



Supporting Information

for

One-pot Ugi-azide and Heck reactions for the synthesis of heterocyclic systems containing tetrazole and 1,2,3,4-tetrahydroisoquinoline

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General reaction procedures, compound characterization data, and copies of NMR spectra

Table of contents

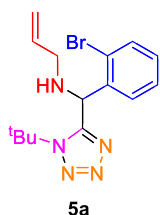
1. General information.....	S1
2. Analytical data of products.....	S1
3. X-ray report of 6d and 8c	S6
4. ¹ H NMR, ¹³ C NMR of products 5a , 6 and 8	S8

1. General information

Chemicals and solvents were purchased from commercial source and used without further purification. ^1H (300 MHz, 400 MHz), ^{13}C NMR spectra (75 MHz or 126 MHz) were recorded on a Bruker NMR spectrometer. LC-MS were performed on an Agilent 2100 system with C18 column (5.0 μm , 6.0 \times 50 mm). The mobile phases were MeOH and H_2O both containing 0.05% trifluoroacetic acid. A linear gradient was used to increase from 25:75 (v/v) MeOH/ H_2O to 100% MeOH in 7.0 min at a flow rate of 0.7 mL/min. UV detections were conducted at 210 nm, 254 nm, and 365 nm. Low resolution mass spectra were recorded in APCI (atmospheric pressure chemical ionization). HRMS were performed on Agilent 6540 Q-TOF mass spectrometer (ESI). Flash column chromatography was performed using silica gel (200–300 mesh).

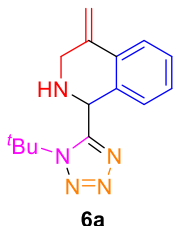
2. Analytical data of products

N-((2-Bromophenyl)(1-(*tert*-butyl)-1*H*-tetrazol-5-yl)methyl)prop-2-en-1-amine (5a)



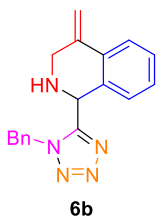
White solid, 321mg, 92% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.59 (dd, $J = 7.9, 1.5$ Hz, 1H), 7.20 (dd, $J = 7.5, 1.4$ Hz, 1H), 7.16–7.11 (m, 1H), 7.08 (dd, $J = 7.6, 1.8$ Hz, 1H), 5.94 (dddd, $J = 18.4, 9.5, 7.2, 5.4$ Hz, 1H), 5.72 (s, 1H), 5.10 (t, $J = 1.5$ Hz, 1H), 5.07 (dd, $J = 6.2, 1.6$ Hz, 1H), 3.42–3.32 (m, 1H), 3.19–3.12 (m, 1H), 2.36 (s, 1H), 1.57 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.7, 138.2, 136.0, 133.6, 130.0, 129.0, 128.3, 124.3, 117.6, 61.6, 56.2, 50.9, 29.8. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{20}\text{BrN}_5$ ($[\text{M}+\text{Na}]^+$): 372.0800, found 372.0792.

1-(1-(*tert*-Butyl)-1*H*-tetrazol-5-yl)-4-methylene-1,2,3,4-tetrahydroisoquinoline (6a)



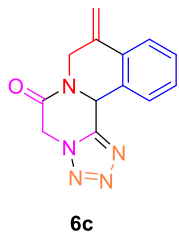
Light yellow oil, 161mg, 60% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.73 (dd, $J = 8.0, 1.4$ Hz, 1H), 7.29 (d, $J = 7.5$ Hz, 1H), 7.17 (d, $J = 1.3$ Hz, 1H), 6.66 (d, $J = 7.7$ Hz, 1H), 5.74 (s, 1H), 5.61 (s, 1H), 5.04 (s, 1H), 3.80 (d, $J = 15.2$ Hz, 1H), 3.68 (s, 1H), 2.03 (d, $J = 16.7$ Hz, 1H), 1.85 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.5, 138.8, 133.9, 133.0, 128.2, 128.0, 126.7, 124.5, 108.3, 62.1, 53.1, 48.6, 30.2. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{19}\text{N}_5$ ($[\text{M}+\text{Na}]^+$): 292.1538, found 292.1520.

1-(1-Benzyl-1*H*-tetrazol-5-yl)-4-methylene-1,2,3,4-tetrahydroisoquinoline (6b)



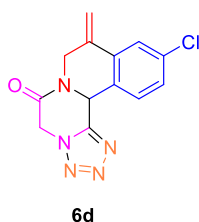
yellow oil, 174 mg, 58 yield. ^1H NMR (300 MHz, Chloroform-*d*) δ 7.67 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.21 (dd, $J = 5.2, 2.2$ Hz, 4H), 7.09–7.03 (m, 2H), 6.99 (td, $J = 7.6, 1.3$ Hz, 1H), 6.52 (d, $J = 7.8$ Hz, 1H), 5.66–5.55 (m, 3H), 5.48 (d, $J = 14.9$ Hz, 1H), 5.04 (d, $J = 1.4$ Hz, 1H), 3.68–3.54 (m, 2H), 2.47 (s, 1H). ^{13}C NMR (101 MHz, DMSO-*d*₆) δ 150.4, 133.5, 128.5, 127.6, 126.9, 123.5, 123.2, 123.0, 122.9, 122.7, 121.9, 119., 103.2, 72.4, 72.1, 71.8, 47.1, 46.2, 43.6. HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{17}\text{N}_5$ ($[\text{M}+\text{Na}]^+$): 326.1832, found 326.1817.

9-Methylene-9,13b-dihydro-8*H*-tetrazolo[5',1':3,4]pyrazino[2,1-*a*]isoquinolin-6(5*H*)-one (6c)



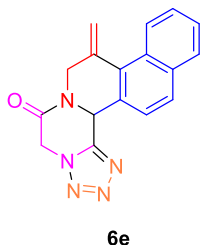
Light yellow solid, 192 mg, 76% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, $J = 7.6$ Hz, 1H), 7.70 (d, $J = 7.7$ Hz, 1H), 7.34 (dt, $J = 15.8, 7.3$ Hz, 2H), 6.33 (s, 1H), 5.75 (s, 1H), 5.43 (d, $J = 15.0$ Hz, 1H), 5.34 (s, 1H), 5.20 (d, $J = 18.0$ Hz, 1H), 4.98 (d, $J = 18.0$ Hz, 1H), 3.91 (d, $J = 15.0$ Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.5, 147.9, 135.5, 132.57, 129.8, 129.2, 129.0, 125.9, 124.9, 112.0, 53.7, 48.0, 47.8. HRMS (ESI) calcd for $\text{C}_{13}\text{H}_{11}\text{N}_5\text{O}$ ($[\text{M}+\text{Na}]^+$): 276.0866, found 276.0861.

11-Chloro-9-methylene-9,13b-dihydro-8H-tetrazolo[5',1':3,4]pyrazino[2,1-a]isoquinolin-6(5H)-one (6d)



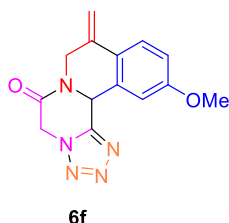
White solid, 215 mg, 75% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 8.5 Hz, 1H), 7.68 (d, *J* = 1.9 Hz, 1H), 7.31 (dd, *J* = 8.5, 1.9 Hz, 1H), 6.31 (s, 1H), 5.77 (s, 1H), 5.45 (d, *J* = 15.1 Hz, 1H), 5.42 (s, 1H), 5.24 (d, *J* = 18.0 Hz, 1H), 5.03 (d, *J* = 18.0 Hz, 1H), 3.90 (d, *J* = 15.0 Hz, 1H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 159.4, 147.7, 135.4, 134.5, 134.3, 129.0, 128.1, 127.6, 124.9, 113.3, 53.3, 47.8, 47.6. HRMS (ESI) calcd for C₁₃H₁₀ClN₅O ([M+Na]⁺): 310.0472, found 310.0472.

9-Methylene-9,15b-dihydro-8H-benzo[*g*]tetrazolo[5',1':3,4]pyrazino[2,1-a]isoquinolin-6(5H)-one (6e)



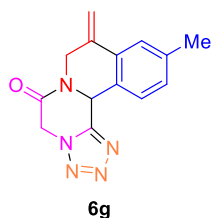
Light yellow solid, 230 mg, 76% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.38 (d, *J* = 8.0 Hz, 1H), 7.91 – 7.85 (m, 1H), 7.78 (d, *J* = 8.6 Hz, 1H), 7.62 – 7.52 (m, 2H), 7.34 (d, *J* = 8.6 Hz, 1H), 6.15 (s, 1H), 5.89 (s, 1H), 5.75 (d, *J* = 1.9 Hz, 1H), 5.24 (d, *J* = 17.9 Hz, 1H), 5.01 (dd, *J* = 16.5, 7.9 Hz, 2H), 4.30 (d, *J* = 15.0 Hz, 1H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 159.2, 147.3, 134.9, 134.1, 132.9, 130.0, 129.5, 128.8, 128.7, 127.5, 126.9, 124.9, 120.6, 120.2, 52.6, 50.0, 47.8. HRMS (ESI) calcd for C₁₇H₁₃N₅O ([M+Na]⁺): 326.1011, found 326.1018.

12-Methoxy-9-methylene-9,13b-dihydro-8H-tetrazolo[5',1':3,4]pyrazino[2,1-a]isoquinolin-6(5H)-one (6f)



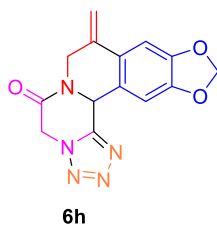
yellow solid, 206 mg, 73% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 8.8 Hz, 1H), 7.30 (d, *J* = 2.0 Hz, 1H), 6.85 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.28 (s, 1H), 5.58 (d, *J* = 1.5 Hz, 1H), 5.38 (d, *J* = 14.9 Hz, 1H), 5.19 (s, 1H), 5.18 – 5.13 (m, 1H), 4.97 (dd, *J* = 17.9, 1.4 Hz, 1H), 3.85 (d, *J* = 14.9 Hz, 1H), 3.77 (s, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 160.0, 159.4, 147.9, 135.0, 131.0, 126.3, 124.9, 115.7, 110.3, 109.5, 55.5, 53.8, 48.1, 47.7. HRMS (ESI) calcd for C₁₄H₁₃N₅O₂ ([M+Na]⁺): 306.0979, found 306.0967.

11-Methyl-9-methylene-9,13b-dihydro-8H-tetrazolo[5',1':3,4]pyrazino[2,1-a]isoquinolin-6(5H)-one (6g)



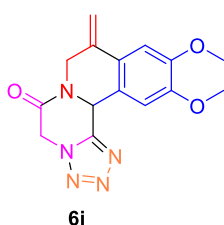
brown solid, 202 mg, 76% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 8.1 Hz, 1H), 7.51 (s, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 6.29 (s, 1H), 5.74 (s, 1H), 5.42 (d, *J* = 15.0 Hz, 1H), 5.32 (s, 1H), 5.20 (d, *J* = 18.0 Hz, 1H), 4.97 (d, *J* = 17.9 Hz, 1H), 3.89 (d, *J* = 15.0 Hz, 1H), 2.35 (s, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 159.5, 148.1, 139.1, 135.6, 132.3, 129.8, 127.0, 125.8, 125.3, 111.7, 53.6, 48.1, 47.8, 21.2. HRMS (ESI) calcd for C₁₄H₁₃N₅O ([M+Na]⁺): 290.1023, found 290.1018.

9-Methylene-9,14b-dihydro-8H-[1,3]dioxolo[4,5-*g*]tetrazolo[5',1':3,4]pyrazino[2,1-a]isoquinolin-6(5H)-one (6h)



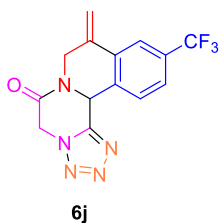
brown solid, 225 mg, 76% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.28 (s, 1H), 7.10 (s, 1H), 6.24 (s, 1H), 5.99 (d, *J* = 1.1 Hz, 1H), 5.94 (d, *J* = 1.1 Hz, 1H), 5.55 (d, *J* = 1.3 Hz, 1H), 5.39 (d, *J* = 14.9 Hz, 1H), 5.24 (s, 1H), 5.20 (d, *J* = 18.1 Hz, 1H), 4.99 (dd, *J* = 18.0, 1.3 Hz, 1H), 3.84 (d, *J* = 14.9 Hz, 1H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 159.5, 148.5, 148.5, 148.0, 135.3, 127.0, 123.9, 110.4, 106.1, 104.5, 101.8, 53.6, 47.9, 47.7. HRMS (ESI) calcd for C₁₄H₁₁N₅O₃ ([M+Na]⁺): 320.0753, found 320.0760.

11,12-Dimethoxy-9-methylene-9,13b-dihydro-8H-tetrazolo[5',1':3,4]pyrazino[2,1-a]isoquinolin-6(5H)-one (6i)



brown solid, 247 mg, 79% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.40 (s, 1H), 7.11 (s, 1H), 6.31 (s, 1H), 5.59 (d, *J* = 1.5 Hz, 1H), 5.43 (d, *J* = 14.8 Hz, 1H), 5.25 (s, 1H), 5.23 – 5.18 (m, 1H), 5.02 (dd, *J* = 18.0, 1.4 Hz, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.84 (d, *J* = 14.8 Hz, 1H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 159.4, 149.9, 149.4, 148.2, 135.2, 125.0, 122.4, 109.5, 108.4, 106.8, 56.1, 56.0, 53.6, 48.1, 47.7. HRMS (ESI) calcd for C₁₅H₁₅N₅O₃ ([M+Na]⁺): 336.1069, found 336.1069.

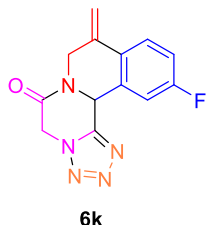
9-Methylene-11-(trifluoromethyl)-9,13b-dihydro-8H-tetrazolo[5',1':3,4]pyrazino[2,1-a]isoquinolin-6(5H)-one (6j)



White solid, 237 mg, 74% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.02 (d, J = 8.3 Hz, 1H), 7.95 (s, 1H), 7.59 (d, J = 8.3 Hz, 1H), 6.38 (s, 1H), 5.86 (s, 1H), 5.53 – 5.48 (m, 2H), 5.26 (d, J = 18.4 Hz, 1H), 5.04 (dd, J = 18.1, 1.2 Hz, 1H), 3.93 (d, J = 15.0 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 159.4, 147.5, 134.4, 133.5, 133.1, 131.8, 131.6, 127.0, 125.5, 121.9, 113.9, 53.5, 47.8, 47.7. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -63.0. HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{10}\text{F}_3\text{N}_5\text{O}$ ($[\text{M}+\text{Na}]^+$): 344.0759, found 344.0735.

