Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information

Transition-Metal-Free S-N Bond Formation Synthesis of 5-Amino-1,2,4-Thiadiazoles form Isothiocyanates with Amidines

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EXPERIMENTAL SECTION

General methods: ^{1}H (400 MHz), ^{13}C (101 MHz) spectra were recorded on a Bruker 400MHz spectrometer in $CDCl_3$ or DMSO-d_6 using TMS as internal standard. HRMS was recorded on a Bruker micrOTOF-Q II. Isothiocyanates were synthesized according to the literatures.[1] Melting points are uncorrected.

General procedure: The mixture of amidines (0.25 mmol), isothiocyanates (0.25 mmol), TMEDA (0.5 mmol) and MeCN (2.0 mL) was stirred at 80 ºC for 16h under air atmosphere. After completion of the reaction, the mixture was concentrated in vacuo and the residue was purified by column chromatography (EtOAc/n-Hexane=1:10) to afford the desired products **3**.

3-phenyl-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3aa**).[2] White solid, mp 154-156 ºC, yield: 62 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.27 - 8.11 (m, 2H), 7.49 - 7.38 (m, 3H), 7.21 - 7.13 (m, 2H), 7.12 - 7.04 (m, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.55, 169.37, 136.72, 134.46, 132.89, 130.35, 130.14, 128.58, 128.00, 119.05, 20.89.

N,3-di-p-tolyl-1,2,4-thiadiazol-5-amine (**3ba**).[2] White solid, mp 180-183 ºC, yield: 63 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 19.8 Hz, 1H), 8.18 - 8.01 (m, 2H), 7.25 - 7.15 (m, 4H), 7.13 - 7.08 (m, 2H), 2.39 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.22, 169.49, 140.26, 136.74, 134.37, 130.36, 130.28, 129.28, 127.91, 118.93, 21.50, 20.88.

3-(4-methoxyphenyl)-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3ca**). White solid, mp 145-147 ºC, yield: 65mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 29.3 Hz, 1H), 8.12 (d, J = 8.9 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 3.83 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.38, 169.13, 161.13, 136.83, 134.28, 130.30, 129.58, 125.84, 119.00, 113.87, 55.36, 20.88. HRMS (ESI-TOF) m/z calcd for C16H15N3OS $[M+H]^+$ 297.0930, found 297.0917.

3-(4-fluorophenyl)-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3da**). White solid, mp 198-200 ºC, yield: 57mg, 80%.^{1}H NMR (400 MHz, DMSO-d_6) δ 10.98 (s, 1H), 8.31 - 8.13 (m, 2H), 7.61 - 7.47 (m, 2H), 7.40 - 7.30 (m, 2H), 7.28 - 7.20 (m, 2H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 179.81, 167.95, 162.43, 137.89, 132.58, 130.36, 130.26, 129.90, 129.87, 118.34, 116.31, 116.09, 20.89. ^{19}F NMR (376 MHz, DMSO) δ -110.80. HRMS (ESI-TOF) m/z calcd for C15H12FN3S $[M+H]^+$ 285.0730, found 285.0748.

3-(4-chlorophenyl)-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3ea**).[2] White solid, mp 220-222 °C, yield: 57 mg, 75%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 8.25 - 8.12 (m, 2H), 7.64 - 7.56 (m, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.28 - 7.19 (m, 2H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 179.83, 167.85, 137.83, 135.28, 132.63, 132.01, 130.28, 129.73, 129.35, 118.34, 20.90.

3-(4-bromophenyl)-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3fa**).[2] White solid, mp 240-242 °C, yield: 62 mg, 72%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.99 (s, 1H), 8.20 - 8.01 (m, 2H), 7.79 - 7.69 (m, 2H), 7.59 - 7.45 (m, 2H), 7.30 - 7.18 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 179.90, 167.97, 137.84, 132.68, 132.37, 132.28, 130.29, 129.97, 124.15, 118.40, 20.90.

3-(pyridin-4-yl)-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3ga**).[3] White solid, mp 240-242 °C, yield: 57 mg, 85%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.04 (s, 1H), 8.72 (d, J = 6.0 Hz, 2H), 8.02 (d, J = 6.2 Hz, 2H), 7.52 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 7.4 Hz, 2H), 2.28 (s, 3H).^{13}C NMR (101 MHz, DMSO-d_6) δ 181.18, 167.67, 151.16, 139.99, 138.24, 133.11, 130.30, 122.15, 118.71, 21.06.

3-(pyridin-3-yl)-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3ha**).[3] 78% White solid, mp 238-240 °C, yield: 49 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.27 - 7.11 (m, 7H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.32, 180.30, 137.19, 135.95, 134.44, 130.16, 130.15, 129.43, 126.36, 125.56, 125.53, 21.11.

3-(1H-pyrazol-1-yl)-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3ia**).[4] White solid, mp 200-202 °C, yield: 53 mg, 84%.^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.30 (d, J = 5.6 Hz, 1H), 7.53 (s, 1H), 7.28 - 7.12 (m, 4H), 6.46 - 6.35 (m, 1H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.29, 158.47, 142.86, 136.30, 135.56, 130.43, 128.94, 121.03, 108.04, 21.13.

3-methyl-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3ja**).[2] White solid, mp 144-147 °C, yield: 45 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.22 (d, J = 8.2 Hz, 2H), 7.19 - 7.11 (m, 2H), 2.43 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.34, 169.50, 136.99, 134.90, 130.42, 119.77, 20.93, 19.13.

3-cyclopropyl-N-(p-tolyl)-1,2,4-thiadiazol-5-amine (**3ka**).[2] White solid, mp 135-137 °C, yield: 50 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.12 (d, J = 8.2 Hz, 2H), 7.07 - 7.01 (m, 2H), 2.27 (s, 3H), 2.03 (ddd, J = 13.2, 8.3, 4.9 Hz, 1H), 0.99 (dt, J = 6.2, 3.1 Hz, 2H), 0.89 (dt, J = 8.3, 3.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.22, 174.74, 136.85, 134.37, 130.33, 119.09, 20.88, 13.63, 8.86.

N,3-diphenyl-1,2,4-thiadiazol-5-amine (**3ab**).[4] White solid, mp 174-175 ºC, yield: 51 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.17 - 8.08 (m, 2H), 7.40 - 7.32 (m, 5H), 7.17 (dd, *J* = 2.2, 0.9 Hz, 1H), 7.14 - 7.07 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.58, 168.30, 138.06, 131.78, 129.13, 128.83, 127.54, 126.93, 123.29, 117.33.

3-phenyl-N-(m-tolyl)-1,2,4-thiadiazol-5-amine (**3ac**).[4] White solid, mp 108-110 ºC, yield: 57 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (s, 1H), 8.29 - 8.12 (m, 2H), 7.42 (dd, *J* = 5.1, 1.9 Hz, 3H), 7.27 - 7.16 (m, 1H), 7.00 (dd, *J* = 8.0, 2.3 Hz, 1H), 6.92 (d, *J* = 7.7 Hz, 1H), 6.87 (d, *J* = 2.2 Hz, 1H), 2.25 (d, *J* = 2.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.21, 169.25, 139.92, 139.12, 132.84, 130.20, 129.60, 128.62, 128.08, 125.19, 119.53, 115.25, 21.44.

3-phenyl-N-(o-tolyl)-1,2,4-thiadiazol-5-amine (**3ad**).[4] White solid, mp 167-170 ºC, yield: 54 mg, 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.11 - 7.95 (m, 2H), 7.38 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.34 - 7.21 (m, 4H), 7.20 - 7.14 (m, 1H), 7.10 (td, *J* = 7.4, 1.3 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.10, 169.64, 137.82, 132.88, 131.53, 130.80, 130.06, 128.49, 127.85, 127.65, 126.28, 121.26, 17.72.

N-(4-isopropylphenyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3ae**).[4] White solid, mp 130-132 ºC, yield: 67 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.27 - 8.12 (m, 2H), 7.49 - 7.38 (m, 3H), 7.28 - 7.20 (m, 2H), 7.17 - 7.09 (m, 2H), 2.90 (hept, *J* = 6.9 Hz, 1H), 1.25 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.33, 169.35, 145.42, 136.91, 132.89, 130.13, 128.57, 128.00, 127.77, 118.93, 33.61, 24.01.

N-(4-(tert-butyl)phenyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3af**). White solid, mp 145-147 ºC, 74mg, 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.12 - 8.02 (m, 2H), 7.32 - 7.23 (m, 5H), 7.04 - 7.00 (m, 2H), 1.22 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.43, 169.34, 147.59, 136.67, 132.87, 130.14, 128.59, 128.06, 126.65, 118.60, 34.48, 31.36. HRMS (ESI-TOF) m/z calcd for C18H19N3S $[M+H]^+$ 309.1294, found 309.1287

N-(2,4-dimethylphenyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3ag**). White solid, mp 132-135 ºC, 62mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.14 - 7.98 (m, 2H), 7.41 - 7.28 (m, 4H), 7.14 - 7.05 (m, 2H), 2.34 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.05, 169.72, 136.70, 135.34, 132.96, 132.25, 131.71, 129.97, 128.45, 128.14, 127.81, 122.52, 21.03, 17.64. HRMS (ESI-TOF) m/z calcd for C16H15N3S $[M+H]^+$ 281.0981, found 281.0986.

N-(4-methoxyphenyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3ah**).[4] White solid, mp 117-120 ºC, yield: 57 mg, 81%. ^{1}H NMR (400 MHz, CDCl3) δ 8.40 (s, 1H), 8.12 - 8.03 (m,

2H), 7.33 (dd, *J* = 5.2, 2.0 Hz, 3H), 7.16 - 7.08 (m, 2H), 6.87 - 6.80 (m, 2H), 3.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.79, 169.61, 157.21, 132.95, 132.42, 130.08, 128.54, 127.95, 122.07, 115.05, 55.59.

N-(4-ethoxyphenyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3ai**). White solid, mp 135-137 ^{o}C, yield: 63mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.15 - 7.98 (m, 2H), 7.38 - 7.27 (m, 3H), 7.13 - 7.03 (m, 2H), 6.85 - 6.74 (m, 2H), 3.94 (q, *J* = 7.0 Hz, 2H), 1.34 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.01, 169.58, 156.59, 132.92, 132.30, 130.08, 128.53, 127.96, 122.15, 115.55, 63.82, 14.84. HRMS (ESI-TOF) m/z calcd for C16H15N3OS $[M+H]^+$ 297.0930, found 297.0919.

N-(4-fluorophenyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3aj**).[4] White solid, mp 170-172 ^{o}C, yield: 58 mg, 84%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.06 (s, 1H), 8.29 - 8.13 (m, 2H), 7.78 - 7.67 (m, 2H), 7.57 - 7.49 (m, 3H), 7.33 - 7.24 (m, 2H).^{13}C NMR (101 MHz, DMSO) δ 179.59, 168.99, 159.45, 157.07, 136.86, 136.84, 133.18, 130.66, 129.22, 128.04, 120.00, 119.93, 116.57, 116.34. ^{19}F NMR (376 MHz, DMSO) δ -119.88.

N-(4-chlorophenyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3ak**).[4] White solid, mp 194-196 ^{o}C, yield: 56 mg, 78%.^{1}H NMR (400 MHz, DMSO-d_6) δ 11.12 (s, 1H), 8.20 - 8.18 (m, 2H), 7.72 (d, *J* = 8.9 Hz, 2H), 7.53 - 7.48 (m, 5H). ^{13}C NMR (101 MHz, DMSO) δ 179.55, 169.08, 139.49, 133.16, 130.67, 129.73, 129.23, 128.25, 126.85, 119.74.

N-(3-chlorophenyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3al**).[4] White solid, mp 156-158 ^{o}C, yield: 49mg, 68%. ^{1}H NMR (400 MHz, CDCl3) δ 8.58 (s, 1H), 8.33 - 8.11 (m, 2H), 7.50 - 7.41 (m, 3H), 7.31 - 7.22 (m, 2H), 7.13 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.53, 140.24, 135.51, 132.66, 130.81, 130.37, 128.67, 128.04, 124.21, 118.52, 118.50, 116.12.

N-(naphthalen-1-yl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3am**).[4] White solid, mp 150-152 ^{o}C, yield: 65mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (d, *J* = 4.4 Hz, 1H), 8.13 - 7.98 (m, 3H), 7.89 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.80 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.66 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.56 - 7.45 (m, 3H), 7.33 - 7.25 (m, 1H), 7.18 (dd, *J* = 8.3, 6.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.35, 169.82, 135.45, 134.58, 132.84, 129.94, 128.70, 128.32, 127.83, 127.81, 127.27, 127.00, 126.93, 125.80, 121.30, 119.59.

N-benzyl-3-phenyl-1,2,4-thiadiazol-5-amine (**3an**).[3] White solid, mp 100-103 ^{o}C, yield: 55 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 - 8.00 (m, 2H), 7.38 - 7.22 (m, 8H), 6.85 (s, 1H), 4.40 (d, *J* = 5.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.55, 168.75, 135.06, 132.10, 128.90, 127.87, 127.44, 127.13, 126.84, 126.55, 49.39.

N-(tert-butyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3ao**). Yellow liquid, yield: 50 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 - 8.04 (m, 2H), 7.35 (dd, *J* = 5.2, 2.1 Hz, 3H), 5.85 (s, 1H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.46, 169.18, 133.21,

129.83, 128.45, 127.90, 53.05, 28.53. HRMS (ESI-TOF) m/z calcd for C12H15N3S $[M+H]^+$ 233.0981, found 233.0989.

N-(sec-butyl)-3-phenyl-1,2,4-thiadiazol-5-amine (**3ap**). Yellow liquid, yield: 47 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 - 8.04 (m, 2H), 7.50 - 7.37 (m, 3H), 6.05 (d, *J* = 8.5 Hz, 1H), 3.32 (dh, *J* = 8.3, 6.4 Hz, 1H), 1.60 (qd, *J* = 7.4, 6.3 Hz, 2H), 1.27 (d, *J* = 6.5 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.92, 169.88, 133.24, 129.90, 128.47, 127.92, 55.24, 29.60, 20.15, 10.34. HRMS (ESI-TOF) m/z calcd for C12H15N3S $[M+H]^+$ 233.0981, found 233.0997.

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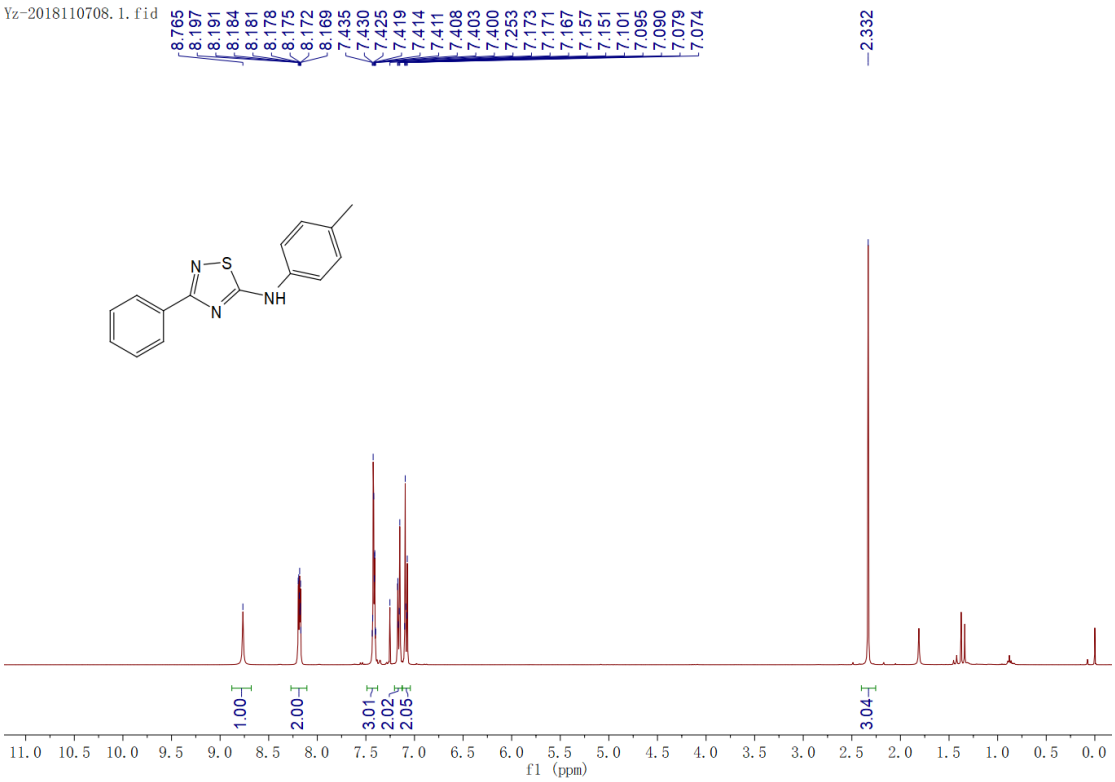

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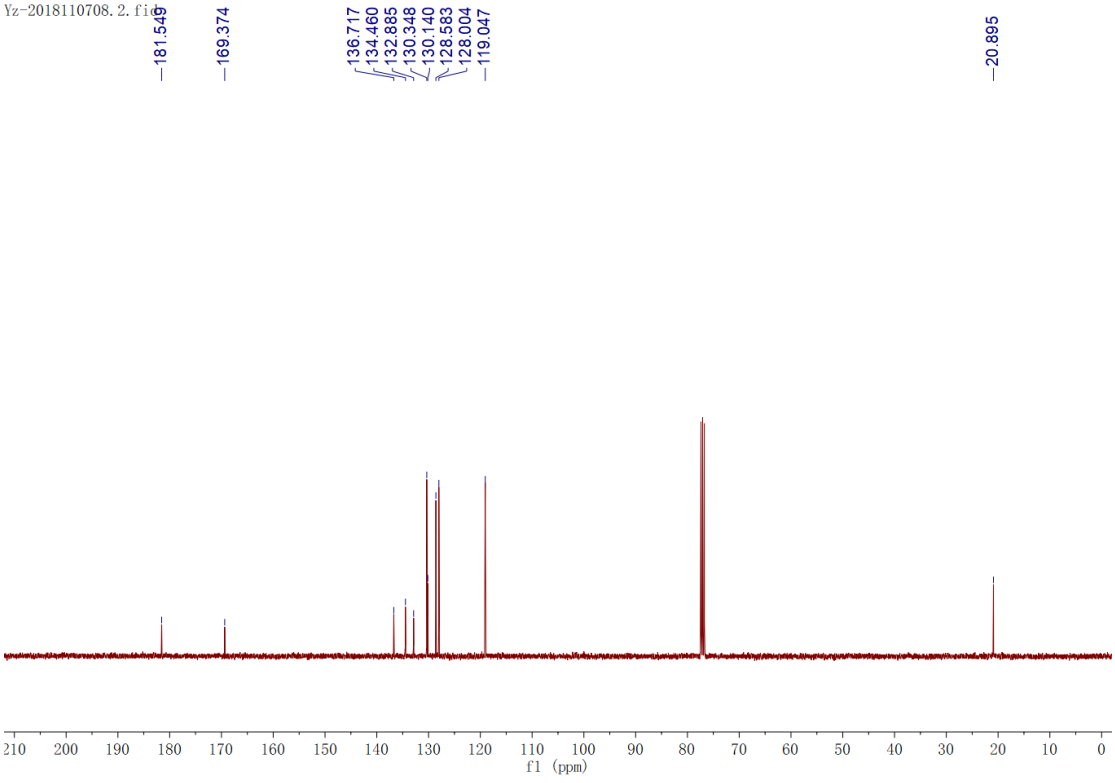

