Acid Promoted Metal Free Synthesis of Trizole-Fused Heterocycles *via* Intramolecular [3+2] Cycloaddition

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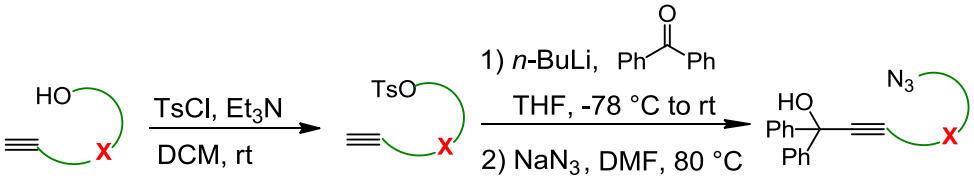
Supporting Information

General information

All chemicals and solvents were of analytical grade and were used without further purifications. All reactions were conducted in oven-dried (135 ℃) glassware under an inert atmosphere of dry nitrogen. The progress of reactions was monitored by silica gel thin layer chromatography (TLC) plates (mesh size 60Å, MERCK). Products were purified by flash column chromatography (FCC) on 40-63 m silica gel 60 (MERCK). ^{1}H and ^{13}C NMR were recorded on Bruker AV-400(400 MHz) or JEOL JNM-ECP500 spectrometer (400MHz or 500MHz for ^{1}H NMR, 100MHz or 126 MHz for ^{13}C NMR). Chemical shifts are reported as δ values in ppm and calibrated by residual solvent peak or tetramethylsilane (δ 0 for ^{1}H NMR). Abbreviations are following: s (singlet), d (doublet), t (triplet), q (quartet), br (broad peak), m (complex multiplet). Mass spectra were measured on HP-1100 LC-MS spectrometer. X-ray crystallography was performed on Rigaku R-AXIS RAPID/S imaging plate diffractometer. Flush column chromatography was performed by MERCK Silica gel 60. The progress of reactions was monitored by silica gel thin layer chromatographyplates (MERCKTLC Silicagel 60 F_{254}). Phosphomolybdic acid ethanol solution, ninhydrin-acetic acid butanol solution and anisaldehyde-acetic acid-sulfuric acid ethanol solution were used as TLC stain.

Experimental Procedure of Azido-Propargyl Alcohol



15 X = CH_2
16 X = O
17 X = S

1 X = CH_2
3 X = O
5 X = S

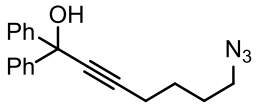
To a stirred solution of corresponding propargyl alcohol and TsCl in dichloromethane

was triethylamine added under nitrogen atmosphere. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography gave tosylate compound.

To a stirred solution of tosylate compound in dry THF under an atmosphere of nitrogen was added dropwise *n*-BuLi at -78 ℃ and the mixture was stirred for 10 min. Benzaldehyde was then added at same temperature. After 4h, the reaction was quenched with water. The mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$. The crude product can be used to the next step without further purification.

To a stirred solution of benzyl alcohols in DMF was added sodium azide at room temperature and the reaction mixture was heated to 50 ℃. After 20 min, the reaction mixture was diluted with ether and was washed with water and brined. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography gave azide as colorless oil.

7-azido-1,1-diphenylhept-2-yn-1-ol(1a)



1a

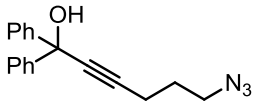
The reaction with tosylate compound(0.255 g, 1.07 mmol), *n*-BuLi (1.55 M in hexane, 0.729 mL, 1.15 mmol) and ketone (0.15 g, 0.823 mmol) in THF (8 mL) followed by followed by collected the organic layer under vacuum affording the product 0.45 g. [silica gel purification (ethyl acetate / hexane = 1 / 8 to 1/3)].

Colorless solid; R_f value 0.28(ethyl acetate/hexane = 1/3); ^{1}H NMR(500 MHz, $CDCl_3$) δ 7.78(d, 2H, *J* = 8.0 Hz), 7.60–7.57(m, 4H), 7.38–7.31(m, 6H), 7.28–7.25(m, 2H), 4.06(t, 2H, *J* = 6.5 Hz), 2.92(s, 1H, OH), 2.44(s, 3H), 2.34(t, 2H, *J* = 7.0 Hz), 1.82(tt, 2H, *J* = 6.5, 6.5 Hz), 1.63(tt, 2H, *J* = 6.5, 7.0 Hz); ^{13}C NMR(126 MHz, $CDCl_3$) δ 145.4, 144.8, 132.9, 129.9, 128.2, 127.8, 127.5, 125.9, 86.9, 83.9, 74.4, 69.9, 28.0, 24.3, 21.6, 18.3; HRMS (ESI) calcd for $C_{26}H_{26}O_4SNa$ $[M+Na]^+$457.14495, found 457.14440.

Then the crude benzyl alcohol with sodium azide (83.47 mg, 1.28 mmol) in DMF (20 ml) followed by silica gel column chromatography (ethyl acetate / hexane = 1/10 to 1/5) gave azide **1a** (0.108 g, 43%) as a colorless oil.

Colorless oil; R_f value 0.47(ethyl acetate/hexane = 1/5); ^{1}H NMR(500 MHz, $CDCl_3$) δ 7.60(m, 4H), 7.33(dd, 4H, *J* = 6.5, 6.5 Hz), 7.27(m, 2H), 3.31(t, 2H, *J* = 6.5 Hz), 2.76(s, 1H, OH), 2.40(t, 2H, *J* = 7.0 Hz), 1.66–1.76(m, 4H); ^{13}C NMR(126 MHz, $CDCl_3$) δ 145.3, 128.2, 127.6, 125.9, 87.2, 83.7, 74.4, 50.9, 28.0, 25.6, 18.5; HRMS (ESI) calcd for $C_{19}H_{19}N_3ONa$ $[M+Na]^+$ 328.1426, found 328.1424.

6-azido-1,1-diphenylhex-2-yn-1-ol (1b)



1b

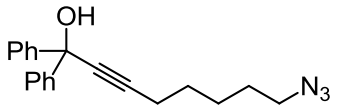
The reaction with tosylate (0.543 g, 2.15 mmol), *n*-BuLi (1.58 M in hexane, 1.46 mL, 2.30 mmol) and ketone (0.28 g, 1.54 mmol) in THF (15 mL) followed by followed by collected the organic layer under vacuum affording the product 2.2 g. [silica gel purification (ethyl acetate / hexane = 1 / 8 to 1/4)].

Colorless oil; R_f value 0.25(ethyl acetate/hexane = 1/4); IR (NaCl, neat) ν_{max} 3502, 3060, 3029, 2958, 1598, 1491, 1449, 1360, 1175 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$) δ 7.75(d, 2H, *J* = 7.5 Hz), 7.53(m, 4H), 7.23–7.32(m, 8H), 4.15(t, 2H, *J* = 6.0 Hz), 2.76(s, 1H), 2.43(t, 2H, *J* = 6.5 Hz), 2.39(s, 3H), 1.90(tt, 2H, *J* = 6.5, 6.0 Hz); ^{13}C NMR(126 MHz, $CDCl_3$) δ 145.1, 144.8, 132.8, 129.9, 128.2, 127.9, 127.6, 125.9, 85.5, 84.4, 74.3, 68.8, 27.7, 21.6, 15.2; LRMS (EI) 420(M^+, 0.8%), 403(5), 343(100), 220(53), 105(71); HRMS (EI) calcd for $C_{25}H_{24}O_4S$ (M^+) 420.1395, found 420.1397.

Then the crude benzyl alcohol with sodium azide (0.124 g, 1.9 mmol) in DMF (5 ml) followed by silica gel column chromatography (ethyl acetate / hexane = 1/10 to 1/5) gave azide **1b** (0.32 g, 70%) as a colorless oil.

Colorless oil; R_f value 0.50(ethyl acetate/hexane = 1/4); IR (NaCl, neat) ν_{max} 3426, 2933, 2099, 1490, 1449 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$) δ 7.59(m, 4H), 7.31(m, 4H), 7.27(m, 2H), 3.43(t, 2H, *J* = 6.5 Hz), 2.75(s, 1H), 2.48(t, 2H, *J* = 7.0 Hz), 1.85(tt, 2H, *J* = 7.0, 6.5 Hz); ^{13}C NMR(126 MHz, $CDCl_3$) δ 145.2, 128.2, 127.6, 125.9, 86.2, 84.2, 74.4, 50.2, 27.7, 16.2; HRMS (CI) calcd for $C_{18}H_{18}N_3O$ $[M+H]^+$ 292.1450, found 292.1455.

8-azido-1,1-diphenyloct-2-yn-1-ol（1c）



1c

To a stirred solution of hept-6-yn-1-ol (700.0 mg, 6.05 mmol) and TsCl (1.27 mg, 6.66 mmol) in dichloromethane (6 ml) was added triethylamine (1.01 mL, 7.26 mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate/ Petroleum ether = 1/25) gave tosylate compound **15c** (1.15 g, 71.7%) as a colorless oil.

Colorless oil; R_f value 0.63(ethyl acetate/Petroleum ether = 1/5); ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, 2H , *J* = 8.4 Hz), 7.34 (d, 2H, *J* = 8.0 Hz), 4.02 (t, 2H, *J* = 6.4 Hz), 2.45 (s, 3H), 2.14 (td, 2H, *J* = 6.8, 2.4 Hz), 1.92 (t, 1H, *J* = 2.4 Hz), 1.66 (tt, 2H, *J* = 6.8，6.8 Hz), 1.51-1.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 133.1, 129.8,

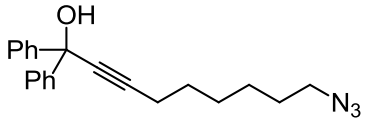
127.9, 84.0, 70.3, 68.5, 28.3, 27.7, 24.5, 21.7, 18.2; HRMS (ESI) calcd for $C_{14}H_{19}O_3S$ $[M+H]^+$ 267.1055, found 267.1048.

The reaction with tosylate **15c** (0.25 g, 1.37 mmol), *n*-BuLi (1.58 M in hexane, 1.20 mL, 1.92 mmol) and ketone (0.475 g, 1.78 mmol) in THF (15 mL) followed by collected the organic layer under vacuum affording the product 0.581 g.

Then the crude benzyl alcohol with sodium azide (0.101 g, 1.56 mmol) in DMF (5 ml) followed by silica gel column chromatography (ethyl acetate/ petroleum ether= 20/1 to 10/1) gave azide **1c** (0.331 g, 80%) as a colorless oil.

R*f* value 0.475(ethyl acetate/petroleum ether = 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 4H, *J* = 7.2 Hz), 7.34 (dd, 4H, *J* = 7.2, 7.6 Hz), 7.27–7.24 (m, 2H), 3.26 (t, 2H, *J* = 6.4 Hz), 2.76 (s, 1H), 2.37 (t, 2H, *J* = 7.0 Hz), 1.64–1.59 (m, 4H), 1.55–1.48 (m, 2H)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 128.1, 127.5, 125.9, 87.6, 83.5, 74.4, 51.2, 28.3, 28.0, 25.9, 18.7； HRMS (ESI) calcd for $C_{20}H_{22}N_3O$ $[M+H]^+$ 320.1763, found 320.1763.

9-azido-1,1-diphenylnon-2-yn-1-ol（1d）



1d

To a stirred solution of oct-7-yn-1-ol (0.4g，3.46mmol) and TsCl (0.725g，3.80mmol) in dichloromethane (30 ml) was added triethylamine (0.577mL，420mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate/ Petroleum ether= 1/40 to 1/30) gave tosylate compound **15d** (0.721 g, 78%) as a colorless oil.

Colorless oil; R_f value 0.55(ethyl acetate/ Petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, 2H , *J* = 8.4 Hz), 7.34 (d, 2H, *J* = 8.0 Hz), 4.02 (t, 2H, *J* = 6.4 Hz), 2.45 (s, 3H), 2.14 (td, 2H, *J* = 6.8, 2.4 Hz), 1.92 (t, 1H, *J* = 2.4 Hz), 1.68-1.63 (m, 2H), 1.50-1.44 (m, 2H), 1.38-1.32 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ145.4, 144.6, 128.0, 125.8, 87.3, 74.3, 70.2, 28.12, 27.6, 24.5, 21.5, 18.5; HRMS (ESI) calcd for $C_{15}H_{21}O_3S$ $[M+H]^+$ 281.1211, found 281.1216.

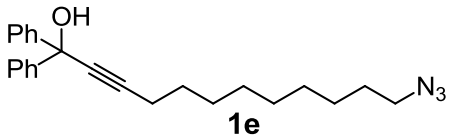
The reaction with tosylate **15d** (1.00 g, 2.74 mmol), *n*-BuLi (1.60 M in hexane, 2.40 mL, 3.84 mmol) and ketone (0.50 g, 1.78 mmol) in THF (27 mL) followed by collected the organic layer under vacuum affording the product 1.20 g.

Then the crude benzyl alcohol with sodium azide (0.200 g, 3.11 mmol) in DMF (5 ml)

followed by silica gel column chromatography (ethyl acetate/ petroleum ether= 20/1 to 10/1) gave azide **1d** (0.825 g, 95 %) as a colorless oil.

R*f* value 0.475(ethyl acetate/ petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 4H, *J* = 7.2 Hz), 7.32 (dd, 4H, *J* = 7.2, 7.6 Hz), 7.27 – 7.23 (m, 2H), 3.25 (t, 2H, *J* = 6.8 Hz), 2.79 (s, 1H), 2.36 (t, 2H, *J* = 6.8 Hz), 1.64 – 1.56 (m, 4H), 1.50 – 1.36 (m, 4H)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 128.1, 127.5, 125.9, 87.9, 83.3, 74.4, 51.3, 28.7, 28.32, 28.27, 26.1, 18.8； HRMS (ESI) calcd for $C_{21}H_{24}N_3O$ $[M+H]^+$ 334.1919, found 334.1914.

9-azido-1,1-diphenylnon-2-yn-1-ol（1e）



1e

To a stirred solution of oct-7-yn-1-ol (0.3 g，1.71 mmol) and TsCl (0.360 g，1.88 mmol) in dichloromethane (10 ml) was added triethylamine (0.285 mL，2.05 mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate / Petroleum ether = 1/100 to 1/60) gave tosylate compound **15e** (0.525 g, 95.1%) as a colorless oil.

Colorless oil; R_f value 0.47(ethyl acetate/ Petroleum ether= 1/10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, 2H , *J* = 8.4 Hz), 7.34 (d, 2H, *J* = 8.4 Hz), 4.01 (t, 2H, *J* = 6.8 Hz), 2.45 (s, 3H), 2.17 (td, 2H, *J* = 7.2, 2.4 Hz), 1.94 (t, 1H, *J* = 2.4 Hz), 1.66-1.59 (m, 2H), 1.54-1.46 (m, 2H), 1.37-1.32 (m, 2H), 1.30-1.23 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 133.2, 129.8, 127.8, 84.7, 70.6, 68.1, 29.2，28,9, 28.8，28.6, 28.4, 25.3, 21.6, 18.3; HRMS (ESI) calcd for $C_{18}H_{27}O_3S$ $[M+H]^+$ 323.1681, found 323.1685.

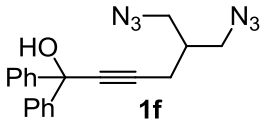
The reaction with tosylate **15e** (0.433g, 1.34 mmol), *n*-BuLi (1.60 M in hexane, 0.900 mL, 1.44 mmol) and ketone (0.188 g, 1.03 mmol) in THF (10 mL) followed by collected the organic layer under vacuum affording the product 0.470 g.

Then the crude benzyl alcohol with sodium azide (0.073g, 1.12 mmol) in DMF (5 ml) followed by silica gel column chromatography (ethyl acetate/petroleum ether = 20/1 to 10/1) gave azide **1e** (0.234 g, 67 %) as a colorless oil.

R*f* value 0.475(ethyl acetate/petroleum ether = 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 4H, *J* = 7.2 Hz), 7.32 (dd, 4H, *J* = 7.2, 8.0 Hz), 7.27–7.23 (m, 2H), 3.25 (t, 2H, *J* = 6.8 Hz), 2.74 (s, 1H), 2.34 (t, 2H, *J* = 6.8 Hz), 1.62–1.55 (m, 6H), 1.44–1.30 (m, 8H)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.5, 128.1, 127.4, 126.0, 88.2, 83.1, 74.4,

51.4, 29.3, 29.0, 28.9, 28.82, 28.78, 28.5, 26.7, 18.9；HRMS (ESI) calcd for $C_{24}H_{30}N_3O$ $[M+H]^+$ 376.2389, found 376.2389.

8-azido-1,1-diphenyloct-2-yn-1-ol（1f）



1f

To a stirred solution of 2-(prop-2-yn-1-yl)propane-1,3-diol (120.0 mg, 1.05 mmol) and TsCl (561.2 mg, 2.94 mmol) in dichloromethane (10 ml) was added triethylamine (0.511 mL, 3.68 mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate/ Petroleum ether= 1/40 to 1/15) gave tosylate compound (0.373g, 84%) as a colorless oil.

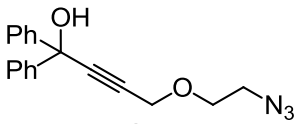
Colorless oil; R_f value 0.45(ethyl acetate/petroleum ether = 1/10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 2H , *J* = 8.0 Hz), 7.36 (d, 2H, *J* = 8.0 Hz), 4.02 (d, 4H, *J* = 2.8Hz), 2.46 (s, 6H), 2.24 (s, 3H), 1.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 132.2, 130.0, 127.9, 79.1, 71.1, 67.9, 37.3, 21.7, 17.2; HRMS (ESI) calcd for $C_{20}H_{23}O_6S$ $[M+H]^+$ 423.0936, found 423.0936.

The reaction with tosylate **15f** (0.334 g, 0.790 mmol), *n*-BuLi (1.60 M in hexane, 0.576 mL, 0.922 mmol) and ketone (0.120 g, 0.659 mmol) in THF (8 mL) followed by collected the organic layer under vacuum affording the product 0.370 g.

Then the crude benzyl alcohol with sodium azide (0.103 g, 1.59 mmol) in DMF (5 ml) followed by silica gel column chromatography (ethyl acetate/petroleum ether = 20/1 to 10/1) gave azide **1f** (0.148 g, 81%) as a colorless oil.

R*f* value 0.45(ethyl acetate/petroleum ether = 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, 4H, *J* = 6.4 Hz), 7.34 (dd, 4H, *J* = 7.2, 7.6 Hz), 7.28 (d, 2H, *J* = 6.4 Hz), 3.44 (d, 4H, *J* = 6.0 Hz), 2.74 (br, 1H), 2.49 (d, 2H, *J* = 6.8 Hz), 2.09–2.03 (m, 1H)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 128.3, 127.7, 125.9, 85.9, 83.8, 74.5, 52.0, 38.2, 19.6； HRMS (ESI) calcd for $C_{19}H_{19}N_6O$ $[M+H]^+$ 347.1620, found 347.1623.

4-(2-azidoethoxy)-1,1-diphenylbut-2-yn-1-ol (3a)



3a

To a stirred solution of 2-(prop-2-yn-1-yloxy)ethanol (0.7 g，6.99 mmol) and TsCl (1.60 g，8.39 mmol) in dichloromethane (10 ml) was added triethylamine (3.49 mL，

24.47 mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate/ Petroleum ether= 1/20 to 1/10 to 1/2) gave tosylate compound **16a** (1.62 g, 91%) as a colorless oil.

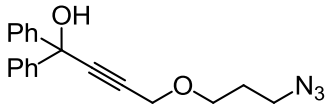
Colorless oil; R_f value 0.3(ethyl acetate/ Petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80(d, 2H , *J* = 8.0 Hz), 7.34 (d, 2H, *J* = 8.0 Hz), 4.19 (t, 2H, *J* = 4.8 Hz), 4.11 (s, 2H), 3.72 (t, 2H, *J* = 4.4 Hz), 2.44 (s, 3H), 2.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 132.9, 129.8, 127.9, 78.9, 75.0, 68.8, 67.1, 58.3, 21.6; HRMS (ESI) calcd for $C_{12}H_{14}O_4S$ $[M]^+$ 254.0613, found 254.0610.

The reaction with tosylate **16a** (1.09g，4.28mmol), *n*-BuLi (1.60 M in hexane, 2.88ml，4.61mmol) and ketone (0.6g，3.29mmol) in THF (33 mL) followed by collected the organic layer under vacuum affording the product 1.2 g.

Then the crude benzyl alcohol with sodium azide (0.214g, 3.3 mmol) in DMF (5 ml) followed by silica gel column chromatography (ethyl acetate/ petroleum ether= 20/1 to 10/1) gave azide **3a** (0.625 g, 74 %) as a colorless oil.

R*f* value 0.35(ethyl acetate/ petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 4H, *J* = 7.6 Hz), 7.34 (dd, 4H, *J* = 7.2, 7.6 Hz), 7.27 (d, 2H, *J* = 7.2 Hz), 4.38 (s, 2H), 3.73 (t, 2H, *J* = 4.8 Hz), 3.42 (t, 2H, *J* = 4.8 Hz), 2.82 (br, 1H)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 128.3, 127.8, 125.9, 89.5, 82.8, 74.4, 68.5, 58.8, 50.6； HRMS (ESI) calcd for $C_{18}H_{17}N_3O_2Na$ $[M+Na]^+$ 330.1218, found 330.1217.

4-(3-azidopropoxy)-1,1-diphenylbut-2-yn-1-ol（3b）



3b

To a stirred solution of 3-(prop-2-yn-1-yloxy)propan-1-ol (0.8 g，7.01 mmol) and TsCl (1.60 g，8.41 mmol) in dichloromethane (10 ml) was added triethylamine (3.50 mL，24.53 mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate/ Petroleum ether= 1/20 to 1/10 to 1/2) gave tosylate compound **16b** (1.57 g, 83%) as a colorless oil.

Colorless oil; R_f value 0.3(ethyl acetate/ Petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79(d, 2H , *J* = 8.4 Hz), 7.35 (d, 2H, *J* = 8.0 Hz), 4.13 (t, 2H, *J* = 6.4 Hz), 4.03 (s, 2H), 3.53 (t, 2H, *J* = 6.0 Hz), 2.43 (s, 3H), 2.40 (s, 1H), 1.93 (tt, 2H, *J* = 6.0, 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ144.7, 133.0, 129.8, 127.9, 79.4, 74.5, 67.5, 65.4, 58.2, 29.1, 21.6; HRMS (ESI) calcd for $C_{13}H_{17}O_4S$ $[M+H]^+$ 269.0848, found

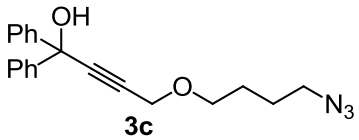
269.0844.

The reaction with tosylate **16b** (1.04g，3.89mmol), *n*-BuLi (1.60 M in hexane, 2.62ml，4.19mmol) and ketone (0.545g，2.99mmol) in THF (33 mL) followed by collected the organic layer under vacuum affording the product 1.15g.

Then the crude benzyl alcohol with sodium azide (0.200g, 3.06mmol) in DMF (5 ml) followed by silica gel column chromatography (ethyl acetate/ petroleum ether= 10/1 to 5/1) gave azide **3b** (0.730 g, 89 %) as a colorless oil.

R*f* value 0.38(ethyl acetate/ petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 4H, *J* = 7.6 Hz), 7.34 (dd, 4H, *J* = 7.2, 7.6 Hz), 7.28 (d, 2H, *J* = 7.2 Hz), 4.31 (s, 2H), 3.63 (t, 2H, *J* = 6.0 Hz), 3.42 (t, 2H, *J* = 6.4 Hz), 2.93 (br, 1H)，1.86 (tt, 2H, *J* = 6.0, 6.4 Hz)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 128.2, 127.7, 125.9, 89.1, 83.1, 74.2, 66.5, 58.5, 48.2, 28.9；HRMS (ESI) calcd for $C_{19}H_{19}N_3O_2Na$ $[M+Na]^+$ 344.1375, found 344.1373.

4-(4-azidobutoxy)-1,1-diphenylbut-2-yn-1-ol（3c）



3c

To a stirred solution of 4-(prop-2-yn-1-yloxy)butan-1-ol (1.57 g，12.25 mmol) and TsCl (2.80 g，14.70 mmol) in dichloromethane (10 ml) was added triethylamine 6.11 mL，42.87 mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate/ Petroleum ether= 1/15 to 1/10) gave tosylate compound **16c** (2.75 g, 80%) as a colorless oil.

Colorless oil; R_f value 0.40(ethyl acetate/ Petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78(d, 2H , *J* = 8.4 Hz), 7.34 (d, 2H, *J* = 8.0 Hz), 4.08-4.03 (m, 4H), 3.47 (t, 2H, *J* = 6.0 Hz), 2.45 (s, 3H), 2.40 (s, 1H), 1.78-1.71 (m, 2H), 1.65-1.58 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 133.1, 129.8, 127.8, 79.7, 74.3, 70.3, 68.9, 58.0, 25.7, 25.4, 21.6; HRMS (ESI) calcd for $C_{14}H_{19}O_4S$ $[M+H]^+$ 283.1004, found 283.1008.

