Iridium-Catalyzed double C-H Amidation of *s*-Tetrazines

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Contents

I. General Information.

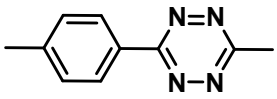
All commercially available organic compounds were purchased from Sigma-Aldrich, adamas-beta and Shanghai GeorGene Biotech Co., Ltd. in China. Unless otherwise noted, all commercial reagents and solvents were used without additional purification. The substrates **1** were prepared according to literature methods.[1] Water was purified with a Millipore Milli-Q system. NMR spectra were recorded on Bruker AM-500 instruments. Chemical shifts are reported in δ (ppm) referenced to TMS as an internal standard for ^{1}H NMR and $CDCl_3$ (δ 77.0) or DMSO-d_6 (δ 39.5) for ^{13}C NMR. High-resolution mass spectra were obtained on High-resolution mass spectra (HRMS-ESI) were obtained on an Agilent Technologies 6230 Accurate Mass TOF LC/MS instrument or an AB Sciex 4600 QTOF MS instrument.

All reagents and DNA headpiece HP-NH2 (5'- / 5phos / GAGTCA / iSp9 / iUniAmM / iSp9 / TGACTCCC-3') were obtained from commercial sources unless otherwise noted and used as received. All on-DNA reactions were performed in 1.5 mL or 5 mL Eppendorf tubes. On-DNA reactions in the studies of reaction condition optimization and substrate scope extension were analyzed by UPLC-MS. Typically, samples were dissolved in an appropriate amount of distilled and deionized water (ddH_2O) and injected into a reverse-phase chromatography column (Xbridge Oligonucleotide BEH C18 column, 1.7 μm, 2.1×50 mm). The elution was carried out as followings: 5–95% solvent B over 4.5 min, 0.4 mL/min, λ = 260 nm; solvent A: 0.75% v/v hexafluoroisopropanol/ 0.038% v/v triethylamine in methanol/water = 5/95; solvent B: 0.75% v/v hexafluoroisopropanol/ 0.038% v/v triethylamine in methanol/water = 90/10. The effluents were analyzed by a Xevo G2-XS Q-TOF with electrospray ionization source was used for detection.

II. Experimental Procedures and Characterizations:

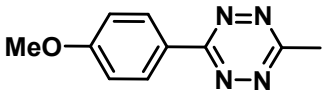
General procedure for the Synthesis and Characterization of 1.[1]

A solution of 4-methylbenzonitrile (586 mg, 5 mmol), acetonitrile (1.7 mL, 40 mmol) and 3-mercaptopropionic acid (0.44 mL, 5 mmol) in ethanol (1 mL) was cooled to 0 **°C**. To this mixture was added dropwise hydrazine hydrate (3.9 mL, 80 mmol). The reaction mixture was stirred at room temperature for 18 h. An ice water solution of $NaNO_2$ (5.175, 75 mmol) was slowly added into the reaction mixture, followed by slow addition of 1M HCl during which the solution was stirred intensely and turned bright red, and gas evolved. Addition of 1M HCl continued until gas evolution ceased and the pH value was 3-4. Then, the reaction mixture was extracted with dichloromethane before washing with saturated salt water. The extract was combined, dried over sodium sulfate and concentrated in vacuo. The crude residue was purified on silica column chromatography (PE : DCM = 2 : 1) to afford the desired product **1b** as a pink solid in 41% yield (382 mg).



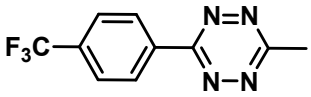
1b

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 3.07 (s, 2H), 2.47 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 164.1, 143.2, 130.0, 129.0, 127.8, 21.6, 21.1. HRMS (ESI): Calcd for $C_{10}H_{11}N_4$: $[M+H]^+$ 187.0984, found: m/z 187.0982.



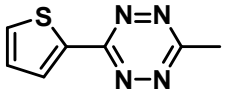
1c

Pink solid, 35% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 3.90 (s, 3H), 3.04 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 163.7, 163.2, 129.7, 124.1, 114.6, 55.4, 21.0. HRMS (ESI): Calcd for $C_{10}H_{11}N_4O$: $[M+H]^+$ 203.0933, found: m/z 203.0937.



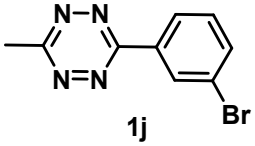
1g

Pink solid, 31% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 8.2 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H), 3.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 163.2, 135.1, 134.1 (q, *J* = 32.9 Hz), 128.2, 126.2 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 272.4 Hz), 21.2. HRMS (ESI): Calcd for $C_{10}H_8F_3N_4$: $[M+H]^+$ 241.0701, found: m/z 241.0701.



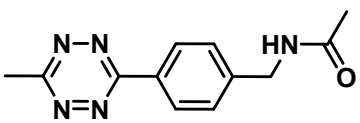
1i

Pink solid, 45% yield.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 3.7 Hz, 1H), 7.66 (d, *J* = 4.9 Hz, 1H), 7.24 (t, *J* = 4.3 Hz, 1H), 3.03 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 162.0, 135.7, 132.3, 131.0, 128.8, 21.1. HRMS (ESI): Calcd for $C_7H_7N_4S$: $[M+H]^+$ 179.0391, found: m/z 179.0391.



1j

Pink solid, 48% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.53 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.47 (t, *J* = 7.9 Hz, 1H), 3.12 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.7, 163.1, 135.5, 133.7, 130.8, 130.8, 126.4, 123.4, 21.2. HRMS (ESI): Calcd for $C_9H_8N_4Br$: $[M+H]^+$ 250.9932, found: m/z 250.9958.



1h

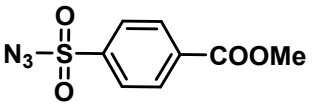
To a 25 mL test tube was combined (4-(6-methyl-1,2,4,5-tetrazin-3-yl)phenyl)methanamine

(commercial available, 1.006 g, 5 mmol, 1 equiv), TEA (1.1 mL, 7.5 mmol, 1.5 equiv) and 20 mL CH_2Cl_2, then Ac_2O (0.57 mL, 6 mmol, 1.2 equiv) was added at 0 °C and the mixture was stirred at room temperature for 2 h. Then water (20 mL) was added and extracted with CH_2Cl_2 (15 mL x 2), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (CH_2Cl_2/MeOH, 100 : 1) to afford **1h** (1.156 g, 95%).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 6.02 (s, 1H), 4.54 (d, *J* = 5.9 Hz, 2H), 3.09 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 167.2, 163.8, 143.2, 130.9, 128.4, 128.2, 43.3, 23.2, 21.1. HRMS (ESI): Calcd for $C_{12}H_{14}N_5O$: $[M+H]^+$ 244.1198, found: m/z 244.1195.

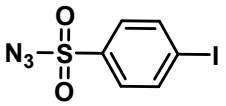
Procedure for the Synthesis and Characterization of 2.

Methyl 4-(chlorosulfonyl)benzoate (2.347 g, 10.0 mmol) was dissolved in acetone (30 mL) and water (30 mL). The solution was cooled to 0 °C and NaN_3 (715 mg, 11.0 mmol) was added. The reaction was stirred for 2 h. The acetone was removed under vacuum and the remaining water layer was extracted with EtOAc (50 mL), the EtOAc layer was washed with brine, dried on Na_2SO_4 and concentrated. The residue was purified on silica gel column chromatography (PE/DCM, 10 : 1) to afford **2f** (2.29 g, 95%).



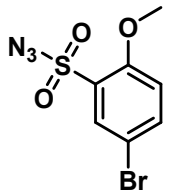
2f

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, *J* = 7.9 Hz, 2H), 8.03 (d, *J* = 8.0 Hz, 2H), 3.98 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 142.0, 135.7, 130.8, 127.5, 52.9.



2h

97% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 138.0, 128.6, 103.0.

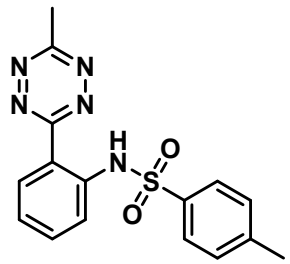


2i

93% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 2.0 Hz, 1H), 7.72 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.00 (d, *J* = 8.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 138.8, 132.6, 129.0, 114.1, 112.5, 56.7.

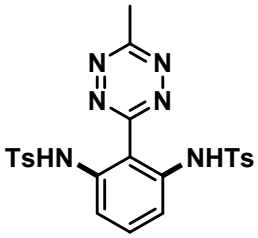
General Procedure for the Synthesis and Characterization of 4 and/or 3.

To a 10 mL test tube was combined **1** (0.2 mmol, 1 equiv), **2** (0.5 mmol, 2.5 equiv), $[IrCp^*Cl_2]_2$ (6.4 mg, 4 mol %), $AgNTf_2$ (12 mg, 16 mol %), $AgOCOCF_3$ (9 mg, 20 mol %) and 2 mL DCE, then the reaction was stirred at 100 °C for 3 h. The solvent was removed and the residue was purified by silica gel chromatography using PE/EA to afford the title compounds.



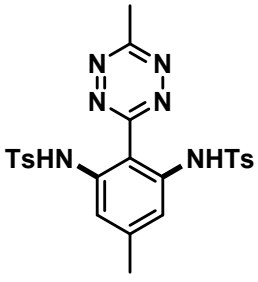
3a

Pink solid, 55% yield (60 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.56 (s, 1H), 8.49 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 7.9 Hz, 2H), 3.10 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 164.5, 143.9, 138.1, 136.1, 133.7, 130.3, 129.4, 127.0, 124.9, 122.9, 120.4, 21.4, 21.1. HRMS (ESI): Calcd for $C_{16}H_{16}N_5O_2S$: $[M+H]^+$ 342.1025, found: m/z 342.1016.



4a

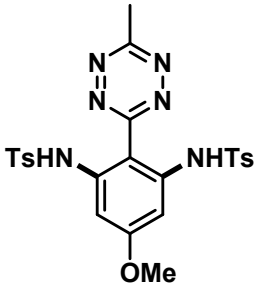
Pink solid, 93% yield.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (s, 2H), 7.66 – 7.56 (m, 3H), 7.08 (d, *J* = 7.8 Hz, 4H), 6.92 (d, *J* = 7.8 Hz, 4H), 3.06 (s, 3H), 2.30 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 163.4, 144.1, 136.5, 135.0, 133.2, 129.3, 126.3, 125.8, 118.9, 21.4, 21.2. HRMS (ESI): Calcd for $C_{23}H_{23}N_6O_4S_2$: $[M+H]^+$ 511.1222, found: m/z 511.1214.



4b

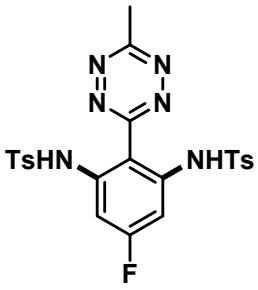
Pink solid, 88% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (s, 2H), 7.44 (s, 2H), 7.06 (d, *J* = 8.0 Hz, 4H), 6.89 (d, *J* = 8.0 Hz, 4H), 3.01 (s, 3H), 2.46 (s, 3H), 2.27 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 163.4, 144.6, 144.0, 136.3, 134.9, 129.1, 126.4, 126.2, 115.9, 21.8, 21.3, 21.1.

HRMS (ESI): Calcd for $C_{24}H_{25}N_6O_4S_2$: $[M+H]^+$ 525.1379, found: m/z 525.1390.



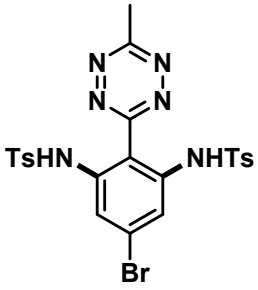
4c

Pink solid, 92% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.71 (s, 2H), 7.23 (d, *J* = 7.9 Hz, 4H), 7.11 (s, 2H), 6.97 (d, *J* = 7.9 Hz, 4H), 3.89 (s, 3H), 3.03 (s, 3H), 2.30 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 163.8, 162.8, 144.1, 139.0, 135.2, 129.3, 126.5, 109.1, 108.3, 55.8, 21.4, 21.0. HRMS (ESI): Calcd for $C_{24}H_{25}N_6O_5S_2$: $[M+H]^+$ 541.1328, found: m/z 541.1321.



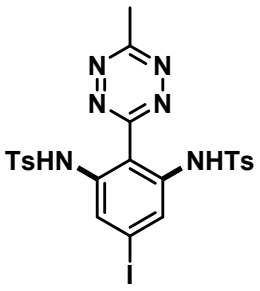
4d

Pink solid, 85% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (s, 2H), 7.33 – 7.27 (m, 6H), 7.03 (d, *J* = 7.8 Hz, 4H), 3.09 (s, 3H), 2.33 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.78, 164.4 (d, *J* = 254.7 Hz), 163.6, 144.4, 139.7 (d, *J* = 13.4 Hz), 135.1, 111.1 (d, *J* = 3.7 Hz), 109.8 (d, *J* = 25.6 Hz), 21.5, 21.2. HRMS (ESI): Calcd for $C_{23}H_{22}FN_6O_4S_2$: $[M+H]^+$ 529.1128, found: m/z 529.1103.



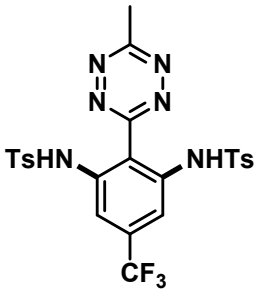
4e

Pink solid, 73% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.29 (s, 2H), 7.75 (s, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 6.98 (d, *J* = 7.9 Hz, 2H), 3.06 (s, 3H), 2.31 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 163.4, 144.4, 137.8, 134.9, 129.4, 127.3, 127.0, 126.5, 115.8, 21.4, 21.2. HRMS (ESI): Calcd for $C_{23}H_{22}BrN_6O_4S_2$: $[M+H]^+$ 589.0327, found: m/z 589.0317



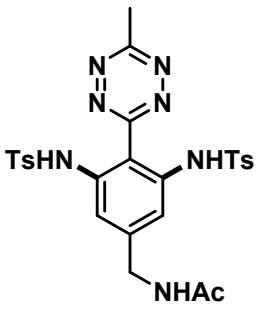
4f

Pink solid, 78% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.31 (s, 2H), 7.77 (s, 2H), 7.19 (d, J = 7.8 Hz, 4H), 6.98 (d, J = 7.9 Hz, 4H), 3.07 (s, 3H), 2.33 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 163.4, 144.4, 137.8, 134.9, 129.4, 127.4, 127.2, 126.5, 115.8, 21.5, 21.2. HRMS (ESI): Calcd for $C_{23}H_{22}IN_6O_4S_2$: $[M+H]^+$ 637.0189, found: m/z 637.0185.



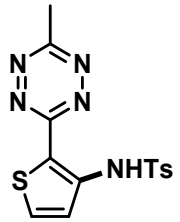
4g

Pink solid, 83% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.27 (s, 2H), 7.81 (s, 2H), 7.21 (d, J = 7.9 Hz, 4H), 7.00 (d, J = 7.8 Hz, 4H), 3.11 (s, 3H), 2.33 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 163.1, 144.6, 137.9, 134.9, 134.8 (q, J = 34.3 Hz), 134.6, 126.6, 122.5 (q, J = 273.3 Hz), 120.5 (q, J = 3.6 Hz), 119.7, 21.5, 21.3. HRMS (ESI): Calcd for $C_{24}H_{22}F_3N_6O_4S_2$: $[M+H]^+$ 579.1096, found: m/z 579.1090.



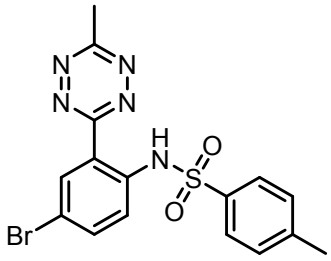
4h

Pink solid, 88% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.60 (s, 2H), 8.37 (t, J = 6.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 4H), 7.29 (d, J = 8.0 Hz, 4H), 7.02 (s, 2H), 4.11 (d, J = 6.1 Hz, 2H), 3.06 (s, 3H), 2.35 (s, 6H), 1.84 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.1, 165.7, 163.7, 143.8, 143.3, 136.5, 129.5, 126.7, 120.6, 119.1, 41.5, 22.4, 21.0. HRMS (ESI): Calcd for $C_{26}H_{28}N_7O_5S_2$: $[M+H]^+$ 582.1593, found: m/z 582.1573.



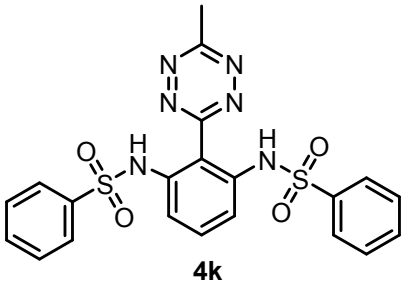
4i

Pink solid, 98% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.12 (s, 1H), 7.75 (d, *J* = 7.7 Hz, 2H), 7.56 – 7.50 (m, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 3.04 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.79, 162.55, 144.25, 141.00, 136.44, 132.54, 129.79, 127.04, 121.99, 114.18, 77.00, 21.53, 21.21. HRMS (ESI): Calcd for $C_{14}H_{14}N_5O_2S_2$: $[M+H]^+$ 348.0589, found: m/z 348.0595.



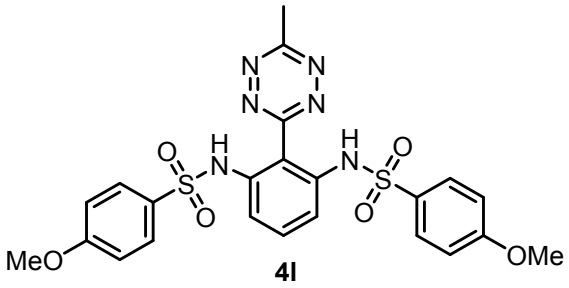
3j

Pink solid, 87% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.56 (s, 1H), 8.63 (s, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 3.12 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 163.6, 144.2, 137.2, 136.4, 135.8, 132.6, 129.5, 126.9, 124.1, 121.6, 117.9, 21.4, 21.2. HRMS (ESI): Calcd for $C_{16}H_{15}BrN_5O_2S$: $[M+H]^+$ 420.0130, found: m/z 420.0126.



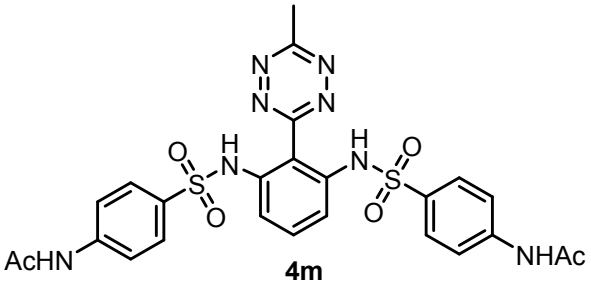
4k

Pink solid, 91% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.12 (s, 2H), 7.68 – 7.59 (m, 3H), 7.40 (t, *J* = 7.4 Hz, 2H), 7.30 – 7.26 (m, 4H), 7.19 (t, *J* = 7.5 Hz, 4H), 3.08 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 163.5, 138.0, 136.5, 133.3, 133.0, 128.8, 126.3, 125.5, 118.4, 21.2. HRMS (ESI): Calcd for $C_{21}H_{19}N_6O_4S_2$: $[M+H]^+$ 483.0909, found: m/z 483.0894.



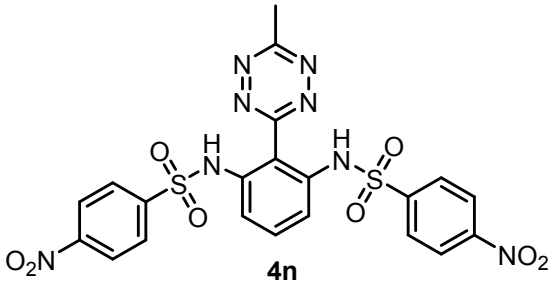
4l

Pink solid, 95% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.58 (s, 2H), 7.48 (d, J = 8.7 Hz, 4H), 7.35 (t, J = 8.2 Hz, 1H), 7.06 (d, J = 8.2 Hz, 2H), 7.00 (d, J = 8.7 Hz, 4H), 3.81 (s, 6H), 3.08 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.7, 163.8, 162.5, 136.7, 131.5, 130.8, 128.9, 122.6, 120.8, 114.2, 55.6, 21.0. HRMS (ESI): Calcd for $C_{23}H_{23}N_6O_6S_2$: $[M+H]^+$ 543.1120, found: m/z 543.1093.



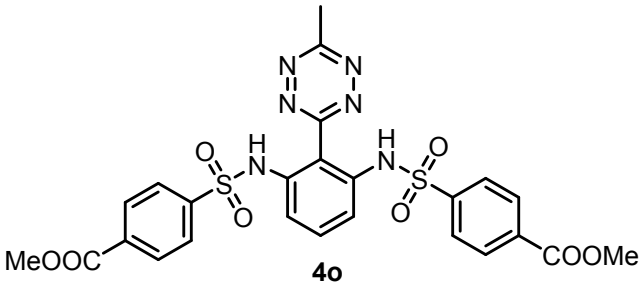
4m

Pink solid, 56% yield. ^{1}H NMR (500 MHz, DMSO) δ 10.34 (s, 2H), 9.63 (s, 2H), 7.67 (d, J = 8.6 Hz, 4H), 7.47 (d, J = 8.5 Hz, 4H), 7.35 (t, J = 8.2 Hz, 1H), 7.04 (d, J = 8.2 Hz, 2H), 3.06 (s, 3H), 2.08 (s, 6H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.0, 165.7, 163.8, 143.2, 136.6, 132.7, 131.4, 127.8, 123.2, 121.3, 118.3, 24.1, 21.0. HRMS (ESI): Calcd for $C_{25}H_{25}N_8O_6S_2$: $[M+H]^+$ 597.1338, found: m/z 597.1327.



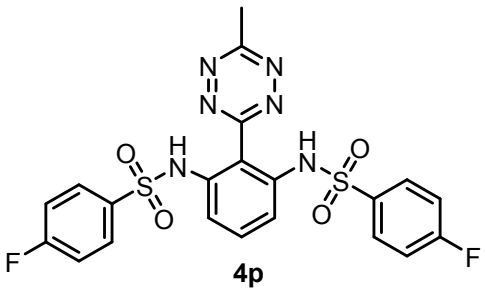
4n

Pink solid, 63% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.19 (s, 2H), 8.32 (d, J = 8.4 Hz, 4H), 7.73 (d, J = 8.4 Hz, 4H), 7.50 (t, J = 8.1 Hz, 1H), 7.24 (d, J = 8.1 Hz, 2H), 3.02 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.9, 163.4, 149.7, 144.8, 135.8, 132.0, 128.1, 124.9, 124.4, 123.7, 20.9. HRMS (ESI): Calcd for $C_{21}H_{17}N_8O_8S_2$: $[M+H]^+$ 573.0611, found: m/z 573.0600.



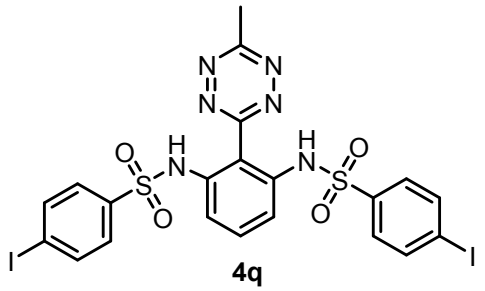
4o

Pink solid, 65% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.15 (s, 2H), 7.83 (d, *J* = 8.0 Hz, 4H), 7.60 (s, 3H), 7.36 (d, *J* = 8.1 Hz, 4H), 3.95 (s, 6H), 3.08 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 165.0, 163.5, 141.9, 136.3, 134.2, 133.5, 129.9, 126.5, 125.3, 118.2, 52.8, 21.2. HRMS (ESI): Calcd for $C_{25}H_{23}N_6O_8S_2$: $[M+H]^+$ 599.1019, found: m/z 599.1017.



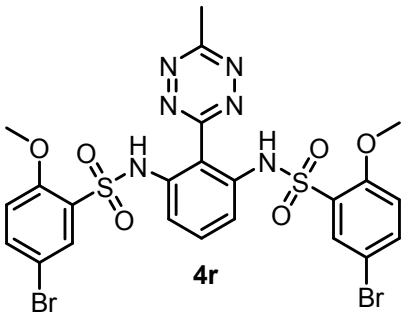
4p

Pink solid, 85% yield. ^{1}H NMR (500 MHz, DMSO) δ 9.79 (s, 2H), 7.58 (dd, *J* = 8.1, 5.3 Hz, 4H), 7.43 (t, *J* = 8.2 Hz, 1H), 7.35 (t, *J* = 8.6 Hz, 4H), 7.14 (d, *J* = 8.2 Hz, 2H), 3.06 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.8, 164.4 (d, *J* = 251.5 Hz), 163.6, 136.3, 135.5, 131.6, 129.7 (d, *J* = 9.7 Hz), 123.8, 123.8, 122.1, 116.3 (d, *J* = 22.9 Hz), 21.0. HRMS (ESI): Calcd for $C_{21}H_{17}F_2N_6O_4S_2$: $[M+H]^+$ 519.0721, found: m/z 519.0715.



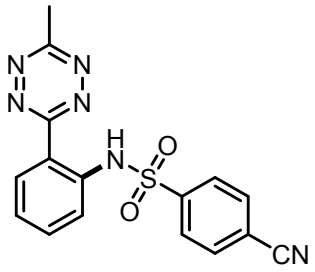
4q

Pink solid, 72% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.87 (s, 2H), 7.89 (d, *J* = 7.9 Hz, 4H), 7.44 (t, *J* = 8.2 Hz, 1H), 7.26 (d, *J* = 7.9 Hz, 4H), 7.14 (d, *J* = 8.2 Hz, 2H), 3.07 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.8, 163.6, 138.9, 138.0, 136.2, 131.8, 128.2, 124.0, 122.4, 101.3, 21.0. HRMS (ESI): Calcd for $C_{21}H_{17}I_2N_6O_4S_2$: $[M+H]^+$ 734.8842, found: m/z 734.8847.



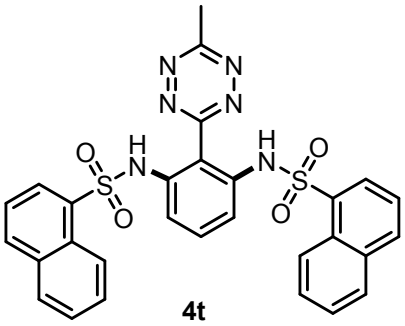
4r

Pink solid, 81% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.71 (s, 2H), 7.75 (dd, J = 8.8, 1.5 Hz, 2H), 7.48 (d, J = 2.1 Hz, 2H), 7.46 (t, J = 8.0 Hz, 1H), 7.17 (d, J = 8.2 Hz, 2H), 7.10 (d, J = 8.9 Hz, 2H), 3.63 (s, 6H), 3.01 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.6, 163.7, 155.6, 149.0, 137.3, 136.4, 131.4, 130.8, 128.6, 123.5, 115.3, 110.7, 56.2, 21.0. HRMS (ESI): Calcd for $C_{23}H_{21}Br_2N_6O_6S_2$: $[M+H]^+$ 698.9331, found: m/z 698.9328.



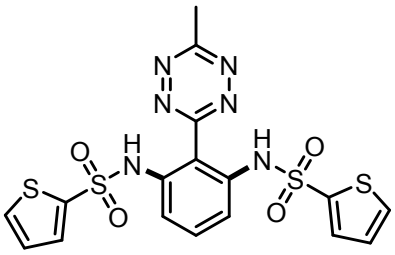
3s

Pink solid, 61% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.96 (s, 1H), 8.60 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.3 Hz, 1H), 7.63 (d, J = 8.1 Hz, 2H), 7.57 (t, J = 7.8 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 3.13 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 164.4, 143.4, 137.5, 134.0, 132.7, 130.6, 127.6, 125.2, 121.7, 119.6, 116.9, 116.7, 21.2. HRMS (ESI): Calcd for $C_{16}H_{13}N_6O_2S$: $[M+H]^+$ 353.0821, found: m/z 353.0816.



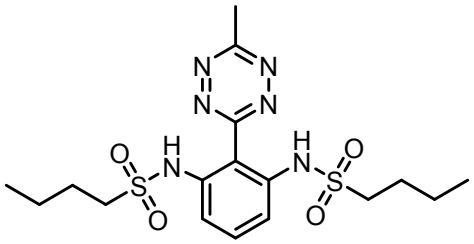
4t

Pink solid, 93% yield. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.10 (s, 2H), 8.26 (d, J = 8.6 Hz, 2H), 8.15 (d, J = 8.2 Hz, 2H), 8.02 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 7.3 Hz, 2H), 7.62 (t, J = 7.5 Hz, 2H), 7.52 (t, J = 7.7 Hz, 2H), 7.47 (t, J = 7.8 Hz, 2H), 7.29 (t, J = 8.2 Hz, 1H), 7.02 (d, J = 8.2 Hz, 2H), 2.71 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.1, 163.2, 135.8, 134.3, 133.5, 131.3, 128.9, 127.8, 126.8, 126.8, 124.9, 124.3, 124.1, 21.0. HRMS (ESI): Calcd for $C_{29}H_{23}N_6O_4S_2$: $[M+H]^+$ 583.1222, found: m/z 583.1437.



4u

Pink solid, 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.28 (s, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.67 – 7.62 (m, 1H), 7.35 (d, *J* = 4.9 Hz, 2H), 7.04 (d, *J* = 3.6 Hz, 2H), 6.80 (t, *J* = 4.3 Hz, 2H), 3.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 163.6, 138.7, 136.4, 133.4, 132.6, 132.3, 127.3, 125.6, 21.2. HRMS (ESI): Calcd for $C_{17}H_{15}N_6O_4S_4$: $[M+H]^+$ 495.0038, found: m/z 495.0029.

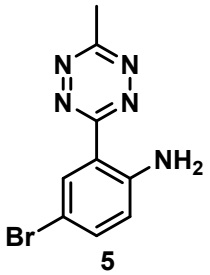


4v

Pink solid, 92% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.58 (s, 2H), 7.60 – 7.52 (m, 3H), 3.16 (s, 3H), 3.14 – 3.06 (m, 4H), 1.67 (p, *J* = 7.5 Hz, 4H), 1.41 – 1.31 (m, 4H), 0.85 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 164.9, 138.7, 133.7, 117.5, 112.1, 52.6, 25.3, 21.3, 13.4. HRMS (ESI): Calcd for $C_{17}H_{27}N_6O_4S_2$: $[M+H]^+$ 443.1535, found: m/z 443.1523.

Procedure for the deprotection of 5.

3j (126 mg, 0.3 mmol) was added cold H_2SO_4 (1.0 mL) slowly at 0 °C and stirred at room temperature for 2 h. The reaction mixture was cooled to 0 °C and quenched by cold water (30 mL) and then saturated aqueous $NaHCO_3$ (20 mL) slowly, extracted with CH_2Cl_2 (20 mL x 3), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (CH_2Cl_2/MeOH, 20 : 1) to afford **5** (69 mg, 87%) as a pink solid.

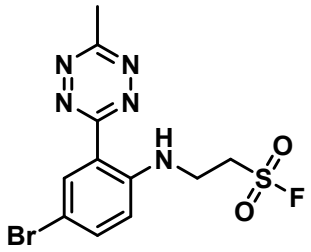


5

^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 8.40 (s, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.11 (s, 2H), 6.90 (d, *J* = 8.8 Hz, 1H), 2.97 (s, 3H). ^{13}C NMR (125 MHz, DMSO-*d*$_6$) δ 164.9, 164.0, 148.7, 135.4, 130.7, 119.4, 113.0, 106.2, 20.8. HRMS (ESI): Calcd for $C_9H_9BrN_5$: $[M+H]^+$ 266.0041, found: m/z 266.0055.

Procedure for the synthesis of 6.

To a stirring solution of **5** (53 mg, 0.2 mmol) in DMF (1.0 mL) was added ESF (34 μL, 0.4 mmol) at room temperature. After t stirring at 60 °C for 3h, the mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (CH_2Cl_2/MeOH, 50 : 1) to afford **6** (60 mg, 80%) as a pink solid.

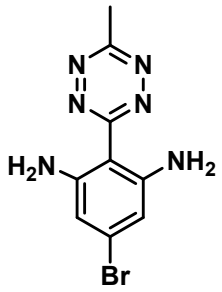


6

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.69 (s, 1H), 7.56 (d, J = 8.8 Hz, 1H), 6.72 (d, J = 8.9 Hz, 1H), 4.03 – 3.95 (m, 2H), 3.75 – 3.68 (m, 2H), 3.10 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 164.4, 146.4, 136.8, 133.0, 115.1, 112.8, 109.4, 49.6 (d, J = 14.8 Hz), 37.3, 21.1. HRMS (ESI): Calcd for $C_{11}H_{12}BrFN_5O_2S$: $[M+H]^+$ 375.9879, found: m/z 375.9892.

Procedure for the synthesie of 7.

4e (177 mg, 0.3 mmol) was added cold H_2SO_4 (1.0 mL) slowly at 0 °C and stirred at room temperature for 2 h. The reaction mixture was cooled to 0 °C and quenched by cold water (30 mL) and then saturated aqueous $NaHCO_3$ (20 mL) slowly, extracted with CH_2Cl_2 (20 mL x 3), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (CH_2Cl_2/MeOH, 20 : 1) to afford **5** (72 mg, 85%) as a pink solid.

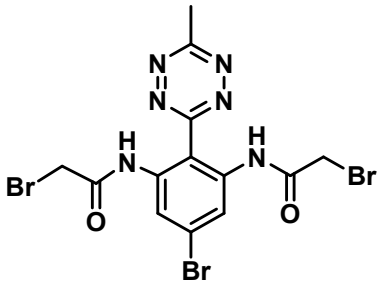


7

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.29 (s, 2H), 6.22 and 3.03 (a pair of s, 4H), 3.05 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 163.2, 151.1, 128.0, 108.2, 97.4, 21.0. HRMS (ESI): Calcd for $C_9H_{10}BrN_5$: $[M+H]^+$ 281.0150, found: m/z 281.0176.

Procedure for the synthesis of 8.

To a 25 mL test tube was combined **7** (28mg, 0.1 mmol), bromoacetyl chloride (18 μL, 0.22 mmol) and 3 mL CH_2Cl_2, then TEA (42 μL, 0.3 mmol) was added at 0 °C and the mixture was stirred at room temperature for 2 h. Then water (20 mL) was added and extracted with CH_2Cl_2 (10 mL x 2), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (CH_2Cl_2/acetone, 2 : 1) to afford **8** (31 mg, 60%) as a pink solid.

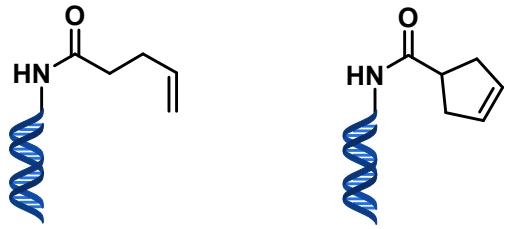


8

^{1}H NMR (500 MHz, $CDCl_3$) δ 11.12 (s, 2H), 8.30 (s, 2H), 3.98 (s, 4H), 3.19 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 164.5 (two peaks, 164.54 and 164.49), 137.9, 127.4, 123.6, 111.9, 29.3, 21.4. HRMS (ESI): Calcd for $C_{13}H_{12}Br_3N_6O_2$: $[M+H]^+$ 520.8572, found: m/z 520.8583.

