Supporting Information

Synthesis, Crystal Structures and Biological Activity Evaluation of Novel Xanthine Derivatives Containing Pyrethroid Moiety

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1. The data for the intermediates

*2-Iodoethyl-2,2,3,3-tetramethylcyclopropane-1-carboxylate (**1**)*: colorless sticky oil, yield 61%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (t, J = 6.9 Hz, 2H, CH_2), 3.29 (t, J = 6.9 Hz, 2H, CH_2), 1.25 (s, 6H, cyclopropane-CH_3 × 2), 1.21 (s, 1H, cyclopropane-H), 1.20 (s, 6H, cyclopropane-CH_3 × 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.48, 62.93, 34.56, 29.58, 22.52, 15.62.

*2-Iodoethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**2**)*: colorless sticky oil, yield 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (d, J = 9.4 Hz, 1H, CH=), 4.33-4.24 (m, 2H, CH_2), 3.24 (t, J = 6.9 Hz, 2H, CH_2), 2.14 (t, J = 8.8 Hz, 1H, cyclopropane-H), 1.97 (d, J = 8.4 Hz, 1H, cyclopropane-H), 1.25 (d, J = 6.9 Hz, 6H, cyclopropane-CH_3 × 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.38, 129.75 (q, J = 4.3 Hz), 120.20 (q, J = 271.7 Hz), 121.58 (q, J = 37.4 Hz), 64.48, 32.48, 30.77, 28.64, 28.02, 14.69.

*1,7-Dimethyl-3,7-dihydro-1H-purine-2,6-dione (**5a**)*: white solid, m.p. 296-299 °C(lit.[1] m.p. 297-299 °C), yield 70%, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.82 (s, 1H, NH), 7.90 (s, 1H, Imidazole-H), 3.83 (s, 3H, N-CH_3), 3.15 (s, 3H, N-CH_3).

*1-Isopropyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione (**5b**)*: white solid, m.p. 235-237 °C, yield 76%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.77 (s, 1H, N-H), 7.56 (s, 1H, imidazole-H), 5.36-5.21 (m, 1H, CH), 4.00 (s, 3H, N-CH_3), 1.54 (d, J = 6.9 Hz, 6H, CH_3 × 2).

*1-(Cyclopropylmethyl)-7-methyl-3,7-dihydro-1H-purine-2,6-dione (**5c**)*: white solid, m.p. 224-226 °C, yield 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H, N-H), 7.56 (s, 1H, imidazole-H), 4.02 (s, 3H, N-CH_3), 3.91 (d, J = 7.2 Hz, 2H, N-CH_2), 1.39-1.24 (m, 1H, cyclopropane-CH), 0.59-0.35 (m, 4H, cyclopropane-CH_2 × 2).

*8-Bromo-1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione (**B1**)*: white solid, m.p. 295-297 °C (lit.[2] m.p. 303 °C), yield 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.54 (s, 3H, N-CH_3), 3.41 (s, 3H, N-CH_3).

*1,3-Dimethyl-8-(trifluoromethyl)-3,7-dihydro-1H-purine-2,6-dione (**B2**)*: white solid, m.p. 234-236 °C(lit.[3] m.p. 234-237 °C), yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.78 (s, 1H, N-H), 3.70 (s, 3H, N-CH_3), 3.54 (s, 3H, N-CH_3).

*8-Chloro-3,7-dimethyl-3,7-dihydro-1H-purine-2,6-dione (**B3**)*: white solid, m.p. 291-293 °C(lit.[4] m.p. 290 °C), yield 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H, N-H), 3.87 (s, 3H, N-CH_3), 3.44 (s, 3H, N-CH_3).

*8-Chloro-1,7-dimethyl-3,7-dihydro-1H-purine-2,6-dione (**B4**)*: white solid, m.p. 285-288 °C(lit.[5] m.p. 284 °C), yield 79%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (s, 1H, N-H), 3.81 (s, 3H, N-CH_3), 3.16 (s, 3H, N-CH_3).

2. References

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3. The data for the title compounds

*2-(1,3-Dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**Ia**)*: white solid, m.p. 120-121 °C, yield 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H, imidazole-H), 4.52–4.45 (m, 2H, CH_2), 4.39–4.30 (m, 2H, CH_2), 3.53 (s, 3H, N-CH_3), 3.34 (s, 3H, N-CH_3), 1.12 (s, 6H, cyclopropane-CH_3 × 2), 1.11 (s, 6H, cyclopropane-CH_3 × 2), 1.05 (s, 1H, cyclopropane-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.32, 155.20, 151.64, 148.93, 141.59, 106.72, 61.65, 46.19, 35.28, 30.88, 29.75, 27.95, 23.45, 16.42. HRMS (Maldi) calcd for $C_{17}H_{25}N_4O_4$ $[M+H]^+$ 349.1870, found 349.1872.

*2-(8-Chloro-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**Ib**)*: white solid, m.p. 119-120 °C, yield 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57 (t, J = 4.9 Hz, 2H, CH_2), 4.43 (t, J = 4.9 Hz, 2H, CH_2), 3.56 (s, 3H, N-CH_3), 3.41 (s, 3H, N-CH_3), 1.18 (s, 6H, cyclopropane-CH_3 × 2), 1.16 (s, 6H, cyclopropane-CH_3 × 2), 1.10 (s, 1H, cyclopropane-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.44, 154.32, 151.33, 147.38, 139.23, 107.72, 61.11, 45.78, 35.38, 31.02, 29.87, 28.07, 23.49, 16.40. HRMS (Maldi) calcd for $C_{17}H_{23}ClN_4NaO_4$

$[M+Na]^+$ 405.1300, found 405.1300.

*2-(8-Bromo-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**Ic**)*: white solid, m.p. 121-123 °C, yield 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57 (s, 2H, CH_2), 4.45 (s, 2H, CH_2), 3.57 (s, 3H, N-CH_3), 3.40 (s, 3H, N-CH_3), 1.25 (s, 6H, cyclopropane-CH_3 × 2), 1.18 (s, 6H, cyclopropane-CH_3 × 2), 1.11 (s, 1H, cyclopropane-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.40, 154.14, 151.28, 148.31, 128.22, 108.81, 65.39, 61.08, 46.85, 35.39, 30.95, 29.87, 28.07, 23.50, 16.41. HRMS (Maldi) calcd for $C_{17}H_{24}BrN_4O_4$ $[M+H]^+$ 427.0975, found 427.0975.

*2-(3-Isobutyl-1-methyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**Id**)*: white solid, m.p. 136-137 °C, yield 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H, imidazole-H), 4.57-4.51 (m, 2H, CH_2), 4.44-4.39 (m, 2H, CH_2), 3.94 (d, J = 7.5 Hz, 2H, N-CH_2), 3.41 (s, 3H, N-CH_3), 2.32 (td, J = 13.9, 7.0 Hz, 1H, CH), 1.18 (s, 6H, cyclopropane-CH_3 × 2), 1.17 (s, 6H, cyclopropane-CH_3 × 2), 1.12 (s, 1H, cyclopropane-H), 0.96 (d, J = 6.7 Hz, 6H, CH_3 × 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.39, 155.35, 151.60, 149.09, 141.45, 106.68, 61.72, 50.59, 46.17, 35.37, 30.89, 27.98, 27.36, 23.48, 19.98, 16.47. HRMS (Maldi) calcd for $C_{20}H_{30}N_4NaO_4$ $[M+Na]^+$ 413.2159, found 413.2158.

*2-(1,3-Dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**Ie**)*: white solid, m.p. 126-128 °C, yield 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H, imidazole-H), 6.81 (d, J = 9.3 Hz, 1H, CH=CCF_3Cl), 4.62-4.51 (m, 2H, CH_2), 4.50-4.42 (m, 2H, CH_2), 3.60 (s, 3H, N-CH_3), 3.42 (s, 3H, N-CH_3), 2.18 (t, J = 8.8 Hz, 1H, cyclopropane-H), 1.90 (d, J = 8.4 Hz, 1H, cyclopropane-H), 1.28 (s, 3H, cyclopropane-CH_3), 1.24 (s, 3H, cyclopropane-CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.54, 155.16, 151.57, 149.00, 141.47, 129.54 (q, J = 4.2 Hz), 122.00 (q, J = 37.4 Hz), 120.30 (q, J = 272.7 Hz), 106.68, 62.64, 45.96, 32.30, 31.10, 29.71, 28.98, 28.20, 27.91, 14.66. HRMS (Maldi) calcd for $C_{18}H_{21}ClF_3N_4O_4$ $[M+H]^+$ 449.1198, found 449.1193.

*2-(8-Chloro-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**If**)*: white solid, m.p. 137-139 °C, yield 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (d, J = 9.4 Hz, 1H, CH=CCF_3Cl), 4.61-4.52 (m, 2H, CH_2), 4.49-4.42 (m, 2H, CH_2), 3.54 (s, 3H, N-CH_3), 3.38 (s, 3H, N-CH_3), 2.17 (t, J = 8.9 Hz, 1H,

cyclopropane-H), 1.86 (d, *J* = 8.4 Hz, 1H, cyclopropane-H), 1.24 (d, *J* = 7.9 Hz, 6H, cyclopropane-CH_3 × 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.67, 154.15, 151.19, 147.36, 138.94, 129.60 (q, *J* = 4.0 Hz), 121.91(q, *J* = 38.4 Hz), 120.31(q, *J* = 272.7 Hz), 107.60, 62.21, 32.37, 31.18, 29.78, 29.06, 28.22, 27.97, 14.63. HRMS (Maldi) calcd for $C_{18}H_{20}Cl_2F_3N_4O_4$ $[M+H]^+$ 483.0808, found 483.0807.

*2-(8-Bromo-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**Ig**)*: white solid, m.p. 139-141 °C, yield 63%. ^1H NMR (400 MHz, $CDCl_3$) δ 6.83 (d, *J* = 9.4 Hz, 1H, CH=CCF_3Cl), 4.62-4.57 (m, 2H, CH_2), 4.52-4.47 (m, 2H, CH_2), 3.56 (s, 3H, N-CH_3), 3.39 (s, 3H, N-CH_3), 2.19 (t, *J* = 4.9 Hz, 1H, cyclopropane-H), 1.93 (d, *J* = 8.4 Hz, 1H, cyclopropane-H), 1.30 (s, 3H, cyclopropane-CH_3), 1.26 (s, 3H, cyclopropane-CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.63, 154.04, 151.11, 148.29, 129.73 (q, *J* = 4.3 Hz), 128.03, 121.72 (q, *J* = 36.4 Hz), 120.27 (q, *J* = 271.7 Hz), 116.23, 108.65, 62.18, 46.46, 32.42, 31.12, 29.75, 29.05, 28.15, 27.93, 14.60. HRMS (Maldi) calcd for $C_{18}H_{20}BrClF_3N_4O_4$ $[M+H]^+$ 527.0303, found 527.0307.

*2-(-1,3-Dimethyl-2,6-dioxo-8-(trifluoromethyl)-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethyl-cyclopropane-1-carboxylate (**Ih**)*: white solid, m.p. 130-132 °C, yield 61%. ^1H NMR (400 MHz, $CDCl_3$) δ 6.80 (d, *J* = 9.4 Hz, 1H, CH=CCF_3Cl), 4.74 (t, *J* = 10.1 Hz, 2H, CH_2), 4.61-4.47 (m, 2H, CH_2), 3.61 (s, 3H, N-CH_3), 3.43 (s, 3H, N-CH_3), 2.18 (t, *J* = 8.9 Hz, 1H, cyclopropane-H), 1.87 (d, *J* = 8.4 Hz, 1H, cyclopropane-H), 1.27 (s, 3H, cyclopropane-CH_3), 1.24 (s, 3H, cyclopropane-CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.65, 155.16, 151.25, 147.00, 139.00 (q, *J* = 39.9 Hz), 129.51 (q, *J* = 4.3 Hz), 121.99 (q, *J* = 138.4 Hz), 119.23 (q, *J* = 272.7 Hz), 119.01 (q, *J* = 272.7 Hz), 109.10, 62.25, 46.44, 32.23, 31.20, 29.89, 29.08, 28.25, 28.16, 14.54. HRMS (Maldi) calcd for $C_{19}H_{20}ClF_6N_4O_4$ $[M+H]^+$ 517.1072, found 517.1075.

*2-(3-Isobutyl-1-methyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**Ii**)*: white solid, m.p. 130-131 °C, yield 62%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H, imidazole-H), 6.83 (d, *J* = 9.3 Hz, 2H, CH=CCF_3Cl), 4.62-4.38 (m, 4H, CH_2-CH_2), 3.94 (d, *J* = 7.5 Hz, 2H, N-CH_2), 3.41 (s, 3H, N-CH_3), 2.37-2.25 (m, 1H, CH), 2.18 (t, *J* = 8.8 Hz, 1H, cyclopropane-H), 1.91 (d, *J* = 8.4 Hz, 1H, cyclopropane-H), 1.29 (s, 3H, cyclopropane-CH_3), 1.24 (s, 3H, cyclopropane-CH_3),

0.96 (d, J = 6.7 Hz, 6H, CH_3 × 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.59, 155.32, 151.54, 149.17, 141.32, 129.50 (q, J = 4.4 Hz), 122.12 (q, J = 37.37 Hz), 120.32 (q, J = 272.7 Hz), 106.65, 62.72, 50.60, 45.93, 32.35, 31.14, 28.99, 28.26, 27.97, 27.35, 19.95, 14.74. HRMS (Maldi) calcd for $C_{21}H_{26}ClF_3N_4NaO_4$ $[M+Na]^+$ 513.1487 found 513.1486.

*2-(8-Chloro-3,7-dimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1H-purin-1-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**Ij**)*: white solid, m.p. 129-130 °C, yield 69%. ^1H NMR (400 MHz, $CDCl_3$) δ 4.29 (s, 4H, CH_2-CH_2), 3.95 (s, 3H, N-CH_3), 3.54 (s, 3H, N-CH_3), 1.20 (s, 6H, cyclopropane-CH_3 × 2), 1.16 (s, 6H, cyclopropane-CH_3 × 2), 1.14 (s, 1H, cyclopropane-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.86, 154.32, 151.07, 147.28, 139.02, 108.23, 99.99, 60.49, 40.30, 35.55, 32.69, 30.32, 29.79, 23.53, 16.45. HRMS (Maldi) calcd for $C_{17}H_{23}ClN_4NaO_4$ $[M+Na]^+$ 405.1300, found 405.1302.

*2-(3,7-Dimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1H-purin-1-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**Ik**)*: white solid, m.p. 117-119 °C, yield 71%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 1H, imidazole-H), 6.91 (d, J = 8.5 Hz, 1H, imidazole-H), 4.38-4.25 (m, 4H, CH_2-CH_2), 3.98 (s, 3H, N-CH_3), 3.57 (s, 3H, N-CH_3), 2.20-2.07 (m, 1H, cyclopropane-H), 1.97-1.91 (m, 1H, cyclopropane-H), 1.28 (s, 6H, cyclopropane-CH_3 × 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.09, 155.08, 151.45, 148.91, 141.61, 130.23 (q, J = 4.04 Hz), 121.32 (q, J = 37.4 Hz), 120.39 (q, J = 272.7 Hz), 107.45, 61.67, 39.98, 33.50, 32.66, 30.89, 29.66, 28.75, 28.33, 14.75. HRMS (Maldi) calcd for $C_{18}H_{21}ClF_3N_4O_4$ $[M+H]^+$ 449.1198 found 449.1197.

*2-(8-Chloro-3,7-dimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1H-purin-1-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**Il**)*: white solid, m.p. 106-108 °C, yield 54%. ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 (d, J = 9.5 Hz, 1H, CH=CCF_3Cl), 4.35-4.23 (m, 4H, CH_2-CH_2), 3.94 (s, 3H, N-CH_3), 3.54 (s, 3H, N-CH_3), 2.14 (t, J = 8.9 Hz, 1H, cyclopropane-H), 1.94 (d, J = 8.4 Hz, 2H, cyclopropane-H), 1.28 (d, J = 2.7 Hz, 6H, cyclopropane-CH_3 × 2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.10, 154.26, 151.04, 147.30, 139.20, 130.20 (q, J = 4.5 Hz), 120.38 (q, J = 271.7 Hz), 121.38 (q, J = 37.4 Hz), 108.12, 61.61, 40.12, 32.65, 30.92, 29.76, 28.79, 28.35, 14.77. HRMS (Maldi) calcd for $C_{18}H_{20}Cl_2F_3N_4O_4$ $[M+H]^+$ 483.0808, found 483.0808.

*2-(1,7-Dimethyl-2,6-dioxo-1,2,6,7-tetrahydro-3H-purin-3-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**Im**)*: white solid, m.p. 101-102 °C, yield 62%. ^1H

NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H, imidazole-H), 4.44-4.35 (m, 4H, CH_2-CH_2), 3.99 (s, 3H, N-CH_3), 3.41 (s, 3H, N-CH_3), 1.17 (s, 6H, cyclopropane-CH_3 × 2), 1.13 (s, 6H, cyclopropane-CH_3 × 2), 1.08 (s, 1H, cyclopropane-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.73, 155.49, 151.40, 148.47, 141.23, 107.67, 60.25, 42.52, 35.46, 33.55, 30.35, 27.91, 23.51, 16.41. HRMS (Maldi) calcd for $C_{17}H_{25}N_4O_4$ $[M+H]^+$ 349.1870, found 349.1871.

*2-(1-Isopropyl-7-methyl-2,6-dioxo-1,2,6,7-tetrahydro-3H-purin-3-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**In**)*: white solid, m.p. 104-105 °C, yield 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H, imidazole-H), 5.28 (td, J = 13.9, 6.9 Hz, 1H, CH), 4.41-4.31 (m, 4H, CH_2-CH_2), 3.98 (s, 3H, N-CH_3), 1.51 (d, J = 7.2 Hz, 6H, CH_3 × 2), 1.18 (s, 6H, cyclopropane-CH_3 × 2), 1.12 (s, 6H, cyclopropane-CH_3 × 2), 1.07 (s, 1H, cyclopropane-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.71, 155.89, 148.43, 141.13, 132.92, 107.81, 60.28, 42.19, 35.49, 33.57, 30.27, 23.50, 19.50, 16.44. HRMS (Maldi) calcd for $C_{19}H_{28}N_4NaO_4$ $[M+Na]^+$ 399.2003, found 399.2009.

*2-(1-(Cyclopropylmethyl)-7-methyl-2,6-dioxo-1,2,6,7-tetrahydro-3H-purin-3-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**Io**)*: white solid, m.p. 105-107 °C, yield 53%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H, imidazole-H), 4.39 (s, 4H, CH_2-CH_2), 3.99 (s, 3H, N-CH_3), 3.91 (d, J = 7.0 Hz, 2H, N-CH_2), 1.32-1.23 (m, 1H, cyclopropane-H), 1.18 (s, 6H, cyclopropane-CH_3 × 2), 1.12 (s, 6H, cyclopropane-CH_3 × 2), 1.08 (s, 1H, cyclopropane-H), 0.47–0.43 (m, 4H, cyclopropane-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.72, 155.57, 151.46, 148.51, 141.18, 100.01, 60.32, 45.67, 42.39, 35.48, 33.54, 30.30, 23.50, 16.43, 10.10, 3.85. HRMS (Maldi) calcd for $C_{20}H_{28}N_4NaO_4$ $[M+Na]^+$ 411.2003, found 411.2003.

*2-(8-Chloro-1,7-dimethyl-2,6-dioxo-1,2,6,7-tetrahydro-3H-purin-3-yl)ethyl 2,2,3,3-tetramethylcyclopropane-1-carboxylate (**Ip**)*: white solid, m.p. 111-112 °C, yield 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42-4.31 (m, 4H, CH_2-CH_2), 3.96 (s, 3H, N-CH_3), 3.40 (s, 3H, N-CH_3), 1.17 (s, 6H, cyclopropane-CH_3 × 2), 1.14 (s, 6H, cyclopropane-CH_3 × 2), 1.08 (s, 1H, cyclopropane-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.74, 154.65, 150.98, 146.88, 138.78, 108.33, 60.23, 42.80, 35.46, 32.67, 30.47, 27.98, 23.49, 16.39. HRMS (Maldi) calcd for $C_{17}H_{23}ClN_4NaO_4$ $[M+Na]^+$ 405.1300, found 405.1301.

*2-(1,7-Dimethyl-2,6-dioxo-1,2,6,7-tetrahydro-3H-purin-3-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**Iq**)*: white solid, m.p. 132-134 °C, yield 48%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H,

imidazole-H), 6.88 (d, J = 8.8 Hz, 1H, CH=CCF$_3$Cl), 4.46-4.43 (m, 2H, CH$_2$), 4.41-4.38 (m, 2H, CH$_2$), 3.99 (s, 3H, N-CH$_3$), 3.41 (s, 3H, N-CH$_3$), 2.11 (t, J = 8.8 Hz, 1H, cyclopropane-H), 1.87 (d, J = 8.4 Hz, 1H, cyclopropane-H), 1.25 (s, 6H, cyclopropane-CH$_3$ × 2). ^{13}C NMR (101 MHz, CDCl$_3$) δ 169.99, 155.36, 151.42, 148.35, 141.25, 130.13 (q, J = 4.3 Hz), 121.52 (q, J = 38.4 Hz), 120.40 (q, J = 275.7 Hz), 107.65, 61.47, 42.30, 33.55, 32.60, 30.98, 28.80, 28.35, 27.90, 14.75. HRMS (Maldi) calcd for C$_{18}$H$_{21}$ClF$_3$N$_4$O$_4$ [M+H]$^+$ 449.1198, found 449.1196.

*2-(1-(Cyclopropylmethyl)-7-methyl-2,6-dioxo-1,2,6,7-tetrahydro-3H-purin-3-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**Ir**)*: white solid, m.p. 126-128 °C, yield 56%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.47 (s, 1H, imidazole-H), 6.89 (d, J = 9.4 Hz, 1H, CH=CCF$_3$Cl), 4.48-4.33 (m, 4H, CH$_2$-CH$_2$), 3.99 (s, 3H, N-CH$_3$), 3.90 (d, J = 7.1 Hz, 2H, N-CH$_2$), 2.12 (t, J = 8.9 Hz, 1H), 1.88 (d, J = 8.4 Hz, 1H, cyclopropane-H), 1.31-1.29 (m, 1H, cyclopropane-H), 1.25 (s, 6H, cyclopropane-CH$_3$ × 2), 0.63-0.25 (m, 4H, cyclopropane-H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 169.99, 155.45, 151.50, 148.39, 141.20, 130.13 (q, J = 5.5 Hz), 121.49 (q, J = 37.4 Hz), 120.40 (q, J = 271.7 Hz), 107.80, 61.53, 45.69, 42.18, 33.54, 32.61, 30.97, 28.77, 28.35, 14.76, 10.08, 3.80. HRMS (Maldi) calcd for C$_{21}$H$_{25}$ClF$_3$N$_4$O$_4$ [M+H]$^+$ 489.1511, found 489.1506.

*2-(8-Chloro-1,7-dimethyl-2,6-dioxo-1,2,6,7-tetrahydro-3H-purin-3-yl)ethyl (1R,3R)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylate (**Is**)*: white solid, m.p. 126-127 °C, yield 66%. ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.88 (d, J = 9.4 Hz, 1H, CH=CCF$_3$Cl), 4.45-4.30 (m, 4H, CH$_2$-CH$_2$), 3.95 (s, 3H, N-CH$_3$), 3.39 (s, 3H, N-CH$_3$), 2.13 (t, J = 8.0 Hz, 1H, cyclopropane-H), 1.88 (d, J = 8.3 Hz, 1H, cyclopropane-H), 1.26 (d, J = 6.5 Hz, 6H, cyclopropane-CH$_3$ × 2). ^{13}C NMR (101 MHz, CDCl$_3$) δ 170.0, 154.5, 150.9, 146.7, 141.3, 138.8, 130.0 (q, J = 4.4 Hz), 121.6 (q, J = 37.4 Hz), 120.3 (q, J = 272.7 Hz), 108.3, 61.4, 42.50, 32.6, 32.5, 31.0, 28.8, 28.3, 27.9, 14.7. HRMS (Maldi) calcd for C$_{18}$H$_{20}$Cl$_2$F$_3$N$_4$O$_4$ [M+H]$^+$ 483.0808, found 483.0808.

4. The NMR spectra of the intermediate compounds.

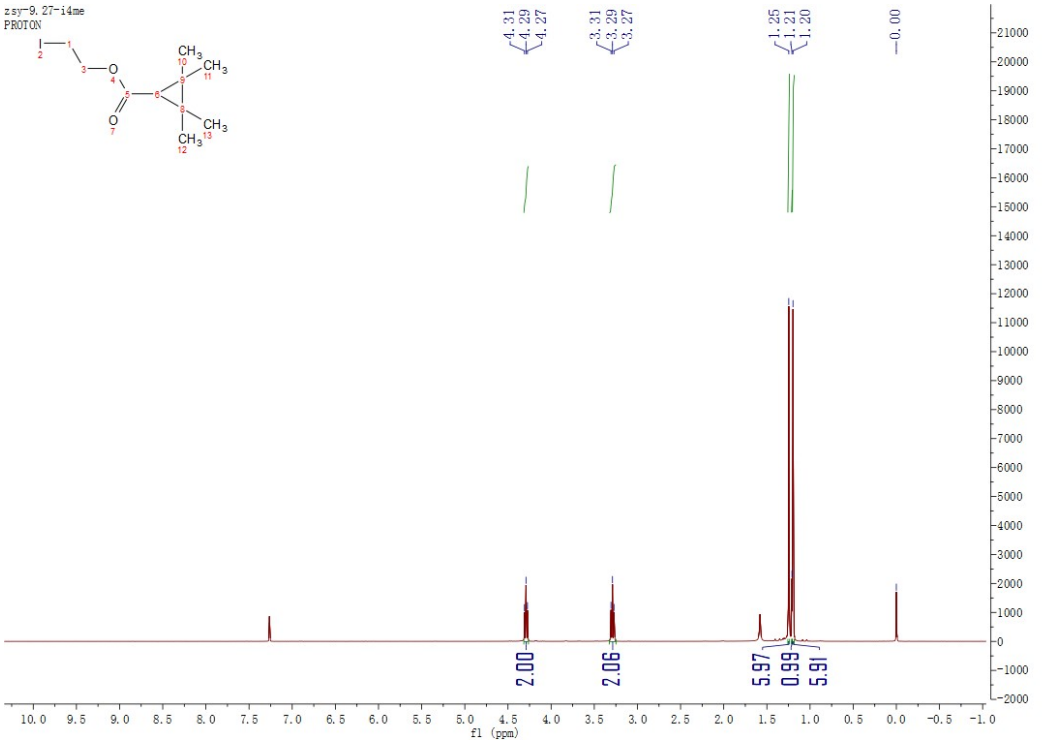

Fig. S1. The ^{1}H NMR spectrum of intermediate **1**.