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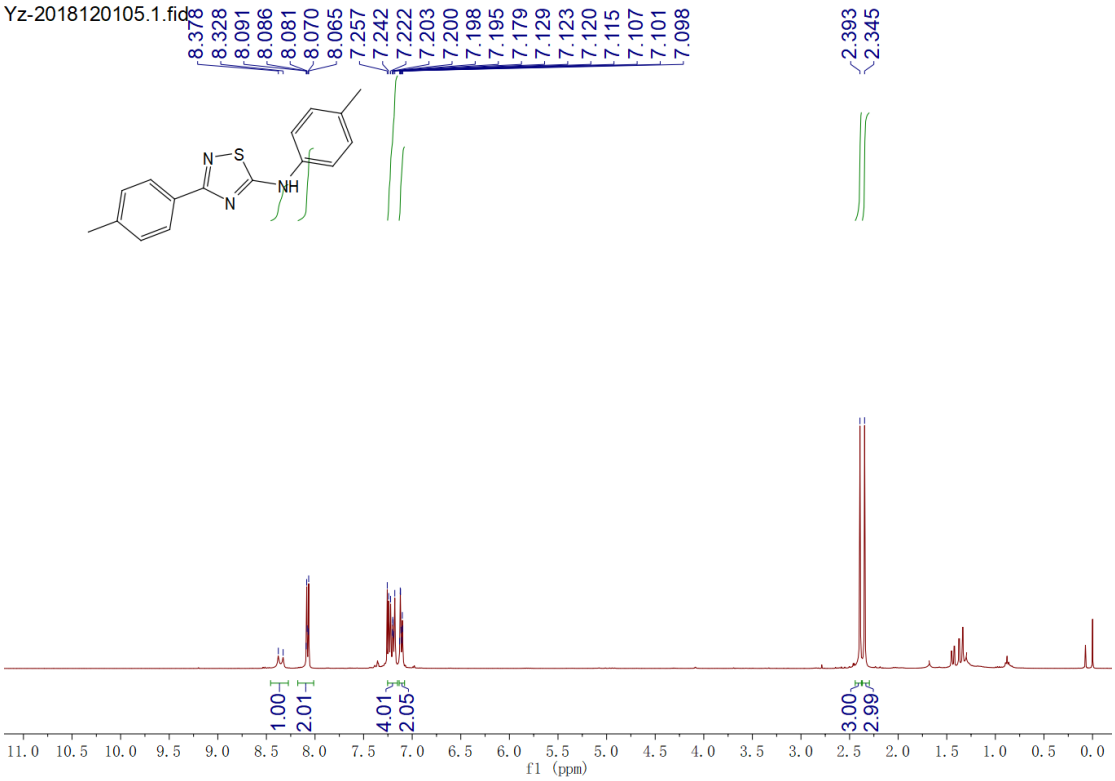

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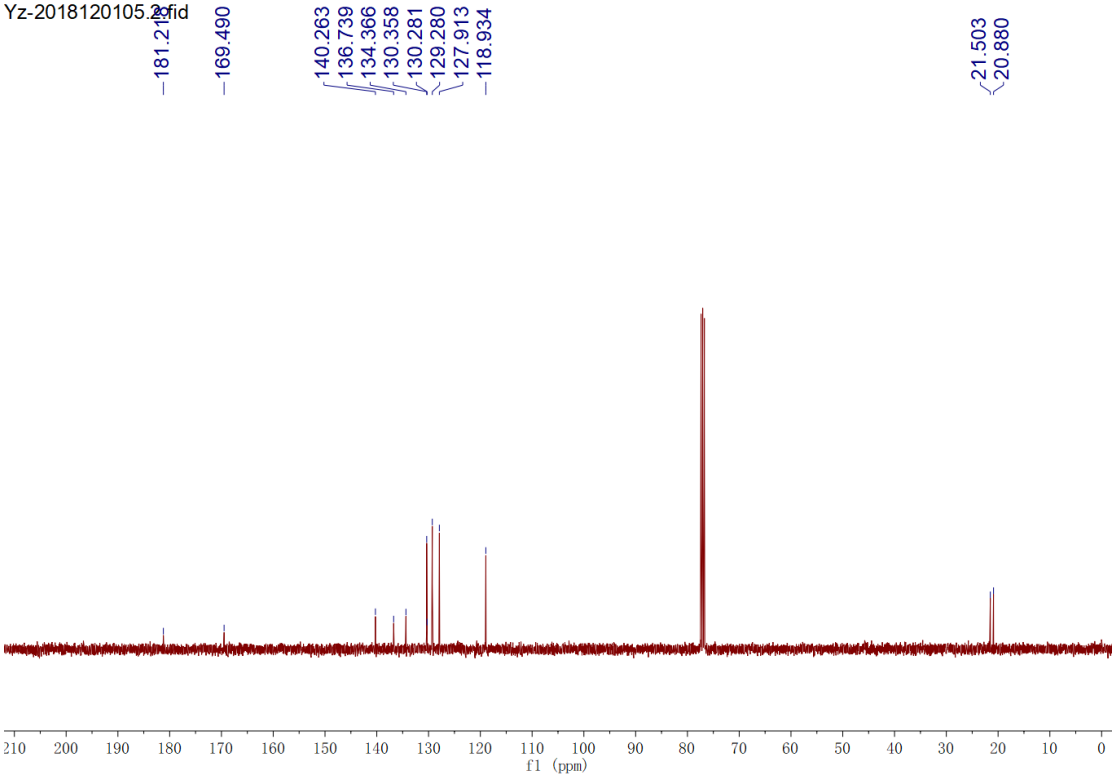

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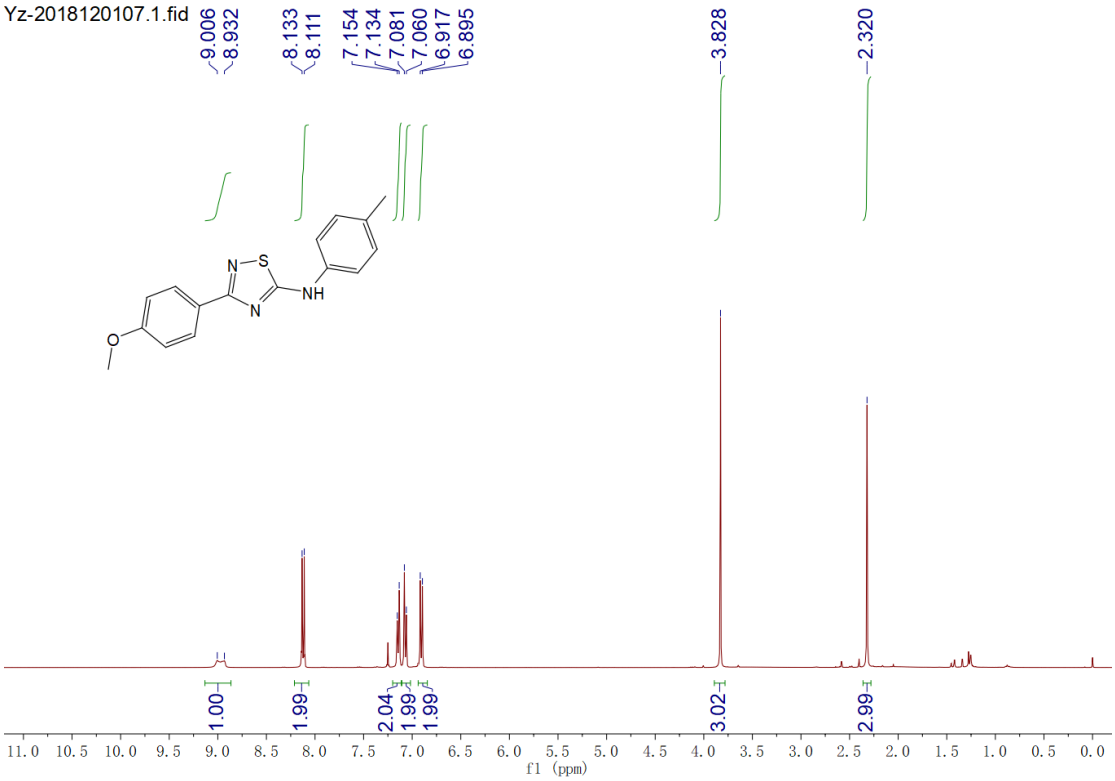

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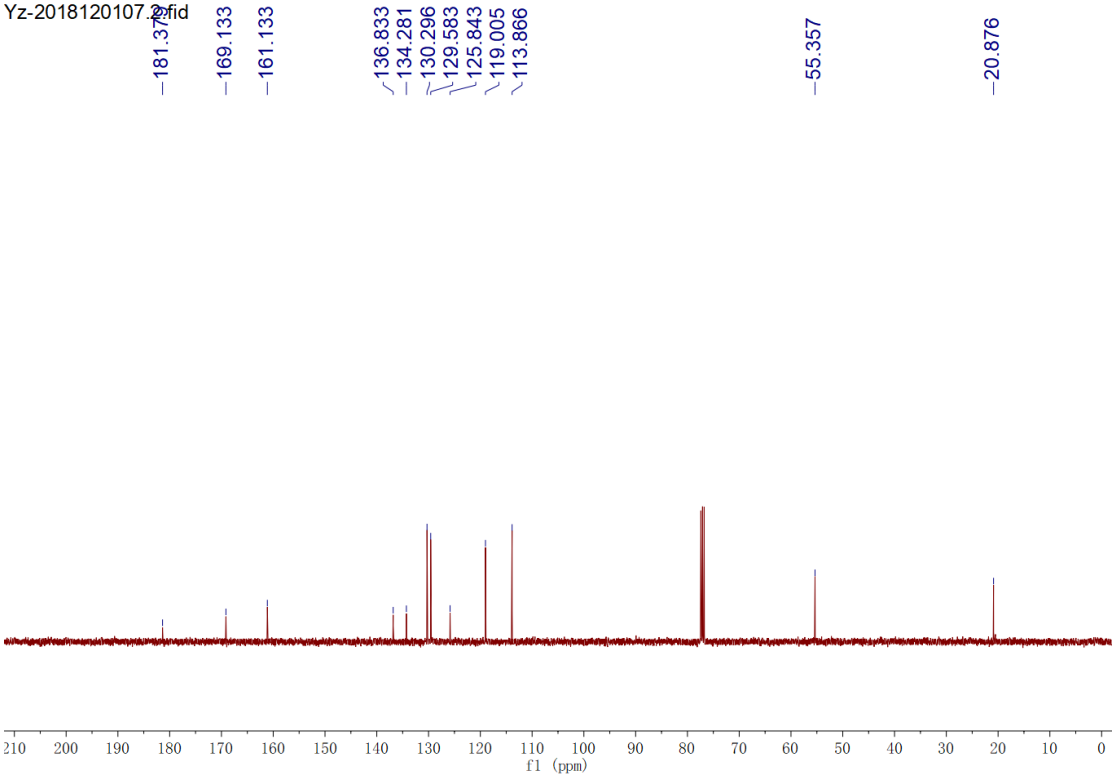

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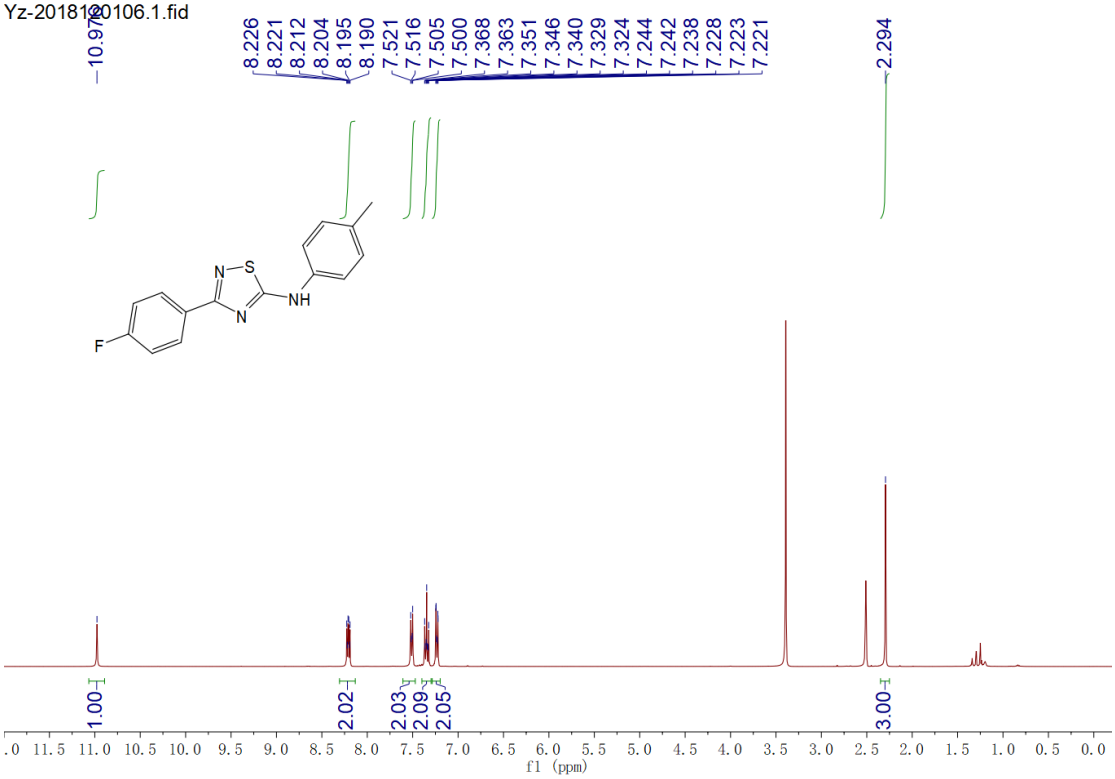

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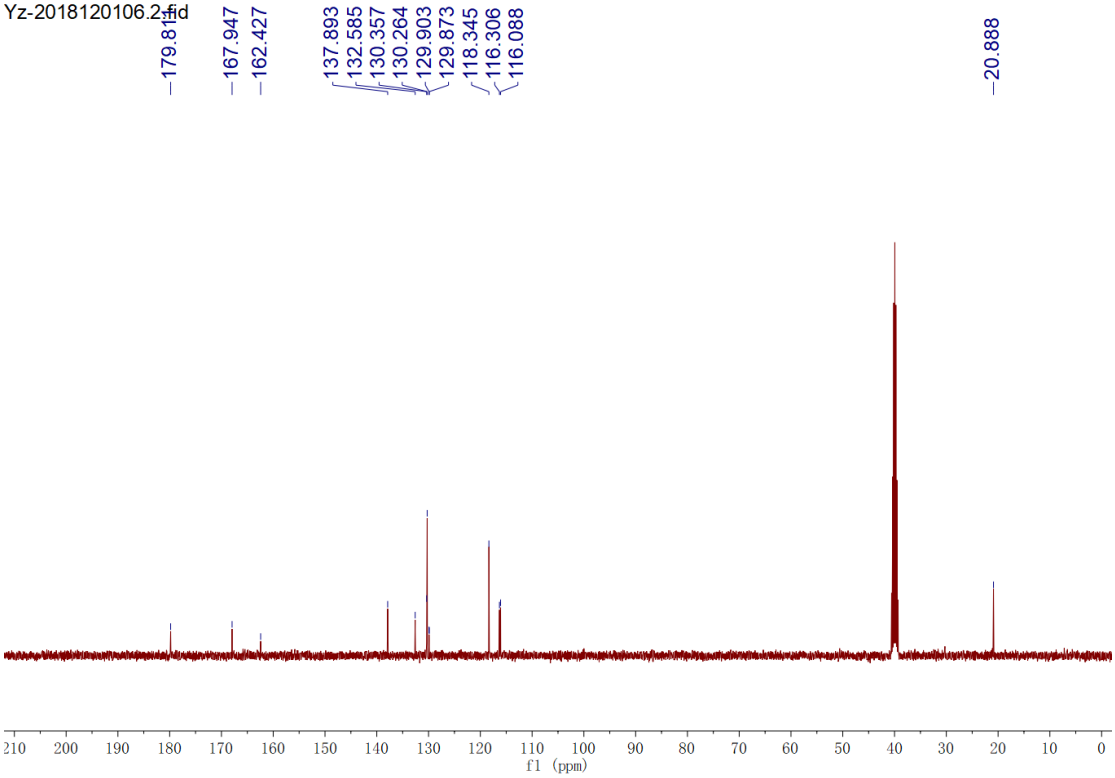

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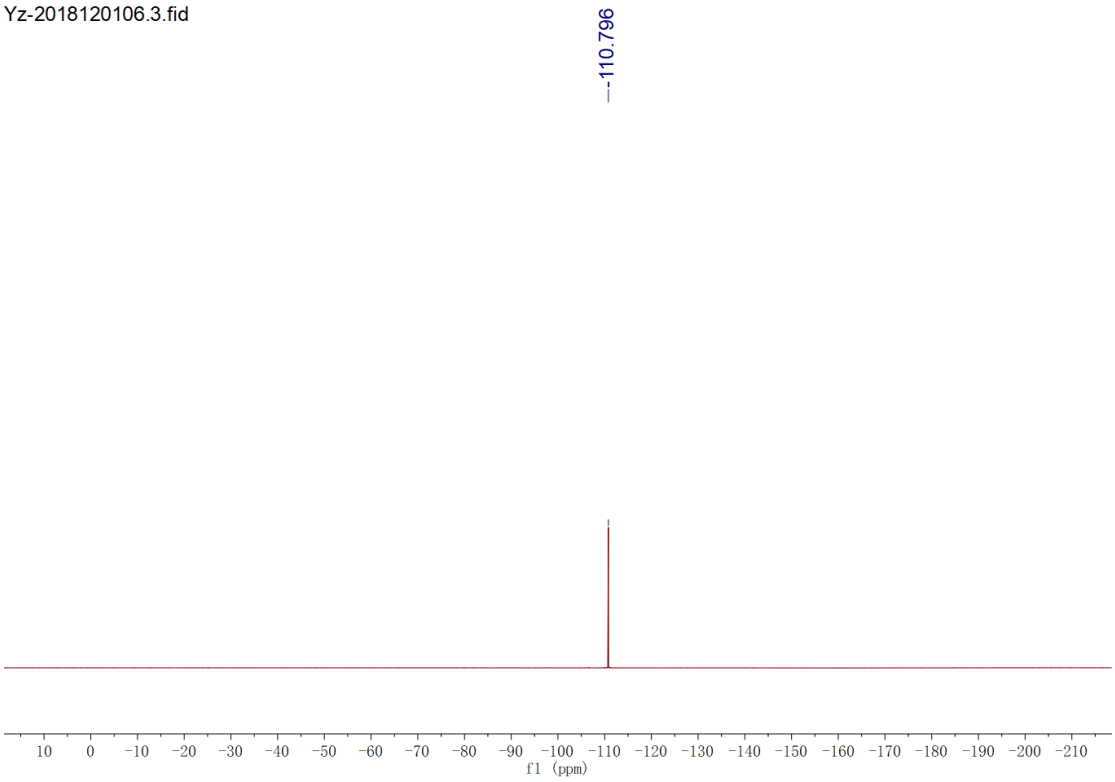

