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Supporting Information

Mild Copper (II)-Catalyzed Synthesis of Multisubstituted 1,2,4-Triazoles from Amidines with Nitriles via N−N/C−N Coupling

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Content

Typical Experimental Procedure

General information

All reactions were carried out in flame-dried reaction vessels. Reaction temperatures are reported as the temperature of the bath surrounding the reaction vessel. The commercially available chemicals were used without further purification. All the N-arylamidines used were synthesized according to reference.[1] All new compounds were fully characterized. Melting points were determined on a melting point apparatus in open capillaries and are uncorrected. 1H and ^{13}C NMR spectra were recorded on a 300 MHz or a 500 MHz NMR spectrometers using $CDCl_3$ or DMSO-d_6 as solvent and TMS as an internal standard. High resolution mass spectral (HRMS) data were obtained with an ionization mode of ESI or APCI on Agilent 6200 LC/MS TOF.

General procedures for 1,3,5-trisubstituted-1H-1,2,4-triazoles

N-arylamidines (1 mmol), nitrile (1.5-2 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.1 mmol), Na_2CO_3 (2 mmol) and 1,10-phenanthroline (0.1 mmol) were stirred in toluene (2 mL) under reflux in air for 24 h in pre-heated oil bath. After cooling to room temperature, the reaction was extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtrated, concentrated and purified by column chromatography on silica gel (300-400 mesh) to give **3aa-3da** with petroleum ether/ethyl acetate as the eluent.

General procedures for 3,5-disubstituted-1H-1,2,4-triazoles.

Benzamidine hydrochloride (1 mmol), nitrile (1.5 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.03 mmol), Na_2CO_3 (3 mmol) were stirred in toluene (2 mL) under reflux in air for 24 h in pre-heated oil bath. After cooling to room temperature, the reaction was extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtrated, concentrated and purified by column chromatography on silica gel (300-400 mesh) to give **5aa-5da** with petroleum ether/ethyl acetate as the eluent.

Characterization data for the products

1,3,5-triphenyl-1,2,4-triazole(3aa)[2]. Red-brown solid, mp 100-103 °C, Lit.m.p: 105-106 °C, Yield 75 %; ^{1}H NMR (300MHz, $CDCl_3$) δ 8.26-8.23 (m, 2H), 7.57-7.33 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 155.1, 138.7, 131.1, 130.4, 129.8, 129.4, 129.2, 129.0, 128.4, 127.0, 125.8.

3-(4-chlorophenyl)-1,5-diphenyl-1,2,4-triazole(3ab). Light red solid, mp 98-101 °C, Yield 76 %; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 6.9 Hz, 2H), 7.45-7.33 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.38 , 155.3, 138.5, 135.7, 130.5, 129.8, 129.6, 129.3, 129.2, 129.0, 128.3, 125.8; $C_{20}H_{15}N_3Cl$ ($[M + H]^+$) 332.0954, found 332.0949.

1,5-diphenyl-3-(4-(trifluoromethyl)phenyl)-1,2,4-triazole(3ac). White solid, mp 125-127 °C, Yield 82%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 6.6 Hz, 2H), 7.44-7.34(m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 155.5, 138.4, 134.5, 131.4(q, *J* = 32.3 Hz), 130.6, 129.9, 129.5, 129.3, 129.1, 128.0, 127.2, 125.9 (q, *J* = 3.8 Hz), 124.6(q, *J* = 270.4 Hz). HRMS (ESI) calcd for $C_{21}H_{15}N_3F_3$ ($[M + H]^+$) 366.1218, found 366.1213;

3-(4-methoxyphenyl)-1,5-diphenyl-1,2,4-triazole(3ad). Red-brown solid, mp 128-130 °C, Yield 56 %; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 6.9 Hz, 2H), 7.40-7.31 (m, 8H), 6.98 (d, *J* = 8.4 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 161.1, 155.0, 138.8, 130.4, 129.8, 129.4, 129.1, 129.0, 128.5, 128.5, 125.8, 114.4, 55.7; HRMS (ESI) calcd for $C_{21}H_{18}N_3O$ ($[M + H]^+$) 328.1450, found 328.1447.

1,5-diphenyl-3-(p-tolyl)-1,2,4-triazole(3ae). White solid, mp131-132°C, Yield 73 %; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.00(d, *J* = 8.1 Hz, 2H), 7.49-7.37(m, 10H), 7.30(d, *J* = 7.8 Hz,

2H), 2.34(s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.6, 155.3, 139.9, 138.8, 131.0, 130.4, 130.3, 130.0, 129.6, 129.5, 128.6, 128.5, 126.8, 126.6, 21.8; HRMS (ESI) calcd for $C_{21}H_{18}N_3$ ([M + H]$^+$) 312.1501, found 312.1495.

1,5-diphenyl-3-(o-tolyl)-1,2,4-triazole(3af). White solid, mp 87-89 °C, Yield 52 %; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d，*J* = 3 Hz，1H)，7.57 (d，*J* = 6 Hz，2H)，7.43-7.31 (m, 11H), 2.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 154.1, 138.7, 137.7, 131.5, 130.3, 130.3, 130.0, 129.7, 129.4, 129.4, 129.1, 129.0, 128.5, 126.2, 125.7, 22.3; HRMS (ESI) calcd for $C_{21}H_{18}N_3$ ([M + H]$^+$) 312.1501, found 312.1493.

3-(2-chlorophenyl)-1,5-diphenyl-1,2,4-triazole(3ag). White solid, mp 107-109 °C, Yield 56 %; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03-8.01 (m, 1H), 7.58-7.50 (m, 3H), 7.43-7.34 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 154.5, 138.5, 133.4, 132.0, 131.1, 130.6, 130.5, 130.3, 129.8, 129.4, 129.3, 129.0, 128.2, 127.1, 125.8. HRMS (ESI) calcd for $C_{20}H_{15}N_3Cl$ ([M + H]$^+$) 332.0954, found 332.0949.

3-(1,5-diphenyl-1H-1,2,4-triazol-3-yl)pyridine(3ah). White solid, mp109-110°C, Yield 81%; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.27(s, 1H), 8.65(d, *J* = 4.5 Hz, 1H), 8.41(d, *J* = 8.1 Hz, 1H), 7.57-7.38(m, 11H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 159.1, 155.3, 150.9, 147.5, 138.2, 133.8, 130.8, 130.0, 129.9, 129.2, 129.1, 127.8, 126.8, 126.3, 124.5; HRMS (ESI) calcd for $C_{19}H_{15}N_4$([M + H]$^+$) 298.1296, found 298.1291.

1,3-diphenyl-5-(p-tolyl)-1,2,4-triazole(3ba). White solid, mp 84-86 °C, Yield 72%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, *J*=8.7Hz, 2H), 7.50-7.44 (m,10H), 7.16 (d, *J* = 7.8 Hz, 2H), 2.36(s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 155.3, 140.5, 138.7, 131.1, 129.7, 129.7, 129.6, 129.2, 129.1, 128.9, 126.9, 125.8, 125.4, 21.8. HRMS (ESI) calcd for $C_{21}H_{18}N_3$ ([M + H]$^+$)

312.1501, found 312.1495.

3-(4-chlorophenyl)-1-phenyl-5-(p-tolyl)-1,2,4-triazole(3bb). Pink solid, mp 119-121 °C, Yield 82 %; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.4Hz, 2H), 7.44-7.42 (m, 9H), 7.17 (d, *J* = 7.8Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3, 155.4, 140.7, 138.7, 135.6, 129.8, 129.7, 129.2, 129.2, 129.2, 128.3, 125.8, 125.3, 21.82; $C_{21}H_{18}N_3Cl$ ($[M + H]^+$) 346.1111, found 346.1106.

1-phenyl-5-(p-tolyl)-3-(4-(trifluoromethyl)phenyl)-1,2,4-triazole(3bc). White solid, mp 95-97 °C, Yield 85 %; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 7.8, 2H), 7.71 (d, *J* = 7.8Hz, 2H), 7.44 (w, 7H), 7.17 (d, *J* = 7.5Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8, 138.6, 138.2, 134.7, 134.3, 131.4(q, *J* = 32.2 Hz), 130.1, 129.9, 129.8, 129.7, 129.7, 127.2, 126.4, 125.9 (q, *J* = 3.8 Hz), 124.6(q, *J* = 270.5 Hz), 21.7; HRMS (ESI) calcd for $C_{22}H_{16}N_3F_3$ ($[M + H]^+$) 380.1375, found 380.1369.

1-phenyl-3,5-di-p-tolyl-1,2,4-triazole(3be). Gray solid, mp 100-103 °C, Yield 69 %;; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.1 Hz, 2H), 7.45-7.42 (m, 7H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 2.40 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 155.1, 140.5, 139.7, 138.9, 130.6, 129.7, 129.7, 129.7, 129.3, 129.1, 128.5, 127.0, 125.8, 125.6; HRMS (ESI) calcd for $C_{22}H_{20}N_3$ ($[M + H]^+$) 326.1657, found 326.1652.

5-(4-chlorophenyl)-3-phenyl-1-(p-tolyl)-1H-1,2,4-triazole(3ca). Red-brown solid, mp 107-109 °C, Yield 65 %; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24-8.21(m, 2H), 7.53-7.44(m, 5H), 7.35-7.27(m, 5H), 7.14-7.11(d, *J* = 7.5 Hz, 1H), 2.40(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.4, 152.1, 138.4, 136.5, 134.6, 129, 128.7, 128.4, 128.0, 127.7, 127.6, 127.3, 127.1, 125.1, 125.0, 124.5, 123.9, 121.1, 19.4; HRMS (ESI) calcd for $C_{21}H_{18}N_3Cl$ ($[M + H]^+$) 346.1111, found

346.1106;

1-(4-chlorophenyl)-3-phenyl-5-(p-tolyl)-1H-1,2,4-triazole(3da). White solid, mp 142-144 °C, Yield 70 %; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23-8.21 (m, 2H), 7.49-7.35 (m, 9H), 7.18 (d, *J* = 7.8 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5, 153.4, 138.9, 135.4, 132.9, 129.2, 128.7, 128.4, 128.0, 127.9, 127.4, 127.1, 125.1, 125.0, 123.4, 121.1, 20.0; HRMS (ESI) calcd for $C_{21}H_{18}N_3Cl$ ($[M + H]^+$) 346.1111, found 346.1106.

3,5-diphenyl-1H-1,2,4-triazole(5aa)[3]. White solid, mp 188-190 °C, Lit.m.p: 190-191 °C, Yield 89 %; ^{1}H NMR (300 MHz, DMSO-d_6) δ 14.56 (s, 1H), 8.10 (b, 4H), 7.58-7.48 (m, 6H); ^{13}CNMR (75MHz, DMSO-d_6) δ 162.5, 155.9, 132.1, 131.0, 129.9, 129.5, 128.1, 127.0, 126.7.

3-(4-chlorophenyl)-5-phenyl-1H-1,2,4-triazole(5ab). White solid, mp 232-234 °C, Yield 91 %; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.57(s, 1H), 8.21-8.15 (m, 3H), 7.85 (t, J = 7.5 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.60-7.51 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.6, 161.6, 156.1, 155.0, 135.8, 134.6, 131.2, 130.0, 129.7, 128.8, 128.5, 128.1, 127.1, 126.9; HRMS (ESI) calcd for$C_{14}H_{11}N_3Cl$ ($[M + H]^+$) 256.0641, found 256.0636.

5-phenyl-3-(4-(trifluoromethyl)phenyl)-1H-1,2,4-triazole(5ac)[3]. White solid, mp 218-219 °C, Lit.m.p: 214-216 °C, Yield 96 %; ^{1}H NMR (300 MHz, DMSO-d_6) δ 14.83-14.76 (m, 1H), 8.32 (d, *J* = 7.8 Hz, 2H), 8.11 (d, *J* = 6.9 Hz, 2H), 7.99-7.86 (m, 2H), 7.58-7.49 (m, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.2, 156.3, 135.9, 131.1, 129.7 (d, *J* = 27.1 Hz), 127.8, 127.6, 127.2, 126.9 (d, *J* = 16.5 Hz), 126.4, 123.2.

3-(4-methoxyphenyl)-5-phenyl-1H-1,2,4-triazole(5ad). White solid, mp 164-165 °C, Yield 83 %; ^{1}H NMR (300 MHz, DMSO-d_6) δ 14.48(s, 1H), 8.17-8.08(m, 4H), 7.56-7.54(m, 3H), 7.15-7.12(m, 2H), 3.85(s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.2, 161.5, 161.2, 160.7, 156.3,

155.8, 132.3, 131.1, 130.9, 129.9, 129.7, 129.5, 128.6, 128.2, 127.8, 127.2, 126.7, 126.4, 115.3, 114.8, 56.1, 55.9; HRMS (ESI) calcd for $C_{15}H_{14}N_3O$ ($[M + H]^+$) 252.1137, found 252.1127.

5-phenyl-3-(p-tolyl)-1H-1,2,4-triazole(5ae)[4a]. White solid, mp 189-190 °C, Yield 90 %; ^{1}H NMR (300 MHz, DMSO-d_6) δ 14.48-14.44 (m, 1H), 8.11-7.96 (m, 2H), 7.98-7.96 (m, 2H), 7.57-7.29 (m, 5H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 162.5, 162.3, 155.9, 155.7, 140.8, 139.2, 132.2, 131.0, 130.5, 130.1, 129.9, 129.8, 129.5, 128.1, 126.9, 126.7, 125.3.

5-phenyl-3-(o-tolyl)-1H-1,2,4-triazole(5af)[4b](1:1). White solid, mp 165-166°C, Yield 78 %; ^{1}H NMR (500 MHz, DMSO-d_6) δ 14.56 (s, 1H), 14.25 (s, 1H), 8.08 (s, 4H), 8.00 (d, J = 5.5 Hz, 1H), 7.69 (d, J = 6.5 Hz, 1H), 7.58-7.33 (m, 12H), 2.64 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.3, 162.1, 156.2, 155.0, 137.5, 137.2, 132.0, 131.0, 130.7, 129.9, 129.6, 128.2, 126.8, 22.6, 21.4.

3-(2-chlorophenyl)-5-phenyl-1H-1,2,4-triazole(5ag)(1:1). White solid, mp 166-167 °C, Yield 71 %; ^{1}H NMR (500 MHz, DMSO-d_6) δ 14.69 (s, 1H), 14.40 (s, 1H), 8.39-7.44 (m, 18H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.2, 161.1, 155.4, 153.6, 132.5, 132.4, 132.3, 132.0, 131.2, 130.0, 129.6, 128.4, 128.0, 127.0, 126.8;HRMS (ESI) calcd for $C_{14}H_{11}N_3Cl$ ($[M + H]^+$) 256.0641, found 256.0632.

3-cyclohexyl-5phenyl-1H-1,2,4-triazole(5ah). White solid, mp 119-120°C, Yield 78 %; ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.60(s, 1H), 7.96(d, J = 6.3 Hz, 2H), 7.41-7.35 (m, 3H), 2.82-2.75(m, 1H), 1.95(d, J = 11.7 Hz, 2H), 1.77-1.64(m, 3H), 1.58-1.46(m, 2H), 1.41-1.16(m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.2, 161.3, 132.6, 129.8, 129.4, 126.5, 36.2, 31.8, 26.3, 26.2; HRMS (ESI) calcd for $C_{14}H_{18}N_3$ ($[M + H]^+$) 228.1501, found 228.1495.

5-(4-bromophenyl)-3-phenyl-1H-1,2,4-triazole(5ba)[4c]. White solid, mp 260-262 °C, Yield 88 %;

^{1}H NMR (500 MHz, DMSO-d_6) δ14.63 (s, 1H), 8.08-8.04 (m, 4H), 7.81-7.70 (m, 2H), 7.60-7.44 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.6, 156.2, 132.7, 130.9, 129.8, 128.8, 126.9, 123.5;

5-(4-bromophenyl)-3-(4-(trifluoromethyl)phenyl)-1H-1,2,4-triazole(5bc). White solid, mp 223-235 °C, Yield 94 %; ^{1}H NMR (500 MHz, DMSO-d_6) δ 14.89-14.82 (m, 1H), 8.30-8.29 (m, 2H), 8.05-8.03 (m, 2H), 7.96-7.71 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.9, 161.3, 155.4, 154.8, 135.7, 133.0, 132.6, 131.6, 131.1, 129.0, 127.7, 127.3, 127.0, 126.6, 124.7, 124.0; HRMS (ESI) calcd for $C_{15}H_{10}N_3F_3Br$ ($[M + H]^+$) 368.0010, found 367.9999.

5-(4-bromophenyl)-3-(4-methoxyphenyl)-1H-1,2,4-triazole(5bd). White solid, mp 230-232 °C, Yield 75 %; ^{1}H NMR (300 MHz, DMSO-d_6) δ 14.43 (s, 1H), 8.03-8.01 (m, 4H), 7.72 (b, 2H), 7.12 (b, 2H), 3.84(s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.6, 156.0, 132.5, 131.4, 128.7, 123.0, 120.2, 115.3, 56.1; HRMS (ESI) calcd for $C_{15}H_{13}N_3OBr$ ($[M + H]^+$) 330.0242, found 330.0234.

3-phenyl-5-(p-tolyl)-1H-1,2,4-triazole(5ca). White solid, mp 180-181 °C, Yield 93 %; ^{1}H NMR (500 MHz, DMSO-d_6) δ14.48-14.44 (m, 1H), 8.11-7.97 (m, 4H), 7.58-7.30 (m, 5H), 2.39-2.37(m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.3, 155.9, 140.5, 130.3, 129.7, 126.3, 21.8;HRMS (ESI) calcd for $C_{15}H_{14}N_3$ ($[M + H]^+$) 236.1188, found 236.1184.

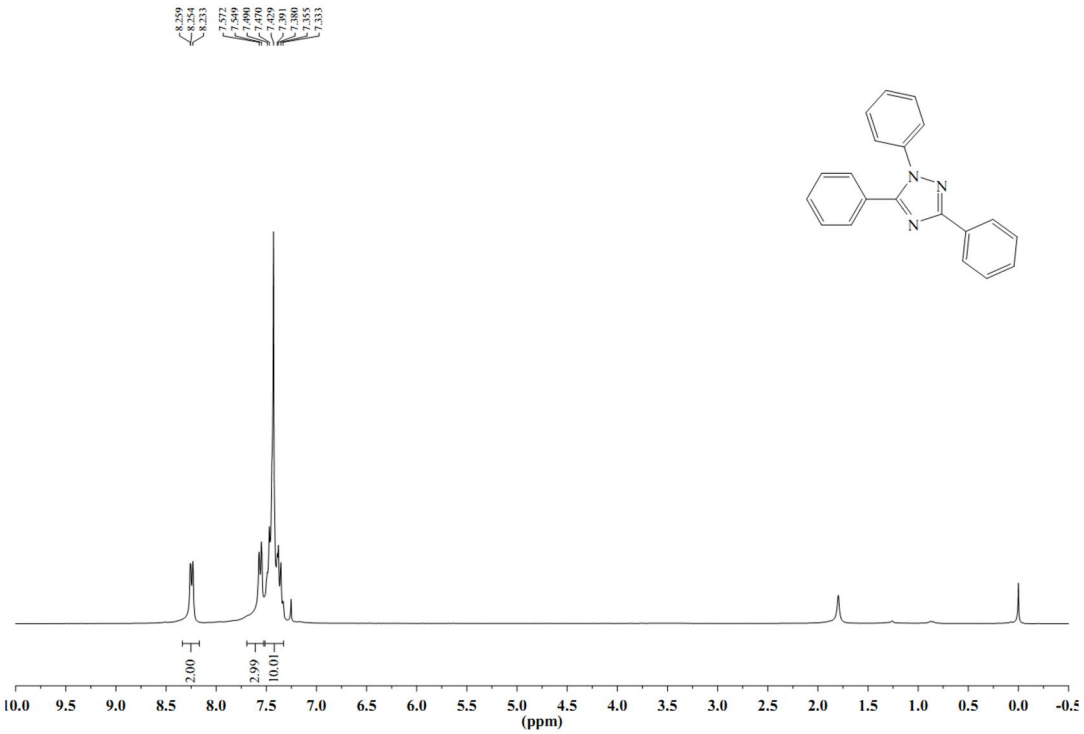
3-(4-chlorophenyl)-5-(p-tolyl)-1H-1,2,4-triazole(5cb). White solid, mp 272-274 °C, Yield 92 %; ^{1}H NMR (500 MHz, DMSO-d_6) δ 14.52 (s, 1H), 8.10-8.09 (d, J = 4.8 Hz, 2H), 7.98-7.97 (d, J = 4.5 Hz, 2H), 7.60-7.58(m, 2H), 7.36-7.35(m, 2H), 2.38(s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 162.5, 156.0, 140.6, 139.3, 132.4, 130.3, 129.6, 126.9, 125.5, 21.7; HRMS (APCI) calcd for $C_{15}H_{13}N_3Cl$ ($[M + H]^+$) 270.0798, found 270.0788.