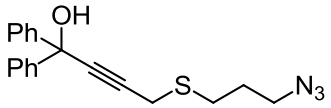
The reaction with tosylate **16c** (1.01g，3.57mmol), *n*-BuLi (1.60 M in hexane, 2.40ml，3.84mmol) and ketone (0.500g，2.74mmol) in THF (27 mL) followed by collected the organic layer under vacuum affording the product 0.945g.

Then the crude benzyl alcohol with sodium azide (0.159g, 2.44mmol) in DMF (5 ml) followed by silica gel column chromatography (ethyl acetate/ petroleum ether= 20/1

to 8/1) gave azide **3c** (0.532 g, 78 %) as a colorless oil.

R*f* value 0.39(ethyl acetate/ petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 4H, *J* = 7.6 Hz), 7.34 (dd, 4H, *J* = 7.2, 7.6 Hz), 7.28 (d, 2H, *J* = 7.2 Hz), 4.30 (s, 2H), 3.57 (t, 2H, *J* = 6.0 Hz), 3.27 (t, 2H, *J* = 6.4 Hz), 2.87 (br, 1H)，1.67 (tt, 4H, *J* = 6.4, 6.0 Hz)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 128.2, 127.6, 125.9, 88.9, 83.3, 74.2, 69.2, 58.3, 51.0, 26.5, 25.6； HRMS (ESI) calcd for $C_{20}H_{21}N_3O_2Na$ $[M+Na]^+$ 358.1531, found 358.1527.

4-(3-azidopropoxy)-1,1-diphenylbut-2-yn-1-ol（5）



5

To a stirred solution of 3-(prop-2-yn-1-ylthio)propan-1-ol (0.680g，5.22mmol) and TsCl (1.19 g，6.27 mmol) in dichloromethane (10 ml) was added triethylamine (1.44 mL，18.28 mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate/ Petroleum ether= 1/25 to 1/10) gave tosylate compound **17** (1.17 g, 79%) as a colorless oil.

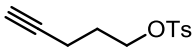
Colorless oil; R_f value 0.42(ethyl acetate/ Petroleum ether= 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79(d, 2H , *J* = 8.4 Hz), 7.35 (d, 2H, *J* = 8.4 Hz), 4.15 (t, 2H, *J* = 6.4 Hz), 3.18 (s, 2H), 2.73 (t, 2H, *J* = 6.0 Hz), 2.45 (s, 3H), 2.22 (s, 1H), 1.96 (tt, 2H, *J* = 6.0, 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 132.8, 129.8, 127.8, 79.5, 71.2, 68.6, 28.1, 27.3, 21.6, 19.0; HRMS (ESI) calcd for $C_{13}H_{17}O_3S_2$ $[M+H]^+$ 285.0619, found 285.0619.

The reaction with tosylate **17** (0.594g，2.09mmol), *n*-BuLi (1.60 M in hexane, 1.41mL，2.25mmol) and ketone (0.293g，1.61mmol) in THF (16 mL) followed by collected the organic layer under vacuum affording the product 0.69g.

Then the crude benzyl alcohol with sodium azide (0.155g, 3.06mmol) in DMF (5 ml) followed by silica gel column chromatography (ethyl acetate/ petroleum ether= 10/1 to 5/1) gave azide **5** (0.320 g, 64%) as a colorless oil.

R*f* value 0.40(ethyl acetate/petroleum ether = 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, 4H, *J* = 7.6 Hz), 7.33 (dd, 4H, *J* = 7.2, 7.6 Hz), 7.28 (d, 2H, *J* = 7.2 Hz), 3.42 (s, 2H), 3.35 (t, 2H, *J* = 6.4 Hz), 2.74 (t, 2H, *J* = 6.8 Hz), 1.86 (tt, 2H, *J* = 6.8, 6.4 Hz)； ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 128.2, 127.7, 125.9, 86.0, 83.3, 74.4, 49.9, 28.7, 28.2, 19.7； HRMS (ESI) calcd for $C_{19}H_{20}N_3OS$ $[M+H]^+$338.1327, found 338.1325.

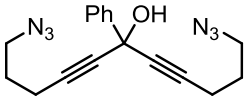
pent-4-yn-1-yl 4-methylbenzenesulfonate



To a stirred solution of 4-pentyn-1-ol **1** (100.0 mg, 1.19 mmol) and TsCl (249.3 mg, 1.31 mmol) in dichloromethane (12 ml) was added dropwise triethylamine (0.2 mL, 1.43 mmol) at 0 ℃, then reaction mixture was allowed to warm up to ambient temperature. After 2 h, the mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$ followed by silica gel column chromatography (ethyl acetate / hexane = 1/10) gave tosylate (220 mg, 77.7%) as a colorless oil.

Colorless oil; R_f value 0.53(ethyl acetate / hexane = 1/3);IR (NaCl, neat) ν_{max} = 3291, 2962, 1598, 1360, 1176 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, 2H, *J* = 8.5 Hz), 7.35 (d, 2H, *J* = 8.5 Hz), 4.14 (t, 2H, *J* = 6.0 Hz), 2.45 (s, 3H), 2.25 (td, 2H, *J* = 6.5, 2.5 Hz), 1.88 (t, 1H, *J* = 2.5 Hz), 1.86 (tt, 2H, *J* = 6.5, 6.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.8, 132.9, 129.8, 127.9, 82.1, 69.4, 68.7, 27.7, 21.6, 14.7; HRMS (ESI) calcd for $C_{12}H_{14}O_3SNa$ $[M+Na]^+$ 261.0561, found 261.0561.

1,11-diazido-6-phenylundeca-4,7-diyn-6-ol(7a)



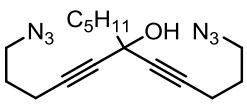
7a

The reaction with pent-4-yn-1-yl 4-methylbenzenesulfonate (1.19 g, 4.98 mmol), *n*-BuLi (1.55 M in hexane, 3.49 mL, 5.23 mmol) and chloride (0.35 g, 2.49 mmol) in THF (25 mL) followed by followed by collected the organic layer under vacuum affording the crude product 2.89 g. The crude product can be used to the next step without further purification.

Then the crude benzyl alcohol with sodium azide (388.5 mg, 5.98 mmol) in DMF (25 ml) followed by silica gel column chromatography (ethyl acetate / hexane = 1/20 to 1/10 to 1/2) gave azide **7a** (0.724 g, 90%) as a colorless oil.

Colorless oil; R_f value 0.51(ethyl acetate/hexane = 1/2); IR (NaCl, neat) ν_{max} 3398, 2935, 2099, 1449, 1255 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$) δ 7.76(m, 2H), 7.35–7.41(m, 3H), 3.41(t, 4H, *J* = 7.0 Hz), 2.86(m, 1H, OH), 2.42(t, 4H, *J* = 7.0 Hz), 1.82(tt, 4H, *J* = 7.0, 7.0 Hz); ^{13}C NMR(126 MHz, $CDCl_3$) δ 142.4, 128.5, 128.4, 125.6, 83.9, 82.0, 65.0, 50.1, 27.5, 16.1; HRMS (ESI) calcd for $C_{17}H_{18}N_6ONa$ $[M+Na]^+$ 345.1440, found 345.1436.

1,11-diazido-6-pentylundeca-4,7-diyn-6-ol(7b)



7b

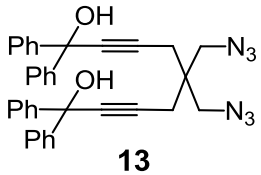
The reaction with pent-4-yn-1-yl 4-methylbenzenesulfonate (0.915 g, 3.84 mmol), *n*-BuLi (1.55 M in hexane, 2.8 mL, 4.22 mmol) and ester (0.25 g, 1.92 mmol) in THF

(20 mL) followed by followed by collected the organic layer under vacuum affording the crude product 1.10 g. The crude product can be used to the next step without further purification.

Then the crude benzyl alcohol with sodium azide (299.6 mg, 4.61 mmol) in DMF (38 ml) followed by silica gel column chromatography (ethyl acetate / hexane = 1/15 to 1/5 to 1/1) gave azide **7b** (0.521 g, 86%) as a colorless oil.

Colorless oil; R_f value 0.45(ethyl acetate/hexane = 1/2); IR (NaCl, neat) ν_{max} 3420, 2930, 2098, 1254 cm^{-1}; ^1H NMR(500 MHz, $CDCl_3$) δ 3.40(t, 4H, *J* = 7.0 Hz), 2.45(s, 1H, OH), 2.35(t, 4H, *J* = 7.0 Hz), 1.84–1.76(m, 6H), 1.57–1.51(m, 2H), 1.36–1.31(m, 4H), 0.90(t, 3H, *J* = 7.0 Hz); ^{13}C NMR(126 MHz, $CDCl_3$) δ 82.2, 81.9, 63.7, 50.1, 44.1, 31.4, 27.5, 24.3, 22.5, 16.0, 14.0; HRMS (ESI) calcd for $C_{16}H_{24}N_6ONa$ $[M+Na]^+$ 339.1909, found 339.1901.

5,5-bis(azidomethyl)-1,1,9,9-tetraphenylnona-2,7-diyne-1,9-diol (13)

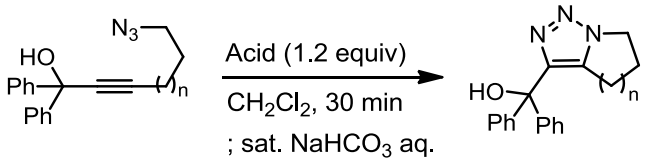


13

To a stirred solution of azide compound **12**[1] (0.044 g, 0.218 mmol) in dry THF (5.5 mL)under an atmosphere of nitrogen was added dropwise *n*-BuLi (1.60 M in hexane, 0.326 mL, 0.522 mmol) at -78 ℃ and the mixture was stirred for 30 min. Ketone (0.099 g, 0.544 mmol) was then added at same temperature. After 4h, the reaction was quenched with water. The mixture was diluted with ethyl acetate and was washed with water and brine. Drying collected organic layer over $MgSO_4$followed by silica gel column chromatography gave **13** (112.9 mg, 92%) as colorless oil. [silica gel purification (ethyl acetate / hexane = 1 / 40 to 1/20 to 1/10)].

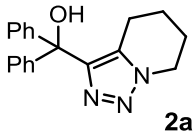
Colorless oil; R_f value 0.45(ethyl acetate/hexane = 1/5); ^1H NMR(400 MHz, $CDCl_3$) δ 7.57(d, 8H, *J* = 7.2 Hz), 7.32(dd, 8H, *J* = 6.8, 7.2 Hz), 7.28–7.25(m, 4H), 3.37 (s, 4H), 2.82(s, 2H), 2.47(s, 4H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 144.9, 128.3, 127.8, 125.8, 86.9, 82.5, 74.5, 54.4, 42.5, 23.7; HRMS (EI) calcd for $C_{35}H_{30}N_6O_2$ $[M^+]$ 566.2430, found 566.2434.

General Experimental Procedure of triazolations



To the mixture of propargyl alcohol (1.0 equiv) in dichloromethane (0.1 M to alcohols) under nitrogen atmosphere, acid (1.2 equiv) was added at ambient temperature. After 30 minutes, the reaction was quenched with saturated sodium bicarbonate aqueous solution, and was washed with brine. Drying the organic layer over magnesium sulfate followed by concentration in vacuo and silica gel column chromatography afforded triazole.

Diphenyl(4,5,6,7-tetrahydro-[1,2,3]triazolo[1,5-a]pyridin-3-yl)methanol (2a).

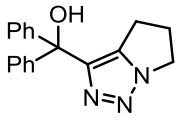


2a

To the mixture of azido-propargyl alcohol **1a** (47.0 mg, 0.154 mmol) in dichloromethane (2 mL) under nitrogen atmosphere, TFA (38.5 μL, 0.173 mmol, 1.2 equiv) was added at ambient temperature. After 30 minutes, the reaction was quenched with saturated sodium bicarbonate aqueous solution, and was washed with brine. Drying the organic layer over magnesium sulfate followed by concentration in vacuo and silica gel column chromatography afforded triazole (ethyl acetate/ petroleum ether = 1/4 to 1/1) afforded **2a** (44.1mg, 94%).

Colorless oil; R_f value 0.22 (ethyl acetate/petroleum ether = 1/2); ^{1}H NMR(500 MHz, $CDCl_3$) δ 7.32–7.28(m, 10H), 4.34(t, 2H, *J* = 6.0 Hz), 4.28(br, 1H, OH), 2.00(t, 2H, *J* = 7.0 Hz), 1.93(m, 2H), 1.67(m, 2H); ^{13}C NMR(126 MHz, $CDCl_3$) δ 147.7, 145.2, 131.0, 127.9, 127.7, 127.5, 77.4, 46.6, 22.2, 20.6, 19.9; HRMS (ESI) calcd for $C_{19}H_{19}N_3ONa$ $[M+Na]^+$ 328.1426, found 328.1426.

(5,6-dihydro-4H-pyrrolo[1,2-c][1,2,3]triazol-3-yl)diphenylmethanol (2b).

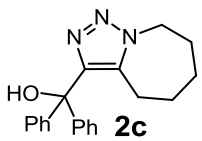


2b

The reaction with propargyl alcohol (57.2mg, 0.196mmol) and TFA (0.015mL, 0.236 mmol) in dichloromethane (2 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/5) afforded triazole **3c** (56.1mg, 98%).

White crystal; R_f value 0.10 (EtOAc/petroleum ether = 1/2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.25 (m, 10H), 4.24 (t, 2H, *J* = 7.5 Hz), 4.19 (br-s, 1H, OH), 2.56 (tt, 2H, *J* = 7.5, 7.5 Hz), 2.07 (t, 2H, *J* = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5, 145.1, 140.2, 127.8, 127.34, 127.29, 76.6, 46.2, 27.9, 20.8; HRMS (ESI) calcd for $C_{18}H_{17}N_3ONa$ $[M+Na]^+$ 314.1269, found 314.1267.

diphenyl(5,6,7,8-tetrahydro-4H-[1,2,3]triazolo[1,5-a]azepin-3-yl)methanol (2c)



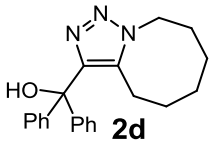
2c

The reaction with propargyl alcohol (67.7mg, 0.212mmol) and TFA (0.016mL, 0.254 mmol) in dichloromethane (2 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/20) afforded triazole **2c** (58.4mg, 86%).

White solid; R*f* value 0.37 (ethyl acetate/ petroleum ether= 1/10);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.29 (m, 8H), 7.21-7.19 (m, 2H), 6.58 (s, 1H), 3.20 (t, 2H, *J* = 6.8 Hz), 2.24 (t, 2H, *J* = 6.8 Hz), 1.53-1.45(m, 4H), 1.23-1.18(m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 139.0, 129.5, 128.4, 128.3, 126.6, 77.2, 51.2, 42.8, 28.6, 26.2, 23.7;

HRMS (ESI) calcd for $C_{20}H_{21}N_3ONa$ $[M+Na]^+$ 342.1582, found 342.1582.

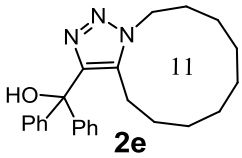
(4,5,6,7,8,9-hexahydro-[1,2,3]triazolo[1,5-a]azocin-3-yl)diphenylmethanol (2d)



2d

The reaction with propargyl alcohol (55.1mg, 0.165mmol) and TFA (0.013mL, 0.198 mmol) in dichloromethane (2 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/20) afforded triazole **3d** (46.8mg, 84%).
White solid; R*f* value 0.4 (ethyl acetate/ petroleum ether= 1/10);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.29 (m, 8H), 7.21-7.19 (m, 2H), 6.58 (s, 1H), 3.22 (t, 2H, *J* = 6.8 Hz), 2.23 (t, 2H, *J* = 6.8 Hz), 1.57-1.46(m, 4H), 1.30-1.23(m, 2H), 1.21-1.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 139.0, 129.5, 128.4, 128.3, 126.6, 77.2, 51.3, 42.9, 28.59, 28.57, 26.4, 24.0; HRMS (ESI) calcd for $C_{21}H_{23}N_3ONa$ $[M+Na]^+$ 356.1739, found 356.1747.

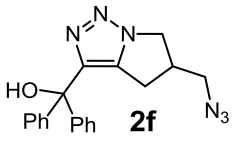
(5,6,7,8,9,10,11,12-octahydro-4H-[1,2,3]triazolo[1,5-a][1]azacycloundecin-3-yl)diphenylmethanol (2e)



2e

The reaction with propargyl alcohol (48.7mg, 0.130mmol) and TFA (0.010mL, 0.156 mmol) in dichloromethane (2 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/10) afforded triazole **2e** (35.6mg, 73%).
White solid; R*f* value 0.45 (ethyl acetate/ petroleum ether= 1/10);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.28 (m, 8H), 7.20-7.19 (m, 2H), 6.58 (s, 1H), 3.25 (t, 2H, *J* = 6.8 Hz), 2.23 (t, 2H, *J* = 6.8 Hz), 1.61-1.54(m, 2H), 1.52-1.45(m, 2H), 1.35-1.31 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 139.0, 129.5, 128.4, 128.2, 126.6, 77.2, 51.4, 43.2, 29.22, 29.18, 29.1, 29.0, 28.8, 26.6, 24.3; HRMS (ESI) calcd for $C_{24}H_{30}N_3O$ $[M+H]^+$ 376.2389, found 376.2388.

(5-(azidomethyl)-5,6-dihydro-4H-pyrrolo[1,2-c][1,2,3]triazol-3-yl)diphenylmethanol (2f)

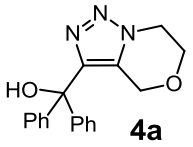


2f

The reaction with propargyl alcohol (56.7mg, 0.164mmol) and TFA (0.015mL, 0.196 mmol) in dichloromethane (2 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/10 to 1/5 to 1/1) afforded triazole **2f** (56.7mg, 85%).
White solid; R*f* value 0.38 (ethyl acetate/ petroleum ether= 1/1);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 10H), 4.44 (dd, 1H, *J* = 8.4, 12.0 Hz), 4.12 (dd, 1H, *J* = 8.4, 12.0 Hz), 3.49-3.38(m, 2H), 3.24-3.17(m, 1H), 2.20 (dd, 1H, *J* = 8.4, 12.0 Hz), 1.92 (dd,

1H, *J* = 8.4, 12.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 145.2, 138.9, 128.0, 127.6, 127.3, 76.6, 53.5, 49.5, 42.3, 25.0; HRMS (ESI) calcd for $C_{19}H_{19}N_6O$ $[M+H]^+$ 347.1620, found 347.1627.

(6,7-dihydro-4H-[1,2,3]triazolo[5,1-c][1,4]oxazin-3-yl)diphenylmethanol (4a)

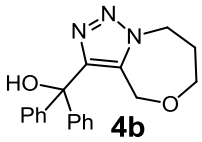


4a

The reaction with propargyl alcohol (60.0mg, 0.195mmol) and BF_3 OEt_2 (0.029mL, 0.234mmol) in dichloromethane (2 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/15 to 1/2 to 1/1) afforded triazole **4a** (59.2mg, 99%).

White solid; R*f* value 0.25(ethyl acetate/ petroleum ether= 1/2);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 10H), 4.35 (t, 2H, *J* = 4.2 Hz), 4.12 (s, 2H), 3.99 (s, 1H), 3.93 (t, 2H, *J* = 4.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.9, 145.1, 134.5, 128.1, 127.8, 127.4, 77.2, 63.0, 62.5, 45.7; HRMS (ESI) calcd for $C_{18}H_{18}N_3O_2$ $[M+H]^+$ 308.1399, found 308.1402.

diphenyl(4,6,7,8-tetrahydro-[1,2,3]triazolo[5,1-c][1,4]oxazepin-3-yl)methanol (4b)

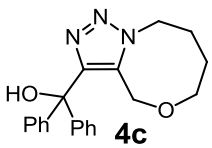


4b

The reaction with propargyl alcohol (100.0mg, 0.311mmol) and BF_3 OEt_2 (0.046mL, 0.373 mmol) in dichloromethane (4 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/5 to 1/2 to 1/1) afforded triazole **4b** (92.2mg, 92%).

White solid; R*f* value 0.18 (ethyl acetate/ petroleum ether= 1/2);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.29 (m, 10H), 4.65 (t, 2H, *J* = 4.2 Hz), 4.08 (s, 2H), 4.03 (s, 1H), 3.95 (t, 2H, *J* = 4.2 Hz), 2.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 145.0, 134.2, 128.1, 127.8, 127.6, 77.6, 73.6, 62.1, 50.3, 29.0; HRMS (ESI) calcd for $C_{19}H_{20}N_3O_2$ $[M+H]^+$ 322.1556, found 322.1562.

diphenyl(6,7,8,9-tetrahydro-4H-[1,2,3]triazolo[5,1-c][1,4]oxazocin-3-yl)methanol (4c)



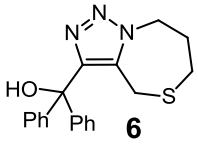
4c

The reaction with propargyl alcohol (45.0mg, 0.134mmol) and BF_3 OEt_2 (0.020mL, 0.349 mmol) in dichloromethane (4 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/5 to 1/2 to 1/1) afforded triazole **4c** (38.4 mg,

85%).

White solid; R*f* value 0.25 (ethyl acetate/ petroleum ether= 1/2);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 10H), 4.81 (t, 2H, *J* = 4.2 Hz), 4.10 (s, 2H), 3.65 (t, 2H, *J* = 4.2 Hz), 1.98 (tt, 2H, *J* = 4.2, 4.2 Hz), 1.52 (tt, 2H, *J* = 4.2, 4.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 144.9, 134.8, 128.2, 127.9, 127.7, 71.7, 63.4, 49.7, 29.7, 27.5, 24.5; HRMS (ESI) calcd for $C_{20}H_{22}N_3O_2$ $[M+H]^+$ 336.1712, found 336.1712.

diphenyl(4,6,7,8-tetrahydro-[1,2,3]triazolo[5,1-c][1,4]thiazepin-3-yl)methanol(6)

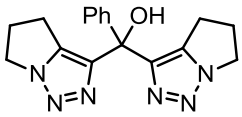


6

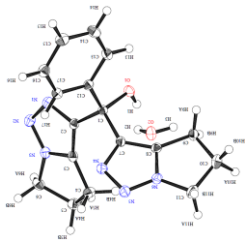
The reaction with propargyl alcohol (98.0mg, 0.290mmol) and BF_3 OEt_2 (0.043mL, 0.349 mmol) in dichloromethane (4 ml) followed by silica gel column purification (ethyl acetate/ petroleum ether = 1/5 to 1/2 to 1/1) afforded triazole **6** (74.6mg, 76%).

White crystal; R*f* value 0.28 (ethyl acetate/petroleum ether = 1/1);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.28 (m, 10H), 4.57 (t, 2H, *J* = 4.8 Hz), 3.12 (s, 2H), 2.92–2.89 (m, 2H), 2.17–2.12 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 144.8, 136.0, 128.1, 127.8, 127.7, 77.5, 50.5, 34.3, 28.8, 23.9; HRMS (ESI) calcd for $C_{19}H_{20}N_3OS$ $[M+H]^+$ 338.1327, found 338.1320.

bis(5,6-dihydro-4*H*-pyrrolo[1,2-c][1,2,3]triazol-3-yl)(phenyl)methanol(8a)



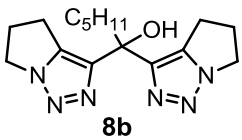
8a



The reaction with propargyl alcohol (117.6 mg, 0.372 mmol) and TsOH H_2O (83.3mg, 0.438 mmol) in dichloromethane (4 ml) followed by silica gel column purification (ethyl acetate/hexane = 1/5 to 1/2 to 1/1 to ethyl acetate then methaol/dichloromethane = 1/30 to 1/20 to 1/10) afforded triazole **8a** (100.8mg, 86%).

White crystal; R_f value 0.14(dichloromethane/methanol = 10/1); ^{1}H NMR(500 MHz, $CDCl_3$) δ 7.57–7.55 (m, 2H), 7.31–7.28 (m, 2H), 7.25–7.22 (m, 1H), 5.72(s, 1H, OH), 4.30–4.19 (m, 4H), 2.64–2.43 (m, 8H); ^{13}C NMR(126 MHz, $CDCl_3$) δ 144.8, 143.9, 140.2, 127.9, 127.4, 126.3, 71.9, 46.3, 27.9, 21.3; HRMS (ESI) calcd for $C_{17}H_{18}N_6ONa$ $[M+Na]^+$ 345.1440, found 345.1430.

