# Cobalt-Catalyzed Synthesis of Aryl Ketones and Aldehydes from Redox-Active Esters

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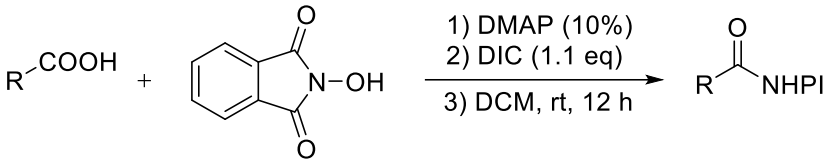
## Contents

## 1. General Information

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Organic solutions were concentrated under reduced pressure on a rotary evaporator or an oil pump. Reactions were monitored through thin layer chromatography (TLC) on silica gel-precoated glass plates. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed using Qingdao Haiyang flash silica gel (200-300 mesh). Infrared spectra were recorded using a Bruker Optics TENSOR 27 instrument. $^{1}H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ using a 500 MHz NMR instrument (referenced internally to $Me_4Si$). $^{1}H$ NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and integral. Data for $^{13}C$ NMR spectra are reported in terms of chemical shift. Accurate mass measurements were performed using an Agilent instrument with the ESI-MS technique. Melting points were determined on a Stuard SMP3 melting point apparatus.

## 2. General Procedure for Preparation of NHPI Esters [1]

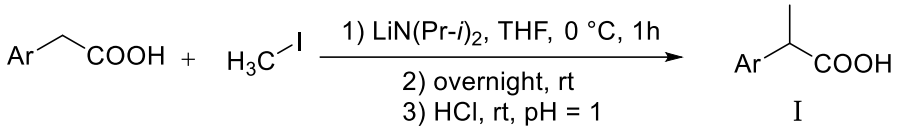



To a solution of 4-dimethylaminopyridine (DMAP, 122 mg, 1.0 mmol, 10 mol %) in $CH_2Cl_2$ (30 mL), *N*-hydroxyphthalimide (NHPI, 1.63 g, 10 mmol, 1.00 equiv) and the corresponding acids (10 mmol, 1.0 equiv) were successively added. The solution was then allowed to stir vigorously at room temperature, and *N,N'*-diisopropylcarbodiimide (DIC, 1.26 g, 10 mmol, 1.0 equiv) was added over 5 minutes by syringe. The reaction mixture was allowed to stir until the acid was consumed (monitored by TLC). The reaction mixture was then filtered, and the residue was washed by $CH_2Cl_2$. The organic phase was dried over anhydrous $Na_2SO_4$ and filtered. Silica gel was added, and the mixture

was concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel using cyclohexane/EtOAc as eluent afforded the desired esters.

Most of aliphatic acids were commercially available and used directly without further purification. Other acids were synthesized according to the following procedures.

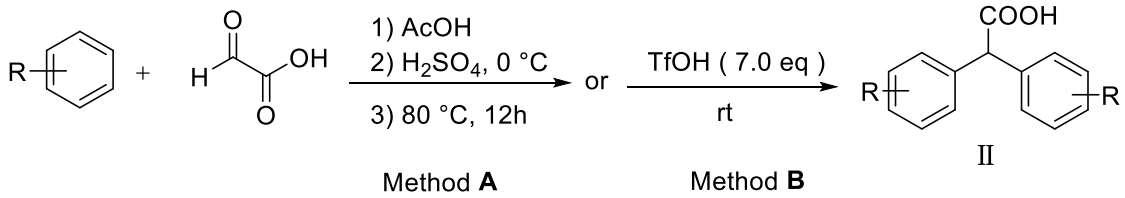
**2.1. General Procedure for Preparation of Acids I**




Ar = 4-biphenyl, α-naphthyl, β-naphthyl

Following the procedure outlined by Smith,[2] *n*-BuLi (2.2 equiv) was added to a solution of *i*-$Pr_2NH$ (2.2 equiv) in anhydrous THF in a flame-dried round-bottomed flask under a $N_2$ atmosphere at 0 ℃. The LDA solution was stirred for 30 minutes, arylacetic acid (1.0 equiv) was added and the reaction mixture was stirred for 1 h at 0 ℃. Alkyl halide (2.2 equiv) was added and the reaction mixture was stirred overnight at room temperature. HCl (20 mL) was added until pH was 1. The aqueous layer was extracted with EtOAc (3 × 20 mL). The organic layers were combined, dried over $Na_2SO_4$, filtered and concentrated in vacuo to give the crude *α*-substituted aryl acetic acid I.

**2.2. General Procedure for Preparation of Acids II**




**Method A** [3]

Aromatic compound (10 mmol, 2.0 equiv) was added to a solution of glyoxylic acid monohydrate (5.0 mmol, 1.0 equiv) in AcOH (6 mL). The mixture was then cooled to 0 ℃, conc. $H_2SO_4$ (5 mL) was added dropwise, and stirred at 80 ℃ for 12 h. After cooling to room temperature, the reaction mixture was quenched with water (10 mL) and a dark brown solid was precipitated. The solid was

washed with water (2 × 10 mL) followed by n-hexane (3 × 10 mL). The yellow solid can further be purified by trituration with n-hexane and EtOAc to get the desired acid as a white solid.

**Method B** [4]

The glyoxylic acid, 50% (0.6 g, 4 mmol), was mixed with arenes (5 mL) in a bottle and cooled to 0 ℃. Then TfOH (28 mmol) was added slowly. The reaction mixture was warmed up to room temperature and stirred over specific period of time. The reaction progress was monitored by TLC (3:1 hexanes/ethyl acetate). After the reaction was complete, the mixture was poured over ice, neutralized with sodium bicarbonate, and extracted with diethyl ether (3 × 15 mL). The organic extracts were combined, washed with water and dried over anhydrous $Na_2SO_4$. The solvent was removed by vacuum evaporation and crude products were purified by column chromatography on silica gel (200–300 mesh) using hexane/ethyl acetate (85:15) as eluent.

**3. General Procedure for Co-Catalyzed Decarboxylative Oxidation of NHPI Esters**

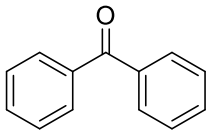
To a 10 ml reaction tube equipped with a stir bar was added the NHPI esters **a** (0.15 mmol, 1.0 equiv), the catalyst $Co(OAc)_2$ (0.015 mmol, 10 mol%) and the ligand 2,2':6',2"-terpyridine (0.03 mmol, 20 mol%) under air atmosphere. Then the solvent DMF (1 mL) was added via a syringe. The reaction mixture was vigorously stirred at 100 ℃ and monitored by TLC. After the reaction was complete, the mixture was directly purified by column chromatography on silica gel (petroleum ether/EtOAc as the eluent) to furnish the corresponding product.

Control experiment under oxygen atmosphere: To a 10 ml reaction tube equipped with a stir bar was added the NHPI esters **a** (0.15 mmol, 1.0 equiv), the catalyst $Co(OAc)_2$ (0.015 mmol, 10 mol%) and the ligand 2,2':6',2"-terpyridine (0.03 mmol, 20 mol%). Then the solvent DMF (1 mL) was added via a syringe. The reaction mixture was degassed for 10 min and refilled with $O_2$ for 3 times. The mixture was vigorously stirred at 100 ℃ and monitored by TLC. After 4 h, the mixture was directly

purified by column chromatography on silica gel (petroleum ether/EtOAc as the eluent) to furnish the corresponding product.

## 4. Characterization Data for Products

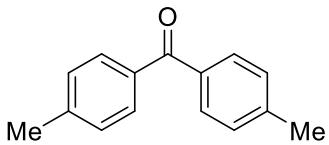
**benzophenone (1b)[5]**




**1b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). White solid, 24.8 mg, 91% yield (24.5 mg, 90% yield, under $O_2$). mp = 48 - 50 ℃. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.3 Hz, 4H), 7.59 (t, *J* = 7.5 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 4H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ196.9, 137.7, 132.6, 130.2, 128.4.

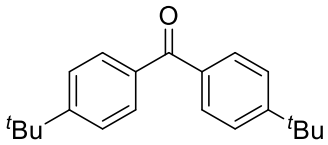
**di-*p*-tolylmethanone (2b)[6]**




**2b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Yellow solid, 25.6 mg, 81% yield. mp = 90 - 92 ℃. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 4H), 7.19 (d, *J* = 7.9 Hz, 4H), 2.35 (s, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 196.6, 143.3, 135.6, 130.5, 129.2, 21.9.

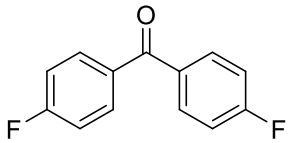
**bis(4-(tert-butyl)phenyl)methanone (3b)[6]**




**3b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). White solid, 37.5 mg, 85% yield. mp = 133 - 135 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.5 Hz, 4H), 7.49 (d, *J* = 8.4 Hz, 4H), 1.37 (s, 18H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 196.3, 156.0, 135.2, 130.1, 125.2, 35.2, 31.2.

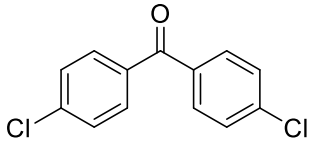
**bis(4-fluorophenyl)methanone (4b)[6]**




**4b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Yellow solid, 30.1 mg, 92% yield. mp = 102 -104 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.76 - 7.71 (m, 4H), 7.11 - 7.06 (m, 4H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 192.8, 164.4 (d, *J* = 254.5 Hz), 132.7 (d, *J* = 2.5 Hz), 131.5 (d, *J* = 8.8 Hz), 114.56 (d, *J* = 21.4 Hz).

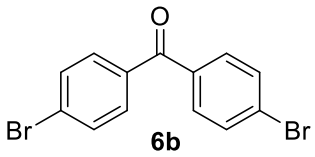
**bis(4-chlorophenyl)methanone (5b)[6]**




**5b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Yellow solid, 26.2 mg, 70% yield. mp = 147 - 149 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.67 - 7.63 (m, 4H), 7.42 - 7.38 (m, 4H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 193.3, 138.2, 134.5, 130.3, 127.8.

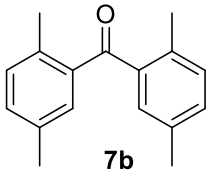
**bis(4-bromophenyl)methanone (6b)[7]**




**6b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Yellow solid, 25.7 mg, 51% yield. mp = 177 - 179 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.64 - 7.45 (m, 8H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 193.5, 134.9, 130.8, 130.4, 126.8.

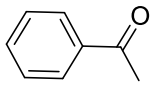
**bis(2,5-dimethylphenyl)methanone (7b)[6]**




**7b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 29.7 mg, 83% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 7.7, 1.9 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 7.04 (d, *J* = 1.9 Hz, 2H), 2.29 (s, 6H), 2.21 (s, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 200.2, 138.1, 134.0, 133.9, 130.7, 130.3, 129.6, 19.8, 19.1.

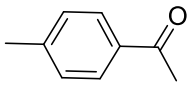
**acetophenone (8b)[5]**




**8b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 11.4 mg, 63% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.3 Hz, 2H), 7.55 – 7.50 (m, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 2.57 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 198.1, 137.1, 133.1, 128.6, 128.3, 26.6.

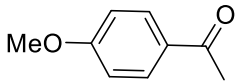
**1-(p-tolyl)ethan-1-one (9b)[5]**



**9b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 15.5 mg, 77% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 2.47 (s, 3H), 2.31 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 196.8, 142.8, 133.7, 128.2, 127.4, 25.5, 20.6.

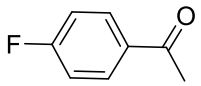
**1-(4-methoxyphenyl)ethan-1-one (10b)[7]**



**10b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). White solid, 18.0 mg, 80% yield. mp = 36 - 38 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.9 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 2H), 2.48 (s, 2H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 195.8, 162.5, 129.6, 129.3, 112.7, 54.5, 25.3.

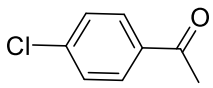
**1-(4-fluorophenyl)ethan-1-one (11b)[7]**



**11b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 12.6 mg, 61% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.92 - 7.87 (m, 2H), 7.06 – 7.01 (m, 2H), 2.50 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 195.5, 164.8 (d, *J* = 254.3 Hz), 132.6 (d, *J* = 4.4 Hz), 129.9 (d, *J* = 9.1 Hz), 114.6 (d, *J* = 21.6 Hz), 25.5.

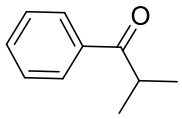
**1-(4-chlorophenyl)ethan-1-one (12b)[5]**



**12b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 18.3 mg, 79% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 2H), 2.49 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 195.8, 138.5, 134.4, 128.7, 127.8, 25.5.

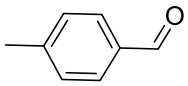
**2-methyl-1-phenylpropan-1-one (13b)[8]**



**13b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 18.4 mg, 83% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.85 (m, 2H), 7.49 – 7.43 (m, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 3.52 – 3.42 (m, 1H), 1.13 (d, *J* = 6.9 Hz, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 203.5, 135.2, 131.8, 127.6, 127.3, 34.3, 18.1.

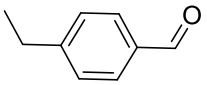
**4-methylbenzaldehyde (14b)[9]**



**14b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 13.2 mg, 73% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 2.32 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 191.0, 144.5, 133.2, 128.8, 128.7, 20.8.

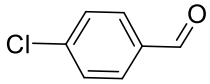
**4-ethylbenzaldehyde (15b)[10]**



**15b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 15.1 mg, 75% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.18 (t, *J* = 7.7 Hz, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 191.0, 150.7, 133.4, 129.0, 127.5, 28.1, 14.1.

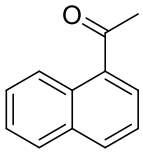
**4-chlorobenzaldehyde (16b)[11]**



**16b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). White solid, 13.9 mg, 66% yield. mp = 47 - 49 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 189.9, 139.9, 133.7, 129.9, 128.4.

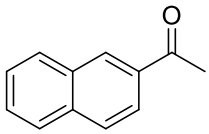
**1-(naphthalen-1-yl)ethan-1-one (17b)[7]**



**17b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Yellow solid, 16.8 mg, 66% yield. mp = 34 - 36 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, *J* = 8.5 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 7.3 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.48 (t, *J* = 7.0 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 2.61 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 200.8, 134.3, 132.9, 132.0, 129.1, 127.7, 127.4, 127.0, 125.4, 125.0, 123.3, 28.9.

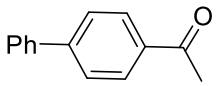
**1-(naphthalen-2-yl)ethan-1-one (18b)[12]**



**18b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). White solid, 18.6 mg, 73% yield. mp = 56 - 58 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.78 (t, *J* = 7.8 Hz, 2H), 7.52 – 7.43 (m, 2H), 2.63 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 197.1, 134.6, 133.5, 131.5, 129.2, 128.5, 127.44, 127.38, 126.8, 125.7, 122.9, 25.6.

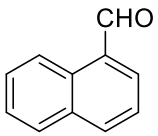
**1-([1,1'-biphenyl]-4-yl)ethan-1-one (19b)[7]**



**19b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). White solid, 22.6 mg, 77% yield. mp = 121 - 123 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.9 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 2.64 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 196.8, 144.8, 138.9, 134.9, 128.0, 127.9, 127.2, 126.3, 126.2, 25.6.

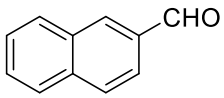
**1-naphthaldehyde (20b)[11]**



**20b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Liquid, 15.2 mg, 65% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 10.26 (s, 1H), 9.13 (d, *J* = 8.7 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 7.0 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.56 (t, *J* = 7.1 Hz, 1H), 7.49 – 7.42 (m, 2H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 192.5, 135.6, 134.2, 132.7, 130.3, 129.5, 128.0, 127.4, 125.9, 123.8.

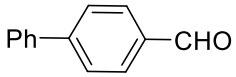
**2-naphthaldehyde (21b)[9]**




**21b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Yellow solid, 16.6 mg, 71% yield. mp = 61 - 63 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.24 (s, 1H), 7.91 (d, *J* = 6.9 Hz, 1H), 7.88 – 7.80 (m, 3H), 7.55 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.50 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 191.3, 135.4, 133.5, 133.1, 131.6, 128.5, 128.09, 128.08, 127.1, 126.1, 121.7.

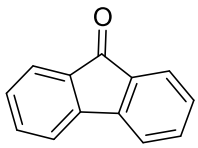
**[1,1'-biphenyl]-4-carbaldehyde (22b)[11]**




**22b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). White solid, 18.6 mg, 68% yield. mp = 60 - 62 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 7.1 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 190.9, 146.2, 138.7, 134.2, 129.3, 128.0, 127.5, 126.7, 126.4.

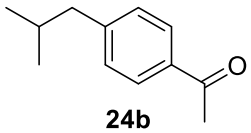
**9*H*-fluoren-9-one (23b)[7]**



**23b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Yellow solid, 25.7 mg, 95% yield. mp = 84 - 86 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.3 Hz, 2H), 7.42 – 7.33 (m, 4H), 7.21 – 7.15 (m, 2H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 192.9, 143.4, 133.7, 133.1, 128.0, 123.3, 119.3.

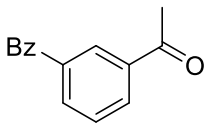
**1-(4-isobutylphenyl)ethan-1-one (24b)[9]**



**24b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 20:1). Liquid, 16.4 mg, 62% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 2.52 (s, 3H), 2.46 (d, *J* = 7.2 Hz, 2H), 1.88 - 1.79 (m, 1H), 0.84 (d, *J* = 6.6 Hz, 6H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 197.0, 146.6, 134.0, 128.3, 127.3, 44.4, 29.1, 25.5, 21.3.

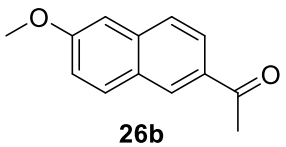
**1-(3-benzoylphenyl)ethan-1-one (25b)[11]**



**25b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 20:1). Liquid, 27.2 mg, 81% yield. $^{1}$H NMR (500 MHz, $CDCl_3$) $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.29 (t, *J* = 1.8 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.75 – 7.71 (m, 2H), 7.57 – 7.51 (m, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 2.58 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 196.3, 194.9, 137.1, 136.2, 136.0, 133.2, 131.9, 130.8, 129.0, 128.7, 127.7, 127.5, 25.7.

