[3+3] Annulation of Allylic Phosphoryl-Stabilized Carbanions / Phosphorus Ylides and Vinyl Azide: A Practice Strategy to Polyfunctionalized Anilines

Shen Liu, ‡ Wenteng Chen, ‡ Jin Luo and Yongping Yu*,

Zhejiang Province Key Laboratory of Anti-Cancer Drug Research, College of Pharmaceutical Science, Zhejiang University, Hangzhou 310058, P. R. China.

‡ Shen Liu and Wenteng Chen contributed equally to this work.

* Corresponding author, E-mail: yyu@zju.edu.cn; Tel: +86-571-88208452.

Supporting Information

List of contents

General Information:

All solvents were purified according to standard methods prior to use. Reactions were run under an atmosphere of nitrogen unless mentioned otherwise. Purifications of reaction products were carried out by chromatography using silica gel (200–300 mesh). Melting points were recorded on a BÜCHI B-540 melting point apparatus. Infrared spectra were recorded on FTIR spectrophotometer. NMR spectra were recorded for ^{1}H NMR at 500 MHz and for ^{13}C NMR at 125 MHz. For ^{1}H NMR, tetramethylsilane (TMS) served as internal standard (δ=0) and data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constant(s) in Hz. For ^{13}C NMR, TMS (δ=0) or $CDCl_3$ (δ=77.26) was used as internal standard and spectra were obtained with complete proton decoupling. HPLC analysis and the HRMS of all biologically evaluated compounds was confirmed on a Agilent 1290 HPLC-6224 Time of Fight Mass Spectrometer using PhenomenexLuna 5µ C18, 100 Å, 150 X 4.60 mm 5 micron column at a flow rate of 0.5ml/min using liner gradients buffer B in A (B: CH_3OH containing 0.1 % formic acid, A: H_2O containing 0.1% formic acid). Mobile phase B was increased linearly from 5% to 95% over 7 min and 95% over the next 2 min, after which the column was equilibrated to 5% for 1 min.

The starting material **2** were prepared according to literature methods.[1, 2]

General Procedure for the Synthesis of 3

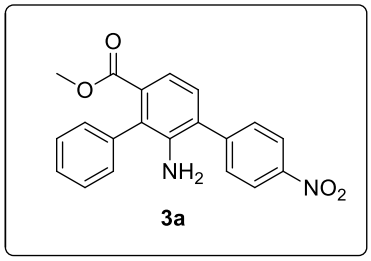
Pathway A: A mixture of phosphorus ylides (**1a**) (1.0 mmol), vinyl azide **2** (1.0 mmol) and EtONa (3.0 mmol) was stirred in DCM (2 ml) at room temperature for 1.0 h. The reaction mixture was quenched with water (10 ml), and then extracted three times with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by chromatography to afford **3a-3o**.

Pathway B: A mixture of allylic phosphoryl-stabilized carbanions (**1b**) (1.0 mmol), vinyl azide **2** (1.0 mmol) and MeONa (5.0 mmol) was stirred in DCM (2 ml) at room

temperature for 1.0 h. The reaction mixture was quenched with water (10 ml), and then extracted three times with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated. Purification of the crude product by chromatography to afford **3p-3w**.

Characterization Data

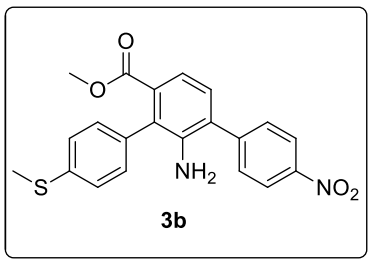
2-Phenyl-3-methoxycarbonyl-6-(4-nitrophenyl) aniline (3a)



3a

Yellow solid, m.p.178.0-178.4ºC.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38-8.29 (m, 2H), 7.74-7.70 (m, 2H), 7.49 (m, 2H), 7.44-7.39 (m, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.32 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 1H), 3.73 (s, 2H), 3.59 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$), δ 168.2, 147.3, 145.9, 141.7, 137.2, 132.1, 130.0, 129.2, 129.1, 128.9, 128.2, 127.9, 127.8, 124.2, 119.3, 51.8. HRMS (ESI) calcd. for $C_{20}H_{17}N_2O_4[M+H]^+$= 349.1183, found 349.1184.

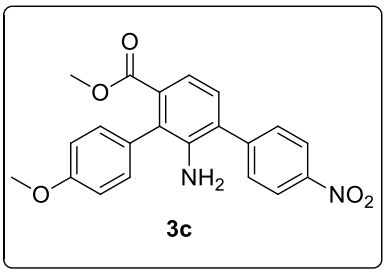
2-(4-Methylthio)phenyl-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3b):



3b

Yellow solid, m.p.58.0-58.4 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.33-7.35 (m, 3H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.16 (d, *J* = 7.8 Hz, 1H), 3.71 (s, 2H), 3.61 (s, 3H), 2.53 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 145.8, 141.9, 138.2, 133.6, 132.1, 130.0, 129.7, 129.1, 127.5, 126.9, 126.6, 124.2, 123.9, 119.3, 51.9,15.5. HRMS (ESI) calcd for $C_{21}H_{19}N_2O_4S$ $[M+H]^+$ = 395.1060, found 395.1060.

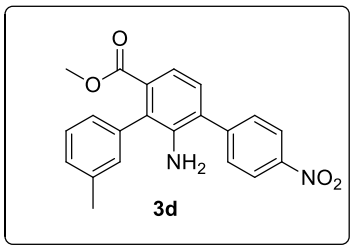
2-(4-Methoxyphenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3c):



3c

Yellow solid , m.p. 159.0-159.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.6 Hz, 2H), 7.70 (d, *J* = 8.6 Hz,2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 2H), 3.86 (s, 3H), 3.73 (s, 2H), 3.60 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 159.1, 147.3, 146.0, 142.1, 132.6, 130.4, 130.0, 129.0, 128.9, 127.8, 127.7, 124.2, 119.1, 114.4, 55.2, 51.9. HRMS (ESI) calcd for $C_{21}H_{19}N_2O_5$ $[M+H]^+$= 379.1288, found 379.1288.

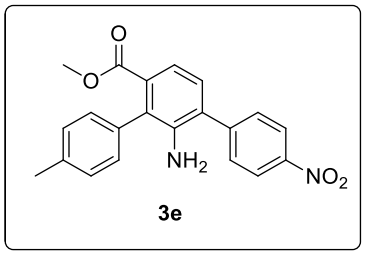
2-(3-Methylphenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3d):



3d

Yellow solid, m.p.125.0-125.4°C.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.35 (m, 2H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.12 (s, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 3.72 (s, 2H), 3.58 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 147.2, 146.0, 141.7, 138.5, 137.0, 132.2, 130.0, 129.7, 129.0, 128.8, 128.5, 128.3, 127.8, 126.2, 124.2, 119.2, 51.8, 21.4. HRMS (ESI) calcd. for $C_{21}H_{19}N_2O_4$ $[M+H]^+$= 363.1339, found 363.1339.

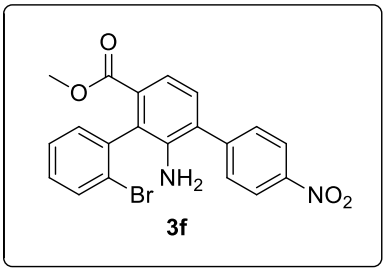
2-(4-Methylphenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3e):



3e

Yellow solid, m.p. 129.6-130.0°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.5 Hz, 2H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.29 (m, 2H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 1H), 3.75(s,2H),3.62 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2, 147.2, 146.0, 141.9, 137.4, 134.0, 132.2, 130.0, 129.7, 129.3, 129.0, 128.9, 127.8, 124.2, 119.1, 51.9, 21.3. HRMS (ESI) calcd. for $C_{21}H_{19}N_2O_4$ $[M+H]^+$= 363.1339, found 363.1338.

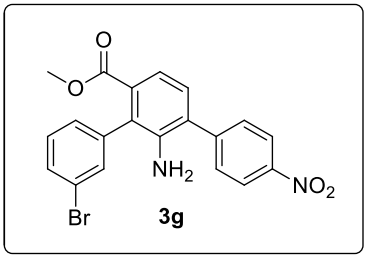
2-(2-Bromophenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3f):



3f

Yellow solid, m.p.151.2-152.0 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.3 Hz, 2H), 7.72 (m, 3H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.29 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 3.63 (s, 3H), 3.60 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 147.4, 145.7, 141.6, 138.4, 133.0, 130.9,130.9, 130.0, 129.6, 129.4,128.6, 127.9, 127.7, 124.2, 124.1, 119.9, 51.9. HRMS (ESI) calcd. for $C_{20}H_{16}BrN_2O_4$ $[M+H]^+$= 427.0288, found 427.0287.

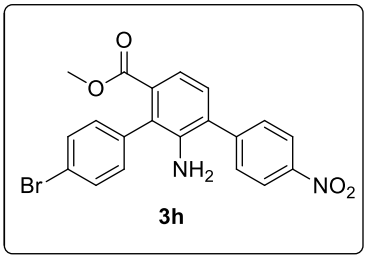
2-(3-Bromophenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3g):



3g

Yellow solid, m.p.156.2-156.7 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.47 (s, 1H), 7.37 (m, 2H), 7.25 (d, *J* = 9.0 Hz, 1H), 7.18 (d, *J* = 7.9 Hz, 1H), 3.71 (s, 2H), 3.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 147.3, 145.6, 141.6, 139.4, 132.2, 131.7, 130.9, 130.4, 130.0, 129.5, 128.2, 128.0, 126.6, 124.3, 122.9, 119.5, 52.0. HRMS (ESI) calcd. for $C_{20}H_{16}BrN_2O_4$ $[M+H]^+$= 427.0288, found 427.0288.

2-(4-Bromophenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3h):

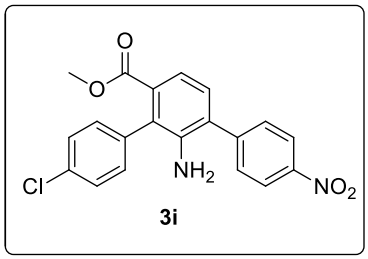


3h

Orange solid, m.p. 151.0-151.4ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.5 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.24 -7.10 (m, 3H), 3.67 (s, 2H), 3.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 147.4, 145.6, 141.6, 136.2, 132.1, 131.8, 131.0, 130.0, 129.4, 128.2, 126.9, 124.3, 122.0,

119.5, 51.9. HRMS (ESI) calcd. for $C_{20}H_{16}BrN_2O_4$ $[M+H]^+$= 427.0288, found 427.0288.

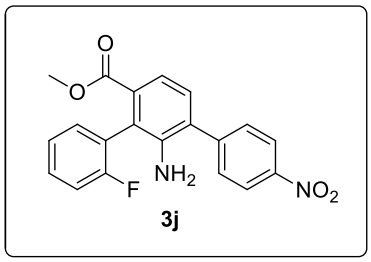
2-(4-Chlorophenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3i):



3i

Yellow solid, m.p.158.1-158.4 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.7 Hz,2H), 7.69 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 1H), 3.68 (s, 2H), 3.61 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 147.3, 145.6, 141.7, 135.7, 133.8, 131.8, 130.7, 130.0, 129.4, 129.2, 128.1, 126.9, 124.3, 119.5, 52.0. HRMS (ESI) calcd. for $C_{20}H_{16}ClN_2O_4$ $[M+H]^+$= 383.0793, found 383.0794.

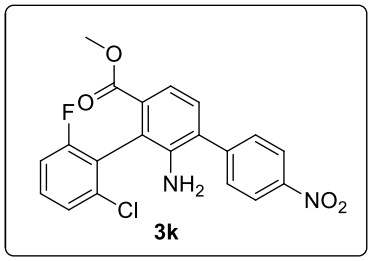
2-(2-Fluorophenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3j):



3j

Yellow solid, m.p.146.9-147.2 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 7.9 Hz, 2H), 7.71 (d, J = 7.9 Hz, 2H), 7.48 (d, J = 8.0 Hz, 1H), 7.45-7.37 (m, 1H), 7.29-7.26(m, 2H), 7.22-7.18(m, 2H), 3.69 (s, 2H), 3.64 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 161.1,158.7, 147.3, 145.6, 142.1, 131.8, 131.2, 130.1,130.0, 129.7, 128.5, 124.6,124.5, 124.2, 122.0,120.0, 116.0, 115.8, 52.0. HRMS (ESI) calcd. for $C_{20}H_{16}FN_2O_4$ $[M+H]^+$= 367.1089, found 367.1089.

2-(2-Fluoro-6-chlorophenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3k):

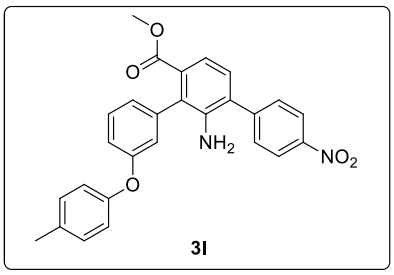


3k

Yellow solid, m.p.220.9-221.6 ºC.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 7.9 Hz, 2H), 7.72 (d, *J* = 7.9 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.39-7.32 (m, 2H), 7.26-7.25 (m, 1H), 7.17-7.11 (m, 1H), 3.69 (s, 3H), 3.63 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ

166.4, 161.5, 159.0, 147.5, 145.4, 141.9, 135.1,135.0, 131.0, 130.2,130.1,130.0, 129.0, 125.5, 124.8,124.6, 124.2, 120.5, 119.6, 114.5, 114.2, 52.0. HRMS (ESI) calcd. for $C_{20}H_{15}ClFN_2O_4$ $[M+H]^+$= 401.0699, found 401.0698.

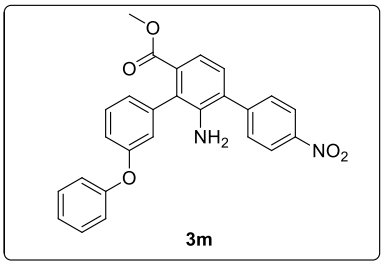
2-(3-(p-tolyloxy)phenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3l):



3l

Yellow solid, m.p.62.0-62.2 ^oC.^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.14-7.12 (m, 3H), 7.02-7.00 (m, 2H), 6.94-6.92(m, 3H), 3.74 (s, 2H), 3.63 (s, 3H), 2.33 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 158.3, 154.5, 147.3, 145.8, 141.6, 138.8, 133.1, 132.0, 130.3,130.2, 130.0, 129.2, 127.9, 127.4, 124.2, 123.6, 119.3,119.2,119.1, 117.8, 51.9, 20.7. HRMS (ESI) calcd. for $C_{27}H_{23}N_2O_5$ $[M+H]^+$= 455.1601, found 455.1603.

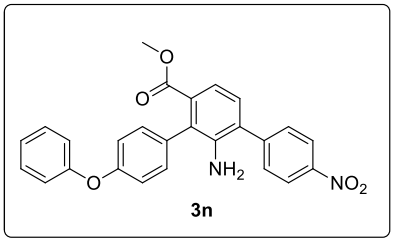
2-(3-Phenoxyphenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3m):



3m

Yellow solid, m.p.145.2-145.9^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.44 (t, J = 7.8 Hz, 1H), 7.34- 7.32 (m, 3H), 7.15 (d, *J* = 7.9 Hz, 1H), 7.12-7.10 (m, 1H), 7.06-7.02 (m, 4H), 6.97-6.95 (m, 1H), 3.74 (s, 2H), 3.64(s,3H).^{13}C NMR(101MHz,$CDCl_3$) δ 167.9, 157.7, 157.1, 147.3, 145.8, 141.6, 139.0, 132.0, 130.3, 130.0, 129.7, 129.2, 128.0, 127.4, 124.2, 124.1, 123.4, 119.8, 119.3, 118.8, 118.3, 51.9. HRMS (ESI) calcd. for $C_{26}H_{21}N_2O_5$ $[M+H]^+$= 441.1445, found 455.1447.

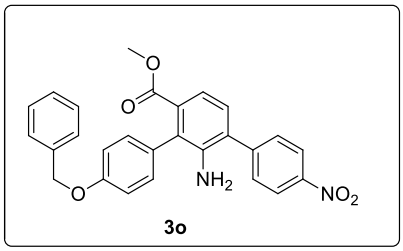
2-(4-Phenoxyphenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3n):



3n

Yellow solid, m.p.145.8-146.4 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.1 Hz, 2H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.41-7.29 (m, 4H), 7.17-7.14 (m, 2H), 7.10-7.07 (m, 5H), 3.75 (s, 2H), 3.63 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 157.1, 156.7, 147.3, 145.9, 141.9, 132.4, 131.9, 131.6, 130.7, 130.0, 129.8, 129.1, 127.8 ,124.2, 123.6, 119.3, 119.3, 118.9, 51.9. HRMS (ESI) calcd. for $C_{26}H_{21}N_2O_5$ $[M+H]^+$= 441.1445, found 441.1442.

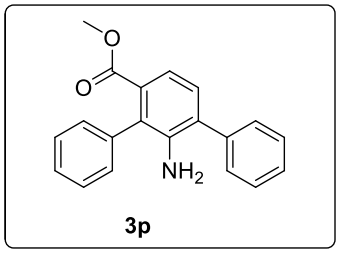
2-(4-benzyloxyphenyl)-3-methoxycarbonyl-6-(4-nitrophenyl)aniline(3o):



3o

Yellow solid, m.p.152.3-152.5 ºC.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.47-7.45(m, 2H), 7.41-7.38 (m, 2H), 7.35-7.33(m, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.15-7.13 (m, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 5.11 (s, 2H), 3.73 (s, 2H), 3.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 158.3, 147.2, 146.0, 142.1, 136.8, 130.4, 130.0, 129.3, 128.9, 128.6, 128.0, 127.8, 127.7, 127.6, 127.4, 124.2, 119.1, 115.3, 70.0, 51.9. HRMS (ESI) calcd. for $C_{27}H_{23}N_2O_5$ $[M+H]^+$= 455.1601, found 455.1601.

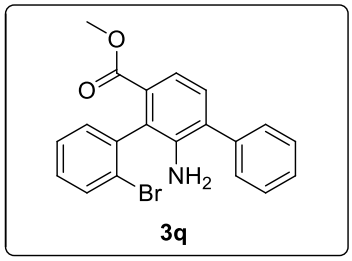
2,6-Diphenyl-3-methoxycarbonylaniline(3p):



3p

Yellow solid, m.p.82.8-83.1ºC;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49-7.42 (m, 6H), 7.38 (d, *J* = 7.1 Hz, 2H), 7.32 (t, *J* = 9.1 Hz, 3H), 7.17 (d, *J* = 7.9 Hz, 1H), 3.72 (s, 2H), 3.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$), δ 168.5, 141.9, 139.0, 137.9 , 130.8, 130.7, 129.3, 129.2, 129.0, 128.9, 128.8, 127.7, 127.6, 127.5, 119.0, 51.7. HRMS (ESI) calcd. for $C_{20}H_{18}NO_2$ $[M+H]^+$= 304.1332, found 304.1331.

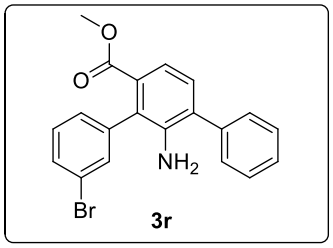
2-(2'-Bromophenyl)-3-methoxycarbonyl-6-phenylaniline(3q):



3q

Yellow solid, m.p.127.8-128.2ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.3 Hz, 1H), 7.60-7.51 (m, 3H), 7.49 (t, J = 7.6 Hz, 2H), 7.46-7.42 (m, 1H), 7.40 (m, 1H), 7.34-7.28 (m, 2H), 7.25 (m, 1H), 3.66 (s, 3H);^{13}C NMR (125 MHz, $CDCl_3$), δ: 167.2, 141.8, 139.0, 138.7, 132.9, 131.4, 130.9, 129.7, 129.4, 129.2, 129.0,128.9, 127.9, 127.8,127.2, 124.2, 119.7, 51.9. HRMS (ESI) calcd. for $C_{20}H_{17}BrNO_2$ $[M+H]^+$= 382.0437, found 382.0439.

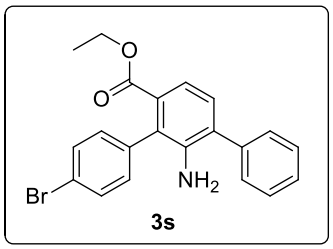
2-(3'-Bromophenyl)-3-methoxycarbonyl-6-phenylaniline(3r):



3r

Yellow solid, m.p.154.1-154.5ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56-7.52 (m, 1H), 7.52 – 7.47 (m, 5H), 7.43 – 7.38 (m, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 3.73 (s, 2H), 3.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0 , 141.9 , 140.1, 138.7, 132.2, 131.0, 130.6, 130.3, 129.7, 129.0, 128.9, 128.2, 128.1, 127.9, 126.0, 122.7, 119.4, 51.9. HRMS (ESI) calcd. for $C_{20}H_{17}BrNO_2$ $[M+H]^+$= 382.0437, found 382.0438.

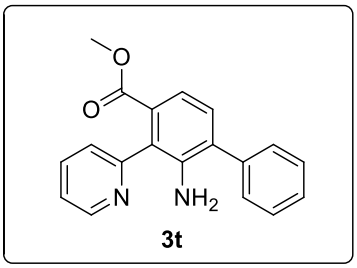
2-(4'-Bromophenyl)-3-ethoxycarbonyl-6-phenylaniline (3s):



3s

Yellow solid, m.p.58.5-58.9ºC; ^{1}H NMR (500 MHz, $CDCl_3$)δ 7.65-7.55 (m, 2H), 7.47 (d, J = 4.4 Hz, 4H), 7.39-7.33 (m, 2H), 7.22-7.17 (m, 3H), 4.04 (q, J = 7.1 Hz, 2H), 3.69 (s, 2H), 1.02 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ,δ: 167.9, 141.7, 138.7, 137.1, 132.0,131.2, 131.0, 130.8, 129.6, 129.0, 129.0, 127.8, 126.1, 121.6, 119.3, 60.7, 13.7. HRMS (ESI) calcd. for $C_{21}H_{19}BrNO_2$ $[M+H]^+$= 396.0594, found 396.0594.

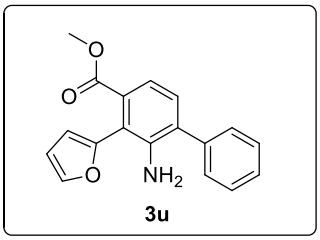
2-(2-Pyridinyl)-3-methoxycarbonyl-6-phenylaniline(3t):



3t

Yellow solid, m.p.93.9-94.3°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.2 Hz, 1H), 7.80 (m, 1H), 7.48-7.47 (m, 4H), 7.44-7.38 (m, 2H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.31-7.29 (m, 1H), 7.22 (d, *J* = 7.9 Hz, 1H), 4.29 (s, 2H), 3.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 157.9, 149.4, 142.6, 138.7, 136.7, 132.0, 130.7, 130.1, 129.1, 129.0, 127.8, 125.8, 125.1, 122.1, 119.7, 51.8. HRMS (ESI) calcd. for $C_{19}H_{17}N_2O_2$ $[M+H]^+$= 305.1285, found 305.1290.

