Supplementary Material

A Potential Lead for Insect Growth Regulator: Design, Synthesis, and Biological Activity Evaluation of Novel Hexacyclic Pyrazolamide Derivatives

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Content

Table S1. The price and manufacturer of the starting reagents (From Chemical Book)

Reagent.	Price	Manufacturer	Reagent.	Price	Manufacturer
Cyclohexanone	**¥ 49 /500mL**	**Macklin**	**Cyclohexanone**	**¥ 69 /1L**	**J&K Scientific**
Cycloheptanone	**¥ 1802/500mL**	**Macklin**	**Cycloheptanone**	**¥ 378 /0.1L**	**J&K Scientific**

Table S2. Comparison of the yields of hexacyclic and heptacyclic intermediates [1]

Intermediates (hexacyclic)[a]	yield (%)	Intermediates (heptacyclic)[b]	yield (%)
Intermediate 3[a]	75	**Intermediate 3[b]**	68
Intermediate 4[a]	58	**Intermediate 4[b]**	50

"a" represents the intermediate synthesized in this work; "b" represents the intermediate synthesized in our previous work [1]. Intermediate 3[b] represents ethyl 2-oxo-2-(2-oxocycloheptyl) acetate. Intermediate 4[b] represents ethyl 2-phenyl-2,4,5,6,7,8-hexahydrocyclohepta[c]pyrazol63-carboxylate

Table S3. Comparison of the yields of hexacyclic and heptacyclic compounds [1].

Compd[a].	R	yield (%)	Compd[b].	R	yield (%)
6a	**3-Br**	**48**	**D-08**	**3-Br**	**22**
6b	**4-Br**	**56**	**D-09**	**4-Br**	**49**
6c	**3-Et**	**59**	**D-23**	**3-Et**	**54**
6d	**4-Et**	**72**	**D-24**	**4-Et**	**64**
6e	**4-OCH_3**	**56**	**D-15**	**4-OCH_3**	**16**
6f	**4-tBu**	**76**	**D-27**	**4-tBu**	**74**

"a" represents the compound synthesized in this work; "b" represents the compound synthesized in our previous work [1].

[1] Jiang, B.; Jin, X.; Dong, Y.; Guo, B.; Cui, L.; Deng, X.; Zhang, L.; Yang, Q.; Li, Y.; Yang, X.; Smagghe, G. Design, Synthesis, and Biological Activity of Novel Heptacyclic Pyrazolamide Derivatives: A New Candidate of Dual-Target Insect Growth Regulators. *J Agric Food Chem.* **2020**, *68*, 6347-6354.

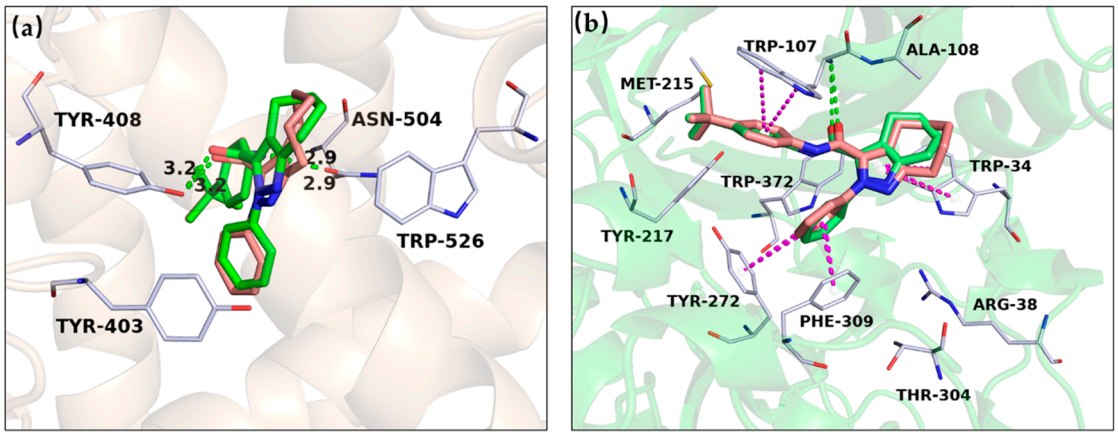


Figure S1. Predicted binding modes of **6f** and **D-27** with EcR and *Of*ChtI. (a) Superimposed conformations of the **6f** (green) and **D-27** (red) with EcR; (b) Superimposed conformations of the **6f** (green) and **D-27** (red) with *Of*ChtI.

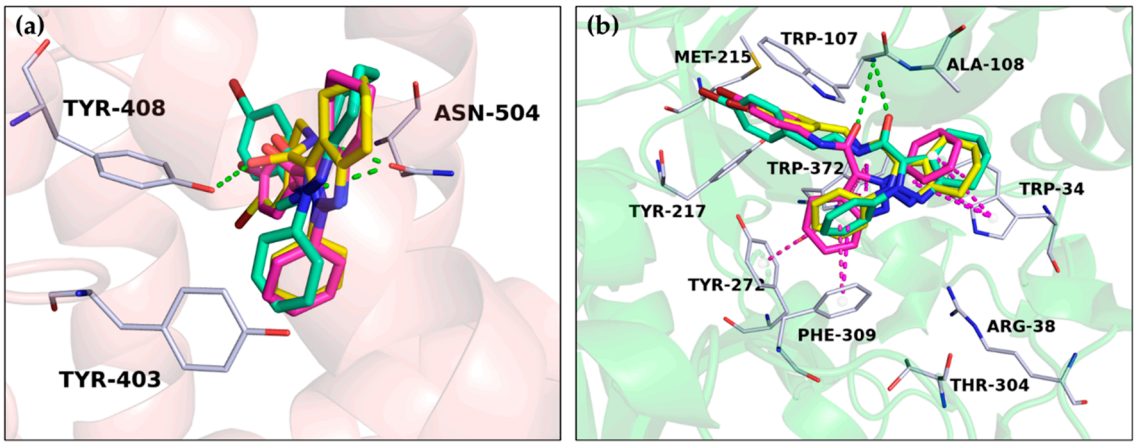


Figure S2. Predicted binding modes of **6b**, **6j**, and **6u** with EcR and *Of*ChtI. (a) Superimposed conformations of the **6b** (purple) **6j** (yellow) and **6u** (cyan) with EcR; (b) **6b** (purple) **6j** (yellow) and **6u** (cyan) with *Of*ChtI.

The HPLC chromatogram of 6j.

The samples were analyzed using an Agilent 1290 high-performance liquid chromatography system (Agilent Technologies, Santa Clara, CA, USA). Analysis conditions are listed in **Table S4**.

Table S4. Elution gradient and analysis conditions of HPLC.

Time（min）	Flow（mL/ min）	A%	B%
0	0.3	90.0	10.0
1.0	0.3	90.0	10.0
2.5	0.3	10.0	90.0
4.0	0.3	10.0	90.0
4.1	0.3	90.0	10.0
5.0	0.3	90.0	10.0

A: Acetonitrile

B: 0.2% formic acid aqueous solution

Column: Agilent Poroshell 120 EC-C18 (2.1 mm × 100 mm, particle size 1.9 μm)

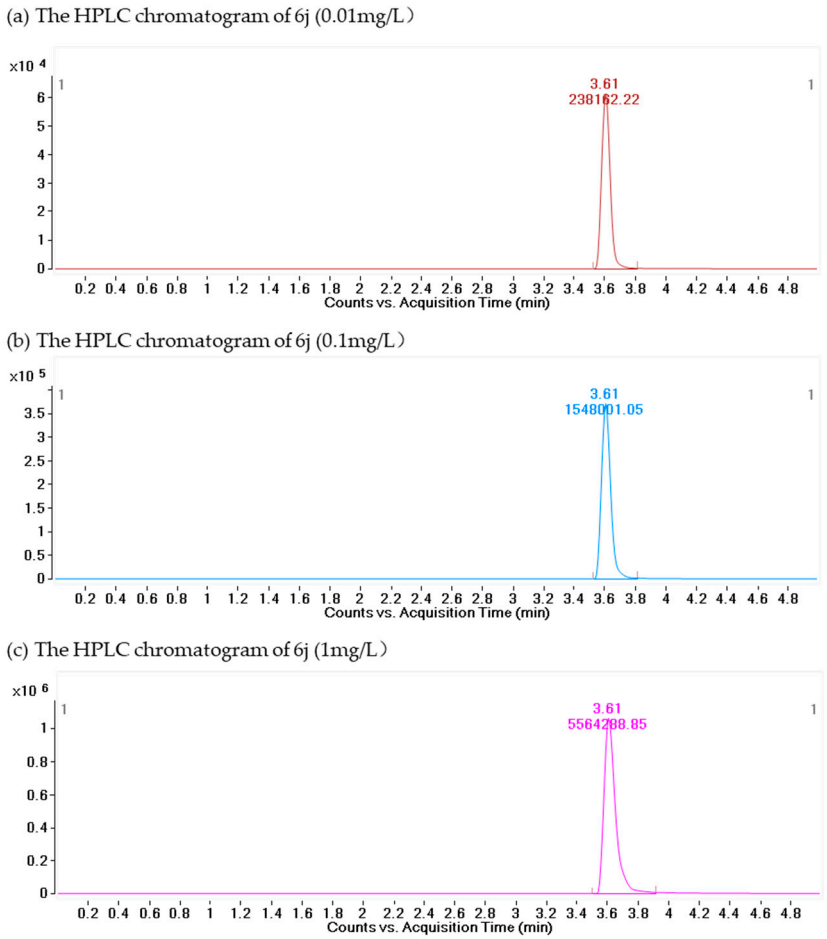


Figure S3. The HPLC chromatogram of **6j**. (a) The HPLC chromatogram of **6j** (0.01 mg/L); (b) The HPLC chromatogram of **6j** (0.1 mg/L); (c) The HPLC chromatogram of **6j** (1 mg/L).

Physical and chemical properties, NMR and HRMS spectra data of 6a~6x

(N-(3-bromophenyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide) **(6a)**: white solid, yield 48%, m.p. 168-169℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.98 (t, J = 9.0 Hz, 1H), 7.77–7.28 (m, 9H), 2.73 (t, J = 6.1 Hz, 2H), 2.63 (t, J = 6.1 Hz, 2H), 1.81–1.67 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.11, 149.75, 141.24, 130.34, 128.83, 128.29, 128.08, 127.86, 125.98, 124.96, 123.19, 119.70, 110.02, 23.26, 22.94, 22.92, 22.33. HRMS (ESI) calcd for $C_{20}H_{18}BrN_3O$ $(M+H)^+$ 396.0706, found 396.0709.

N-(4-bromophenyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6b):** white solid, yield 56%, m.p. 226-227℃. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.26 (m, 7H), 7.20–7.08 (m, 3H), 2.75 (t, J = 5.9 Hz, 2H), 2.68 (t, J = 6.1 Hz, 2H), 1.83–1.71 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.02, 149.58, 138.86, 135.22, 131.66, 131.01, 128.29, 127.39, 124.00, 120.29, 120.06, 116.37, 22.26, 21.93, 21.82, 20.79. HRMS (ESI) calcd for $C_{20}H_{18}BrN_3O$ $(M+H)^+$ 396.0706, found 396.0706.

N-(3-ethylphenyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide Chemical Formula **(6c)**: white solid, yield 59%, m.p. 154-155℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.46 (s, 1H), 7.55–7.39 (m, 6H), 7.36–7.19 (m, 2H), 6.96 (d, J = 7.6 Hz, 1H), 2.69 (t, J = 5.1 Hz, 4H), 2.57 (q, J = 7.6 Hz, 2H), 1.84-1.71 (m, 4H), 1.16 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.56, 149.66, 144.88, 140.35, 139.03, 134.85, 129.49, 129.17, 127.40, 124.03, 123.27, 119.50, 118.79, 117.62, 28.70, 23.32, 23.15, 23.00, 20.66, 15.95. HRMS (ESI) calcd for $C_{22}H_{23}N_3O$ $(M+H)^+$ 346.1914, found 346.1916.

N-(4-ethylphenyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6d)**: white solid, yield 72%, m.p. 189-190℃.^{1}H NMR (500 MHz, DMSO-d_6) δ 10.45 (s, 1H), 7.55–7.41 (m, 6H), 7.34–7.27 (m, 1H), 7.16 (d, J = 8.3 Hz, 2H), 2.71–2.63(m, 4H), 2.55 (q, J = 7.6 Hz, 2H), 1.85–1.70 (m, 4H), 1.15 (t, J = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.44, 149.66, 140.35, 140.09, 136.71, 134.89, 129.47, 128.46, 127.36, 123.19, 120.25, 118.70, 28.13, 23.32, 23.15, 23.01, 20.63, 16.24. HRMS (ESI) calcd for $C_{22}H_{23}N_3O$ $(M+H)^+$ 346.1914, found 346.1915.

N-(4-methoxyphenyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6e)**: white solid, yield 56%, m.p. 210-221℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.38 (s, 1H), 7.57–7.40 (m, 6H), 7.36–7.27 (m, 1H), 6.90 (d, J = 8.8 Hz, 2H), 3.73 (d, J = 3.1 Hz, 3H), 2.73–2.62(m, 4H), 1.86–1.68 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.20, 156.31, 149.65, 140.37, 134.93, 132.12, 129.47, 127.34, 123.17, 121.72, 118.61, 114.41, 55.71, 23.33, 23.16, 23.02, 20.64. HRMS (ESI) calcd for $C_{21}H_{21}N_3O_2$ $(M+H)^+$ 348.1707, found 348.1708.

N-(4-(tert-butyl)phenyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6f)**: white solid, yield 76%, m.p. 155-156℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.45 (s, 1H), 7.54 (d, J = 8.6 Hz, 2H), 7.45–7.41 (m, 4H), 7.36–7.28 (m, 3H), 2.68 (q, J = 6.2 Hz, 4H), 1.85–1.71 (m, 4H), 1.26 (s, 9H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 159.46, 149.66, 146.97, 140.34, 136.46, 134.89, 129.48, 127.35, 125.88, 123.16, 119.92, 118.69, 34.54, 31.63, 23.33, 23.16, 23.02, 20.61. HRMS (ESI) calcd for $C_{24}H_{27}N_3O$ $(M+H)^+$ 374.2227, found 374.2224.

N-(3-fluorobenzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6g)**: white solid, yield 64%, m.p. 214-215℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.02 (t, J = 6.0 Hz, 1H), 7.42–7.28 (m, 6H), 7.15–7.02 (m, 3H), 4.41 (d, J = 6.0 Hz, 2H), 2.68–2.57 (m, 4H)., 1.82–1.67 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.64 (d, J = 243.2 Hz), 161.32, 149.56, 142.41 (d, J = 7.2 Hz), 140.41, 134.56, 130.73 (d, J = 8.7 Hz), 129.25, 127.33, 123.84 (d, J = 2.8 Hz), 123.40, 118.22, 114.52 (d, J = 21.7 Hz), 114.15 (d, J = 20.9 Hz), 42.52, 23.30, 23.14, 23.04, 20.70. HRMS (ESI) calcd for $C_{21}H_{20}FN_3O$ $(M+H)^+$ 350.1663, found 350.1661.

N-(4-fluorobenzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6h)**: white solid, yield 68%, m.p. 189-190℃.^{1}H NMR (500 MHz, DMSO-d_6) δ 8.99 (t, J = 6.0 Hz, 1H), 7.40–7.27 (m, 7H), 7.19–7.13 (m, 2H), 4.37 (d, J = 6.0 Hz, 2H), 2.67–2.58 (m, 4H), 1.81–1.66 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.30, 149.53, 140.48, 137.66, 134.48, 132.91, 129.54, 129.50, 129.32, 128.18, 127.37, 123.59, 122.90, 118.34, 43.42, 23.32, 23.15, 23.07, 20.79. HRMS (ESI) calcd for $C_{21}H_{20}FN_3O$ $(M+H)^+$ 350.1663, found 350.1665.

N-(3-bromobenzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6i):** white solid, yield 64%, m.p. 217-218℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.02 (t, J = 6.1 Hz, 1H), 7.52–7.24

(m, 9H), 4.39 (d, *J* = 6.1 Hz, 2H), 2.68–2.59(m, 4H), 1.82–1.68 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.30, 149.58, 142.30, 140.37, 134.48, 130.99, 130.57, 130.24, 129.29, 127.33, 126.94, 123.32, 122.07, 118.27, 42.42, 23.29, 23.14, 23.03, 20.73. HRMS (ESI) calcd for $C_{21}H_{20}BrN_3O$ $(M+H)^+$ 410.0863, found 410.0859.

N-(4-bromobenzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide**(6j):** white solid, yield 65%, m.p. 220-221℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.93 (t, *J* = 6.0 Hz, 1H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.35–7.21 (m, 5H), 7.15 (d, *J* = 8.3 Hz, 2H), 4.28 (d, *J* = 6.0 Hz, 2H), 2.62–2.49 (m, 4H), 1.75–1.60 (m, 4H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.24, 149.54, 140.40, 138.92, 134.54, 131.65, 130.13, 129.29, 127.32, 123.38, 120.42, 118.21, 42.39, 23.29, 23.14, 23.04, 20.69. HRMS (ESI) calcd for $C_{21}H_{20}BrN_3O$ $(M+H)^+$ 410.0863, found 410.0864.

2-phenyl-N-(3-(trifluoromethoxy)benzyl)-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6k):** white solid, yield 60%, m.p. 198-199℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.05 (t, *J* = 6.1 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.39–7.24 (m, 8H), 4.44 (d, *J* = 6.1 Hz, 2H), 2.68–2.59 (m, 4H), 1.83–1.67 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.30, 149.54, 146.60, 140.44, 134.41, 131.54, 129.96, 129.40, 129.29, 127.93, 127.33, 123.48, 121.11, 118.35, 37.52, 23.30, 23.13, 23.04, 20.67. HRMS (ESI) calcd for $C_{22}H_{20}F_3N_3O_2$ $(M+H)^+$ 416.1580, found 416.1583.

2-phenyl-N-(4-(trifluoromethoxy)benzyl)-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6l):** white solid, yield 72%, m.p. 214-215℃.^{1}H NMR (500 MHz, DMSO-d_6) δ 8.98 (t, *J* = 5.9 Hz, 1H), 7.44 – 7.29 (m, 9H), 4.47 (d, *J* = 5.9 Hz, 2H), 2.69–2.60 (m, 4H), 1.81–1.69 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.27, 149.55, 147.71, 140.39, 138.96, 134.54, 129.72, 129.24, 127.28, 123.37, 121.44, 118.21, 42.32, 23.29, 23.14, 23.04, 20.69. HRMS (ESI) calcd for $C_{22}H_{20}F_3N_3O_2$ $(M+H)^+$ 416.1580, found 416.1583.

N-(3-methylbenzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6m):** white solid, yield 77%, m.p. 200-201℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.88 (t, *J* = 5.8 Hz, 1H), 7.40–7.28 (m, 5H), 7.21–7.11 (m, 4H), 4.37 (d, *J* = 5.8 Hz, 2H), 2.67–2.58 (m, 4H), 2.26 (s, 3H), 1.81–1.67 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.20, 149.52, 140.44, 139.33, 137.80, 134.71, 129.26, 128.68, 128.43, 127.98, 127.24, 124.91, 123.30, 118.14, 42.91, 23.31, 23.16, 23.05, 21.51, 20.72. HRMS (ESI) calcd for $C_{22}H_{23}N_3O$ $(M+H)^+$ 346.1914, found 346.1915.

N-(4-methylbenzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide (**6n):** white solid, yield 72%, m.p. 201-202℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.94 (t, *J* = 6.0 Hz, 1H), 7.40–7.28 (m, 5H), 7.18–7.10 (m, 4H), 4.34 (d, *J* = 6.0 Hz, 2H), 2.68–2.57 (m, 4H), 2.29 (s, 3H), 1.81–1.67 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.15, 149.50, 140.43, 136.44, 136.40, 134.73, 129.30, 129.27, 127.84, 127.23, 123.29, 118.10, 42.70, 23.30, 23.16, 23.05, 21.16, 20.69. HRMS (ESI) calcd for $C_{22}H_{23}N_3O$ $(M+H)^+$ 346.1914, found 346.1913.

N-(4-ethylbenzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6o):** white solid, yield 57%, m.p. 177-178℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.95 (t, *J* = 6.0 Hz, 1H), 7.41–7.27 (m, 5H), 7.20–7.12 (m, 4H), 4.35 (d, *J* = 6.0 Hz, 2H), 2.68–2.55 (m, 6H), 1.81–1.66 (m, 4H), 1.17 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.17, 149.50, 142.87, 140.44, 136.64, 134.74, 129.26, 128.13, 127.89, 127.20, 123.28, 118.09, 42.74, 28.32, 23.31, 23.16, 23.05, 20.70, 16.22. HRMS (ESI) calcd for $C_{23}H_{25}N_3O$ $(M+H)^+$ 360.2070, found 360.2071.

N-(4-methoxybenzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6p)**: white solid, yield 86%, m.p. 181-182℃ , ^{1}H NMR (300 MHz, DMSO) δ 8.94 (t, *J* = 6.0 Hz, 1H), 7.43–7.17 (m, 7H), 6.91 (d, *J* = 8.6 Hz, 2H), 4.34 (d, *J* = 6.0 Hz, 2H), 3.76 (s, 3H), 2.70–2.57(m, 4H), 1.85–1.66 (m, 4H). ^{13}C NMR (151 MHz, DMSO-d$_6$) δ 161.08, 158.74, 149.49, 140.40, 134.73, 131.38, 129.27, 129.20, 127.20, 123.22, 118.07, 114.15, 55.55, 42.40, 23.30, 23.15, 23.04, 20.67. HRMS (ESI) calcd for $C_{22}H_{23}N_3O_2$ $(M+H)^+$ 362.1863, found 362.1864.

N-(4-(tert-butyl)benzyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6q):** white solid, yield 84%, m.p. 162-163℃.^{1}H NMR (300 MHz, DMSO-d_6) δ 8.95 (t, *J* = 5.9 Hz, 1H), 7.48–7.26 (m, 7H), 7.21 (d, *J* = 8.2 Hz, 2H), 4.37 (d, *J* = 6.0 Hz, 2H,), 2.75-2.56 (m, 4H), 1.88-1.65 (m, 4H), 1.30 (s, 9H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 161.18, 149.75, 149.49, 140.41, 136.33, 134.72, 129.25, 127.59, 127.17, 125.49, 123.25, 118.08, 42.66, 34.67, 31.66, 23.30, 23.16, 23.05, 20.71. HRMS (ESI) calcd for $C_{25}H_{29}N_3O$ $(M+H)^+$ 388.2383, found 388.2382.

N-(3-fluorophenethyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6r):** white solid, yield 68%, m.p. 165-166℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.47 (t, *J* = 5.5 Hz, 1H), 7.44–

7.25 (m, 6H), 7.11–7.03 (m, 3H), 3.50 (dd, *J* = 12.7, 6.7 Hz, 2H), 2.84 (t, *J* = 6.9 Hz, 2H), 2.62 (t, *J* = 6.2 Hz, 2H), 2.47 (t, *J* = 6.1 Hz, 2H), 1.80–1.64 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.68 (d, *J* = 243.0 Hz), 161.04, 149.42, 142.64 (d, *J* = 7.2 Hz), 140.43, 134.67, 130.55 (d, *J* = 8.1 Hz), 129.25, 127.13, 125.40, 123.09, 118.08, 115.92 (d, *J* = 20.5 Hz), 113.40 (d, *J* = 21.1 Hz), 40.26, 34.63, 23.27, 23.15, 23.02, 20.59. HRMS (ESI) calcd for $C_{22}H_{22}FN_3O$ $(M+H)^+$ 364.1820, found 364.1821.

