Supporting Information

Palladium-Catalyzed Cross-Coupling Reaction of Organoindiums with Aryl Halides in Aqueous Media

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Instrumentation and Materials

^{1}H NMR (300 MHz) and ^{13}C NMR (75.3 MHz) spectra were taken on a Varian GEMINI 300 spectrometer in $CDCl_3$ as a solvent, and chemical shifts were given in δ value with tetramethylsilane as an internal standard. TLC analyses were performed on commercial glass plates bearing 0.25-mm layer of Merck Silica gel $60F_{254}$. Silica gel (Wakogel 200 mesh) was used for column chromatography.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl before use. Distilled water and methanol were purchased from Wako Pure Chemicals and used as they were. DMF was dried with molecular sieves 4A. Dioxane was dried over slices of sodium. Anhydrous indium trichloride was purchased from Mitsuwa Pure Chemicals and was dried in a reaction flask carefully under reduced pressure (0.5 torr) by heating with a hair dryer for 1 min immediately before use. Tris(dibenzylideneacetone)dipalladium ($Pd_2(dba)_3 \cdot CHCl_3$) was prepared according to the literature.[1] Trifurylphosphine was prepared by treating phosphorus trichloride (10 mmol) with furyllithium (32 mmol), prepared from furan (33 mmol) and *n*-butyllithium (1.6 M hexane solution, 32 mmol) in refluxing ether (30 mL).

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[1] Ukai, T.; Kawazura, H.; Ishii, Y. *J. Organomet. Chem.* **1974**, *65*, 253.

Reaction of Triorganoindium with 3-Iodoanisole in Aqueous THF

The reaction of triphenylindium with 3-iodoanisole was representative. Phenylmagnesium bromide (1.0 M THF solution, 3.0 mL, 3.0 mmol) was added dropwise to a solution of indium trichloride (221 mg, 1.0 mmol in 1 mL of THF) under argon. After the mixture was stirred for 30 min, water (1.0 mL) and 3-iodoanisole (702 mg, 3.0 mmol) were introduced to the reaction flask. After the addition of water, the solution turned into a white suspension. The palladium complex, prepared by mixing $Pd_2(dba)_3•CHCl_3$ (10 mg, 0.01 mmol) and trifurylphosphine (14 mg, 0.06 mmol) in THF (1 mL) in another reaction flask, was then added by a syringe. The whole mixture was stirred at reflux for 2.5 h. Bath temperature was 80 ˚C. After the mixture was cooled, water (10 mL) was added, and the product was extracted with hexane (10 mL × 3). Combined organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo. Silica gel column purification afforded 0.386 g of 3-methoxybiphenyl (2.1 mmol) and 0.211 g of 3-iodoanisole (0.90 mmol).

Partial Hydrolysis of Triphenylindium to Form Diphenylindium Hydroxide

Phenylmagnesium bromide (1.0 M THF solution, 3.0 mL, 3.0 mmol) was added to a THF solution of indium trichloride (0.221 g, 1.0 mmol / 1 mL) at 25 ˚C under argon. Tetramethylsilane (0.14 mL, 1.0 mmol) was then added as an internal standard. After the clear solution was stirred for 15 min, 0.6 mL of the solution was taken up with a syringe and was put in an NMR tube that contained a capillary tube filled with benzene-d_6. The ^{13}C NMR experiment of the NMR sample showed Chart 1. On the other hand, water (1.0 mL) was added to the remaining solution of triphenylindium to give a suspension. The suspension was stirred for 5 min and then stood undisturbed. The supernatant was similarly taken up and was measured by ^{13}C NMR (Chart 2). The production of benzene was confirmed. Rough calculations based on the integration of **B** (2C) and **E** (6C) indicated the formation of diphenylindium hydroxide. The fact that two phenyl groups are on the indium center was also obvious because the coupling reaction yielded 0. 21 mmol of the product as shown in Scheme 1.

Formation of Diphenylindium Hydroxide from Diphenylindium Chloride by the Action of Water

A THF solution of phenylmagnesium bromide (1.0 M, 2.0 mL, 2.0 mmol) was added dropwise to indium trichloride (0.221 g, 1.0 mmol) in THF (1 mL) at 25 ˚C under an argon atmosphere. Tetramethylsilane (0.14 mL. 1.0 mmol) was added and the whole mixture was stirred for 15 min. Water (1.0 mL) was added to the solution. The resulting suspension was stirred for 5 min. After the stirring was stopped, an NMR tube containing a capillary filled with benzene-d_6 was charged with the supernatant (0.6 mL). The ^{13}C NMR chart is Chart 3, which is quite similar to Chart 2. Therefore, diphenylindium chloride was converted into diphenylindium hydroxide by the addition of water.

Procedure for Coupling Reaction of Diphenylindium Species with Aryl Halide in Aqueous Media

The reaction of 3-iodoanisole is representative. Indium trichloride (0.144 g, 0.65 mmol) was placed in a reaction flask under argon and was dissolved with 1 mL of THF. Phenylmagnesium bromide (1.0 M THF solution, 1.3 mL, 1.3 mmol) was added dropwise to indium trichloride at 25 ˚C. The whole mixture was stirred for 30 min to prepare diphenylindium chloride. Water (0.50 mL) and 3-iodoanisole (0.234 g, 1.0 mmol) was then added. The palladium-trifurylphosphine complex, prepared from $Pd_2(dba)_3•CHCl_3$ (2.5 mg, 0.0025 mmol) and trifurylphosphine (3.5 mg, 0.015 mmol) in THF (1 mL) in another reaction flask, was introduced by a syringe. The resulting mixture was heated at reflux for 3 h. After water (10 mL) was added to the reaction flask, the product was extracted with hexane (10 mL × 3). Concentration followed by silica gel column purification afforded 3-methoxybiphenyl (0.184 g, 1.0 mmol) as a colorless oil in 100% yield.

Coupling Reaction with Phenylindium Compound with 4-Iodobenzoic Acid in a THF/Water Mixed Solvent

Indium trichloride (0.487 g, 2.2 mmol) in THF (3.0 mL) was treated with phenylmagnesium bromide (1.0 M THF solution, 2.2 mL, 2.2 mmol) at 25 ˚C under argon for 30 min. Water (0.50 mL), sodium hydrogencarbonate (0.420 g, 5.0 mmol), 4-iodobenzoic acid (**1i**, 0.248 g, 1.0 mmol), and the palladium complex (0.005 mmol in 1 mL of THF) were sequentially added. The mixture was heated at reflux for 4 h. After cooling, 1M HCl (10 mL) was added and the mixture was then extracted with ethyl acetate (20 mL × 3). Combined organic layer was dried over Na_2SO_4 and the solvent was evaporated. The crude product was dissolved in DMF (6 mL). After allyl bromide (0.34 mL, 3.0 mmol) and K_2CO_3 were added, the mixture was stirred at 25 ˚C overnight. Extractive workup followed by silica gel column purification provided 0.214 g of allyl 4-biphenylcarboxylate (0.90 mmol) in 90% yield.