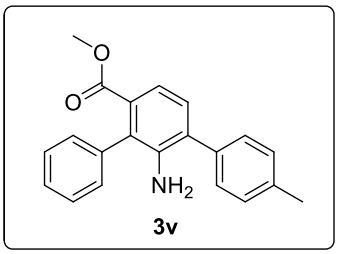
2-(2-Furanyl)-3-methoxycarbonyl-6-phenylaniline(3u):



3u

Brown solid, m.p.72.3-72.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.51-7.46 (m, 4H), 7.42-7.38 m, 1H), 7.27 (d, *J* = 8.1 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.59-6.51 (m, 2H), 4.19 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 149.4, 143.0, 142.5, 138.5, 132.1, 130.9, 130.5, 129.1, 129.0, 127.9, 119.0, 115.5, 111.1, 109.4, 52.2. HRMS (ESI) calcd. for $C_{18}H_{16}NO_3$ $[M+H]^+$= 294.1125, found 294.1124.

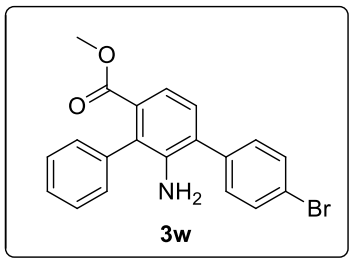
2-Phenyl-3-methoxycarbonyl-6-(4-methylphenyl)aniline(3v):



3v

Yellow solid, m.p.89.9-90.3°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.43-7.37 (m, 3H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.33 (m, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 1H), 3.75 (s, 2H), 3.58 (m, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 142.0, 138.0, 137.5, 135.9, 130.7, 130.5, 129.6, 129.2, 128.9,128.8, 128.3, 127.6, 127.4, 119.1, 51.7, 29.7. HRMS (ESI) calcd. for $C_{21}H_{20}NO_2$ $[M+H]^+$= 318.1489, found 318.1489.

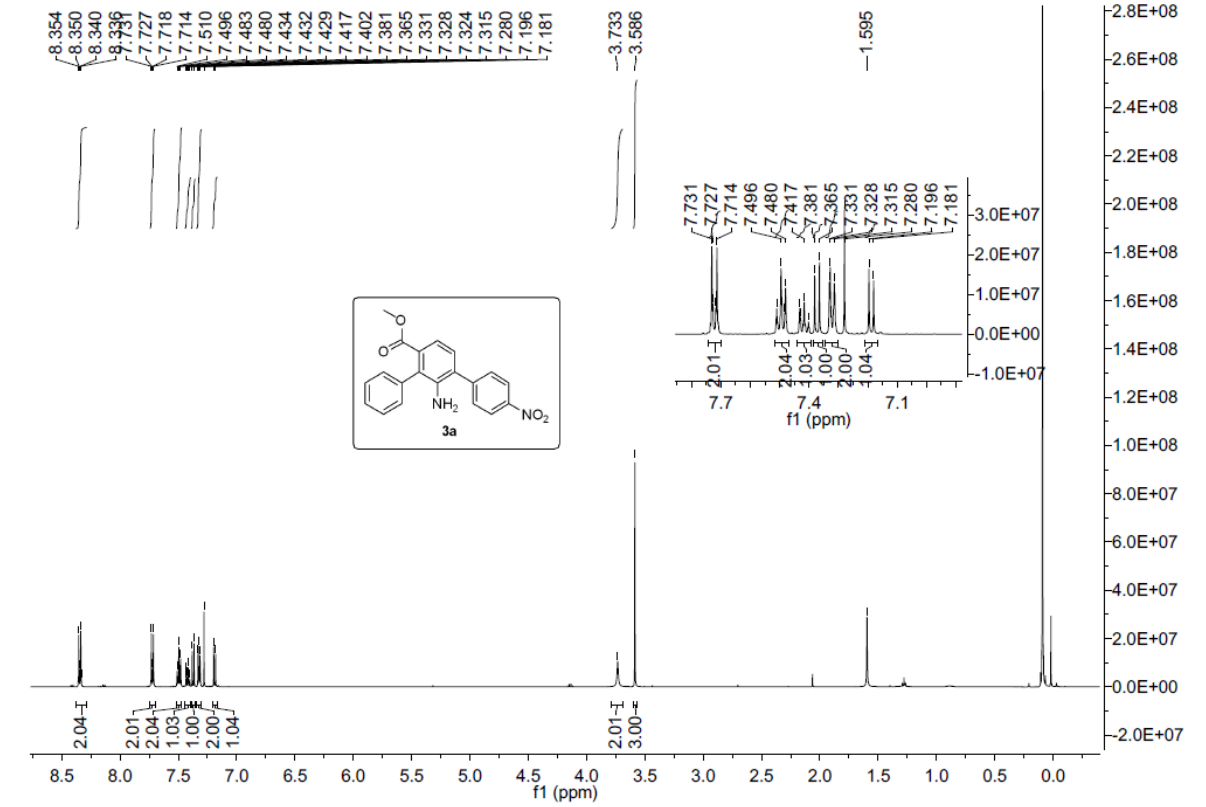
2-Phenyl-3-methoxycarbonyl-6-(4-bromophenyl)aniline(3w):

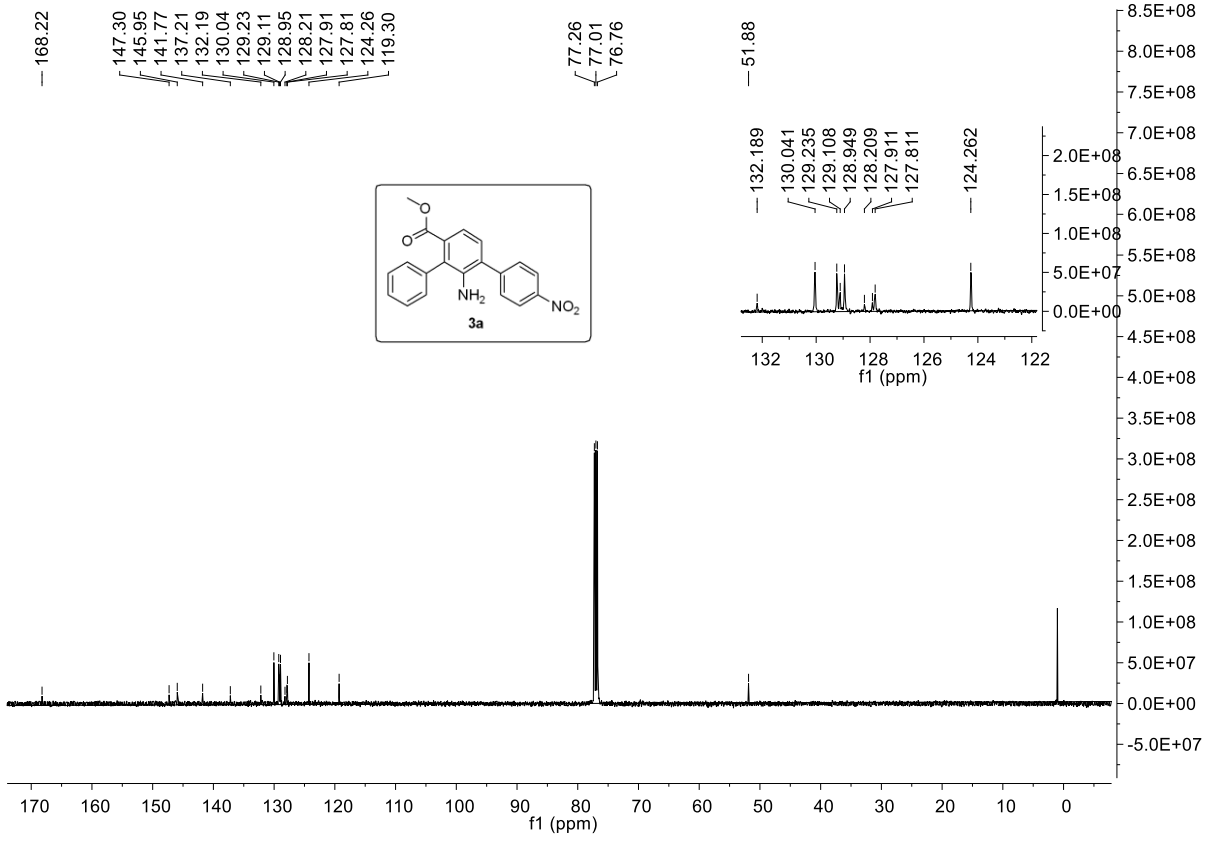


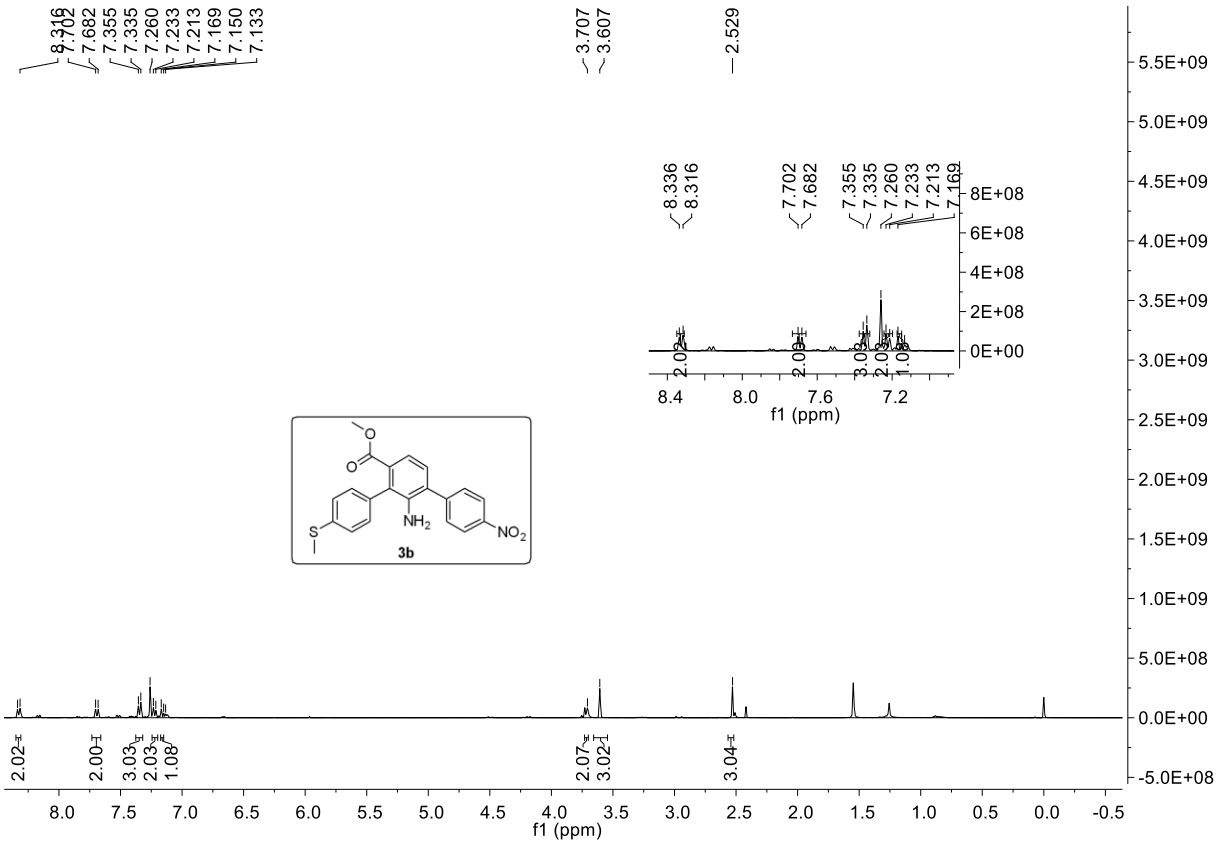
3w

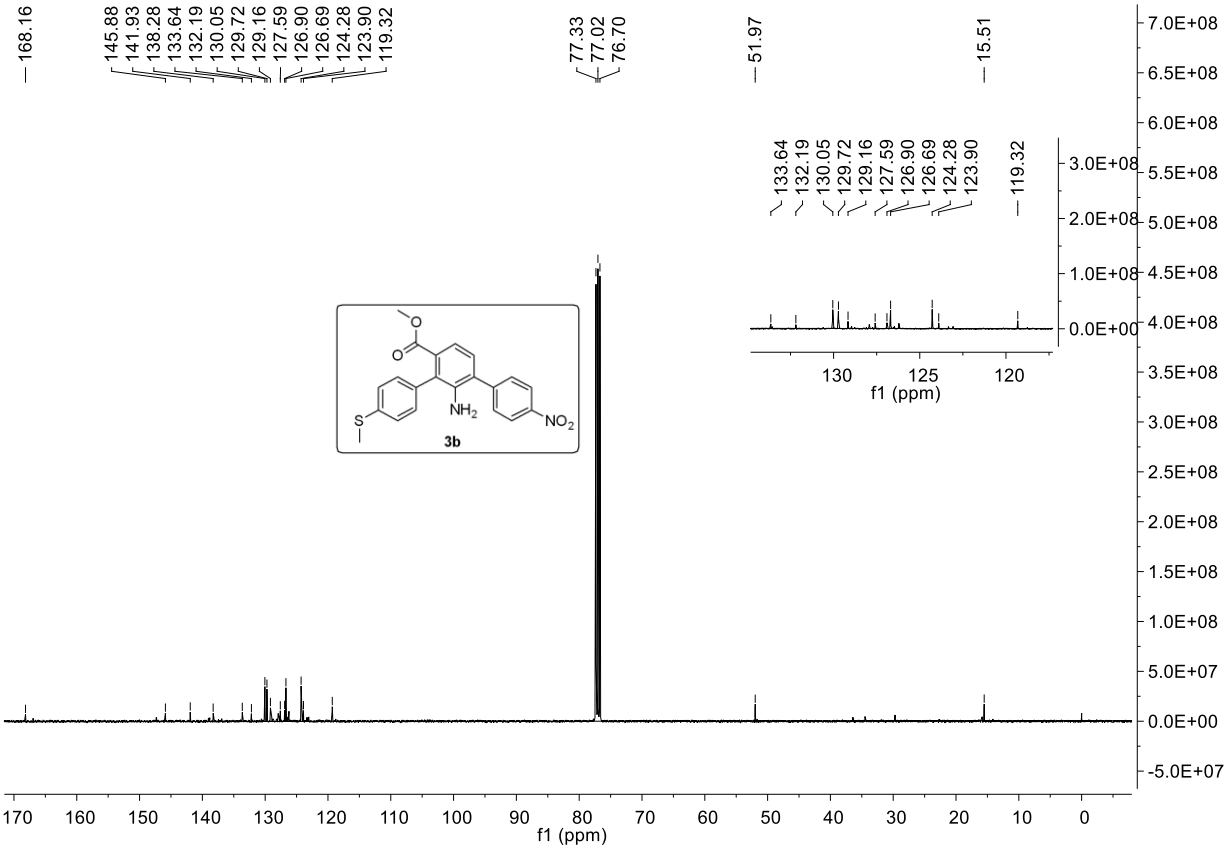
Yellow solid, m.p.130.9-131.7°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.4 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 8.0 Hz, 3H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 7.0 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 1H), 3.71 (s, 2H), 3.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 141.8, 137.8, 137.6, 132.1, 131.1，130.7, 129.3, 129.2, 129.1, 128.8, 127.8, 127.6, 121.9, 119.1, 51.8. HRMS (ESI) calcd. for $C_{20}H_{17}BrNO_2$ $[M+H]^+$= 382.0437, found 382.0437

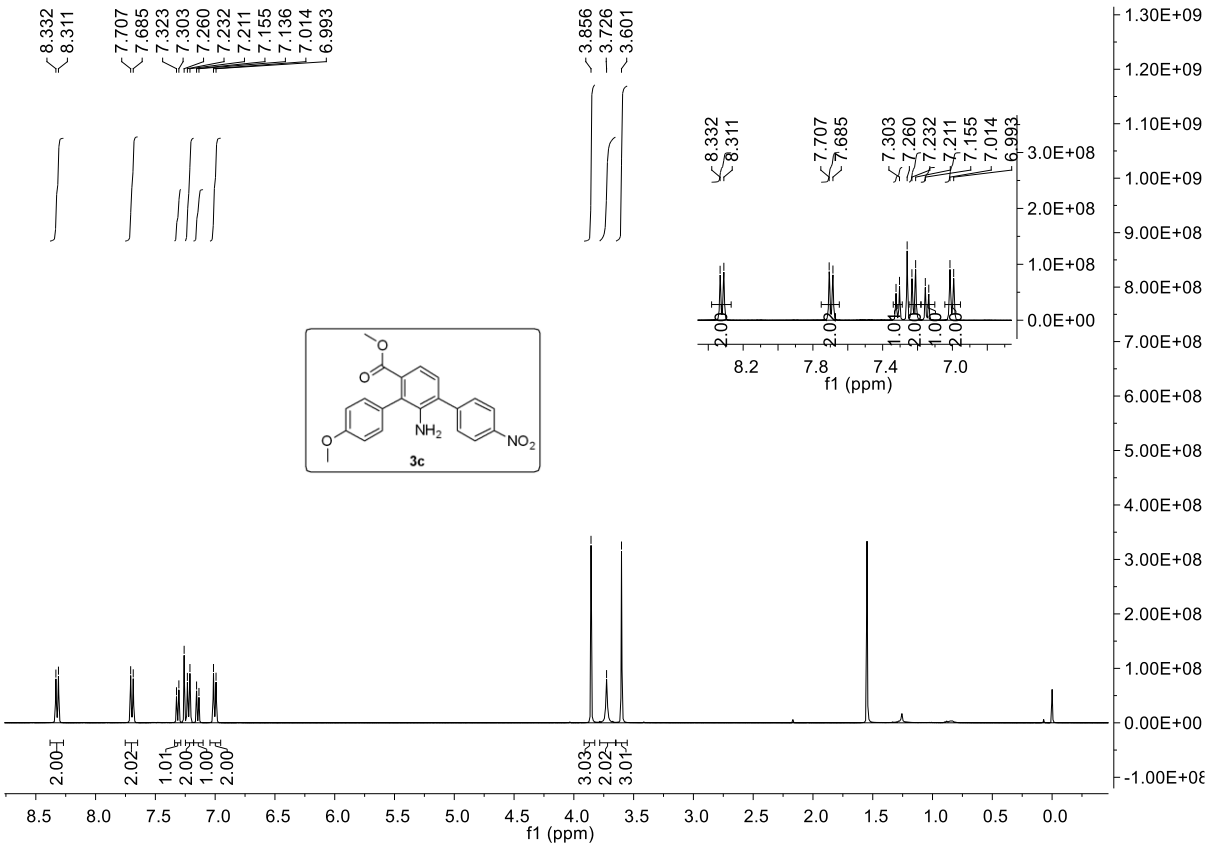
^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) Spectra of 3:

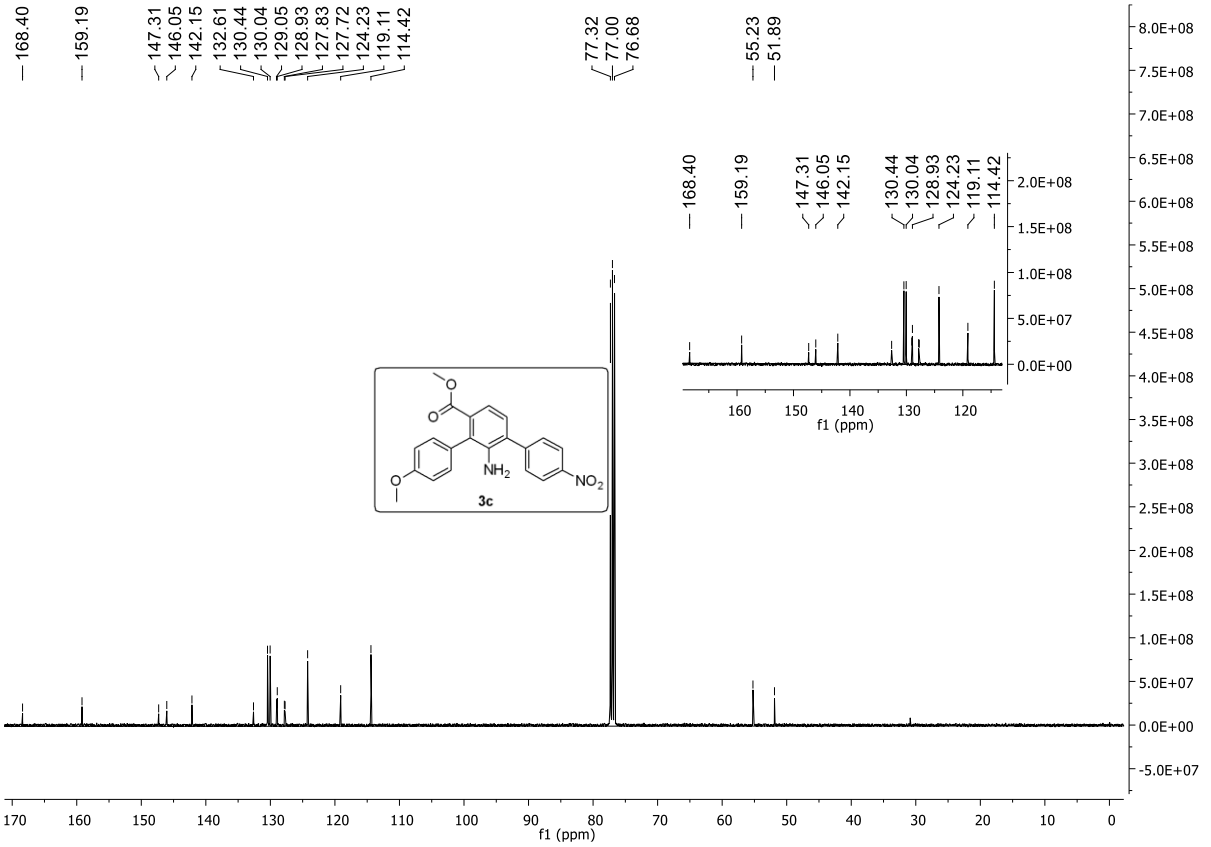


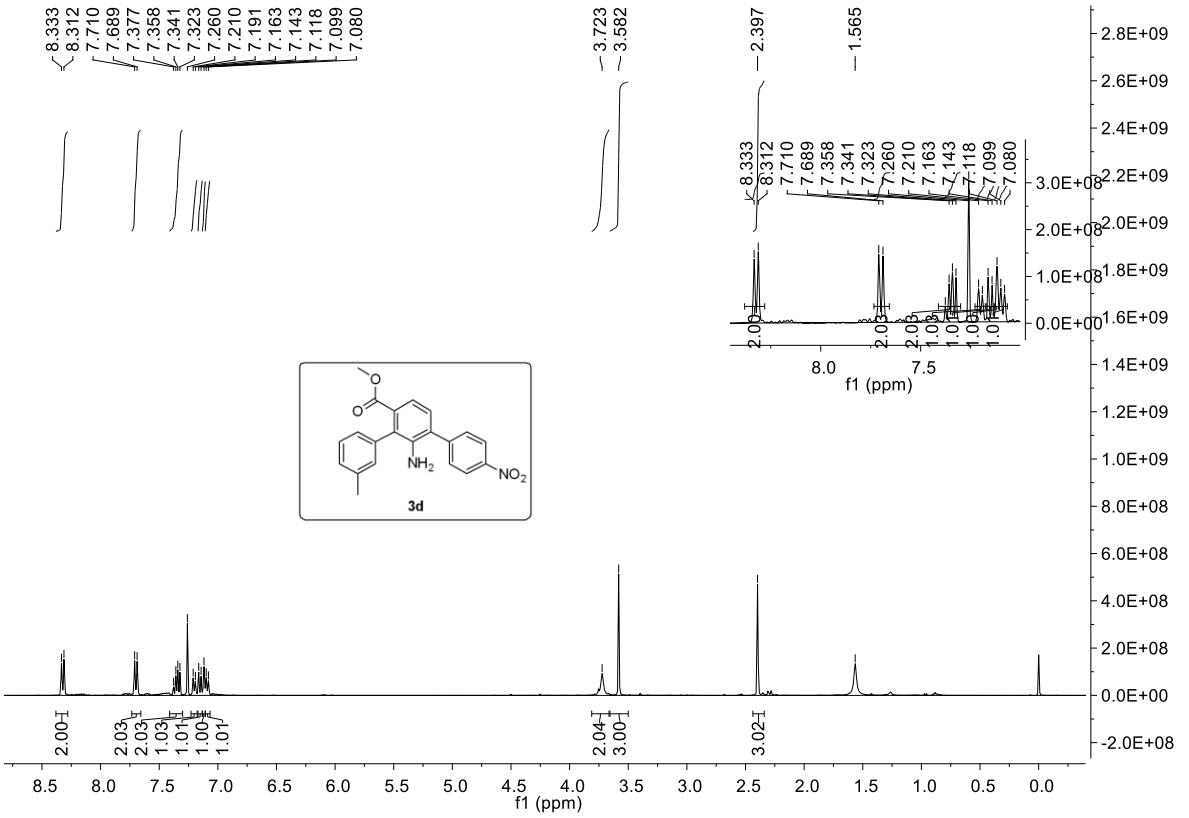


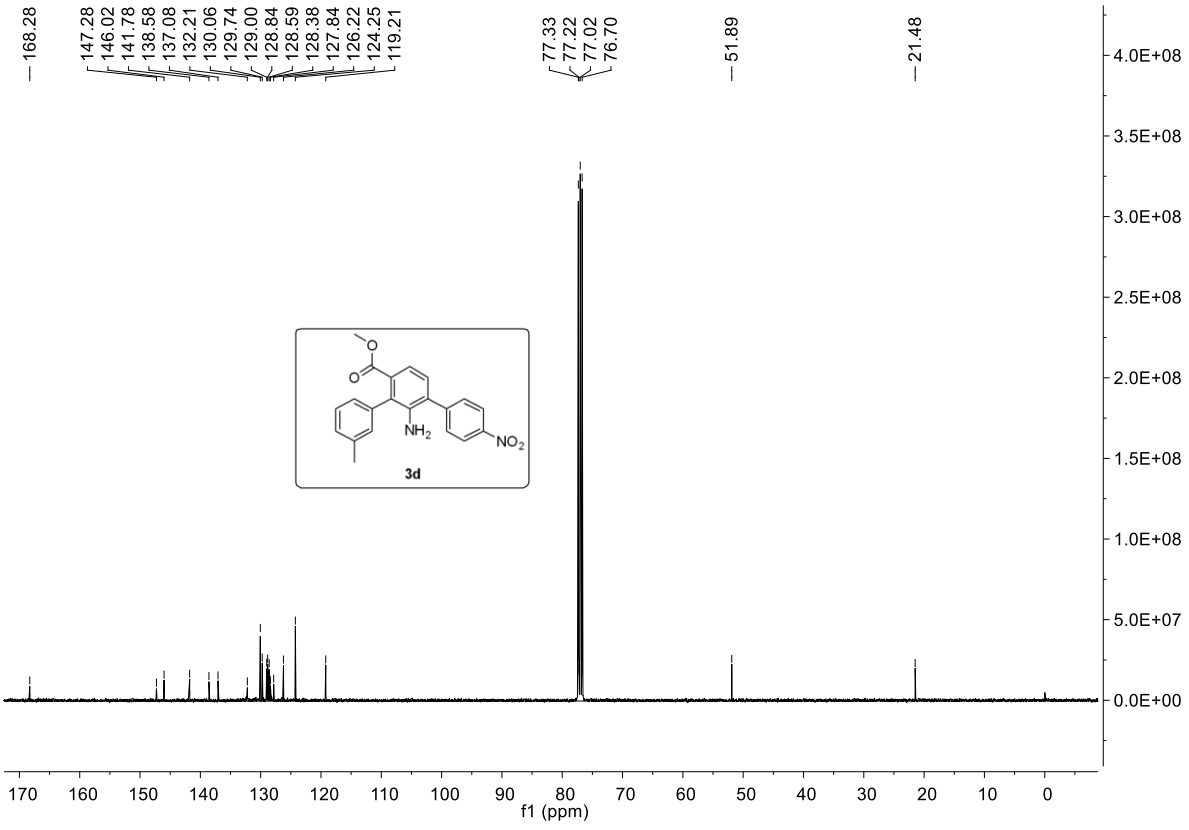

8.316
7.702
7.682
7.355
7.335
7.260
7.233
7.213
7.169
7.150
7.133
3.707
3.607
2.529
2.02
2.00
3.03
2.03
1.08
2.07
3.02
3.04
3b
f1 (ppm)

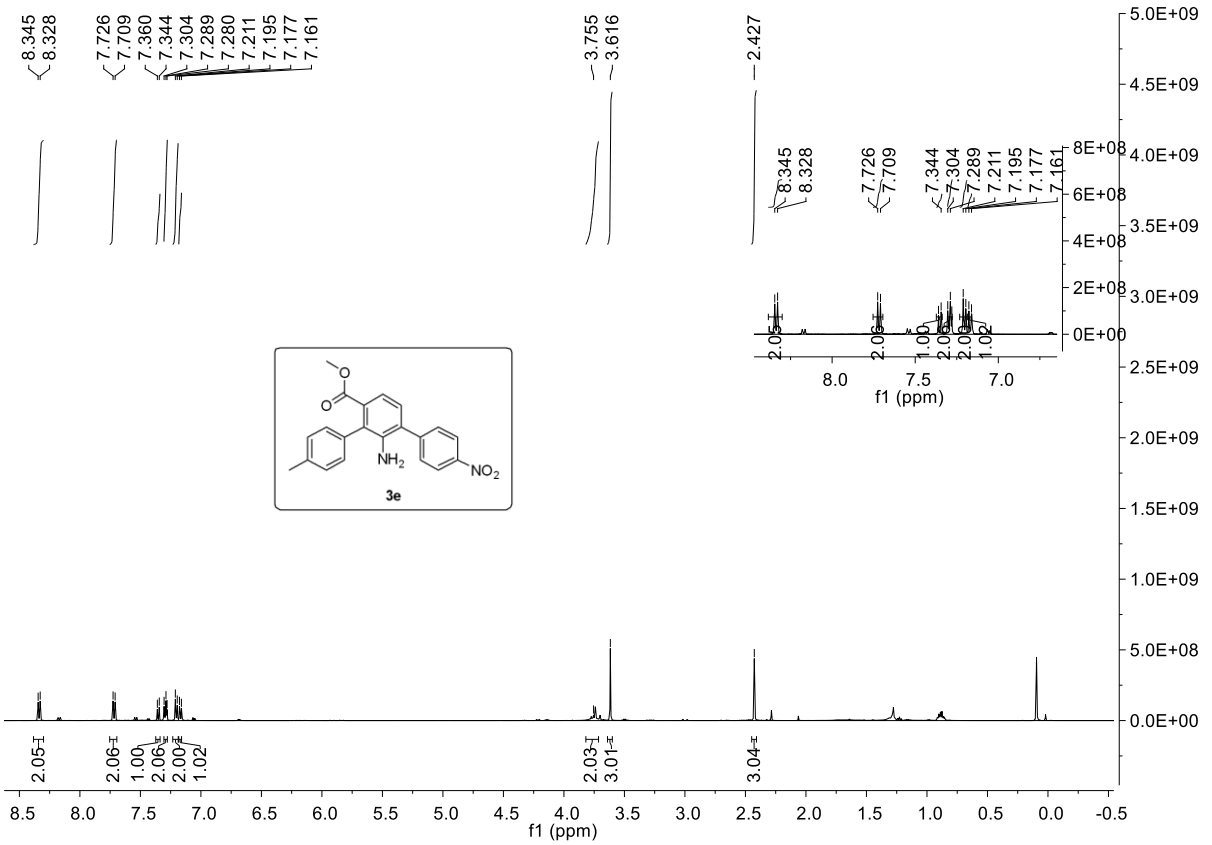

168.16
145.88
141.93
138.28
133.64
132.19
130.05
129.72
129.16
127.59
126.90
126.69
124.28
123.90
119.32
77.33
77.02
76.70
51.97
15.51
3b
f1 (ppm)

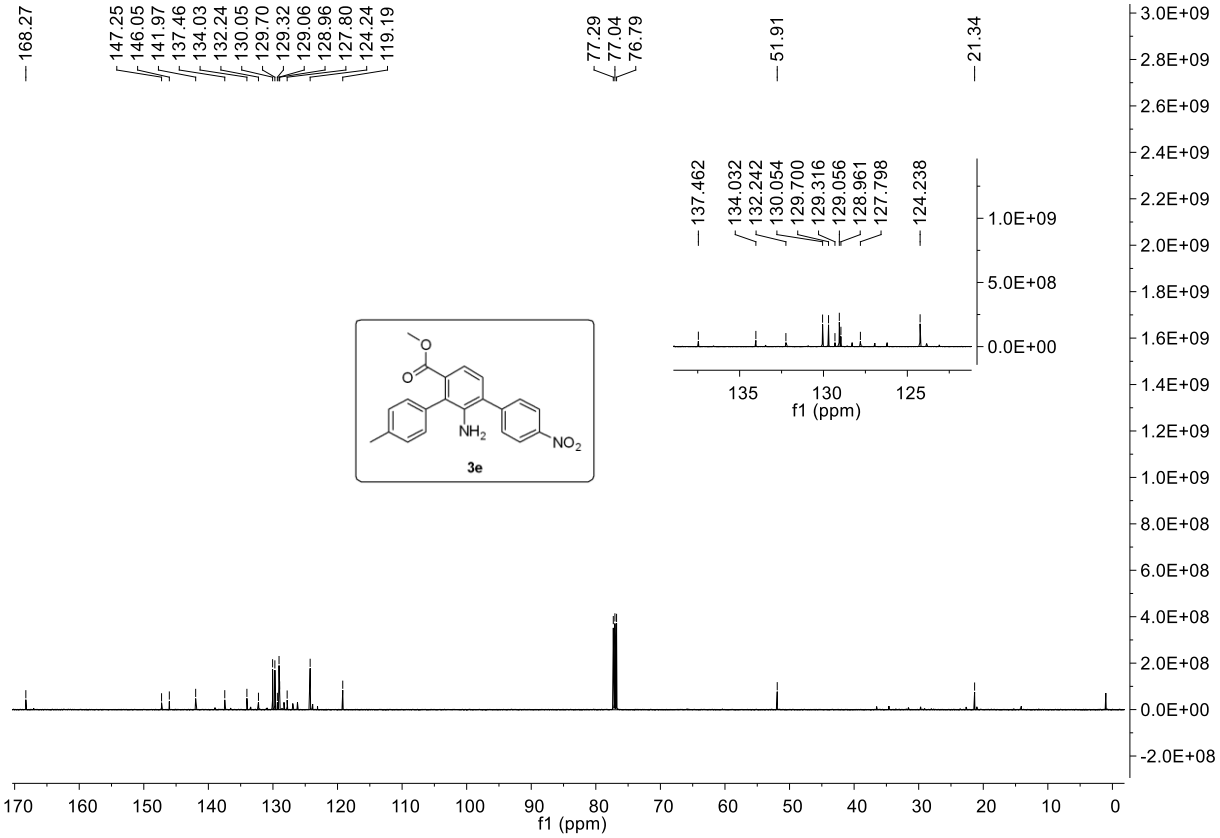

8.332
8.311
7.707
7.685
7.323
7.303
7.260
7.232
7.211
7.155
7.136
7.014
6.993
3.856
3.726
3.601
3c
f1 (ppm)

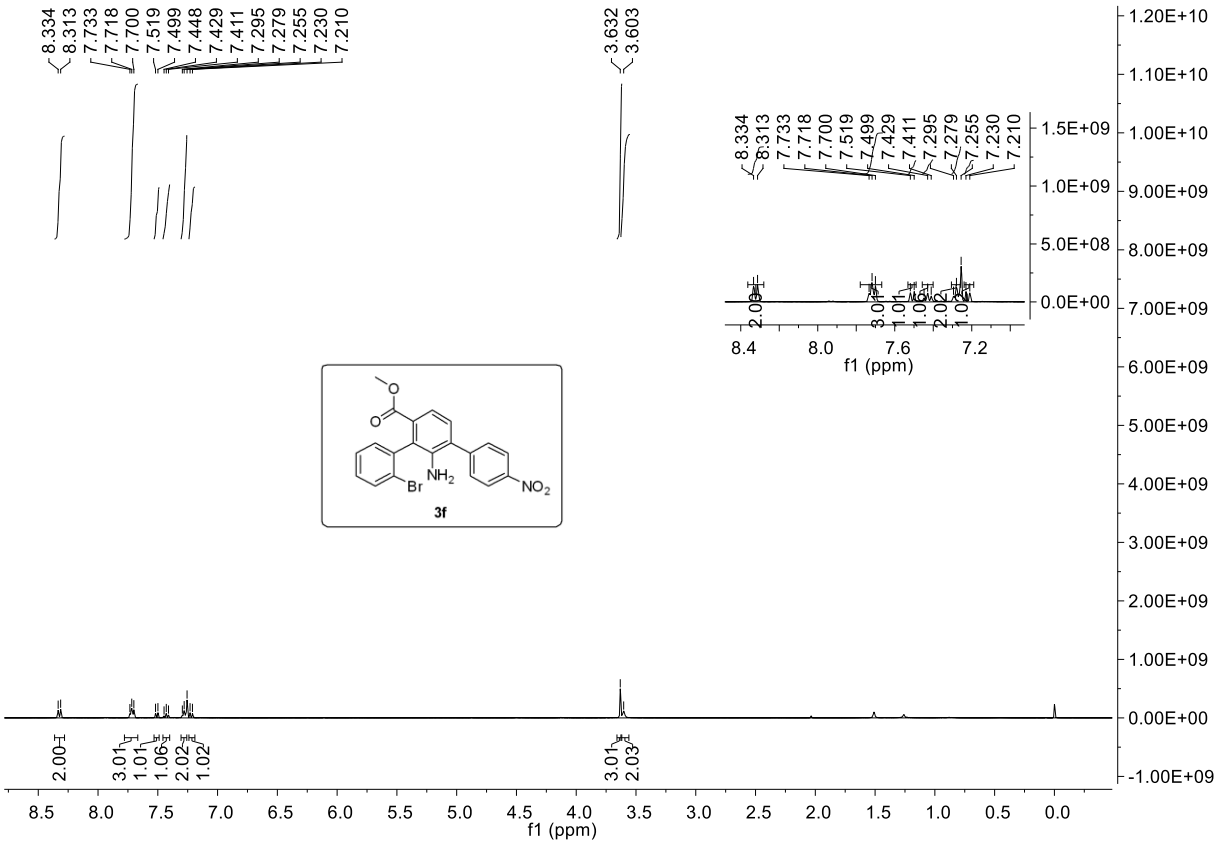

168.40
159.19
147.31
146.05
142.15
132.61
130.44
130.04
129.05
128.93
127.83
127.72
124.23
119.11
114.42
77.32
77.00
76.68
55.23
51.89
3c
f1 (ppm)

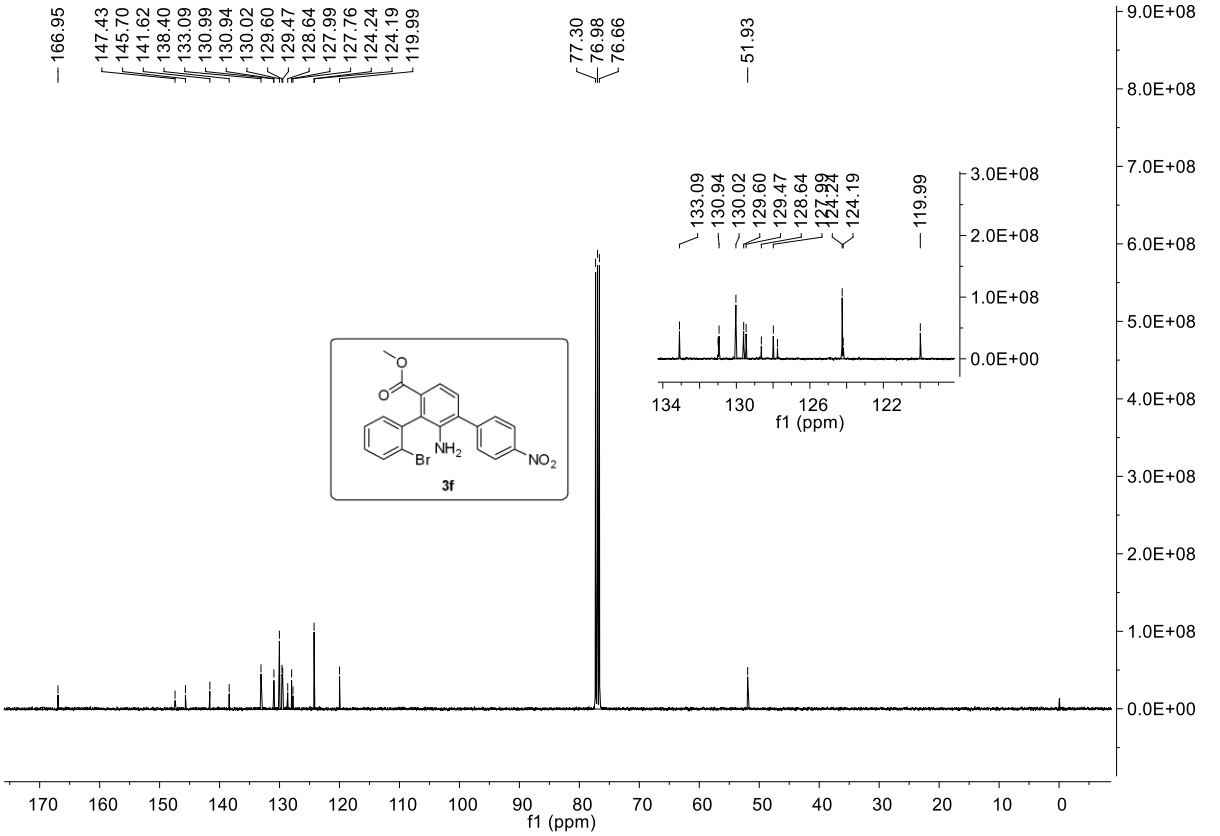

8.333
8.312
7.710
7.689
7.377
7.358
7.341
7.323
7.260
7.210
7.191
7.163
7.143
7.118
7.099
7.080
3.723
3.582
2.397
1.565
3d
f1 (ppm)

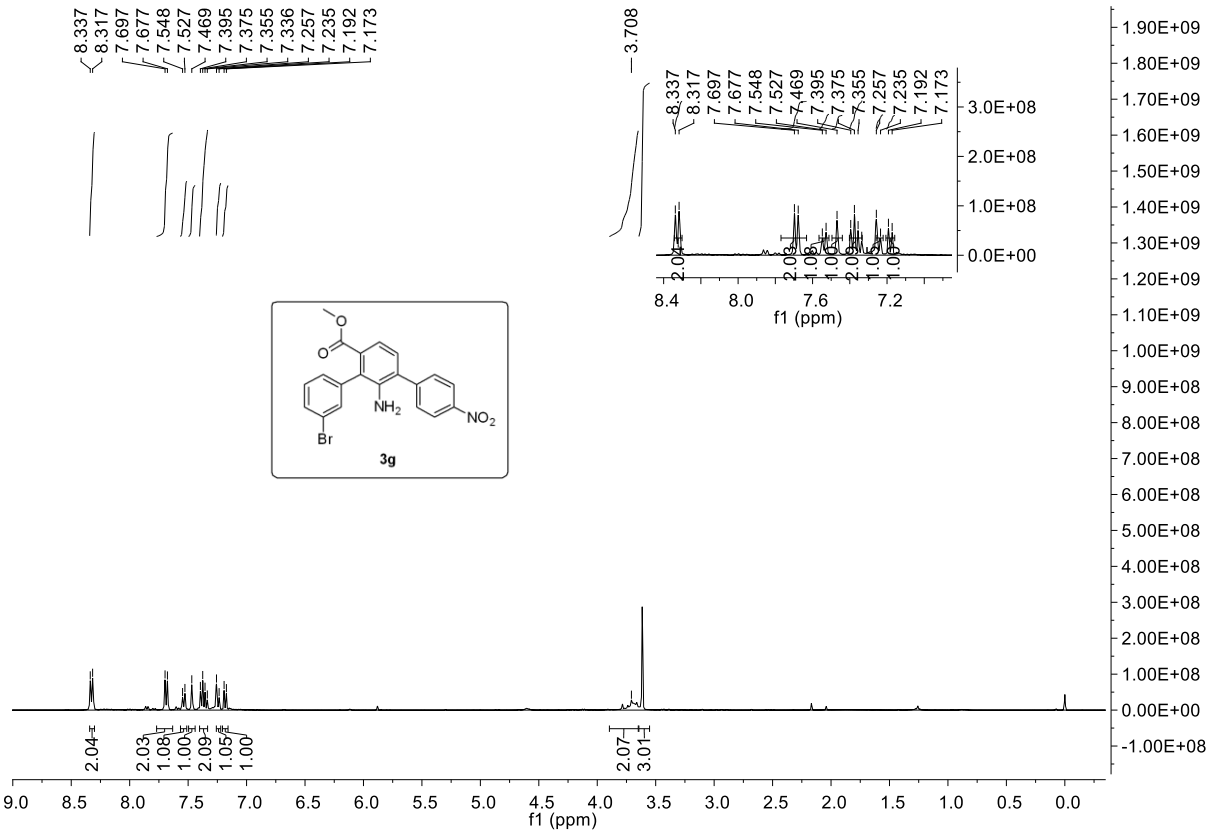

168.28
147.28
146.02
141.78
138.58
137.08
132.21
130.06
129.74
129.00
128.84
128.59
128.38
127.84
126.22
124.25
119.21
77.33
77.22
77.02
76.70
51.89
21.48
3d
f1 (ppm)