N-(4-fluorophenethyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6s):** white solid, yield 83%, m.p. 203-204℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (t, *J* = 5.5 Hz, 1H), 7.43–7.22 (m, 7H), 7.12 (t, *J* = 8.8 Hz, 2H), 3.46 (dd, *J* = 12.8, 6.8 Hz, 2H), 2.79 (t, *J* = 6.9 Hz, 2H), 2.62 (t, *J* = 6.1 Hz, 2H), 2.48 (t, *J* = 6.1 Hz, 2H), 1.82–1.62 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.36 (d, *J* = 241.7 Hz), 161.00, 149.42, 140.44, 135.75 (d, *J* = 2.7 Hz), 134.70, 131.03, 130.97, 129.23, 127.13, 123.13, 118.07, 115.48, 115.31, 40.63, 34.17, 23.27, 23.15, 23.01, 20.59. HRMS (ESI) calcd for $C_{22}H_{22}FN_3O$ $(M+H)^+$ 364.1820, found 364.1821.

N-(3-bromophenethyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6t):** white solid, yield 61%, m.p. 185-186℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.46 (t, *J* = 5.5 Hz, 1H), 7.47–7.35 (m, 4H), 7.32–7.23 (m, 5H), 3.48 (q, *J* = 6.4 Hz, 2H), 2.81 (t, *J* = 6.7 Hz, 2H), 2.61 (t, *J* = 6.1 Hz, 2H), 2.45 (t, *J* = 6.0 Hz, 2H), 1.78–1.65 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.04, 149.41, 142.65, 140.42, 134.66, 132.12, 130.88, 129.52, 129.27, 128.41, 127.12, 123.07, 122.06, 118.08, 40.39, 34.46, 23.28, 23.16, 23.08, 20.64. HRMS (ESI) calcd for $C_{22}H_{22}BrN_3O$ $(M+H)^+$ 424.1019, found 424.1020.

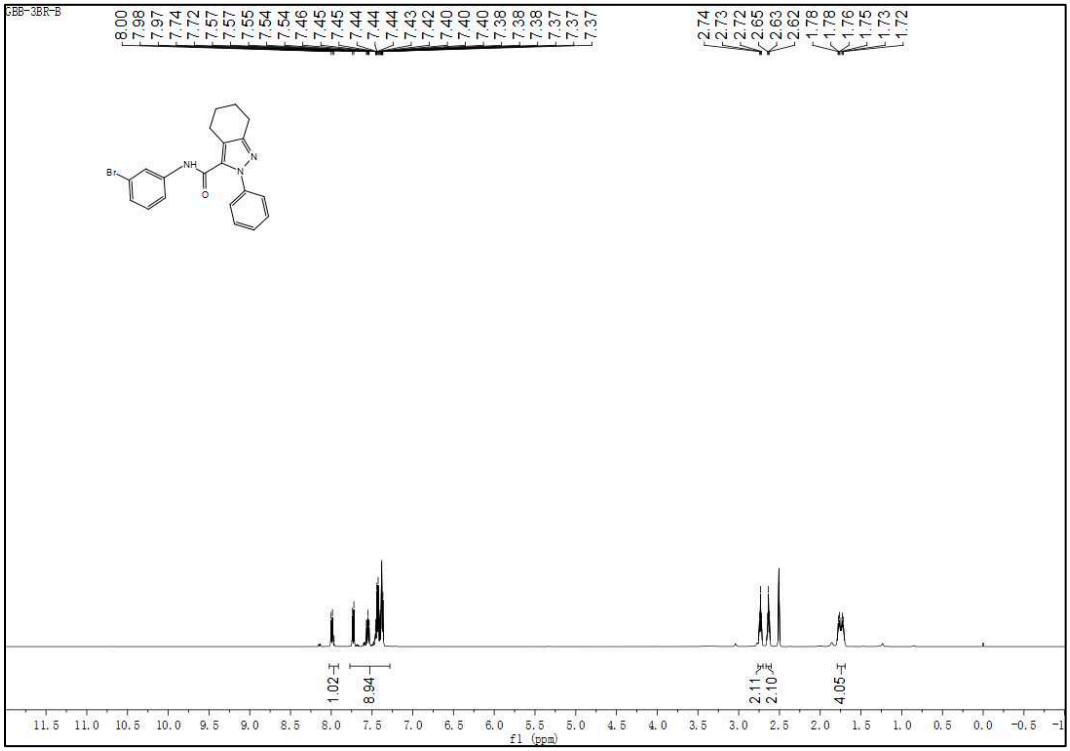
N-(4-bromophenethyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6u):** white solid; yield 77%, m.p. 209-210℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.43 (t, *J* = 5.6 Hz, 1H), 7.51–7.36 (m, 4H), 7.32–7.17 (m, 5H), 3.47 (q, *J* = 6.8 Hz, 2H), 2.78 (t, *J* = 6.9 Hz, 2H), 2.61 (t, *J* = 6.2 Hz, 2H), 2.45 (t, *J* = 6.1 Hz, 2H), 1.78–1.63 (m, 4H).^{13}C NMR (126 MHz, DMSO-d_6) δ 160.99, 149.42, 140.43, 139.11, 134.67, 131.56, 129.24, 127.12, 123.12, 119.74, 118.09, 34.37, 23.28, 23.15, 23.02, 20.58. ESI-HRMS (m/z) found: 424.1019 (calcd. for $C_{22}H_{22}BrN_3O$ $[M+H]^+$: 424.1019). HRMS (ESI) calcd for $C_{22}H_{22}BrN_3O$ $(M+H)^+$ 424.1019, found 424.1019.

N-(4-methylphenethyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6v)**: white solid, yield 76%, m.p. 184-185℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.44 (t, *J* = 5.6 Hz, 1H), 7.43–7.07 (m, 9H), 3.43 (dd, *J* = 13.0, 7.0 Hz, 2H), 2.75 (t, *J* = 7.2 Hz, 2H), 2.62 (t, *J* = 6.2 Hz, 2H), 2.49–2.43 (m, 2H), 2.27 (s, 3H), 1.79–1.62 (m, 4H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.97, 149.41, 140.44, 136.47, 135.52, 134.74, 129.33, 129.25, 129.06, 127.12, 123.12, 118.08, 40.77, 34.70, 23.28, 23.16, 23.03, 21.12, 20.59. HRMS (ESI) calcd for $C_{23}H_{25}N_3O$ $(M+H)^+$ 360.2070, found 360.2069.

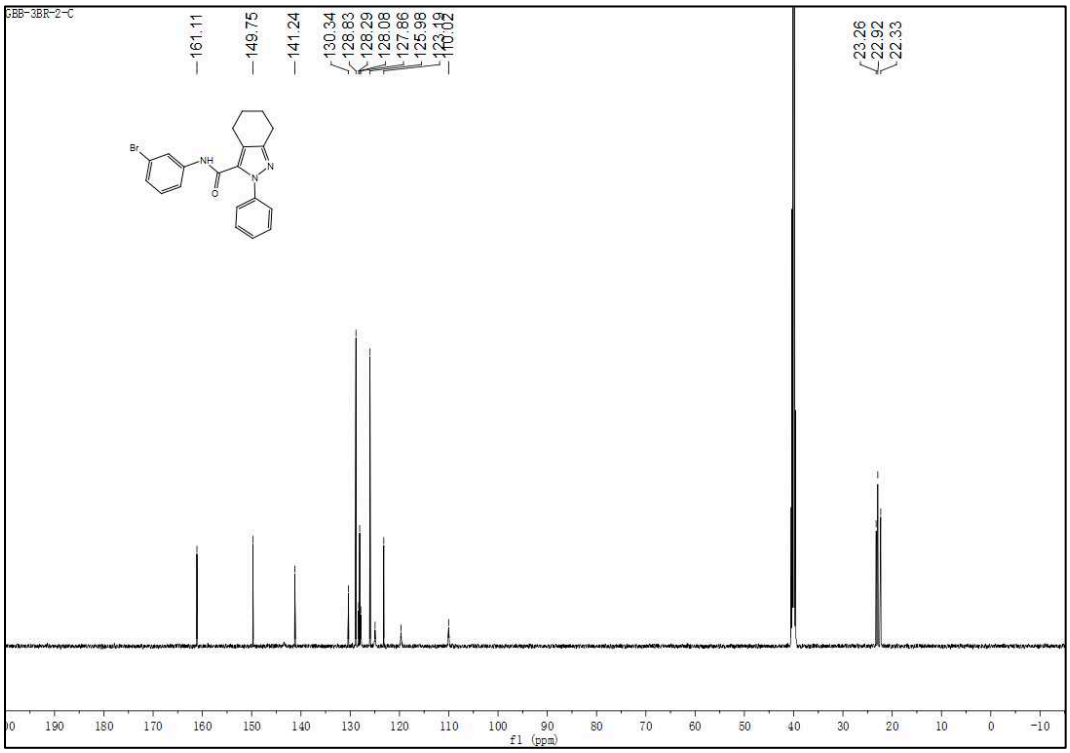
N-(4-ethylphenethyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6w)**: white solid, yield 73%, m.p. 130-131℃. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (t, *J* = 5.6 Hz, 1H), 7.41–7.36 (m, 2H), 7.33–7.28 (m, 3H), 7.16–7.09 (m, 4H), 3.44 (dd, *J* = 13.0, 7.0 Hz, 2H), 2.76 (t, *J* = 7.2 Hz, 2H), 2.64–2.54 (m, 4H), 2.45 (t, *J* = 6.2 Hz, 2H), 1.78–1.63 (m, 4H), 1.16 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 160.99, 149.41, 141.95, 140.45, 136.73, 134.76, 129.26, 129.09, 128.14, 127.12, 123.13, 118.07, 40.72, 34.67, 28.28, 23.28, 23.16, 23.03, 20.56, 16.18. HRMS (ESI) calcd for $C_{24}H_{27}N_3O$ $(M+H)^+$ 374.2227, found 374.2229.

N-(4-methoxyphenethyl)-2-phenyl-4,5,6,7-tetrahydro-2H-indazole-5-carboxamide **(6x)**: white solid, yield 90%, m.p. 187-188℃. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.43 (t, *J* = 5.7 Hz, 1H), 7.48–7.11 (m, 7H), 6.94–6.81 (m, 2H), 3.74 (s, 3H), 3.44 (dd, *J* = 12.8, 7.1 Hz, 2H), 2.75 (t, *J* = 7.1 Hz, 2H), 2.64 (t, *J* = 6.0 Hz, 2H), 2.51–2.47 (m, 2H), 1.84 – 1.54 (m, 4H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 160.94, 158.19, 149.40, 140.43, 134.74, 131.43, 130.16, 129.24, 127.11, 123.11, 118.06, 114.17, 55.46, 40.90, 34.22, 23.28, 23.15, 23.02, 20.60. HRMS (ESI) calcd for $C_{23}H_{25}N_3O_2$ $(M+Na)^+$ 398.1839, found 398.1840.

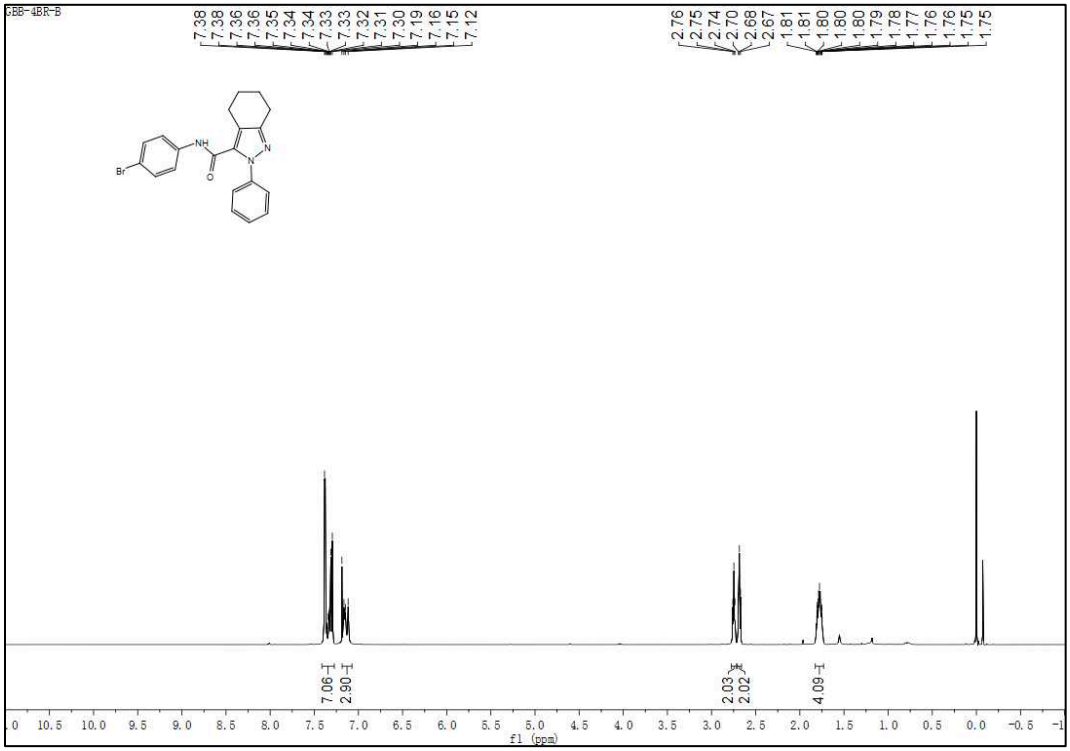
[1]H NMR and [13]C NMR spectra of target compounds