Hydrolysis of Trivinylindium

Vinylmagnesium bromide (1.0 M THF solution, 3.0 mL, 3.0 mmol) was added to a THF solution of indium trichloride (0.221 g, 1.0 mmol). *p*-Xylene (0.25 mL, 2.0 mmol) was added to the solution as an internal standard. The ^{13}C NMR experiments were conducted as described in the measurement of the phenylindium compounds. A capillary filled with $CDCl_3$ was used for locking. Chart 4 was obtained before the addition of water, and Chart 5 after the addition. The calculations based on the integrations of **B** and **C** in Chart 4 and 5 suggest that one of the three vinyl groups was disappeared.

Hydrolysis of Triethylindium

Similar experiments were performed, giving Chart 6 (before the addition of water) and Chart 7 (after the addition). The change of the integration of **B**, compared with the integration of **C**, indicates the formation of organoindium that consists of two ethyl groups and one indium.

Trimethylindium in Aqueous THF

Trimethylindium was prepared from indium trichloride (0.111 g, 0.5 mmol in 1 mL of THF) and methyllithium (1.1 M ether solution, 1.36 mL, 1.5 mmol). The ratio of the integration of **A** to the integration of **B** did not change upon addition of water. Trimethylindium seemed stable in water (Chart 8 and 9).

Decomposition of Tri(1-octynyl)indium

Tri(1-octynyl)indium was prepared by mixing octynyllithium (*n*-BuLi + $n\text{-}C_6H_{13}C{\equiv}CH$) with indium trichloride. Before the addition of water, **A** and **B** in Chart 10 indicated the acetylenic carbons. However, **A** and **B** were completely disappeared upon addition of water (Chart 11). Formation of 1-octyne was observed.

Procedure for Coupling Reaction with Divinyl-, or Diethylindium in a THF/Water Mixed Solvent

The reaction of vinylindium with **1a** is representative. Vinylmagnesium bromide (1.0 M THF solution, 1.3 mL, 1.3 mmol) was added to a solution of indium trichloride (0.144 g, 0.65 mmol) in THF (1.0 mL) under argon. After the mixture was stirred for 30 min, water (0.5 mL), 3-iodoanisole (**1a**, 0.234 g, 1.0 mmol), and the palladium complex prepared as above (0.005 mmol in 1 mL of THF) were sequentially added. The mixture was heated at reflux for 3 h. Workup and silica gel column purification provided 0.129 g of 3-methoxystyrene (**3a**, 0.96 mmol) in 96% yield.

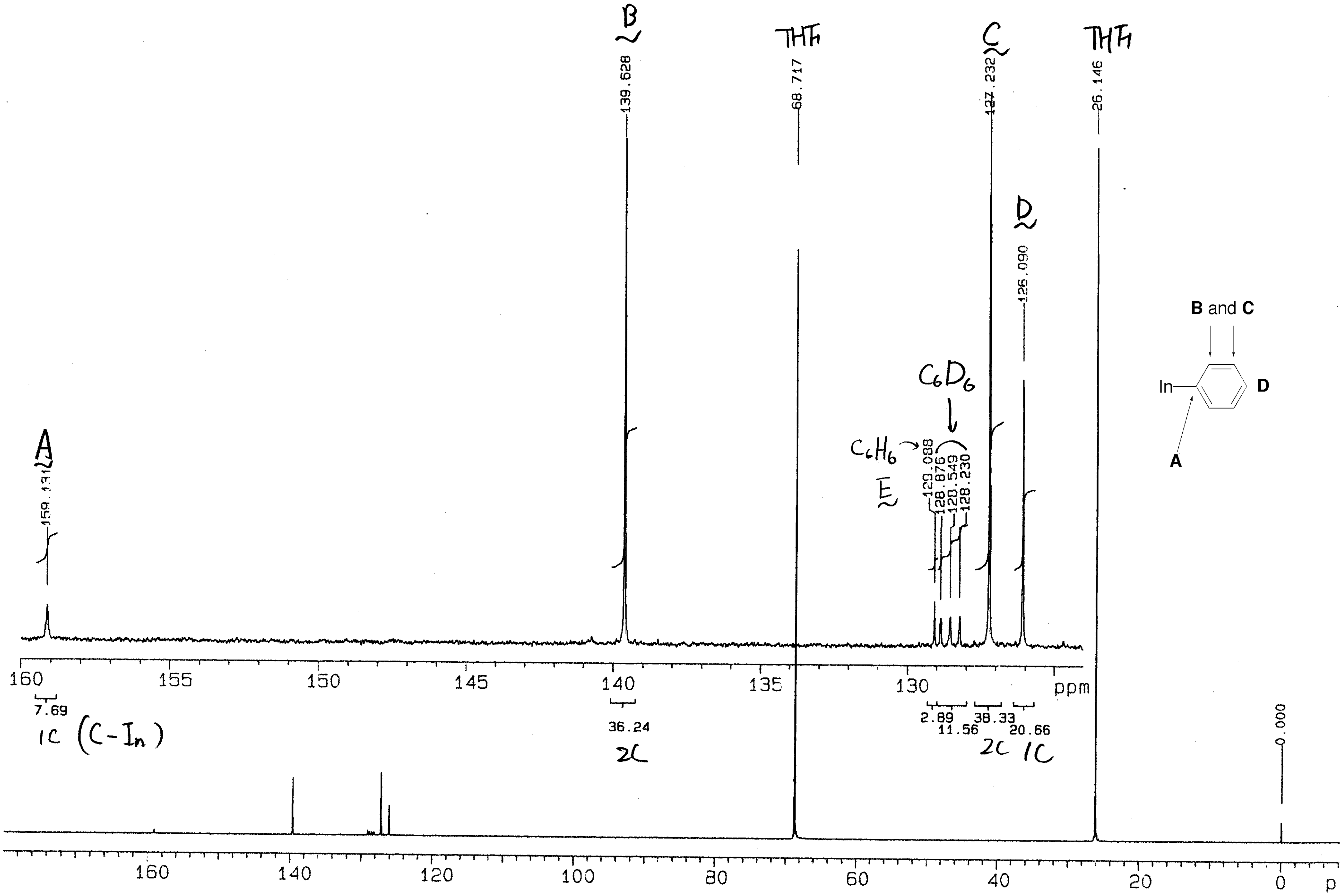
A
159.131
1C (C-In)
7.69
B
139.628
36.24
2C
THF
68.717
C
127.232
THF
26.146
D
126.090
C6D6
C6H6
E
129.088
128.876
128.549
128.230
2.89
11.56
38.33
20.66
2C
1C
160
155
150
145
140
135
130
ppm
0.000
160
140
120
100
80
60
40
20
0
p
B and C
In
D
A

Chart 1.