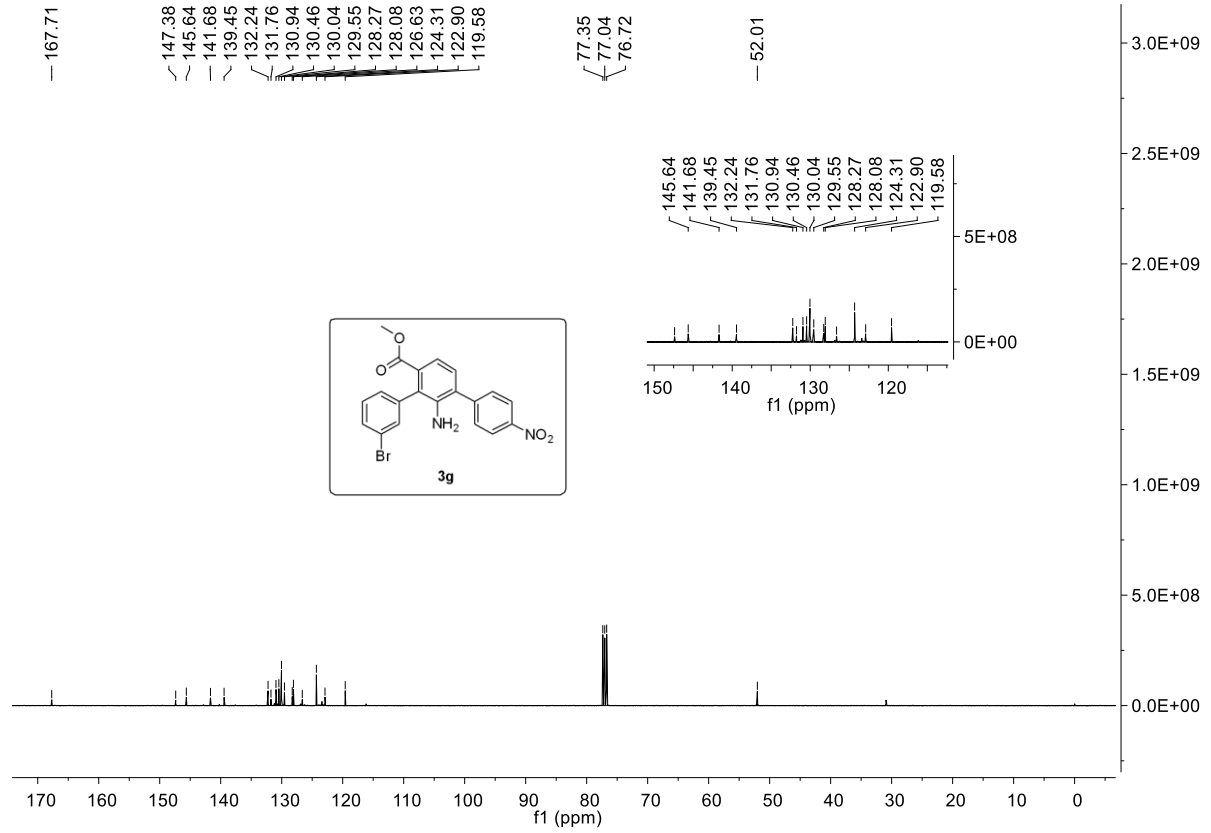

8.345
8.328
7.726
7.709
7.360
7.344
7.304
7.289
7.280
7.211
7.195
7.177
7.161
3.755
3.616
2.427
2.05
2.06
1.00
2.06
2.00
1.02
2.03
3.01
3.04
f1 (ppm)
NH2
NO2
3e

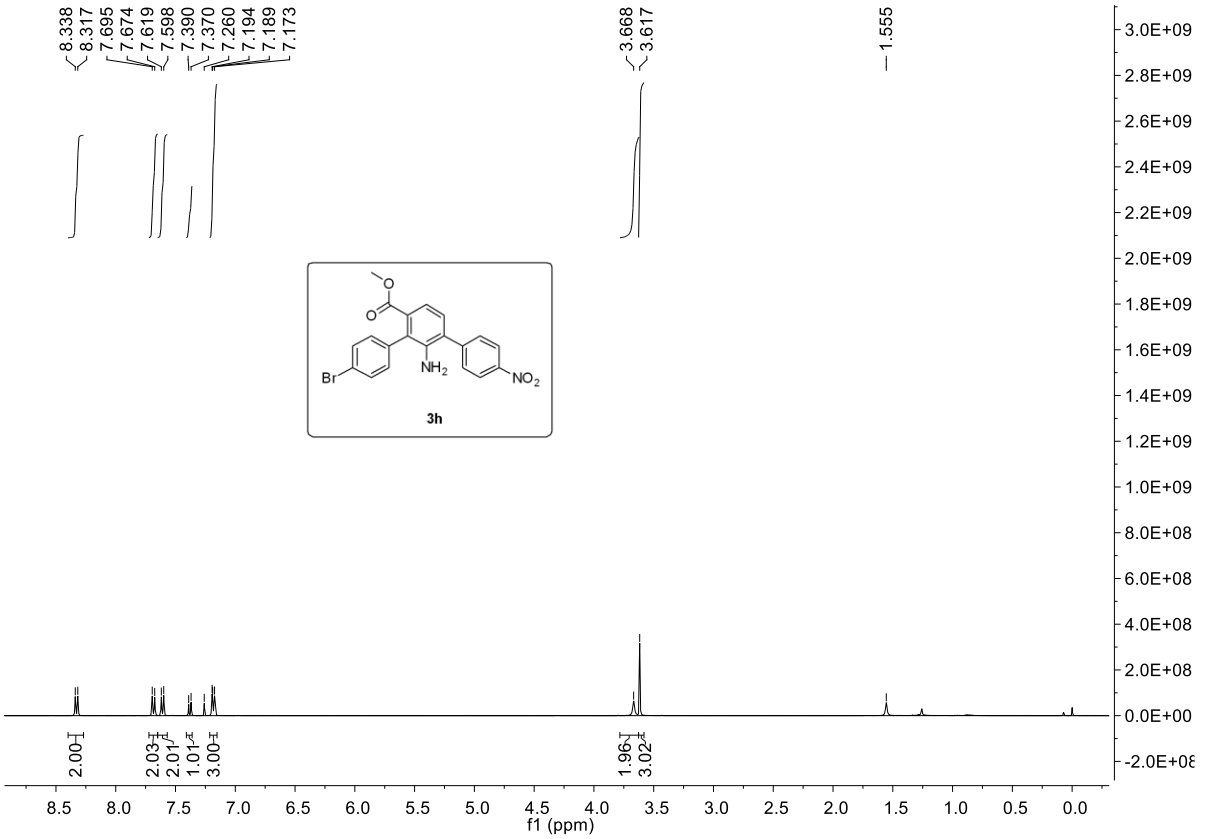

168.27
147.25
146.05
141.97
137.46
134.03
132.24
130.05
129.70
129.32
129.06
128.96
127.80
124.24
119.19
77.29
77.04
76.79
51.91
21.34
f1 (ppm)
NH2
NO2
3e

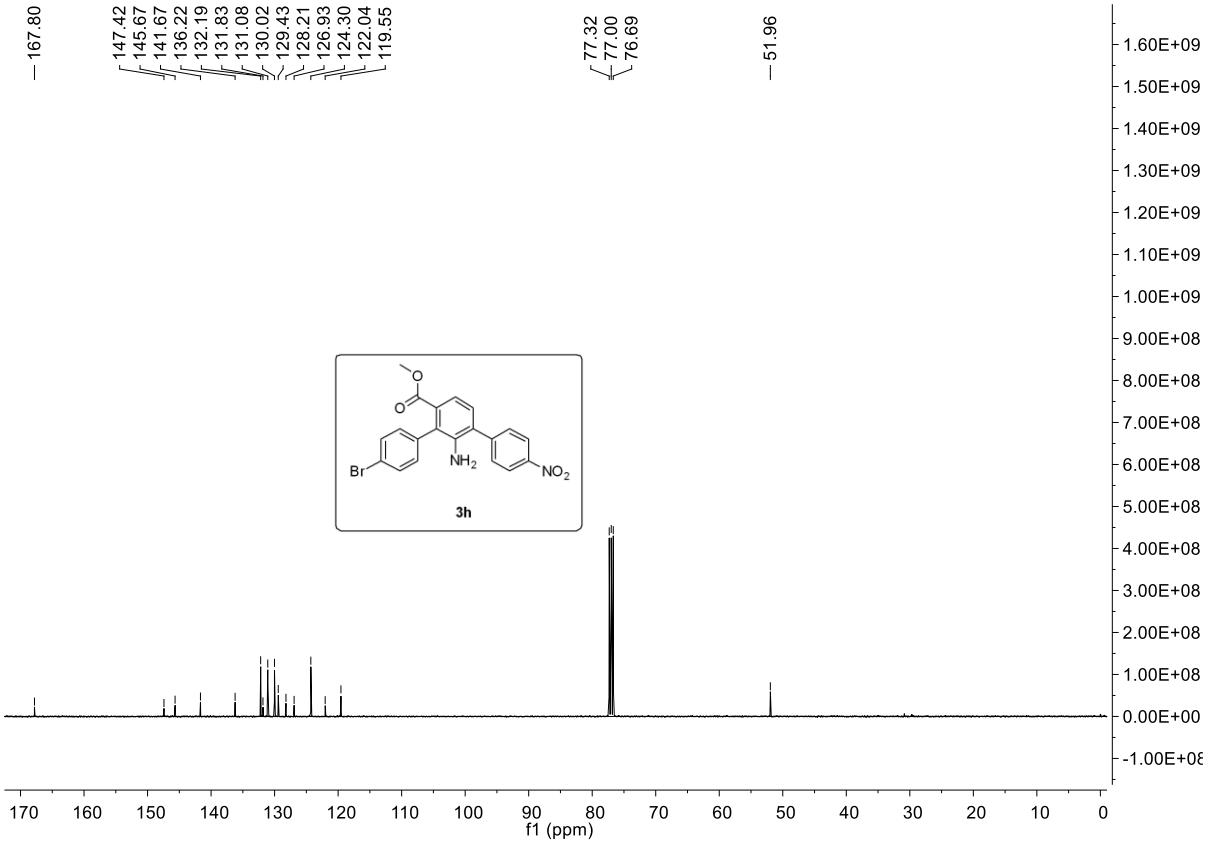

8.334
8.313
7.733
7.718
7.700
7.519
7.499
7.448
7.429
7.411
7.295
7.279
7.255
7.230
7.210
3.632
3.603
2.00
3.01
1.01
1.06
2.02
1.02
3.01
2.03
f1 (ppm)
3f

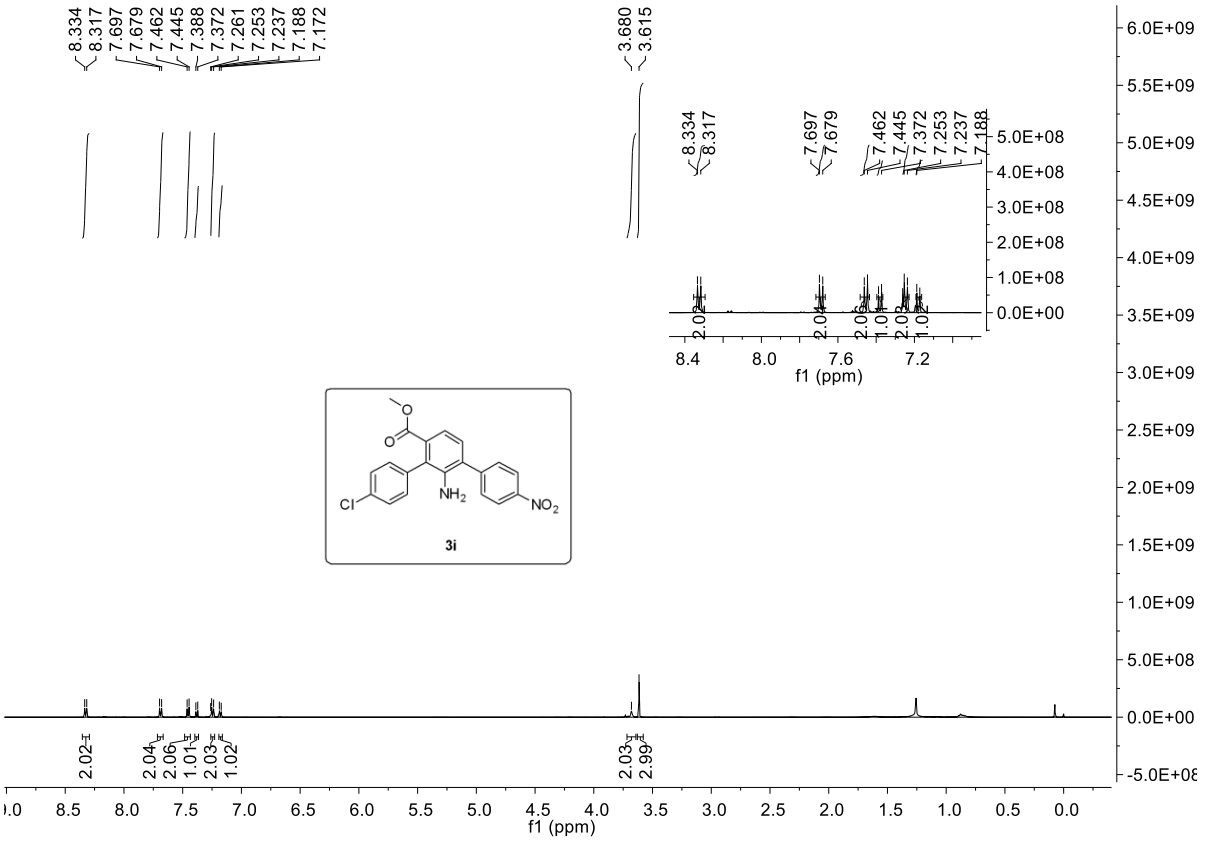

166.95
147.43
145.70
141.62
138.40
133.09
130.99
130.94
130.02
129.60
129.47
128.64
127.99
127.76
124.24
124.19
119.99
77.30
76.98
76.66
51.93
f1 (ppm)
3f

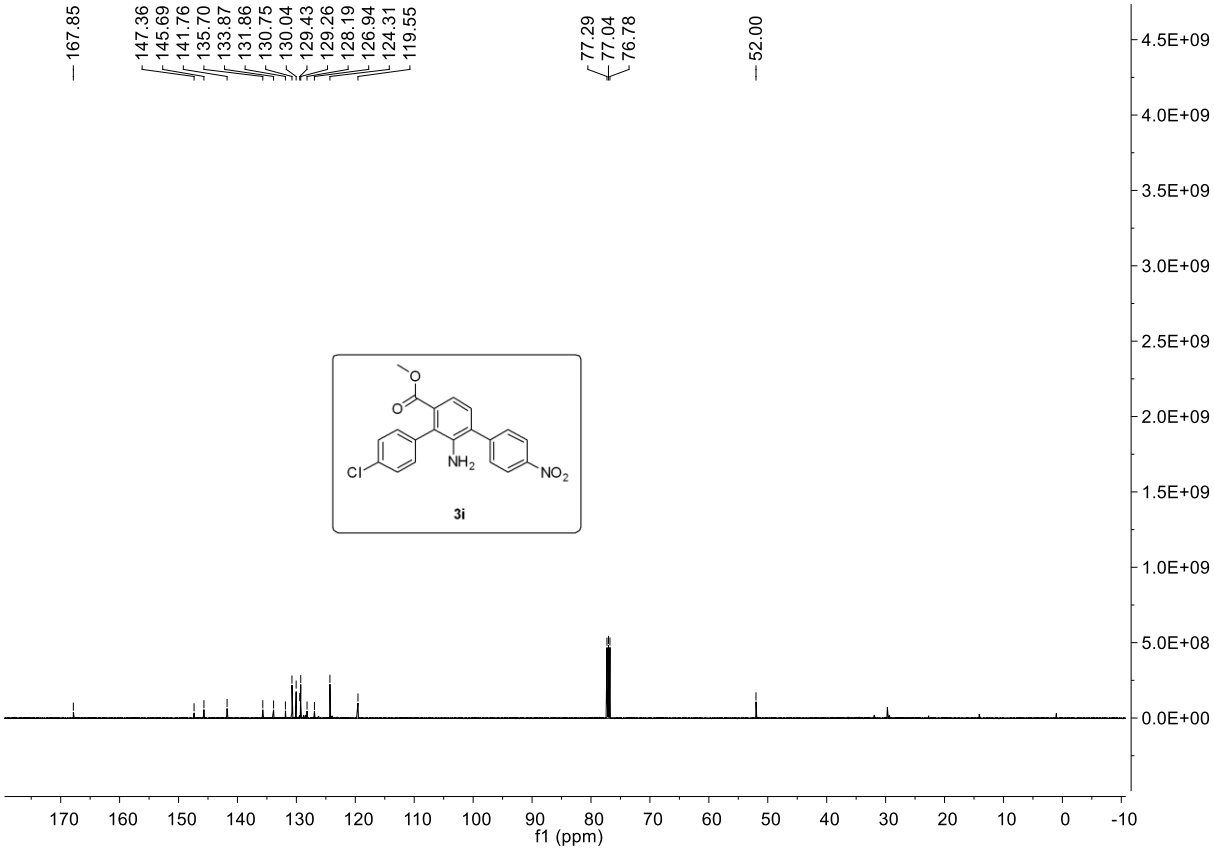

8.337
8.317
7.697
7.677
7.548
7.527
7.469
7.395
7.375
7.355
7.336
7.257
7.235
7.192
7.173
3.708
NH2
NO2
Br
3g
f1 (ppm)

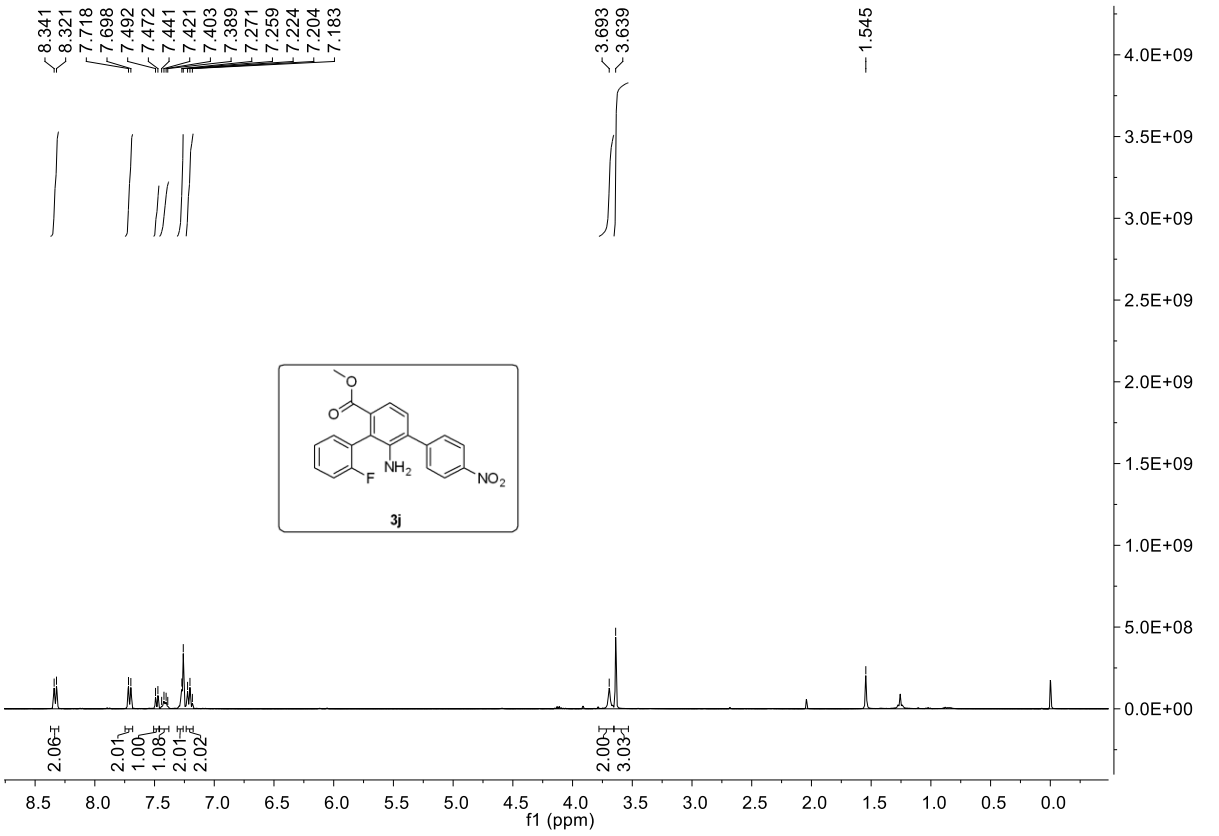

167.71
147.38
145.64
141.68
139.45
132.24
131.76
130.94
130.46
130.04
129.55
128.27
128.08
126.63
124.31
122.90
119.58
77.35
77.04
76.72
52.01
NH2
NO2
Br
3g
f1 (ppm)

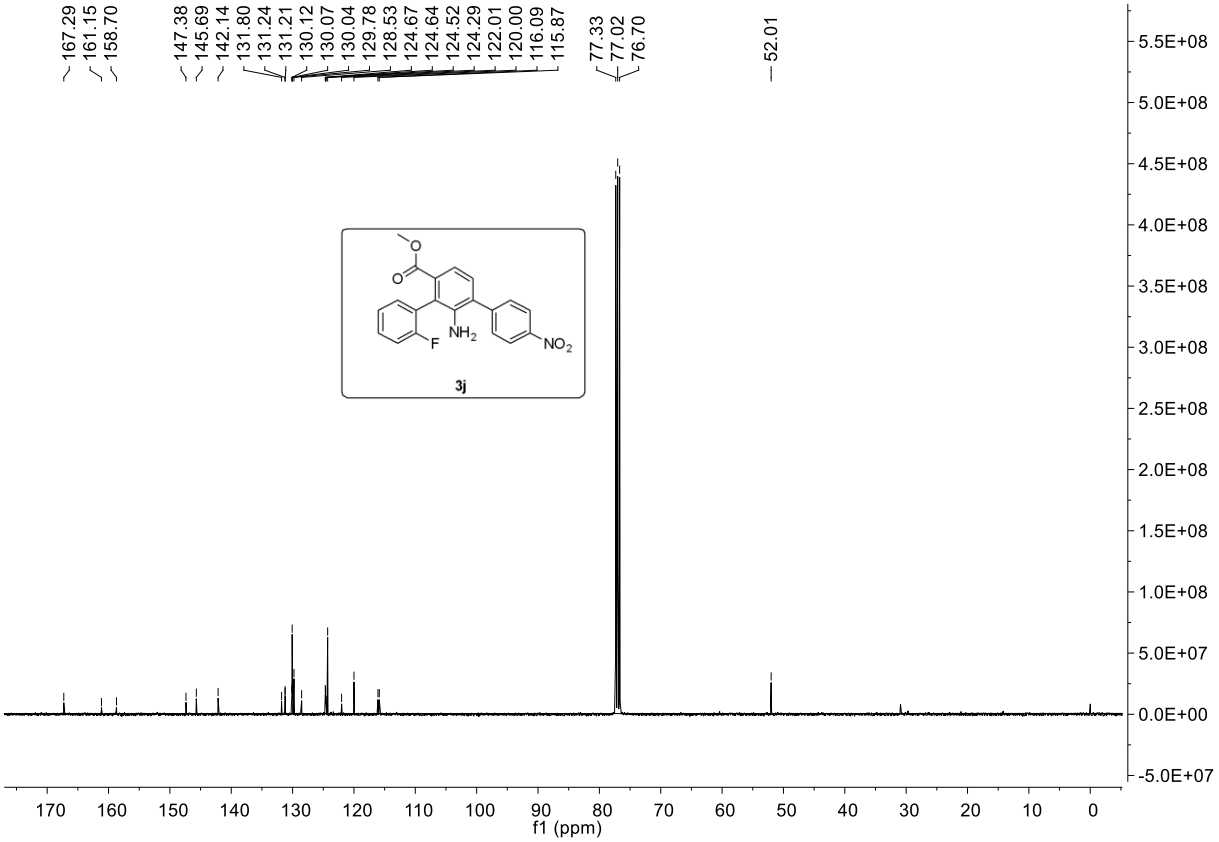

8.338
8.317
7.695
7.674
7.619
7.598
7.390
7.370
7.260
7.194
7.189
7.173
3.668
3.617
1.555
2.00
2.03
2.01
1.01
3.00
1.96
3.02
3h
f1 (ppm)