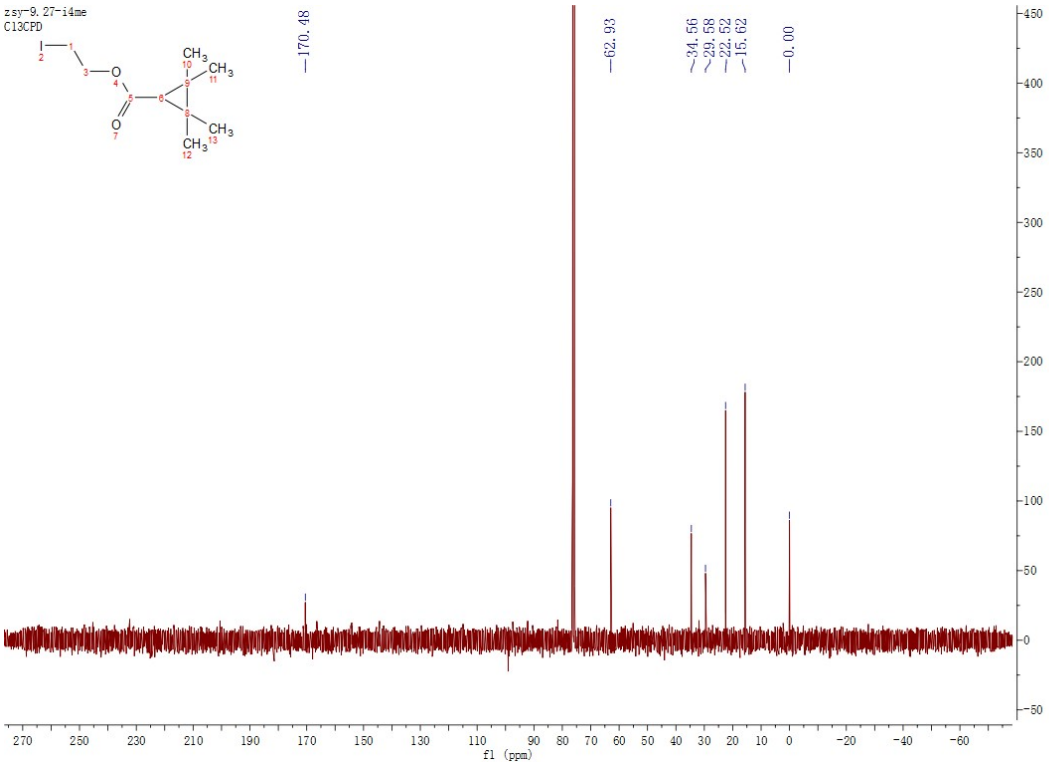

Fig. S2. The ^{13}C NMR spectrum of intermediate **1**.

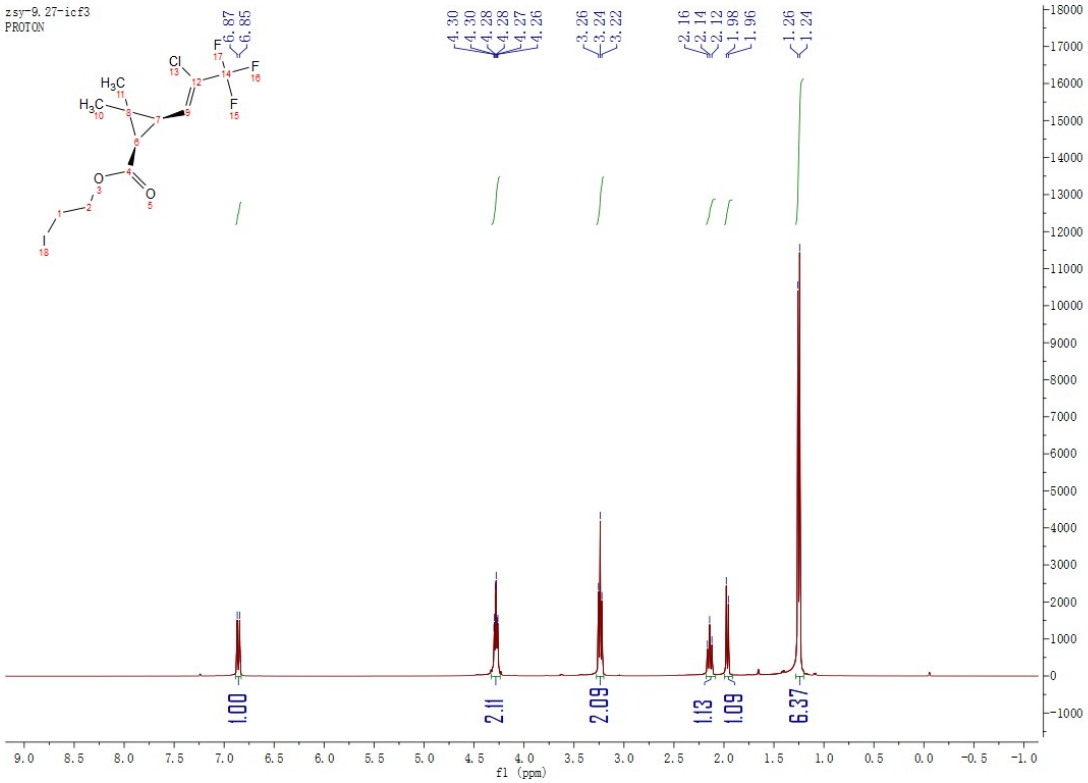

Fig. S3. The ^{1}H NMR spectrum of intermediate **2**.

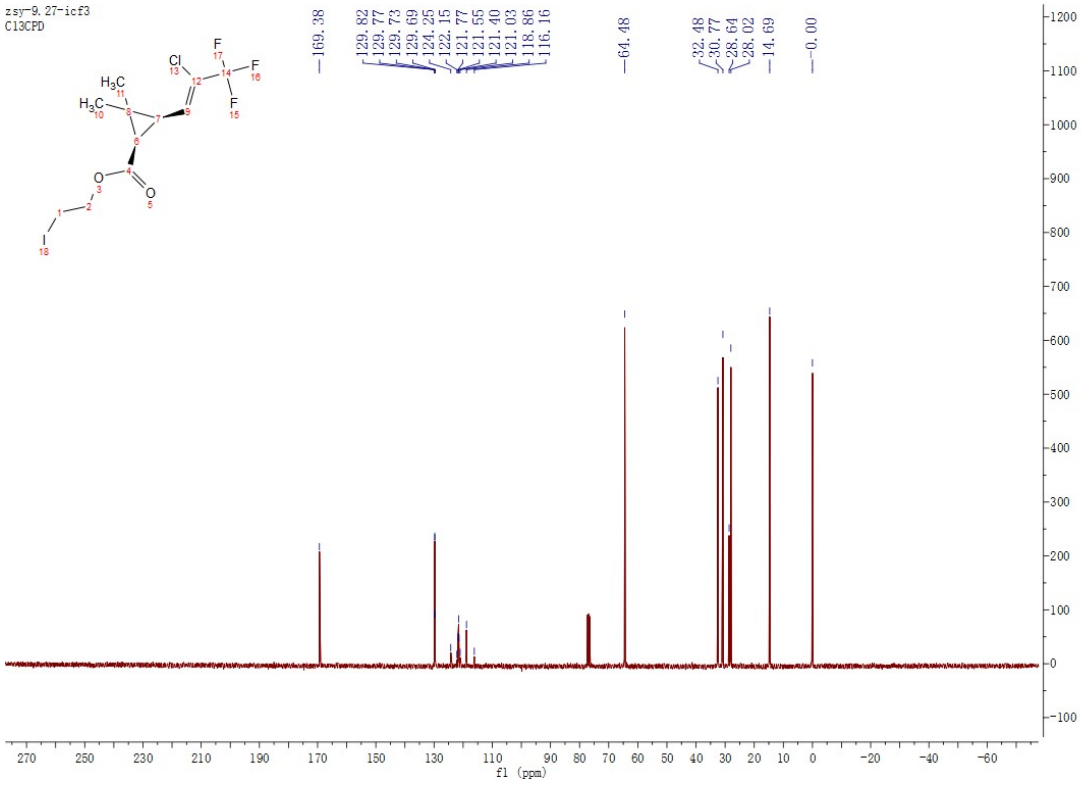

Fig. S4. The ^{13}C NMR spectrum of intermediate **2**.

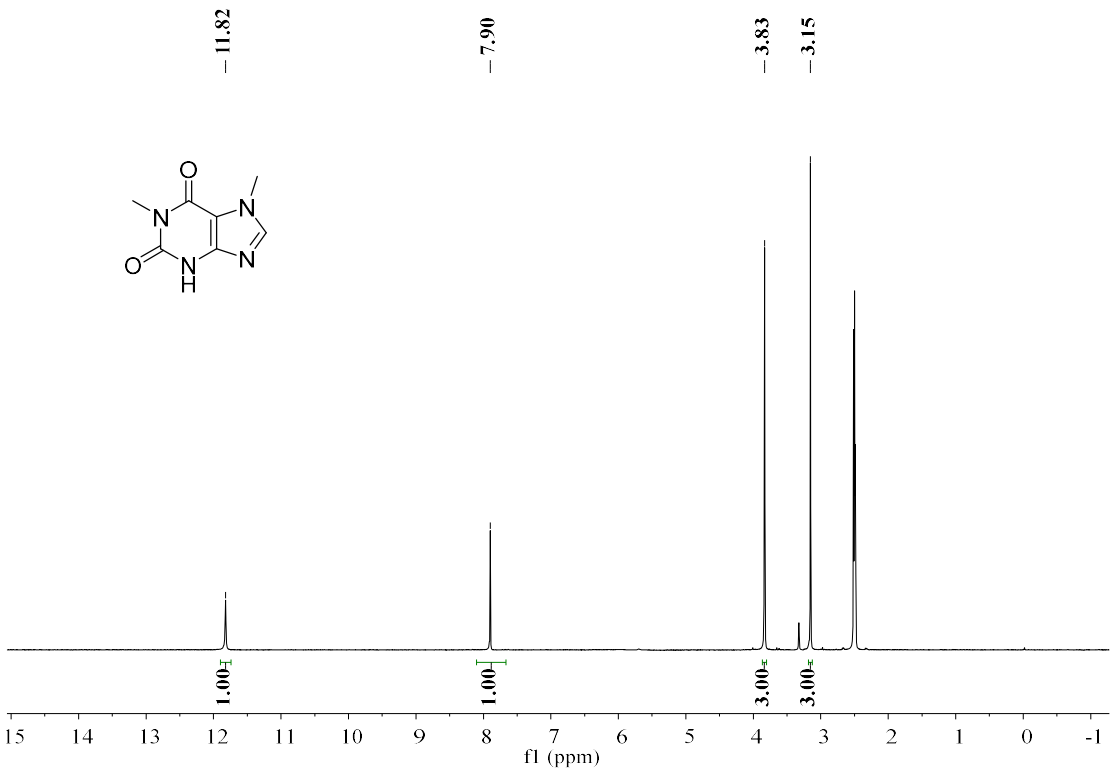

Fig. S5. The ^{1}H NMR spectrum of intermediate **5a**.

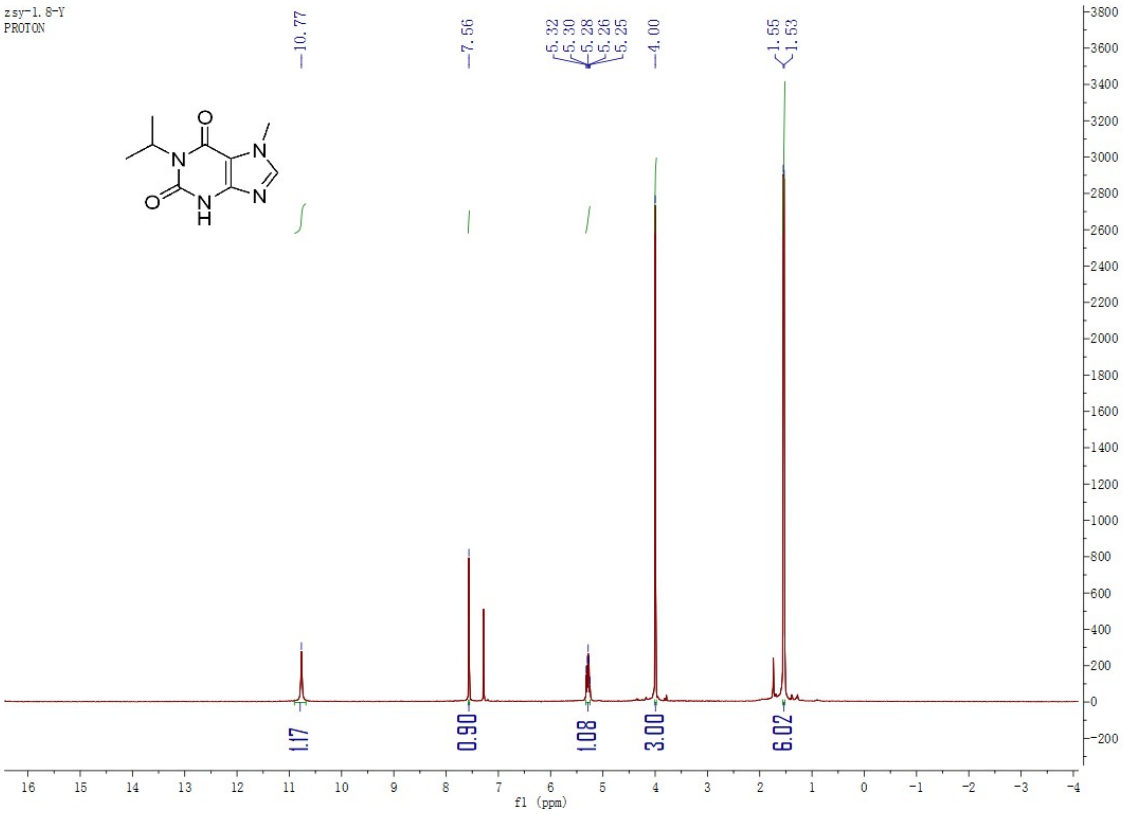

Fig. S6. The ^{1}H NMR spectrum of intermediate **5b**.

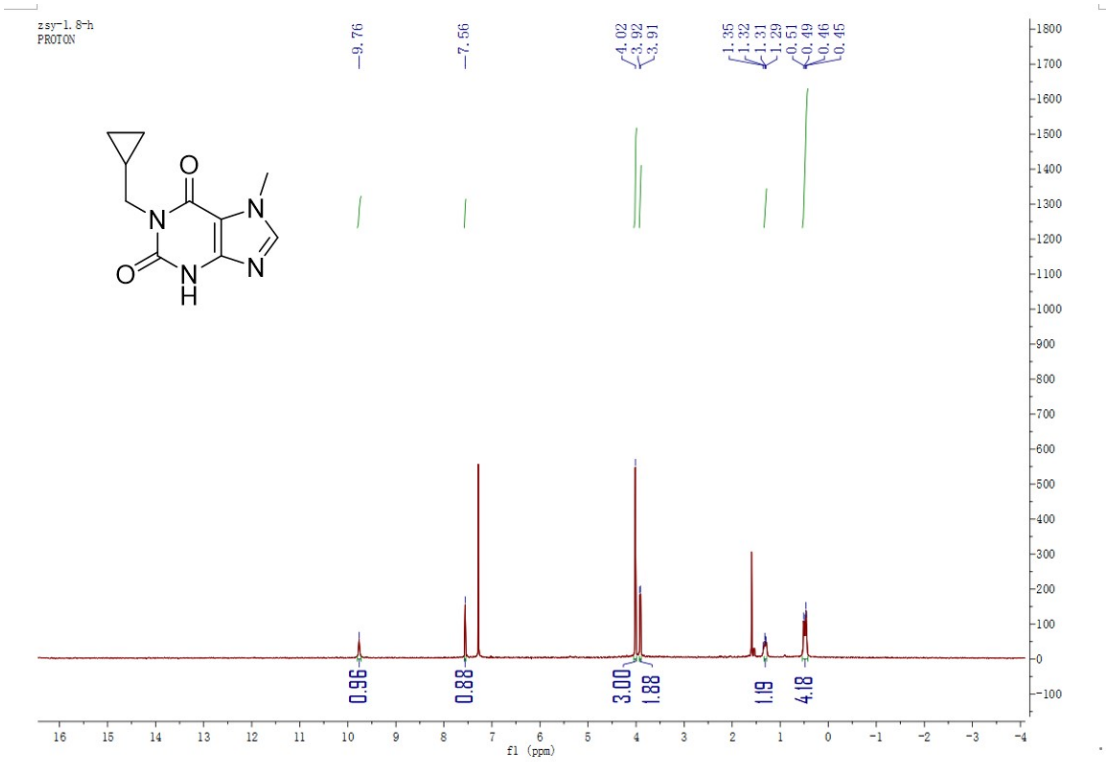

Fig. S7. The ^{1}H NMR spectrum of intermediate **5c**.

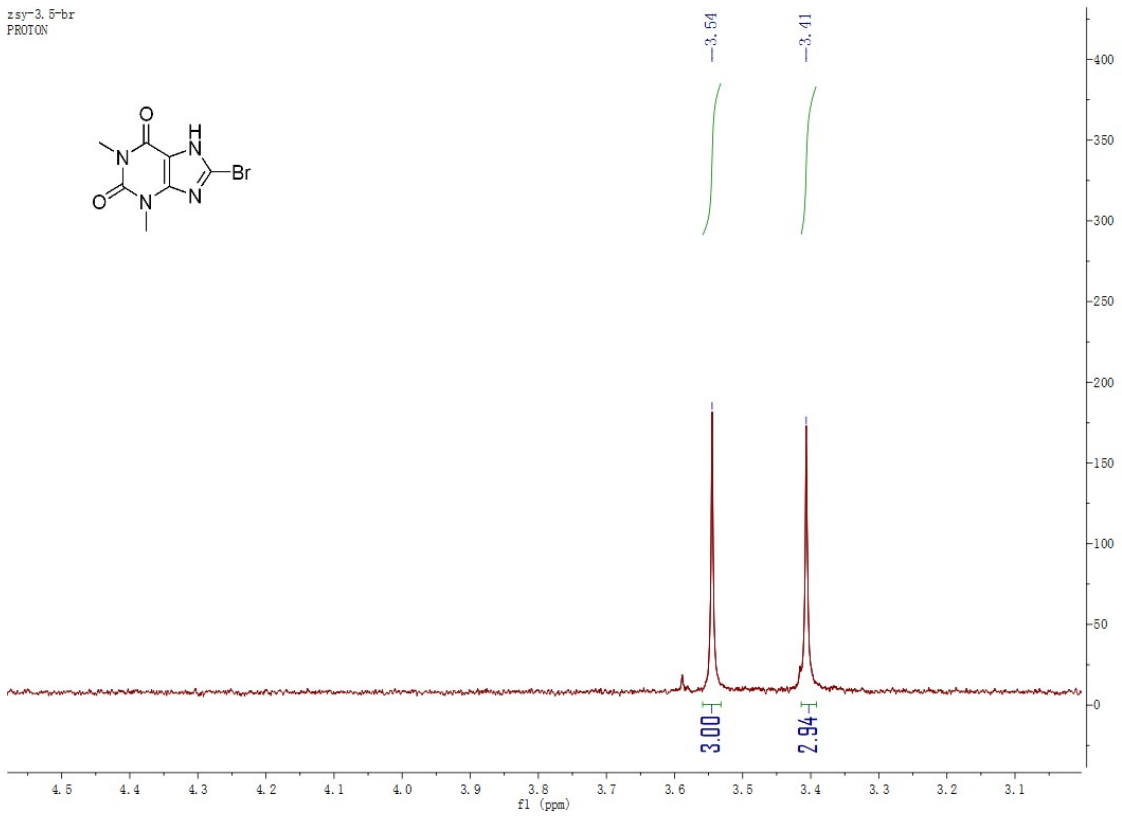

Fig. S8. The ^{1}H NMR spectrum of intermediate **B1**.

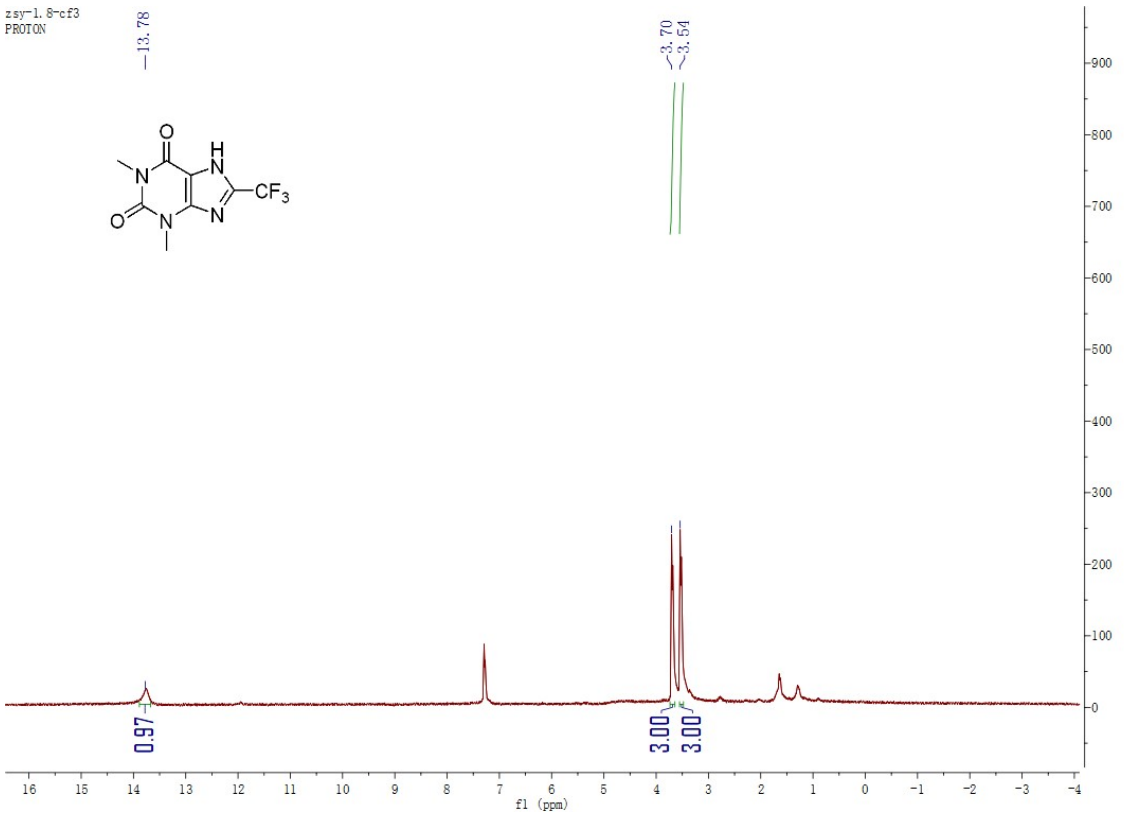

Fig. S9. The ^{1}H NMR spectrum of intermediate **B2**.

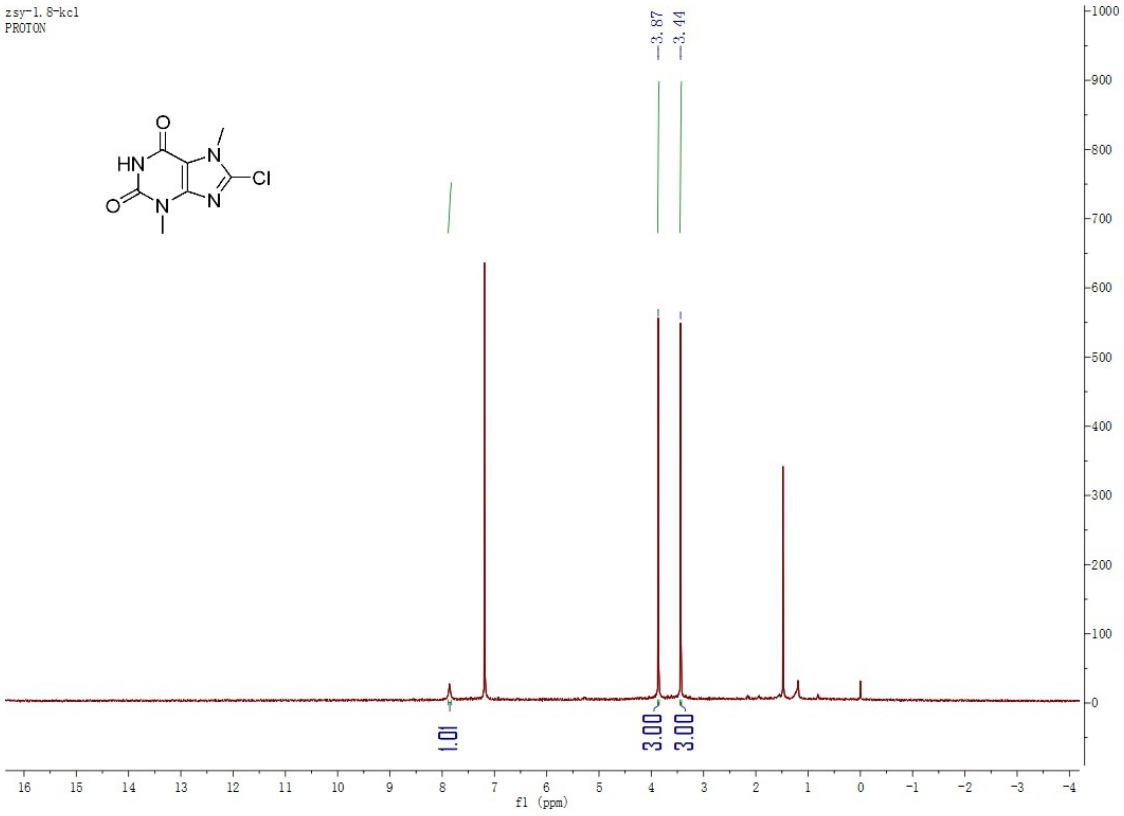

Fig. S10. The ^{1}H NMR spectrum of intermediate **B3**.