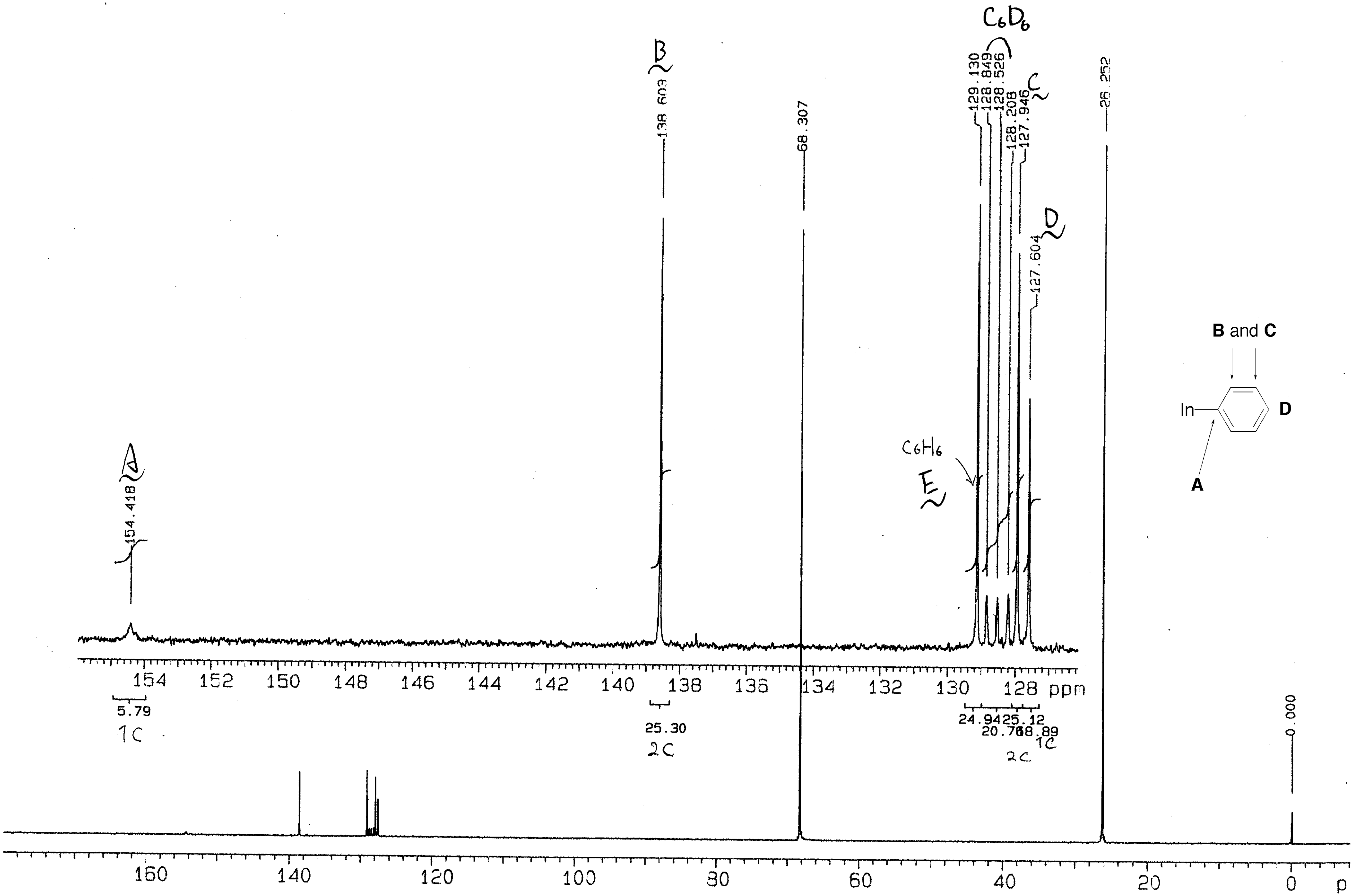
C6D6
B
C
D
A
E
C6H6
154.418
138.603
68.307
129.130
128.849
128.526
128.208
127.946
127.604
26.252
0.000
154
152
150
148
146
144
142
140
138
136
134
132
130
128 ppm
5.79
1C
25.30
2C
24.94
25.12
20.76
68.89
1C
2C
160
140
120
100
80
60
40
20
0
p
B and C
In
D
A

Chart 2.

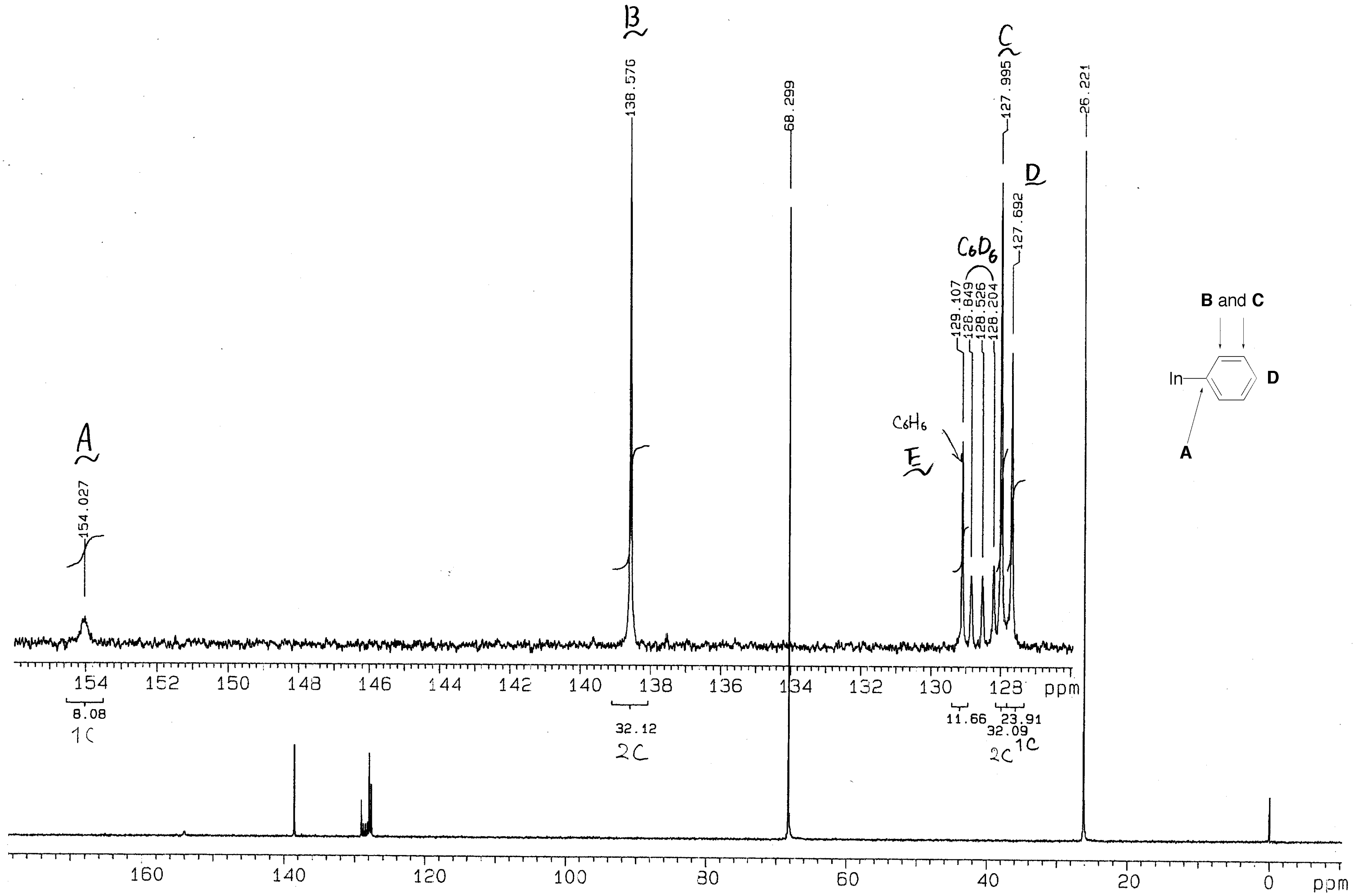
B
138.576
68.299
C
127.995
26.221
D
127.692
C6D6
129.107
128.849
128.526
128.204
B and C
In
D
A
C6H6
E
A
154.027
154
152
150
148
146
144
142
140
138
136
134
132
130
128
ppm
8.08
1C
32.12
2C
11.66
23.91
32.09
2C
1C
160
140
120
100
80
60
40
20
0
ppm

Chart 3.