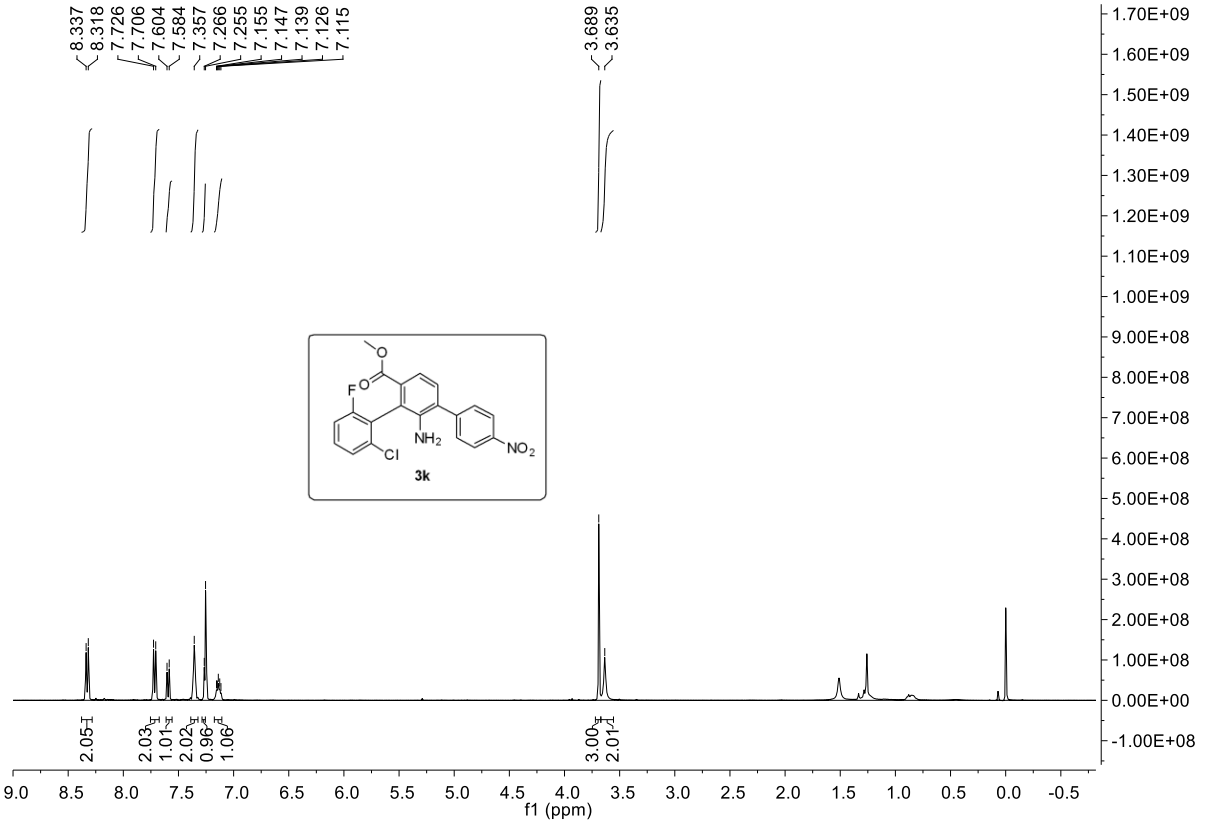

167.80
147.42
145.67
141.67
136.22
132.19
131.83
131.08
130.02
129.43
128.21
126.93
124.30
122.04
119.55
77.32
77.00
76.69
51.96
3h
f1 (ppm)

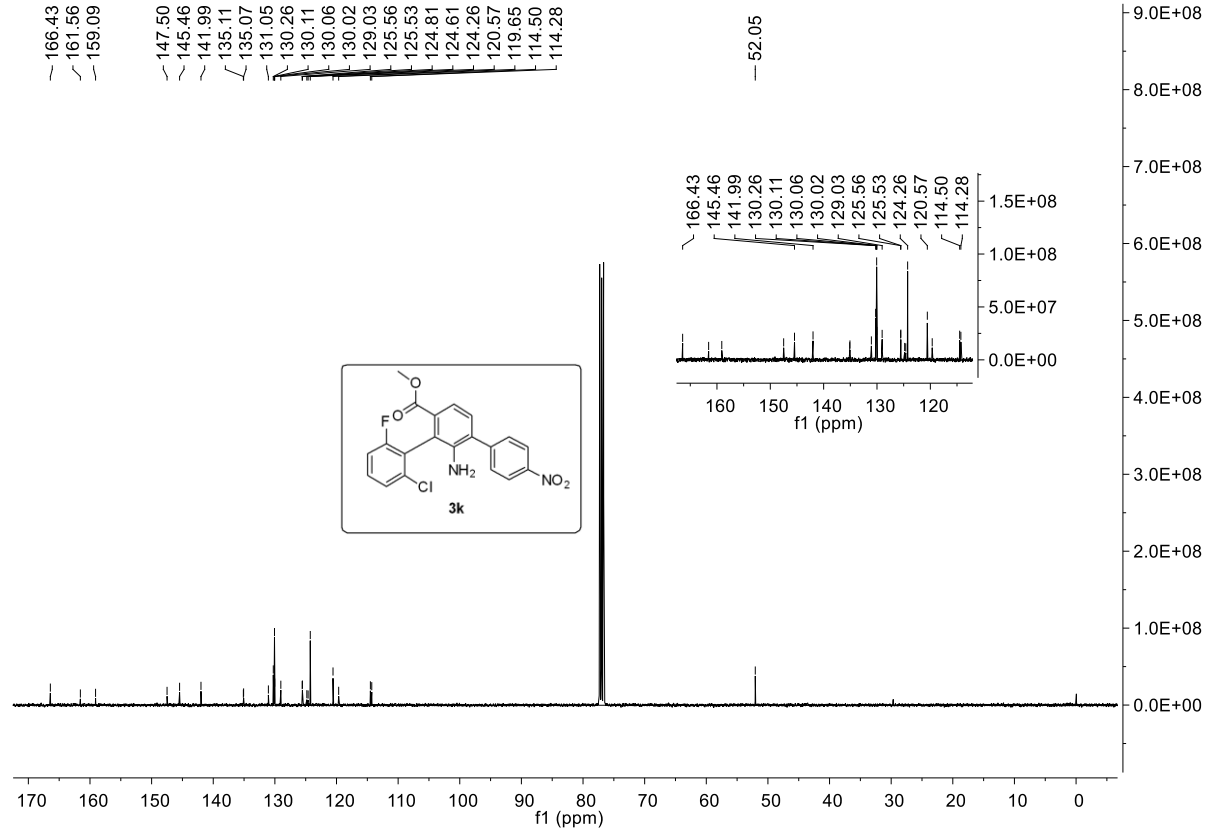

8.334
8.317
7.697
7.679
7.462
7.445
7.388
7.372
7.261
7.253
7.237
7.188
7.172
3.680
3.615
Cl
NH2
NO2
3i
2.02
2.04
2.06
1.01
2.03
1.02
2.03
2.99
f1 (ppm)

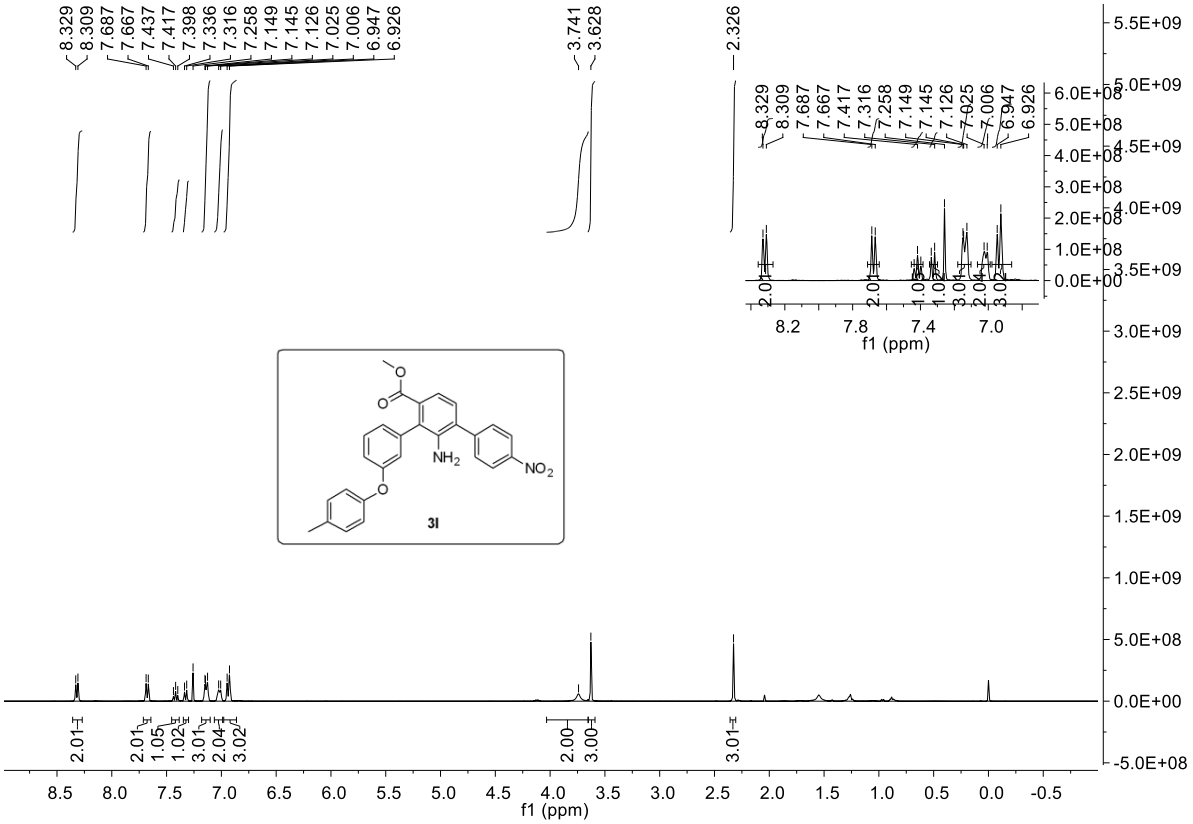

167.85
147.36
145.69
141.76
135.70
133.87
131.86
130.75
130.04
129.43
129.26
128.19
126.94
124.31
119.55
77.29
77.04
76.78
52.00
Cl
NH2
NO2
3i
f1 (ppm)

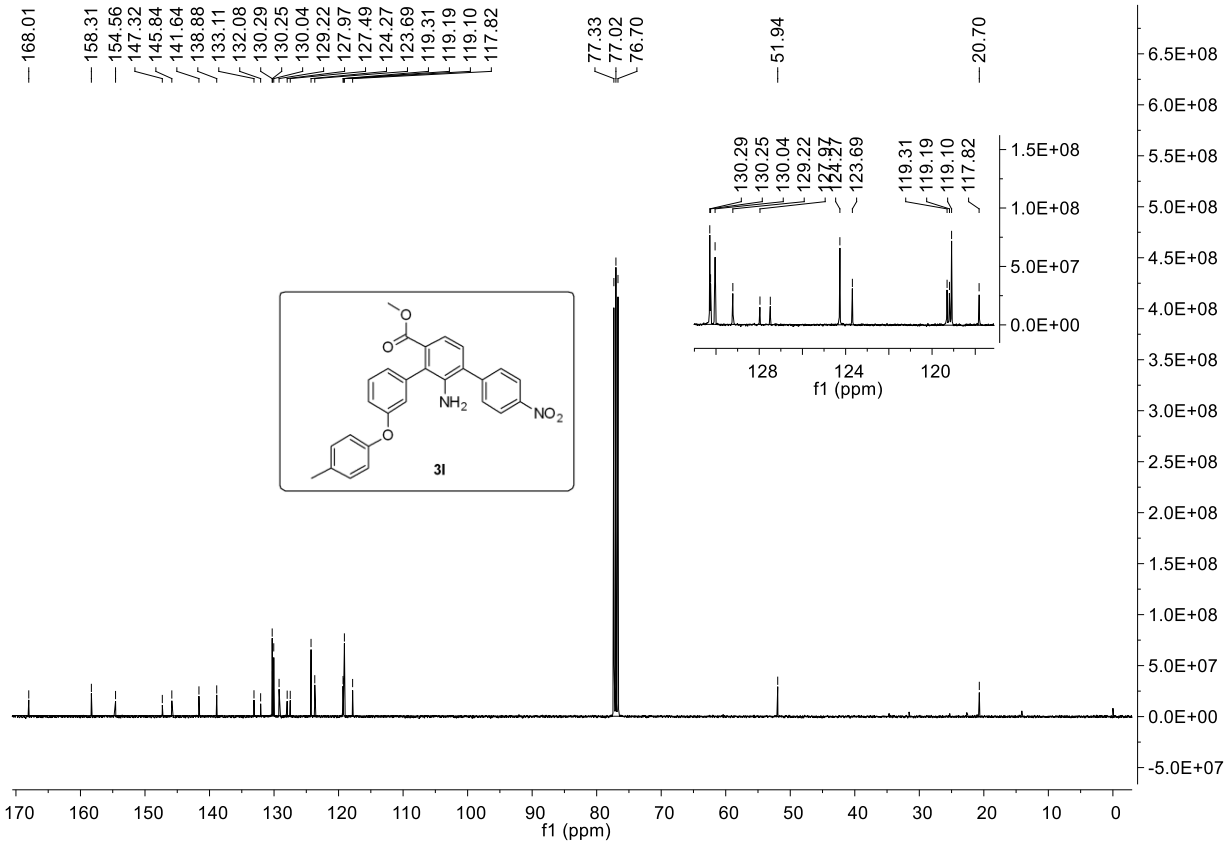

8.341
8.321
7.718
7.698
7.492
7.472
7.441
7.421
7.403
7.389
7.271
7.259
7.224
7.204
7.183
3.693
3.639
1.545
2.06
2.01
1.00
1.08
2.01
2.02
2.00
3.03
3j
f1 (ppm)

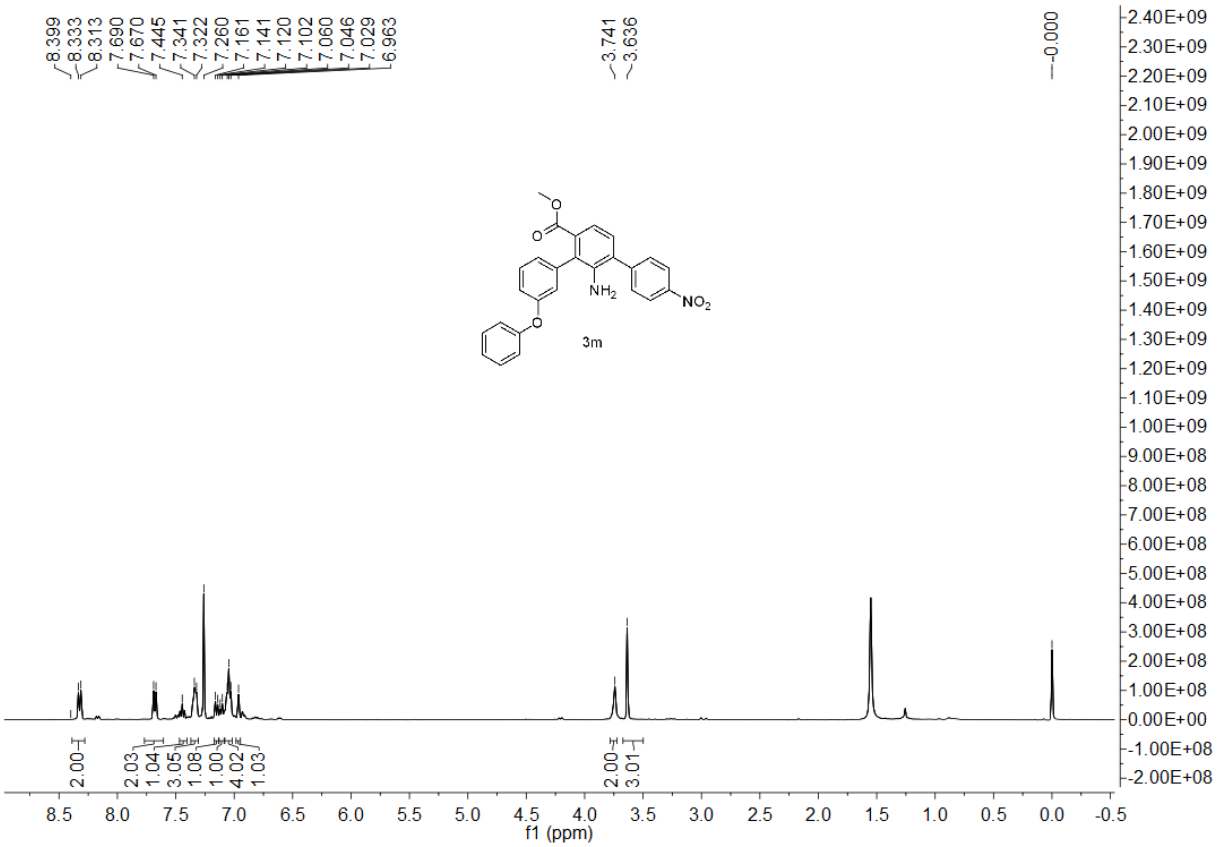

167.29
161.15
158.70
147.38
145.69
142.14
131.80
131.24
131.21
130.12
130.07
130.04
129.78
128.53
124.67
124.64
124.52
124.29
122.01
120.00
116.09
115.87
77.33
77.02
76.70
52.01
3j
f1 (ppm)

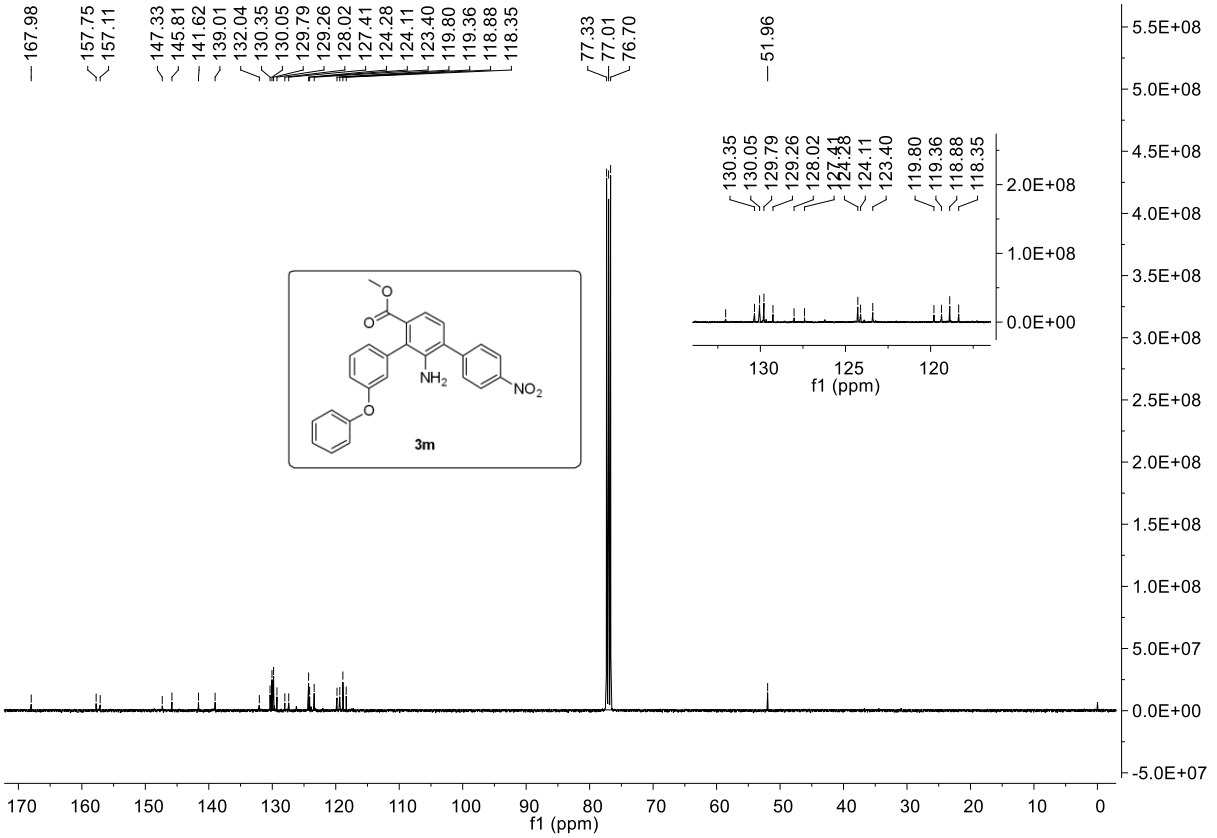

8.337
8.318
7.726
7.706
7.604
7.584
7.357
7.266
7.255
7.155
7.147
7.139
7.126
7.115
3.689
3.635
3k
2.05
2.03
1.01
2.02
0.96
1.06
3.00
2.01
f1 (ppm)

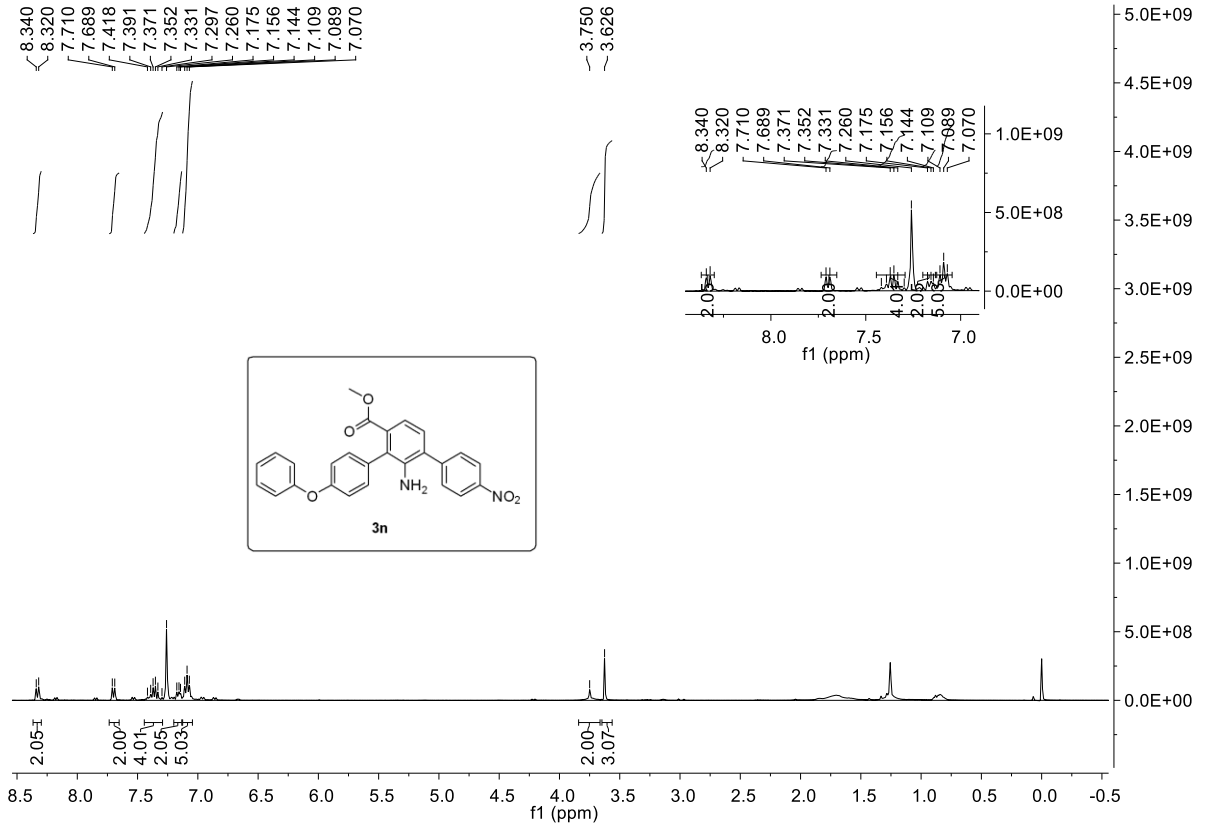

166.43
161.56
159.09
147.50
145.46
141.99
135.11
135.07
131.05
130.26
130.11
130.06
130.02
129.03
125.56
125.53
124.81
124.61
124.26
120.57
119.65
114.50
114.28
52.05
3k
f1 (ppm)