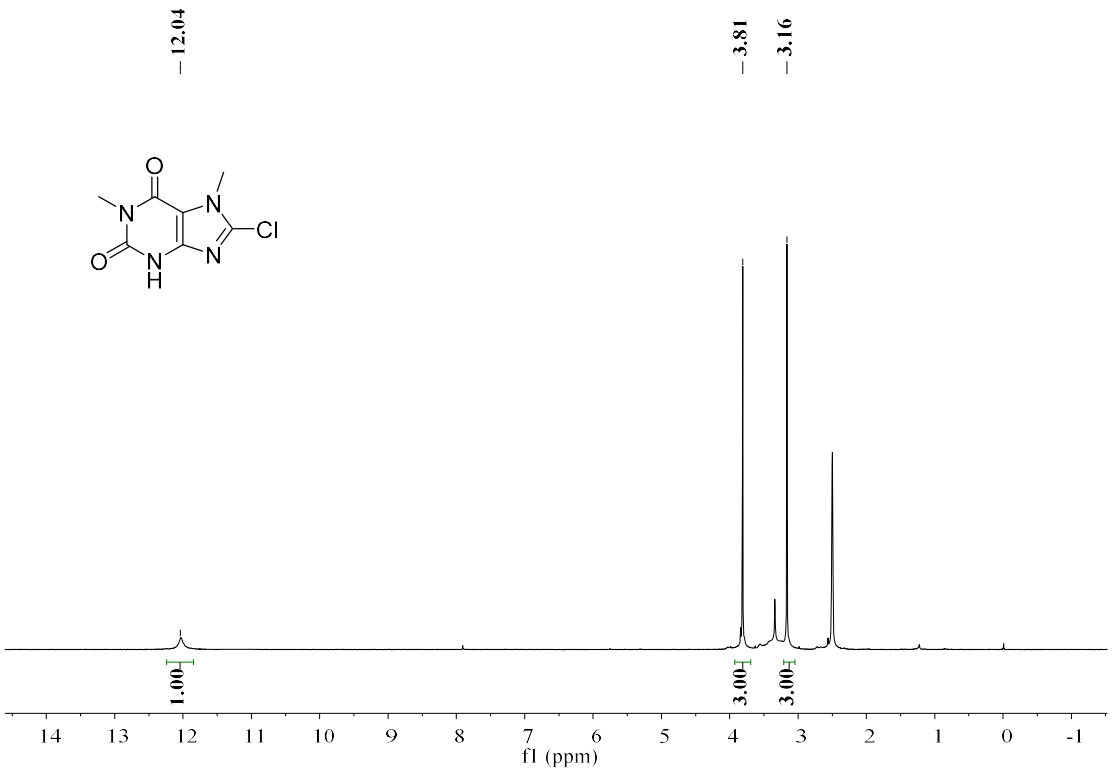

Fig. S11. The ^{1}H NMR spectrum of intermediate **B4**.

5. The NMR and HRMS spectra of the title compounds

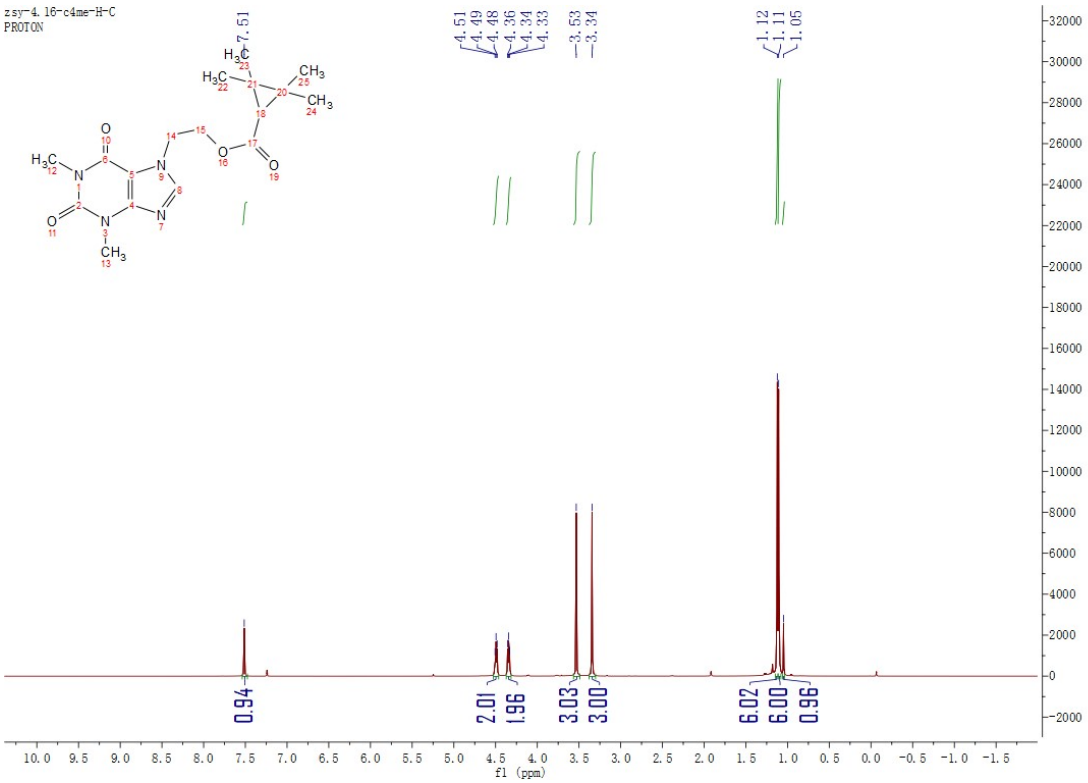

Fig. S12. The ^{1}H NMR spectrum of compound **Ia**.

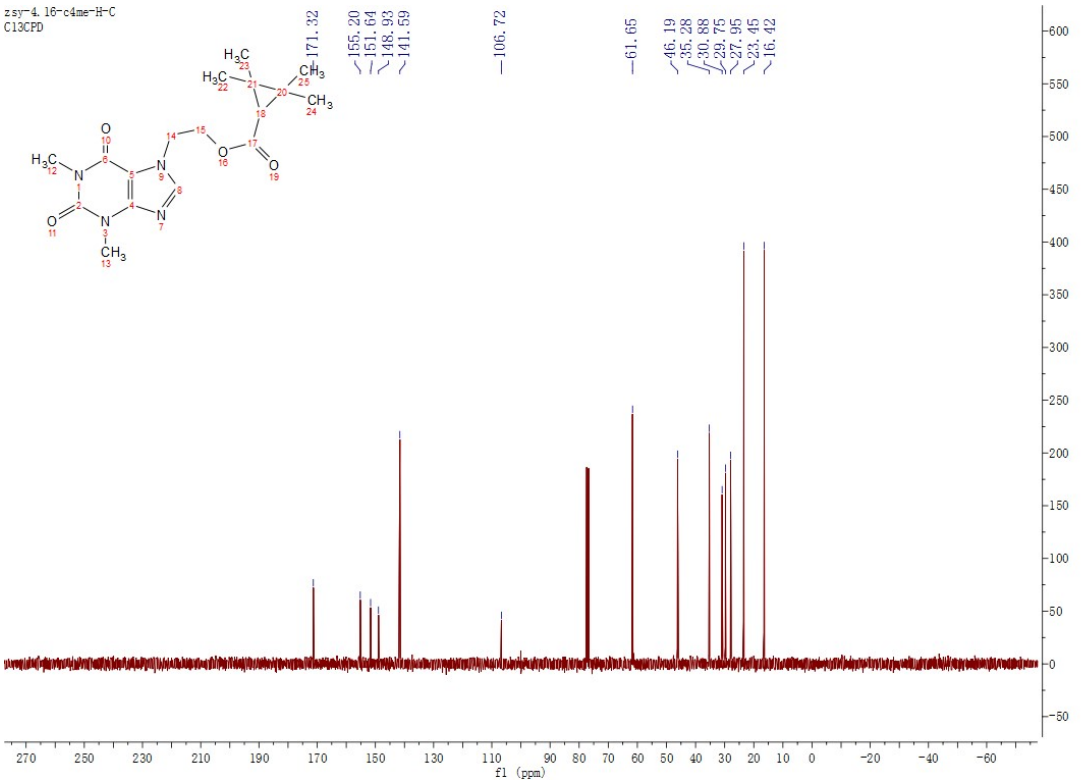

Fig. S13. The ^{13}C NMR spectrum of compound **Ia**.

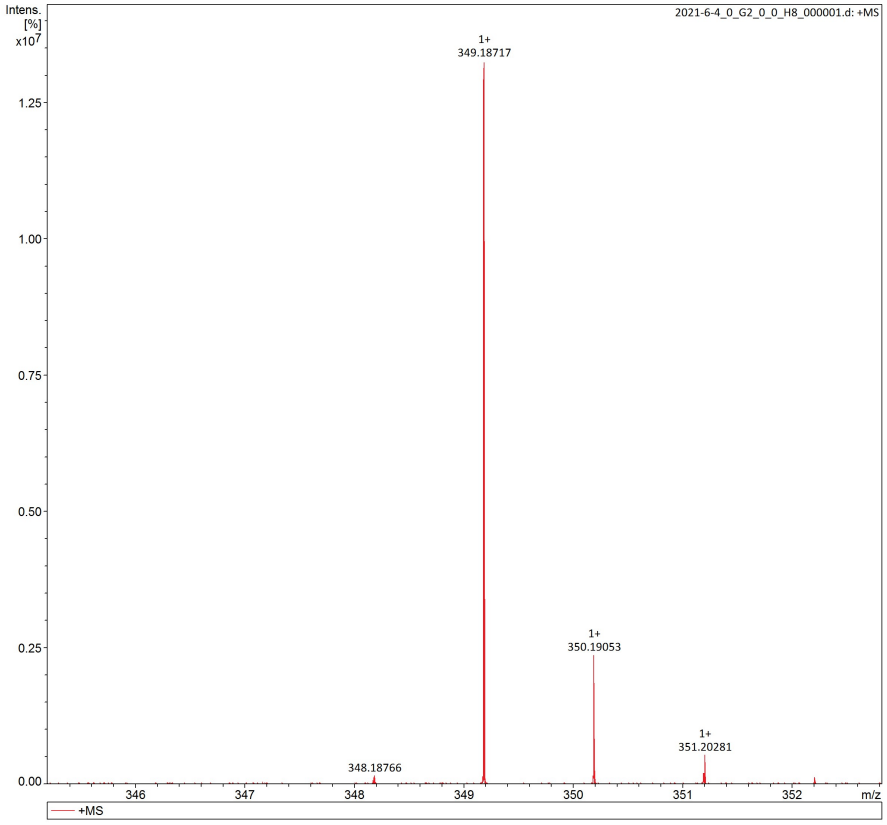

Fig. S14. The HRMS spectrum of compound **Ia**.

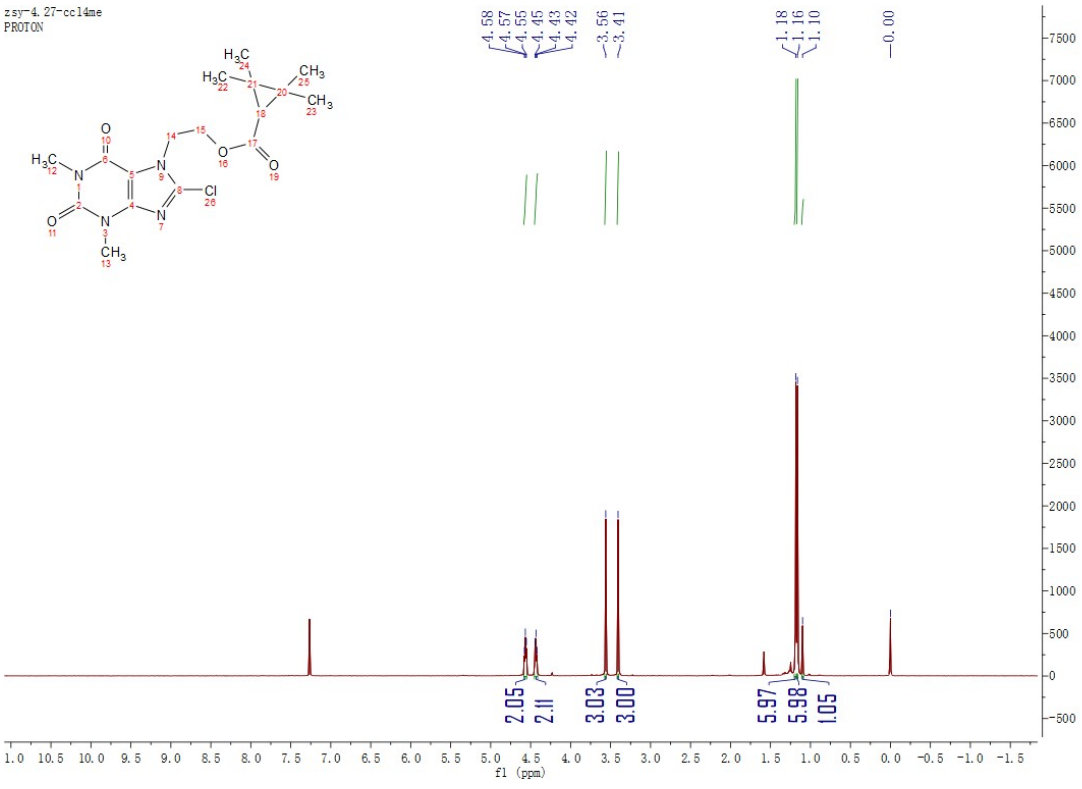

Fig. S15. The ^{1}H NMR spectrum of compound **Ib**.

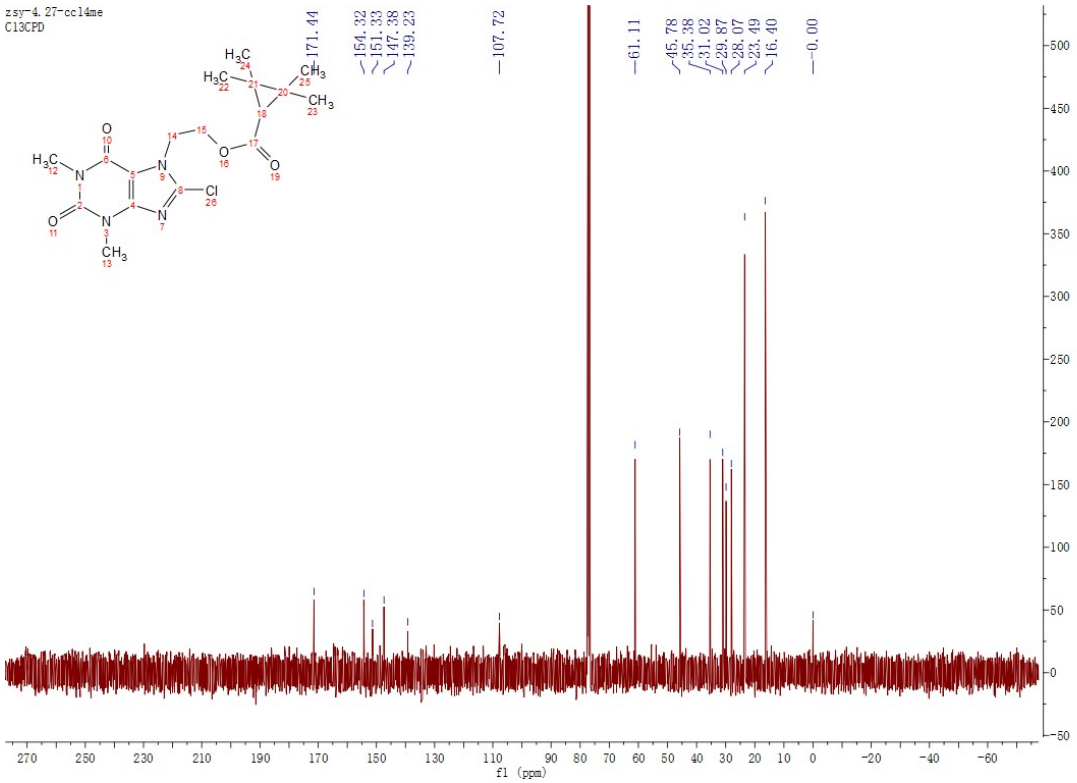

Fig. S16. The ^{13}C NMR spectrum of compound **Ib**.

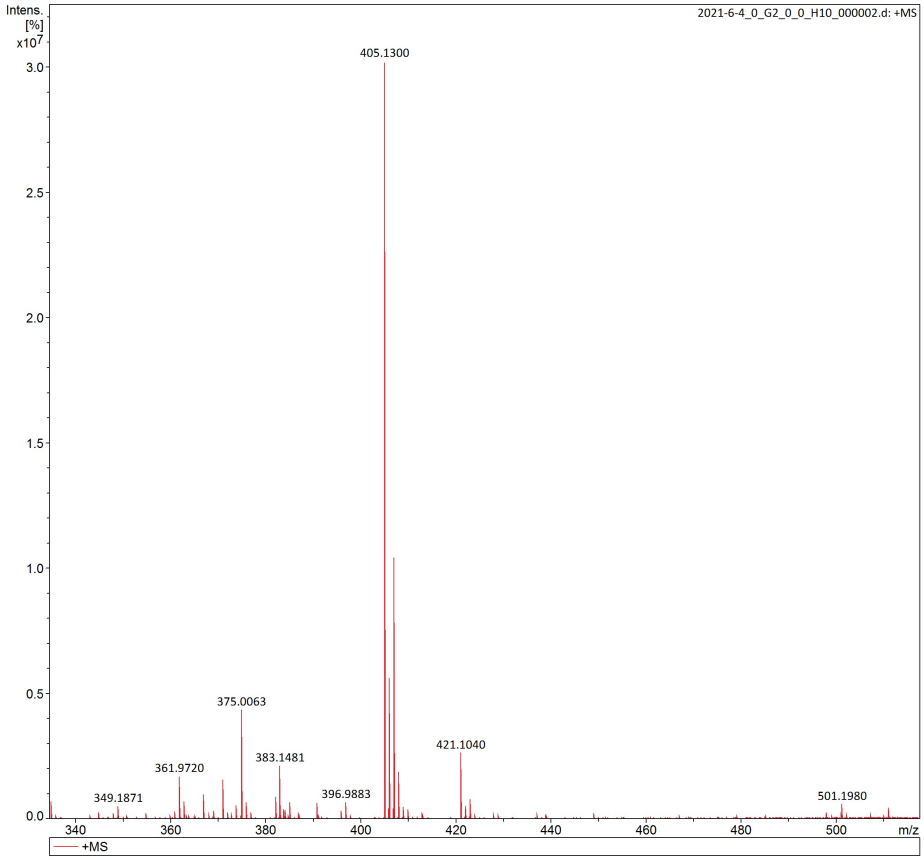

Fig. S17. The HRMS spectrum of compound **Ib**.

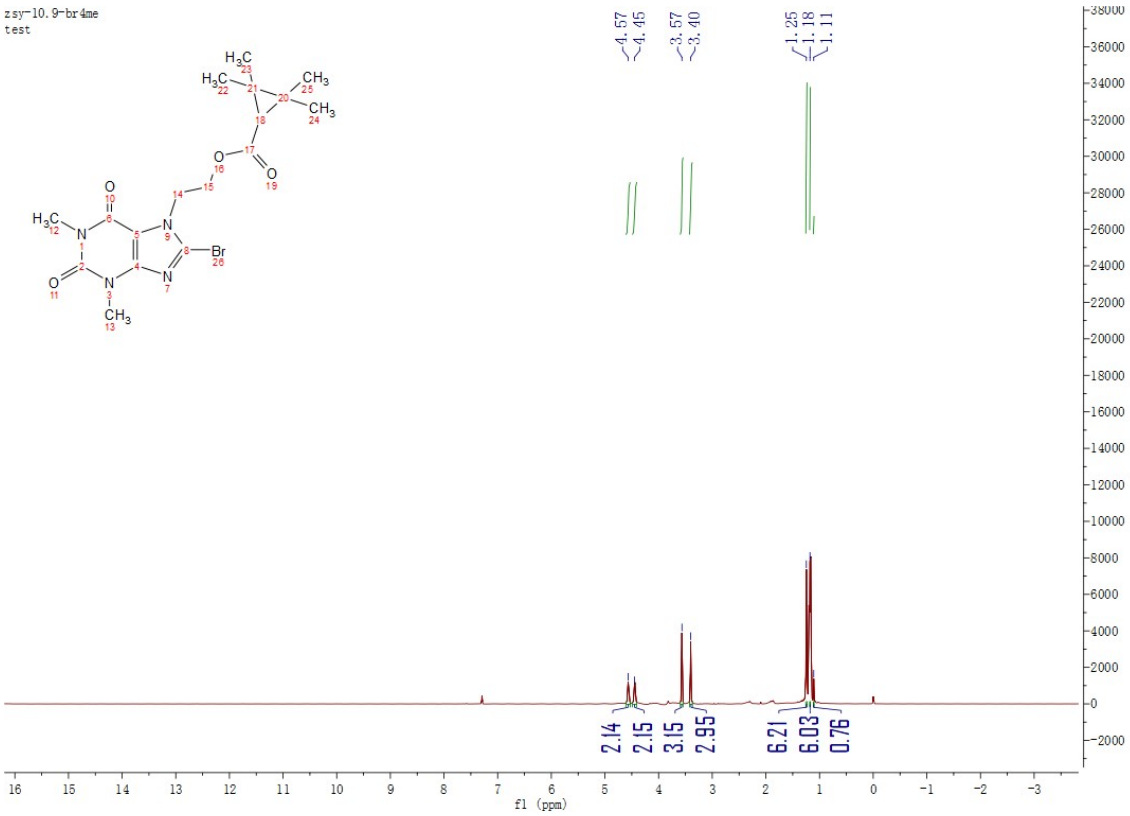

Fig. S18. The ^{1}H NMR spectrum of compound **Ic**.

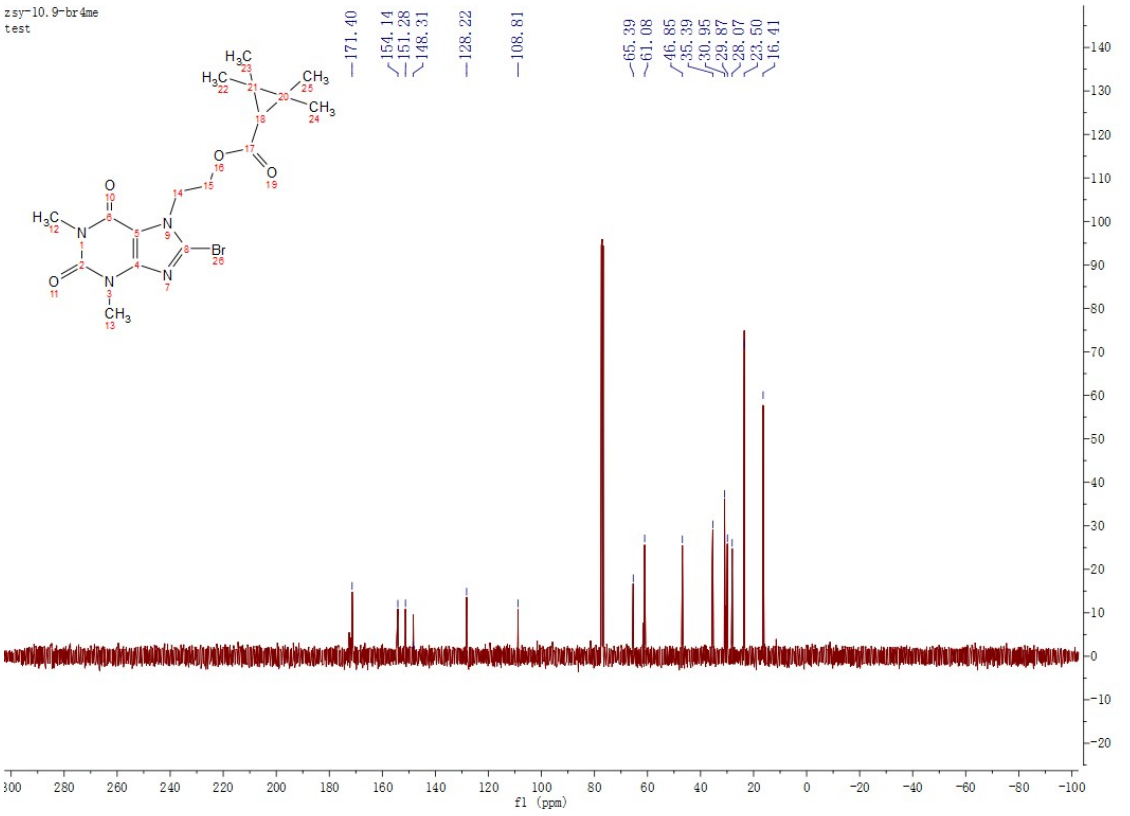

Fig. S19. The ^{13}C NMR spectrum of compound **Ic**.

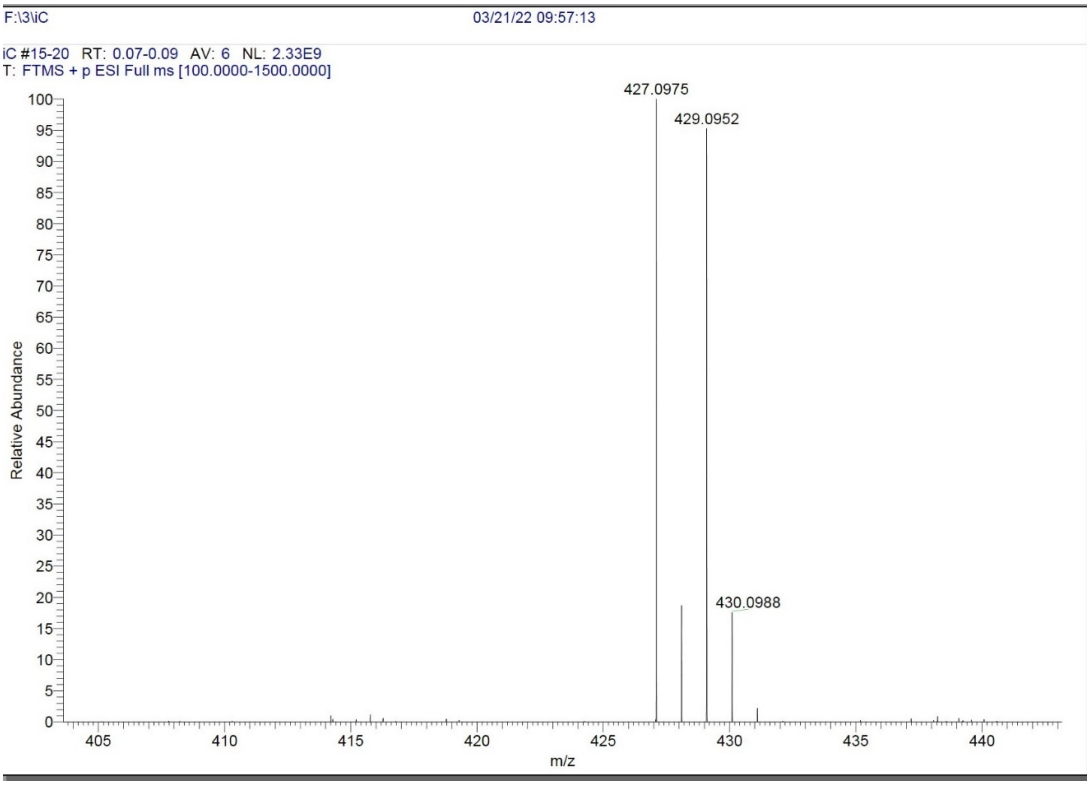

Fig. S20. The HRMS spectrum of compound **Ic**.