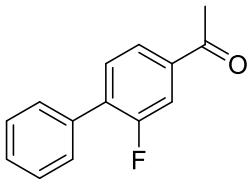
**1-(6-methoxynaphthalen-2-yl)ethan-1-one (26b)[12]**



**26b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). Yellow solid, 25.0 mg, 83% yield. mp = 106 - 108 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 1.7 Hz, 1H), 7.93 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.15 - 7.06 (m, 2H), 3.87 (s, 3H), 2.62 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 196.9, 158.8, 136.3, 131.6, 130.1, 129.1, 126.8, 126.1, 123.6, 118.7, 104.7, 54.4, 25.5

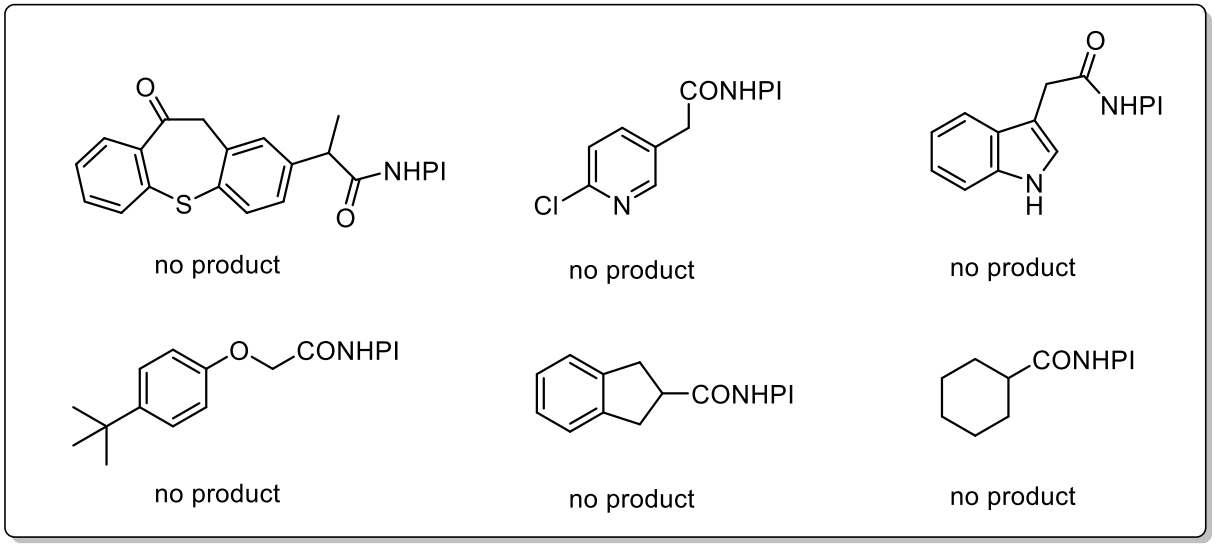
**1-(2-fluoro-[1,1'-biphenyl]-4-yl)ethan-1-one (27b)[11]**



**27b**

Prepared according to the general procedure as described above and purified by flash chromatography (PE/EtOAc 30:1). White solid, 25.0 mg, 78% yield. mp = 94 - 96 ℃. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.74 (dd, *J* = 11.2, 1.7 Hz, 1H), 7.60 – 7.53 (m, 3H), 7.50 – 7.45 (m, 2H),, 7.45 – 7.40 (m, 1H), 2.63 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 195.5, 158.7 (d, *J* = 249.9 Hz), 136.8 (d, *J* = 6.7 Hz), 133.7, 132.8 (d, *J* = 14.6 Hz), 129.9 (d, *J* = 3.4 Hz), 128.0 (d, *J* = 3.6 Hz), 127.6, 127.5, 123.3 (d, *J* = 3.4 Hz), 114.9 (d, *J* = 23.8 Hz), 25.6.

## 5. Unsuccessful Substrates

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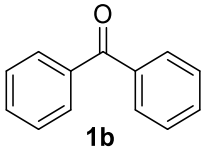
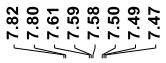
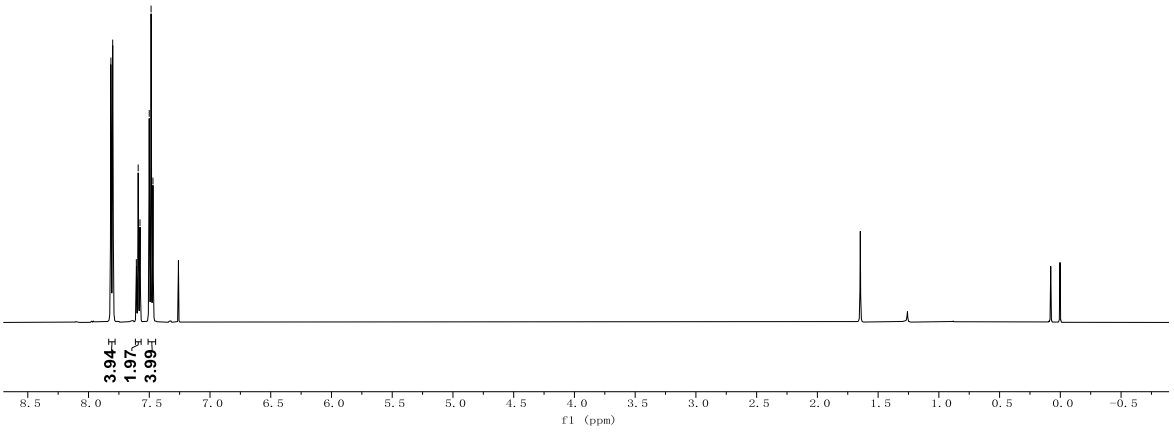
## 7. NMR Spectra

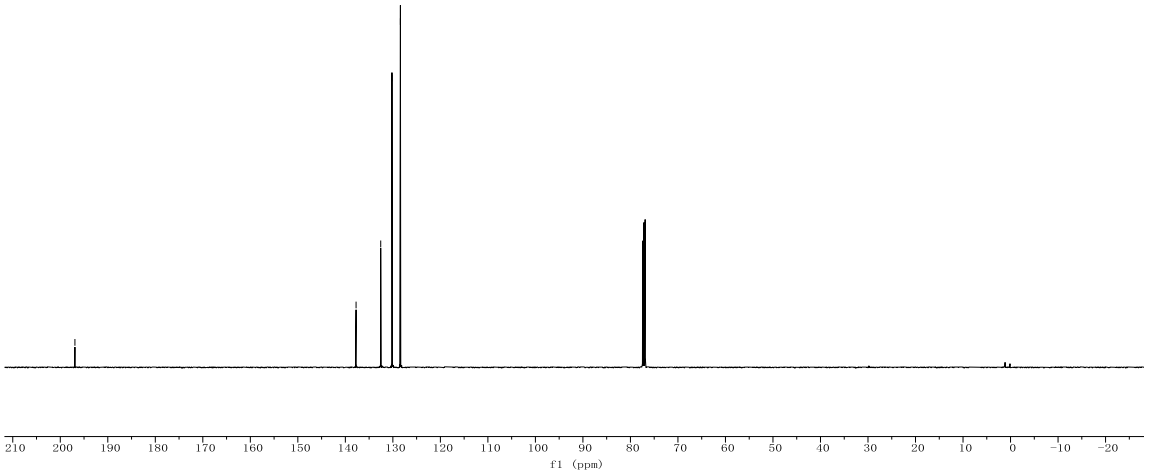


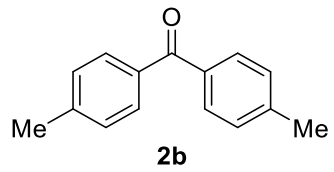
1b



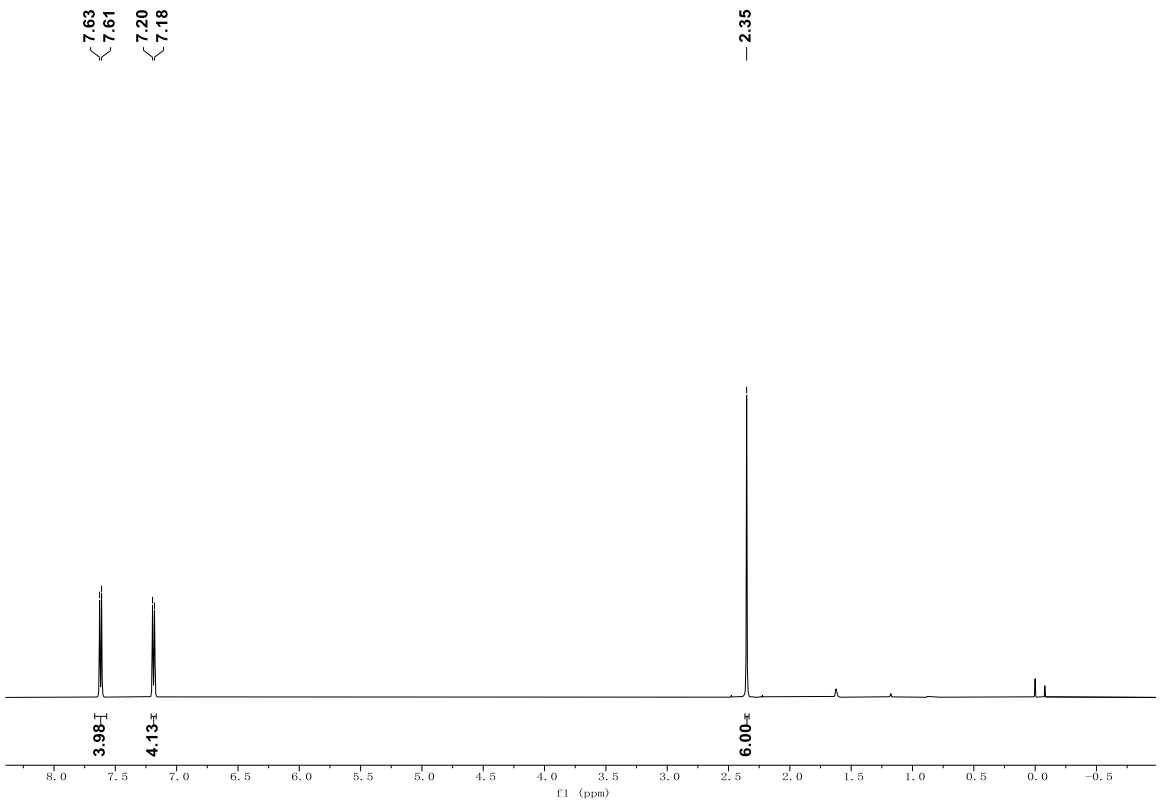



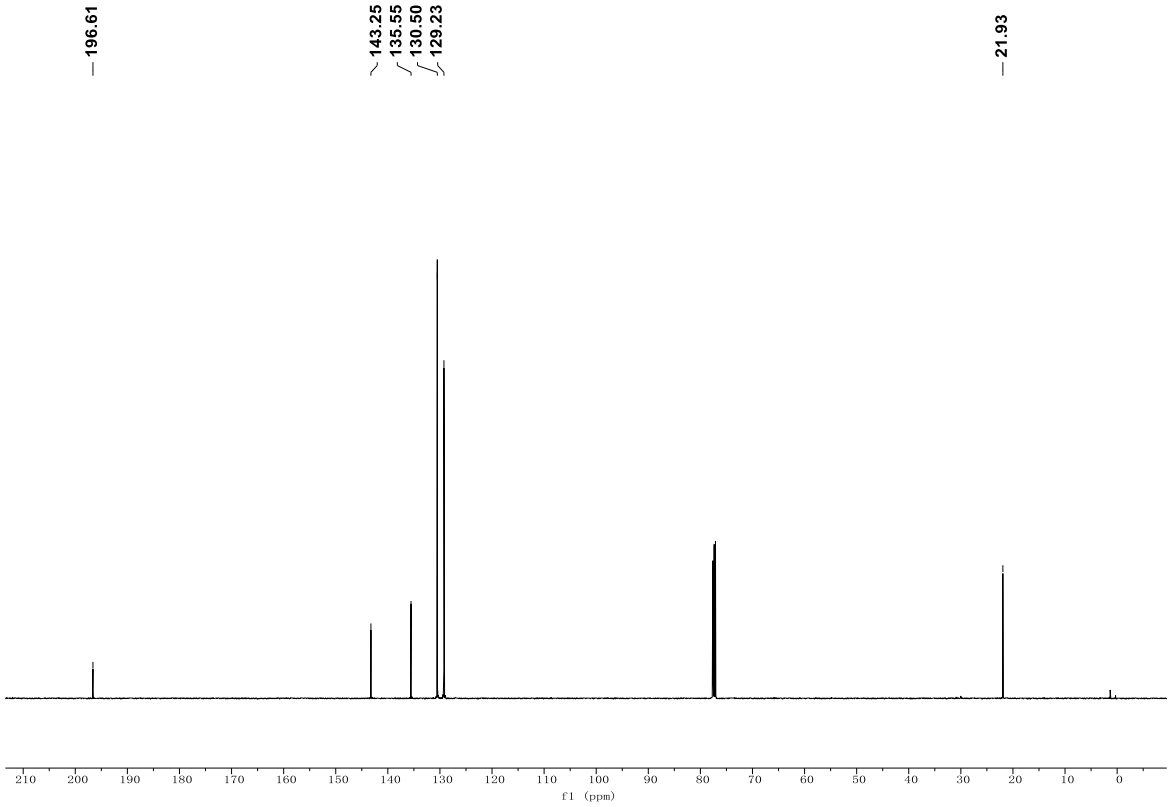


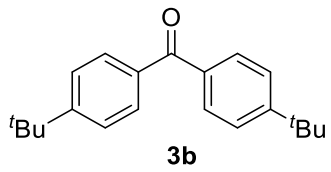



O
Me
Me

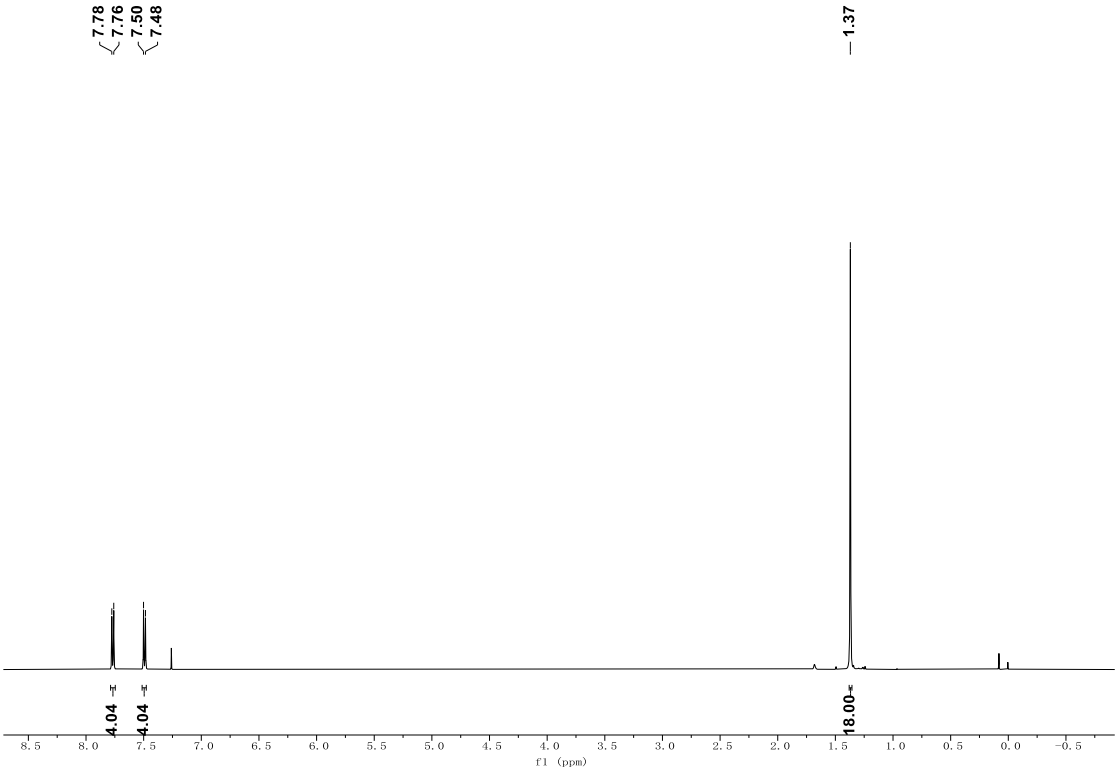
**2b**

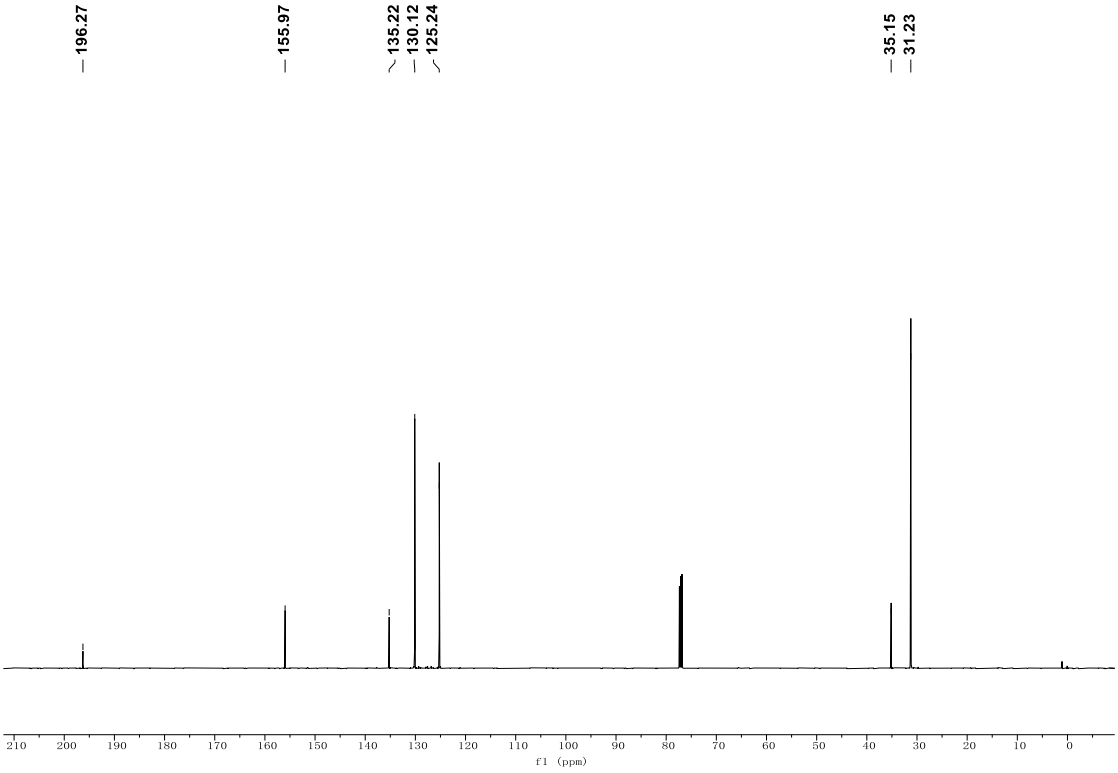

7.63
7.61
7.20
7.18
2.35
3.98
4.13
6.00
f1 (ppm)

