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Carbozincation of Enynes Catalyzed by Titanium(IV) Alkoxides and Alkylmagnesium Derivatives

Jean-Luc Montchamp and Ei-ichi Negishi*

Supplementary Data

Cyclization of 1-Phenyl-6-hepten-1-yne with Et_2Zn in the Presence of a Catalytic Amount of EtMgBr / ClTi(OPr-*i*)$_3$. Representative Procedure. To a solution of 1-phenyl-6-hepten-1-yne (0.335 g, 2 mmol) and Et_2Zn (1 M in hexanes, 5 mL, 5 mmol) in ether (5 mL) was added ClTi(OPr-*i*)$_3$ (0.5 M in hexanes, 0.4 mL, 0.2 mmol). Ethylmagnesium bromide (3 M in Et_2O, 0.13 mL, 0.4 mmol) was then added and the reaction mixture rapidly turned black. **(a) Protonolysis**. After 2.5 h at 23 °C, the mixture was poured into 3 N aqueous HCl, and ether was added. The organic layer was washed with brine, dried over $MgSO_4$, concentrated, and purified on silica gel (pentane) to afford (*E*)-1-(benzylidene)-2-methylcyclopentane[a] (entry 3, compound **3**, 0.310 g, 1.8 mmol, 90%): ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.17 (d, *J* = 7 Hz, 3 H), 1.55-1.75 (m, 2 H), 1.75-1.9 (m, 2 H), 2.5-2.65 (m, 3 H), 6.22 (d, *J* = 2 Hz, 1 H), 7.25-7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 19.32, 24.66, 31.49, 34.53, 40.86, 120.06, 125.54, 128.00, 128.08, 128.22, 128.25, 138.85, 151.54. **(b) Deuterolysis.** Deuterolysis with 3 N DCl in D_2O at 0 °C afforded (*E*)-1-(α-deuteriobenzylidene)-2-deuteriomethylcyclopentane (entry 3, compound **4**, 90% by GLC based on mesitylene as the internal standard): ^{13}C NMR ($CDCl_3$, Me_4Si) δ 19.04 (t, *J* = 20 Hz), 24.70, 31.50, 34.54, 40.82, 119.71 (t, *J* = 23 Hz), 125.57, 128.00, 128.12, 138.82, 151.52; ≥86% D at the vinylic position and ≥99% D at the methyl by ^{13}C NMR. **(c) Iodinolysis.** To a solution of 1-phenyl-6-hepten-1-yne (0.335 g, 2 mmol) and Et_2Zn (1 M in hexanes, 2 mL, 2 mmol) in ether (5 mL) and hexanes (3 mL) was added ClTi(OPr-*i*) (0.5 M in hexanes, 0.4 mL, 0.2 mmol) followed by ethylmagnesium bromide (3 M in Et_2O, 0.13 mL, 0.4 mmol). After 3.5 h at 23 °C, the reaction mixture was cooled to -78 °C, and a solution of I_2 (1.26 g, 5 mmol) in THF (10 mL) was added via cannula. The reaction mixture was warmed to 23 °C, and stirred overnight. The mixture was then partitioned between 3 N aqueous HCl and ether. The organic layer was washed with water and aqueous $Na_2S_2O_3$. Drying over $MgSO_4$, concentration, and purification on silica gel (pentane) provided (*Z*)-1-(α-iodobenzylidene)-2-(iodomethyl)cyclopentane (entry 3, compound **5**, 0.491 g, 1.15 mmol, 59%): ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.65-1.9 (m, 3 H), 1.95-2.1 (m, 1 H), 2.2-2.45 (m, 2 H), 3.0-3.1 (m, 1 H), 3.27 (dd, *J* = 10, 10 Hz, 1 H), 3.63 (dd, *J* = 10, 3 Hz, 1 H), 7.25-7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 10.89, 25.11, 32.28, 33.44, 52.63, 92.56, 127.71, 128.00, 128.10, 128.21, 128.44, 143.91, 152.90; IR (neat) 2956, 1489, 1441, 1172, 753, 697; HRMS calcd for $C_{13}H_{14}I_2$ (M+H-HI) 297.0140, found 297.0139. **(d) Reaction with $MeOCH_2Br$.** The reaction mixture containing the organozinc product **2** obtained as in **(c)** was cooled to -78 °C, and freshly distilled $MeOCH_2Br$ (90%, 0.20 mL, 2.2 mmol) was added neat via syringe. The reaction mixture was warmed to 23 °C, and stirred overnight. The reaction mixture was poured into 3 N aqueous HCl and ether. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated to a yellow oil. Purification by chromatography on silica gel (pentane) provided 1-(1'-

phenylethenyl)-bicyclo[3.1.0]hexane (entry 3, compound **6**, 0.219 g, 1.19 mmol, 61%): ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.7-0.75 (m, 2 H), 1.15-2.0 (m, 6 H), 3.25-3.4 (m, 1 H), 5.1 (d, J = 1.5 Hz, 1 H), 5.22 (d, J = 1.5 Hz, 1 H), 7.15-7.3 (m, 3 H), 7.4-7.45 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 12.91, 21.37, 24.79, 27.68, 32.11, 33.33, 111.71, 127.00, 127.12, 127.96, 128.01, 128.11, 141.08, 151.50; IR (neat) 3026, 2953, 1621, 1492, 1446, 897, 776, 701; HRMS calcd for $C_{14}H_{16}$ (M+H) 185.1330, found 185.1324. Anal. Calcd for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 91.22; H, 8.80.

(*E*)-1-[(Trimethylsilyl)methylene]-2-methylcyclopentane:[a] ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.15 (s, 9 H), 1.12 (d, J = 6 Hz, 3 H), 1.0-2.6 (m, 7 H), 5.3-5.4 (m, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ -0.27, 18.86, 24.26, 32.58, 34.78, 41.78, 116.11, 167.50.

(*Z*)-1-[(Trimethylsilyl)iodomethylene]-2-(iodomethyl)cyclopentane:[a] ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.25 (s, 9 H), 1.85-2.0 (m, 4 H), 2.4-2.5 (m, 2 H), 2.95-3.2 (m, 2 H), 3.60 (dd, J = 9, 3 Hz, 1 H);); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 0.94, 9.49, 25.59, 31.24, 33.87, 56.79, 103.85, 163.27.

1-(1'-Trimethylsilylethenyl)-bicyclo[3.1.0]hexane: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.11 (s, 9 H), 0.45-0.5 (m, 2 H), 1.2-1.35 (m, 2 H), 1.55-1.85 (m, 4 H), 3.25-3.35 (m, 1 H), 5.31 (d, J = 3 Hz, 1 H), 5.60 (d, J = 3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ -0.28, 12.88, 21.29, 23.77, 27.68, 33.19, 35.17, 123.91, 154.90; HRMS calcd for $C_{10}H_{20}Si$ (M+H) 181.1412, found 181.1410.

(*E*)-1-Ethylidene-2-methylcyclopentane:[a] ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.03 (d, J = 7 Hz, 3 H), 1.2-1.4 (m, 2 H), 1.59 (d, J = 7 Hz, 3 H), 1.7-2.05 (m, 2 H), 2.05-2.5 (m, 3 H), 5.0-5.4 (m, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.53, 18.93, 23.89, 28.88, 35.62, 38.87, 113.08, 148.57.

(*Z*)-1-(1'-Iodoethylidene)-2-(iodomethyl)cyclopentane: ^{1}H NMR ($CDCl_3$, Me_4-Si) δ 1.80-2.0 (m, 4 H), 2.35-2.4 (m, 5 H), 2.95-3.05 (m, 2 H), 3.5-3.6 (m, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 9.88, 24.66, 30.83, 31.04, 31.90, 53.42, 90.59, 149.22; HRMS calcd for $C_8H_{12}I_2$ (M+H-HI) 234.9984, found 234.9983.

(*E*)-3-(Benzylidene)-4-methyloxolane:[b] ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.18 (d, J = 7 Hz, 3 H), 2.75-2.95 (m, 1 H), 3.35 (t, J = 8 Hz, 1 H), 4.04 (t, J = 8 Hz, 1 H), 4.6-4.7 (m, 2 H), 6.26 (d, J = 2 Hz, 1 H), 7.1-7.45 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 16.29, 39.69, 70.12, 74.13, 119.86, 126.36, 127.77, 128.14, 128.35, 128.40, 137.51, 146.25; HRMS calcd for $C_{12}H_{14}O$ (M+H) 175.1123, found 175.1117.

(*Z*)-3-(α-Iodobenzylidene)-4-(iodomethyl)oxolane: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.25-3.4 (m, 2 H), 3.63 (dd, J = 7, 2 Hz, 1 H), 4.0-4.1 (m, 2 H), 4.14 (d, J = 14 Hz, 1 H), 4.41 (d, J = 14 Hz, 1 H), 7.2-7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 6.20, 53.59, 70.21, 73.05, 91.60, 126.83, 127.73, 128.42, 128.49, 137.51, 149.33; HRMS calcd for $C_{12}H_{12}I_2O$ (M+H) 426.9056, found 426.9055.

