Electronic Supplementary Material (ESI) for Chemical Communications

Copper-Catalyzed Direct Oxidative Annulation of *N*-Iminopyridinium Ylides with Terminal Alkynes Using O_2 as Oxidant

(Supporting Information)

Shengtao Ding,[†] Yuepeng Yan,[†] and Ning Jiao[*,†,‡]

[†] State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Xue Yuan Rd. 38, Beijing 100191, China,

[‡] State Key Laboratory of Organometallic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China.

E-mail: jiaoning@bjmu.edu.cn

Fax: (+86)10-82805297

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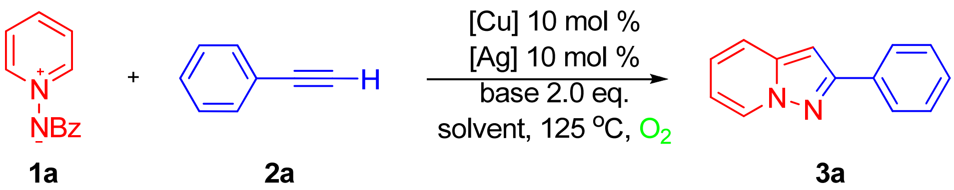
General Information

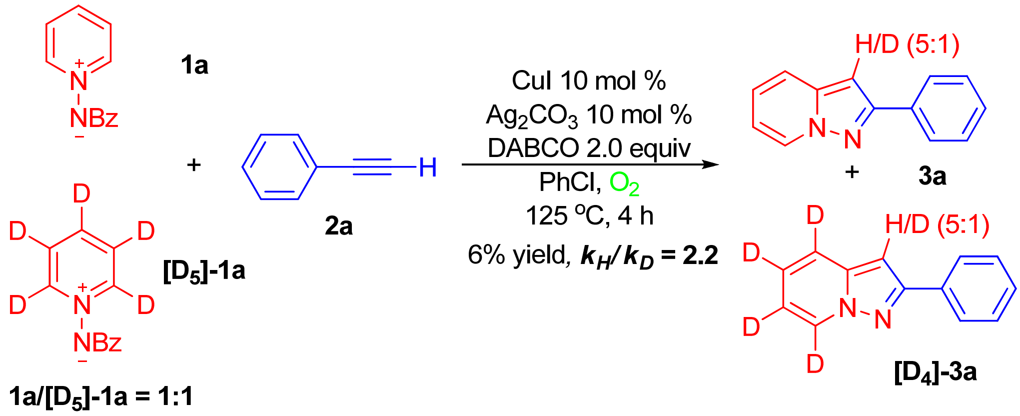
All manipulations were conducted with a standard Schlenk technique under oxygen atmosphere (1 atm). ^{1}H-NMR spectra were recorded with a Bruker AVIII-400 spectrometer. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in $CDCl_3$ as an internal standard. ^{13}C-NMR spectra were obtained by the same NMR spectrometer and were calibrated with $CDCl_3$ (δ = 77.00 ppm). Mass spectra were recorded by PE SCLEX QSTAR spectrometer. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Compounds **1a**,[1] **1b** – **1f** [2] were synthesized according to related literatures.

Table S1. Optimization of the reaction conditions.[a]



entry	[Cu]	[Ag]	base	solvent	yield(%)[b]
1	CuI			PhCl	trace
2	CuI	Ag_2CO_3		PhCl	27
3	CuI	Ag_2CO_3	Na_2CO_3	PhCl	55
4	CuI	Ag_2CO_3	K_2CO_3	PhCl	<5
5	CuI	Ag_2CO_3	Cs_2CO_3	PhCl	<5
6	CuI	Ag_2CO_3	DABCO	PhCl	74
7	CuI		DABCO	PhCl	20
8	$Cu(OAc)_2$	Ag_2CO_3	DABCO	PhCl	23
9	CuCN	Ag_2CO_3	DABCO	PhCl	40
10	$CuBr_2$	Ag_2CO_3	DABCO	PhCl	20
11	$CuCl_2$	Ag_2CO_3	DABCO	PhCl	35
12	CuI	AgOAc	DABCO	PhCl	45
13	CuI	Ag_2O	DABCO	PhCl	38
14	CuI	AgOBz	DABCO	PhCl	49
15	CuI	AgOTs	DABCO	PhCl	52
16	CuI	Ag_2CO_3	DABCO	DMF	<5
17	CuI	Ag_2CO_3	DABCO	DMSO	0
18	CuI	Ag_2CO_3	DABCO	NMP	0
19[c]	CuI	Ag_2CO_3	DABCO	PhCl	36
20[d]	CuI	Ag_2CO_3	DABCO	PhCl	20

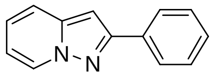
[a] General condition: **1a** (0.2 mmol), **2a** (0.6 mmol), additives, solvent (2 mL) under O_2 (1 atm) for 48 h. [b] Isolated yields. [c] The reaction was carried out under 100 °C. [d] The reaction was carried out under air.



Scheme S1. Kinetic isotope effect experiment.

Experimental procedures and characterization of products

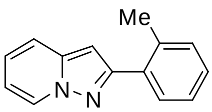
1. 2-Phenylpyrazolo[1,5-*a*]pyridine (3a) [3]



3a

Typical procedure: Substrate **1a** (39.6 mg, 0.20 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv) were added to a 20 mL Schlenk tube under O_2, followed by addition of **2a** (66 µl, 0.60 mmol) and PhCl (2.0 mL). The formed mixture was stirred at 125 ºC under O_2 (1 atm.) for 48 h as monitored by TLC. The solution was then cooled to rt., diluted with ethyl acetate (15 mL), and evaporated under vaccum. The crude product was purified by column chromatography on silica gel (hexane : ethyl acetate = 10:1) to afford 29.3 mg (74%) of product **3a**: light yellow solid; m.p. 95-97 ^{o}C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1944, 1889, 1632, 1512, 1470, 1332, 762 cm^{-1}; ^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 7.2 Hz, 1 H), 7.96 (d, *J* = 8.0 Hz, 2 H), 7.51-7.42 (m, 3 H), 7.36 (t, *J* = 7.2 Hz, 1 H), 7.06 (t, *J* = 8.0 Hz, 1 H), 6.78 (s, 1 H), 6.71 (dt, *J* = 1.2, 7.2 Hz, 1 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 153.5, 141.6, 133.2, 128.7, 128.5, 128.4, 126.4, 123.4, 117.9, 111.6, 93.7; MS (EI) *m/z* (relative intensity) 194.1 (100) [M]$^{+}$.

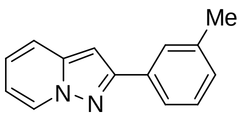
2. 2-*o*-Tolylpyrazolo[1,5-*a*]pyridine (3b) [3]



3b

The reaction of **1a** (39.6 mg, 0.20 mmol), 1-ethynyl-2-methylbenzene (78 µl, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 34.2 mg (82%) of **3b:** light beige solid; m.p. 70-73 ^{o}C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1752, 1633, 1520, 1508, 1461, 1329, 1251, 762 cm^{-1}; ^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 7.2 Hz, 1 H), 7.67 (t, *J* = 3.6 Hz, 1 H), 7.50 (d, *J* = 9.2 Hz, 1 H), 7.30-7.23 (m, 3 H), 7.08 (t, *J* = 8.0 Hz, 1 H), 6.72 (t, *J* = 7.2 Hz, 1 H), 6.62 (s, 1 H), 2.53 (s, 3 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 154.0, 140.7, 136.4, 133.1, 130.8, 129.9, 128.4, 128.1, 125.8, 123.2, 117.8, 111.4, 96.9, 21.1; MS (EI) *m/z* (relative intensity) 208.2 (82), 207.2 (100) [M]$^{+}$.

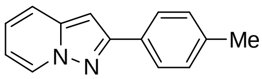
3. 2-*m*-Tolylpyrazolo[1,5-*a*]pyridine (3c)



3c

The reaction of **1a** (39.6 mg, 0.20 mmol), 1-ethynyl-3-methylbenzene (81 μl, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 33.9 mg (81%) of **3c:** light yellow solid; m.p. 87-88 ^oC (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1755, 1634, 1520, 1467, 1419, 1331, 1256, 772, 733 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.46 (d, J = 6.8 Hz, 1 H), 7.81 (s, 1H), 7.74 (d, J = 8.0 Hz, 1 H), 7.48 (d, J = 9.2 Hz, 1 H), 7.34 (t, J = 7.6 Hz, 1 H), 7.18 (d, J = 7.2 Hz, 1 H), 7.06 (t, J = 7.6 Hz, 1 H), 6.77 (s, 1 H), 6.70 (t, J = 6.8 Hz, 1 H), 2.42 (s, 3 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 153.7, 141.6, 138.3, 133.1, 129.2, 128.6, 128.4, 127.0, 123.6, 123.3, 117.8, 111.6, 93.7, 21.4; MS (EI) *m/z* (relative intensity) 208.2 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{14}H_{13}N_2$ $(M + H)^+$ 209.1073, found 209.1077.

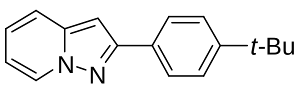
4. 2-*p*-Tolylpyrazolo[1,5-*a*]pyridine (3d) [3]



3d

The reaction of **1a** (39.6 mg, 0.20 mmol), 1-ethynyl-4-methylbenzene (78 μl, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 31.6 mg (76%) of **3d:** light yellow solid; m.p. 106-108 ^oC (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1909, 1633, 1514, 1474, 1331, 1255, 825, 778, 763 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.45 (d, J = 6.8 Hz, 1 H), 7.85 (d, J = 8.0 Hz, 2 H), 7.48 (d, J = 8.8 Hz, 1 H), 7.25 (d, J = 7.2 Hz, 2 H), 7.06 (t, J = 8.0 Hz, 1 H), 6.75 (s, 1 H), 6.70 (t, J = 6.4 Hz, 1 H), 2.39 (s, 3 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 153.6, 141.6, 138.2, 130.4, 129.4, 128.5, 126.3, 123.3, 117.8, 111.5, 93.4, 21.3; MS (EI) *m/z* (relative intensity) 208.2 (100) $[M]^+$.

5. 2-(4-*tert*-Butylphenyl)pyrazolo[1,5-*a*]pyridine (3e)

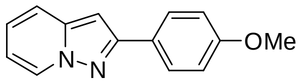


3e

The reaction of **1a** (39.6 mg, 0.20 mmol), 1-*tert*-butyl-4-ethynylbenzene (84 μl, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 36.5 mg (73%) of **3e:**

white solid; m.p. 108-110 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1918, 1751, 1632, 1513, 1473, 1328, 841, 776 cm^{-1}; ^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 6.8 Hz, 1 H), 7.89 (d, *J* = 8.4 Hz, 2 H), 7.49-7.45 (m, 3 H), 7.08-7.02 (m, 1 H), 6.76 (s, 1 H), 6.69 (t, *J* = 6.8 Hz, 1 H), 1.36 (s, 9H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 153.6, 151.4, 141.6, 130.4, 128.5, 126.2, 125.6, 123.3, 117.8, 111.4, 93.5, 34.6, 31.3; MS (EI) *m/z* (relative intensity) 250.2 (36), 235.2 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{17}H_{19}N_2$ $(M + H)^+$ 251.1543, found 251.1548.

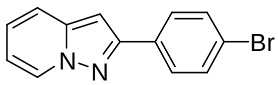
6. 2-(4-Methoxyphenyl)pyrazolo[1,5-*a*]pyridine (3f) [3, 4]



3f

The reaction of **1a** (39.6 mg, 0.20 mmol), 1-ethynyl-4-methoxybenzene (82 µl, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 31.3 mg (70%) of **3f:** white solid; m.p. 111-114 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 2363, 1858, 1631, 1613, 1514, 1463, 1246, 1029, 772 cm^{-1}; ^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 6.4 Hz, 1 H), 7.89 (d, *J* = 8.8 Hz, 2 H), 7.46 (d, *J* = 9.2 Hz, 1 H), 7.05 (t, *J* = 7.6 Hz, 1 H), 6.98 (d, *J* = 9.2 Hz, 2 H), 6.80-6.66 (m, 2 H), 3.84 (s, 3 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 159.9, 153.4, 141.6, 128.4, 127.7, 125.9, 123.3, 117.7, 114.1, 111.3, 93.0, 55.3; MS (EI) *m/z* (relative intensity) 224.2 (100), 209.1 (56) $[M]^+$.

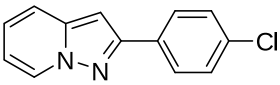
7. 2-(4-Bromophenyl)pyrazolo[1,5-*a*]pyridine (3g)



3g

The reaction of **1a** (39.6 mg, 0.20 mmol), 1-bromo-4-ethynylbenzene (108.6 mg, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 44.9 mg (82%) of **3g:** white solid; m.p. 174-177 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 2851, 1727, 1634, 1506, 1467, 1427, 1069, 1010, 775 cm^{-1}; ^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 6.4 Hz, 1 H), 7.82 (d, *J* = 8.4 Hz, 2 H), 7.56 (d, *J* = 8.0 Hz, 2 H), 7.49 (d, *J* = 8.8 Hz, 1 H), 7.11-7.05 (m, 1 H), 6.76-6.71 (m, 2 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 152.4, 141.7, 132.2, 131.8, 128.5, 128.0, 123.6, 122.4, 117.9, 111.9, 93.7; MS (EI) *m/z* (relative intensity) 272.1 (7), 192.0 (12), 117.0 (20), 62.6 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{13}H_{10}N_2Br$ $(M + H)^+$ 273.0022, found 273.0029.

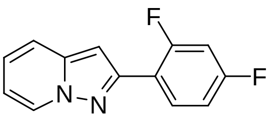
8. 2-(4-Chlorophenyl)pyrazolo[1,5-*a*]pyridine (3h)



3h

The reaction of **1a** (39.6 mg, 0.20 mmol), **2b** (82.0 mg, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 40.5 mg (89%) of **3h:** light yellow solid; m.p. 158-160 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1899, 1634, 1508, 1469, 1090, 1012, 774 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 7.2 Hz, 1 H), 7.89 (d, *J* = 8.4 Hz, 2 H), 7.50 (d, *J* = 9.2 Hz, 1 H), 7.41 (d, *J* = 8.0 Hz, 2 H), 7.09 (t, *J* = 8.0 Hz, 1 H), 6.76-6.72 (m, 2 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 152.3, 141.7, 134.2, 131.8, 128.9, 128.4, 127.7, 123.5, 117.9, 111.9, 93.6; MS (EI) *m/z* (relative intensity) 228.2 (100), 192.1 (31), 62.7 (94) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{13}H_{10}N_2Cl$ $(M + H)^+$ 229.0527, found 229.0532.

9. 2-(2,4-Difluorophenyl)pyrazolo[1,5-*a*]pyridine (3i)

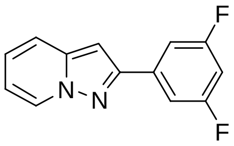


3i

The reaction of **1a** (39.6 mg, 0.20 mmol), 1-ethynyl-2,4-difluorobenzene (85.4 mg, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 35.2 mg (77%) of **3i:** white solid; m.p. 96-98 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1919, 1896, 1765, 1624, 1601, 1515, 1477, 1265, 1140, 973, 844, 767 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 6.4 Hz, 1 H), 8.14 (dd, *J* = 8.4, 15.2 Hz, 1 H), 7.52 (d, *J* = 8.8 Hz, 1 H), 7.09 (t, *J* = 8.0 Hz, 1 H), 7.01-6.85 (m, 3 H), 6.75 (d, *J* = 6.4 Hz, 1 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 162.9 (dd, *J* = 11.8, 213.4 Hz), 160.4 (dd, *J* = 12.3, 216.9 Hz), 147.2, 141.4, 130.0 (dd, *J* = 4.4, 10.0 Hz), 128.3, 123.4, 118.1, 117.6 (dd, *J* = 3.2, 11.3 Hz), 112.1, 111.7 (dd, *J* = 3.5, 20.5 Hz), 104.4 (t, *J* = 26.1 Hz), 97.0 (d, *J* = 10.8 Hz); MS (EI) *m/z* (relative intensity) 230.2 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{13}H_9N_2F_2$ $(M + H)^+$ 231.0728, found 231.0733.

10. 2-(3,5-difluorophenyl)pyrazolo[1,5-*a*]pyridine (3j)

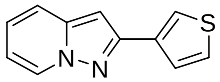
Electronic Supplementary Material (ESI) for Chemical Communications



3j

The reaction of **1a** (39.6 mg, 0.20 mmol), 3-ethynylthiophene (74 μl, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 29.1 mg (63%) of **3j:** white solid; m.p. 99-102 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1919, 1896, 1633, 1602, 1512, 1419, 1115, 989, 763 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 7.2 Hz, 1 H), 7.54-7.45 (m, 3 H), 7.14-7.08 (m, 1 H), 6.83-6.73 (m, 3 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 163.3 (dd, *J* = 12.4, 246.6 Hz), 151.3, 141.7, 136.6 (t, *J* = 9.6 Hz), 128.5, 123.7, 118.1, 112.4, 109.2 (dd, *J* = 7.8, 19.0 Hz), 103.5 (t, *J* = 25.3 Hz), 94.1; MS (EI) *m/z* (relative intensity) 230.2 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{13}H_9N_2F_2$ $(M + H)^+$ 231.0728, found 231.0733.

11. 2-(Thiophen-3-yl)pyrazolo[1,5-*a*]pyridine (3l)

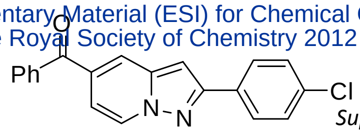


3l

The reaction of **1a** (39.6 mg, 0.20 mmol), 3-ethynylthiophene (59 μl, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 26.8 mg (67%) of **3l:** white solid; m.p. 115-118 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1630, 1513, 1345, 1326, 1252, 858, 775 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 6.8 Hz, 1 H), 7.76 (d, *J* = 0.4 Hz, 1 H), 7.59 (d, *J* = 4.4 Hz, 1 H), 7.48 (d, *J* = 8.8 Hz, 1 H), 7.39 (s, 1 H), 7.11-7.04 (m, 1 H), 6.72 (t, *J* = 6.8 Hz, 1 H), 6.67 (s, 1 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 149.7, 141.4, 135.0, 128.4, 126.3, 126.0, 123.4, 121.9, 117.7, 111.6, 93.9; MS (EI) *m/z* (relative intensity) 200.2 (80), 62.7 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{11}H_9N_2S$ $(M + H)^+$ 201.0481, found 201.0486.

12. 2-(4-Chlorophenyl)-5-benzoylpyrazolo[1,5-*a*]pyridine (3m)

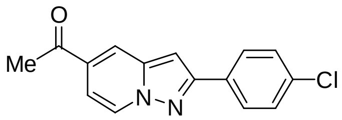
The reaction of **1b** (57.7 mg, 0.20 mmol), **2b** (82.0 mg, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 28.2 mg (42%) of **3m:** light yellow solid; m.p. 161-164 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1787, 1733, 1657, 1525, 1320, 1260, 831, 705 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 7.0 Hz, 1 H), 7.95 (s,



3m

1 H), 7.90 (d, J = 8.0 Hz, 2 H), 7.83 (d, J = 7.2 Hz, 2 H), 7.64 (t, J = 6.8 Hz, 1 H), 7.56-7.50 (m, 2 H), 7.43 (d, J = 8.0 Hz, 2 H), 7.28 (d, J = 7.2 Hz, 1 H), 6.96 (s, 1 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 194.3, 153.6, 140.2, 137.0, 134.7, 133.7, 132.7, 131.1, 129.7, 129.0, 128.9, 128.5, 128.4, 127.7, 121.8, 111.5, 97.1; MS (EI) *m/z* (relative intensity) 332.1 (10), 105.1 (62), 77.0 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{20}H_{14}N_2ClO$ $(M + H)^+$ 333.0789, found 333.0796.

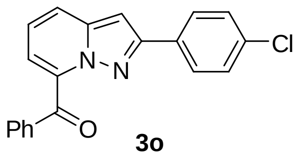
13. 2-(4-Chlorophenyl)-5-acetylpyrazolo[1,5-*a*]pyridine (3n)



3n

The reaction of **1c** (48.1 mg, 0.20 mmol), **2b** (82.0 mg, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 17.8 mg (33%) of **3n:** light yellow solid; m.p. 170-174 ^{o}C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1909, 1866, 1683, 1498, 1476, 1357, 1096, 833, 774 cm^{-1}; ^{1}H NMR: (400 MHz, $CDCl_3$) δ 8.46 (d, J = 7.2 Hz, 1 H), 8.14 (s, 1 H), 7.90 (d, J = 8.0 Hz, 2 H), 7.43 (d, J = 8.0 Hz, 2 H), 7.32 (d, J = 6.0 Hz, 1 H), 6.99 (s, 1 H), 2.65 (s, 3 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 195.6, 153.6, 140.4, 134.7, 133.7, 132.2, 129.0, 128.9, 128.5, 127.7, 119.9, 109.7, 97.3, 26.2; MS (EI) *m/z* (relative intensity) 270.1 (8), 200.2 (16), 49.9 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{15}H_{12}N_2ClO$ $(M + H)^+$ 271.0633, found 271.0631.

