Supporting Information for:

Copper-Catalyzed Radical Cascades of *para*-Quinone Methides with AIBN and H_2O via *α*-Cyanoalkylation by C–C Bond Cleavage: New Access to Benzofuran-2(3*H*)-ones

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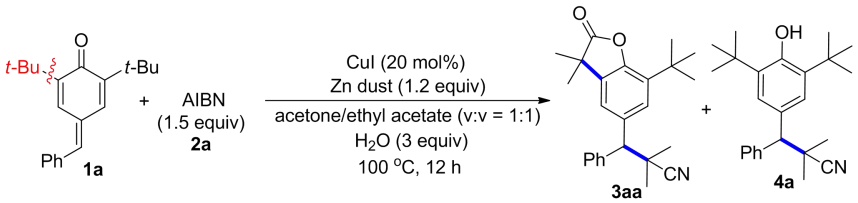
1. General

All manipulations of oxygen- and moisture-sensitive materials were conducted with a Schlenk technique under a nitrogen or argon atmosphere. Solvent were purified and

dried in a standard manner. Flash column chromatography was performed using EM Silica gel 60 (200-400 mesh). Visualization was accomplished with UV light (254 nm) and/or an aqueous alkaline $KMnO_4$ solution followed by heating. ^1H NMR, ^{13}C NMR spectra were recorded on 400 MHz NMR spectrometer with trimethylsilane resonance as the internal standard. Unless otherwise noted, reagents were commercially available and were used without further purification. Preparation of para-Quinone methides **1** were prepared according to literature procedures.[1]

2. Optimization of Reaction Conditions

Table S1 Screening of optimal conditions[a,b]



Entry	Change from the standard conditions	yield (%)[b]	
		3aa	**4a**
1	***none***	***75***	*10*
2	without CuI	13	<5
3	CuBr instead of CuI	52	17
4	CuCl instead of CuCl	63	15
5	$Cu(CH_3CN)_4PF_6$ instead of CuI	66	14
6	[*i*-Pr]CuCl instead of CuI	55	12
7	$Cu(OAc)_2.H_2O$ instead of CuI	59	14
8	Cu instead of CuI	63	13
9	$Fe(NH_4)_2(SO_4)_2.7H_2O$ instead of CuI	17	16
10	$FeCl_2.4H_2O$ instead of CuI	13	14
11	ferrocene instead of CuI	11	18
12	pure acetone as solvent	61	16
13	acetone/ethyl acetate (*v:v* = 1:2) as solvent	72	12
14	Acetone/ethyl acetate (*v:v* = 2:1) as solvent	73	13
15	pure ethyl acetate as solvent	66	11
16	*n*-hexane as solvent	57	15
17	1,4-dioxane as solvent	47	19

Continued (Table S1)

18	CH_3CN as solvent	46	16
19	H_2O as solvent	38	20
20	using 1.0 equiv of AIBN	47	8
21	using 2.0 equiv of AIBN	73	12
22	using 10 mol% CuI	64	10
23	using 30 mol% CuI	74	12
24	using 2.0 equiv. of H_2O	45	11
25	using 4.0 equiv. of H_2O	68	15
26	without Zn	45	12
27	using 2.0 equiv. of Zn dust	71	15
28	at 80 °C	50	13
29	at 120 °C	77	11
30	under O_2	35	<5

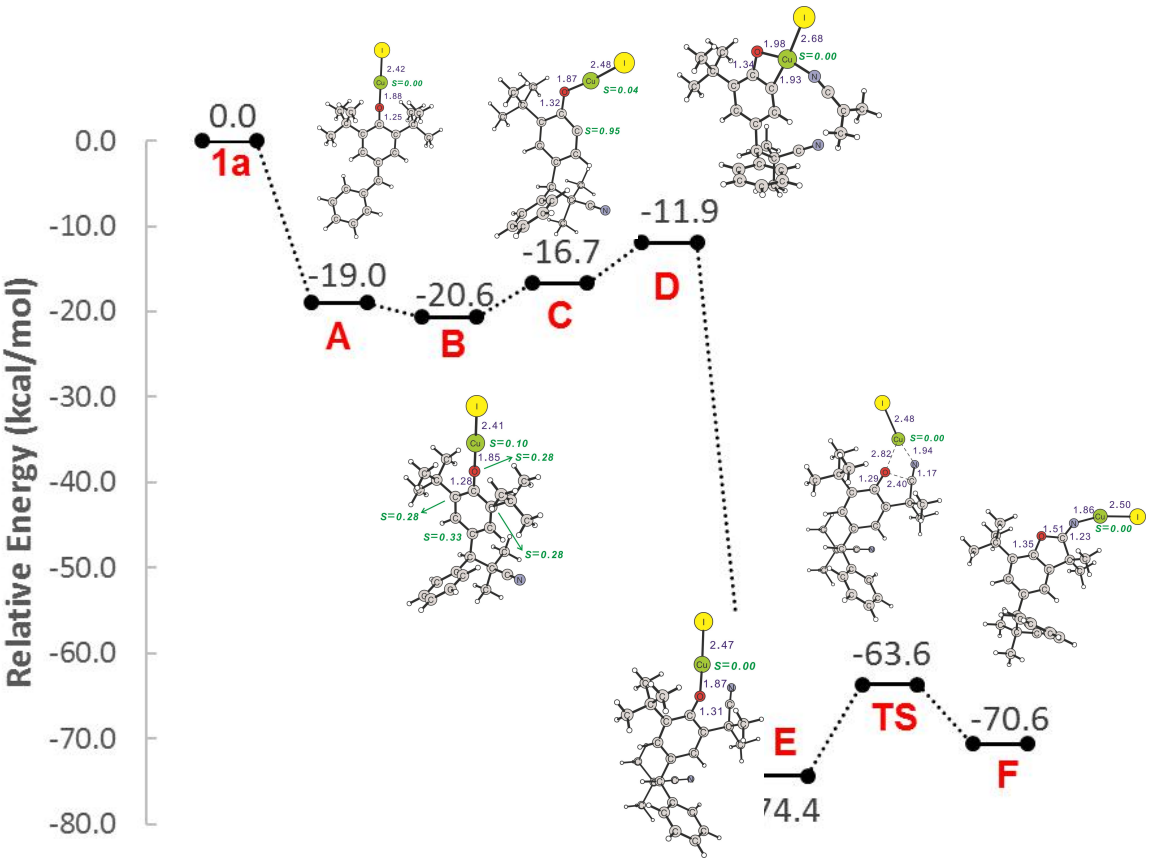
[a] Standard reaction conditions: **1a** (0.3 mmol), AIBN (1.5 equiv.), CuI (20 mol %), Zn dust (1.2 equiv.), H_2O (3 equiv.) and ethyl acetate/acetone (*v: v* = 1:1, 2 mL) under N_2 at 100 °C for 12 h. [*i*-Pr]CuCl = Chloro(1,3-dimesitylimidazol-2-ylidene)copper(I). [b] Yield of the isolated product.

3. Calculations

General: All calculations presented in this paper were performed using unrestricted density functional theory (DFT) with the hybrid functional B3LYP[2–4] as implemented in Gaussian 09 package.[5] Geometry optimizations were carried out with the effective core Stuttgart/Dresden basis set (SDD) for Cu and I,[6-10] and the 6-31G(d,p) basis set for other elements. On the basis of the optimized geometries, more accurate energies were obtained by performing single-point calculations with SDD for Cu and I and a larger 6-311+G (2d,2p) basis set for other elements. Using an empirical formula by Grimme et al,[11-14] dispersion effects were taken into account throughout geometry optimizations and single-point calculations. Solvation effects were also considered by performing single-point calculations at the same theory level as optimizations, using a

conductor-like polarizable continuum model (CPCM)[15-18] method with acetone as the solvent. Frequency calculations were performed at the same level of theory as in the optimizations to further confirm the nature of stationary points and to obtain zero-point energies (ZPE) and entropy effects. The energies reported in this paper are the free energies which have been corrected for dispersion, solvation, ZPE, and entropy effects.

Results and Discussion: A reaction mechanism has been proposed by our density functional calculations, as shown in Scheme S1. The optimized stationary points are given in Figure S1. The oxygen of **1a** can coordinate to a CuI leading to a copper complex A with a quite large exothermicity of 19.0 kcal/mol. Although the ground state of **A** is found to be in the singlet state without any unpaired spin at the complex, it is easy for **A** to react with an isobutyronitrile radical to form **B**. With the assistance of H_2O/Zn, one of *t*-Bu substituent of intermediate **B** can be abstracted as a cation by a hydroxide resulting in a radical species (C) with a slight endothermicity of 3.9 kcal/mol.. Next, with a slight energy cost of 4.8 kcal/mol, another isobutyronitrile radical coordinates to Cu in complex **C** forming a tetra-coordinated copper complex **D** in the singlet state, which is quickly converted to specie **E** *via* a C-C bond formation with a significant exothermicity of 62.5 kcal/mol. Overcoming a barrier of 16.4 kcal/mol, E is transformed to a five-member-ring complex (**F**) through a transition state of C-O bond formation (**TS**).



Scheme S1. Potential energy profile for the reaction mechanism

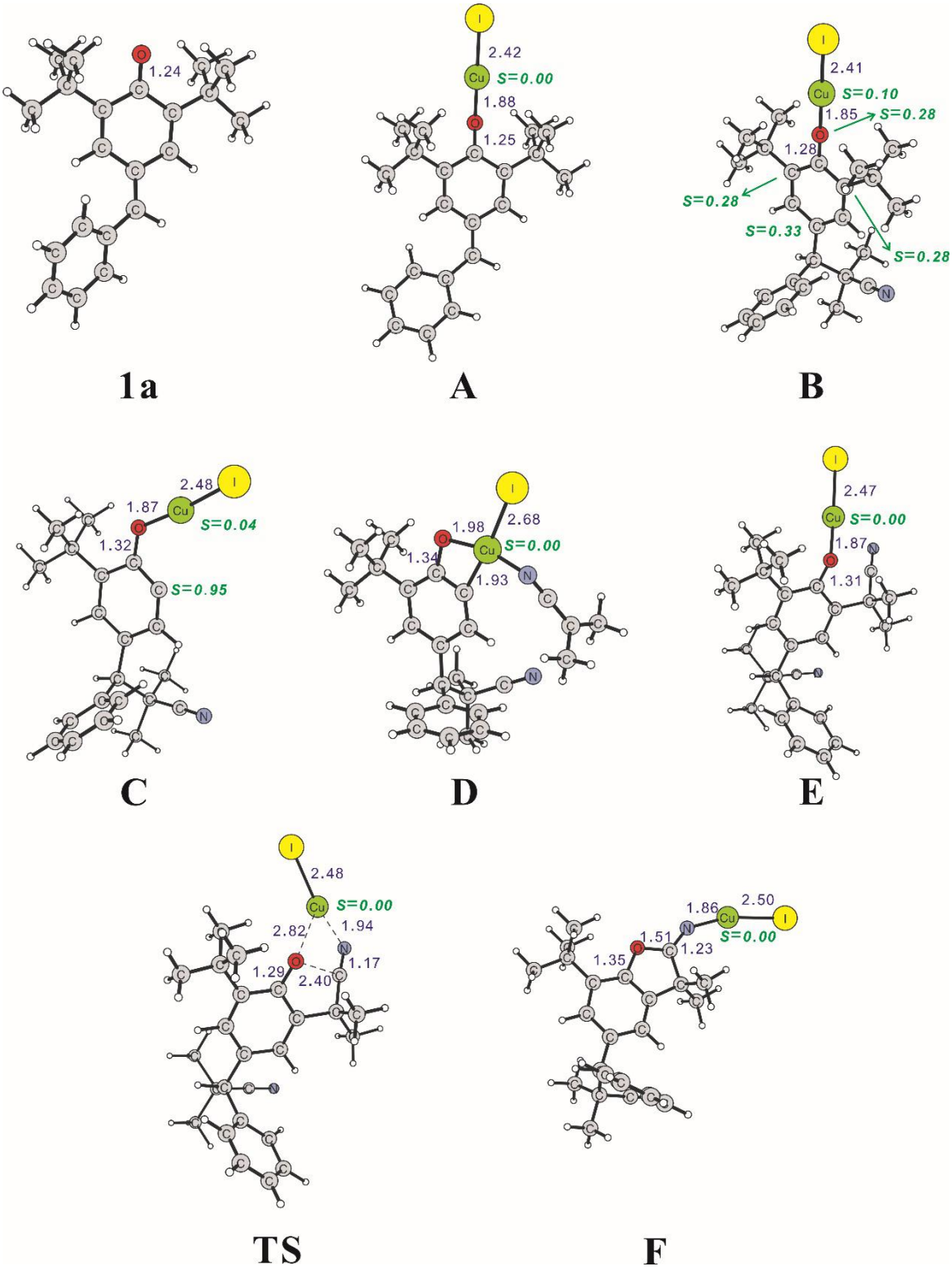
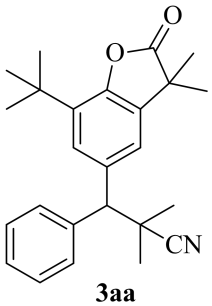


Figure S1. Optimized structures of transition states in the proposed mechanism. All distances are in angstrom (Å). The unpaired spin populations are indicated by "S".

4. Typical Experimental Procedures

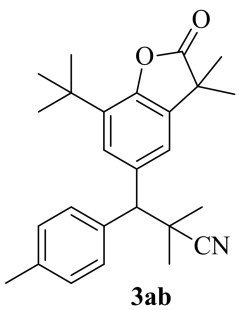
General procedure for the synthesis of benzofuran-2(3H)-ones. To a mixture of p *para*-quinone methides **1** (0.3 mmol), CuI (20 mol%), Zn dust (1.2 equv.), azo

compound **2** (1.5 equiv.) was added acetone/ethyl acetate(*v:v* = 1:1, 2 mL), and then H_2O (3 equiv.). The resulting solution was stirred at 100 °C under N_2 atmosphere (1 atm.) for 12 h. The solvent was evaporated under reduced pressure and the resulted mixture was filtered through a Florisil pad, diluted with Et_2O, and washed with water and then brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by flash chromatography on silica gel (eluent: n-hexane/ethyl acetate) to afford the corresponding *benzofuran-2(3H)-ones* (**3aa-3bh**) in a yield listed in **Table 2** and **3**.



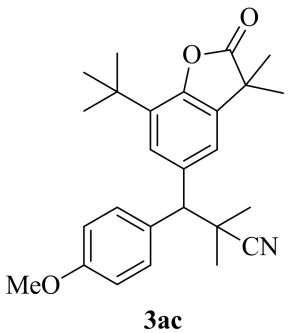
3aa

3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl) -2,2-dimethyl-3-phenylpropanenitrile (**3aa**). White solid (84.5 mg, 75%), m.p. 149.3-150.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 7.2 Hz, 2H), 7.43 (s, 1H), 7.40 – 7.36 (m, 2H), 7.32 – 7.30 (m, 2H), 3.64 (s, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.42 (s, 9H), 1.39 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.1, 149.2, 140.3, 136.2, 134.5, 134.3, 128.9, 128.6, 127.4, 126.5, 124.8, 120.3, 61.3, 42.4, 36.4, 34.4, 29.6, 27.8, 27.5, 25.4, 25.4; IR(KBr): 2026, 1801, 1578, 1436, 1067 cm^{-1}; UV: λ_{max} = 274; HRMS m/z (ESI) calcd for $C_{25}H_{30}NO_2$ $[M+H]^+$ 376.2271, found: 376.2274.



3ab

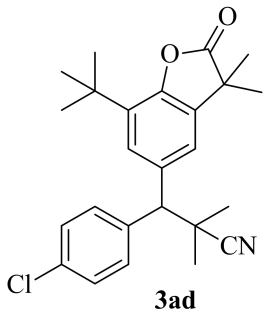
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5 -yl)-2,2-dimethyl-3-(p-tolyl)propanenitrile (**3ab**). White solid (93.5 mg, 80%), m.p. 134.1-135.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 1.6 Hz, 1H), 7.30 (d, *J* = 2.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 3.61 (s, 1H), 2.35 (s, 3H), 1.52 (s, 3H), 1.50 (s, 3H), 1.42 (s, 9H), 1.38 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.2, 149.2, 137.3, 137.1, 136.5, 134.4, 134.2, 129.6, 128.5, 126.5, 124.9, 120.3, 60.9, 42.4, 36.5, 34.4, 29.63, 27.82, 27.5, 25.4, 25.4, 21.0; IR(KBr): 2026, 1806, 1579, 1423, 1054 cm^{-1}; UV: λ_{max} = 273; HRMS *m/z* (ESI) calcd for $C_{26}H_{32}NO_2$ $[M+H]^+$ 390.2428, found: 390.2426.



3ac

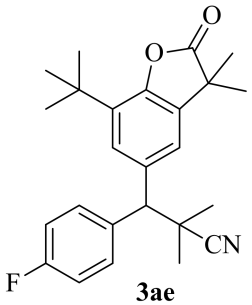
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofura

n-5-yl)-3-(4-methoxyphenyl)-2,2-dimethylpropanenitrile (**3ac**). Yellow solid (76.6 mg, 63%), m.p. 149.5-150.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 1.6 Hz, 1H), 7.28 (d, *J* = 2.0 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 3.60 (s, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.42 (s, 9H), 1.38 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.1, 158.8, 149.1, 136.6, 134.4, 134.3, 132.4, 129.7, 126.4, 124.9, 120.2, 114.2, 60.5, 55.3, 42.4, 36.6, 34.4, 29.6, 27.8, 27.5, 25.4, 25.4; IR(KBr): 2026, 1805, 1579, 1426, 1067 cm^{-1}; UV: λ_{max} = 273; HRMS *m/z* (ESI) calcd for $C_{26}H_{32}NO_3$ $[M+H]^+$ 406.2377, found: 406.2381.



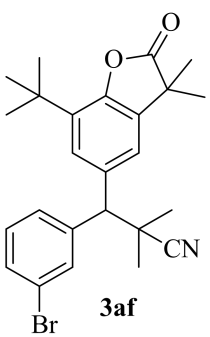
3ad

3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(4-chlorophenyl)-2,2-dimethylpropanenitrile (**3ad**). Yellowish solid (96.6 mg, 81%), m.p. 148.5-149.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.36 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 2.0 Hz, 1H), 3.62 (s, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.42 (s, 9H), 1.38 (d, *J* = 2.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.0, 149.4, 138.8, 135.7, 134.7, 134.5, 133.4, 130.0, 129.1, 126.4, 124.6, 120.2, 60.6, 42.4, 36.3, 34.4, 29.6, 27.7, 27.4, 25.4, 25.4; IR(KBr): 2025, 1801, 1577, 1426, 1065 cm^{-1}; UV: λ_{max} = 274; HRMS m/z (ESI) calcd for $C_{25}H_{29}ClNO_2$ $[M+H]^+$ 410.1881, found: 410.1884.



3ae

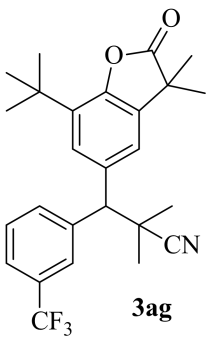
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(4-fluorophenyl)-2,2-dimethylpropanenitrile (**3ae**). White solid (88.5 mg, 75%), m.p. 154.4-155.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56 (dd, *J* = 8.8, 5.2 Hz, 2H), 7.40 (d, *J* = 2.0 Hz, 1H), 7.25 (d, *J* = 2.0 Hz, 1H), 7.07 (t, *J* = 8.8 Hz, 2H), 3.64 (s, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.42 (s, 9H), 1.38 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.0, 163.3 (d, *J* = 247.6 Hz), 149.3, 136.1, 136.0, 134.6, 134. 5, 130.2 (d, *J* = 8.0 Hz), 126.4, 124.6, 120.2, 115.9 (d, *J* = 21.3 Hz), 60.4, 42.4, 36.5, 34.4, 29.6, 27.7, 27.5, 25.4, 25.4; IR(KBr): 2026, 1796, 1580, 1431, 1068 cm^{-1}; UV: λ_{max} = 272, 265; HRMS *m/z* (ESI) calcd for $C_{25}H_{29}FNO_2$ $[M+H]^+$ 394.2177, found: 394.2179.



3af

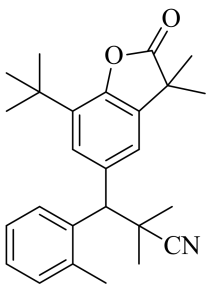
3-(3-bromophenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihy

drobenzofuran-5-yl)-2,2-dimethylpropanenitrile (**3af**). Yellowish solid (76.3 mg, 56%), m.p. 141.3-142.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, *J* = 7.6 Hz, 1H), 7.61 (s, 1H), 7.44 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.40 (d, *J* = 2.0 Hz, 1H), 7.29 (s, 1H), 7.24 (d, *J* = 1.9 Hz, 1H), 3.59 (s, 1H), 1.52 (s, 3H), 1.50 (s, 3H), 1.42 (s, 9H), 1.40 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.0, 149.4, 142.5, 135.4, 134.7, 134.5, 132.3, 130.6, 130.5, 126.6, 126.5, 124.4, 122.8, 120.3, 60.8, 42.4, 36.3, 34.5, 29.6, 27.8, 27.4, 25.4, 25.4; IR(KBr): 2026, 1801, 1578, 1436, 1068 cm^{-1}; UV: λ_{max} = 270; HRMS *m/z* (ESI) calcd for $C_{25}H_{29}BrNO_2$ $[M+H]^+$ 454.1376, found: 454.1375.



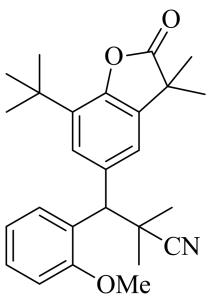
3ag

3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl) -2,2-dimethyl-3-(3-(trifluoromethyl)phenyl)propanenitrile (**3ag**). Yellow oil (67.9 mg, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, *J* = 7.6 Hz, 1H), 7.74 (s, 1H), 7.59-7.52 (m, 2H), 7.44 (d, *J* = 2.0 Hz, 1H), 7.27 (d, *J* = 2.0 Hz, 1H), 3.71 (s, 1H), 1.52 (s, 3H), 1.50 (s, 3H), 1.42 (s, 9H), 1.40 (d, *J* = 3.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.9, 149.5, 141.2, 135.2, 134.7, 134.7, 131.4, 131.3 (q, *J* = 32.4 Hz), 129.5, 126.4, 126.0 (q, *J* = 4.0 Hz), 125.3 (q, *J* = 273.5 Hz), 124.4 (q, *J* = 3.7 Hz), 124.4, 120.3, 60.9, 42.4, 36.4, 34.5, 29.6, 27.7, 27.4, 25.4, 25.4; IR(KBr): 2026, 1805, 1578, 1425, 1066 cm^{-1}; UV: λ_{max} = 271, 264; HRMS *m/z* (ESI) calcd for $C_{26}H_{29}F_3NO_2$ $[M+H]^+$ 444.2145, found: 444.2147.



3ah

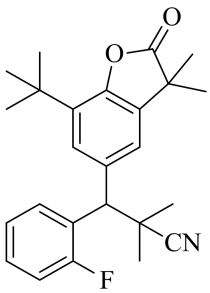
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl) -2,2-dimethyl-3-(o-tolyl)propanenitrile (**3ah**). Yellow solid (64.3 mg, 55%), m.p. 168.1-169.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.32 (m, 2H), 7.21 (d, *J* = 2.0 Hz, 1H), 7.19 – 7.15 (m, 2H), 3.93 (s, 1H), 2.34 (s, 3H), 1.51 (s, 3H), 1.46 (s, 3H), 1.42 – 1.41 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.1, 149.16 138.8, 136.1, 135.2, 134.3, 133.9, 131.1, 127.3, 127.0, 126.7, 126.5, 125.1, 120.9, 55.3, 42.3, 36.5, 34.3, 29.6, 28.6, 26.7, 25.5, 25.3, 20.4; IR(KBr): 2026, 1806, 1580, 1427, 1066 cm^{-1}; UV: λ_{max} = 273; HRMS *m/z* (ESI) calcd for $C_{26}H_{32}NO_2$ $[M+H]^+$ 390.2428, found: 390.2431.



3ai

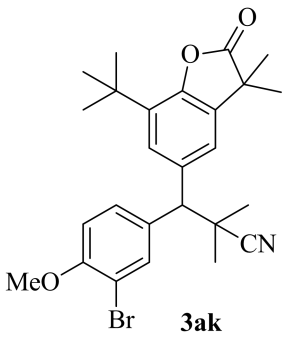
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)

-3-(2-methoxyphenyl)-2,2-dimethylpropanenitrile (**3ai**). Yellow oil (74.2 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.46 (d, *J* = 1.6 Hz, 1H), 7.27 – 7.22 (m, 2H), 7.04 (td, *J* = 7.4, 0.8 Hz, 1H), 6.93 – 6.87 (m, 1H), 4.42 (s, 1H), 3.84 (s, 3H), 1.51 (s, 3H), 1.48 (s, 3H), 1.42 (s, 9H), 1.39 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.3, 156.7, 149.0, 136.4, 134.1, 134.0, 129.0, 128.1, 128.0, 127.0, 125.4, 121.0, 120.8, 110.9, 55.5, 50.3, 42.4, 36.3, 34.4, 29.7, 28.1, 26.8, 25.5, 25.4, 23.4; IR(KBr): 2025, 1806, 1578, 1436, 1067 cm^{-1}; UV: λ_{max} = 275; HRMS *m/z* (ESI) calcd for $C_{26}H_{32}NO_3$ $[M+H]^+$ 406.2377, found: 406.2379.



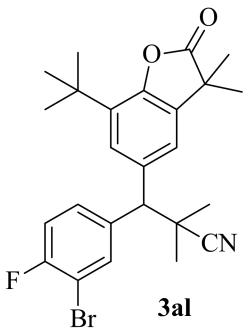
3aj

3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl) -3-(2-fluorophenyl)-2,2-dimethylpropanenitrile (**3aj**). Yellow solid (75.6 mg, 64%), m.p. 114.3-115.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 (td, *J* = 7.6, 2.0 Hz, 1H), 7.47 (d, *J* = 2.0 Hz, 1H), 7.28 – 7.20 (m, 3H), 7.11 – 7.04 (m, 1H), 4.20 (s, 1H), 1.51 (s, 3H), 1.50 (s, 3H), 1.42 – 1.41 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.0, 159.1 (d, *J* = 245.7 Hz), 149.3, 135.2, 134.5 (d, *J* = 8.9 Hz), 128.9 (d, *J* = 8.7 Hz), 128.6, 128.6, 127.6 (d, *J* = 13.5 Hz), 126.7, 124.7, 124.5, 120.6, 115.7 (d, *J* = 23.7 Hz), 50.5, 42.3, 36.3, 34.4, 29.6, 27.7, 27.0, 25.4; IR(KBr): 2026, 1807, 1585, 1423, 1053 cm^{-1}; UV: λ_{max} = 264, 270; HRMS *m/z* (ESI) calcd for $C_{25}H_{29}FNO_2$ $[M+H]^+$ 394.2177, found: 394.2179.



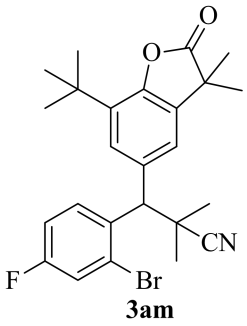
3ak

3-(3-bromo-4-methoxyphenyl)-3-(7-(tert-butyl)-3,3-dimeth yl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropan enitrile (**3ak**). Yellow oil (91.6 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 – 7.62 (m, 2H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.23 (d, *J* = 1.6 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 3.90 (s, 3H), 3.55 (s, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.42 (s, 9H), 1.39 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.4, 154.5, 148.7, 135.3, 134.0, 133.8, 133.5, 133.3, 127.3, 125.7, 124.0, 119.6, 111.6, 111.0, 59.3, 55.6, 41.7, 35.9, 33.8, 29.0, 27.0, 26.9, 24.8, 24.8; IR(KBr): 2026, 1800, 1578, 1436, 1068 cm^{-1}; UV: λ_{max} = 281; HRMS *m/z* (ESI) calcd for $C_{26}H_{31}BrNO_3$ $[M+H]^+$ 484.1482, found: 484.1486.



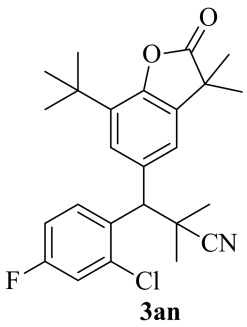
3al

3-(3-bromo-4-fluorophenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile (**3al**). Colourless oil (92.1 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 – 7.62 (m, 2H), 7.38 (d, *J* = 2.0Hz, 1H), 7.22 (d, *J* = 2.0 Hz, 1H), 7.16 (t, *J* = 8.4 Hz, 1H), 3.60 (s, 1H), 1.52 (s, 3H), 1.50 (s, 3H), 1.42 (s, 9H), 1.40 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.9, 157.2 (d, *J* = 249.1 Hz), 149.5, 137.8 (d, *J* = 4.0 Hz), 135.3, 134.8, 134.7, 134.1, 128.6 (d, *J* = 7.2 Hz), 126.3, 124.3, 120.2, 117.0 (d, *J* = 22.3 Hz), 109.4 (d, *J* = 21.1 Hz), 60.0, 42.4, 36.4, 34.5, 29.6, 27.6, 27.5, 25.4, 25.4; IR(KBr): 2026, 1806, 1578, 1436, 1067 cm^{-1}; UV: λ_{max} = 271; HRMS *m/z* (ESI) calcd for $C_{25}H_{28}BrFNO_2$ $[M+H]^+$ 472.1282, found: 472.1285.



3am

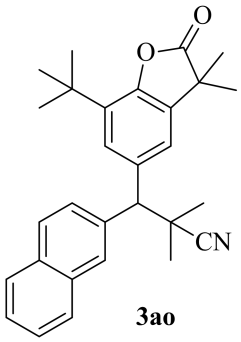
3-(2-bromo-4-fluorophenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile (**3am**). Orange red solid (77.9 mg, 55%), m.p. 198.5-199.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.13 (dd, *J* = 8.8, 6.0Hz, 1H), 7.45 (d, *J* = 2.0Hz, 1H), 7.36 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.25 (d, *J* = 2.0 Hz, 1H), 7.19 – 7.14 (m, 1H), 4.40 (s, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.43 (s, 3H), 1.42 – 1.41 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.0, 159.8 (d, *J* = 252.6 Hz), 149.4, 135.7 (d, *J* = 3.7 Hz), 134.6, 134.6, 134.4, 129.2 (d, *J* = 8.4 Hz), 126.8, 125.8 (d, *J* = 9.2 Hz), 124.7, 120.7, 120.5, 115.6 (d, *J* = 21.0 Hz), 56.7, 42.3, 36.6, 34.4, 29.6, 28.0, 26.7, 25.4, 25.3; IR(KBr): 2026, 1808, 1577, 1424, 1066 cm^{-1}; UV: λ_{max} = 270; HRMS *m/z* (ESI) calcd for $C_{25}H_{28}BrFNO_2$ $[M+H]^+$ 472.1282, found: 472.1280.



3an

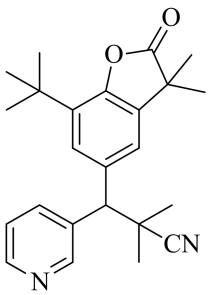
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(2-chloro-4-fluorophenyl)-2,2-dimethylpropanenitrile (**3an**). Yellow solid (55.2 mg, 43%), m.p. 181.4-182.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (dd, *J* = 8.8, 6.0 Hz, 1H), 7.43 (d, *J* = 2.0 Hz, 1H), 7.23 (d, *J* = 2.0 Hz, 1H), 7.17 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.14 – 7.09 (m, 1H), 4.39 (s, 1H), 1.51 (s, 3H), 1.49

(s, 3H), 1.42 (t, J = 5.0 Hz, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.9, 162.4 (d, J = 251.5 Hz), 149.4, 135.1 (d, J = 9.9 Hz), 134.7, 134.6, 134.5, 134.2 (d, J = 3.9 Hz), 129.4 (d, J = 8.7 Hz), 126.8, 124.7, 120.5, 117.4 (d, J = 24.5 Hz), 115.0 (d, J = 21.1 Hz), 54.0, 42.3, 36.4, 34.4, 29.6, 28.0, 26.7, 25.4, 25.4; IR(KBr): 2026, 1798, 1580, 1423, 1067 cm^{-1}; UV: λ_{max} = 270 , 277; HRMS *m/z* (ESI) calcd for $C_{25}H_{28}ClFNO_2$ $[M+H]^+$ 428.1787, found: 428.1789.



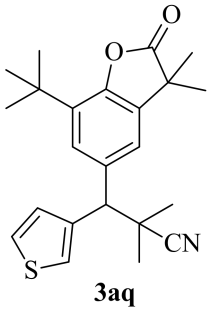
3ao

3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(naphthalen-2-yl)propanenitrile (**3ao**). Yellowish solid (107.2 mg, 84%), m.p. 62.3-63.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (s, 1H), 7.80 – 7.86 (m, 2H), 7.84 – 7.79 (m, 2H), 7.54 – 7.47 (m, 3H), 7.36 (d, J = 2.0 Hz, 1H), 3.83 (s, 1H), 1.52 (s, 3H), 1.49 (s, 3H), 1.46 – 1.41 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.1, 149.3, 137.8, 136.2, 134.5, 134.4, 133.4, 132.6, 128.7, 128.0, 127.7, 127.6, 126.6, 126.4, 126.3, 126.2, 124.9, 120.4, 61.4, 42.4, 36.4, 34.4, 29.6, 28.0, 27.6, 25.4, 23.5; IR(KBr): 2026, 1805, 1579, 1435, 1067 cm^{-1}; UV: λ_{max} = 269; HRMS *m/z* (ESI) calcd for $C_{29}H_{32}NO_2$ $[M+H]^+$ 426.2428, found: 426.2428.



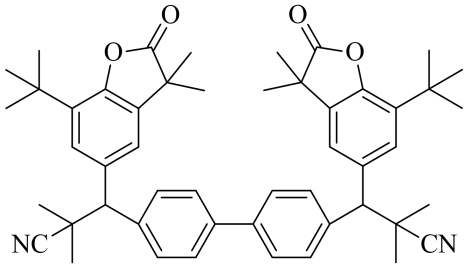
3ap

3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(pyridin-3-yl)propanenitrile (**3ap**). Brown solid (82mg, 73%), m.p. 162.3-163.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.66 (d, J = 2.0 Hz, 1H), 8.56 (dd, J = 4.8, 1.6 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.41 (d, J = 1.6 Hz, 1H), 7.36 (dd, J = 8.0, 4.8 Hz, 1H), 7.25 (d, J = 2.0 Hz, 1H), 3.68 (s, 1H), 1.51 (s, 3H), 1.49 (s, 3H), 1.43 – 1.37 (m, 15H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.8, 150.5, 149.5, 149.0, 135.9, 135.2, 135.1, 134.8, 134.8, 126.4, 124.3, 123.8, 120.2, 58.5, 42.4, 36.3, 34.5, 29.6, 27.5, 27.5, 25.4, 25.4; IR(KBr): 2026, 1806, 1580, 1423, 1067 cm^{-1}; UV: λ_{max} = 257; HRMS *m/z* (ESI) calcd for $C_{24}H_{29}N_2O_2$ $[M+H]^+$ 377.2224, found: 377.2227.



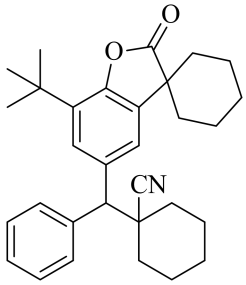
3aq

3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(thiophen-3-yl)propanenitrile (**3aq**). Yellowish solid (68.7 mg, 60%), m.p. 52.5-53.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42 (dd, *J* = 2.4, 1.6 Hz, 1H), 7.38 (d, *J* = 2.0 Hz, 1H), 7.36 – 7.35 (m, 2H), 7.23 (d, *J* = 2.0 Hz, 1H), 3.83 (s, 1H), 1.52 (s, 3H), 1.49 (s, 3H), 1.42 – 1.41 (m, 12H), 1.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.1, 149.3, 140.5, 135.7, 134.4, 134.3, 127.8, 126.6, 126.2, 124.7, 122.5, 120.4, 56.5, 42.3, 37.1, 34.4, 29.7, 29.6, 27.3, 25.4, 23.5; IR(KBr): 2025, 1806, 1578, 1436, 1067 cm^{-1}; UV: λ_{max} = 272, 280; HRMS *m/z* (ESI) calcd for $C_{23}H_{28}NO_2S$ $[M+H]^+$ 382.1835, found: 382.1838.



3ar

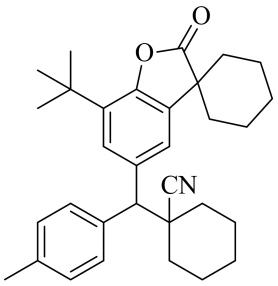
3,3'-([1,1'-biphenyl]-4,4'-diyl)bis(3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile) (**3ar**). Yellow solid (132.6 mg, 59%), m.p. 153.6-154.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, *J* = 8.4 Hz, 4H), 7.60 (d, *J* = 8.4 Hz, 4H), 7.45 (d, *J* = 1.6 Hz, 2H), 7.31 (d, *J* = 1.6 Hz, 2H), 3.68 (s, 2H), 1.52 (s, 6H), 1.50 (s, 6H), 1.43 (s, 24H), 1.40 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 181.1, 149.3, 139.5, 139.4, 136.1, 134.6, 134.4, 129.1, 127.4, 126.5, 124.8, 120.3, 61.0, 42.4, 36.5, 34.4, 29.6, 27.8, 27.5, 25.4, 25.4; IR(KBr): 2026, 1809, 1578, 1436, 1067 cm^{-1}; UV: λ_{max} = 267; HRMS *m/z* (ESI) calcd for $C_{50}H_{57}N_2O_4$ $[M+H]^+$ 749.4313, found: 749.4317.



3as

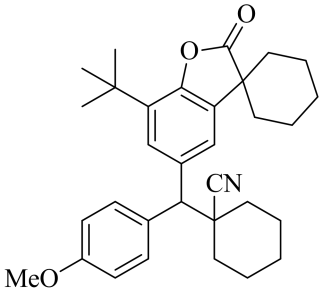
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(phenyl)methyl)cyclohexanecarbonitrile (**3as**). White solid (101.1 mg, 74%), m.p. 72.5-73.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, *J* = 7.2 Hz, 2H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.40 – 7.36 (m, *J* = 9.4, 4.6 Hz, 3H), 7.30 (d, *J* = 7.2 Hz, 1H), 3.66 (s, 1H), 2.03 – 1.83 (m, 7H), 1.81 – 1.59 (m, 13H), 1.41 (s, 9H); ^{13}C

NMR (101 MHz, $CDCl_3$) δ: 179.7, 149.3, 140.1, 135.2, 134.3, 133.8, 128.8, 127.3, 126.7, 123.3, 121.4, 61.5, 45.4, 42.7, 36.2, 35.9, 34.4, 34.1, 34.1, 29.6, 25.1, 24.9, 22.8, 20.8, 20.7; IR(KBr): 2026, 1795, 1580, 1436, 1068 cm^{-1}; UV: λ_{max} = 272; HRMS *m/z* (ESI) calcd for $C_{31}H_{38}NO_2$ $[M+H]^+$ 456.2897, found: 456.2896.



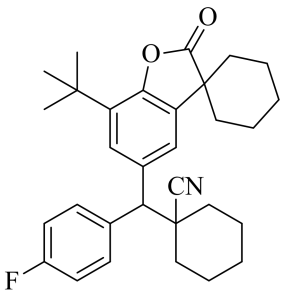
3at

1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(p-tolyl)methyl)cyclohexanecarbonitrile (**3at**). Yellow solid (98.6 mg, 70%), m.p. 103.6-103.9 °C. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.55 (d, *J* = 1.6 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 2.0 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 3.63 (s, 1H), 2.34 (s, 3H), 1.99 – 1.84 (m, 7H), 1.80 – 1.60 (m, 13H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.8, 149.2, 137.1, 137.0, 135.5, 134.3, 133.7, 129.5, 128.7, 126.6, 123.3, 121.3, 61.2, 60.4, 45.4, 42.7, 36.2, 36.0, 34.3, 34.1, 34.1, 29.6, 25.1, 24.9, 22.8, 21.0, 20.8, 20.7; IR(KBr): 2026, 1796, 1586, 1424, 1068 cm^{-1}; UV: λ_{max} = 273; HRMS *m/z* (ESI) calcd for $C_{32}H_{40}NO_2$ $[M+H]^+$ 470.3054, found: 470.3052.



3au

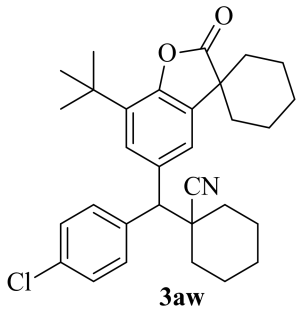
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-methoxyphenyl)methyl)cyclohexanecarbonitrile (**3au**). Yellow solid (91.8 mg, 63%), m.p. 108.2-109.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.54 – 7.52 (m, 3H), 7.34 (d, *J* = 2.0 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 3.62 (s, 1H), 1.99 – 1.87 (m, 7H), 1.79 – 1.63 (m, 13H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.7, 158.8, 149.2, 135.6, 134.3, 133.8, 132.2, 129.8, 126.5, 123.3, 121.2, 114.1, 60.6, 55.3, 45.4, 42.9, 36.1, 36.0, 34.3, 34.1, 34.1, 29.6, 25.1, 24.9, 22.8, 20.8, 20.7; IR(KBr): 2026, 1795, 1579, 1439, 1068 cm^{-1}; UV: λ_{max} = 274; HRMS *m/z* (ESI) calcd for $C_{32}H_{40}NO_3$ $[M+H]^+$ 486.3003, found: 486.3006.



3av

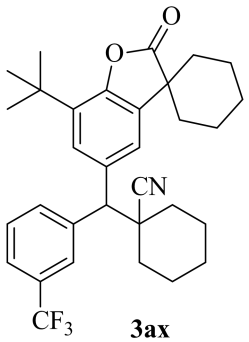
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-fluorophenyl)methyl)cyclohexanecarbonitrile (**3av**). White solid (96.6 mg, 68%), m.p. 98.0-99.2 °C. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.58 (dd, *J* = 8.6, 5.4 Hz, 2H),

7.50 (d, *J* = 2.0 Hz, 1H), 7.33 (d, *J* = 1.6 Hz, 1H), 7.06 (t, *J* = 8.8 Hz, 2H), 3.67 (s, 1H), 1.99 – 1.86 (m, 7H), 1.79 – 1.60 (m, 13H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.6, 163.2 (d, *J* = 247.5 Hz), 149.3, 135.8, 135.0, 134.5, 133.9, 130.4 (d, *J* = 7.9 Hz), 126.5, 123.1, 121.2, 115.8 (d, *J* = 21.2 Hz), 60.6, 45.3, 42.7, 36.1, 36.0, 34.4, 34.1, 34.1, 29.6, 25.1, 24.9, 22.8, 20.8, 20.7; IR(KBr): 2026, 1796, 1580, 1431, 1068 cm^{-1}; UV: λ_{max} = 266, 272; HRMS *m/z* (ESI) calcd for $C_{31}H_{37}FNO_2$ $[M+H]^+$ 474.2803, found: 474.2806.



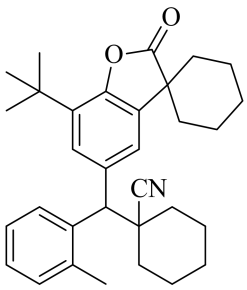
3aw

1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-chlorophenyl)methyl)cyclohexanecarbonitrile (**3aw**). Yellowish solid (113.2 mg, 77%), m.p. 62.3-63.0 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.55 (d, *J* = 8.4Hz, 2H), 7.49 (d, *J* = 1.6 Hz, 1H), 7.35 – 7.32 (m, 3H), 3.65 (s,1H), 1.99 – 1.86 (m, 7H), 1.78 – 1.60 (m, 13H), 1.40 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.6, 149.4, 138.6, 134.7, 134.5, 134.0, 133.3, 130.1, 129.0, 126.5, 123.0, 121.2, 65.9, 60.7, 45.3, 42.6, 36.1, 35.9, 34.4, 34.1, 34.1, 29.6, 25.1, 24.9, 22.7, 20.8, 20.7; IR(KBr): 2026, 1796, 1582, 1417, 1068 cm^{-1}; UV: λ_{max} = 272; HRMS *m/z* (ESI) calcd for $C_{31}H_{37}ClNO_2$ $[M+H]^+$ 490.2507, found: 490.2511.



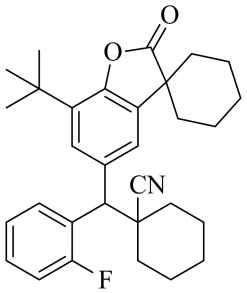
3ax

1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(3-(trifluoromethyl)phenyl)methyl)cyclohexanecarbonitrile (**3ax**). Yellowish solid (95.8 mg, 61%), m.p. 101.5-102.9 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 7.2 Hz, 1H), 7.77 (s, 1H), 7.58 – 7.51 (m, 3H), 7.36 (d, *J* = 2.0 Hz, 1H), 3.74 (s, 1H), 2.01 – 1.85 (m, 7H), 1.85 – 1.64 (m, 13H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.5, 149.6, 141.1, 134.6, 134.2, 134.1, 131.7, 131.2 (d, *J* = 32.3 Hz), 129.4, 126.6, 126.1, 125.3 (d, *J* = 273.5 Hz), 124.3, 122.8, 121.3, 61.2, 45.4, 42.7, 36.1, 35.9, 34.4, 34.1, 34.0, 29.6, 25.0, 24.9, 22.7, 20.7, 20.6; IR(KBr): 2026, 1792, 1578, 1436, 1068 cm^{-1}; UV: λ_{max} = 265, 272; HRMS *m/z* (ESI) calcd for $C_{32}H_{37}F_3NO_2$ $[M+H]^+$ 524.2771, found: 524.2774.



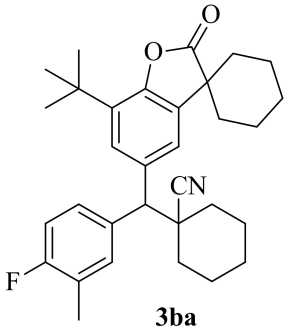
3ay

1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(o-tolyl)methyl)cyclohexanecarbonitrile (**3ay**). Yellowish solid (84.5 mg, 60%), m.p. 186.2-187.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.20 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 1.6 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.18 – 7.15 (m, 2H), 3.98 (s, 1H), 2.35 (s, 3H), 2.00 – 1.82 (m, 7H), 1.81 – 1.60 (m, 13H), 1.40 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.8, 149.2, 138.6, 136.3, 134.2, 134.0, 133.4, 131.1, 127.3, 126.9, 126.7, 126.7, 123.5, 122.1, 55.4, 45.3, 42.7, 36.9, 35.0, 34.3, 34.2, 33.9, 29.6, 25.2, 24.9, 22.9, 22.6, 20.7, 20.6, 20.5; IR(KBr): 2026, 1798, 1577, 1419, 1068 cm^{-1}; UV: λ_{max} = 273; HRMS *m/z* (ESI) calcd for $C_{32}H_{40}NO_2$ $[M+H]^+$ 470.3054, found: 470.3057.



3az

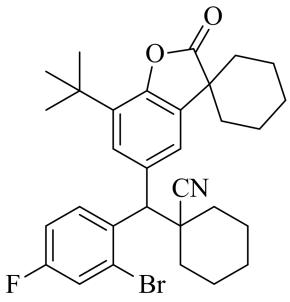
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(2-fluorophenyl)methyl)cyclohexanecarbonitrile (**3az**). White solid (72.5 mg, 51%), m.p. 161.4-162.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (td, *J* = 7.6, 2.2 Hz, 1H), 7.53 (d, *J* = 1.6 Hz, 1H), 7.40 (d, *J* = 2.0 Hz, 1H), 7.27 – 7.21 (m, 2H), 7.09 – 7.04 (m, 1H), 4.24 (s, 1H), 2.00 – 1.85 (m, 7H), 1.81 – 1.63 (m, 13H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.7, 159.3 (d, *J* = 245.6 Hz), 149.4, 134.4, 134.2, 134.0, 128.8, 128.7, 128.6, 127.3 (d, *J* = 13.6 Hz), 126.9, 124.7, 121.6, 115.7 (d, *J* = 23.8 Hz), 50.5, 45.3, 42.6, 36.1, 35.2, 34.4, 34.1, 34.1, 30.3, 29.6, 25.1, 24.9, 22.7, 20.7, 20.6; IR(KBr): 2026, 1798, 1580, 1424, 1068 cm^{-1}; UV: λ_{max} = 264, 270; HRMS *m/z* (ESI) calcd for $C_{31}H_{37}FNO_2$ $[M+H]^+$ 474.2803, found: 474.2806.