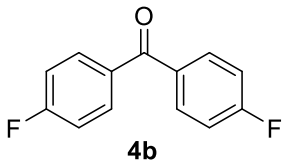

196.61
143.25
135.55
130.50
129.23
21.93
f1 (ppm)


O
tBu
tBu

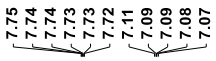
**3b**

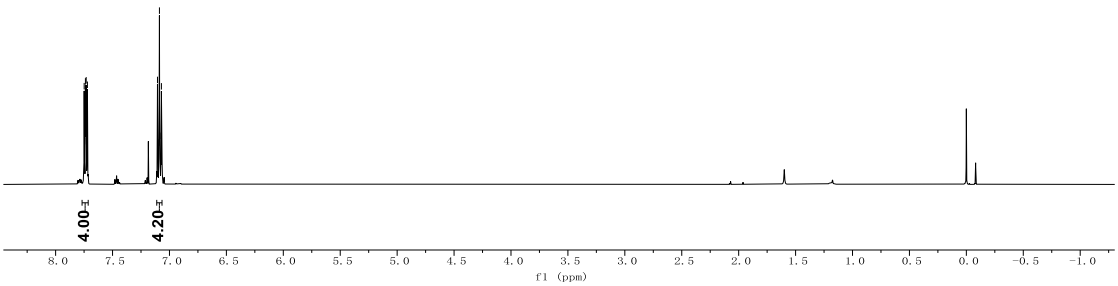

7.78
7.76
7.50
7.48
1.37
4.04
4.04
18.00
f1 (ppm)

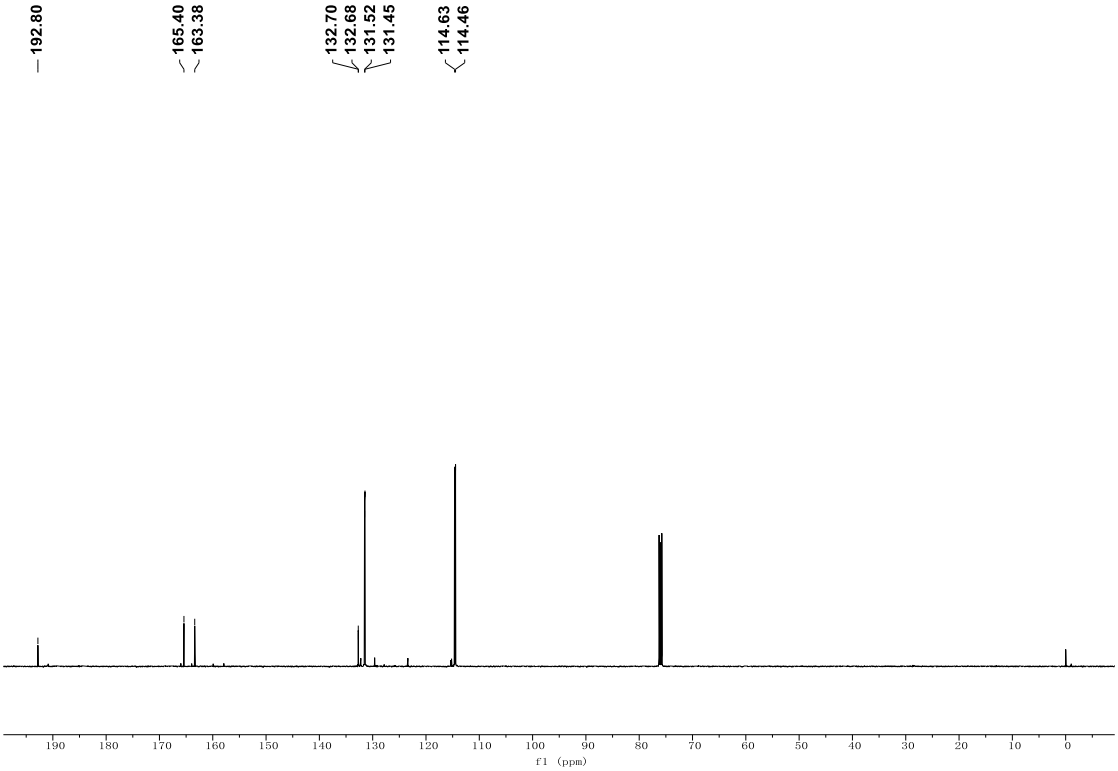

196.27
155.97
135.22
130.12
125.24
35.15
31.23
f1 (ppm)

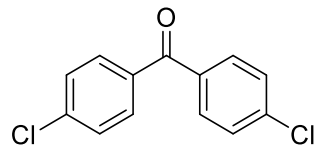

O
F
F

**4b**

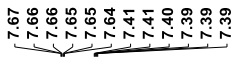

7.75
7.74
7.74
7.73
7.73
7.72
7.11
7.09
7.09
7.08
7.07

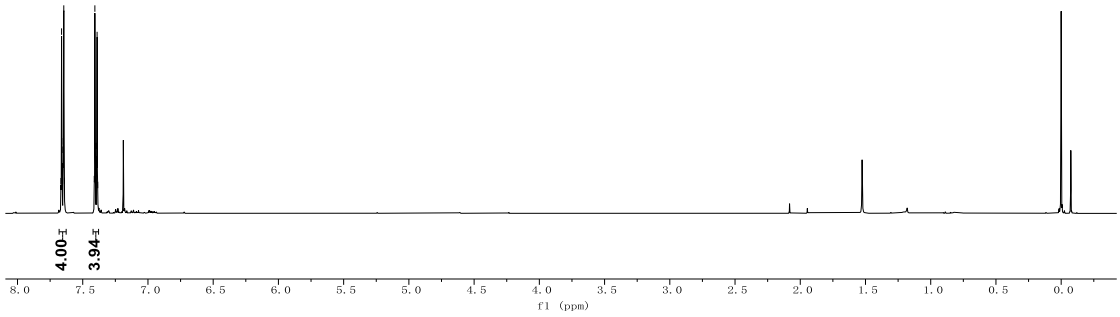

4.00
4.20
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

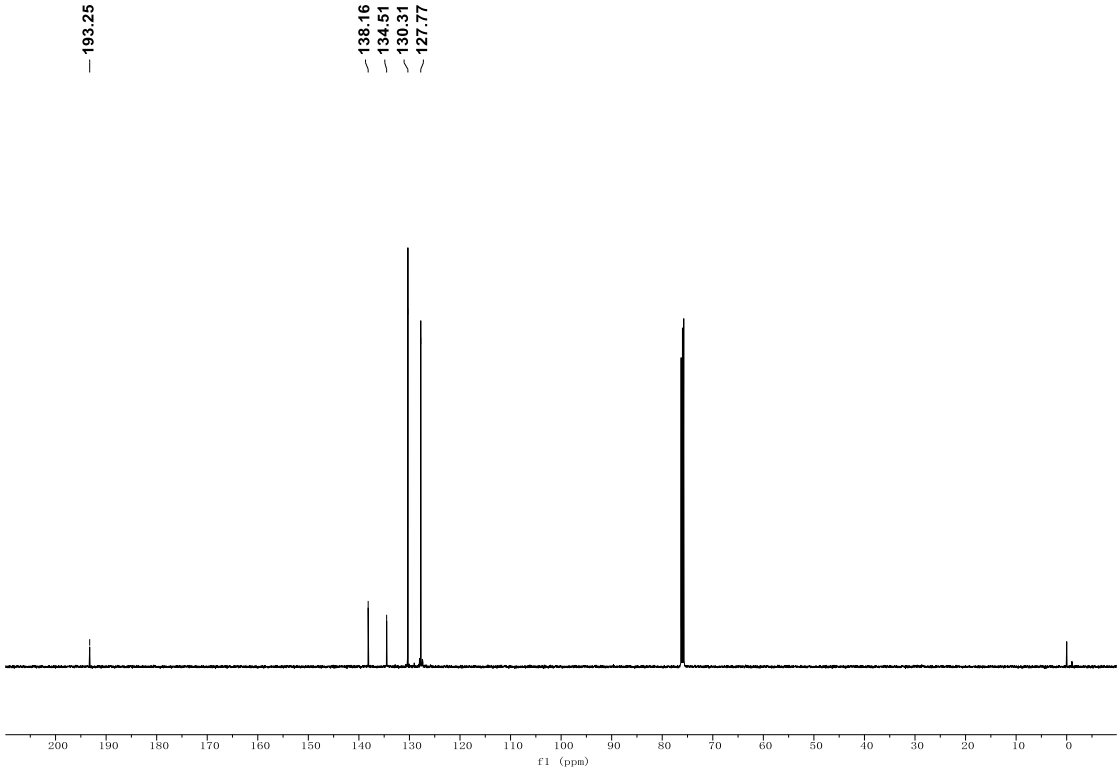

192.80
165.40
163.38
132.70
132.68
131.52
131.45
114.63
114.46
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

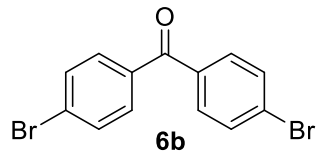

O
Cl
Cl

**5b**


7.67
7.66
7.66
7.65
7.65
7.64
7.41
7.41
7.40
7.39
7.39
7.39

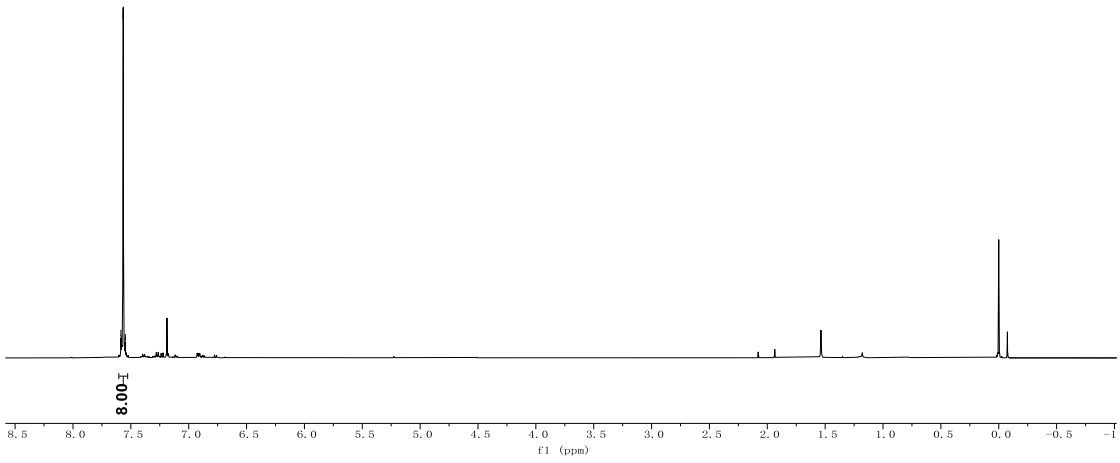

4.00
3.94
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


193.25
138.16
134.51
130.31
127.77
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



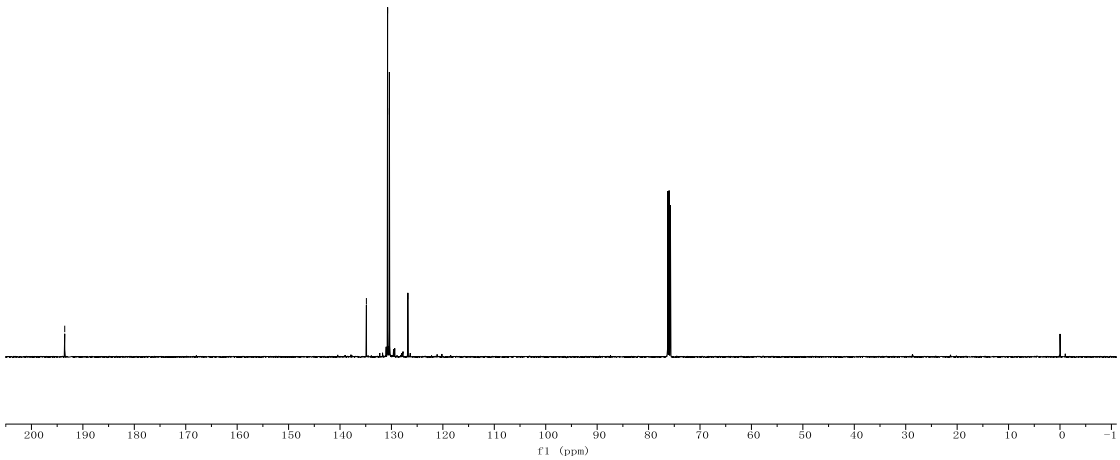

**6b**

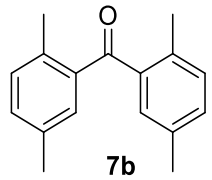
7.59
7.58
7.57
7.57
7.55
7.55




193.53

134.87
130.75
130.40
126.81

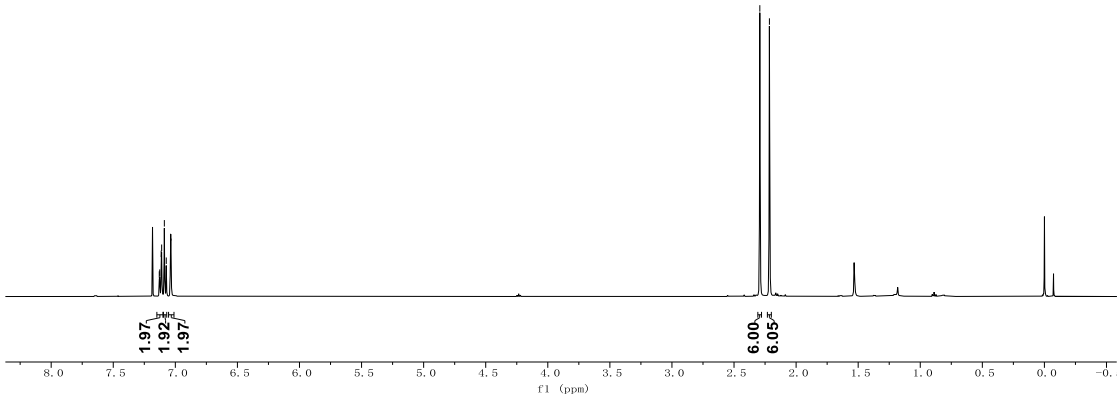



O

**7b**


7.13
7.13
7.11
7.11
7.09
7.07
7.04
7.04

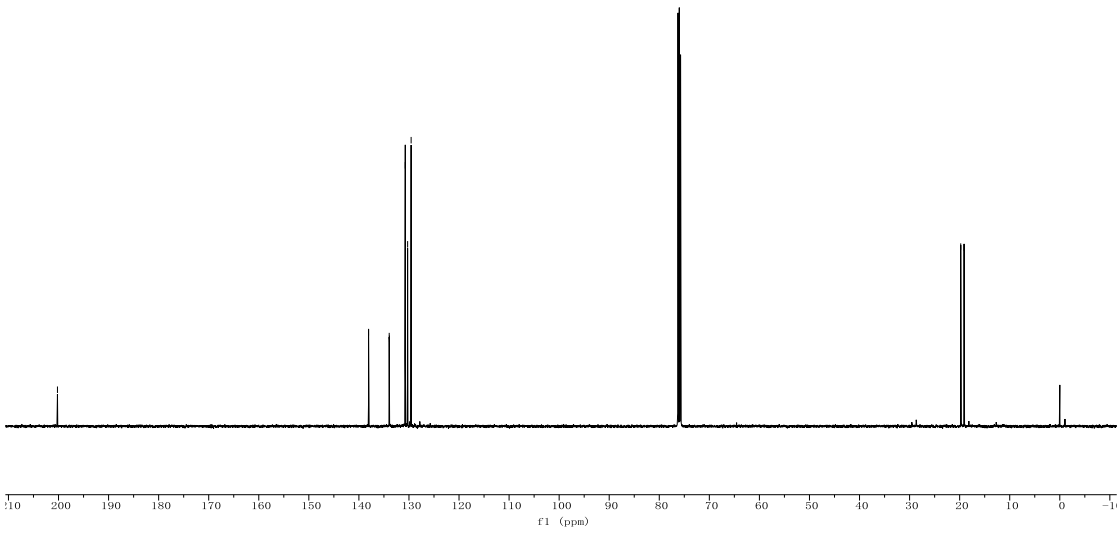

2.29
2.21

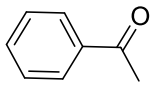

1.97
1.92
1.97
6.00
6.05
f1 (ppm)