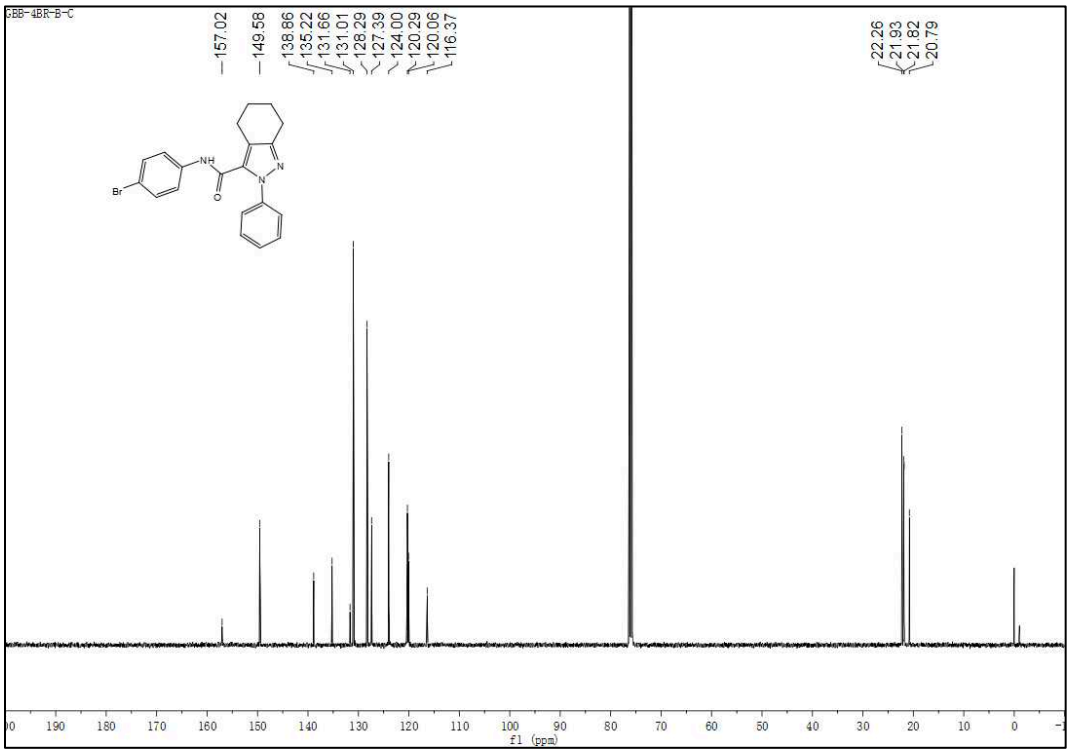
[1]H NMR spectra of compound **6a**



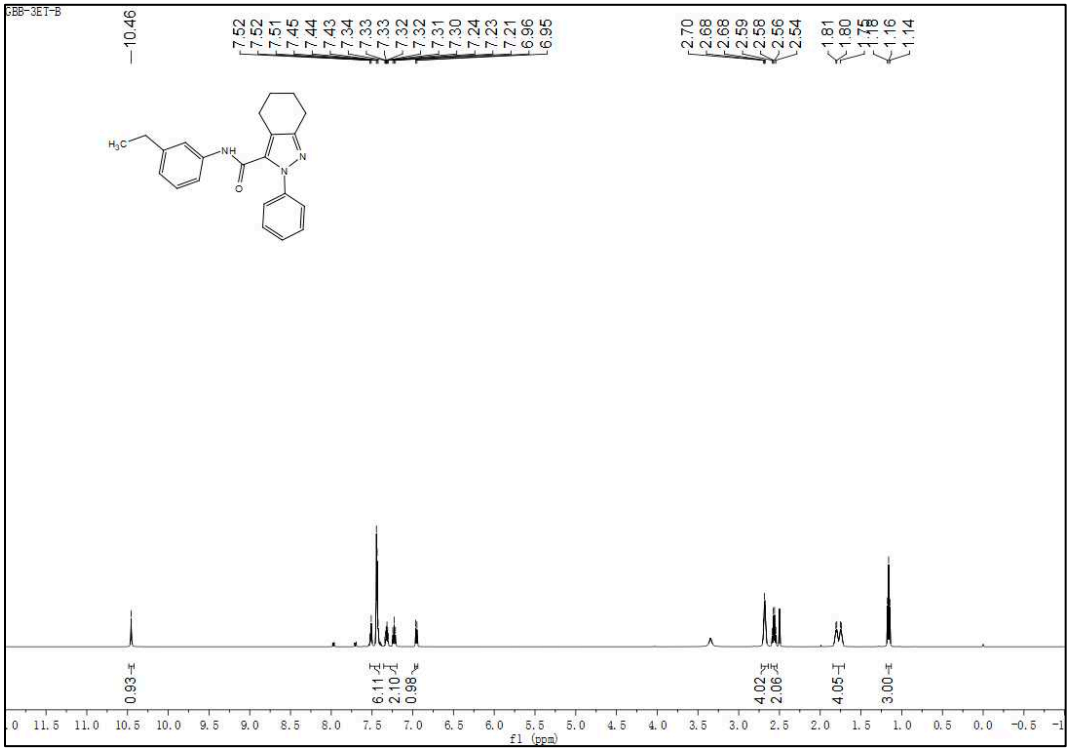
[13]C NMR spectra of compound **6a**



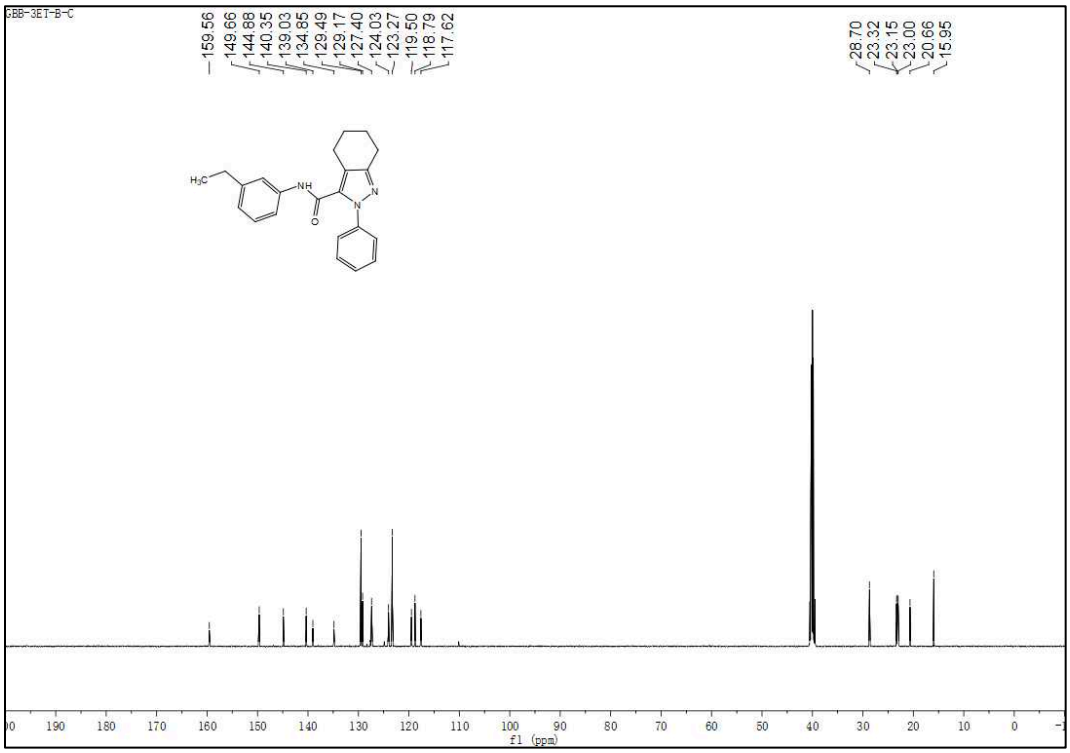
^{1}H NMR spectra of compound **6b**



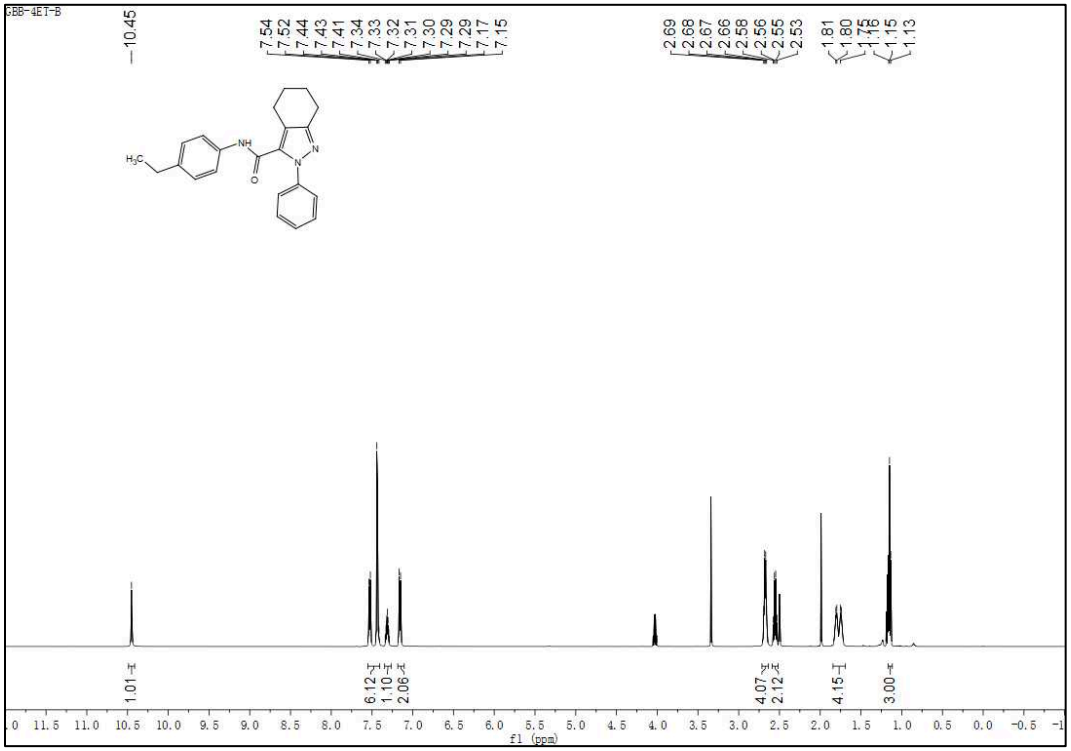
^{13}C NMR spectra of compound **6b**



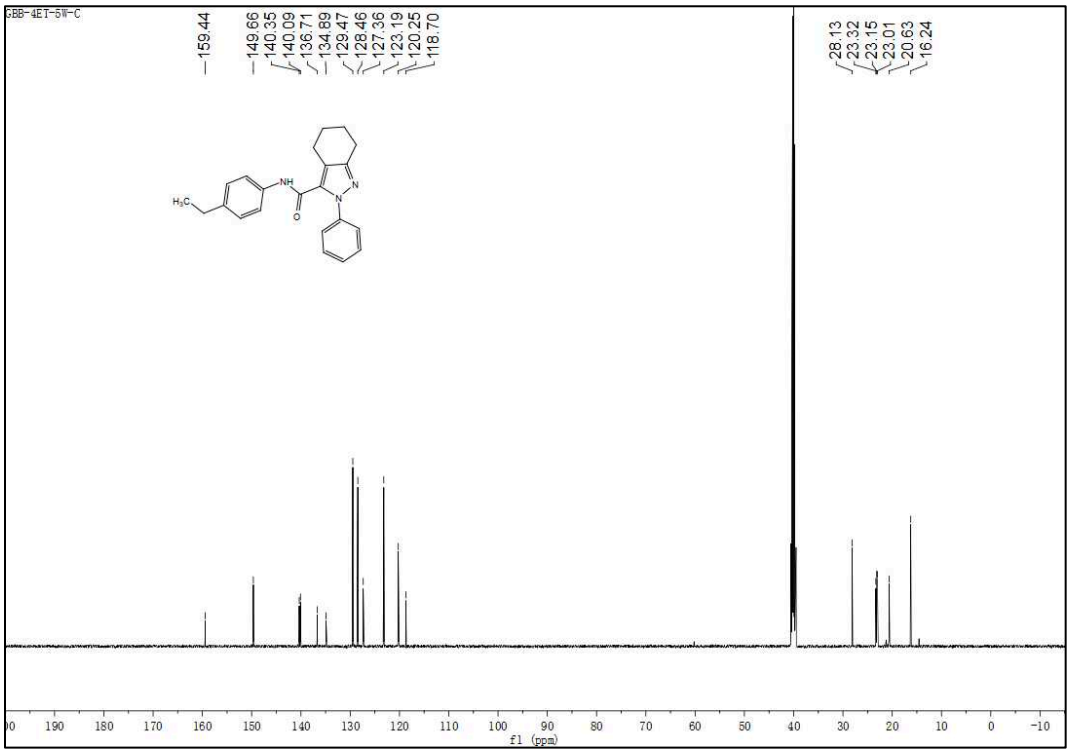
^{1}H NMR spectra of compound **6c**



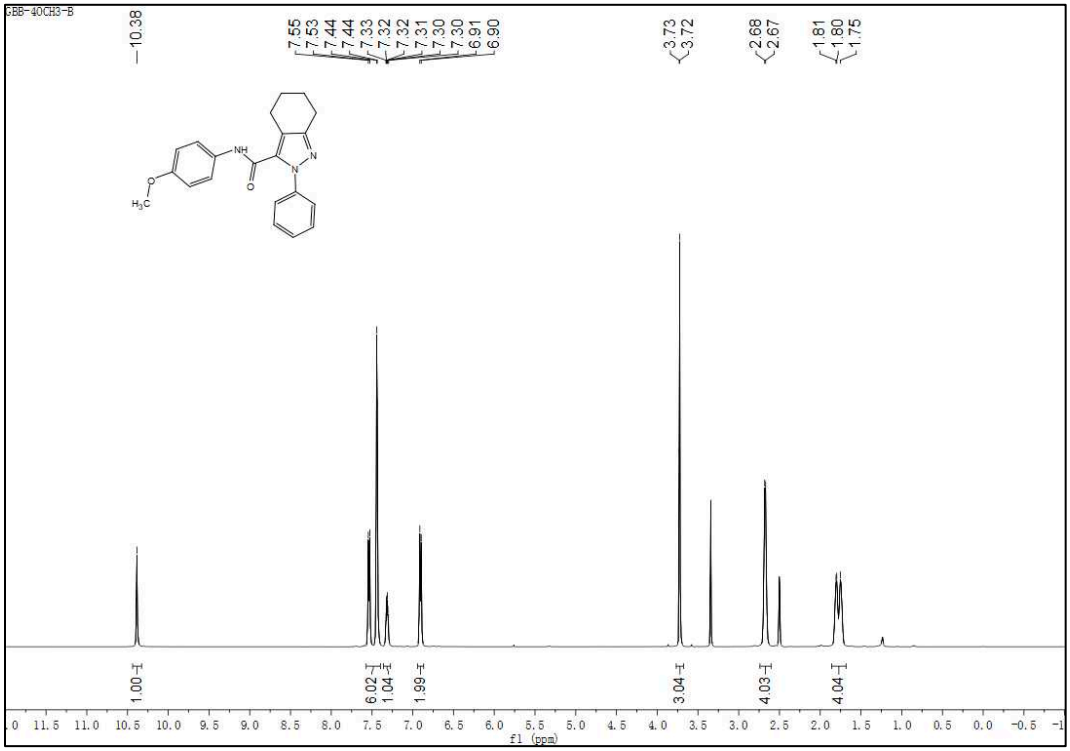
^{13}C NMR spectra of compound **6c**



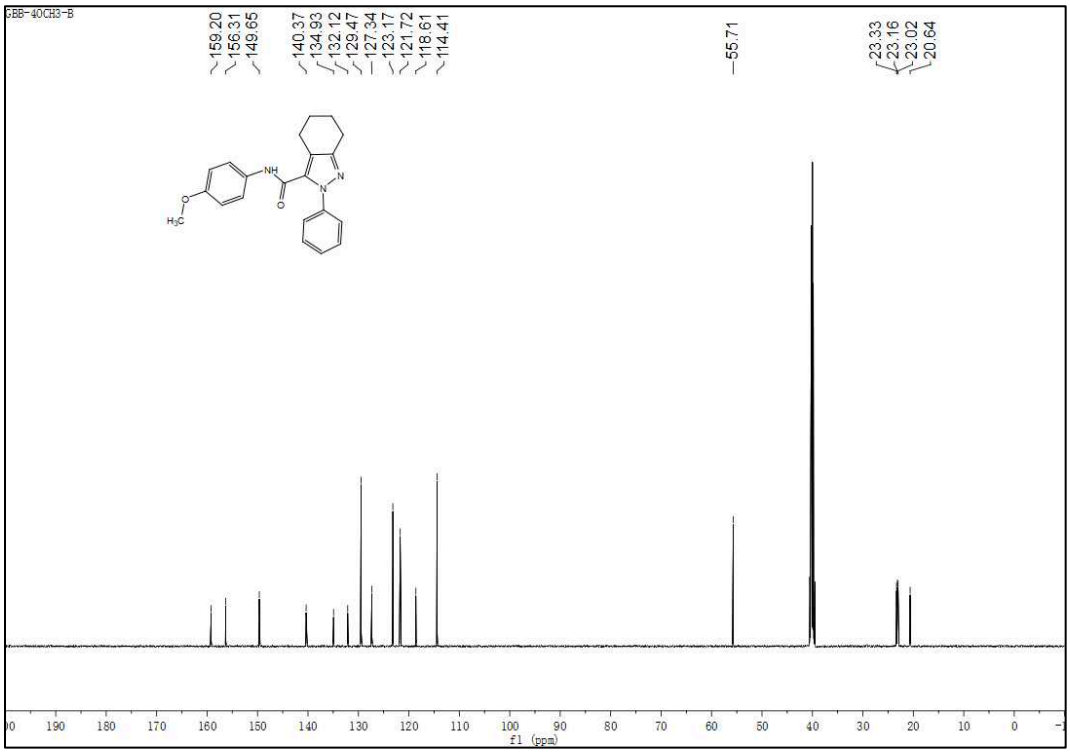
^{1}H NMR spectra of compound **6d**



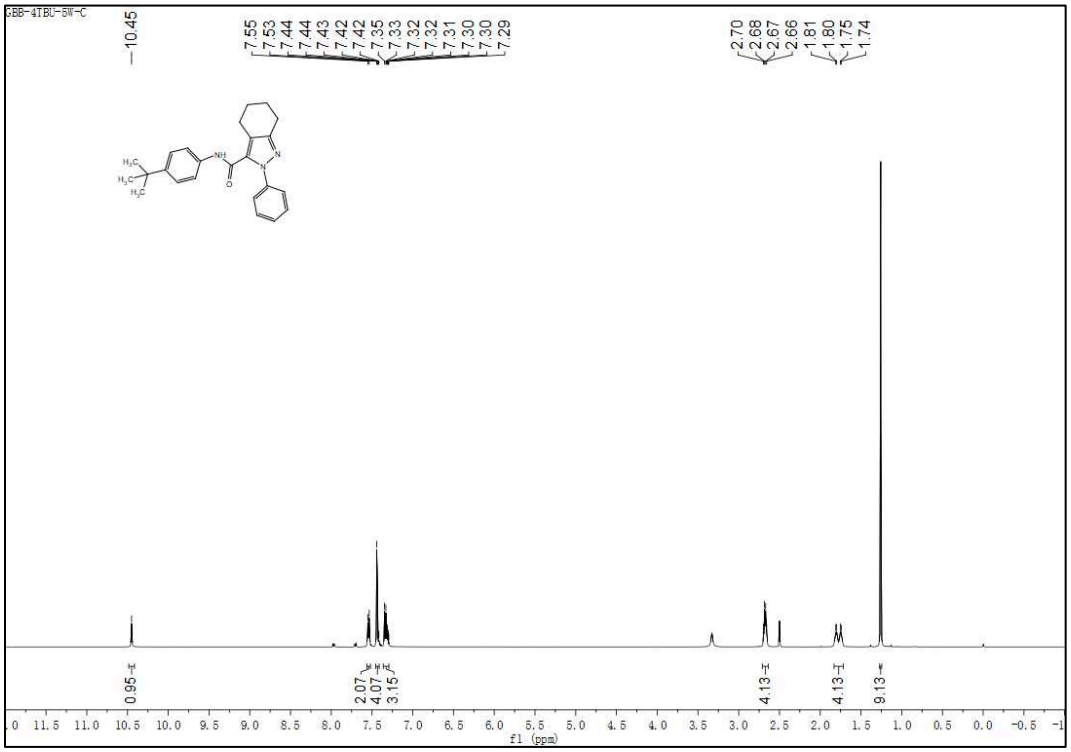
^{13}C NMR spectra of compound **6d**



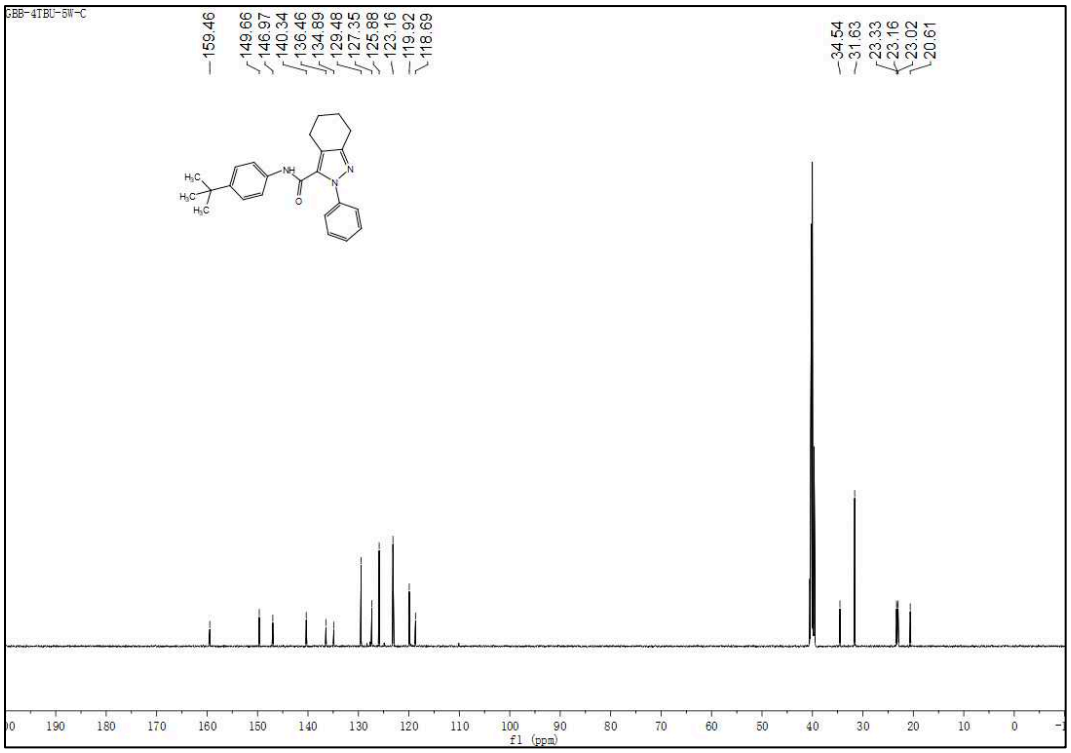
^{1}H NMR spectra of compound **6e**



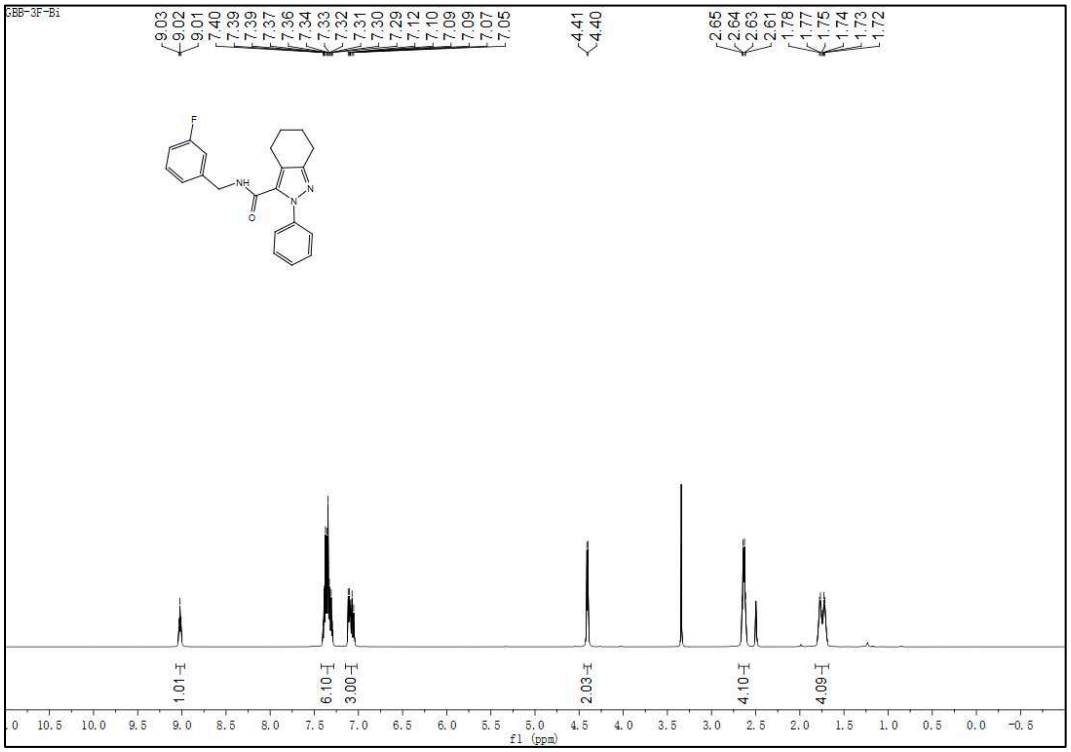
^{13}C NMR spectra of compound **6e**



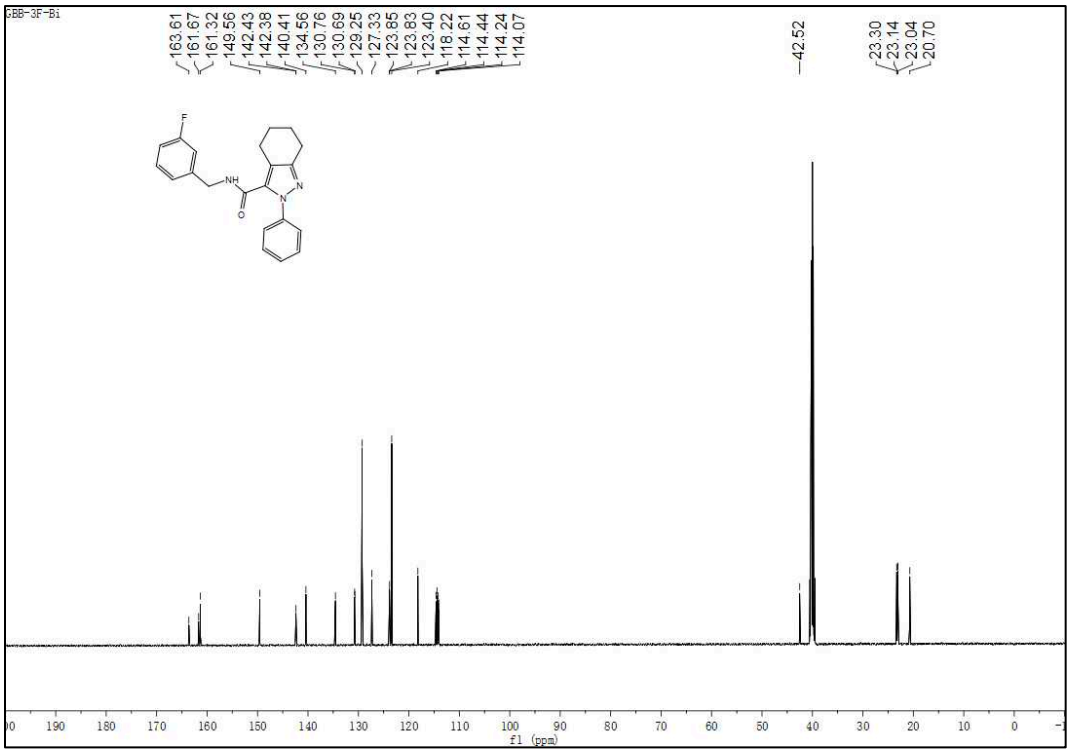
^{1}H NMR spectra of compound **6f**



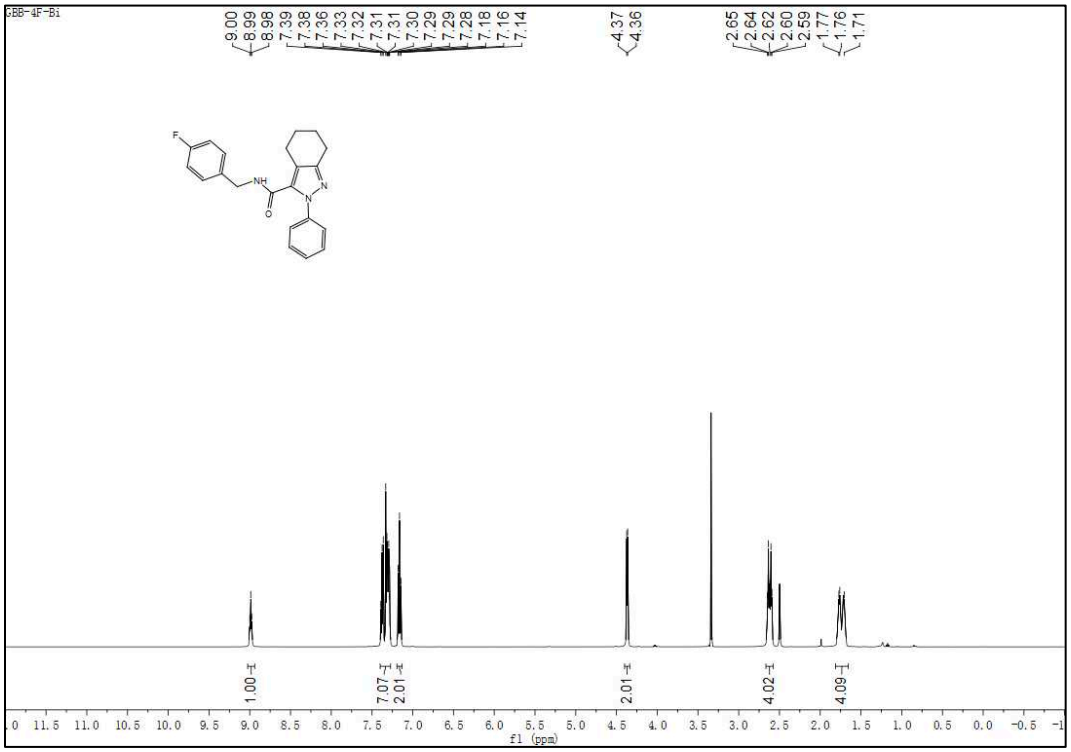
^{13}C NMR spectra of compound **6f**



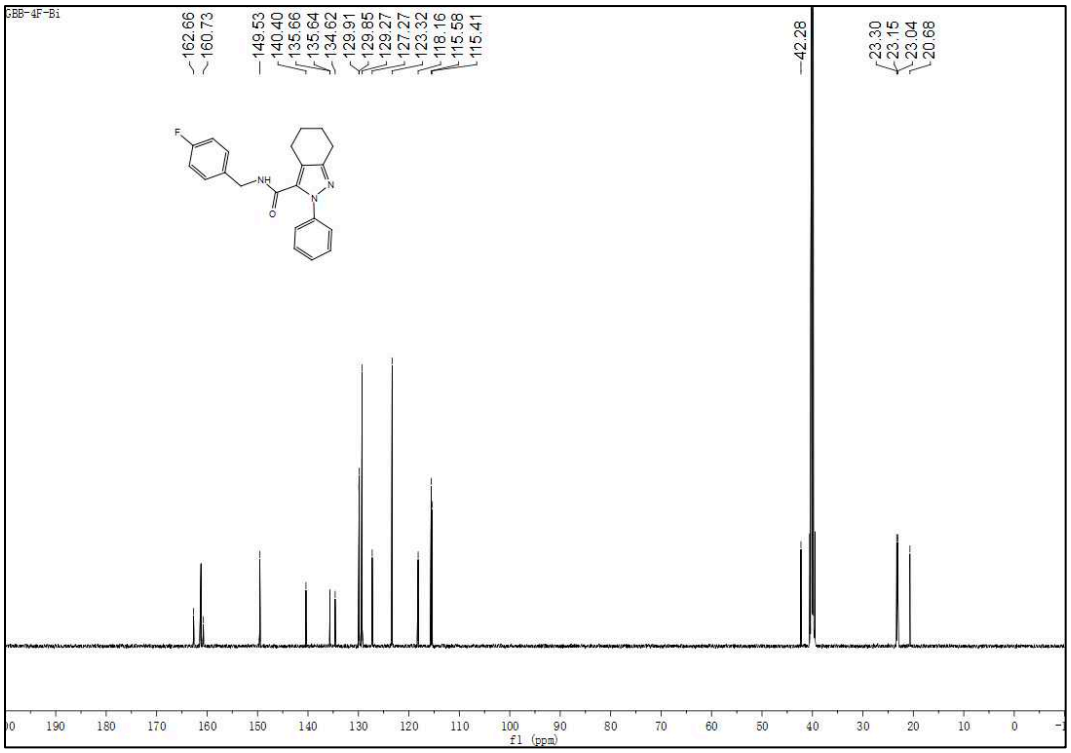