3ba

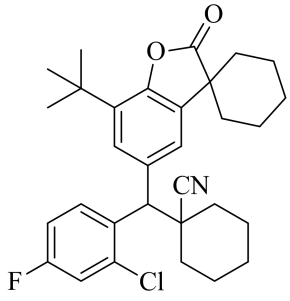
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-fluoro-3-methylphenyl)methyl)cyclohexanecarbonitrile (**3ba**). Yellow solid (87.8 mg, 60%), m.p. 93.2-94.1 °C. ^{1}H NMR (400 MHz, CDCl3) δ: 7.52 (d, *J* = 1.6 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.36 – 7.33 (m, 2H), 7.01 (t, *J* = 9.0 Hz, 1H), 3.60 (s, 1H), 2.29 (d, *J* = 1.6 Hz, 3H), 2.03 – 1.85 (m, 8H), 1.83 – 1.70 (m, 12H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ:

179.66, 159.4 (d, J = 246.0 Hz), 149.3, 135.6, 135.1, 134.4, 133.9, 132.2, 127.2, 126.5, 125.2 (d, J = 17.4 Hz), 123.1, 121.2, 115.4 (d, J = 22.3 Hz), 60.6, 45.4, 42.7, 36.2, 36.0, 34.4, 34.1, 34.0, 29.6, 25.1, 24.9, 22.8, 22.8, 20.7, 20.7; IR(KBr): 2026, 1805, 1579, 1435, 1067 cm^{-1}; UV: λ_{max} = 267, 273; HRMS *m/z* (ESI) calcd for $C_{32}H_{39}FNO_2$ $[M+H]^+$ 488.2959, found: 488.2963.



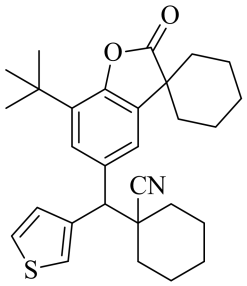
3bb

1-((2-bromo-4-fluorophenyl)(7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)methyl)cyclohexanecarbonitrile (**3bb**). White solid (96.1 mg, 58%), m.p. 148.8-150.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.21 (dd, J = 8.8, 6.0 Hz, 1H), 7.48 (d, J = 1.6 Hz, 1H), 7.40 (d, J = 1.6 Hz, 1H), 7.34 (dd, J = 8.0, 2.8 Hz, 1H), 7.19 – 7.14 (m, 1H), 4.44 (s, 1H), 2.02 – 1.84 (m, 7H), 1.83 – 1.60 (m, 13H), 1.40 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.6, 159.8 (d, J = 252.4 Hz), 149.4, 135.5, 134.4, 133.9, 133.5, 129.4 (d, J = 8.3 Hz), 127.0, 126.0 (d, J = 9.1 Hz), 123.2, 121.6, 120.7 (d, J = 24.1 Hz), 115.5 (d, J = 20.9 Hz), 56.8, 45.3, 42.8, 36.4, 34.9, 34.4, 34.1, 34.0, 29.6, 25.0, 24.9, 22.7, 22.6, 20.8, 20.6; IR(KBr): 2026, 1798, 1578, 1436, 1069 cm^{-1}; UV: λ_{max} = 271; HRMS *m/z* (ESI) calcd for $C_{31}H_{36}BrFNO_2$ $[M+H]^+$ 552.1908, found: 552.1911.



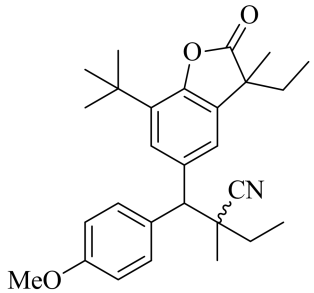
3bc

1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(2-chloro-4-fluorophenyl)methyl)cyclohexanecarbonitrile (**3bc**). White solid (79.3 mg, 52%), m.p. 173.4-174.1 °C. ^{1}H NMR (400 MHz, CDCl3) δ: 8.19 (dd, J = 8.8, 6.0 Hz, 1H), 7.46 (d, J = 1.6 Hz, 1H), 7.38 (d, J = 1.6 Hz, 1H), 7.17 – 7.09 (m, 2H), 4.43 (s, 1H), 1.99 – 1.89 (m, 7H), 1.82 – 1.57 (m, 13H), 1.40 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.5, 159.9 (d, J = 251.3 Hz), 149.4, 135.3 (d, J = 9.9 Hz), 134.4, 134.0, 133.9, 133.6, 129.5 (d, J = 8.6 Hz), 126.9, 123.2, 121.6, 117.4 (d, J = 24.5 Hz), 115.0 (d, J = 21.0 Hz), 54.1, 45.3, 42.7, 36.3, 34.9, 34.4, 34.1, 34.0, 29.6, 25.0, 24.9, 22.7, 22.6, 20.7, 20.6; IR(KBr): 2026, 1798, 1578, 1436, 1068 cm^{-1}; UV: λ_{max} = 270; HRMS *m/z* (ESI) calcd for $C_{31}H_{36}ClFNO_2$ $[M+H]^+$ 508.2413, found: 508.2416.



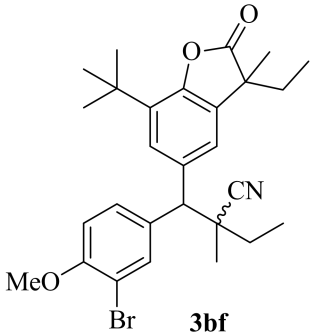
3bd

1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(thiophen-3-yl)methyl)cyclohexanecarbonitrile (**3bd**). Yellow solid (70.6 mg, 51%), m.p. 72.5-73.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, *J* = 2.0 Hz, 1H), 7.42 – 7.41 (m, 1H), 7.40 – 7.38 (m, 1H), 7.36 – 7.34 (m, 1H), 7.32 (d, *J* = 2.0 Hz, 1H), 3.86 (s, 1H), 1.97 – 1.87 (m, 6H), 1.83 – 1.61 (m, 14H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.7, 149.3, 140.3, 134.7, 134.3, 133.7, 127.9, 126.6, 126.1, 123.2, 122.5, 121.5, 56.6, 45.4, 43.4, 35.9, 35.8, 34.3, 34.1, 34.0, 29.6, 25.1, 24.9, 22.9, 22.9, 20.8, 20.7; IR(KBr): 2026, 1795, 1580, 1424, 1068 cm^{-1}; UV: λ_{max} = 272, 281; HRMS *m/z* (ESI) calcd for $C_{29}H_{36}NO_2S$ $[M+H]^+$ 462.2461, found: 462.2463.



3be

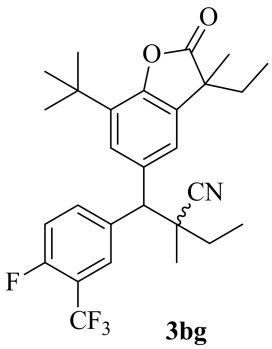
2-((7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)(4-methoxyphenyl)methyl)-2-methylbutanenitrile (**3be**). Yellow solid (67.6 mg, 52%), m.p. 110.1-111.5 °C. d.r. = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53-7.49 (m, 2H), 7.45 (s, 0.5H), 7.34– 7.31 (m, 1H), 7.22 (dd, *J* = 5.2, 2.0 Hz, 0.5H), 6.91 (d, *J* = 8.4 Hz, 2H), 3.81 (s, 3H), 3.64 (d, *J* = 4.0Hz, 1H), 2.07 – 1.95 (m, 1H), 1.89 – 1.79 (m, 1H), 1.50 – 1.48 (m, 4H), 1.41 (d, *J* = 0.8 Hz, 9H), 1.30 – 1.26 (m, 4H), 1.05 (t, *J* = 7.4 Hz, 3H), 0.73 – 0.66 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.7, 158.8, 149.8, 136.6, 134.2, 132.7, 132.3, 129.8, 129.7, 126.8, 126.7, 126.4, 124.1, 120.8, 120.3, 114.2, 114.2, 59.3, 55.2, 47.4, 41.4, 34.3, 34.3, 32.5, 29.6, 23.7, 23.7, 23.5, 23.2, 9.0, 9.0; IR(KBr): 2026, 1801, 1577, 1436, 1068 cm^{-1}; UV: λ_{max} = 273; HRMS *m/z* (ESI) calcd for $C_{28}H_{36}NO_3$ $[M+H]^+$ 434.2690, found: 434.2686.



3bf

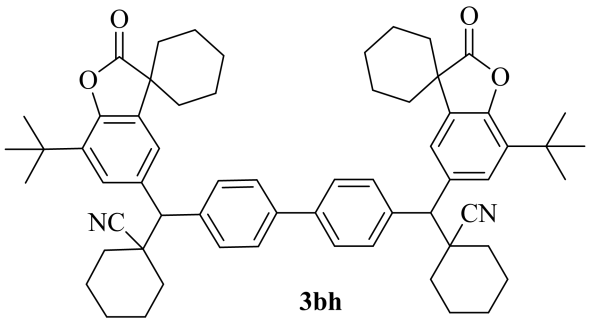
2-((3-bromo-4-methoxyphenyl)(7-(tert-butyl)-3-ethyl-3-methyl-2-oxo-2,3-dihydrobenzofuran-5-yl)methyl)-2-methylbutanenitrile (**3bf**). Yellowish solid (89.2 mg, 58%), m.p. 61.2-62.0 °C. d.r. = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 – 7.62 (m, 2H), 7.42 (d, *J* = 1.6 Hz, 0.5H), 7.32 (dd, *J*

= 7.2, 2.0 Hz, 0.5H), 7.27 (dd, *J* = 3.6, 2.0 Hz, 0.5H), 7.20 (dd, *J* = 5.6, 1.6 Hz, 0.5H), 6.93 (dd, *J* = 8.4, 1.8 Hz, 1H), 3.90 (s, 3H), 3.60 (d, *J* = 4.0 Hz, 1H), 2.03 – 1.94 (m, 1H), 1.89 – 1.79 (m, 1H), 1.65 (s, 1H), 1.51 – 1.48 (m, 4H), 1.41 (s, 9H), 1.31 – 1.26 (m, 4H), 1.06 (dd, *J* = 13.2, 7.0 Hz, 3H), 0.73 – 0.67 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.5, 155.1, 150.0, 135.9, 134.4, 134.3, 134.2, 133.8, 126.8, 126.6, 126.4, 126.3, 123.8, 120.7, 120.2, 112.2, 65.9, 58.9, 56.3, 47.4, 41.3, 34.4, 34.3, 32.5, 29.6, 23.7, 23.7, 23.3, 23.2, 9.0, 8.9; IR(KBr): 2026, 1803, 1580, 1435, 1067 cm^{-1}; UV: λ_{max} = 274; HRMS *m/z* (ESI) calcd for $C_{28}H_{35}BrNO_3$ $[M+H]^+$ 512.1795, found: 512.1797.



3bg

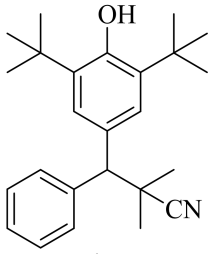
2-((7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)(4-fluoro-3-(trifluoromethyl)phenyl)methyl)-2-methylbutanenitrile (**3bg**). Yellow solid (66.1 mg, 45%), m.p. 123.8-124.8 °C. d.r. = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 – 7.89 (m, 1H), 7.72 – 7.69 (m, 1H), 7.42 (d, *J* = 1.6 Hz, 0.5H), 7.34 (dd, *J* = 7.2, 2.0 Hz, 0.5H), 7.27 – 7.20 (m, 2H), 3.74 (s, 1H), 2.05 – 1.97 (m, 1H), 1.89 – 1.81 (m, 1H), 1.51 – 1.49 (m, 4H), 1.42 (s, 9H), 1.31 – 1.29 (m, 4H), 1.10 – 1.05 (m, 3H), 0.75 – 0.65 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 180.3, 157.7 (d, *J* = 261.4 Hz), 150.2, 135.1, 134.8, 133.6, 126.7, 126.5, 126.2, 123.7 (q, *J* = 273.5 Hz), 123.5, 120.2, 117.7, 117.5, 104.2, 103.0, 59.1, 47.4, 41.2, 34.4, 32.6, 32.0, 29.5, 23.6, 17.9, 15.4, 9.0; IR(KBr): 2026, 1801, 1577, 1419, 1067 cm^{-1}; UV: λ_{max} = 264, 272; HRMS *m/z* (ESI) calcd for $C_{28}H_{32}F_4NO_2$ $[M+H]^+$ 490.2364, found: 490.2362.



3bh

1,1'-([1,1'-biphenyl]-4,4'-diylbis((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)methylene))dicyclohexanecarbonitrile (**3bh**). Yellowish solid (136.4 mg, 50%), m.p. 197.9-199.2 °C. ^{1}H NMR (400 MHz, CDCl3) δ: 7.68 (d, *J* = 8.4 Hz, 4H), 7.58 (d, *J* = 8.4 Hz, 6H), 7.38 (d, *J* = 2.0Hz, 2H), 3.70 (s, 2H), 1.98 – 1.87 (m, 14H), 1.80 – 1.60 (m, 26H), 1.41 (s, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 179.7, 149.4, 139.4, 139.2,

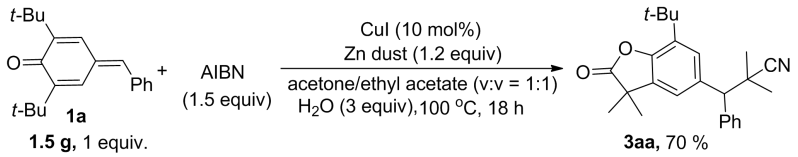
135.0, 134.4, 133.9, 129.3, 127.3, 126.7, 123.2, 121.3, 61.2, 45.4, 42.7, 36.2, 36.0, 34.4, 34.1, 34.1, 29.6, 25.1, 24.9, 22.8, 20.8, 20.7, 20.7; IR(KBr): 2026, 1797, 1579, 1420, 1068 cm^{-1}; UV: λ_{max} = 263; HRMS *m/z* (ESI) calcd for $C_{62}H_{73}N_2O_4$ $[M+H]^+$ 909.5565, found: 909.5568.



4a

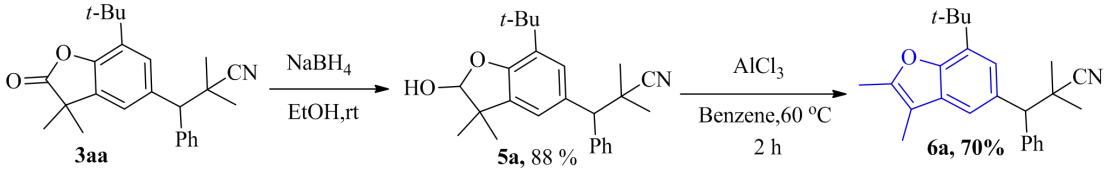
3-(3,5-di-tert-butyl-4-hydroxyphenyl)-2,2-dimethyl-3-phenylpropanenitrile (**4a**). Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.58 (d, *J* = 7.2 Hz, 2H), 7.37 – 7.21 (m, 5H), 5.16 (s, 1H), 3.55 (s, 1H), 1.47 (s, 18H), 1.38 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.9, 141.2, 135.8, 130.8, 128.7, 128.6, 127.0, 125.4, 125.2, 61.4, 36.6, 34.5, 30.3, 30.2, 27.8, 27.6; IR(KBr): 2026, 1578, 1436 cm^{-1}; UV: λ_{max} = 275; HRMS m/z (ESI) calcd for $C_{25}H_{34}NO$ $[M+H]^+$ 364.2635, found: 364.2638.

Procedure for gram-scale synthesis of benzofuran-2(3H)-ones. To a mixture of *para*-quinone methides **1** (1.5g, 5.1 mmol,), CuI (10 mol%), Zn dust (1.2 equv.), azo compound **2** (1.5 equiv.) was added acetone/ethyl acetate (*v:v* = 1:1, 8 mL), and then H_2O (3 equiv.). The resulting solution was stirred at 100 °C under N_2 atmosphere (1 atm.) for 18 h. The solvent was evaporated under reduced pressure and the resulted mixture was filtered through a Florisil pad, diluted with Et_2O, and washed with water and then brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by flash chromatography on silica gel (eluent : *n*-hexane/ethyl acetate = 20:1) to give **3aa** (1.24g, 70%) as a yellowish solid.



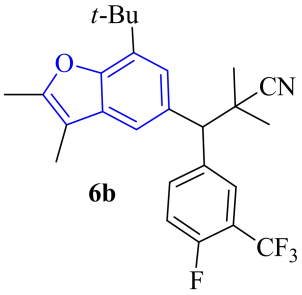
Preparation of benzofuran 6a. To a solution of **3aa** (1.0 mmol) in ethanol (3 mL), $NaBH_4$ (2.0 mmol) was added at 0 °C and stirred for 2-3 h at room temperature. After completion, the reaction was quench with H_2O (0.5 mL) and the solvent was evaporated after fileted over a celite pad. The resulting residue was dissolved in

EtOAc (10 mL) and washed with brine (2 x 20mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel elueting with n-hexane/ethyl acetate (15/1 ─ 8/1) to afford **5a** (332.2 mg, 88%) as white solid (m.p. 149.5-150.6 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.29 – 7.25 (m, 2H), 7.17 (dd, *J* = 5.6, 2.0 Hz, 1H), 5.55 – 5.53 (m, 1H), 3.58 (s, 1H), 2.93 – 2.91 (m, 1H), 1.39 – 1.26 (m, 21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.3, 141.0, 135.9, 133.2, 133.0, 128.7, 128.9, 127.1, 125.9, 125.2, 120.4, 108.0, 61.3, 44.8, 36.6, 34.2, 29.4, 27.9, 27.6, 20.2, 20.2; IR(KBr): 2026, 1578, 1436, 1137 cm^{-1}; UV: λ_{max} = 279; HRMS m/z (ESI) calcd for $C_{25}H_{32}NO_2$ $[M+H]^+$ 378.2428, found: 378.2431.



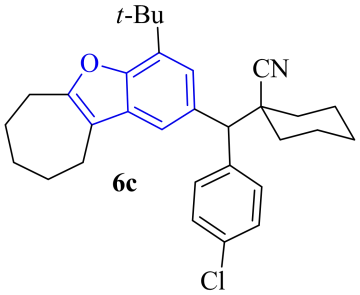
To a solution of above obtained **5a** (113 mg, 0.3 mmol) in dry benzene (2.0 mL) was added $AlCl_3$ (120 mg, 0.9 mmol) under N_2. The reaction mixture was then heated to 60 °C and stirred for 2 h. Following addition of H_2O (10 mL), the resulting mixture was extracted with ethyl acetate (10 mL × 3), and the combined extracts were dried over anhydrous Na_2SO_4. The solvent of filtrate was concentrated under reduced pressure. The residue obtained was purified by flash column chromatography on silica gel (eluent: *n*-hexane/AcOEt (50/1) to afford the benzofuran **6a** as a white solid (75.5 mg, 70% yield, m.p 135.5-137.0 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 7.2 Hz, 2H), 7.44 (d, *J* = 1.6 Hz, 1H), 7.37 – 7.34 (m, 3H), 7.26 (t, *J* = 7.4 Hz, 1H), 3.73 (s, 1H), 2.39 (s, 3H), 2.16 (s, 3H), 1.50 (s, 9H), 1.42 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.15, 150.19, 141.15, 133.98, 131.08, 128.80, 128.65, 127.04, 125.27, 120.84, 116.43, 109.48, 61.62, 36.52, 34.38, 29.90, 27.88, 27.83, 11.96, 8.01; IR(KBr): 2026, 1577, 1436, 1137 cm^{-1}; UV: λ_{max} = 260, 292; HRMS *m/z* (ESI) calcd for $C_{25}H_{30}NO$ $[M+H]^+$ 360.2322, found: 360.2326.

Preparation of benzofuran 6b and 6c. By following the synthetic procedure for **6a**, benzofuran **6b** and **6c** were prepared.



6b

3-(7-(tert-butyl)-2-ethyl-3-methylbenzofuran-5-yl)-3-(4-fluoro-3-(trifluoromethyl)phenyl)-2,2-dimethylpropanenitrile (**6c**). Yellowish solid (88.2 mg, 66%), m.p. 78.5-80.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 – 7.95 (m, 1H), 7.77 (dd, *J* = 6.6, 2.4 Hz, 1H), 7.40 (d, *J* = 1.8 Hz, 1H), 7.34 (d, *J* = 1.9 Hz, 1H), 7.23 (t, *J* = 9.3 Hz, 1H), 3.80 (s, 1H), 2.41 (s, 3H), 2.17 (s, 3H), 1.52 (s, 9H), 1.43 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 160.1 (d, *J* = 257.3 Hz), 151.3, 150.7, 137.5, 134.5, 133.6, 132.9, 131.4, 127.9, 125.2, 124.6, 123.8 (q, *J* = 273.3 Hz), 120.4, 117.4, 116.4, 109.5, 60.6, 36.5, 34.5, 29.9, 27.8, 27.5, 11.9, 7.9; IR(KBr): 2026, 1577, 1420, 1138 cm^{-1}; UV: λ_{max} = 260, 290; HRMS *m/z* (ESI) calcd for $C_{26}H_{28}F_4NO$ $[M+H]^+$ 446.2102, found: 446.2106.



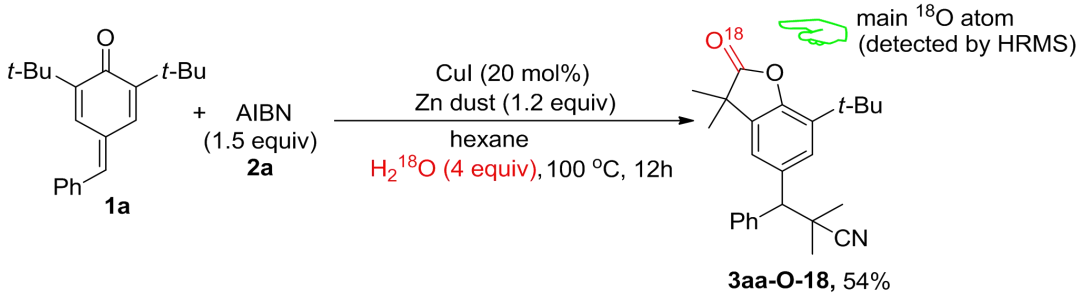
6c

1-((4-(tert-butyl)-7,8,9,10-tetrahydro-6H-cyclohepta[b]benzofuran-2-yl)(4-chlorophenyl)methyl)cyclohexanecarbonitrile (**6b**). White solid (85.3 mg, 60%), m.p. 112.4-113.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 1.6 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 1.6 Hz, 1H), 3.75 (s, 1H), 2.96 – 2.93 (m, 2H), 2.73 – 2.71 (m, 2H), 1.97 – 1.81 (m, 9H), 1.73 – 1.60 (m, 5H), 1.51 (s, 9H), 1.35 – 1.28 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 156.3, 150.7, 139.3, 134.3, 133.0, 132.9, 131.2, 130.4, 128.7, 123.3, 120.8, 116.1, 115.5, 61.1, 42.6, 36.3, 36.0, 34.4, 30.6, 29.9, 29.3, 28.3, 26.4, 25.2, 23.3, 22.8; IR(KBr): 2026, 1577, 1420, 1136 cm^{-1}; UV: λ_{max} = 259, 290; HRMS *m/z* (ESI) calcd for $C_{31}H_{37}ClNO$ $[M+H]^+$ 474.2558, found: 474.2557.

3. Control experiments using $H_2{}^{18}O$, D_2O and acetone-d_6 **according to known method[2]**

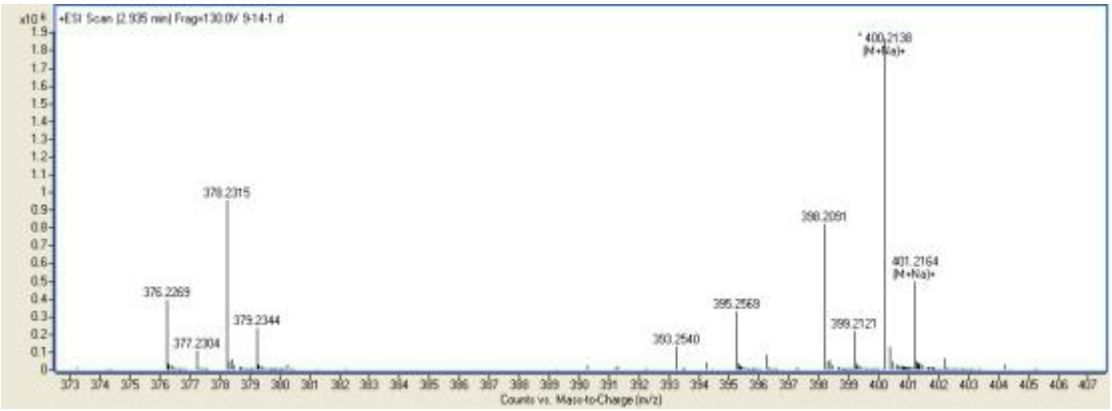
Experiment procedure using $H_2{}^{18}O$: To a mixture of p *para*-quinone methides **1** (0.3 mmol), CuI (20 mol%), Zn dust (1.2 equv.), azo compound **2** (1.5 equiv.) was added n-hexane (2 mL), and then H_2O^{18} (1.2 mmol, about 90% atom of O^{18}). The

resulting solution was stirred at 100 °C under N_2 atmosphere (1 atm.) for 12 h. The solvent was evaporated under reduced pressure and the resulted mixture was filtered through a Florisil pad, diluted with Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by flash chromatography on silica gel (eluent: n-hexane/ethyl acetate) to afford the corresponding 18-lablled *benzofuran-2(3H)-ones* (**3a-O-18**) in a 54% yield. and then the characterization of the product thereby obtained was recorded on HRMS spectrometer. As showed in the HRMS spetra, an ^{18}O-atom was apparrently introduced into the benzofuran-2(3*H*)-one **3aa-O-18**, which suggests that the oxygen atom of the newly-formed carbonyl group originated from H_2O

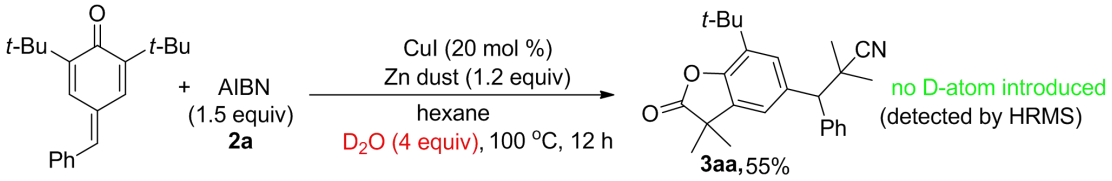


HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
9-14-1	C25 H29 N O 18O	C25 H29 N Na O 18O	400.2138	400.2133	1.25

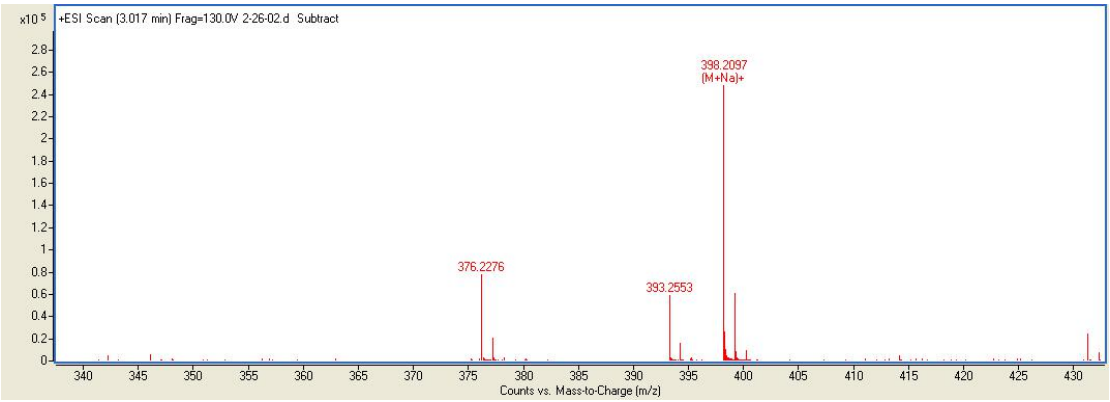


Experiment procedure using D_2O: To a mixture of p *para*-quinone methides **1** (0.3 mmol), CuI (20 mol%), Zn dust (1.2 equv.), azo compound **2** (1.5 equiv.) was added *n*-hexane (2 mL), and then D_2O (1.2 mmol, about 99.9% D-atom). The resulting solution was stirred at 100 °C under N_2 atmosphere (1 atm.) for 12 h. The solvent was evaporated under reduced pressure and the resulted mixture was filtered through a Florisil pad, diluted with Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by flash chromatography on silica gel (eluent: n-hexane/ethyl acetate) to afford the corresponding benzofuran-2(3*H*)-ones in a 55% yield. and then the characterization of the product thereby obtained was recorded on HRMS spectrometer. As showed in the HRMS spetra, no D-atom was apparrently introduced into the benzofuran-2(3*H*)-one **3aa**, which suggests that H_2O in the reaction should act as the oxygen source.



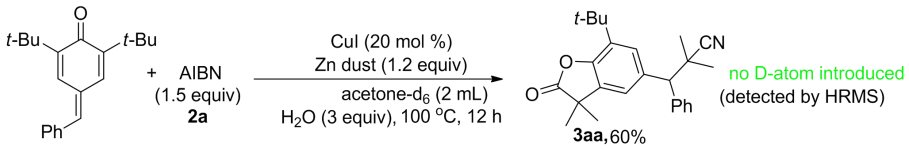
HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
2-26-02	C25 H29 N O2	C25 H29 N Na O2	398.2097	398.2091	1.51



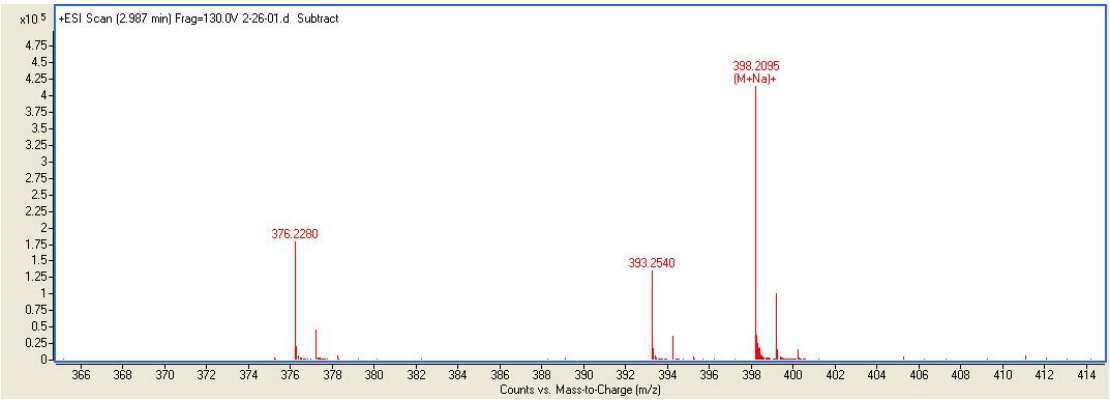
Experiment procedure using acetone-d_6: To a mixture of p *para*-quinone methides **1** (0.3 mmol), CuI (20 mol%), Zn dust (1.2 equv.), azo compound **2** (1.5 equiv.) was added actone-d_6 (2 mL, about 99.9% D-atom), and then H_2O (1.2 mmol). The

resulting solution was stirred at 100 °C under N_2 atmosphere (1 atm.) for 12 h. The solvent was evaporated under reduced pressure and the resulted mixture was filtered through a Florisil pad, diluted with Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The residue was purified by flash chromatography on silica gel (eluent: n-hexane/ethyl acetate) to afford the corresponding benzofuran-2(3*H*)-ones in a 60% yield. and then the characterization of the product thereby obtained was recorded on HRMS spectrometer. As showed in the HRMS spetra, no D-atom was introduced into the benzofuran-2(3*H*)-one **3aa**, which also suggests that H_2O in the reaction should act as the oxygen source.



HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
2-26-01	C25 H29 N O2	C25 H29 N Na O2	398.2095	398.2091	1.00



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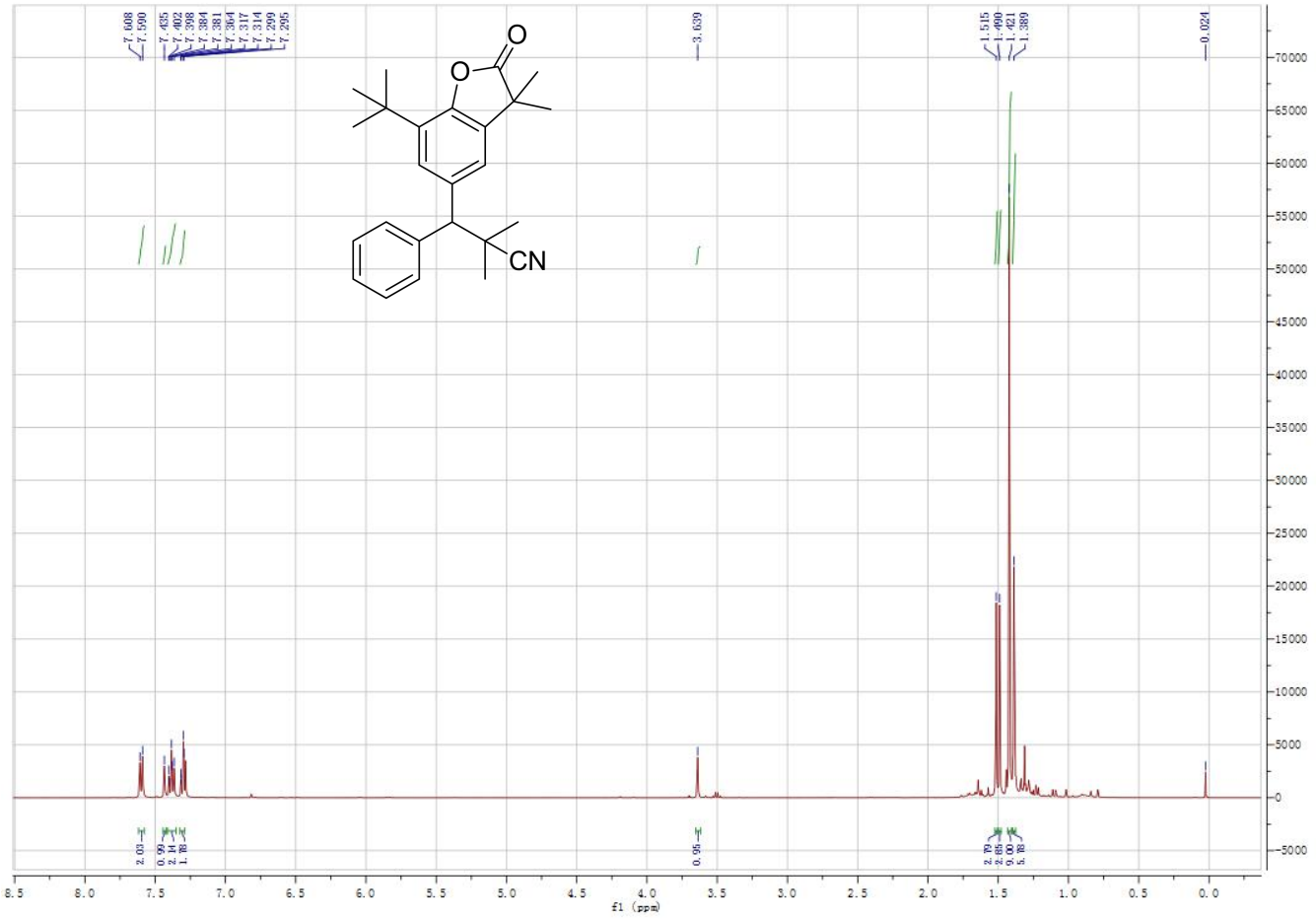
5 Copies of ^{1}H NMR and ^{13}C NMR spectra

3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-phenylpropanenitrile (3aa)



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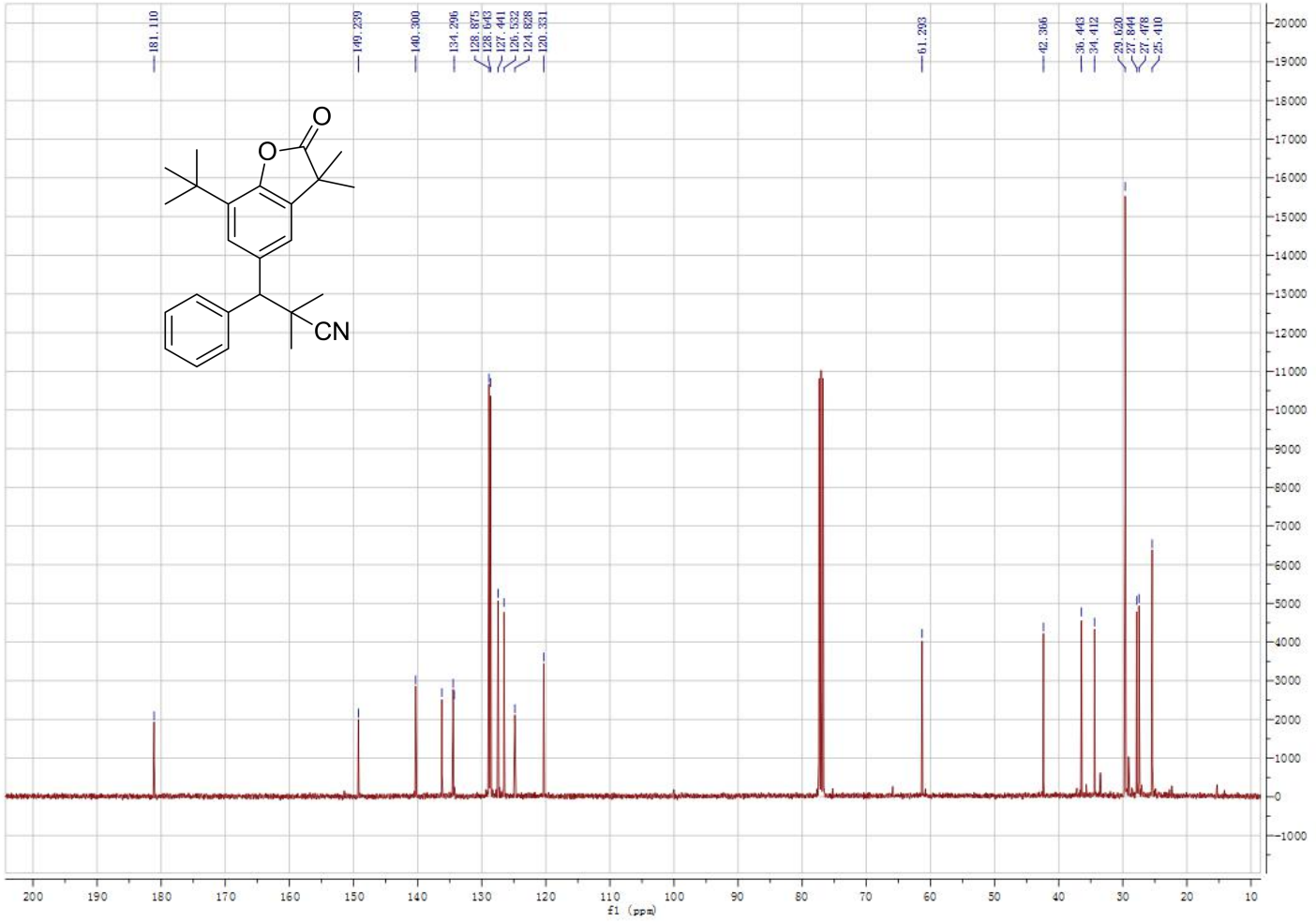
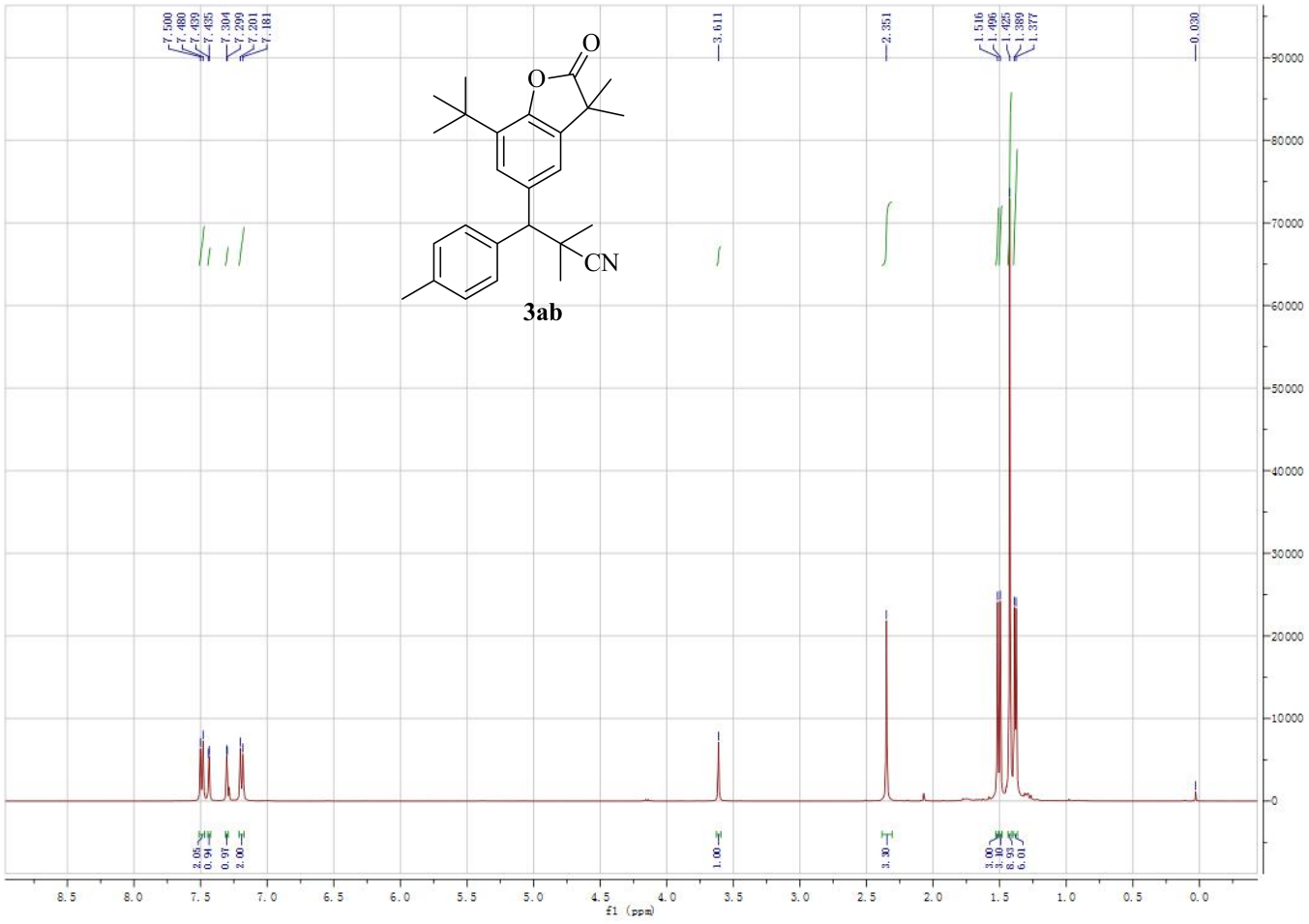


3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(p-tolyl)propanenitrile （3ab）



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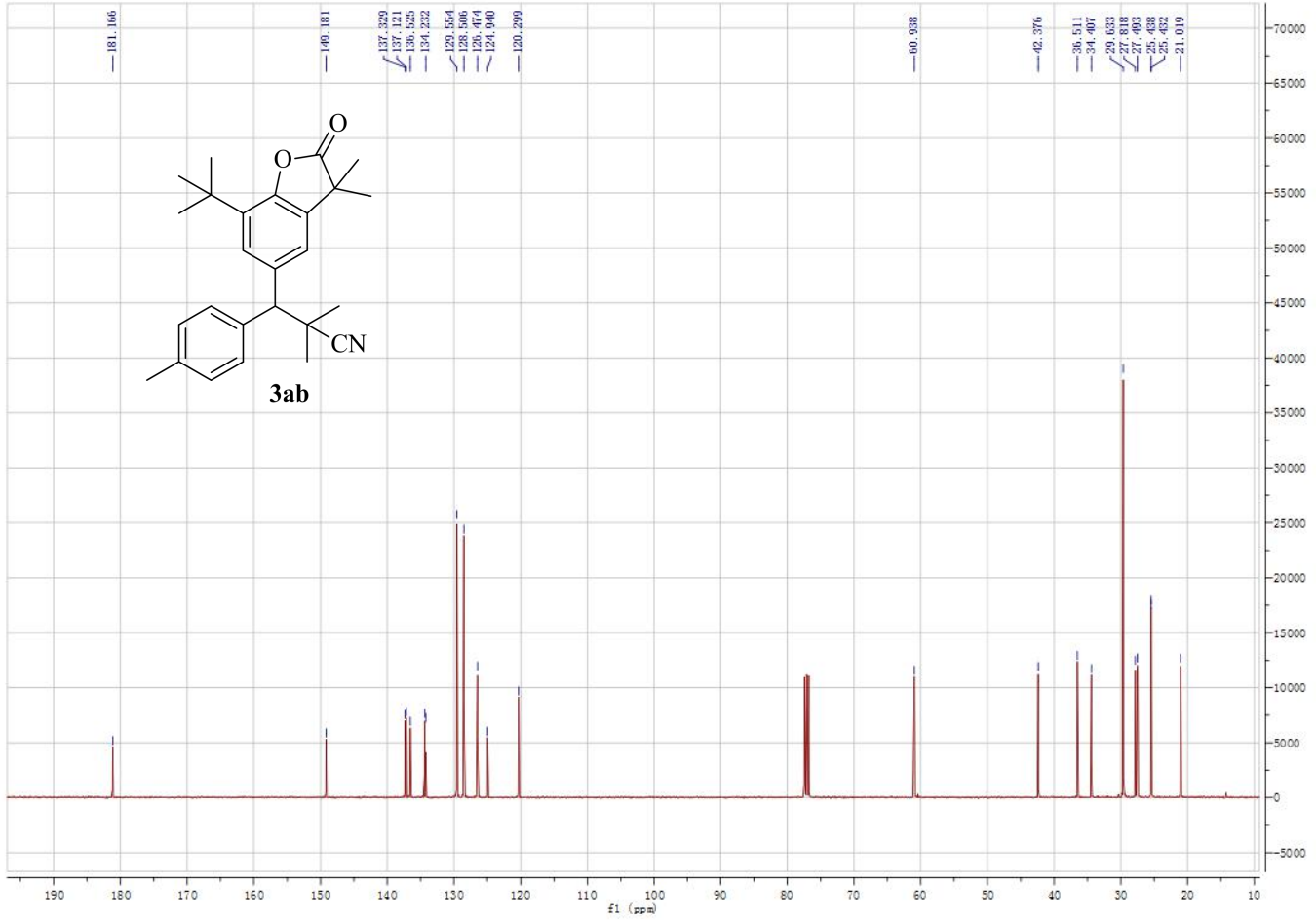

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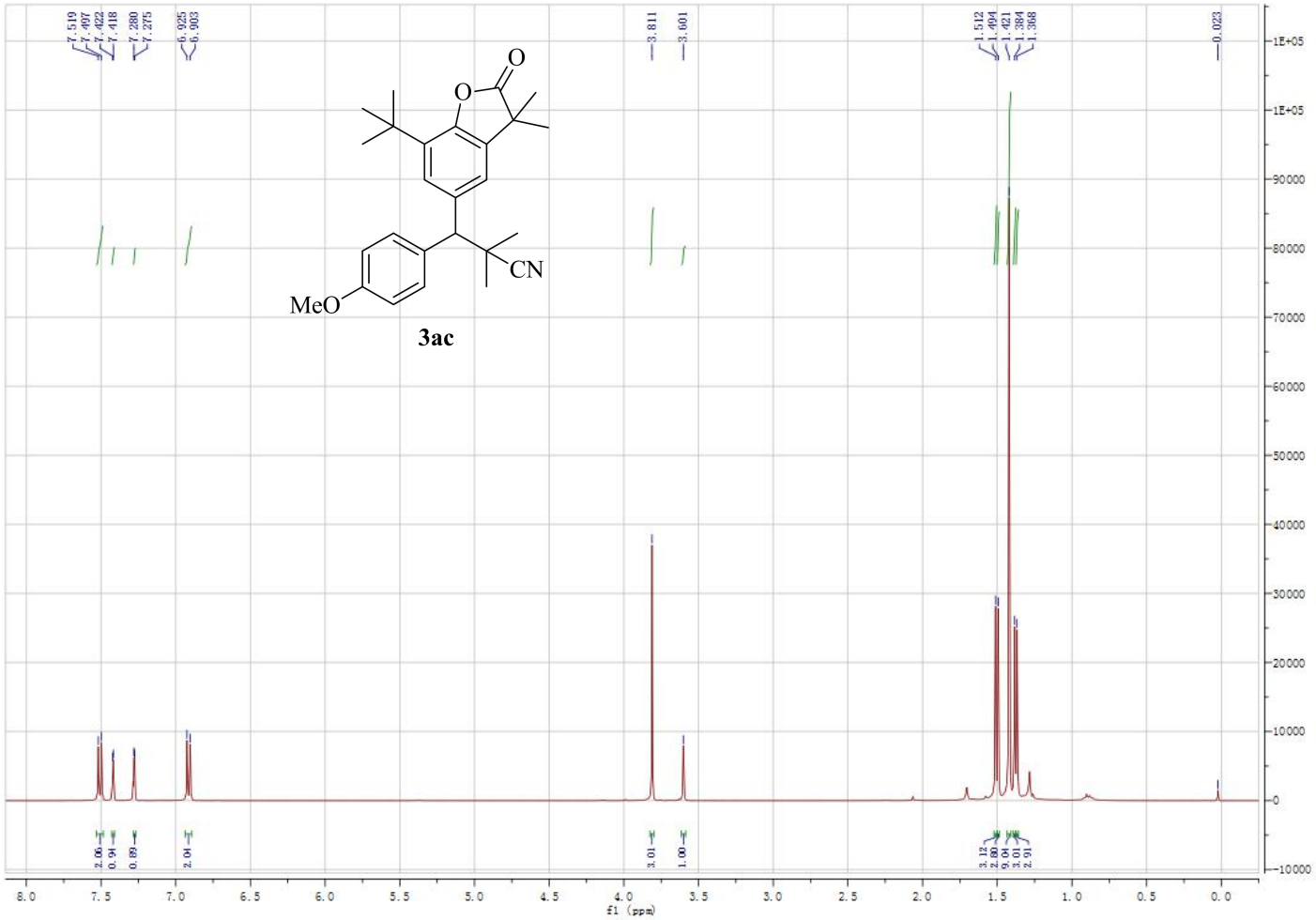