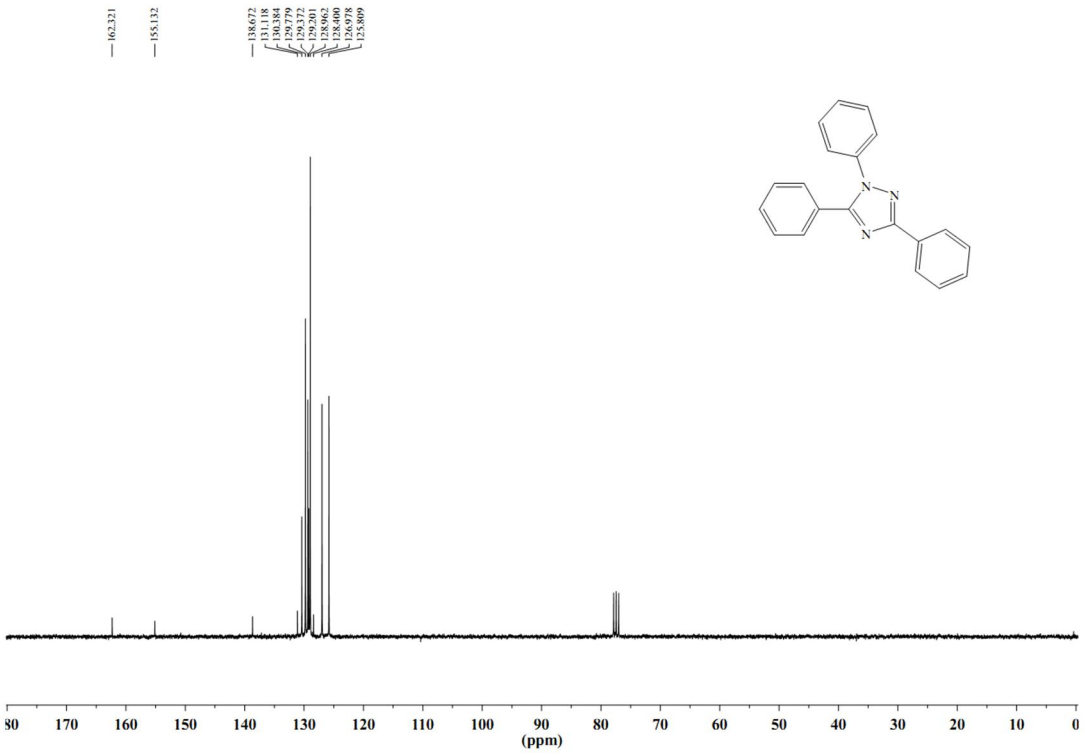
3-(4-methoxyphenyl)-5-(p-tolyl)-1H-1,2,4-triazole(5cd). White solid, mp 216-218 °C, Yield 90 %; ^{1}H NMR (500 MHz, DMSO-d_6) δ 14.25 (s, 1H), 7.99-7.93(m, 4H), 7.30(b, 2H), 7.06(b, 2H),

3.80(s, 3H), 2.34(s, 3H); ^{3}C NMR (125 MHz, DMSO-d_6) δ 162.3, 161.3, 155.7, 139.2, 130.2, 128.4, 126.8, 115.1, 56.1, 21.8; HRMS (ESI) calcd for $C_{16}H_{16}N_3O$ ($[M + H]^+$) 266.1293, found 266.1286;

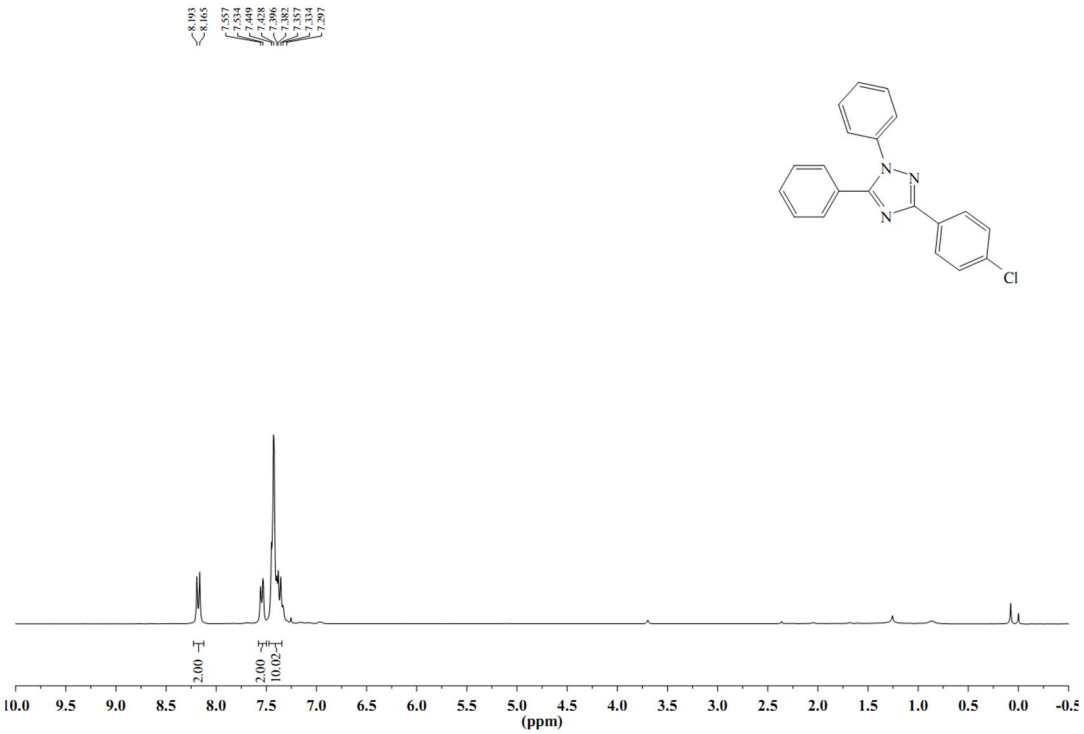
5-methyl-3-phenyl-1H-1,2,4-triazole(5da)[3]. White solid, mp 154-155 °C, Lit.m.p: 163-165 °C, Yield 45 %; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.99-7.97 (m, 2H), 7.40-7.38 (m, 3H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.0, 156.3, 130.1, 130.0, 129.2, 126.8, 12.9.

^{1}H and ^{13}C NMR spectra of the products.





3aa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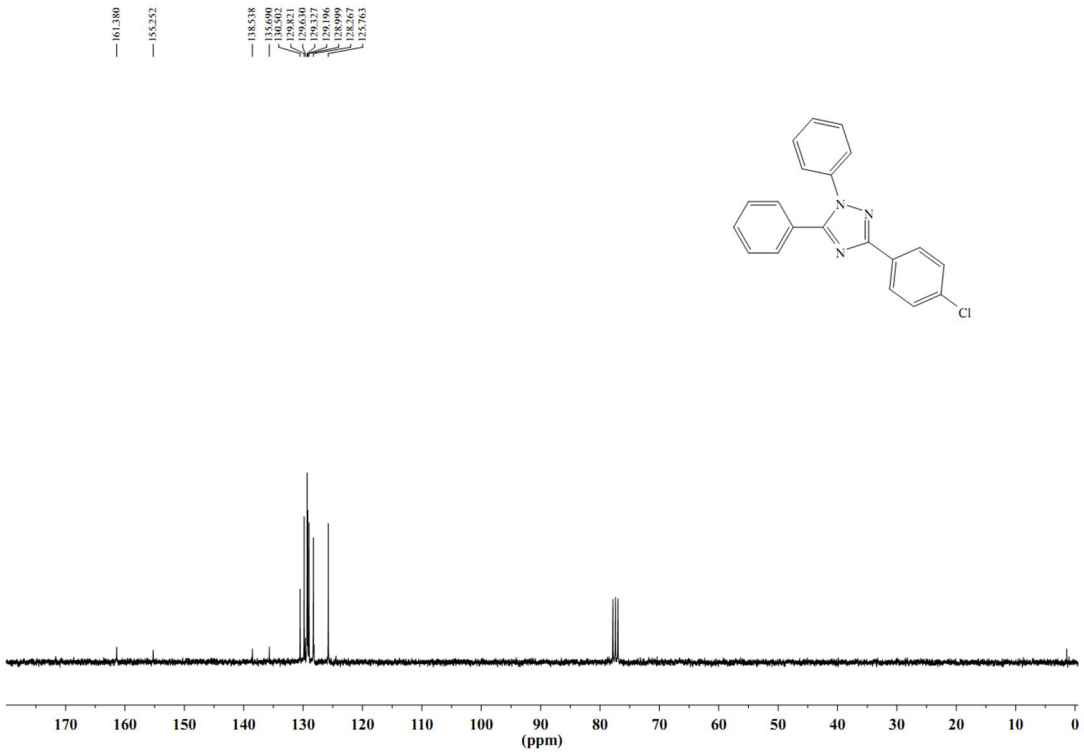
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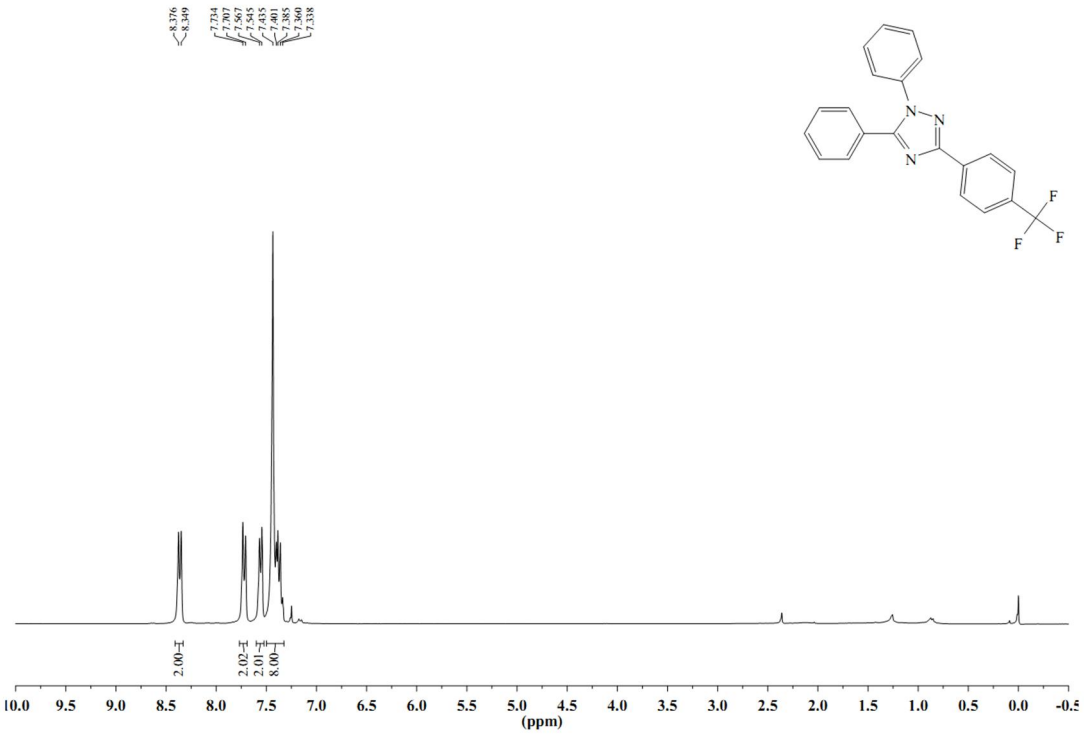
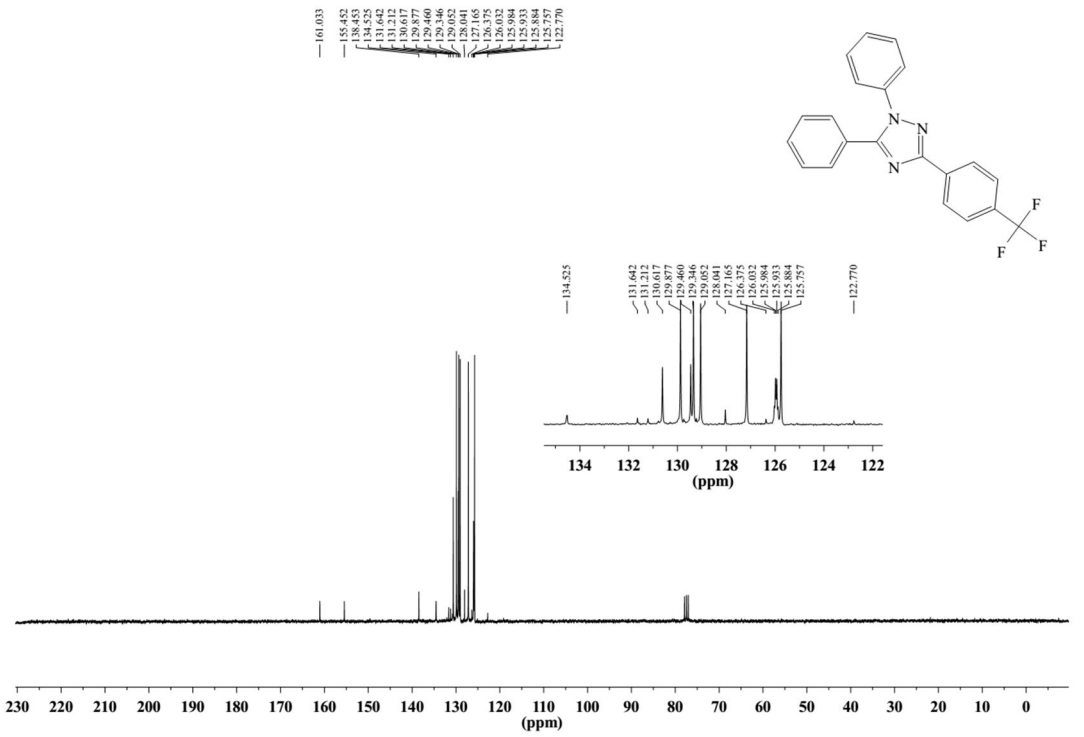
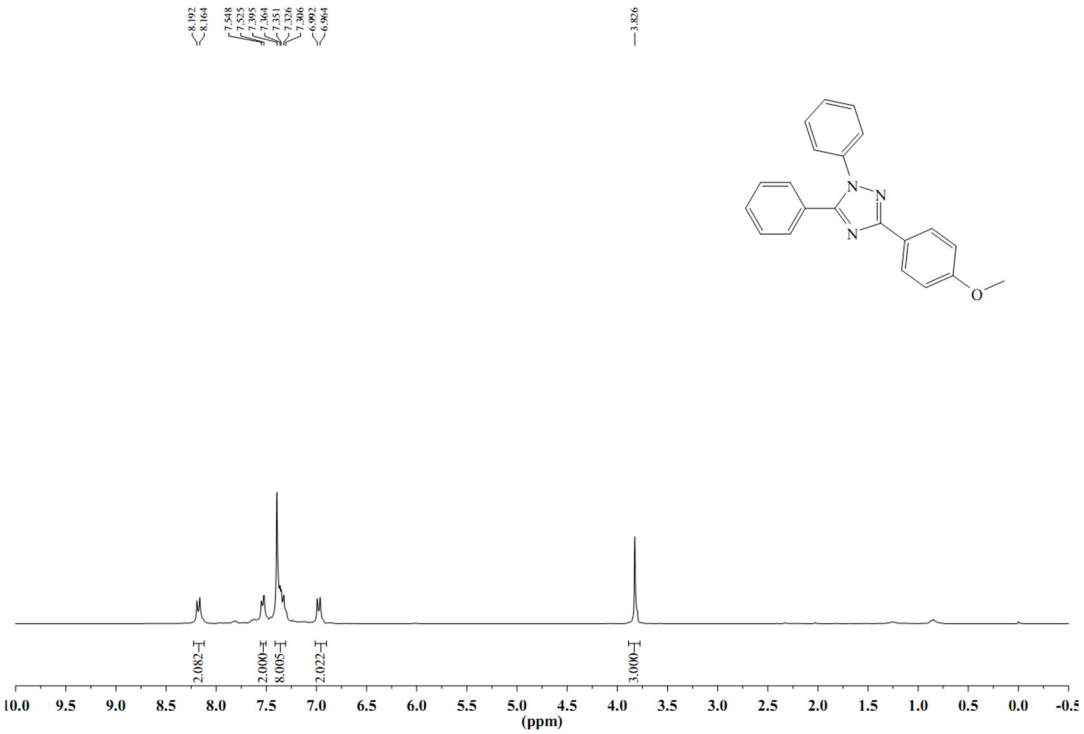
(ppm)

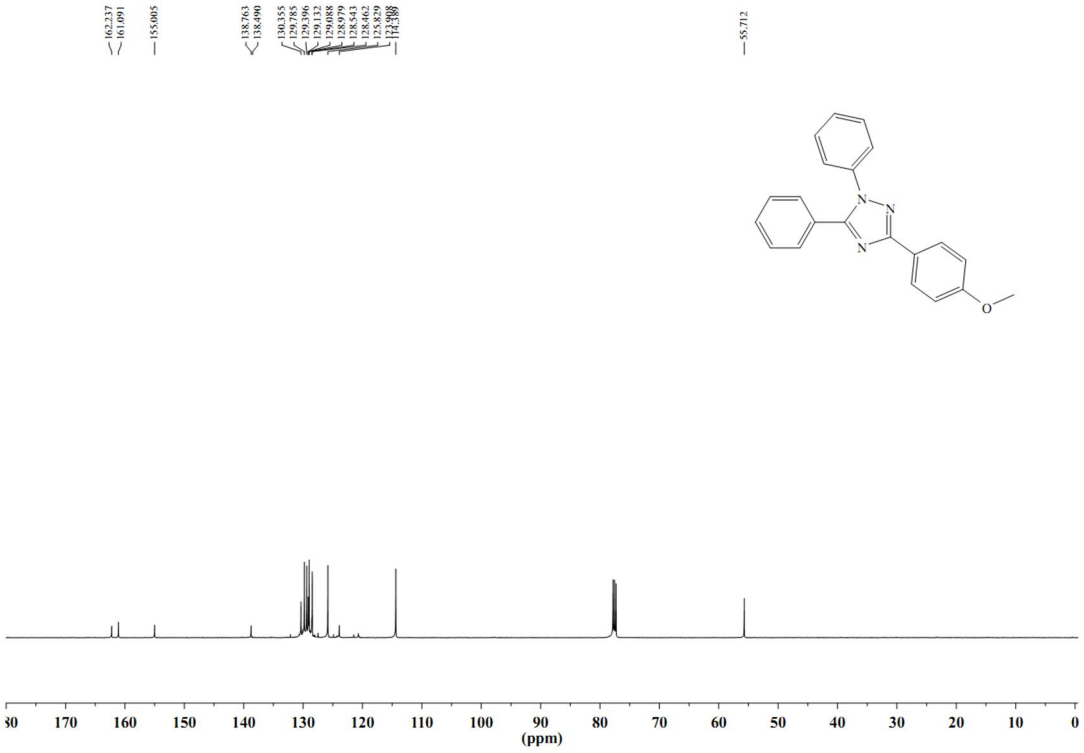
3ab


8.376
8.349
7.734
7.707
7.567
7.545
7.435
7.401
7.385
7.360
7.338
2.00
2.02
2.01
8.00
(ppm)

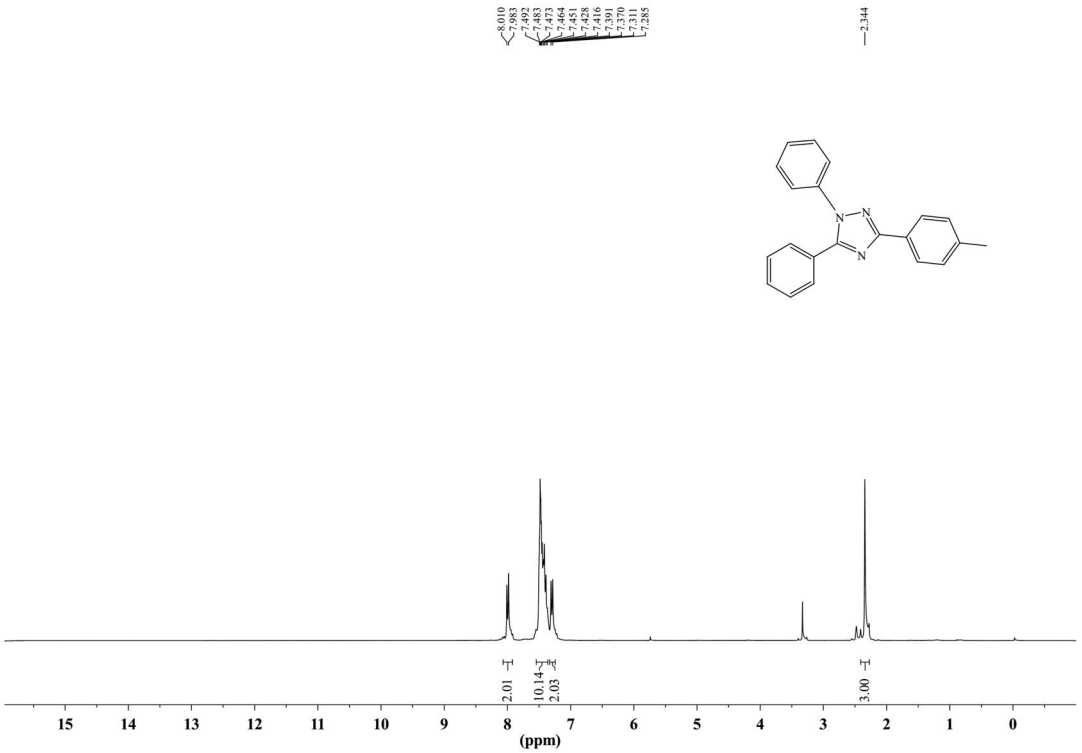

161.033
155.452
138.453
134.525
131.642
131.212
130.617
129.877
129.460
129.346
129.052
128.041
127.165
126.375
126.032
125.984
125.933
125.884
125.757
122.770
(ppm)

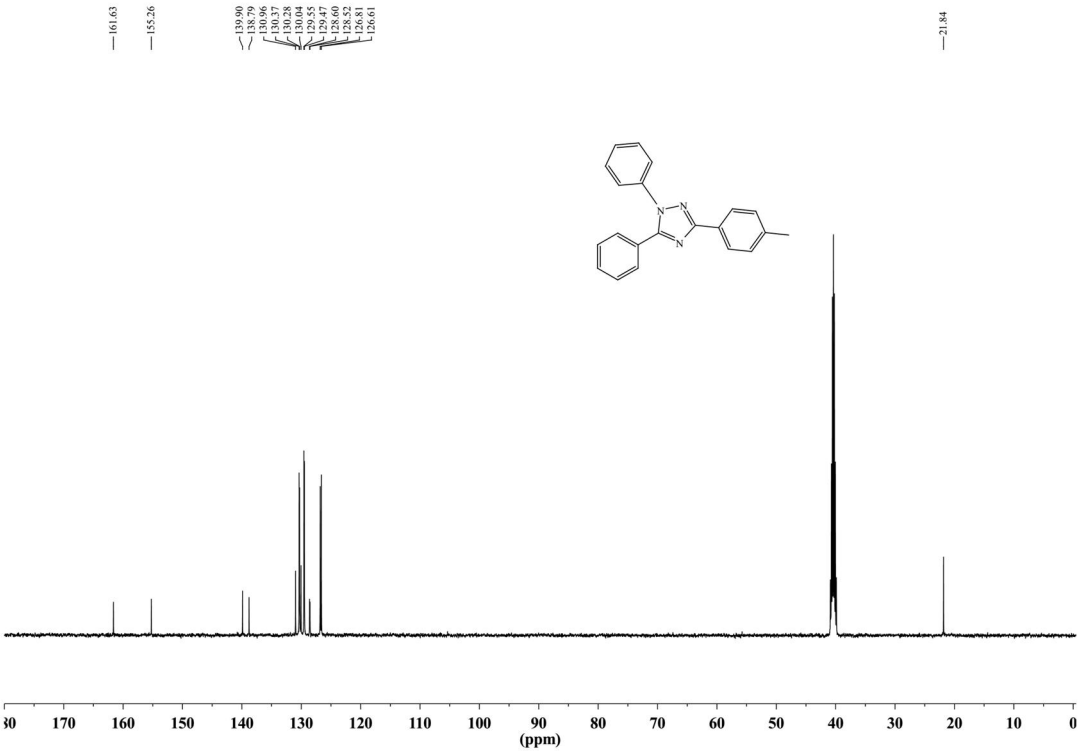
3ac


8.192
8.164
7.548
7.525
7.396
7.364
7.351
7.326
7.306
6.992
6.964
3.826
2.082
2.000
8.005
2.022
3.000
(ppm)