(*E*)-1-[(Trimethylsilyl)methylene]-2-methylcyclohexane:[a] ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.10 (s, 9 H), 1.00 (d, *J* = 7 Hz, 3 H), 1.3-1.5 (m, 4 H), 1.7-2.7 (m, 5 H), 5.08 (s, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 0.39, 18.72, 25.78, 28.95, 34.93, 37.25, 40.65, 116.36, 163.72.

(*E*)-1-[(Trimethylsilyl)deuteriomethylene]-2-deuteriomethylcyclopentane: ^{13}C NMR ($CDCl_3$, Me_4Si) δ 0.41, 18.44 (t, *J* = 19 Hz), 25.82, 29.00, 34.91, 37.24, 40.51, 115.96 (t, *J* = 21 Hz), 163.74; ≥98% D at the vinylic position and ≥97% D at the methyl by ^{13}C NMR.

(*E*)-1-(Benzylidene)-2-methylcyclohexane: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.14 (d, *J* = 7 Hz, 3 H), 1.2-2.1 (m, 8 H), 2.65-2.8 (m, 1 H), 6.20 (s, 1 H), 7.1-7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 18.75, 25.37, 28.28, 28.93, 36.77, 38.92, 119.53, 125.64, 127.89, 128.95, 138.75, 147.26; HRMS calcd for $C_{14}H_{18}$ (M+H) 187.1487; found 187.1486. Anal. Calcd for $C_{14}H_{18}$: C, 90.33; H, 9.67. Found: C, 90.32; H, 9.73.

(*Z*)-1-[(Phenyl)iodomethylene]-2-(iodomethyl)cyclohexane: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.0-1.25 (m, 1 H), 1.4-1.6 (m, 3 H), 1.65-1.75 (m, 2 H), 2.0-2.1 (m, 1 H), 2.35-2.45 (m, 1 H), 3.3-3.5 (m, 3 H), 7.15-7.3 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 8.19, 19.85, 27.33, 27.46, 30.41, 49.32, 96.91, 127.40, 128.01, 128.37, 143.83, 146.19; IR (neat) 3054, 2927, 1486, 1444, 1185, 740, 697; HRMS calcd for $C_{14}H_{16}I_2$ (M+H-HI) 311.0297, found 311.0308.

1-(1'-Phenylethenyl)-bicyclo[4.1.0]heptane: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.45-0.55 (m, 1 H), 0.95-2.0 (m, 9 H), 3.25-3.4 (m, 1 H), 5.03 (d, *J* = 1 Hz, 1 H), 5.23 (d, *J* = 1 Hz, 1 H), 7.15-7.6 (m, 5 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 16.71, 18.90, 20.46, 21.91, 23.54, 24.33, 29.58, 110.88, 126.81, 127.72, 127.88, 128.00, 128.93, 140.58, 154.68; HRMS calcd for $C_{15}H_{18}$ (M+H) 199.1487, found 199.1486. Anal. Calcd for $C_{15}H_{18}$: C, 90.85; H, 9.15. Found: C, 90.59; H, 9.39.

(*E*)-1-(Pentylidene)-2-methylcyclohexane: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.85-0.95 (m, 3 H), 1.00 (d, *J* = 7 Hz, 3 H), 1.2-2.2 (m, 14 H), 2.45-2.55 (m, 1 H), 5.04 (t, *J* = 7 Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 14.02, 18.70, 22.36, 25.62, 26.81, 28.20, 31.60, 32.58, 36.88, 38.44, 118.80, 143.33; HRMS calcd for $C_{12}H_{22}$ (M+H) 167.1800, found 167.1798.

(*E*)-4-(Ethylidene)-3-methyloxane: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.97 (d, *J* = 7 Hz, 3 H), 1.59 (d, *J* = 7 Hz, 3 H), 1.95-2.25 (m, 2 H), 2.3-2.5 (m, 1 H), 3.14 (dd, *J* = 11, 8 Hz, 1 H), 3.45-3.5 (m, 1 H), 3.7-3.8 (m, 2 H), 5.15-5.3 (m, 1 H); ^{13}C NMR ($CDCl_3$, Me_4-Si) δ 14.34, 28.00, 29.67, 38.23, 68.88, 75.13, 114.56, 138.93; HRMS calcd for $C_8H_{14}O$ (M+H) 127.1123, found 127.1122. Anal. Cald for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 75.89; H, 11.08.

Reference

(a) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336.
(b) Miura, K.; Funatsu, M.; Saito, H.; Ito, H.; Hosomi, A. *Tetrahedron Lett.* **1996**, *37*, 9059.

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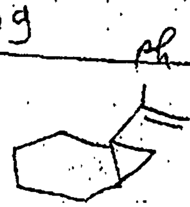

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SUBMITTER

Name Dr Jean-Luc MONTCHAMP
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Date ~~03/16/98~~ 04/03/98

Element	Theory	Found	
C	90.85	90.59	
H	9.15	9.39	

Single ☒ Duplicate ☐

Elements Present: $C_{15}H_{18}$

Analyze for: C, H

Hygroscopic ☐ Explosive ☐

M.P. ____ B.P. ____

To be dried: Yes ☐ No ☒

Temp. ____ Vac. ____ Time ____

FAX Service ☒

FAX Phone# (765) 494 0239

Rush Service ☐ ($5/sample)

Phone Service ☐ ($5/phone call)

Phone No. ____

Date Received APR 07 1998

Remarks:

Date Completed APR 07 1998

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Sample No. VII-512

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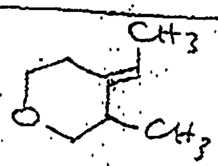

SUBMITTER

Name Dr. Jean-Luc MONTCHAMP
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West Lafayette, IN 47907

Date ~~03/16/98~~ 04/03/98

Element	Theory	Found	
C	76.14	75.89	
H	11.18	11.08	

Single ☒ Duplicate ☐
Elements Present: $C_8H_{14}O$
Analyze for: C, H
Hygroscopic ☐ Explosive ☐
M.P. ______ B.P. ______
To be dried: Yes ☐ No ☒
Temp. ______ Vac. ______ Time ______
FAX Service ☒
FAX Phone# (765) 494 0239
Rush Service ☐ ($5/sample)
Phone Service ☐ ($5/phone call)
Phone No. ______

Date Received APR 07 1998
Remarks: ______ Date Completed APR 07 1998

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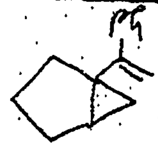

SUBMITTER

Name: Dr. Jean-Luc MONTCHAMP
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Department of Chemistry
West Lafayette, IN 47907
Date: ~~03/16/98~~ 04/03/98

Element	Theory	Found	
C	91.25	91.22	
H	8.75	8.80	

Single ☒ Duplicate ☐
Elements Present: $C_{14}H_{16}$
Analyze for: C, H
Hygroscopic ☐ Explosive ☐
M.P. ______ B.P. ______
To be dried: Yes ☐ No ☒
Temp. ______ Vac. ______ Time ______
FAX Service ☒
FAX Phone# (765) 494 0239
Rush Service ☐ ($5/sample)
Phone Service ☐ ($5/phone call)
Phone No. ______

Date Received APR 07 1998
Remarks:

Date Completed APR 0? 1998

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Sample No. 402 L

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SUBMITTER

Name Dr. Jean-Luc MONTCHAMP
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Date 02/1?/98

Single ☒ Duplicate ☐

Elements Present: $C_{14}H_{18}$

Analyze for: C, H

Hygroscopic ☐ Explosive ☐
M.P. B.P.

To be dried: Yes ☒ No ☐
Temp. RT Vac. 0.02 mmHg Time 2 h

Fax Service ☒
Fax Phone# (765) 494 0239

Rush Service ☐ ($5/sample)
Phone Service ☐ ($5/phone call)
Phone No.

