A Highly Effective Catalyst System for the Pd-Catalyzed Amination of Vinyl Bromides and Chlorides

Chinta Reddy Venkat Reddy, Sameer Urgaonkar[1], and John G. Verkade*

Department of Chemistry, Gilman Hall, Iowa State University, Ames, Iowa 50011

jverkade@iastate.edu

Supporting Information

Table of Contents

[1] Present address: Chemical Biology Program, Broad Institute of Harvard and MIT, 320 Bent Street, Cambridge, MA, 02141.

General Considerations

All reactions were performed under an atmosphere of argon in oven-dried glassware. Toluene was freshly distilled over sodium/benzophenone and stored over 4 Å molecular sieves under an argon atmosphere. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz, respectively. Thin layer chromatography (TLC) was performed using commercially prepared 60 mesh silica gel plates visualized with short-wavelength UV light (254 nm). For convenience, stock solutions of ligands (2 mM) were prepared in toluene and stored under argon. Celite® 521 (Aldrich) was used for the purification of enamines. Electron impact ionization experiments were performed on a Finnigan TSQ700 triple quadrupole mass spectrometer (Finnigan MAT, San Jose, CA) fitted with a Finnigan EI/CI ion source. Accurate mass measurements were performed using a double focusing Kratos MS-50 mass spectrometer (Kratos, NJ). The reported yields are isolated yields and are the average of two runs. All commercially available reagents were used as received. Ligands **1a, 1b** and **1d** were received from Aldrich and used without purification, ligands **1c** and **1e** were prepared according to our previous procedures.[1] All compounds described in Tables 1-4 and Scheme 1 are known in the literature (unless stated otherwise) and were characterized by comparing their ^{1}H and ^{13}C NMR to the previously reported data. In all cases, the comparisons were very favorable. Compound **5e** is new and it was characterized by ^{1}H, ^{13}C, mass (EI) and HRMS analysis. Compound **8b** is known, but since data are not available it was characterized in the same manner as **5e**.

Experimental Procedures

General Procedure for the Synthesis of Enamines from Vinyl Bromides. An oven-dried Schlenk flask equipped with a magnetic stirring bar was charged with NaO-*t*-Bu (1.4 equiv.) and $Pd(OAc)_2$ or $Pd_2(dba)_3$ (0.25 mol %) inside a nitrogen-filled glove box. The flask was capped with a rubber septum, and then it was removed from the glove box. Alkenyl bromide (3.0 mmol), amine (3.0 mmol), ligand (0.5 mol %) and toluene (5 mL) were then successively added. The Schlenk flask was degassed and refilled with argon. Then the flask was placed in an 80 ºC oil bath, and the reaction mixture was stirred until the starting material had been completely consumed as judged by TLC. After completion of the reaction, the mixture was cooled to room temperature, diluted with 30 mL of hexanes and filtered through Celite®. Solvents were evaporated under reduced pressure to afford a residue that consisted of the essentially pure enamine (^{1}H and ^{13}C NMR).

General Procedure for the Synthesis of Imines from Vinyl Bromides. An oven-dried Schlenk flask equipped with a magnetic stirring bar was charged with NaO-*t*-Bu (1.4 equiv.) and $Pd_2(dba)_3$ (0.25 mol %) inside a nitrogen-filled glove box. The flask was capped with a rubber septum, and then it was removed from the glove box. Alkenyl bromide (3.0 mmol), amine (3.0 mmol), ligand (0.5 mol %) and toluene (5 mL) were then successively added. The Schlenk flask was degassed and refilled with argon. Then the flask was placed in an 80 ºC oil bath, and the reaction mixture was stirred until the starting material had been completely consumed as judged by TLC. After completion of the reaction, the mixture was cooled to room temperature, diluted with 30 mL of hexanes and filtered through Celite®. Solvents were evaporated under reduced pressure to afford a residue that consisted of the essentially pure enamine (^{1}H and ^{13}C NMR).

Compound **7d** was purified as follows: After completion of the reaction, the mixture was cooled to room temperature, diluted with 30 mL of hexanes and filtered through Celite®. Solvents were evaporated, the obtained residue was separated by flash chromatography through neutral alumina (25 g) treated with Et_3N (5 g), and then eluted with 200 mL hexanes.

General Procedure for the Synthesis of Enamines from Vinyl Chloride 8. An oven-dried Schlenk flask equipped with a magnetic stirring bar was charged with NaO-*t*-Bu (1.4 equiv.) and $Pd_2(dba)_3$ (2.5 mol %) inside a nitrogen-filled glove box. The flask was capped with a rubber septum, and then it was removed from the glove box. Vinyl chloride **8** (3.0 mmol), amine (3.0 mmol), ligand (5 mol %) and toluene (5 mL) were then successively added. The Schlenk flask was degassed and refilled with argon. Then, the flask was placed in a 115 ºC oil bath and the reaction mixture was stirred until the starting material had been completely consumed as judged by TLC. After completion of the reaction, the mixture was cooled to room temperature, diluted with 30 mL of hexanes and filtered through Celite®. Solvents were evaporated under reduced pressure to afford a residue, which consisted of the essentially pure enamine (^{1}H and ^{13}C NMR).

General Procedure for the Synthesis of 1*H*-Indole 11 by Palladium Catalyzed Cascade Reaction of Alkenyl Bromide 2 with *o*-Bromoaniline 10. An oven-dried Schlenk flask equipped with a magnetic stirring bar was charged with NaO-*t*-Bu (2.8 equiv.), *o*-bromoaniline **10** (3 mmol) and $Pd_2(dba)_3$ (4.0 mol %) inside a nitrogen-filled glove box. The flask was capped with a rubber septum, and removed from the glove box. α-Bromostyrene **2** (3.0 mmol), ligand **1d** (4 mol %) and toluene (5 mL) were then successively added. The Schlenk flask was degassed and refilled with argon. The flask was then placed in an 80 ºC oil bath and the reaction mixture was stirred until **10** had been completely consumed as judged by TLC. The temperature was then raised to 120 ºC and after completion of the reaction (16 h), the mixture was cooled to room temperature, diluted with 50 mL of hexanes and filtered through Celite®. Solvents were evaporated under reduced pressure. Purification by silica gel flash chromatography (hexanes/ethyl acetate, 10:1) afforded 1*H*-indole **11**.

(1) Su, W.; Urgaonkar, S.; McLaughlin, P. A.; Verkade, J. G. *J. Am. Chem. Soc.* **2004**, *126*, 16433.

References for known compounds

4-Styrylmorpholine (Table 3, **5a**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

N-(2-Phenylethyl)-piperidine (Table 3, **5b**). Tillack, A.; Trauthwein, H.; Hartung, C. G.; Eichberger, M.; Jansen, A.; Bellar, M. *Monatsh. Chemie,* **2000**, *131*, 1327.

8-Styryl-1,4-dioxa-8-aza-spiro[4,5]decane (Table 3, **5c**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

Dibenzylstyrylamine (Table 3, **5d**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

Methylphenylstyrylamine (Table 3, **5f**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

N-(2-Phenylethyl)-di-*n*-butylamine (Table 3, **5g**). Tillack, A.; Trauthwein, H.; Hartung, C. G.; Eichberger, M.; Jansen, A.; Bellar, M. *Monatsh. Chemie,* **2000**, *131*, 1327.

N-(2-Phenylethyl)-diethylamine (Table 3, **5h**). Tillack, A.; Trauthwein, H.; Hartung, C. G.; Eichberger, M.; Jansen, A.; Bellar, M. *Monatsh. Chemie,* **2000**, *131*, 1327.

Ethylphenylstyrylamine (Table 3, **5i**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

4-(1-Phenylvinyl)morpholine (Table **1**, **3a**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

8-(1-Phenylvinyl)-1,4-dioxa-8-aza-spiro[4,5]decane (Table 3, **3b**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

Methylphenyl(1-phenylvinyl)amine (Table 3, **3c**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

1-(1-Phenylethen-1-yl)piperidine (Table 3, **3d**). Palecek, J.; Paleta, O. *Synthesis* **2004**, 521.

N-(Cyclohexylidenemethyl)morpholine (Table 3, **6**). Valderrama, J. A.; Gonzalez, M. F.; Valderrama, C. *Tetrahedron* **1999**, *55*, 6039.

(1-Phenylethylidene)*p*-tolylamine (Scheme 1, **7a**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

(4-Fluorophenyl)(1-phenylethylidene)amine (Scheme 1, **7b**). Bodis, J.; Muller, T. E.; Lercher. J. A. *Green Chem.* **2003**, *5*, 227.

N-phenyl-(1-phenylethylidene)amine (Scheme 1, **7c**). Hansen, M. C.; Buchwald, S. L. *Org. Lett.* **2000**, *5*, 713.

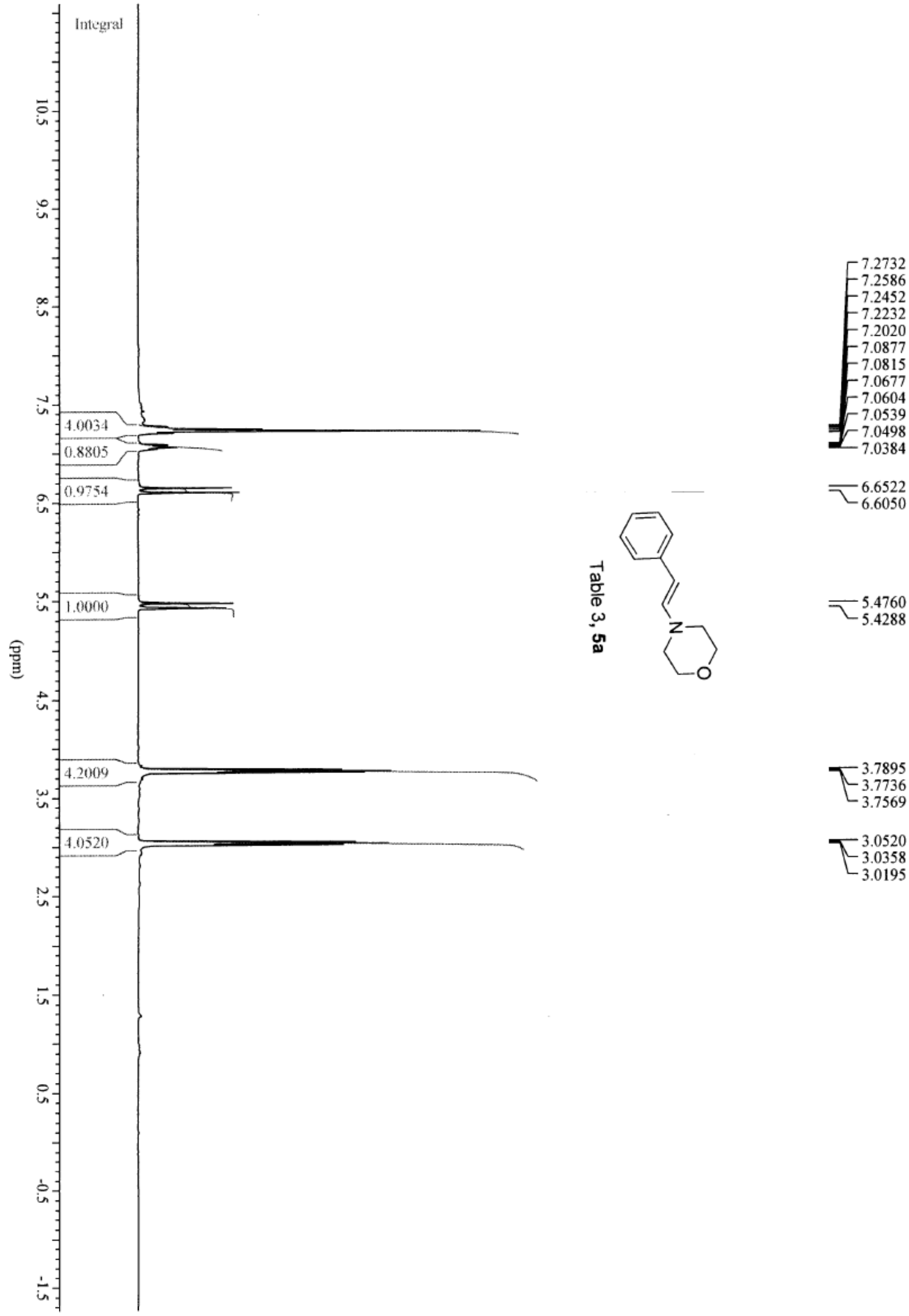
N-(1-phenylethylidene)-2,6-xylylamine (Scheme 1, **7d**). Jousseaume, B.; Vilcot, N.; Ricci, A.; Tiekink, E. R. T. *J. Chem. Soc. Perkin Trans.* **1994**, 2283.

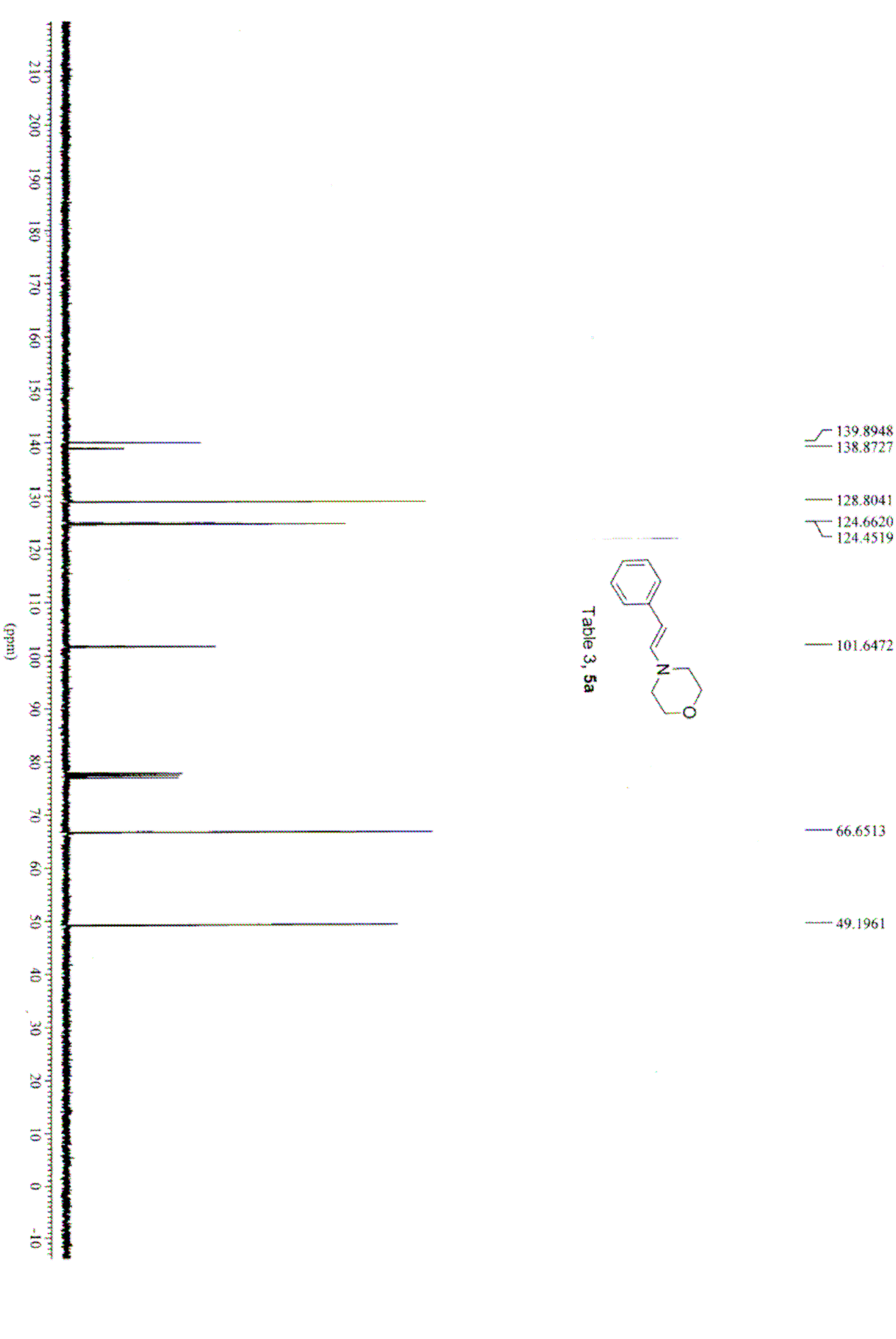
Butyl(1-phenylethylidene)amine (Scheme 1, **7e**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

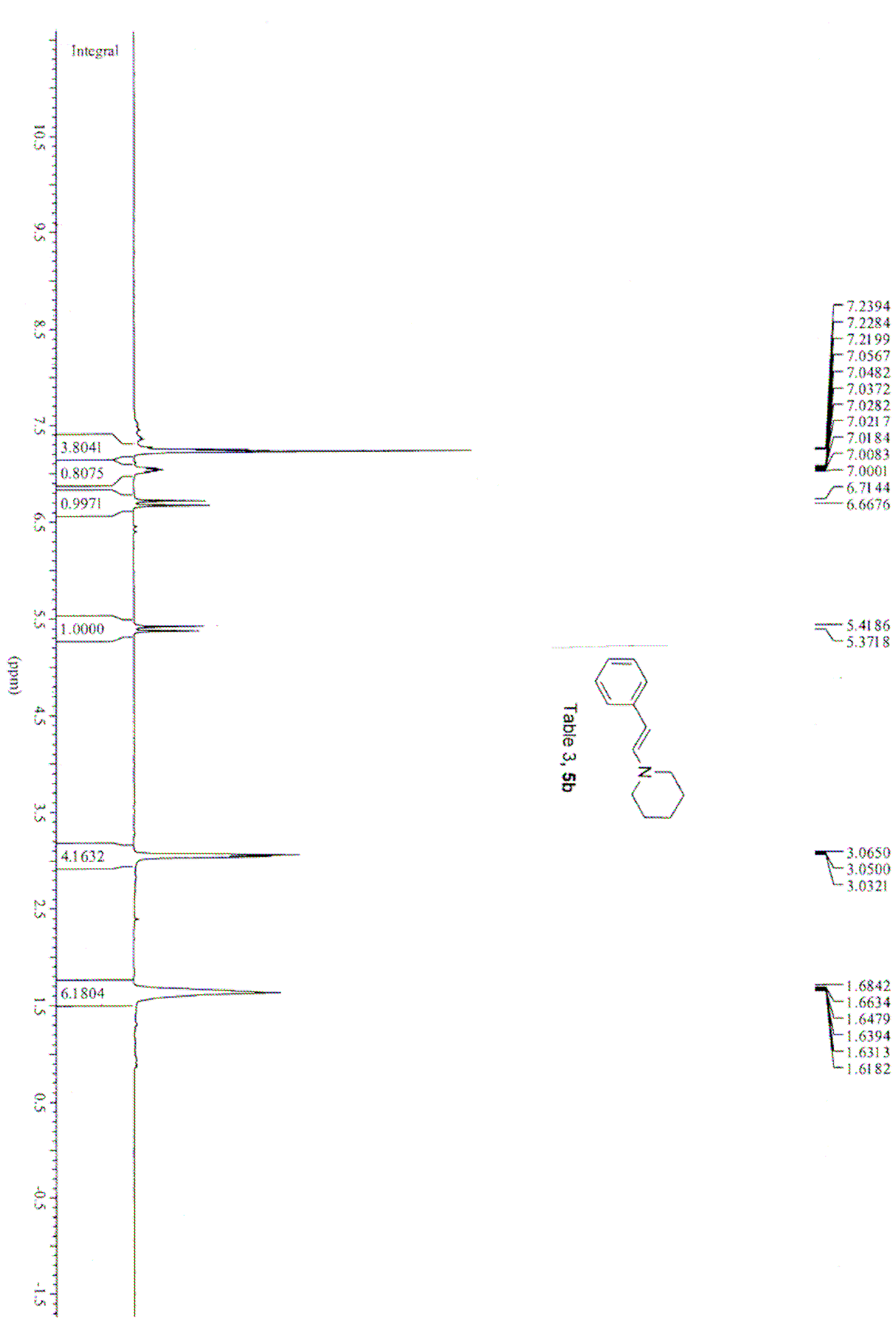
(2-Chlorophenyl)(1-phenylethylidene)amine (Scheme 1, **7f**). Barluenga, J.; Fernandez, M. A.; Aznar, F.; Valdes. C. *Chem. Eur. J.* **2004**, 494.

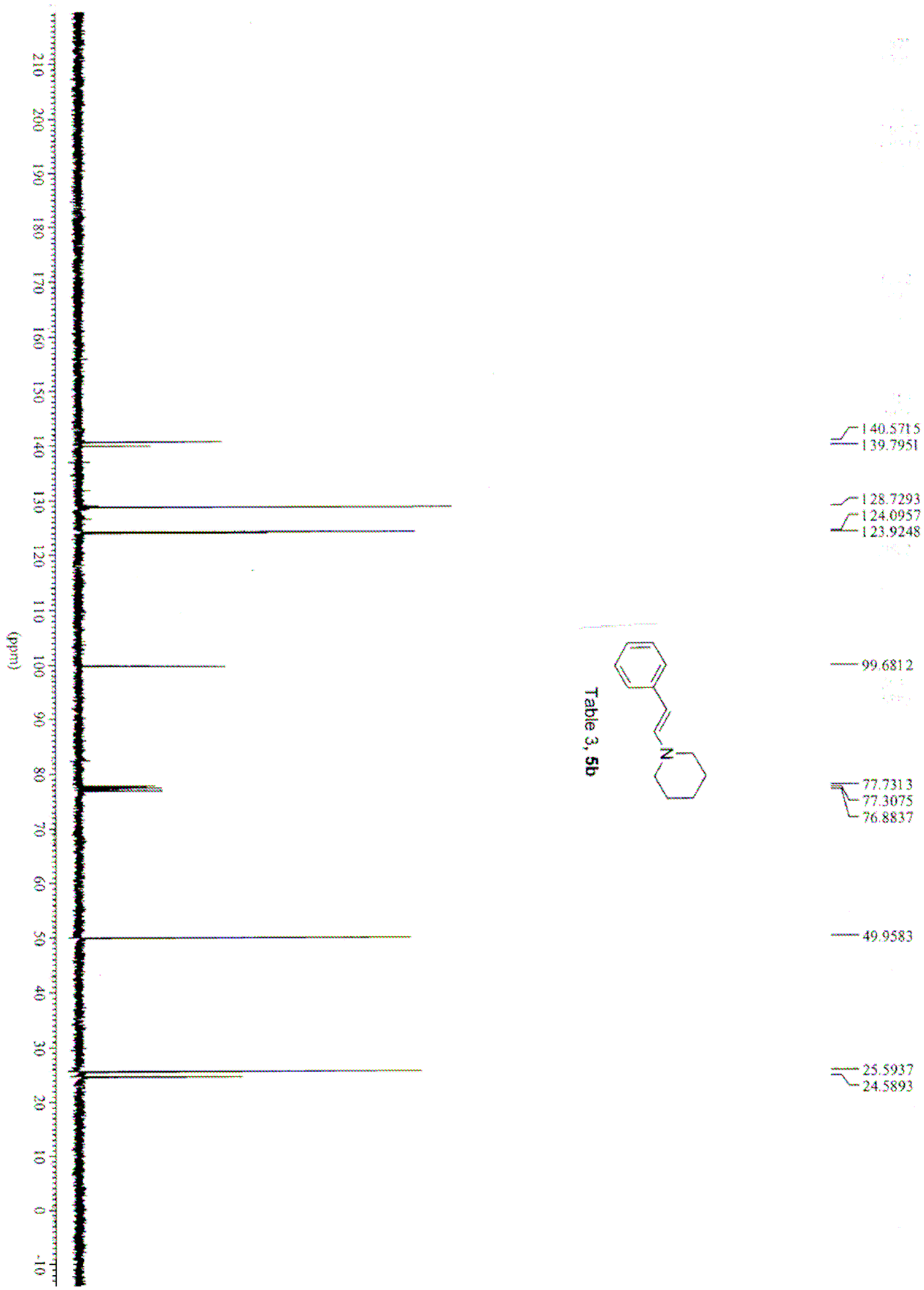
1-Morpholinocyclopentene (Scheme 2, **9a**). www.sigma-aldrich.com (^{1}H and ^{13}C spectra available online)

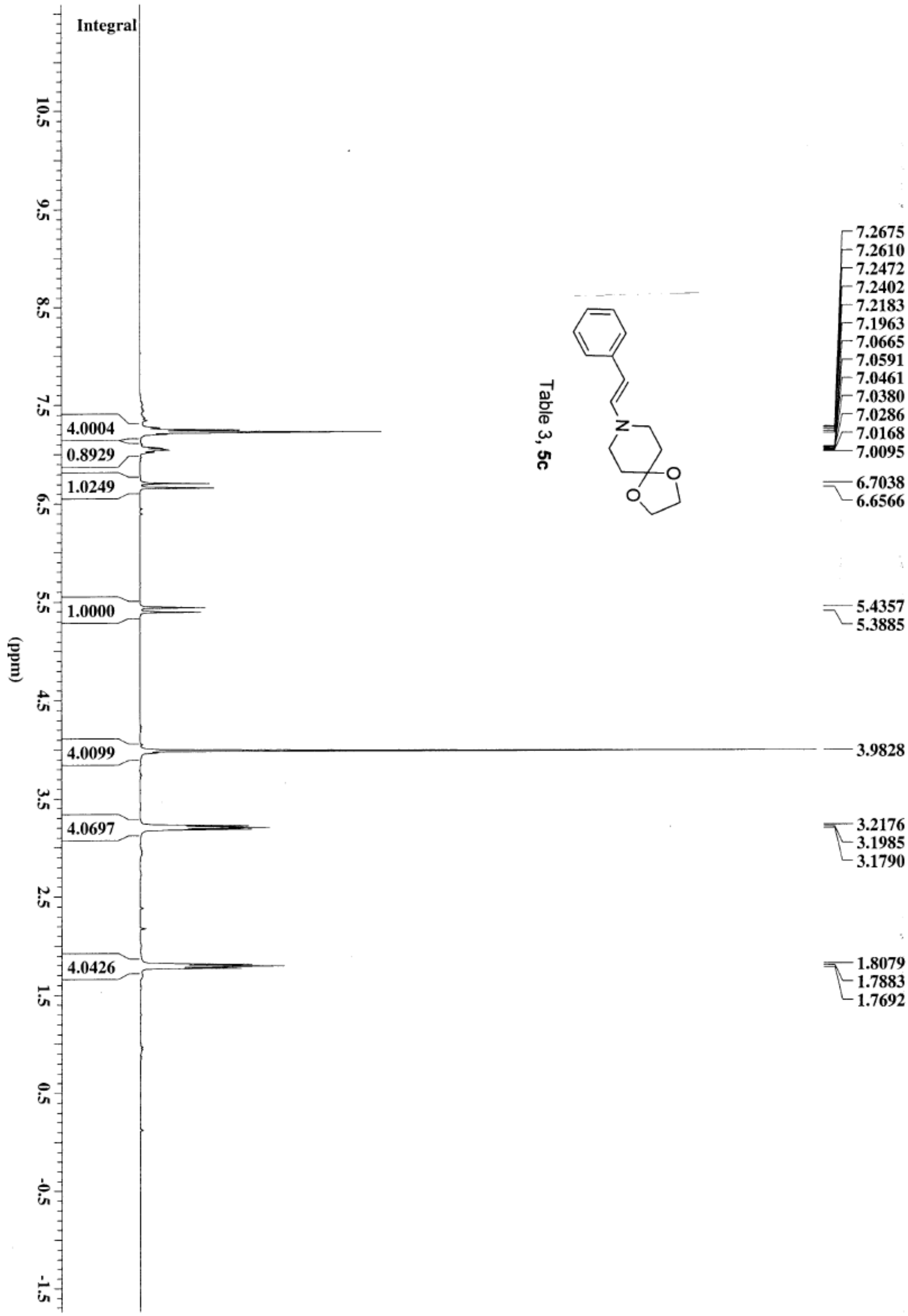
2-Phenylindole (Scheme 3, **11**). Sezen, B.; Sames, D. *J. Am. Chem. Soc.* **2003**, *125*, 5274.