^{1}H NMR spectra of compound **6g**



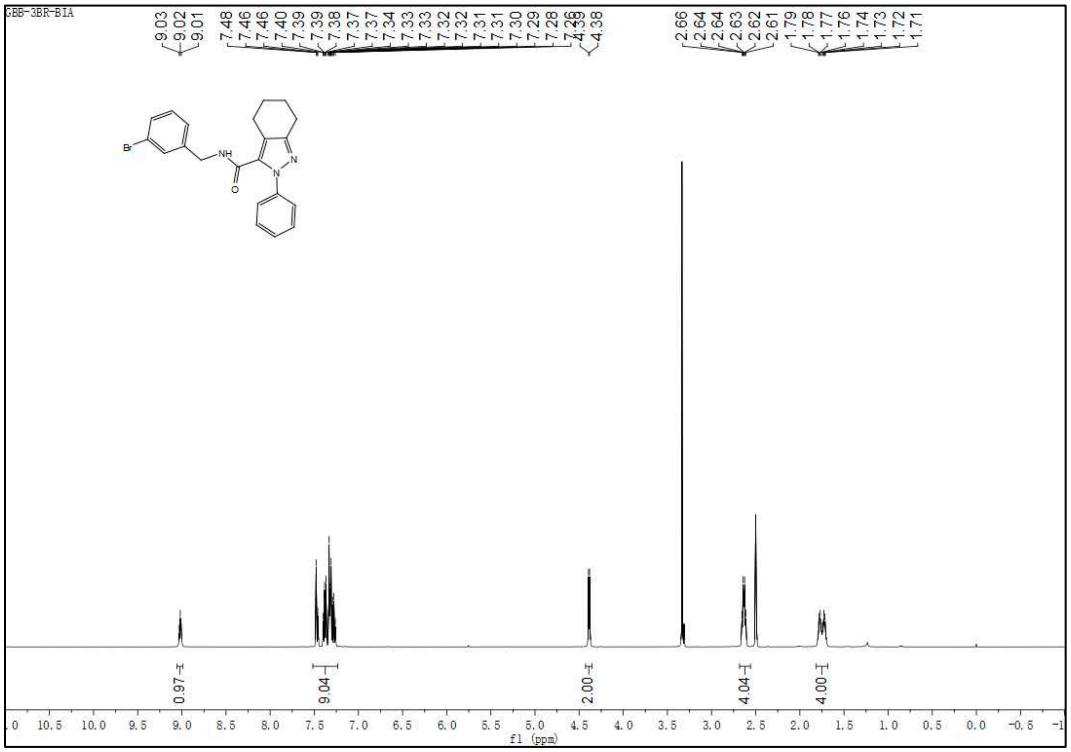
^{13}C NMR spectra of compound **6g**



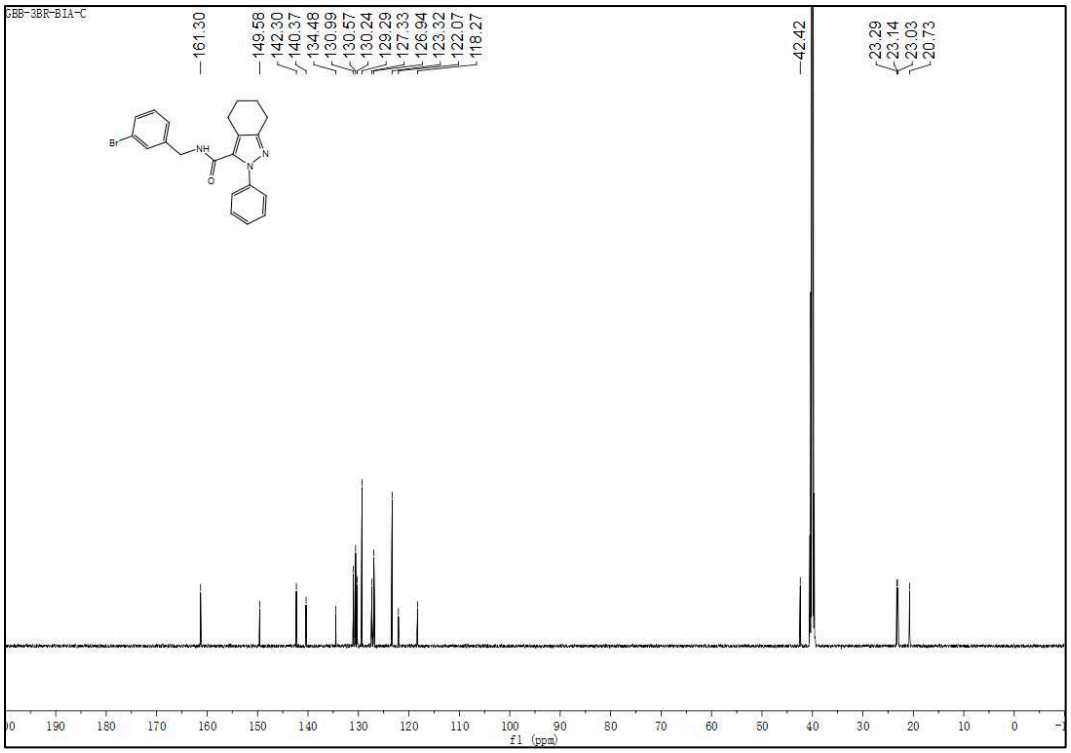
^{1}H NMR spectra of compound **6h**



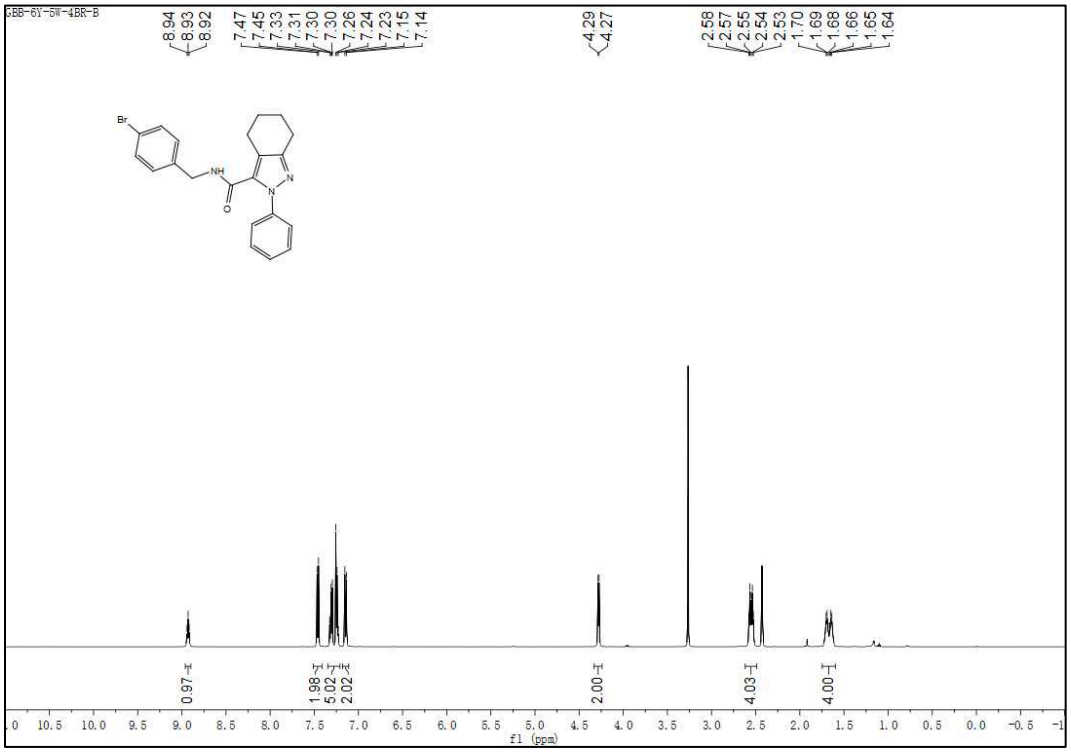
^{13}C NMR spectra of compound **6h**



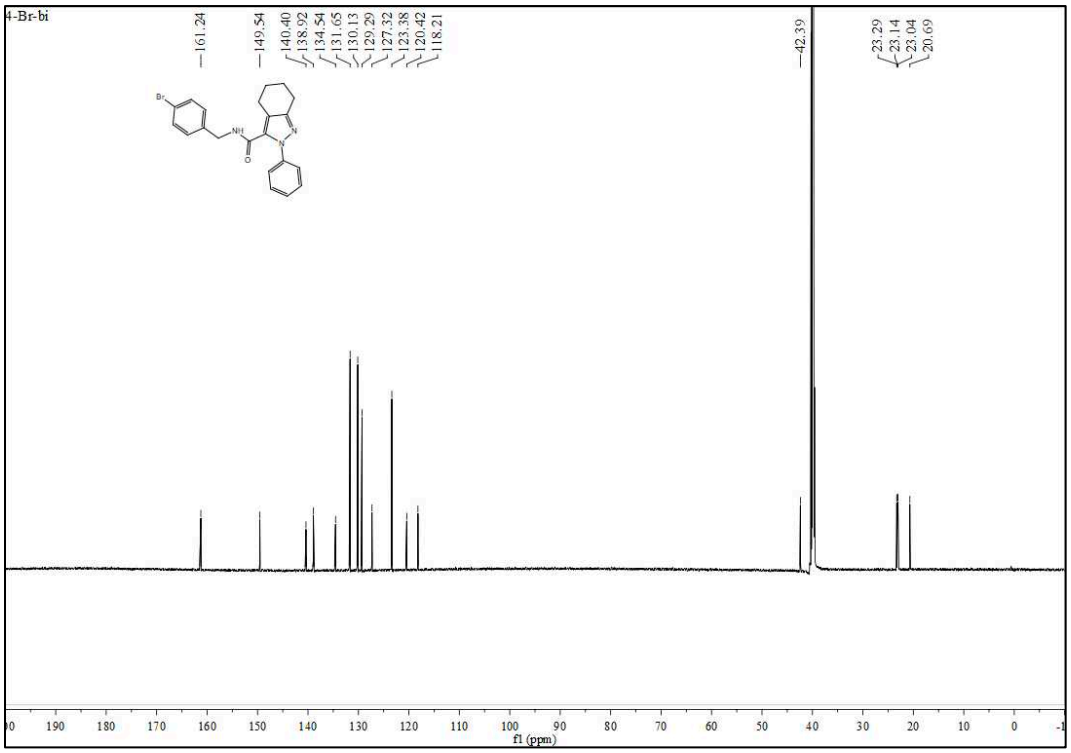
^{1}H NMR spectra of compound **6i**



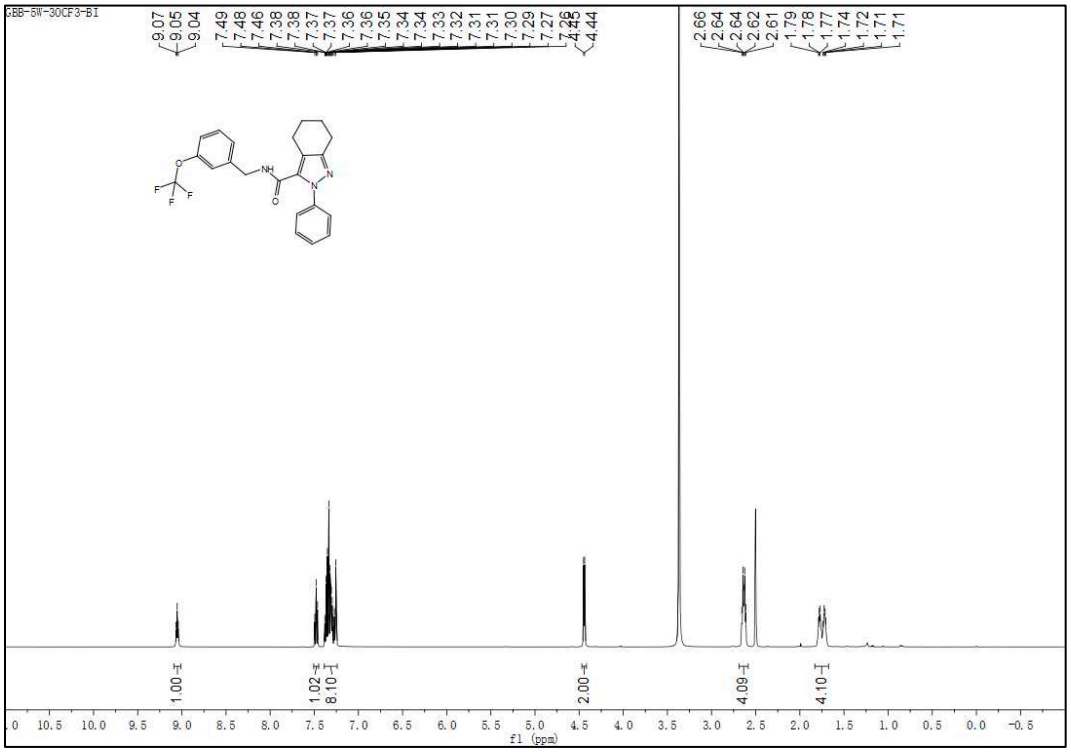
^{13}C NMR spectra of compound **6i**



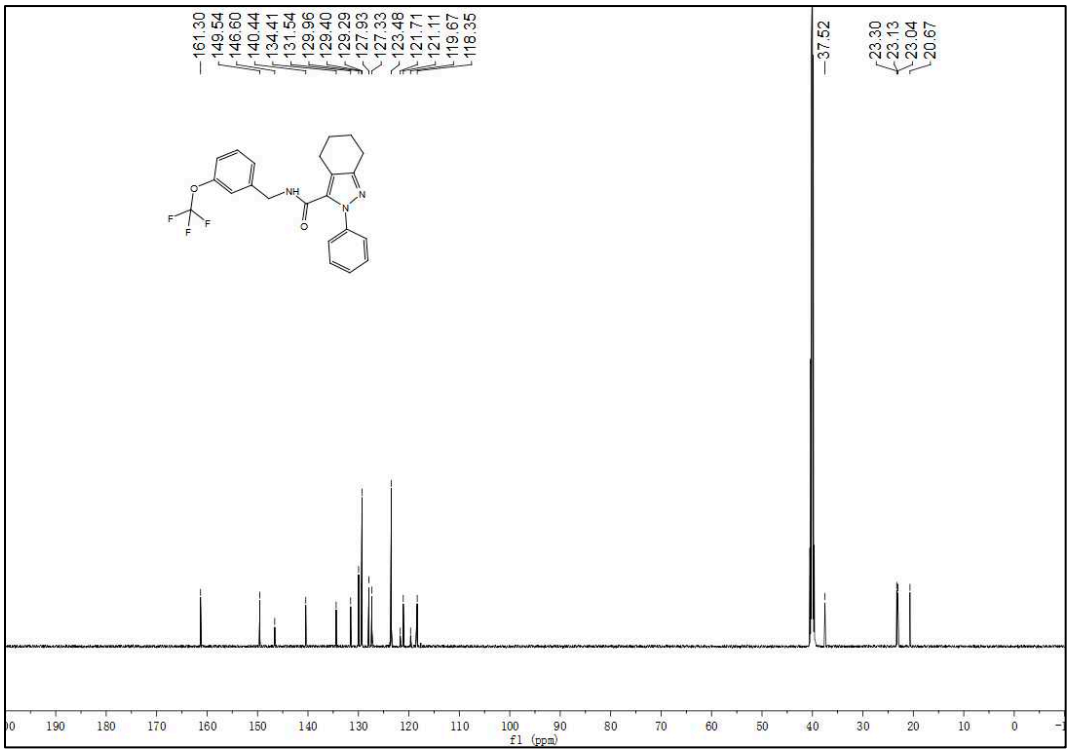
^{1}H NMR spectra of compound **6j**



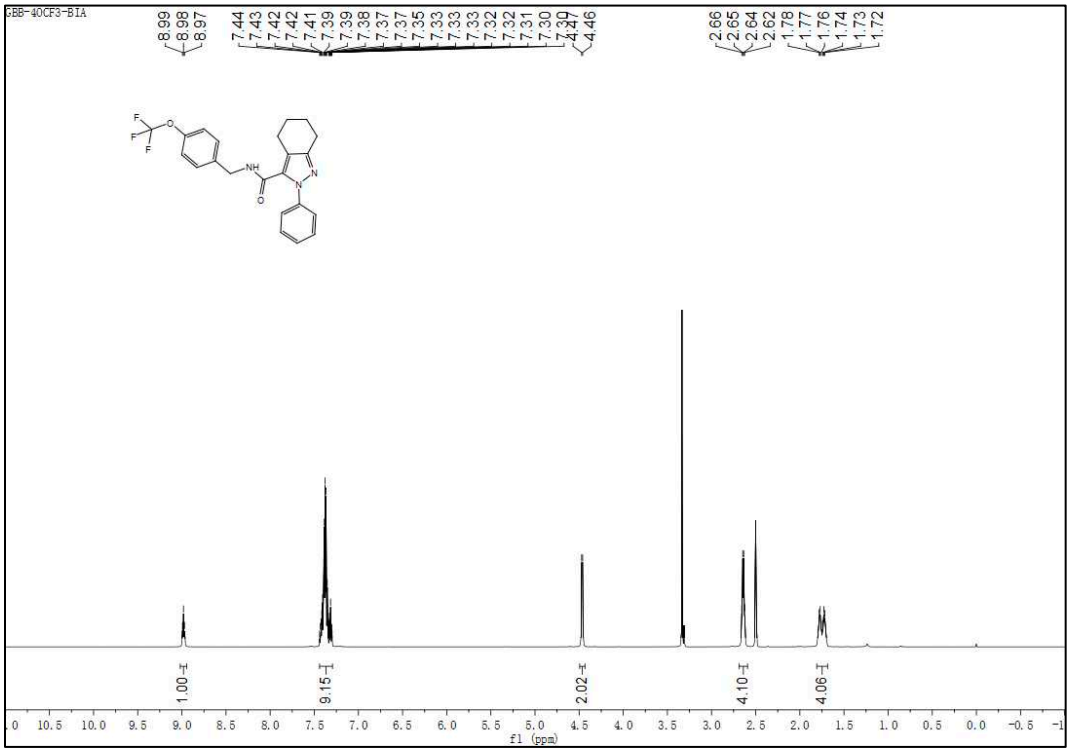
^{13}C NMR spectra of compound **6j**



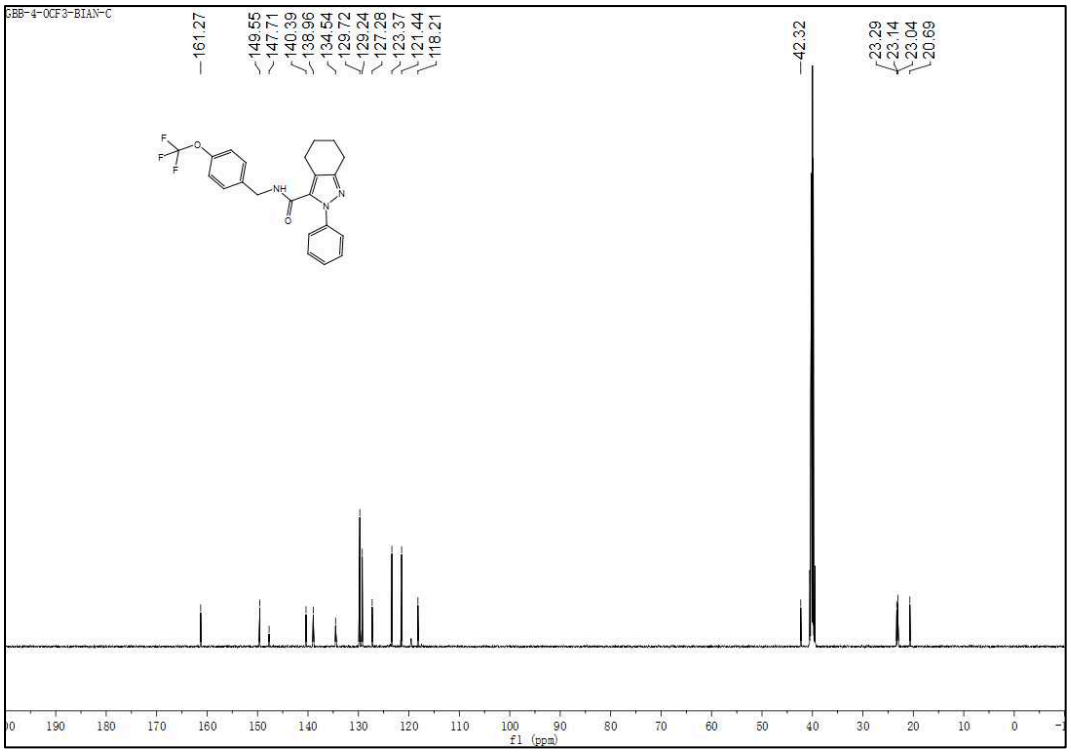
^{1}H NMR spectra of compound **6k**



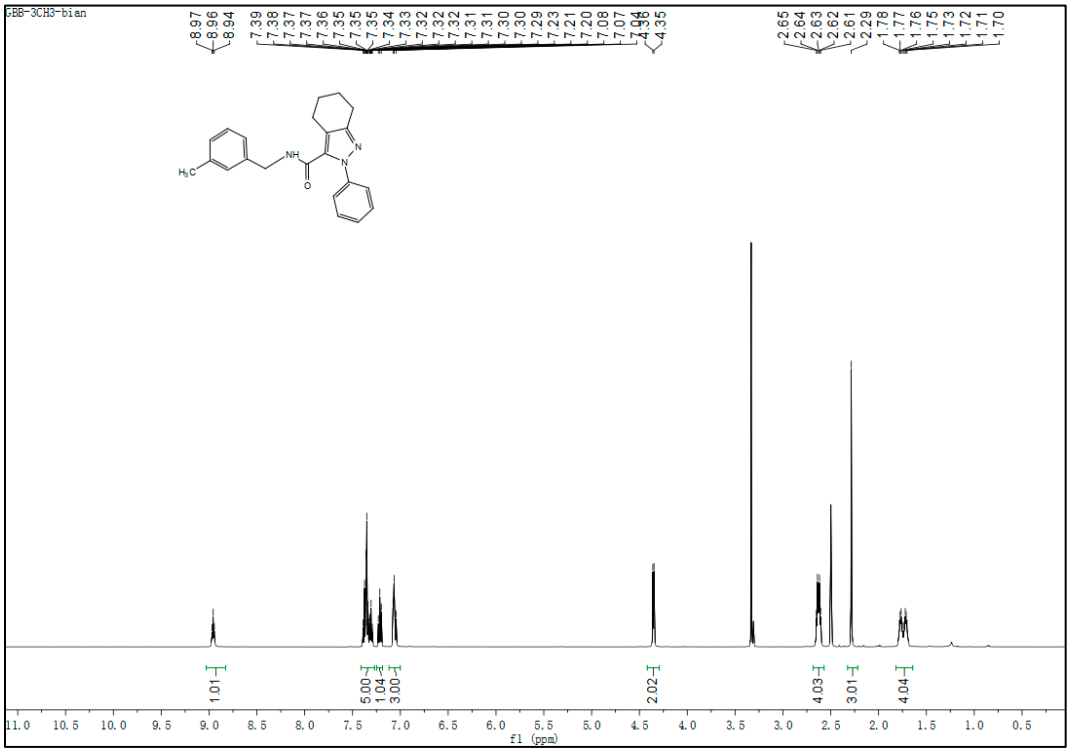
^{13}C NMR spectra of compound **6k**



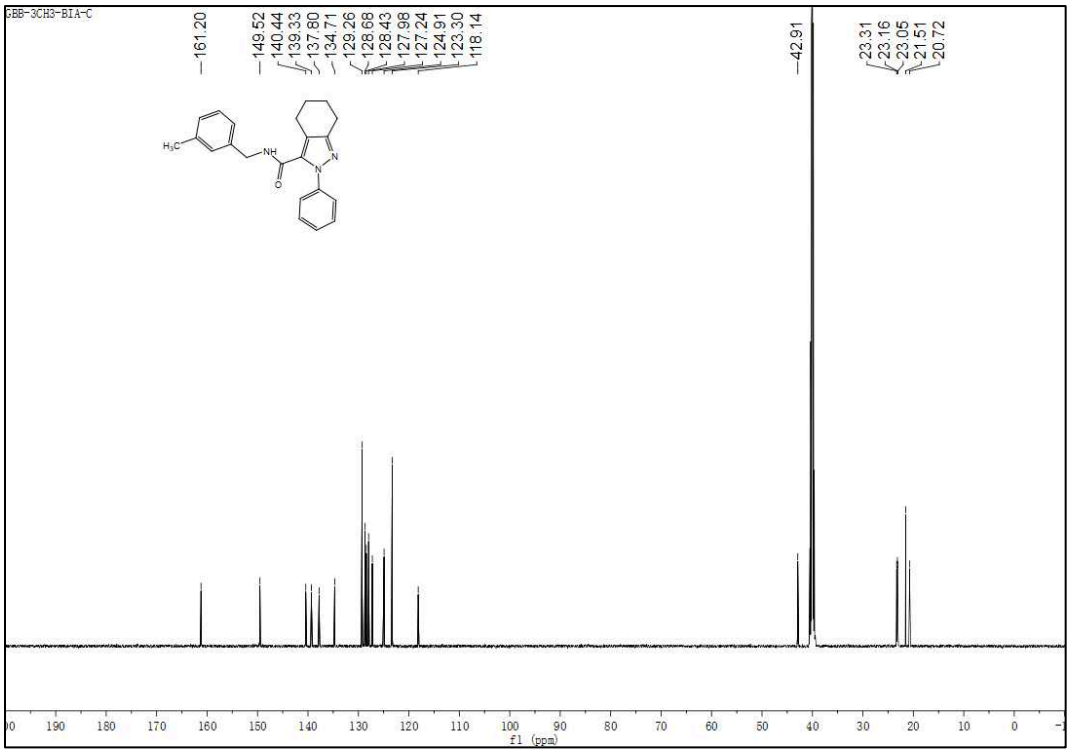
^{1}H NMR spectra of compound **6l**



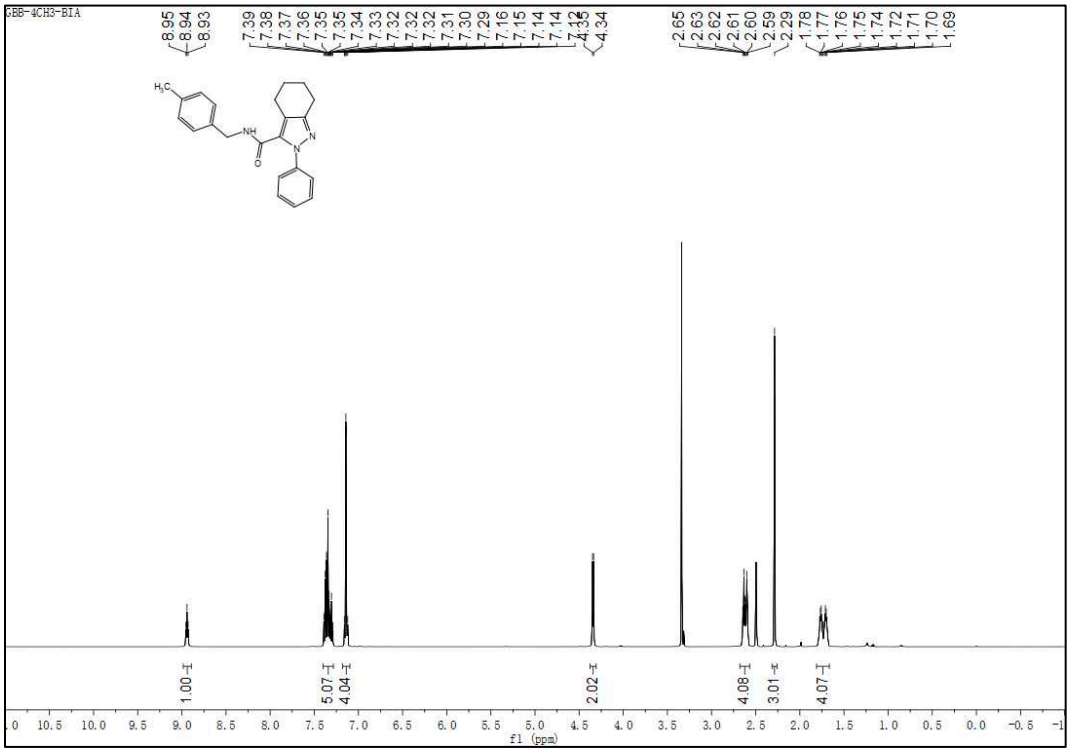
^{13}C NMR spectra of compound **6l**



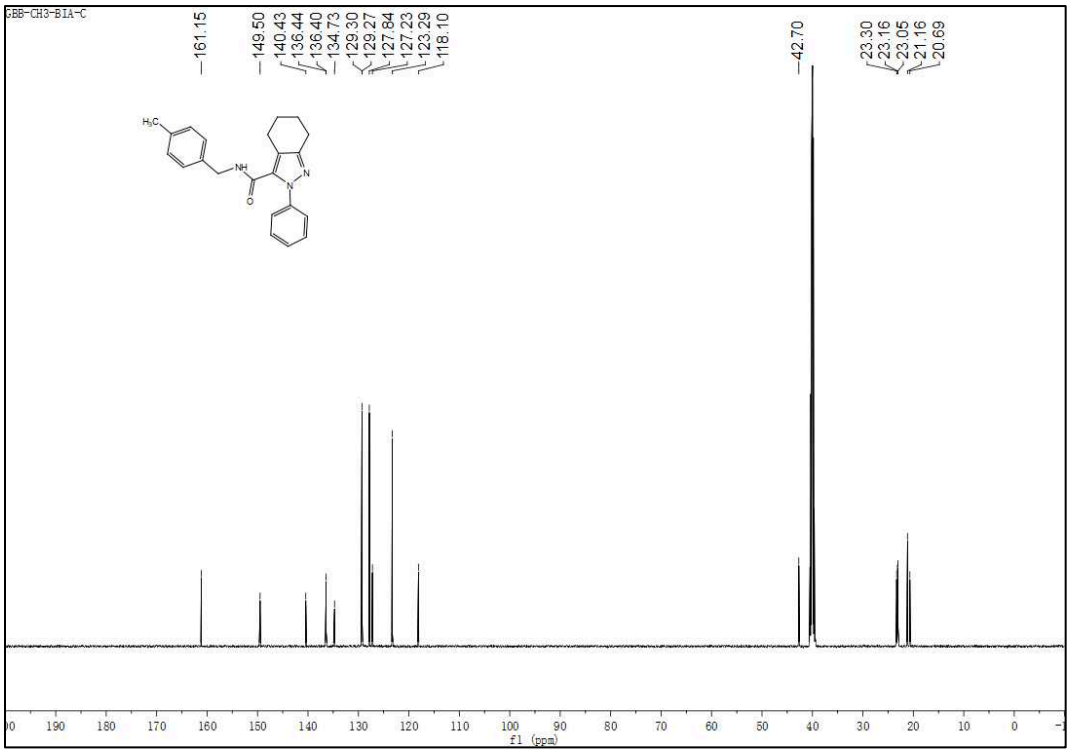
^{1}H NMR spectra of compound **6m**



