Supporting Information

Metal-free, 2-MeTHF mediated C(sp)–H functionalization of alkynes with anilines to access diaryl 1,2-diketones bearing lower E-factors†

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1. Experimental Section

1.1. General Information

All starting materials and commercial reagent were purchased from Alfa Aesar, Sigma Aldrich, Avra, Spectrochem, TCI. Thin Layer Chromatography plates were visualized by exposure to ultraviolet light (UV) with 254 nm of wavelength and then further analyzed by using iodine chamber. Thin-layer chromatography was performed using pre-coated plates. Column chromatography was performed in 120 to 200 mesh size silica gel. The reactions were carried out in round bottom flask and sealed tube. Crude product was examined by SIMADZU GC-MS (Selected Ion Monitoring) and all NMR spectra were recorded by Bruker Avance 400 spectrometer (^{1}H at 400 MHz and ^{13}C at 100 MHz). Chemical shifts for ^{1}H NMR spectra have been reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Simillarly, ^{13}C NMR spectra have been reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: δ 77.0 ppm). The ^{1}H NMR and ^{13}C NMR of the known products were compared with literature reports.

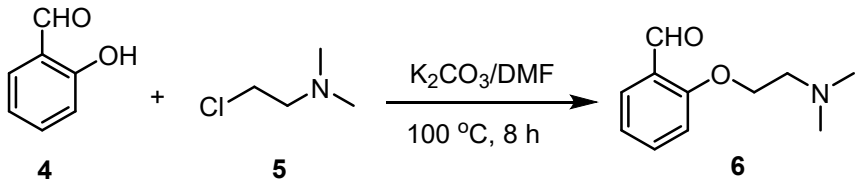
1.2. General procedure for the synthesis of α-diketones (3)

In a 25 mL sealed tube, arylacetylene (**1**, 1 mmol) and aniline (**2**, 1.2 mmol) was added with the mixture of *tert*-butyl nitrite (1.2 equiv.), ascorbic acid (2 equiv.) in 2 mL of 2-MeTHF. The reactions mixture was then stirred under oxygen balloon atmosphere at 50 ℃ for 4 hours. Reaction was monitoring by TLC, after completion of reaction, reaction mass was quenched with EtOAc (3 x 10mL) and then combined organic phase was washed with distilled water (2 x 15mL) and dried over anhydrous $NaSO_4$ followed by concentrating under reduced pressure. Finally, the crude product was purified by column chromatography on silica gel (EtOAc: *n*-Hexane) to afford the desired benzil compounds **3** (up to 87% yield).

1.3. Synthesis of Trifenagrel drug (7)

Step-I

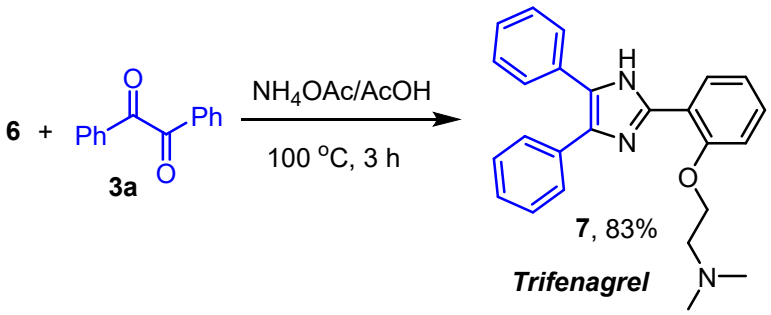
***Synthesis of intermediate* 6**



In a 25mL round bottom flask **4** (244 mg, 2 mmol) was charged in 6 mL dry DMF under N_2 atmosphere followed by K_2CO_3 (828 mg, 6 mmol) was added and stirred the solution until yellow colour was disappeared. After that **5** (428 mg, 4 mmol) was adding to the reaction mixture and stirrer the reaction at 100^0C for 8 hours. After completion of reaction, DMF was removed by ice cold water and the mixture was diluted with DCM (3 X 10 mL) washed the combined organic layer by cold water (3 X 5 mL). Extracted DCM layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (Hexane/EtOAc = 1:2) to isolate 250 mg off white solid of **6** (65% yield).

Step-II

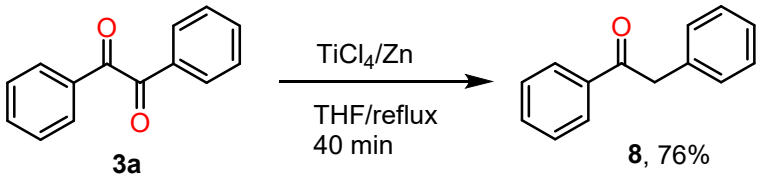
Synthesis of Trifenagrel



In a 15 mL round bottom flask **6** (193 mg, 1 mmol), benzil (210 mg, 1 mmol), NH_4OAc (770 mg, 10 mmol) were charged in 4 mL acetic acid and stirred the reaction mixture at 100^0C for 3h. After completion of the reaction, the mixture was diluted with EtOAc (3 X 10mL) and washed the combined organic layer by saturated sodium bicarbonate aqueous solution (2 X 5mL). Extracted ethyl acetate layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure.

The crude product was purified by column chromatography on silica gel (Hexane/EtOAc = 4:1) to isolate 317 mg white solid of trifenagrel (83% yield).

1.4. Preparation of 2-phenyl acetophenone (8)[1]



In a two neck 15 mL round bottom flask was charged 4 mL of anhydrous THF and Zn-powder (195 mg, 3 mmol) under N_2 atmosphere at room temperature. After a few minutes, $TiCl_4$ (0.3 mL, 1.5 mmol) was slowly added to the suspension of Zn-THF mixture and stirred the reaction mixture at 67^0C for 2 hours, then cold the reaction mixture to room temperature. After that the solution of benzil (105 mg, 0.5 mmol) in 3 mL anhydrous THF was added dropwise to the suspended solution under inert atmosphere and mixture was continuously stirred at room temperature, progress was monitored by TLC and conversion was completed within 15 minutes. After completion of the reaction, the mixture was quenched with diluted HCl and the mixture was diluted with DCM (3 X 10 mL) washed the combined organic layer by cold water (3 X 5 mL). Extracted DCM layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (Hexane/EtOAc = 30:1) to isolate 60 mg orange yellow solid of **8** (76% yield).

1.5. E-factor (E) calculations:[#]

E = *m* (starting/waste materials) – *m* (product)/ *m* (product)

For **3a**: E = [0.102 g (**1a**) + 0.111 g (**2a**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.3 g (silica gel) – 0.182 g (product × yield)] /0.182 g = 12.67

For **3b**: E = [0.116 g (**1b**) + 0.111 g (**2a**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.3 g (silica gel) – 0.168 g (product × yield)] /0.168 g = 13.89

For **3c**: E = [0.136 g (**1c**) + 0.111 g (**2a**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.3 g (silica gel) – 0.190 g (product × yield)] /0.190 g = 12.27

For **3d**: E = [0.181 g (**1d**) + 0.111 g (**2a**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.3 g (silica gel) – 0.208 g (product × yield)] /0.208 g = 11.58

For **3e**: E = [0.181g (**1e**) + 0.111 g (**2a**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.4 g (silica gel) – 0.194 g (product × yield)] /0.194 g = 12.75

For **3f**: E = [0.158 g (**1f**) + 0.111 g (**2a**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.3 g (silica gel) – 0.173 g (product × yield)] /0.173 g = 14.00

For **3g**: E = [0.102 g (**1a**) + 0.128 g (**2b**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.3 g (silica gel) – 0.152 g (product × yield)] /0.152 g = 15.81

For **3h**: E = [0.102 g (**1a**) + 0.152 g (**2c**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.3 g (silica gel) – 0.185 g (product × yield)] /0.185 g = 12.67

For **3i**: E = [0.102 g (**1a**) + 0.206 g (**2d**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.3 g (silica gel) – 0.199 g (product × yield)] /0.199 g = 12.23

For **3j**: E = [0.102 g (**1a**) + 0.206 g (**2e**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.4 g (silica gel) – 0.191 g (product × yield)] /0.191 g = 13.05

For **3k**: E = [0.116 g (**1c**) + 0.128 g (**2b**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.3 g (silica gel) – 0.161 g (product × yield)] /0.161 g = 14.96

For **3l**: E = [0.116 g (**1b**) + 0.152 g (**2c**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.3 g (silica gel) – 0.188 g (product × yield)] /0.188 g = 12.53

For **3m**: E = [0.116 g (**1b**) + 0.206 g (**2d**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.3 g (silica gel) – 0.212 g (product × yield)] /0.212 g = 11.49

For **3n**: E = [0.116 g (**1b**) + 0.178 g (**2f**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.3 g (silica gel) – 0.179 g (product × yield)] /0.179 g = 13.63

For **3o**: E = [0.136 g (**1d**) + 0.152 g (**2c**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.3 g (silica gel) – 0.206 g (product × yield)] /0.206 g = 11.44

For **3p**: E = [0.136 g (**1d**) + 0.206 g (**2e**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.3 g (silica gel) – 0.216 g (product × yield)] /0.216 g = 11.35

For **3q**: E = [0.136 g (**1d**) + 0.178 g (**2f**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.4 g (silica gel) – 0.195 g (product × yield)] /0.195 g = 13.05

For **3r**: E = [0.158 g (**1g**) + 0.128 g (**2b**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.4 g (silica gel) – 0.174 g (product × yield)] /0.174 g = 14.29

For **3s**: E = [0.158 g (**1g**) + 0.152 g (**2c**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.3 g (silica gel) – 0.207 g (product × yield)] /0.207 g = 11.49

For **3t**: E = [0.158 g (**1g**) + 0.206 g (**2e**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.4 g (silica gel) – 0.221 g (product × yield)] /0.221 g = 11.62

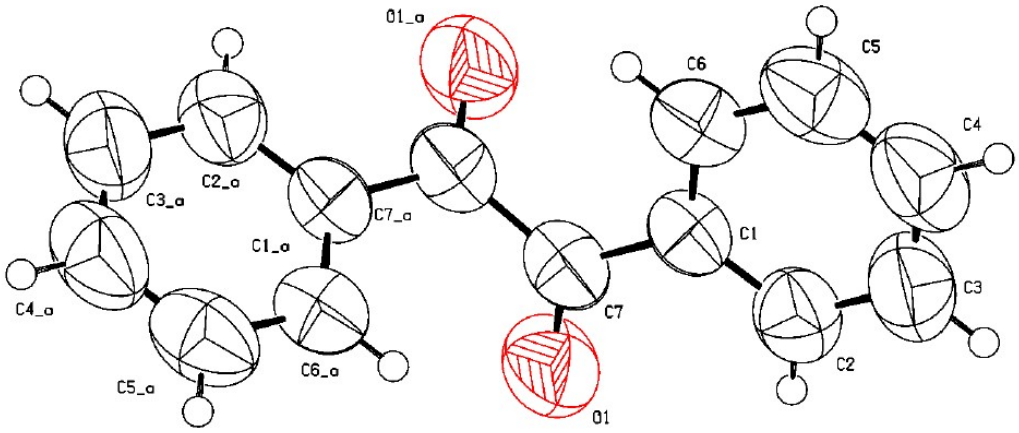
For **3u**: E = [0.181 g (**1f**) + 0.178 g (**2f**) + 0.124 g + 0.352 g + 0.550 g (Na_2SO_4) + 1.4 g (silica gel) – 0.207 g (product × yield)] /0.207 g = 12.45

For **3v**: E = [0.155 g (**1d**) + 0.111 g (**2b**) + 0.124 g + 0.352 g + 0.500 g (Na_2SO_4) + 1.5 g (silica gel) – 0.152 g (product × yield)] /0.152 g = 17.03

[#](The eluent, *n*-hexane and ethyl acetate was recovered and reused for the column chromatography; the amount of water used in the work-up procedure is not accounted)

2. Characterization data

2.1. X-ray crystallographic data for 3a:



ORTEP diagram for the structure 1,2-diphenylethane-1,2-dione **3a**

Wavelength	0.71073
Moiety formula	$C_{14}H_{10}O_2$
Crystal system	Monoclinic
Space group	P 32 2 1
Unit cell dimensions	a=8.415(1) b=8.415(1) c=13.689(2)
	α=90 β=90 γ=120
Volume	839.5(2)
Z	3
R-factor (%)	4.94

The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication with a CCDC reference number CCDC **2237333**.

2.2. GC-MS spectra and data:

ICT-IOC GCMS DATA

Test Date : Sep/16/2022 13:48

Sample Information

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Sample ID	: SB-478_01
Vial #	: 12
Injection Volume	: 1.00
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Org Method File	: D:\SWADHA_01\EI_METHOD SIM.qgm
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Modified	: 9/16/2022 1:46:56 PM

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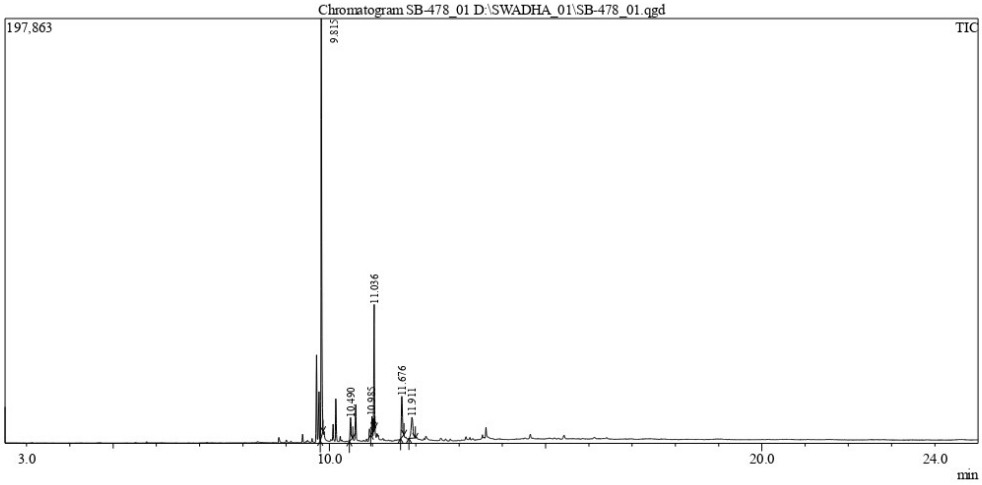

Peak Report TIC

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2	10.490	10.460	10.540	16127	4.37	10573	3.55	1.53	MI	
3	10.985	10.960	11.015	6135	1.66	8076	2.72	0.76	MI	
4	11.036	11.020	11.055	54474	14.77	55135	18.54	0.99	MI	
5	11.676	11.645	11.725	31058	8.42	18995	6.39	1.64	MI	
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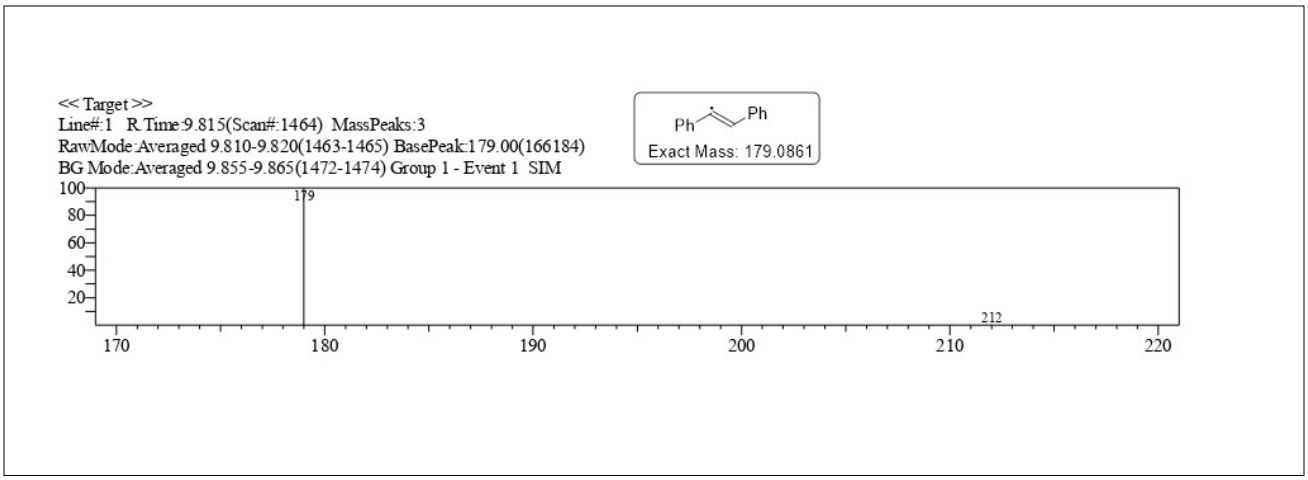
Library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Ph
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40
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179
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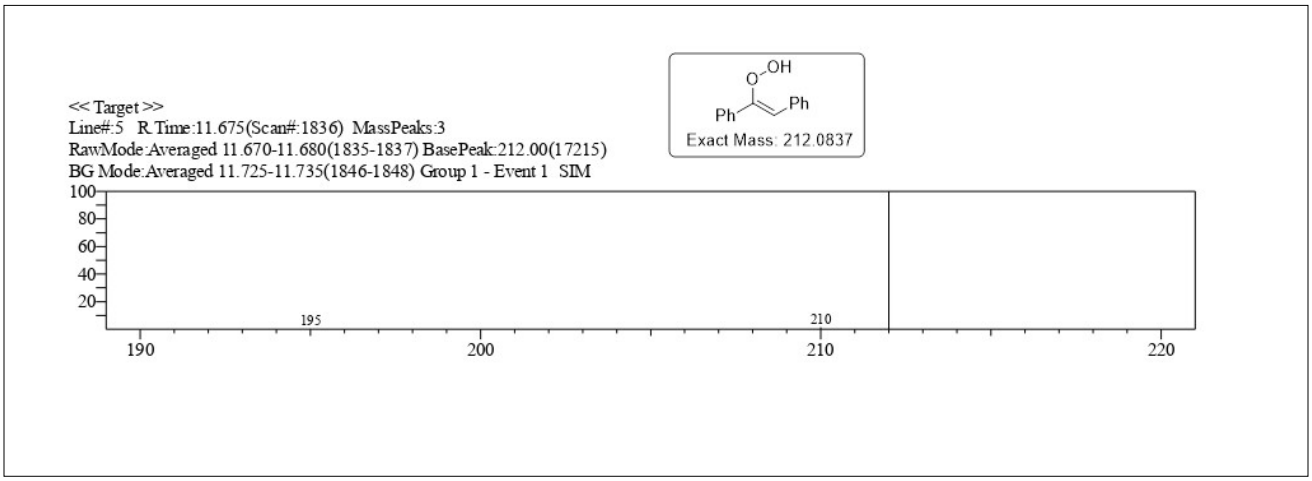
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Ph
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60
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20
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210
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210
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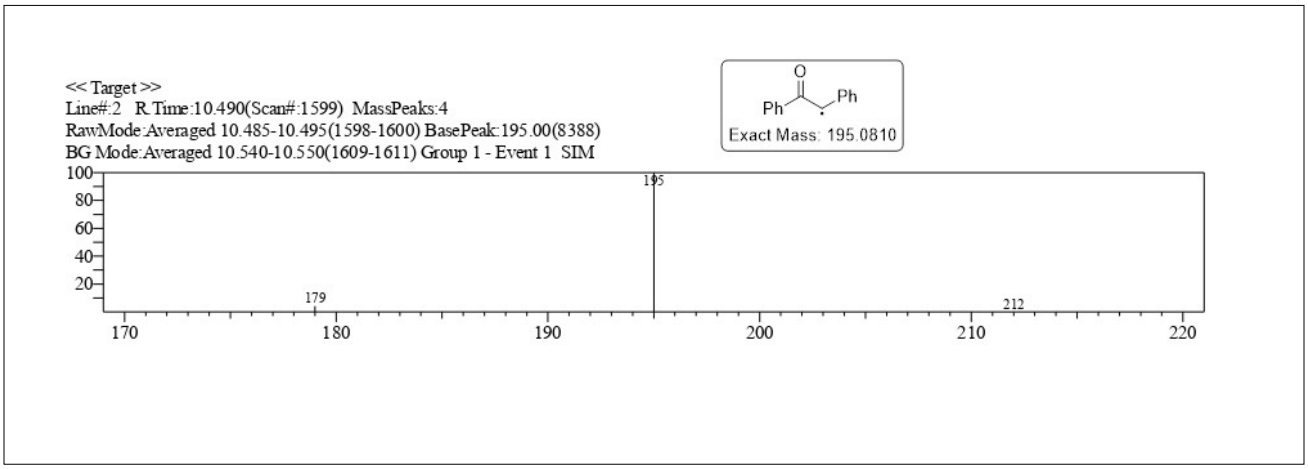
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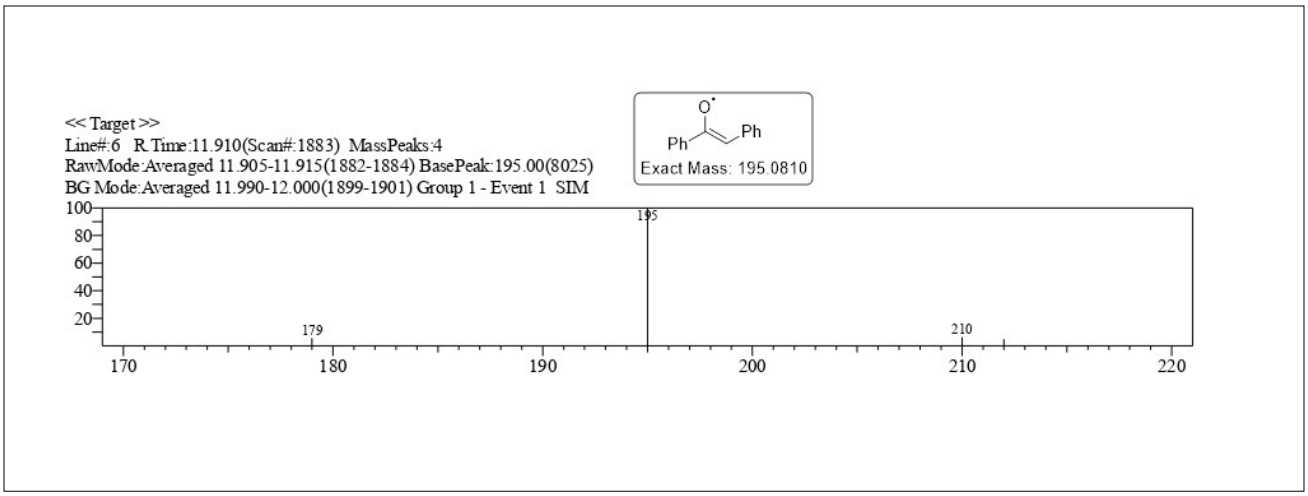
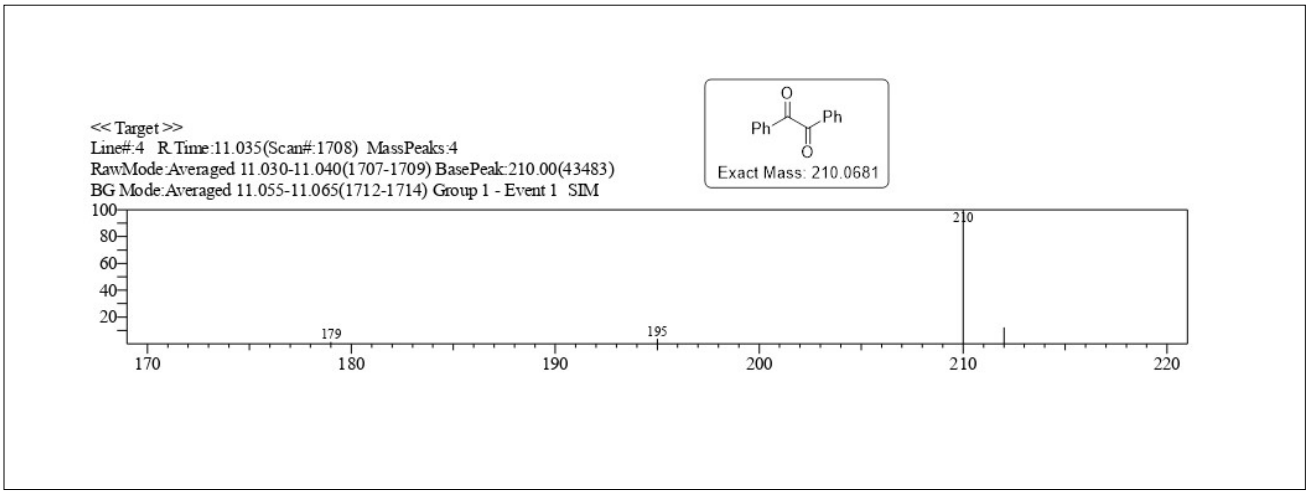
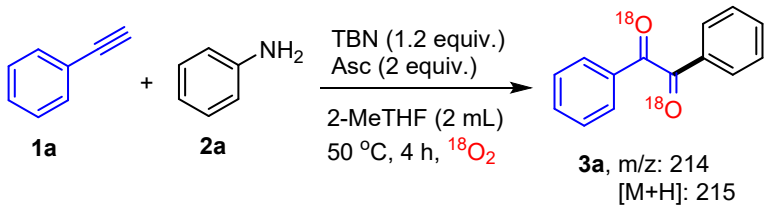