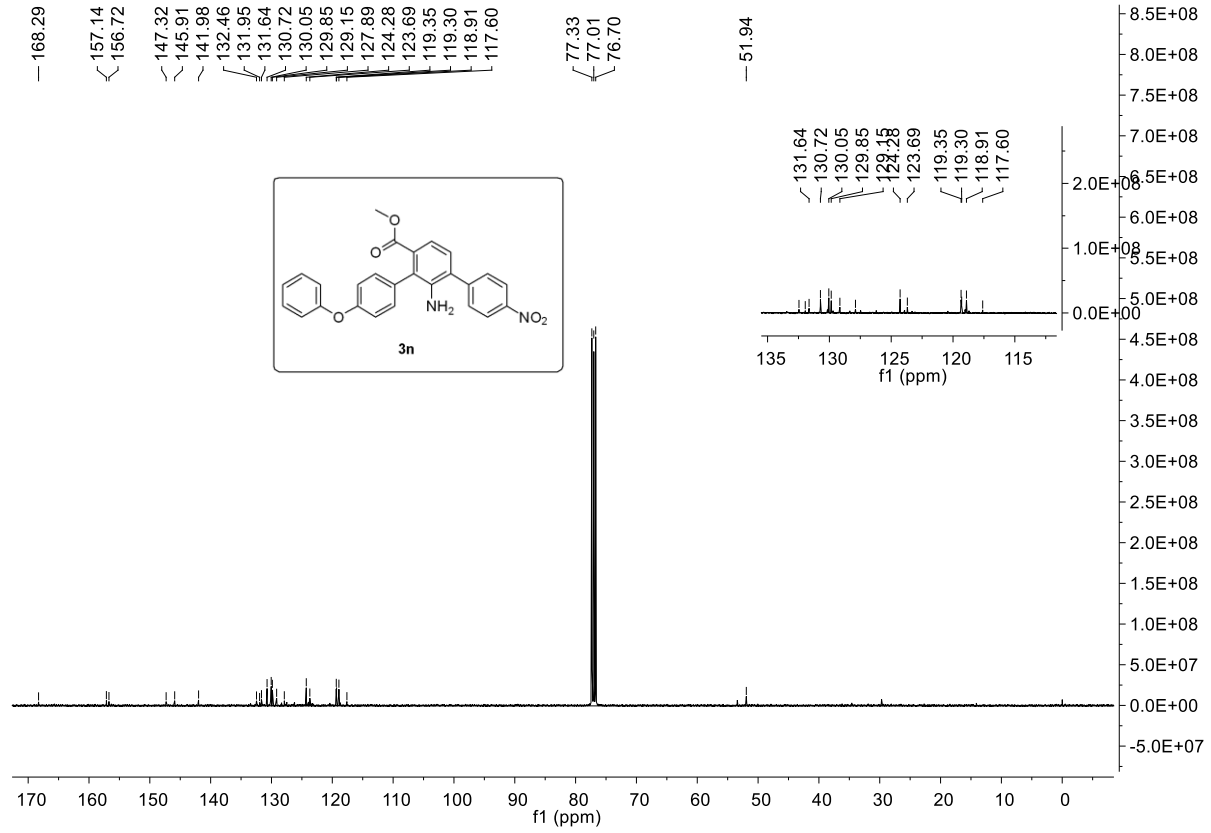

8.329
8.309
7.687
7.667
7.437
7.417
7.398
7.336
7.316
7.258
7.149
7.145
7.126
7.025
7.006
6.947
6.926
3.741
3.628
2.326
NH2
NO2
O
3l
2.01
1.05
1.02
3.01
2.04
3.02
2.00
3.00
f1 (ppm)

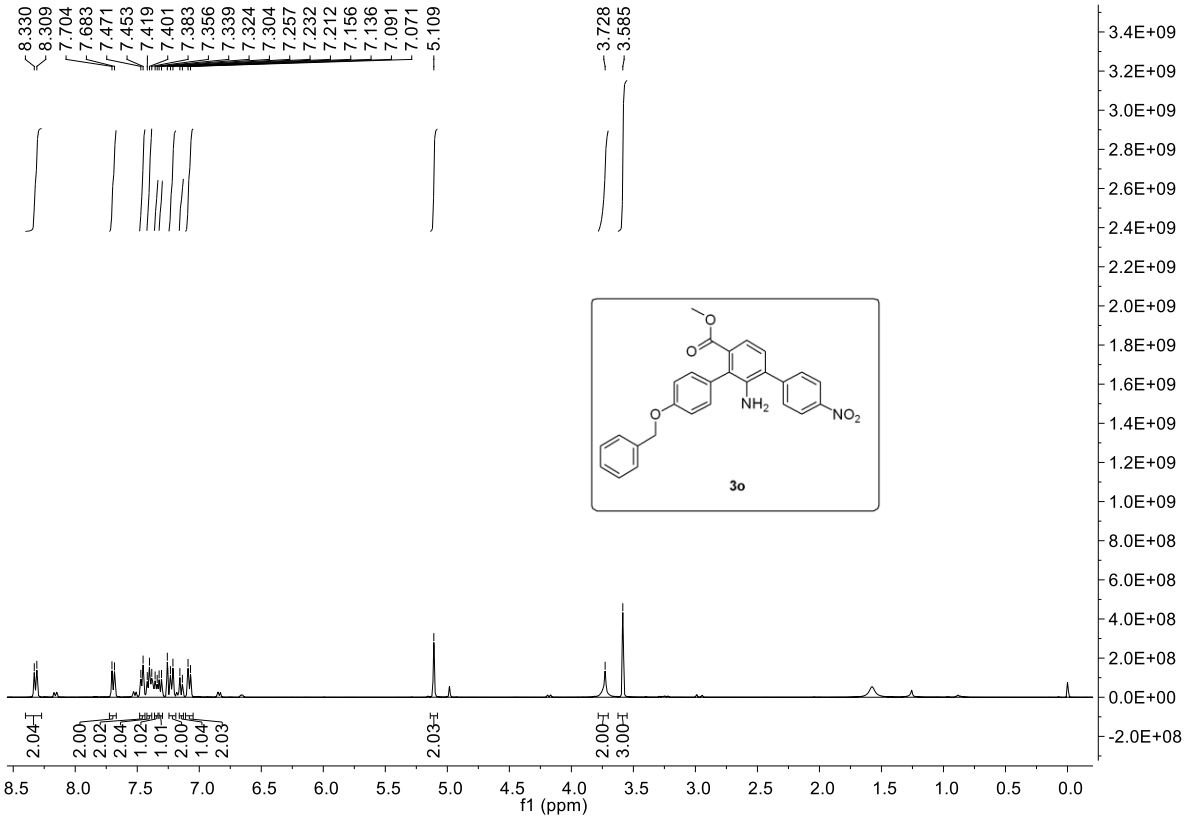

168.01
158.31
154.56
147.32
145.84
141.64
138.88
133.11
132.08
130.29
130.25
130.04
129.22
127.97
127.49
124.27
123.69
119.31
119.19
119.10
117.82
77.33
77.02
76.70
51.94
20.70
NH2
NO2
O
3l
f1 (ppm)

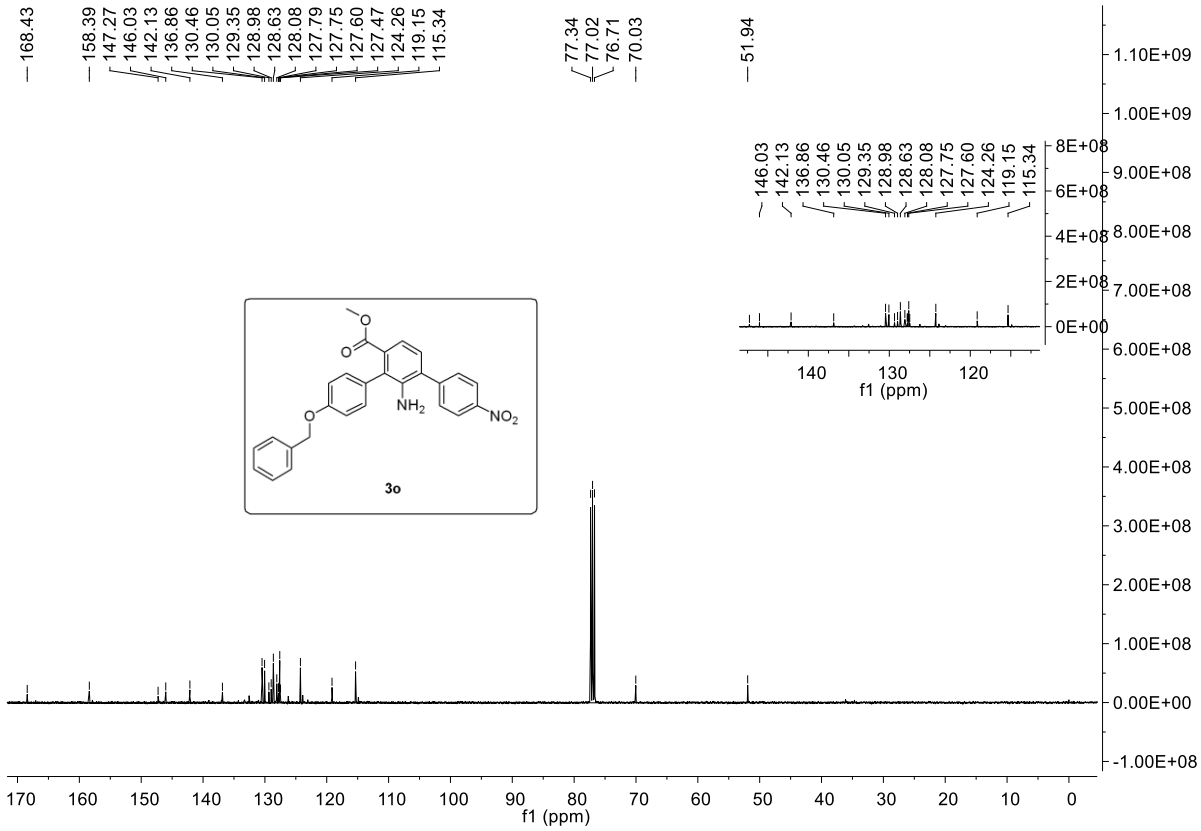

8.399
8.333
8.313
7.690
7.670
7.445
7.341
7.322
7.260
7.161
7.141
7.120
7.102
7.060
7.046
7.029
6.963
3.741
3.636
-0.000
NH2
NO2
3m
2.00
2.03
1.04
3.05
1.08
1.00
4.02
1.03
2.00
3.01
f1 (ppm)

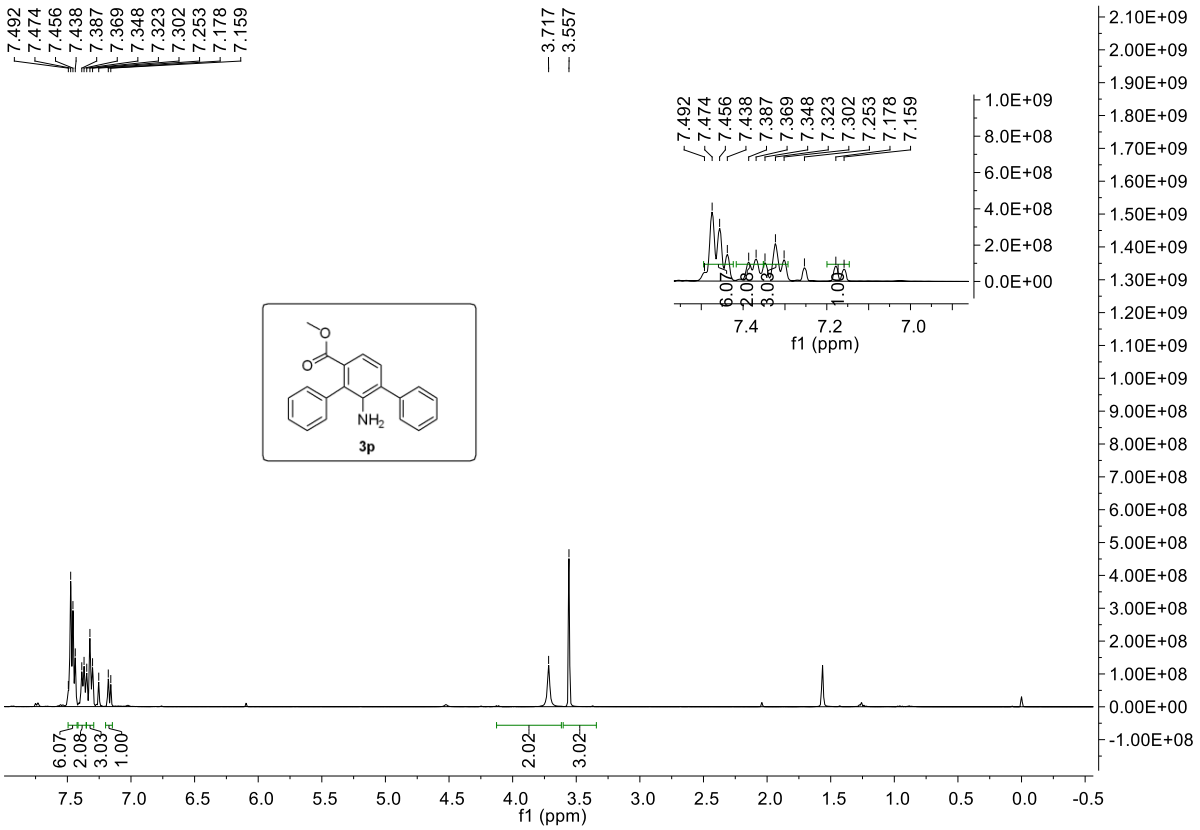

167.98
157.75
157.11
147.33
145.81
141.62
139.01
132.04
130.35
130.05
129.79
129.26
128.02
127.41
124.28
124.11
123.40
119.80
119.36
118.88
118.35
77.33
77.01
76.70
51.96
NH2
NO2
3m
f1 (ppm)

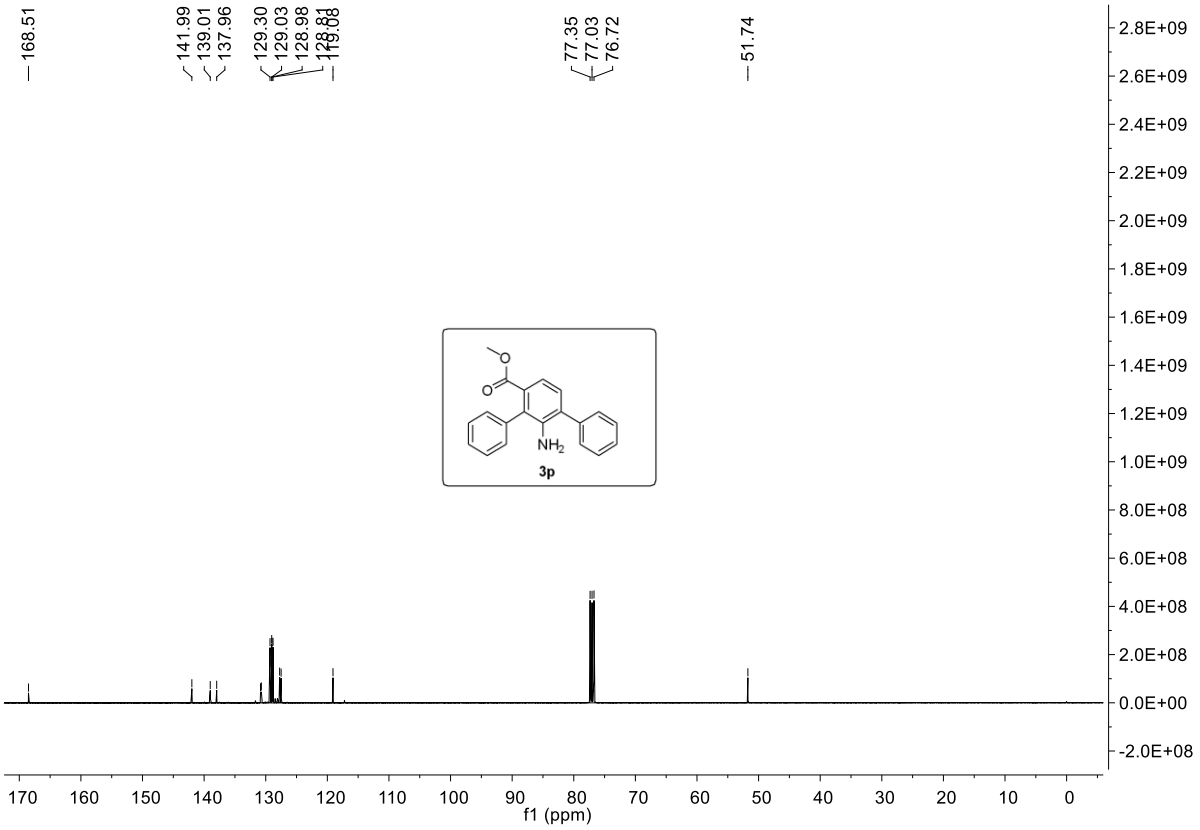

8.340
8.320
7.710
7.689
7.418
7.391
7.371
7.352
7.331
7.297
7.260
7.175
7.156
7.144
7.109
7.089
7.070
3.750
3.626
2.05
2.00
4.01
2.05
5.03
2.00
3.07
f1 (ppm)
3n

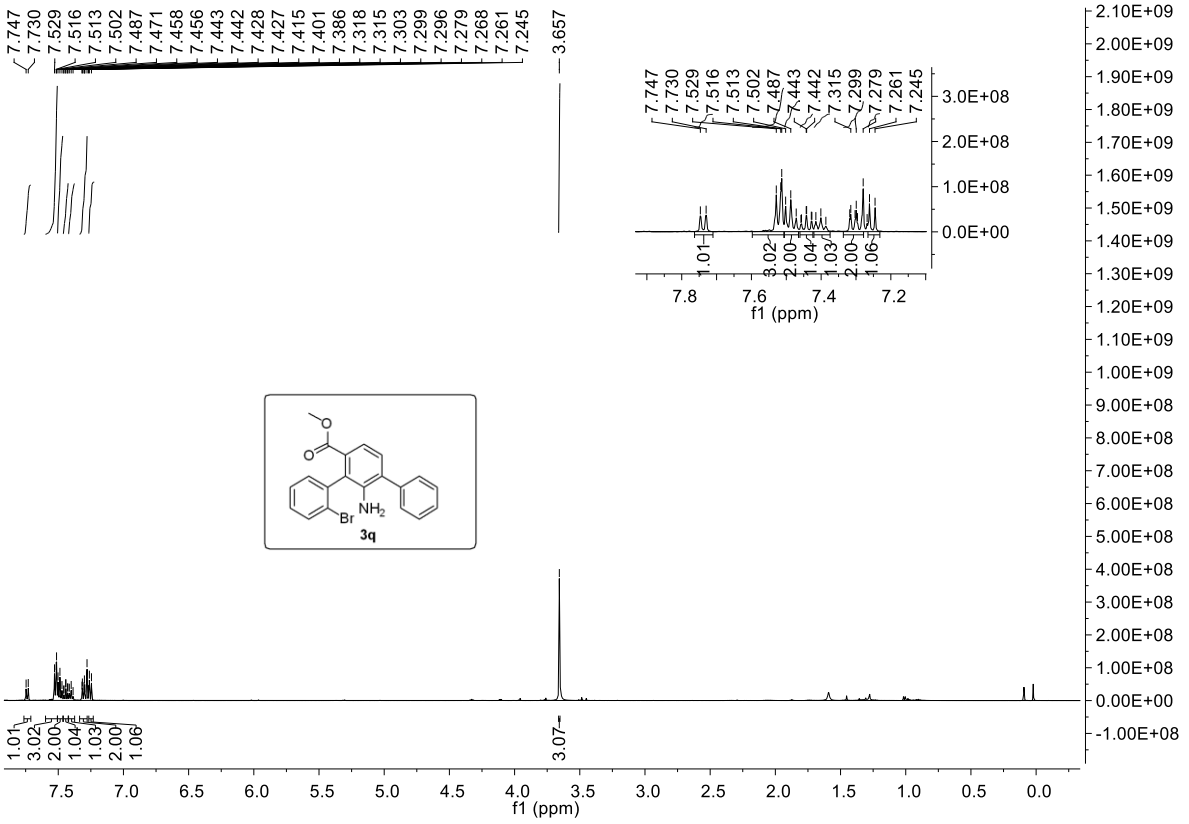

168.29
157.14
156.72
147.32
145.91
141.98
132.46
131.95
131.64
130.72
130.05
129.85
129.15
127.89
124.28
123.69
119.35
119.30
118.91
117.60
77.33
77.01
76.70
51.94
f1 (ppm)
3n

