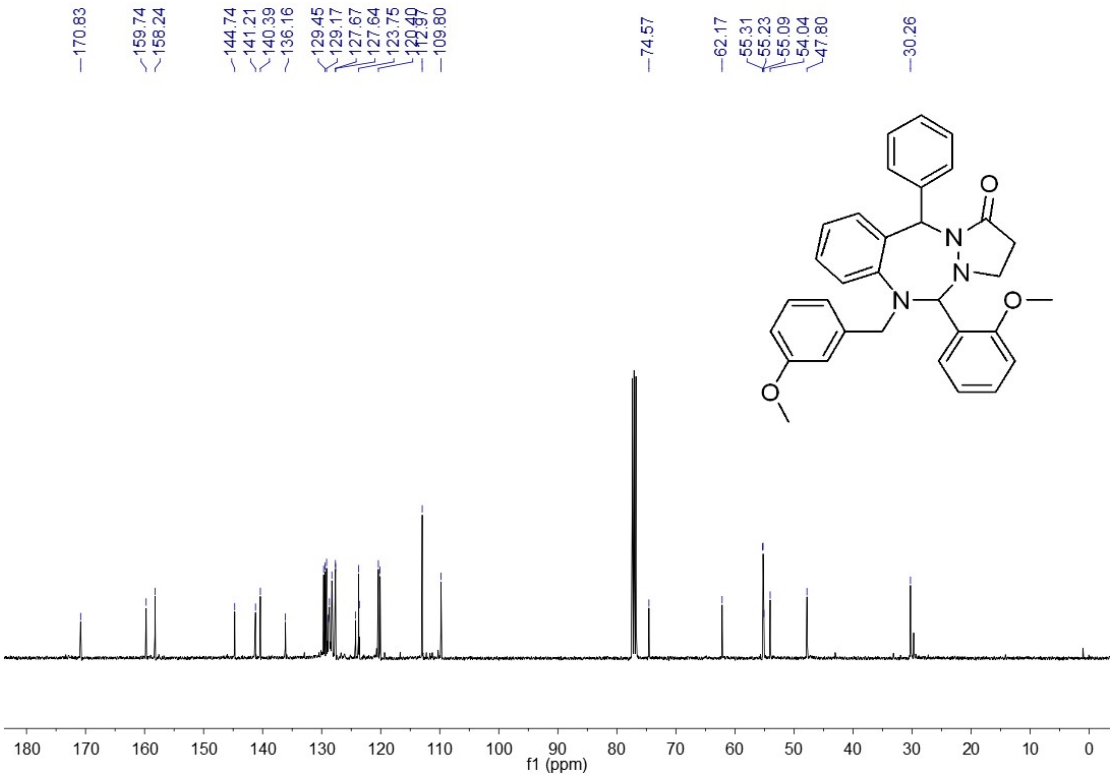

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