Integral
4.0034
0.8805
0.9754
1.0000
4.2009
4.0520
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
Table 3, 5a
7.2732
7.2586
7.2452
7.2232
7.2020
7.0877
7.0815
7.0677
7.0604
7.0539
7.0498
7.0384
6.6522
6.6050
5.4760
5.4288
3.7895
3.7736
3.7569
3.0520
3.0358
3.0195


139.8948
138.8727
128.8041
124.6620
124.4519
101.6472
66.6513
49.1961
Table 3, 5a
(ppm)


Integral
3.8041
0.8075
0.9971
1.0000
4.1632
6.1804
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
Table 3, 5b
7.2394
7.2284
7.2199
7.0567
7.0482
7.0372
7.0282
7.0217
7.0184
7.0083
7.0001
6.7144
6.6676
5.4186
5.3718
3.0650
3.0500
3.0321
1.6842
1.6634
1.6479
1.6394
1.6313
1.6182


140.5715
139.7951
128.7293
124.0957
123.9248
99.6812
77.7313
77.3075
76.8837
49.9583
25.5937
24.5893
Table 3, 5b
(ppm)


Integral
4.0004
0.8929
1.0249
1.0000
4.0099
4.0697
4.0426
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
7.2675
7.2610
7.2472
7.2402
7.2183
7.1963
7.0665
7.0591
7.0461
7.0380
7.0286
7.0168
7.0095
6.7038
6.6566
5.4357
5.3885
3.9828
3.2176
3.1985
3.1790
1.8079
1.7883
1.7692
N
O
O
Table 3, **5c**

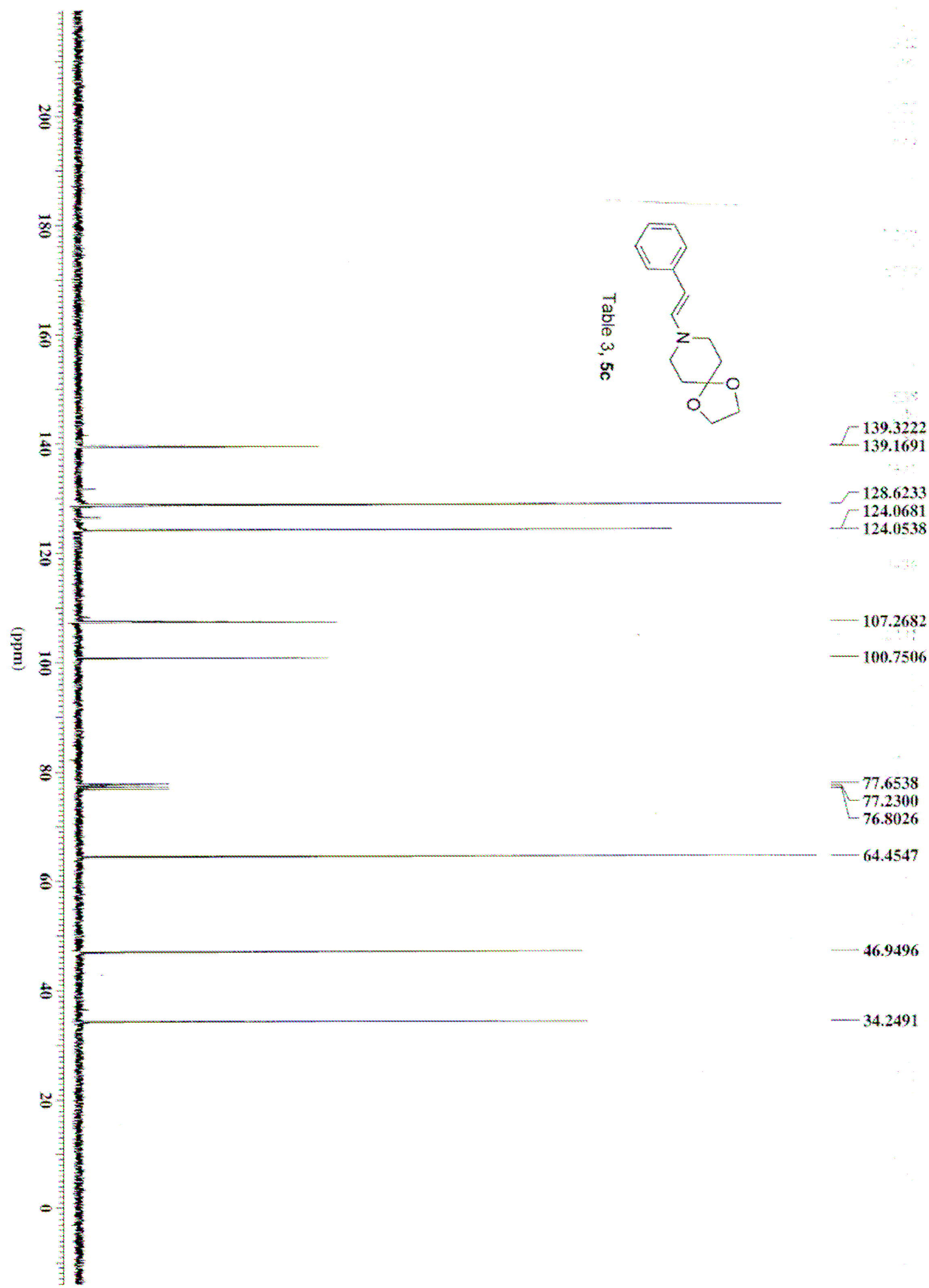
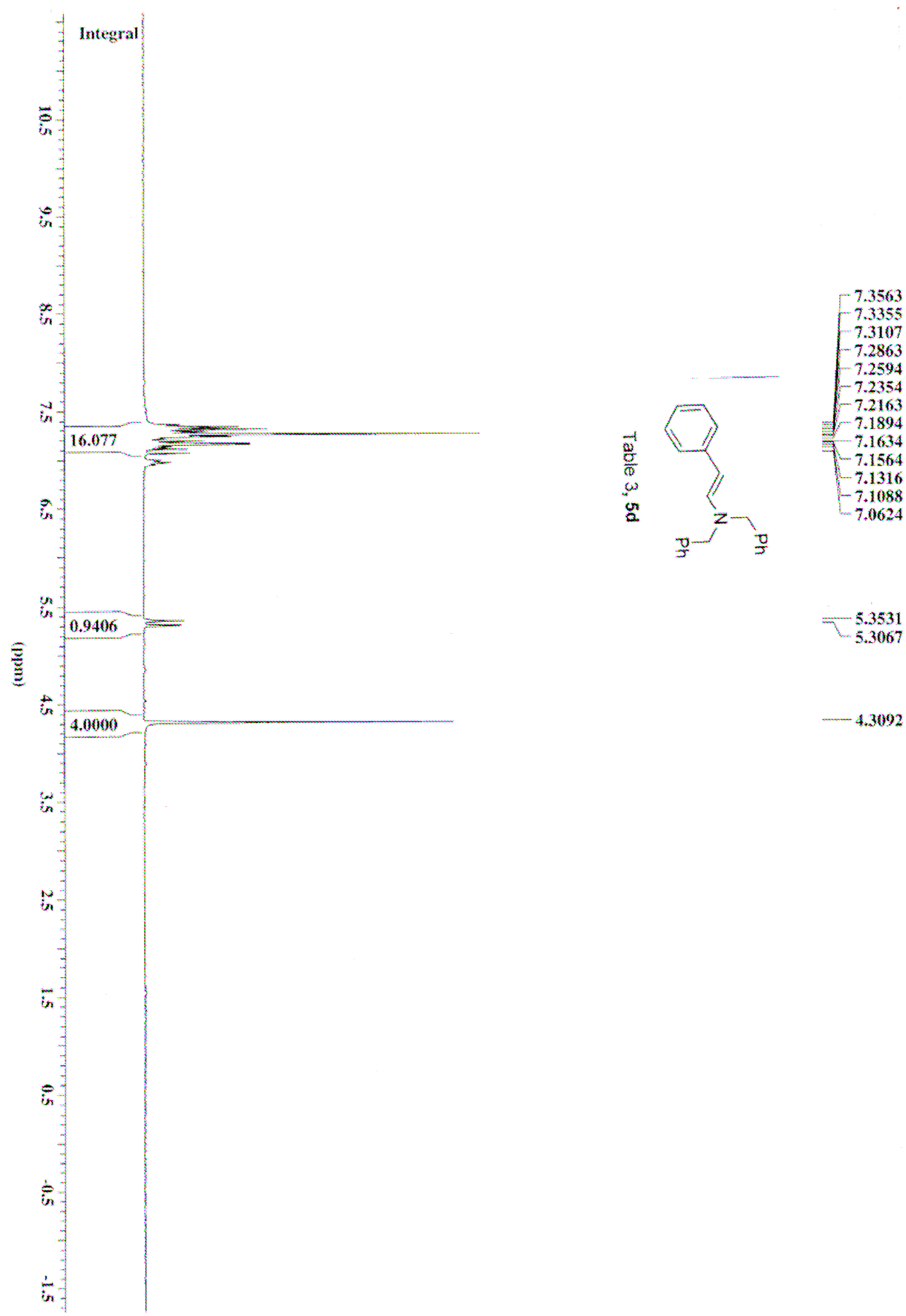
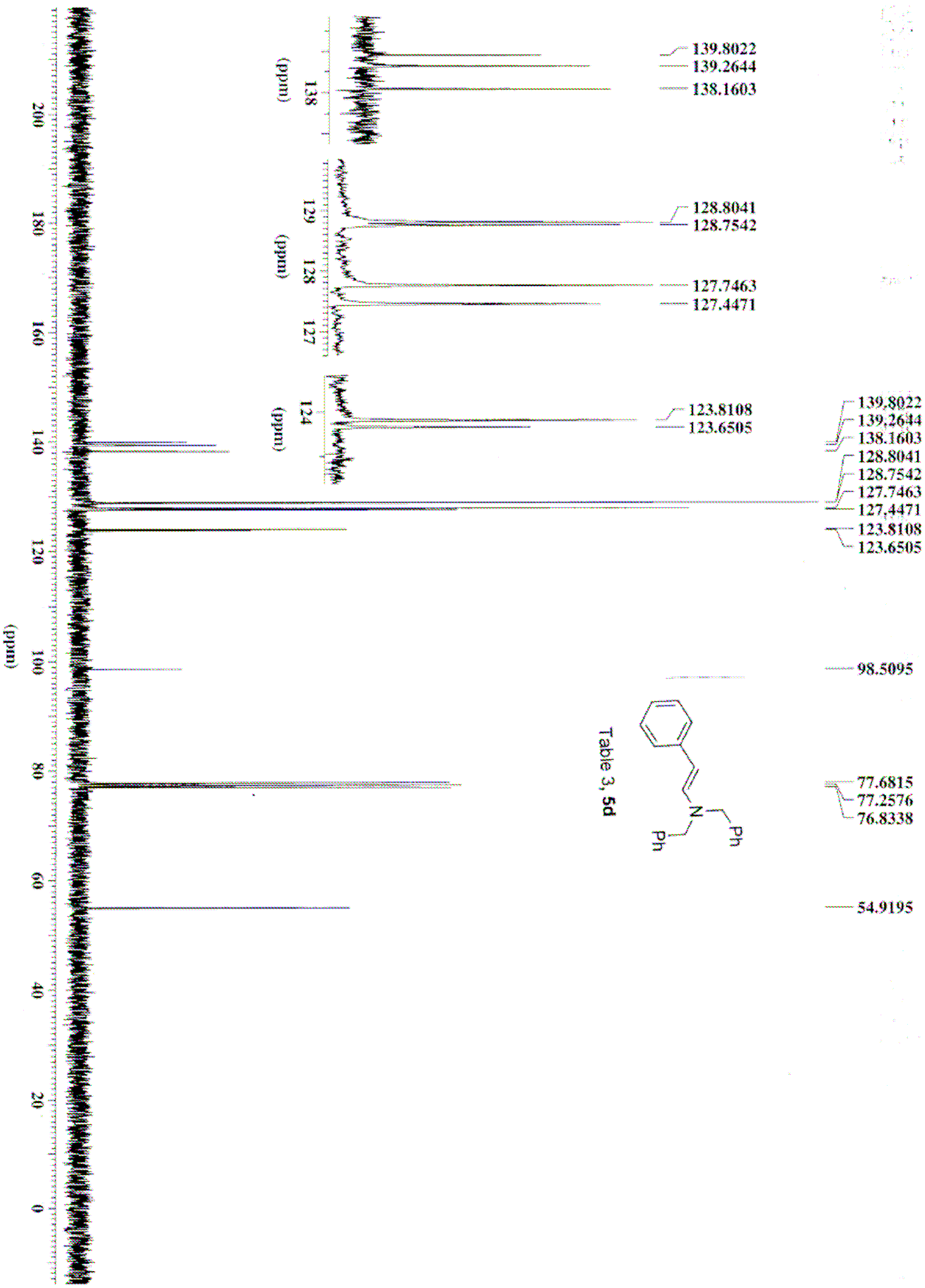
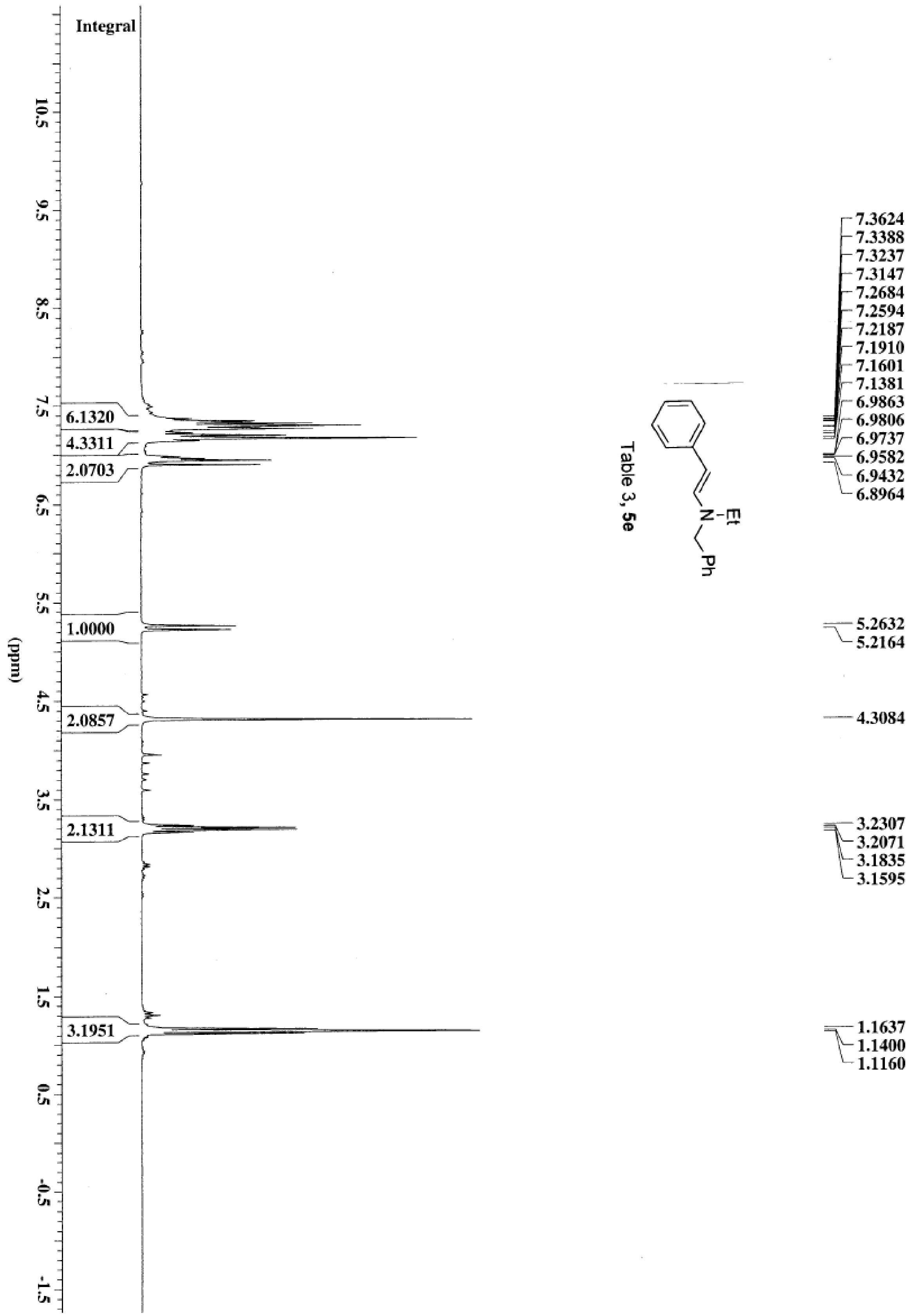


Table 3, 5c
139.3222
139.1691
128.6233
124.0681
124.0538
107.2682
100.7506
77.6538
77.2300
76.8026
64.4547
46.9496
34.2491
(ppm)
200
180
160
140
120
100
80
60
40
20
0


Integral
16.077
0.9406
4.0000
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
Table 3, 5d
Ph
N
Ph
7.3563
7.3355
7.3107
7.2863
7.2594
7.2354
7.2163
7.1894
7.1634
7.1564
7.1316
7.1088
7.0624
5.3531
5.3067
4.3092


139.8022
139.2644
138.1603
128.8041
128.7542
127.7463
127.4471
123.8108
123.6505
98.5095
77.6815
77.2576
76.8338
54.9195
Table 3, 5d
Ph
N
Ph
(ppm)
200
180
160
140
120
100
80
60
40
20
0
138
129
128
127
124


Integral
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
6.1320
4.3311
2.0703
1.0000
2.0857
2.1311
3.1951
Et
N
Ph
Table 3, 5e
7.3624
7.3388
7.3237
7.3147
7.2684
7.2594
7.2187
7.1910
7.1601
7.1381
6.9863
6.9806
6.9737
6.9582
6.9432
6.8964
5.2632
5.2164
4.3084
3.2307
3.2071
3.1835
3.1595
1.1637
1.1400
1.1160

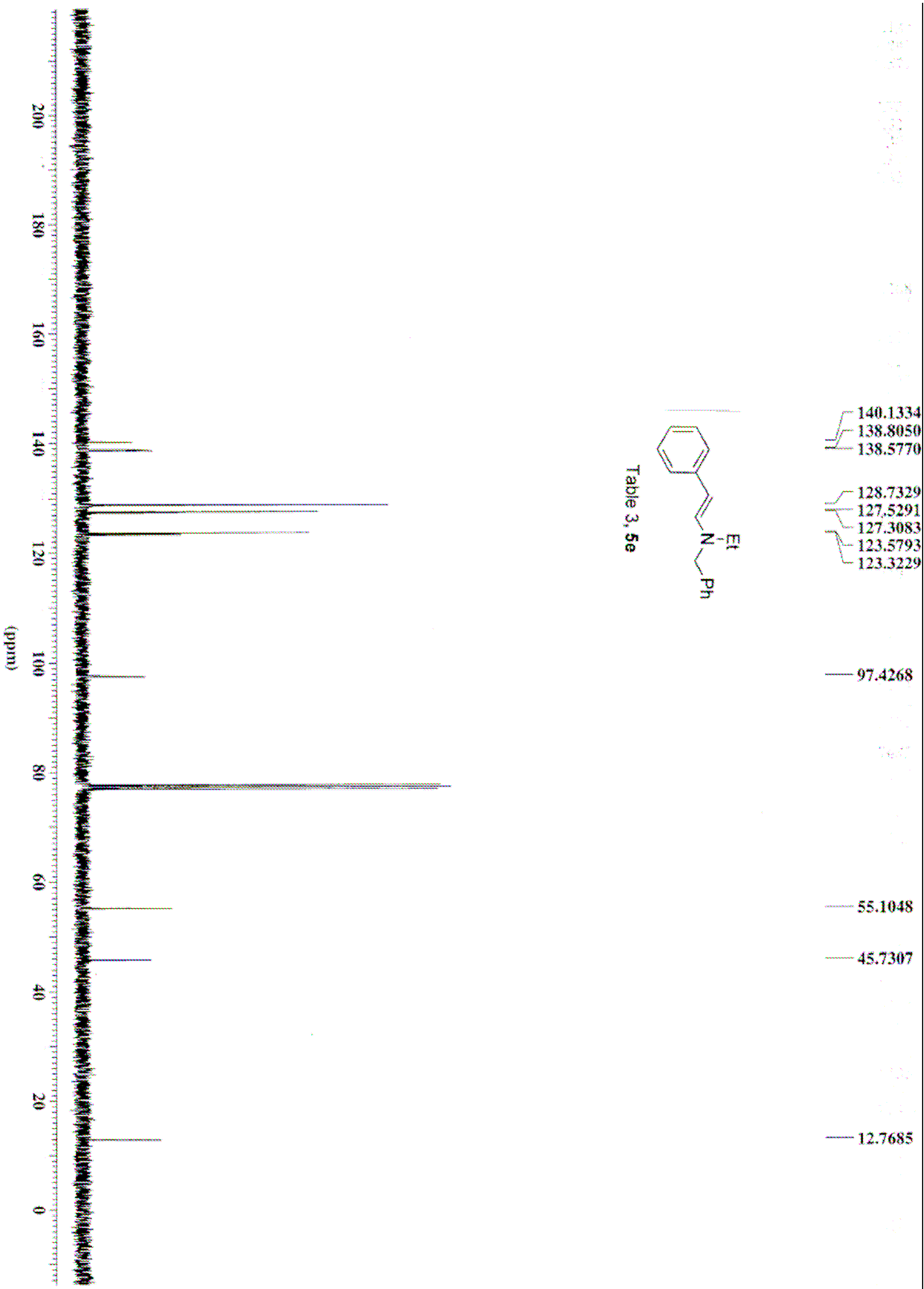


Table 3, 5e
Et
N
Ph
140.1334
138.8050
138.5770
128.7329
127.5291
127.3083
123.5793
123.3229
97.4268
55.1048
45.7307
12.7685
200
180
160
140
120
100
80
60
40
20
0
(ppm)

SPEC: fin031698.dat (03-JUN-05 14:43:04)
Samp: Venkat
Comm: 70 eV EI
Oper: kh
Base: 90.25
Peak: 1000.0 mmu

Study: ms services
Masses: 35.01 > 650.00
Intensity: 9985963

Scan 10 @ 0.42 min (EI +Q1MS LMR UP LR)

Scans: 1 > 12

Client: Venkat
#Peaks: 616
RIC: 54426173

10.0E+06

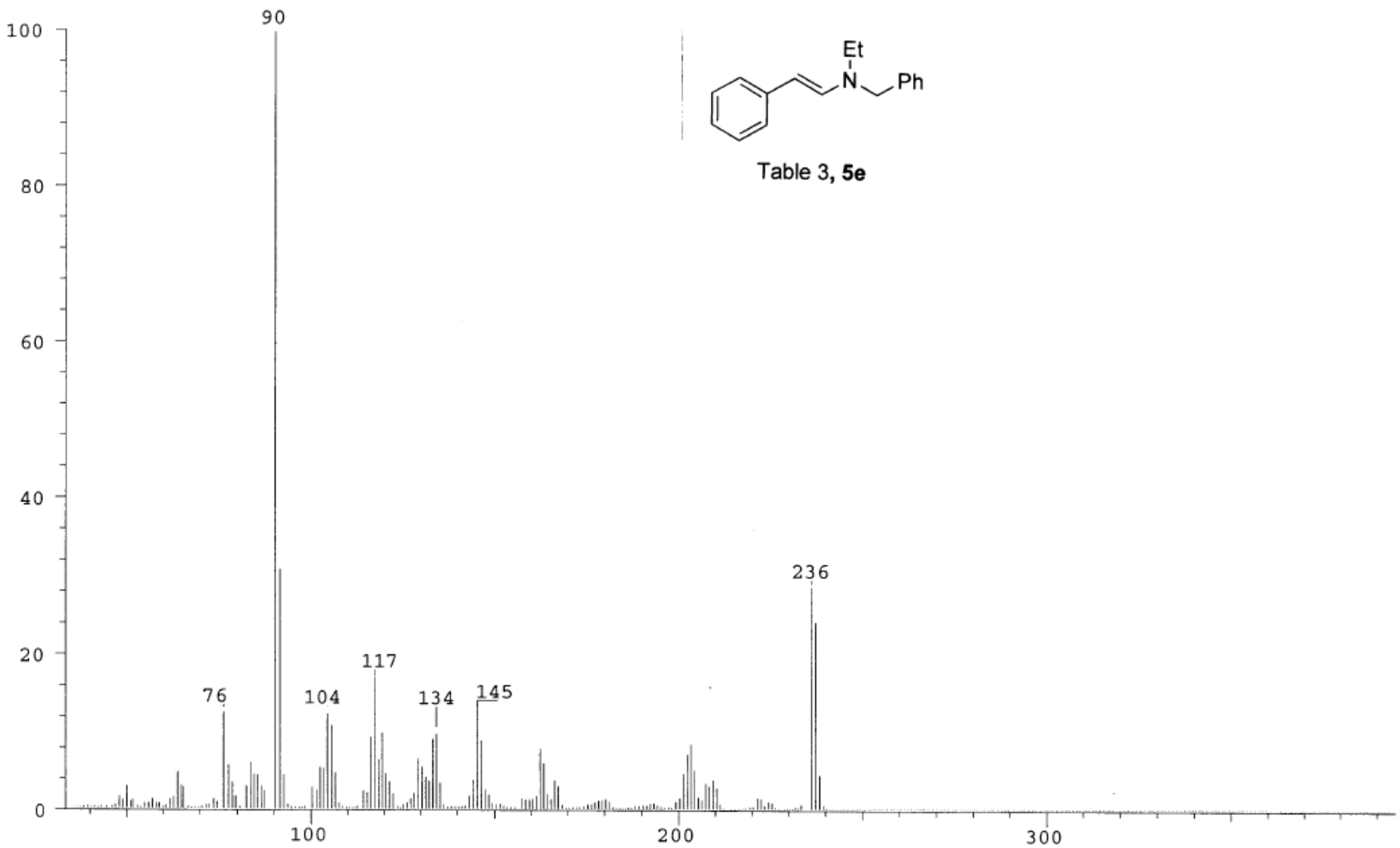


Table 3, **5e**

Date: Fri Jun 3 14:44:00 2005 ICIS: 8.3.0 SP2 for OSF1 (V4.0) build 98-238 from 26-Aug-98

```
LIST:  fin031698                       03-JUN-05  Elapse:  00:25.0     10
Samp:  Venkat                                     Start :  14:43:04    12
Comm:   70 eV EI
Mode:  EI +Q1MS LMR UP LR                         Study :  ms services
Oper:  kh            Client:  Venkat              Inlet :
Base:  90.3                 Inten :  9985963      Masses:  35 > 650
Norm:  90.3                 RIC   :  54426173     #peaks:  616
Peak:  1000.00  mmu
```