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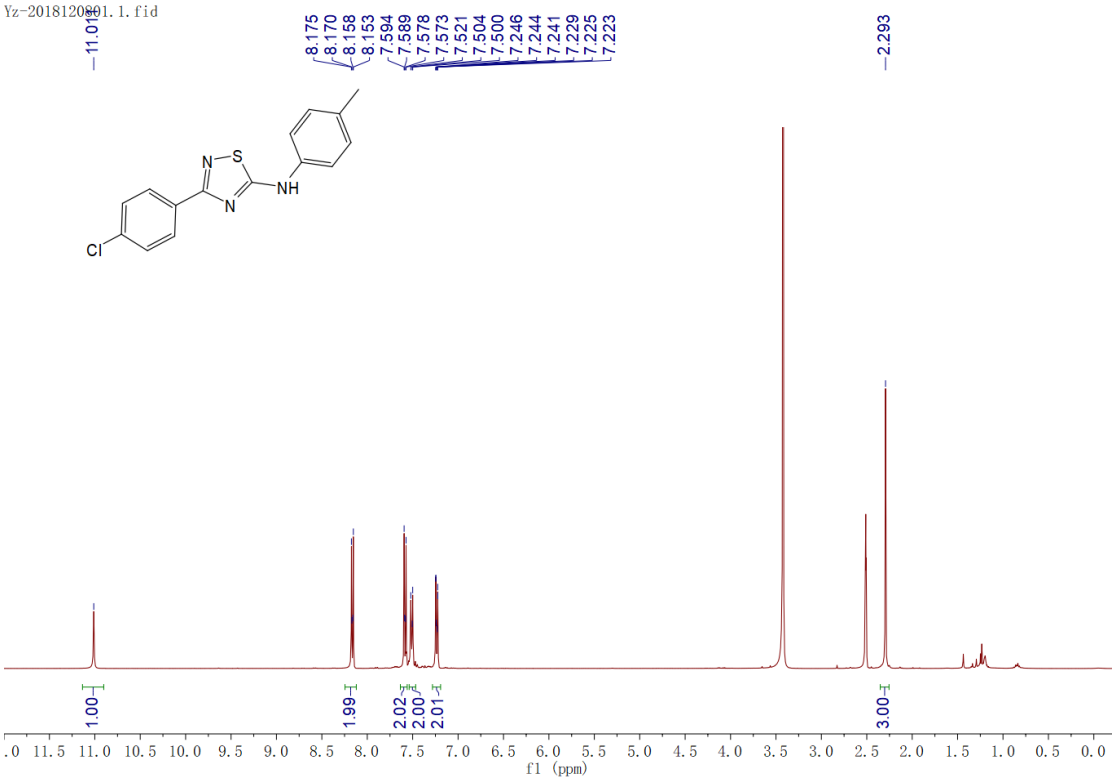

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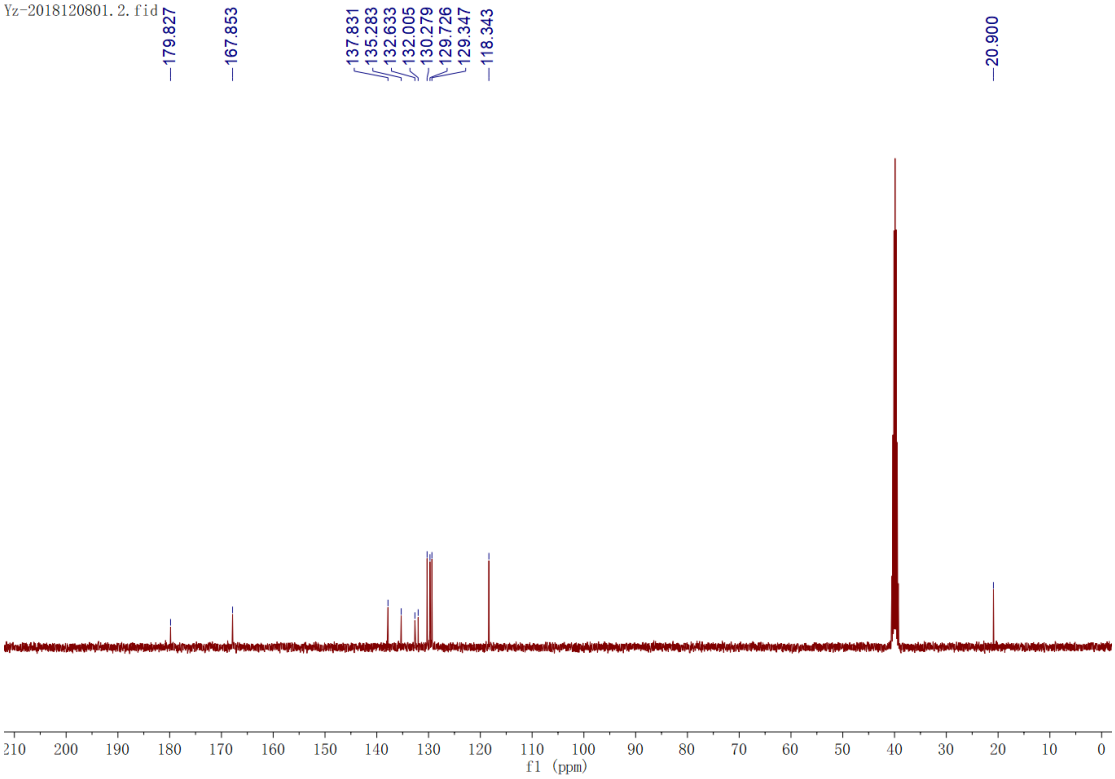

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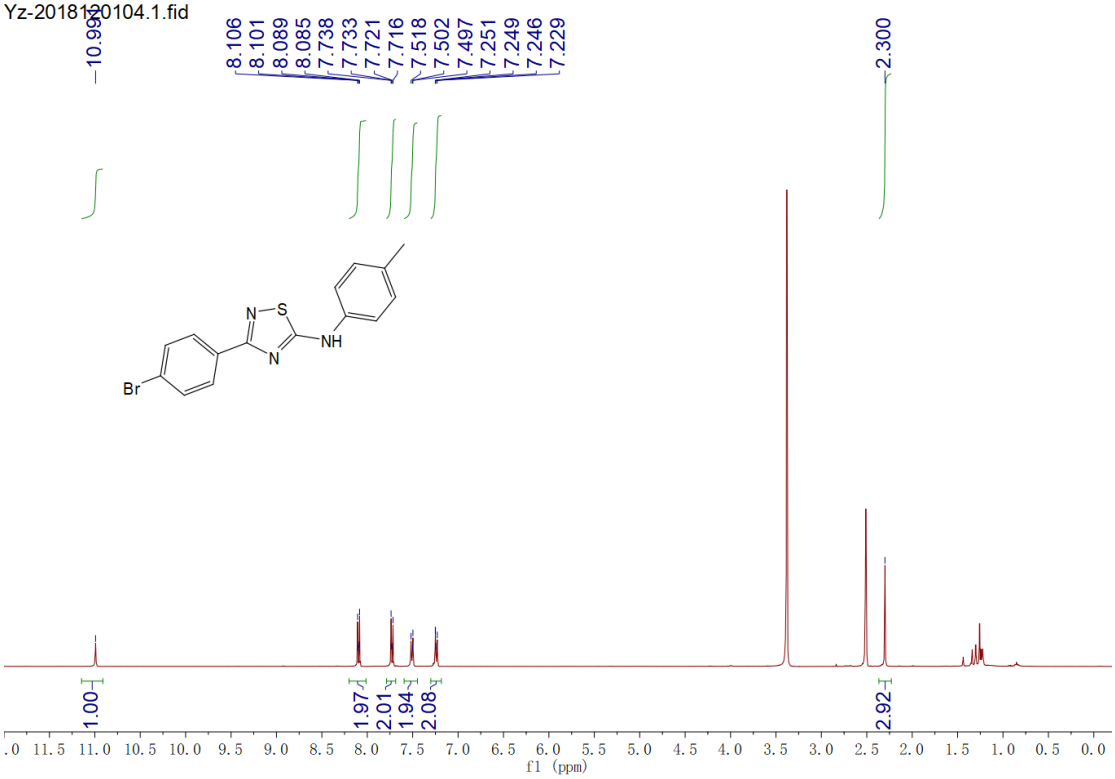

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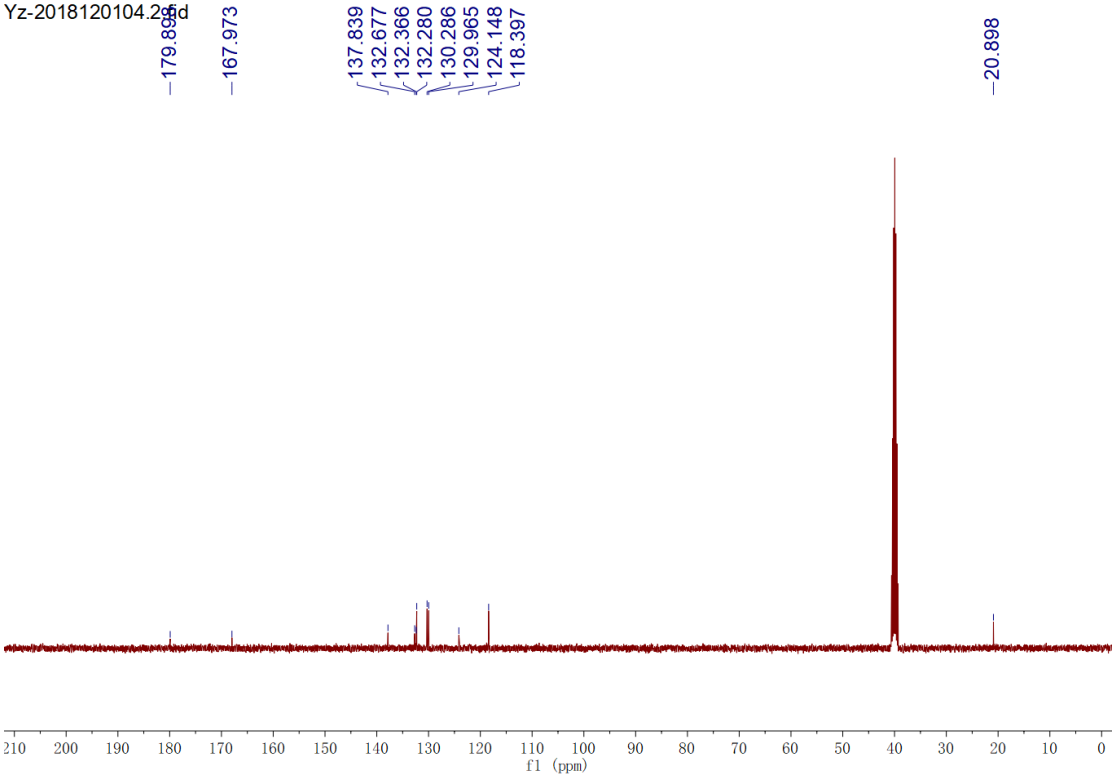

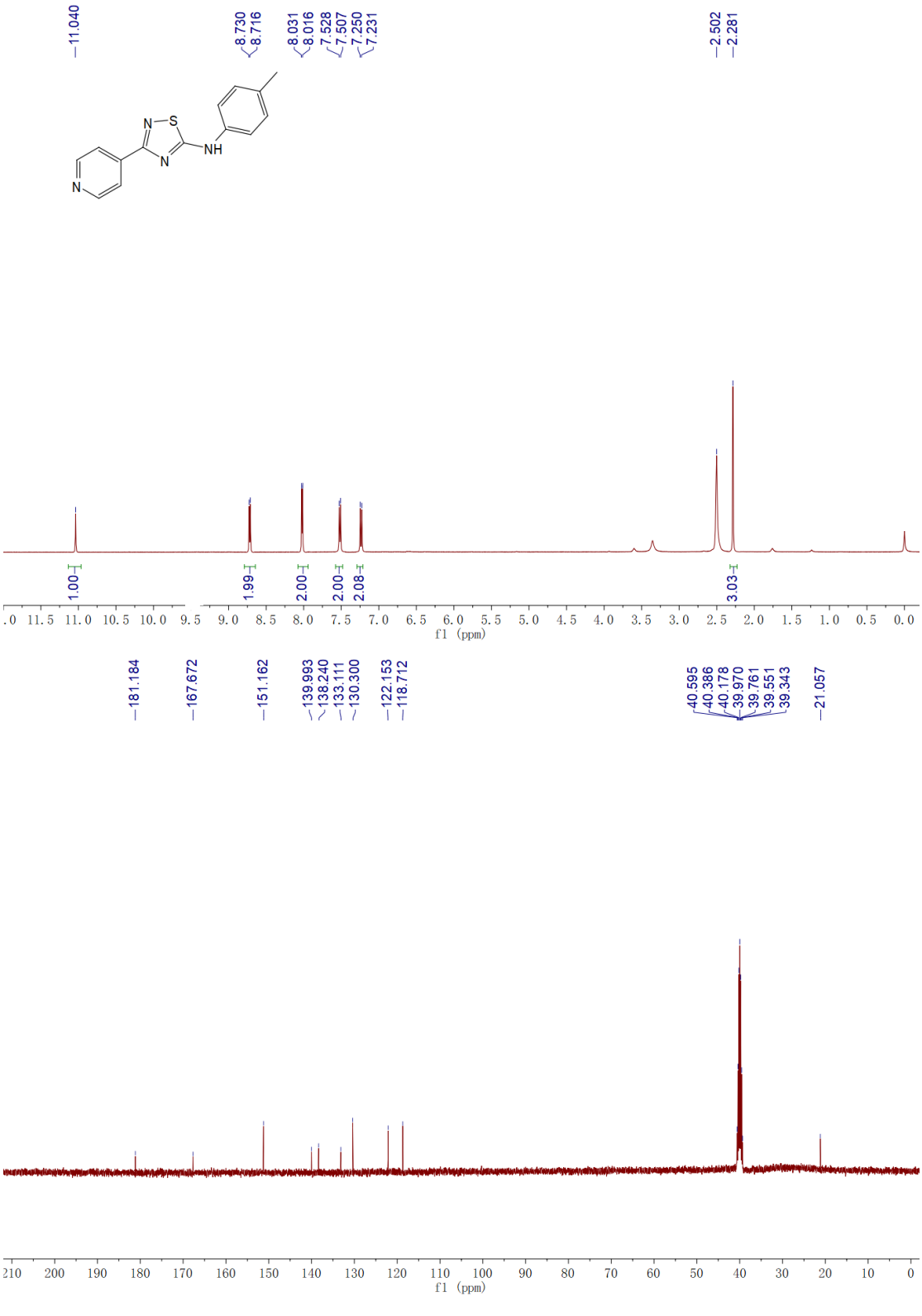
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N
S
N
NH
N
1.00
1.99
2.00
2.00
2.08
3.03
f1 (ppm)
181.184
167.672
151.162
139.993
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f1 (ppm)

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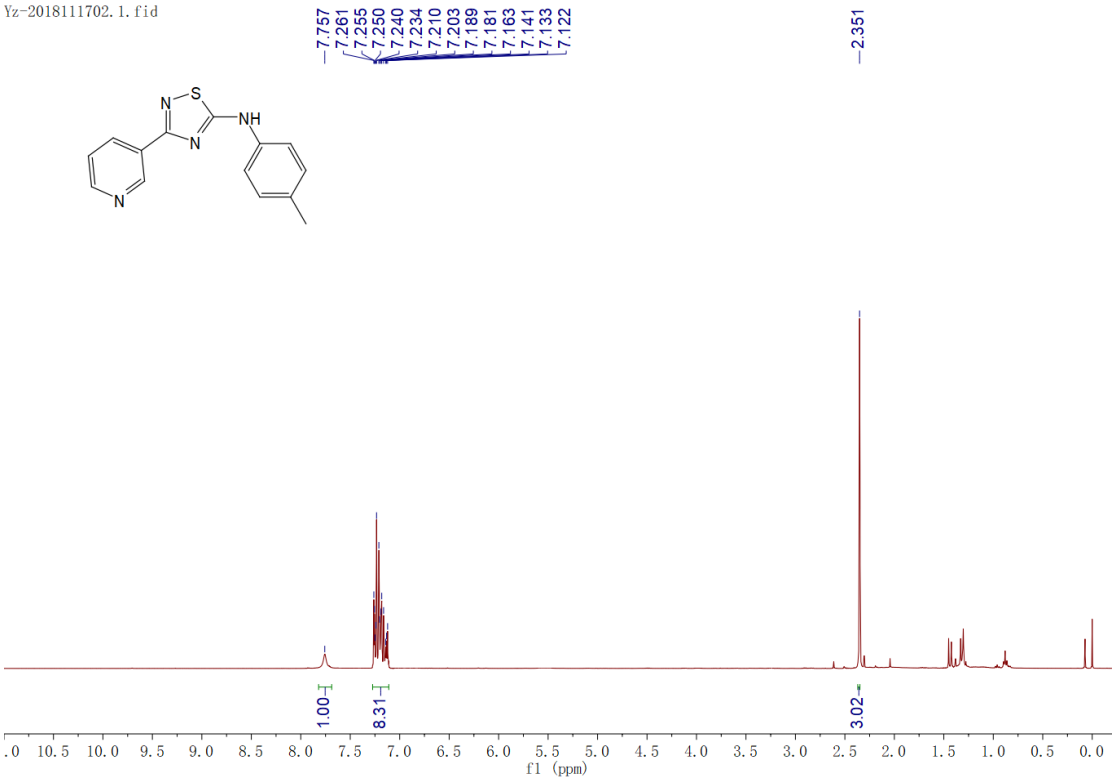

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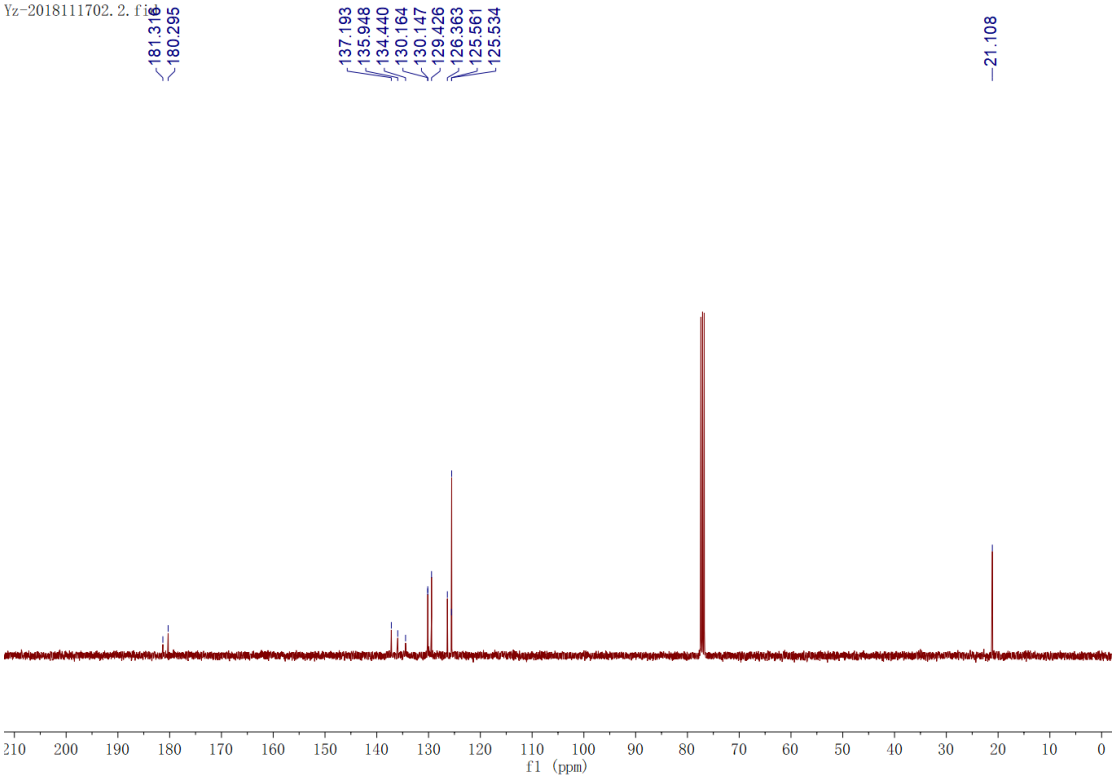