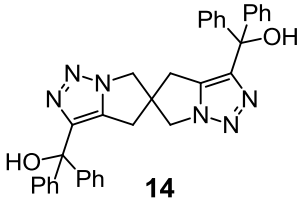
1,1-bis(5,6-dihydro-4*H*-pyrrolo[1,2-c][1,2,3]triazol-3-yl)hexan-1-ol(8b)



8b

The reaction with propargyl alcohol **8b** (127.1 mg, 0.402 mmol) and TMSOTf (0.087 mL, 0.482 mmol) in dichloromethane (4 ml) followed by silica gel column purification (ethyl acetate/hexane = 1/5 to 1/2 to 1/1 to ethyl acetate then methaol/dichloromethane = 1/30 to 1/20 to 1/10) afforded triazole **8b** (92.1mg, 72%).
White crystal; R_f value 0.1(methaol/dichloromethane = 1/20); ^{1}H NMR(500 MHz, $CDCl_3$) δ 4.31 (s, 1H, OH), 4.24 (t, 4H, *J* = 7.5 Hz), 2.98–2.87 (m, 4H), 2.71 (tt, 4H, *J* = 7.5, 7.5 Hz), 2.21–2.17 (m, 2H), 1.30–1.23 (m, 6H), 0.81–0.79 (m, 3H); ^{13}C NMR(126 MHz, $CDCl_3$) δ 144.7, 138.9, 71.3, 46.3, 41.4, 31.8, 28.1, 22.9, 22.5, 21.6, 14.0; HRMS (ESI) calcd for $C_{16}H_{24}N_6ONa$ $[M+Na]^+$ 339.1909, found 339.1903.

(4,4',6,6'-tetrahydro-5,5'-spirobi[pyrrolo[1,2-c][1,2,3]triazole]-3,3'-diyl)bis(diphenylmethanol) (14)

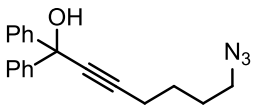


14

To the mixture of propargyl alcohol **13** (26.6 mg, 0.047 mmol) in dichloromethane (1 ml), TsOH H_2O (22.6 mg, 0.117 mmol) was added at ambient temperature. After 30 minutes, the reaction was quenched with saturated sodium bicarbonate aqueous solution, and was washed with brine, followed by silica gel column purification ($MeOH/CH_2Cl_2$ = 1/80 to 1/60 to 1/40 to 1/30) afforded triazole **14** (26.0 mg, 98%).
White solid; R_f value 0.36($MeOH/CH_2Cl_2$ = 1/20); ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.32–7.27(m, 20H), 4.34(d, 2H, *J* = 12.0 Hz), 4.20 (d, 2H, *J* = 12.0 Hz), 2.29(d, 2H, *J* = 16.4 Hz), 2.07(d, 2H, *J* = 16.4 Hz); ^{13}C NMR(100 MHz, DMSO) δ 146.9, 146.3, 138.3, 127.6, 127.0, 126.7, 75.7, 60.1, 55.8, 34.7; HRMS (ESI) calcd for $C_{35}H_{30}N_6O_2Na$ $[M+Na]^+$ 589.2328, found 589.2326.

References

1. Y. Yoshida, S. Takizawa, and H. Sasai, *Tetrahedron:Asymmetry*, 2012, **23**, 843.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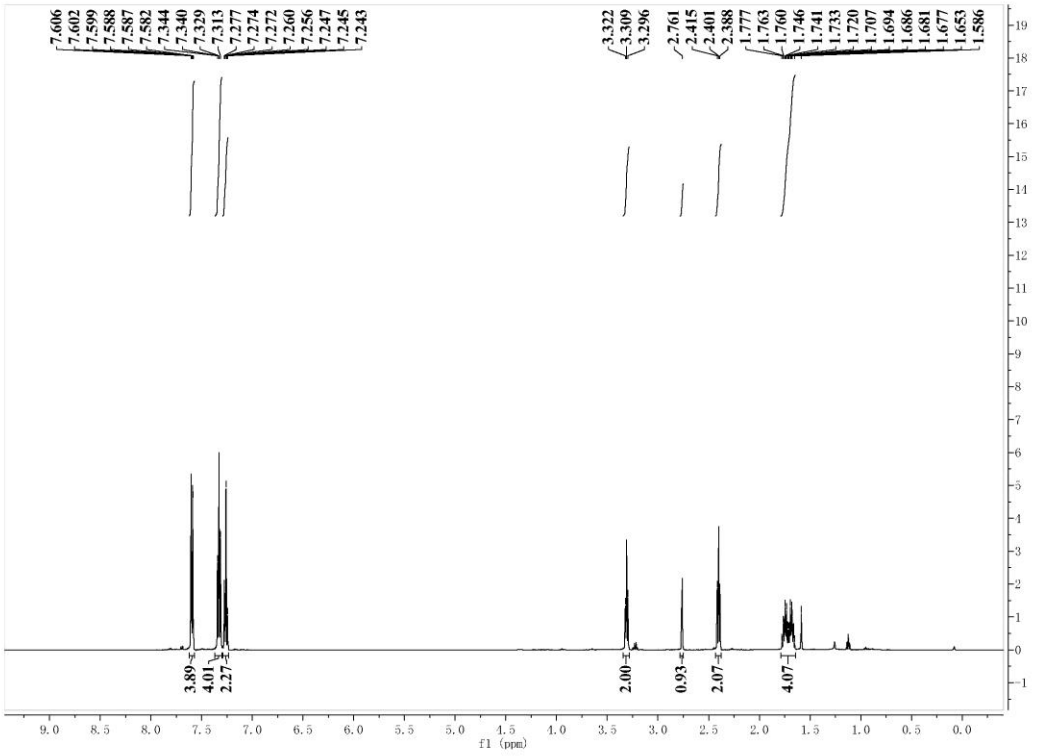
Ph
Ph
N3

1a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7.256
7.247
7.245
7.243
3.322
3.309
3.296
2.761
2.415
2.401
2.388
1.777
1.763
1.760
1.746
1.741
1.733
1.720
1.707
1.694
1.686
1.681
1.677
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1.586
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4.01
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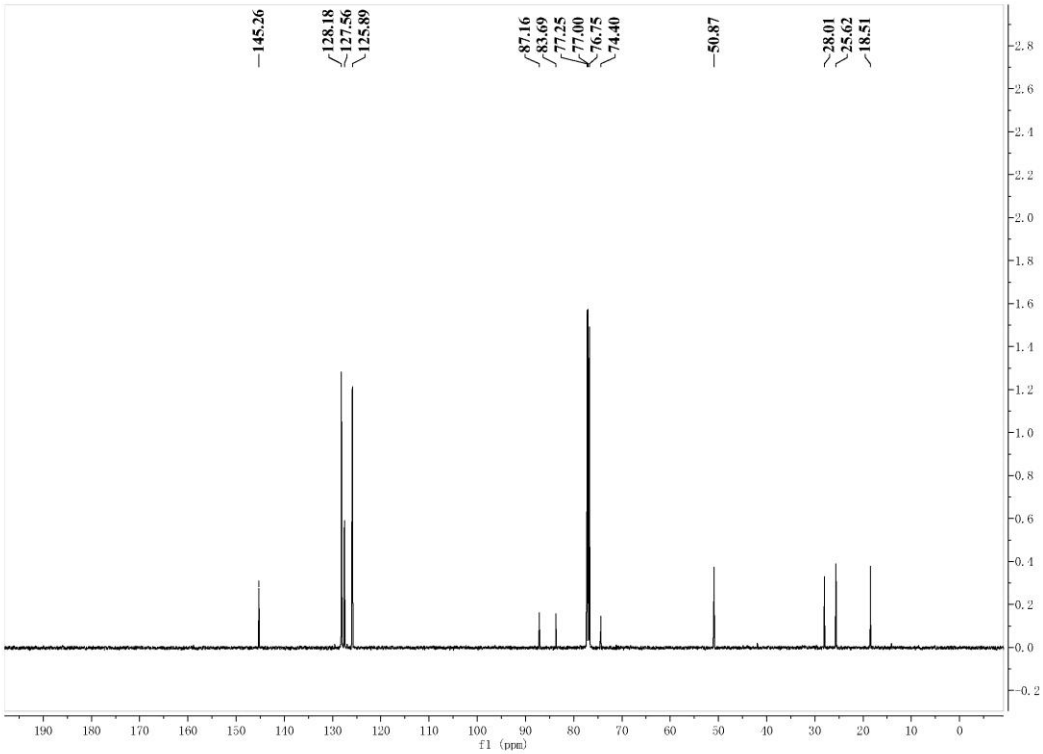
4.07
f1 (ppm)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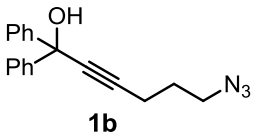
f1 (ppm)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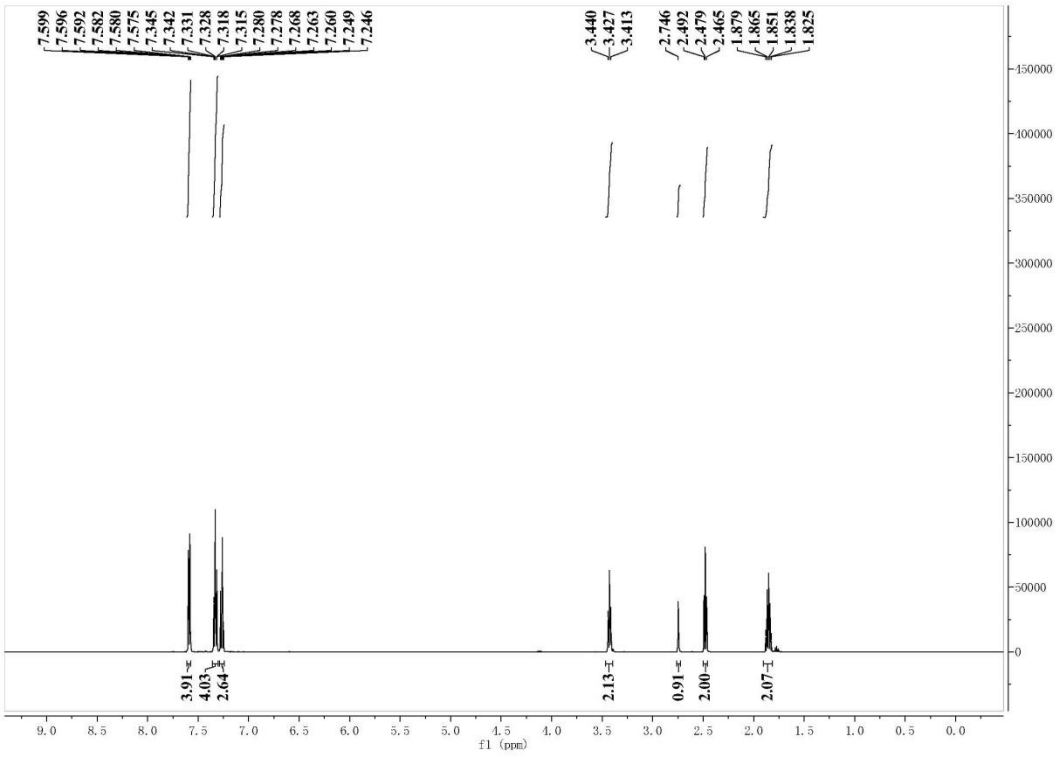
Ph
Ph
N3

1b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7.260
7.249
7.246
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3.427
3.413
2.746
2.492
2.479
2.465
1.879
1.865
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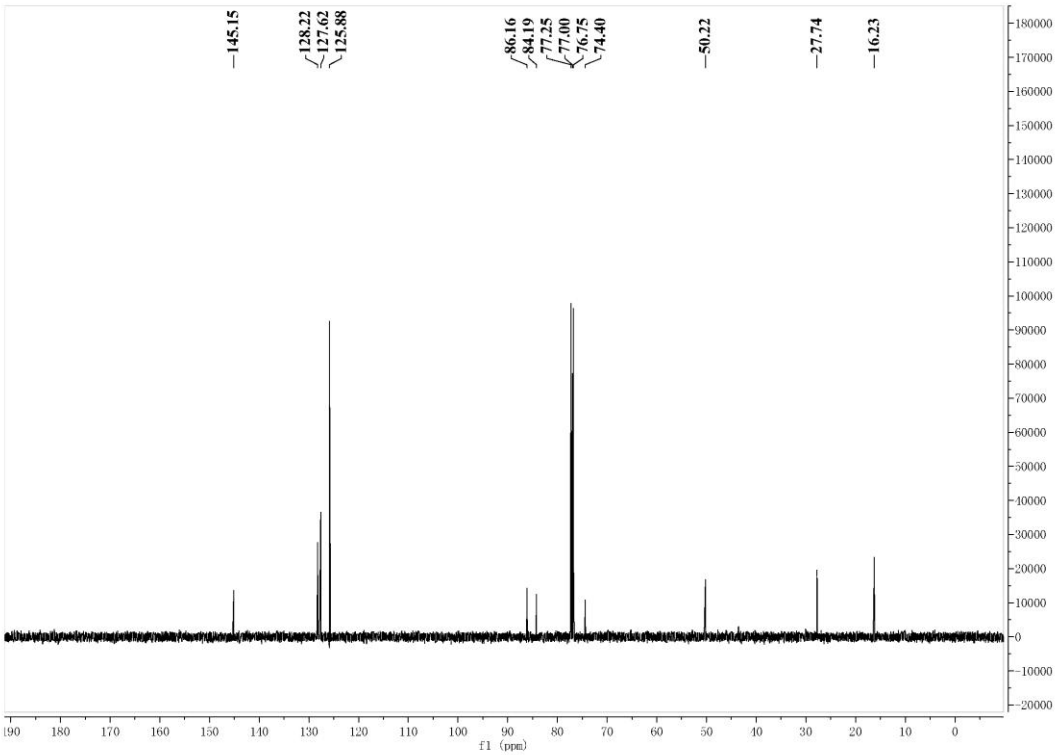
f1 (ppm)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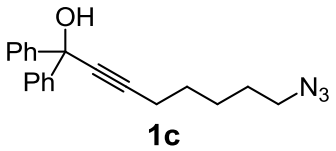
f1 (ppm)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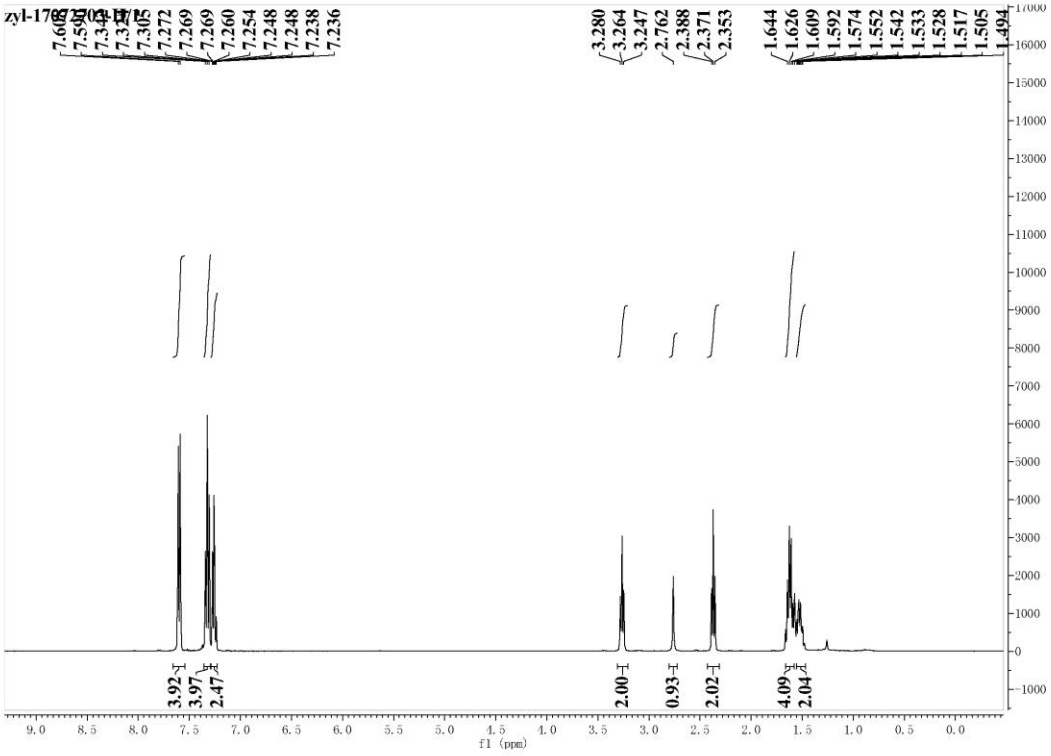
Ph
Ph
N3

1c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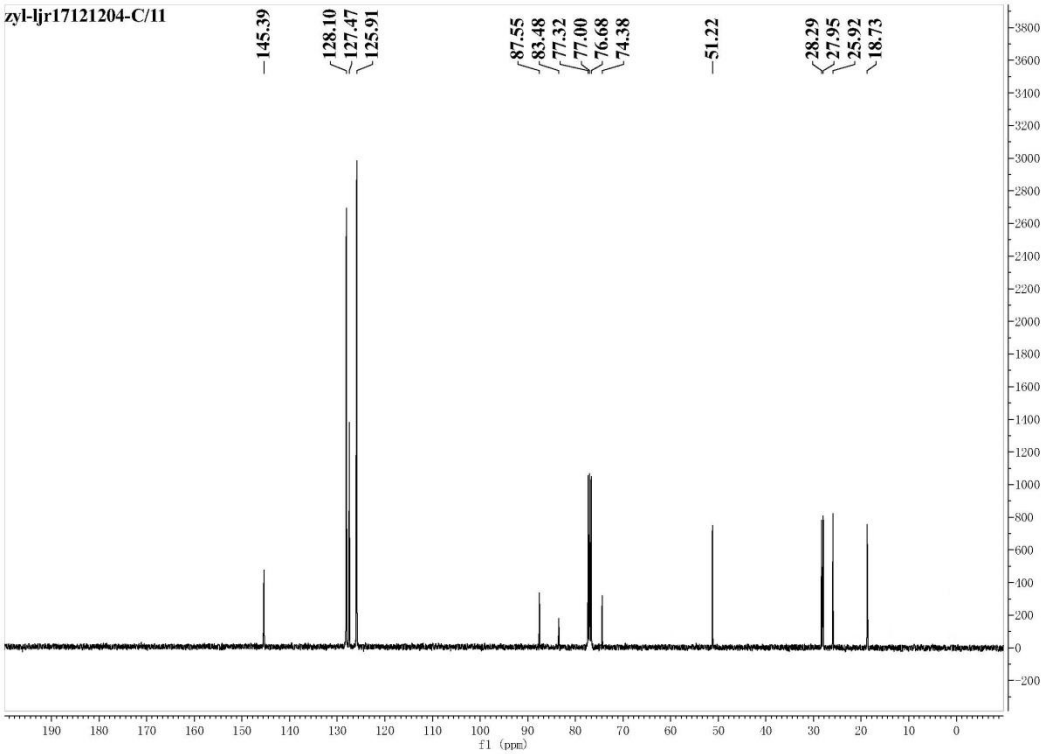
f1 (ppm)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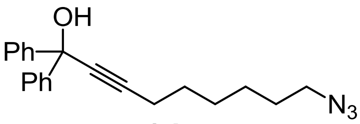
f1 (ppm)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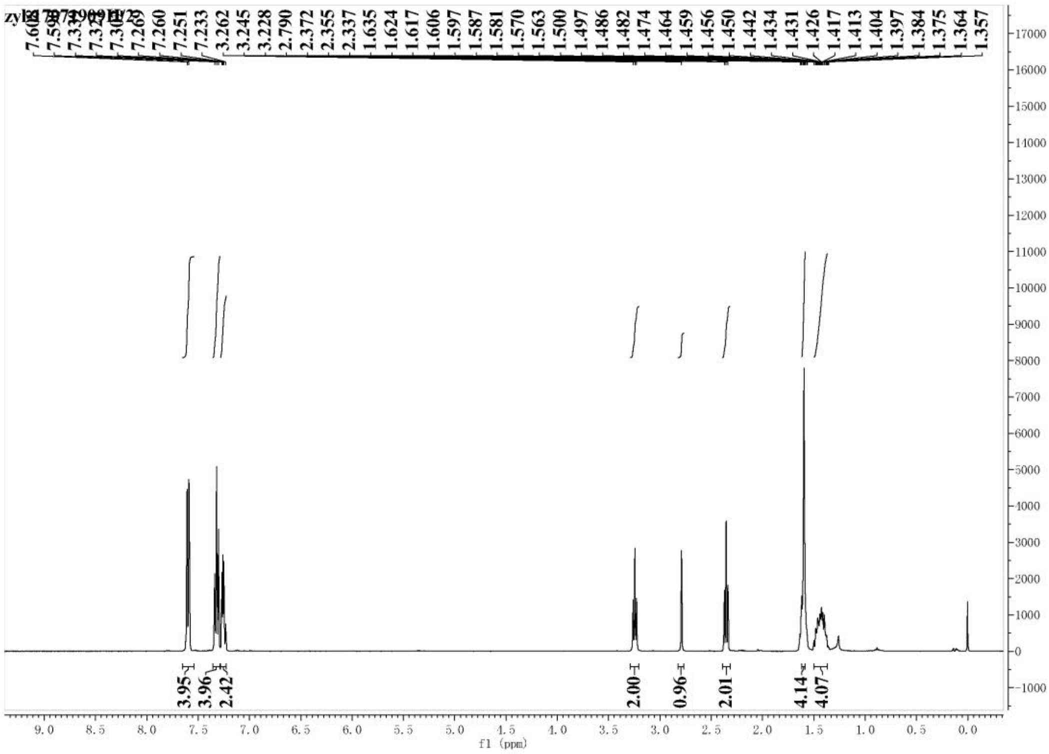
Ph
Ph
N3

1d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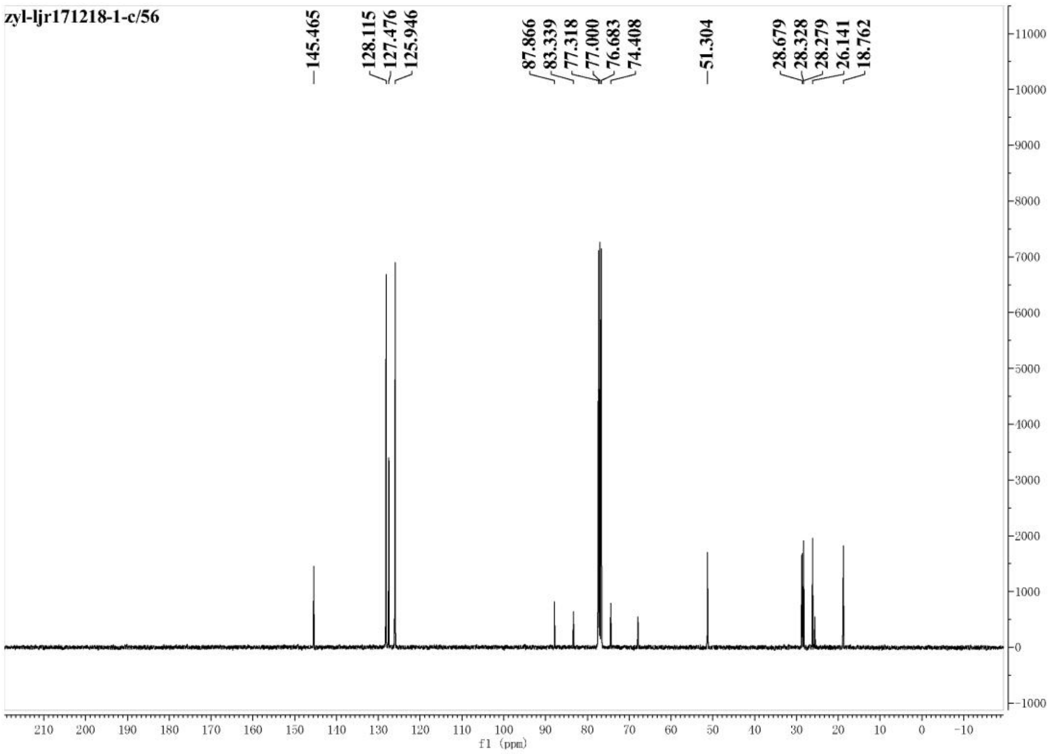
f1 (ppm)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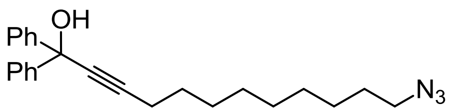
f1 (ppm)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Ph
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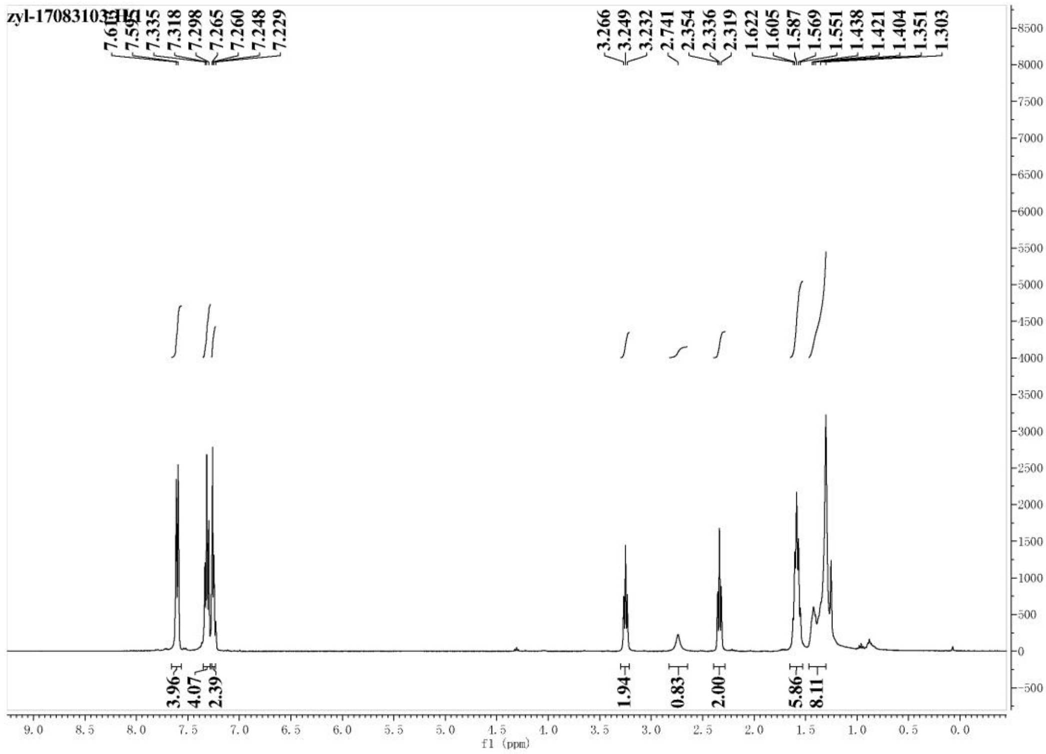
N3