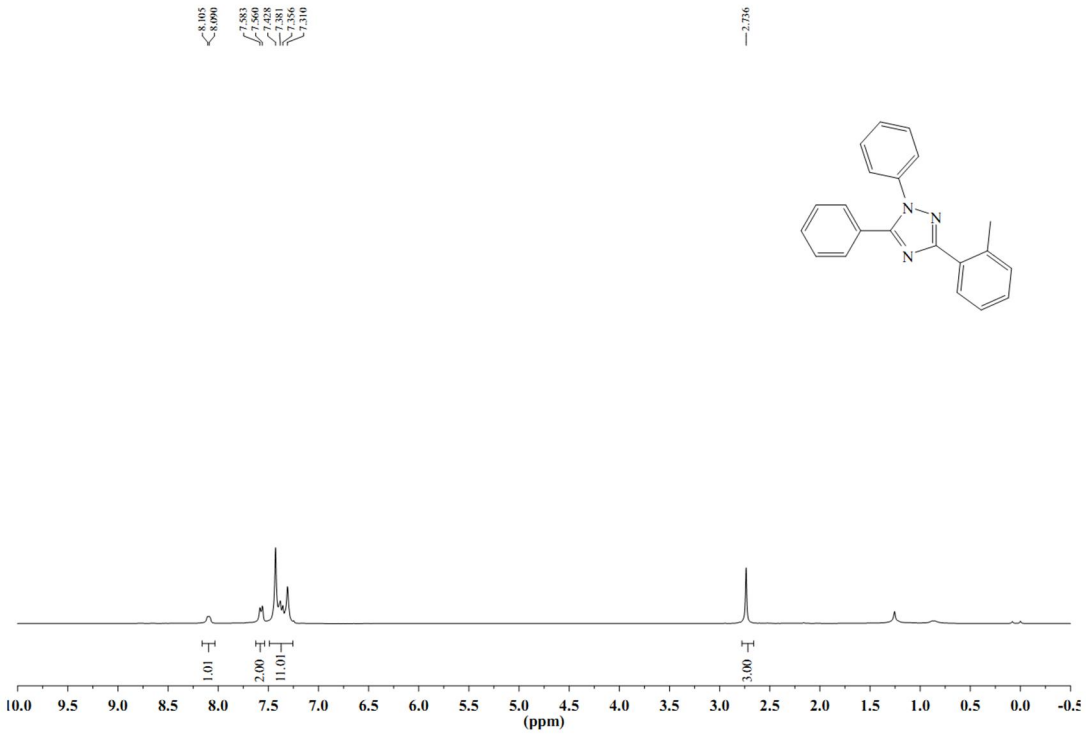

162.237
161.091
155.605
138.763
138.490
130.355
129.395
129.396
129.132
129.088
128.979
128.543
128.462
55.712
(ppm)

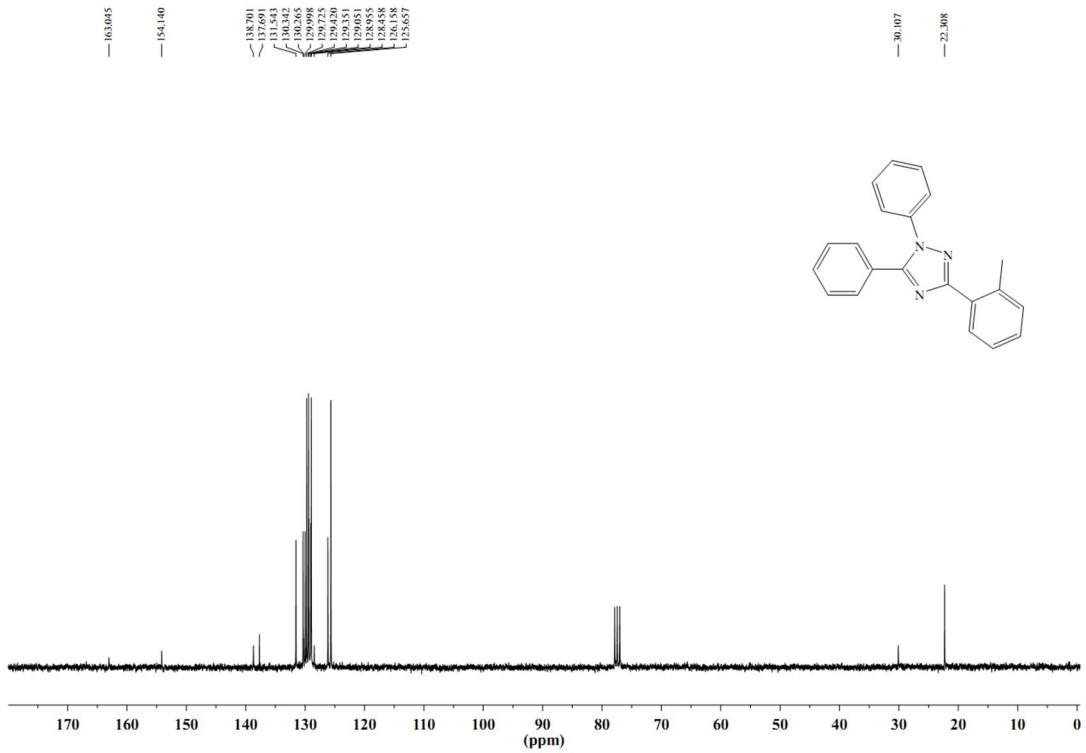
3ad


8.010
7.983
7.492
7.483
7.473
7.464
7.451
7.428
7.416
7.391
7.370
7.311
7.285
2.344
2.01
10.14
2.03
3.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)

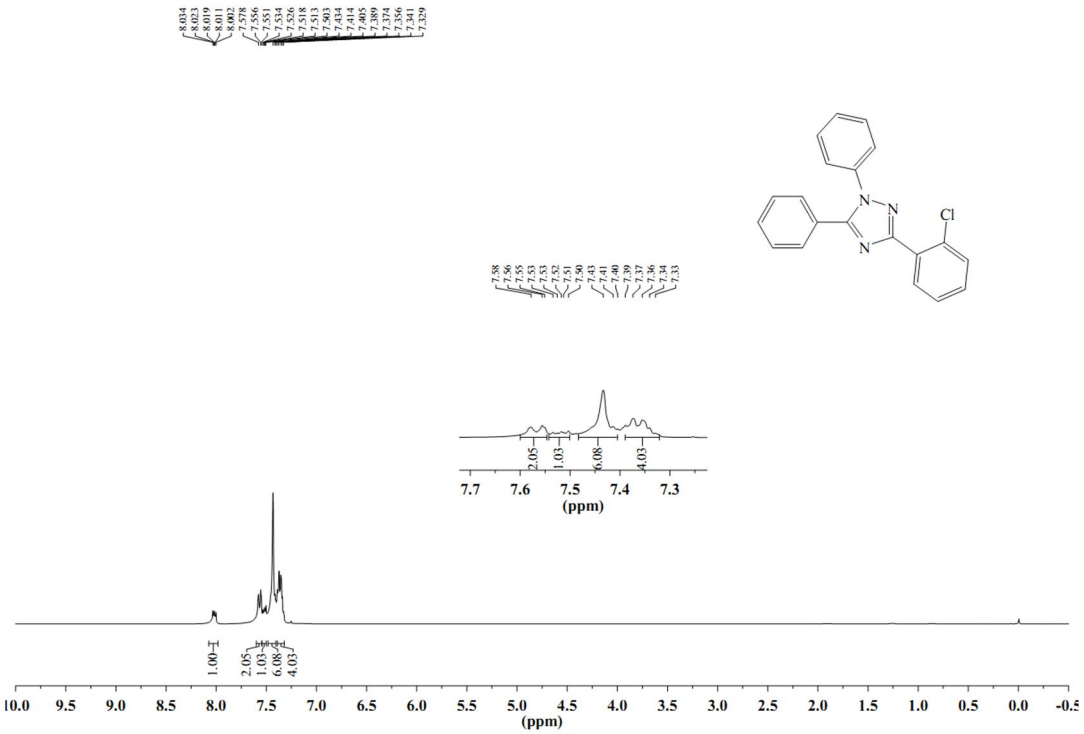

161.63
155.26
139.90
138.79
130.96
130.37
130.28
130.04
129.55
129.47
128.60
128.52
126.81
126.61
21.84
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

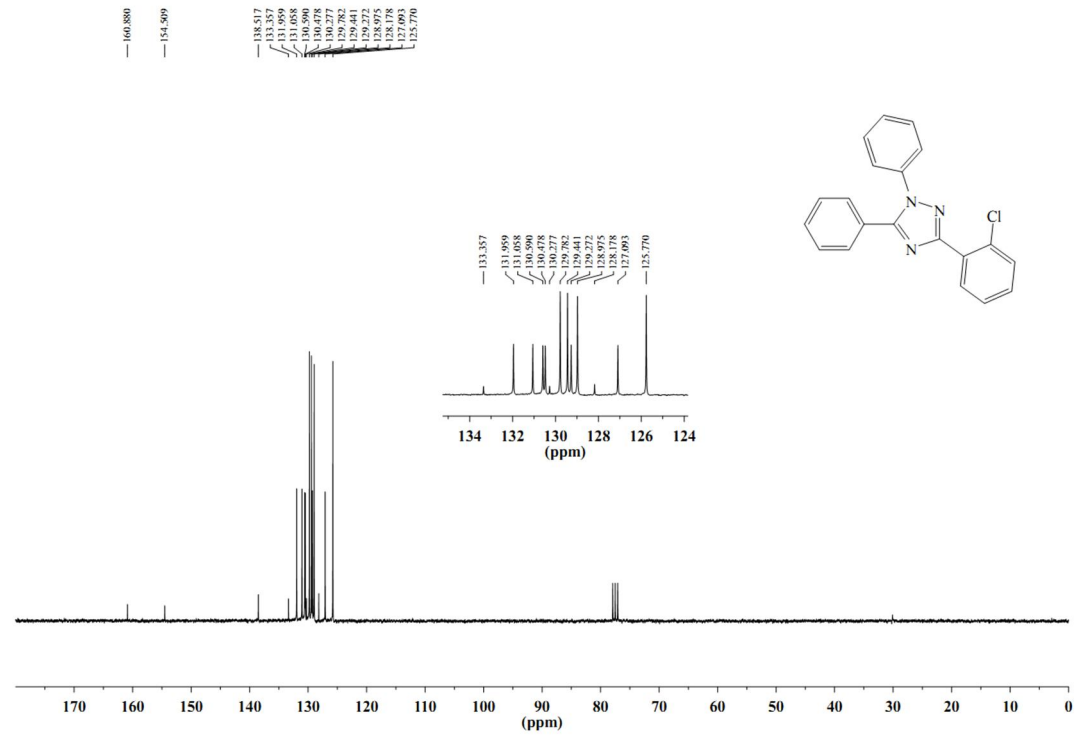
3ae


8.105
8.090
7.583
7.560
7.528
7.381
7.356
7.310
2.736
1.01
2.00
11.01
3.00
(ppm)

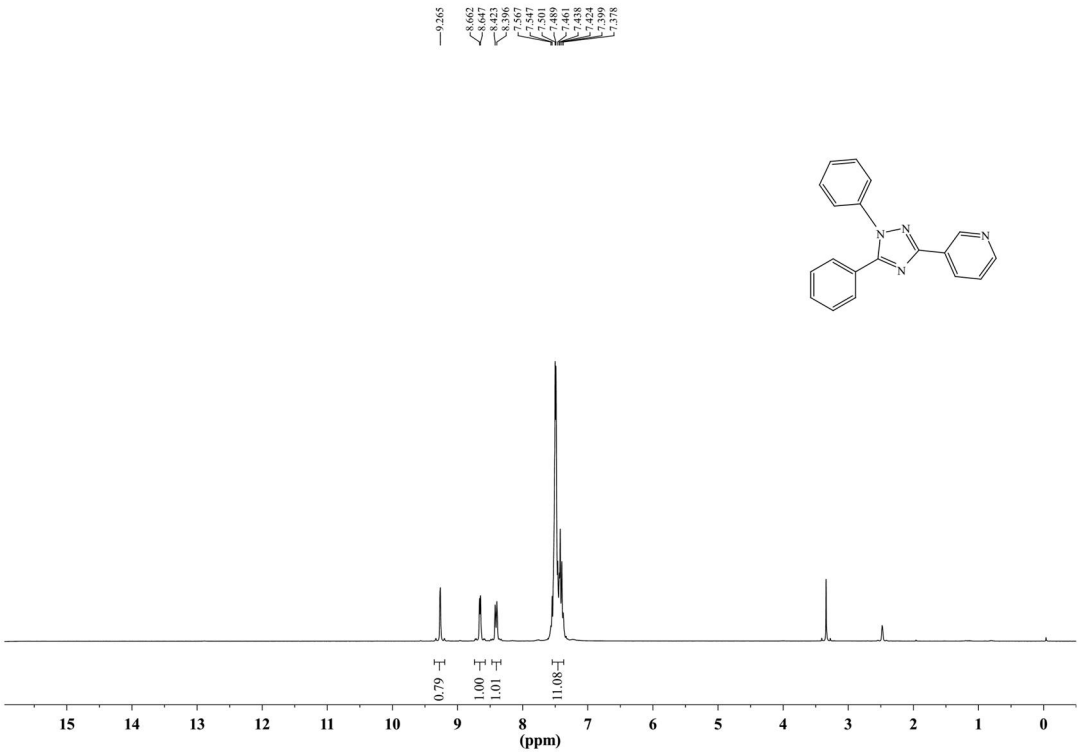

163.045
154.140
138.701
137.691
131.543
130.342
130.265
130.008
129.725
129.420
129.351
129.051
128.955
128.458
126.158
125.657
30.107
22.308
(ppm)

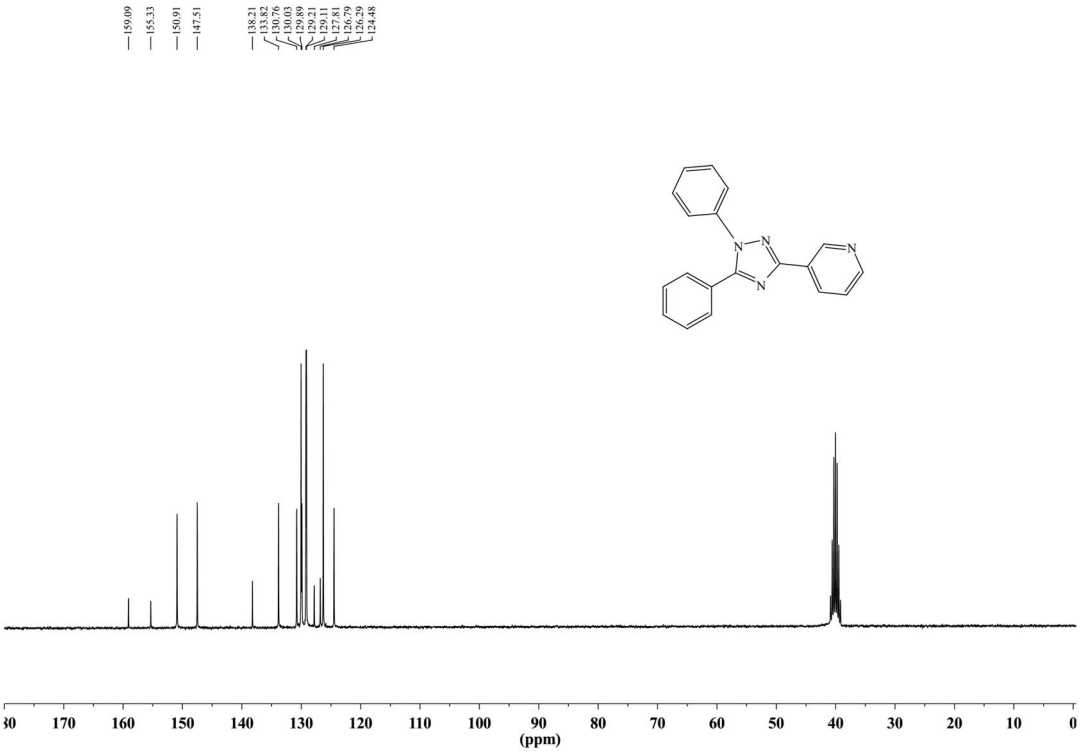
3af


8.034
8.033
8.019
8.011
8.002
7.578
7.556
7.551
7.534
7.526
7.518
7.513
7.503
7.434
7.414
7.405
7.389
7.374
7.356
7.341
7.329
7.58
7.56
7.55
7.53
7.53
7.52
7.51
7.50
7.43
7.41
7.40
7.39
7.37
7.36
7.34
7.33
N
N
N
Cl
2.05
1.03
6.08
4.03
7.7
7.6
7.5
7.4
7.3
(ppm)
1.00
2.05
1.03
6.08
4.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
(ppm)

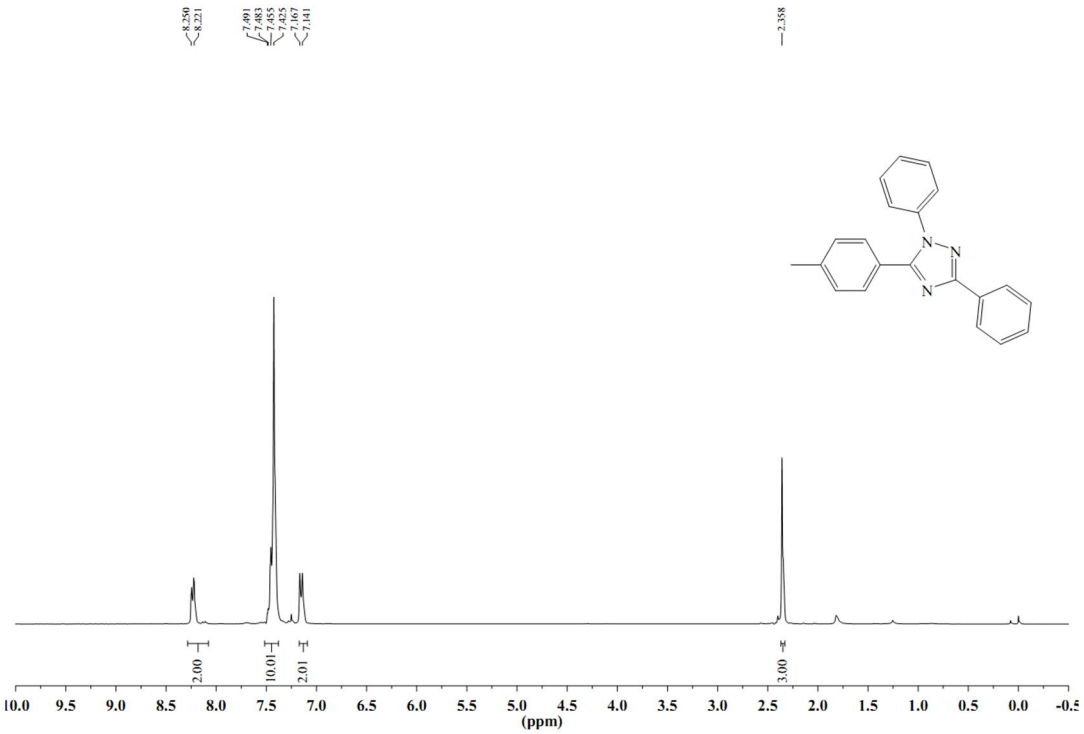

160.880
154.909
138.517
133.357
131.959
131.058
130.590
130.478
130.277
129.782
129.441
129.372
128.975
128.178
127.093
125.770
N
N
N
Cl
134
132
130
128
126
124
(ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

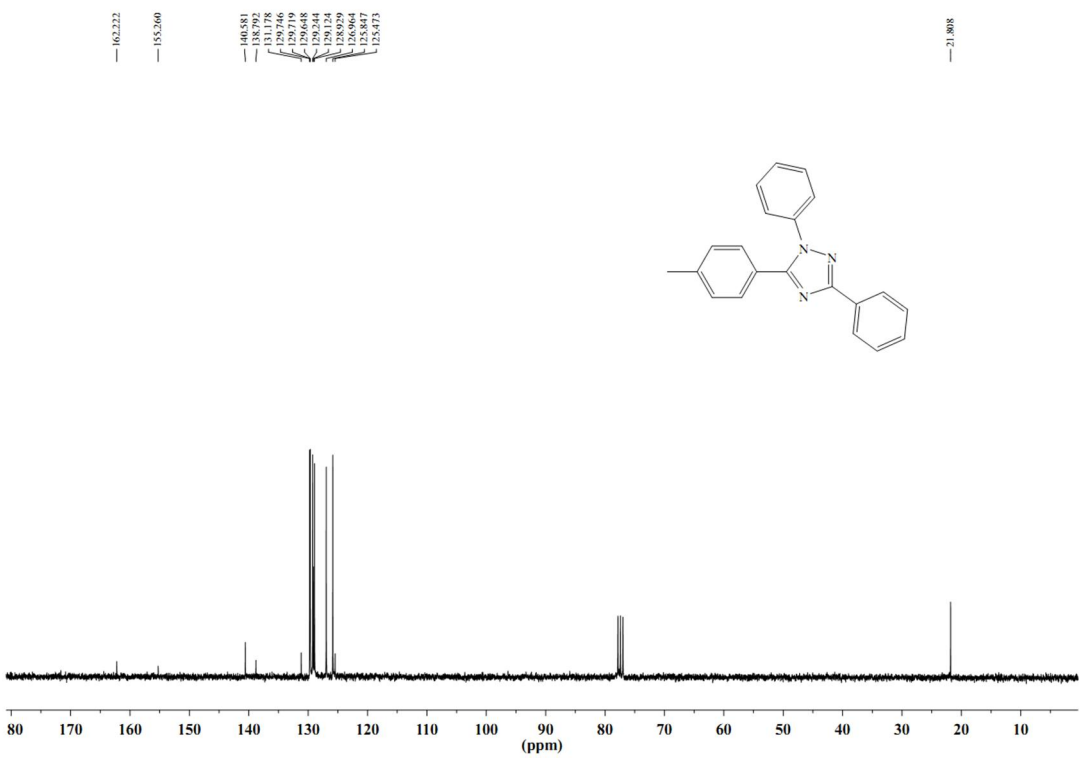
3ag


9.265
8.662
8.647
8.423
8.396
7.567
7.547
7.501
7.489
7.461
7.438
7.424
7.399
7.378
0.79
1.00
1.01
11.08
(ppm)