200.21

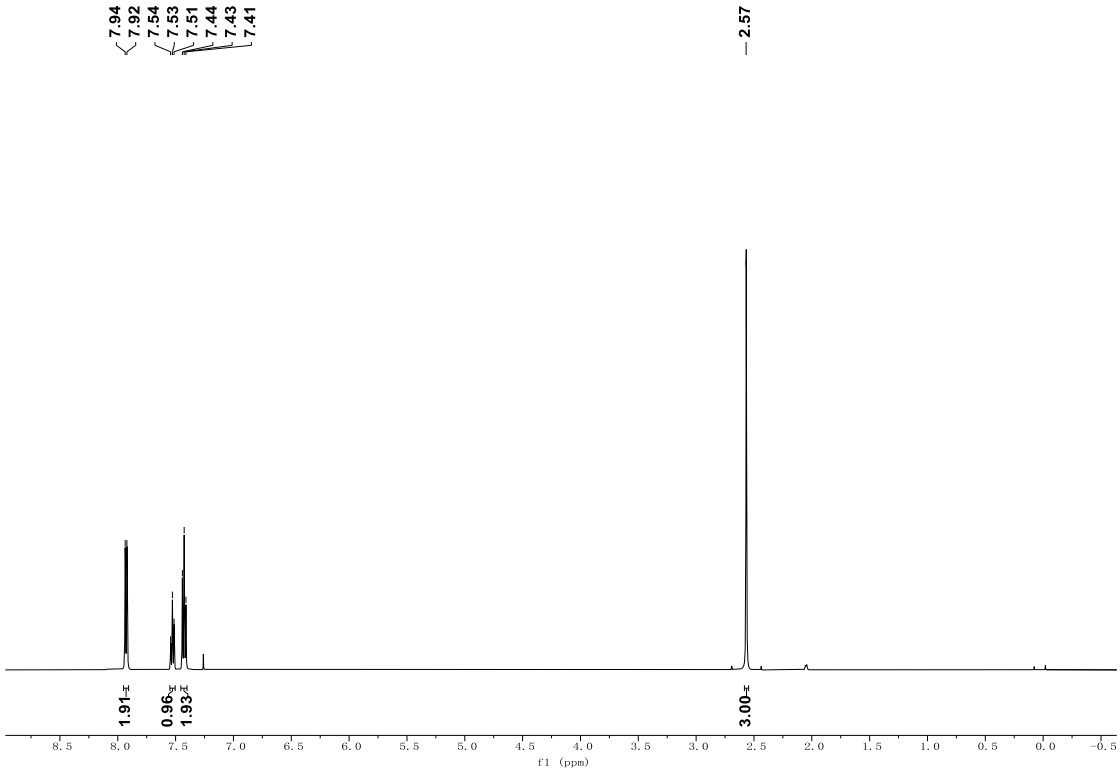

138.07
133.95
133.90
130.74
130.27
129.57

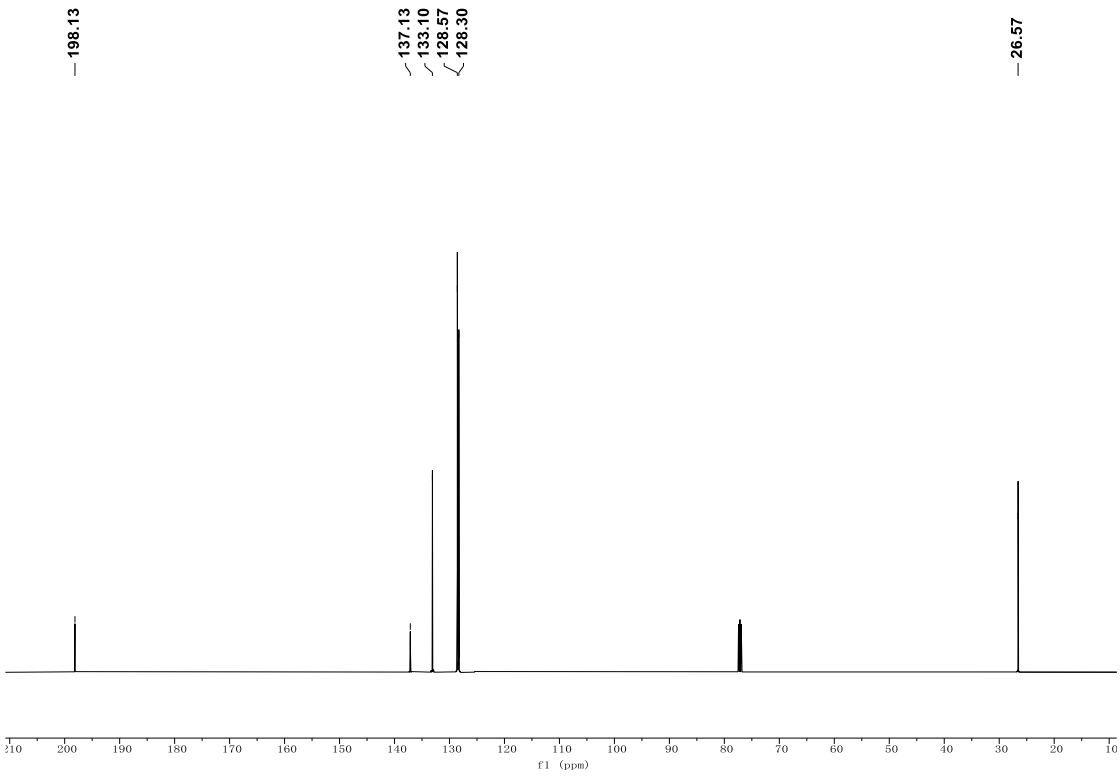

19.79
19.11

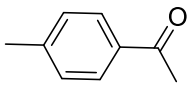

f1 (ppm)



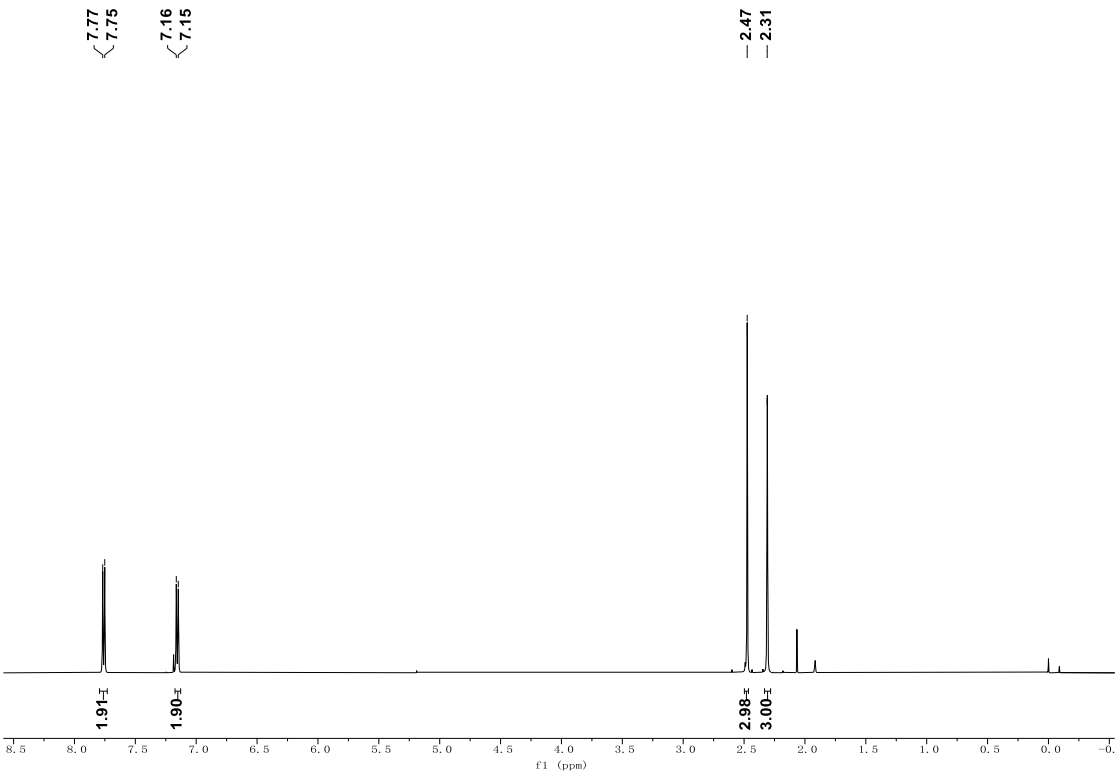
**8b**

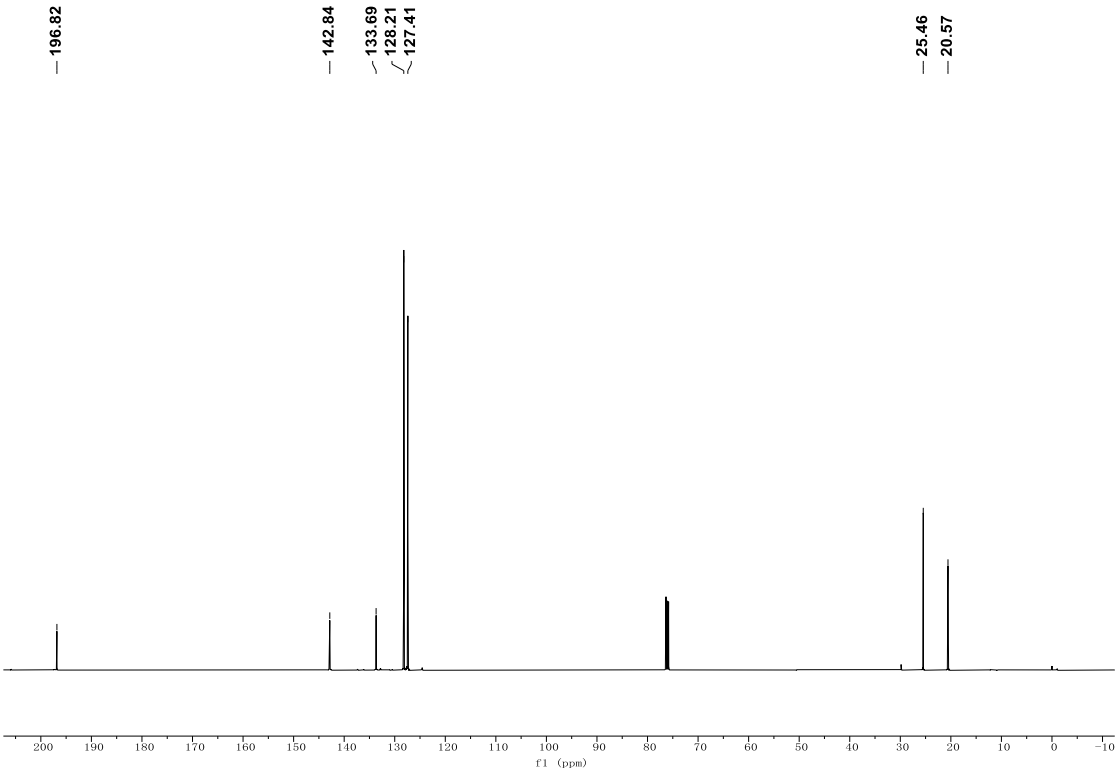

7.94
7.92
7.54
7.53
7.51
7.44
7.43
7.41
2.57
1.91
0.96
1.93
3.00
f1 (ppm)

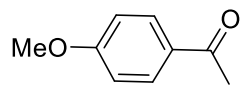

198.13
137.13
133.10
128.57
128.30
26.57
f1 (ppm)



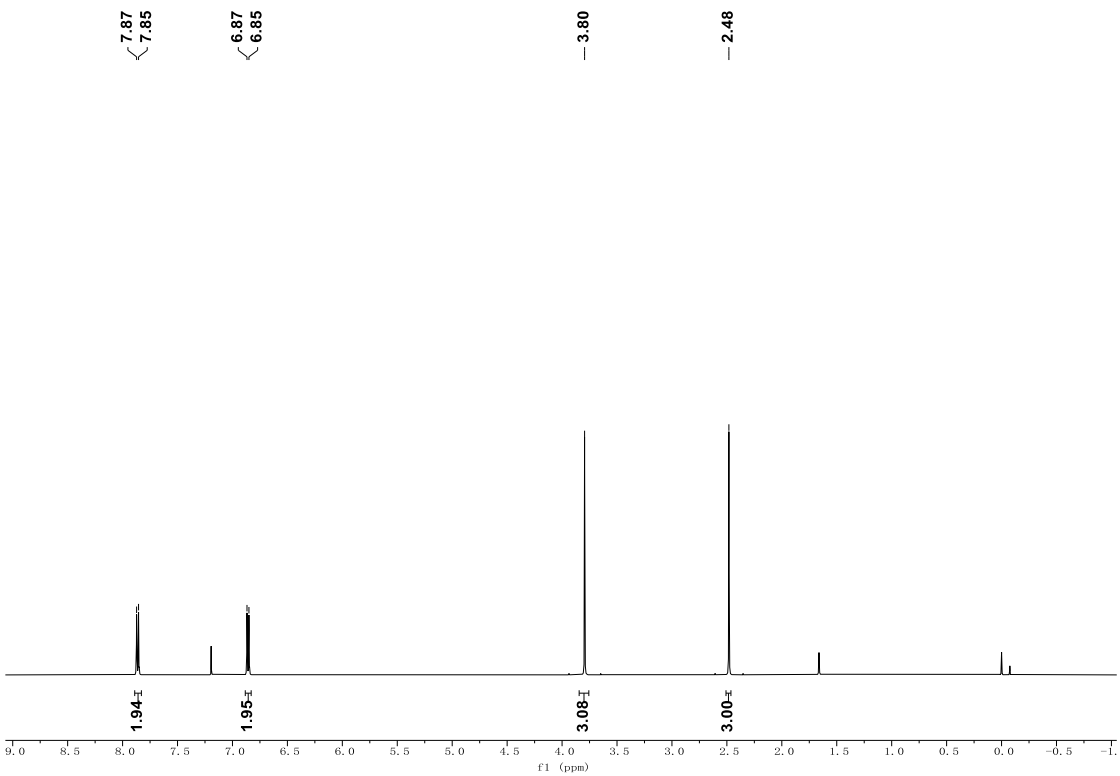
**9b**

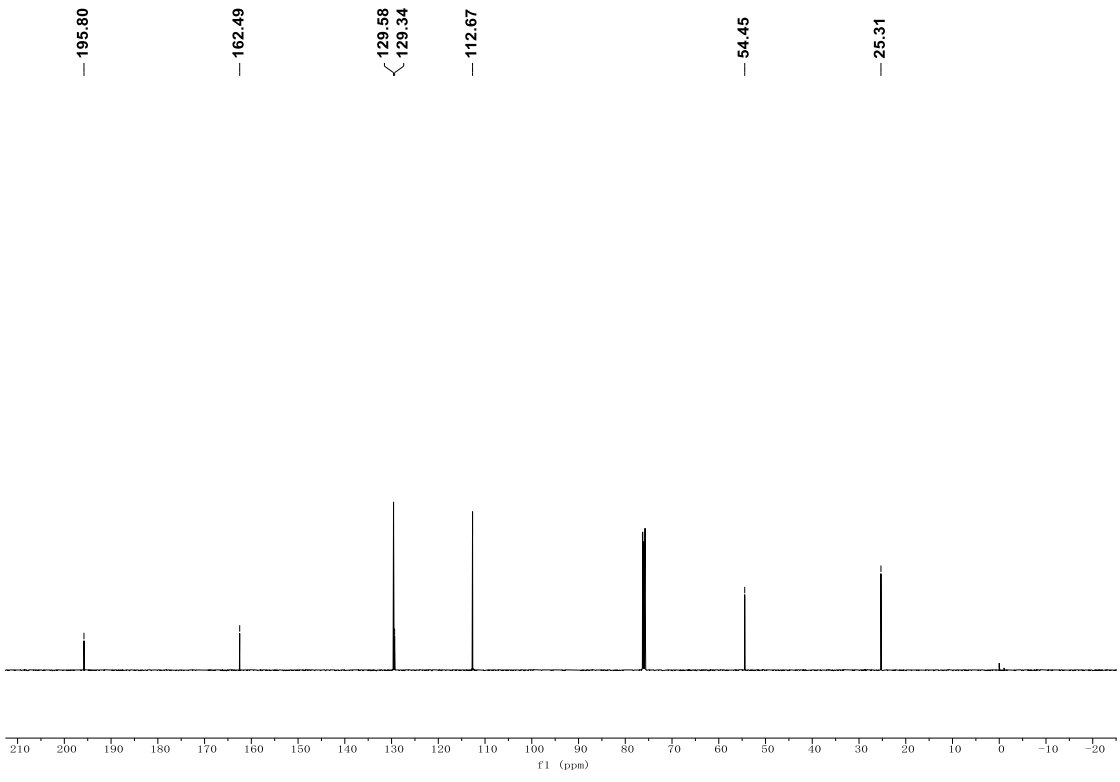

7.77
7.75
7.16
7.15
2.47
2.31
1.91
1.90
2.98
3.00
f1 (ppm)

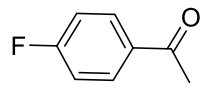

196.82
142.84
133.69
128.21
127.41
25.46
20.57
f1 (ppm)


MeO
O

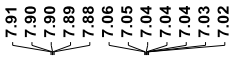
**10b**


7.87
7.85
6.87
6.85
3.80
2.48
1.94
1.95
3.08
3.00
f1 (ppm)

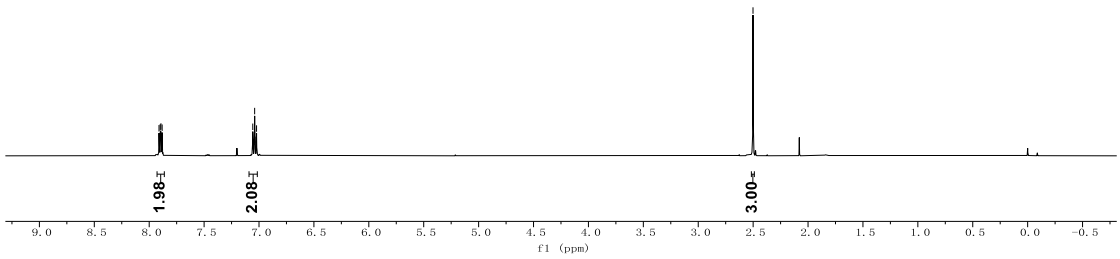

195.80
162.49
129.58
129.34
112.67
54.45
25.31
f1 (ppm)