Element	Theory	Found	
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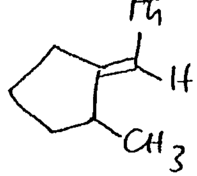
H	[illegible]	[illegible].73	

Date Received FEB 24 1998 Date Completed FEB 24 1998

Remarks:



Carbozincation of Enynes Catalyzed by Titanium(IV) Alkoxides and Alkylmagnesium Derivatives

Jean-Luc Montchamp and Ei-ichi Negishi*

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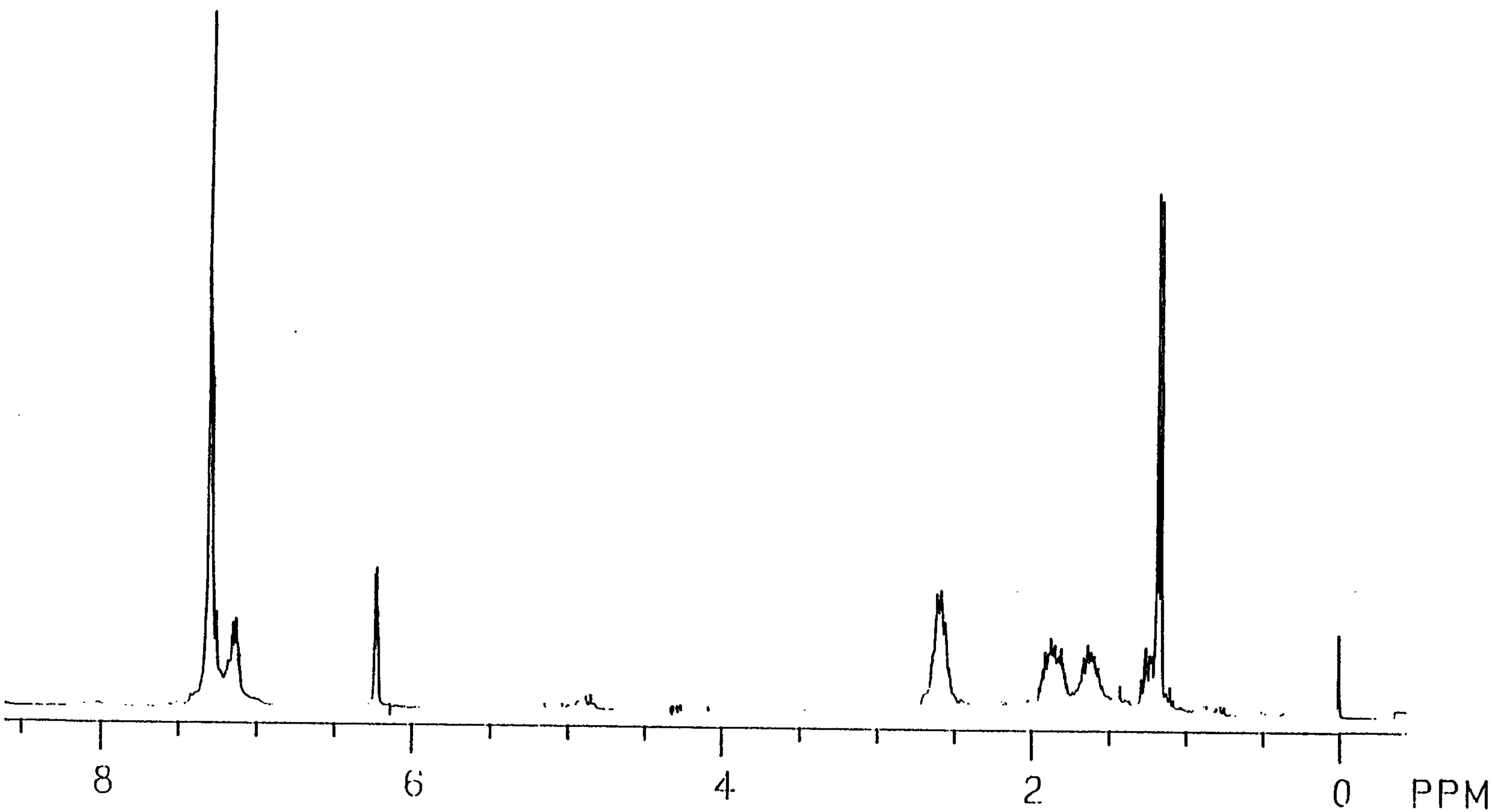

Carbozincation of Enynes Catalyzed by Titanium(IV) Alkoxides and Alkylmagnesium Derivatives

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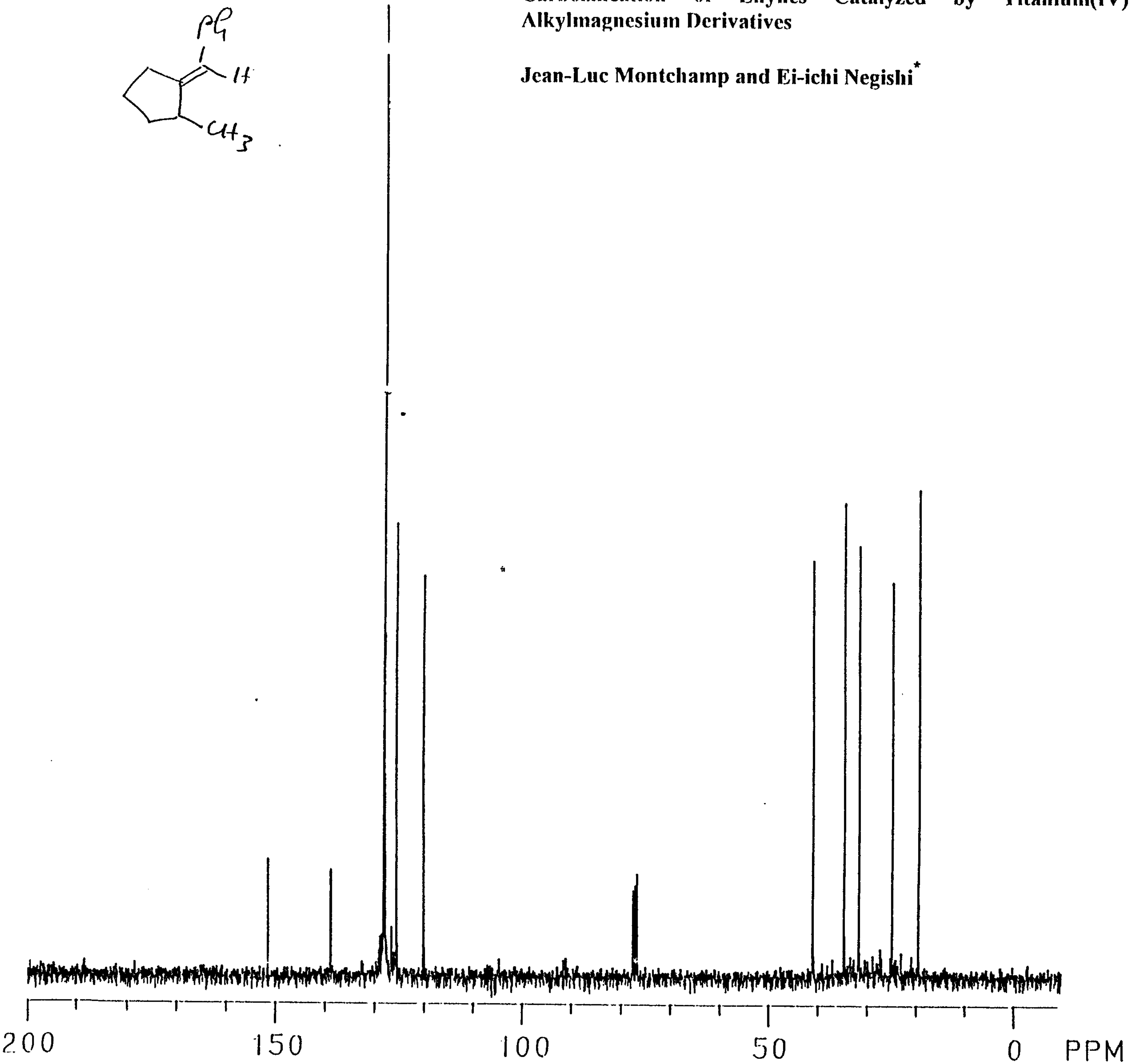