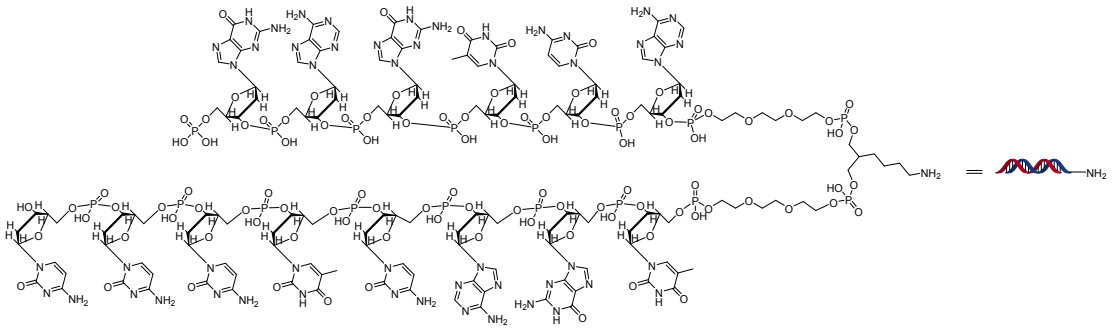
Procedure for the synthesis of HP-A-1 and HP-A-2.

To a solution of DNA headpiece (600 μL, 300 nmol) in borate buffer (250 mM, pH = 9.4), was added a mixture of DMA solution of HATU (60 μL, 200 mM), DIPEA (60 μL, 200 mM) and acids (60 μL, 200 mM). The resultant mixture was vortexed and stood at 25 °C for 8 hours. 5M NaCl (78 μL) and cold ethanol (2.34 mL) were sequentially added, and the resultant mixture was stored at −80 °C for 30 min. The mixture was centrifuged at 4 °C for 30 min at 12000 rpm to remove the supernatant. The resulting pellet was re-dissolved in ddH_2O (300 μL), which was used in following reaction without further purification.



HP-A-1 (97%)

HP-A-2 (100%)

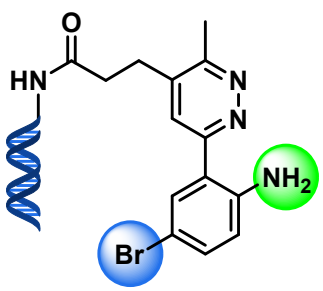


(MW: 4937)

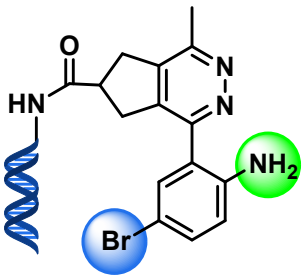
The Structure of DNA Headpiece.

Procedure for the synthesis of HP-1-1 and HP-1-2.

The solution of oxidant system was prepared according the literature (*Org. Lett. 2018, 20, 7186−7191*) procedure: briefly,[2] to a solution of $Cu(ClO_4)_2$ (100 μL, 100 mM in water) was added a solution of 2,2'-bipyridine (100 μL, 100 mM in DMSO). The resultant mixture was vortexed and stood at 20 °C for 5 min. After that, to the reaction mixture was added a solution of TEMPO (100 μL, 100 mM in DMSO) and the resultant mixture was vortexed to give the oxidant solution (300 μL, 33 mM). To a solution of DNA-conjugated alkenes 10 (10 nmol) in water (10 μL) was added a solution of tetrazine **5** (10 μL, 200 mM in DMSO, 2000 nmol). The mixture was vortexed and stood at 20 °C. When UPLC-MS showed that t DNA-conjugated alkenes was consumed completely, a solution of oxidant system (6 μL, 33 mM, 200 nmol) was added to the reaction mixture. The mixture was vortexed and stood at 20 °C for 4 h. Aqueous sodium diethyldithiocarbamic acid (10 μL, 100 mM, 1000 nmol) was added and the reaction mixture was vortexed and centrifuged. To the supernatant were sequentially added aqueous NaCl (3.6 μL, 5.0 M) and cold ethanol (108 μL). The resultant mixture was stored at −80 °C for 30 min and centrifuged at 4 °C for 30 min at 10000 rpm before the resultant supernatant was removed. The pellet was dissolved in deionized water and analyzed by UPLC-MS to determine the conversion.



HP-I-1 (90%)

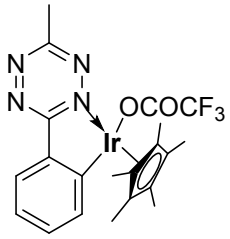


HP-I-2 (91%)

III. Mechanistic Studies

Procedure for the synthesis of complex A.

$AgOCOCF_3$ (88.4 mg, 0.4 mmol) was added to a solution of $[Cp^*IrCl_2]_2$ (80.0 mg, 0.1 mmol) in CH_2Cl_2 (20 mL) in the dark and stirred at room temperature for 30 min. **1a** (17.2 mg, 0.2 mmol) and NaOAc (24.6 mg, 0.3 mmol) were then added. The mixture was stirred at room temperature for 12 h and the solution was filtered. The filtrate was evaporated under vacuum and 10 mL (hexane and methyl *tert*-butyl ether) solvent was added to the residue, the title compound complex A was precipitated and collected by filtration as black solid in 92% yield (112.5 mg).



Complex A

^1H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.7 Hz, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.5 Hz,

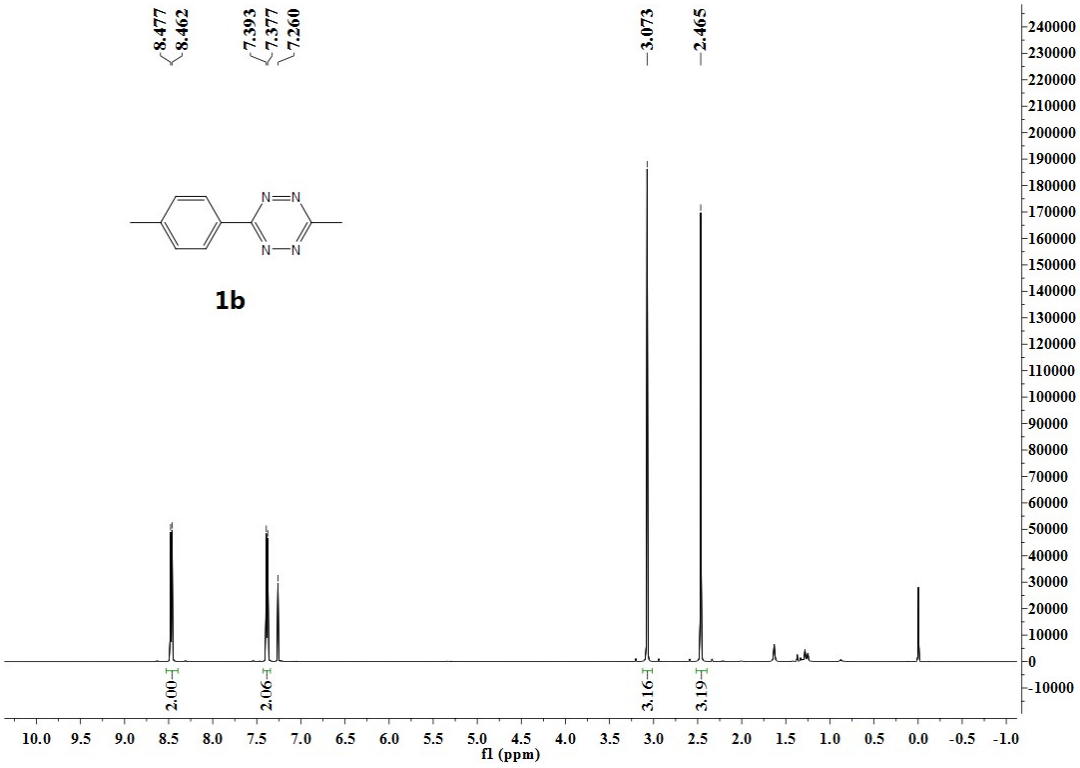
1H), 7.22 (t, J = 7.5 Hz, 1H), 3.14 (s, 3H), 1.74 (s, 15H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 165.8, 163.1 (q, J = 36.3 Hz), 160.9, 135.7, 135.6, 133.7, 127.3, 124.1, 113.9 (q, J = 291.6 Hz), 92.0, 20.8, 8.8. ^{19}F NMR (471 MHz, $CDCl_3$) δ -74.7 (s). HRMS (ESI): Calcd for $C_{19}H_{22}N_6Ir$: $[M\text{-}CF_3CO_2]^+$ 499.1474, found: m/z 499.1456.

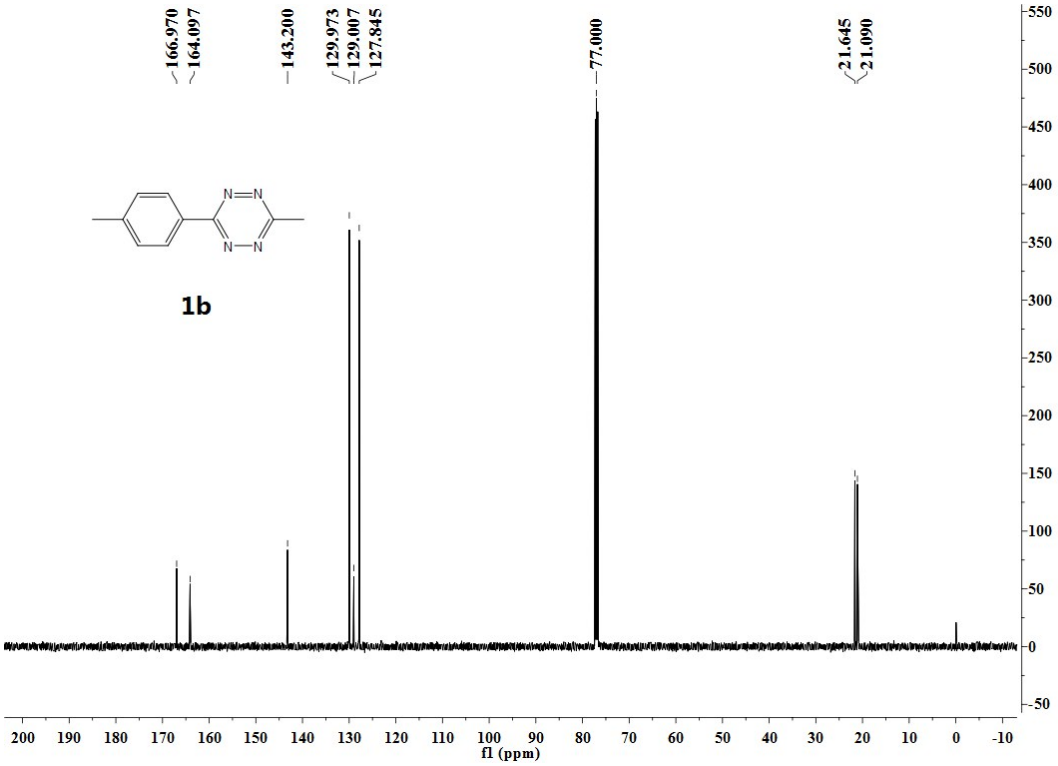
IV. Reference

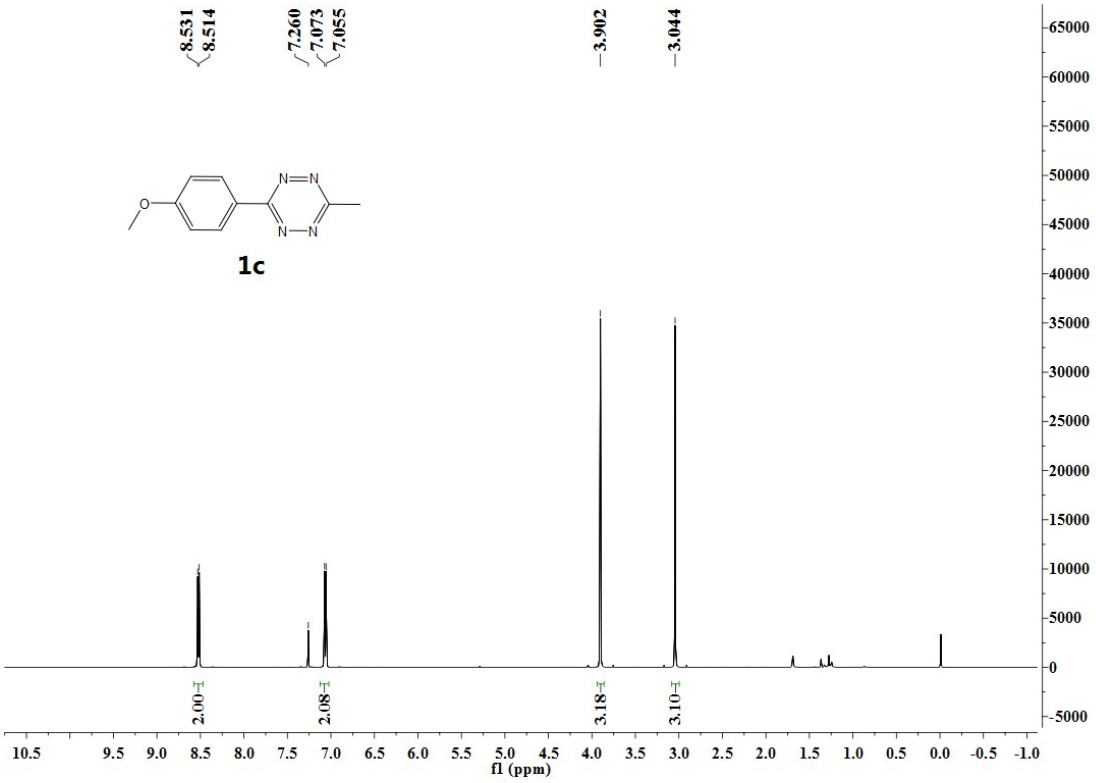
[1] Mao, W.; Shi, W.; Li, J.; Su, D.; Wang, X.; Zhang, L.; Pan, L.; Wu, X.; Wu, H. *Angew. Chem. Int. Ed*. **2019**, *58*, 1106.

[2] Li, H.; Sun, Z.; Wu, W.; Wang, X.; Zhang, M.; Lu, X.; Zhong, W.; Dai, D. *Org. Lett.* **2018**, *20* (22), 7186–7191.