1e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1.569
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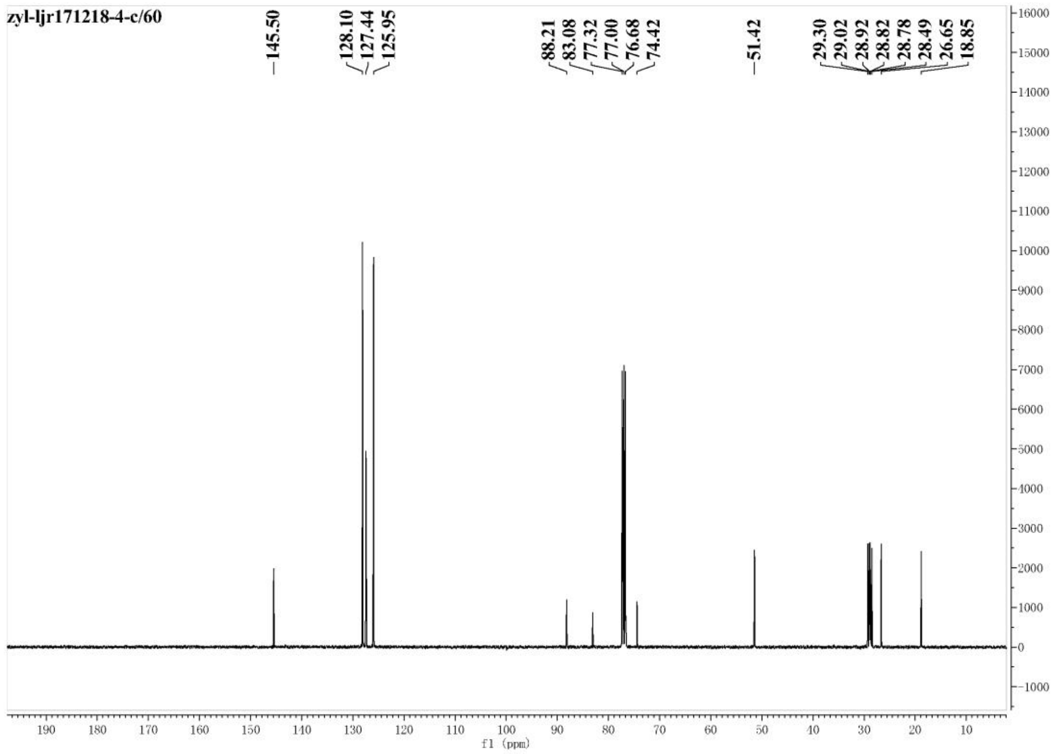
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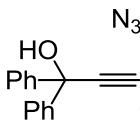
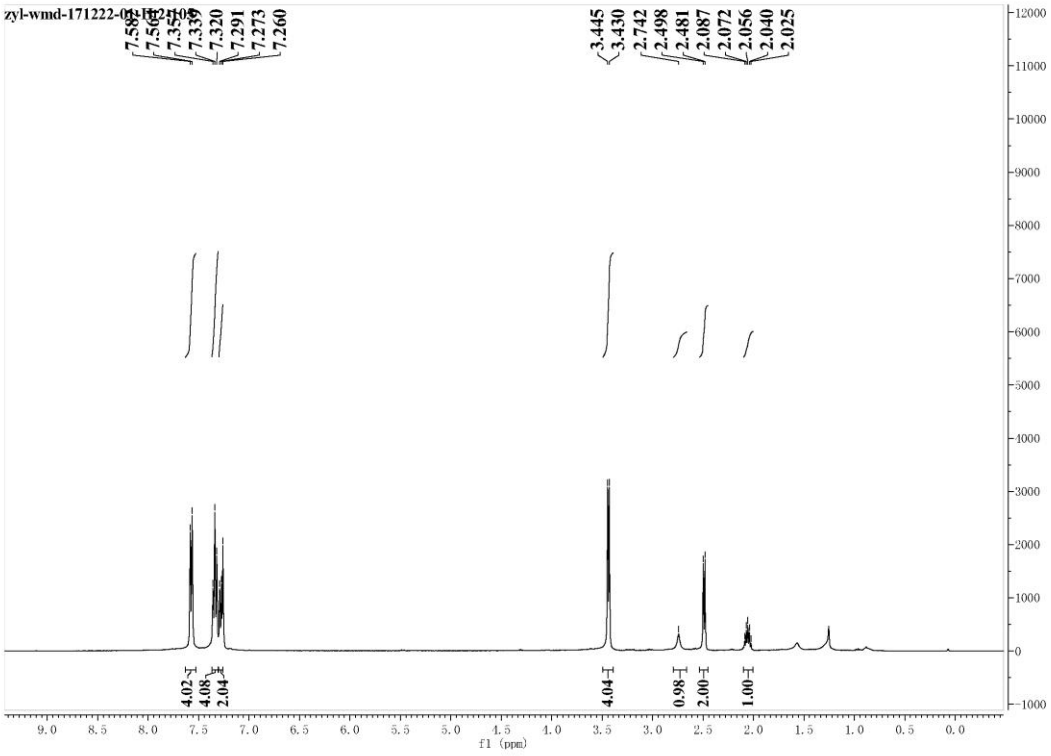
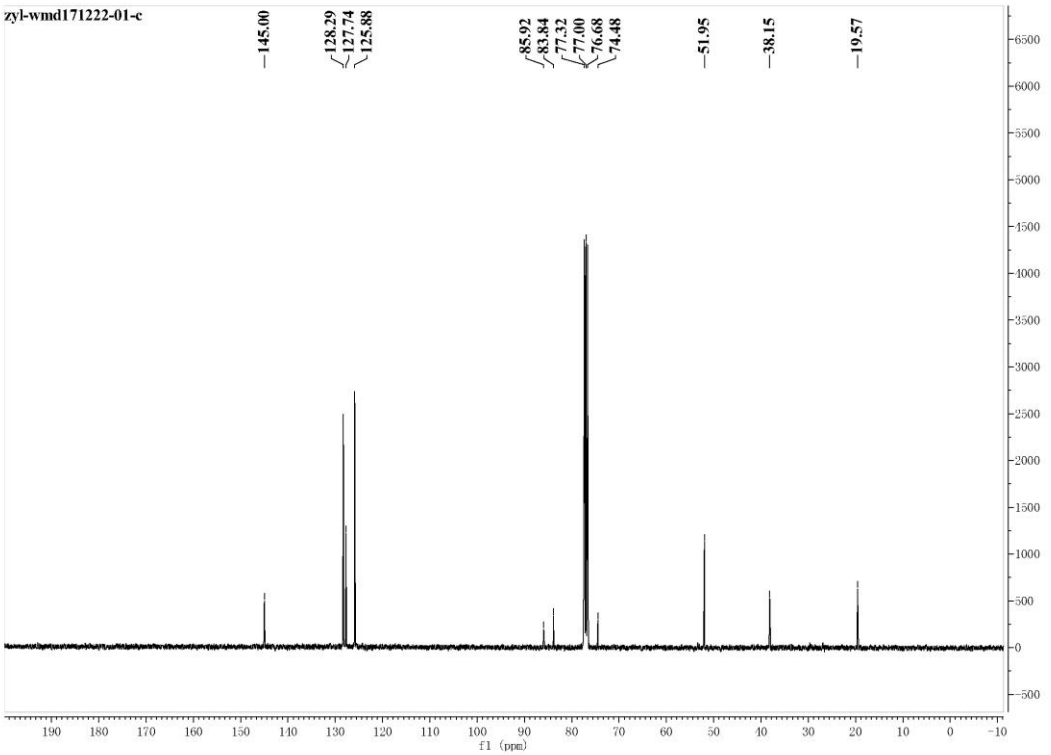
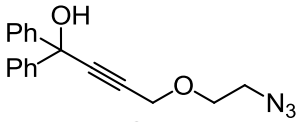
26.65
18.85
f1 (ppm)


N3
N3
HO
Ph
Ph

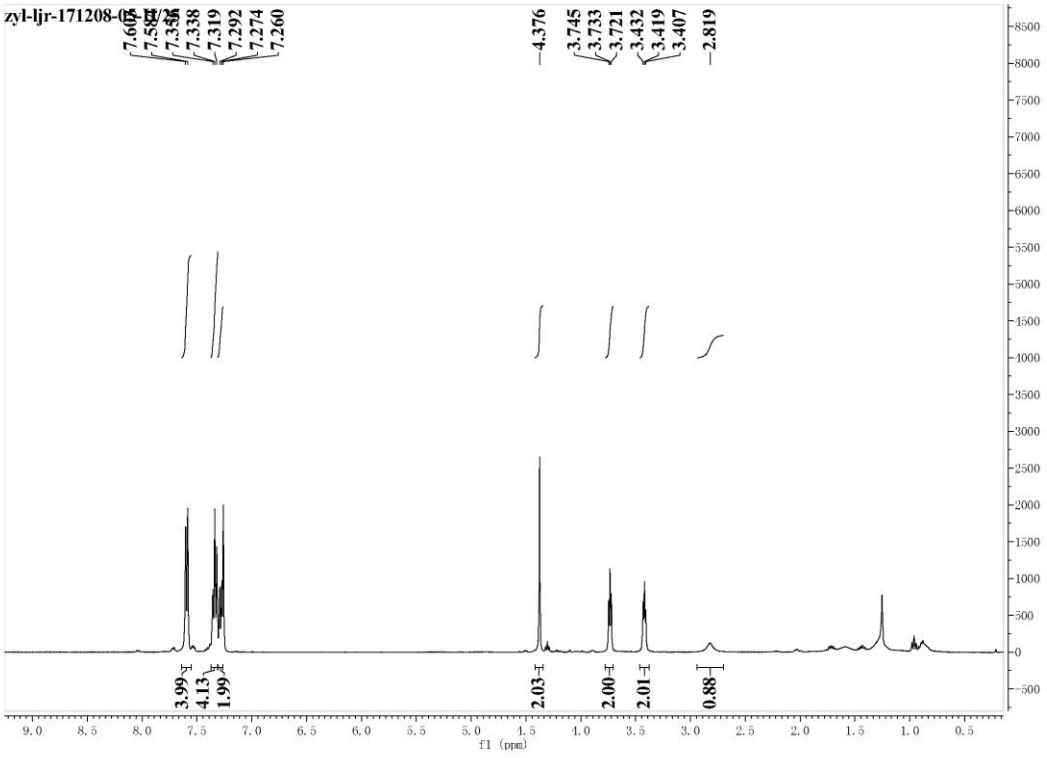
1f

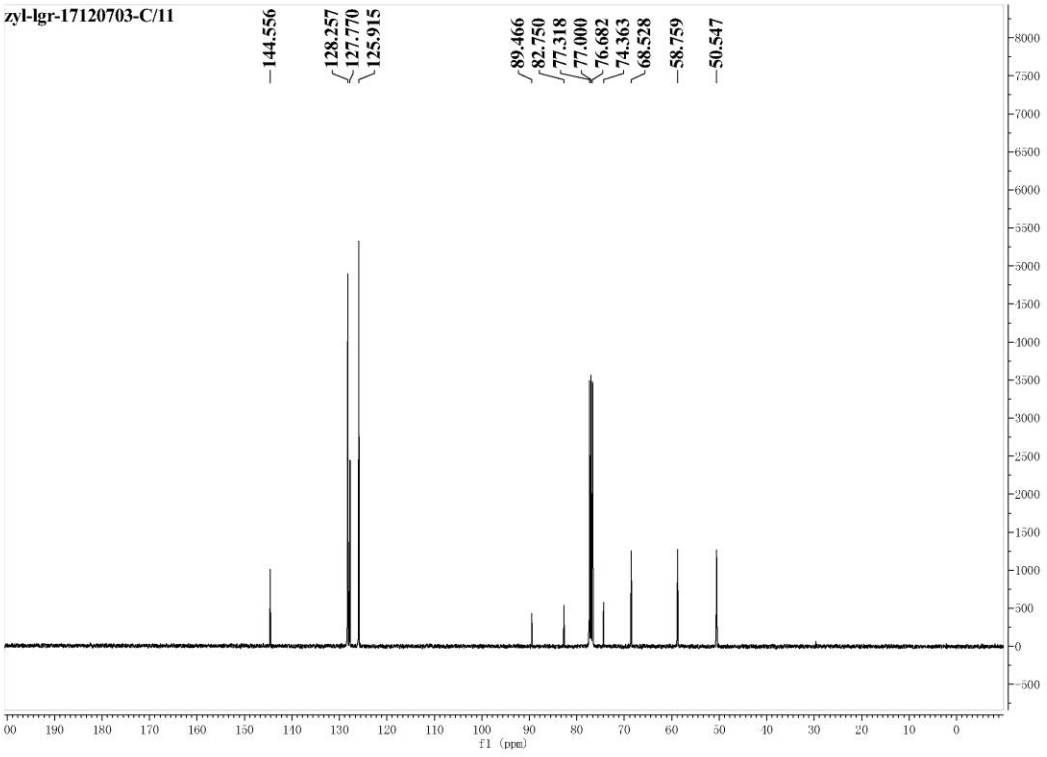

7.587
7.565
7.355
7.339
7.320
7.291
7.273
7.260
3.445
3.430
2.742
2.498
2.481
2.087
2.072
2.056
2.040
2.025
4.02
4.08
2.04
4.04
0.98
2.00
1.00
f1 (ppm)

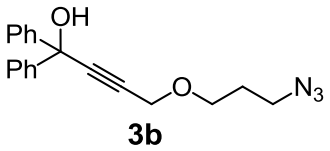

zyl-wmd171222-01-c
145.00
128.29
127.74
125.88
85.92
83.84
77.32
77.00
76.68
74.48
51.95
38.15
19.57
f1 (ppm)


OH
Ph
Ph
O
N3

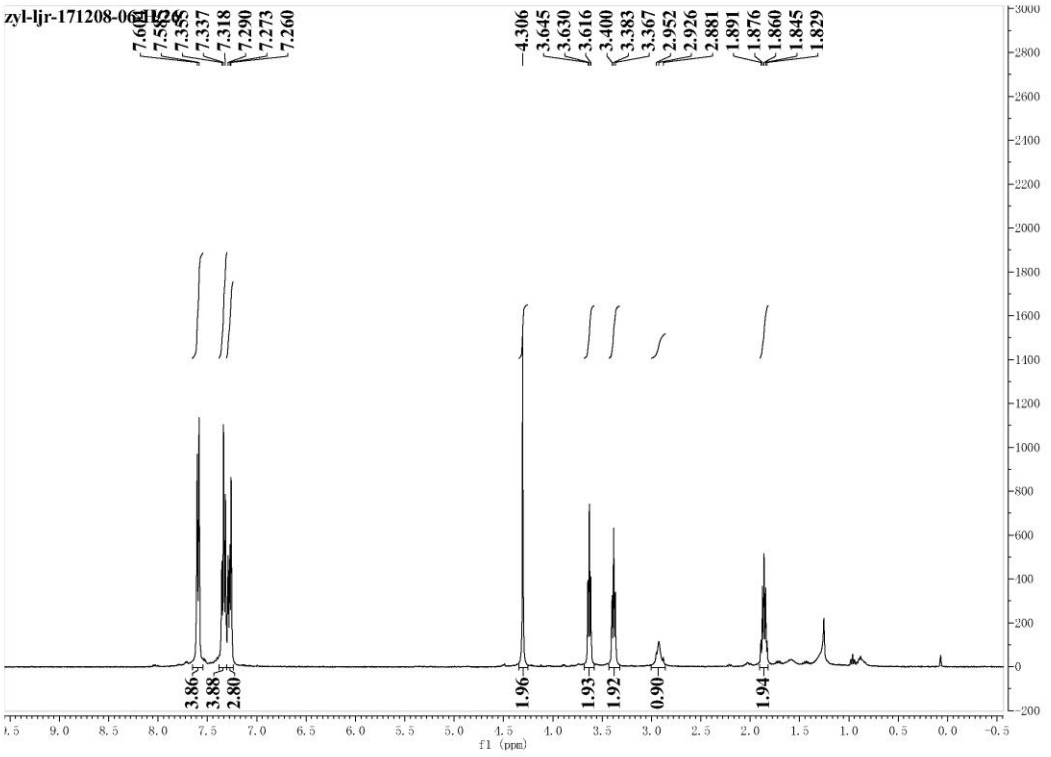
3a

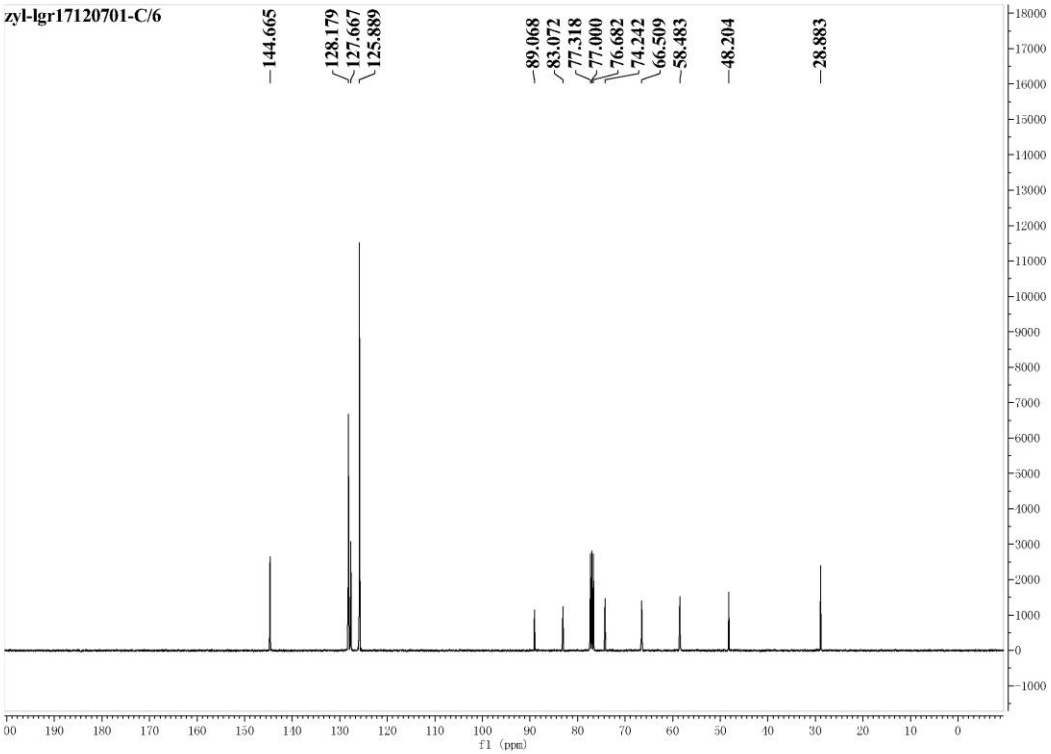

7.600
7.582
7.358
7.338
7.319
7.292
7.274
7.260
4.376
3.745
3.733
3.721
3.432
3.419
3.407
2.819
3.99
4.13
1.99
2.03
2.00
2.01
0.88
f1 (ppm)

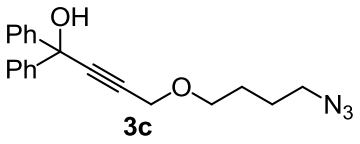

144.556
128.257
127.770
125.915
89.466
82.750
77.318
77.000
76.682
74.363
68.528
58.759
50.547
f1 (ppm)


OH
Ph
Ph
O
N3

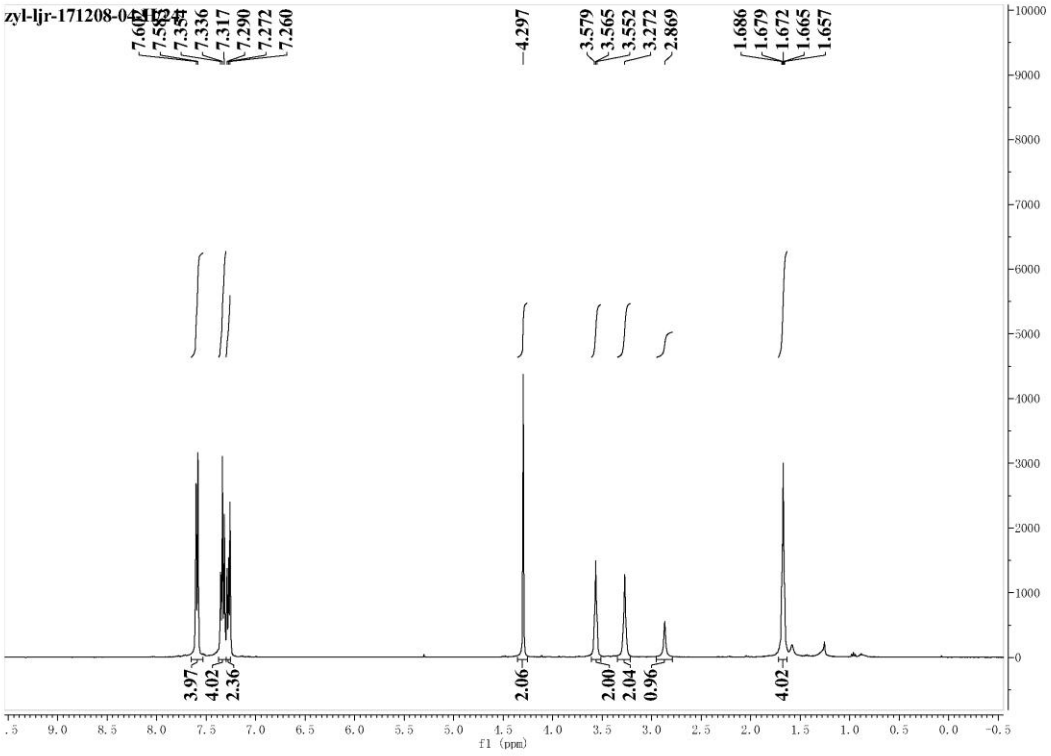
3b

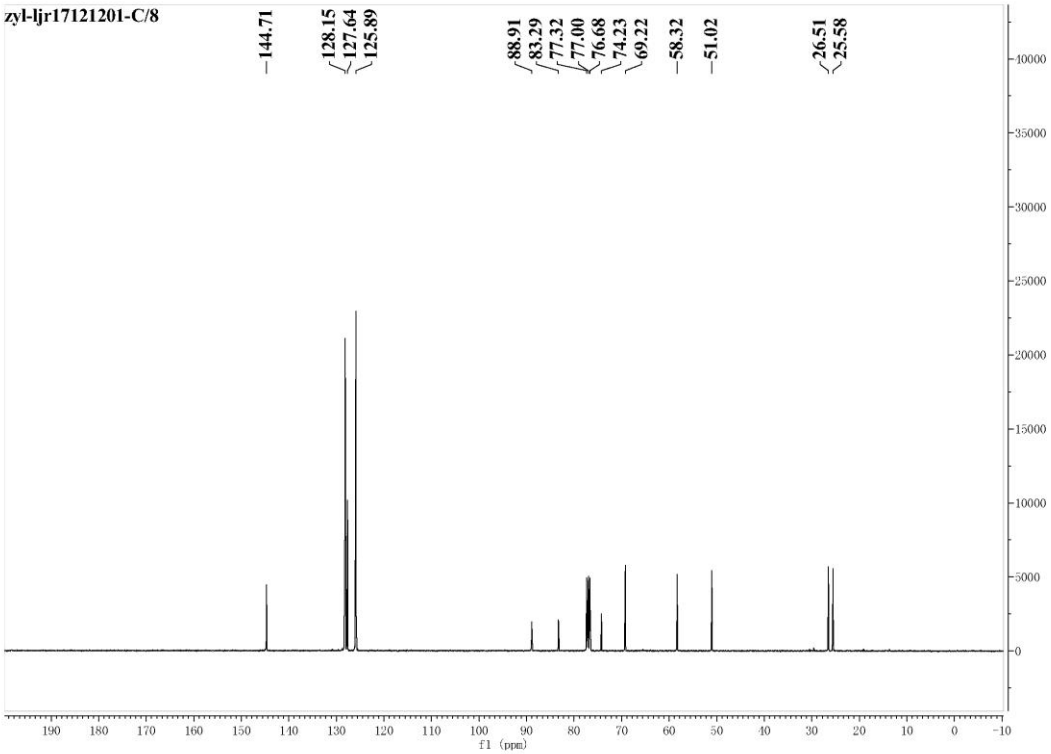

zyl-ljr-171208-06-H26
7.602
7.585
7.355
7.337
7.318
7.290
7.273
7.260
4.306
3.645
3.630
3.616
3.400
3.383
3.367
2.952
2.926
2.881
1.891
1.876
1.860
1.845
1.829
3.86
3.88
2.80
1.96
1.93
1.92
0.90
1.94
f1 (ppm)