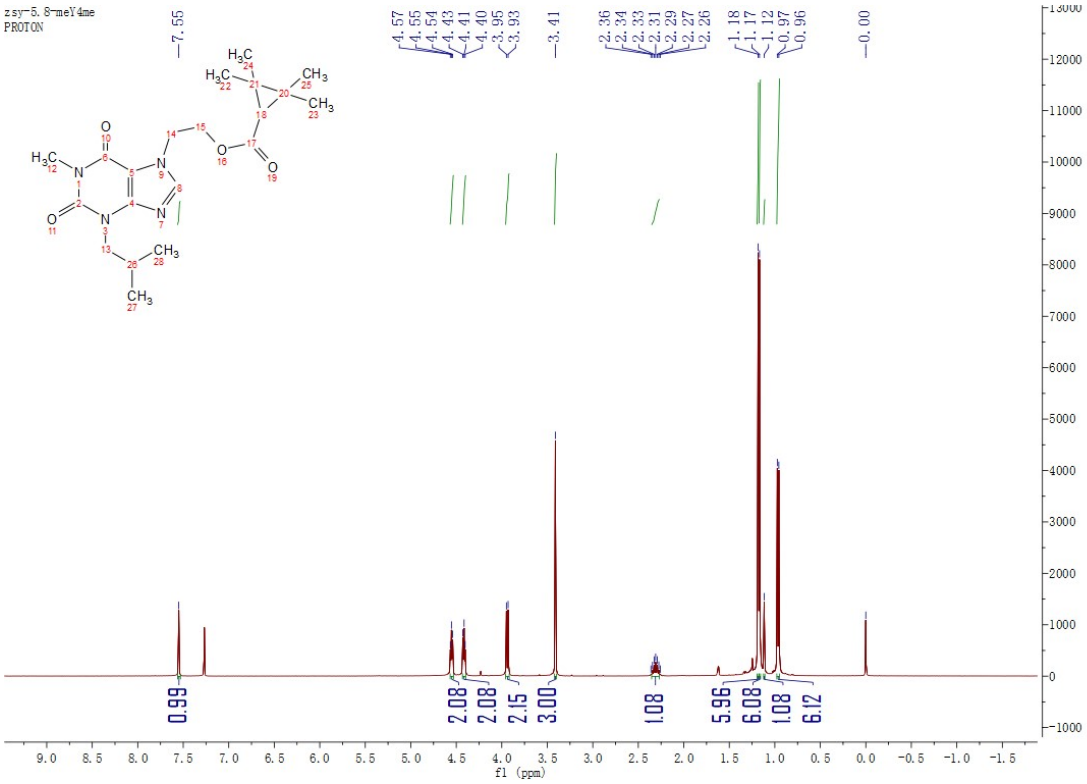

Fig. S21. The ^{1}H NMR spectrum of compound **Id**.

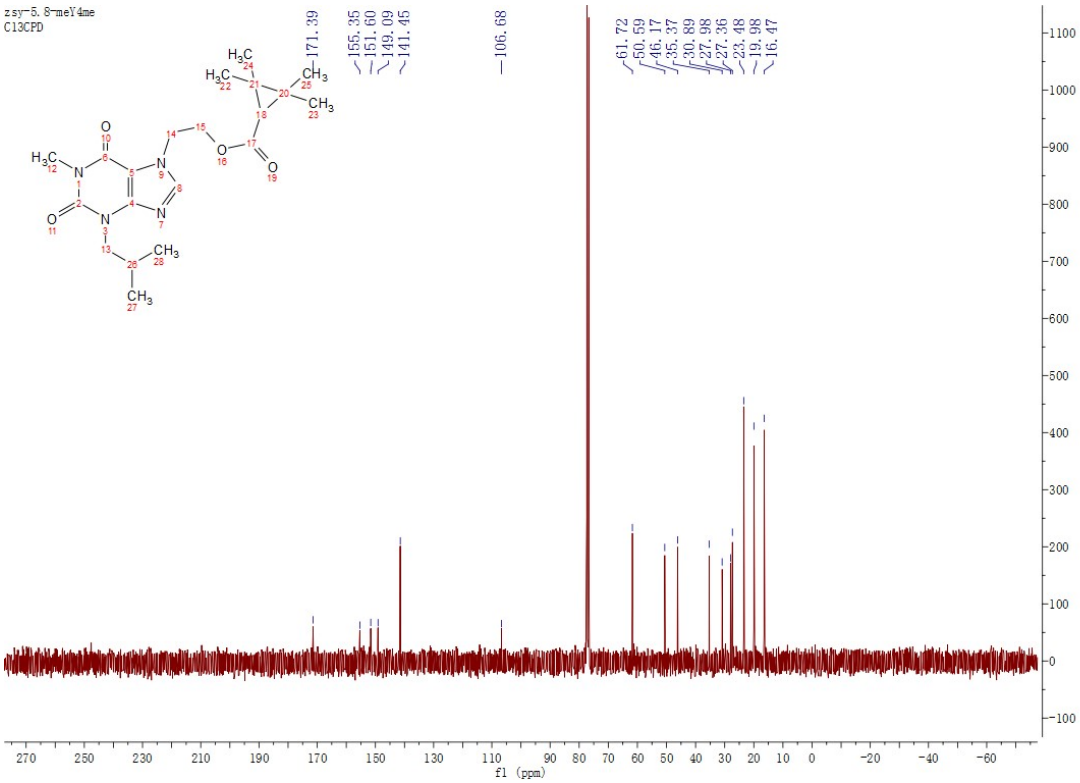

Fig. S22. The ^{13}C NMR spectrum of compound **Id**.

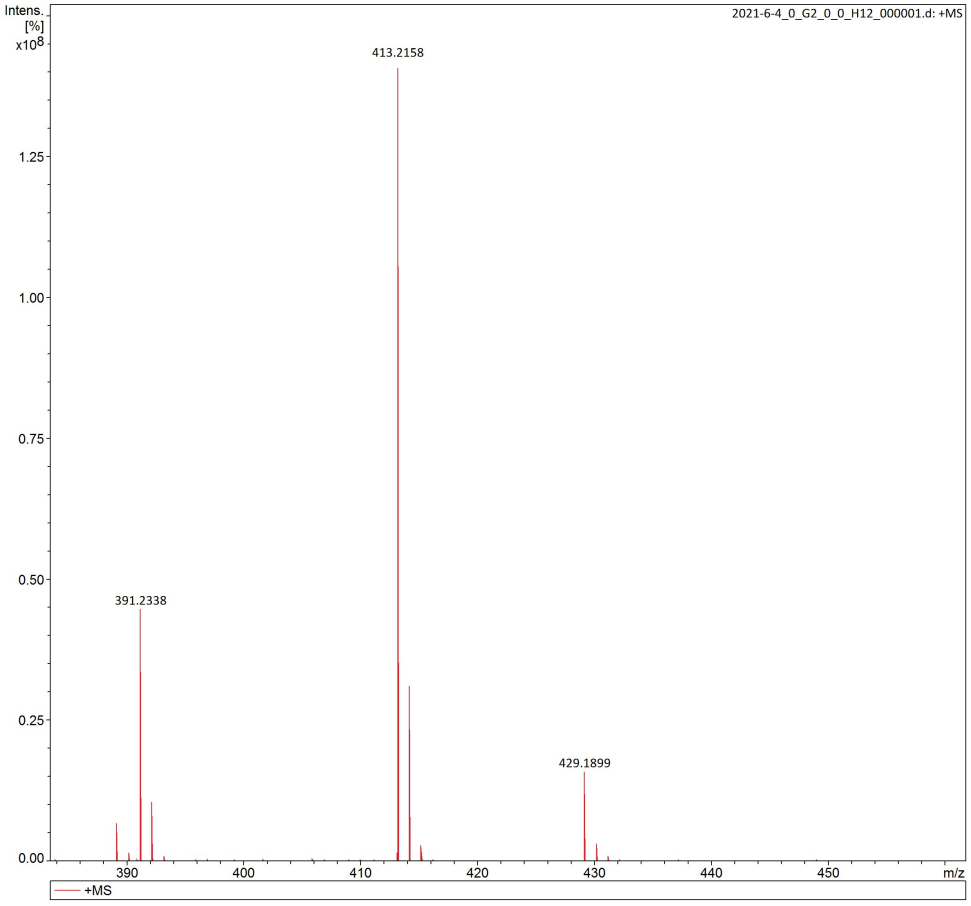

Fig. S23. The HRMS spectrum of compound **Id**.

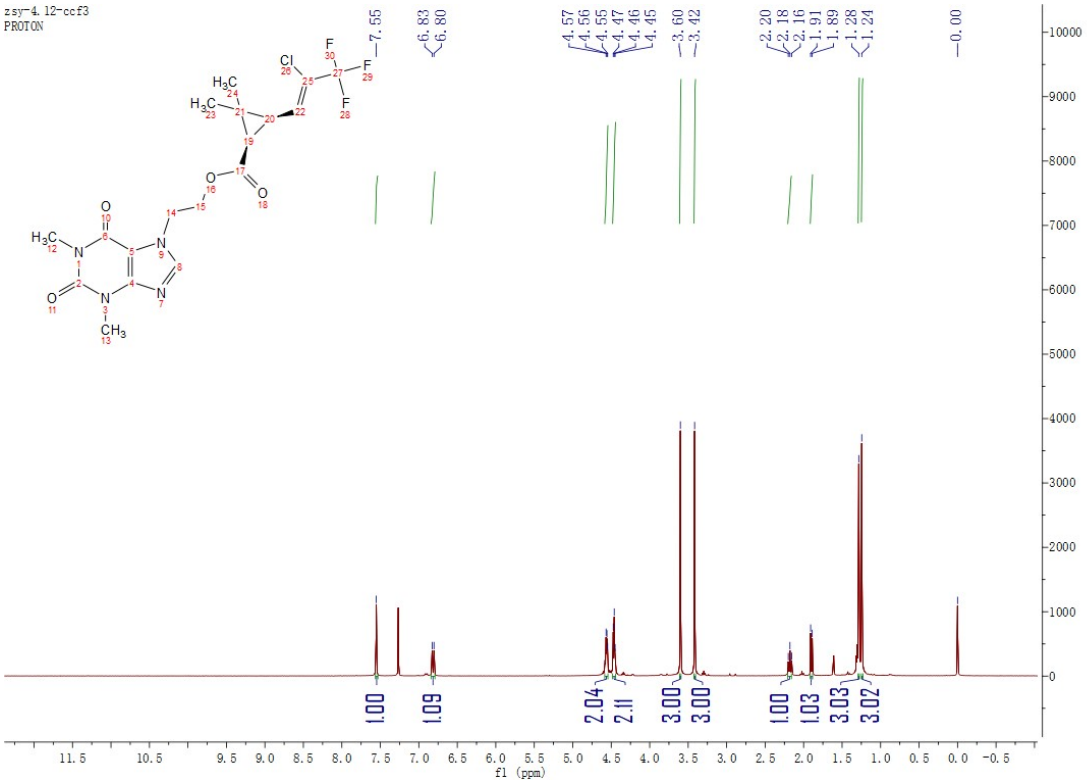

Fig. S24. The ^{1}H NMR spectrum of compound **Ie**.

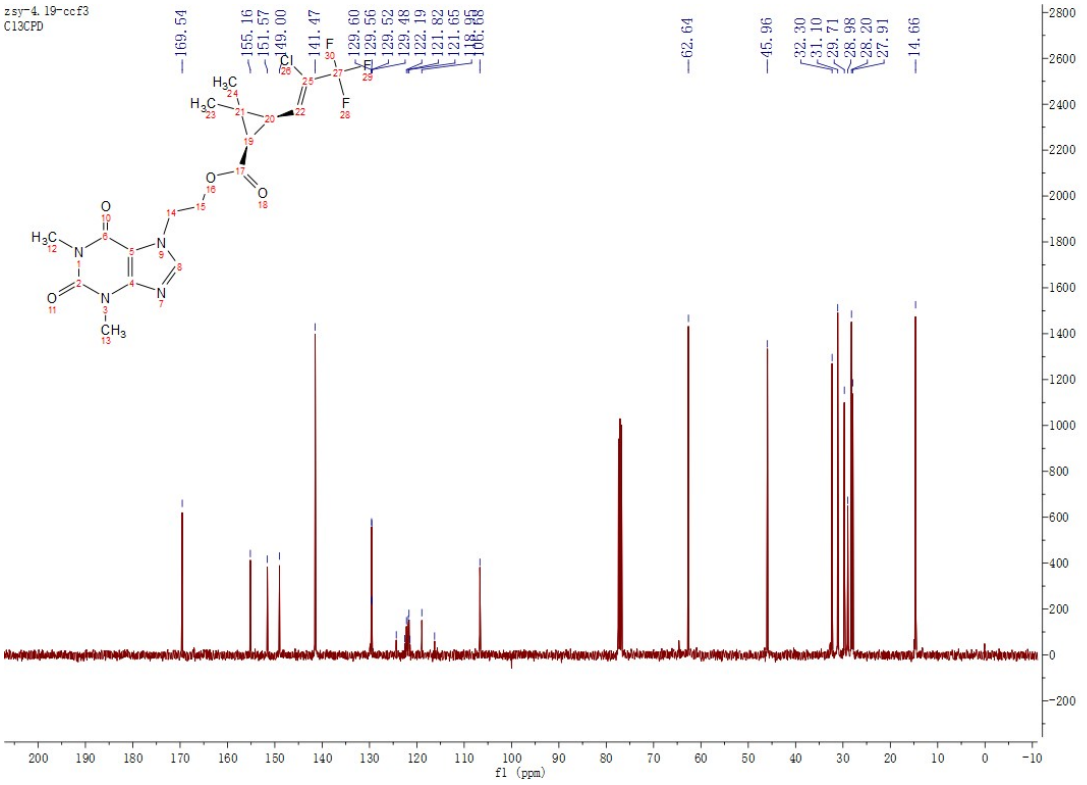

Fig. S25. The ^{13}C NMR spectrum of compound **Ie**.

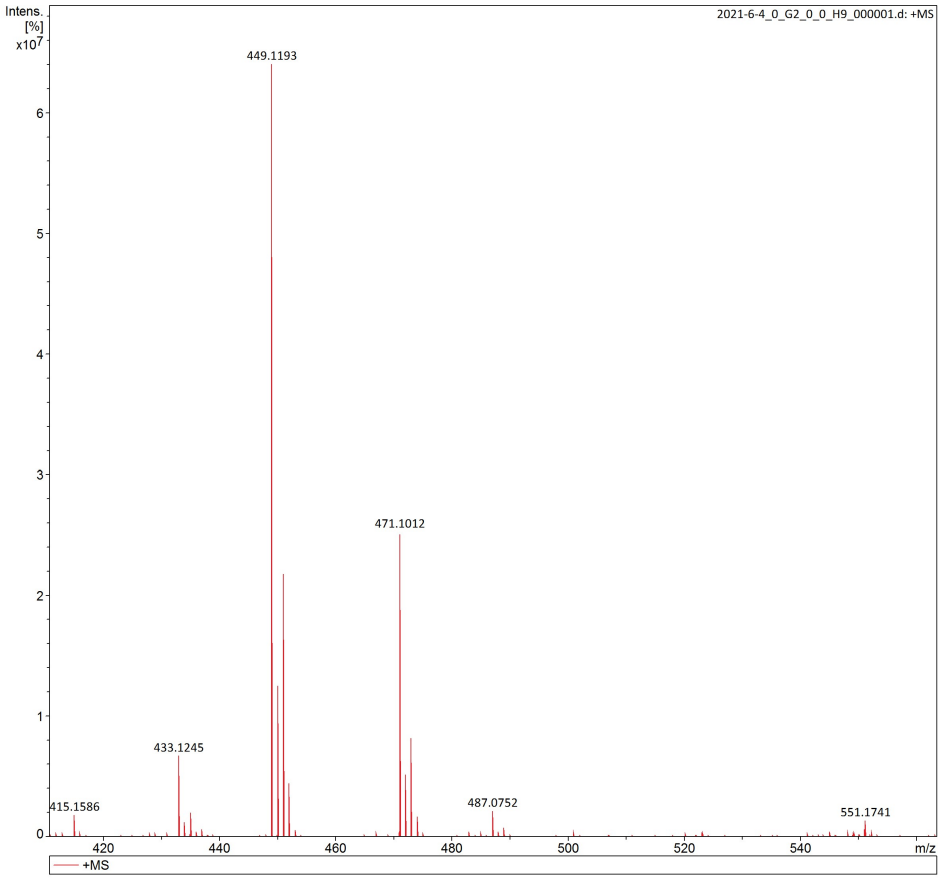

Fig. S26. The HRMS spectrum of compound **Ie**.

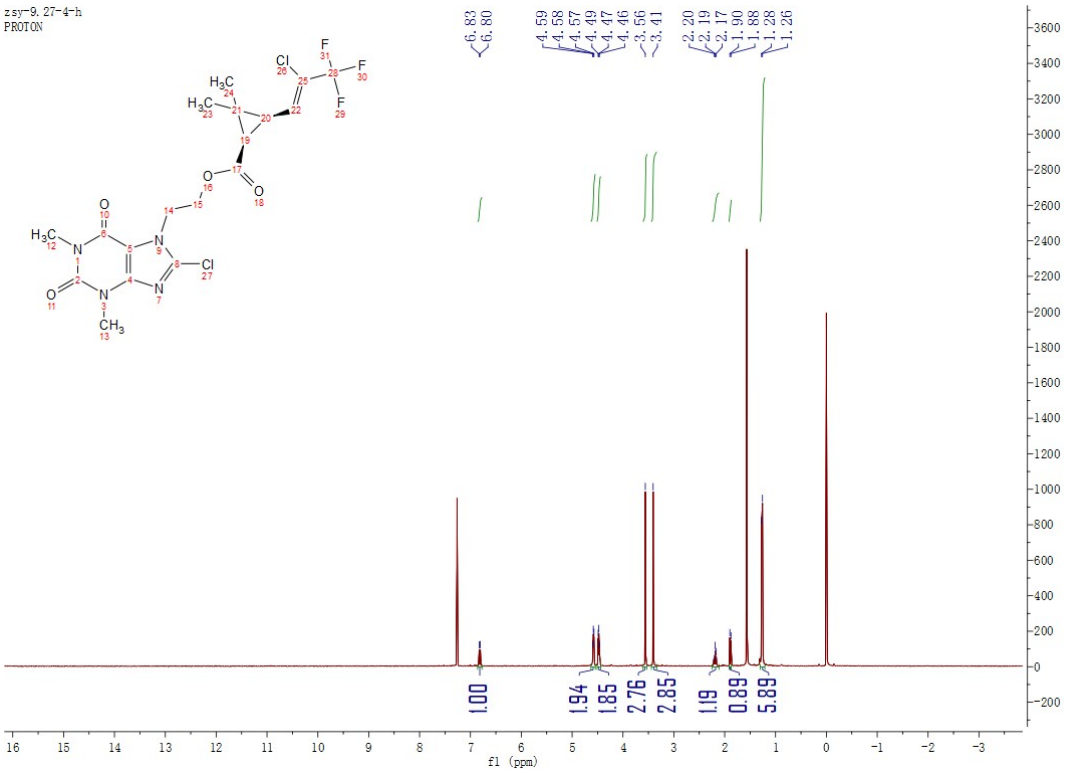

Fig. S27. The ^{1}H NMR spectrum of compound **If**.

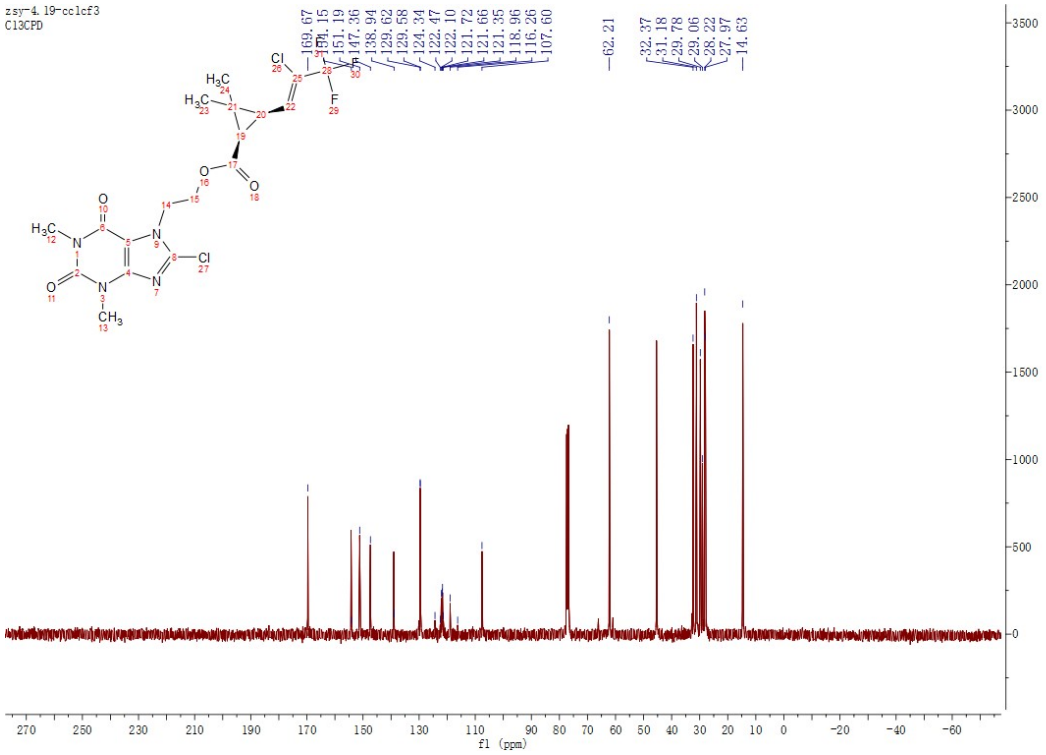

Fig. S28. The ^{13}C NMR spectrum of compound **If**.

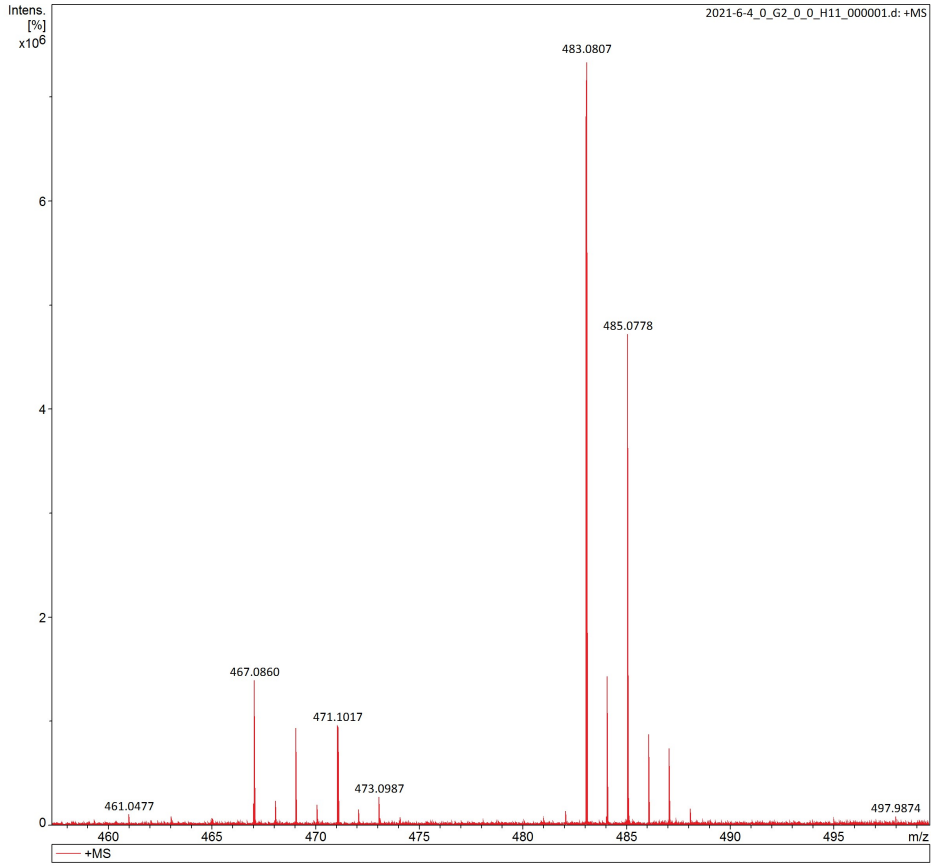

Fig. S29. The HRMS spectrum of compound **If**.

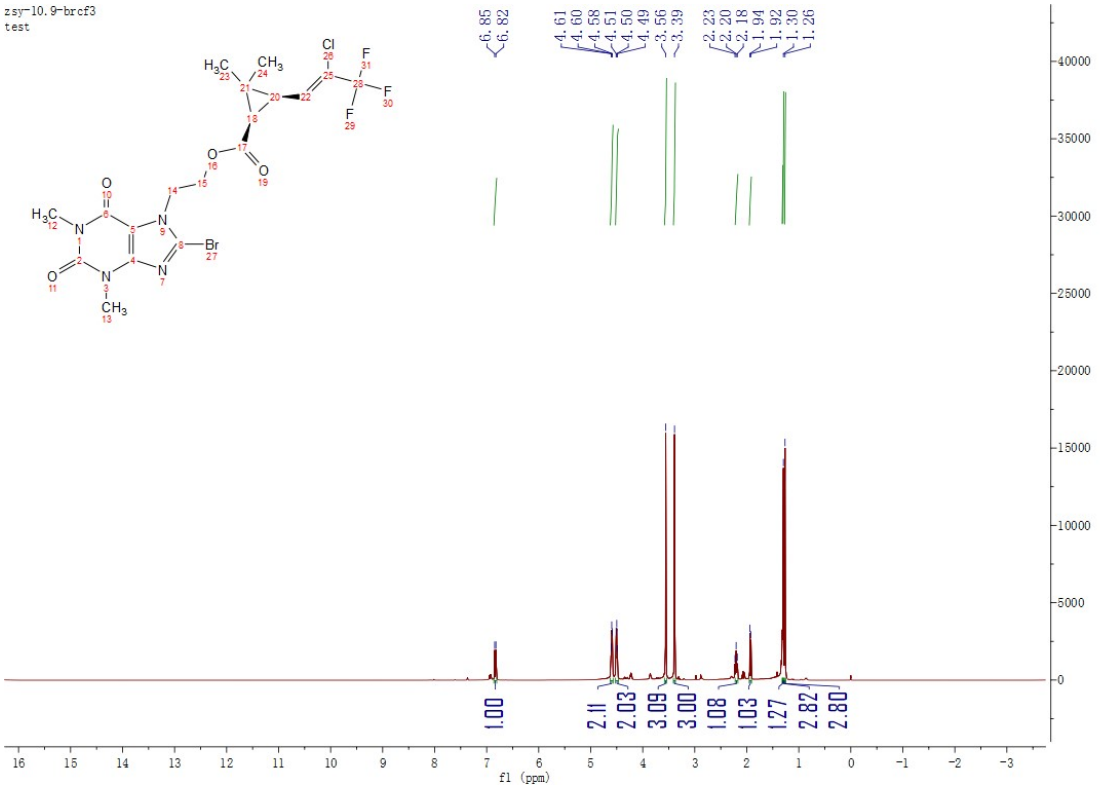

Fig. S30. The ^{1}H NMR spectrum of compound **Ig**.