V. Copies of ^{1}H, ^{13}C NMR, HPLC and MS Spectra.



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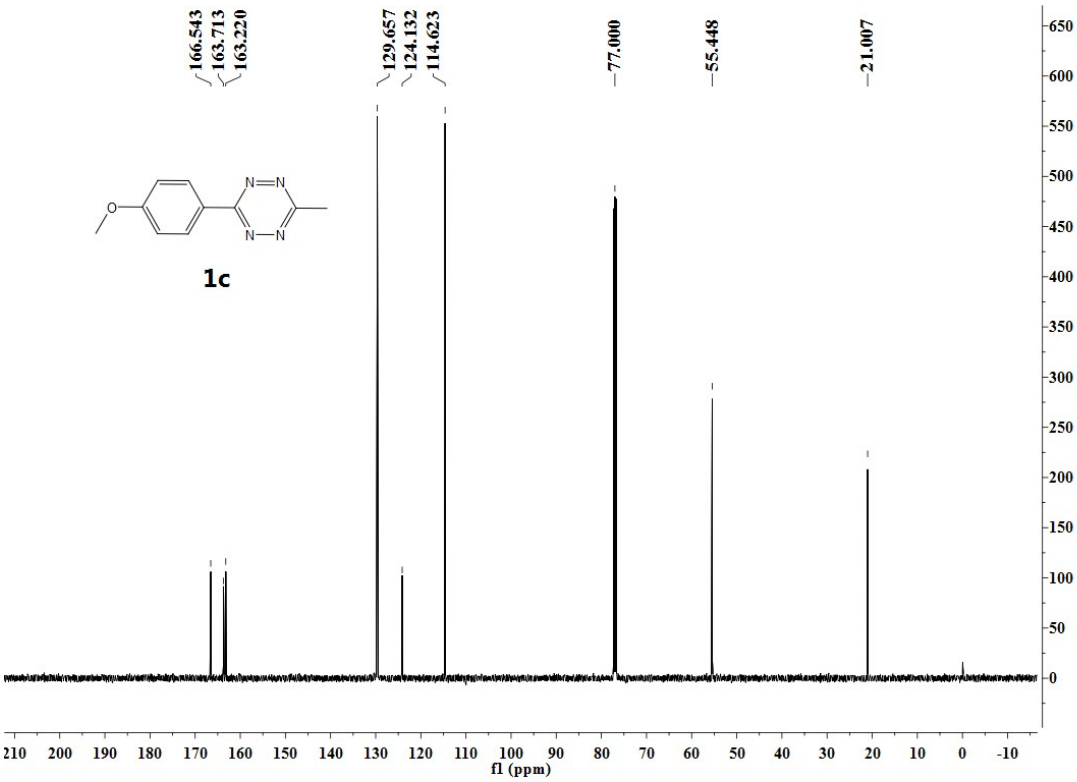
3.10
f1 (ppm)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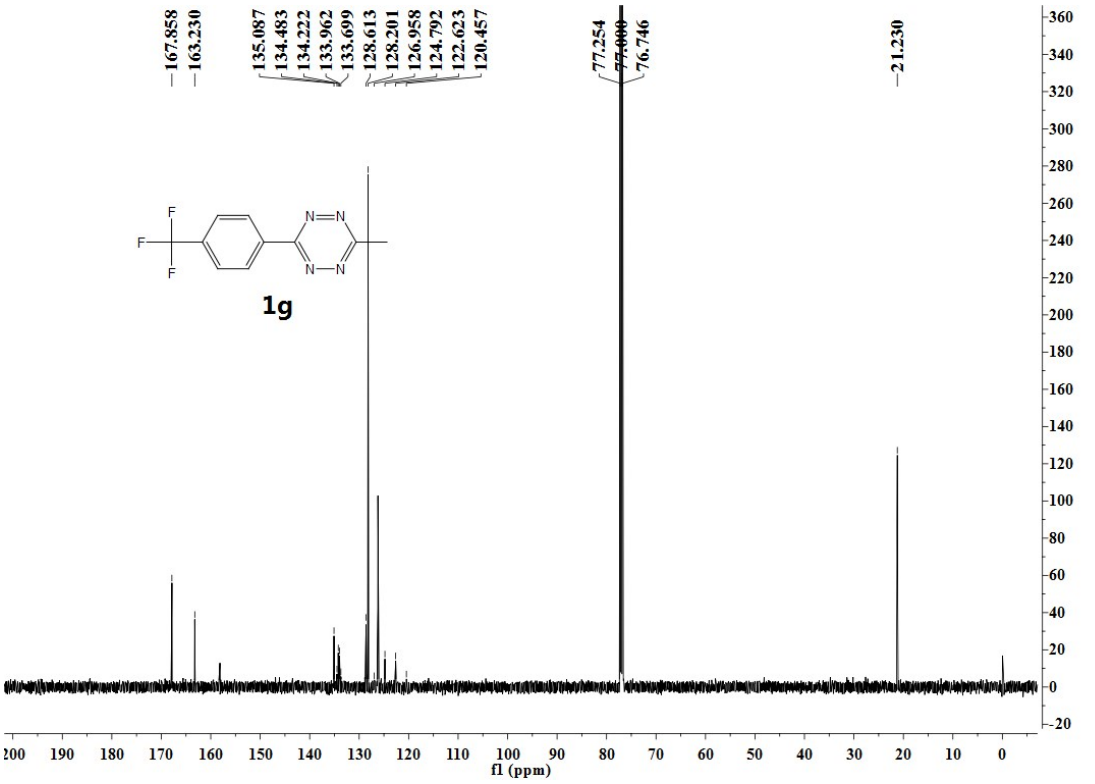
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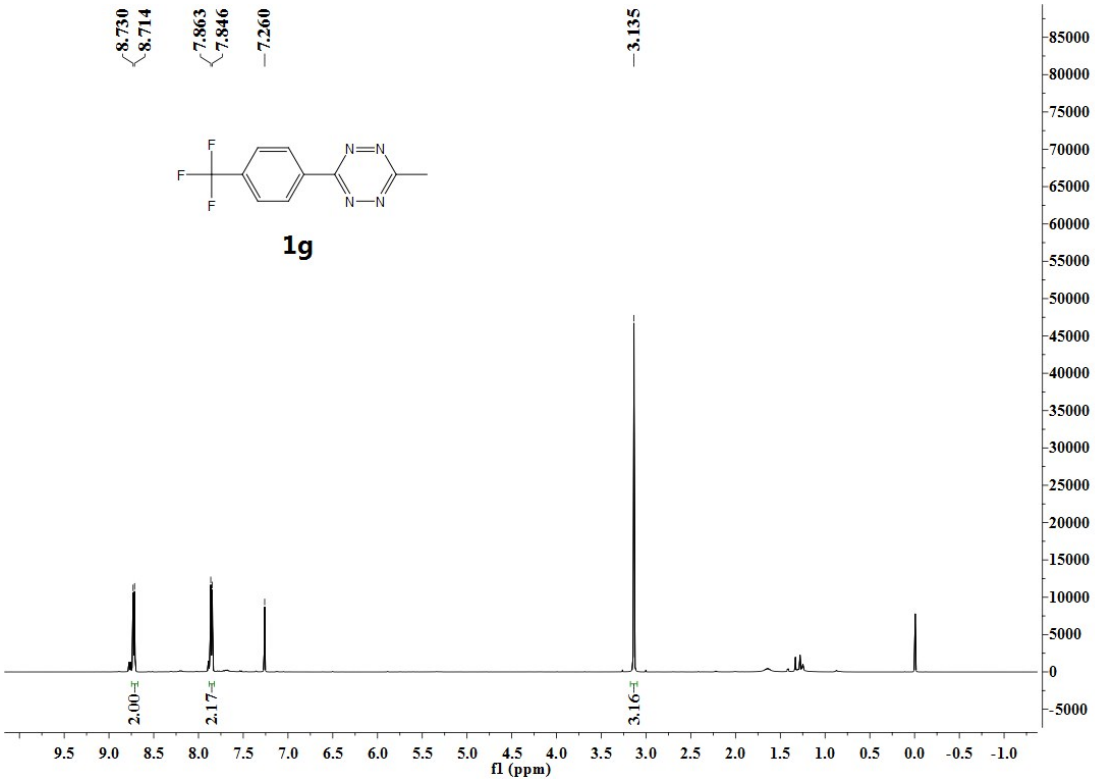
1g
f1 (ppm)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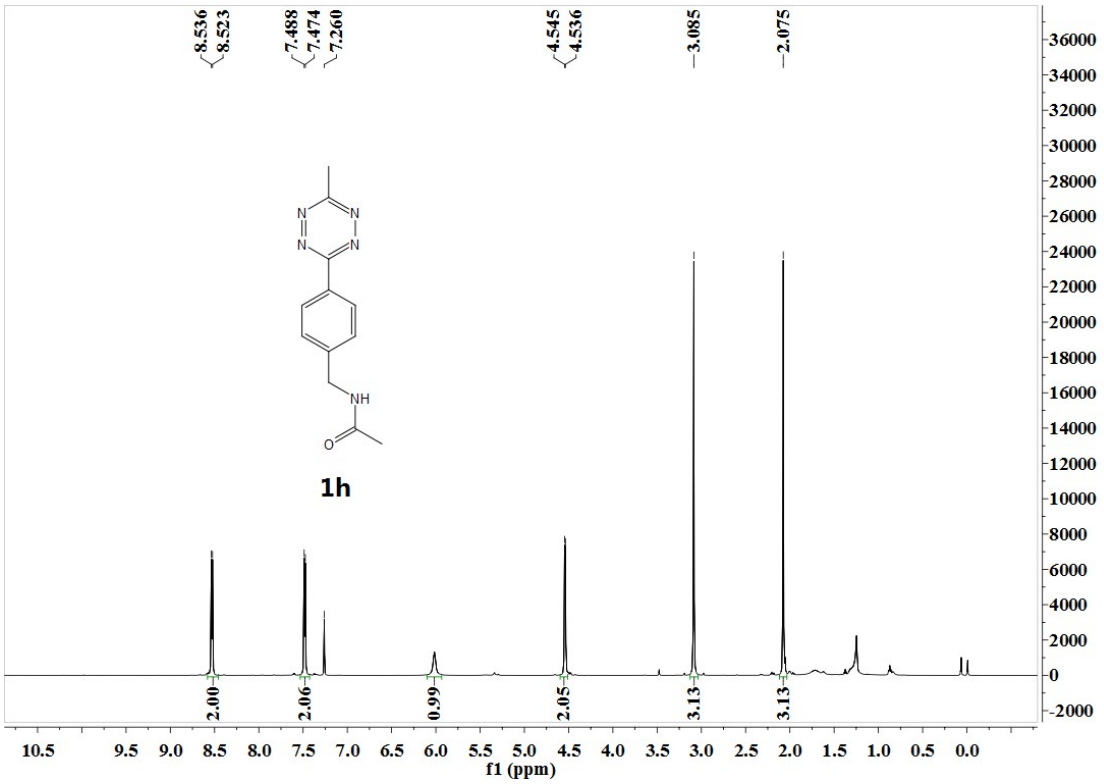
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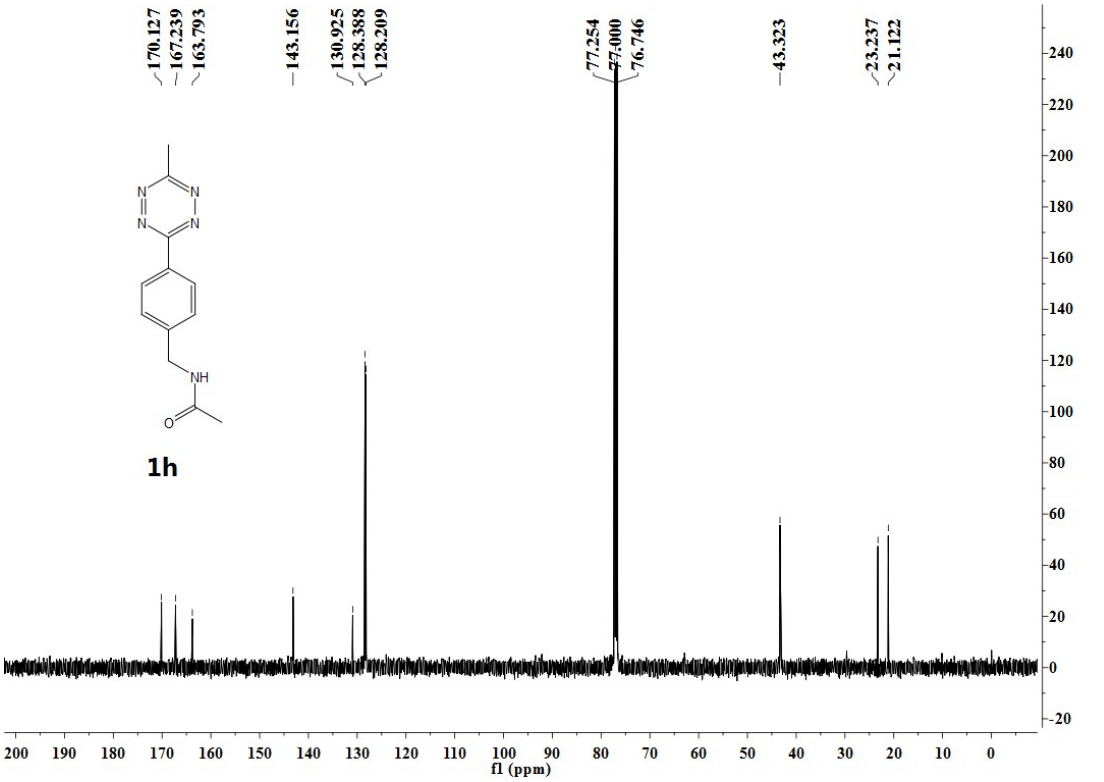
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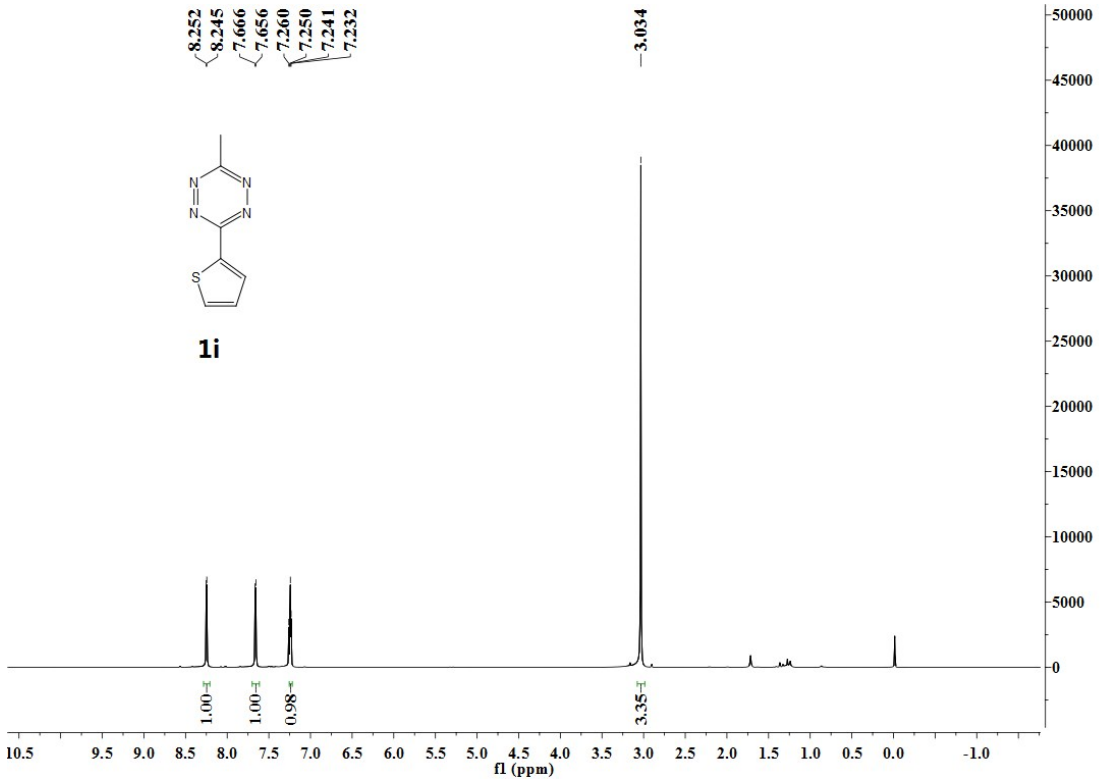
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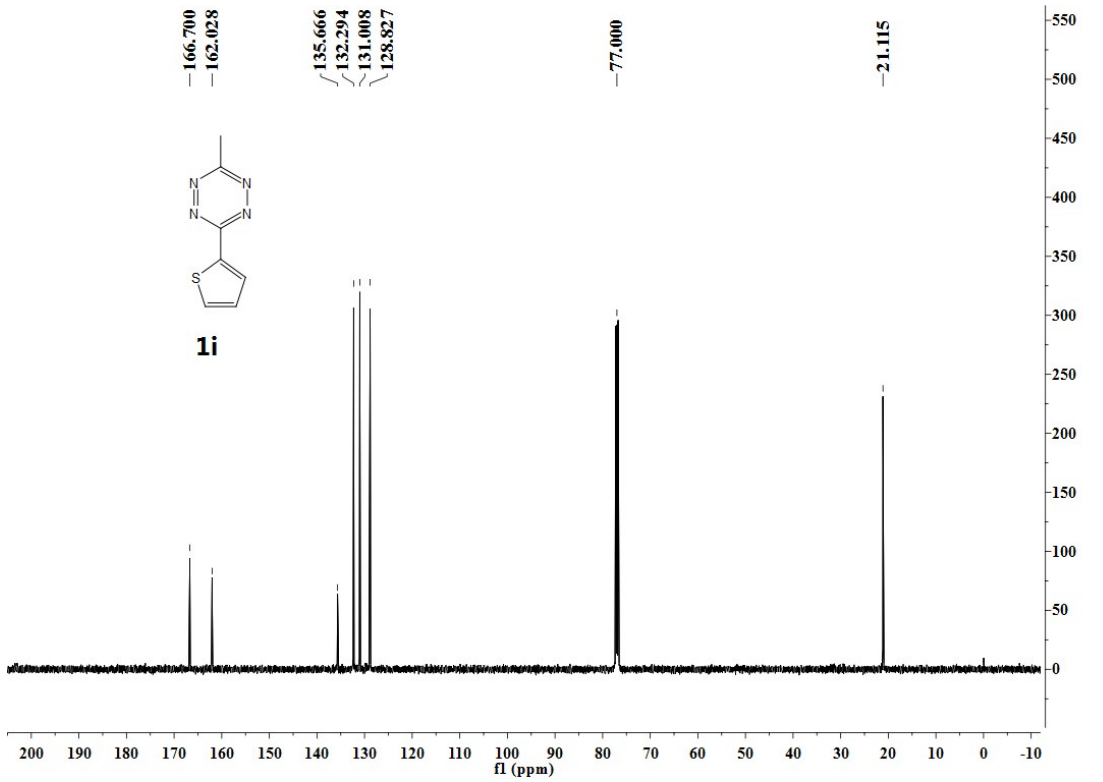
fl (ppm)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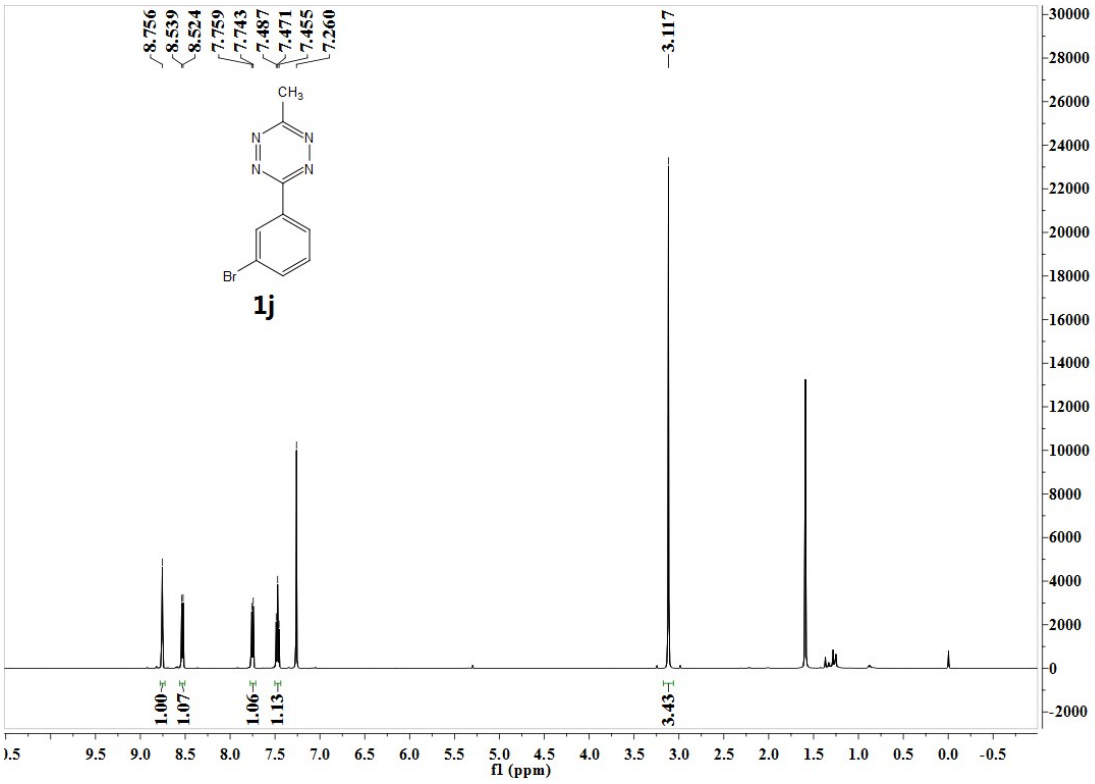
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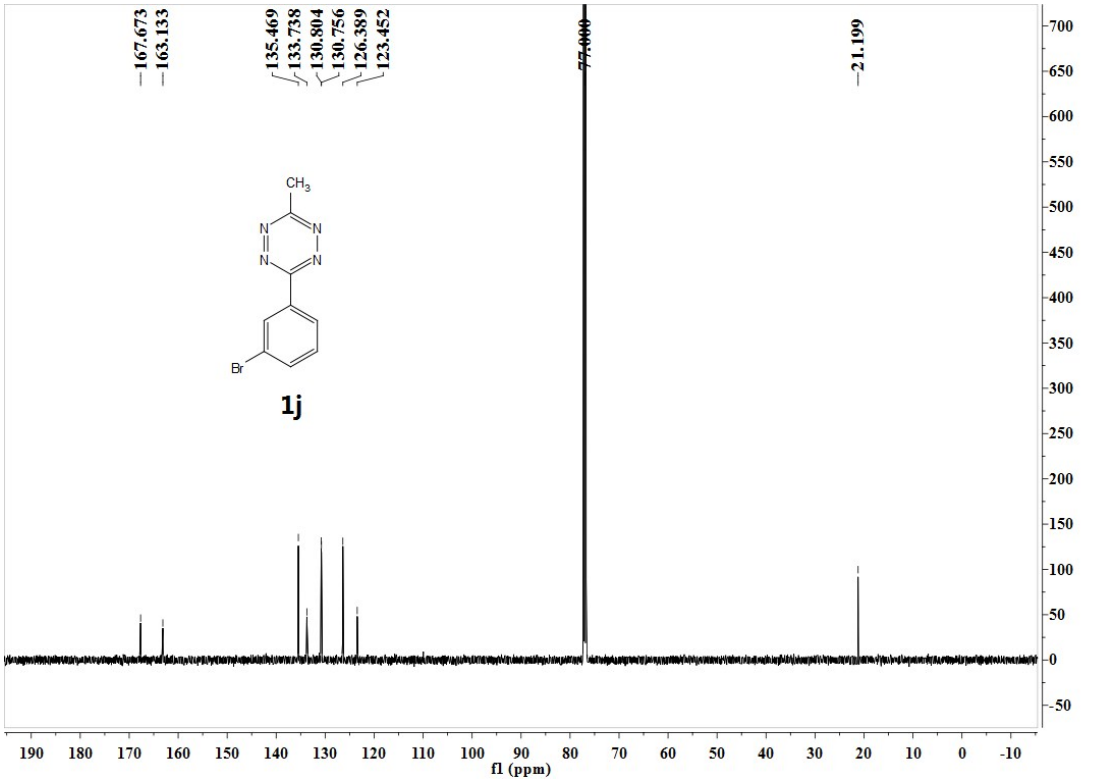
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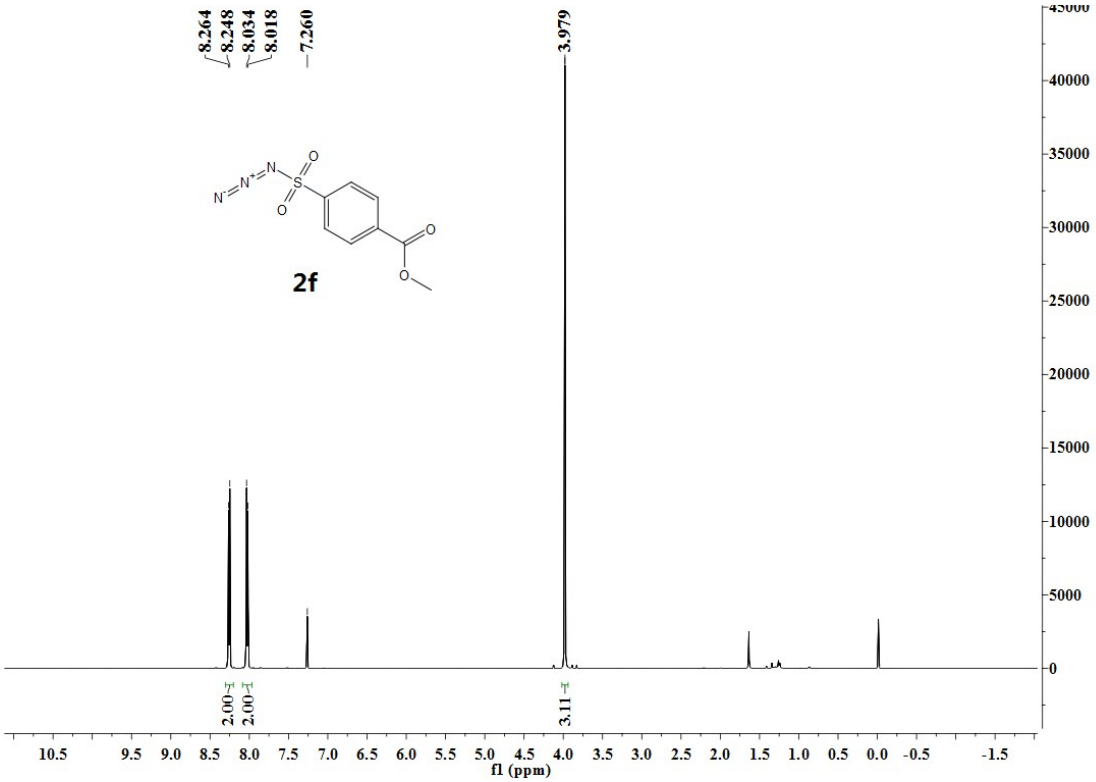
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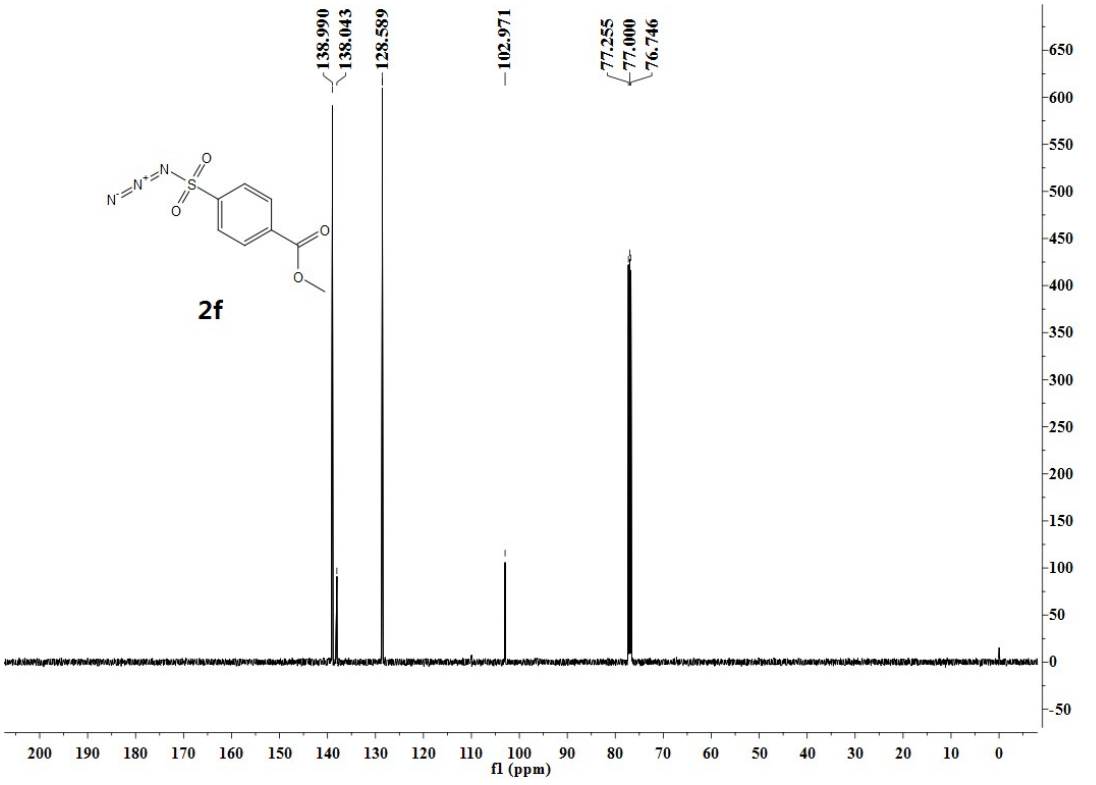
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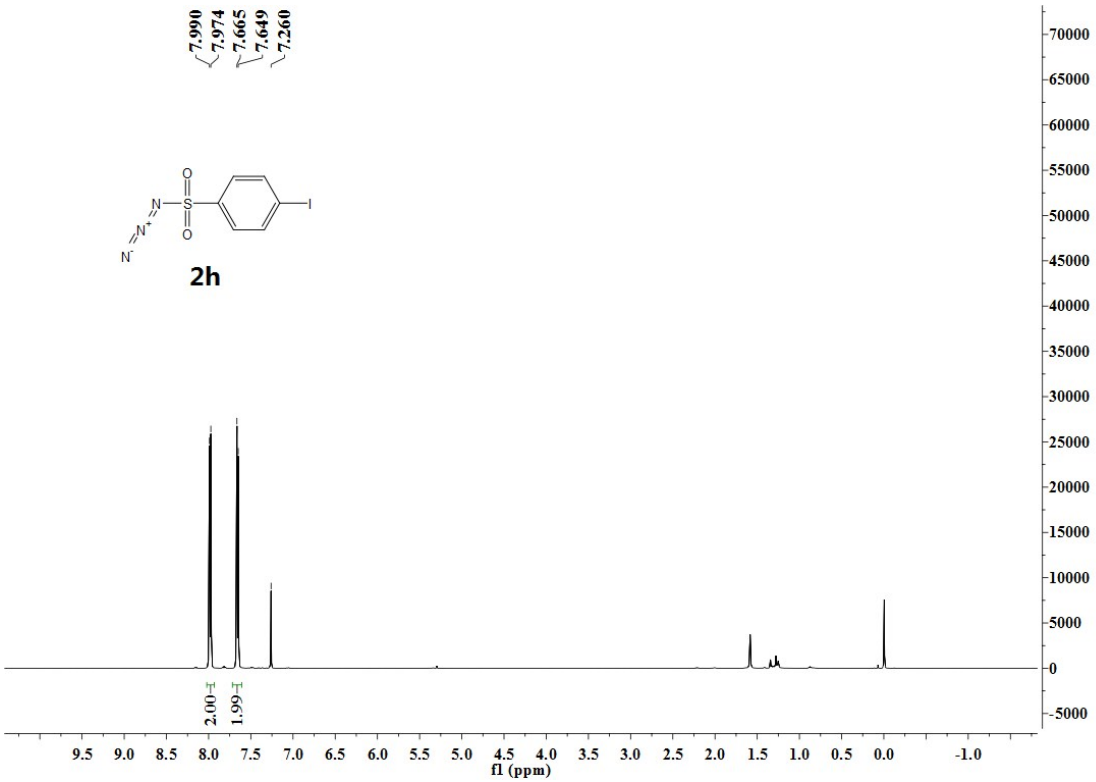
fl (ppm)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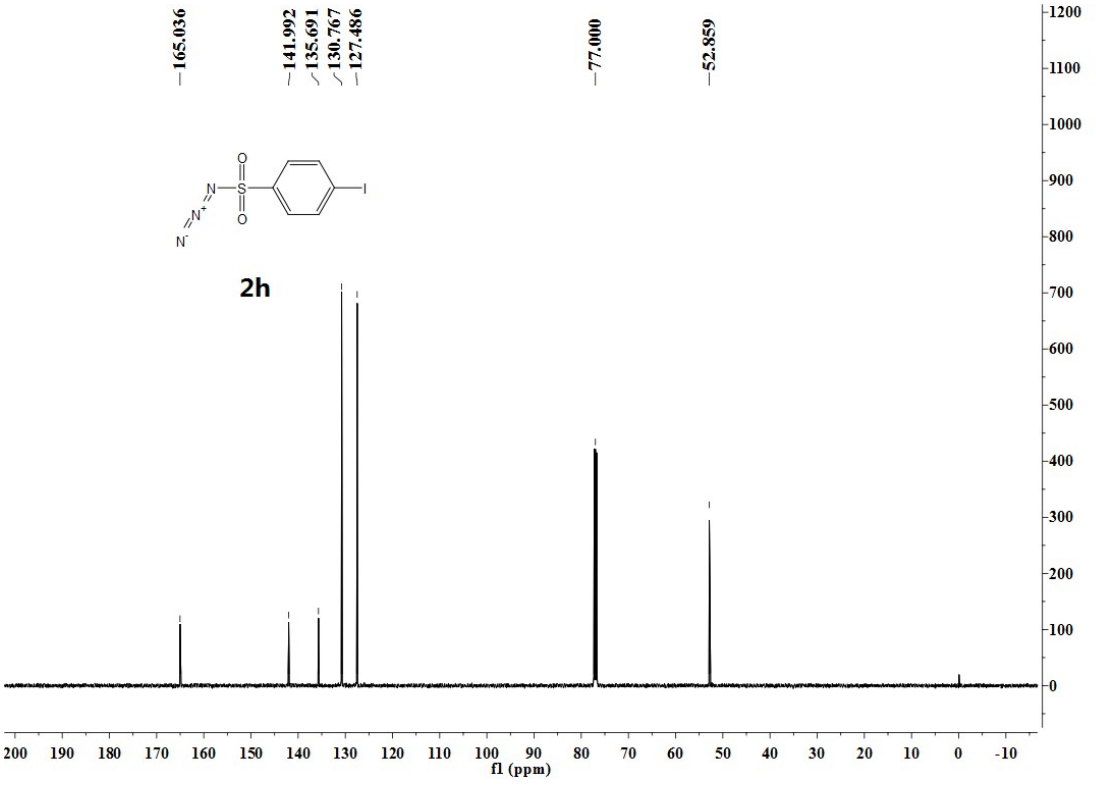
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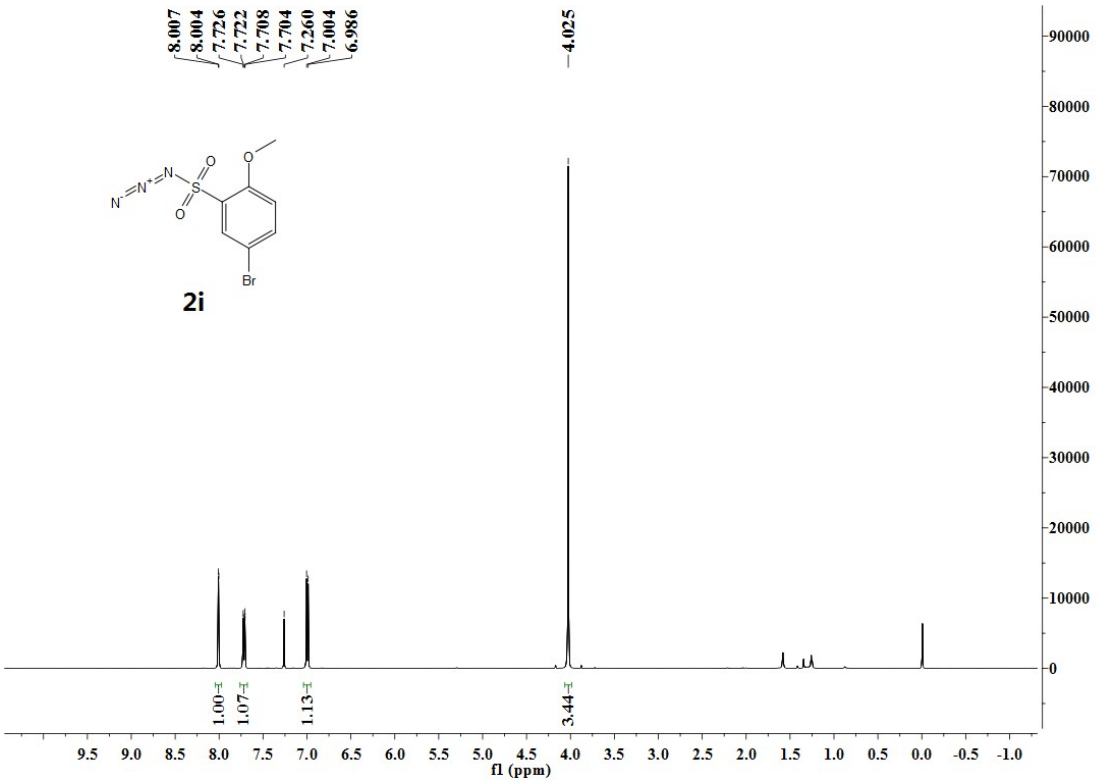
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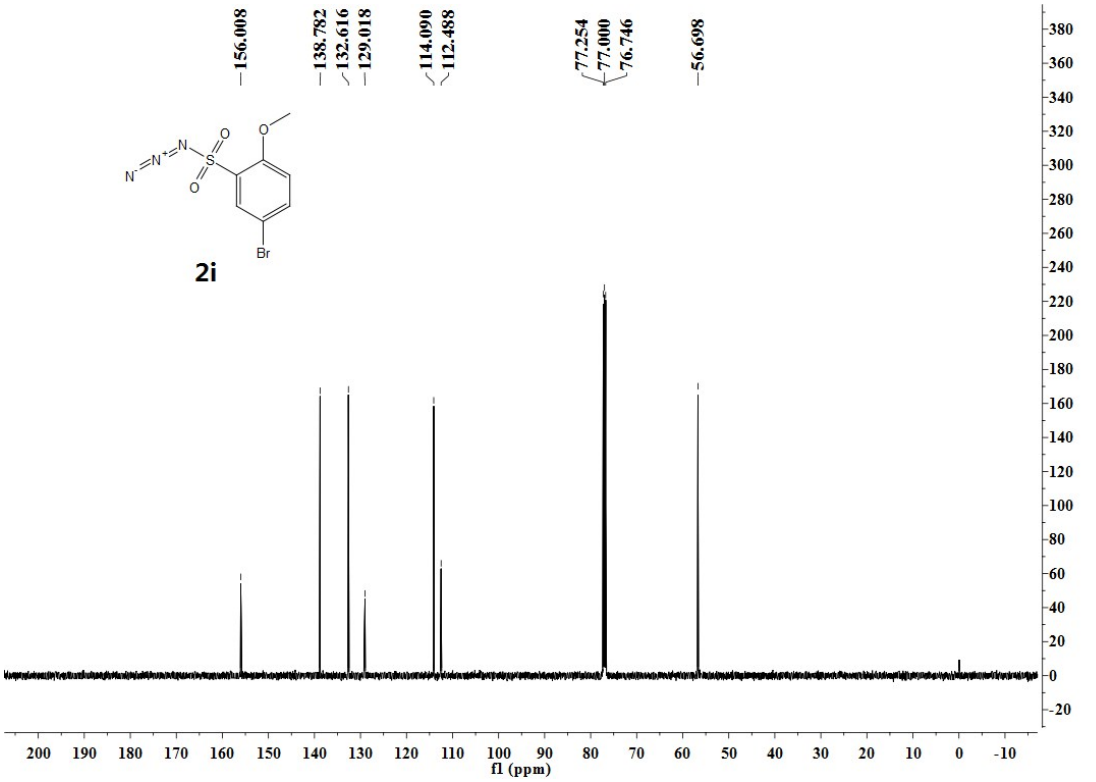
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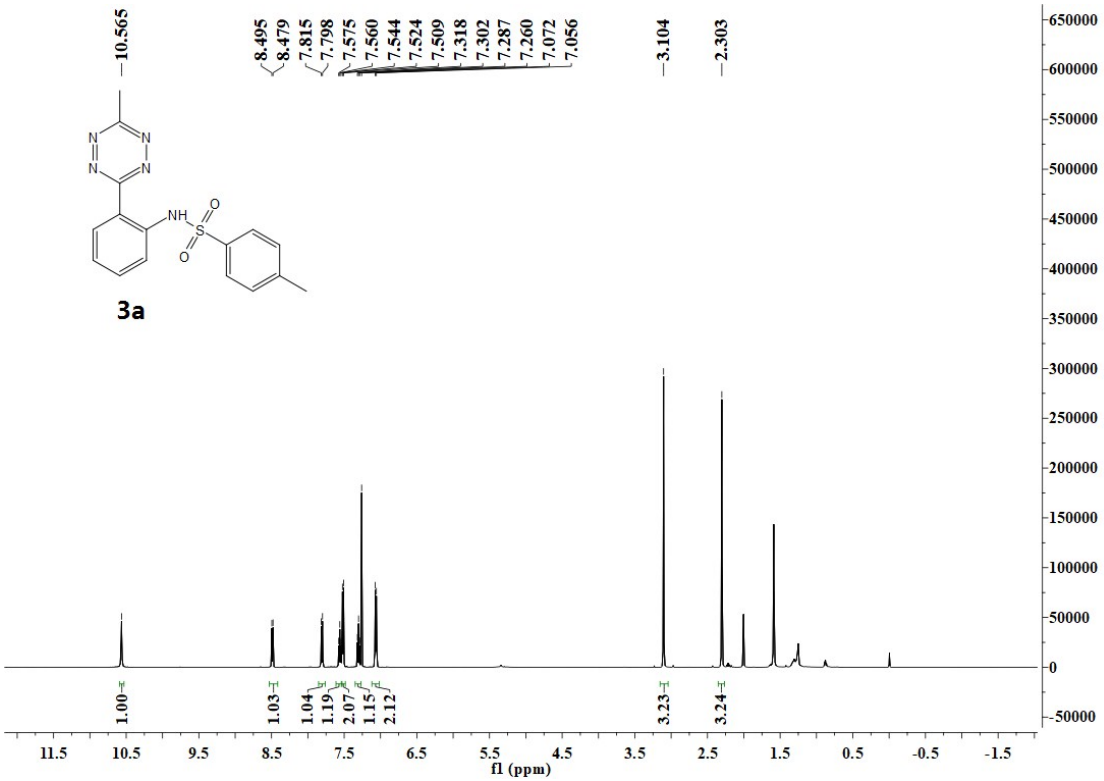
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7.056
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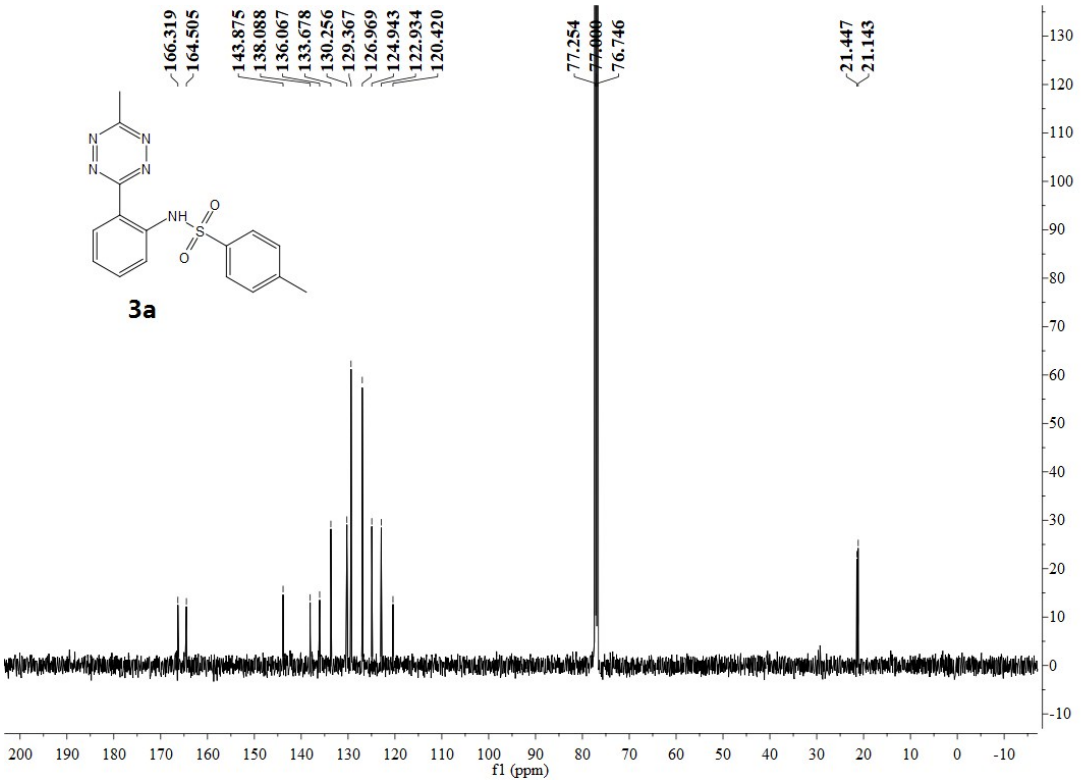