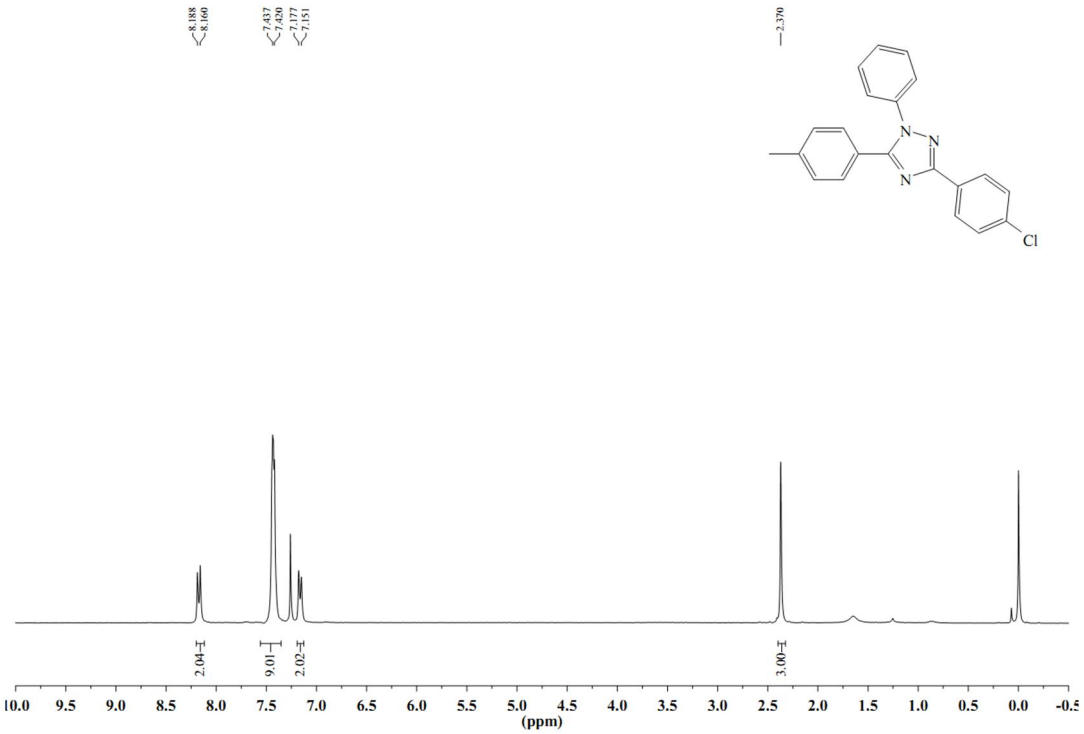

159.09
155.33
150.91
147.51
138.21
133.82
130.76
130.03
129.89
129.21
129.11
127.81
126.79
126.29
124.48
(ppm)

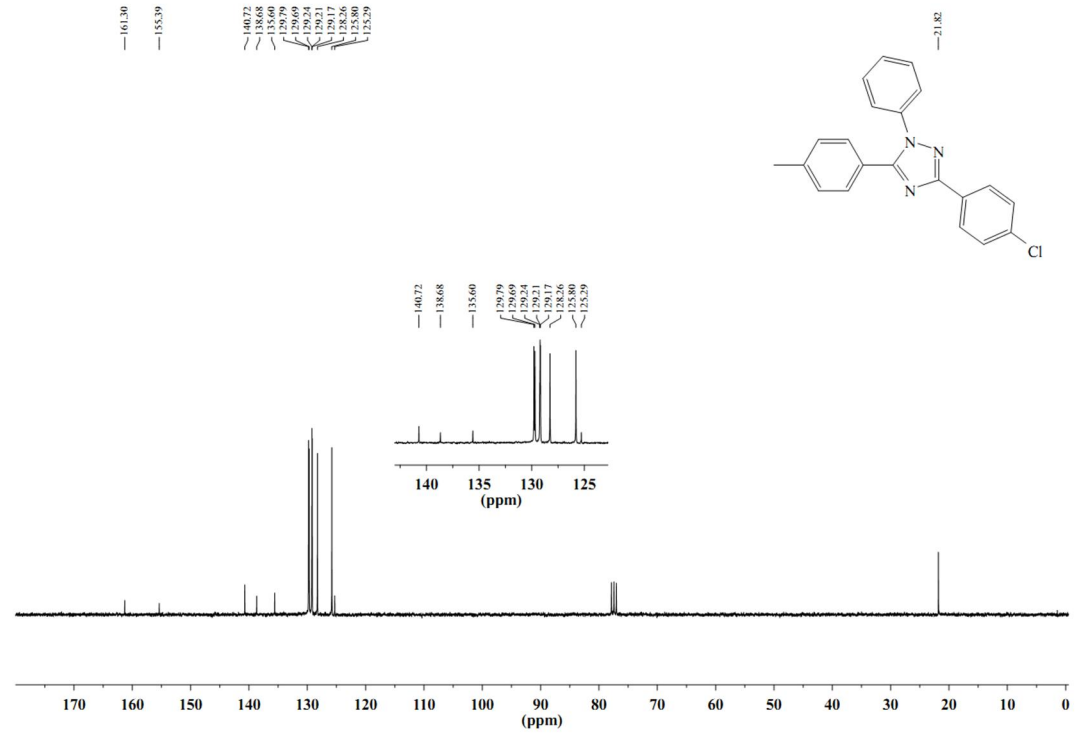
3ah


8.259
8.221
7.491
7.483
7.455
7.425
7.167
7.141
2.358
2.00
10.01
2.01
3.00
(ppm)

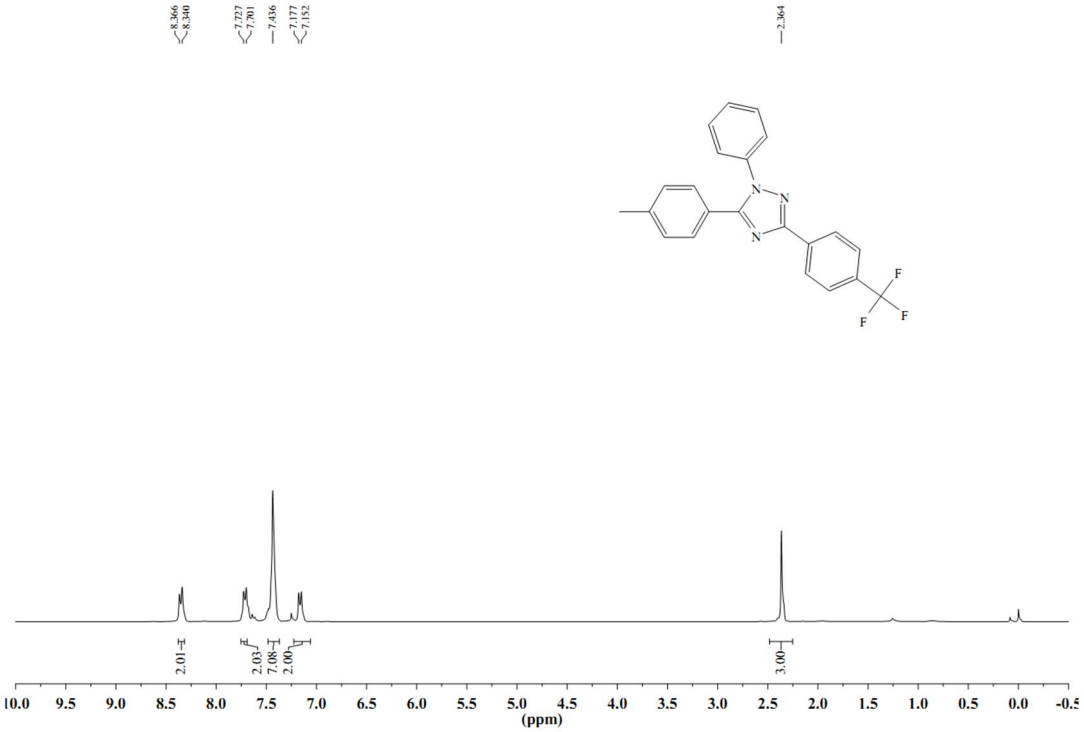

162.222
155.260
140.581
138.792
131.178
130.966
129.719
129.648
129.344
129.124
128.929
126.964
125.847
125.473
21.808
(ppm)

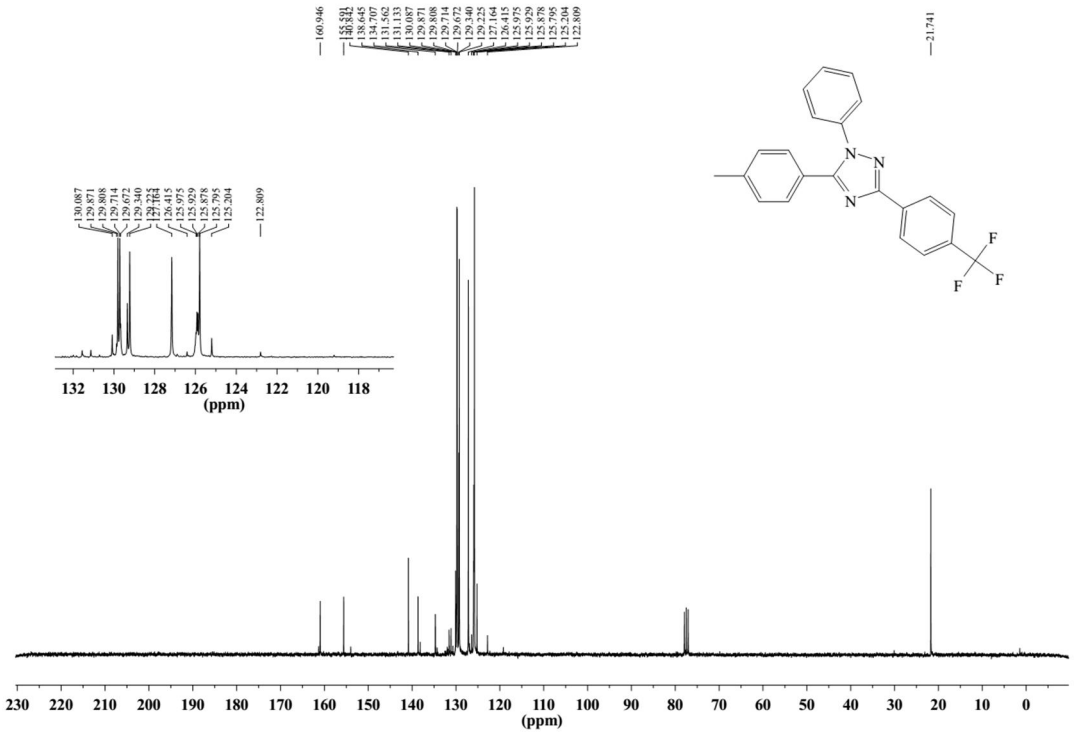
3ba


8.188
8.160
7.437
7.420
7.177
7.151
2.370
N
N
N
Cl
2.04
9.01
2.02
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
(ppm)

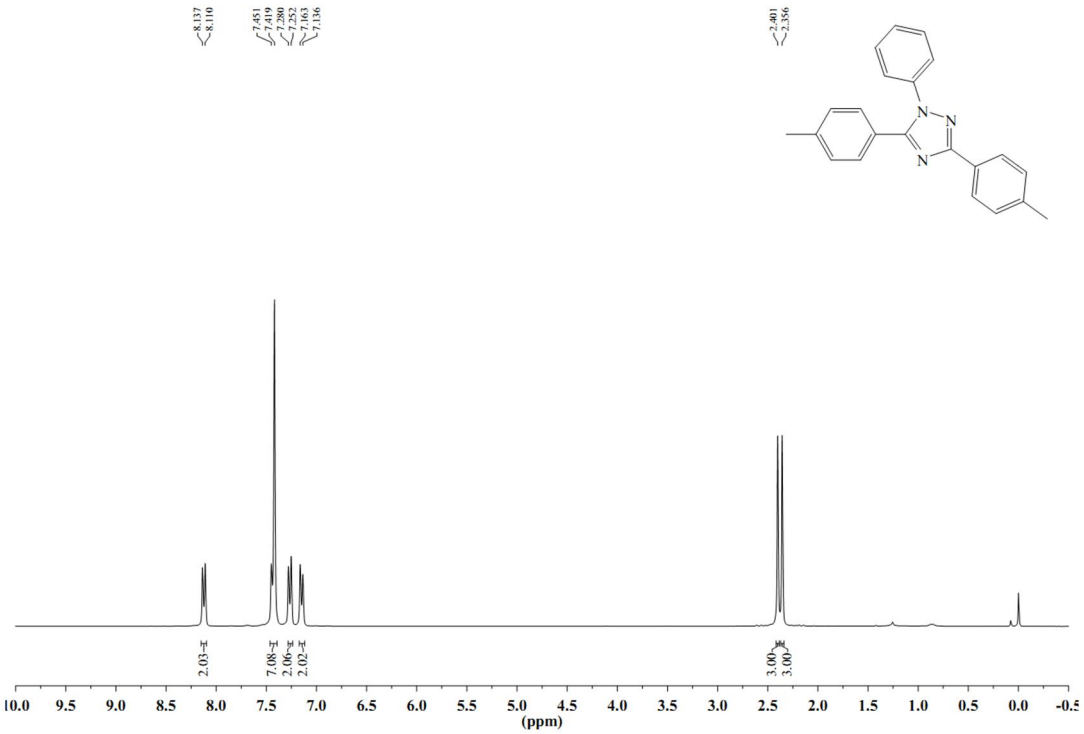

161.30
155.39
140.72
138.68
135.60
129.79
129.69
129.24
129.21
129.17
128.26
125.80
125.29
21.82
N
N
N
Cl
140.72
138.68
135.60
129.79
129.69
129.24
129.21
129.17
128.26
125.80
125.29
140 135 130 125
(ppm)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

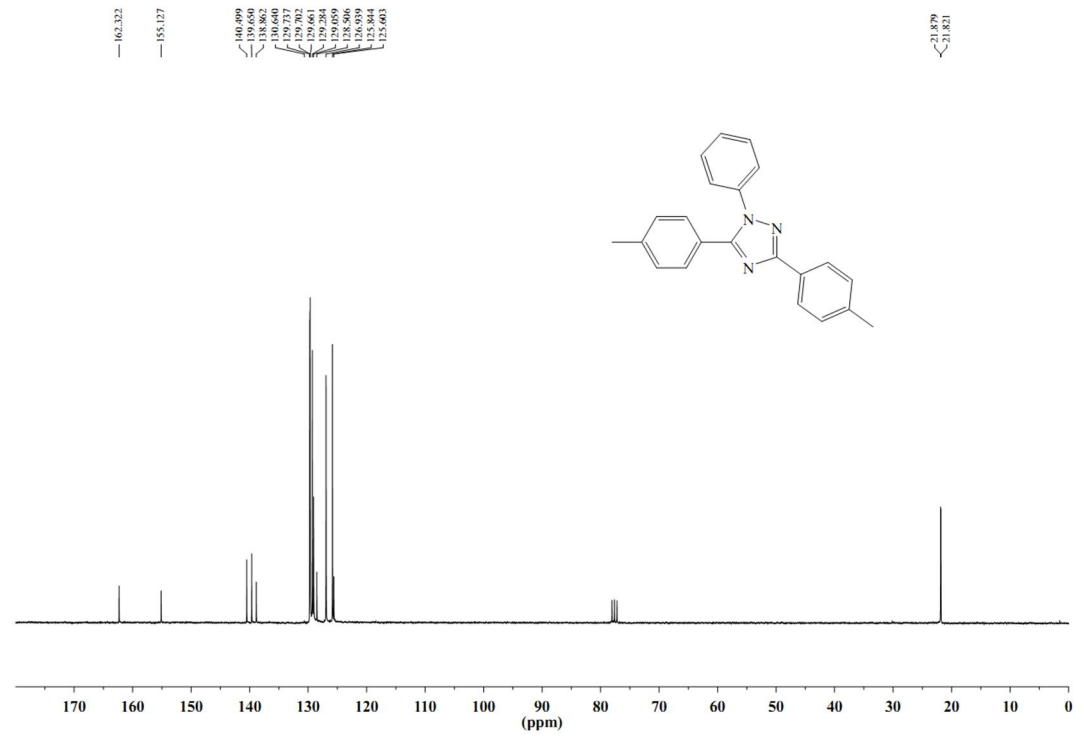
3bb


8.366
8.340
7.727
7.701
7.436
7.177
7.152
2.364
2.01
2.03
7.08
2.00
3.00
(ppm)

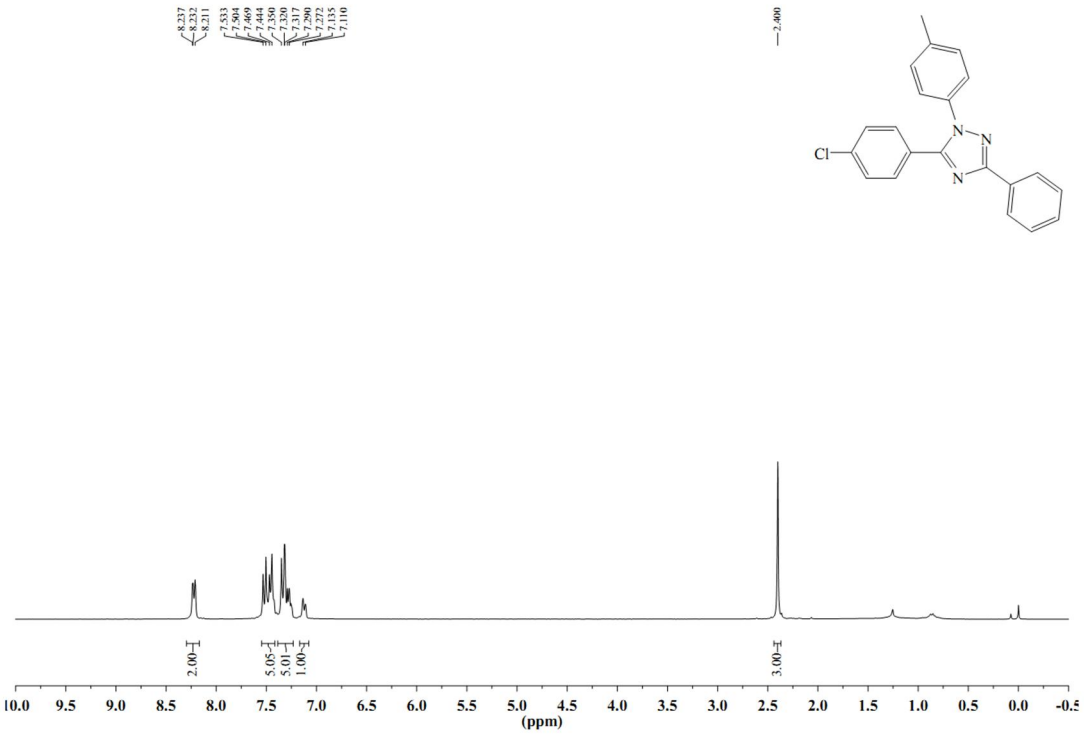

160.946
138.645
134.707
131.562
131.133
130.087
129.871
129.808
129.714
129.672
129.340
129.225
127.164
126.415
125.975
125.929
125.878
125.795
125.204
122.809
21.741
(ppm)

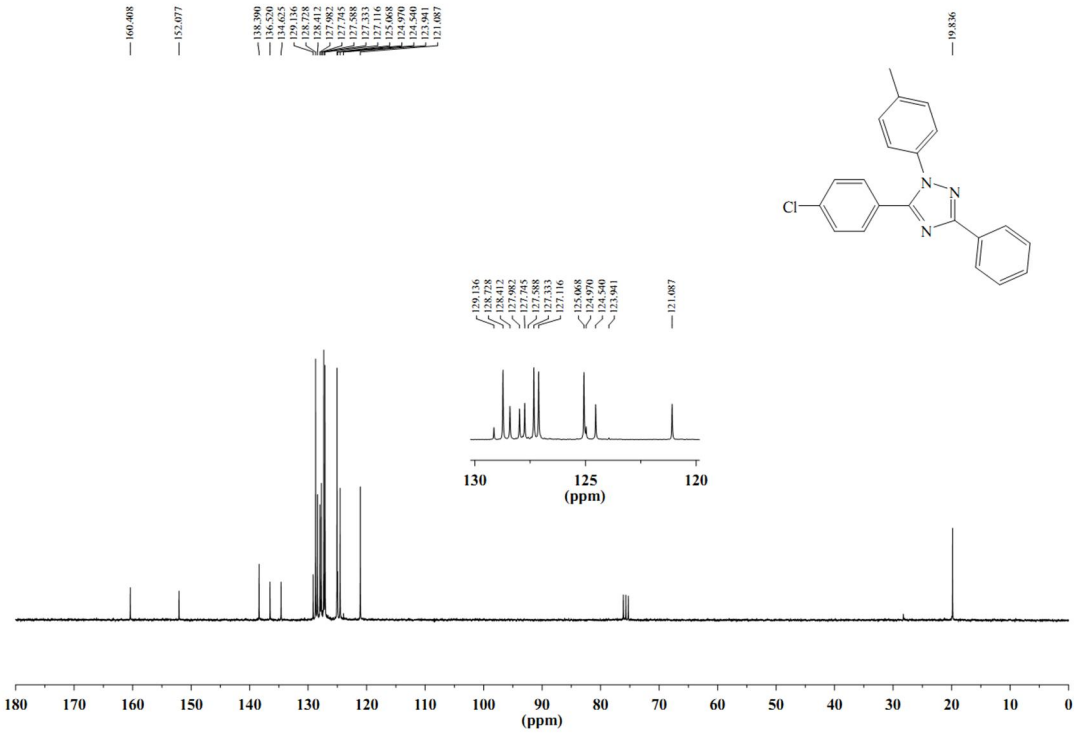
3bc


8.137
8.110
7.451
7.419
7.390
7.253
7.163
7.136
2.401
2.356
2.03
7.08
2.06
2.02
3.00
3.00
(ppm)