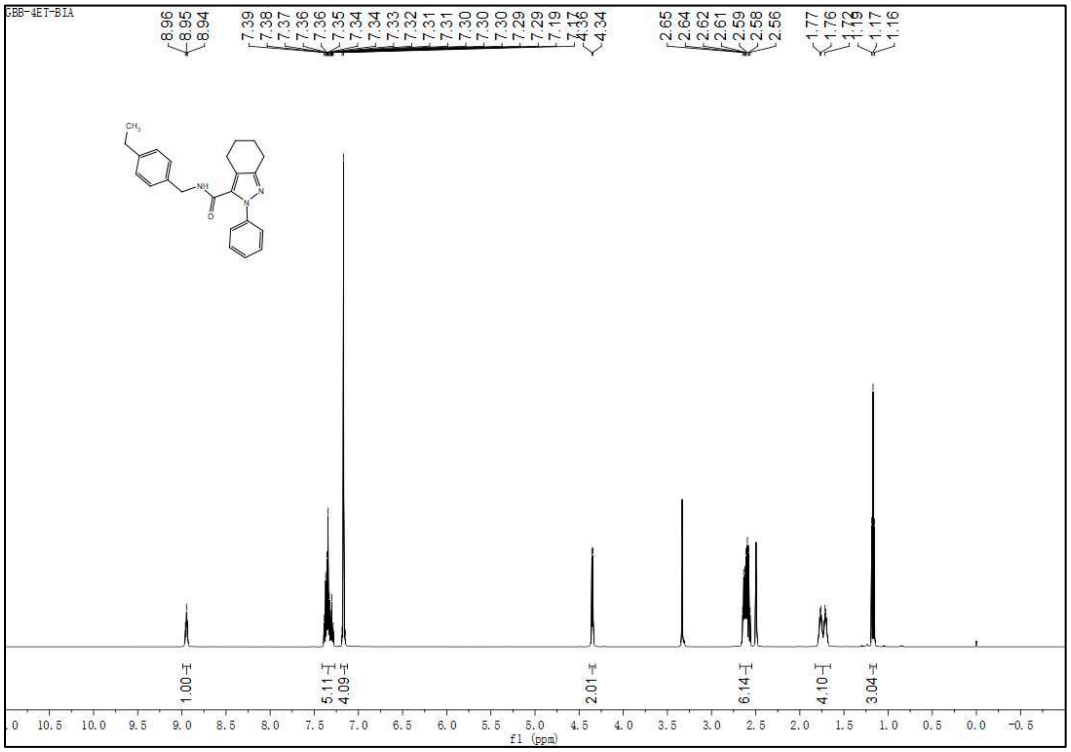
^{13}C NMR spectra of compound **6m**



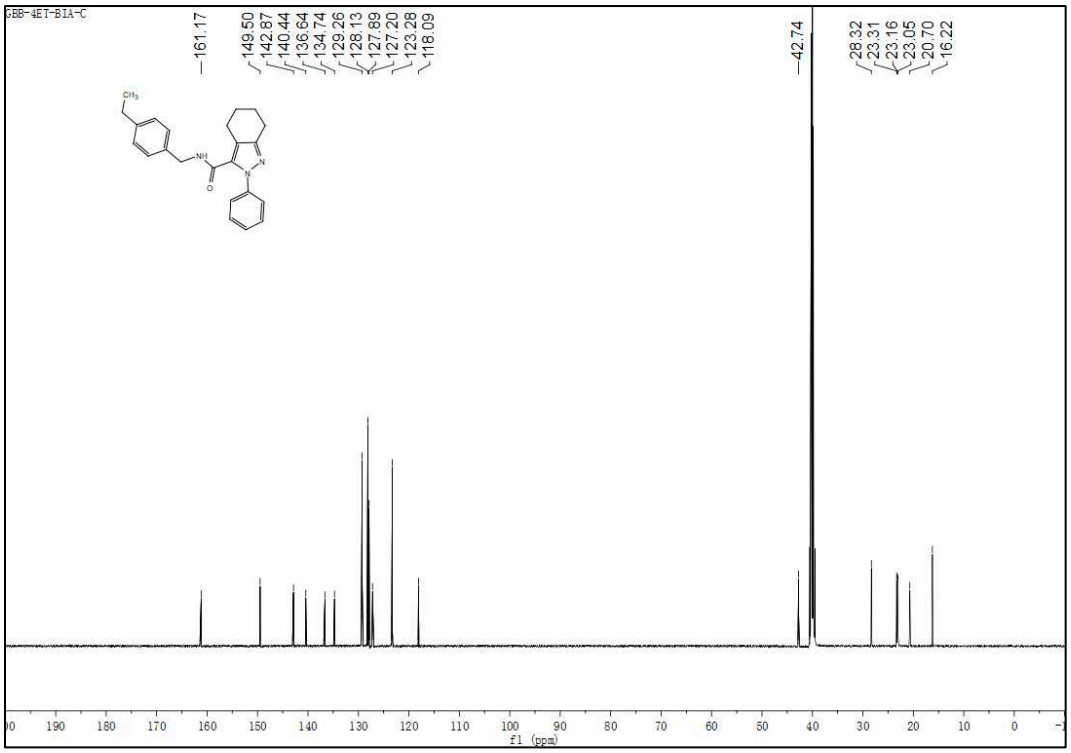
^{1}H NMR spectra of compound **6n**



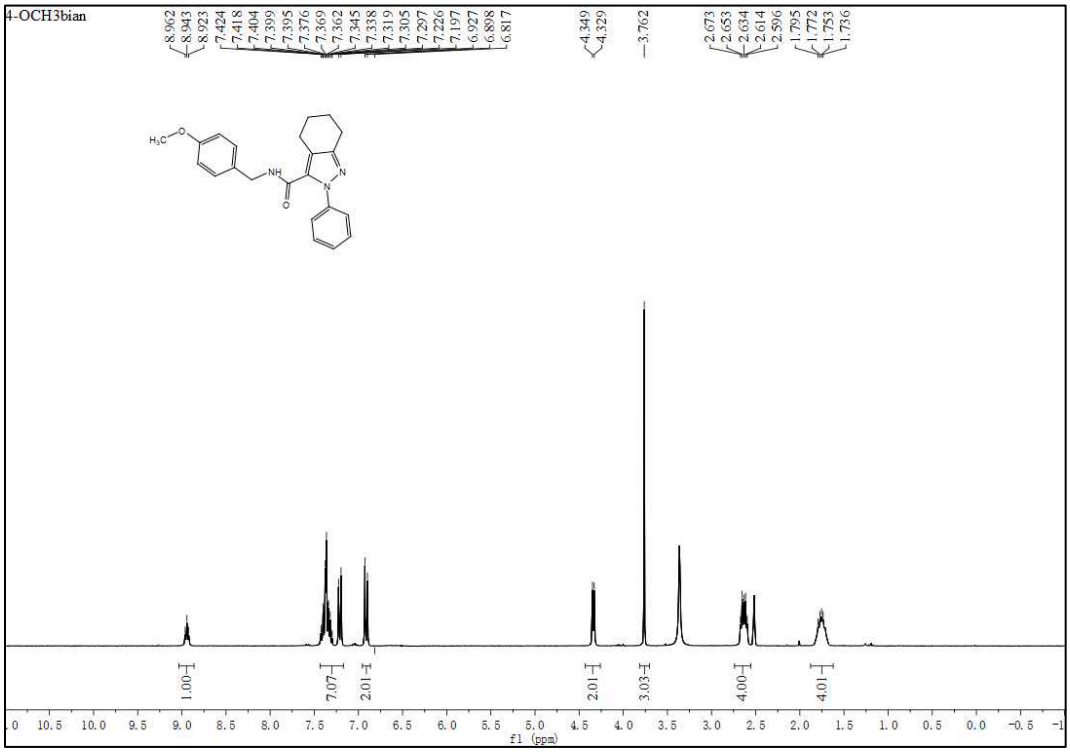
^{13}C NMR spectra of compound **6n**



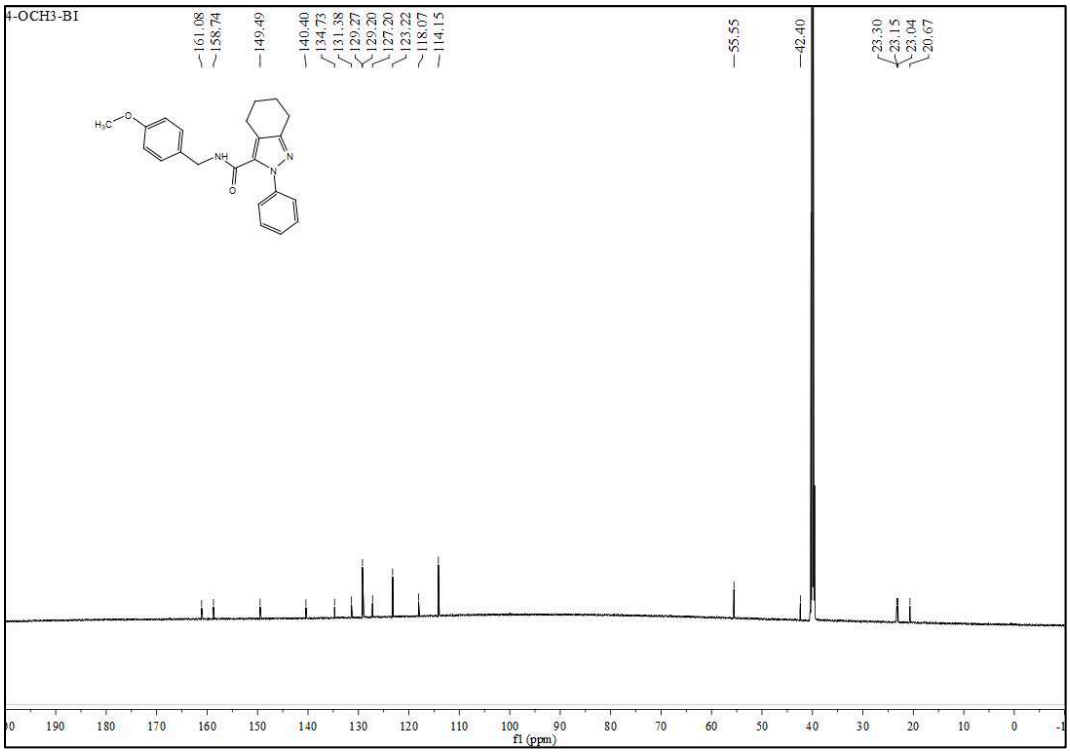
^{1}H NMR spectra of compound **6o**



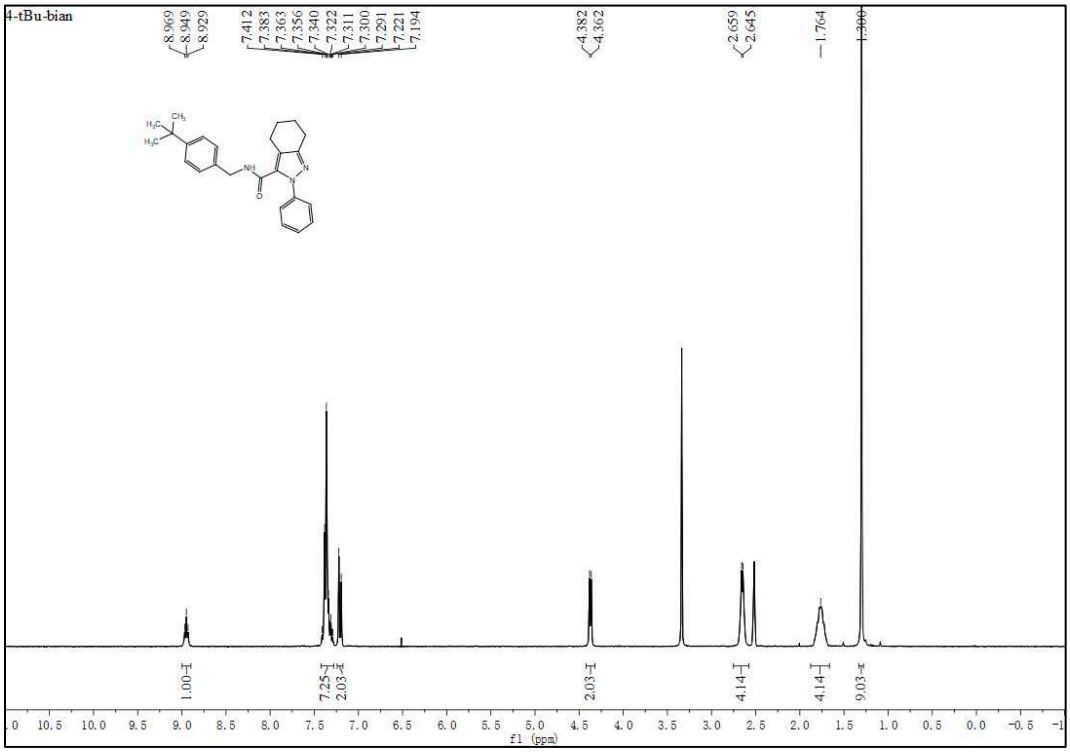
^{13}C NMR spectra of compound **6o**



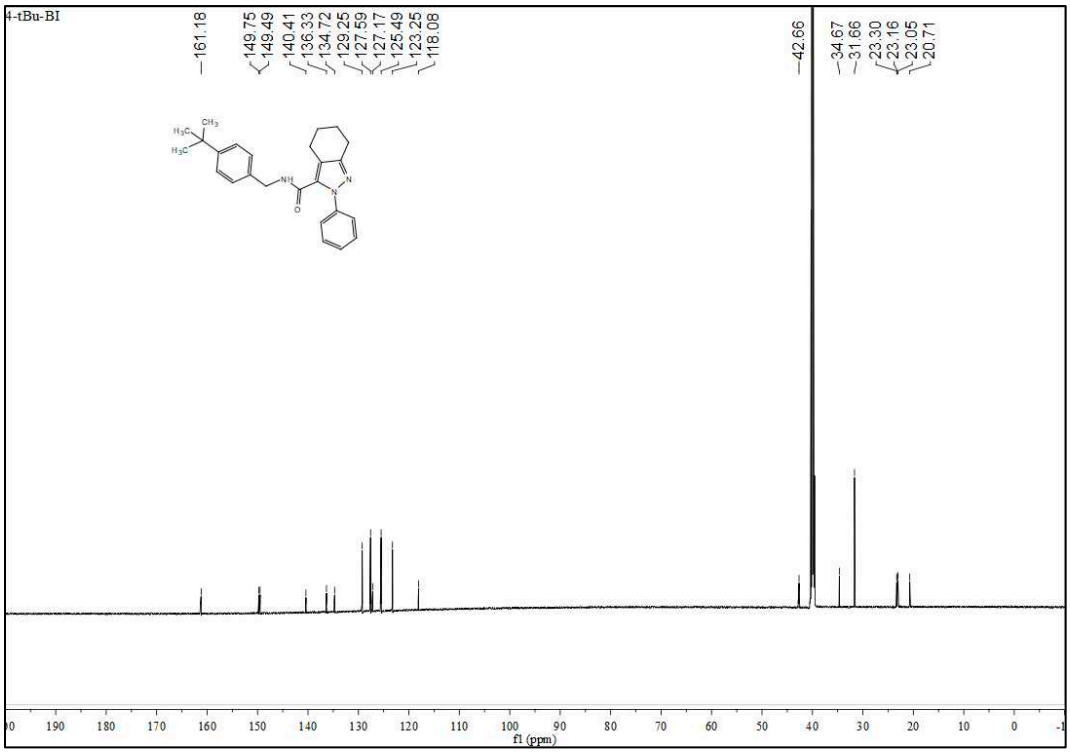
^{1}H NMR spectra of compound **6p**



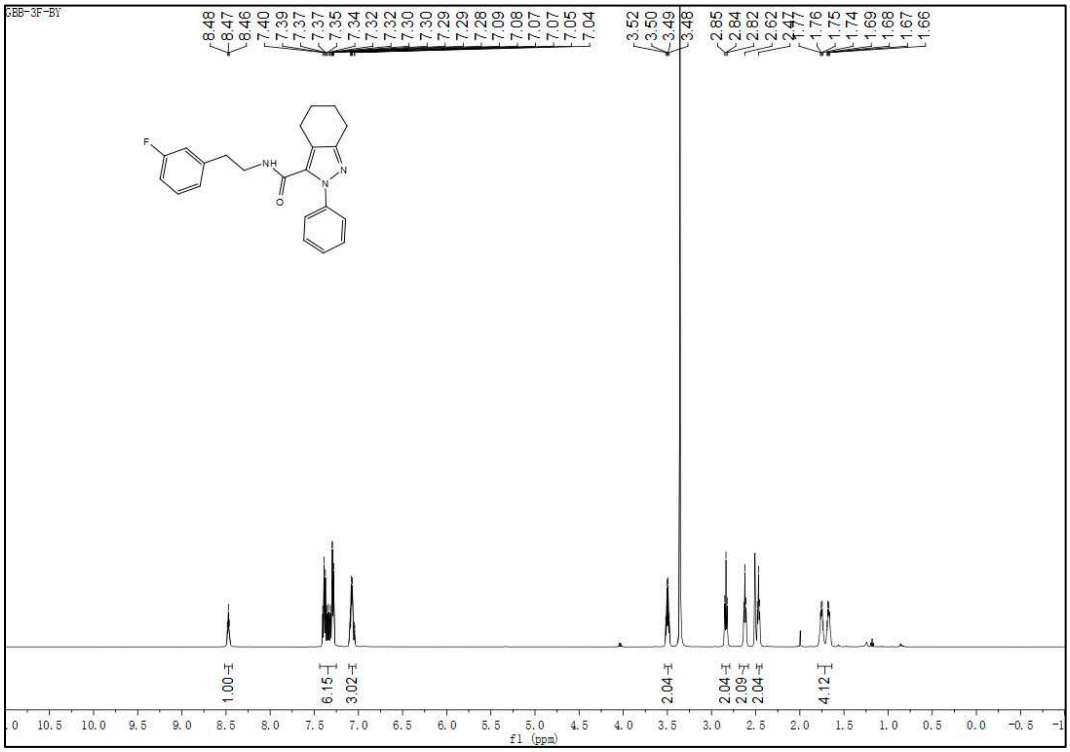
^{13}C NMR spectra of compound **6p**



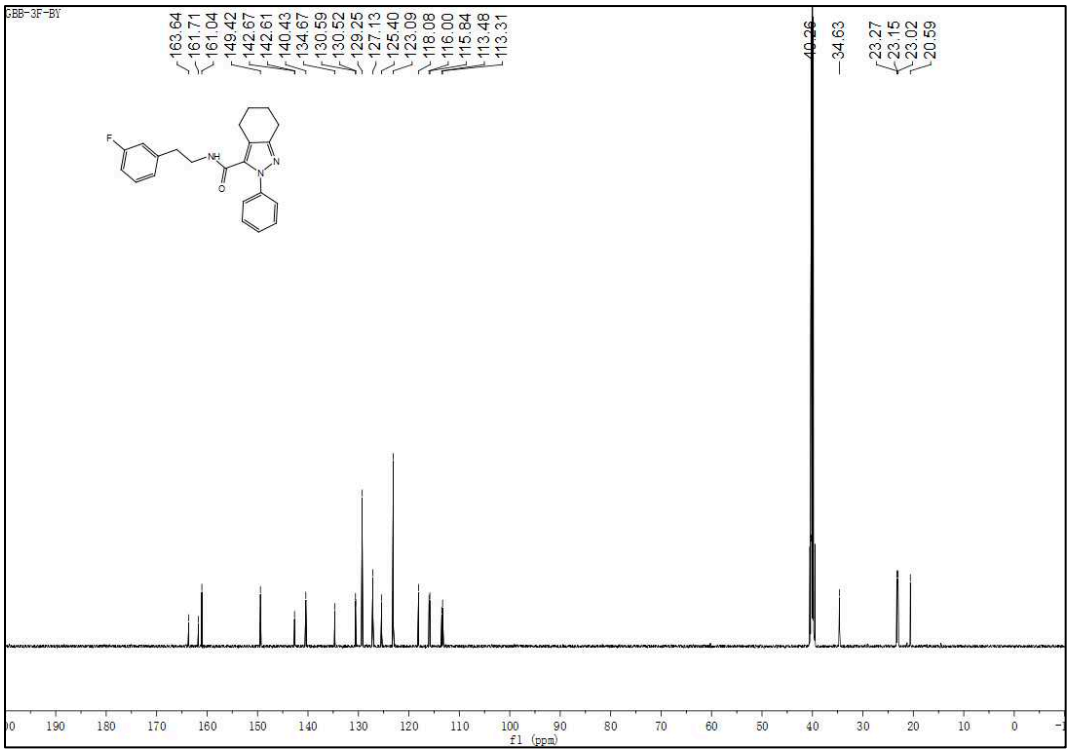
^{1}H NMR spectra of compound **6q**



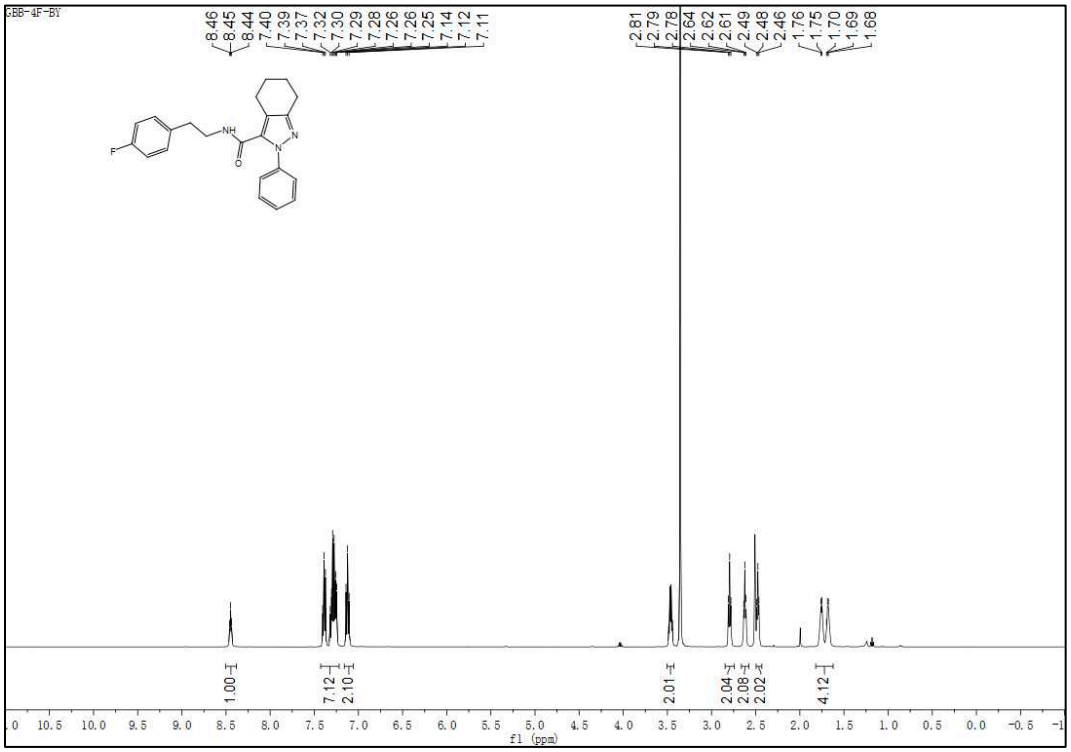
^{13}C NMR spectra of compound **6q**



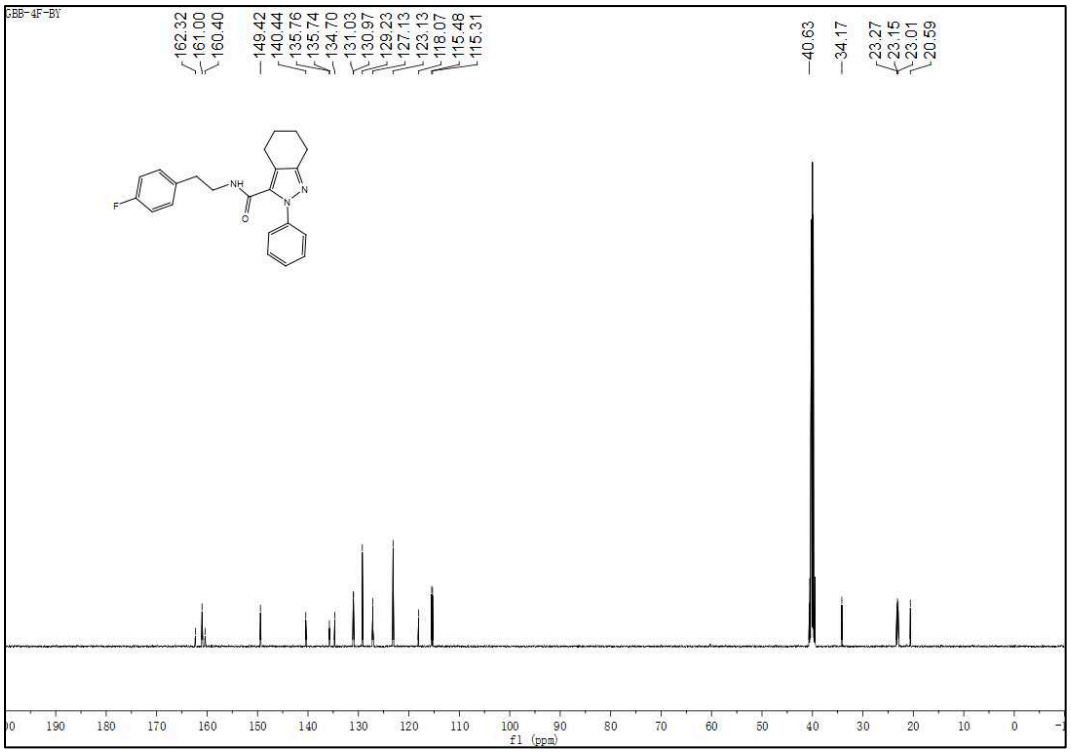
^{1}H NMR spectra of compound **6r**



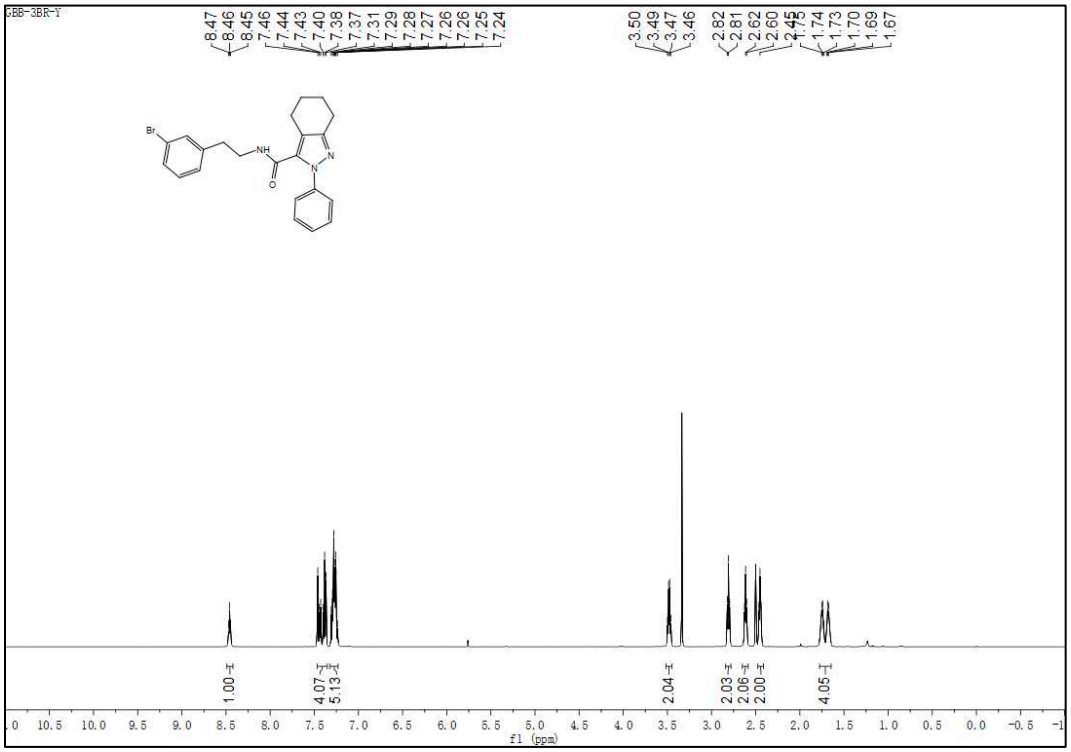
^{13}C NMR spectra of compound **6r**



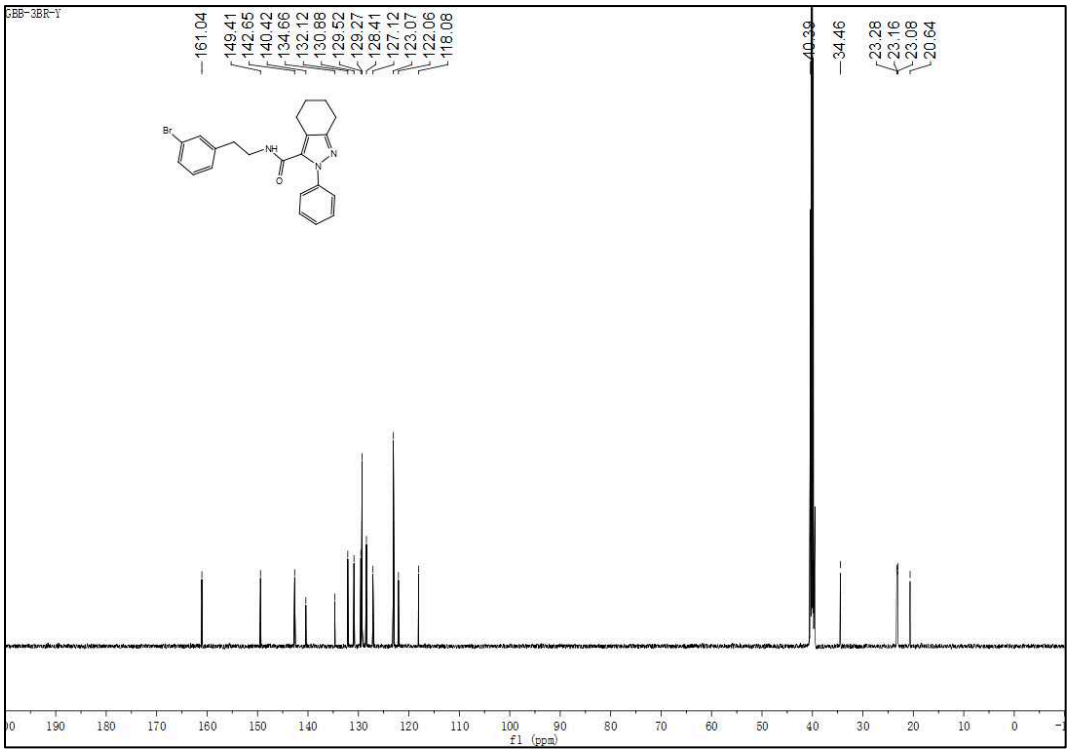
^{1}H NMR spectra of compound **6s**



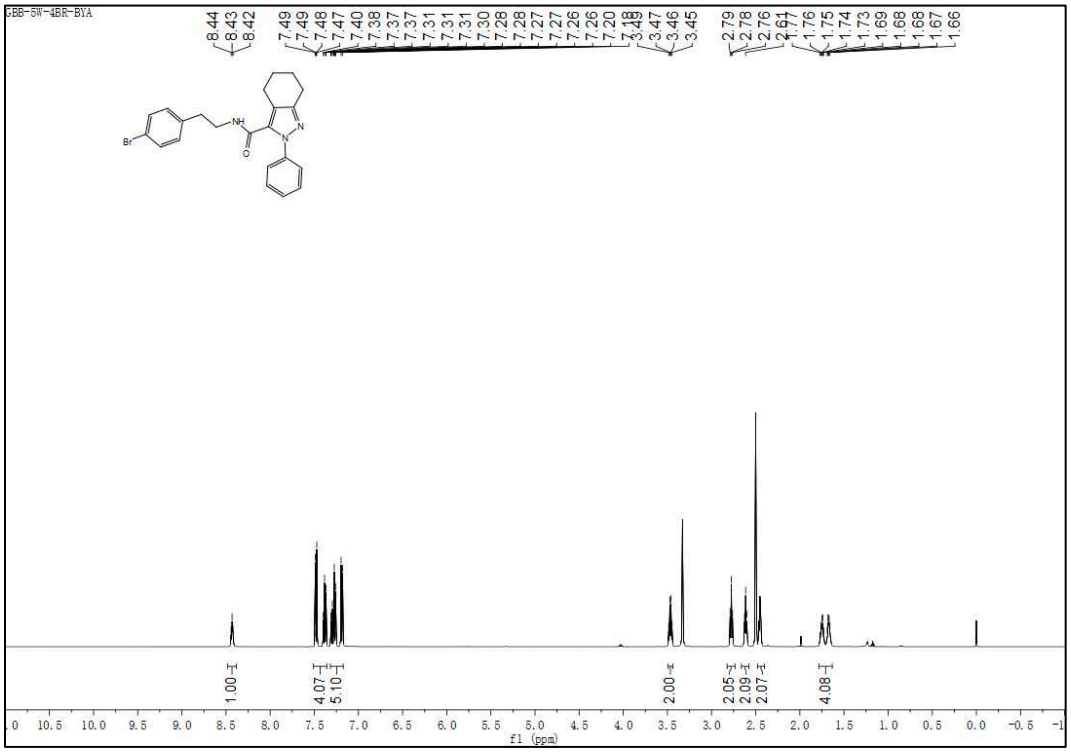
^{13}C NMR spectra of compound **6s**