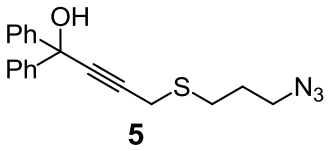

zyl-lgr17120701-C/6
144.665
128.179
127.667
125.889
89.068
83.072
77.318
77.000
76.682
74.242
66.509
58.483
48.204
28.883
f1 (ppm)


OH
Ph
Ph
O
N3

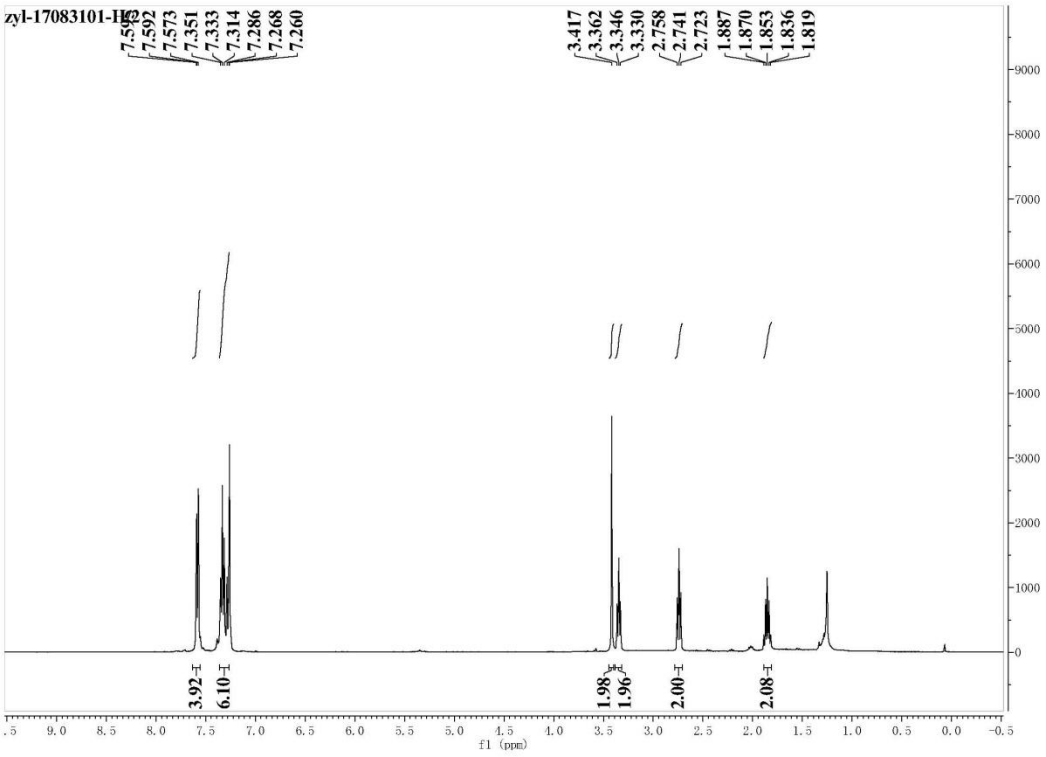
3c

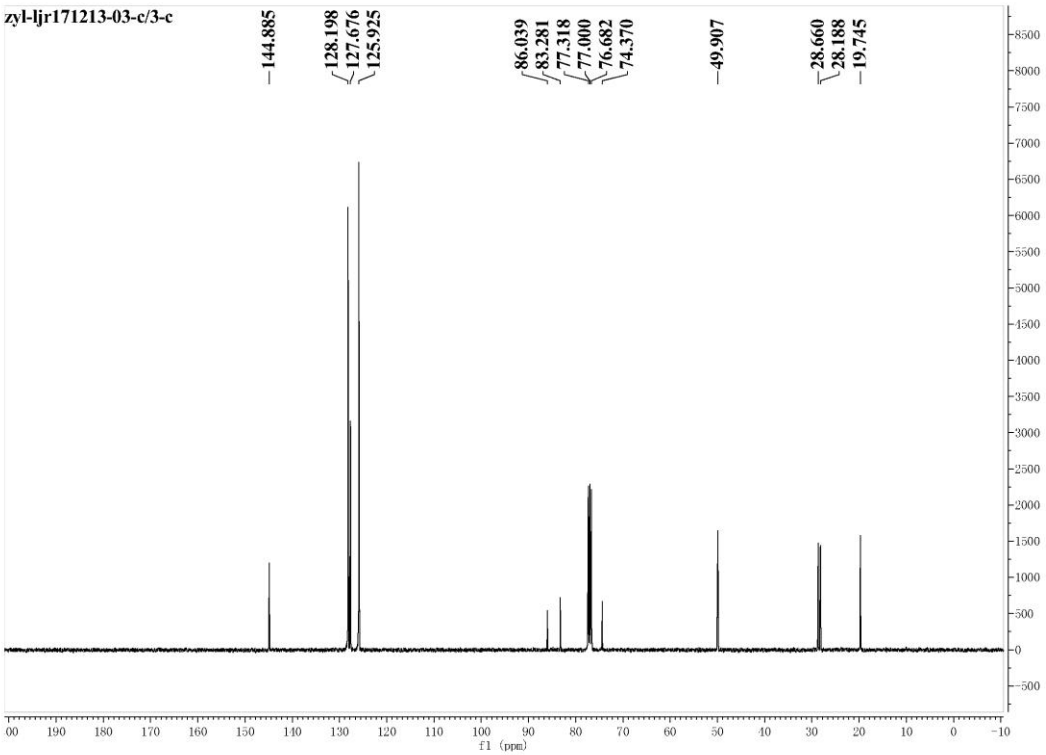

7.604
7.584
7.354
7.336
7.317
7.290
7.272
7.260
4.297
3.579
3.565
3.552
3.272
2.869
1.686
1.679
1.672
1.665
1.657
3.97
4.02
2.36
2.06
2.00
2.04
0.96
4.02
f1 (ppm)

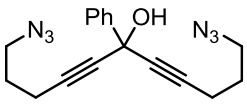

144.71
128.15
127.64
125.89
88.91
83.29
77.32
77.00
76.68
74.23
69.22
58.32
51.02
26.51
25.58
f1 (ppm)


OH
Ph
Ph
S
N3

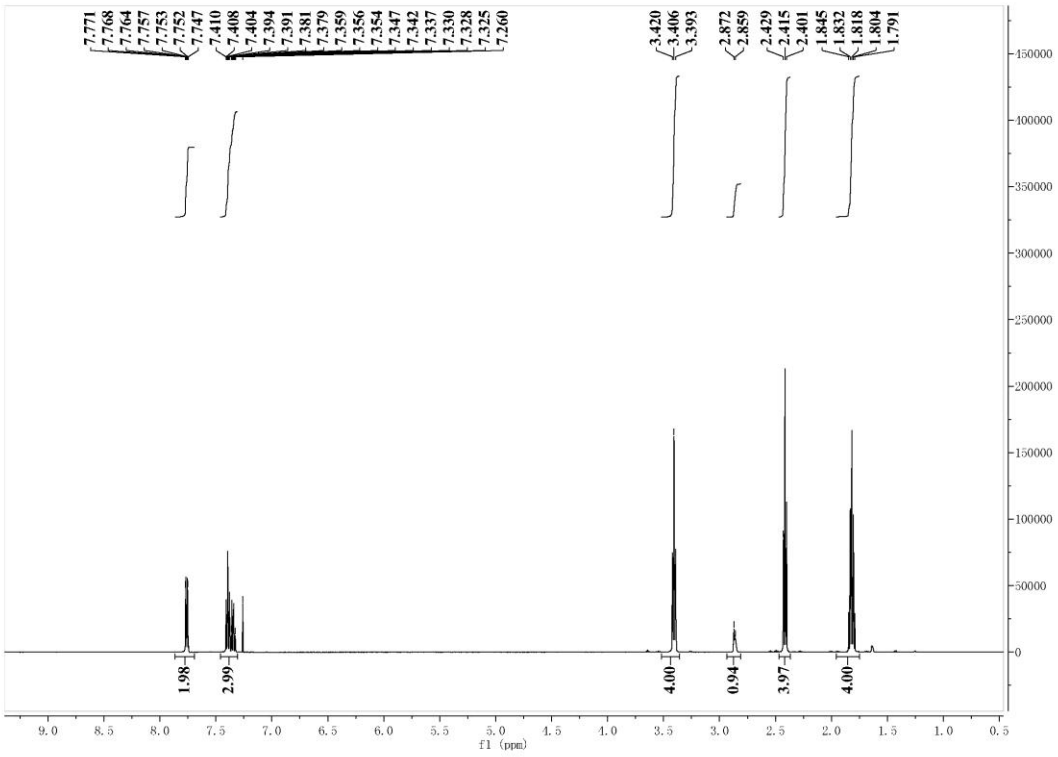
5

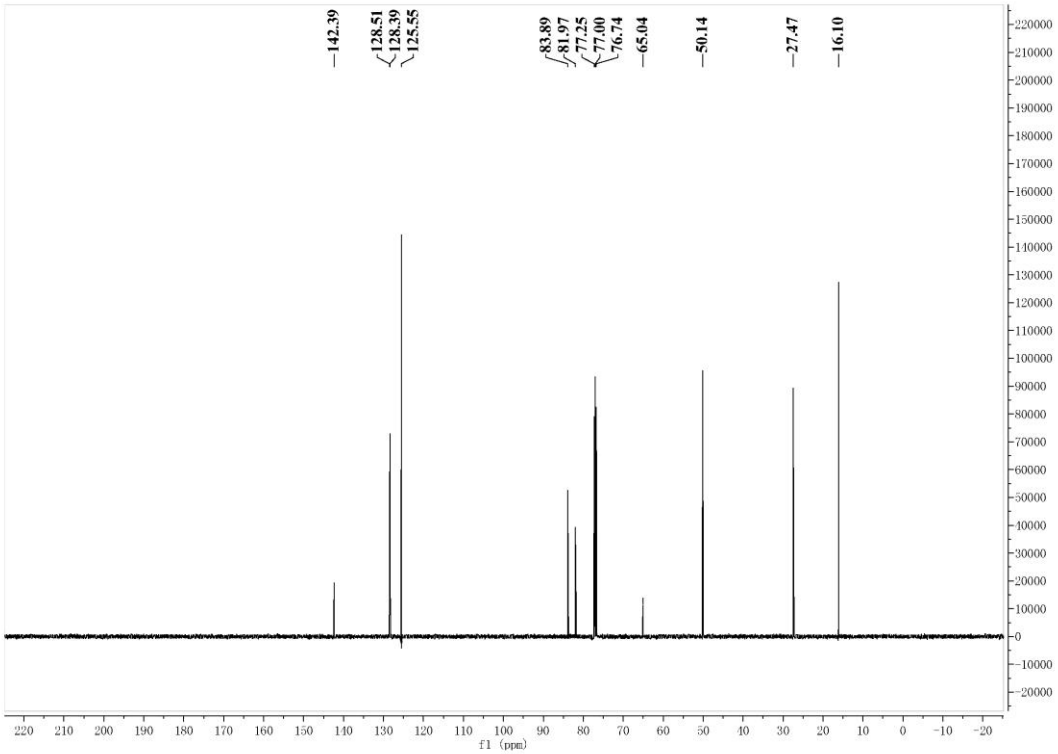

7.595
7.592
7.573
7.351
7.333
7.314
7.286
7.268
7.260
3.417
3.362
3.346
3.330
2.758
2.741
2.723
1.887
1.870
1.853
1.836
1.819
3.92
6.10
1.98
1.96
2.00
2.08
f1 (ppm)

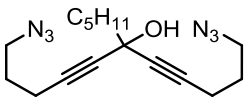

144.885
128.198
127.676
125.925
86.039
83.281
77.318
77.000
76.682
74.370
49.907
28.660
28.188
19.745
f1 (ppm)


N3
Ph
OH
N3

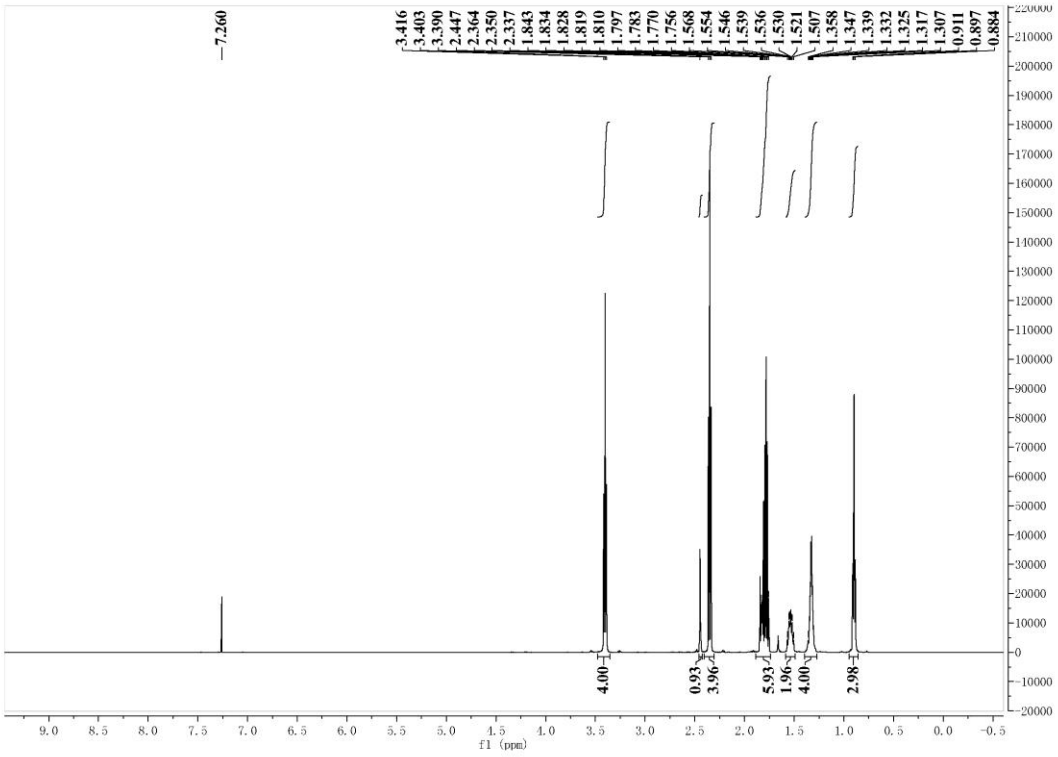
7a

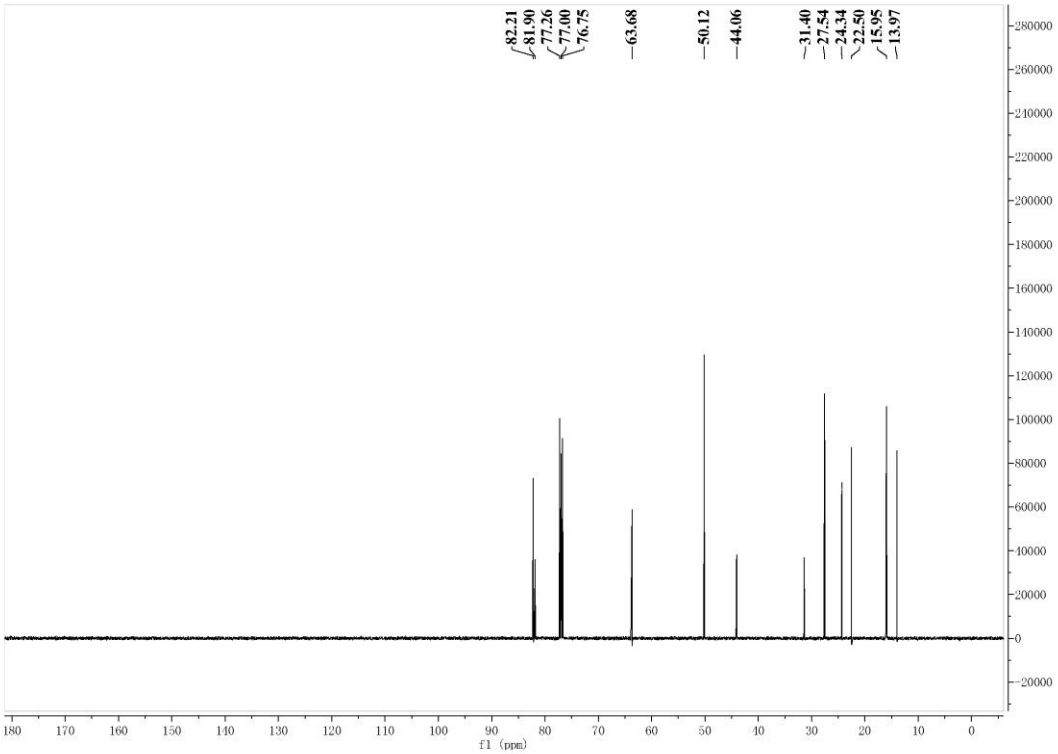

7.771
7.768
7.764
7.757
7.753
7.752
7.747
7.410
7.408
7.404
7.394
7.391
7.381
7.379
7.359
7.356
7.354
7.347
7.342
7.337
7.330
7.328
7.325
7.260
3.420
3.406
3.393
2.872
2.859
2.429
2.415
2.401
1.845
1.832
1.818
1.804
1.791
1.98
2.99
4.00
0.94
3.97
4.00
f1 (ppm)

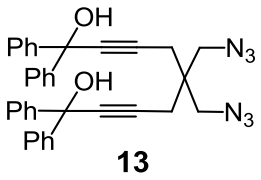

142.39
128.51
128.39
125.55
83.89
81.97
77.25
77.00
76.74
65.04
50.14
27.47
16.10
f1 (ppm)


N3
C5H11
OH
N3

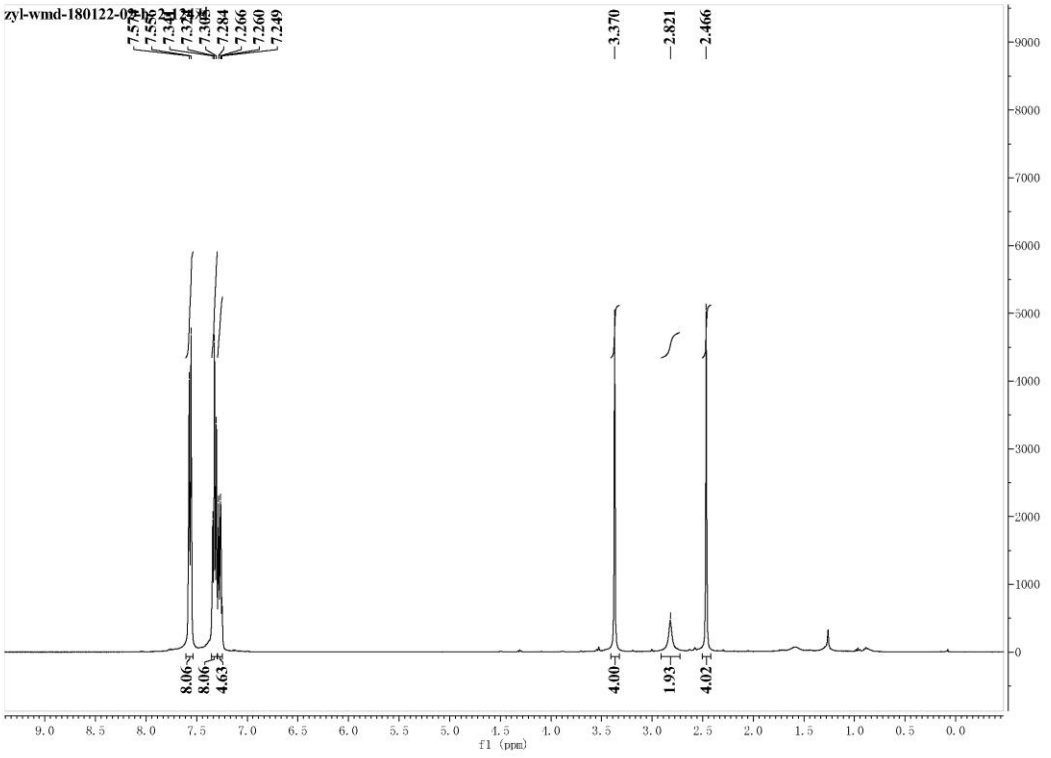
7b

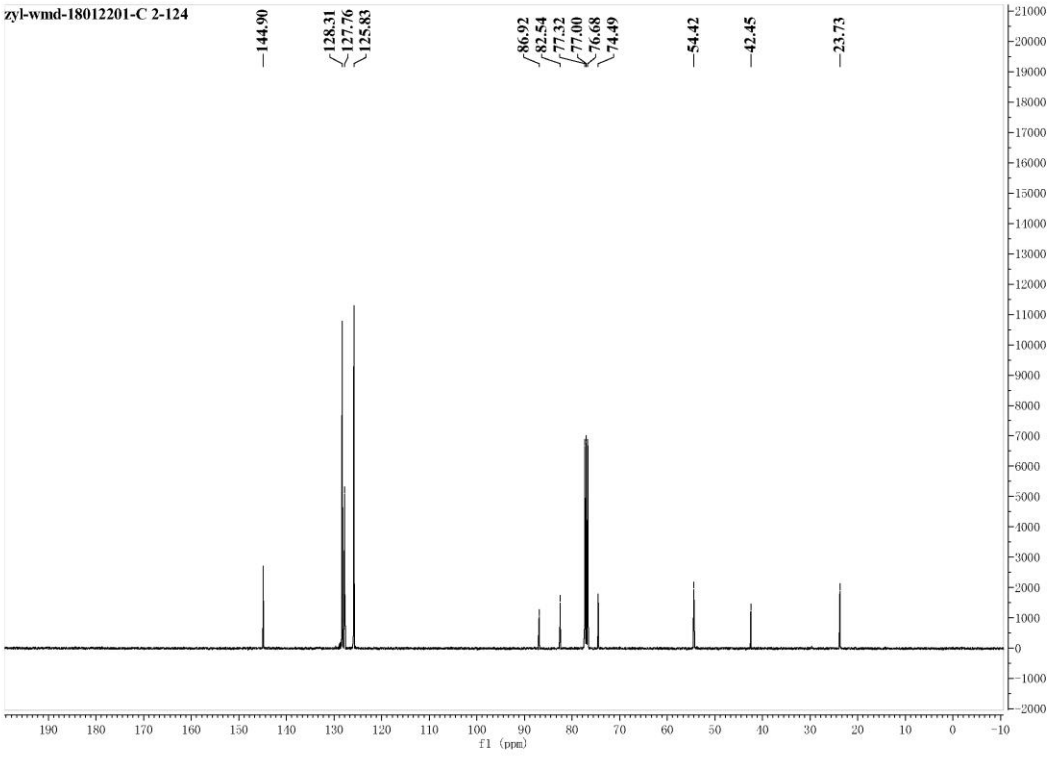

7.260
3.416
3.403
3.390
2.447
2.364
2.350
2.337
1.843
1.834
1.828
1.819
1.810
1.797
1.783
1.770
1.756
1.568
1.554
1.546
1.539
1.536
1.530
1.521
1.507
1.358
1.347
1.339
1.332
1.325
1.317
1.307
0.911
0.897
0.884
4.00
0.93
3.96
5.93
1.96
4.00
2.98
f1 (ppm)

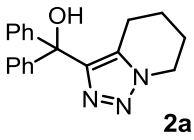

82.21
81.90
77.26
77.00
76.75
63.68
50.12
44.06
31.40
27.54
24.34
22.50
15.95
13.97
f1 (ppm)