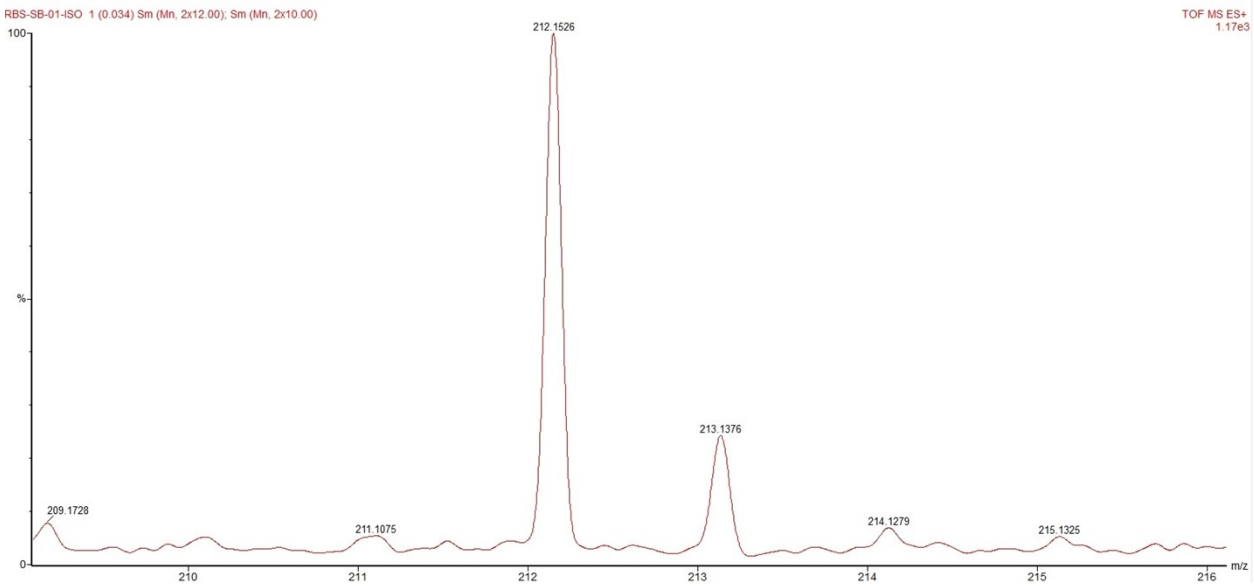


2.3. Isotopic labelling experiments with $^{18}O_2$:

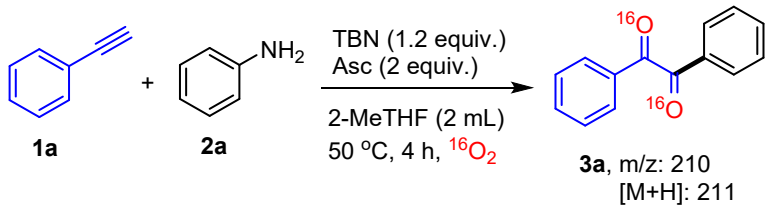


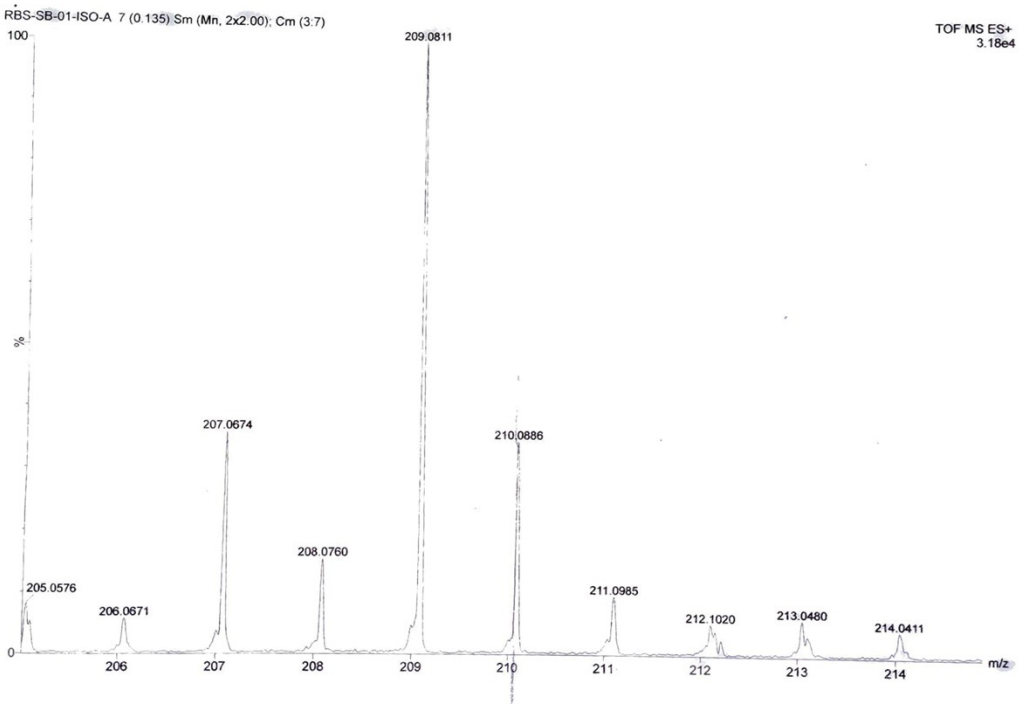
1a + **2a**

3a, m/z: 214
[M+H]: 215



Scheme 1. MS spectrum of ^{18}O-Labeling **3a**





2.4. ^{1}H and ^{13}C data of compounds:

benzil (3a)

Yellow solid (87%, 182 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 6.7 Hz, 4H), 7.62 (s, 2H), 7.49 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.64, 134.95, 133.01, 129.89, 129.07.

1-phenyl-2-(p-tolyl)ethane-1,2-dione (3b)

Yellow solid (75%, 168 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.79, 194.33, 146.24, 134.80, 133.12, 130.61, 130.04, 129.91, 129.76, 128.99, 21.94.

1-(4-chlorophenyl)-2-phenylethane-1,2-dione (3c)

Yellow solid (78%, 175 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 16.5, 7.5 Hz, 4H), 7.67 (t, *J* = 7.3 Hz, 1H), 7.51 (dd, *J* = 15.2, 7.7 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.90, 193.08, 141.63, 135.07, 132.81, 131.32, 131.30, 129.96, 129.46, 129.10.

1-(4-bromophenyl)-2-phenylethane-1,2-dione (3d)

Yellow solid (72%, 208 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.4 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.67 (d, *J* = 7.6 Hz, 3H), 7.52 (t, *J* = 7.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.86, 193.30, 135.09, 132.80, 132.46, 131.77, 131.26, 130.52, 129.96, 129.10.

1-(3-bromophenyl)-2-phenylethane-1,2-dione (3e)

Yellow solid (67%, 193 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.97 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.69 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.57, 192.87, 137.71, 135.16, 134.73, 132.61, 130.58, 130.00, 129.13, 128.58, 123.36.

1-(4-(tert-butyl)phenyl)-2-phenylethane-1,2-dione (3f)

Yellow liquid (65%, 172 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.5 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H), 7.65 (t, *J* = 7.1 Hz, 1H), 7.51 (dd, *J* = 13.2, 7.5 Hz, 4H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.81, 194.32, 134.78, 133.15, 130.50, 129.92, 129.71, 128.99, 126.06, 126.0, 35.41, 31.04.

1-phenyl-2-(p-tolyl)ethane-1,2-dione (3g)

Orange viscus liquid (68%, 152 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.5 Hz, 2H), 7.87 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.30 (d, *J* = 7.7 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.80, 194.33, 146.24, 134.80, 133.13, 130.63, 130.14, 129.67, 129.00, 76.75, 21.94.

1-(4-chlorophenyl)-2-phenylethane-1,2-dione (3h)

Yellow solid (76%, 185 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 16.2, 7.6 Hz, 4H), 7.68 (t, *J* = 7.1 Hz, 1H), 7.51 (dd, *J* = 15.2, 7.6 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.90, 193.09, 141.63, 135.07, 132.81, 131.31, 129.96, 129.46, 129.10.

1-(4-bromophenyl)-2-phenylethane-1,2-dione (3i)

Yellow solid (69%, 199 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.4 Hz, 2H), 7.85 (d, *J* = 7.7 Hz, 2H), 7.67 (d, *J* = 7.7 Hz, 3H), 7.53 (t, *J* = 7.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.86, 193.30, 135.09, 132.80, 132.46, 131.77, 131.26, 130.52, 129.96, 129.10.

1-(3-bromophenyl)-2-phenylethane-1,2-dione (3j)

Yellow solid (66%, 189 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.97 (d, *J* = 7.5 Hz, 2H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 2H), 7.39 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.57, 192.87, 137.71, 135.16, 134.73, 132.61, 130.58, 130.00, 129.13, 128.58, 123.36.

1-(o-tolyl)-2-(p-tolyl)ethane-1,2-dione (3k)

Yellow liquid (68%, 161 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.7 Hz, 2H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.32 (t, *J* = 8.4 Hz, 3H), 7.26 (s, 1H), 2.70 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.98, 194.61, 145.98, 141.32, 133.68, 133.04, 132.53, 131.96, 130.75, 130.07, 129.75, 126.00, 21.92, 21.90.

1-(4-chlorophenyl)-2-(p-tolyl)ethane-1,2-dione (3l)

Yellow solid (73%, 188 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 23.2, 7.6 Hz, 4H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.62, 193.29, 146.46, 141.49, 131.49, 131.23, 130.41, 130.08, 129.82, 129.41, 21.96.

1-(4-bromophenyl)-2-(p-tolyl)ethane-1,2-dione (3m)

Yellow solid (70%, 210 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (t, *J* = 8.0 Hz, 4H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 7.7 Hz, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.57, 193.49, 146.47, 132.40, 131.88, 131.25, 130.39, 130.08, 129.82, 21.96.

1-(4-(tert-butyl)phenyl)-2-(p-tolyl)ethane-1,2-dione (3n)

Yellow liquid (64%, 179 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.84 (m, 4H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 7.7 Hz, 2H), 2.43 (s, 3H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.53, 194.51, 158.91, 146.05, 130.75, 130.61, 130.04, 129.89, 129.70, 126.01, 35.39, 30.99, 21.92.

1,2-bis(4-chlorophenyl)ethane-1,2-dione (3o)

Pale brown solid (74%, 206 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.7 Hz, 4H), 7.50 (d, *J* = 7.9 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.38, 141.85, 131.29, 131.17, 129.53.

1-(3-bromophenyl)-2-(4-chlorophenyl)ethane-1,2-dione (3p)

Yellow solid (67%, 216 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.90 (dd, *J* = 16.3, 7.9 Hz, 3H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.40 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.18, 192.06, 141.94, 137.87, 134.52, 132.59, 131.31, 131.05, 130.62, 129.55, 128.60, 123.40.

1-(4-(tert-butyl)phenyl)-2-(4-chlorophenyl)ethane-1,2-dione (3q)

Yellow gummy liquid (65%, 195 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (t, *J* = 8.8 Hz, 4H), 7.51 (dd, *J* = 19.0, 8.1 Hz, 4H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.63, 193.31, 159.30, 141.48, 131.50, 131.23, 130.28, 129.96, 129.41, 126.12, 30.97, 29.71.

1-(4-(tert-butyl)phenyl)-2-(p-tolyl)ethane-1,2-dione (3r)

Pale Yellow liquid (62%, 173 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 12.6, 8.7 Hz, 4H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 7.6 Hz, 2H), 2.43 (s, 3H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.53, 194.51, 158.91, 146.05, 130.75, 130.61, 130.04, 129.90, 129.71, 126.01, 35.39, 30.99, 21.92.

1-(4-(tert-butyl)phenyl)-2-(4-chlorophenyl)ethane-1,2-dione (3s)

Pale Yellow liquid (69%, 207 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (t, *J* = 8.7 Hz, 4H), 7.51 (dd, *J* = 18.9, 7.9 Hz, 4H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.64, 193.32, 159.30, 141.48, 131.51, 131.24, 130.28, 129.96, 129.41, 126.13, 35.45, 30.98.

1-(3-bromophenyl)-2-(4-(tert-butyl)phenyl)ethane-1,2-dione (3t)

Pale Yellow liquid (64%, 220 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.89 (t, *J* = 6.7 Hz, 3H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 1H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.30, 193.10, 159.40, 137.59, 134.86, 132.53, 130.54, 130.17, 130, 128.56, 126.16, 123.30, 35.46, 30.98.

1-(3-bromophenyl)-2-(4-(tert-butyl)phenyl)ethane-1,2-dione (3u)

Pale Yellow liquid (60%, 206 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 2H), 7.89 (t, *J* = 6.7 Hz, 6H), 7.77 (d, *J* = 7.9 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 4H), 7.38 (t, *J* = 7.8 Hz, 2H), 1.35 (s, 17H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.29, 193.09, 159.40, 137.58, 134.86, 132.53, 130.54, 130.08, 128.56, 126.16, 123.30, 35.46, 30.98.

tert-butyl (2,3-dioxo-3-phenylpropyl)carbamate (3v)

Colourless liquid (58%, 152 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.18 (m, 5H), 4.32 (s, 1H), 3.92 (s, 2H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.01, 190.38, 155.27, 138.93, 129.32, 128.62, 127.50, 127.34, 119.85, 80.08, 71.25, 28.42, 28.35.

2-(2-(4,5-diphenyl-1H-imidazol-2-yl)phenoxy)-N,N-dimethylethan-1-amine (7)

White solid (83%, 318 mg); ^{1}H NMR (400 MHz, DMSO) δ 12.57 (s, 1H), 8.22 (d, *J* = 7.6 Hz, 1H), 7.63 – 7.10 (m, 13H), 4.29 (s, 2H), 2.63 (s, 2H), 1.90 (s, 6H). ^{13}C NMR (101 MHz, DMSO) δ 155.43, 143.39, 129.94, 129.38, 129.18, 128.57, 128.39, 127.06, 122.19, 120.13, 115.09, 66.02, 57.85, 44.49.

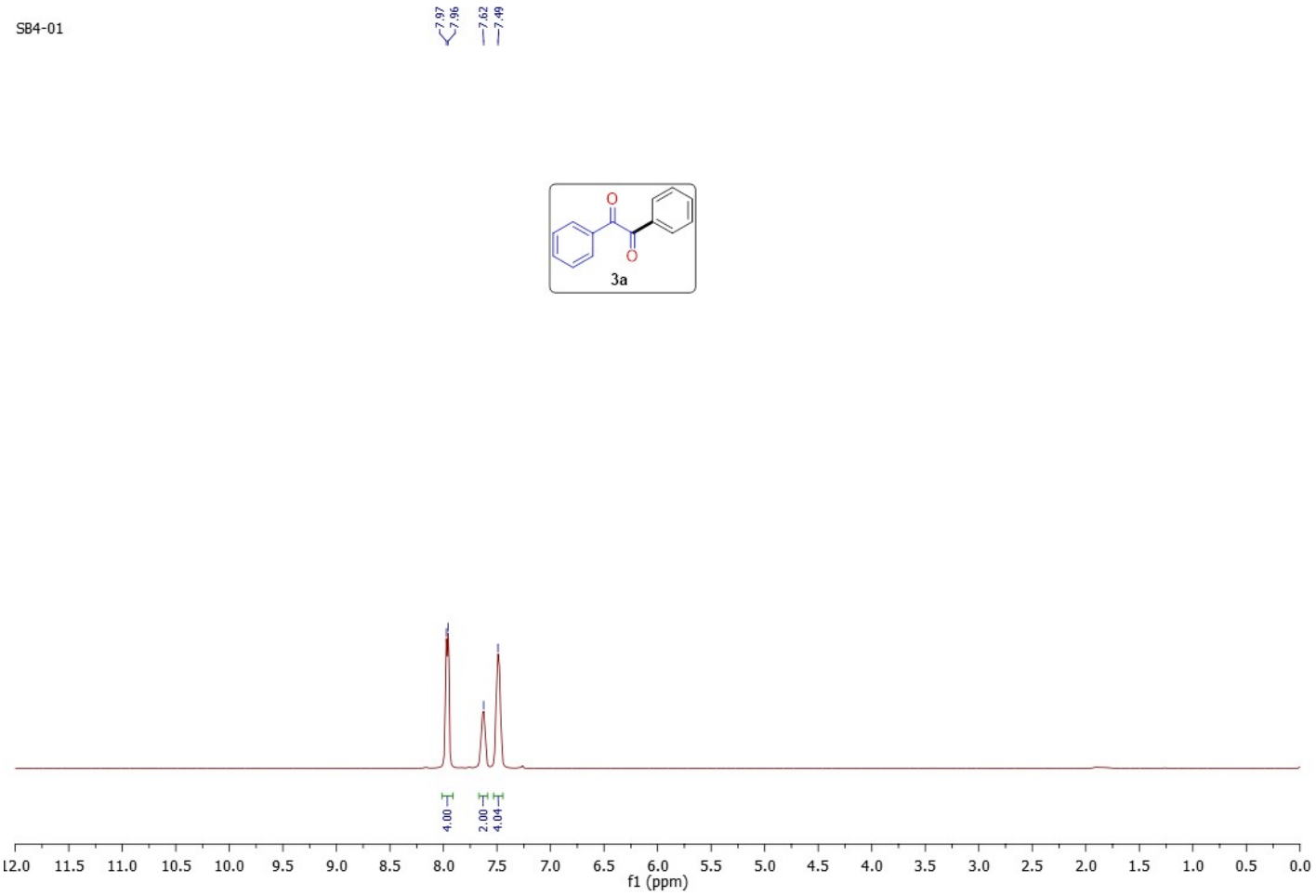
1,2-diphenylethan-1-one (8)

Orange solid (76%, 159 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.4 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.33 – 7.27 (m, 2H), 7.23 (dd, *J* = 13.7, 7.1 Hz, 3H), 4.26 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.65, 136.69, 134.64, 133.21, 129.55, 128.73, 128.70, 128.67, 126.94, 45.54.

3. References

1. W. Lin, M. H. Hu, X. Feng, L. Fu, C. P. Cao, Z. B. Huang, and D. Q. Shi, *Tetrahedron Lett*., 2014, **55**, 2238-2242.

4. ^{1}H and ^{13}C NMR Spectra of Compounds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10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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2.5
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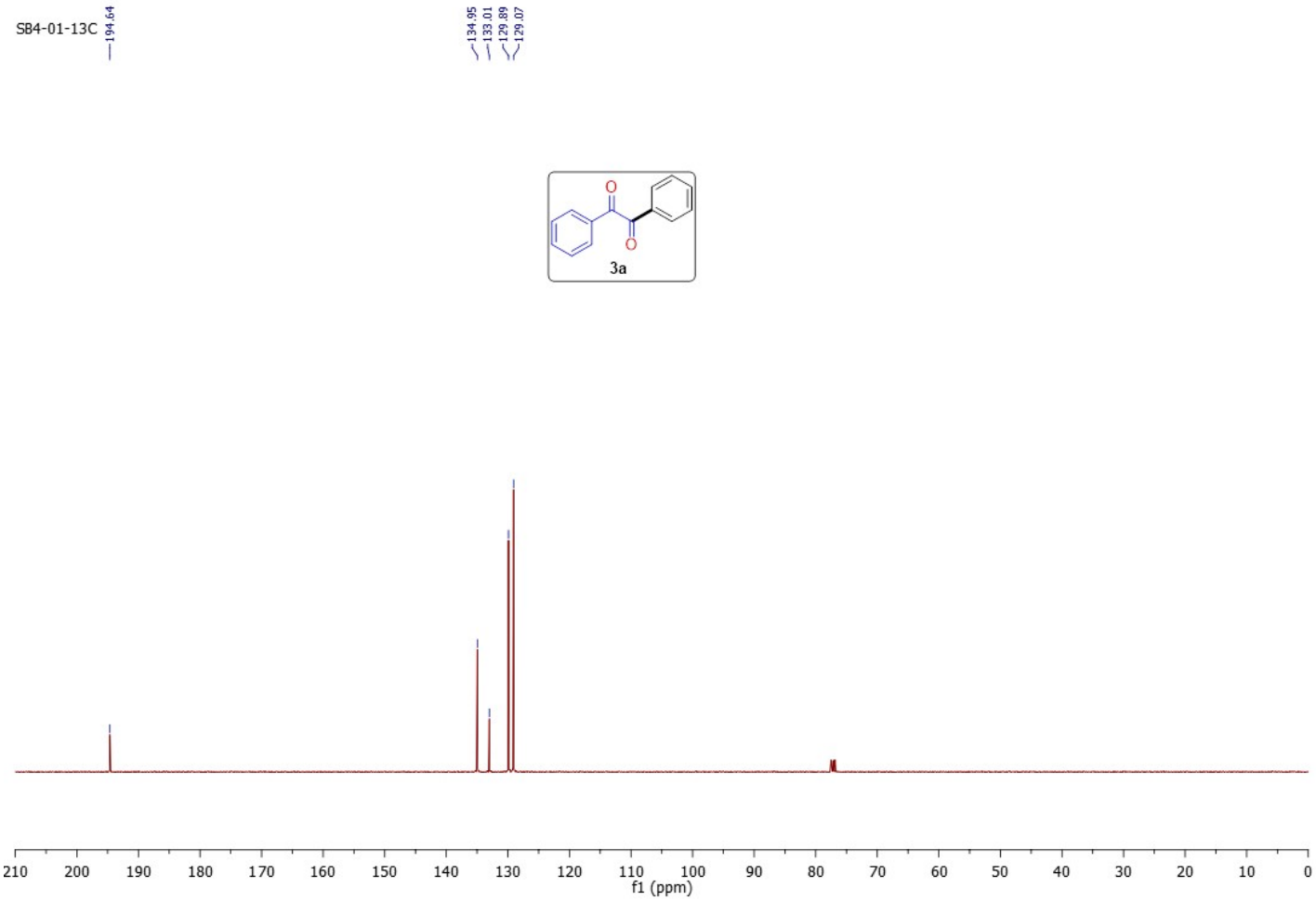
f1 (ppm)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200
190
180
170
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150
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110
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90
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70
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50
40
30
20
10
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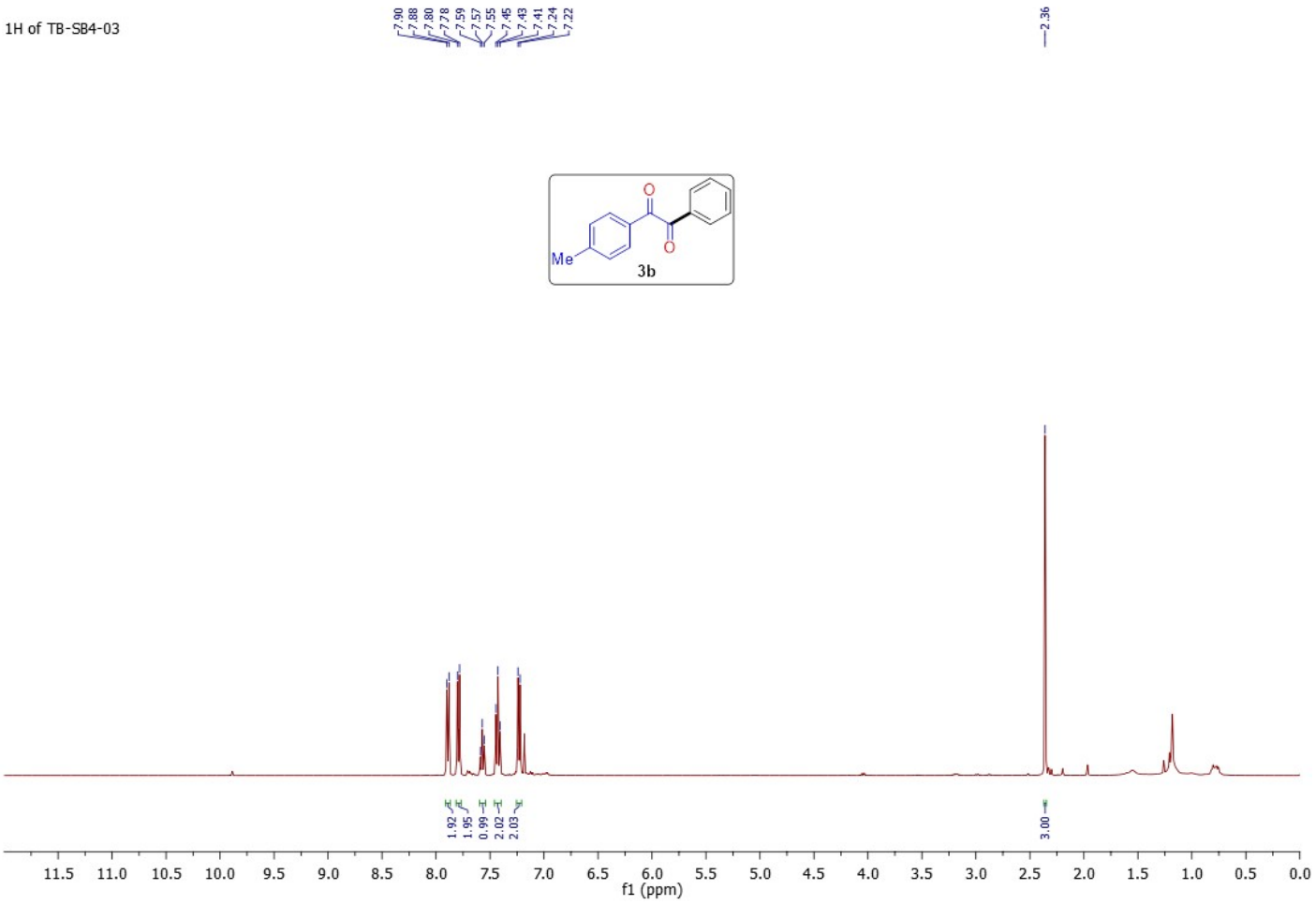
f1 (ppm)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7.55
7.45
7.43
7.41
7.24
7.22
2.36
Me
3b
1.92
1.95
0.99
2.02
2.03
3.00
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
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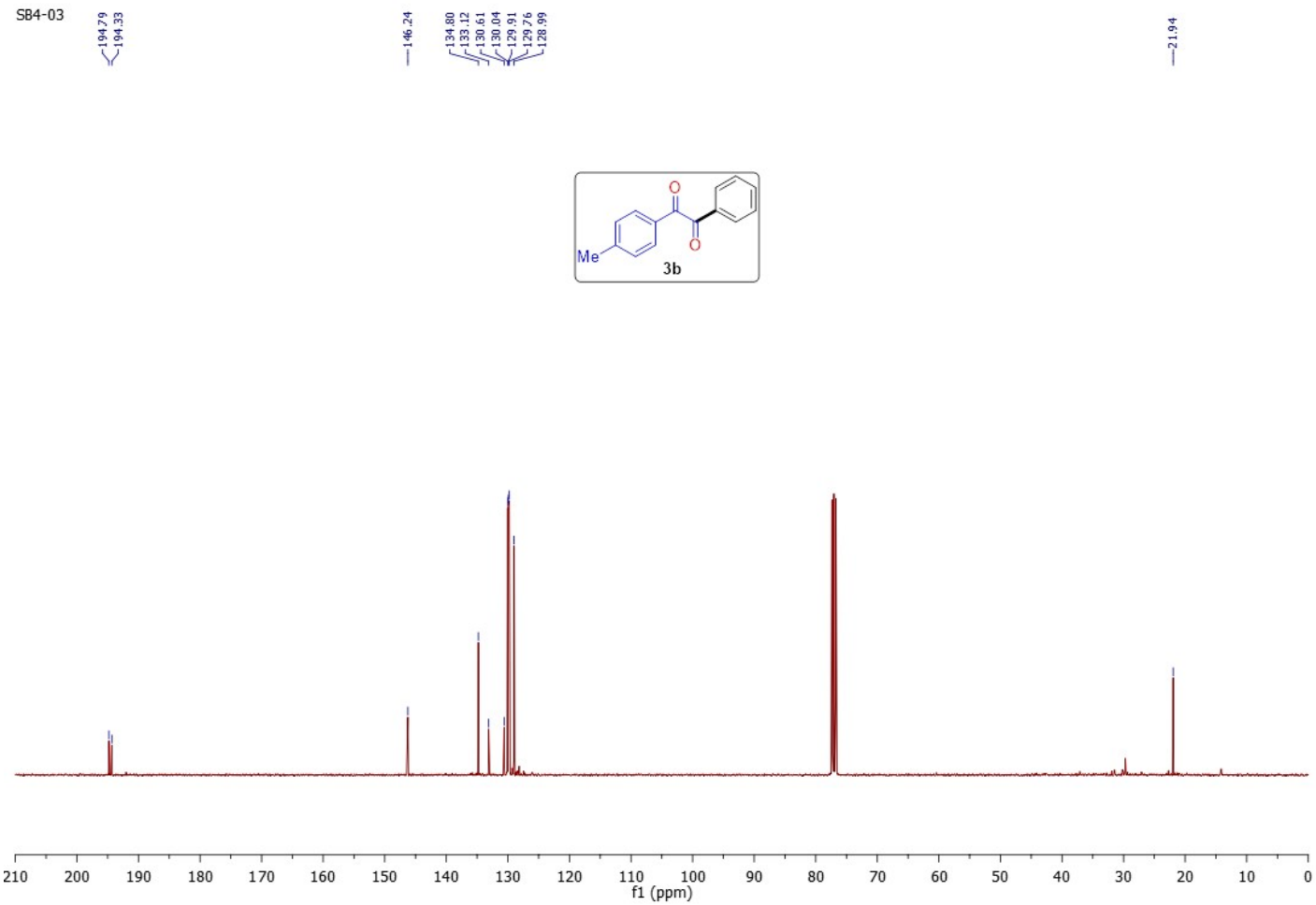
0.0
f1 (ppm)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130.04
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21.94
O
O
Me
3b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