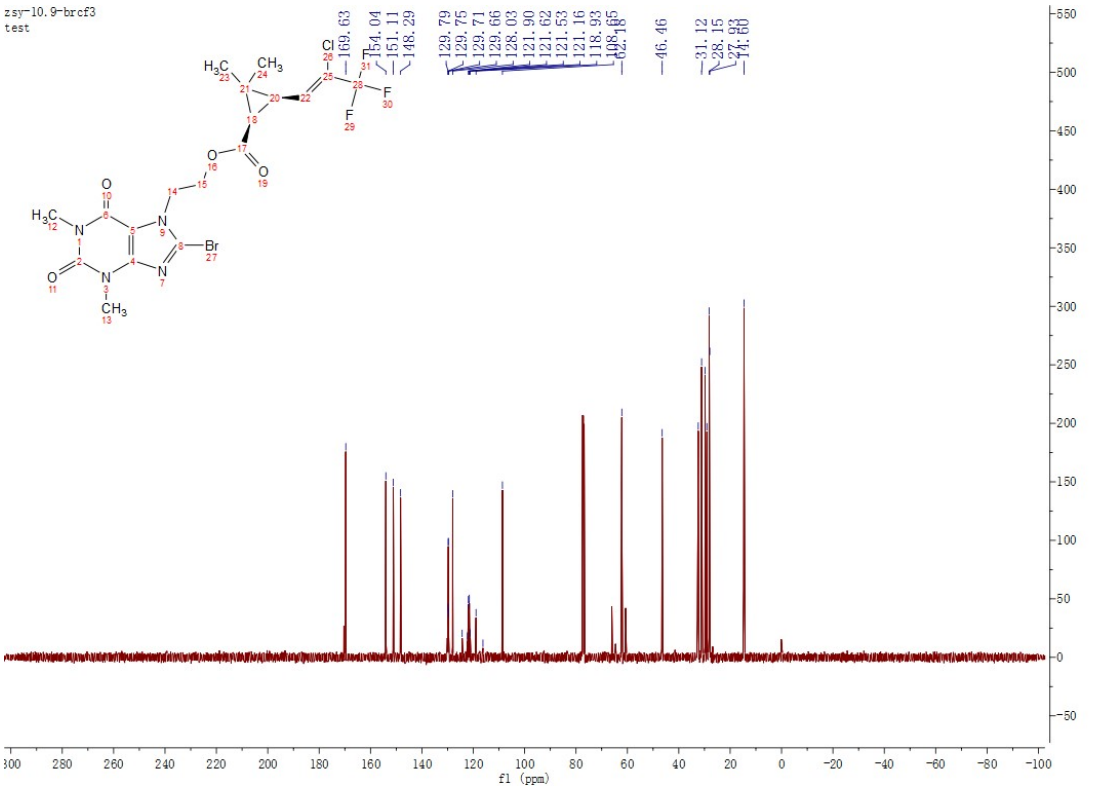

Fig. S31. The ^{13}C NMR spectrum of compound **Ig**.

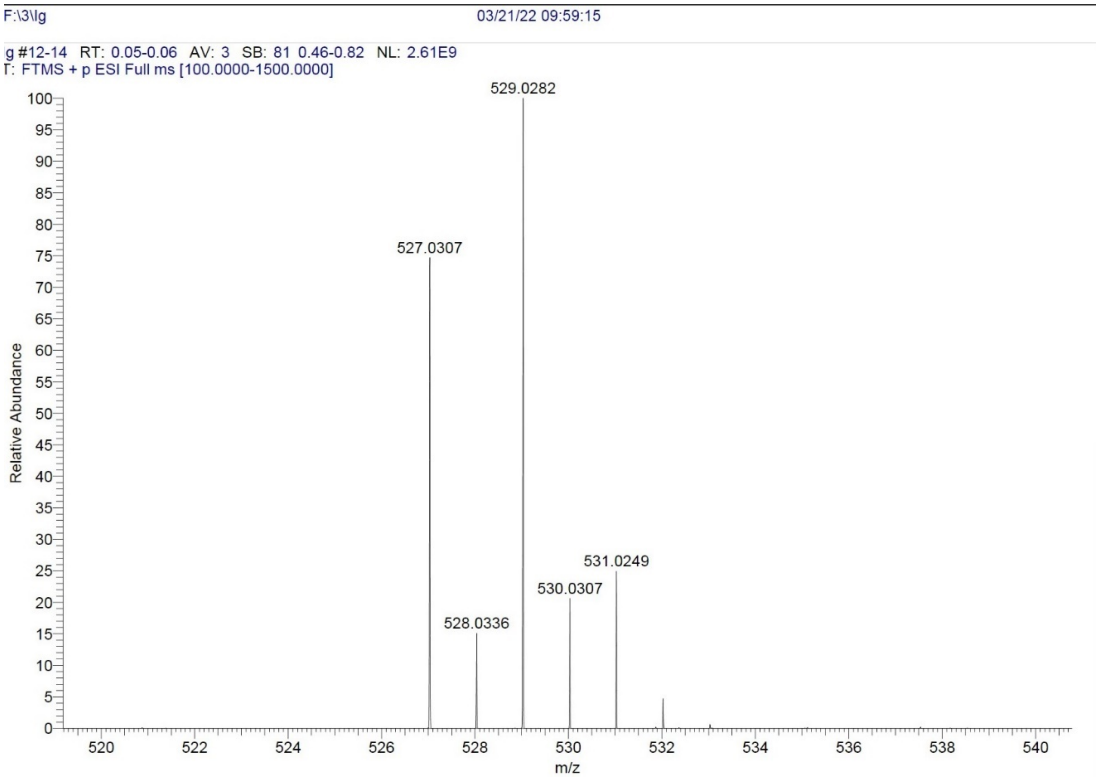

Fig. S32. The HRMS spectrum of compound **Ig**.

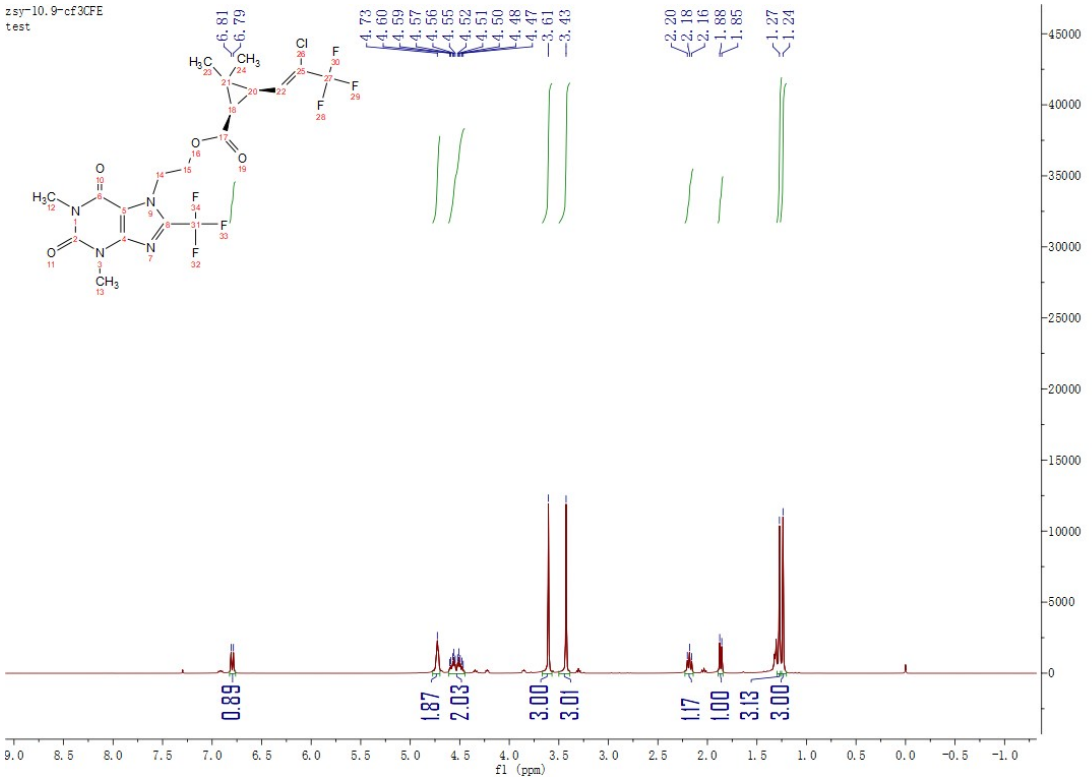

Fig. S33. The ^{1}H NMR spectrum of compound **Ih**.

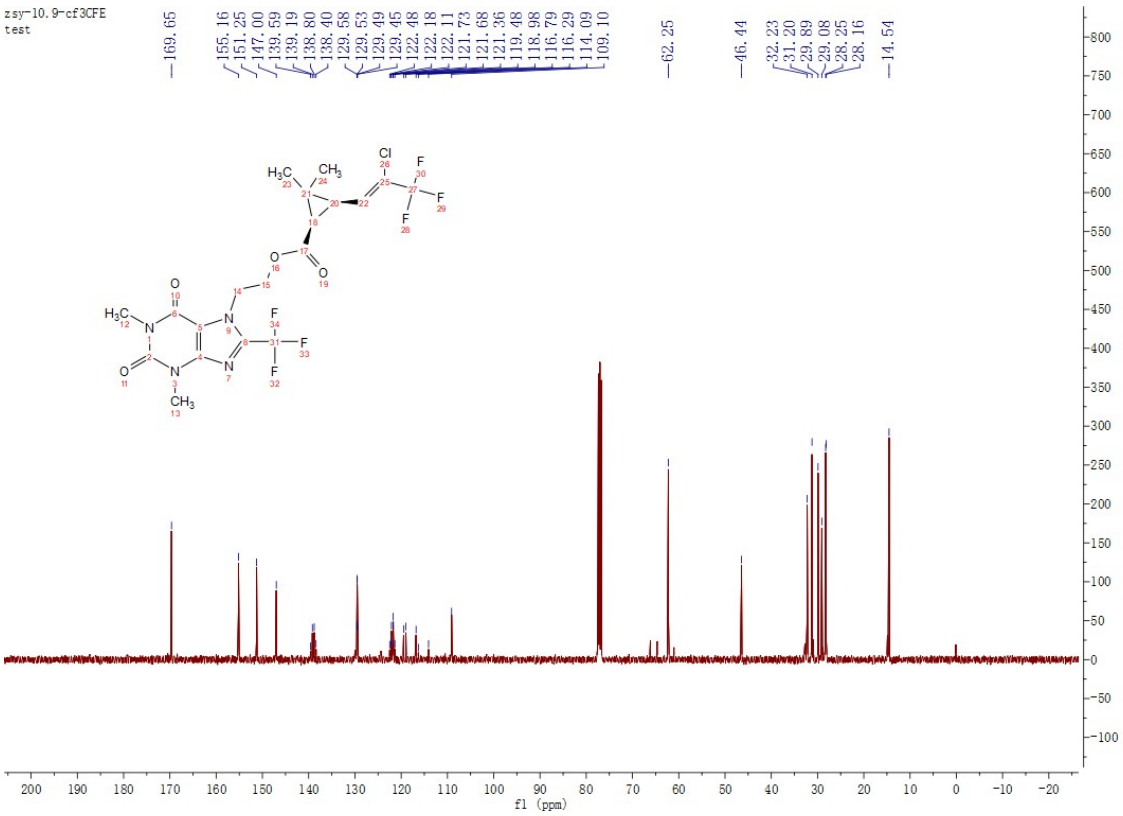

Fig. S34. The ^{13}C NMR spectrum of compound **Ih**.

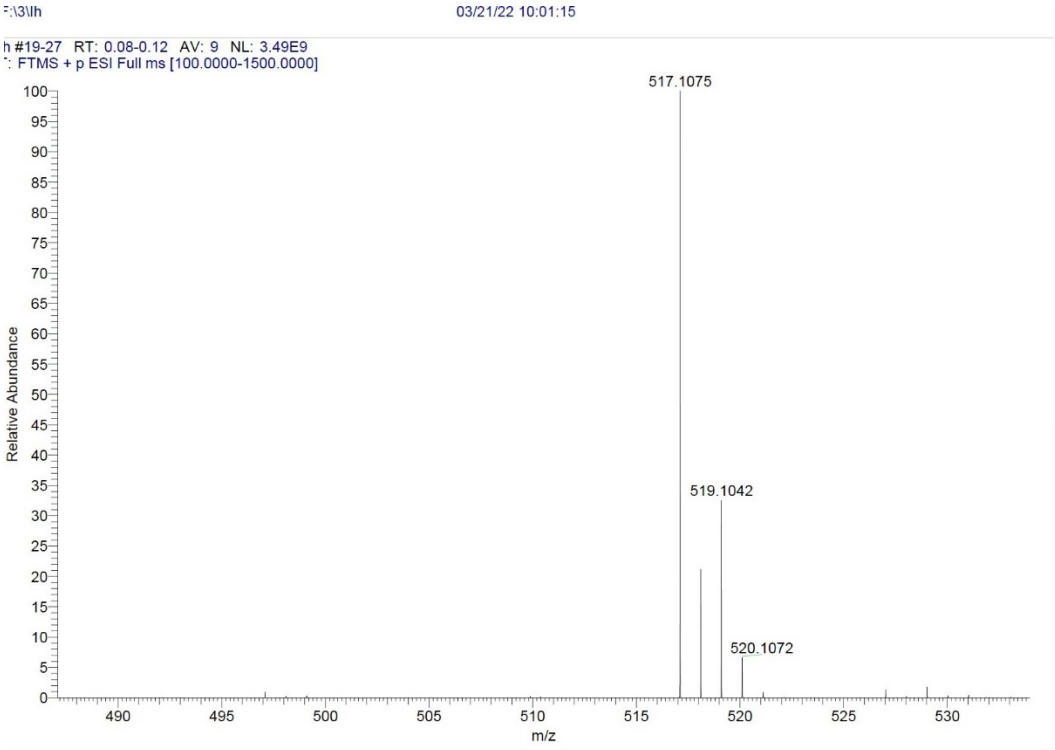

Fig. S35. The HRMS spectrum of compound **Ih**.

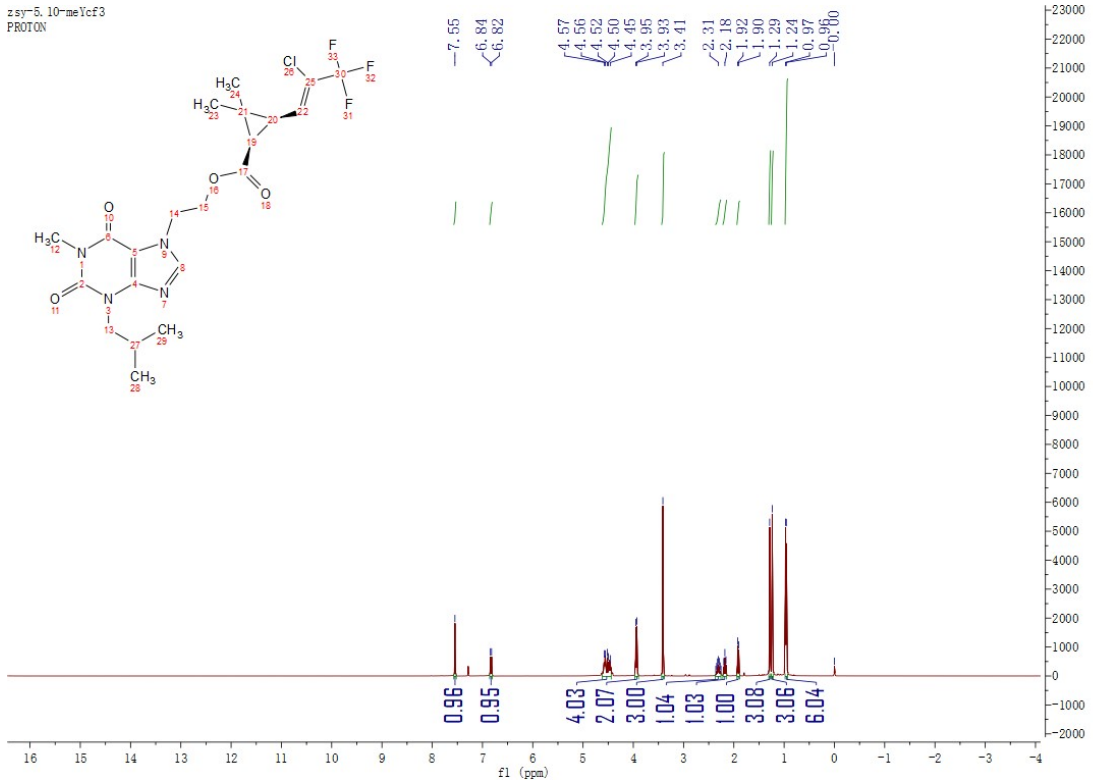

Fig. S36. The ^{1}H NMR spectrum of compound **Ii**.

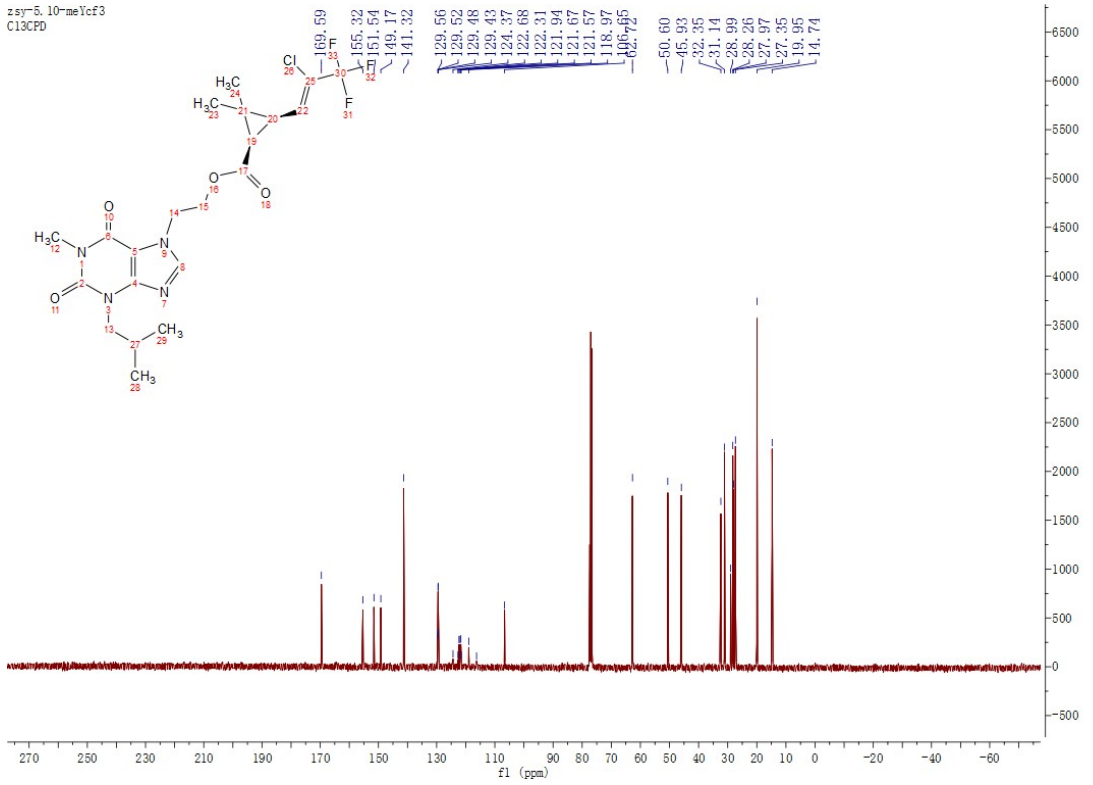

Fig. S37. The ^{13}C NMR spectrum of compound **Ii**.

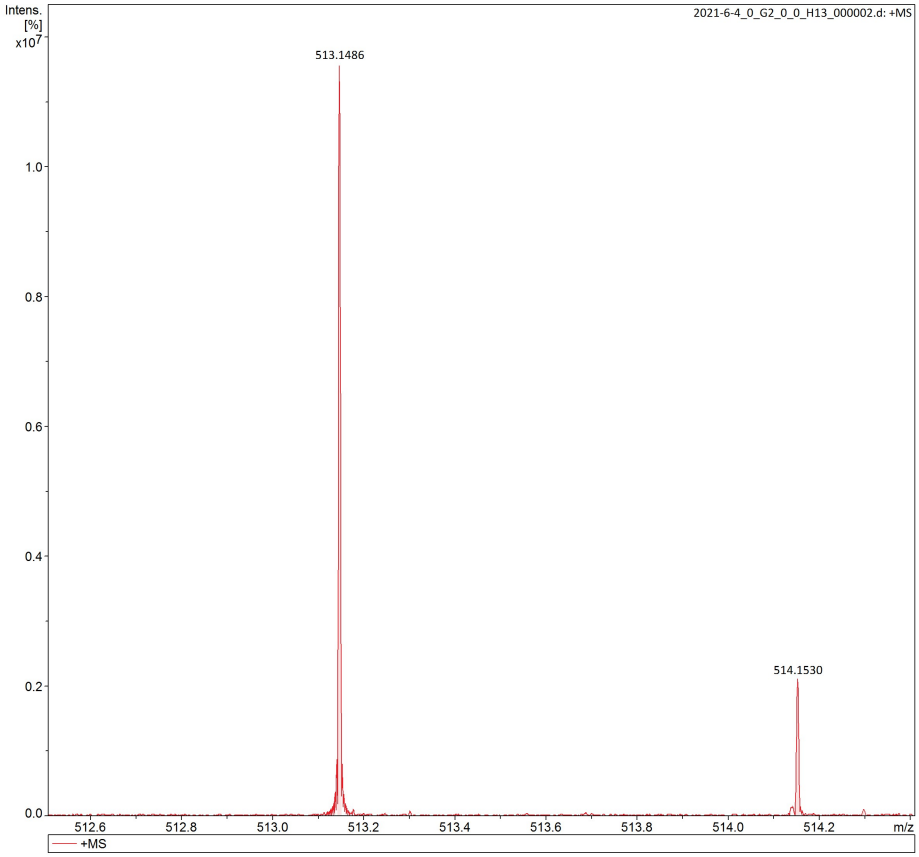

Fig. S38. The HRMS spectrum of compound **Ii**.

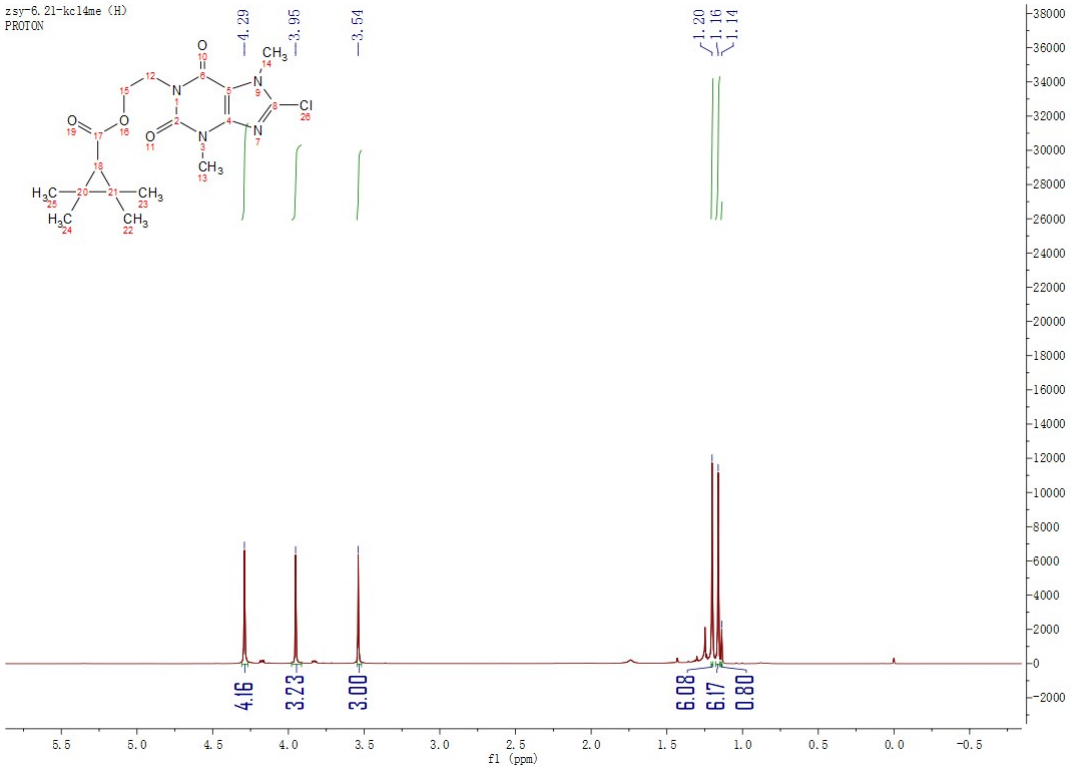

Fig. S39. The ^{1}H NMR spectrum of compound **Ij**.

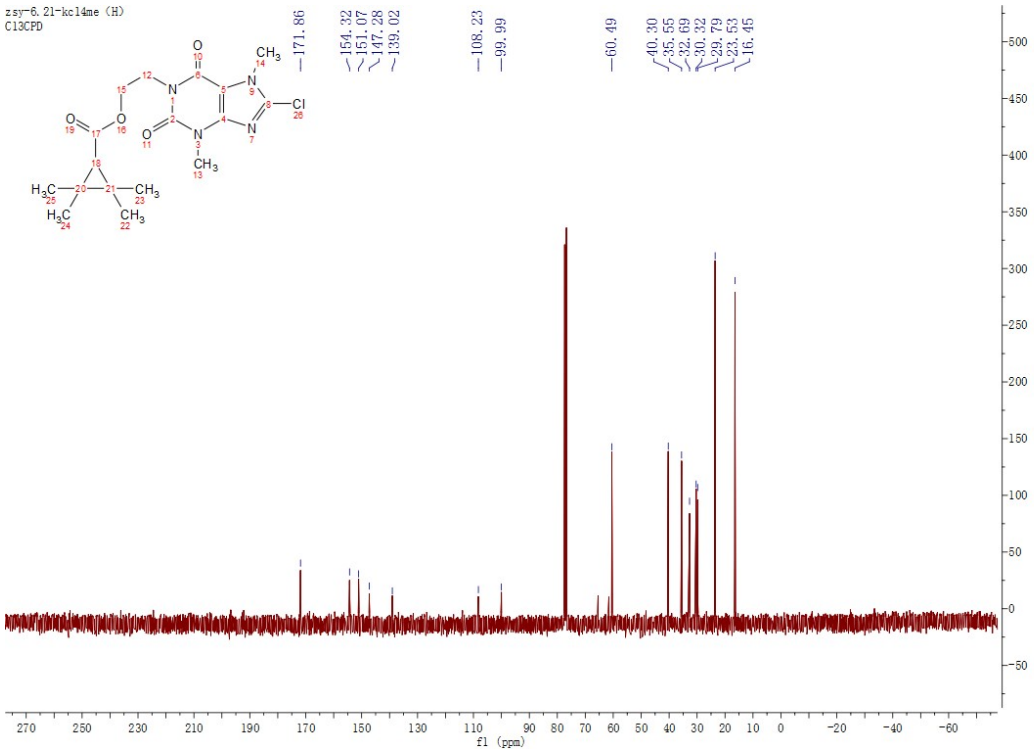

Fig. S40. The ^{13}C NMR spectrum of compound **Ij**.

