Supplementary Information

Amine-promoted three-component cycloaddition of bicyclo[1.1.0]butanes with hydroxylamine and polyformaldehyde: expedient access to 2-oxa-3-azabicyclo[3.1.1]heptanes

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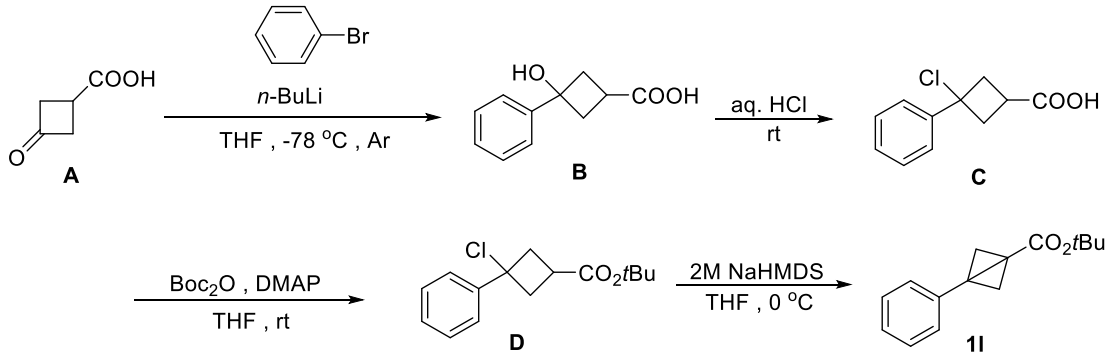
1. General information

Commercially available reagents and solvents were used without any purification. The progress of the reactions was monitored by TLC with silica gel plates, and the visualization was carried out under UV light (254 nm). Melting points were determined using a Büchi B-540 capillary melting point apparatus. NMR spectra were recorded using Bruker Avance III 400 MHz spectrometers and Bruker Avance III 600 MHz spectrometers. Chemical shifts of ^{1}H NMR were reported relative to the solvent signal ($CDCl_3$: δ = 7.26 ppm; DMSO-d_6: δ = 2.50 ppm; Acetone-d_6 = 2.05 ppm). Chemical shifts of ^{13}C NMR were reported relative to the solvent signal ($CDCl_3$: δ = 77.00 ppm; DMSO-d_6: δ = 39.50 ppm. Acetone-d_6 = 29.84 ppm). HRMS spectra were recorded on an electrospray ionization quadrupole time-of-flight (ESI-Q-TOF) mass spectrometer. Column chromatography was performed on silica gel (300-400 mesh).

2. Synthesis of substrates 1

Preparation of bicyclo[1.1.0]butanes[1] **1a**-**1n**. Typical procedure.

(1) Preparation of *tert*-butyl 3-phenylbicyclo[1.1.0]butane-1-carboxylate (**1l**)



Step 1: To a solution of aromatic bromide (2.2 equiv.) in anhydrous THF (0.7 M), *n*-BuLi (2.5 M, 2.2 equiv.) was added dropwise at -78 °C under an argon atmosphere. The reaction mixture was stirred for 1 hour at -78 °C, and then a solution of 3-oxocyclobutane-1-carboxylic acid (1.0 equiv.) in anhydrous THF (2.5 M) was added in one portion, the temperature rising to -25 °C. The mixture was stirred for an additional hour and subsequently quenched with a saturated aqueous solution of NH_4Cl and H_2O (3:2). The reaction mixture was then diluted with hexane, and the organic layer was separated and washed with water. The aqueous layers were combined, acidified with a 2 M solution of $NaHSO_4$, and extracted with MTBE. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting crude material was used directly in the subsequent step without further

purification.

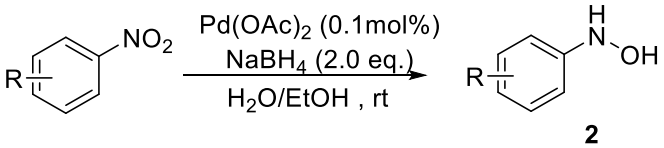
Step 2: To a solution of phenylcyclobutane-1-carboxylic acid (1.0 eq.) in toluene (0.8 M), concentrated HCl (12 eq.) was added dropwise at room temperature. The resulting mixture was stirred at room temperature overnight. The organic phase was separated, washed successively with water and brine (2 times), dried over Na_2SO_4, filtered, and concentrated under reduced pressure to yield the title compound. The crude product was used directly in the subsequent step without further purification.

Step 3: To a solution of 3-chloro-phenylcyclobutane-1-carboxylic acid (1.0 eq.) in THF (0.3 M), di-*tert*-butyl dicarbonate (Boc_2O, 1.2 eq.) and 4-dimethylaminopyridine (DMAP, 0.05 eq.) were added. The reaction mixture was stirred at room temperature overnight, then concentrated under reduced pressure. The residue was dissolved in a 1:1 mixture of MTBE and hexane. The solution was washed sequentially with 1 M $NaHSO_4$, 1 M $NaHCO_3$, and brine, then filtered through silica gel. The organic phase was concentrated under reduced pressure, and the resulting residue was purified by flash chromatography, eluting with a gradient from hexanes to 10% ethyl acetate in hexanes.

Step 4: To a solution of 3-chloro-3-phenylcyclobutane-1-carboxylate (1.0 eq.) in THF (0.4 M), a 2 M solution of NaHMDS (1.2 eq.) was added dropwise at 0–5 °C under an argon atmosphere. The resulting mixture was stirred for 1 hour at the same temperature, after which a 25% aqueous solution of NH_4Cl was added dropwise. The reaction mixture was then diluted with hexane (25 mL). The organic layer was separated, washed with brine, dried over Na_2SO_4, filtered through silica gel, and concentrated under reduced pressure. The residue was purified by flash chromatography, using a gradient elution from hexanes to 10% ethyl acetate in hexanes.

3. Synthesis of substrates 2

Preparation of hydroxylamines[2] **2a-2m**. Typical procedure.

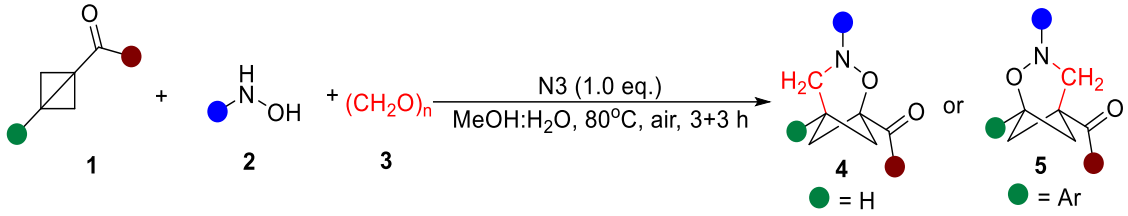


2

Step: In a 20 mL flask, $Pd(OAc)_2$ (0.1 mL of a 10 mM $Pd(OAc)_2/CH_2Cl_2$ solution) was added to a stirred suspension or solution of nitroarene (1.0 mmol) and $NaBH_4$ (2.0 mmol) in a mixture of H_2O (4.0 mL) and EtOH (6.0 mL). The reaction mixture was stirred at room temperature for the required time (3–

8 minutes), as monitored by TLC. The reaction was then extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was recrystallized from CH_2Cl_2/*n*-hexane to yield the desired products **2**.

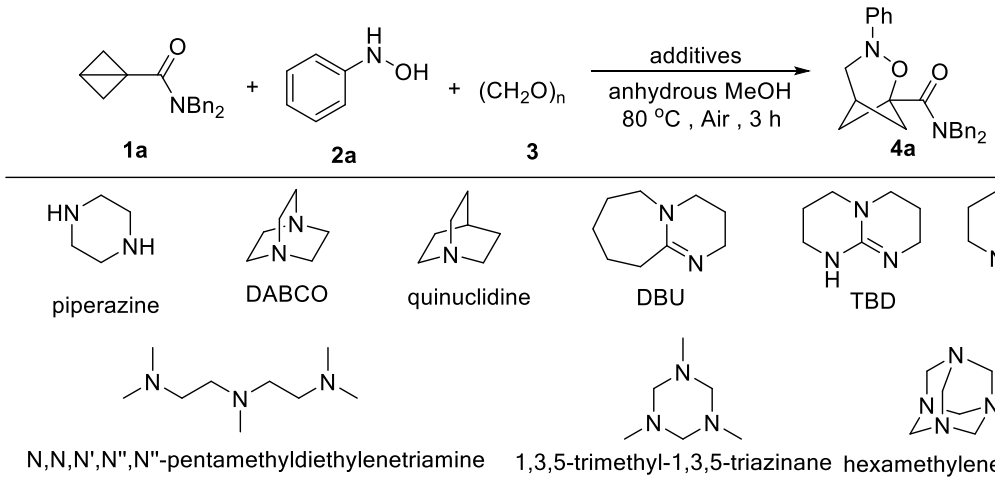
4. General method



An oven-dried 10 mL reaction tube equipped with a magnetic stir bar was charged with **1** (0.2 mmol, 1.0 eq), **2** (0.4 mmol, 2.0 eq), Polyformaldehyde (1.2 mmol, 6.0 eq), **N3** (0.2 mmol, 1.0 eq), MeOH (1.5 mL), and H_2O (0.5 mL). The reaction mixture was placed in a preheated metal block and stir at 80 °C, after reacting 3 h, another 2.0 equivalents of **2a** was added, and then react for 3 h. After the reaction was complete as monitored by TLC, it was quenched with saturated NaCl solution (5 mL) at room temperature, and then extracted with DCM (10 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and then concentrated in vacuum. The residue was purified by flash chromatography on silica gel to afford the desired product **4** or **5**.

5. Optimization of the reaction conditions

Table S1. The screening of additives [a]

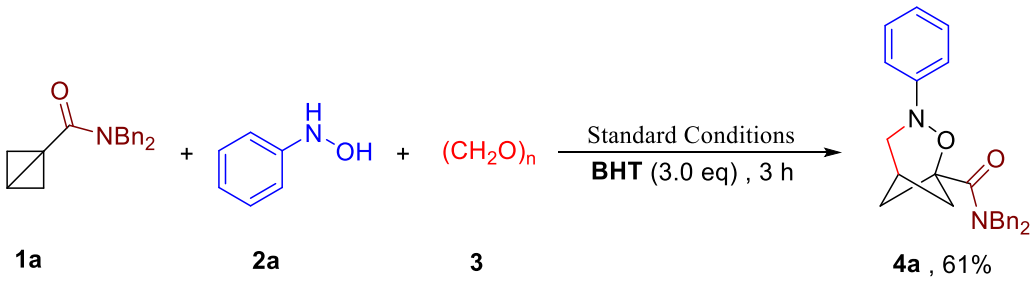


Entry	Additives	Yield (%)
1	Et_2NH	50
2	Ph_2NH	43
3	piperazine	49
4	Et_3N	45
5	DABCO	27
6	quinuclidine	39
7	DBU	49
8	TBD	38
9	MTBD	38
10[c]	Et_2NH	73(71) [b]
11[c]	*N*,*N*,*N*',*N*'',*N*''-pentamethyldiethylenetriamine	58
12[c]	1,3,5-trimethyl-1,3,5-triazinane	82 (77) [b]
13[c]	hexamethylenetetramine	64

[a] Reaction condition:**1a** (0.2 mmol), **2a** (0.4 mmol), polyformaldehyde **3** (1.2 mmol), additive (0.2 mmol), anhydrous MeOH (2 mL), 80 ℃, 3h. Yields were determined by ^{1}H NMR analysis of the unpurified reaction mixture with 1,3,5-trimethoxybenzene as an internal standard. [b] Isolated yield after chromatographic purification in brackets. [c] solvent: MeOH: H_2O = 3:1.

6. Control experiments

a) Radical inhibiting experiment

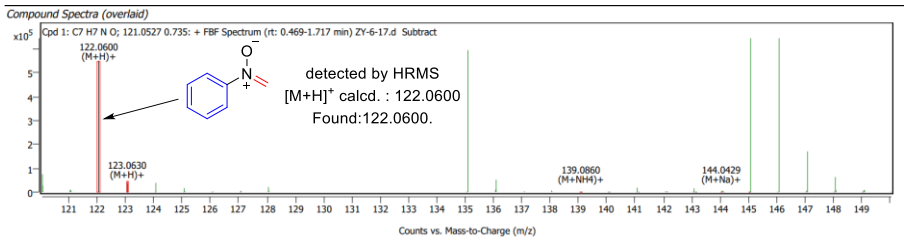


1a **2a** **3** **4a** , 61%

An oven-dried 10 mL Schlenk tube was charged with **1a** (55.5 mg, 0.2 mmol), BHT (132 mg, 0.6 mmol), **2a** (44 mg, 0.4 mmol), Polyformaldehyde (36 mg, 1.2 mmol) and **N3** (25.8 mg, 0.2 mmol) in MeOH (1.5 mL) and H_2O (0.5 mL). The reaction mixture was placed in a preheated metal block and stirred at 80 ℃ for 3 h. After the reaction was complete as monitored by TLC, it was quenched with saturated NaCl solution (5 mL) at room temperature, and then extracted with DCM (10 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4 filtered, and then concentrated in vacuum. The residue was purified by flash chromatography on silica gel to afford the desired product **4a** 48.5 mg (61%).

b) Intermediate trapping experiment

Intermidiate trap by HRMS



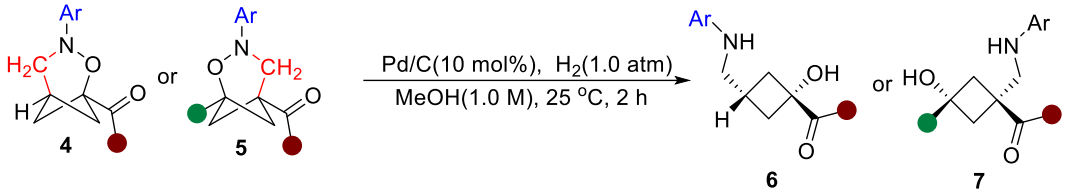
7. Gram-scale synthesis of 4a and derivatization of products 4 and 5

a) Gram-scale synthesis of compound 4a

An oven-dried 100 mL three-necked flask equipped with a magnetic stir bar was charged with **1a** (888 mg, 3.2 mmol), **2a** (697.6 mg, 6.4 mmol), Polyformaldehyde (577 mg, 19.2 mmol), **N3** (413.5 mg, 3.2

mmol), MeOH (24 mL) and H_2O (8 mL). The reaction mixture was stirred at 80 ℃ for 3 h, another 2.0 equivalents of **2a** was added, and react for another 3 h. The reaction was quenched with saturated $NaHCO_3$ solution (15 mL) at room temperature, and then extracted with DCM (30 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and then concentrated in vacuum. The residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate 20/1 to 15/1 afford the desired product **4a** as a white solid (1.1669 g, 91%).

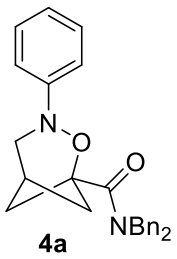
b) Synthesis of products 6 and 7



An oven-dried 10 mL Schlenk tube was charged with solvent of **4** or **5** (0.2 mmol) in MeOH (2.0 mL) was added under argon, then Pd/C (palladium on activated carbon, 5% Pd basis, 10 mol %) was added, and charged H_2 3 times. The reaction mixture was stirred at H_2 atmosphere (1.0 atm) at 25 ℃ for 2 hours. After the reaction was complete as monitored by TLC, it was quenched with saturated $NaHCO_3$ solution (5 mL) at room temperature, and then extracted with DCM (10 mL × 3). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and then concentrated in vacuum. The residue was purified by flash chromatography on silica gel with petroleum ether/ethyl acetate 5/1 to afford the desired product **6** and **7**.

8. Characterization of products

***N,N*-dibenzyl-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4a).**

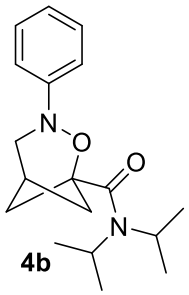


4a

Eluent in chromatography: petroleum ether/ethyl acetate = 20:1, **4a** was isolated as a white solid (76.5 mg, 96 %); M.p.:76.6-78.6 ℃;^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.13 (m, 12H), 6.96 – 6.80

(m, 3H), 4.74 (s, 2H), 4.56 (s, 2H), 3.75 (d, *J* = 3.2 Hz, 2H), 2.78 – 2.68 (m, 1H), 2.63 – 2.53 (m, 2H), 2.43 – 2.31 (m, 2H) ;^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.86, 149.95, 136.77, 136.72, 128.66, 128.63, 128.55, 127.89, 127.36, 127.26, 126.96, 121.20, 113.91, 86.54, 58.44, 49.54, 47.54, 38.07, 28.30. HRMS (ESI) m/z: calcd for $C_{26}H_{27}N_2O_2$ $[M+H]^+$ 399.2067, found: 399.2073.

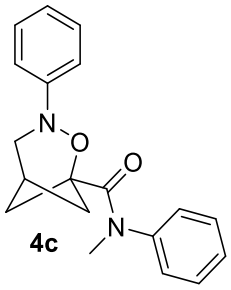
***N,N*-diisopropyl-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4b).**



4b

Eluent in chromatography: petroleum ether/ethyl acetate = 20:1, **4b** was isolated as a white solid (48.4 mg, 80 %); M.p.:120.8-122.8 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (t, *J* = 7.2 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.93 (t, *J* = 7.2 Hz, 1H), 4.57 – 4.39 (m, 1H), 3.74 (d, *J* = 3.2 Hz, 2H), 3.47 – 3.28 (m, 1H), 2.77 – 2.60 (m, 1H), 2.53 -2.36 (m, 2H), 2.35 – 2.19 (m, 2H), 1.43 (d, *J* = 6.8 Hz, 6H), 1.19 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 167.06, 150.29, 128.71, 120.98, 113.70, 87.28, 58.53, 48.16, 46.01, 37.58, 27.92, 20.83, 20.26. HRMS (ESI) m/z: calcd for $C_{18}H_{27}N_2O_2$ $[M+H]^+$ 303.2067, found: 303.2075.

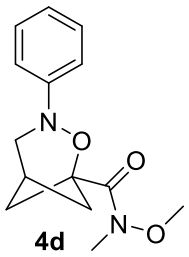
***N*-methyl-*N*,3-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4c).**



4c

Eluent in chromatography: petroleum ether/ethyl acetate = 20:1, **4c** was isolated as a white solid (56.4 mg, 92 %); M.p.:156.3-158.3 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.09 (m, 7H), 7.06 – 6.69 (m, 3H), 3.78 – 3.48 (m, 2H), 3.33 (s, 3H), 2.54 – 2.38 (m, 1H), 2.37 – 2.06 (m, 2H), 1.98 – 1.55 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.13, 150.36, 142.86, 128.92, 128.47, 127.67, 120.74, 113.84, 86.17, 58.65, 38.68, 38.28, 27.75. HRMS (ESI) m/z: calcd for $C_{19}H_{21}N_2O_2$ $[M+H]^+$ 309.1598, found: 309.1604.

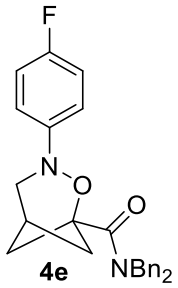
***N*-methoxy-*N*-methyl-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4d).**



4d

Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4d** was isolated as a yellow oil (40.9 mg, 78 %);^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (t, *J* = 8.0 Hz, 2H), 7.07 – 7.01 (m, 2H), 6.92 (t, *J* = 7.4 Hz, 1H), 3.87 – 3.67 (m, 5H), 3.23 (s, 3H), 2.80 – 2.55 (m, 1H), 2.51 – 2.24 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.80, 128.73, 120.89, 117.59, 113.75, 85.54, 61.99, 58.92, 37.32, 32.48, 28.39. HRMS (ESI) m/z: calcd for $C_{14}H_{19}N_2O_3$ $[M+H]^+$ 263.1390, found:.263.1385.

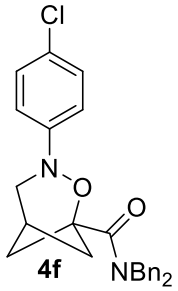
***N,N*-dibenzyl-3-(4-fluorophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4e).**



4e

Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4e** was isolated as a yellow solid (60.8 mg, 73 %); M.p.:122.8-124.8 ℃; ^{1}H NMR (400 MHz, $CDCI_3$) δ 7.43 – 7.27 (m, 6H), 7.24 – 7.11 (m, 4H), 6.90 – 6.83 (m, 2H), 6.83 -6.74 (m, 2H), 4.72 (s, 2H), 4.56 (s, 2H), 3.69 (d, *J* = 4.0 Hz, 2H), 2.78-2.66 (m, 1H), 2.64 – 2.50 (m, 2H), 2.45 – 2.31 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.86, 158.01 (d, *J* = 240.3 Hz), 146.27 (d, *J* = 2.2 Hz), 136.76, 136.74, 128.73, 128.61, 127.98, 127.45, 127.36, 126.98, 115.99 (d, *J* = 7.7 Hz), 115.17 (d, *J* = 22.3 Hz), 86.67, 59.20, 49.51, 47.60, 38.08, 28.36. ^{19}F NMR (376 MHz, $CDCI_3$) δ -122.52. HRMS (ESI) m/z: calcd for $C_{26}H_{26}FN_2O_2$ $[M+H]^+$ 417.1973, found:417.1977.

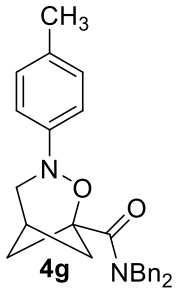
***N,N*-dibenzyl-3-(4-chlorophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4f).**



4f

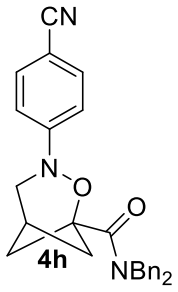
Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4f** was isolated as a yellow solid (73.6 mg, 87 %); M.p.:113.2-115.2 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.26 (m, 6H), 7.25 – 7.14 (m, 4H), 7.11 (d, *J* = 8.0 Hz, 2H), 6.74 (d, *J* = 8.0 Hz, 2H), 4.71 (s, 2H), 4.57 (s, 2H), 3.82 – 3.62 (m, 2H), 2.79 – 2.66 (m, 1H), 2.66 – 2.50 (m, 2H), 2.45 – 2.25 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.68, 148.48, 136.68, 136.67, 128.74, 128.59, 128.51, 127.93, 127.47, 127.36, 126.88, 126.11, 115.19, 86.72, 58.54, 49.48, 47.61, 38.02, 28.23. HRMS (ESI) m/z: calcd for $C_{26}H_{26}ClN_2O_2$ $[M+H]^+$ 433.1677, found:433.1677.

***N,N*-dibenzyl-3-(p-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4g).**



Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4g** was isolated as a yellow solid (49.1 mg, 61 %); M.p.:125.3-126.8 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.10 (m, 10H), 7.01 (d, *J* = 7.6 Hz, 2H), 6.80 (d, *J* = 7.6 Hz, 2H), 4.75 (s, 2H), 4.56 (s, 2H), 3.71 (d, *J* = 4.0 Hz, 2H), 2.77– 2.65 (m, 1H), 2.64 – 2.48 (m, 2H), 2.44 – 2.33 (m, 2H), 2.27 (s, 3H) ; ^{13}C NMR (100 MHz, Chloroform-*d*) δ 169.02, 147.77, 136.83, 136.76, 130.87, 129.17, 128.67, 128.57, 127.90, 127.38, 127.27, 127.03, 114.39, 86.47, 58.85, 49.56, 47.51, 38.11, 28.35, 20.50. HRMS (ESI) m/z: calcd for $C_{27}H_{29}N_2O_2$ $[M+H]^+$ 413.2224, found: 413.2226.

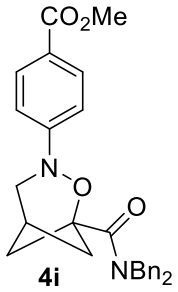
***N,N*-dibenzyl-3-(4-cyanophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4h).**



Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4h** was isolated as a yellow oil (30.5 mg, 36 %);^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.27 (m, 8H), 7.23 – 7.13 (m, 4H), 6.80 – 6.68 (m, 2H), 4.67 (s, 2H), 4.58 (s, 2H), 3.83 (d, *J* = 3.0 Hz, 2H), 2.83 – 2.71 (m, 1H), 2.70 – 2.56 (m, 2H), 2.34

– 2.23 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.11, 152.18, 136.58, 136.55, 133.02, 128.87, 128.67, 128.01, 127.62, 127.52, 126.75, 119.61, 112.44, 102.49, 87.26, 57.09, 49.50, 47.85, 37.93, 28.04. HRMS (ESI) m/z: calcd for $C_{27}H_{26}N_3O_2$ $[M+H]^+$ 424.2020, found: 424.2025.

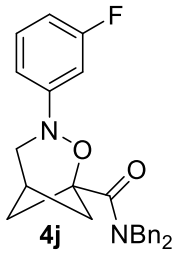
methyl 4-(1-(dibenzylcarbamoyl)-2-oxa-3-azabicyclo[3.1.1]heptan-3-yl)benzoate (4i).



4i

Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4i** was isolated as a yellow solid (42.0 mg, 46 %); M.p.:128.4-130.4 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 – 7.81 (m, 2H), 7.43 – 7.27 (m, 6H), 7.25 – 7.13 (m, 4H), 6.87 – 6.70 (m, 2H), 4.70 (s, 2H), 4.57 (s, 2H), 3.86 (s, 3H), 3.83 (d, *J* = 4.0 Hz, 2H), 2.79 – 2.69 (m, 1H), 2.68 – 2.54 (m, 2H), 2.36 – 2.25 (m, 2H).^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.36, 166.87, 152.92, 136.57, 136.53, 130.67, 128.78, 128.62, 127.90, 127.56, 127.42, 126.82, 121.64, 111.91, 86.96, 57.34, 51.71, 49.52, 47.66, 37.95, 28.09. HRMS (ESI) m/z: calcd for $C_{28}H_{29}N_2O_4$ $[M+H]^+$ 457.2122, found: 457.2126.

***N,N*-dibenzyl-3-(3-fluorophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4j).**

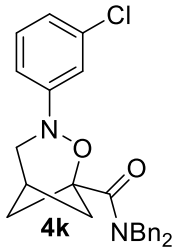


4j

Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4j** was isolated as a yellow solid (64.1 mg, 77 %); M.p.:104.0-106.0 ℃; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.43 – 7.26 (m, 6H), 7.25 – 7.16 (m, 4H), 7.18 – 7.07 (m, 1H), 6.67 – 6.53 (m, 3H), 4.72 (s, 2H), 4.58 (s, 2H), 3.75 (d, *J* = 3.0 Hz, 2H), 2.77 – 2.68 (m, 1H), 2.66 – 2.53 (m, 2H), 2.42 – 2.30 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-d) δ 168.58, 163.24 (d, *J* = 243.9 Hz), 151.52 (d, *J* = 10.1 Hz), 136.62, 136.59, 129.80 (d, *J* = 9.6 Hz), 128.73, 128.61, 127.86, 127.50, 127.36, 126.86, 108.96 (d, *J* = 2.6 Hz), 107.50 (d, *J* = 21.5 Hz), 101.22 (d, *J* = 26.6 Hz),

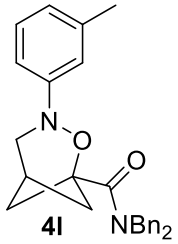
86.75, 58.26, 49.50, 47.59, 38.02, 28.17; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.14. HRMS (ESI) m/z: calcd for $C_{26}H_{26}FN_2O_2$ $[M+H]^+$ 417.1973, found: 417.1978.

***N,N*-dibenzyl-3-(3-chlorophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4k).**



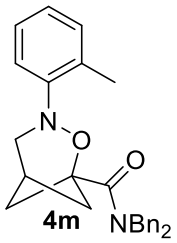
Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4k** was isolated as a yellow oil (62.1 mg, 71 %);^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 6H), 7.23 – 7.16 (m, 4H), 7.13 – 7.05 (m, 1H), 7.01 – 6.92 (m, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.81 – 6.63 (m, 1H), 4.70 (s, 2H), 4.57 (s, 2H), 3.74 (d, *J* = 4.0 Hz, 2H), 2.81 – 2.67 (m, 1H), 2.65 – 2.54 (m, 2H), 2.39 – 2.28 (m, 2H).^{13}C NMR (400 MHz, $CDCl_3$) δ 168.55, 150.99, 136.64, 136.58, 134.61, 129.66, 128.78, 128.63, 127.85, 127.52, 127.35, 126.92, 120.92, 113.90, 111.70, 86.78, 58.34, 49.54, 47.56, 38.05, 28.19. HRMS (ESI) m/z: calcd for $C_{26}H_{26}ClN_2O_2$ $[M+H]^+$ 433.1677, found: 433.1678.

***N,N*-dibenzyl-3-(m-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4l).**



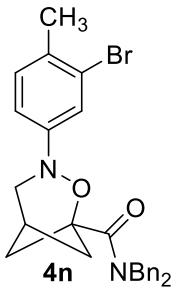
Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4l** was isolated as a white solid (73.4 mg, 89 %); M.p.:103.6-105.6 ℃;^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 6H), 7.25 – 7.17 (m, 4H), 7.10 (t, *J* = 8.0 Hz, 1H), 6.80 – 6.76 (m, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.71 – 6.67 (m, 1H), 4.75 (s, 2H), 4.57 (s, 2H), 3.75 (d, *J* = 4.0 Hz, 2H), 2.78 – 2.67 (m, 1H), 2.63 – 2.53 (m, 2H), 2.43 – 2.32 (m, 2H), 2.24 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.93, 149.98, 138.50, 136.79, 136.74, 128.68, 128.56, 128.51, 127.87, 127.41, 127.28, 127.06, 122.12, 114.76, 110.92, 86.51, 58.50, 49.56, 47.44, 38.08, 28.32, 21.60. HRMS (ESI) m/z: calcd for $C_{27}H_{29}N_2O_2$ $[M+H]^+$ 413.2224, found:413.2227.

***N,N*-dibenzyl-3-(o-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4m).**



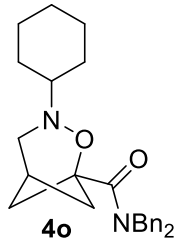
Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4m** was isolated as a yellow solid (31.2 mg, 45 %); M.p.:92.8-94.8 ℃; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.39 (d, *J* = 8.0 Hz, 1H), 7.32 – 7.17 (m, 6H), 7.16 – 7.05 (m, 6H), 7.05 – 6.98 (m, 1H), 4.63 (s, 2H), 4.45 (s, 2H), 3.44 (d, *J* = 3.2 Hz, 2H), 2.67 – 2.58 (m, 1H), 2.56 – 2.45 (m, 4H), 2.27 – 2.20 (m, 3H). ^{13}C NMR (100 MHz, Chloroform-d) δ 169.17, 148.51, 136.88, 136.85, 131.13, 130.41, 128.49, 128.11, 127.28, 127.20, 126.53, 125.23, 120.47, 86.57, 60.60, 49.53, 47.47, 38.34, 28.92, 17.90. HRMS (ESI) m/z: calcd for $C_{27}H_{29}N_2O_2$ $[M+H]^+$ 413.2224, found: 413.2229.