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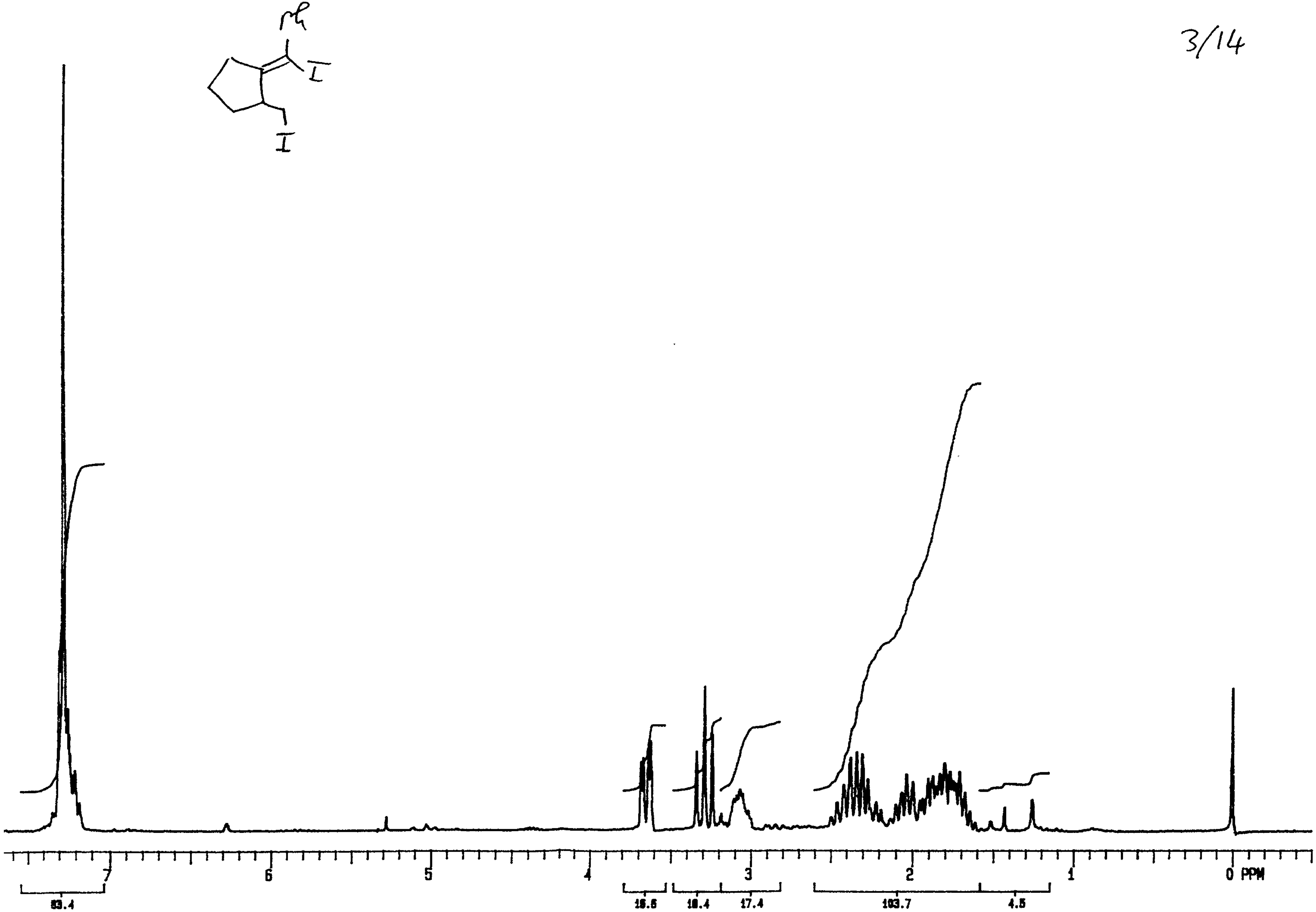

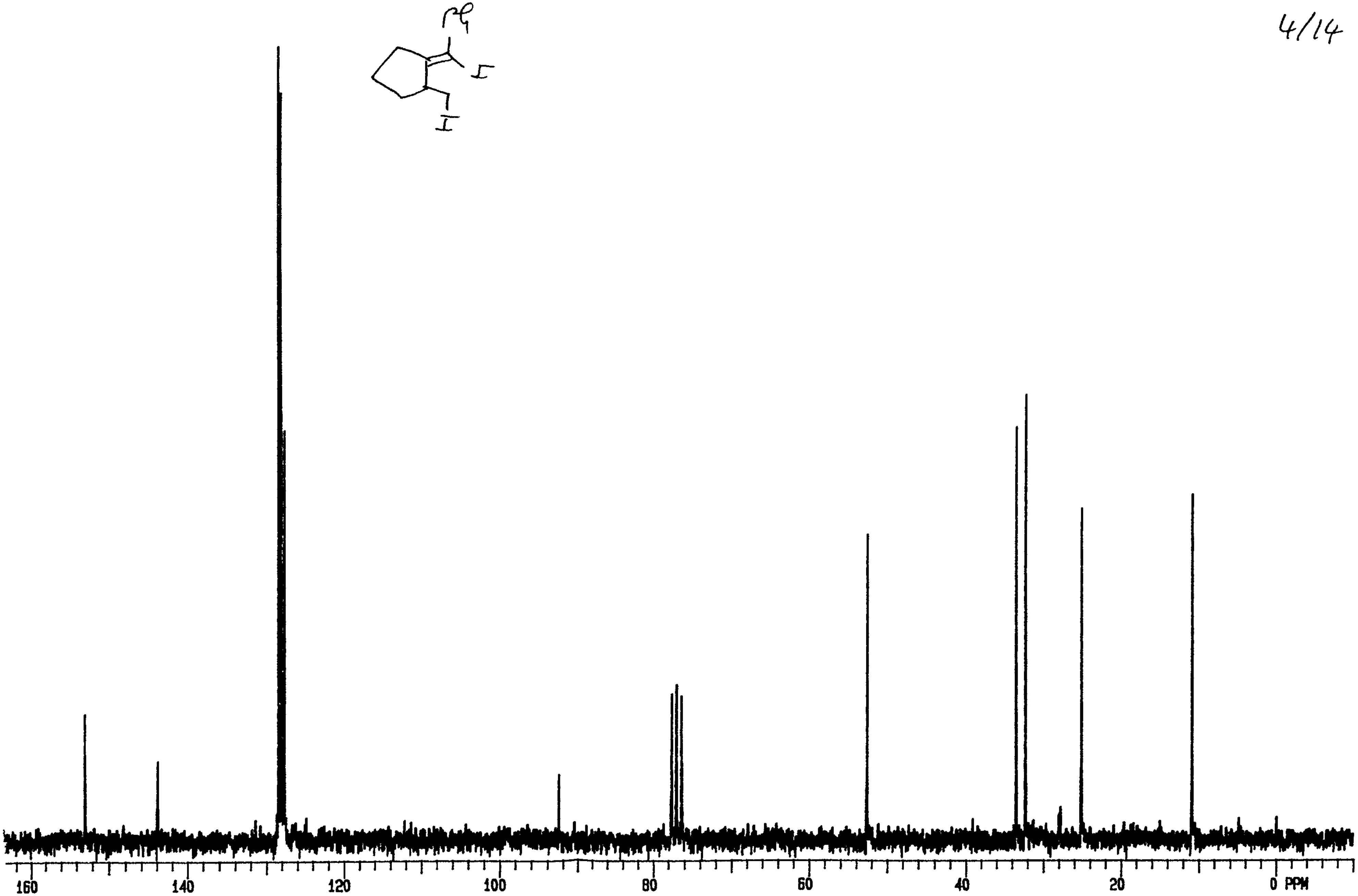
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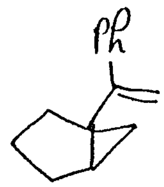
Carbozincation of Enynes Catalyzed by Titanium(IV) Alkoxides and Alkylmagnesium Derivatives

Jean-Luc Montchamp and Ei-ichi Negishi*



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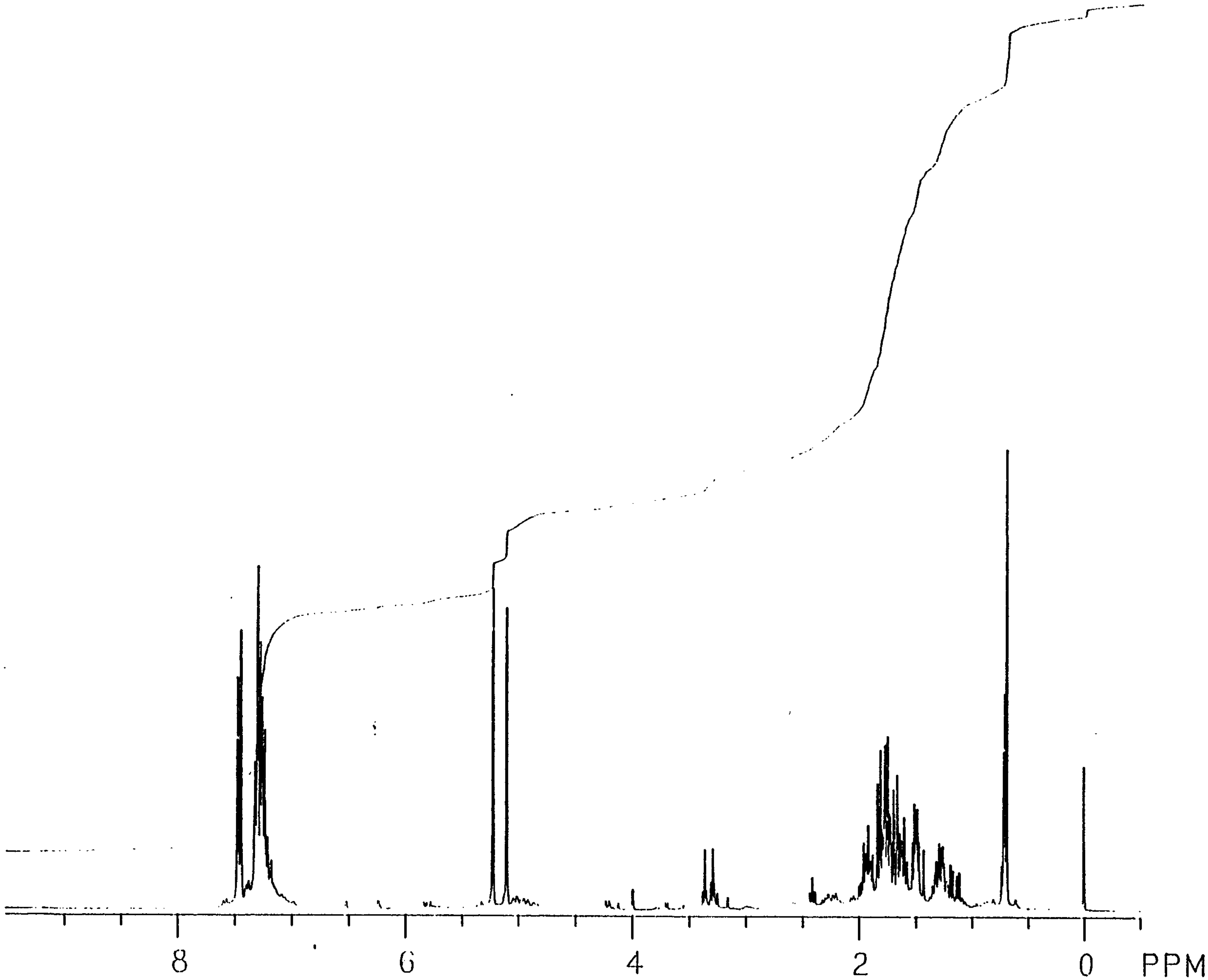