14. 2-(4-Chlorophenyl)-7-benzoylpyrazolo[1,5-*a*]pyridine (3o)

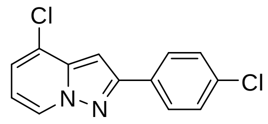


3o

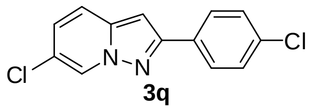
The reaction of **1d** (60.2 mg, 0.20 mmol), **2b** (82.0 mg, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 26.3 mg (40%) of **3o:** light yellow solid; m.p. 140-143 ^{o}C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 2225, 1729, 1599, 1524, 1474, 1437, 1334, 1092, 1013, 822, 770 cm^{-1}; ^{1}H NMR: (400 MHz, $CDCl_3$) δ 7.86 (d, J = 7.2 Hz, 2 H), 7.72 (d, J = 8.0 Hz, 2 H), 7.69-7.58 (m, 2 H), 7.46 (t, J = 7.2 Hz, 2 H), 7.31 (d, J = 8.0 Hz, 2 H), 7.18 (t, J = 7.6 Hz, 1 H), 6.95 (d, J = 6.4 Hz, 1 H), 6.85 (s, 1 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 189.5, 152.6, 142.3, 136.8, 136.2, 134.3, 133.9, 133.7, 131.4, 129.9, 128.9, 128.7, 128.6, 127.8, 122.7, 120.1, 113.8, 94.2; MS (EI) *m/z* (relative intensity) 332.1 (2), 105.1 (29), 77.0 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{20}H_{14}N_2ClO$ $(M + H)^+$ 333.0789, found 333.0794.

15. 4-Chloro-2-(4-chlorophenyl)pyrazolo[1,5-*a*]pyridine (3p)

6-Chloro-2-(4-chlorophenyl)pyrazolo[1,5-*a*]pyridine (3q)



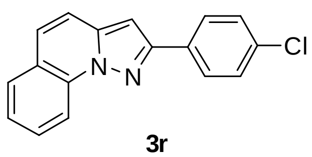
3p



3q

The reaction of **1e** (46.6 mg, 0.20 mmol), **2b** (82.0 mg, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 28.4 mg (54%) of **3p** & **3q** (2.4:1). **3p:** light yellow solid; m.p. 157-160 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1899, 1771, 1629, 1510, 1463, 1094, 830, 755 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 6.8 Hz, 1 H), 7.90 (d, *J* = 8.0 Hz, 2 H), 7.42 (d, *J* = 8.0 Hz, 2 H), 7.14 (d, *J* = 7.2 Hz, 1 H), 6.90 (s, 1 H), 6.68 (t, *J* = 7.2 Hz, 1 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 152.7, 140.8, 134.6, 131.2, 129.0, 127.8, 123.8, 122.7, 111.3, 94.1; MS (EI) *m/z* (relative intensity) 262.1 (73), 111.0 (70), 75.1 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{13}H_9N_2Cl_2$ $(M + H)^+$ 263.0137, found 263.0143. **3q:** light yellow; m.p. 125-128 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1765, 1463, 1245, 800 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.50 (s, 1 H), 7.86 (d, *J* = 8.0 Hz, 2 H), 7.47-7.39 (m, 3 H), 7.08 (d, *J* = 9.2 Hz, 1 H), 6.78 (s, 1 H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 153.0, 140.1, 134.5, 131.3, 129.0, 127.7, 126.6, 125.2, 120.0, 118.1, 94.4; MS (EI) *m/z* (relative intensity) 262.1 (75), 110.9 (83), 75.1 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{13}H_9N_2Cl_2$ $(M + H)^+$ 263.0137, found 263.0142.

16. 2-(4-Chlorophenyl)pyrazolo[1,5-*a*]quinoline (3r)

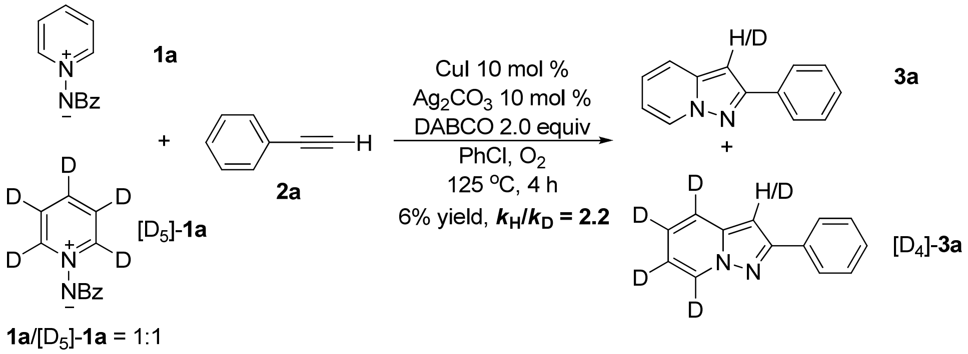


3r

The reaction of **1f** (49.7 mg, 0.20 mmol), **2b** (82.0 mg, 0.60 mmol), CuI (3.8 mg, 10 mol %), Ag_2CO_3 (5.5 mg, 10 mol %), DABCO (44.8 mg, 2.0 equiv), in PhCl (2.0 mL) under oxygen for 48 h afforded 45.5 mg (82%) of **3r:** white solid; m.p. 155-158 °C (*n*-hexane/ethyl acetate); IR: (KBr) ν_{max} 1913, 1614, 1462, 1422, 1090, 812, 753 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 8.63 (d, *J* = 8.0 Hz, 1 H), 7.96 (d, *J* = 7.6 Hz, 2 H), 7.72 (d, *J* = 7.6 Hz, 1 H), 7.66 (t, *J* = 7.2 Hz, 1 H), 7.44-7.37 (m, 5 H), 6.82 (s, 1 H);

^{13}C NMR: (100 MHz, $CDCl_3$) δ 151.7, 139.4, 134.8, 134.0, 133.7, 132.0, 129.4, 128.9, 128.3, 127.6, 124.8, 124.6, 123.3, 116.5, 115.6, 96.6; MS (EI) *m/z* (relative intensity) 278.2 (50), 139.9 (90), 74.7 (100) $[M]^+$; HRMS *m/z* (ESI) calcd. for $C_{17}H_{12}N_2Cl$ $(M + H)^+$ 279.0684, found 279.0690.

Kinetic Isotopic Experiment Study



Compound [D_5]-**1a** was synthesized according to the reported procedure.[5] Substrates **1a** (39.6 mg, 0.20 mmol), [D_5]-**1a** (40.6 mg, 0.20 mmol), CuI (7.6 mg, 10 mol %), Ag_2CO_3 (11.0 mg, 10 mol %), DABCO (89.6 mg, 2.0 equiv) were added to a 20 mL Schlenk tube and the tube was purged with O_2 for three times, followed by addition of **2a** (132 μl, 0.60 mmol) and PhCl (4.0 mL). The formed mixture was stirred at 125 ºC under O_2 (1 atm.) for 4 h. The solution was then cooled to rt., diluted with ethyl acetate (15 mL), and evaporated under vaccum. The crude product was purified by column chromatography on silica gel (hexane : ethyl acetate = 10:1) to afford 4.6 mg (6%) of the product. Compared with the standard ^{1}H NMR spectrum of 3a, the integration of the peak at 7.97 ppm was 2.84 instead of 2.00, at 7.48-7.43 ppm was 2.94 instead of 2.00, at 7.40-7.34 ppm was 1.47 instead of 1.00, in 6.80 was 1.20 instead of 1.00.

$k_H/k_D = (2/0.84 + 2/0.94 + 1/0.47)/3 = (2.38 + 2.13 + 2.13)/3 = 2.21$

Meanwhile, the percentage of the deuterium incorporation at C-3 position could be calculated as follow:

$[(1 + 1/2.21) – 1.20]/(1 + 1/2.21) = 17\%$

This result indicated the protonation process in this transformation.

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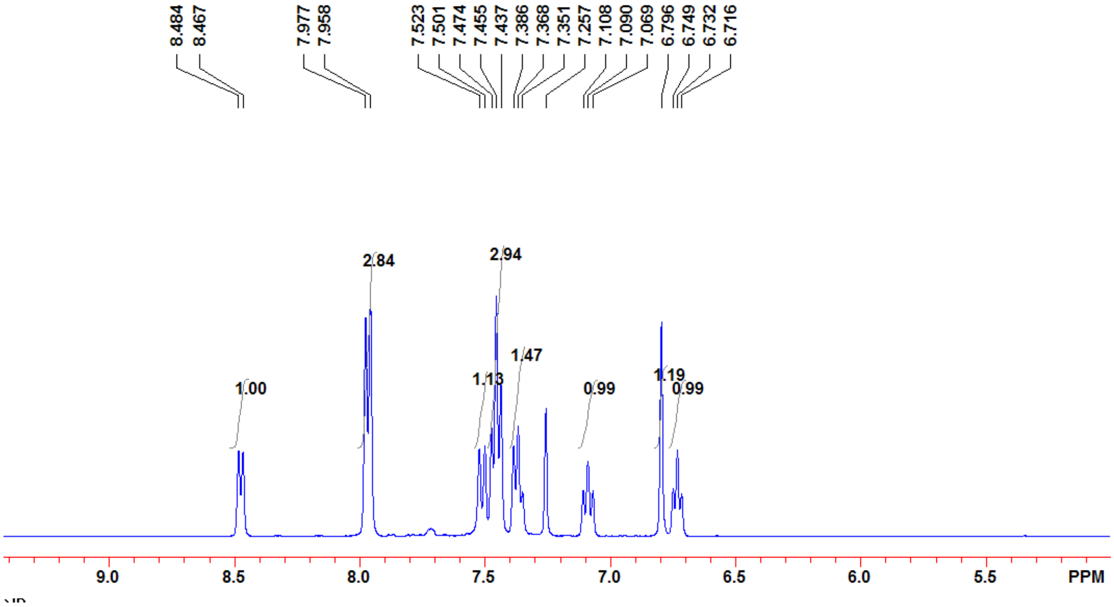
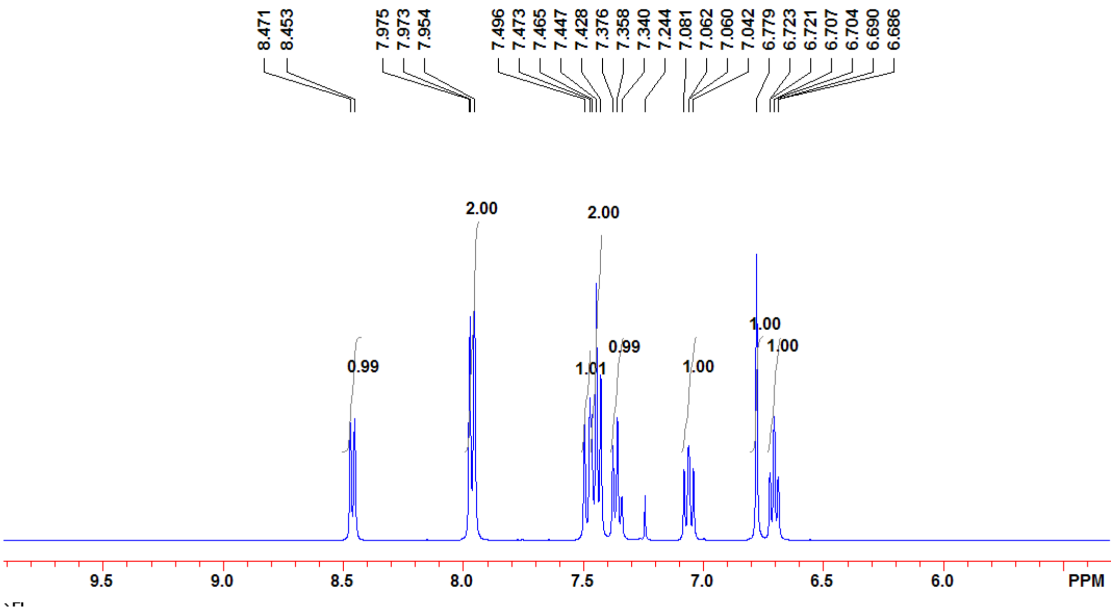
^{1}H NMR spectrum of the product



Standard ^{1}H NMR spectrum of **3a**



References

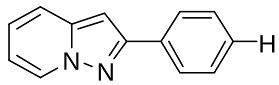
1 A. Balasubramanlan, J. M. McIntosh, V. Snieckus, *J. Org. Chem.* 1970, **35**, 433.

2 C. Y. Legault, A. B. Charette, *J. Org. Chem.* 2003, **68**, 7119.

3 (a) J. J. Mousseau, A. Fortier, A. B. Charette, *Org. Lett.* 2010, **12**, 516; (b) J. J. Mousseau, J. A. Bull, C. L. Ladd, A. Fortier, D. S. Roman, A. B. Charette, *J. Org. Chem.* 2011, **76**, 8243; (c) Y. Miki, O. Tomii, H. Nakao, M. Kubo, H. Hachiken, S. Takemura, M. Ikeda, *J. Heterocyclic Chem.* 1988, **25**, 327; (d) K. Harju, I. Kylaenlahti, T. Paananen, M. Polamo, J. Nielsen, J. Yli-Kauhaluoma, *J. Comb. Chem.* 2006, **8**, 344; (e) T. Tsuchiya, H. Sashida, *J. Chem. Soc., Chem. Commun.* 1980, 1109.

4 W. Chai, J. G. Breitenbucher, A. Kwok, X. Li, V. Wong, N. I. Carruthers, T. W. Lovenberg, C. Mazur, S. J. Wilson, F. U. Axe, T. K. Jones, *Bioorg. Med. Chem. Lett.* 2003, **13**, 1767.

5 J. J. Mousseau, J. A. Bull, A. B. Charette, *Angew. Chem. Int. Ed.* 2010, **49**, 1115.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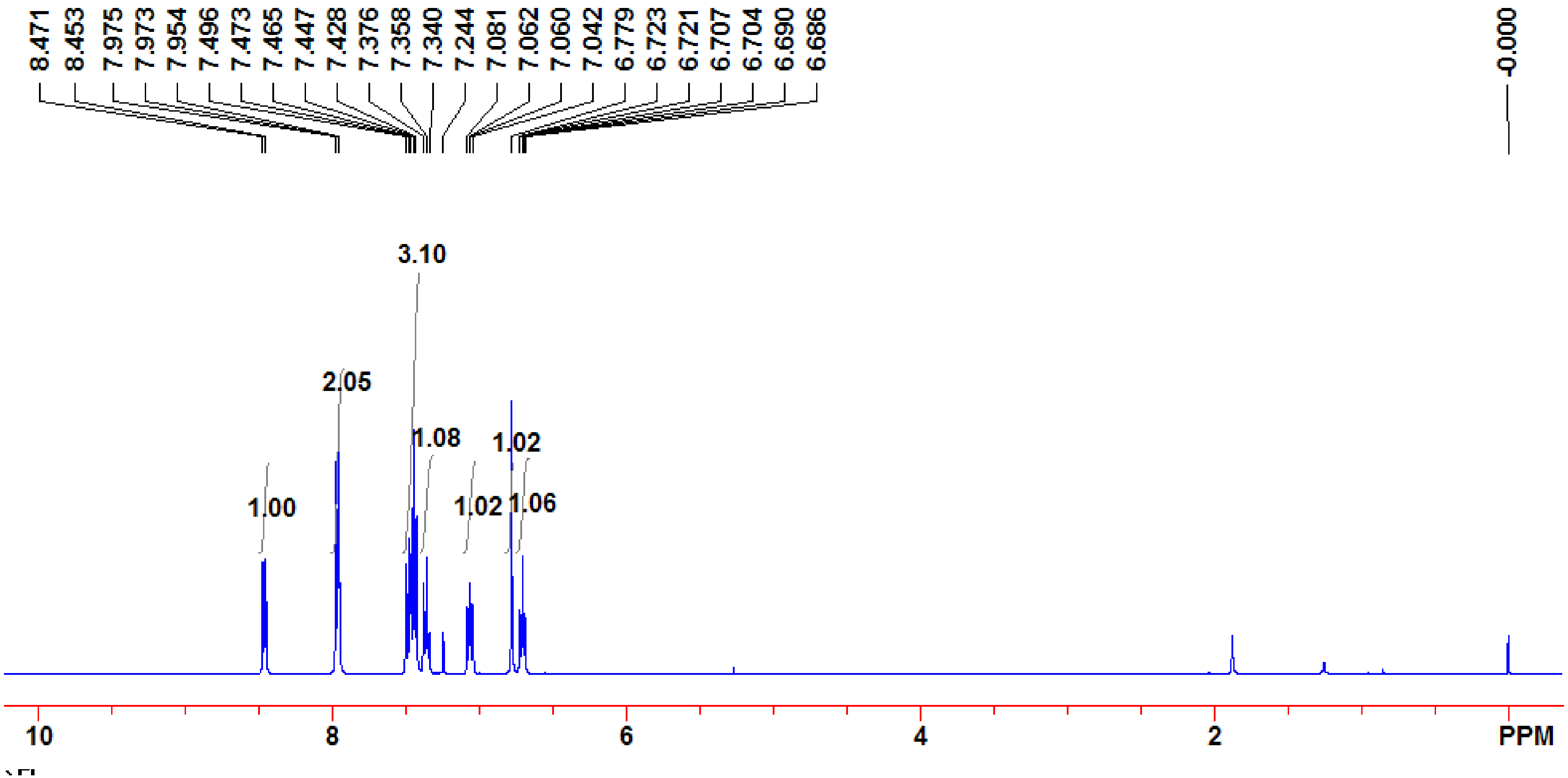
3a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7.060
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6.721
6.707
6.704
6.690
6.686
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2.05
1.08
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1.06
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6
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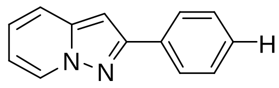
2
PPM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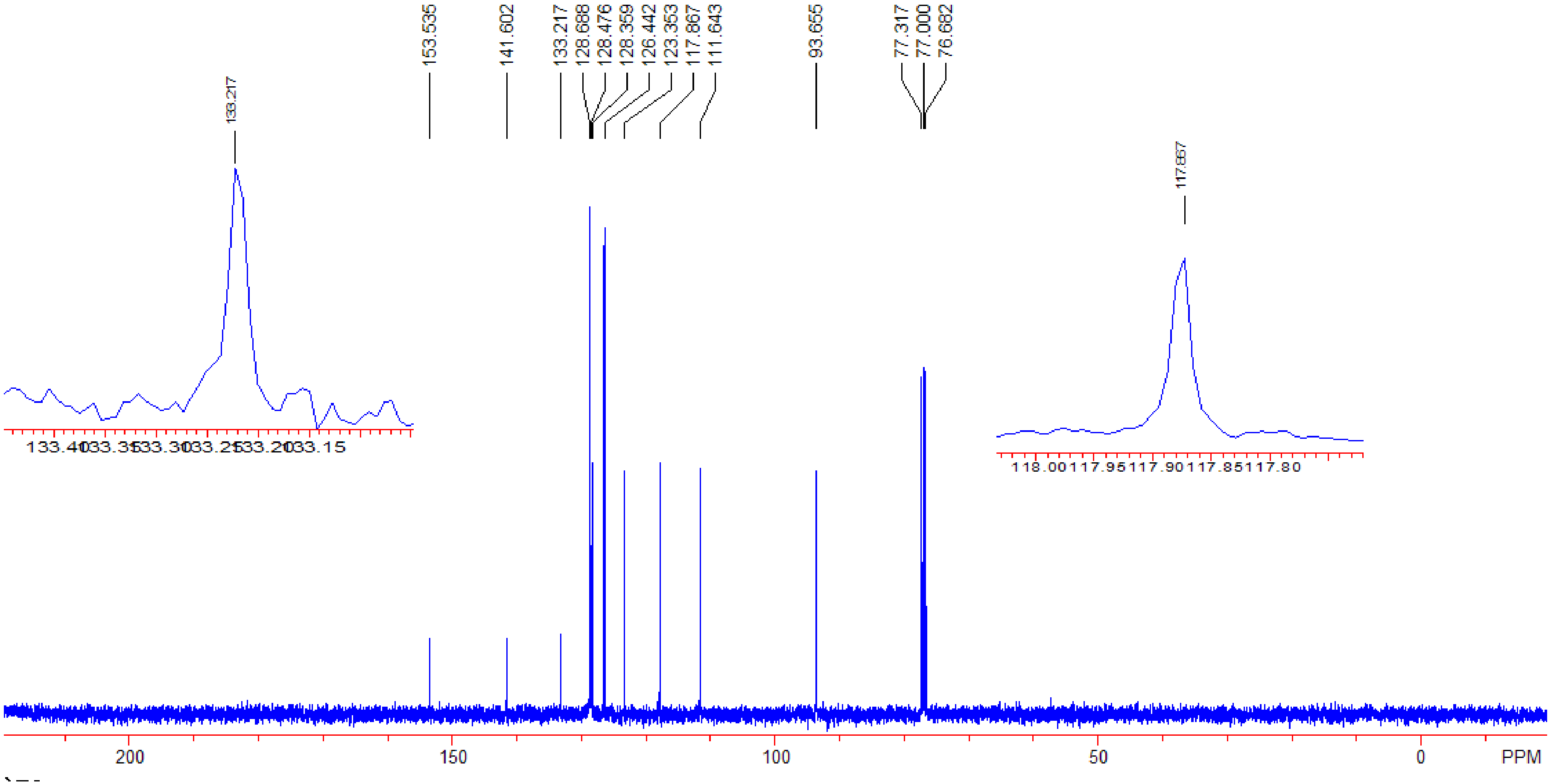
N
H