No.	Mass	699017 Intensity	%RA	%RIC	Flags
1	76.	1242204	12.44	2.28	F
2	90.	9985963	100.00	18.35	F
3	92.	3070211	30.75	5.64	F
4	104.	1222938	12.25	2.25	F
5	106.	1073174	10.75	1.97	F
6	116.	922130	9.23	1.69	F
7	117.	1691219	16.94	3.11	F
8	119.	978587	9.80	1.80	F
9	133.	896335	8.98	1.65	F
10	134.	965152	9.67	1.77	F
11	145.	1300367	13.02	2.39	F
12	146.	881215	8.82	1.62	F
13	162.	770462	7.72	1.42	F
14	202.	703375	7.04	1.29	F
15	203.	826232	8.27	1.52	F
16	236.	2849573	28.54	5.24	F
17	237.	2409808	24.13	4.43	F

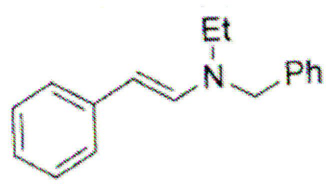


Table 3, **5e**

Manual Peak Matching Report
For Accurate Mass Determination

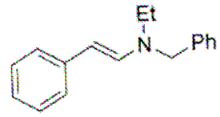


Table 3, **5e**

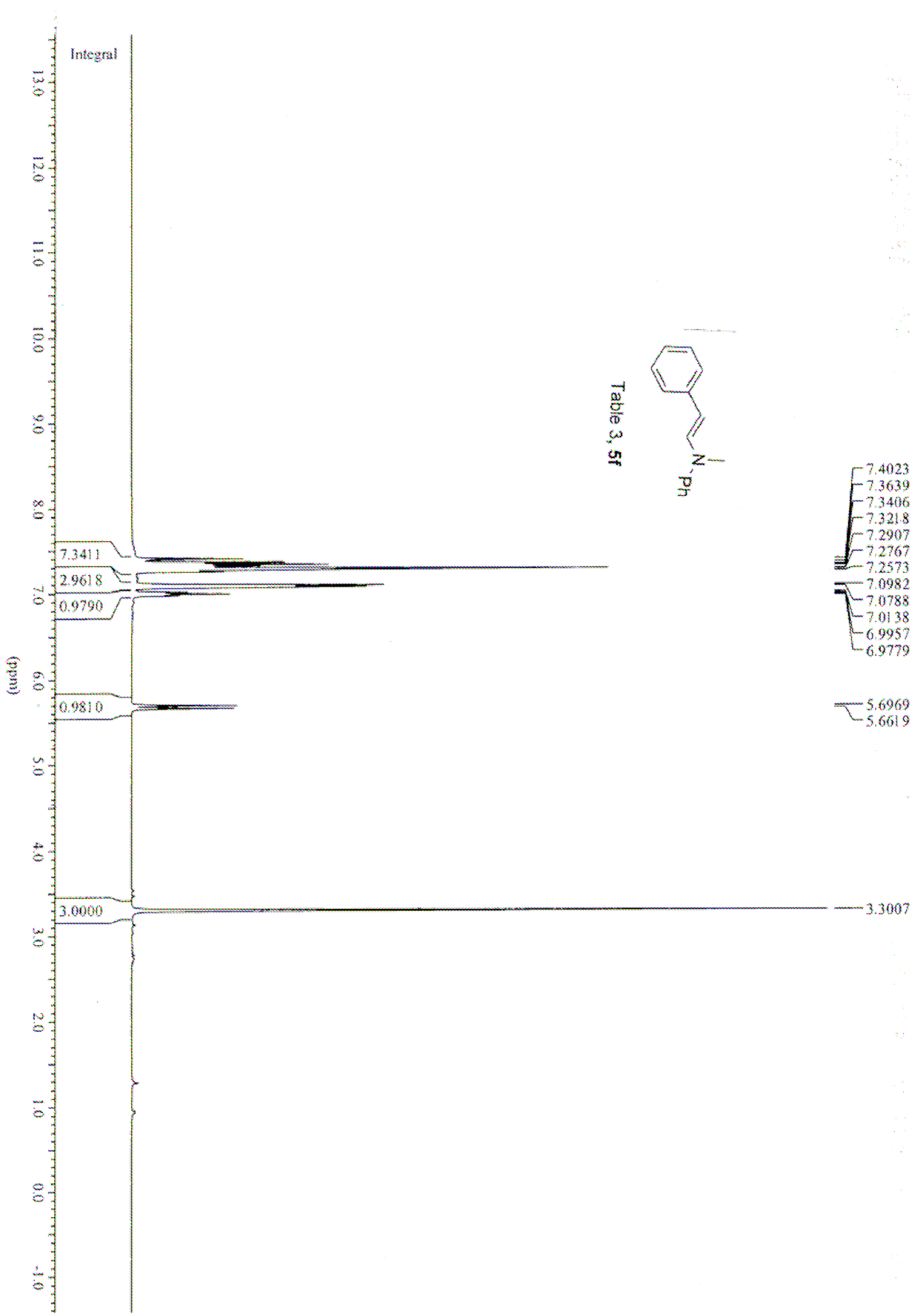
Theoretical mass	Experimental mass	PFK matching mass	Deviation*
237.15175	237.15205	230.98562	1.3 ppm

* The deviation is obtained from the following equation:

$$\text{deviation} = \frac{\text{experimental mass} - \text{theoretical mass}}{\text{nominal mass}}$$

Where nominal mass takes in account only ^{12}C, ^{1}H, ^{16}O, ^{14}N etc...

Theoretical mass correspond to the mass of the most abundant isotope peak


Integral
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
(ppm)
7.3411
2.9618
0.9790
0.9810
3.0000
Table 3, 5f
N
Ph
7.4023
7.3639
7.3406
7.3218
7.2907
7.2767
7.2573
7.0982
7.0788
7.0138
6.9957
6.9779
5.6969
5.6619
3.3007

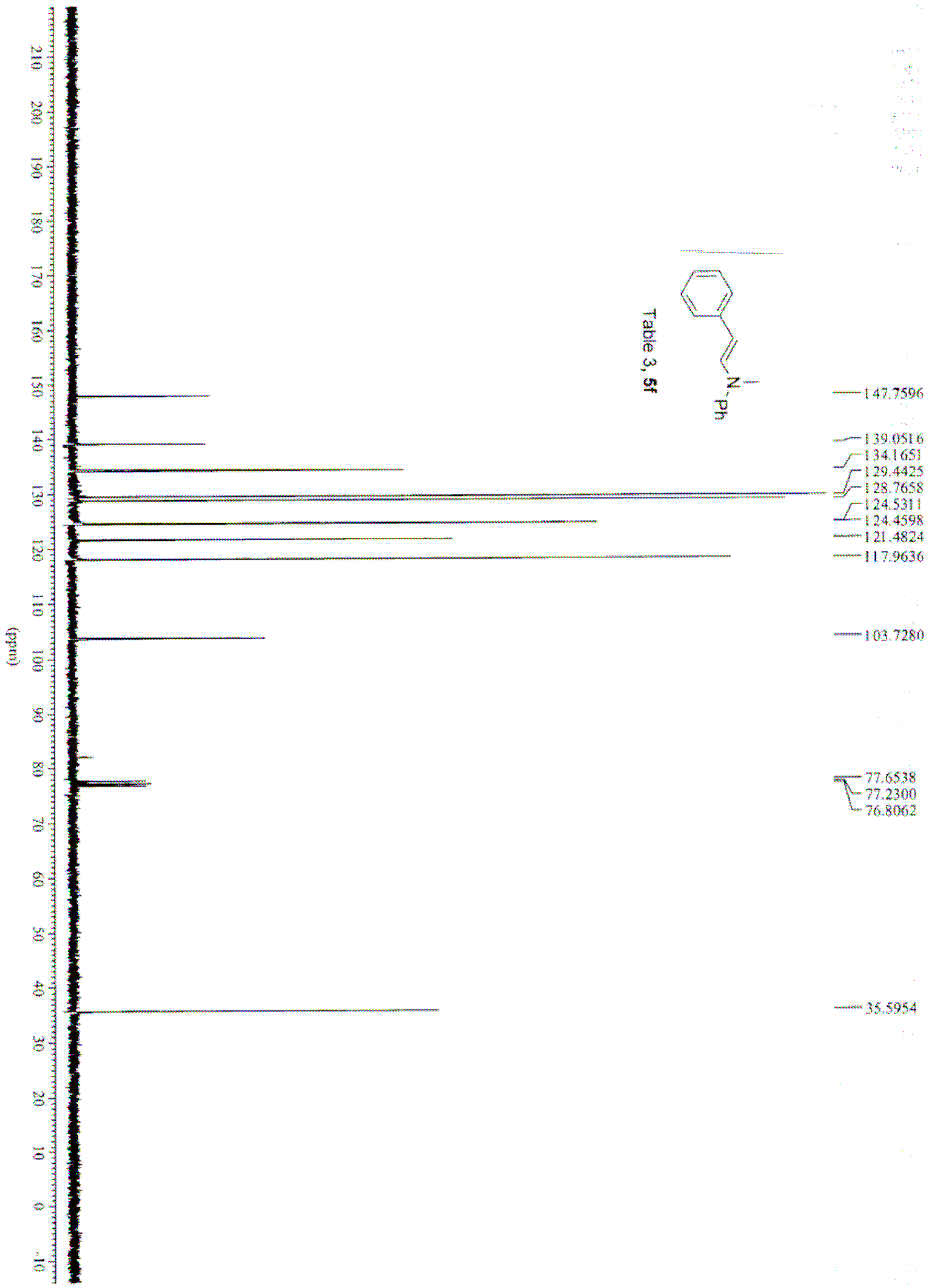
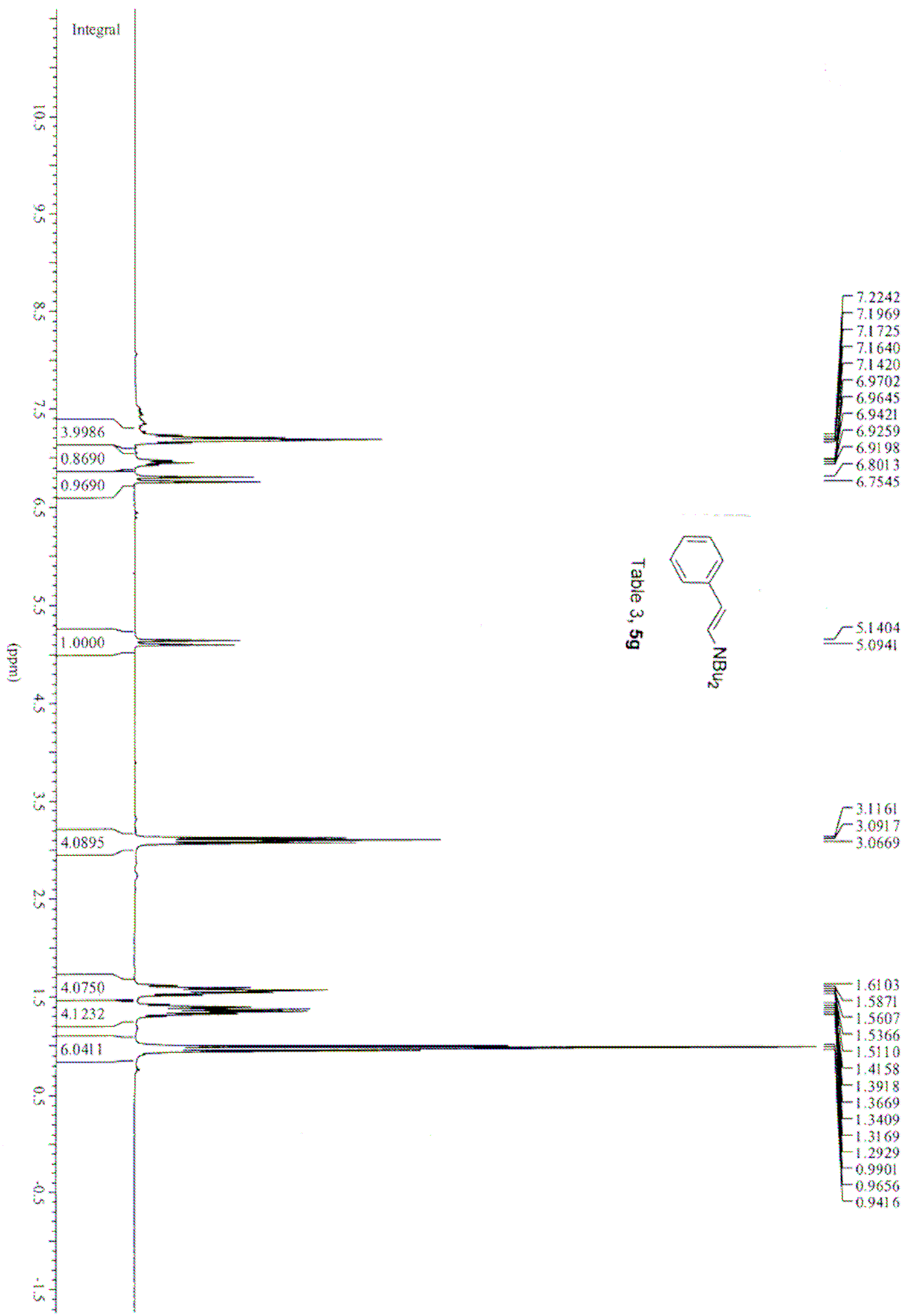
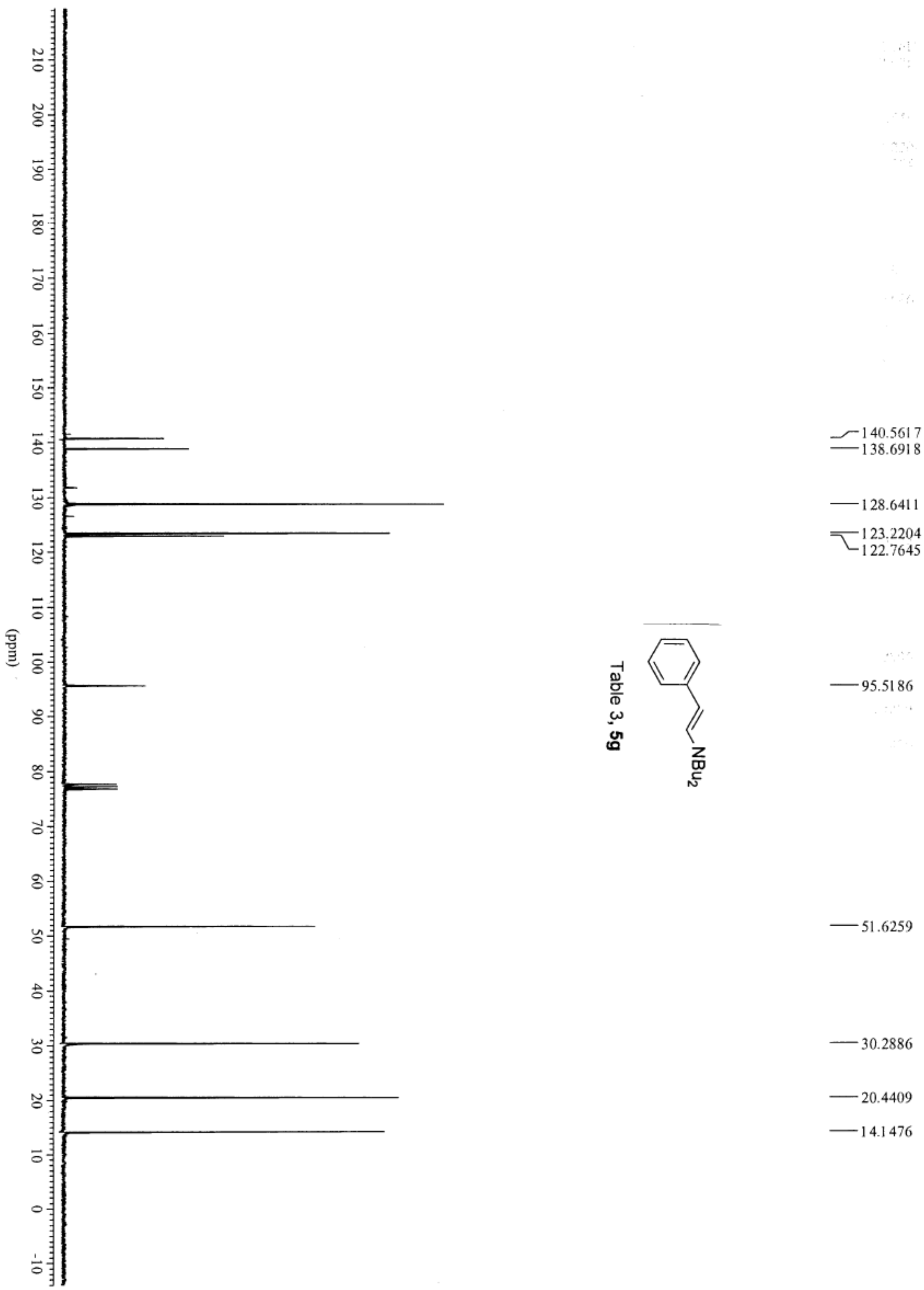
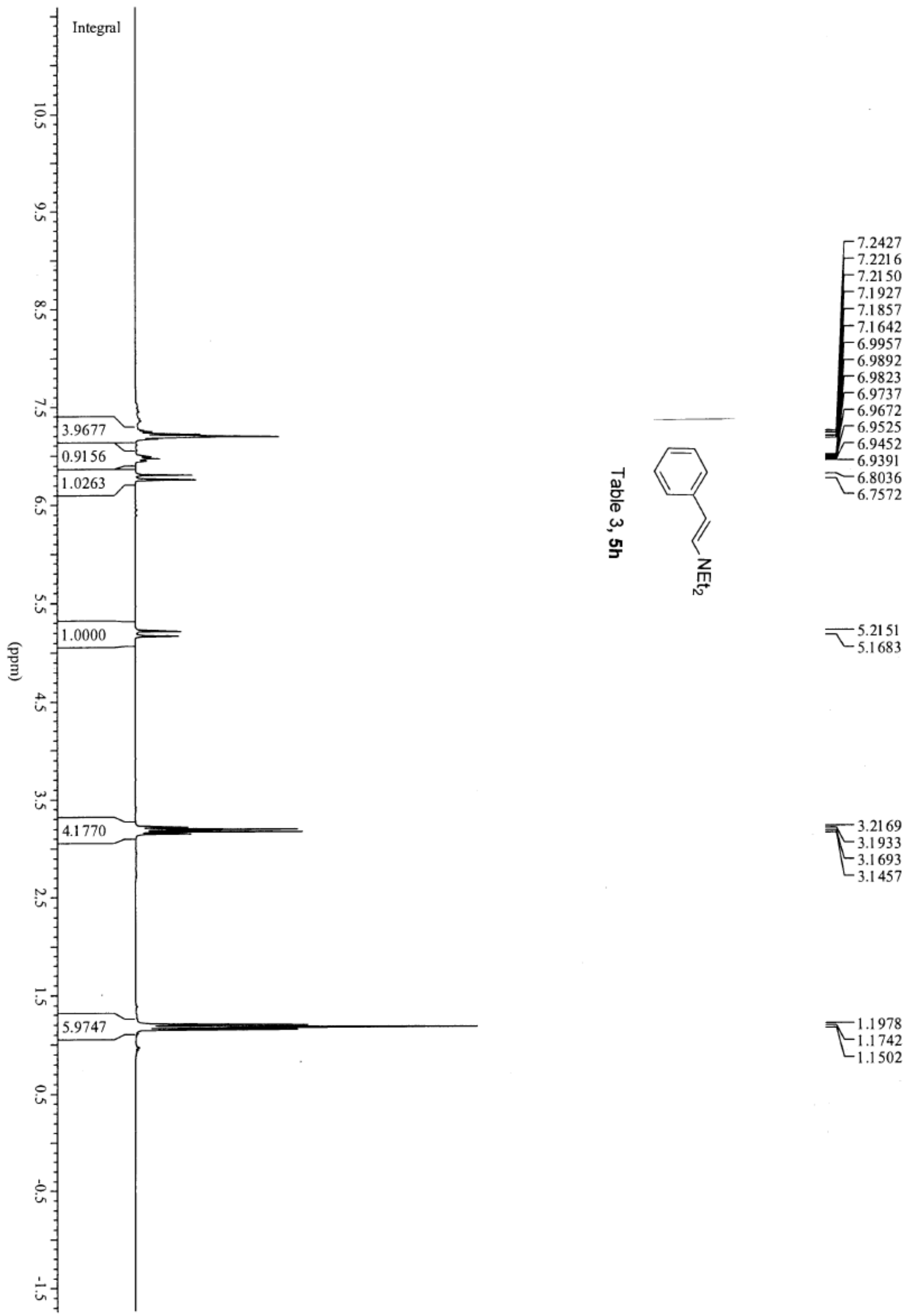


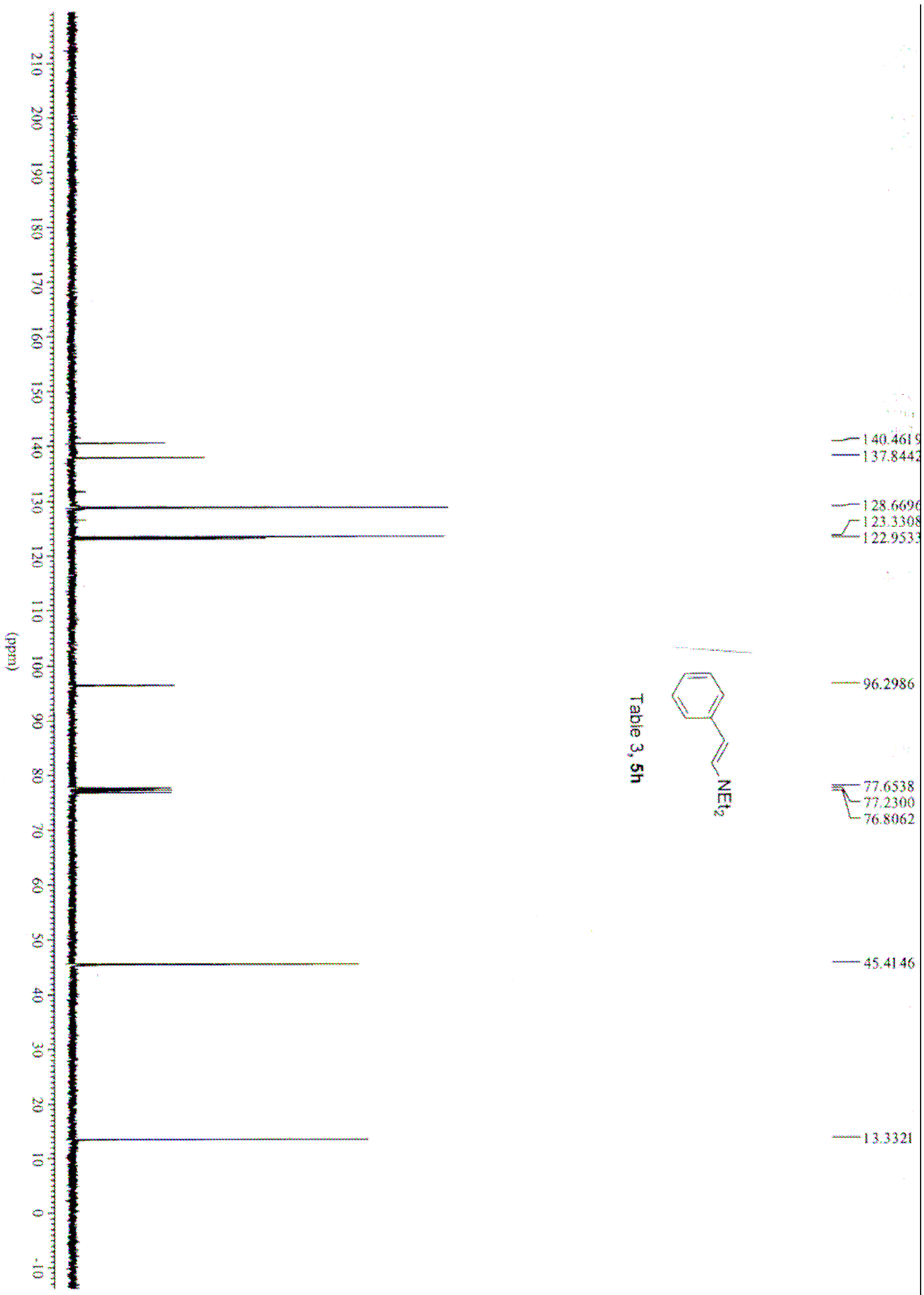
Table 3, 5f
N
Ph
147.7596
139.0516
134.1651
129.4425
128.7658
124.5311
124.4598
121.4824
117.9636
103.7280
77.6538
77.2300
76.8062
35.5954
(ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