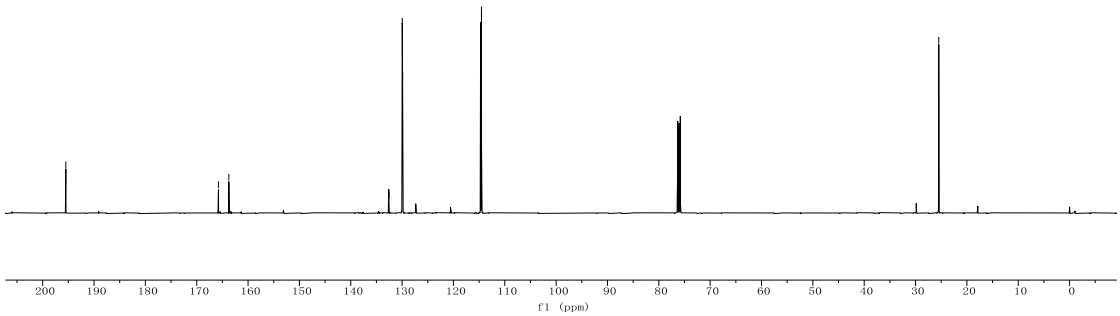
**11b**

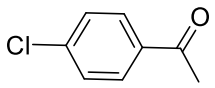

7.91
7.90
7.90
7.89
7.88
7.06
7.05
7.04
7.04
7.04
7.03
7.02


2.50

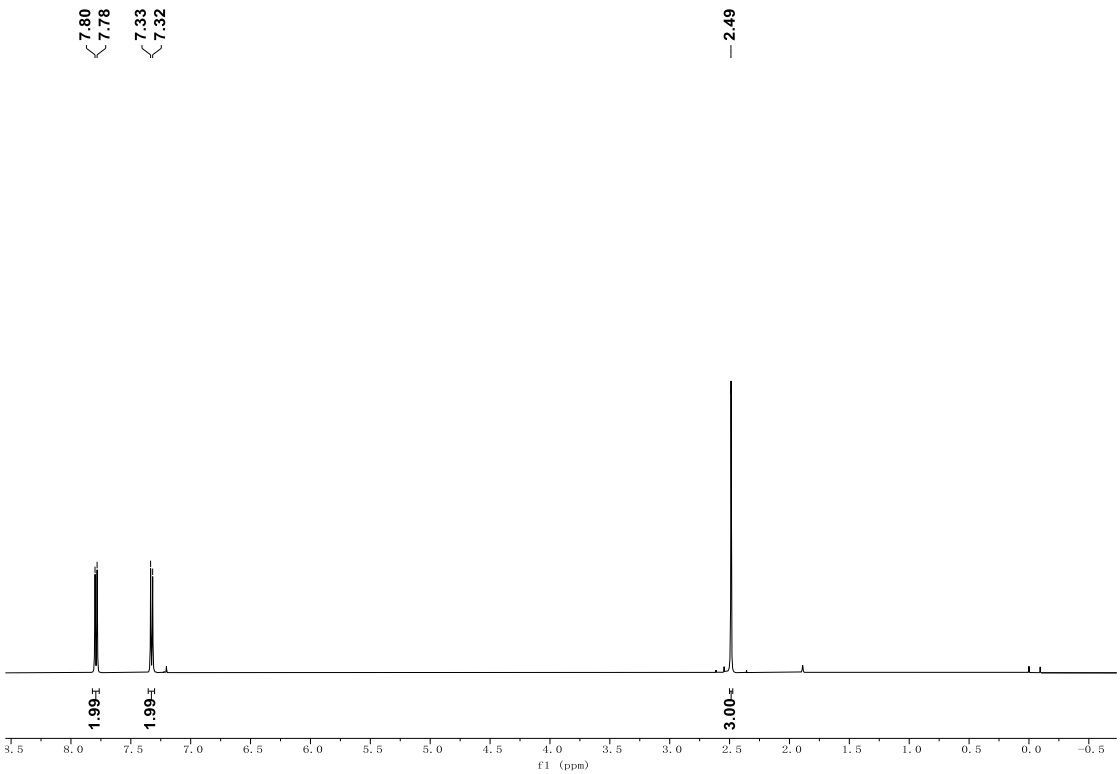

1.98
2.08
3.00
f1 (ppm)

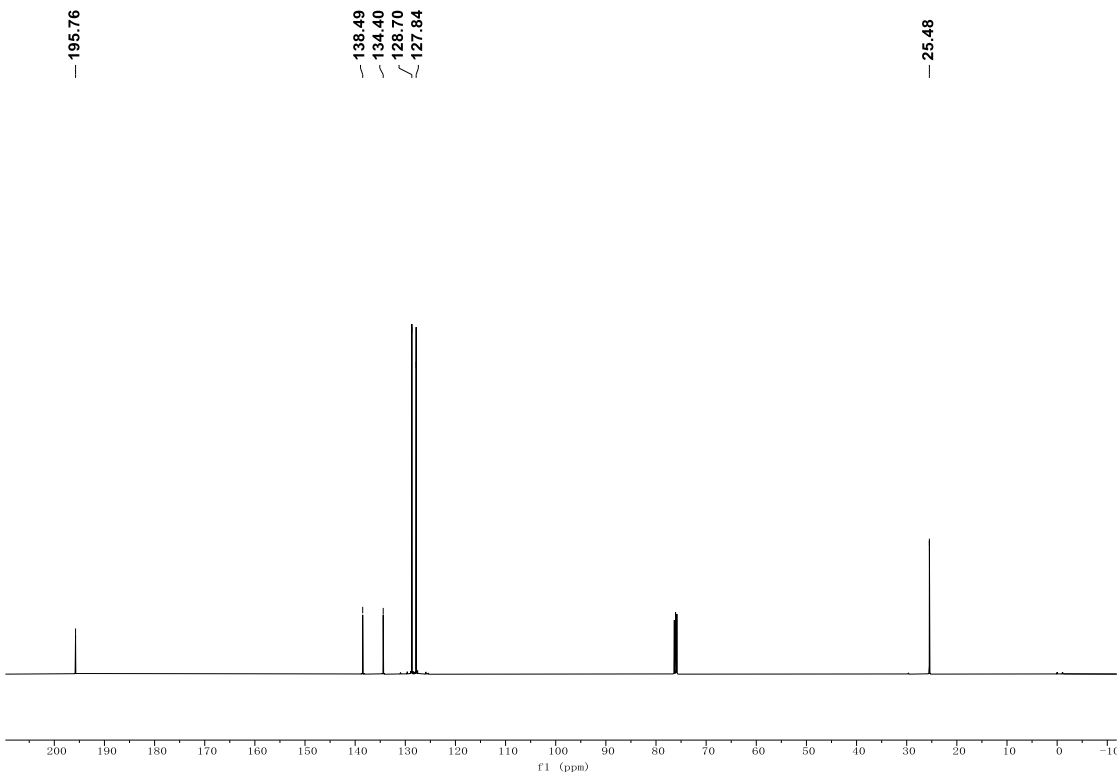

195.49
165.77
163.74
132.61
132.57
129.97
129.90
114.71
114.54
25.48

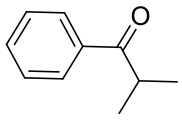

f1 (ppm)


Cl
O

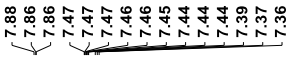
**12b**

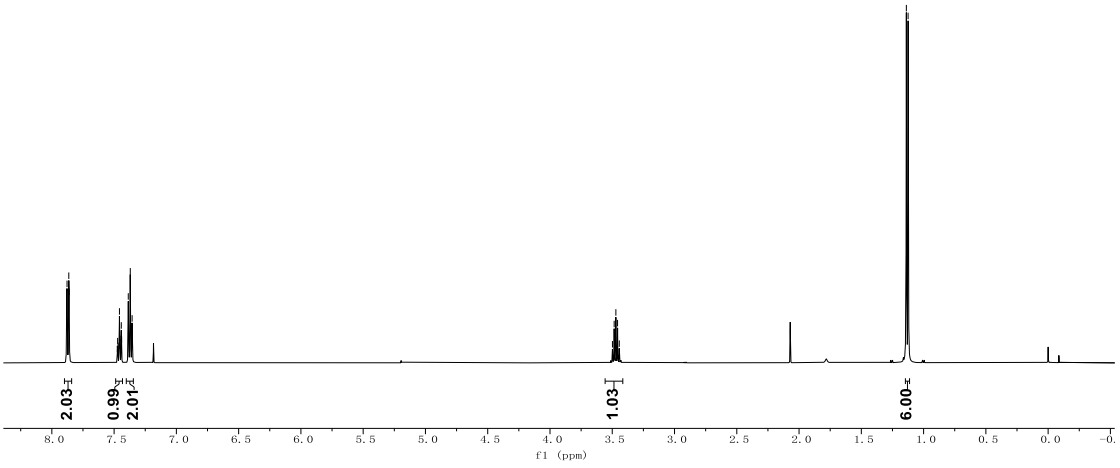

7.80
7.78
7.33
7.32
2.49
1.99
1.99
3.00
f1 (ppm)

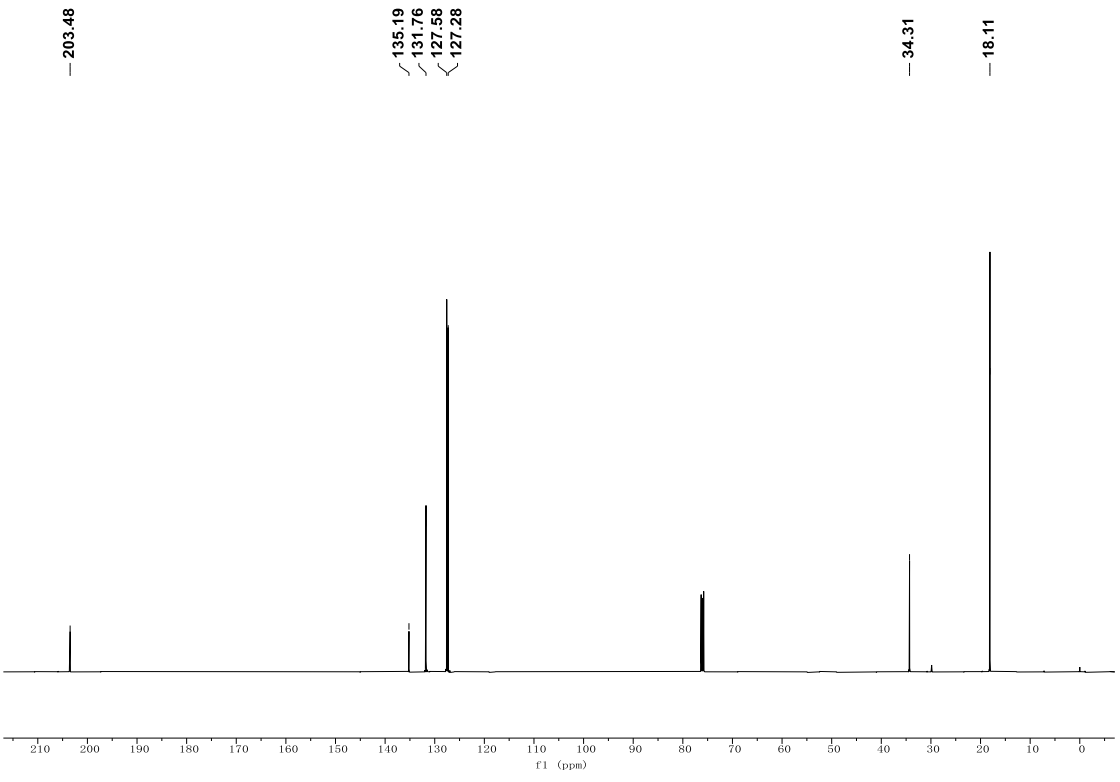

195.76
138.49
134.40
128.70
127.84
25.48
f1 (ppm)

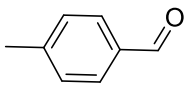


**13b**

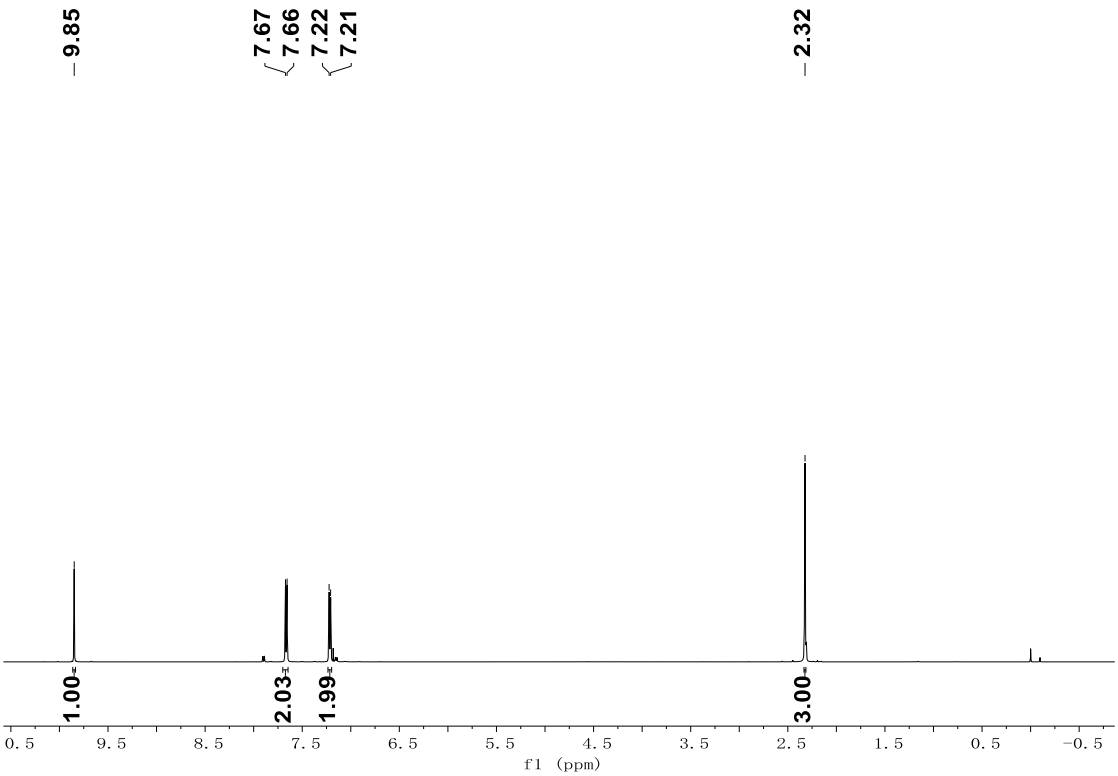

7.88
7.86
7.86
7.47
7.47
7.47
7.46
7.46
7.45
7.44
7.44
7.44
7.39
7.37
7.36
3.50
3.48
3.47
3.46
3.44
1.14
1.12

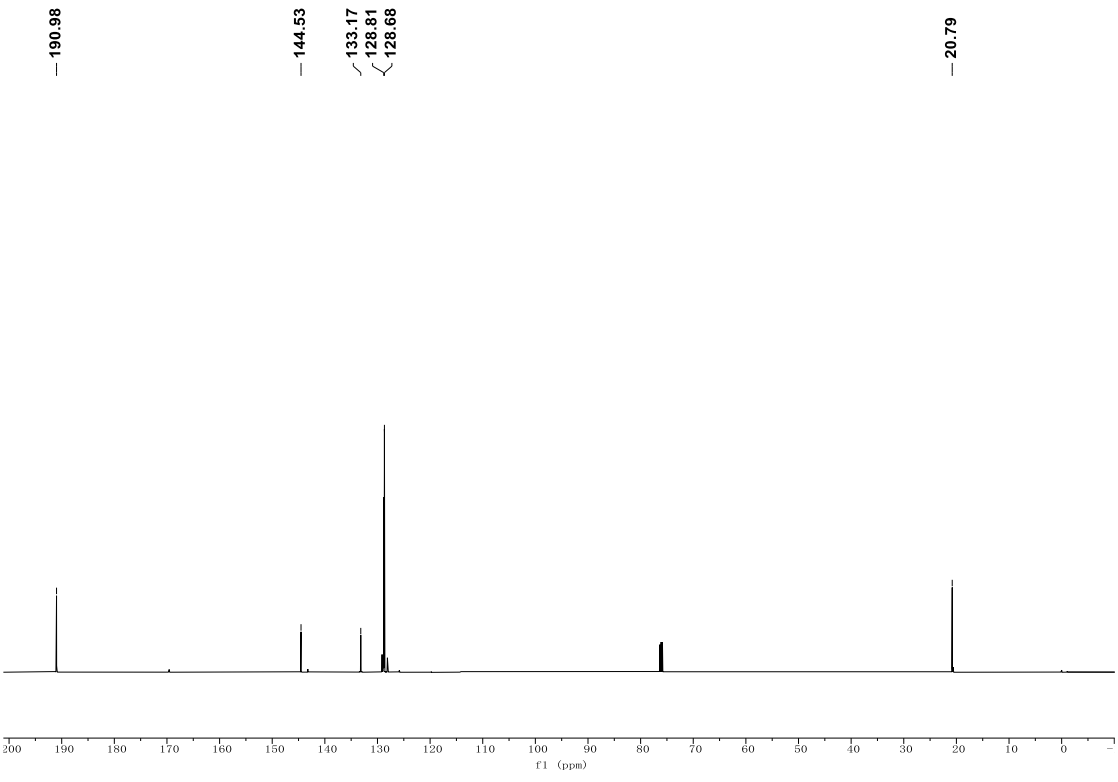

2.03
0.99
2.01
1.03
6.00
f1 (ppm)

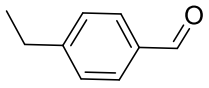

203.48
135.19
131.76
127.58
127.28
34.31
18.11
f1 (ppm)



