Supporting information:

Regioselective Synthesis of Substituted Naphthalenes: A Novel *de Novo* Approach Based on a Metal-Free Protocol for Cocyclization of *o*-Alkynylbenzaldehyde Derivatives with either Alkynes or Alkenes

José Barluenga,* Henar Vázquez-Villa, Alfredo Ballesteros, José M. González

Instituto Universitario de Química Organometálica "Enrique Moles"-Unidad Asociada al C.S.I.C., Universidad de Oviedo; Julián Claveria, 8; 33006 Oviedo Spain

Contents

Experimental section:

General: All reactions were conducted using oven-dried glassware under an atmosphere of nitrogen. Dichloromethane was distilled before used from P_2O_5, and DMF was distilled from $MgSO_4$. The solvents used in column chromatography, hexane and ethyl acetate, were obtained from commercial suppliers and used without further distillation. TLC was performed on aluminium-backed plates coated with silica gel 60 with F_{254} indicator (Merck). Flash chromatography was carried out on silica gel. NMR spectra were measured at room temperature on a Bruker AC-200 MHz or Bruker DPX-300 MHz spectrometers. 2D NMR experiments were recorded on a Bruker AMX-400 MHz. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (deuterochloroform: δ 7.26 ppm in ^1H spectra, δ 77.00 ppm in ^{13}C spectra). Carbon multiplicities were assigned by DEPT techniques.

Starting materials: 2-Alkynylbenzaldehydes were prepared by Sonogashira coupling reaction of 2-bromobenzaldehyde with various terminal alkynes. [1]

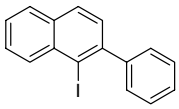
All commercially available compounds were used as received. IPy_2BF_4 is a commercially available reagent from Aldrich, Novabiochem and Galchimia.

General procedure for the synthesis of naphthalene derivatives 3 and 4 using IPy_2BF_4 and HBF_4: IPy_2BF_4 (0.37g, 1 mmol, 1 equiv) was dissolved in dry CH_2Cl_2 (10 mL). The solution was cooled at 0°C and tetrafluoroboric acid, 54% solution in diethyl ether (0.28 mL, 2.2 mmol, 2.2 equiv) was added. After 10 min., the corresponding 2-alkynylbenzaldehyde (1 mmol, 1 equiv) was added and the solution was stirred during 30 min. at room temperature. After this time, the corresponding alkyne or alkene (1.2 mmol, 1.2 equiv) was added and the solution was further stirred at room temperature (reaction times are given in Table 1 and 2). The reaction mixture was quenched with saturated aqueous $NaHCO_3$ and vigorously stirred. The organic

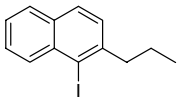
[1] Roesch, K. R., Larock, R. C. *J. Org. Chem.* **2002**, *67*, 86.

layer was washed with a 5% aqueous solution of $Na_2S_2O_3$ (50 mL) and water (50 mL); dried over sodium sulphate and concentrated. The crude were purified by flash column chromatography (silica gel, hexane/EtOAc) to afford pure compounds **3**, **4**.

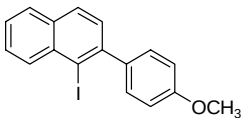
Spectroscopic data of compounds 3and 4:



1-Iodo-2-phenylnaphthalene 3a. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8,5 (d, *J* = 8.2 Hz, 1H),7.9 (m, 2H), 7.8-7.3 (m, 8H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 146.0 (C), 145.9 (C), 134.8 (C), 133.3 (CH), 132.8 (C), 129.4 (2 x CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 127.8 (2 x CH), 127.5 (2 x CH), 126.4 (CH), 104.0 (C-I). HRMS (EI) Calcd for $C_{16}H_{11}I$ 329.9905, Found 329.9906.

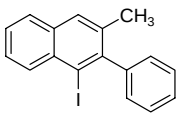


1-Iodo-2-propylnaphthalene 3b. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.3 (d, *J* = 8.5 Hz, 1H), 7.8-7.75 (m, 2H), 7.6-7.4 (m, 2H), 7.35 (d, *J* = 8.3 Hz, 1H), 3.0 (m, 2H), 1.8 (m, 2H), 1.1 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 144.5 (C), 135.1 (C), 132.6 (CH), 132.5 (C), 128.4 (CH), 128.0 (CH), 127.5 (CH), 127.4 (CH), 125.6 (CH), 105.1 (C-I), 44.7 (CH_2), 23.7 (CH_2), 13.9 (CH_3). HRMS (EI) Calcd for $C_{13}H_{13}I$ 296.0062, Found 296.0067.



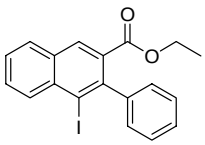
1-Iodo-2-(4-methoxyphenyl)naphthalene 3c. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.4 (d, *J* = 7.9 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 2H), 7.65 (m, 1H), 7.55 (m, 1H), 7.45 (d, *J* = 8.3 Hz, 1H), 7.4 (d, *J* = 8.8 Hz, 2H), 7.0 (d, *J* = 8.8 Hz, 2H),

3.9 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 158.9 (C), 145.7 (C), 138.5 (C), 134.9 (C), 133.4 (CH), 132.7 (C), 130.6 (2 x CH), 128.3 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 126.3 (CH), 113.2 (2 x CH), 104.5 (C-I), 55.2 (CH_3). HRMS (EI) Calcd for $C_{17}H_{13}IO$ 360.0011, Found 360.0015.

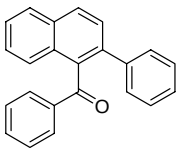


1-Iodo-3-methyl-2-phenylnaphthalene 3d. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.2 (d, *J* = 7.4 Hz, 1H), 7.7 (m, 2H), 7.6-7.4 (m, 5H), 7.2 (m, 2H), 2.2 (s, 3H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 146.9 (C), 145.8 (C), 134.9 (C), 133.5 (2 x C), 133.2 (CH),

128.9 (2 x CH), 128.6 (CH), 128.3 (2 x CH), 127.4 (CH), 127.3 (CH), 127.0 (CH), 126.5 (CH), 106.0 (C-I), 22.8 (CH_3. HRMS (EI) Calcd for $C_{17}H_{13}I$ 344.0062, Found 344.0068.

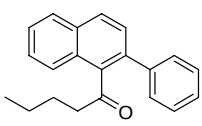


4-Iodo-3-phenylnaphthalene-2-carboxylic acid ethyl ester 3e ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.4 (s, 1H), 8.35 (d, *J* = 8.8 Hz, 1H), 7.9 (d, *J* = 8.0 Hz, 1H) 7.7 (m, 1H), 7.6 (m, 1H), 7.55-7.4 (m, 3H), 7.3 (m, 2H), 4.0 (q, *J* = 7.1 Hz, 2H), 1.0 (t, *J* = 7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 167.1 (C=O), 145.2 (C), 143.7 (C), 135.8 (C), 133.4 (CH), 131.8 (C), 130.7 (CH), 130.3 (C), 129.7 (CH), 129.3 (2 x CH), 129.0 (CH), 127.5 (2 x CH), 127.4 (CH), 127.2 (CH), 107.8 (C-I), 61.0 (CH_2), 13.5 (CH_3). HRMS (EI) Calcd for $C_{19}H_{15}IO_2$ 402.0117, Found 402.0125.



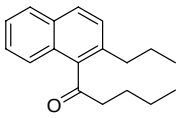
Phenyl-(2-phenylnaphthalen-1-yl)-methanone 4a. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.1 (d, *J* = 8.6 Hz, 1H), 8.0 (d, *J* = 8.5 Hz, 1H), 7.8 (d, *J* = 8.4 Hz, 1H), 7.7 (m, 2H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.6-7.4 (m, 5H), 7.3-7.2 (m, 5H).

^{13}C-NMR ($CDCl_3$, 75 MHz): 199.5 (C=O)), 140.1 (C), 137.8 (C), 137.3 (C), 137.6 (C), 133.1 (CH), 132.3 (C), 130.5 (C), 129.4 (CH), 129.35 (2 x CH), 129.3 (2x CH), 128.1 (2 x CH), 18.05 (2 x CH), 128.0 (CH), 127.6 (CH), 127.3 (CH), 127.1 (CH), 126.2 (CH), 125.4 (CH). HRMS (EI) Calcf for $C_{23}H_{16}O$ 308.1201, Found 308.1208.

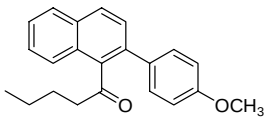


1-(2-Phenylnaphthalen-1-yl)-pentan-1-one 4b. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.0-7.8 (m, 3H), 7.6-7.4 (m, 8H), 2.3 (t, *J* = 7.2 Hz, 2H), 1.45 (m, 2H), 1.1 (m, 2H), 0.7 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 209.9 (C=O), 140.3 (C),

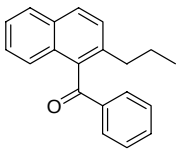
138.4 (C), 135.8 (C), 135.1 (C), 132.4 (C), 129.4 (2 x CH), 129.2 (CH), 128.6 (2 x CH), 128.1 (CH), 127.8 (CH), 127.4 (CH), 127.3 (CH), 126.2 (CH), 124.8 (CH), 44.8 (CH_2), 25.6 (CH_2), 21.9 (CH_2), 13.6 (CH_3). HRMS (EI) Calcd for $C_{21}H_{20}O$ 288.1514, Found 288.1518.