3a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PPM

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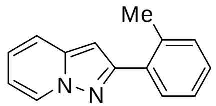

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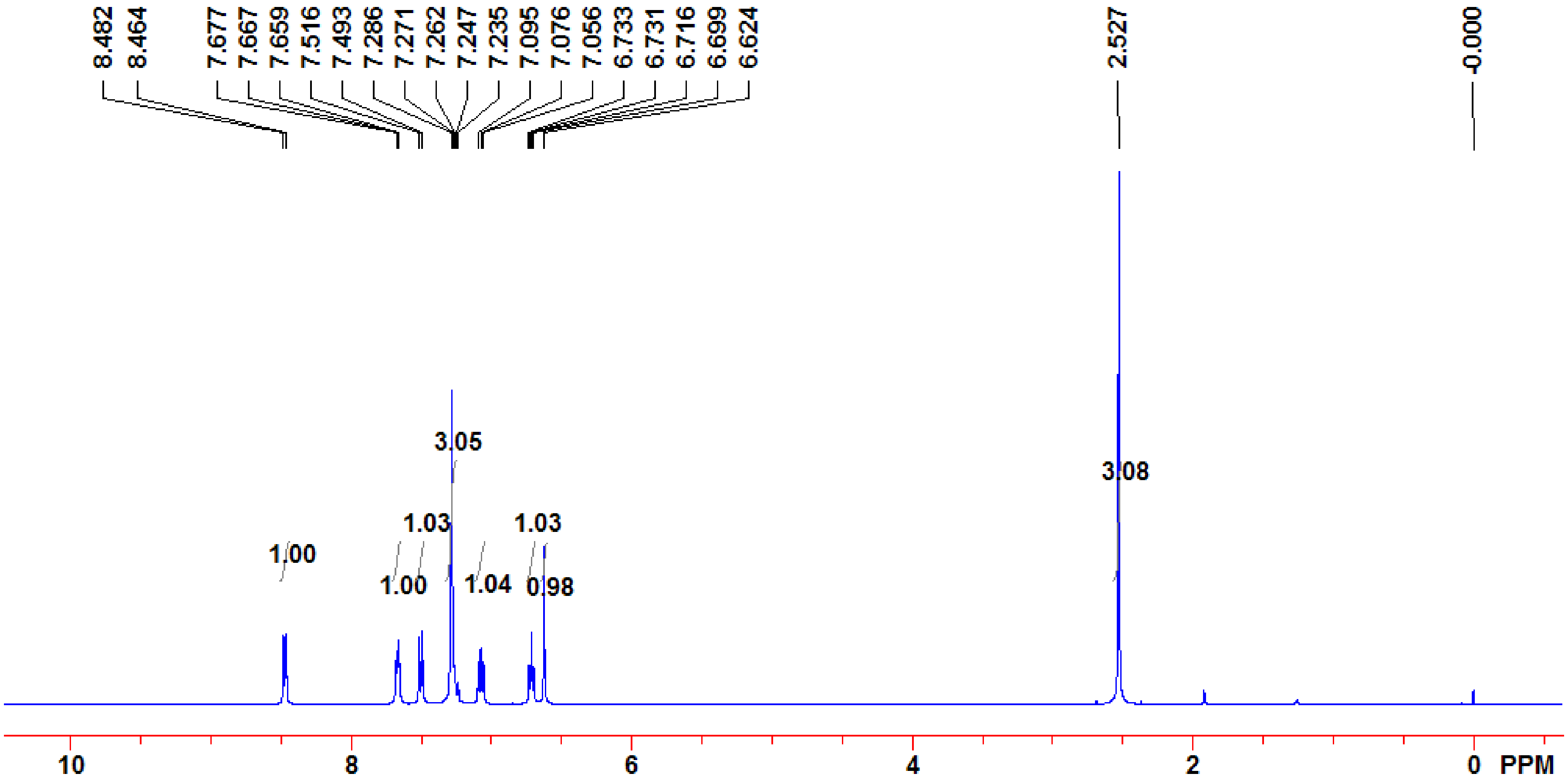

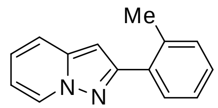
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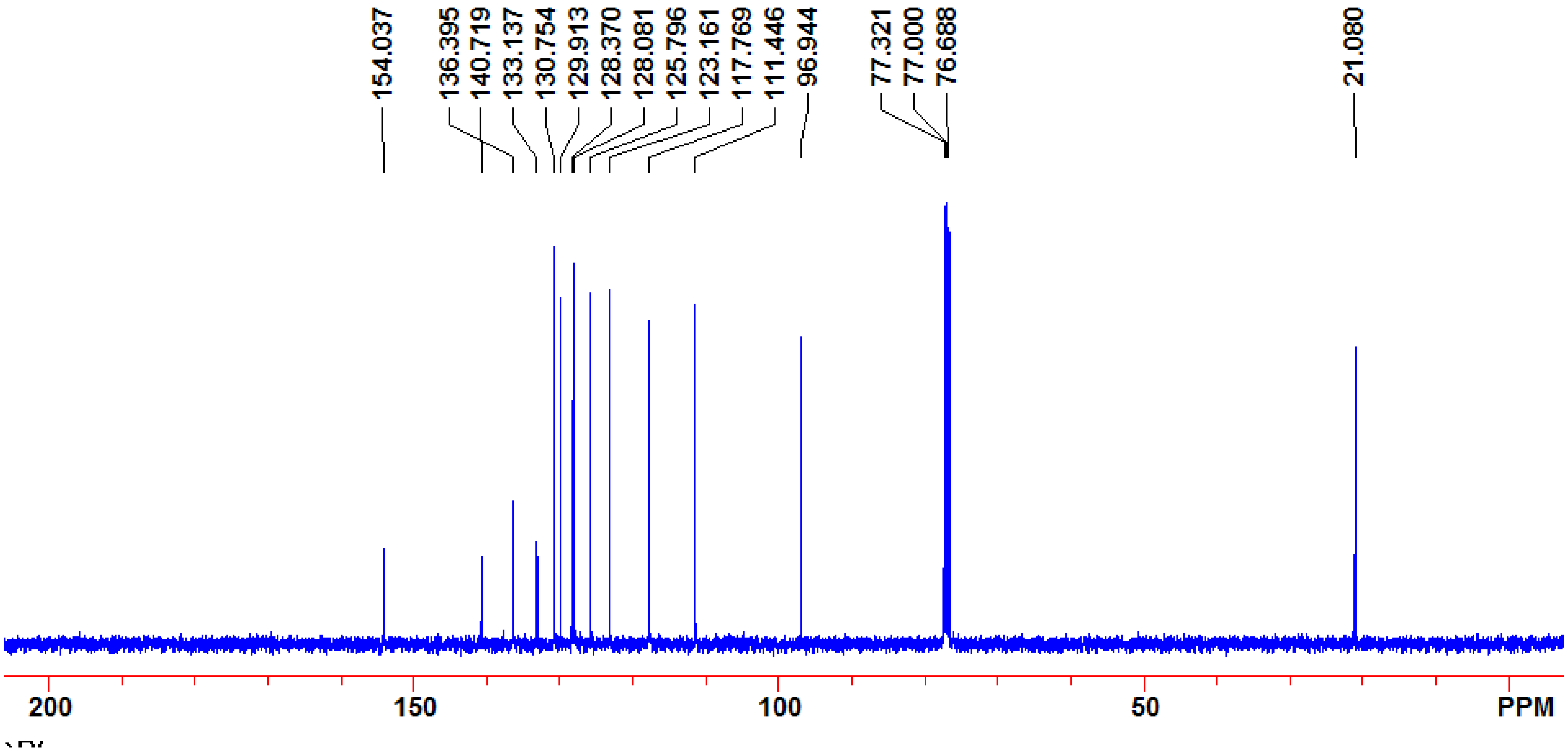
3b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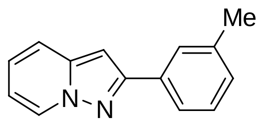
PPM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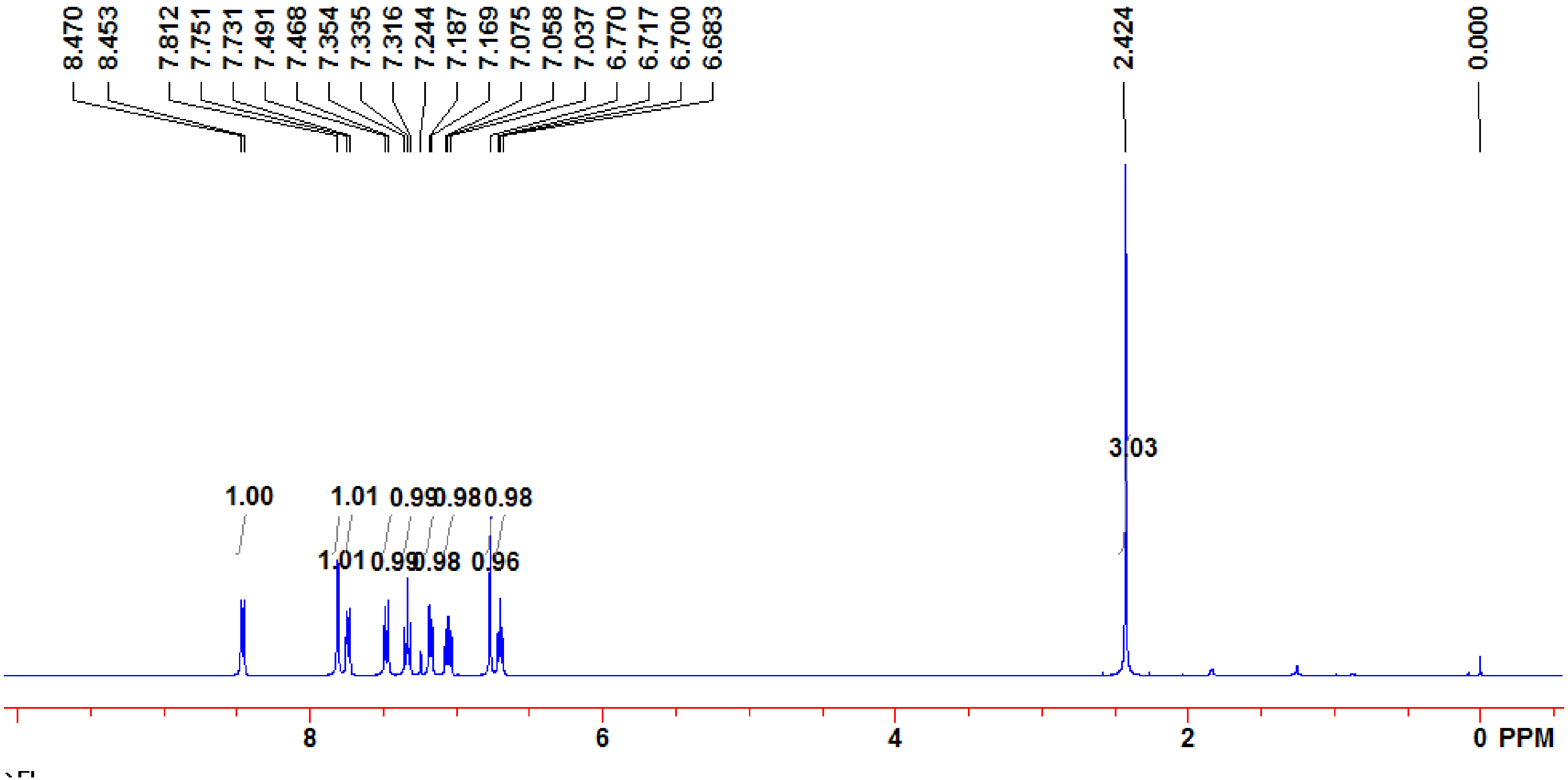
3c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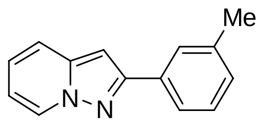
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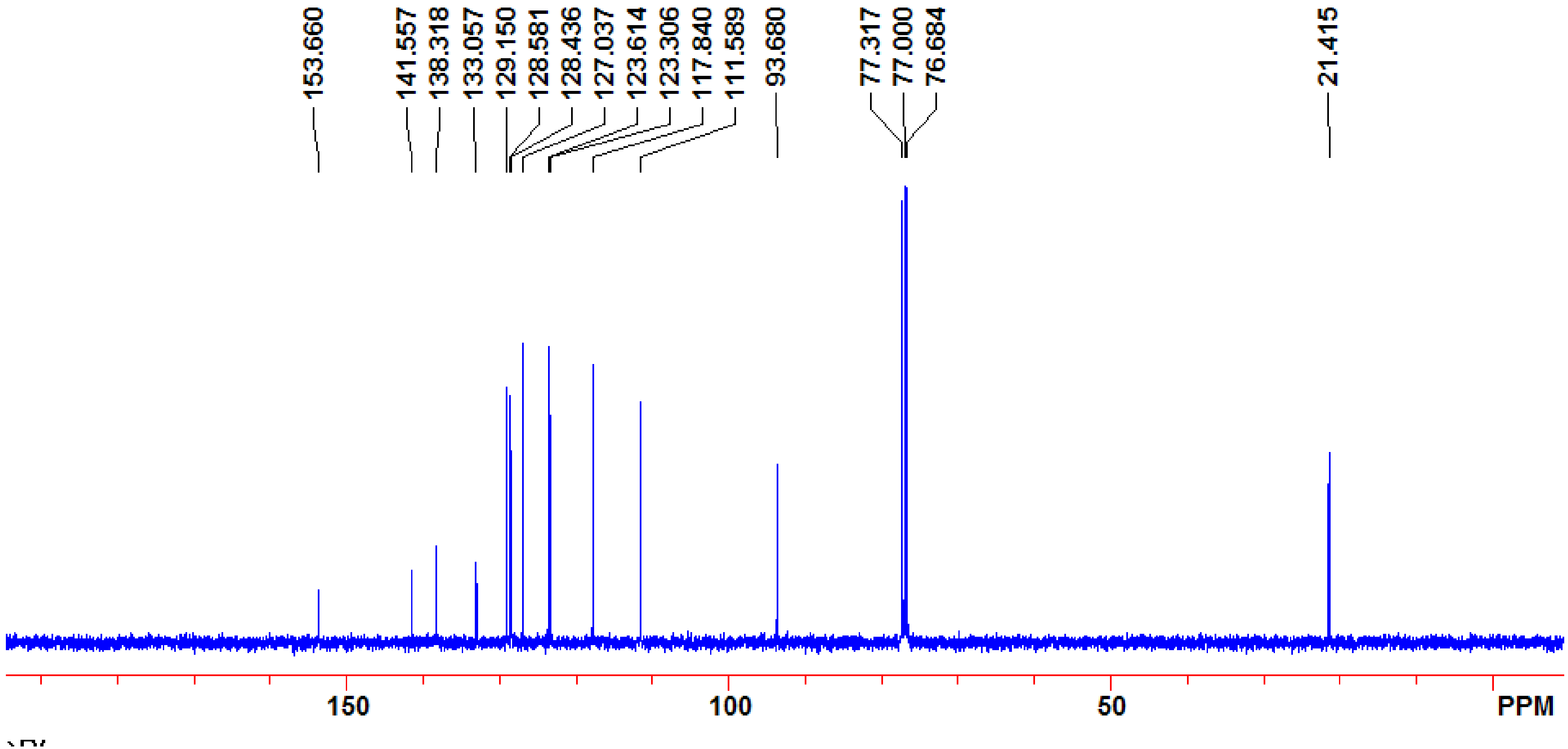
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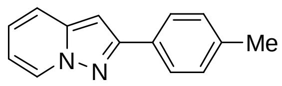
PPM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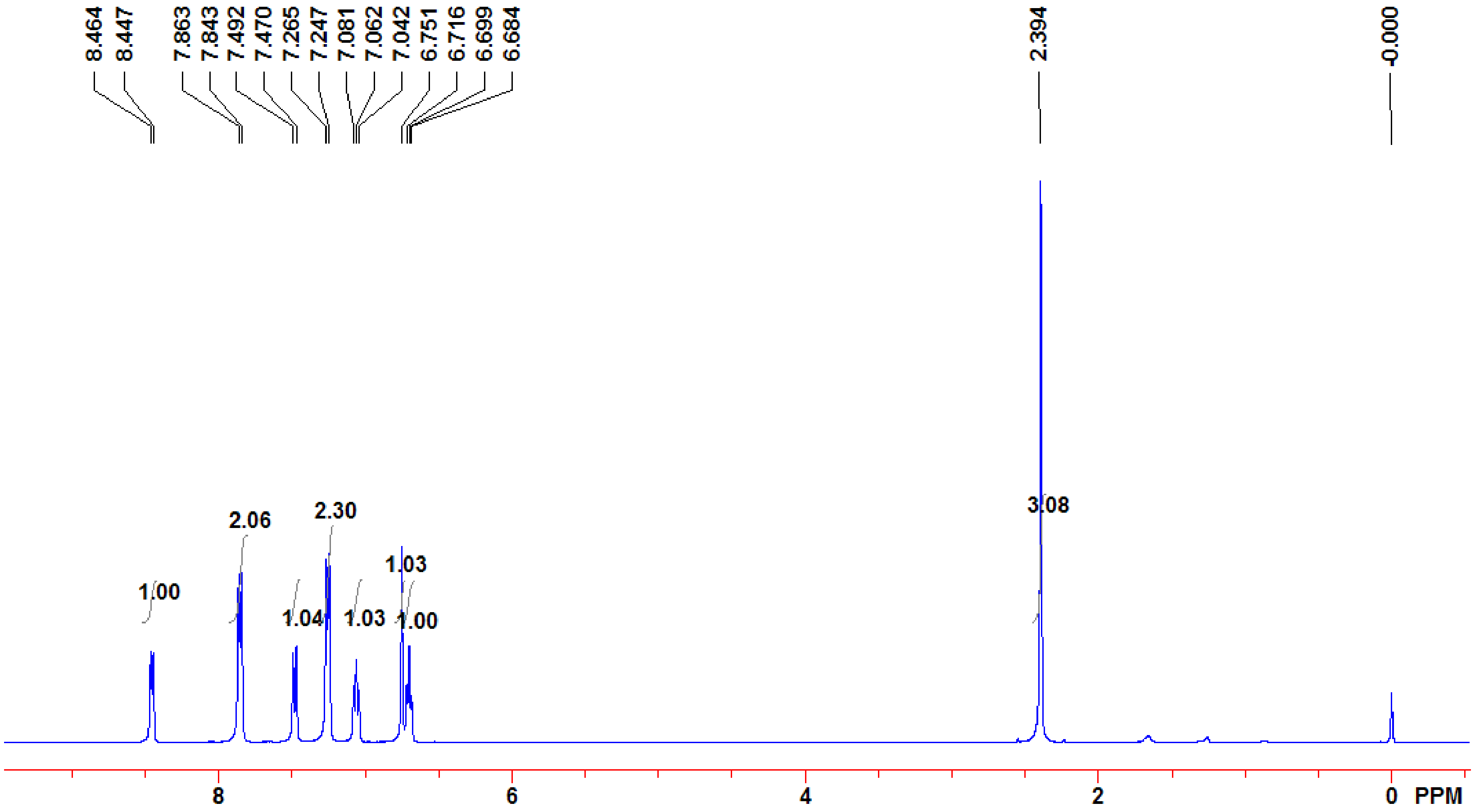
3d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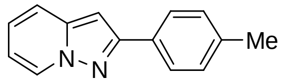
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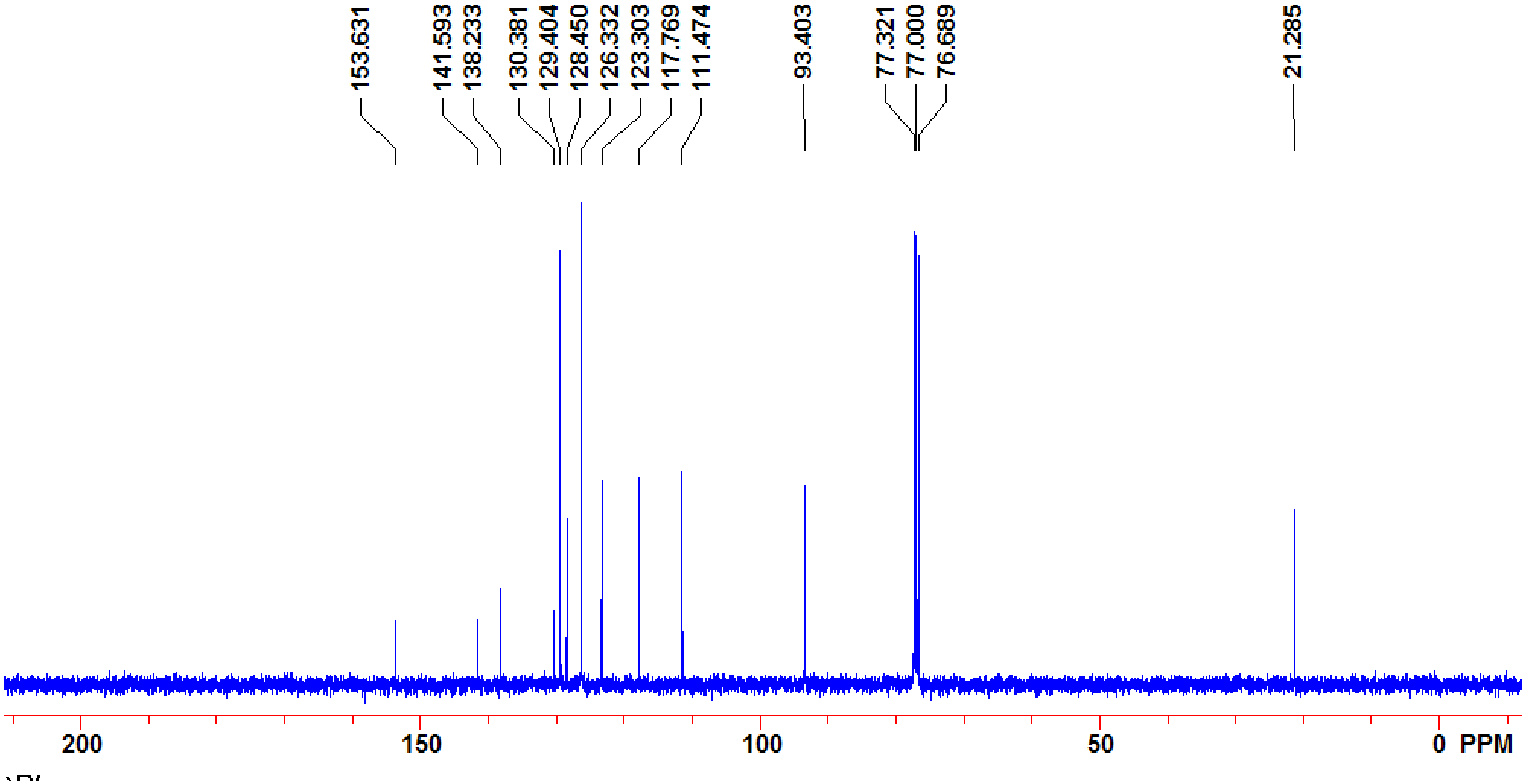
3d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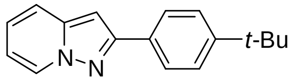
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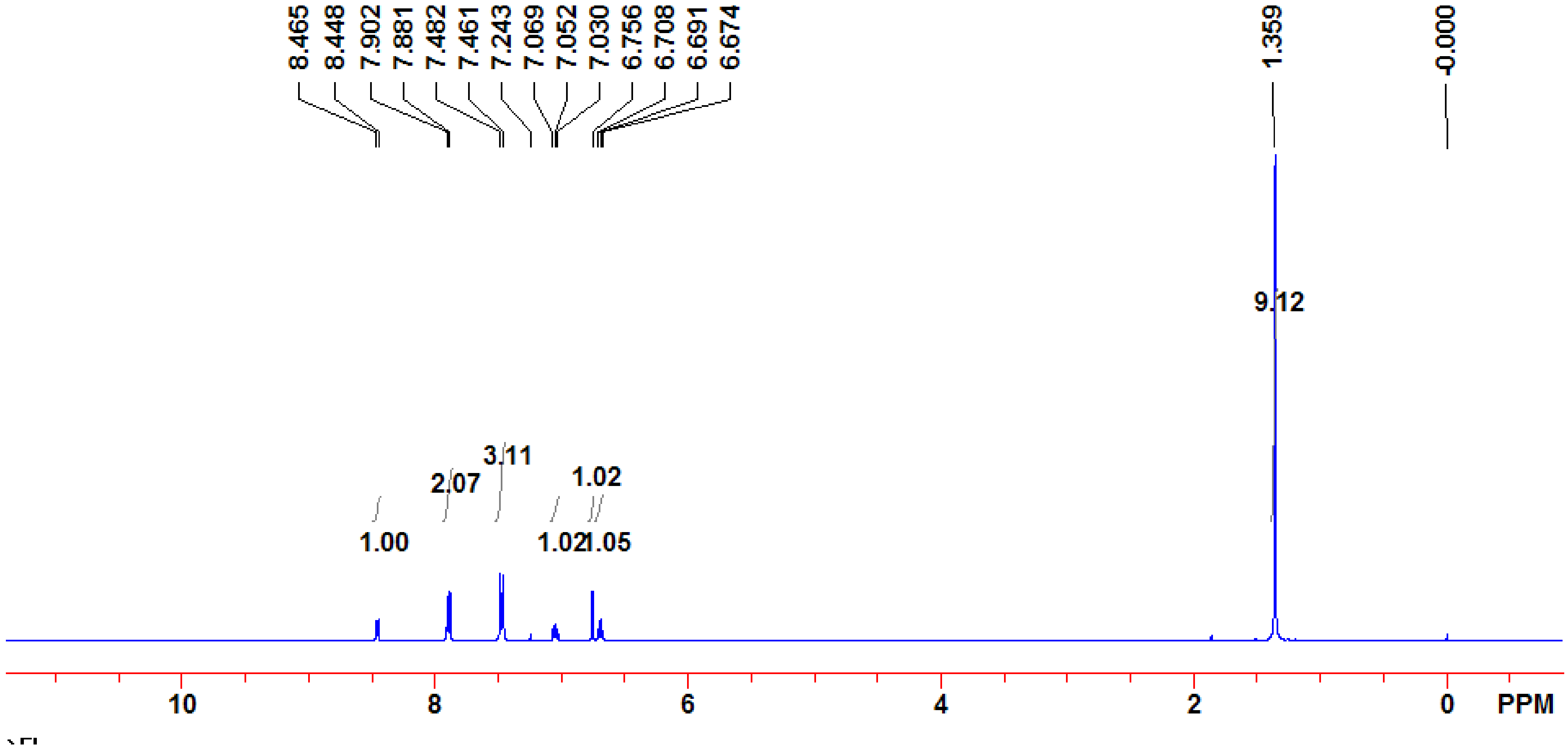
N
t-Bu