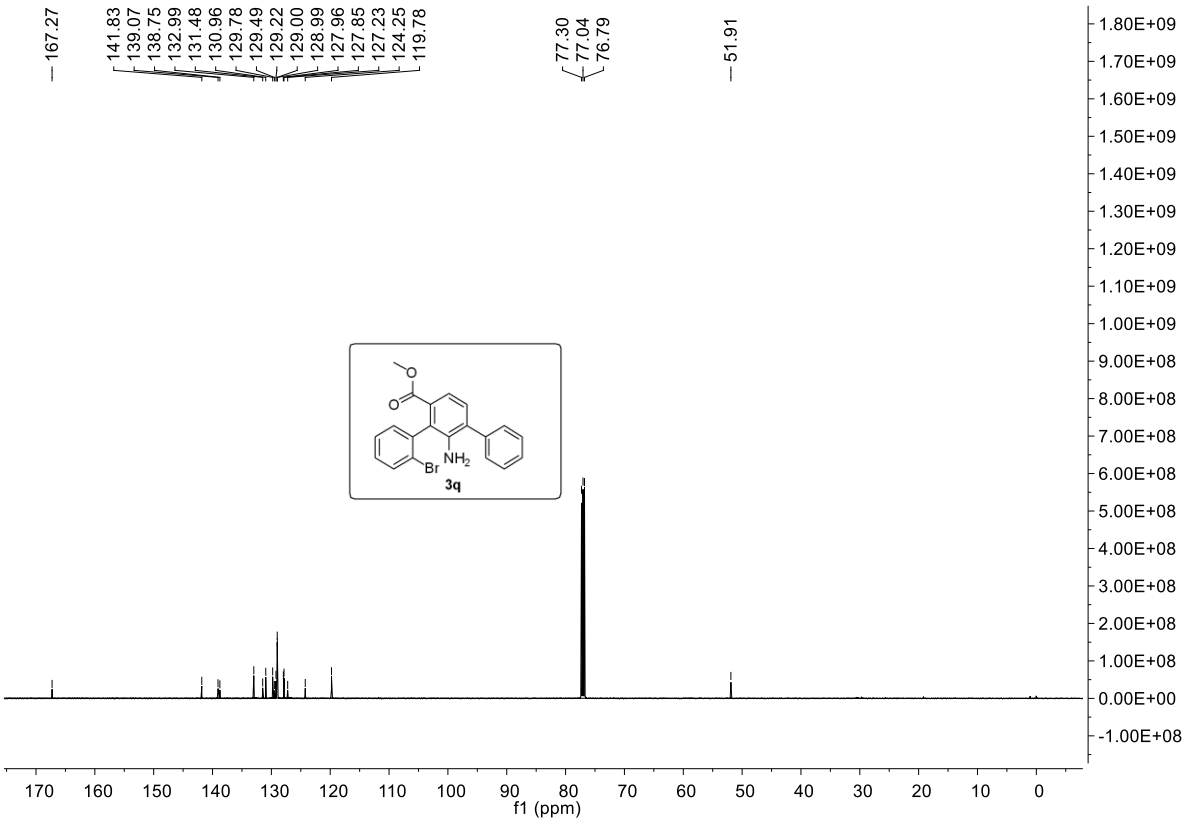

8.330
8.309
7.704
7.683
7.471
7.453
7.419
7.401
7.383
7.356
7.339
7.324
7.304
7.257
7.232
7.212
7.156
7.136
7.091
7.071
5.109
3.728
3.585
NH2
NO2
3o
2.04
2.00
2.02
2.04
1.02
1.01
2.00
1.04
2.03
2.03
2.00
3.00
f1 (ppm)

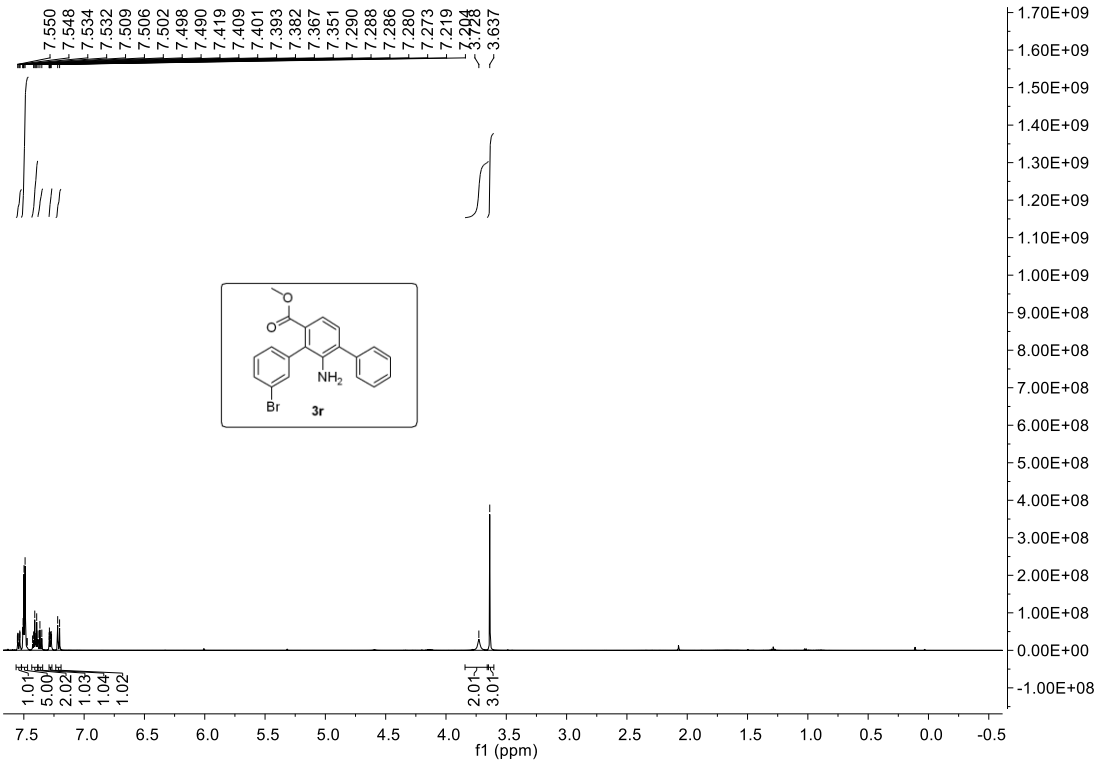

168.43
158.39
147.27
146.03
142.13
136.86
130.46
130.05
129.35
128.98
128.63
128.08
127.79
127.75
127.60
127.47
124.26
119.15
115.34
77.34
77.02
76.71
70.03
51.94
NH2
NO2
3o
f1 (ppm)

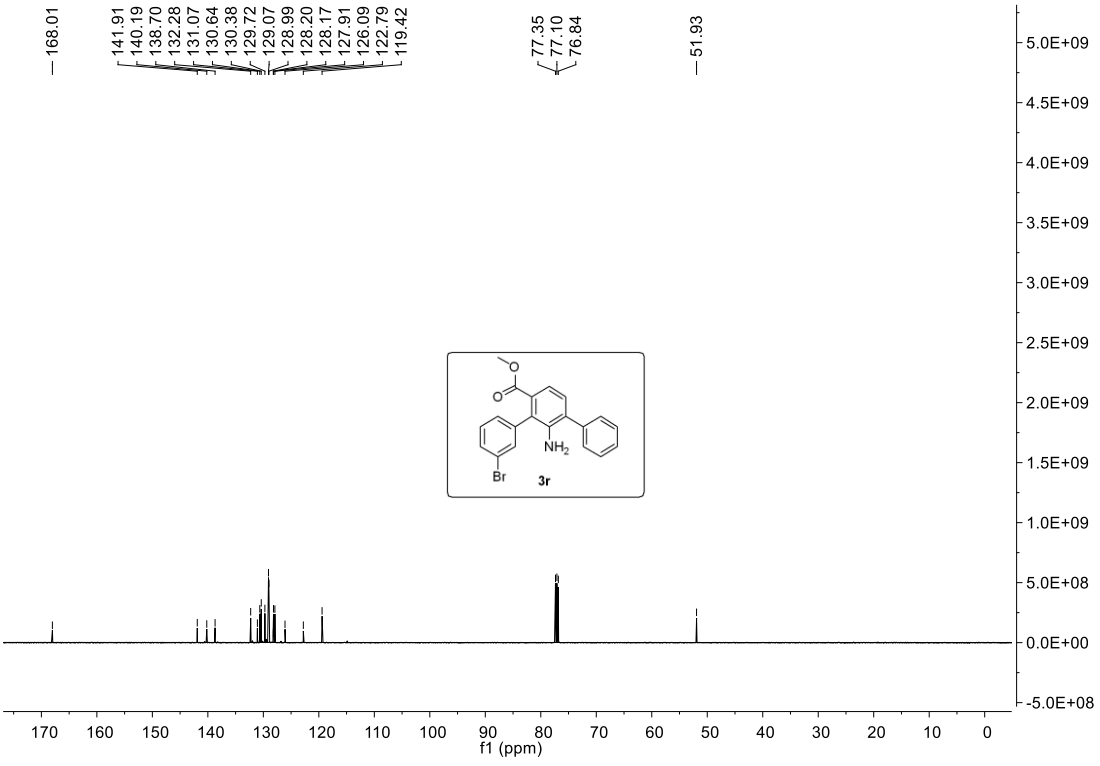

7.492
7.474
7.456
7.438
7.387
7.369
7.348
7.323
7.302
7.253
7.178
7.159
3.717
3.557
6.07
2.08
3.03
1.00
2.02
3.02
NH2
3p
f1 (ppm)

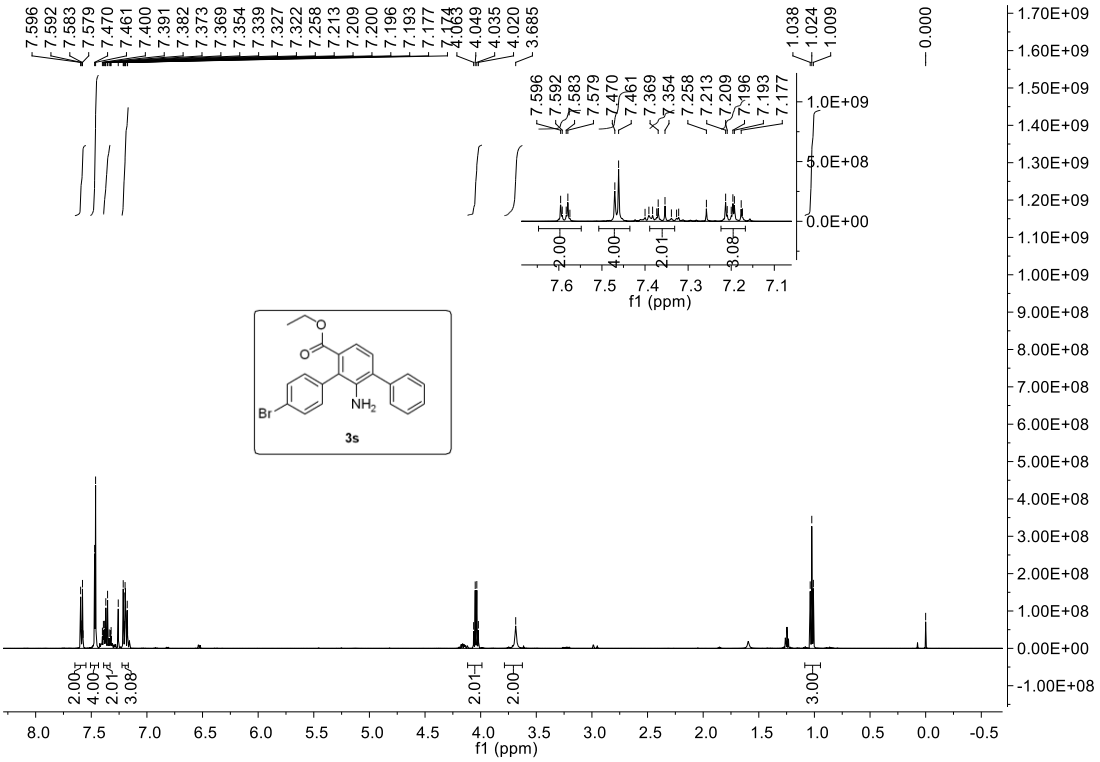

168.51
141.99
139.01
137.96
129.30
129.03
128.98
77.35
77.03
76.72
51.74
NH2
3p
f1 (ppm)

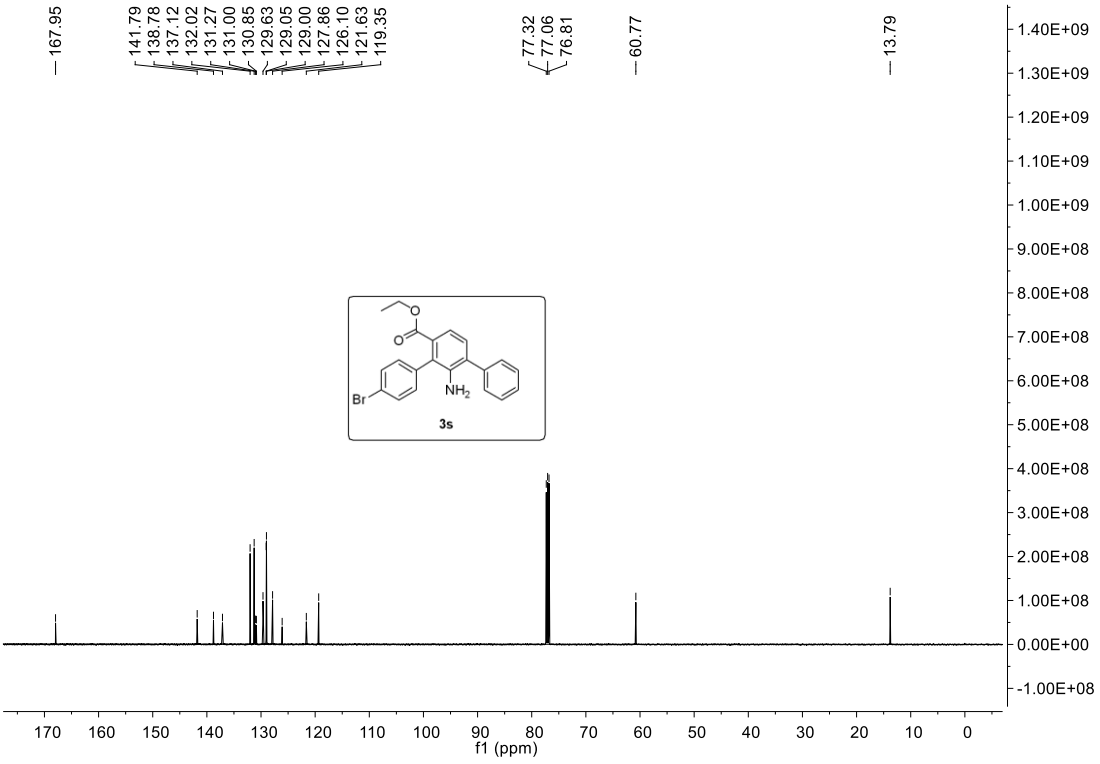

7.747
7.730
7.529
7.516
7.513
7.502
7.487
7.471
7.458
7.456
7.443
7.442
7.428
7.427
7.415
7.401
7.386
7.318
7.315
7.303
7.299
7.296
7.279
7.268
7.261
7.245
3.657
1.01
3.02
2.00
1.04
1.03
2.00
1.06
3.07
f1 (ppm)
3q

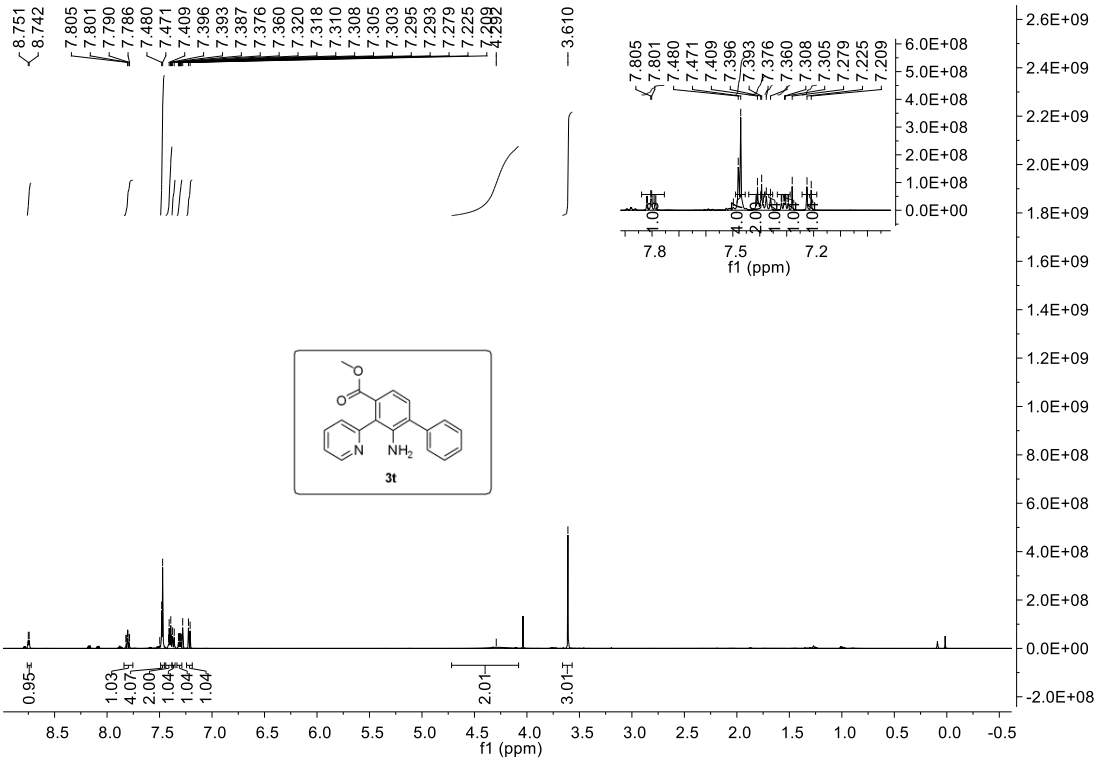

167.27
141.83
139.07
138.75
132.99
131.48
130.96
129.78
129.49
129.22
129.00
128.99
127.96
127.85
127.23
124.25
119.78
77.30
77.04
76.79
51.91
f1 (ppm)
3q

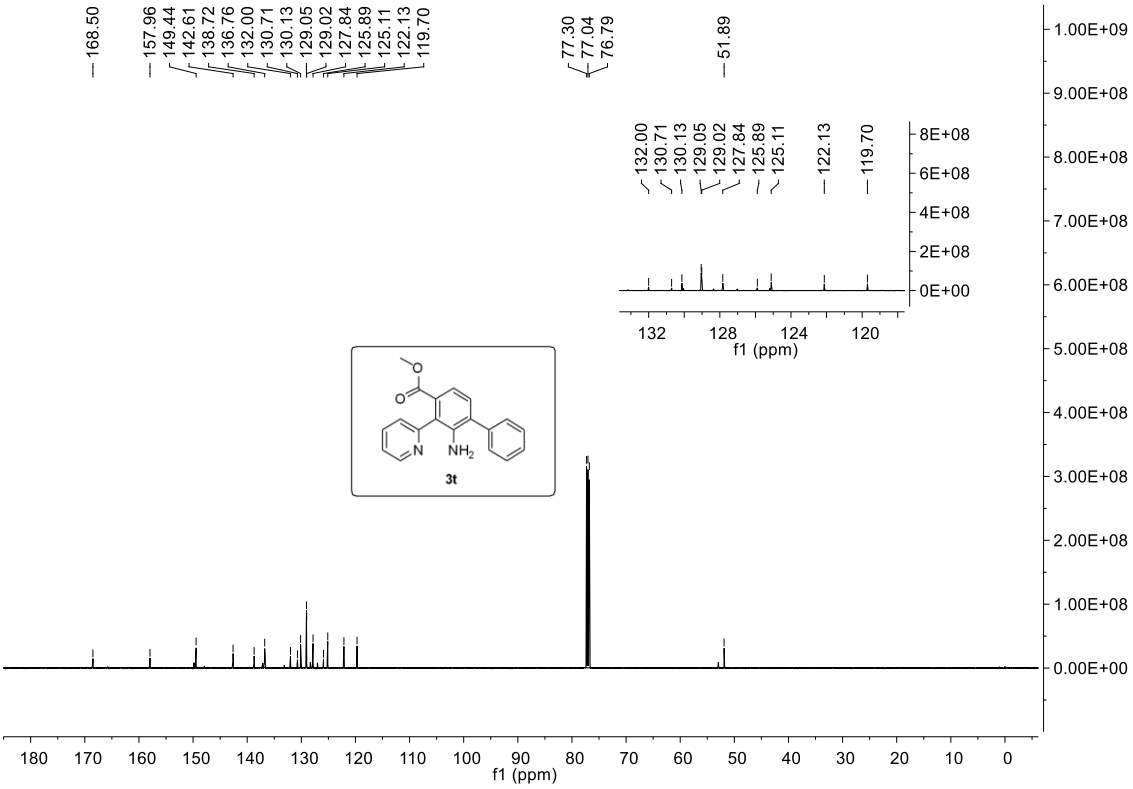

7.550
7.548
7.534
7.532
7.509
7.506
7.502
7.498
7.490
7.419
7.409
7.401
7.393
7.382
7.367
7.351
7.290
7.288
7.286
7.280
7.273
7.219
7.204
3.728
3.637
NH2
Br
3r
1.01
5.00
2.02
1.03
1.04
1.02
2.01
3.01
f1 (ppm)

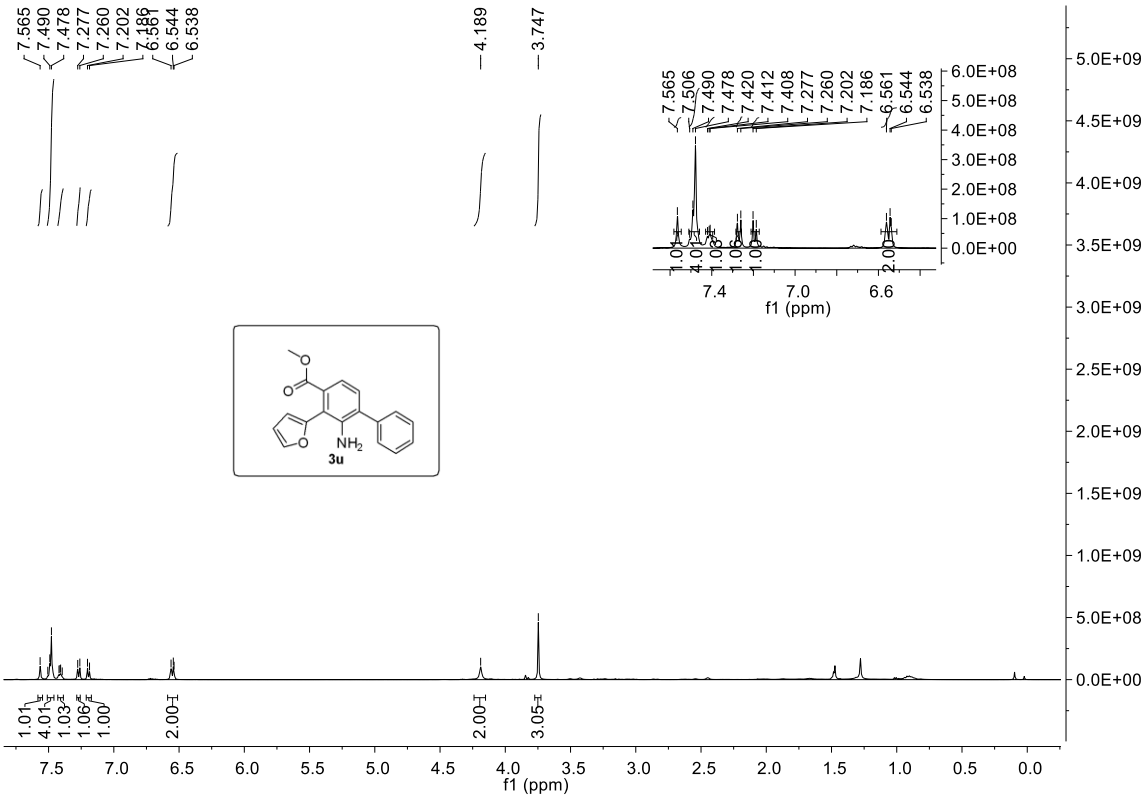

168.01
141.91
140.19
138.70
132.28
131.07
130.64
130.38
129.72
129.07
128.99
128.20
128.17
127.91
126.09
122.79
119.42
77.35
77.10
76.84
51.93
NH2
Br
3r
f1 (ppm)