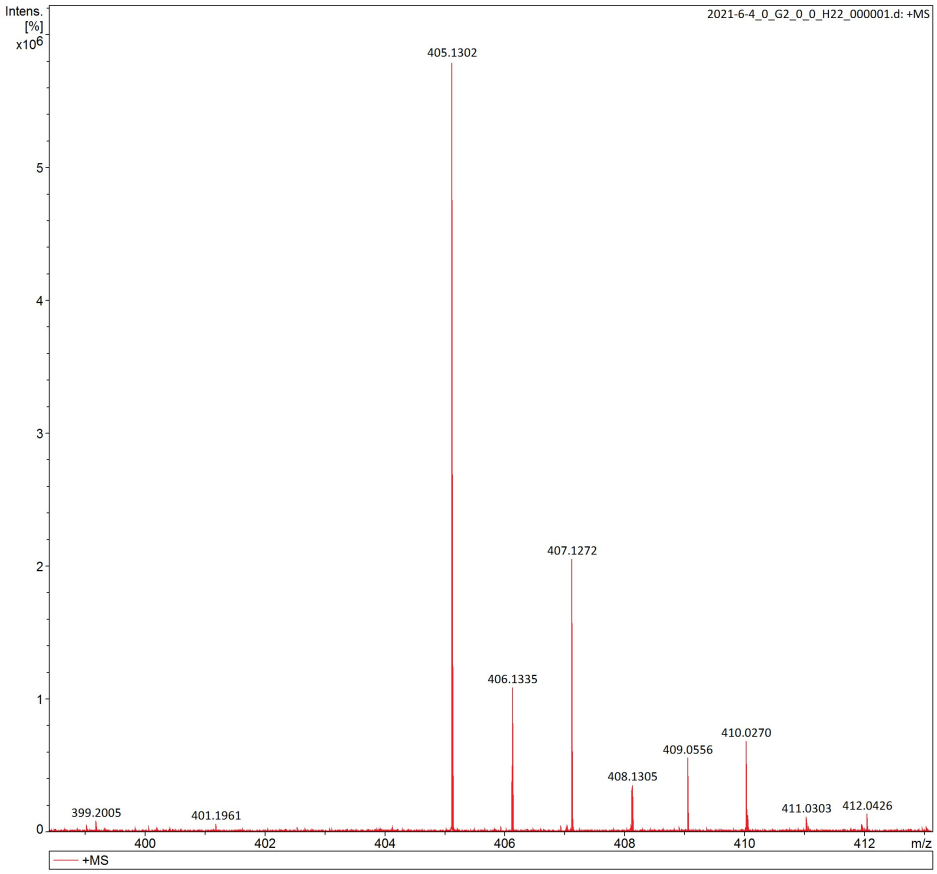

Fig. S41. The HRMS spectrum of compound **Ij**.

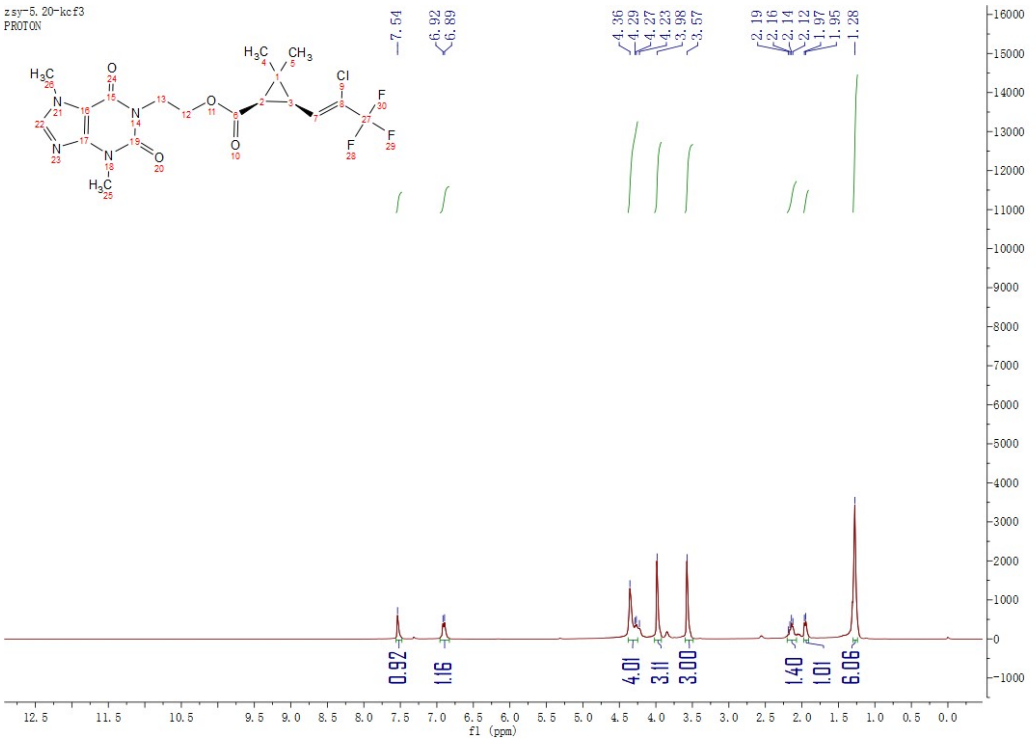

Fig. S42. The ^{1}H NMR spectrum of compound **Ik**.

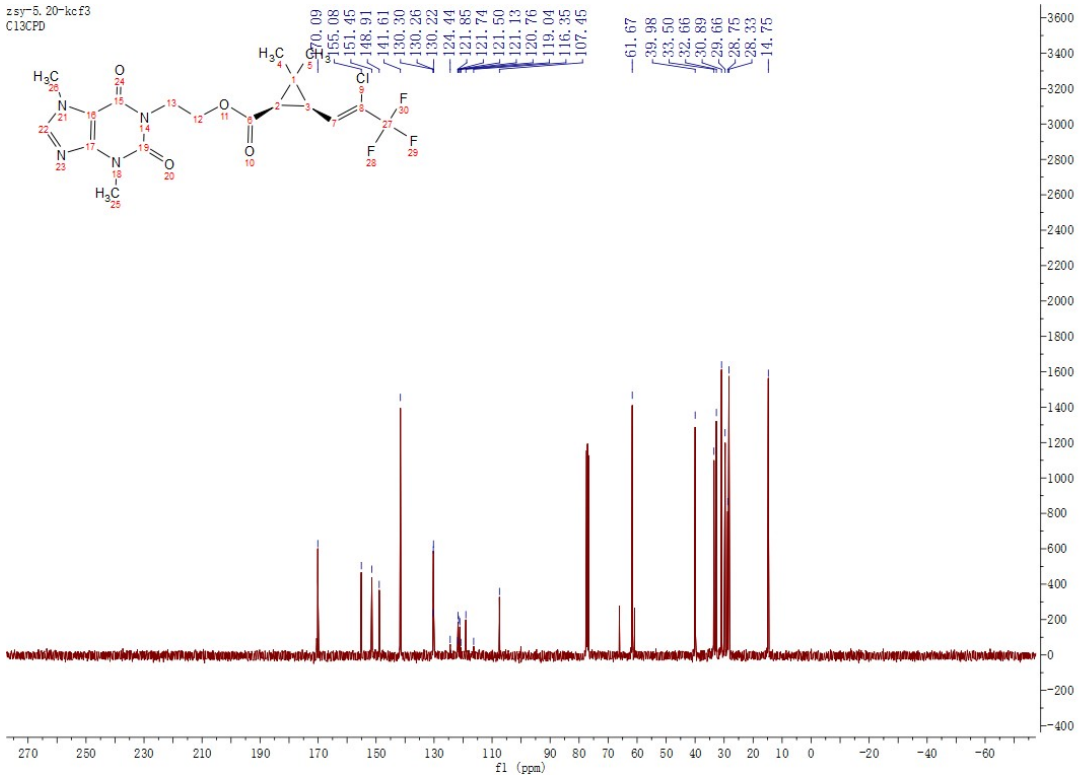

Fig. S43. The ^{13}C NMR spectrum of compound **Ik**.

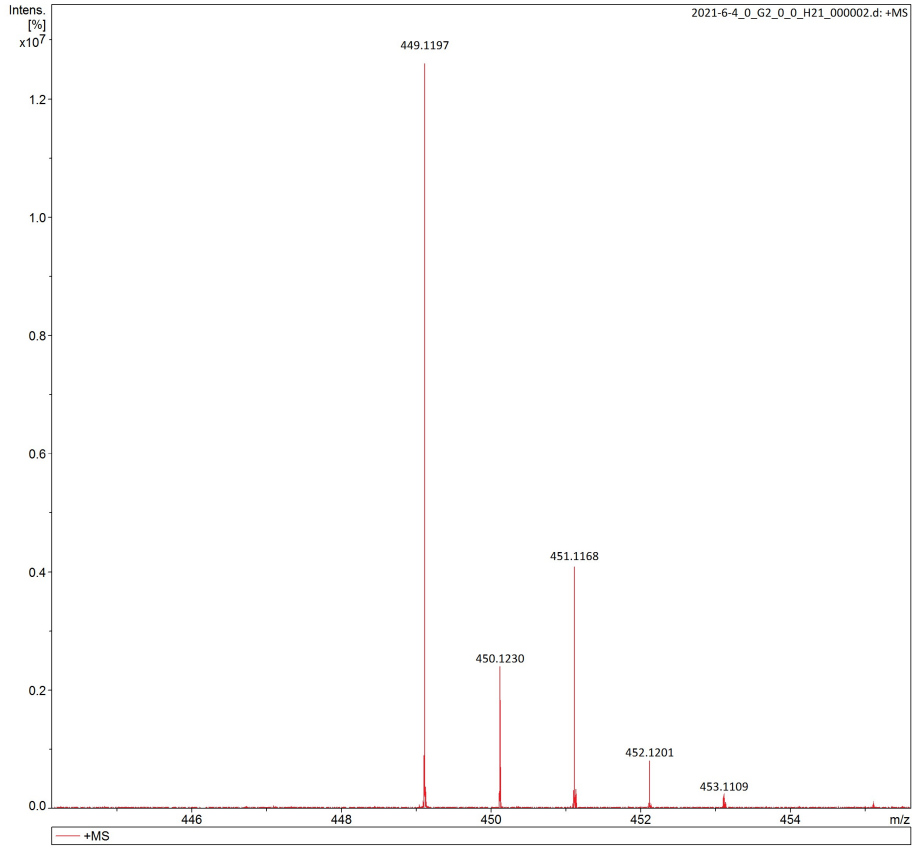

Fig. S44. The HRMS spectrum of compound **Ik**.

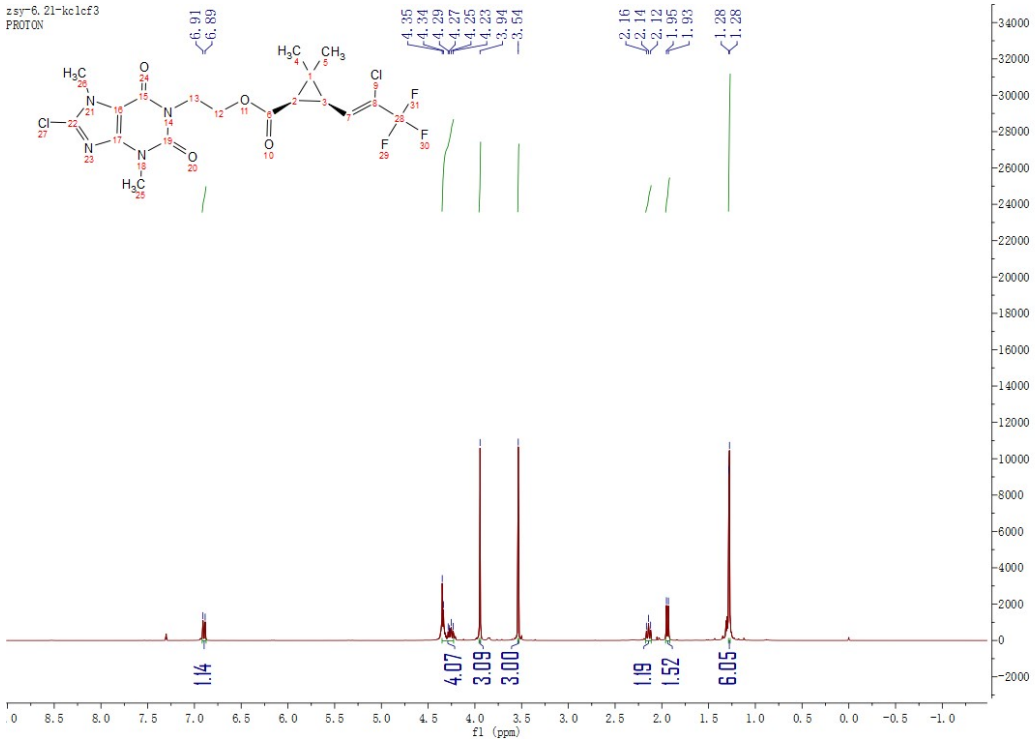

Fig. S45. The ^{1}H NMR spectrum of compound **Il**.

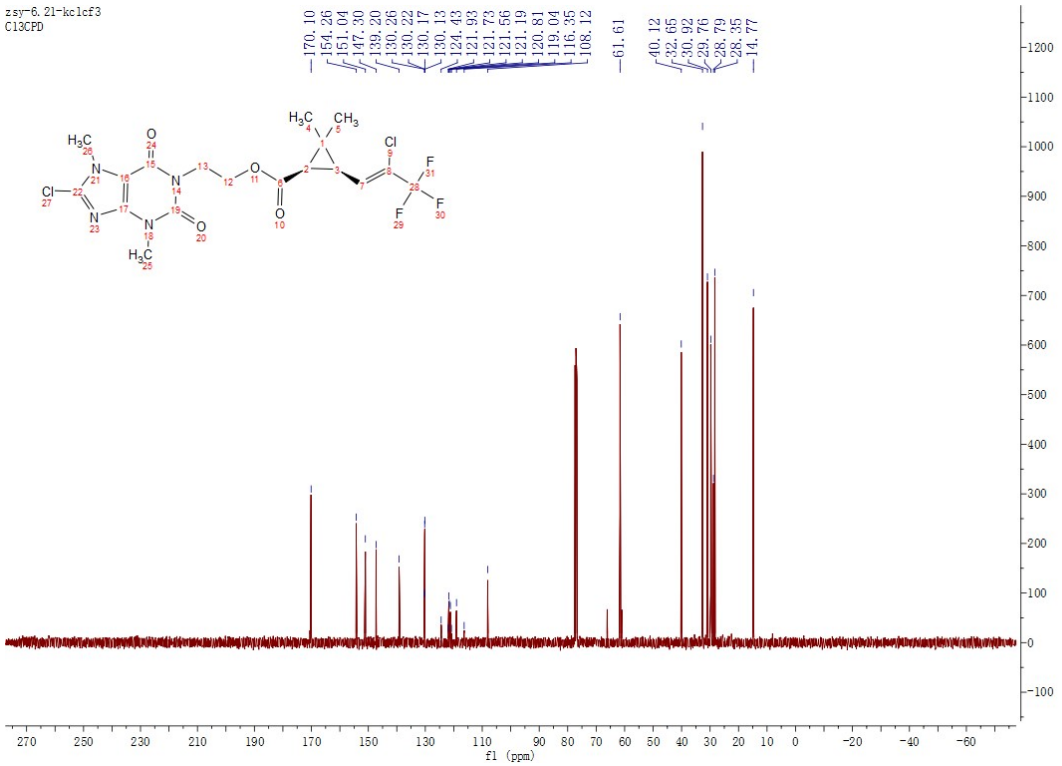

Fig. S46. The ^{13}C NMR spectrum of compound **II**.

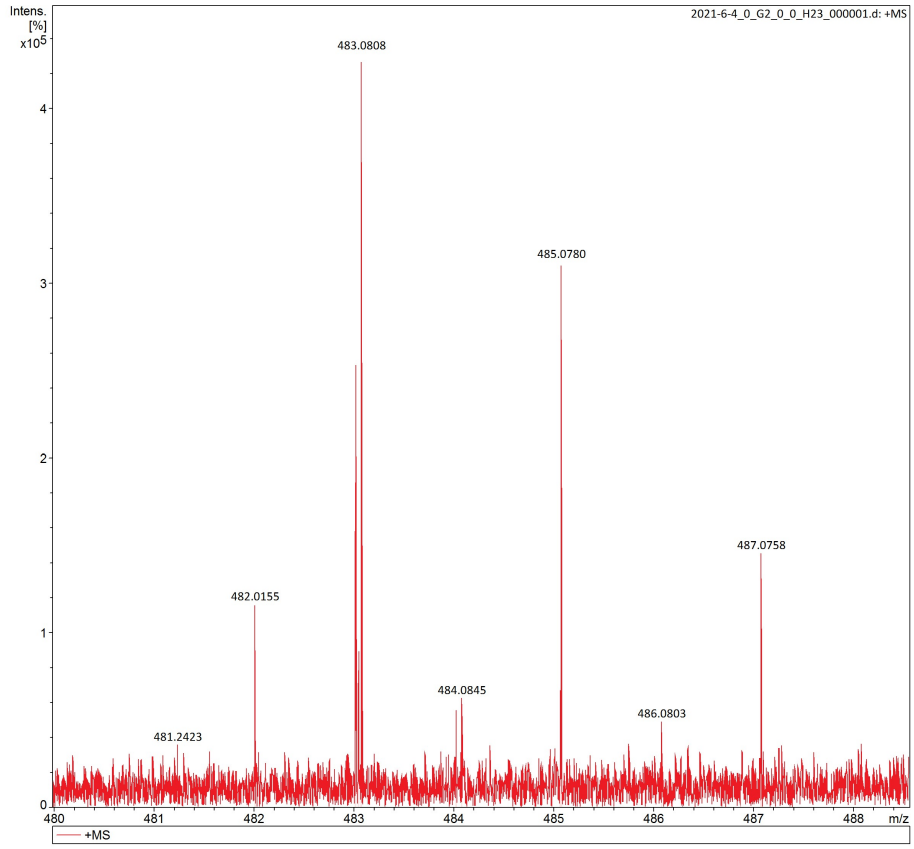

Fig. S47. The HRMS spectrum of compound **II**.

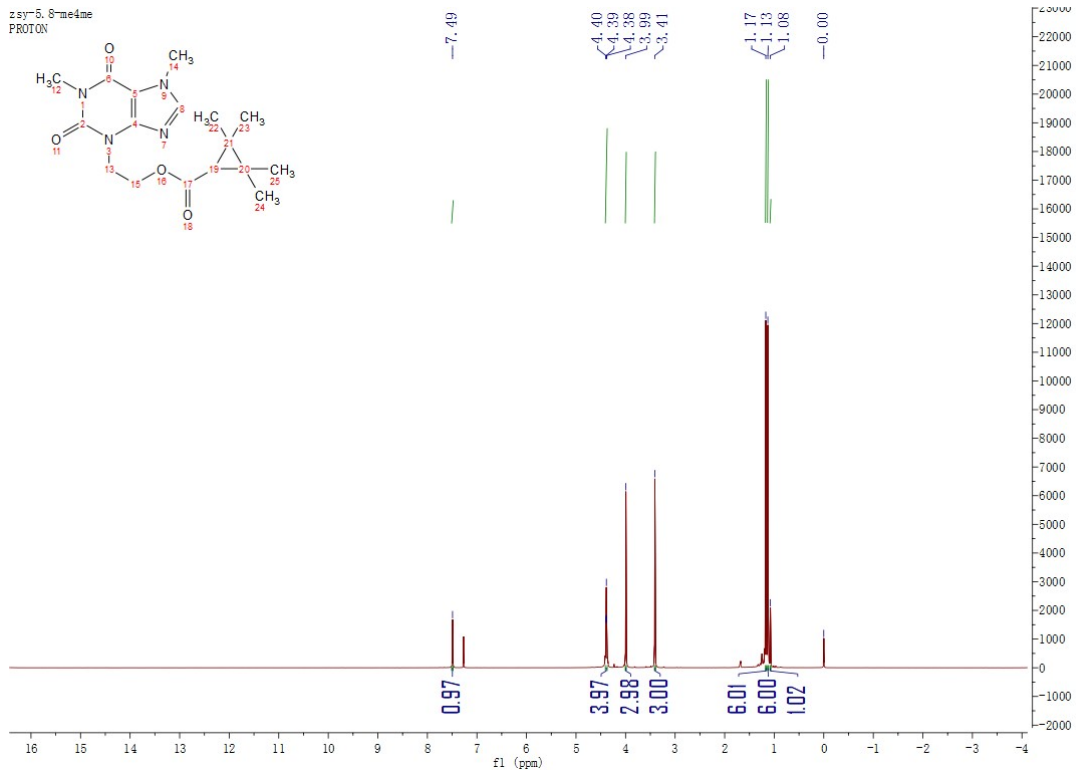

Fig. S48. The ^{1}H NMR spectrum of compound **Im**.

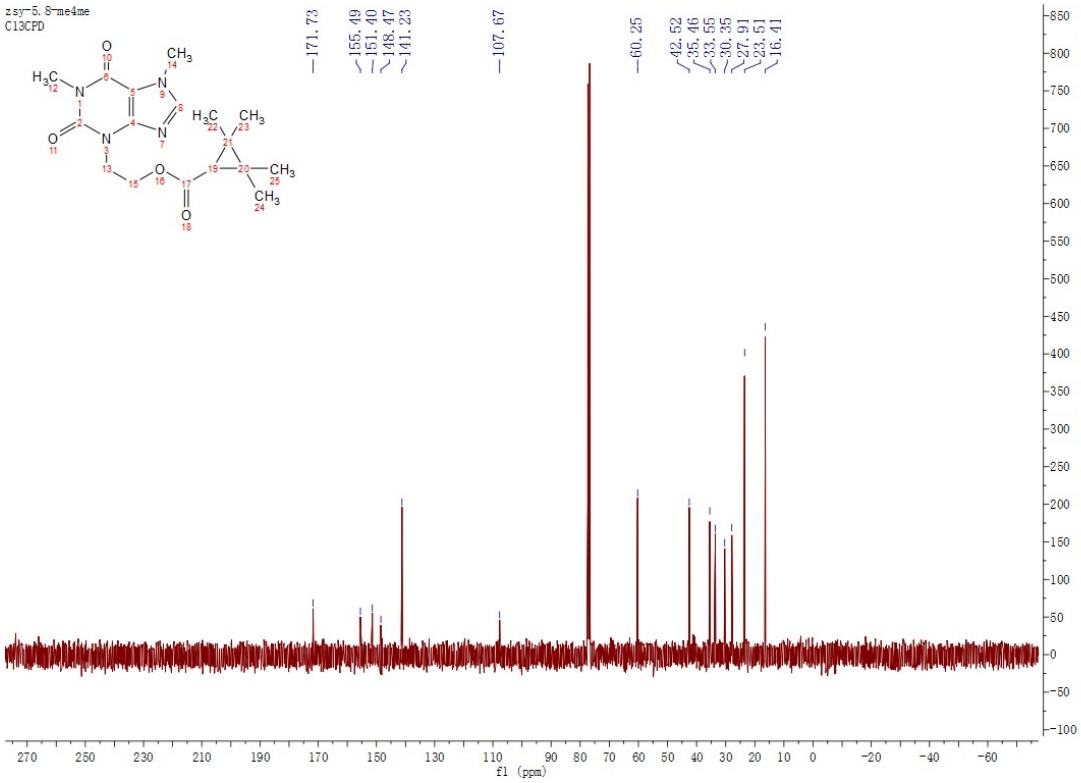

Fig. S49. The ^{13}C NMR spectrum of compound **Im**.

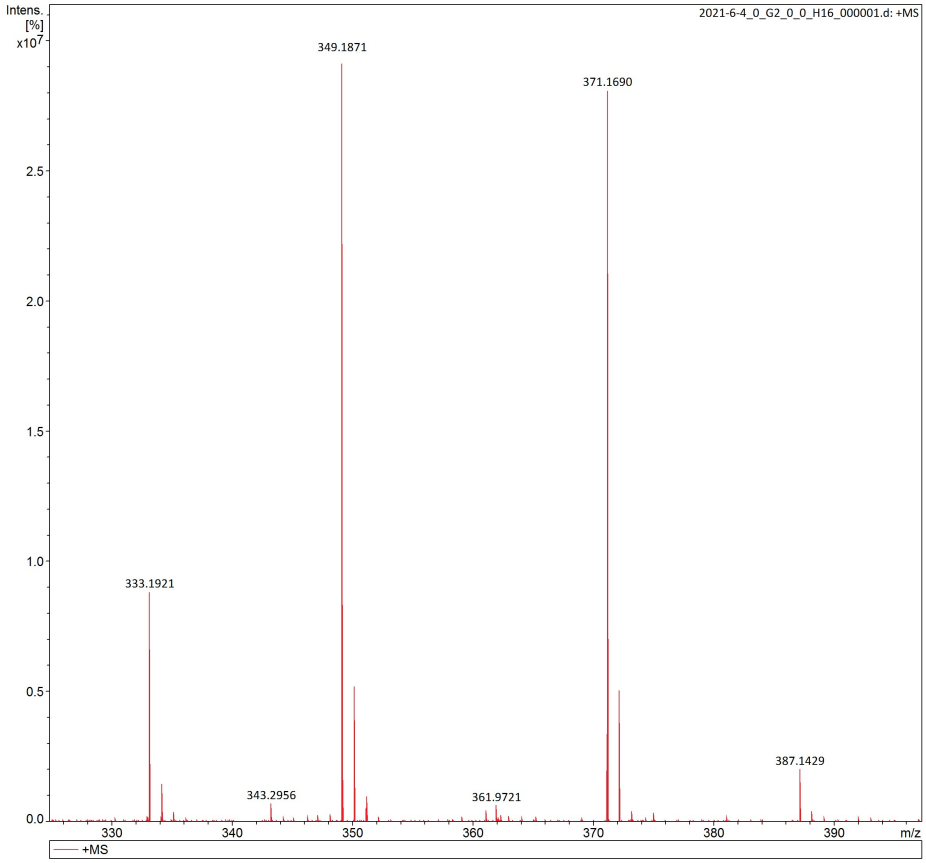

Fig. S50. The HRMS spectrum of compound **Im**.