SB4-02


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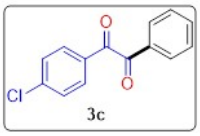
7.52
7.50
7.48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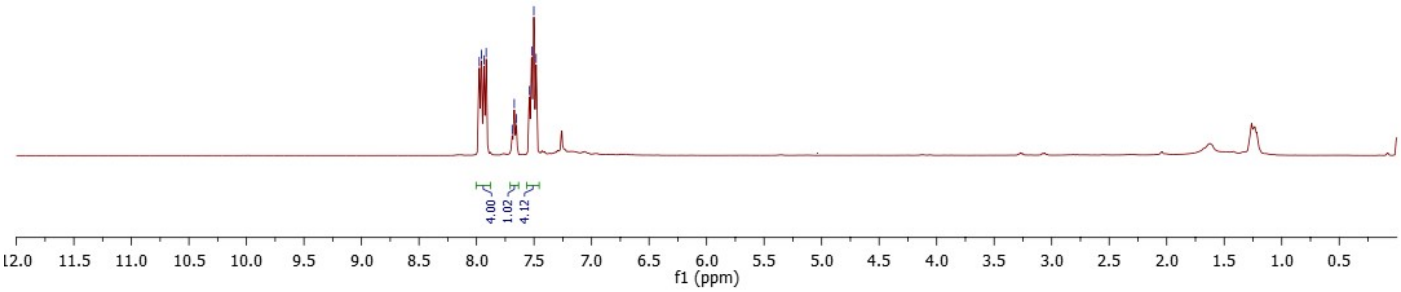
O
Cl

3c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1.02
4.12
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
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6.5
6.0
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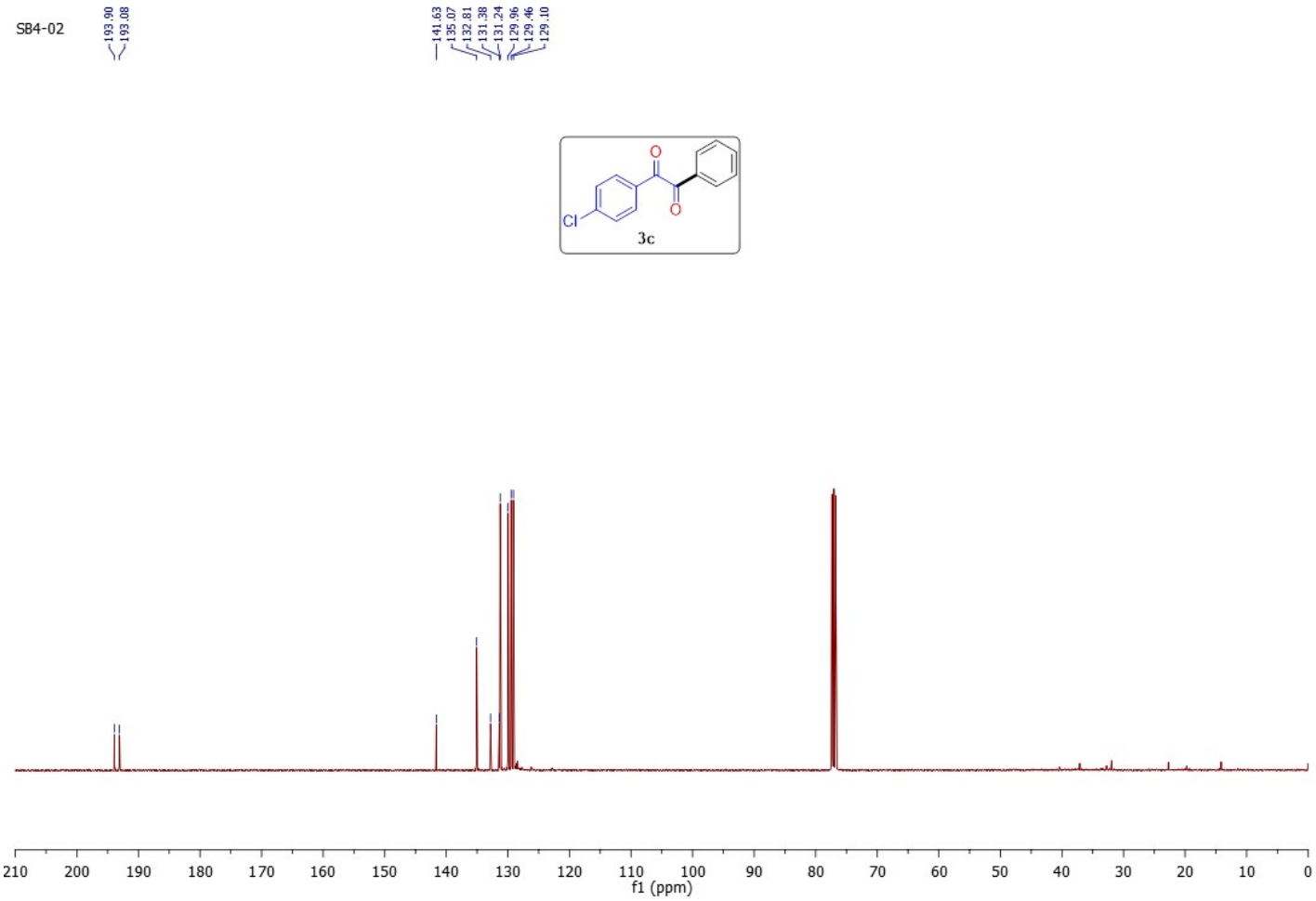
0.5
f1 (ppm)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131.24
129.96
129.46
129.10
O
O
Cl
3c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

SB4-07


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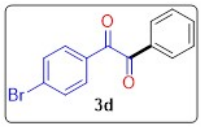
7.52
7.51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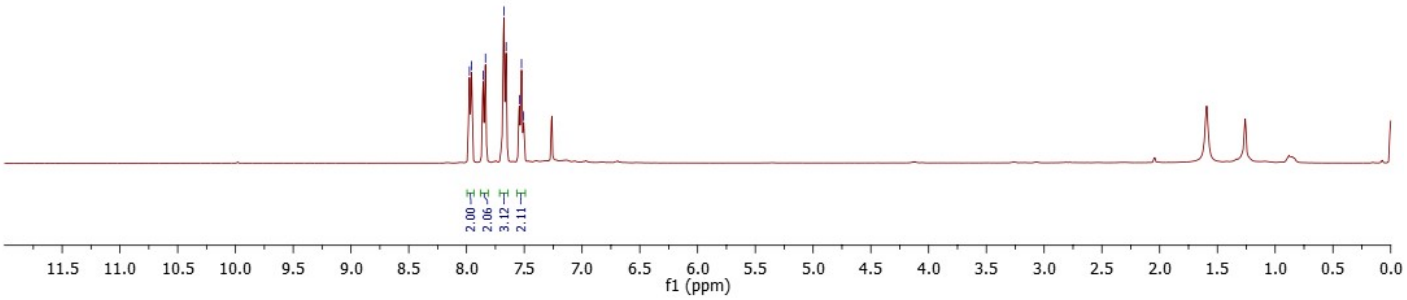
O
Br
3d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7.0
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6.0
5.5
5.0
4.5
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3.5
3.0
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1.0
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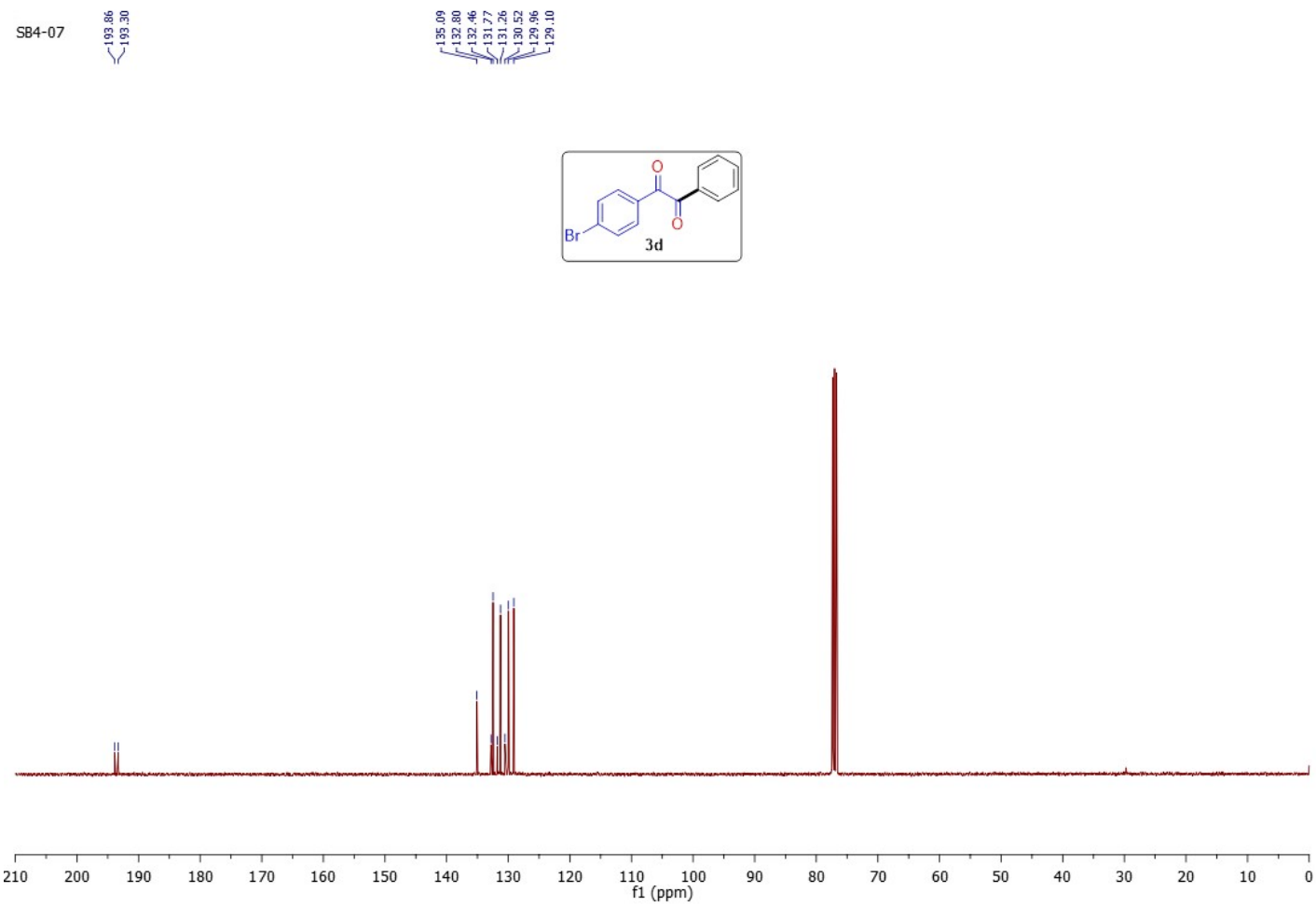
0.0
f1 (ppm)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129.96
129.10
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O
Br
3d
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

SB4-08


8.14
7.98
7.96
7.90
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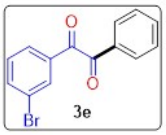
7.41
7.40
7.38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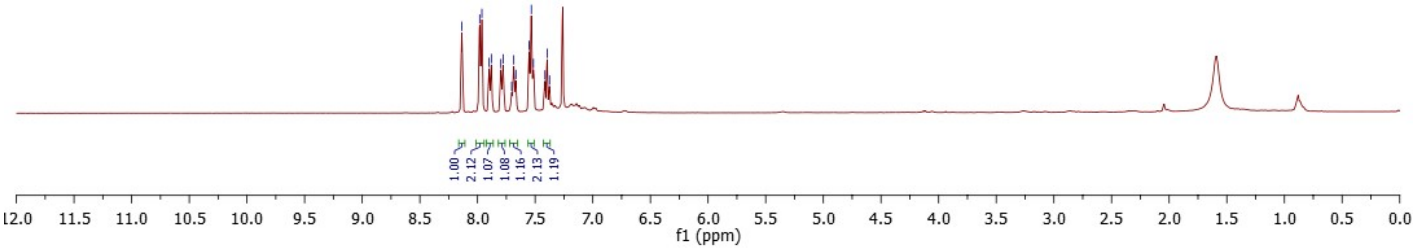
O
Br

3e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7.0
6.5
6.0
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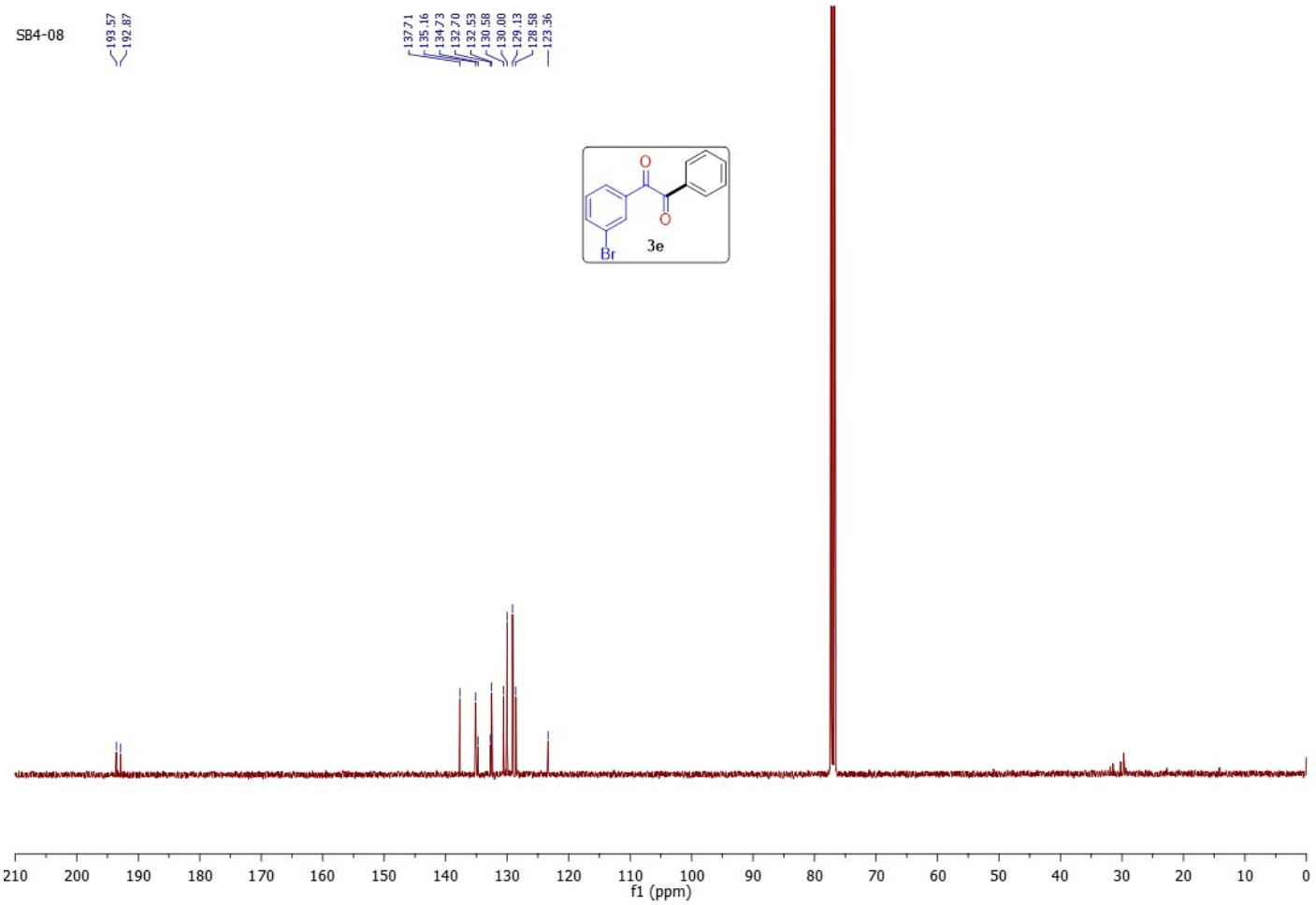
f1 (ppm)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O
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3e
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200
190
180
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130
120
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90
80
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50
40
30
20
10
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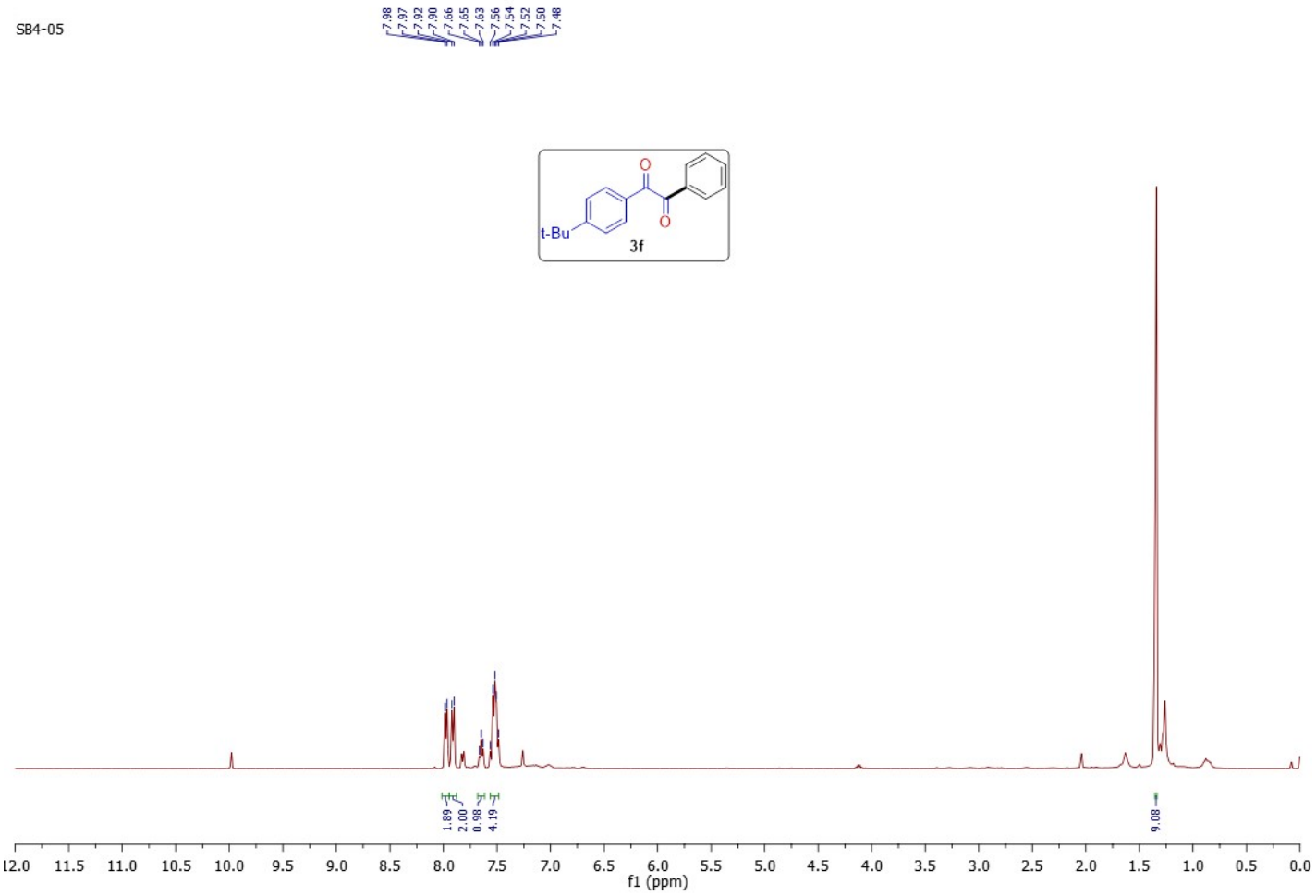
f1 (ppm)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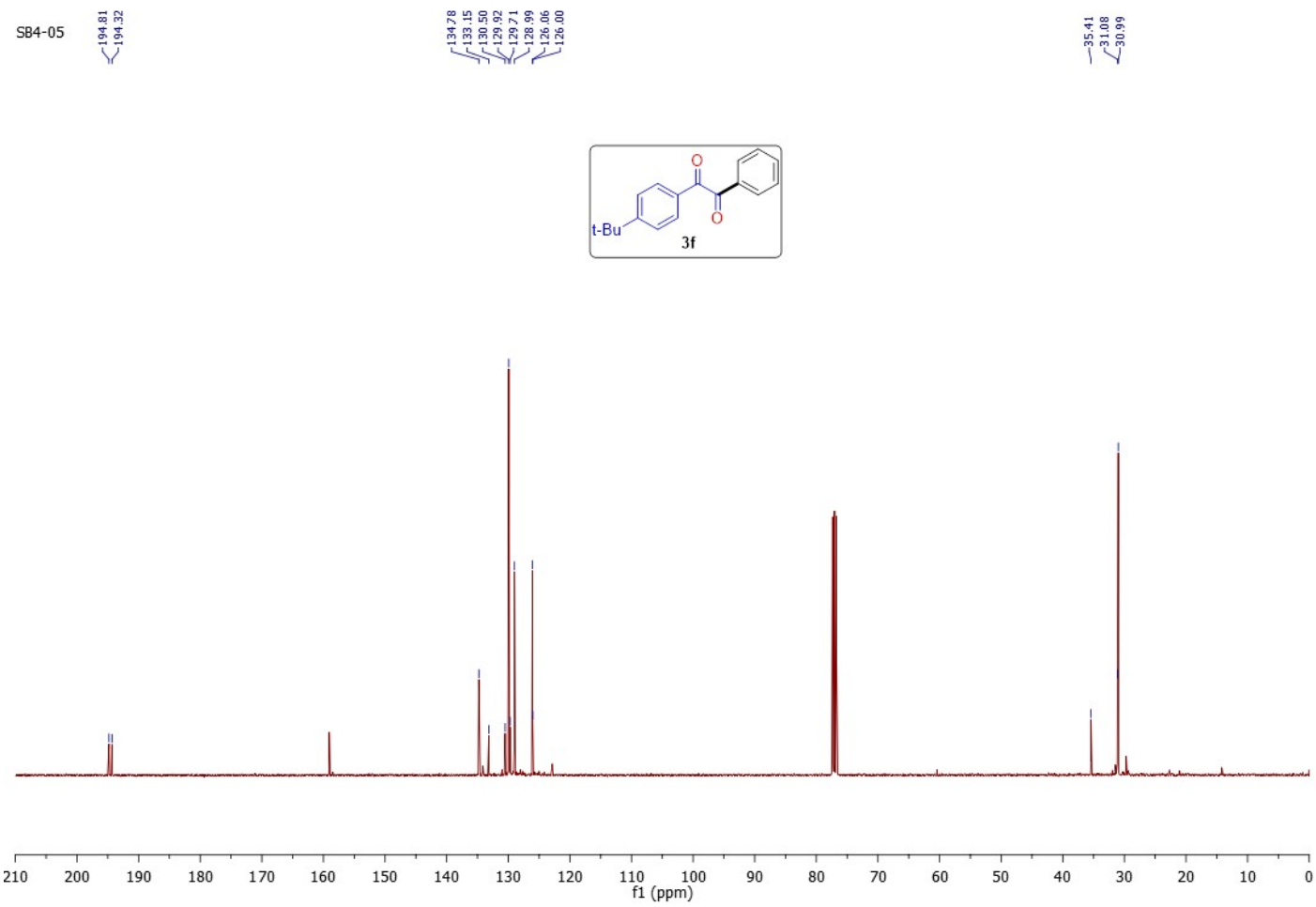
9.08
f1 (ppm)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129.92
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126.00
35.41
31.08
30.99
O
O
t-Bu
3f
210
200
190
180
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50
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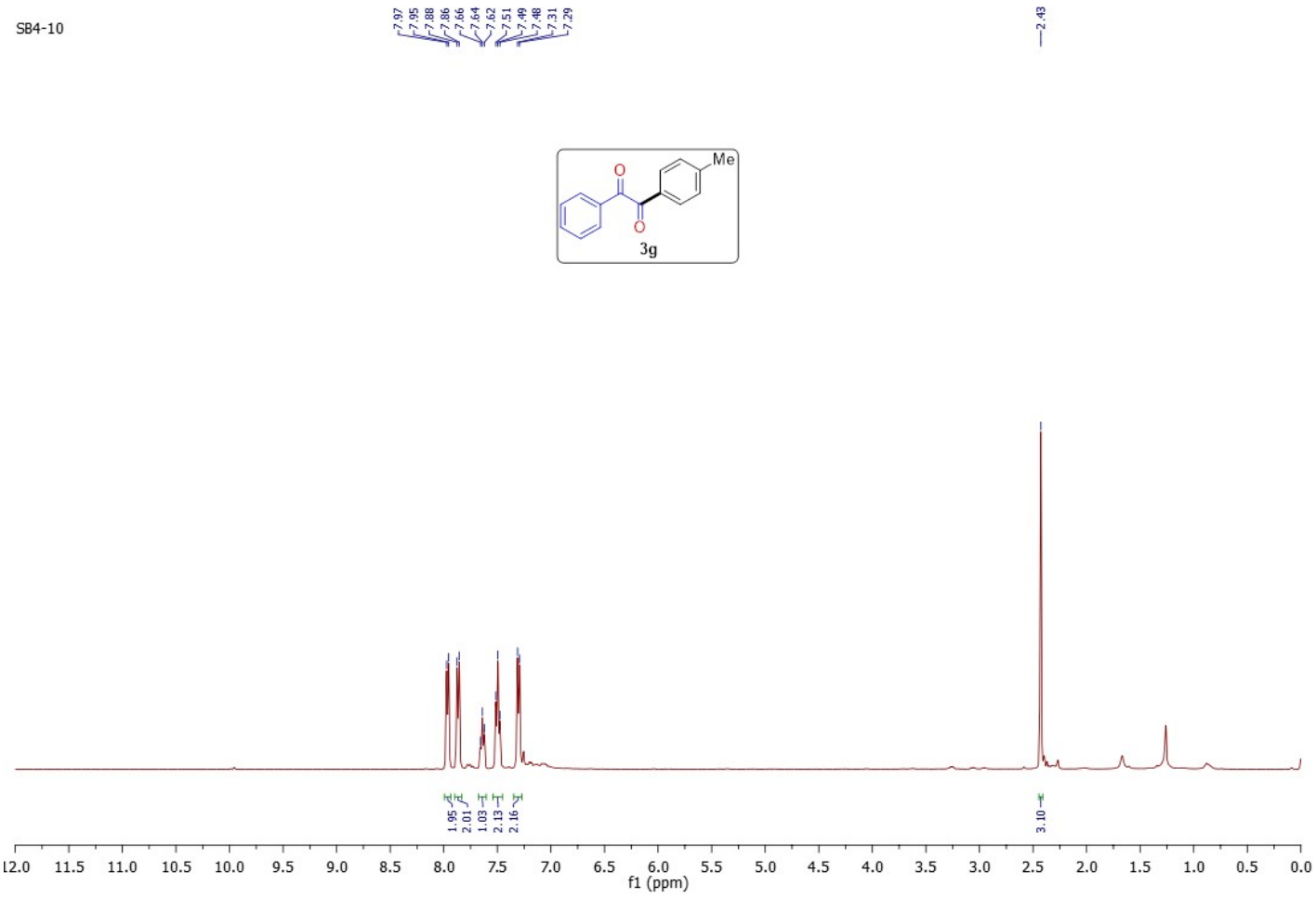
f1 (ppm)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2.43
Me
O
O
3g
1.95
2.01
1.03
2.13
2.16
3.10
12.0
11.5
11.0
10.5
10.0
9.5
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8.5
8.0
7.5
7.0
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6.0
5.5
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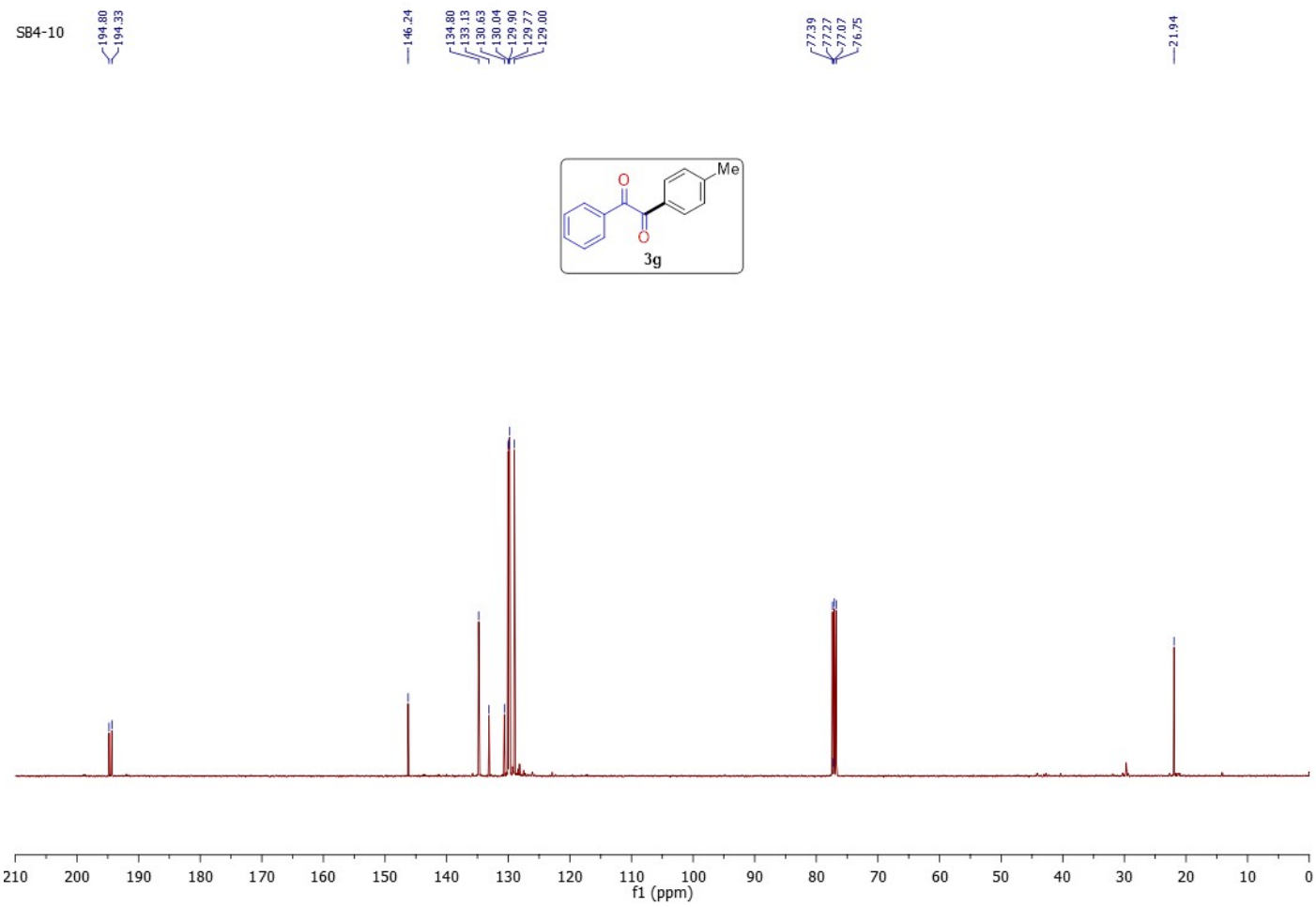
f1 (ppm)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77.27
77.07
76.75
21.94
O
O
Me
3g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