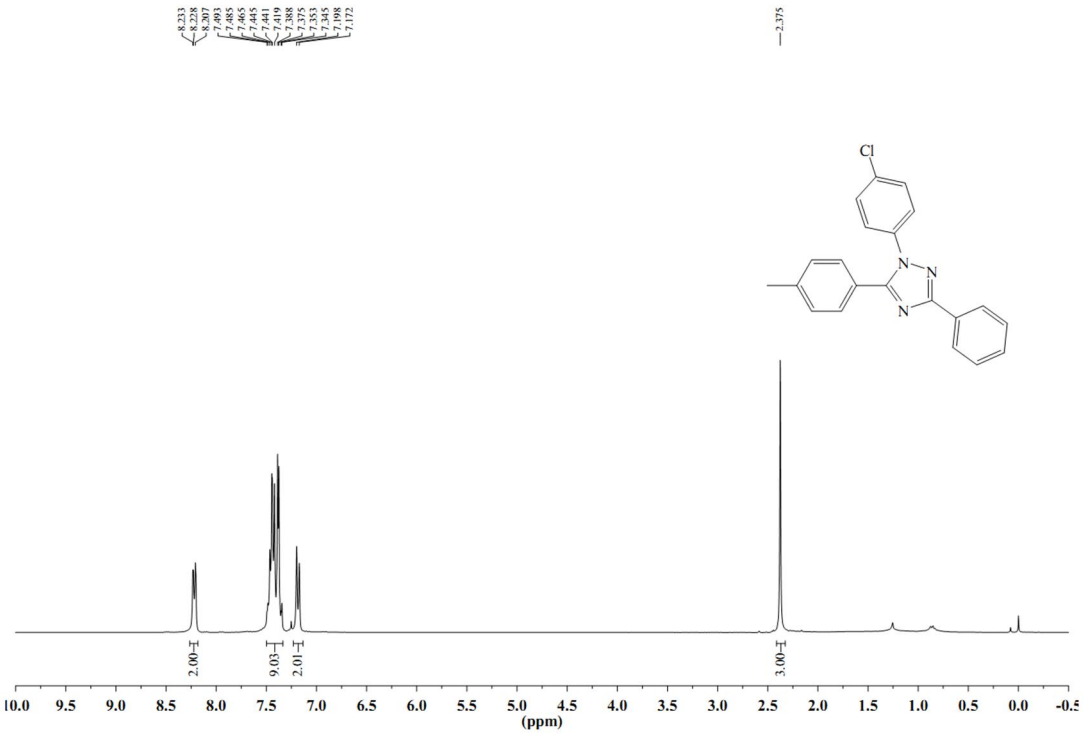

162.322
155.127
140.499
139.650
138.862
130.640
129.737
129.702
129.661
129.284
129.169
128.906
126.939
125.844
125.603
21.879
21.821
(ppm)

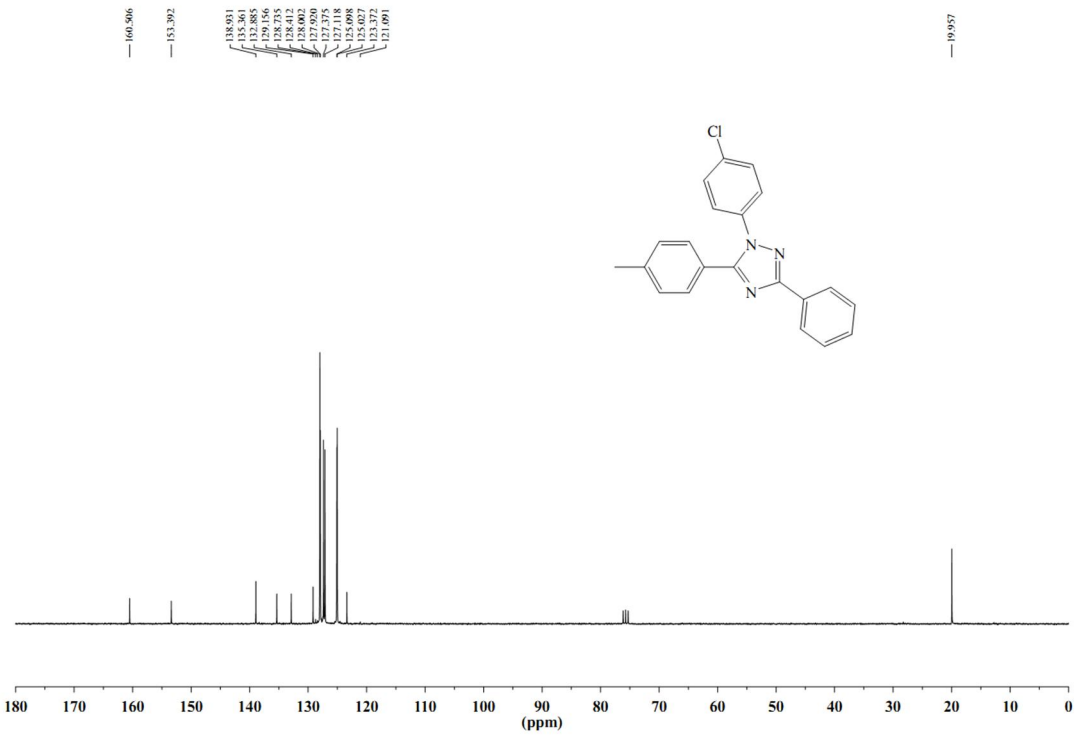
3be


8.237
8.232
8.211
7.533
7.504
7.469
7.444
7.350
7.330
7.317
7.299
7.272
7.135
7.110
2.400
Cl
N
N
N
2.00
5.05
5.01
1.00
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
(ppm)

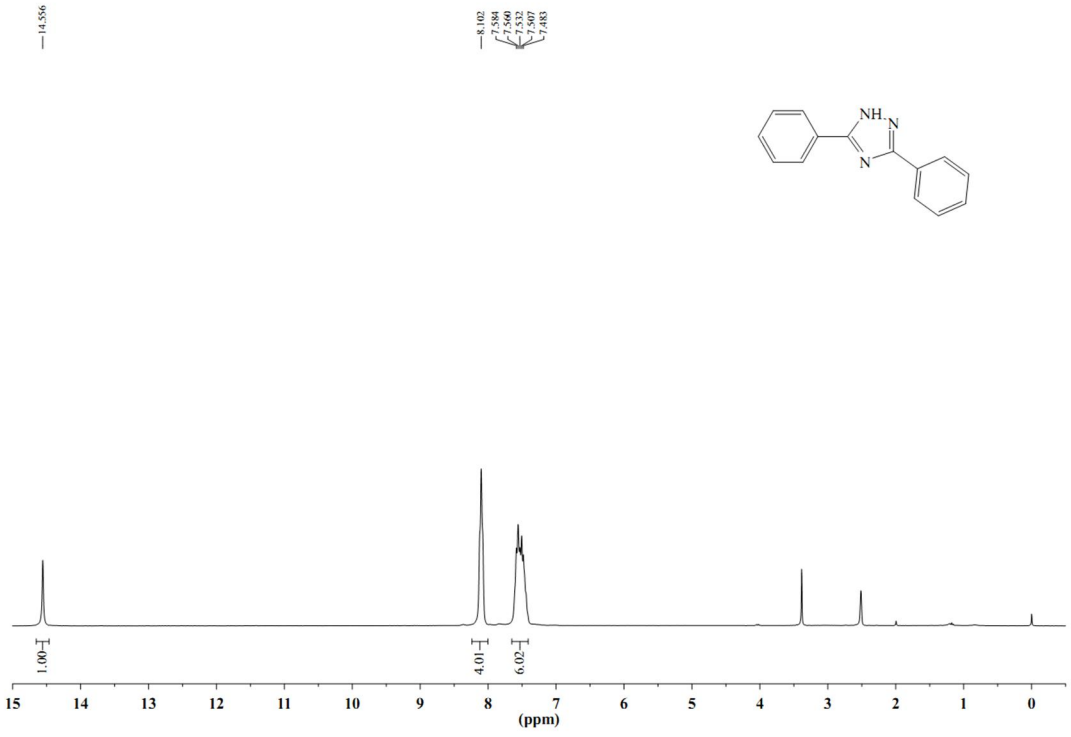

160.408
152.077
138.390
136.520
134.625
130.156
128.728
128.412
127.982
127.745
127.588
127.333
127.116
125.068
124.970
124.540
123.941
121.087
19.836
Cl
N
N
N
129.136
128.728
128.412
127.982
127.745
127.588
127.333
127.116
125.068
124.970
124.540
123.941
121.087
130
125
120
(ppm)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

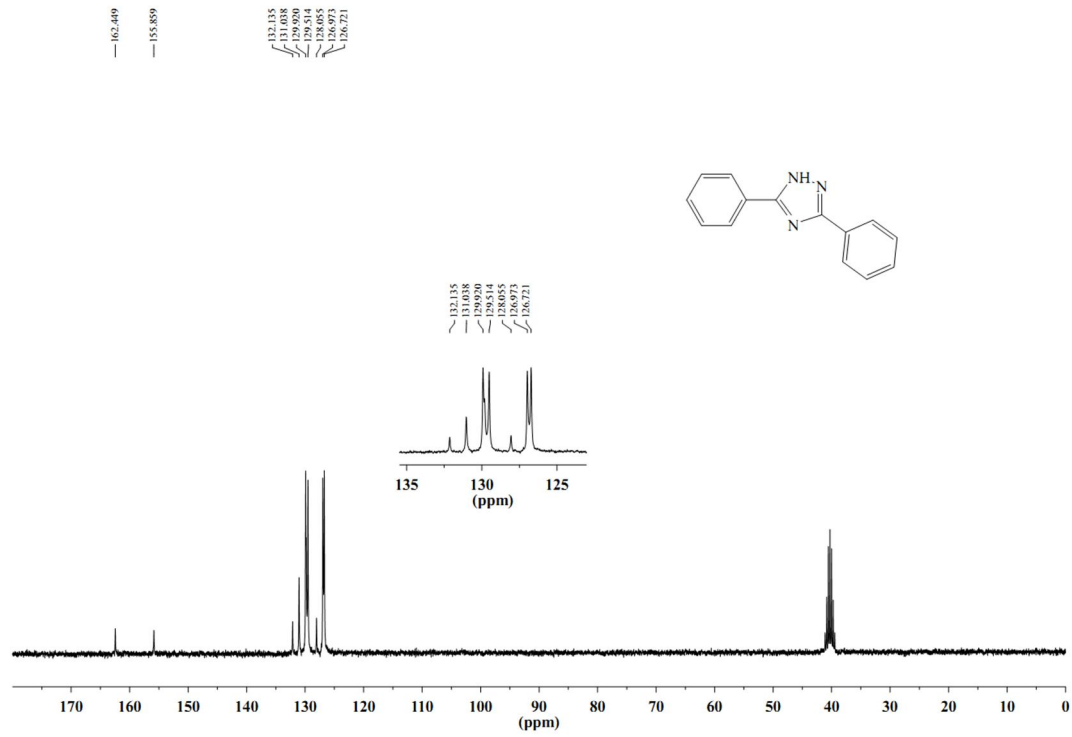
3ca


8.233
8.228
8.207
7.493
7.485
7.465
7.445
7.441
7.419
7.388
7.375
7.353
7.345
7.198
7.172
2.375
Cl
N
N
N
2.00
9.03
2.01
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
(ppm)

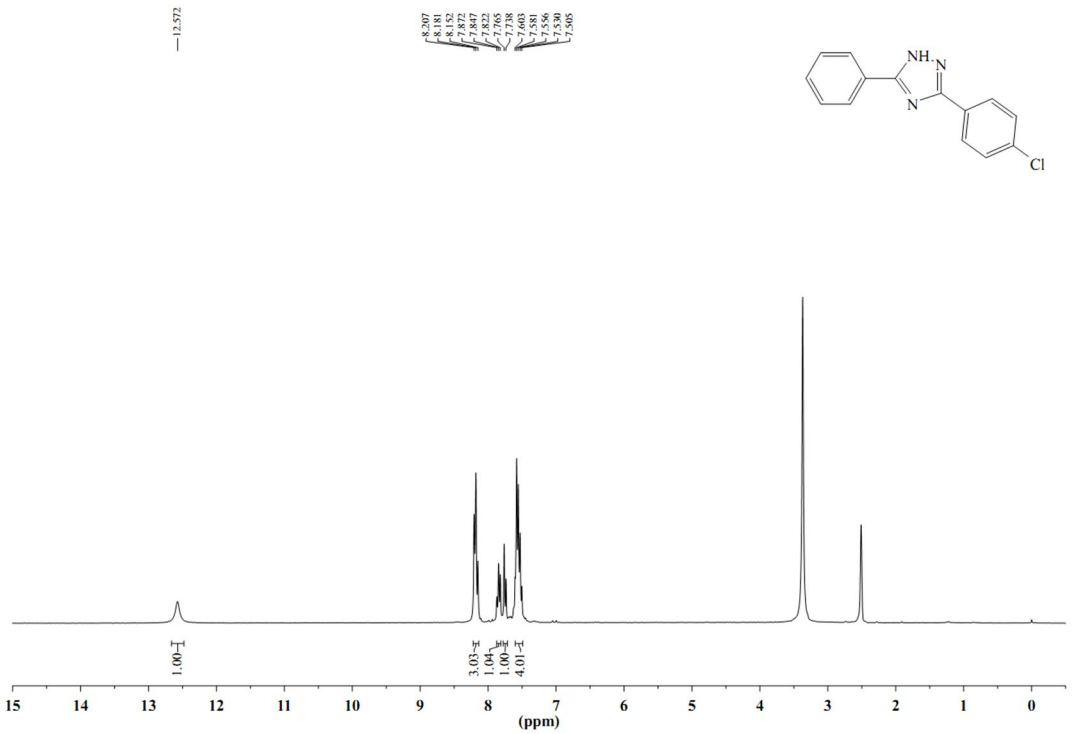

160.506
153.392
138.931
135.361
132.885
130.156
128.735
128.412
128.002
127.920
127.375
127.118
126.998
125.027
123.372
121.091
19.957
Cl
N
N
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

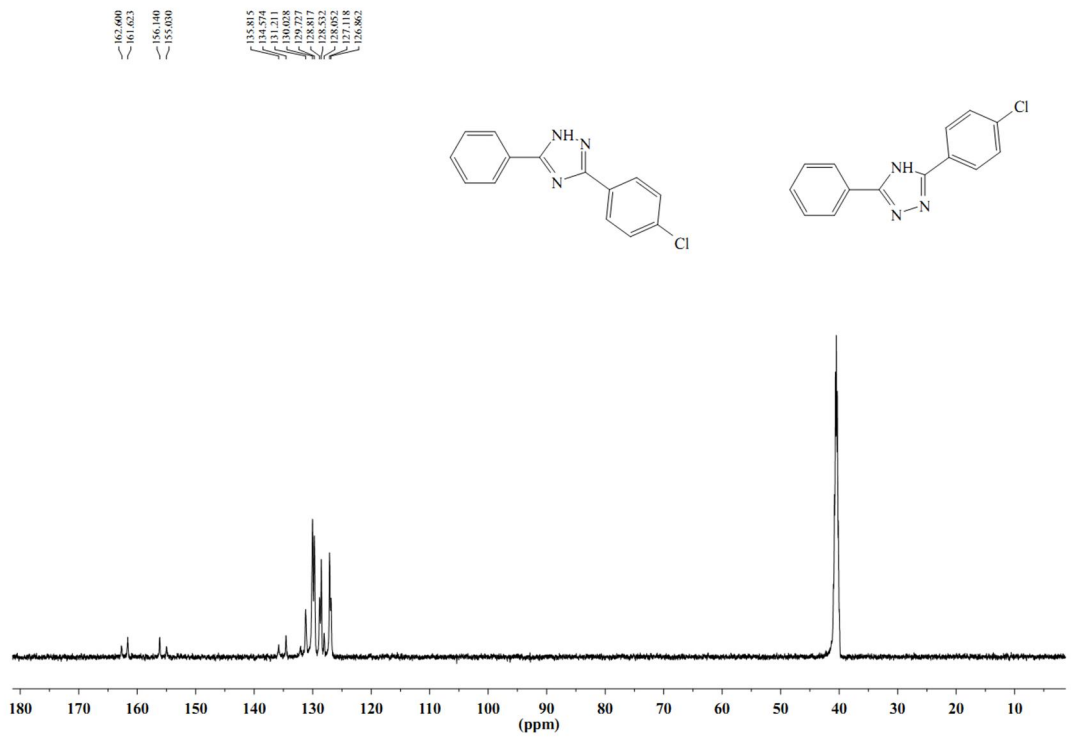
3da


14.556
8.102
7.584
7.560
7.532
7.507
7.483
NH
N
N
1.00
4.01
6.02
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
(ppm)

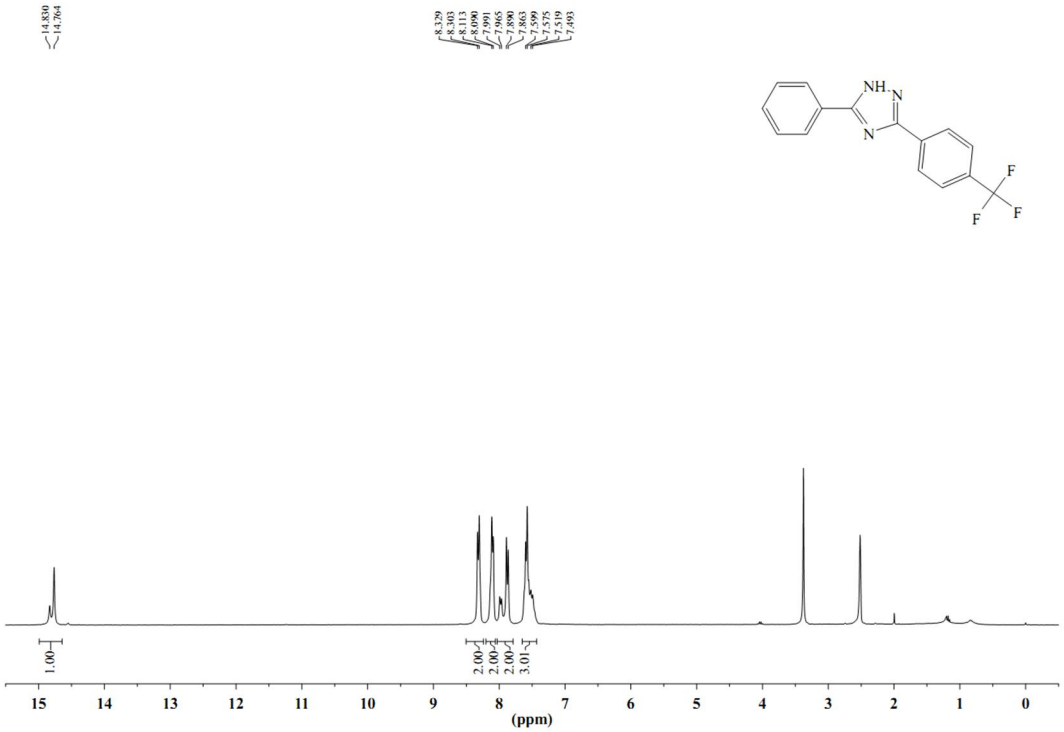

162.449
155.859
132.135
131.038
129.920
129.514
128.055
126.973
126.721
NH
N
N
135
130
125
(ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

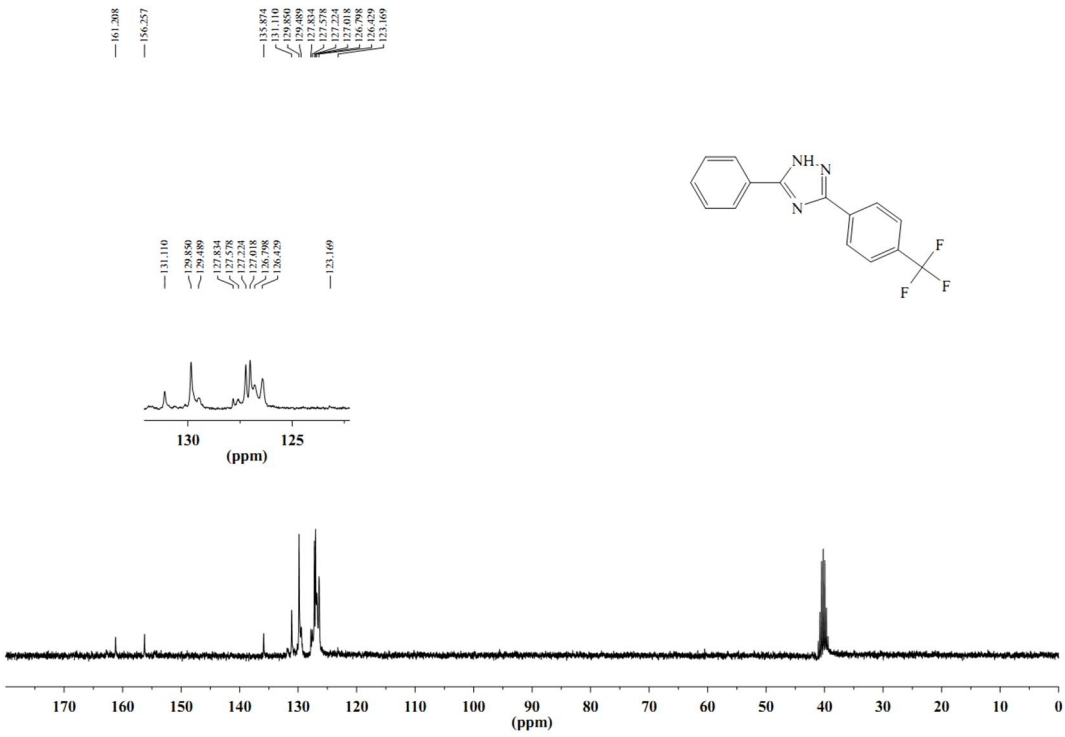
5aa


12.572
8.207
8.181
8.152
7.872
7.847
7.822
7.765
7.738
7.603
7.581
7.556
7.530
7.505
NH
N
N
Cl
1.00
3.03
1.04
1.00
4.01
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)