OH
Ph
Ph
N3
OH
Ph
Ph
N3

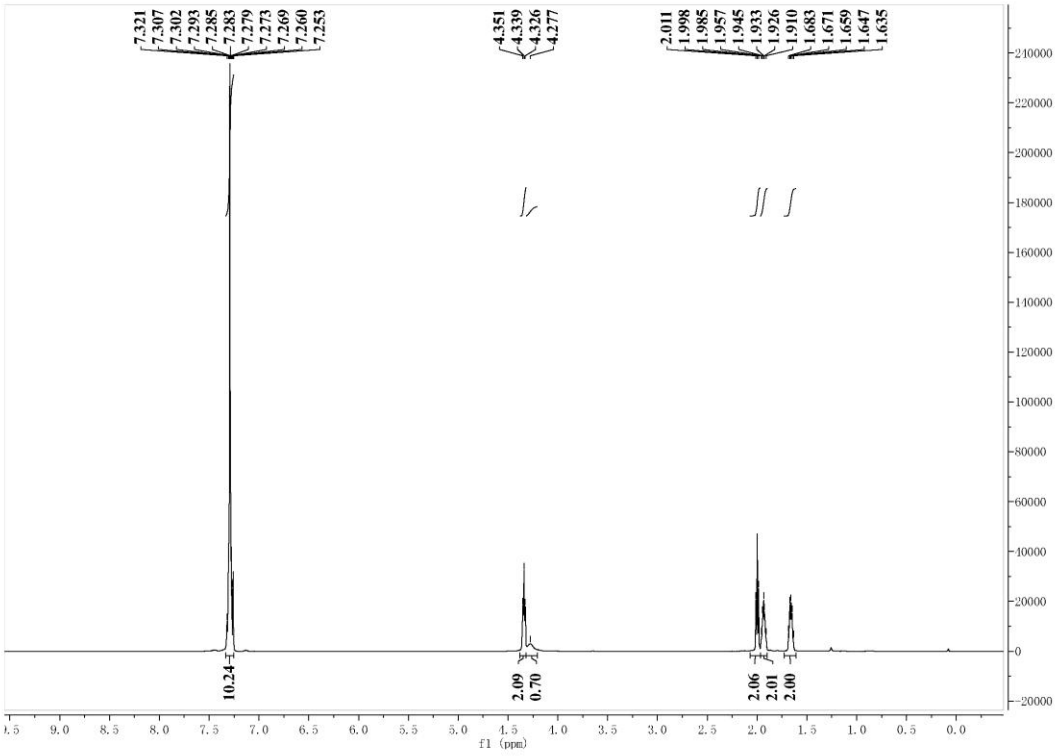
13

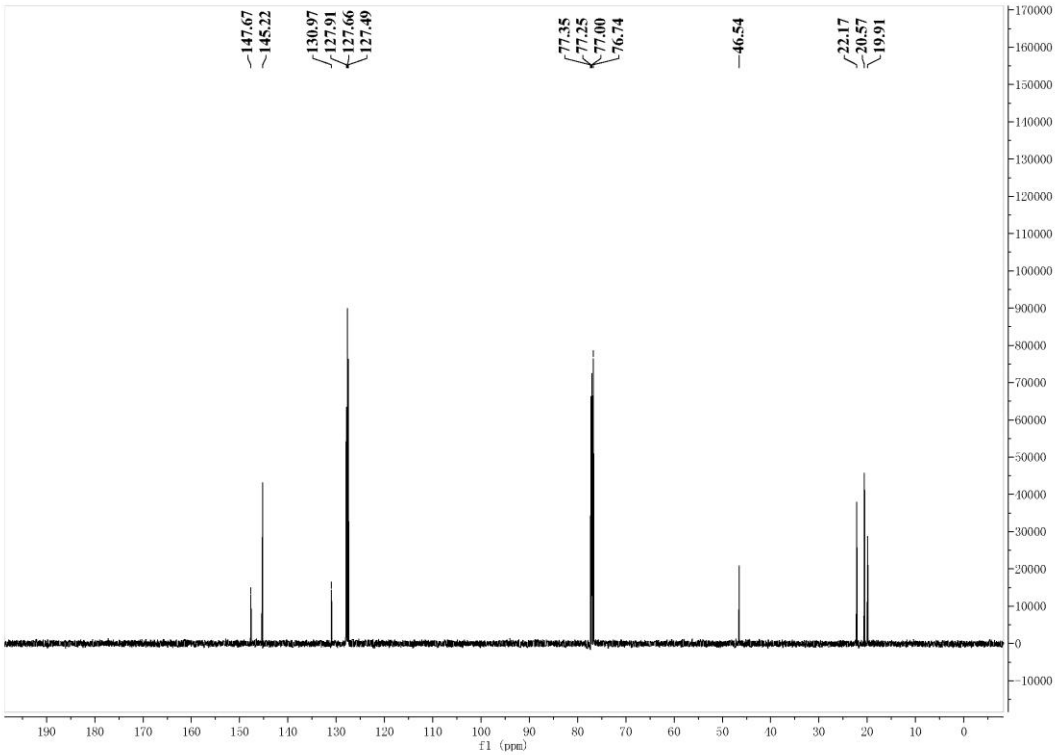

zyl-wmd-180122-02-h-2
7.572
7.556
7.341
7.324
7.308
7.284
7.266
7.260
7.249
3.370
2.821
2.466
8.06
8.06
4.63
4.00
1.93
4.02
f1 (ppm)

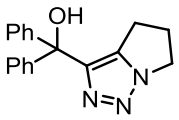

zyl-wmd-18012201-C 2-124
144.90
128.31
127.76
125.83
86.92
82.54
77.32
77.00
76.68
74.49
54.42
42.45
23.73
f1 (ppm)


OH
Ph
Ph
N
N=N

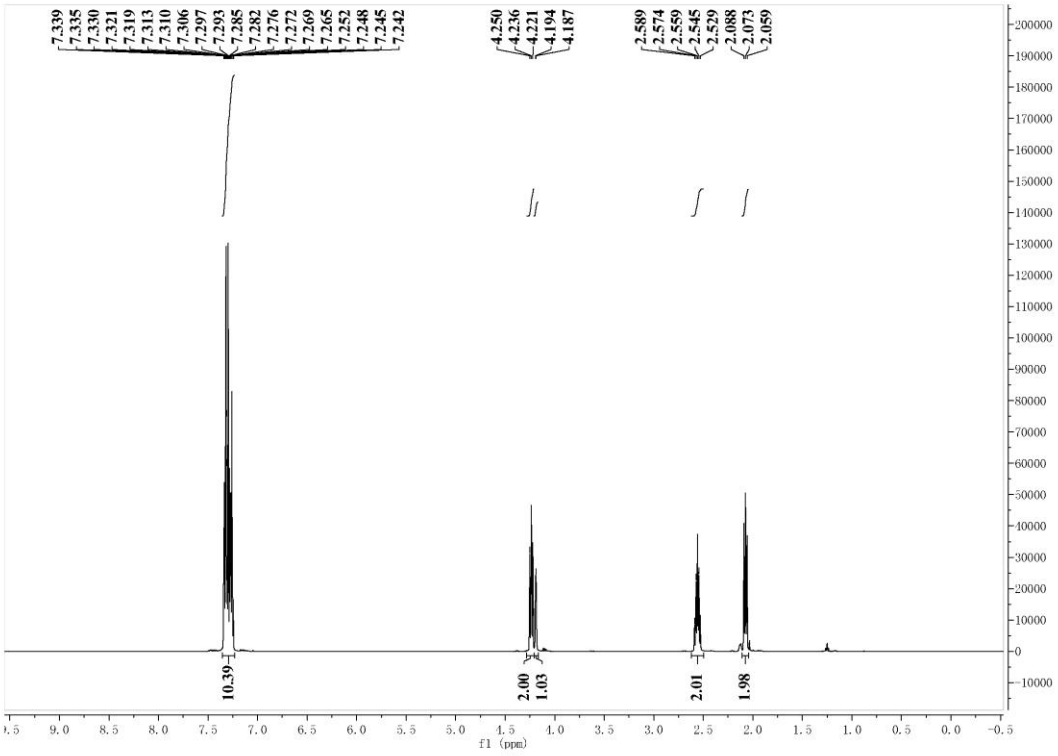
2a

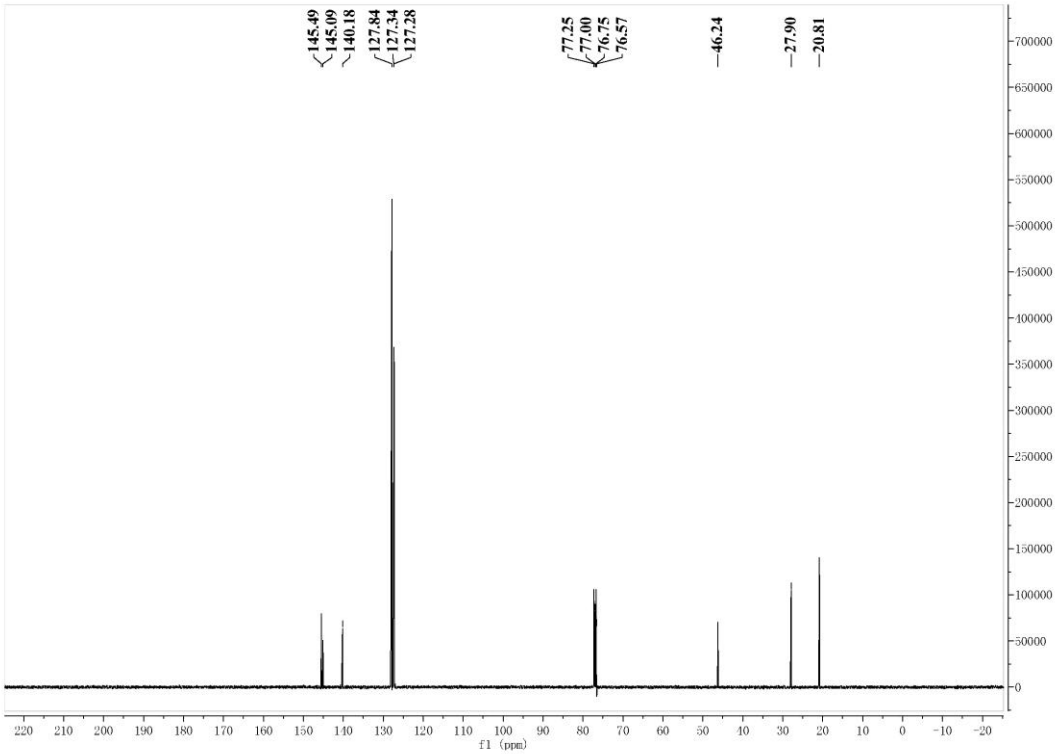

7.321
7.307
7.302
7.293
7.285
7.283
7.279
7.273
7.269
7.260
7.253
4.351
4.339
4.326
4.277
2.011
1.998
1.985
1.957
1.945
1.933
1.926
1.910
1.683
1.671
1.659
1.647
1.635
10.24
2.09
0.70
2.06
2.01
2.00
f1 (ppm)

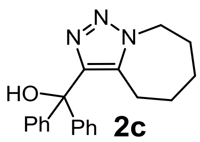

147.67
145.22
130.97
127.91
127.66
127.49
77.35
77.25
77.00
76.74
46.54
22.17
20.57
19.91
f1 (ppm)


OH
Ph
Ph
N
N=N

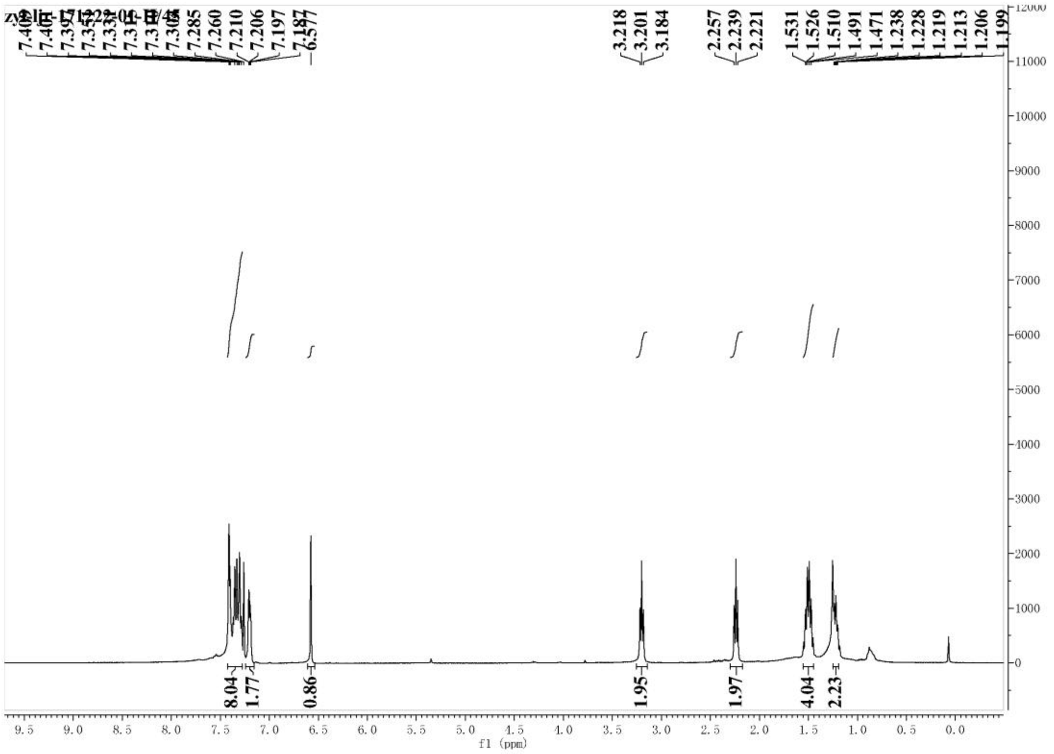
2b

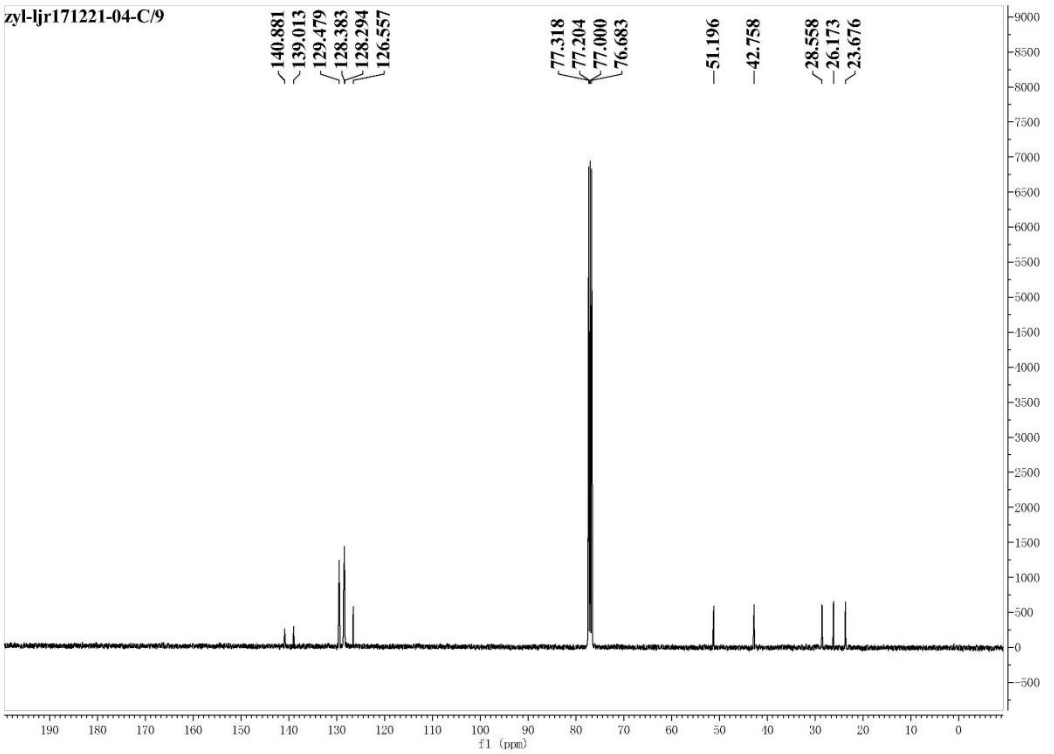

7.339
7.335
7.330
7.321
7.319
7.313
7.310
7.306
7.297
7.293
7.285
7.282
7.276
7.272
7.269
7.265
7.252
7.248
7.245
7.242
4.250
4.236
4.221
4.194
4.187
2.589
2.574
2.559
2.545
2.529
2.088
2.073
2.059
10.39
2.00
1.03
2.01
1.98
f1 (ppm)

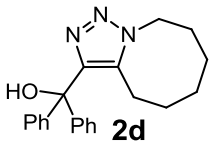

145.49
145.09
140.18
127.84
127.34
127.28
77.25
77.00
76.75
76.57
46.24
27.90
20.81
f1 (ppm)



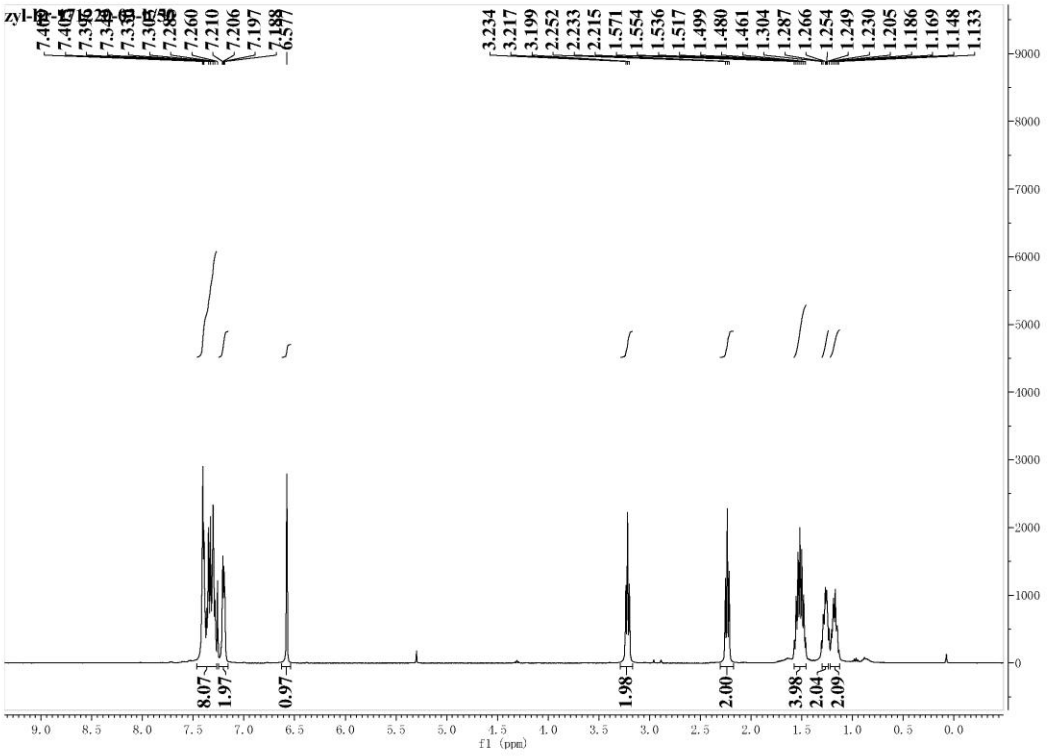
2c

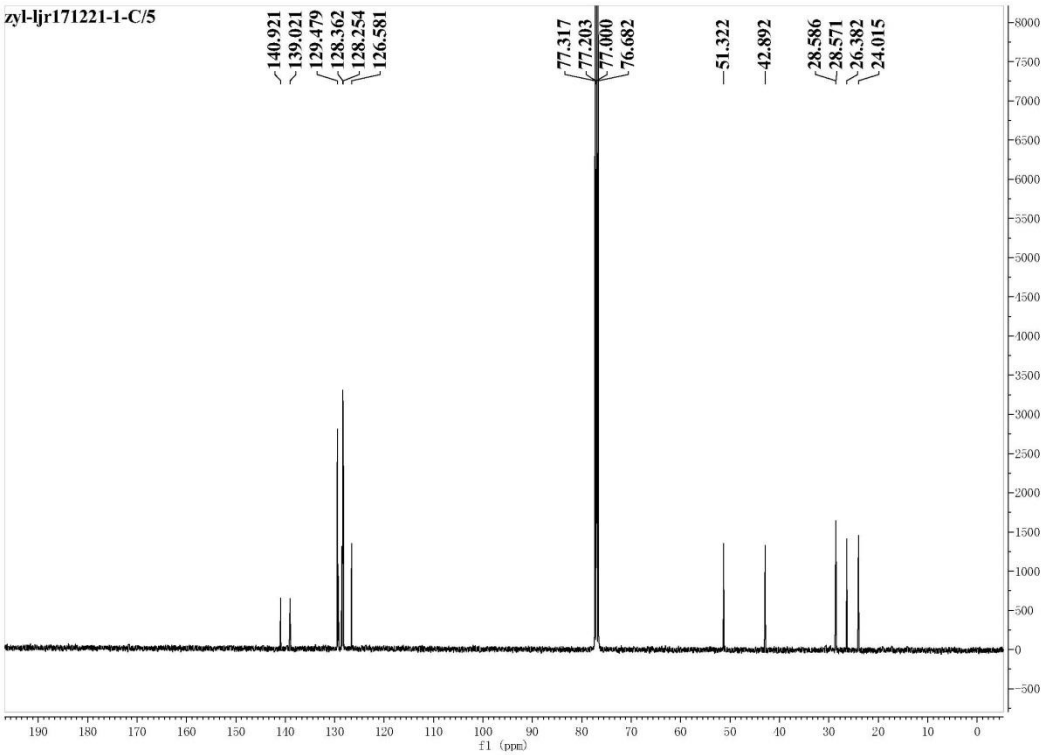

zyl-ljr-171221-04-H/44
7.401
7.397
7.355
7.333
7.310
7.306
7.285
7.260
7.210
7.206
7.197
7.187
6.577
3.218
3.201
3.184
2.257
2.239
2.221
1.531
1.526
1.510
1.491
1.471
1.238
1.228
1.219
1.213
1.206
1.199
8.04
1.77
0.86
1.95
1.97
4.04
2.23
f1 (ppm)

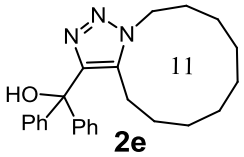

zyl-ljr171221-04-C/9
140.881
139.013
129.479
128.383
128.294
126.557
77.318
77.204
77.000
76.683
51.196
42.758
28.558
26.173
23.676
f1 (ppm)