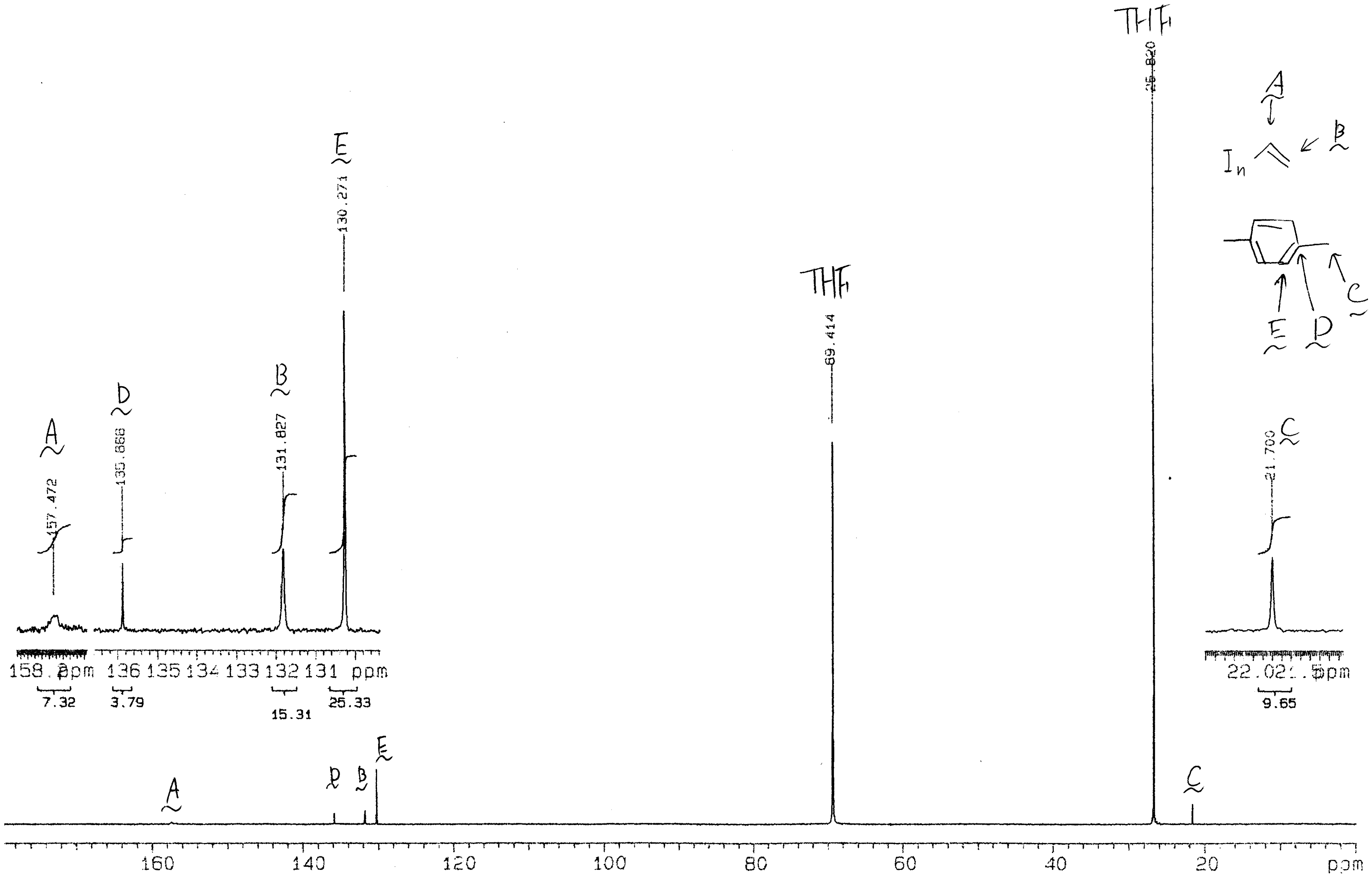
THF
25.820
E
130.271
THF
69.414
B
131.827
D
135.866
A
157.472
C
21.700
A
B
In
C
E
D
ppm
136
135
134
133
132
131
ppm
7.32
3.79
15.31
25.33
22.0
21.5
ppm
9.65
A
D
B
E
C
160
140
120
100
80
60
40
20
ppm