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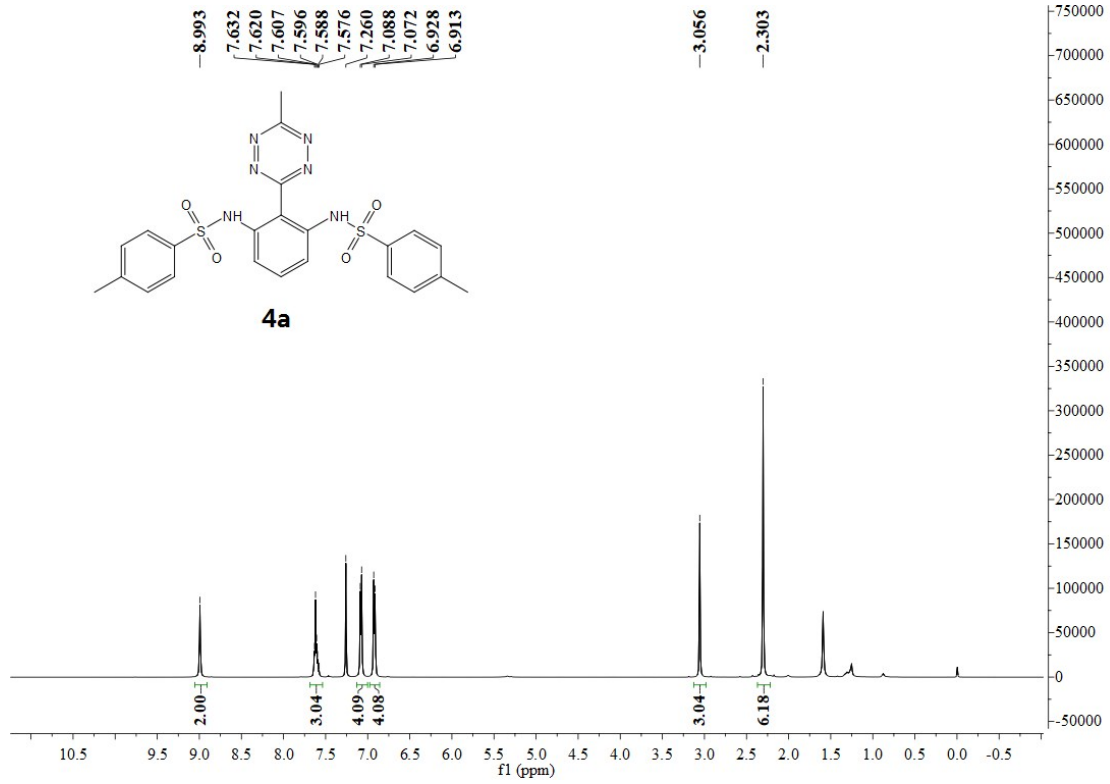
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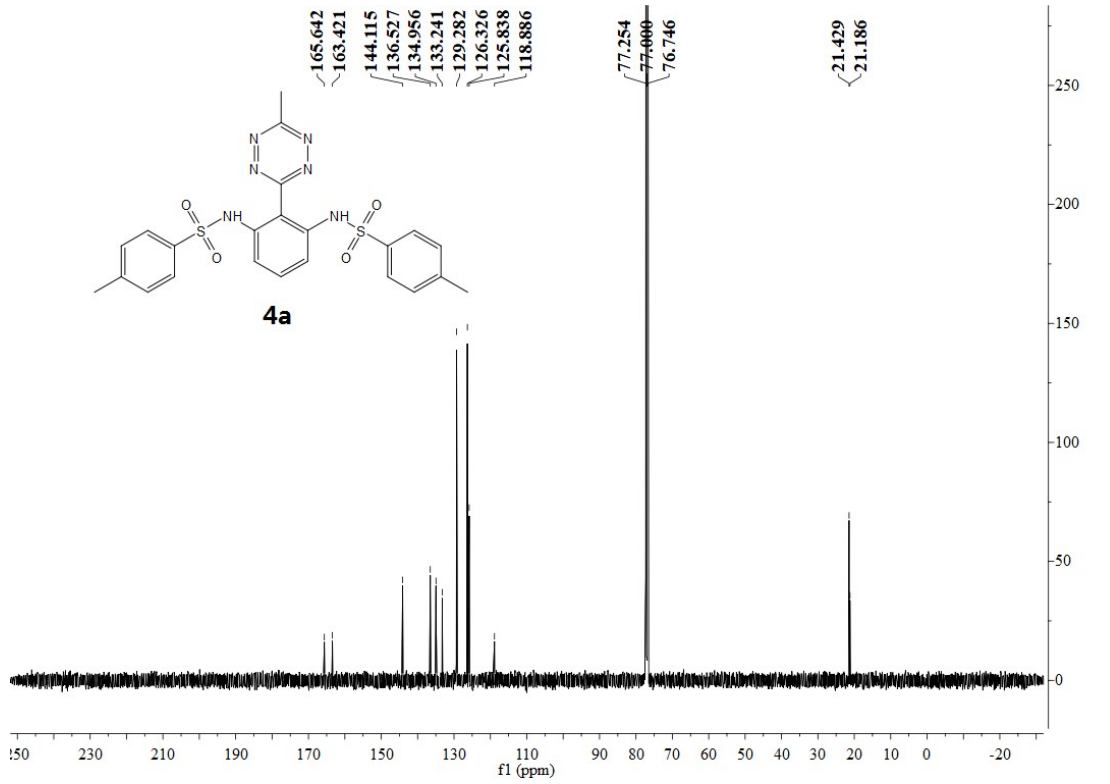
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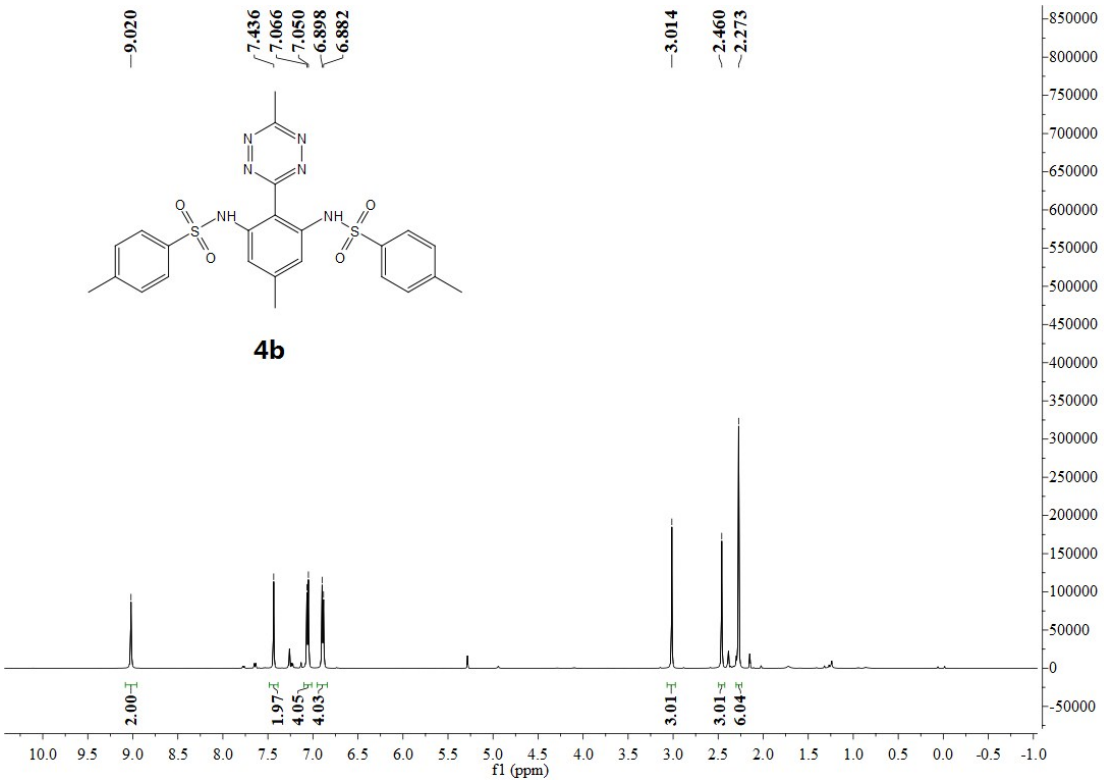
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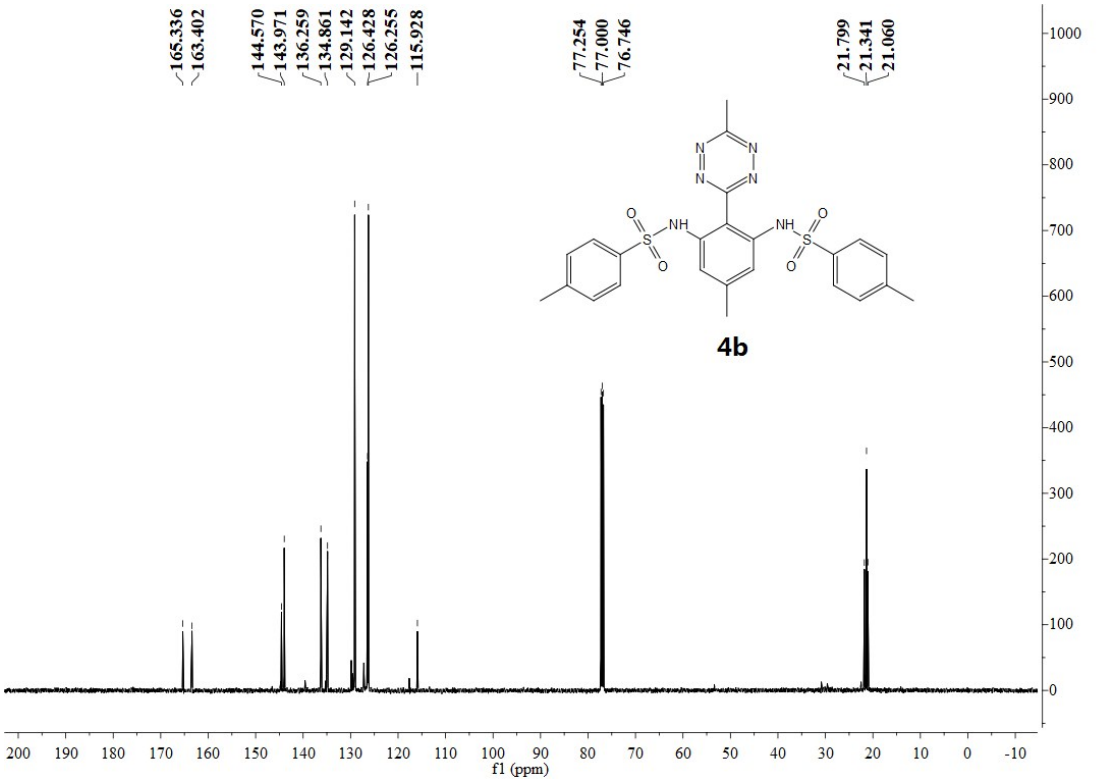
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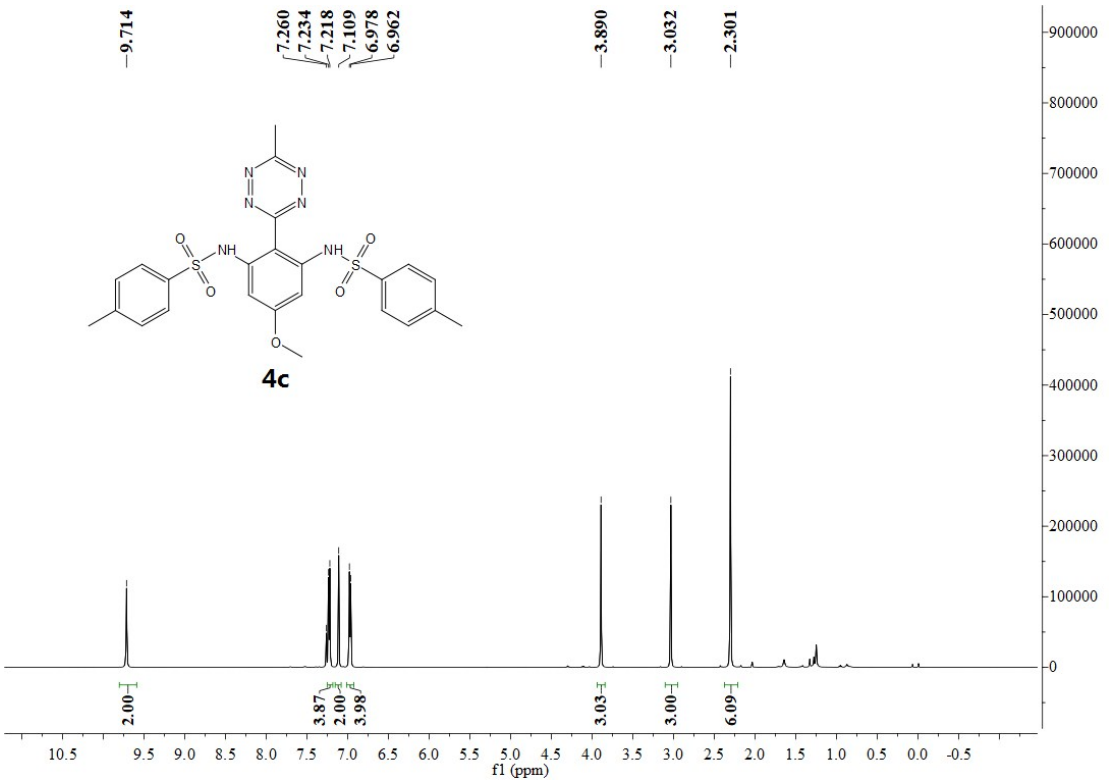
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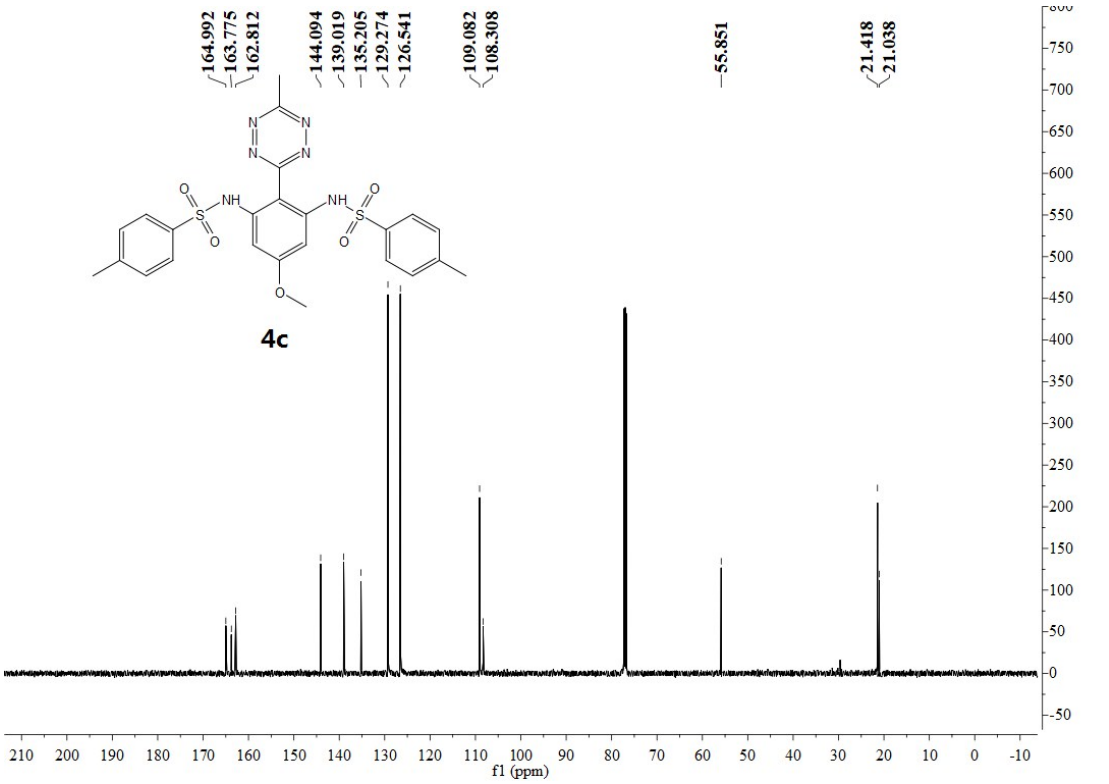
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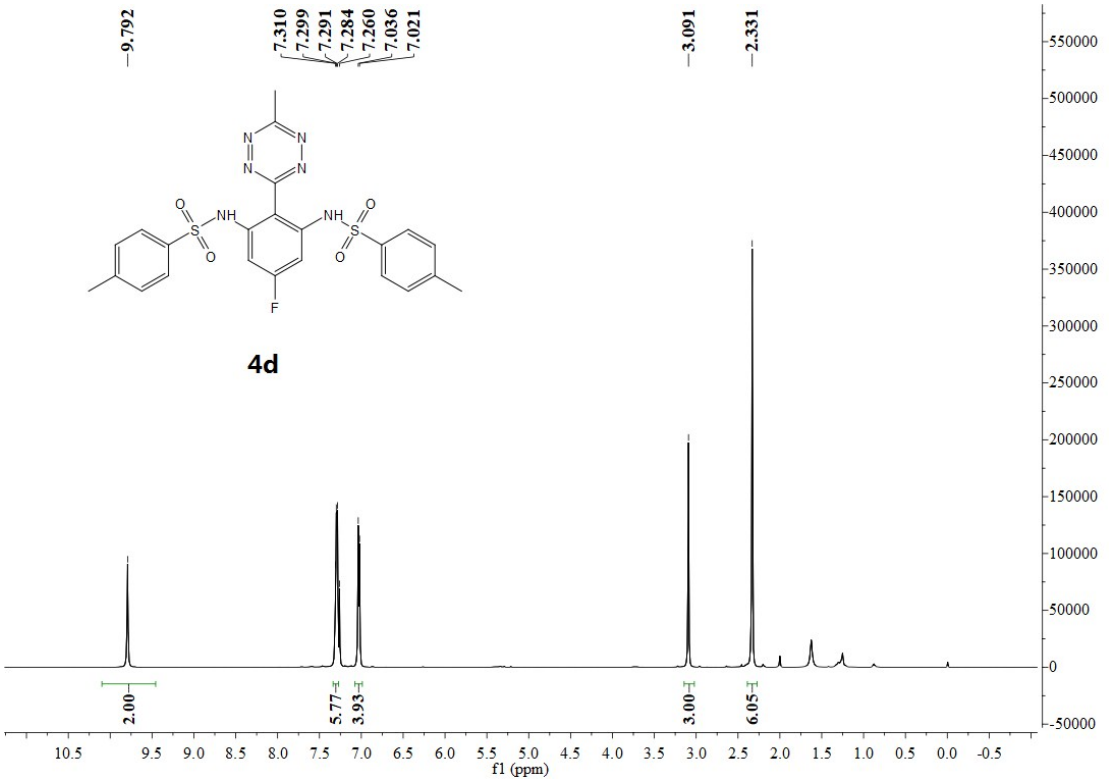
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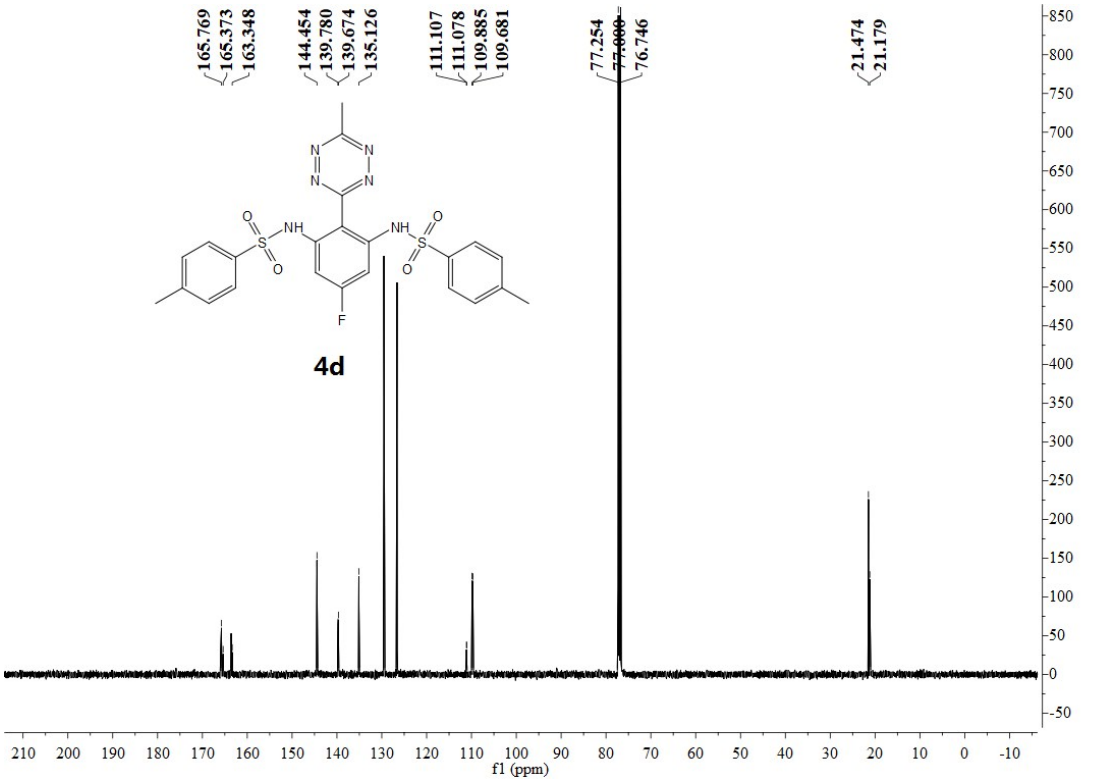
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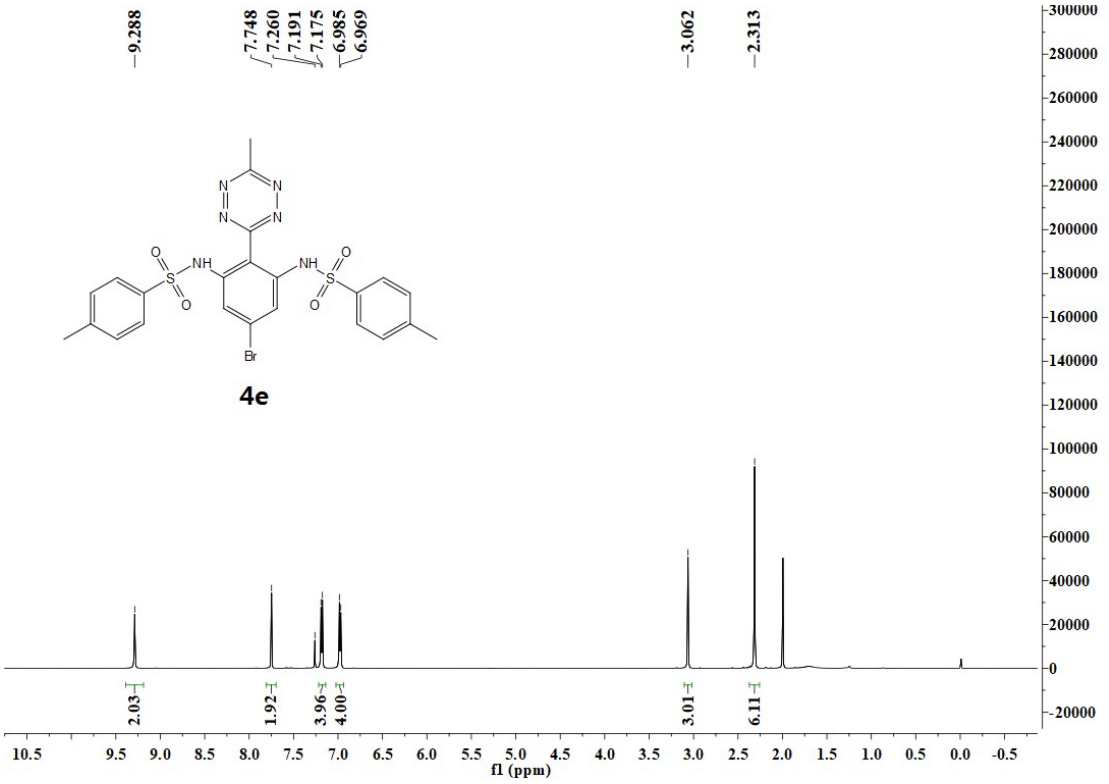
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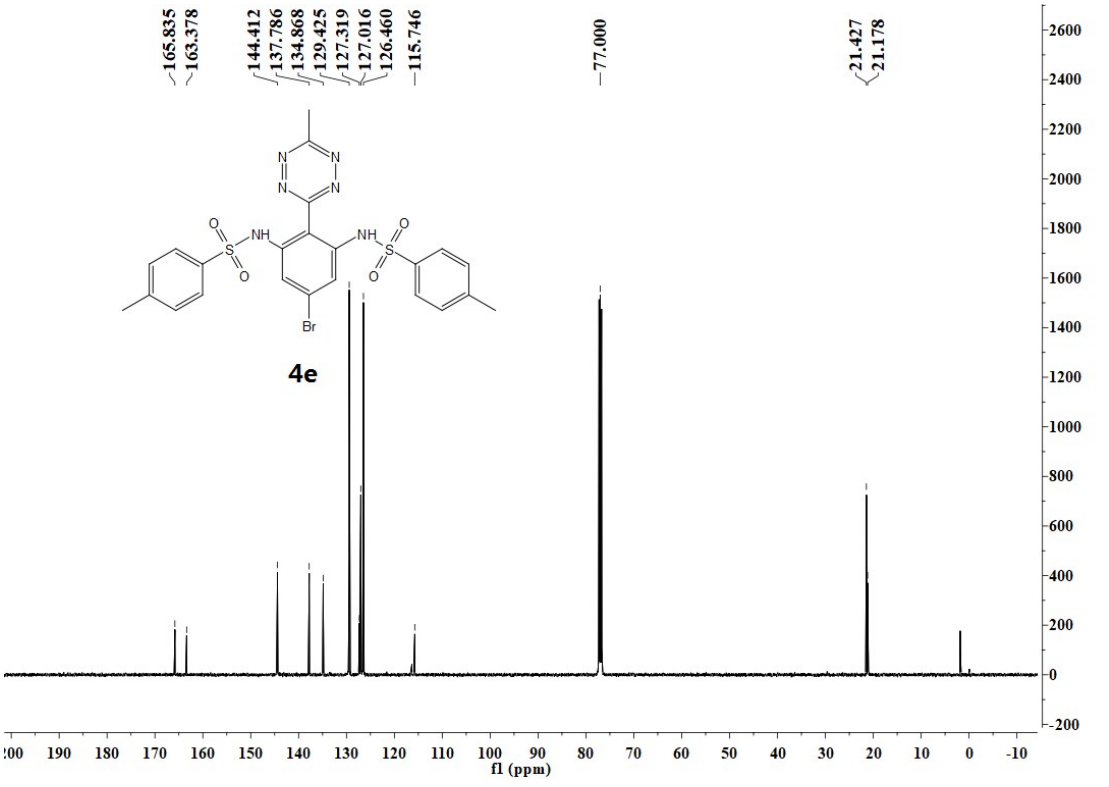
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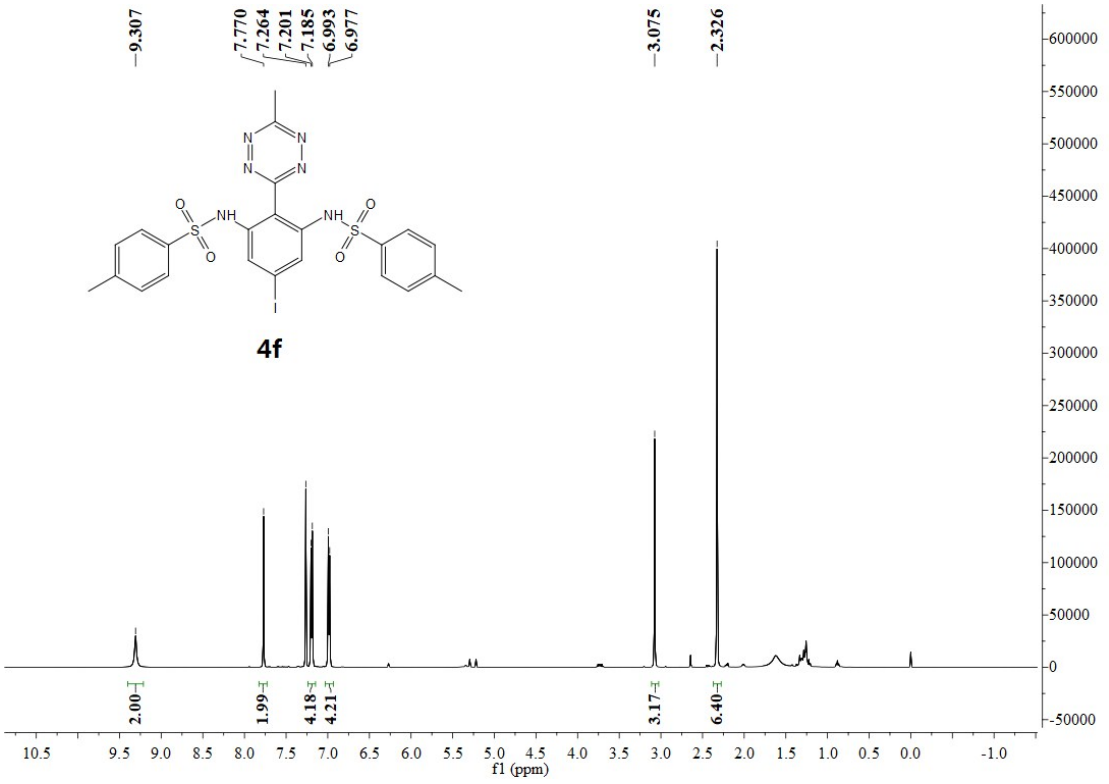
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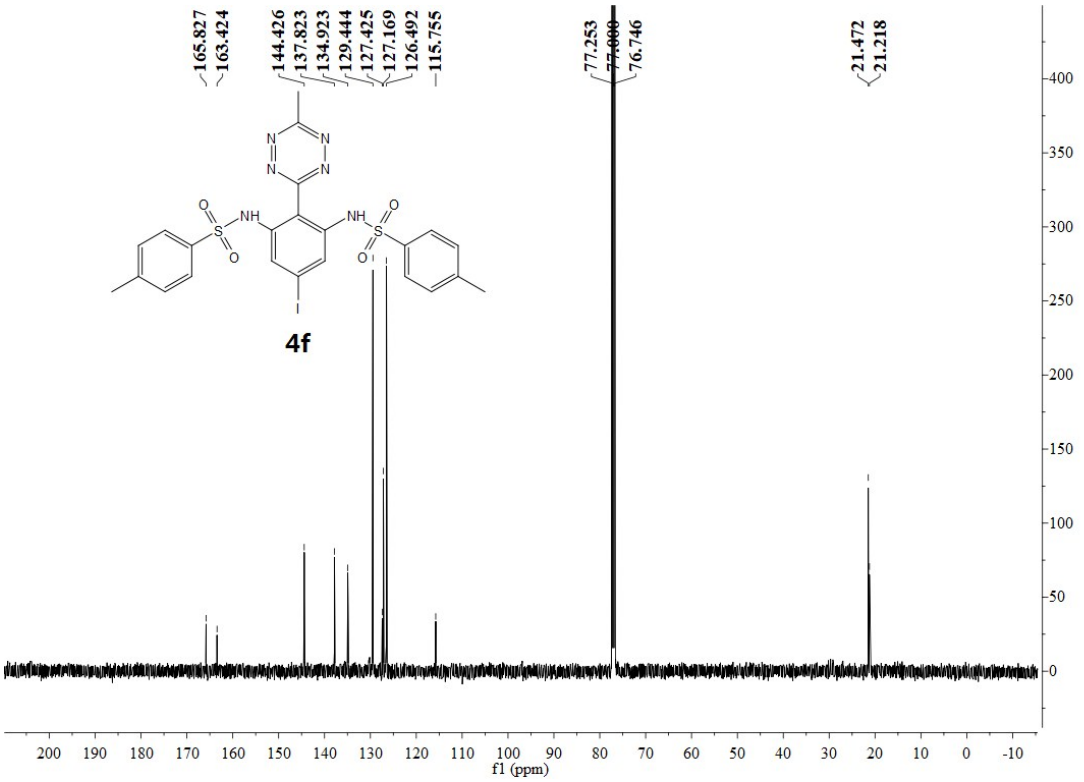
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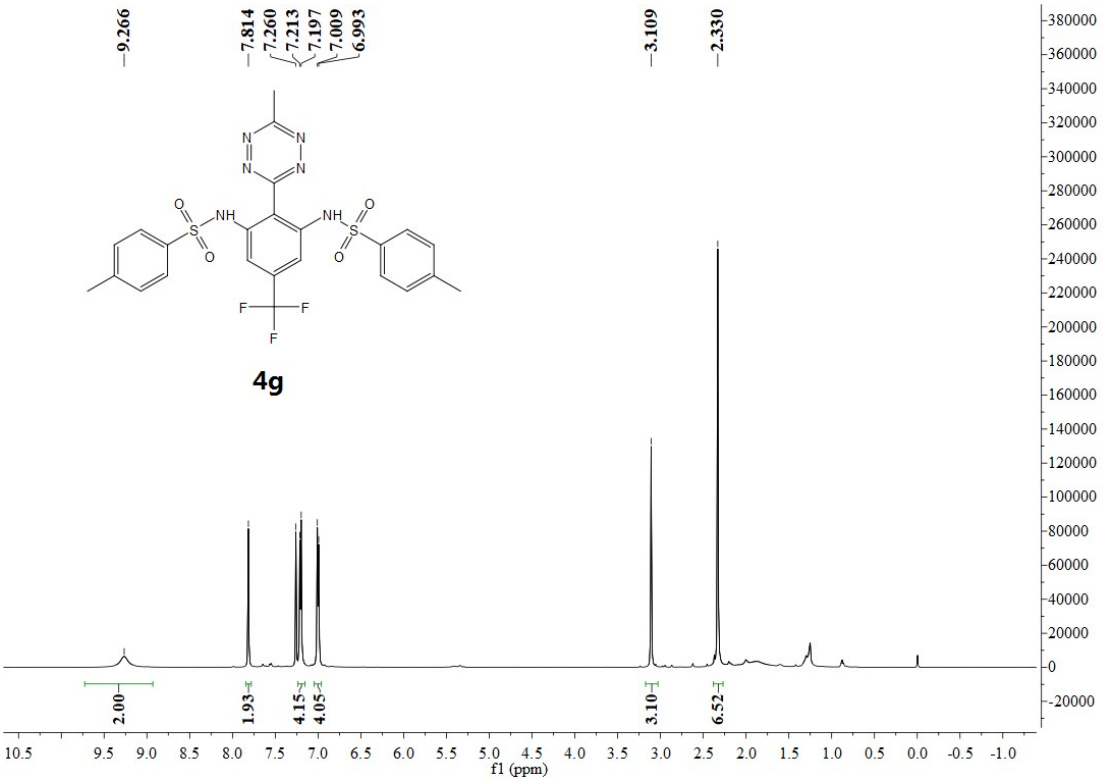
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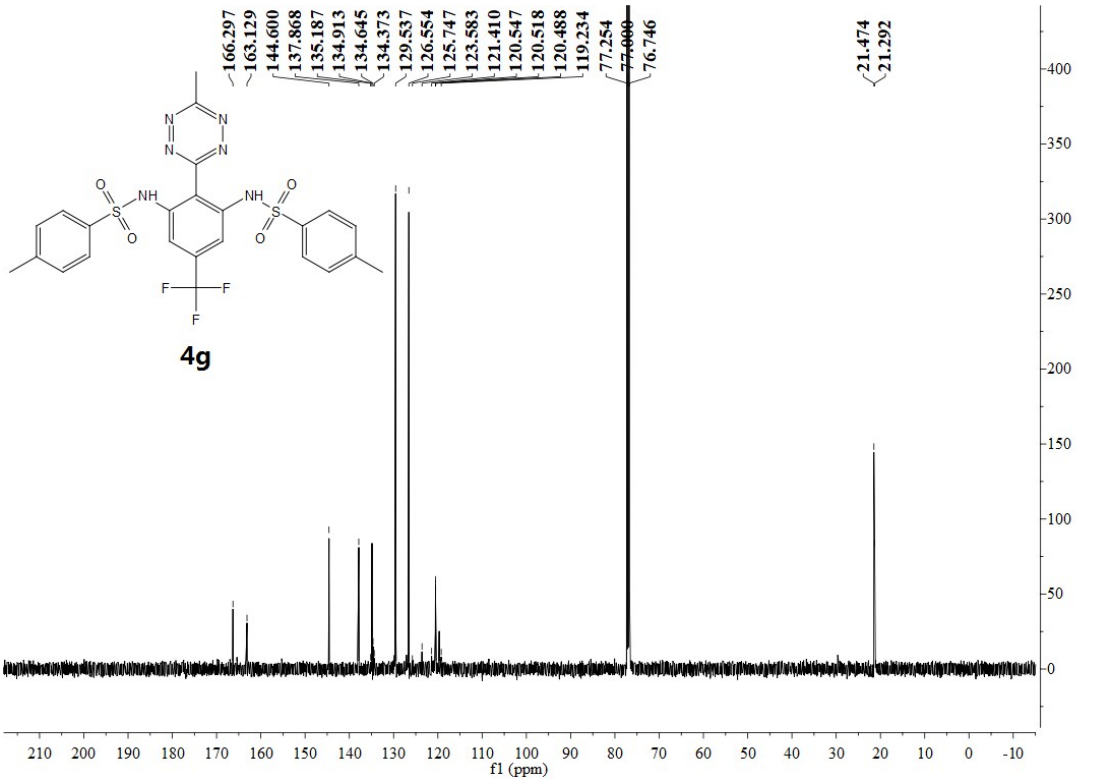
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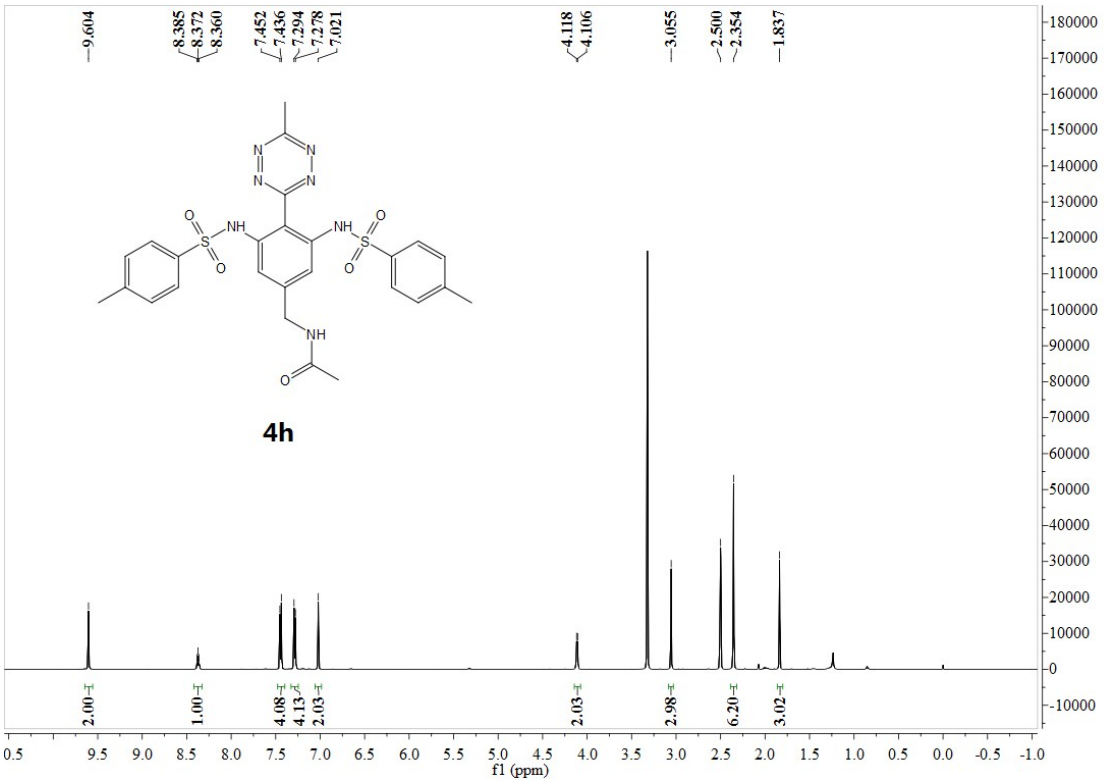
4g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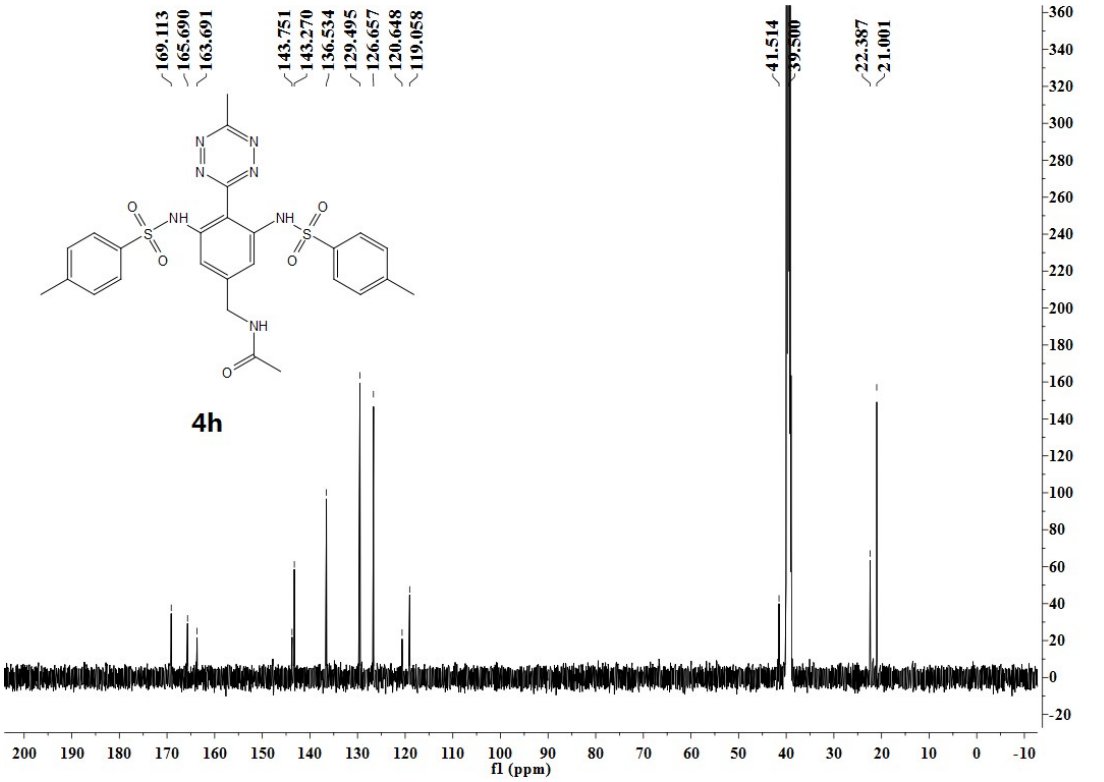
3.02
f1 (ppm)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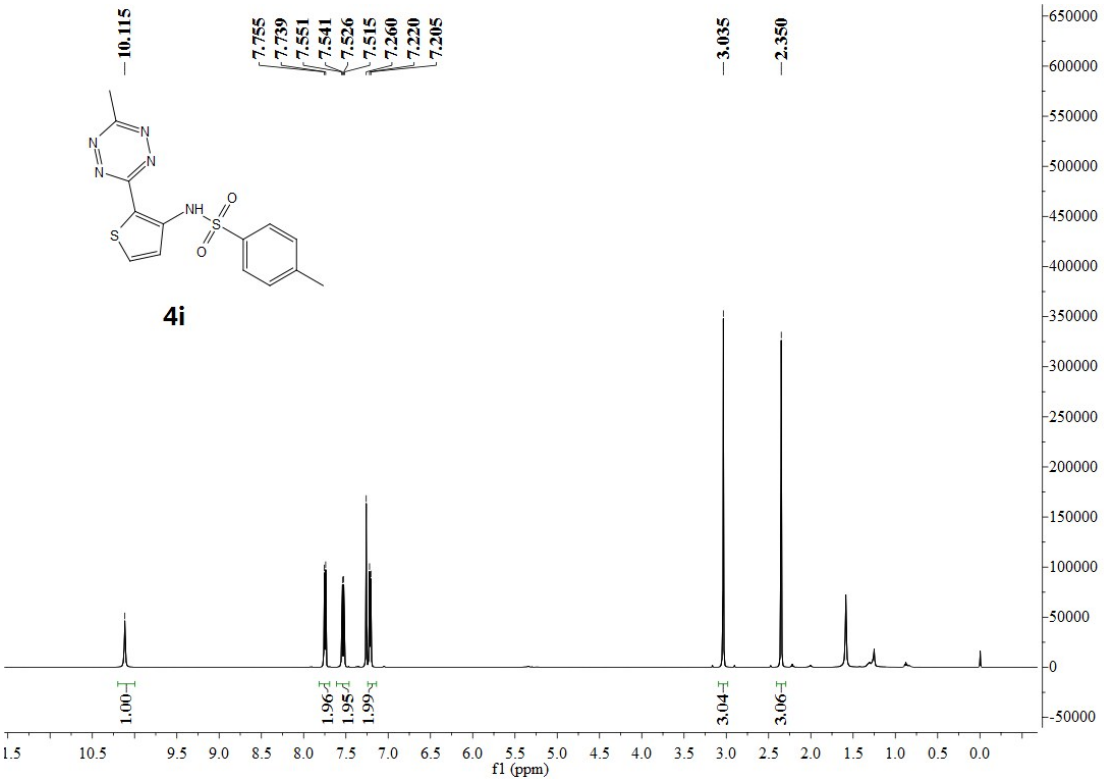
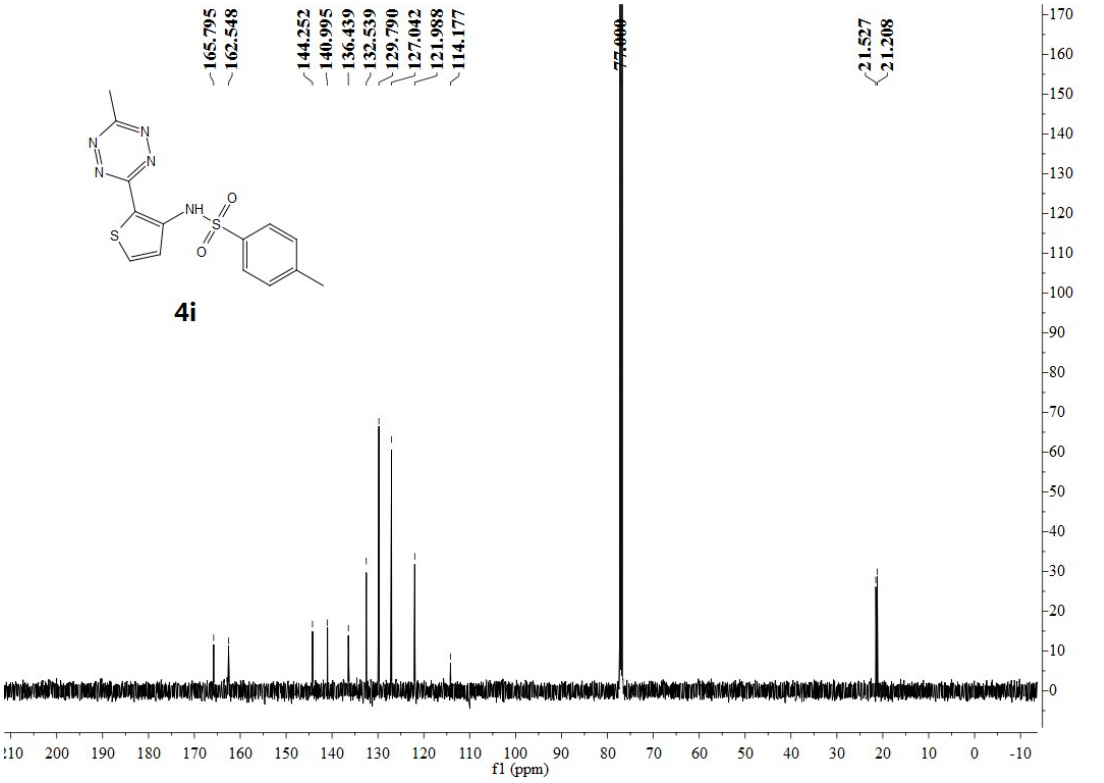
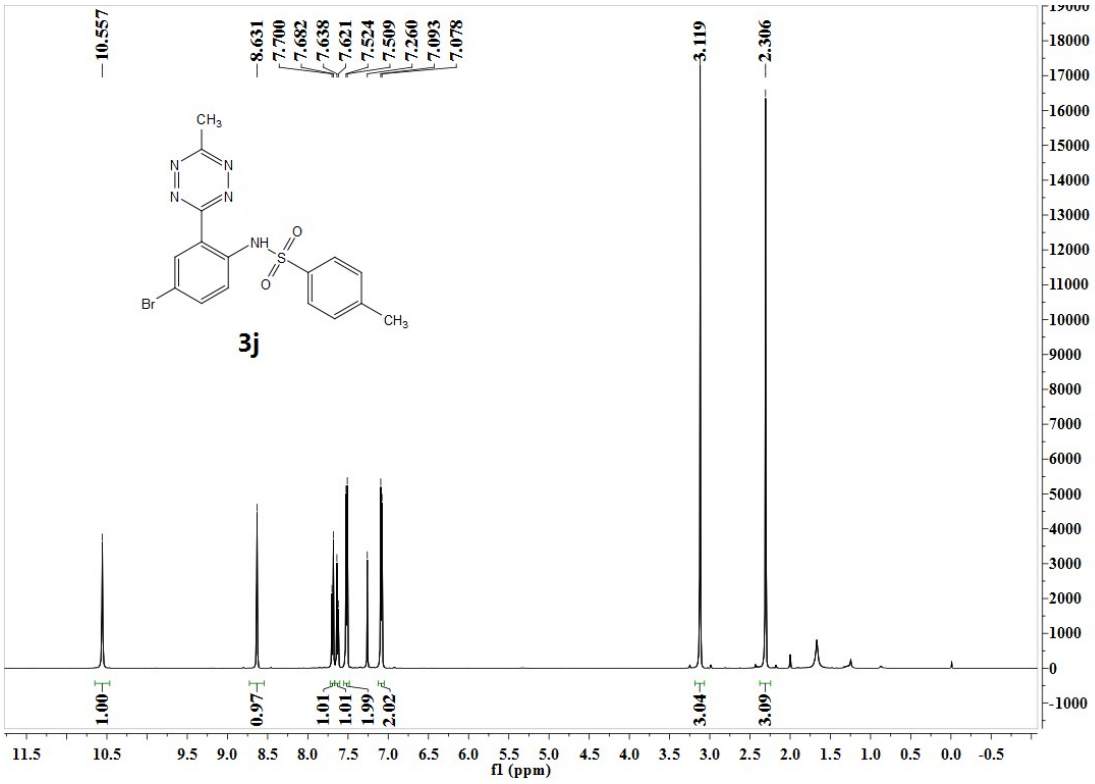
165.690
163.691
143.751
143.270
136.534
129.495
126.657
120.648
119.058
41.514
39.500
22.387
21.001
4h
f1 (ppm)