3ac

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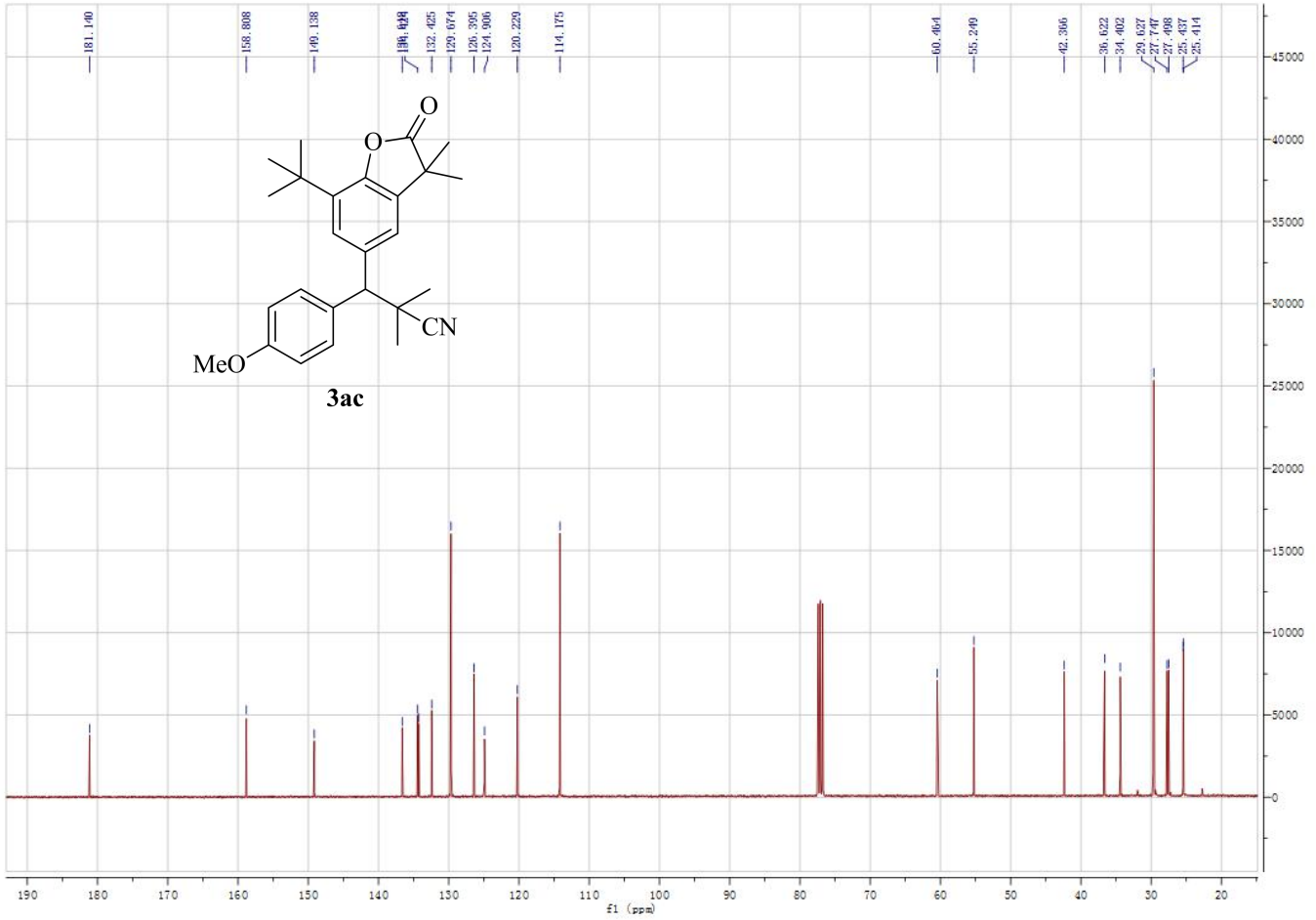

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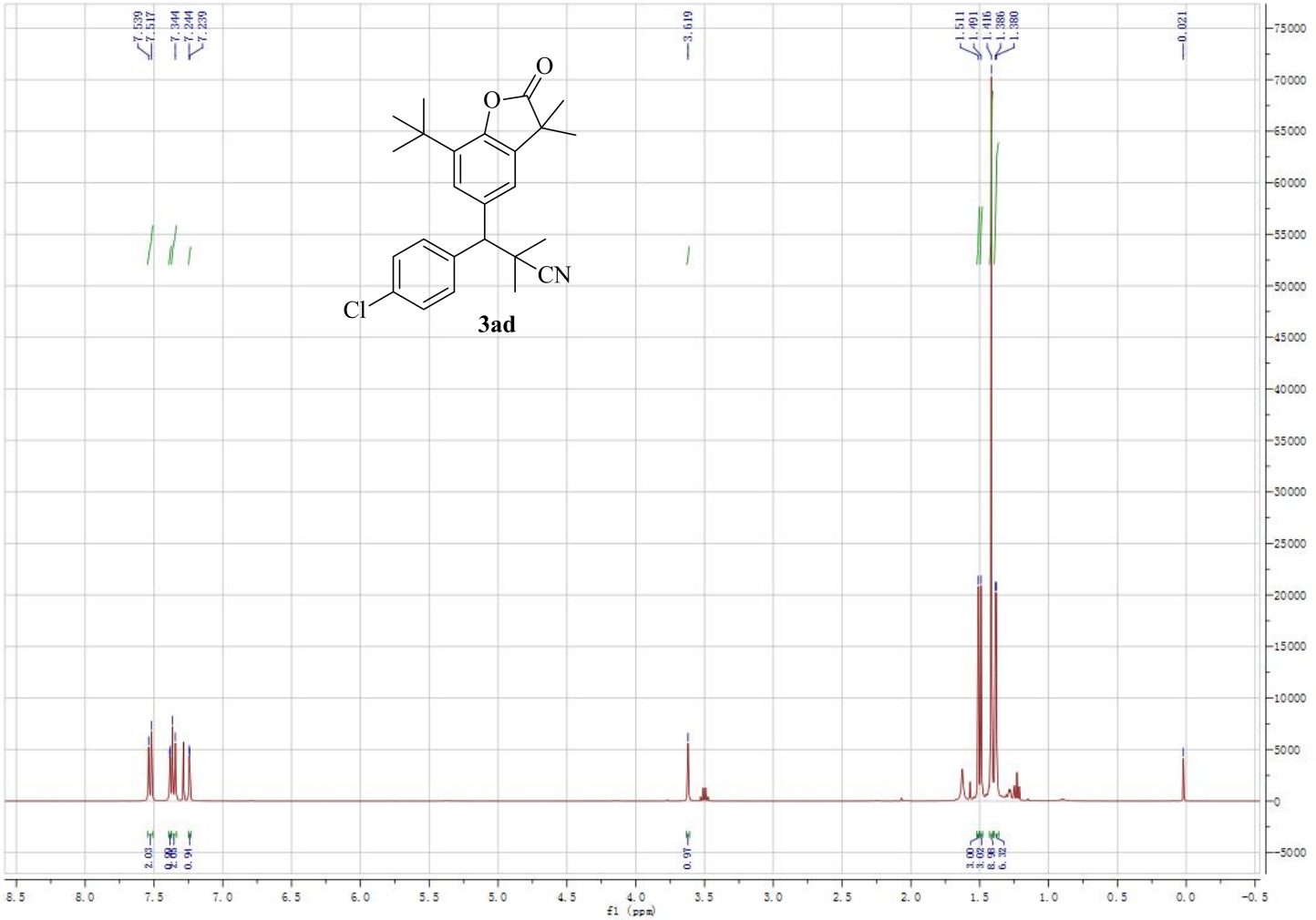

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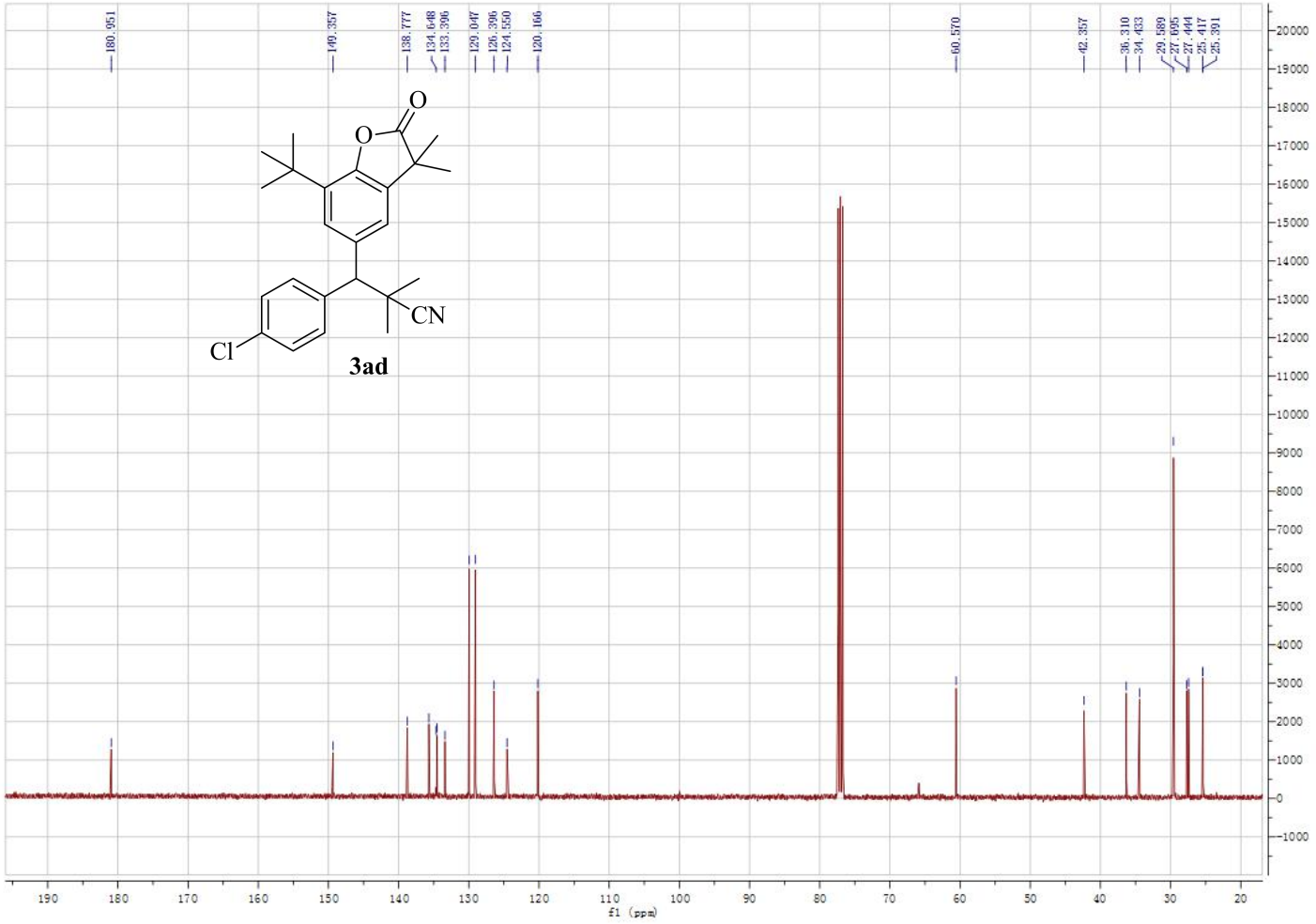

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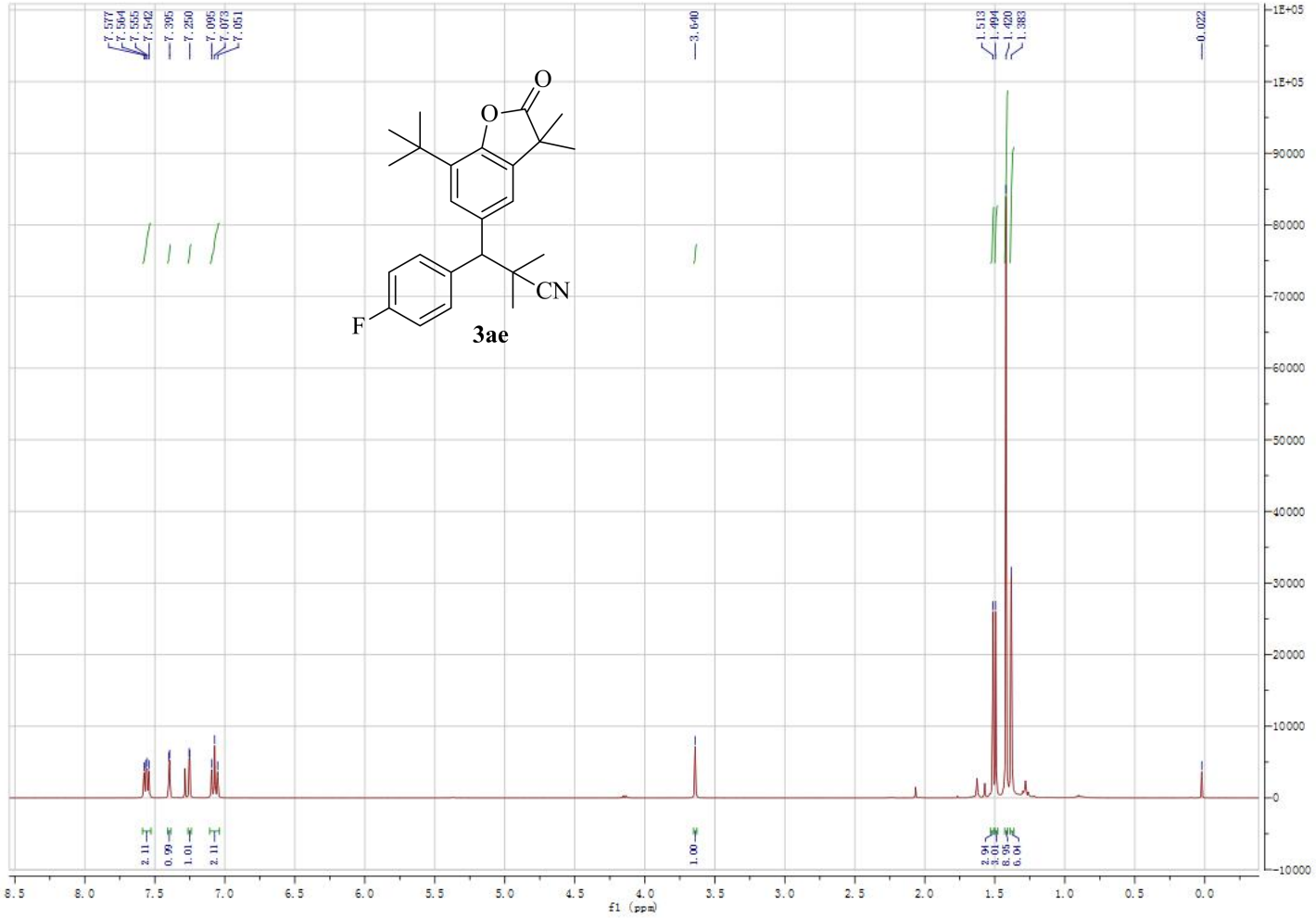

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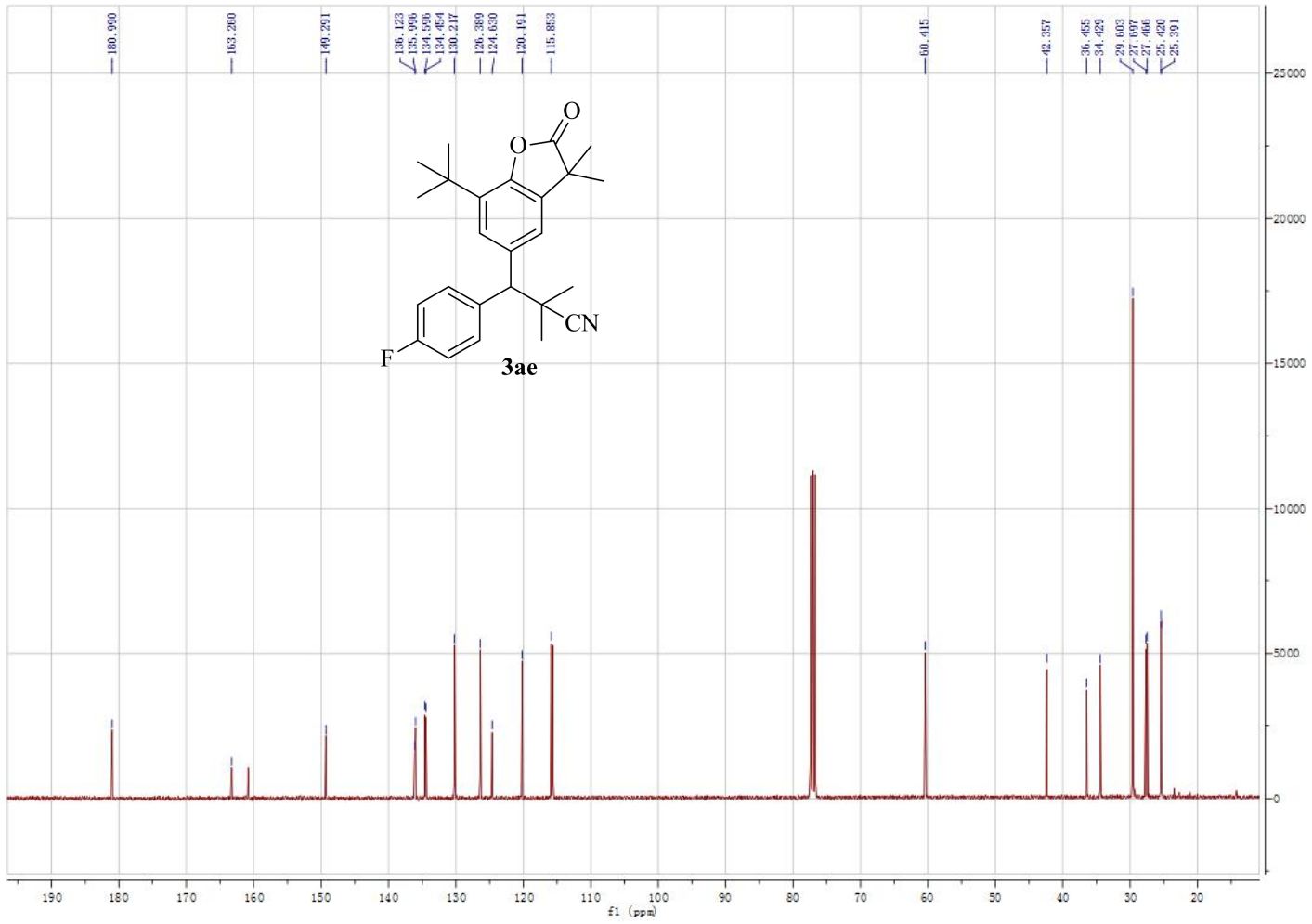

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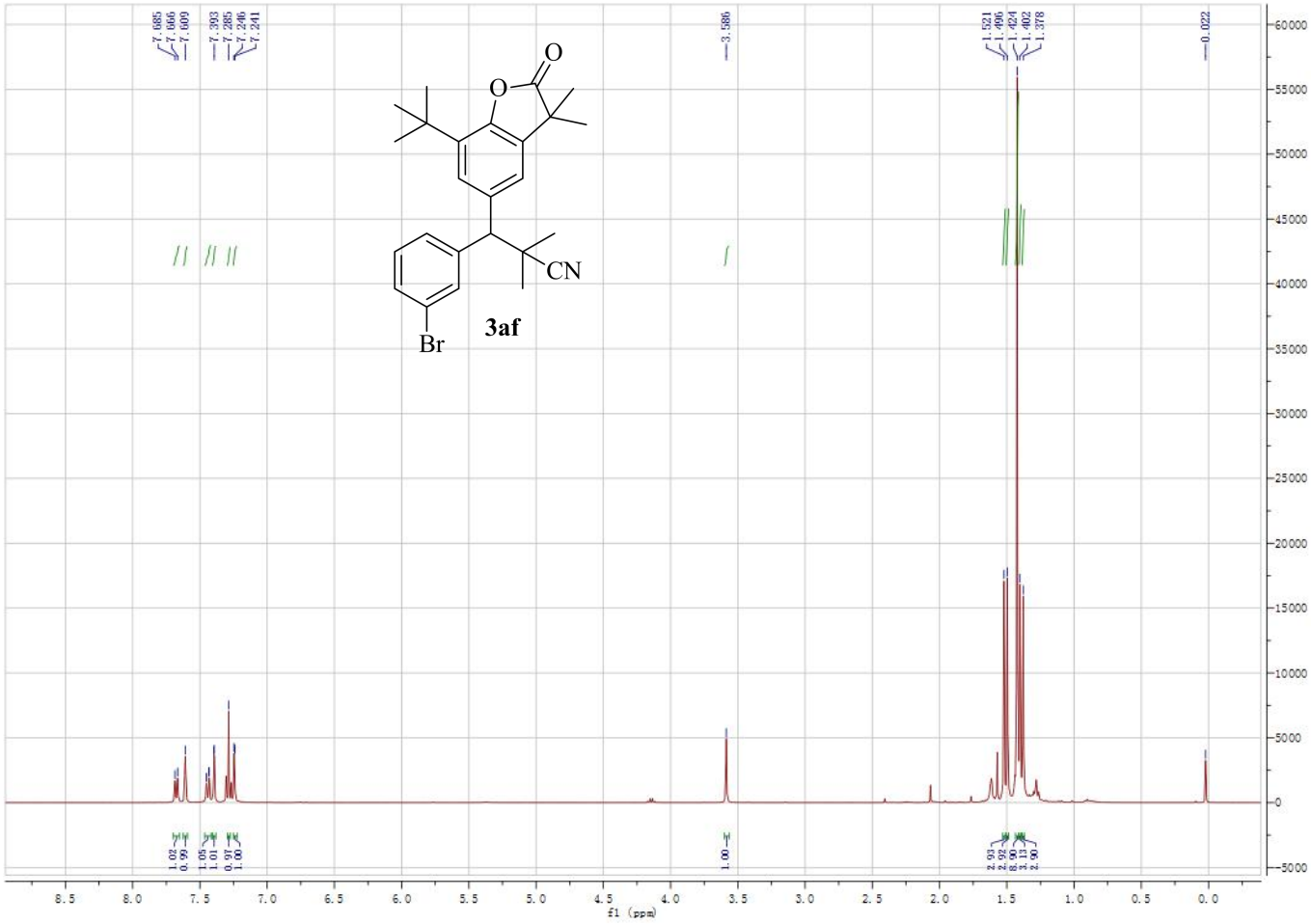

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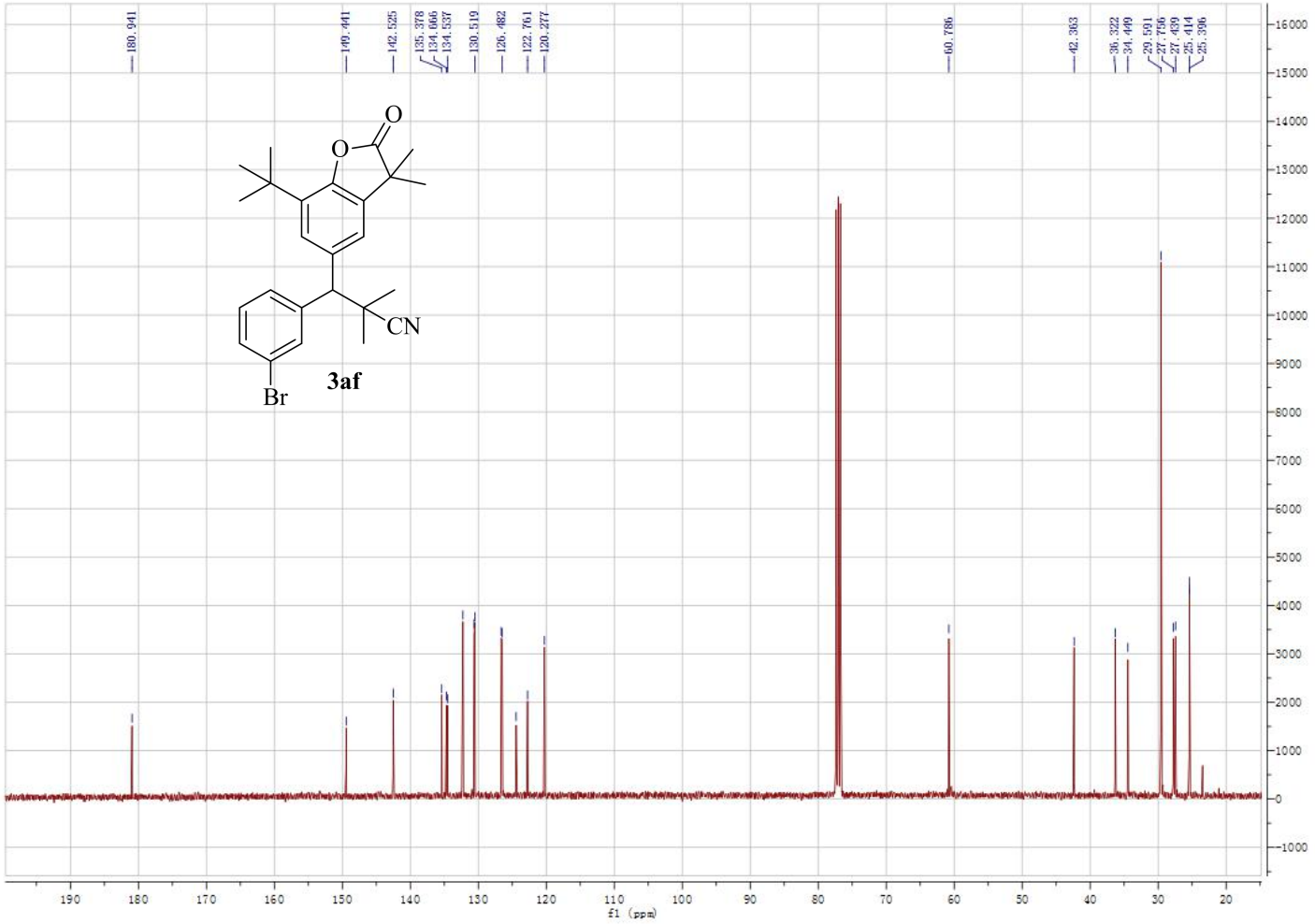
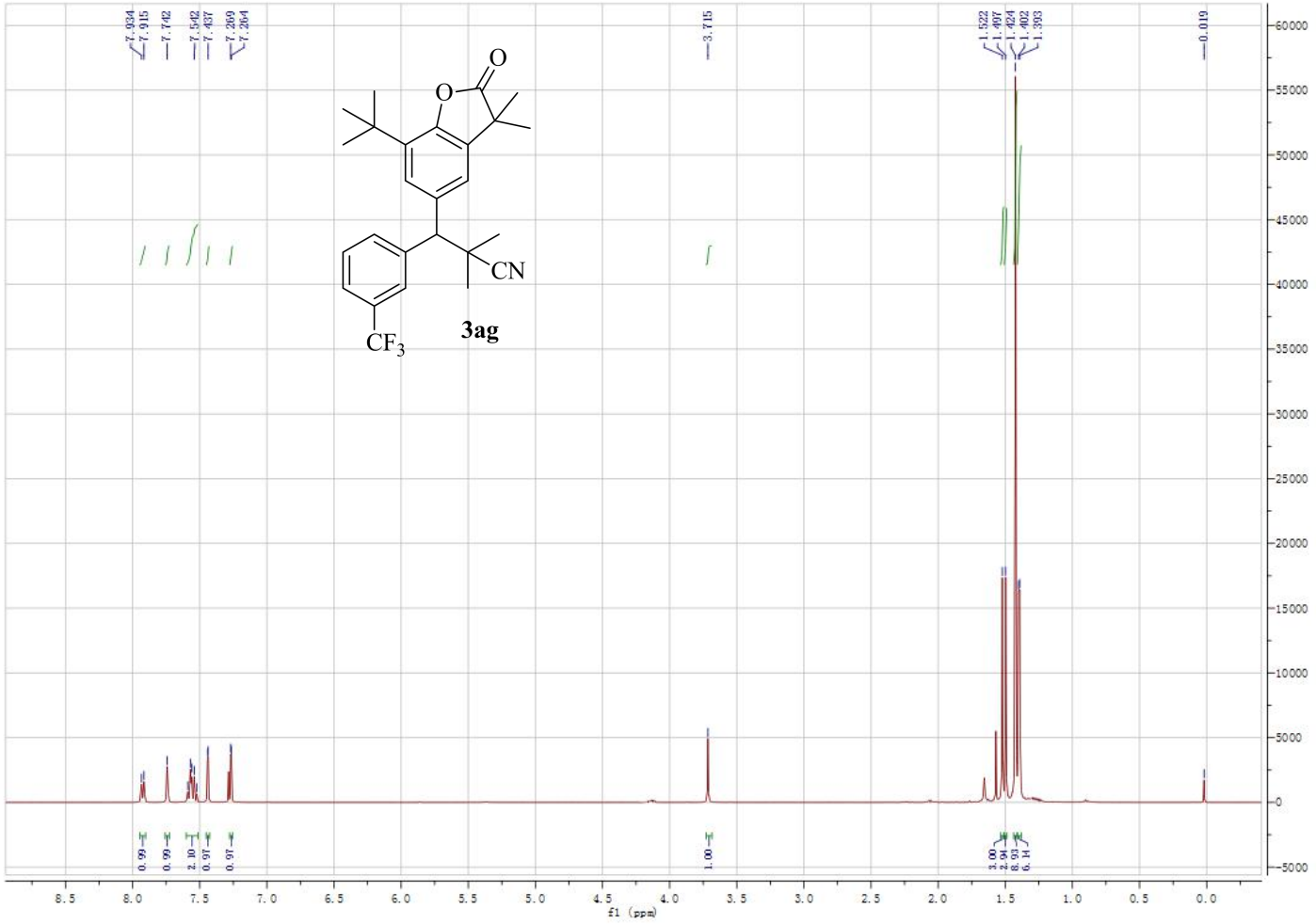
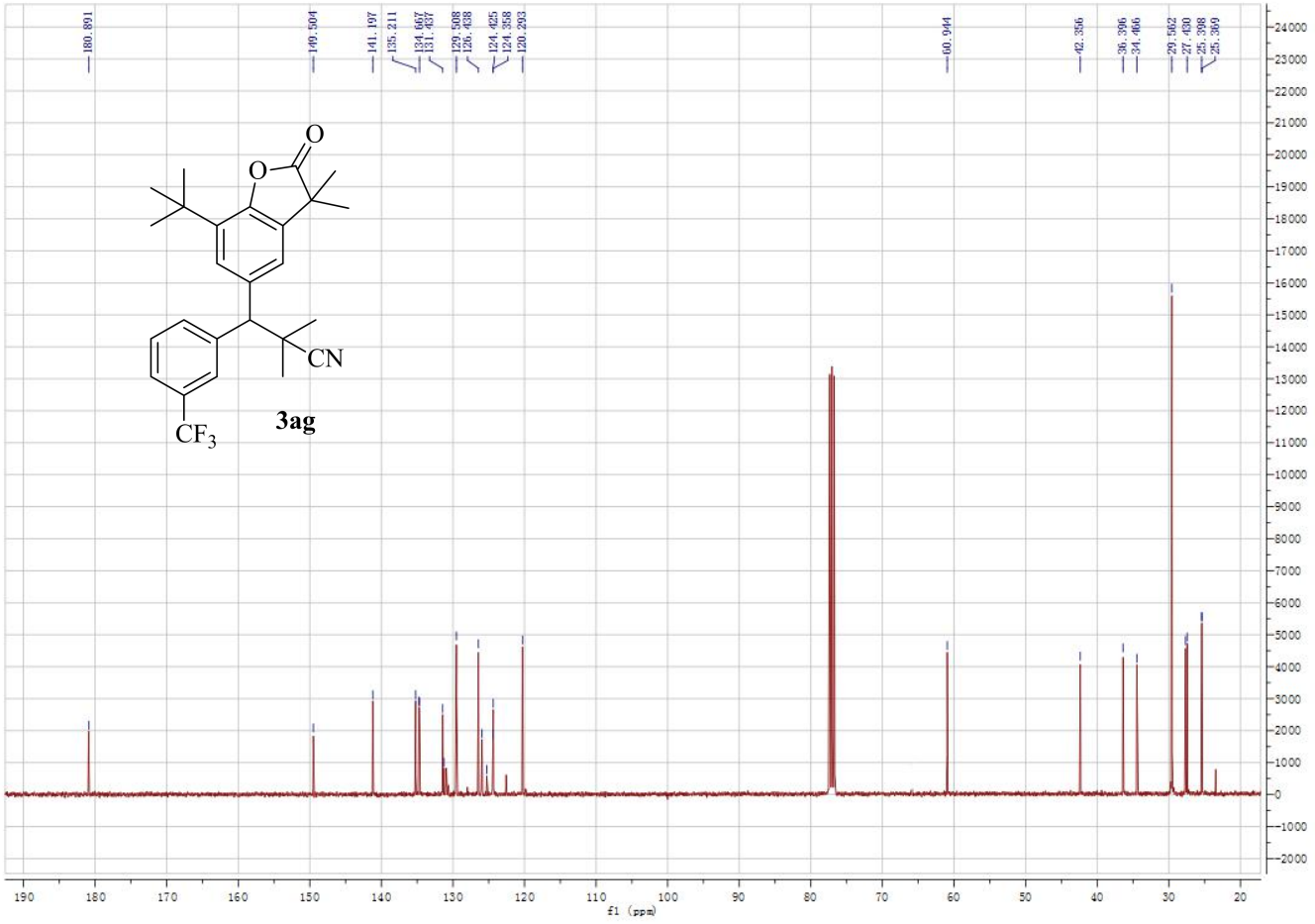


3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(3-(trifluoromethyl)phenyl)propanenitrile（3ag）



3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(3-(trifluoromethyl)phenyl)propanenitrile（3ag）



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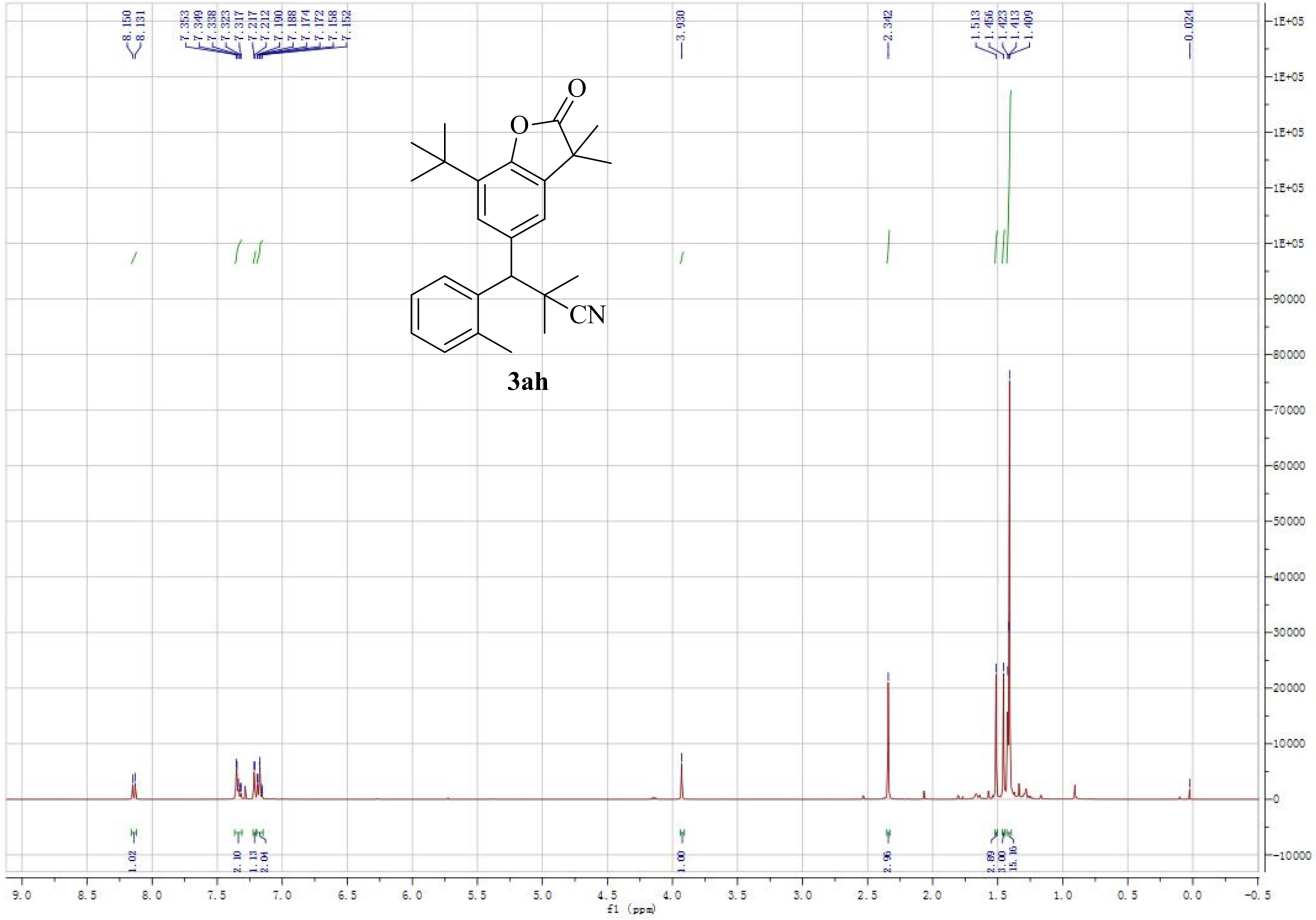

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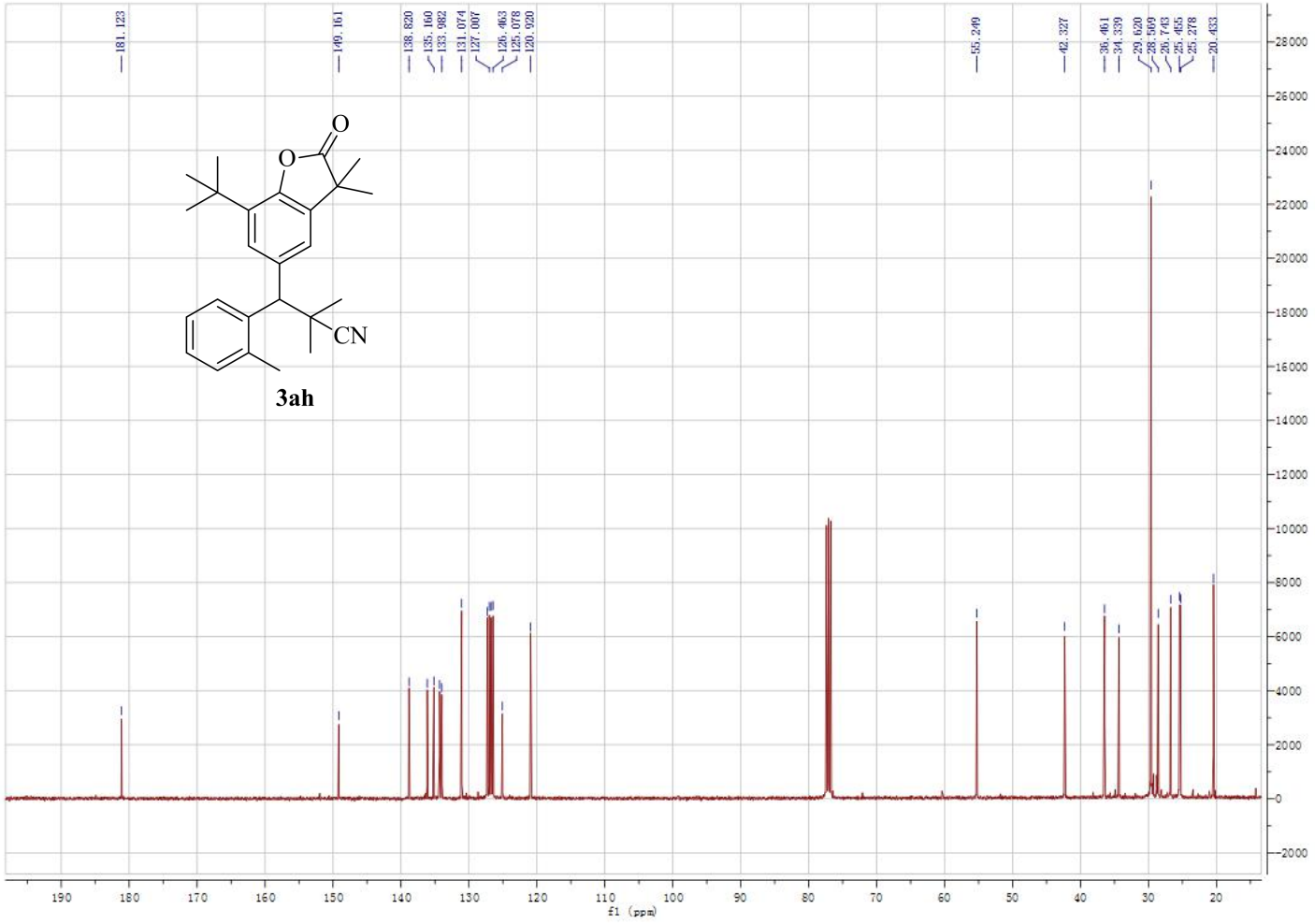
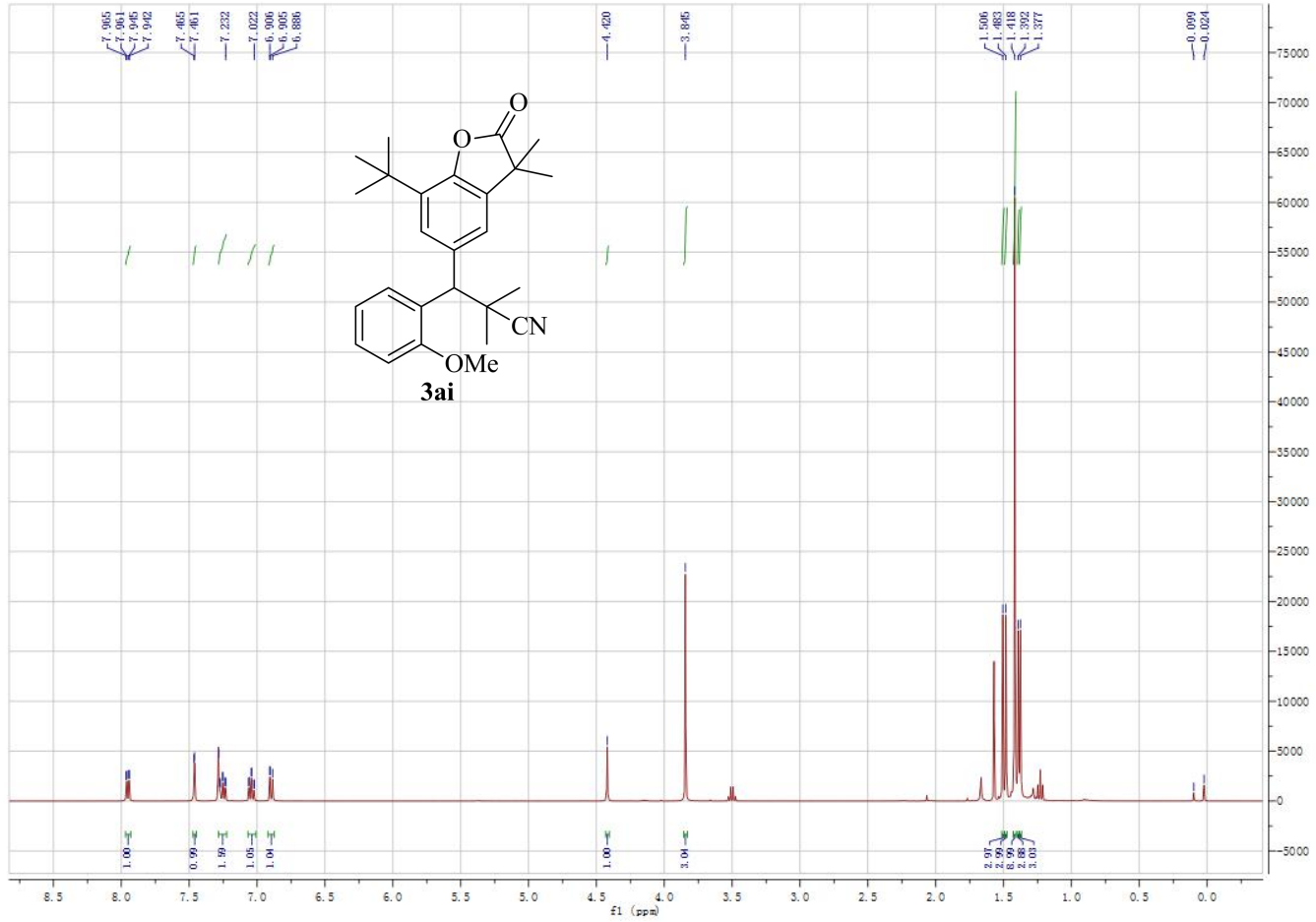
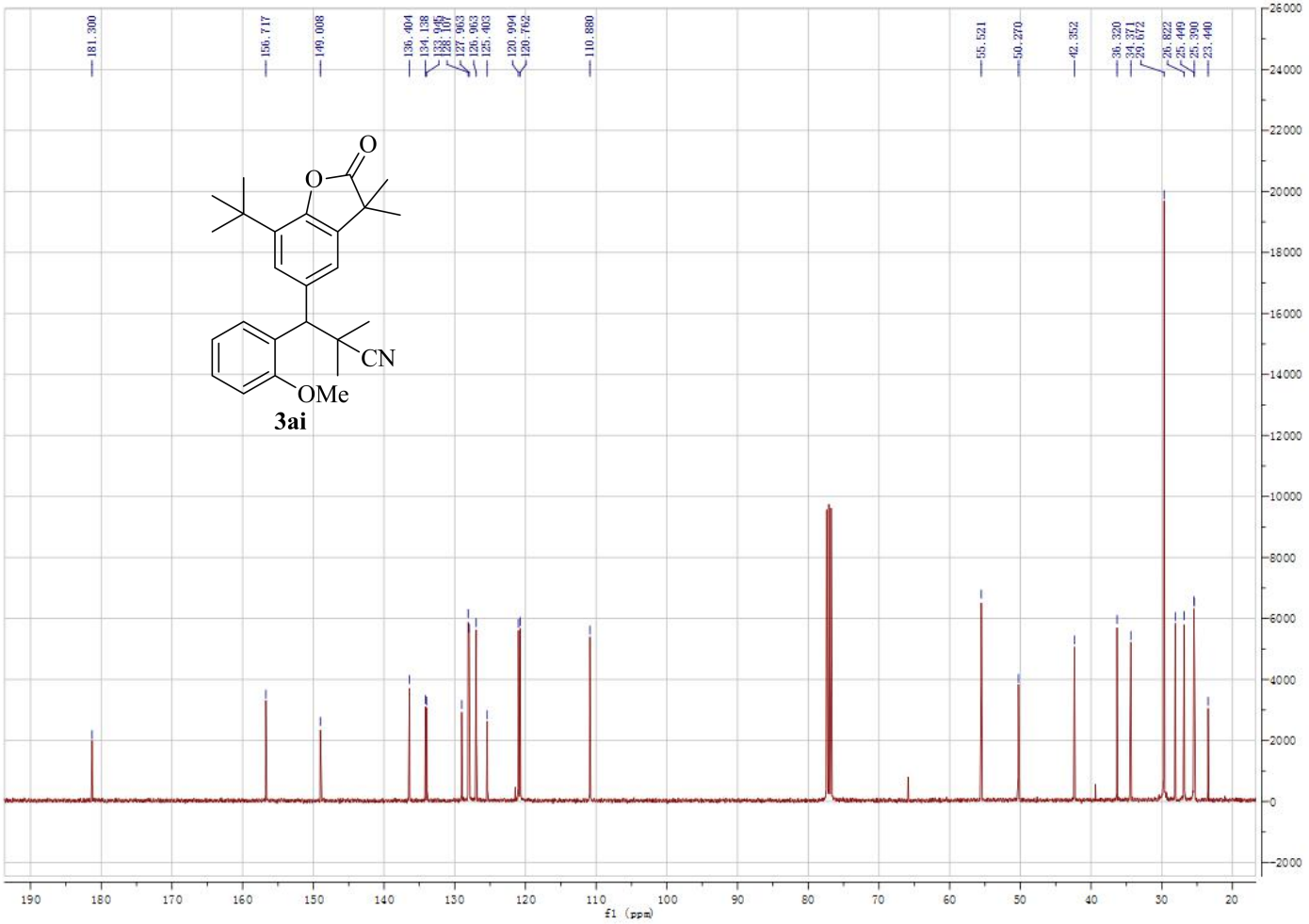