Chart 4

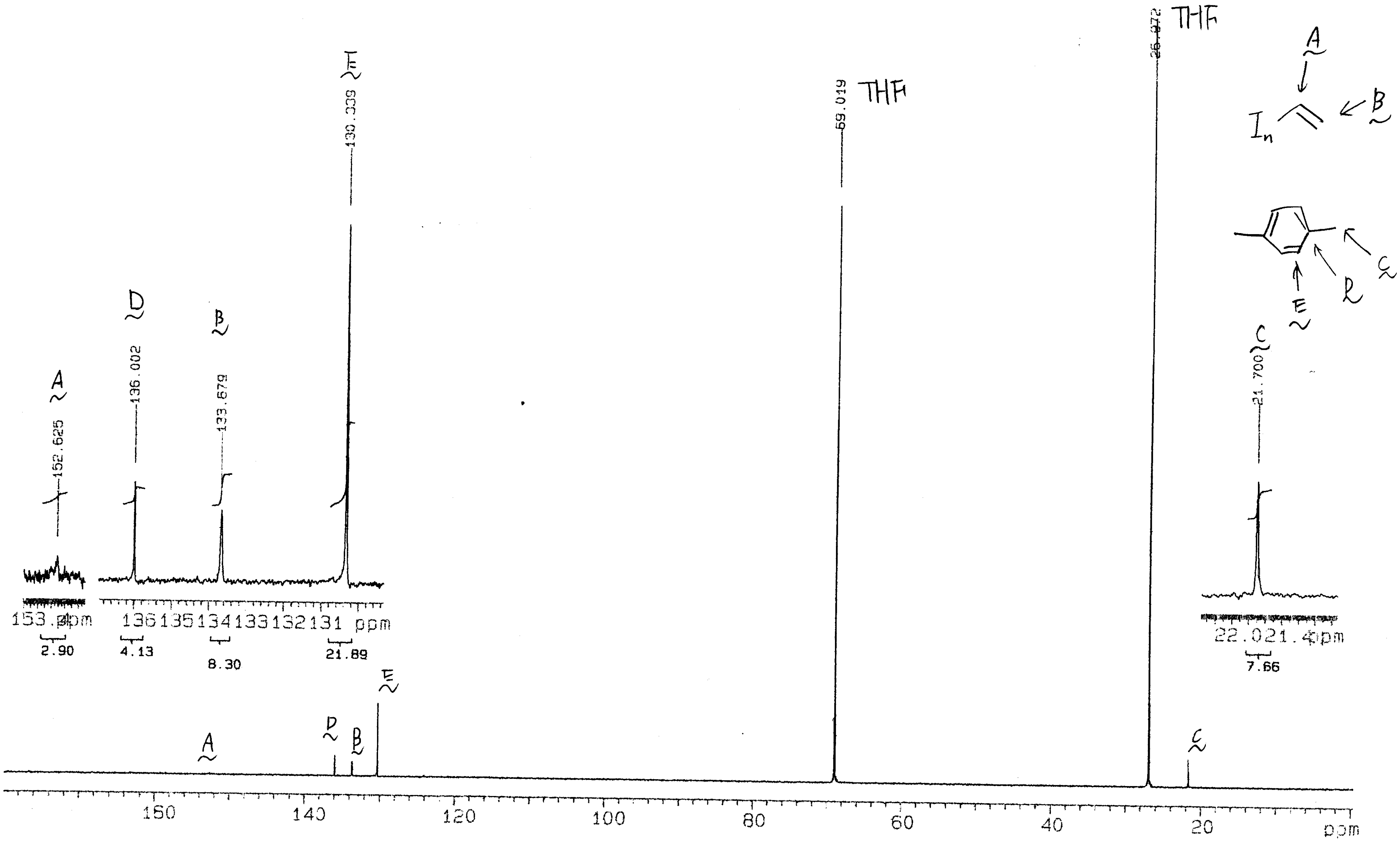
26.872
THF
69.019
THF
130.339
E
136.002
D
133.679
B
152.625
A
153.2ppm
136 135 134 133 132 131 ppm
2.90
4.13
8.30
21.89
21.700
C
22.0 21.4ppm
7.66
A
B
I_n
C
D
E
A
D
B
E
C
160
140
120
100
80
60
40
20
ppm

Chart 5

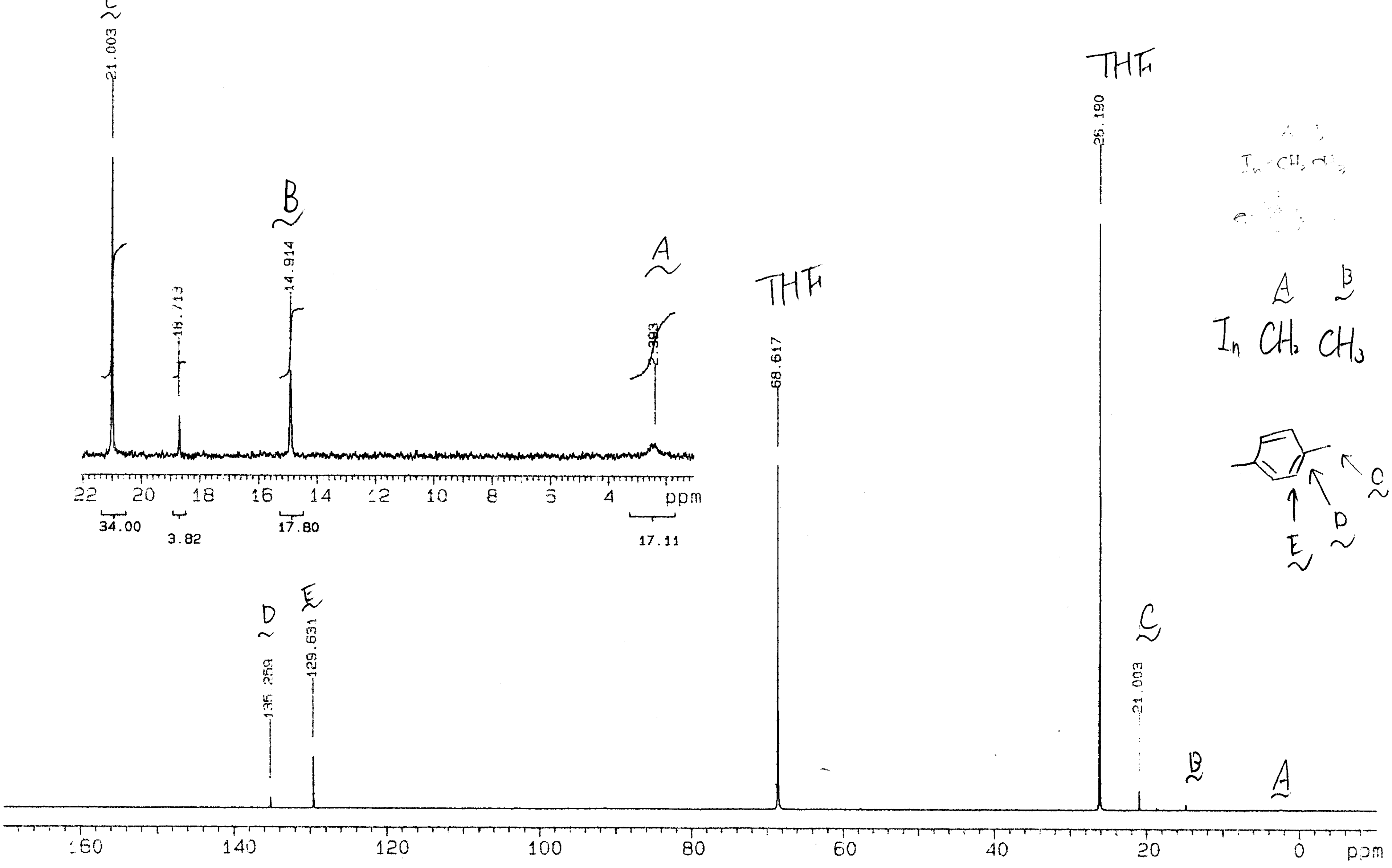
C
21.003
18.713
B
14.914
A
2.393
22
20
18
16
14
12
10
8
6
4
ppm
34.00
3.82
17.80
17.11
THF
68.617
THF
26.190
A B
$In\ CH_2\ CH_3$
C
D
E
D
135.259
E
129.631
C
21.003
B
A
160
140
120
100
80
60
40
20
0
ppm