***N,N*-dibenzyl-3-(3-bromo-4-methylphenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4n).**



Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4n** was isolated as a yellow oil (55.3 mg, 57 %);^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.27 (m, 6H), 7.24 – 7.16 (m, 5H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.75 – 6.65 (m, 1H), 4.70 (s, 2H), 4.56 (s, 2H), 3.70 (d, *J* = 3.0 Hz, 2H), 2.75 – 2.67 (m, 1H), 2.62 – 2.52 (m, 2H), 2.39 – 2.32 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.67, 149.04, 136.64, 136.62, 130.49, 130.24, 128.77, 128.63, 127.81, 127.49, 127.31, 126.99, 124.92, 117.84, 113.14, 86.65, 58.75, 49.54, 47.46, 38.07, 28.21, 21.90. HRMS (ESI) m/z: calcd for $C_{27}H_{28}BrN_2O_2$ $[M+H]^+$ 491.1329, found: 491.1327.

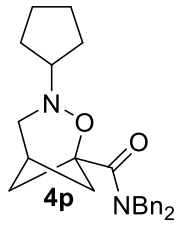
***N,N*-dibenzyl-3-cyclohexyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4o).**



4o

Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4o** was isolated as a colorless oil (66.3 mg, 82 %); ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.37 – 7.22 (m, 6H), 7.18 – 7.12 (m, 4H), 4.68 (s, 2H), 4.49 (s, 2H), 3.22 – 3.03 (m, 2H), 2.60 – 2.50 (m, 2H), 2.45 – 2.13 (m, 4H), 1.91 – 1.81 (m, 2H), 1.70 – 1.62 (m, 2H), 1.59 – 1.51 (m, 1H), 1.24 – 1.09 (m, 5H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.85, 137.23, 136.86, 128.46, 128.41, 127.79, 127.15, 127.06, 127.03, 85.35, 64.85, 58.40, 49.50, 47.22, 38.06, 29.08, 28.50, 25.95, 24.45. HRMS (ESI) m/z: calcd for $C_{26}H_{33}N_2O_2$ $[M+H]^+$ 405.2537, found: 405.2557.

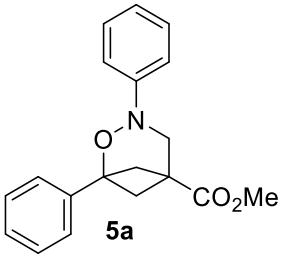
***N,N*-dibenzyl-3-cyclopentyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4p).**



4p

Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **4p** was isolated as a yellow solid (59.4 mg, 76 %); M.p.:85.2-86.6 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.21 (m, 6H), 7.20 – 7.07 (m, 4H), 4.68 (s, 2H), 4.48 (s, 2H), 3.28 – 2.91 (m, 3H), 2.58– 2.07 (br, 5H), 1.77 – 1.64 (m, 2H), 1.64 – 1.53 (m, 2H), 1.53 – 1.40 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 169.78, 137.18, 136.85, 128.52, 128.45, 127.76, 127.23, 127.18, 127.06, 85.49, 68.30, 60.66, 49.55, 47.14, 37.89, 29.87, 28.53, 24.37. HRMS (ESI) m/z: calcd for $C_{25}H_{31}N_2O_2$ $[M+H]^+$ 391.2380, found: 391.2380.

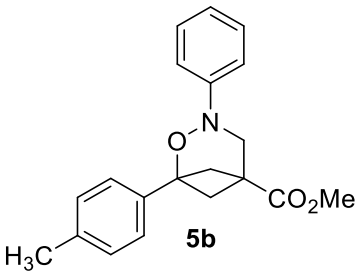
Methyl 3,5-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate (5a).



5a

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5a** was isolated as a colorless oil (35.9 mg, 58%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.33 (m, 5H), 7.33 – 7.27 (m, 2H), 7.14 – 7.07 (m, 2H), 6.98 – 6.90 (m, 1H), 4.03 (s, 2H), 3.79 (s, 3H), 2.77 – 2.66 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.79, 150.07, 140.07, 128.85, 128.42, 128.26, 125.62, 120.96, 113.83, 83.38, 57.50, 52.27, 42.11, 41.85. HRMS (ESI) m/z: calcd for $C_{19}H_{20}NO_3$ $[M+H]^+$ 310.1438, found: 310.1440.

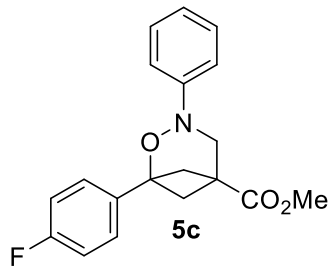
Methyl 3-phenyl-5-(p-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate (5b).



5b

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5b** was isolated as a yellow oil (41.4 mg, 64%);^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 4H), 7.25 – 7.20 (m, 2H), 7.14 – 7.07 (m, 2H), 6.98 – 6.89 (m, 1H), 4.03 (s, 2H), 3.79 (s, 3H), 2.79 – 2.62 (m, 4H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.83, 150.12, 138.08, 137.25, 129.07, 128.83, 125.56, 120.85, 113.78, 83.32, 57.45, 52.24, 42.08, 41.87, 21.21. HRMS (ESI) m/z: calcd for $C_{20}H_{22}NO_3$ $[M+H]^+$ 324.1594, found: 324.1602.

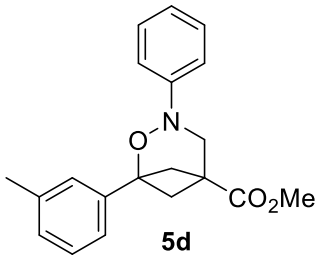
Methyl 5-(4-fluorophenyl)-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate (5c).



5c

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5c** was isolated as a yellow oil (38.0 mg, 58%); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.38 (m, 2H), 7.34 – 7.27 (m, 2H), 7.14 – 7.05 (m, 4H), 6.99 – 6.91 (m, 1H), 4.02 (s, 2H), 3.79 (s, 3H), 2.74 – 2.65 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.64, 162.60 (d, J = 247.1 Hz), 149.93, 136.08, 128.87, 127.51 (d, J = 8.3 Hz), 121.11, 115.32 (d, J = 21.6 Hz), 113.87, 82.87, 57.46, 52.30, 42.12, 41.77. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.56. HRMS (ESI) m/z: calcd for $C_{19}H_{19}FNO_3$ $[M+H]^+$ 328.1343, found: 328.1345.

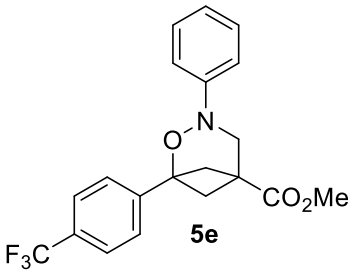
Methyl 3-phenyl-1-(m-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-5-carboxylate (5d)



5d

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5d** was isolated as a colorless oil (26.5 mg, 41%); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.24 (m, 5H), 7.18 (d, *J* = 4.0 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.97 – 6.92 (m, 1H), 4.04 (s, 2H), 3.79 (s, 3H), 2.80 – 2.65 (m, 4H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.81, 150.10, 140.00, 138.06, 129.00, 128.82, 128.32, 126.29, 122.66, 120.91, 113.84, 83.38, 57.53, 52.24, 42.06, 41.84, 21.47. HRMS (ESI) m/z: calcd for $C_{20}H_{22}NO_3$ $[M+H]^+$ 324.1594, found:324.1602.

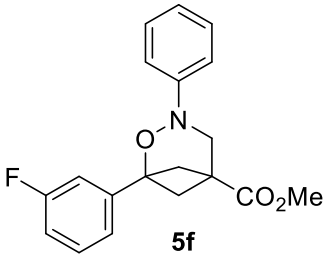
Methyl 3-phenyl-5-(4-(trifluoromethyl)phenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate (5e).



5e

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5e** was isolated as a colorless oil (30.5 mg, 39%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.28 (m, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.02 -6.91 (m, 1H), 4.04 (s, 2H), 3.80 (s, 3H), 2.85 – 2.62 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.48, 149.79, 143.75, 130.40 (q, *J* = 32.6 Hz), 128.91, 126.03, 125.45 (q, *J* = 3.8 Hz), 124.00 (q, *J* = 270 Hz), 121.36, 113.98, 82.81, 57.62, 52.37, 42.28, 41.82. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.57. HRMS (ESI) m/z: calcd for $C_{20}H_{19}F_3NO_3$ $[M+H]^+$ 378.1312, found: 378.1317.

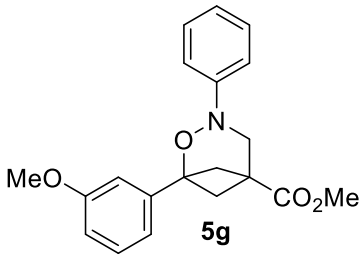
Methyl 5-(3-fluorophenyl)-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate (5f).



5f

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5f** was isolated as a colorless oil (24.9 mg, 38%); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.35 (m, 1H), 7.34 – 7.28 (m, 2H), 7.23 (d, *J* = 8.1 Hz, 1H), 7.20 – 7.14 (m, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.08 – 7.00 (m, 1H), 6.99 – 6.93 (m, 1H), 4.02 (s, 2H), 3.80 (s, 3H), 2.78 – 2.64 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.56, 162.83 (d, *J* = 246.3 Hz), 149.85, 142.56 (d, *J* = 7.1 Hz), 130.04 (d, *J* = 8.2 Hz), 128.88, 121.23, 121.19 (d, *J* = 3.0 Hz), 115.16 (d, *J* = 21.1 Hz), 113.94, 112.82 (d, *J* = 22.1 Hz), 82.80 (d, *J* = 1.8 Hz), 57.56, 52.32, 42.32, 41.75. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -112.59. HRMS (ESI) m/z: calcd for $C_{19}H_{19}FNO_3$ $[M+H]^+$ 328.1343, found: 328.1351.

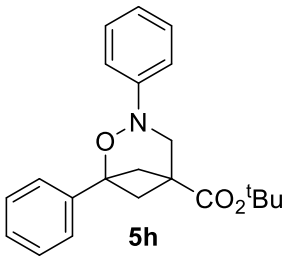
Methyl 5-(3-methoxyphenyl)-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate (5g).



5g

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5g** was isolated as a yellow oil (43.4 mg, 64%); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.27 (m, 3H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.07 – 6.98 (m, 2H), 6.97 – 6.87 (m, 2H), 4.03 (s, 2H), 3.85 (s, 3H), 3.79 (s, 3H), 2.78 – 2.64 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.72, 159.67, 150.07, 141.66, 129.50, 128.84, 120.97, 117.91, 113.85, 113.62, 111.48, 83.29, 57.53, 55.29, 52.24, 42.18, 41.82. HRMS (ESI) m/z: calcd for $C_{20}H_{22}NO_4$ $[M+H]^+$ 340.1543, found: 340.1549.

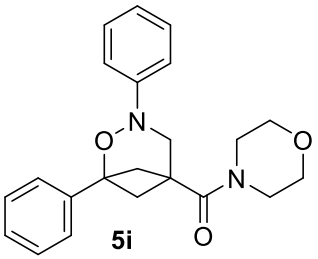
***tert*-Butyl 3,5-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate (5h).**



5h

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5h** was isolated as a yellow solid (47.1 mg, 67%); M.p.:85.3-87.3 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.27 (m, 7H), 7.17 – 7.06 (m, 2H), 6.99 – 6.89 (m, 1H), 4.01 (s, 2H), 2.68 (s, 4H), 1.53 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.63, 150.25, 140.27, 128.80, 128.38, 128.19, 125.68, 120.79, 113.79, 83.19, 81.35, 57.67, 42.71, 41.88, 28.00. HRMS (ESI) m/z: calcd for $C_{22}H_{26}NO_3$ $[M+H]^+$ 352.1907, found: 352.1897.

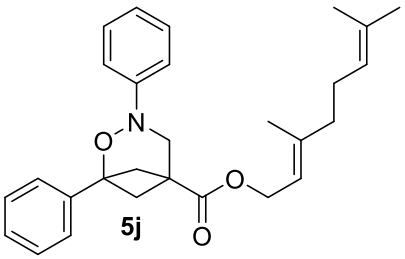
(3,5-Diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-1-yl)(morpholino)methanone (5i).



5i

Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5i** was isolated as a yellow solid 44.5 mg, 61 %); M.p.:176.3-178.3 ℃;^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.25 (m, 7H), 7.12 – 7.04 (m, 2H), 6.95 (t, *J* = 7.3 Hz, 1H), 3.92 (s, 2H), 3.82 – 3.47 (m, 8H), 2.91 – 2.77 (m, 2H), 2.72 – 2.58 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 171.43, 149.89, 139.85, 128.91, 128.42, 128.24, 125.58, 121.32, 114.05, 82.42, 66.75, 58.68, 46.27, 43.67, 42.48. HRMS (ESI) m/z: calcd for $C_{22}H_{25}N_2O_3$ $[M+H]^+$ 365.1860, found: 365.1854.

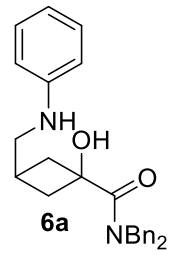
(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 3,5-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate (5j).



5j

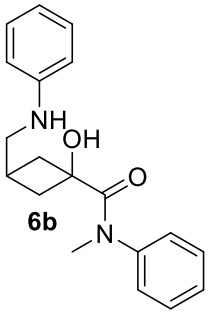
Eluent in chromatography: petroleum ether/ethyl acetate = 100:1, **5j** was isolated as a colorless oil (40.1 mg, 47 %); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.40 (m, 4H), 7.39 – 7.34 (m, 1H), 7.33 – 7.27 (m, 2H), 7.15 – 7.07 (m, 2H), 6.98 – 6.89 (m, 1H), 5.44 – 5.32 (m, 1H), 5.16 – 5.06 (m, 1H), 4.71 (d, *J* = 7.1 Hz, 2H), 4.04 (s, 2H), 2.80 – 2.64 (m, 4H), 2.21 – 2.04 (m, 4H), 1.75 (s, 3H), 1.70 (s, 3H), 1.62 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.33, 150.15, 142.67, 140.17, 131.85, 128.82, 128.40, 128.24, 125.67, 123.62, 120.90, 117.97, 113.85, 83.37, 62.09, 57.57, 42.04, 42.00, 39.49, 26.22, 25.68, 17.70, 16.53. HRMS (ESI) m/z: calcd for $C_{28}H_{34}NO_3$ $[M+H]^+$ 432.2533, found: 432.2537.

***N*,*N*-dibenzyl-1-hydroxy-3-((phenylamino)methyl)cyclobutane-1-carboxamide(6a).**



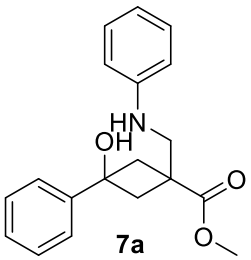
Eluent in chromatography: petroleum ether/ethyl acetate = 3:1, **6a** was isolated as a white solid (56.9 mg, 71 %); M.p.:156.3-158.3 ℃;^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.00 (m, 12H), 6.78 – 6.68 (m, 1H), 6.67 – 6.53 (m, 2H), 4.58 (s, 2H), 4.49 (s, 2H), 3.45 (br, 1H),3.25 (d, *J* = 6.8 Hz, 2H), 3.07 – 2.97 (m, 2H), 2.43 – 2.29 (m, 1H), 2.03 – 1.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.19, 148.22, 136.97, 136.62, 129.21, 128.63, 127.99, 127.48, 127.33, 117.53, 112.91, 73.92, 50.01, 49.55, 47.38, 38.50, 25.91. HRMS (ESI) m/z: calcd for $C_{26}H_{29}N_2O_2$ $[M+H]^+$ 401.2224, found: 401.2219.

1-Hydroxy-*N*-methyl-*N*-phenyl-3-((phenylamino)methyl)cyclobutane-1-carboxamide (6b).



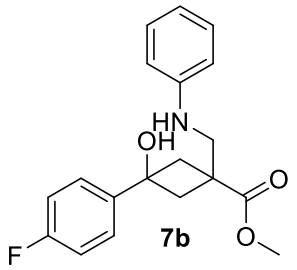
Eluent in chromatography: petroleum ether/ethyl acetate = 3:1, **6b** was isolated as a white solid (49.7 mg, 80 %); M.p.:113.6-115.6 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.36 (m, 2H), 7.35 – 7.25 (m, 3H), 7.21 – 7.07 (m, 2H), 6.73 – 6.63 (m, 1H), 6.56 (d, *J* = 7.2 Hz, 2H), 3.46 (br, 1H), 3.32 (s, 3H), 3.17 (d, *J* = 7.2 Hz, 2H), 2.83 – 2.63 (m, 2H), 2.31 – 2.11 (m, 1H), 1.79 – 1.55 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.38, 148.28, 143.52, 129.30, 129.13, 127.62, 127.26, 117.20, 112.71, 74.82, 49.27, 39.40, 38.12, 25.93. HRMS (ESI) m/z: calcd for $C_{19}H_{23}N_2O_2$ $[M+H]^+$ 311.1754, found:311.1764.

Methyl 3-hydroxy-3-phenyl-1-((phenylamino)methyl)cyclobutane-1-carboxylate (7a).



Eluent in chromatography: petroleum ether/ethyl acetate = 10:1, **7a** was isolated as a colorless oil (43.0 mg, 69 %); ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 8.0 Hz, 2H), 7.42 – 7.34 (m, 2H), 7.33 – 7.24 (m, 1H), 7.23 – 7.16 (m, 2H), 6.80 – 6.69 (m, 3H), 3.77 (s, 2H), 3.68 (s, 3H), 3.14 – 3.04 (m, 2H), 2.58 – 2.45 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.28, 148.31, 145.97, 129.27, 128.54, 127.52, 124.73, 117.79, 113.16, 73.13, 52.26, 50.18, 42.90, 41.12. HRMS (ESI) m/z: calcd for $C_{19}H_{22}NO_3$ $[M+H]^+$ 312.1594, found:312.1605.

Methyl 3-(4-fluorophenyl)-3-hydroxy-1-((phenylamino)methyl)cyclobutane-1-carboxylate (7b).



7b

Eluent in chromatography: petroleum ether/ethyl acetate = 10:1, **7b** was isolated as a white solid (46.8 mg, 71 %); M.p.:78.7-79.8 ℃; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.39 (m, 2H), 7.24 – 7.16 (m, 2H), 7.09 – 7.01 (m, 2H), 6.79 – 6.68 (m, 3H), 3.74 (s, 2H), 3.68 (s, 3H), 3.09 – 2.99 (m, 2H), 2.56 – 2.45 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 176.19, 162.03 (d, *J* = 246.2 Hz), 148.25, 141.85 (d, *J* = 3.2 Hz), 129.28, 126.64 (d, *J* = 8.2 Hz), 117.93, 115.24 (d, *J* = 21.3 Hz), 113.21, 72.62, 52.31, 50.13, 43.11, 41.00. ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.01. HRMS (ESI) m/z: calcd for $C_{19}H_{21}FNO_3$ $[M+H]^+$ 330.1500, found:330.1494.

9. DFT computations

Computational details: All density functional theory (DFT) calculations were carried out using Gaussian 09 package.[3] Geometry optimizations and vibrational frequencies were calculated at the B3LYP[4] level of theory with Grimme D3 correction[5]. A basis set of 6-31G(d,p)[6] is employed for all atoms in the gas phase. Frequencies calculations were used to determine the structures to be minima (no imaginary frequency) or transition states (only one imaginary frequency) and to obtain the thermal correction to free energies. Furthermore, solvation single-point energy calculations were performed at the wβ97xd/6-311++G(d,p)[7]-SMD level of theory in methonal solvent with SMD[8] contiummn solvation model to obtain more accurate energies. In order to compensate for the overestimation of the entropic, a

correction factor which consists on half (0.5) of the entropy correction for ΔG values at 298 K was applied.[9] The calculated optimized structures are visualized using CYLview.[10]

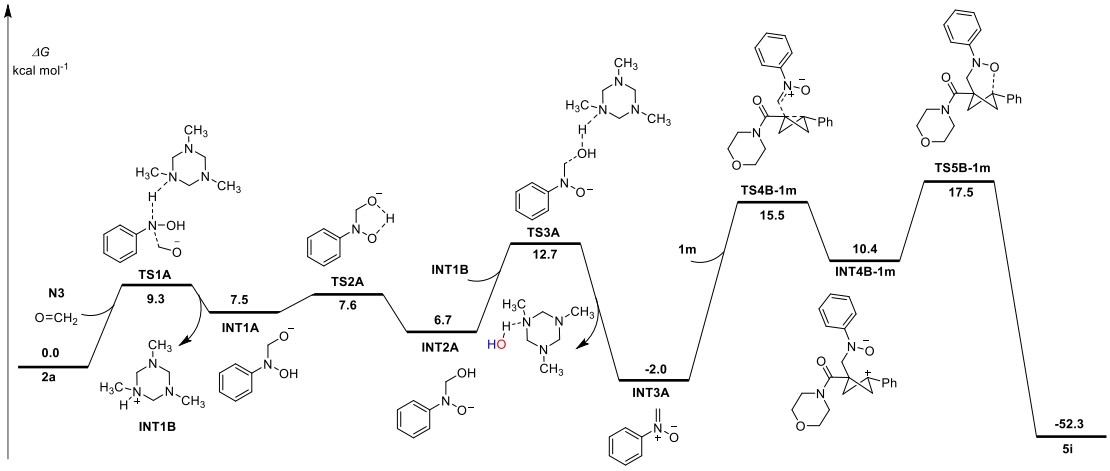


Fig. S1. The calculated energy profile for the generation of 5i.

Table S2. The calculated energies of stationary points (in Hartree/Particle).

Structure	E_{ele}	H_{corr}	G_{corr}	H_{sol}	0.5TS	G_{sol}
2a	-362.758129	0.129406	0.090603	-362.628723	0.019402	-362.648124
N3	-401.893915	0.230507	0.186950	-401.663408	0.021779	-401.685186
CH_2O	-114.502574	0.030484	0.005009	-114.472090	0.012738	-114.484827
TS1A	-879.165434	0.395554	0.328768	-878.769880	0.033393	-878.803273
INT1A	-476.790718	0.147768	0.103960	-476.642950	0.021904	-476.664854
INT1B	-402.364775	0.245814	0.201210	-402.118961	0.022302	-402.141263
TS2A	-476.788137	0.144821	0.101775	-476.643316	0.021523	-476.664839
INT2A	-476.792597	0.148627	0.104042	-476.643970	0.022293	-476.666262
TS3A	-879.158360	0.394195	0.326879	-878.764165	0.033658	-878.797823
INT3A	-400.829321	0.134655	0.094713	-400.694666	0.019971	-400.714637
N3-H_2O	-478.349704	0.258738	0.207738	-478.090966	0.025500	-478.116466
1a	-865.336397	0.353486	0.286252	-864.982911	0.033617	-865.016528
TS4A	-1266.137011	0.489319	0.403301	-1265.647692	0.043009	-1265.690701
INT4A	-1266.136680	0.489655	0.401886	-1265.647025	0.043885	-1265.690909

TS4B	-1266.127734	0.488699	0.404205	-1265.639035	0.042247	-1265.681282
INT4B	-1266.131868	0.488721	0.404234	-1265.643147	0.042244	-1265.685390
TS4A-concerted	-1266.096632	0.487777	0.402192	-1265.608855	0.042793	-1265.651647
TS5A	-1266.133623	0.489444	0.404832	-1265.644179	0.042306	-1265.686485
4a	-1266.237667	0.493168	0.409847	-1265.744499	0.041661	-1265.786159
1m	-786.940718	0.310823	0.250923	-786.629895	0.029950	-786.659845
TS4A-1m	-1187.737025	0.446427	0.367062	-1187.290598	0.039683	-1187.330280
INT4A-1m	-1187.736960	0.446913	0.368335	-1187.290047	0.039289	-1187.329336
TS4B-1m	-1187.754719	0.446722	0.369801	-1187.307997	0.038461	-1187.346457
INT4B-1m	-1187.764090	0.447796	0.370960	-1187.316294	0.038418	-1187.354712
TS4B-1m-concerted	-1187.704826	0.444659	0.365201	-1187.260167	0.039729	-1187.299896
TS5B-1m	-1187.752395	0.447062	0.370987	-1187.305333	0.038038	-1187.343370
5i	-1187.840610	0.450012	0.372855	-1187.390598	0.038579	-1187.429176

Note: ZPE = zero-point vibrational energy; H_{corr} = thermal correction to enthalpy; G_{corr} = thermal correction to Gibbs free energy; E_{ele} = the electronic energies in solvent; 0.5TS = 1/2 of the entropy, H_{sol} = ethalpies in solvent; G_{sol} = Gibbs free energies in solvent.

Mulliken charge analysis of **1a**

Natural Population

Atom	No	Natural Charge	Core	Valence	Rydberg	Total
C	1	-0.15861	1.99890	4.14040	0.01931	6.15861
C	2	0.71615	1.99918	3.24445	0.04022	5.28385
O	3	-0.72459	1.99980	6.70809	0.01670	8.72459
N	4	-0.47746	1.99932	5.46619	0.01195	7.47746
C	5	-0.28441	1.99927	4.26871	0.01643	6.28441
H	6	0.27063	0.00000	0.72754	0.00184	0.72937
H	7	0.27566	0.00000	0.72268	0.00166	0.72434
C	8	-0.28581	1.99928	4.26898	0.01755	6.28581
H	9	0.28238	0.00000	0.71546	0.00216	0.71762
H	10	0.27021	0.00000	0.72823	0.00155	0.72979
C	11	-0.06504	1.99905	4.05133	0.01466	6.06504
C	12	-0.25982	1.99905	4.24790	0.01287	6.25982
C	13	-0.25134	1.99905	4.23941	0.01287	6.25134
C	14	-0.24864	1.99913	4.23529	0.01422	6.24864
H	15	0.26233	0.00000	0.73616	0.00152	0.73767
C	16	-0.25010	1.99914	4.23697	0.01399	6.25010
H	17	0.26141	0.00000	0.73727	0.00132	0.73859
C	18	-0.26389	1.99913	4.25107	0.01368	6.26389
H	19	0.26304	0.00000	0.73579	0.00117	0.73696
H	20	0.26322	0.00000	0.73561	0.00116	0.73678
H	21	0.26239	0.00000	0.73648	0.00113	0.73761
C	22	-0.05663	1.99905	4.04302	0.01456	6.05663
C	23	-0.26111	1.99906	4.24897	0.01308	6.26111
C	24	-0.25251	1.99906	4.24064	0.01281	6.25251

C	25	-0.24934	1.99913	4.23600	0.01421	6.24934
H	26	0.25763	0.00000	0.74091	0.00146	0.74237
C	27	-0.25094	1.99914	4.23784	0.01397	6.25094
H	28	0.26028	0.00000	0.73840	0.00132	0.73972
C	29	-0.26630	1.99913	4.25348	0.01369	6.26630
H	30	0.26208	0.00000	0.73675	0.00117	0.73792
H	31	0.26247	0.00000	0.73636	0.00117	0.73753
H	32	0.26164	0.00000	0.73723	0.00113	0.73836
C	33	-0.45540	1.99929	4.44180	0.01431	6.45540
H	34	0.25147	0.00000	0.74641	0.00212	0.74853
H	35	0.26174	0.00000	0.73685	0.00142	0.73826
C	36	-0.45500	1.99928	4.44052	0.01520	6.45500
H	37	0.26490	0.00000	0.73352	0.00158	0.73510
H	38	0.24525	0.00000	0.75273	0.00202	0.75475
C	39	-0.22147	1.99906	4.20622	0.01620	6.22147
H	40	0.28355	0.00000	0.71534	0.00111	0.71645

==========

* Total *	-0.00000	41.98250	105.65703	0.36047	148.00000

Mulliken charge analysis of **1m**

			Natural Population			
	Natural					
Atom	No	Charge	Core	Valence	Rydberg	Total
C	1	-0.12244	1.99881	4.10620	0.01743	6.12244
C	2	-0.00097	1.99896	3.98261	0.01939	6.00097
C	3	0.71088	1.99917	3.24822	0.04173	5.28912
O	4	-0.74279	1.99980	6.72627	0.01673	8.74279

C	5	-0.44501	1.99920	4.42915	0.01667	6.44501
H	6	0.26115	0.00000	0.73702	0.00183	0.73885
H	7	0.27168	0.00000	0.72647	0.00185	0.72832
C	8	-0.45473	1.99919	4.43998	0.01555	6.45473
H	9	0.26479	0.00000	0.73346	0.00175	0.73521
H	10	0.26300	0.00000	0.73505	0.00195	0.73700
C	11	-0.08148	1.99900	4.06576	0.01671	6.08148
C	12	-0.24739	1.99908	4.23556	0.01274	6.24739
C	13	-0.24210	1.99908	4.22981	0.01320	6.24210
C	14	-0.25078	1.99914	4.23748	0.01416	6.25078
H	15	0.26079	0.00000	0.73780	0.00141	0.73921
C	16	-0.24987	1.99914	4.23666	0.01407	6.24987
H	17	0.26285	0.00000	0.73578	0.00137	0.73715
C	18	-0.26428	1.99913	4.25142	0.01372	6.26428
H	19	0.26373	0.00000	0.73510	0.00117	0.73627
H	20	0.26380	0.00000	0.73504	0.00116	0.73620
H	21	0.26262	0.00000	0.73625	0.00112	0.73738
C	22	-0.30472	1.99934	4.29026	0.01512	6.30472
C	23	-0.30944	1.99935	4.29401	0.01609	6.30944
C	24	-0.13080	1.99929	4.11258	0.01893	6.13080
H	25	0.25323	0.00000	0.74408	0.00269	0.74677
H	26	0.27430	0.00000	0.72428	0.00142	0.72570
C	27	-0.13267	1.99929	4.11420	0.01918	6.13267
H	28	0.24985	0.00000	0.74769	0.00246	0.75015
H	29	0.27927	0.00000	0.71847	0.00226	0.72073
H	30	0.25386	0.00000	0.74492	0.00122	0.74614
H	31	0.21652	0.00000	0.78104	0.00244	0.78348
H	32	0.25358	0.00000	0.74522	0.00121	0.74642
H	33	0.21861	0.00000	0.77863	0.00276	0.78139

N	34	-0.48478	1.99930	5.47213	0.01335	7.48478
O	35	-0.62028	1.99981	6.60781	0.01266	8.62028

==========

* Total *	-0.00000	35.98607	93.67643	0.33750	130.00000

Cartesian Coordinate (unit:angstrom)