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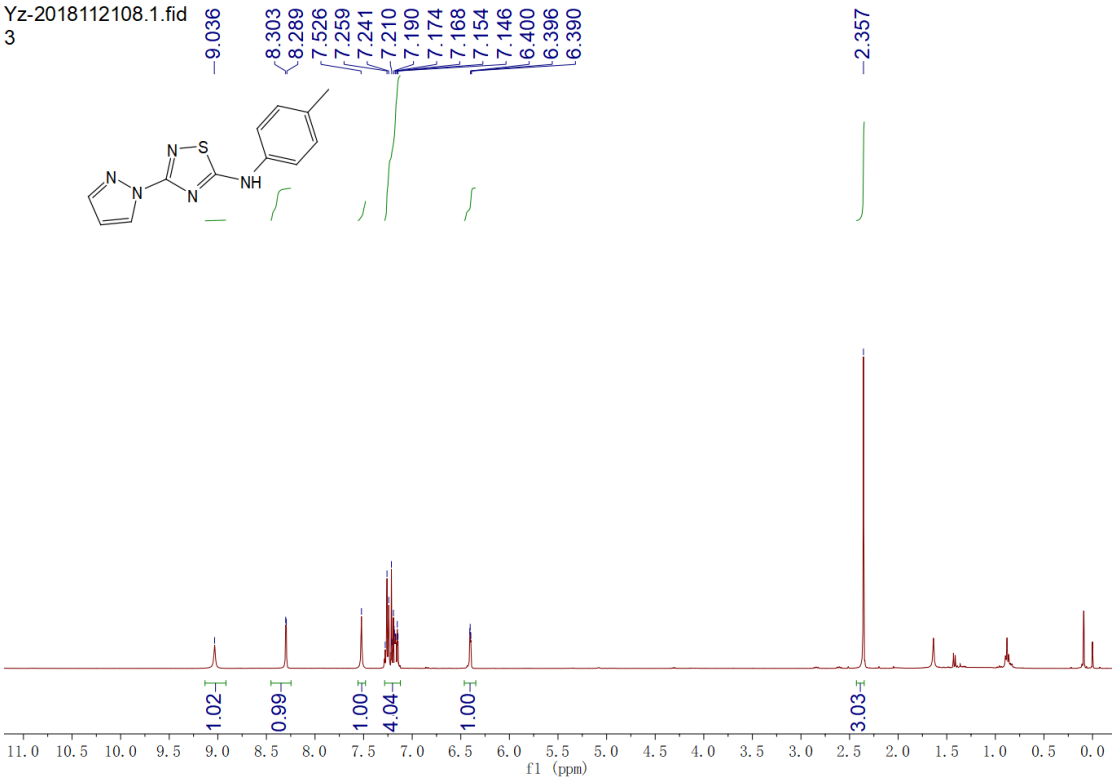

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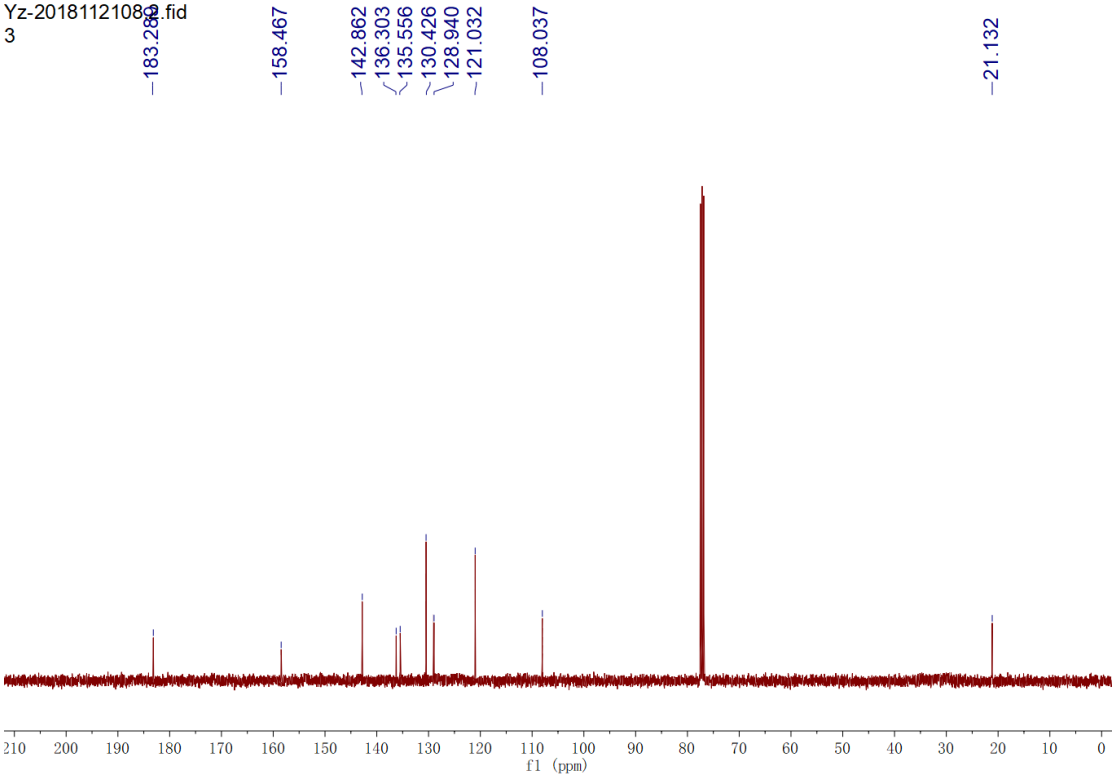

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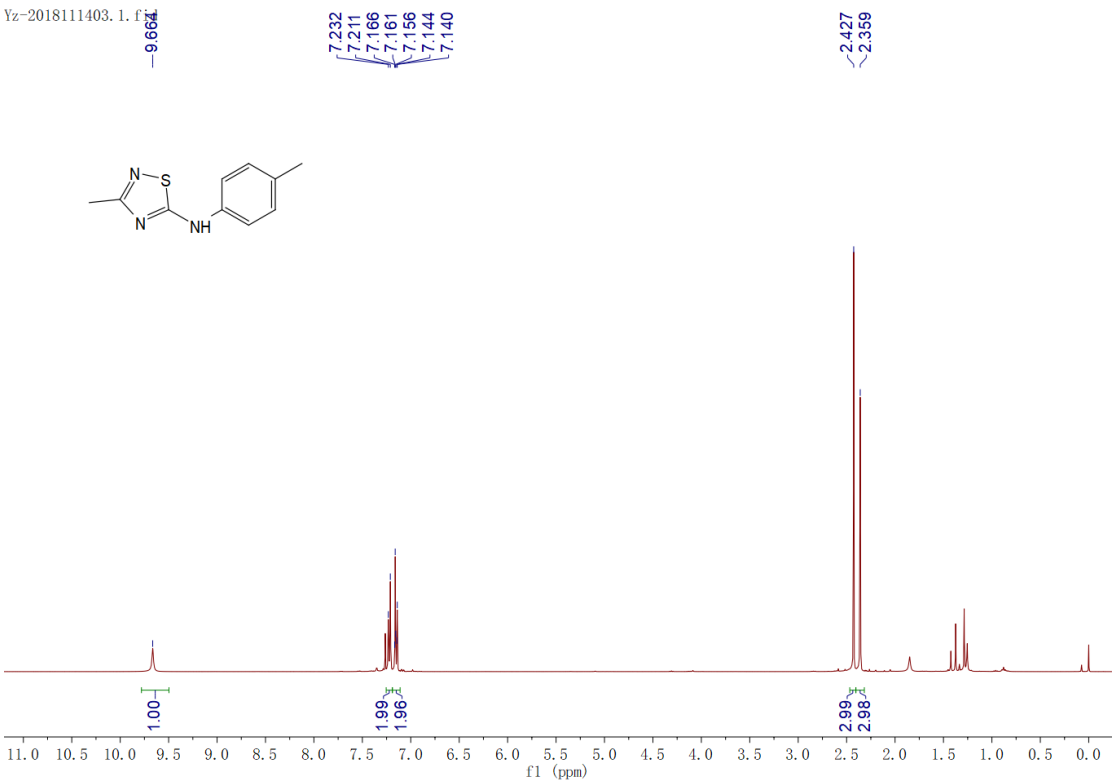

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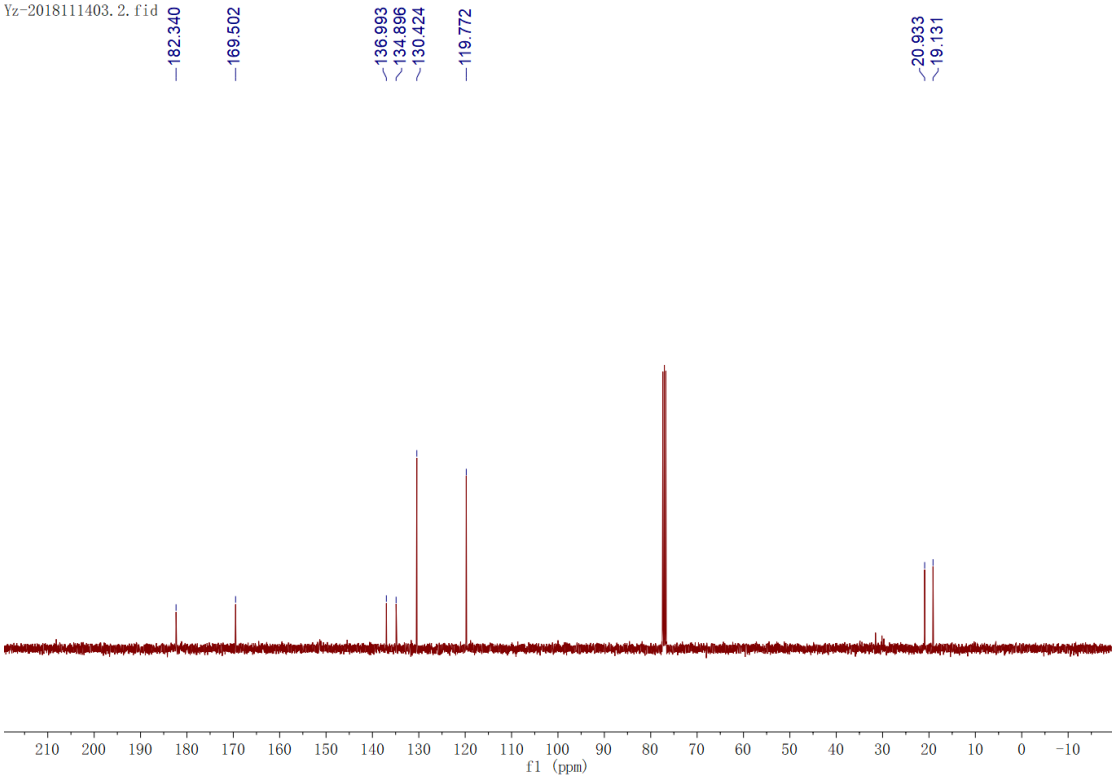

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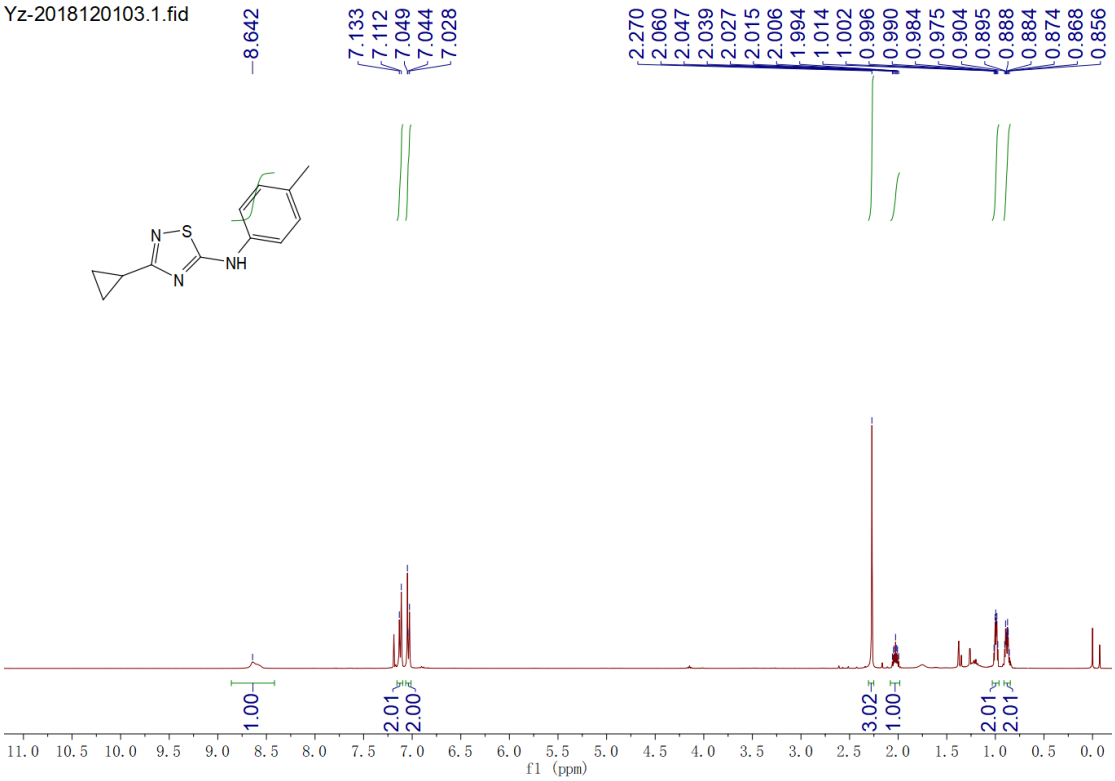

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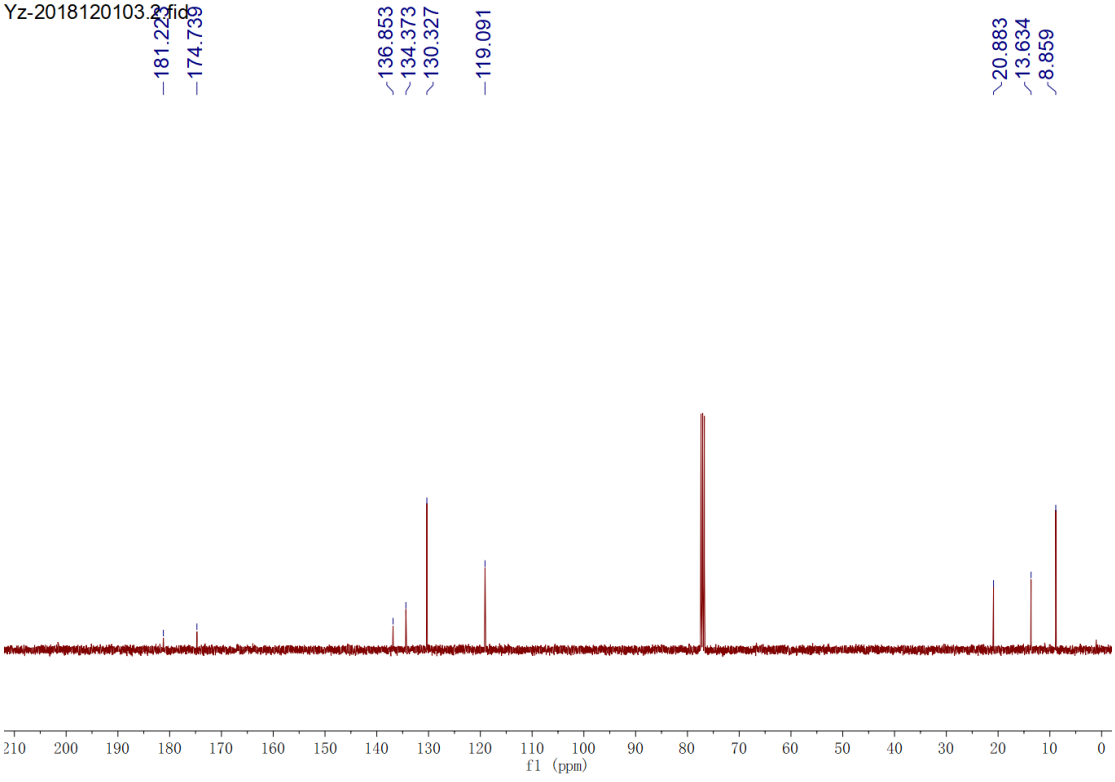

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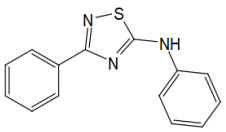