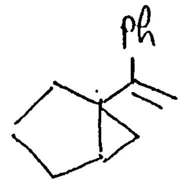

Carbozincation of Enynes Catalyzed by Titanium(IV) Alkoxides and Alkylmagnesium Derivatives

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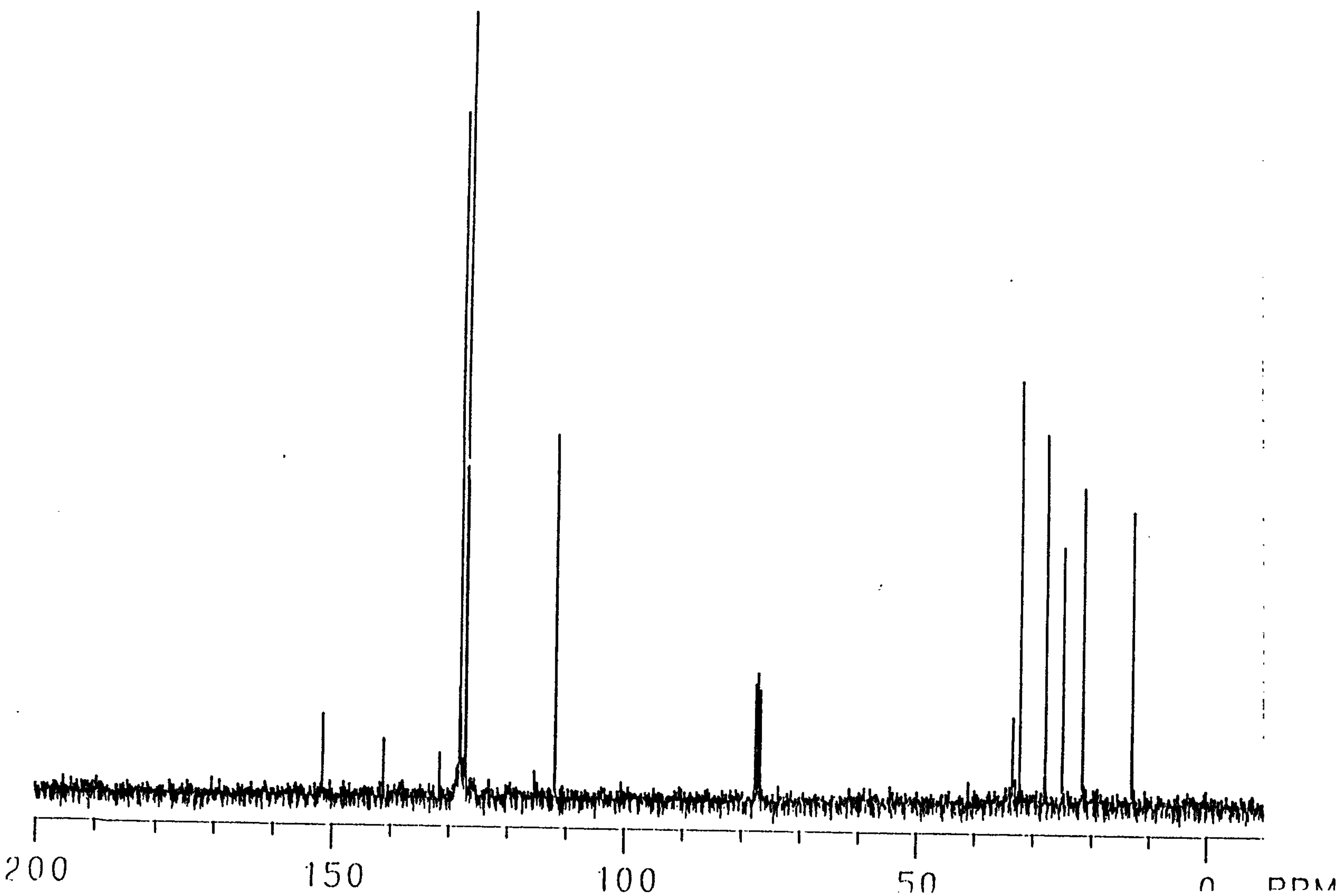

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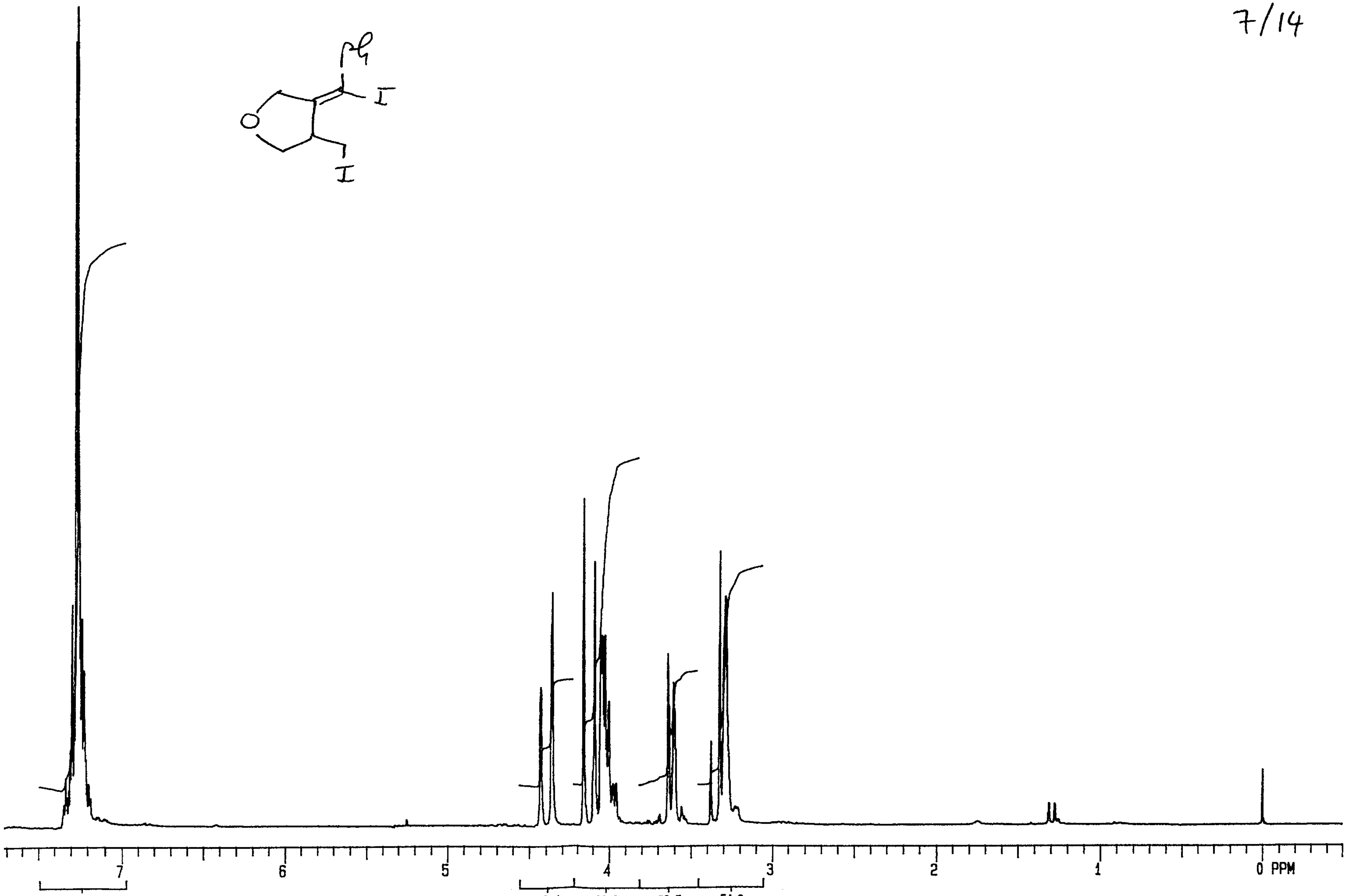