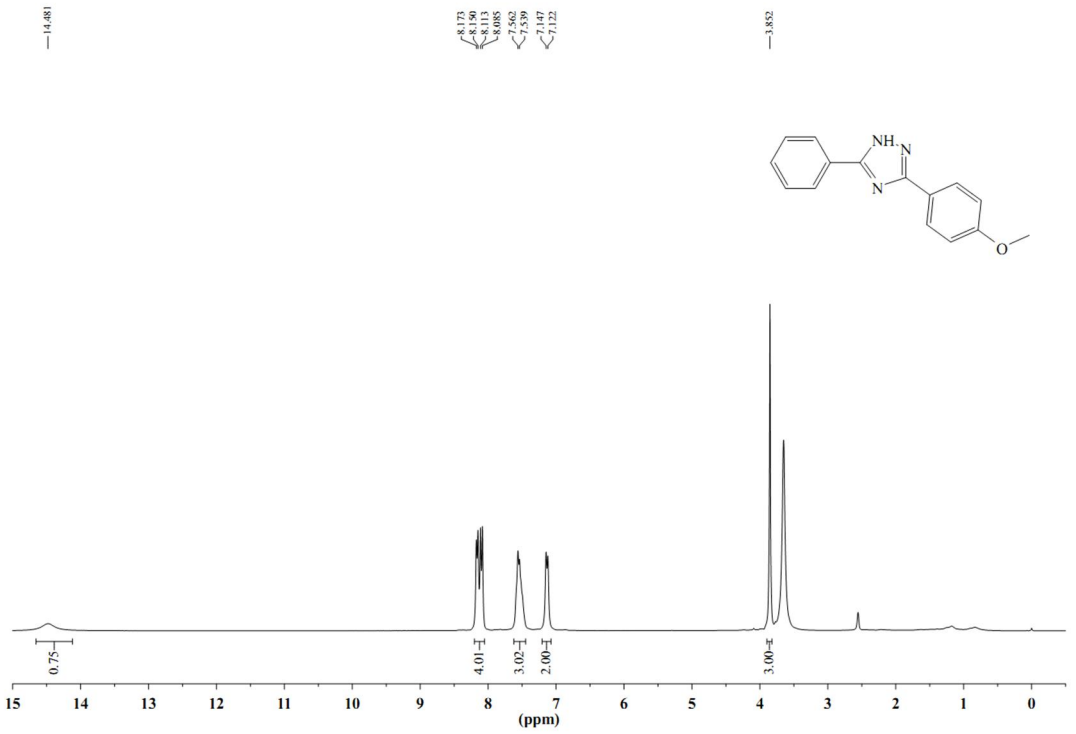

162.690
161.623
156.140
155.030
135.815
134.574
131.211
130.028
129.727
128.817
128.532
128.052
127.118
126.862
NH
N
N
Cl
Cl
NH
N
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

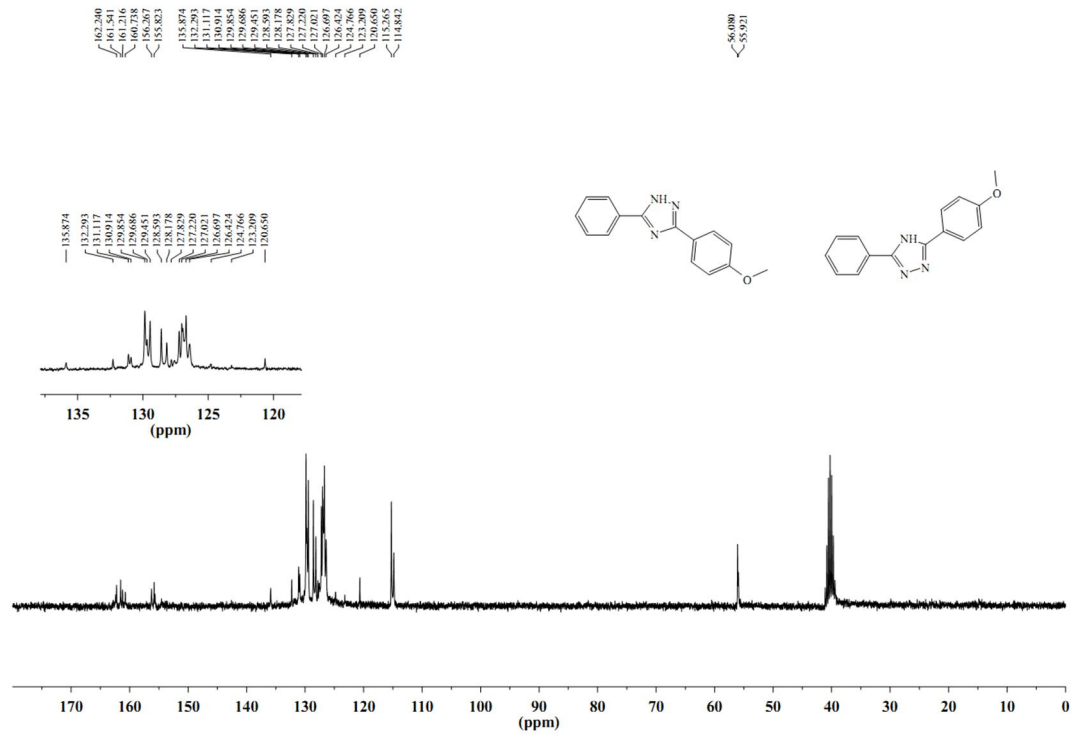
5ab


14.830
14.764
8.329
8.305
8.113
8.090
7.991
7.965
7.890
7.863
7.599
7.575
7.519
7.493
NH
N
N
F
F
F
1.00
2.00
2.00
2.00
3.01
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
(ppm)


161.208
156.257
135.874
131.110
129.850
129.489
127.834
127.578
127.234
127.018
126.798
126.429
123.169
NH
N
N
F
F
F
130
125
(ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

5ac


14.481
8.173
8.170
8.115
8.085
7.562
7.539
7.147
7.122
3.852
NH
N
N
O
0.75
4.01
3.02
2.00
3.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)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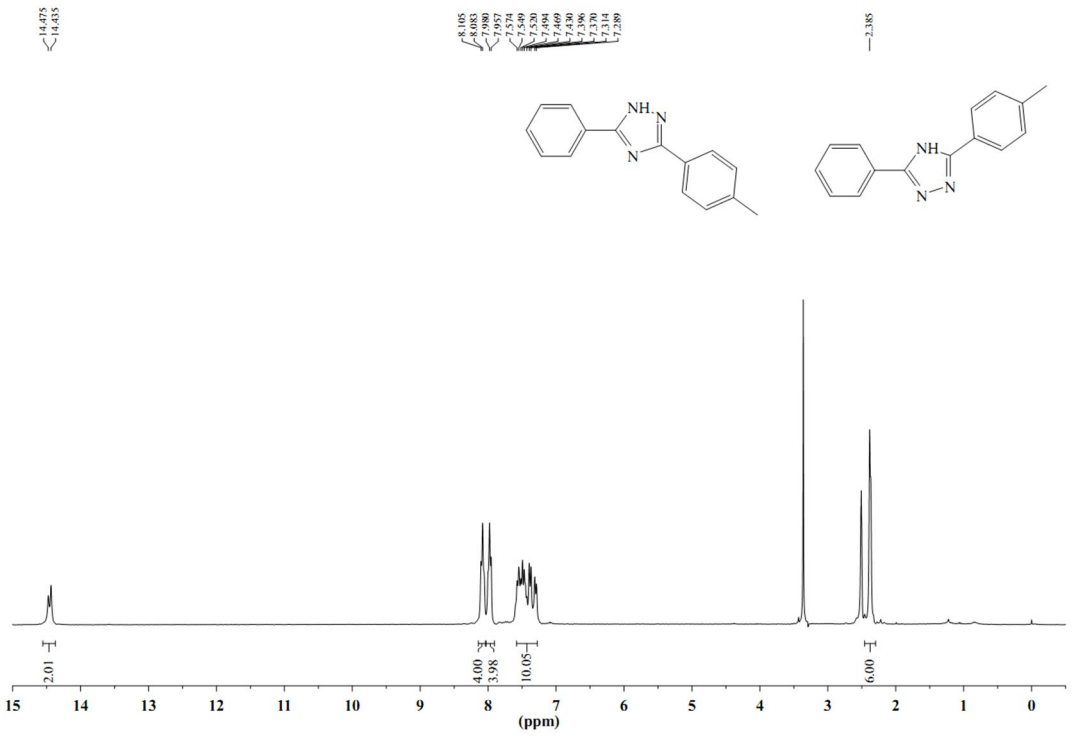
161.541
160.216
160.738
156.267
155.823
135.874
132.293
131.117
130.914
129.854
129.686
129.451
128.593
128.178
127.829
127.230
127.021
126.697
126.424
124.766
123.309
120.650
115.265
114.842
56.080
55.921
NH
N
N
O
135 130 125 120
(ppm)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

5ad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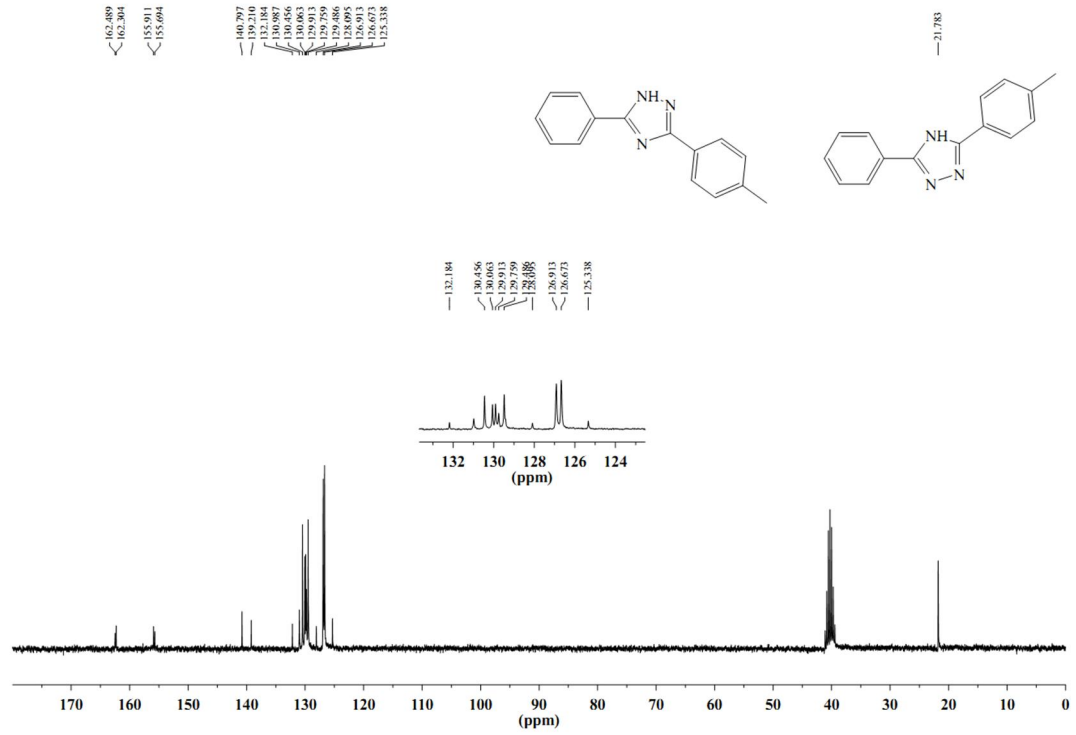
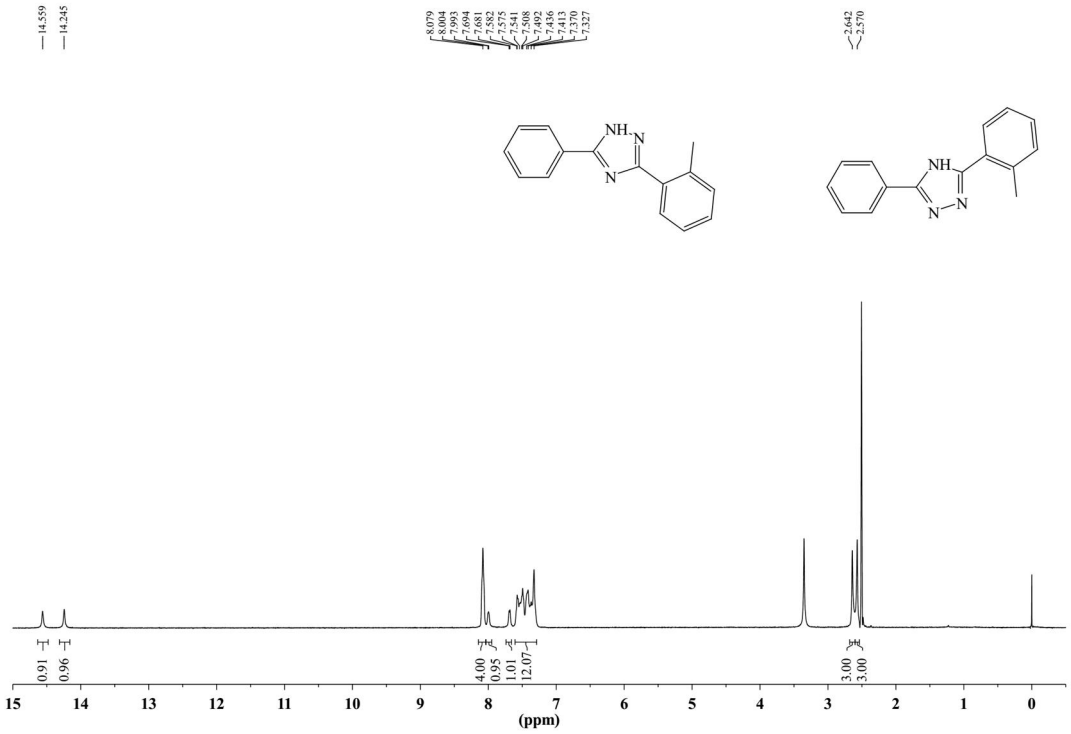
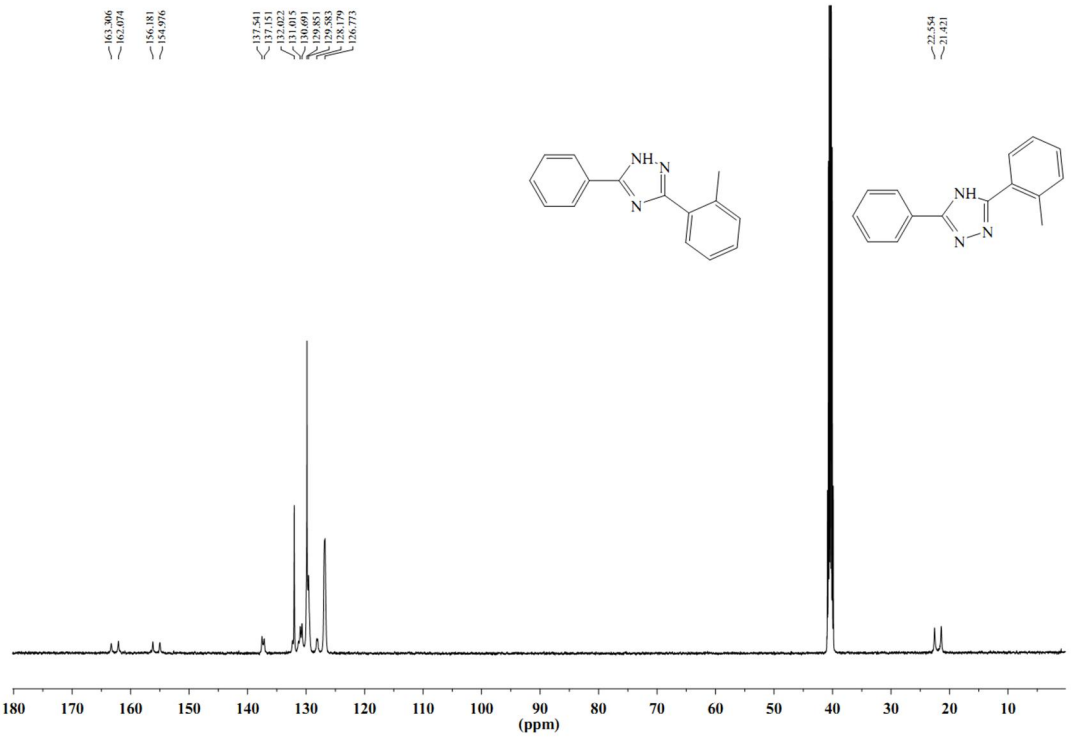
14.435
8.105
8.083
7.980
7.957
7.574
7.549
7.530
7.494
7.469
7.448
7.396
7.370
7.314
7.289
2.385
NH
N
N
2.01
4.00
3.98
10.05
6.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)

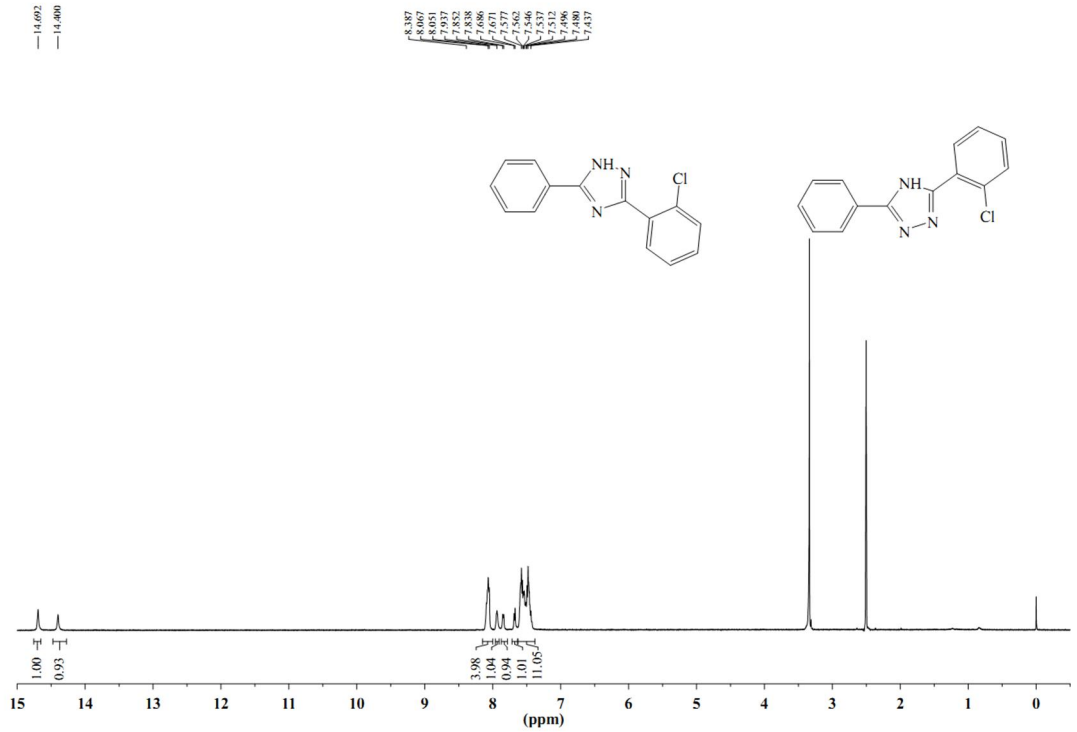

162.489
162.304
155.911
155.694
140.797
139.210
132.184
130.987
130.456
130.063
129.913
129.759
129.486
128.095
126.913
126.673
125.338
21.783
NH
N
N
132 130 128 126 124
(ppm)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

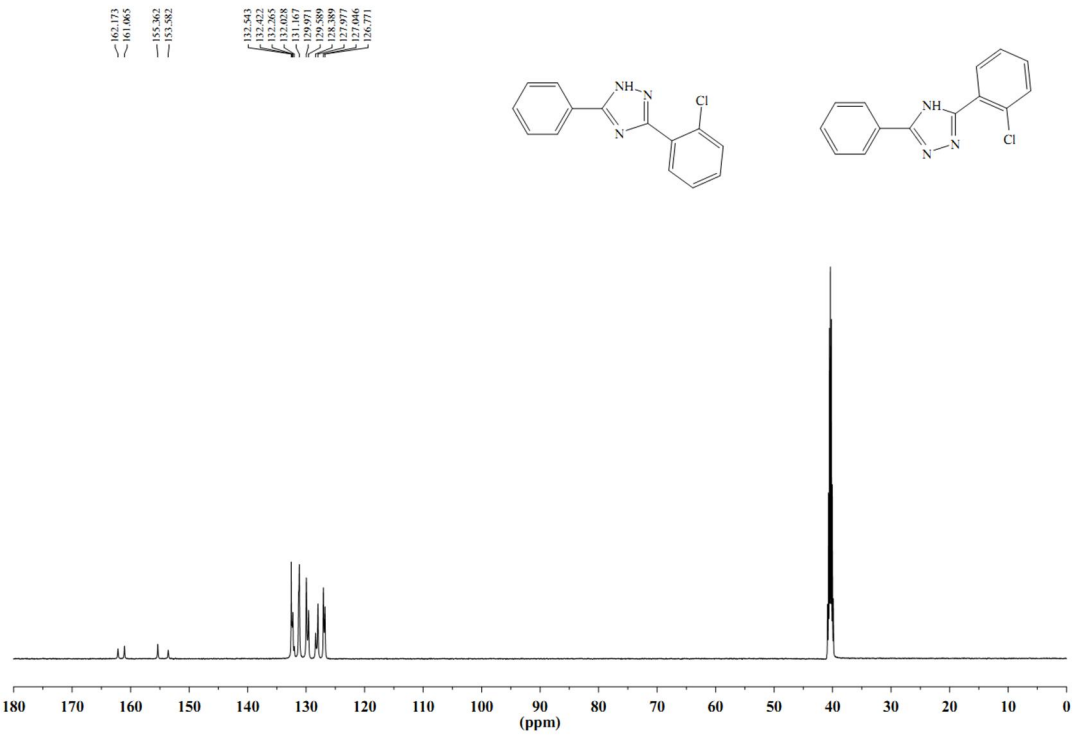
5ae


14.559
14.245
8.079
8.004
7.993
7.694
7.681
7.582
7.575
7.541
7.508
7.492
7.436
7.413
7.370
7.327
2.642
2.570
NH
N
N
0.91
0.96
4.00
0.95
1.01
12.07
3.00
3.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)