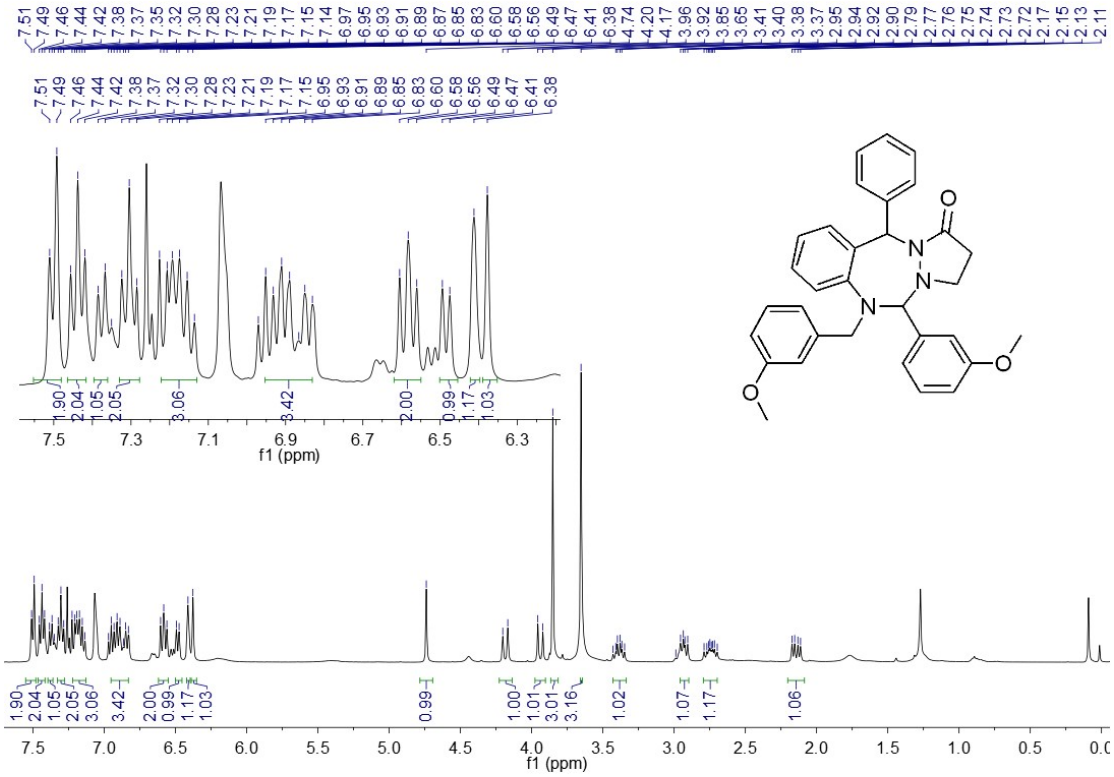
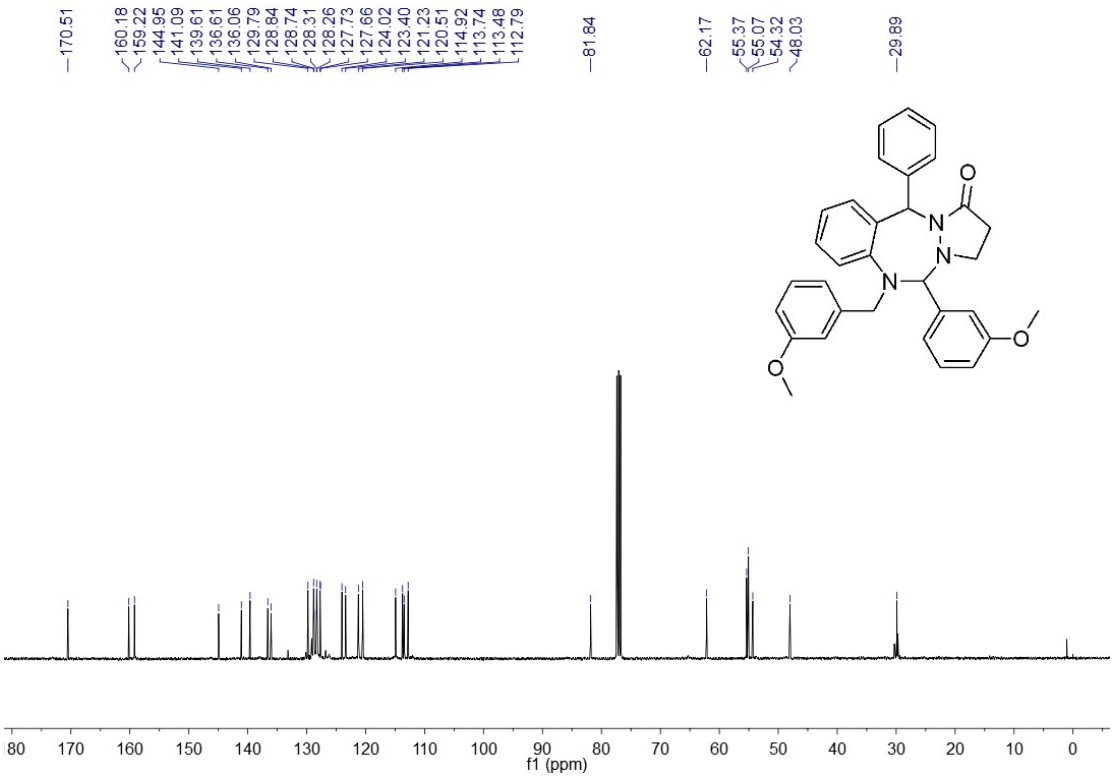