SB4-13


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7.94
7.92
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7.66
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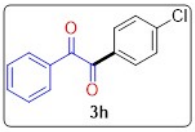
7.52
7.50
7.49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Cl
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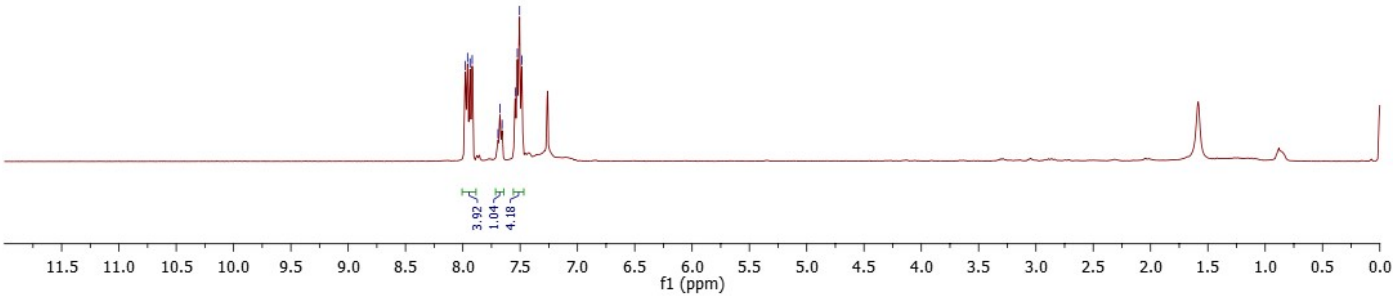
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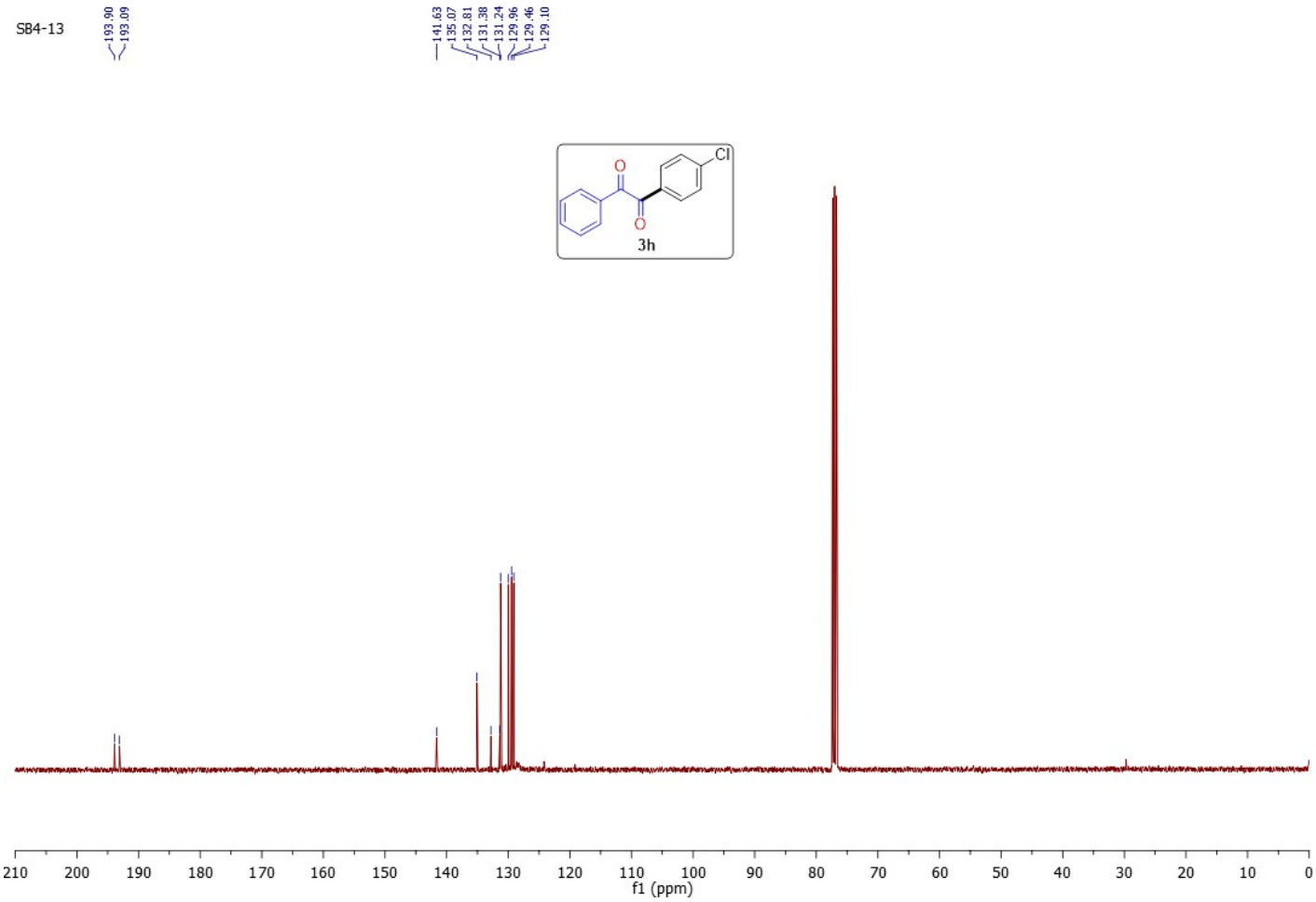
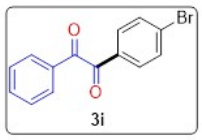
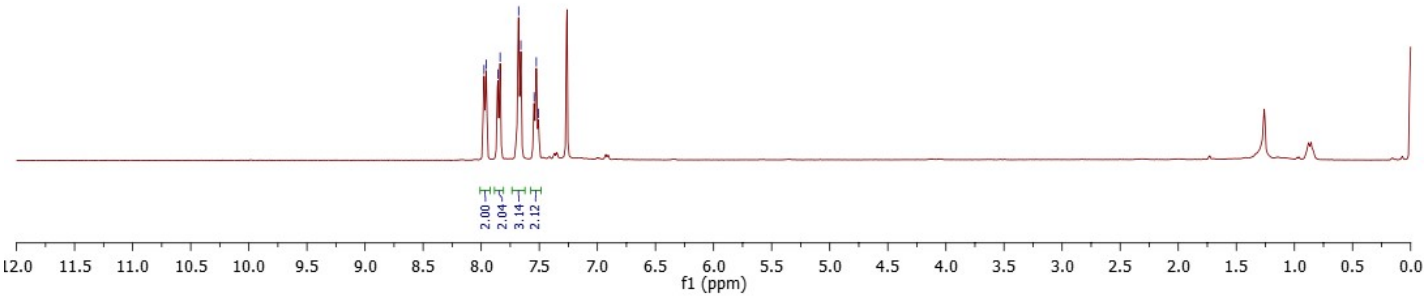
1.04
4.18
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

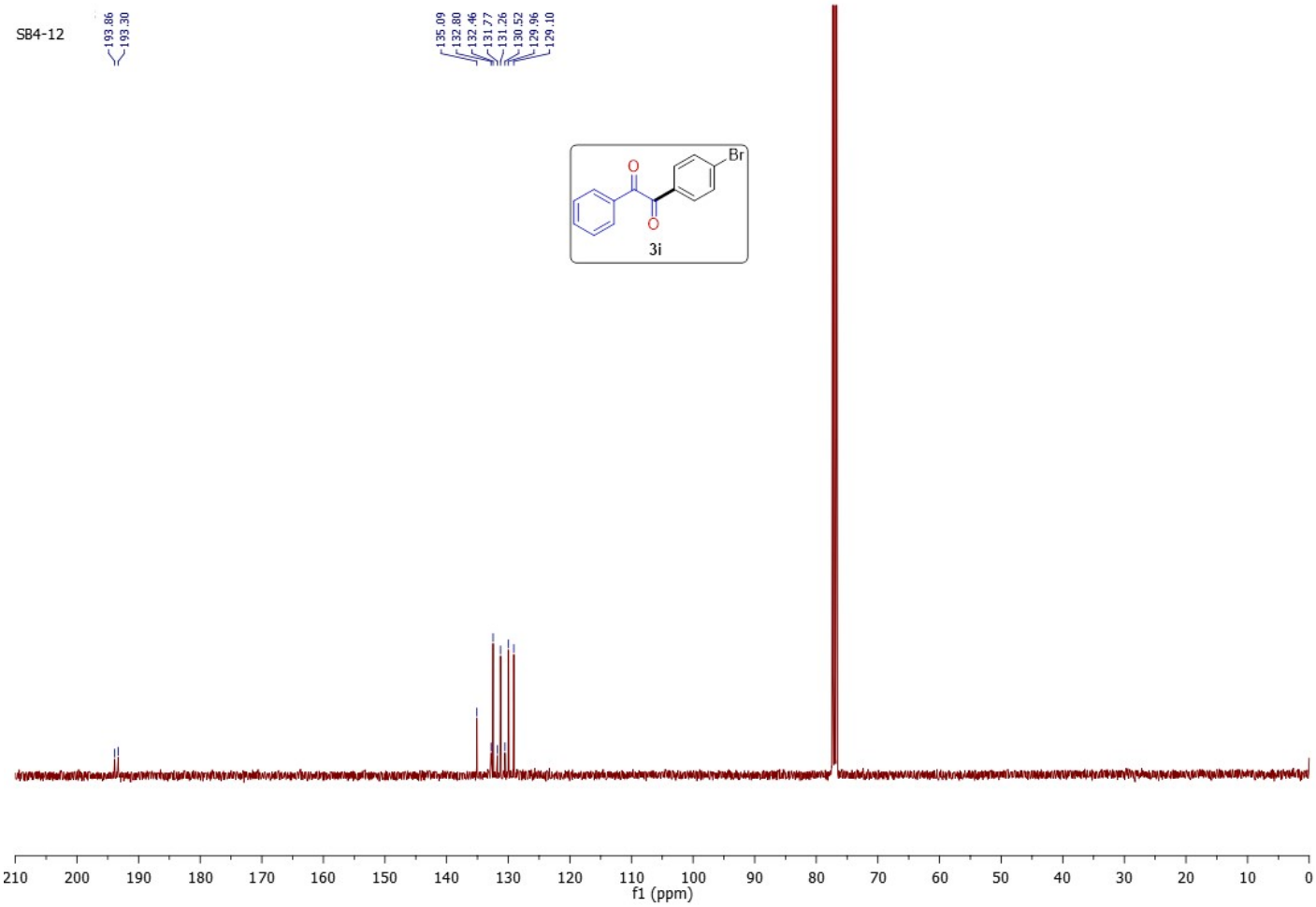

SB4-13
193.90
193.09
141.63
135.07
132.81
131.38
131.24
129.96
129.46
129.10
O
O
Cl
3h
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

SB4-12

7.98
7.96
7.86
7.84
7.68
7.66
7.54
7.53
7.51

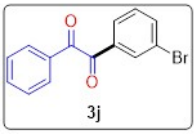

O
O
Br
3i


2.00
2.04
3.14
2.12
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
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)

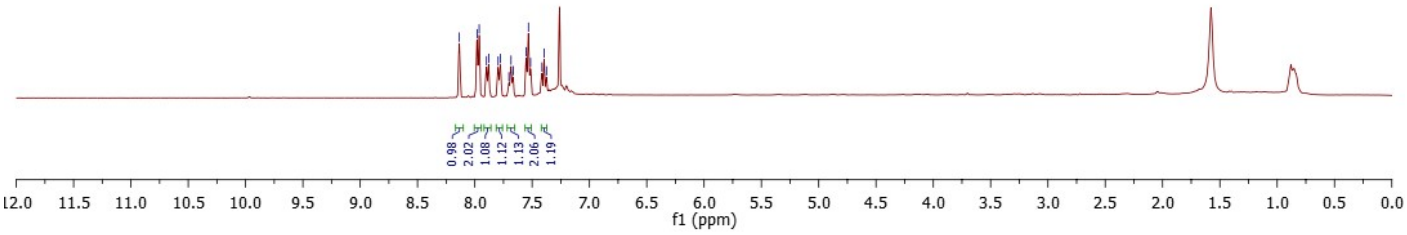

SB4-12
193.86
193.30
135.09
132.80
132.46
131.77
131.26
130.52
129.96
129.10
Br
O
O
3i
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