6j

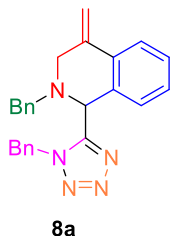
12-Fluoro-9-methylene-9,13b-dihydro-8H-tetrazolo[5',1':3,4]pyrazino[2,1-a]isoquinolin-6(5H)-one (6k)



Light yellow solid, 208 mg, 77% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.70 (dd, J = 8.8, 5.5 Hz, 1H), 7.59 (dd, J = 9.4, 2.4 Hz, 1H), 7.08 (td, J = 8.4, 2.6 Hz, 1H), 6.32 (s, 1H), 5.69 (s, 1H), 5.45 (d, J = 15.0 Hz, 1H), 5.34 (s, 1H), 5.24 (d, J = 18.0 Hz, 1H), 5.06 – 4.99 (m, 1H), 3.90 (d, J = 15.0 Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.6, 161.6, 159.4, 147.6, 134.5, 131.7, 128.7, 127.0, 127.0, 116.7, 116.6, 113.4, 113.2, 111.8, 53.5, 47.9, 47.8. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -109.9. HRMS (ESI) calcd for $\text{C}_{13}\text{H}_{10}\text{FN}_5\text{O}$ ($[\text{M}+\text{Na}]^+$): 294.0771, found 294.0767.

6k

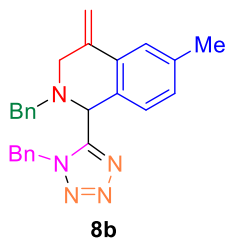
2-Benzyl-1-(1-benzyl-1H-tetrazol-5-yl)-4-methylene-1,2,3,4-tetrahydroisoquinoline (8a)



Light yellow solid, 290 mg, 74% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.74 – 7.66 (m, 1H), 7.37 – 7.29 (m, 3H), 7.25 – 7.14 (m, 6H), 7.03 (d, J = 1.3 Hz, 1H), 6.86 – 6.78 (m, 2H), 6.53 (d, J = 7.8 Hz, 1H), 5.70 (s, 1H), 5.58 (d, J = 15.0 Hz, 1H), 5.36 (s, 1H), 5.23 (d, J = 15.0 Hz, 1H), 5.09 (s, 1H), 3.70 (dd, J = 27.4, 13.5 Hz, 2H), 3.51 (d, J = 13.5 Hz, 1H), 3.28 – 3.20 (m, 1H). ^{13}C NMR (101 MHz, DMSO-*d*₆) δ 155.9, 137.7, 136.7, 135.0, 132.7, 130.9, 129.5, 129.2, 128.9, 128.8, 128.7, 128.6, 128.4, 128.2, 127.9, 124.2, 111.0, 57.5, 56.5, 51.4, 50.7. HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{23}\text{N}_5$ ($[\text{M}+\text{Na}]^+$): 416.1851, found 416.1834.

8a

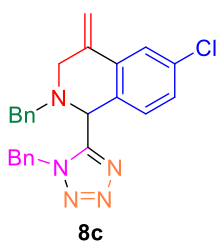
2-Benzyl-1-(1-benzyl-1H-tetrazol-5-yl)-6-methyl-4-methylene-1,2,3,4-tetrahydroisoquinoline (8b)



Colorless oil, 288 mg, 71% yield. ^1H NMR (300 MHz, DMSO-*d*₆) δ 7.71 – 7.63 (m, 1H), 7.31 (d, J = 2.2 Hz, 2H), 7.30 – 7.28 (m, 2H), 7.27 (d, J = 1.9 Hz, 2H), 7.14 (dd, J = 7.0, 2.5 Hz, 2H), 7.07 – 6.95 (m, 3H), 6.63 (d, J = 7.9 Hz, 1H), 5.82 (s, 1H), 5.78 – 5.70 (m, 1H), 5.51 (t, J = 7.7 Hz, 2H), 4.99 (s, 1H), 3.74 – 3.49 (m, 3H), 3.17 (d, J = 14.5 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (75 MHz, DMSO-*d*₆) δ 156.0, 137.7, 137.6, 136.9, 135.0, 132.4, 129.8, 129.5, 129.1, 129.0, 128.8, 128.6, 128.5, 128.2, 128.1, 127.9, 124.4, 110.7, 57.6, 56.4, 51.6, 50.7, 21.3. HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{25}\text{N}_5$ ($[\text{M}+\text{Na}]^+$): 430.2008, found 430.2052.

8b

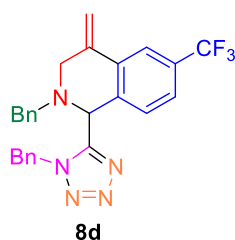
2-Benzyl-1-(1-benzyl-1H-tetrazol-5-yl)-6-chloro-4-methylene-1,2,3,4-tetrahydroisoquinoline (8c)



Light yellow solid, 281 mg, 66 % yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.93 (d, J = 2.2 Hz, 1H), 7.35 – 7.31 (m, 3H), 7.26 (dt, J = 5.9, 2.5 Hz, 4H), 7.16 – 7.10 (m, 2H), 7.08 (dd, J = 4.5, 1.8 Hz, 2H), 6.89 (d, J = 8.3 Hz, 1H), 5.97 (s, 1H), 5.74 (d, J = 15.5 Hz, 1H), 5.56 (d, J = 15.6 Hz, 2H), 5.08 (s, 1H), 3.68 (d, J = 13.0 Hz, 1H), 3.57 (d, J = 13.1 Hz, 1H), 3.50 (d, J = 14.7 Hz, 1H), 3.19 (d, J = 14.9 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.4, 142.4, 140.0, 139.8, 139.5, 138.1, 135.7, 134.3, 133.9, 133.6, 133.4, 133.3, 132.8, 132.7, 128.6, 117.8, 62.0, 60.7, 55.4. HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{22}\text{ClN}_5$ ($[\text{M}+\text{Na}]^+$): 450.1461, found 450.1505.

8c

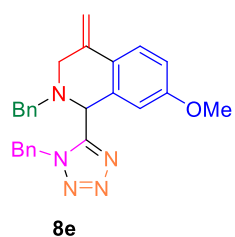
2-Benzyl-1-(1-benzyl-1H-tetrazol-5-yl)-4-methylene-6-(trifluoromethyl)-1,2,3,4-tetrahydroisoquinoline (**8d**)



Light yellow solid, 331 mg, 72% yield. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.19 (d, *J* = 1.9 Hz, 1H), 7.55 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.34 – 7.30 (m, 3H), 7.26 (d, *J* = 2.5 Hz, 3H), 7.18 – 7.11 (m, 3H), 7.11 – 7.05 (m, 2H), 6.07 (d, *J* = 1.3 Hz, 1H), 5.77 (d, *J* = 15.5 Hz, 1H), 5.71 (d, *J* = 3.6 Hz, 1H), 5.60 (d, *J* = 15.5 Hz, 1H), 5.15 (s, 1H), 3.71 (d, *J* = 13.1 Hz, 1H), 3.64 – 3.50 (m, 2H), 3.24 (d, *J* = 15.0 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 155.5, 137.6, 135.2, 134.0, 134.9, 133.8, 130.3, 129.5, 129.5, 129.3, 129.1, 129.1, 129.1, 129.0, 128.8, 128.6, 128.6, 128.1, 128.0, 127.9, 125.9, 125.0, 124.9, 123.2, 121.1, 121.1, 113.6, 57.3, 56.2, 50.7. ¹⁹F NMR (376 MHz, DMSO-*d*₆) δ -61.1. HRMS (ESI) calcd for C₂₆H₂₂F₃N₅ ([M+Na]⁺):

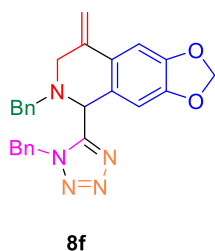
484.1725, found 484.1752.

2-Benzyl-1-(1-benzyl-1H-tetrazol-5-yl)-7-methoxy-4-methylene-1,2,3,4-tetrahydroisoquinoline (**8e**)



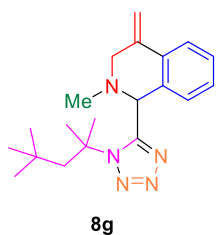
Light yellow solid, 287 mg, 68% yield. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.80 (d, *J* = 8.8 Hz, 1H), 7.34 – 7.30 (m, 3H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.27 (d, *J* = 1.9 Hz, 2H), 7.19 – 7.10 (m, 2H), 7.10 – 7.01 (m, 2H), 6.91 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.28 (d, *J* = 2.6 Hz, 1H), 5.74 (s, 3H), 5.68 (s, 1H), 5.55 – 5.48 (m, 2H), 4.87 (s, 1H), 3.66 (d, *J* = 13.1 Hz, 1H), 3.61 (s, 3H), 3.17 (d, *J* = 14.7 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 159.7, 155.8, 137.8, 136.3, 135.1, 132.2, 129.5, 129.1, 128.8, 128.6, 128.1, 127.9, 125.8, 125.5, 115.1, 112.7, 108.6, 57.5, 56.5, 55.6, 55.3, 51.5, 50.7. HRMS (ESI) calcd for C₂₆H₂₅N₅O ([M+Na]⁺): 446.1957, found 446.1961.

6-Benzyl-5-(1-benzyl-1H-tetrazol-5-yl)-8-methylene-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*]isoquinoline (**8f**)



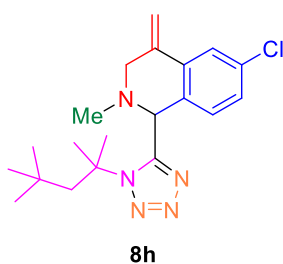
Light yellow solid, 319 mg, 73% yield. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.39 (s, 1H), 7.36 – 7.30 (m, 3H), 7.27 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.17 – 7.10 (m, 2H), 7.09 – 7.02 (m, 2H), 6.27 (s, 1H), 6.02 (d, *J* = 1.0 Hz, 1H), 5.98 (d, *J* = 1.0 Hz, 1H), 5.74 – 5.68 (m, 2H), 5.52 (d, *J* = 15.4 Hz, 1H), 5.42 (s, 1H), 4.89 (s, 1H), 3.74 – 3.55 (m, 2H), 3.54 – 3.45 (m, 1H), 3.14 (d, *J* = 14.7 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 155.9, 148.1, 148.0, 137.8, 136.4, 135.1, 129.5, 129.1, 128.8, 128.6, 128.1, 127.9, 127.0, 124.7, 109.7, 107.8, 103.7, 101.7, 57.4, 56.5, 51.3, 50.6. HRMS (ESI) calcd for C₂₆H₂₃N₅O₂ ([M+Na]⁺): 460.1749, found 460.1803.

2-Methyl-4-methylene-1-(1-(2,4,4-trimethylpentan-2-yl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline (**8g**)



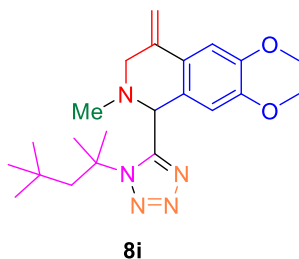
White solid, 230 mg, 68% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 7.9 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 5.76 (s, 1H), 5.33 (s, 1H), 5.12 (s, 1H), 3.85 (d, *J* = 14.4 Hz, 1H), 3.23 (d, *J* = 14.4 Hz, 1H), 2.43 (s, 3H), 2.11 (d, *J* = 14.7 Hz, 2H), 1.81 (s, 6H), 0.85 (s, 9H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 155.0, 132.4, 128.4, 127.8, 123.8, 110.0, 53.3, 31.6, 30.8, 29.8. HRMS (ESI) calcd for C₂₀H₂₉N₅ ([M+Na]⁺): 362.2321, found 362.2314.

6-Chloro-2-methyl-4-methylene-1-(1-(2,4,4-trimethylpentan-2-yl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline (**8h**)



Light yellow solid, 257 mg, 69% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 2.2 Hz, 1H), 7.16 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 5.72 (s, 1H), 5.23 (s, 1H), 5.13 (s, 1H), 3.77 (d, *J* = 14.8 Hz, 1H), 3.18 (d, *J* = 14.7 Hz, 1H), 2.40 (s, 3H), 2.19 (d, *J* = 15.3 Hz, 1H), 2.05 (d, *J* = 14.9 Hz, 1H), 1.80 (s, 6H), 0.82 (s, 9H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 154.5, 134.2, 133.9, 129.6, 128.5, 123.8, 111.6, 66.3, 53.3, 31.6, 30.8, 30.1, 29.7. HRMS (ESI) calcd for C₂₀H₂₈ClN₅ ([M+Na]⁺): 396.1931, found 396.1923.

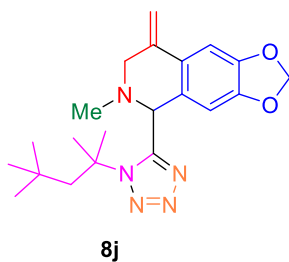
6,7-Dimethoxy-2-methyl-4-methylene-1-(1-(2,4,4-trimethylpentan-2-yl)-1H-tetrazol-5-yl)-1,2,3,4-tetrahydroisoquinoline (**8i**)



Light yellow solid, 263 mg, 66% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.16 (s, 1H), 6.18 (s, 1H), 5.54 (s, 1H), 5.22 (s, 1H), 4.99 (s, 1H), 3.90 (s, 3H), 3.74 (dd, $J = 14.3, 2.7$ Hz, 1H), 3.69 (s, 3H), 3.16 (d, $J = 14.3$ Hz, 1H), 2.38 (s, 3H), 2.13 (d, $J = 10.3$ Hz, 2H), 1.76 (d, $J = 8.8$ Hz, 6H), 0.82 (s, 9H).

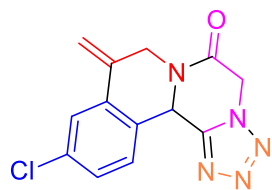
^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.07, 149.6, 148.7, 125.2, 108.0, 105.9, 55.9, 55.8, 53.3, 31.6, 30.9, 30.1. HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{33}\text{N}_5\text{O}_2$ ($[\text{M}+\text{Na}]^+$): 422.2532, found 422.2106

6-Methyl-8-methylene-5-(1-(2,4,4-trimethylpentan-2-yl)-1H-tetrazol-5-yl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-*g*]isoquinoline (**8j**)



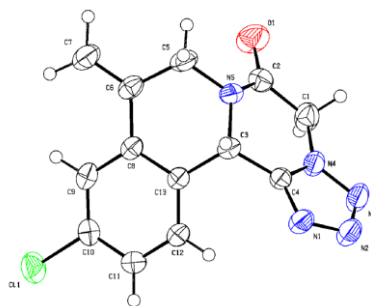
White solid, 252 mg, 66% yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.18 (s, 1H), 6.22 (s, 1H), 5.94 (d, $J = 1.2$ Hz, 1H), 5.91 (d, $J = 1.3$ Hz, 1H), 5.53 (s, 1H), 5.15 (s, 1H), 4.98 (s, 1H), 3.75 (d, $J = 14.6$ Hz, 1H), 3.13 (d, $J = 14.6$ Hz, 1H), 2.41 (s, 3H), 2.20 (d, $J = 15.4$ Hz, 1H), 2.06 (s, 1H), 1.83 (d, $J = 13.0$ Hz, 6H), 0.84 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.9, 148.1, 147.7, 126.7, 108.6, 107.3, 103.4, 101.2, 53.2, 31.6, 30.8, 29.6. HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{29}\text{N}_5\text{O}_2$ ($[\text{M}+\text{Na}]^+$): 406.2219, found 406.2231.