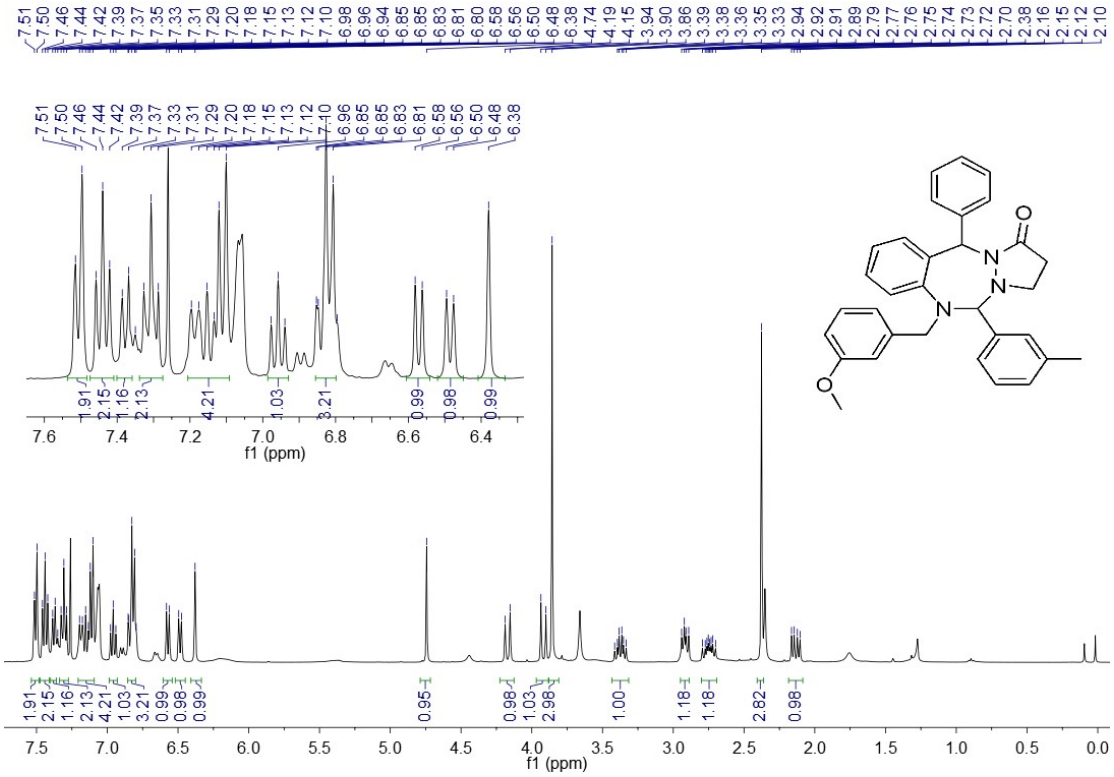
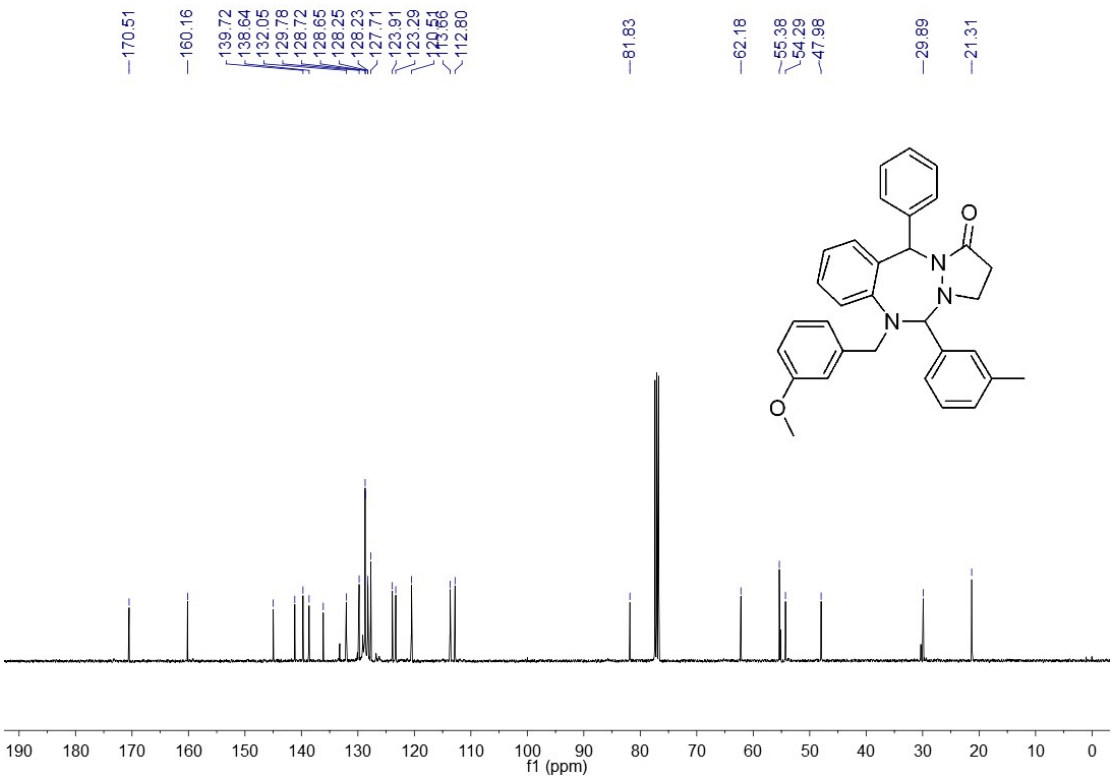