N
N
N
HO
Ph
Ph

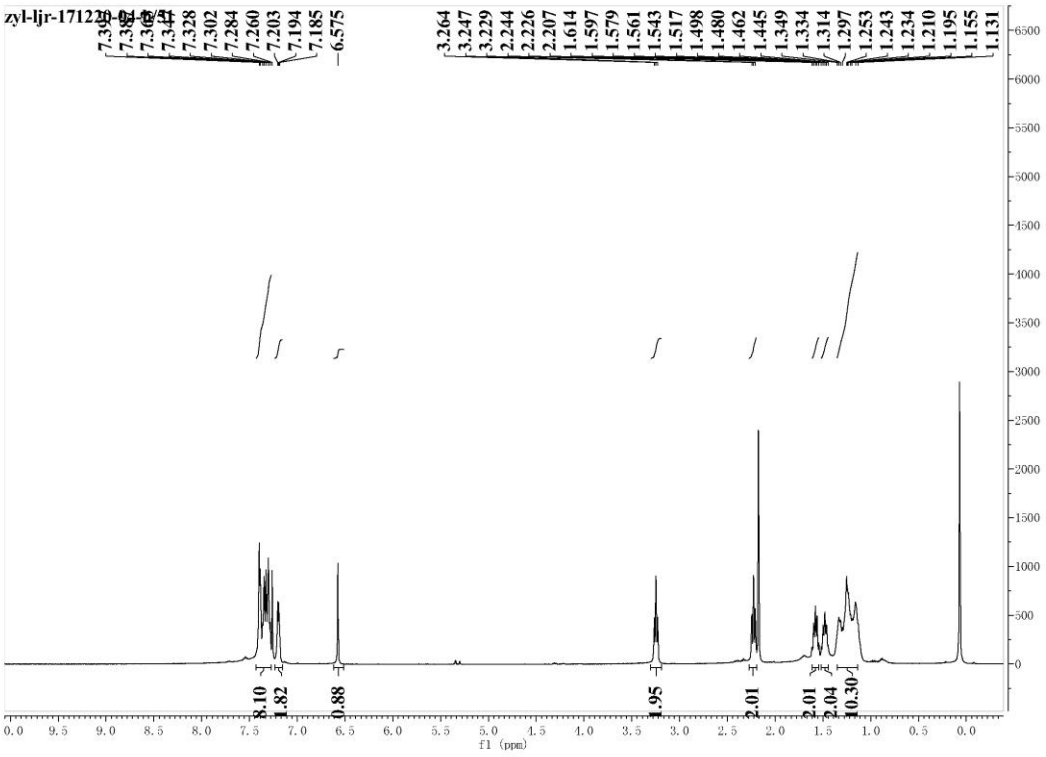
2d

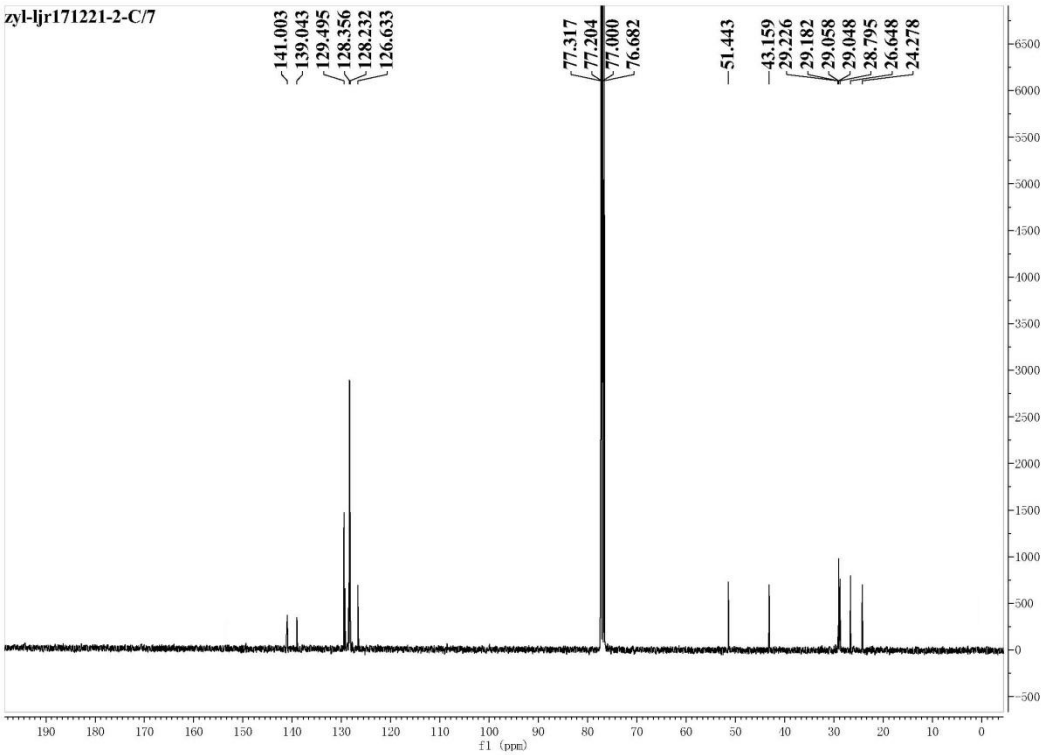

7.577
7.260
7.210
7.206
7.197
3.234
3.217
3.199
2.252
2.233
2.215
1.571
1.554
1.536
1.517
1.499
1.480
1.461
1.304
1.287
1.266
1.254
1.249
1.230
1.205
1.186
1.169
1.148
1.133
8.07
1.97
0.97
1.98
2.00
3.98
2.04
2.09
f1 (ppm)

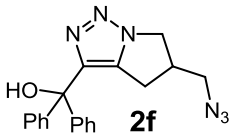

zyl-ljr171221-1-C/5
140.921
139.021
129.479
128.362
128.254
126.581
77.317
77.203
77.000
76.682
51.322
42.892
28.586
28.571
26.382
24.015
f1 (ppm)


N
N
N
11
HO
Ph
Ph

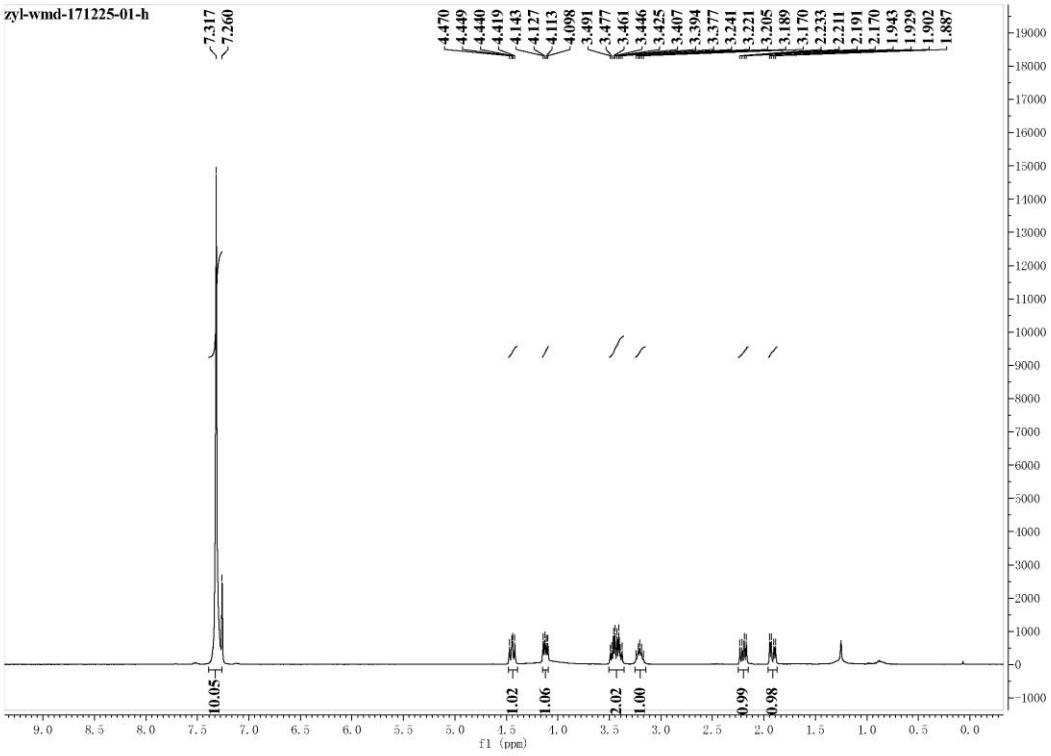
2e

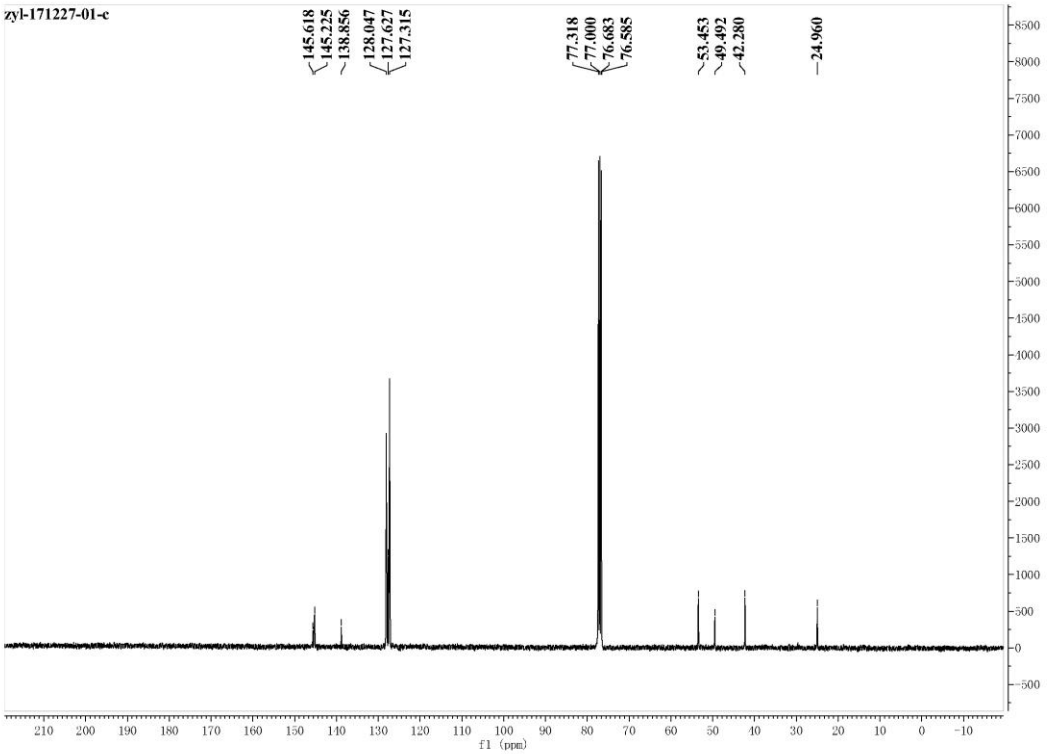

7.328
7.302
7.284
7.260
7.203
7.194
7.185
6.575
3.264
3.247
3.229
2.244
2.226
2.207
1.614
1.597
1.579
1.561
1.543
1.517
1.498
1.480
1.462
1.445
1.349
1.334
1.314
1.297
1.253
1.243
1.234
1.210
1.195
1.155
1.131
8.10
1.82
0.88
1.95
2.01
2.01
2.04
10.30
f1 (ppm)

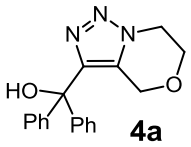

zyl-ljr171221-2-C/7
141.003
139.043
129.495
128.356
128.232
126.633
77.317
77.204
77.000
76.682
51.443
43.159
29.226
29.182
29.058
29.048
28.795
26.648
24.278
f1 (ppm)


HO
Ph
Ph
N3

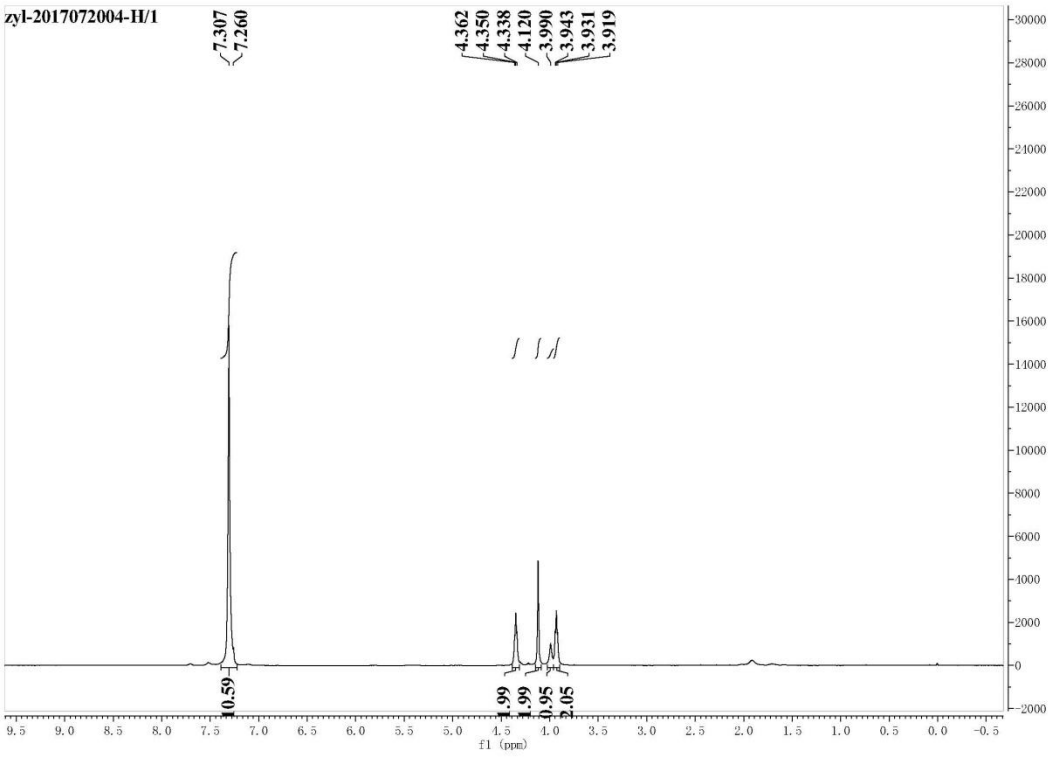
2f

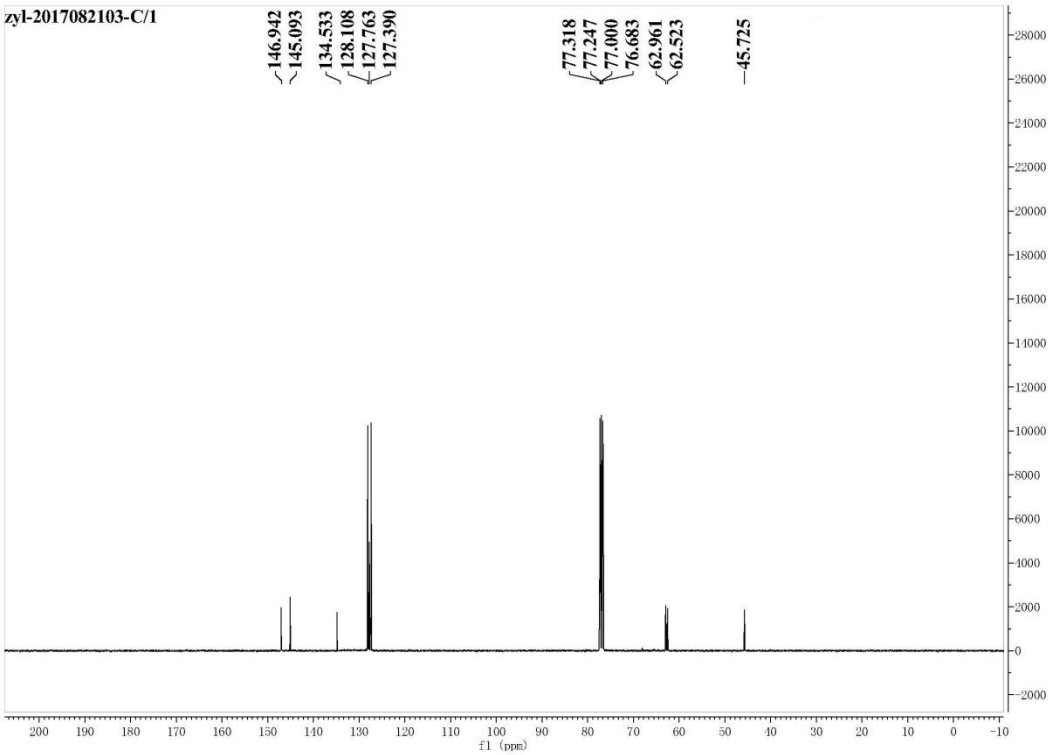

zyl-wmd-171225-01-h
7.317
7.260
4.470
4.449
4.440
4.419
4.143
4.127
4.113
4.098
3.491
3.477
3.461
3.446
3.425
3.407
3.394
3.377
3.241
3.221
3.205
3.189
3.170
2.233
2.211
2.191
2.170
1.943
1.929
1.902
1.887
10.05
1.02
1.06
2.02
1.00
0.99
0.98
f1 (ppm)

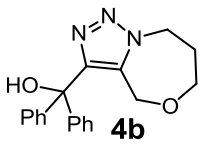

zyl-171227-01-c
145.618
145.225
138.856
128.047
127.627
127.315
77.318
77.000
76.683
76.585
53.453
49.492
42.280
24.960
f1 (ppm)


N
N
N
HO
Ph
Ph
O

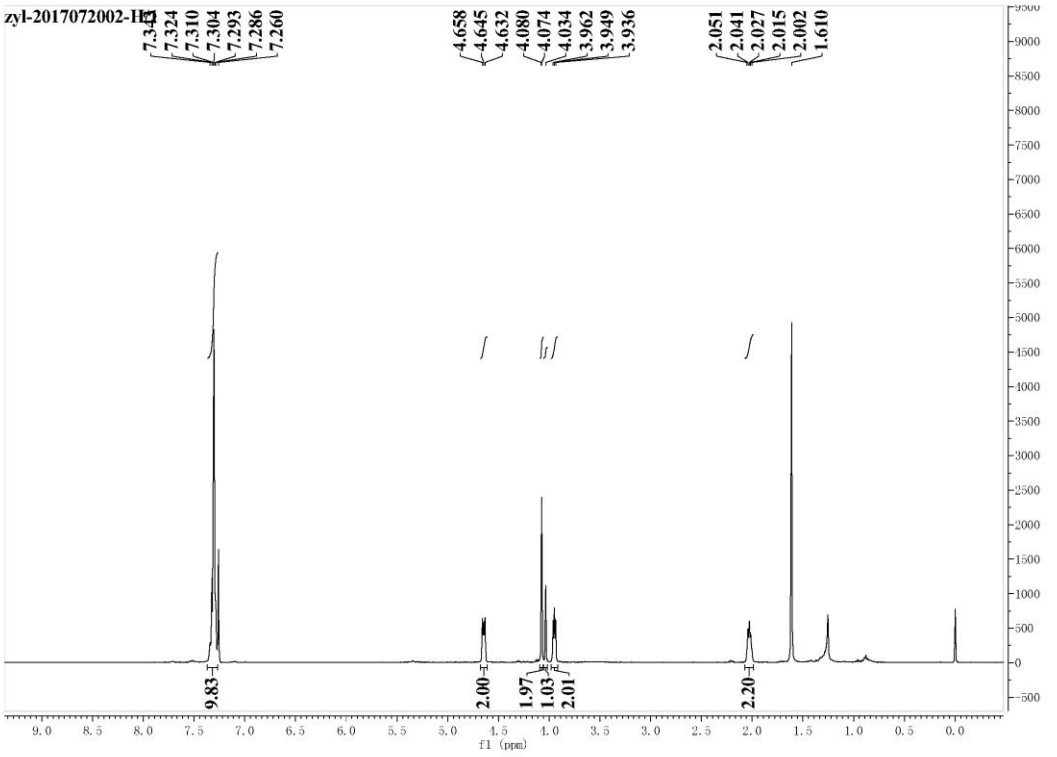
4a

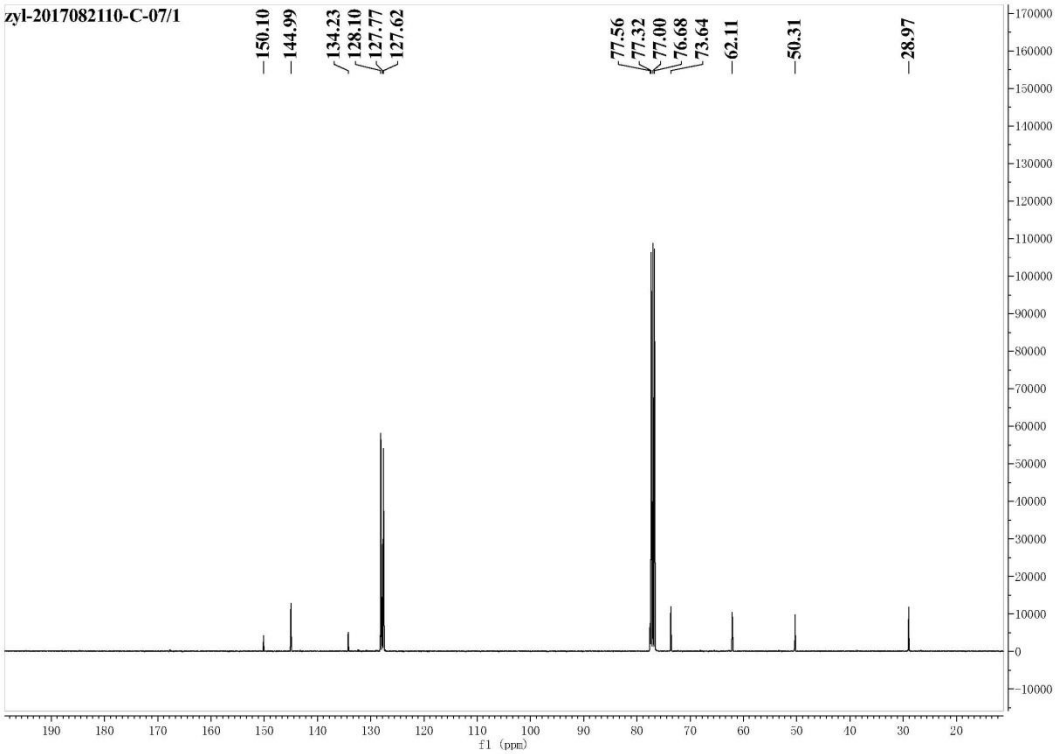

zyl-2017072004-H/1
7.307
7.260
4.362
4.350
4.338
4.120
3.990
3.943
3.931
3.919
10.59
1.99
1.99
0.95
2.05
f1 (ppm)

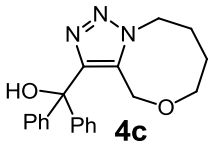

zyl-2017082103-C/1
146.942
145.093
134.533
128.108
127.763
127.390
77.318
77.247
77.000
76.683
62.961
62.523
45.725
f1 (ppm)


HO
Ph
Ph
N
N
N
O

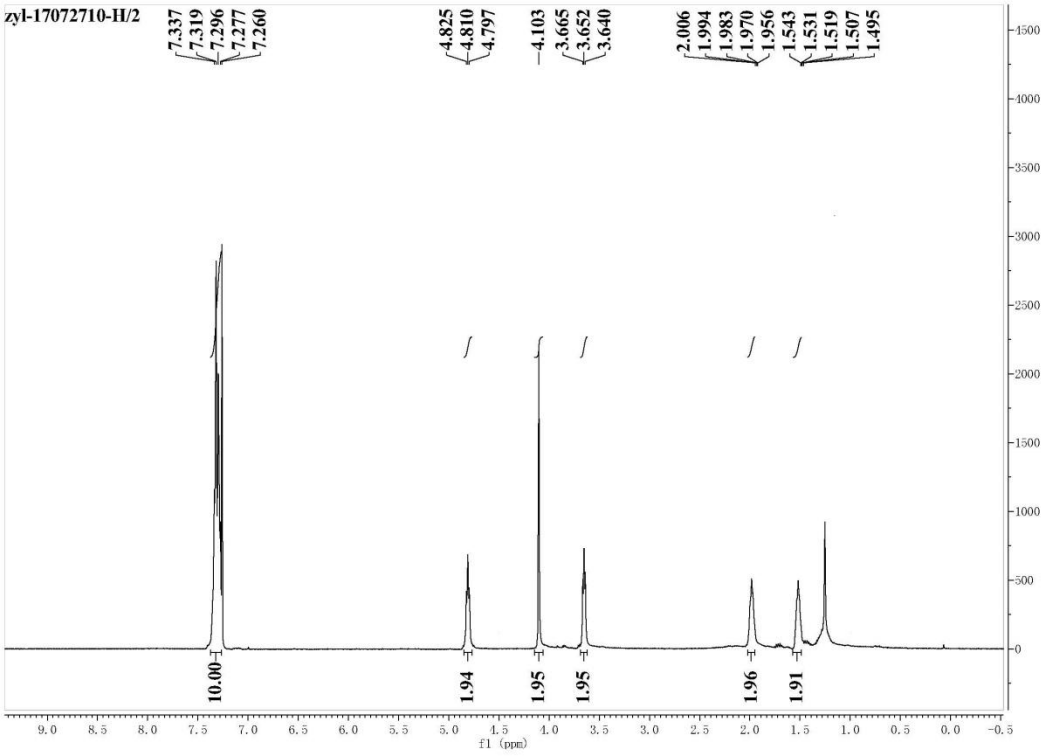
4b

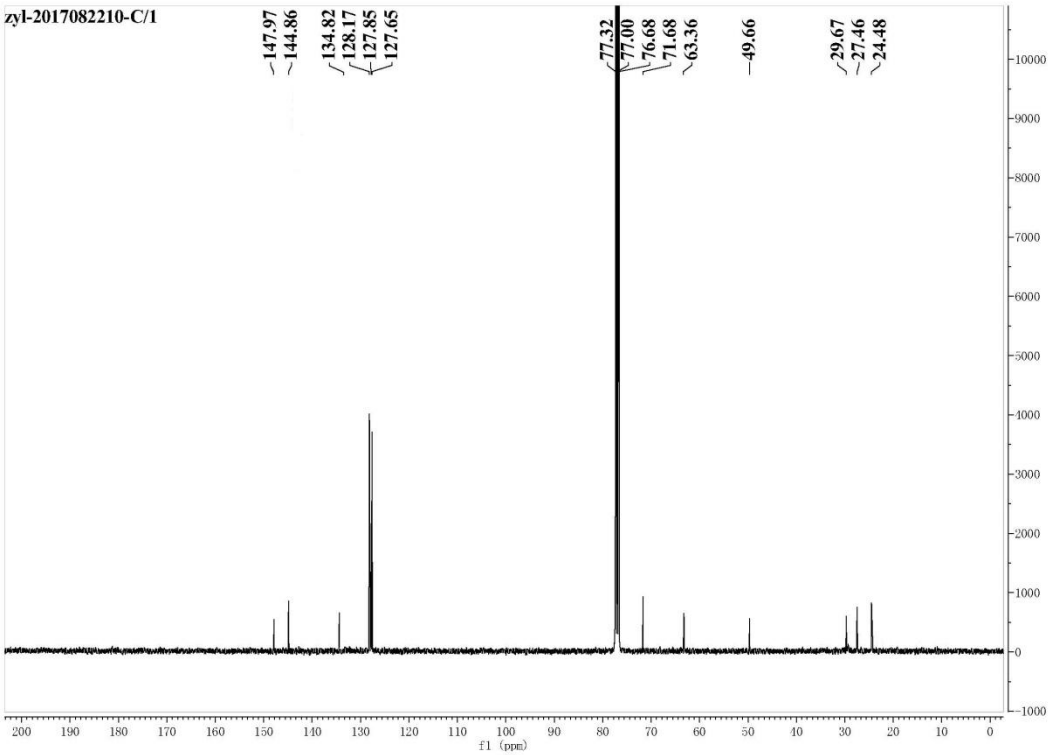

zyl-2017072002-H-1
7.344
7.324
7.310
7.304
7.293
7.286
7.260
4.658
4.645
4.632
4.080
4.074
4.034
3.962
3.949
3.936
2.051
2.041
2.027
2.015
2.002
1.610
9.83
2.00
1.97
1.03
2.01
2.20
f1 (ppm)