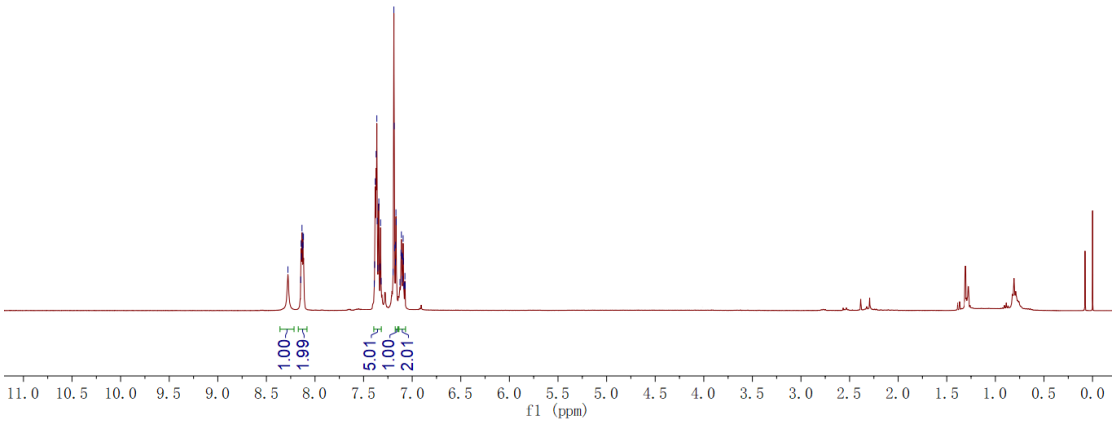

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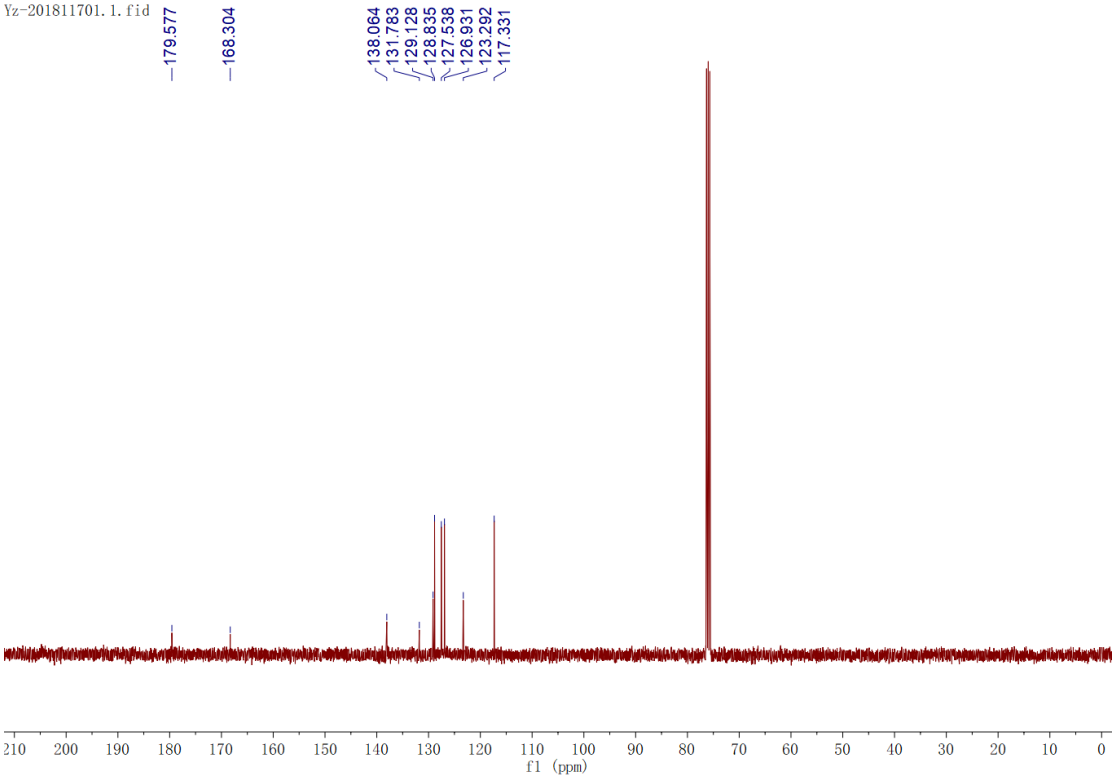

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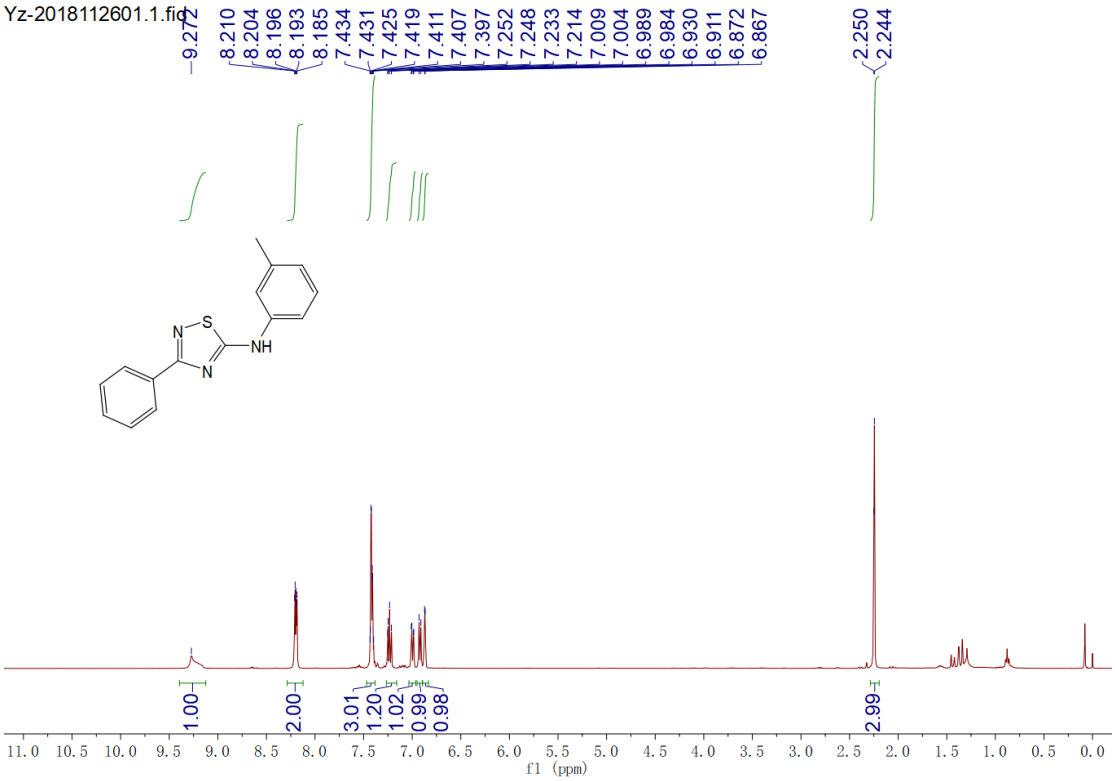

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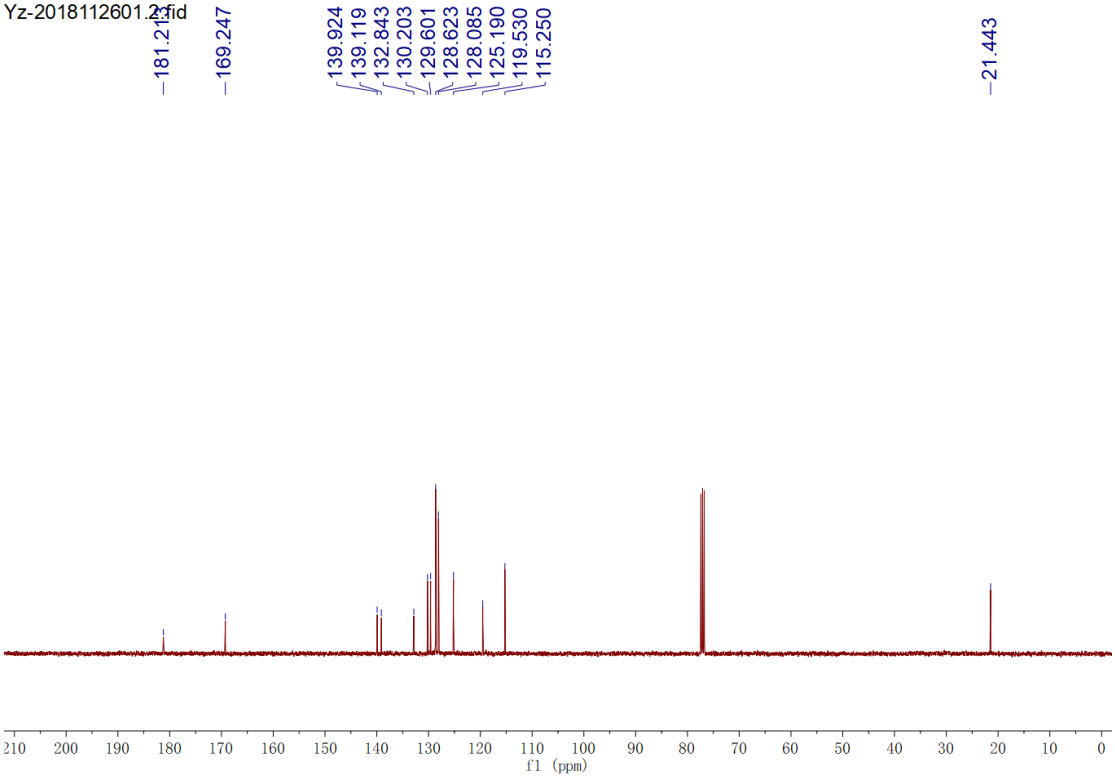

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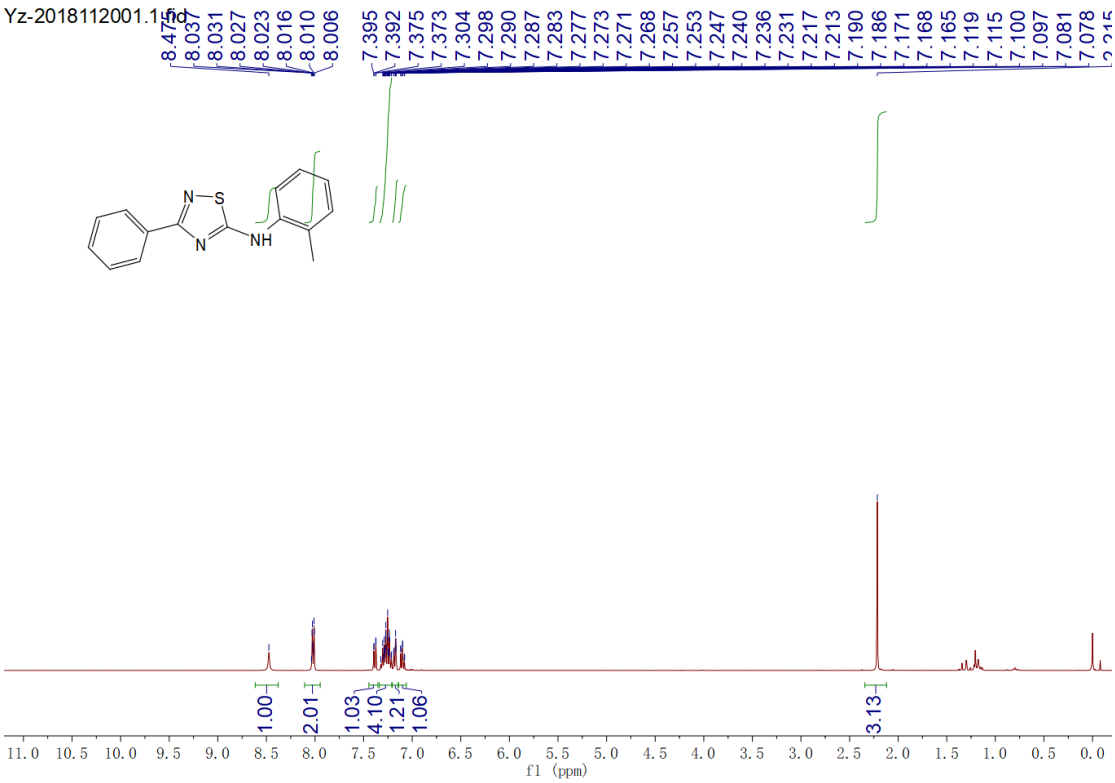

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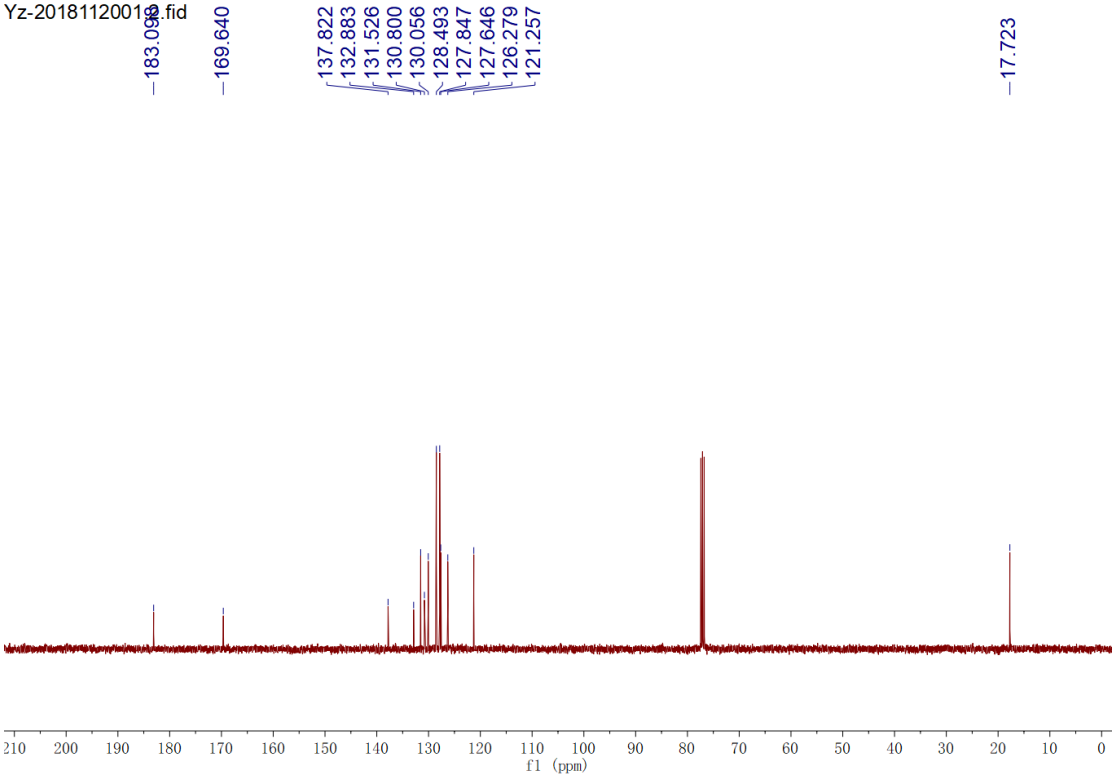

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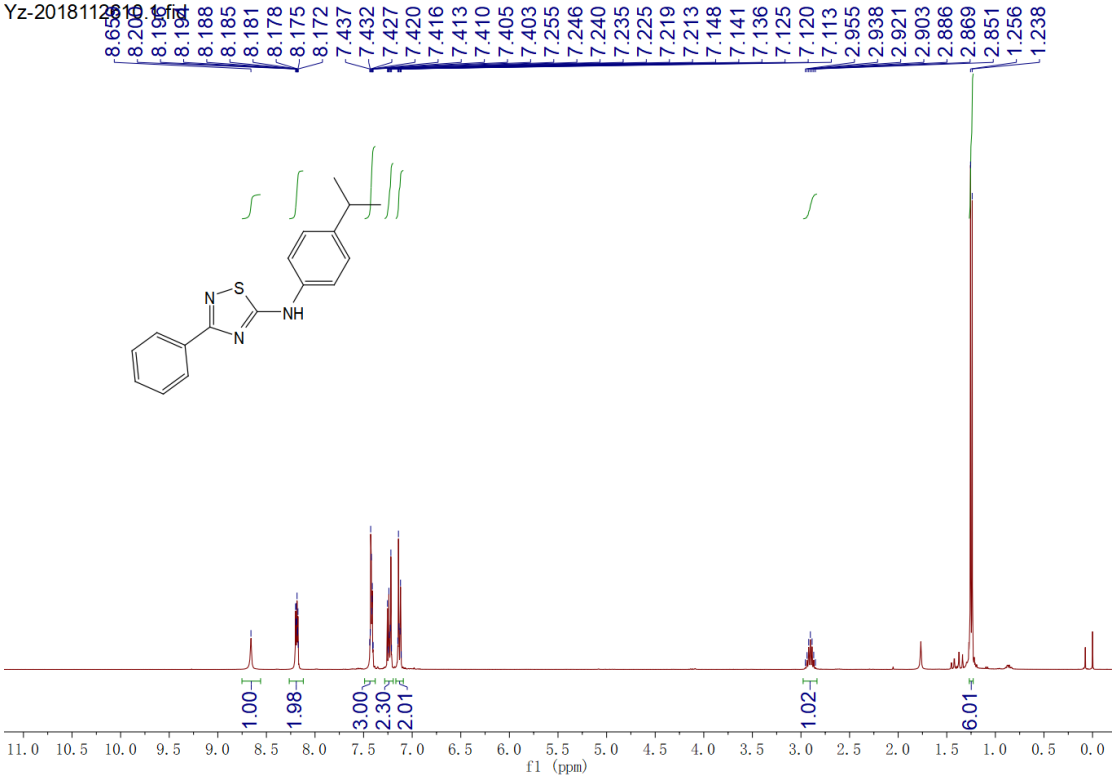

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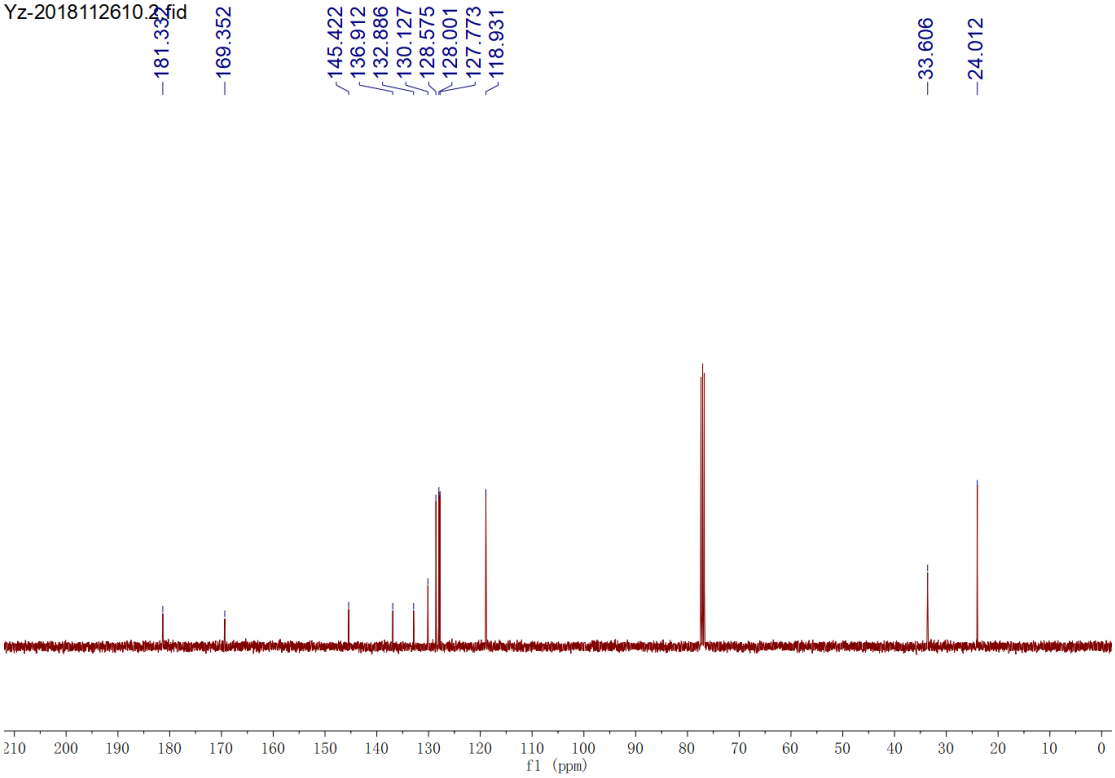