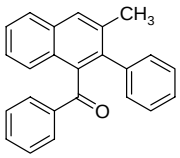
1-(2-Propylnaphthalen-1-yl)-pentan-1-one 4c. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.8 (m, 2H), 7.6-7.45 (m, 3H), 7.3 (d, *J* = 8.5 Hz, 1H), 2.9 (t, *J* = 7.5 Hz, 2H), 2.6 (m, 2H), 1.9-1.65 (m, 2H), 1.5 (m, 2H), 1.0 (m, 6H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 210.5 (C=O), 138.6 (C), 134.9 (C), 131.7 (C), 129.2 (C), 128.6 (CH), 128.1 (CH), 127.3 (CH), 126.6 (CH), 125.4 (CH), 124.1 (CH), 45.7 (CH_2), 35.5 (CH_2), 25.6 (CH_2), 24.7 (CH_2), 22.4 (CH_2), 14.1 (CH_3). 13.9 (CH_3). HRMS (EI) Calcd for $C_{18}H_{22}O$ 254.1671, Found 254.1671.



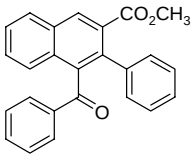
1-[2-(4-Methoxyphenyl)-naphthalen-1-yl]-pentan-1-one 4d. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.0-7.8 (m, 3H), 7.55 (m, 3H), 7.4 (d, *J* = 8.8 Hz, 2H), 7.0 (d, *J* = 8.8 Hz, 2H), 3.9 (s, 3H), 2.3 (t, *J* = 7.4 Hz, 2H), 1.5 (m, 2H), 1.15 (m, 2H), 0.75 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 210.2 (C=O), 159.4 (C), 138.0 (C), 135.5 (C), 132.6 (C), 132.2 (C), 130.5 (2 x CH), 129.2 (C), 129.1 (CH), 128.1 (CH), 127.5 (CH), 127.2 (CH), 126.0 (CH), 124.6 (CH), 114.1 (2 x CH), 55.3 (CH_3), 44.7 (CH_2), 25.7 (CH_2), 22.0 (CH_2), 13.6 (CH_3). HRMS (EI) Calcd for $C_{22}H_{22}O_2$ 318.1620, Found 318.1633.



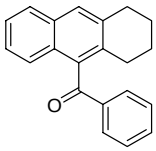
Phenyl-(2-propylnaphthalen-1-yl)-methanone 4e. ^{1}H-NMR ($CDCl_3$, 200 MHz): 8.0-7.8 (m, 4H), 7.6-7.3 (m, 7H), 2.6 (t, *J* = 7.8 Hz, 2H), 1.6 (m, 2H), 1.3 (m, 2H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 200.2 (C=O), 137.8 (C), 137.2 (C), 135.5 (C), 133.6 (CH), 131.6 (C), 130.6 (C), 129.7 (2 x CH), 128.9 (CH), 128.6 (2 x CH), 127.9 (CH), 127.3 (CH), 126.5 (CH), 125.4 (CH), 33.35 (CH_2), 33.3 (CH_2), 22.5 (CH_2), 13.7 (CH_3). HRMS (EI) Calcd for $C_{21}H_{20}O$ 288.1514, Found 288.1514.



(3-Methyl-2-phenylnaphthalen-1-yl)-phenylmethanone 4f. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.9 (m, 2H), 7.7 (m, 3H), 7.6-7.0 (m, 10H), 2.35 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 199.4, 138.1, 137.9, 136.8, 134.0, 132.9, 132.6, 129.2, 129.0, 128.95, 128.0, 127.6, 127.3, 127.0, 126.2, 126.1, 125.2, 20.9. HRMS (EI) Calcd for $C_{24}H_{18}O$ 322.1356, Found 322.1360.

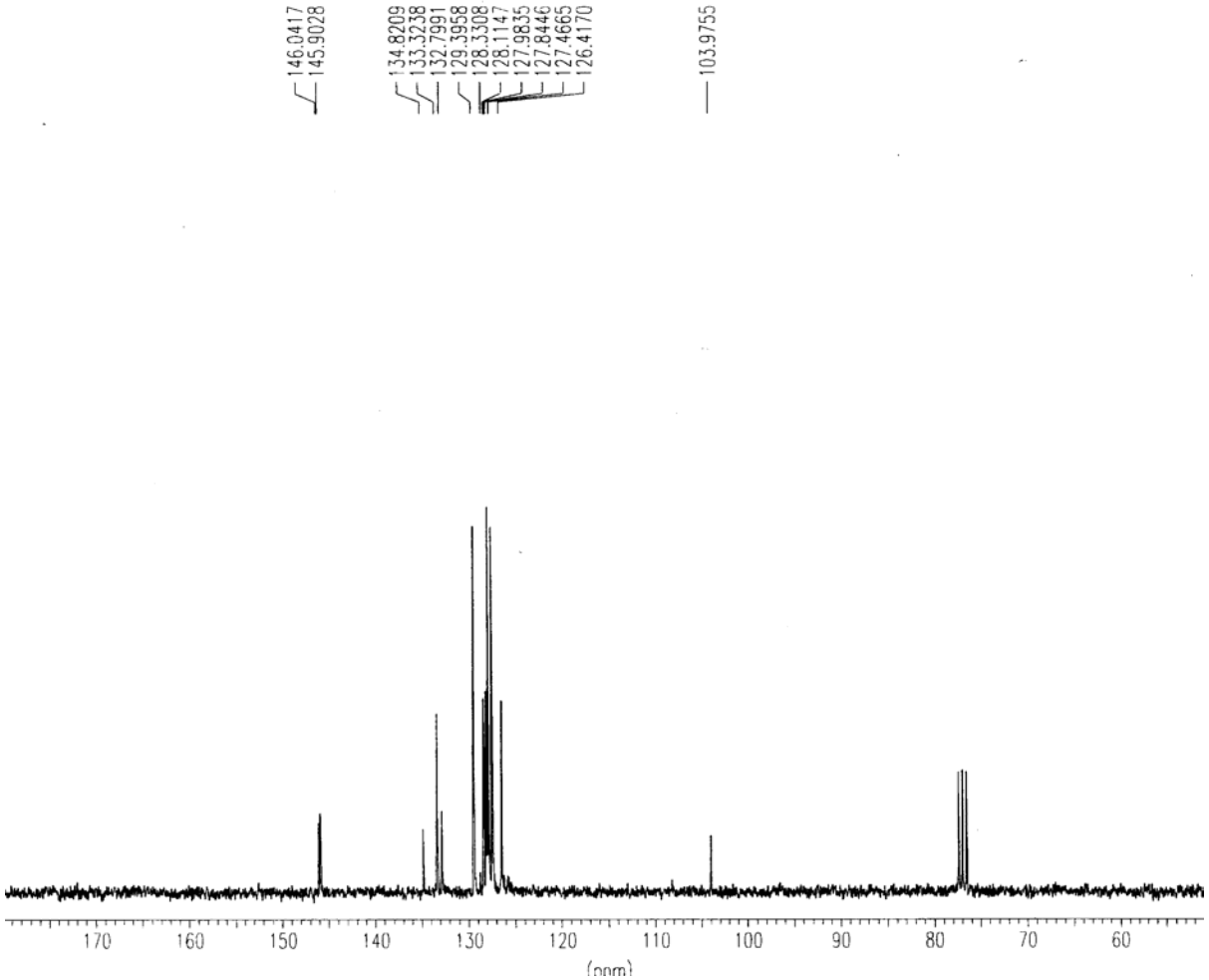


4-Benzoyl-3-phenylnaphthalene-2-carboxylic acid methyl ester 4g ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.6 (s, 1H), 8.0 (dd, *J* = 7.1, 1.4 Hz, 1H), 7.7 (m, 1H), 7.65-7.5 (m, 5H), 7.4 (m, 1H), 7.35-6.8 (m, 6H), 3.6 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 198.6, 168.2, 138.2, 138.1, 137.7, 135.7, 133.2, 131.7, 131.5, 131.4, 129.4, 129.3, 129.0, 128.2, 127.4, 127.2, 127.1, 125.4, 52.0. HRMS (EI) Calcd for $C_{25}H_{18}O_3$ 366.1256, Found 366.1256.

