Supporting Information

Synthesis of multiple-substituted dihydrofurans via palladium-catalysed coupling between 2,3-alkadienols and pronucleophiles

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General Information

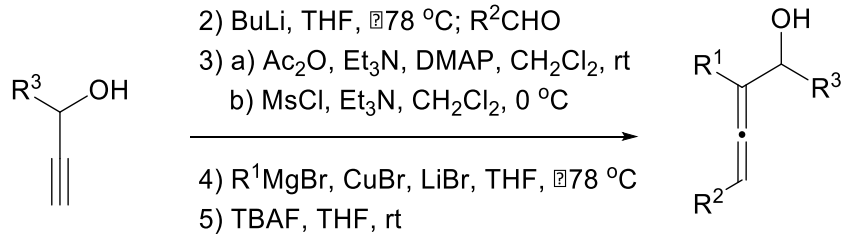
All commercially available reagents and anhydrous solvents including tetrahydrofuran (THF), dichloromethane (DCM), 1,4-dioxane, and cyclohexane were purchased and used without further purification. Anhydrous toluene and methanol were obtained by distillation from sodium and magnesium, respectively. All reactions were monitored by thin layer chromatography (TLC) performed on 0.25 mm silica gel glass plates (60 F_{254}) using UV light and ethanolic *p*-anisaldehyde-sulfuric acid, ethanolic molybdatophosphoric acid, aqueous cerium sulfate-hexaammonium heptamolybdate-sulfuric acid, or aqueous potassium permanganate-potassium carbonate-sodium hydroxide solutions as visualizing agents. Flash column chromatography was carried out with silica gel (spherical, neutral, 100–210 μm grade). Preparative thin layer chromatography were performed on 0.75 mm Wakogel® B-5F PLC plates. Yields refer to chromatographically and spectroscopically homogenous materials. Melting points

were measured on a melting point apparatus and were uncorrected. Only the strongest and/or structurally important absorptions of infrared (IR) spectra are reported in reciprocal centimeters (cm^{-1}). ^{1}H NMR spectra (400 MHz and 600 MHz), $^{13}C\{^{1}H\}$NMR spectra (100 MHz and 151 MHz), and $^{31}P\{^{1}H\}$NMR spectra (243 MHz) were recorded in the indicated solvent. Chemical shifts (δ) are reported in delta (d) units, parts per million (ppm). Chemical shifts for ^{1}H NMR spectra are given relative to signals for internal tetramethylsilane (0 ppm) or residual nondeuterated solvents, i.e., chloroform (7.26 ppm). Chemical shifts for ^{13}C NMR spectra are given relative to the signal for chloroform-*d* (77.0 ppm). Chemical shifts for ^{31}P NMR spectra are given relative to the signal for external 85% phosphoric acid (0 ppm). Multiplicities are reported by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (double doublet), dt (double triplet), dq (double quartet), br–s (broad singlet). Coupling constants (*J*) are represented in hertz (Hz). ^{1}H and ^{13}C NMR chemical shifts were assigned using a combination of COSY, NOESY, HMQC, and HMBC. Low and high-resolution mass spectra were measured on TOF-MS with EI, FAB, or ESI probe.

Experimental Procedures

The allenol **1a**[1], **1b**[2], **1c**[3], **1d**[4], **1f**[5], and **1i**[6] were prepared according to the literature procedure.

General procedure for synthesis **1e**, **1g**, and **1h**



To a solution of 2-propyn-1-ol (for **1e** and **1h**) or 3-butyn-2-ol (for **1g**) (1.0 equiv) in anhydrous CH_2Cl_2 (0.5 M) were added TBSCl (1.3 equiv) and imidazole (1.3 equiv) at 0 °C under argon. The resulting mixture was warmed to room temperature and stirred at the same temperature for 4 h. Then, the reaction mixture was treated with saturated aqueous NH_4Cl and extracted with EtOAc, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give crude TBS ehter, which was used for the next step without further purification.

To a solution of the crude TBS ether (1.0 equiv) in anhydrous THF (0.5 M) was added BuLi (2.6 M in hexane) (1.1 equiv) at –78 °C under argon. The mixture was stirred at the same temperature for 30 min before addition of benzaldehyde (for **1e**, 1.2 equiv) or acetaldehyde (for **1g** and **1h**, 2 equiv) at –78 °C. The resulting mixture was warmed to 0 °C and stirred at the same temperature for 1 h. Then, the reaction mixture was treated with saturated aqueous NH_4Cl, extracted with Et_2O, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give crude propargyl alcohol, which was used for the next step without further purification.

To a solution of the crude propargyl alcohol (1.0 equiv) in anhydrous CH_2Cl_2 (0.5 M) were added triethylamine (2.0 equiv), DMAP (0.20 equiv) and Ac_2O (2.0 equiv) (for **1e**) or triethylamine (2.0 equiv) and MsCl (1.5 equiv) (for **1g** and **1h**) at 0 °C under argon. The resulting mixture was warmed to room temperature and stirred

at the same temperature for 4 h. Then, the reaction mixture was treated with saturated aqueous NH_4Cl and extracted with Et_2O, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give crude acetate or mesylate, which was used for the next step without further purification.

To a solution of CuI (2.0 equiv) and LiBr (2.0 equiv) in anhydrous THF (1.0 M) was added 1.0 M MeMgBr (for **1e**) or PhMgBr (for **1g** and **1h**) solution in THF (2.0 equiv) at –78 °C under argon. The mixture was stirred at the same temperature for 30 min before addition of a solution of acetate (for **1g** and **1h**) or mesylate (for **1e**) (1.0 equiv) in anhydrous THF (1.0 M) at –78 °C. After being stirred at the same temperature for 1 h, the reaction mixture was treated with saturated aqueous NH_4Cl, extracted with Et_2O, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give crude allene, which was used for the next step without further purification.

To a solution of crude allene (1.0 equiv) in anhydrous THF (0.5 M) was added 1.0 M TBAF solution in THF (1.2 equiv) at 0 °C under argon. The resulting mixture was warmed to room temperature and stirred at the same temperature for 30 min. Then, the reaction mixture was treated with saturated aqueous NH_4Cl, extracted with EtOAc, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo*. The residue was purified by silica gel column chromatography eluting with 4–10% EtOAc/hexane to give allenol.

2-Methyl-4-phenylbuta-2,3-dien-1-ol (**1e**) was obtained from 2-propyn-1-ol. Each quantity of substrates and products and yield of crude products and isolated ones are shown in Table S1. All the analytical data of **1e** were in good agreement with values reported in the literature.[7]

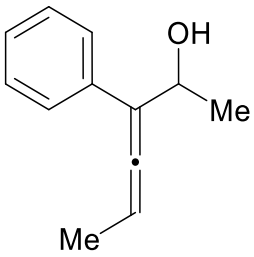
Table S1

reaction	substrate (g or mL, mmol)	product (g)	crude yield
1	2-propyn-1-ol 1.77 mL, 30 mmol	TBS ether 5.20 g	quant
2	TBS ether 1.73 g, 10 mmol	propargyl alcohol 2.80 g	quant
3	propargyl alcohol 840 mg, 3.0 mmol	propargyl acetate 960 mg	quant
4	propargyl acetate 320 mg, 1.0 mmol	allene 209 mg	76%
5	allene 318 mg, 1.1 mmol	**1e** 151 mg	90% (isolated yield)

3-Phenylhexa-3,4-dien-2-ol (**1g**) was obtained as an inseparable 1:1 diastereomeric mixture from 3-butyn-2-ol. Each quantity of substrates and products and yield of crude products and isolated ones are shown in Table S2.

Table S2

reaction	substrate (mg or μL, mmol)	product (mg)	crude yield
1	3-propyn-2-ol 784 μL, 10 mmol	TBS ether 1.79 g	97%
2	TBS ether 550 mg, 3.0 mmol	propargyl alcohol 686 mg	quant
3	propargyl alcohol 686 mg, 3.0 mmol	propargyl mesylate 836 mg	quant
4	propargyl mesylate 800 mg, 2.7 mmol	allene 830 mg	99%
5	allene 830 mg, 2.7 mmol	**1g** 237 mg	50% (isolated yield)



Coloress oil. Rf = 0.40 (25% EtOAc/hexane). IR (neat): 3384 (br), 2976, 2925, 1948, 1597, 1495, 1448, 1370, 1081, 1026, 966, 903, 875, 761, 694 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.6 Hz, 2H), 7.30 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.19 (t, *J* = 7.6 Hz, 1H), 5.62 (q, *J* = 6.8 Hz, 1H), 4.79 (q, *J* = 6.0 Hz, 1H), 2.20–2.03 (m, 1H), 1.83–1.75 (m, 3H), 1.44–1.34 (m, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 202.7, 202.5, 135.49, 135.45, 128.4, 126.8, 126.7, 126.6, 111.2, 111.1, 91.8, 65.8, 65.7, 22.7, 22.6, 14.14, 14.06. LRMS m/z (relative intensity) 174 (M, 35), 145 (25), 129 (100), 115 (94), 183 (52), 77 (27). HRMS (EI) calcd for $C_{12}H_{14}O$ 174.1045, found 174.1029 (M).

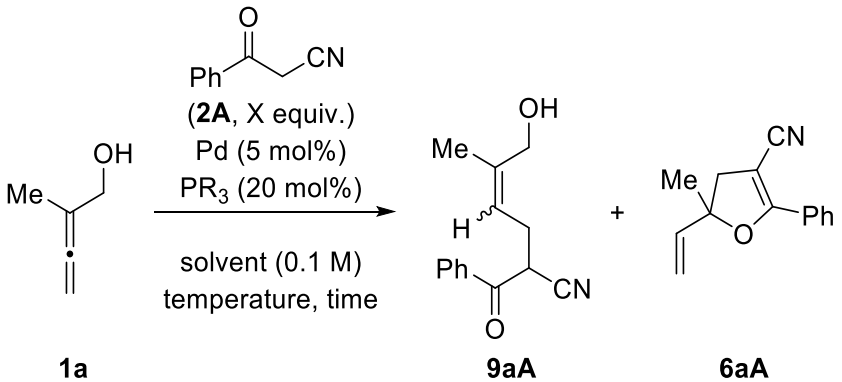
2-Phenylpenta-2,3-dien-1-ol (**1h**) was obtained from 2-propyn-1-ol. Each quantity of

substrates and products and yield of crude products and isolated ones are shown in Table S3. All the analytical data of **1h** were in good agreement with values reported in the literature.[8]

Table S3

reaction	substrate (g or mL, mmol)	product (g)	crude yield
1	2-propyn-1-ol 1.77 mL, 30 mmol	TBS ether 5.20 g	quant
2	TBS ether 2.60 g, 15 mmol	propargyl alcohol 3.30 g	quant
3	propargyl alcohol 1.71 g, 7.8 mmol	propargyl mesylate 2.28 g	quant
4	propargyl mesylate 2.00 g, 6.7 mmol	allene 2.06 g	quant
5	allene 2.06 g, 6.7 mmol	**1h** 685 mg	64% (isolated yield)

General procedure for optimization of reaction conditions for the coupling reaction between **1a** and **2A** (Table 1 and S4)



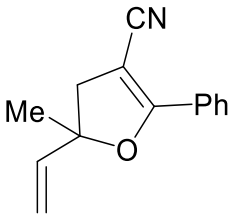
To a test tube containing allenic alcohol **1a** (1 equiv), benzoylacetonitrile (**2A**) (X

equiv), and $Pd(PPh_3)_4$ (5 mol%) was added anhydrous solvent (0.10 M) under argon. The resulting mixture was sealed with a screw cap and stirred at 65 °C (entries 1–5), 50 °C (entry 6), or 80 °C (entries 7–10) for the time described in Table S4. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The residue was purified by preparative TLC eluting with 25% EtOAc/hexane to give **6aA** and 1.2:1 (*E*)- and (*Z*)-mixture of **9aA**, the latter of which can be separated by preparative TLC eluting with 50% EtOAc/hexane.

Table S4

entry	solvent	**1a** (mg)	**2A** (mg, X equiv)	$Pd(PPh_3)_4$ (mg)	**time (h)**	**9aA** (mg, %)	**6aA** (mg, %)
1	toluene	8.4	29.0, 2.0	5.9	4	12.3, 54	trace
2	THF	8.4	29.0, 2.0	5.9	2	16.0, 70	trace
3	1,4-dioxane	8.4	29.0, 2.0	5.9	2	14.7, 64	trace
4	CH_2Cl_2	8.4	29.0, 2.0	5.9	2	14.3, 63	1.0, 5
5	MeOH	8.4	29.0, 2.0	5.9	4	4.1, 18	12.2, 58
6	MeOH	8.4	29.0, 2.0	5.9	36	1.6, 7	4.6, 22
7	MeOH	8.4	29.0, 2.0	5.9	1.5	2.7, 12	14.3, 68
8	MeOH	8.4	21.8, 1.5	5.9	28	2.8, 12	8.0, 38
9	MeOH	8.4	44.0, 3.0	5.9	1	5.7, 25	8.9, 42
10	MeOH	42.0	14.5, 0.2	5.9	24	0, 0	0, 0

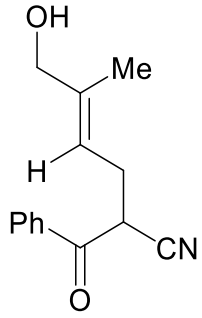
5-Methyl-2-phenyl-5-vinyl-4,5-dihydrofuran-3-carbonitrile (**6aA**)



Colorless oil. Rf = 0.55 (20% EtOAc/hexane). IR (neat): 2978, 2929, 2864, 2204, 1620, 1496, 1448, 1351, 1263, 1074, 929, 771, 691 cm^{-1}. ^1H-NMR (400 MHz, $CDCl_3$): δ 7.97

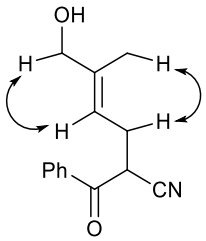
(dd, J = 8.0, 1.6 Hz, 2H), 7.48–7.41 (m, 3H), 6.01 (dd, J = 10.8, 17.2 Hz, 1H), 5.32 (d, J = 17.2 Hz, 1H), 5.18 (d, J = 10.8 Hz, 1H), 3.05 (d, J = 14.4 Hz, 1H), 2.92 (d, J = 14.4 Hz, 1H), 1.59 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.7, 140.2, 131.3, 128.6, 128.2, 127.1, 117.8, 113.7, 88.3, 78.4, 43.4, 26.1. LRMS m/z (relative intensity) 211 (M, 64), 182 (43), 168 (26), 105 (100). HRMS (EI) calcd for $C_{14}H_{13}NO$ 211.0997, found 211.0996 (M).

(*E*)-2-Benzoyl-6-hydroxy-5-methylhex-4-enenitrile (**(*E*)-9aA**)



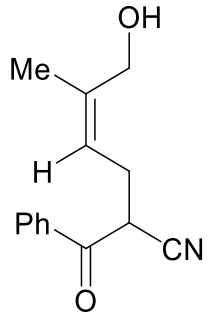
Colorless oil. Rf = 0.40 (50% EtOAc/hexane). IR (neat): 3391(br), 2922, 2251, 2209, 2179, 1693, 1597, 1448, 1261, 1226, 1002, 699 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 7.6 Hz, 2H), 7.66 (t, J = 7.6 Hz, 1H), 7.53 (dd, J = 7.6, 7.6 Hz, 2H), 5.52 (t, J = 7.2 Hz, 1H), 4.37 (t, J = 7.2 Hz, 1H), 4.04–4.02 (m, 2H), 2.81–2.75 (m, 2H), 1.86–1.79 (m, 1H), 1.68 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 190.3, 140.2, 134.6, 134.0, 129.1, 128.8, 118.1, 117.1, 67.9, 39.8, 27.9, 13.9. LRMS m/z (relative intensity) 211 (M–H_2O, 2), 196 (2), 146 (4), 105 (100) , 105 (100), 77 (21). HRMS (EI) calcd for $C_{14}H_{13}NO$ 211.0997, found 211.1011 (M–H_2O).

The *E*-configuration of **9aA** was determined by NOESY correlation as shown below.



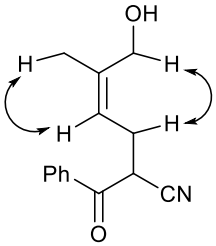
NOESY correlation of (*E*)-**9aA**

(*Z*)-2-Benzoyl-6-hydroxy-5-methylhex-4-enenitrile ((*Z*)-**9aA**)



Colorless oil. Rf = 0.45 (50% EtOAc/hexane). IR (neat): 3412(br), 2921, 2250, 2207, 1692, 1597, 1449, 1002, 697 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.0 Hz, 2H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.53 (dd, *J* = 8.0, 7.6 Hz, 2H), 5.36 (t, *J* = 8.0 Hz, 1H), 4.36 (t, *J* = 6.8 Hz, 1H), 4.16–4.12 (m, 2H), 2.90–2.75 (m, 2H), 1.84 (s, 3H), 1.69–1.64 (m, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 190.2, 140.4, 134.6, 134.0, 129.1, 128.8, 120.9, 117.4, 61.4, 40.2, 27.8, 21.6. LRMS m/z (relative intensity) 211 (M–H_2O, 2), 196 (6), 149 (17), 105 (100), 77 (19). HRMS (EI) calcd for $C_{14}H_{13}NO$ 211.0997, found 211.0978 (M–H_2O).

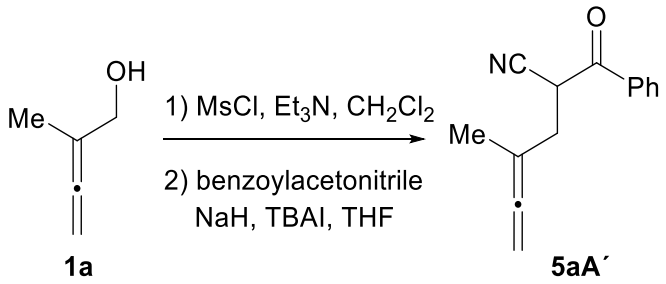
The *Z*-configuration of **9aA** was determined by NOESY correlation as shown below.



NOESY correlation of (*Z*)-**9aA**

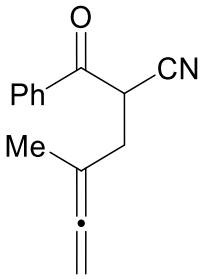
Conventional synthesis of **6aA** for the structure determination

2-Benzoyl-4-methylhexa-4,5-dienenitrile (**5aA'**)



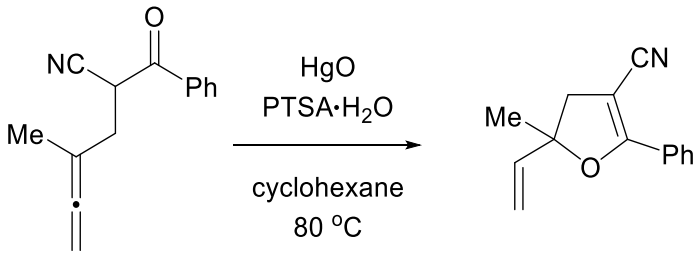
To a solution of **1a** (42.1 mg, 0.50 mmol) in anhydrous CH_2Cl_2 (5 mL) were added Et_3N (210 µL, 1.5 mmol) and MsCl (145 µL, 1.5 mmol) at 0 ºC. After being stirred at the same temperature for 15 min, the reaction mixture was treated with saturated aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give crude mesylate, which was used for the next reaction without further purification.

To a solution of benzoylacetonitrile (**2A**) (290 mg, 2.00 mmol) in anhydrous THF (5 mL) was added NaH (60% dispersion in mineral oil, 80 mg, 2.0 mmol) at 0 ºC. The mixture was stirred at the same temperature for 30 min before addition of a solution of the crude mesylate in THF (1 mL) and TBAI (277 mg, 0.75 mmol) at 0 °C. The resulting mixture was warmed to room temperature and stirred for 1.5 h. Then, the reaction mixture was treated with saturated aqueous NH_4Cl, extracted with Et_2O, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo,* The residue was purified by silica gel column chromatography eluting with 4–20% EtOAc/hexane to give 2-benzoyl-4-methylhexa-4,5-dienenitrile (**5aA'**) (33.8 mg, 32%).



Colorless oil. Rf = 0.55 (25% EtOAc/hexane). IR (neat): 3382, 3062, 2983, 2921, 2242, 2207, 1961, 1697, 1597, 1448, 1256, 858, 694 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.65 (t, *J* = 6.8 Hz, 1H), 7.52 (dd, *J* = 8.4, 6.8 Hz, 2H), 4.85–4.77 (m, 1H), 4.74–4.66 (m, 1H), 4.46 (dd, *J* = 8.0, 6.0 Hz, 1H), 2.78–2.67 (m, 1H), 2.60–2.50 (m, 1H), 1.78 (t, *J* = 2.8 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 205.4, 189.9, 134.4, 134.2, 129.0, 128.7, 117.2, 95.3, 77.9, 37.7, 32.4, 18.8. LRMS m/z (relative intensity) 211 (M, 21), 196 (13), 145 (10), 105 (100), 77 (33). HRMS (EI) calcd for $C_{14}H_{13}NO$ 211.0997, found 211.0962 (M).

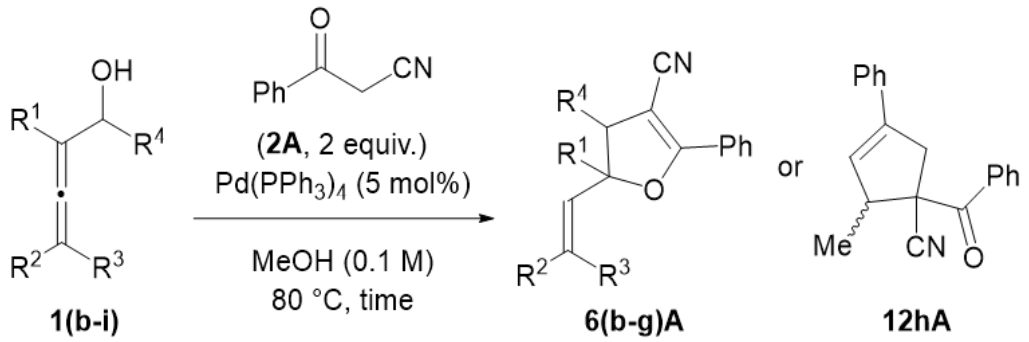
5-Methyl-2-phenyl-5-vinyl-4,5-dihydrofuran-3-carbonitrile (**6aA**)



5aA´ **6aA**

To a test tube containing **5aA'** (12.7 mg, 0.0600 mmol), HgO (1.3 mg, 10 mol%), and PTSA·H_2O (1.2 mg, 12 mol%) was added anhydrous cyclohexane (0.6 mL) under argon. The resulting mixture was sealed with a screw cap and stirred at 80 °C for 3 h. The reaction mixture was cooled to room temperature and basified with saturated aqueous $NaHCO_3$. The mixture was extracted with Et_2O, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo*. The residue was purified by preparative TLC eluting with 20% EtOAc/hexane to give **6aA** (12.5 mg, 98%).

General procedure for the dehydrative coupling between **1b–i** and **2A** (Table 2 and S5)

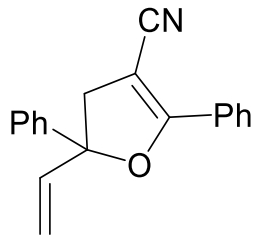


To a test tube containing allenic alcohol **1b–1i** (1 equiv), benzoylacetonitrile (**2A**) (2 equiv), and $Pd(PPh_3)_4$ (5 mol%) was added anhydrous MeOH (0.10 M) under argon. The resulting mixture was sealed with a screw cap and stirred at 80 °C for the time described in Table S5. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The residue was purified by preparative TLC to give **6(b–g)A** or **12hA**.

Table S5

entry	**1** (mg)	**2A** (mg)	$Pd(PPh_3)_4$ (mg)	time (h)	product (mg, %)
1	**1b**, 14.0	29.0	5.9	1.5	**6bA**, 19.2, 71
2	**1c**, 22.7	24.4	5.0	1.5	**6cA**, 15.7,47
3	**1d**, 9.8	29.0	5.9	1.5	**6dA**, 10.1, 45
4	**1e**, 16.0	29.0	5.9	1.5	**6eA**, 12.3, 43
5	**1f**, 17.4	29.0	5.9	1.5	**6fA**, 19.5, 65
6	**1g**, 17.4	29.0	5.8	1.5	**6gA**, 22.2, 74 (dr = 1:1)
7	**1h**, 16.0	29.0	5.9	2.0	**12hA**, major : 12.8, 45 minor : 10.2, 35
8	**1i**, 7.0	29.0	5.9	24	0, 0

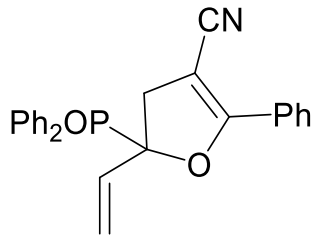
2,5-Diphenyl-5-vinyl-4,5-dihydrofuran-3-carbonitrile (**6bA**)



Isolated by preparative TLC eluting with 25% EtOAc/hexane

Pale yellow oil. Rf = 0.60 (20% EtOAc/hexane). IR (neat): 3060, 2925, 2204, 1624, 1495, 1448, 1350, 1261, 1151, 1076, 930, 771, 690 cm^{-1}.^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.07 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.53–7.45 (m, 3H), 7.45–7.30 (m, 5H), 6.19 (dd, *J* = 10.4, 17.6 Hz, 1H), 5.31 (d, *J* = 17.6 Hz, 1H), 5.27 (d, *J* = 10.4 Hz, 1H), 3.44 (d, *J* = 14.4 Hz, 1H), 3.39 (d, *J* = 14.4 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.4, 142.5, 139.6, 131.5, 128.8, 128.7, 128.04, 127.98, 127.1, 125.0, 117.4, 114.7, 91.2, 78.8, 44.1. LRMS m/z (relative intensity) 273 (M, 83), 244 (61), 168 (42), 105 (100). HRMS (EI) calcd for $C_{19}H_{15}NO$ 273.1154, found 273.1149 (M).

5-(Diphenylphosphoryl)-2-phenyl-5-vinyl-4,5-dihydrofuran-3-carbonitrile (**6cA**)

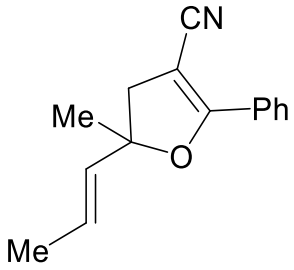


Isolated by preparative TLC eluting with 50% EtOAc/hexane

Colorless oil. Rf = 0.55 (50% EtOAc/hexane). IR (neat): 3443, 3060, 2208, 1628, 1438, 1346, 1256, 1197, 1117, 931, 753, 725, 698 cm^{-1}. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.03 (dd, *J* = 10.8, 7.6 Hz, 2H), 7.87 (dd, *J* = 10.8, 7.6 Hz, 2H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.56–7.45 (m, 6H), 7.38 (ddd, *J* = 7.6, 7.6, 3.2 Hz, 2H), 6.20 (ddd, *J* = 17.2, 10.8, 3.6 Hz, 1H), 5.42 (dd, *J* = 17.2, 3.6 Hz, 1H), 5.33 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.68 (dd, *J* = 15.0, 19.2 Hz, 1H), 3.16 (dd, *J* = 15.0, 15.0 Hz, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 165.2 (d, *J* = 3.2 Hz), 134.5 (d, *J* = 3.3 Hz), 132.7 (d, *J*

= 2.8 Hz), 132.5 (d, *J* = 2.8 Hz), 132.2 (d, *J* = 8.6 Hz), 132.0 (d, *J* = 8.7 Hz), 131.7, 129.0 (d, *J* = 91.7 Hz), 128.9, 128.7 (d, *J* = 11.5 Hz), 128.6 (d, *J* = 11.8 Hz), 128.4 (d, *J* = 88.5 Hz), 127.2, 126.8, 117.5 (d, *J* = 7.3 Hz), 116.2, 89.3 (d, *J* = 85.8 Hz), 80.4 (d, *J* = 3.9 Hz), 40.0 (d, *J* = 2.8 Hz). ^{31}P-NMR (243 MHz, $CDCl_3$): δ 28.3. HRMS (ESI) calcd for $C_{25}H_{21}NO_2P$ 398.1304, found 398.1289 $(M+H)^+$.

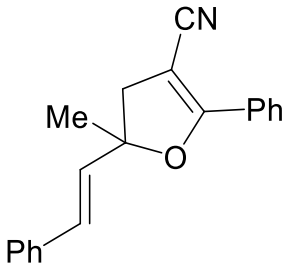
(*E*)-5-Methyl-2-phenyl-5-(prop-1-en-1-yl)-4,5-dihydrofuran-3-carbonitrile (**6dA**)



Isolated by preparative TLC eluting with 25% EtOAc/hexane

Pale yellow oil. Rf = 0.60 (20% EtOAc/hexane). IR (neat): 2974, 2929, 2861, 2204, 1620, 1496, 1448, 1353, 1260, 771, 691 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.95 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.48–7.40 (m, 3H), 5.77 (dq, *J* = 15.6, 6.0 Hz, 1H), 5.67 (dq, *J* = 15.6, 1.2 Hz, 1H), 3.03 (d, *J* = 14.8 Hz, 1H), 2.88 (d, *J* = 14.8 Hz, 1H), 1.74 (dd, *J* = 6.0, 1.2 Hz, 3H), 1.56 (s, 3H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 165.7, 133.4, 131.2, 128.6, 128.4, 127.1, 125.3, 118.0, 88.3, 78.3, 43.7, 26.3, 17.7. LRMS m/z (relative intensity) 225 (M, 46), 210 (77), 105 (100). HRMS (EI) calcd for $C_{15}H_{15}NO$ 225.1154, found 225.1147 (M).

(*E*)-5-Methyl-2-phenyl-5-styryl-4,5-dihydrofuran-3-carbonitrile (**6eA**)

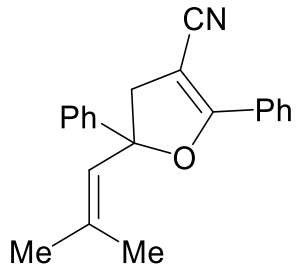


Isolated by preparative TLC eluting with 25% EtOAc/hexane

Pale yellow oil. Rf = 0.70 (25% EtOAc/hexane). IR (neat): 3027, 2928, 2863, 2203,

1621, 1495, 1448, 1352, 1259, 1062, 968, 770, 750, 691 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.51–7.43 (m, 3H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.33 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.26 (t, *J* = 7.2 Hz, 1H), 6.65 (d, *J* = 16.0 Hz, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 3.16 (d, *J* = 14.4 Hz, 1H), 3.01 (d, *J* = 14.4 Hz, 1H), 1.70 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.6, 135.9, 131.4, 131.3, 128.9, 128.7, 128.2, 128.1, 127.1, 126.7, 117.8, 88.4, 78.5, 43.9, 26.5. LRMS m/z (relative intensity) 287 (M, 92), 272 (16), 182 (25), 105 (100). HRMS (EI) calcd for $C_{20}H_{17}NO$ 287.1310, found 287.1293 (M).

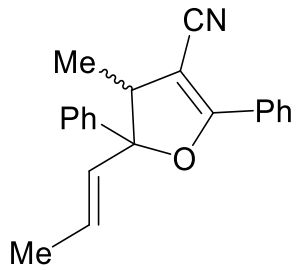
5-(2-Methylprop-1-en-1-yl)-2,5-diphenyl-4,5-dihydrofuran-3-carbonitrile (**6fA**)



Isolated by preparative TLC eluting with 25% EtOAc/hexane

Pale yellow oil. Rf = 0.60 (20% EtOAc/hexane). IR (neat): 3060, 3027, 2914, 2864, 2203, 1624, 1494, 1447, 1349, 1259, 1149, 769, 691 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.52–7.42 (m, 3H), 7.42–7.27 (m, 5H), 5.76 (dd, *J* = 1.2, 1.2 Hz, 1H), 3.42 (d, *J* = 14.8 Hz, 1H), 3.33 (d, *J* = 14.8 Hz, 1H), 1.81 (d, *J* = 1.2 Hz, 3H), 1.61 (d, *J* = 1.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.5, 145.0, 140.3, 131.3, 128.7, 128.6, 128.5, 128.2, 127.6, 127.2, 124.9, 117.7, 90.7, 78.2, 48.2, 26.6, 19.8. HRMS (ESI) calcd for $C_{21}H_{20}NO$ 302.1539, found 302.1533 $(M+H)^+$.

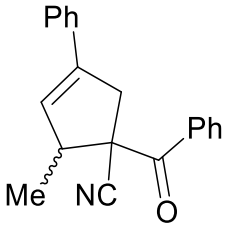
(*E*)-4-Methyl-2,5-diphenyl-5-(prop-1-en-1-yl)-4,5-dihydrofuran-3-carbonitrile (**6gA**)



Isolated as an inseparable 1:1 diastereomeric mixture by preparative TLC eluting with 25% EtOAc/hexane

Colorless oil. Rf = 0.65 (25% EtOAc/hexane). IR (neat): 3060, 3030, 2968, 2931, 2200, 1626, 1495, 1448, 1347, 1245, 1154, 970, 924, 772, 691 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.15–8.04 (m, 2H), 7.52–7.46 (m, 3H), 7.46–7.27 (m, 5H), 5.90 (d, *J* = 15.6 Hz, 0.5H), 5.88–5.72 (m, 0.5H), 5.79 (d, *J* = 15.6 Hz, 0.5H), 5.63 (dq, *J* = 15.6, 6.4 Hz, 0.5H), 3.62 (q, *J* = 7.2 Hz, 0.5H), 3.47 (q, *J* = 7.2 Hz, 0.5H), 1.75 (d, *J* = 6.4 Hz, 1.5H), 1.73 (d, *J* = 6.4 Hz, 1.5H), 1.39 (d, *J* = 7.2 Hz, 1.5H), 0.82 (d, *J* = 7.2 Hz, 1.5H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 164.3, 164.1, 143.9, 139.1, 132.9, 131.4, 129.3, 128.7, 128.5, 128.2, 128.15, 128.13, 128.11, 127.8, 127.7, 127.6, 127.2, 127.11, 127.10, 126.0, 125.9, 124.7, 117.7, 117.4, 93.7, 93.4, 86.2, 86.0, 49.8, 47.6, 17.85, 17.81, 17.1, 16.1. HRMS (ESI) calcd for $C_{21}H_{20}NO$ 302.1539, found 302.1532 $(M+H)^+$.

1-Benzoyl-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile (**12hA**)

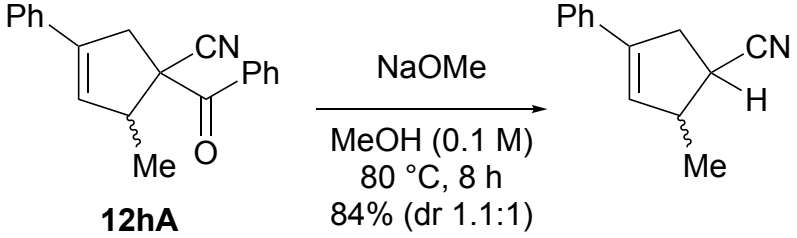


Isolated by preparative TLC eluting with 25% EtOAc/hexane

Faster-moving major diastereomer: Colorless oil. Rf = 0.60 (25% EtOAc/hexane). IR (neat): 3060, 3029, 2969, 2930, 2236, 1696, 1597, 1579, 1496, 1448, 1235, 757, 695 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.4 Hz, 2H), 7.62 (t, *J* = 8.0 Hz, 1H), 7.53 (dd, *J* = 8.4, 8.0 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.34 (dd, *J* = 8.0, 6.8 Hz, 2H), 7.28 (t, *J* = 6.8 Hz, 1H), 5.98 (s, 1H), 3.76 (q, *J* = 7.2 Hz, 1H), 3.72 (d, *J* = 16.4 Hz, 1H), 3.53 (d, *J* = 16.4 Hz, 1H), 1.52 (d, *J* = 7.2 Hz, 3H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 191.2, 138.0, 134.2, 133.9, 133.2, 129.6, 128.8, 128.5, 128.1, 127.4, 125.7, 120.4, 54.8, 47.0, 43.1, 17.8. LRMS m/z (relative intensity) 287 (M, 12), 272 (14), 246 (15), 105 (100). HRMS (EI) calcd for $C_{20}H_{17}NO$ 287.1310, found 287.1302 (M).

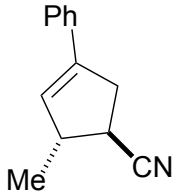
Slower-moving minor diastereomer: Colorless oil. Rf = 0.57 (25% EtOAc/hexane). IR (neat): 3060, 3029, 2969, 2930, 2236, 1696, 1597, 1579, 1496, 1448, 1235, 757, 695 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.0 Hz, 2H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.55 (dd, *J* = 8.0, 7.6 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.38 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.31 (t, *J* = 8.0 Hz, 1H), 6.07 (s, 1H), 4.11 (d, *J* = 16.4 Hz, 1H), 3.89 (q, *J* = 6.8 Hz, 1H), 3.14 (d, *J* = 16.4 Hz, 1H), 0.91 (d, *J* = 6.8 Hz, 3H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 191.0, 139.1, 134.6, 134.4, 134.1, 129.3, 128.9, 128.6, 128.2, 126.3, 125.8, 123.5, 54.7, 50.8, 40.2, 16.0. LRMS m/z (relative intensity) 287 (M, 12), 272 (14), 246 (15), 105 (100). HRMS (EI) calcd for $C_{20}H_{17}NO$ 287.1310, found 287.1302 (M).

Retro-Claisen reaction of **12hA** for the structure determination



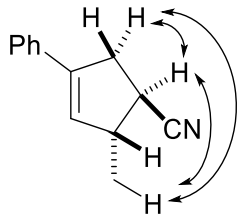
To a test tube containing a 6:5 diastereomeric mixture of **12hA** (28.7 mg, 0.0999 mmol) were added anhydrous MeOH (1.0 mL) and NaOMe (11.0 mg, 0.204 mmol) under argon. The resulting mixture was sealed with a screw cap and stirred at 80 °C for 8 h. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The residue was purified by preparative TLC eluting with eluting with 20% EtOAc/hexane to give (1*R**,2*R**)-2-methyl-4-phenylcyclopent-3–ene-1-carbonitrile (7.3 mg, 44%) and (1*R**,2*S**)-2-methyl-4-phenylcyclopent-3-ene–1-carbonitrile (6.6 mg, 40%).