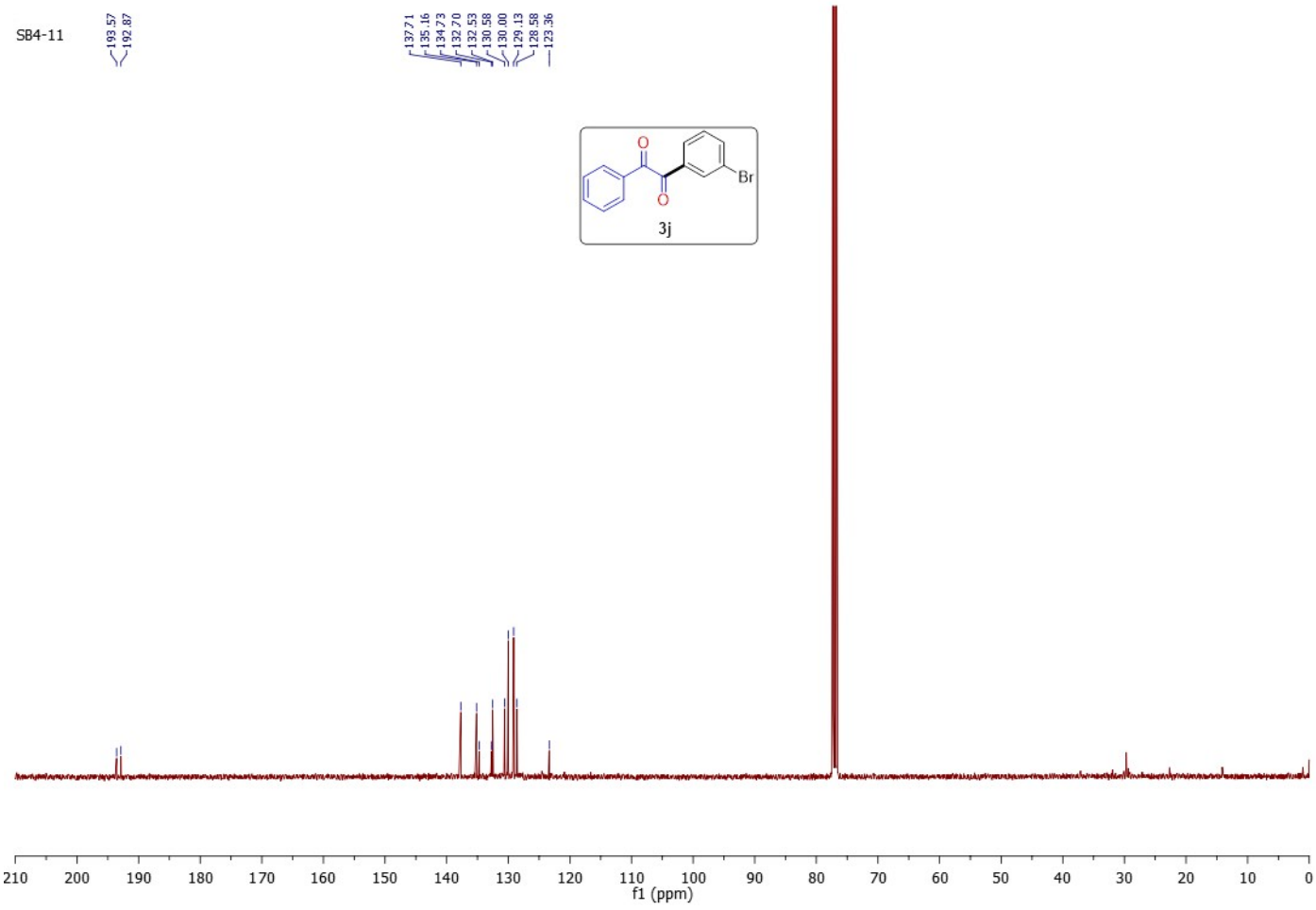
SB4-11

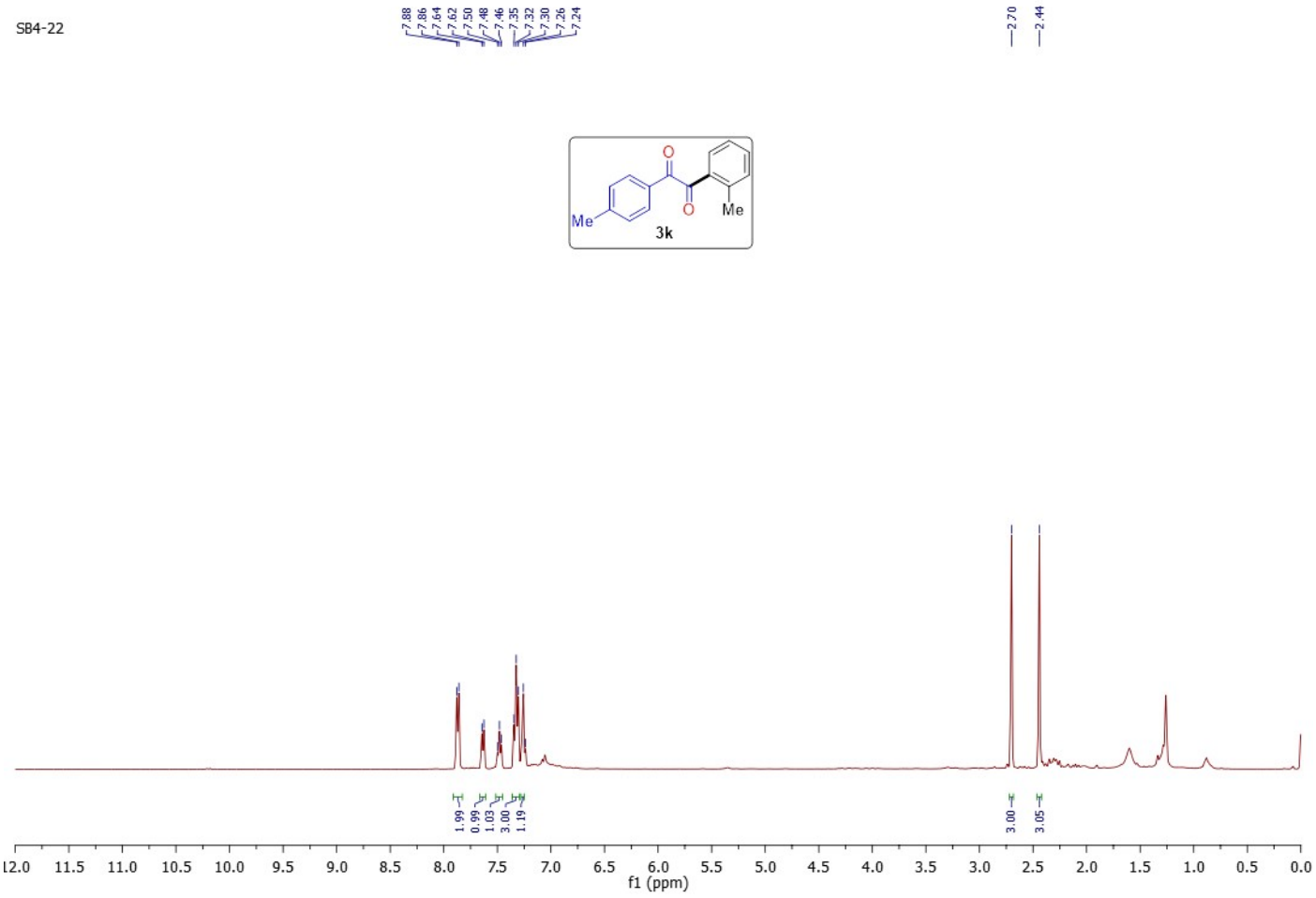

8.13
7.98
7.96
7.90
7.88
7.80
7.78
7.70
7.68
7.67
7.55
7.53
7.51
7.41
7.39
7.37

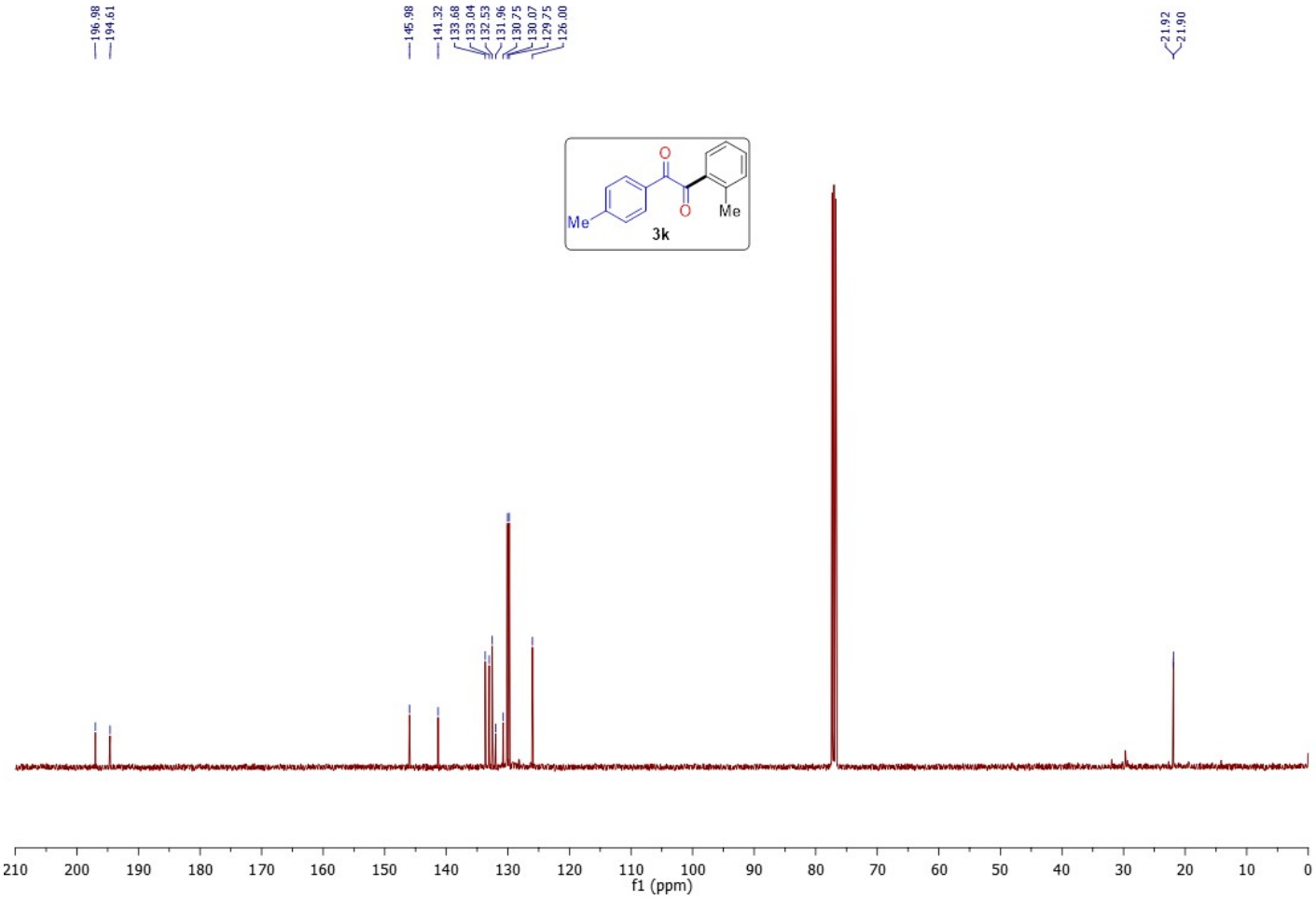

O
O
Br

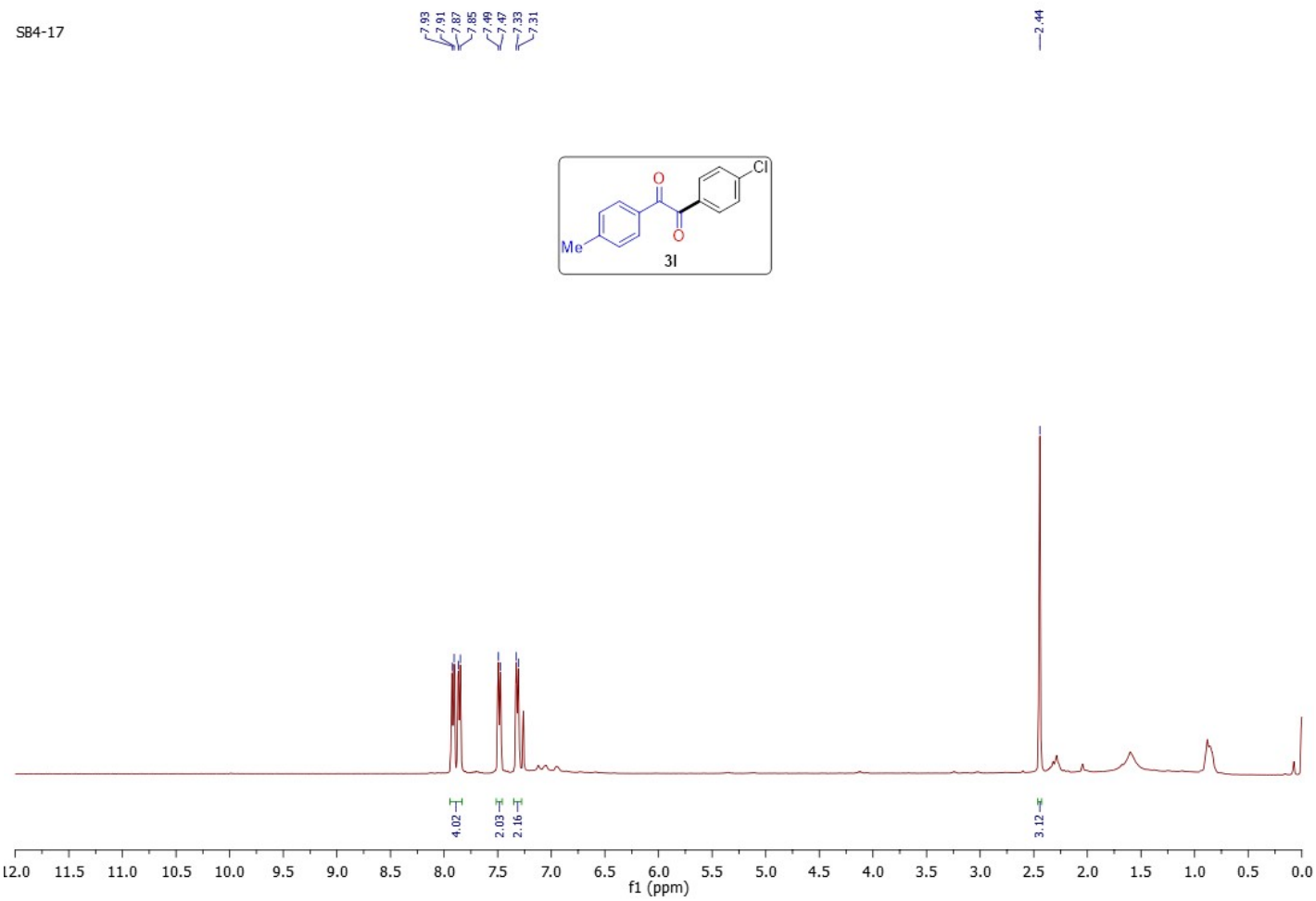
3j

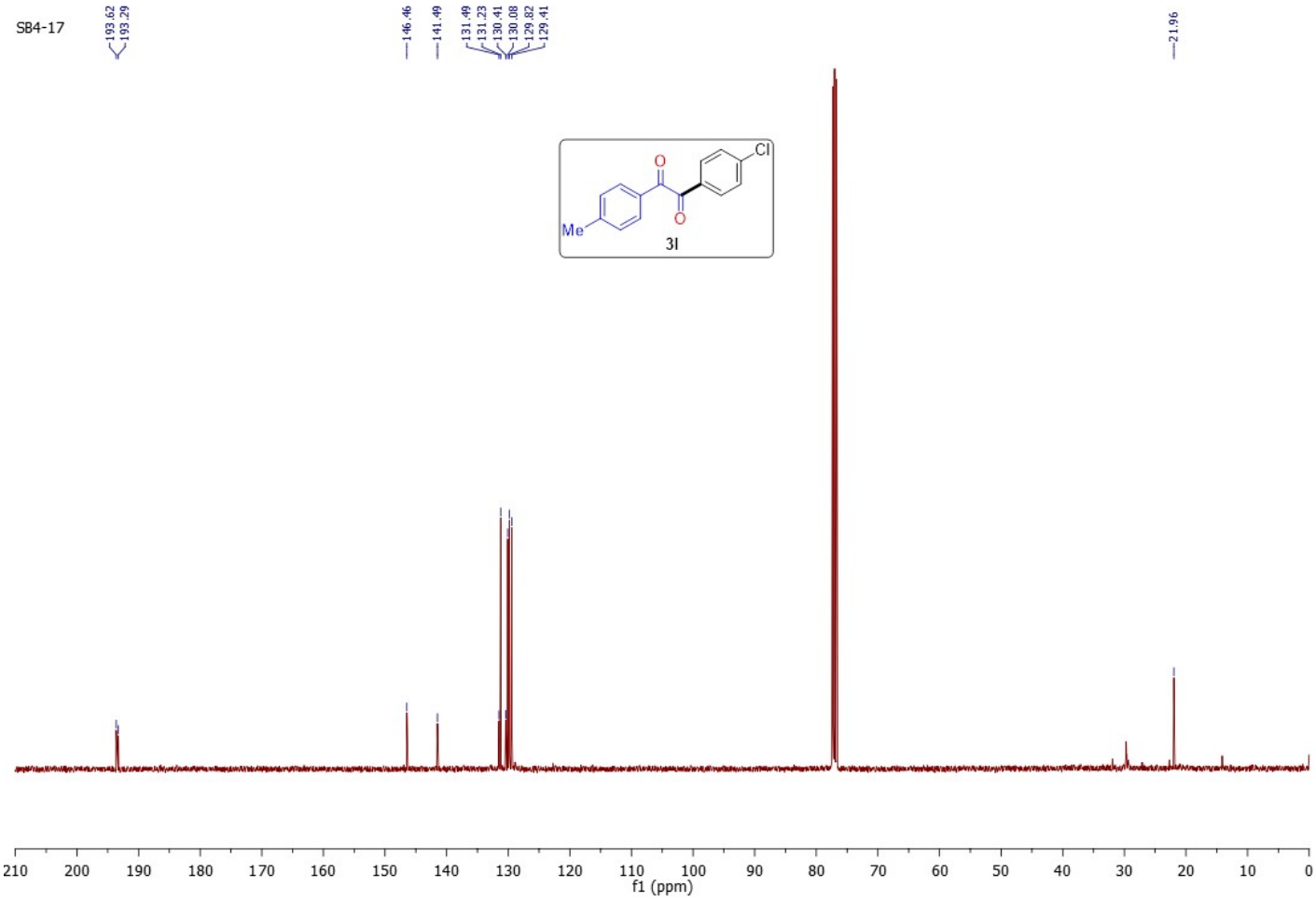

0.98
2.02
1.08
1.12
1.13
2.06
1.19
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

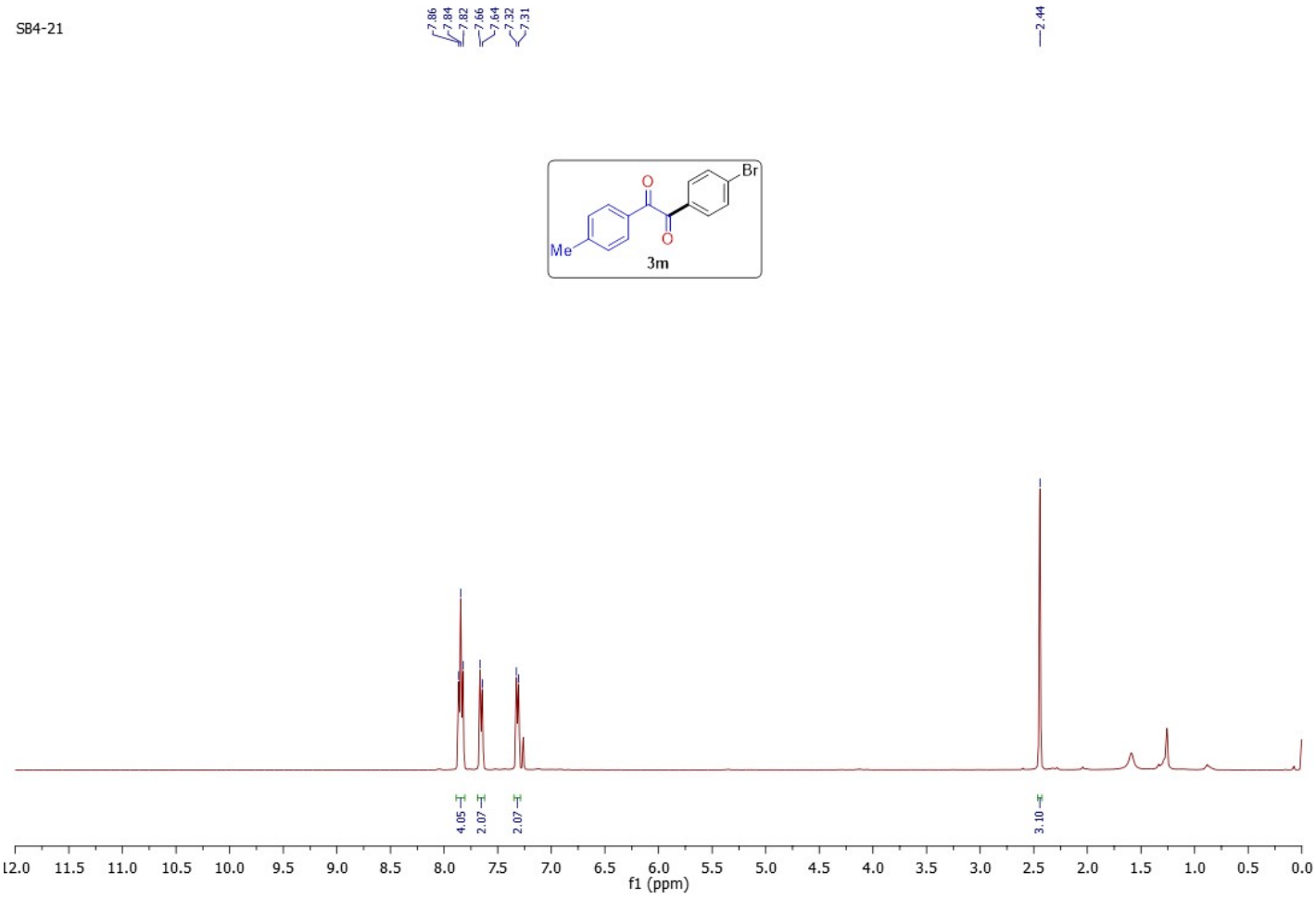

SB4-11
193.57
192.87
137.71
135.16
134.73
132.70
132.53
130.58
130.00
129.13
128.58
123.36
O
O
Br
3j
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

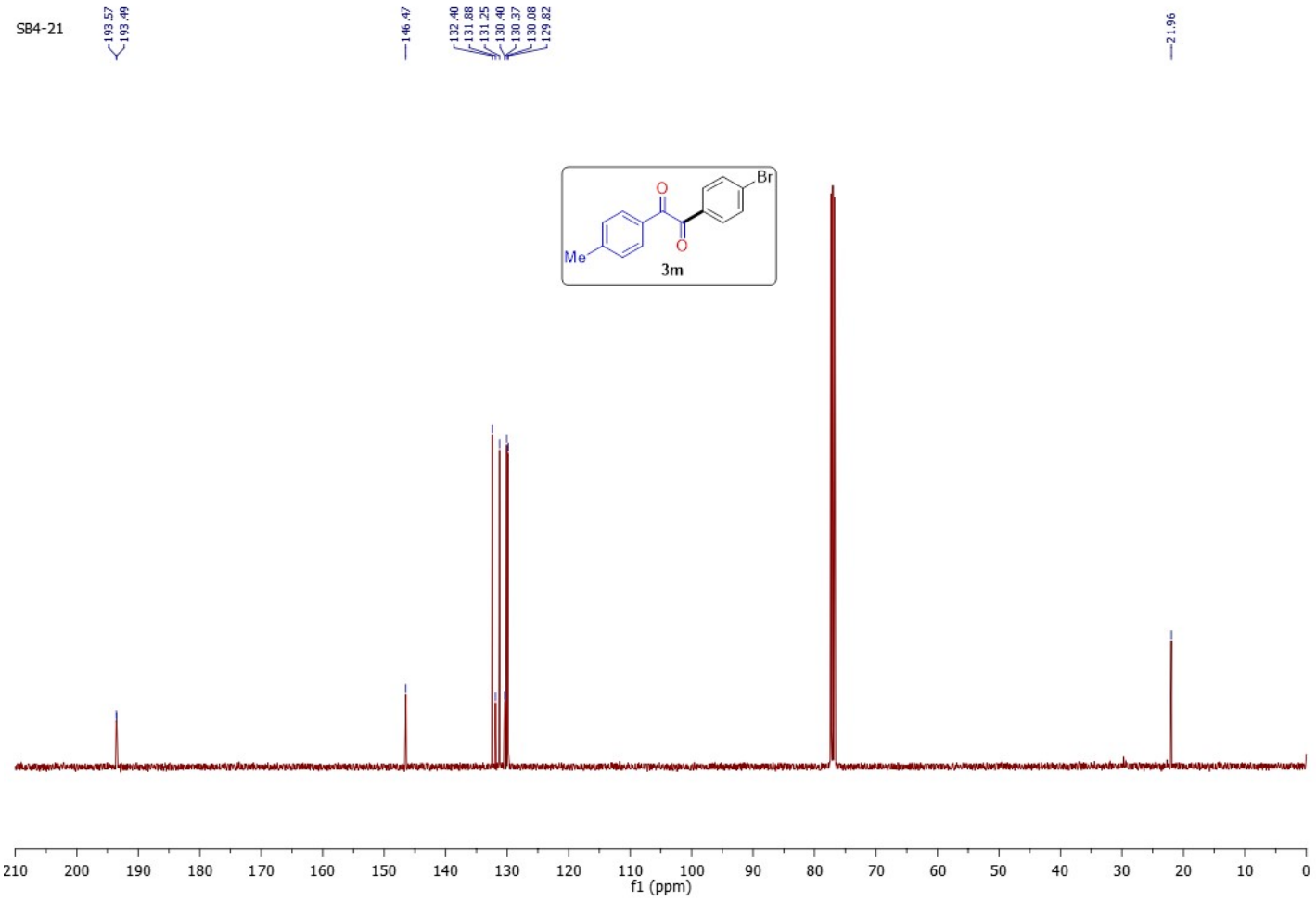

SB4-22
7.88
7.86
7.64
7.62
7.50
7.48
7.46
7.35
7.32
7.30
7.26
7.24
2.70
2.44
O
O
Me
Me
3k
1.99
0.99
1.03
3.00
1.19
3.00
3.05
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

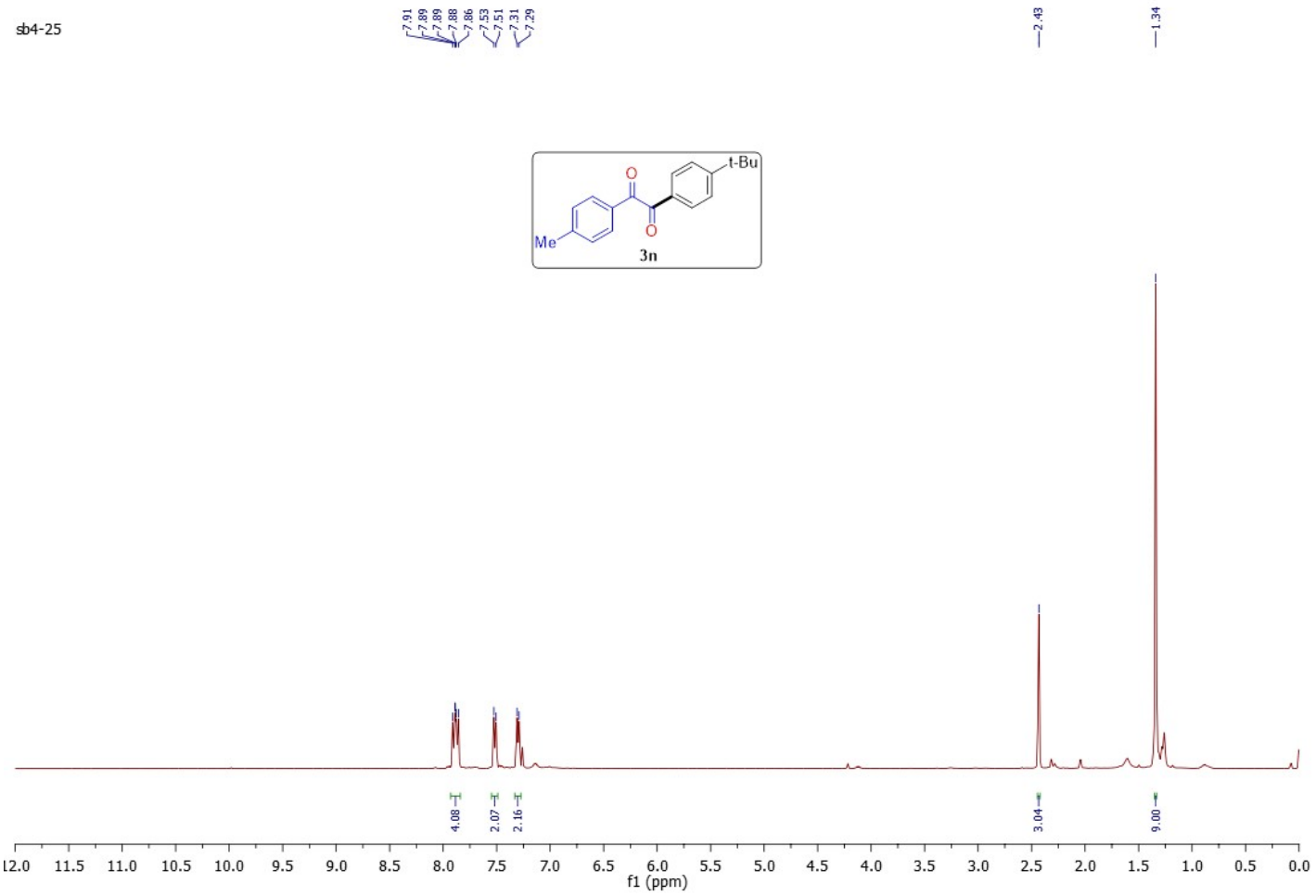

196.98
194.61
145.98
141.32
133.68
133.04
132.53
131.96
130.75
130.07
129.75
126.00
21.92
21.90
O
O
Me
Me
3k
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