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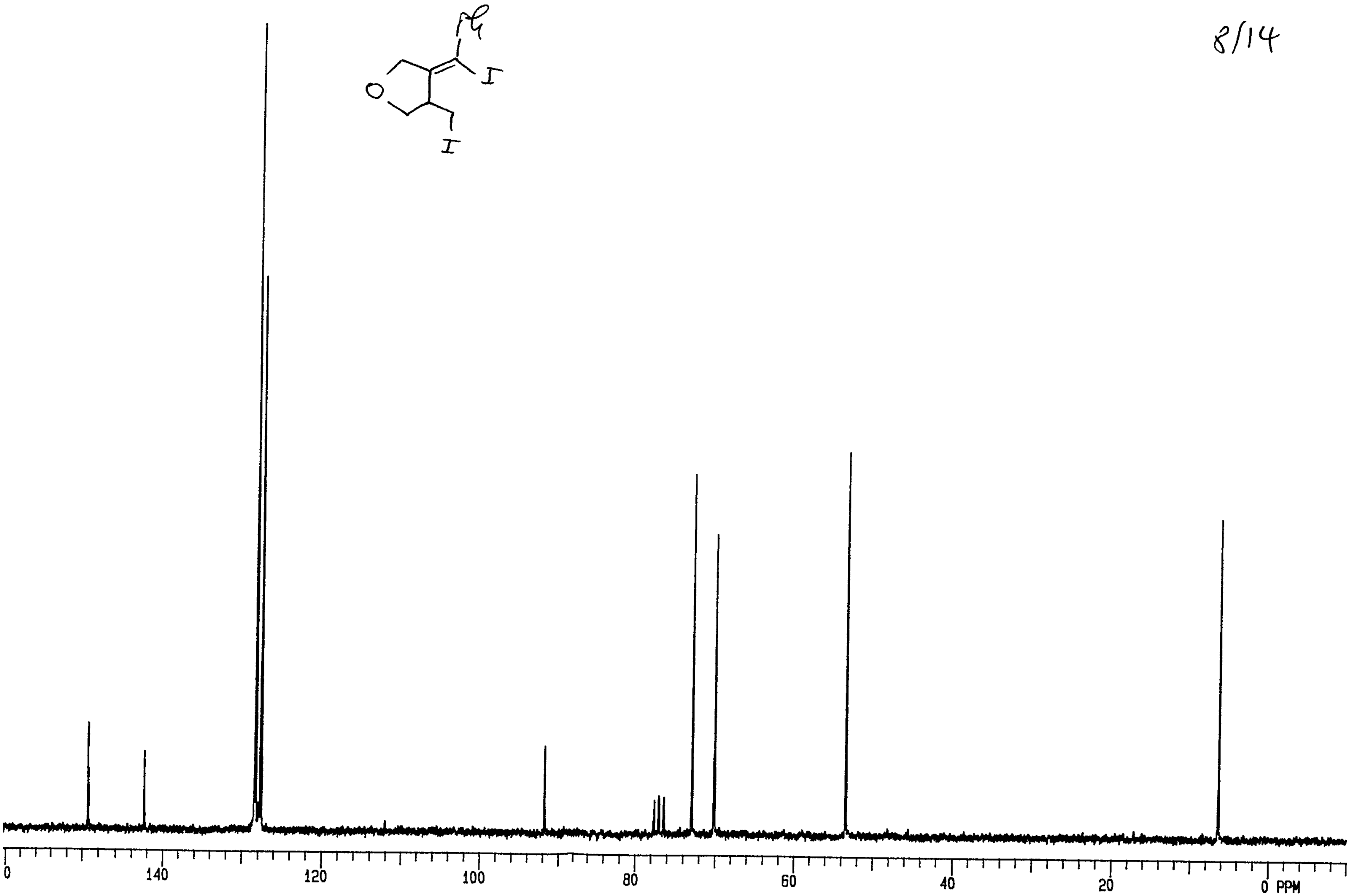

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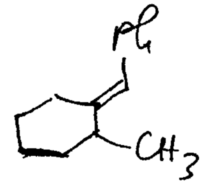

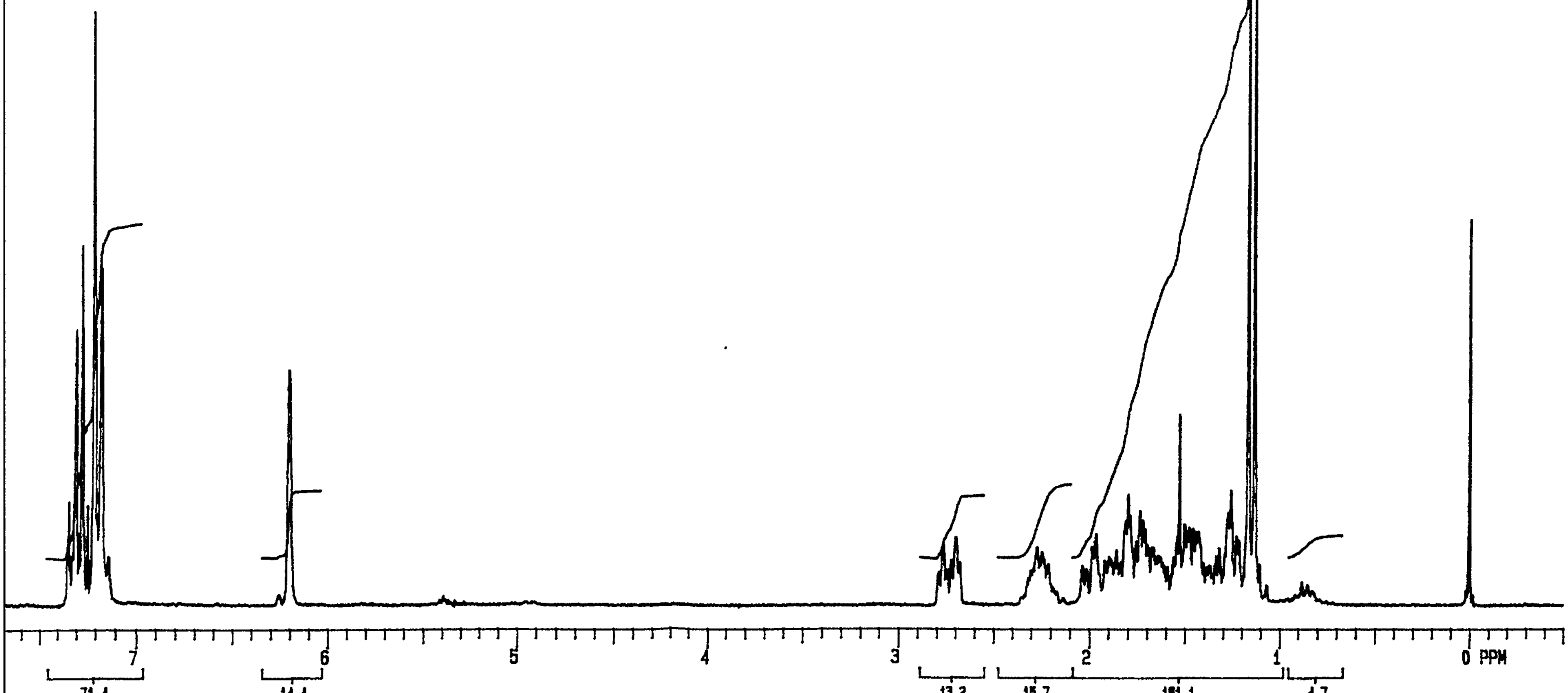

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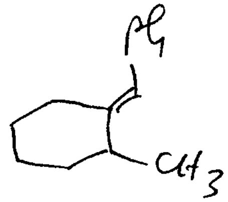