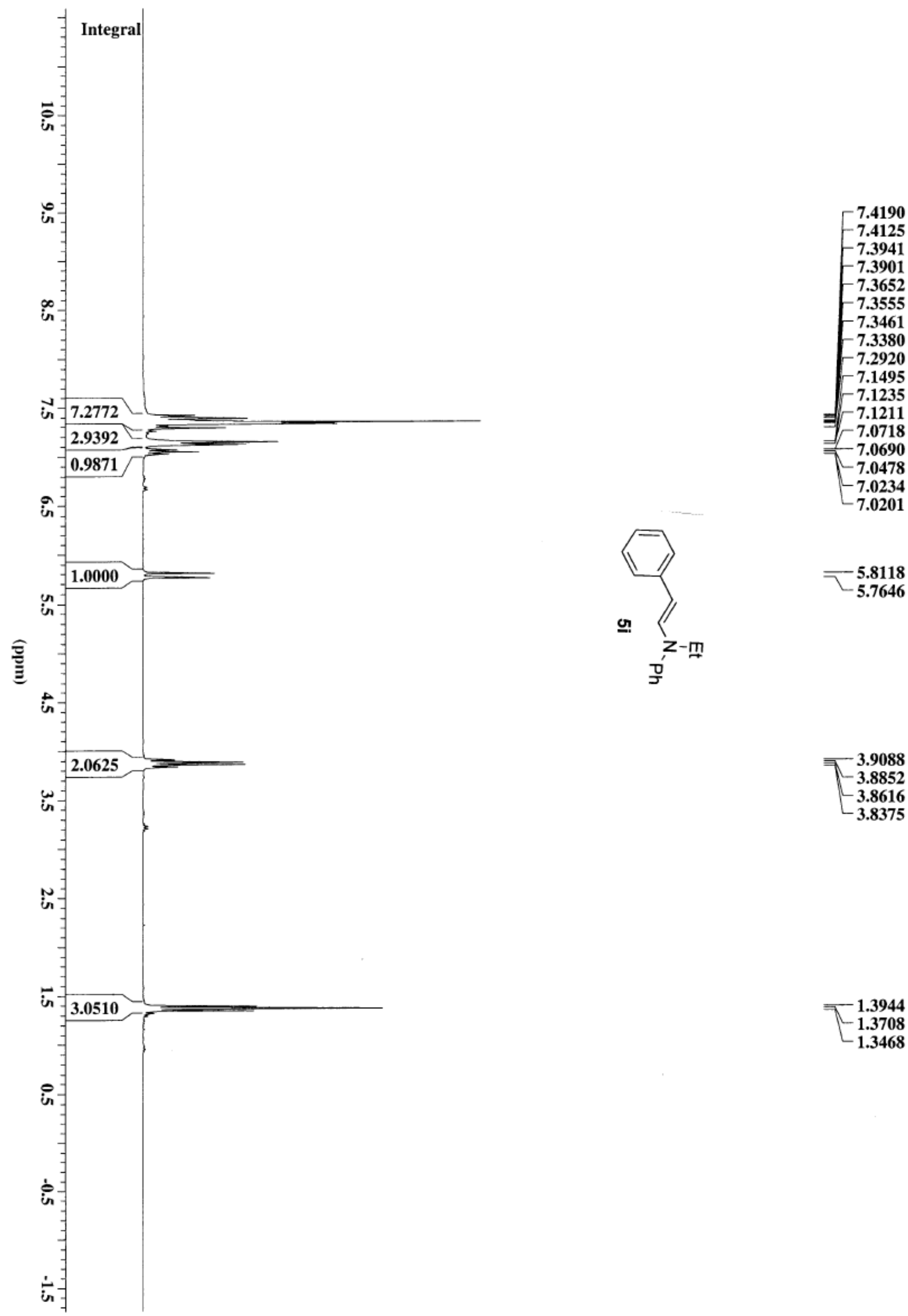

Integral
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
3.9986
0.8690
0.9690
1.0000
4.0895
4.0750
4.1232
6.0411
7.2242
7.1969
7.1725
7.1640
7.1420
6.9702
6.9645
6.9421
6.9259
6.9198
6.8013
6.7545
5.1404
5.0941
3.1161
3.0917
3.0669
1.6103
1.5871
1.5607
1.5366
1.5110
1.4158
1.3918
1.3669
1.3409
1.3169
1.2929
0.9901
0.9656
0.9416
NBu2
Table 3, 5g

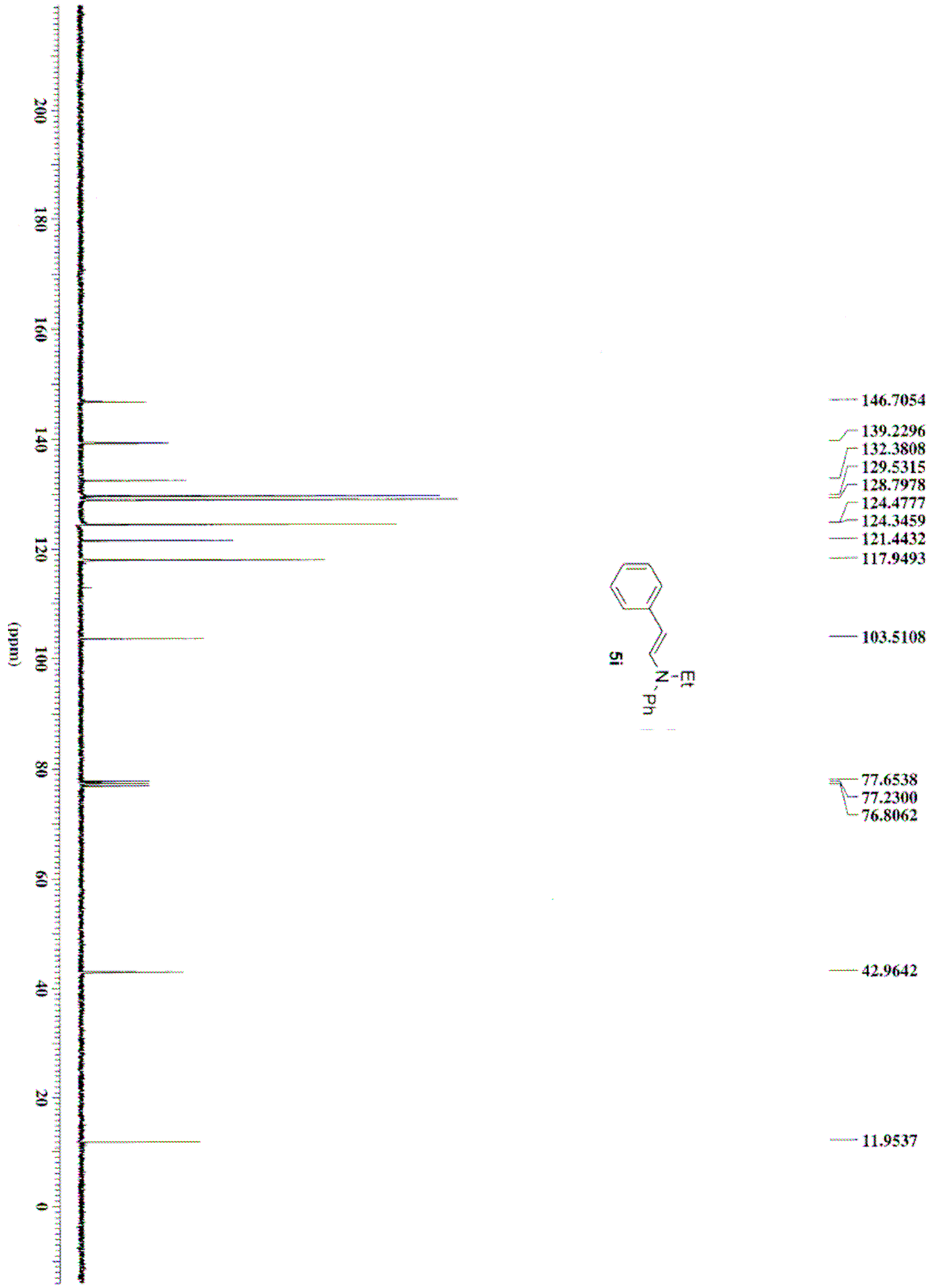


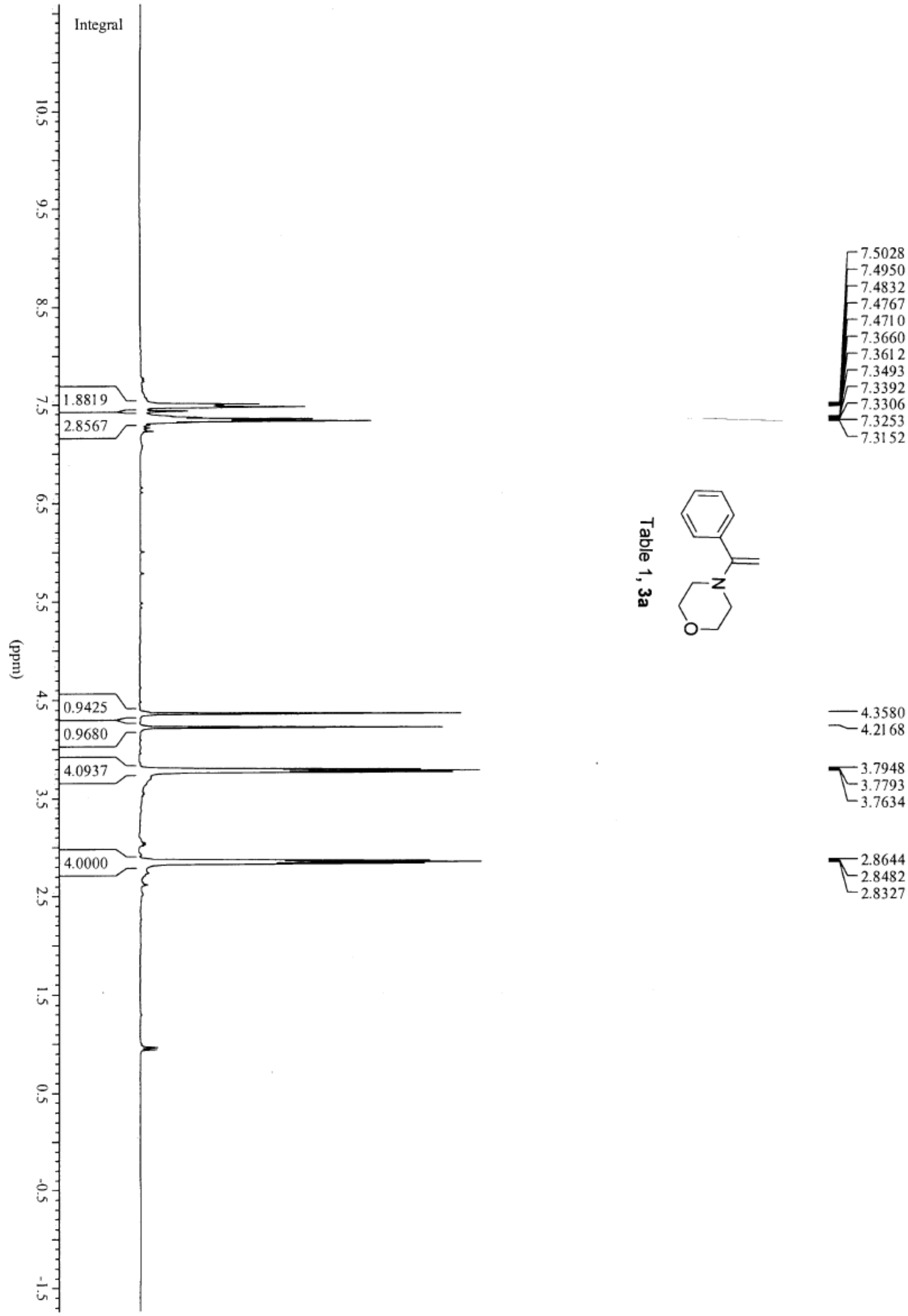
140.5617
138.6918
128.6411
123.2204
122.7645
95.5186
51.6259
30.2886
20.4409
14.1476
Table 3, 5g
NBu2
(ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


Integral
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
3.9677
0.9156
1.0263
1.0000
4.1770
5.9747
7.2427
7.2216
7.2150
7.1927
7.1857
7.1642
6.9957
6.9892
6.9823
6.9737
6.9672
6.9525
6.9452
6.9391
6.8036
6.7572
5.2151
5.1683
3.2169
3.1933
3.1693
3.1457
1.1978
1.1742
1.1502
NEt2
Table 3, 5h


140.4619
137.8442
128.6696
123.3308
122.9533
96.2986
77.6538
77.2300
76.8062
45.4146
13.3321
Table 3, 5h
NEt2
(ppm)


Integral
7.2772
2.9392
0.9871
1.0000
2.0625
3.0510
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
7.4190
7.4125
7.3941
7.3901
7.3652
7.3555
7.3461
7.3380
7.2920
7.1495
7.1235
7.1211
7.0718
7.0690
7.0478
7.0234
7.0201
5.8118
5.7646
3.9088
3.8852
3.8616
3.8375
1.3944
1.3708
1.3468
Et
N
Ph
5i


146.7054
139.2296
132.3808
129.5315
128.7978
124.4777
124.3459
121.4432
117.9493
103.5108
77.6538
77.2300
76.8062
42.9642
11.9537
5i
Et
N
Ph
(ppm)
200
180
160
140
120
100
80
60
40
20
0


Integral
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
1.8819
2.8567
0.9425
0.9680
4.0937
4.0000
7.5028
7.4950
7.4832
7.4767
7.4710
7.3660
7.3612
7.3493
7.3392
7.3306
7.3253
7.3152
4.3580
4.2168
3.7948
3.7793
3.7634
2.8644
2.8482
2.8327
N
O
Table 1, 3a

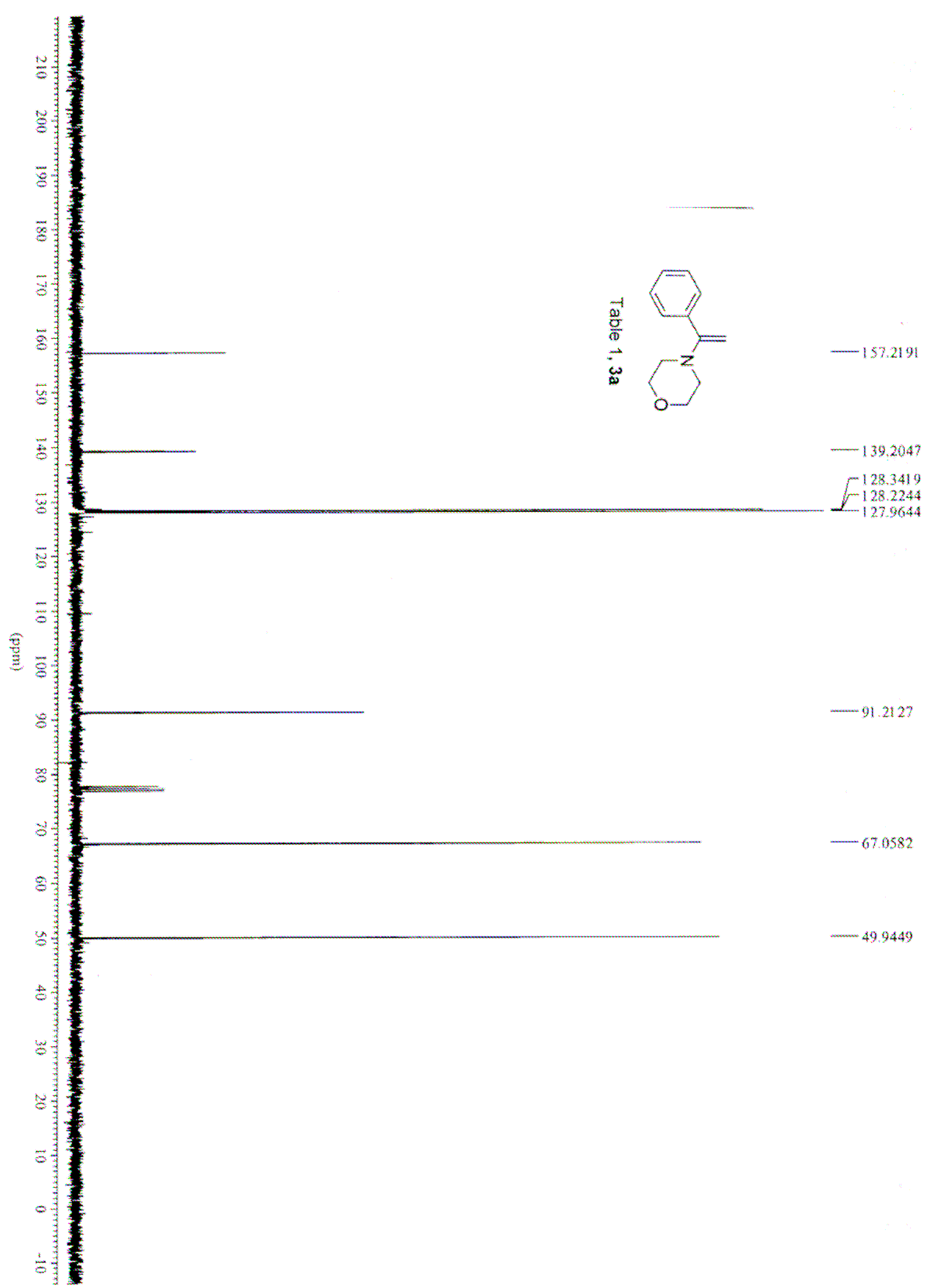
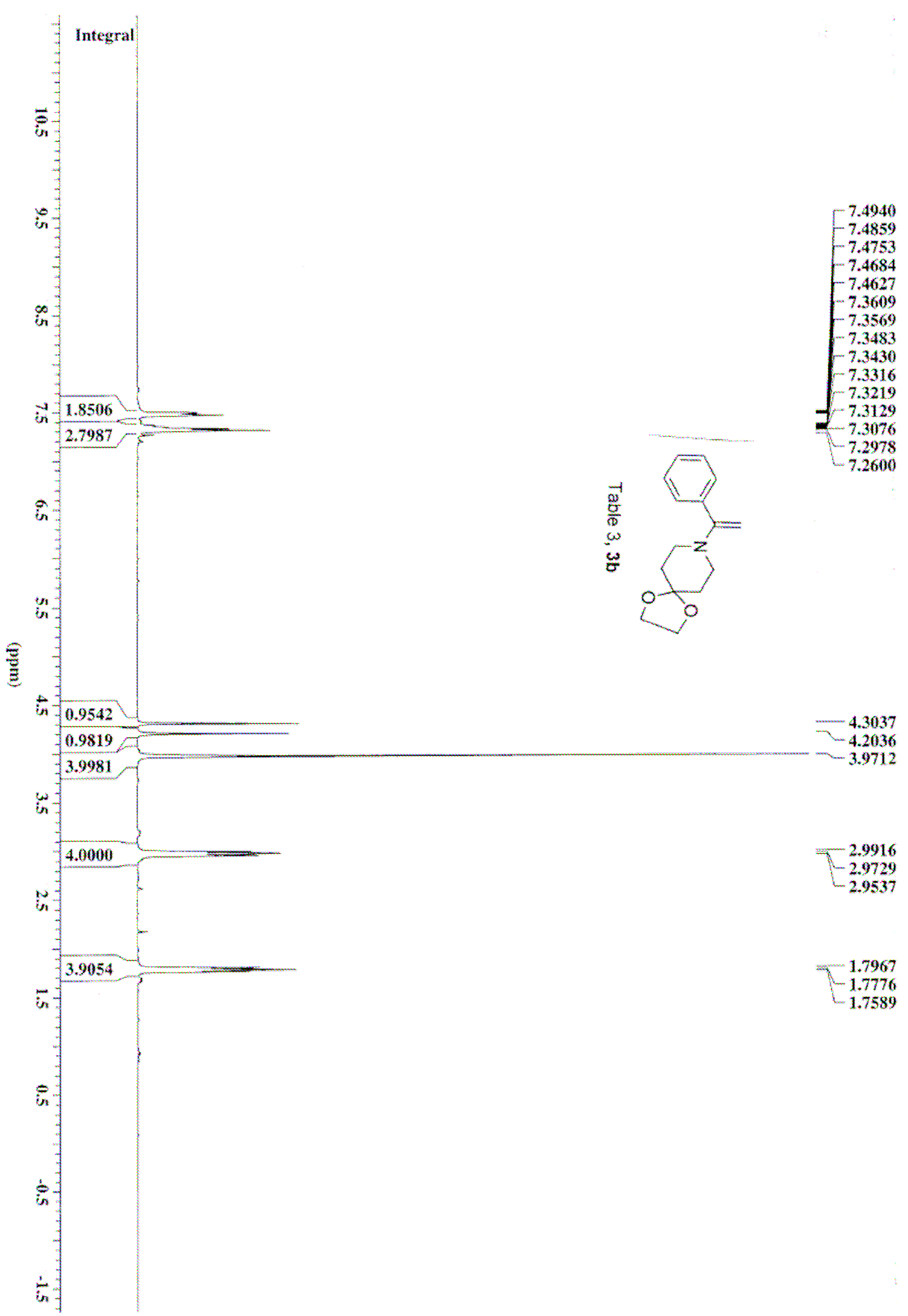


Table 1, 3a
157.2191
139.2047
128.3419
128.2244
127.9644
91.2127
67.0582
49.9449
(ppm)


Integral
1.8506
2.7987
0.9542
0.9819
3.9981
4.0000
3.9054
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
7.4940
7.4859
7.4753
7.4684
7.4627
7.3609
7.3569
7.3483
7.3430
7.3316
7.3219
7.3129
7.3076
7.2978
7.2600
4.3037
4.2036
3.9712
2.9916
2.9729
2.9537
1.7967
1.7776
1.7589
Table 3, 3b
N
O
O

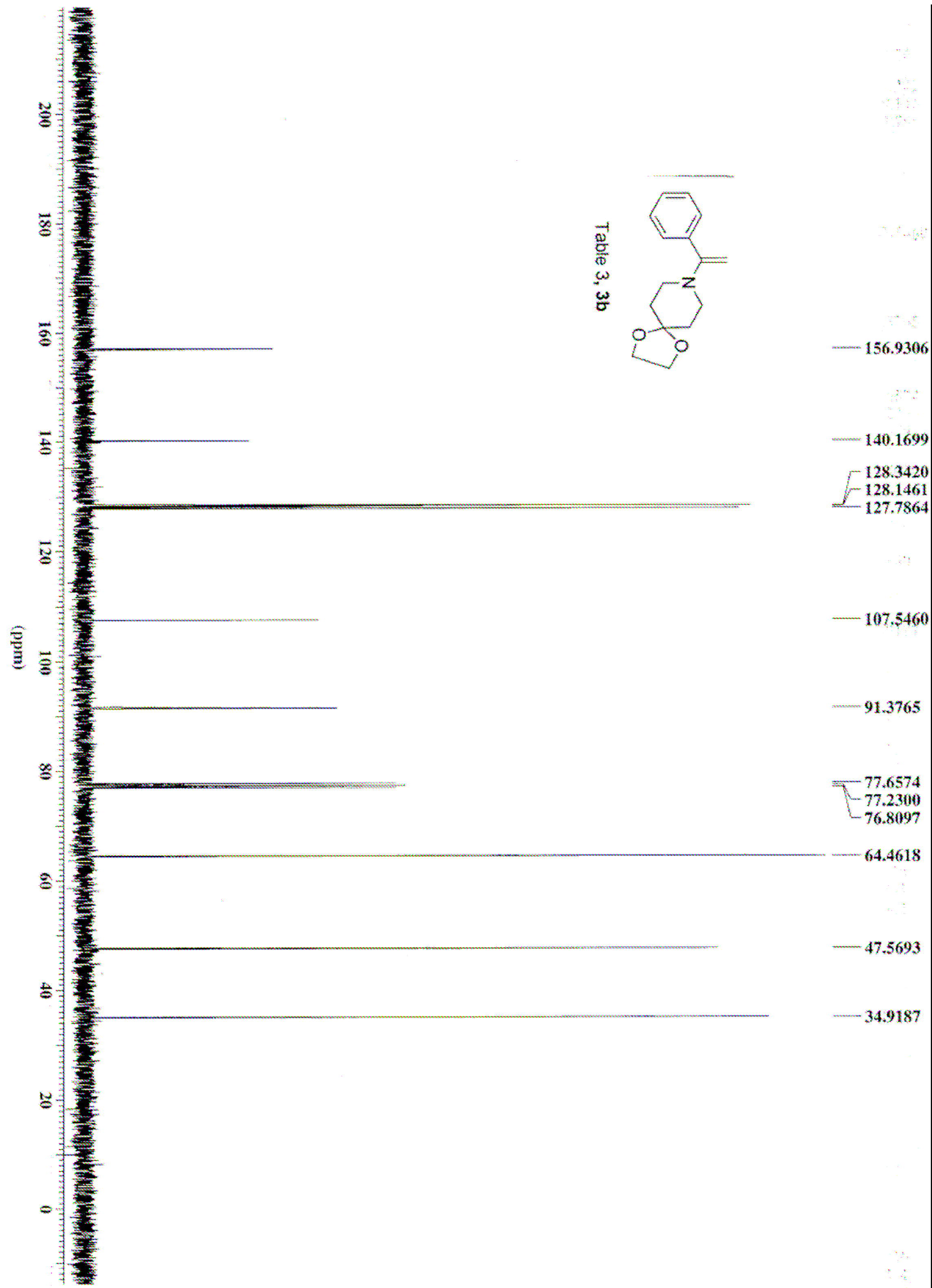
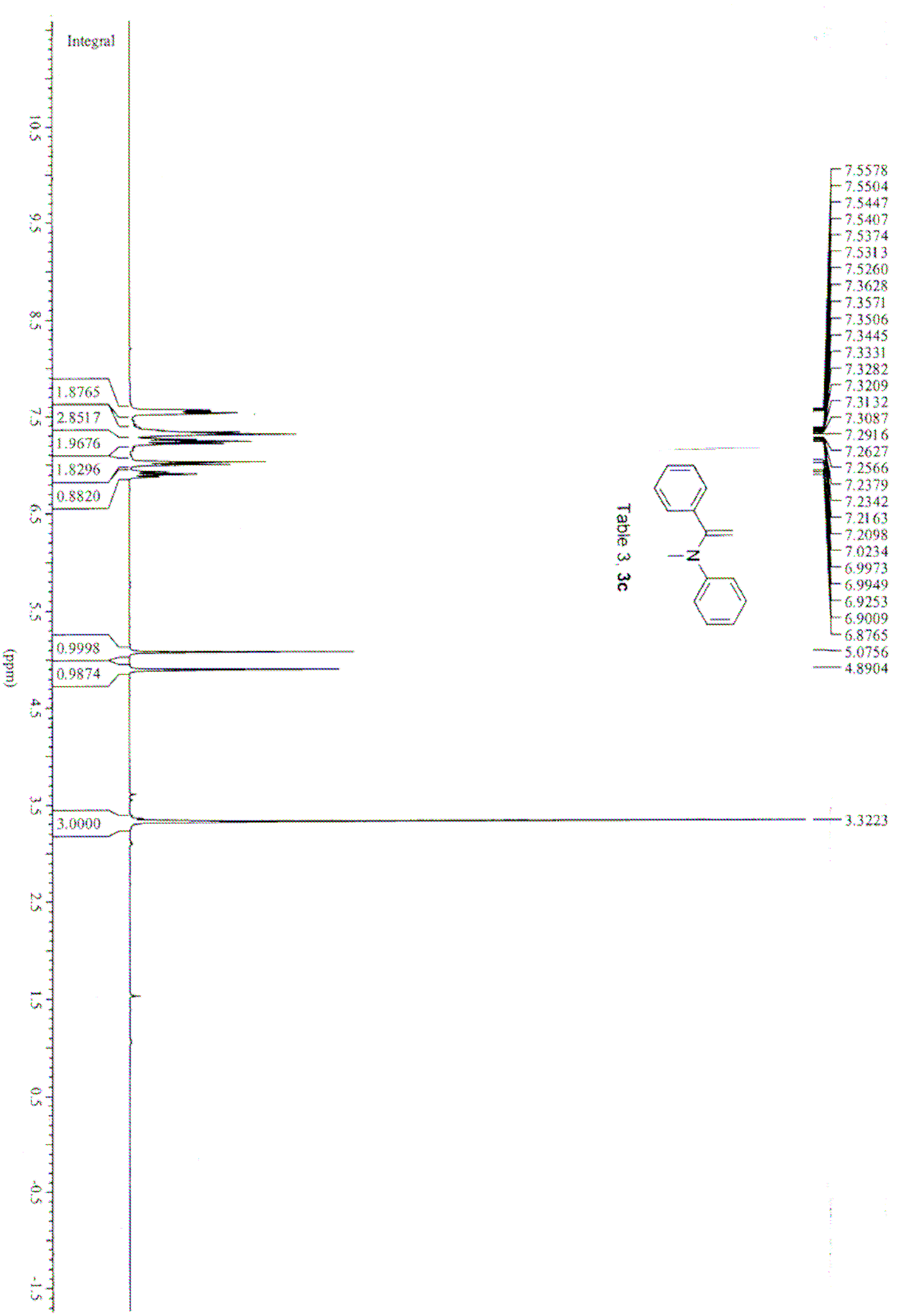