10.115
7.755
7.739
7.551
7.541
7.526
7.515
7.260
7.220
7.205
3.035
2.350
4i
1.00
1.96
1.95
1.99
3.04
3.06
f1 (ppm)


165.795
162.548
144.252
140.995
136.439
132.539
129.790
127.042
121.988
114.177
77.000
21.527
21.208
4i
f1 (ppm)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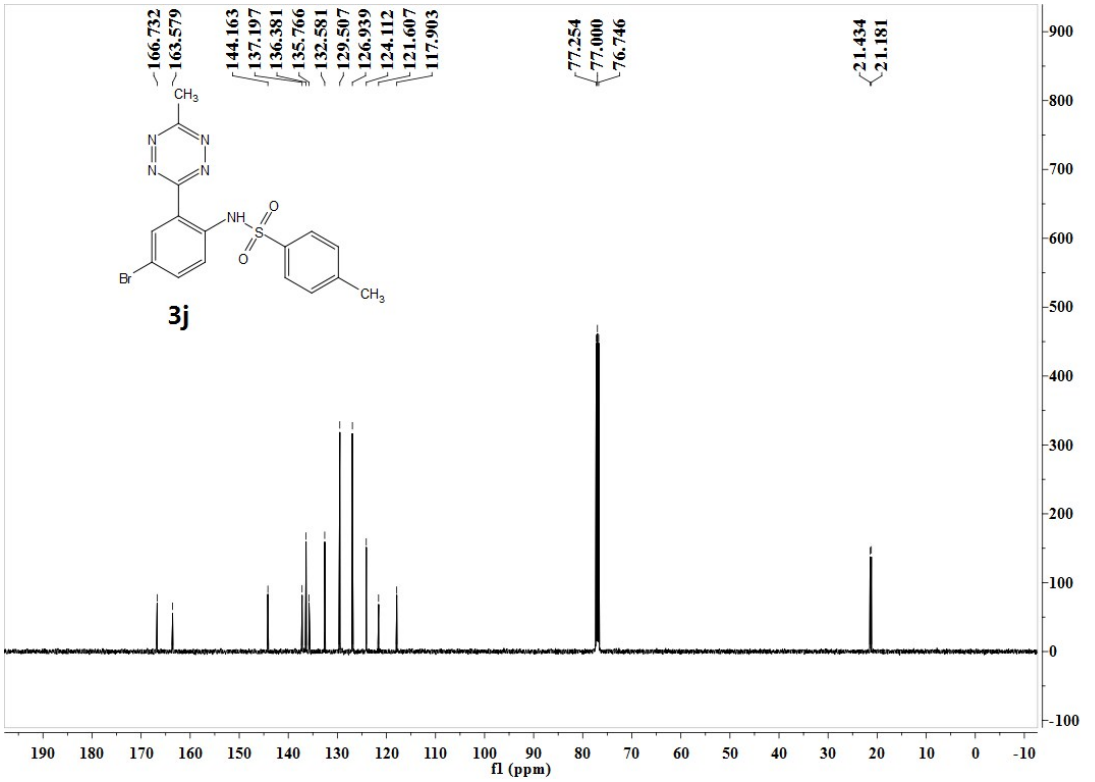
8.631
7.700
7.682
7.638
7.621
7.524
7.509
7.260
7.093
7.078
3.119
2.306
3j
1.00
0.97
1.01
1.01
1.99
2.02
3.04
3.09
fl (ppm)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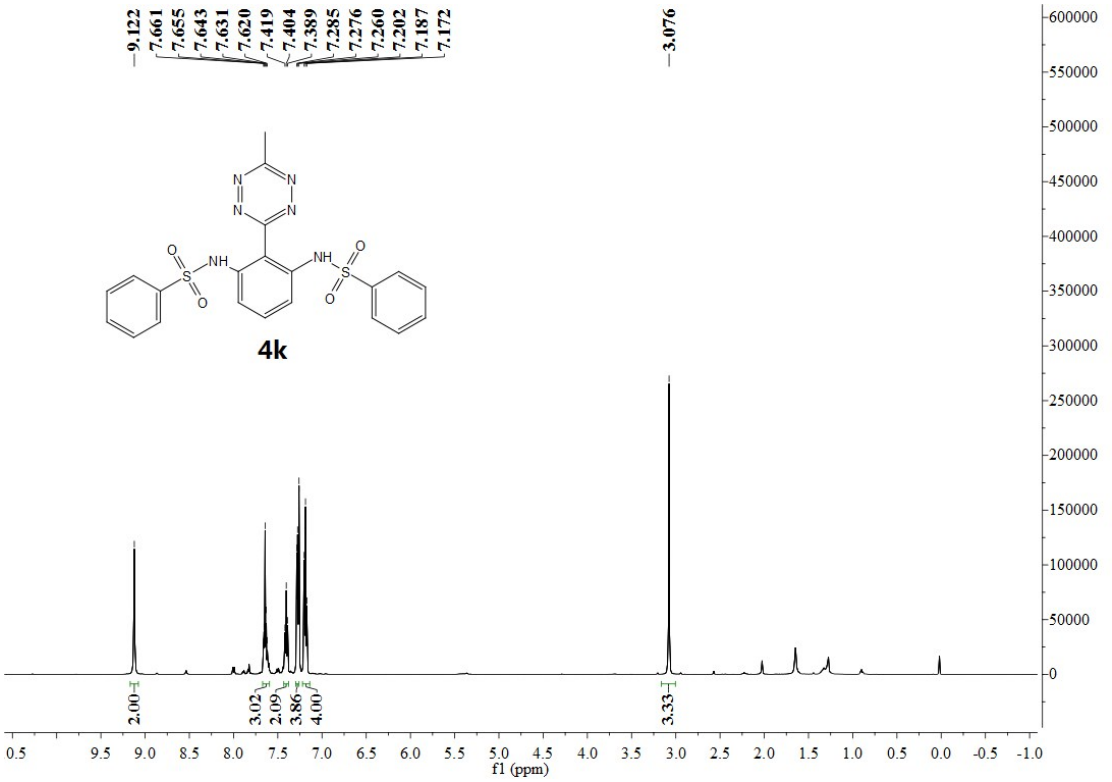
163.579
144.163
137.197
136.381
135.766
132.581
129.507
126.939
124.112
121.607
117.903
77.254
77.000
76.746
21.434
21.181
3j
fl (ppm)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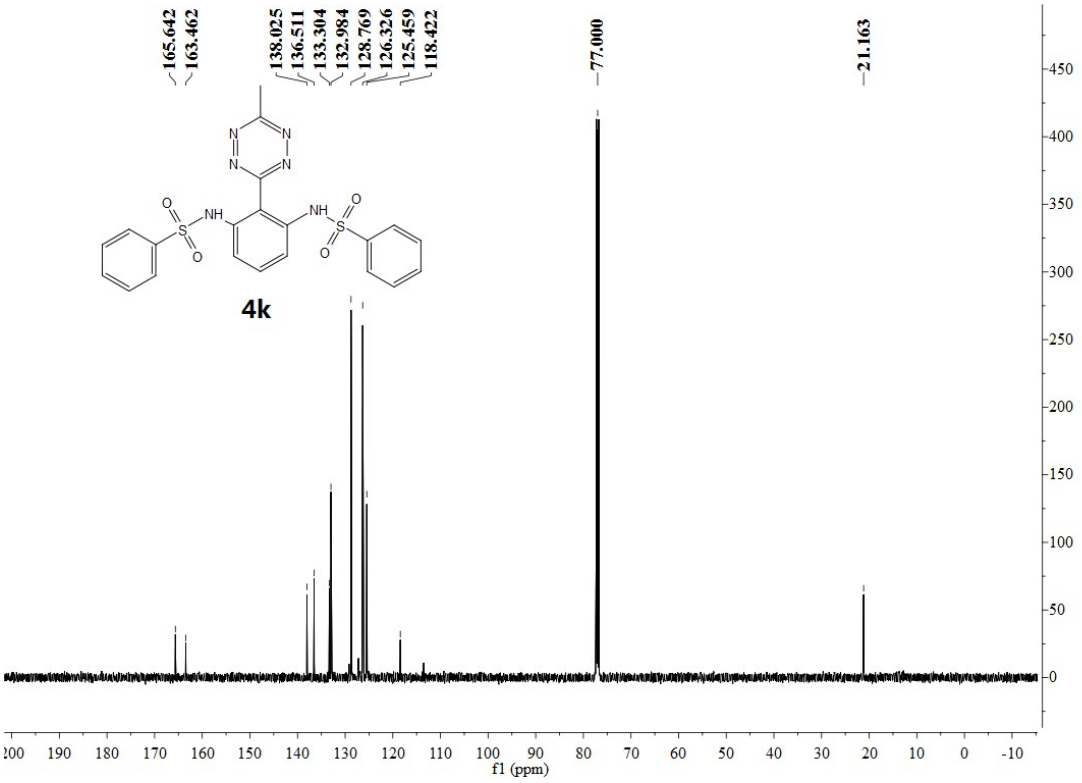
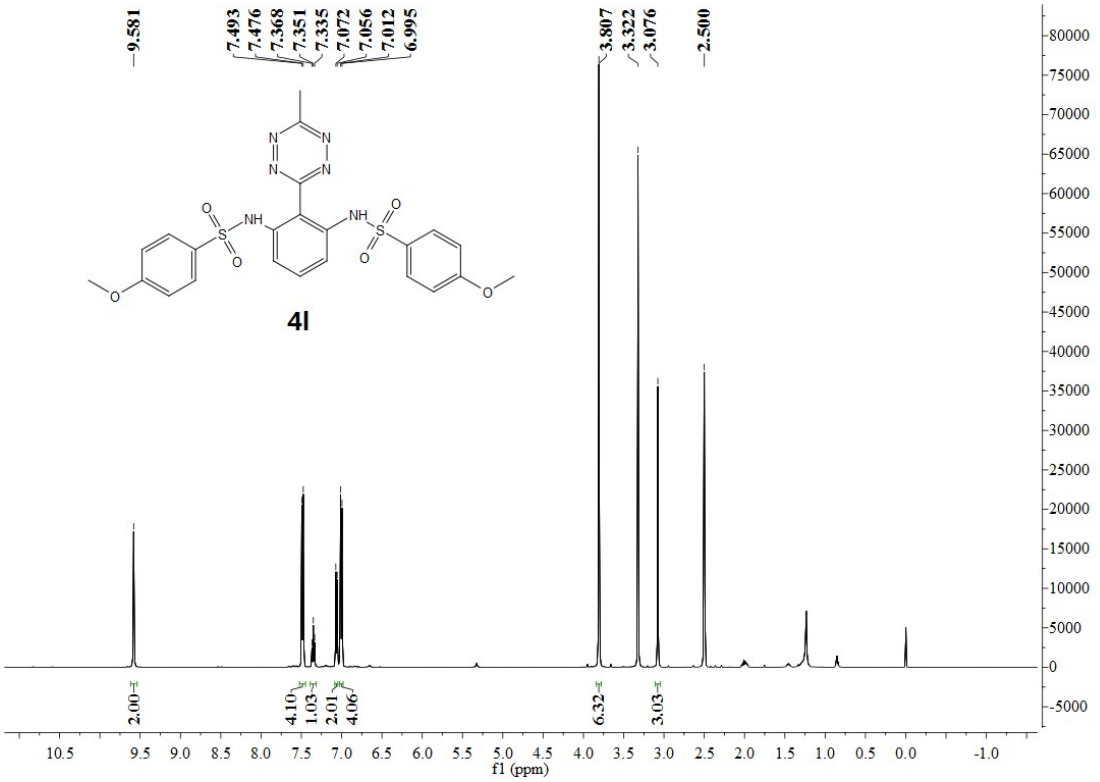
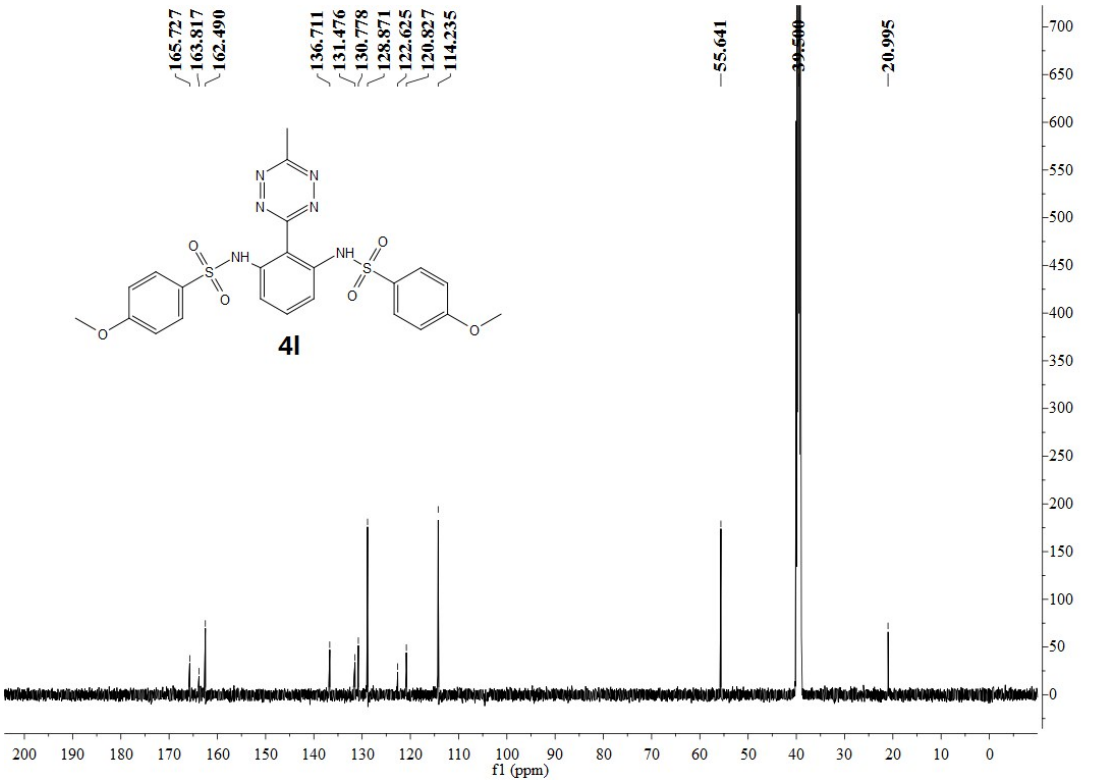
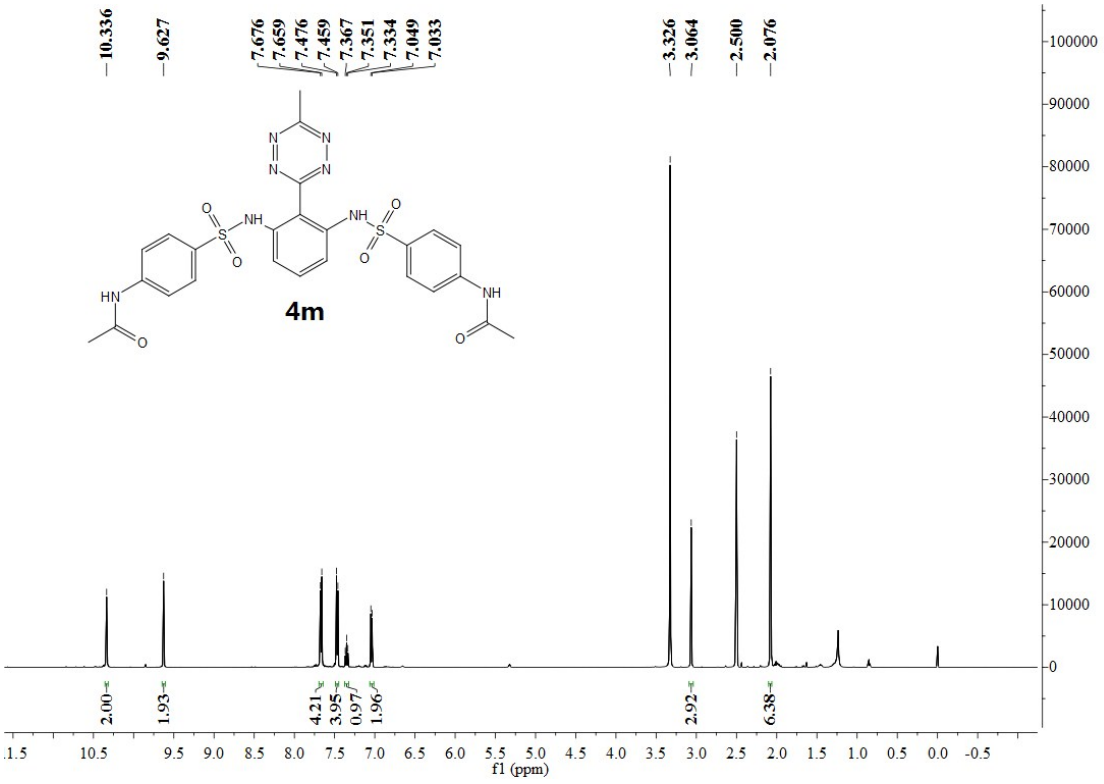
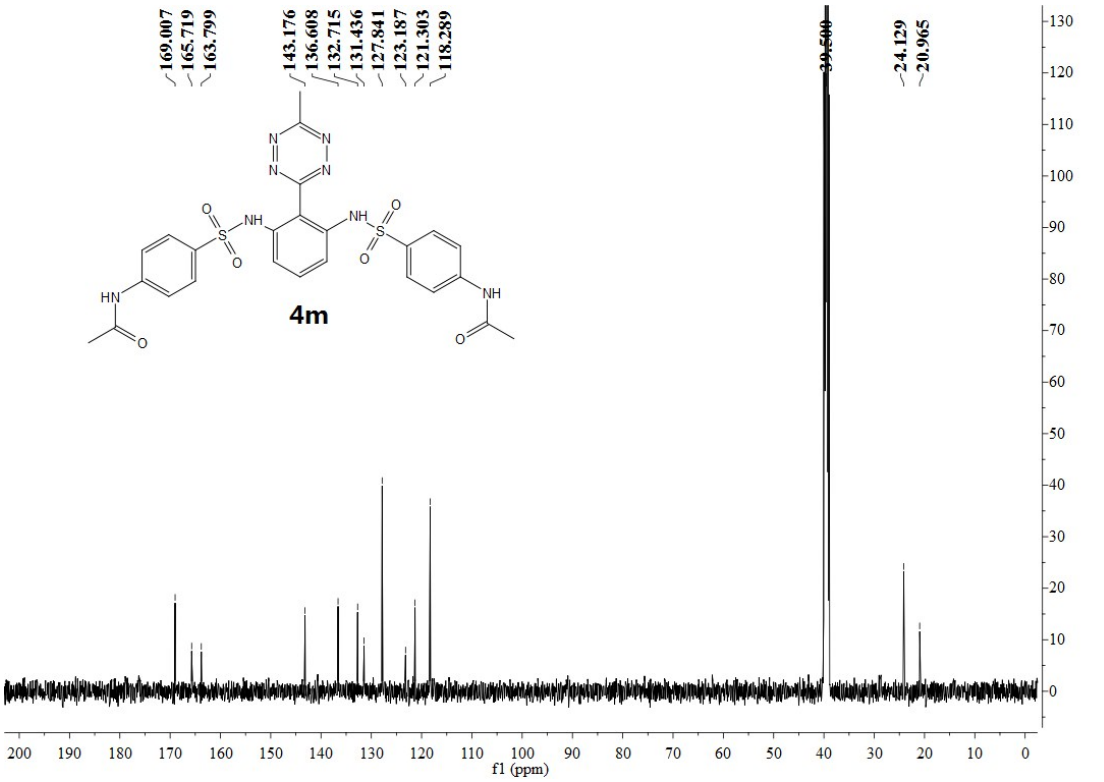
7.661
7.655
7.643
7.631
7.620
7.419
7.404
7.389
7.285
7.276
7.260
7.202
7.187
7.172
3.076
4k
2.00
3.02
2.09
3.86
4.00
3.33
f1 (ppm)


165.642
163.462
138.025
136.511
133.304
132.984
128.769
126.326
125.459
118.422
77.000
21.163
4k
f1 (ppm)


9.581
7.493
7.476
7.368
7.351
7.335
7.072
7.056
7.012
6.995
3.807
3.322
3.076
2.500
4l
2.00
4.10
1.03
2.01
4.06
6.32
3.03
f1 (ppm)


165.727
163.817
162.490
136.711
131.476
130.778
128.871
122.625
120.827
114.235
55.641
39.500
20.995
4l
f1 (ppm)


10.336
9.627
7.676
7.659
7.476
7.459
7.367
7.351
7.334
7.049
7.033
3.326
3.064
2.500
2.076
4m
2.00
1.93
4.21
3.95
0.97
1.96
2.92
6.38
f1 (ppm)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163.799
143.176
136.608
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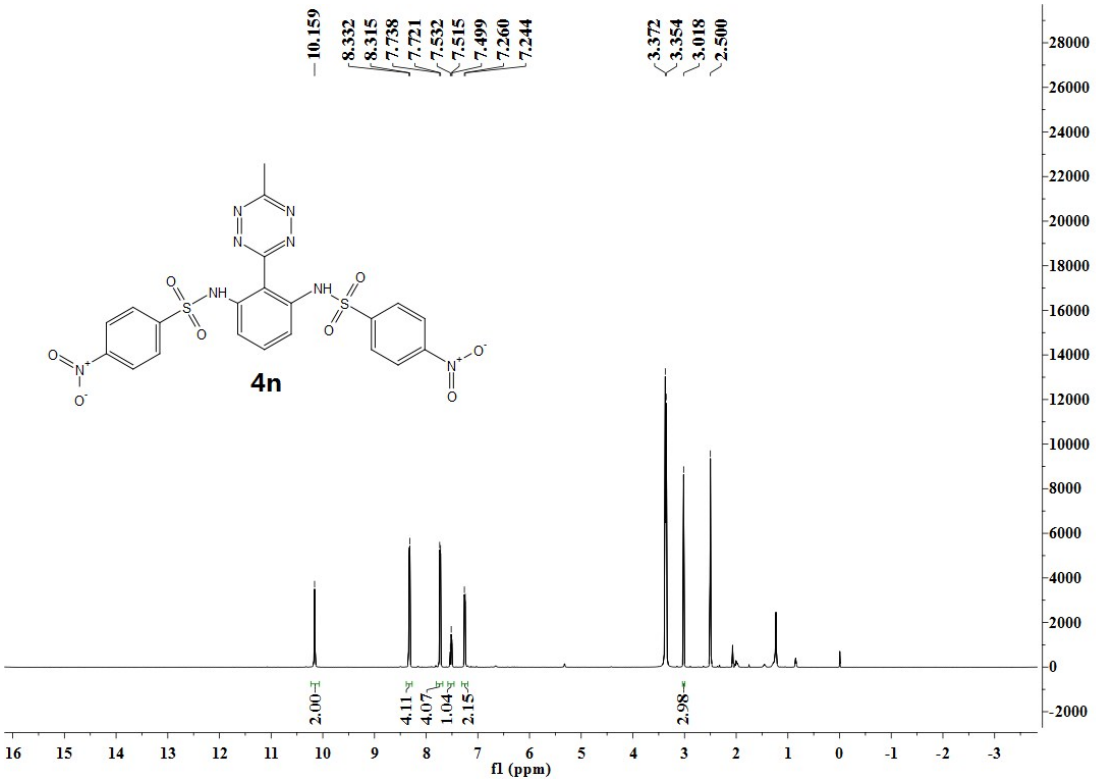
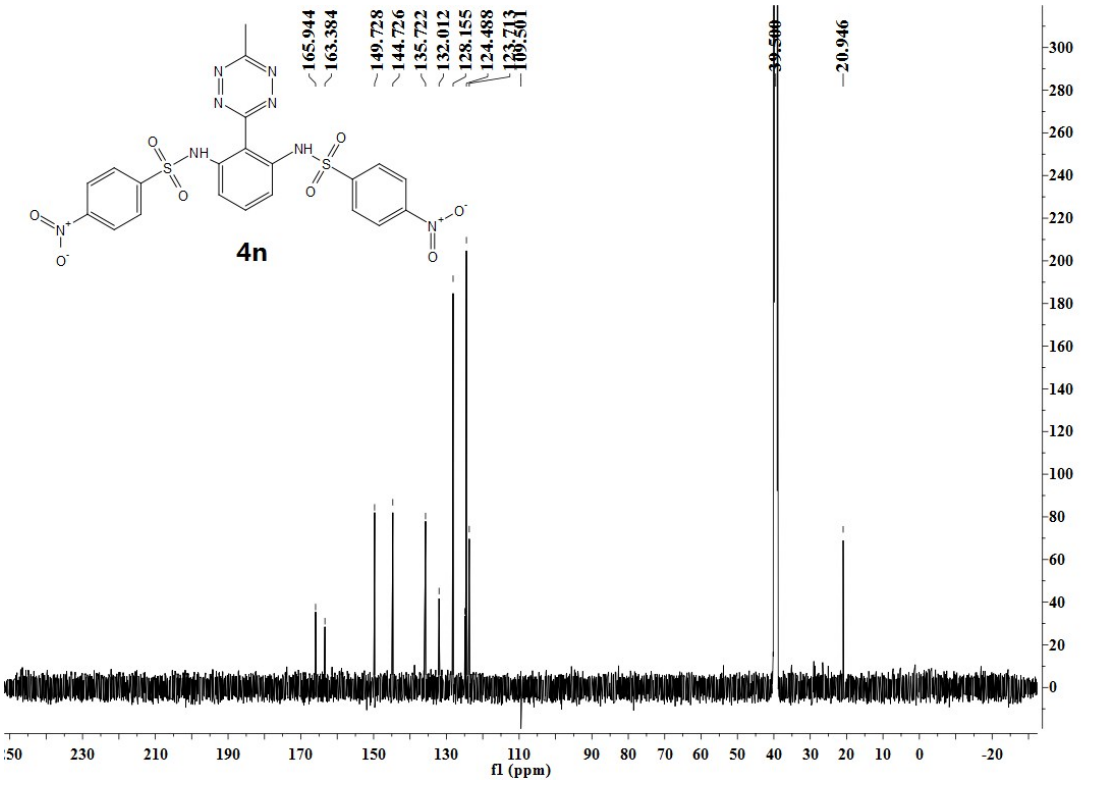
127.841
123.187
121.303
118.289
39.500
24.129
20.965
4m
f1 (ppm)


10.159
8.332
8.315
7.738
7.721
7.532
7.515
7.499
7.260
7.244
3.372
3.354
3.018
2.500
4n
2.00
4.11
4.07
1.04
2.15
2.98
fl (ppm)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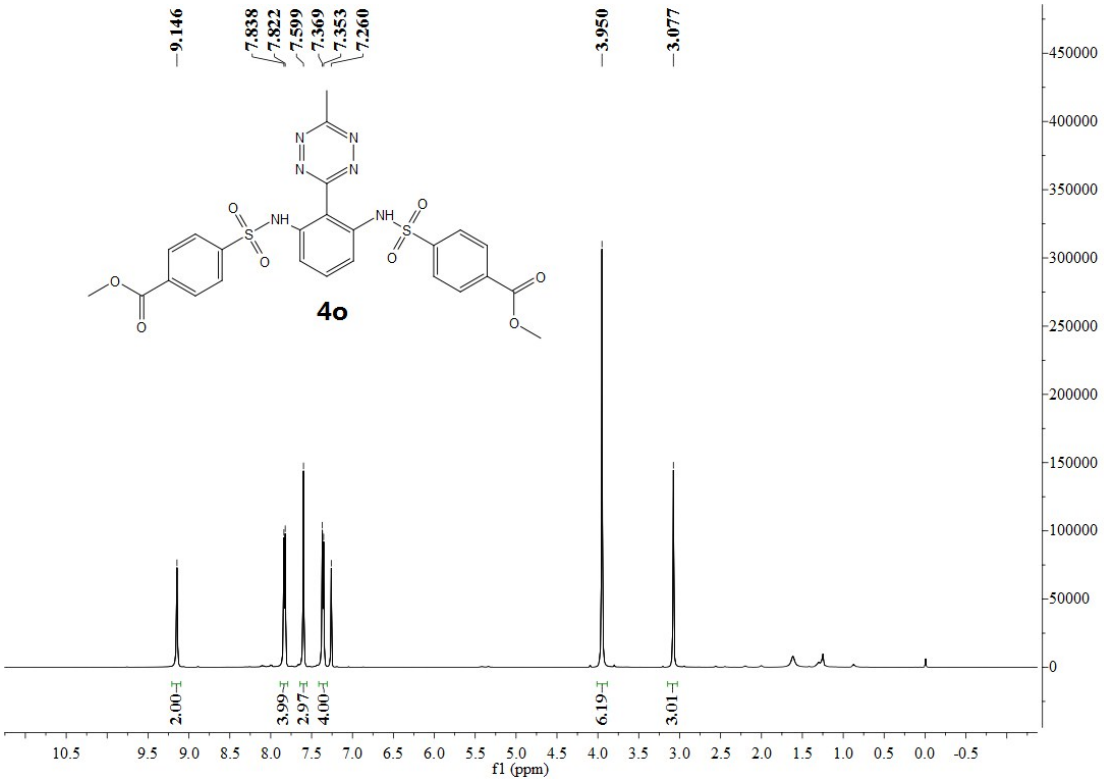
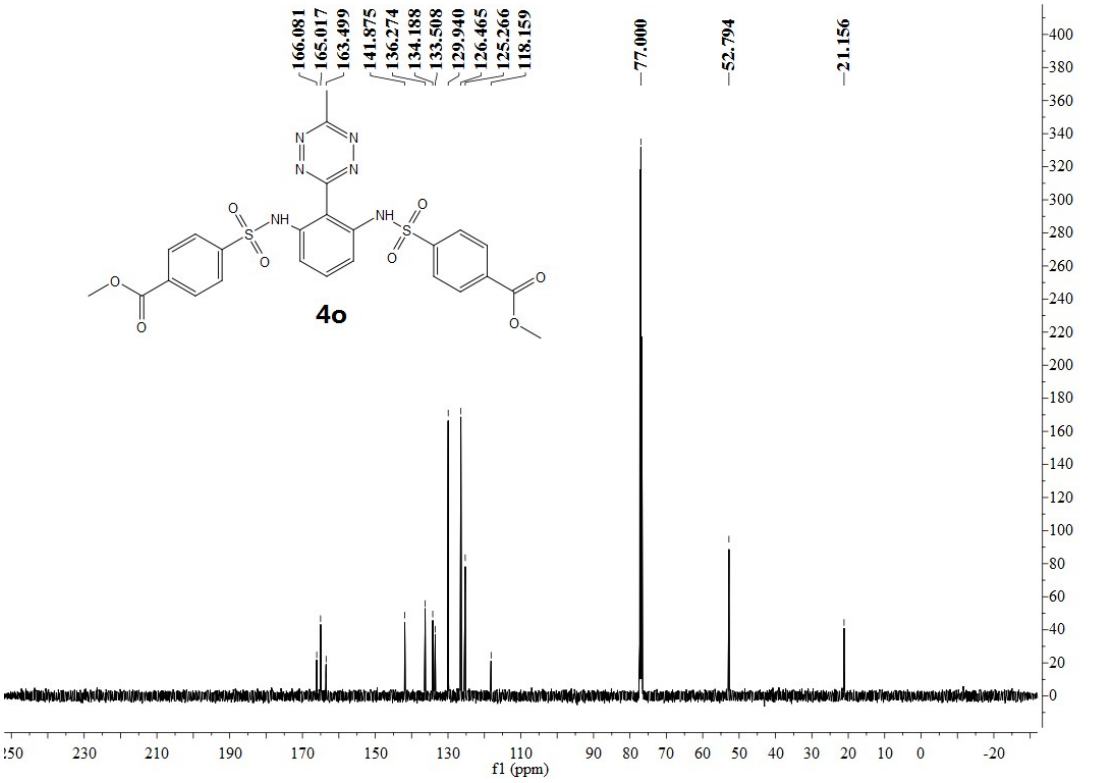
149.728
144.726
135.722
132.012
128.155
124.488
39.500
20.946
4n
fl (ppm)