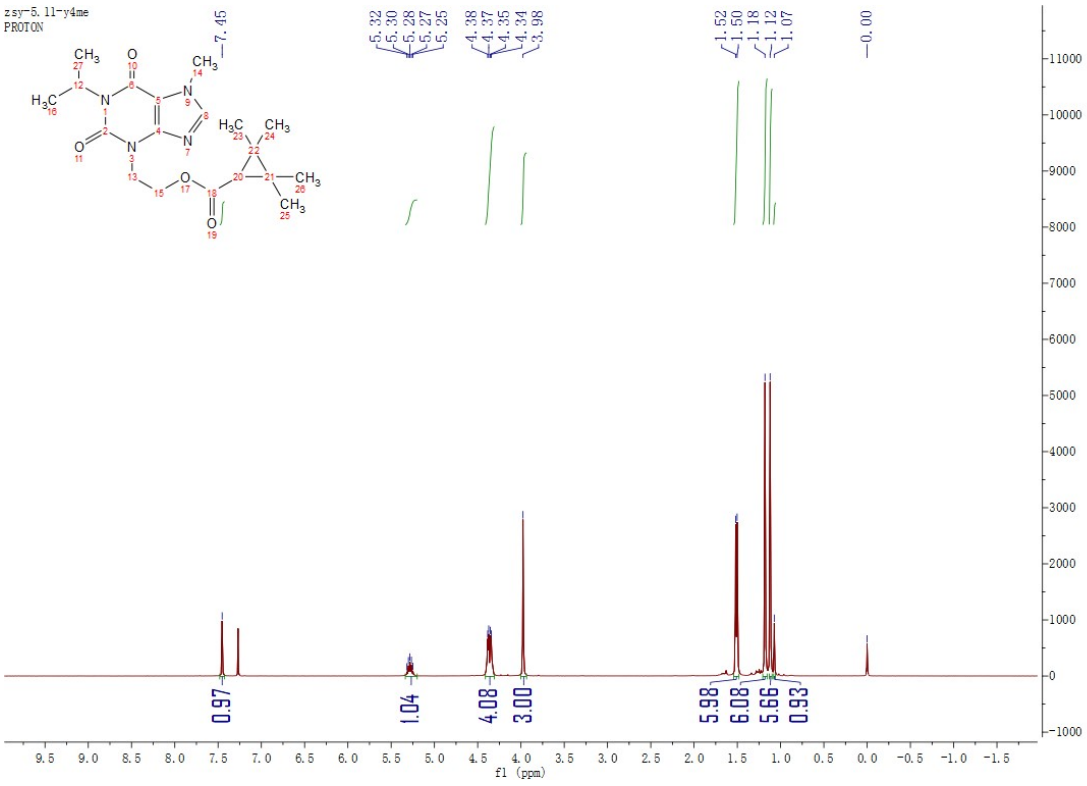

Fig. S51. The ^{1}H NMR spectrum of compound **In**.

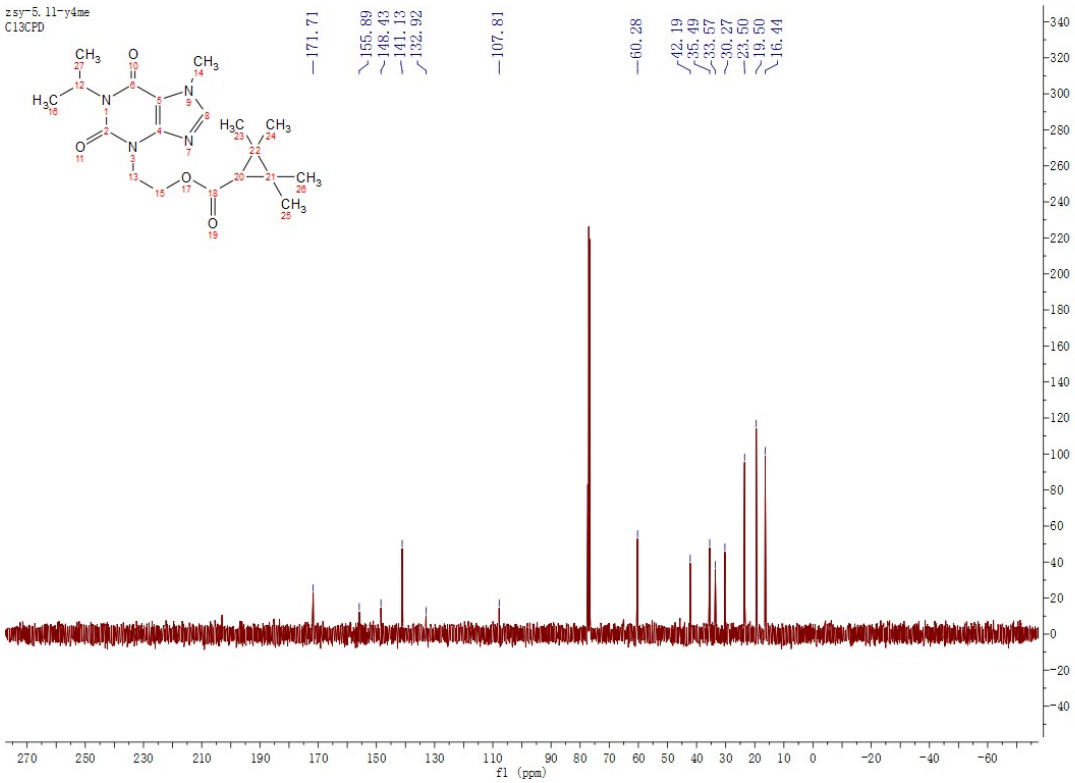

Fig. S52. The ^{13}C NMR spectrum of compound **In**.

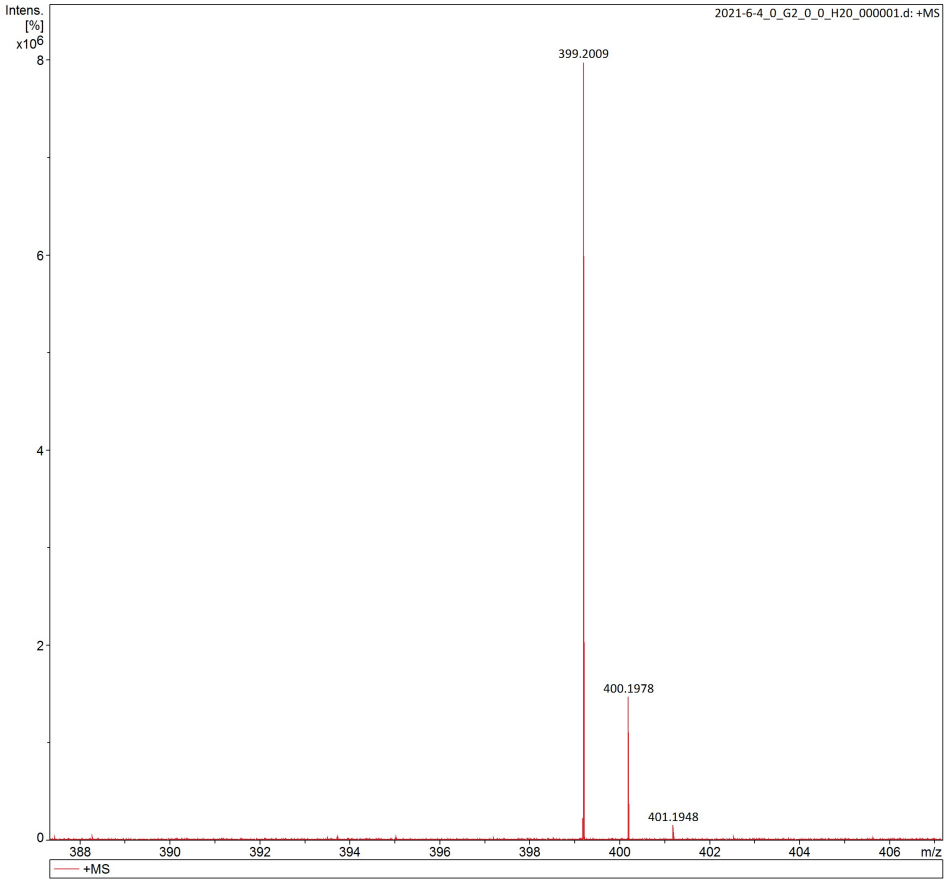

Fig. S53. The HRMS spectrum of compound **In**.

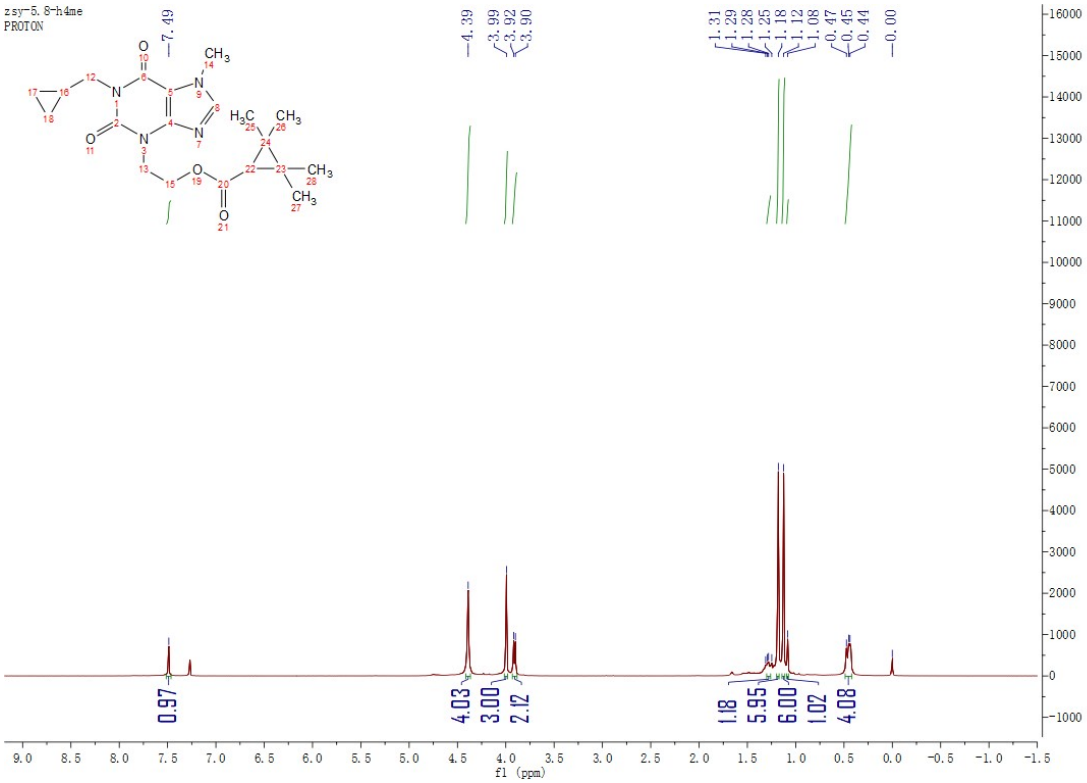

Fig. S54. The ^{1}H NMR spectrum of compound **Io**.

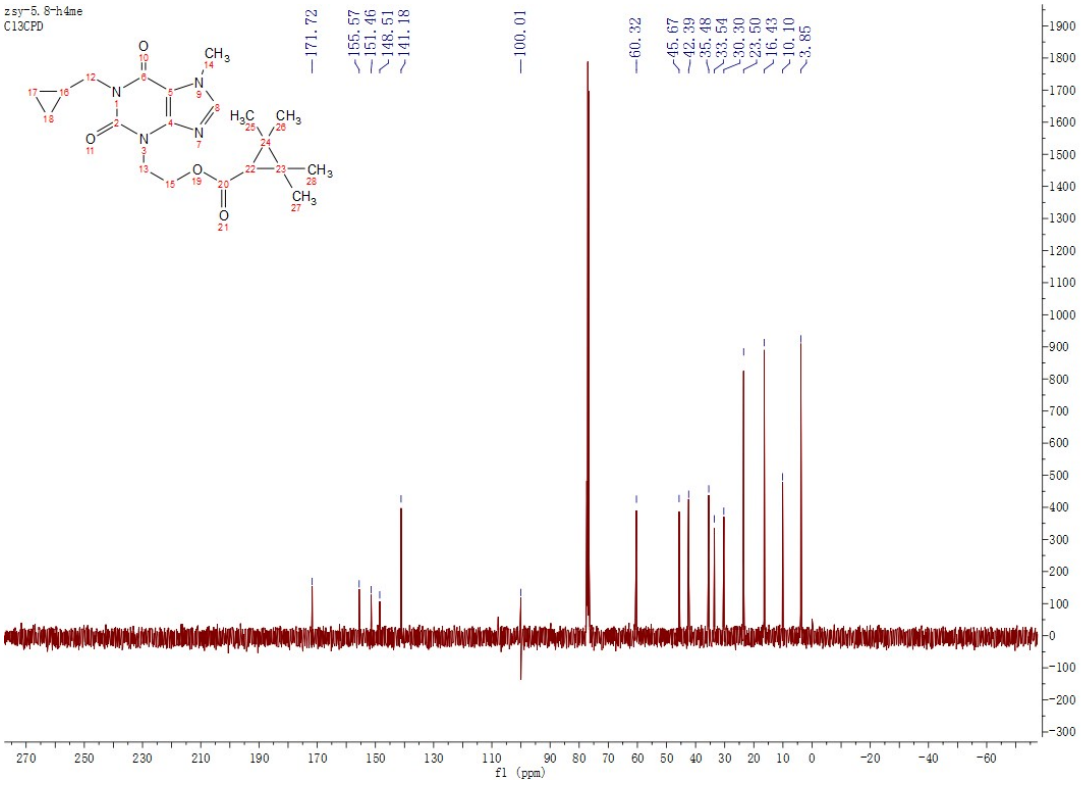

Fig. S55. The ^{13}C NMR spectrum of compound **Io**.

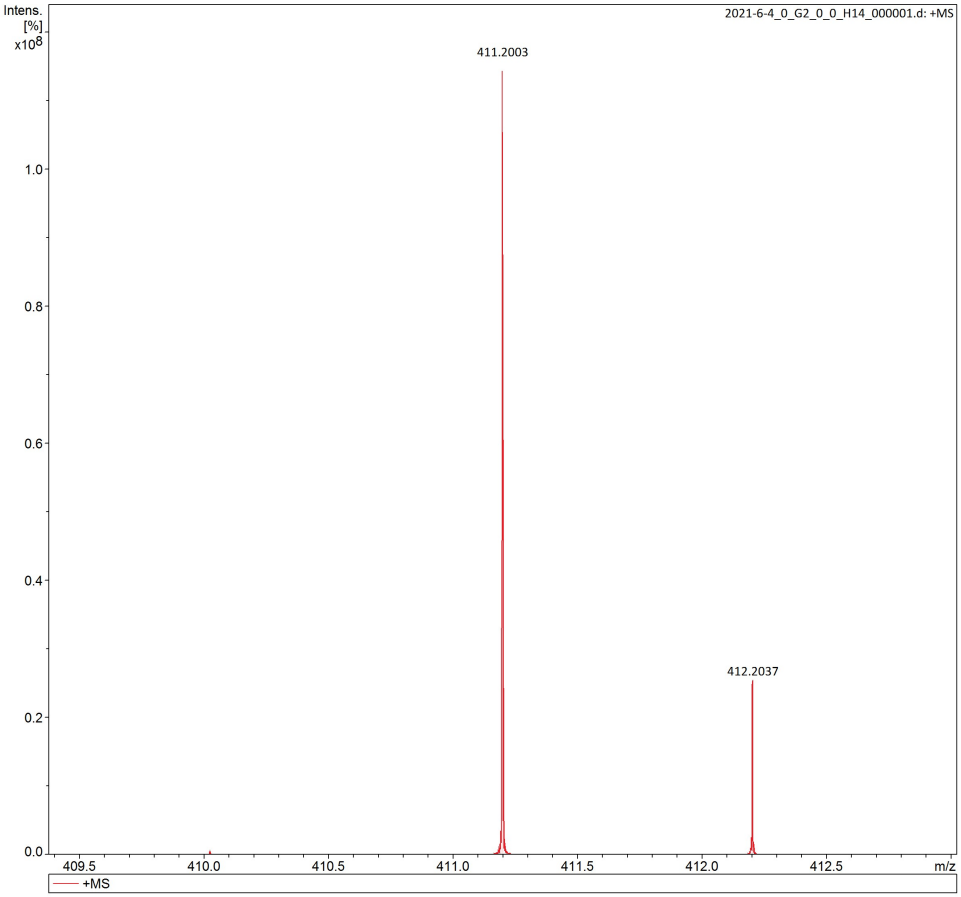

Fig. S56. The HRMS spectrum of compound **Io**.

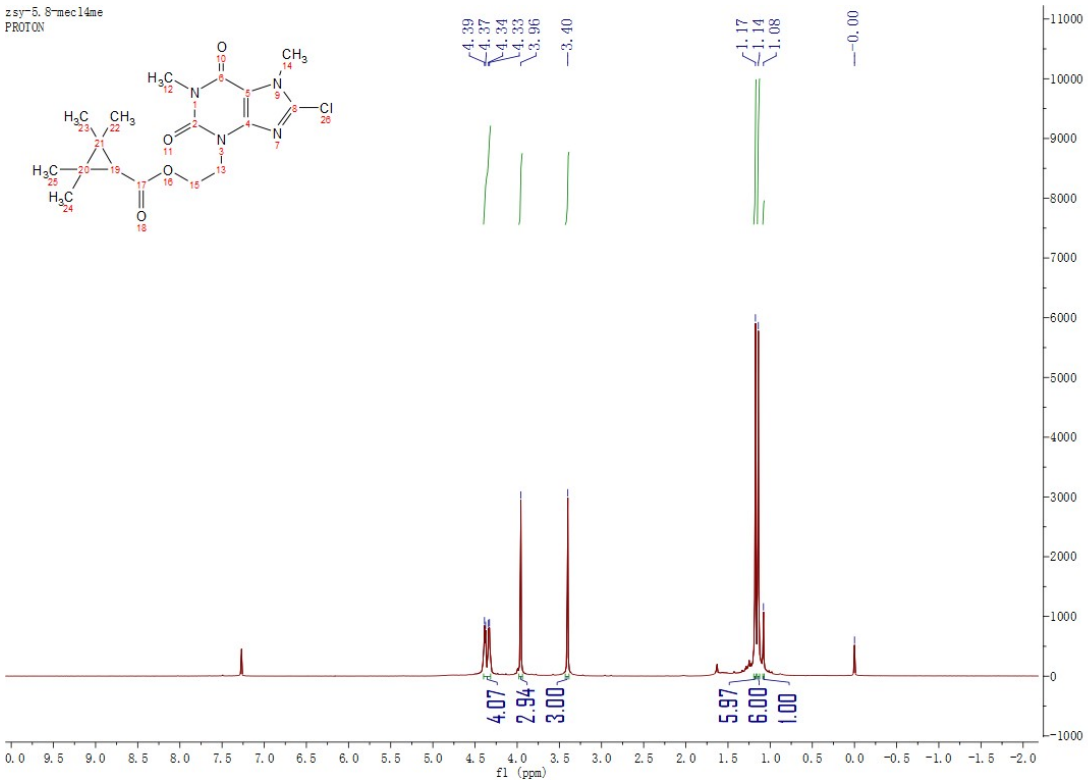

Fig. S57. The ^{1}H NMR spectrum of compound **Ip**.

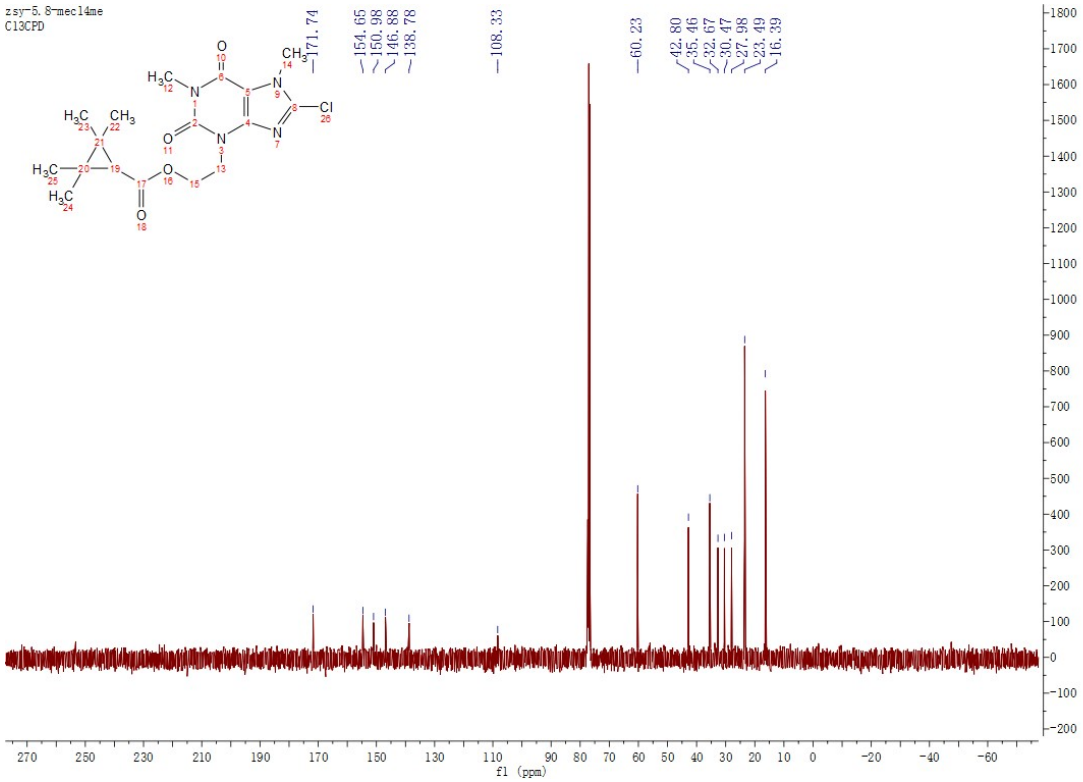

Fig. S58. The ^{13}C NMR spectrum of compound **Ip**.

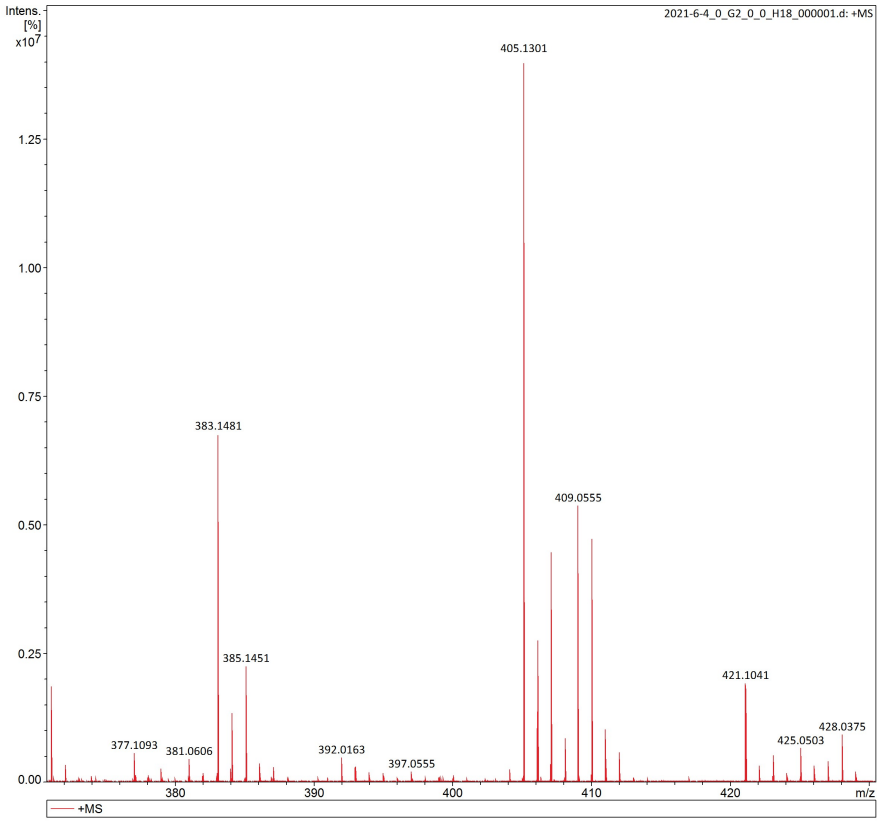

Fig. S59. The HRMS spectrum of compound **Ip**.

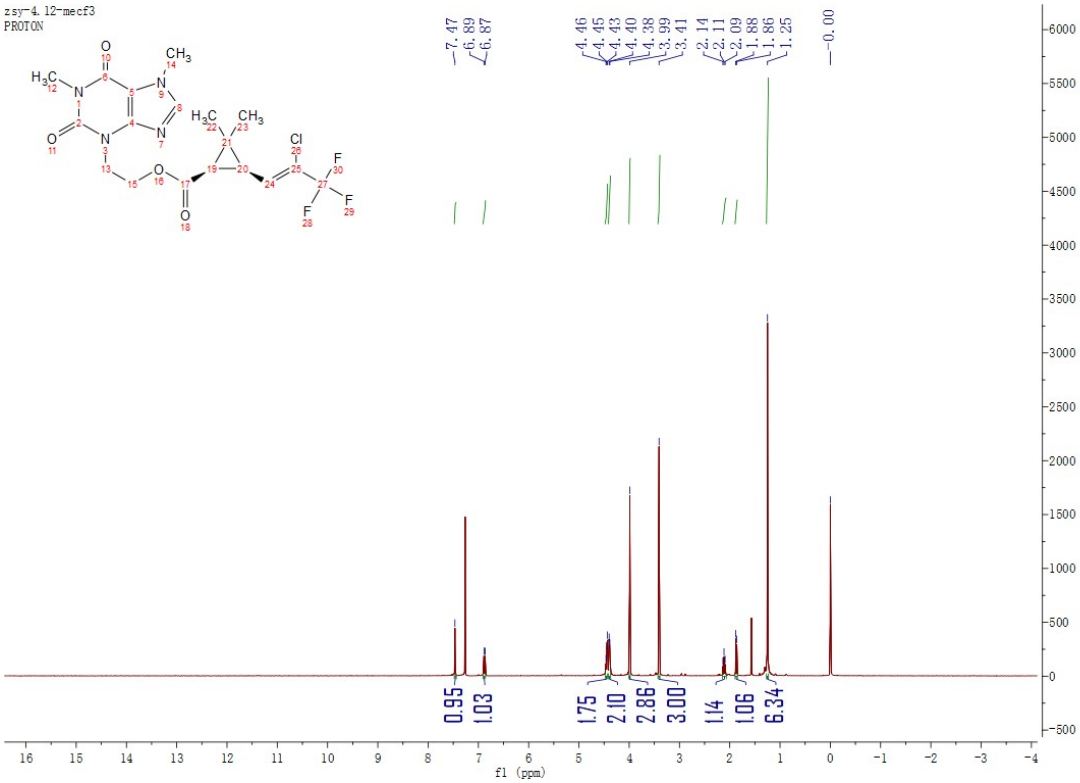

Fig. S60. The ^{1}H NMR spectrum of compound **Iq**.