2a

C	2.279989	0.327784	0.041199
C	1.845696	-1.000158	0.045277
C	0.487045	-1.300756	-0.004479
C	-0.459899	-0.266732	-0.066557
C	-0.030290	1.065150	-0.068658
C	1.333623	1.351806	-0.013283
H	3.339649	0.558909	0.084151
H	2.567992	-1.810097	0.093851
H	0.156283	-2.336795	-0.002987
H	-0.767772	1.857671	-0.094673
H	1.655971	2.389348	-0.009183
N	-1.826651	-0.609738	-0.212636
H	-2.057547	-1.437661	0.332002
O	-2.707570	0.415035	0.254280
H	-3.184445	0.663948	-0.549945

N3

C	1.181522	0.668715	0.640034
C	0.000058	-1.278410	-0.102999
C	-1.181722	0.668844	0.639762
H	0.000106	-2.087071	-0.843728
H	1.200271	0.323657	1.693805
H	2.080062	1.270885	0.468606
H	-2.080127	1.271047	0.467854
H	-1.200834	0.323897	1.693522
H	-0.000039	-1.758924	0.912140
N	-1.201098	-0.470798	-0.288287
N	1.201123	-0.470715	-0.287995
N	-0.000036	1.493523	0.462907
C	0.000005	2.216410	-0.813929
H	-0.884627	2.859648	-0.858289
H	0.885187	2.858886	-0.858582
H	-0.000481	1.551838	-1.686849
C	-2.406293	-1.269855	-0.140966
H	-2.517291	-1.721683	0.864525
H	-3.285387	-0.644590	-0.327454
H	-2.407376	-2.081153	-0.876432
C	2.406435	-1.269665	-0.141122
H	2.517508	-1.722040	0.864115
H	2.407652	-2.080545	-0.877048
H	3.285419	-0.644144	-0.327240

CH_2O

C	-0.000006	0.529027	0.000000
H	0.937942	1.124849	0.000000
H	-0.937864	1.125001	0.000000
O	-0.000006	-0.678001	0.000000

TS1A

C	4.258113	1.508417	0.257559
C	2.950499	1.962052	0.452927
C	1.870838	1.099532	0.273335
C	2.091505	-0.239738	-0.084286
C	3.403047	-0.695397	-0.284309
C	4.475676	0.180431	-0.116749
H	5.097656	2.184853	0.388102
H	2.770286	2.997173	0.731025
H	0.847254	1.446833	0.380380
H	3.559475	-1.728411	-0.572421
H	5.489184	-0.179716	-0.272367
H	-0.857903	-0.848119	-0.198820
O	1.210480	-2.148075	-1.164201
H	1.335092	-1.661086	-1.993117
C	-2.876992	-0.706527	0.424971
C	-1.800692	0.516111	-1.450146
C	-2.760868	1.655622	0.439368
H	-0.943780	0.484006	-2.129293
H	-3.836657	-0.706024	-0.107841
H	-2.720044	-1.618129	0.996956
H	-2.625252	2.527582	1.084760
H	-3.741947	1.749180	-0.065811
H	-2.732976	0.541787	-2.048539
N	-1.661732	1.635825	-0.544766
N	-2.759245	0.452622	1.242475
C	-1.691378	0.413840	2.259581
H	-1.996066	1.024736	3.115471
H	-1.522315	-0.621181	2.560549
H	-0.737605	0.793210	1.874236
C	-1.492661	2.893411	-1.259705
H	-2.360499	3.162756	-1.889011
H	-1.333164	3.698322	-0.537050
H	-0.606283	2.835790	-1.898957
C	-1.929098	-1.976885	-1.499526
H	-2.938687	-2.047774	-1.912059
H	-1.187714	-1.940680	-2.297234
H	-1.681694	-2.802001	-0.829295
N	-1.804451	-0.749479	-0.669890
N	0.949023	-1.084452	-0.194686
C	0.611215	-1.889228	1.172267
H	0.892280	-1.103154	1.918092
H	1.419795	-2.659574	1.177441
O	-0.624082	-2.307155	1.186847

INT1A

C	-2.211599	-1.286531	-0.030334
C	-0.837908	-1.195918	-0.216700
C	-0.181884	0.068511	-0.197106
C	-0.985787	1.219100	0.025910
C	-2.358281	1.099935	0.208336
C	-2.997840	-0.146493	0.183243
H	-2.680771	-2.269651	-0.050972

H	-0.252570	-2.092427	-0.395240
H	-0.490586	2.181286	0.060036
H	-2.945295	2.001942	0.380201
H	-4.072864	-0.227353	0.322440
O	1.744599	1.399928	-0.217854
H	2.642310	0.983999	0.135958
N	1.153159	0.141258	-0.447415
C	2.170704	-0.940915	0.138068
H	2.216843	-1.720387	-0.665768
H	1.613475	-1.407725	0.995627
O	3.294515	-0.318006	0.427993

INT1B

C	1.096894	0.877453	0.606537
C	0.090288	-1.342118	0.031063
C	-1.242741	0.535096	0.689676
H	0.162989	-2.220848	-0.615049
H	1.238659	0.494574	1.622293
H	1.920477	1.536590	0.328321
H	-2.199942	1.026629	0.509739
H	-1.204430	0.227639	1.749453
H	0.249291	-1.654875	1.079775
N	-1.127897	-0.623097	-0.216397
N	-0.160866	1.477889	0.439043
C	-0.336518	2.307024	-0.762597
H	-1.231962	2.919284	-0.637824
H	0.516143	2.982092	-0.866302
H	-0.452948	1.717813	-1.683343
C	-2.309848	-1.492996	-0.217704
H	-2.508899	-1.952788	0.762547
H	-3.181519	-0.902281	-0.507412
H	-2.180024	-2.286855	-0.957999
C	2.585037	-1.072363	-0.137227
H	2.713032	-1.368110	0.905095
H	2.636520	-1.952163	-0.780539
H	3.363528	-0.361605	-0.417041
H	1.119898	-0.122716	-1.264002
N	1.251694	-0.419785	-0.292102

TS2A

C	-2.217402	-1.288742	-0.010855
C	-0.836201	-1.203263	-0.131579
C	-0.183802	0.067196	-0.132113
C	-1.004032	1.224867	0.007527
C	-2.380953	1.104837	0.127639
C	-3.017955	-0.145652	0.119223
H	-2.682374	-2.274453	-0.015011
H	-0.245823	-2.107861	-0.238321
H	-0.509116	2.187799	0.026389
H	-2.977830	2.010387	0.237081
H	-4.098025	-0.226154	0.210437
O	1.777006	1.391130	-0.114895
H	2.788804	0.813062	0.133608
N	1.149463	0.164248	-0.313157
C	2.145127	-0.936224	0.077606
H	2.135470	-1.684481	-0.748932
H	1.723143	-1.453827	0.975907
O	3.321847	-0.310170	0.273177

INT2A

C	3.031467	-0.173393	-0.000077
C	2.203851	-1.304941	0.000002
C	0.818333	-1.205527	0.000014
C	0.182121	0.080602	-0.000178
C	1.034726	1.232084	-0.000096
C	2.410952	1.089850	-0.000067
H	4.114037	-0.269167	0.000176
H	2.652547	-2.298845	0.000144
H	0.218158	-2.110012	0.000151
H	0.551934	2.201320	-0.000123
H	3.028272	1.988910	-0.000084
O	-1.772620	1.443132	0.000608
N	-1.148704	0.224320	-0.000433
C	-2.098993	-0.917023	0.000599
H	-1.910182	-1.551930	0.892786
H	-1.909338	-1.554284	-0.889599
O	-3.368761	-0.369386	-0.000787
H	-3.068202	0.623880	-0.000177

TS3A

C	-4.728438	-0.676681	0.766193
C	-4.047022	-1.377890	-0.232484
C	-2.903937	-0.847206	-0.826914
C	-2.438969	0.425159	-0.437601
C	-3.104864	1.119361	0.587441
C	-4.241696	0.568882	1.173333
H	-5.612798	-1.102308	1.230760
H	-4.394435	-2.361072	-0.539359
H	-2.341432	-1.436204	-1.542516
H	-2.698597	2.077652	0.883925
H	-4.753234	1.119938	1.958316
H	0.843734	-0.860285	-0.365382
O	-0.701472	2.043087	-0.324677
C	2.410609	-1.606113	0.957637
C	1.365894	0.624946	1.048485
C	3.696518	0.367838	0.601646
H	0.454219	1.194279	0.763731
H	2.574625	-1.588994	2.042706
H	2.230012	-2.635198	0.637068
H	4.537048	0.774169	0.031852
H	3.936869	0.456640	1.679324
H	1.565154	0.673206	2.139714
N	2.476881	1.078262	0.247078
N	3.553720	-1.056914	0.289012
C	3.605352	-1.316647	-1.153312
H	4.610567	-1.083889	-1.517227
H	3.417050	-2.377622	-1.340816
H	2.881535	-0.716451	-1.719657
C	2.559263	2.531663	0.169589
H	2.780538	3.012172	1.139477
H	3.350027	2.810250	-0.534687
H	1.598782	2.897956	-0.203299
C	-0.011045	-1.381555	1.476401
H	0.216876	-1.395192	2.546221
H	-0.892482	-0.767129	1.292302
H	-0.204716	-2.396086	1.123525

N	1.132061	-0.820814	0.717615	C	0.228082	-1.288022	-0.218018
N	-1.295447	1.019860	-1.006839	C	1.607102	0.652576	-0.468533
C	-0.693200	0.493716	-2.083035	H	-0.044249	-2.101557	0.463488
H	-1.341199	0.014147	-2.810618	H	-0.268897	0.356269	-2.295540
H	0.082532	1.145592	-2.467884	H	-1.502860	1.309949	-1.434421
O	0.250319	-0.975119	-1.680395	H	2.392317	1.240124	0.017603
H	0.887255	-1.094924	-2.399243	H	1.994978	0.314273	-1.451151
				H	0.574182	-1.750297	-1.177614

INT3A

C	1.829119	-1.184983	-0.213780	N	1.279133	-0.489452	0.393383
C	0.436447	-1.185058	-0.187088	N	0.449841	1.495062	-0.711819
C	-0.237523	0.019200	0.007228	C	0.020785	2.242432	0.479055
C	0.454576	1.212290	0.213852	H	0.854574	2.861617	0.823780
C	1.849733	1.198566	0.192707	H	-0.796002	2.914842	0.195324
C	2.538216	0.004590	-0.027586	H	-0.311973	1.605264	1.307443
H	2.361670	-2.117089	-0.375220	C	2.445328	-1.294773	0.716376
H	-0.144969	-2.091329	-0.303357	H	2.924993	-1.753994	-0.170071
H	-0.082289	2.131585	0.419917	H	3.191342	-0.670815	1.218211
H	2.396010	2.121177	0.362597	H	2.161633	-2.098232	1.403412
H	3.623811	-0.001201	-0.041474	C	-2.043208	-1.253523	-1.045597
N	-1.702245	-0.031507	0.020115	H	-1.774732	-1.697543	-2.020484
C	-2.395727	0.977913	-0.448969	H	-2.321999	-2.058581	-0.359501
H	-1.888949	1.816649	-0.898851	H	-2.919770	-0.614868	-1.190567
H	-3.471260	0.899524	-0.395530	N	-0.963259	-0.466379	-0.458790
O	-2.215919	-1.099235	0.484116	O	-1.912450	-0.080344	2.210063
				H	-2.571938	0.620865	2.144918

N3-H_2O

H	-1.557569	-0.147283	1.296346	C	-0.920888	2.595387	-0.520039
C	-0.605495	0.697659	-1.298466	C	-2.006507	3.496795	0.031286

1a

H	-2.224865	3.627119	1.081941	H	5.171528	0.894243	-0.521957
C	0.056419	1.883272	0.342000	H	4.045418	-3.256307	-0.588869
O	0.791627	2.523556	1.097310	H	5.695866	-1.467416	-1.093538
N	0.086722	0.509066	0.287086	C	-0.888746	4.085156	-0.752581
C	-0.485257	-0.291746	-0.786950	H	-1.077308	4.451276	-1.764174
H	-0.833884	0.377755	-1.575430	H	-0.129537	4.625292	-0.193581
H	0.316657	-0.897668	-1.228961	C	-2.370361	2.350367	-0.855984
C	0.973752	-0.207261	1.217098	H	-2.849860	1.493618	-0.387766
H	1.120528	0.443205	2.080270	H	-2.714114	2.549808	-1.874451
H	0.447342	-1.109334	1.545632				
C	-1.617702	-1.206144	-0.347093	**TS4A**			
C	-2.368878	-0.945999	0.803928	C	-0.206681	-1.919218	-0.209836
C	-1.941026	-2.324407	-1.125275	C	1.044258	-1.101581	-0.346774
C	-3.429346	-1.780011	1.164582	C	0.469291	-3.216260	0.108951
H	-2.110190	-0.092519	1.423669	H	1.033776	-0.047240	-0.089242
C	-3.002806	-3.155743	-0.770756	H	1.650249	-1.292964	-1.237583
H	-1.355304	-2.544486	-2.015016	H	-0.075931	-3.901472	0.754876
C	-3.751932	-2.885278	0.377012	H	0.984573	-3.708594	-0.719353
H	-4.000435	-1.566280	2.063517	C	4.273441	-0.699148	-0.189504
H	-3.241291	-4.018793	-1.385708	C	5.144993	-0.357395	-1.231943
H	-4.575564	-3.535146	0.657207	C	3.752730	0.296357	0.652434
C	2.303848	-0.571548	0.590195	C	5.500067	0.974090	-1.419657
C	3.238018	0.433779	0.299010	H	5.510774	-1.148609	-1.873471
C	2.605057	-1.897437	0.262706	C	4.103592	1.628055	0.439349
C	4.451886	0.110165	-0.303861	H	3.049278	0.056209	1.439381
H	2.994129	1.461719	0.550019	C	4.979160	1.972958	-0.591210
C	3.822737	-2.222321	-0.341110	H	6.180638	1.235407	-2.224403
H	1.883013	-2.680122	0.484259	H	3.665547	2.396243	1.068003
C	4.748032	-1.218339	-0.625026	H	5.246716	3.012468	-0.753473

O	-2.050619	-2.399587	1.174052	H	1.667137	4.709278	1.201501
N	-1.932394	-0.263837	0.367644	O	4.131634	-2.864113	-1.055551
C	-1.495247	0.702816	-0.626424	C	3.188614	-2.514933	1.007764
H	-2.389622	1.130176	-1.099050	H	3.156475	-3.596143	1.061289
H	-0.960965	0.182328	-1.425517	H	3.373075	-1.988500	1.937404
C	-3.139427	0.099206	1.124844	N	3.906757	-2.081969	-0.060439
H	-3.185457	-0.566300	1.987840	C	1.303129	-2.111463	0.756245
H	-3.010800	1.126482	1.483627	C	-1.450710	-1.559151	0.487124
C	-4.406187	-0.011550	0.300363	H	0.998356	-1.816935	1.759316
C	-5.103476	1.130671	-0.105970				
C	-4.875342	-1.274180	-0.092586	**INT4A**			
C	-6.255293	1.020945	-0.890025	C	-0.110658	-1.852957	-0.432132
H	-4.746207	2.112257	0.197609	C	0.750486	-3.058251	-0.307090
C	-6.023116	-1.383716	-0.874682	C	0.984147	-1.007785	-0.984217
H	-4.326564	-2.156248	0.223394	H	0.667738	-3.740315	-1.165884
C	-6.716368	-0.237113	-1.275795	H	0.668765	-3.646322	0.612056
H	-6.788145	1.916212	-1.197736	H	0.973999	-0.785120	-2.059860
H	-6.381454	-2.365486	-1.171260	H	1.185285	-0.031927	-0.475890
H	-7.611386	-0.326446	-1.884803	N	3.351434	-0.474131	0.667476
C	-0.631586	1.833465	-0.079584	O	2.533116	0.523860	0.728543
C	-0.240412	2.870966	-0.935809	C	4.658553	-0.280764	0.201751
C	-0.184940	1.850847	1.245672	C	5.102626	1.040097	-0.012571
C	0.585897	3.896934	-0.481101	C	5.539591	-1.357592	-0.029347
H	-0.580468	2.868614	-1.969006	C	6.402280	1.268796	-0.444320
C	0.637959	2.881828	1.706685	H	4.409754	1.851800	0.166869
H	-0.478706	1.045270	1.911520	C	6.838660	-1.105159	-0.457026
C	1.027973	3.906895	0.844841	H	5.216465	-2.382217	0.108566
H	0.885228	4.689838	-1.160320	C	7.281429	0.203616	-0.667634
H	0.971293	2.882465	2.740790	H	6.734506	2.289693	-0.607799

H	7.508563	-1.941218	-0.634039	H	-7.119196	1.249538	-0.802634
H	8.296208	0.390311	-1.003862	H	-6.367580	-2.983066	-0.659746
O	-1.758713	-2.559210	1.051235	H	-7.829263	-1.078841	-1.305634
N	-1.971438	-0.416229	0.259477	C	2.698827	-1.767977	0.764889
C	-3.103216	-0.173573	1.160724	H	3.402525	-2.548375	1.057915
H	-3.035453	0.863660	1.506296	H	1.938063	-1.651106	1.544721
H	-2.975063	-0.835976	2.017593	C	1.988583	-2.113815	-0.561457
C	-1.792496	0.555373	-0.809293	H	2.704921	-2.439607	-1.321958
H	-1.121034	0.132071	-1.558537	C	-1.332749	-1.644793	0.320723
H	-2.756357	0.696867	-1.316947				
C	-1.273543	1.901671	-0.333461	**TS4B**			
C	-0.289928	1.984806	0.658997	C	0.011329	-2.389496	2.515519
C	-1.757632	3.081728	-0.908948	C	0.701213	-3.423244	1.716028
C	0.215401	3.224082	1.051124	C	0.892687	-1.246983	2.149308
H	0.091062	1.080588	1.120376	H	0.115397	-4.223867	1.270249
C	-1.256272	4.323350	-0.515039	H	1.665371	-3.775466	2.108774
H	-2.533145	3.027539	-1.669720	H	0.458109	-0.248702	2.130732
C	-0.265429	4.397089	0.465746	H	1.874588	-1.238239	2.637349
H	0.989835	3.267569	1.810982	N	2.680331	-1.290934	-0.942747
H	-1.643045	5.231208	-0.969375	O	2.096221	-1.284110	-2.102463
H	0.126415	5.362275	0.773557	C	3.454053	-0.155138	-0.574382
C	-4.442436	-0.419294	0.494258	C	3.706847	0.802726	-1.570688
C	-5.268459	0.646939	0.124055	C	3.950880	0.046830	0.725333
C	-4.846109	-1.730591	0.201951	C	4.449605	1.938681	-1.266180
C	-6.485464	0.412921	-0.521895	H	3.310680	0.620423	-2.560745
H	-4.956620	1.665446	0.344455	C	4.693357	1.189167	1.012540
C	-6.059840	-1.964110	-0.441699	H	3.751152	-0.664487	1.516503
H	-4.191692	-2.550672	0.482728	C	4.946920	2.142707	0.023747
C	-6.883161	-0.893553	-0.804945	H	4.642087	2.671252	-2.044607

H	5.066655	1.337617	2.021373	C	-1.540117	1.416944	1.115264
H	5.519652	3.034457	0.257786	C	-0.734179	4.017441	0.516839
C	-0.251017	-1.977860	-0.155651	H	0.689816	3.099409	-0.815731
O	-0.838495	-2.994808	-0.528655	C	-2.166678	2.500793	1.730669
C	0.891322	-2.130947	0.866338	H	-1.880307	0.406466	1.316325
C	2.381422	-2.309878	-0.057959	C	-1.765440	3.804191	1.434380
H	3.137617	-2.473492	0.707342	H	-0.418597	5.028861	0.277105
H	2.135411	-3.205147	-0.623881	H	-2.977870	2.324796	2.430908
C	0.230646	0.465226	-0.449822	H	-2.256812	4.648575	1.908869
C	-1.589621	-0.682505	-1.703071				
H	0.647889	0.753593	-1.421680	**INT4B**			
H	1.097362	0.229630	0.161680	C	-0.673318	-4.521836	-0.042428
H	-1.294703	0.117072	-2.387432	C	0.012952	-4.082408	-1.278096
H	-1.545582	-1.629730	-2.244141	C	-0.774476	-3.162852	0.520736
N	-0.566920	-0.741669	-0.637225	H	-0.669546	-3.859741	-2.112682
H	-1.070364	-2.303438	2.544233	H	0.848212	-4.663329	-1.684788
C	-2.989673	-0.433382	-1.179180	H	-1.751529	-2.670799	0.409838
C	-3.626940	0.792373	-1.394095	H	-0.446606	-2.991842	1.565427
C	-3.650585	-1.422848	-0.436469	N	1.933673	-1.796607	1.064012
C	-4.897668	1.036599	-0.871135	O	1.259112	-2.006249	2.161389
H	-3.113773	1.570609	-1.952800	C	2.619798	-0.595842	0.869835
C	-4.917768	-1.177617	0.091639	C	2.649598	0.333606	1.931544
H	-3.157554	-2.376753	-0.279112	C	3.311465	-0.298819	-0.326234
C	-5.544727	0.052972	-0.122722	C	3.371330	1.512932	1.801449
H	-5.376081	1.996868	-1.040937	H	2.108888	0.091517	2.836995
H	-5.420738	-1.950289	0.666658	C	4.048470	0.877024	-0.423386
H	-6.532269	0.241580	0.288718	H	3.256123	-0.957302	-1.184001
C	-0.509961	1.622260	0.191105	C	4.089404	1.791500	0.633639
C	-0.113044	2.932314	-0.101487	H	3.381830	2.220112	2.625749

H	4.581147	1.088135	-1.346042	C	0.943624	2.528809	-1.033317
H	4.665041	2.707323	0.545258	C	-1.161481	4.276685	-0.499704
C	0.134101	-1.482203	-1.445175	H	-2.437733	2.725721	-1.283094
O	0.532054	-1.592044	-2.607083	C	1.199682	3.770383	-0.455551
C	0.288609	-2.714566	-0.541012	H	1.759815	1.840104	-1.220986
C	1.718048	-2.790033	0.047100	C	0.146977	4.650497	-0.190656
H	2.449519	-2.713334	-0.756294	H	-1.985841	4.952505	-0.291050
H	1.800305	-3.774478	0.535834	H	2.220918	4.042806	-0.207018
C	-0.635809	0.778082	-1.928654	H	0.345532	5.619758	0.257771
C	-0.811005	-0.077478	0.420010				
H	-1.673179	0.722906	-2.278919	**TS4A-concerted**			
H	0.012560	0.577203	-2.782188	C	-0.743483	-3.265993	0.065725
H	-0.419330	-0.859176	1.069263	C	-1.090687	-2.701401	1.419039
H	-0.321359	0.838618	0.762689	C	-0.052215	-1.799673	0.814265
N	-0.399216	-0.318970	-0.961386	C	0.721275	-2.915654	0.149617
H	-0.781895	-5.498120	0.413240	H	-1.207651	-4.082457	-0.480604
C	-2.312576	0.066282	0.595557	H	-0.779783	-3.278478	2.306736
C	-3.221756	-0.556970	-0.266962	H	-2.086949	-2.278735	1.560832
C	-2.809139	0.829216	1.659074	H	1.354024	-3.530070	0.813089
C	-4.597758	-0.429911	-0.065440	H	1.252327	-2.710555	-0.782740
H	-2.848496	-1.132243	-1.109616	C	-1.859723	-2.250301	-1.606220
C	-4.182103	0.953049	1.867028	H	-0.973256	-2.319796	-2.222575
H	-2.112017	1.334175	2.322923	H	-2.679237	-2.938935	-1.765808
C	-5.082421	0.323216	1.004123	N	-2.151746	-1.033376	-1.145839
H	-5.289144	-0.916561	-0.747413	O	-1.163603	-0.244513	-0.899561
H	-4.550219	1.548760	2.697380	C	-3.437535	-0.693919	-0.593316
H	-6.152128	0.425038	1.161019	C	-3.480520	0.061414	0.583236
C	-0.366296	2.144808	-1.344768	C	-4.608249	-1.082733	-1.249867
C	-1.416151	3.026434	-1.067399	C	-4.722619	0.401833	1.113473

H	-2.555525	0.337090	1.077774	C	3.632148	-1.205232	0.797166
C	-5.843084	-0.733539	-0.703728	C	5.209724	-1.553429	-1.474040
H	-4.555210	-1.623917	-2.188908	H	3.657674	-0.490643	-2.521283
C	-5.903699	0.007312	0.477776	C	4.855017	-1.874321	0.890166
H	-4.765455	0.974705	2.034604	H	3.014322	-1.068879	1.679062
H	-6.755863	-1.028228	-1.212399	C	5.646807	-2.052460	-0.243950
H	-6.866465	0.280686	0.898561	H	5.820880	-1.683884	-2.362722
C	0.163653	-0.393033	1.228349	H	5.187087	-2.256138	1.851527
O	-0.516133	0.043214	2.166431	H	6.597333	-2.572896	-0.172190
N	1.190086	0.338386	0.675720				
C	1.849867	0.004902	-0.575509	**TS5A**			
H	1.994581	0.941320	-1.127639	C	0.000214	-1.644512	-0.803025
H	1.159465	-0.578845	-1.186333	C	-1.196620	-0.764393	-0.734074
C	1.543534	1.620110	1.281466	C	-0.769790	-2.847887	-1.252137
H	1.099168	1.629990	2.279293	H	-1.123588	0.277983	-1.058254
H	2.634270	1.654190	1.395835	H	-1.708823	-0.775268	0.249215
C	1.073891	2.833199	0.496949	H	-0.303030	-3.442468	-2.042834
C	-0.167639	2.837094	-0.152234	H	-1.105171	-3.511171	-0.446287
C	1.871107	3.982045	0.446552	N	-3.658418	-1.926472	0.147542
C	-0.599356	3.976570	-0.831555	C	-4.302246	-0.747415	0.583434
H	-0.781907	1.943172	-0.145398	C	-4.455878	0.376337	-0.254868
C	1.434989	5.124472	-0.226542	C	-4.775318	-0.703683	1.908863
H	2.841760	3.982424	0.937682	C	-5.082126	1.516758	0.235922
C	0.195739	5.124467	-0.868225	H	-4.065253	0.377761	-1.265250
H	-1.561985	3.965904	-1.335440	C	-5.404520	0.443145	2.375283
H	2.066184	6.008296	-0.256997	H	-4.635984	-1.576229	2.533607
H	-0.144580	6.009429	-1.398508	C	-5.564149	1.559652	1.547433
C	3.187204	-0.704092	-0.429148	H	-5.188589	2.381574	-0.411806
C	3.991237	-0.882542	-1.562707	H	-5.774295	0.467452	3.396024

H	-6.053493	2.453561	1.920466	H	4.047399	-2.408836	-0.153954
O	2.080062	-2.292084	-1.638983	C	5.921488	0.377221	1.790444
C	3.368738	0.053667	-1.037871	H	4.863117	1.749209	0.505738
C	1.406588	0.664025	0.346332	C	6.139914	-0.960136	2.119518
H	3.444064	1.117458	-1.290298	H	5.635651	-3.009283	1.672364
H	3.571324	-0.531775	-1.935880	H	6.439693	1.164462	2.330787
H	0.575995	0.151591	0.838805	H	6.830686	-1.219423	2.916791
H	2.158190	0.826866	1.131037	C	-1.890772	-1.819712	-1.635565
N	1.977266	-0.216892	-0.658793	H	-1.829021	-1.556446	-2.695855
O	-3.421550	-2.872337	0.973277				
C	-3.361187	-2.172109	-1.254724	**4a**			
H	-3.530202	-3.239336	-1.408581	C	1.203531	-3.674541	-0.299536
H	-4.059497	-1.606881	-1.872872	C	0.077172	-2.760685	-0.860925
C	1.409047	-1.425279	-1.049180	C	0.194566	-2.022194	0.509924
C	0.943031	2.012906	-0.183429	C	0.646426	-3.368512	1.116568
C	0.711105	2.227883	-1.545663	H	1.267613	-4.714019	-0.629864
C	0.715984	3.063125	0.714525	H	-0.882790	-3.279014	-0.914806
C	0.253645	3.466275	-2.001837	H	0.259960	-2.191015	-1.773403
H	0.897924	1.418214	-2.244696	H	-0.208090	-3.989424	1.386547
C	0.254056	4.298453	0.262822	H	1.351112	-3.297172	1.949086
H	0.902946	2.909908	1.775076	C	2.541550	-2.945046	-0.481009
C	0.021089	4.504373	-1.099501	H	3.260453	-3.249294	0.296891
H	0.082609	3.618996	-3.063754	H	2.971458	-3.178912	-1.460559
H	0.081560	5.102836	0.972202	N	2.287676	-1.498791	-0.485473
H	-0.333065	5.468137	-1.453292	O	1.319422	-1.126008	0.544840
C	4.358252	-0.294984	0.056755	C	3.382523	-0.611848	-0.440014
C	4.580410	-1.638411	0.395318	C	3.189464	0.729060	-0.066613
C	5.032319	0.706041	0.763490	C	4.663553	-1.026171	-0.845404
C	5.466530	-1.966336	1.419386	C	4.248977	1.628456	-0.108278

H	2.214924	1.057426	0.259190	C	0.259701	2.193932	1.265521
C	5.712926	-0.107291	-0.894527	C	0.340481	4.258005	-0.606884
H	4.852305	-2.054680	-1.128430	H	-0.649348	2.880531	-1.934536
C	5.519085	1.223019	-0.526154	C	0.828286	3.422515	1.604455
H	4.069197	2.658183	0.187930	H	0.236816	1.381788	1.985228
H	6.693777	-0.446829	-1.215481	C	0.874523	4.457060	0.667815
H	6.342280	1.929794	-0.560405	H	0.366303	5.059428	-1.339550
C	-1.054936	-1.364041	1.095547	H	1.239004	3.568924	2.599176
O	-1.732407	-2.017154	1.889622	H	1.317867	5.412933	0.930716
N	-1.414222	-0.110776	0.684688				
C	-0.818729	0.630217	-0.425049	**1m**			
H	-1.583806	0.765519	-1.200398	C	-0.054066	1.836179	0.044752
H	-0.014339	0.041294	-0.862635	C	1.367110	1.519153	0.539363
C	-2.667022	0.453997	1.220382	C	-0.743158	0.944282	-0.916422
H	-2.846261	-0.022725	2.184217	O	-0.264648	0.761594	-2.037609
H	-2.504406	1.523032	1.384020	C	1.113063	2.705963	-0.330627
C	-3.835144	0.230848	0.283221	H	1.169677	3.703762	0.110405
C	-4.405149	-1.045447	0.165737	H	1.438512	2.642454	-1.364921
C	-4.328947	1.273132	-0.508545	C	0.248147	1.703310	1.516209
C	-5.453920	-1.267120	-0.724908	H	-0.097257	0.797493	2.012237
H	-4.011958	-1.851933	0.777341	H	0.208909	2.598398	2.142403
C	-5.380254	1.051187	-1.401611	C	2.170674	0.305818	0.320397
H	-3.887386	2.263444	-0.423408	C	2.525121	-0.492827	1.418251
C	-5.944733	-0.219628	-1.510422	C	2.581238	-0.086041	-0.965199
H	-5.893200	-2.257485	-0.805535	C	3.270730	-1.658032	1.239542
H	-5.756200	1.869392	-2.009259	H	2.222133	-0.189040	2.416053
H	-6.763632	-0.394754	-2.202216	C	3.324575	-1.250891	-1.138698
C	-0.269584	1.984886	-0.013112	H	2.278236	0.498837	-1.825456
C	-0.233005	3.030851	-0.941189	C	3.674549	-2.040593	-0.039952