Table 3, 3b
156.9306
140.1699
128.3420
128.1461
127.7864
107.5460
91.3765
77.6574
77.2300
76.8097
64.4618
47.5693
34.9187
(ppm)
200
180
160
140
120
100
80
60
40
20
0


Integral
1.8765
2.8517
1.9676
1.8296
0.8820
0.9998
0.9874
3.0000
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
7.5578
7.5504
7.5447
7.5407
7.5374
7.5313
7.5260
7.3628
7.3571
7.3506
7.3445
7.3331
7.3282
7.3209
7.3132
7.3087
7.2916
7.2627
7.2566
7.2379
7.2342
7.2163
7.2098
7.0234
6.9973
6.9949
6.9253
6.9009
6.8765
5.0756
4.8904
3.3223
N
Table 3, 3c

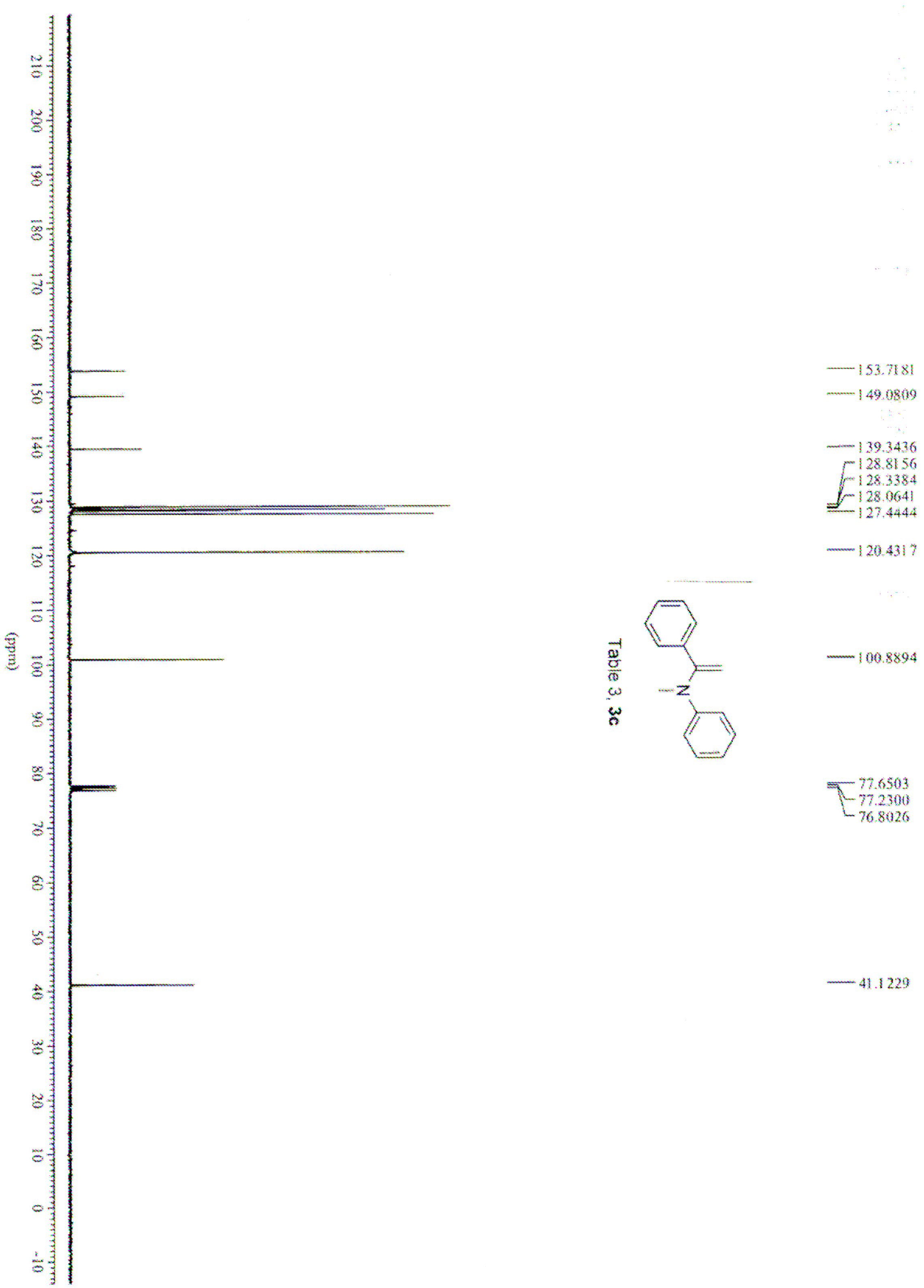
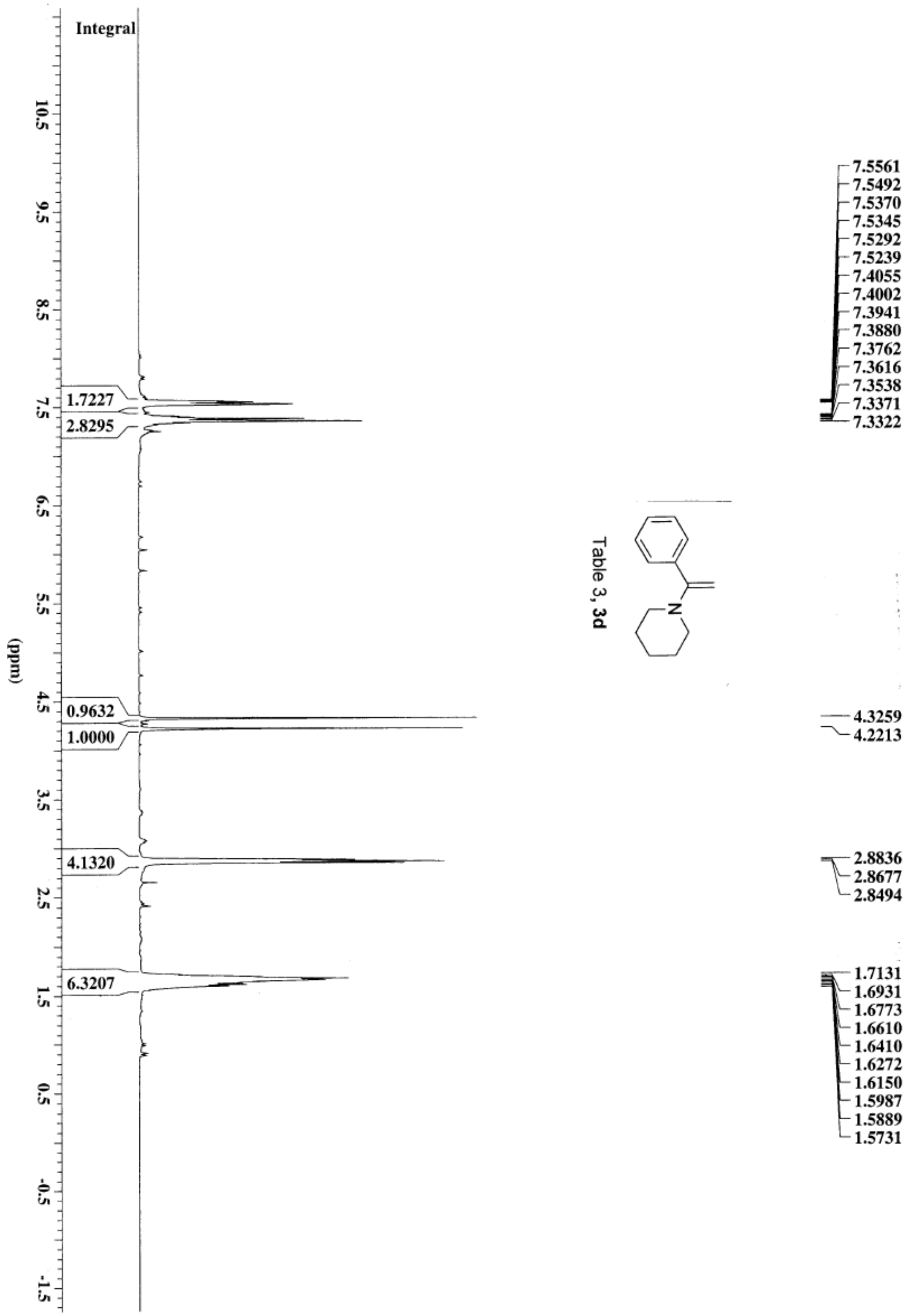
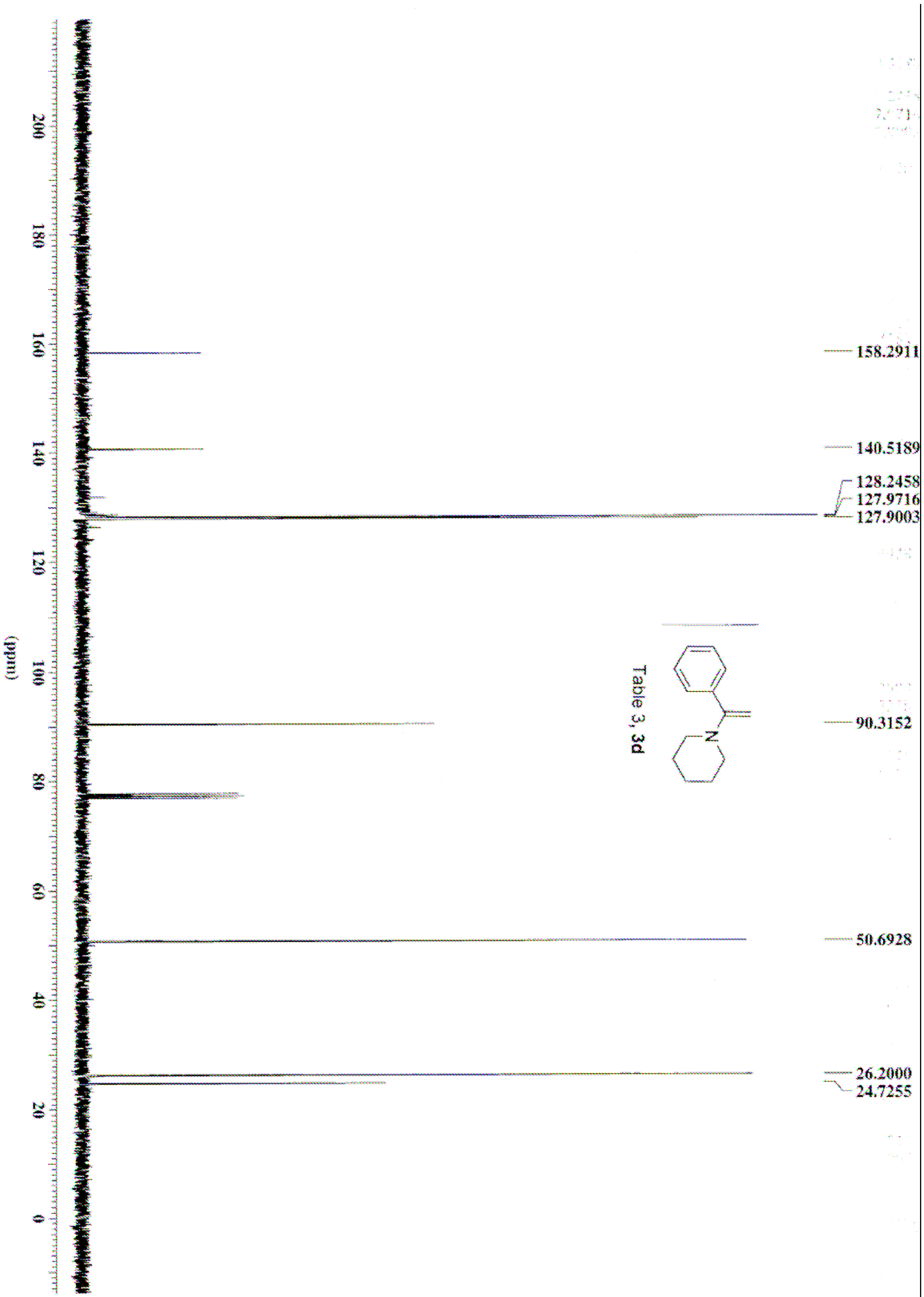
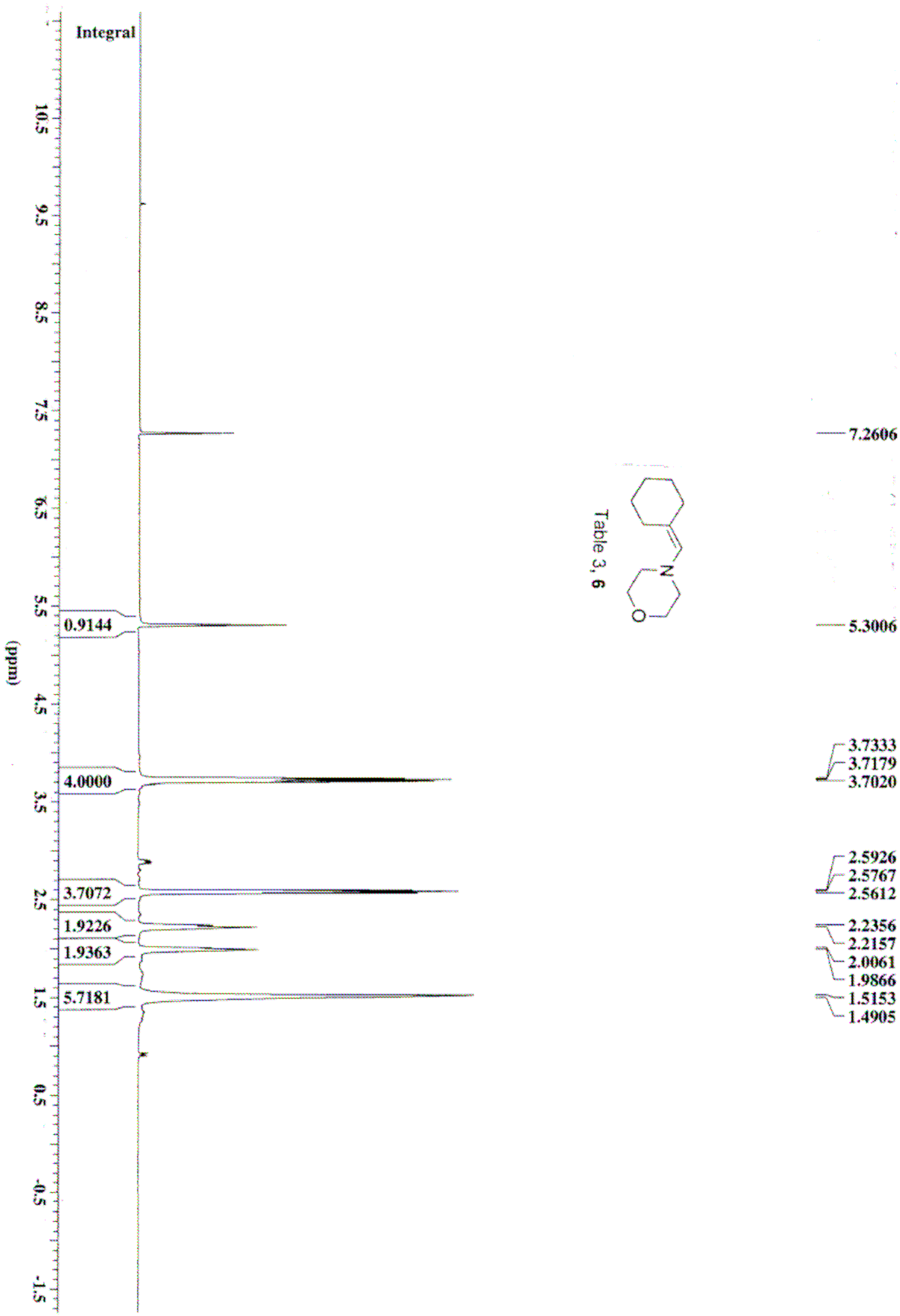
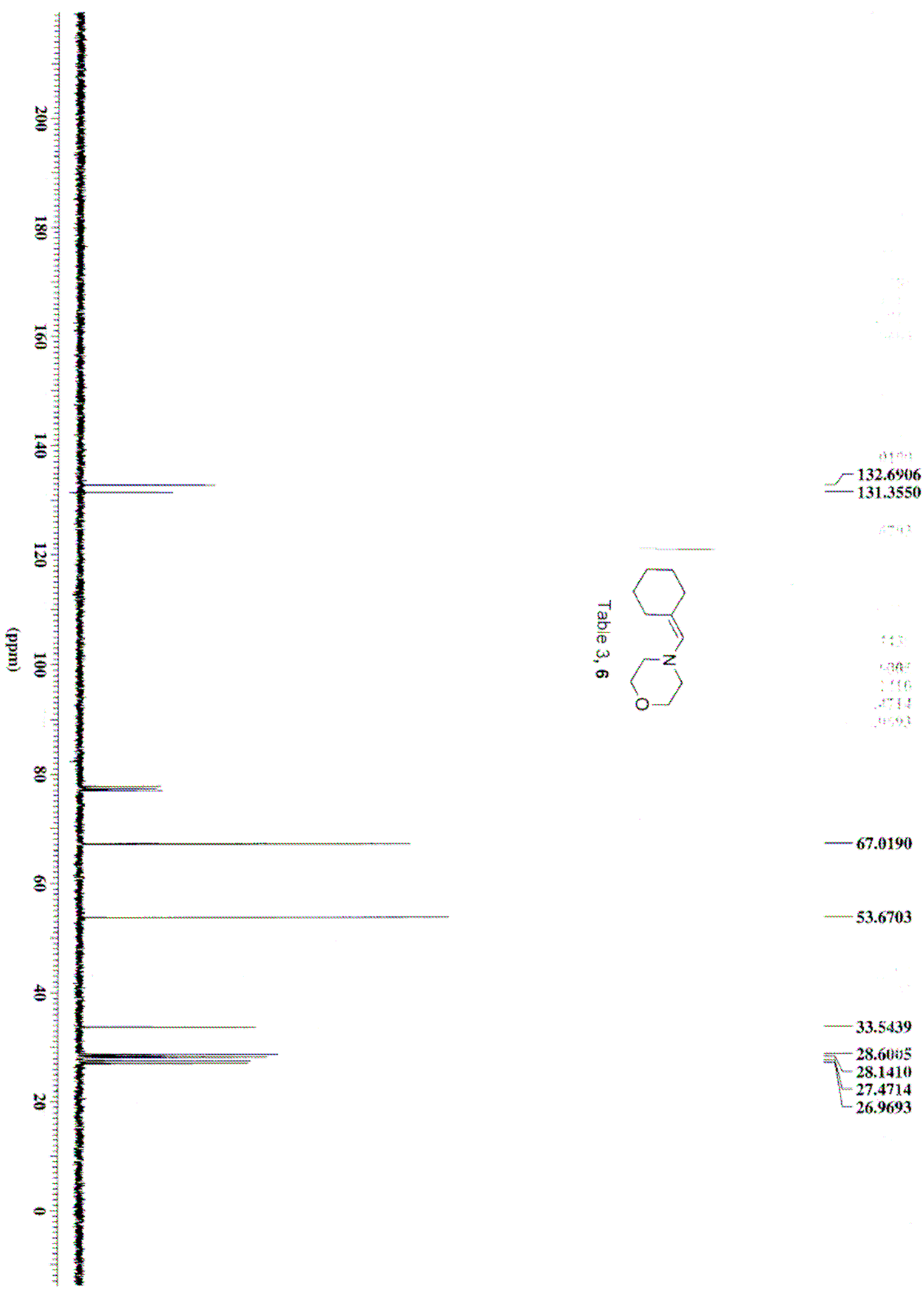


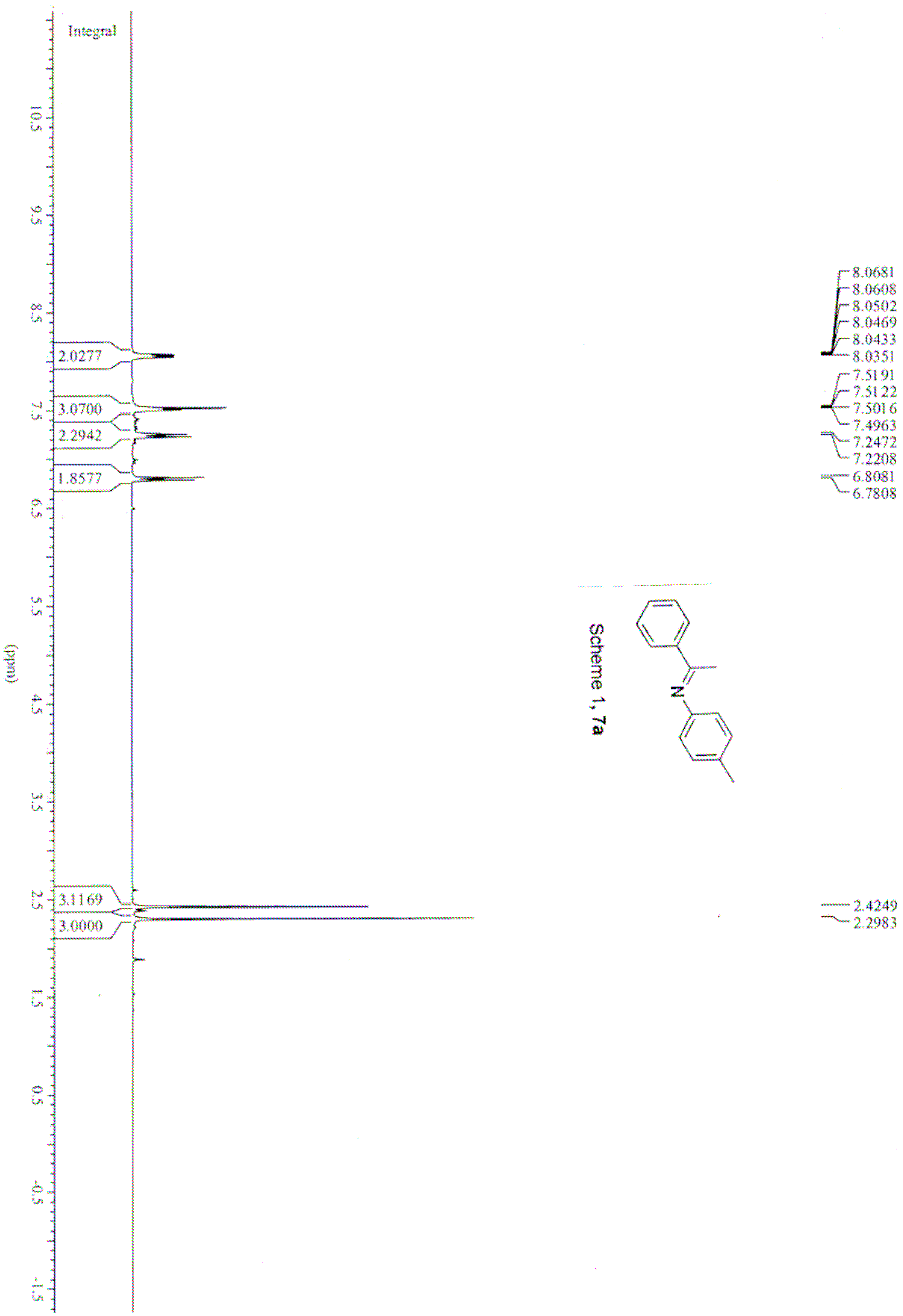
Table 3, 3c
153.7181
149.0809
139.3436
128.8156
128.3384
128.0641
127.4444
120.4317
100.8894
77.6503
77.2300
76.8026
41.1229
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
(ppm)

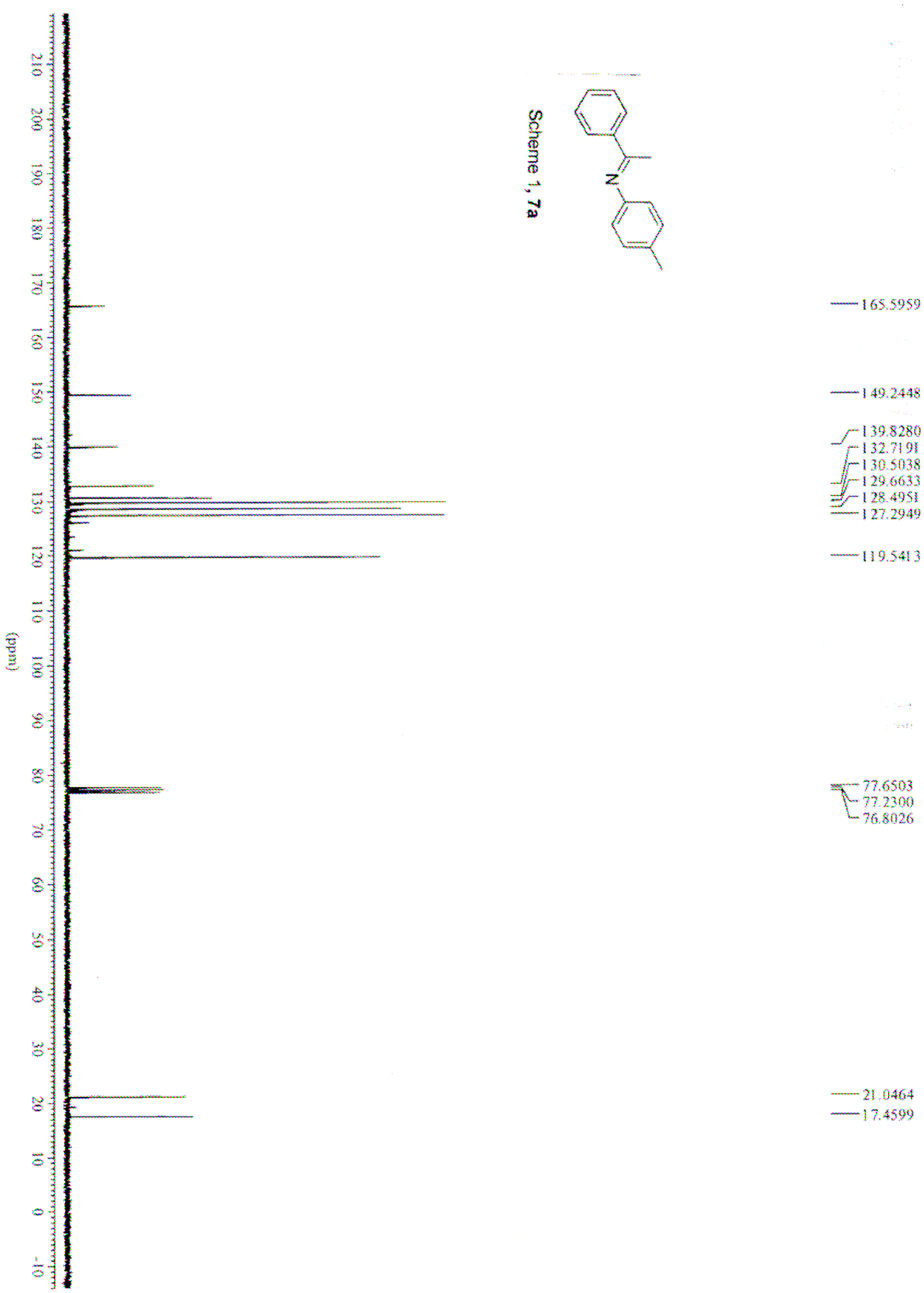

Integral
1.7227
2.8295
0.9632
1.0000
4.1320
6.3207
(ppm)
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
7.5561
7.5492
7.5370
7.5345
7.5292
7.5239
7.4055
7.4002
7.3941
7.3880
7.3762
7.3616
7.3538
7.3371
7.3322
4.3259
4.2213
2.8836
2.8677
2.8494
1.7131
1.6931
1.6773
1.6610
1.6410
1.6272
1.6150
1.5987
1.5889
1.5731
N
Table 3, **3d**