9.146
7.838
7.822
7.599
7.369
7.353
7.260
3.950
3.077
4o
2.00
3.99
2.97
4.00
6.19
3.01
f1 (ppm)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165.017
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141.875
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133.508
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125.266
118.159
77.000
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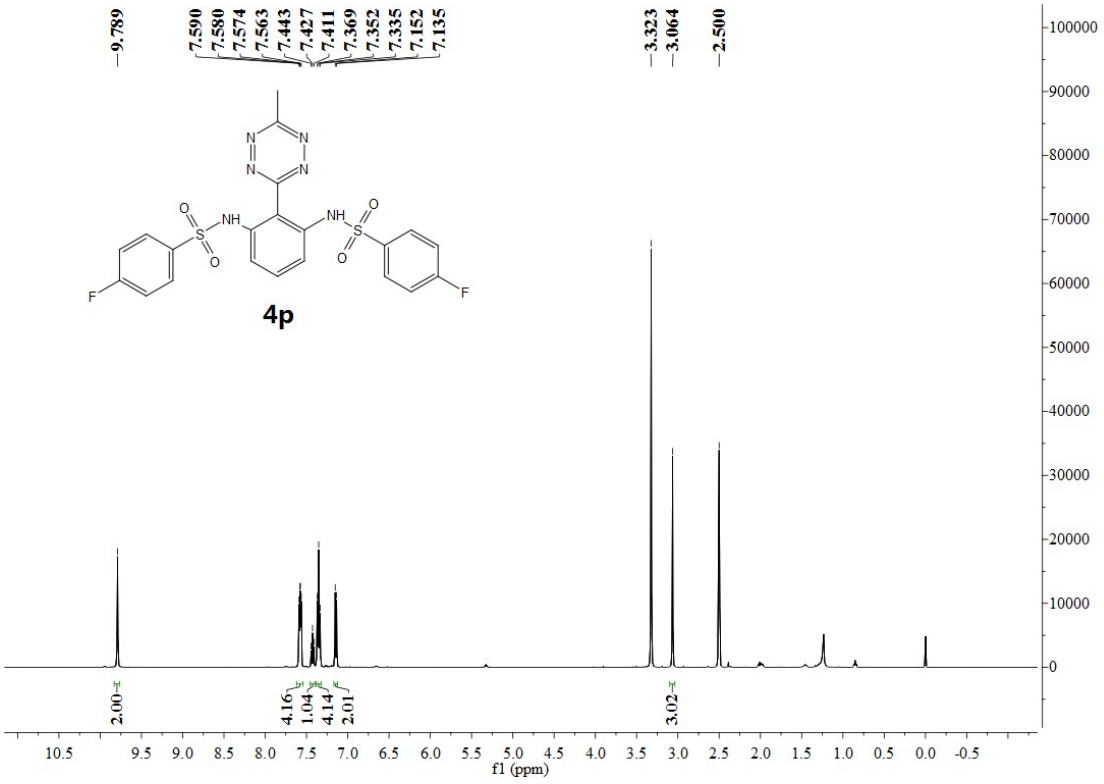
21.156
4o
f1 (ppm)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7.580
7.574
7.563
7.443
7.427
7.411
7.369
7.352
7.335
7.152
7.135
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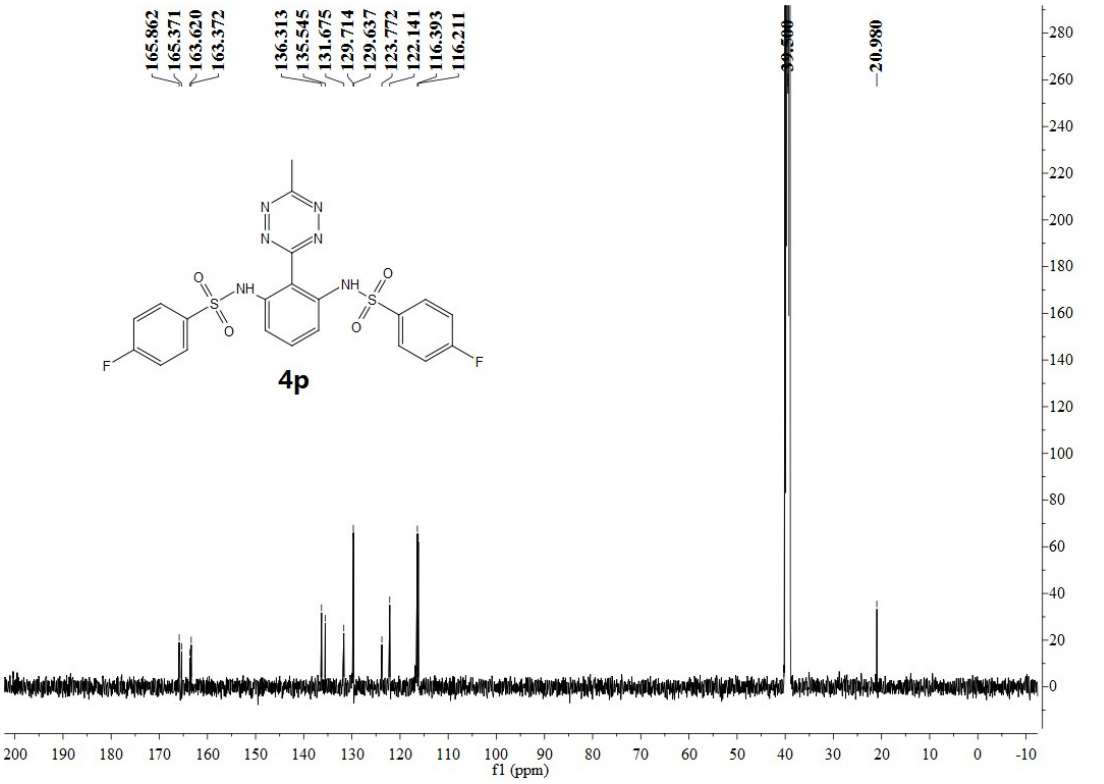
3.064
2.500
4p
2.00
4.16
1.04
4.14
2.01
3.02
f1 (ppm)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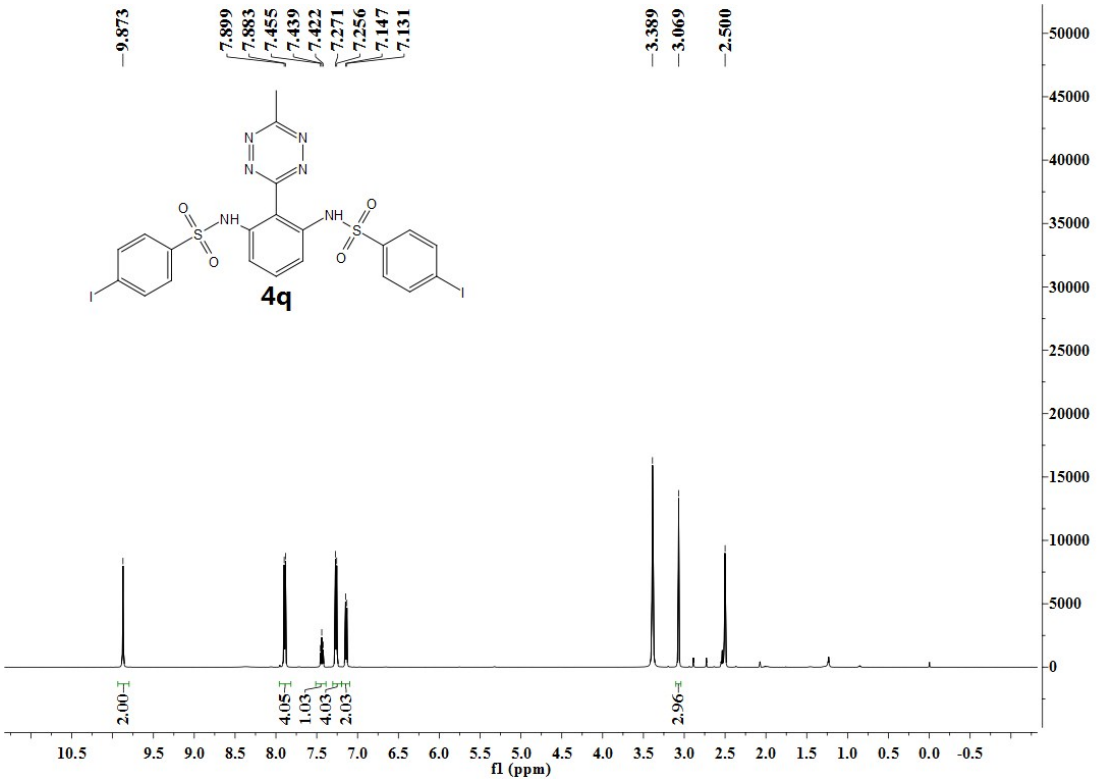
165.371
163.620
163.372
136.313
135.545
131.675
129.714
129.637
123.772
122.141
116.393
116.211
39.500
20.980
4p
f1 (ppm)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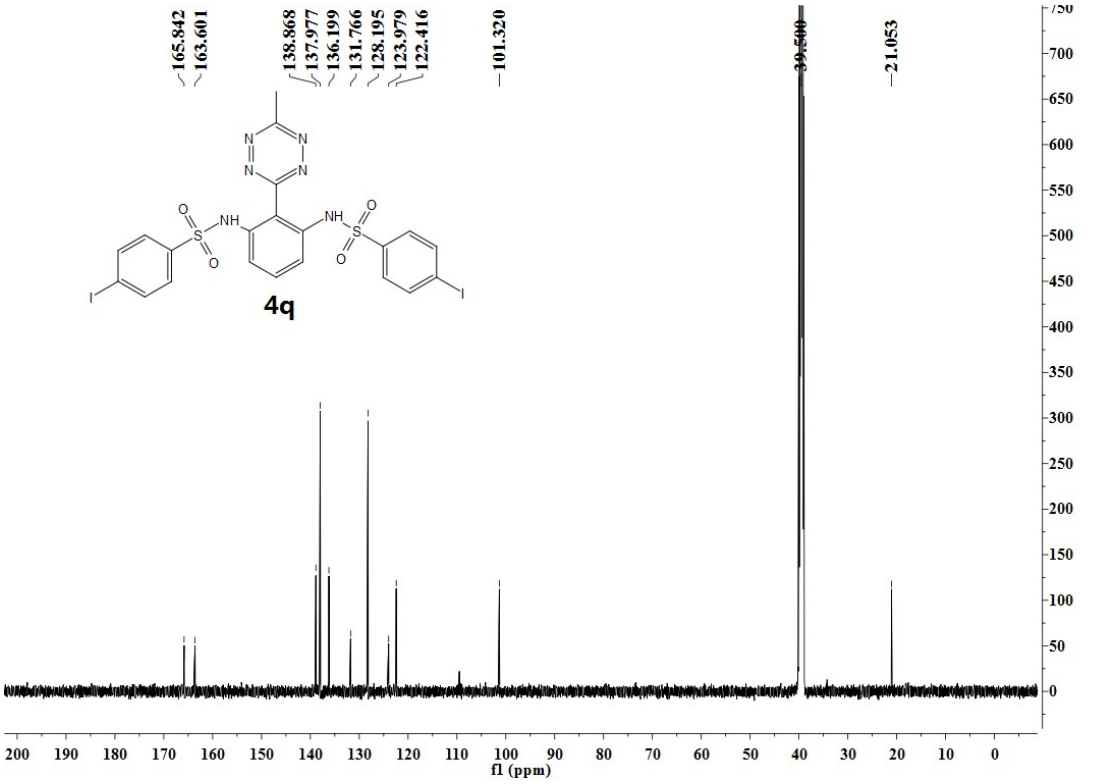
7.883
7.455
7.439
7.422
7.271
7.256
7.147
7.131
3.389
3.069
2.500
4q
2.00
4.05
1.03
4.03
2.03
2.96
f1 (ppm)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163.601
138.868
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123.979
122.416
101.320
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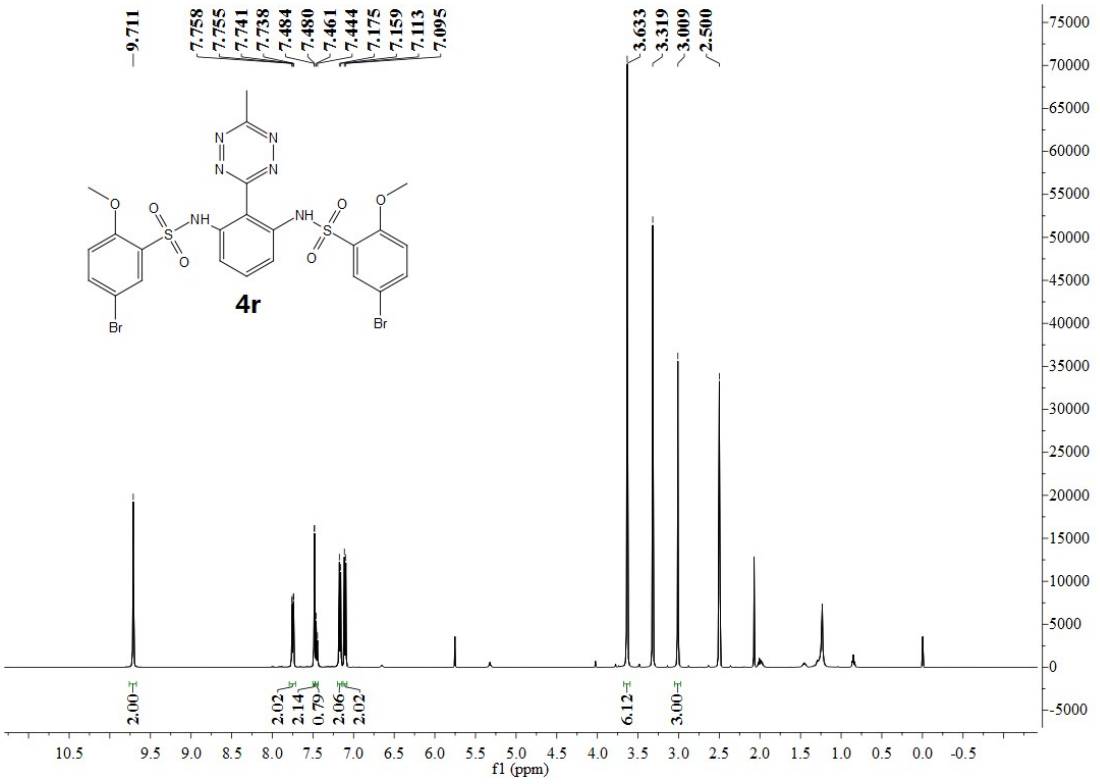
4q
f1 (ppm)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7.461
7.444
7.175
7.159
7.113
7.095
3.633
3.319
3.009
2.500
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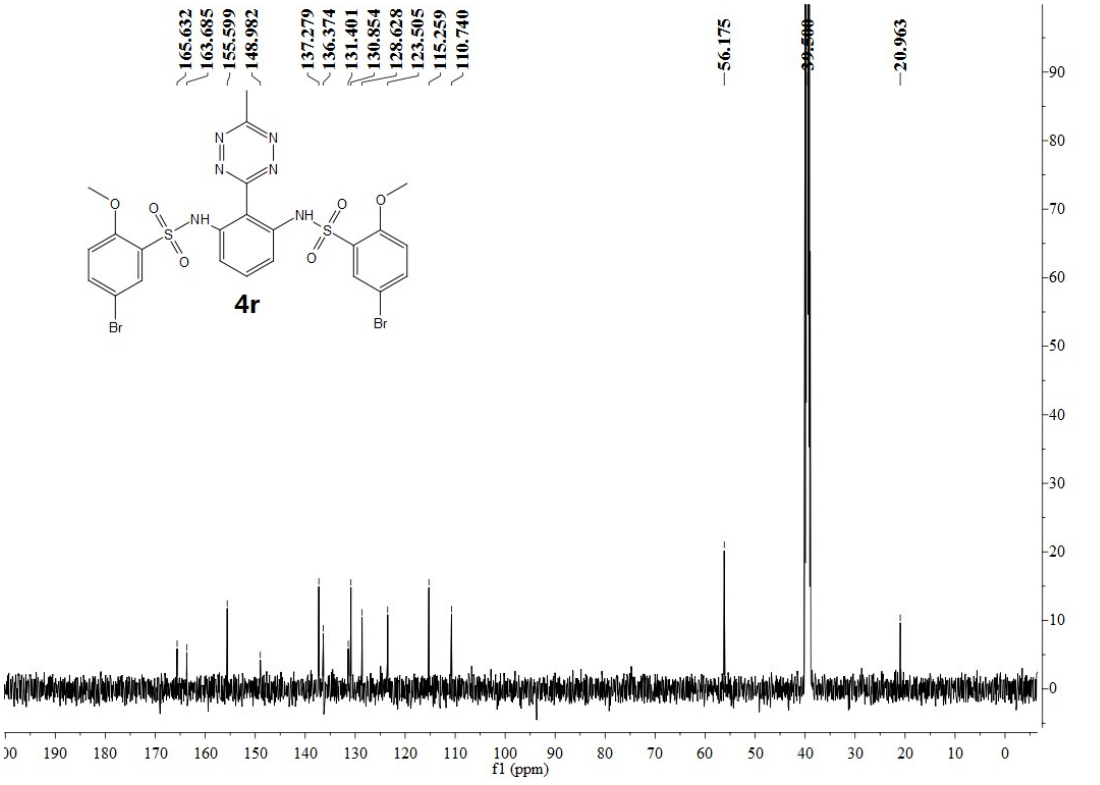
2.00
2.02
2.14
0.79
2.06
2.02
6.12
3.00
f1 (ppm)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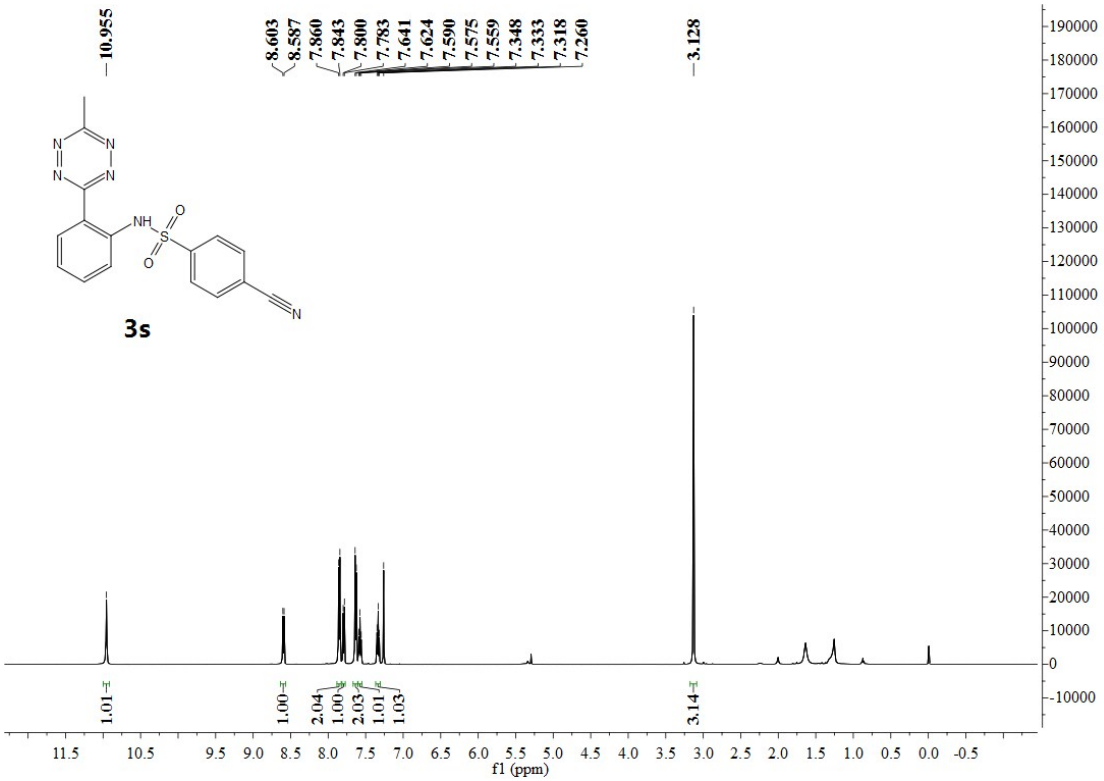
f1 (ppm)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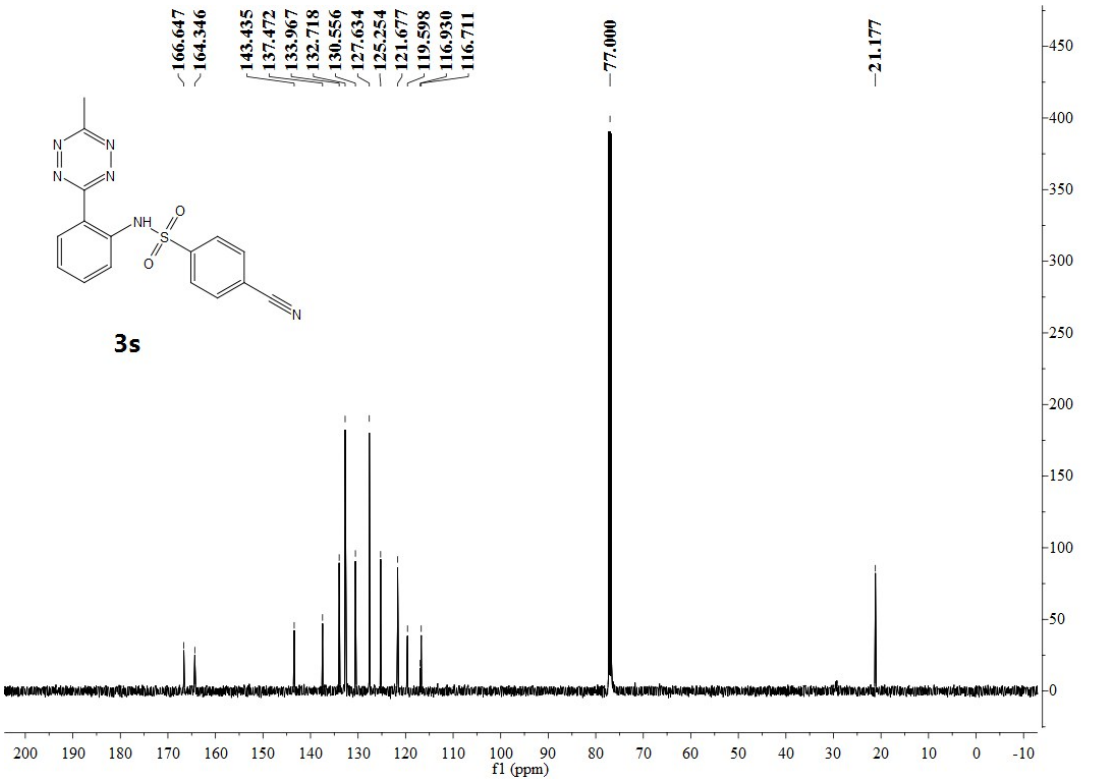
7.590
7.575
7.559
7.348
7.333
7.318
7.260
3.128
3s
1.01
1.00
2.04
1.00
2.03
1.01
1.03
3.14
f1 (ppm)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119.598
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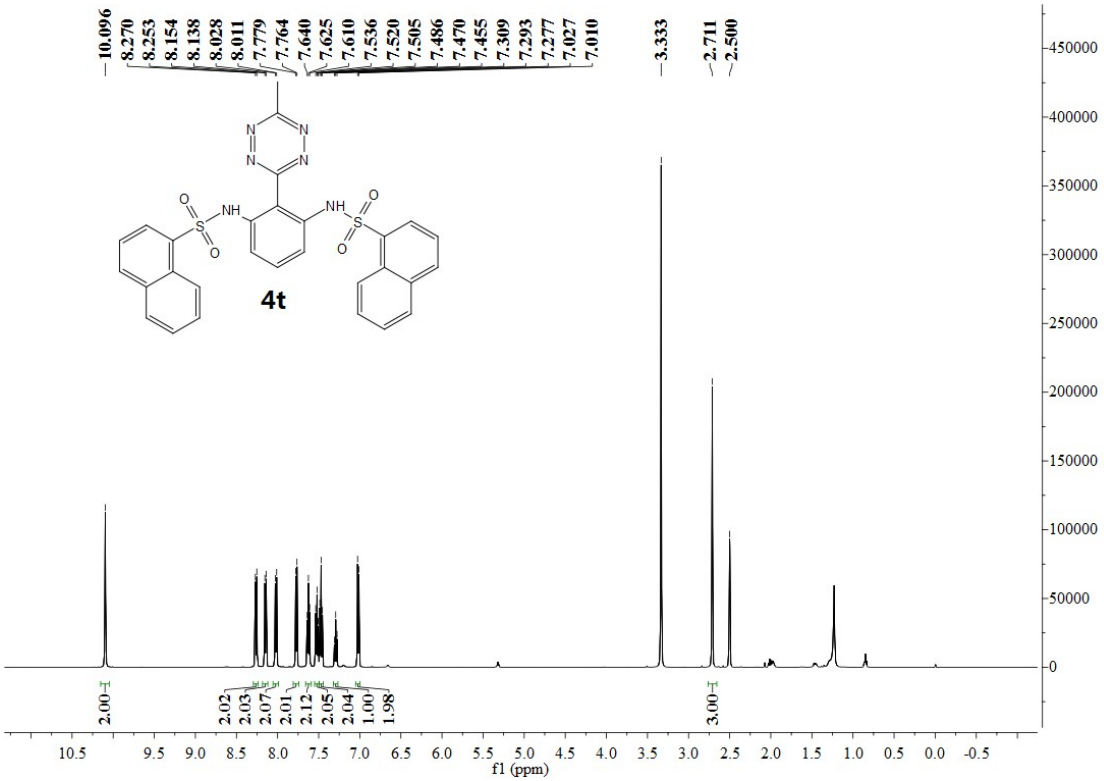
116.711
77.000
21.177
3s
f1 (ppm)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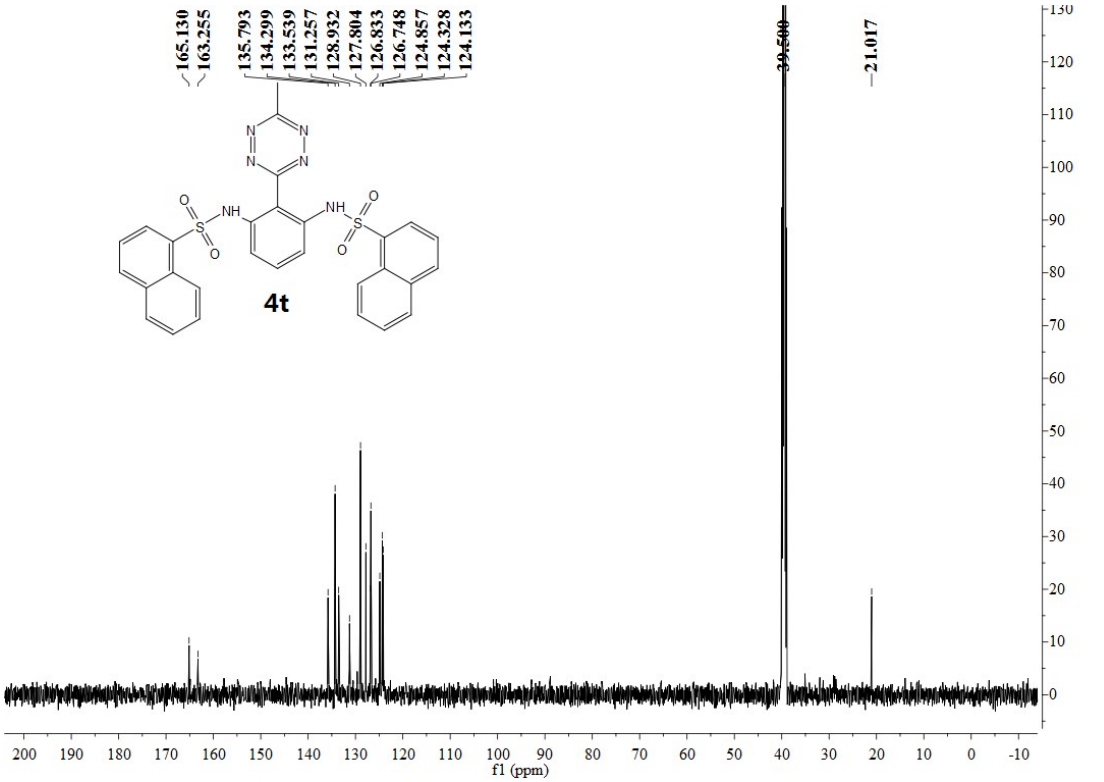
8.253
8.154
8.138
8.028
8.011
7.779
7.764
7.640
7.625
7.610
7.536
7.520
7.505
7.486
7.470
7.455
7.309
7.293
7.277
7.027
7.010
3.333
2.711
2.500
4t
f1 (ppm)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134.299
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128.932
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126.833
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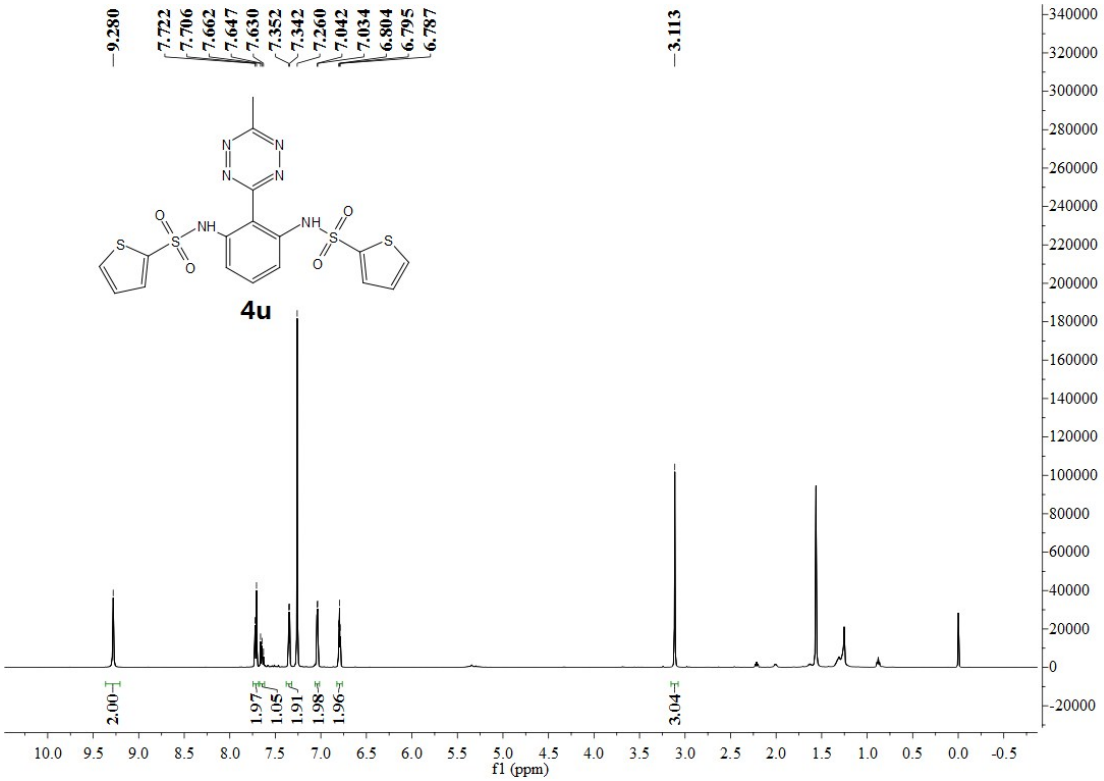
124.857
124.328
124.133
39.500
21.017
4t
f1 (ppm)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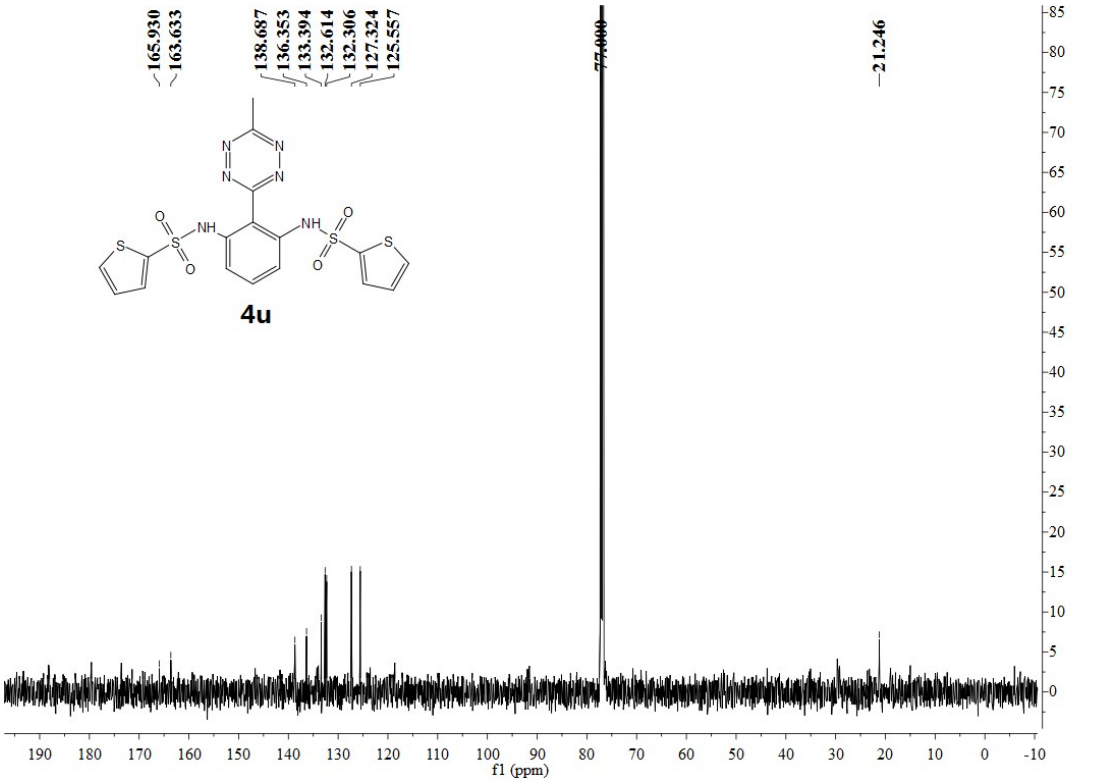
7.647
7.630
7.352
7.342
7.260
7.042
7.034
6.804
6.795
6.787
3.113
4u
2.00
1.97
1.05
1.91
1.98
1.96
3.04
f1 (ppm)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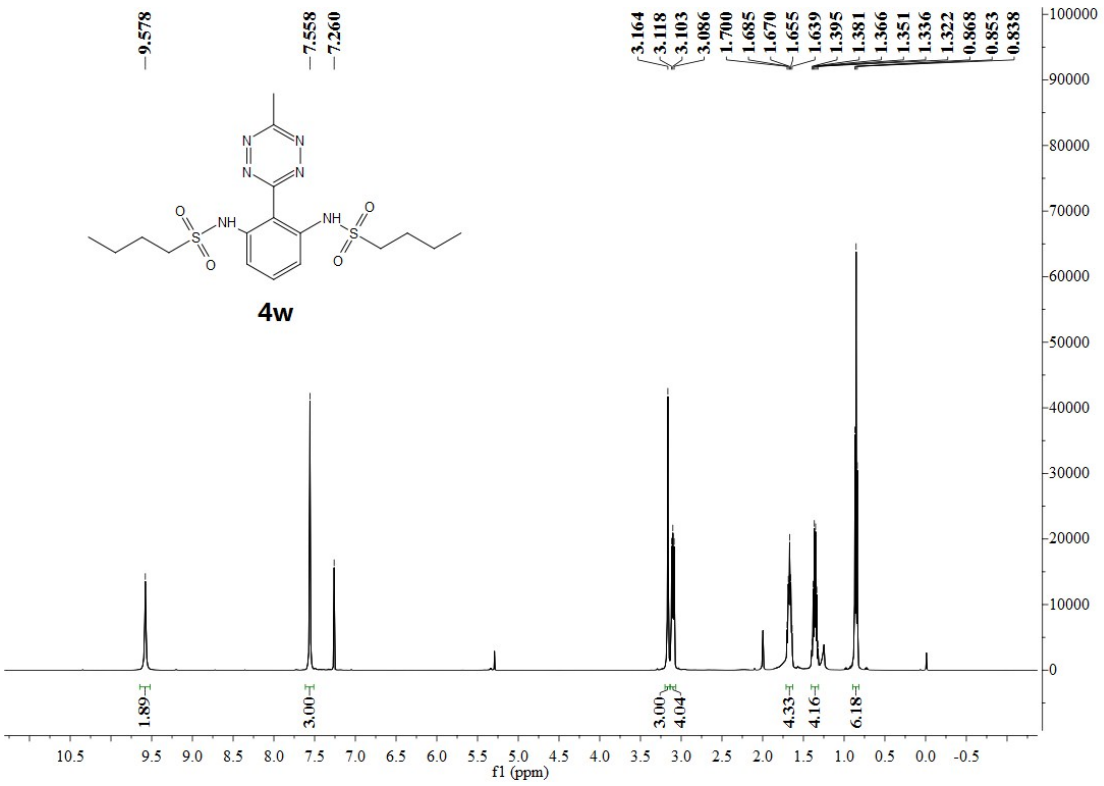
136.353
133.394
132.614
132.306
127.324
125.557
77.000
21.246
4u
f1 (ppm)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7.260
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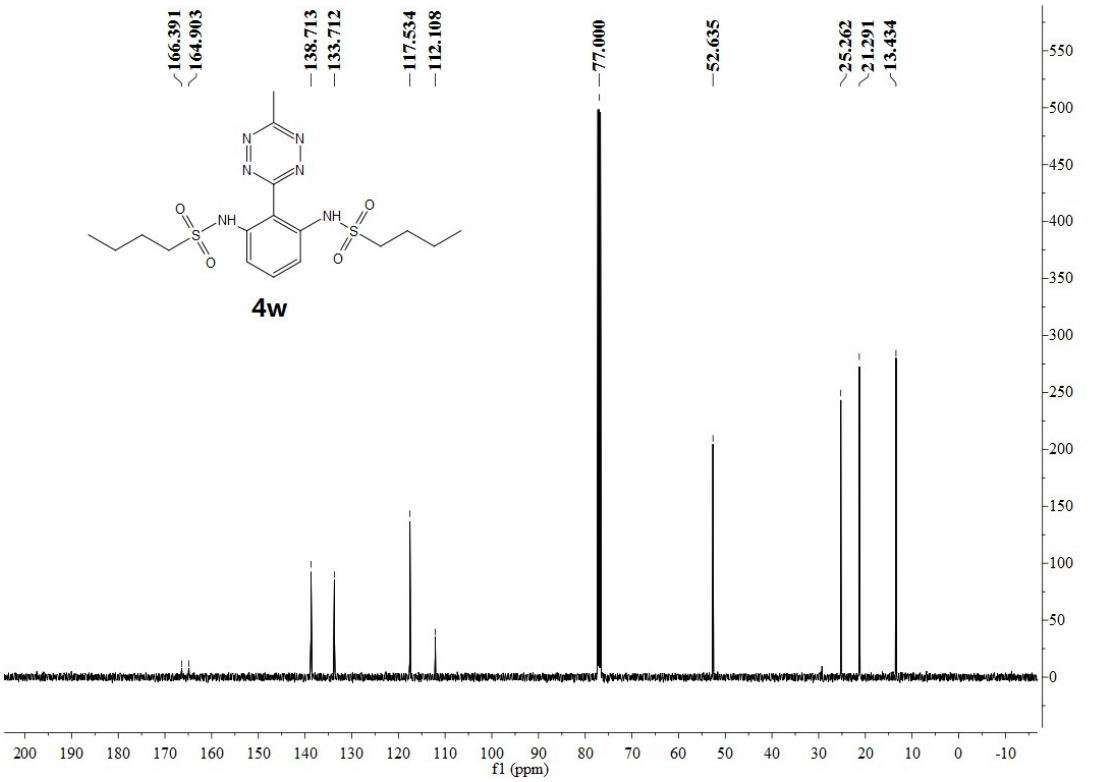
3.118
3.103
3.086
1.700
1.685
1.670
1.655
1.639
1.395
1.381
1.366
1.351
1.336
1.322
0.868
0.853
0.838
4w
1.89
3.00
3.00
4.04
4.33
4.16
6.18
f1 (ppm)