Chart 6

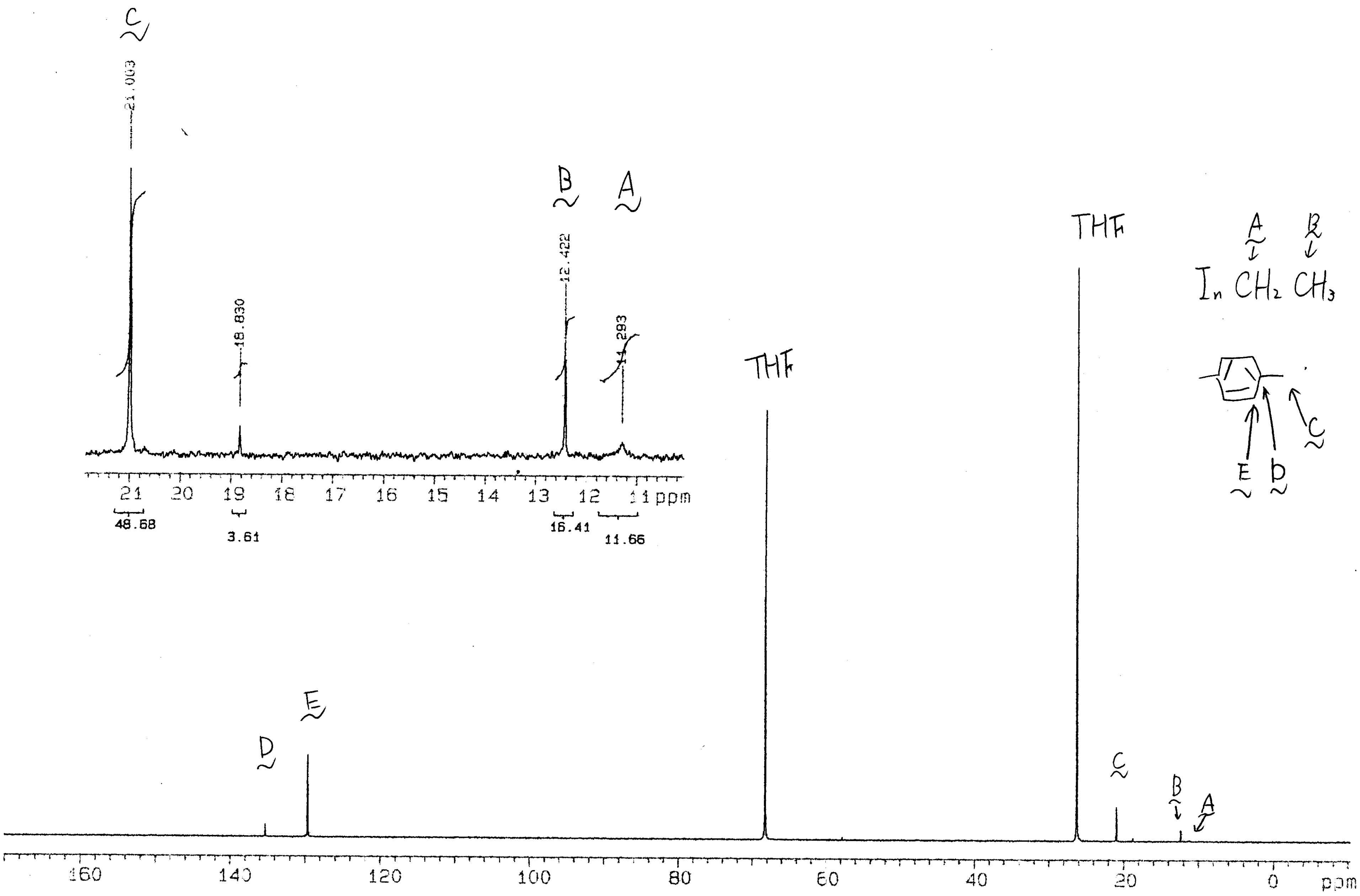
C
21.003
18.830
B
12.422
A
11.293
21
20
19
18
17
16
15
14
13
12
11 ppm
48.68
3.61
16.41
11.66
THF
THF
A
B
In CH₂ CH₃
E
b
C
D
E
C
B
A
160
140
120
100
80
60
40
20
0
ppm

Chart 7

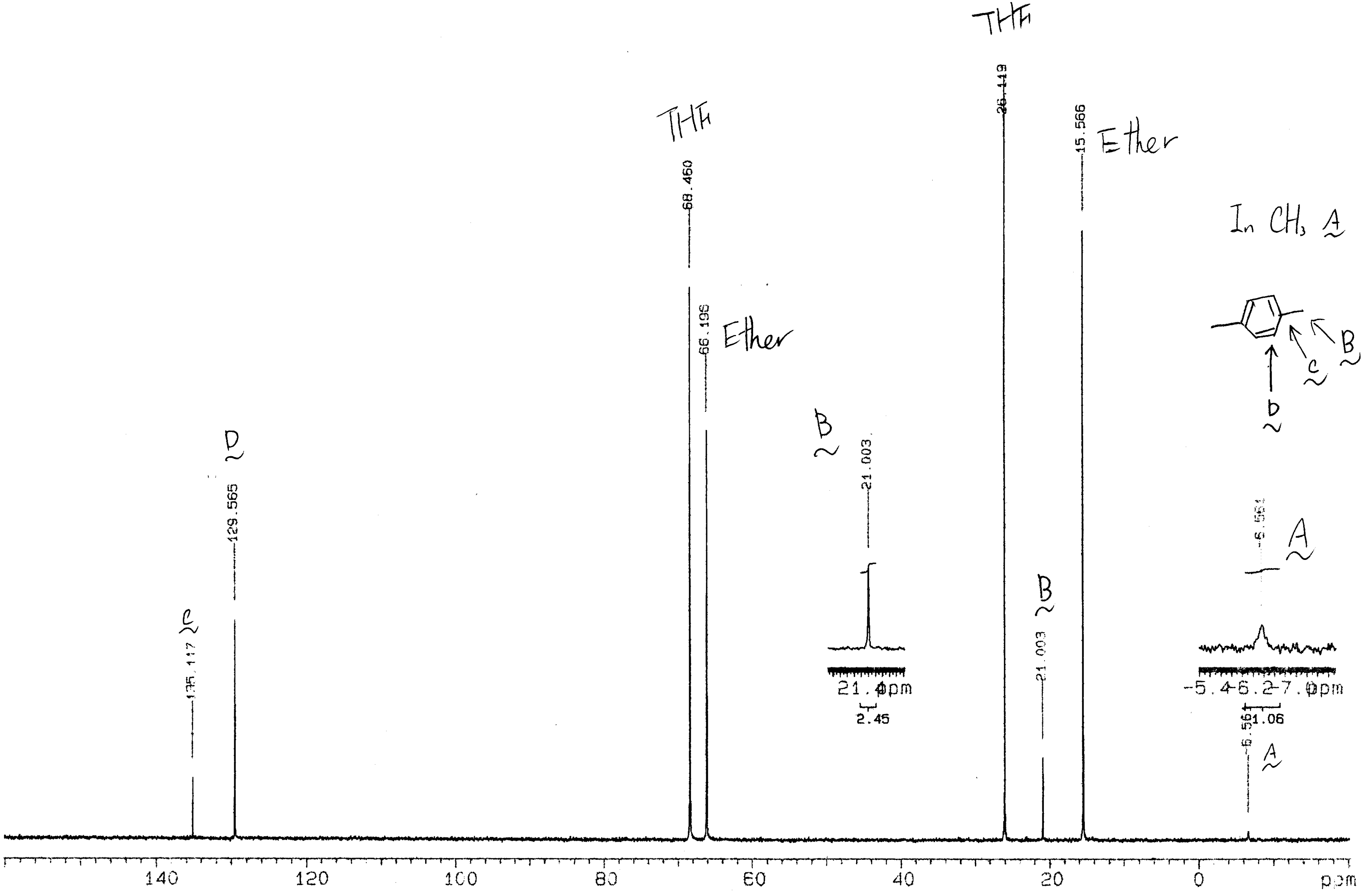
THF
68.450
THF
26.119
15.566
Ether
66.196
Ether
In CH3 A
B
c
b
D
129.565
c
135.117
B
21.003
21.0ppm
2.45
B
21.003
-6.564
A
-5.4-6.2-7.0ppm
-6.56
1.06
A
140
120
100
80
60
40
20
0
ppm