3. X-ray report of 6d and 8c



6d

CCDC: 2164364



Bond precision: C-C = 0.0020 Å Wavelength=0.71073
Cell: a=8.5083(11) b=14.3480(17) c=10.4672(13)
 alpha=90 beta=105.064(2) gamma=90
Temperature: 296 K

	Calculated	Reported
Volume	1233.9(3)	1233.9(3)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C13 H10 Cl N5 O	?
Sum formula	C13 H10 Cl N5 O	C13 H10 Cl N5 O
Mr	287.71	287.71
Dx, g cm ⁻³	1.549	1.549
Z	4	4
Mu (mm ⁻¹)	0.313	0.313
F000	592.0	592.0
F000'	592.78	
h, k, lmax	10, 17, 12	10, 17, 12
Nref	2165	2159
Tmin, Tmax	0.922, 0.928	
Tmin'	0.922	

Correction method= Not given

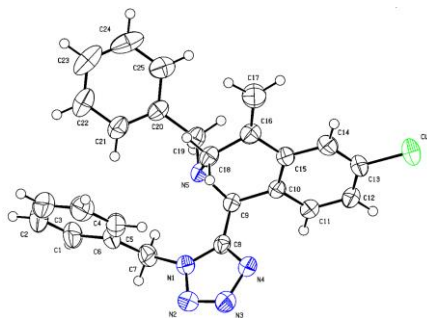
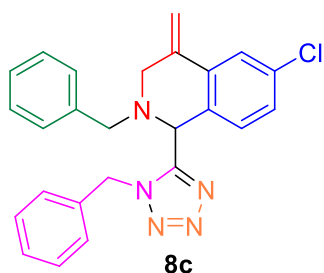
Data completeness= 0.997 Theta(max)= 24.993

R(reflections)= 0.0316(1864)

wR2(reflections)=
0.0829(2159)

S = 1.086

Npar= 190



CCDC: 2321622

Bond precision: C-C = 0.0034 Å

Wavelength=0.71073

Cell: a=21.3467 (15)
alpha=90

b=14.9952 (11)
beta=90.794 (1)

c=6.8948 (5)
gamma=90

Temperature: 296 K

	Calculated	Reported
Volume	2206.8 (3)	2206.8 (3)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C ₂₅ H ₂₂ Cl N ₅	?
Sum formula	C ₂₅ H ₂₂ Cl N ₅	C ₂₅ H ₂₂ Cl N ₅
Mr	427.93	427.92
Dx, g cm ⁻³	1.288	1.288
Z	4	4
Mu (mm ⁻¹)	0.195	0.195
F ₀₀₀	896.0	896.0
F ₀₀₀ '	896.86	
h, k, lmax	25, 17, 8	25, 17, 8
Nref	3888	3882
Tmin, Tmax	0.954, 0.973	
Tmin'	0.951	

Correction method= Not given

Data completeness= 0.998

Theta(max)= 24.999

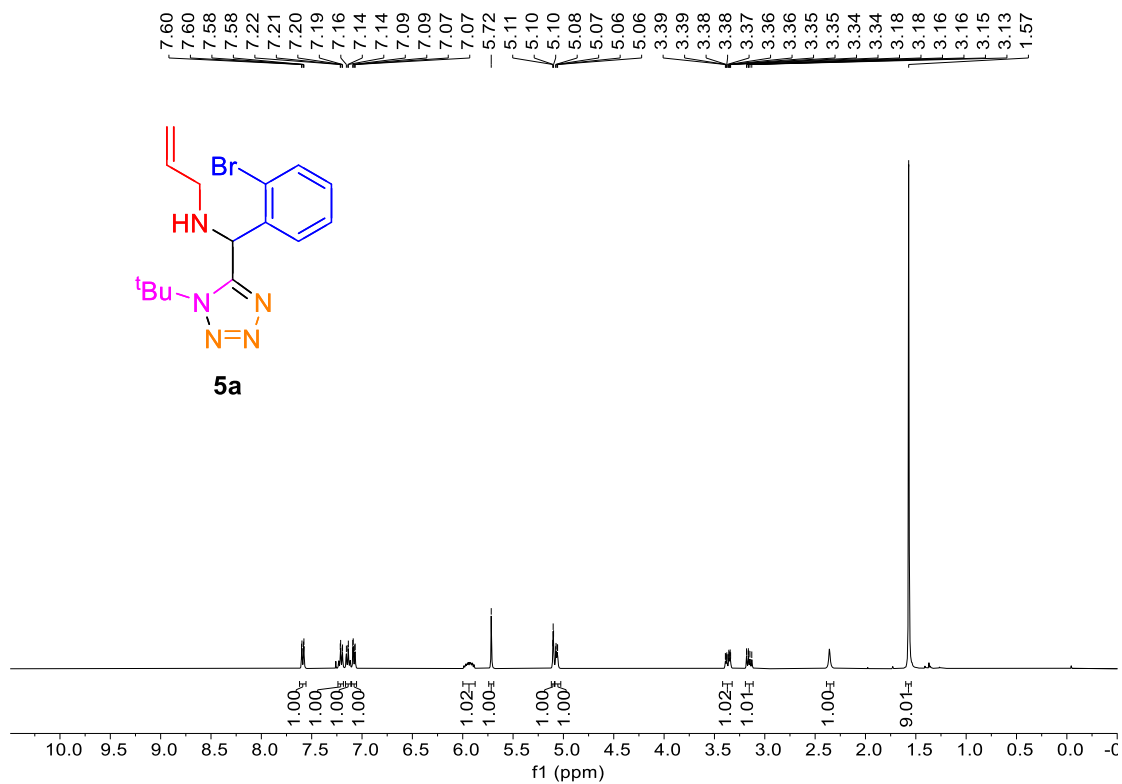
R(reflections)= 0.0424 (2407)

wR2(reflections)=
0.1147 (3882)

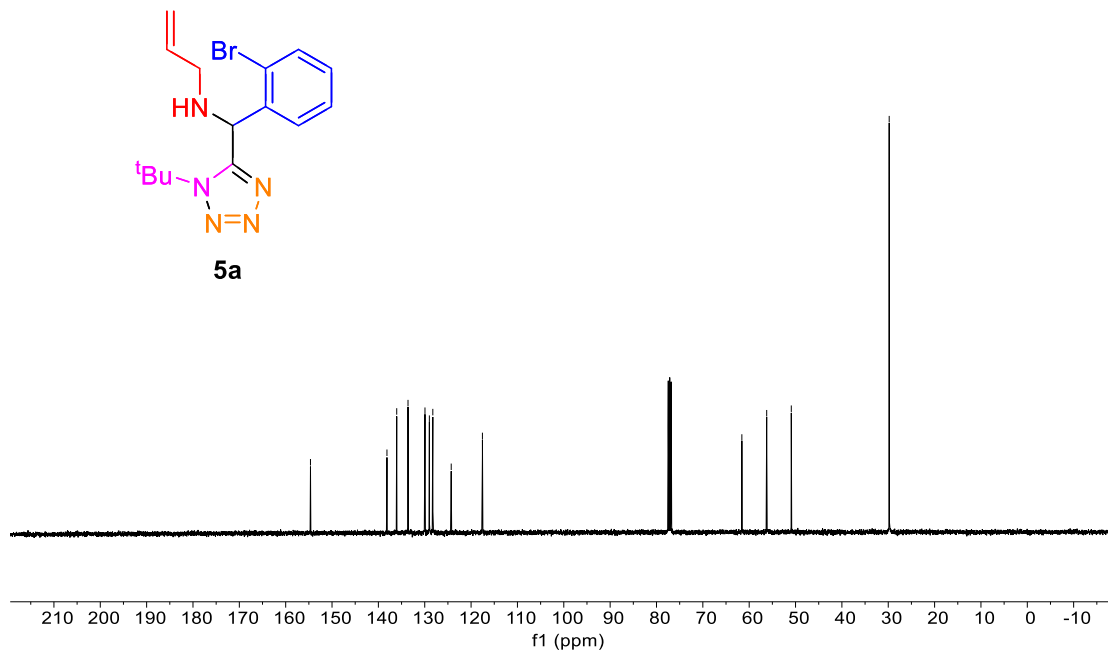
S = 0.862

Npar= 288

4. ^1H NMR, ^{13}C NMR of products 5a, 6 and 8

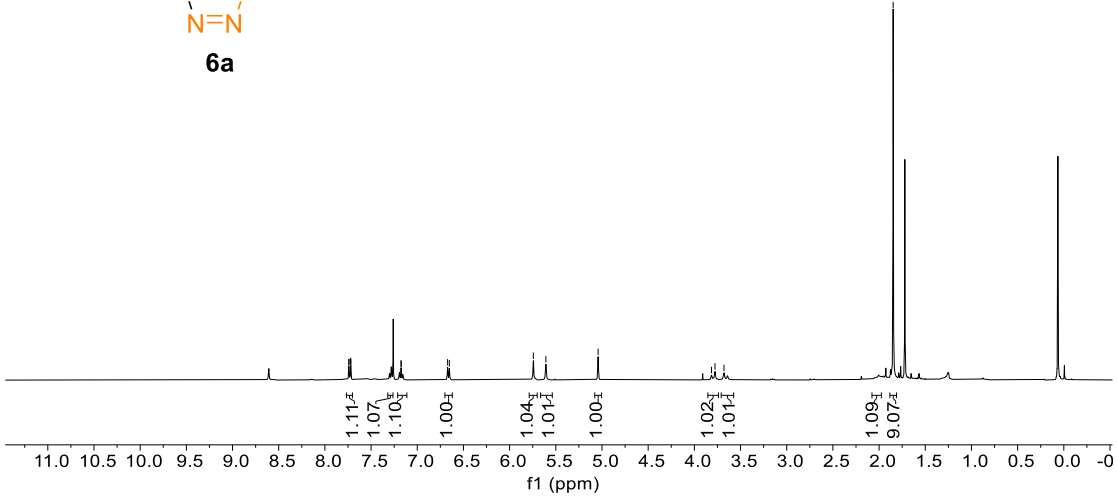
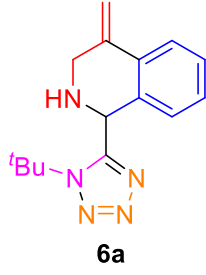


maxinoming08_35.fid
njw



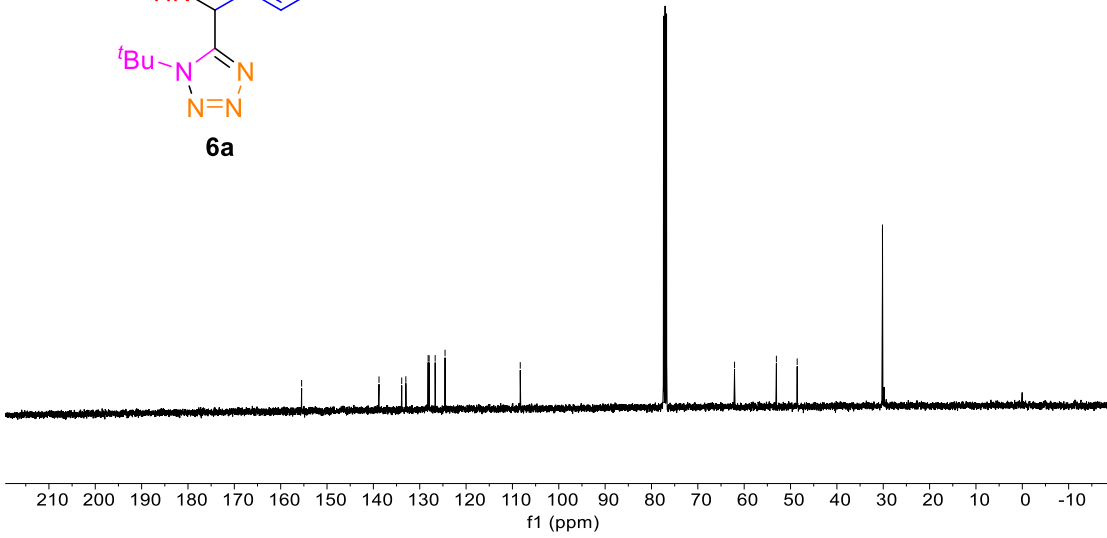
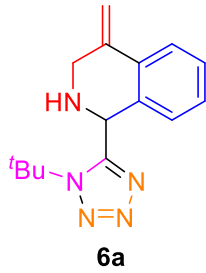
maxiaoming08_6.fid
njw-2

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7.72
7.72
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7.17
6.67
6.65
5.74
5.61
5.04
3.81
3.78
3.68
1.85

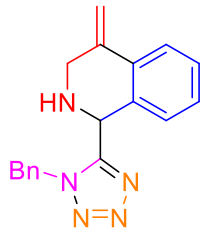


maxiaoming08_150.fid
njw-1 c

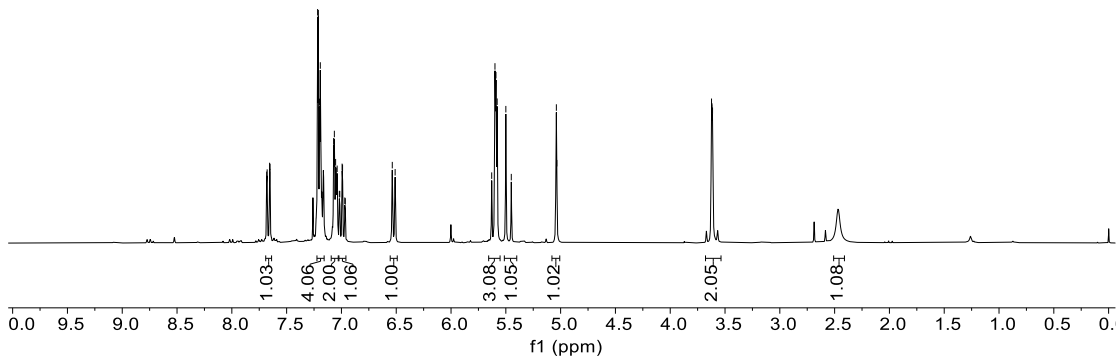
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128.0
126.7
124.5
108.3
62.1
53.1
48.6
30.2