166.391
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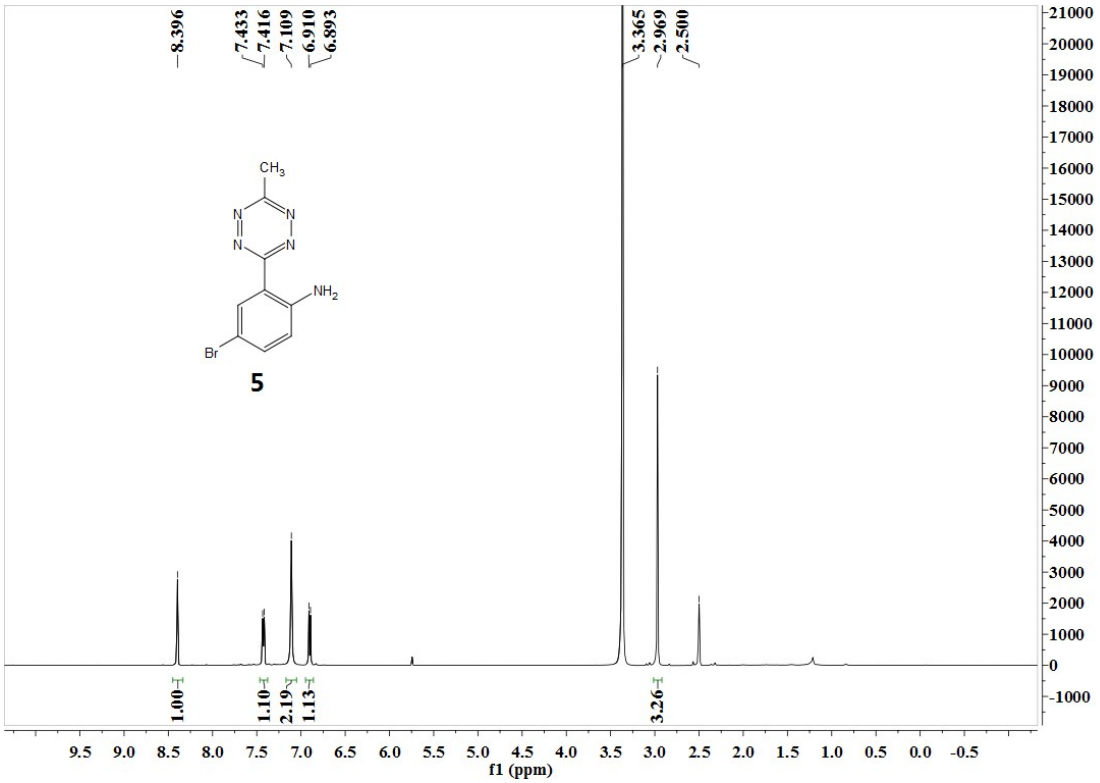
112.108
77.000
52.635
25.262
21.291
13.434
4w
f1 (ppm)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7.109
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6.893
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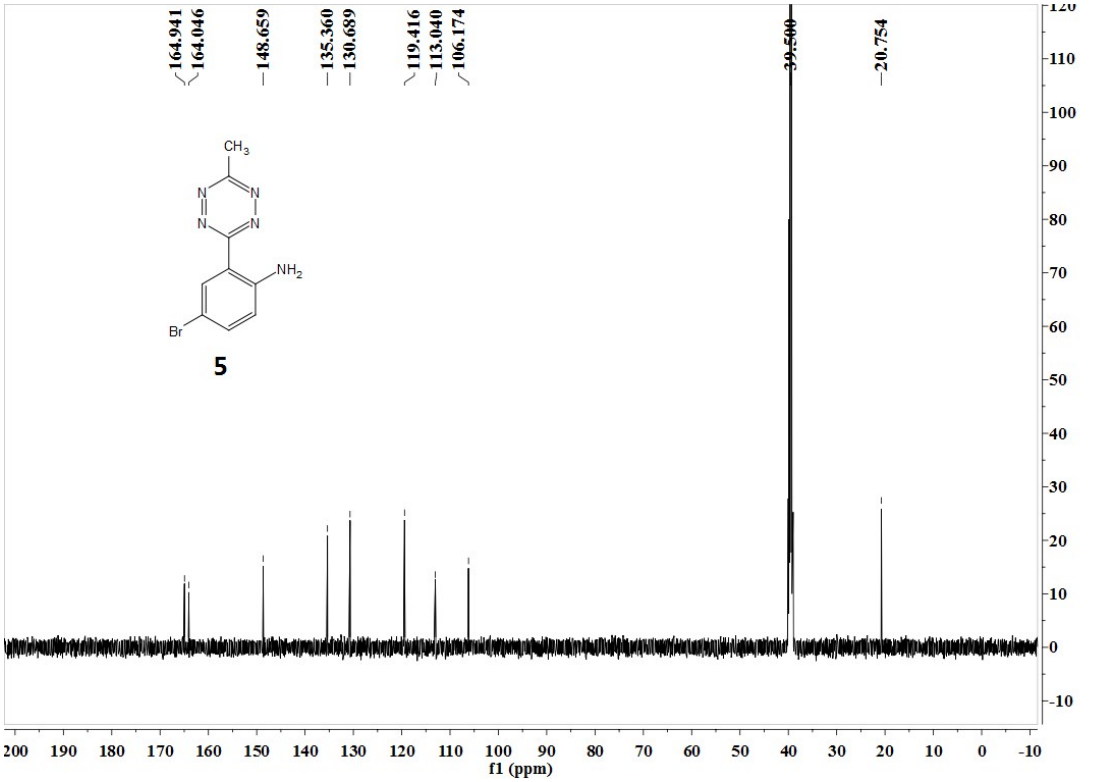
2.969
2.500
1.00
1.10
2.19
1.13
3.26
f1 (ppm)

5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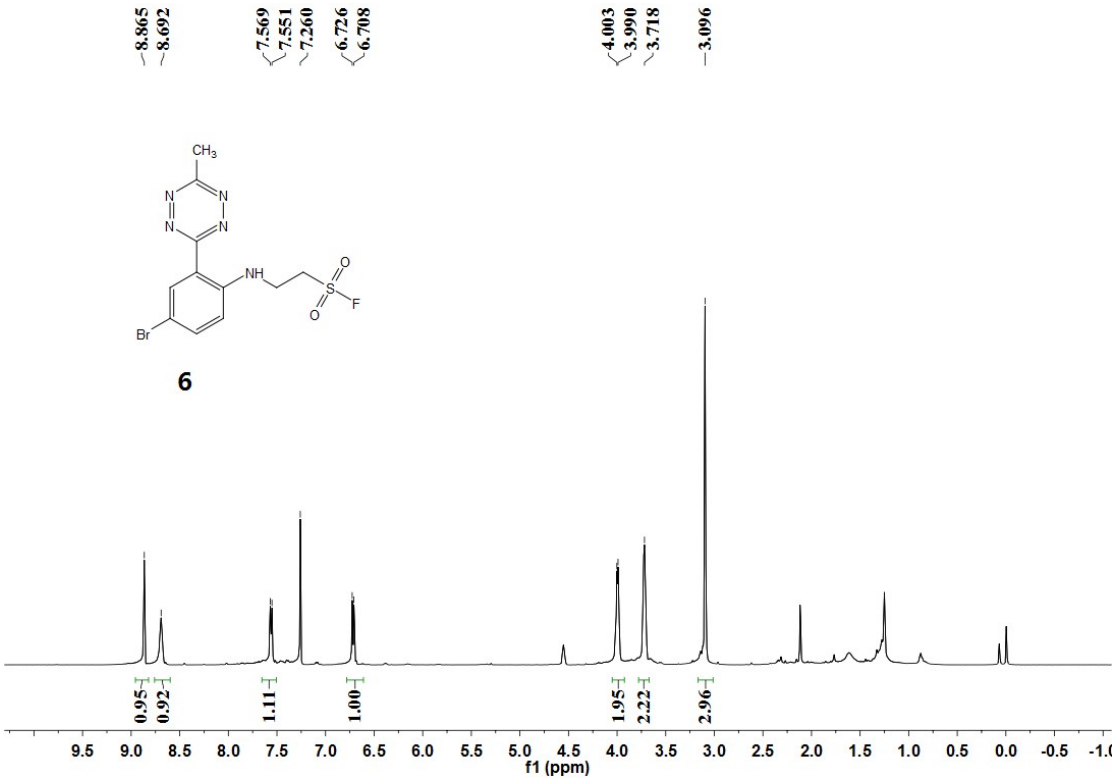
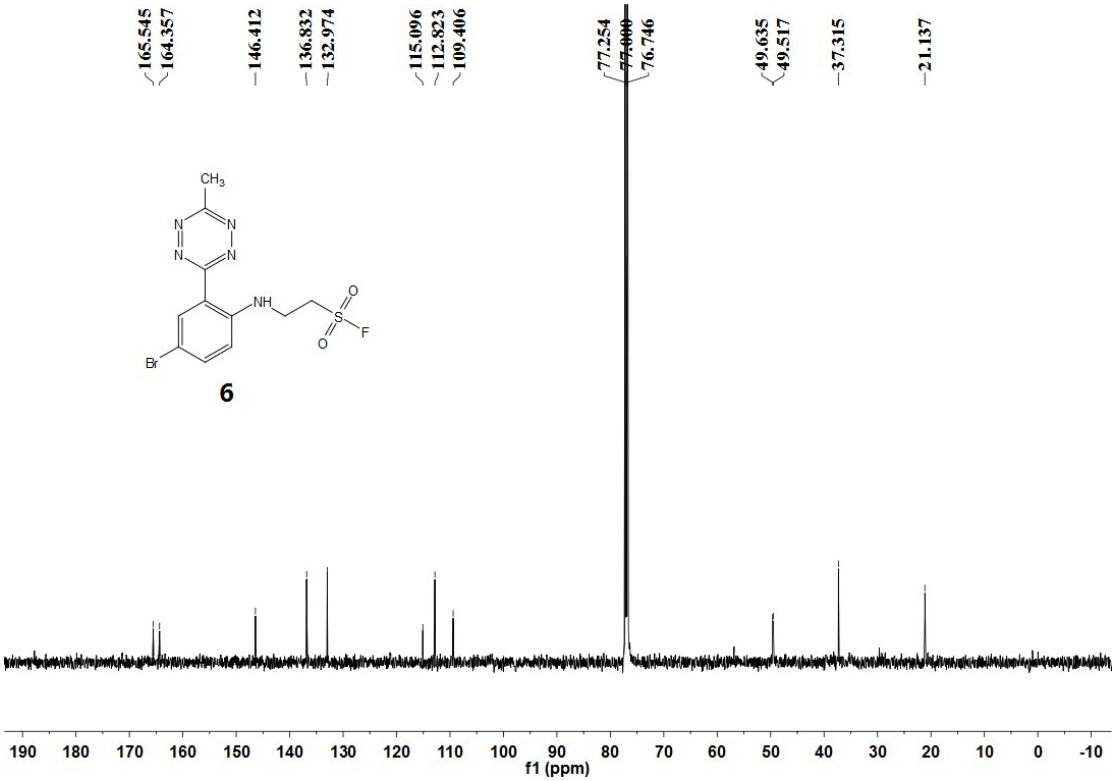
164.046
148.659
135.360
130.689
119.416
113.040
106.174
39.500
20.754
f1 (ppm)

5


8.865
8.692
7.569
7.551
7.260
6.726
6.708
4.003
3.990
3.718
3.096
CH3
N
N
N
N
NH
S
O
O
F
Br
6
0.95
0.92
1.11
1.00
1.95
2.22
2.96
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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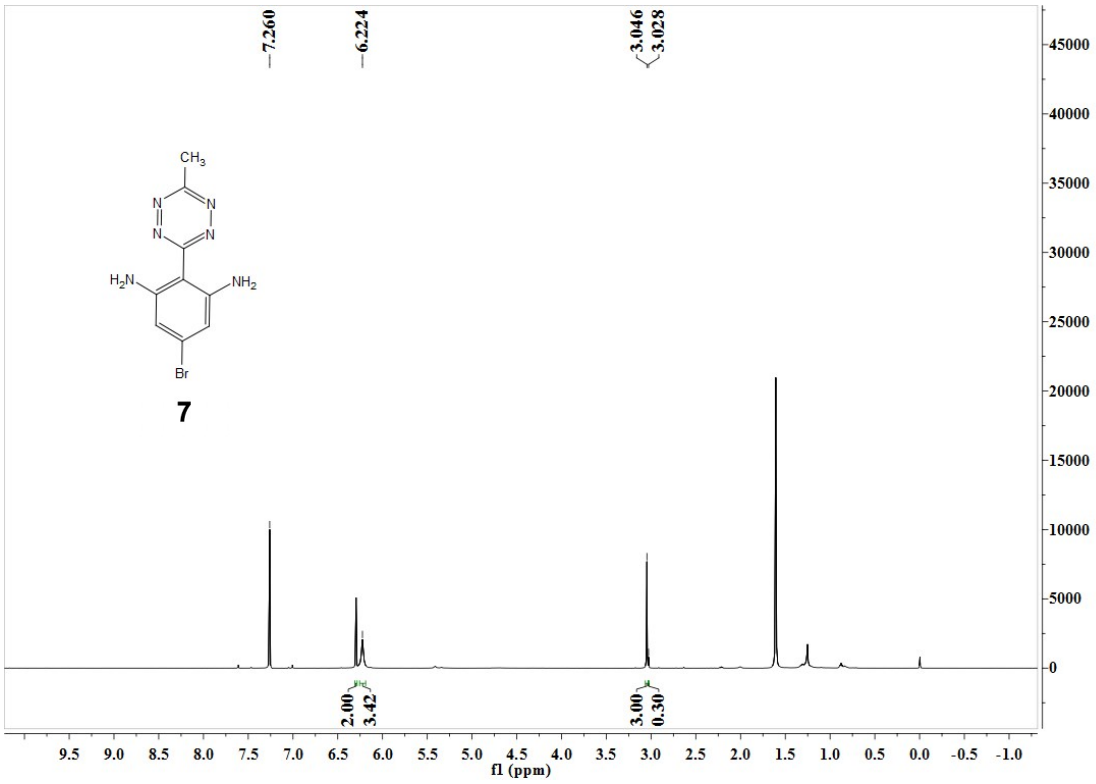
136.832
132.974
115.096
112.823
109.406
77.254
77.000
76.746
49.635
49.517
37.315
21.137
CH3
N
N
N
N
NH
S
O
O
F
Br
6
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.260
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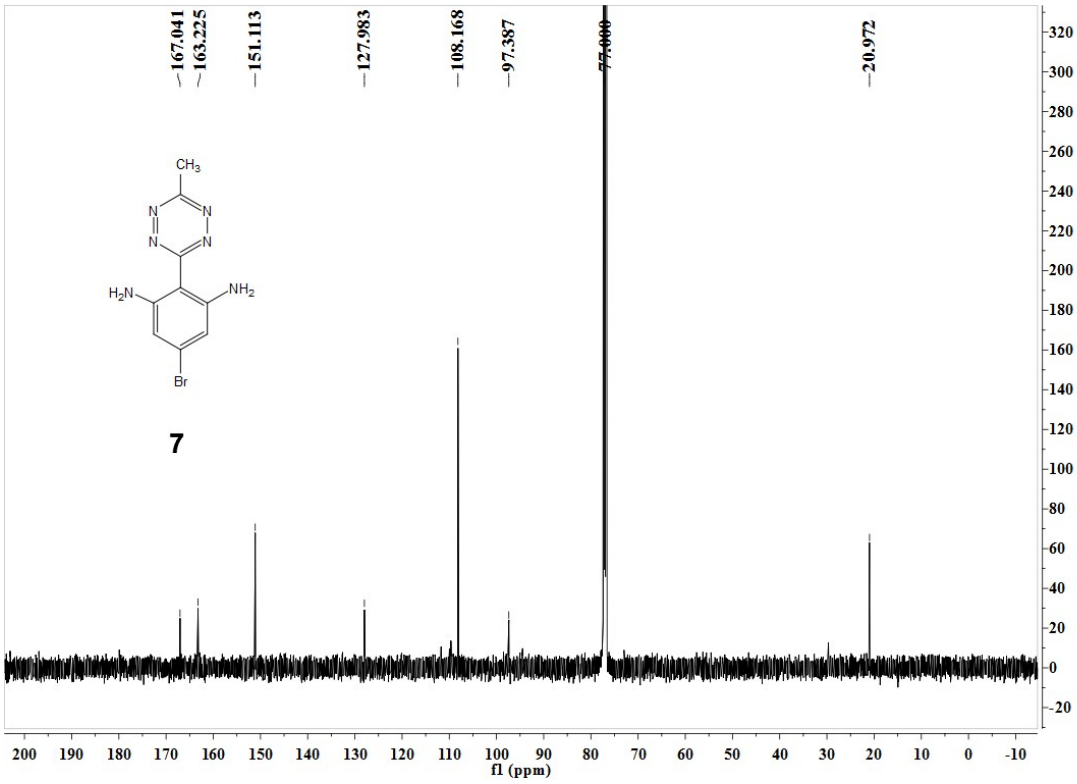
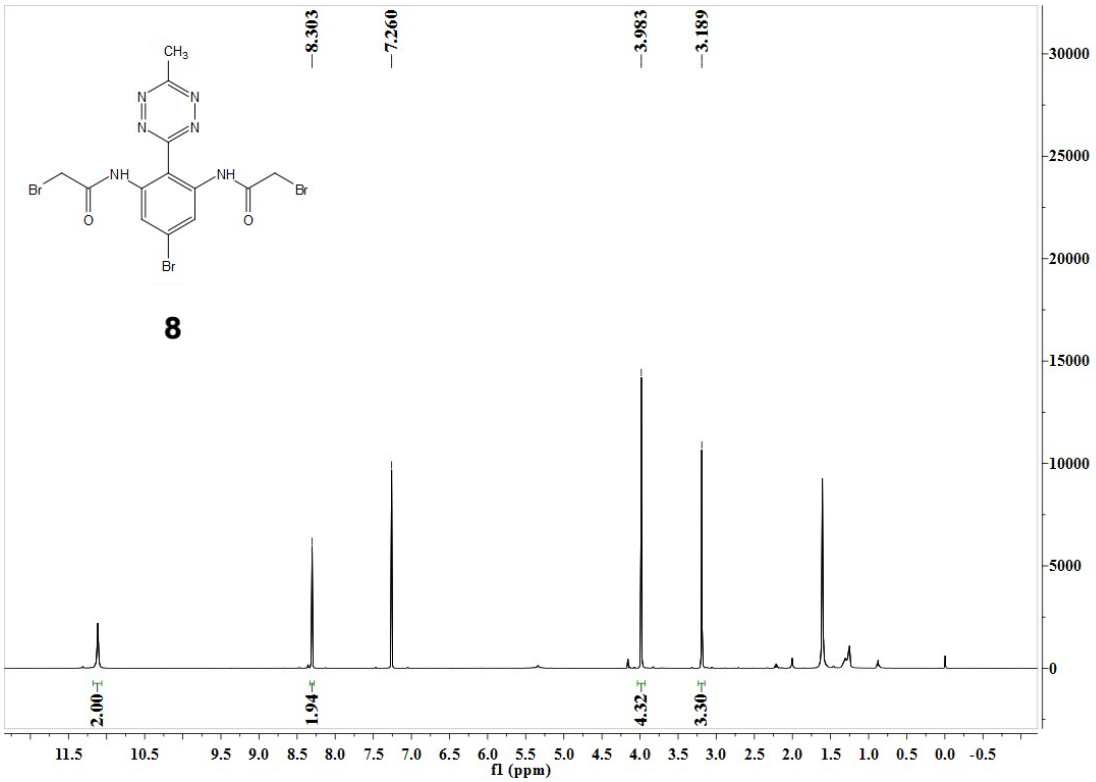
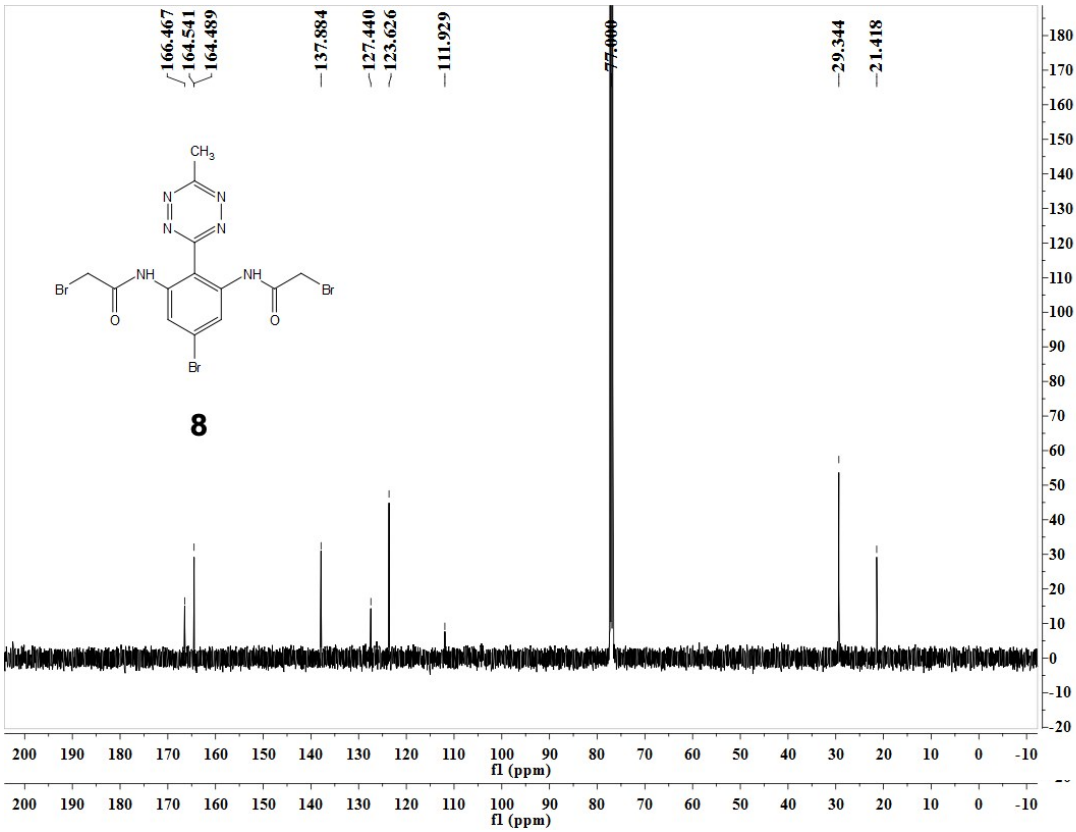
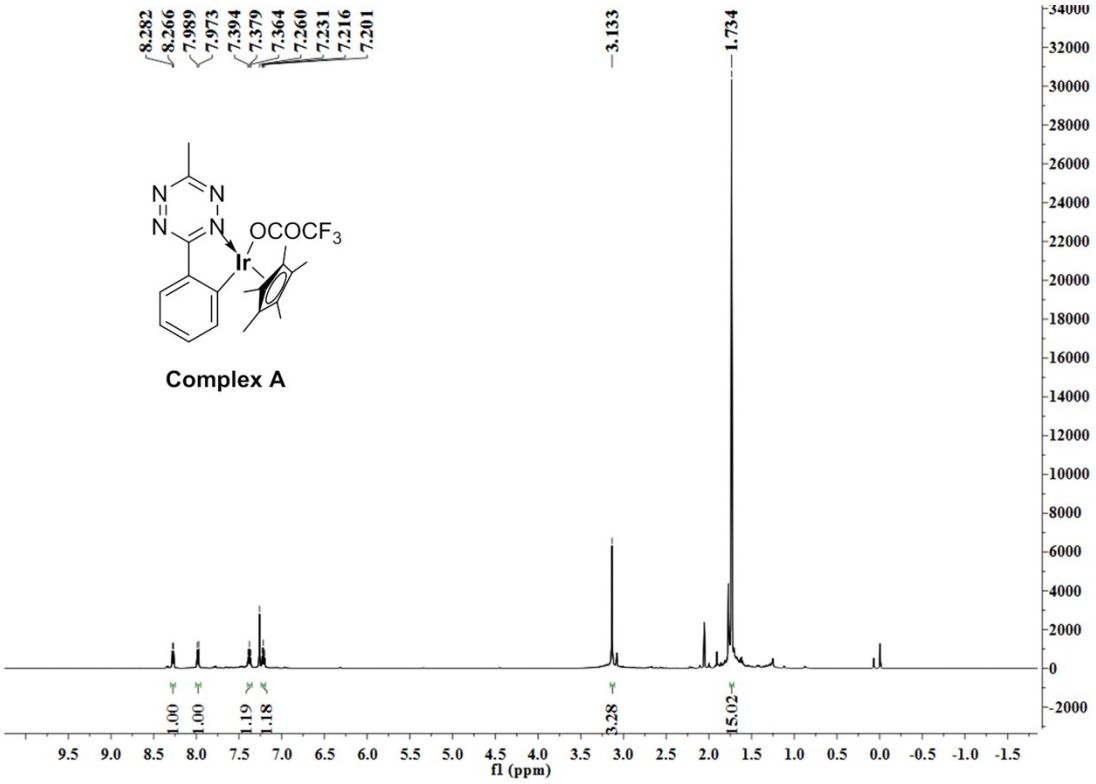
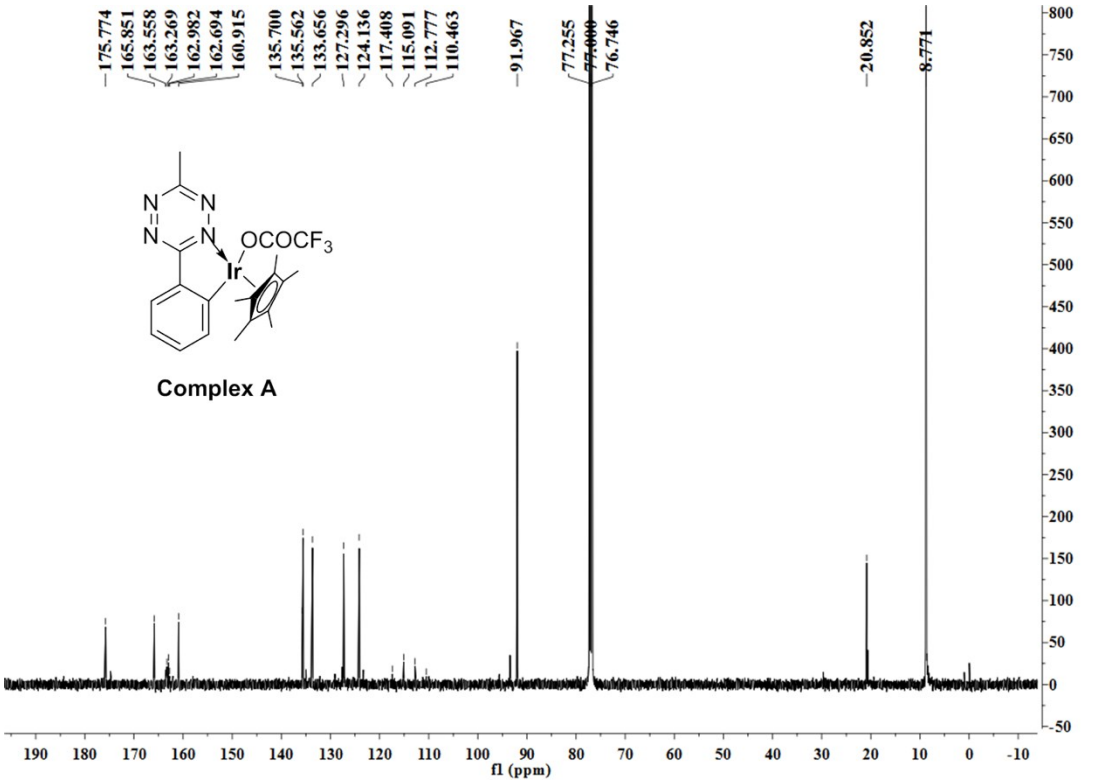
3.046
3.028
2.00
3.42
3.00
0.30
fl (ppm)
7