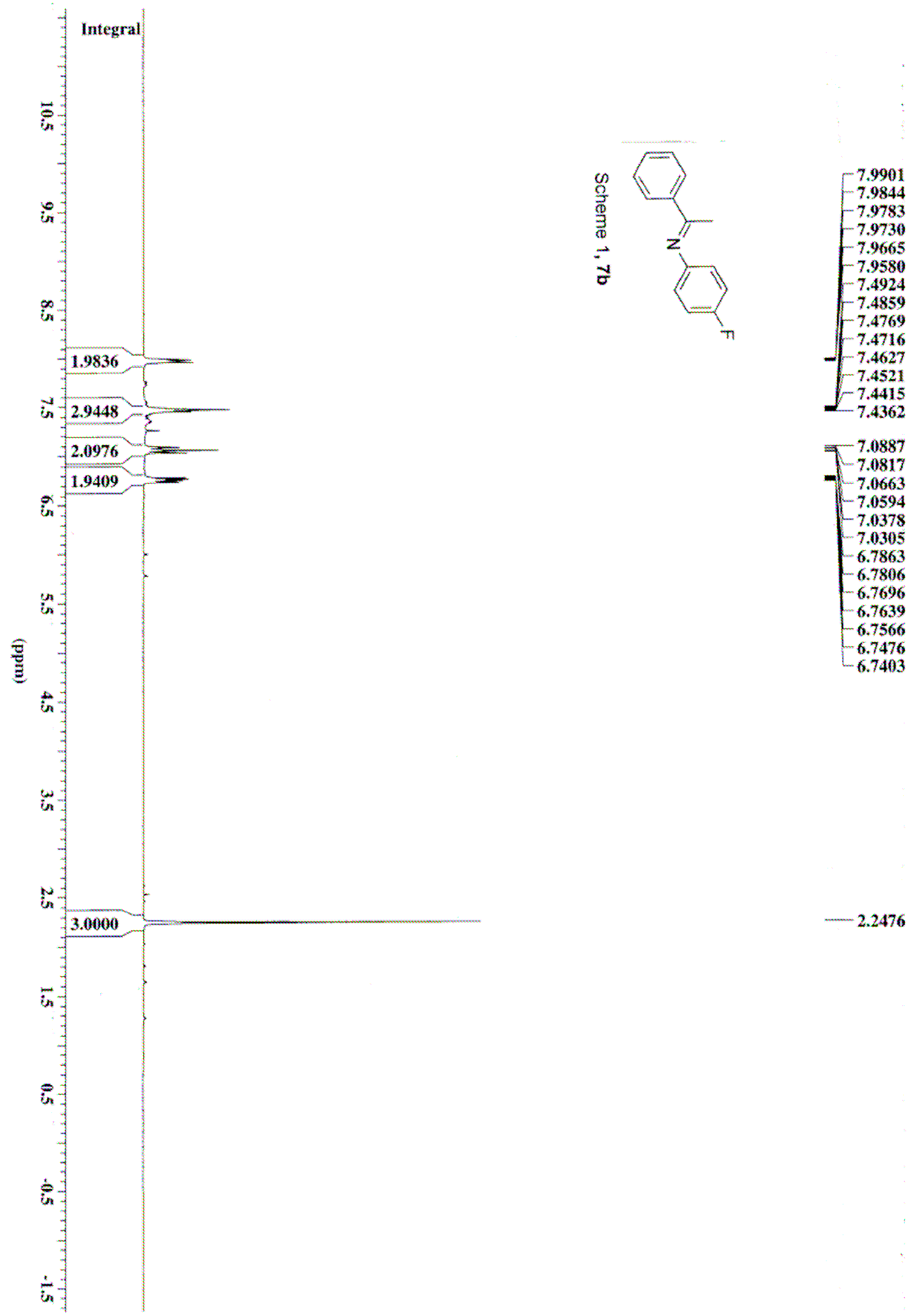

158.2911
140.5189
128.2458
127.9716
127.9003
90.3152
50.6928
26.2000
24.7255
Table 3, 3d
N
(ppm)
200
180
160
140
120
100
80
60
40
20
0

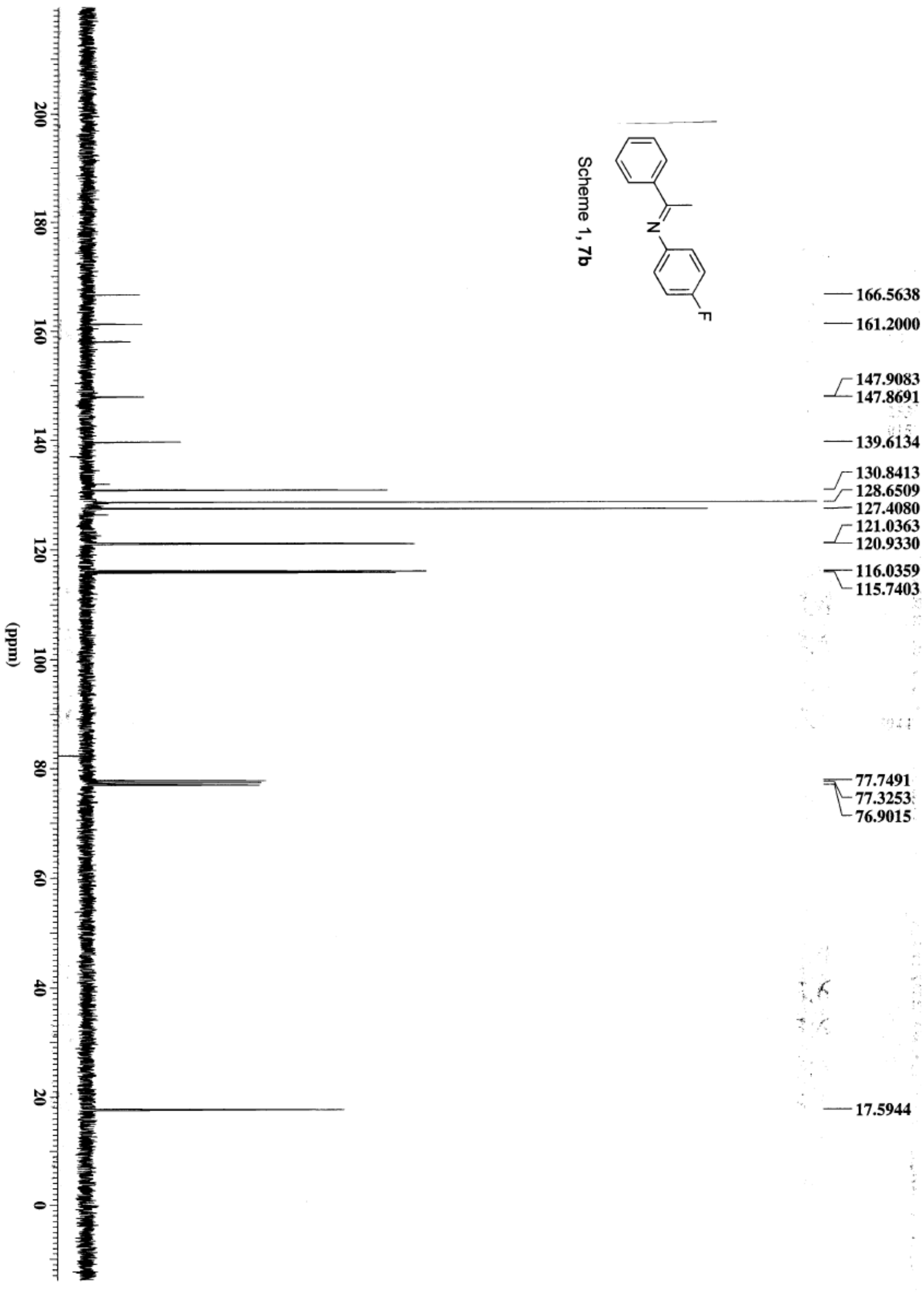

Integral
0.9144
4.0000
3.7072
1.9226
1.9363
5.7181
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
Table 3, 6
N
O
7.2606
5.3006
3.7333
3.7179
3.7020
2.5926
2.5767
2.5612
2.2356
2.2157
2.0061
1.9866
1.5153
1.4905

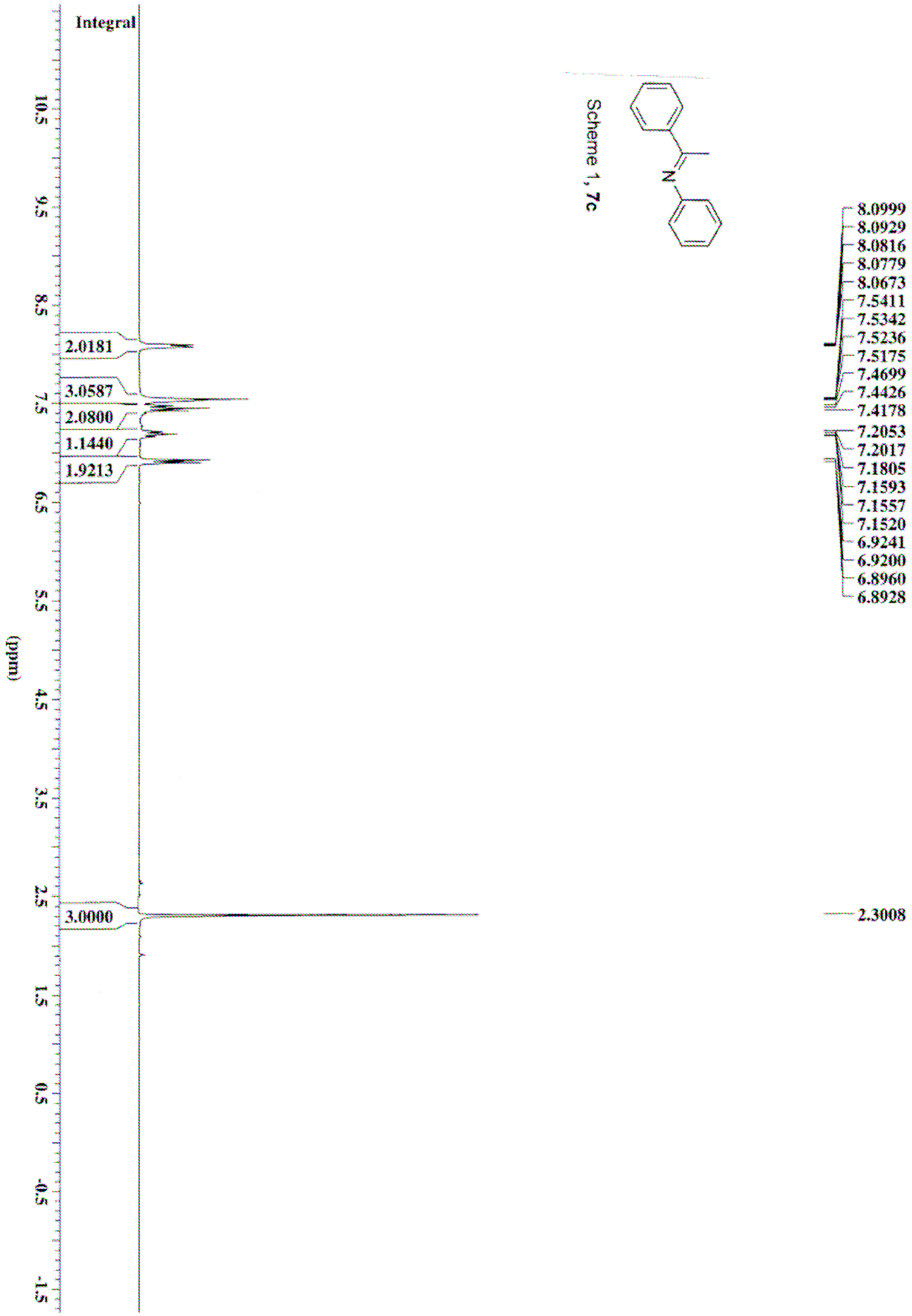

132.6906
131.3550
67.0190
53.6703
33.5439
28.6005
28.1410
27.4714
26.9693
Table 3, 6
(ppm)
200
180
160
140
120
100
80
60
40
20
0

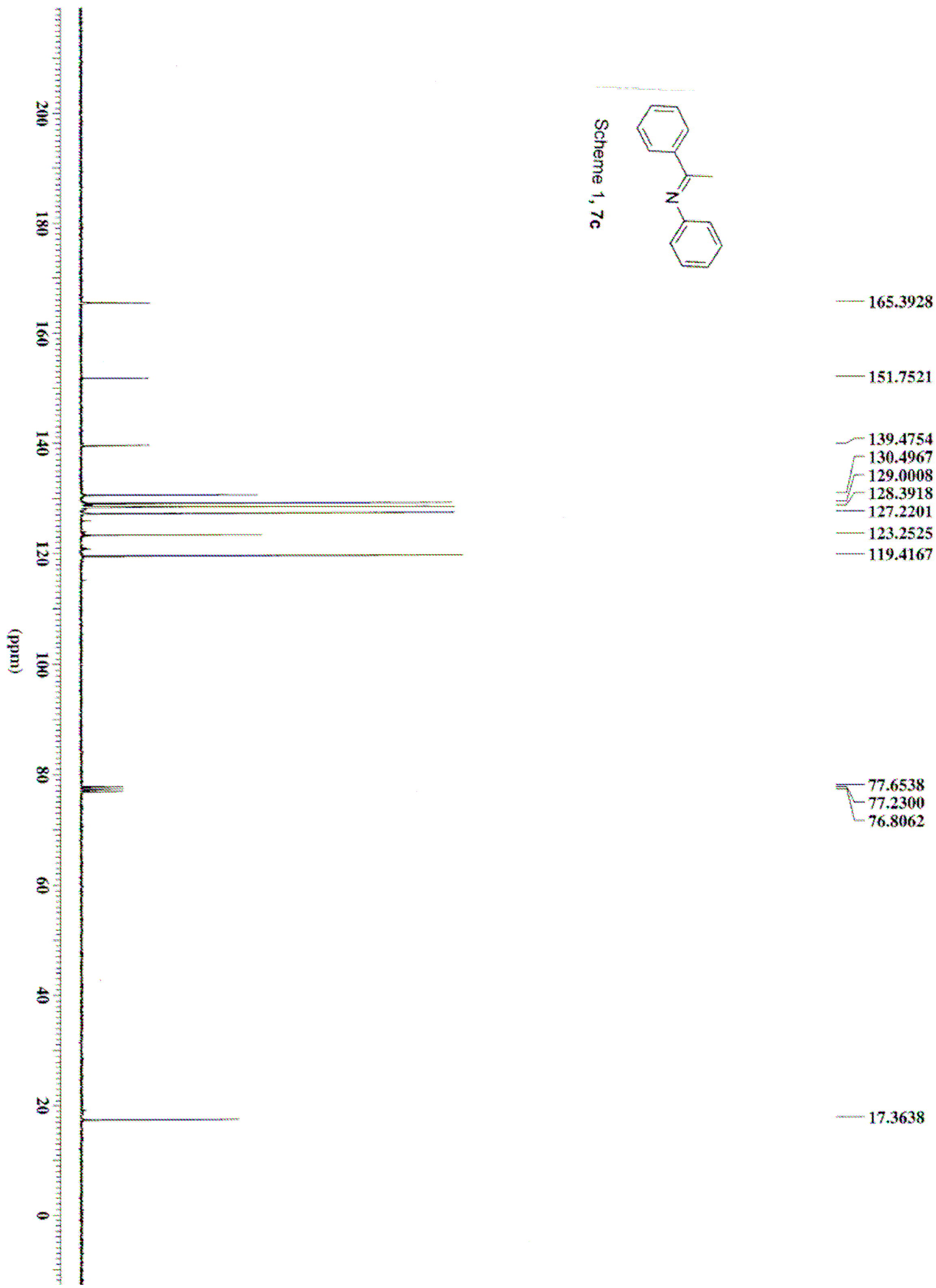

Integral
2.0277
3.0700
2.2942
1.8577
3.1169
3.0000
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
8.0681
8.0608
8.0502
8.0469
8.0433
8.0351
7.5191
7.5122
7.5016
7.4963
7.2472
7.2208
6.8081
6.7808
2.4249
2.2983
N
Scheme 1, 7a

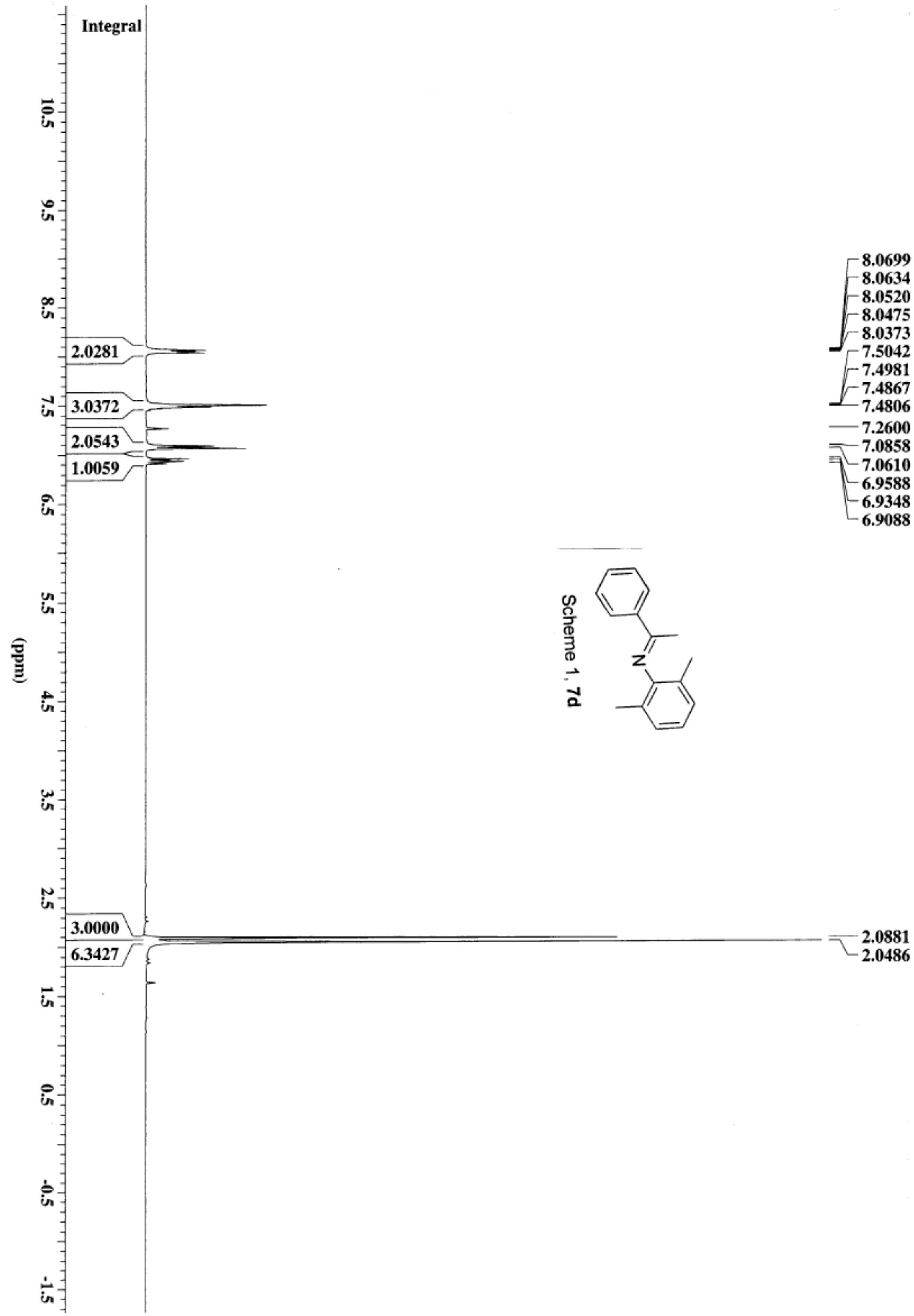

Scheme 1, 7a
N
165.5959
149.2448
139.8280
132.7191
130.5038
129.6633
128.4951
127.2949
119.5413
77.6503
77.2300
76.8026
21.0464
17.4599
(ppm)

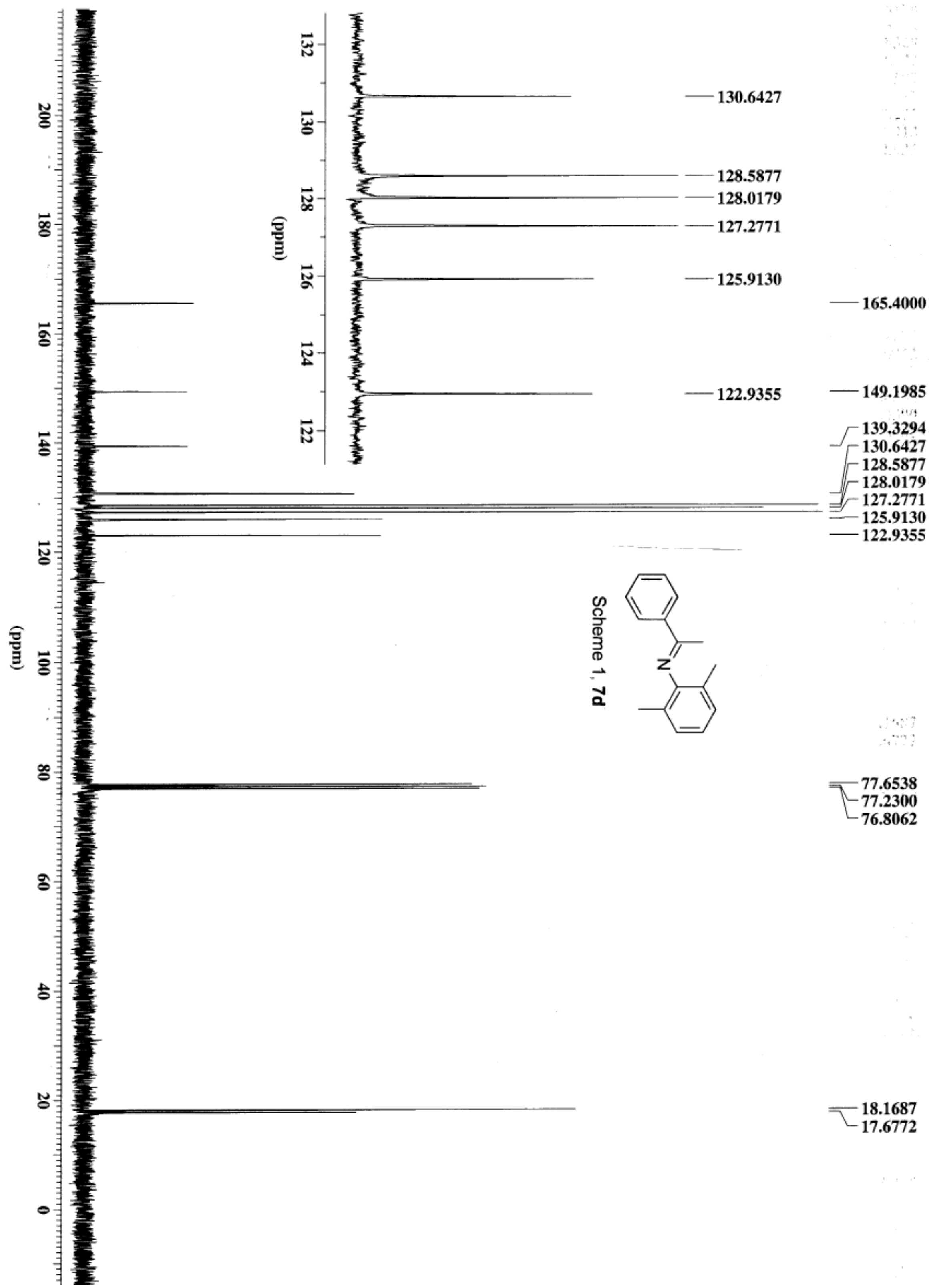

Integral
Scheme 1, 7b
1.9836
2.9448
2.0976
1.9409
3.0000
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
7.9901
7.9844
7.9783
7.9730
7.9665
7.9580
7.4924
7.4859
7.4769
7.4716
7.4627
7.4521
7.4415
7.4362
7.0887
7.0817
7.0663
7.0594
7.0378
7.0305
6.7863
6.7806
6.7696
6.7639
6.7566
6.7476
6.7403
2.2476