H	3.539437	-2.262851	2.100937	C	5.154060	1.812843	0.218169
H	3.626903	-1.547703	-2.138857	H	4.997308	0.505298	-1.507116
H	4.256953	-2.946304	-0.181301	C	3.560862	1.391612	1.981578
C	-2.755690	0.697924	0.596124	H	2.177870	-0.211876	1.660587
C	-2.455308	-0.752917	-1.338581	C	4.630590	2.132492	1.474183
C	-3.170611	-0.528730	1.409538	H	5.985455	2.382978	-0.185335
H	-3.658230	1.154458	0.162677	H	3.141866	1.634367	2.953529
H	-2.270285	1.442343	1.224778	H	5.049487	2.951352	2.050526
C	-2.882731	-1.928154	-0.460244	O	-2.857915	-1.057552	-1.809445
H	-3.330403	-0.348019	-1.867049	O	3.422810	-1.124559	-2.043755
H	-1.714056	-1.054384	-2.079295	C	2.040964	-1.859925	-0.360042
H	-3.917941	-0.258416	2.161353	H	1.983590	-2.771578	-0.943357
H	-2.285839	-0.943648	1.922134	H	2.023792	-2.002967	0.713604
H	-3.424607	-2.673220	-1.049498	N	3.032792	-1.039471	-0.818836
H	-1.987153	-2.403075	-0.027043	C	0.339509	-1.139398	-0.697772
N	-1.866391	0.278202	-0.484929	C	-2.142477	-0.069629	-1.601231
O	-3.769366	-1.512238	0.576137	C	-2.105678	2.424717	-1.142274
				C	-3.995396	1.055938	-0.453146
TS4A-1m				C	-2.144660	3.118238	0.221266
C	-0.700806	-0.116558	-1.870836	H	-2.731154	2.997560	-1.844249
C	0.376531	0.373796	-0.949393	H	-1.094464	2.398925	-1.547905
C	-0.065210	-1.435202	-2.164560	C	-3.967462	1.783310	0.891345
H	0.105002	1.043106	-0.134961	H	-4.699330	1.558285	-1.133187
H	1.308307	0.690464	-1.426519	H	-4.306020	0.016711	-0.340172
H	-0.745955	-2.260804	-2.363546	H	-1.849196	4.167922	0.132053
H	0.797499	-1.420248	-2.831000	H	-1.446752	2.611679	0.910456
C	3.549679	0.023514	-0.010152	H	-4.975879	1.879846	1.303689
C	4.618871	0.768144	-0.527999	H	-3.346799	1.206482	1.596851
C	3.015498	0.338593	1.250790	N	-2.646655	1.076724	-1.008926

O	-3.460598	3.110545	0.757443
C	-0.527710	-1.645550	0.417853
C	-0.656566	-0.918196	1.612790
C	-1.175447	-2.884720	0.319306
C	-1.433804	-1.401608	2.664519
H	-0.155704	0.038413	1.720446
C	-1.950593	-3.369806	1.371621
H	-1.085366	-3.467725	-0.590071
C	-2.086985	-2.629871	2.546713
H	-1.527113	-0.818279	3.576032
H	-2.453805	-4.326496	1.268933
H	-2.692596	-3.008060	3.364720

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C	-0.344936	-1.156127	-0.158109
C	0.671587	-0.896768	0.998438
C	1.741314	-1.369949	0.076710
C	0.774680	-2.049401	-0.826733
H	0.500563	-1.565825	1.853425
H	0.673705	0.137324	1.386421
H	0.584499	-3.090520	-0.528890
H	0.949358	-2.025388	-1.907227
C	-0.466334	0.135113	-1.020158
H	0.560510	0.407297	-1.314500
H	-1.074477	-0.048039	-1.906554
N	-0.970756	1.261477	-0.272686
O	-0.134762	1.766144	0.573881
C	-2.294442	1.717283	-0.308663
C	-2.608519	2.896631	0.397452
C	-3.306487	1.036882	-1.017631
C	-3.907288	3.386400	0.377816
H	-1.818255	3.398848	0.940059
C	-4.599081	1.548296	-1.027305
H	-3.106038	0.093874	-1.509402
C	-4.910888	2.722494	-0.336285
H	-4.139512	4.297405	0.921337
H	-5.373748	1.011329	-1.566055
H	-5.924364	3.110670	-0.346882
C	3.171074	-1.274867	-0.088571
O	3.750085	-2.088245	-0.830278
C	3.377399	1.033458	0.882462
C	5.337551	-0.365964	0.555921
C	3.940676	1.978801	-0.186807
H	3.703894	1.367625	1.874834
H	2.291299	1.070708	0.842428
C	5.822789	0.611642	-0.516458
H	5.752416	-0.070407	1.527489
H	5.645569	-1.384568	0.318999
H	3.666279	3.014313	0.036110
H	3.509129	1.705318	-1.165734
H	6.915471	0.663309	-0.537061
H	5.463463	0.271231	-1.500430
N	3.876612	-0.328567	0.657404
O	5.359182	1.932100	-0.241952
C	-1.694915	-1.744391	0.159390
C	-2.313767	-2.632006	-0.730346
C	-2.395581	-1.332110	1.299802
C	-3.607293	-3.095714	-0.487541

H	-1.779017	-2.960145	-1.618141	C	0.222154	-0.448986	0.821337
C	-3.689192	-1.792649	1.543727	O	0.438003	-0.540711	2.035783
H	-1.930818	-0.630440	1.986619	C	0.276650	-1.715479	-0.004785
C	-4.299181	-2.674690	0.650047	C	-1.540583	-2.457633	-0.004209
H	-4.073248	-3.786659	-1.184172	H	-1.269538	-3.342253	-0.570017
H	-4.222488	-1.457857	2.428451	H	-1.737308	-2.590358	1.052990
H	-5.306226	-3.033949	0.839688	C	3.051149	-0.995919	-0.117837
				C	3.513402	-0.142100	-1.145649
TS4B-1m				C	3.609930	-0.848814	1.171532
C	2.013500	-1.963794	-0.391378	C	4.475720	0.828443	-0.889477
C	1.226756	-2.763621	0.585125	H	3.119454	-0.255261	-2.150469
C	0.922495	-1.799371	-1.397932	C	4.567683	0.127493	1.421018
H	1.447120	-2.680273	1.645570	H	3.268143	-1.484167	1.979849
H	0.976664	-3.785725	0.277246	C	5.004512	0.973744	0.396770
H	0.943082	-0.921549	-2.035447	H	4.815888	1.473246	-1.694410
H	0.613803	-2.690069	-1.952616	H	4.974562	0.233486	2.422332
N	-2.366062	-1.637842	-0.683360	H	5.753926	1.733284	0.597058
O	-2.288630	-1.607254	-1.981390	C	-0.620239	1.029823	-1.088530
C	-3.184011	-0.653980	-0.034349	C	0.137272	1.975395	1.013901
C	-4.157775	-0.020590	-0.816329	C	0.273029	2.021703	-1.831374
C	-3.011921	-0.294174	1.311382	H	-1.600828	1.495916	-0.927040
C	-4.975207	0.950820	-0.244839	H	-0.801794	0.120408	-1.657342
H	-4.241141	-0.305926	-1.857045	C	1.006210	2.943449	0.208559
C	-3.831663	0.687761	1.863856	H	-0.846298	2.421549	1.214480
H	-2.217680	-0.718575	1.914124	H	0.608524	1.716906	1.961697
C	-4.818886	1.310294	1.095796	H	-0.190607	2.317283	-2.777005
H	-5.734087	1.433507	-0.853405	H	1.251250	1.558743	-2.042996
H	-3.684778	0.974610	2.900700	H	1.083018	3.906577	0.721754
H	-5.451044	2.075434	1.535544	H	2.015981	2.514770	0.103871

N	-0.038076	0.751850	0.227941
O	0.447077	3.214665	-1.074020

INT4B-1m

C	-2.733014	0.546305	-0.202941
C	-1.955798	0.859160	-1.442348
C	-1.516908	0.555983	0.661359
H	-1.898694	1.931939	-1.666010
H	-2.192586	0.333238	-2.373007
H	-1.358686	1.501144	1.197750
H	-1.365740	-0.275117	1.367746
N	0.588949	-1.611247	-0.049477
O	0.075284	-1.866027	1.121788
C	1.953081	-1.771143	-0.275461
C	2.704739	-2.491032	0.679609
C	2.606794	-1.219285	-1.400928
C	4.071679	-2.658338	0.501630
H	2.185007	-2.895985	1.538205
C	3.976480	-1.403535	-1.557585
H	2.070965	-0.603892	-2.113609
C	4.721075	-2.120784	-0.615517
H	4.638404	-3.215044	1.242371
H	4.469632	-0.965519	-2.420484
H	5.790313	-2.251999	-0.746138
C	0.533465	1.366804	-0.936119
O	0.689099	1.735520	-2.103855
C	-0.661333	0.454471	-0.647371
C	-0.325989	-1.012384	-0.992449
H	0.061940	-1.071974	-2.010055
H	-1.263103	-1.583307	-0.921273
C	2.426309	2.727508	-0.230543
C	1.372621	1.270300	1.456732
C	3.781049	2.269972	0.299536
H	2.150170	3.669772	0.263003
H	2.448205	2.883751	-1.308874
C	2.792048	0.929113	1.927308
H	0.964520	2.069655	2.091915
H	0.761835	0.375545	1.568002
H	4.523722	3.063145	0.173129
H	4.115217	1.376672	-0.252030
H	2.781518	0.749180	3.006085
H	3.135764	0.015209	1.424746
N	1.394388	1.724659	0.061605
O	3.705052	1.993277	1.693145
C	-4.059236	0.146970	0.021497
C	-5.018118	0.147315	-1.034475
C	-4.496153	-0.257545	1.317543
C	-6.329142	-0.232161	-0.800243
H	-4.708326	0.456787	-2.028176
C	-5.811336	-0.632628	1.535821
H	-3.779136	-0.276115	2.132440
C	-6.737655	-0.624514	0.482963
H	-7.045857	-0.224751	-1.616351
H	-6.125381	-0.940023	2.529054
H	-7.766515	-0.921656	0.659939

TS4B-1m-concerted

C	-0.959388	-1.532877	0.763719

C	-0.493204	-0.479337	1.736446	H	3.884823	1.693170	0.467682
C	0.807307	-0.723102	0.998403	C	4.528469	-1.803899	-0.895136
C	0.405719	-2.076890	0.427439	H	4.145657	-1.924010	1.221495
H	-0.525580	-0.756638	2.807170	H	2.753232	-2.324370	0.202498
H	-0.957382	0.510294	1.630544	H	6.077394	1.064452	-0.684830
H	0.709418	-2.988973	0.980389	H	4.635760	0.711602	-1.675879
H	0.581982	-2.264530	-0.645490	H	4.949550	-2.813394	-0.923702
N	-0.632260	0.931948	-1.130198	H	3.953004	-1.634742	-1.821847
C	-1.218253	2.177741	-0.664235	N	3.146278	-0.257019	0.390486
C	-0.548928	2.986637	0.256719	O	5.627227	-0.906833	-0.824664
C	-2.482295	2.507596	-1.152240	C	-2.261365	-1.965767	0.387444
C	-1.160288	4.173608	0.663111	C	-3.407415	-1.333836	0.923726
H	0.390863	2.660557	0.694974	C	-2.431967	-3.063717	-0.485743
C	-3.074643	3.698370	-0.738087	C	-4.676317	-1.791106	0.599960
H	-2.976294	1.823721	-1.831893	H	-3.279585	-0.482122	1.583962
C	-2.413183	4.536197	0.164105	C	-3.706121	-3.514611	-0.805762
H	-0.658844	4.805498	1.389680	H	-1.556199	-3.548478	-0.905050
H	-4.054654	3.970503	-1.118083	C	-4.831072	-2.882259	-0.264922
H	-2.880569	5.460966	0.488883	H	-5.551456	-1.301376	1.016501
C	1.959151	0.139243	1.030637	H	-3.829259	-4.359744	-1.476434
O	1.899738	1.261578	1.574510	H	-5.825884	-3.239033	-0.514678
C	0.658569	0.794236	-1.292337				
H	1.012404	-0.145545	-1.685150	**TS5B-1m**			
H	1.313195	1.636974	-1.137349	C	2.395098	-0.751183	-0.011759
O	-1.430156	-0.069007	-1.276716	C	1.762101	-1.517356	-1.145653
C	4.273282	0.674292	0.452204	C	0.428625	-0.794181	-0.745371
C	3.597047	-1.645817	0.306630	C	1.080167	-0.479516	0.647385
C	5.179221	0.443826	-0.753590	H	1.745012	-2.606439	-0.996373
H	4.849882	0.523636	1.378601	H	2.110295	-1.328603	-2.168555

H	0.824746	-1.258133	1.381537	N	-1.711686	-1.842377	0.123500
H	0.897063	0.500127	1.089869	C	3.710072	-0.362708	0.251303
N	-0.020082	1.669283	-0.890156	C	4.037941	0.435516	1.389794
C	-1.310627	2.084384	-0.588893	C	4.776051	-0.763846	-0.610779
C	-2.452572	1.421798	-1.098372	C	5.348569	0.791847	1.648388
C	-1.480048	3.222092	0.234701	H	3.238737	0.770221	2.043417
C	-3.721337	1.901535	-0.789553	C	6.083240	-0.398599	-0.336327
H	-2.357353	0.544960	-1.726770	H	4.548414	-1.365577	-1.485295
C	-2.756333	3.669487	0.540208	C	6.382028	0.379033	0.791638
H	-0.592120	3.719659	0.602753	H	5.579663	1.401139	2.517271
C	-3.889618	3.019737	0.032417	H	6.881828	-0.714604	-1.001272
H	-4.589573	1.389334	-1.194347	H	7.408093	0.666062	0.998939
H	-2.873322	4.541549	1.177289	O	1.016986	2.348193	-0.520465
H	-4.884600	3.382105	0.269059	C	0.282282	0.464365	-1.653089
C	-0.797972	-1.699652	-0.890470	H	-0.456364	0.271839	-2.432807
O	-0.901219	-2.323315	-1.947572	H	1.228611	0.689639	-2.142334
C	-2.656777	-2.964450	0.052210				
C	-1.792059	-1.062232	1.361724	**5i**			
C	-4.061902	-2.515674	0.434729	C	-0.942550	-1.146305	-0.361167
H	-2.330624	-3.743852	0.755565	C	0.337234	-0.915068	0.488859
H	-2.627299	-3.366084	-0.960589	C	0.886777	-0.176243	-0.781159
C	-3.251405	-0.741581	1.705832	C	-0.035231	-1.105089	-1.614071
H	-1.346748	-1.630077	2.190767	H	0.856594	-1.861980	0.653545
H	-1.258216	-0.120459	1.246578	H	0.220298	-0.369933	1.426300
H	-4.732780	-3.377725	0.489416	H	0.469612	-2.047946	-1.828402
H	-4.450323	-1.814430	-0.322530	H	-0.484463	-0.700211	-2.523426
H	-3.299004	-0.306725	2.708269	N	-0.953987	1.221744	-0.047002
H	-3.645508	-0.009594	0.988959	C	-1.785669	2.357071	-0.024295
O	-4.064444	-1.906825	1.720211	C	-1.264948	3.637751	-0.279924

C	-3.140687	2.231661	0.333791	H	-1.135822	-3.592503	-1.601108
C	-2.078765	4.763395	-0.151528	C	-3.597237	-3.232873	1.368480
H	-0.231317	3.767178	-0.578325	H	-2.812092	-1.233970	1.569712
C	-3.940297	3.364835	0.443986	C	-3.541377	-4.429969	0.649528
H	-3.552935	1.246805	0.508539	H	-2.607425	-5.478245	-0.985937
C	-3.419501	4.639783	0.209142	H	-4.291388	-3.127741	2.197331
H	-1.655429	5.744003	-0.350033	H	-4.190488	-5.258354	0.917813
H	-4.985307	3.247001	0.716857	O	-1.749381	0.056822	-0.378900
H	-4.049654	5.518883	0.299311	C	0.287614	1.246984	-0.821748
C	2.363429	-0.230132	-1.158075	H	0.142422	1.562706	-1.866811
O	2.703115	-0.785617	-2.200254				
C	4.705246	0.281112	-0.647927				
C	3.039729	0.866729	1.029498				
C	5.412727	-0.566356	0.409559				
H	5.131431	1.292537	-0.650891				
H	4.805300	-0.156587	-1.641080				
C	3.807993	-0.000059	2.033155				
H	3.404286	1.900493	1.097300				
H	1.979366	0.865865	1.270679				
H	6.495025	-0.561358	0.252665				
H	5.051084	-1.605739	0.344287				
H	3.727815	0.417421	3.041276				
H	3.375985	-1.015544	2.036238				
O	5.191548	-0.046777	1.718849				
N	3.278042	0.373509	-0.326818				
C	-1.865184	-2.289712	-0.045415				
C	-1.818618	-3.488056	-0.764091				
C	-2.765896	-2.170025	1.022737				
C	-2.651559	-4.553915	-0.417338				

10. Crystallographic data for compound 4a and 5i

Date of **4a** and **5i**: Details of the X-ray experiments and crystal data are summarized below. CCDC 2365302 and CCDC 2365303 contains the supplementary crystallographic data, and can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

Table S3. Crystal data and structure refinement for 4a.

Identification code	mo_230612_ZY_5_80_0m
Empirical formula	$C_{26}H_{26}N_2O_2$
Formula weight	398.49
Temperature/K	170.00
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	7.8217(3)
b/Å	28.8712(10)
c/Å	10.0160(3)
α/°	90
β/°	109.4000(10)
γ/°	90
Volume/Å^3	2133.41(13)
Z	4
ρ_{calc}g/cm^3	1.241
μ/mm^{-1}	0.079
F(000)	848.0
Crystal size/mm^3	0.42 × 0.25 × 0.23
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.536 to 54.99
Index ranges	-10 ≤ h ≤ 10, -37 ≤ k ≤ 37, -12 ≤ l ≤ 13
Reflections collected	30701
Independent reflections	4889 [R_{int} = 0.0407, R_{sigma} = 0.0265]
Data/restraints/parameters	4889/21/281
Goodness-of-fit on F^2	1.061
Final R indexes [I>=2σ (I)]	R_1 = 0.0458, wR_2 = 0.1005

Final R indexes [all data]	R_1 = 0.0602, wR_2 = 0.1108
Largest diff. peak/hole / e Å^{-3}	0.18/-0.18

Table S4. Crystal data and structure refinement for 5i.

Identification code	240325_ZY_6_142
Empirical formula	$C_{22}H_{24}N_2O_3$
Formula weight	364.43
Temperature/K	170.00
Crystal system	orthorhombic
Space group	$Pna2_1$
a/Å	11.2419(4)
b/Å	12.3869(5)
c/Å	13.4125(6)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1867.72(13)
Z	4
ρ_{calc}g/cm^3	1.296
μ/mm^{-1}	0.443
F(000)	776.0
Crystal size/mm^3	0.1 × 0.06 × 0.04
Radiation	GaKα (λ = 1.34139)
2Θ range for data collection/°	8.454 to 121.32
Index ranges	-14 ≤ h ≤ 14, -16 ≤ k ≤ 16, -17 ≤ l ≤ 17
Reflections collected	61419
Independent reflections	4289 [R_{int} = 0.0405, R_{sigma} = 0.0234]
Data/restraints/parameters	4289/22/254
Goodness-of-fit on F^2	1.064
Final R indexes [I>=2σ (I)]	R_1 = 0.0305, wR_2 = 0.0776
Final R indexes [all data]	R_1 = 0.0330, wR_2 = 0.0790
Largest diff. peak/hole / e Å^{-3}	0.14/-0.19
Flack parameter	-0.01(4)

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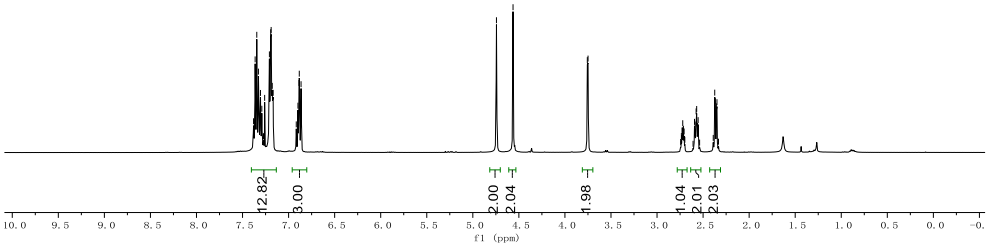
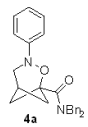
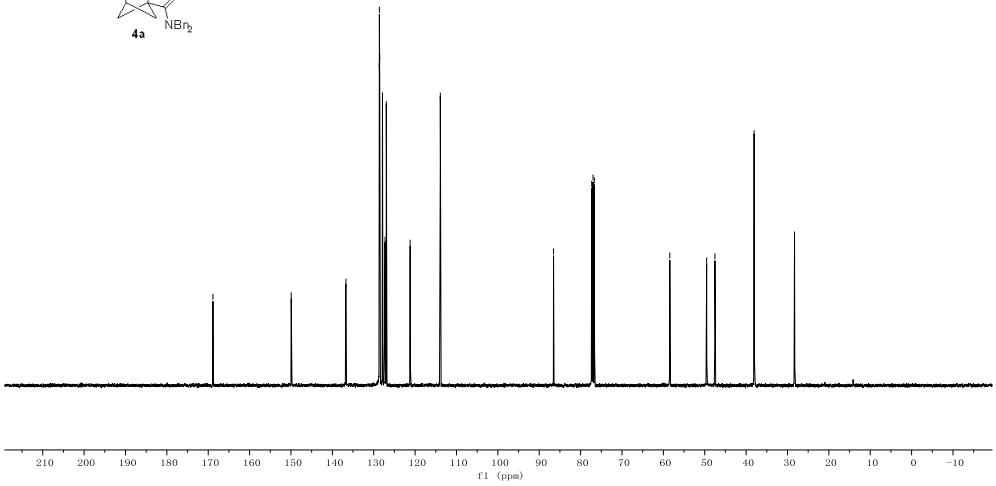
12. Copies of ^{1}H, ^{13}C NMR, and ^{19}F NMR spectra of compounds

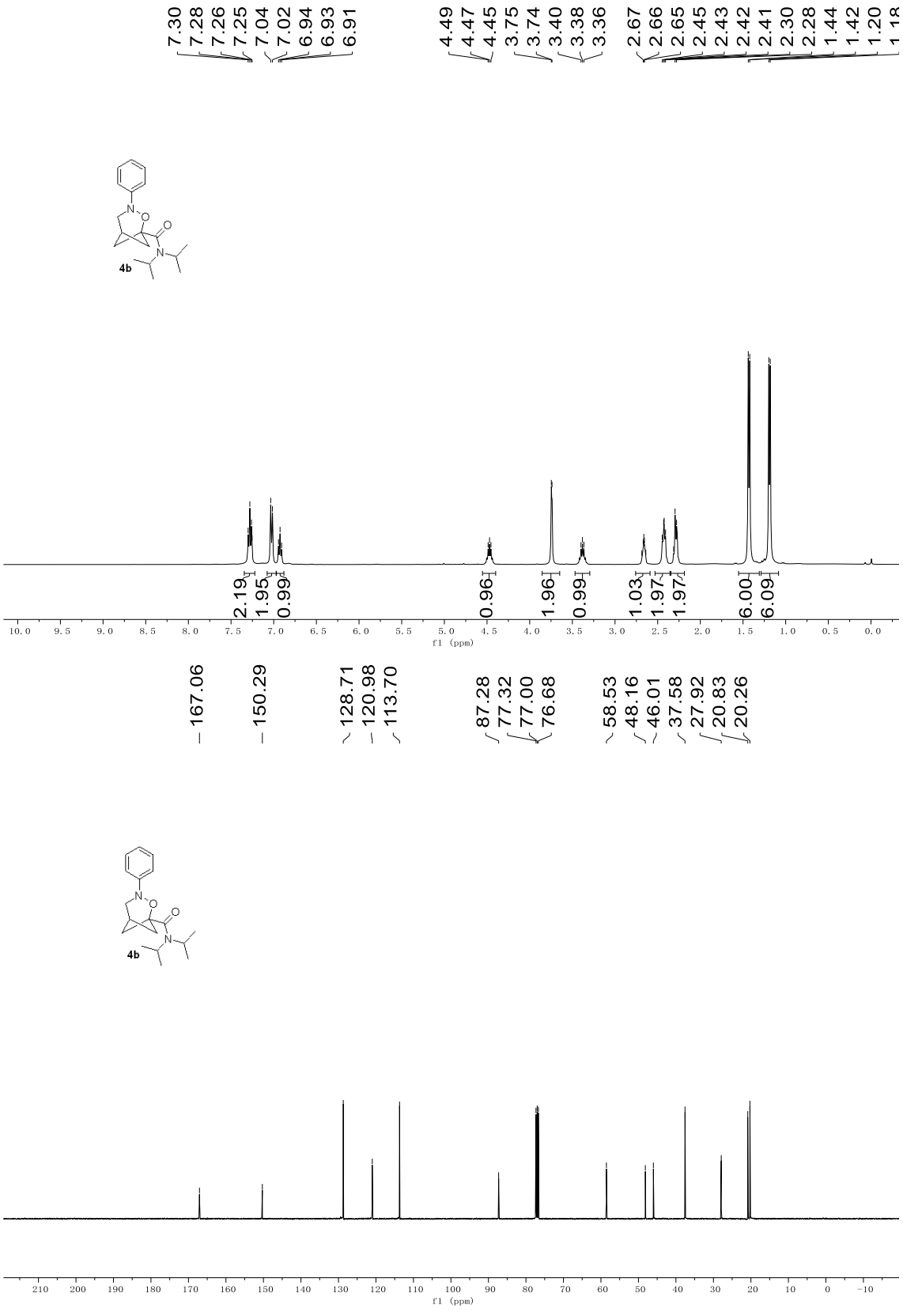
***N,N*-dibenzyl-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide.(4a)**



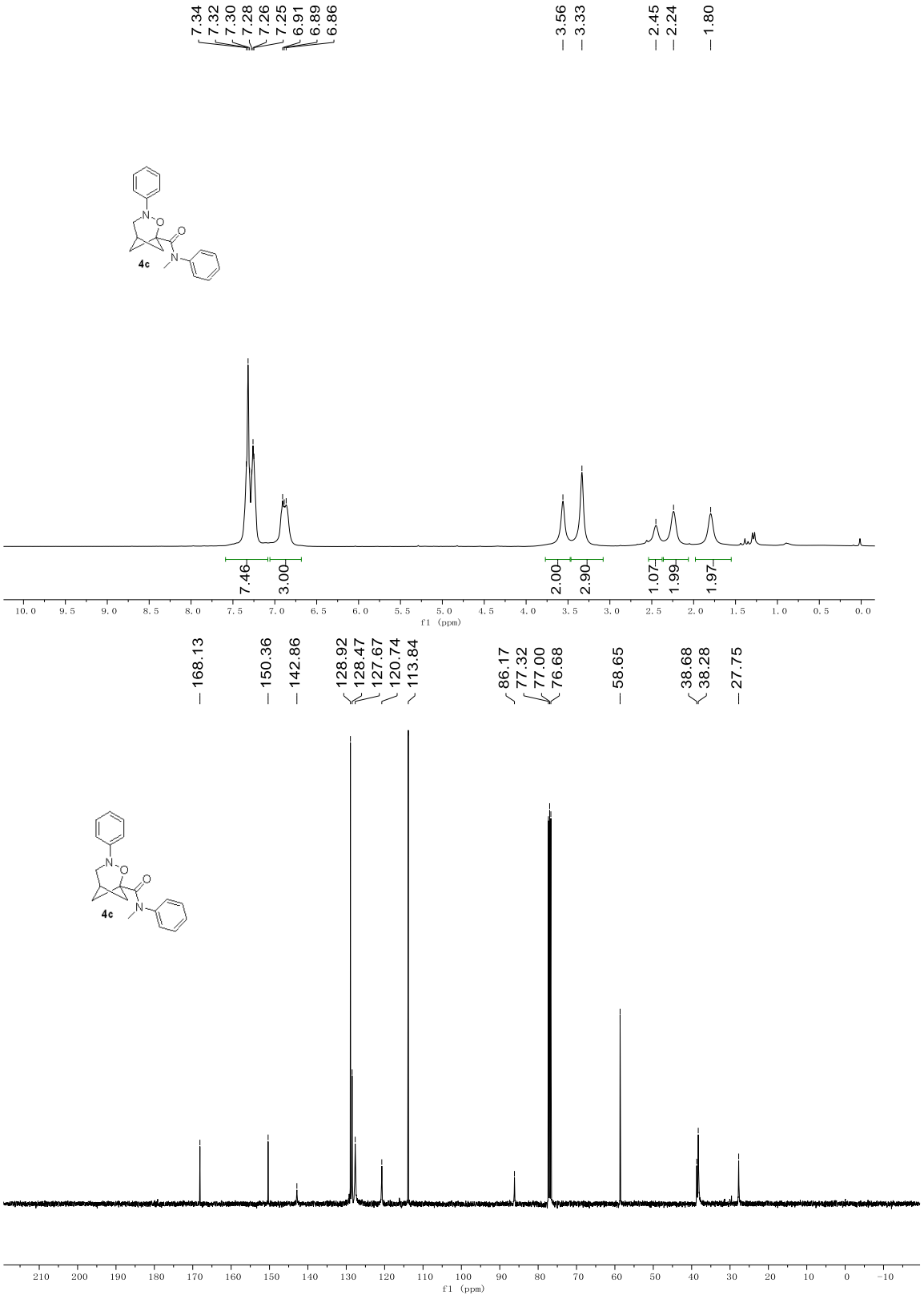




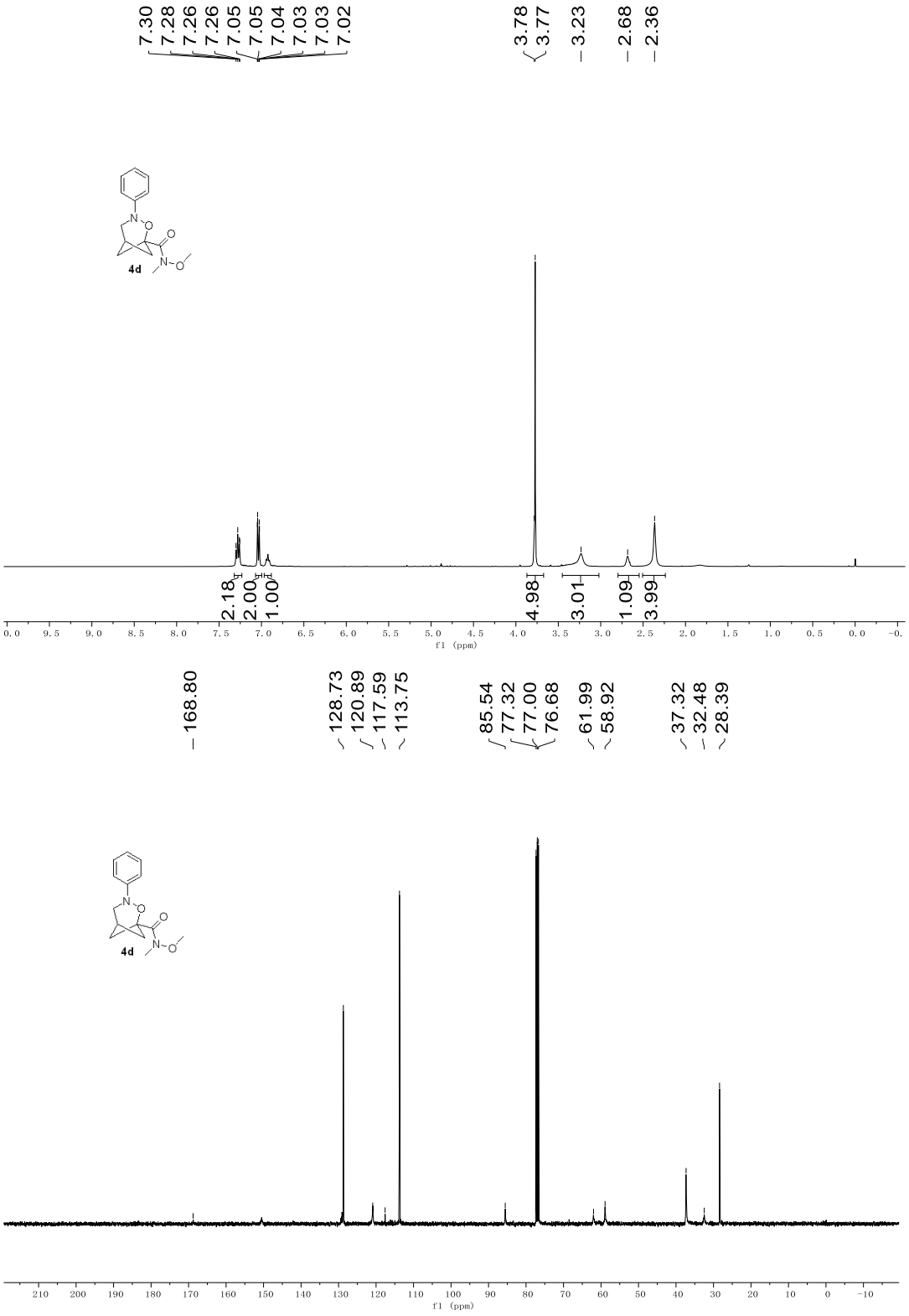
***N,N*-diisopropyl-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide. (4b)**