(1*R**,2*R**)-2-Methyl-4-phenylcyclopent-3-ene-1-carbonitrile



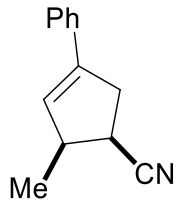
Faster-moving major diastereomer: Colorless oil. Rf = 0.55 (20% EtOAc/hexane). IR (neat): 3056, 2961, 2927, 2870, 2238, 1495, 1447, 756, 693 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.39–7.25 (m, 5H), 6.02–6.00 (m, 1H), 3.31–3.26 (m, 1H), 3.26–3.17 (m, 1H), 3.16–3.02 (m, 1H), 2.78–2.67 (m, 1H), 1.29 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 139.6, 134.7, 129.1, 128.5, 127.9, 125.6, 122.3, 46.4, 37.7, 34.6, 19.7. LRMS m/z (relative intensity) 183 (M, 66), 168 (100), 141 (13). HRMS (EI) calcd for $C_{13}H_{13}N$ 183.1048, found 183.1069 (M).

The *trans*-configuration of (1*R**,2*R**)-2-methyl-4-phenylcyclopent-3-ene-1–carbonitrile was determined by NOESY correlation as shown below.



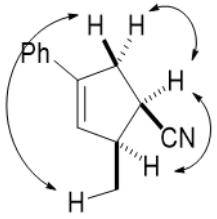
NOESY correlation of (1*R**,2*R**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile

(1*R**,2*S**)-2-Methyl-4-phenylcyclopent-3-ene-1-carbonitrile



Slower-moving minor diastereomer: Colorless oil. Rf = 0.52 (20% EtOAc/hexane). IR (neat): 3057, 2964, 2929, 2871, 2239, 1495, 1447, 756, 694 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.40–7.24 (m, 5H), 6.07 (ddd, J = 2.0, 2.0, 3.6 Hz. 1H), 3.43–3.36 (m, 1H), 3.21–3.16 (m, 1H), 3.13–3.09 (m, 2H), 1.30 (d, J = 6.8 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 139.3, 134.8, 129.3, 128.5, 127.9, 155.6, 121.0, 41.6, 36.9, 32.5, 17.1. LRMS m/z (relative intensity) 183 (M, 63), 168 (100), 141 (13). HRMS (EI) calcd for $C_{13}H_{13}N$ 183.1048, found 183.1069 (M).

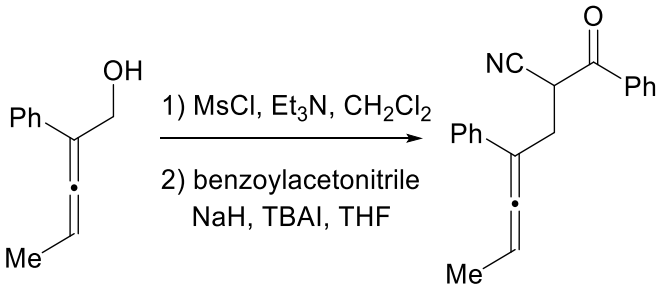
The *cis*-configuration of (1*R**,2*S**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile was determined by NOESY correlation as shown below.



NOESY correlation of (1*R**,2*S**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile

Conventional synthesis of **6hA** and **12hA** for the structure determination

2-Benzoyl-4-phenylhepta-4,5-dienenitrile (**5hA'**)

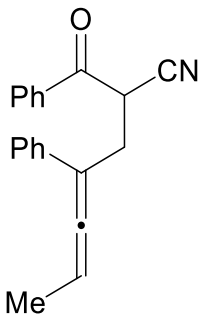


1h **5hA´**

To a solution of **1h** (80.1 mg, 0.50 mmol) in anhydrous CH_2Cl_2 (5 mL) were added Et_3N (210 μL, 1.5 mmol) and MsCl (145 μL, 1.5 mmol) at 0 °C. After being stirred at the same temperature for 15 min, the reaction mixture was treated with saturated aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give crude mesylate, which was used for the next reaction without further purification.

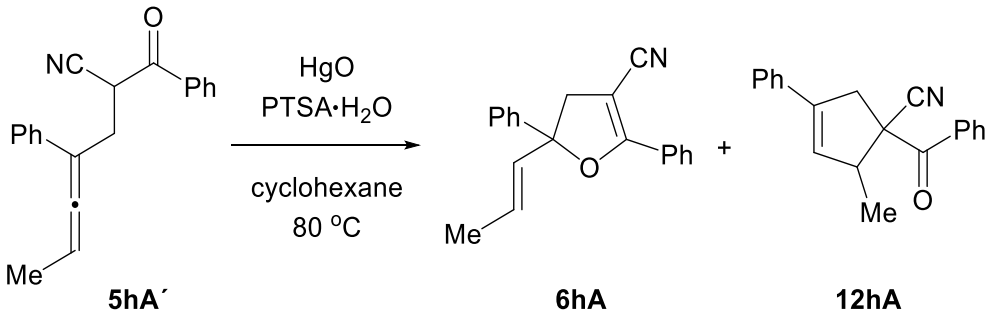
To a solution of benzoylacetonitrile (**2A**) (290 mg, 2.00 mmol) in anhydrous THF (5 mL) was added NaH (60% dispersion in mineral oil, 80 mg, 2.0 mmol) at 0 °C. The mixture was stirred at the same temperature for 30 min before addition of a solution of the crude mesylate in THF (1 mL) and TBAI (277 mg, 0.75 mmol) at 0 °C. The resulting mixture was warmed to room temperature and stirred for 3 h. Then, the reaction mixture was treated with saturated aqueous NH_4Cl, extracted with

Et_2O, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo*. The residue was purified by silica gel column chromatography eluting with 3–15% EtOAc/hexane to give 2-benzoyl-4-phenylhepta-4,5-dienenitrile (**5hA'**) as an inseparable diastereomeric mixture (57.5 mg, 45%).



Colorless oil. Rf = 0.55 (20% EtOAc/hexane). IR (neat): 3421, 3062, 3027, 2983, 2936, 2247, 2209, 1964, 1723, 1690, 1598, 1494, 1270, 1231, 757, 699 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.02–7.97 (m, 2H), 7.69–7.61 (m, 1H), 7.55–7.51 (m, 2H), 7.40–7.28 (m, 4H), 7.28–7.21 (m, 1H), 5.66–5.52 (m, 1H), 4.62–4.55 (m, 1H), 3.35 (ddd, *J* = 15.2, 7.2, 3.6 Hz, 0.5H), 3.20 (ddd, *J* = 15.6, 9.2, 3.6 Hz, 0.5H), 3.09 (ddd, *J* = 15.6, 8.4, 2.8 Hz, 0.5H), 3.03 (ddd, *J* = 15.2, 7.2, 2.8 Hz, 0.5H), 1.79 (d, *J* = 6.8 Hz, 1.5H), 1.56 (d, *J* = 6.8 Hz, 1.5H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 204.0, 203.9, 190.1, 189.5, 135.60, 135.55, 134.5, 134.4, 134.2, 129.09, 129.08, 128.8, 128.61, 128.60, 127.3, 125.9, 125.8, 117.1, 101.8, 101.7, 93.1, 92.7, 37.9, 37.3, 29.8, 29.7, 14.1, 14.0. LRMS m/z (relative intensity) 287 (M, 20), 272 (13), 182 (10), 105 (100). HRMS (EI) calcd for $C_{20}H_{17}NO$ 287.1310, found 287.1307 (M).

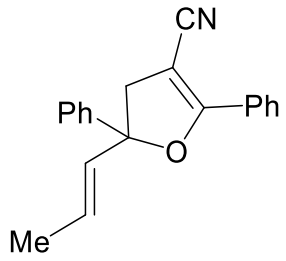
(*E*)-2,5-Diphenyl-5-(prop-1-en-1-yl)-4,5-dihydrofuran-3-carbonitrile (**6hA**) and 1-benzoyl-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile (**12hA**)



5hA´ **6hA** **12hA**

To a test tube containing **5hA'** (14.4 mg, 0.0500 mmol), HgO (1.1 mg, 10 mol%), and PTSA·H_2O (1.0 mg, 12 mol%) was added anhydrous cyclohexane (0.5 mL) under argon. The resulting mixture was sealed with a screw cap and stirred at 80 °C for 3 h. The reaction mixture was cooled to room temperature and basified with saturated aqueous $NaHCO_3$. The mixture was extracted with Et_2O, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo*. The residue was purified by preparative TLC eluting with 25% EtOAc/hexane to give dihydrofurane **6hA** (1.9 mg, 13%) and cyclopentene **12hA** (9.5 mg, 66%) as faster- and slower-moving components, respectively.

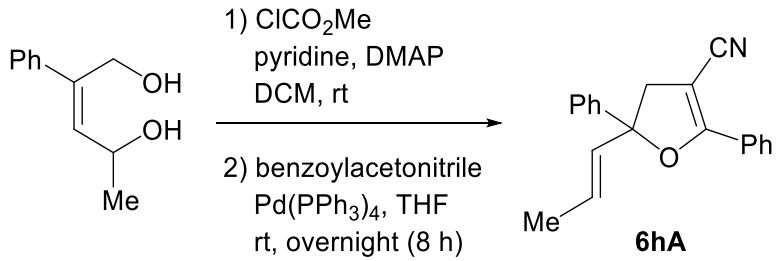
(*E*)-2,5-Diphenyl-5-(prop-1-en-1-yl)-4,5-dihydrofuran-3-carbonitrile (**6hA**)



Pale yellow oil. Rf = 0.68 (25% EtOAc/hexane). IR (neat): 3060, 3030, 2916, 2855, 2203, 1625, 1495, 1447, 1350, 1258, 1152, 965, 771, 691 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.55－7.42 (m, 3H), 7.42－7.25 (m, 5H), 5.85 (dq, *J* = 15.2, 1.6 Hz, 1H), 5.68 (dq, *J* = 6.4, 15.2 Hz, 1H), 3.42 (d, *J* = 14.6 Hz, 1H), 3.35 (d, *J* = 14.6 Hz, 1H), 1.74 (dd, *J* = 6.4, 1.6 Hz, 3H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 165.4, 143.3, 133.1, 131.4, 128.7, 128.6, 128.1, 127.9, 127.2, 126.9, 125.1, 117.6, 91.3, 78.7, 44.5, 17.7. LRMS m/z (relative intensity) 287 (M, 61), 272 (40), 258 (25), 182(21), 130(16), 105 (100). HRMS (EI) calcd for $C_{20}H_{17}NO$ 287.1310, found

287.1307 (M).

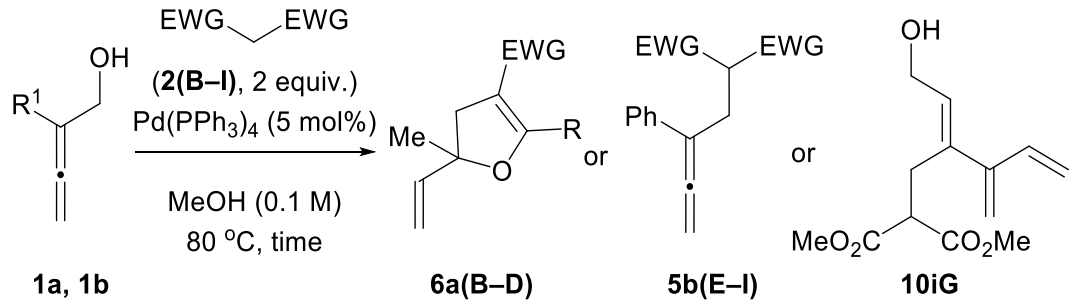
Alternative Synthesis of **6hA**



To a solution of (*Z*)-2-phenylpent-2-ene-1,4-diol[9] (28.0 mg, 0.157 mmol) in anhydrous CH_2Cl_2 (0.45 mL) were added $ClCO_2Me$ (60.7 μL, 0.785 mmol), pyridine (79.0 μL, 0.983 mmol), and DMAP (2.0 mg, 0.016 mmol) successively at 0 ºC. The resulting mixture was warmed to room temperature and stirred for 3 h. Then, the reaction mixture was treated with saturated aqueous NH_4Cl, extracted with EtOAc, washed with water and brine, dried over $MgSO_4$, and concentrated in *vacuo* to give crude dicarbonate (47.1 mg, quant.), which was used for the next reaction without further purification.

To a test tube containing the crude dicarbonate (15.7 mg, 0.0534 mmol), benzoylacetonitrile (**2A**) (8.5 mg, 0.059 mmol) and $Pd(PPh_3)_4$ (3.0 mg, 5 mol%) was added anhydrous MeOH (0.5 mL) under argon. The resulting mixture was sealed with a screw cap and stirred at room temperature for 8 h. The mixture was concentrated in *vacuo* and the residue was purified by preparative TLC eluting with 20% EtOAc/hexane to give dihydrofurane **6hA** (8.2 mg, 54% from (*Z*)-2-phenylpent-2-ene-1,4-diol over 2 steps).

General procedure for the dehydrative coupling between **1a–b** and **2B–I** (Table 3 and S6)

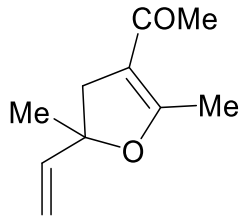


To a test tube containing allenic alcohol **1a** or **1b** (1 equiv), pronucleophile **2B–I** (2 equiv), and $Pd(PPh_3)_4$ (5 mol%) was added anhydrous MeOH (0.10 M) under argon. The resulting mixture was sealed with a screw cap and stirred at 80 °C for the time described in Table S6. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The residue was purified by preparative TLC to give **6a(B–D)**, **5b(E–I)**, or **10iG**.

Table S6

entry	**1** (mg)	**2** (mg or μL)	$Pd(PPh_3)_4$ (mg)	time (h)	product (mg, %)
1	**1a**, 16.8	**2B**, 41.2 μL	11.7	1.5	**6aB**, 16.2, 49
2	**1a**, 16.8	**2C**, 43.2 μL	11.6	1.5	**6aC**, 20.7, 57
3	**1a**, 16.8	**2D**, 56.1 mg	11.8	1.5	**6aD**, 17.7, 43
4	**1b**, 14.7	**2E**, 25.2 mg	5.8	1.5	**5bE**, 13.0, 51
5	**1b**, 14.9	**2F**, 25.3 μL	6.0	1.5	**5bF**, 14.8, 53
6	**1b**, 14.6	**2G**, 22.8 μL	5.9	2.0	**5bG**, 15.5, 60
7	**1b**, 14.6	**2H**, 12.6 μL	5.9	2.0	**5bH**, 12.3, 58
8	**1b**, 14.6	**2I**, 59.2 mg	5.9	1.5	**5bI**, 20.4, 48
9	**1i**, 7.0	**2G**, 22.8 μL	5.9	2.0	**10iG**, 14.7, 58

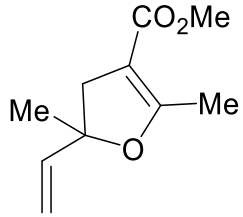
1-(2,5-Dimethyl-5-vinyl-4,5-dihydrofuran-3-yl)ethan-1-one (**6aB**)[10]



Isolated by preparative TLC eluting with 33% EtOAc/hexane

Colorless oil. Rf = 0.65 (25% EtOAc/hexane). IR (neat): 3438 (br), 3061, 3028, 2935, 1715, 1600, 1494, 1448, 1361, 1233, 937, 761, 701 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.95 (dd, *J* = 10.8, 17.2 Hz, 1H), 5.22 (d, *J* = 17.2 Hz, 1H), 5.10 (d, *J* = 10.8 Hz, 1H), 2.92 (dq, *J* = 14.0, 1.2 Hz, 1H), 2.78 (dq, *J* = 14.0, 1.2 Hz, 1H), 2.24 (dd, *J* = 1.2, 1.2 Hz, 3H), 2.18 (s, 3H) , 1.47 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 194.5, 166.4, 141.1, 112.8, 111.5, 87.1, 42.5, 29.3, 26.3, 15.2. HRMS (ESI) calcd for $C_{10}H_{14}O_2$ 166.0994, found 166.0992 (M).

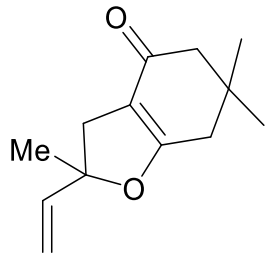
Methyl 2,5-dimethyl-5-vinyl-4,5-dihydrofuran-3-carboxylate (**6aC**)[11]



Isolated by preparative TLC eluting with 33% EtOAc/hexane

Colorless oil. Rf = 0.55 (20% EtOAc/hexane). IR (neat): 2977, 2950, 2928, 2868, 1705, 1646, 1438, 1384, 1243, 1190, 1135, 1072, 984, 926, 762 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.95 (dd, *J* = 10.4, 17.6 Hz, 1H), 5.22 (d, *J* = 17.6 Hz, 1H), 5.09 (d, *J* = 10.4 Hz, 1H), 3.69 (s, 3H), 2.86 (d, *J* = 14.4 Hz, 1H), 2.71 (d, *J* = 14.4 Hz, 1H), 2.21 (s, 3H), 1.46 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 166.9, 166.7, 141.2, 112.6, 100.8, 87.0, 50.8, 41.6, 26.3, 14.2. LRMS m/z (relative intensity) 182 (M, 80), 139 (100), 135 (96), 198 (100), 123 (30), 107 (56). HRMS (EI) calcd for $C_{10}H_{14}O_3$ 182.0943, found 182.0954 (M).

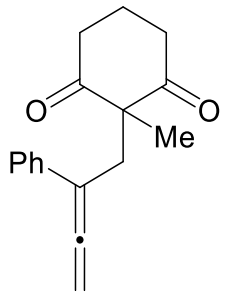
2,6,6-Trimethyl-2-vinyl-3,5,6,7-tetrahydrobenzofuran-4(2*H*)-one (**6aD**)[12]



Isolated by preparative TLC eluting with 25% EtOAc/hexane

Colorless oil. Rf = 0.45 (25% EtOAc/hexane). IR (neat): 3423 (br), 2961, 2934, 2873, 1726, 1620, 1406, 1242, 1034, 928, 755 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.97 (dd, J = 11.2, 17.2 Hz, 1H), 5.23 (d, J = 17.2 Hz, 1H), 5.12 (d, J = 11.2 Hz, 1H), 2.82 (d, J = 14.4 Hz, 1H), 2.67 (d, J = 14.4 Hz, 1H), 2.29 (s, 2H), 2.23 (s, 2H), 1.51 (s, 3H), 1.11 (s, 3H), 1.10 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 195.0, 175.0, 140.7, 113.1, 110.9, 91.4, 50.9, 37.9, 37.8, 34.1, 28.7, 28.6, 26.4. HRMS (ESI) calcd for $C_{13}H_{19}O_2$ 207.1380, found 207.1377 $(M+H)^+$.

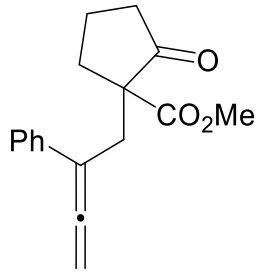
2-Methyl-2-(2-phenylbuta-2,3-dien-1-yl)cyclohexane-1,3-dione (**5bE**)



Isolated by preparative TLC eluting with 33% EtOAc/hexane

Pale yellow oil. Rf = 0.45 (25% EtOAc/hexane). IR (neat): 2959, 2910, 1943, 1726, 1697, 1596, 1493, 1453, 1318, 1283, 1132, 1022, 860, 765, 697 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.37 (d, J = 8.0 Hz, 2H), 7.29 (dd, J = 8.0, 7.2 Hz, 2H), 7.19 (t, J = 7.2 Hz, 1H), 5.00 (t, J = 4.0 Hz, 2H), 3.02 (t, J = 4.0 Hz, 2H), 2.74 (dt, J = 16.8, 7.6 Hz, 2H), 2.63 (dt, J = 16.8, 6.0 Hz, 2H), 2.12–2.02 (m, 2H), 1.40 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 209.8, 208.7, 135.9, 128.3, 126.9, 126.1, 102.5, 81.2, 63.8, 37.7, 34.4, 25.6, 17.5. LRMS m/z (relative intensity) 254 (M, 24), 239 (12), 126 (18), 198 (100), 183 (52), 128 (23). HRMS (EI) calcd for $C_{17}H_{18}O_2$ 254.1307, found 254.1273 (M).

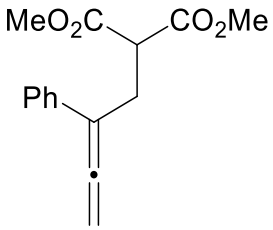
Methyl 2-oxo-1-(2-phenylbuta-2,3-dien-1-yl)cyclopentane-1-carboxylate (**5bF**)



Isolated by preparative TLC eluting with 33% EtOAc/hexane

Pale yellow oil. Rf = 0.60 (25% EtOAc/hexane). IR (neat): 2952, 1942, 1752, 1725, 1596, 1494, 1449, 1217, 1164, 1108, 854, 766, 697 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.31 (dd, *J* = 8.4, 7.6 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 5.11–5.02 (m, 2H), 3.63 (s, 3H), 3.28 (dt, *J* = 15.2, 3.2 Hz, 1H), 2.72－2.64 (m, 1H), 2.60 (dt, *J* = 15.2, 3.2 Hz, 1H), 2.47–2.37 (m, 1H), 2.32–2.22 (m, 1H), 2.10–1.99 (m, 2H), 1.99–1.87 (m, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 214.2, 208.9, 170.4, 136.0, 128.4, 127.0, 126.1, 101.4, 79.6, 60.4, 52.5, 37.9, 33.8, 32.4, 19.6. HRMS (ESI) calcd for $C_{17}H_{18}NaO_3$ 293.1148, found 293.1140 $(M+Na)^+$.

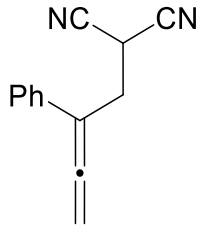
Dimethyl 2-(2-phenylbuta-2,3-dien-1-yl)malonate (**5bG**)



Isolated by preparative TLC eluting with 25% EtOAc/hexane

Pale yellow oil. Rf = 0.60 (25% EtOAc/hexane). IR (neat): 2954, 1943, 1736, 1687, 1437, 1276, 1155, 1029, 764, 700 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.6 Hz, 2H), 7.33 (dd, *J* = 7.6, 7.2 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 5.13 (t, *J* = 3.2 Hz, 1H), 3.74 (s, 6H), 3.71 (t, *J* = 7.6 Hz, 1H), 3.05 (dt, *J* = 7.6, 3.2 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 207.6, 169.4, 135.2, 128.5, 127.1, 125.9, 102.6, 80.2, 52.6, 50.4, 28.4. HRMS (ESI) calcd for $C_{15}H_{16}NaO_4$ 283.0941, found 283.0935 $(M+Na)^+$.

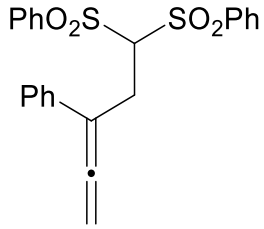
2-(2-Phenylbuta-2,3-dien-1-yl)malononitrile (**5bH**)



Isolated by preparative TLC eluting with 25% EtOAc/hexane

Pale yellow oil. Rf = 0.45 (25% EtOAc/hexane). IR (neat): 3059, 2359, 1943, 1597, 1495, 1453, 1028, 869, 766, 695 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.42–7.27 (m, 5H), 5.44 (t, *J* = 3.6 Hz, 2H), 3.94 (t, *J* = 7.2 Hz, 1H), 3.15 (dt, *J* = 7.2, 3.6 Hz, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 207.4, 133.3, 129.0, 128.0, 125.7, 112.3, 100.1, 82.9, 31.1, 21.5. LRMS m/z (relative intensity) 194 (M, 36), 167 (62), 154 (29), 140 (27), 128 (100), 115 (27). HRMS (EI) calcd for $C_{13}H_{10}N_2$ 194.0844, found 194.0868 (M).

(3-Phenylpenta-3,4-diene-1,1-diyldisulfonyl)dibenzene (**5bI**)

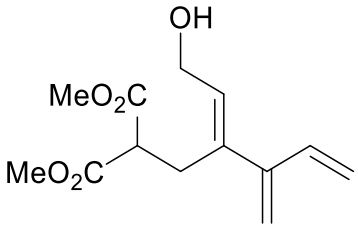


Isolated by preparative TLC eluting with 25% EtOAc/hexane

Colorless oil. Rf = 0.50 (25% EtOAc/hexane). IR (neat): 3056, 2923, 1670, 1594, 1446, 1287, 1251, 1147, 1082, 1004, 779, 747, 716, 685 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.4 Hz, 4H), 7.68 (t, *J* = 6.8 Hz, 2H), 7.54 (dd, *J* = 8.4, 6.8 Hz, 4H), 7.31–7.21 (m, 3H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.06 (t, *J* = 2.8 Hz, 2H), 4.79 (t, *J* = 5.4 Hz, 1H), 3.37 (dt, *J* = 5.4, 2.8 Hz, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 208.0, 138.3, 134.5, 133.9, 129.5, 129.0, 128.6, 127.5, 126.1, 101.8, 81.2, 81.1, 26.0. HRMS (ESI) calcd for $C_{23}H_{20}NaO_4S_2$ 447.0695, found 447.0687 $(M+Na)^+$.

Dimethyl (*E*)-2-(2-(2-hydroxyethylidene)-3-methylenepent-4-en-1-yl)malonate

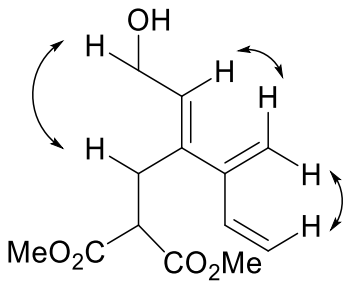
(**10iG**)



Isolated by preparative TLC eluting with 50% EtOAc/hexane

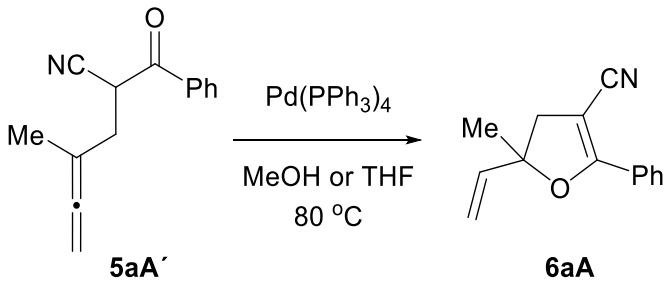
Pale yellow oil. Rf = 0.50 (50% EtOAc/hexane). IR (neat): 3437 (br), 2955, 1732, 1437, 1241, 1159, 1159, 1027, 772 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.35 (dd, *J* = 17.2, 10.4 Hz, 1H), 5.79 (t, *J* = 6.8 Hz, 1H), 5.22 (d, *J* = 17.2 Hz, 1H), 5.17 (s, 1H), 5.16 (d, *J* = 10.4 Hz, 1H), 5.00 (s, 1H), 4.31–4.24 (m, 2H), 3.72 (s, 6H), 3.55 (t, *J* = 8.0 Hz, 1H), 2.91 (d, *J* = 8.0 Hz, 2H), 2.20–2.12 (m, 1H). ^{13}C-NMR (151 MHz, $CDCl_3$): δ 169.6, 147.4, 137.3, 137.0, 131.1, 116.9, 116.3, 58.5, 52.7, 50.1, 28.4. HRMS (ESI) calcd for $C_{13}H_{18}NaO_5$ 277.1046, found 277.1042 $(M+Na)^+$.

The *E*-configuration of **10iG** was determined by NOESY correlation as shown below.



NOESY correlation of **10iG**

Pd-catalyzed cyclisation of **5aA'** (Scheme 3 and Table S7)



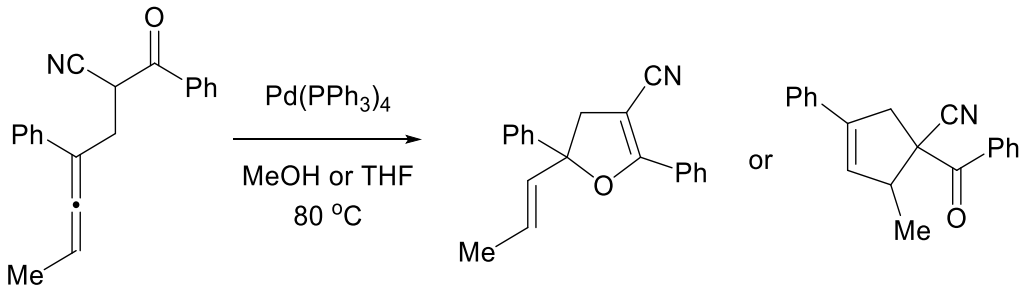
To a test tube containing **5aA'** (1 equiv) and $Pd(PPh_3)_4$ (5 mol% for entries 1, 2, 0

mol% for entry 3) was added anhydrous solvent (0.10 M) under argon. The resulting mixture was sealed with a screw cap and stirred at 80 °C for 1.5 h. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The residue was purified by preparative TLC eluting with 20% EtOAc/hexane to give **6aA**.

Table S7

entry	conditions	**5aA'** (mg)	$Pd(PPh_3)_4$ (mg)	solvent	**6aA** (mg, %)
1	A	9.8	2.6	THF	9.5, 97
2	B	10.5	2.9	MeOH	10.5, quant
3	C	10.2	0	MeOH	<1, trace

Pd-catalyzed cyclisation of **5hA'** (Scheme 3 and Table S8)



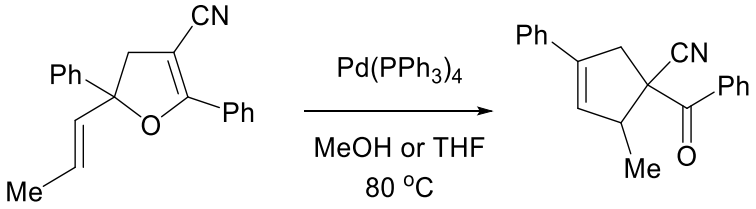
5hA´ **6hA** **12hA**

To a test tube containing **5hA'** (1 equiv) and $Pd(PPh_3)_4$ (5 mol% for entries 1, 2, 0 mol% for entry 3) was added anhydrous solvent (0.10 M) under argon. The resulting mixture was sealed with a screw cap and stirred at 80 °C for 1.5 h. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The residue was purified by preparative TLC eluting with 20% EtOAc/hexane to give **6hA** (for entry 1) or **12hA** (for entry 2).

Table S8

entry	conditions	**5hA'** (mg)	$Pd(PPh_3)_4$ (mg)	solvent	product (mg, %)
1	A	8.8	2.0	THF	**6hA**, 6.9, 78
2	B	14.4	2.9	MeOH	**12hA**, 14.4, quant
3	C	9.2	0	MeOH	0 mg, 0

Rearrangement of **6hA** to **12hA** (Scheme 3 and Table S9)



6hA **12hA**

To a test tube containing **6hA** (1 equiv) and $Pd(PPh_3)_4$ (5 mol% for entries 1, 2, 0 mol% for entry 3) was added anhydrous solvent (0.10 M) under argon. The resulting mixture was sealed with a screw cap and stirred at 80 °C for 2 h. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The residue was purified by preparative TLC eluting with 20% EtOAc/hexane to give **12hA** (for entry 1).

Table S9

entry	conditions	**6hA** (mg)	$Pd(PPh_3)_4$ (mg)	solvent	product (mg, %)
1	A	9.8	2.0	MeOH	**12hA**, 6.8, 70
2	B	9.6	2.0	THF	0 mg, 0
3	C	7.6	0	MeOH	0 mg, 0

References

[1] S. P. Cook and S. J. Danisefsky, *Org. Lett.*, 2006, **8**, 5693.

[2] J. Li, W. Kong, C. Fu and S. Ma, *J. Org. Chem.*, 2009, **74**, 5104.

[3] T. Liu, J. Dong, S.-J. Cao, L.-C. Guo and L. Wu, *RSC Advances*, 2014, **4**, 61722.

[4] I. Alonso, H. Faustino, F. López and J. L. Mascareñas, *Angew. Chem. Int. Ed.*, 2011, **50**, 11496; L.-I. Olsson and A. Clafesson, *Acta Chem. Scand. B*, 1979, **33**, 679.

[5] I. Diaf, G. Lemiére and E. Duñach, *Angew. Chem. Int. Ed.*, 2014, **53**, 4177.

[6] H. Luo and S. Ma, *Eur. J. Org. Chem.*, 2013, 3041.

[7] X. Tang, S. Woodward and N. Krause, *Eur. J. Org. Chem.*, 2009, 2836.

[8] M. Yang, N. Yokokawa, H.Ohmiya and M. Sawamura, *Org. Lett.*, 2012, **14**, 816.

[9] W. Guo, L. Martínez-Rodríguez, E. Martin, E. C. Escudero-Adán, and A. W. Kleij, *Angew. Chem. Int. Ed.*, 2016, **55**, 11037.

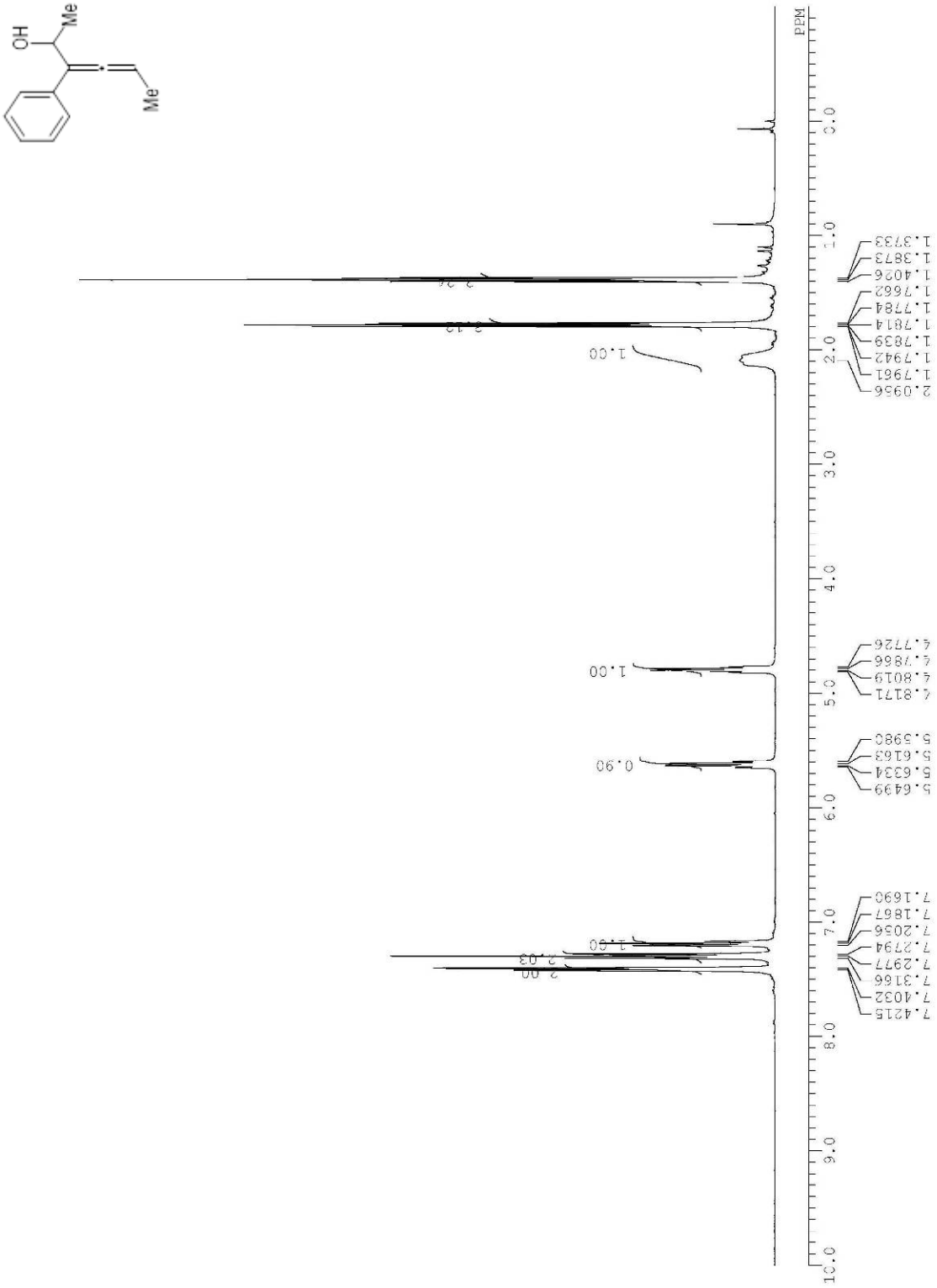
[10] T. Delair, A. Doutheau and J. Gore, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1981, **30**, 125.

[11] T. Delair, A. Doutheau and J. Gore, *Bull. Soc. Chim. Fr.*, 1988, 125.