3maxim
rwj-2

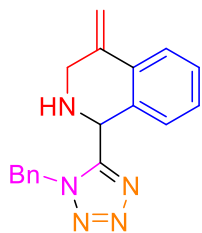


6b

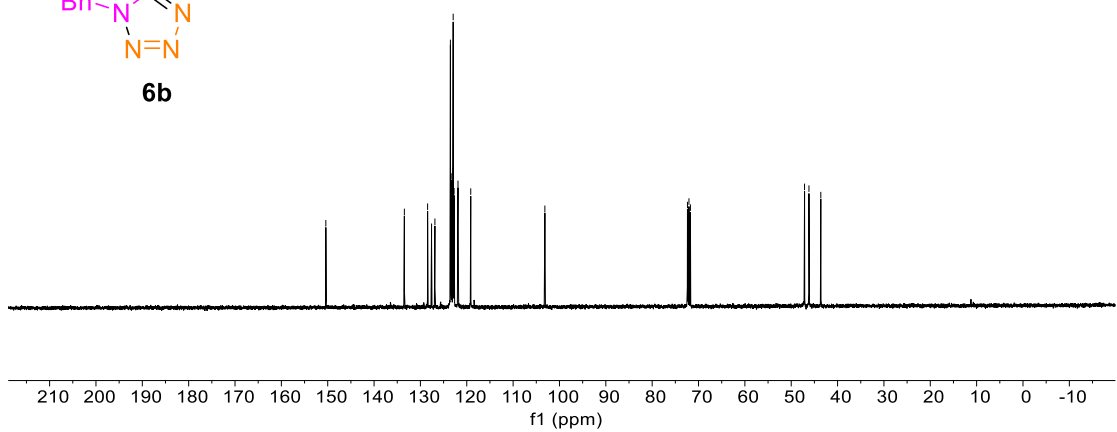


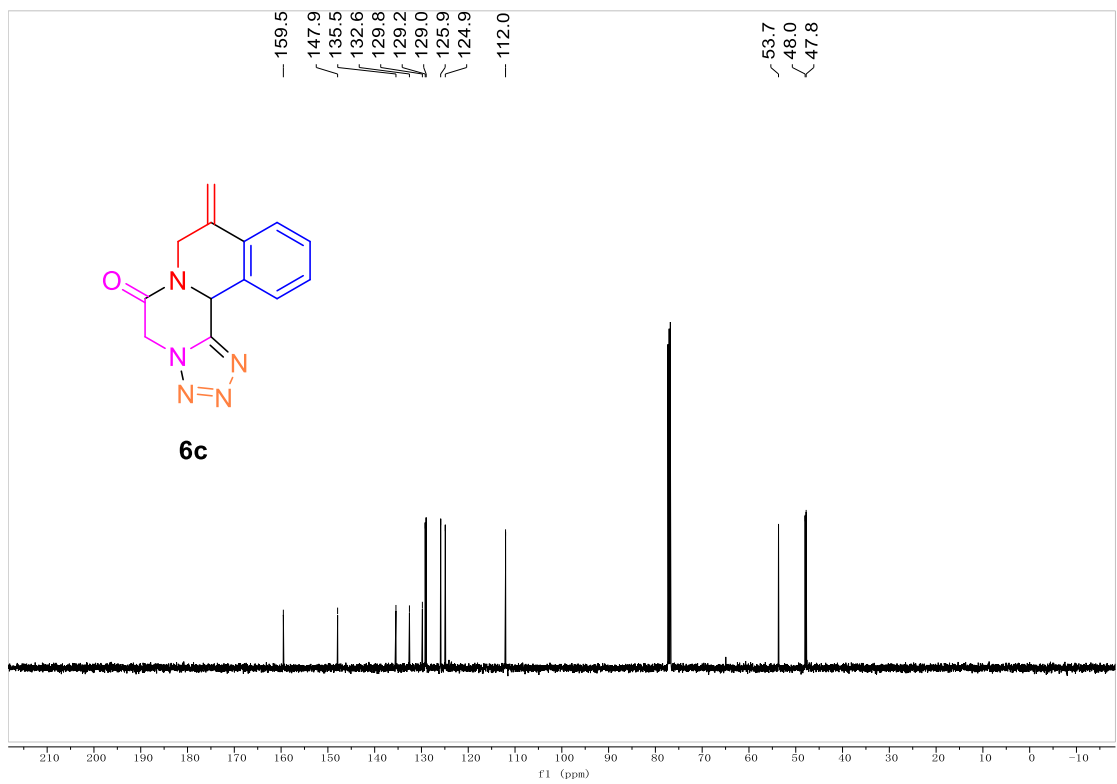
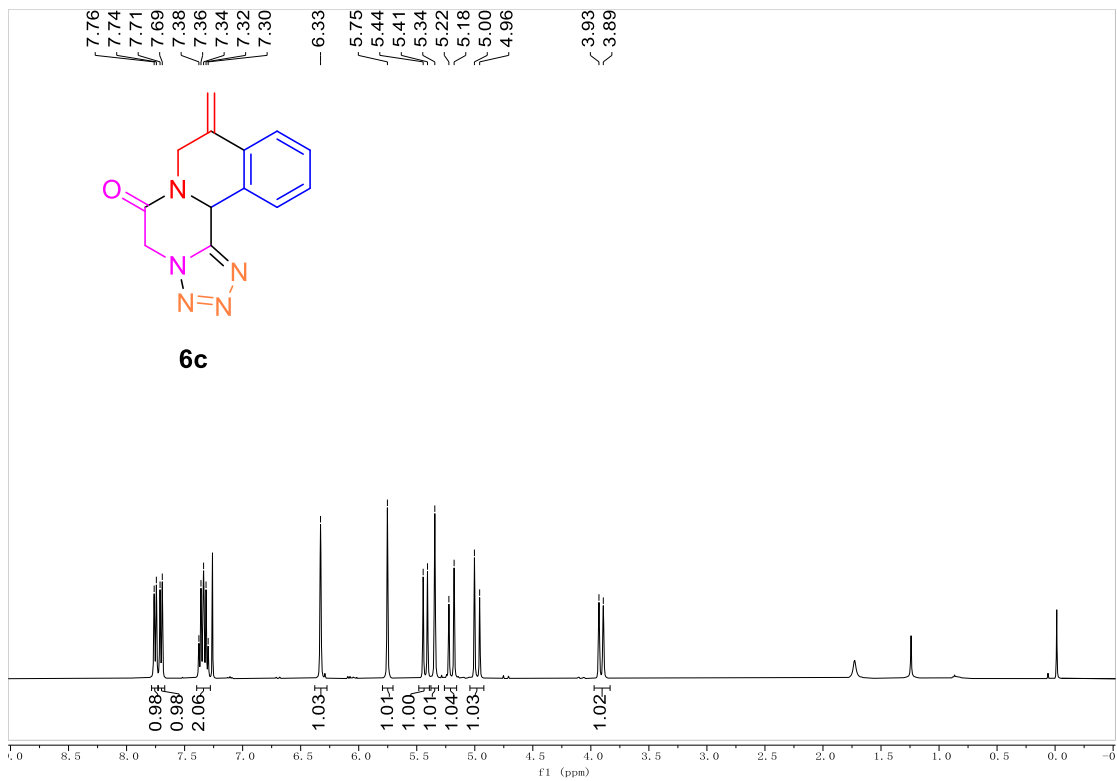
maxiaomg08_148.fid
rwj-2

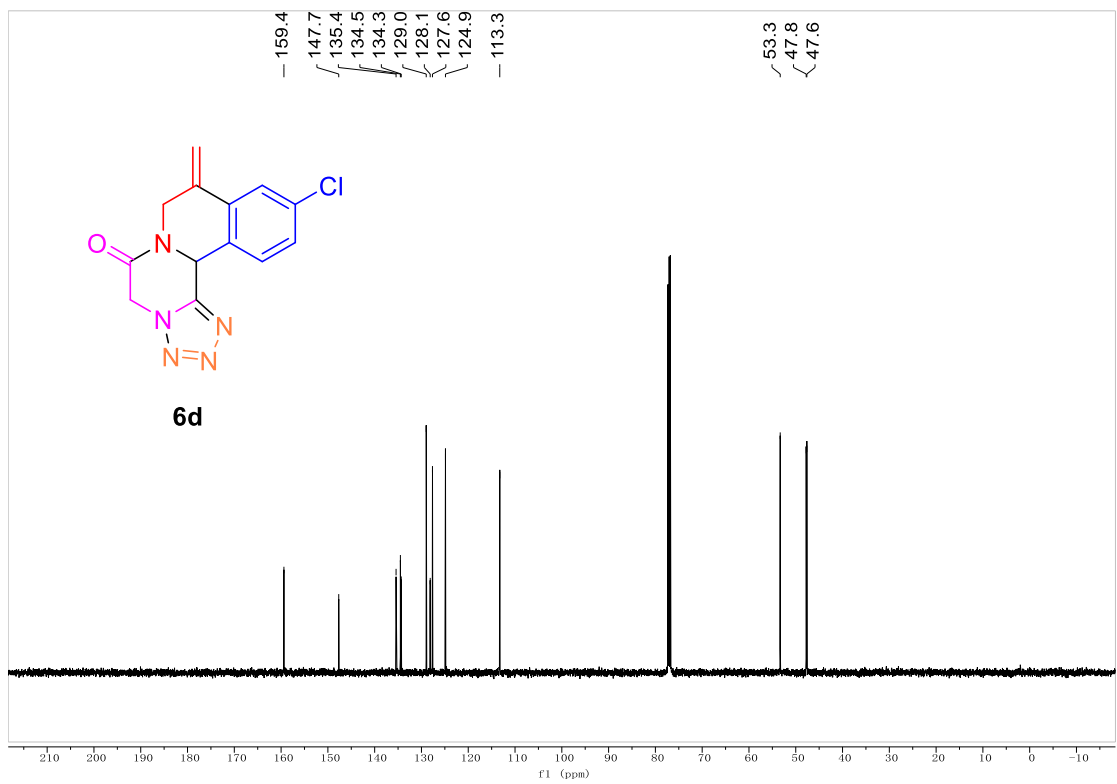
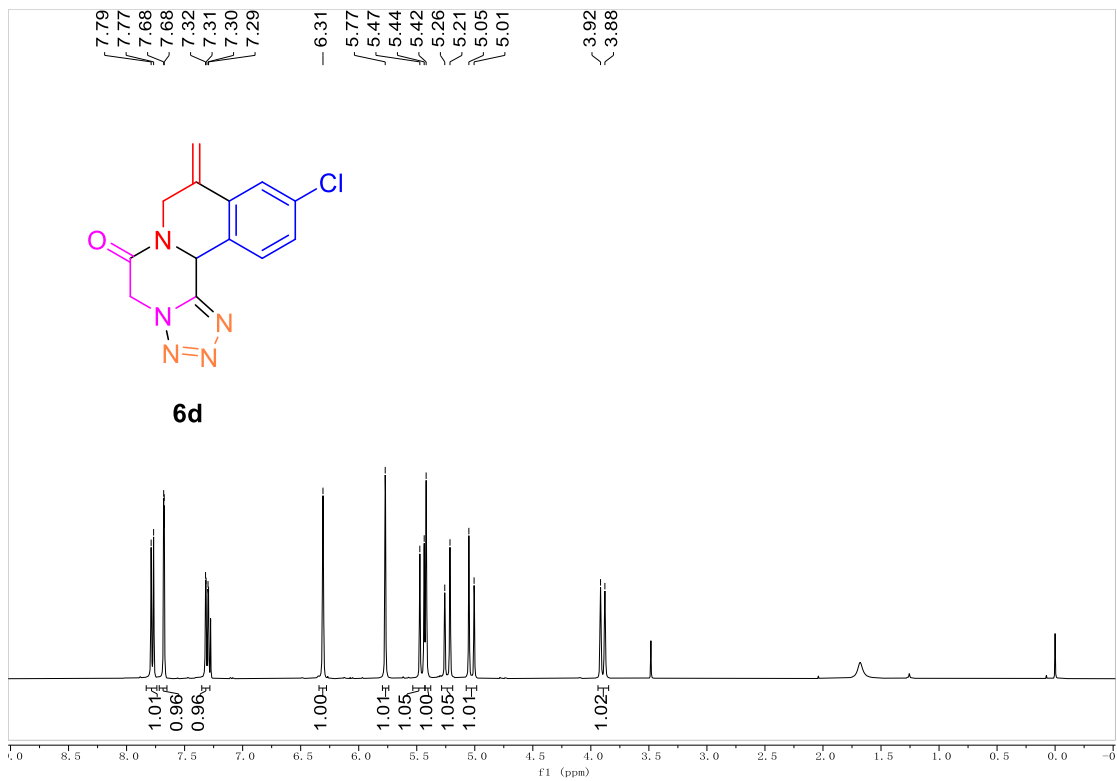
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122.9
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119.1
- 103.2
72.4
72.1
71.7
47.1
46.2
43.6

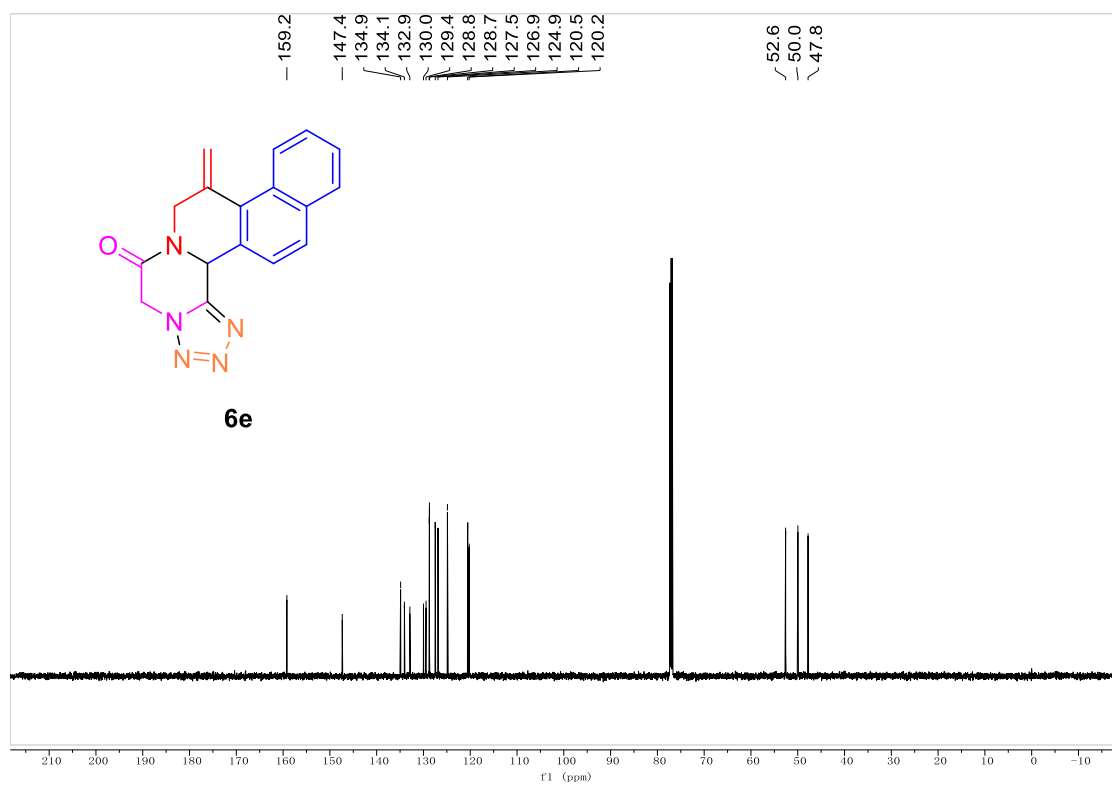
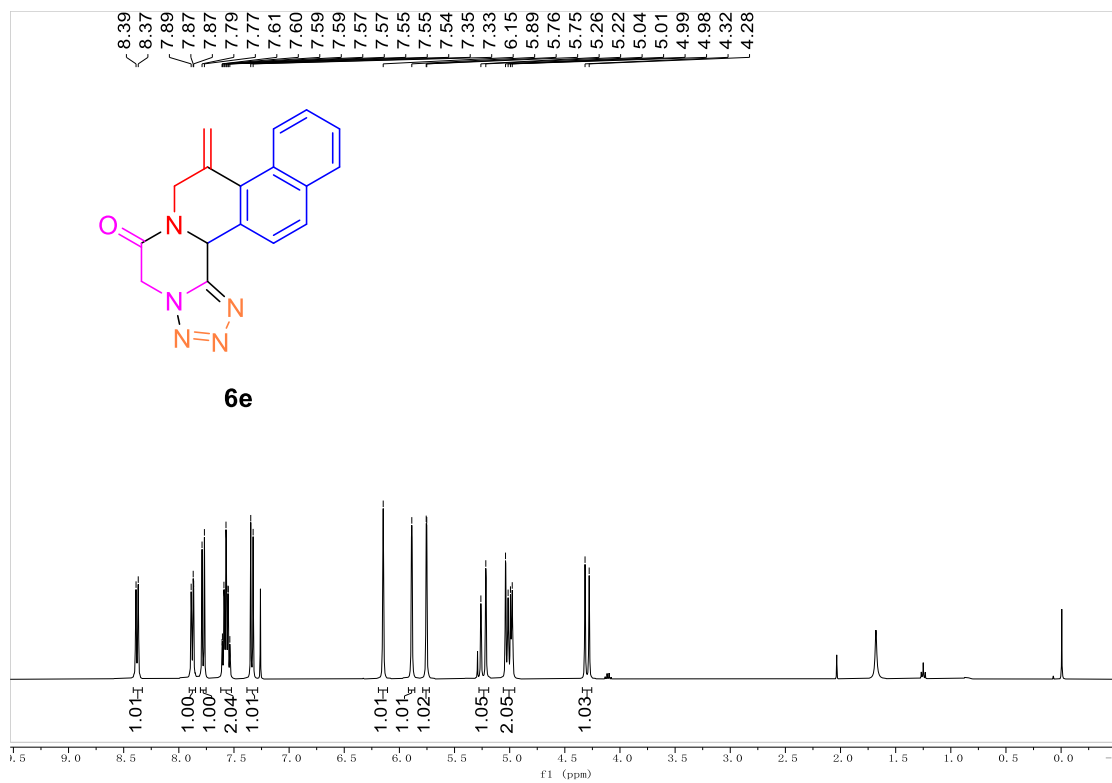