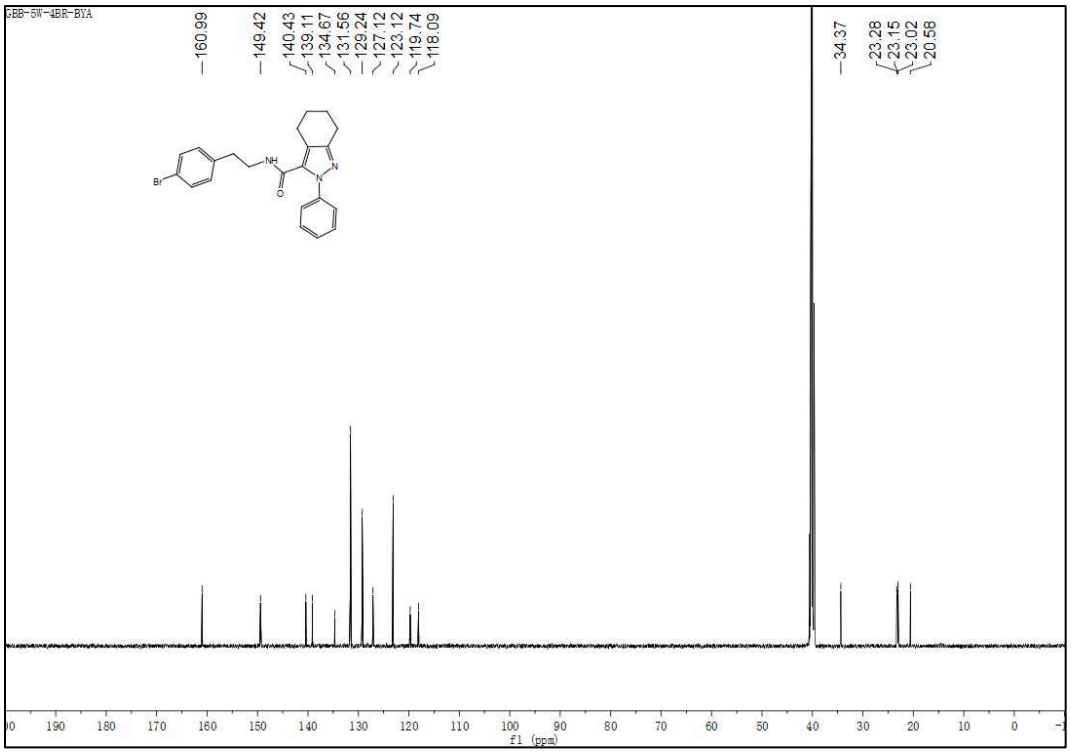
^{1}H NMR spectra of compound **6t**



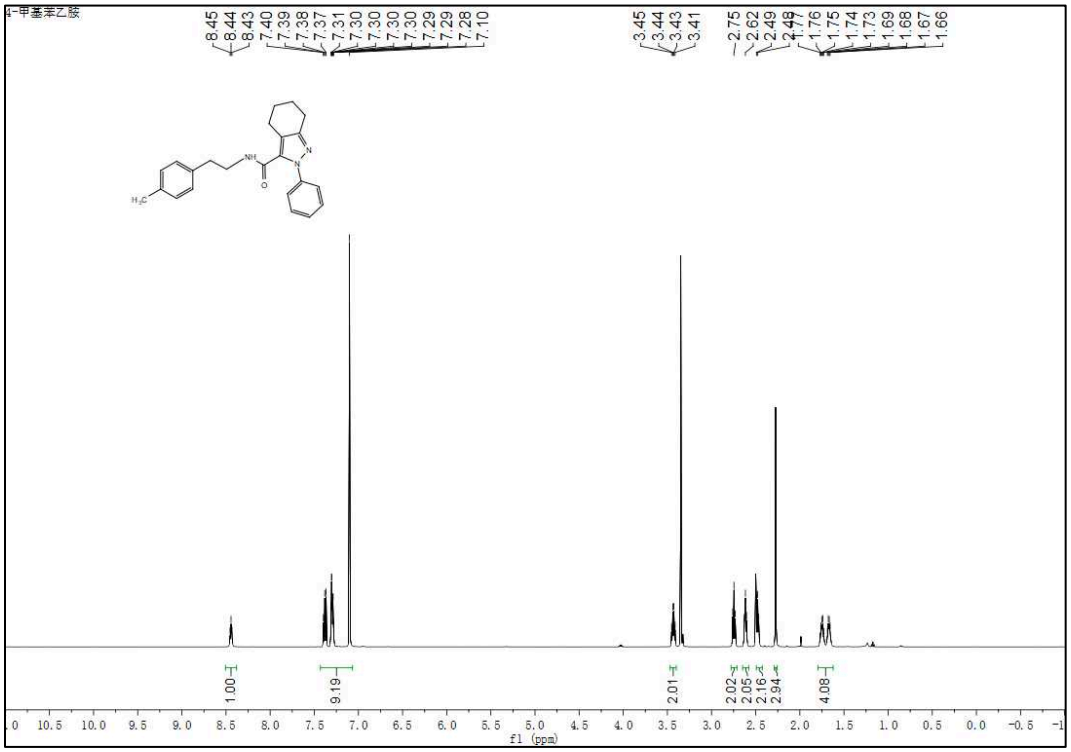
^{13}C NMR spectra of compound **6t**



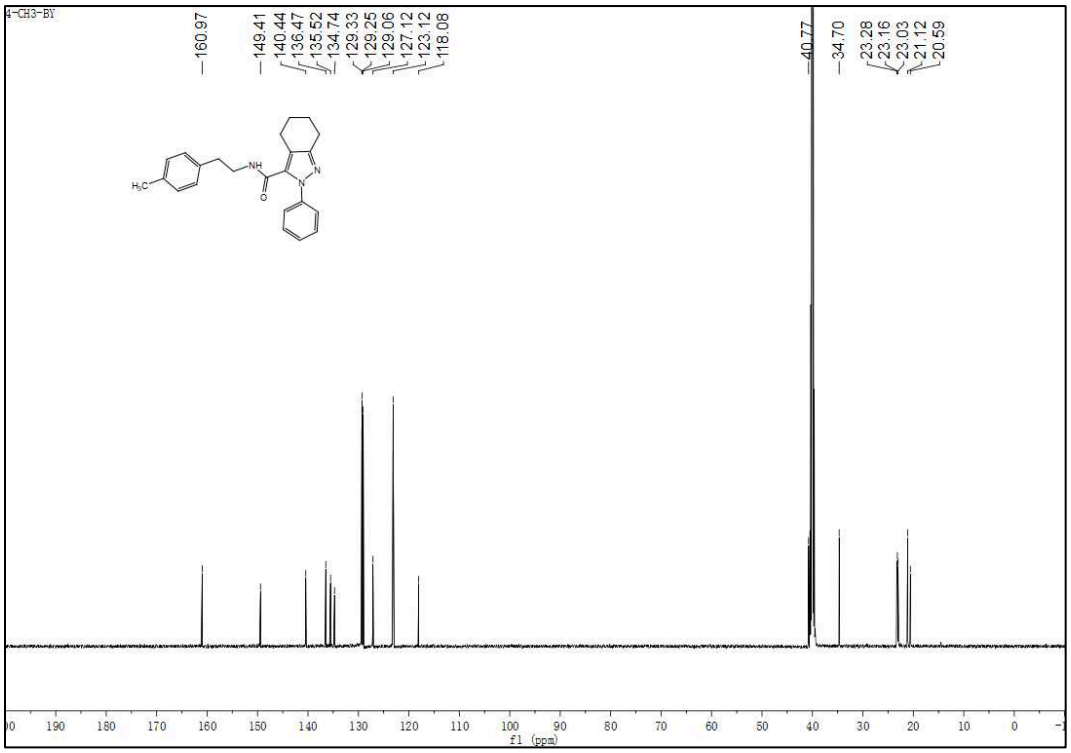
^{1}H NMR spectra of compound **6u**



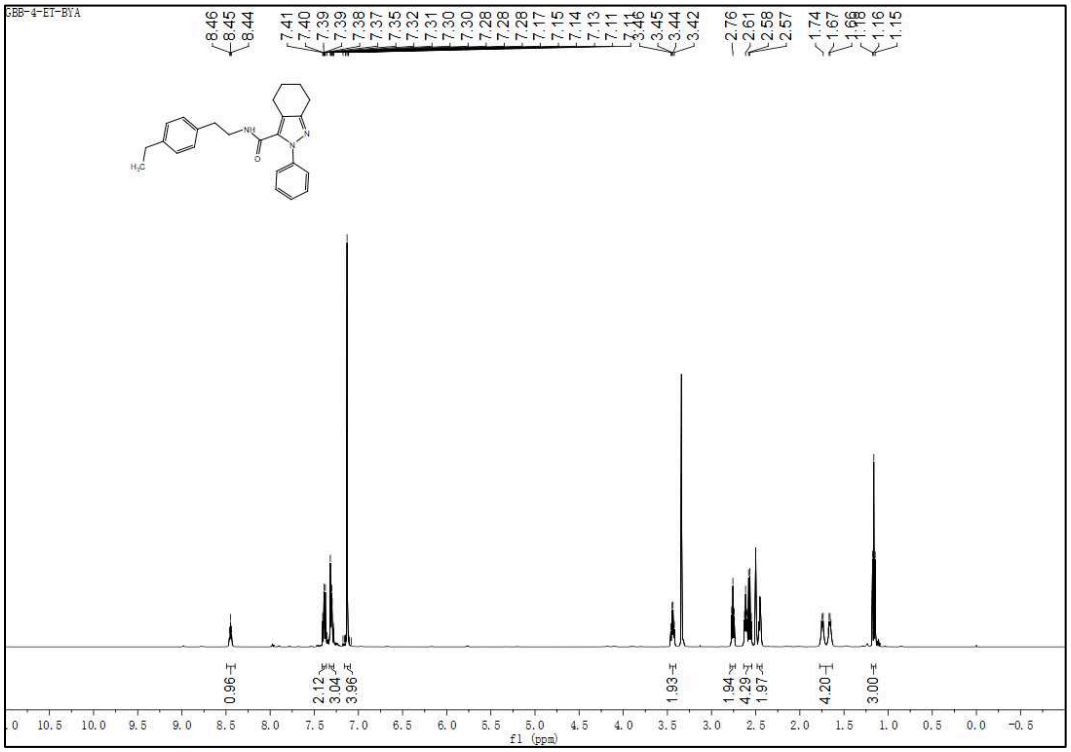
^{13}C NMR spectra of compound **6u**



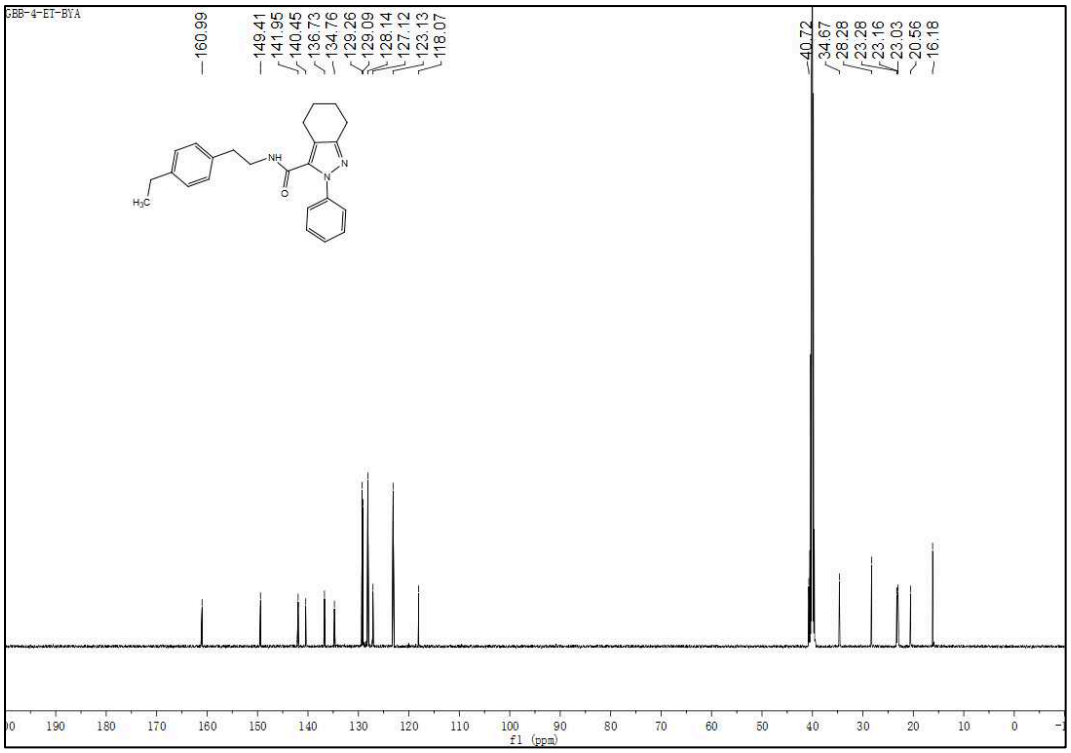
^{1}H NMR spectra of compound **6v**



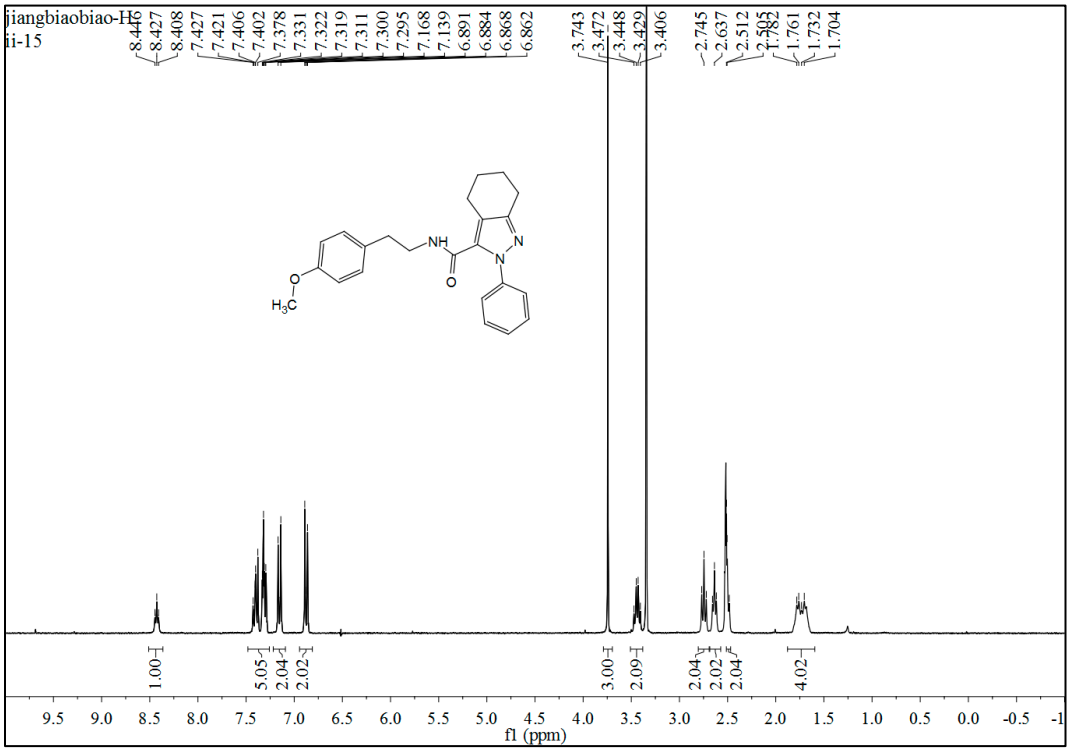
^{13}C NMR spectra of compound **6v**



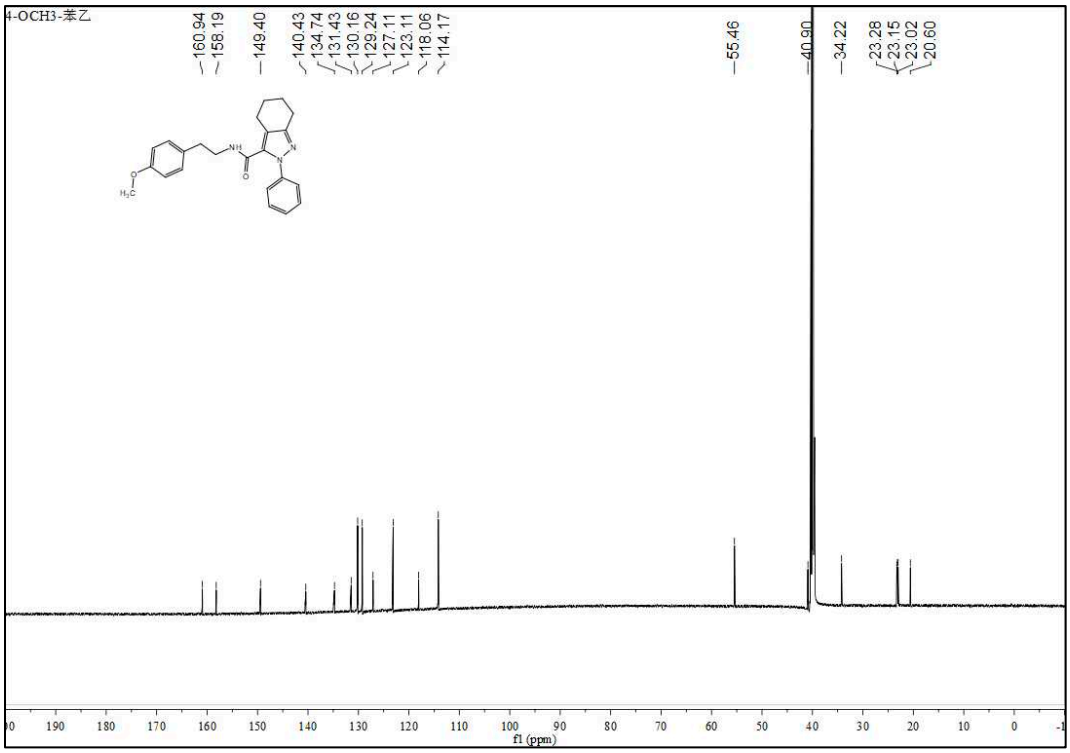
^{1}H NMR spectra of compound **6w**



^{13}C NMR spectra of compound **6w**



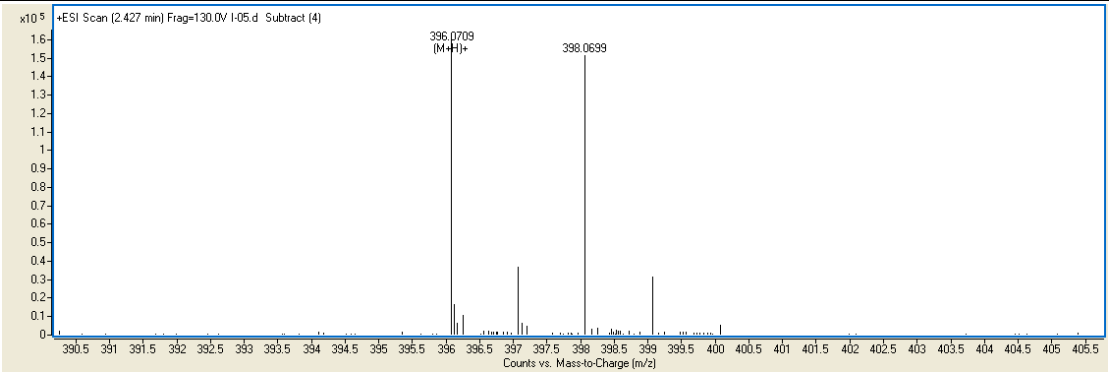
^{1}H NMR spectra of compound **6x**



^{13}C NMR spectra of compound **6x**

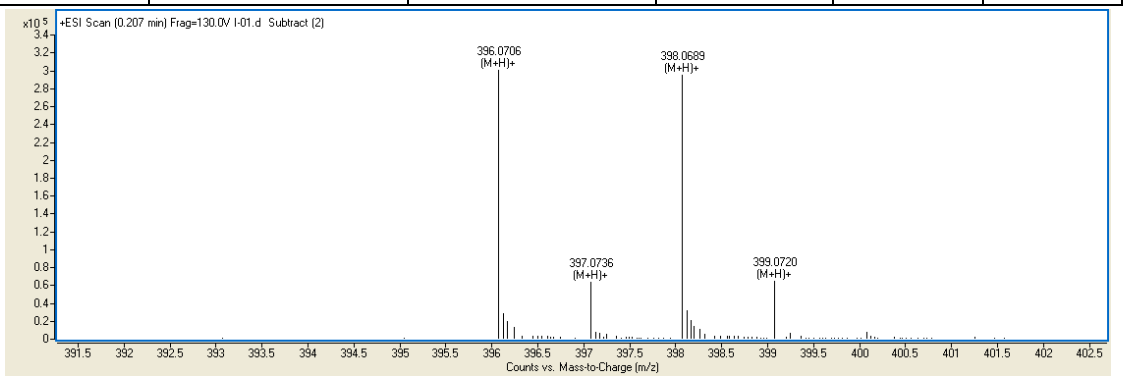
HRMS Spectrum of **6a**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6a	$C_{20}H_{18}BrN_3O$	$C_{20}H_{19}BrN_3O$	396.0709	396.0706	0.76



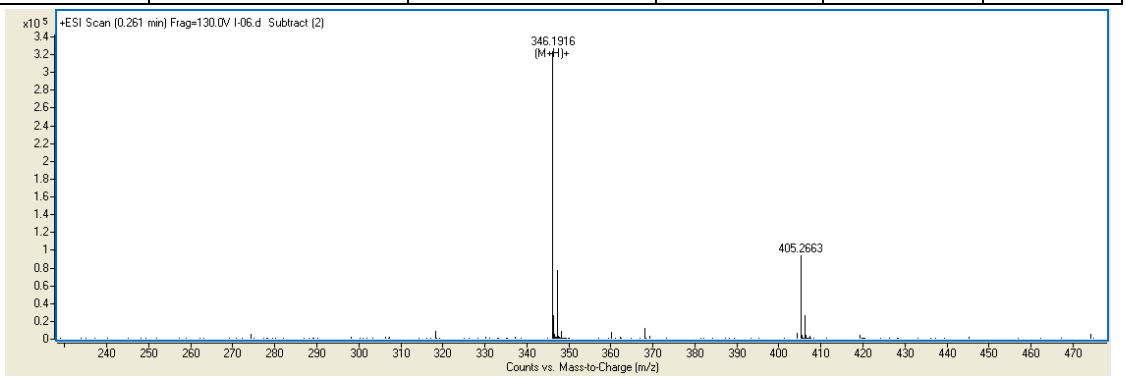