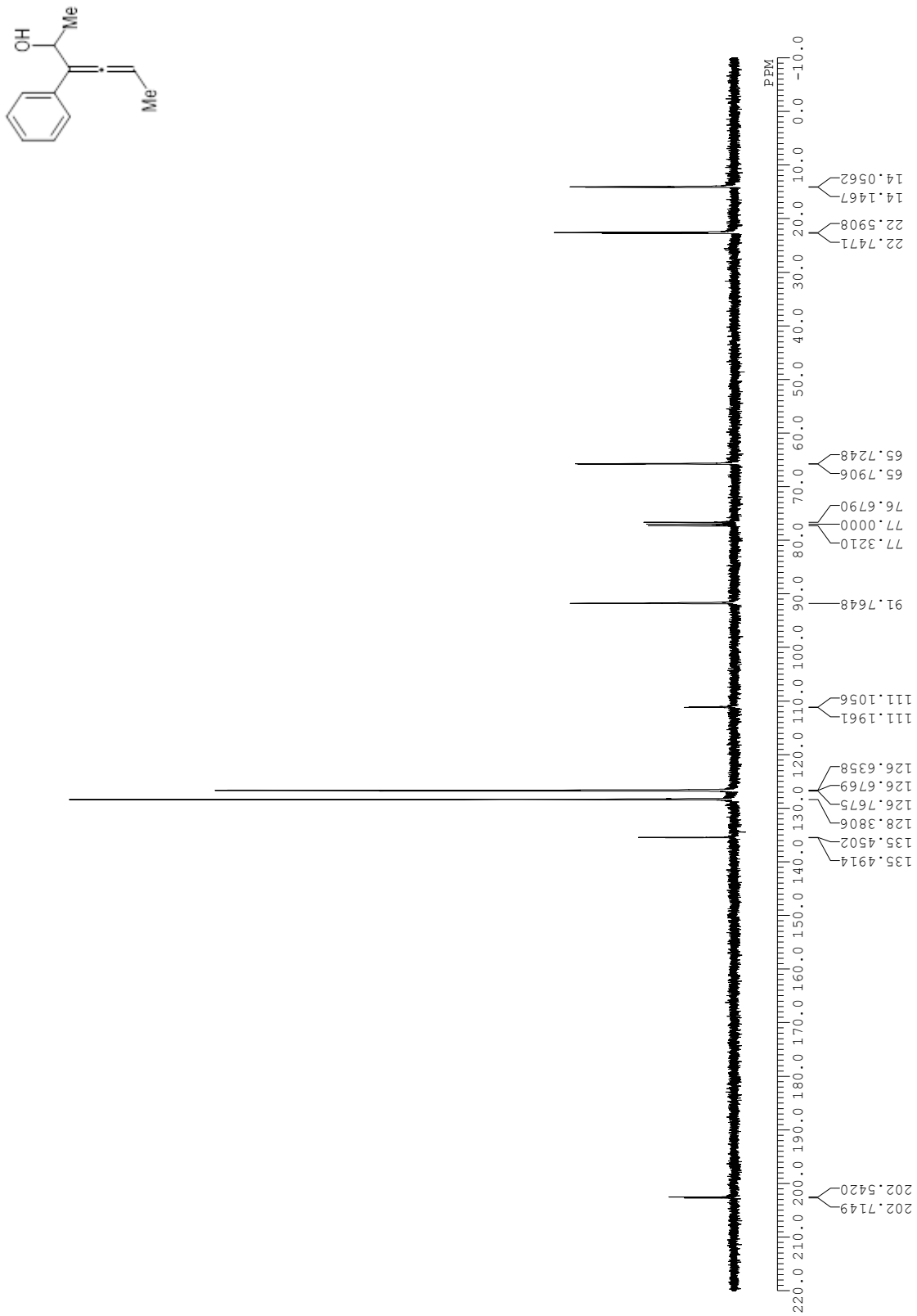
[12] S. Fernandes, S. V. Bhat, *Synth. Commun.*, 2014, **19**, 2892.

NMR spectra

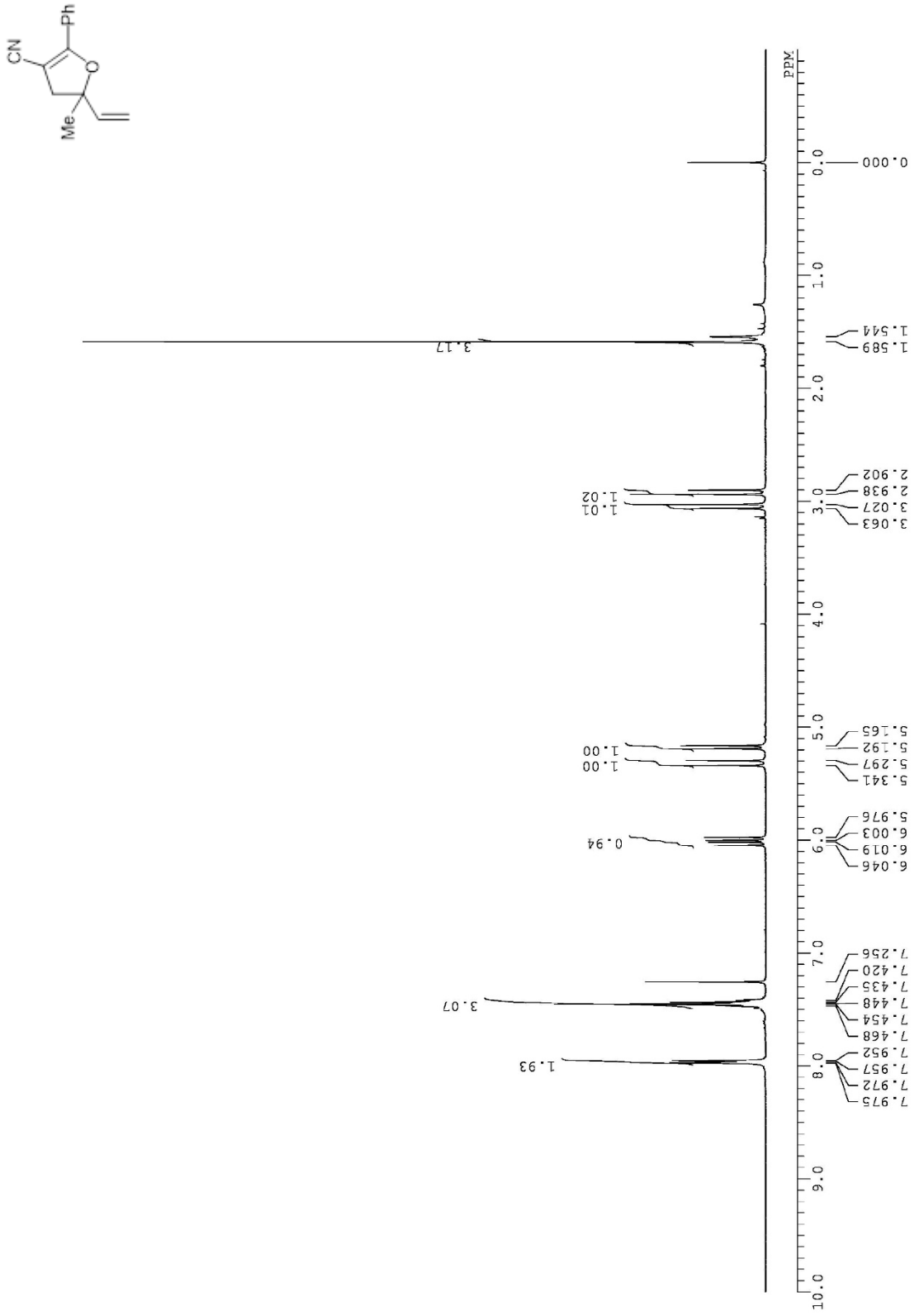
^{1}H NMR spectrum of **1g**



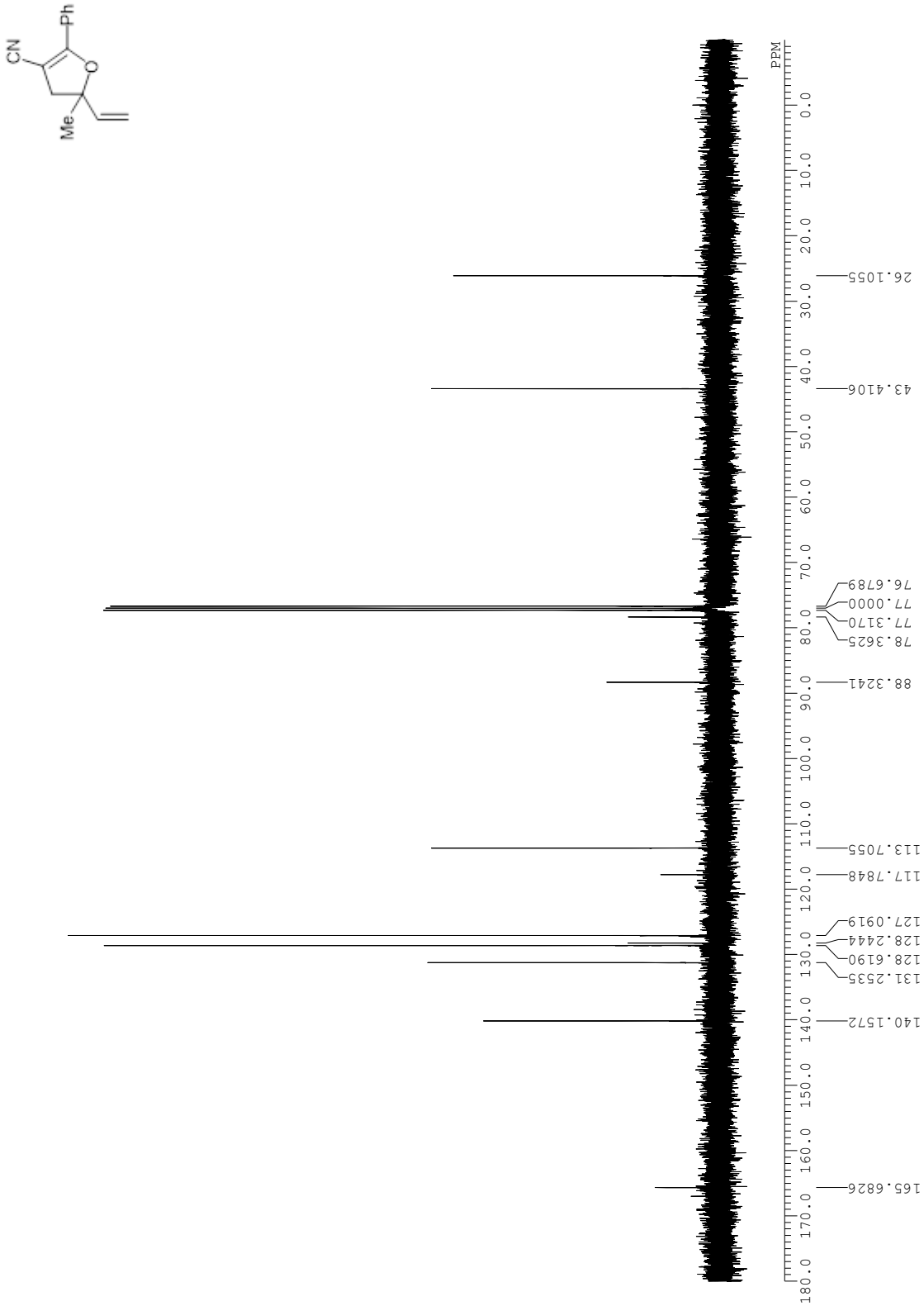
^{13}C NMR spectrum of **1g**



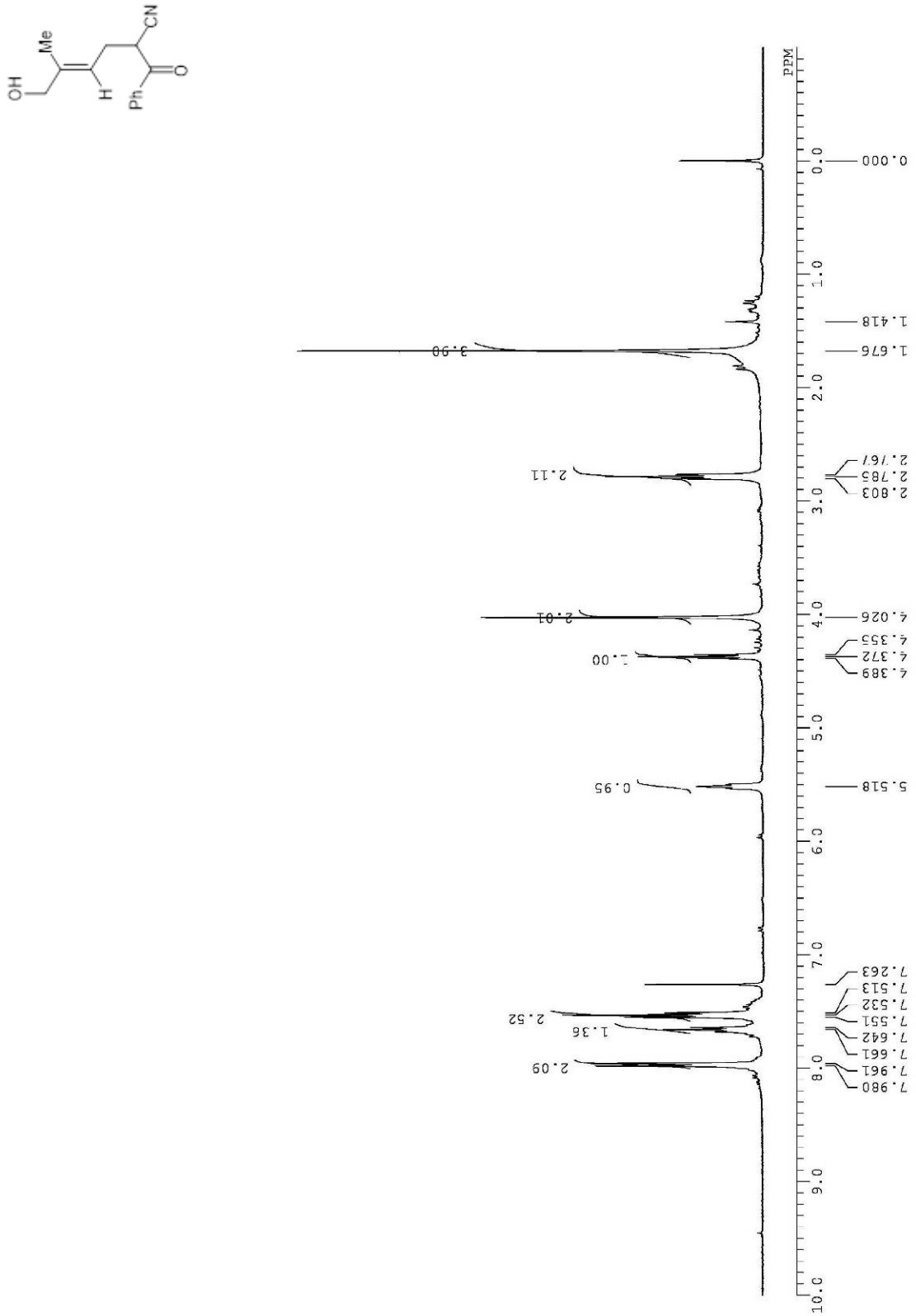
^{1}H NMR spectrum of **6aA**



^{13}C NMR spectrum of **6aA**



^{1}H NMR spectrum of **(*E*)-9aA**



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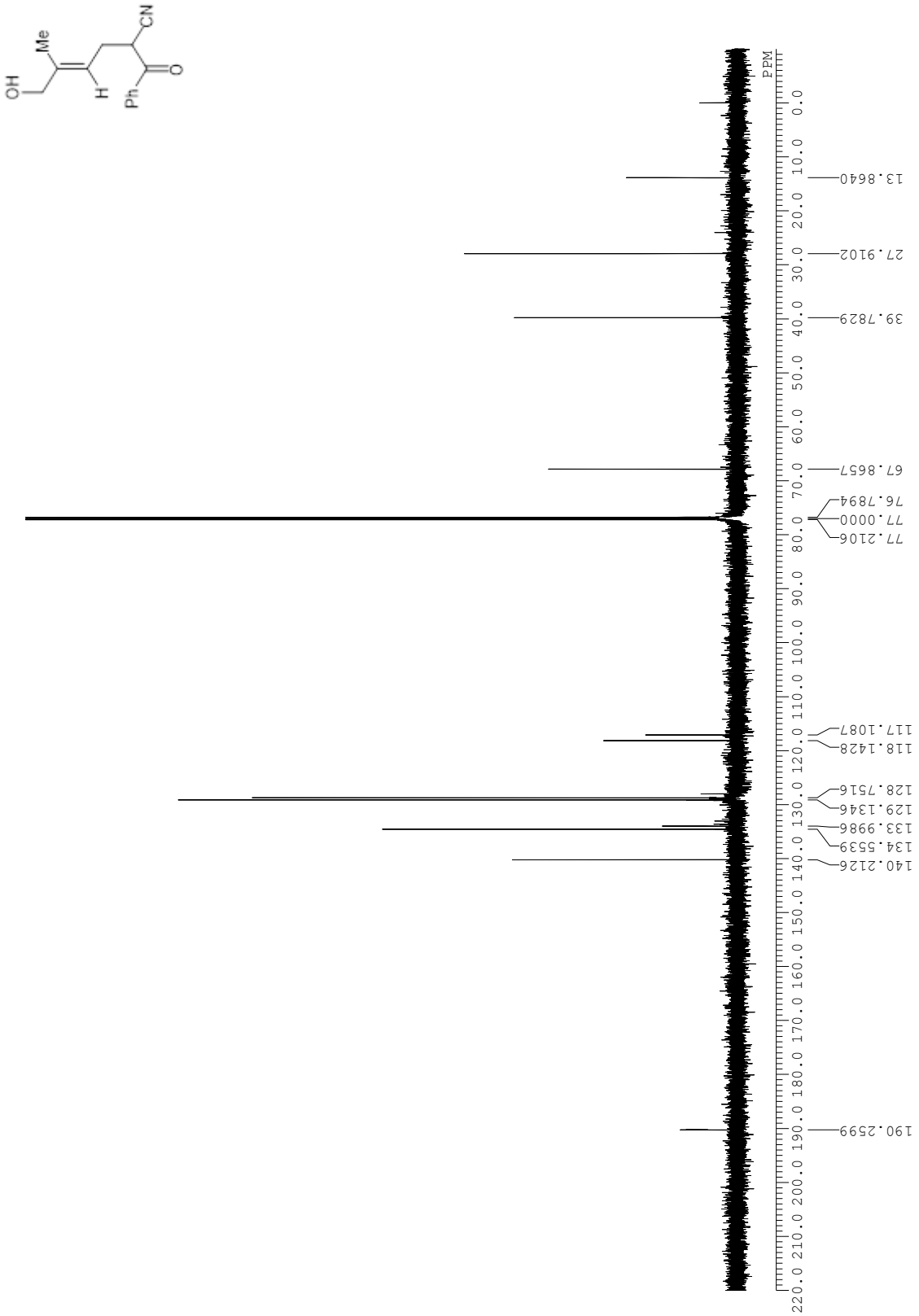
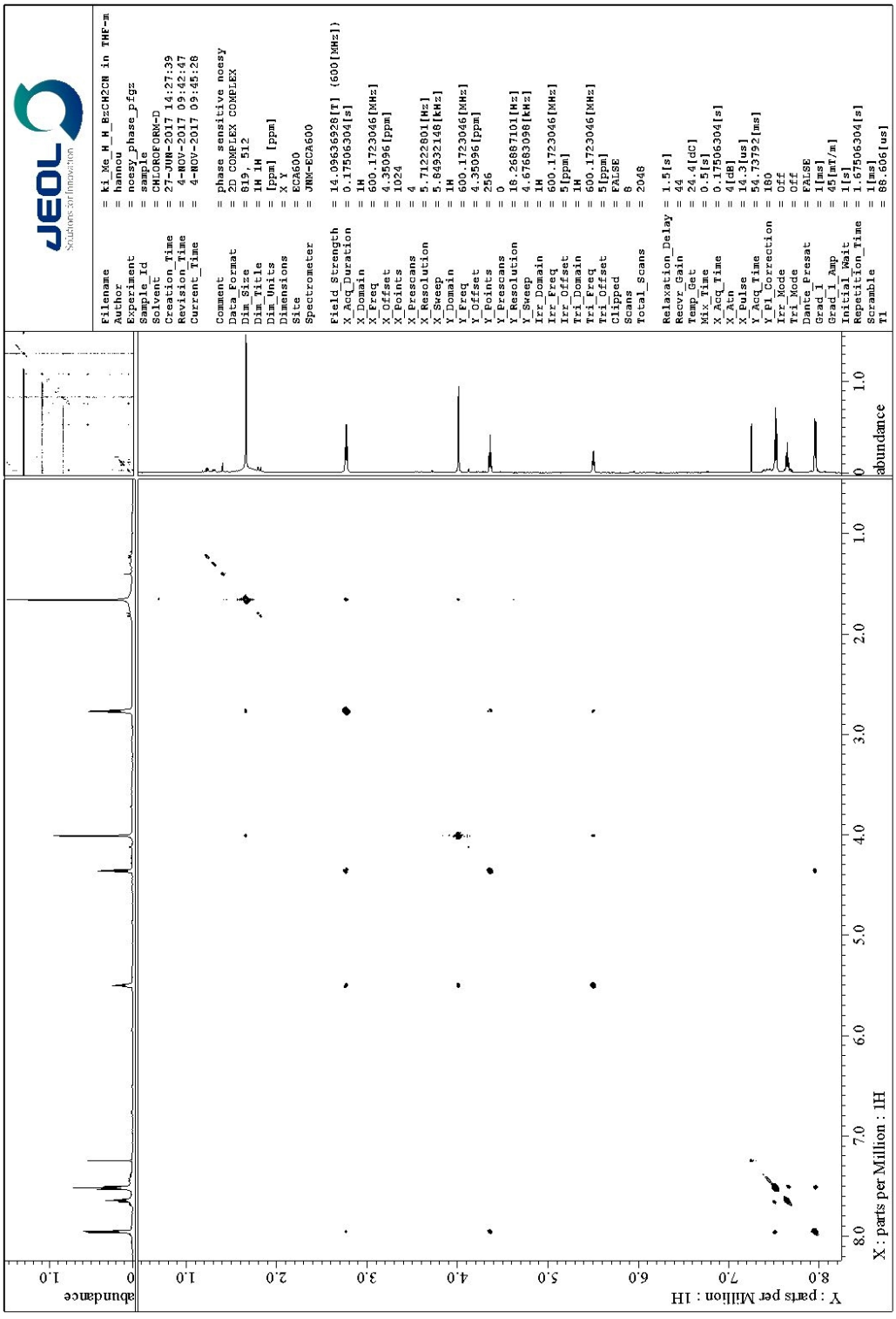


NOESY spectrum of (*E*)-**9aA**



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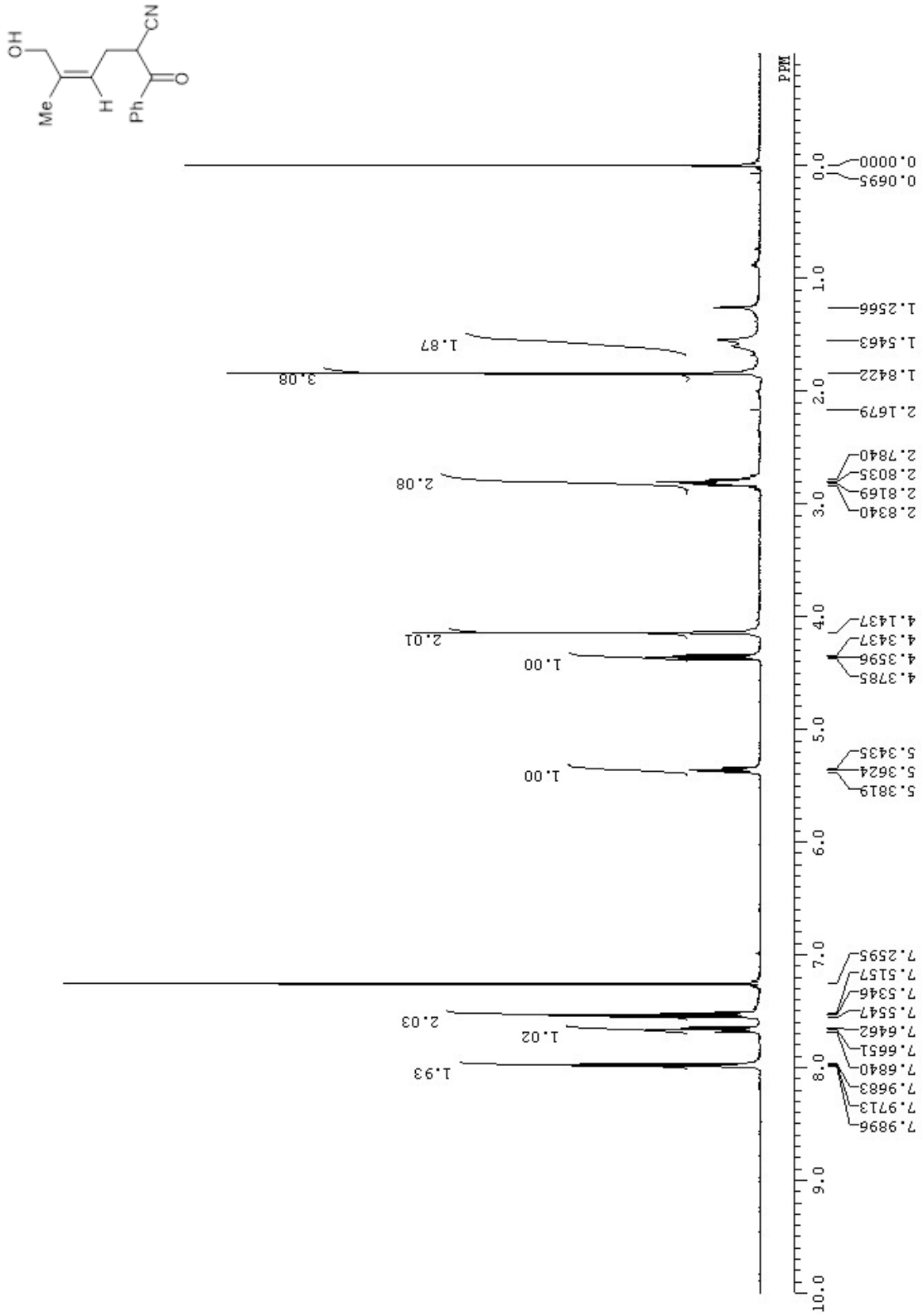
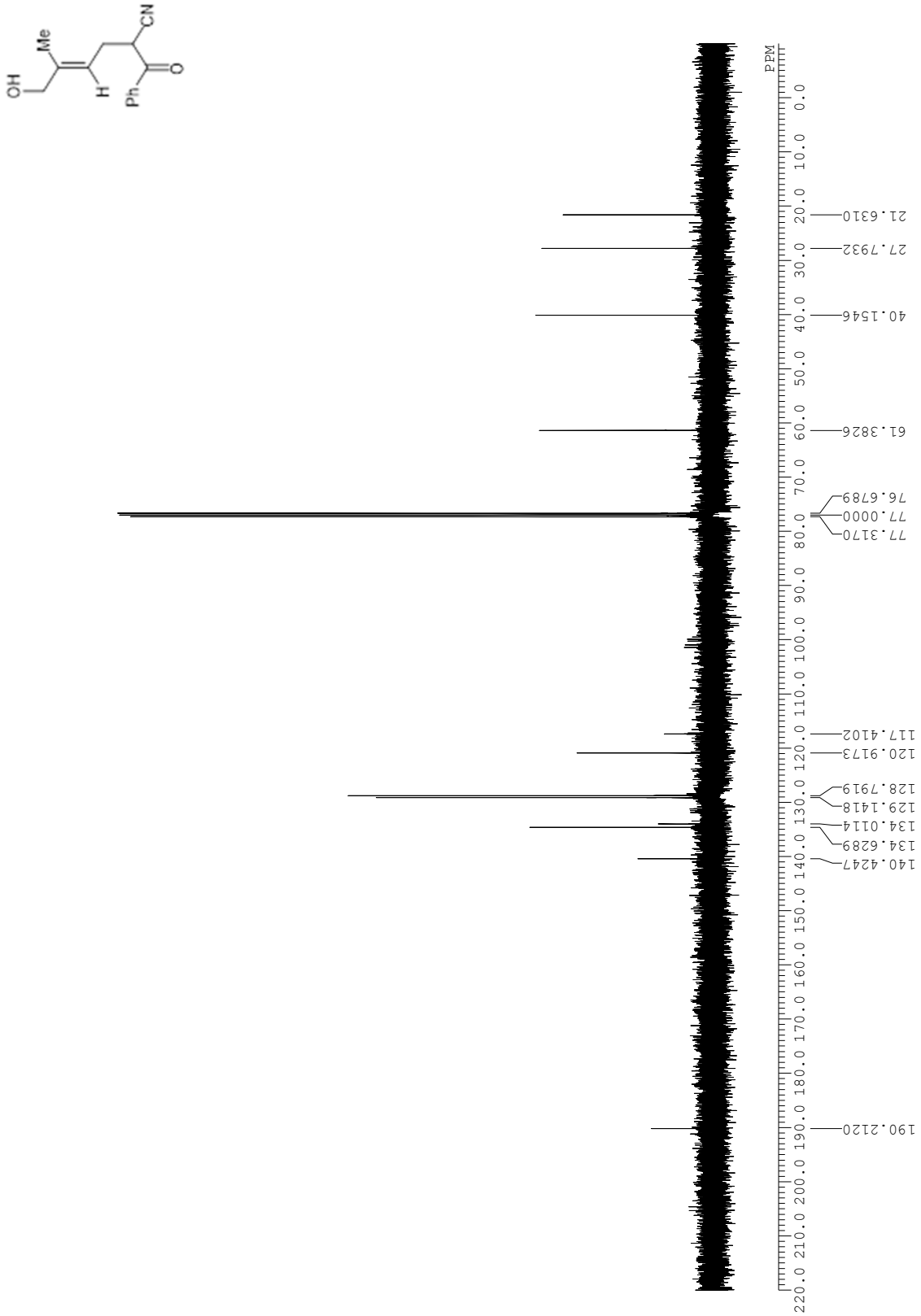
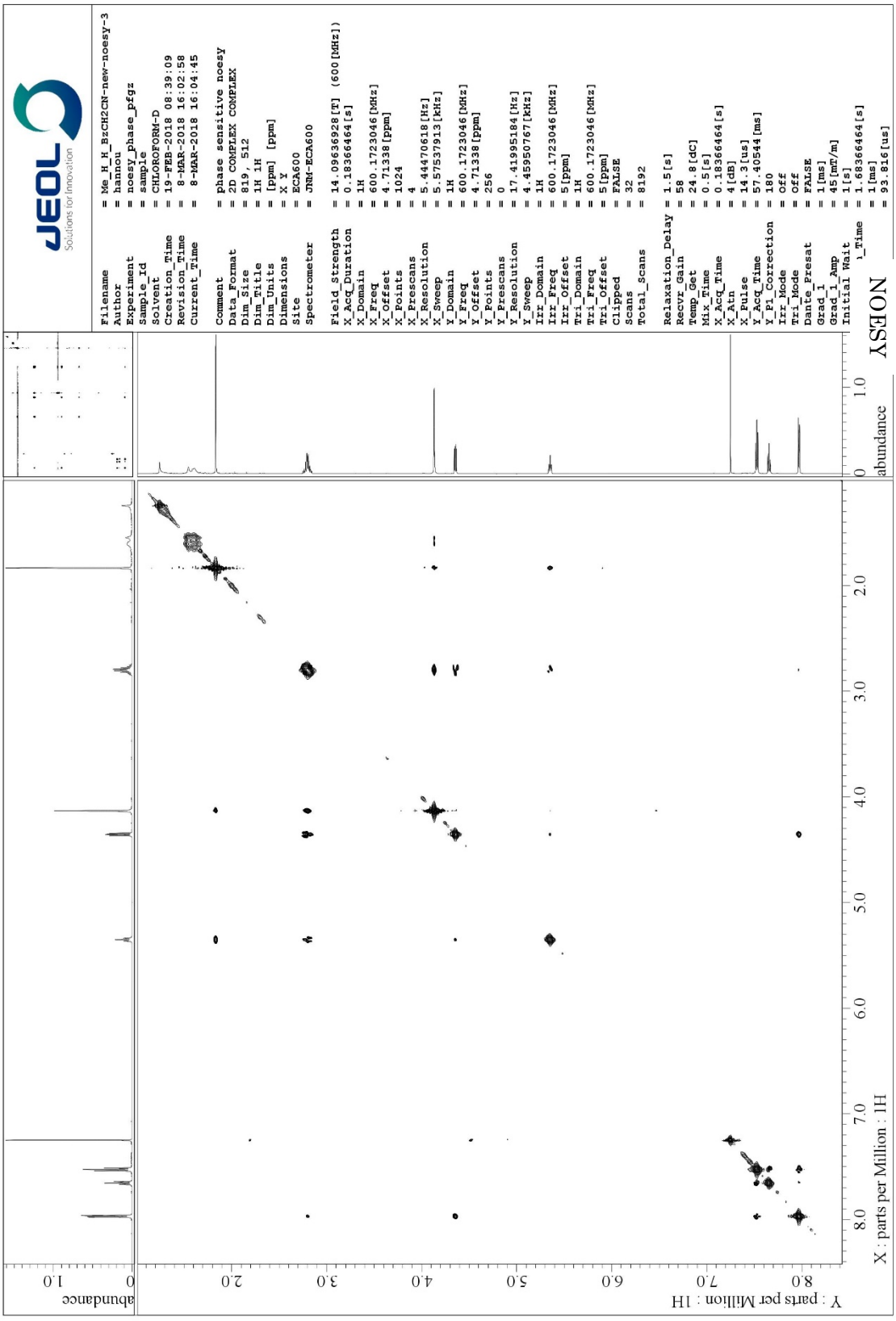