3e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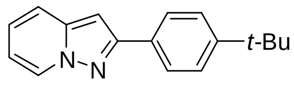

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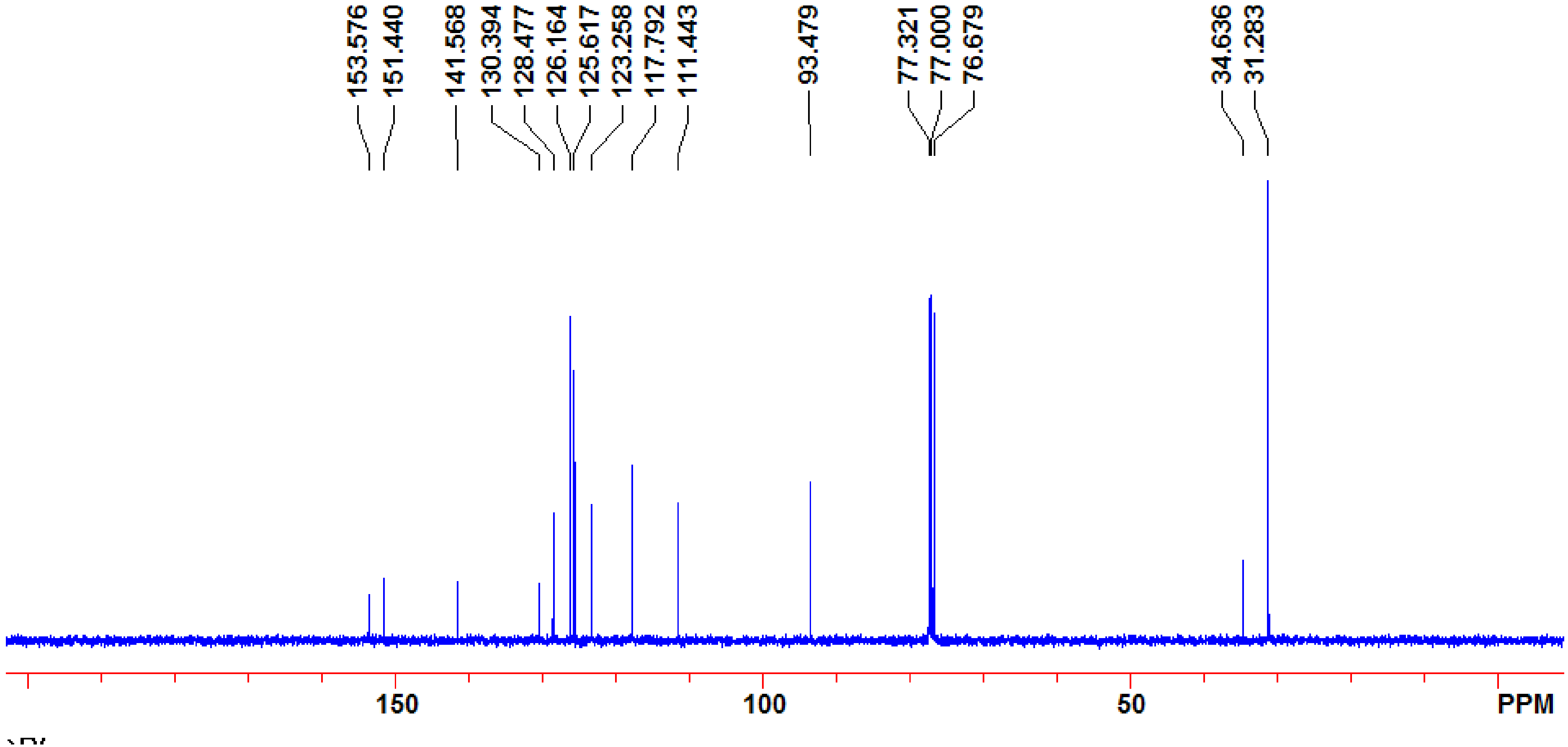
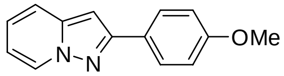


Electronic Supplementary Material (ESI) for Chemical Communications



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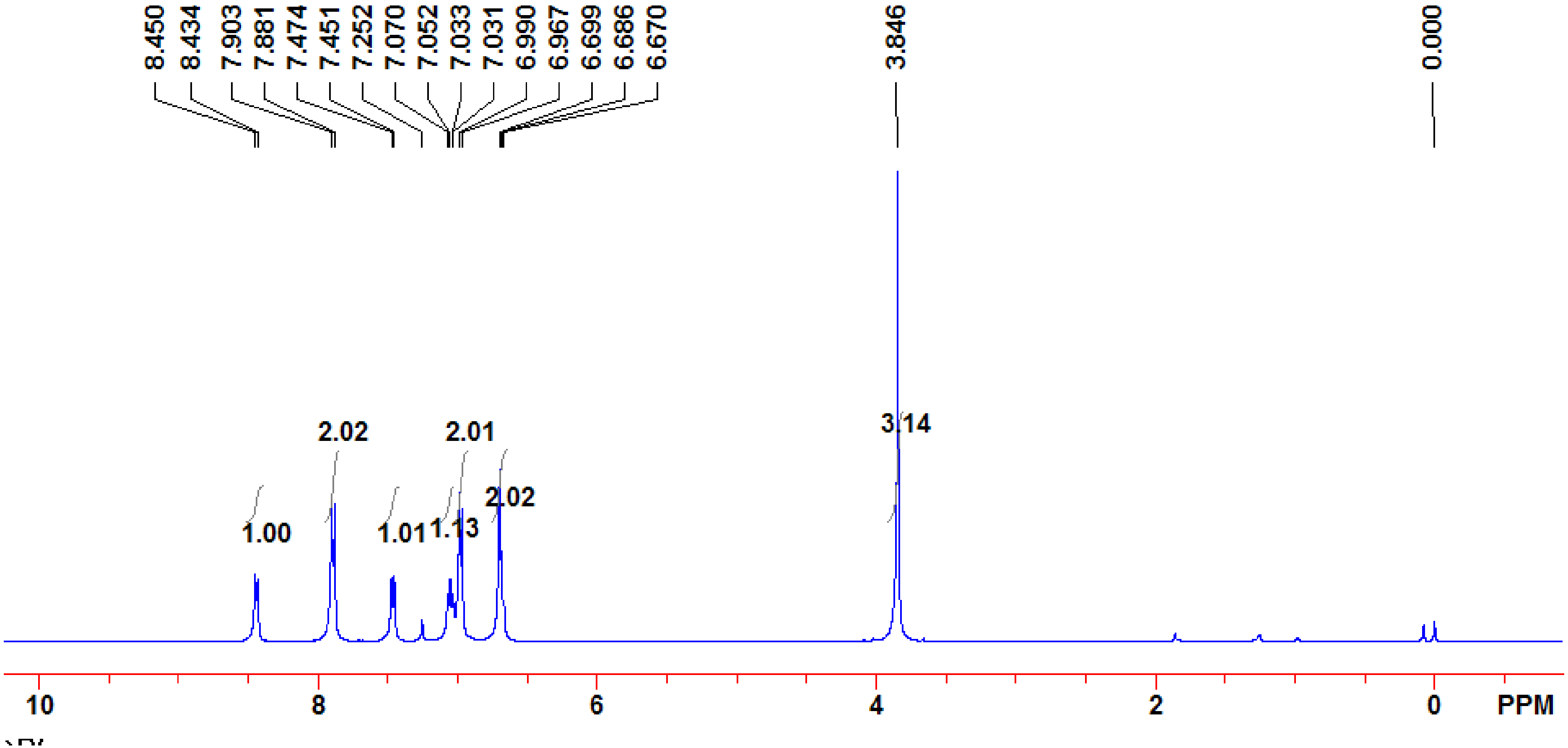

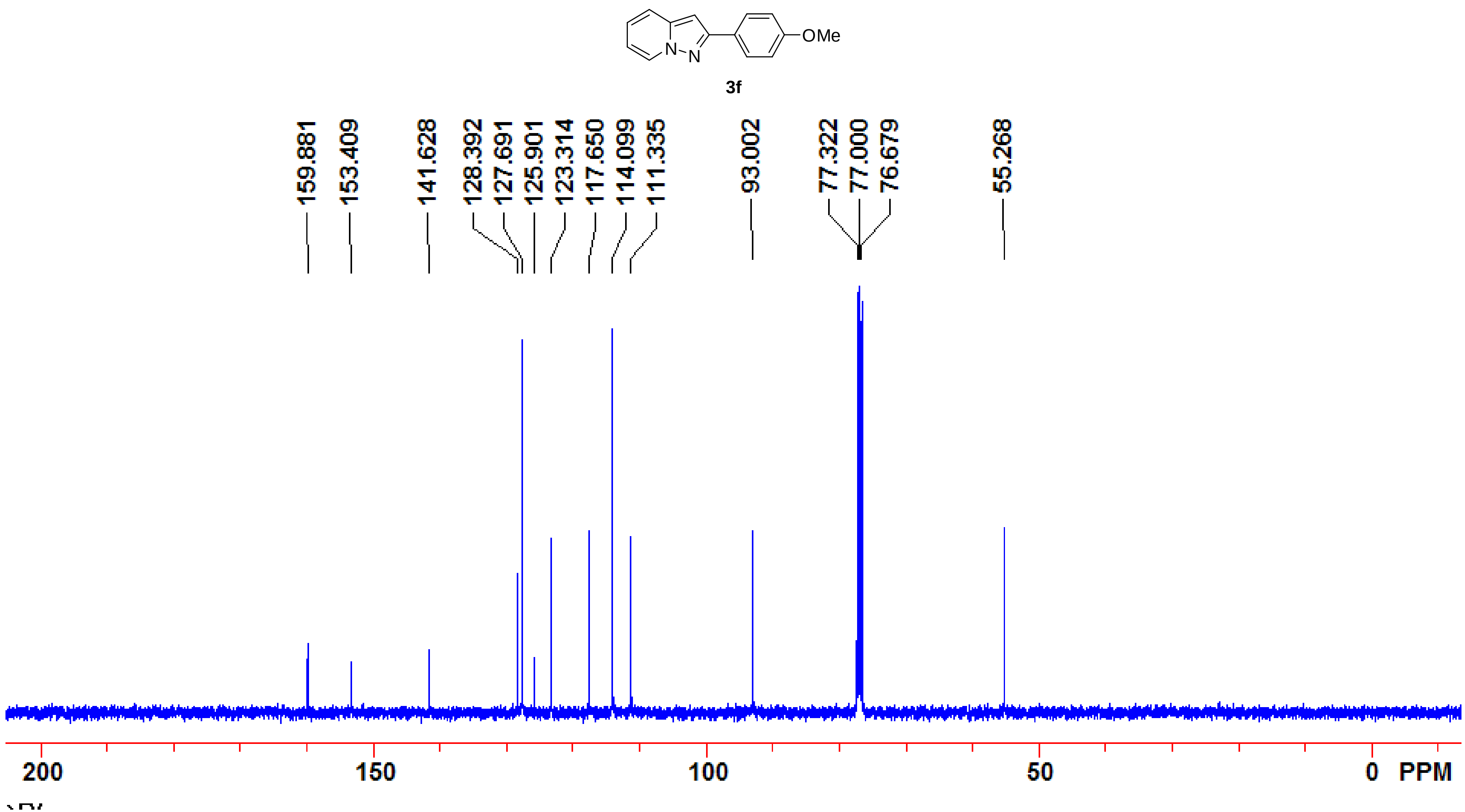
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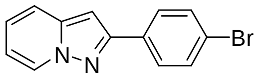
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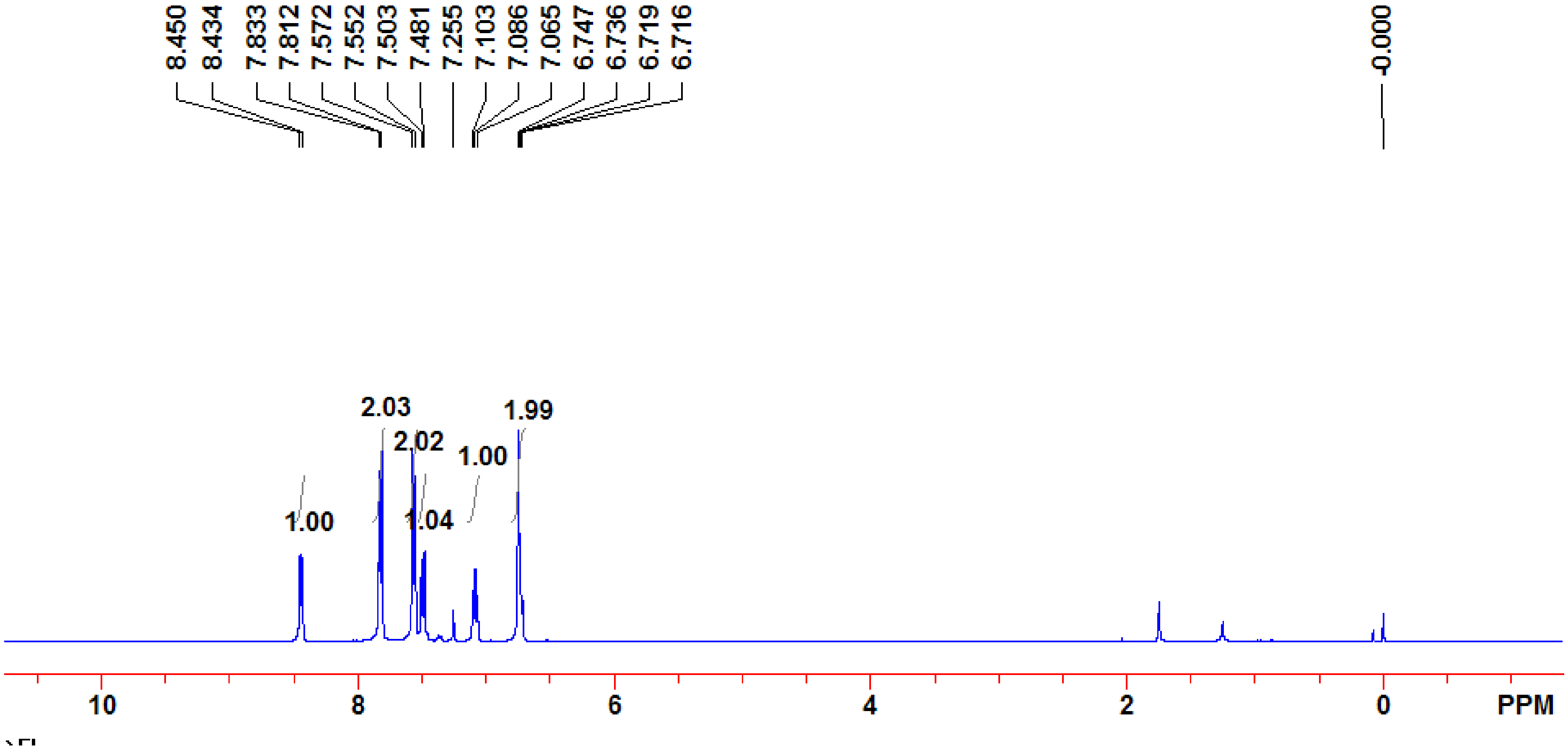
Br