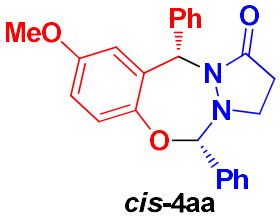


6bf

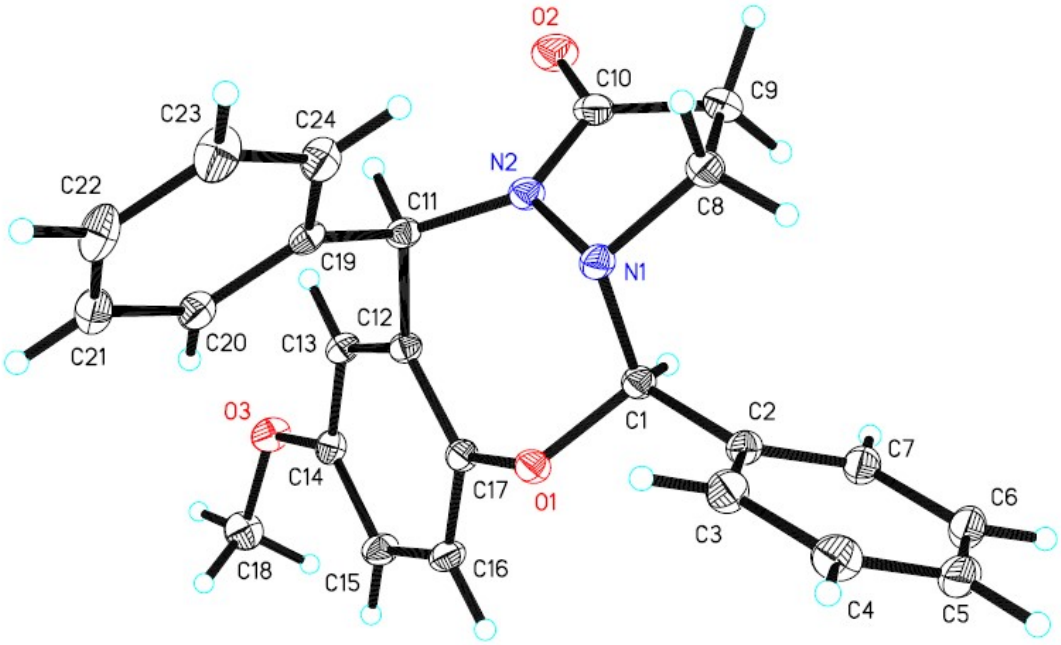

7.51 7.50 7.46 7.44 7.42 7.39 7.37 7.35 7.33 7.31 7.29 7.20 7.18 7.15 7.13 7.12 7.10 6.98 6.96 6.94 6.85 6.85 6.83 6.81 6.80 6.58 6.56 6.50 6.48 6.38 4.74 4.19 4.15 3.94 3.90 3.86 3.39 3.38 3.36 3.35 3.33 2.94 2.92 2.91 2.89 2.79 2.77 2.76 2.75 2.74 2.73 2.72 2.70 2.38 2.16 2.15 2.12 2.10
1.91 2.15 1.16 2.13 4.21 1.03 3.21 0.99 0.98 0.99
f1 (ppm)