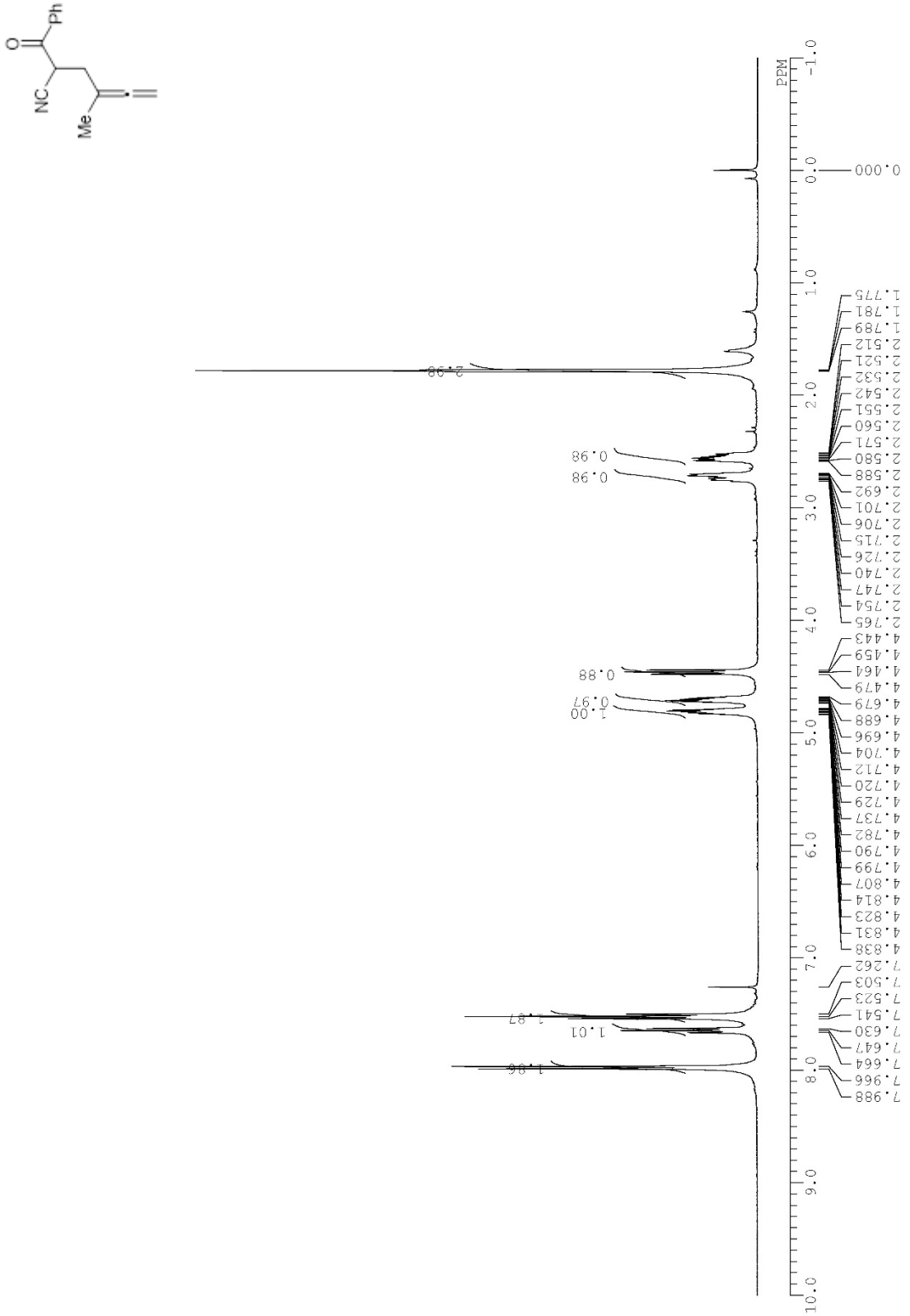
^{13}C NMR spectrum of **(*Z*)-9aA**



NOESY spectrum of (*Z*)-**9aA**



^{1}H NMR spectrum of **5aA'**



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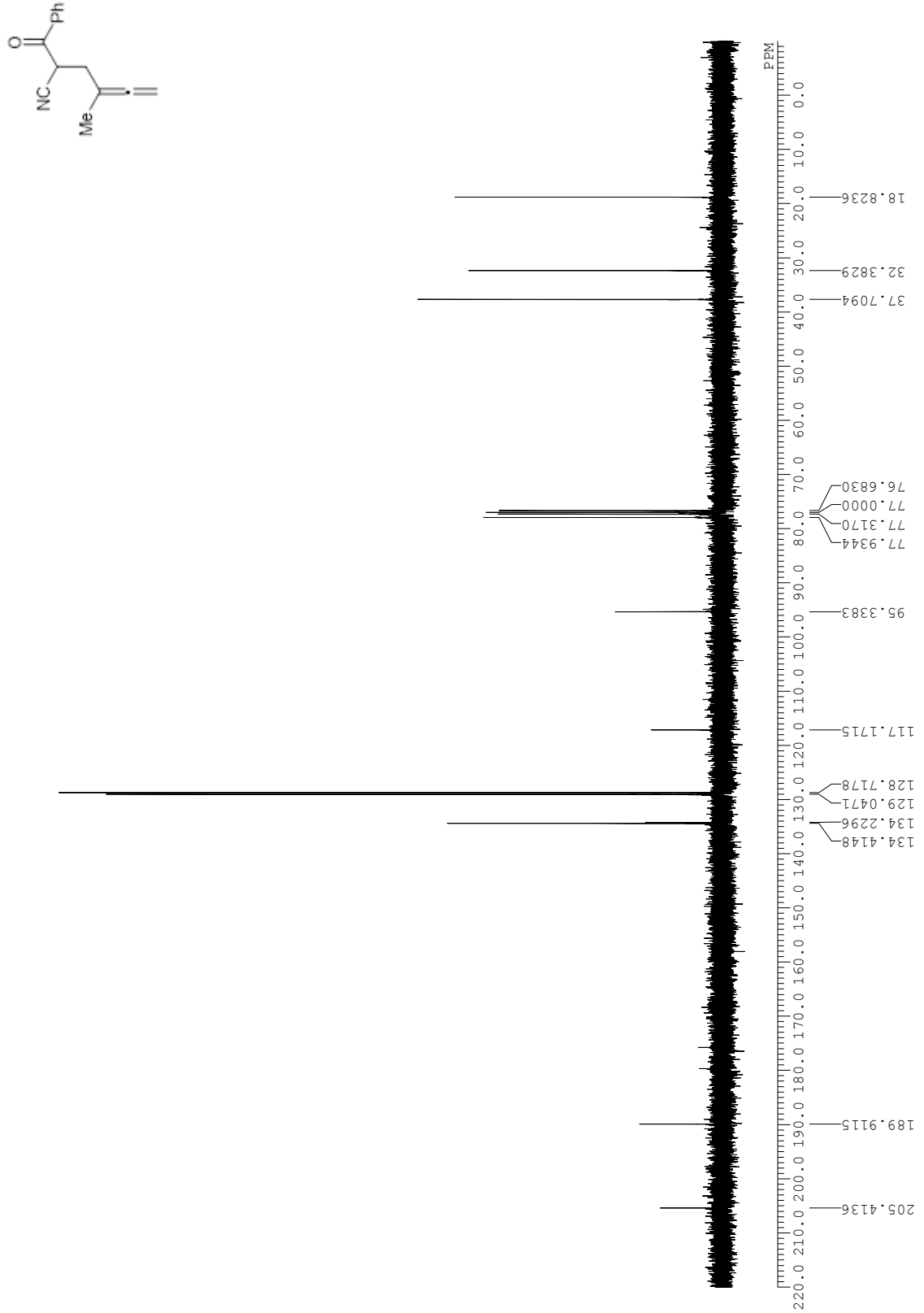
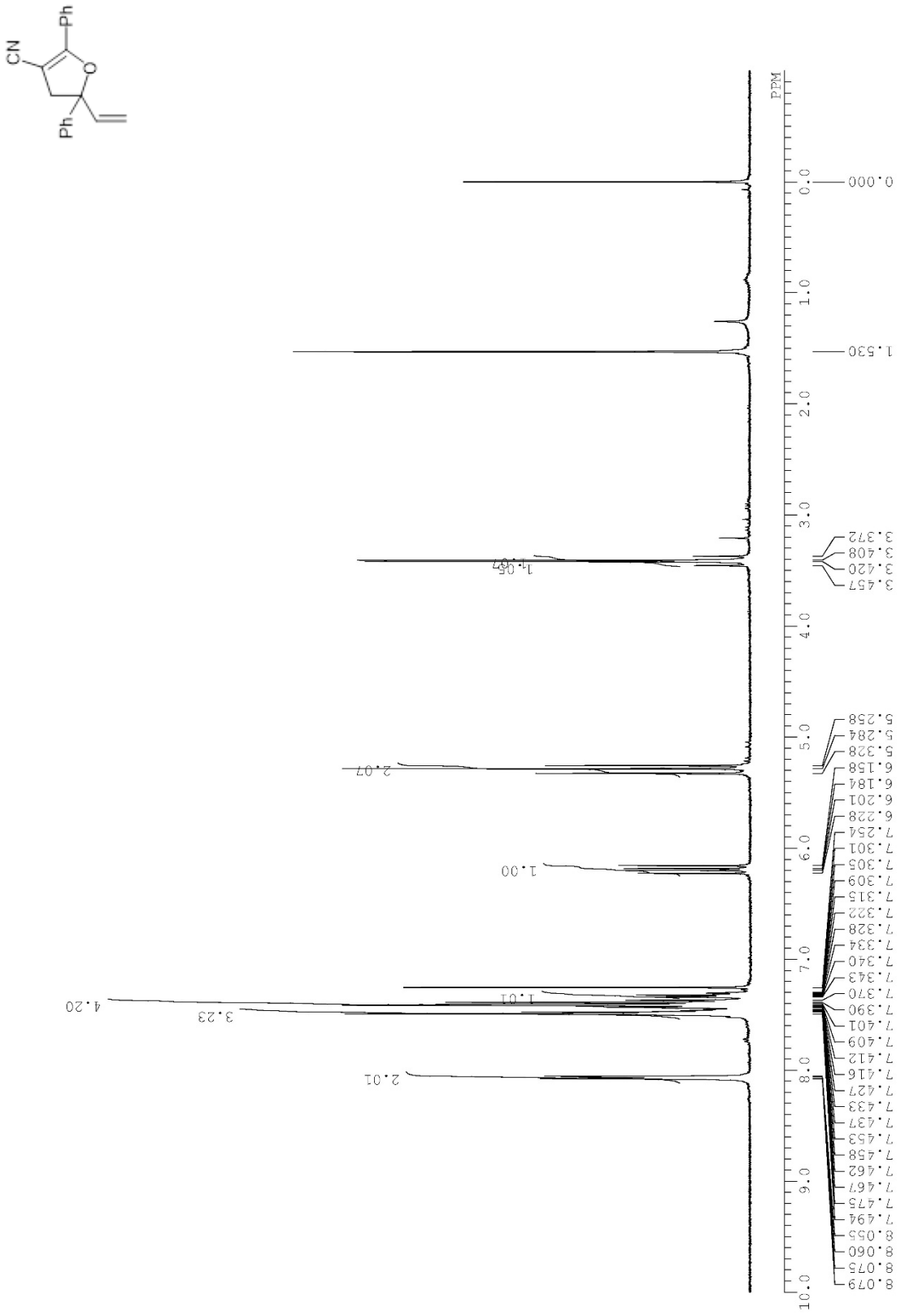
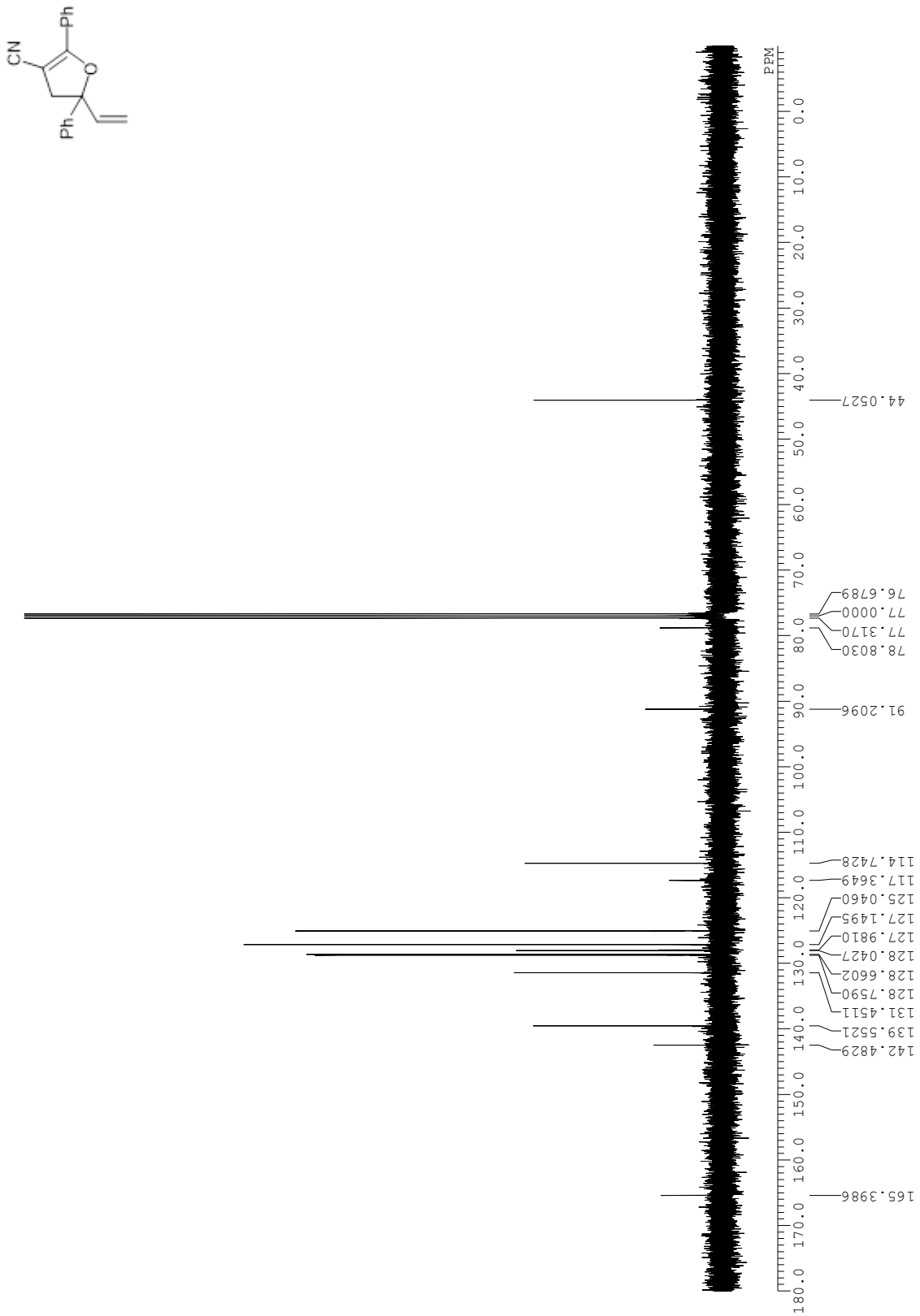


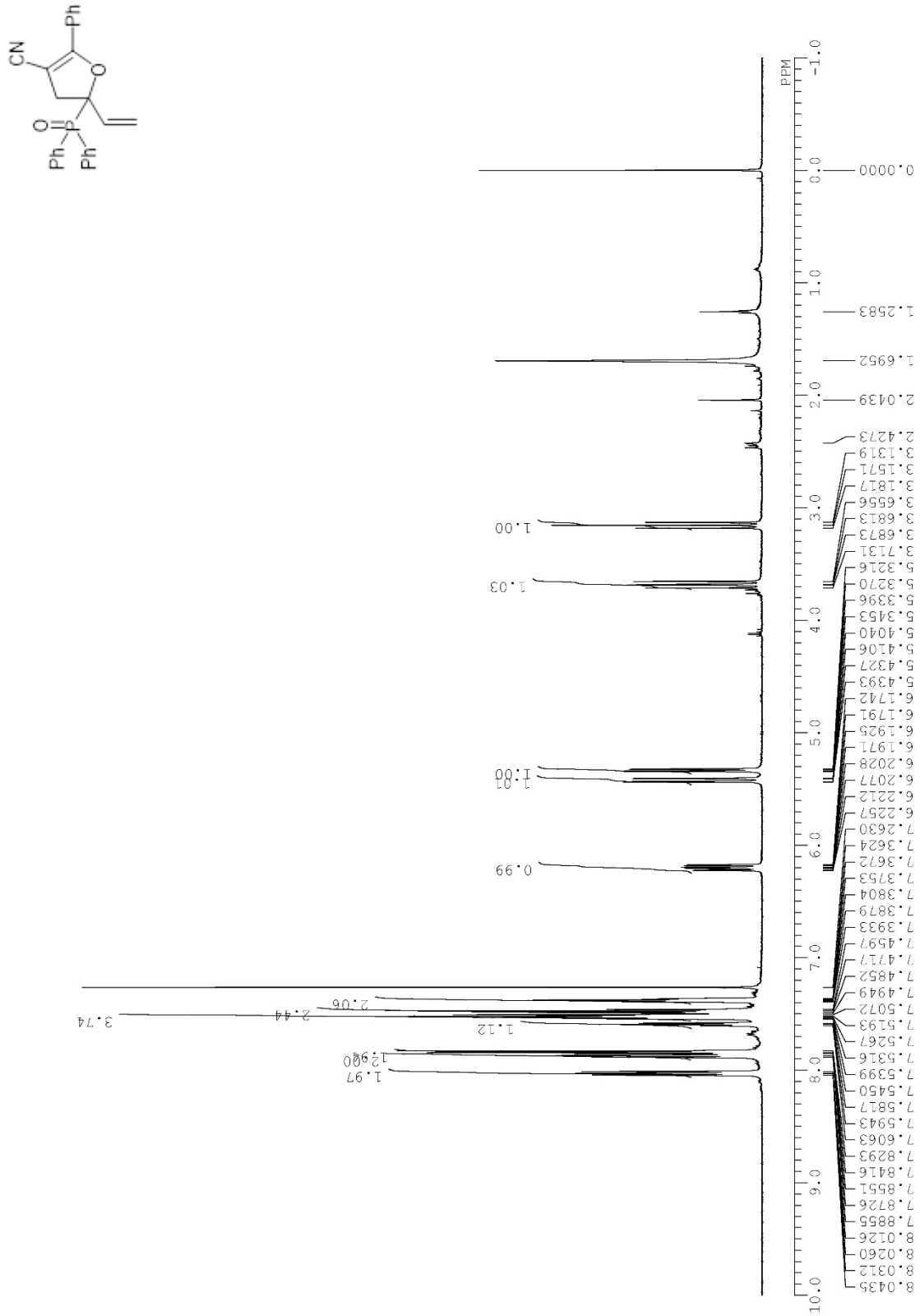
^{1}H NMR spectrum of **6bA**



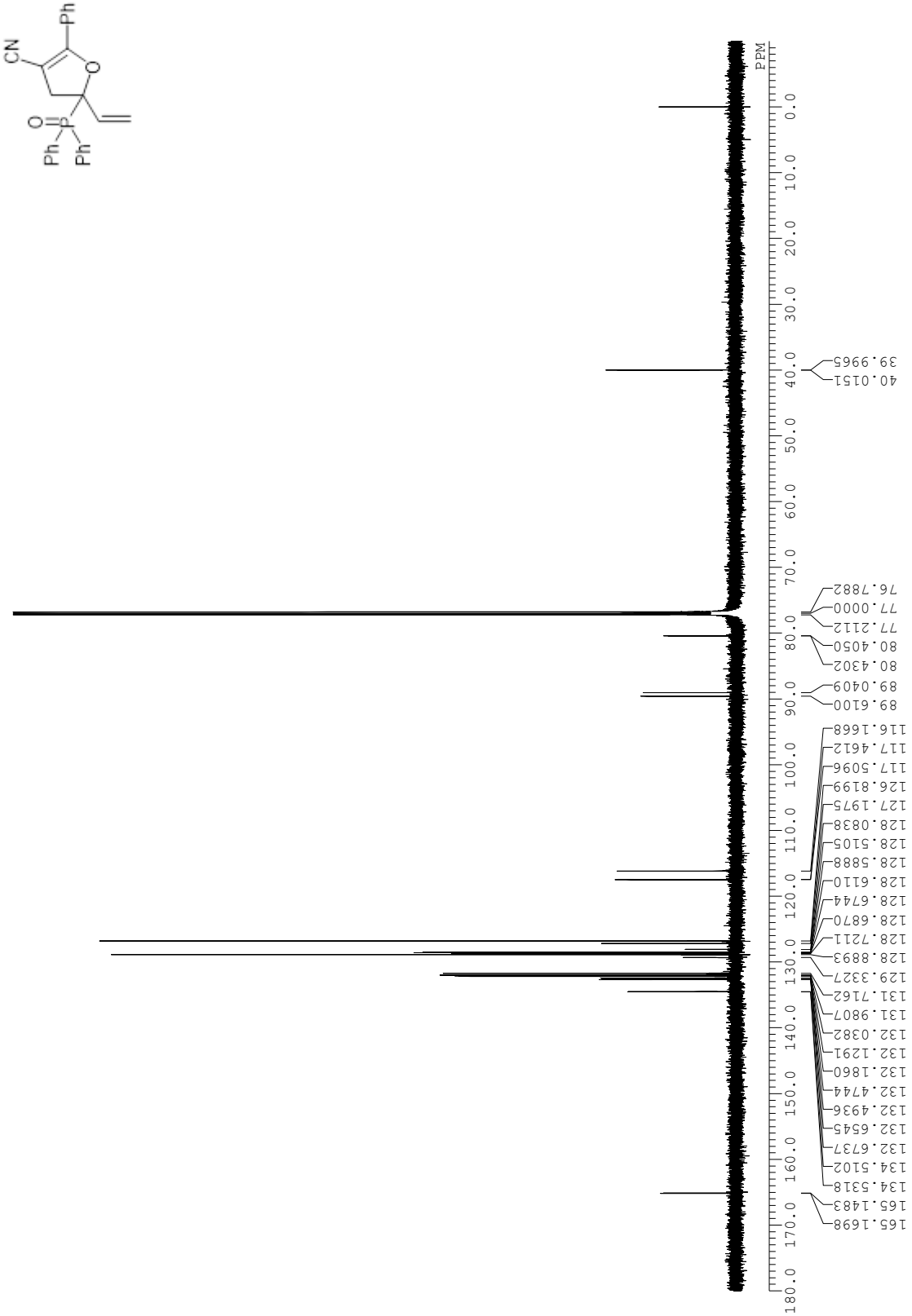
^{13}C NMR spectrum of **6bA**



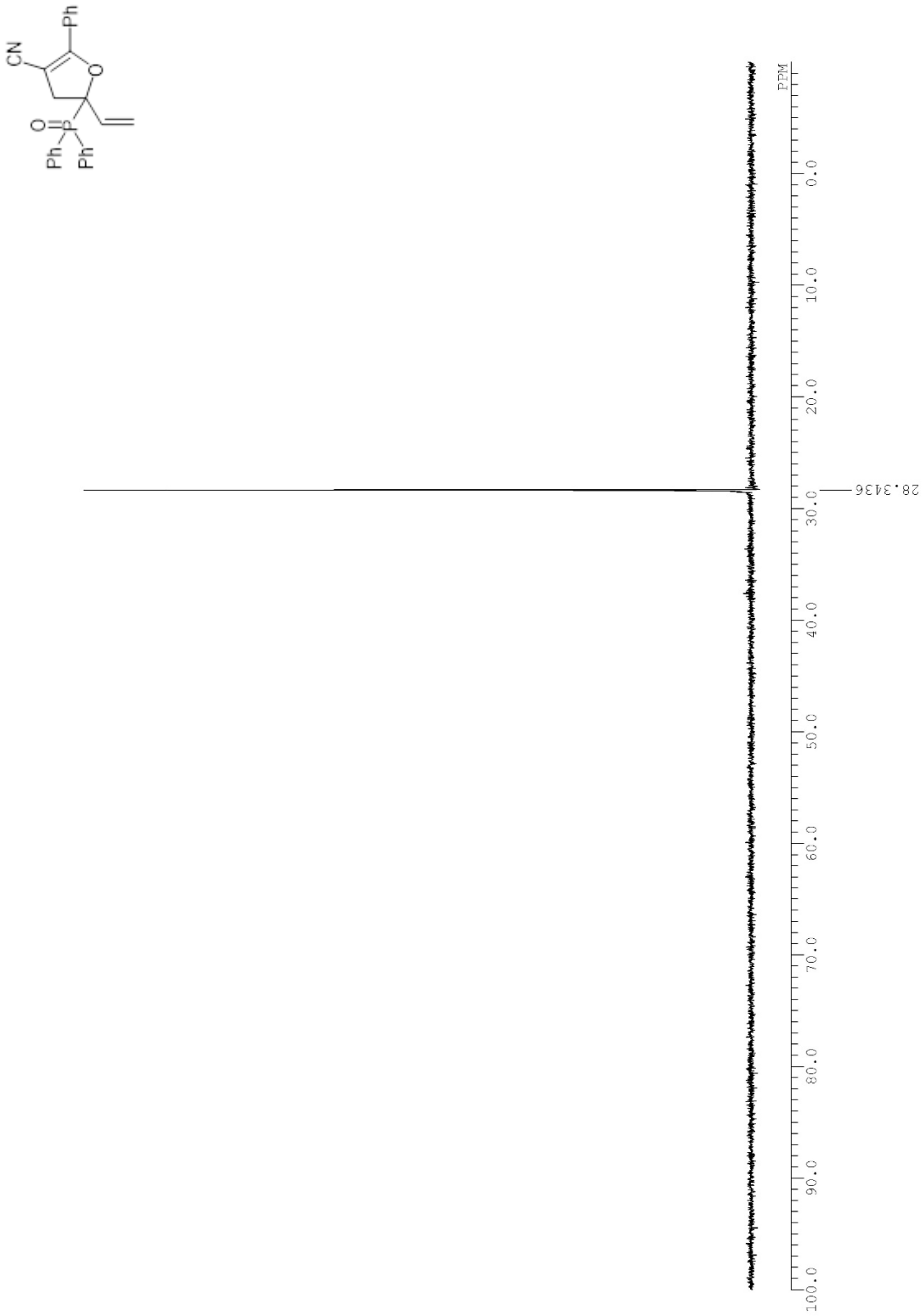
^{1}H NMR spectrum of **6cA**



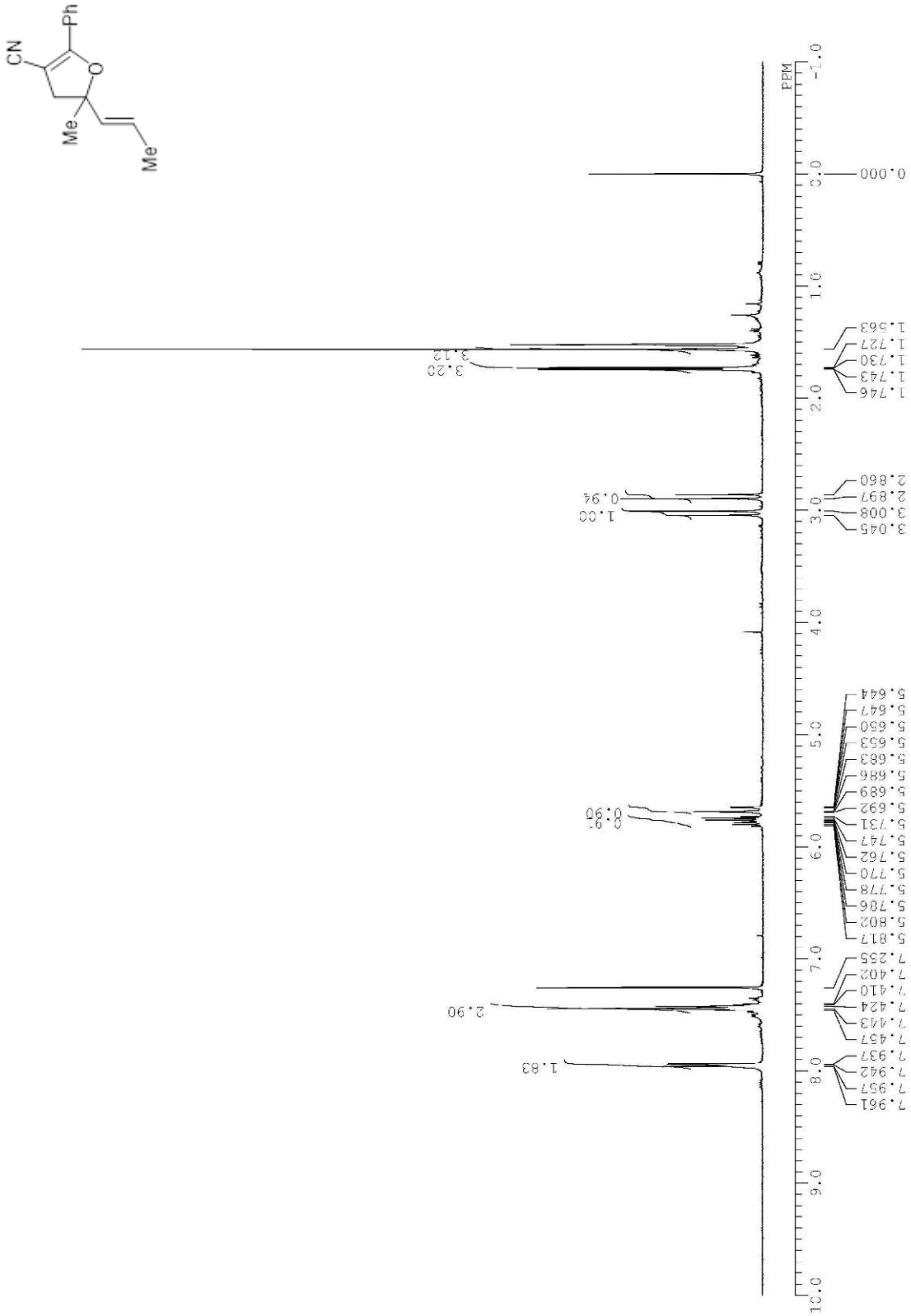
^{13}C NMR spectrum of **6cA**



^{31}P NMR spectrum of **6cA**



^{1}H NMR spectrum of **6dA**



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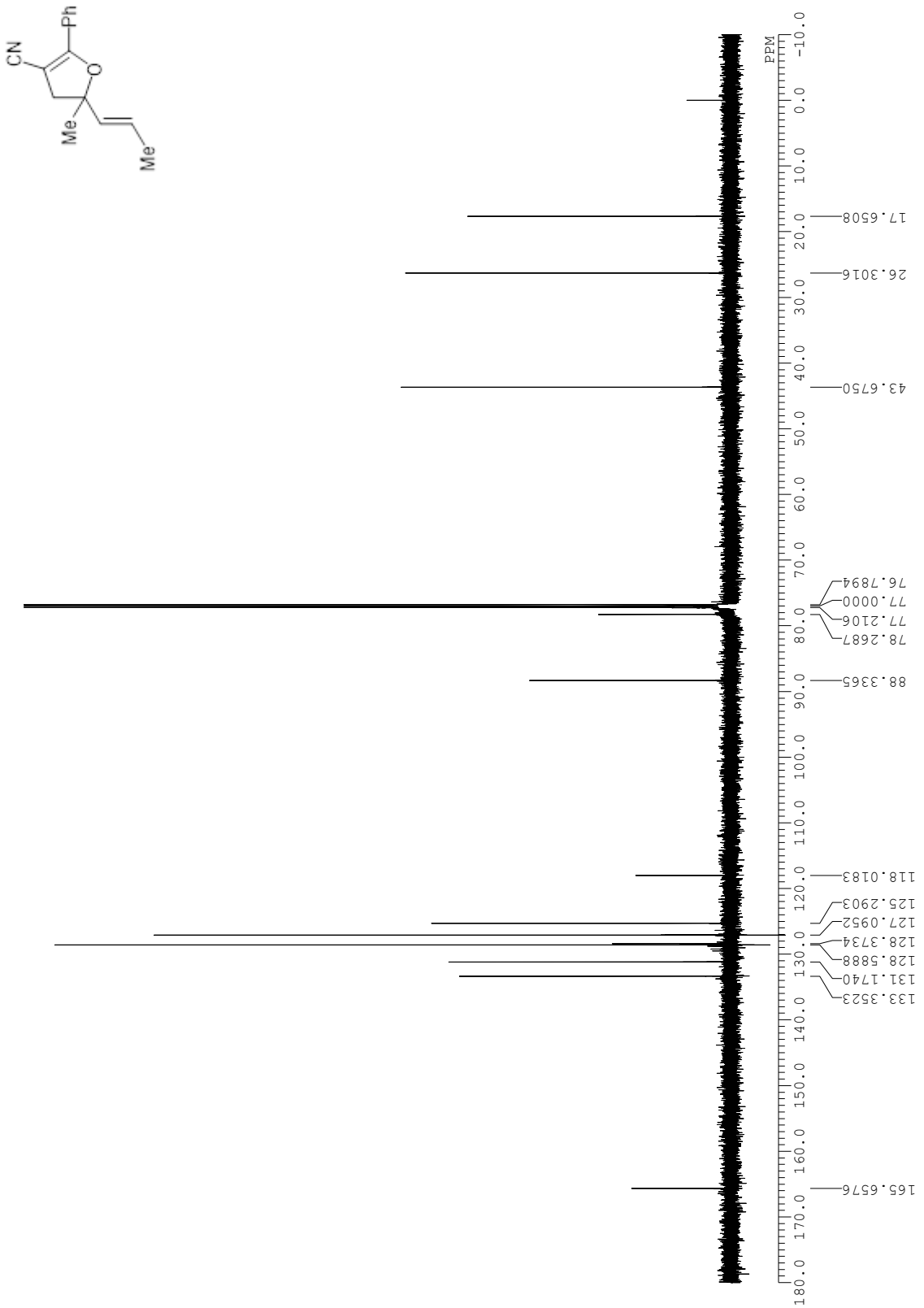

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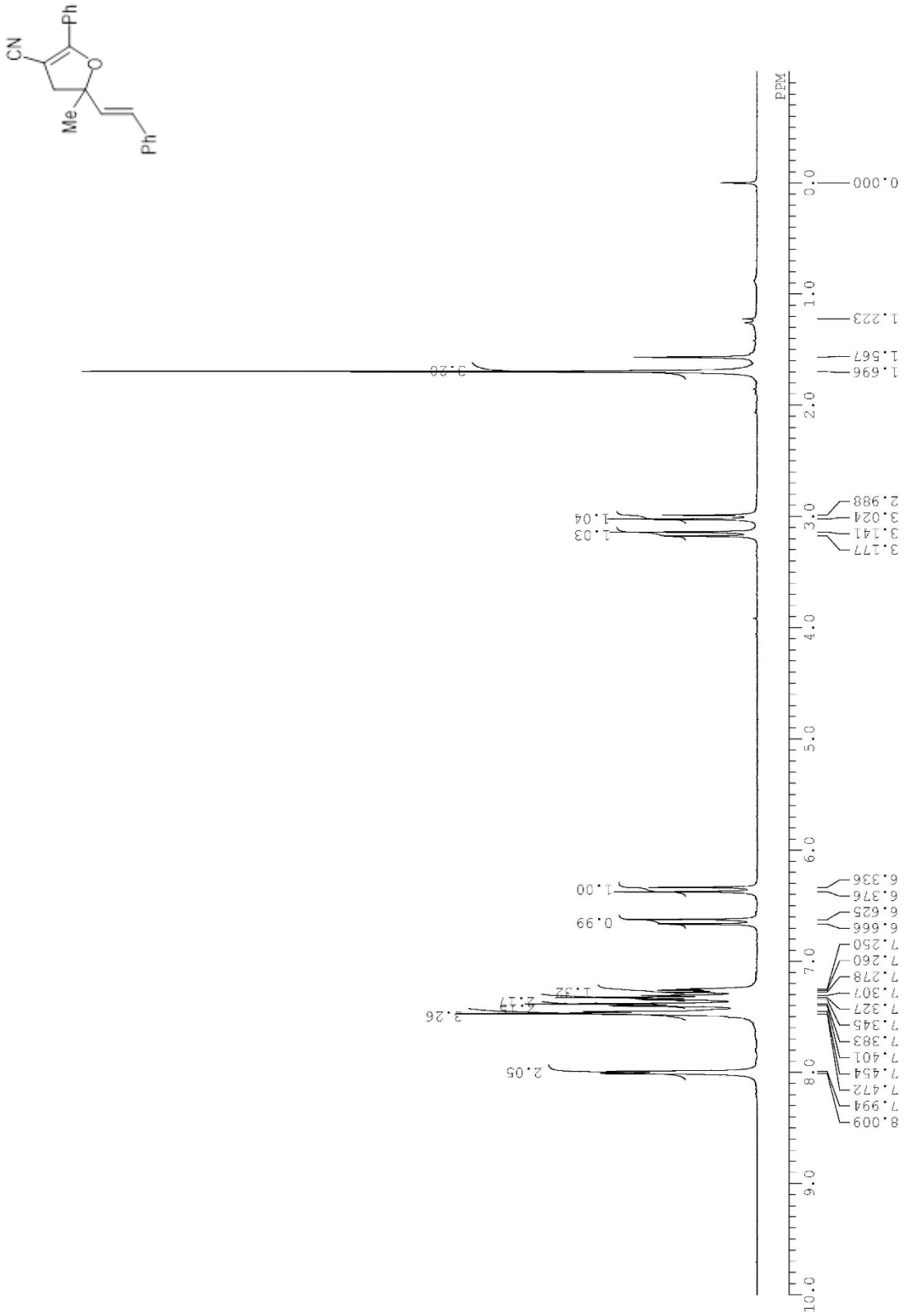

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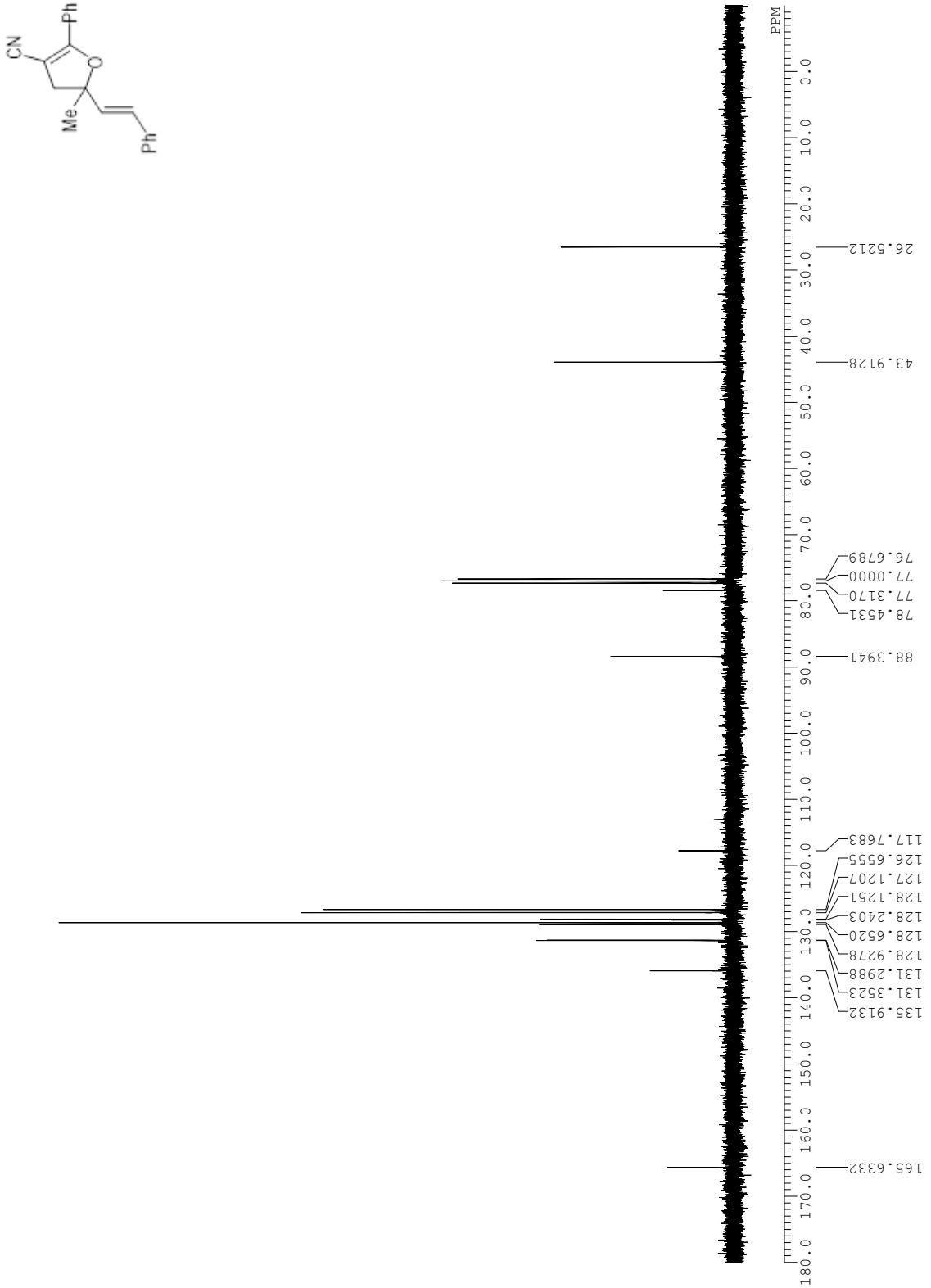

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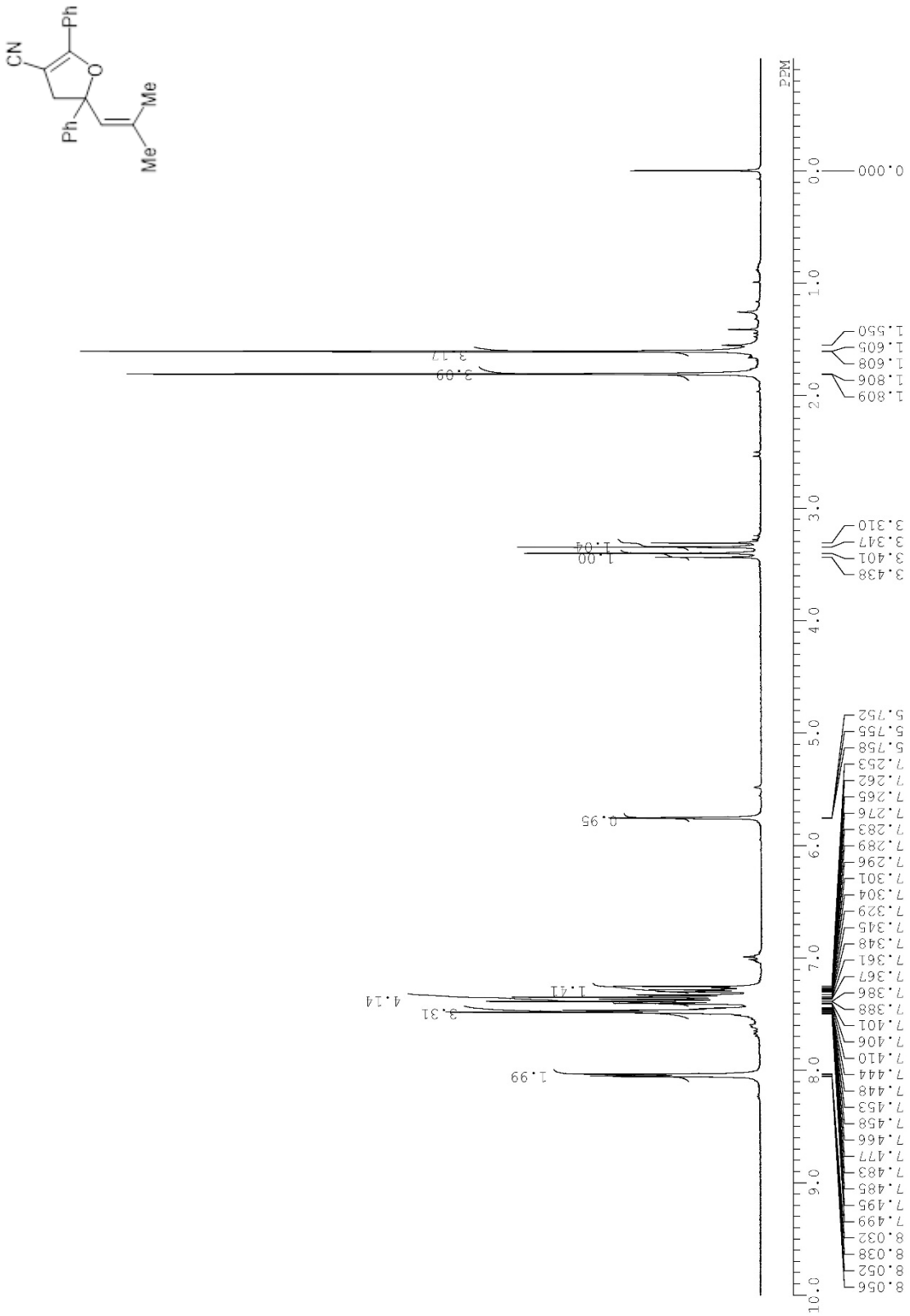