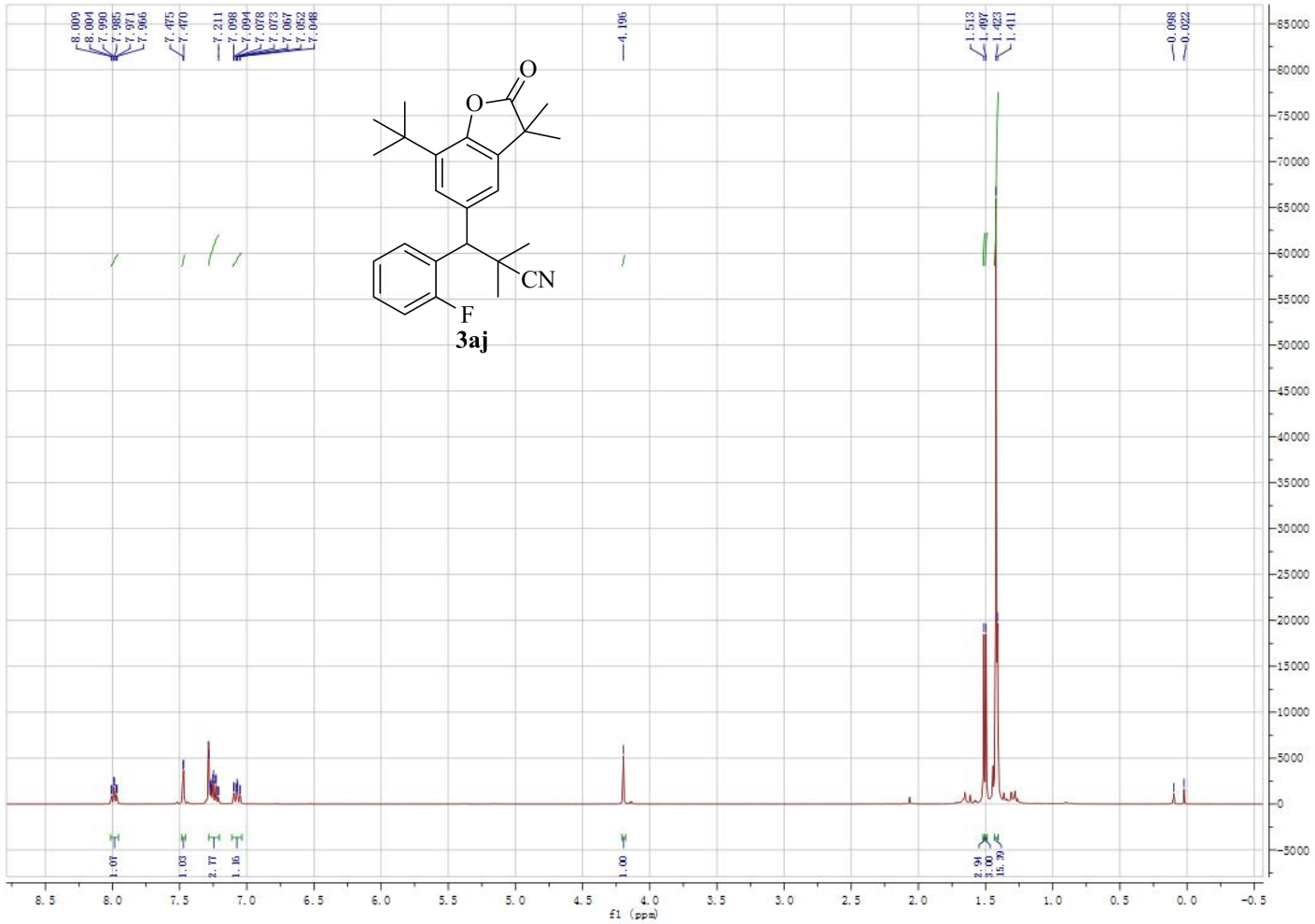
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(2-methoxyphenyl)-2,2-dimethylpropanenitrile (3ai)



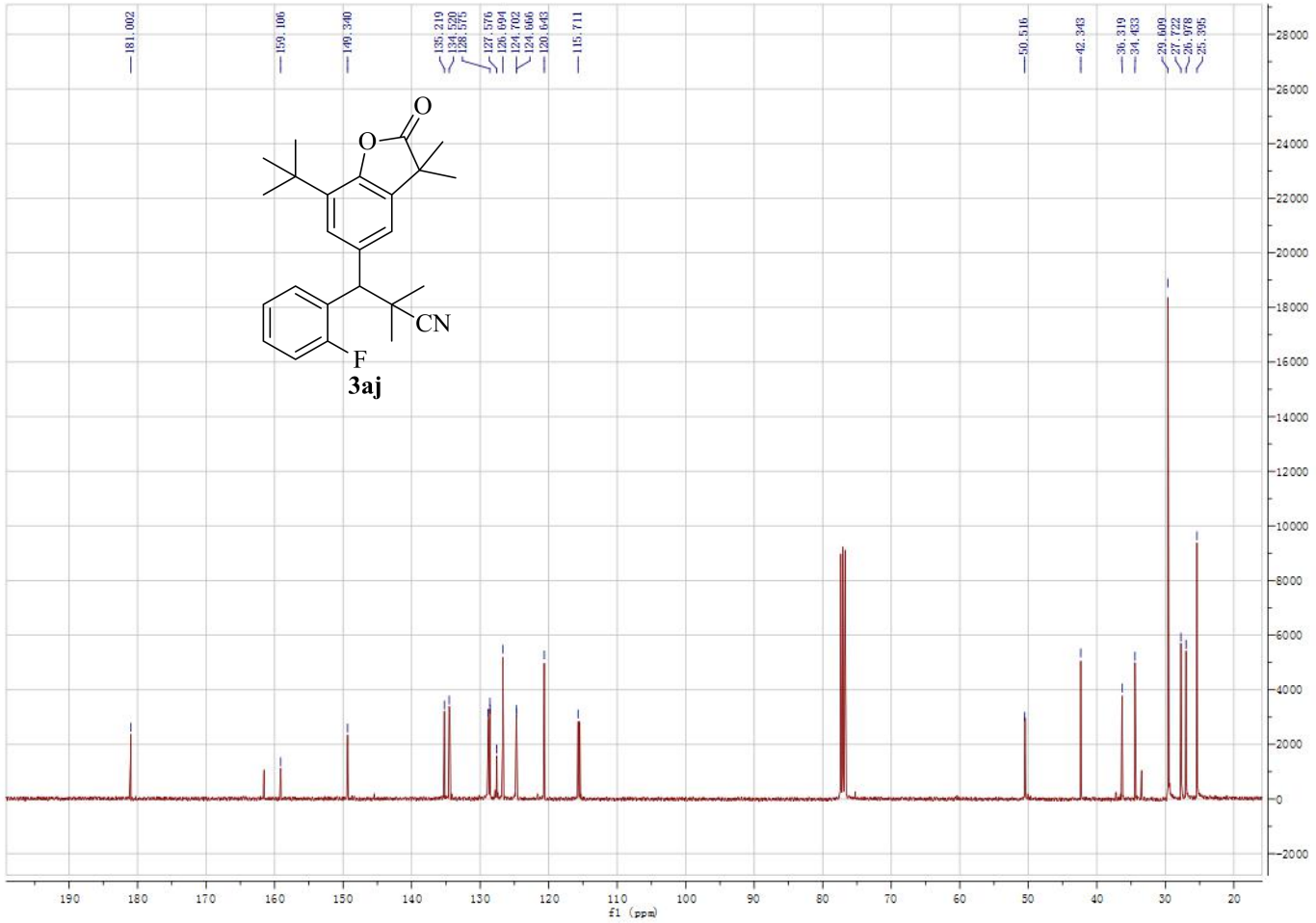
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(2-methoxyphenyl)-2,2-dimethylpropanenitrile (3ai)



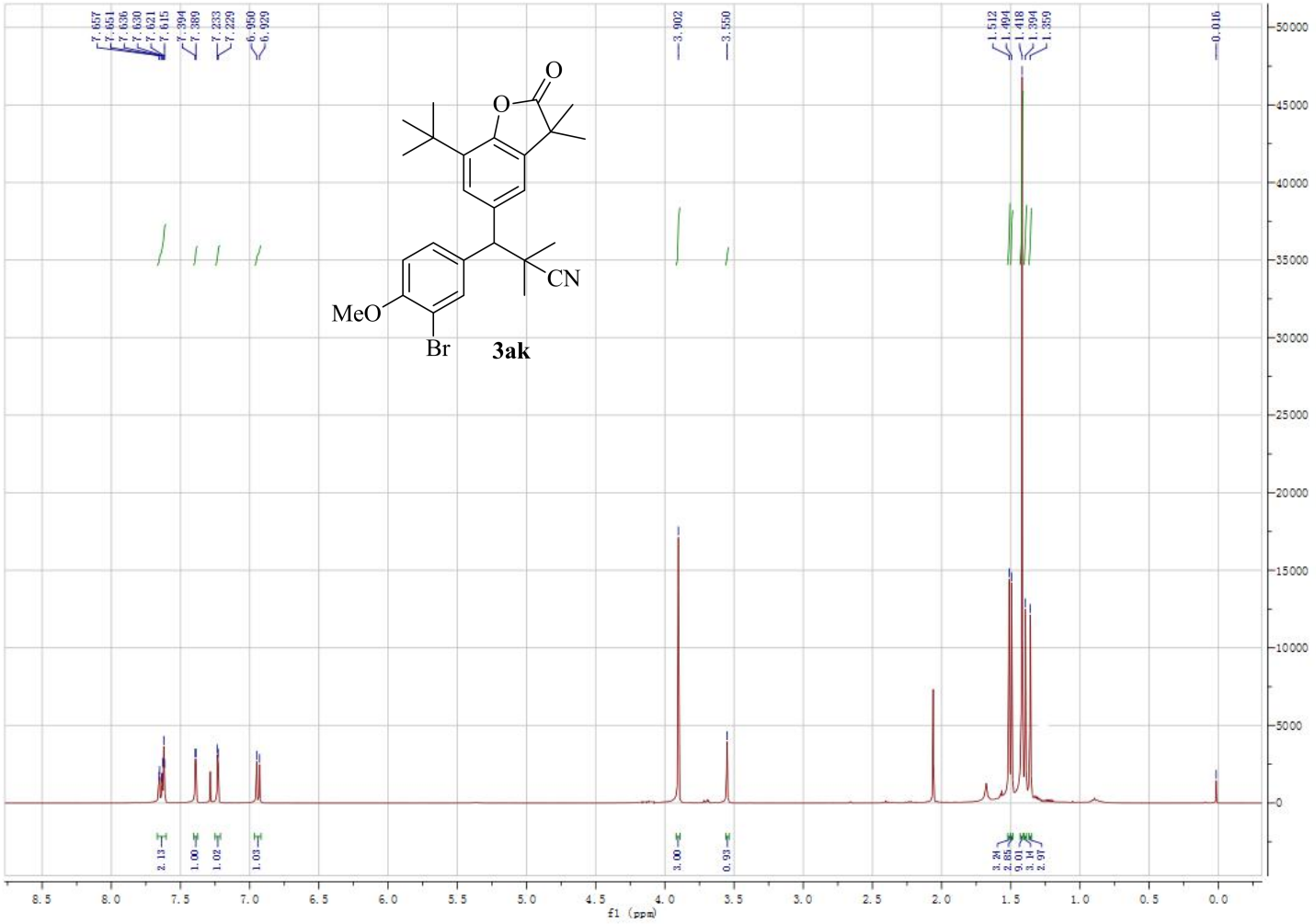
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(2-fluorophenyl)-2,2-dimethylpropanenitrile (3aj)



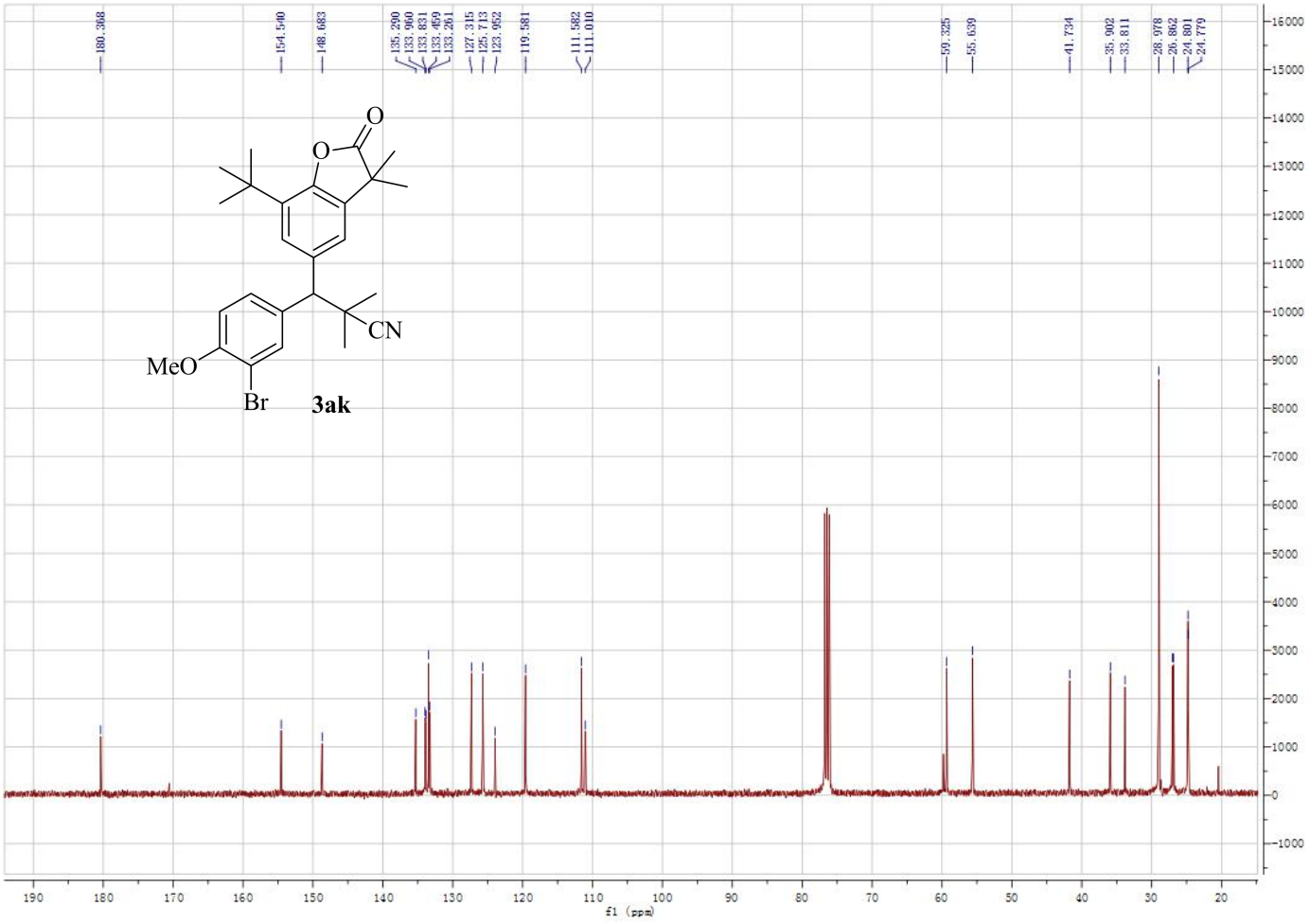
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(2-fluorophenyl)-2,2-dimethylpropanenitrile (3aj)



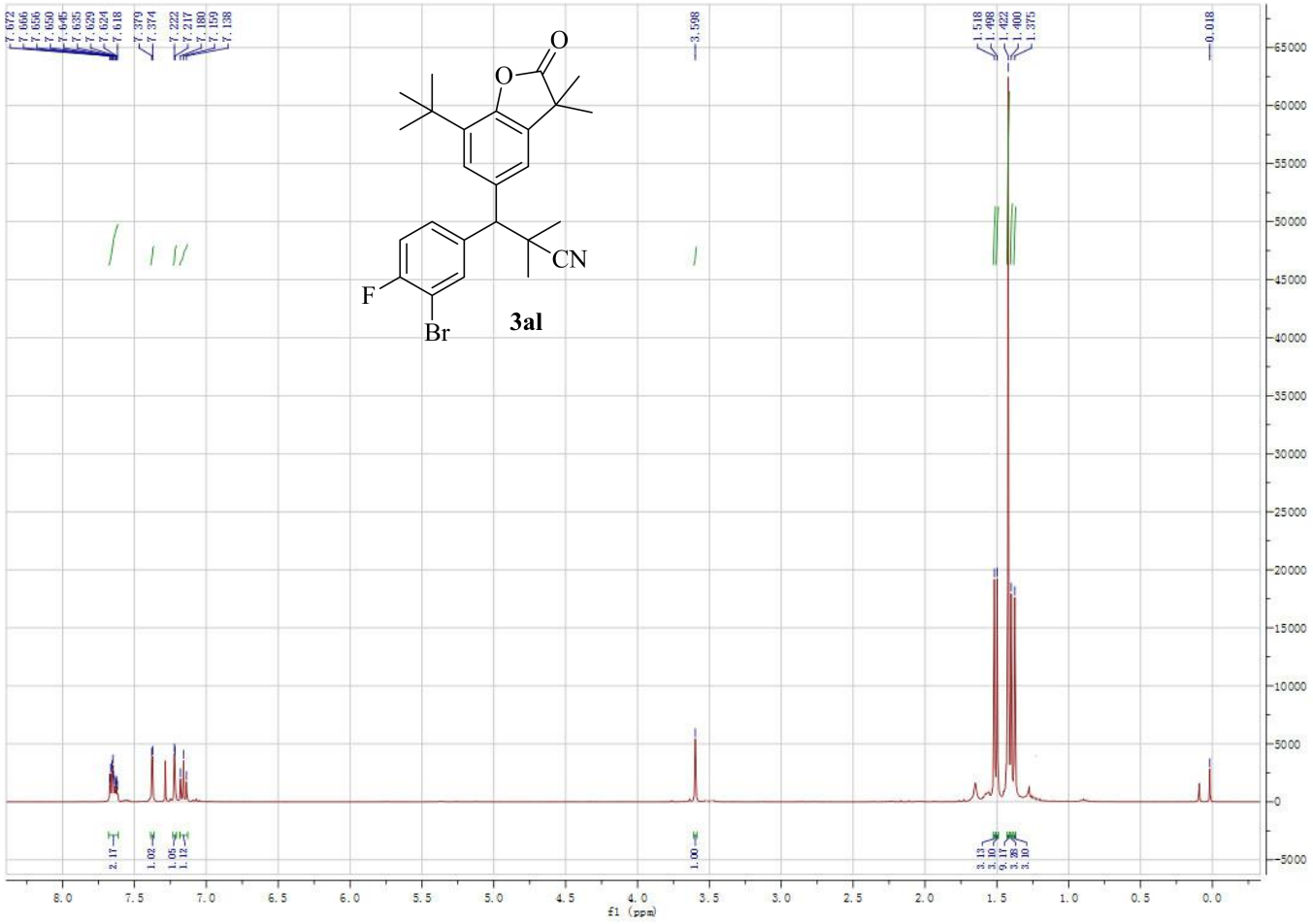
3-(3-bromo-4-methoxyphenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile（3ak）



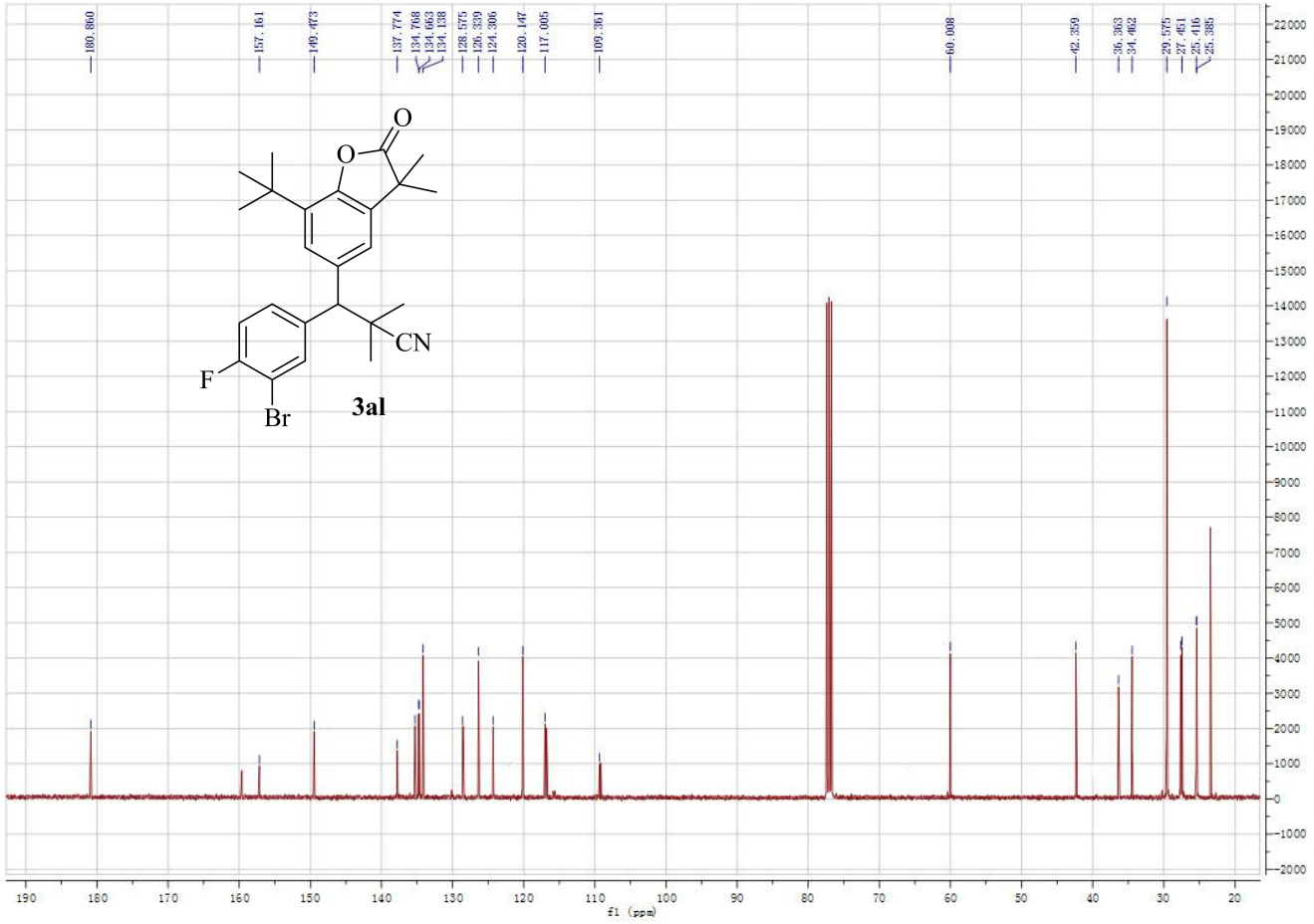
3-(3-bromo-4-methoxyphenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile（3ak）



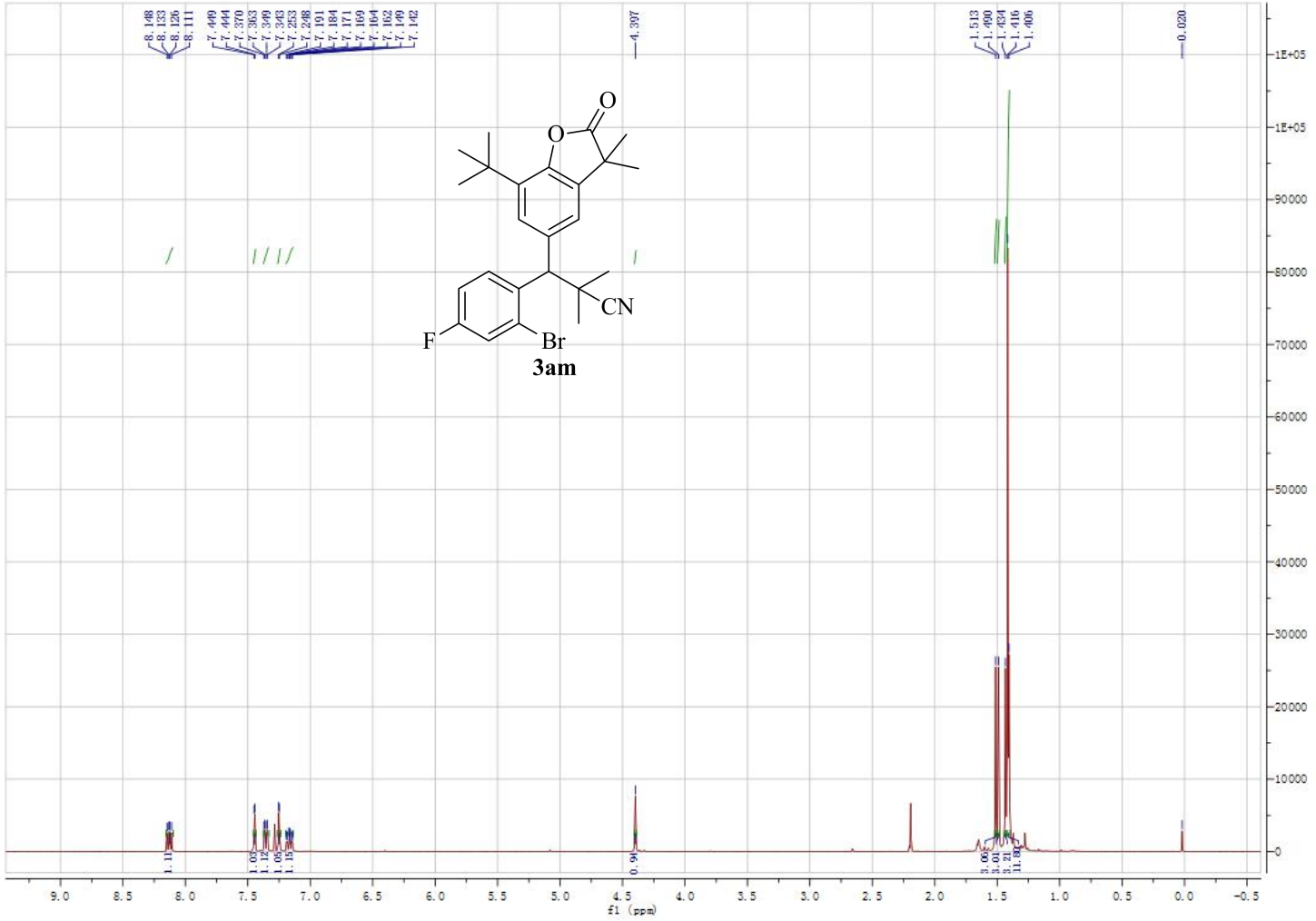
3-(3-bromo-4-fluorophenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile （3al）



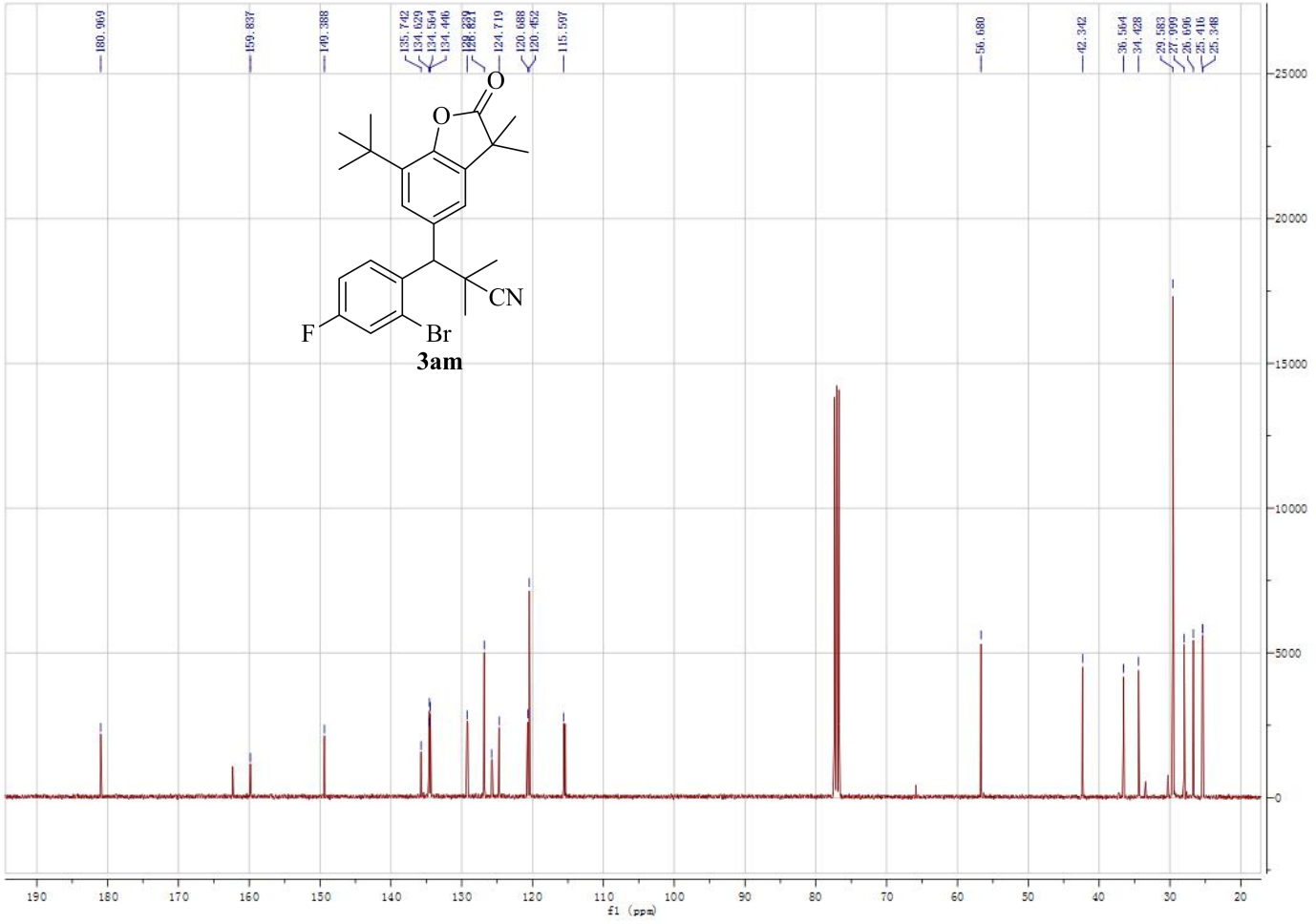
3-(3-bromo-4-fluorophenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile （3al）



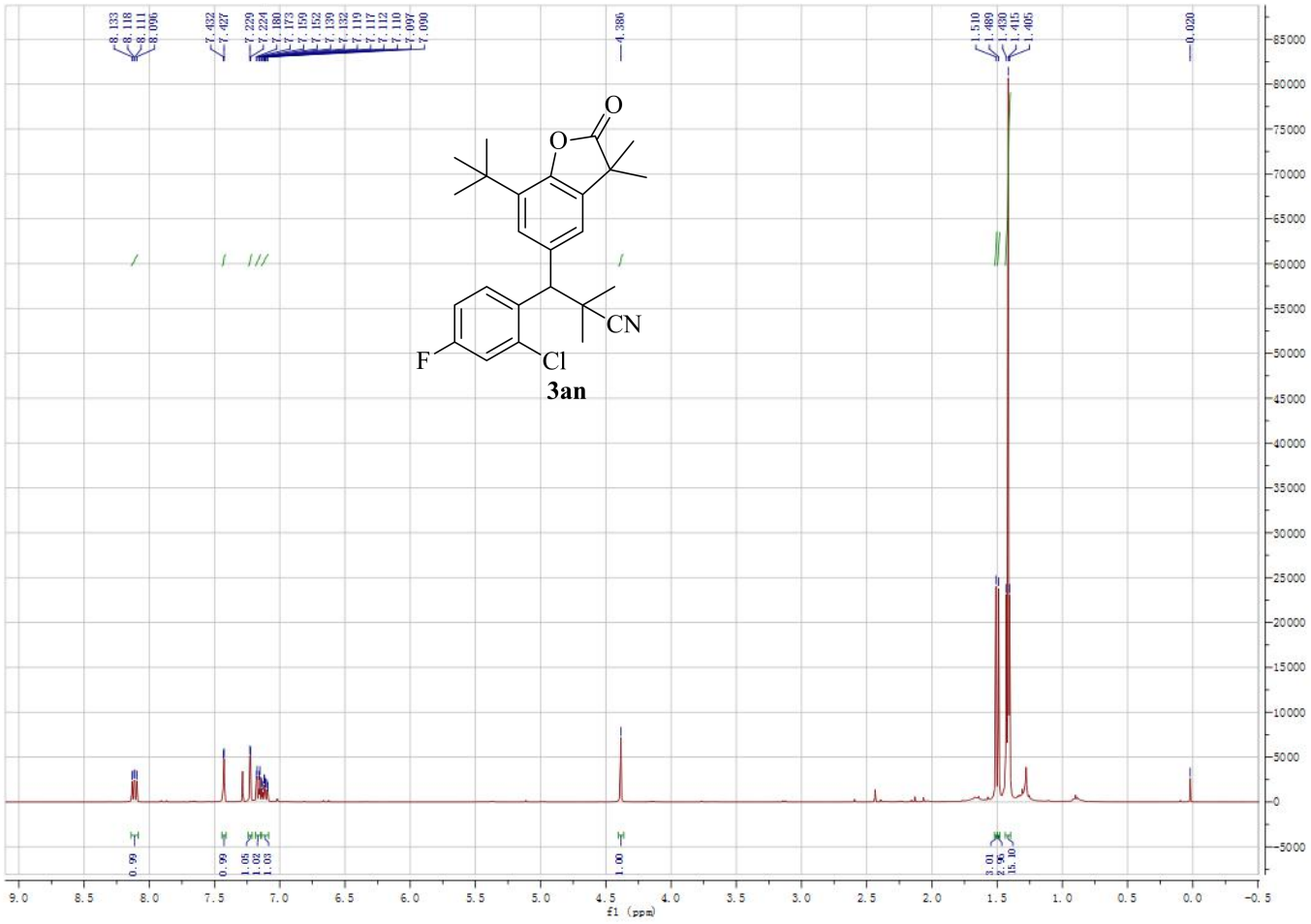
3-(2-bromo-4-fluorophenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile (3am)



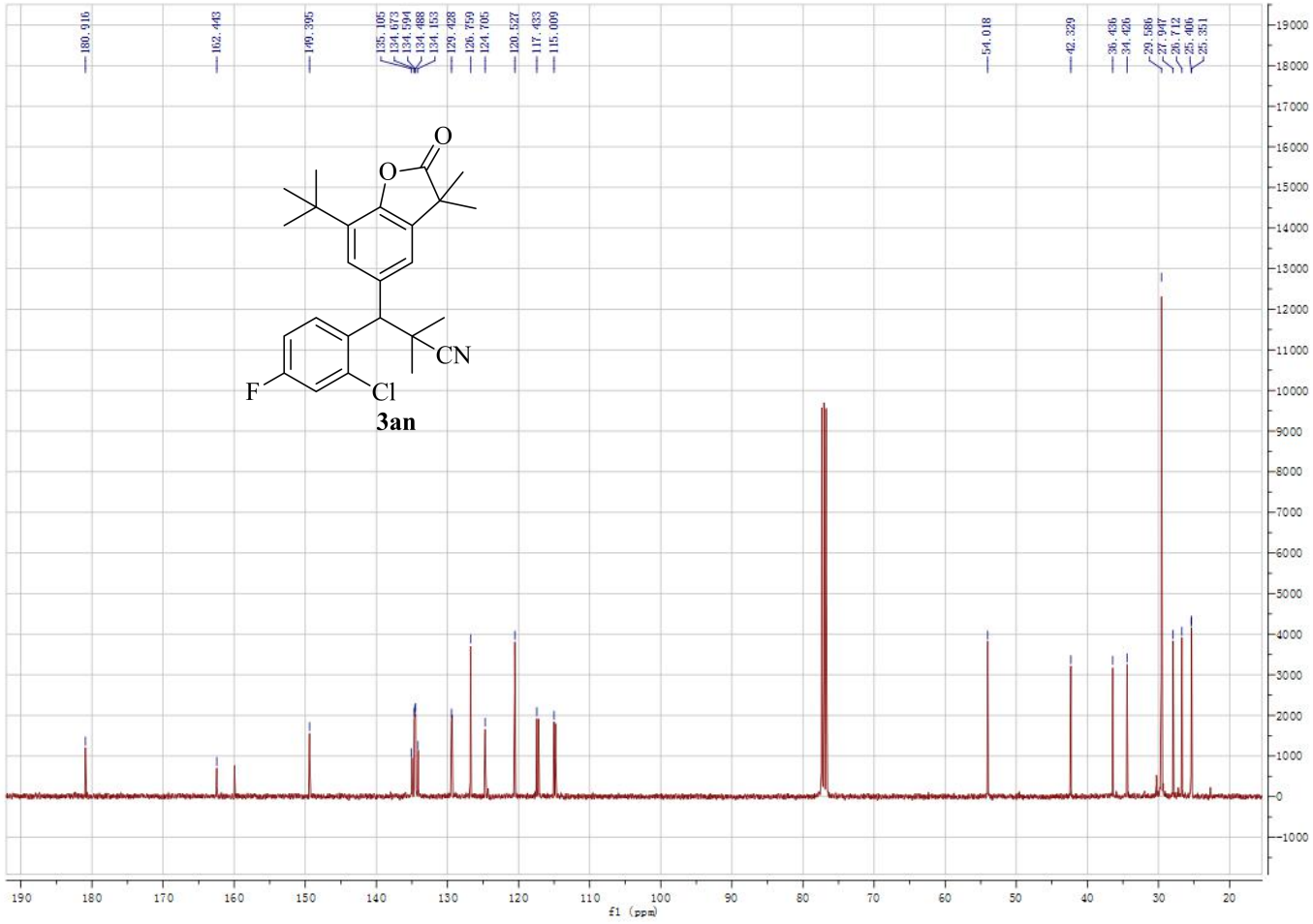
3-(2-bromo-4-fluorophenyl)-3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile (3am)



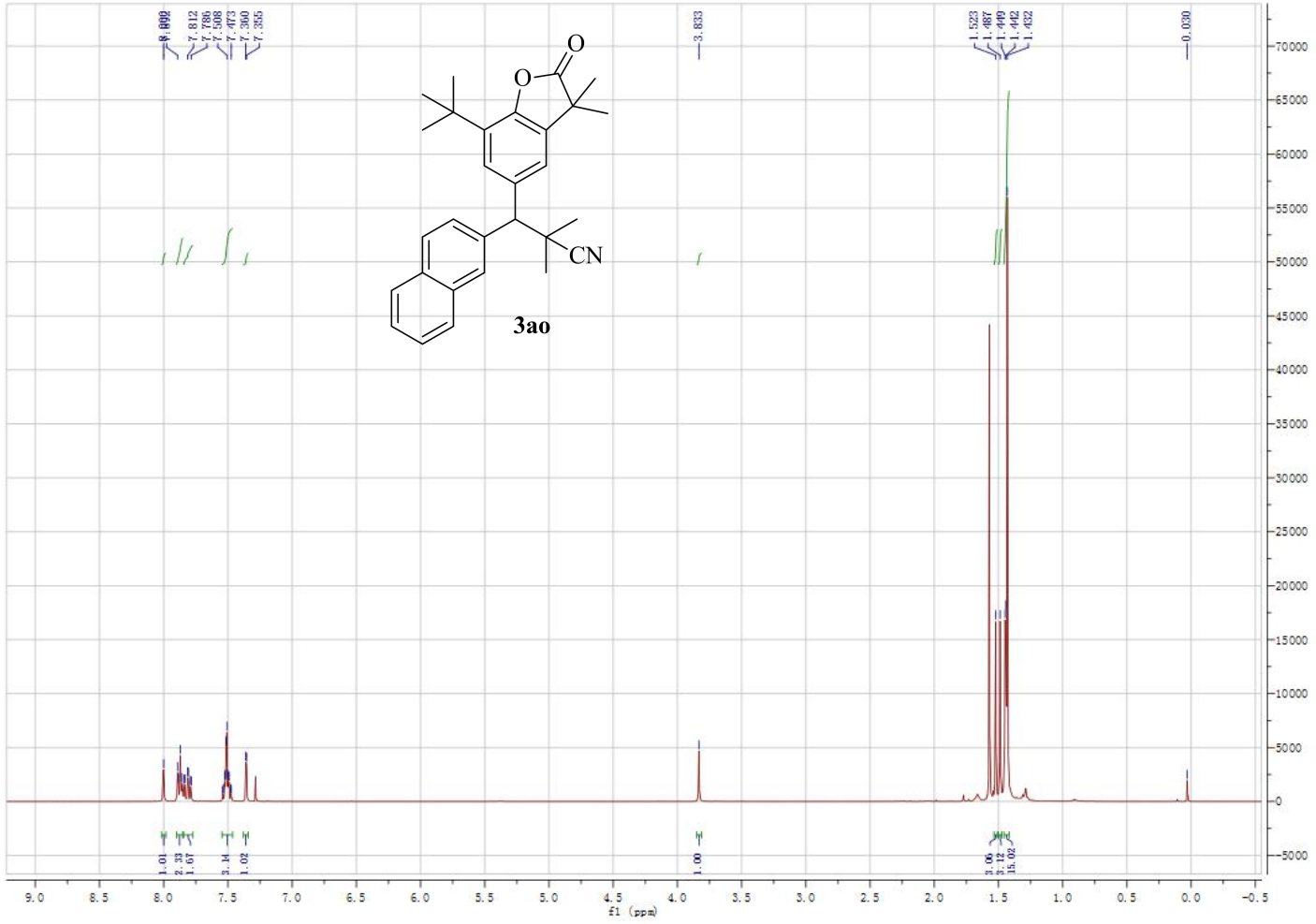
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(2-chloro-4-fluorophenyl)-2,2-dimethylpropanenitrile （3an）



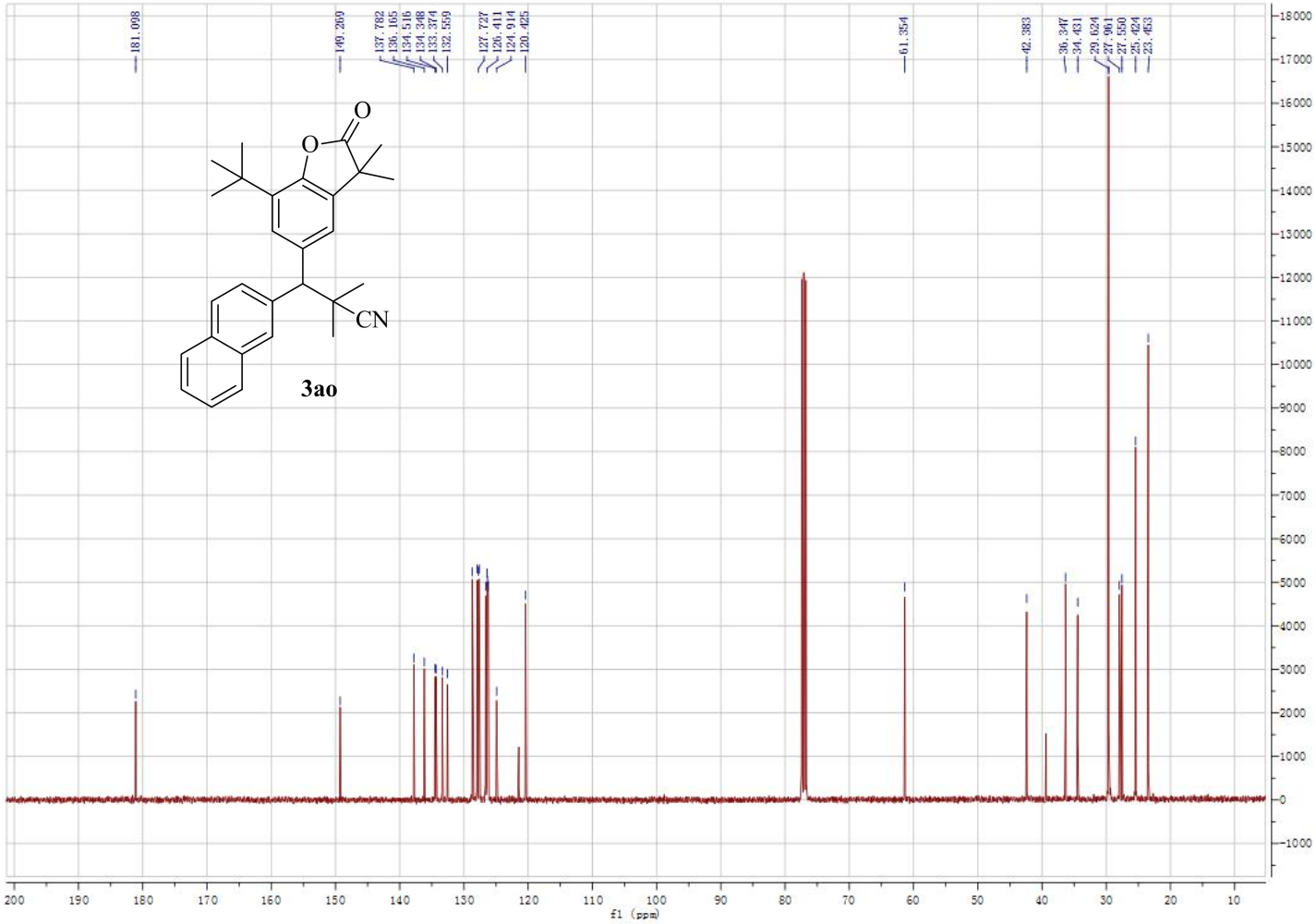
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-3-(2-chloro-4-fluorophenyl)-2,2-dimethylpropanenitrile （3an）