HRMS Spectrum of **6b**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6b	$C_{20}H_{19}BrN_3O$	$C_{20}H_{19}BrN_3O$	396.0706	396.0706	0



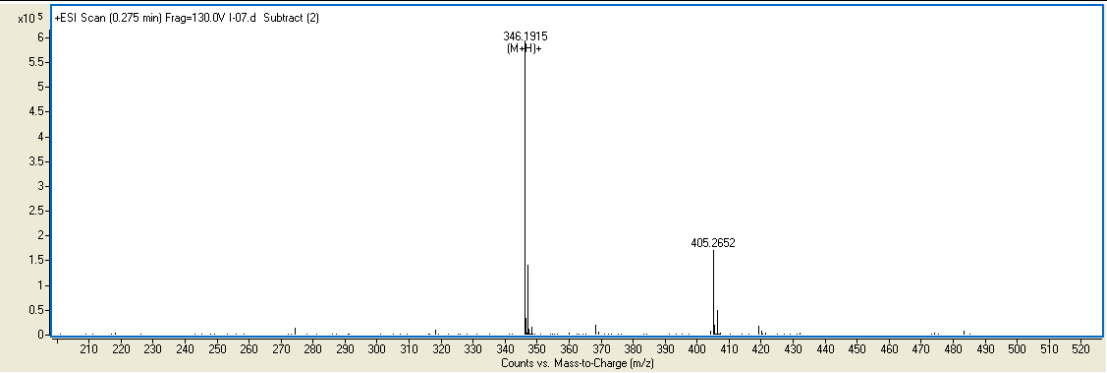
HRMS Spectrum of **6c**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6c	$C_{22}H_{23}N_3O$	$C_{22}H_{24}N_3O$	346.1916	346.1914	0.58



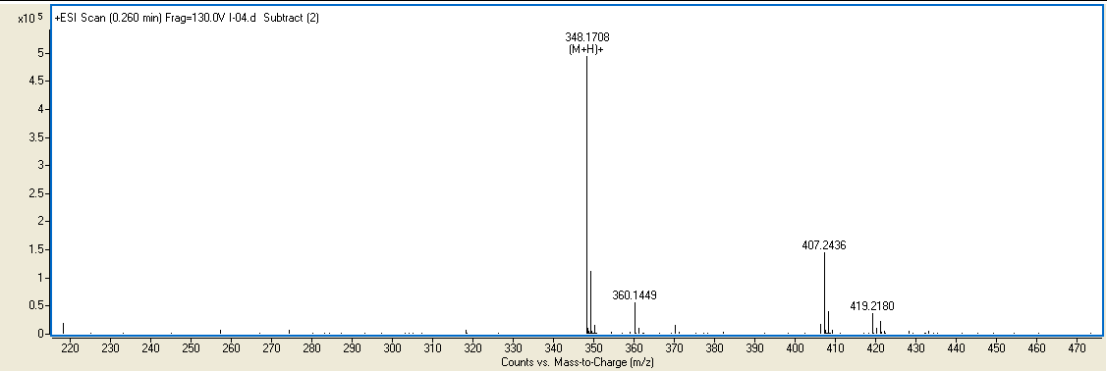
HRMS Spectrum of **6d**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6d	$C_{22}H_{23}N_3O$	$C_{22}H_{24}N_3O$	346.1915	346.1914	0.29



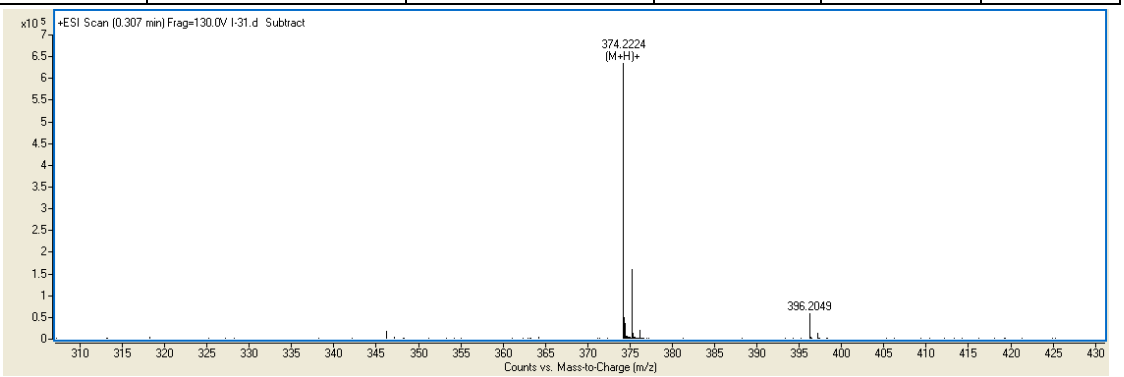
HRMS Spectrum of **6e**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6e	$C_{21}H_{21}N_3O_2$	$C_{21}H_{21}N_3O_2$	348.1708	348.1707	0.29



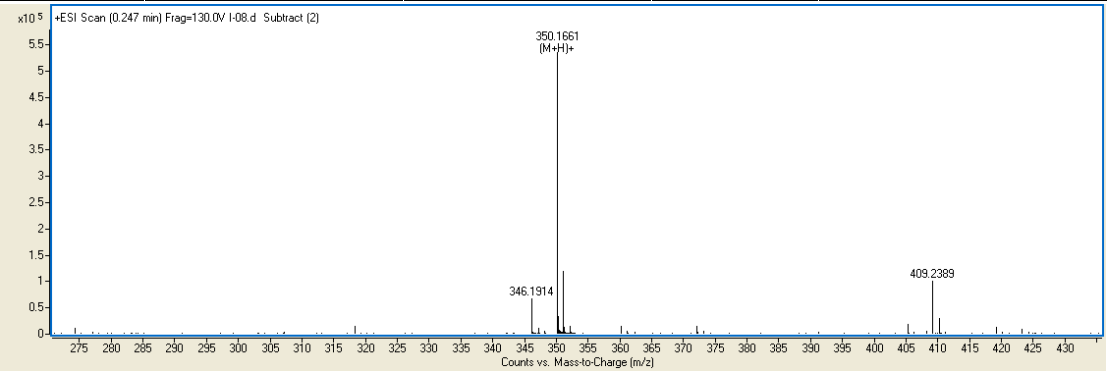
HRMS Spectrum of **6f**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6f	$C_{24}H_{27}N_3O$	$C_{24}H_{28}N_3O$	374.2224	374.2227	0.80



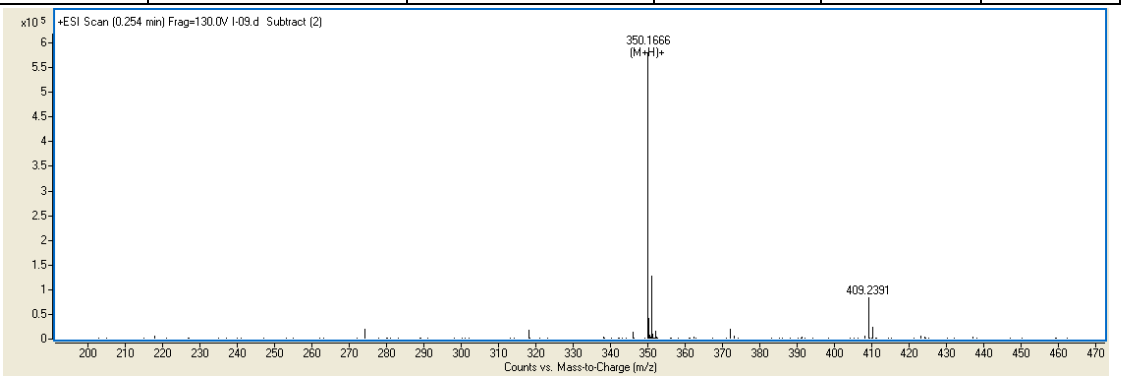
HRMS Spectrum of **6g**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6g	$C_{21}H_{20}FN_3O$	$C_{21}H_{21}FN_3O$	350.1661	350.1663	0.57