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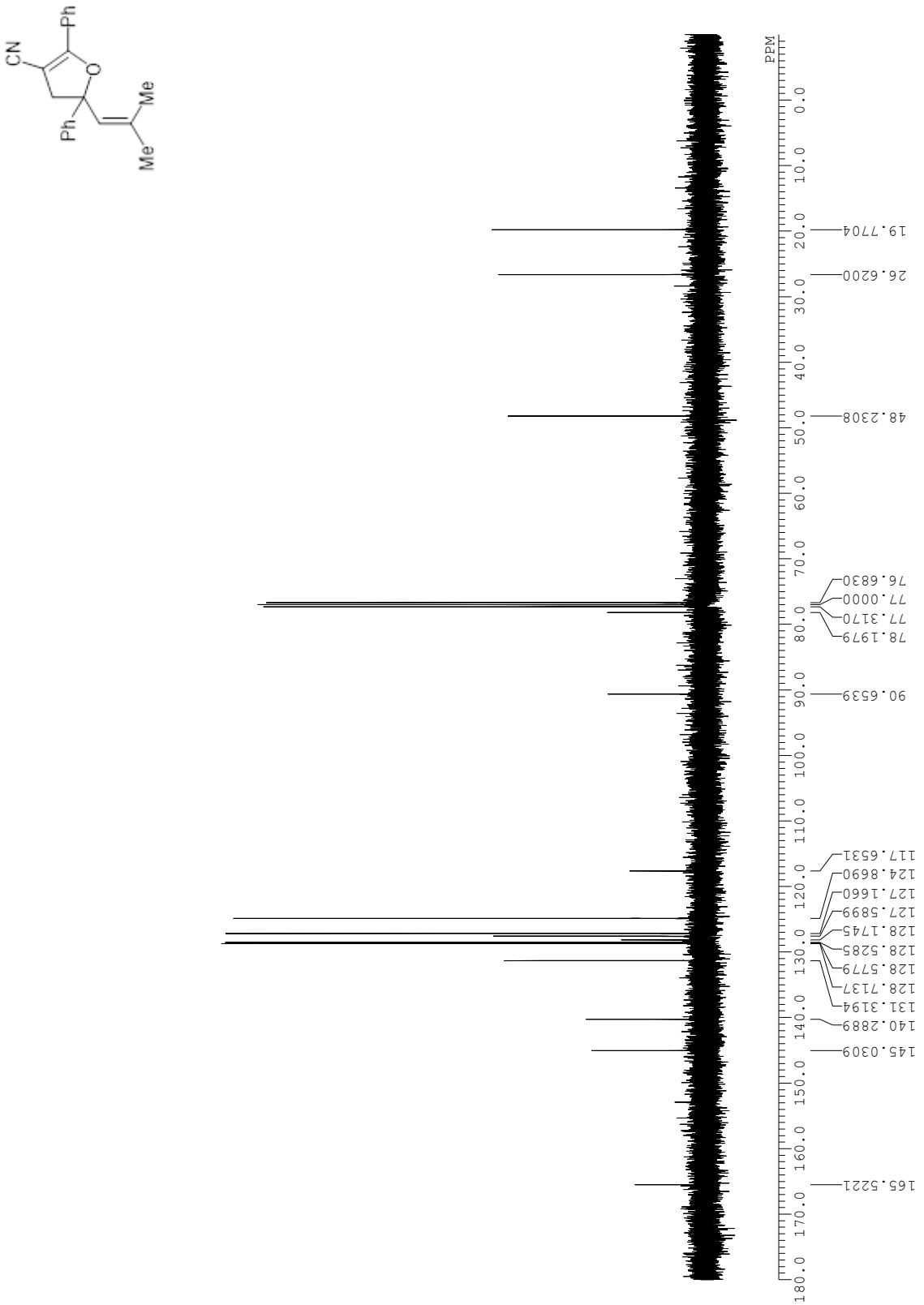
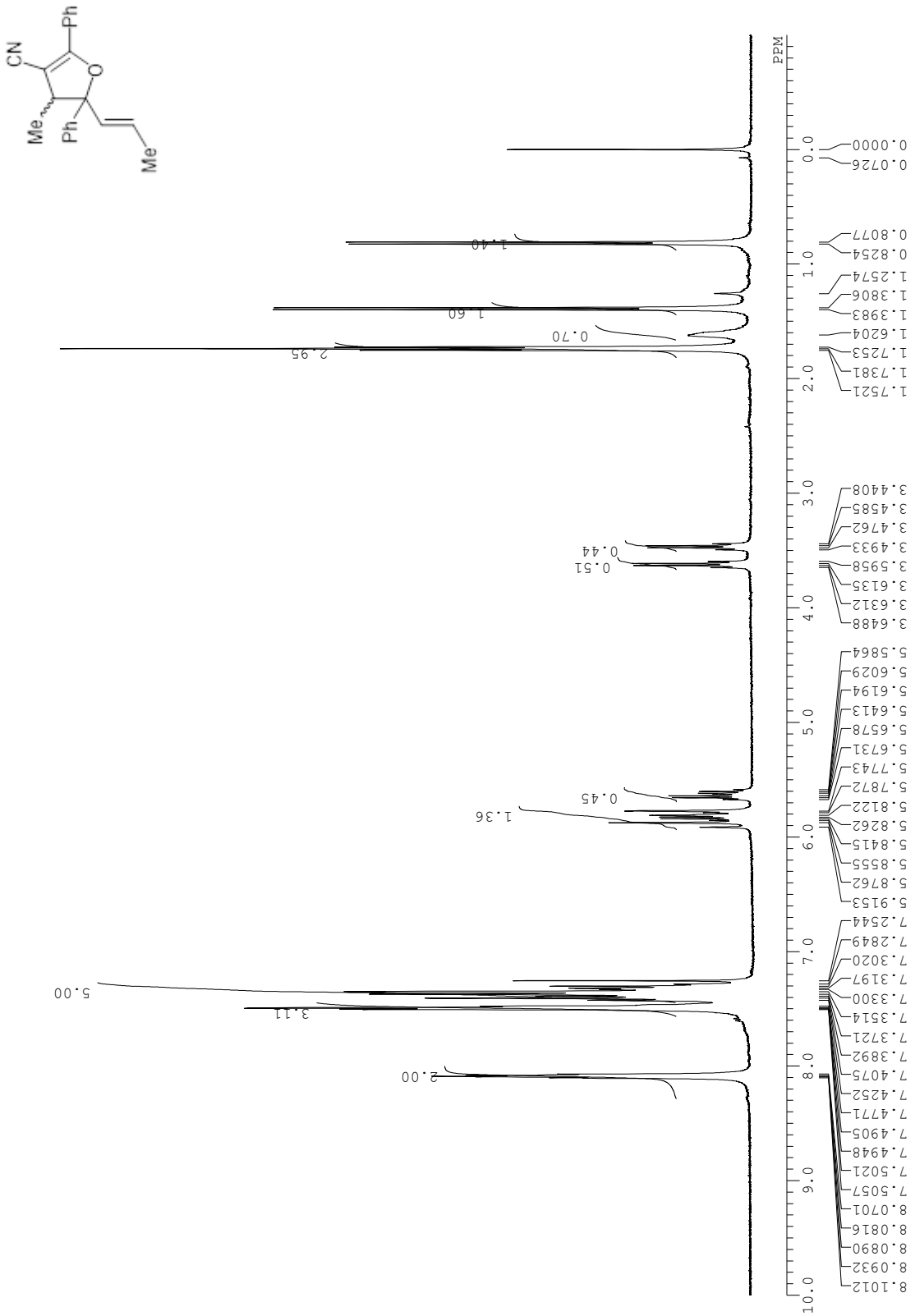
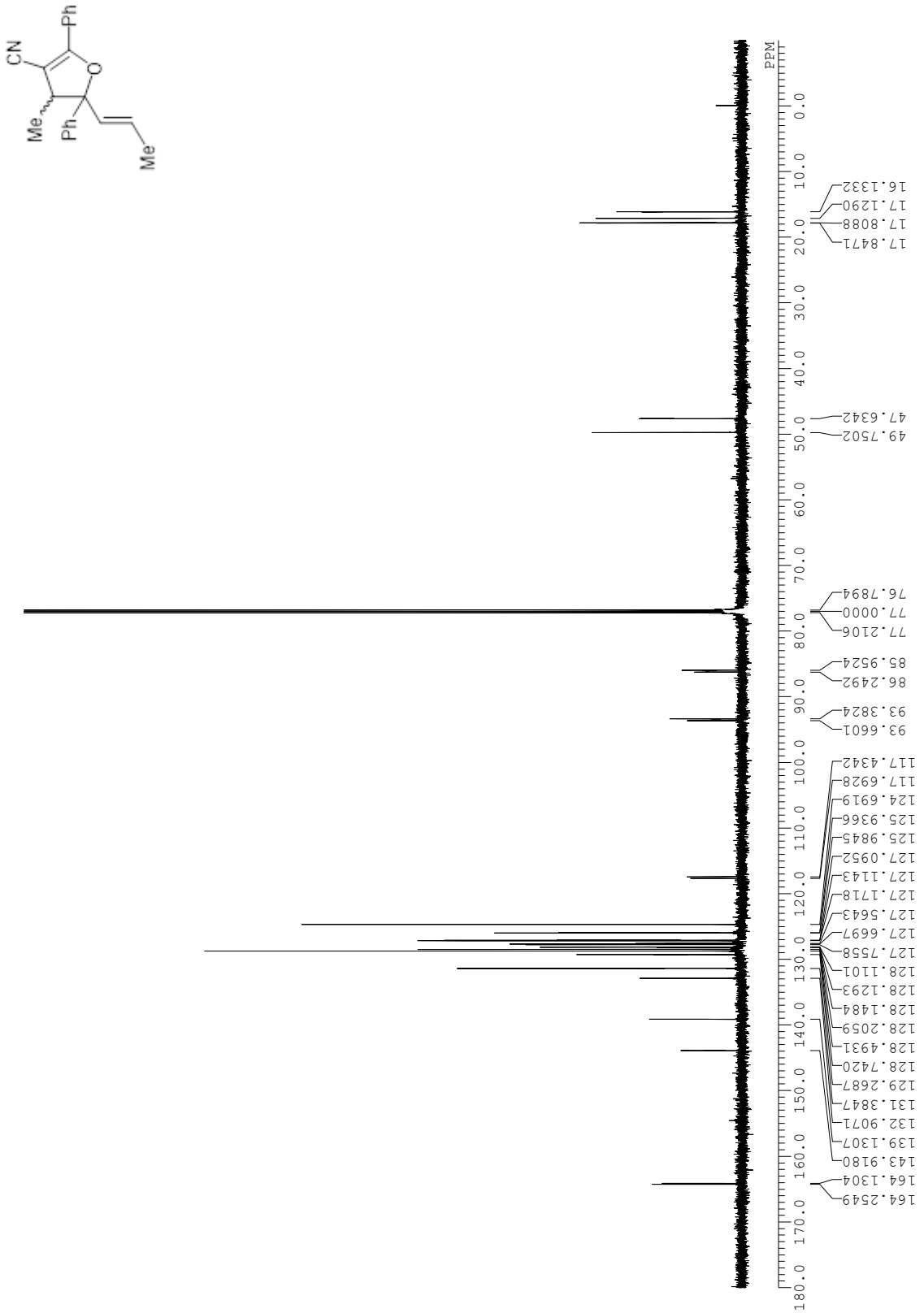


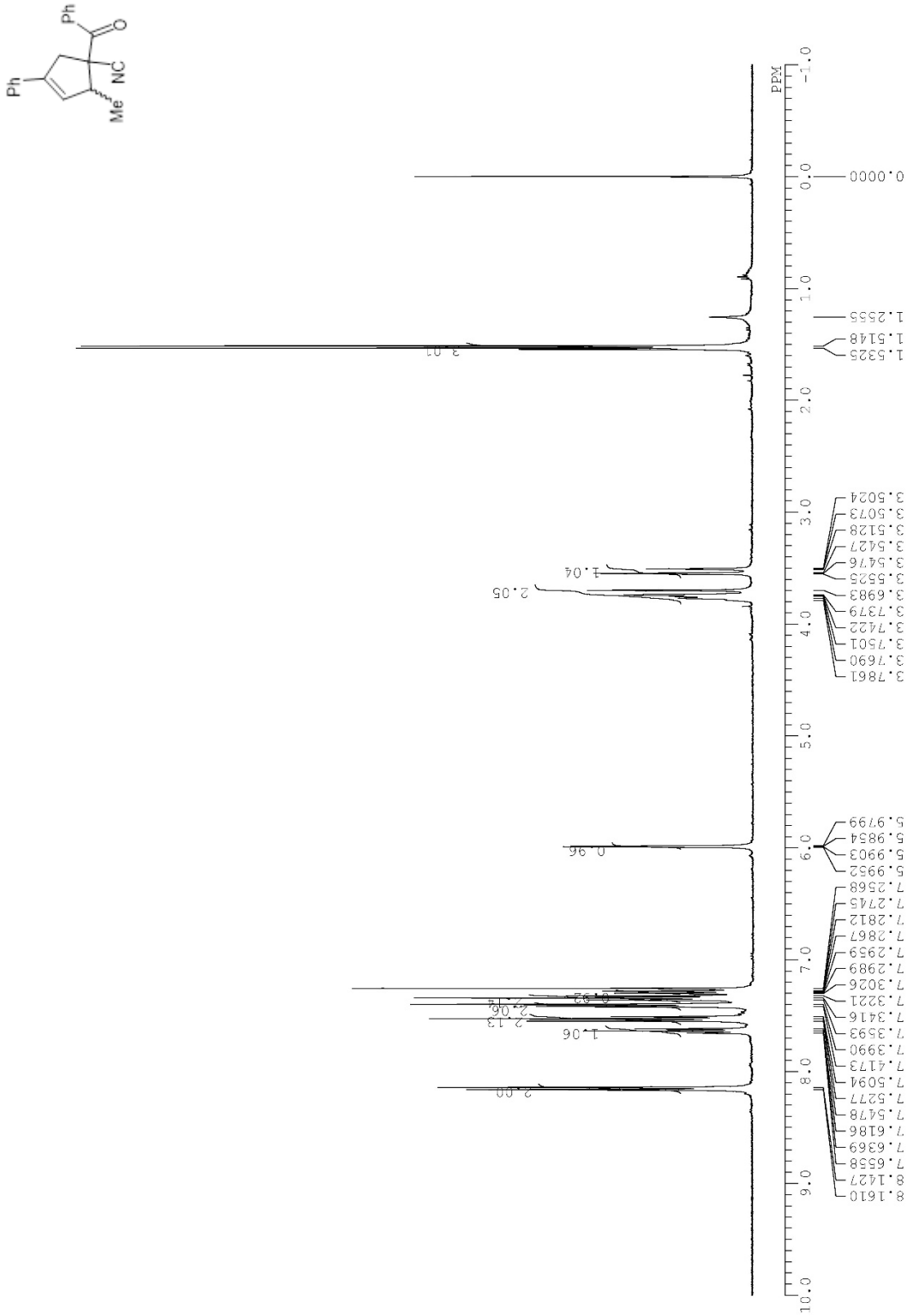
^{1}H NMR spectrum of **6gA**



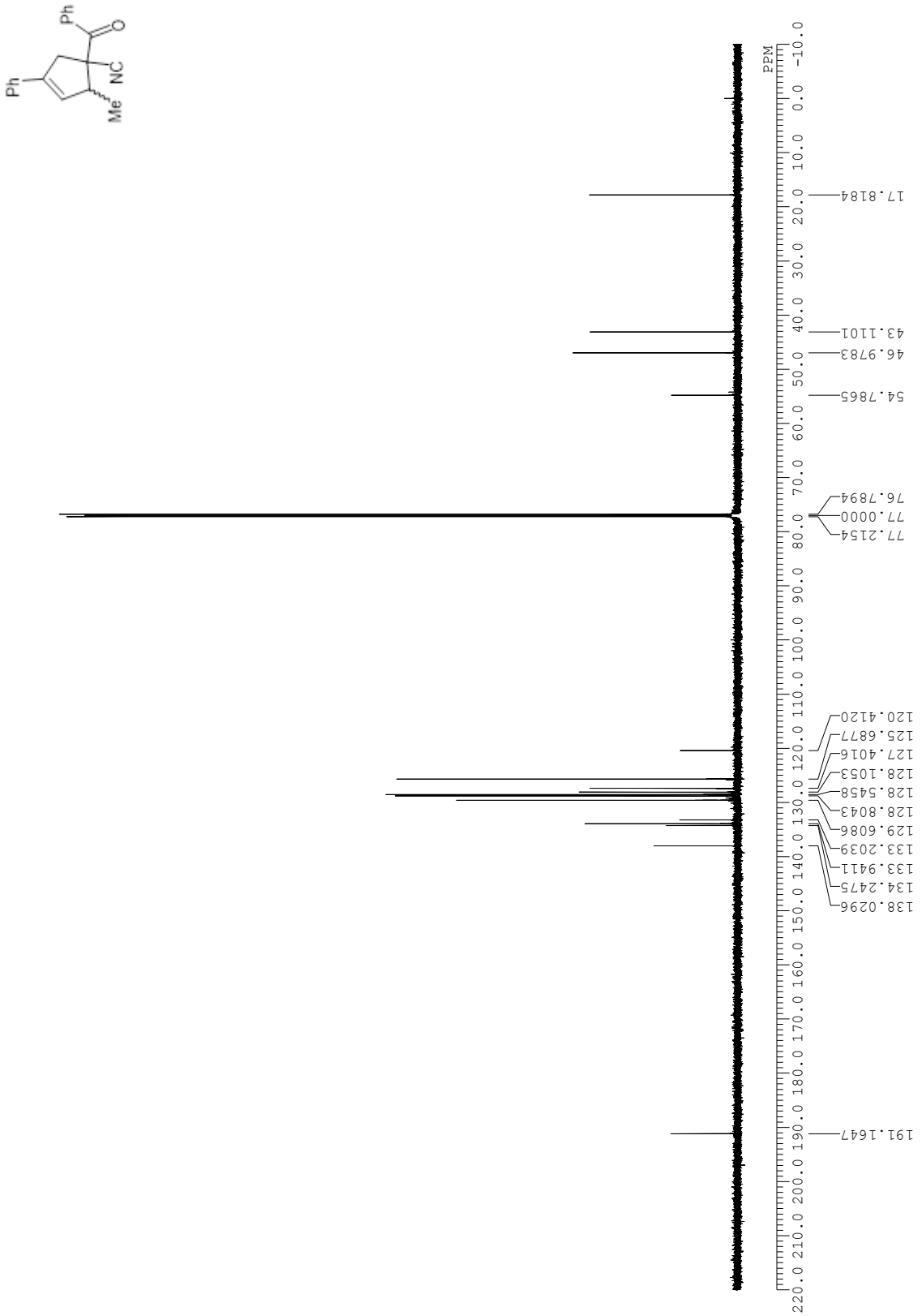
^{13}C NMR spectrum of **6gA**



^{1}H NMR spectrum of **12hA** (major diastereomer)



^{13}C NMR spectrum of **12hA** (major diastereomer)



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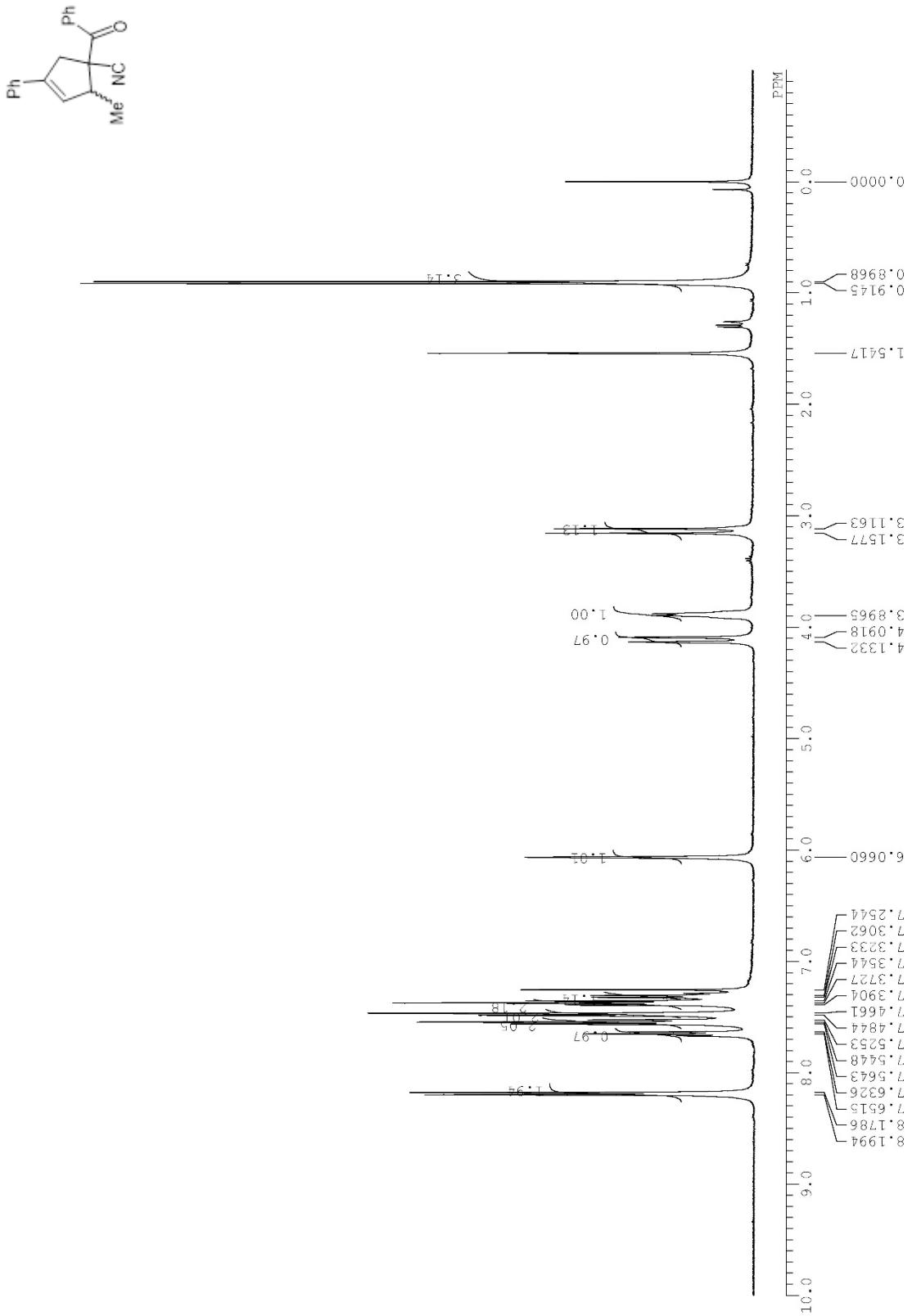
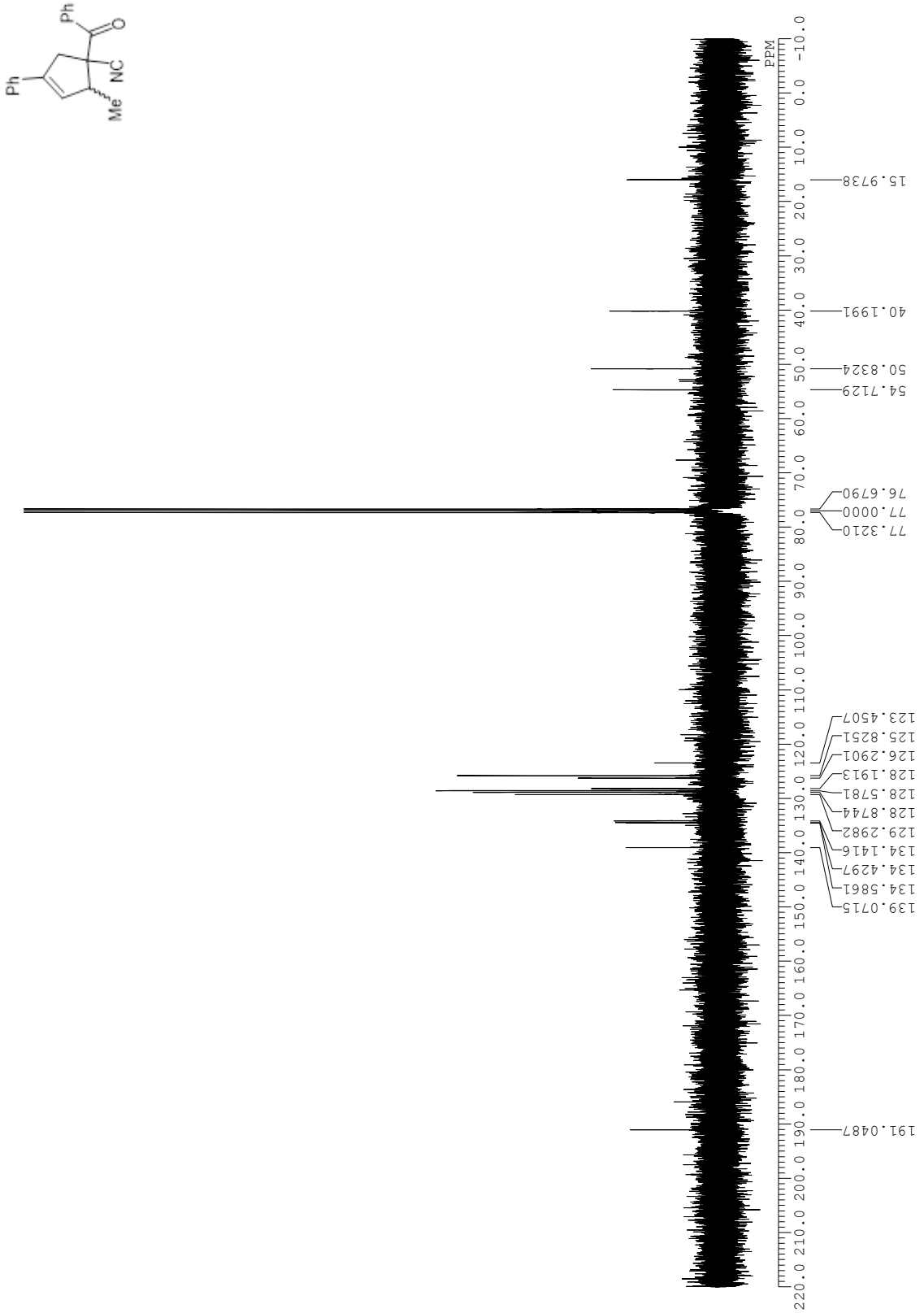
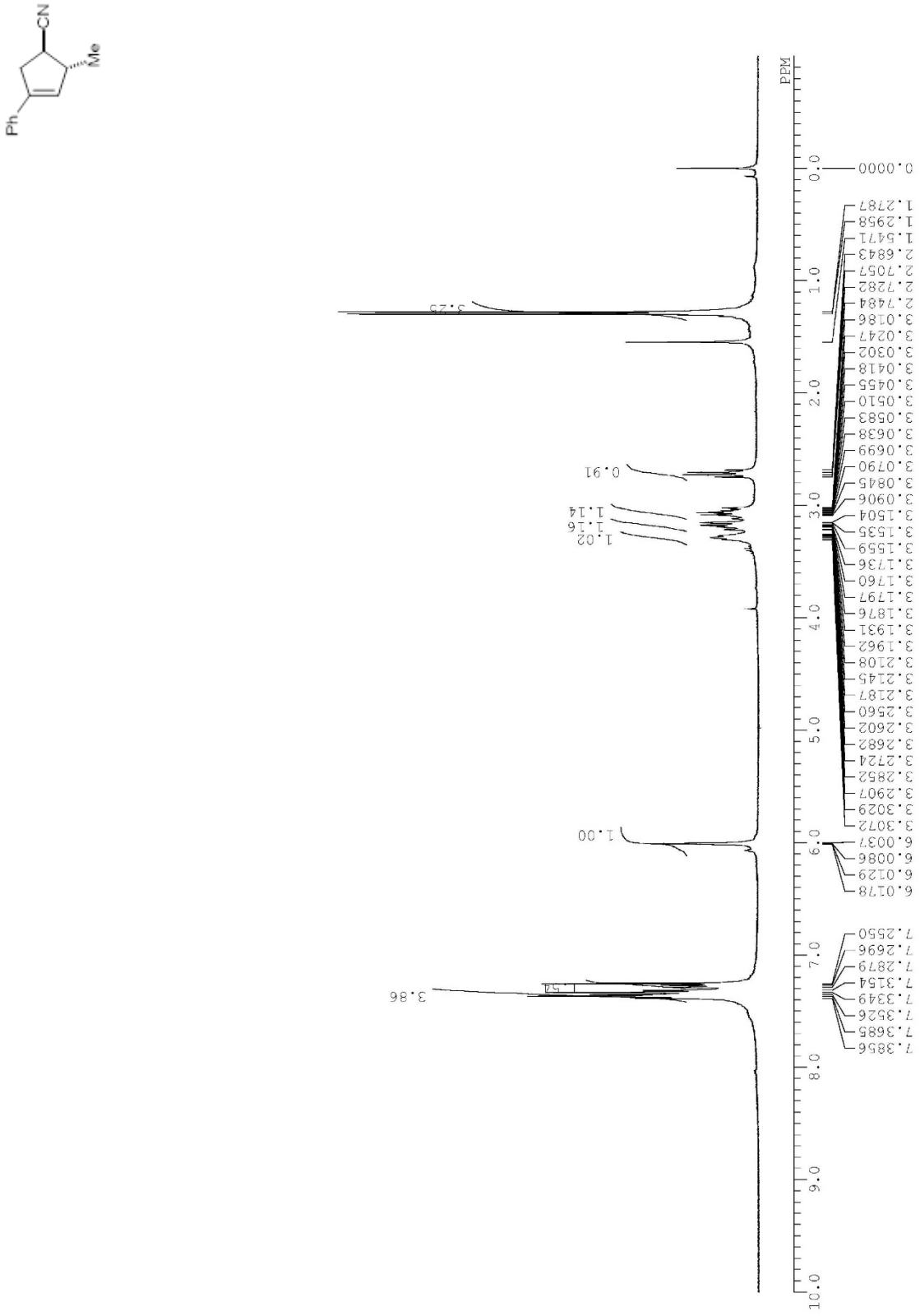


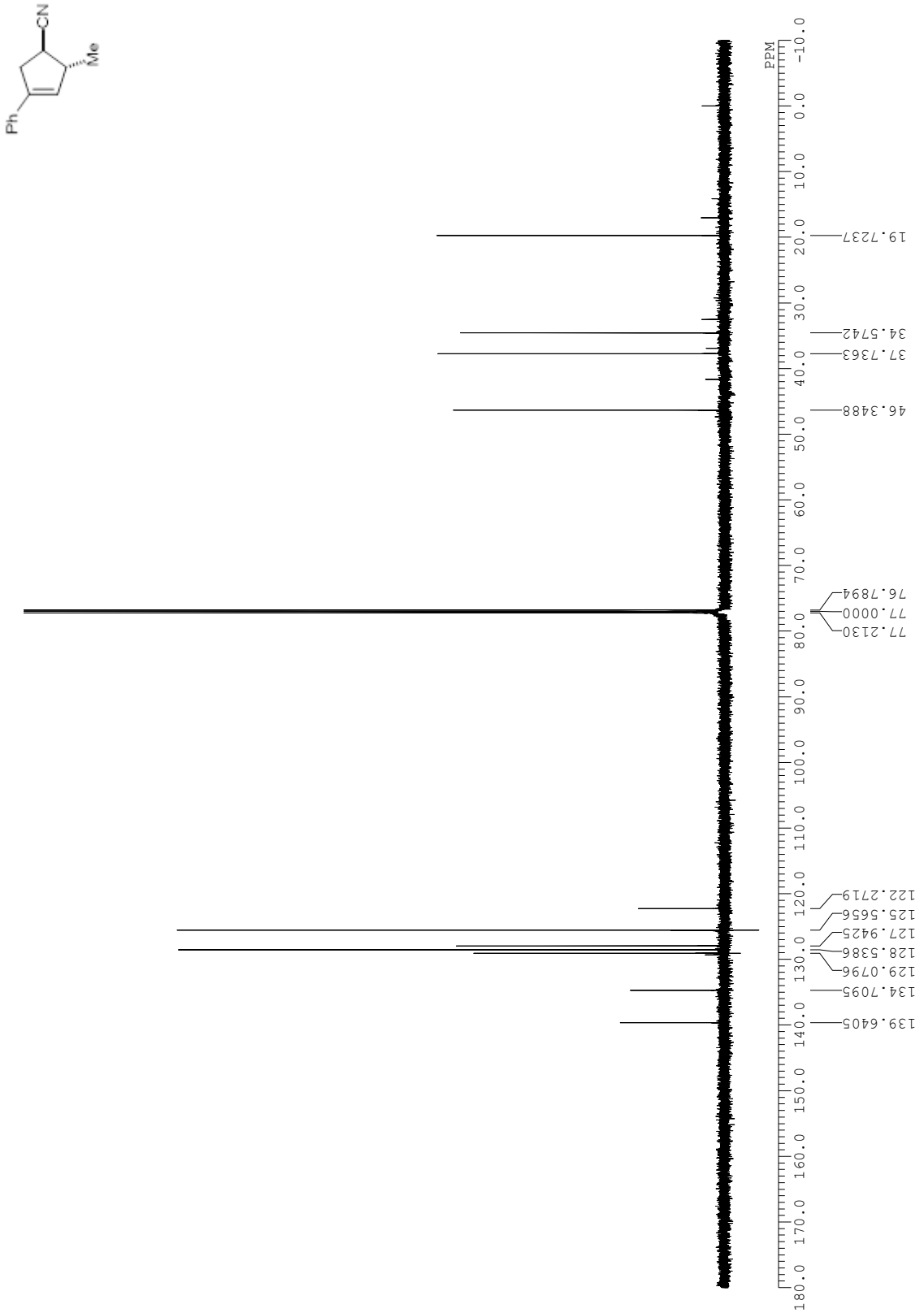
^{13}C NMR spectrum of **12hA** (minor diastereomer)



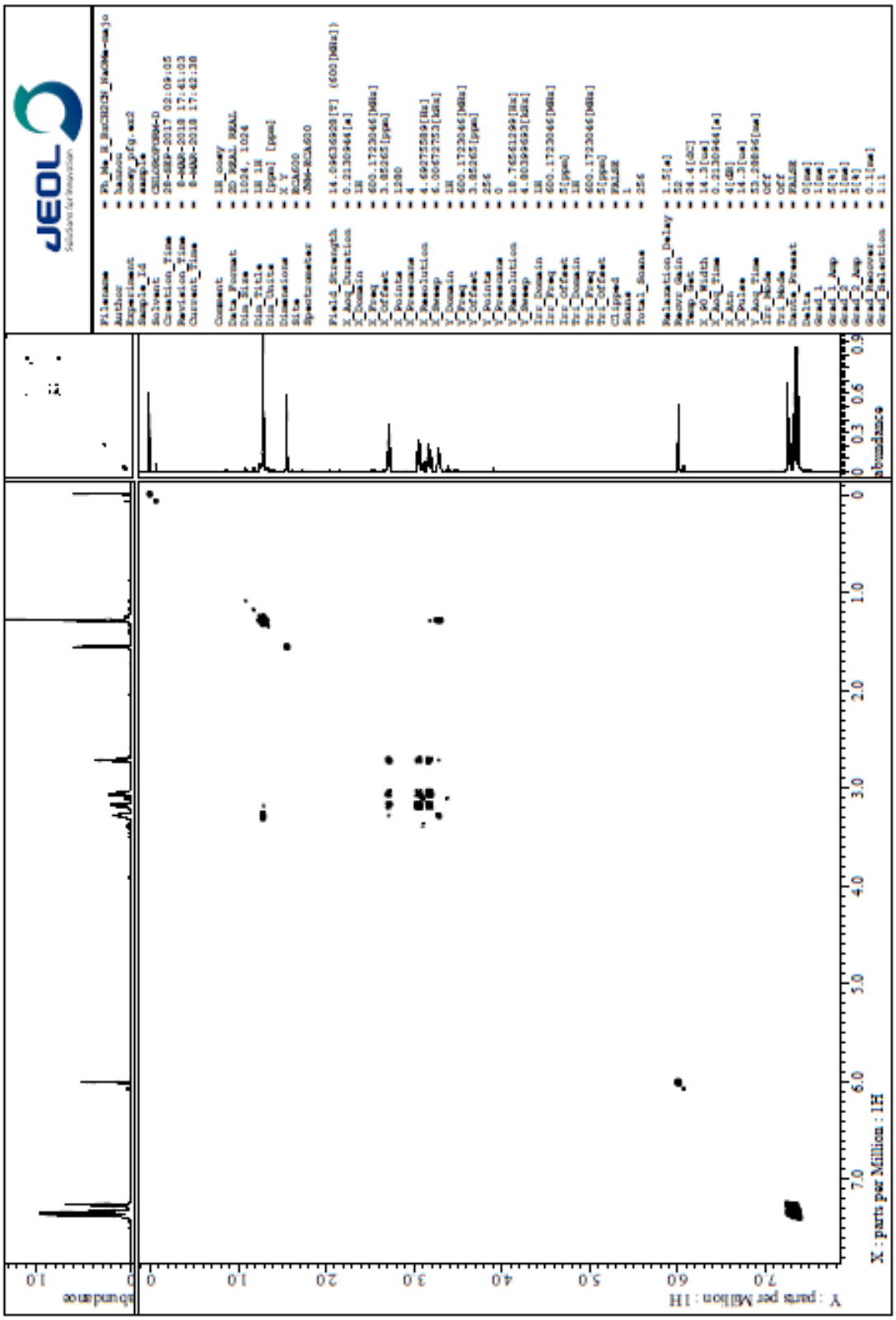
^{1}H NMR spectrum of (1*R**,2*R**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