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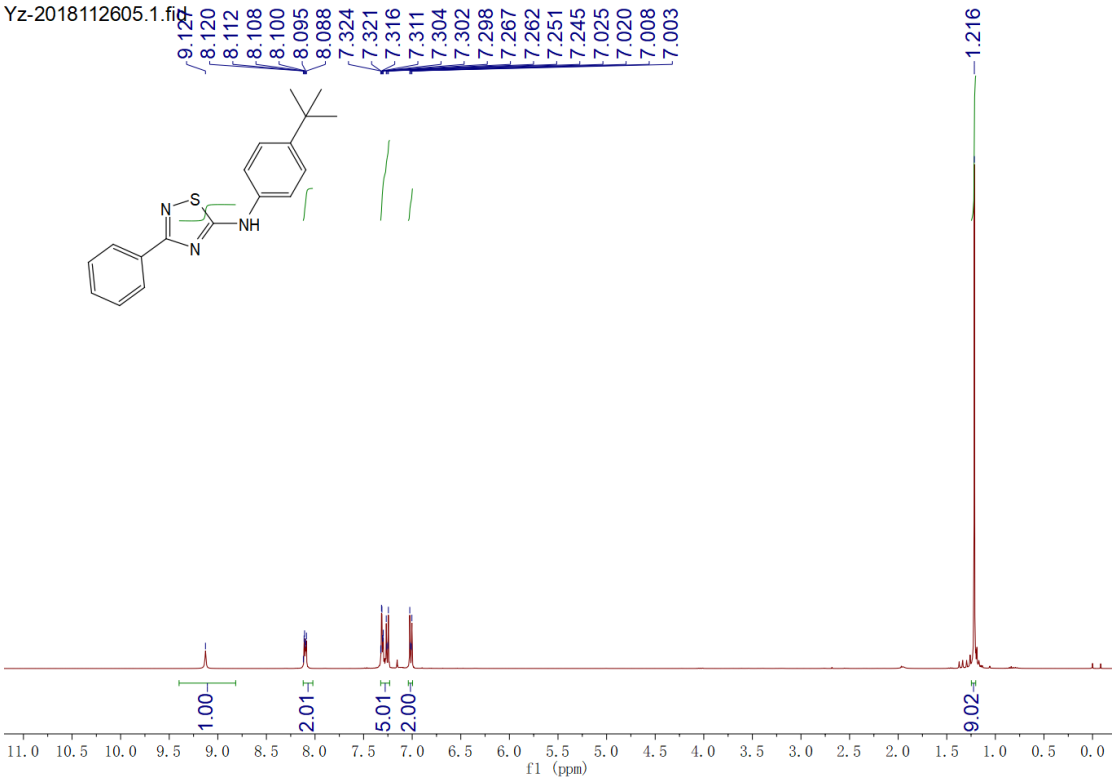

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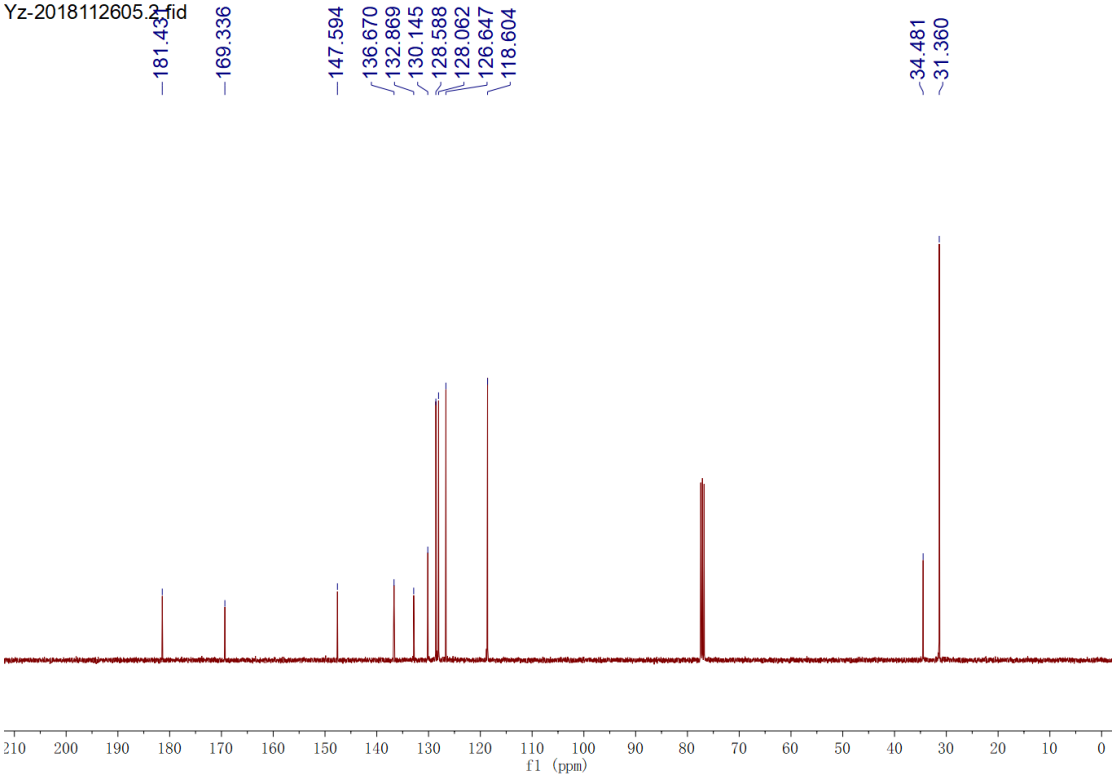

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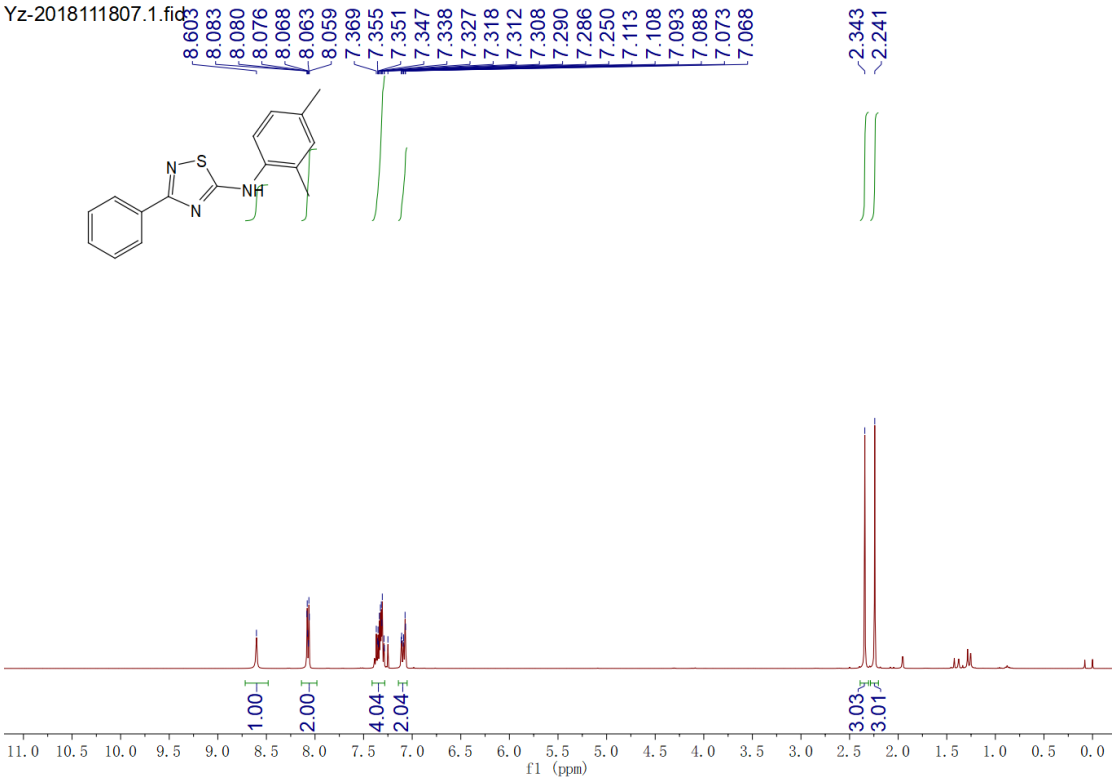

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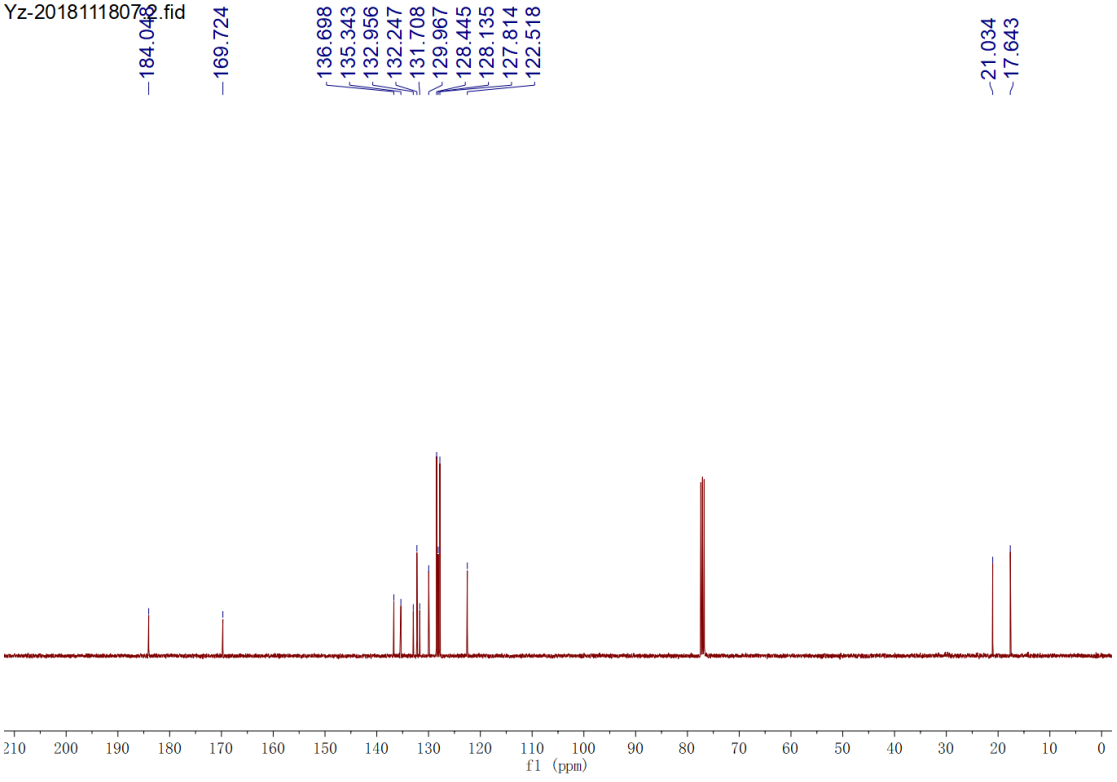

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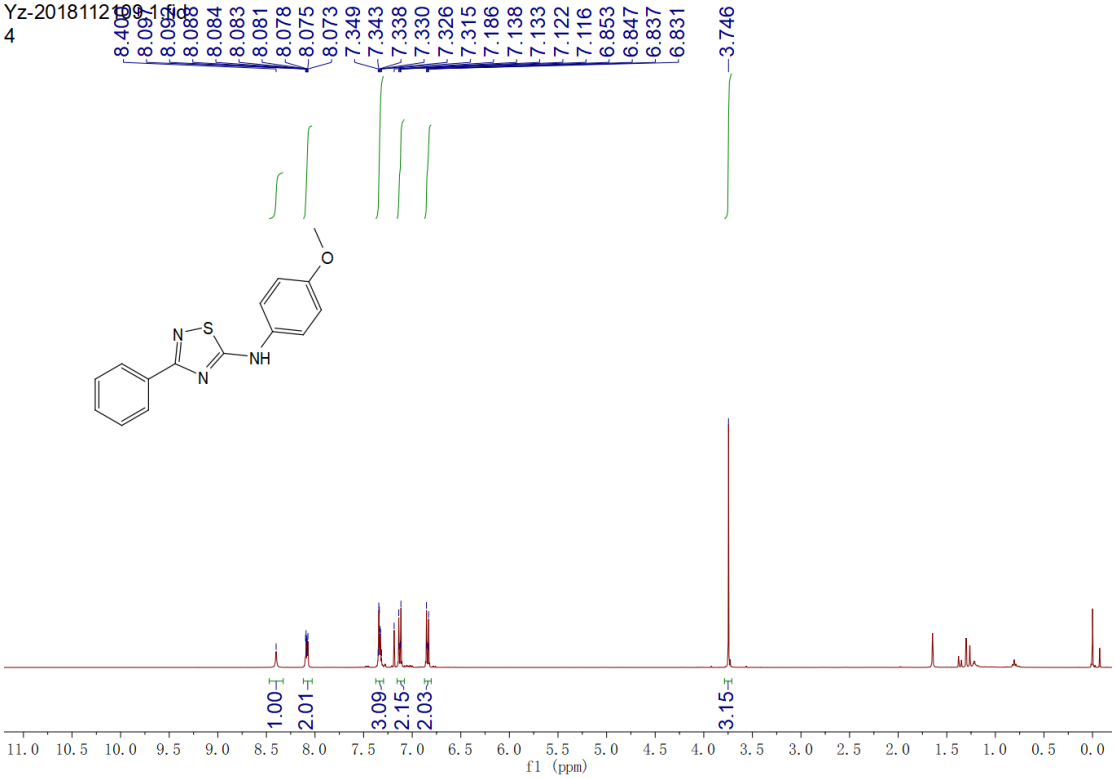

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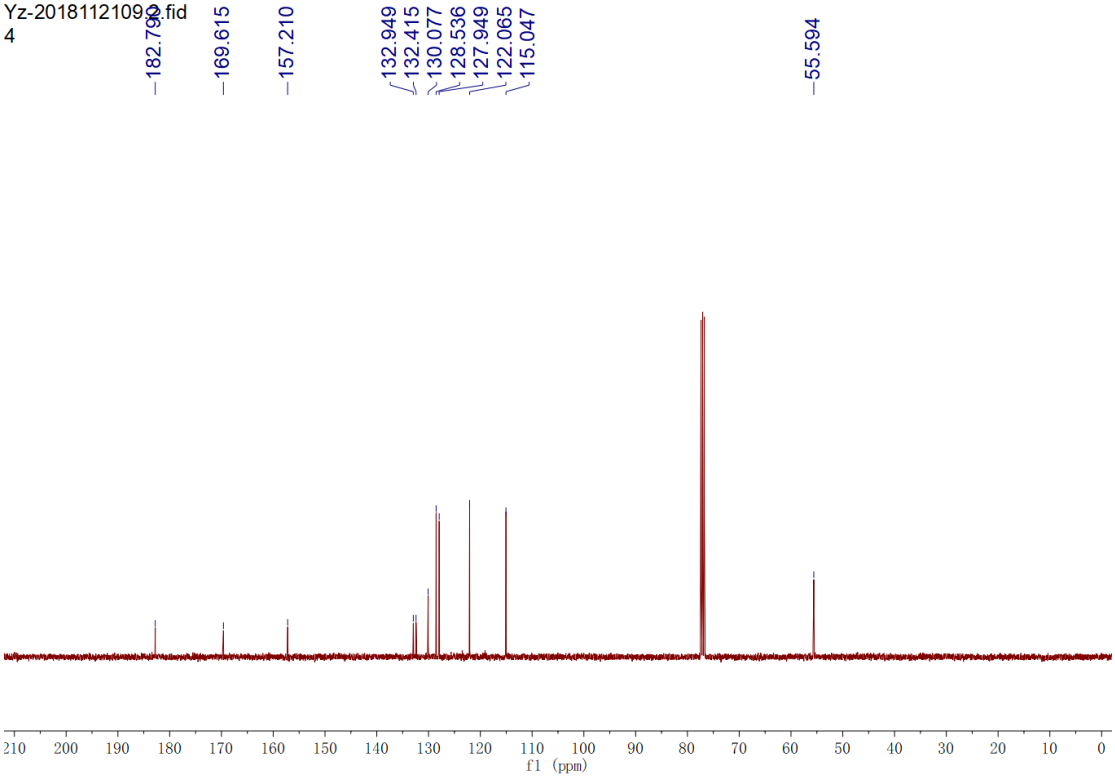

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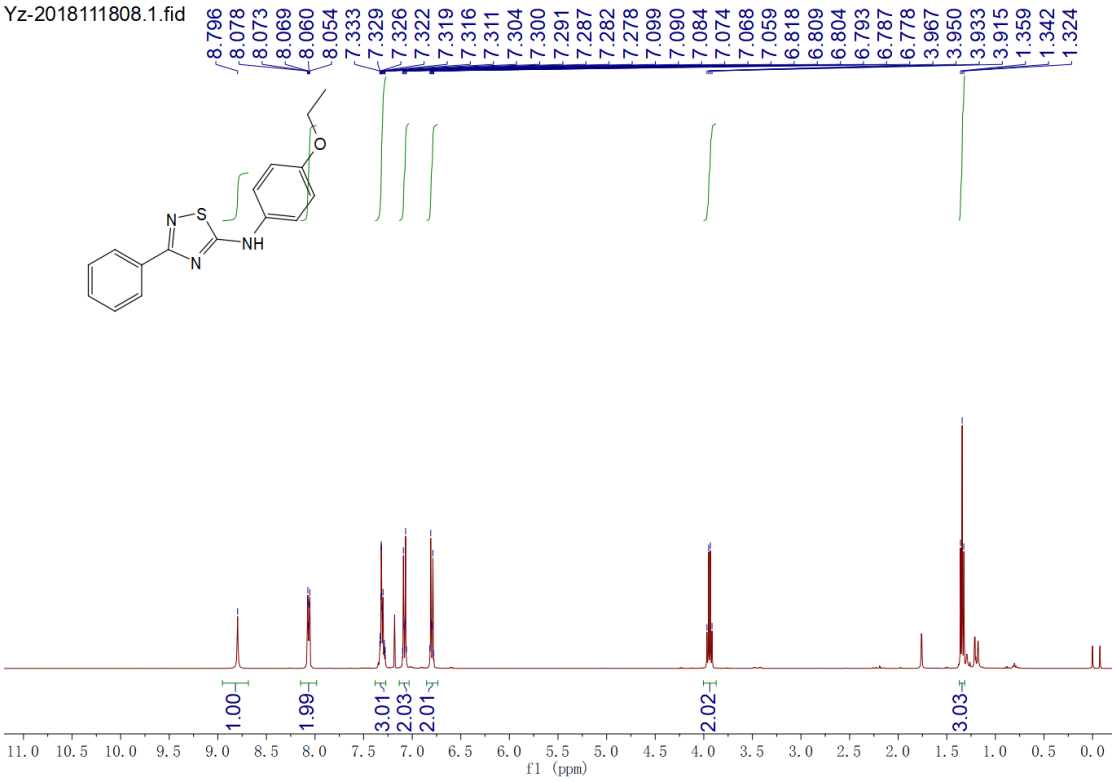