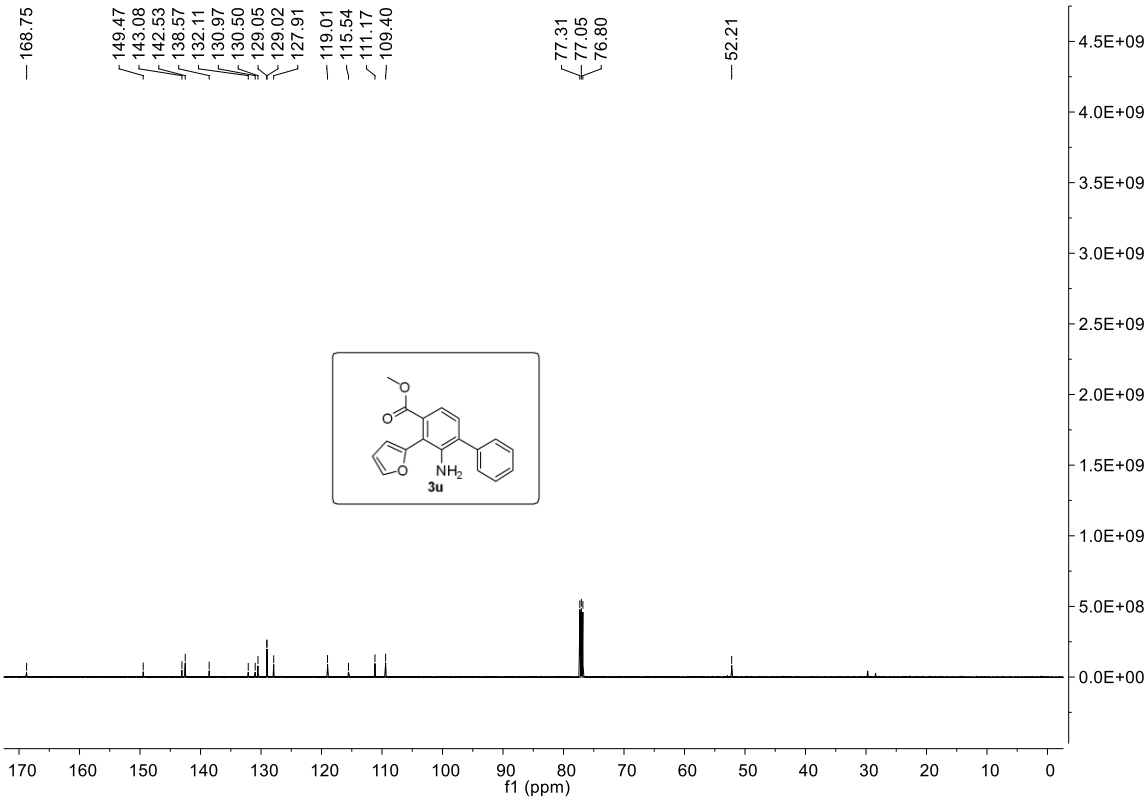

7.596
7.592
7.583
7.579
7.470
7.461
7.400
7.391
7.382
7.373
7.369
7.354
7.339
7.327
7.322
7.258
7.213
7.209
7.200
7.196
7.193
7.177
7.174
7.163
4.049
4.035
4.020
3.685
1.038
1.024
1.009
0.000
2.00
4.00
2.01
3.08
2.01
2.00
3.00
f1 (ppm)
Br
NH2
3s

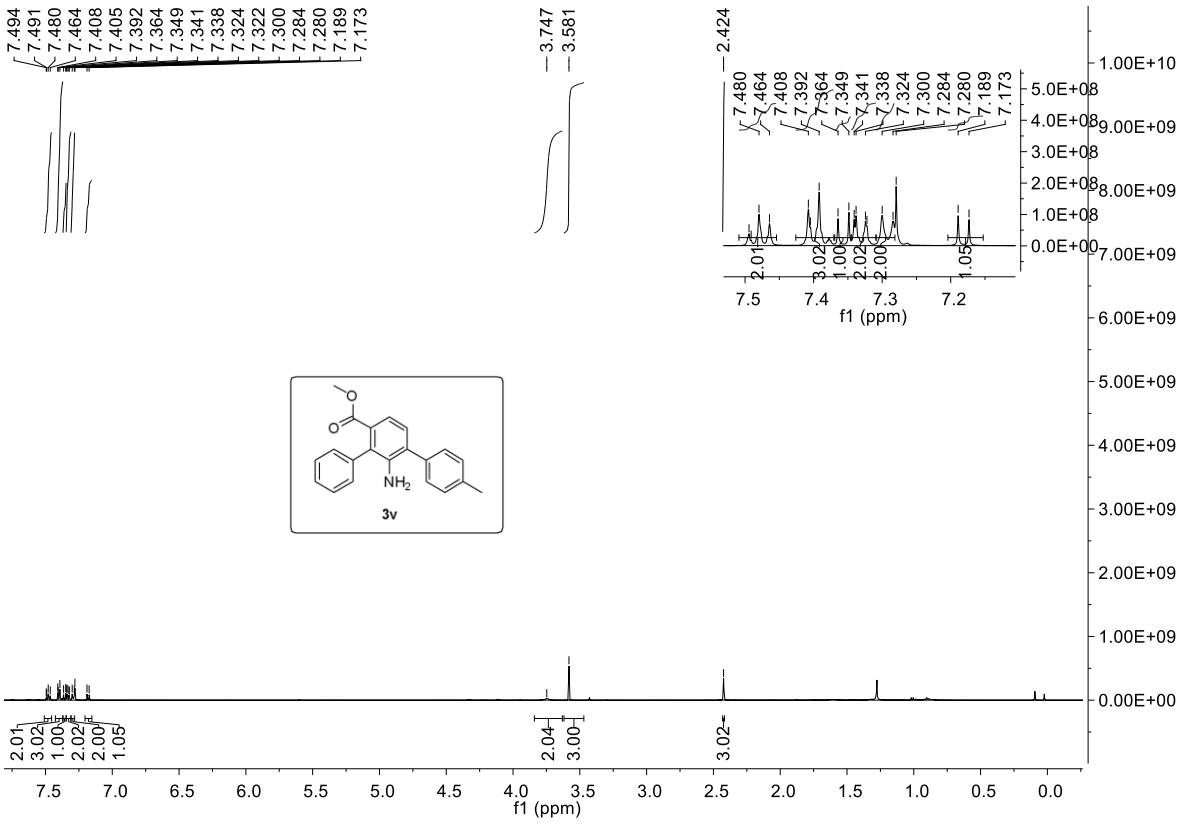

167.95
141.79
138.78
137.12
132.02
131.27
131.00
130.85
129.63
129.05
129.00
127.86
126.10
121.63
119.35
77.32
77.06
76.81
60.77
13.79
f1 (ppm)
Br
NH2
3s

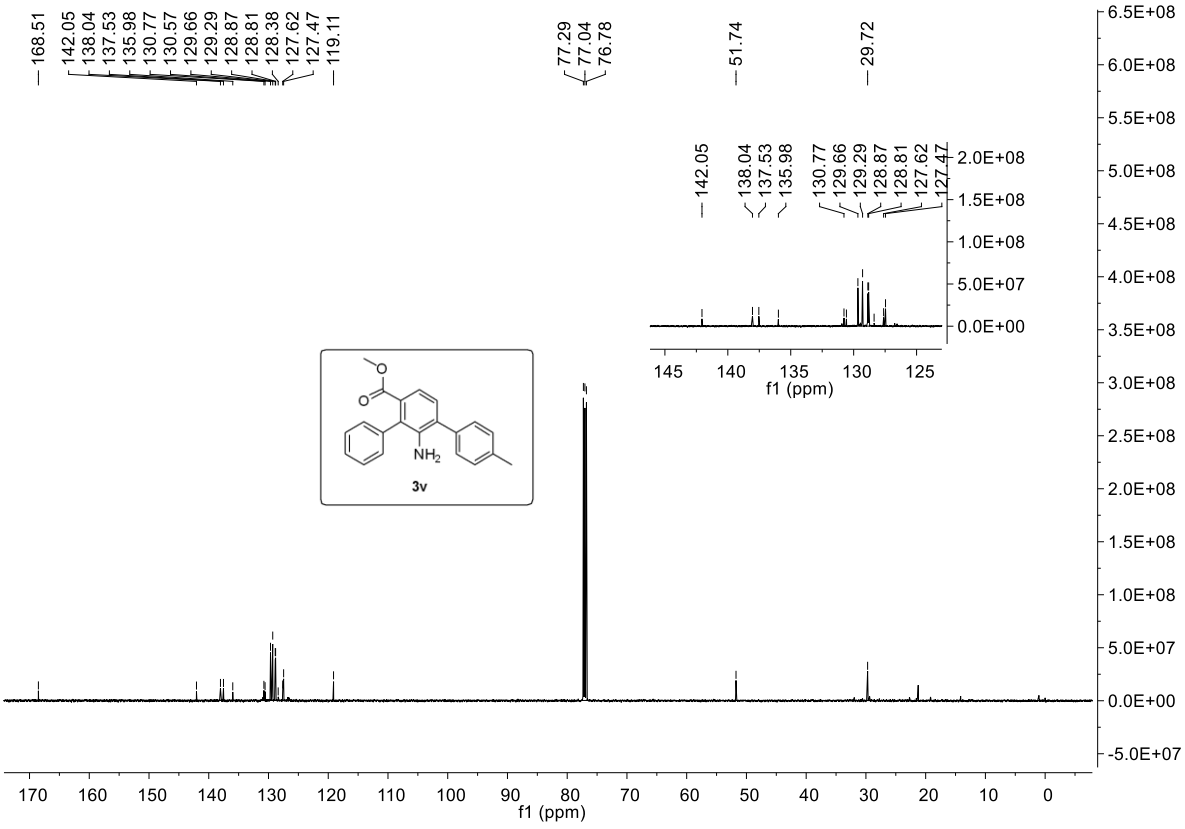

8.751
8.742
7.805
7.801
7.790
7.786
7.480
7.471
7.409
7.396
7.393
7.387
7.376
7.360
7.320
7.318
7.310
7.308
7.305
7.303
7.295
7.293
7.279
7.225
7.209
4.292
3.610
f1 (ppm)
3t

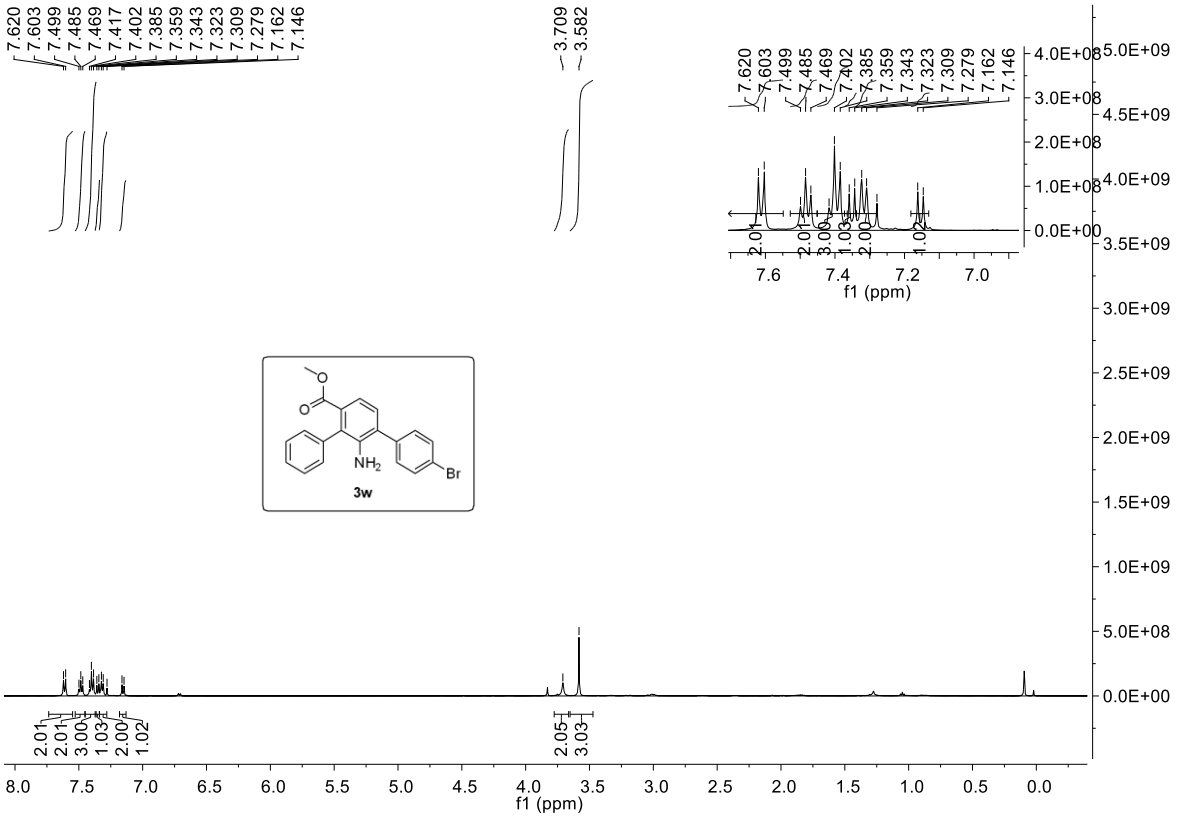

168.50
157.96
149.44
142.61
138.72
136.76
132.00
130.71
130.13
129.05
129.02
127.84
125.89
125.11
122.13
119.70
77.30
77.04
76.79
51.89
f1 (ppm)
3t

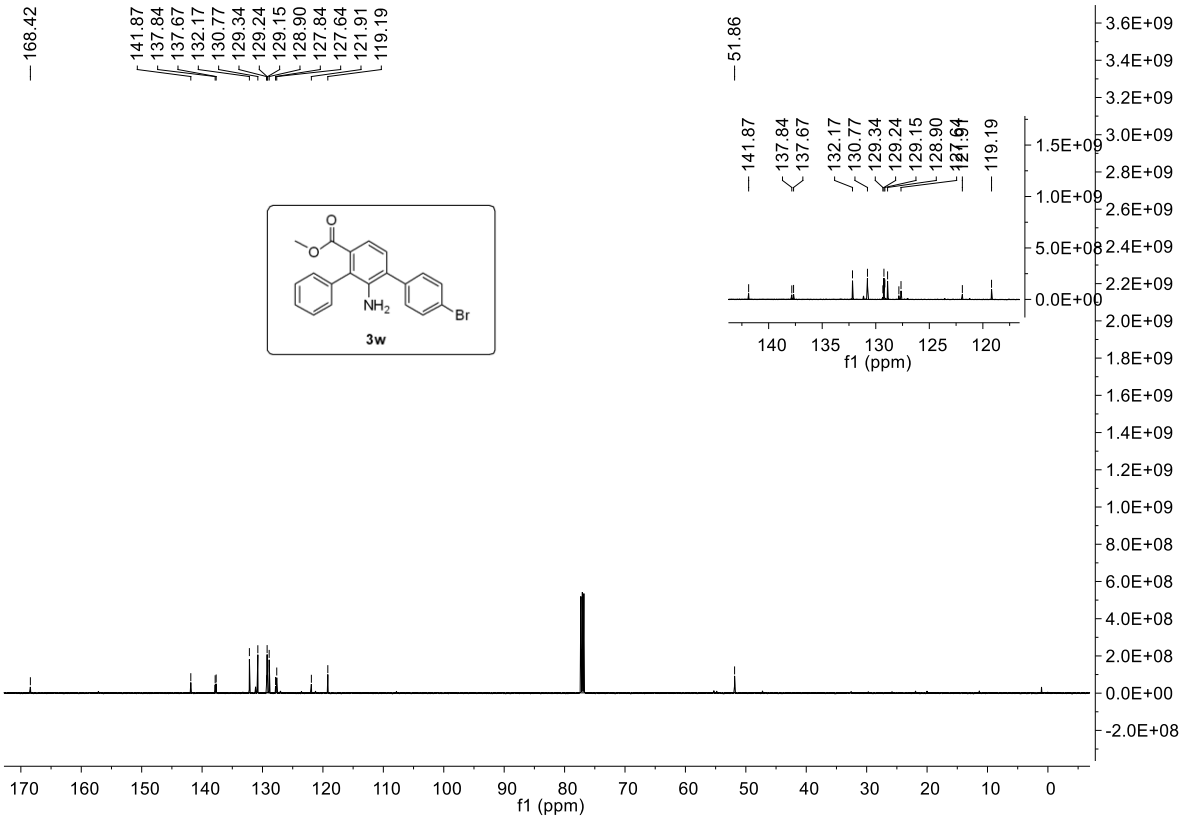

7.565
7.490
7.478
7.277
7.260
7.202
7.186
6.561
6.544
6.538
4.189
3.747
1.01
4.01
1.03
1.06
1.00
2.00
2.00
3.05
NH2
3u
f1 (ppm)


168.75
149.47
143.08
142.53
138.57
132.11
130.97
130.50
129.05
129.02
127.91
119.01
115.54
111.17
109.40
77.31
77.05
76.80
52.21
NH2
3u
f1 (ppm)


7.494
7.491
7.480
7.464
7.408
7.405
7.392
7.364
7.349
7.341
7.338
7.324
7.322
7.300
7.284
7.280
7.189
7.173
3.747
3.581
2.424
2.01
3.02
1.00
2.02
2.00
1.05
2.04
3.00
3.02
f1 (ppm)
3v


168.51
142.05
138.04
137.53
135.98
130.77
130.57
129.66
129.29
128.87
128.81
128.38
127.62
127.47
119.11
77.29
77.04
76.78
51.74
29.72
f1 (ppm)
3v


7.620
7.603
7.499
7.485
7.469
7.417
7.402
7.385
7.359
7.343
7.323
7.309
7.279
7.162
7.146
3.709
3.582
2.01
2.01
3.00
1.03
2.00
1.02
2.05
3.03
f1 (ppm)
3w


168.42
141.87
137.84
137.67
132.17
130.77
129.34
129.24
129.15
128.90
127.84
127.64
121.91
119.19
51.86
f1 (ppm)
3w

6. X-ray crystallography Data of 3c (CCDC No: 1005572):

Single crystals of compound **3c** were measured on a Rigaku RAXIS-RAPID single-crystal diffractometer. The recrystallization solvent of **3c** was DCM:EtOH (1:1).

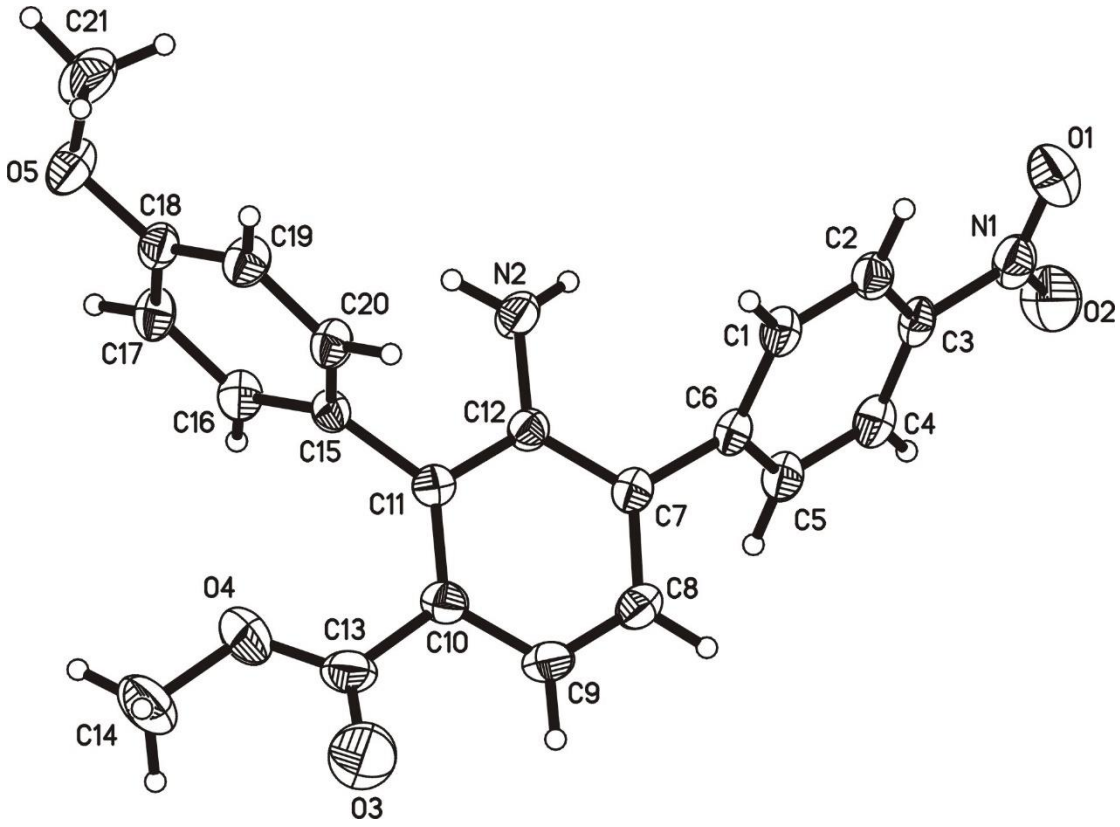


Figure S1 X-ray crystal structure of **3c**

Table S1 X-ray crystallography data of **3c**

Formula moiety	$C_{21}H_{18}N_2O_5$
Formula sum	$C_{21}H_{18}N_2O_5$
Formula weight	378.37
Temperature	293 K
Crystal system	monoclinic
Space group	C 2/c
Unit cell dimensions	a=34.026(3) Å
	b=8.1856(7) Å
	c=13.2003 (9) Å

	alpha = 90 deg.
	beta = 94.279(7) deg.
	gamma = 90 deg.
Volume	3666.3 (5) $Å^3$
Z	8
Calculated density	1.371 g/cm^3
Absorption coefficient	0.099mm^{-1}
F(000)	1584
Crystal size	0.39 x 0.35 x 0.23 mm
Theta range for data collection	3.2 to 25.3 deg.
Reflections collected / unique	7332 / 3342 [R(int) = 0.0345]
Data / restraints / parameters	3342 / 0 / 262
Goodness-of-fit on F2	1.029
Final R indices [I>2sigma(I)]	R1 = 0.0482, wR2 = 0.1178
R indices (all data)	R1 = 0.0709, wR2 = 0.1354

References:

1. (a) Wang, Y.-F.; Toh, K. K.; Chiba, S.; Narasaka, K. *Org. Lett.* **2008**, 10, 5019. (b) Chiba, S.; Wang, Y.-F.; Lapointe, G.; Narasaka, K. *Org. Lett.* **2008**, 10, 313.(c)Wang, Y.-F.; Chiba, S. *J. Am. Chem. Soc.* **2009**, 131, 12570.(d) Subban K., Ekambaram R.,Raghavachary R. *Tetrahedron Lett.* **2009**, 50, 2389.
2. Thomas L. Gilchrist and Ricardo Mendonca, *ARKIVOC* **2000**, 769.