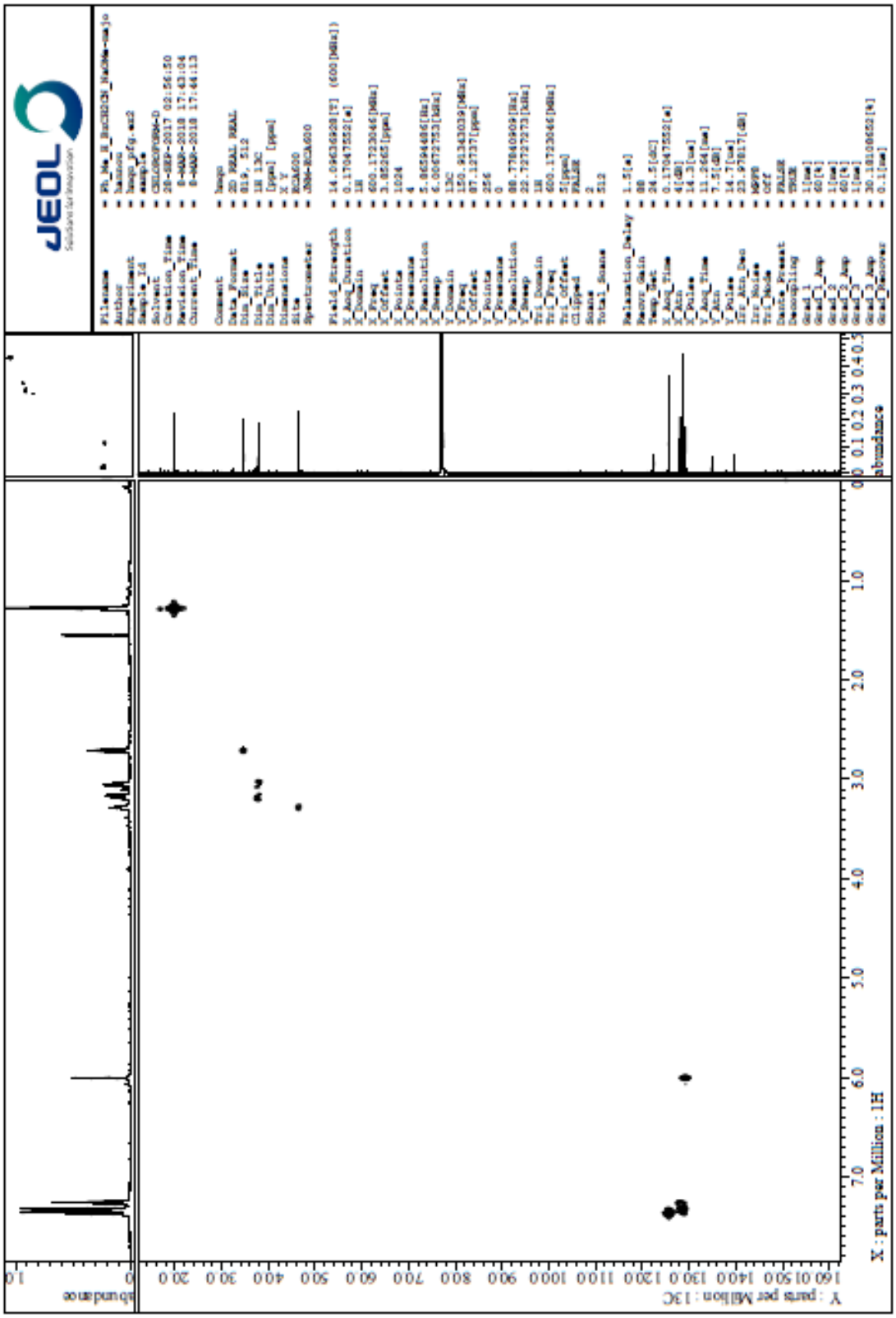
^{13}C NMR spectrum of (1*R**,2*R**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



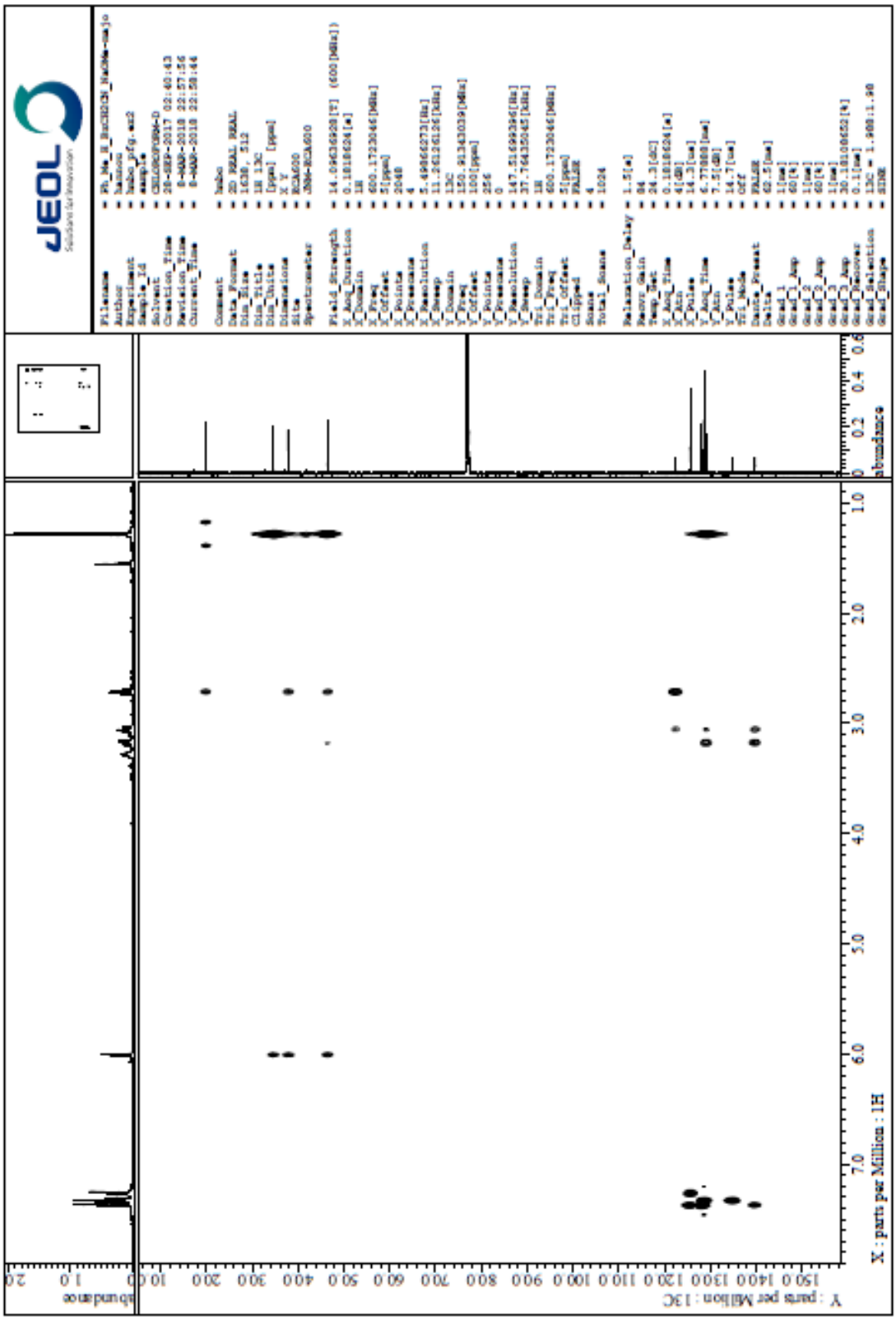
COSY spectrum of (1*R**,2*R**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



HMQC spectrum of (1*R**,2*R**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



HMBC spectrum of (1*R**,2*R**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



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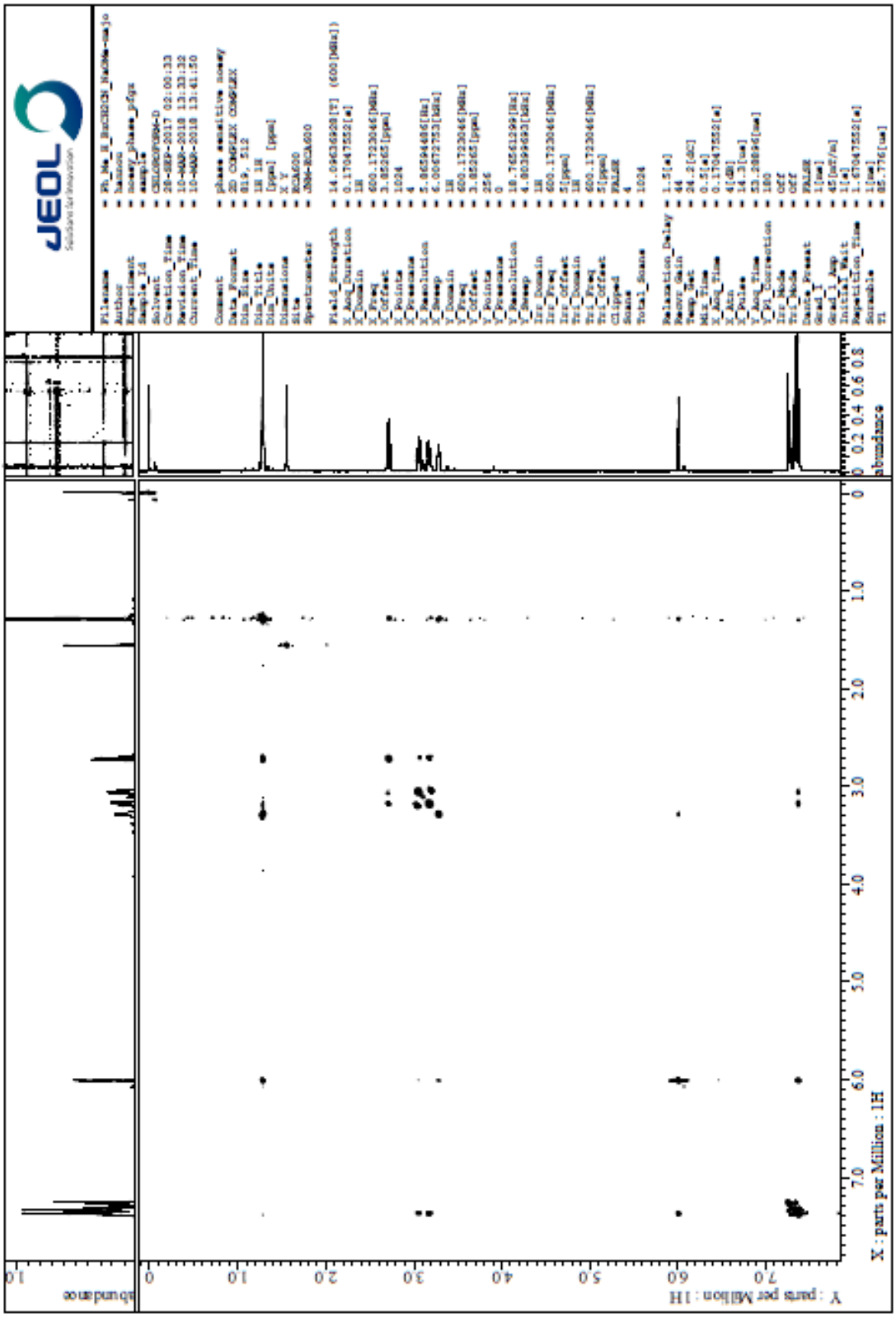
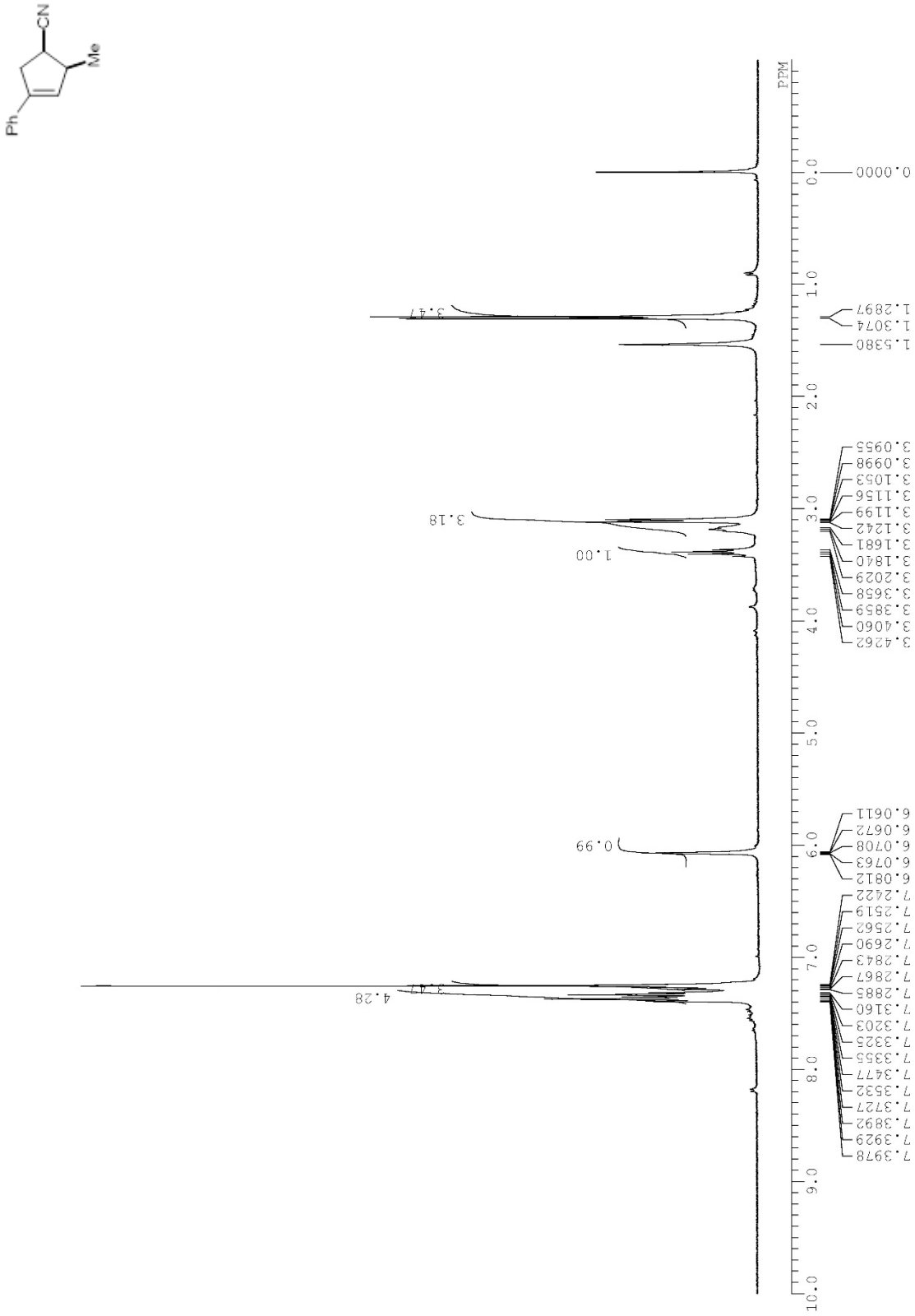


^{1}H NMR spectrum of (1*R**,2*S**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



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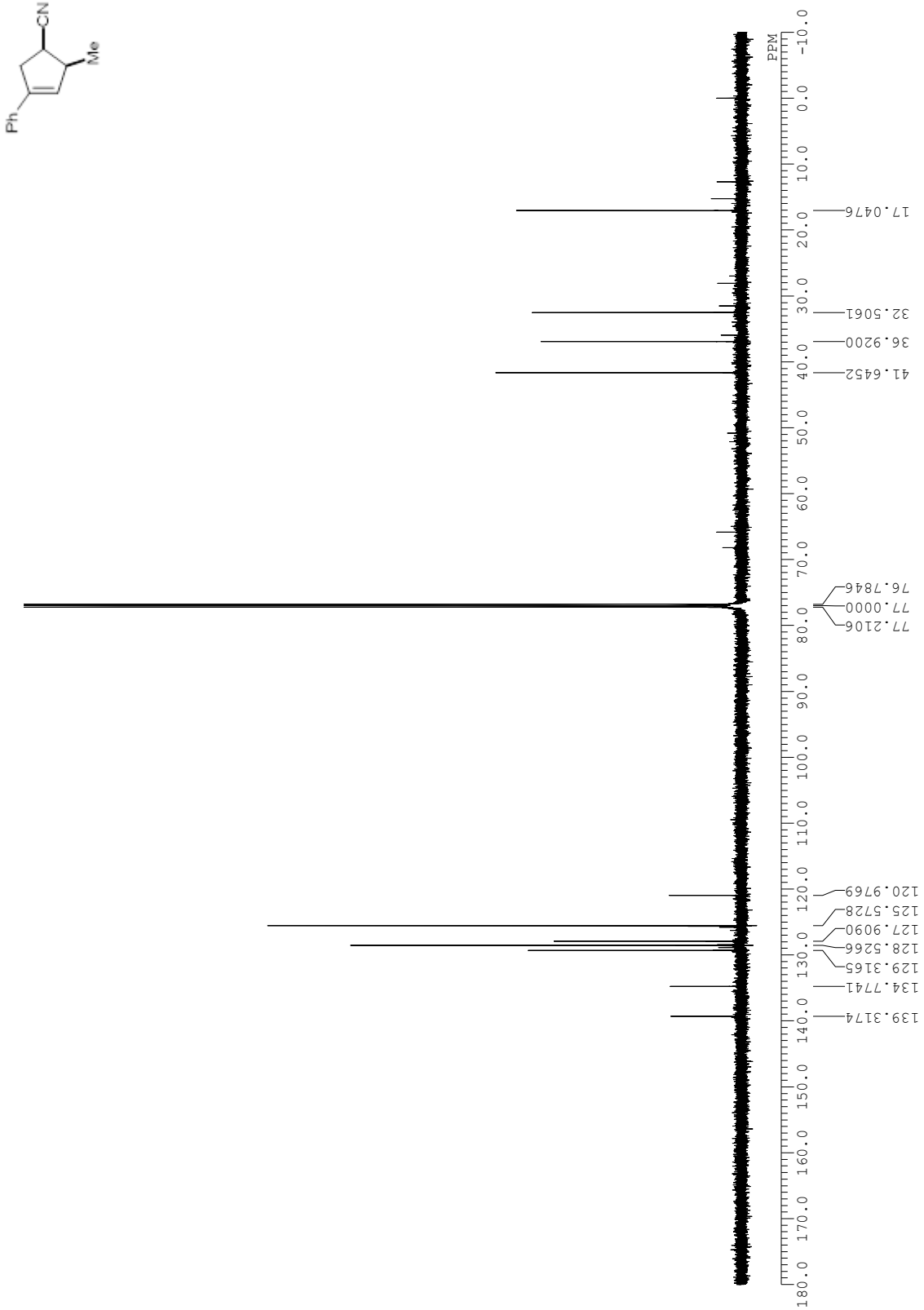
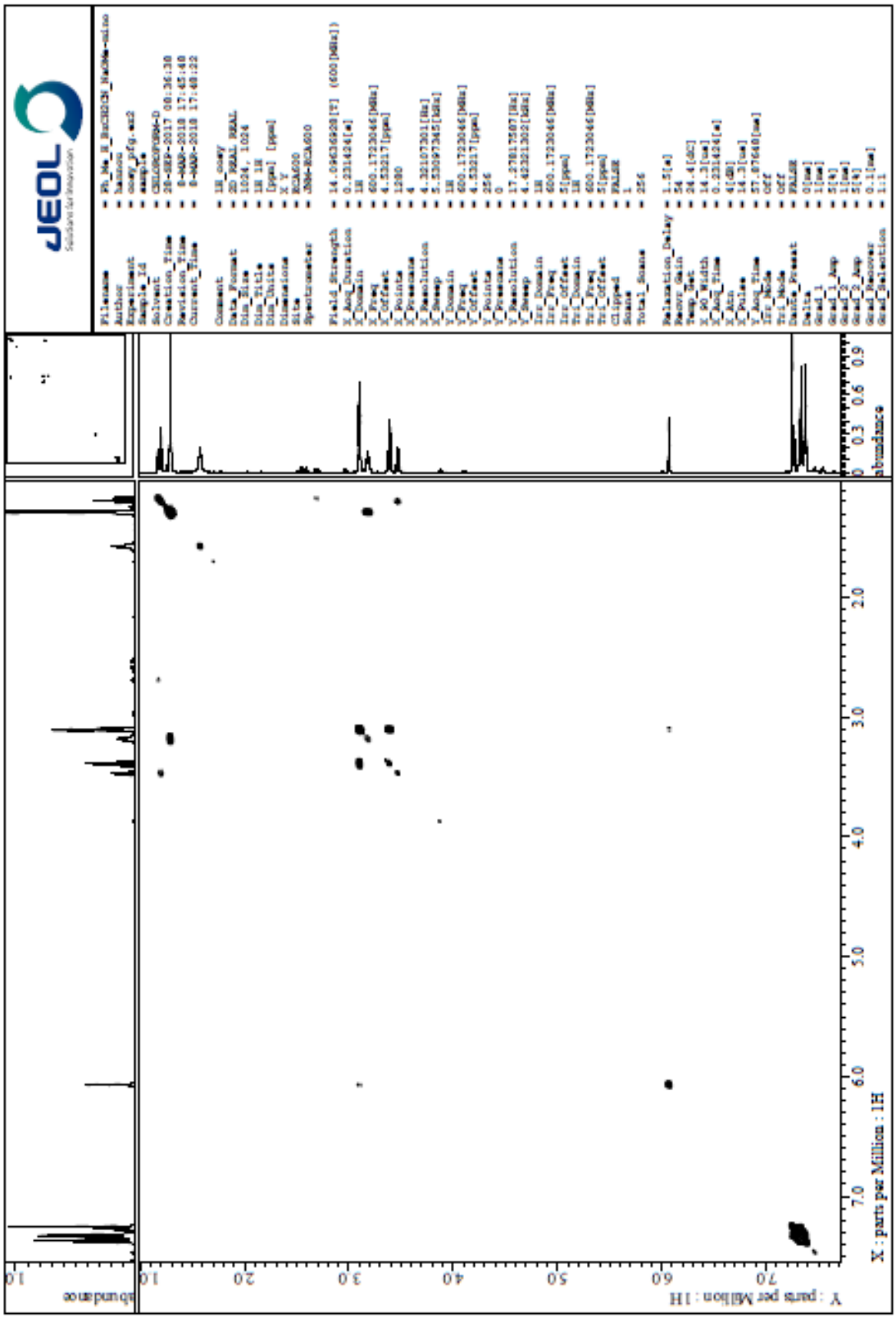
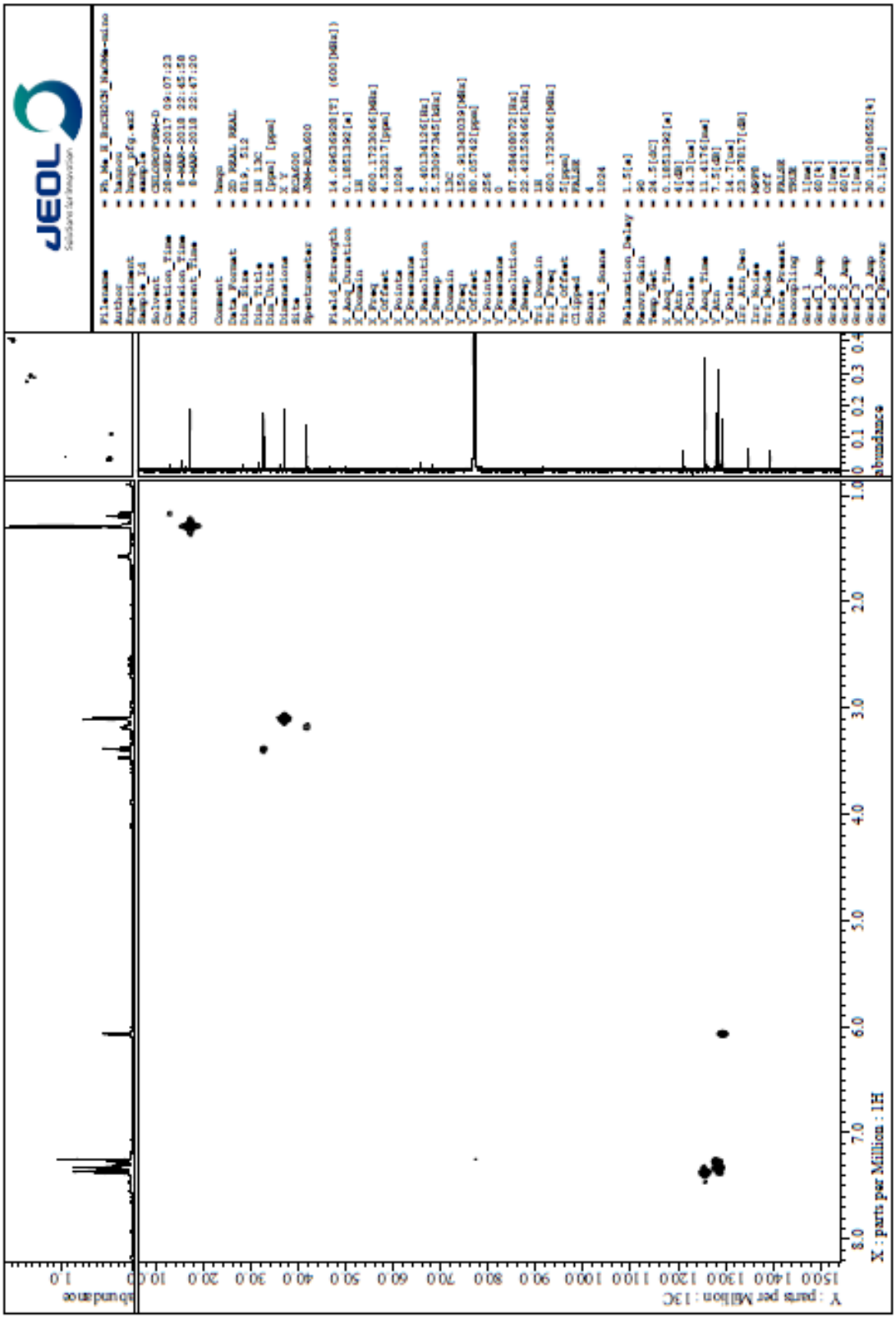


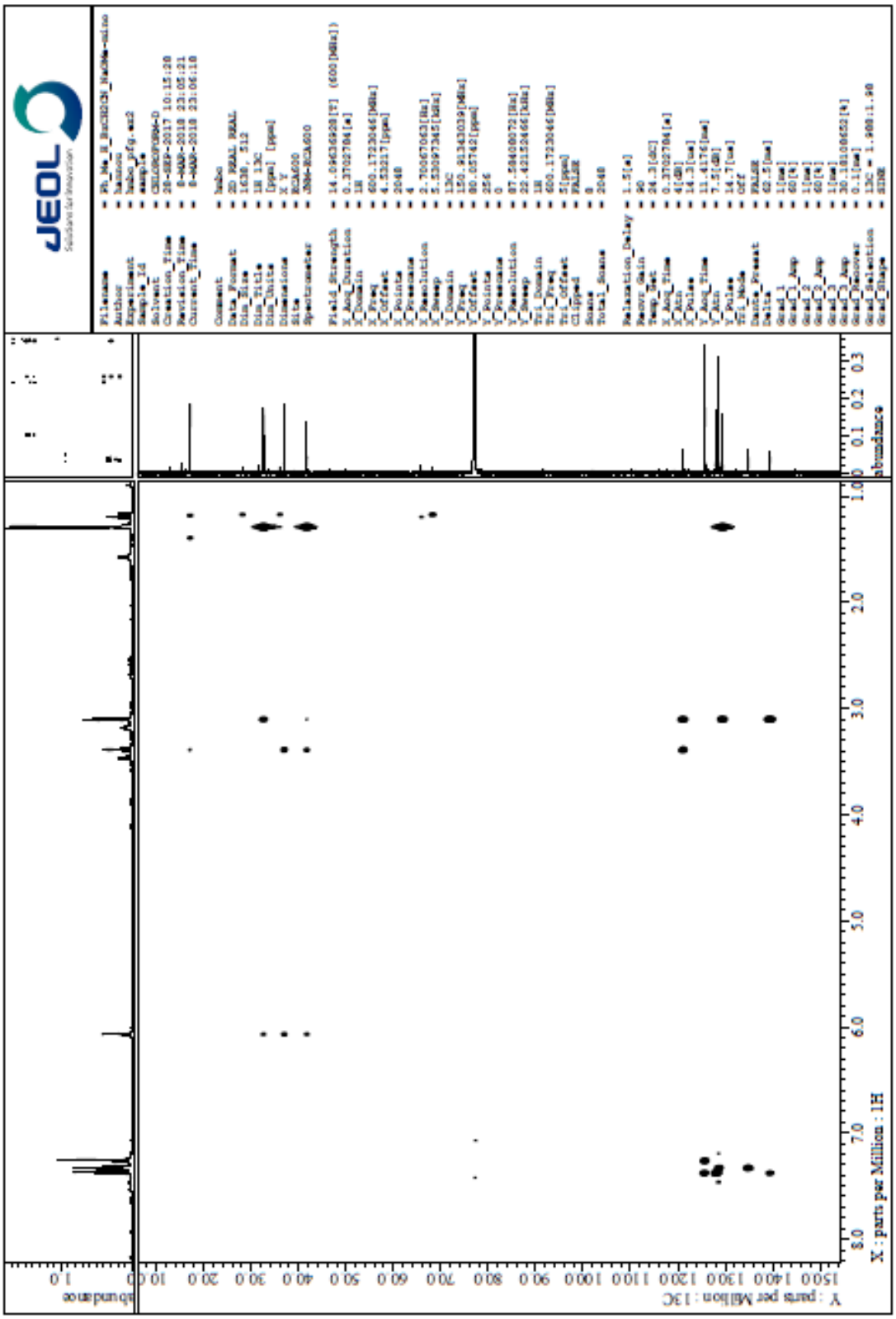
COSY spectrum of (1*R**,2*S**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



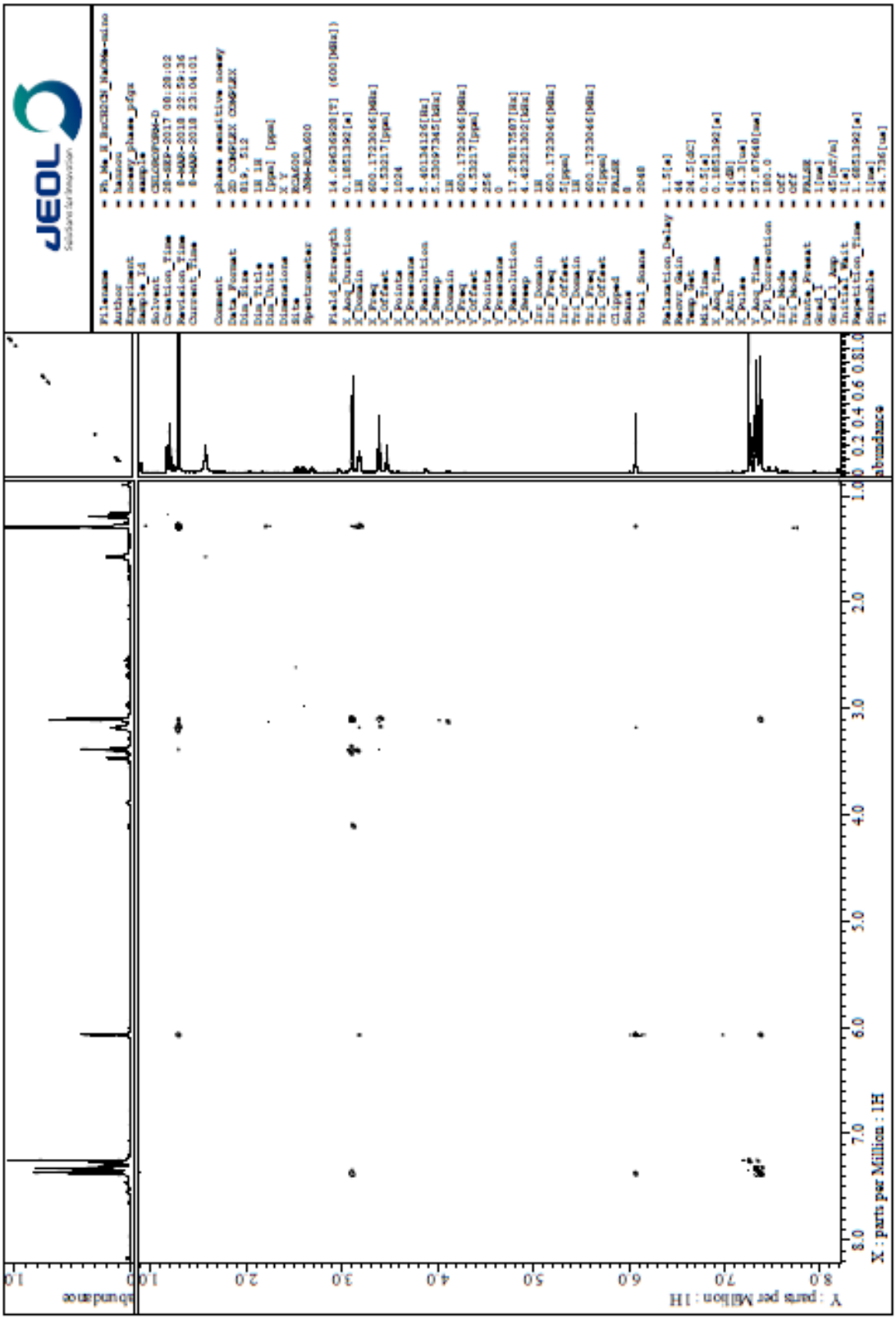
HMQC spectrum of (1*R**,2*S**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



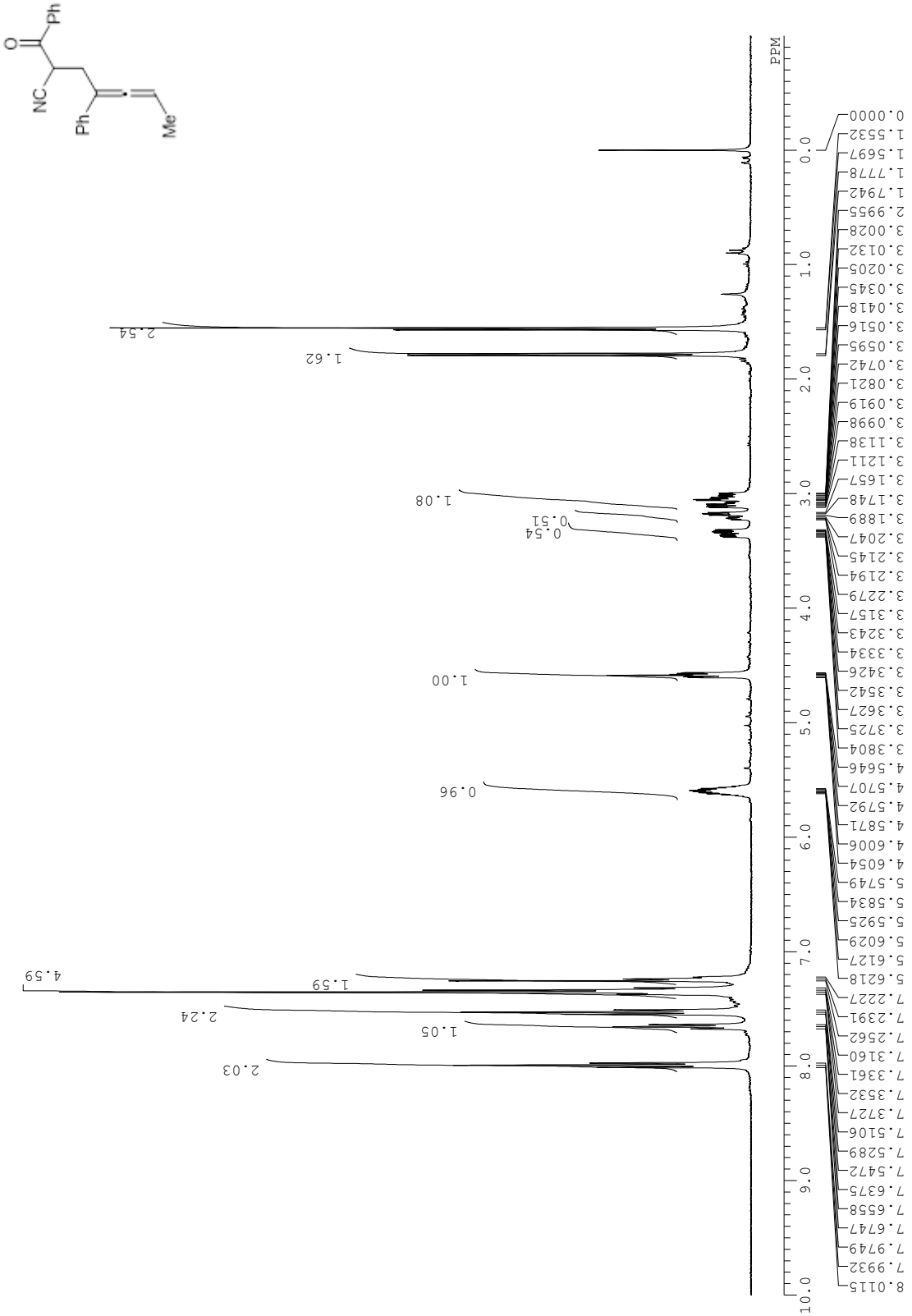
HMBC spectrum of (1*R**,2*S**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