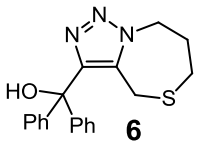

zyl-2017082110-C-07/1
150.10
144.99
134.23
128.10
127.77
127.62
77.56
77.32
77.00
76.68
73.64
62.11
50.31
28.97
f1 (ppm)


HO
Ph
Ph
O
N
N
N

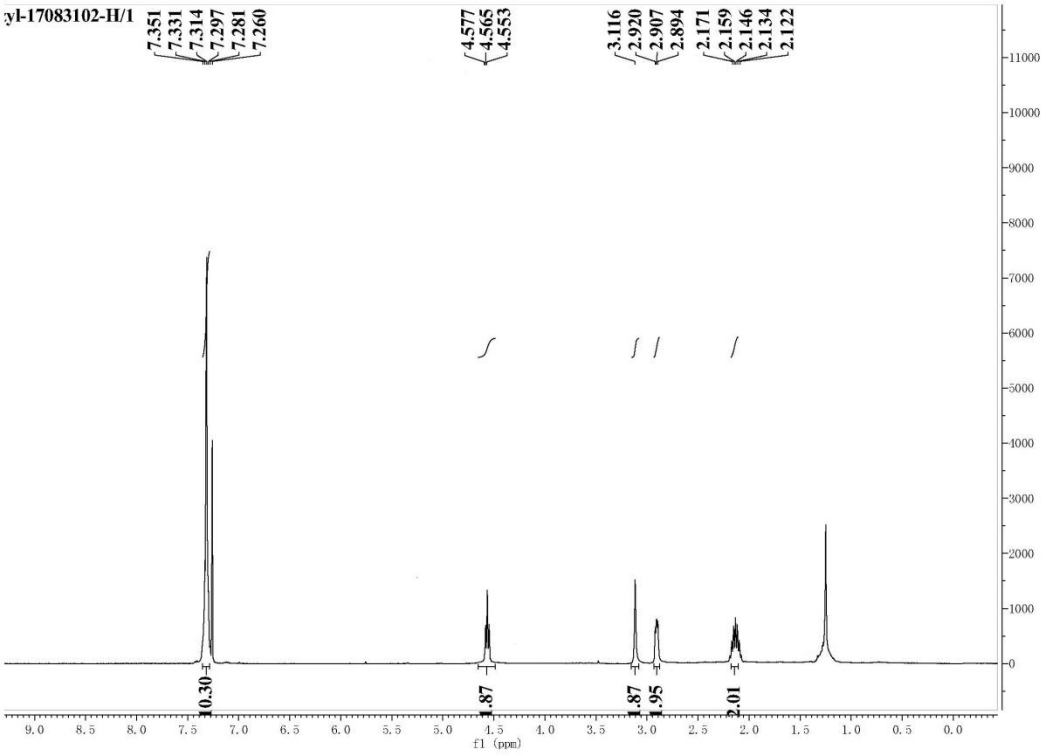
4c

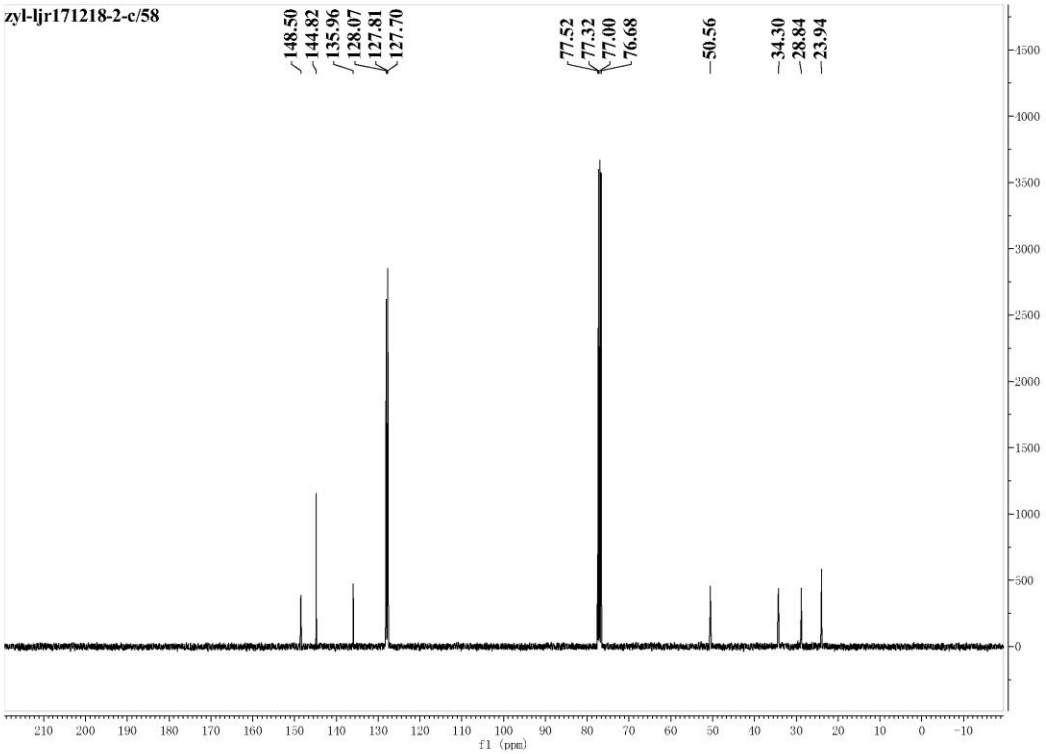

zyl-17072710-H/2
7.337
7.319
7.296
7.277
7.260
4.825
4.810
4.797
4.103
3.665
3.652
3.640
2.006
1.994
1.983
1.970
1.956
1.543
1.531
1.519
1.507
1.495
10.00
1.94
1.95
1.95
1.96
1.91
f1 (ppm)

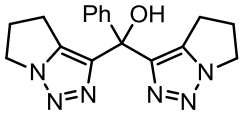

zyl-2017082210-C/1
147.97
144.86
134.82
128.17
127.85
127.65
77.32
77.00
76.68
71.68
63.36
49.66
29.67
27.46
24.48
f1 (ppm)


N
N
N
HO
Ph
Ph
S

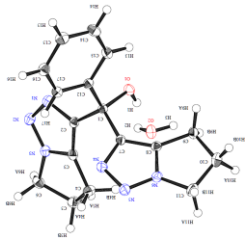
6

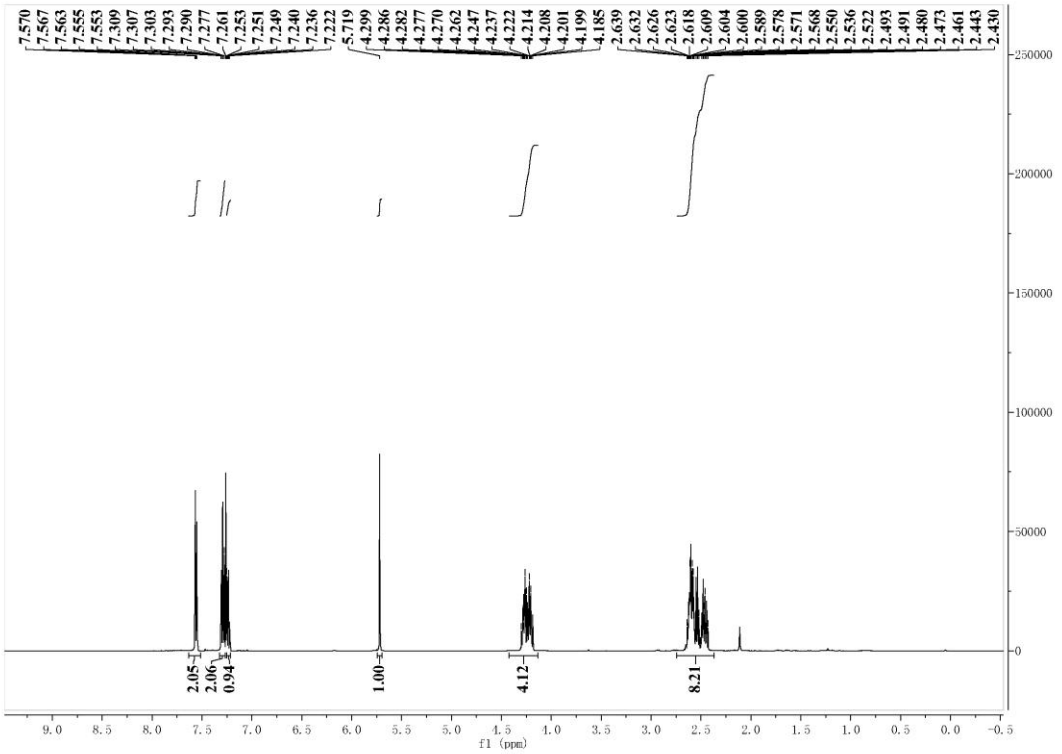

zyl-17083102-H/1
7.351
7.331
7.314
7.297
7.281
7.260
4.577
4.565
4.553
3.116
2.920
2.907
2.894
2.171
2.159
2.146
2.134
2.122
10.30
1.87
1.87
1.95
2.01
f1 (ppm)

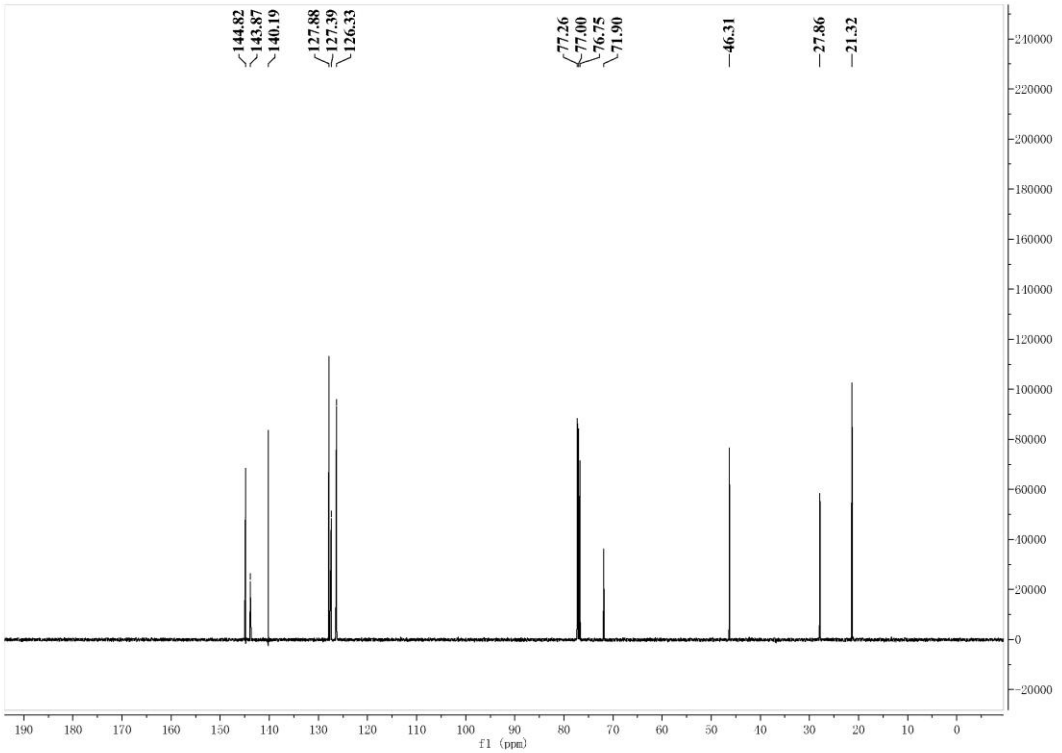

zyl-ljr171218-2-c/58
148.50
144.82
135.96
128.07
127.81
127.70
77.52
77.32
77.00
76.68
50.56
34.30
28.84
23.94
f1 (ppm)

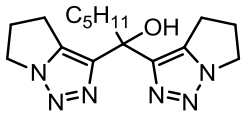

Ph
OH
N
N=N
N=N
N

8a

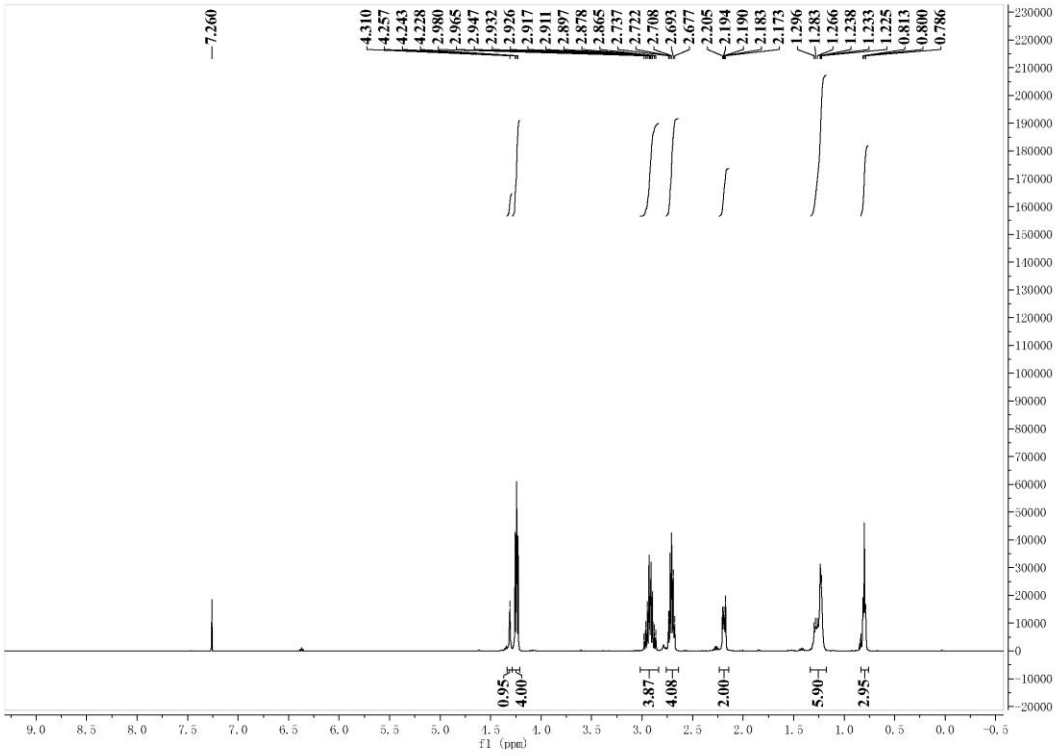


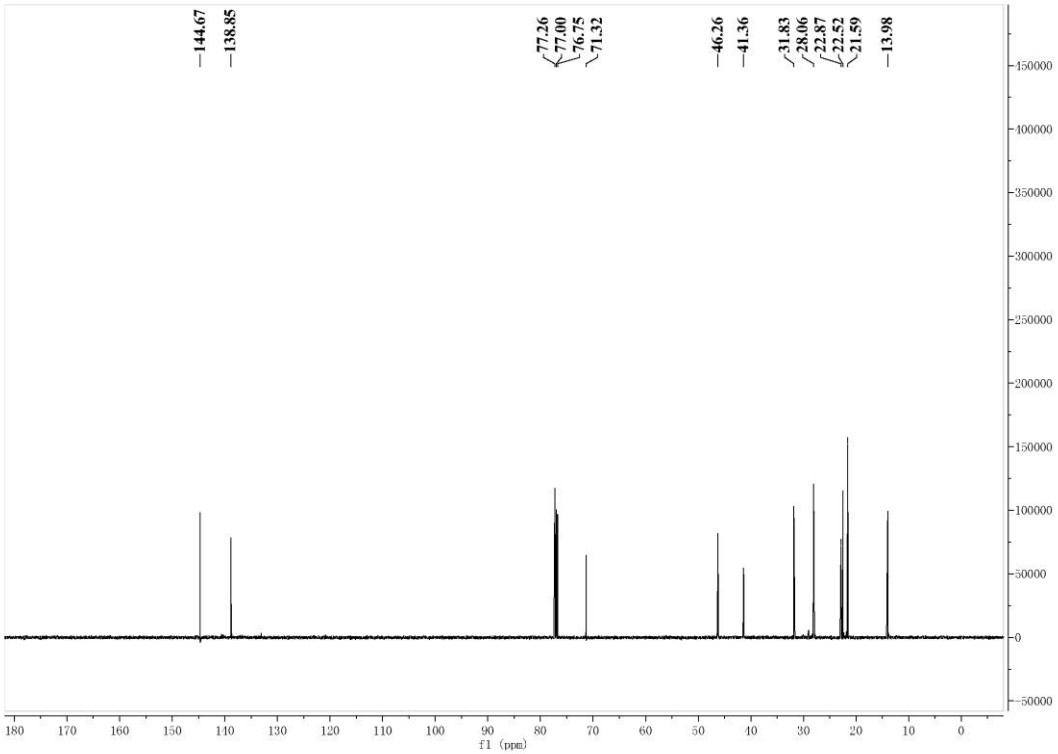

7.570
7.567
7.563
7.555
7.553
7.309
7.307
7.303
7.293
7.290
7.277
7.261
7.253
7.251
7.249
7.240
7.236
7.222
5.719
4.299
4.286
4.282
4.277
4.270
4.262
4.247
4.237
4.222
4.214
4.208
4.201
4.199
4.185
2.639
2.632
2.626
2.623
2.618
2.609
2.604
2.600
2.589
2.578
2.571
2.568
2.550
2.536
2.522
2.493
2.491
2.480
2.473
2.461
2.443
2.430
2.05
2.06
0.94
1.00
4.12
8.21
f1 (ppm)

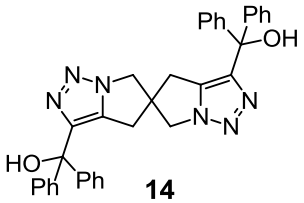

144.82
143.87
140.19
127.88
127.39
126.33
77.26
77.00
76.75
71.90
46.31
27.86
21.32
f1 (ppm)


C5H11
OH
N
N=N
N=N
N

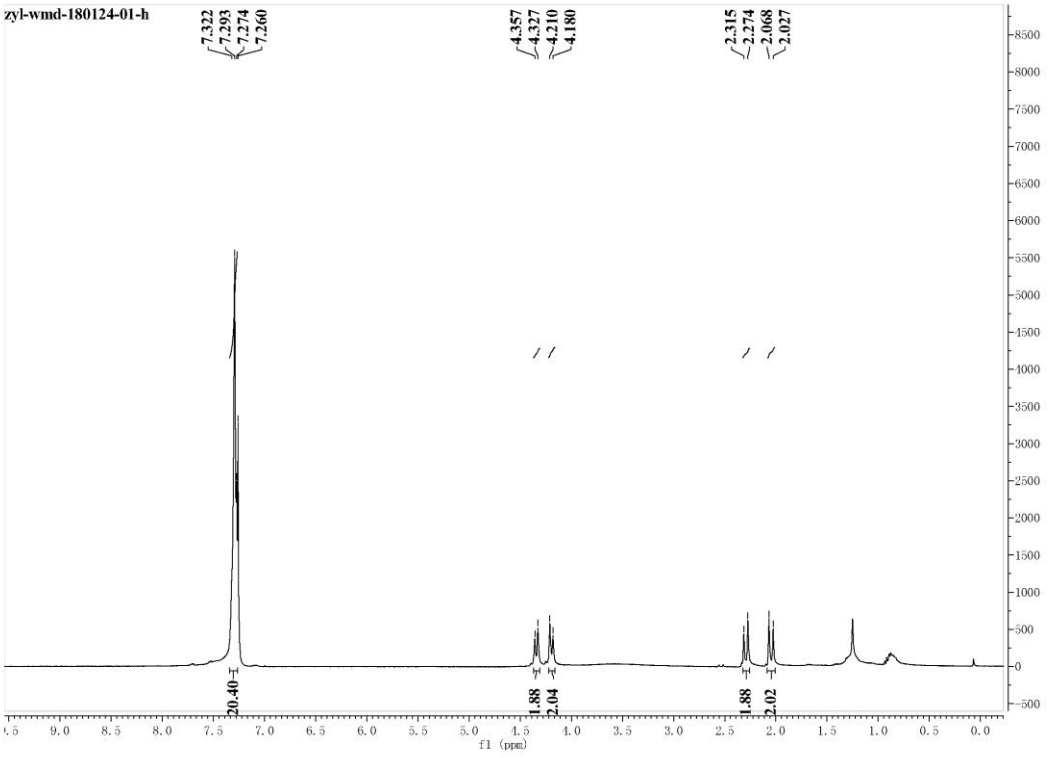
8b

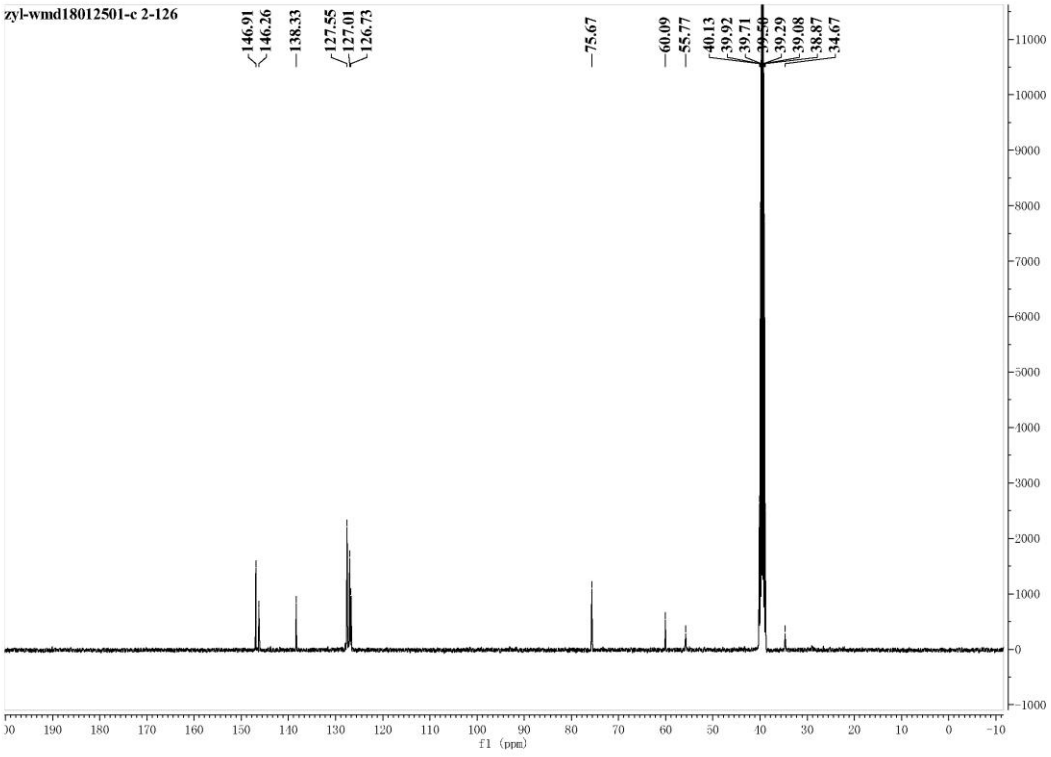

7.260
4.310
4.257
4.243
4.228
2.980
2.965
2.947
2.932
2.926
2.917
2.911
2.897
2.878
2.865
2.737
2.722
2.708
2.693
2.677
2.205
2.194
2.190
2.183
2.173
1.296
1.283
1.266
1.238
1.233
1.225
0.813
0.800
0.786
0.95
4.00
3.87
4.08
2.00
5.90
2.95
f1 (ppm)


144.67
138.85
77.26
77.00
76.75
71.32
46.26
41.36
31.83
28.06
22.87
22.52
21.59
13.98
f1 (ppm)


Ph
Ph
OH
N
N
N
N
N
N
HO
Ph
Ph

14


zyl-wmd-180124-01-h
7.322
7.293
7.274
7.260
4.357
4.327
4.210
4.180
2.315
2.274
2.068
2.027
20.40
1.88
2.04
1.88
2.02
f1 (ppm)


zyl-wmd18012501-c 2-126
146.91
146.26
138.33
127.55
127.01
126.73
75.67
60.09
55.77
40.13
39.92
39.71
39.50
39.29
39.08
38.87
34.67
f1 (ppm)