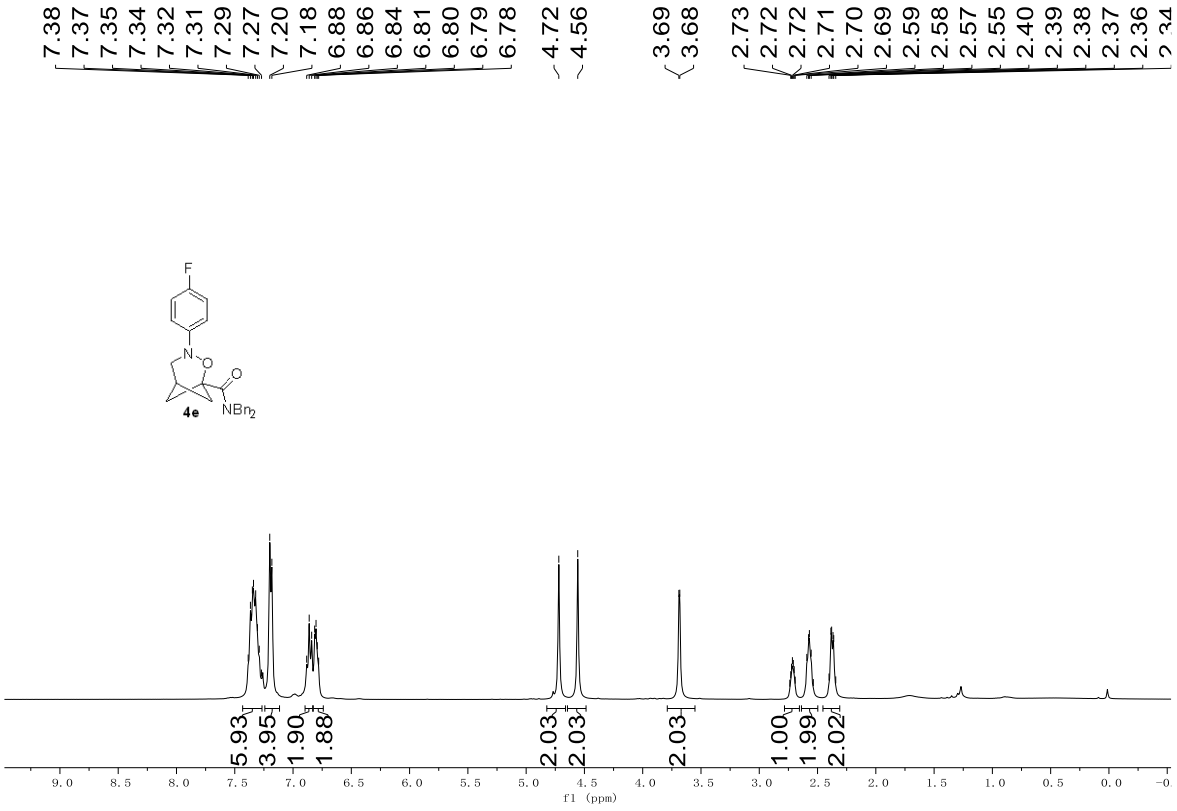
***N*-methyl-*N*,3-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide. (4c)**

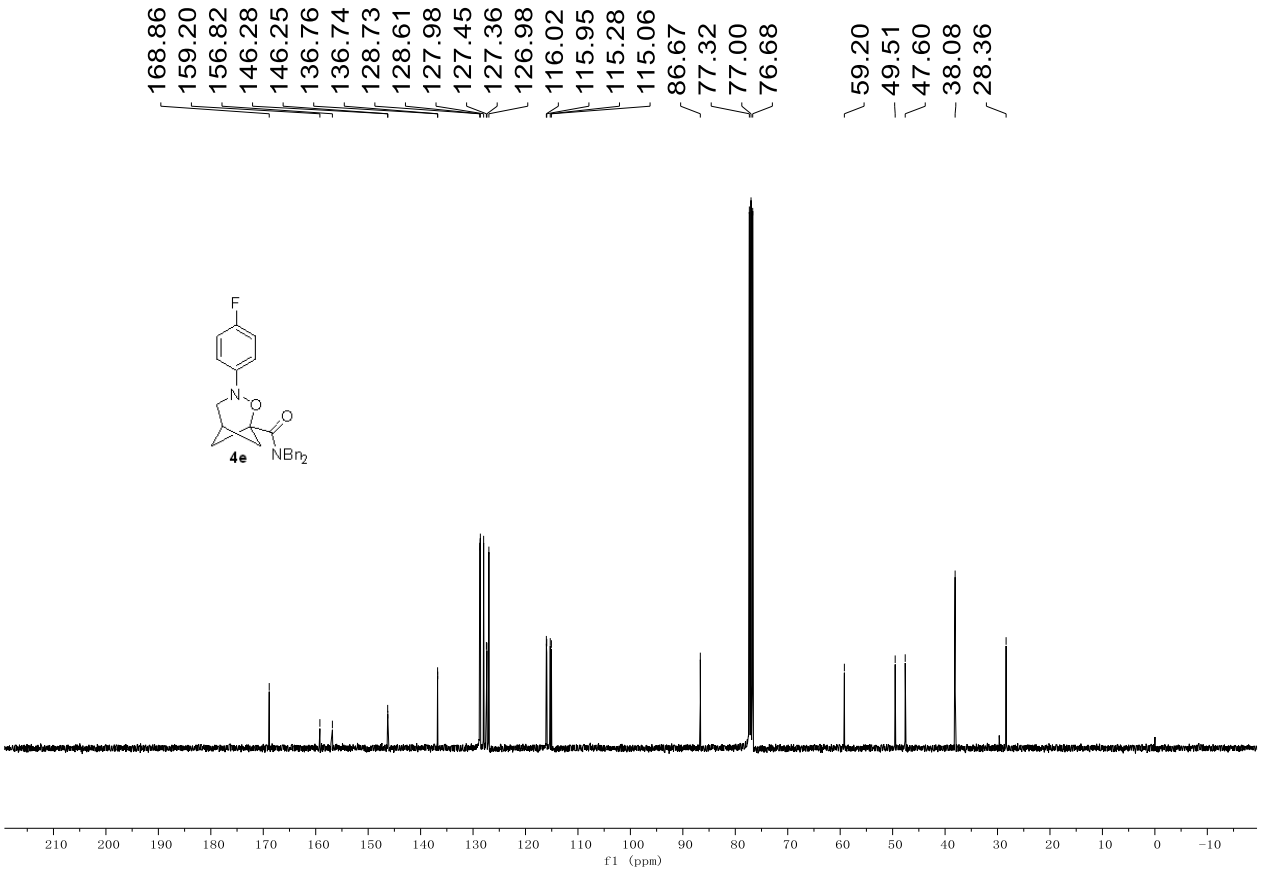


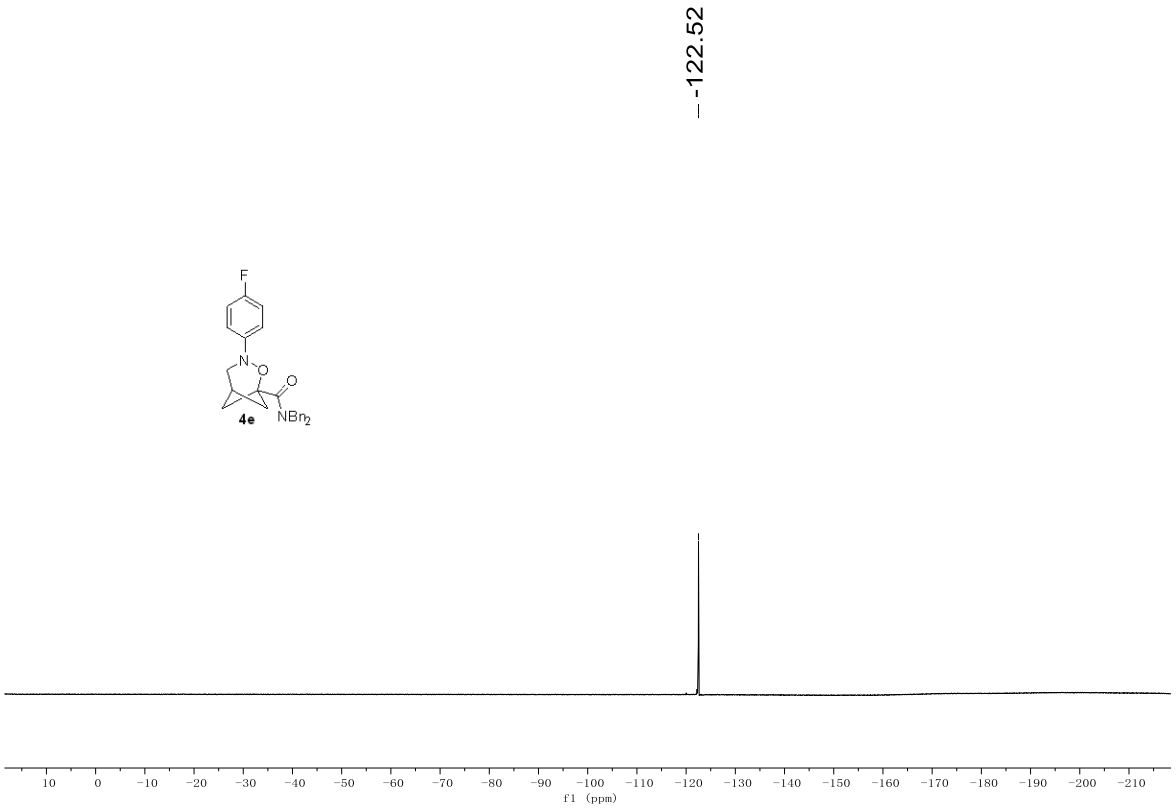
***N*-methoxy-*N*-methyl-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide. (4d)**



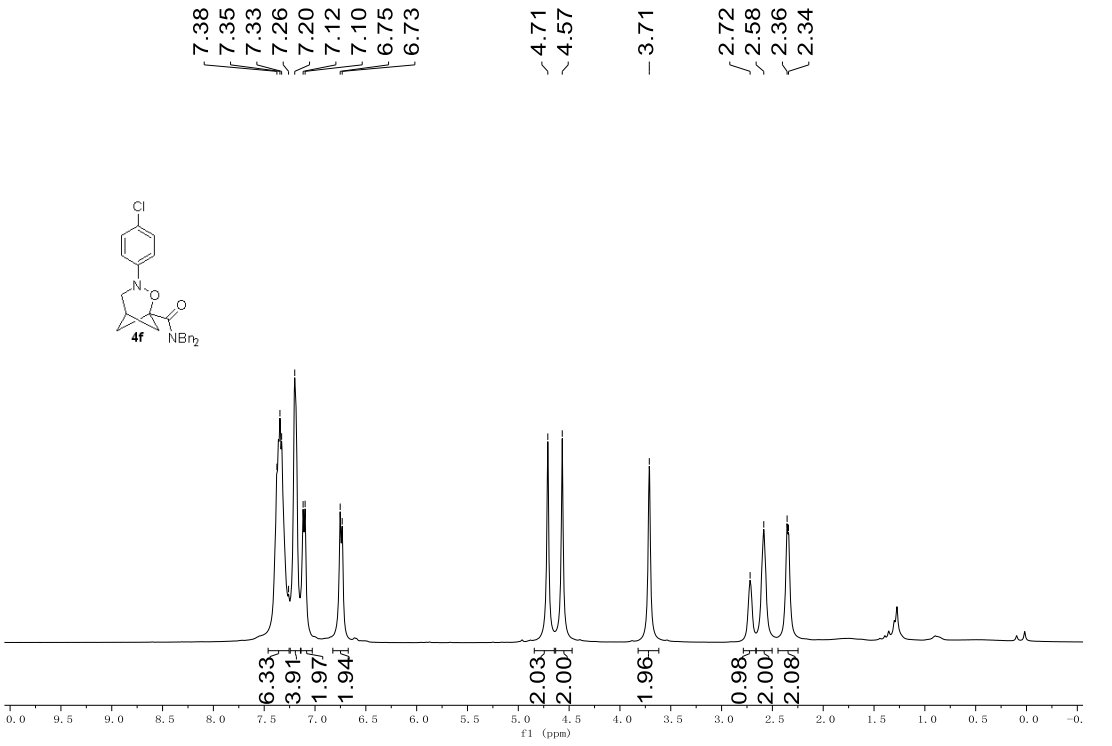
***N,N*-dibenzyl-3-(4-fluorophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide.(4e)**

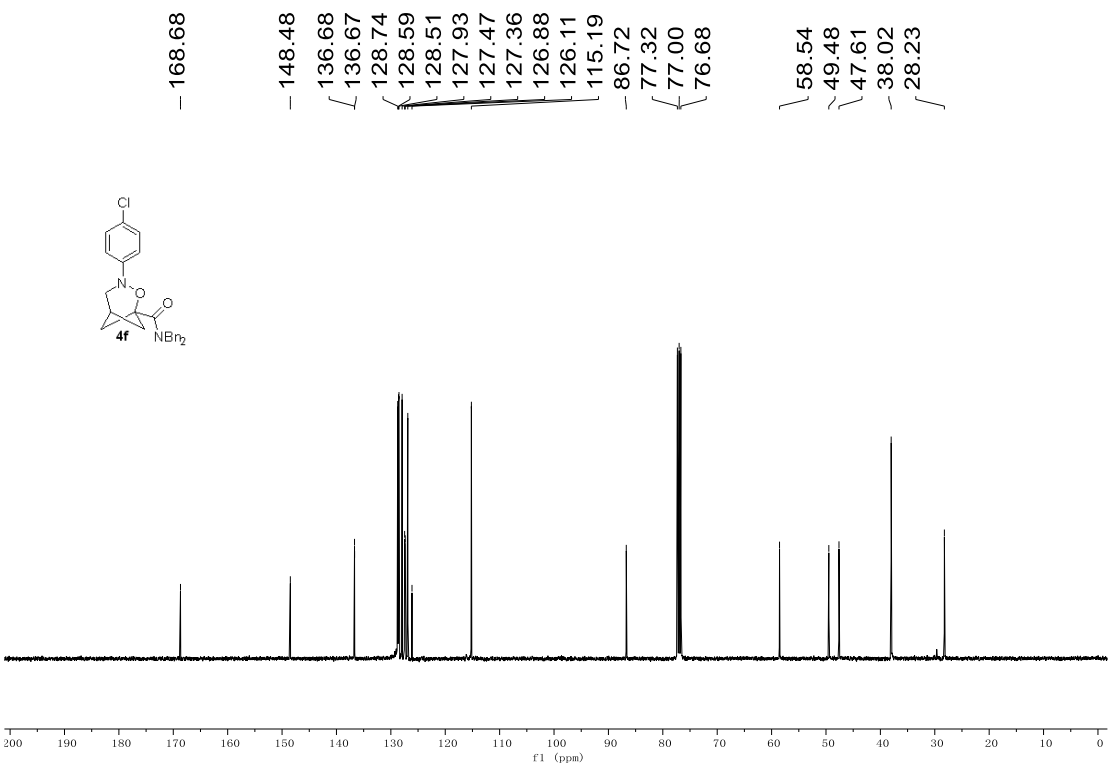



168.86
159.20
156.82
146.28
146.25
136.76
136.74
128.73
128.61
127.98
127.45
127.36
126.98
116.02
115.95
115.28
115.06
86.67
77.32
77.00
76.68
59.20
49.51
47.60
38.08
28.36
F
N
O
O
NBn2
4e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

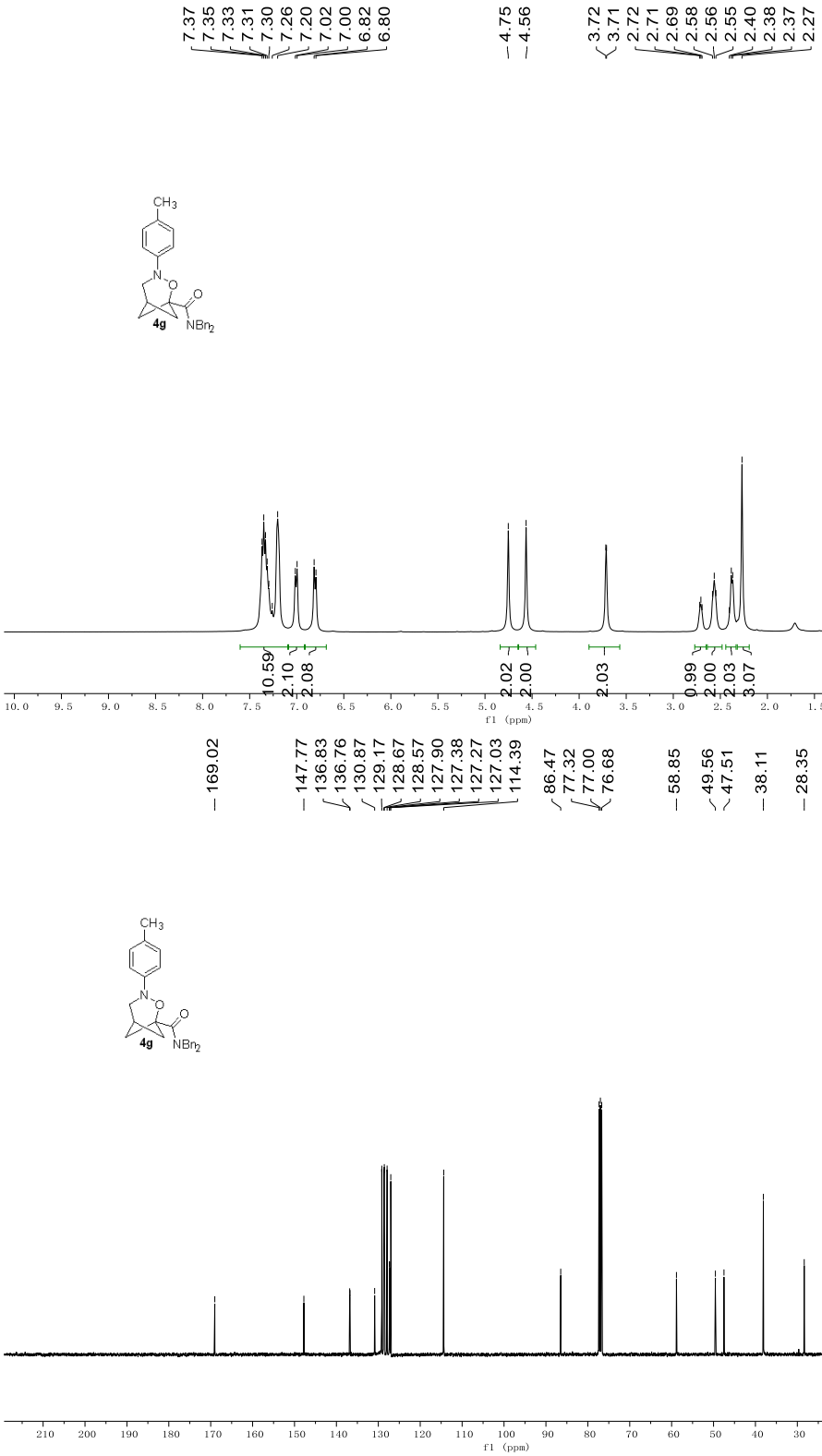

-122.52
F
N
O
O
NBn2
4e
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

***N*,*N*-dibenzyl-3-(4-chlorophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide.(4f)**

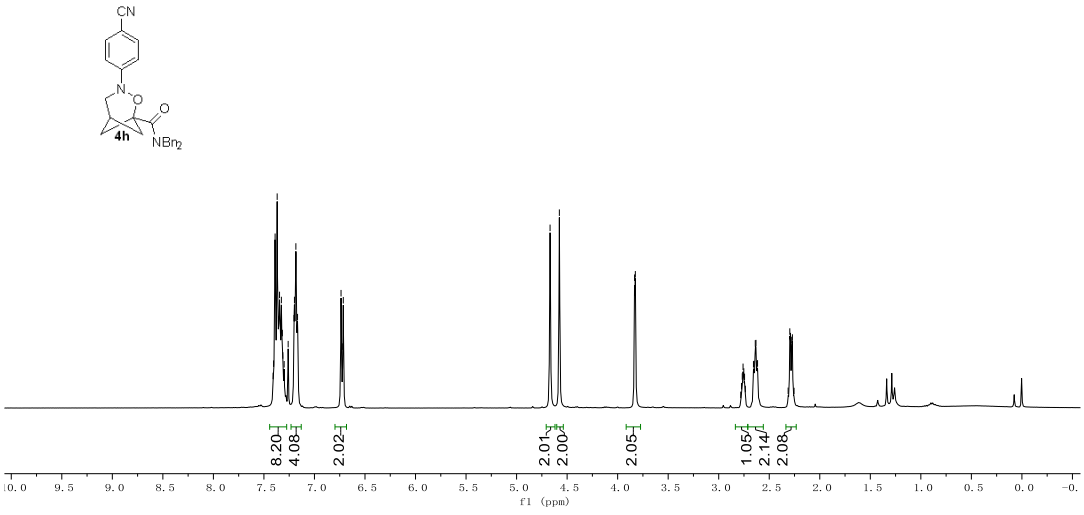


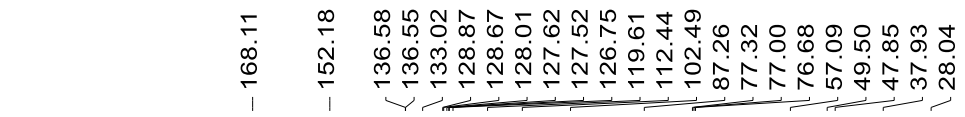


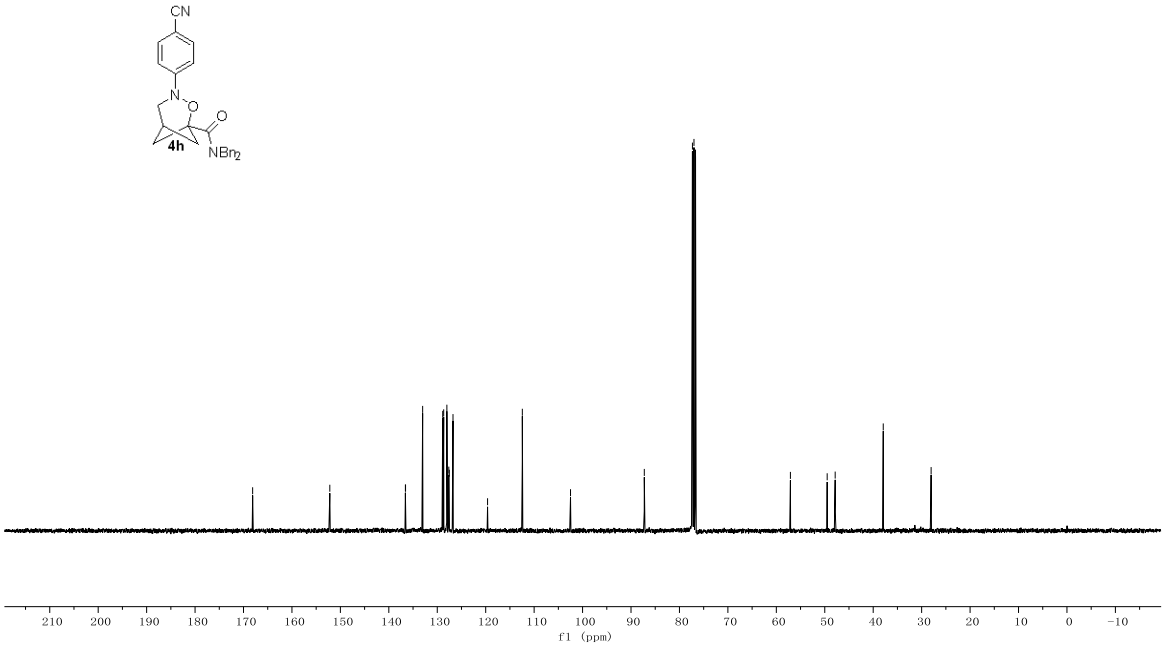
***N,N*-dibenzyl-3-(p-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide.(4g)**



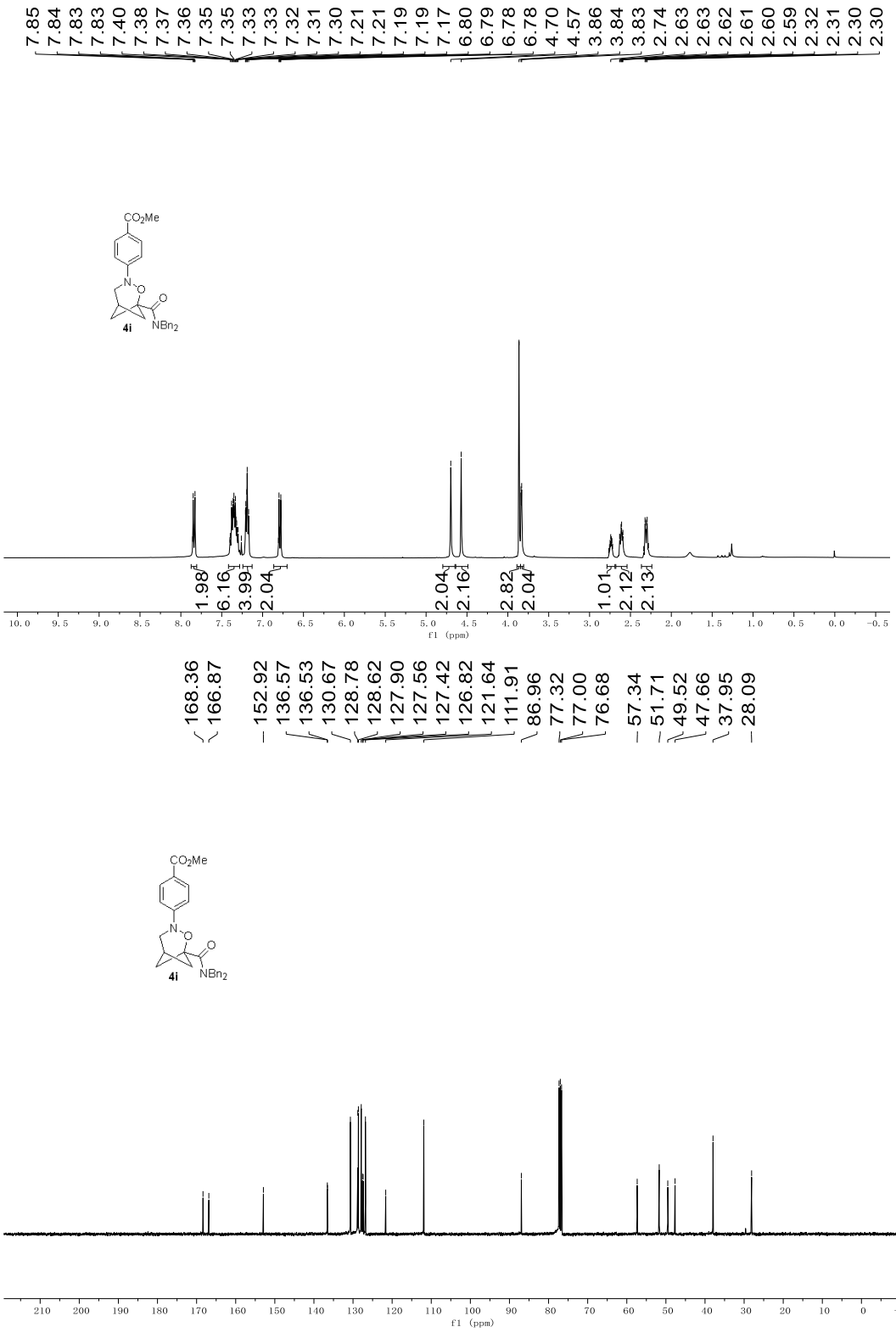
***N,N*-dibenzyl-3-(4-cyanophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide.(4h)**