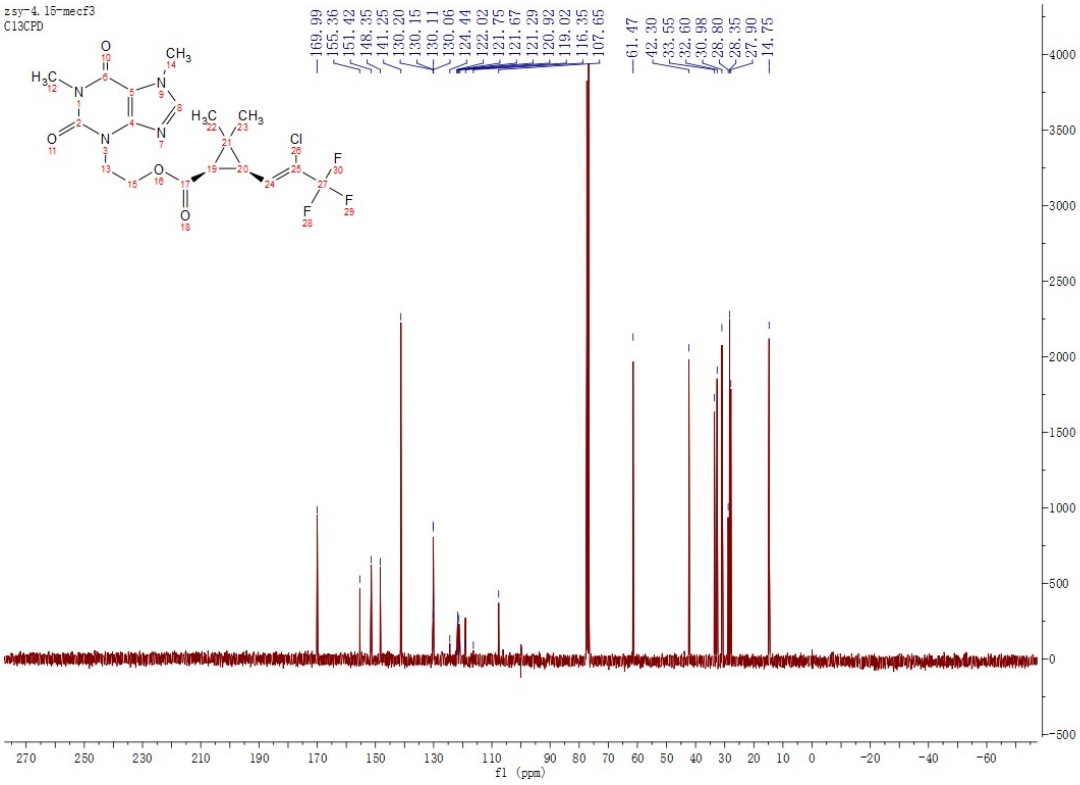

Fig. S61. The ^{13}C NMR spectrum of compound **Iq**.

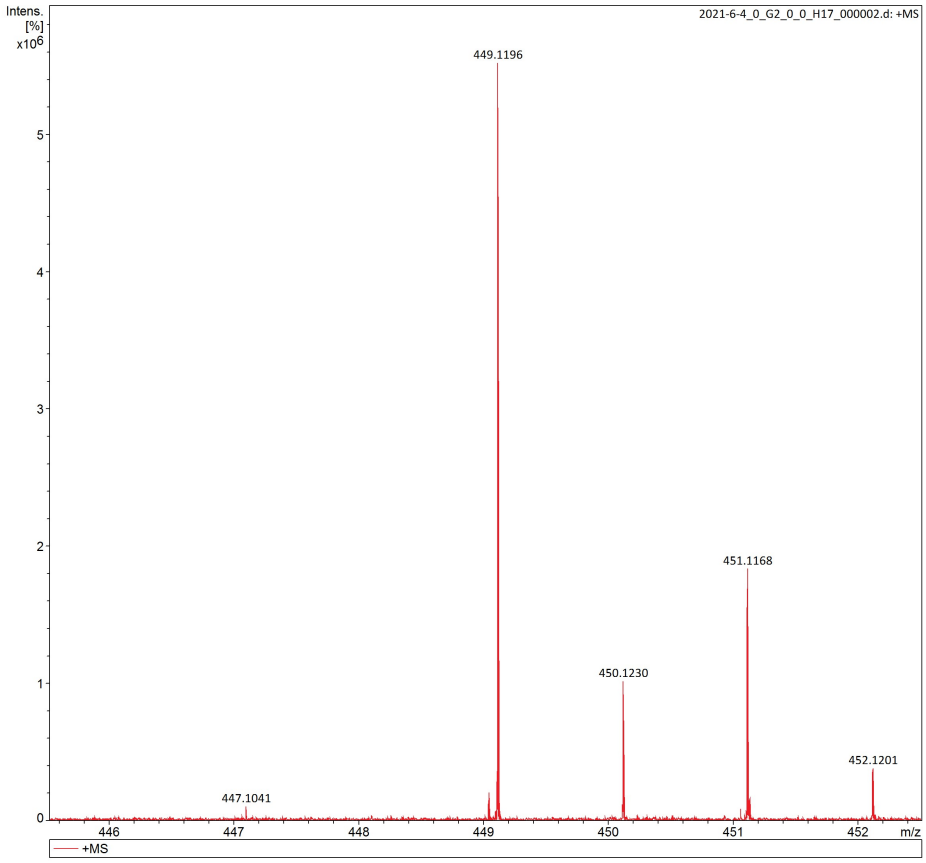

Fig. S62. The HRMS spectrum of compound **Iq**.

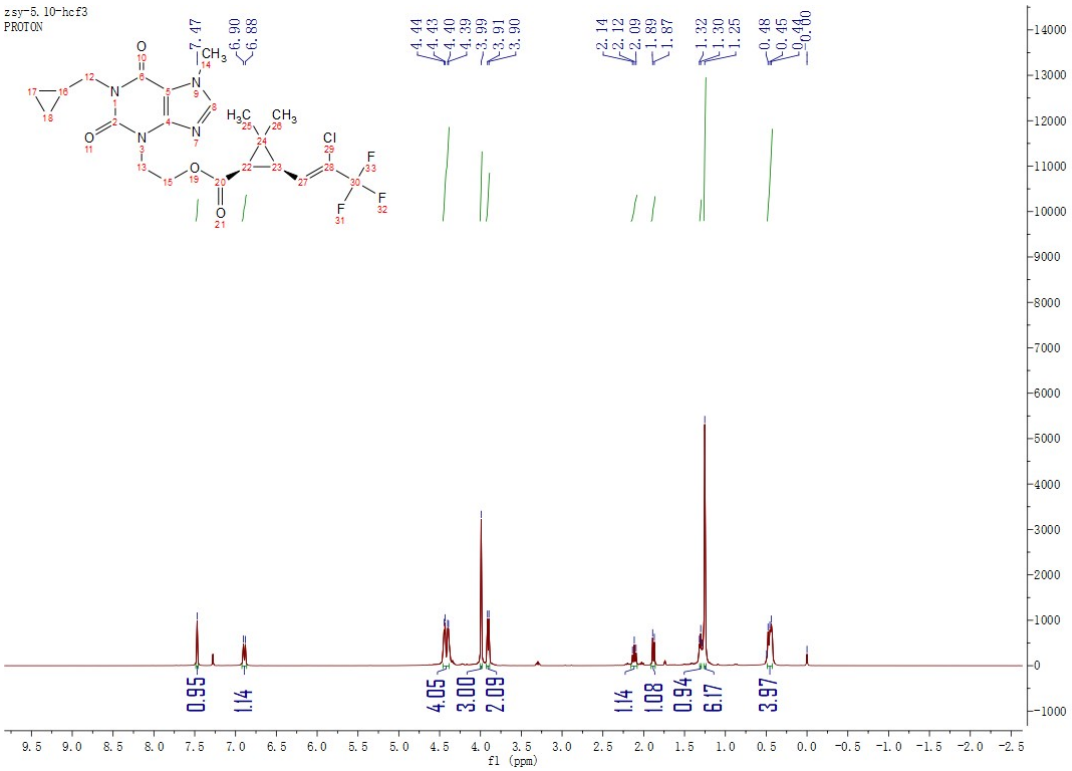

Fig. S63. The ^{1}H NMR spectrum of compound **Ir**.

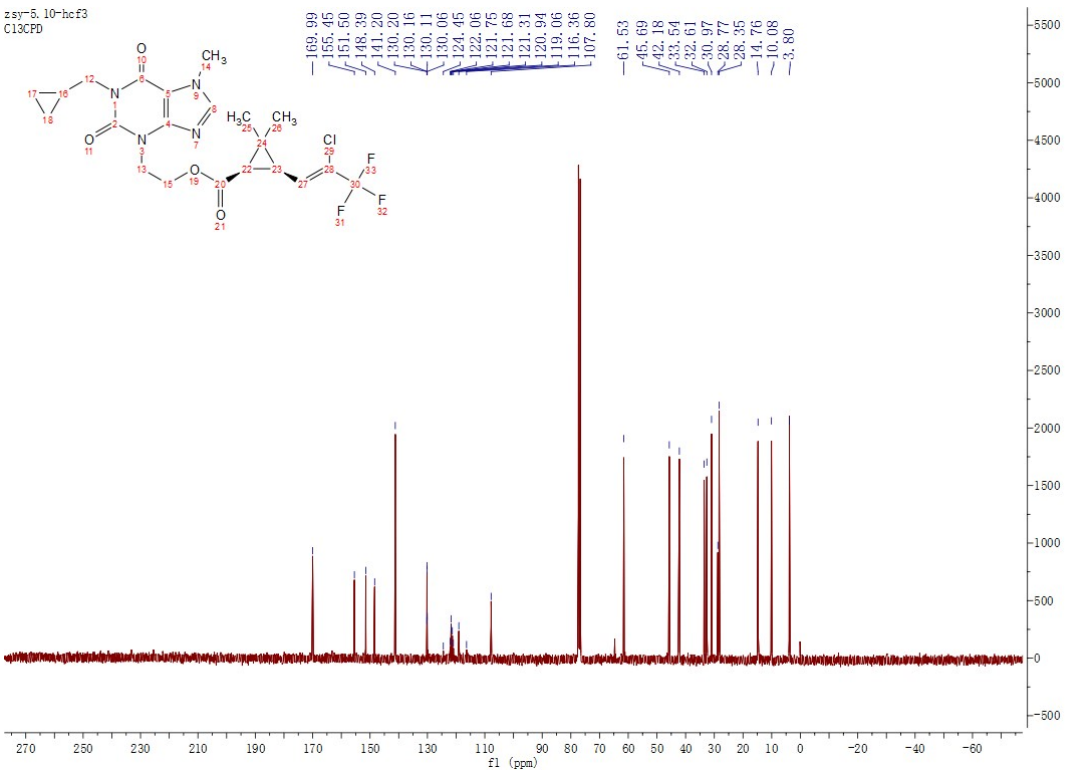

Fig. S64. The ^{13}C NMR spectrum of compound **Ir**.

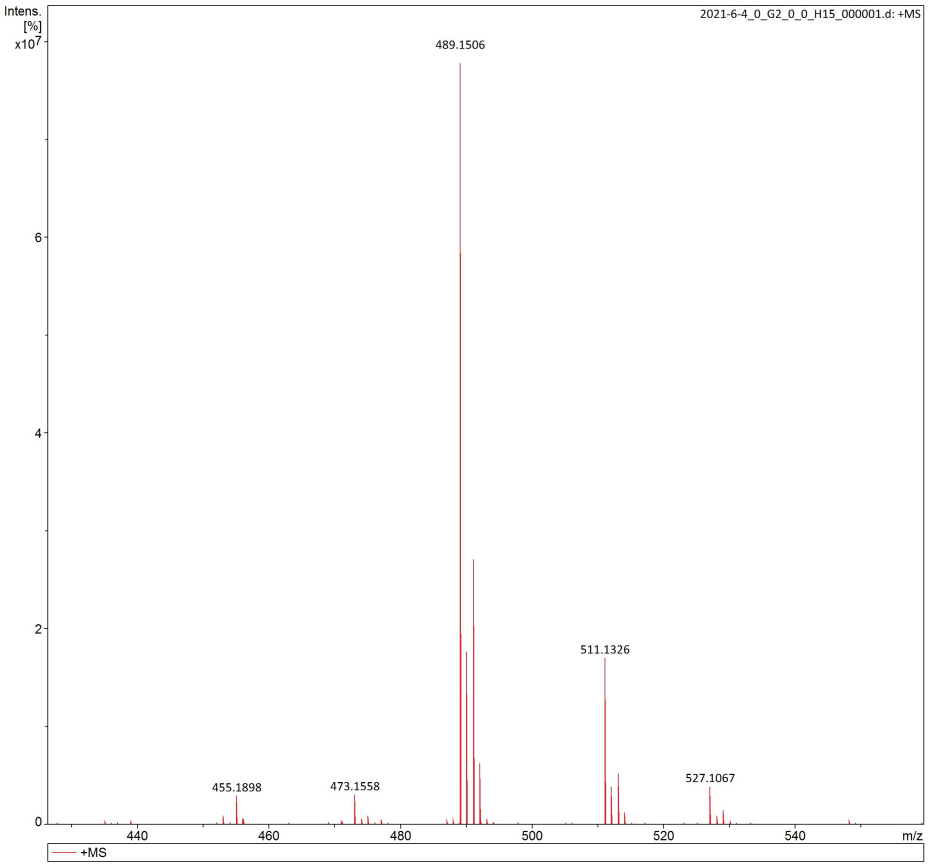

Fig. S65. The HRMS spectrum of compound **Ir**.

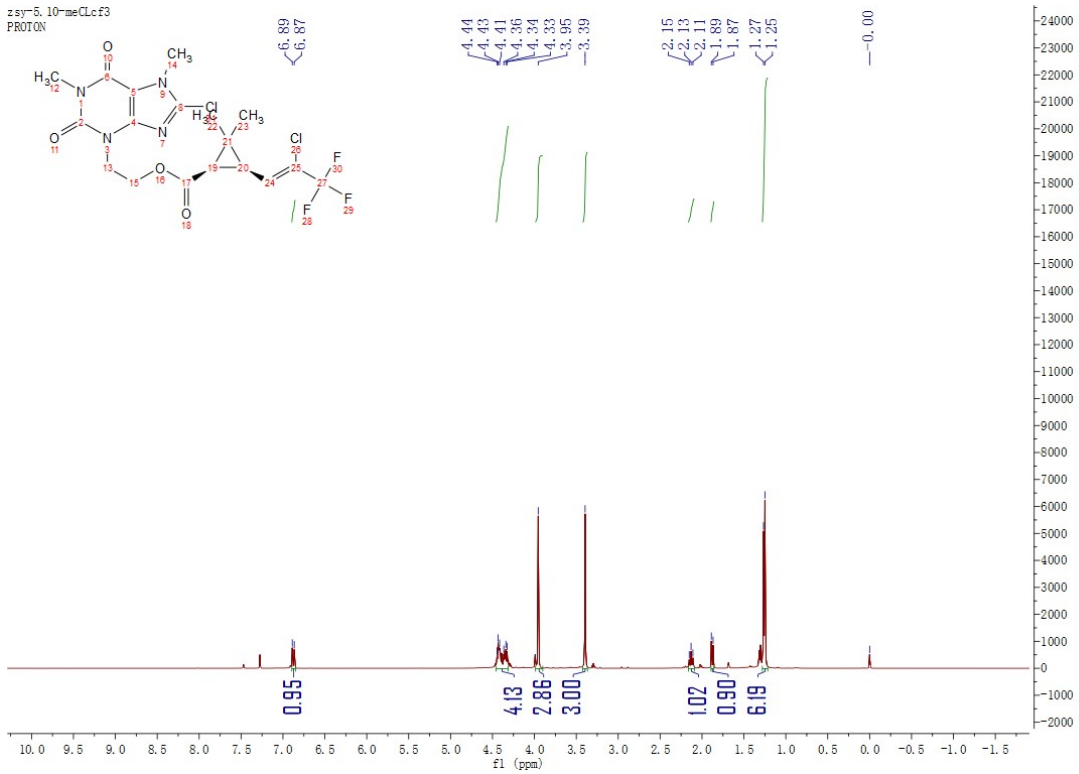

Fig. S66. The ^{1}H NMR spectrum of compound **Is**.

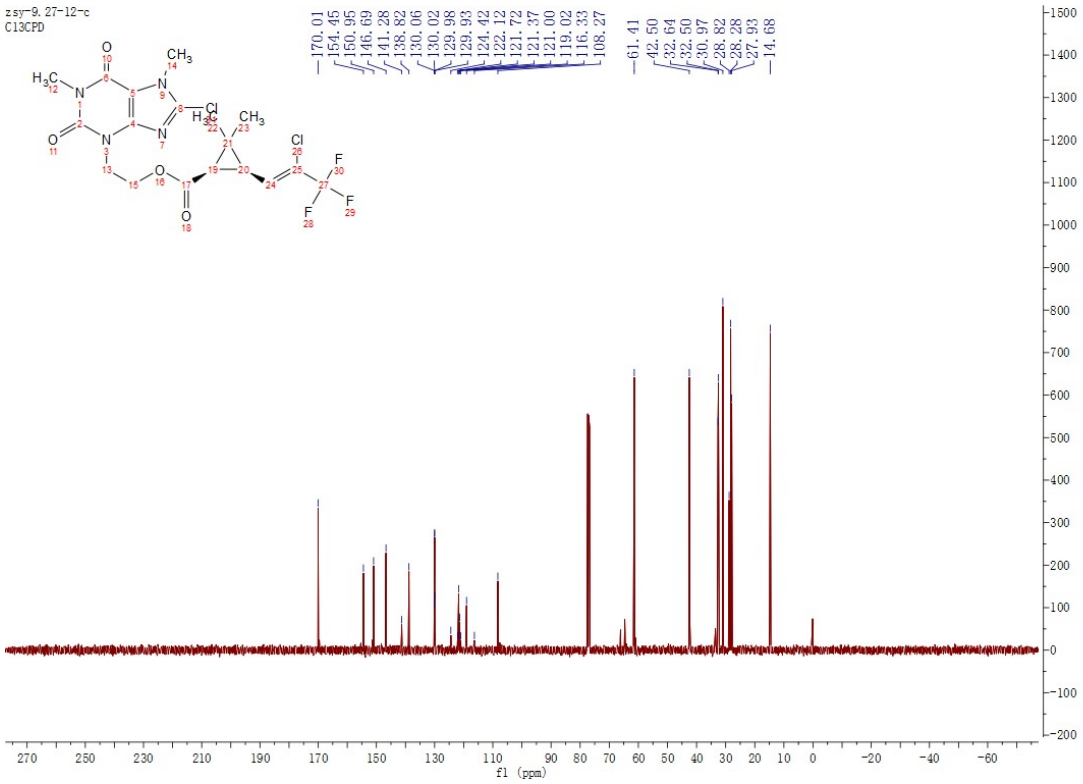

Fig. S67. The ^{13}C NMR spectrum of compound **Is**.

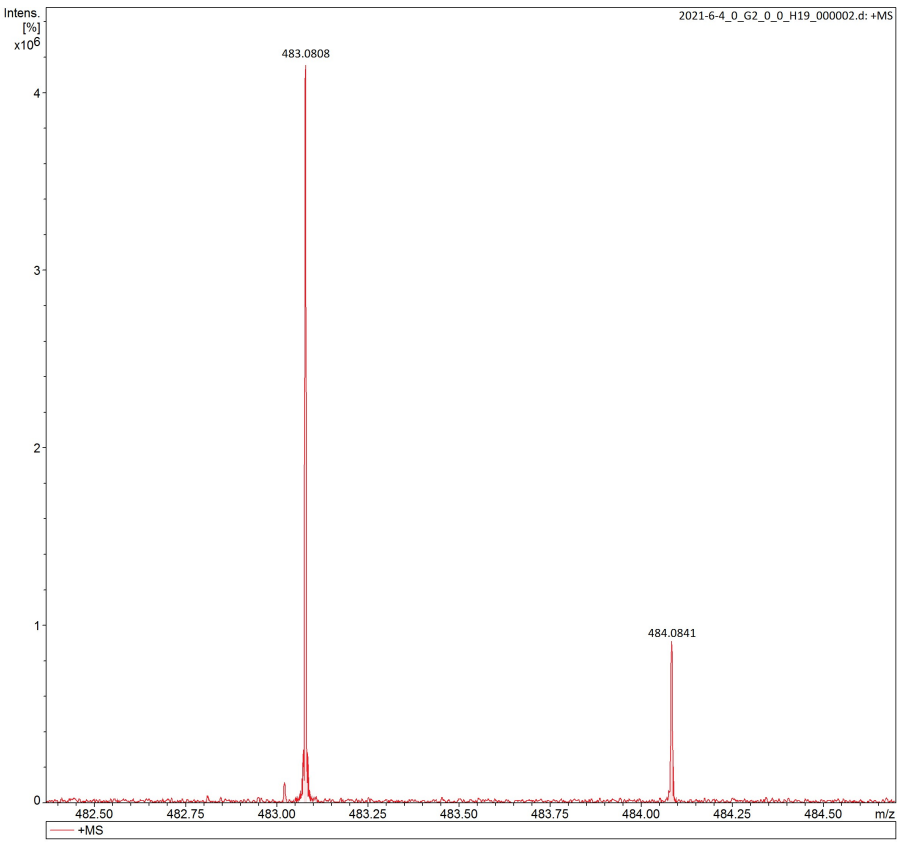

Fig. S68. The HRMS spectrum of compound **Is**.

6. Crystal structure determination data

Table S1. Crystal data and structure refinement for compound **In**.

Identification code	**In**
Formula sum	$C_{19}H_{28}N_4O_4$
Formula weight	376.45 g/mol
Crystal system	monoclinic
Space-group	P 1 21/c 1
a/Å	13.1190(6)
b/Å	8.5470(3)
c/Å	18.8312(8)
α/°	90
β/°	108.512(5)
γ/°	90
Cell volume	2002.25(15) $Å^3$
Z	4
Calc. density	1.249 g/cm^3
μ/mm-1	0.089
F(000)	808
Crystal size/mm3	0.22 × 0.2 × 0.17
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.59 to 64.91
Index ranges	-19 ≤ h ≤ 18, -12 ≤ k ≤ 12, -27 ≤ l ≤ 27
Reflections collected	29323

Table S2. Partial bond length data of compound **In**.

Atom 1	Atom 2	d 1,2 [A]	Atom 1	Atom 2	d 1,2 [A]
O1	C1	1.2238	N4	C5	1.3366
O2	C2	1.2253		C4	1.3625
O3	C12	1.3443	C2	C3	1.427
	C11	1.4497	C3	C4	1.3705
O4	C12	1.2121	C6	C7	1.5199

N1	C1	1.3801		C8	1.5213
	C4	1.3803	C10	C11	1.513
	C10	1.4692	C12	C13	1.4719
N2	C1	1.4079	C14	C15	1.5012
	C2	1.41		C16	1.5133
	C6	1.4933		C17	1.5169
N3	C5	1.3458		C13	1.5372
	C3	1.3897	C15	C18	1.5123
	C9	1.4616		C19	1.5214
				C13	1.5326

Table S3. Partial bond angle data of compound **In**.

Atom 1	Atom 2	Atom 3	Angle 2,1,3	Atom 1	Atom 2	Atom 3	Angle 2,1,3
N1	C1	C4	119.791	C5	N4	N3	114.395
	C1	C10	118.903	C6	N2	C8	110.36
	C4	C10	121.274		N2	C7	112.062
N2	C1	C2	125.966		C7	C8	114.681
	C1	C6	115.377	C10	N1	C11	112.208
	C2	C6	118.549	C11	O3	C10	108.937
N3	C5	C3	105.44	C12	O4	O3	122.891
	C5	C9	127.359		O4	C13	126.828
	C3	C9	127.125		O3	C13	110.277
N4	C5	C4	102.597	C13	C12	C15	123.885
C1	O1	N1	120.684		C12	C14	121.417
	O1	N2	121.77		C15	C14	58.552
	N1	N2	117.545	C14	C15	C16	120.803
C2	O2	N2	122.069		C15	C17	119.755
	O2	C3	126.093		C15	C13	60.571
	N2	C3	111.836		C17	C13	119.089
C3	C4	N3	105.154	C15	C14	C18	121.206
	C4	C2	123.742		C14	C19	119.98
	N3	C2	131.088		C18	C19	110.911
C4	N4	C3	112.412		C18	C13	119.857
	N4	N1	126.506				
	C3	N1	121.08				

Table S4. Crystal data and structure refinement for compound **Iq**.

Identification code	**Iq**
Formula sum	$C_{18}H_{20}ClF_3N_4O_4$
Formula weight	448.83 g/mol

Crystal system	triclinic
Space-group	P-1
a/Å	7.8481(8)
b/Å	9.1014(10)
c/Å	15.7661(14)
α/°	98.224(8)
β/°	100.532(9)
γ/°	110.659(10)
Cell volume	1009.28(19) $Å^3$
Z	2
Calc. density	1.477 g/cm^3
μ/mm-1	0.250
F(000)	464
Crystal size/mm3	0.23 × 0.2 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.39 to 65.75
Index ranges	-11 ≤ h ≤ 11, -13 ≤ k ≤ 13, -23 ≤ l ≤ 23
Reflections collected	15146

Table S5. Partial bond length data of compound **Iq**.

Atom 1	Atom 2	d 1,2 [A]	Atom 1	Atom 2	d 1,2 [A]
O002	C00E	1.3584	C00D	N00B	1.3585
	C00H	1.4449		C00F	1.3739
O003	C00C	1.2259	C00F	C1	1.4232
O004	C00E	1.2077	C00G	C00H	1.5226
O008	C1	1.2269	N00I	C1	1.4116
N009	C00D	1.3858		C00P	1.4753
	C00C	1.3867	C00J	C2	1.3231
	C00G	1.4711		C00R	1.4944
N00A	C3	1.3441		Cl00	1.7321
	C00F	1.3851	C00K	C2	1.4595
	C00Q	1.4643		C00M	1.5152
N00B	C3	1.3381		C00L	1.5479
	C00D	1.3585	C00L	C00M	1.5194

C00C	O003	1.2259		C00E	1.4799
	N00I	1.4047	C00M	C00O	1.5151
				C00S	1.5217

Table S6. Partial bond angle data of compound **Iq**.

Atom 1	Atom 2	Atom 3	Angle 2,1,3	Atom 1	Atom 2	Atom 3	Angle 2,1,3
O002	C00E	C00H	114.785	N00I	C00C	C1	126.674
N009	C00D	C00C	119.544		C00C	C00P	116.372
	C00D	C00G	120.992		C1	C00P	116.951
	C00C	C00G	119.462	C00J	C2	C00R	123.899
N00A	C3	C00F	105.851		C2	Cl00	123.434
	C3	C00Q	126.404		C00R	Cl00	112.639
	C00F	C00Q	127.67	C00K	C2	C00M	122.571
N00B	C3	C00D	102.567		C2	C00L	119.797
C00C	O003	N009	121.299		C00M	C00L	59.467
	O003	N00I	121.748	C00L	C00E	C00M	122.804
	N009	N00I	116.947		C00E	C00K	118.658
C00D	N00B	C00F	112.588		C00M	C00K	59.197
	N00B	N009	125.756	C00M	C00O	C00K	121.232
	C00F	N009	121.653		C00O	C00L	120.957
C00E	O004	O002	122.93		C00O	C00S	114.061
	O004	C00L	127.532		C00K	C00L	61.336
	O002	C00L	109.52	C2	C00J	C00K	125.462
C00F	C00D	N00A	104.823	C1	O008	N00I	120.732
	C00D	C1	123.087		O008	C00F	127.249
	N00A	C1	132.063		N00I	C00F	112.018
C00G	N009	C00H	111.733	C3	N00B	N00A	114.167
C00H	O002	C00G	109.887				