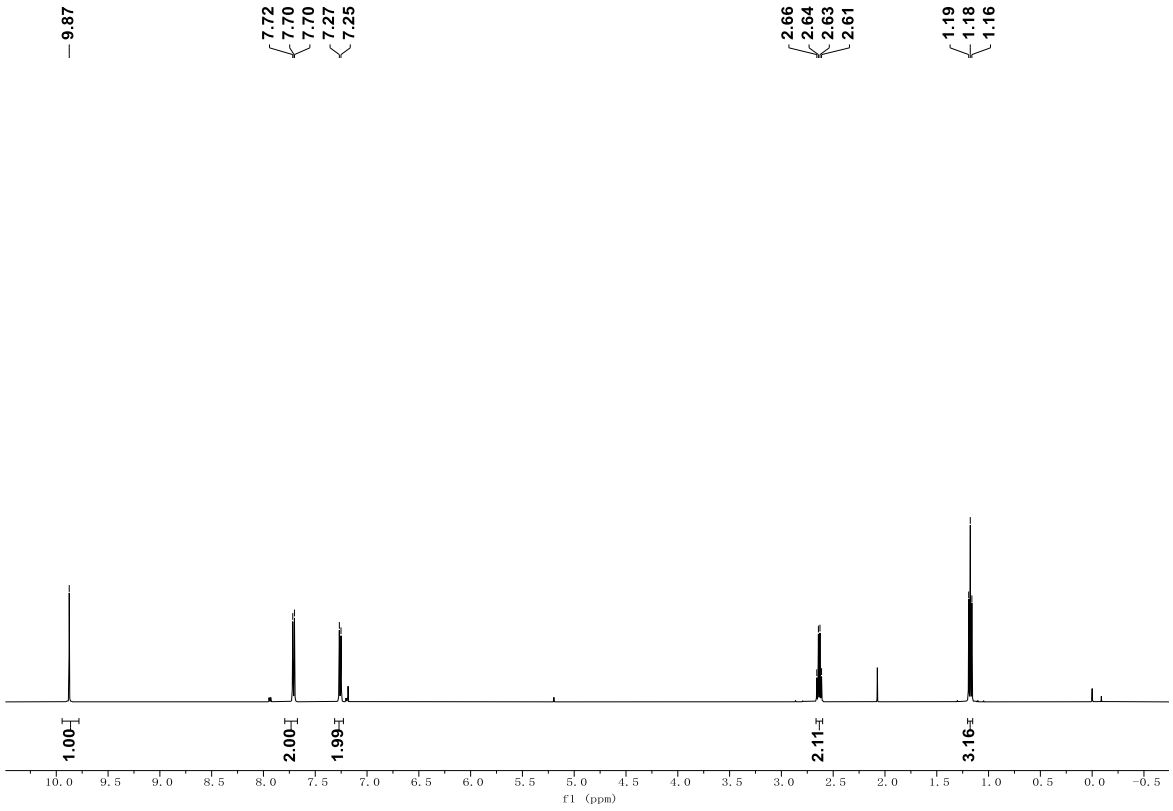
**14b**

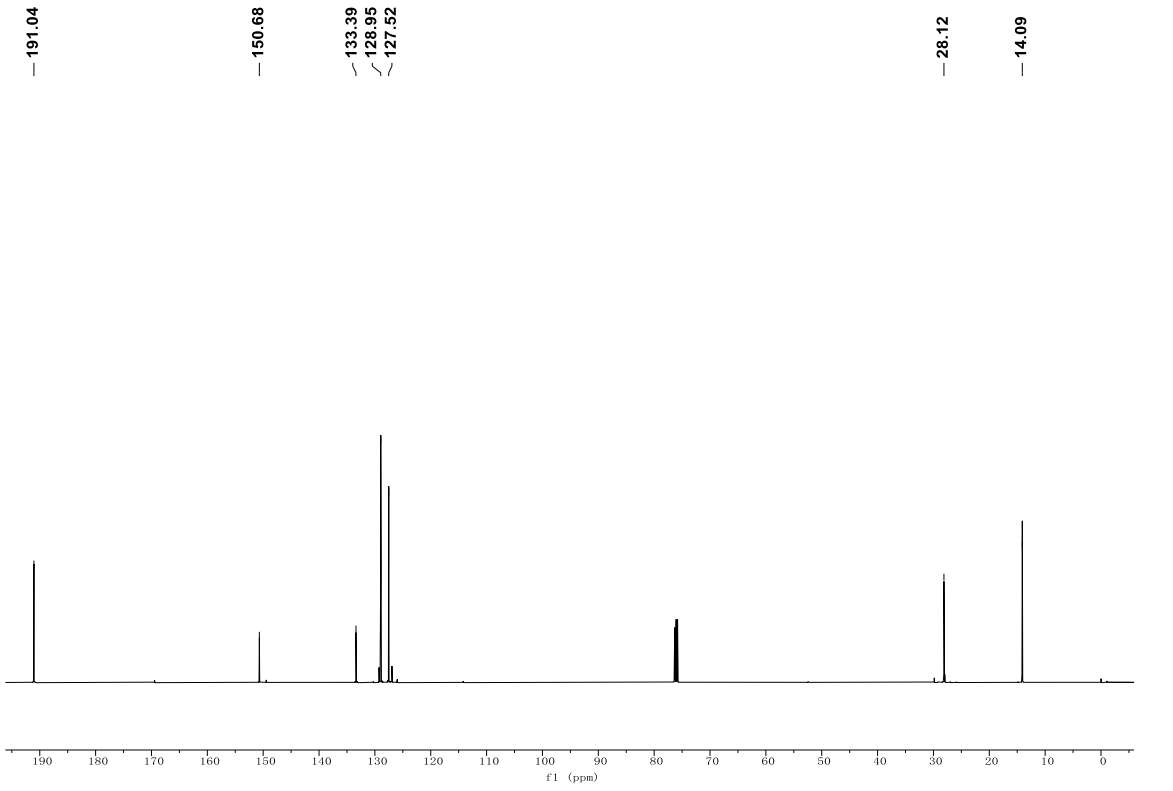

9.85
7.67
7.66
7.22
7.21
2.32
1.00
2.03
1.99
3.00
f1 (ppm)

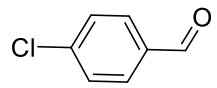

190.98
144.53
133.17
128.81
128.68
20.79
f1 (ppm)



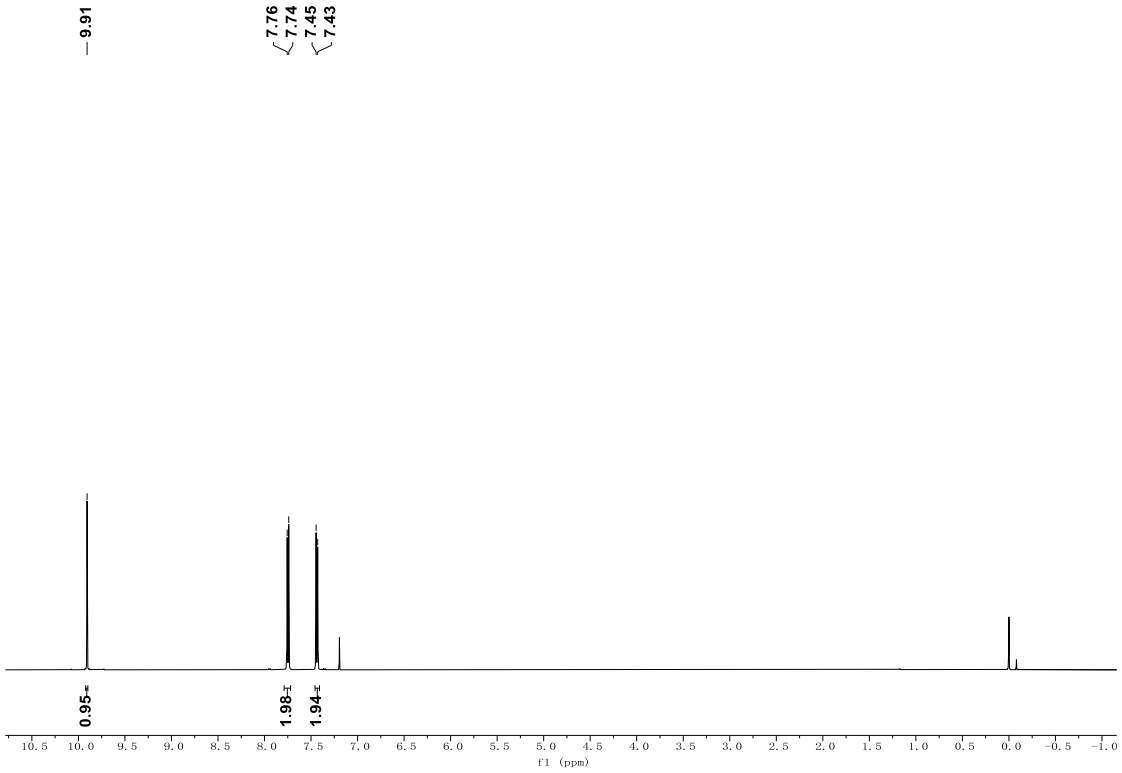
**15b**

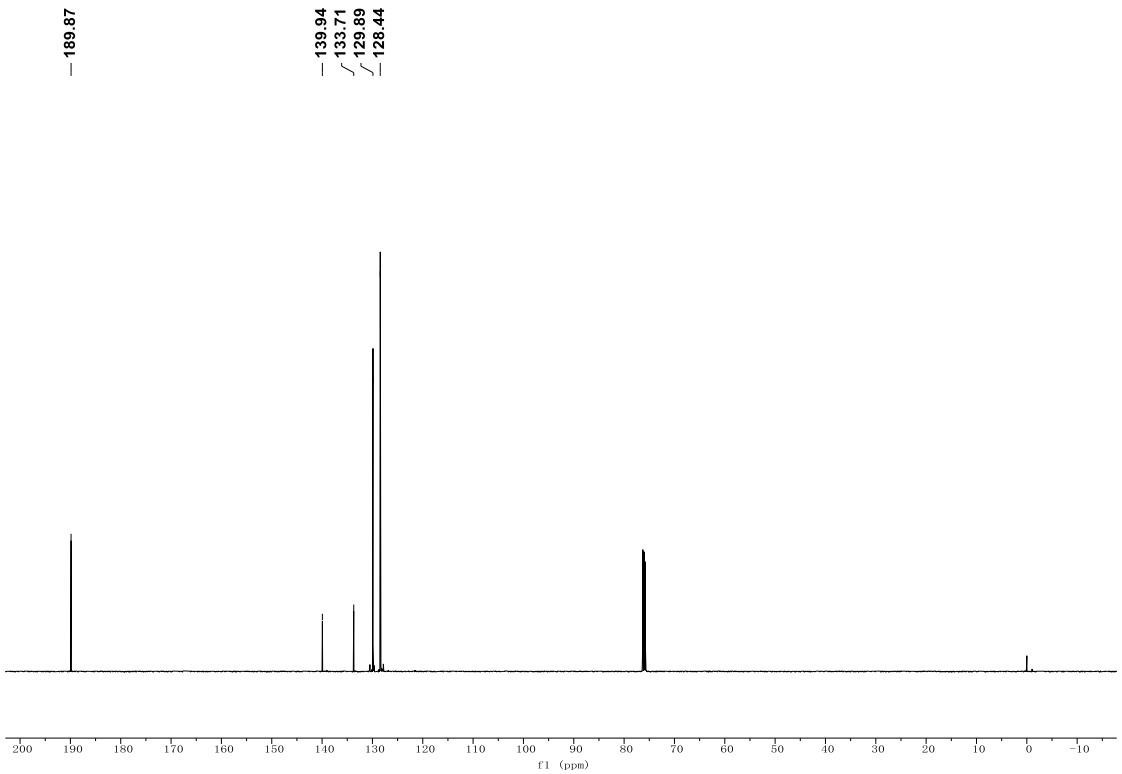

9.87
7.72
7.70
7.70
7.27
7.25
2.66
2.64
2.63
2.61
1.19
1.18
1.16
1.00
2.00
1.99
2.11
3.16
f1 (ppm)

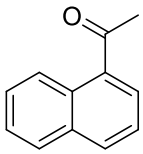

191.04
150.68
133.39
128.95
127.52
28.12
14.09
f1 (ppm)


Cl
O

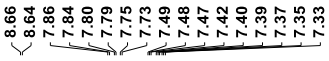
**16b**

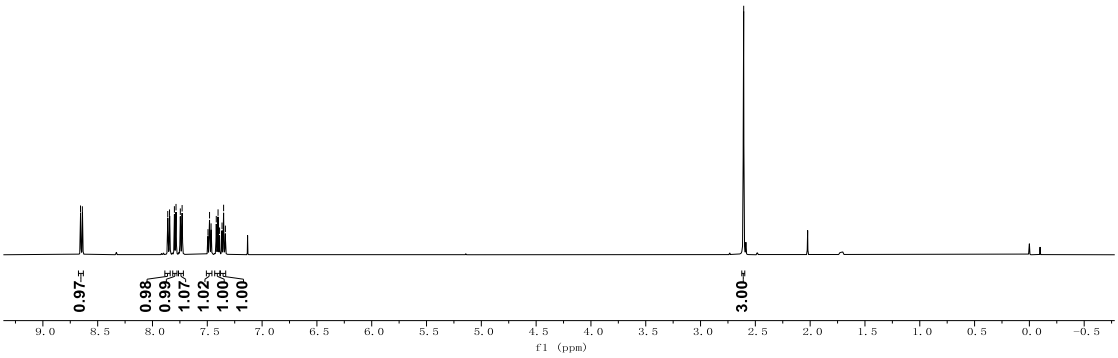

9.91
7.76
7.74
7.45
7.43
0.95
1.98
1.94
f1 (ppm)

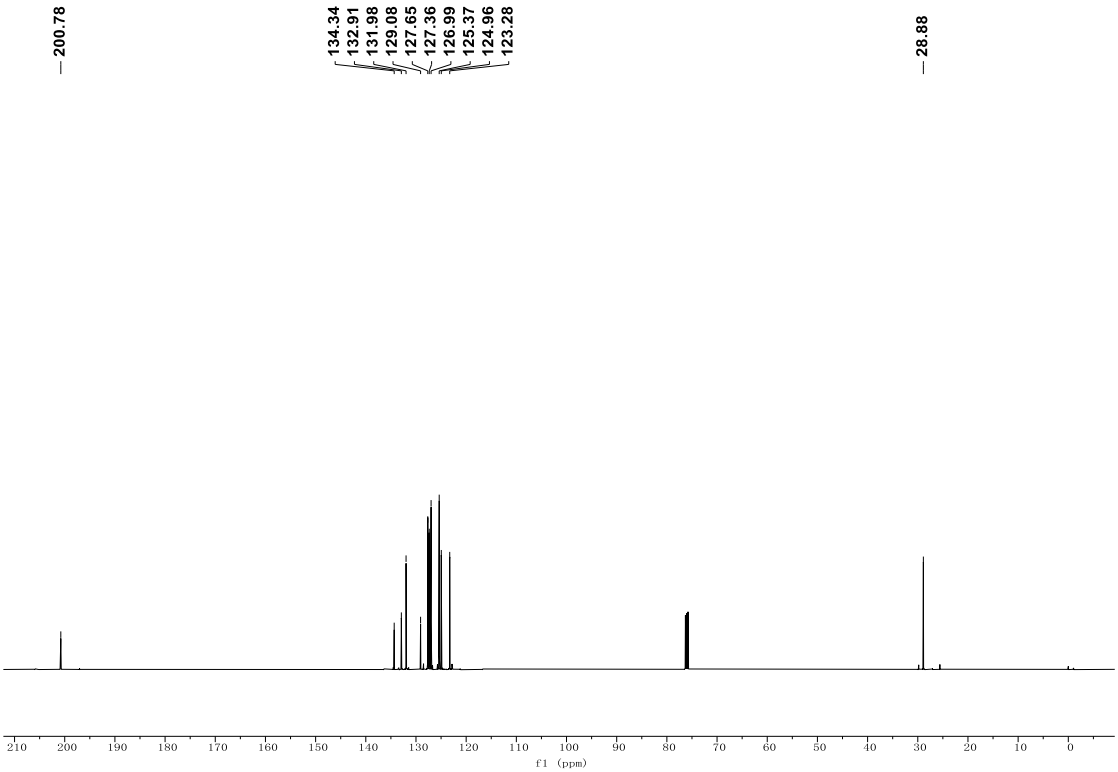

189.87
139.94
133.71
129.89
128.44
f1 (ppm)

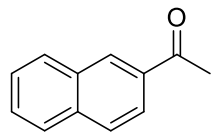


**17b**

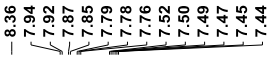

8.66
8.64
7.86
7.84
7.80
7.79
7.75
7.73
7.49
7.48
7.47
7.42
7.40
7.39
7.37
7.35
7.33
2.61


0.97
0.98
0.99
1.07
1.02
1.00
1.00
3.00
f1 (ppm)

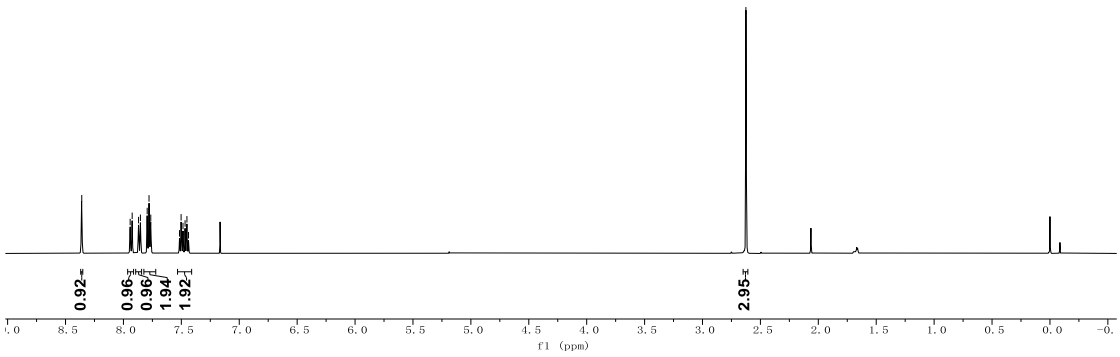

200.78
134.34
132.91
131.98
129.08
127.65
127.36
126.99
125.37
124.96
123.28
28.88
f1 (ppm)