0.95 0.98 1.03 2.98 1.00 1.18 1.18 2.82 0.98
f1 (ppm)


170.51 160.16 139.72 138.64 132.05 129.78 128.72 128.65 128.25 128.23 127.71 123.91 123.29 120.51 113.66 112.80 81.83 62.18 55.38 54.29 47.98 29.89 21.31
f1 (ppm)

6. X-ray single crystal data for compounds 4aa and 6aa



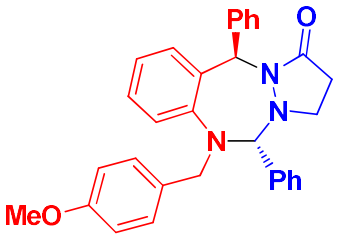
cis-4aa



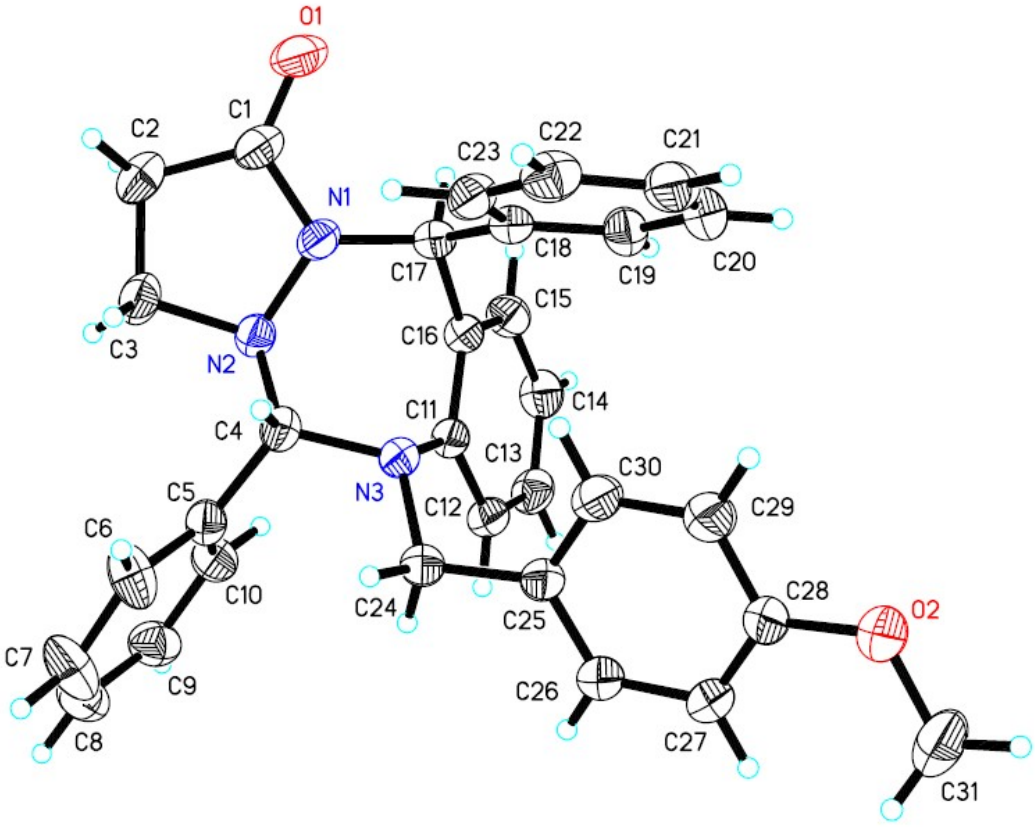
The thermal ellipsoid was drawn at the 30% probability level.