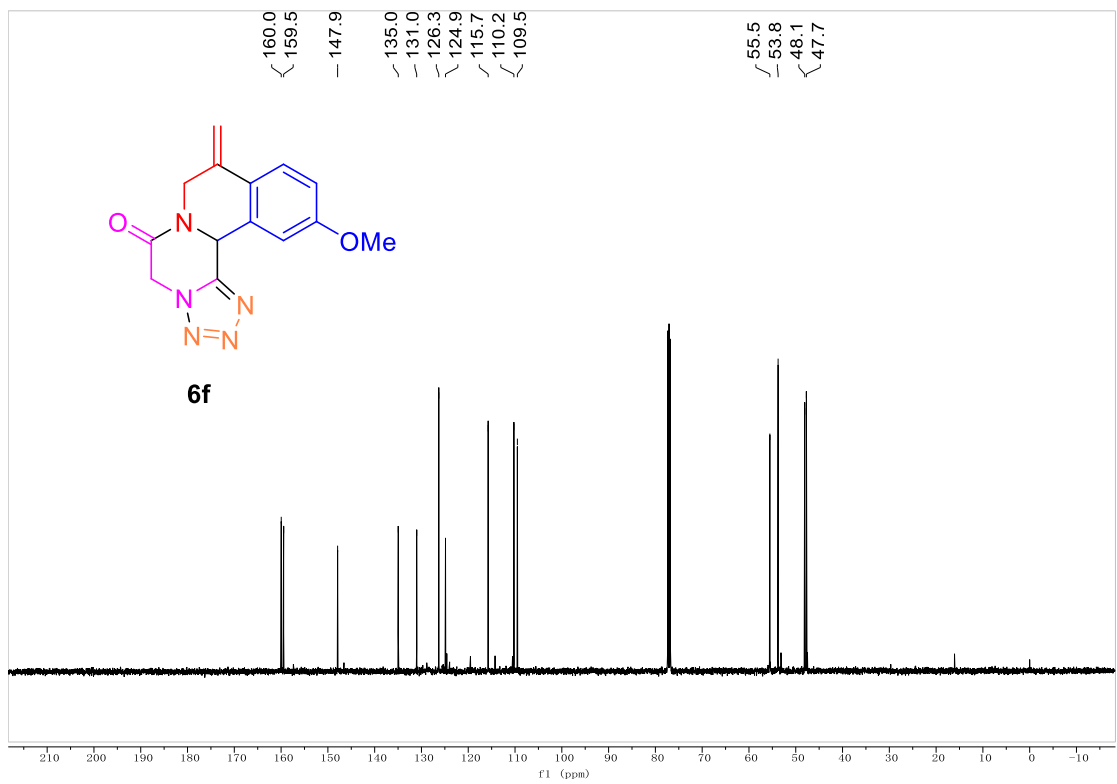
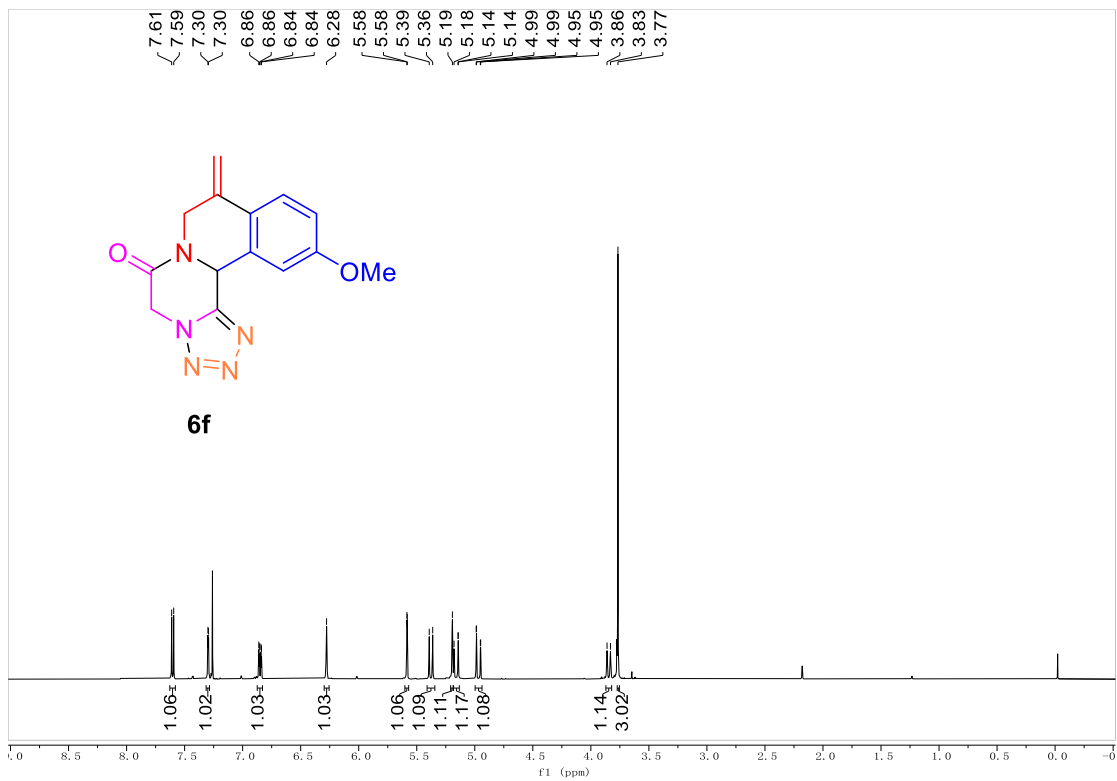
6b

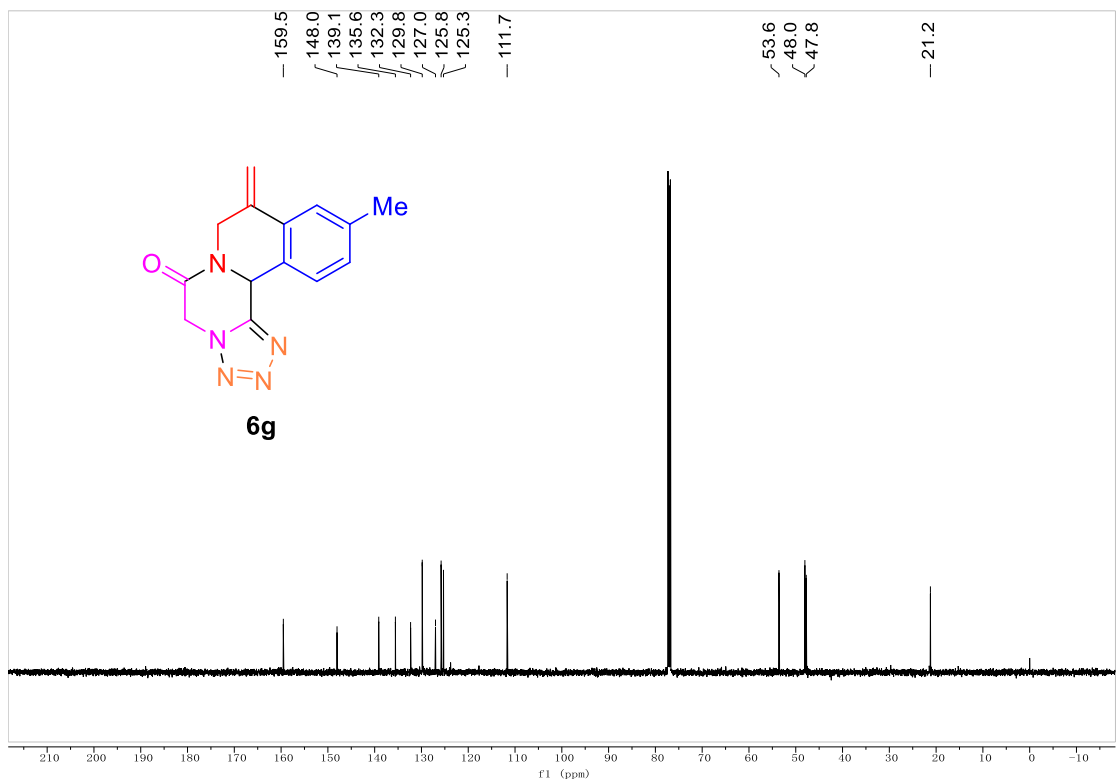
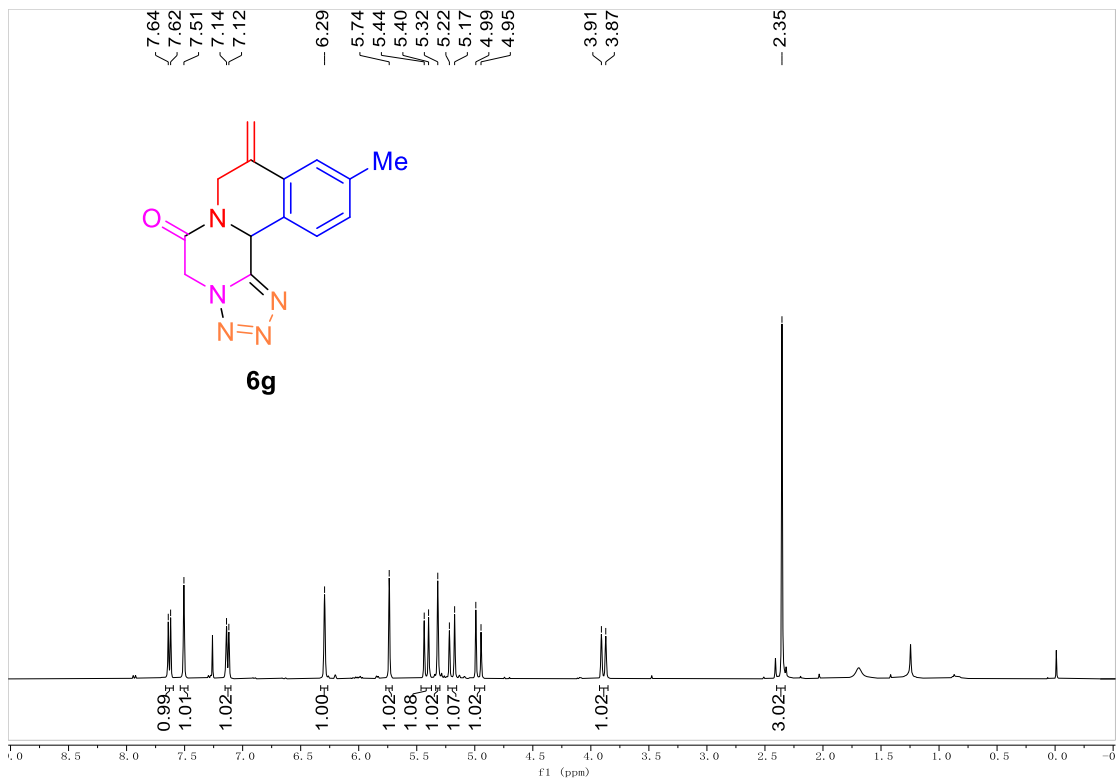