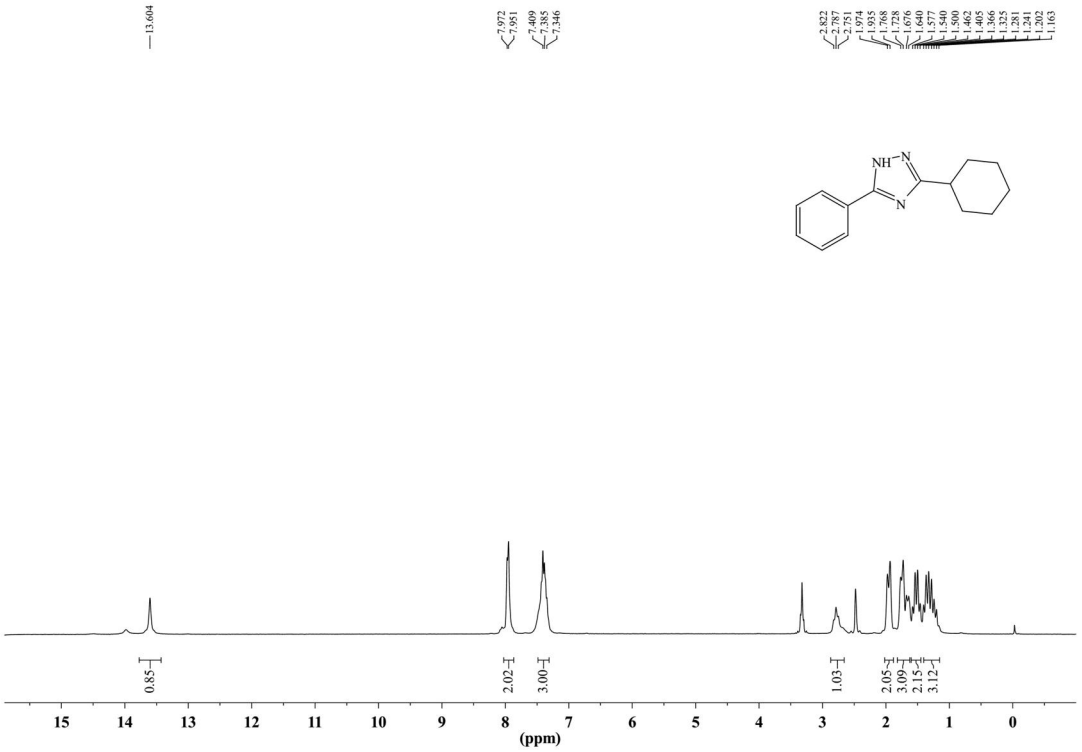

163.306
162.074
156.181
154.976
137.541
137.151
132.022
131.015
130.601
129.851
129.583
128.179
126.773
22.554
21.421
NH
N
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

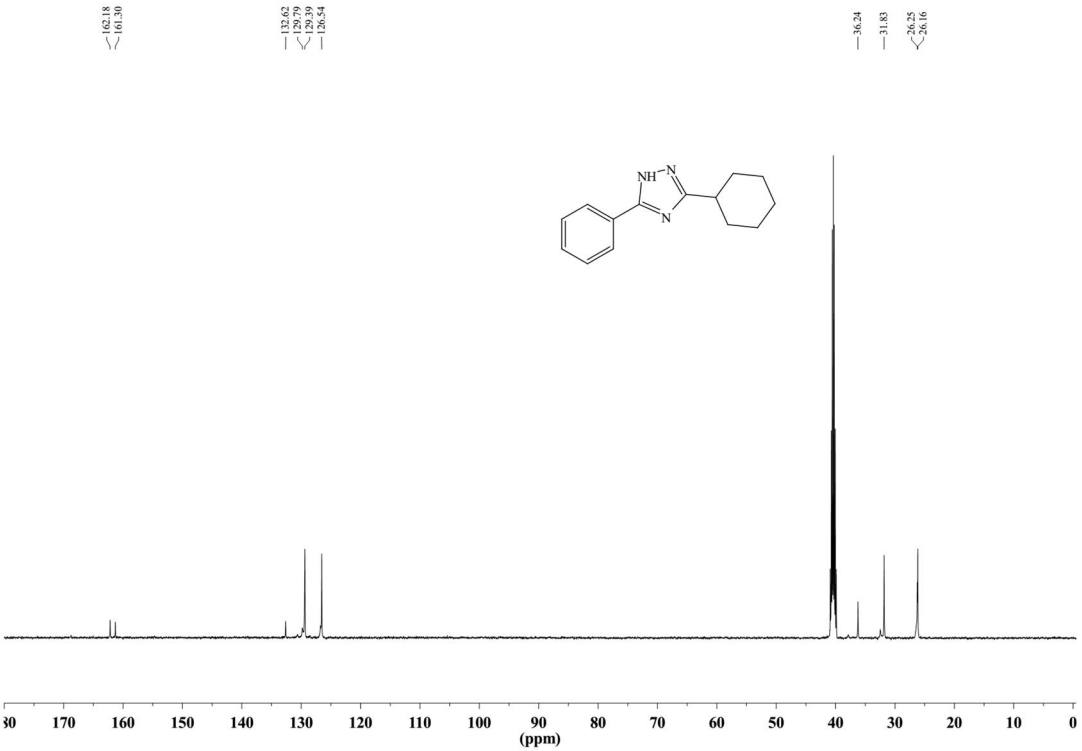
5af


14.692
14.400
8.387
8.067
8.051
7.937
7.852
7.838
7.686
7.671
7.577
7.562
7.546
7.537
7.512
7.496
7.480
7.437
NH
N
N
Cl
1.00
0.93
3.98
1.04
0.94
1.01
11.05
(ppm)

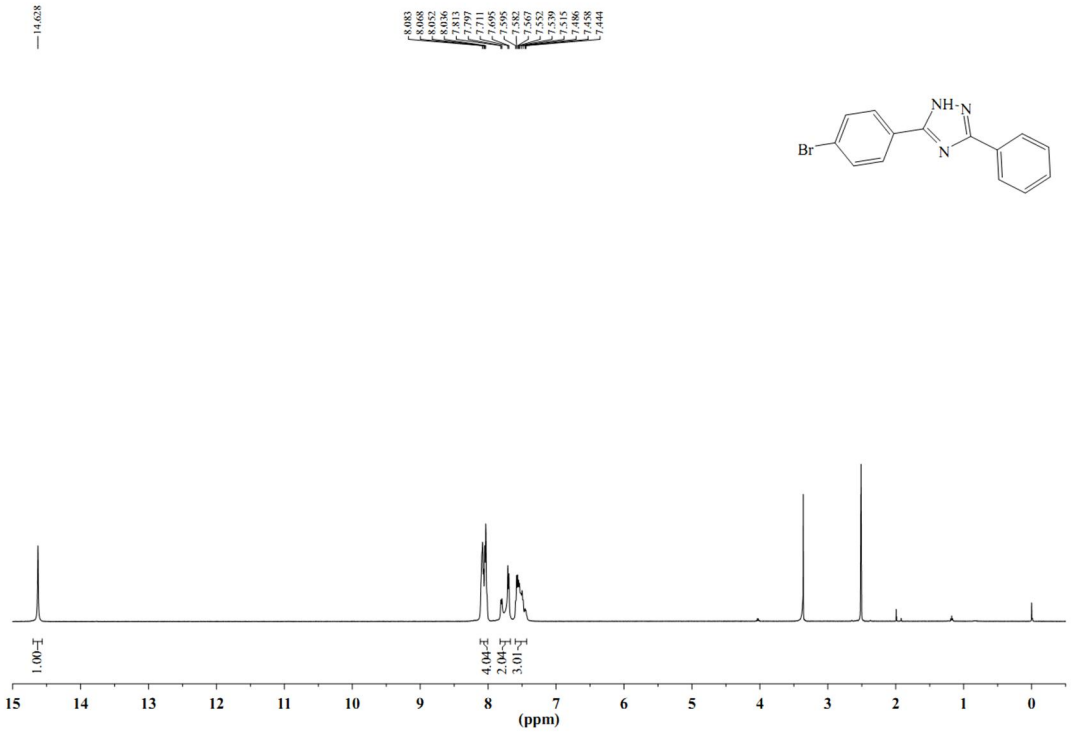

162.173
161.065
155.362
153.582
132.543
132.422
132.265
132.028
131.167
129.971
129.569
128.389
127.977
127.046
126.771
NH
N
N
Cl
(ppm)

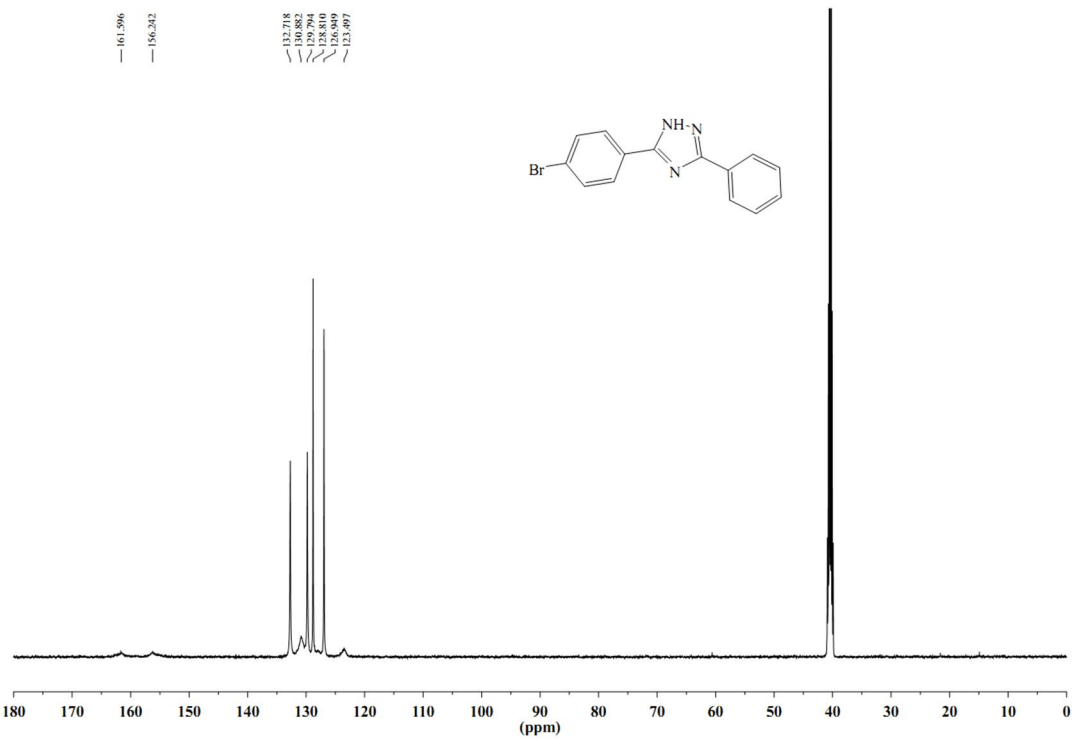
5ag


13.604
7.972
7.951
7.409
7.385
7.346
2.822
2.787
2.751
1.974
1.935
1.768
1.728
1.706
1.640
1.577
1.540
1.500
1.462
1.405
1.366
1.325
1.281
1.241
1.202
1.163
NH
N
N
0.85
2.02
3.00
1.03
2.05
3.09
2.15
3.12
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)

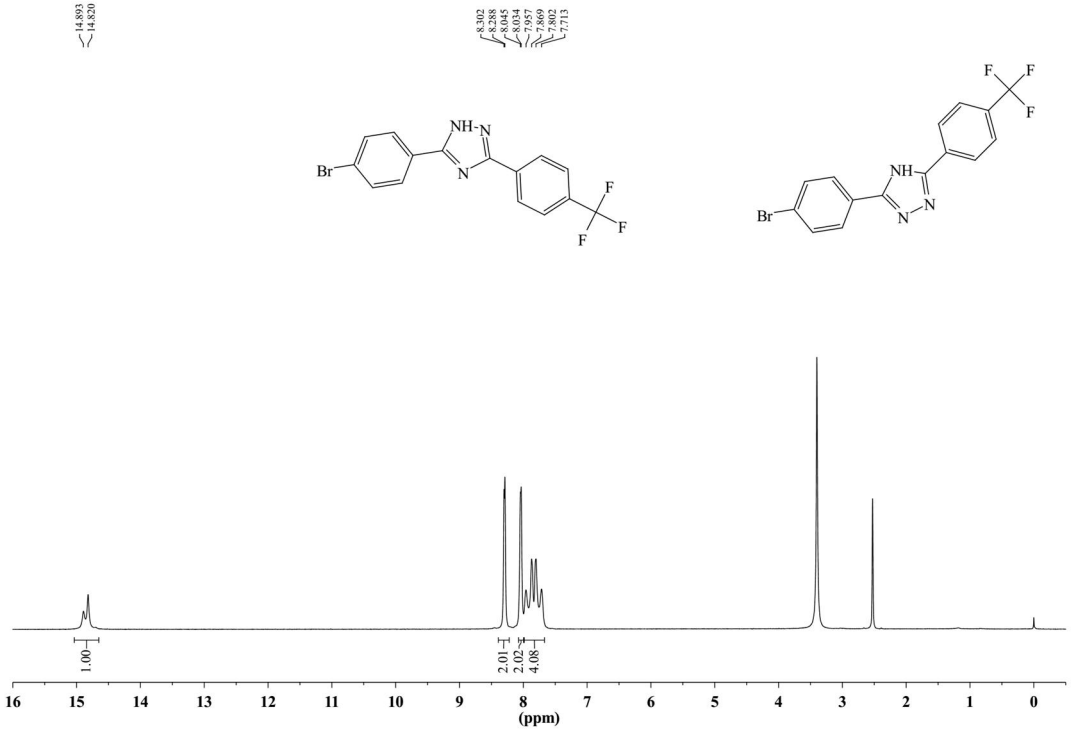

162.18
161.30
132.62
129.79
129.39
126.54
36.24
31.83
26.25
26.16
NH
N
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

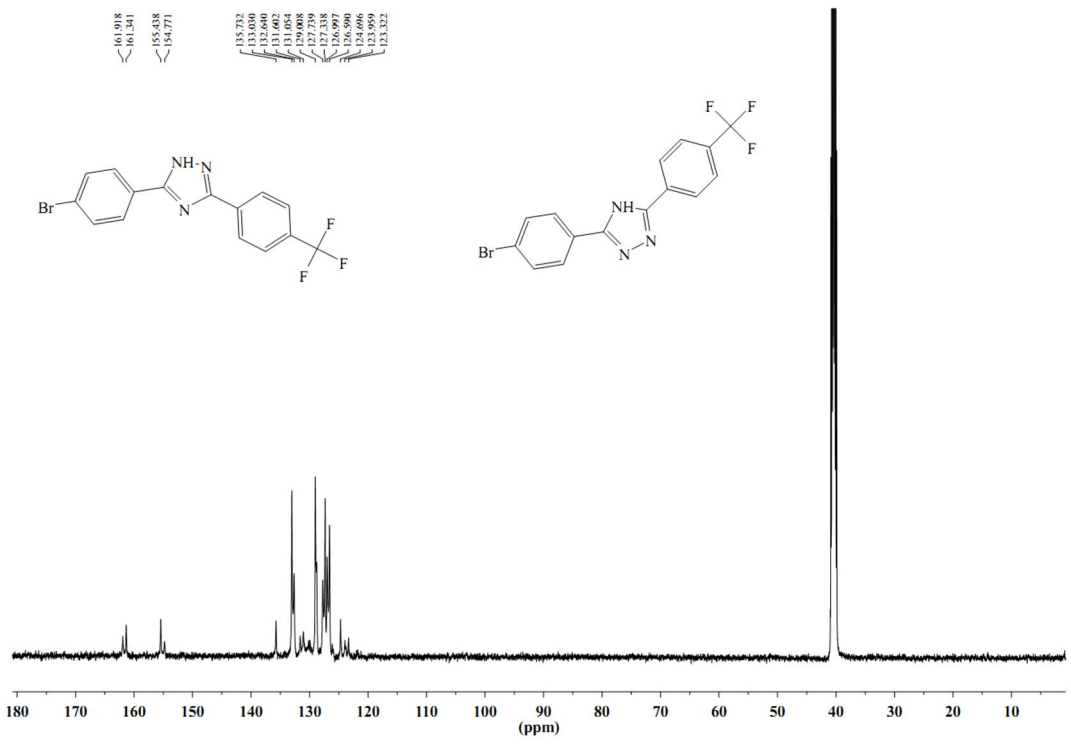
5ah


14.628
8.083
8.068
8.052
8.036
7.813
7.797
7.711
7.695
7.595
7.582
7.567
7.552
7.539
7.515
7.486
7.458
7.444
NH
N
N
Br
1.00
4.04
2.04
3.01
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)

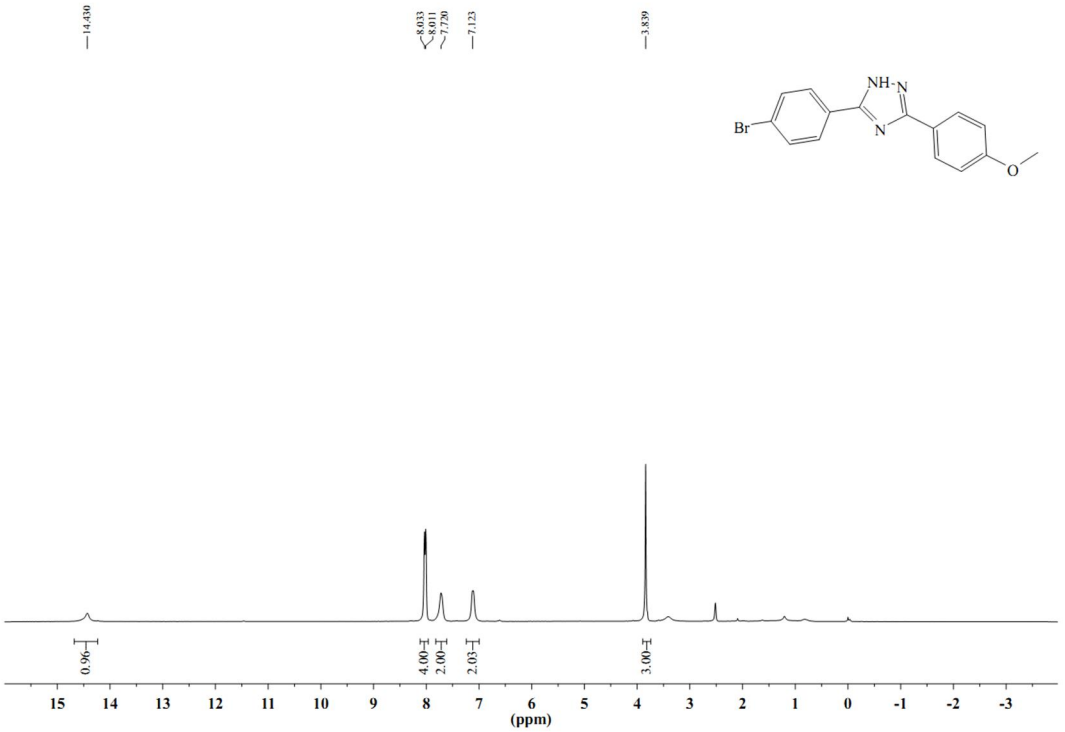

161.596
156.242
132.718
130.882
129.794
128.810
126.949
123.497
NH
N
N
Br
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

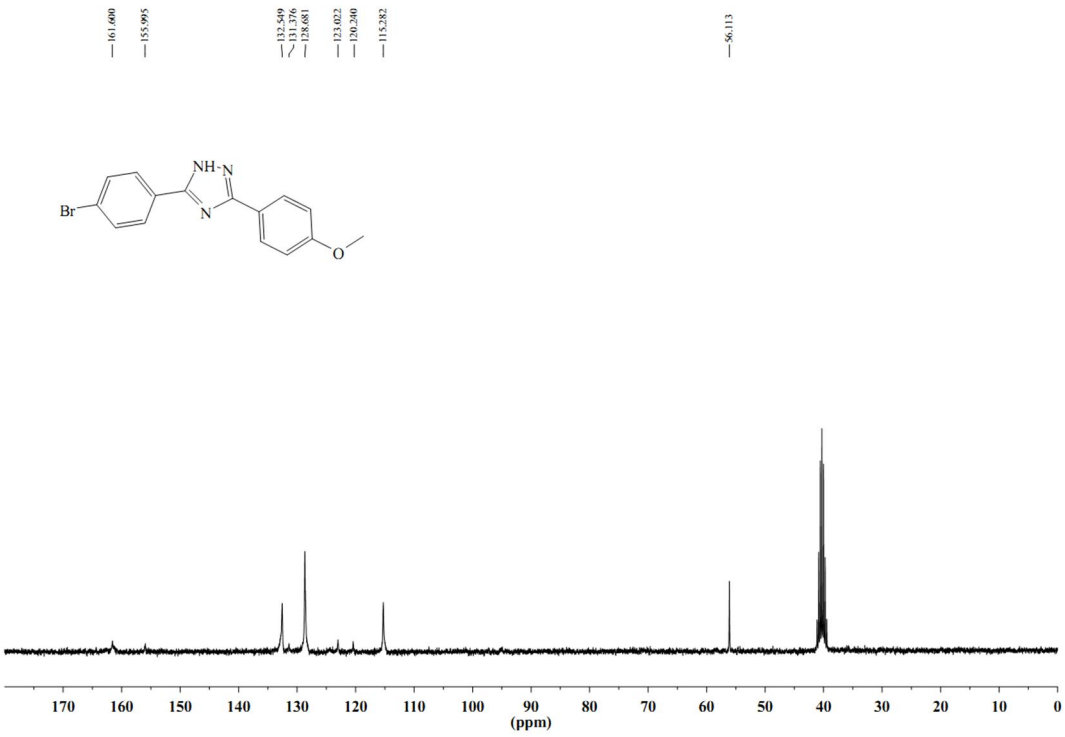
5ba


14.893
14.820
8.302
8.288
8.045
8.034
7.957
7.869
7.802
7.713
NH
N
N
Br
F
F
F
1.00
2.01
2.02
4.08
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)