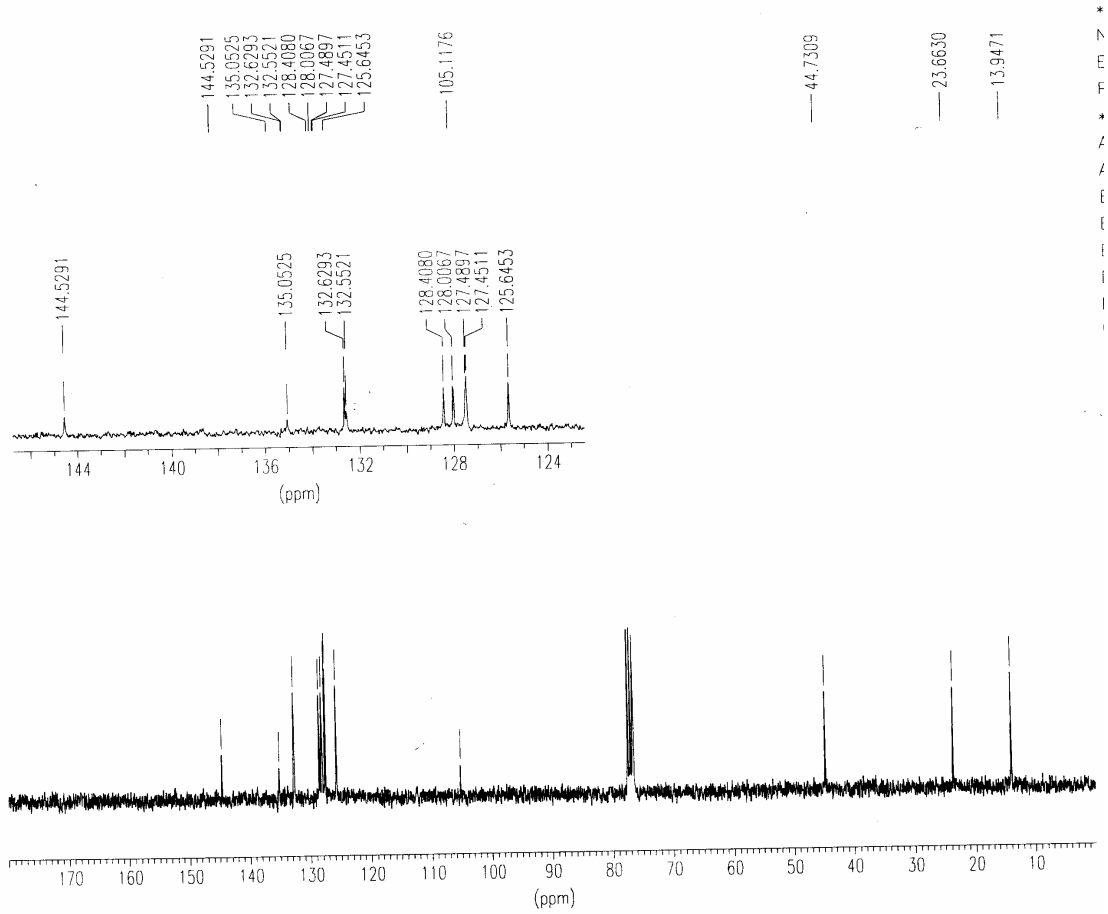


Phenyl-(1,2,3,4-tetrahydroanthracen-9-yl)-methanone 4h. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.85 (d, *J* = 7.2 Hz, 1H), 7.8 (d, *J* = 8.2 Hz, 1H), 7.7 (s, 1H), 7.6 (t, *J* = 7.4 Hz, 1H), 7.5-7.2 (m, 5H), 3.1 (m, 2H), 3.0-2.5 (m, 2H), 2.0-1.8 (m, 4H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 200.7 (C=O), 137.3 (C), 135.7 (2 x C), 133.6 (CH), 132.6 (C), 131.6 (C), 129,5 (2 x CH), 129.0 (C), 128.7 (2 x CH), 127.9 (CH), 127.3 (CH), 125.5 (CH), 125.2 (CH), 125.5 (CH), 30.0 (CH_2), 27.1 (CH_2), 22.75 (CH_2), 22.7 (CH_2). HRMS (EI) Calcd for $C_{21}H_{18}O$ 286.1358, Found 286.1358.

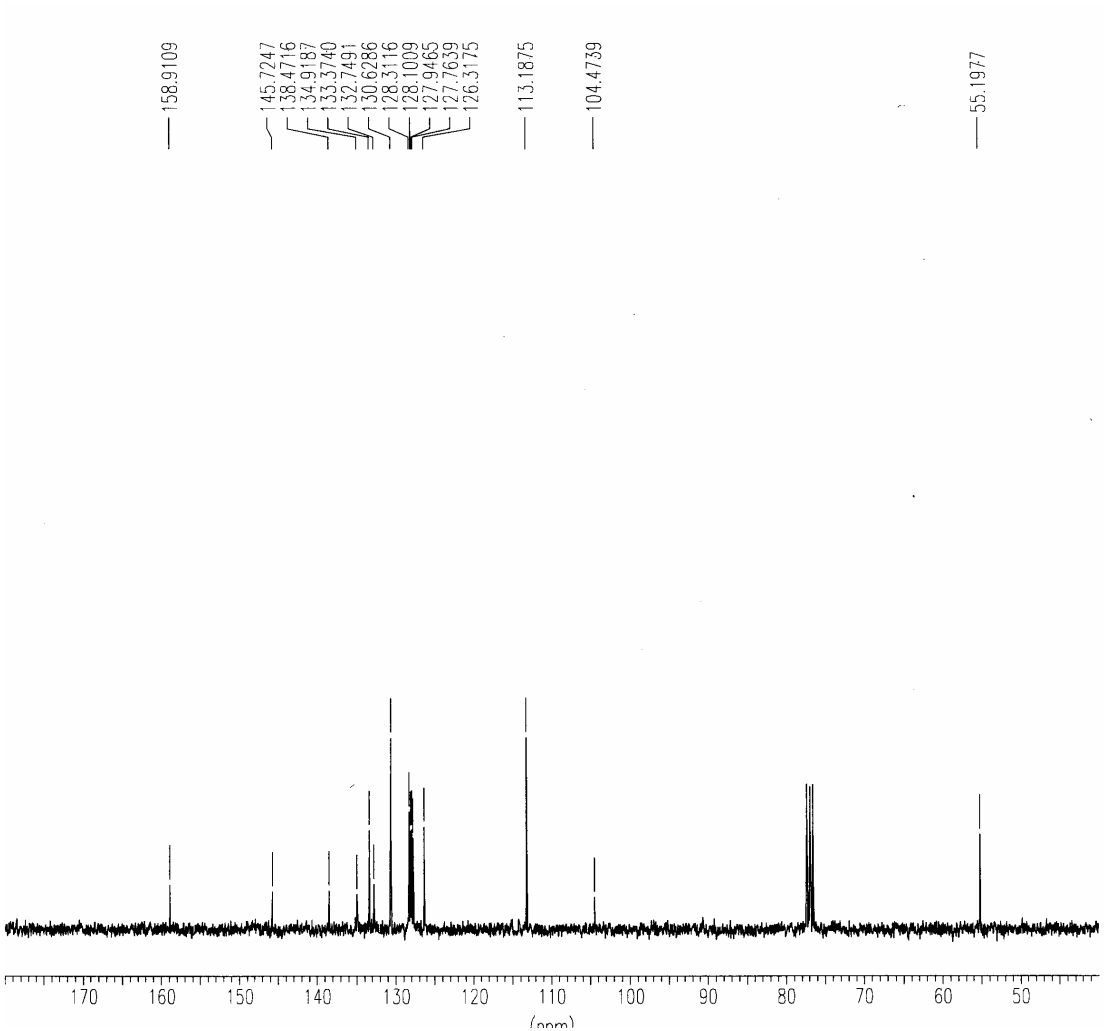
Compound 3a:


146.0417
145.9028
134.8209
133.3238
132.7991
129.3958
128.3308
128.1147
127.9835
127.8446
127.4665
126.4170
103.9755
170
160
150
140
130
120
110
100
90
80
70
60
(ppm)

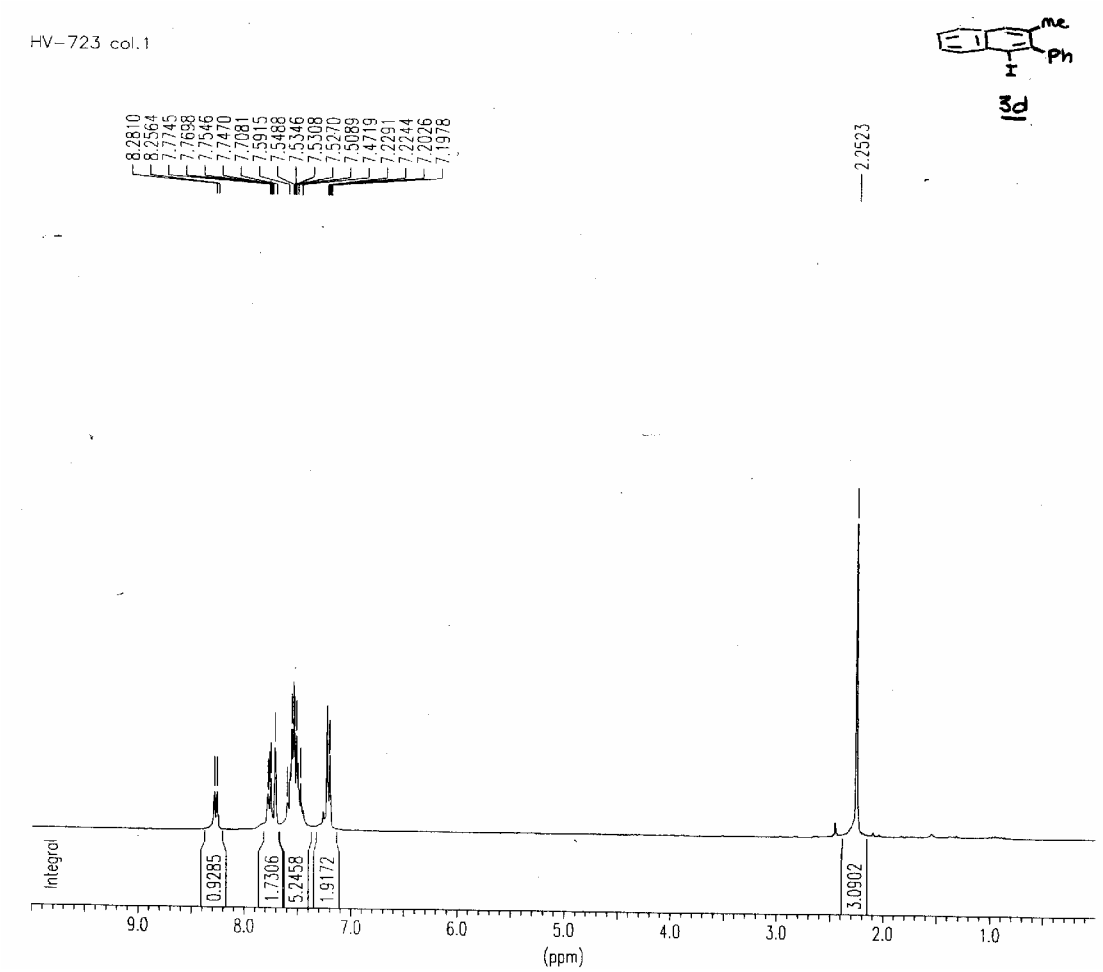
Compound 3b:


144.5291
135.0525
132.6293
132.5521
128.4080
128.0067
127.4897
127.4511
125.6453
105.1176
44.7309
23.6630
13.9471
(ppm)
(ppm)

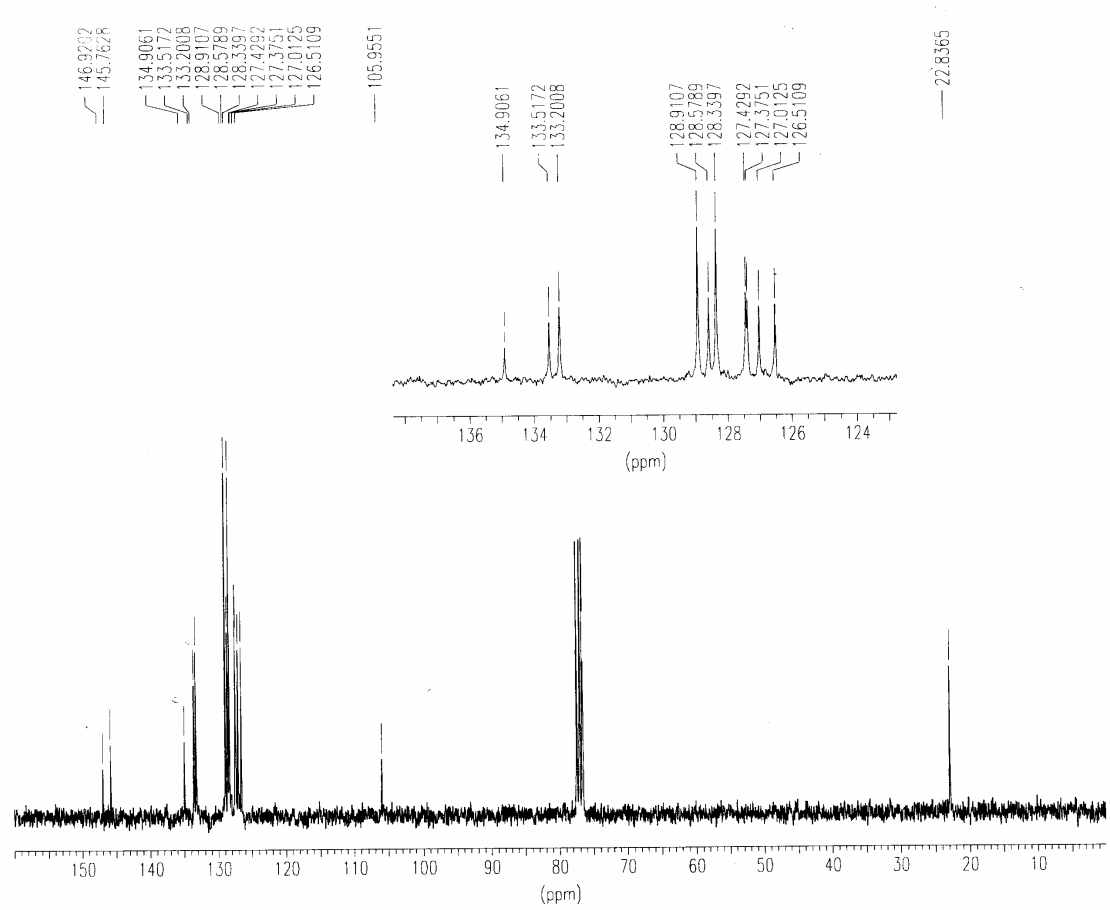
Compound 3c:


158.9109
145.7247
138.4716
134.9187
133.3740
132.7491
130.6286
128.3116
128.1009
127.9465
127.7639
126.3175
113.1875
104.4739
55.1977
170
160
150
140
130
120
110
100
90
80
70
60
50
(ppm)

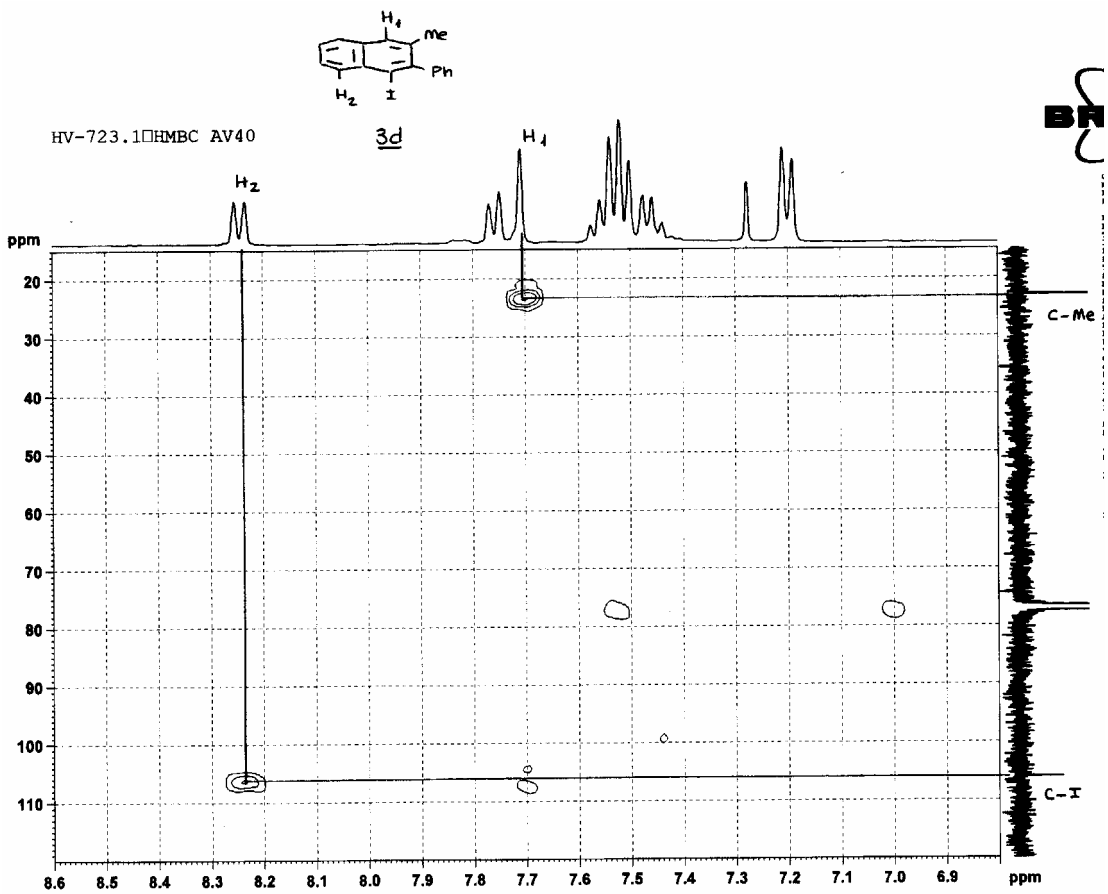
Compound 3d:


HV-723 col.1
me
Ph
I
3d
8.2810
8.2564
7.7745
7.7698
7.7546
7.7470
7.7081
7.5915
7.5488
7.5346
7.5308
7.5270
7.5089
7.4719
7.2291
7.2244
7.2026
7.1978
2.2523
Integral
0.9285
1.7306
5.2458
1.9172
3.0902
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
(ppm)