**18b**

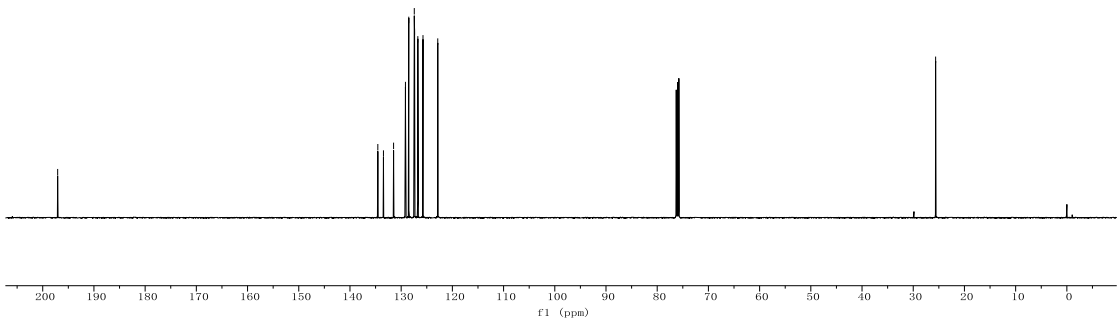

8.36
7.94
7.92
7.87
7.85
7.79
7.78
7.76
7.52
7.50
7.49
7.47
7.45
7.44

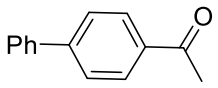

2.63


0.92
0.96
0.96
1.94
1.92
2.95
f1 (ppm)

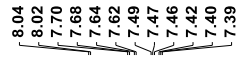

197.08
134.56
133.46
131.48
129.16
128.52
127.44
127.38
126.75
125.74
122.85


25.63

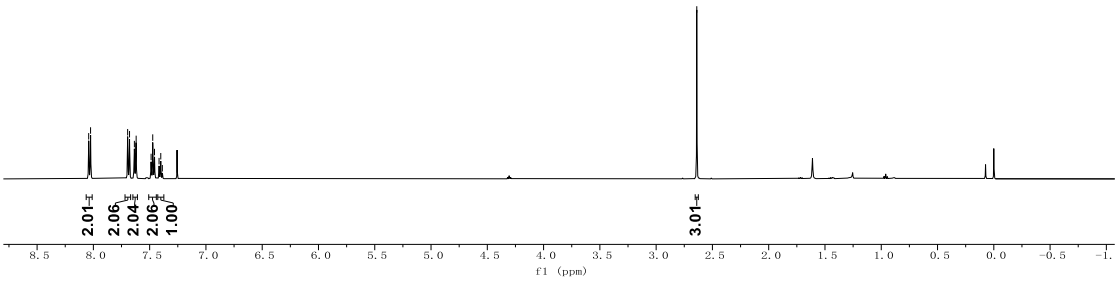

f1 (ppm)


Ph
O

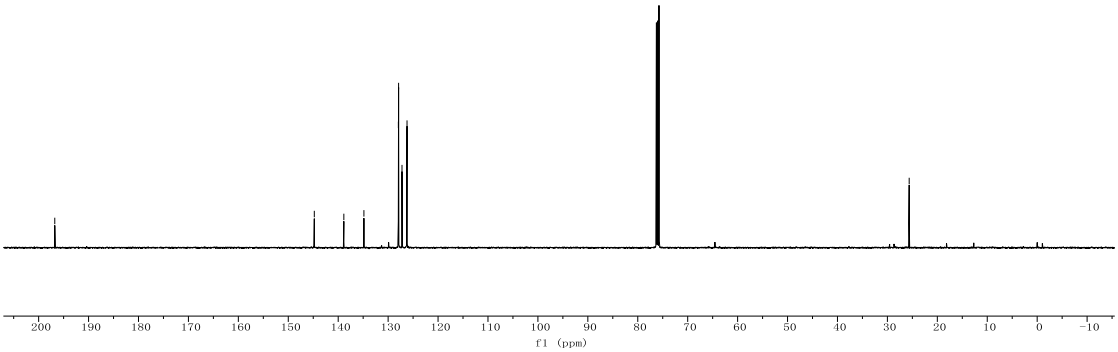
**19b**

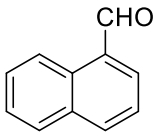

8.04
8.02
7.70
7.68
7.64
7.62
7.49
7.47
7.46
7.42
7.40
7.39


2.64


2.01
2.06
2.04
2.06
1.00
3.01
f1 (ppm)

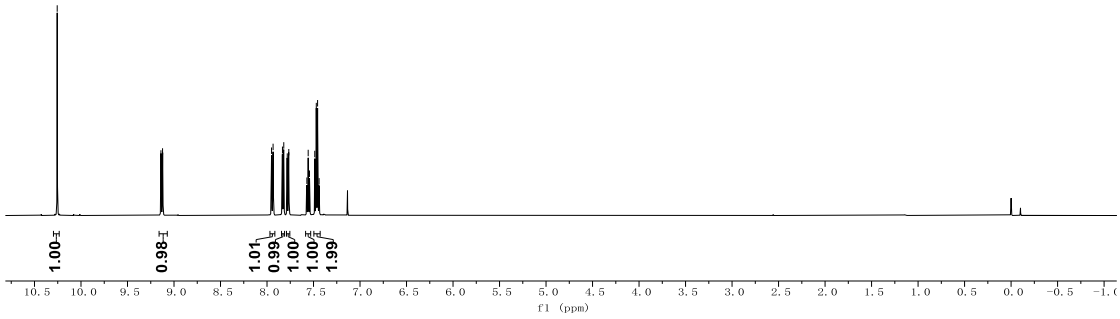

196.77
144.78
138.87
134.85
127.95
127.90
127.22
126.26
126.21
25.64


f1 (ppm)

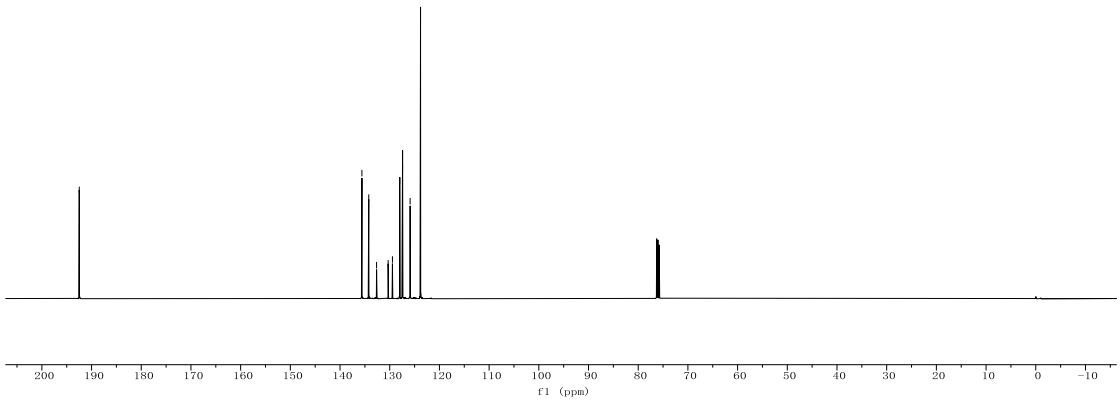

CHO

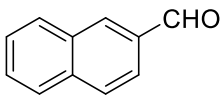
**20b**


10.26
9.14
9.12
7.95
7.93
7.83
7.82
7.78
7.77
7.57
7.56
7.54
7.49
7.47
7.46
7.44

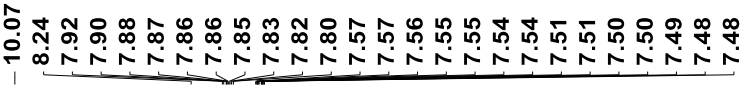

1.00
0.98
1.01
0.99
1.00
1.00
1.99
f1 (ppm)

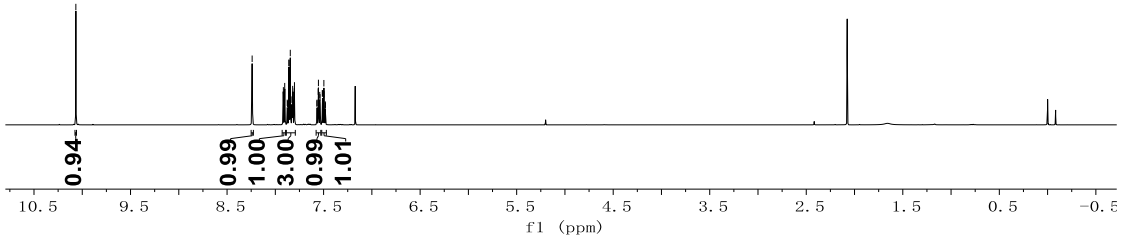

192.48
135.59
134.22
132.65
130.32
129.45
127.99
127.42
125.89
123.81

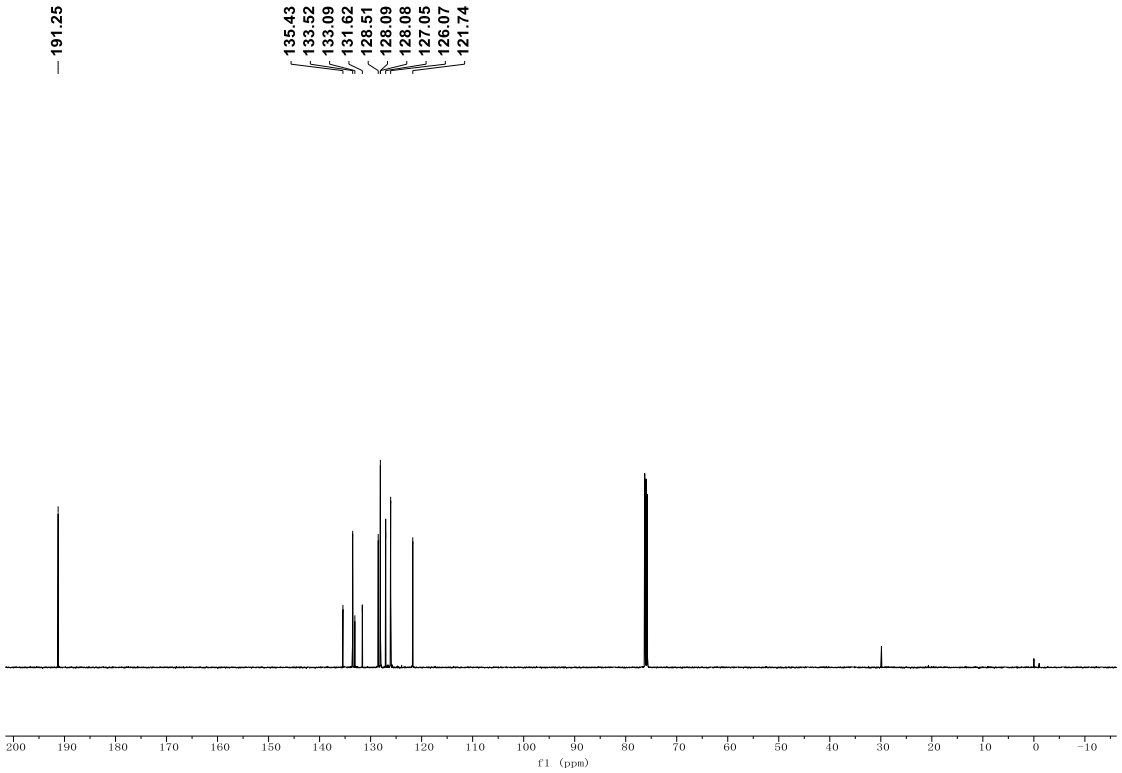

f1 (ppm)

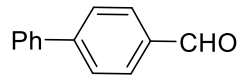

CHO

**21b**

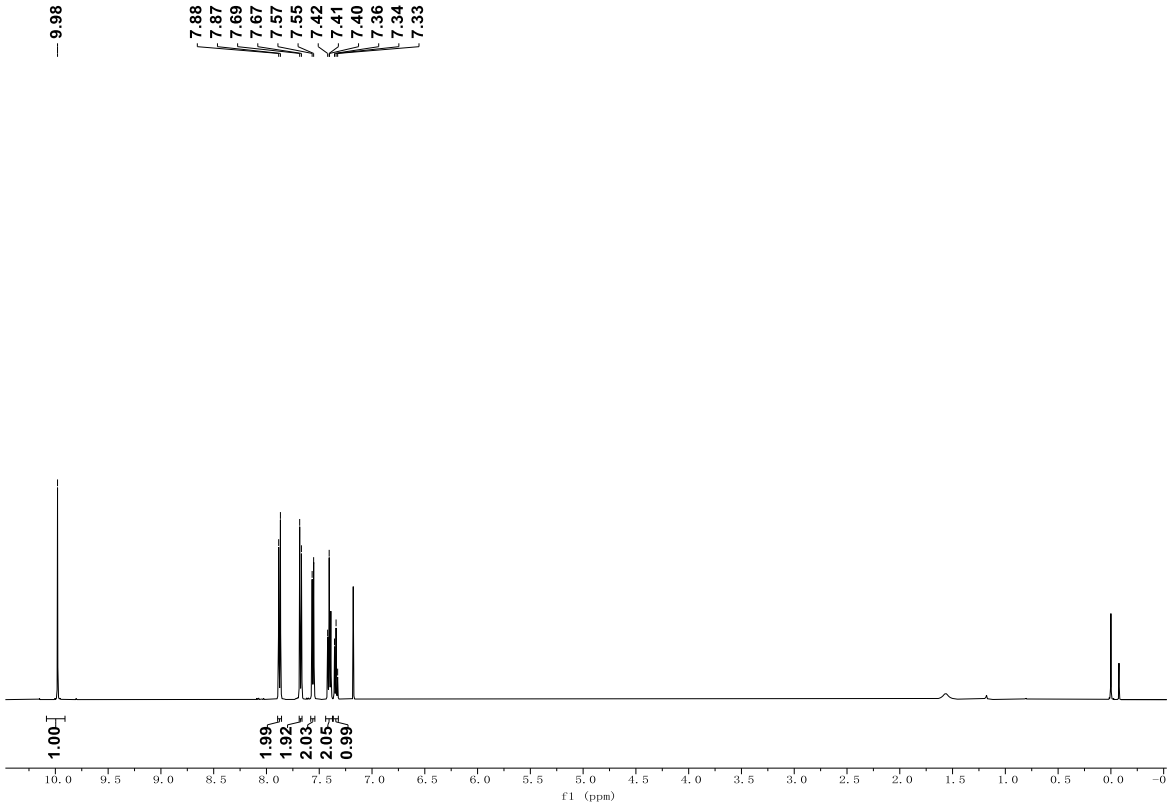

10.07
8.24
7.92
7.90
7.88
7.87
7.86
7.86
7.85
7.83
7.82
7.80
7.57
7.57
7.56
7.55
7.55
7.54
7.54
7.51
7.51
7.50
7.50
7.49
7.48
7.48

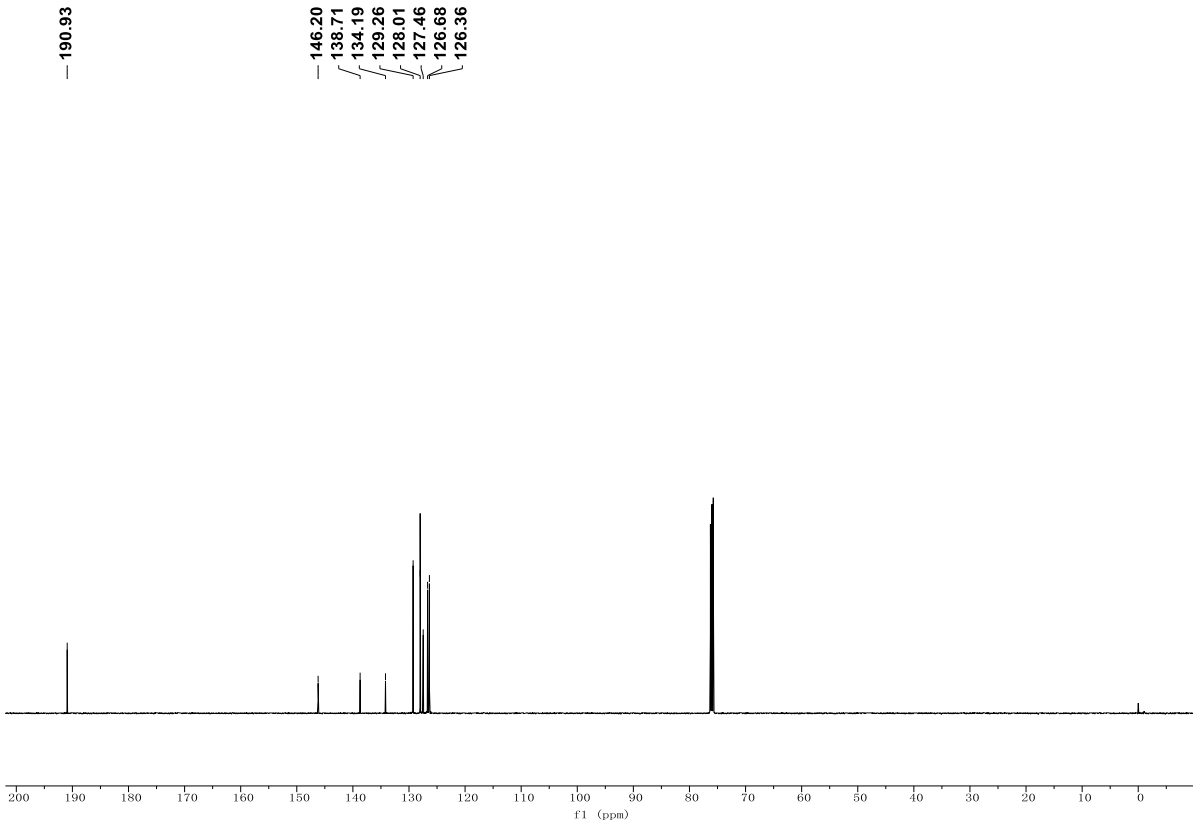

0.94
0.99
1.00
3.00
0.99
1.01
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

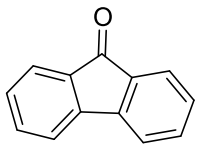

191.25
135.43
133.52
133.09
131.62
128.51
128.09
128.08
127.05
126.07
121.74
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Ph
CHO