Chart 8

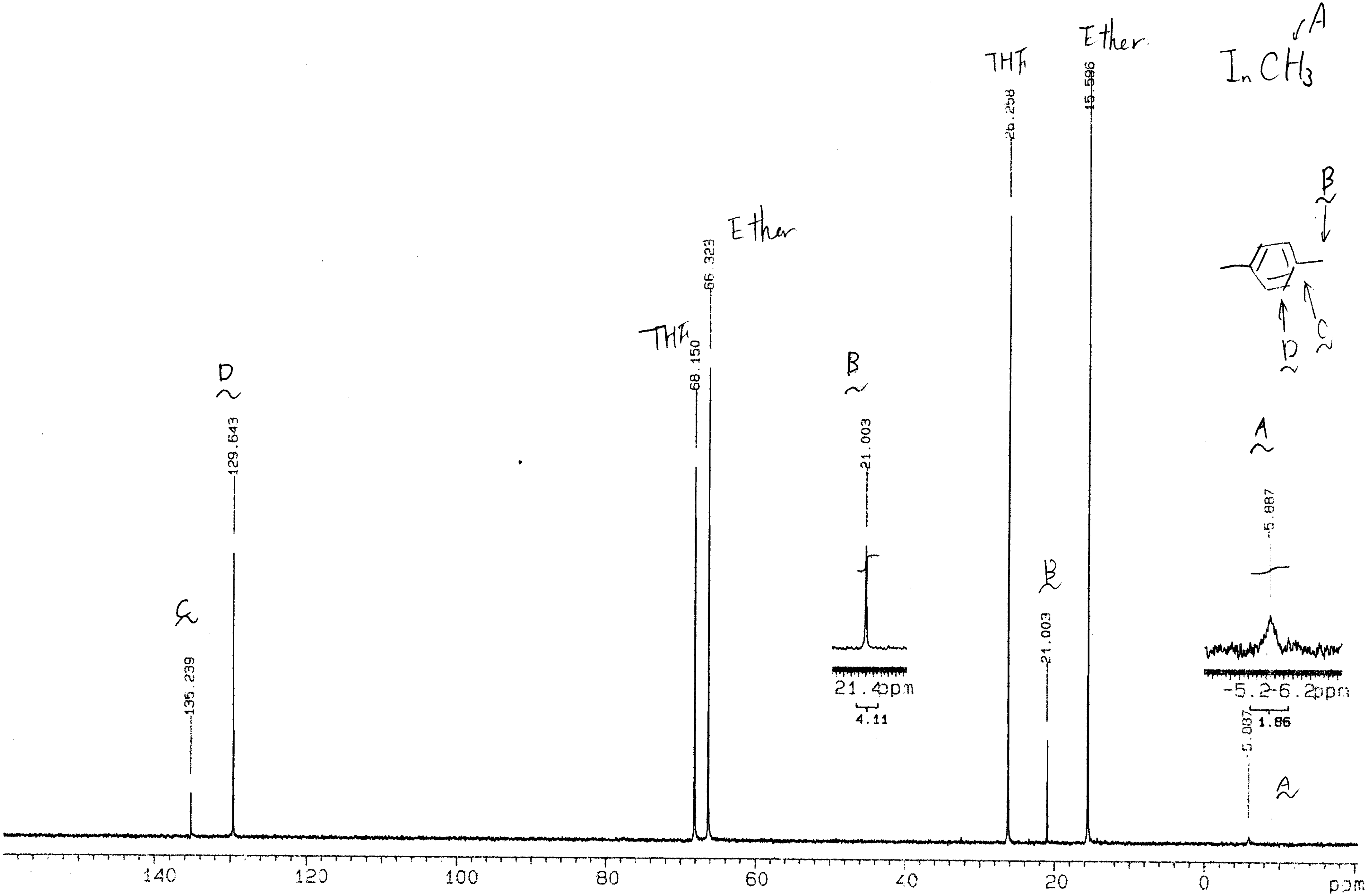In CH3
A
Ether
15.596
THF
26.258
Ether
66.323
THF
68.150
B
21.003
21.4ppm
4.11
D
129.643
C
135.239
B
21.003
A
-5.887
-5.2-6.2ppm
1.86
-5.887
A
B
C
D
140
120
100
80
60
40
20
0
ppm