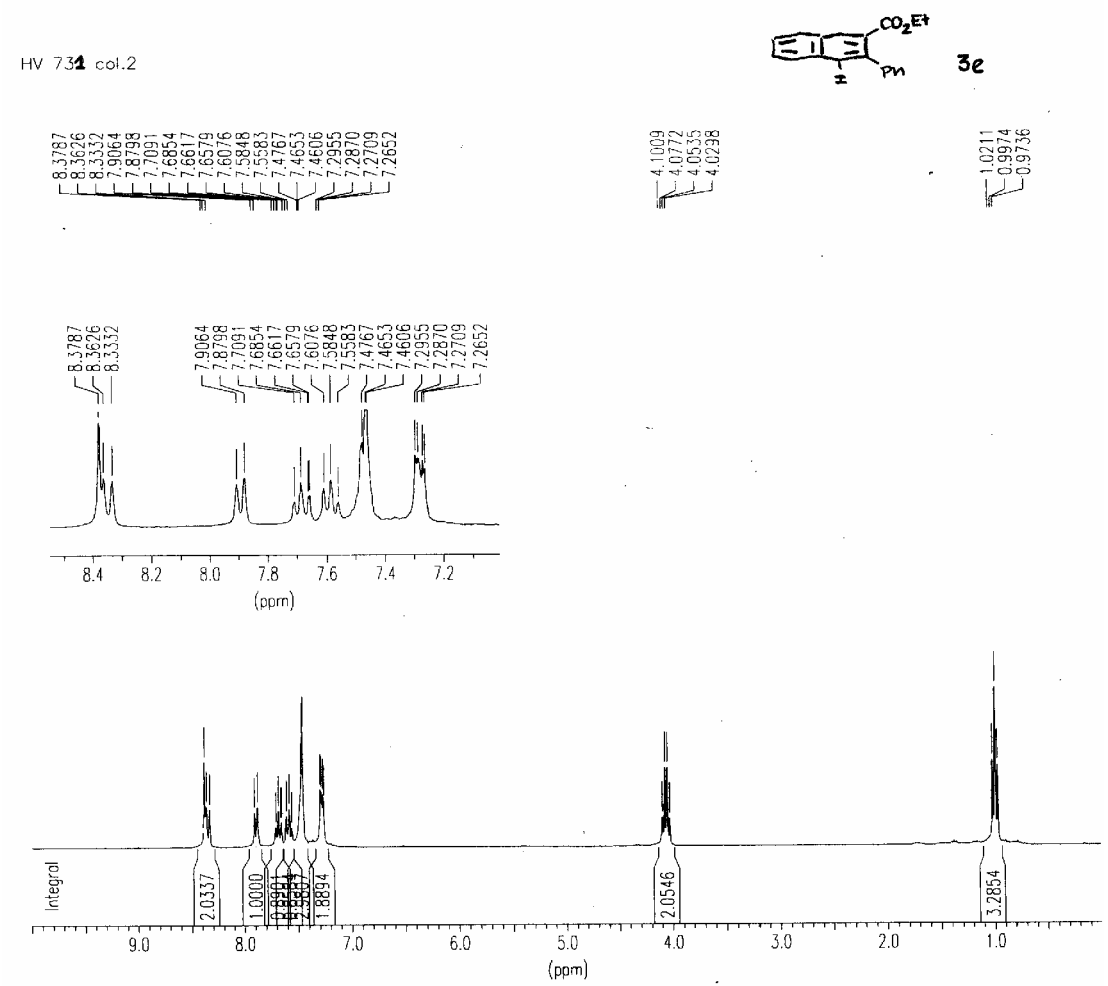
Compound 3d:


146.9232
145.7628
134.9061
133.5172
133.2008
128.9107
128.5789
128.3397
127.4292
127.3751
127.0125
126.5109
105.9551
22.8365
(ppm)
(ppm)

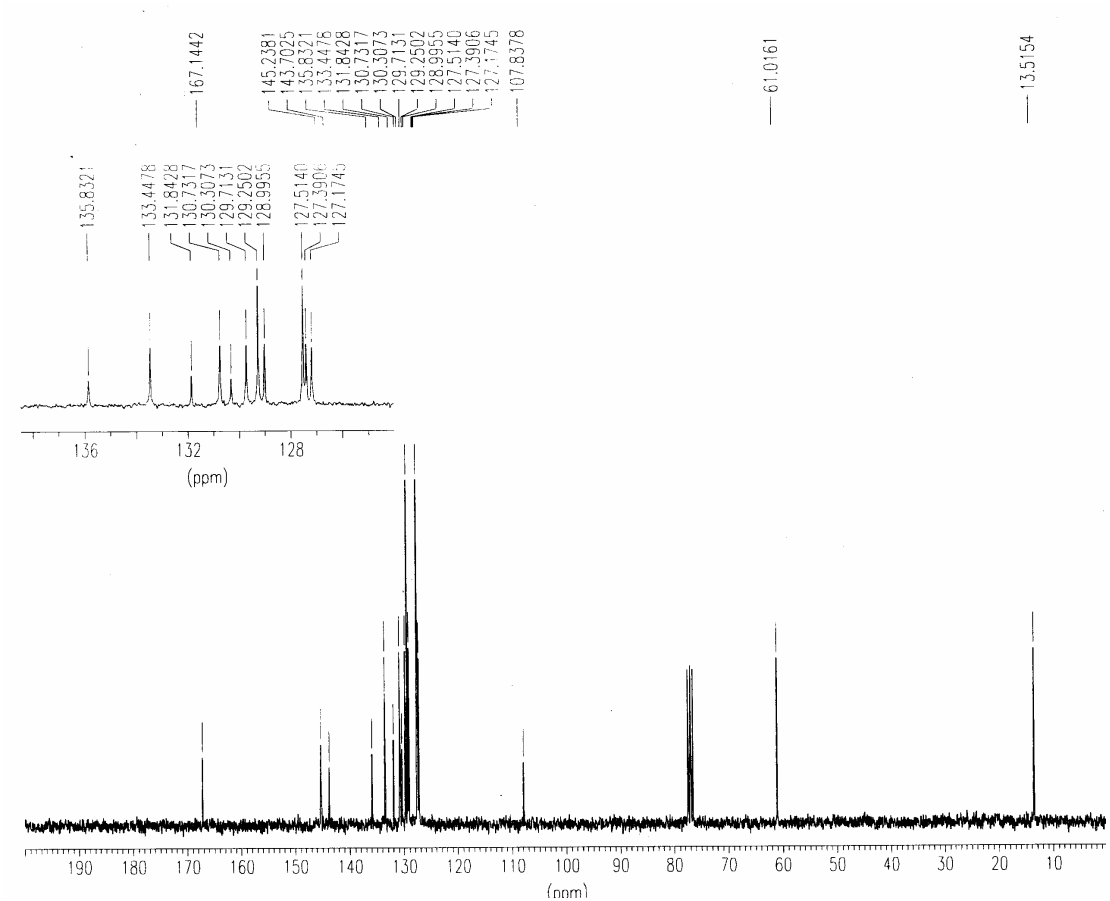
Compound 3d:


H4
me
Ph
H2
I
HV-723.1□HMBC AV40
3d
H1
H2
ppm
20
30
40
50
60
70
80
90
100
110
C-Me
C-I
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
ppm

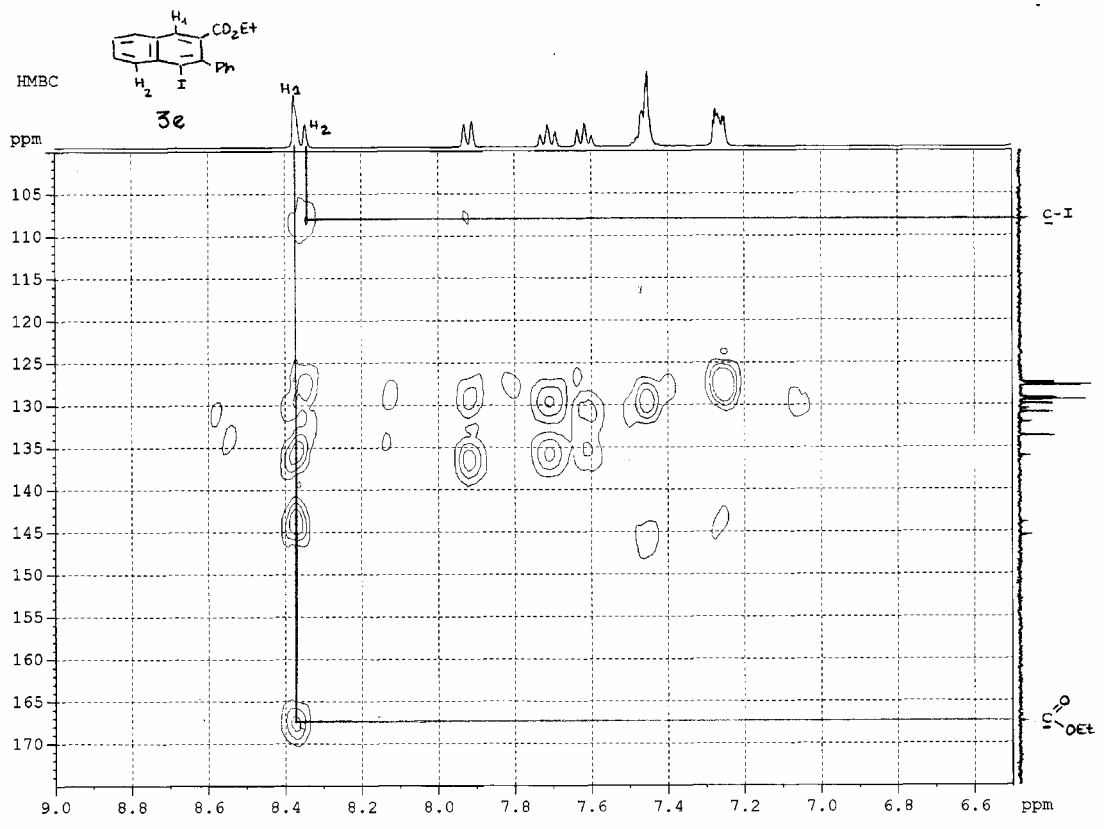
Compound 3e:


HV 731 col.2
3e
8.3787
8.3626
8.3332
7.9064
7.8798
7.7091
7.6854
7.6617
7.6579
7.6076
7.5848
7.5583
7.4767
7.4653
7.4606
7.2955
7.2870
7.2709
7.2652
4.1009
4.0772
4.0535
4.0298
1.0211
0.9974
0.9736
8.4
8.2
8.0
7.8
7.6
7.4
7.2
(ppm)
Integral
2.0337
1.0000
1.8894
2.0546
3.2854
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
(ppm)