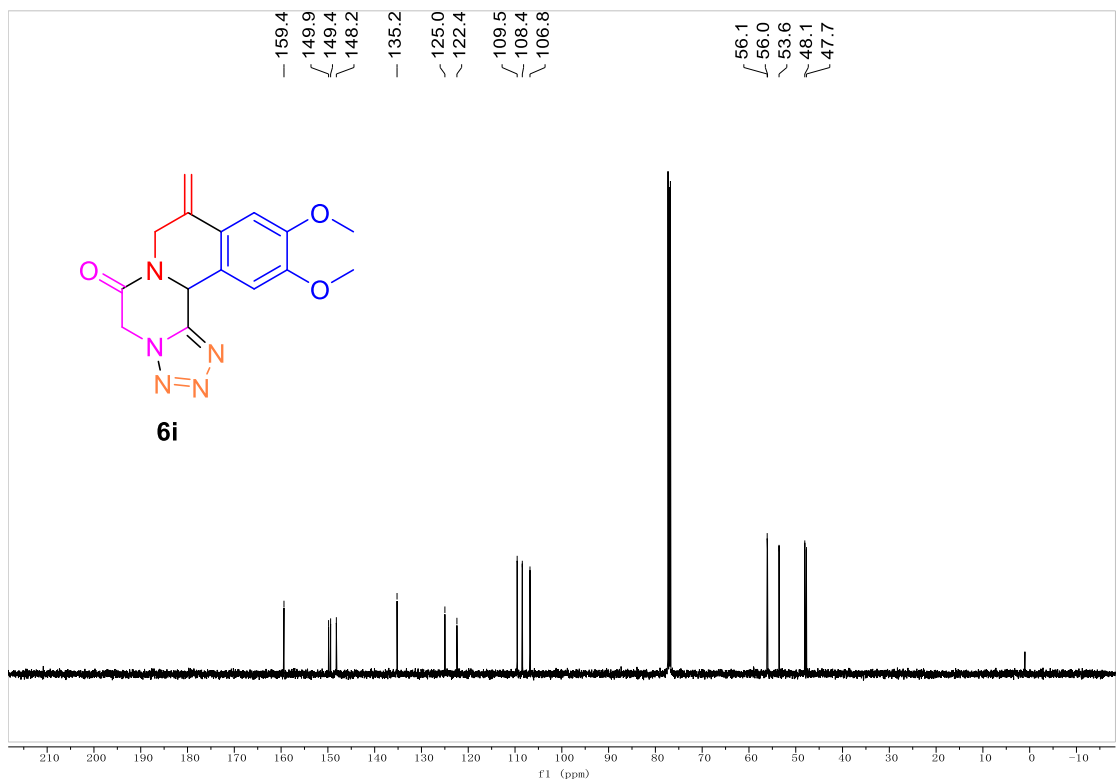
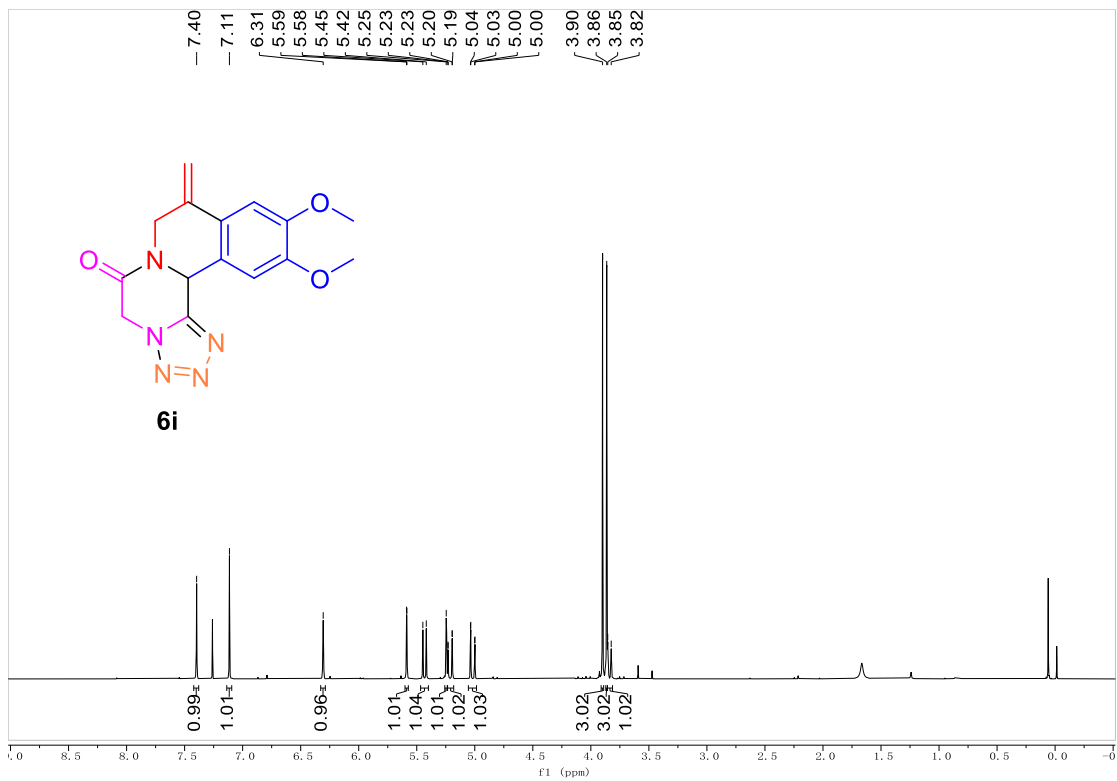


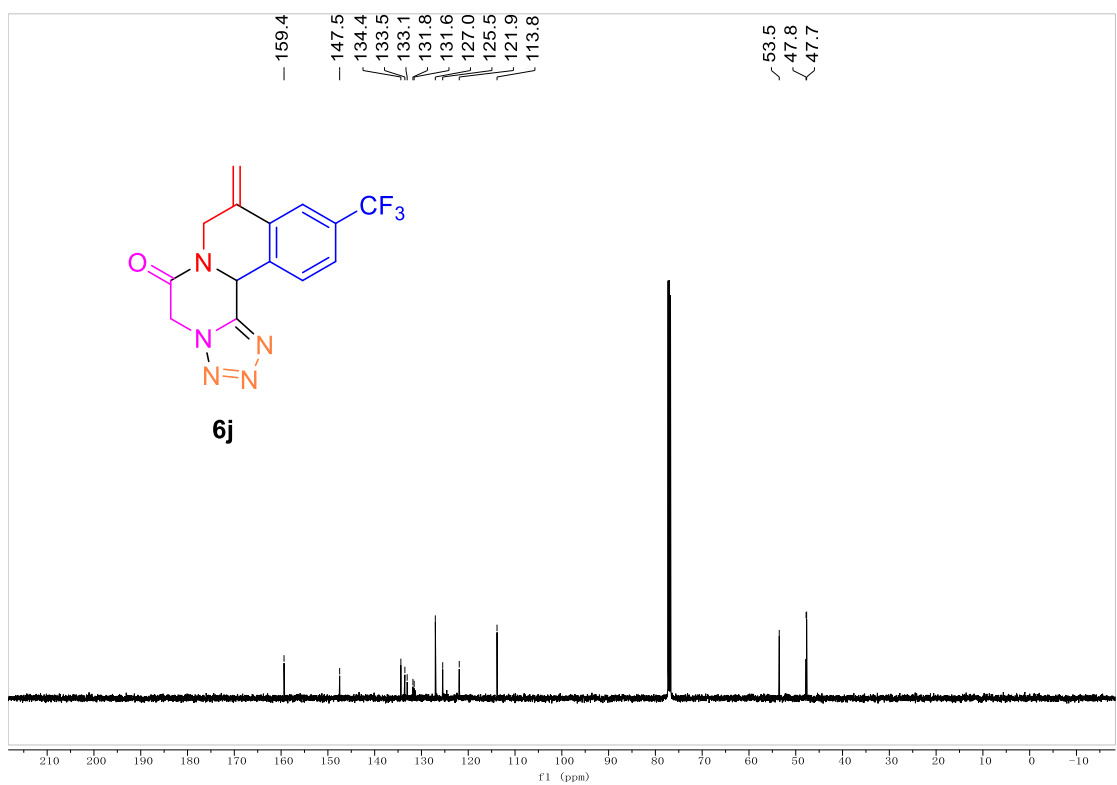
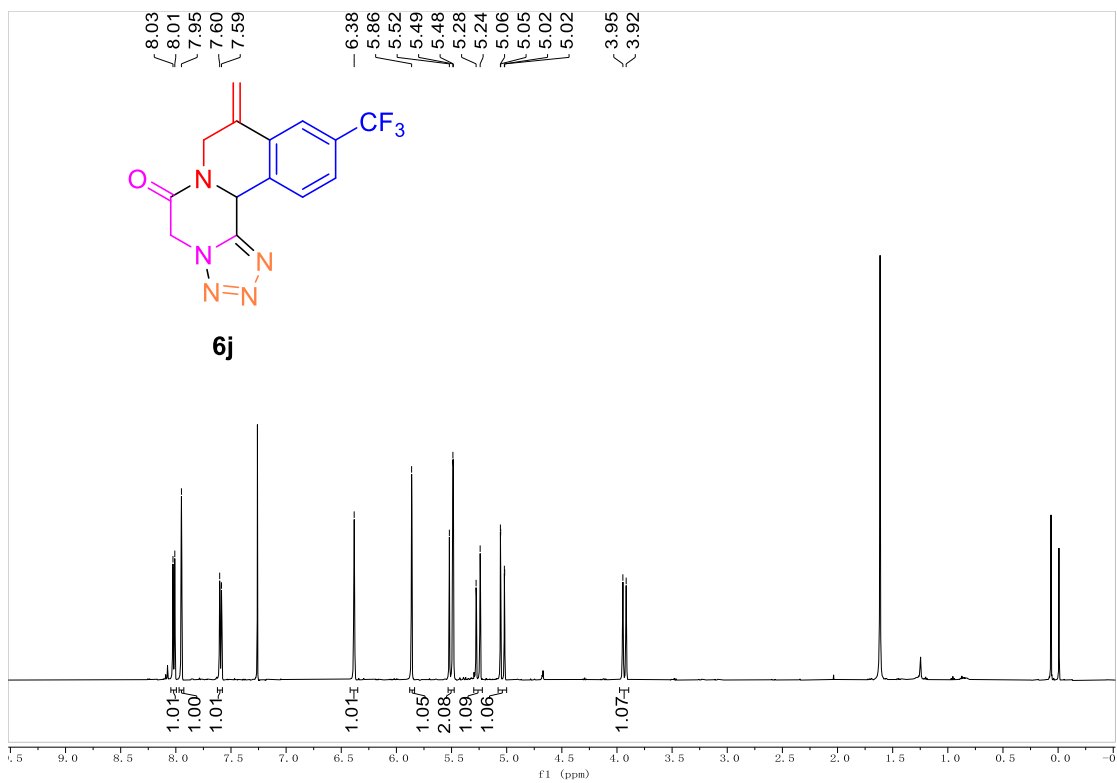


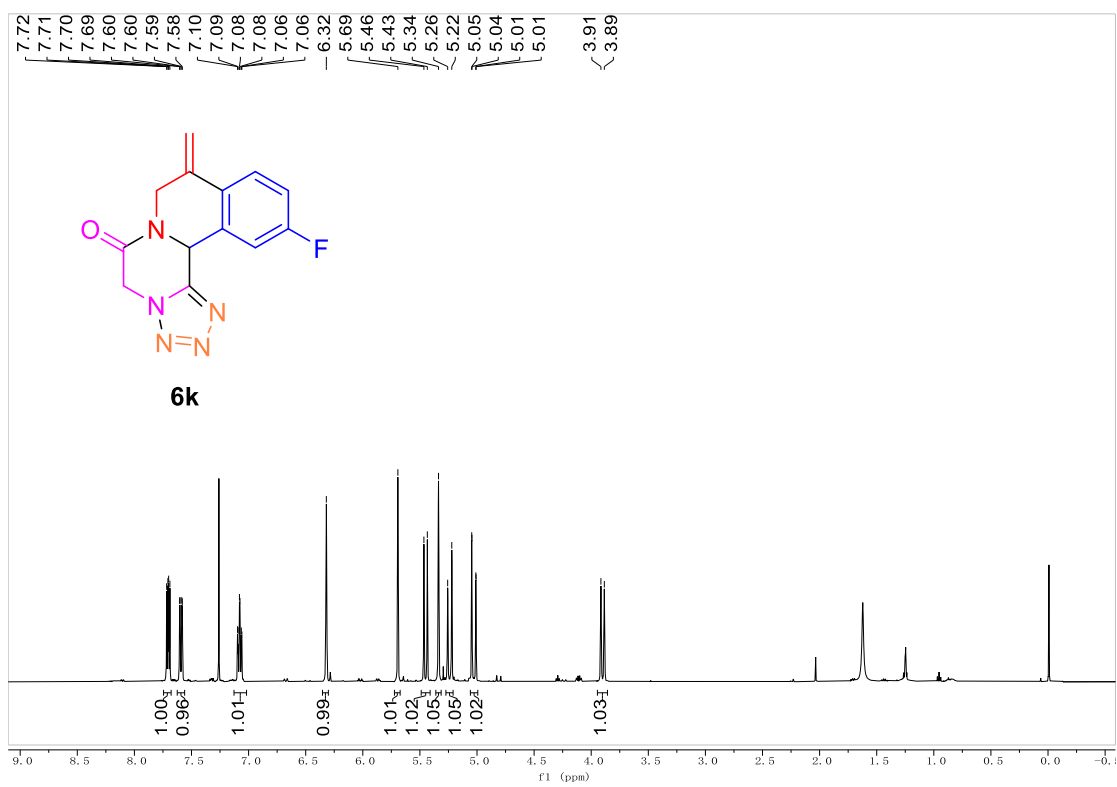
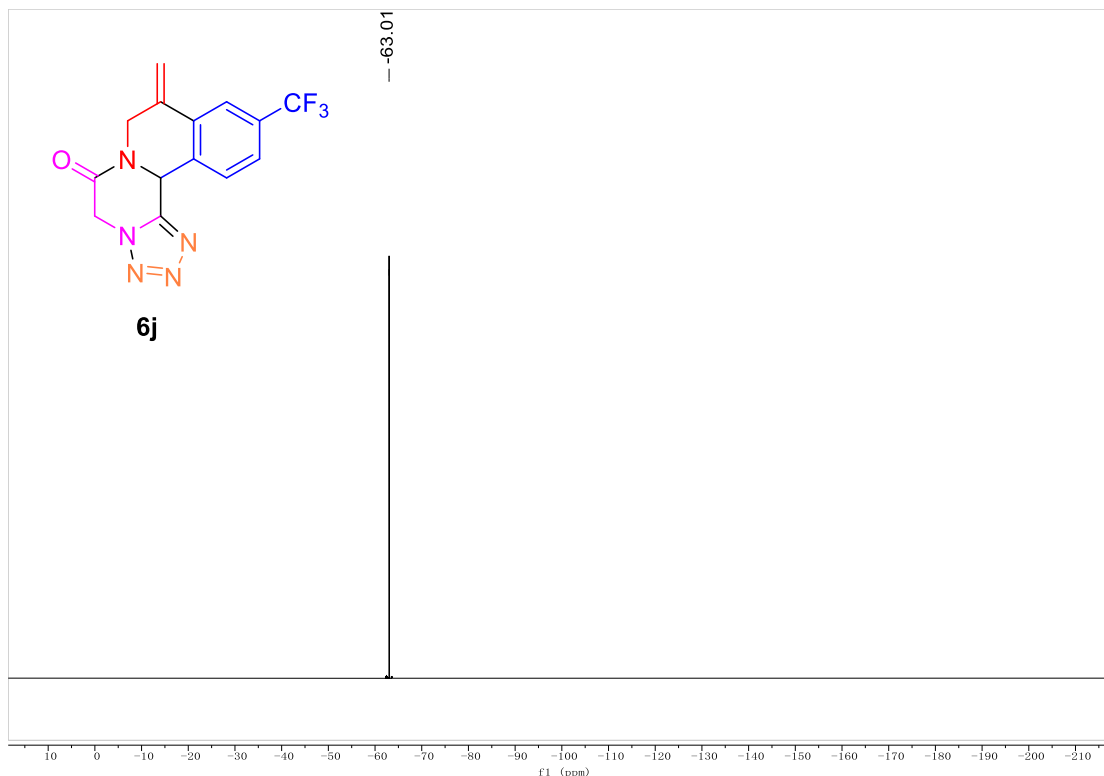