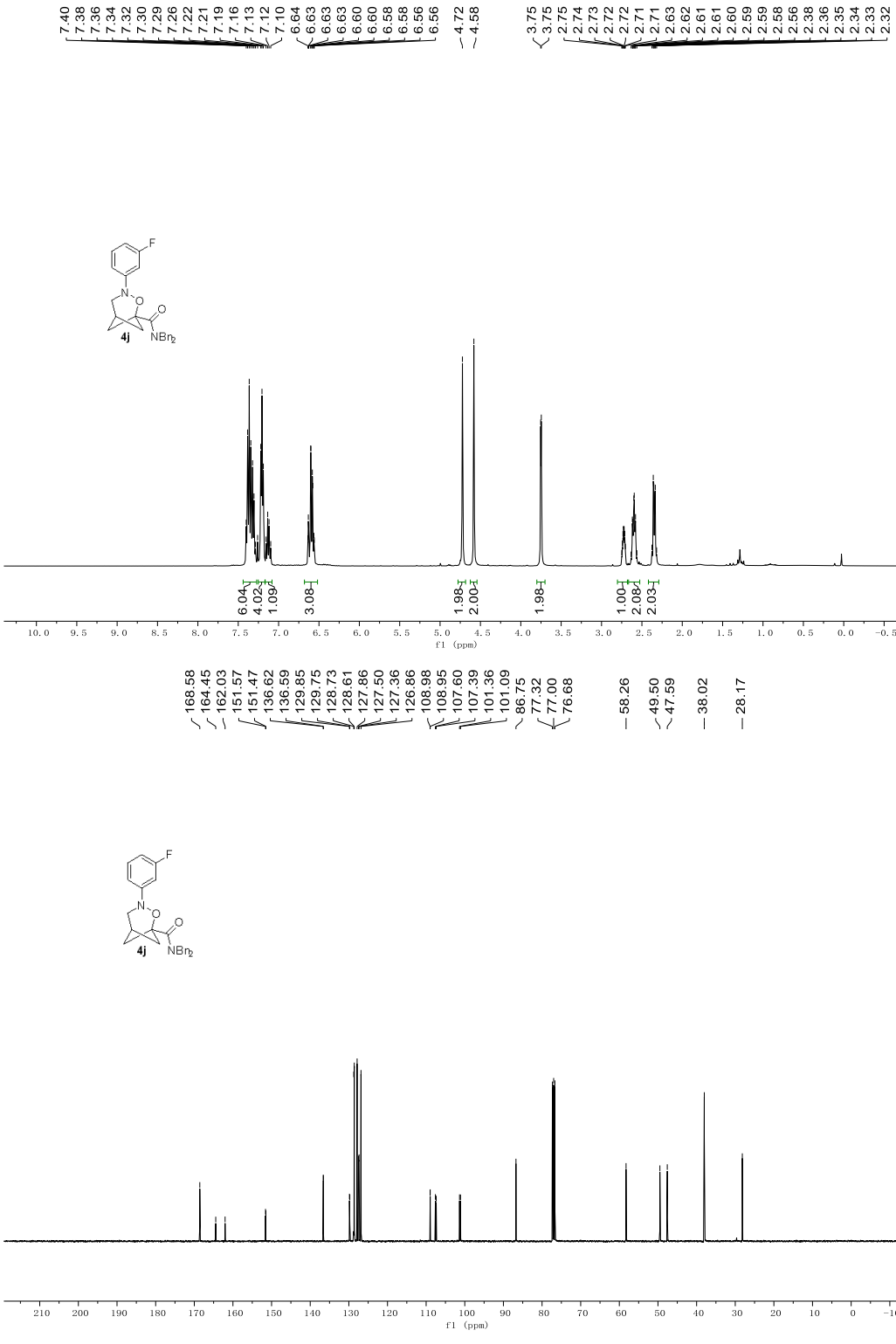


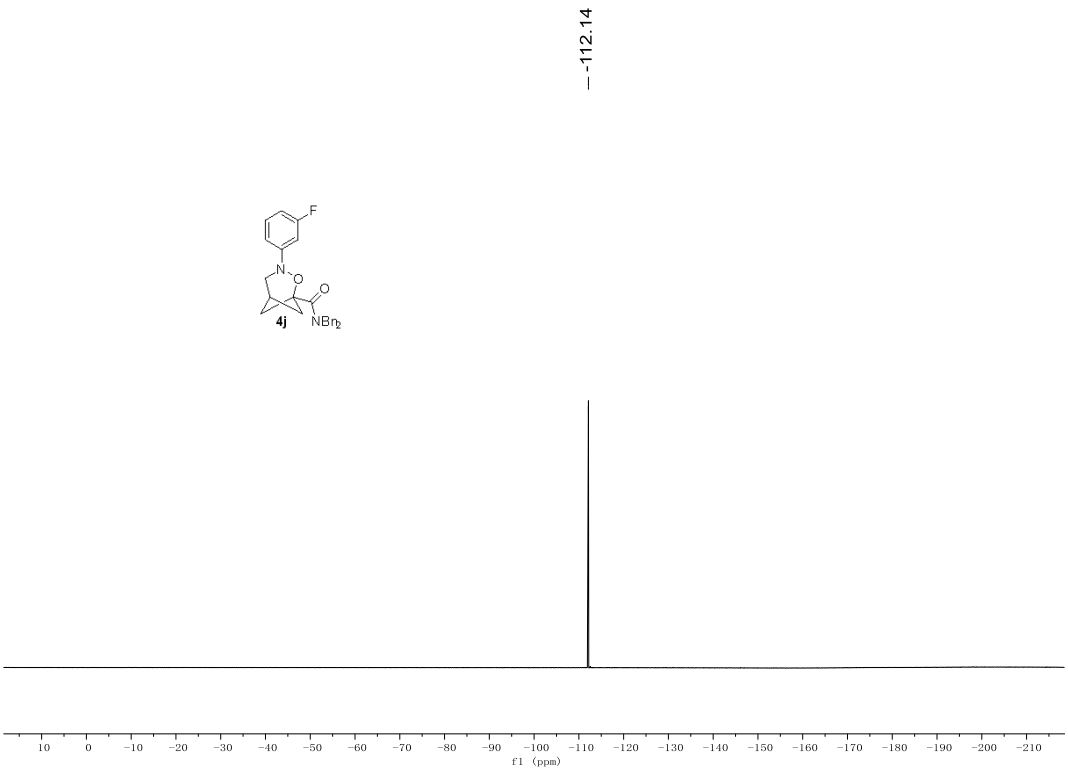


methyl 4-(1-(dibenzylcarbamoyl)-2-oxa-3-azabicyclo[3.1.1]heptan-3-yl)benzoate.(4i)

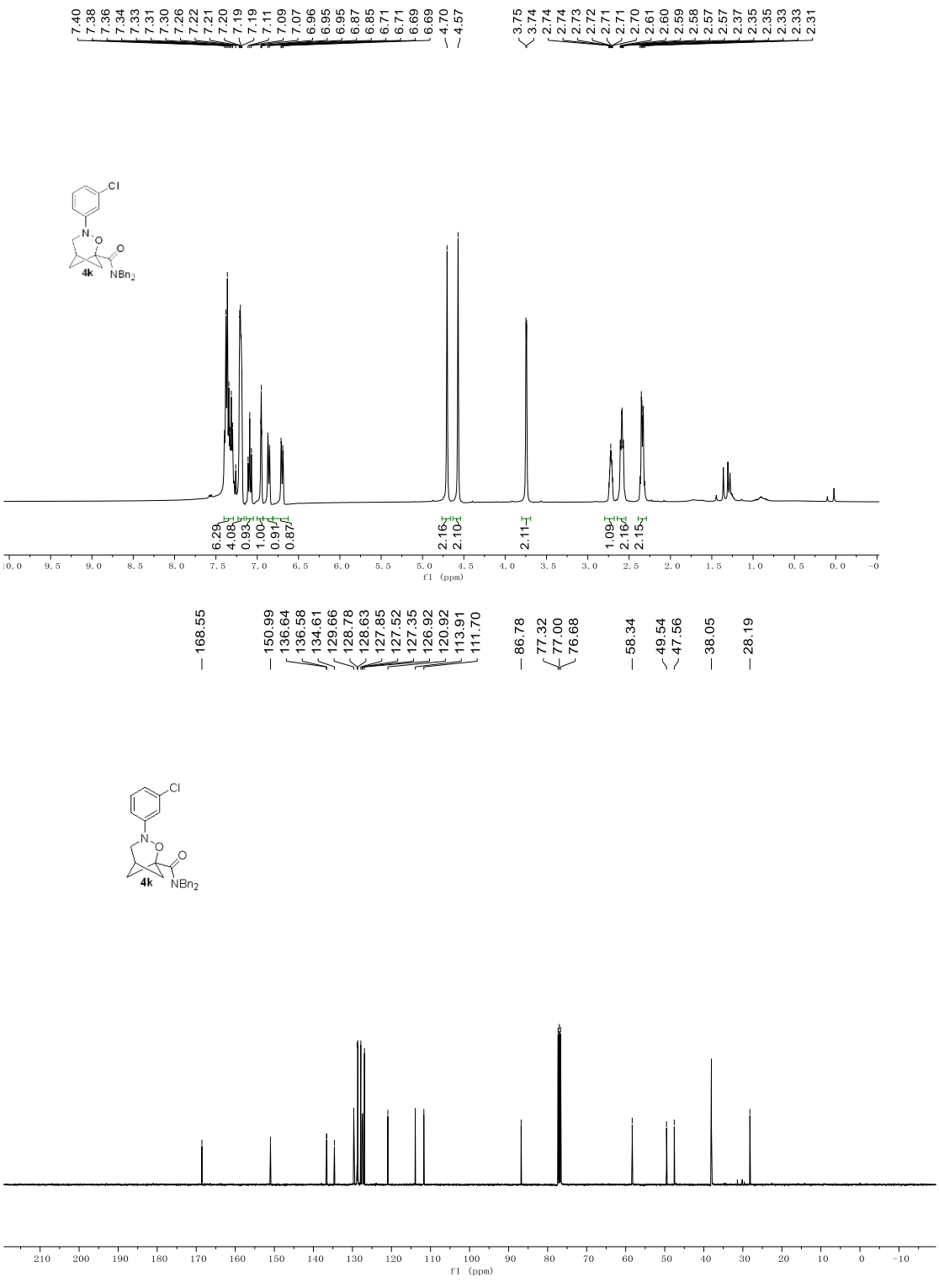


***N,N*-dibenzyl-3-(3-fluorophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide. (4j)**

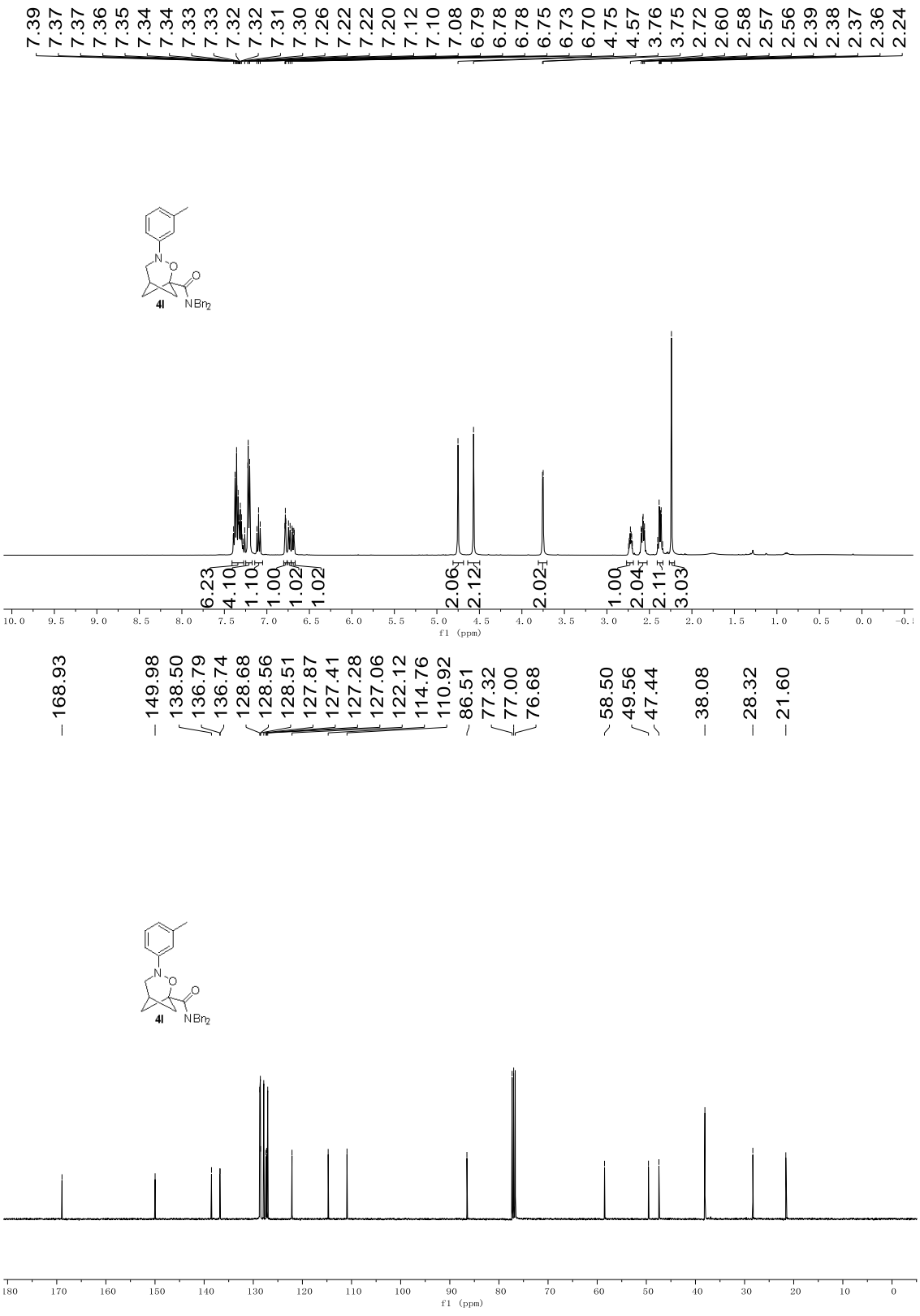



-112.14
F
N
O
O
NBn2
4j
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

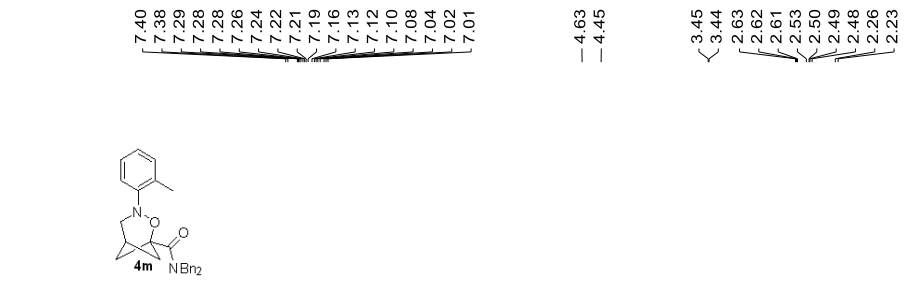
***N*,*N*-dibenzyl-3-(3-chlorophenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide.(4k)**

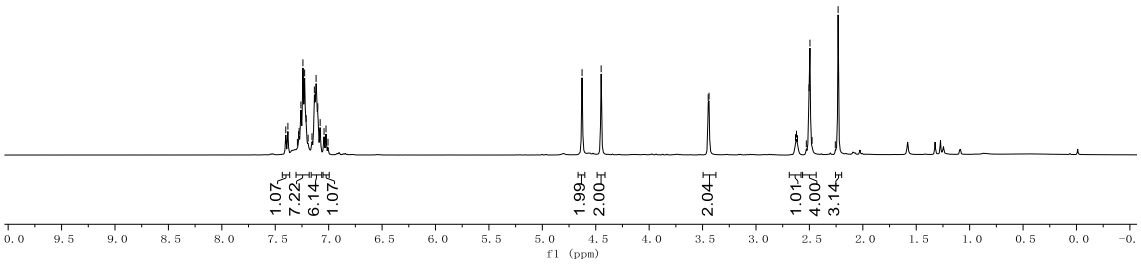


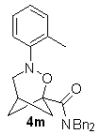
***N,N*-dibenzyl-3-(m-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide.(4l)**



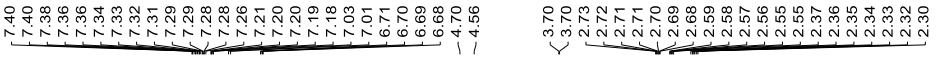
***N,N*-dibenzyl-3-(o-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide. (4m)**

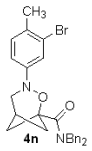


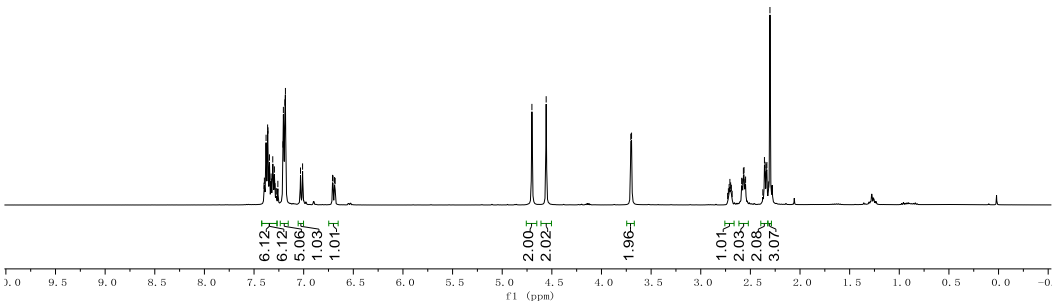


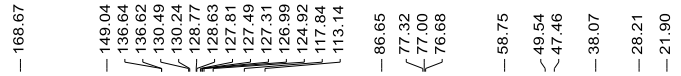


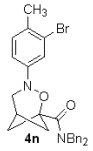
***N,N*-dibenzyl-3-(3-bromo-4-methylphenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide.(4n)**

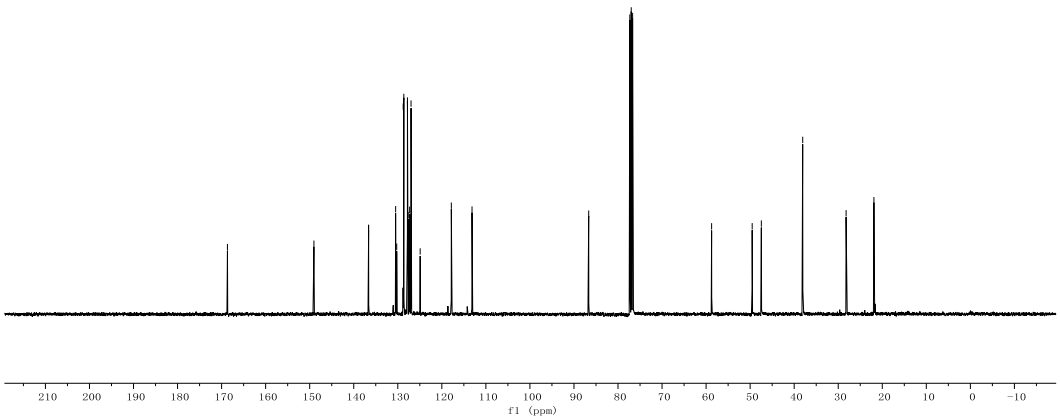




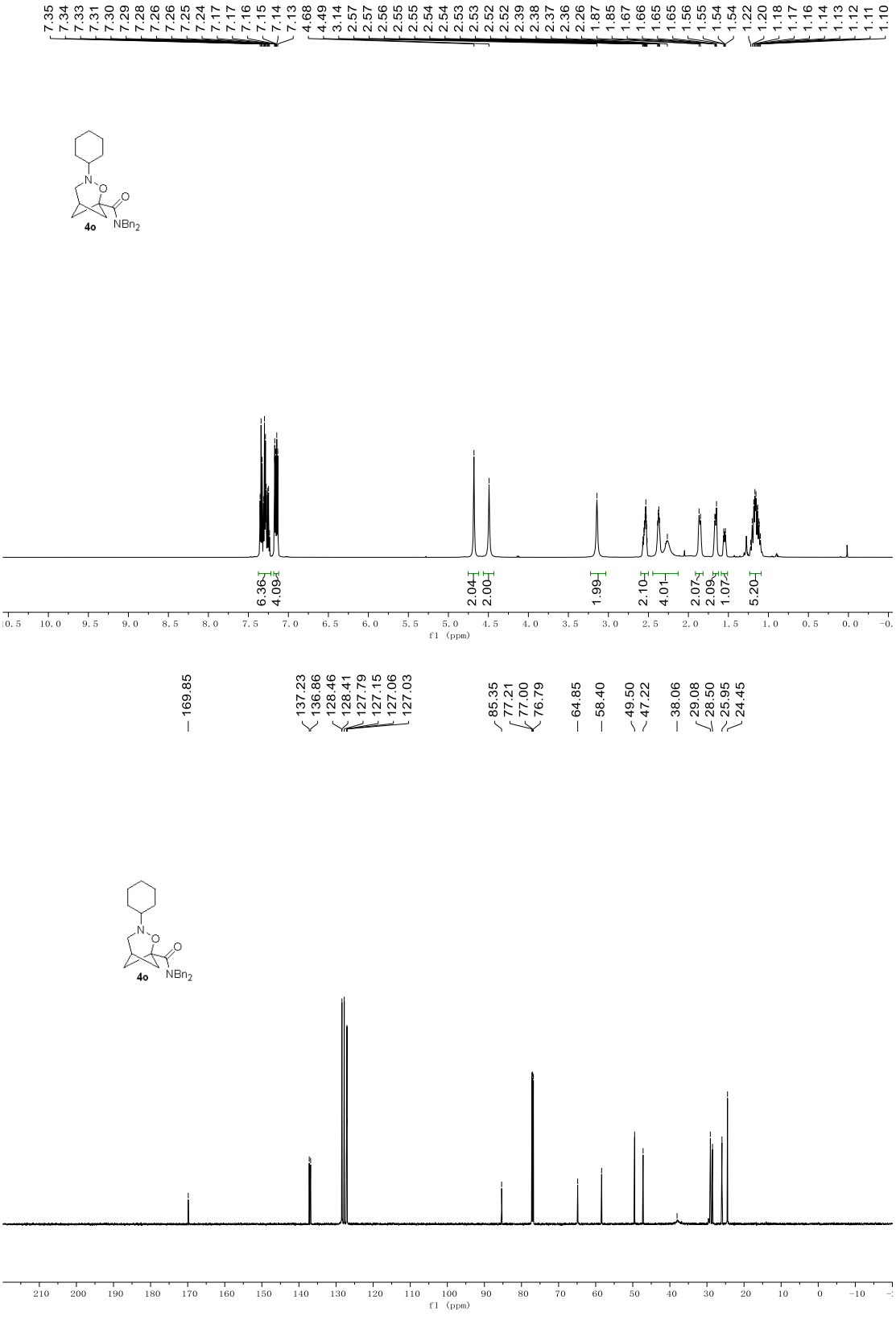




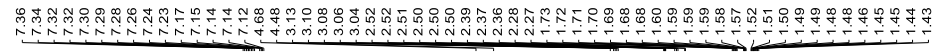


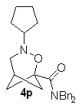


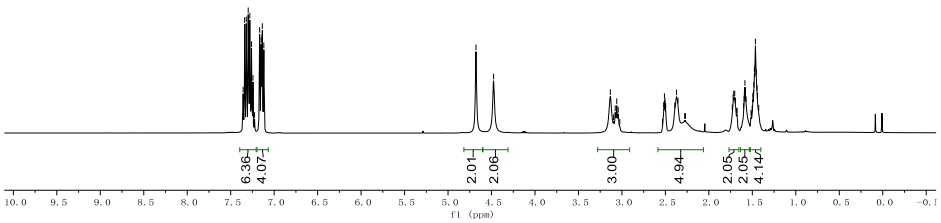
***N,N*-dibenzyl-3-cyclohexyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide (4o).**

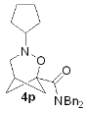


***N,N*-dibenzyl-3-cyclopentyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxamide(4p)**

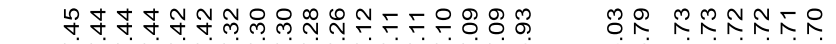


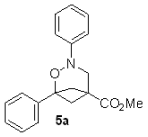


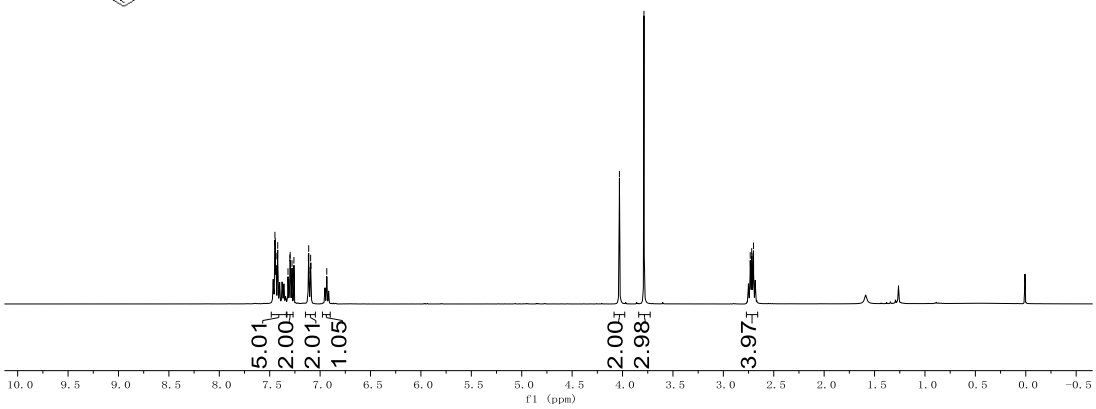


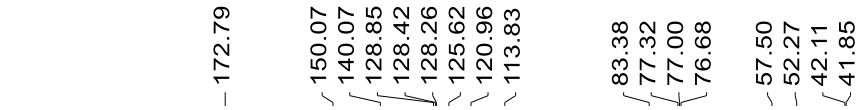


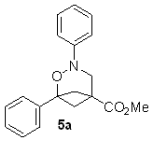
Methyl 3,5-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate.(5a)