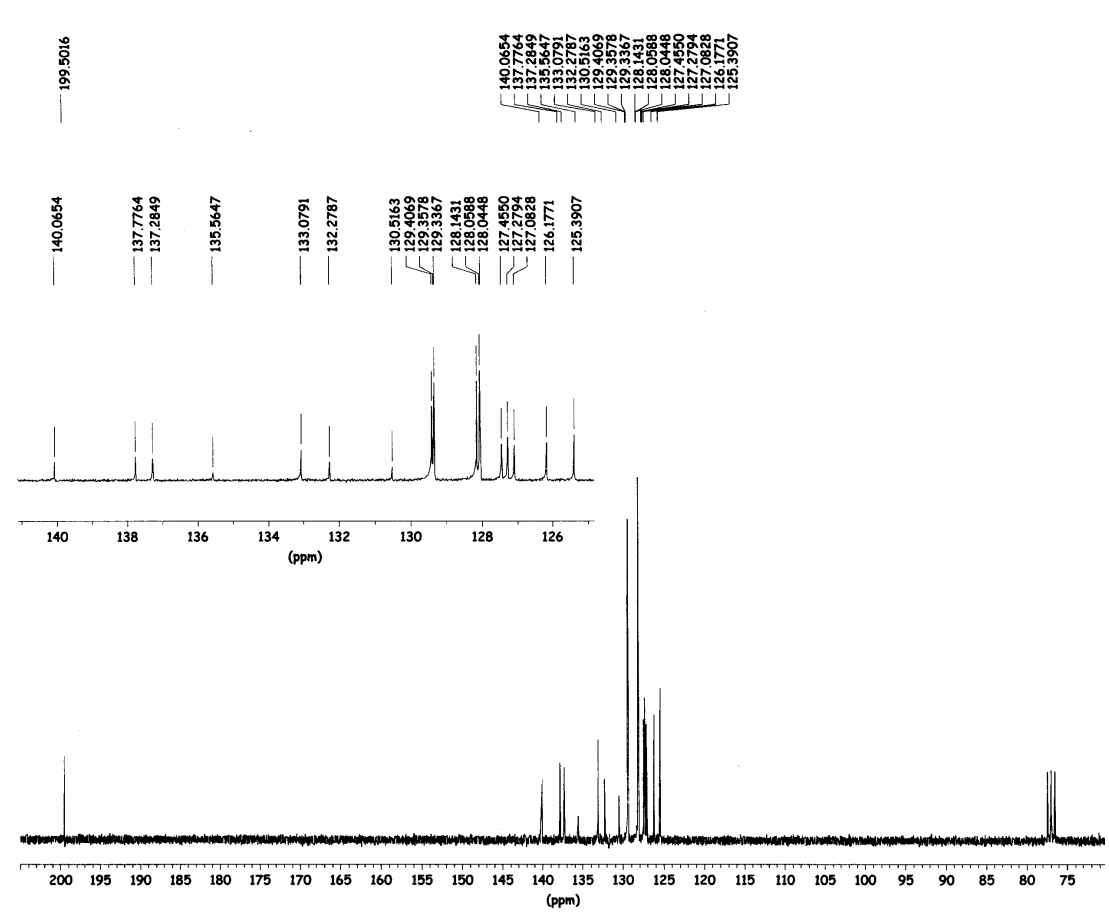
Compound 3e:


167.1442
145.2381
143.7025
135.8321
133.4476
131.8428
130.7317
130.3073
129.7131
129.2502
128.9955
127.5140
127.3906
127.1745
107.8378
61.0161
13.5154
135.8321
133.4478
131.8428
130.7317
130.3073
129.7131
129.2502
128.9955
127.5140
127.3906
127.1745
136
132
128
(ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

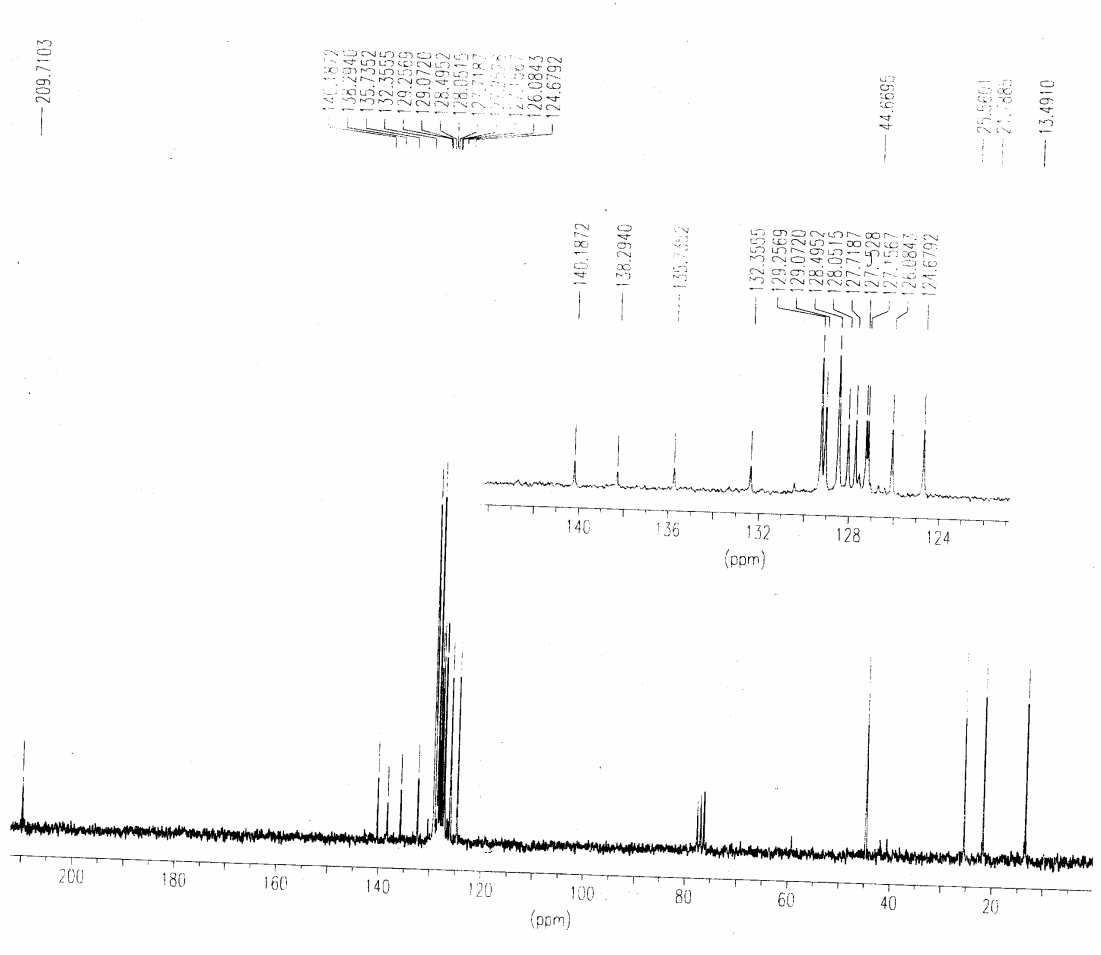
Compound 3e:


HMBC
3e
ppm
105
110
115
120
125
130
135
140
145
150
155
160
165
170
9.0
8.8
8.6
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
ppm
C-I
OEt

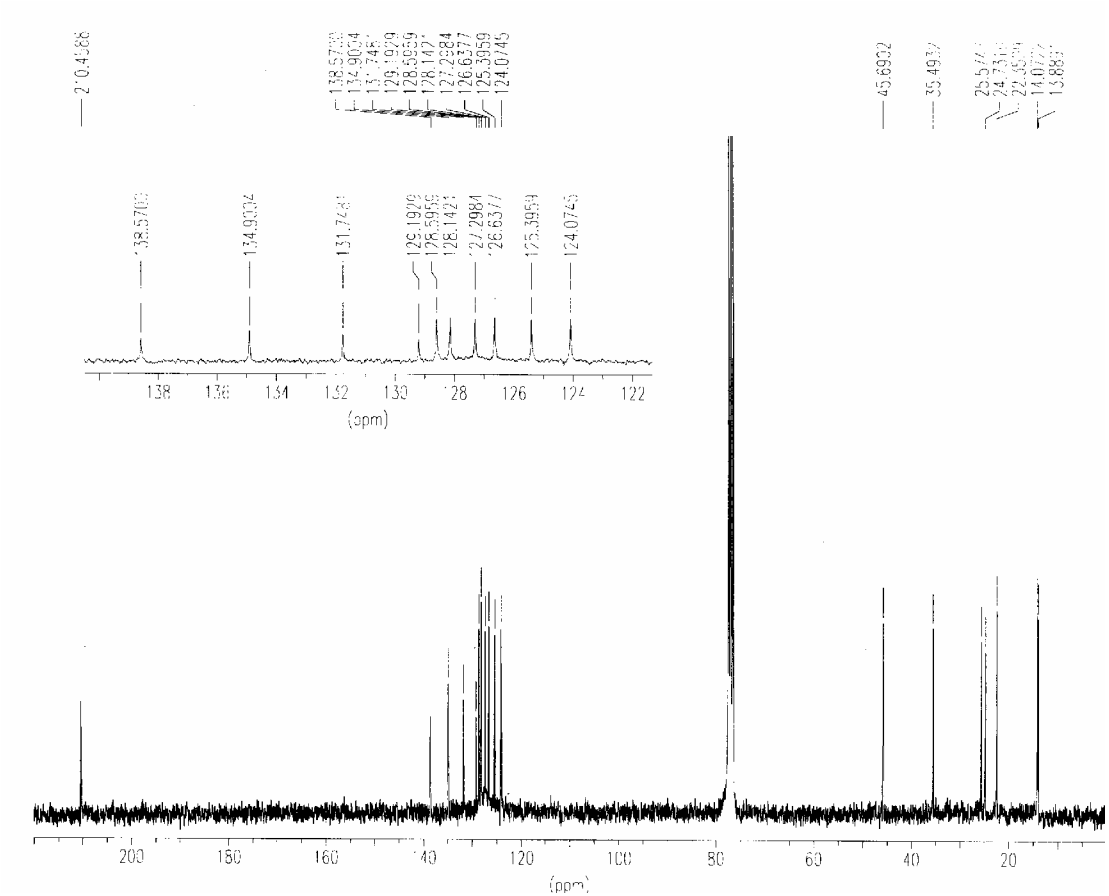
Compound 4a:


199.5016
140.0654
137.7764
137.2849
135.5647
133.0791
132.2787
130.5163
129.4069
129.3578
129.3367
128.1431
128.0588
128.0448
127.4550
127.2794
127.0828
126.1771
125.3907
(ppm)
(ppm)

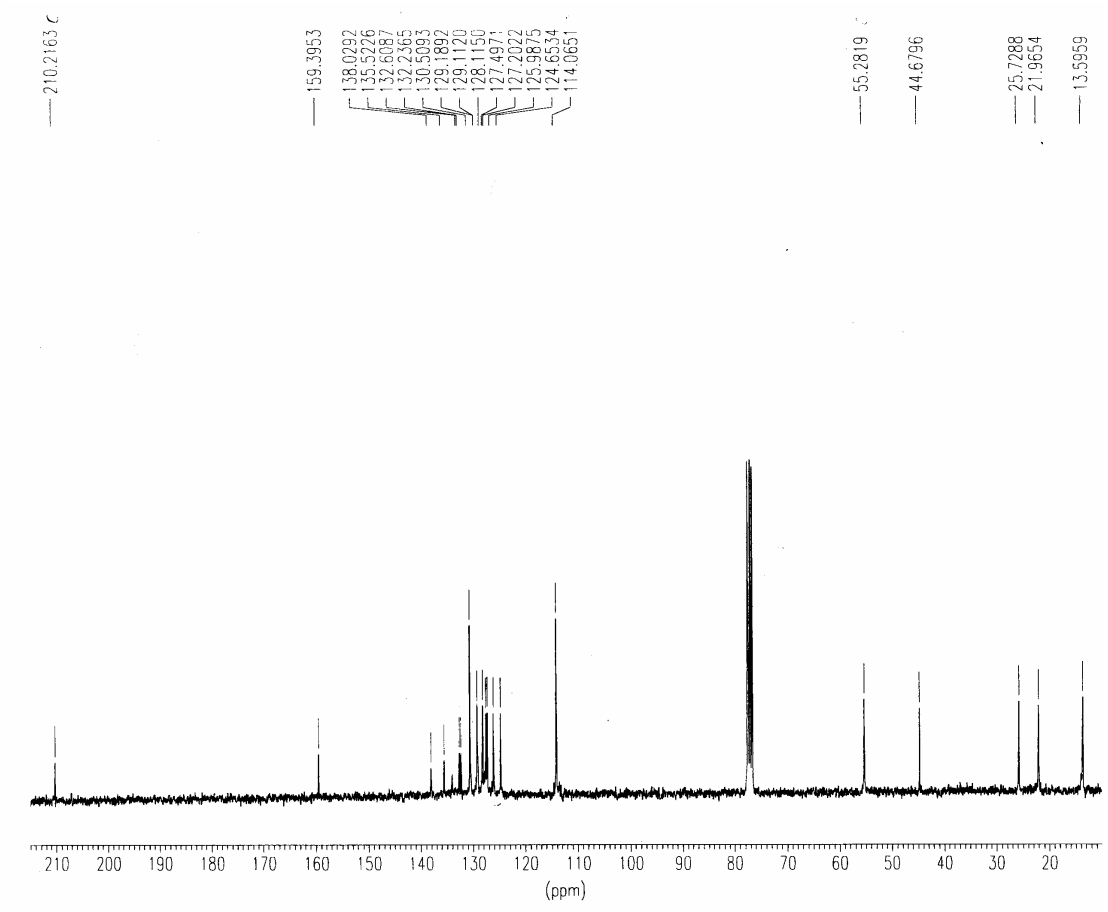
Compound 4b:


209.7103
140.1872
138.2940
135.7352
132.3555
129.2569
129.0720
128.4952
128.0515
127.7187
126.0843
124.6792
44.6695
13.4910
(ppm)
(ppm)

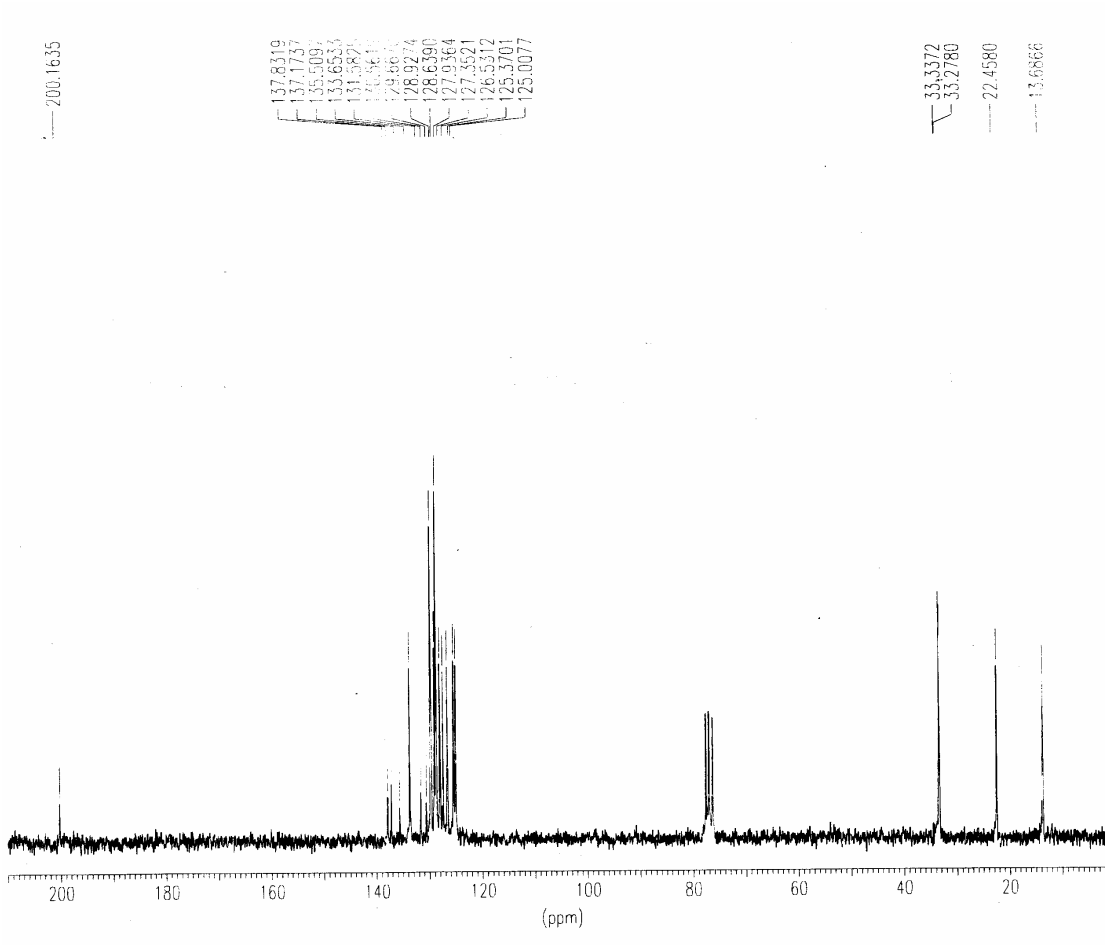
Compound 4c:


138.5700
134.9034
131.7481
129.1929
128.5959
128.1421
127.2984
126.6377
125.3959
124.0745
45.6932
35.4937
25.5777
24.7316
22.3594
14.0777
13.8837
138
136
134
132
130
128
126
124
122
(ppm)
200
180
160
140
120
100
80
60
40
20
(ppm)