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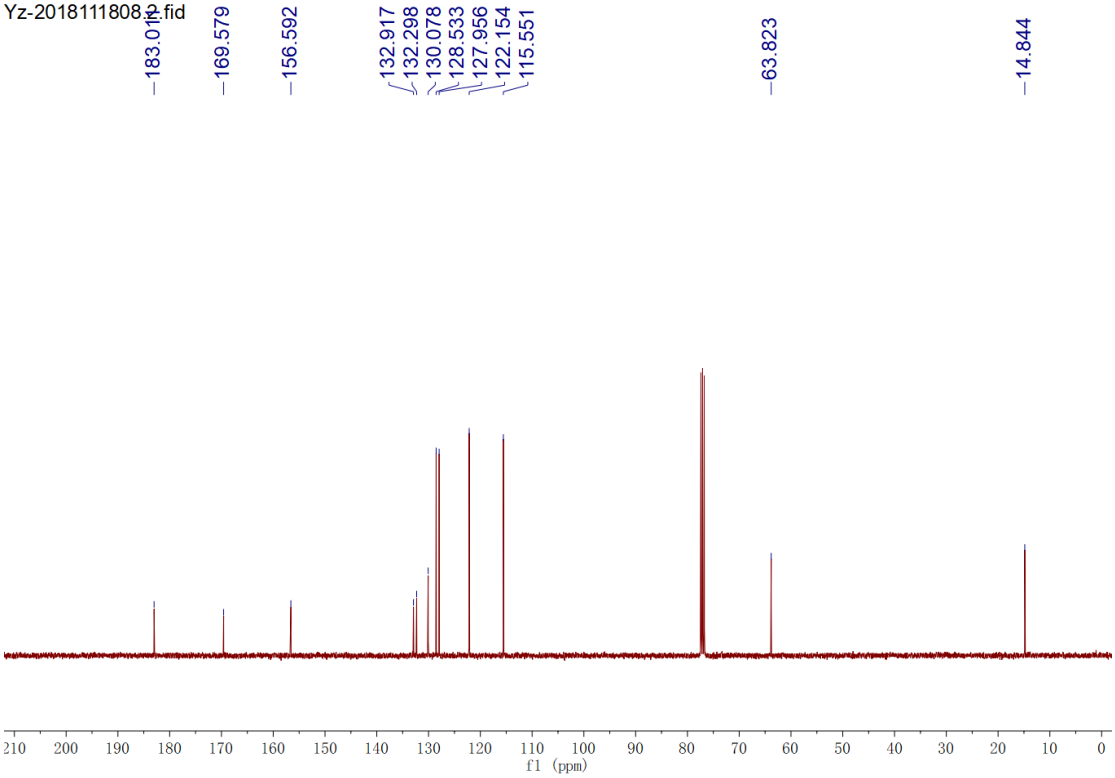

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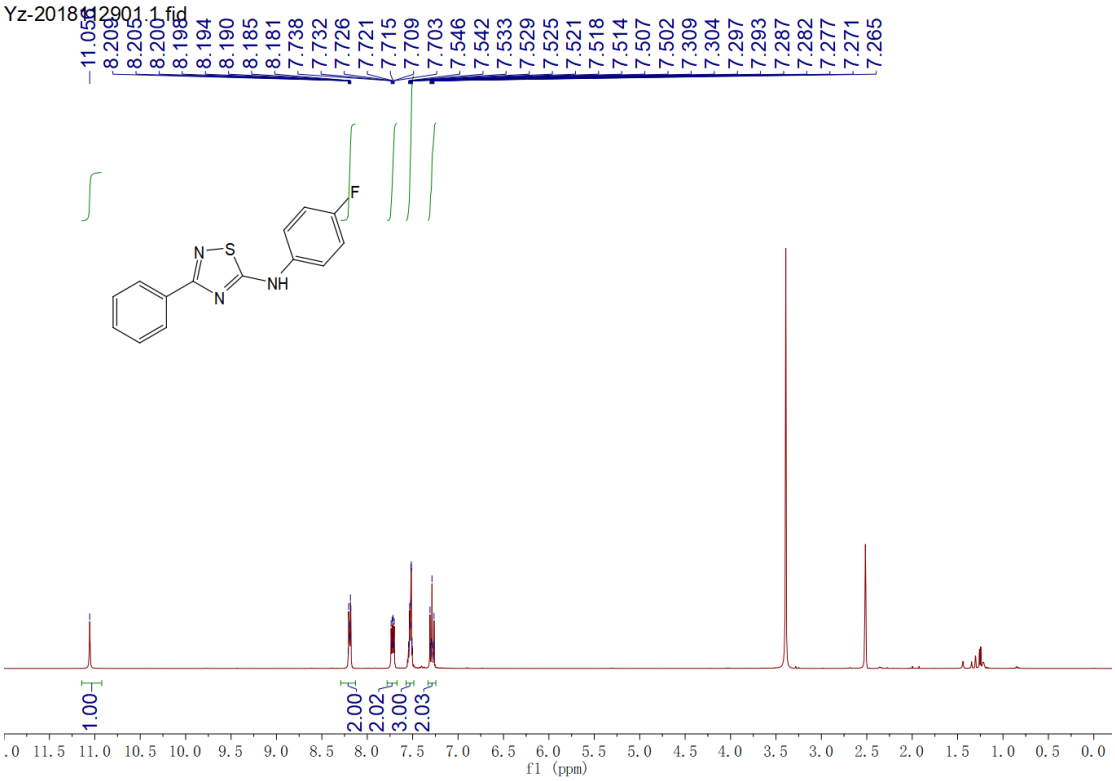

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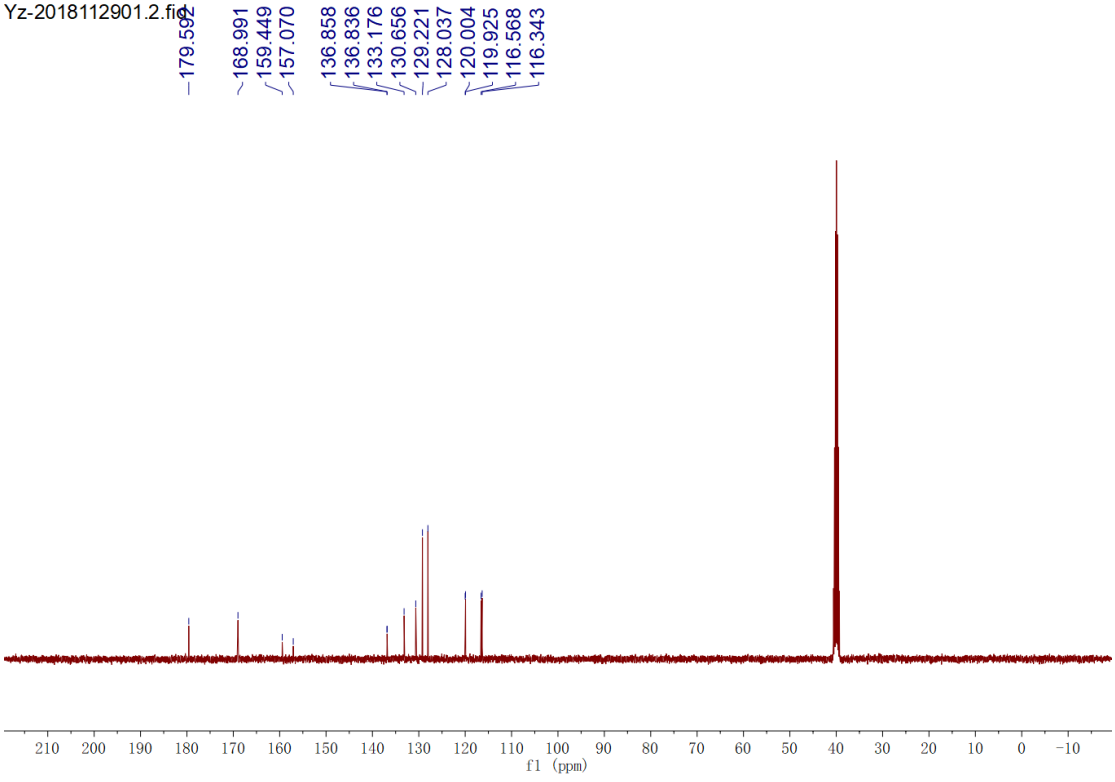

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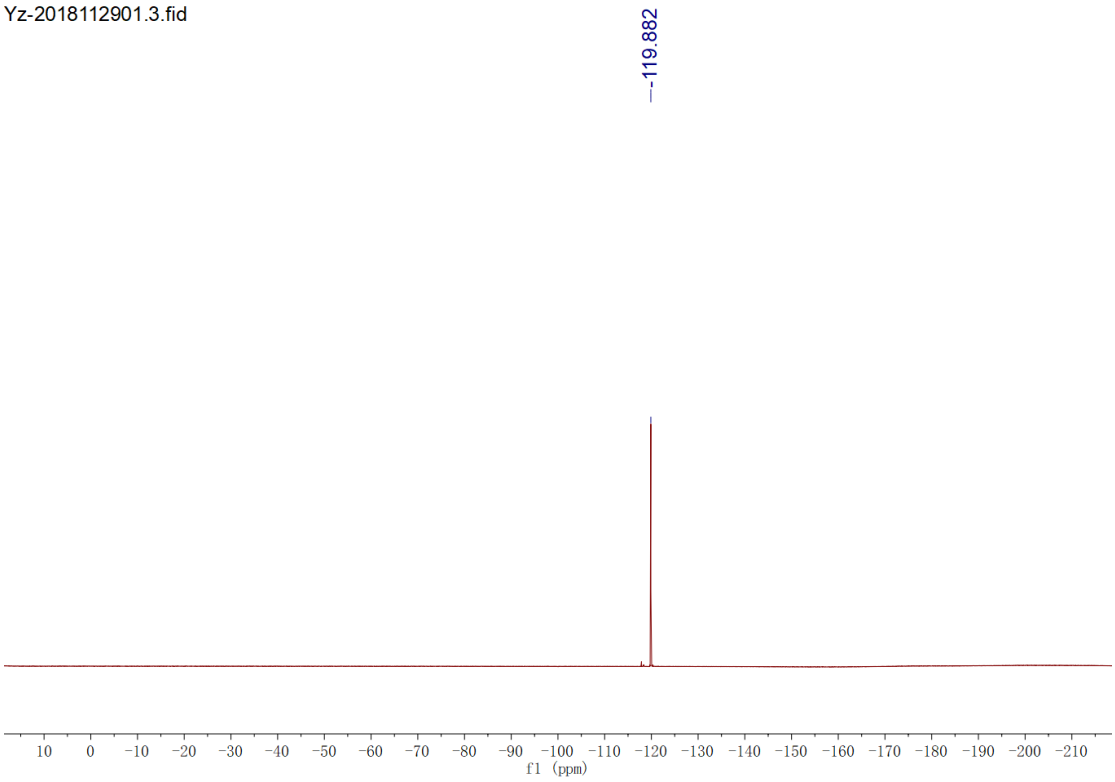

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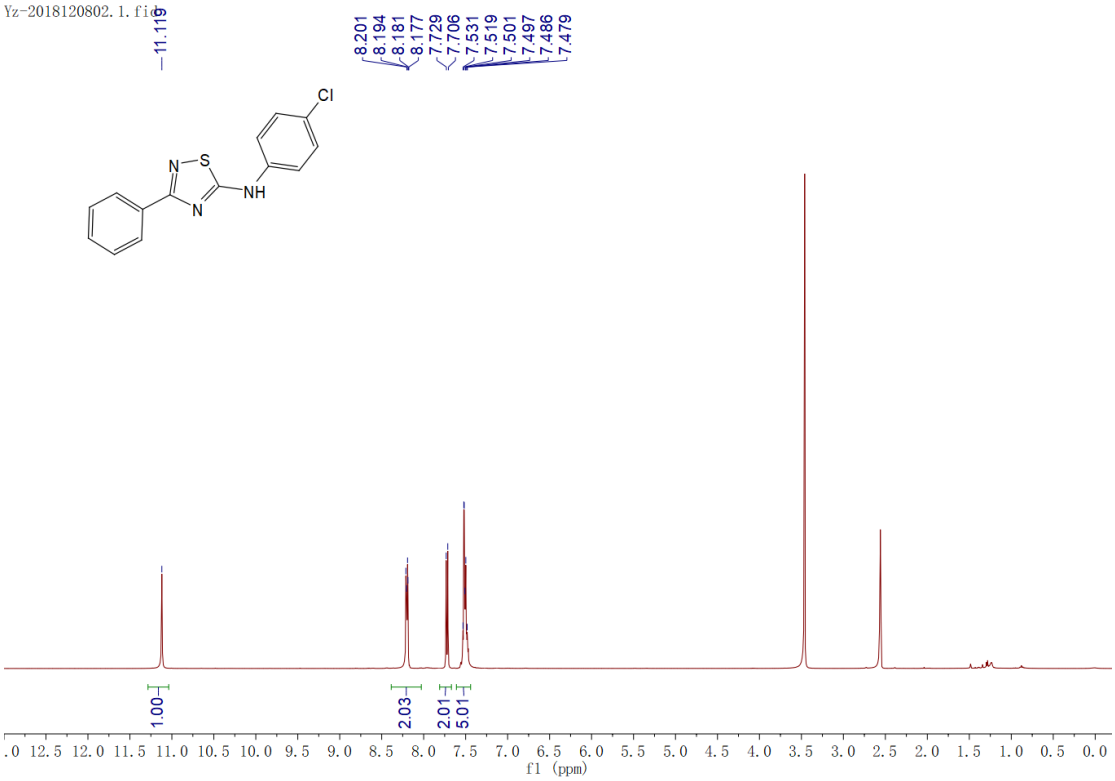

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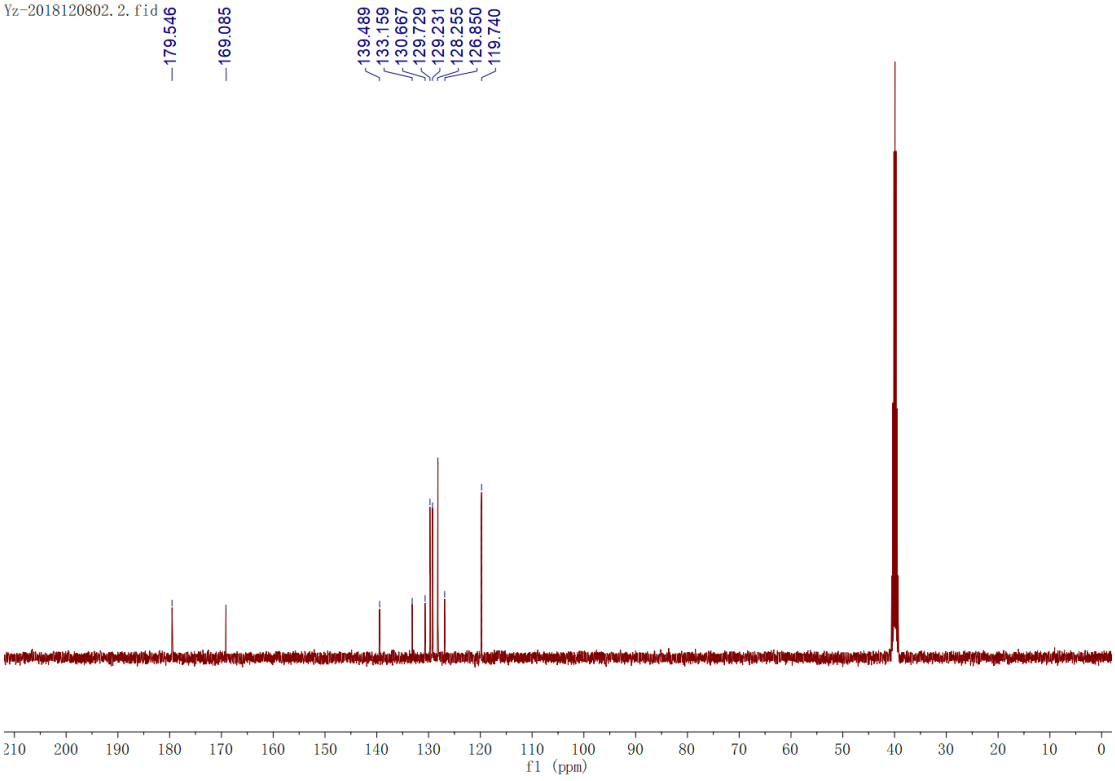

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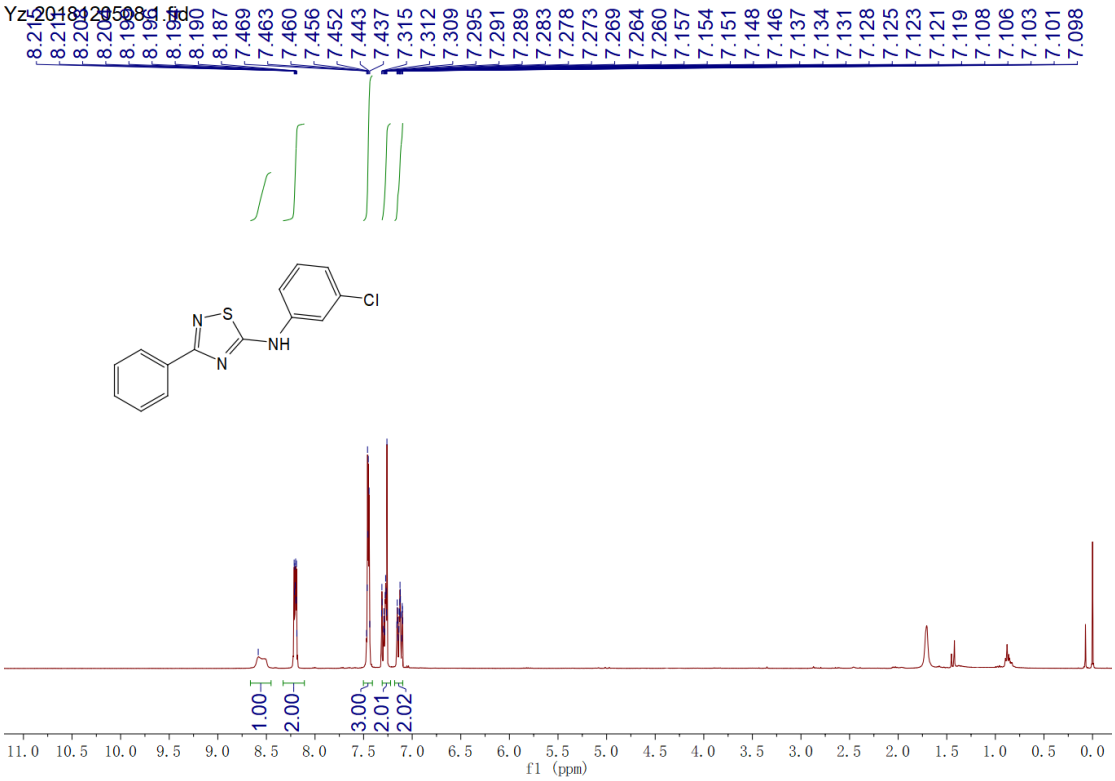