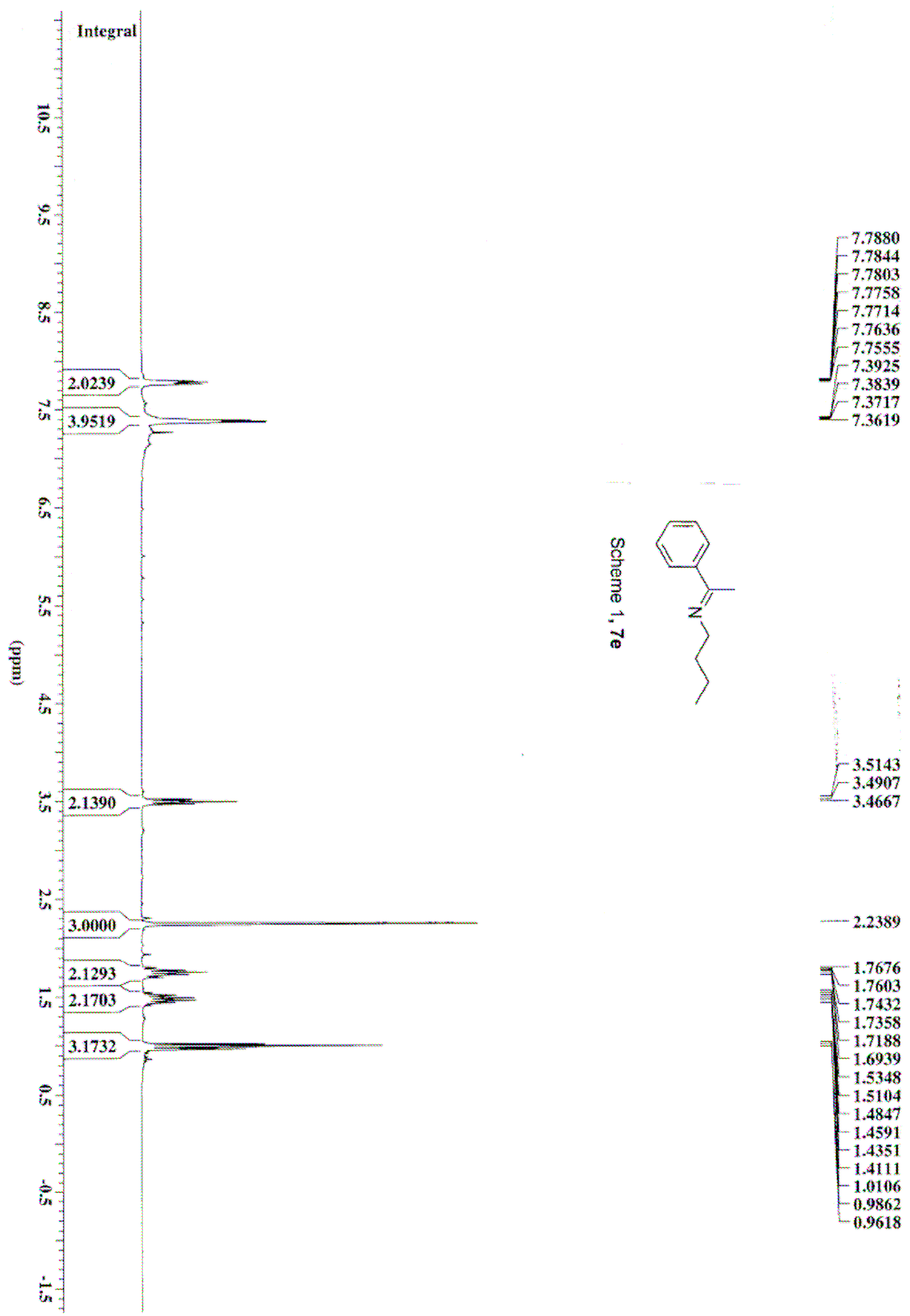

Scheme 1, 7b
F
N
166.5638
161.2000
147.9083
147.8691
139.6134
130.8413
128.6509
127.4080
121.0363
120.9330
116.0359
115.7403
77.7491
77.3253
76.9015
17.5944
(ppm)
200
180
160
140
120
100
80
60
40
20
0

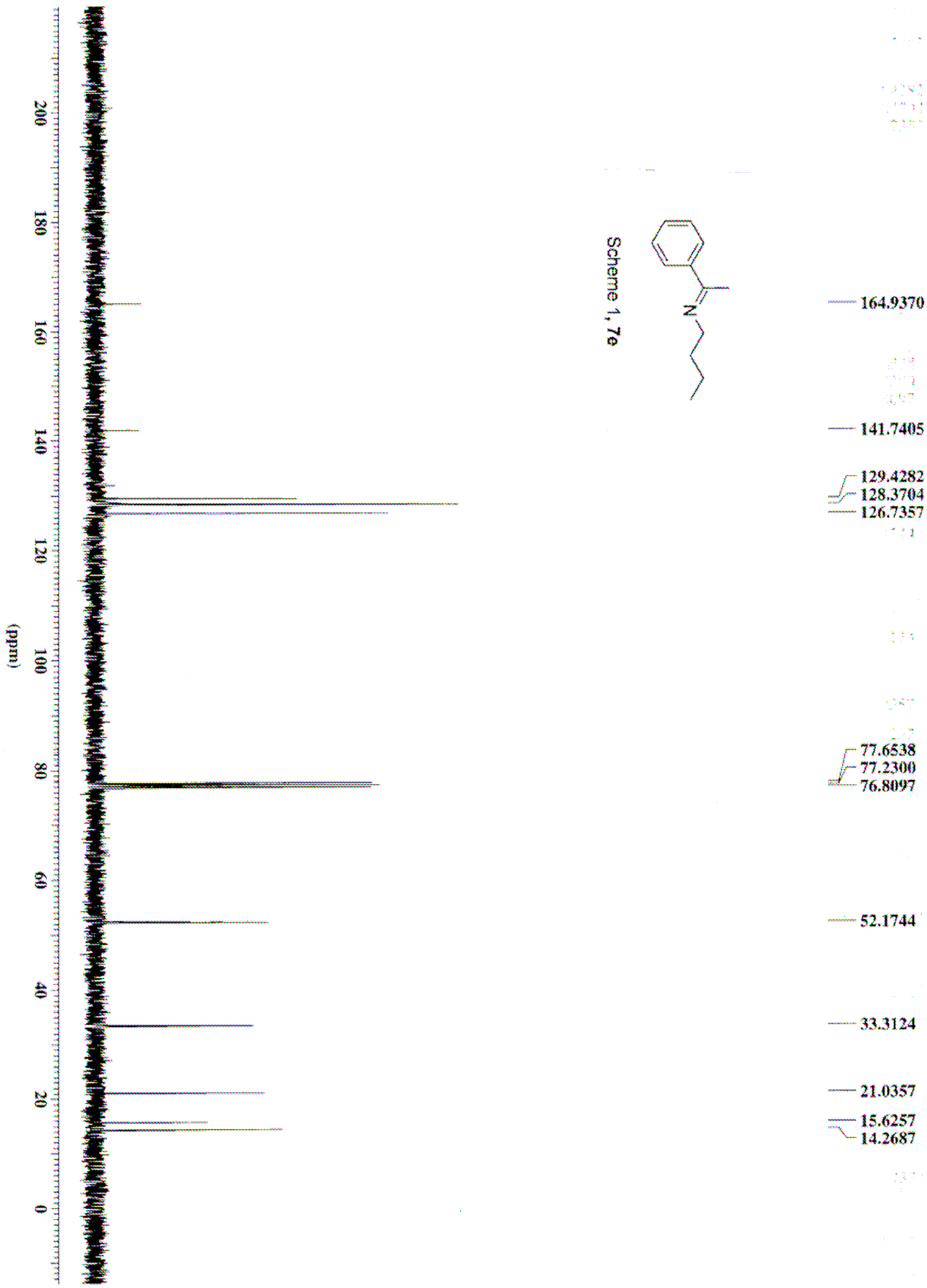

Integral
Scheme 1, 7c
8.0999
8.0929
8.0816
8.0779
8.0673
7.5411
7.5342
7.5236
7.5175
7.4699
7.4426
7.4178
7.2053
7.2017
7.1805
7.1593
7.1557
7.1520
6.9241
6.9200
6.8960
6.8928
2.3008
2.0181
3.0587
2.0800
1.1440
1.9213
3.0000
(ppm)

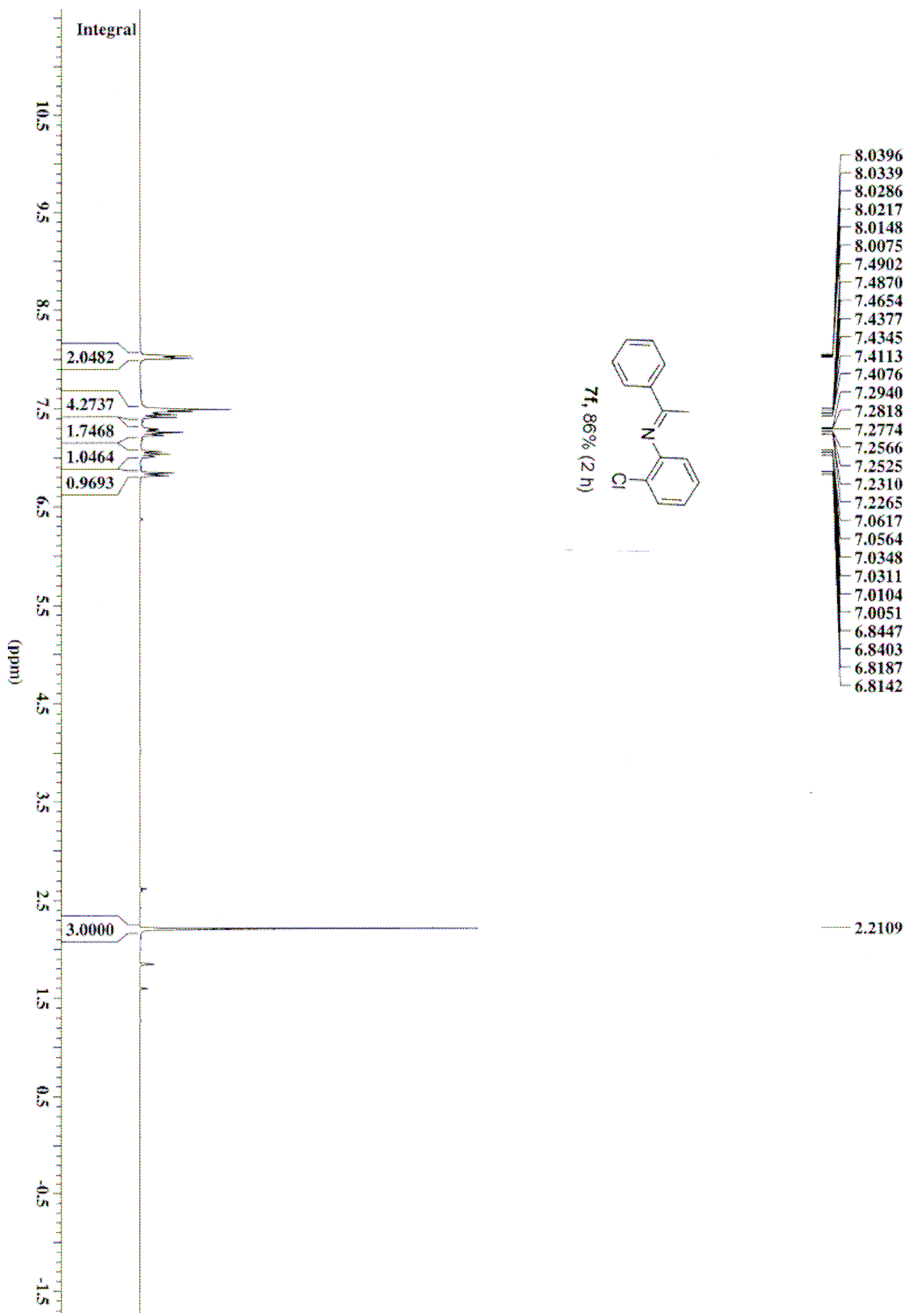

Scheme 1, 7c
165.3928
151.7521
139.4754
130.4967
129.0008
128.3918
127.2201
123.2525
119.4167
77.6538
77.2300
76.8062
17.3638
200
180
160
140
120
100
80
60
40
20
0
(ppm)

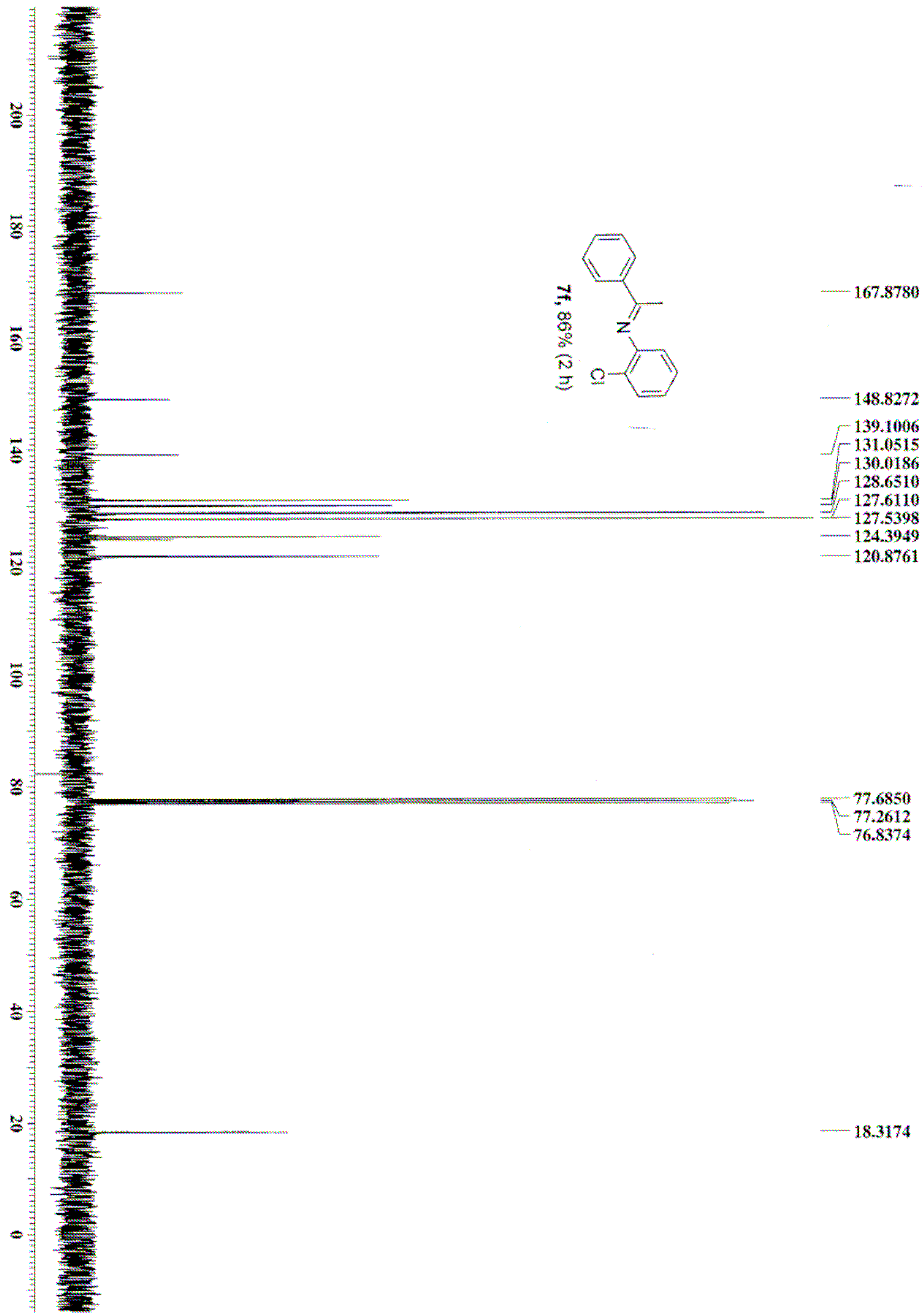

Integral
2.0281
3.0372
2.0543
1.0059
3.0000
6.3427
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
8.0699
8.0634
8.0520
8.0475
8.0373
7.5042
7.4981
7.4867
7.4806
7.2600
7.0858
7.0610
6.9588
6.9348
6.9088
2.0881
2.0486
N
Scheme 1, 7d

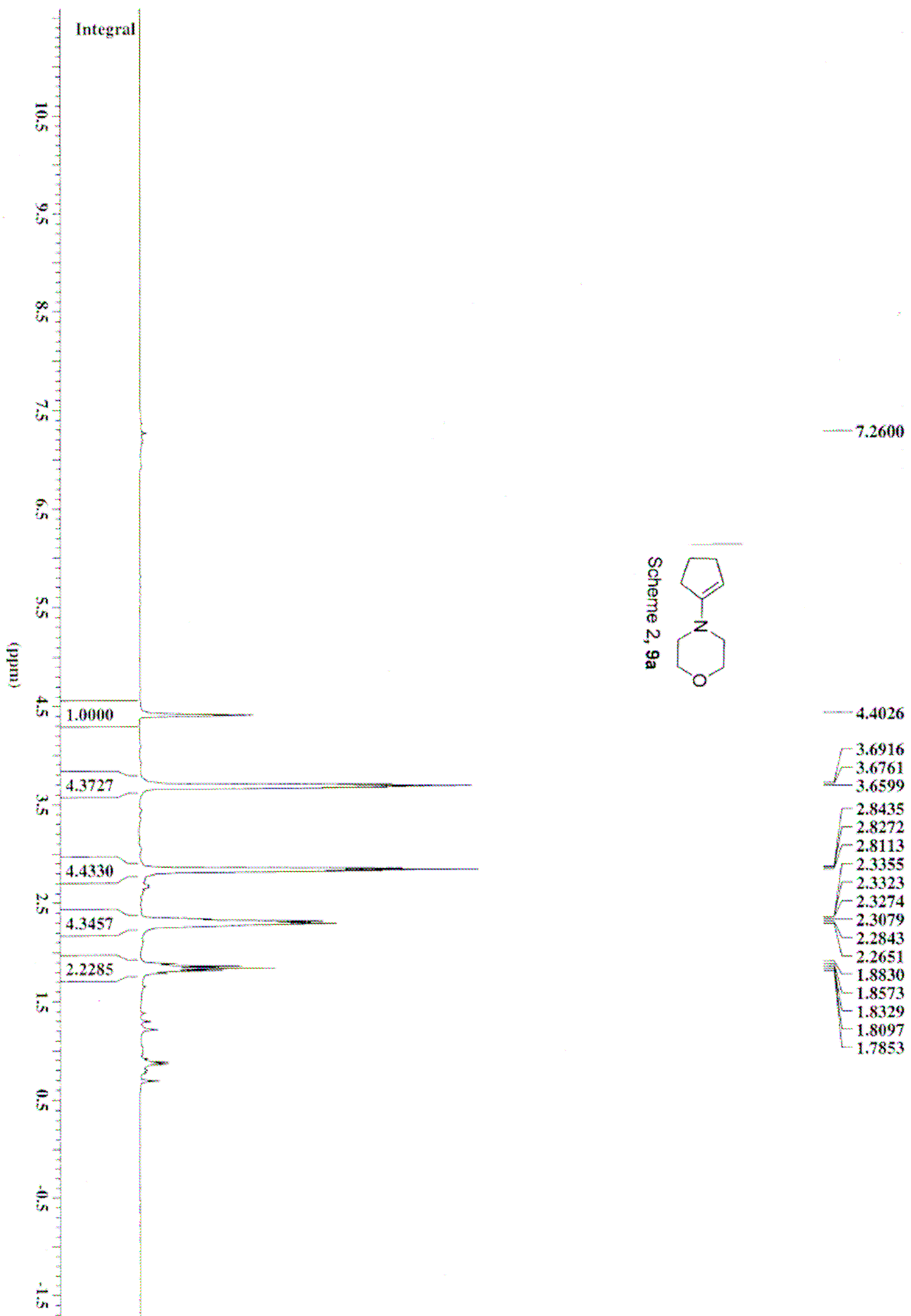

130.6427
128.5877
128.0179
127.2771
125.9130
122.9355
165.4000
149.1985
139.3294
130.6427
128.5877
128.0179
127.2771
125.9130
122.9355
77.6538
77.2300
76.8062
18.1687
17.6772
(ppm)
(ppm)
Scheme 1, 7d

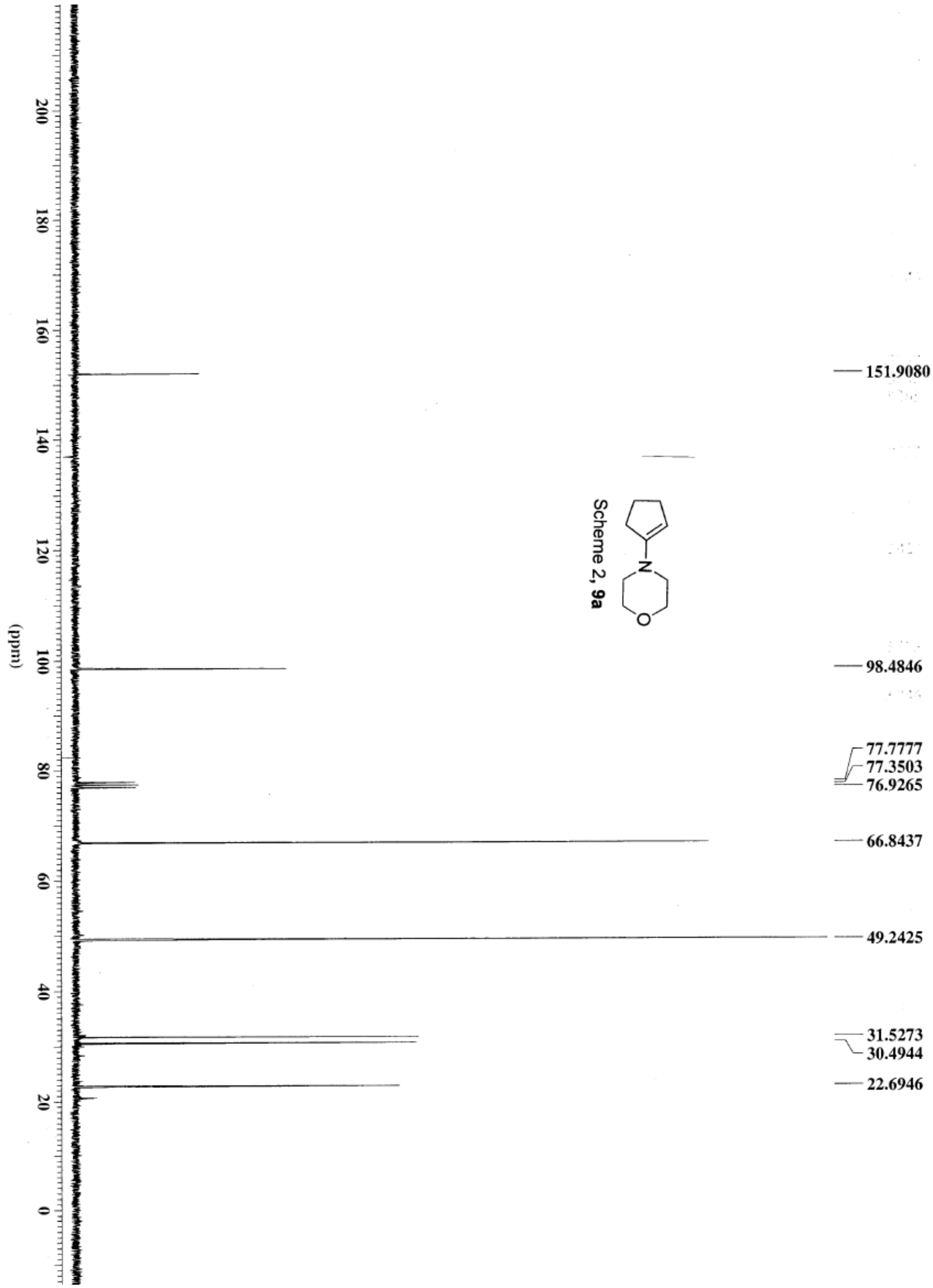

Integral
(ppm)
Scheme 1, 7e
N

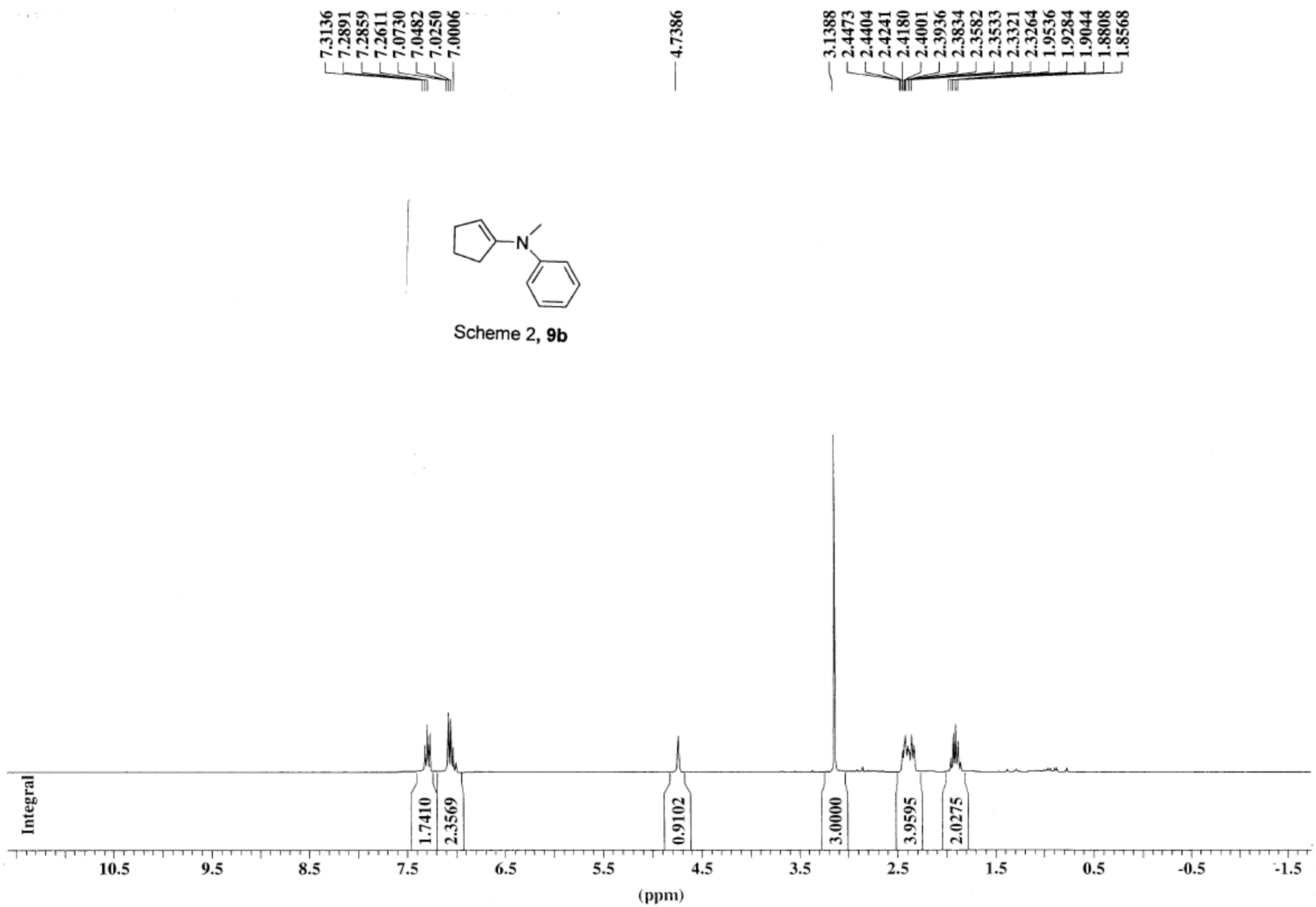

Scheme 1, 7e
164.9370
141.7405
129.4282
128.3704
126.7357
77.6538
77.2300
76.8097
52.1744
33.3124
21.0357
15.6257
14.2687
200
180
160
140
120
100
80
60
40
20
0
(ppm)