NOESY spectrum of (1*R**,2*S**)-2-methyl-4-phenylcyclopent-3-ene-1-carbonitrile



^{1}H NMR spectrum of **5hA'**



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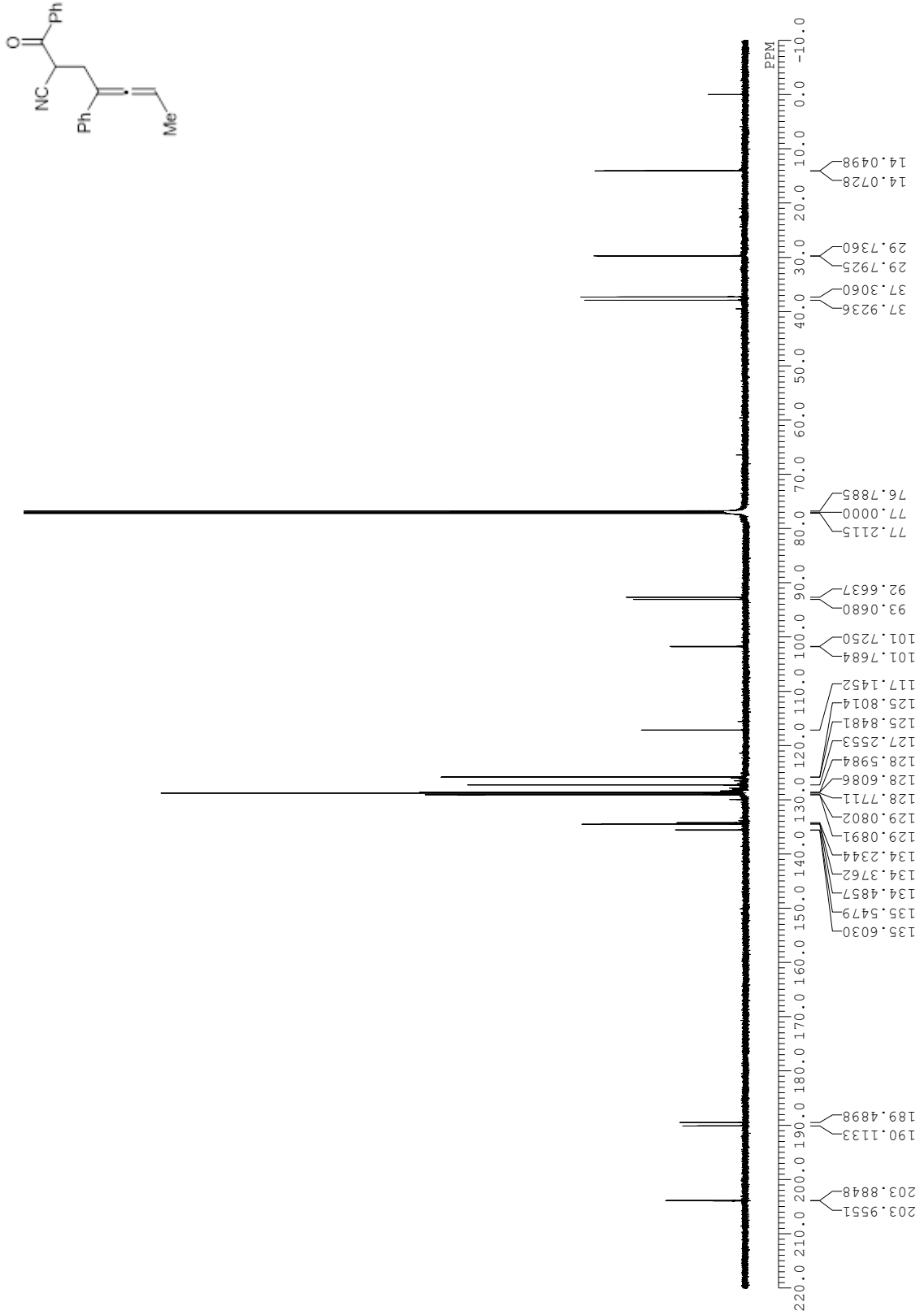
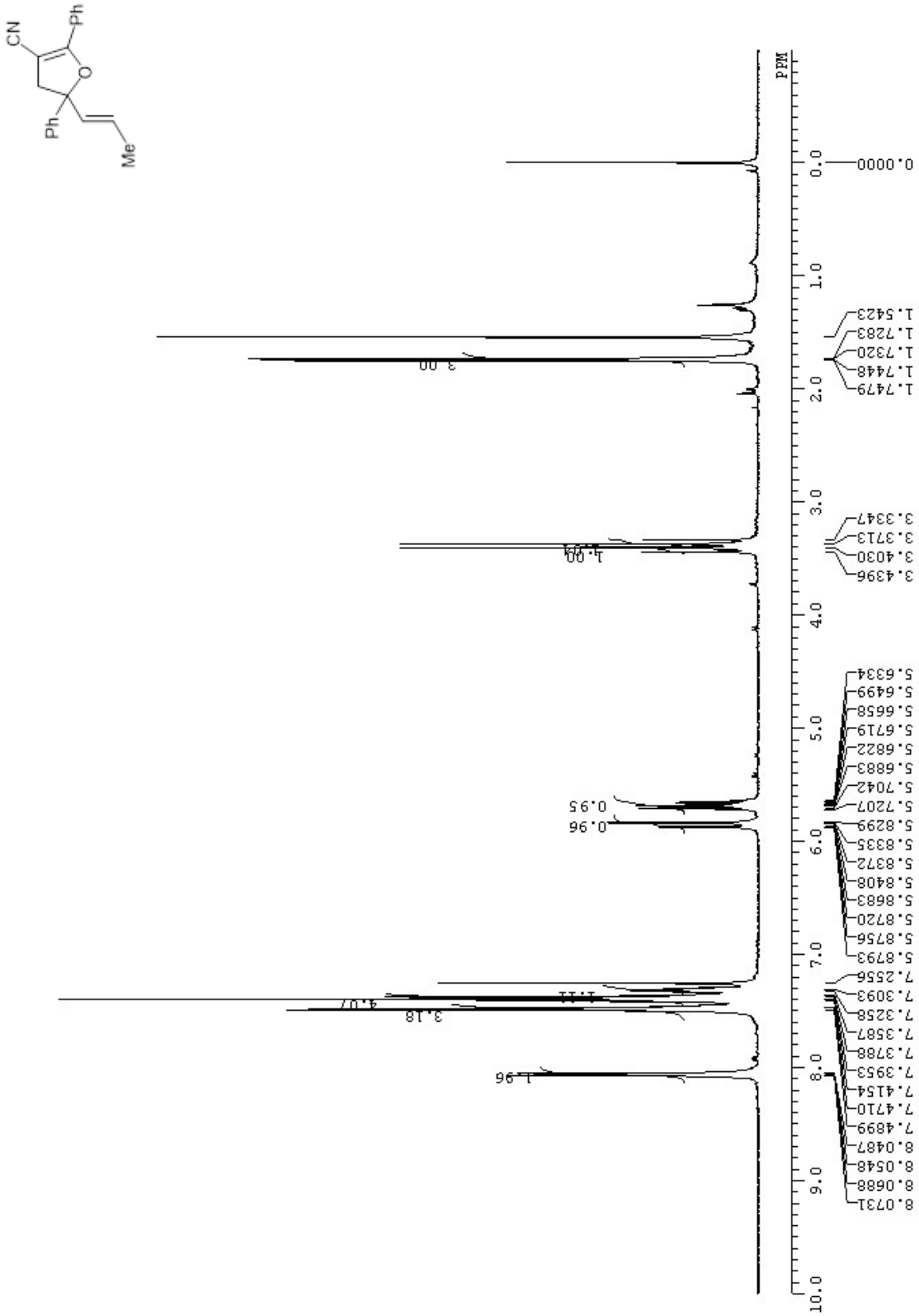


^{1}H NMR spectrum of **6hA**



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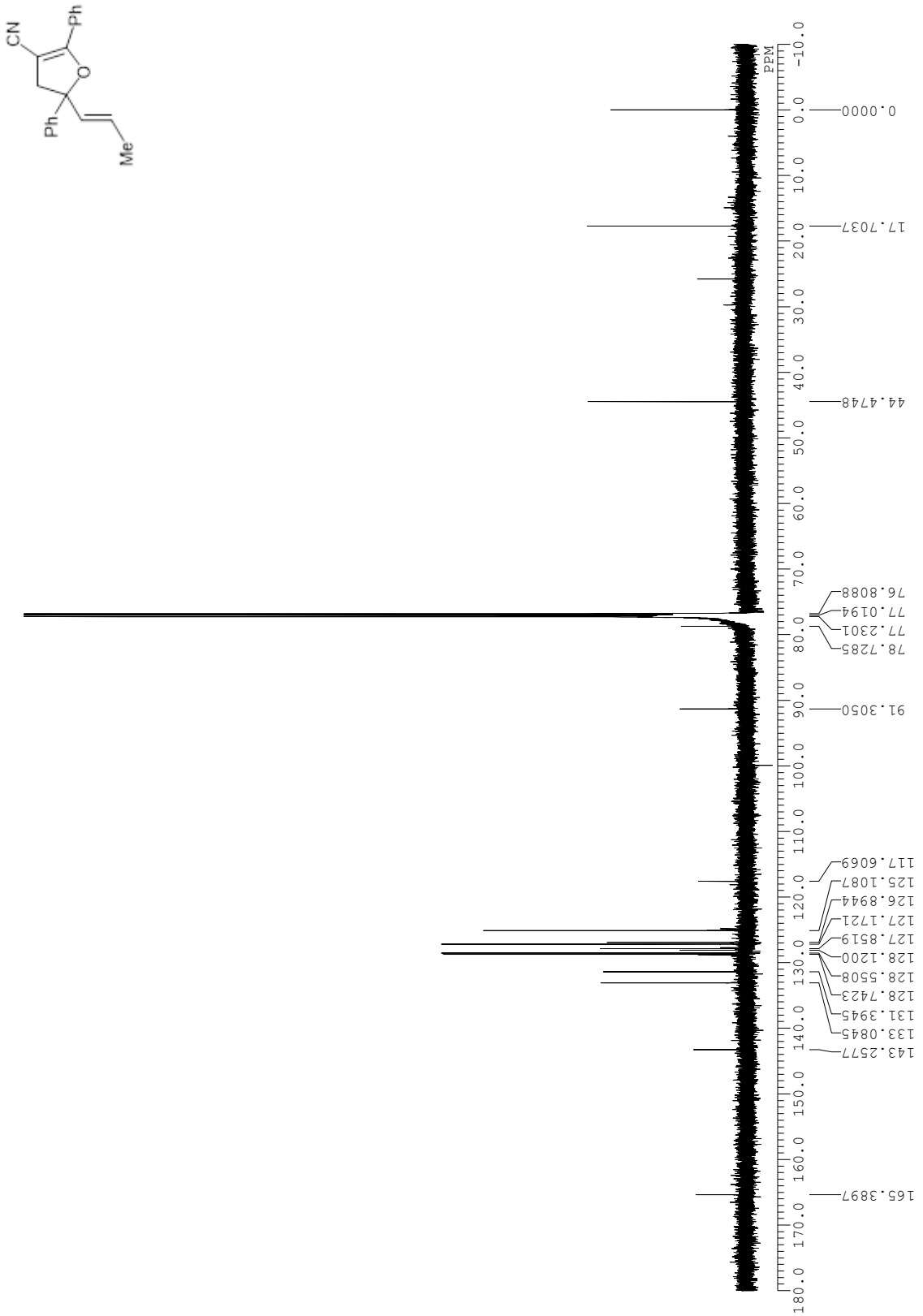
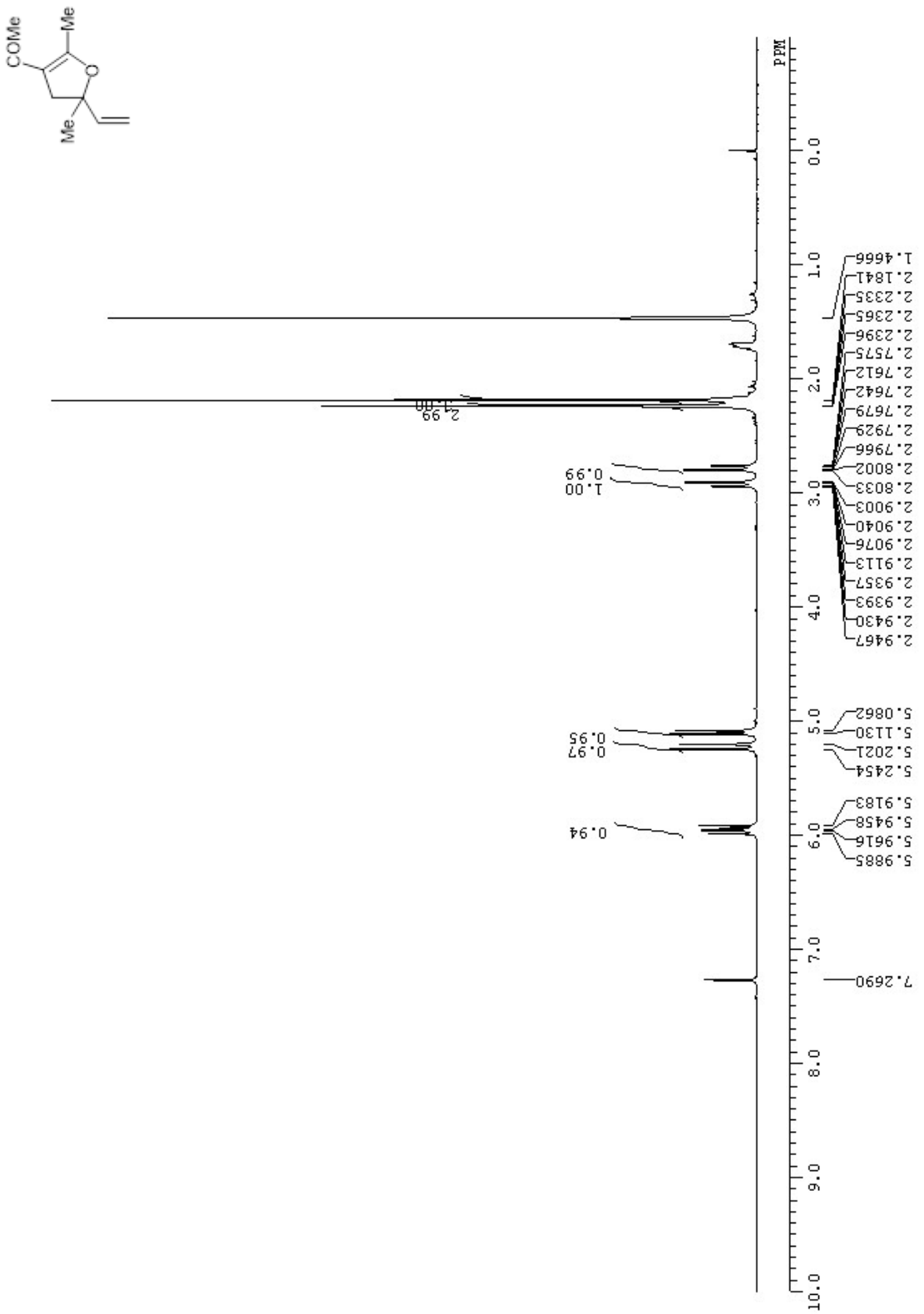
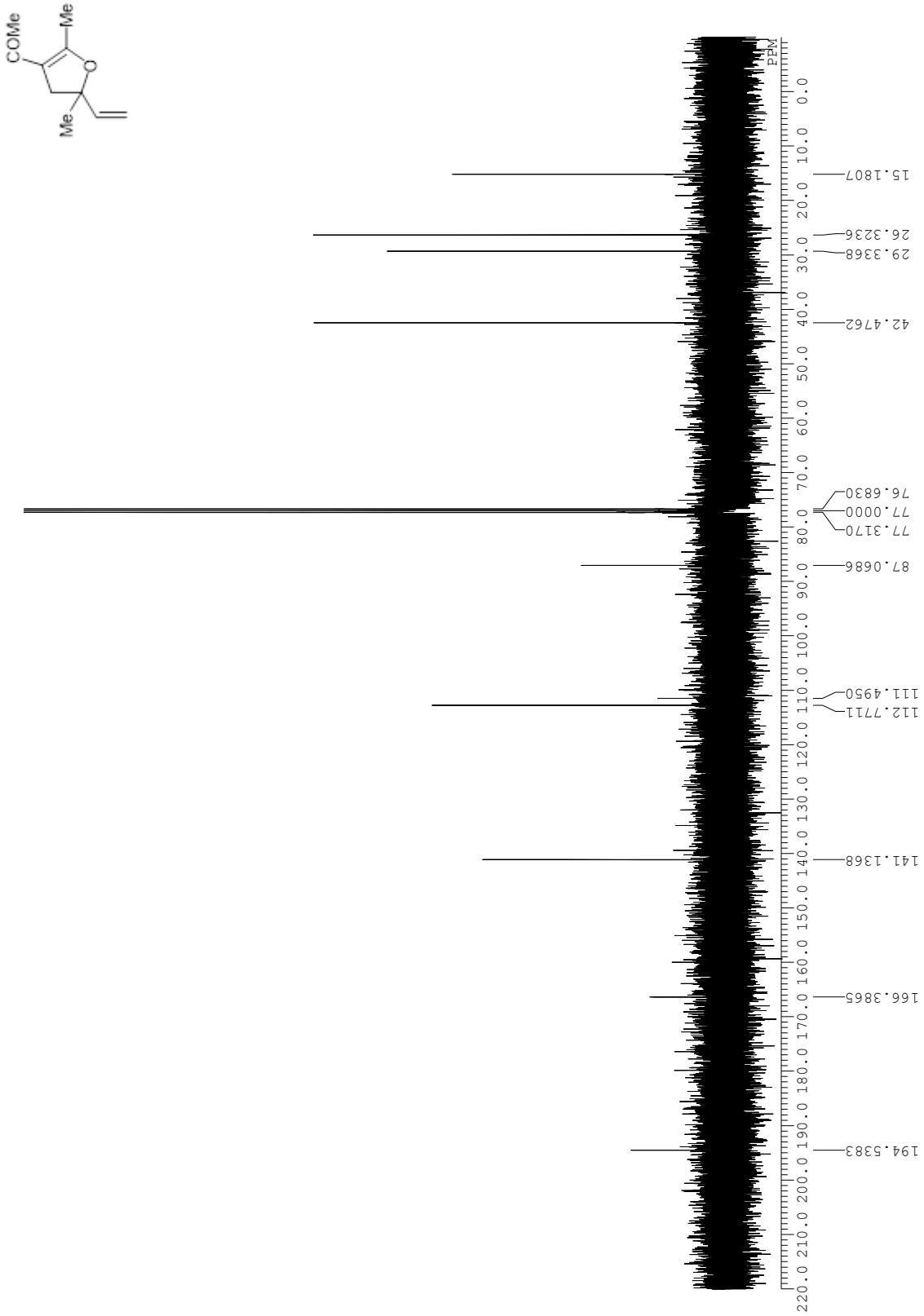