Empirical formula	C24 H22 N2 O3	
Formula weight	386.43	
Temperature	130 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 1 2/c 1	
Unit cell dimensions	a = 25.295(3) Å	α= 90°.
	b = 10.0831(10) Å	β= 125.9700(10)°.
	c = 19.1963(19) Å	γ = 90°.
Volume	3962.4(7) $Å^3$	
Z	8	
Density (calculated)	1.296 Mg/m^3	
Absorption coefficient	0.086 mm^{-1}	
F(000)	1632	
Crystal size	0.25 x 0.2 x 0.15 mm^3	

Theta range for data collection	1.990 to 30.745°.
Index ranges	-36<=h<=36, -12<=k<=14, -27<=l<=27
Reflections collected	19824
Independent reflections	6161 [R(int) = 0.0351]
Completeness to theta = 26.000°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7461 and 0.7007
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6161 / 0 / 263
Goodness-of-fit on F^2	1.009
Final R indices [I>2sigma(I)]	R1 = 0.0441, wR2 = 0.1031
R indices (all data)	R1 = 0.0752, wR2 = 0.1204
Extinction coefficient	n/a
Largest diff. peak and hole	0.296 and -0.288 e.$Å^{-3}$



trans-6aa



The thermal ellipsoid was drawn at the 30% probability level.

Empirical formula	C31 H29 N3 O2	
Formula weight	475.57	
Temperature	296 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 9.6097(5) Å	α= 90°.
	b = 9.4290(6) Å	β= 97.692(3)°.
	c = 27.1720(12) Å	γ = 90°.
Volume	2439.9(2) $Å^3$	
Z	4	
Density (calculated)	1.295 Mg/m^3	
Absorption coefficient	0.645 mm^{-1}	

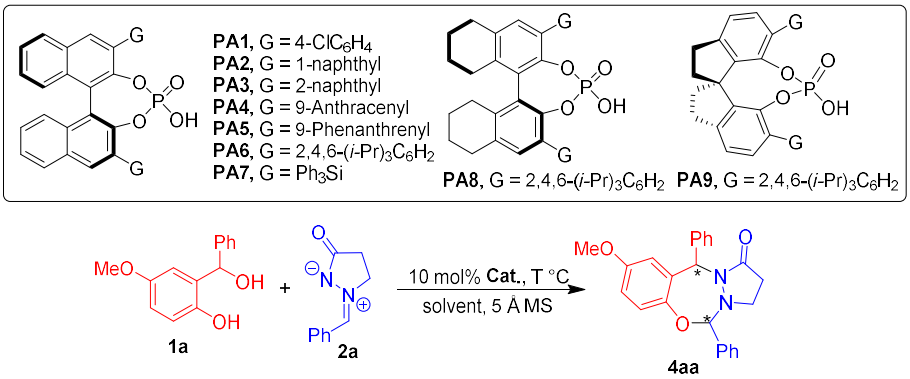
F(000)	1008
Crystal size	0.2 x 0.12 x 0.08 mm^3
Theta range for data collection	4.969 to 69.496°.
Index ranges	-11<=h<=11, -7<=k<=11, -32<=l<=32
Reflections collected	17788
Independent reflections	4470 [R(int) = 0.0405]
Completeness to theta = 67.679°	98.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7532 and 0.5626
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4470 / 12 / 326
Goodness-of-fit on F^2	1.026
Final R indices [I>2sigma(I)]	R1 = 0.0513, wR2 = 0.1378
R indices (all data)	R1 = 0.0649, wR2 = 0.1490
Extinction coefficient	n/a
Largest diff. peak and hole	0.370 and -0.215 e.$Å^{-3}$