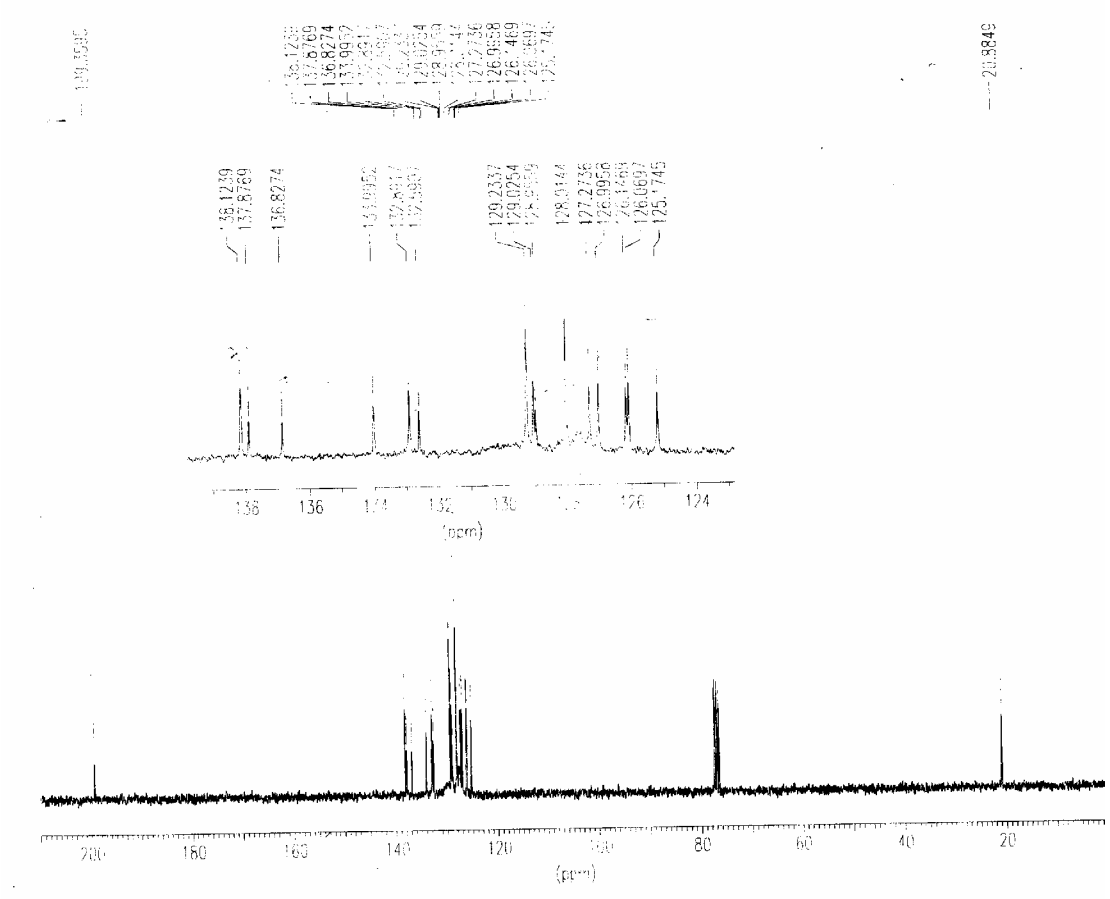
Compound 4d:


210.2163
159.3953
138.0292
135.5226
132.6087
132.2565
130.5093
129.1892
129.1120
128.1150
127.4971
127.2022
125.9875
124.6534
114.0651
55.2819
44.6796
25.7288
21.9654
13.5959
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
(ppm)

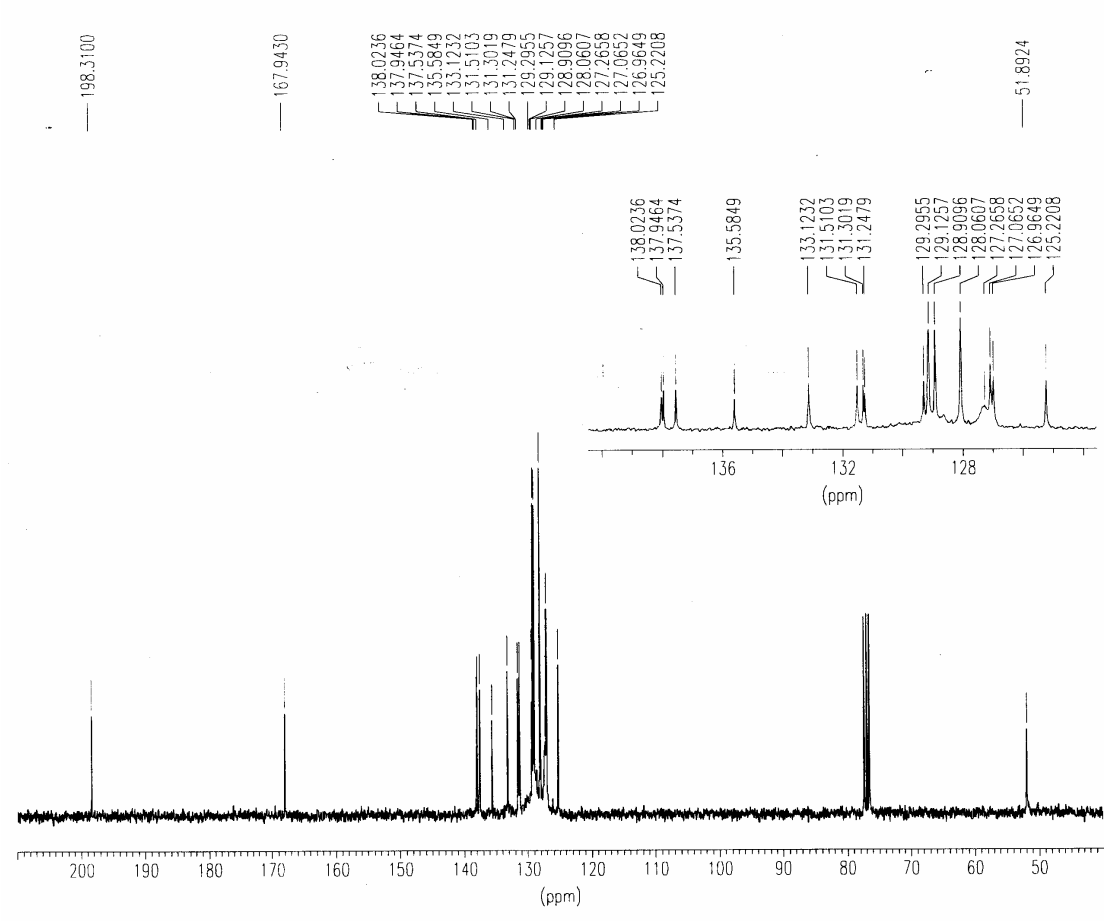
Compound 4e:


200.1635
137.8319
137.1737
135.5097
133.6533
131.5827
128.9274
128.6390
127.9364
127.3521
126.5312
125.3701
125.0077
33.3372
33.2780
22.4580
13.6866
200
180
160
140
120
100
80
60
40
20
(ppm)

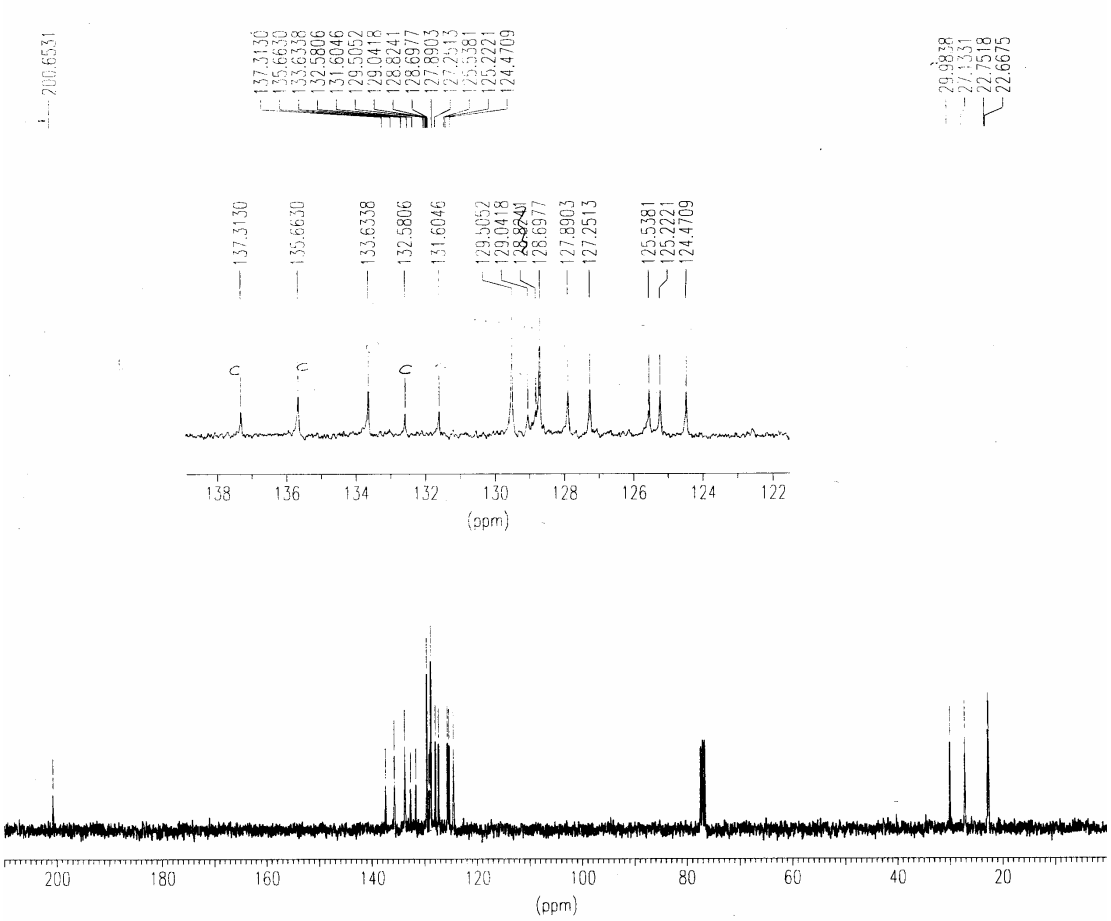
Compound 4f:



Compound 4g:


198.3100
167.9430
138.0236
137.9464
137.5374
135.5849
133.1232
131.5103
131.3019
131.2479
129.2955
129.1257
128.9096
128.0607
127.2658
127.0652
126.9649
125.2208
51.8924
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
(ppm)
136
132
128
(ppm)

Compound 4h:


200.6531
137.3130
135.6630
133.6338
132.5806
131.6046
129.5052
129.0418
128.8241
128.6977
127.8903
127.2513
125.5381
125.2221
124.4709
29.9838
27.1331
22.7518
22.6675
138
136
134
132
130
128
126
124
122
(ppm)
200
180
160
140
120
100
80
60
40
20
(ppm)