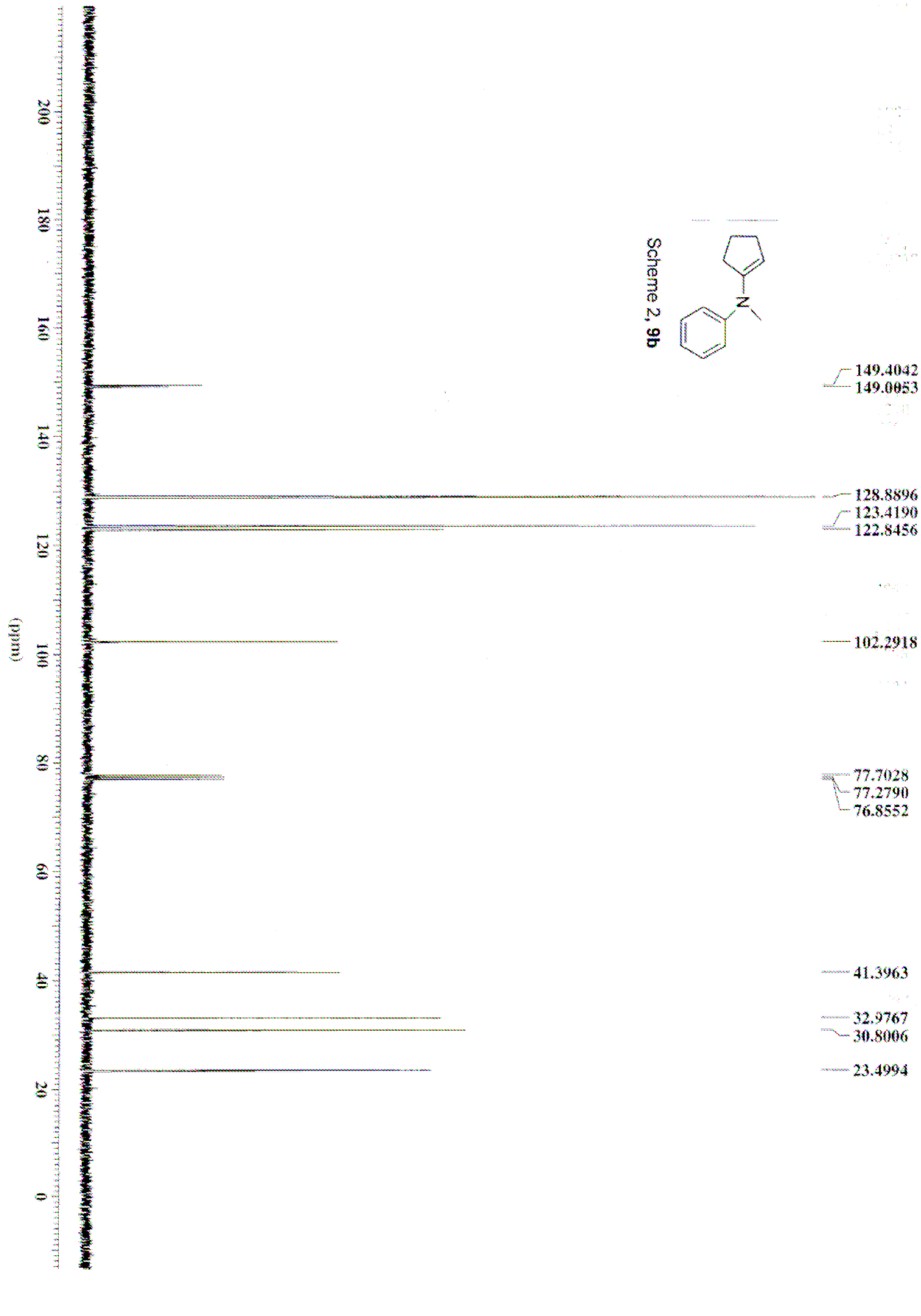

Integral
2.0482
4.2737
1.7468
1.0464
0.9693
3.0000
(ppm)
7l, 86% (2 h)
8.0396
8.0339
8.0286
8.0217
8.0148
8.0075
7.4902
7.4870
7.4654
7.4377
7.4345
7.4113
7.4076
7.2940
7.2818
7.2774
7.2566
7.2525
7.2310
7.2265
7.0617
7.0564
7.0348
7.0311
7.0104
7.0051
6.8447
6.8403
6.8187
6.8142
2.2109

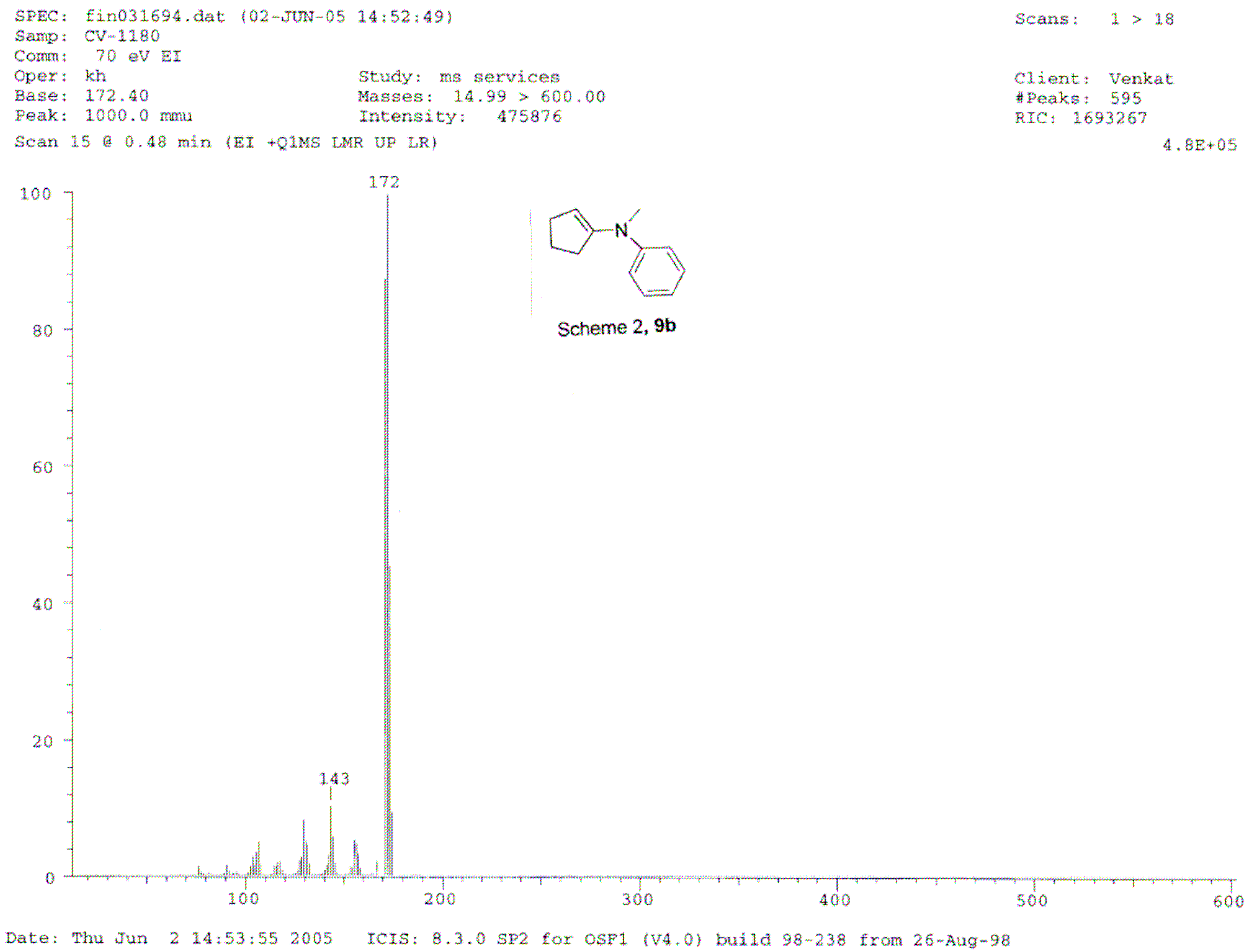

7f, 86% (2 h)
Cl
N
167.8780
148.8272
139.1006
131.0515
130.0186
128.6510
127.6110
127.5398
124.3949
120.8761
77.6850
77.2612
76.8374
18.3174
200
180
160
140
120
100
80
60
40
20
0
(ppm)


Integral
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)
1.0000
4.3727
4.4330
4.3457
2.2285
7.2600
Scheme 2, 9a
4.4026
3.6916
3.6761
3.6599
2.8435
2.8272
2.8113
2.3355
2.3323
2.3274
2.3079
2.2843
2.2651
1.8830
1.8573
1.8329
1.8097
1.7853


151.9080
98.4846
77.7777
77.3503
76.9265
66.8437
49.2425
31.5273
30.4944
22.6946
200
180
160
140
120
100
80
60
40
20
0
(ppm)
Scheme 2, **9a**
N
O

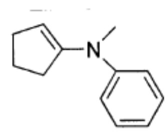

7.3136
7.2891
7.2859
7.2611
7.0730
7.0482
7.0250
7.0006
4.7386
3.1388
2.4473
2.4404
2.4241
2.4180
2.4001
2.3936
2.3834
2.3582
2.3533
2.3321
2.3264
1.9536
1.9284
1.9044
1.8808
1.8568
N
Scheme 2, **9b**
Integral
1.7410
2.3569
0.9102
3.0000
3.9595
2.0275
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)


Scheme 2, 9b
149.4042
149.0053
128.8896
123.4190
122.8456
102.2918
77.7028
77.2790
76.8552
41.3963
32.9767
30.8006
23.4994
(ppm)
200
180
160
140
120
100
80
60
40
20
0


SPEC: fin031694.dat (02-JUN-05 14:52:49)
Samp: CV-1180
Comm: 70 eV EI
Oper: kh
Base: 172.40
Peak: 1000.0 mmu
Study: ms services
Masses: 14.99 > 600.00
Intensity: 475876
Scans: 1 > 18
Client: Venkat
#Peaks: 595
RIC: 1693267
Scan 15 @ 0.48 min (EI +Q1MS LMR UP LR)
4.8E+05
172
143
N
Scheme 2, 9b
100
80
60
40
20
0
100
200
300
400
500
600
Date: Thu Jun 2 14:53:55 2005 ICIS: 8.3.0 SP2 for OSF1 (V4.0) build 98-238 from 26-Aug-98

```
LIST:  fin031694                          02-JUN-05   Elapse:  00:28.6      15
Samp:  CV-1180                                        Start :  14:52:49     18
Comm:   70 eV EI
Mode:  EI +Q1MS LMR UP LR                             Study :  ms services
Oper:  kh            Client:  Venkat                  Inlet :
Base:  172.4               Inten :  475876            Masses:  15 > 600
Norm:  172.4               RIC   :  1693267           #peaks:  595
Peak:  1000.00  mmu
```

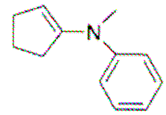
No.	Mass	Intensity (33311)	%RA	%RIC	Flags
1	129.	39149	8.23	2.31	F
2	143.	48766	10.25	2.88	F
3	171.	417179	87.67	24.64	F
4	172.	475876	100.00	28.10	F
5	173.	216118	45.41	12.76	F
6	175.	44273	9.30	2.61	F



Scheme 2, **9b**

Date: Thu Jun 2 14:53:59 2005   ICIS: 8.3.0 SP2 for OSF1 (V4.0) build 98-238 from 26-Aug-98

Manual Peak Matching Report
For Accurate Mass Determination



Scheme 2, **9b**

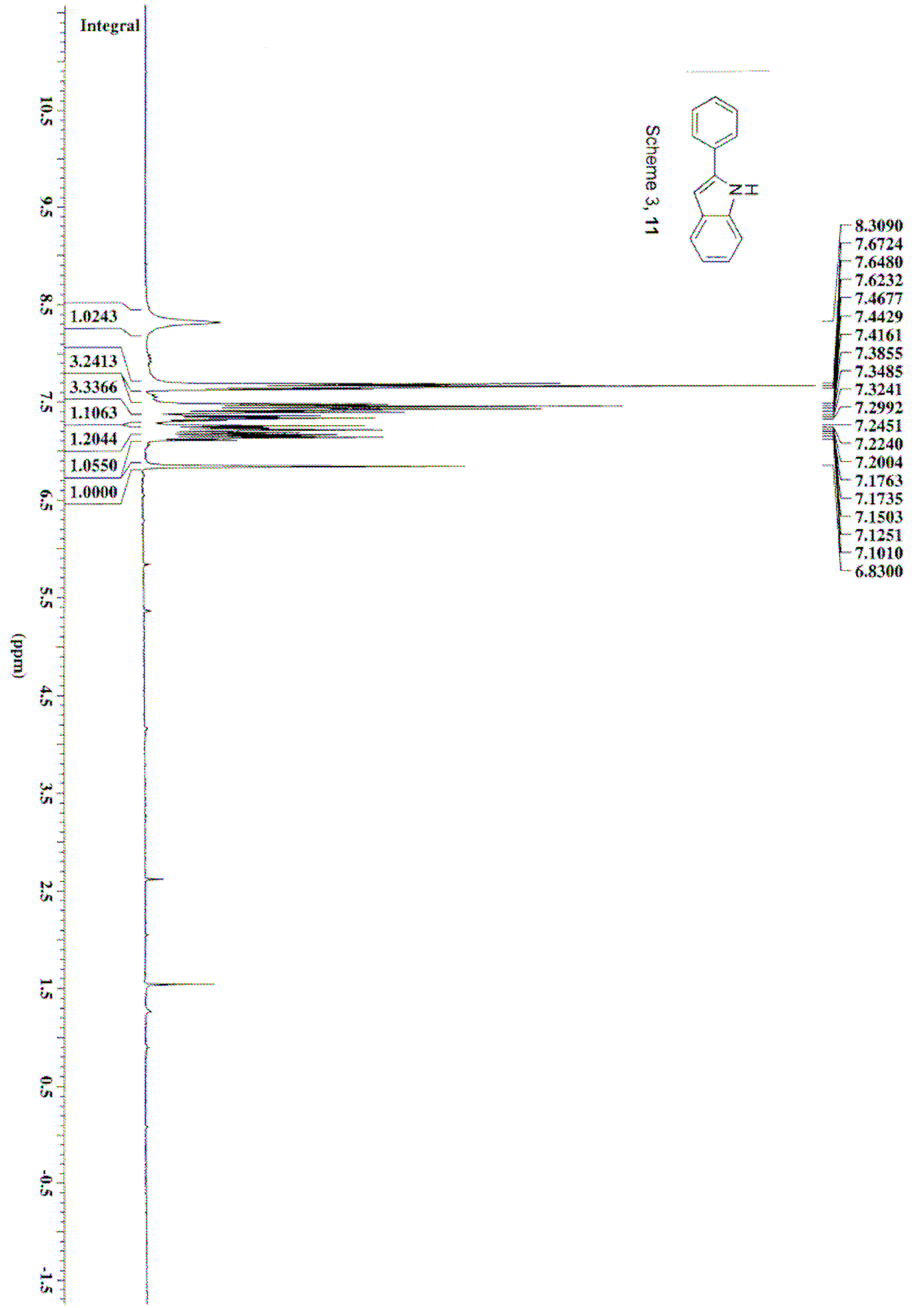
Theoretical mass	Experimental mass	PFK matching mass	Deviation*
173.12045	173.12069	168.98882	1.4 ppm

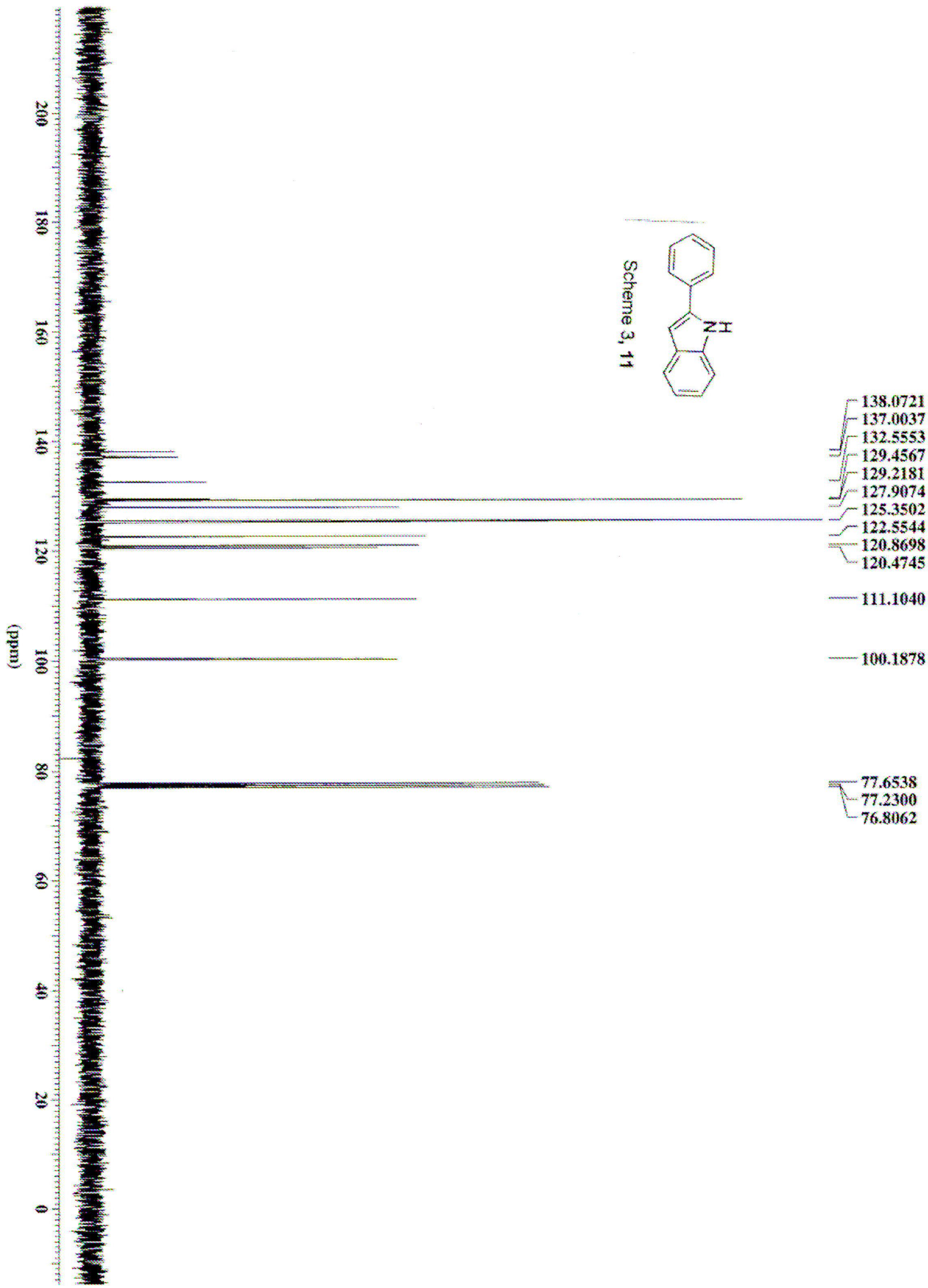
* The deviation is obtained from the following equation:

$$\text{deviation} = \frac{\text{experimental mass} - \text{theoretical mass}}{\text{nominal mass}}$$

Where nominal mass takes in account only ^{12}C, ^{1}H, ^{16}O, ^{14}N etc...

Theoretical mass correspond to the mass of the most abundant isotope peak

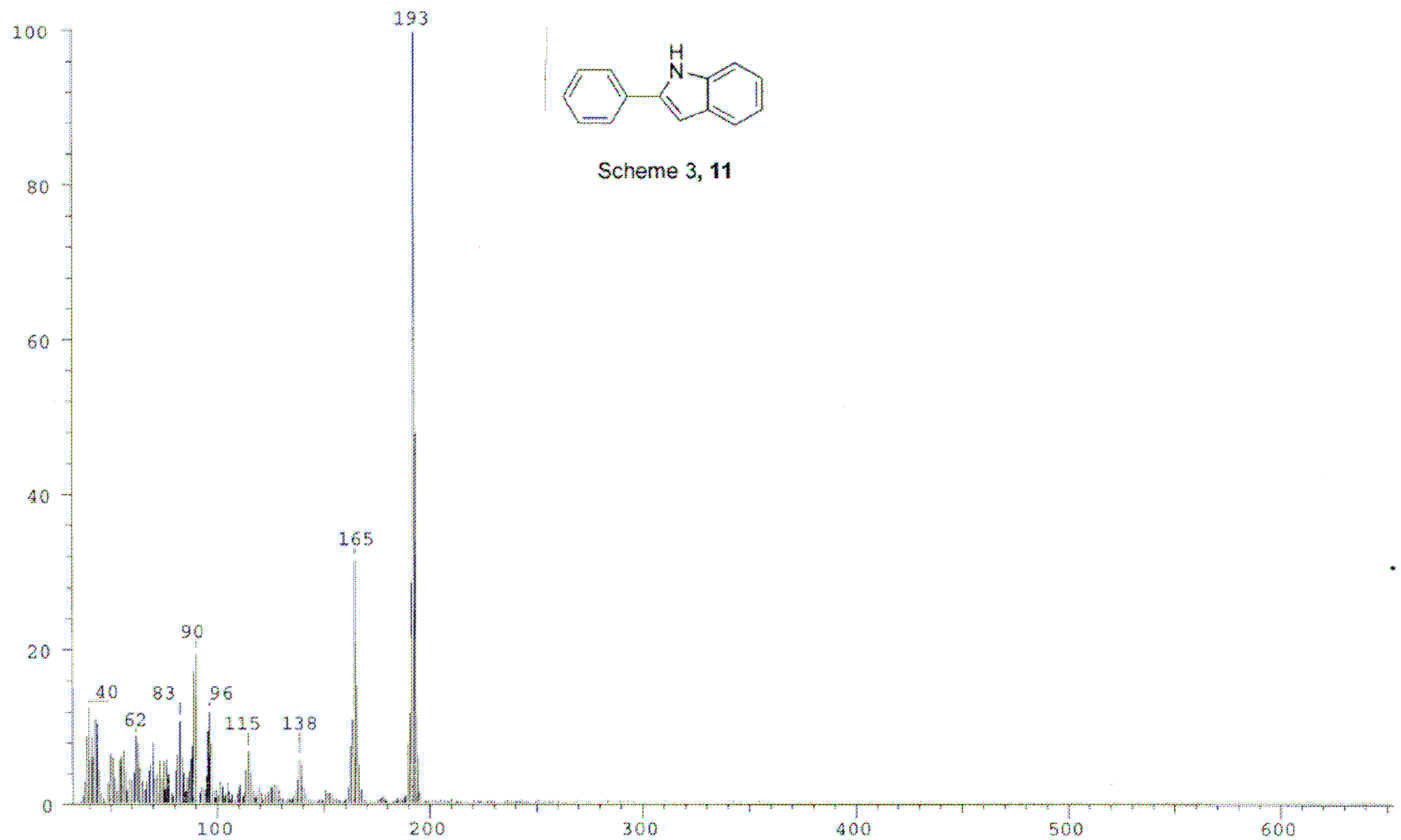

Scheme 3, 11
Integral
1.0243
3.2413
3.3366
1.1063
1.2044
1.0550
1.0000
8.3090
7.6724
7.6480
7.6232
7.4677
7.4429
7.4161
7.3855
7.3485
7.3241
7.2992
7.2451
7.2240
7.2004
7.1763
7.1735
7.1503
7.1251
7.1010
6.8300
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
(ppm)


Scheme 3, 11
138.0721
137.0037
132.5553
129.4567
129.2181
127.9074
125.3502
122.5544
120.8698
120.4745
111.1040
100.1878
77.6538
77.2300
76.8062
200
180
160
140
120
100
80
60
40
20
0
(ppm)

SPEC: fin031846.dat (15-JUN-05 14:35:40)
Samp: CVR-1269
Comm: 70 eV EI
Oper: kh
Base: 192.68
Peak: 1000.0 mmu
Scan 10 @ 0.36 min (EI +Q1MS LMR UP LR)

Study: MS services
Masses: 35.01 > 650.00
Intensity: 162146

Scans: 1 > 11
Client: Venkate
#Peaks: 583
RIC: 1163942
1.6E+05

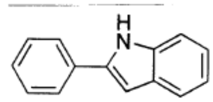


Scheme 3, **11**

Date: Wed Jun 15 14:36:23 2005 ICIS: 8.3.0 SP2 for OSF1 (V4.0) build 98-238 from 26-Aug-98

```
LIST:  fin031846                                15-JUN-05   Elapse:   00:21.6        10
Samp:  CVR-1269                                             Start :   14:35:40       11
Comm:  70 eV EI
Mode:  EI +Q1MS LMR UP LR                                   Study :   MS services
Oper:  kh           Client:   Venkate                       Inlet :
Base:  192.7                Inten :   162146                Masses:   35 > 650
Norm:  192.7                RIC   :   1163942               #peaks:   583
Peak:  1000.00  mmu
```

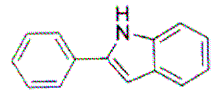
No.	Mass	14593 Intensity	%RA	%RIC	Flags
1	40.	19960	12.31	1.71	F
2	43.	17593	10.85	1.51	FM
3	43.	16595	10.23	1.43	FM
4	83.	17228	10.62	1.48	FM
5	89.	27649	17.05	2.38	F
6	90.	31331	19.32	2.69	F
7	95.	15088	9.31	1.30	F
8	96.	19006	11.72	1.63	F
9	163.	17640	10.88	1.52	FM
10	165.	50875	31.38	4.37	F
11	166.	24732	15.25	2.12	FM
12	191.	18818	11.61	1.62	F
13	192.	46487	28.67	3.99	F
14	193.	162146	100.00	13.93	F
15	194.	77834	48.00	6.69	F



Scheme 3, **11**

Date: Wed Jun 15 14:36:26 2005   ICIS: 8.3.0 SP2 for OSF1 (V4.0) build 98-238 from 26-Aug-98

Manual Peak Matching Report
For Accurate Mass Determination



Scheme 3, **11**

Theoretical mass	Experimental mass	PFK matching mass	Deviation*
193.08915	193.08945	180.98882	1.5 ppm

* The deviation is obtained from the following equation:

$$\text{deviation} = \frac{\text{experimental mass - theoretical mass}}{\text{nominal mass}}$$

Where nominal mass takes in account only ^{12}C, ^{1}H, ^{16}O, ^{14}N etc...

Theoretical mass correspond to the mass of the most abundant isotope peak