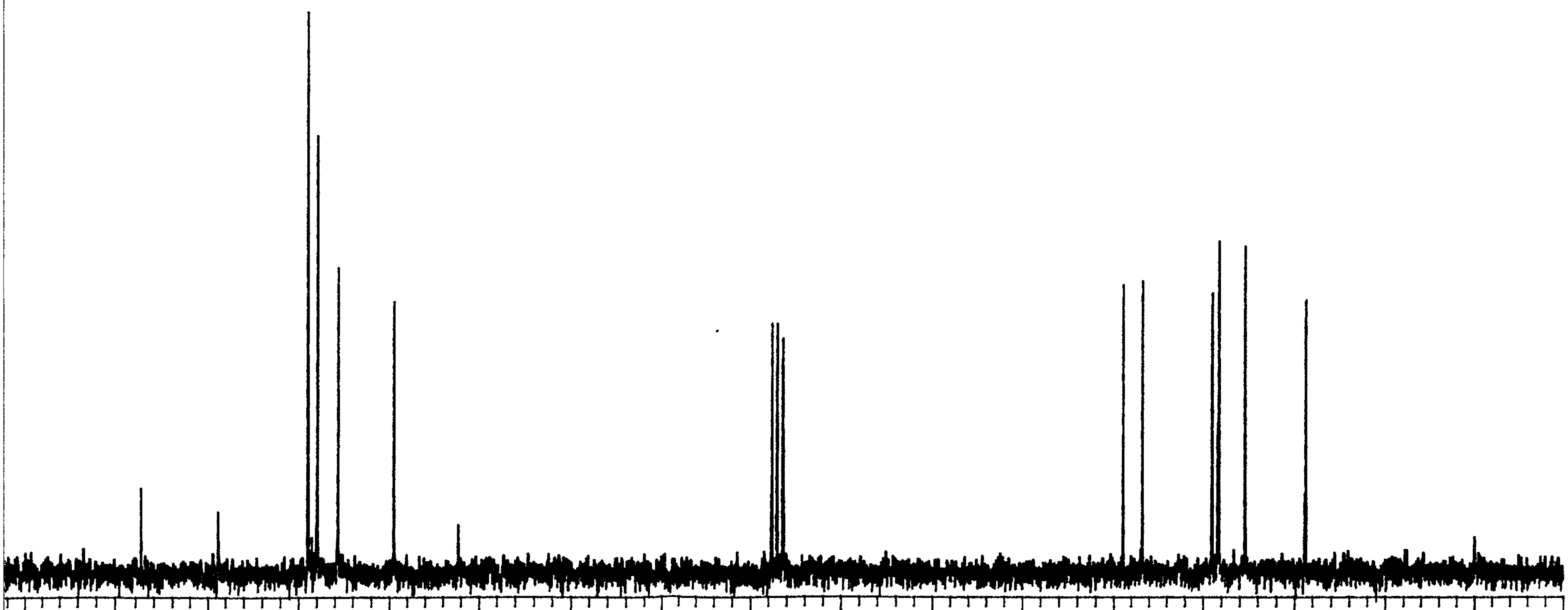

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Jean-Luc Montchamp and Ei-ichi Negishi*

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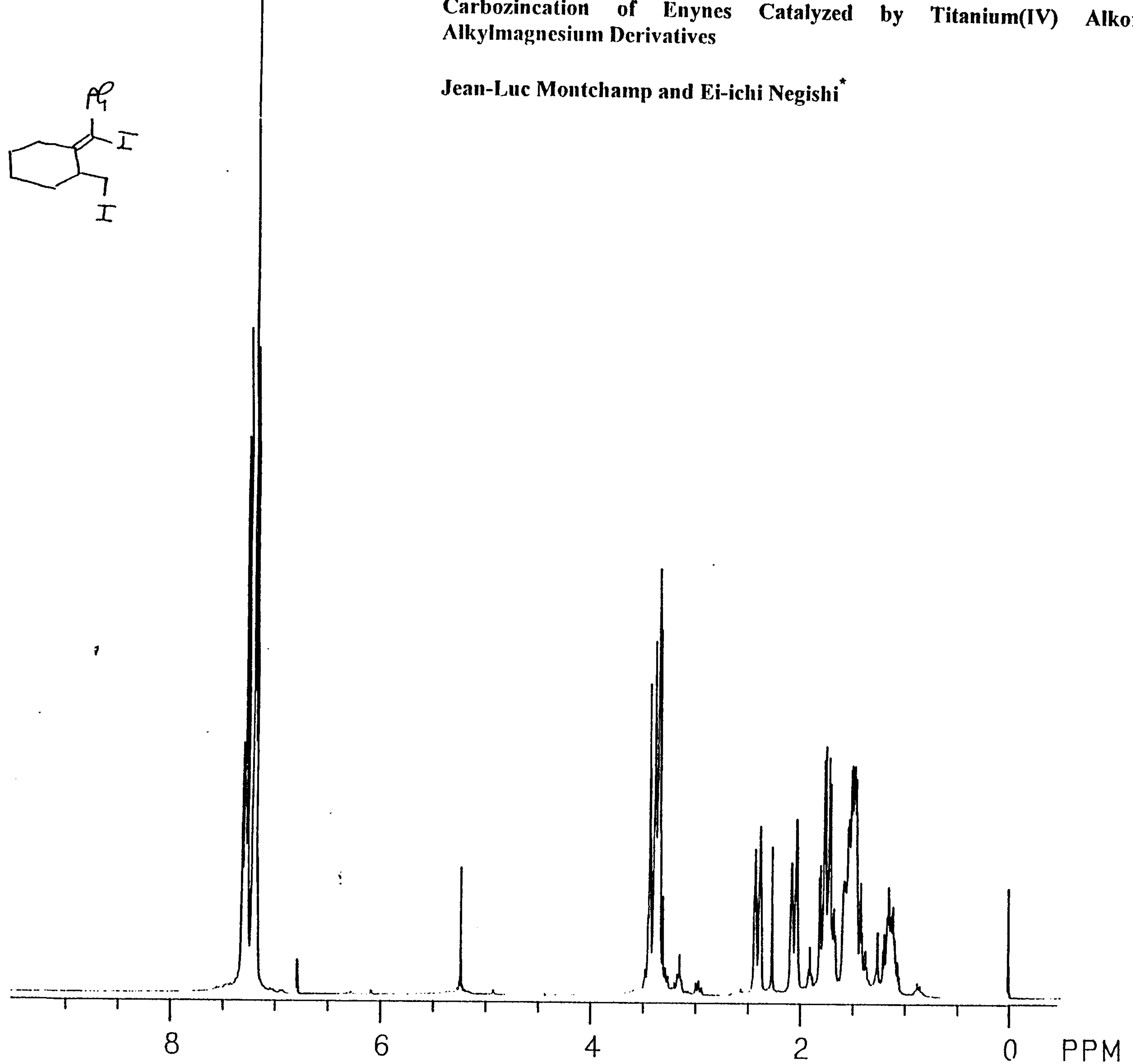

Carbozincation of Enynes Catalyzed by Titanium(IV) Alkoxides and Alkylmagnesium Derivatives

Jean-Luc Montchamp and Ei-ichi Negishi*

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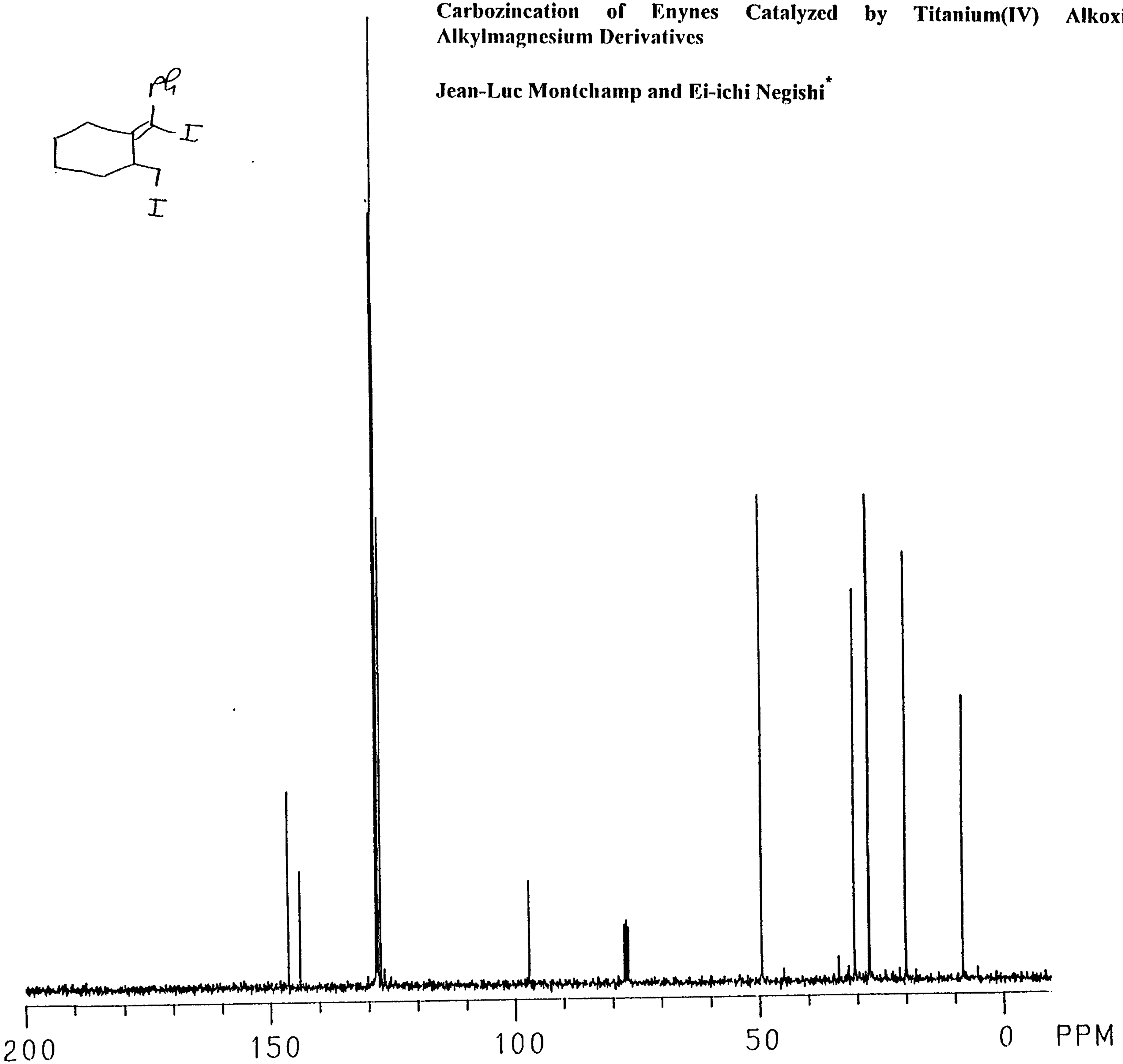