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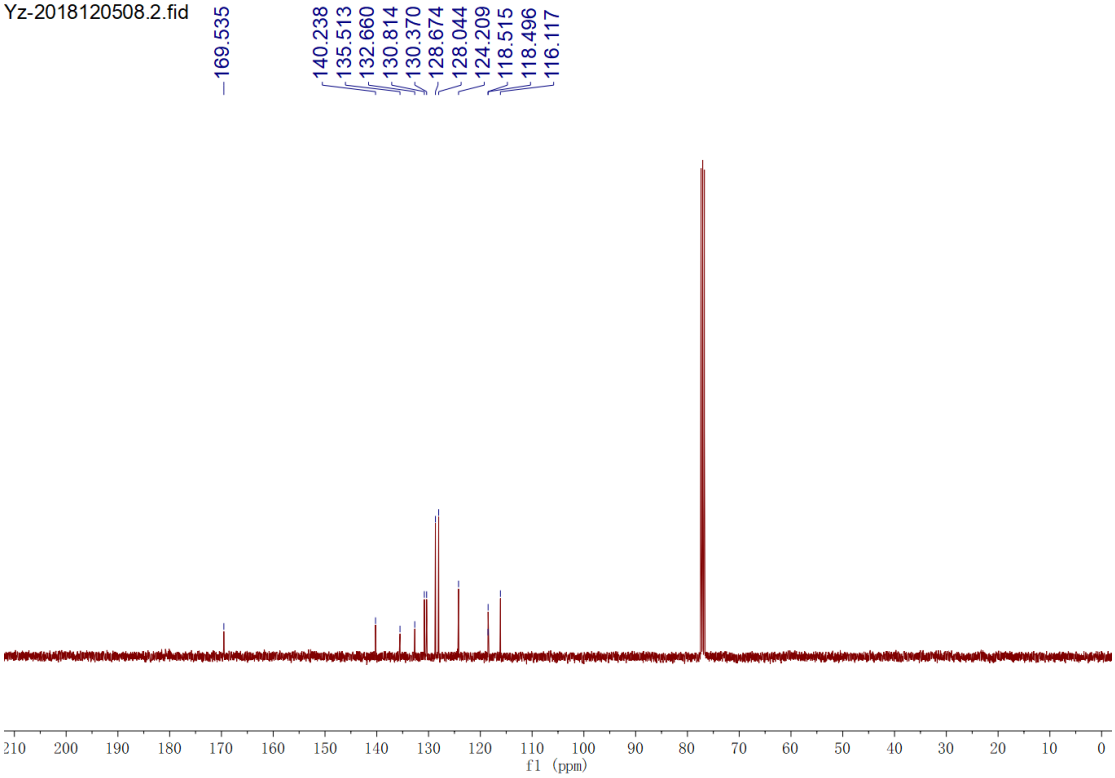

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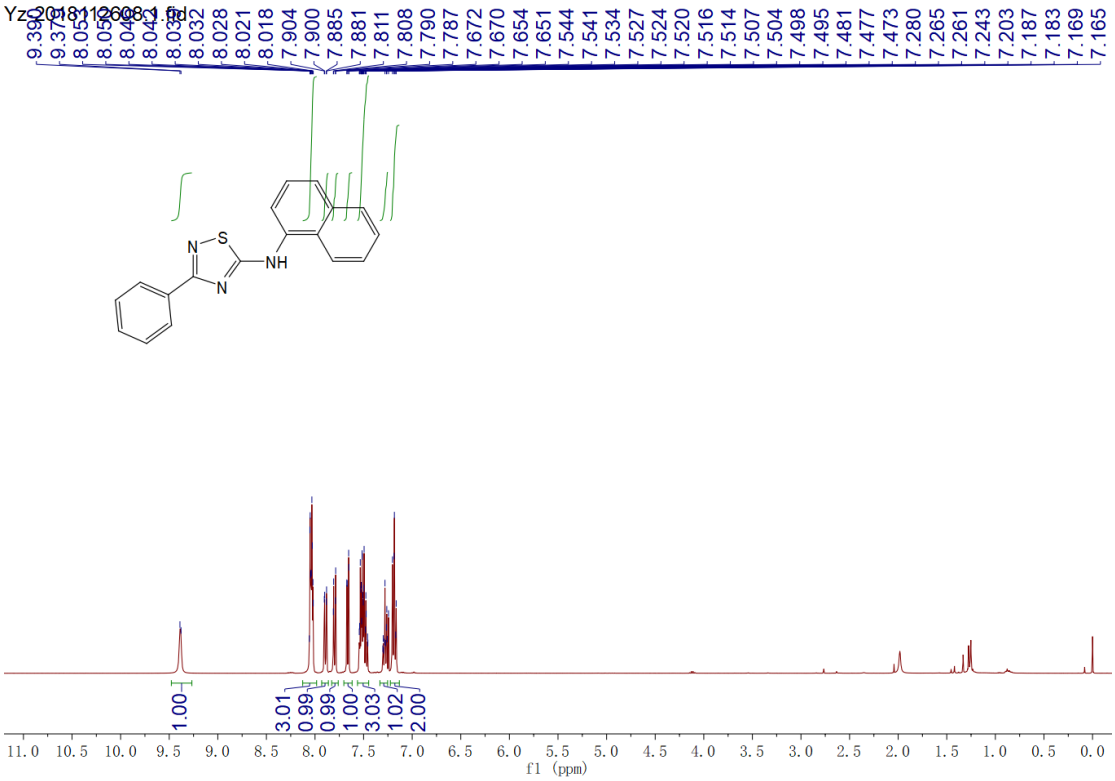

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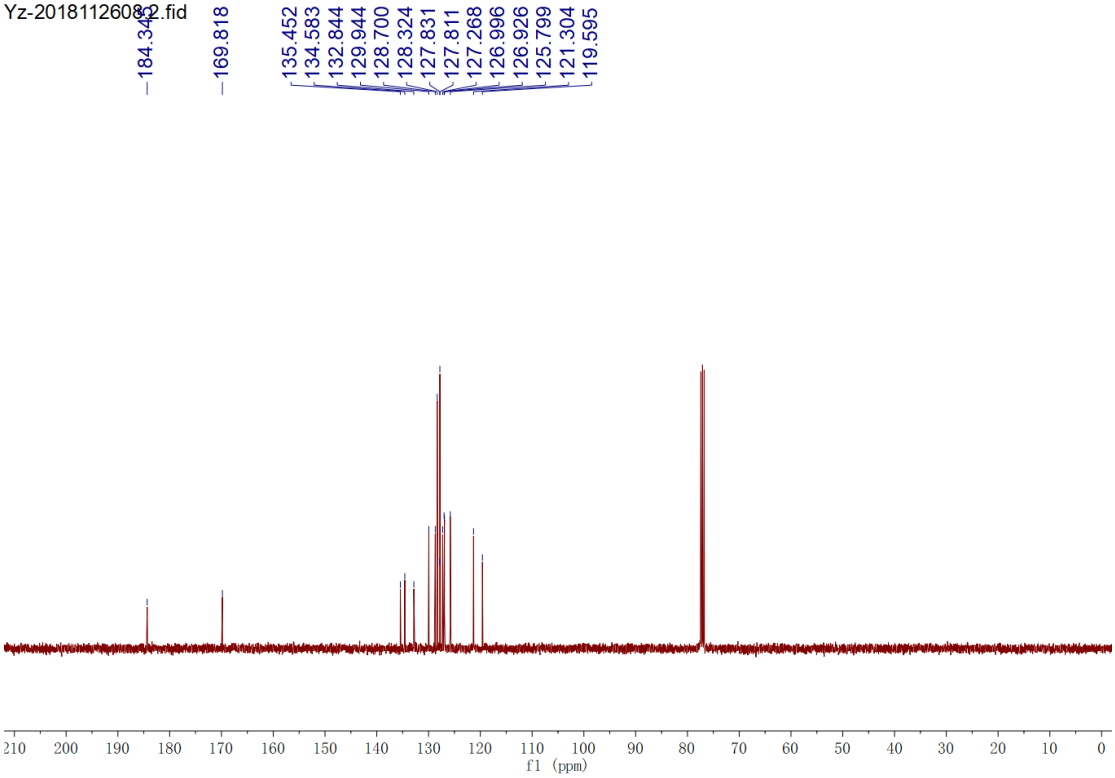

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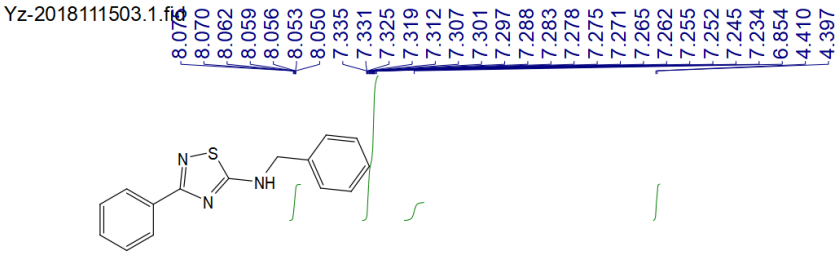

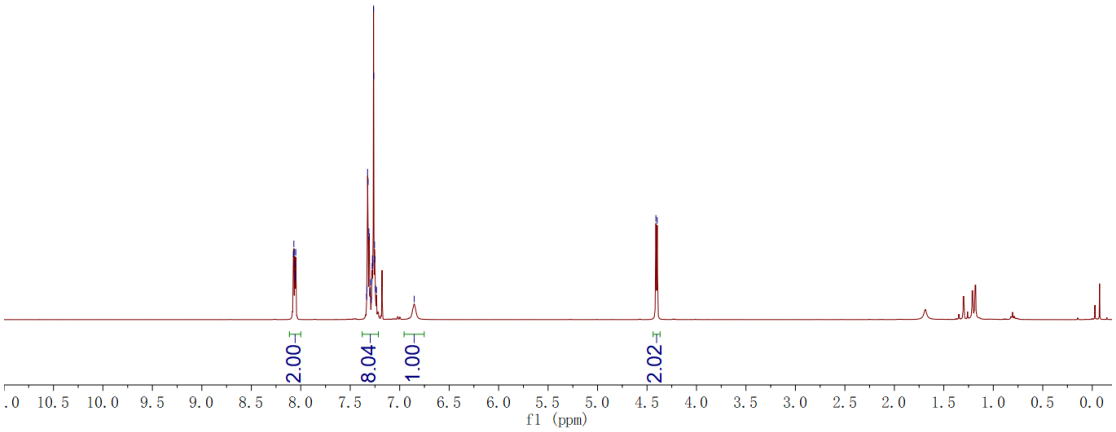

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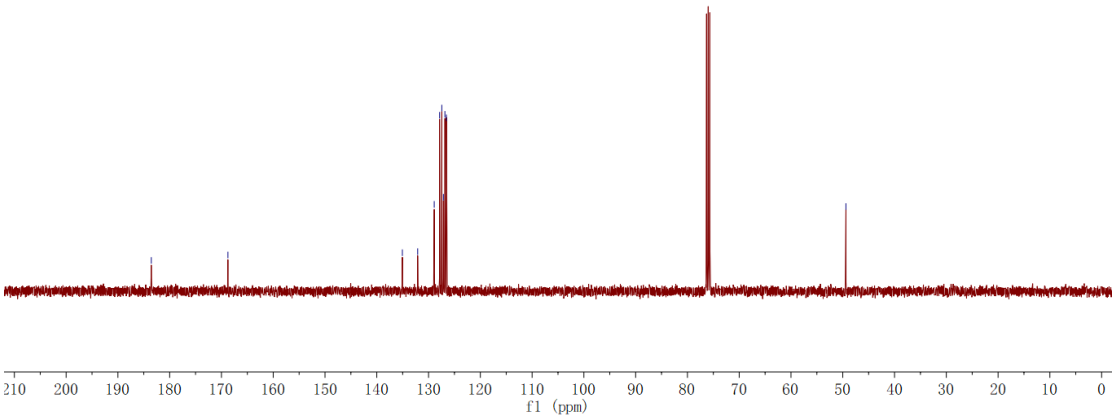

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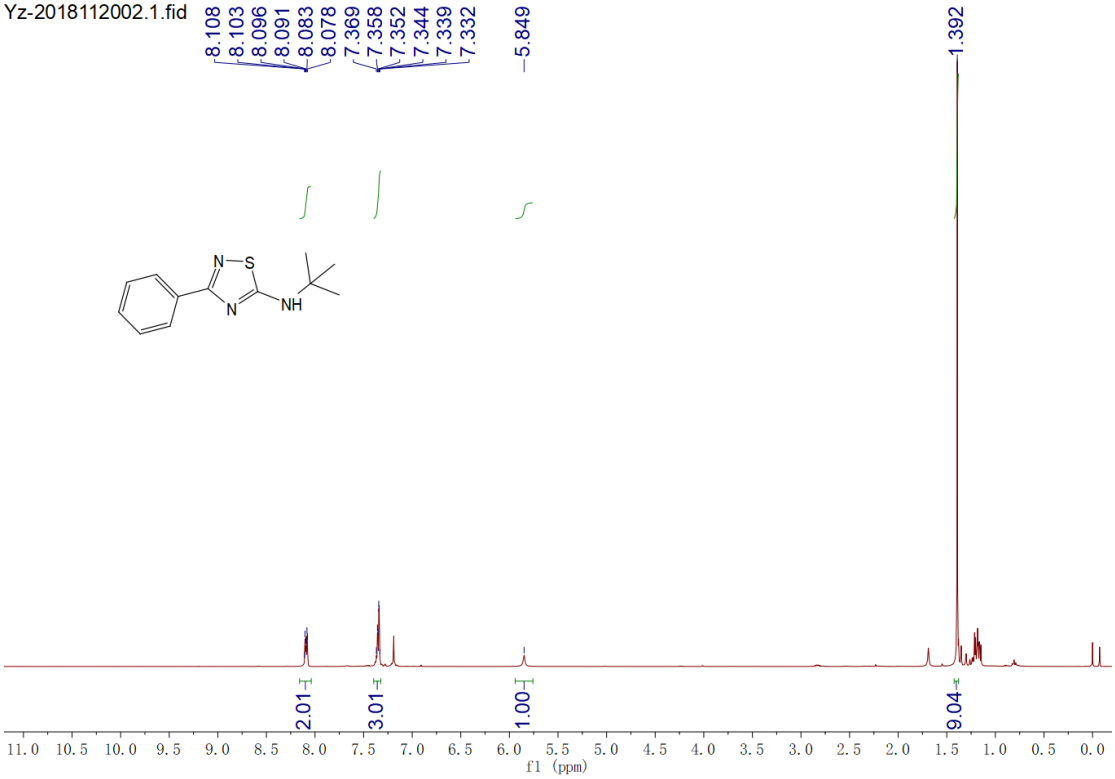

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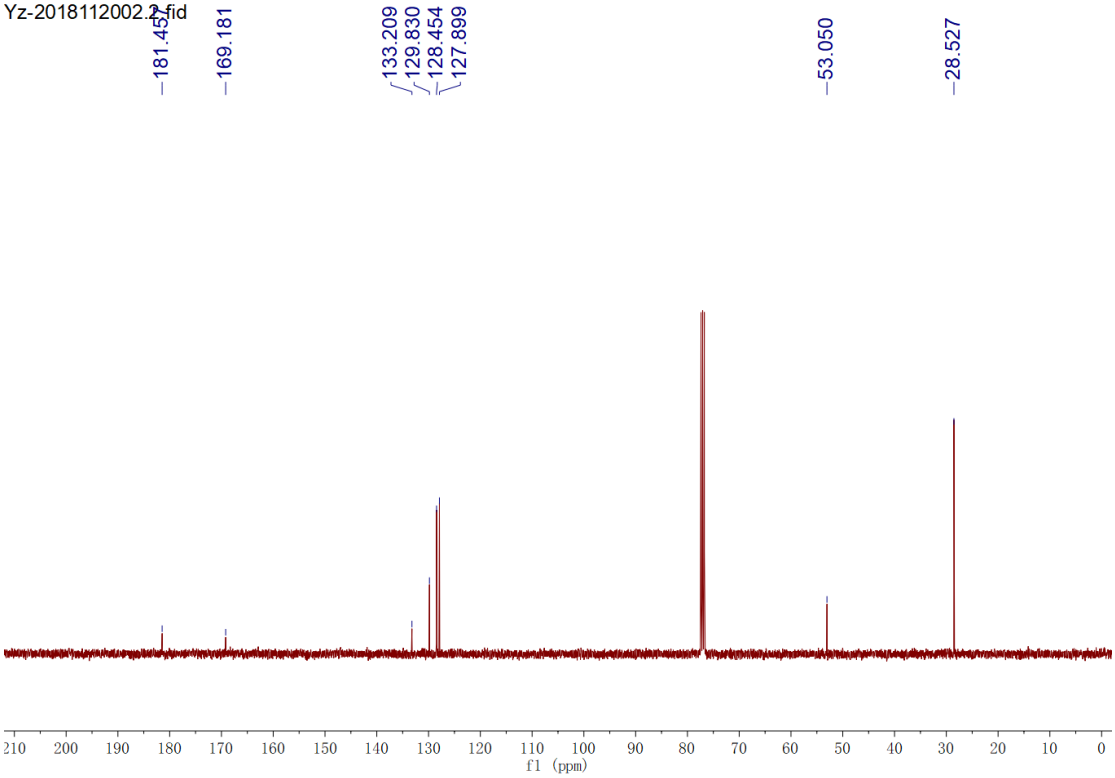

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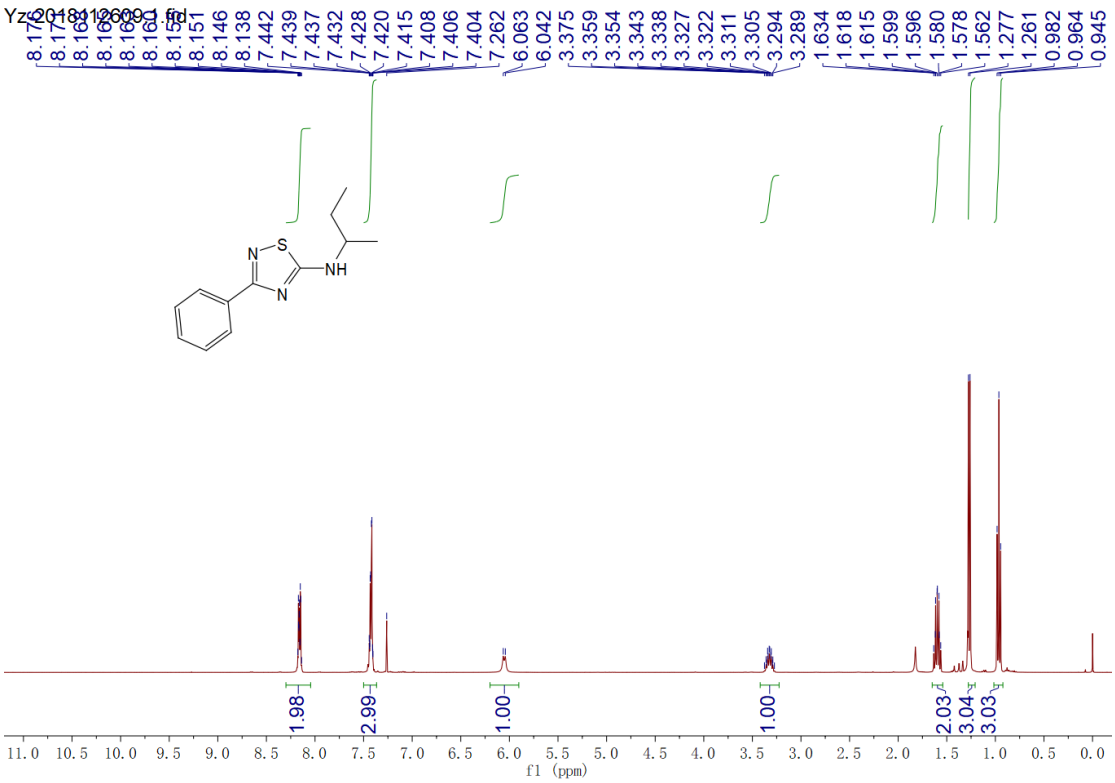

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