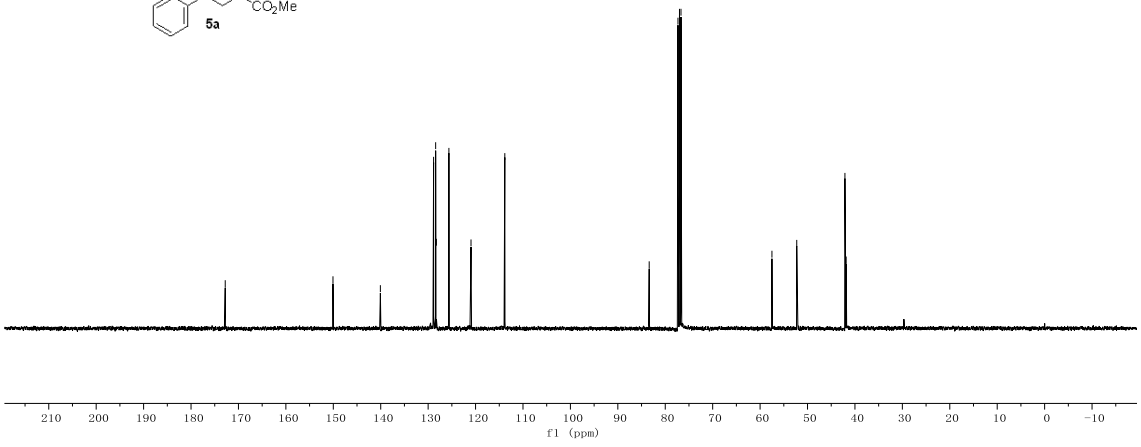




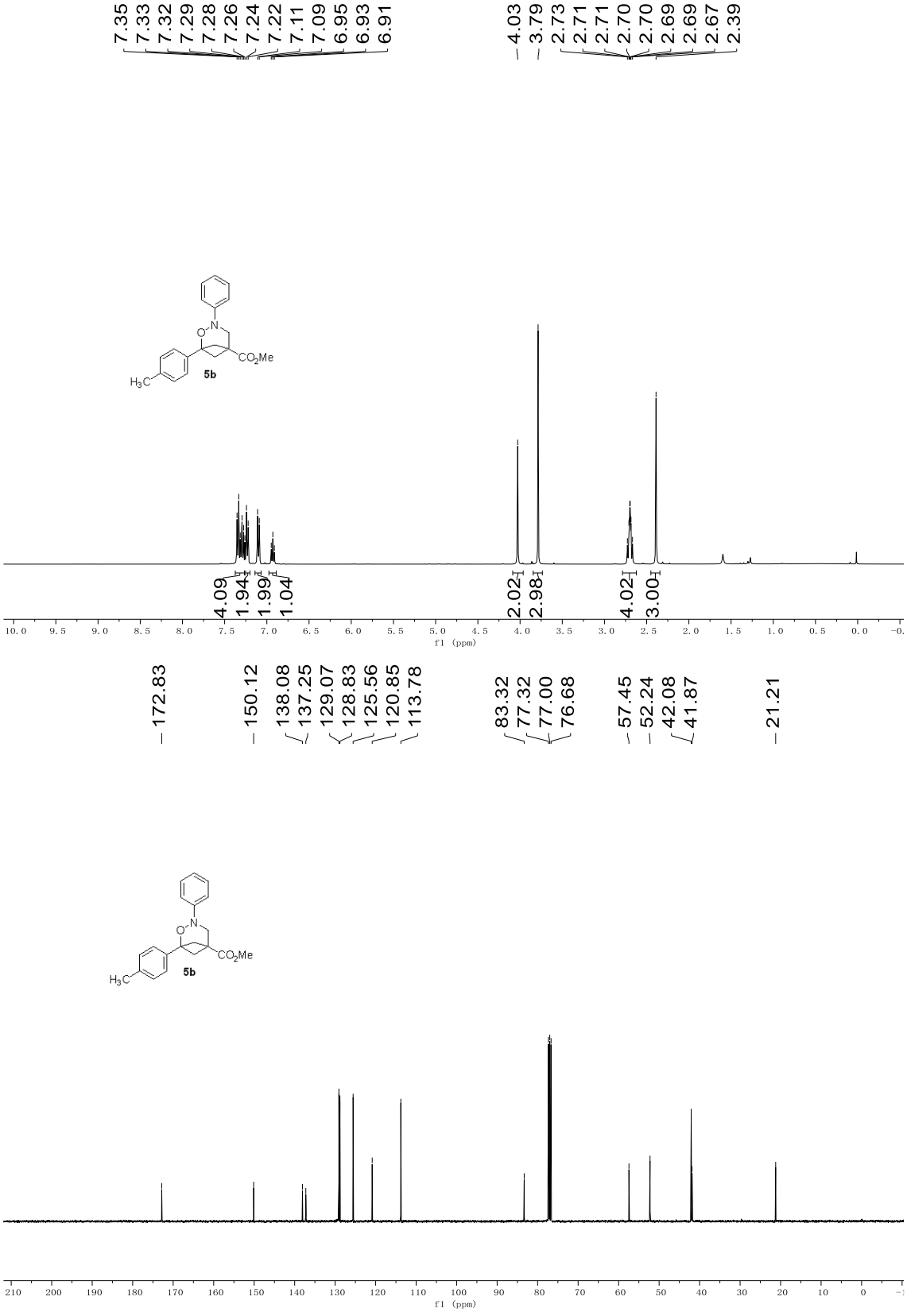




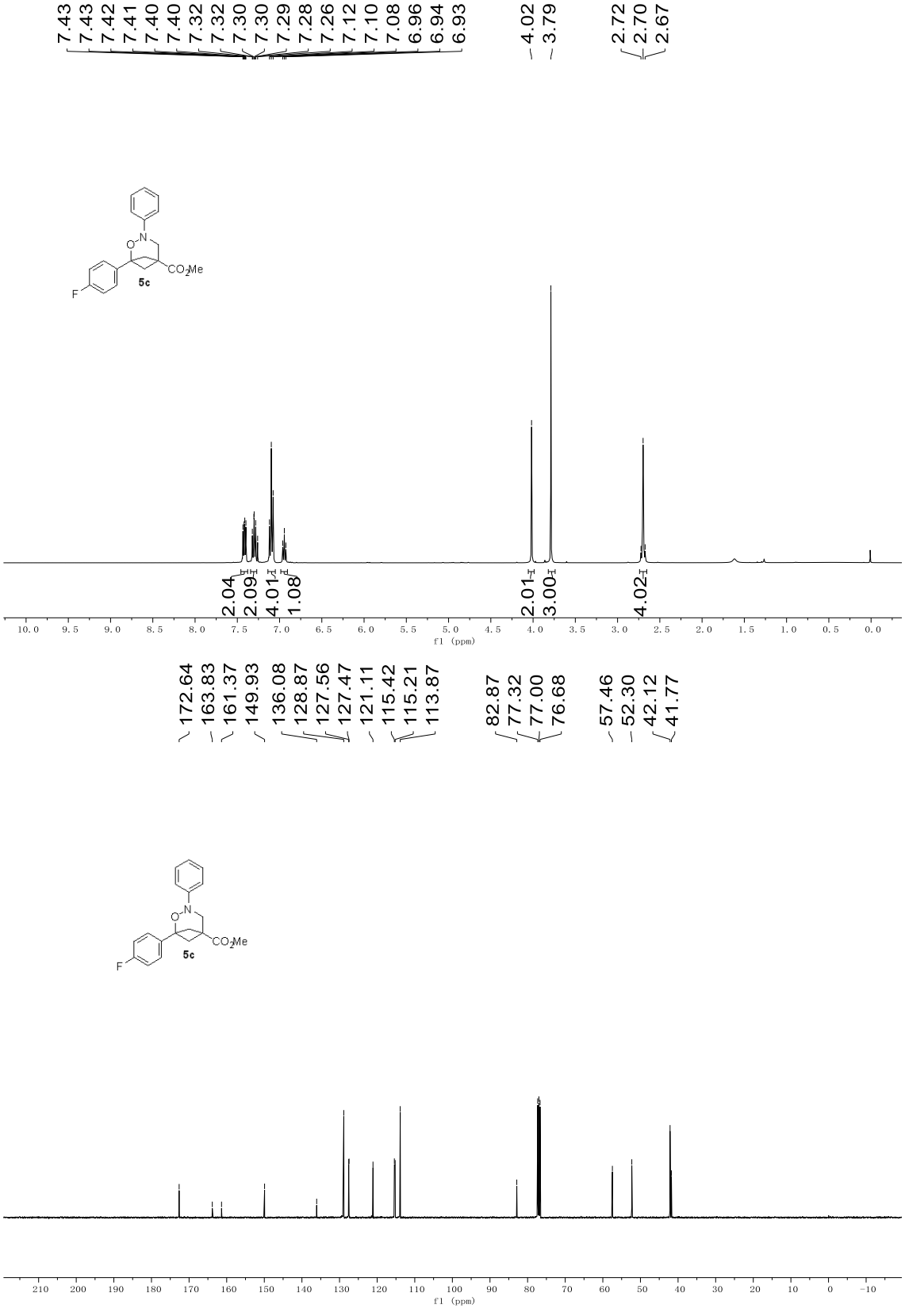


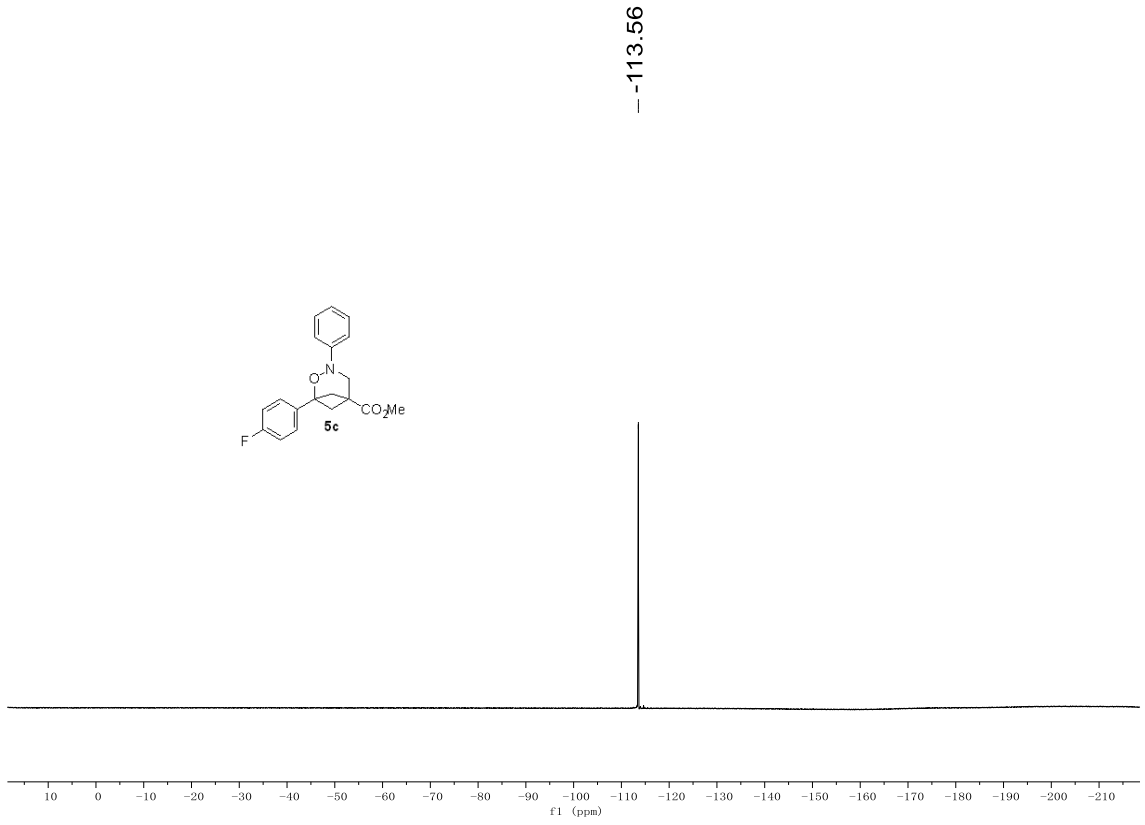


Methyl 3-phenyl-5-(p-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate.(5b)

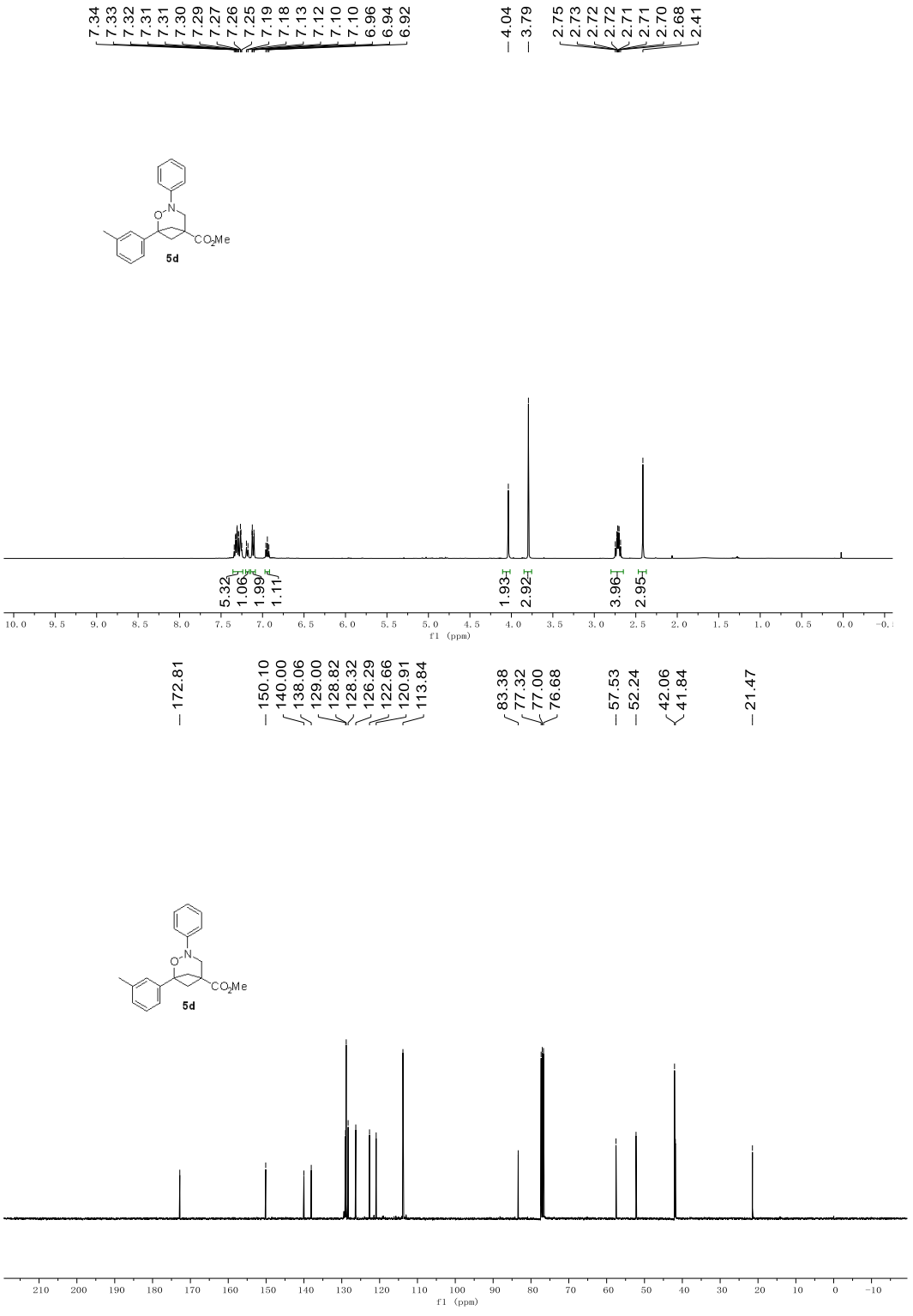


Methyl 5-(4-fluorophenyl)-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate.(5c)

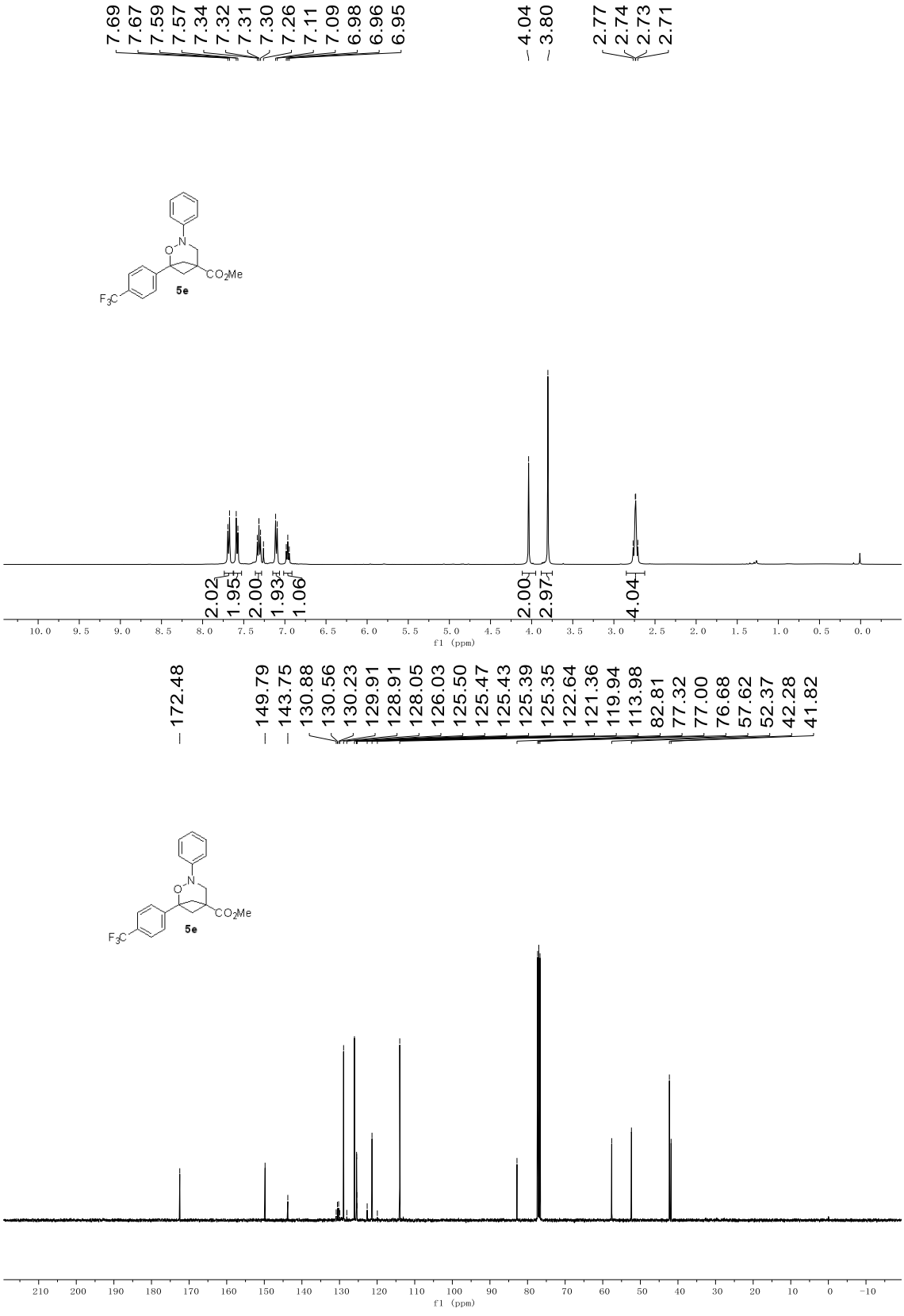


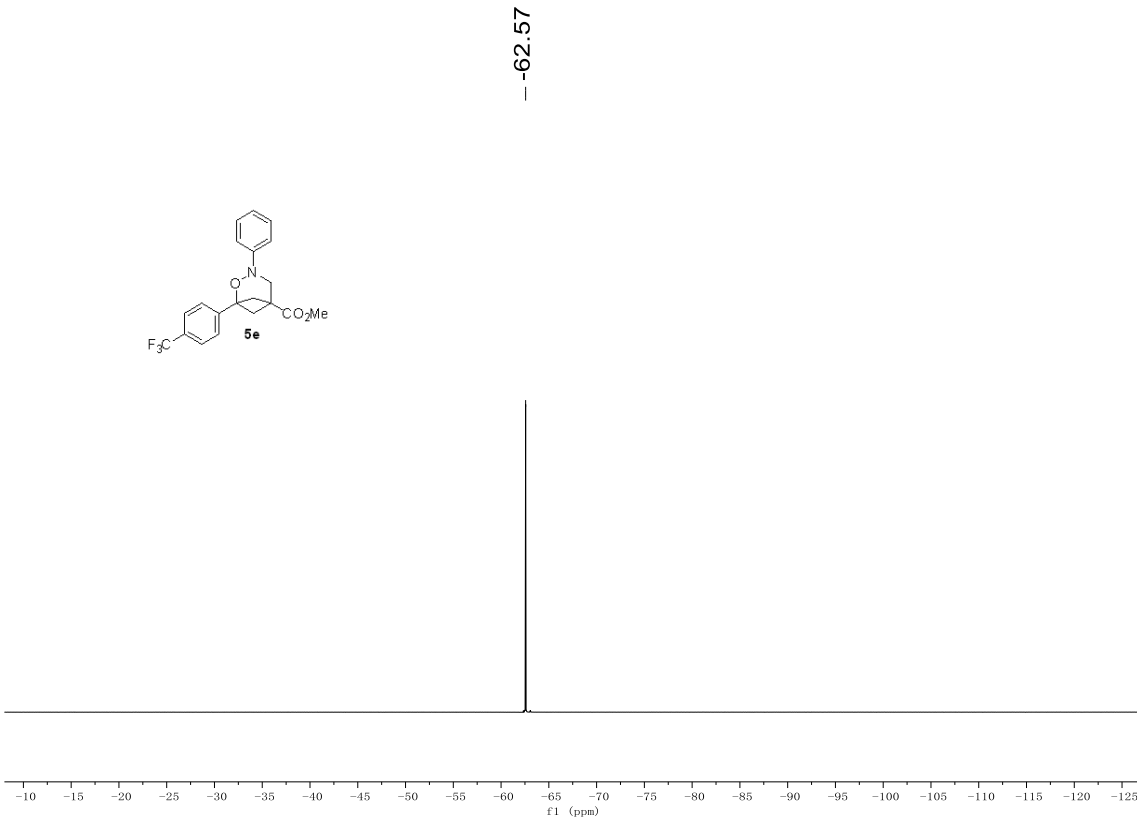

-113.56
O
N
CO2Me
F
5c
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

Methyl 3-phenyl-1-(m-tolyl)-2-oxa-3-azabicyclo[3.1.1]heptane-5-carboxylate (5d)

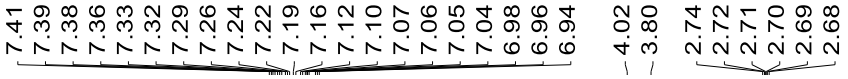


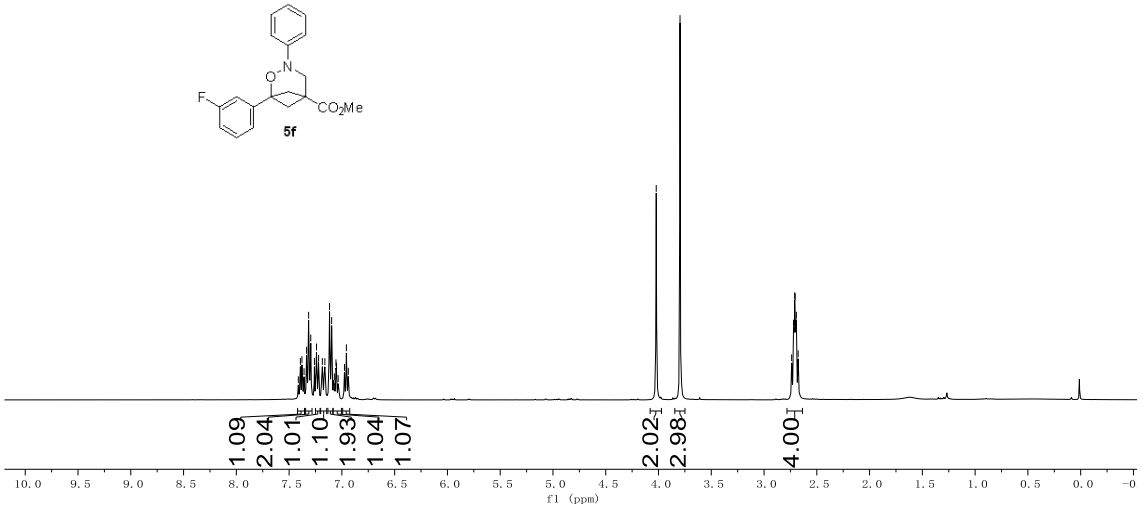
Methyl 3-phenyl-5-(4-(trifluoromethyl)phenyl)-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate.(5e)

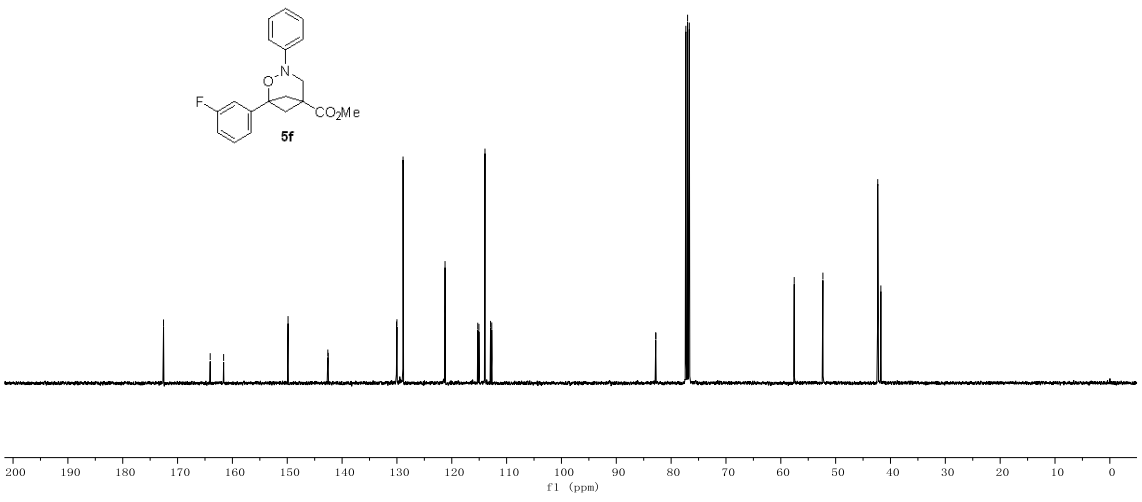


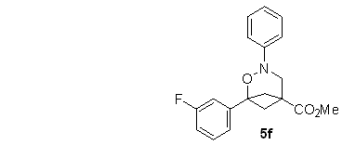

-62.57
N
O
CO2Me
F3C
5e
−10 −15 −20 −25 −30 −35 −40 −45 −50 −55 −60 −65 −70 −75 −80 −85 −90 −95 −100 −105 −110 −115 −120 −125
f1 (ppm)

Methyl 5-(3-fluorophenyl)-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate.(5f)





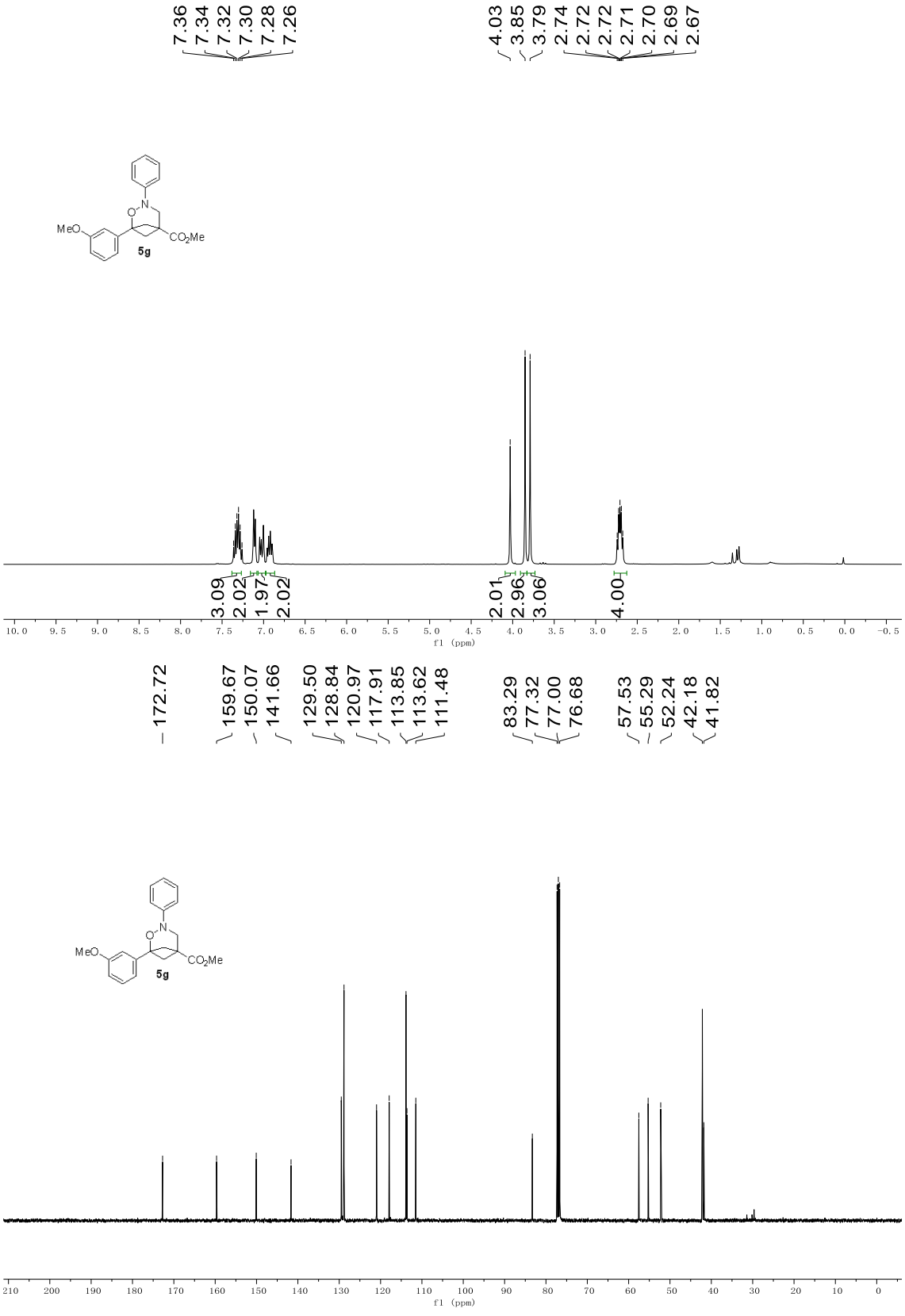



F
O
N
CO2Me

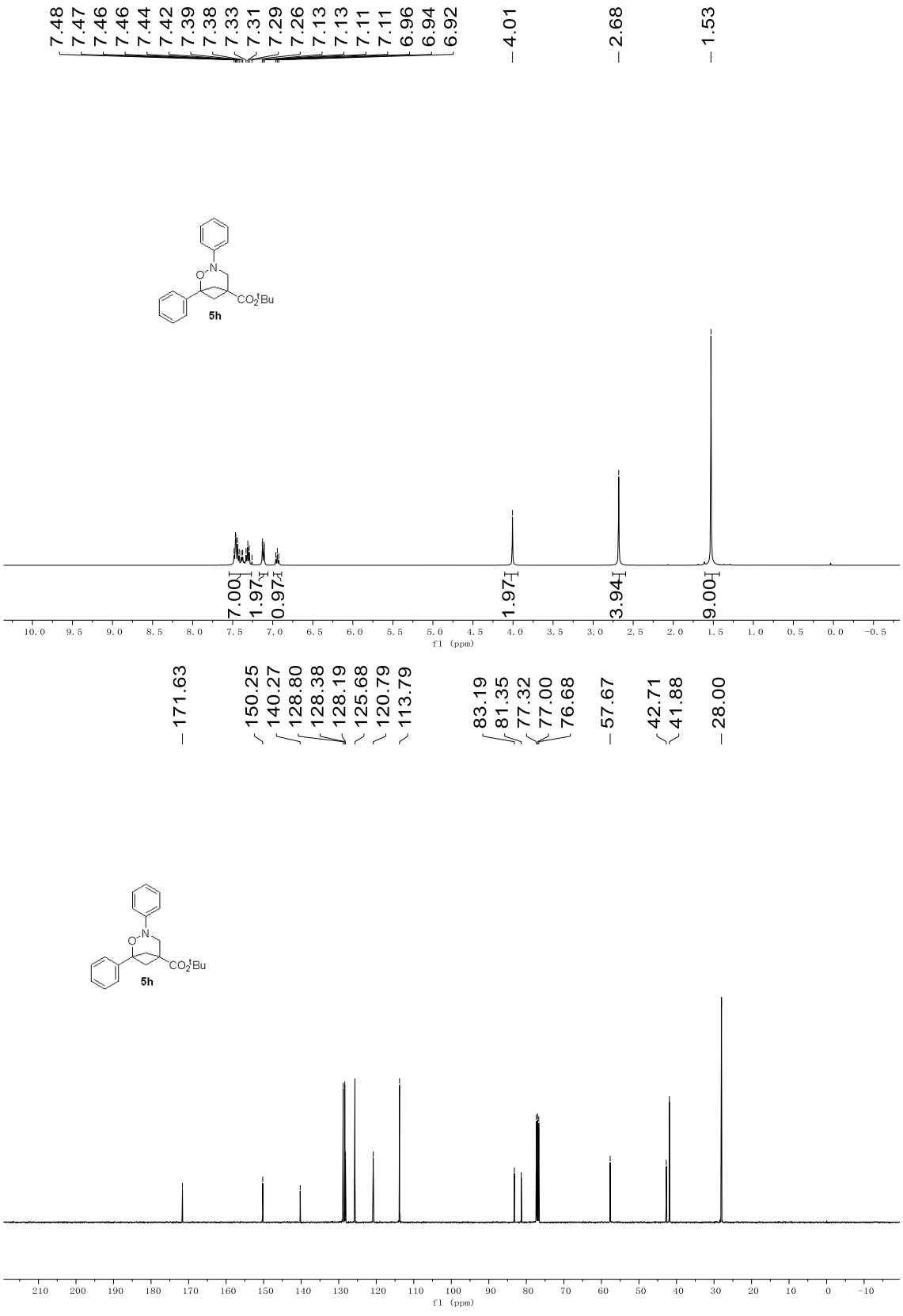
5f

-112.59
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

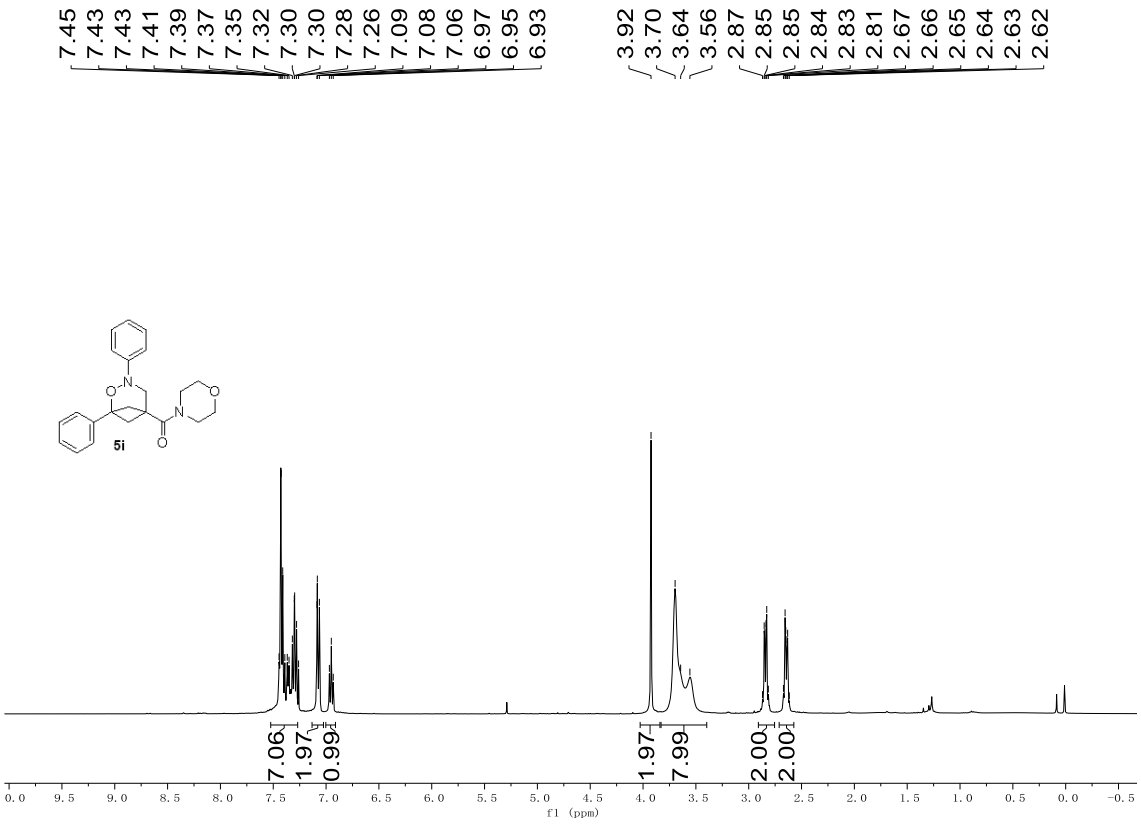
Methyl 5-(3-methoxyphenyl)-3-phenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate.(5g)