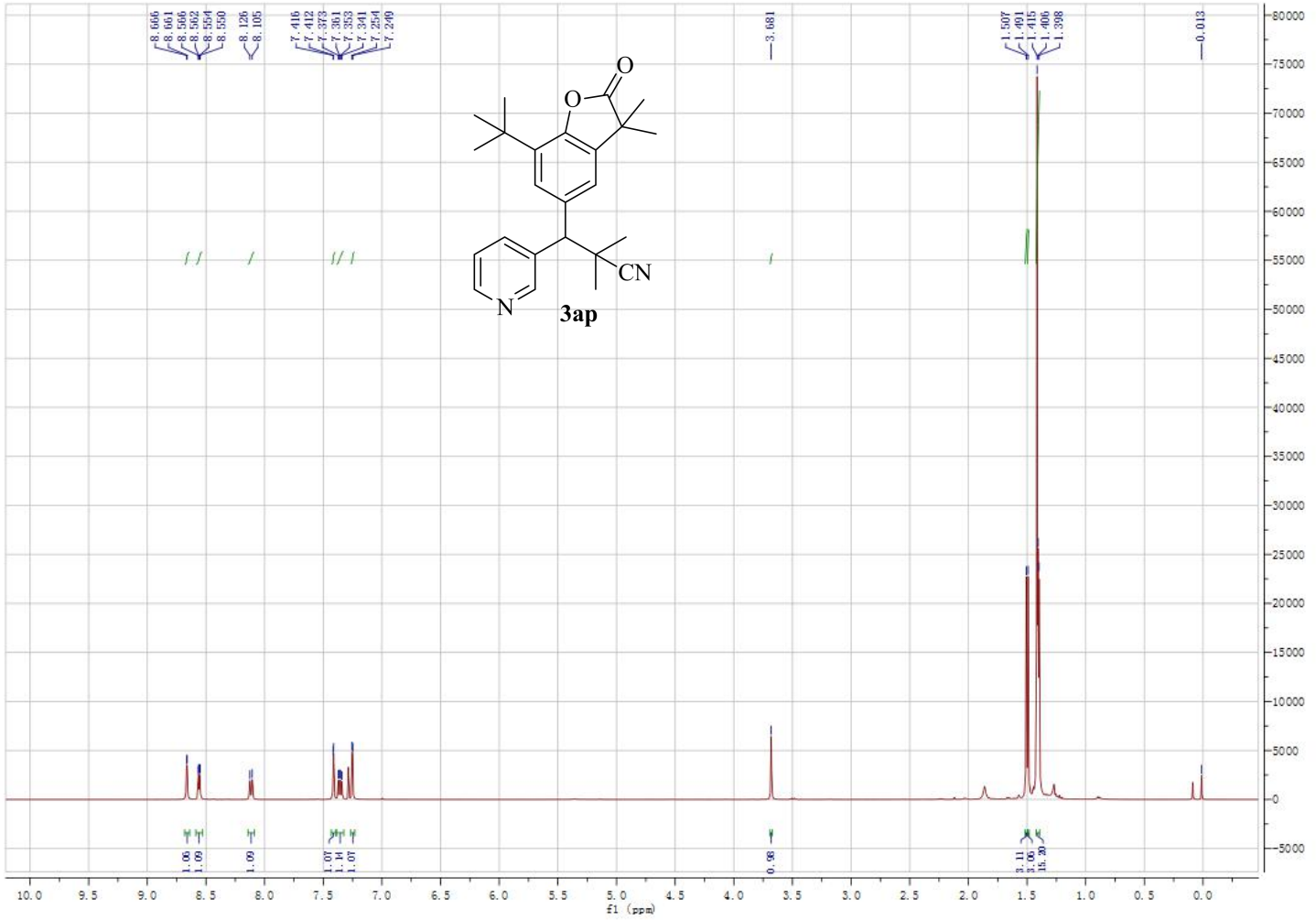
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(naphthalen-2-yl)propanenitrile （3ao）



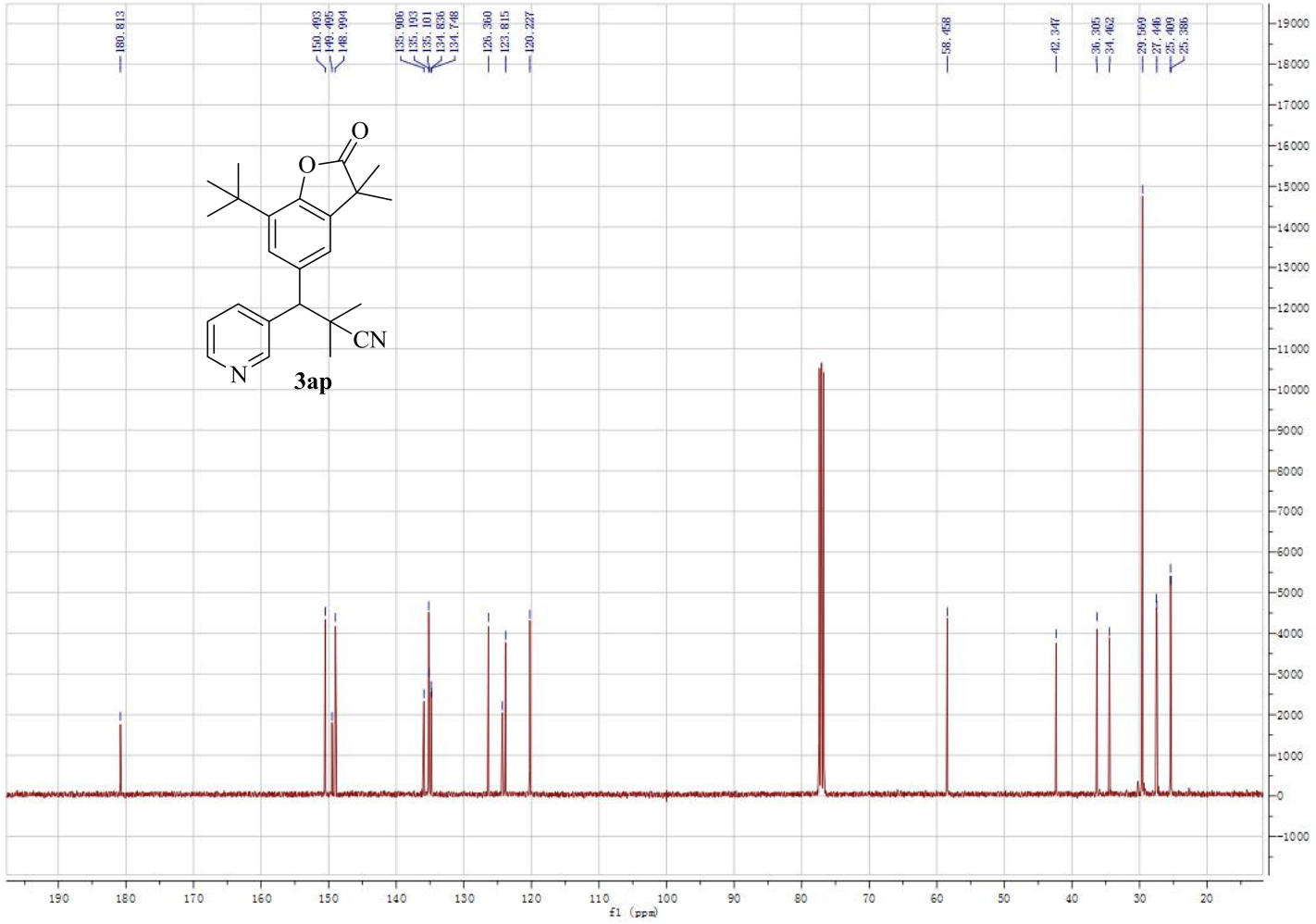
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(naphthalen-2-yl)propanenitrile （3ao）



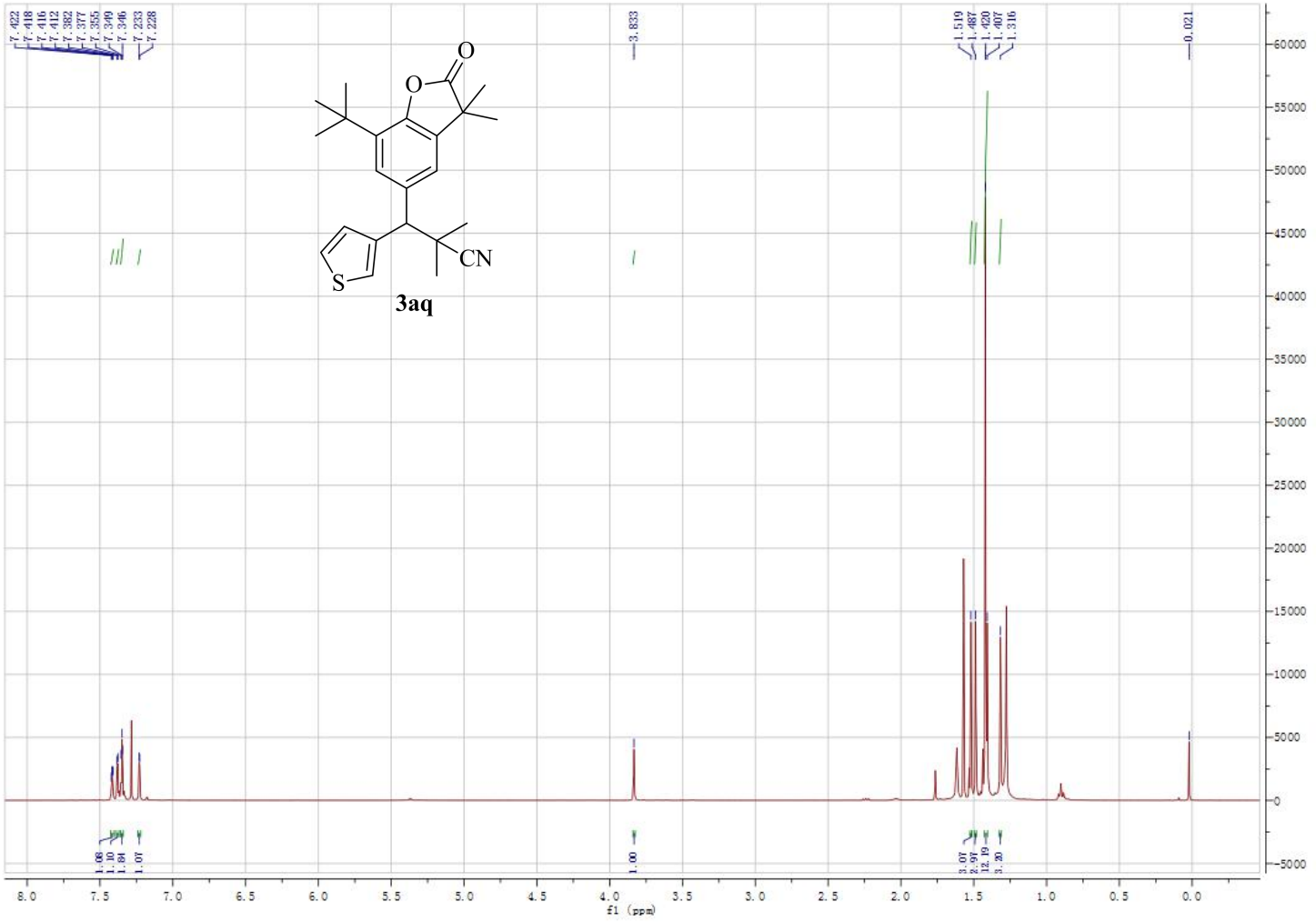
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(pyridin-3-yl)propanenitrile （3ap）



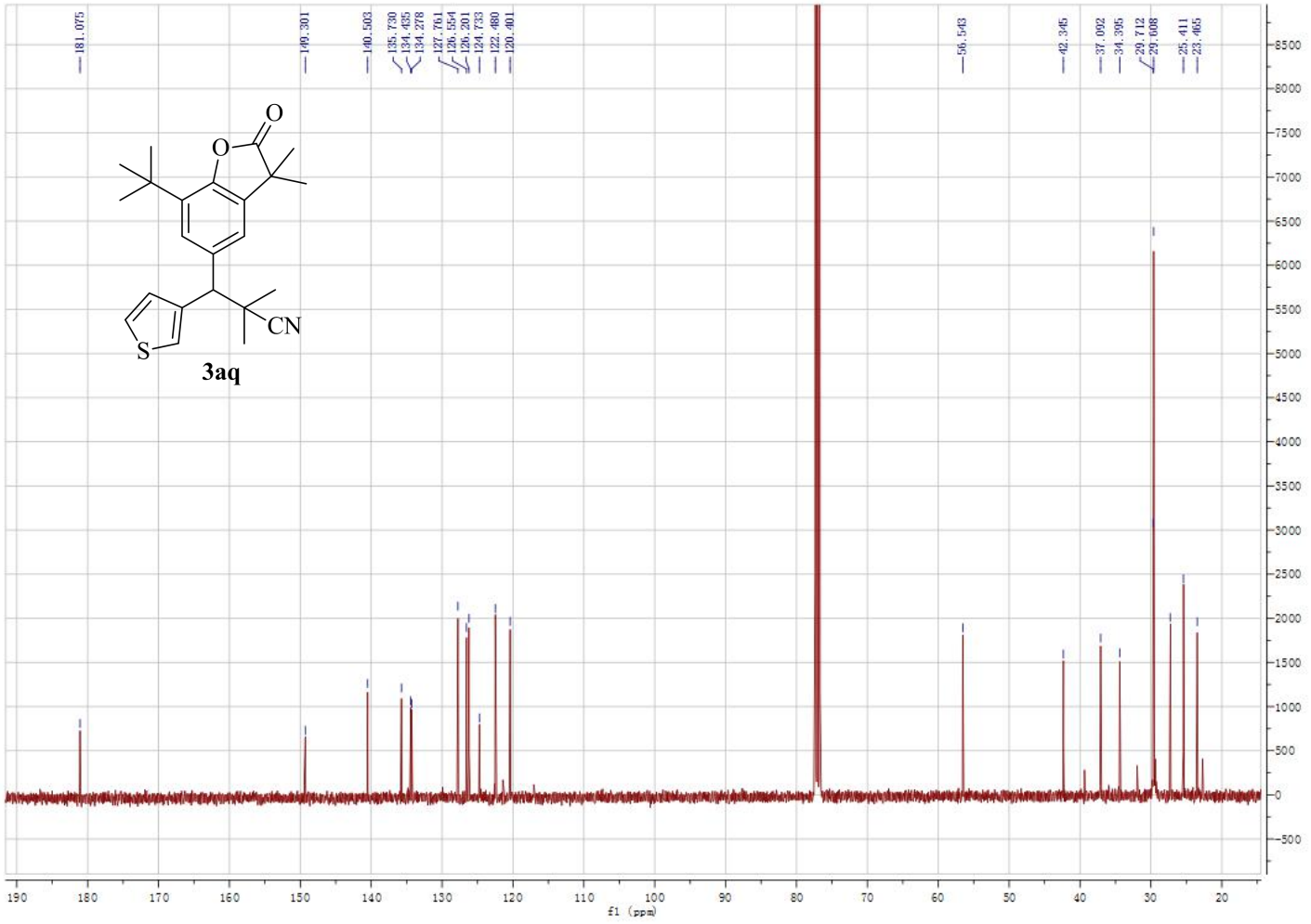
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(pyridin-3-yl)propanenitrile （3ap）



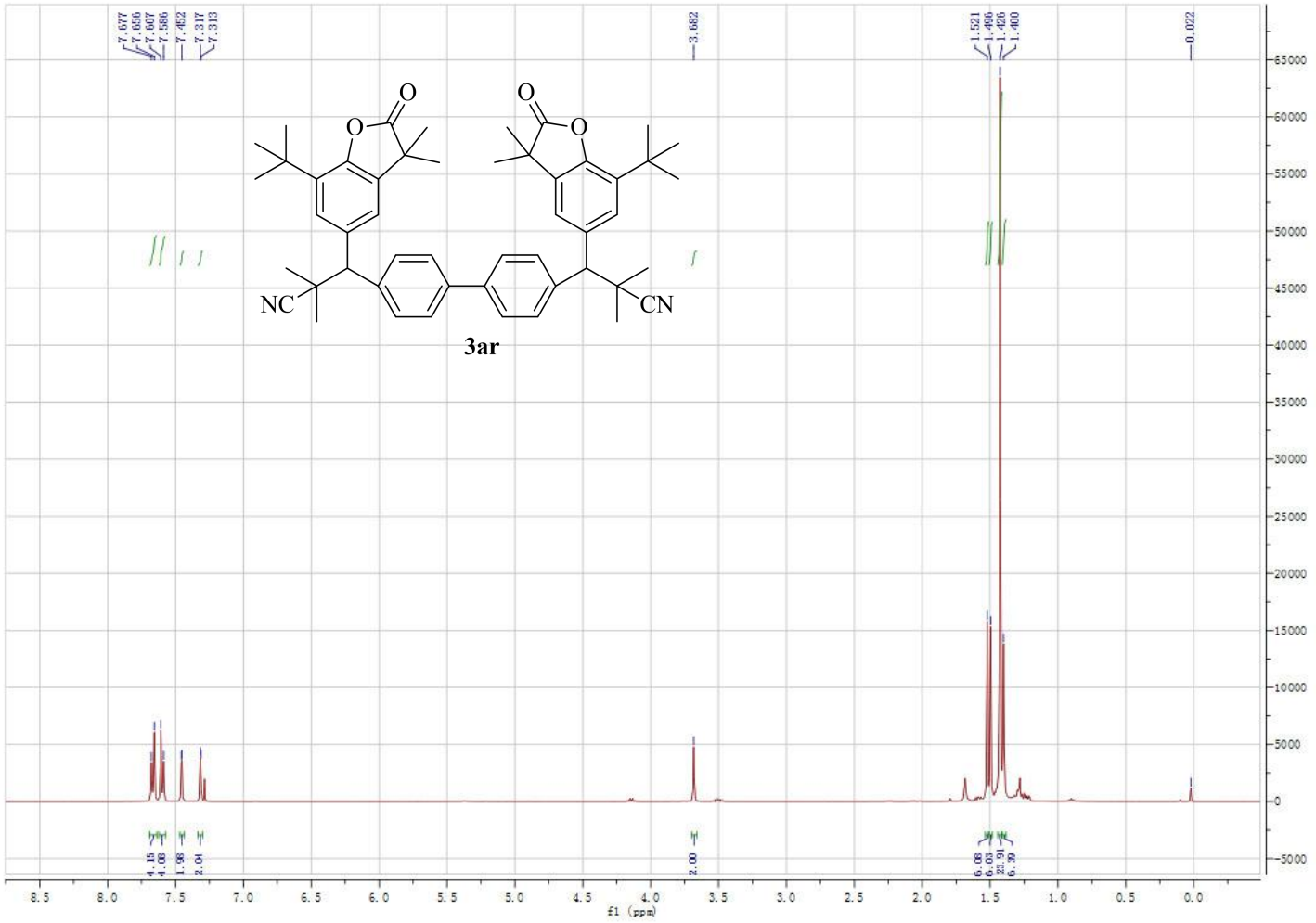
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(thiophen-3-yl)propanenitrile (3aq)



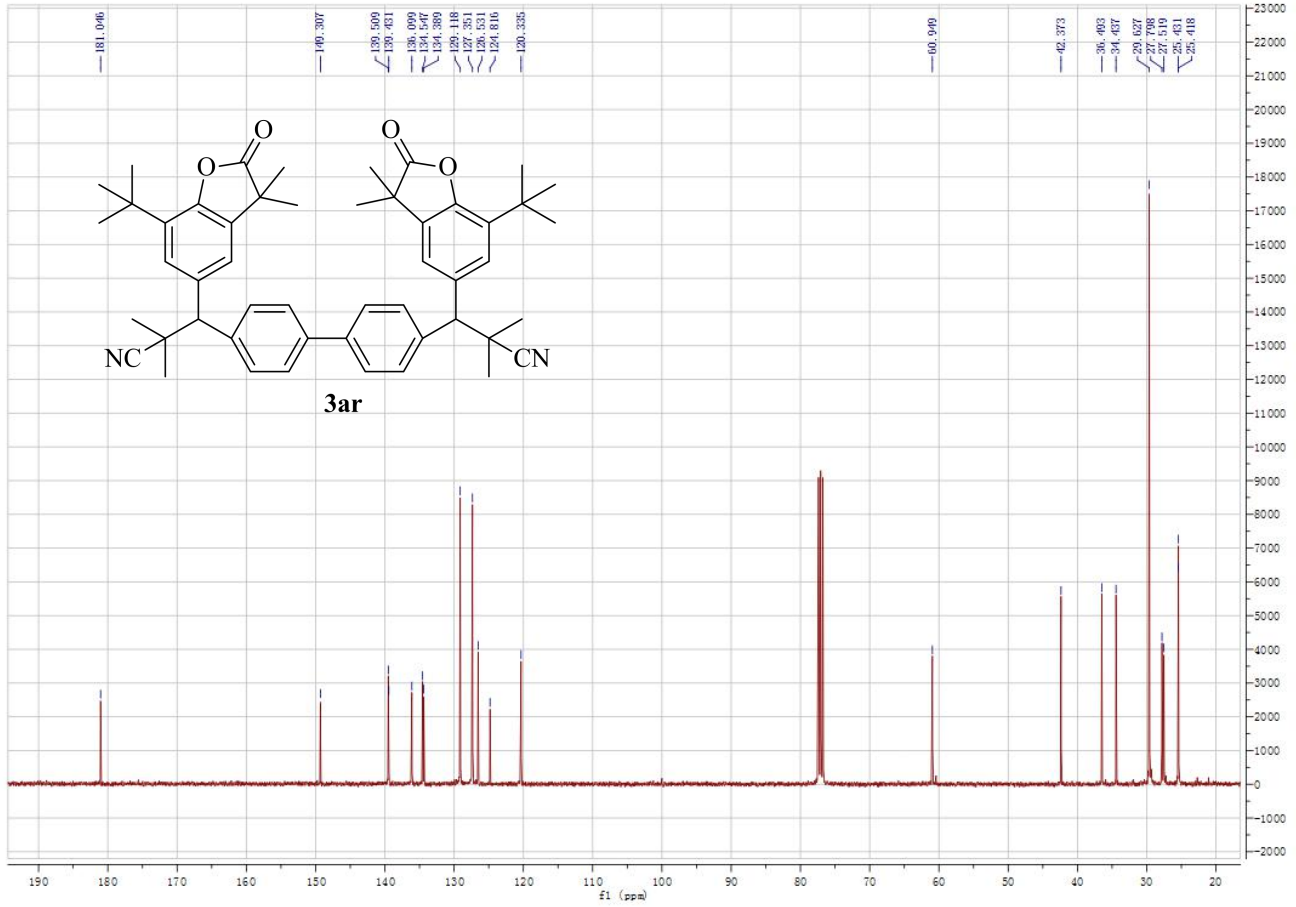
3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-(thiophen-3-yl)propanenitrile (3aq)



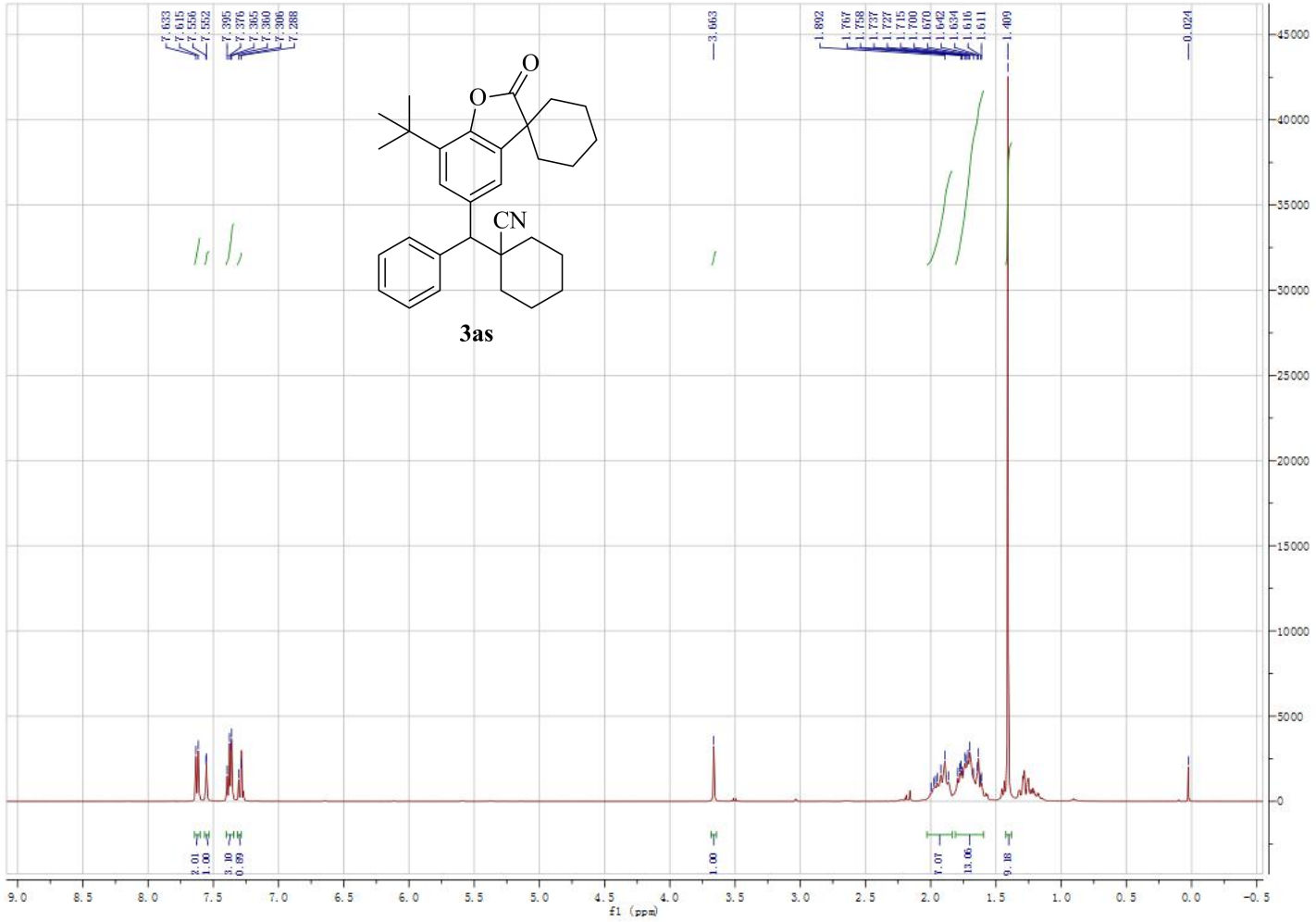
3,3'-([1,1'-biphenyl]-4,4'-diyl)bis(3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile) (3ar)



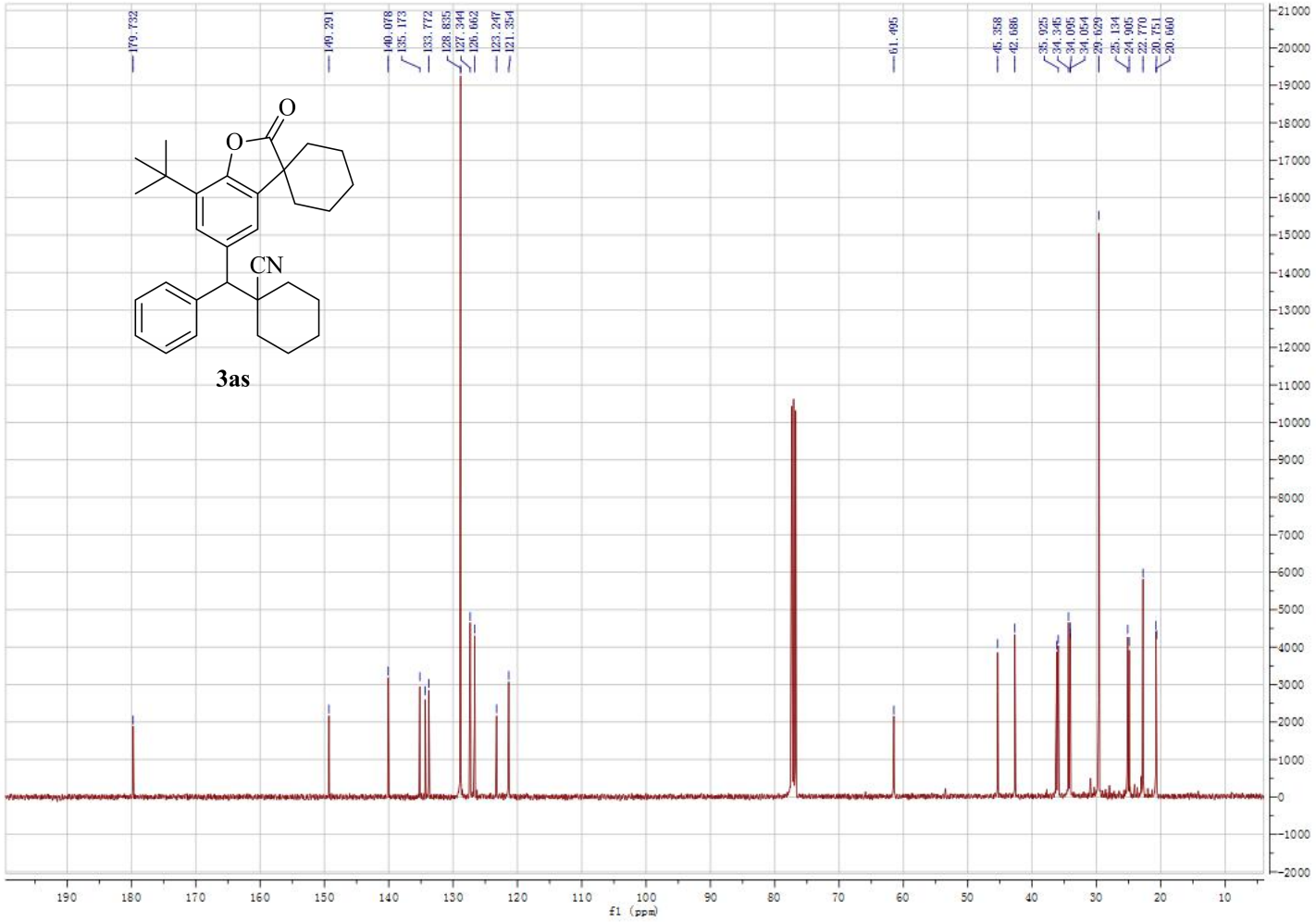
3,3'-([1,1'-biphenyl]-4,4'-diyl)bis(3-(7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)-2,2-dimethylpropanenitrile) (3ar)



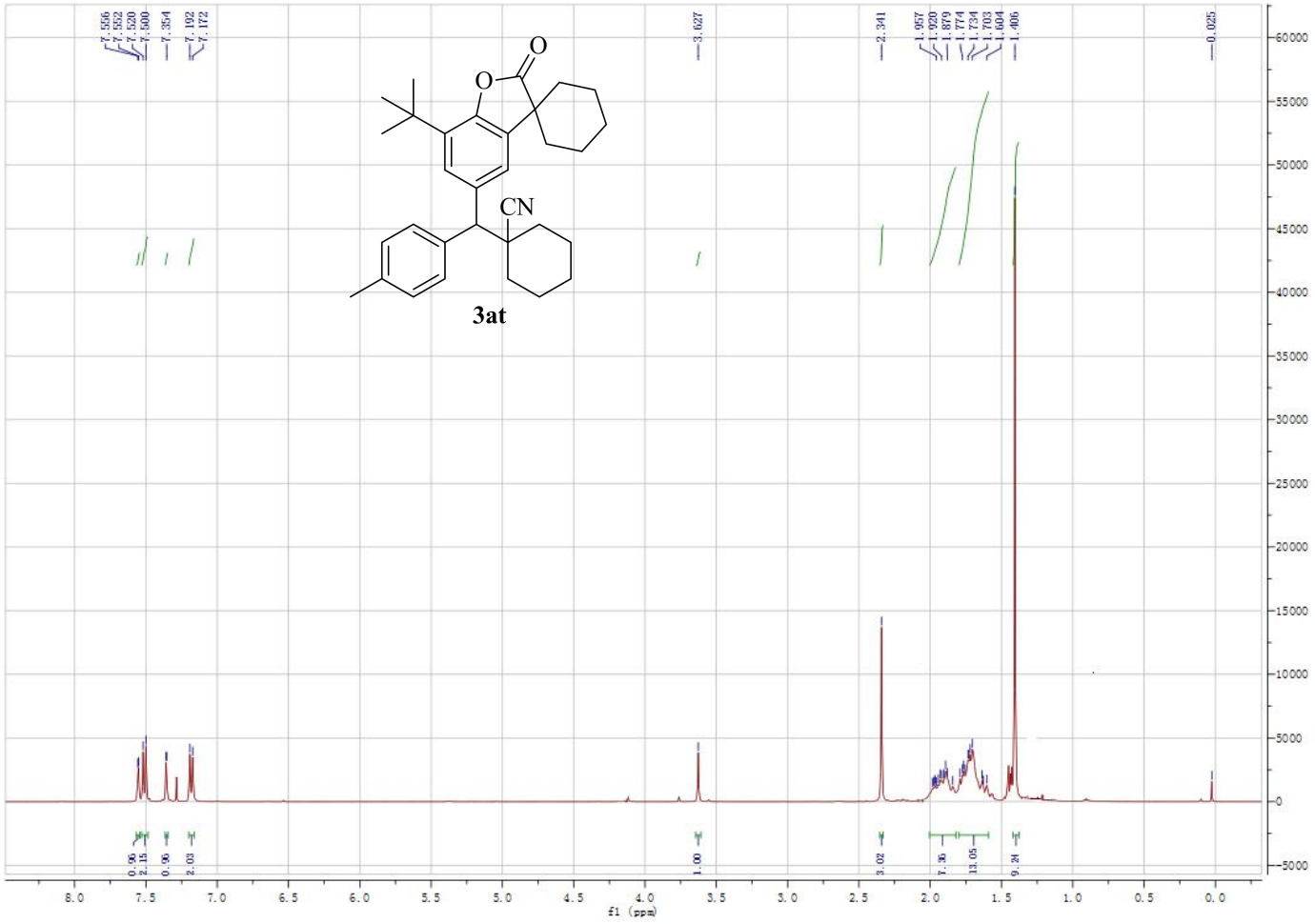
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(phenyl)methyl)cyclohexanecarbonitrile (3as)



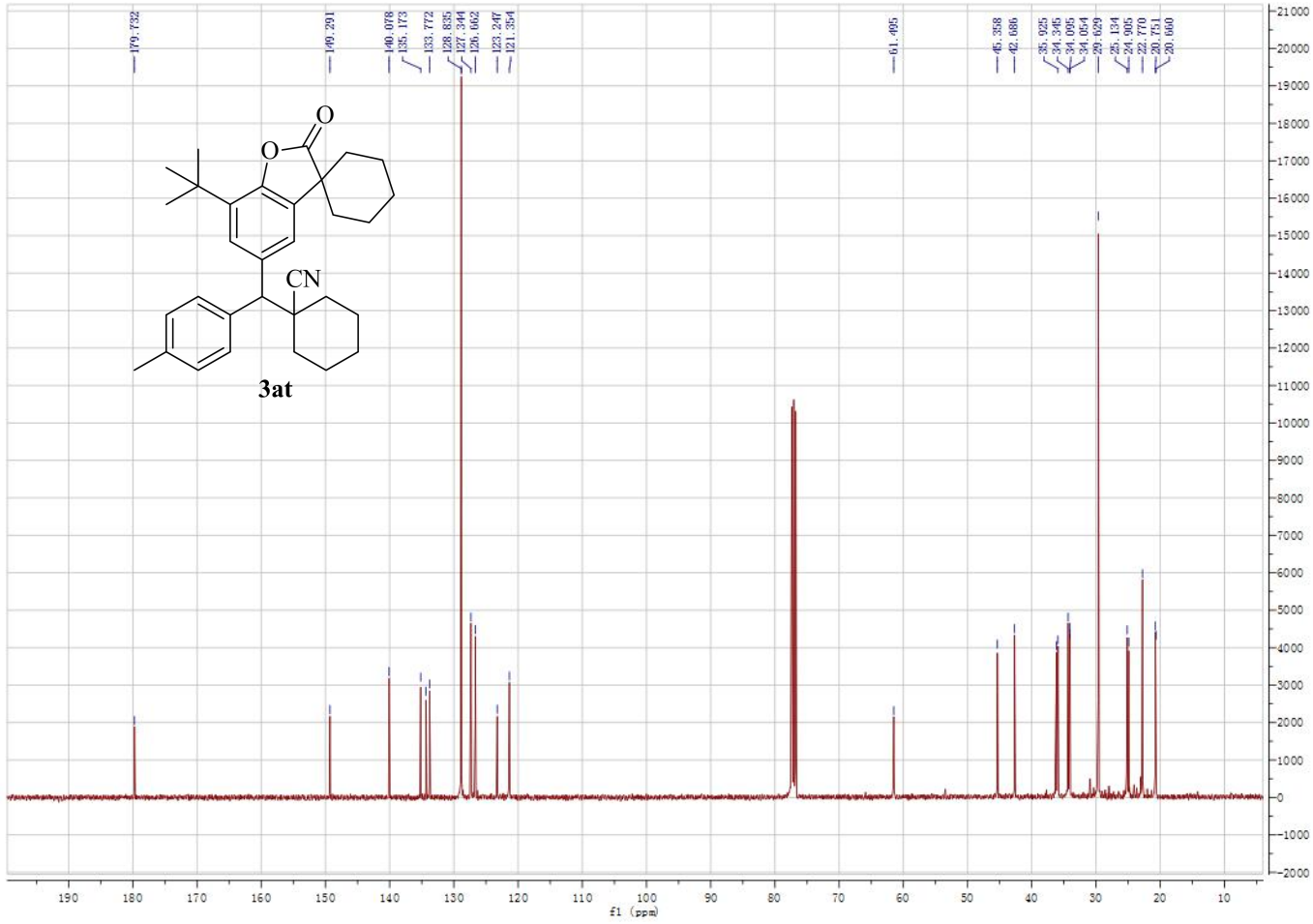
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(phenyl)methyl)cyclohexanecarbonitrile (3as)



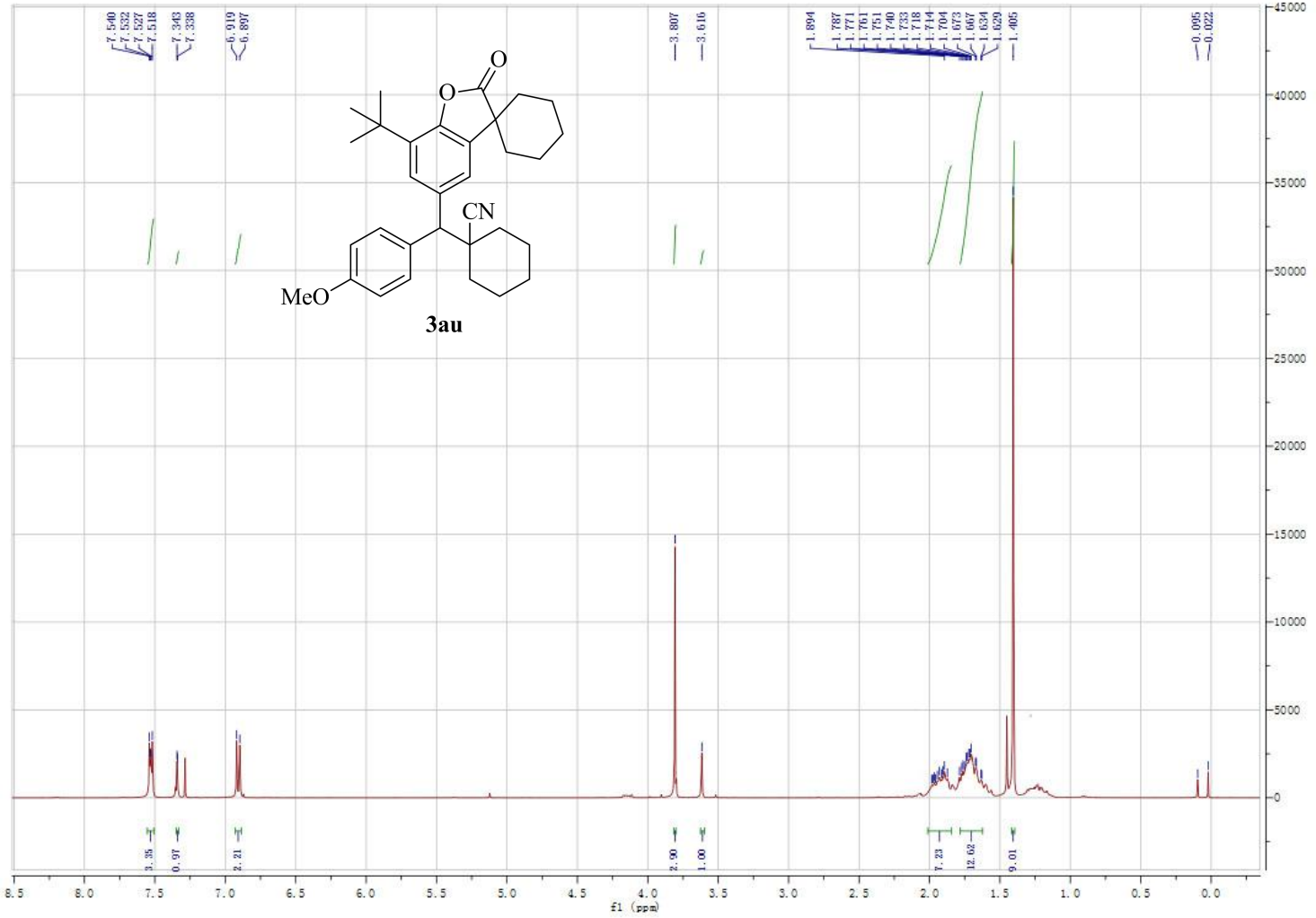
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(p-tolyl)methyl)cyclohexanecarbonitrile (3at)



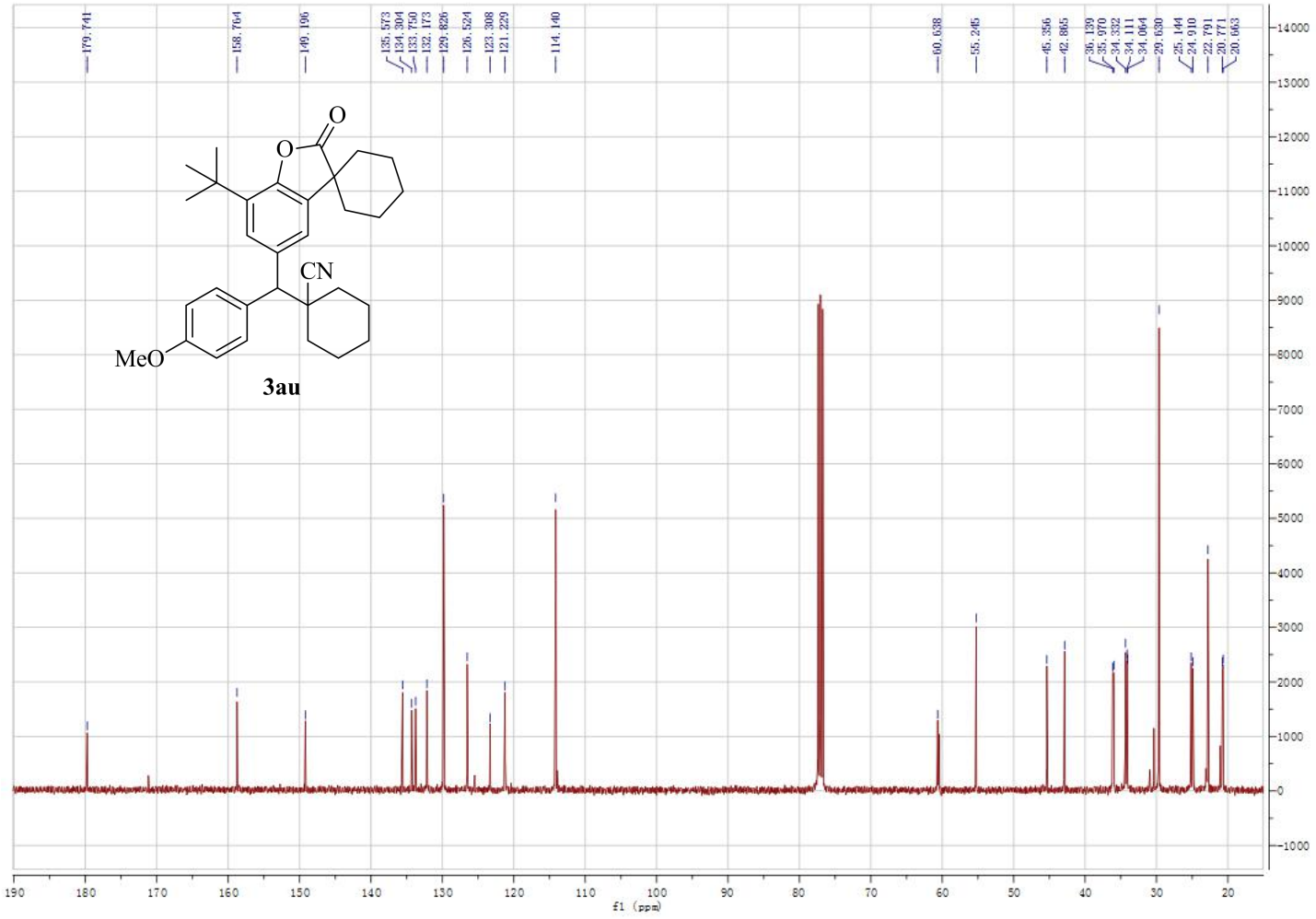
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(p-tolyl)methyl)cyclohexanecarbonitrile (3at)



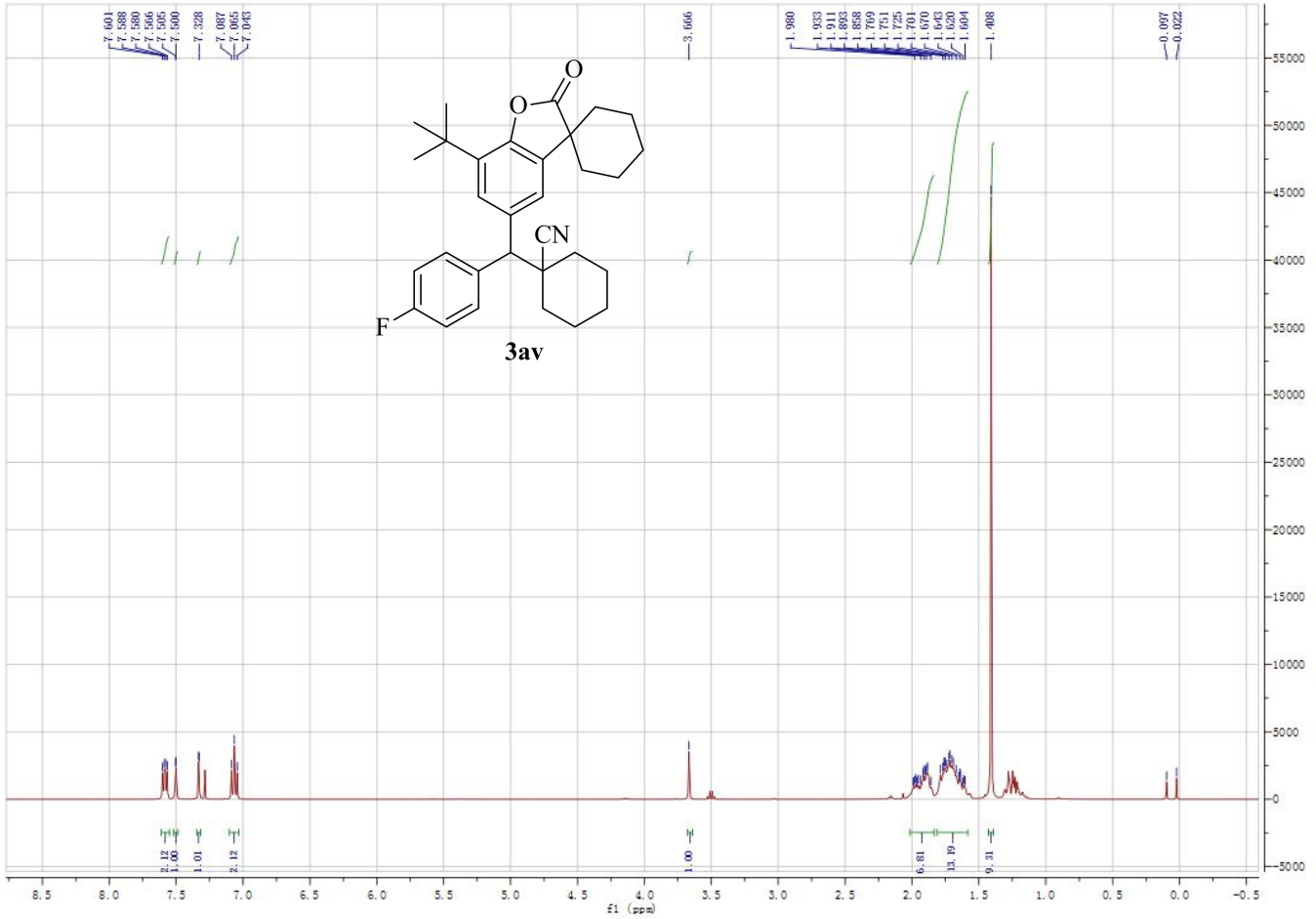
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-methoxyphenyl)methyl)cyclohexanecarbonitrile (3au)