3g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8.434
7.833
7.812
7.572
7.552
7.503
7.481
7.255
7.103
7.086
7.065
6.747
6.736
6.719
6.716
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2.02
1.00
1.99
1.00
1.04
10
8
6
4
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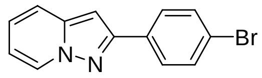
0
PPM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N
N

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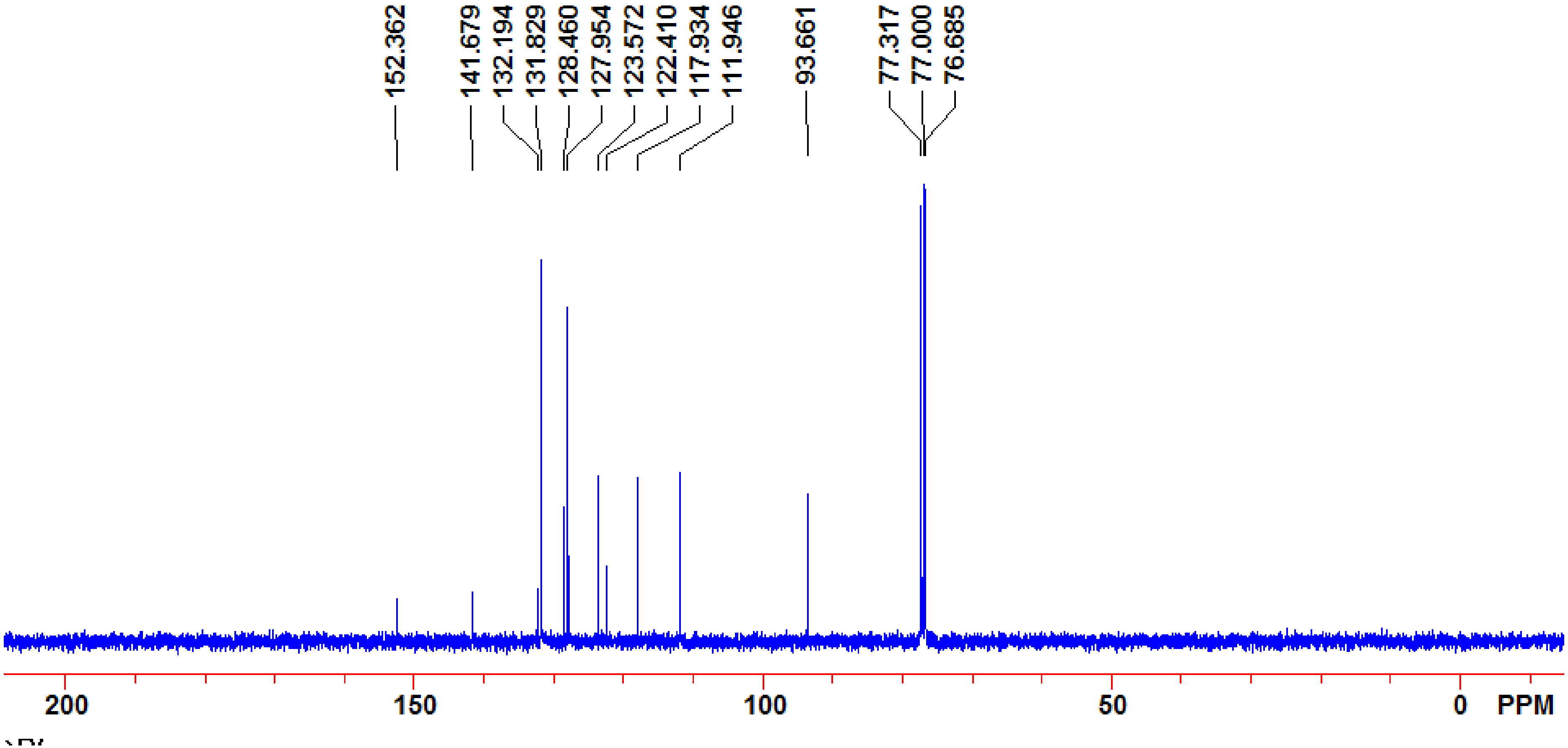
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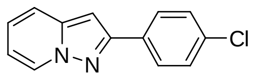
141.679
132.194
131.829
128.460
127.954
123.572
122.410
117.934
111.946
93.661
77.317
77.000
76.685
200
150
100
50
0
PPM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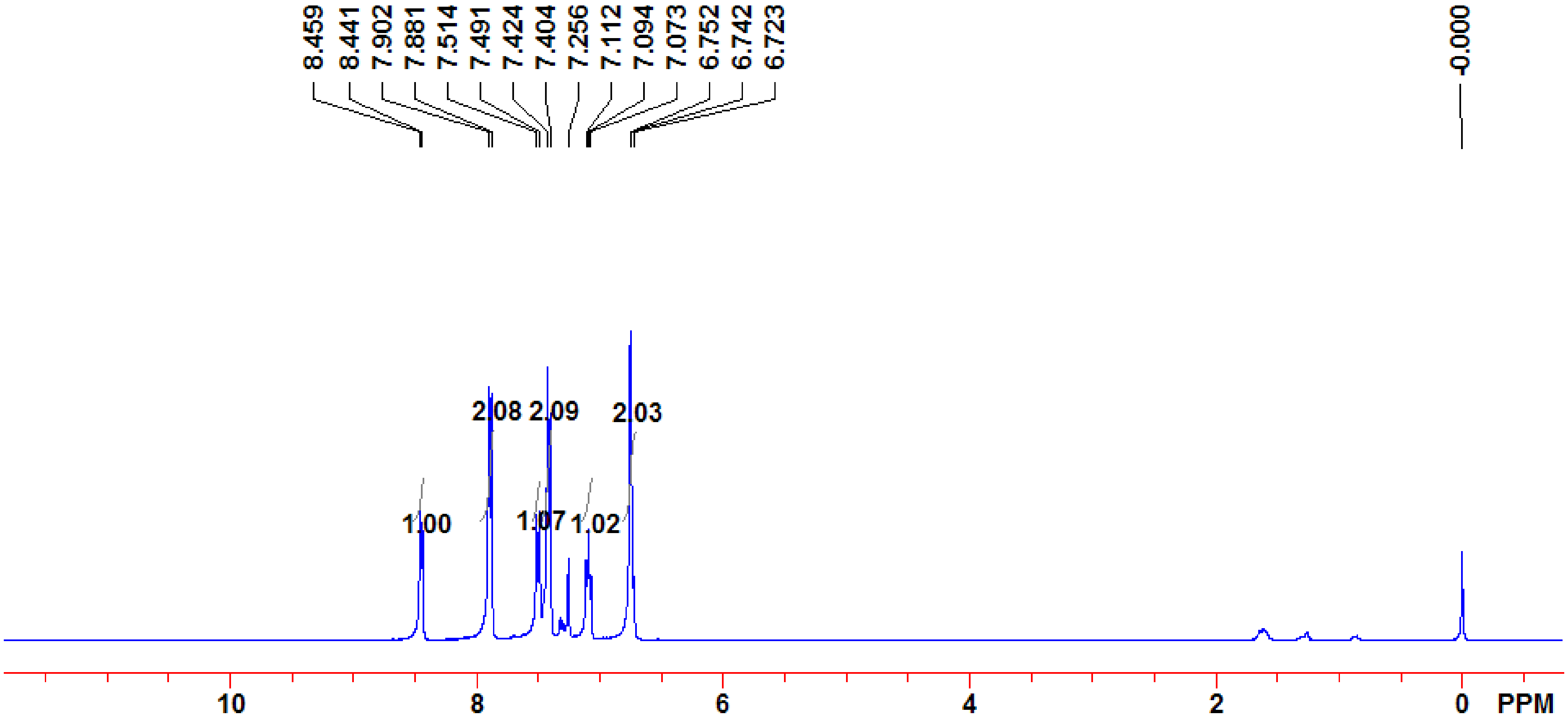
N
Cl

3h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8.441
7.902
7.881
7.514
7.491
7.424
7.404
7.256
7.112
7.094
7.073
6.752
6.742
6.723
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2.09
2.03
1.00
1.07
1.02
10
8
6
4
2
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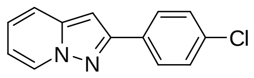
PPM



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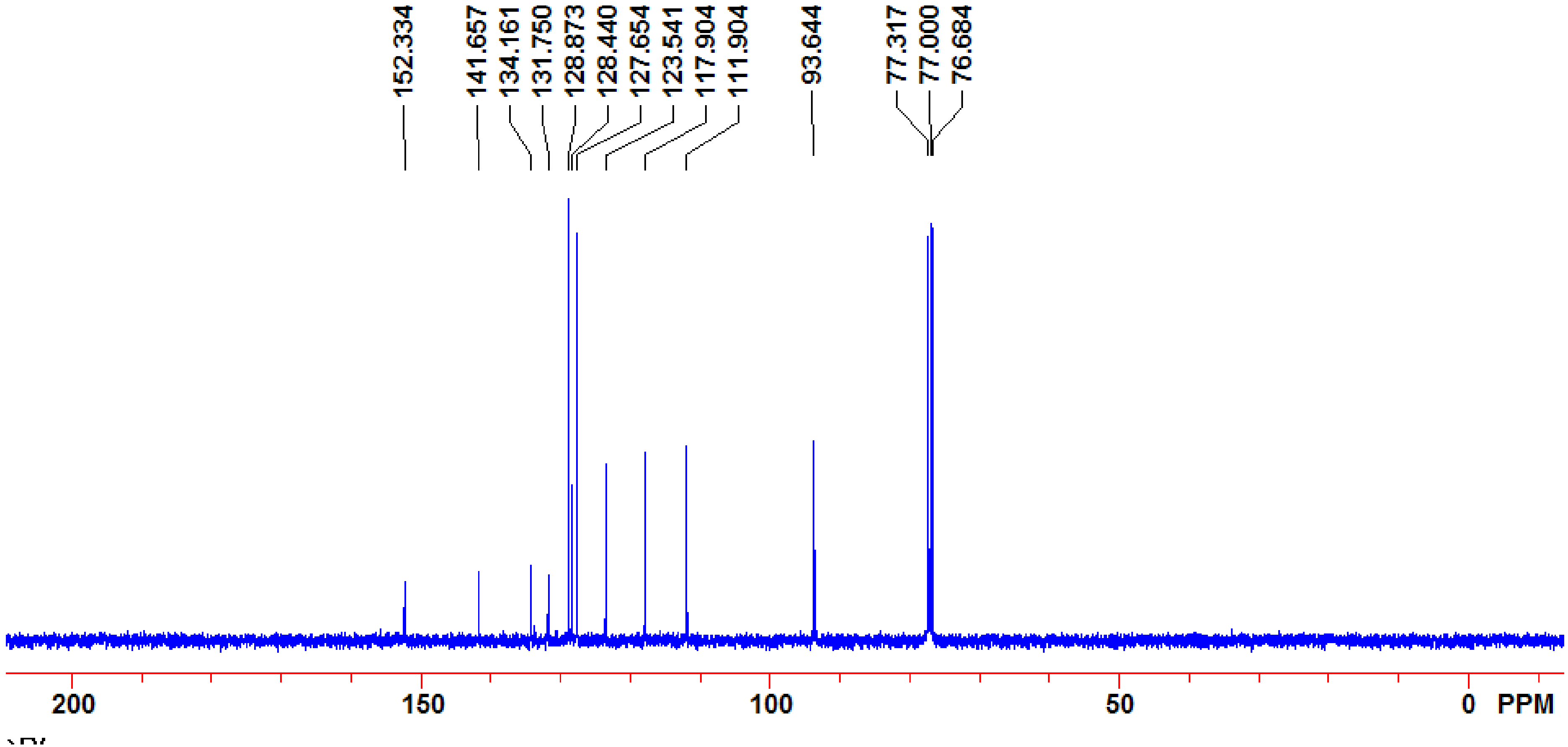
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76.684
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150
100
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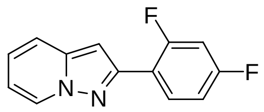
PPM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F
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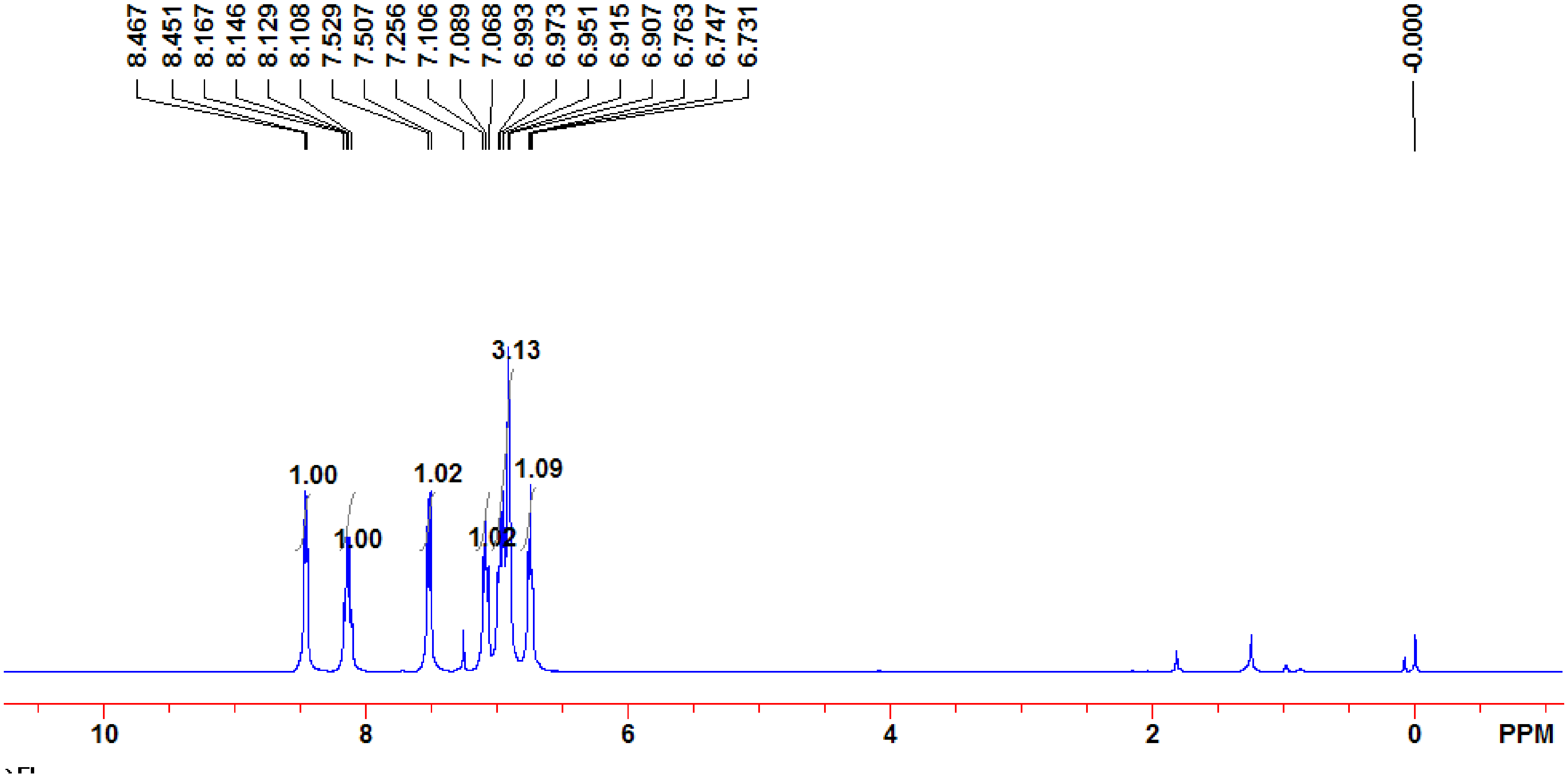
N

3i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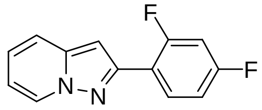
8.451
8.167
8.146
8.129
8.108
7.529
7.507
7.256
7.106
7.089
7.068
6.993
6.973
6.951
6.915
6.907
6.763
6.747
6.731
-0.000
3.13
1.00
1.02
1.09
1.00
1.02
10
8
6
4
2
0
PPM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F
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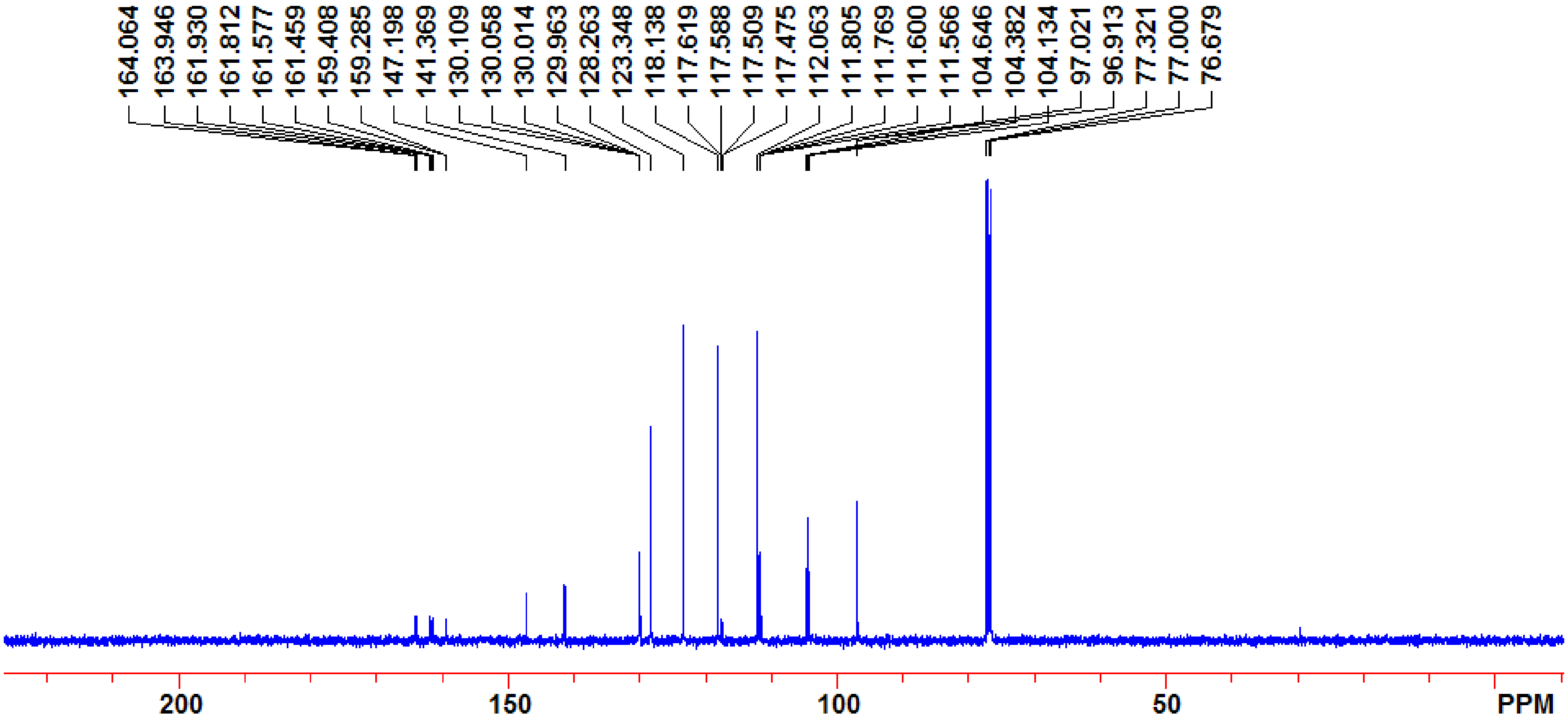
3i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161.930
161.812
161.577
161.459
159.408
159.285
147.198
141.369
130.109
130.058
130.014
129.963
128.263
123.348
118.138
117.619
117.588
117.509
117.475
112.063
111.805
111.769
111.600
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104.134
97.021
96.913
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77.000
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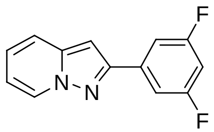
150
100
50
PPM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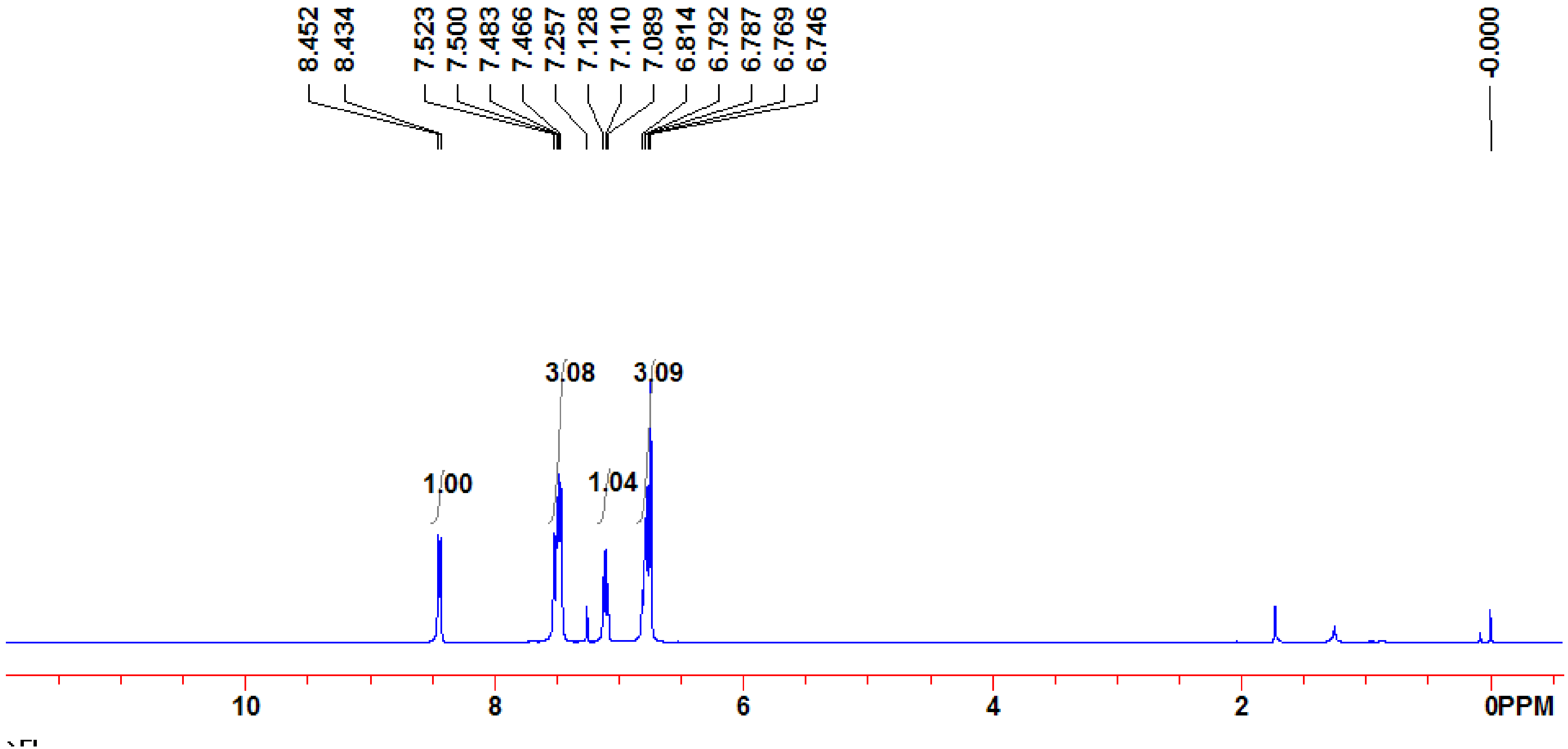
N
N
F