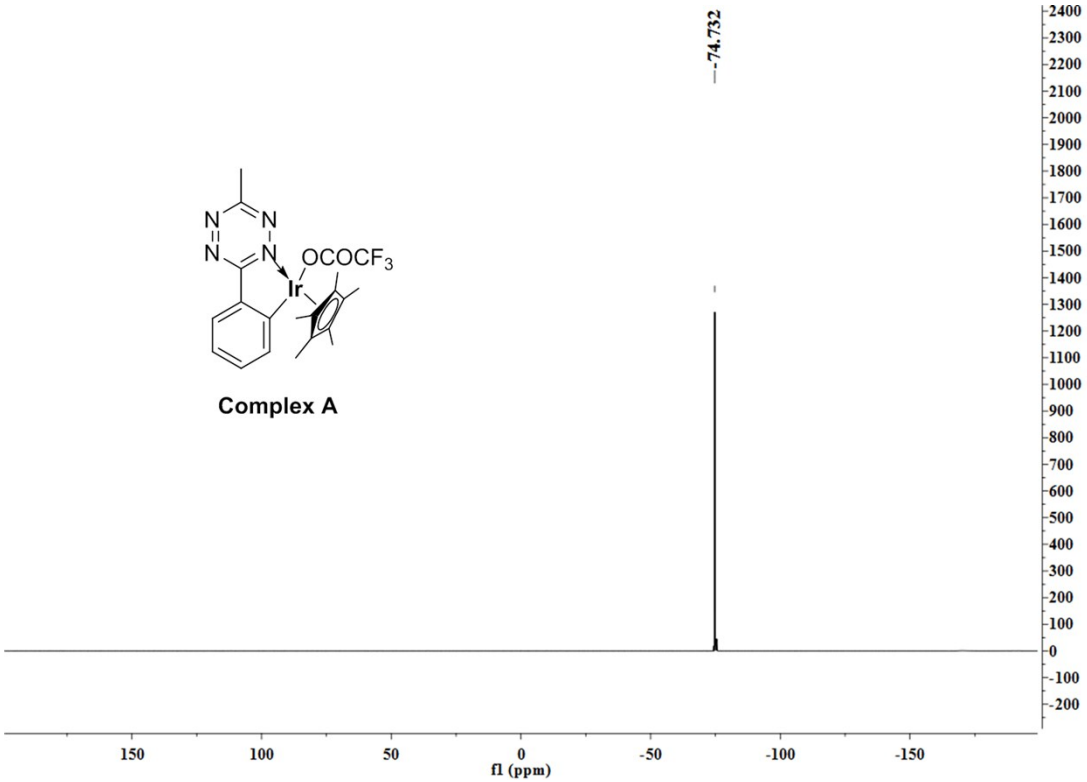

167.041
163.225
151.113
127.983
108.168
97.387
77.000
20.972
fl (ppm)
7

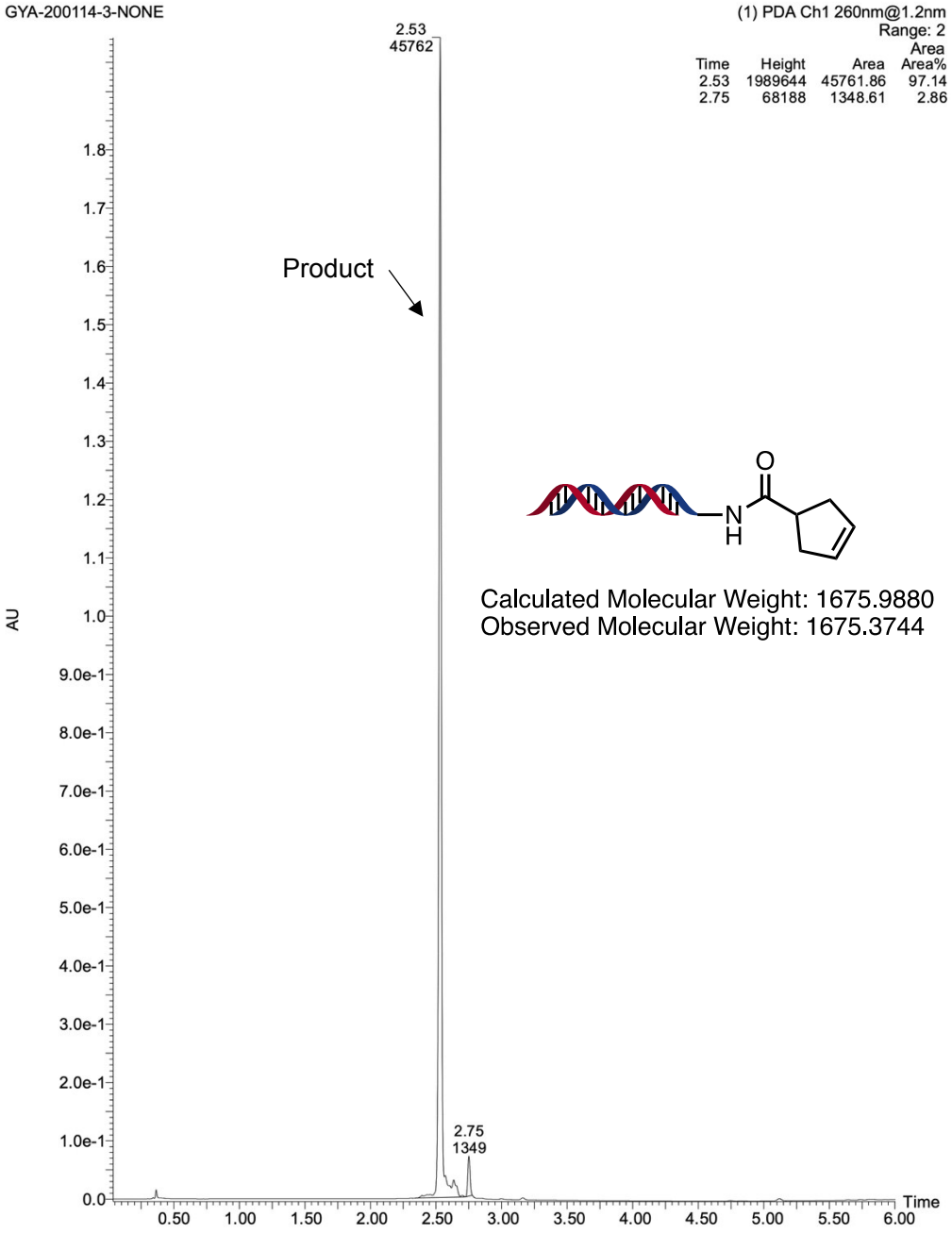

8.303
7.260
3.983
3.189
2.00
1.94
4.32
3.30
f1 (ppm)
8


166.467
164.541
164.489
137.884
127.440
123.626
111.929
77.000
29.344
21.418
f1 (ppm)
8

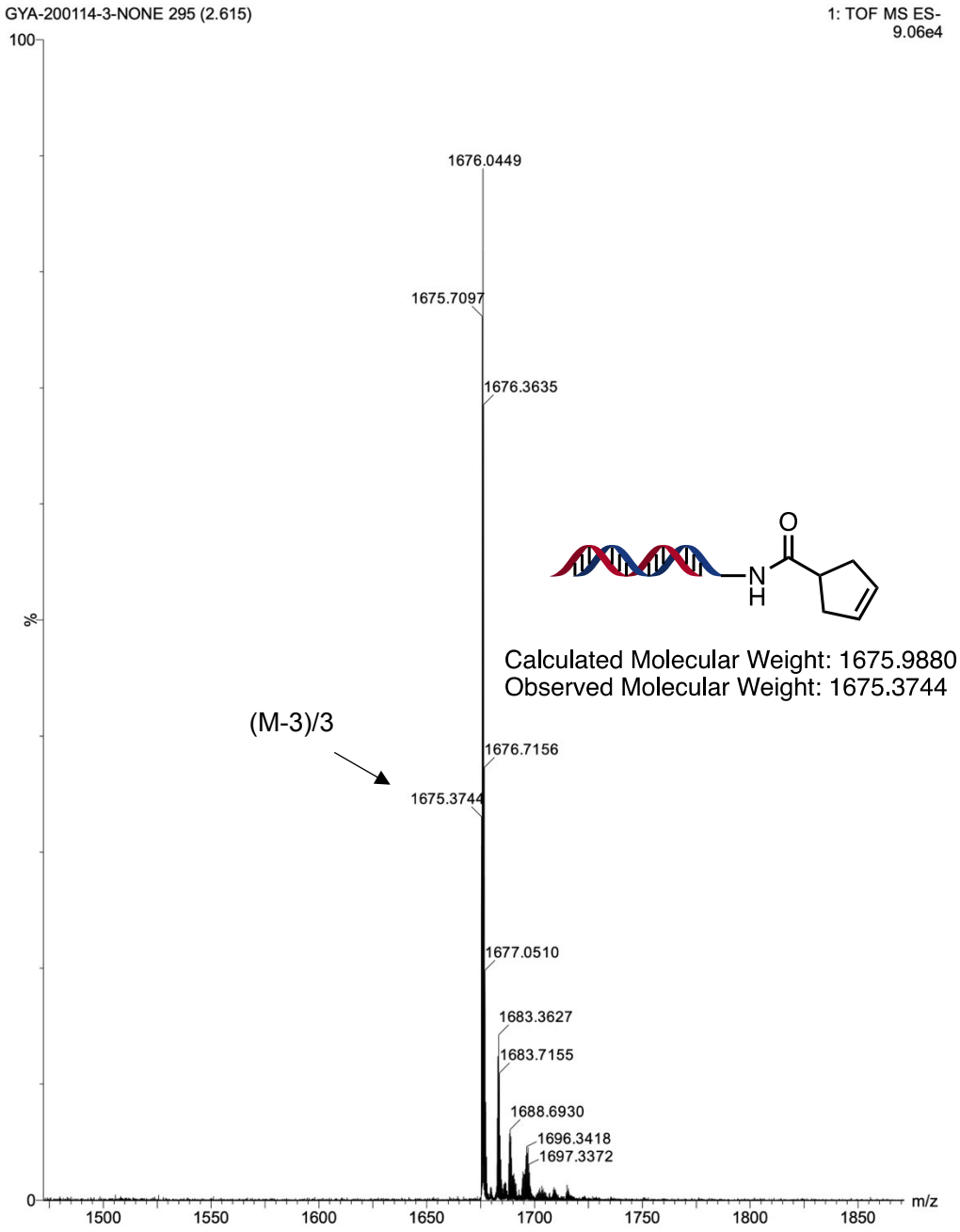

8.282
8.266
7.989
7.973
7.394
7.379
7.364
7.260
7.231
7.216
7.201
3.133
1.734
OCOCF3
Ir
Complex A
1.00
1.00
1.19
1.18
3.28
15.02
fl (ppm)

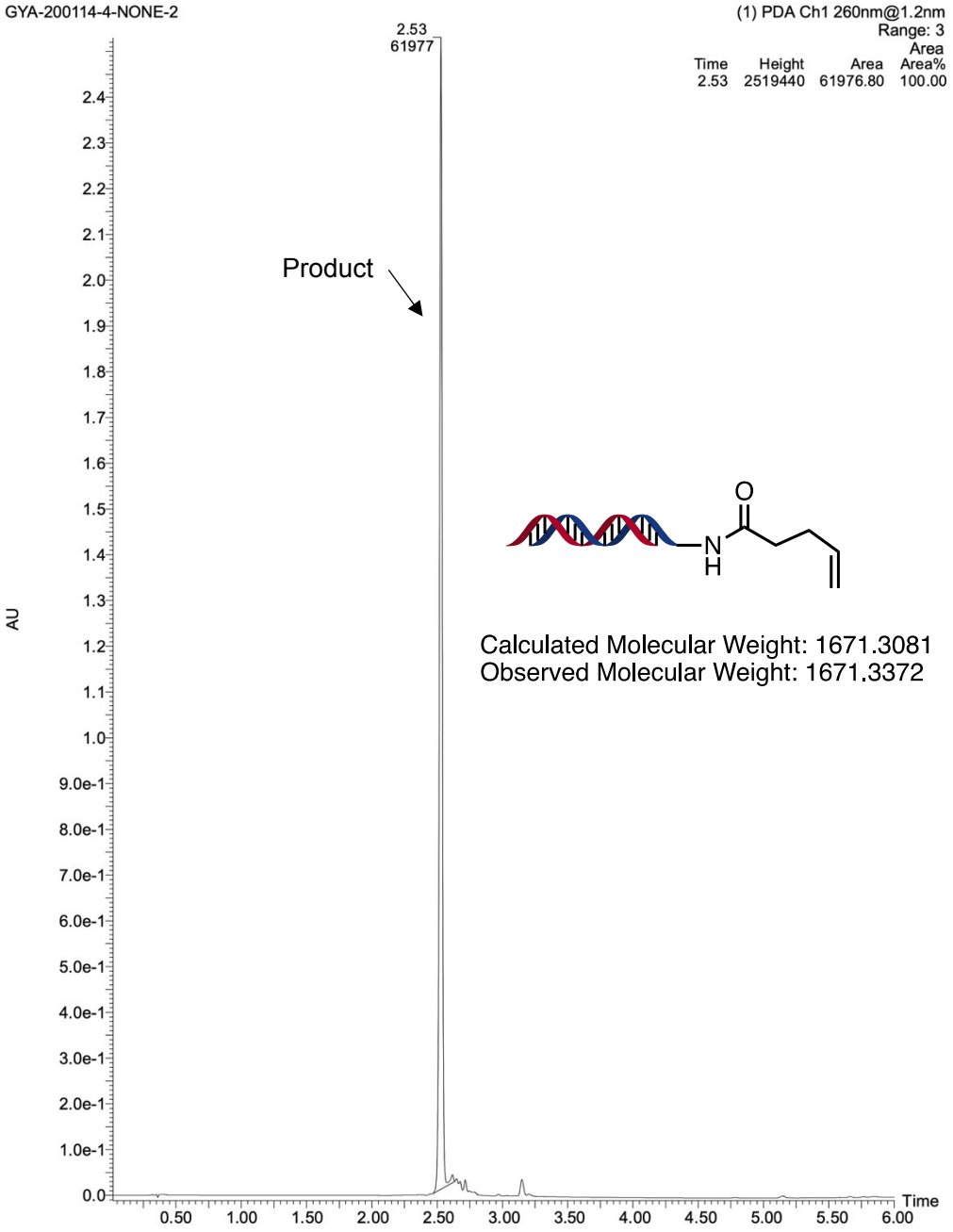

175.774
165.851
163.558
163.269
162.982
162.694
160.915
135.700
135.562
133.656
127.296
124.136
117.408
115.091
112.777
110.463
91.967
77.255
77.000
76.746
20.852
8.771
OCOCF3
Ir
Complex A
fl (ppm)

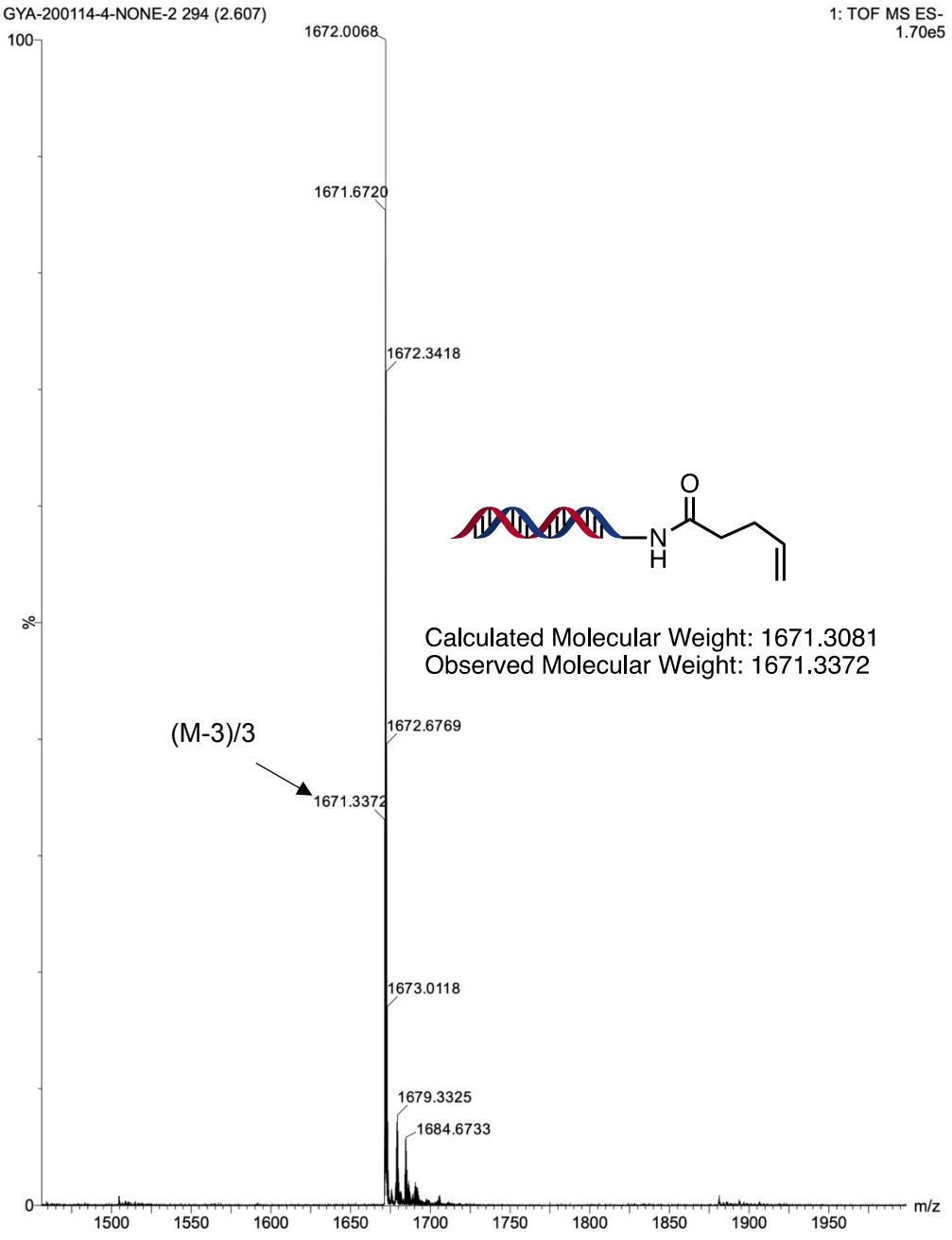

-74.732
OCOCF3
Ir
Complex A
150
100
50
0
-50
-100
-150
f1 (ppm)

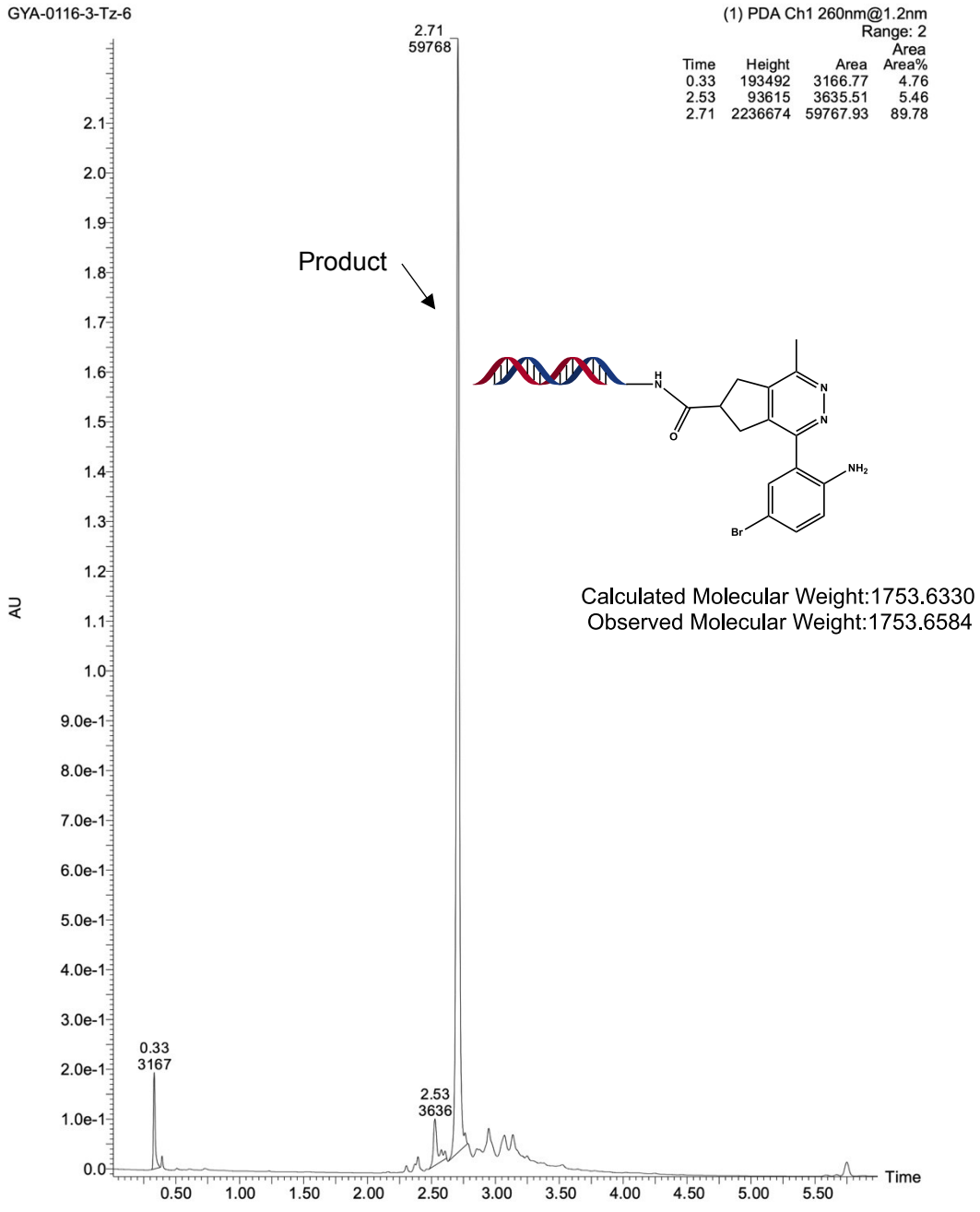


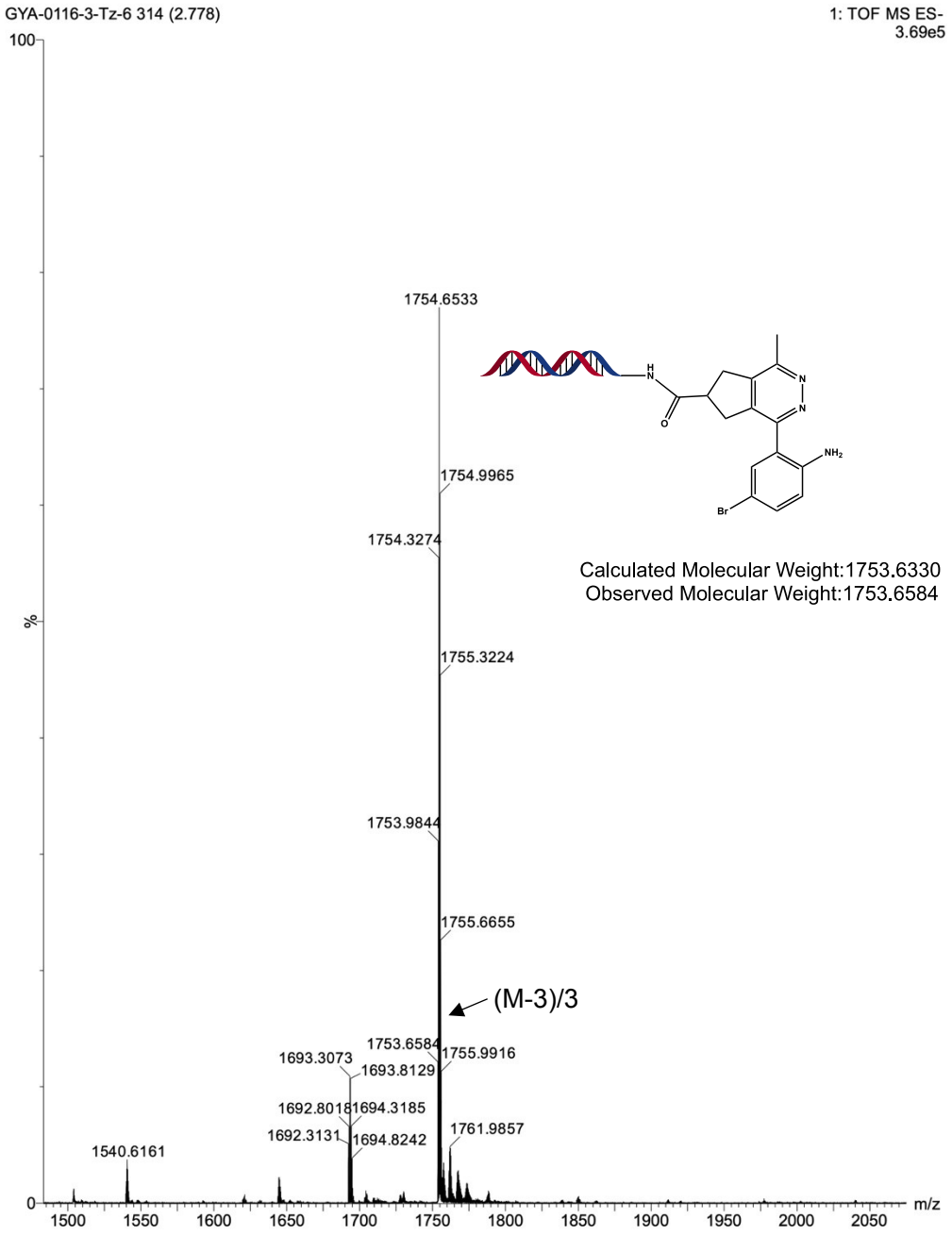
Calculated Molecular Weight: 1675.9880
Observed Molecular Weight: 1675.3744

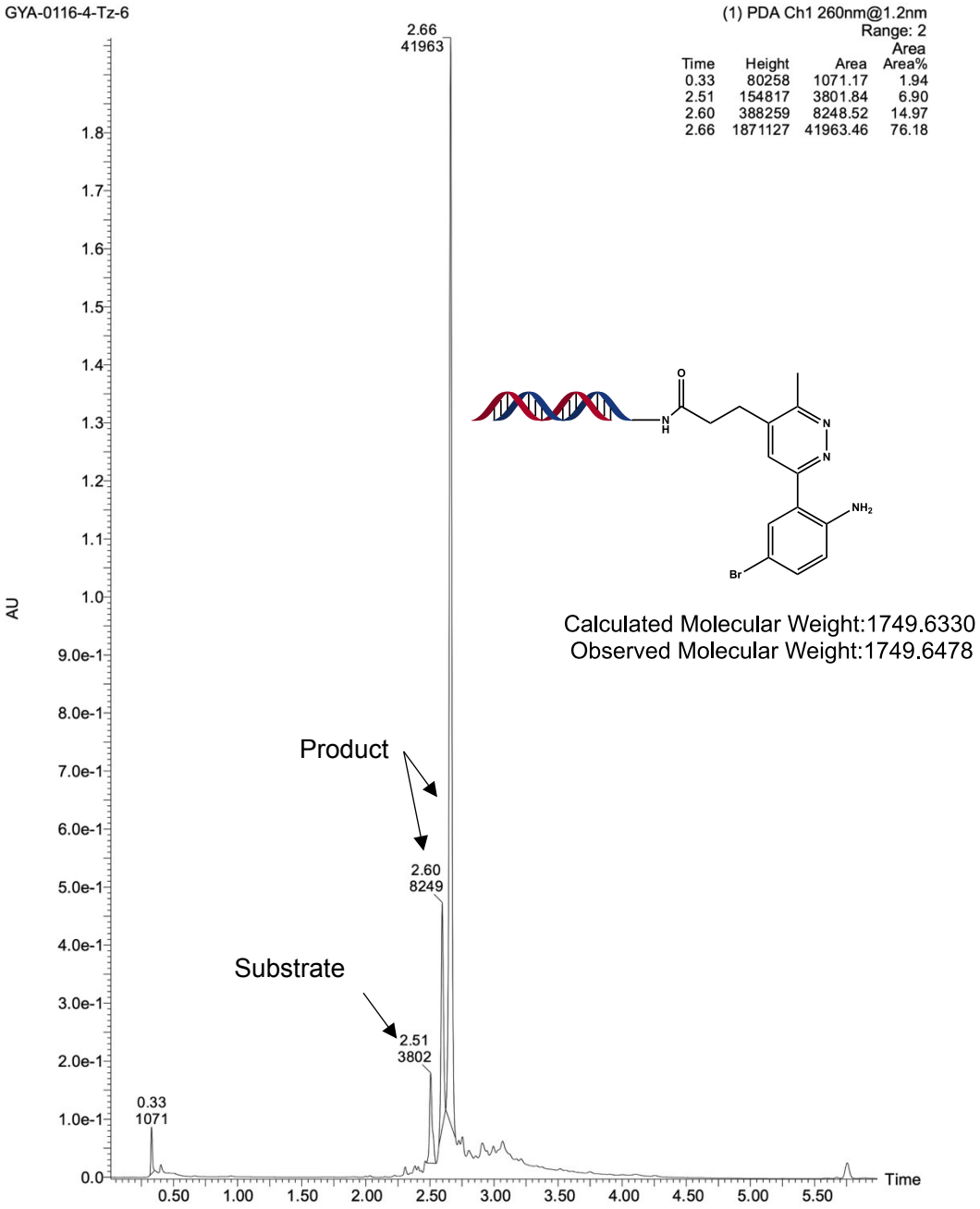

GYA-200114-3-NONE 295 (2.615)
1: TOF MS ES-
9.06e4
100
%
0
1676.0449
1675.7097
1676.3635
1676.7156
1675.3744
1677.0510
1683.3627
1683.7155
1688.6930
1696.3418
1697.3372
(M-3)/3
O
N
H
Calculated Molecular Weight: 1675.9880
Observed Molecular Weight: 1675.3744
1500
1550
1600
1650
1700
1750
1800
1850
m/z

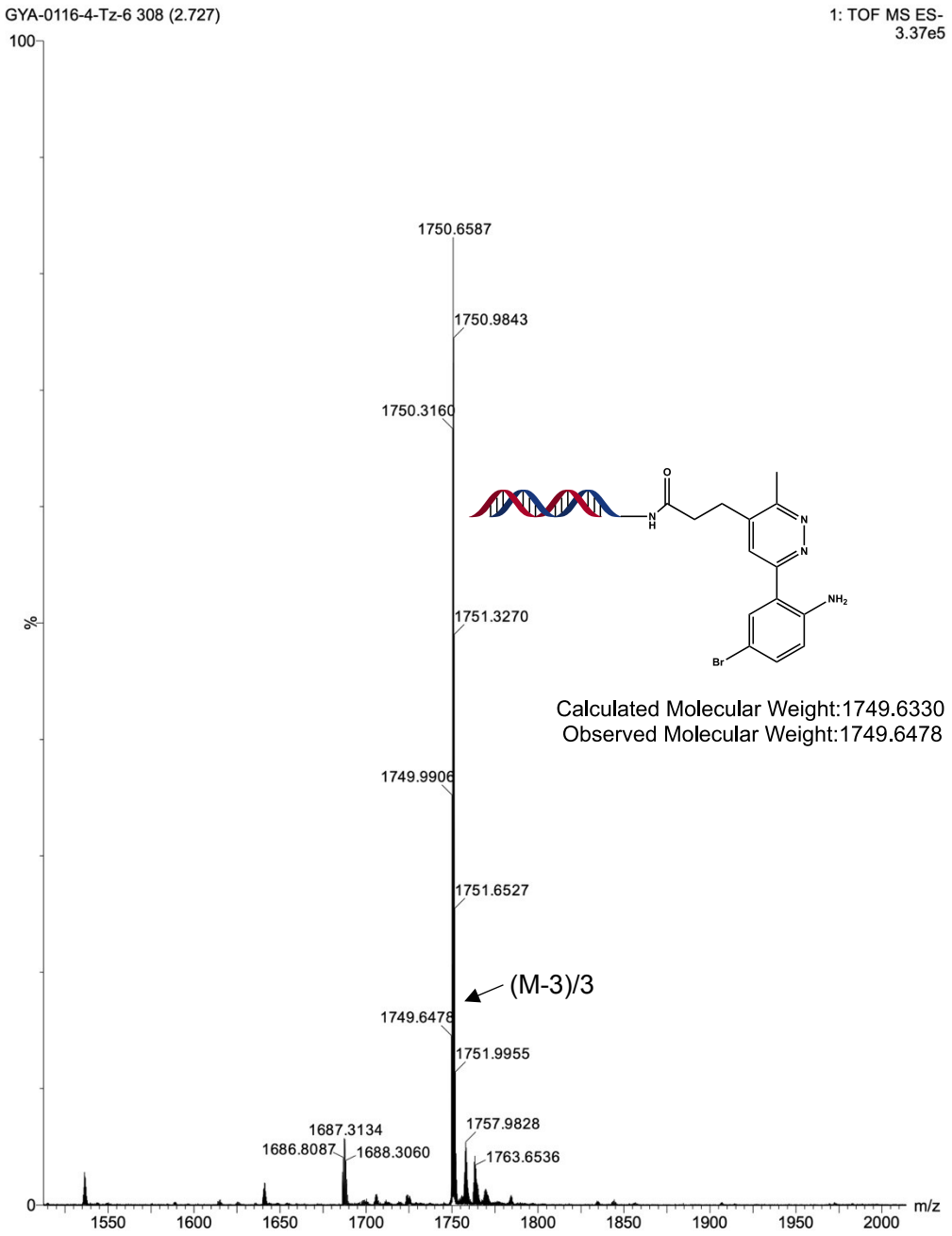

GYA-200114-4-NONE-2
(1) PDA Ch1 260nm@1.2nm
Range: 3
Area
Time Height Area Area%
2.53 2519440 61976.80 100.00
2.53
61977
Product
AU
Time
Calculated Molecular Weight: 1671.3081
Observed Molecular Weight: 1671.3372


GYA-200114-4-NONE-2 294 (2.607)
1: TOF MS ES-
1.70e5
100
%
0
1672.0068
1671.6720
1672.3418
1672.6769
1671.3372
1673.0118
1679.3325
1684.6733
(M-3)/3
O
N
H
Calculated Molecular Weight: 1671.3081
Observed Molecular Weight: 1671.3372
1500
1550
1600
1650
1700
1750
1800
1850
1900
1950
m/z


GYA-0116-3-Tz-6
(1) PDA Ch1 260nm@1.2nm
Range: 2
Time Height Area Area%
0.33 193492 3166.77 4.76
2.53 93615 3635.51 5.46
2.71 2236674 59767.93 89.78
2.71
59768
Product
AU
0.33
3167
2.53
3636
Time
Calculated Molecular Weight:1753.6330
Observed Molecular Weight:1753.6584


GYA-0116-3-Tz-6 314 (2.778)
1: TOF MS ES-
3.69e5
100
%
0
1754.6533
1754.9965
1754.3274
1755.3224
1753.9844
1755.6655
(M-3)/3
1753.6584
1755.9916
1693.3073
1693.8129
1692.8018
1694.3185
1692.3131
1694.8242
1761.9857
1540.6161
Calculated Molecular Weight:1753.6330
Observed Molecular Weight:1753.6584
1500
1550
1600
1650
1700
1750
1800
1850
1900
1950
2000
2050
m/z


GYA-0116-4-Tz-6
(1) PDA Ch1 260nm@1.2nm
Range: 2
Time Height Area Area Area%
0.33 80258 1071.17 1.94
2.51 154817 3801.84 6.90
2.60 388259 8248.52 14.97
2.66 1871127 41963.46 76.18
2.66
41963
AU
Product
2.60
8249
Substrate
2.51
3802
0.33
1071
Time
Calculated Molecular Weight:1749.6330
Observed Molecular Weight:1749.6478


GYA-0116-4-Tz-6 308 (2.727)
1: TOF MS ES-
3.37e5
100
%
0
1750.6587
1750.9843
1750.3160
1751.3270
1749.9906
1751.6527
(M-3)/3
1749.6478
1751.9955
1687.3134
1686.8087
1688.3060
1757.9828
1763.6536
1550
1600
1650
1700
1750
1800
1850
1900
1950
2000
m/z
O
N
H
N
N
NH2
Br
Calculated Molecular Weight:1749.6330
Observed Molecular Weight:1749.6478