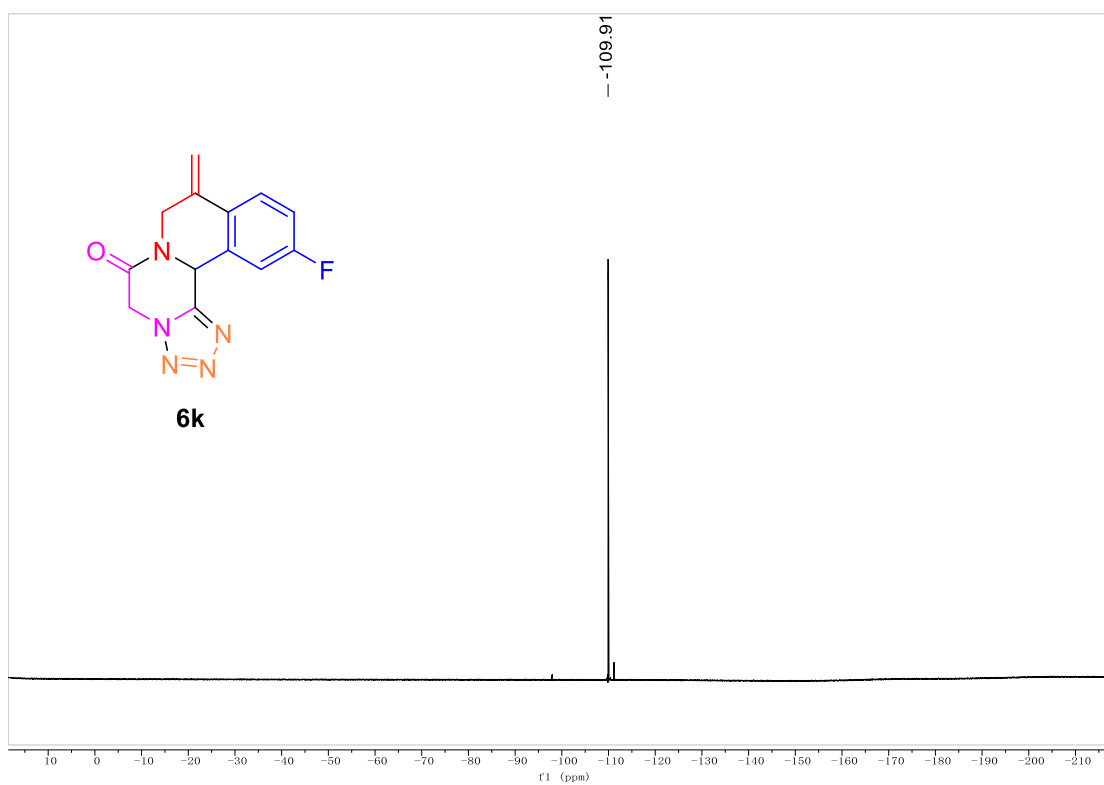
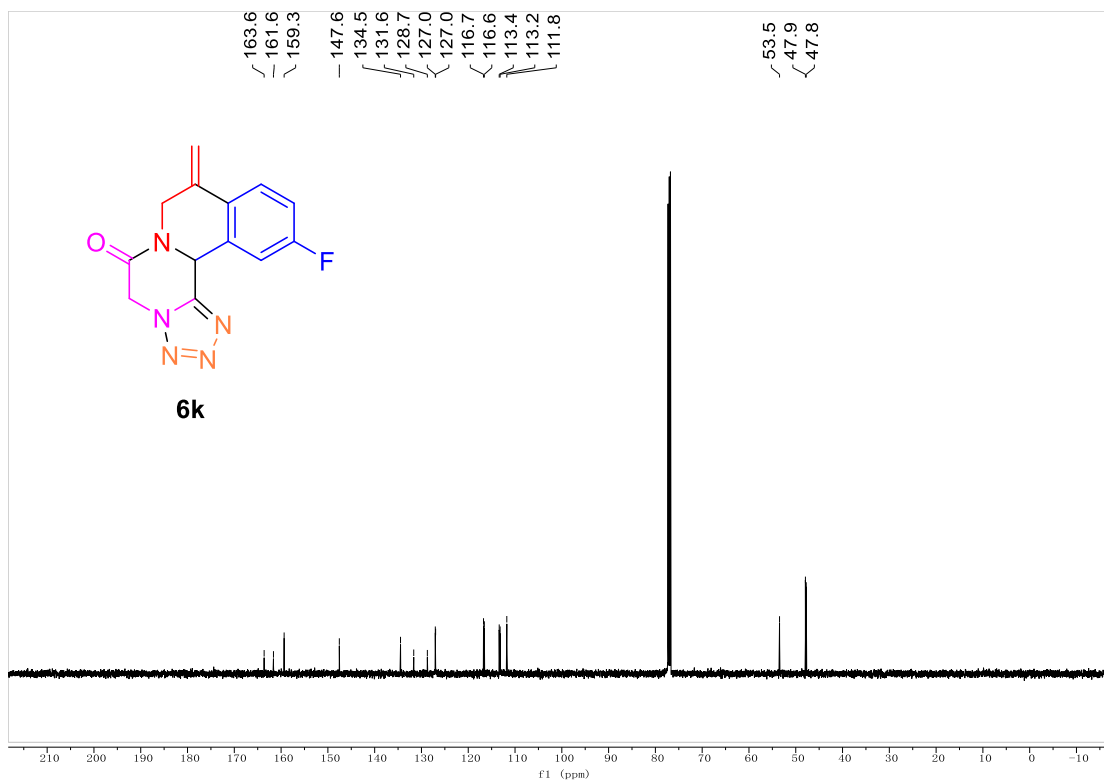




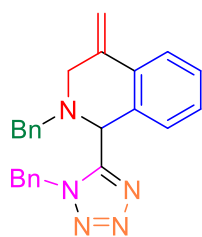




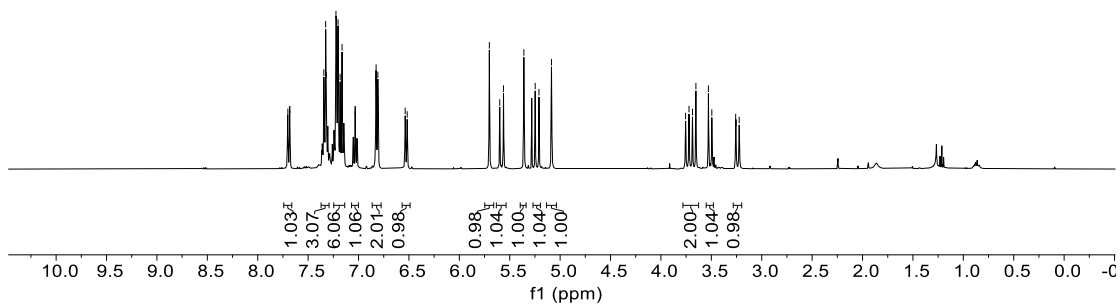




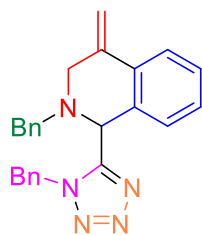
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6.81
6.54
6.52
5.70
5.60
5.56
5.36
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3.53
3.49
3.26
3.25
3.22



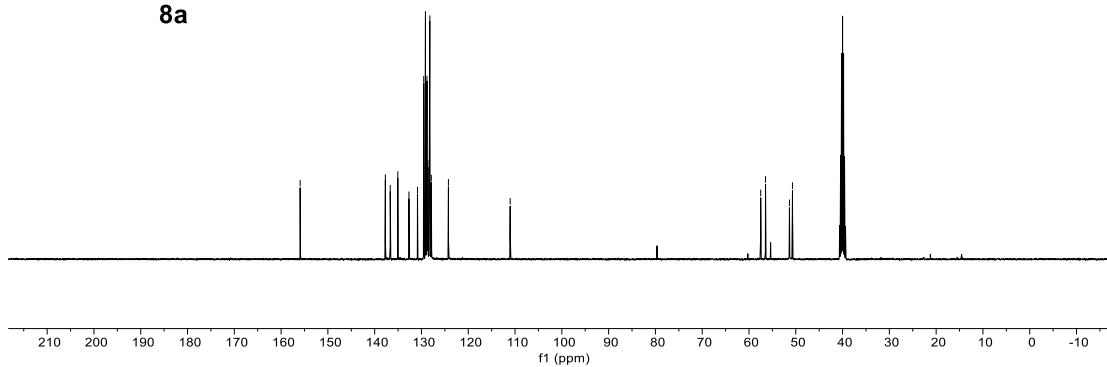
8a



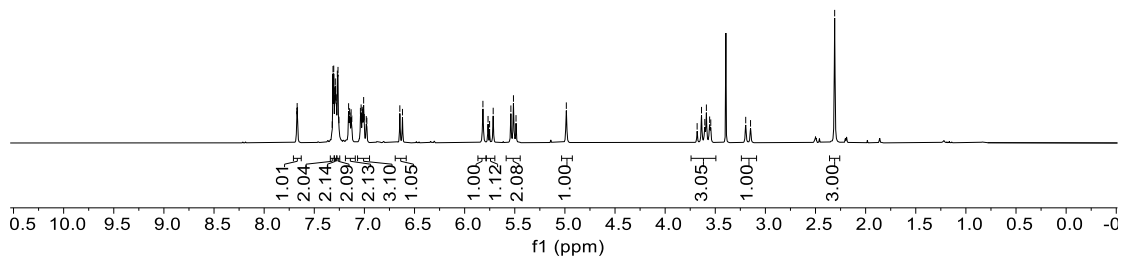
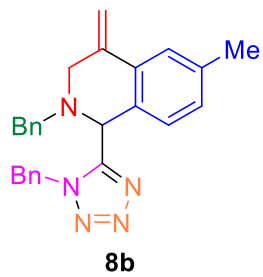
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129.1
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124.2
111.0
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56.5
51.4
50.7



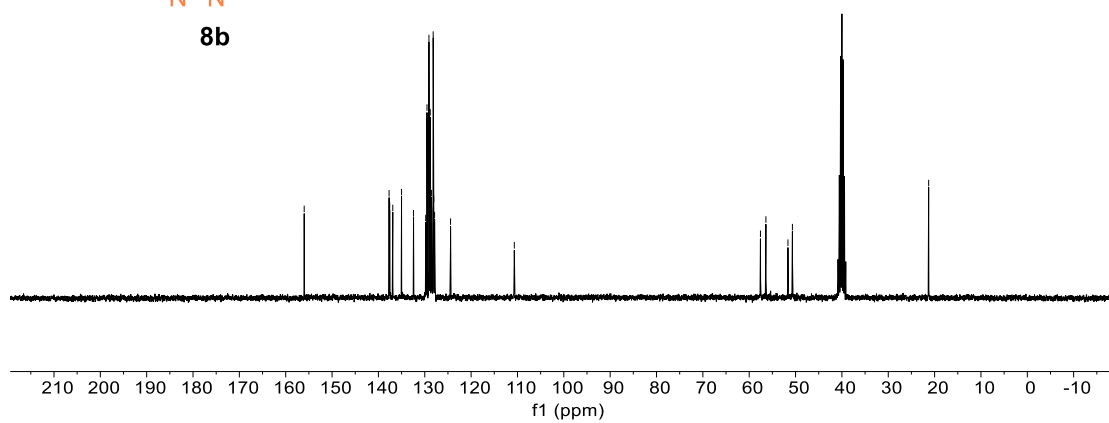
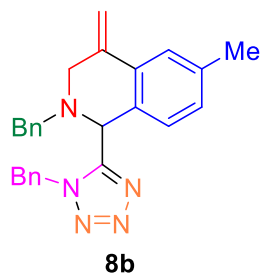
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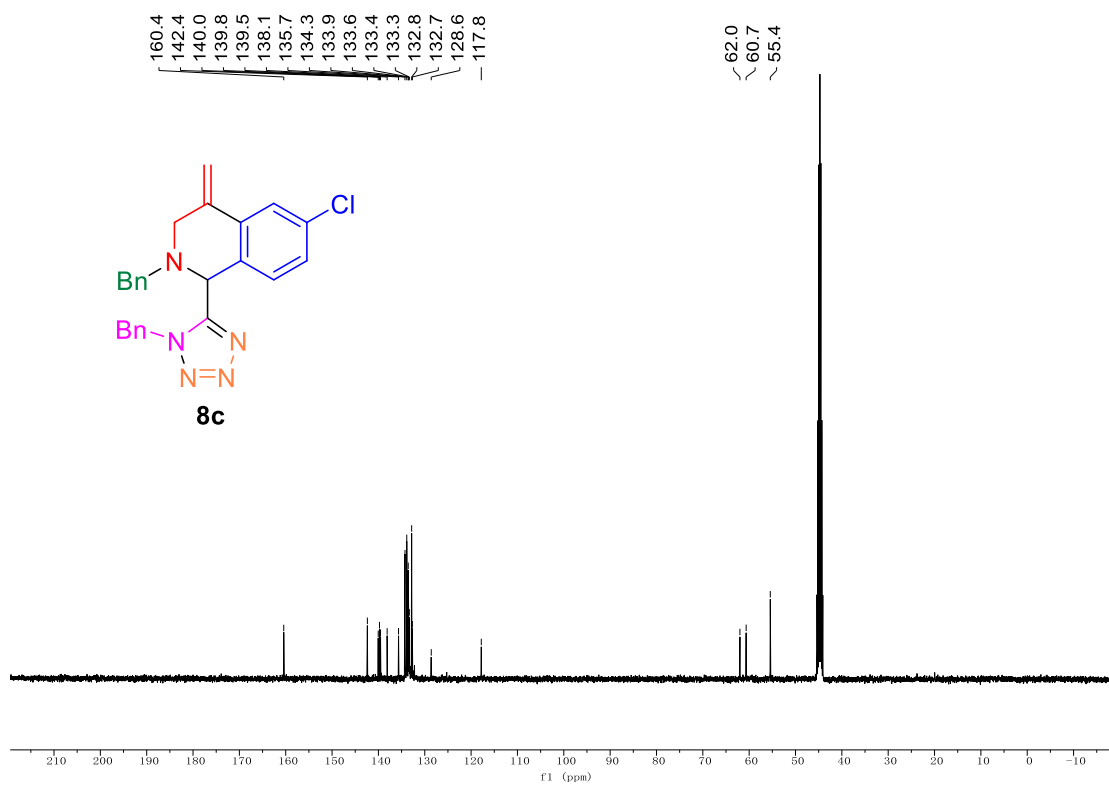
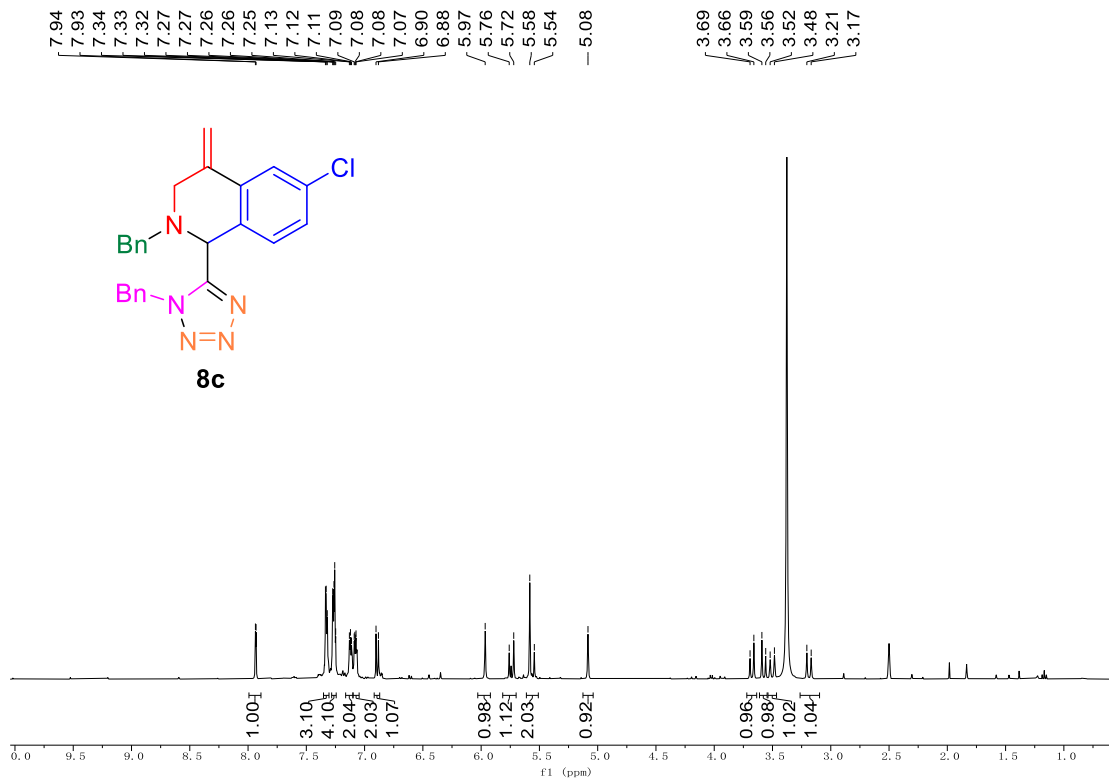