3j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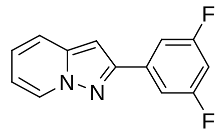
8.434
7.523
7.500
7.483
7.466
7.257
7.128
7.110
7.089
6.814
6.792
6.787
6.769
6.746
-0.000
1.00
3.08
1.04
3.09
10
8
6
4
2
0PPM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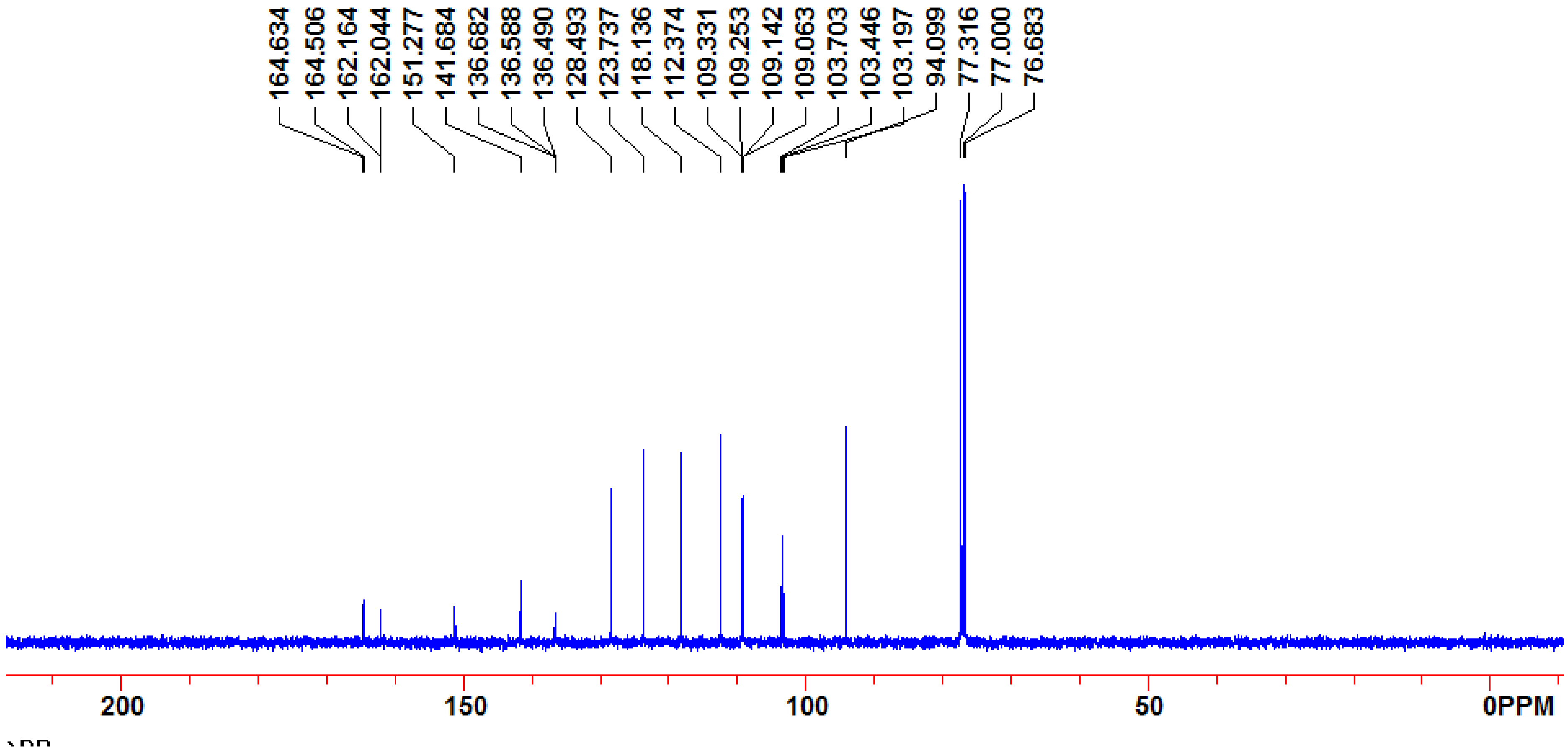
N
F

3j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162.164
162.044
151.277
141.684
136.682
136.588
136.490
128.493
123.737
118.136
112.374
109.331
109.253
109.142
109.063
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103.446
103.197
94.099
77.316
77.000
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200
150
100
50
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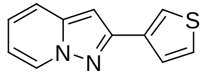
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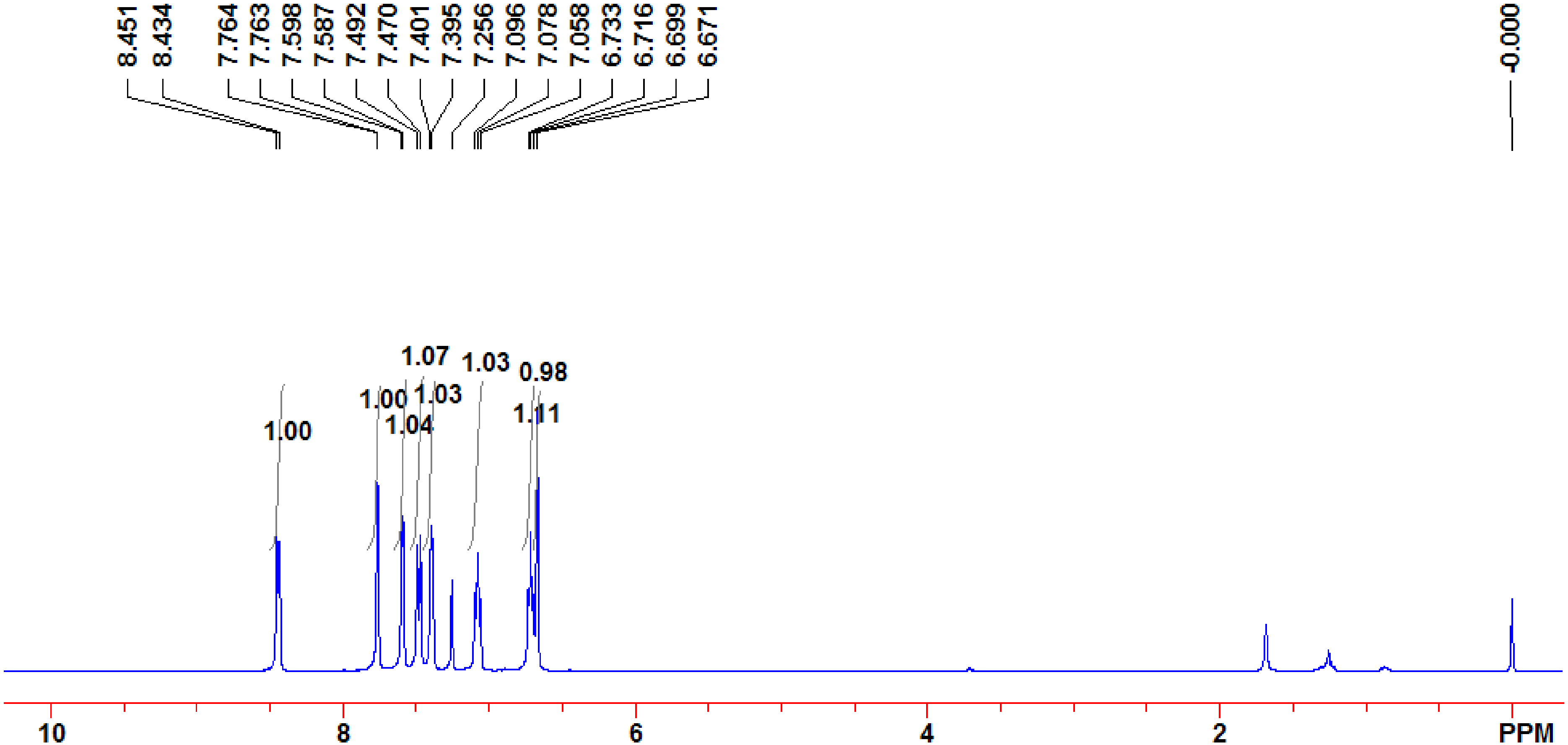
S

3l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8.434
7.764
7.763
7.598
7.587
7.492
7.470
7.401
7.395
7.256
7.096
7.078
7.058
6.733
6.716
6.699
6.671
-0.000
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1.00
1.04
1.07
1.03
1.03
0.98
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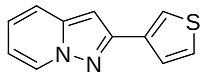
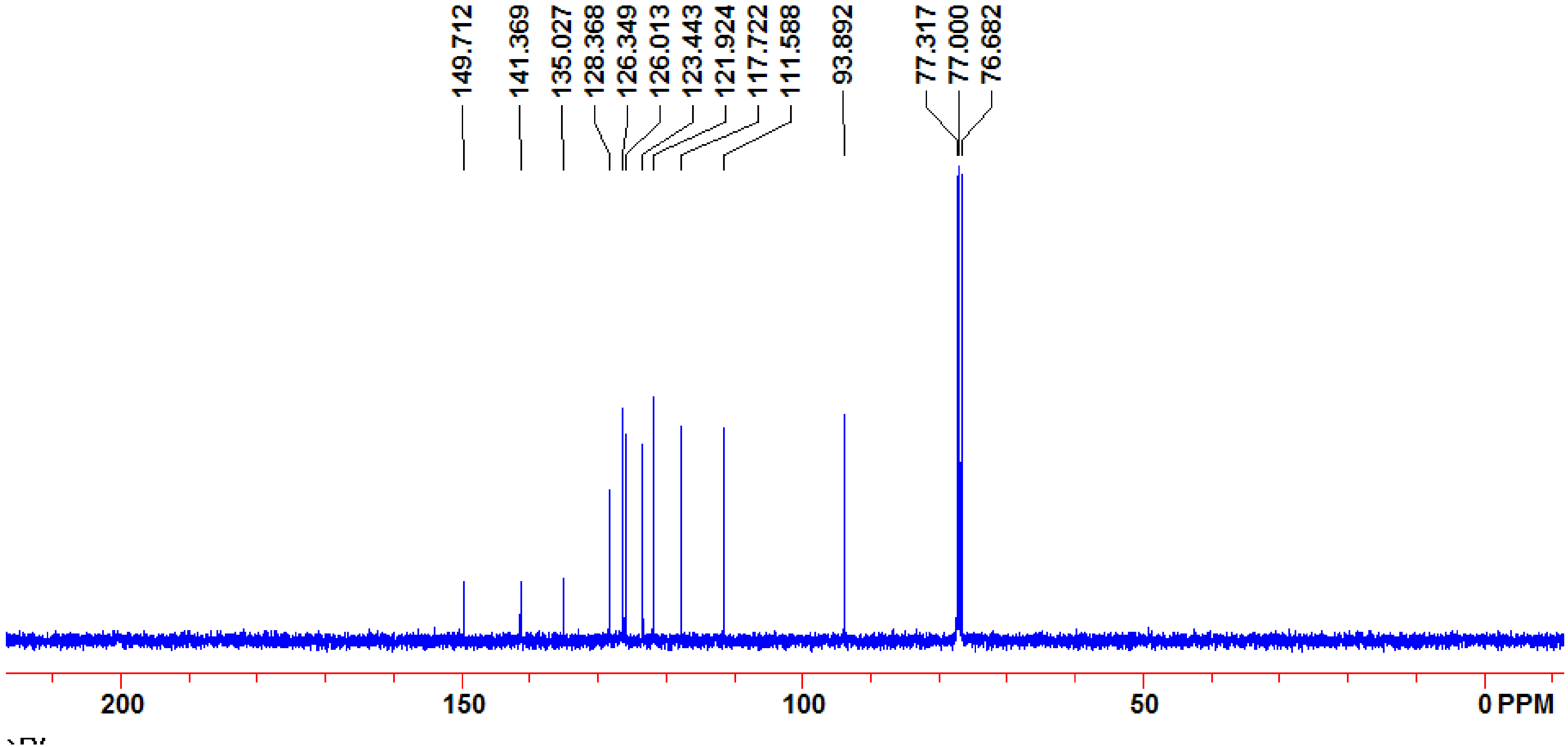
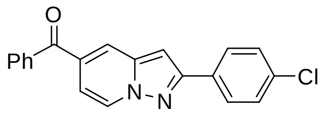
8
6
4
2
PPM


S
N
N

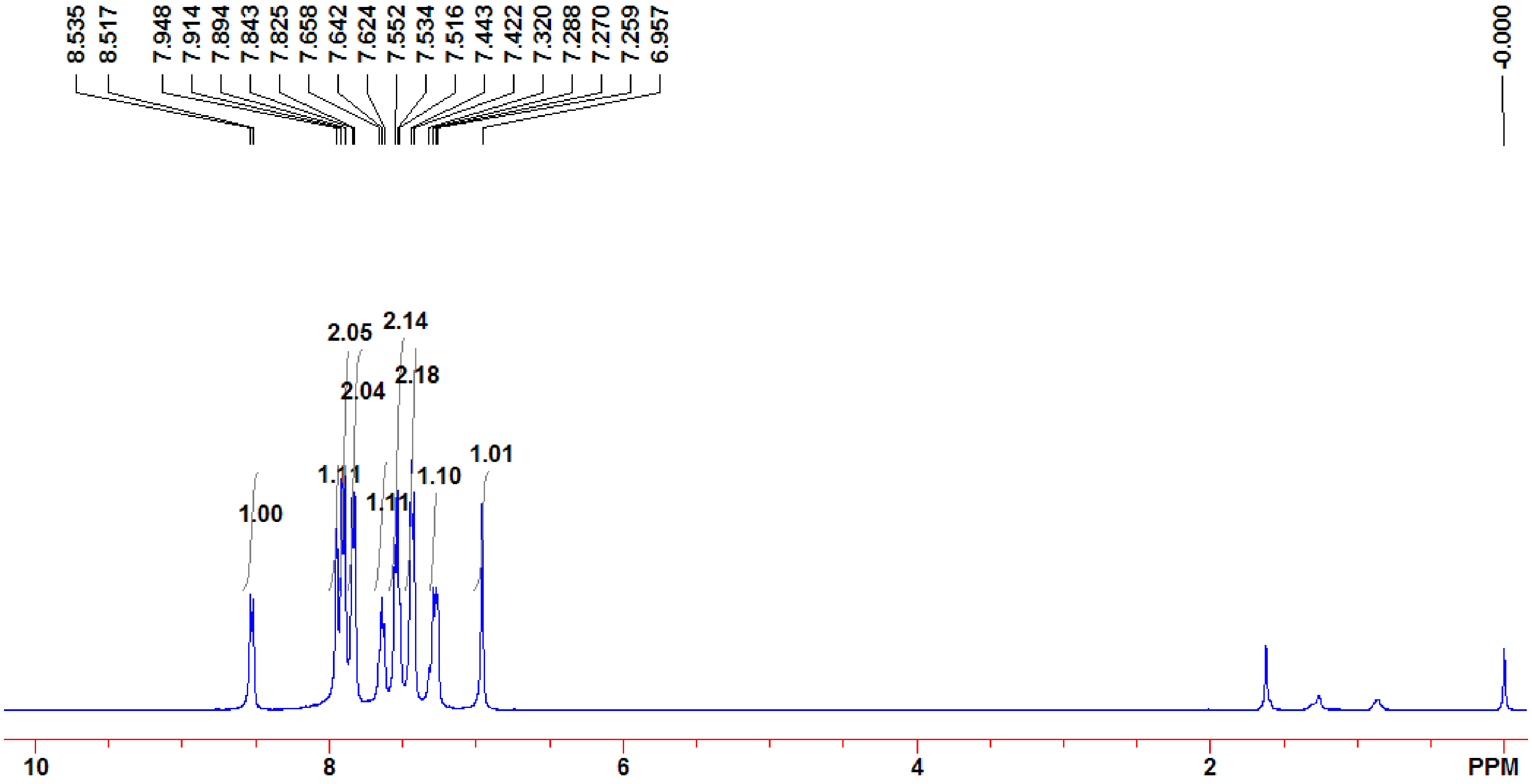
3l

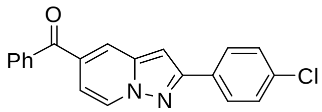

149.712
141.369
135.027
128.368
126.349
126.013
123.443
121.924
117.722
111.588
93.892
77.317
77.000
76.682
200
150
100
50
0 PPM