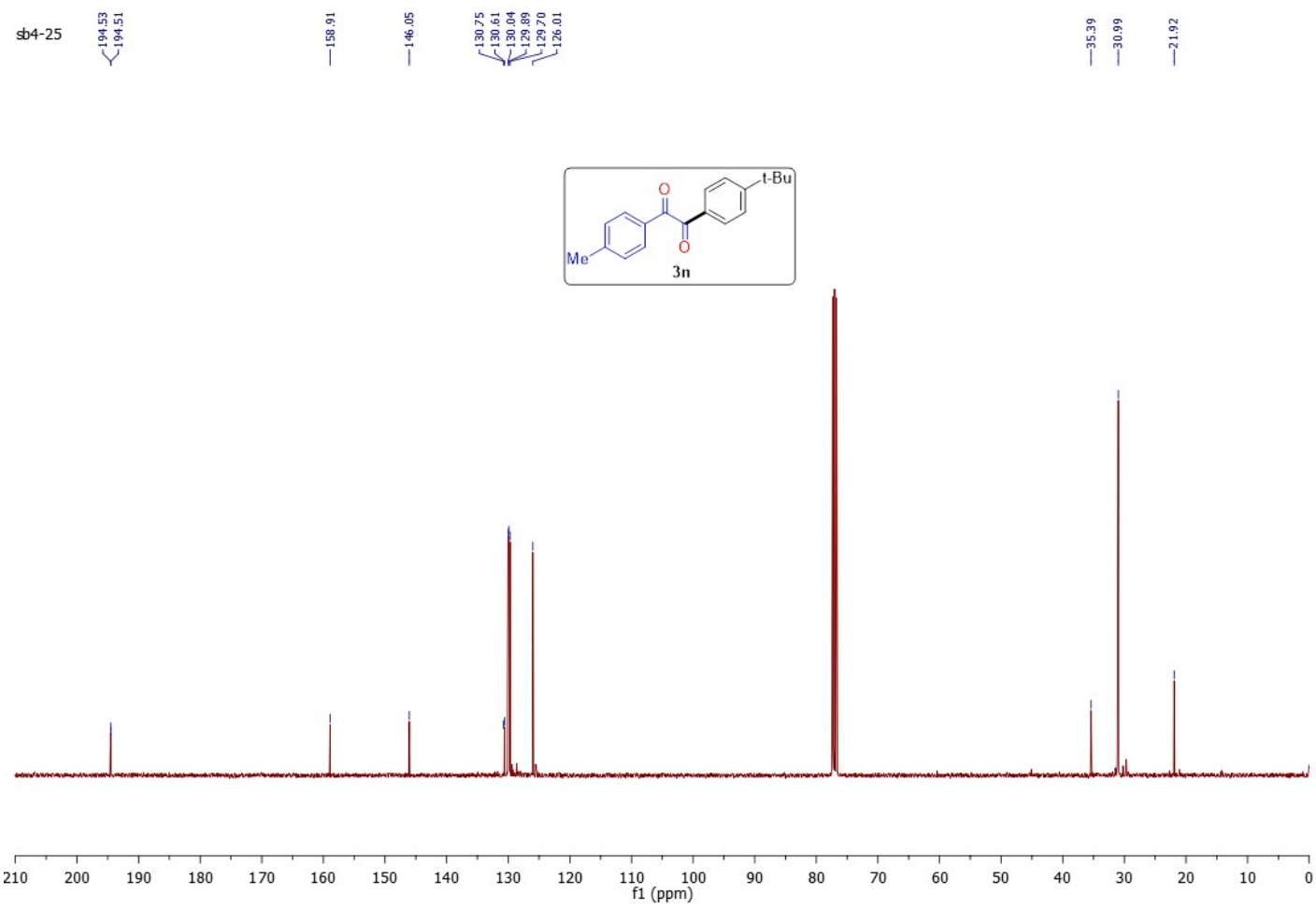

SB4-17
7.93
7.91
7.87
7.85
7.49
7.47
7.33
7.31
2.44
O
O
Cl
Me
3l
4.02
2.03
2.16
3.12
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


SB4-17
193.62
193.29
146.46
141.49
131.49
131.23
130.41
130.08
129.82
129.41
21.96
O
O
Cl
Me
3l
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

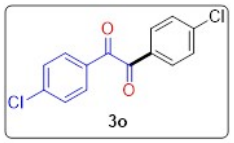

SB4-21
7.86
7.84
7.82
7.66
7.64
7.32
7.31
2.44
Br
O
O
Me
3m
4.05
2.07
2.07
3.10
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


SB4-21
193.57
193.49
146.47
132.40
131.88
131.25
130.40
130.37
130.08
129.82
21.96
Br
O
O
Me
3m
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

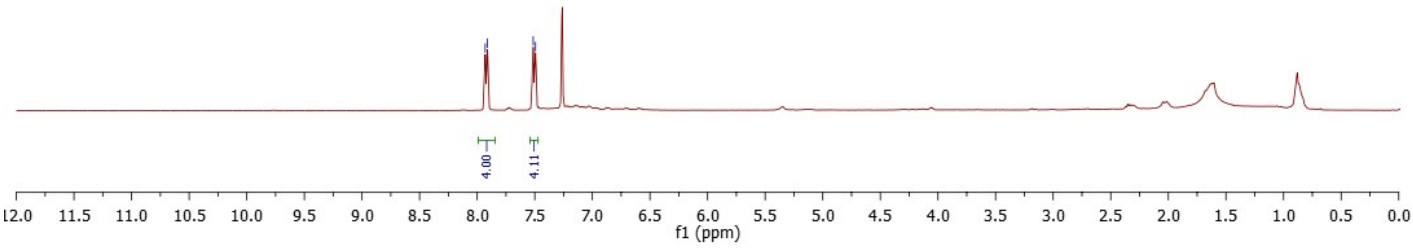

sb4-25
7.91
7.89
7.89
7.88
7.86
7.53
7.51
7.31
7.29
2.43
1.34
t-Bu
O
O
Me
3n
4.08
2.07
2.16
3.04
9.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

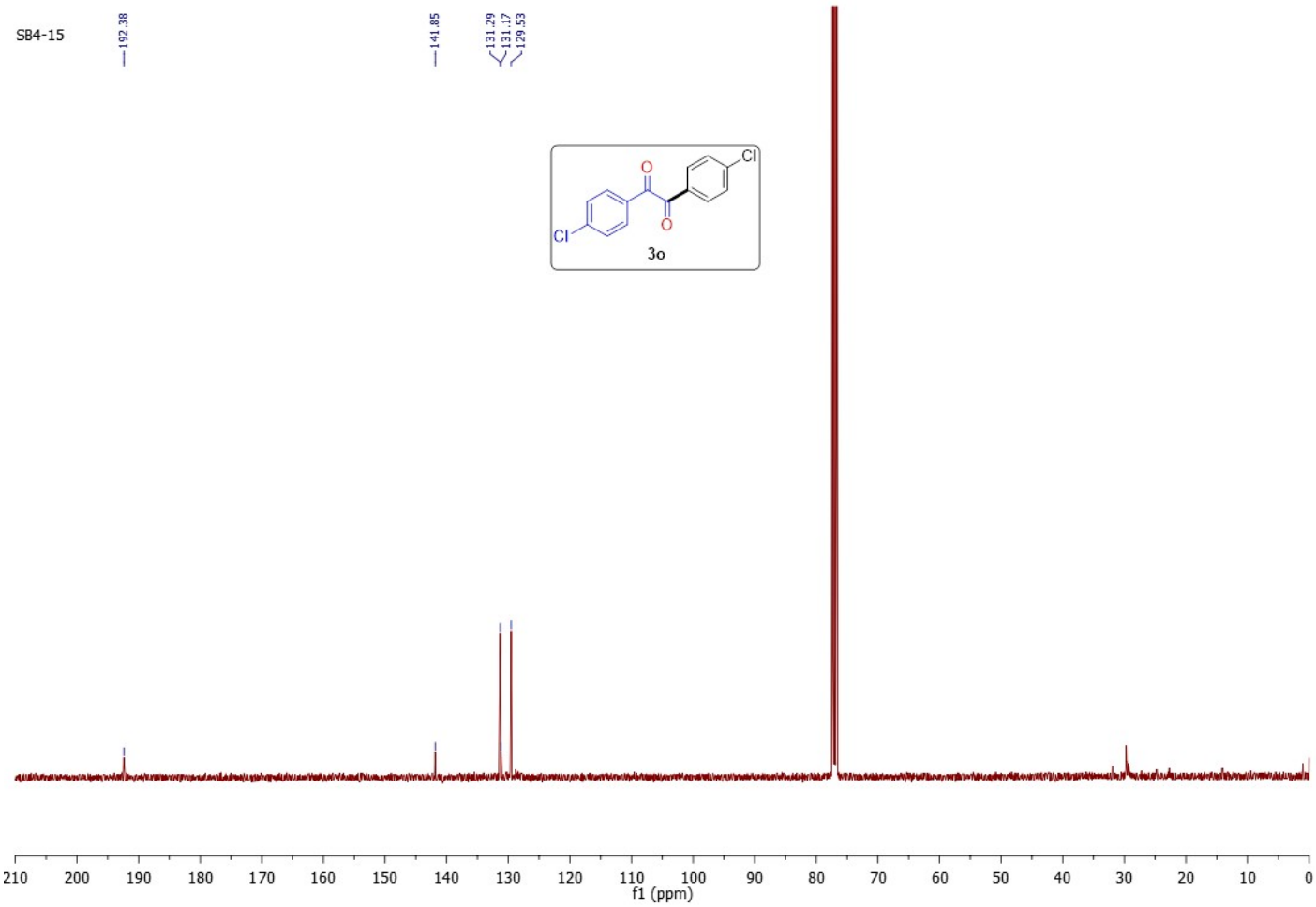

sb4-25
194.53
194.51
158.91
146.05
130.75
130.61
130.04
129.89
129.70
126.01
35.39
30.99
21.92
t-Bu
O
O
Me
3n
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

SB4-15


Cl
O
O
Cl

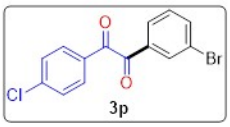
3o


7.93
7.91
7.51
7.49
4.00
4.11
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 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)

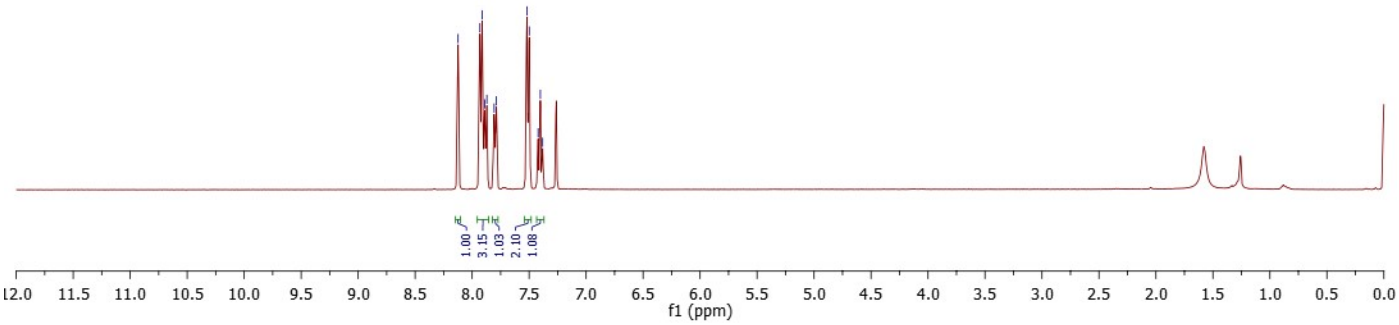

SB4-15
192.38
141.85
131.29
131.17
129.53
Cl
O
O
Cl
3o
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