Chart 9

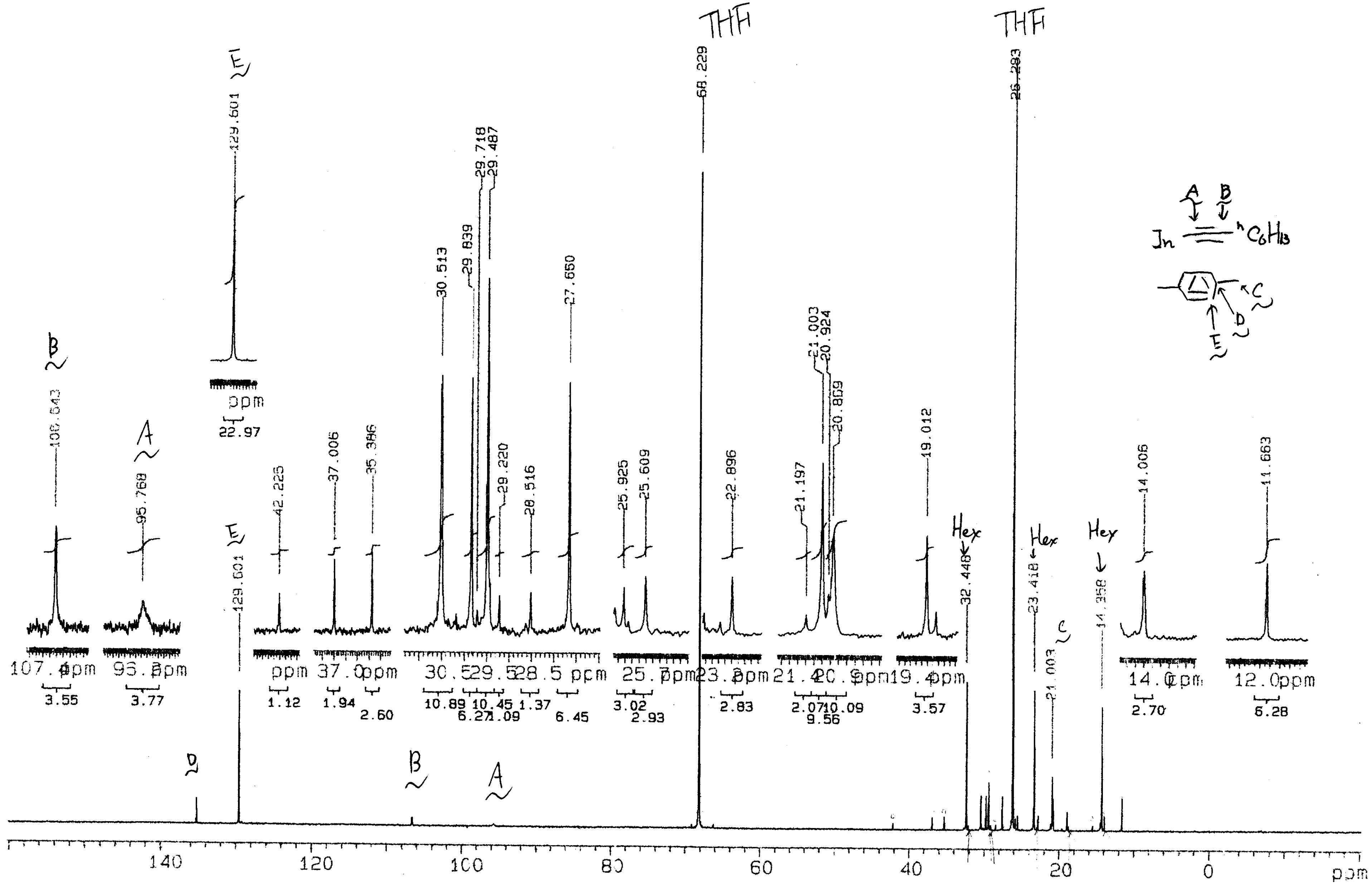
THF
THF
E
129.601
ppm
22.97
B
106.643
A
95.768
42.225
37.006
35.386
30.513
29.839
29.718
29.487
29.220
28.516
27.650
25.925
25.609
22.896
21.197
21.003
20.924
20.809
19.012
14.006
11.663
68.229
26.283
E
129.601
Hex
32.448
Hex
23.418
C
21.003
Hex
14.358
107.4 ppm
95.8 ppm
ppm
37.0 ppm
30.5
29.5
28.5 ppm
25.7 ppm
23.3 ppm
21.4
20.9 ppm
19.4 ppm
14.0 ppm
12.0 ppm
3.55
3.77
1.12
1.94
2.60
10.89
6.27
10.45
1.09
1.37
6.45
3.02
2.93
2.83
2.07
10.09
9.56
3.57
2.70
6.28
D
B
A
A
B
In
$^nC_6H_{13}$
C
D
E
140
120
100
80
60
40
20
0
ppm

Chart 10

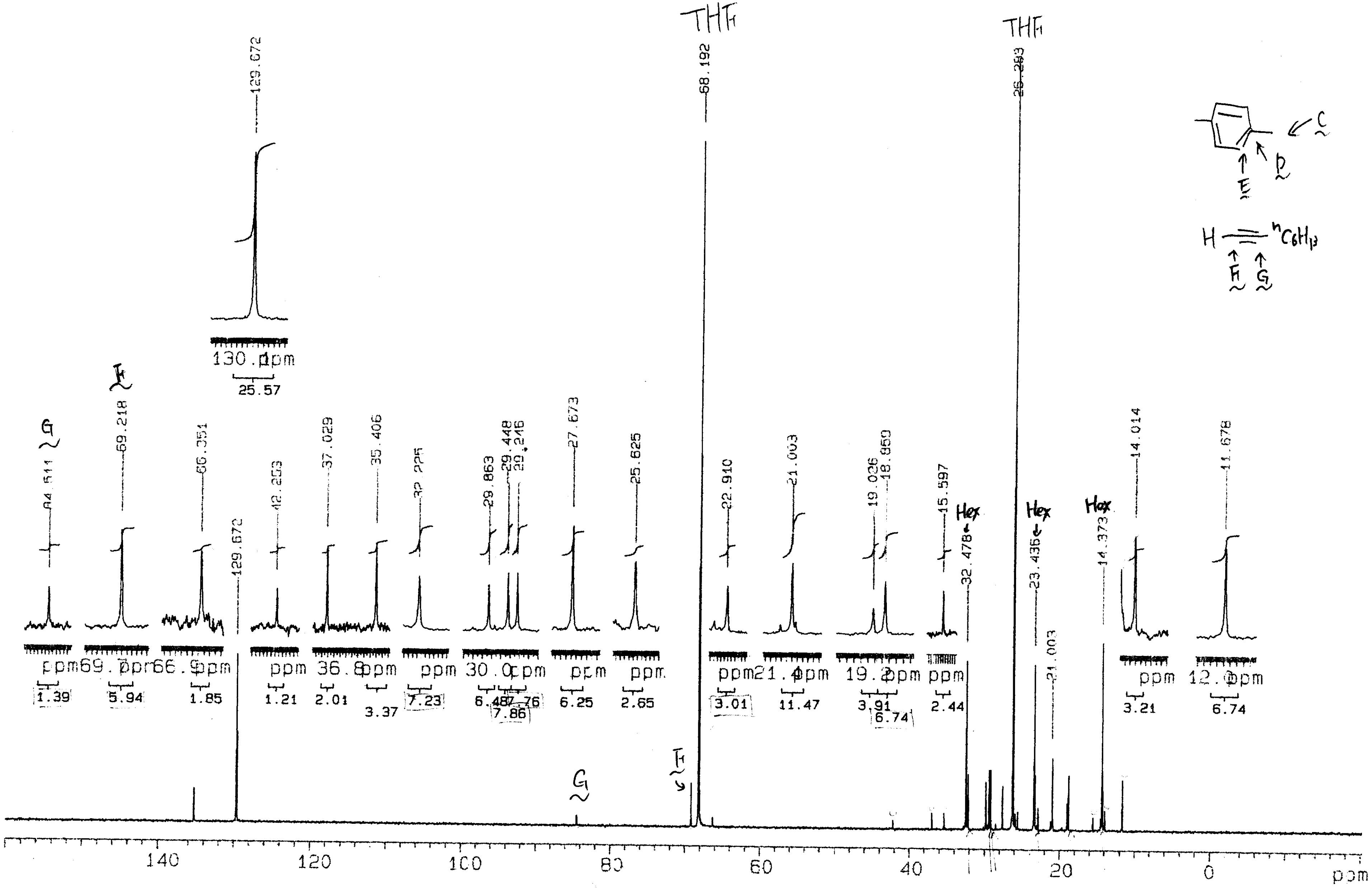
THF
THF
129.672
130.0 ppm
25.57
G
F
84.511
69.218
66.351
129.672
42.253
37.029
35.406
32.225
29.863
29.448
29.246
27.673
25.625
22.910
21.003
19.026
18.859
15.597
Hex
32.478
Hex
23.436
21.003
Hex
14.373
14.014
11.678
69.7 ppm
66.9 ppm
36.8 ppm
30.0 ppm
21.4 ppm
19.2 ppm
12.0 ppm
1.39
5.94
1.85
1.21
2.01
3.37
7.23
6.48
7.86
7.76
6.25
2.65
3.01
11.47
3.91
6.74
2.44
3.21
6.74
C
D
E
H
$^{n}C_6H_{13}$
F
G
140
120
100
80
60
40
20
0
ppm

Chart 11