Electronic Supplementary Material (ESI) for Chemical Communications

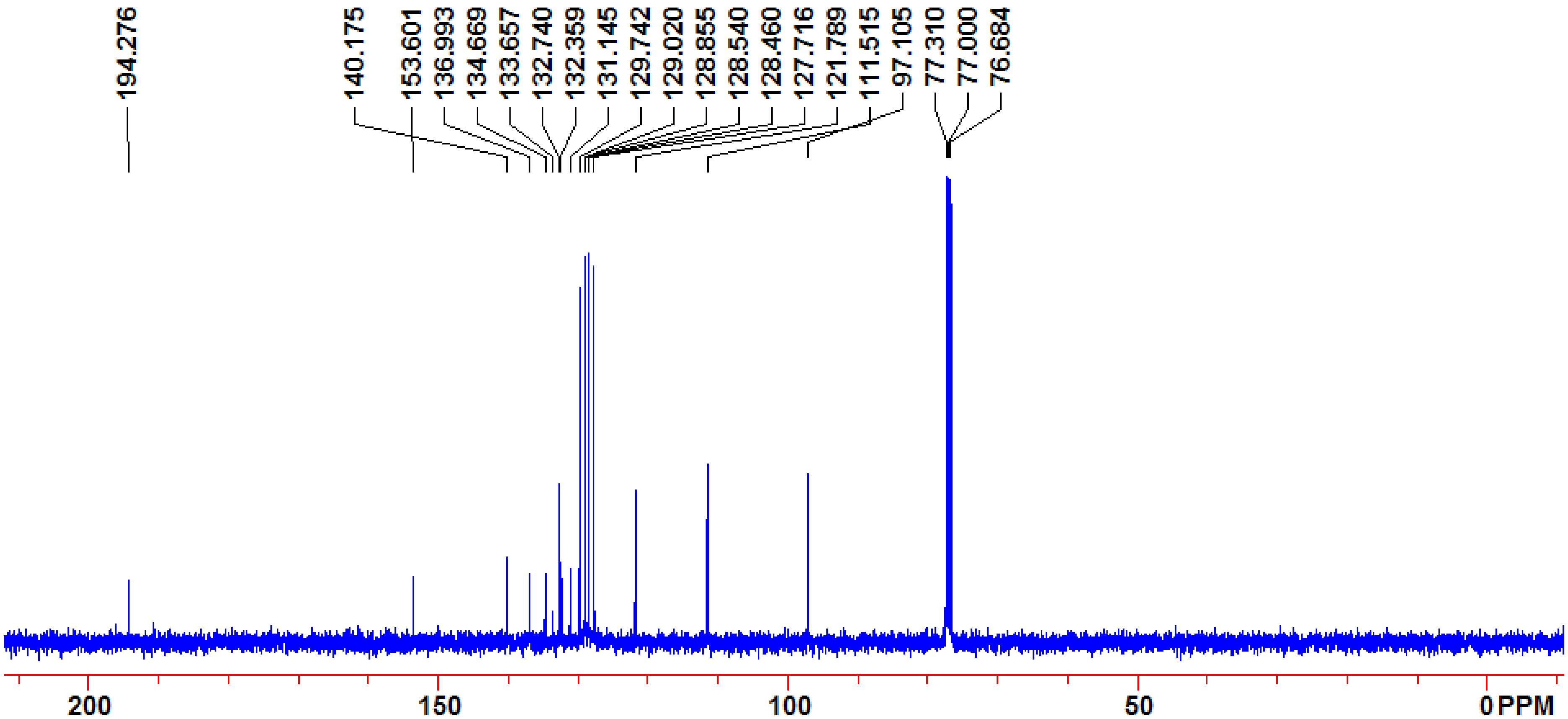


3m




O
Ph
N
N
Cl

3m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153.601
136.993
134.669
133.657
132.740
132.359
131.145
129.742
129.020
128.855
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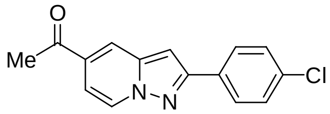
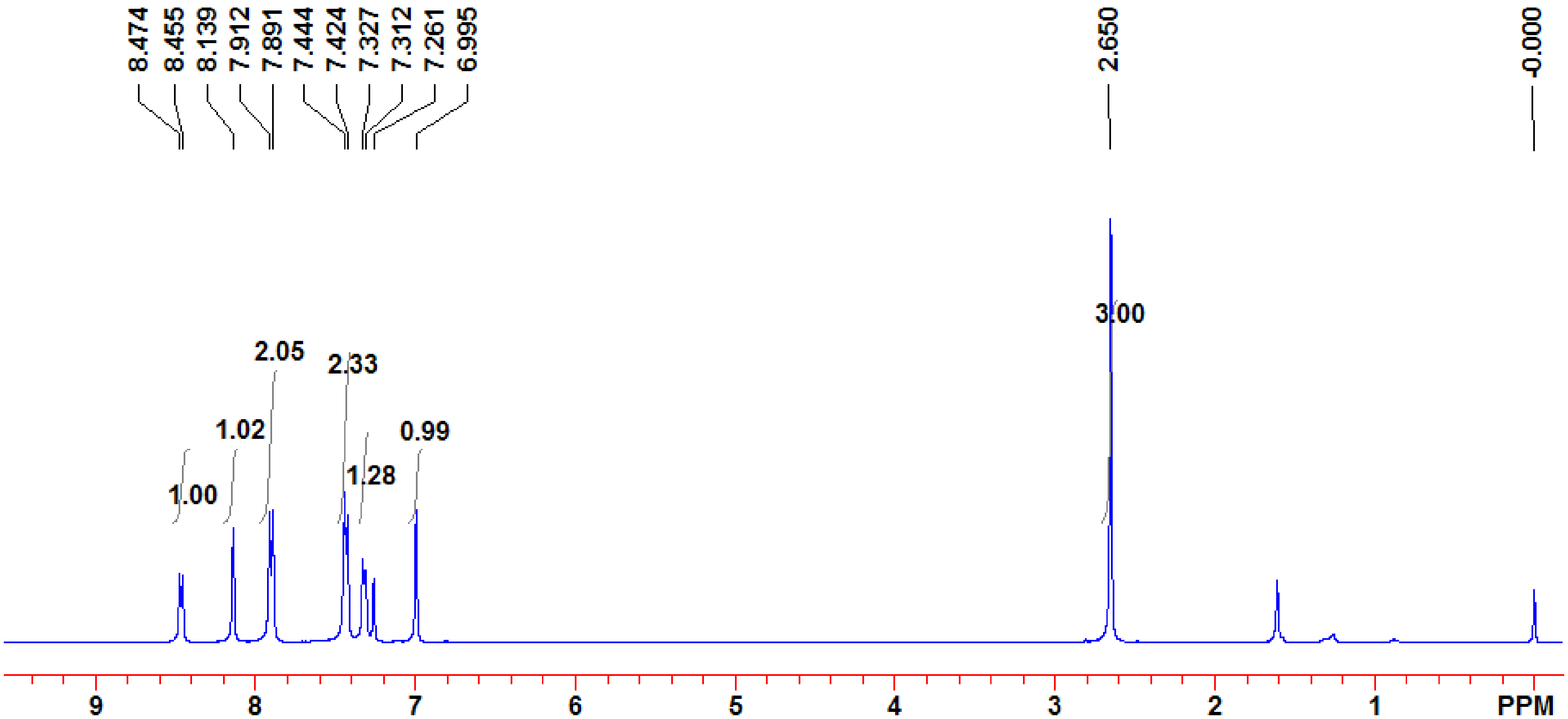
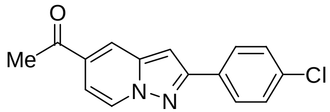
200
150
100
50
0 PPM


O
Me
N
N
Cl

3n


8.474
8.455
8.139
7.912
7.891
7.444
7.424
7.327
7.312
7.261
6.995
2.650
-0.000
1.00
1.02
2.05
2.33
1.28
0.99
3.00
9
8
7
6
5
4
3
2
1
PPM

Electronic Supplementary Material (ESI) for Chemical Communications



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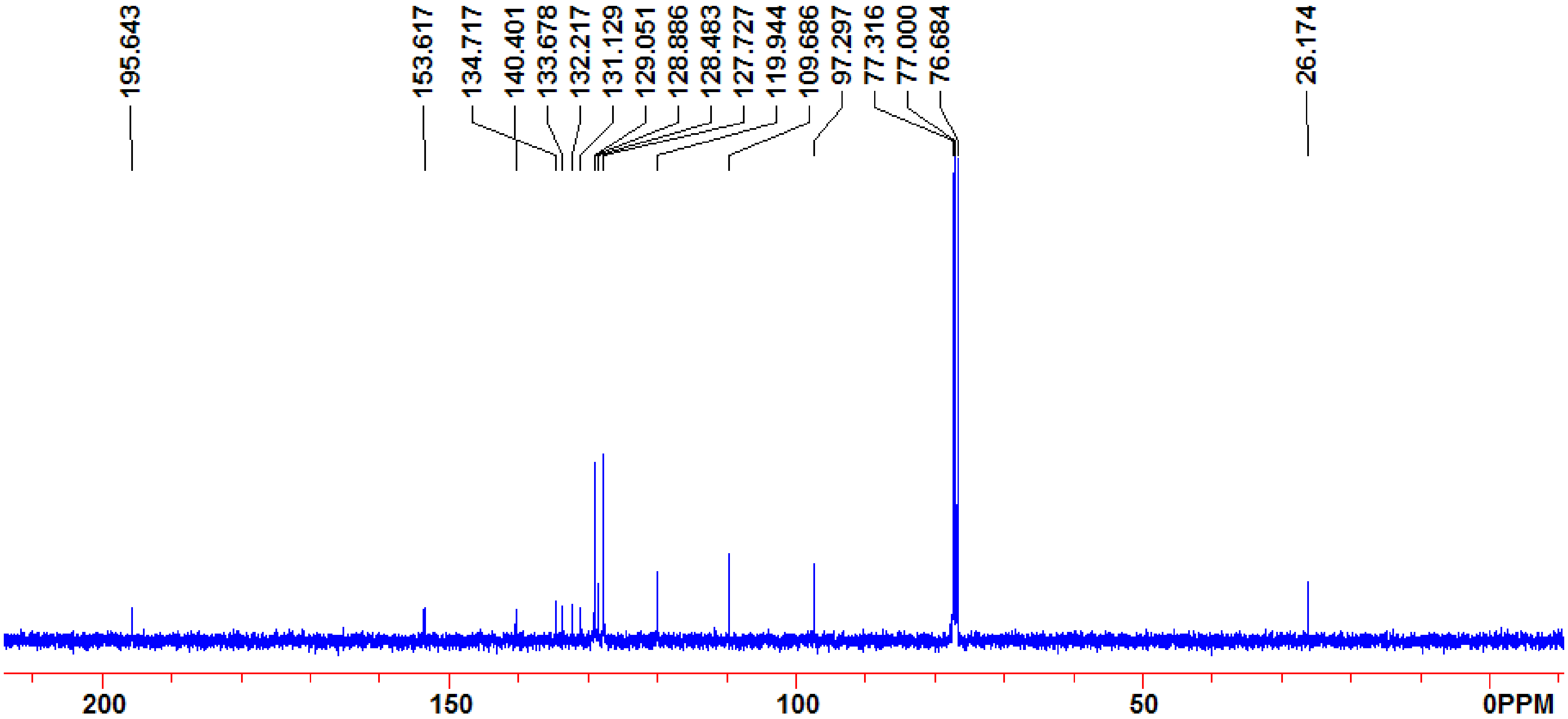
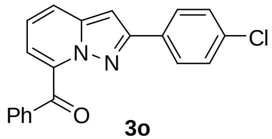
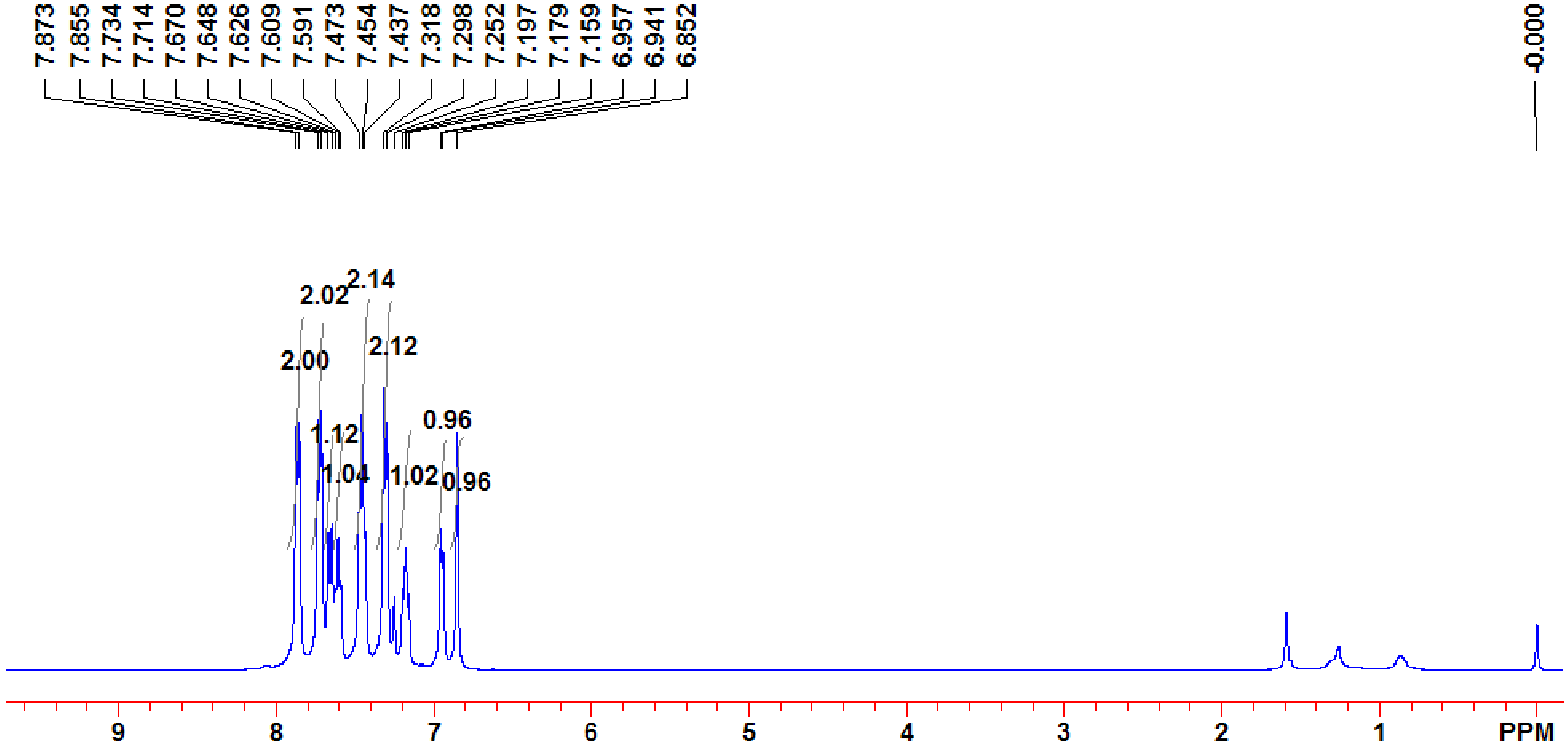



Cl
N
N
Ph
O

3o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7.670
7.648
7.626
7.609
7.591
7.473
7.454
7.437
7.318
7.298
7.252
7.197
7.179
7.159
6.957
6.941
6.852
-0.000
2.00
2.02
2.14
2.12
1.12
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1.02
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0.96
9
8
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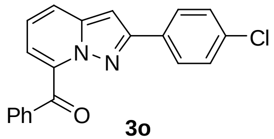
6
5
4
3
2
1
PPM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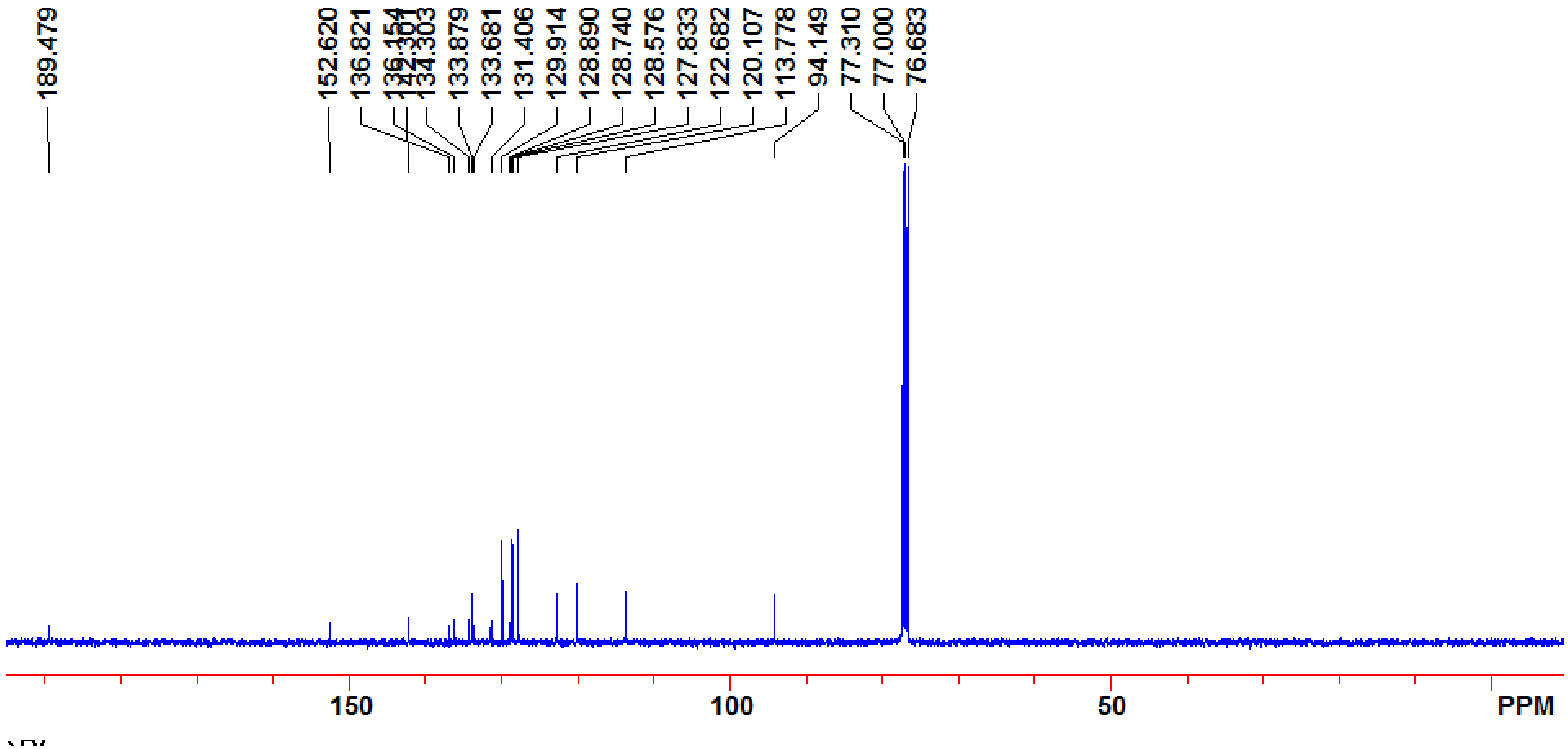
N
Cl
Ph
O

3o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136.154
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134.303
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133.681
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129.914
128.890
128.740
128.576
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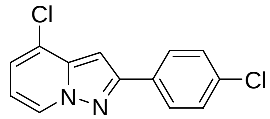
122.682
120.107
113.778
94.149
77.310
77.000
76.683
150
100
50
PPM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N
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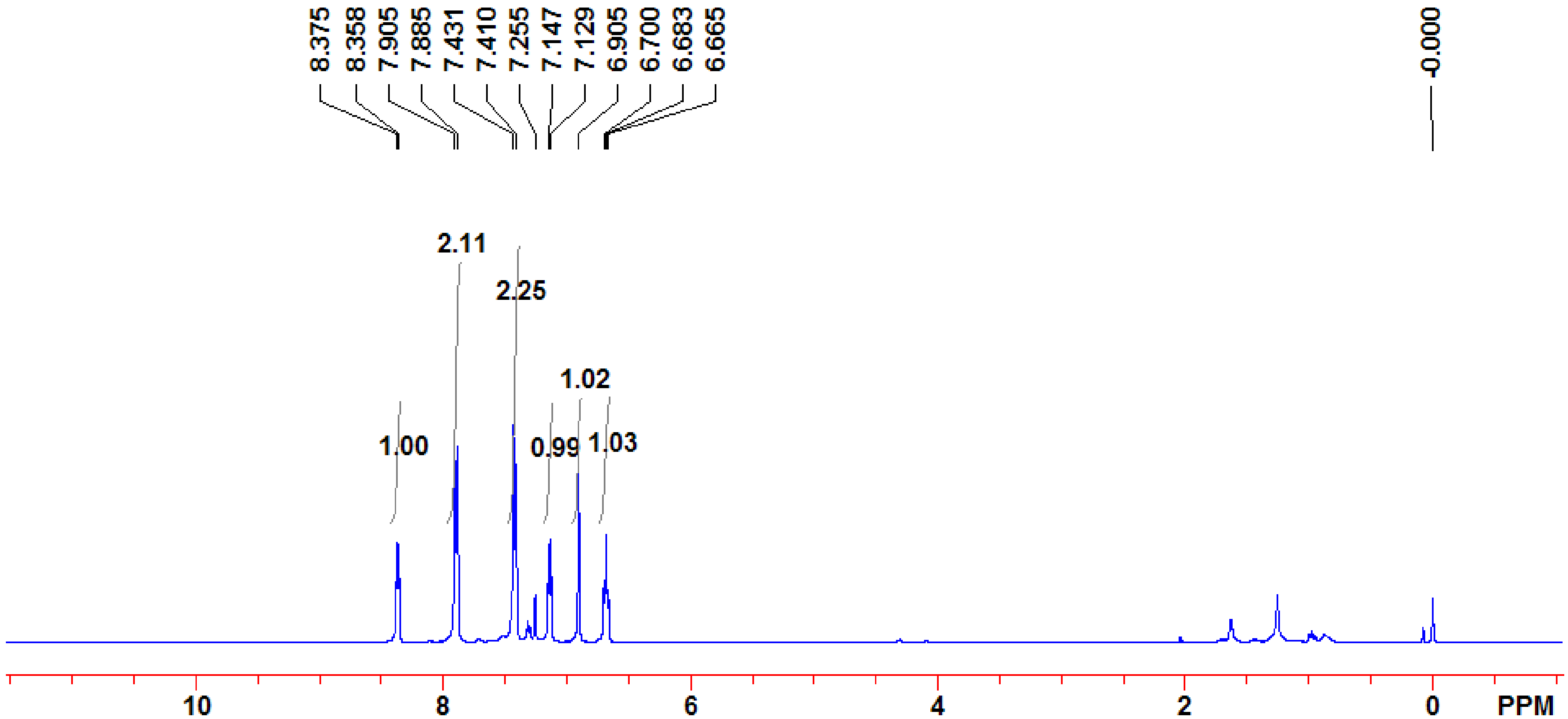
Cl