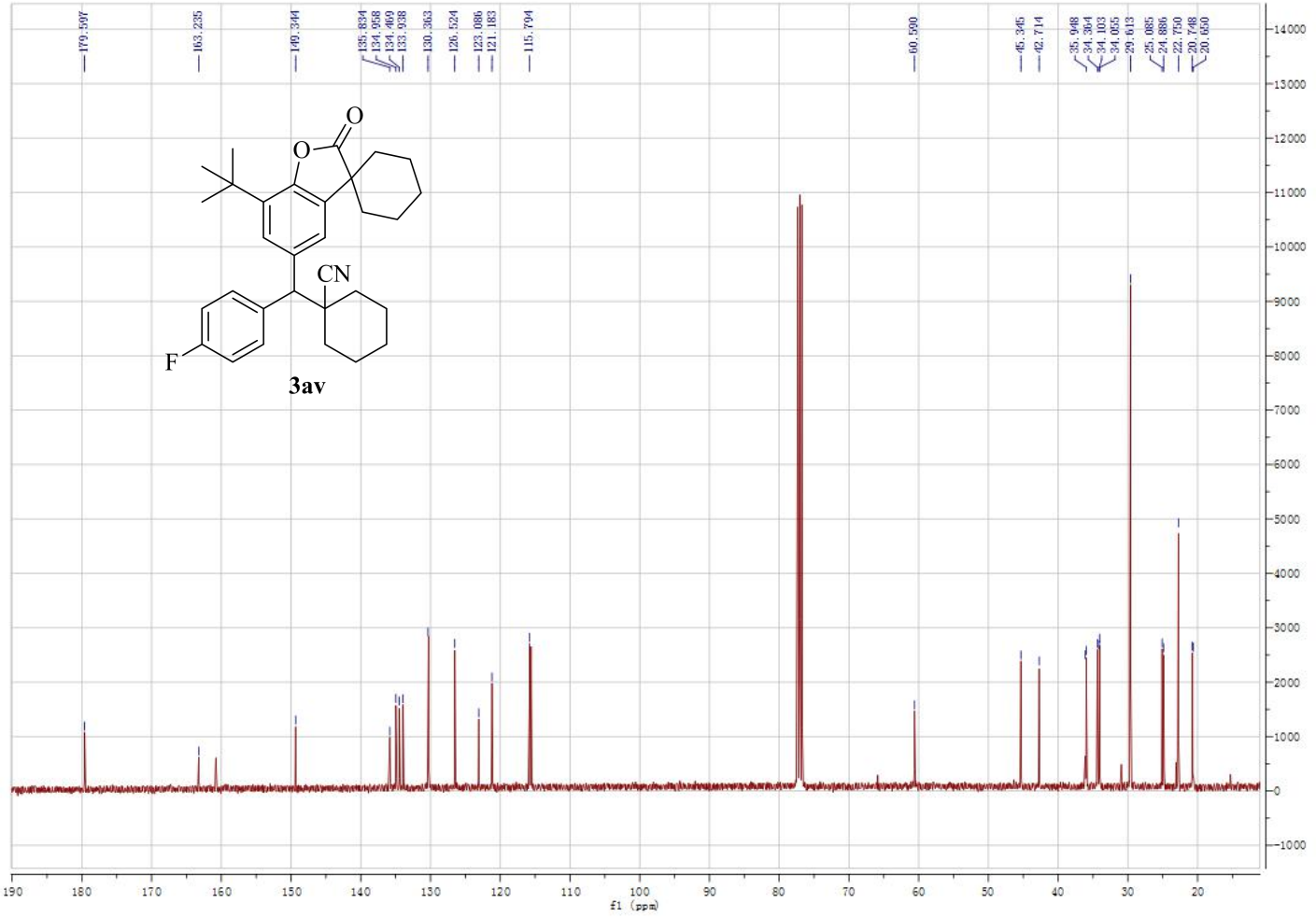
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-methoxyphenyl)methyl)cyclohexanecarbonitrile (3au)



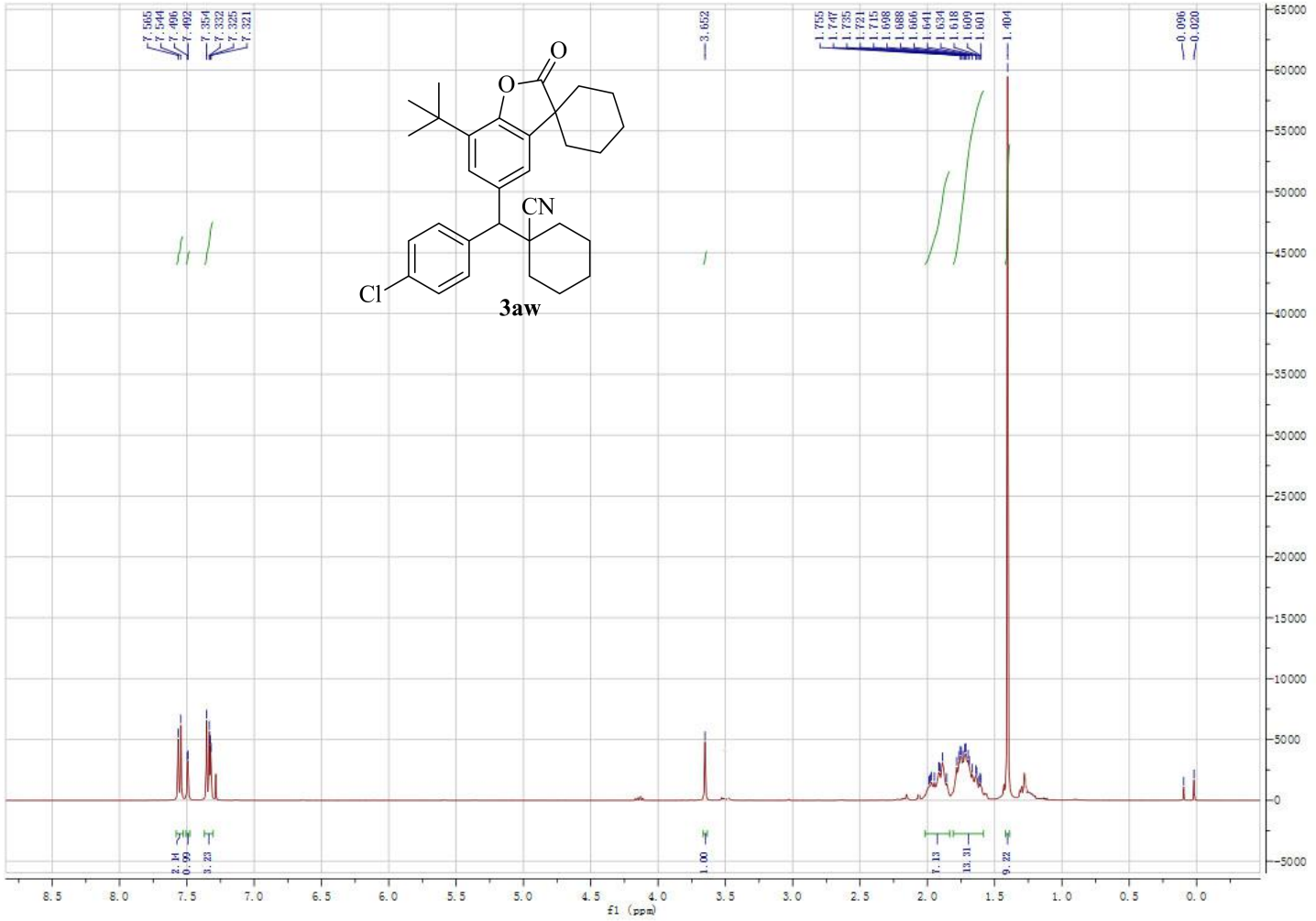
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-fluorophenyl)methyl)cyclohexanecarbonitrile (3av)



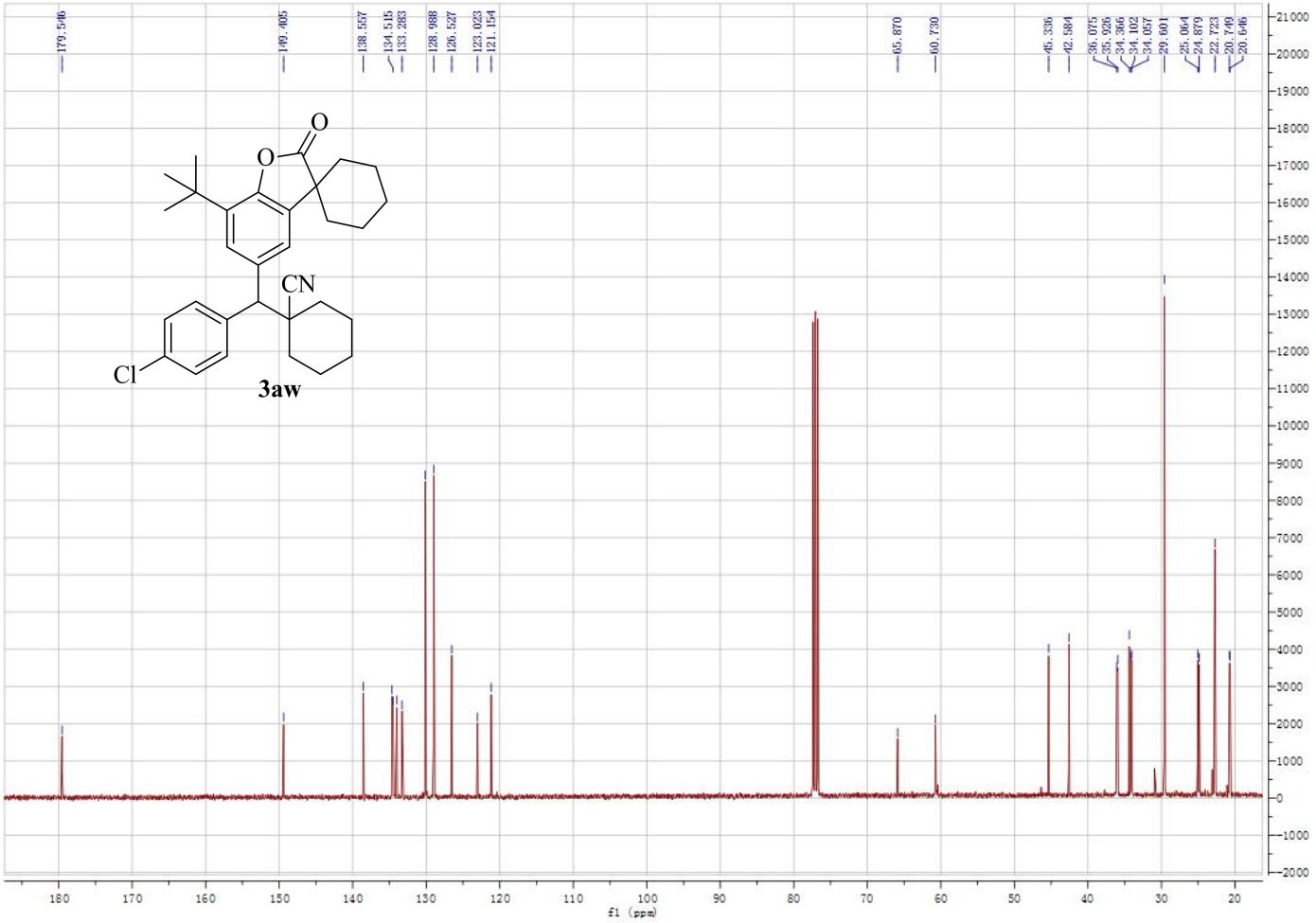
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-fluorophenyl)methyl)cyclohexanecarbonitrile (3av)



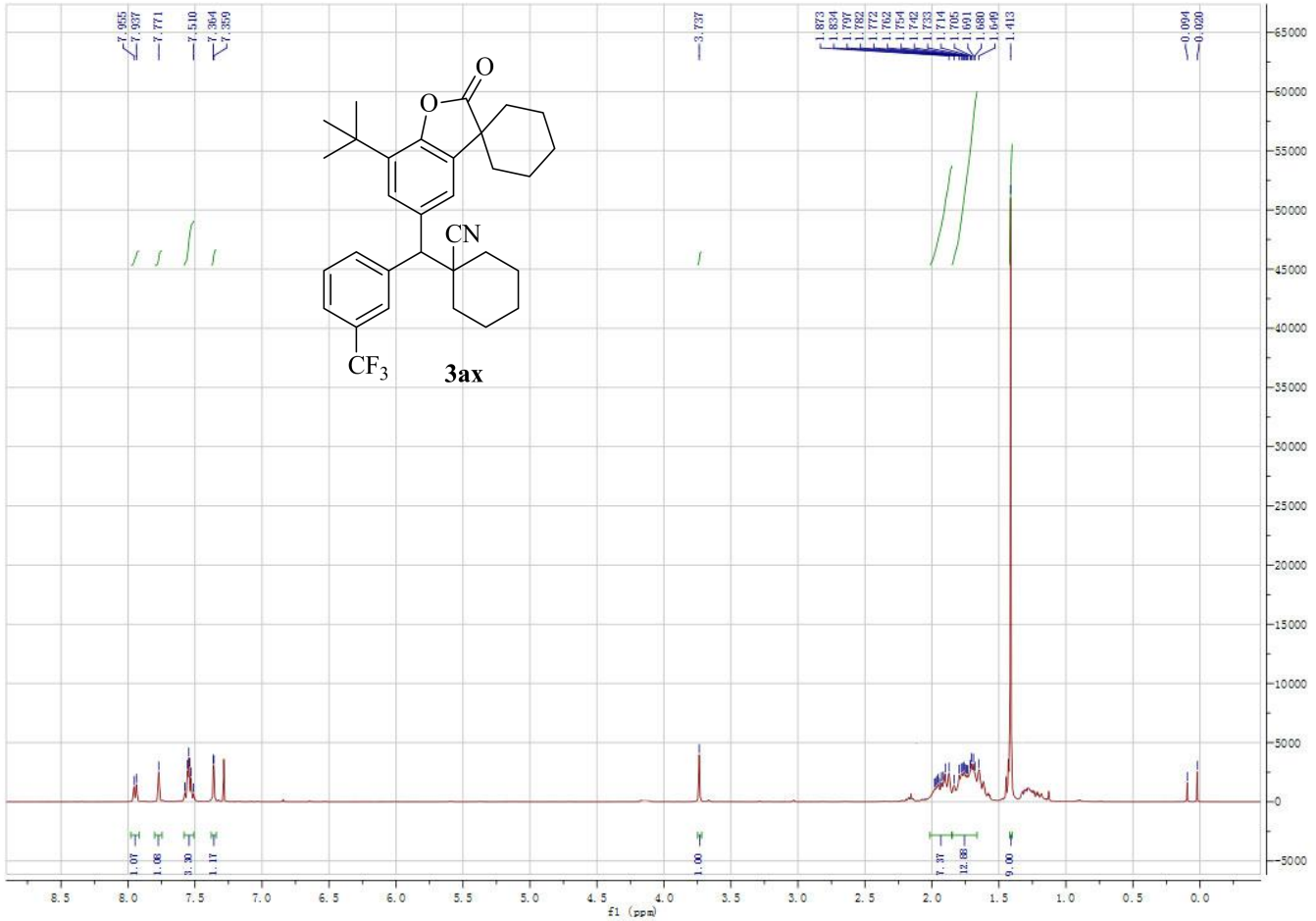
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-chlorophenyl)methyl)cyclohexanecarbonitrile (3aw)



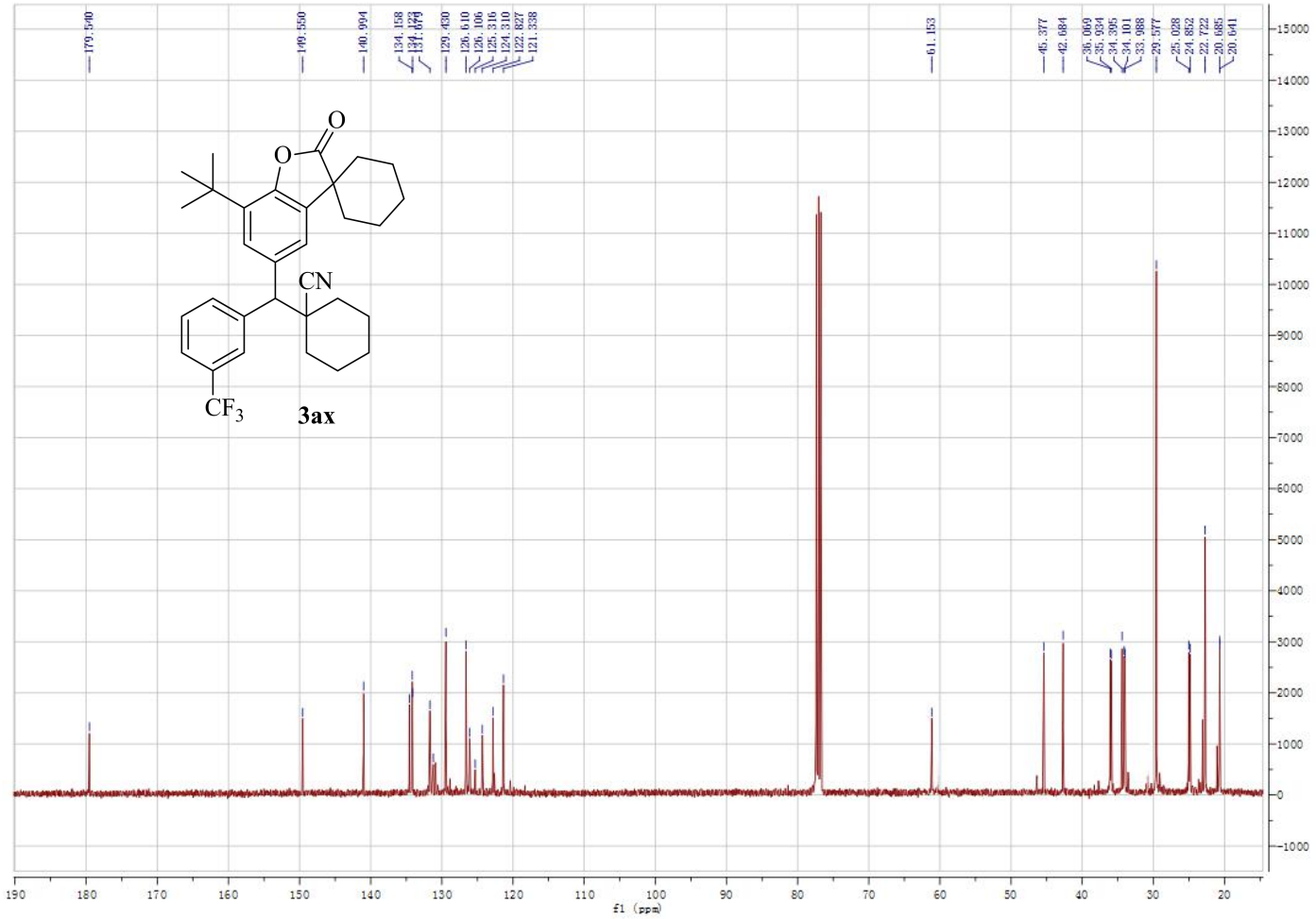
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-chlorophenyl)methyl)cyclohexanecarbonitrile (3aw)



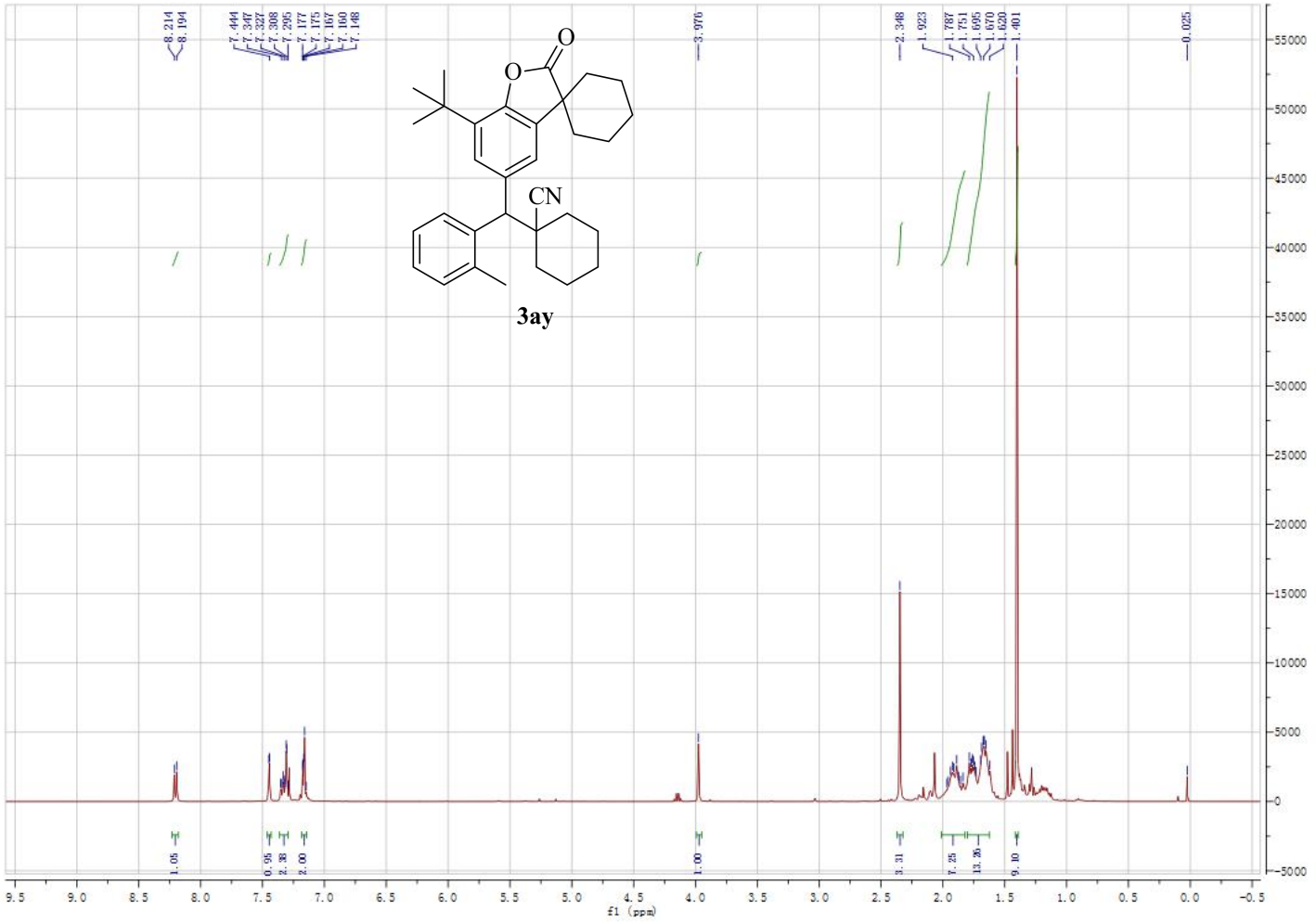
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(3-(trifluoromethyl)phenyl)methyl)cyclohexanecarbonitrile (3ax)



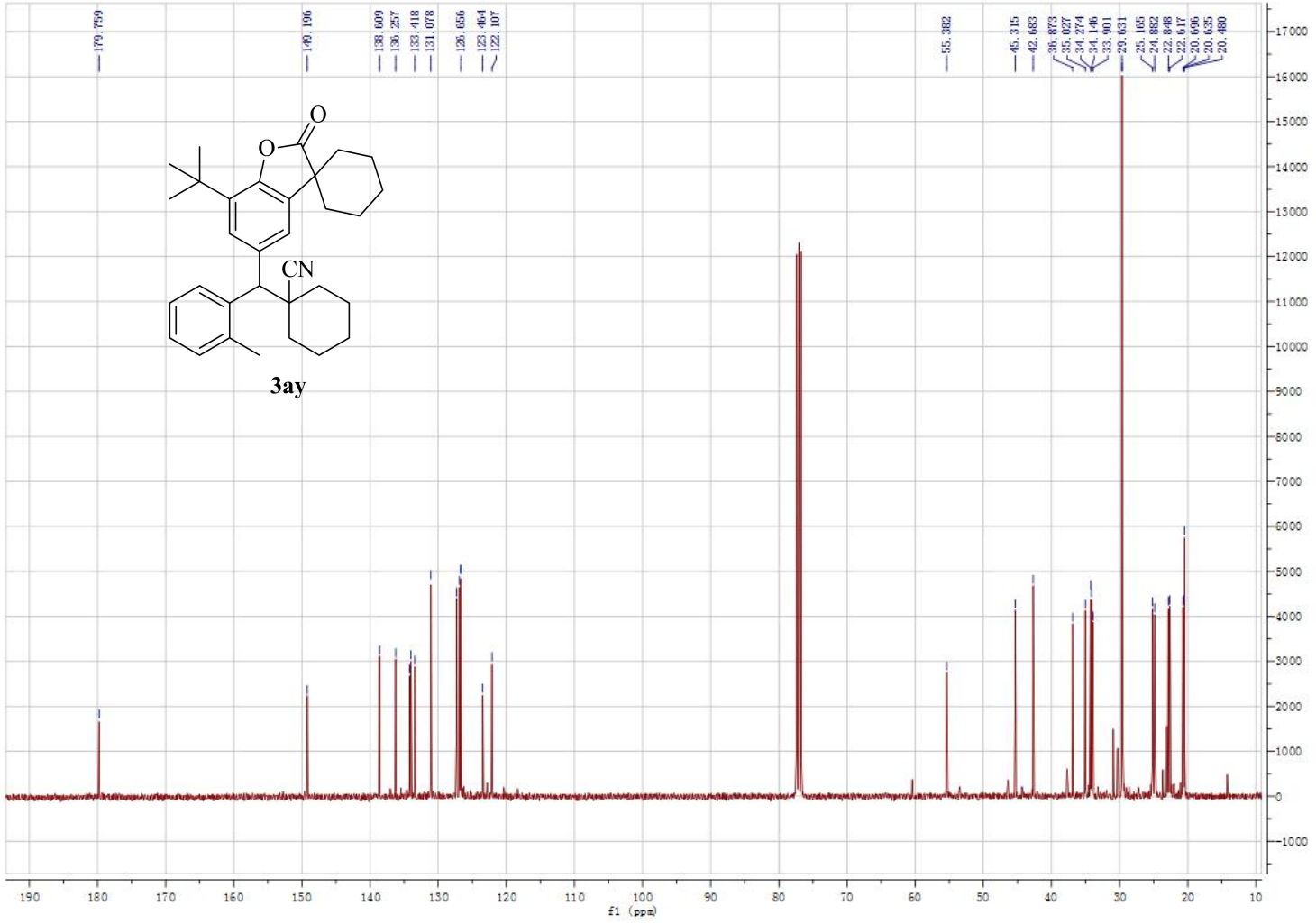
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(3-(trifluoromethyl)phenyl)methyl)cyclohexanecarbonitrile (3ax)



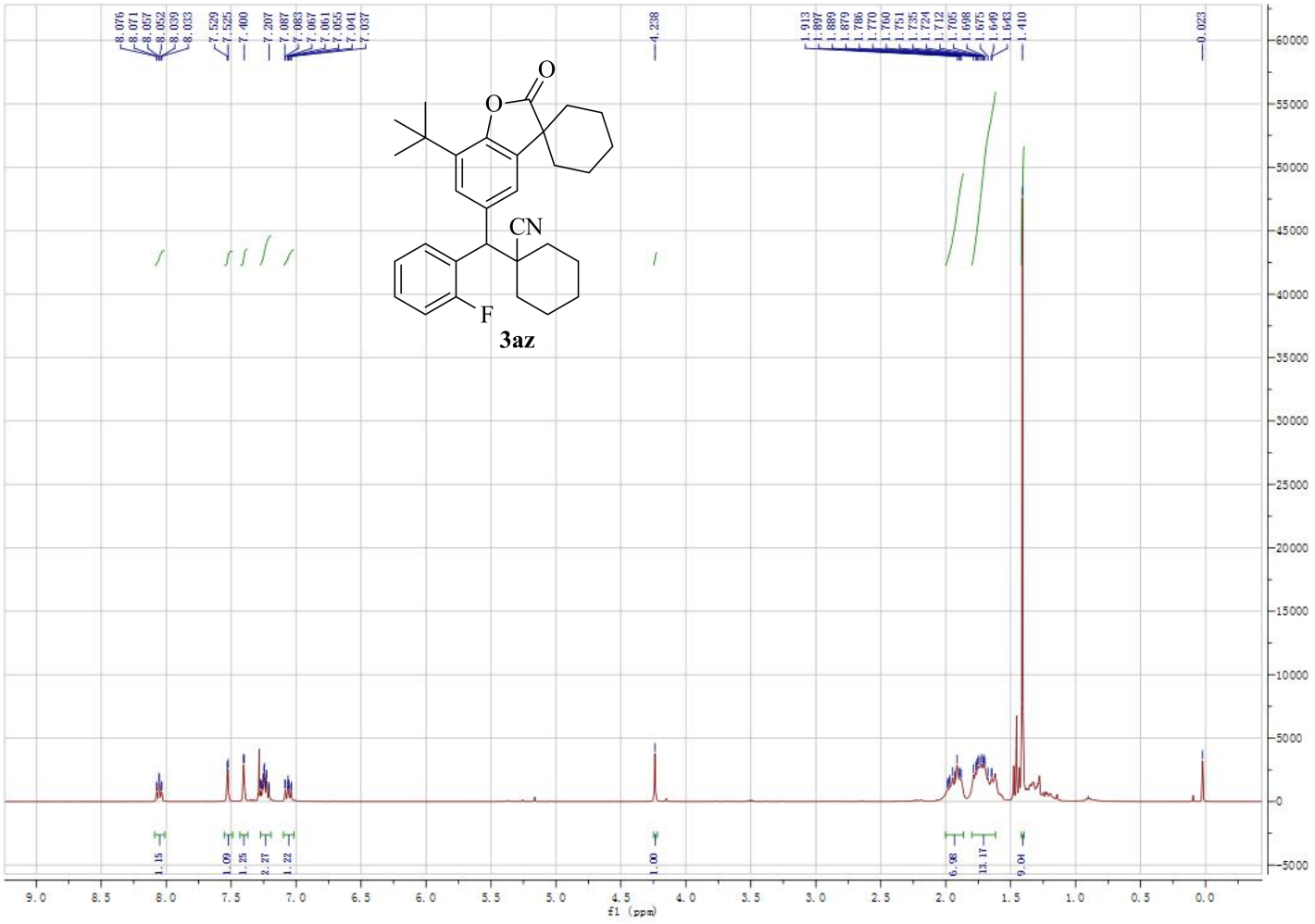
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(o-tolyl)methyl)cyclohexanecarbonitrile (3ay)



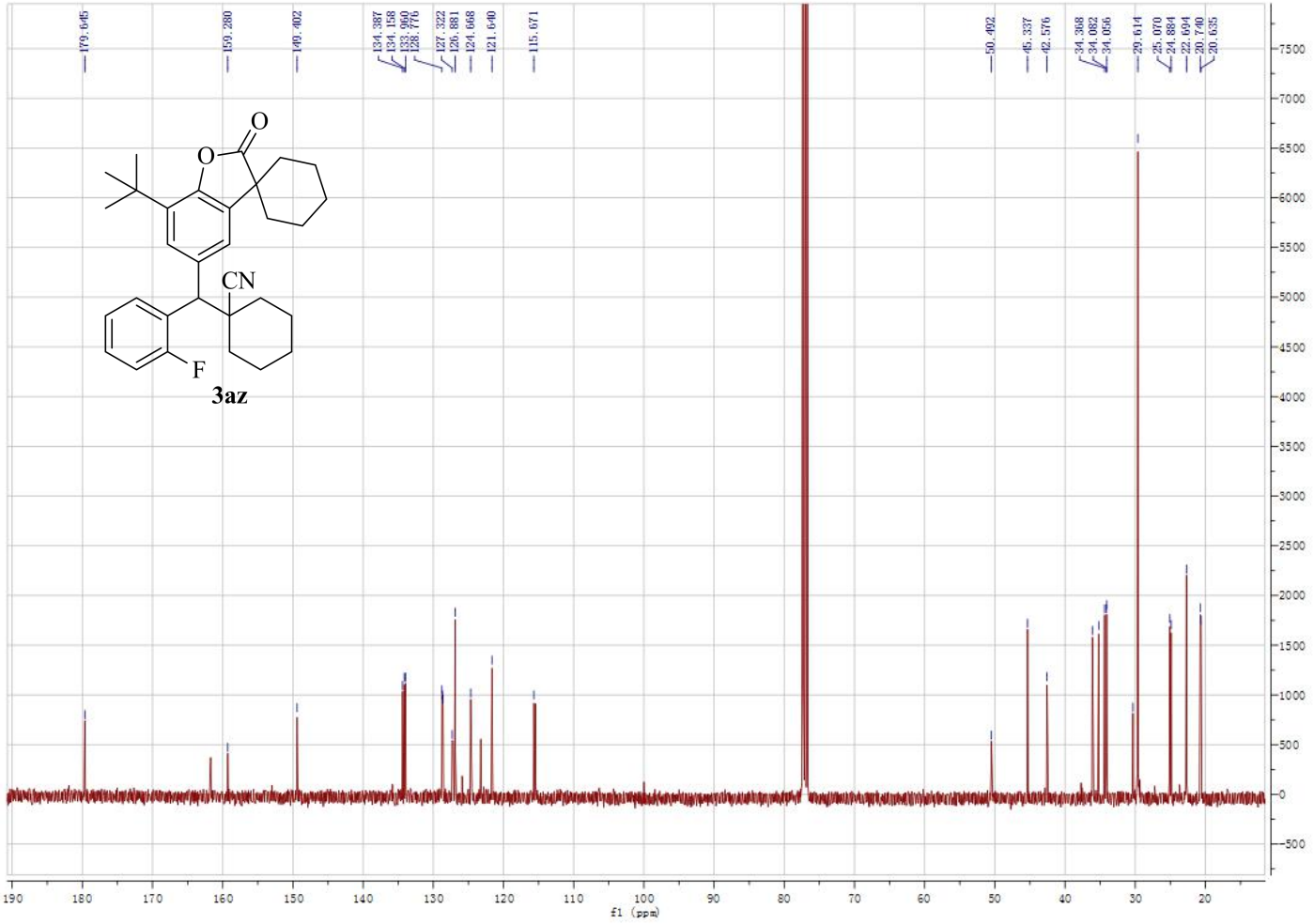
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(o-tolyl)methyl)cyclohexanecarbonitrile (3ay)



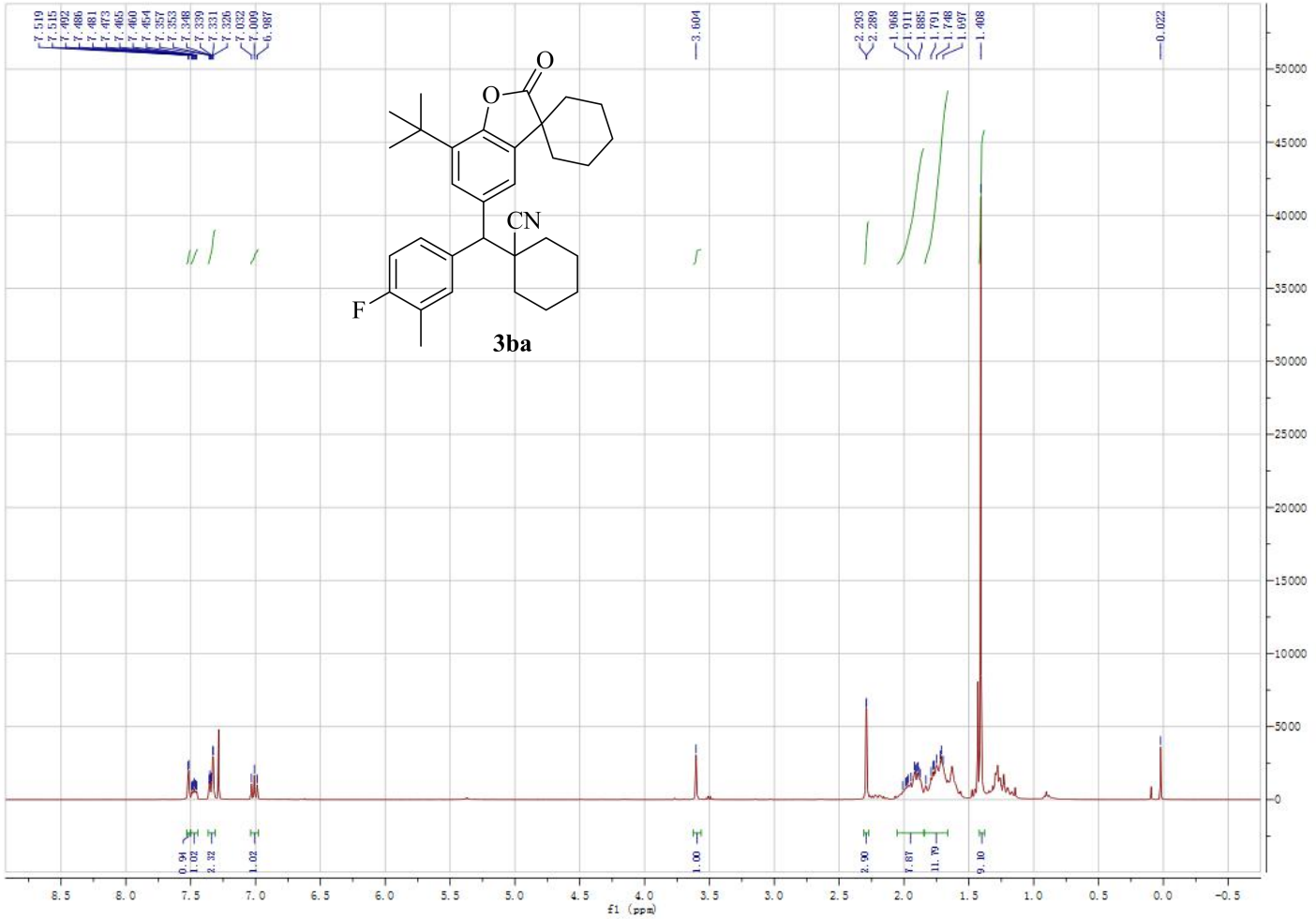
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(2-fluorophenyl)methyl)cyclohexanecarbonitrile (3az)



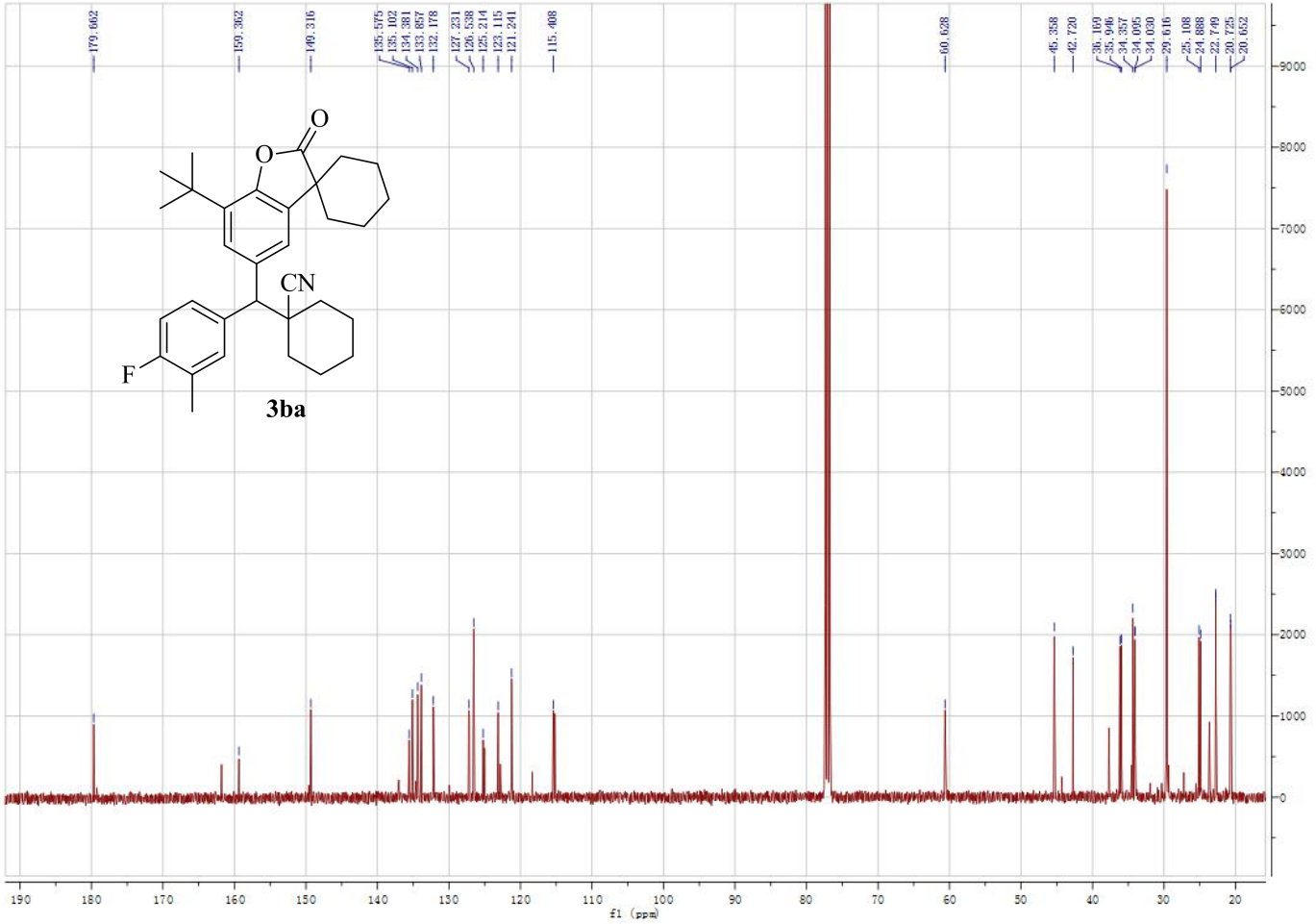
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(2-fluorophenyl)methyl)cyclohexanecarbonitrile (3az)



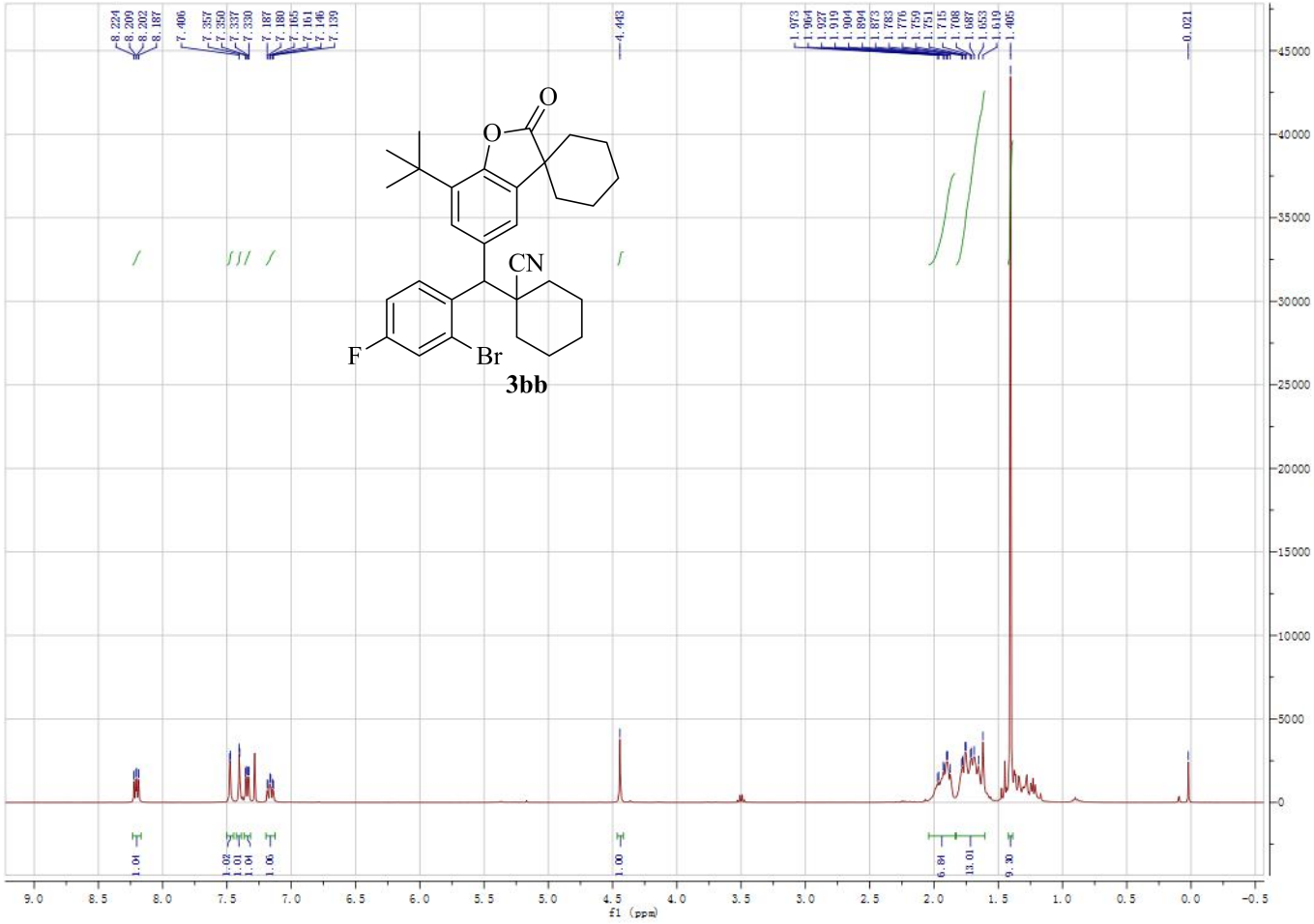
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-fluoro-3-methylphenyl)methyl)cyclohexanecarbonitrile (3ba)



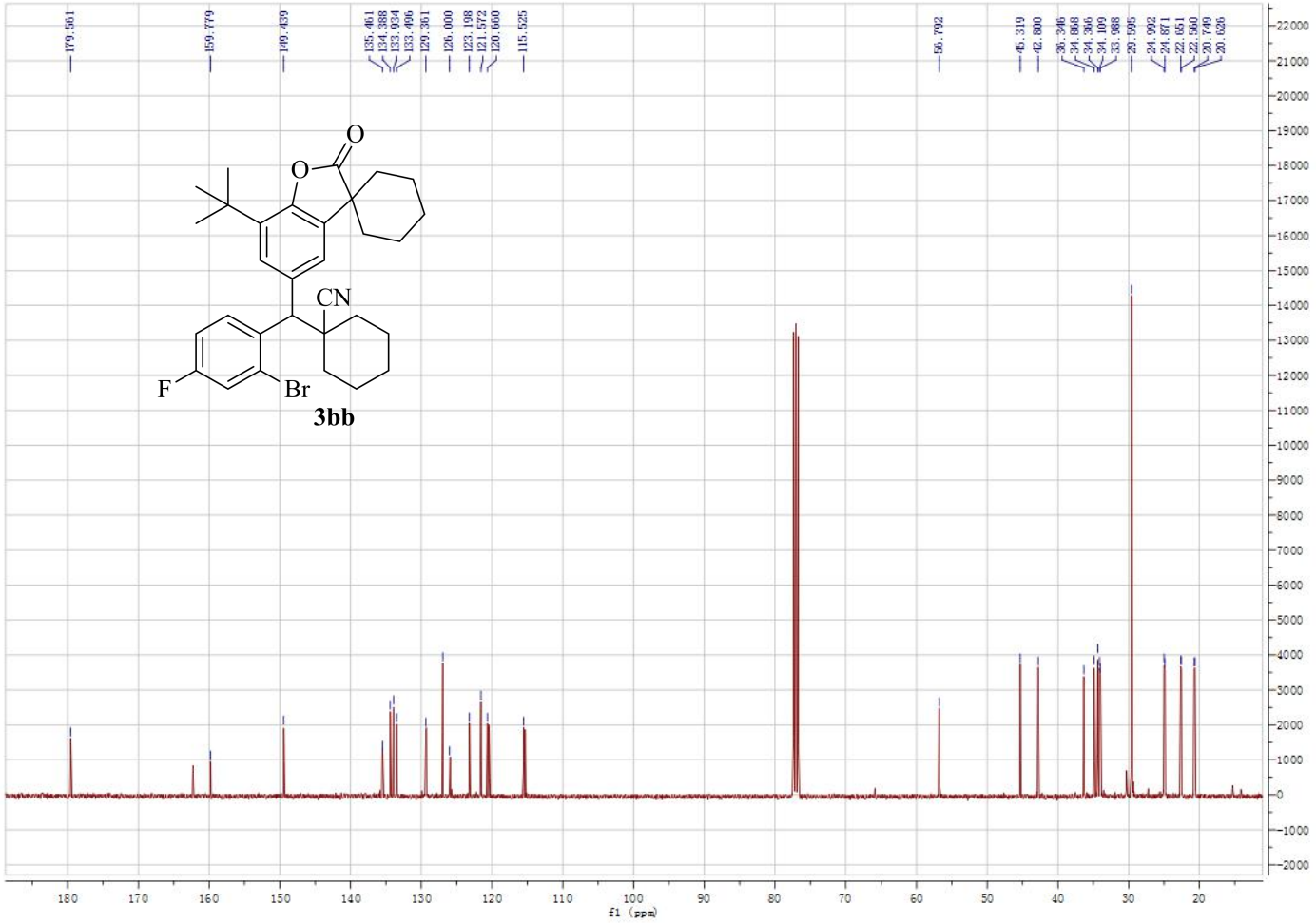
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(4-fluoro-3-methylphenyl)methyl)cyclohexanecarbonitrile (3ba)