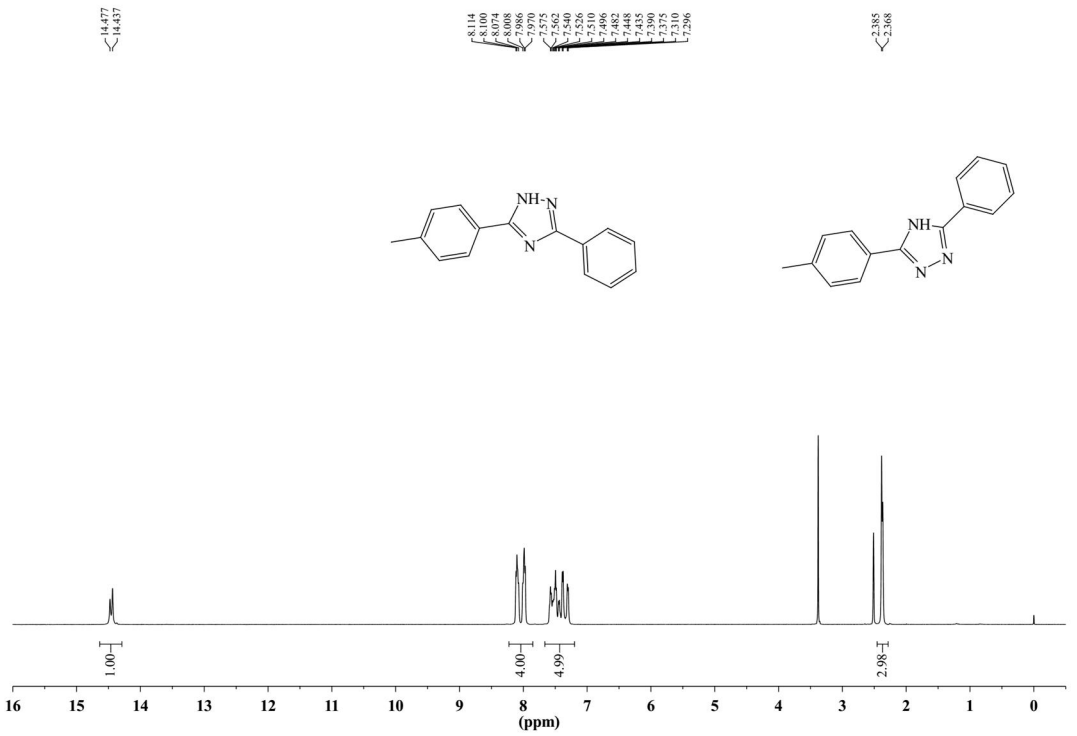

161.918
161.341
155.438
154.771
135.732
133.030
132.640
131.662
131.054
129.008
127.739
127.338
126.997
126.990
124.606
123.959
123.322
NH
N
N
Br
F
F
F
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

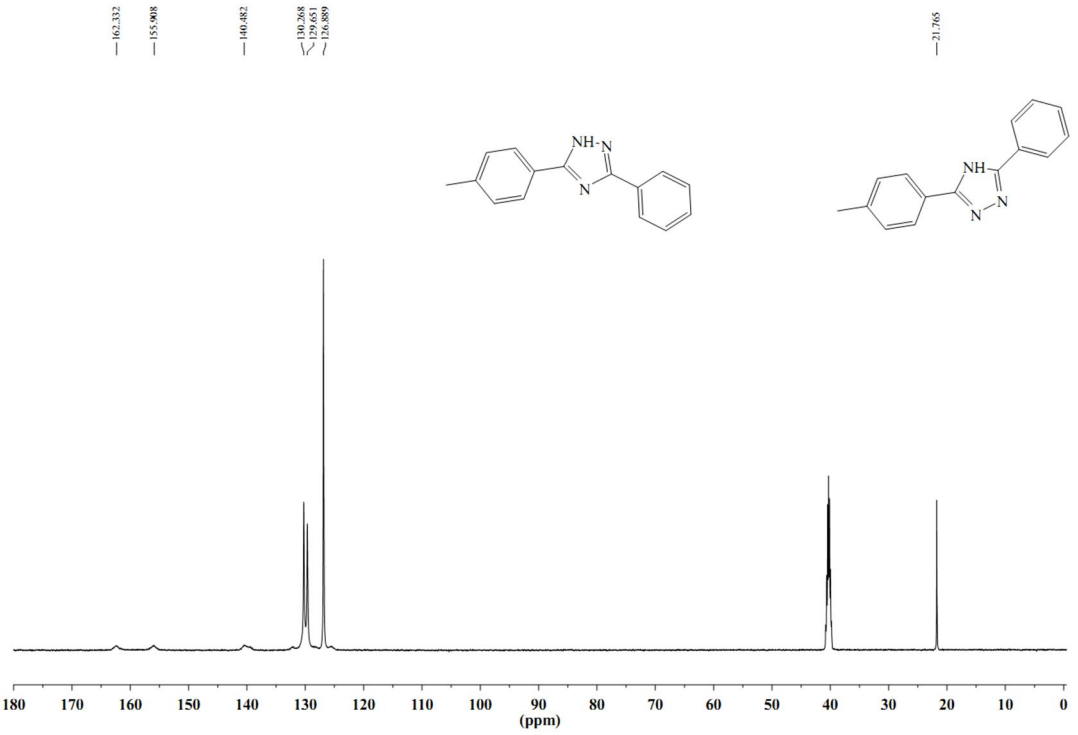
5bc


14.430
8.033
8.011
7.730
7.123
3.839
NH
N
Br
N
O
0.96
4.00
2.00
2.03
3.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
(ppm)

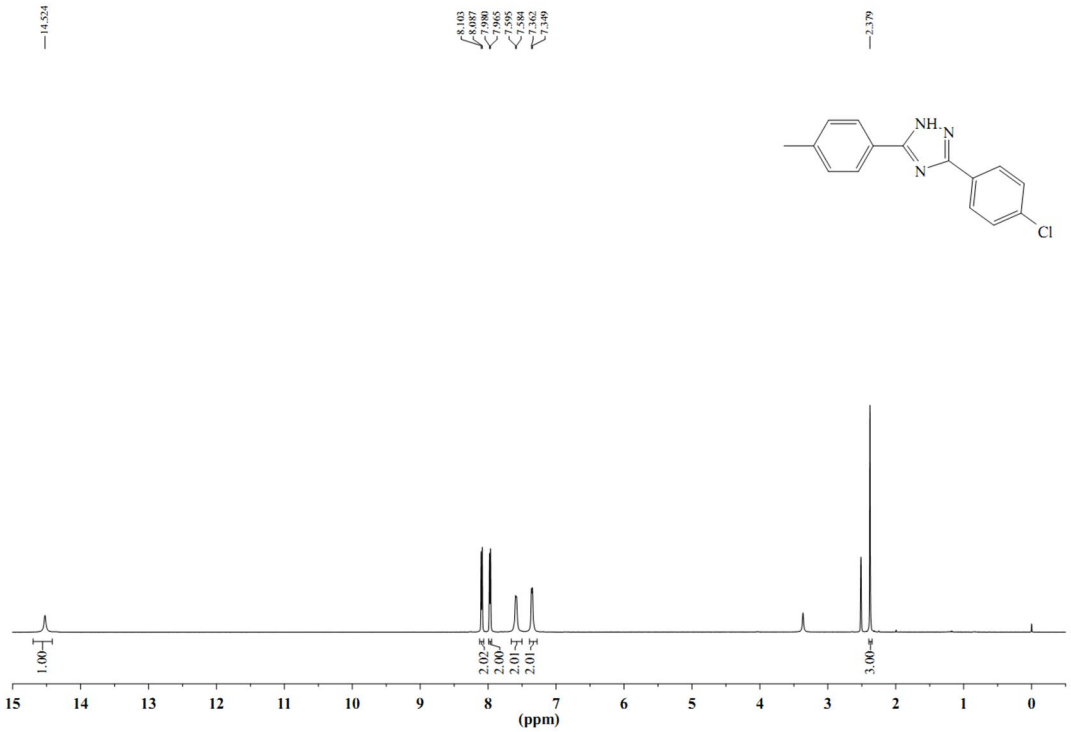

161.690
155.995
132.549
131.376
128.681
123.022
120.240
115.282
56.113
NH
N
Br
N
O
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

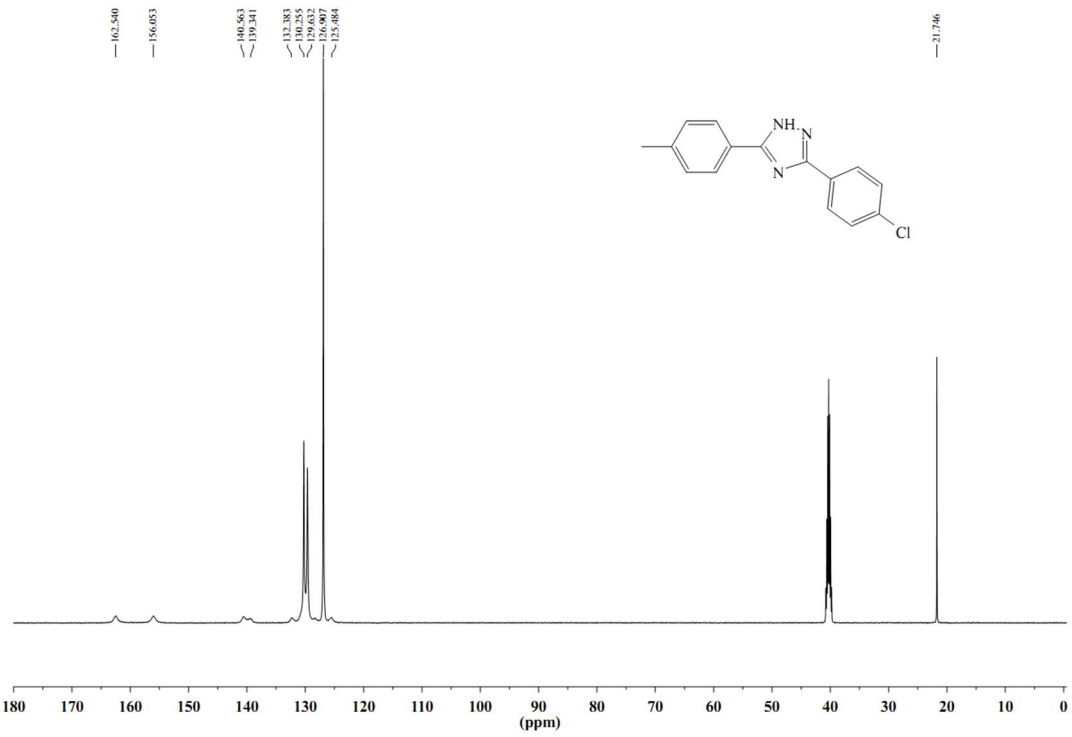
5bd


14.477
14.437
8.114
8.100
8.074
8.008
7.986
7.970
7.575
7.560
7.540
7.526
7.510
7.496
7.482
7.448
7.435
7.390
7.375
7.310
7.296
2.385
2.368
NH
N
N
1.00
4.00
4.99
2.98
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
(ppm)

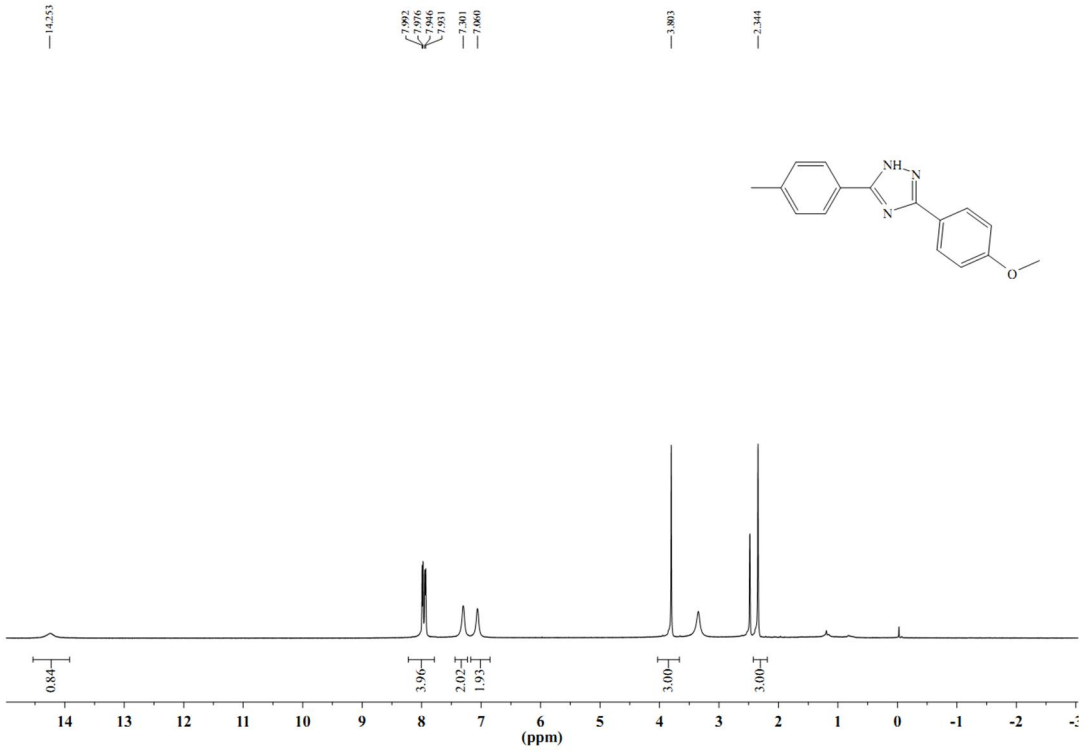

162.332
155.908
140.482
130.268
129.651
126.889
21.765
NH
N
N
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)

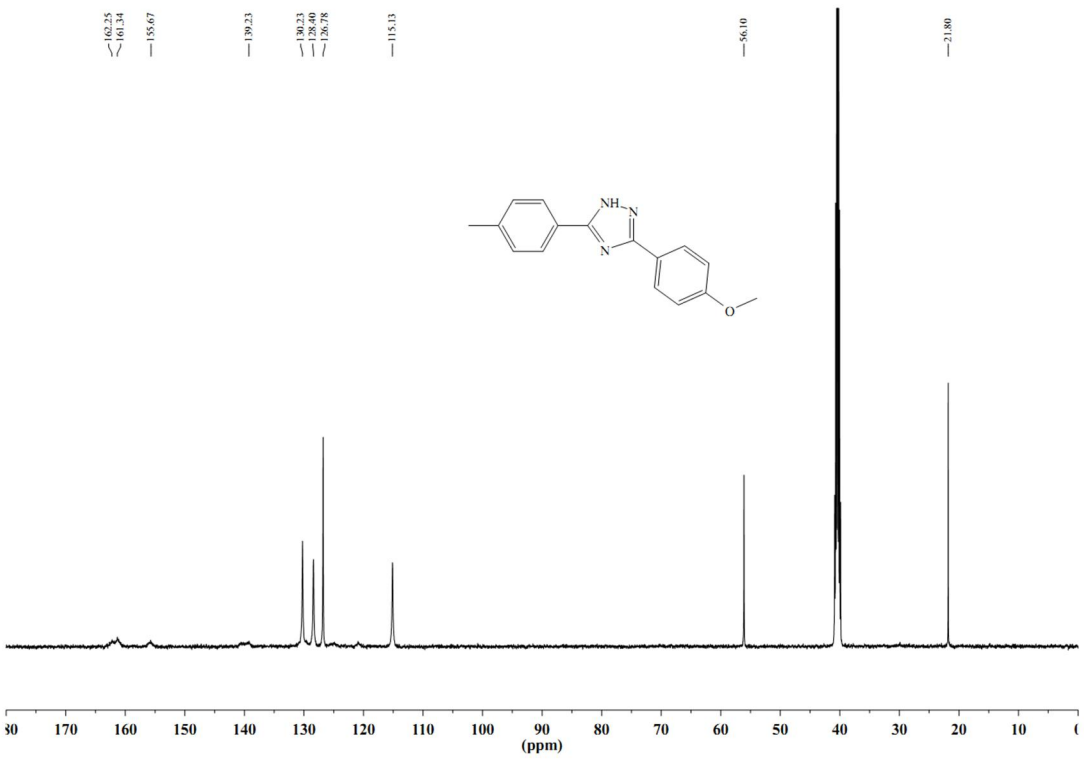
5ca


14.524
8.103
8.087
7.980
7.965
7.595
7.584
7.362
7.349
2.379
NH
N
N
Cl
1.00
2.02
2.00
2.01
2.01
3.00
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
(ppm)

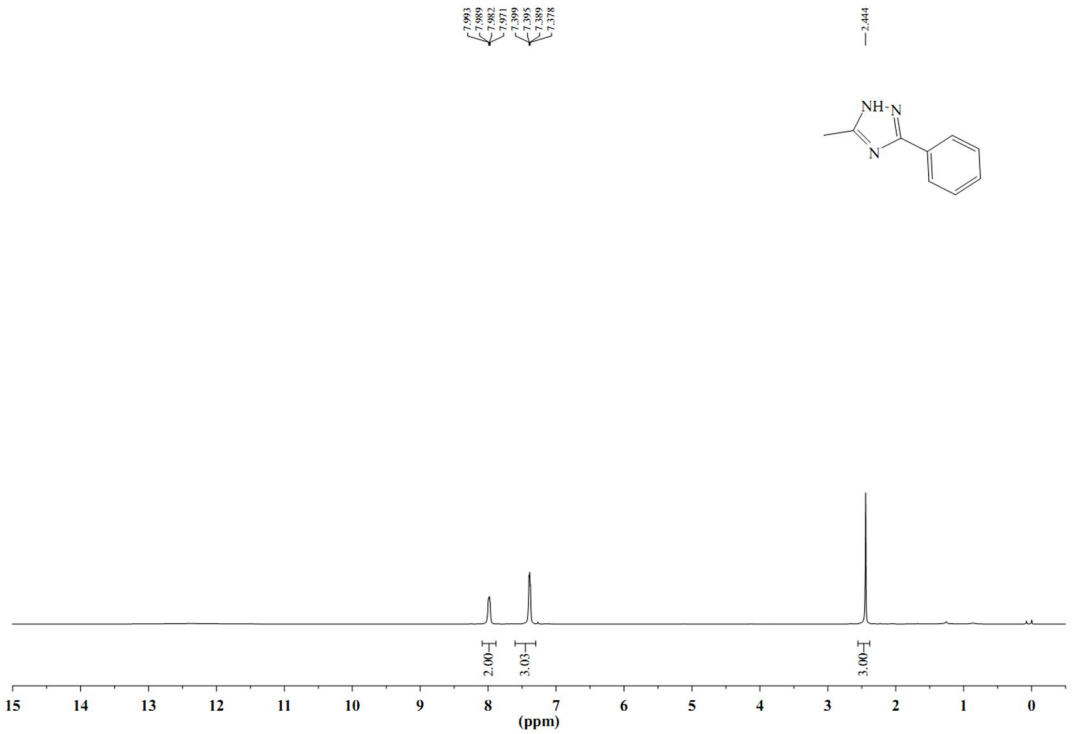

162.540
156.053
140.563
139.341
132.383
130.255
129.632
126.907
125.484
21.746
NH
N
N
Cl
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

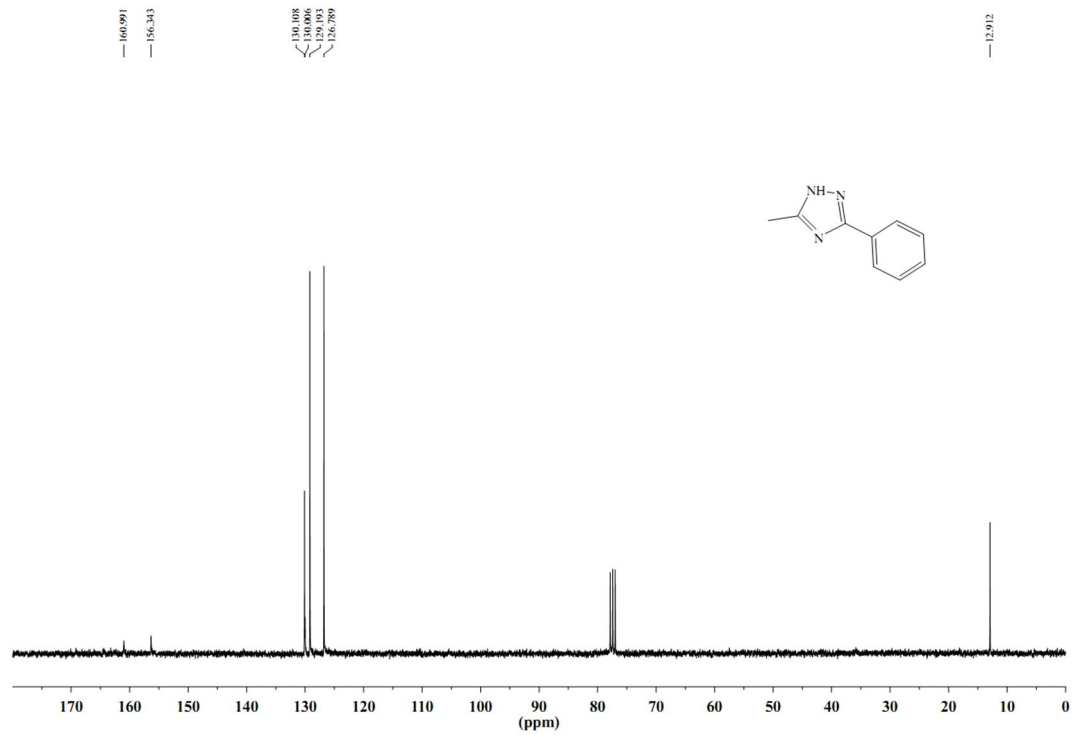
5cb


14.253
7.992
7.976
7.946
7.931
7.301
7.060
3.803
2.344
NH
N
N
O
0.84
3.96
2.02
1.93
3.00
3.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2
(ppm)


162.25
161.34
155.67
139.23
130.23
128.40
126.78
115.13
56.10
21.80
NH
N
N
O
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

5cd


7.993
7.989
7.982
7.971
7.399
7.395
7.389
7.378
2.444
NH
N
N
2.00
3.03
3.00
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
(ppm)


160.991
156.343
130.108
130.006
129.193
126.789
12.912
NH
N
N
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

5da

References

(1) (a) Y. Wang, H. G. Wang, J. Q. Peng and Q. Zhu, *Org. Lett.*, 2011, **13**, 4604-4607; (b) Y. Nishimura and Y. Yasui, *Tetrahedron*, 2012, **68**, 3342–3350.

(2) M. M. Guru and T. Punniyamurthy, *J. Org. Chem.*, 2012, **77**, 5063–5073.

(3) S. Ueda and H. Nagasawa, *J. Am. Chem. Soc.*, 2009, **131**, 15080–15081.

(4) (a) O. R. Gautun and R. J. Carlesen. *Molecules*, 2001, **6**, 969–978; (b) O. S. Amedeo, C. Pietro and G. Giulio, *J. Med. Chem.*, 1983, **26**, 1187–1192; (c) J. Glinka, D. Fiscus, C. B. Rao and H. Shechter, *Tetrahedron Lett.*, 1987, **28**, 3221–3224.