7. Investigation on the enantioselectivity of the reaction

We investigated the enantioselectivity of the reaction by using chiral catalysts. As shown in Table 2 below, we initially tried the catalytic asymmetric version of the [4+3] cyclization of **1a** with **2a** in dichloromethane (DCM) at 35 °C for the consideration that higher reaction temperature may lead to racemization of the product **4aa**. A series of BINOL-derived chiral phosphoric acids **PA1-PA7** were screened (entries 1-7), which found that only **PA1**, **PA3**, **PA5-PA6** could catalyze the reaction under this condition. However, they exhibited very low catalytic activity in terms of both the yield and the enantioselectivity. Among them, 2,4,6-triisopropylphenyl-substituted phosphoric acid **PA6** could catalyze the reaction to afford the product **4aa** in 20% ee (entry 6). In order to further improve the enantioselectivity, we changed the backbone of catalyst from BINOL to H_8-BINOL and SPINOL (entries 8-9). However, **PA8** was inferior to **PA6** with regard to the yield (entry 8), and **PA9** failed to catalyze the reaction (entry 9). So, **PA6** was selected as the optimal catalyst for further condition optimization. The evaluation of different class of solvents (entries 6 and 10-16) revealed that only DCM and toluene could facilitate the reaction, and toluene as an arene-type solvent could deliver the reaction in a higher enantioselectivity (24% ee) than DCM (entry 10 vs 6). In order to find more suitable solvent, several arene-type solvents were carefully evaluated (entries 17-22), which disclosed that *o*-xylene could deliver the reaction in the highest enantioselectivity of 28% ee (entry 20). Unfortunately, the yield was still in an extremely low level of 16%. Considering the reaction at 35 °C was very sluggish, we tentatively elevated the reaction temperature to improve the yield (entries 23-24). Increasing the reaction temperature could indeed improve the yield within a shorter reaction time (entries 23-24). However, the enantioselectivity at 50 °C was decreased to 20% ee (entry 23), and only a racemic product **4aa** was generated at 65 °C (entry 24). To balance the reactivity and the enantioselectivity, 50 °C was chosen as a reaction temperature for further condition optimization. Subsequently, the molar ratio was modulated for the aim to increase the yield without the sacrifice of the enantioselectivity (entries 25-30). Although increasing the stoichiometry of **1a** was

helpful to improve the yield (entries 25-27), the enantioselectivity dropped dramatically. On the other hand, increasing the stoichiometry of **2a** could not benefit the yield and the enantioselectivity. At this point, we found that if the yield was improved, the enantioselectivity would be decreased. Because there is an acetal and an aminal group in the structure of product **4aa**, which has a tendency to undergo reversed reaction under acidic conditions, so we decided to investigate whether the product **4aa** could easily racemize or not.

Table 2. Screening of chiral catalysts and condition optimization[a]