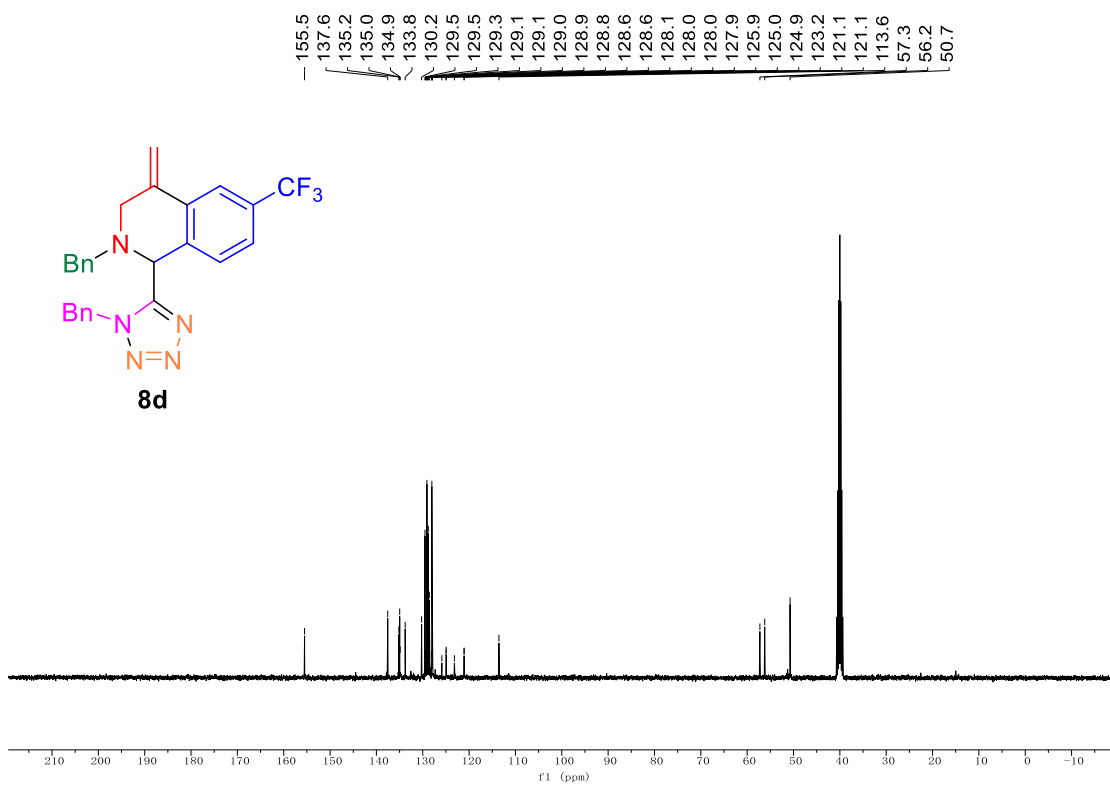
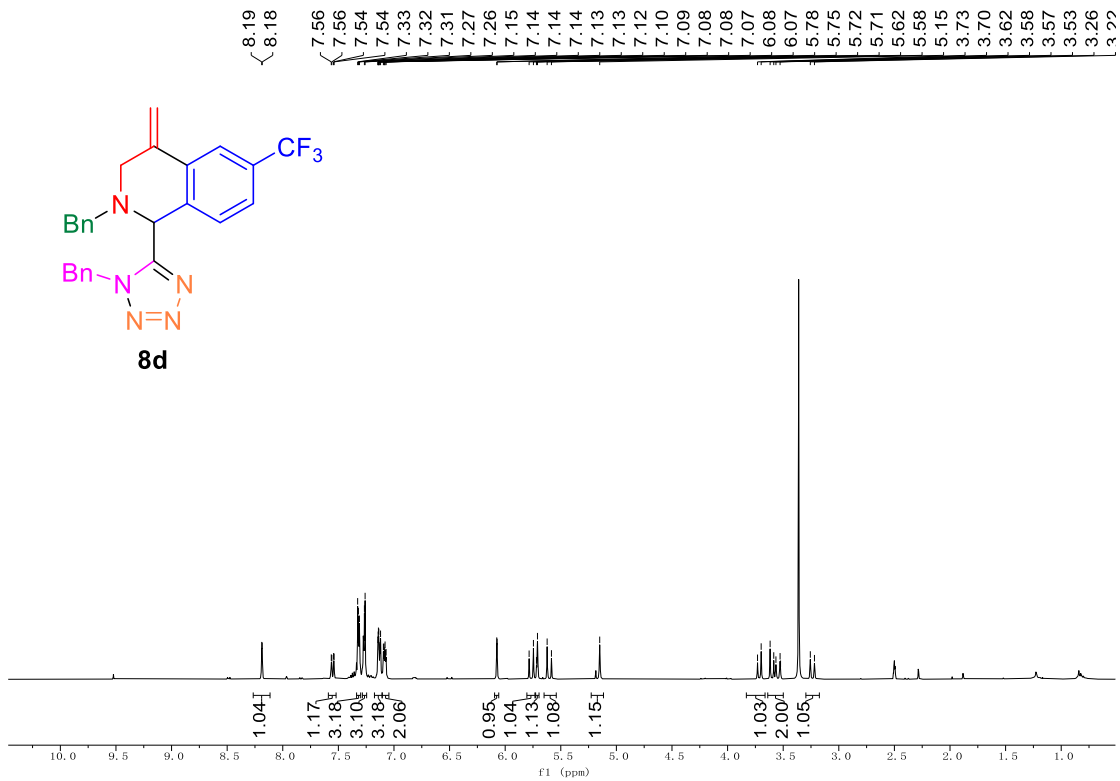
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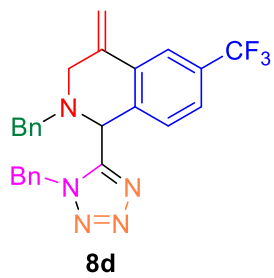


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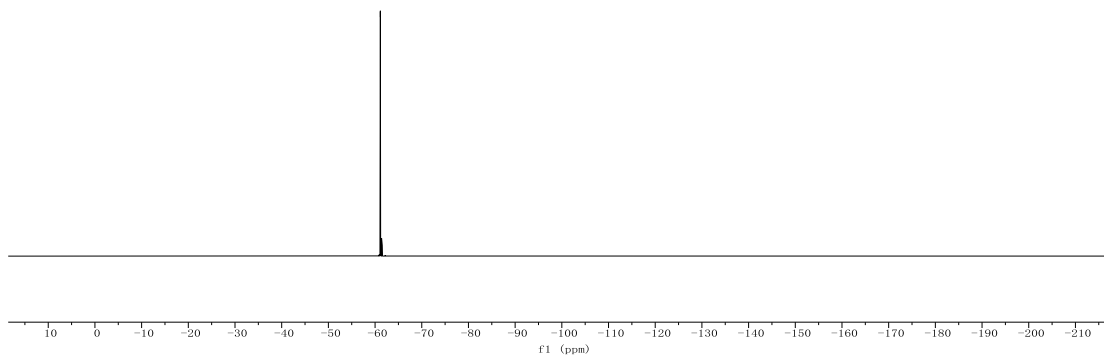




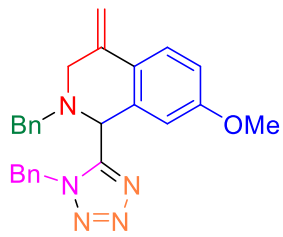




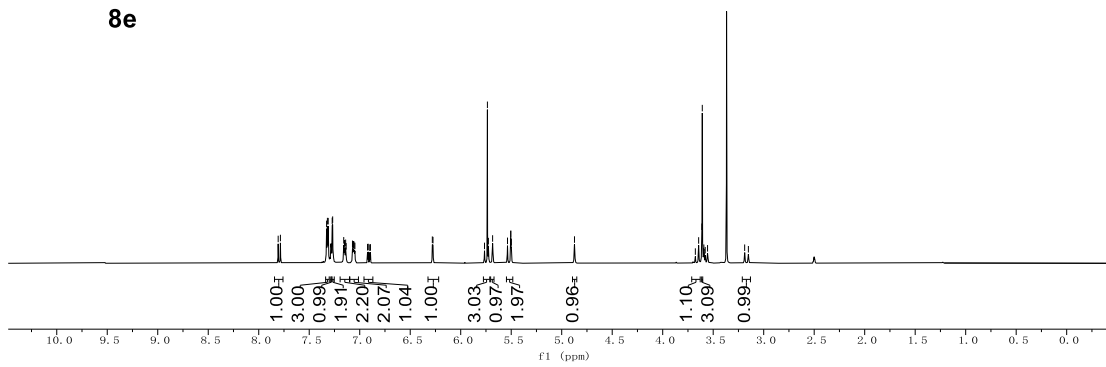
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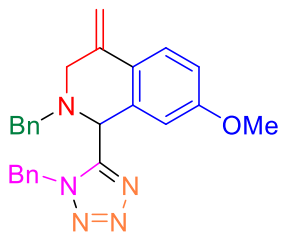
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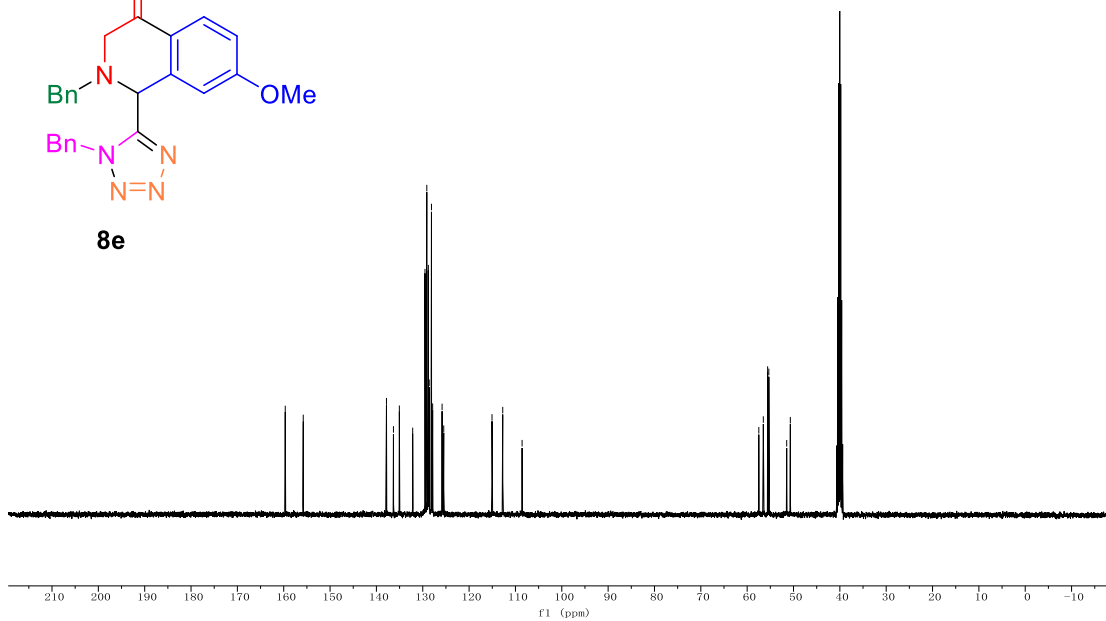
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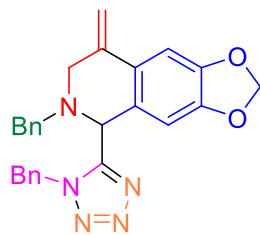
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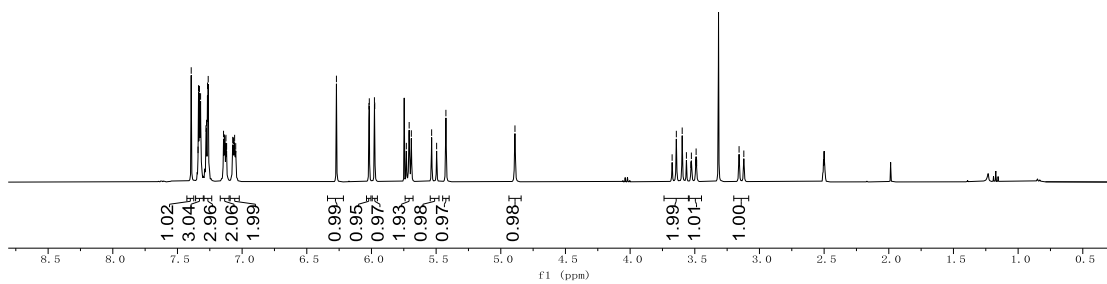
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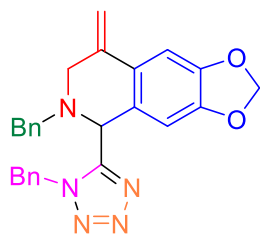
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