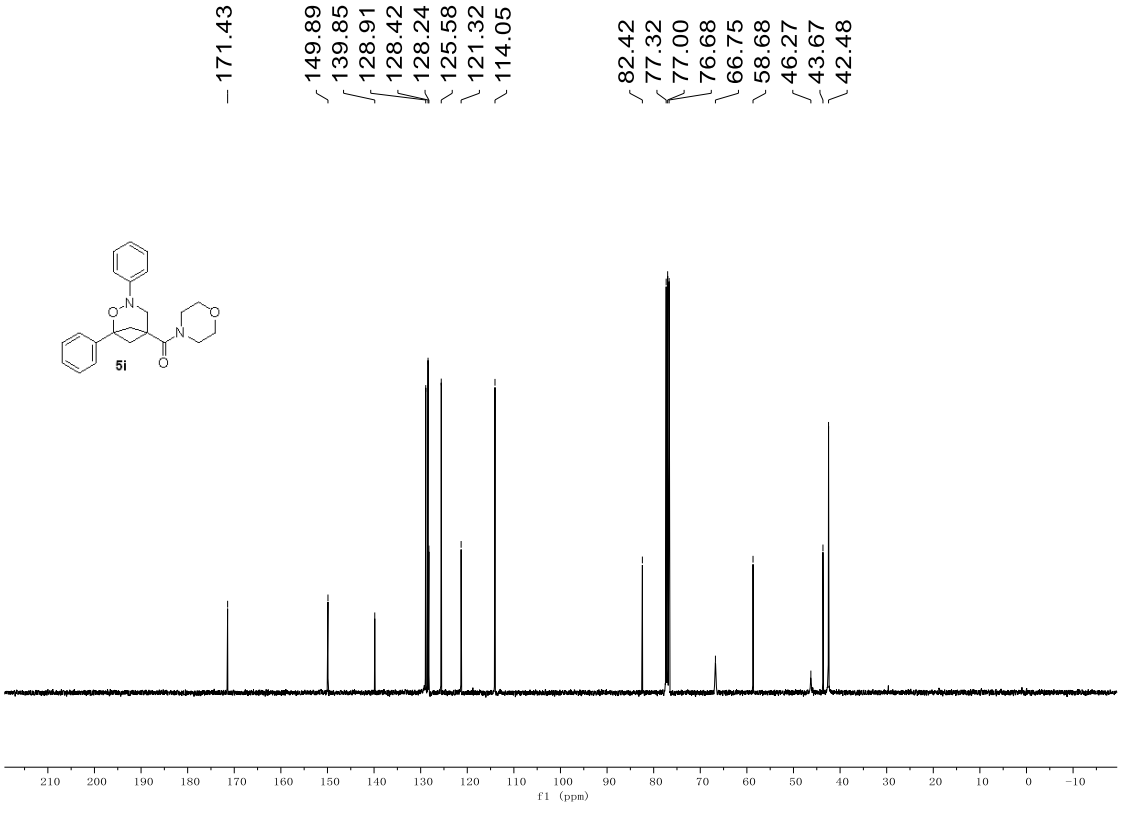


***tert*-butyl 3,5-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate. (5h)**

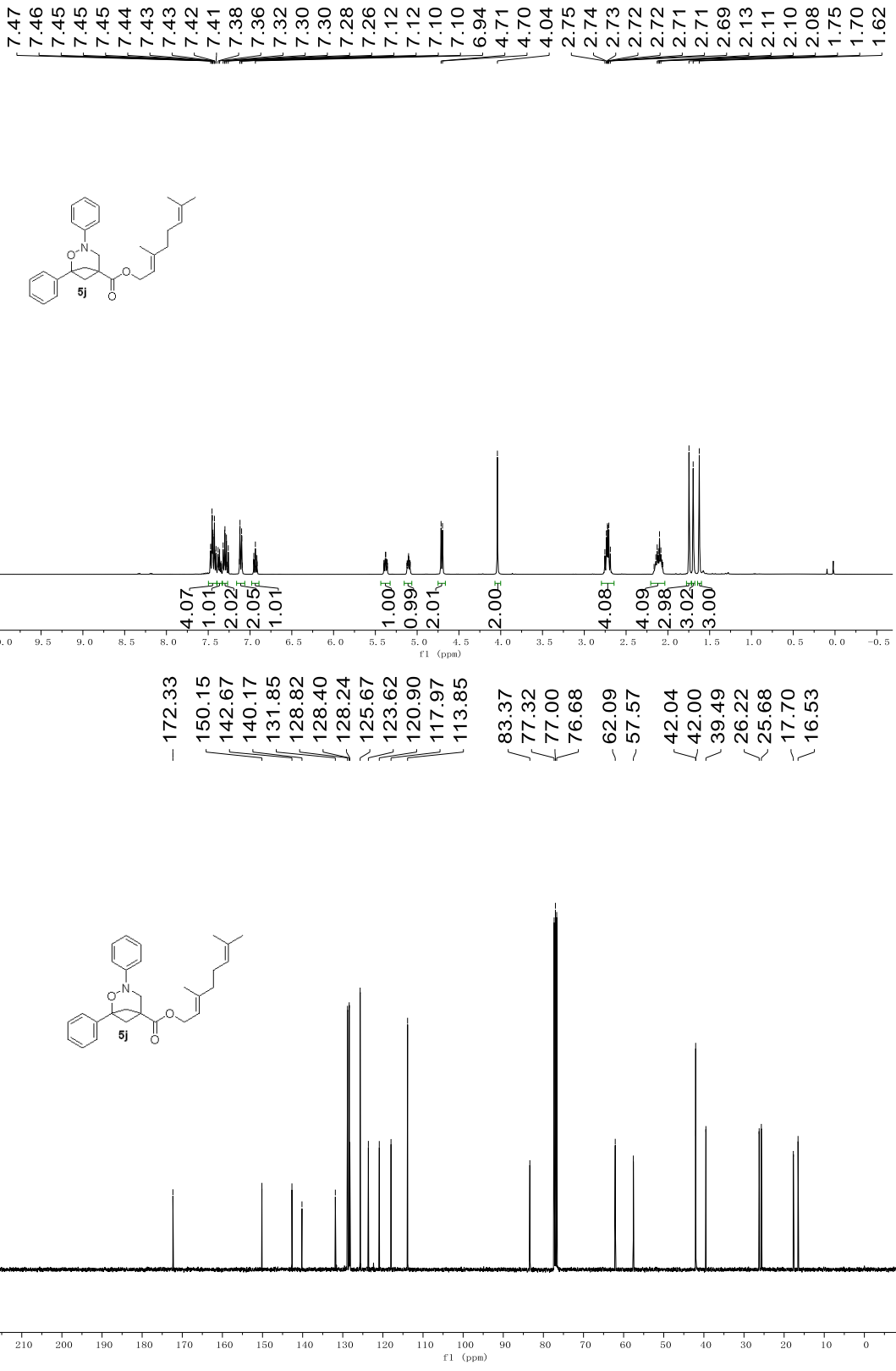


(3,5-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptan-1-yl)(morpholino)methanone. (5i)

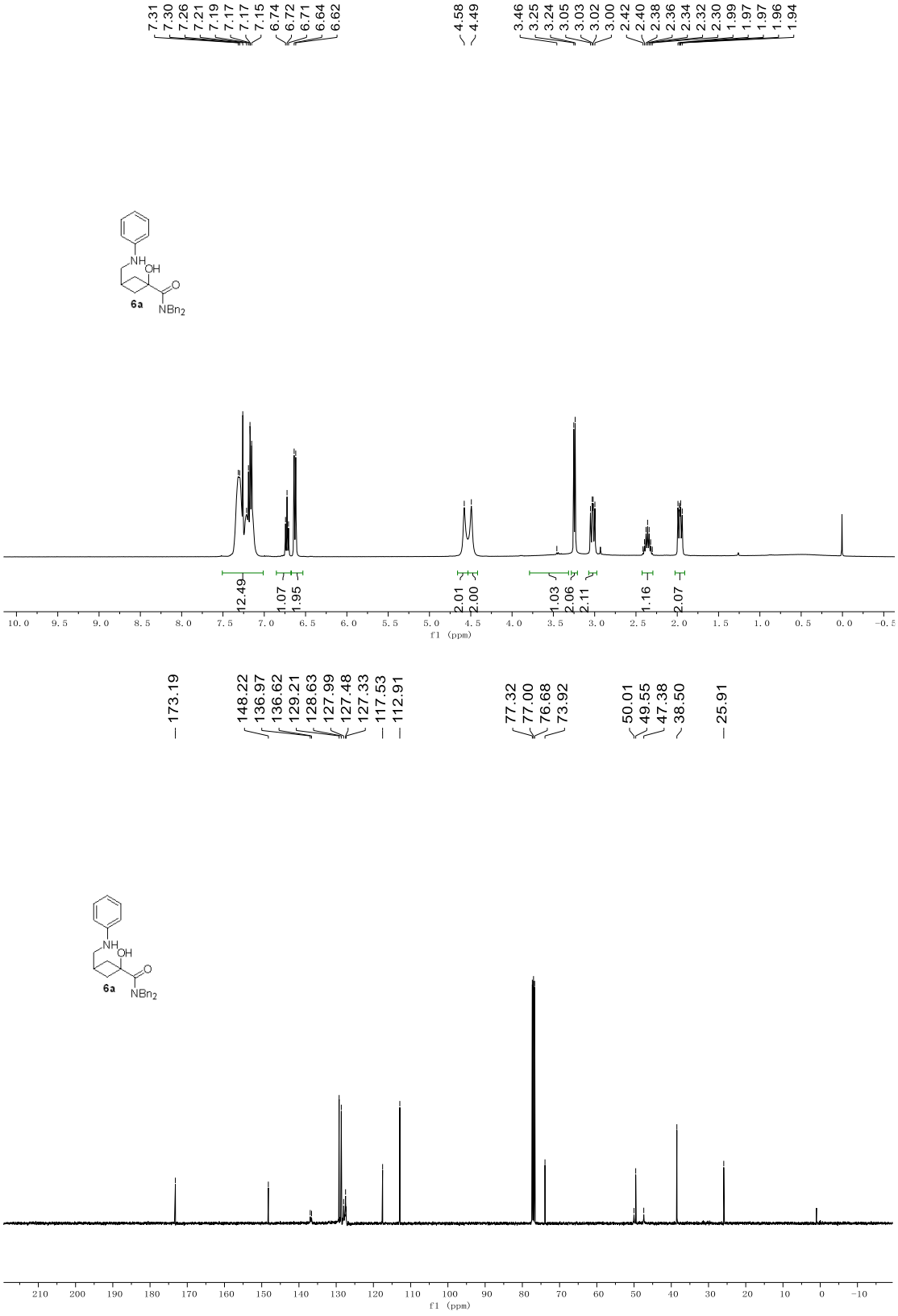




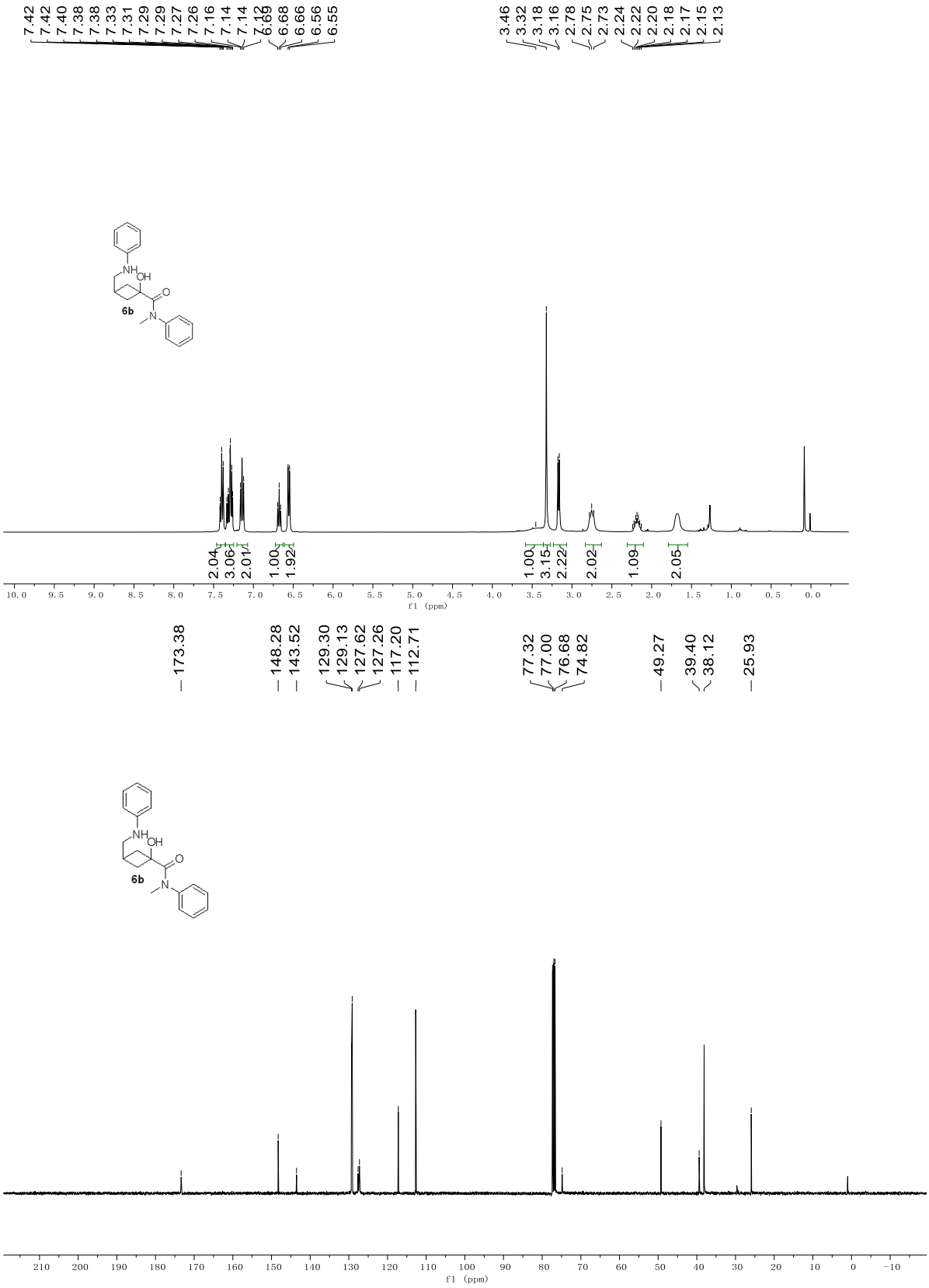
(E)-3,7-dimethylocta-2,6-dien-1-yl 3,5-diphenyl-2-oxa-3-azabicyclo[3.1.1]heptane-1-carboxylate.(5j)



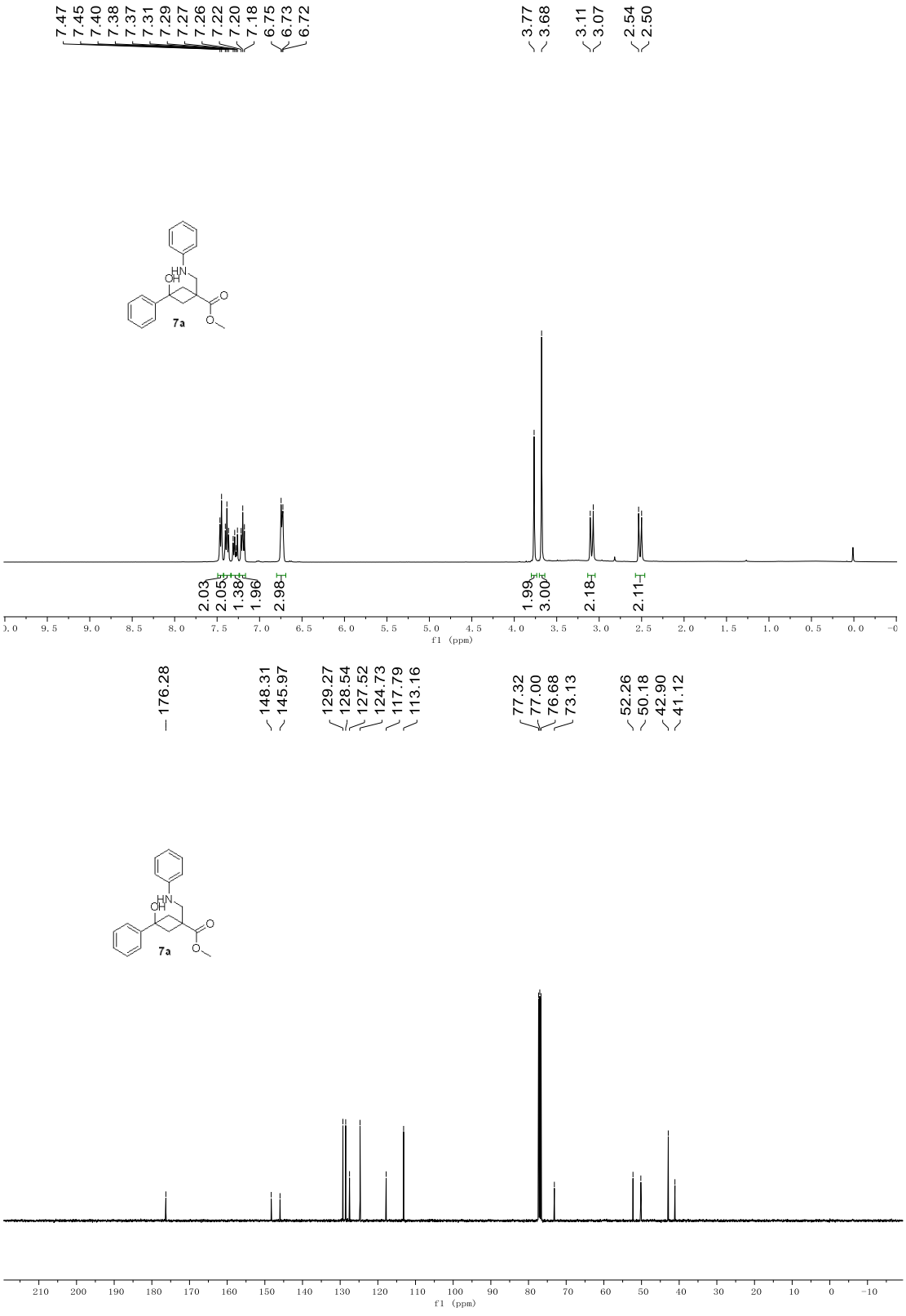
***N*,*N*-dibenzyl-1-hydroxy-3-((phenylamino)methyl)cyclobutane-1-carboxamide.(6a)**



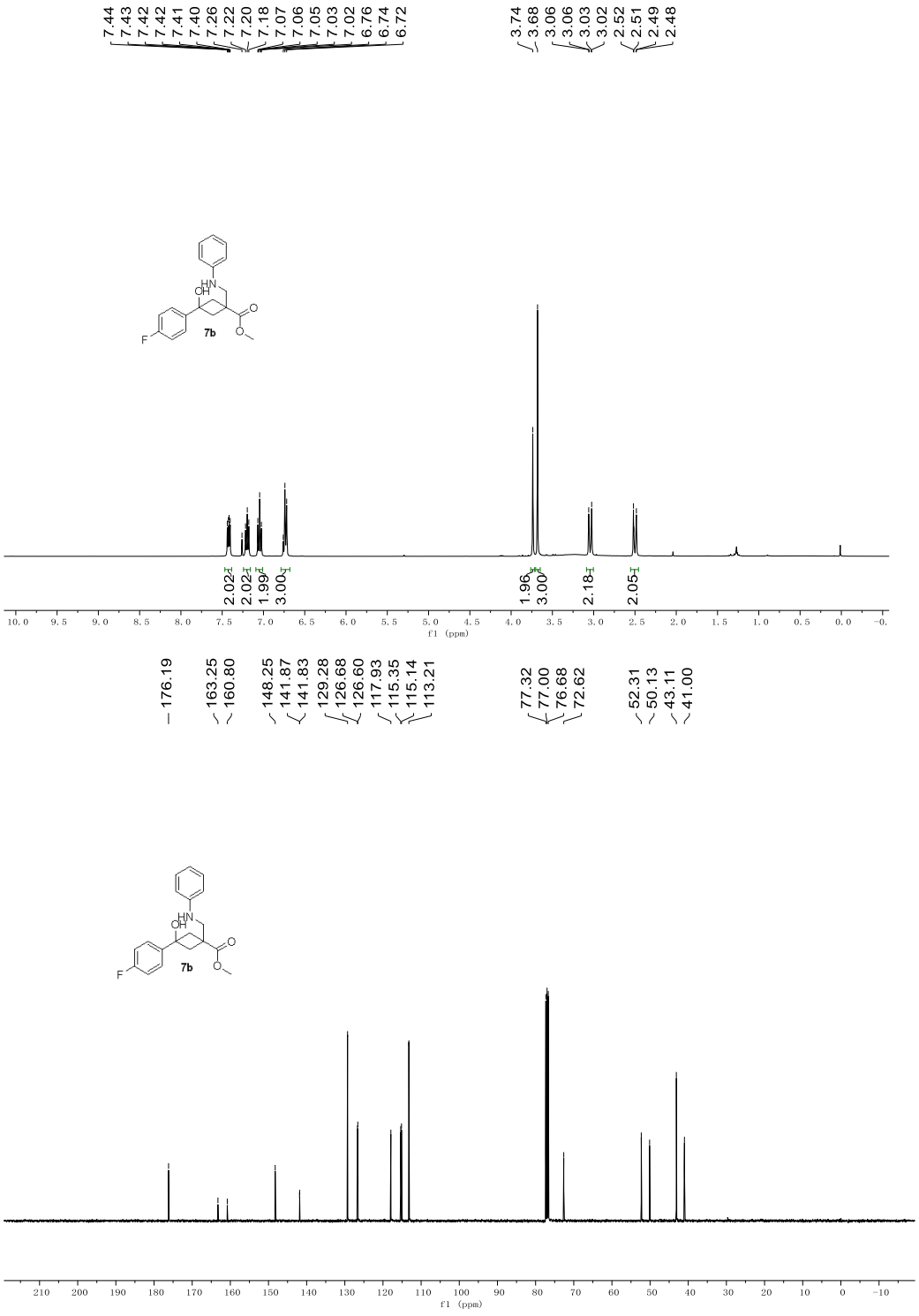
1-Hydroxy-*N*-methyl-*N*-phenyl-3-((phenylamino)methyl)cyclobutane-1-carboxamide.(6b)

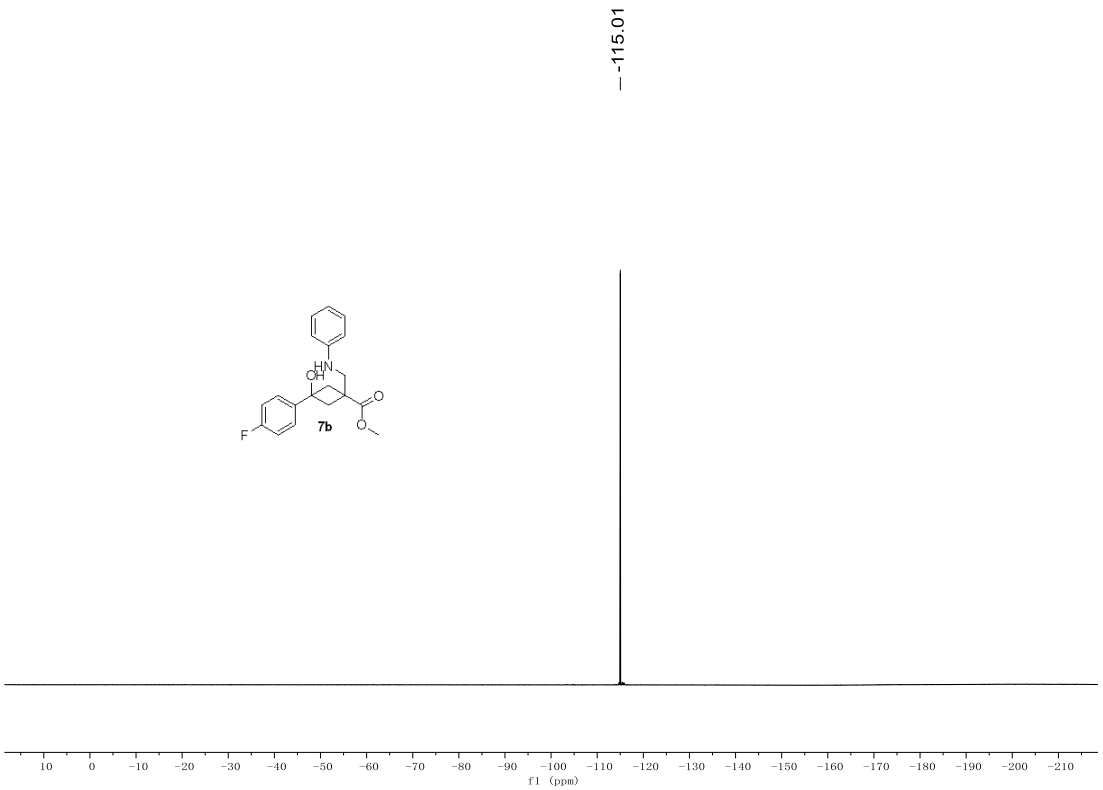


Methyl 3-hydroxy-3-phenyl-1-((phenylamino)methyl)cyclobutane-1-carboxylate.(7a)

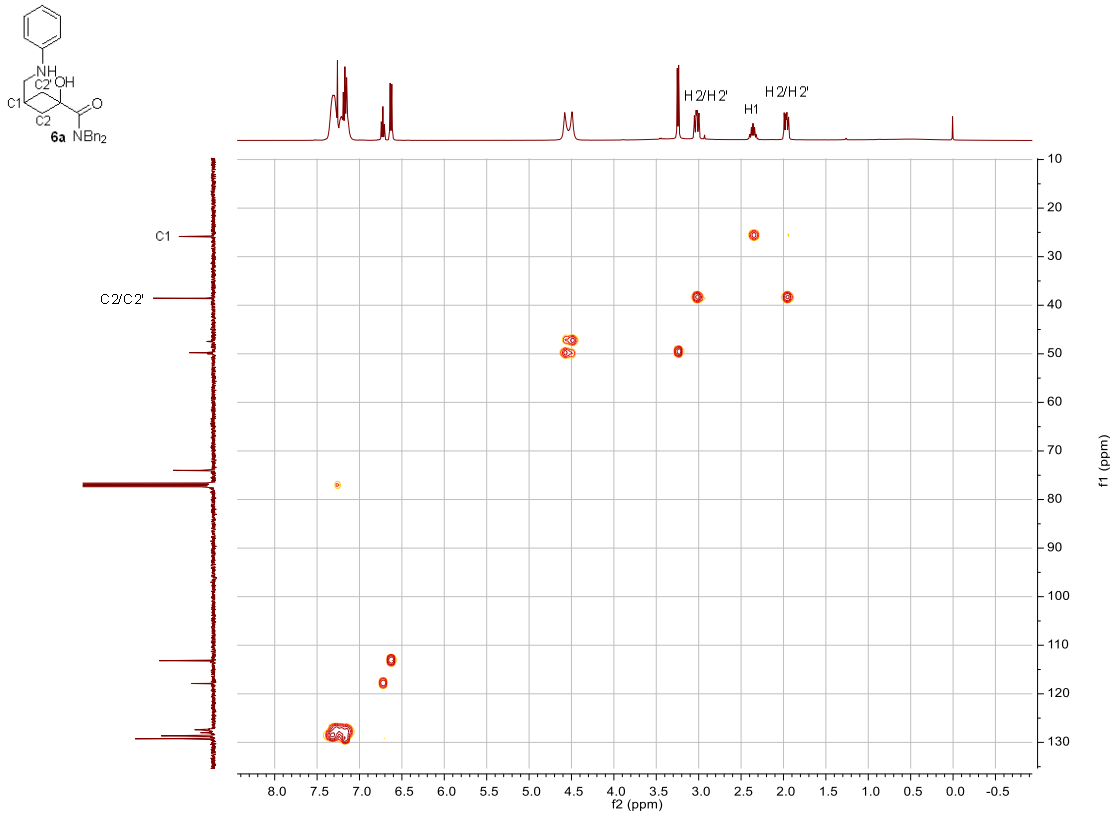


Methyl 3-(4-fluorophenyl)-3-hydroxy-1-((phenylamino)methyl)cyclobutane-1-carboxylate.(7b)





HMBC spectrum of **6a** in $CDCl_3$ (600 MHz)



^{1}H -^{1}H COSY spectrum of **6a** in $CDCl_3$ (600 MHz)