3p


8.375
8.358
7.905
7.885
7.431
7.410
7.255
7.147
7.129
6.905
6.700
6.683
6.665
-0.000
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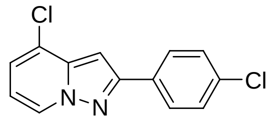
2.25
1.02
1.00
0.99
1.03
10
8
6
4
2
0
PPM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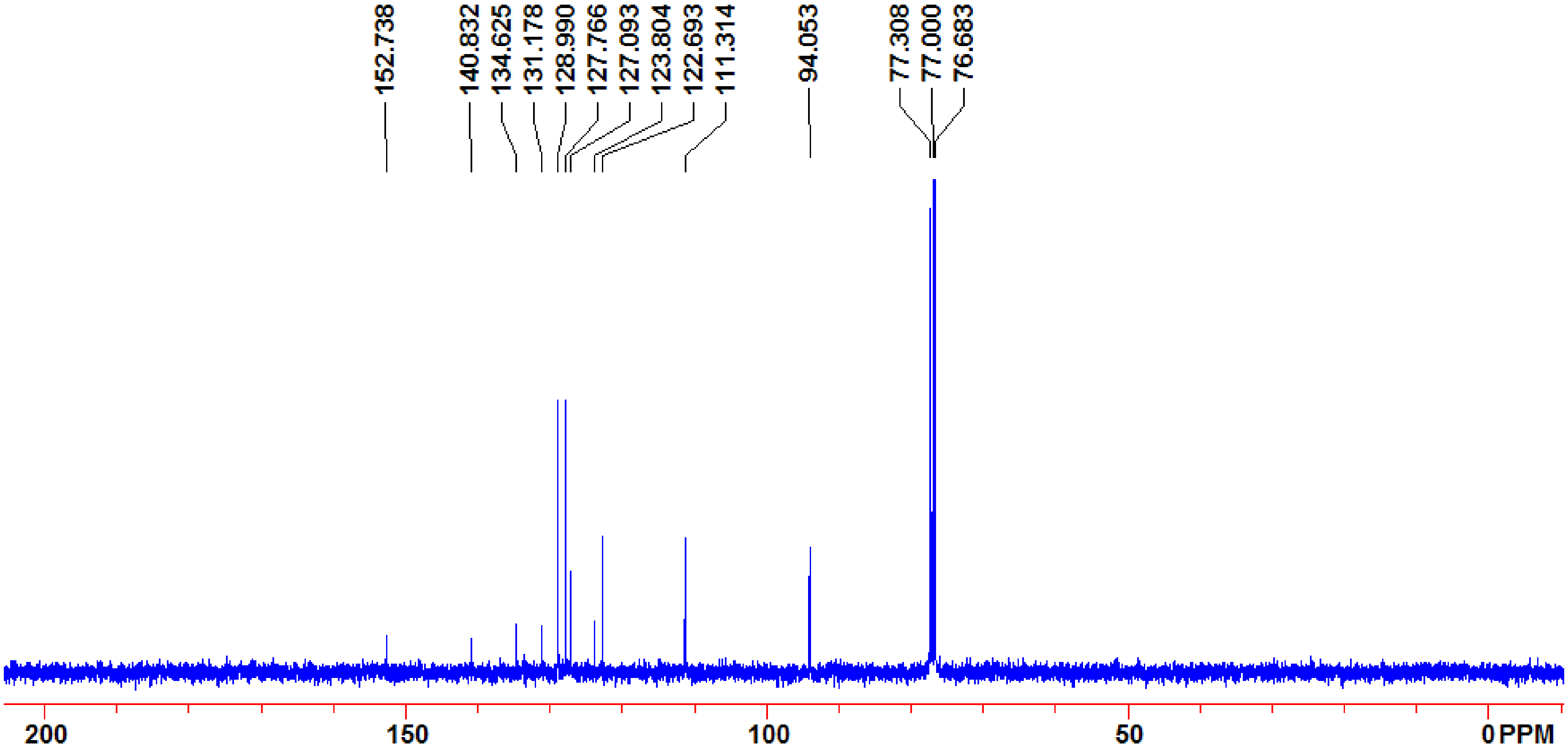
Cl

3p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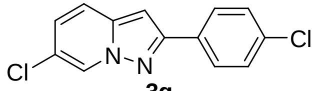
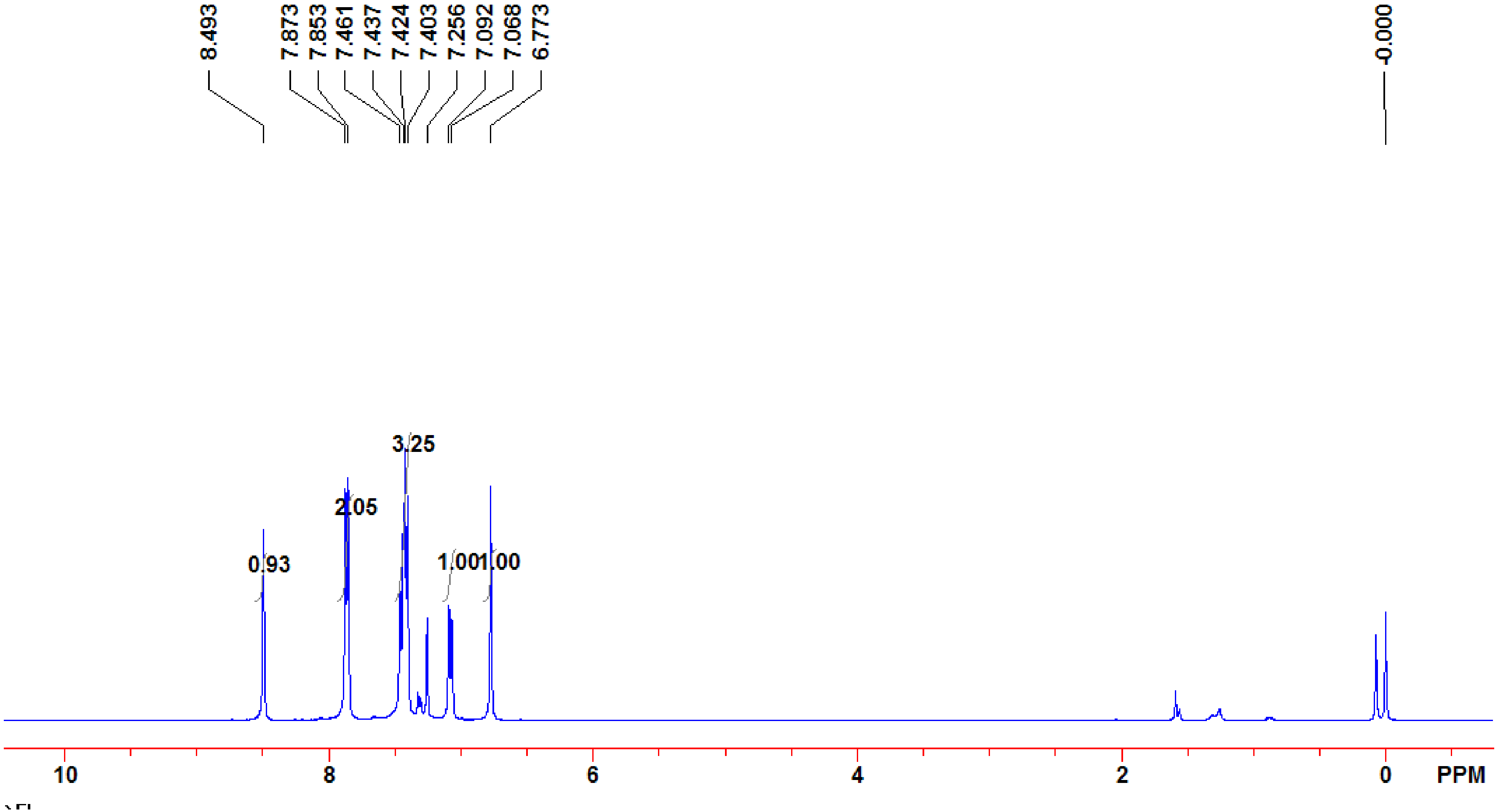
127.093
123.804
122.693
111.314
94.053
77.308
77.000
76.683
200
150
100
50
0 PPM


Cl
N
N
Cl

3q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7.437
7.424
7.403
7.256
7.092
7.068
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3.25
2.05
0.93
1.00
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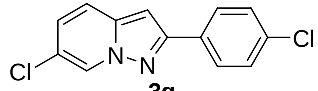
10
8
6
4
2
0
PPM



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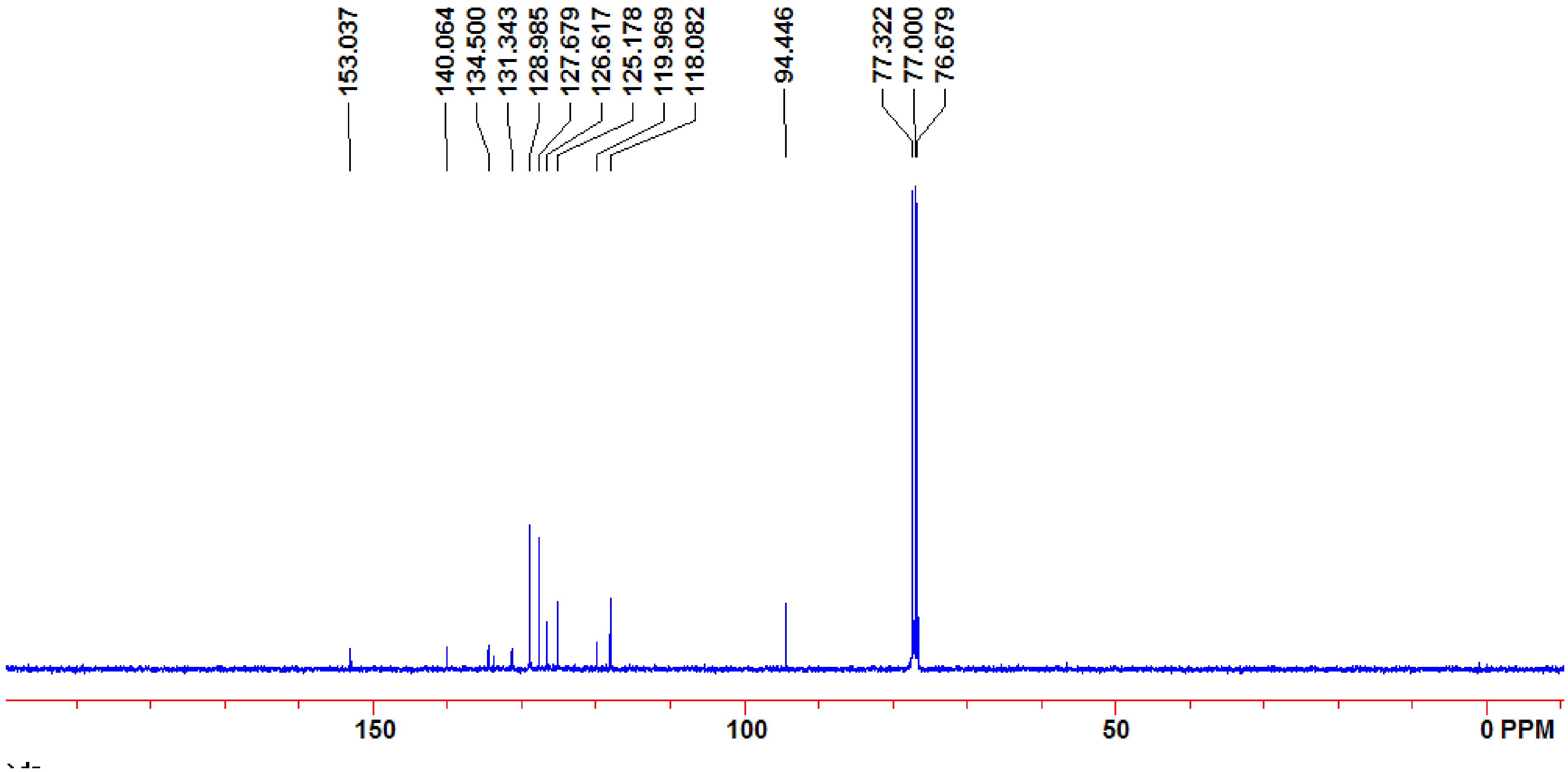
153.037
140.064
134.500
131.343
128.985
127.679
126.617
125.178
119.969
118.082
94.446
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77.000
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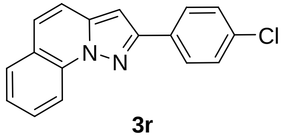
150
100
50
0 PPM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Cl

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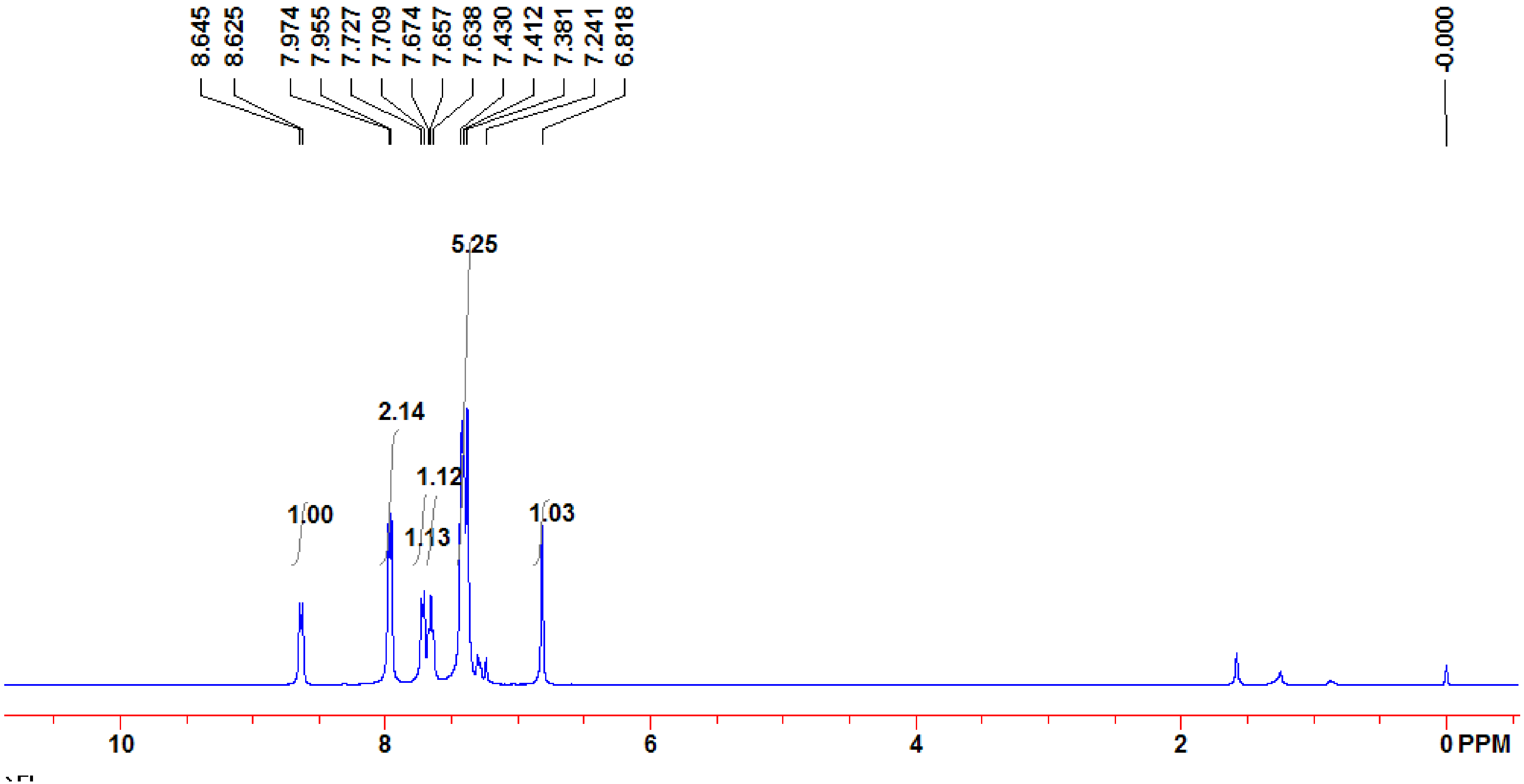
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7.727
7.709
7.674
7.657
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7.430
7.412
7.381
7.241
6.818
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2.14
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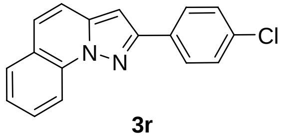
1.00
1.13
1.03
10
8
6
4
2
0 PPM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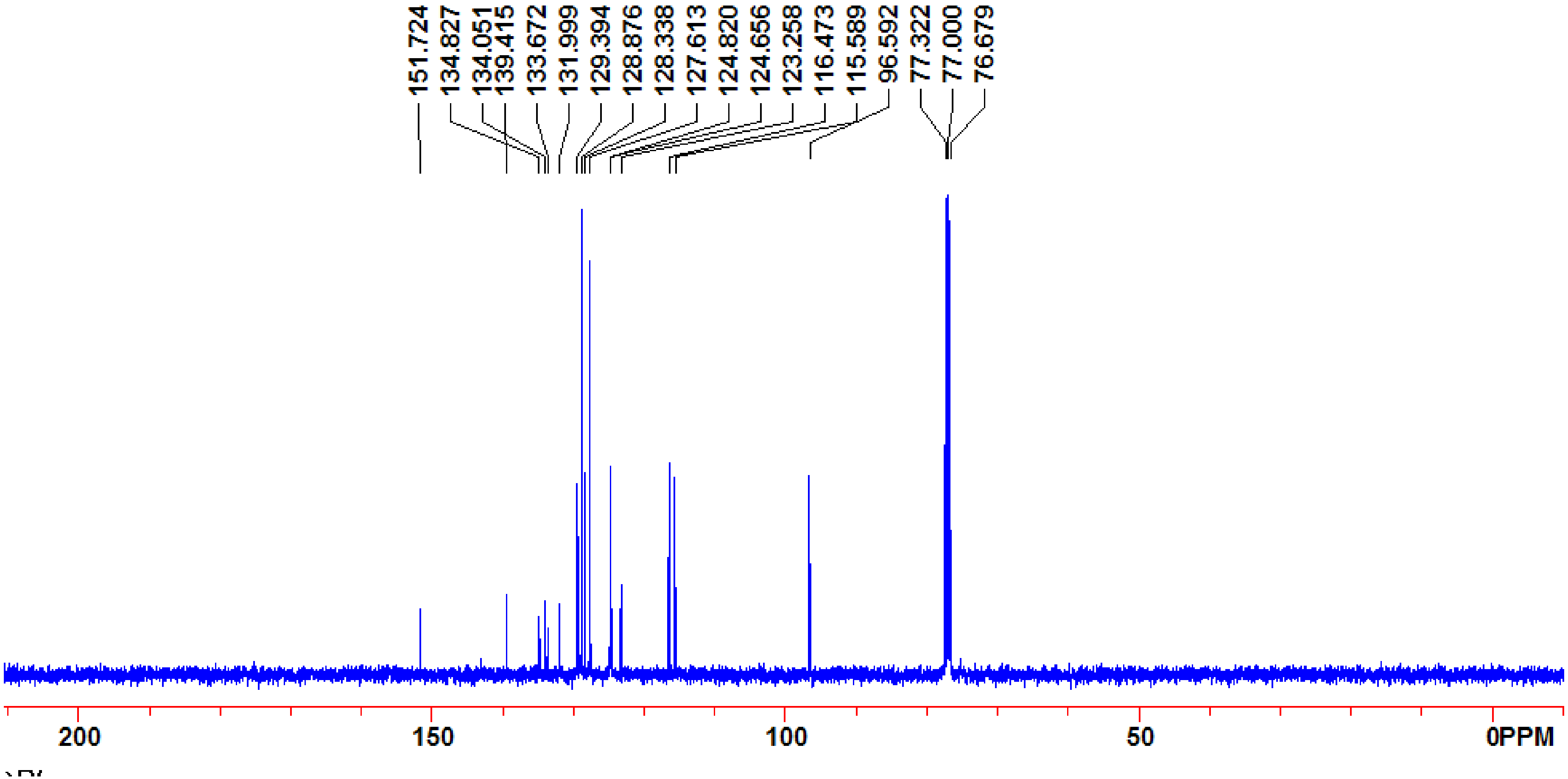
N
Cl

3r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128.876
128.338
127.613
124.820
124.656
123.258
116.473
115.589
96.592
77.322
77.000
76.679
200
150
100
50
0PPM