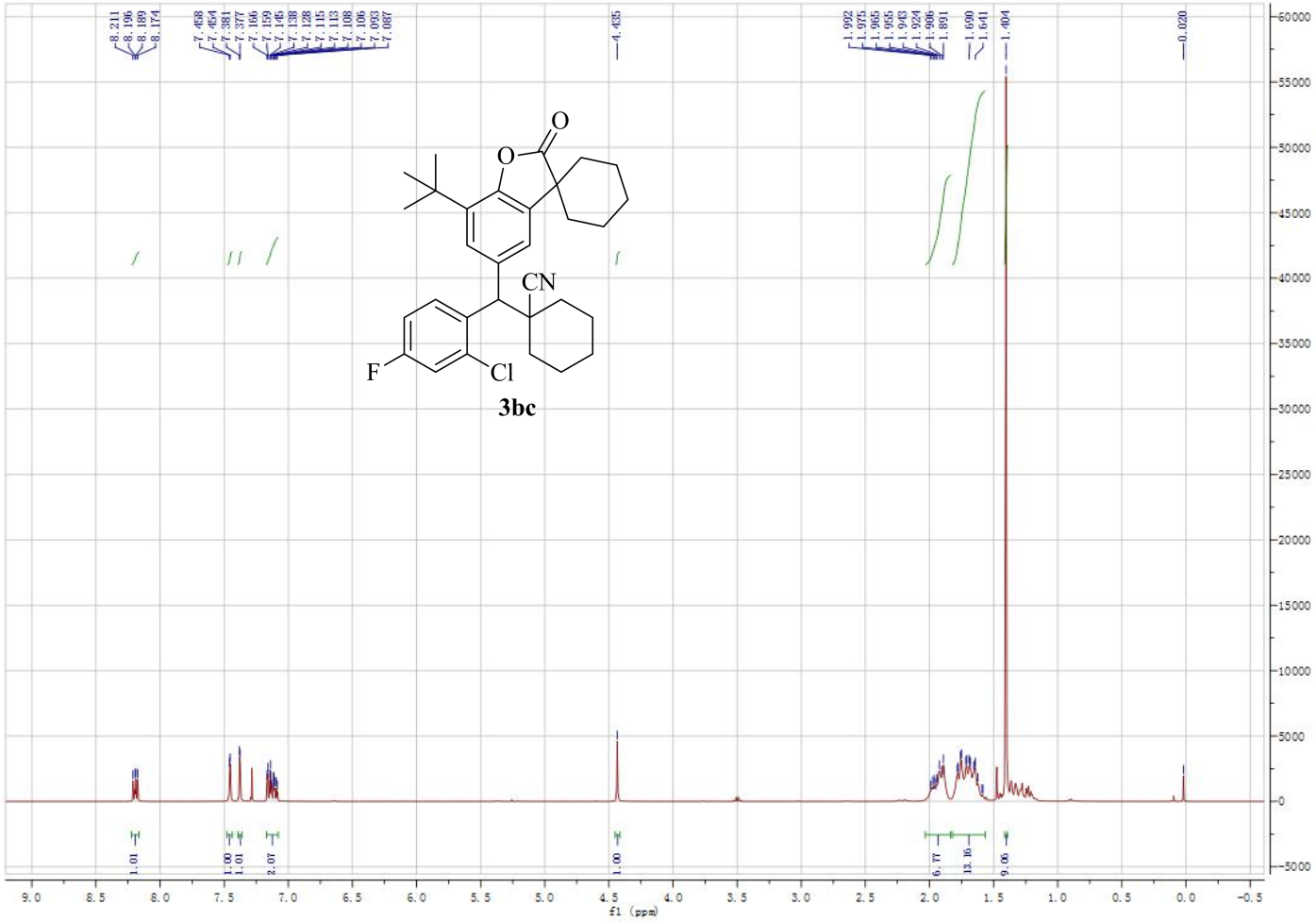
1-((2-bromo-4-fluorophenyl)(7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)methyl)cyclohexanecarbonitrile (3bb)



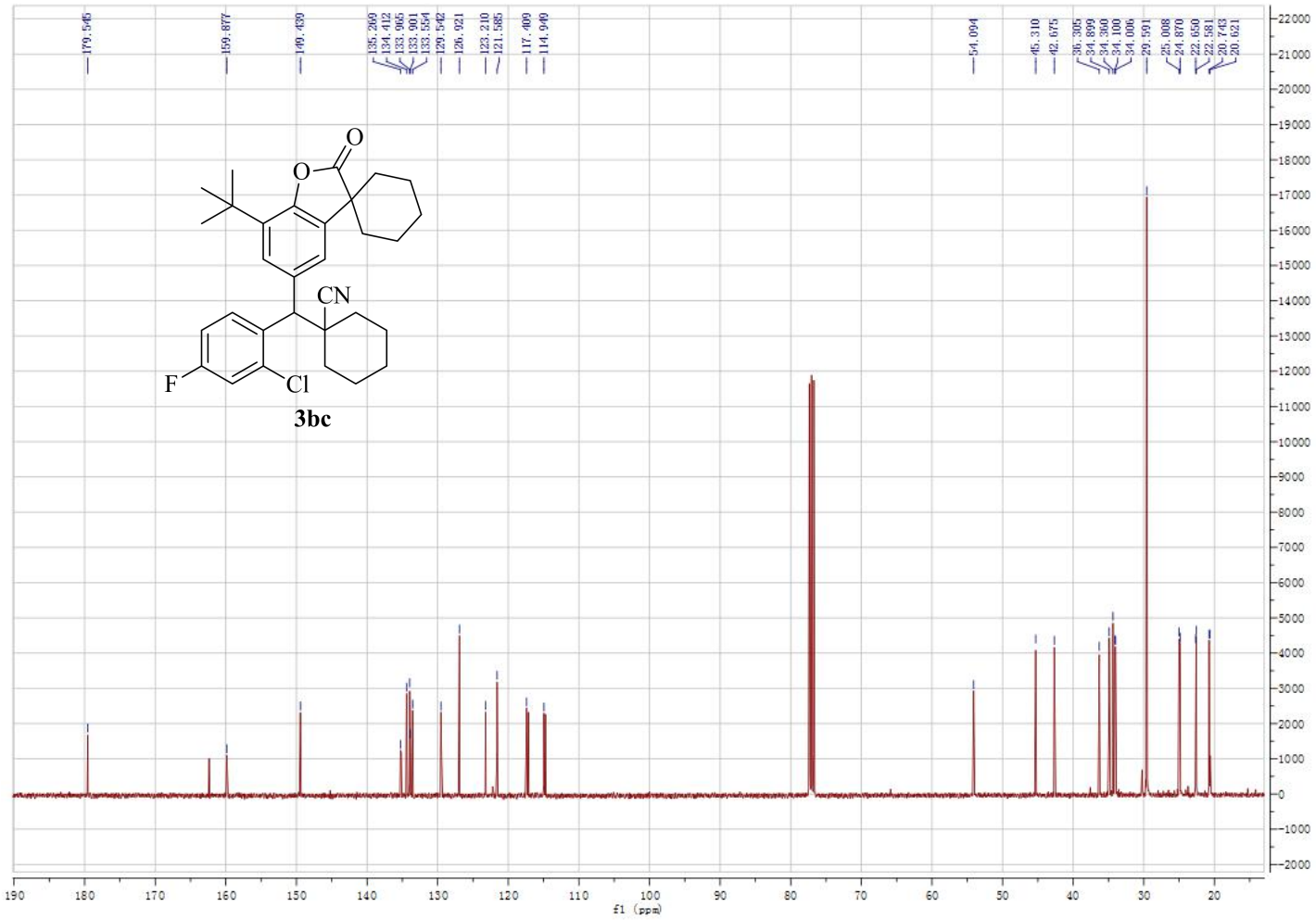
1-((2-bromo-4-fluorophenyl)(7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)methyl)cyclohexanecarbonitrile (3bb)



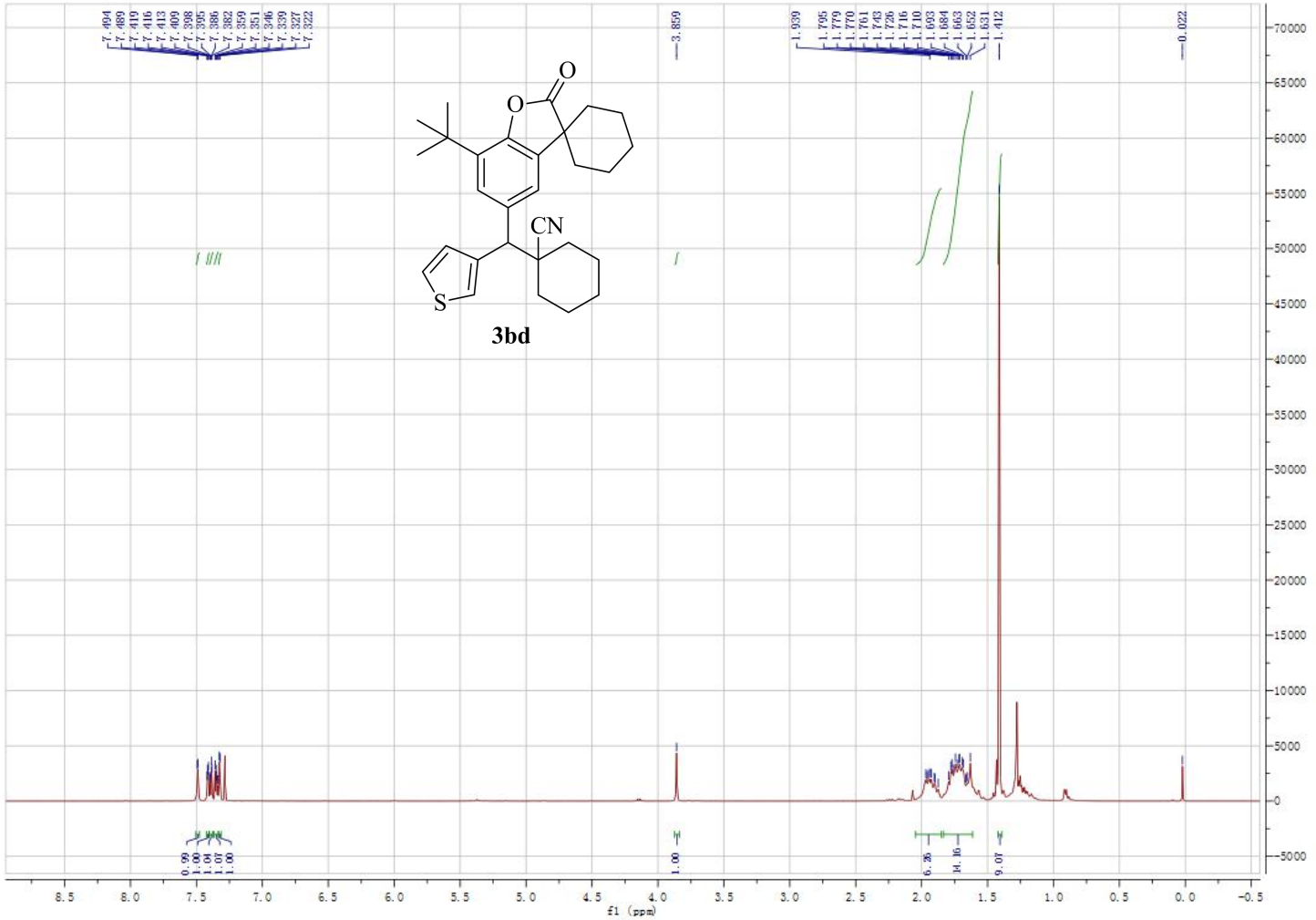
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(2-chloro-4-fluorophenyl)methyl)cyclohexanecarbonitrile (3bc)



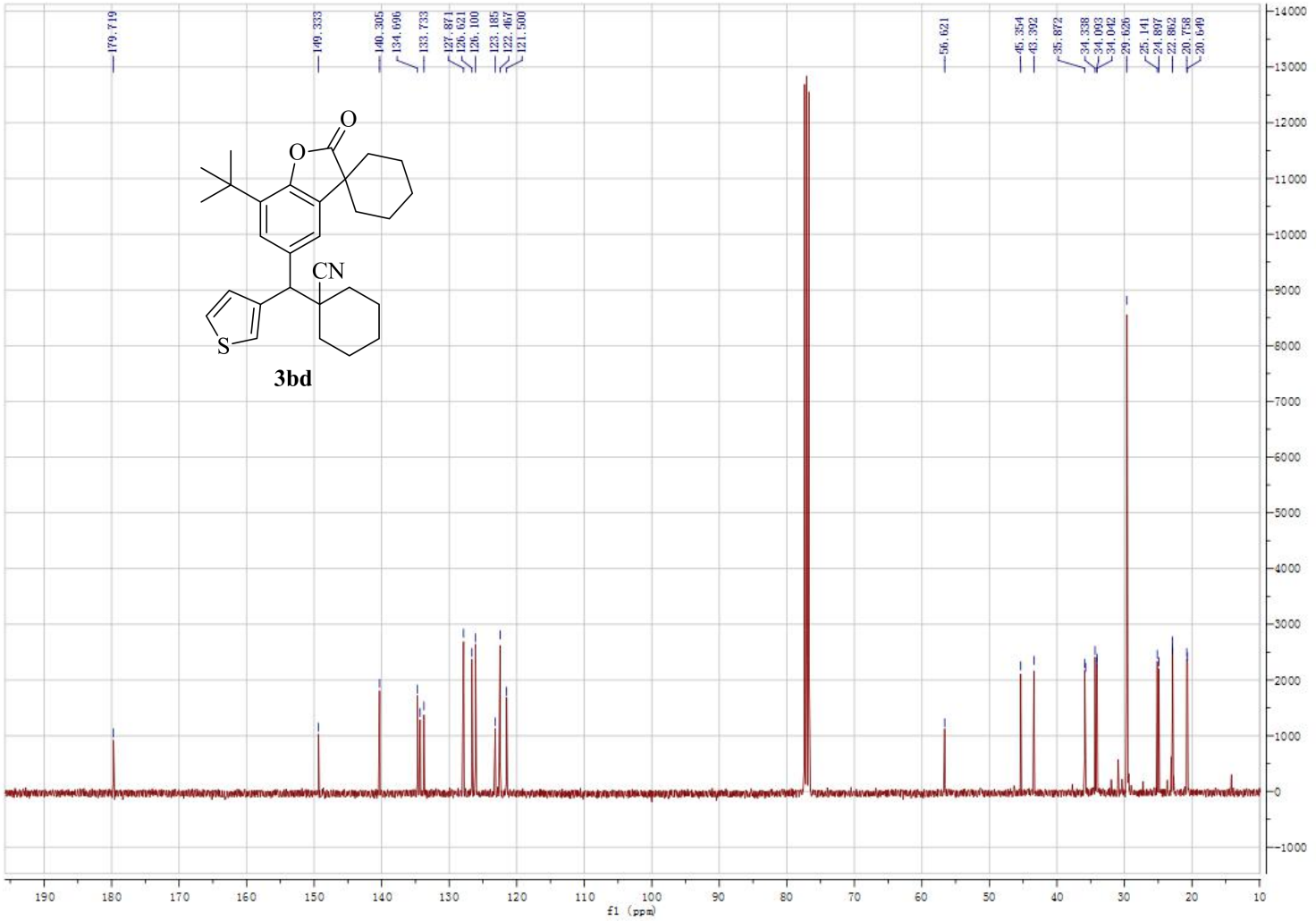
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(2-chloro-4-fluorophenyl)methyl)cyclohexanecarbonitrile (3bc)



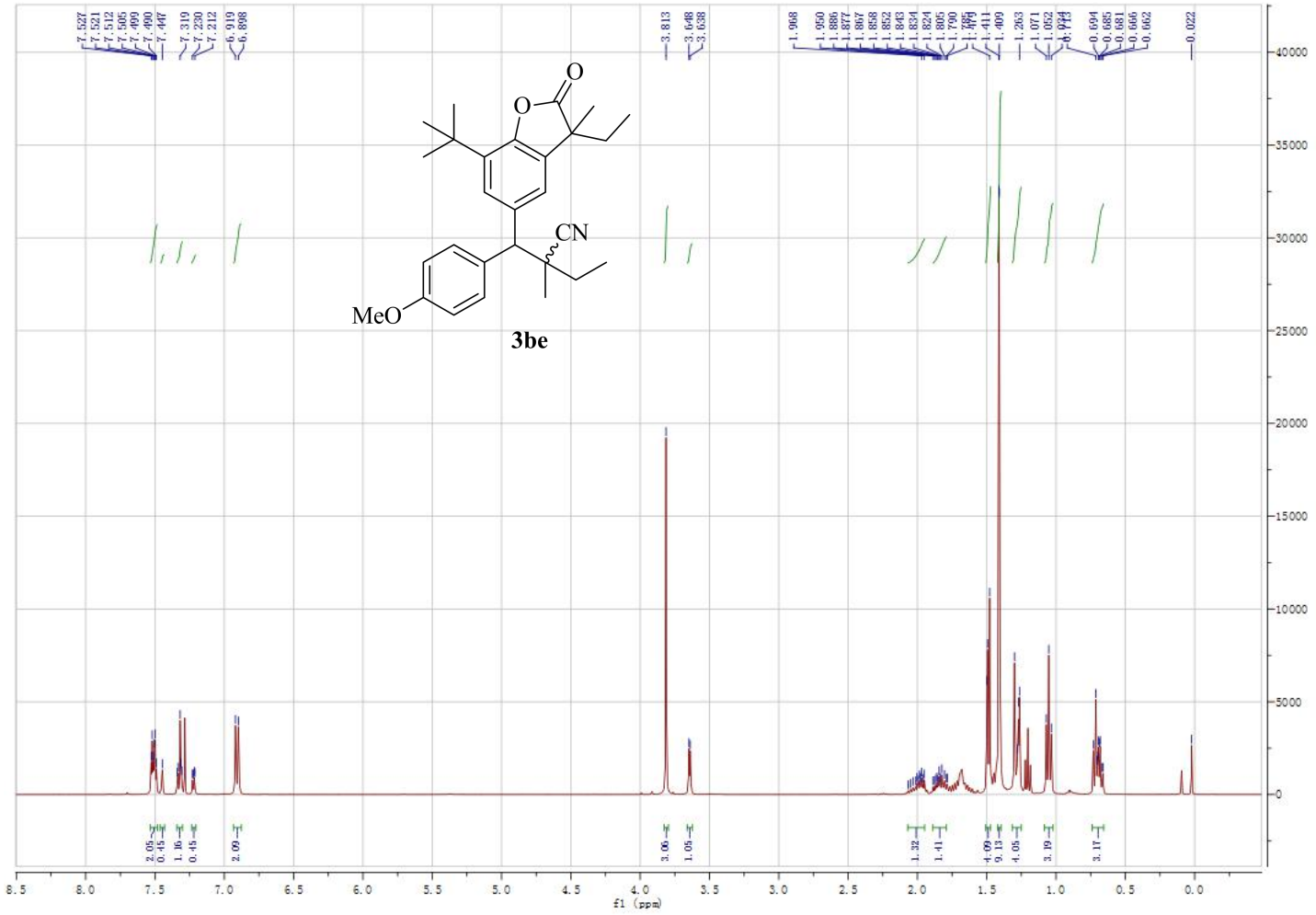
1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(thiophen-3-yl)methyl)cyclohexanecarbonitrile (3bd)



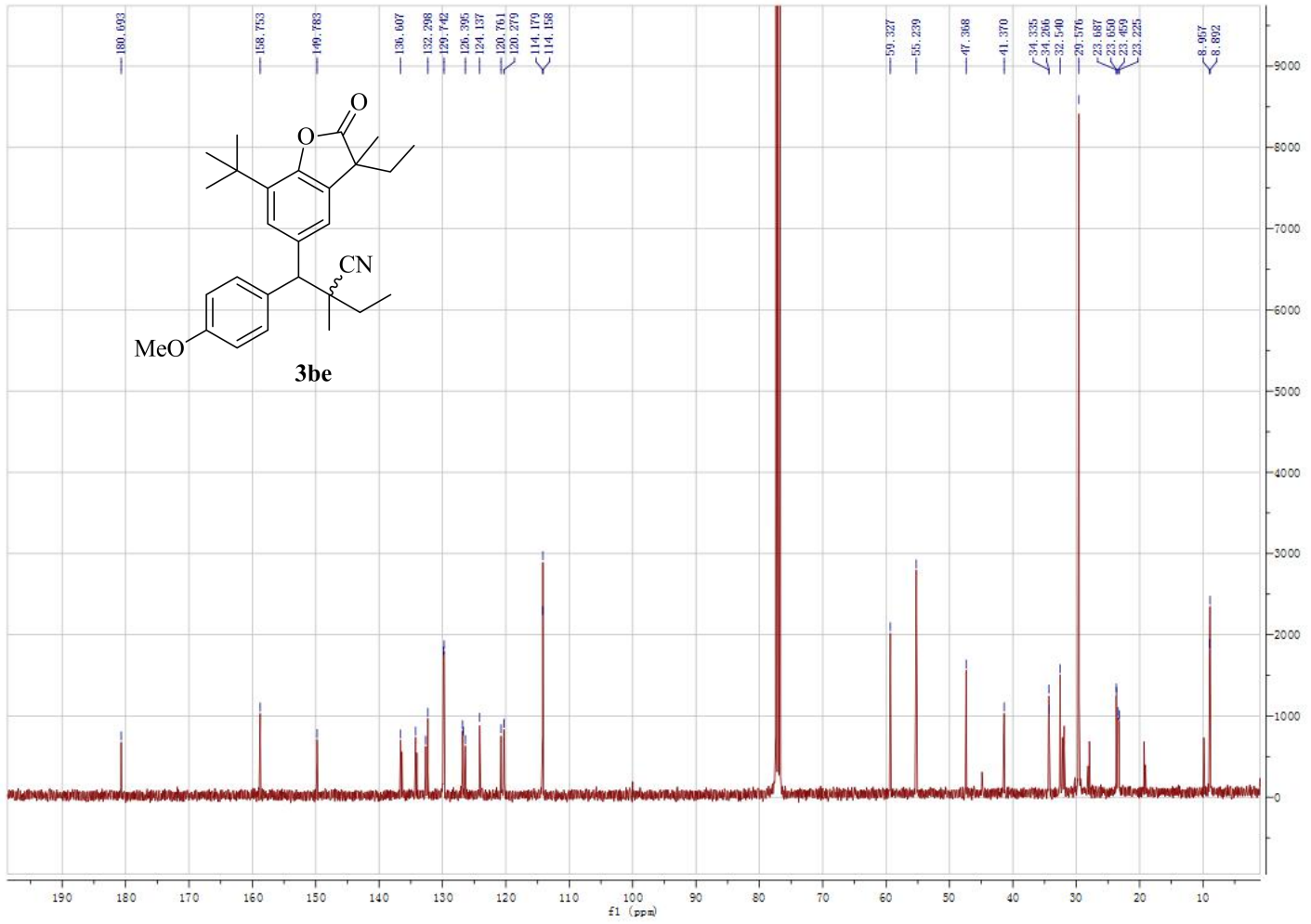
9-19-03, **1-((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)(thiophen-3-yl)methyl)cyclohexanecarbonitrile (3bd)**



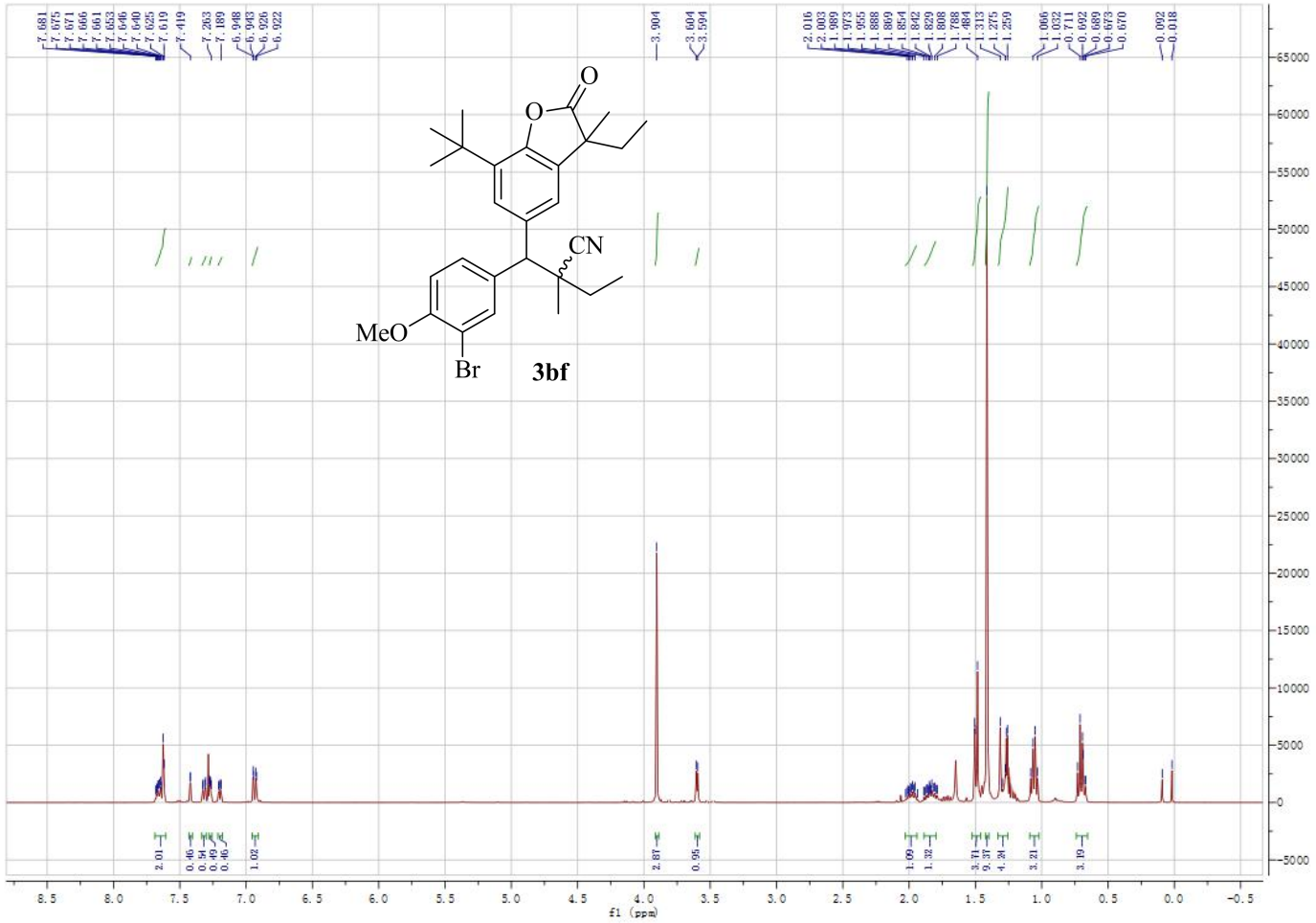
2-((7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)(4-methoxyphenyl)methyl)-2-methylbutanenitrile (3be)



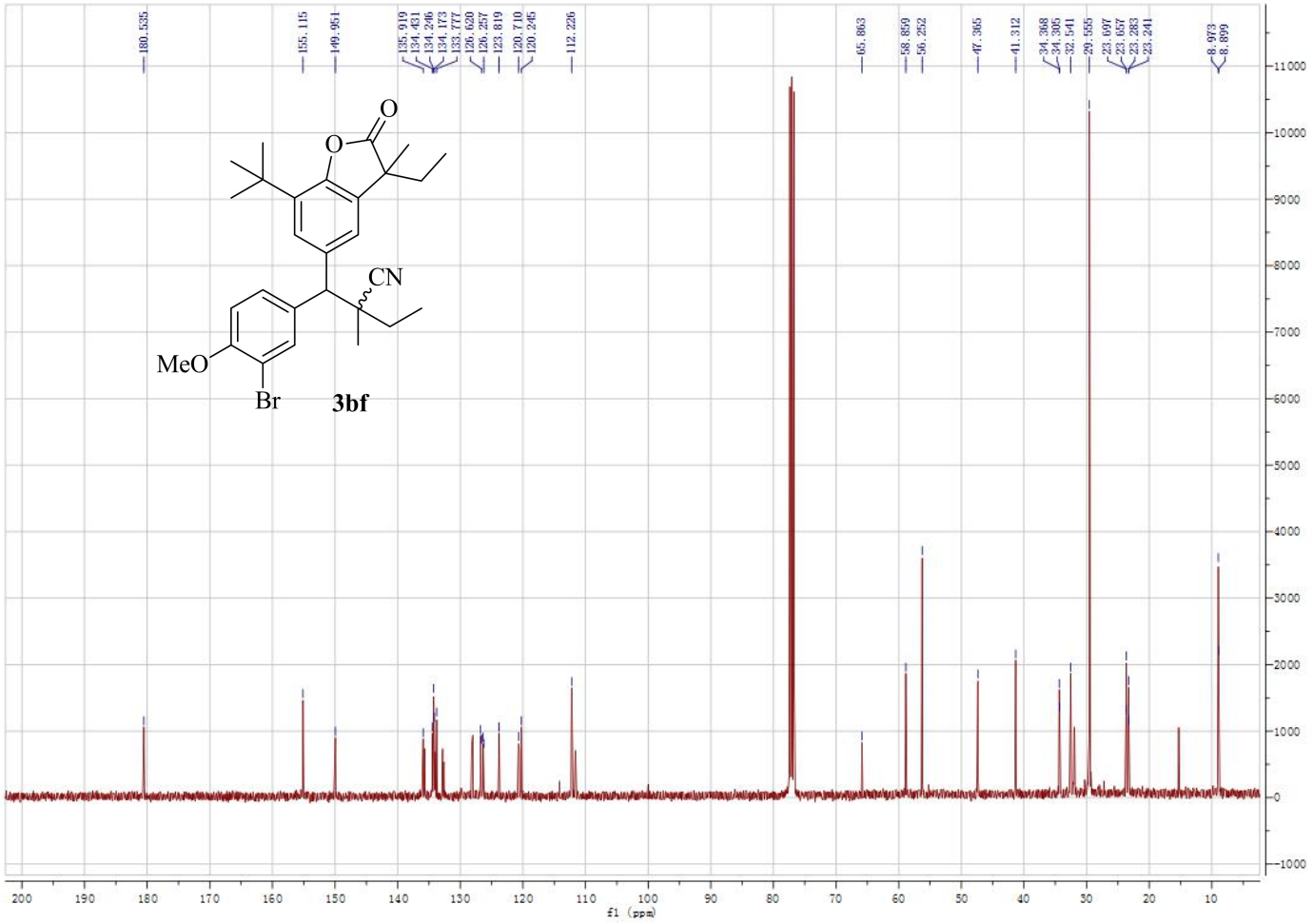
2-((7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)(4-methoxyphenyl)methyl)-2-methylbutanenitrile (3be)



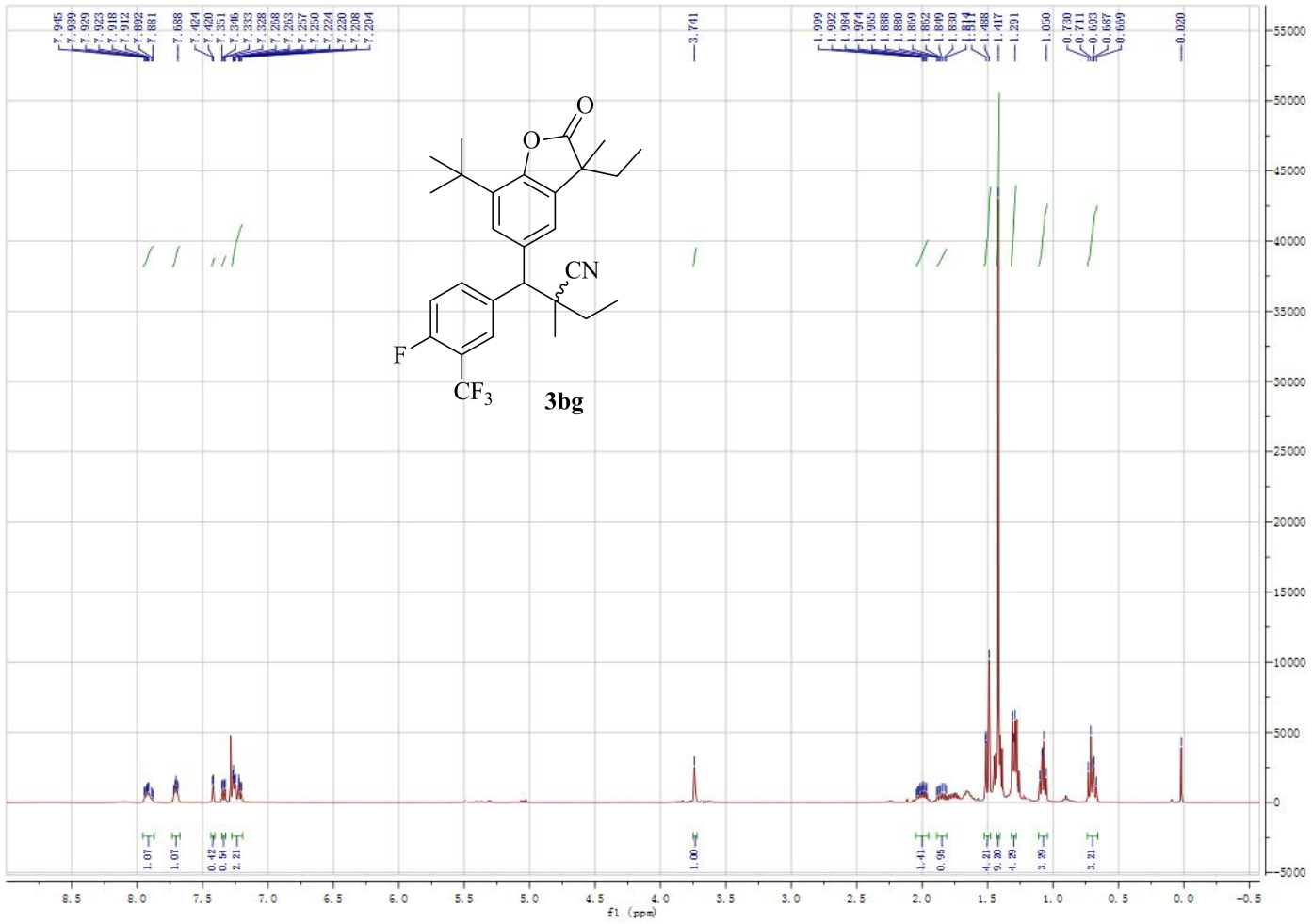
2-((3-bromo-4-methoxyphenyl)(7-(tert-butyl)-3-ethyl-3-methyl-2-oxo-2,3-dihydrobenzofuran-5-yl)methyl)-2-methylbutanenitrile (3bf)



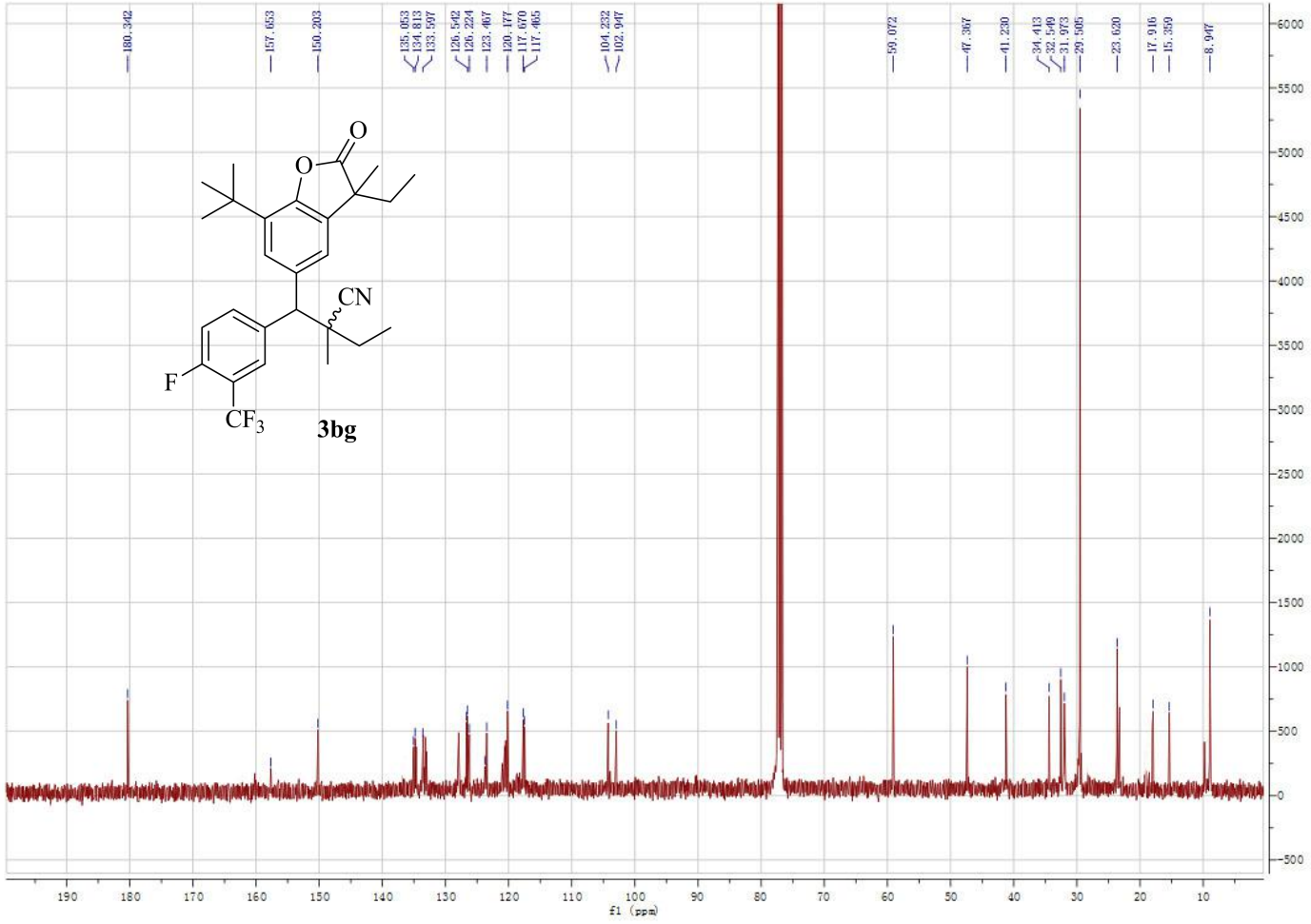
2-((3-bromo-4-methoxyphenyl)(7-(tert-butyl)-3-ethyl-3-methyl-2-oxo-2,3-dihydrobenzofuran-5-yl)methyl)-2-methylbutanenitrile (3bf)



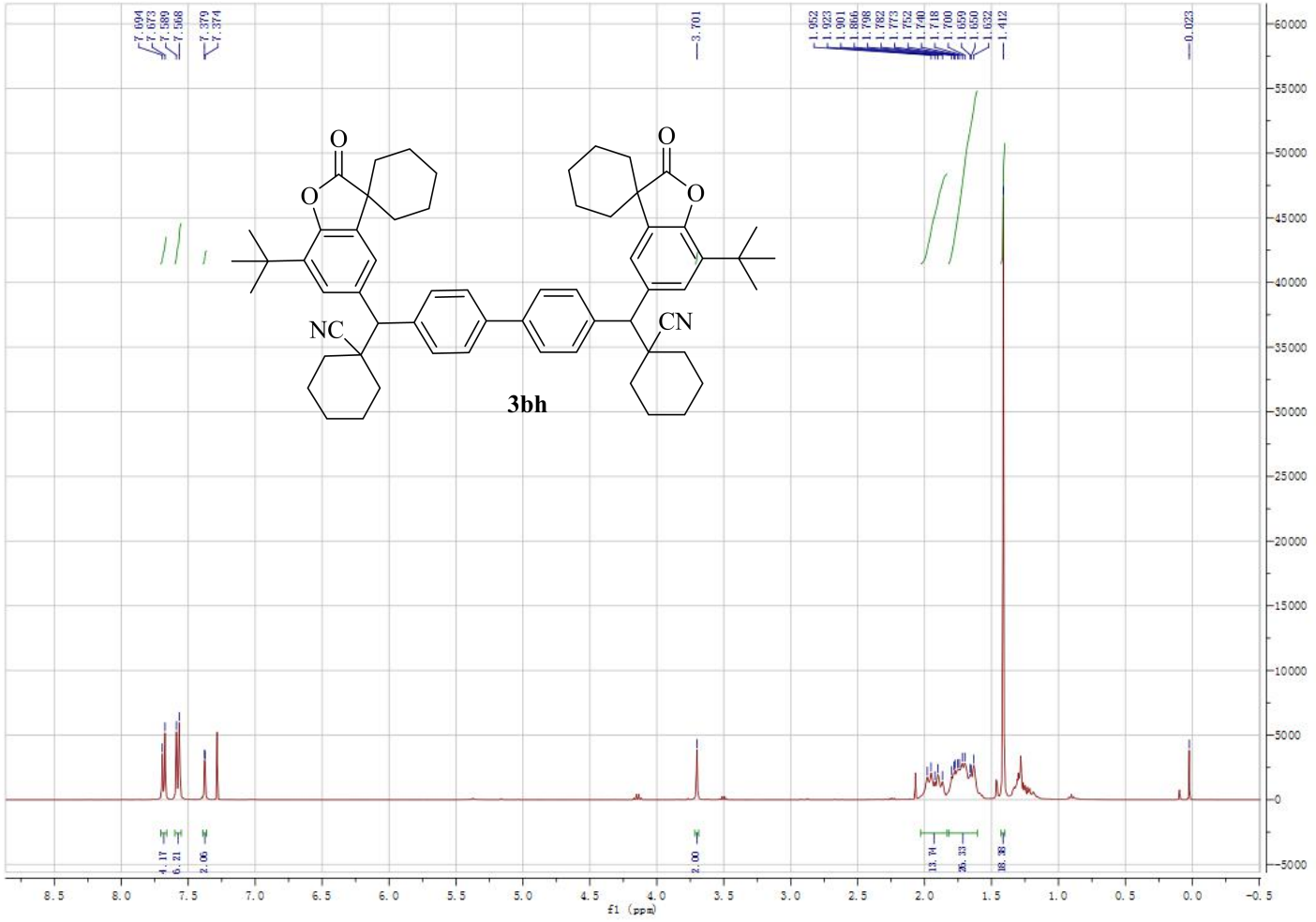
2-((7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)(4-fluoro-3-(trifluoromethyl)phenyl)methyl)-2-methylbutanenitrile (3bg)



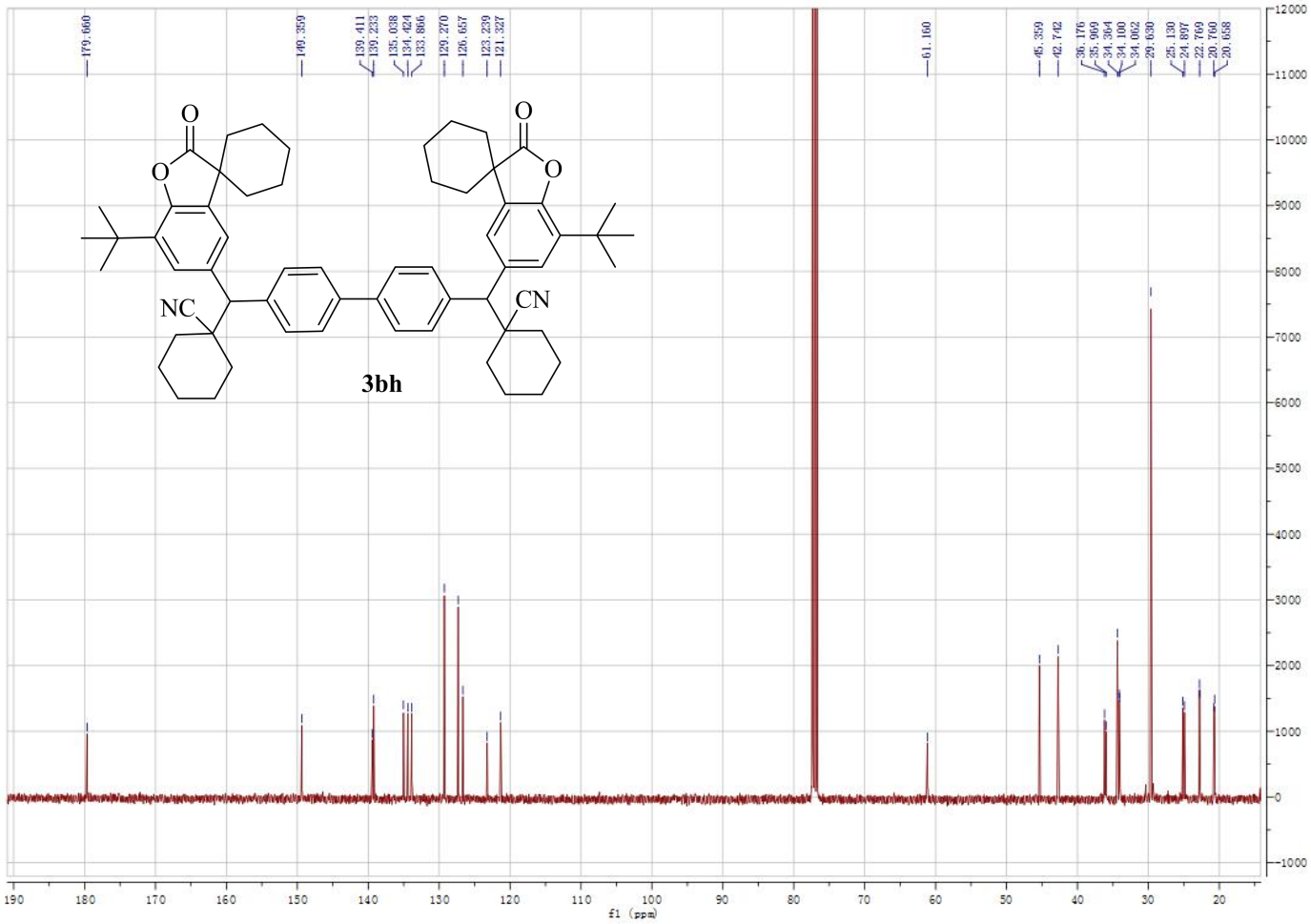
2-((7-(tert-butyl)-3,3-dimethyl-2-oxo-2,3-dihydrobenzofuran-5-yl)(4-fluoro-3-(trifluoromethyl)phenyl)methyl)-2-methylbutanenitrile (3bg)



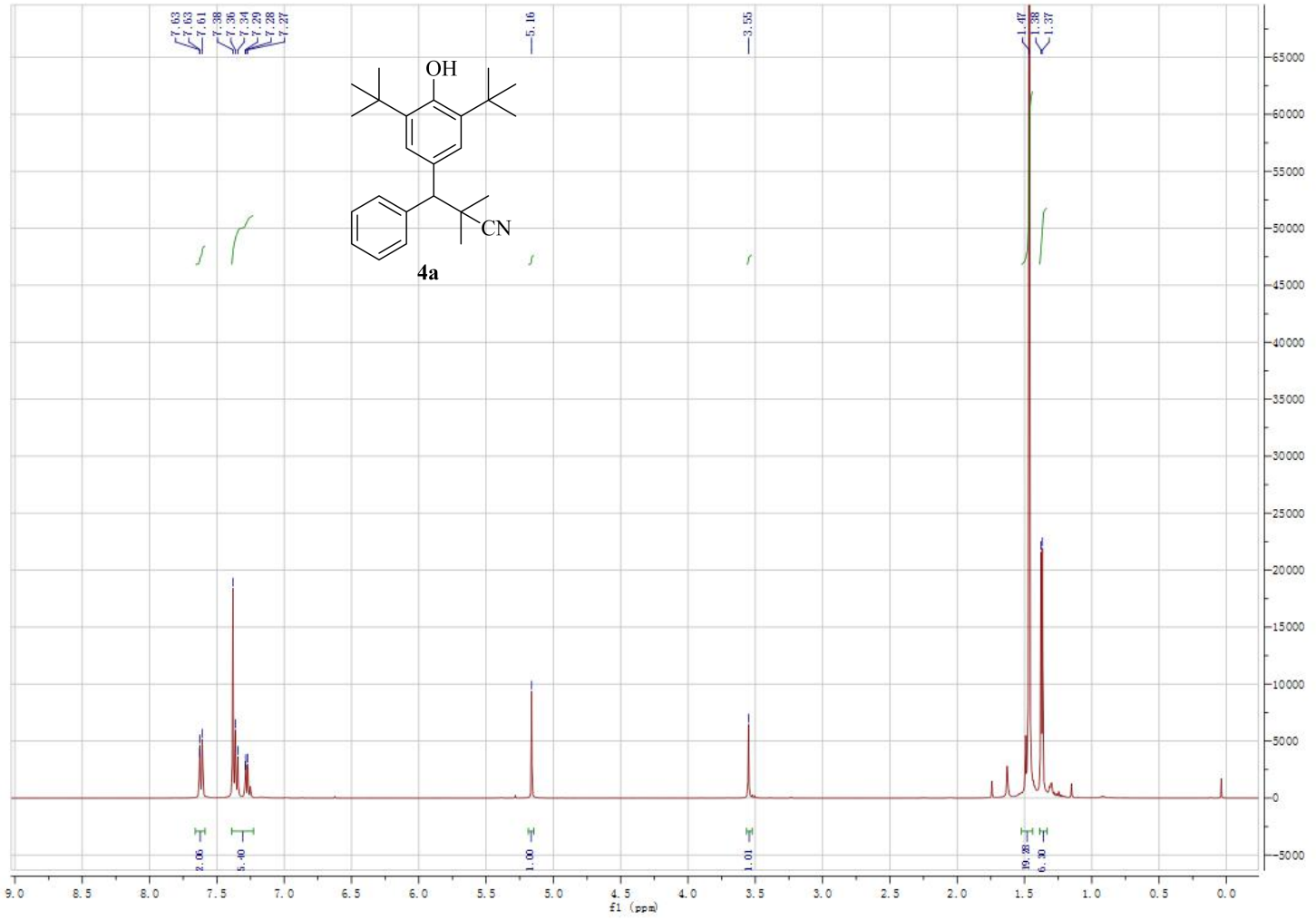
1,1'-([1,1'-biphenyl]-4,4'-diylbis((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)methylene))dicyclohexanecarbonitrile (3bh)