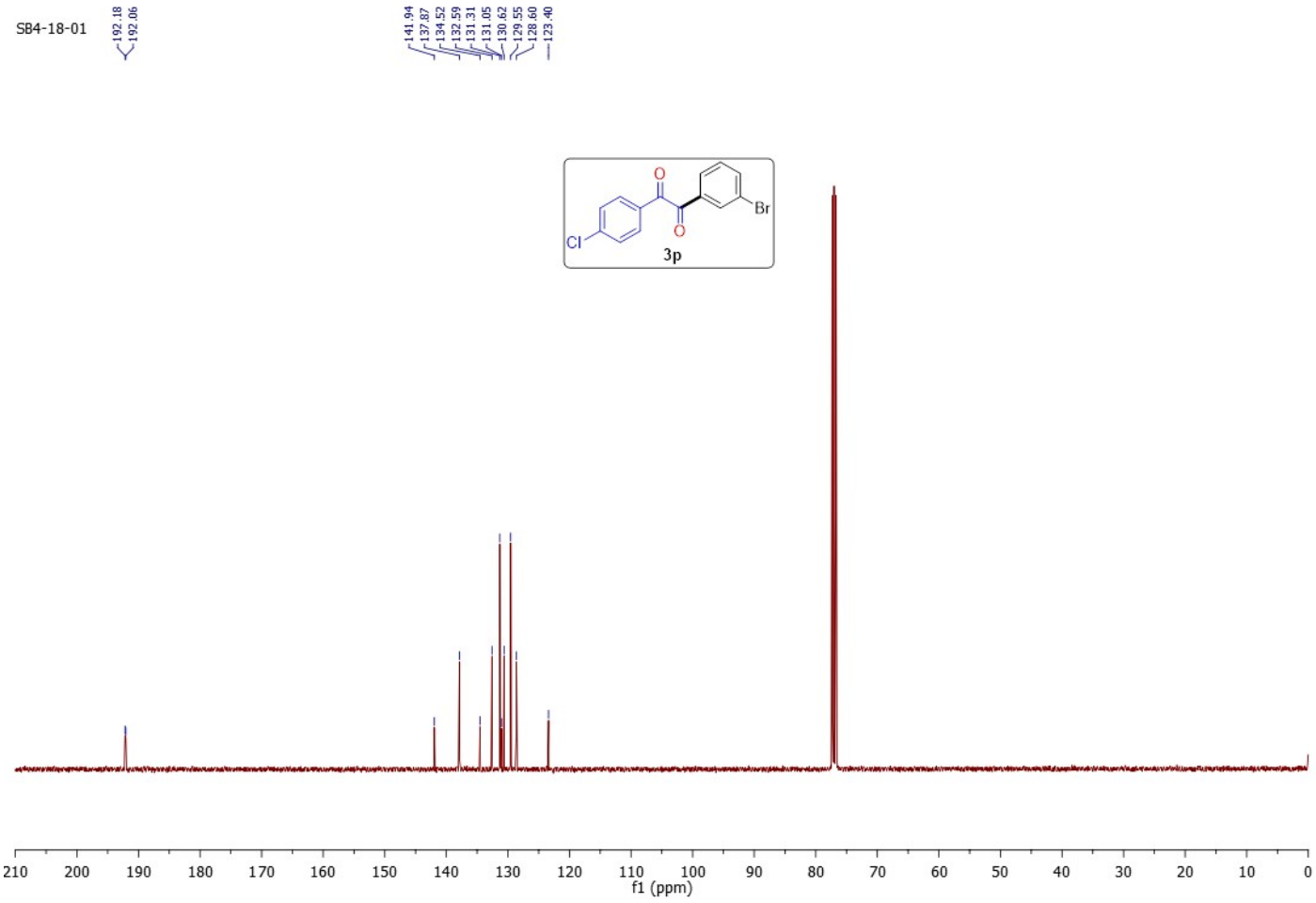
SB4-18-01

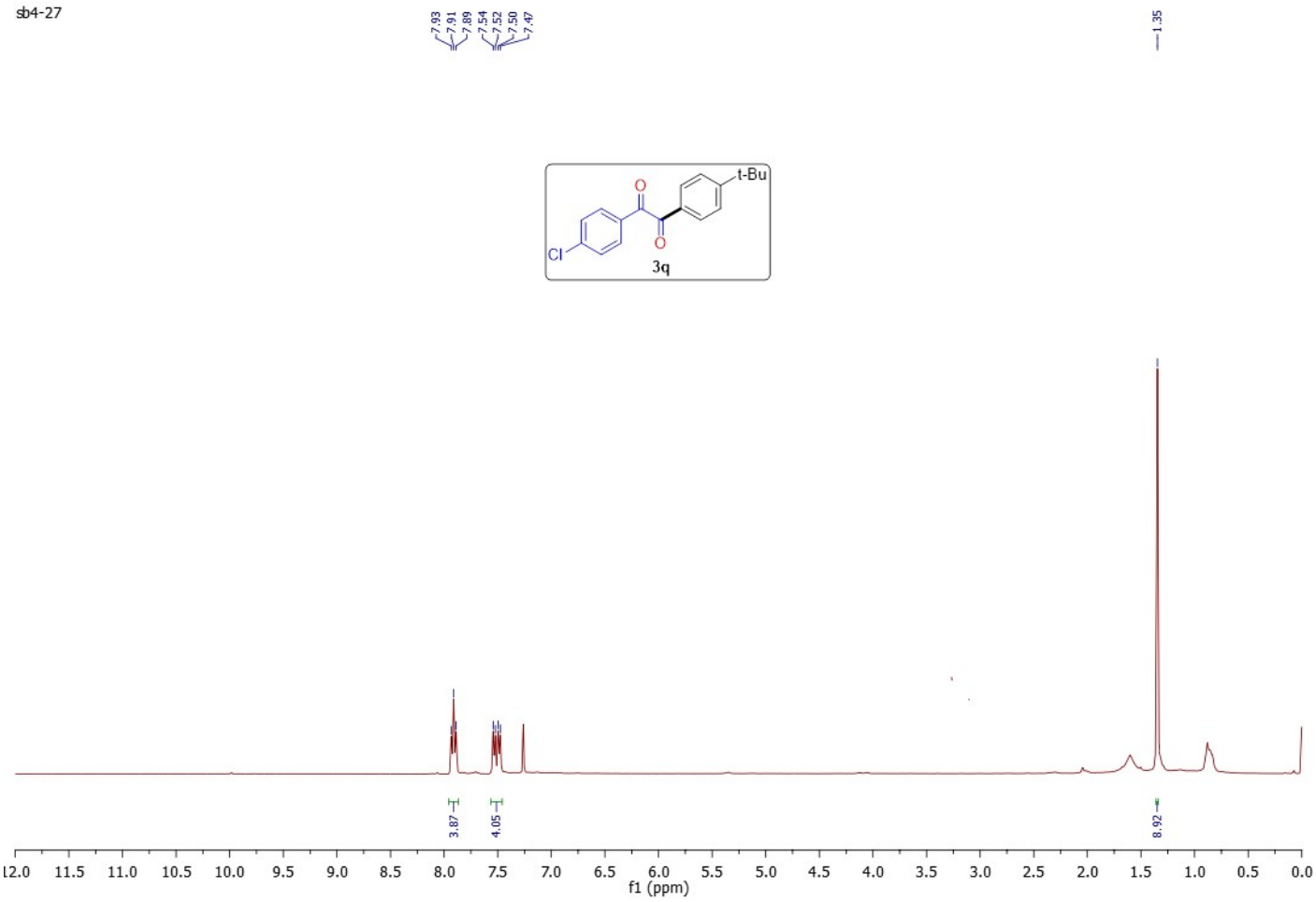

8.12
7.93
7.91
7.89
7.87
7.81
7.79
7.52
7.50
7.42
7.40
7.38

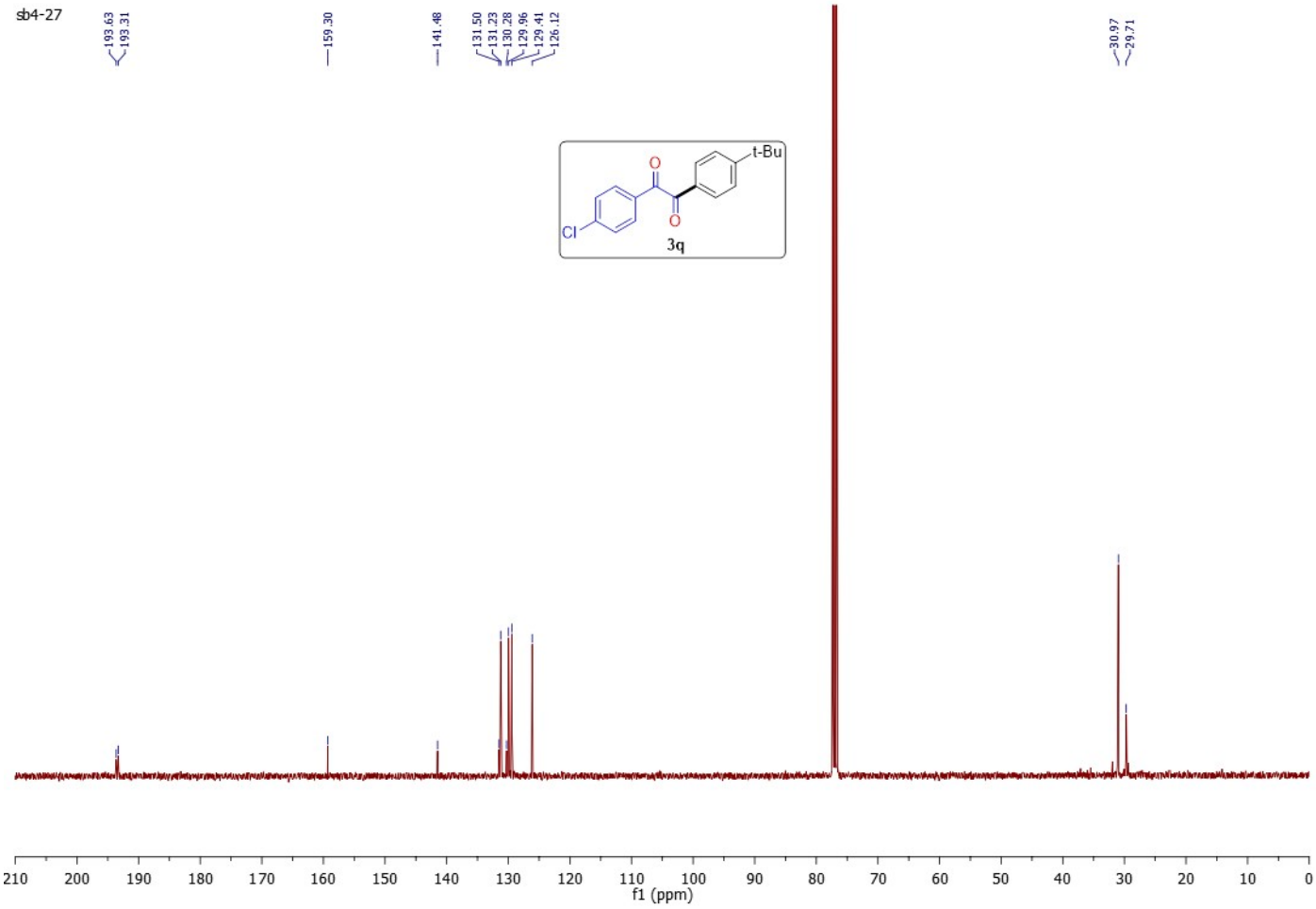

O
O
Br
Cl

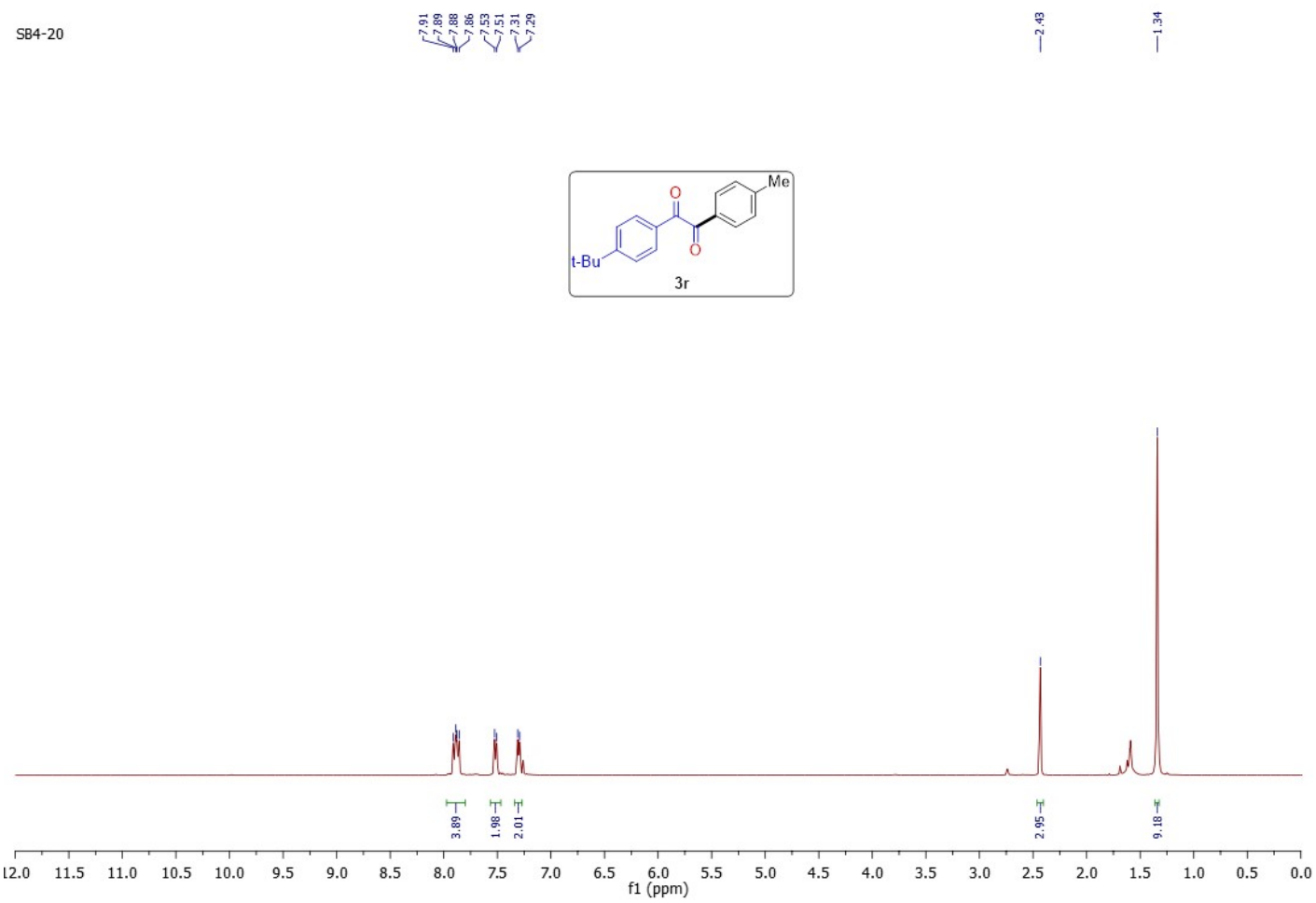
3p

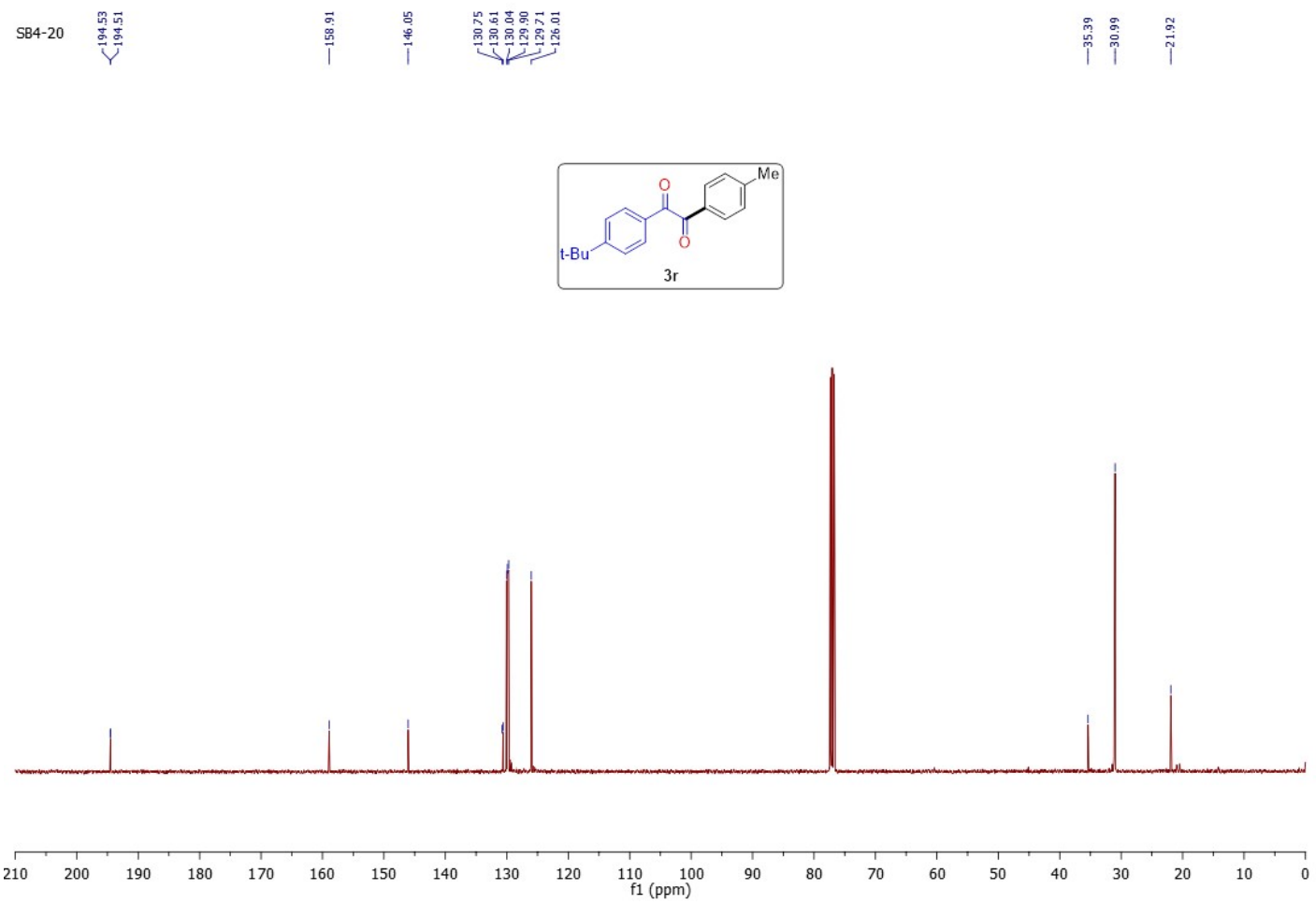

1.00
3.15
1.03
2.10
1.08
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

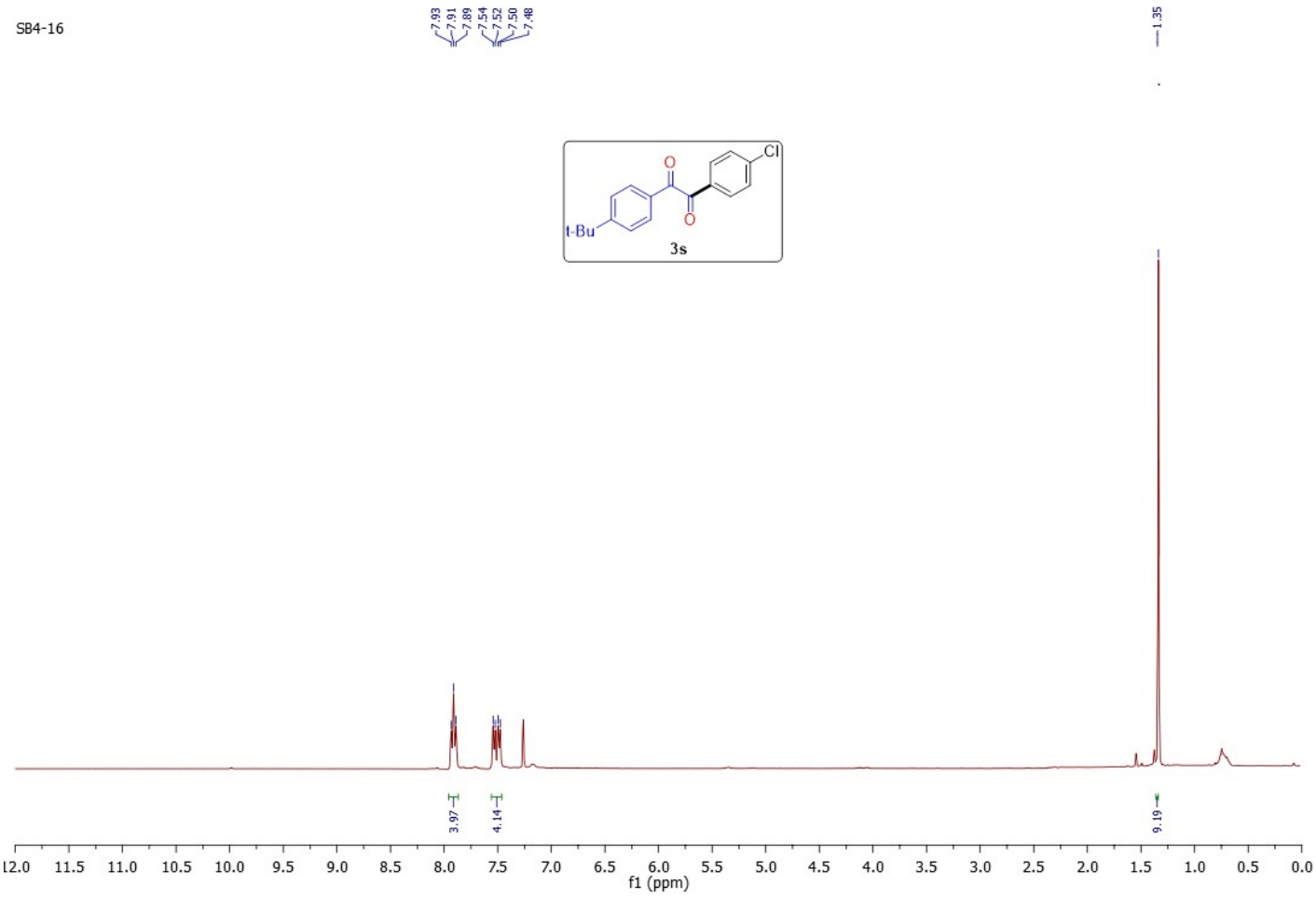

SB4-18-01
192.18
192.06
141.94
137.87
134.52
132.59
131.31
131.05
130.62
129.55
128.60
123.40
O
O
Cl
Br
3p
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

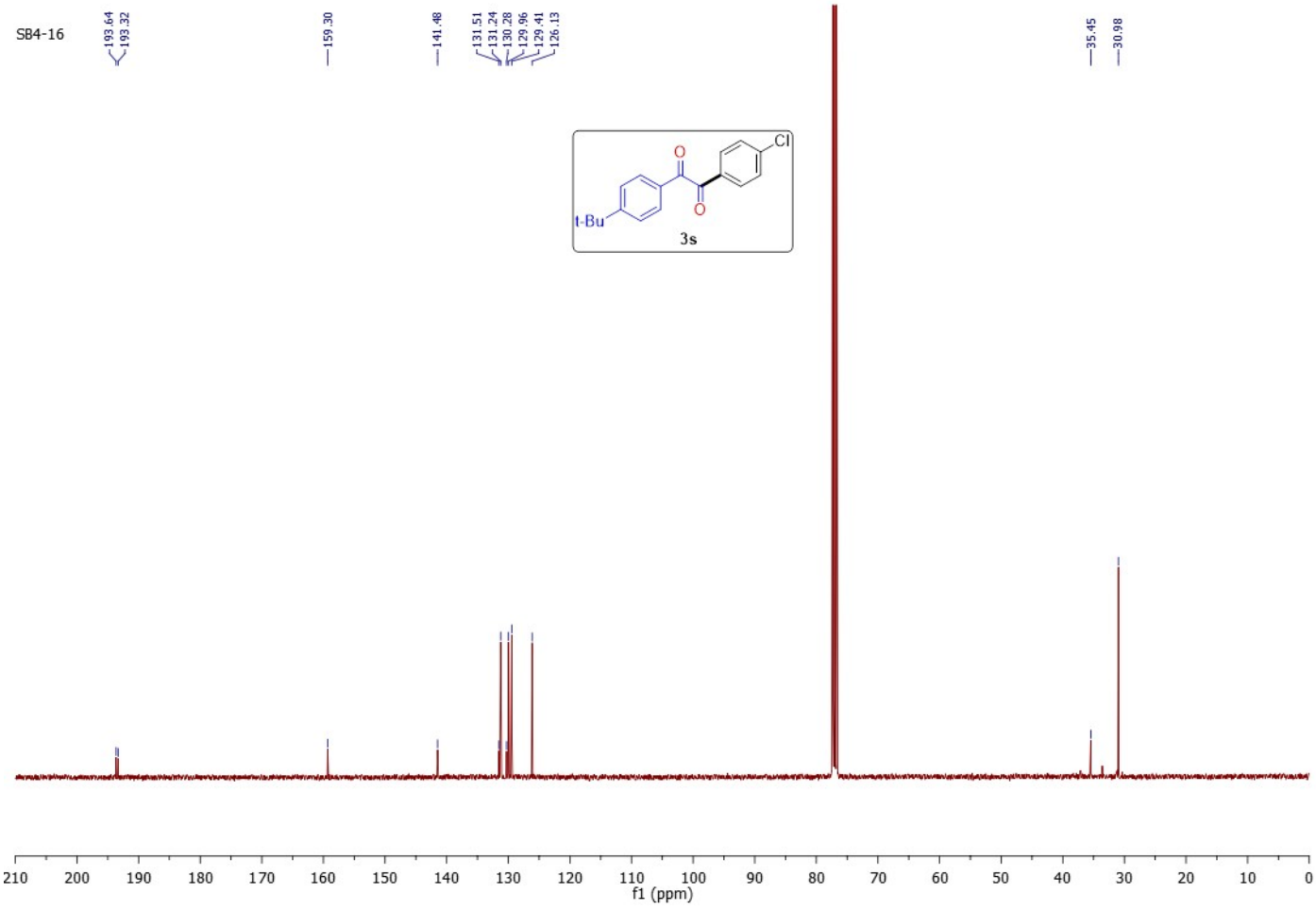

sb4-27
7.93
7.91
7.89
7.54
7.52
7.50
7.47
1.35
t-Bu
O
O
Cl
3q
3.87
4.05
8.92
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

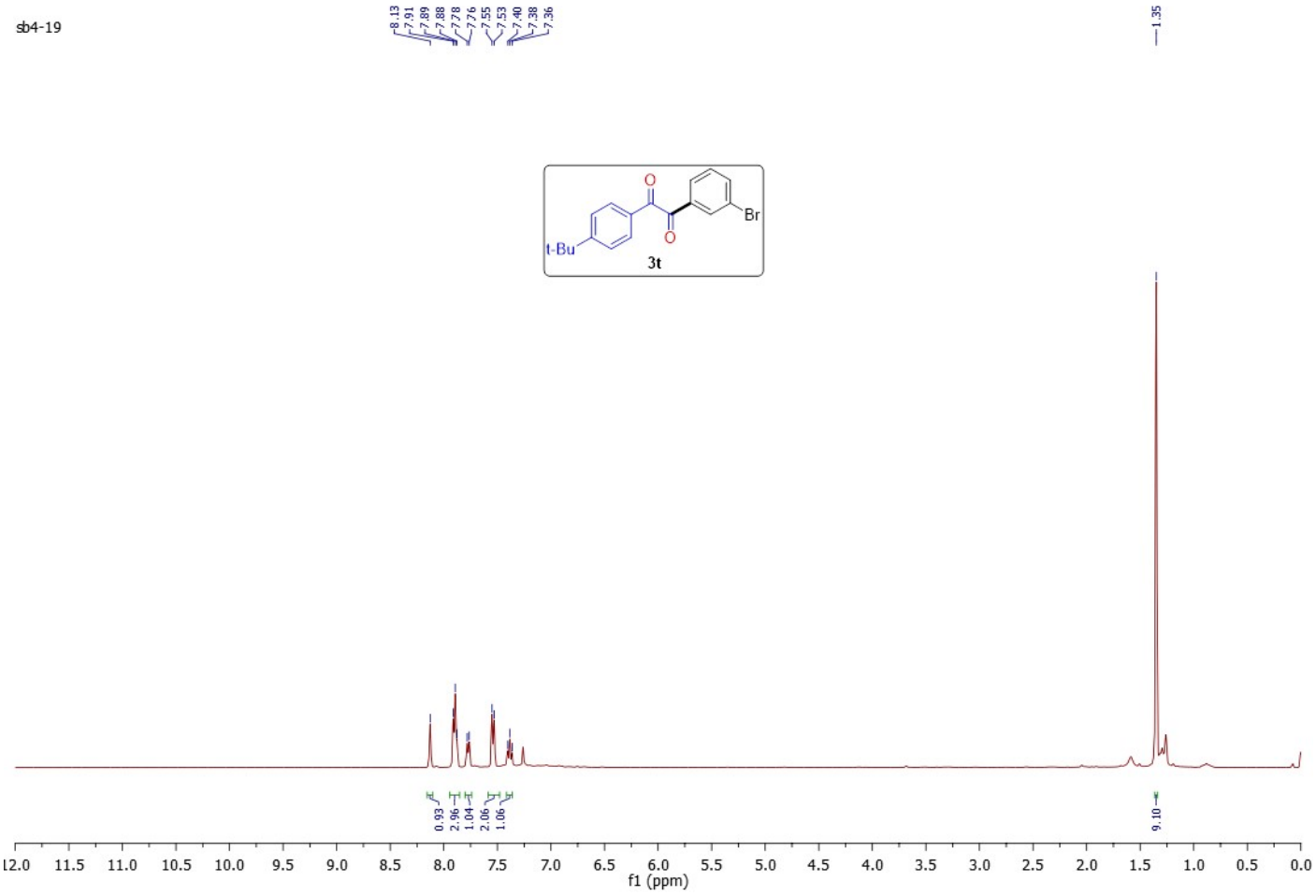

sb4-27
193.63
193.31
159.30
141.48
131.50
131.23
130.28
129.96
129.41
126.12
30.97
29.71
t-Bu
O
O
Cl
3q
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

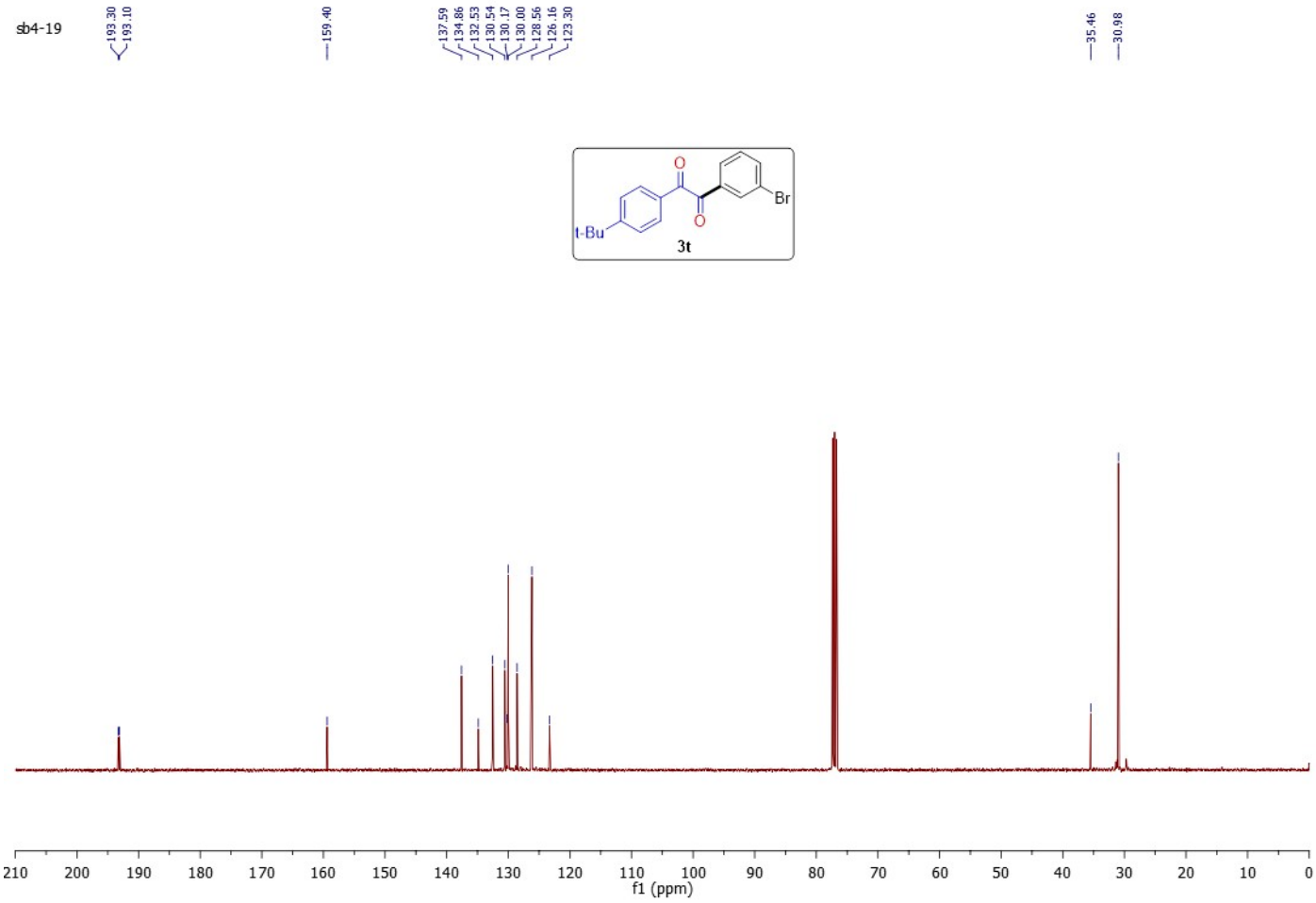

SB4-20
7.91
7.89
7.88
7.86
7.53
7.51
7.31
7.29
2.43
1.34
Me
O
O
t-Bu
3r
3.89
1.98
2.01
2.95
9.18
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


SB4-20
194.53
194.51
158.91
146.05
130.75
130.61
130.04
129.90
129.71
126.01
35.39
30.99
21.92
Me
O
O
t-Bu
3r
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

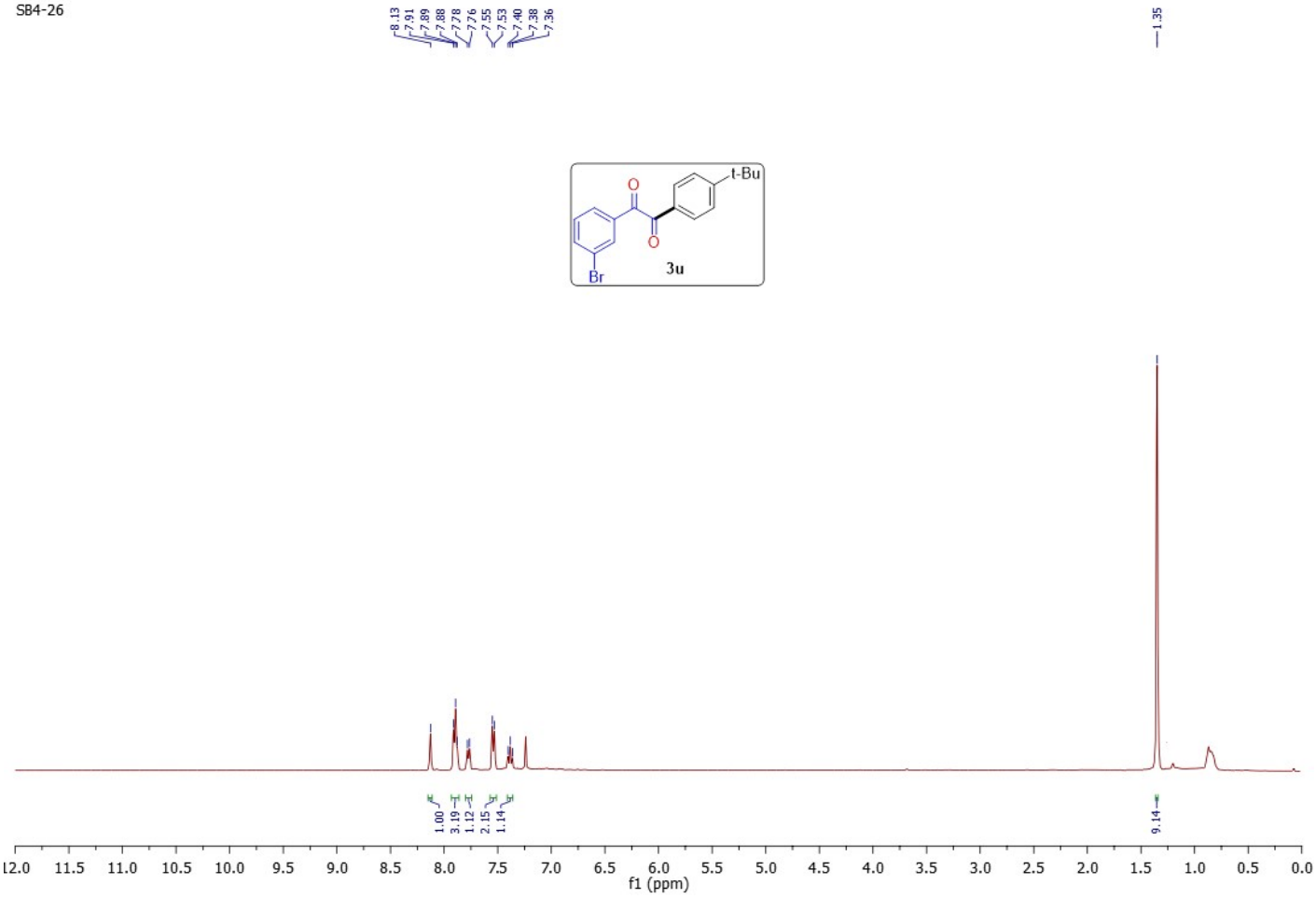

SB4-16
7.93
7.91
7.89
7.54
7.52
7.50
7.48
1.35
O
O
Cl
t-Bu
3s
3.97
4.14
9.19
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

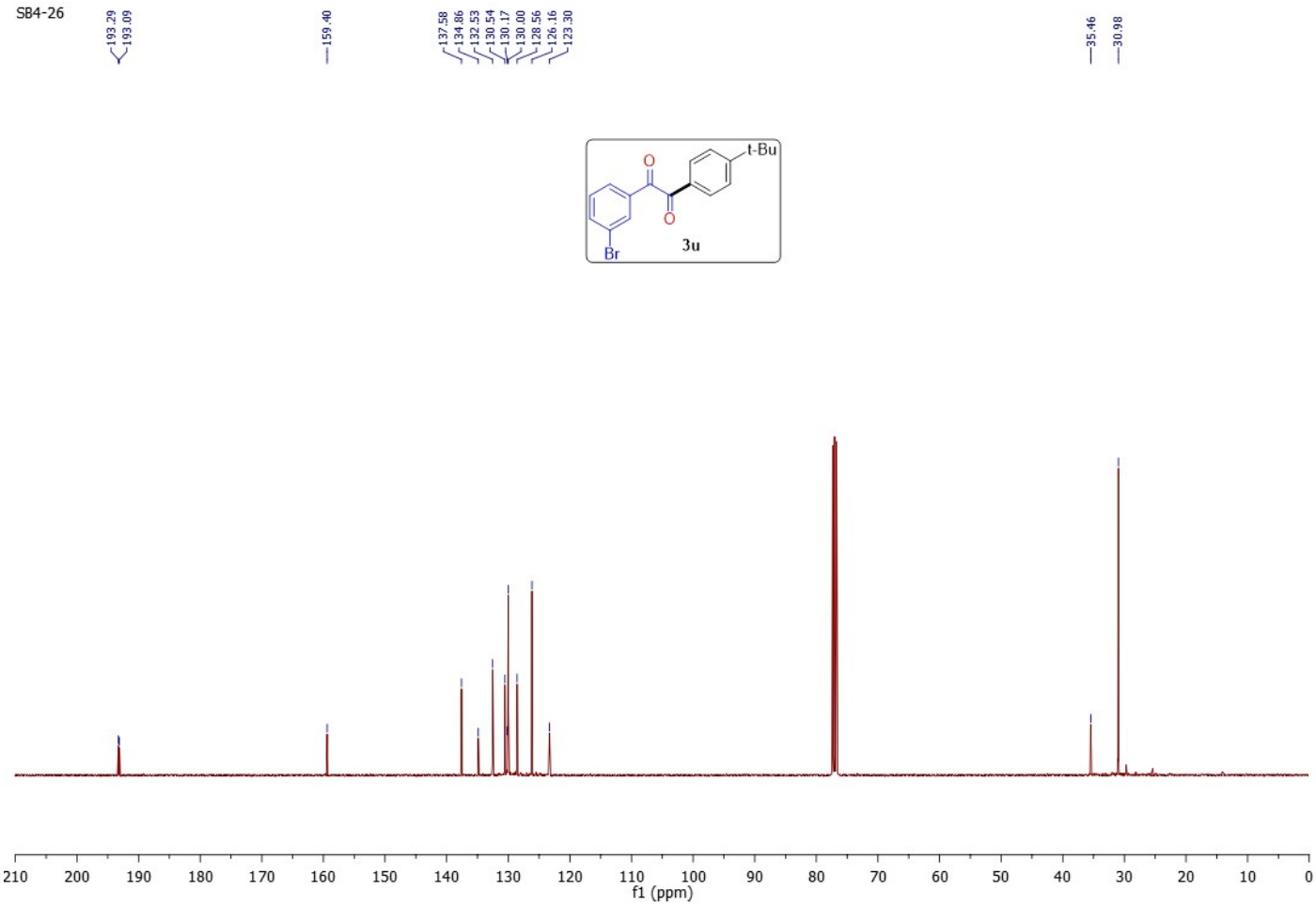

SB4-16
193.64
193.32
159.30
141.48
131.51
131.24
130.28
129.96
129.41
126.13
35.45
30.98
O
O
Cl
t-Bu
3s
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