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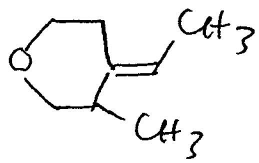

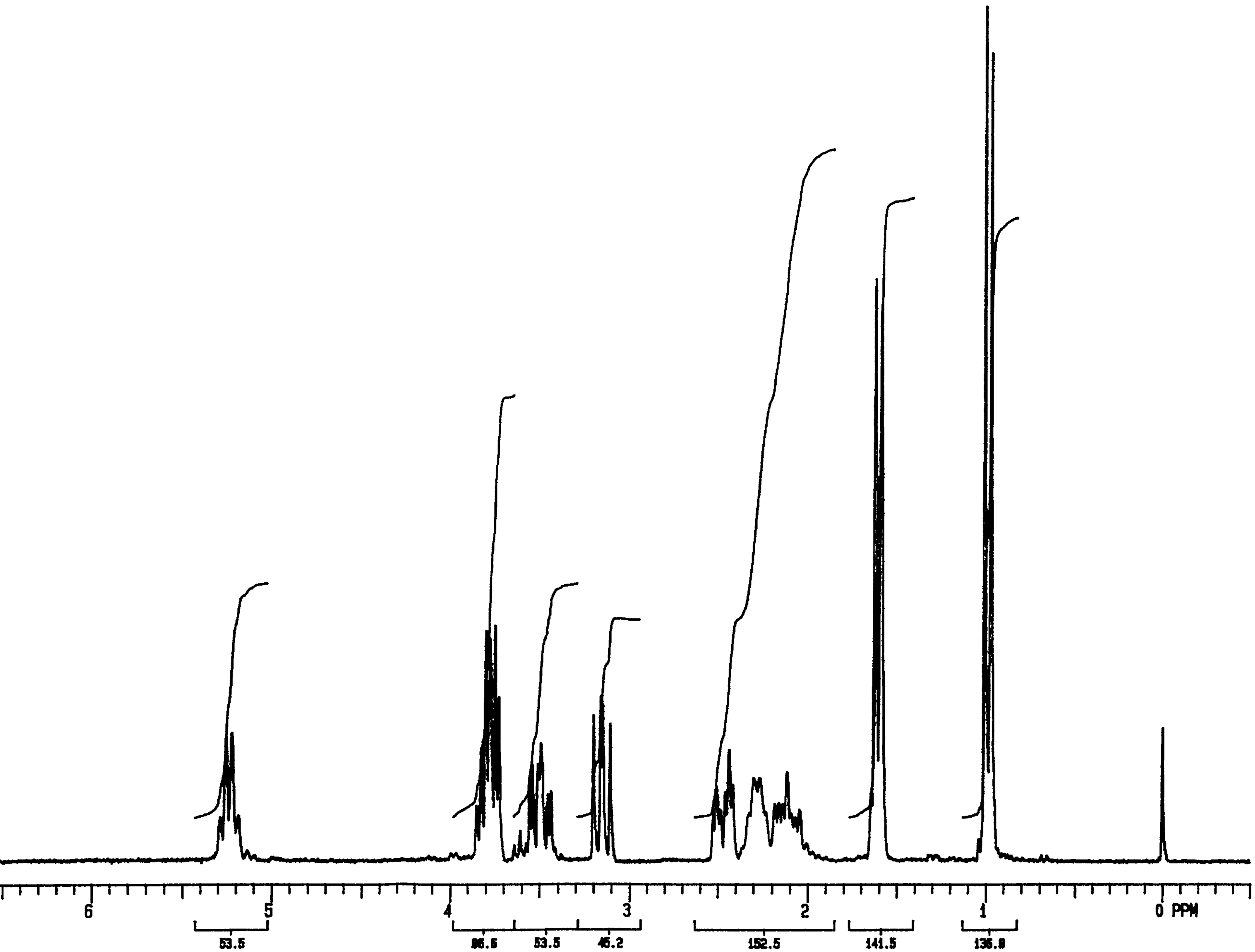

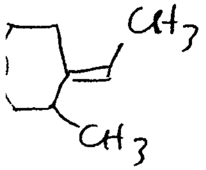
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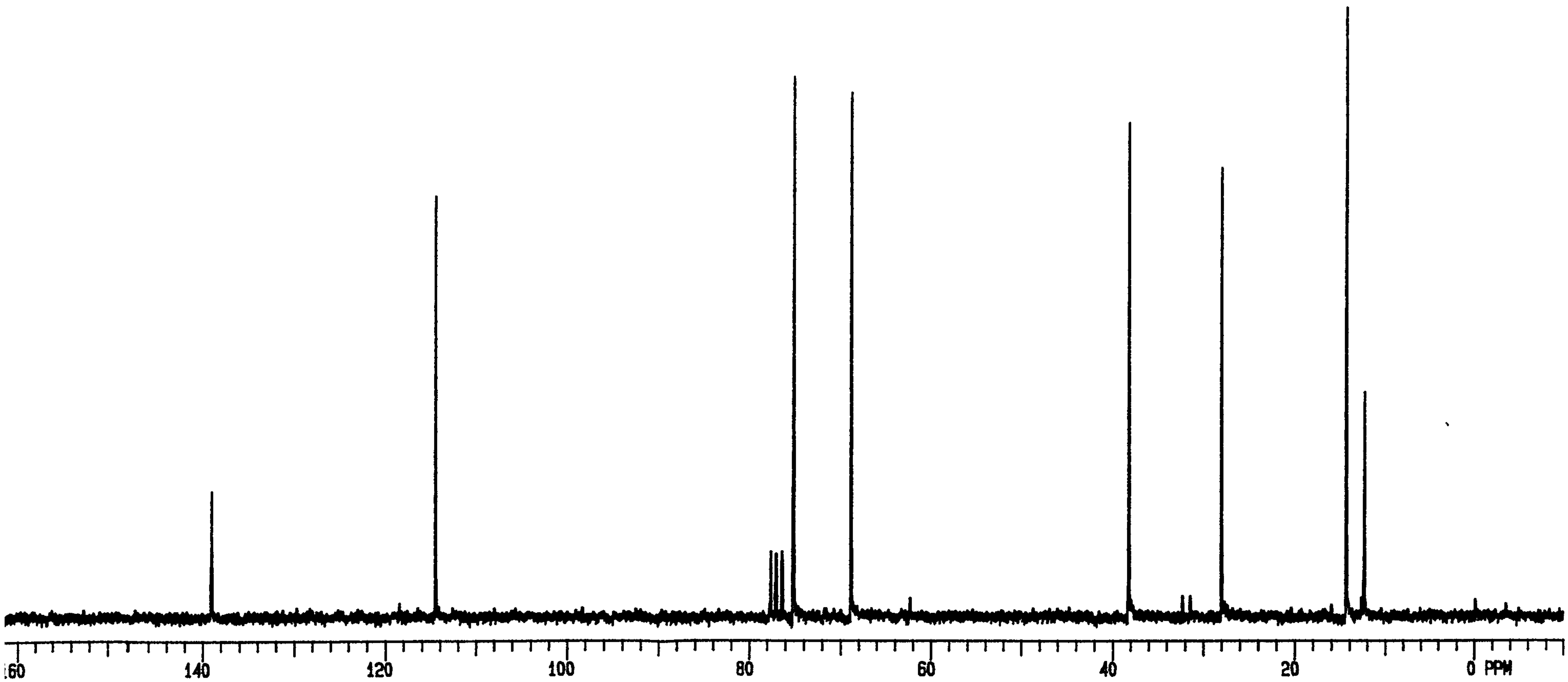
CH3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