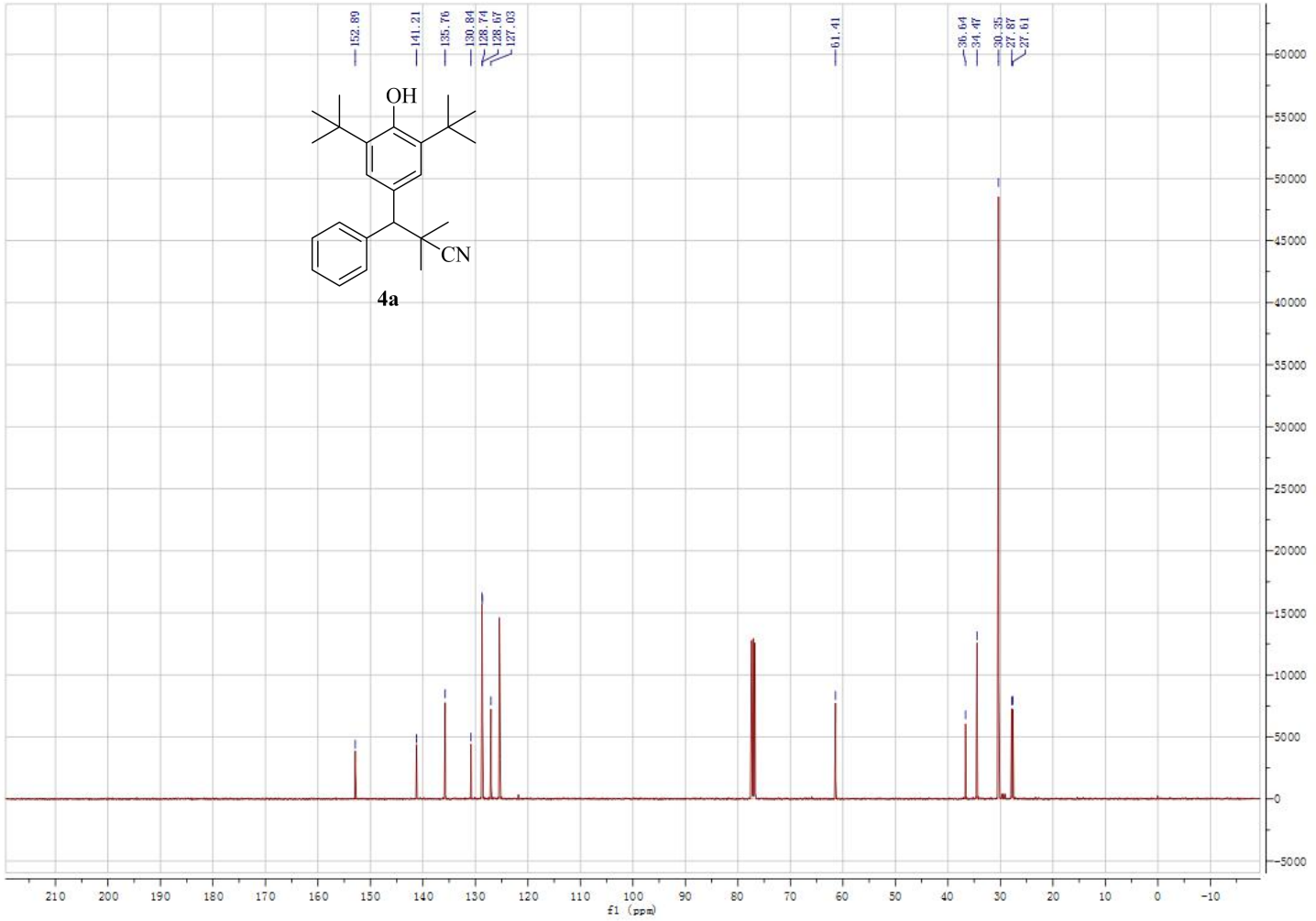
1,1'-([1,1'-biphenyl]-4,4'-diylbis((7-(tert-butyl)-2-oxo-2H-spiro[benzofuran-3,1'-cyclohexan]-5-yl)methylene))dicyclohexanecarbonitrile (3bh)



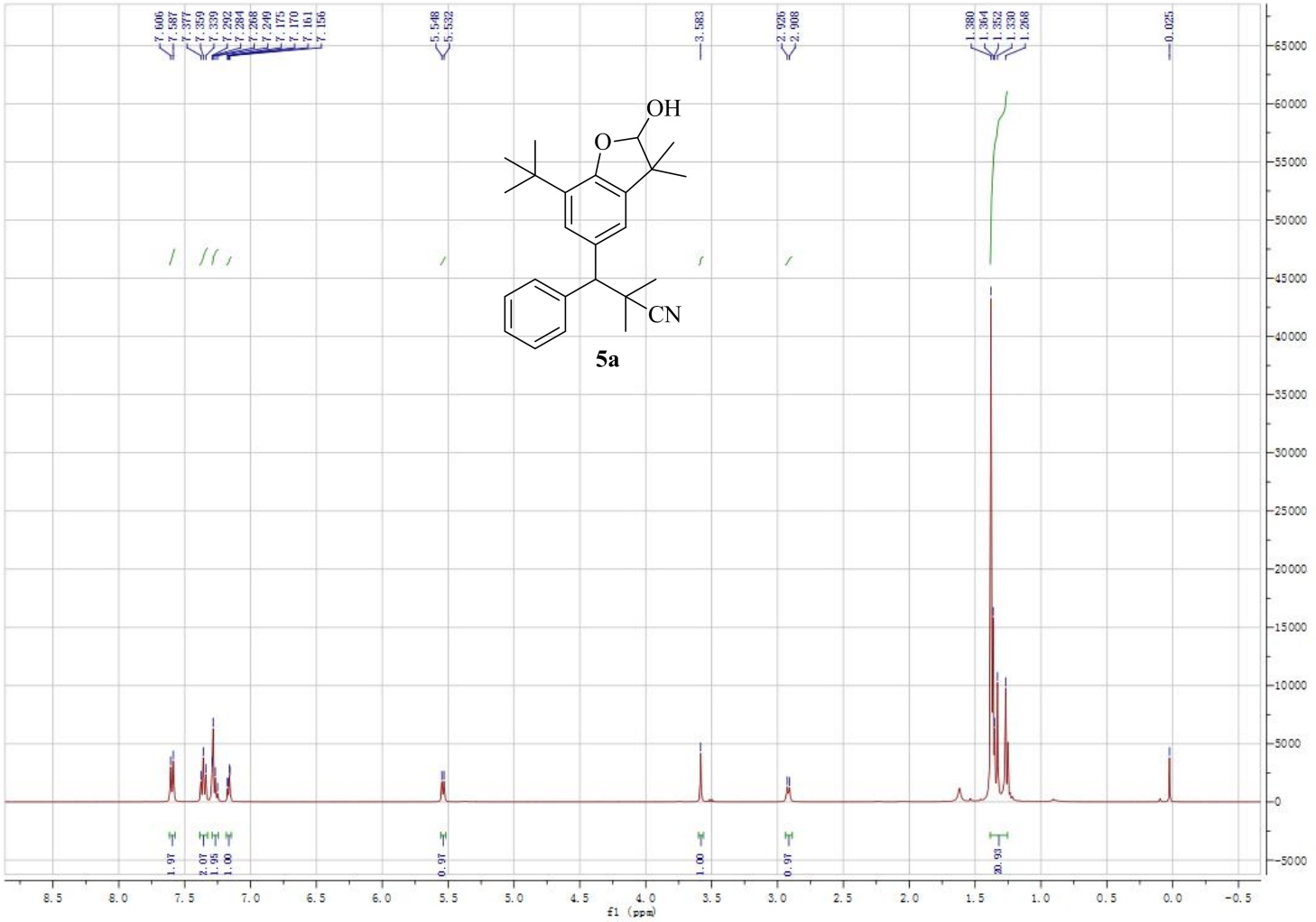
3-(3,5-di-tert-butyl-4-hydroxyphenyl)-2,2-dimethyl-3-phenylpropanenitrile (4a)



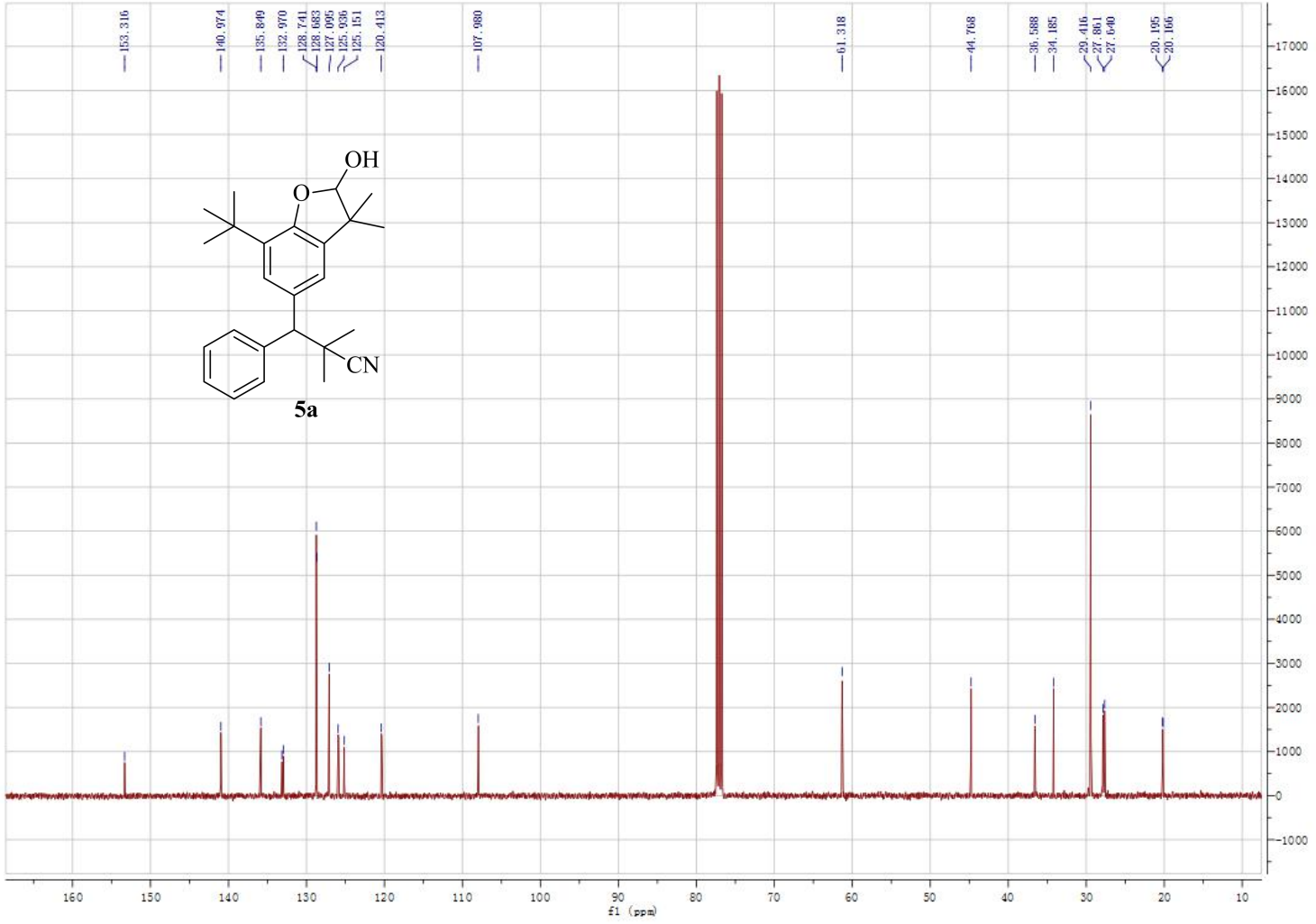
3-(3,5-di-tert-butyl-4-hydroxyphenyl)-2,2-dimethyl-3-phenylpropanenitrile (4a)



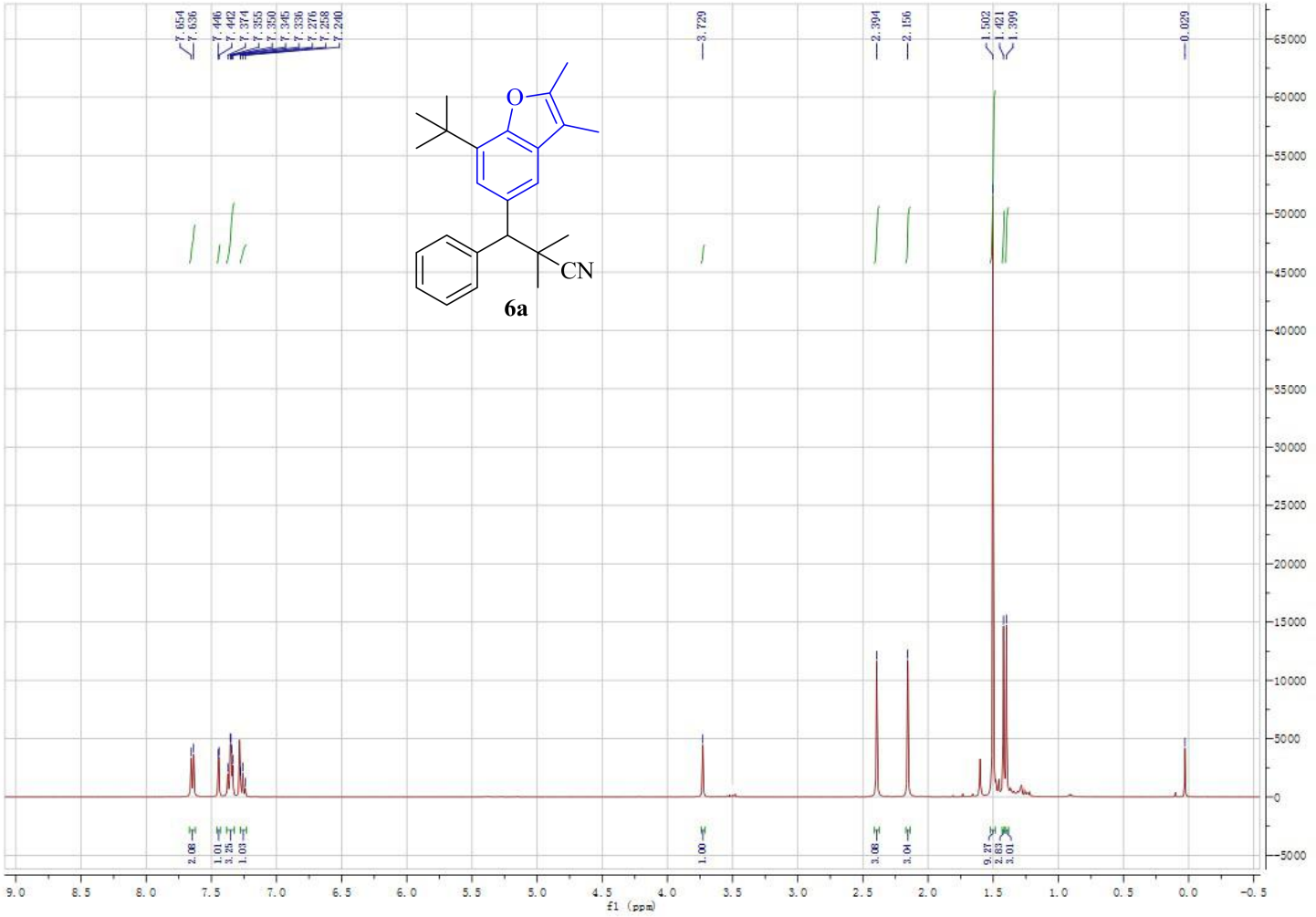
3-(7-(tert-butyl)-2-hydroxy-3,3-dimethyl-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-phenylpropanenitrile (5a)



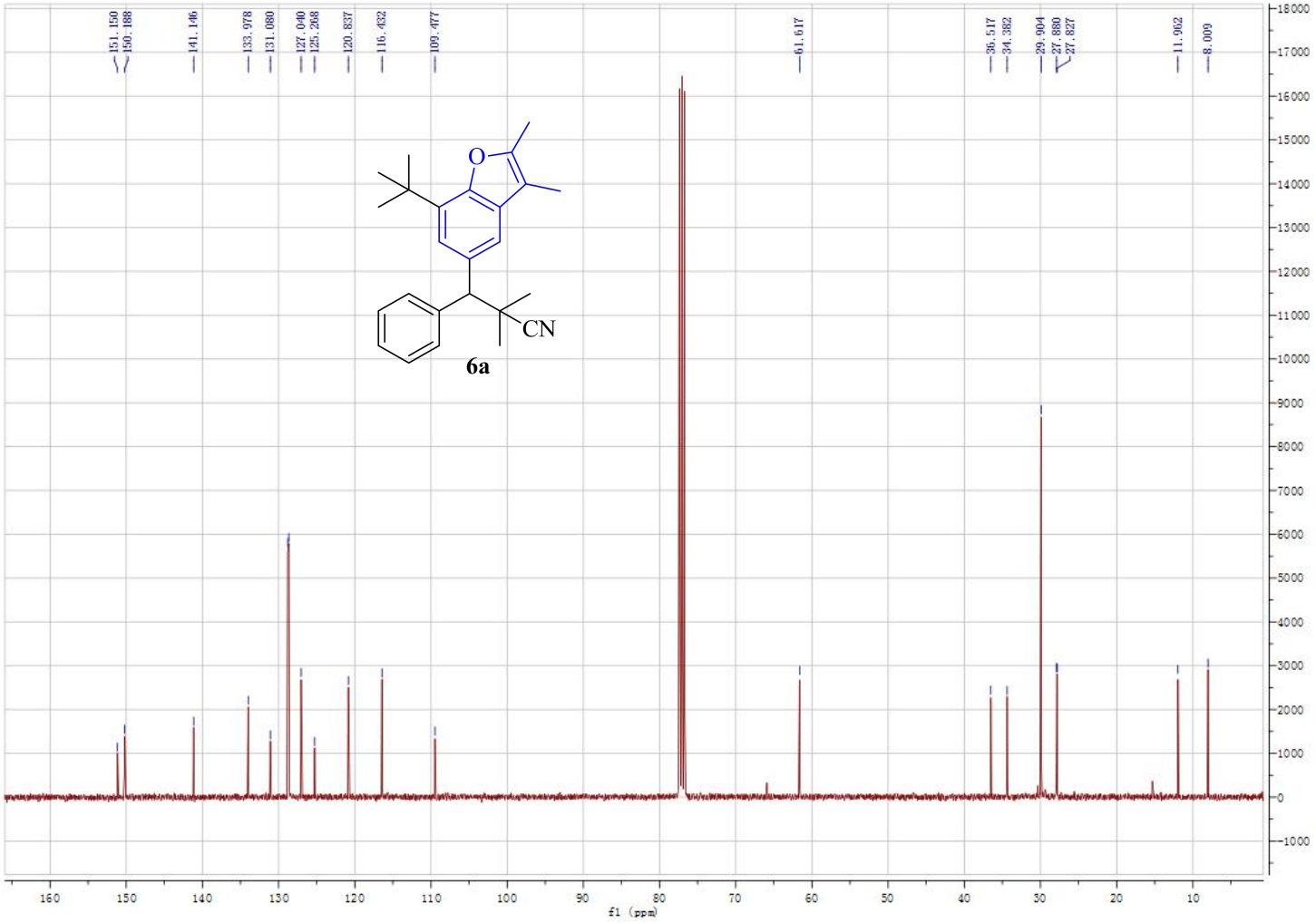
3-(7-(tert-butyl)-2-hydroxy-3,3-dimethyl-2,3-dihydrobenzofuran-5-yl)-2,2-dimethyl-3-phenylpropanenitrile (5a)



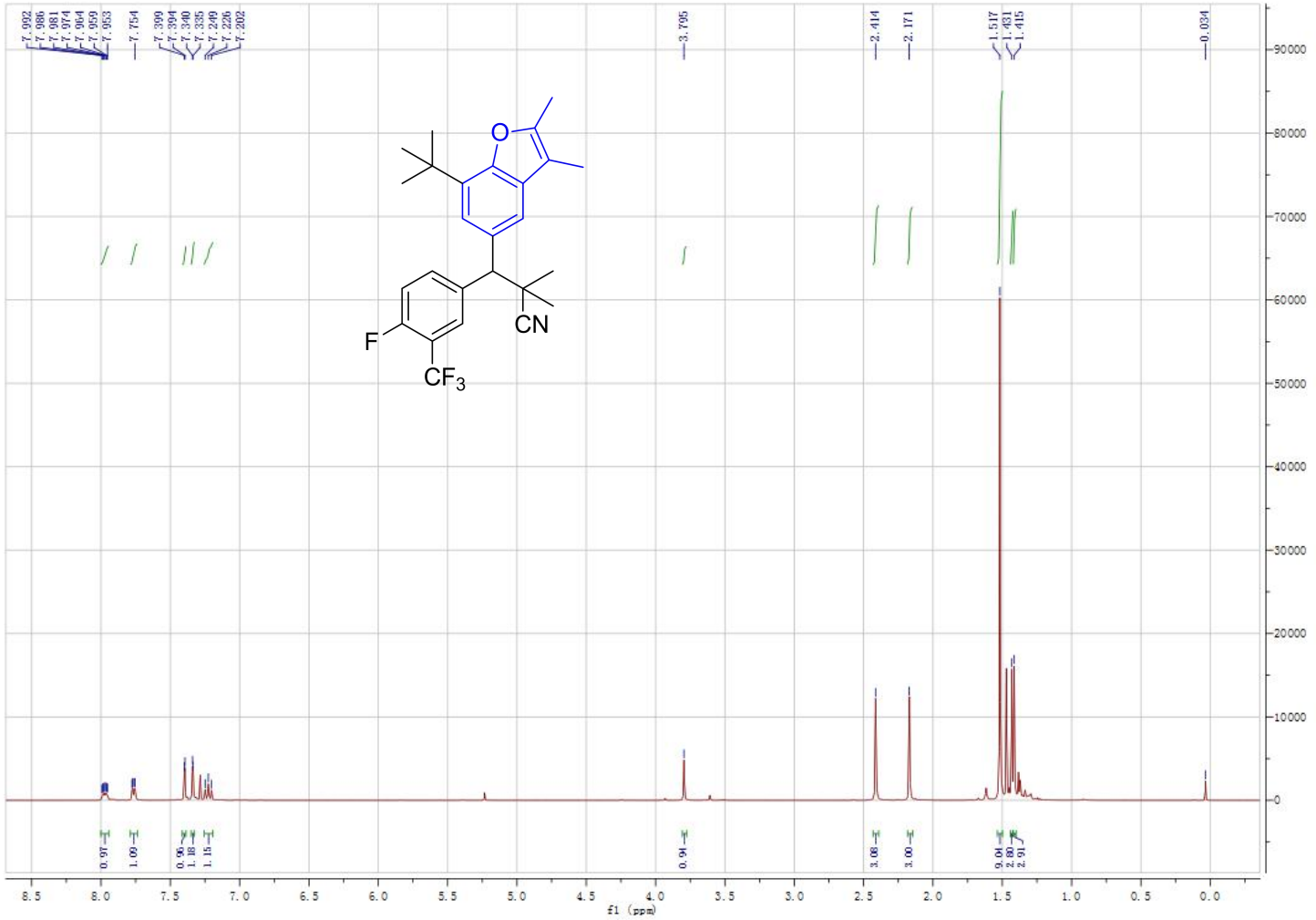
3-(7-(tert-butyl)-2,3-dimethylbenzofuran-5-yl)-2,2-dimethyl-3-phenylpropanenitrile (6a)12-5-5



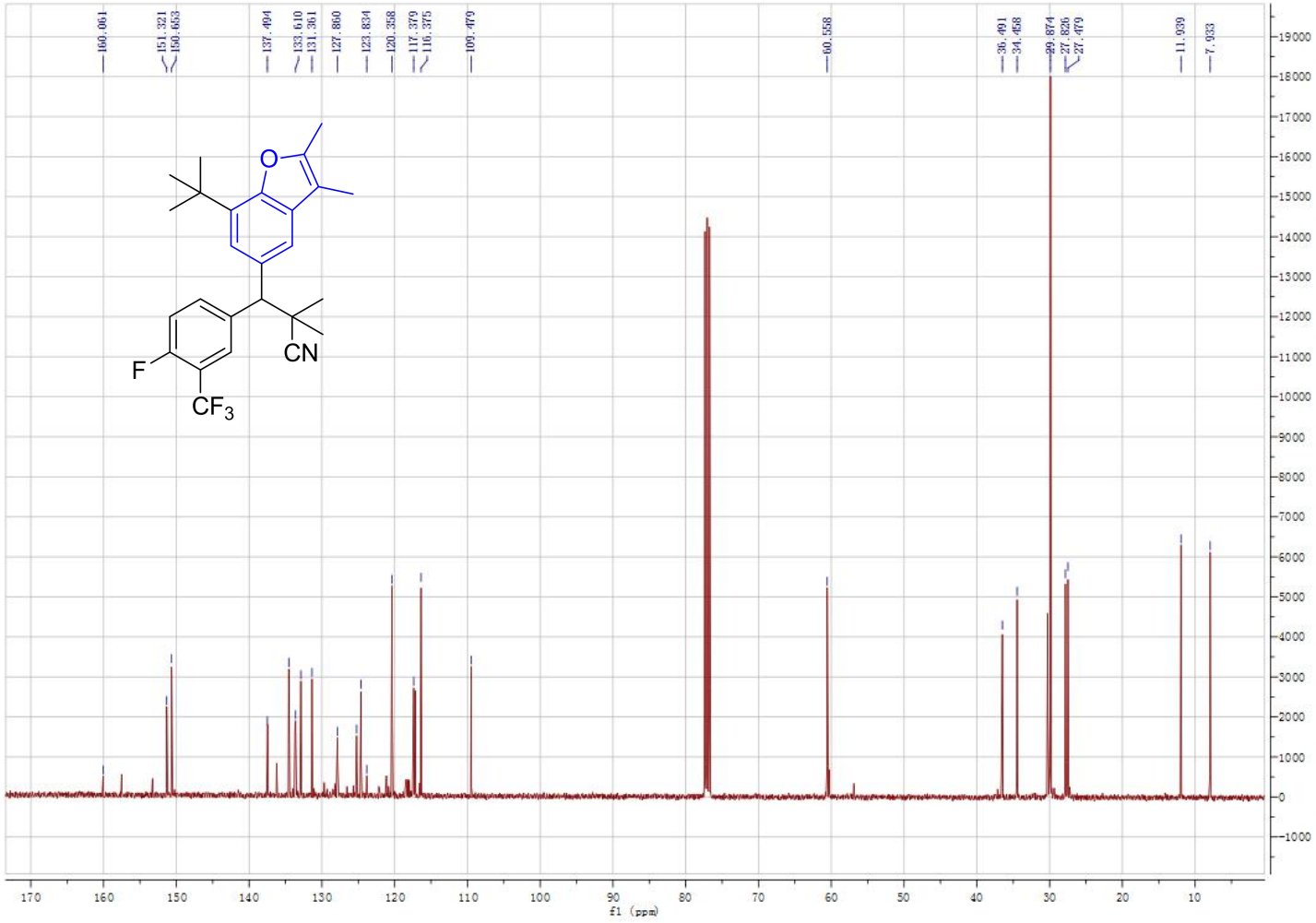
3-(7-(tert-butyl)-2,3-dimethylbenzofuran-5-yl)-2,2-dimethyl-3-phenylpropanenitrile (6a)12-5-5



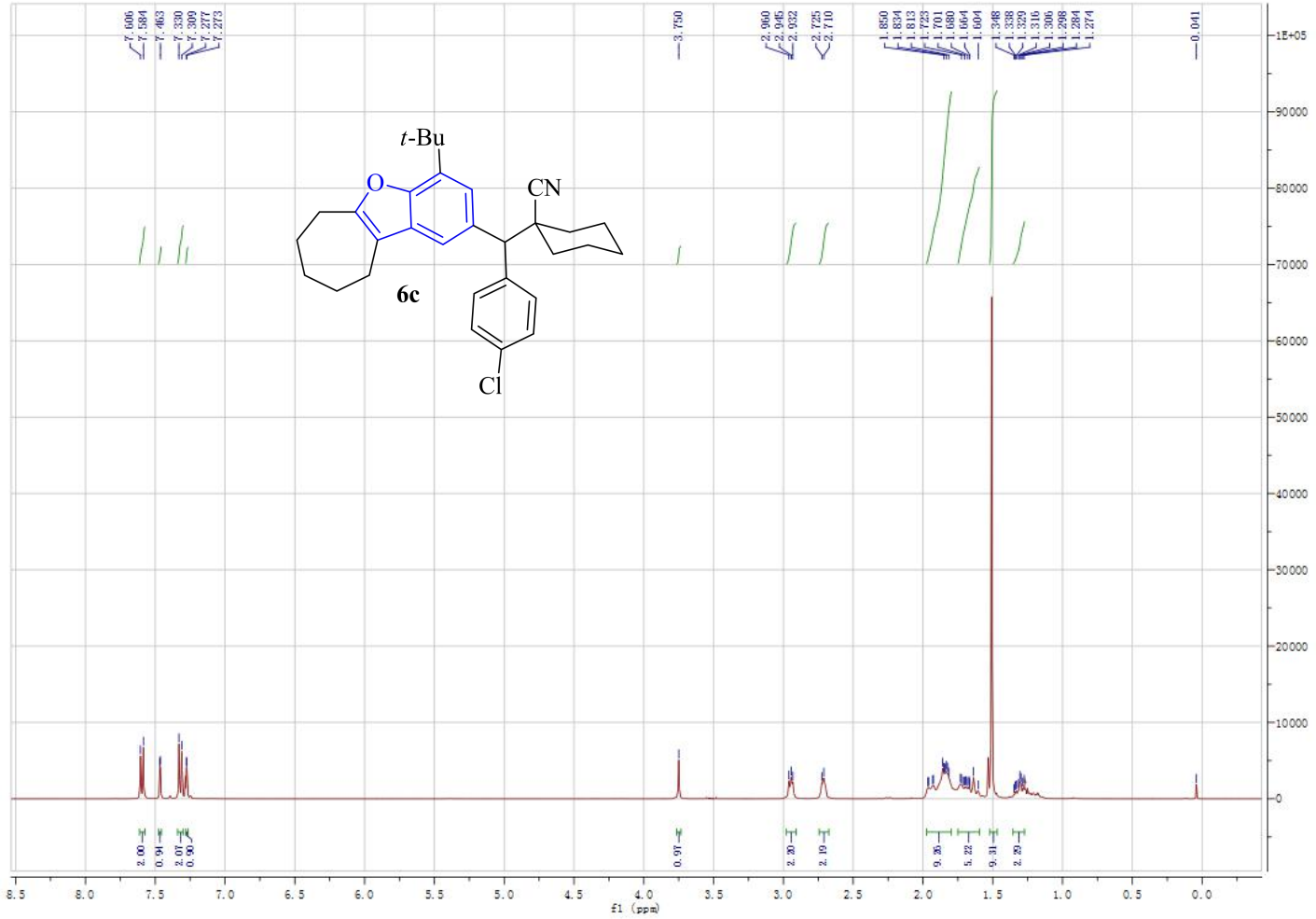
3-(7-(tert-butyl)-2,3-dimethylbenzofuran-5-yl)-3-(4-fluoro-3-(trifluoromethyl)phenyl)-2,2-dimethylpropanenitrile (6b)



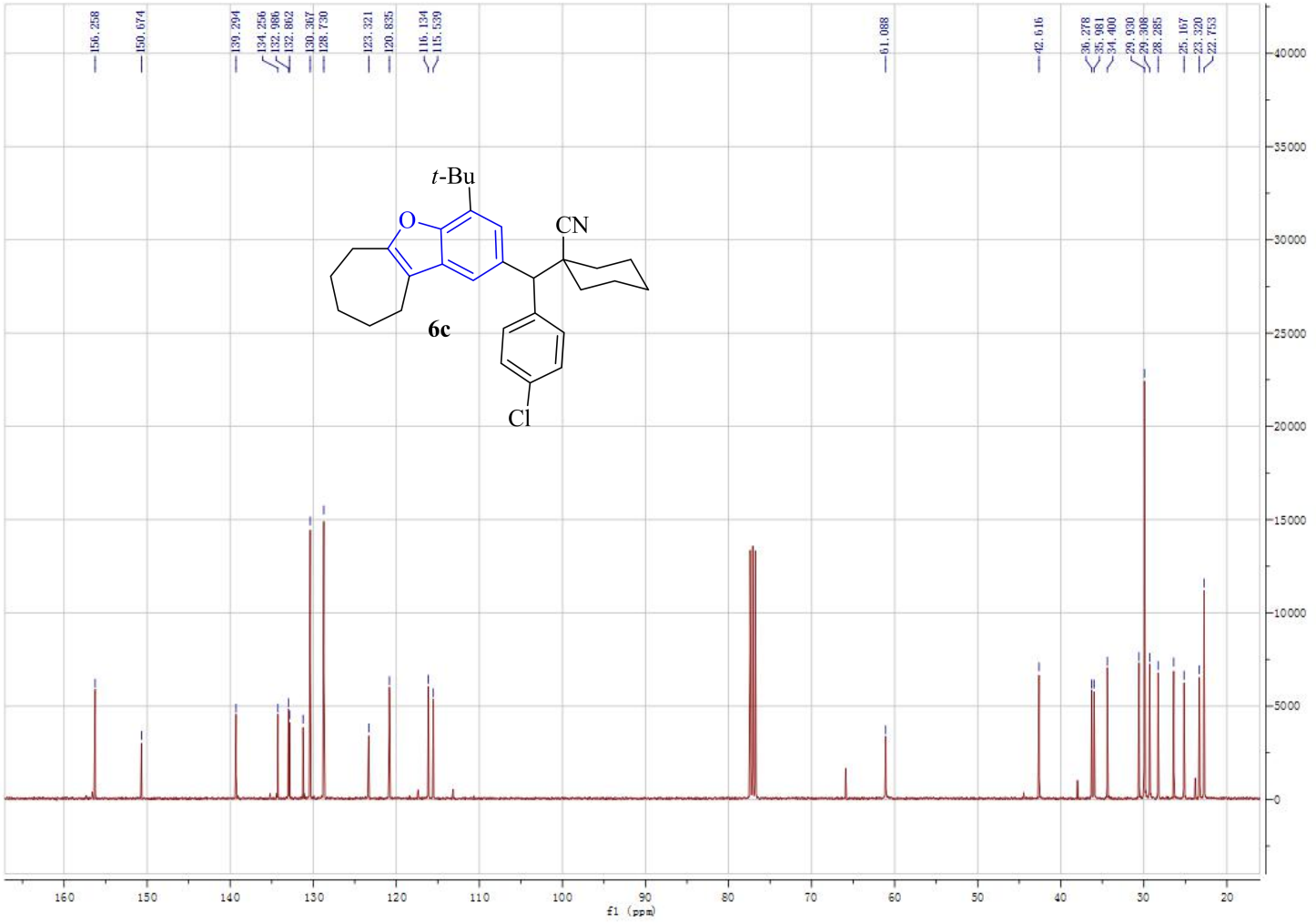
3-(7-(tert-butyl)-2,3-dimethylbenzofuran-5-yl)-3-(4-fluoro-3-(trifluoromethyl)phenyl)-2,2-dimethylpropanenitrile (6b)

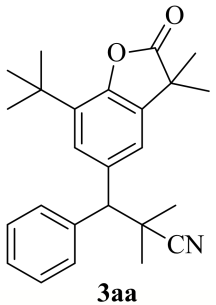


1-((4-(tert-butyl)-6,7,8,9,10,10a-hexahydro-5aH-cyclohepta[b]benzofuran-2-yl)(4-chlorophenyl)methyl)cyclohexanecarbonitrile (6c)



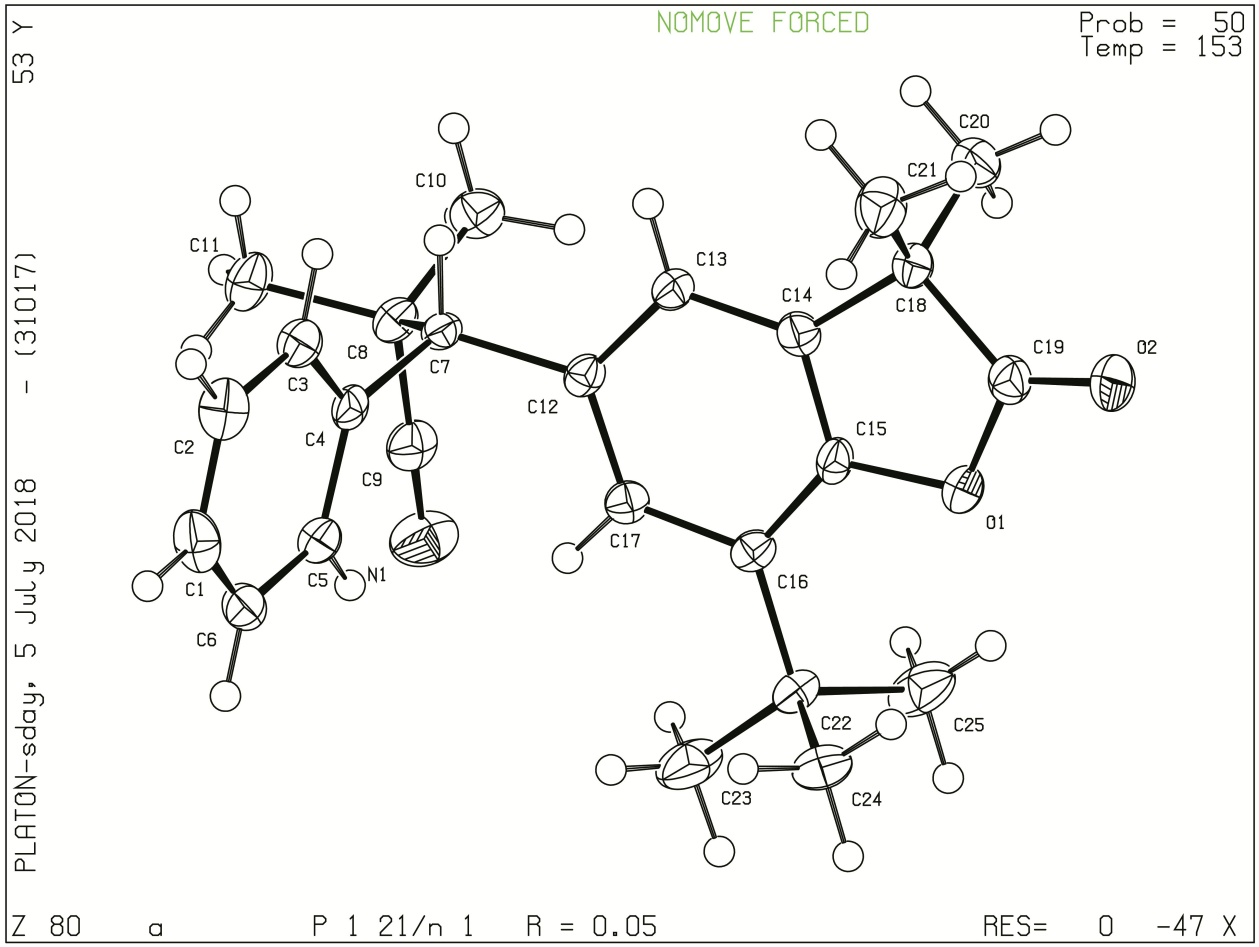
1-((4-(tert-butyl)-6,7,8,9,10,10a-hexahydro-5aH-cyclohepta[b]benzofuran-2-yl)(4-chlorophenyl)methyl)cyclohexanecarbonitrile (6c)



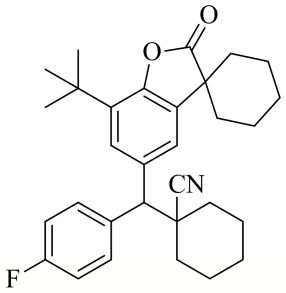


3aa

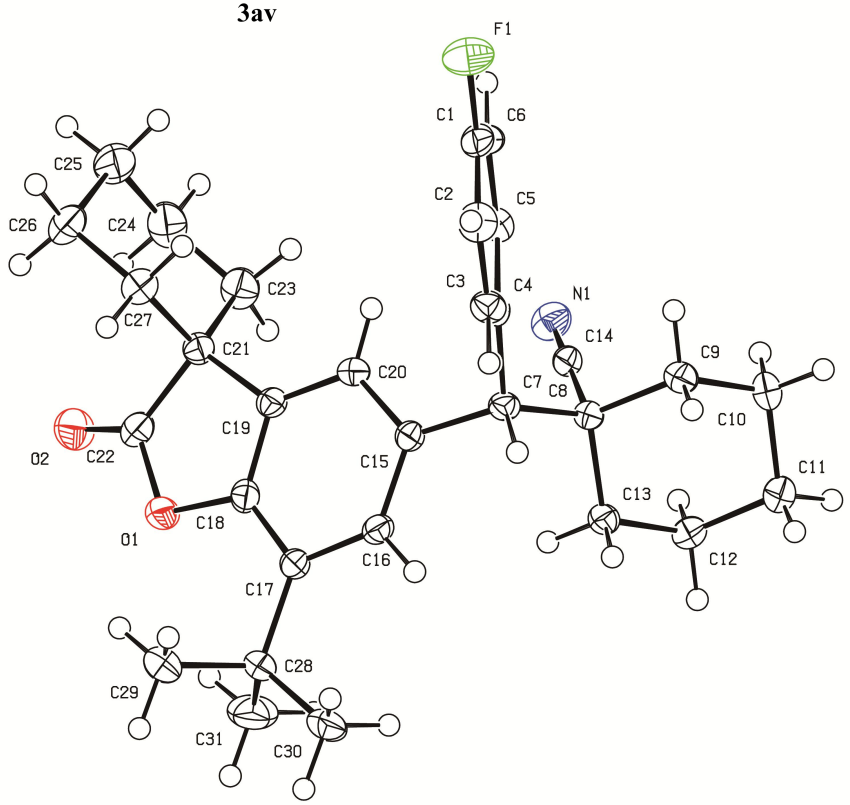
6. X-ray of 3aa



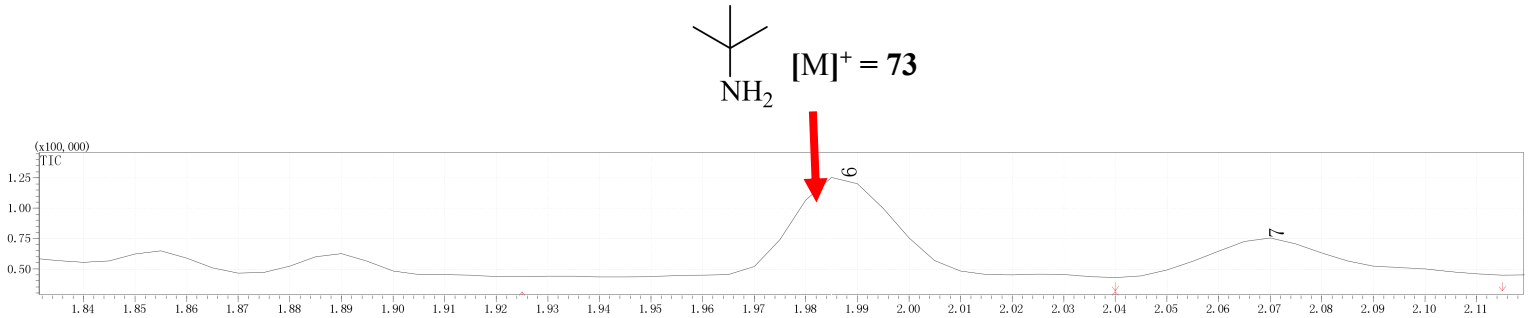
6、X-ray of 3av

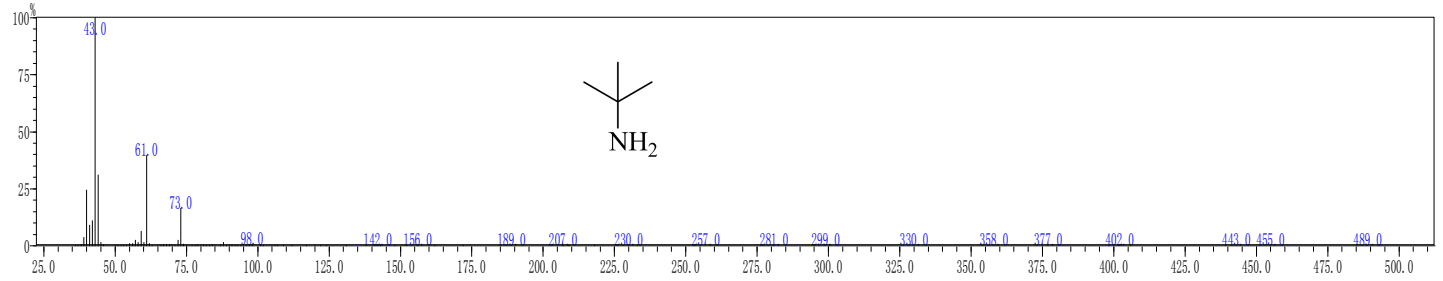


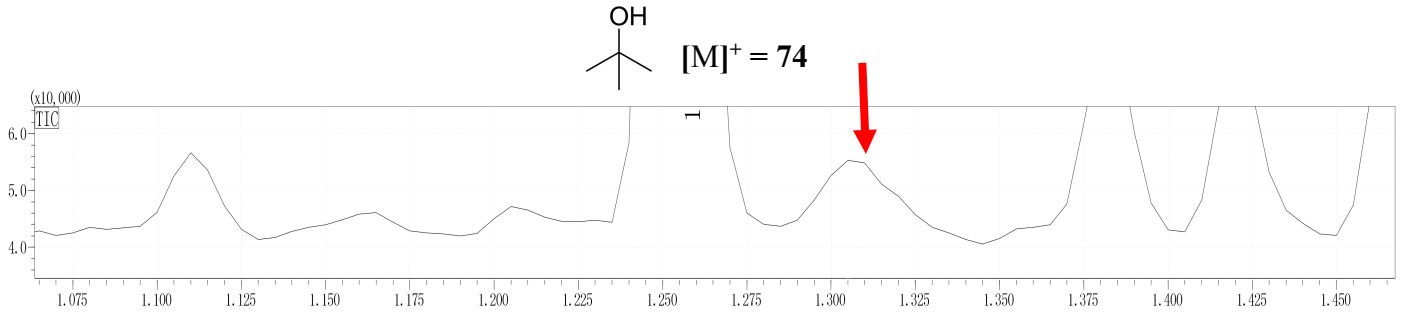
3av

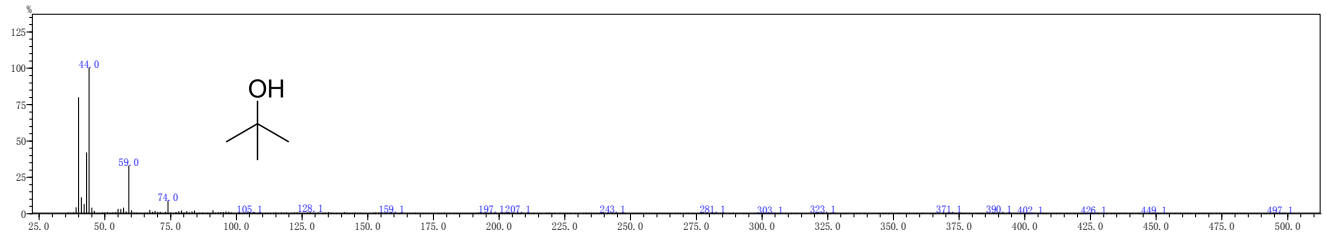


7. Observation of side-product *tert*-butylamine (*t*-BuNH$_2$)and *tert*-butanol (*t*-BuOH).






OH
[M]+ = 74
(x10,000)
TIC
6.0
5.0
4.0
1
1.075
1.100
1.125
1.150
1.175
1.200
1.225
1.250
1.275
1.300
1.325
1.350
1.375
1.400
1.425
1.450


%
125
100
75
50
25
0
44.0
59.0
74.0
OH
25.0
50.0
75.0
100.0
125.0
150.0
175.0
200.0
225.0
250.0
275.0
300.0
325.0
350.0
375.0
400.0
425.0
450.0
475.0
500.0