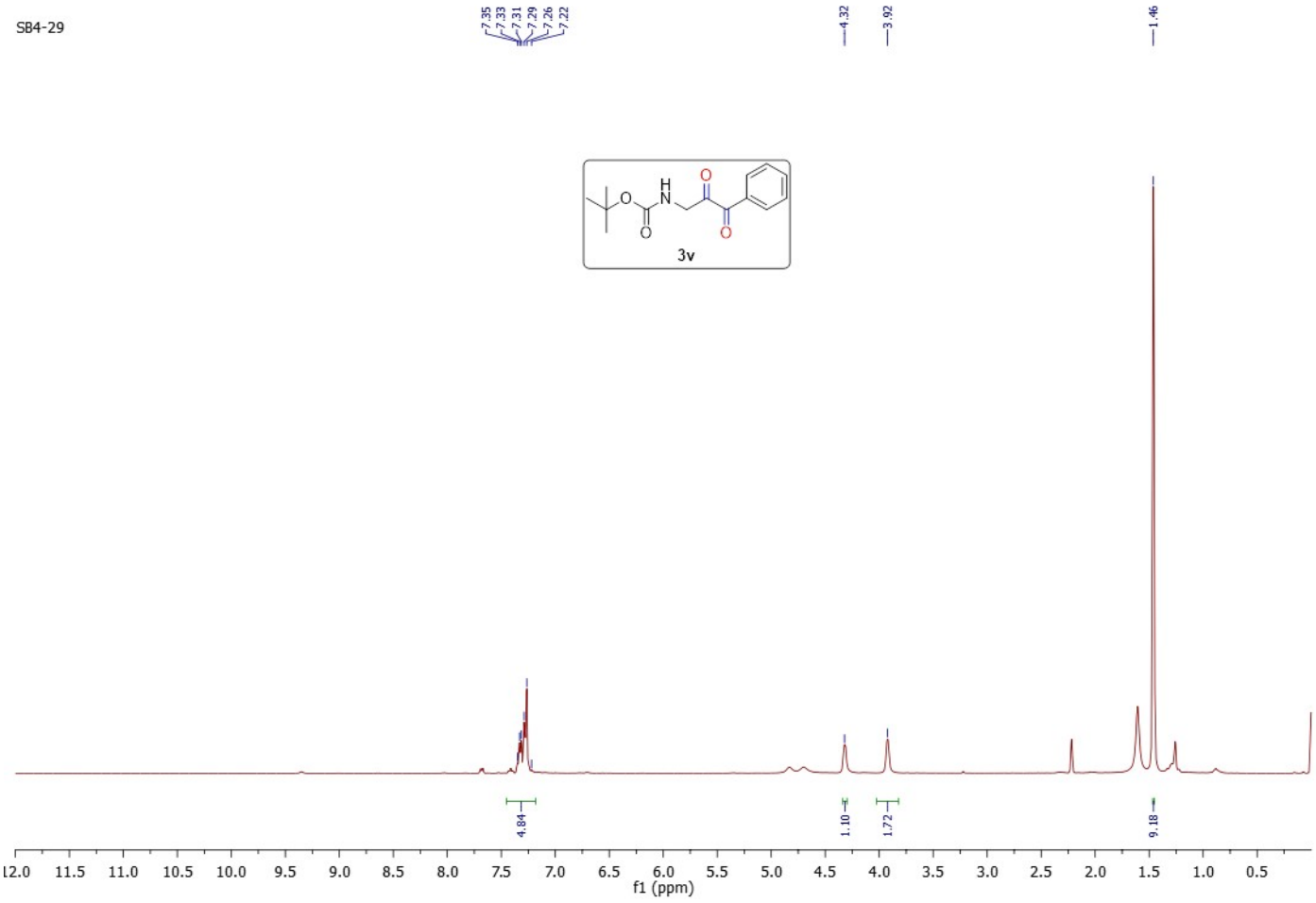

sb4-19
8.13
7.91
7.89
7.88
7.78
7.76
7.55
7.53
7.40
7.38
7.36
1.35
O
O
Br
t-Bu
3t
0.93
2.96
1.04
2.06
1.06
9.10
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

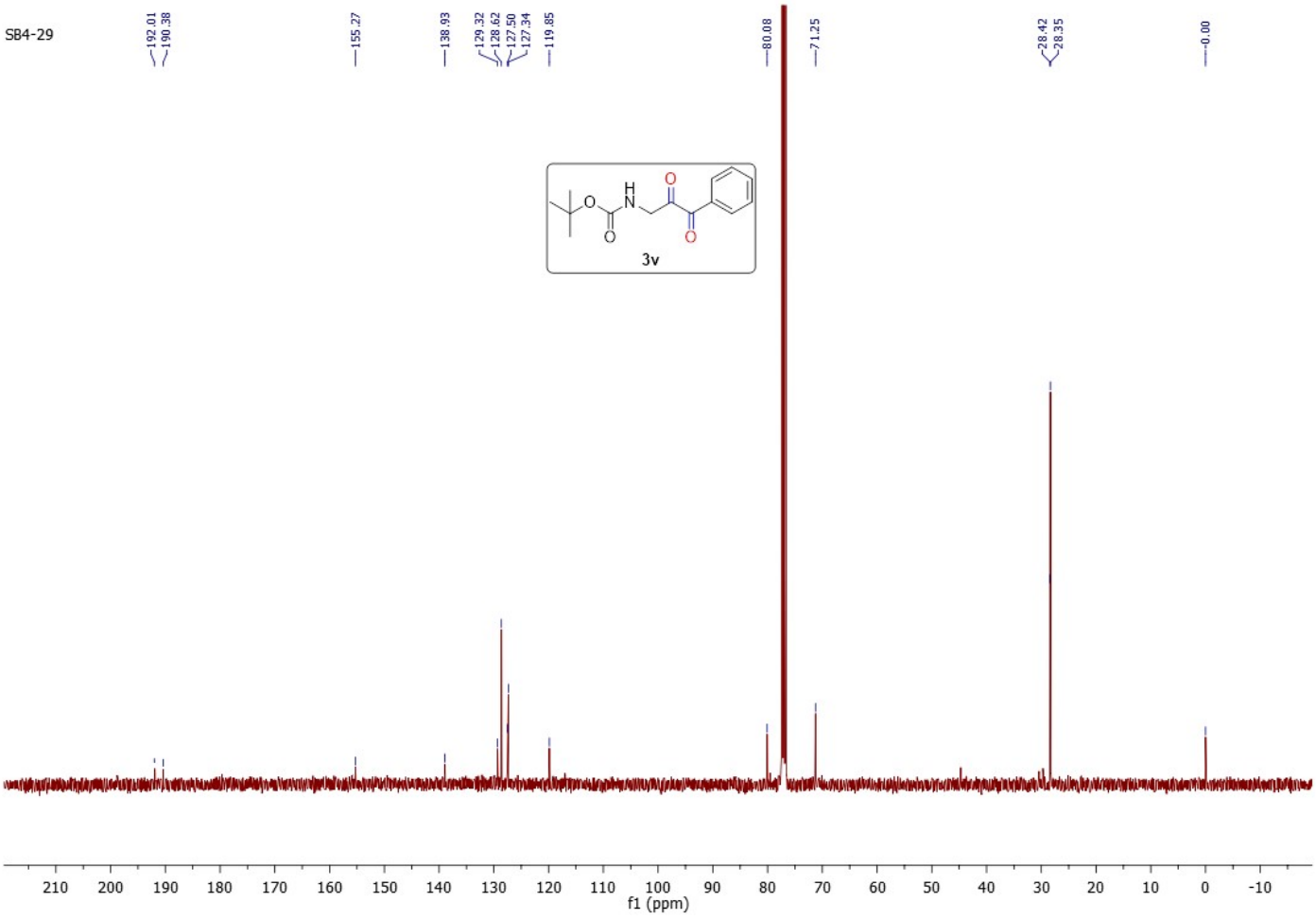

sb4-19
193.30
193.10
159.40
137.59
134.86
132.53
130.54
130.17
130.00
128.56
126.16
123.30
35.46
30.98
O
O
Br
t-Bu
3t
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

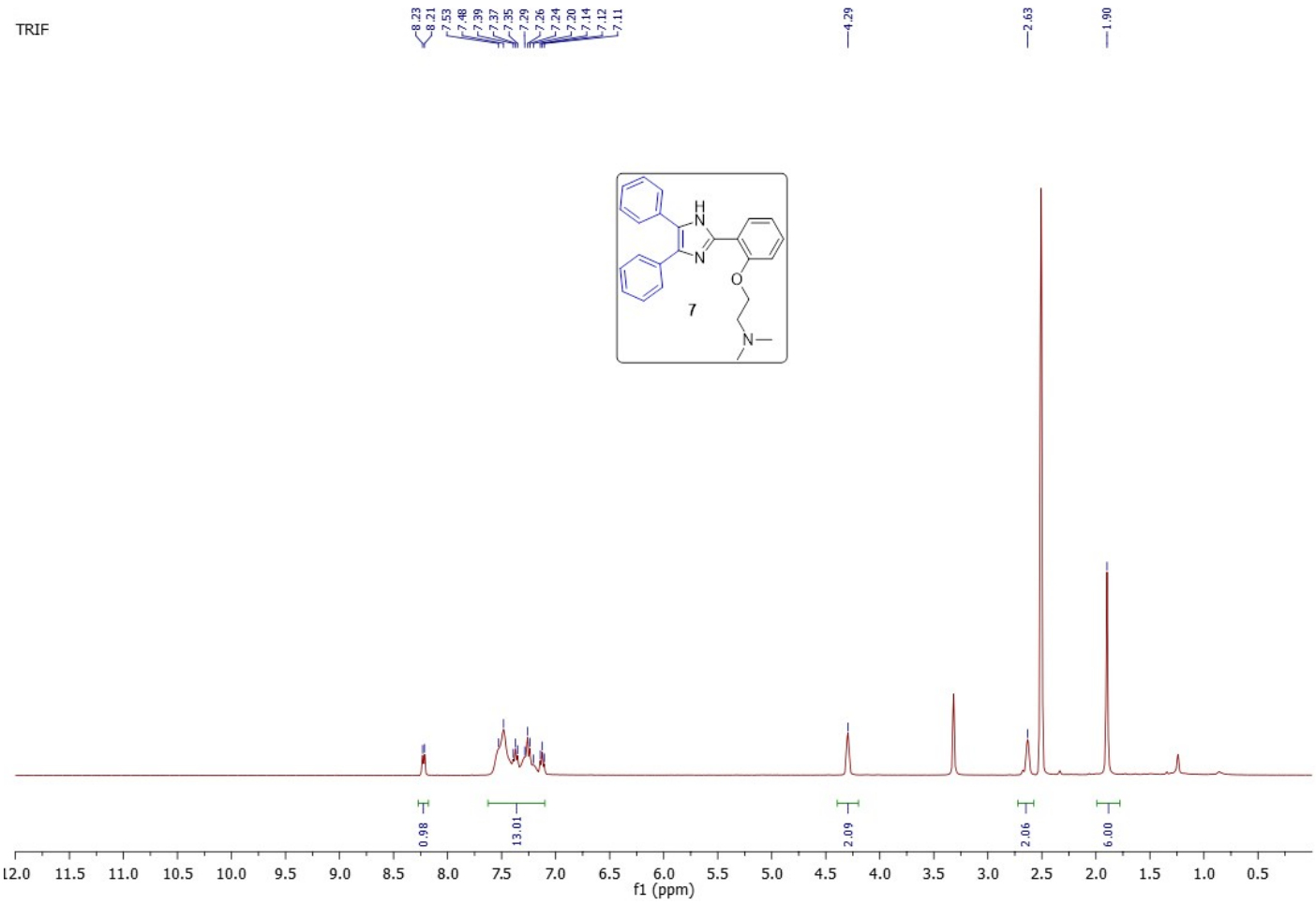
SB4-26

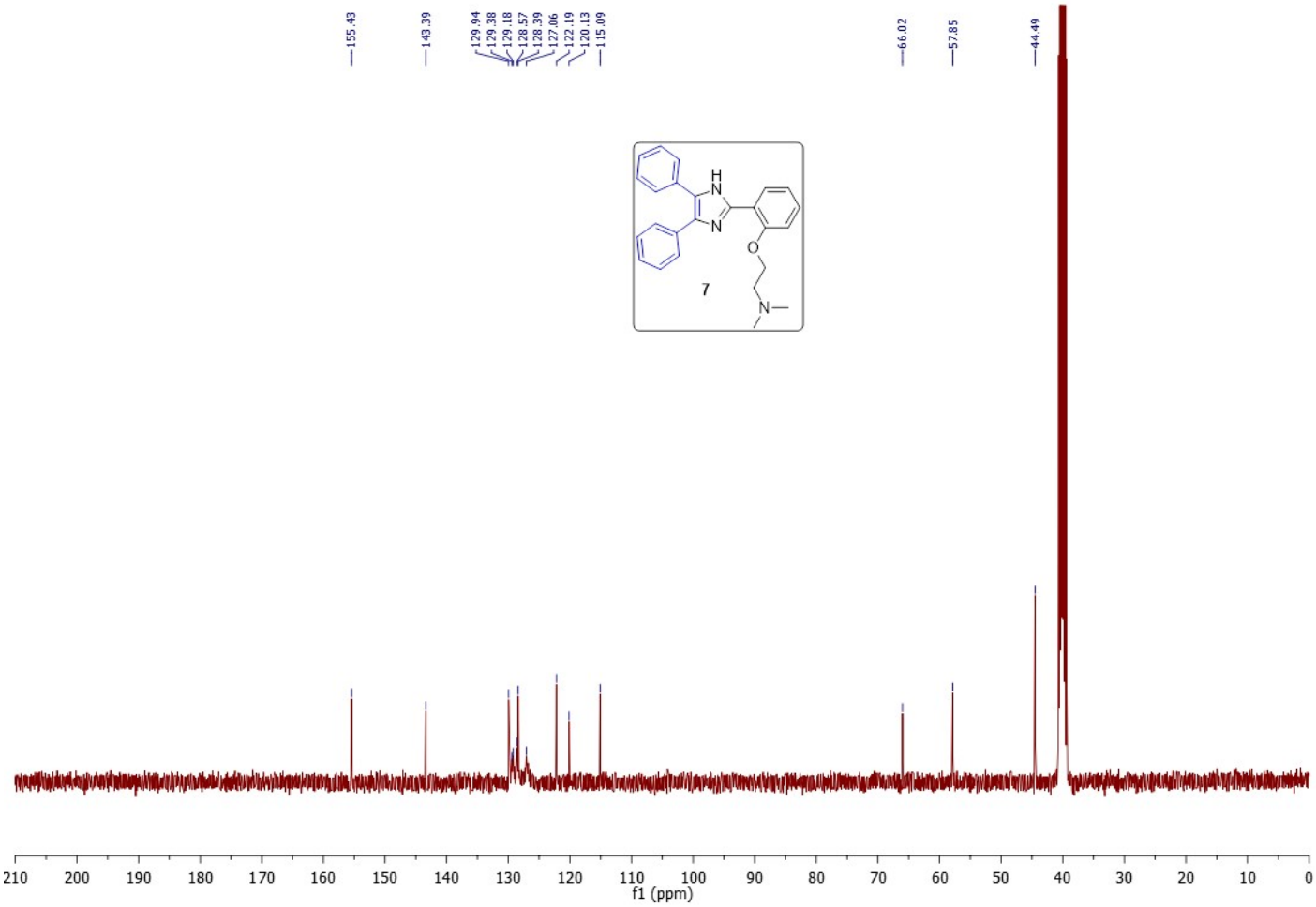

8.13
7.91
7.89
7.88
7.78
7.76
7.55
7.53
7.40
7.38
7.36
1.35
t-Bu
O
O
Br
3u
1.00
3.19
1.12
2.15
1.14
9.14
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

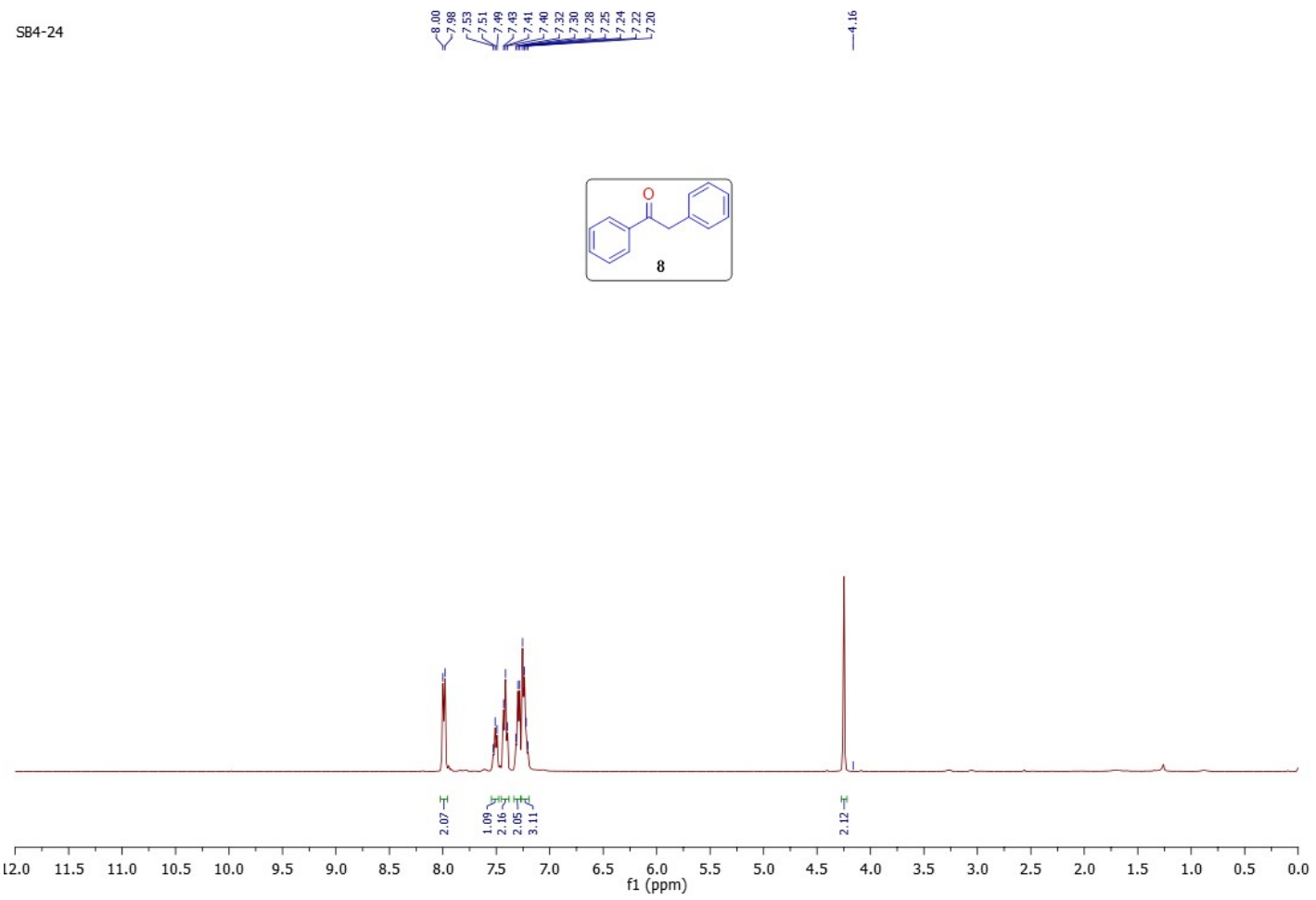

SB4-26
193.29
193.09
159.40
137.58
134.86
132.53
130.54
130.17
130.00
128.56
126.16
123.30
35.46
30.98
t-Bu
O
O
Br
3u
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

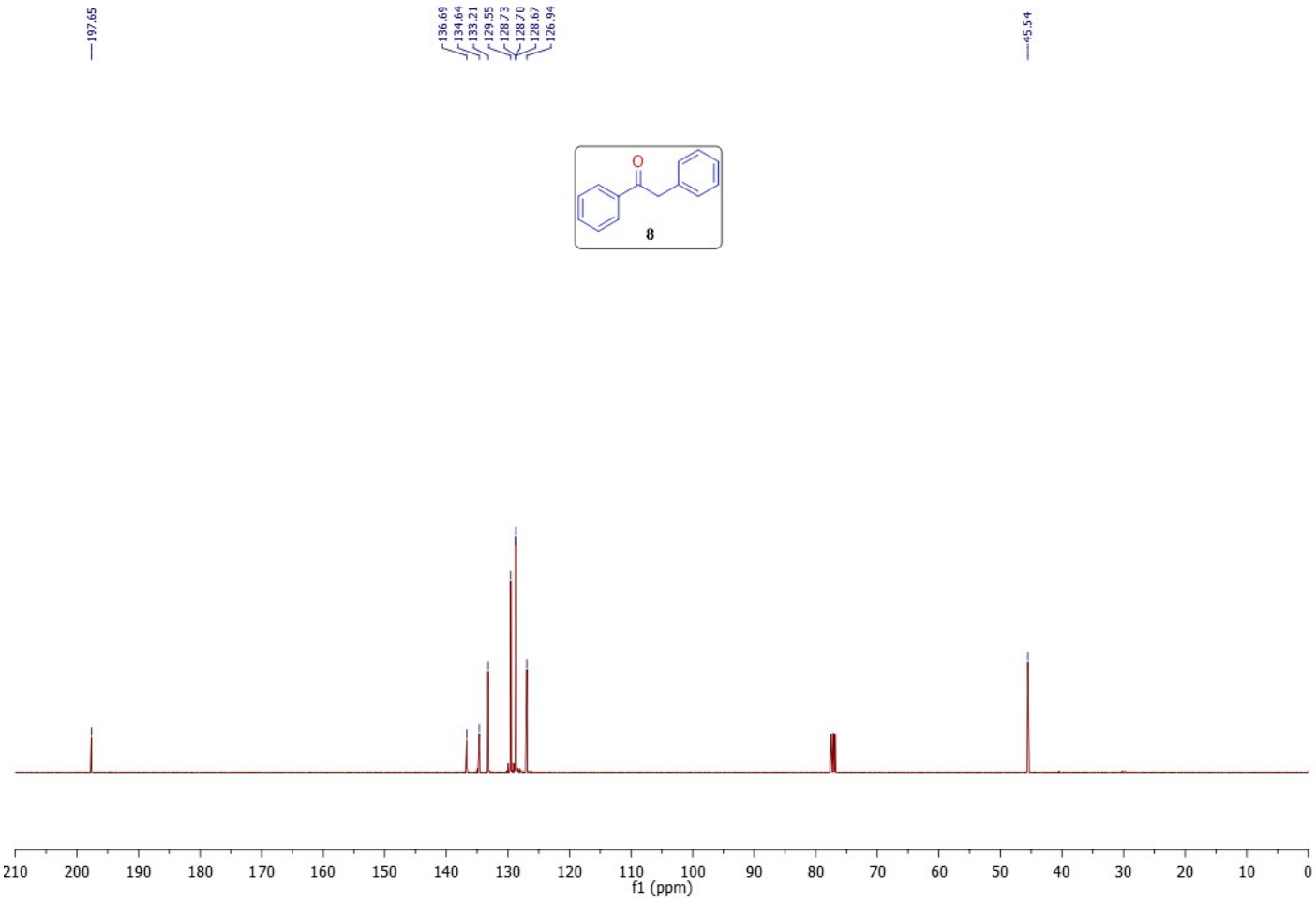

SB4-29
7.35
7.33
7.31
7.29
7.26
7.22
4.32
3.92
1.46
3v
4.84
1.10
1.72
9.18
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


SB4-29
192.01
190.38
155.27
138.93
129.32
128.62
127.50
127.34
119.85
80.08
71.25
28.42
28.35
0.00
3v
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)


TRIF
8.23
8.21
7.53
7.48
7.39
7.37
7.35
7.29
7.26
7.24
7.20
7.14
7.12
7.11
4.29
2.63
1.90
7
0.98
13.01
2.09
2.06
6.00
f1 (ppm)


155.43
143.39
129.94
129.38
129.18
128.57
128.39
127.06
122.19
120.13
115.09
66.02
57.85
44.49
H
N
N
O
N
7
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


SB4-24
8.00
7.98
7.53
7.51
7.49
7.43
7.41
7.40
7.32
7.30
7.28
7.25
7.24
7.22
7.20
4.16
O
8
2.07
1.09
2.16
2.05
3.11
2.12
f1 (ppm)


197.65
136.69
134.64
133.21
129.55
128.73
128.70
128.67
126.94
45.54
O
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)