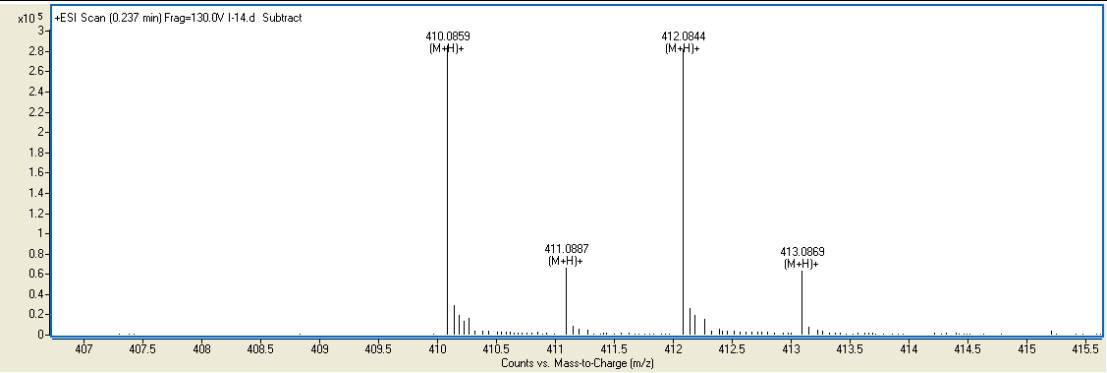
HRMS Spectrum of **6h**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6h	$C_{21}H_{20}FN_3O$	$C_{21}H_{21}FN_3O$	350.1665	350.1663	0.57



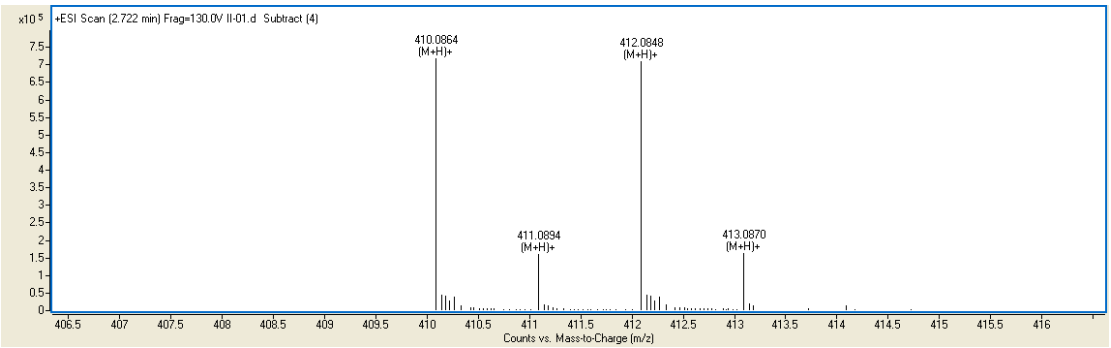
HRMS Spectrum of **6i**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6i	$C_{21}H_{20}BrN_3O$	$C_{21}H_{21}BrN_3O$	410.0859	410.0863	0.98



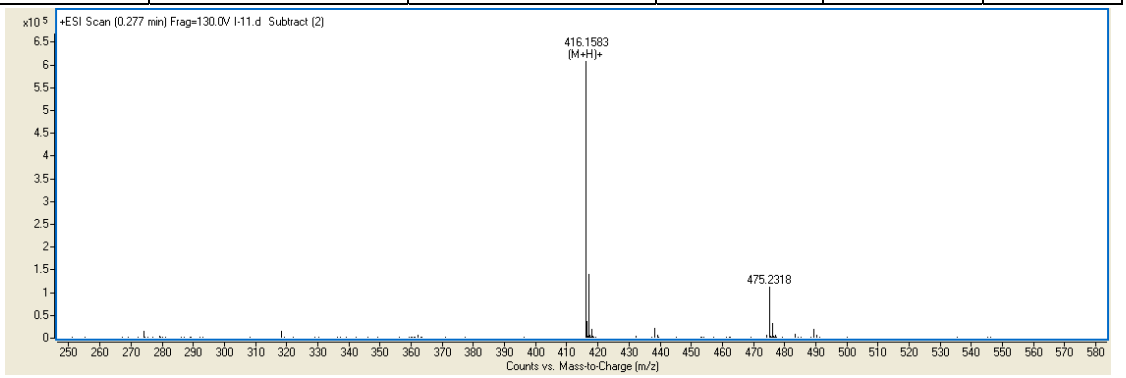
HRMS Spectrum of **6j**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6j	$C_{21}H_{20}BrN_3O$	$C_{21}H_{21}BrN_3O$	410.0864	410.0863	0.24



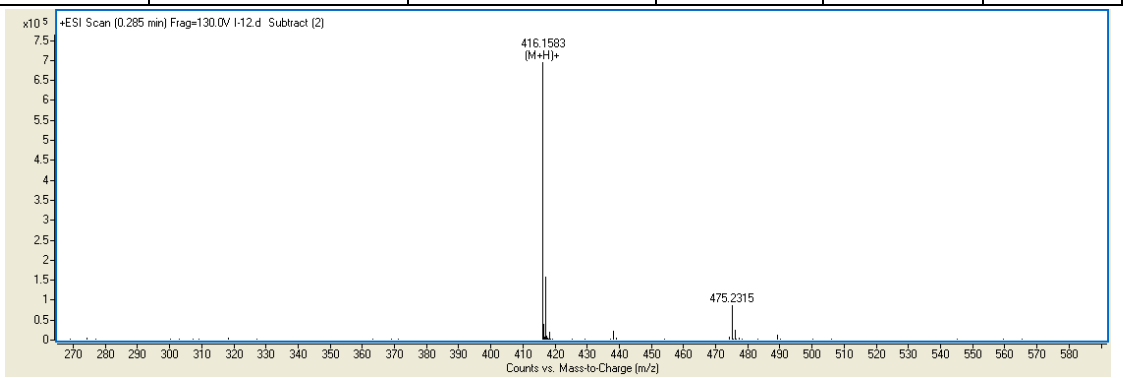
HRMS Spectrum of **6k**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6k	$C_{22}H_{20}F_3N_3O_2$	$C_{22}H_{21}F_3N_3O_2$	416.1583	416.1580	0.72



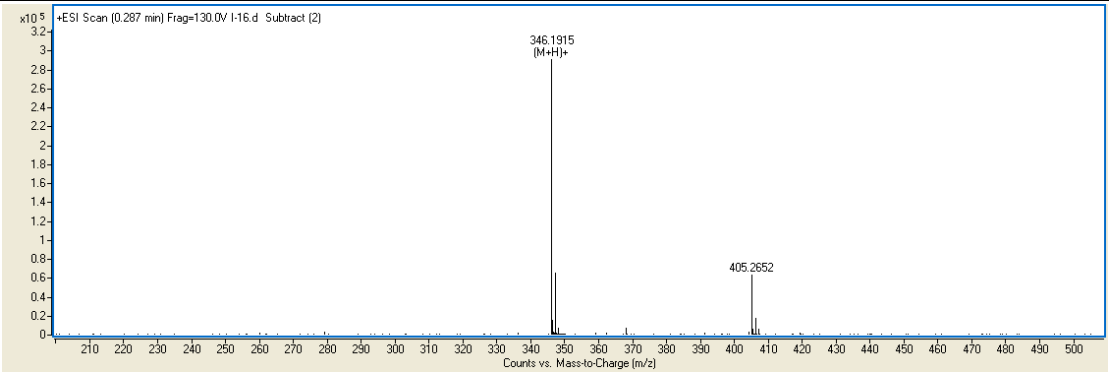
HRMS Spectrum of **6l**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6l	$C_{22}H_{20}F_3N_3O_2$	$C_{22}H_{21}F_3N_3O_2$	416.1583	416.1580	0.72



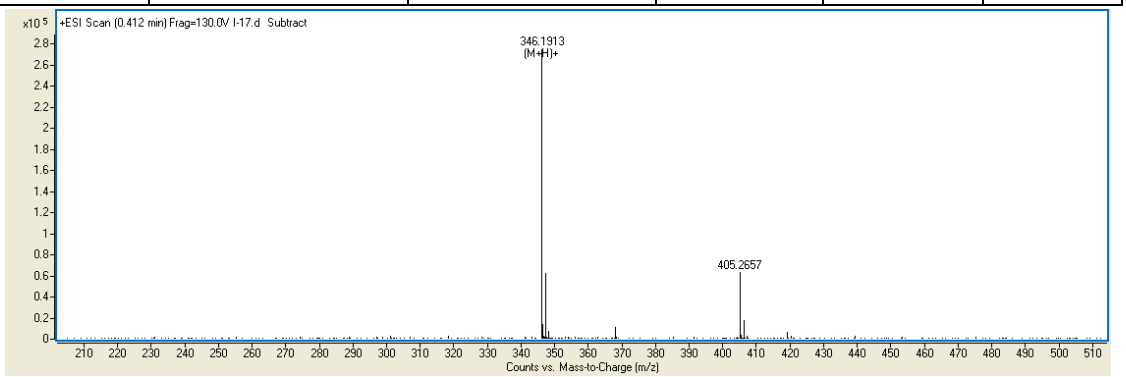
HRMS Spectrum of **6m**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6m	$C_{22}H_{23}N_3O$	$C_{22}H_{24}N_3O$	346.1915	346.1914	0.29



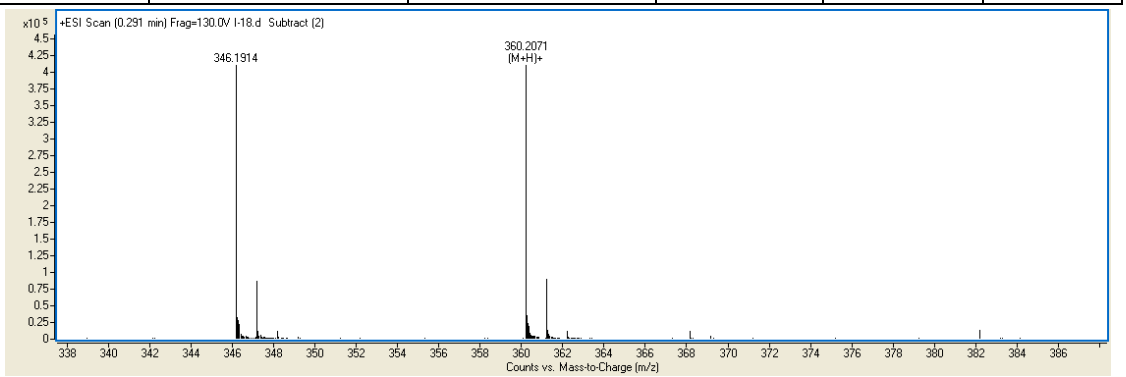
HRMS Spectrum of **6n**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6n	$C_{22}H_{23}N_3O$	$C_{22}H_{24}N_3O$	346.1913	346.1914	0.29



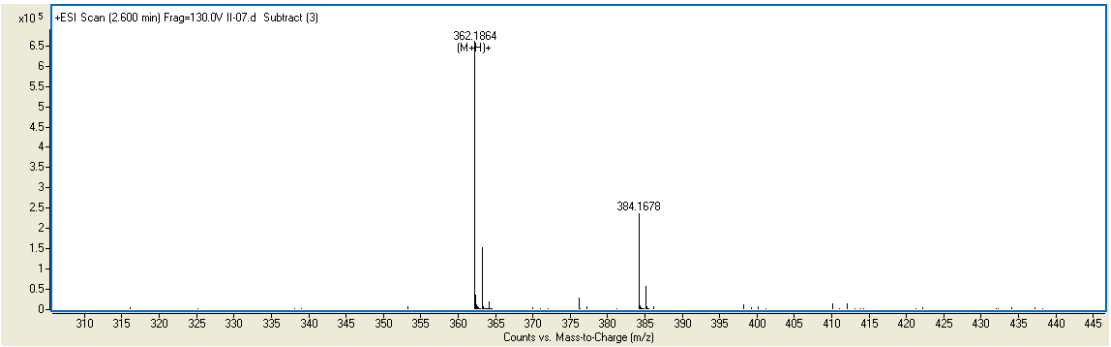
HRMS Spectrum of **6o**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6o	$C_{23}H_{25}N_3O$	$C_{23}H_{26}N_3O$	360.2071	360.2070	0.28



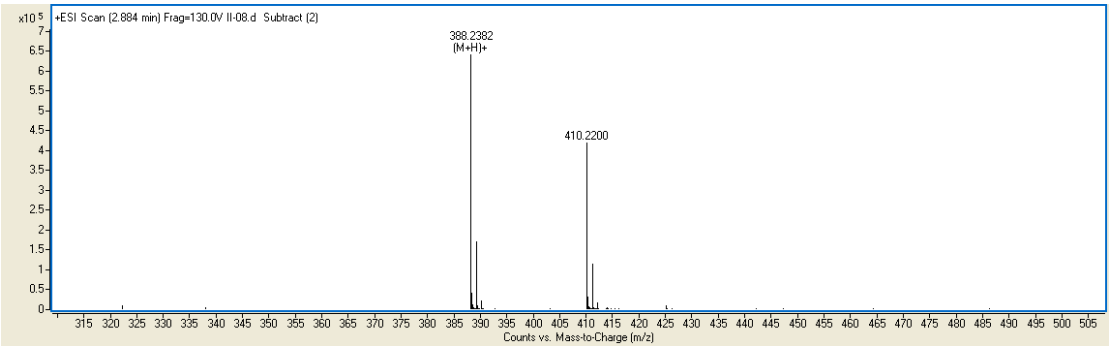
HRMS Spectrum of **6p**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6p	$C_{22}H_{23}N_3O2$	$C_{22}H_{24}N_3O2$	362.1864	362.1863	0.28



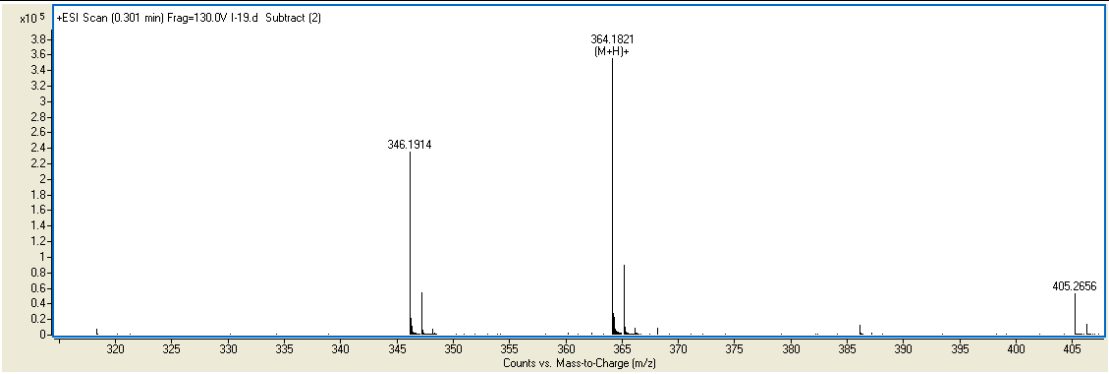
HRMS Spectrum of **6q**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6q	$C_{25}H_{29}N_3O$	$C_{25}H_{30}N_3O$	388.2382	388.2383	0.26



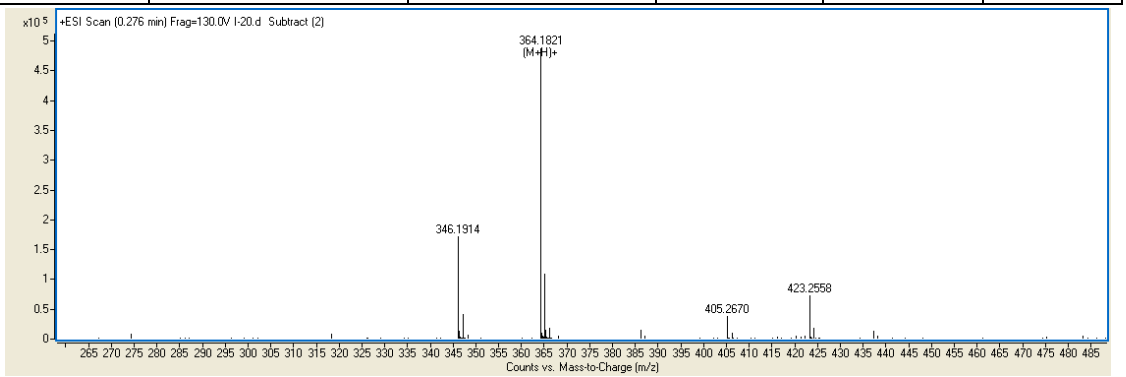
HRMS Spectrum of **6r**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6r	$C_{22}H_{22}FN_3O$	$C_{22}H_{23}FN_3O$	364.1821	364.1820	0.27



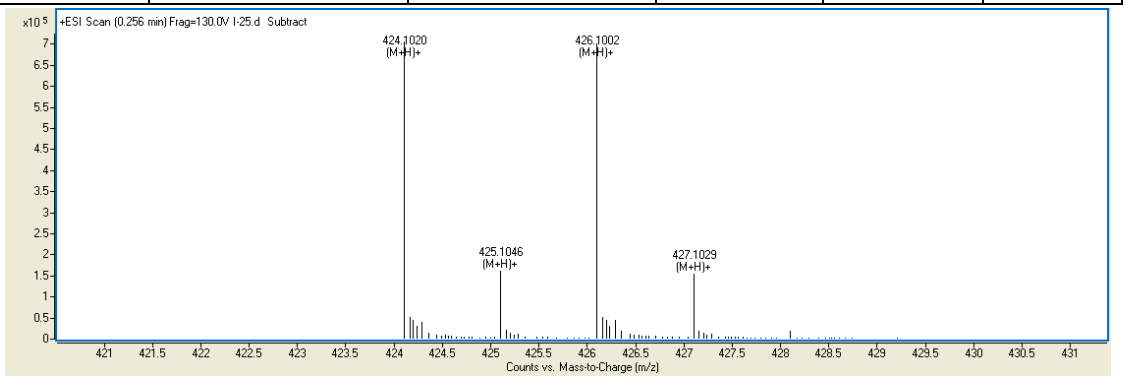
HRMS Spectrum **of 6s**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6s	$C_{22}H_{22}FN_3O$	$C_{22}H_{23}FN_3O$	364.1821	364.1820	0.27



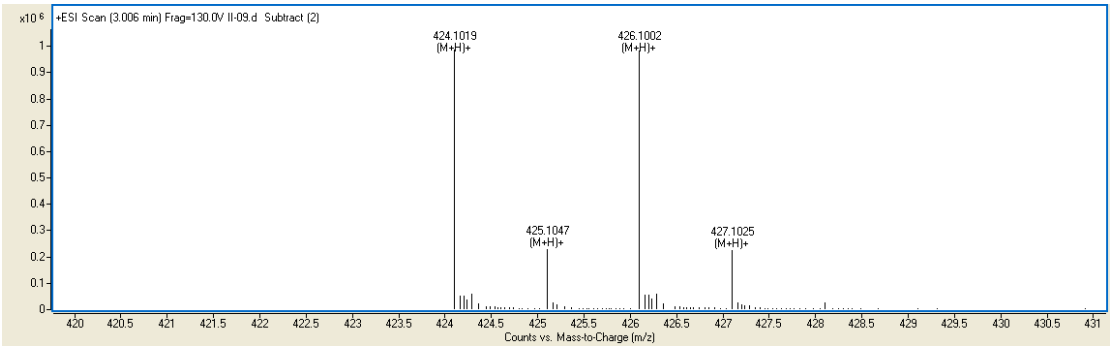
HRMS Spectrum of **6t**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6t	$C_{22}H_{22}BrN_3O$	$C_{22}H_{23}BrN_3O$	424.1020	424.1019	0.24



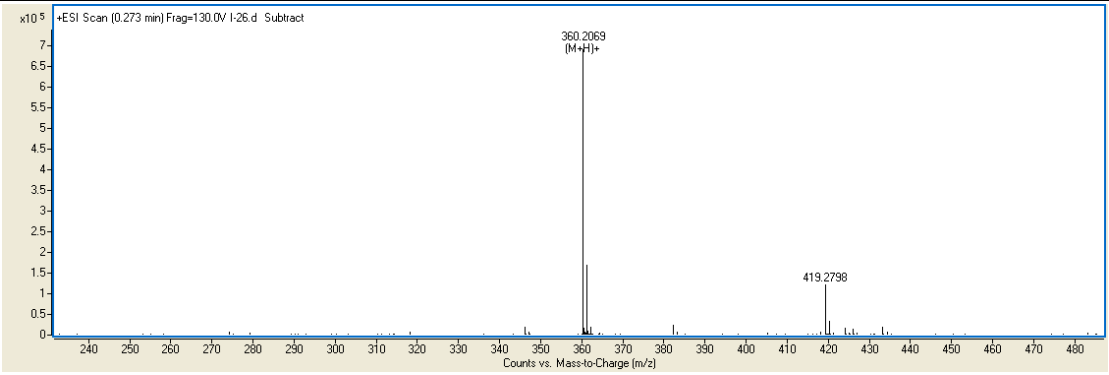
HRMS Spectrum of **6u**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6u	$C_{22}H_{22}BrN_3O$	$C_{22}H_{23}BrN_3O$	424.1019	424.1019	0



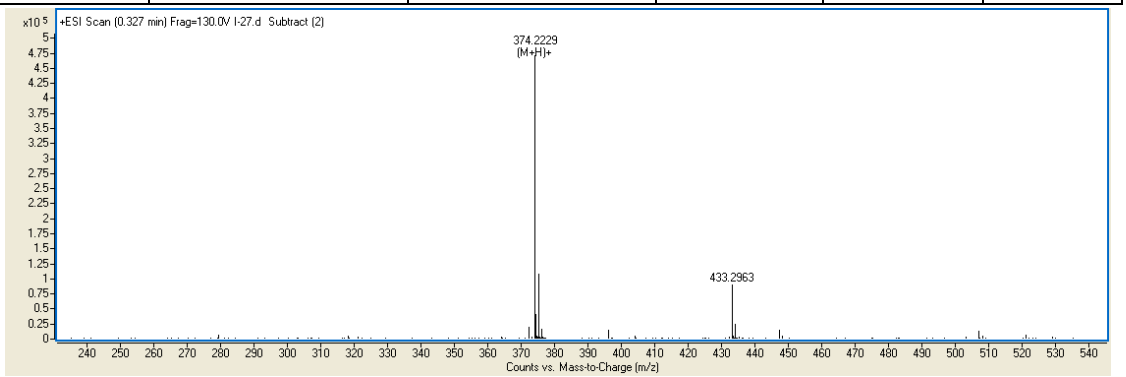
HRMS Spectrum of **6v**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6v	$C_{23}H_{25}N_3O$	$C_{23}H_{26}N_3O$	360.2069	360.2070	0.28



HRMS Spectrum of **6w**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6w	$C_{24}H_{27}N_3O$	$C_{24}H_{28}N_3O$	374.2229	374.2227	0.53



HRMS Spectrum of **6x**

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
6x	$C_{23}H_{25}N_3O_2$	$C_{23}H_{25}N_3\ NaO_2$	398.1840	398.1839	0.25