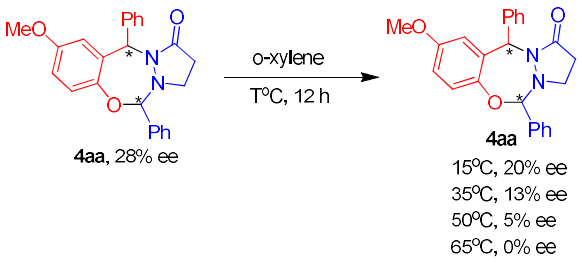


entry	**Cat.**	T (°C)	solvent	reaction time	**1a:2a**	yield (%)	ee (%)
1	**PA1**	35	DCM	36h	1:1.5	23	1
2	**PA2**	35	DCM	36h	1:1.5	N.R.	-
3	**PA3**	35	DCM	36h	1:1.5	17	3
4	**PA4**	35	DCM	36h	1:1.5	N.R.	-
5	**PA5**	35	DCM	36h	1:1.5	11	14
6	**PA6**	35	DCM	36h	1:1.5	15	20
7	**PA7**	35	DCM	36h	1:1.5	N.R.	-
8	**PA8**	35	DCM	36h	1:1.5	13	20
9	**PA9**	35	DCM	36h	1:1.5	N.R.	-
10	**PA6**	35	Toluene	36h	1:1.5	17	24
11	**PA6**	35	EtOAc	36h	1:1.5	N.R.	-
12	**PA6**	35	n-Hexane	36h	1:1.5	N.R.	-
13	**PA6**	35	MeOH	36h	1:1.5	N.R.	-
14	**PA6**	35	CH_3CN	36h	1:1.5	N.R.	-
15	**PA6**	35	Acetone	36h	1:1.5	N.R.	-
16	**PA6**	35	THF	36h	1:1.5	N.R.	-
17	**PA6**	35	PhF	36h	1:1.5	12	22
18	**PA6**	35	PhCl	36h	1:1.5	18	24
19	**PA6**	35	PhBr	36h	1:1.5	10	26
20	**PA6**	35	*o*-xylene	36h	1:1.5	16	28

21	**PA6**	35	*m*-xylene	36h	1:1.5	13	20
22	**PA6**	35	*p*-xylene	36h	1:1.5	13	24
23	**PA6**	50	*o*-xylene	24h	1:1.5	24	20
24	**PA6**	65	*o*-xylene	24h	1:1.5	36	0
25	**PA6**	50	*o*-xylene	24h	2:1	20	16
26	**PA6**	50	*o*-xylene	24h	3:1	27	6
27	**PA6**	50	*o*-xylene	24h	4:1	38	0
28	**PA6**	50	*o*-xylene	24h	1:2	19	20
29	**PA6**	50	*o*-xylene	24h	1:3	23	18
30	**PA6**	50	*o*-xylene	24h	1:4	21	18

[a]Unless indicated otherwise, the reaction was carried out in 0.1 mmol scale in the presence of 10 mol% **cat.** in solvent (1 mL) with 5 Å MS (100 mg). [b]Isolated yield and only one diastereomer was observed in all cases. [c]The ee value was determined by HPLC. N.R. = No reaction.

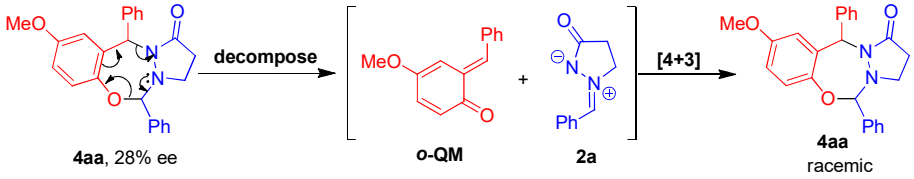
As illustrated in Scheme 1, we performed a series experiments to investigate whether the product **4aa** could easily racemize or not. Compound **4aa** with 28% ee was dissolved in *o*-xylene and stirred for 12 h at different temperatures ranging from 15ºC to 65ºC. It was found that different degree of racemization occurred at these temperatures. With the increasing of the temperature, the enantioselectivity of compound **4aa** dropped greatly. For example, at 35ºC, the enantioselectivity of compound **4aa** was decreased to 13% ee. At 65ºC, compound **4aa** was totally racemized into a racemic compound. So, it is not surprising that in our previous attempts (Table 2), we found it was very difficult to control the enantioselectivity of the [4+3] cyclization.



Scheme 1. Investigation on the racemization of product **4aa**

In order to explain the phenomenon of racemization, we suggested a possible pathway (Scheme 2). Due to the existence of an acetal and an aminal group in the structure of compound **4aa**, this compound underwent a reversed [4+3] cyclization to decompose into o-QM and azomethine imine **2a**, which rapidly performed a [4+3]

cyclization again to regenerate compound **4aa**. In this process, the chemical bonds around the two chiral centers broke and regenerated, which resulted in the racemization of compound **4aa**.



Scheme 2. Suggested pathway of racemization