**22b**

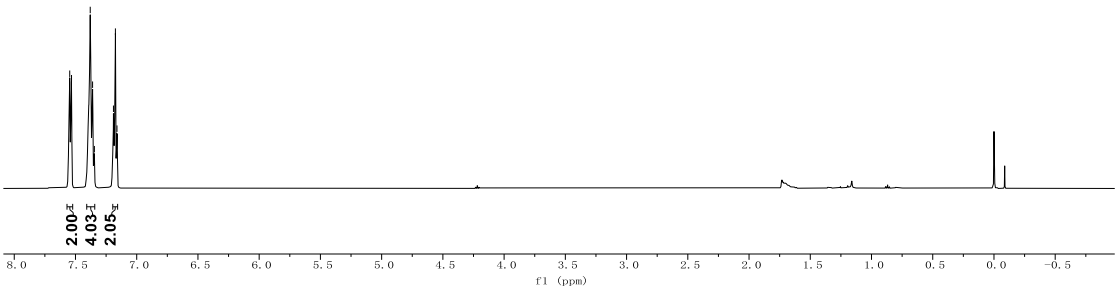

9.98
7.88
7.87
7.69
7.67
7.57
7.55
7.42
7.41
7.40
7.36
7.34
7.33
1.00
1.99
1.92
2.03
2.05
0.99
f1 (ppm)


190.93
146.20
138.71
134.19
129.26
128.01
127.46
126.68
126.36
f1 (ppm)

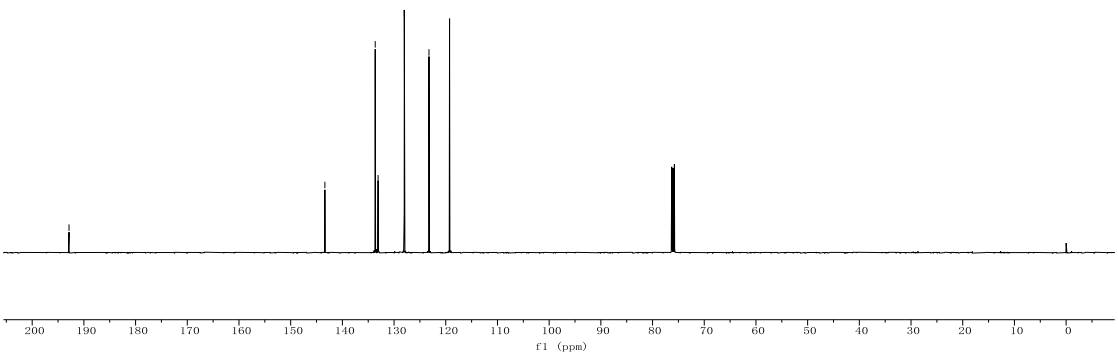


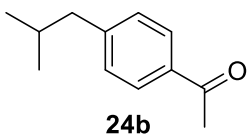
**23b**

7.55
7.53
7.38
7.36
7.35
7.19
7.19
7.17
7.16



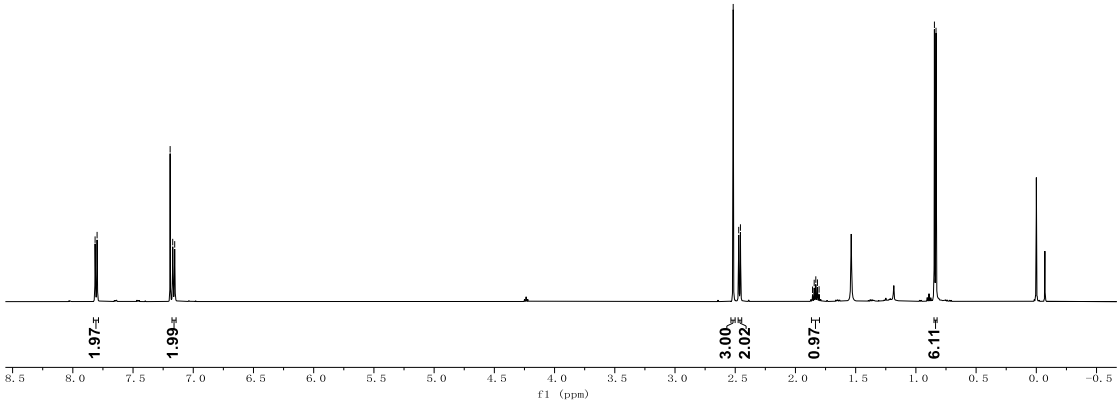

192.88
143.38
133.65
133.09
128.02
123.25
119.27



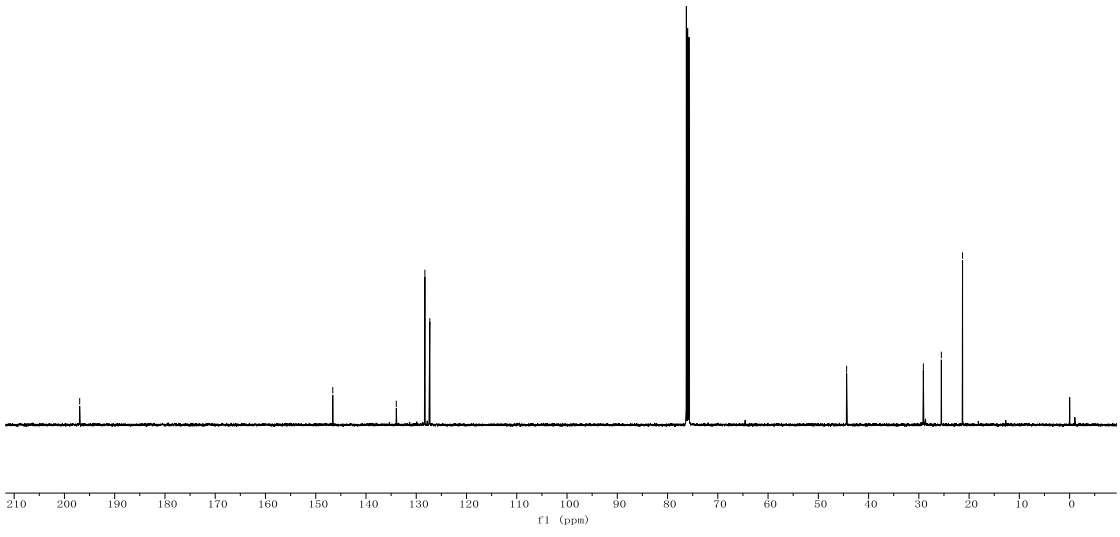


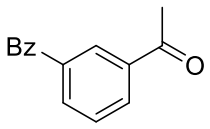
**24b**


7.82
7.80
7.19
7.17
7.15
2.52
2.47
2.46
1.86
1.84
1.83
1.82
1.80
0.85
0.83


1.97
1.99
3.00
2.02
0.97
6.11
f1 (ppm)

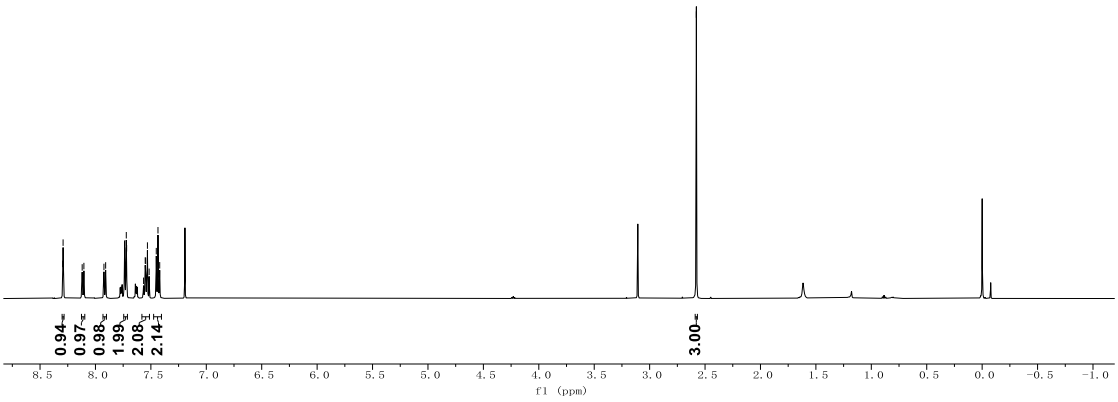

196.97
146.61
133.96
128.28
127.30
44.37
29.10
25.52
21.31


f1 (ppm)

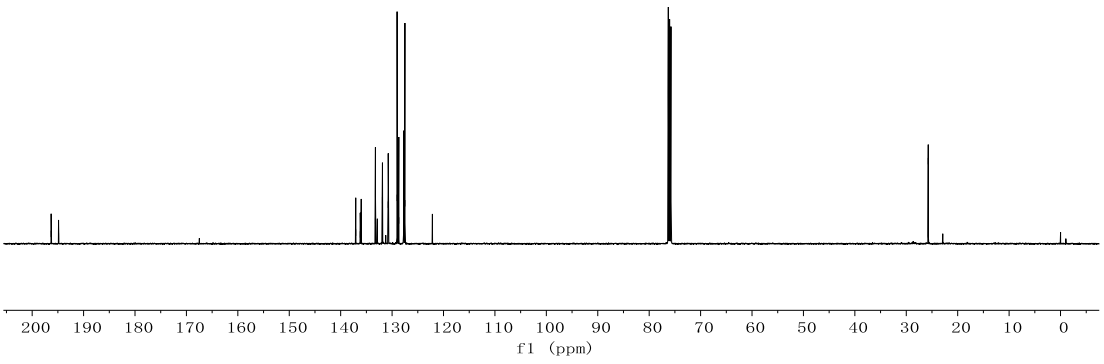

Bz
O

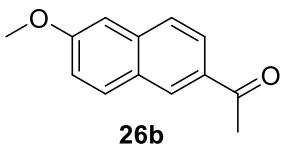
**25b**


8.30
8.29
8.29
8.12
8.10
7.92
7.91
7.74
7.74
7.72
7.72
7.57
7.55
7.55
7.53
7.52
7.45
7.44
7.42
2.58

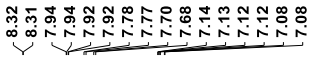

0.94
0.97
0.98
1.99
2.08
2.14
3.00
f1 (ppm)

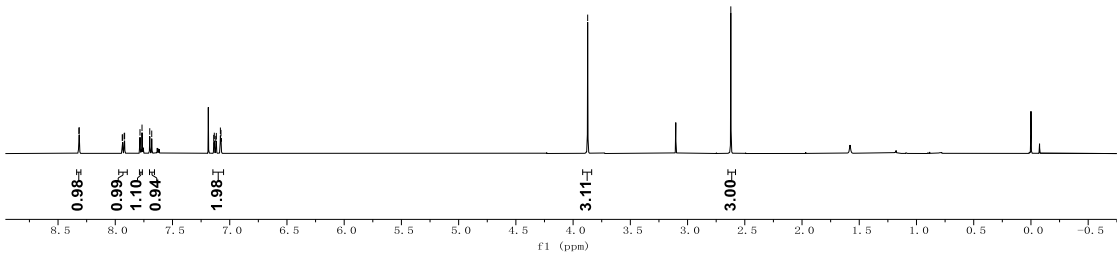

196.31
194.87
137.07
136.19
136.00
133.24
131.88
130.75
129.03
128.69
127.74
127.51
25.73


f1 (ppm)

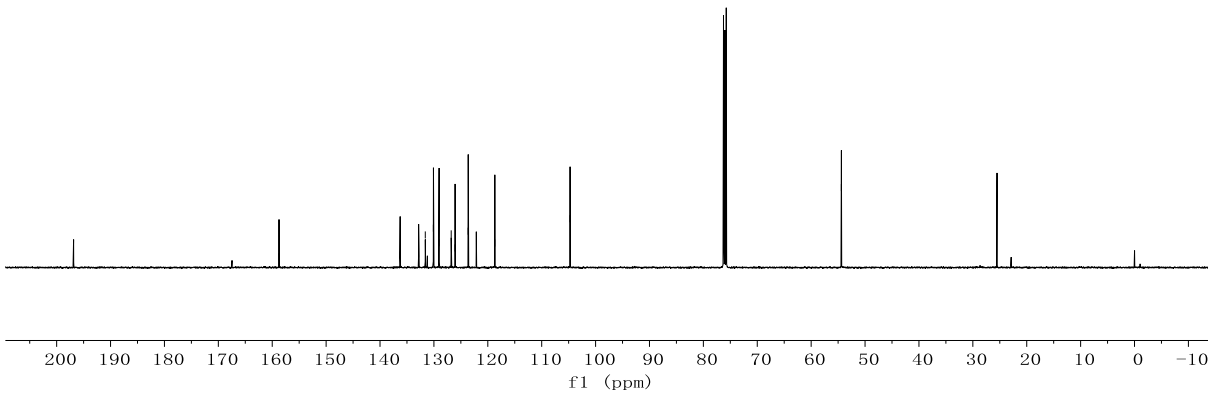


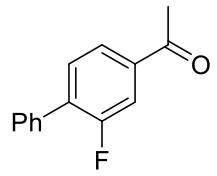
**26b**


8.32
8.31
7.94
7.94
7.92
7.92
7.78
7.77
7.70
7.68
7.14
7.13
7.12
7.12
7.08
7.08
3.87
2.62

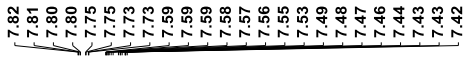

0.98
0.99
1.10
0.94
1.98
3.11
3.00
f1 (ppm)


196.88
158.75
136.27
131.60
130.10
129.05
126.79
126.08
123.64
118.71
104.74
54.39
25.51

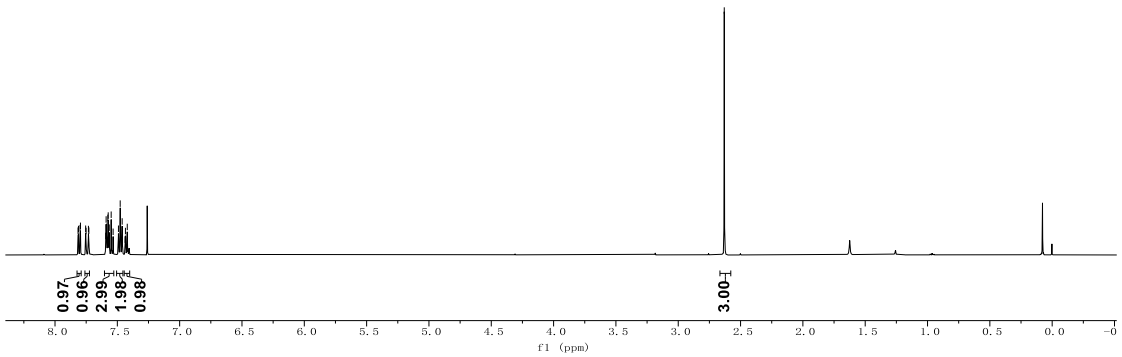

f1 (ppm)

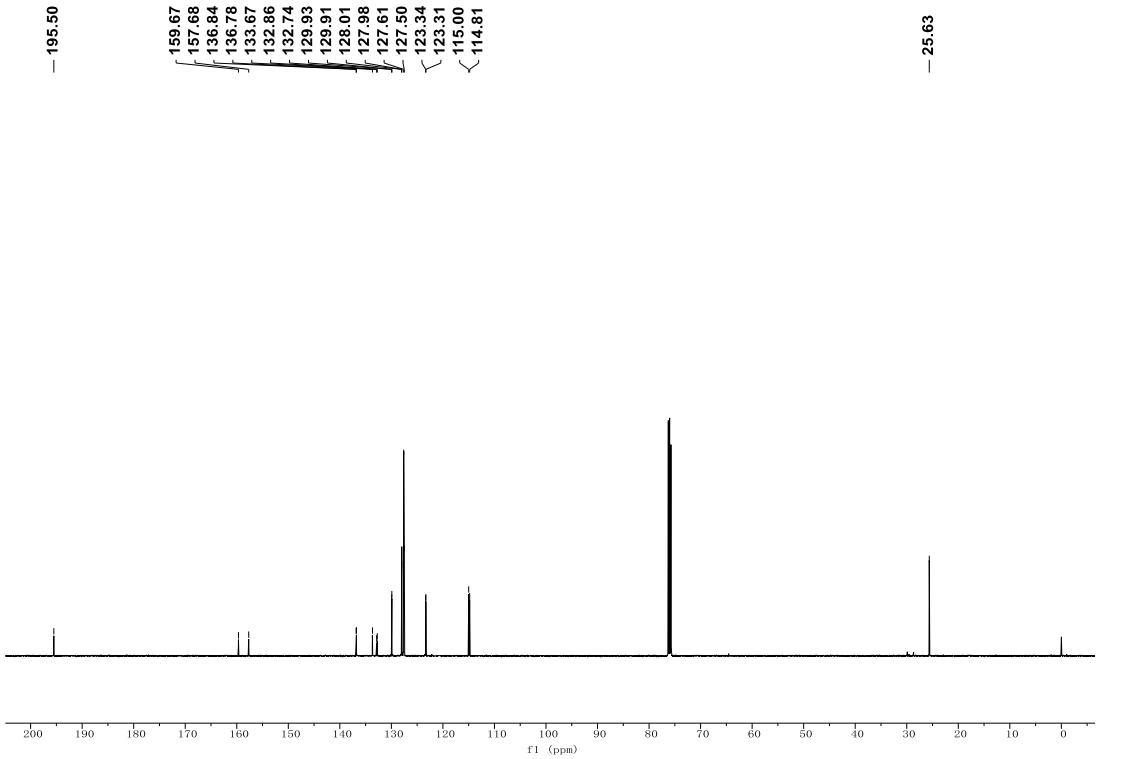

O
Ph
F

**27b**


7.82
7.81
7.80
7.80
7.75
7.75
7.73
7.73
7.59
7.59
7.59
7.58
7.57
7.56
7.55
7.53
7.49
7.48
7.47
7.46
7.44
7.43
7.43
7.42


2.63


0.97
0.96
2.99
1.98
0.98
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


195.50
159.67
157.68
136.84
136.78
133.67
132.86
132.74
129.93
129.91
128.01
127.98
127.61
127.50
123.34
123.31
115.00
114.81
25.63
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)