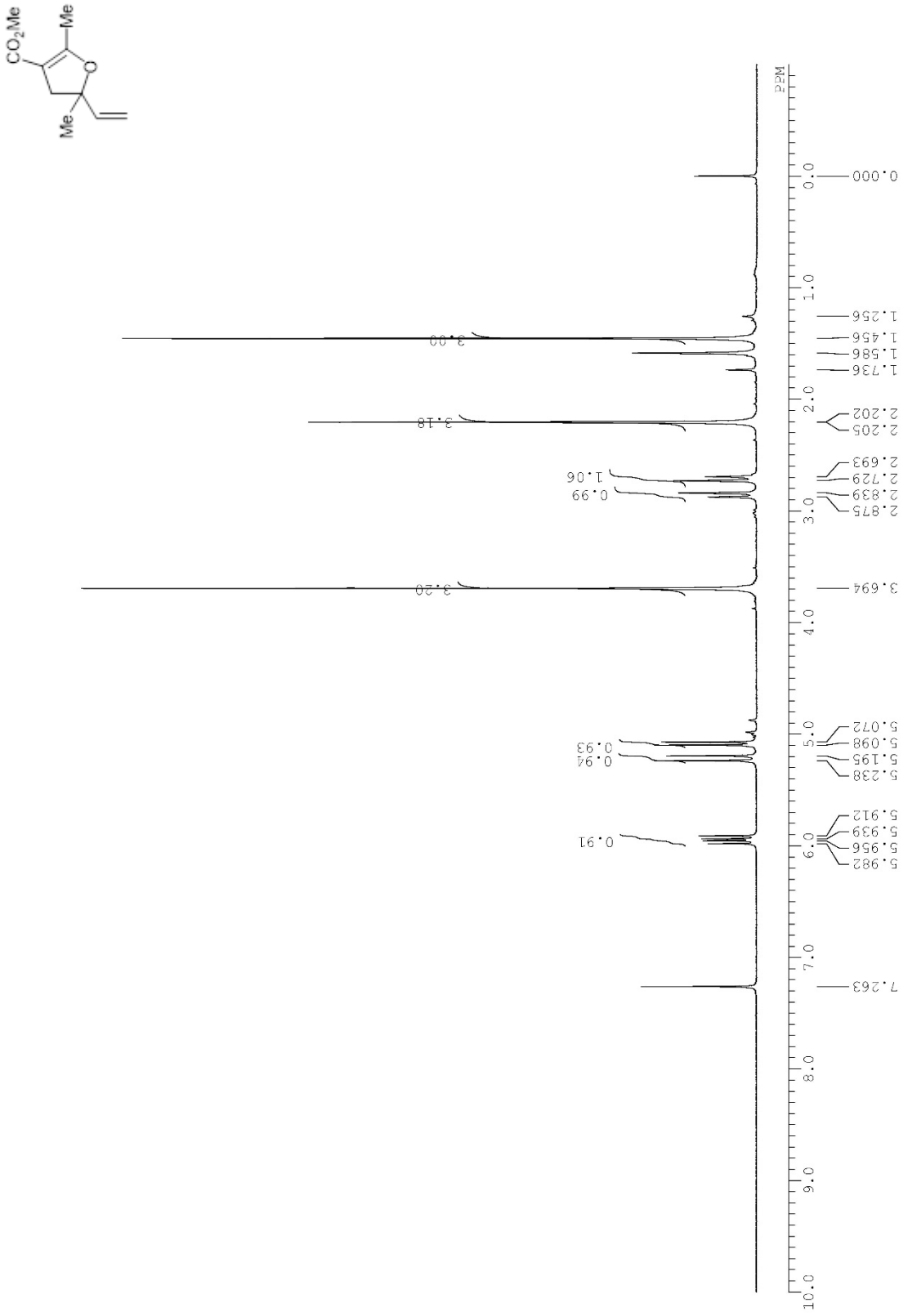
^{1}H NMR spectrum of **6aB**



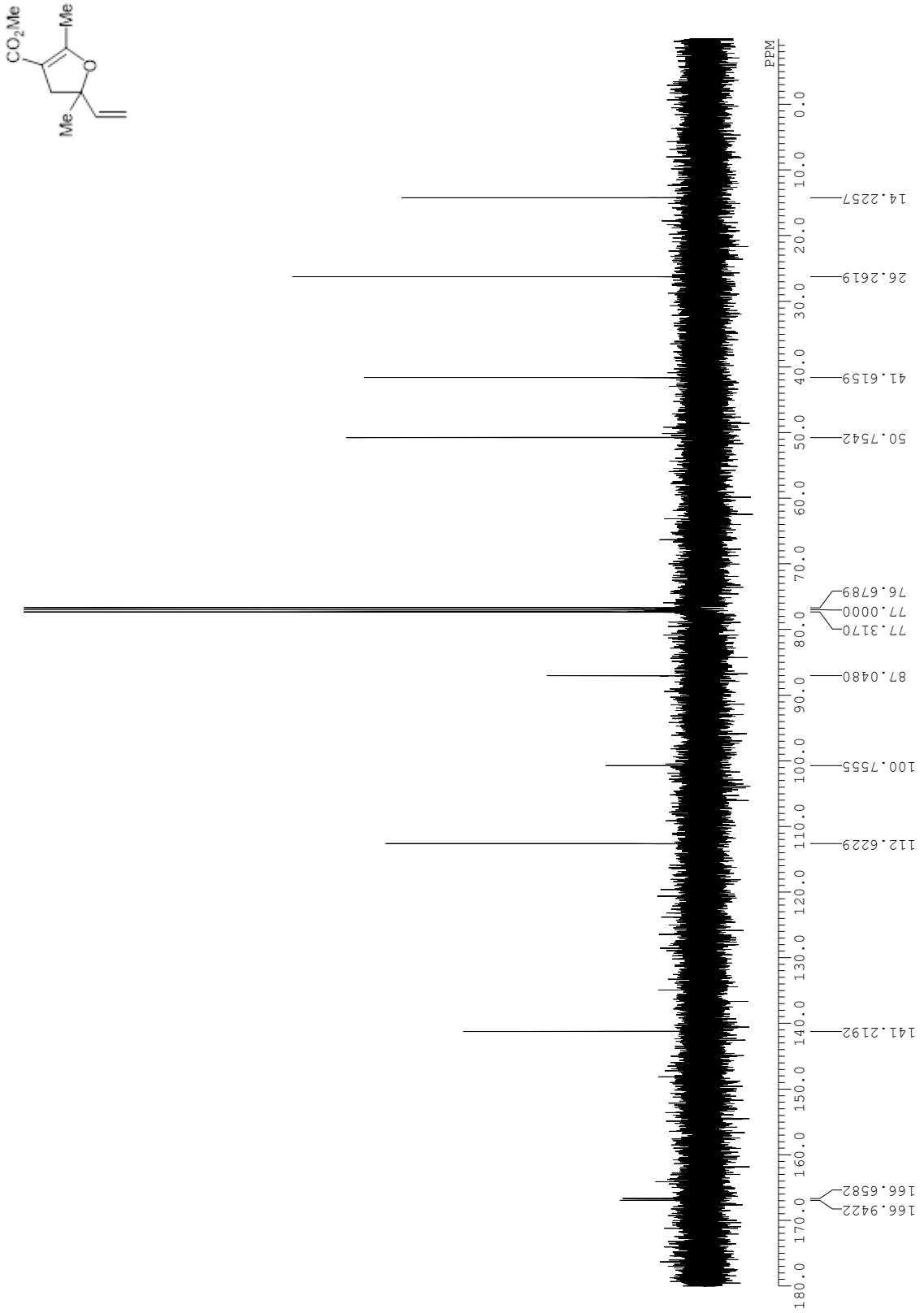
^{13}C NMR spectrum of **6aB**



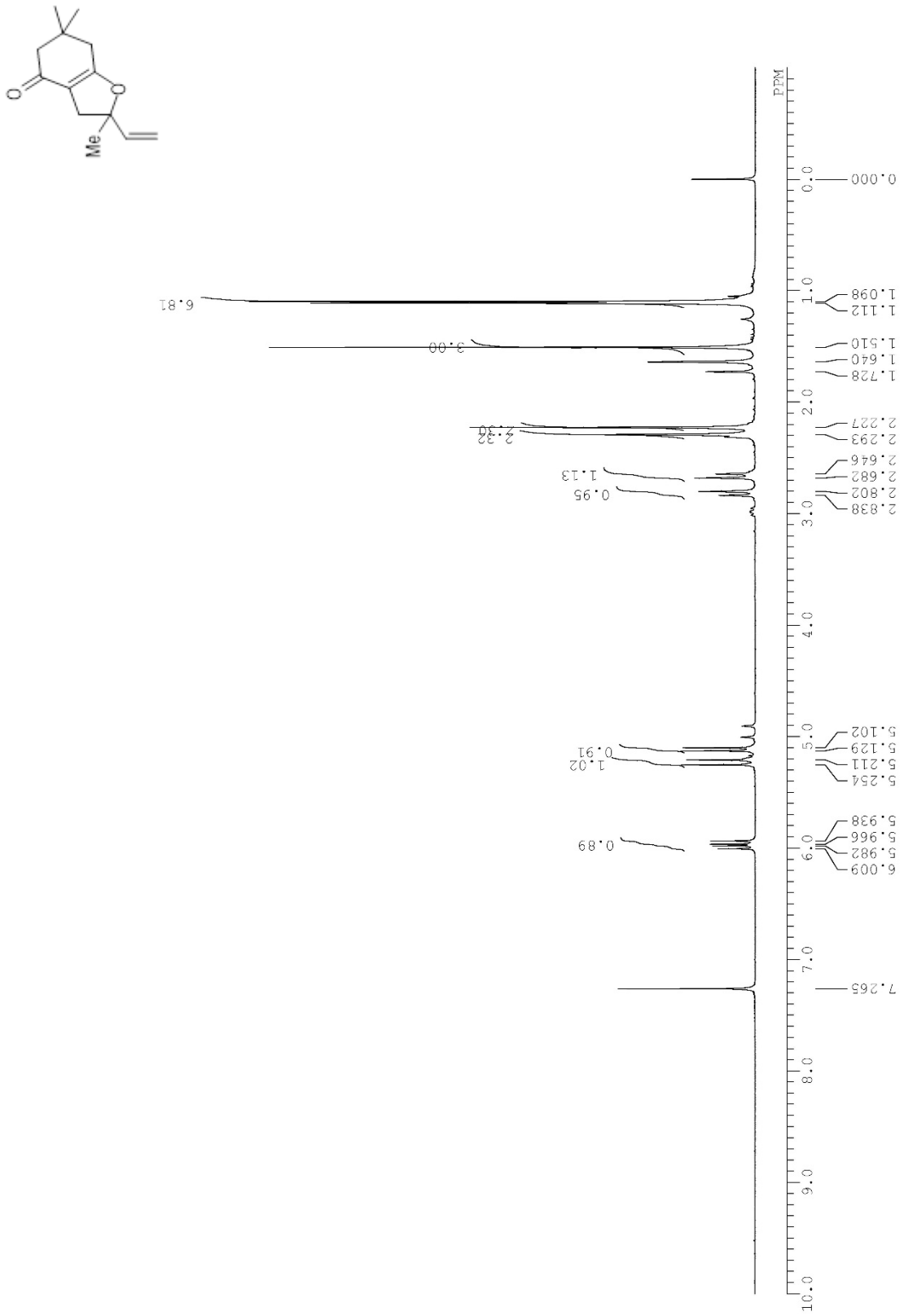
^{1}H NMR spectrum of **6aC**



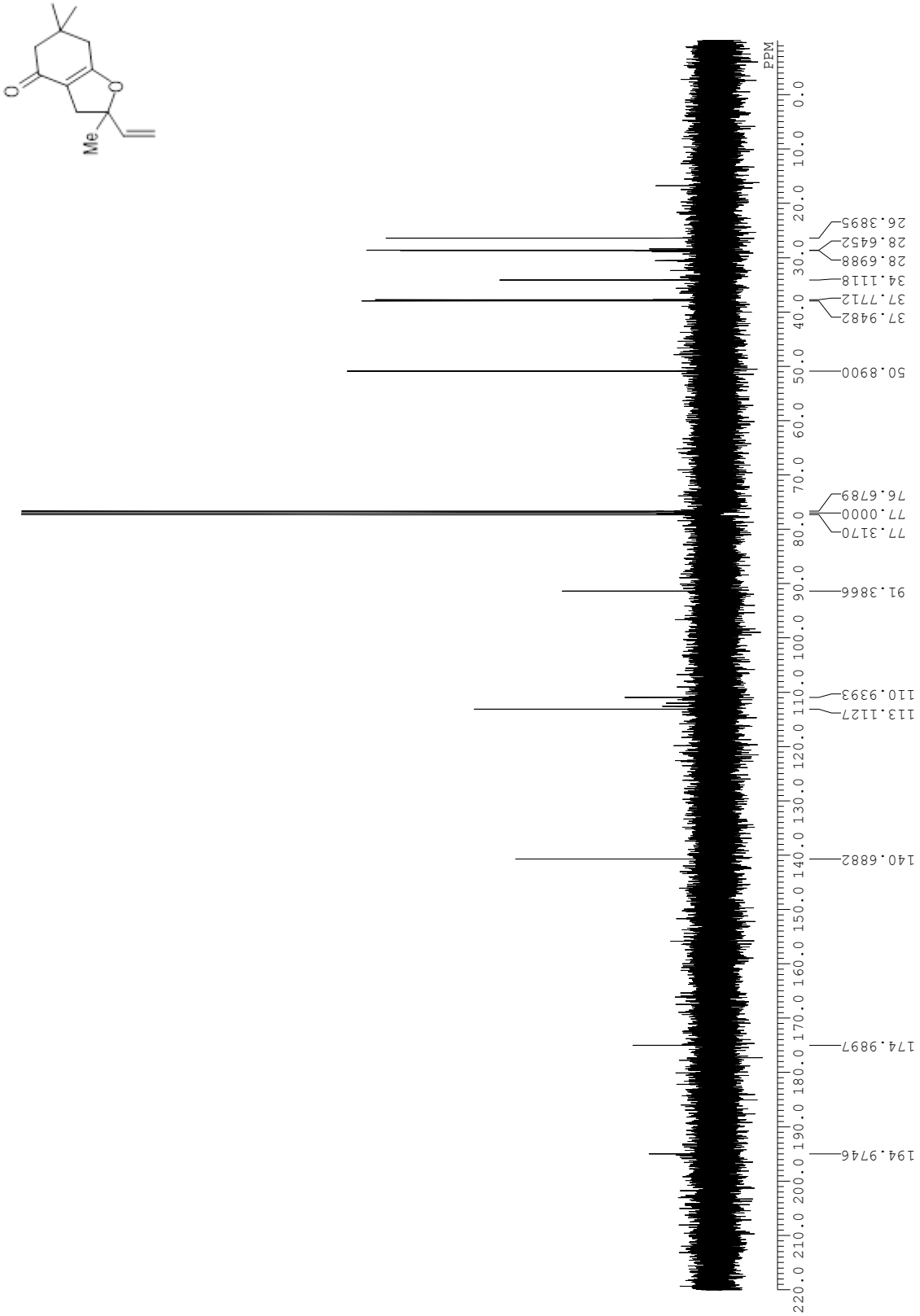
^{13}C NMR spectrum of **6aC**



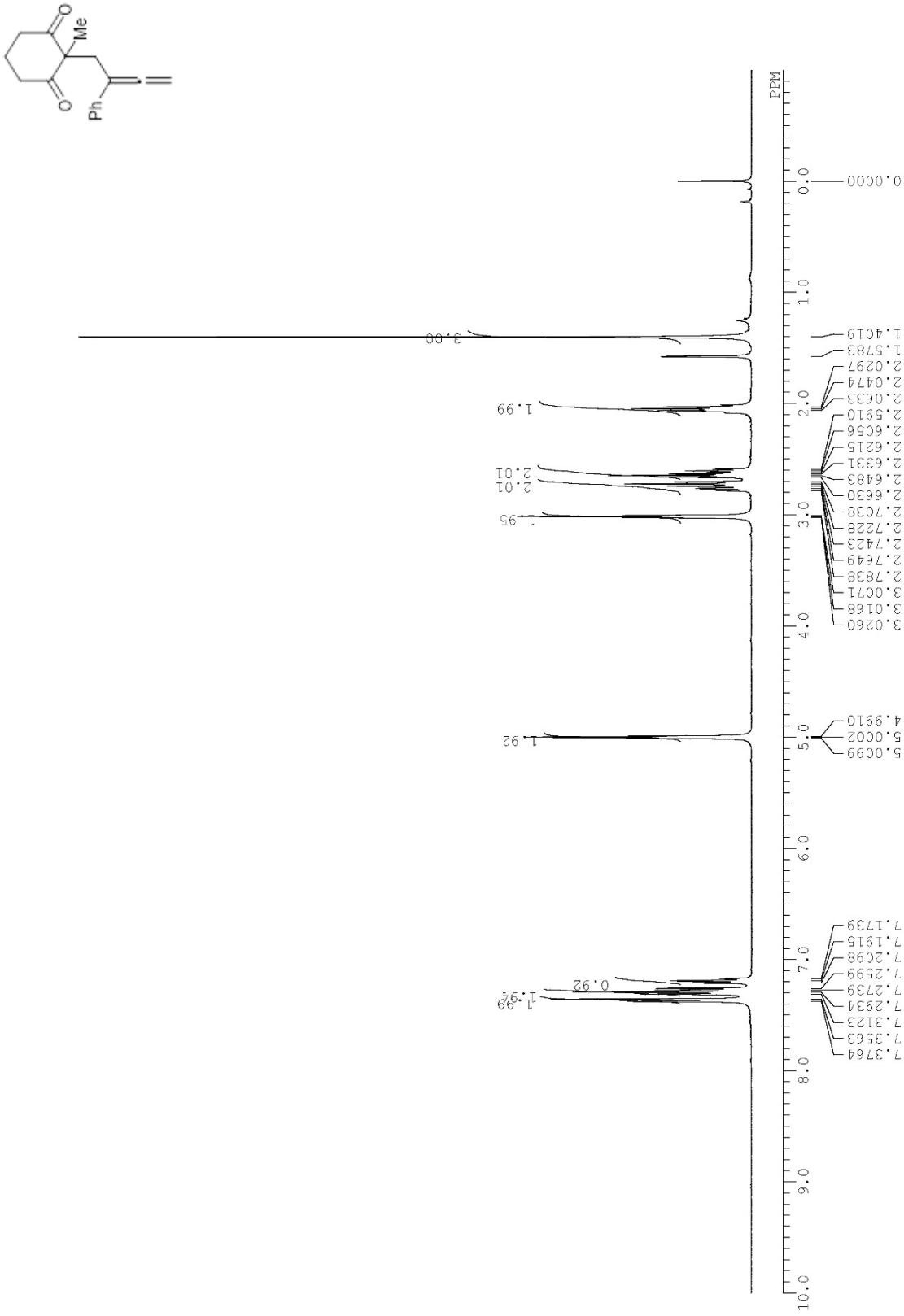
^{1}H NMR spectrum of **6aD**



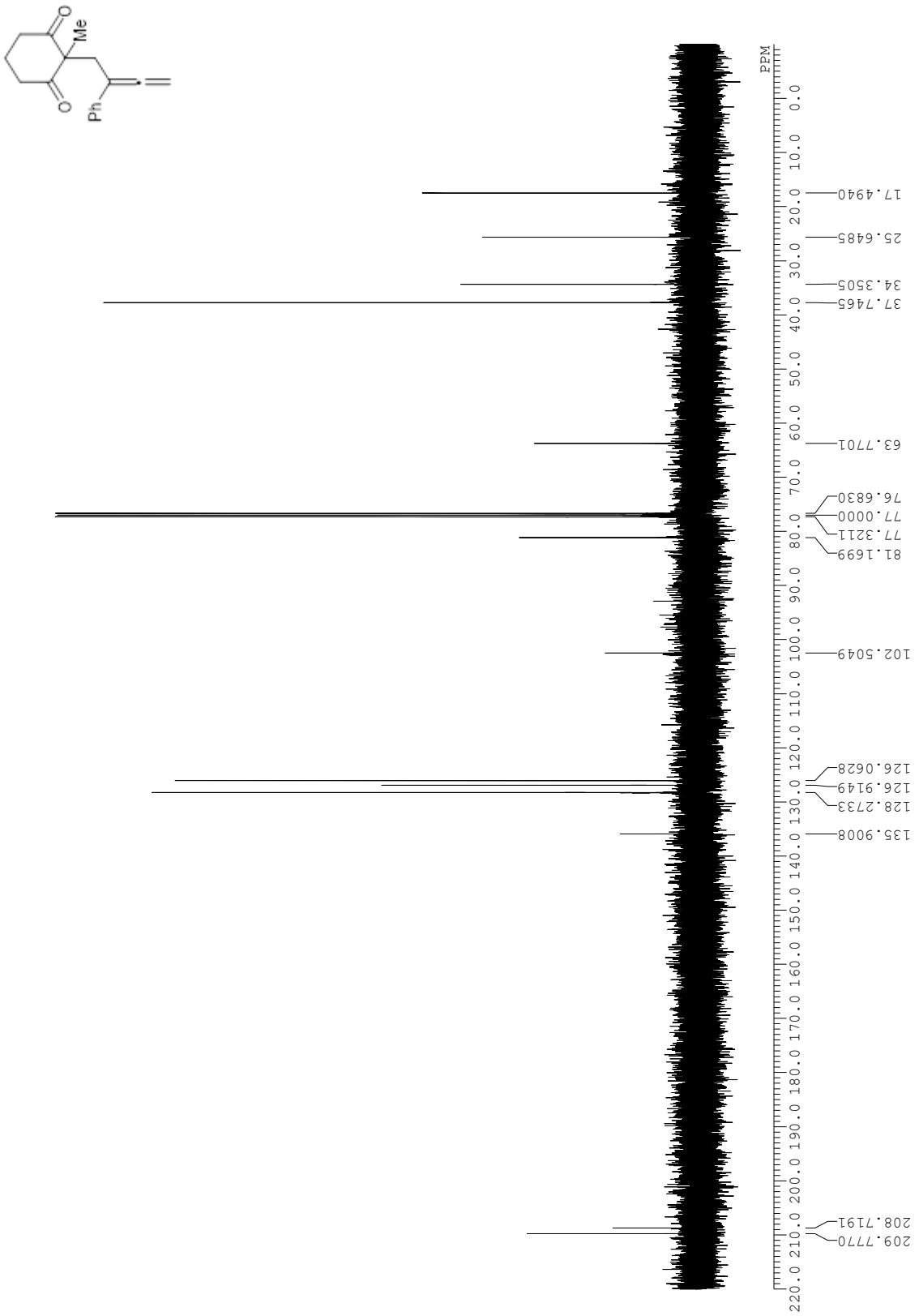
^{13}C NMR spectrum of **6aD**



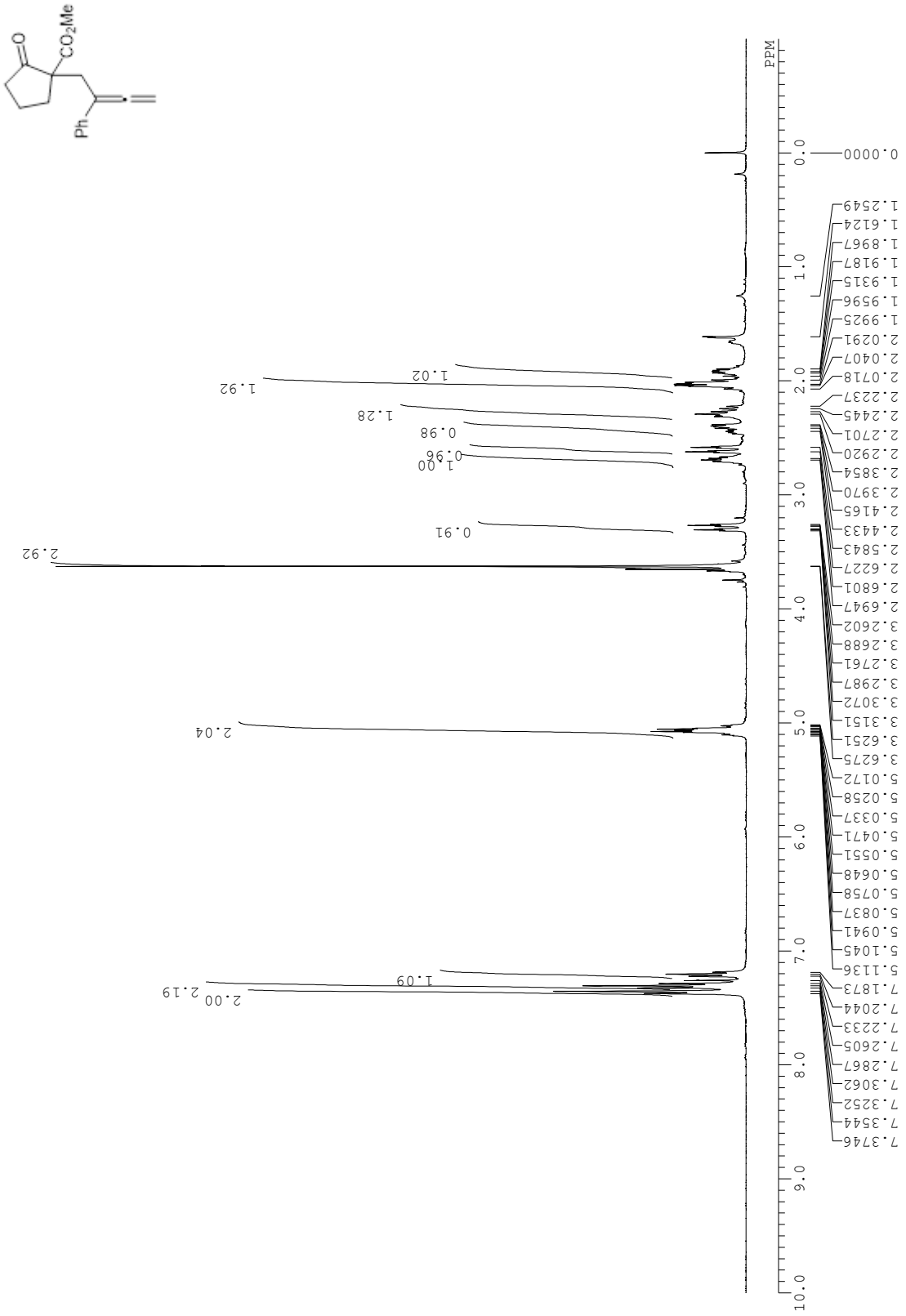
^{1}H NMR spectrum of **5bE**



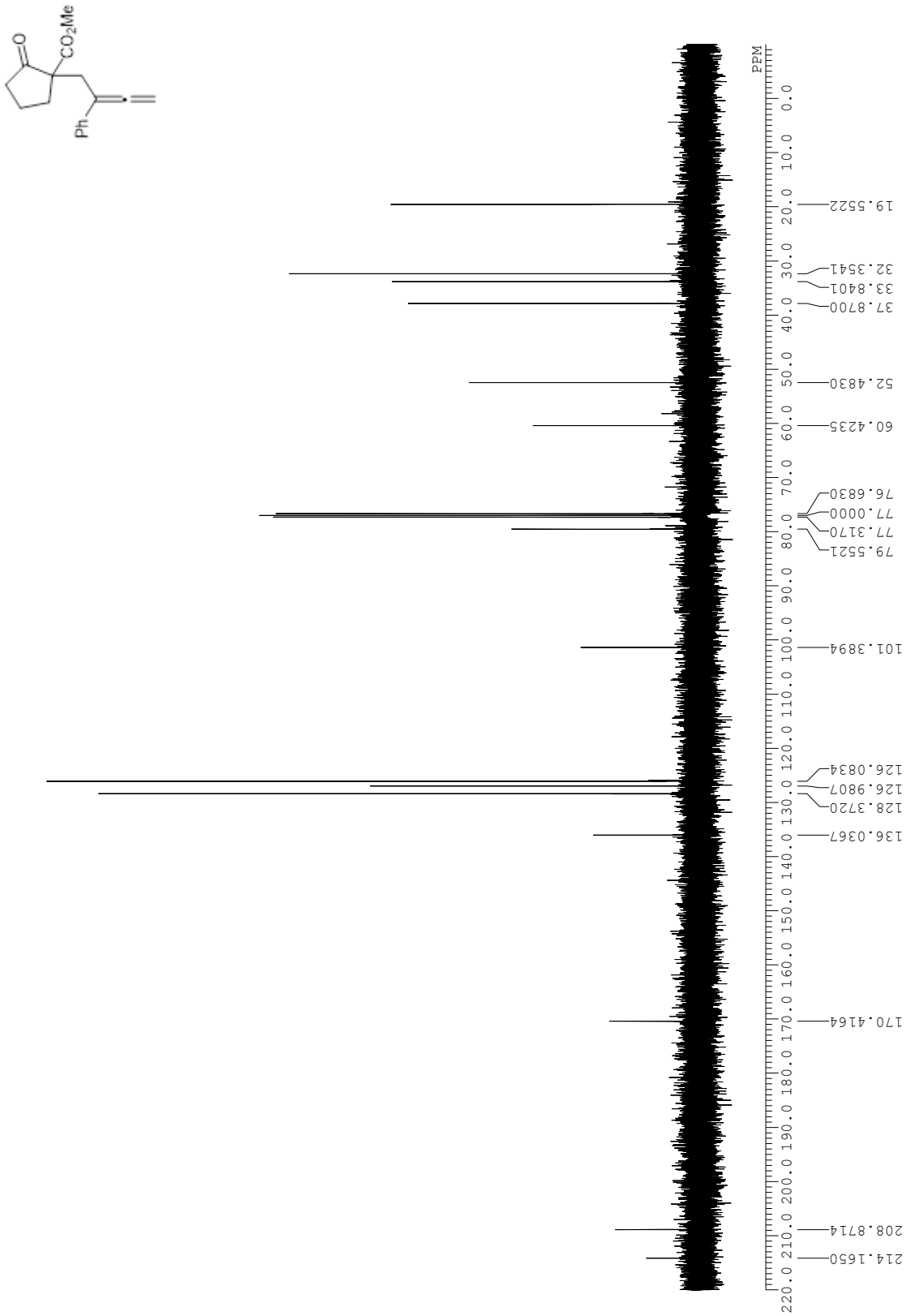
^{13}C NMR spectrum of **5bE**



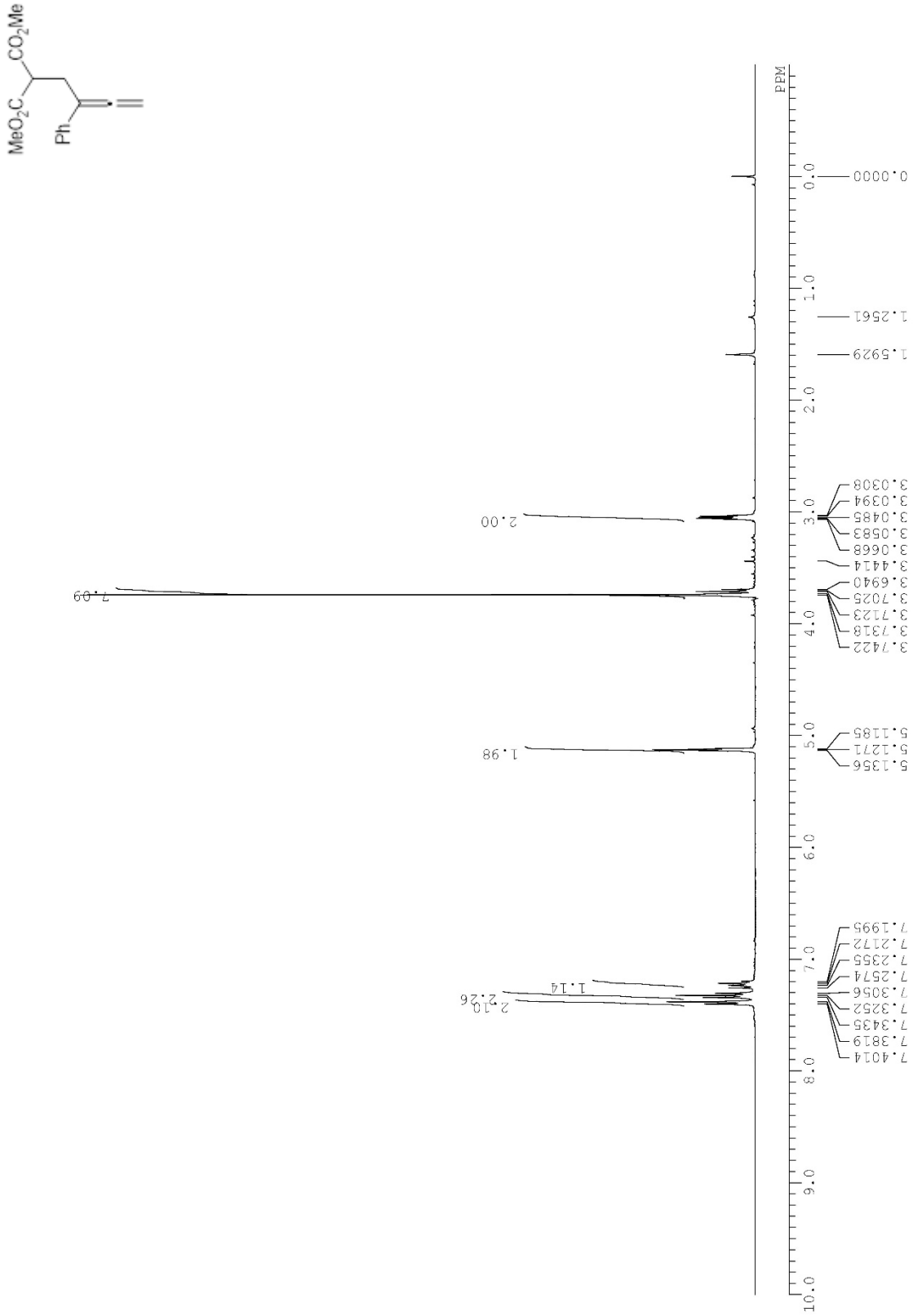
^{1}H NMR spectrum of **5bF**



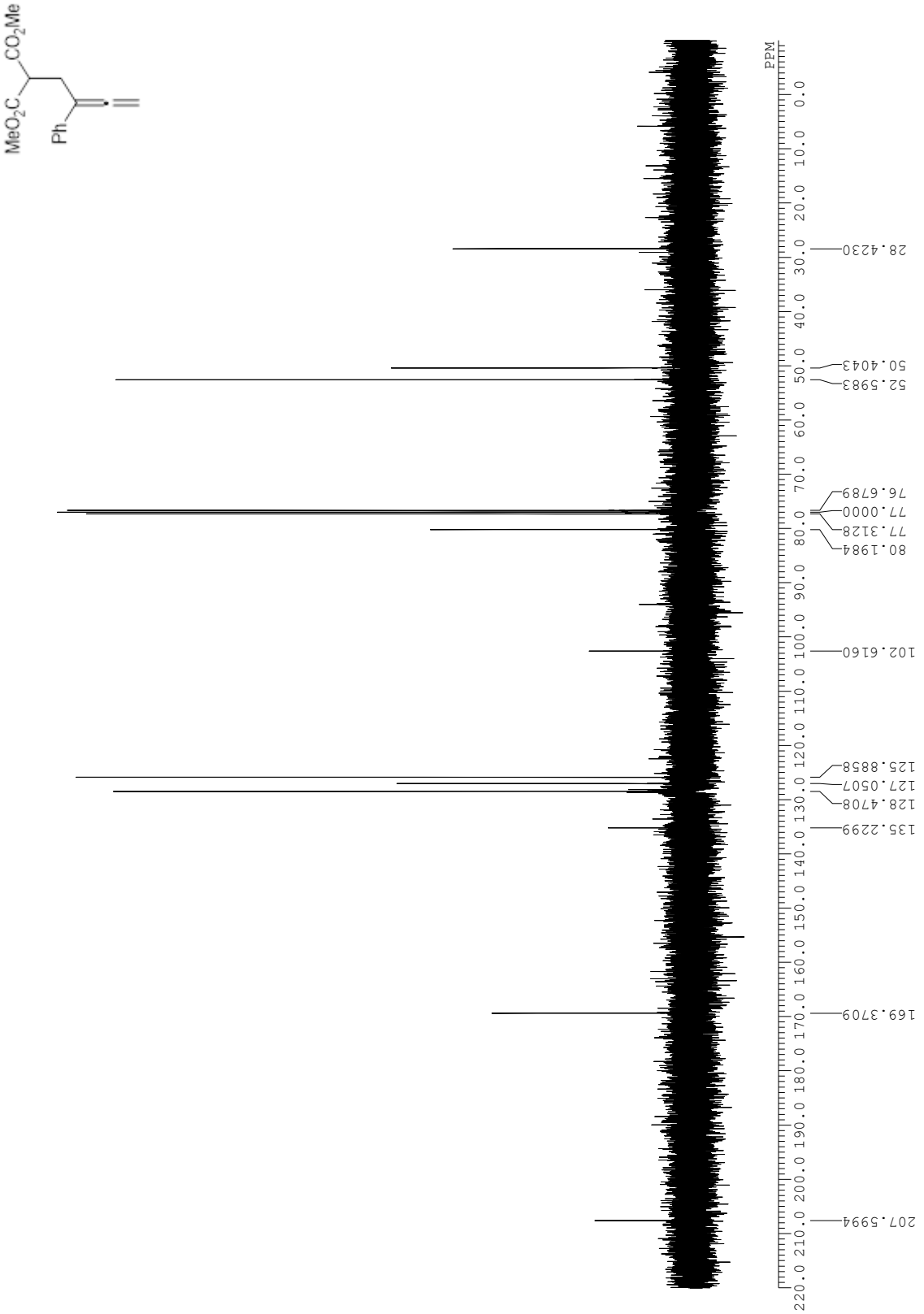
^{13}C NMR spectrum of **5bF**



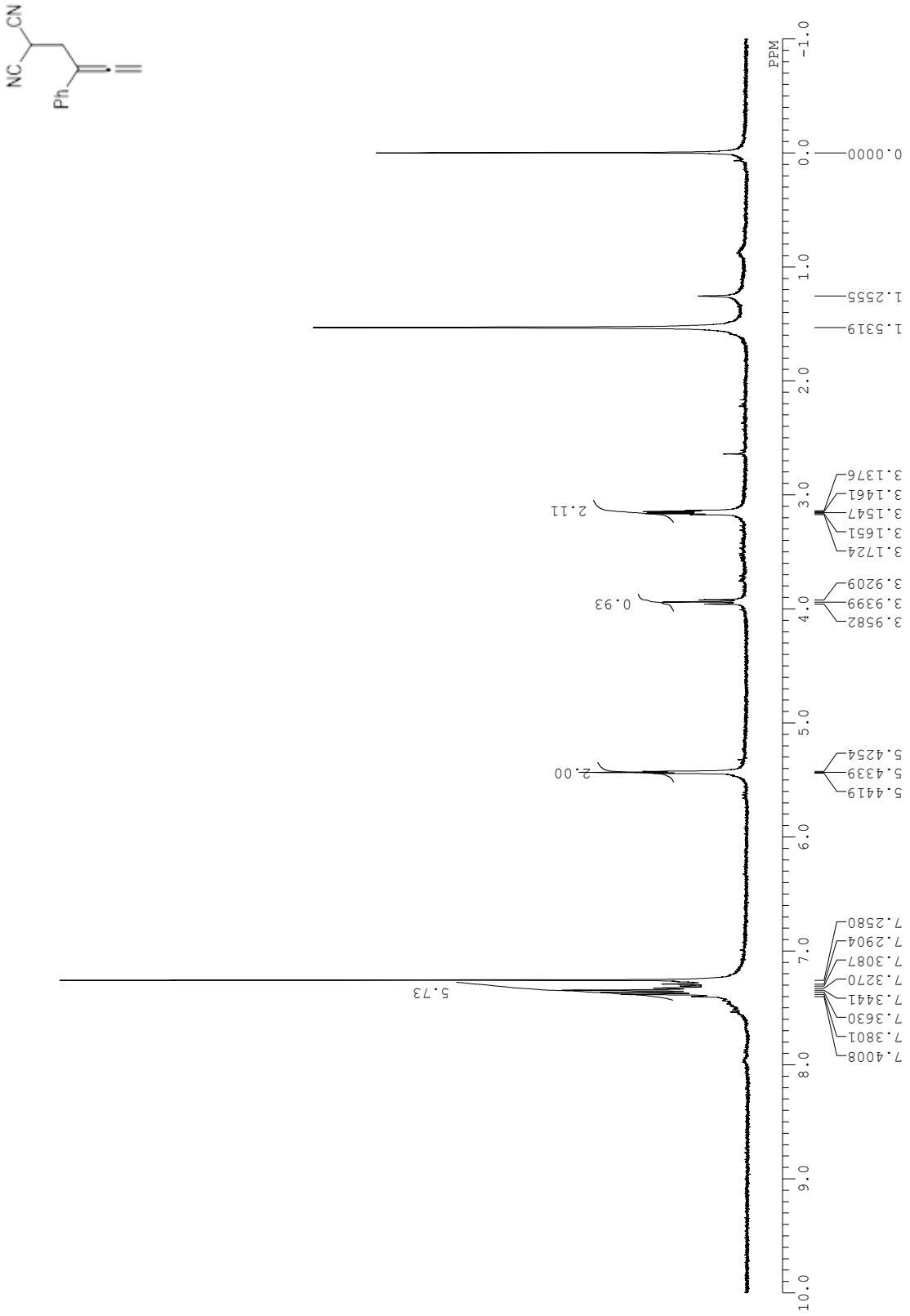
^{1}H NMR spectrum of **5bG**



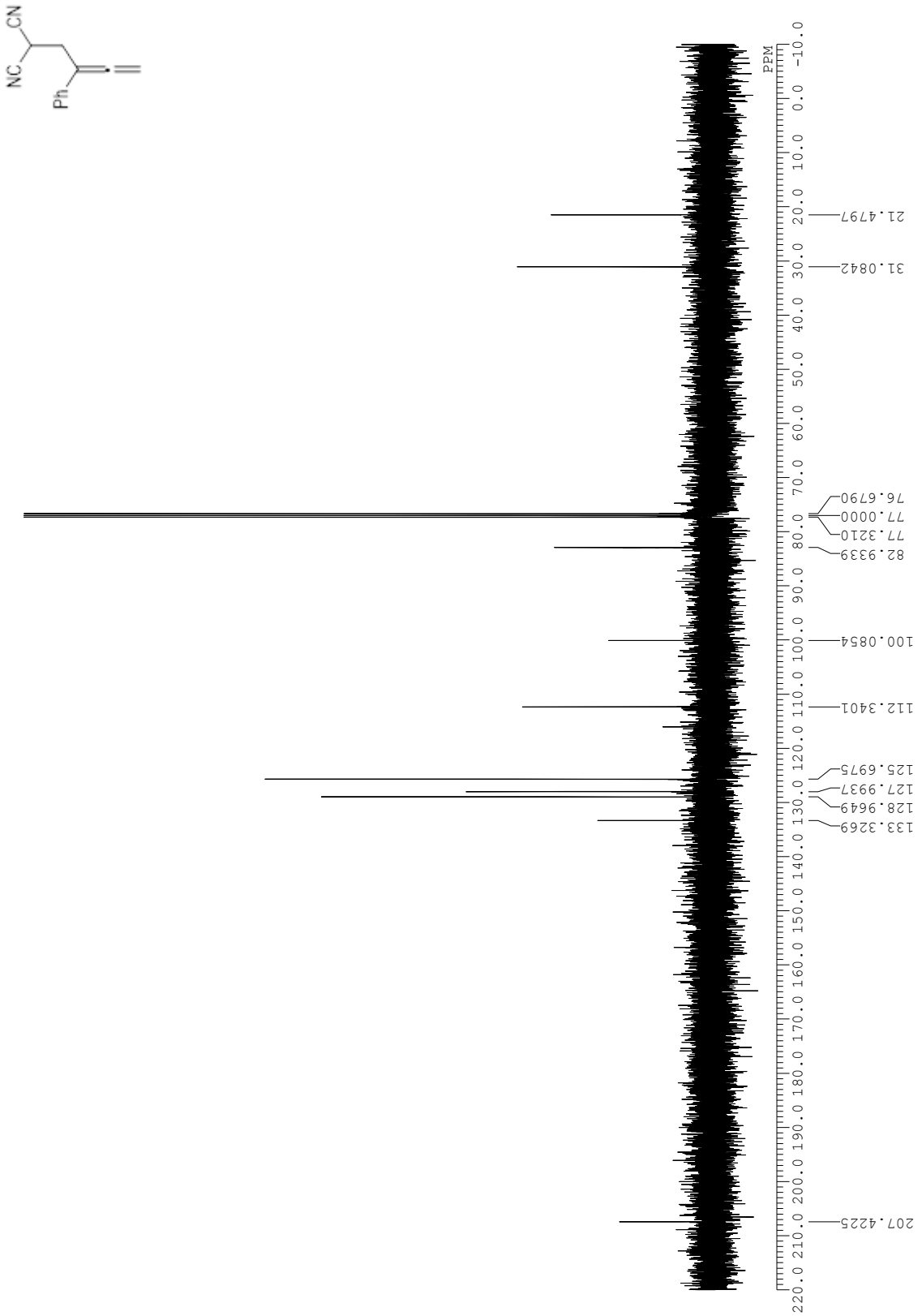
^{13}C NMR spectrum of **5bG**



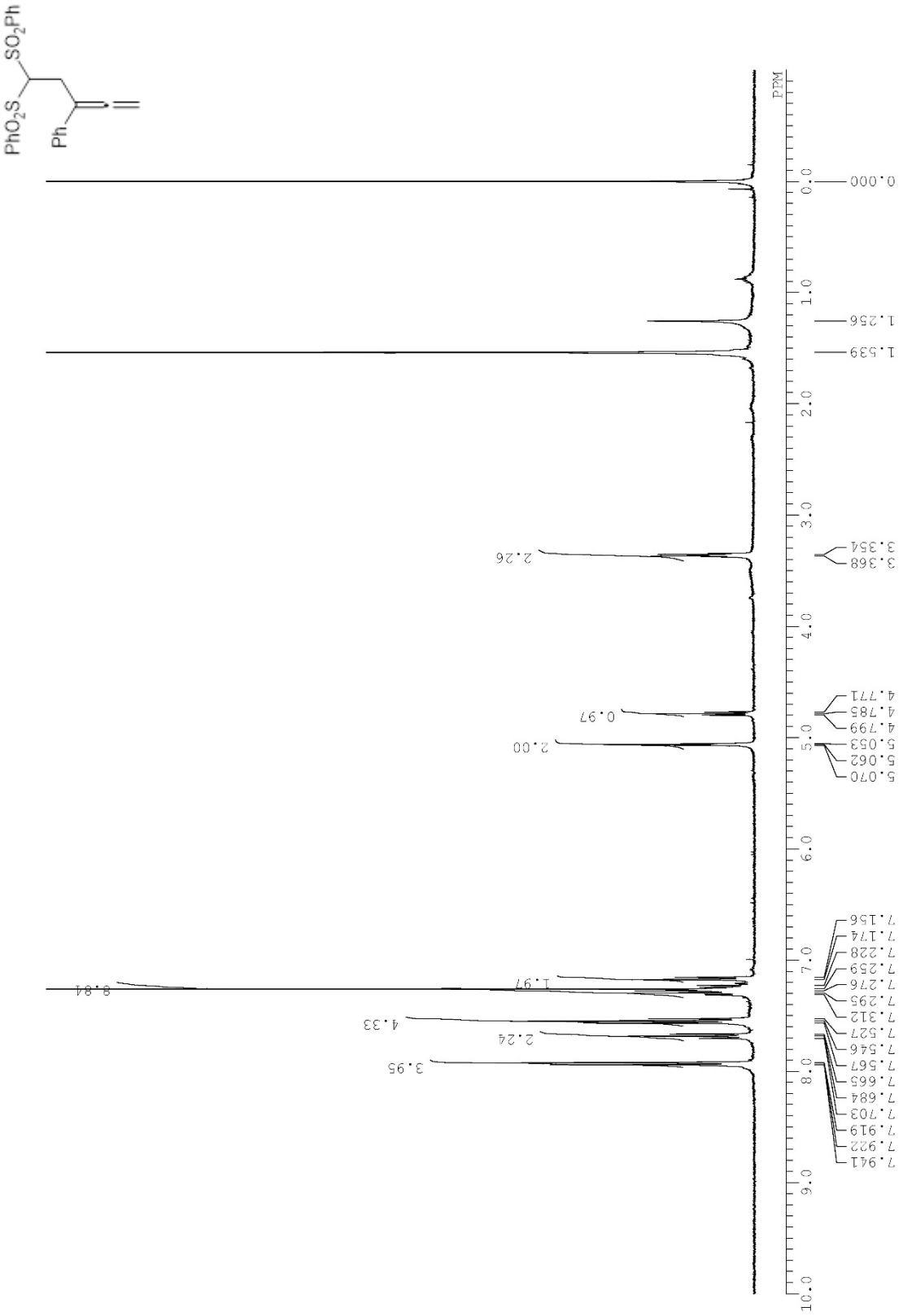
^{1}H NMR spectrum of **5bH**



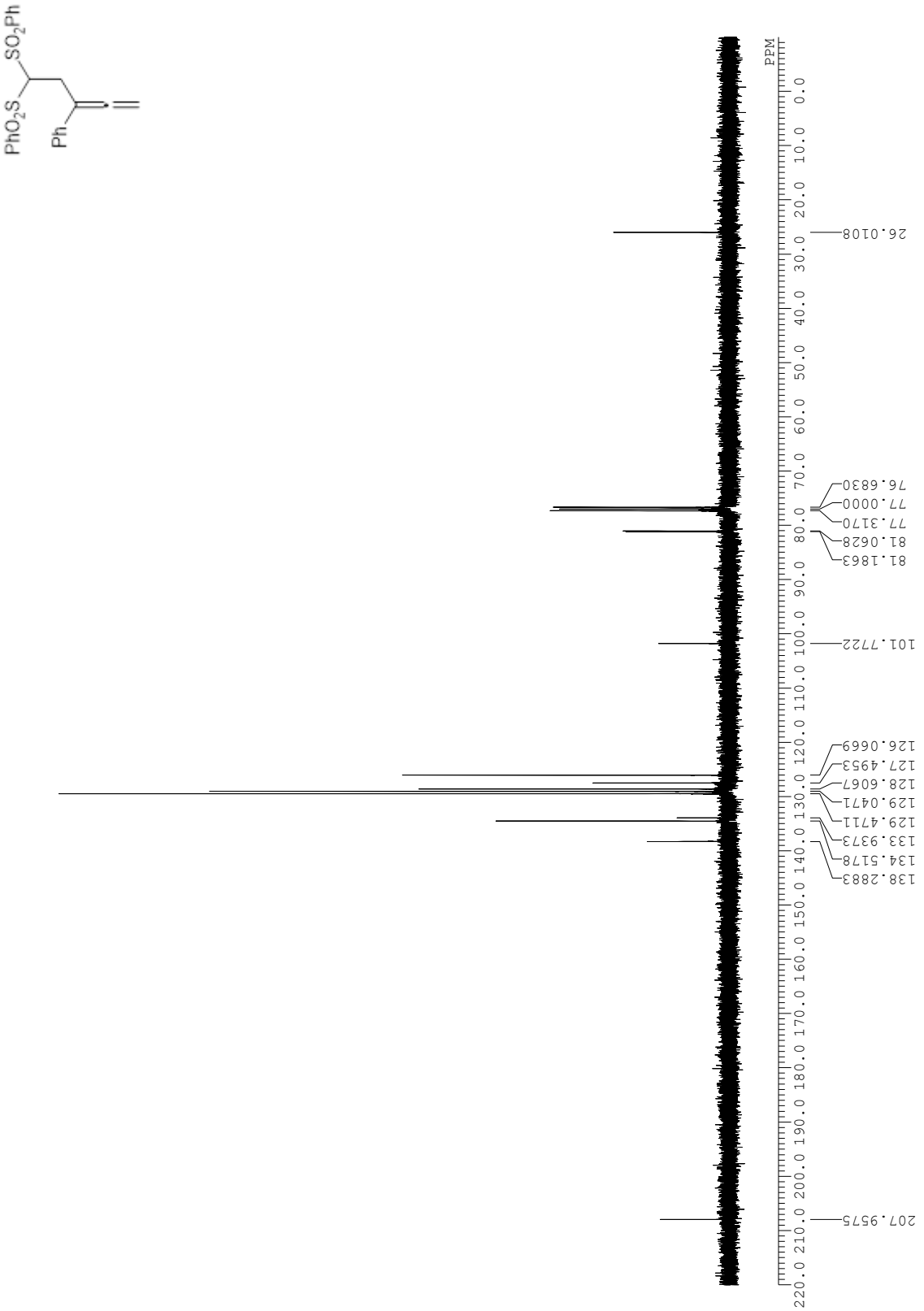
^{13}C NMR spectrum of **5bH**



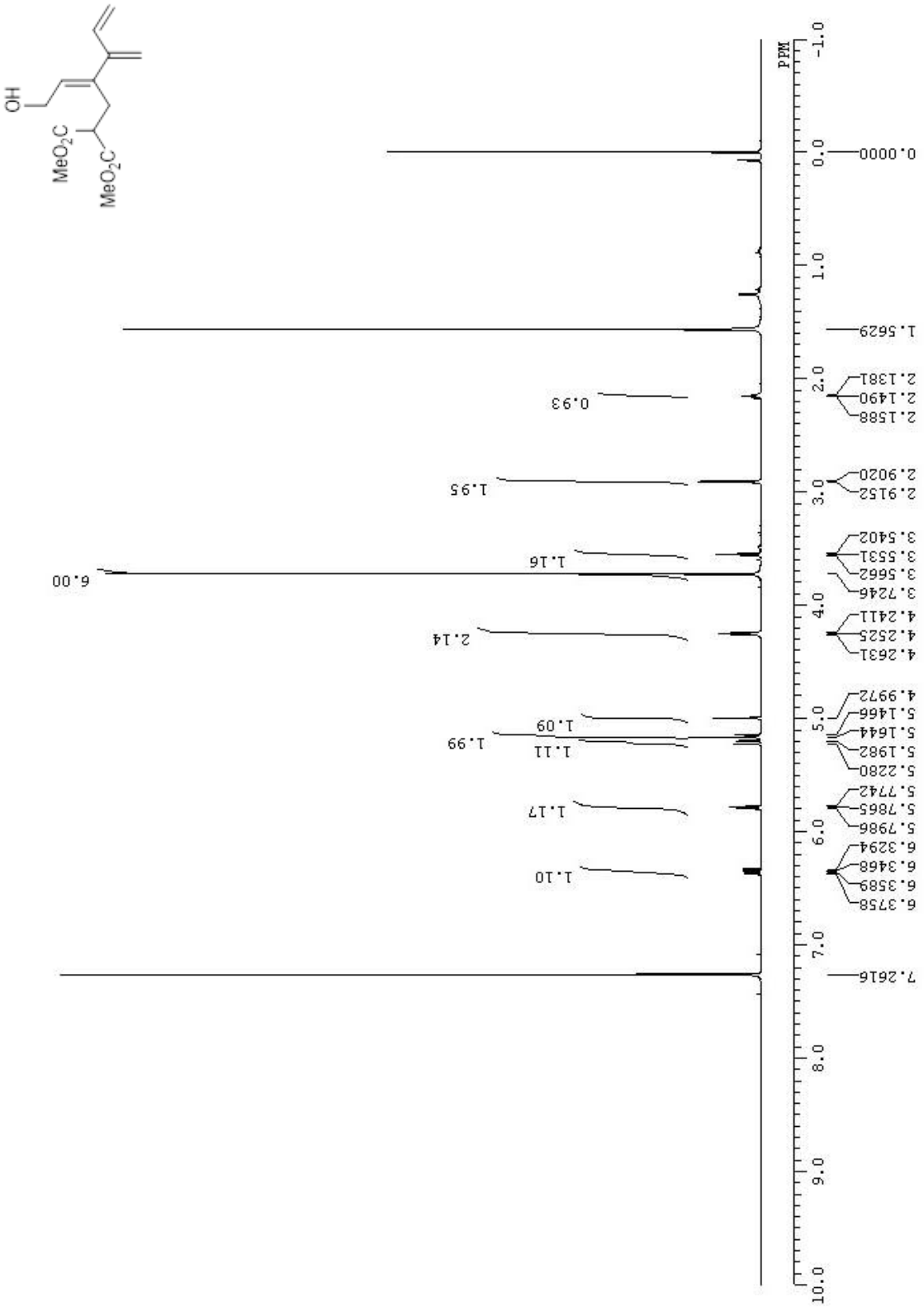
^{1}H NMR spectrum of **5bl**



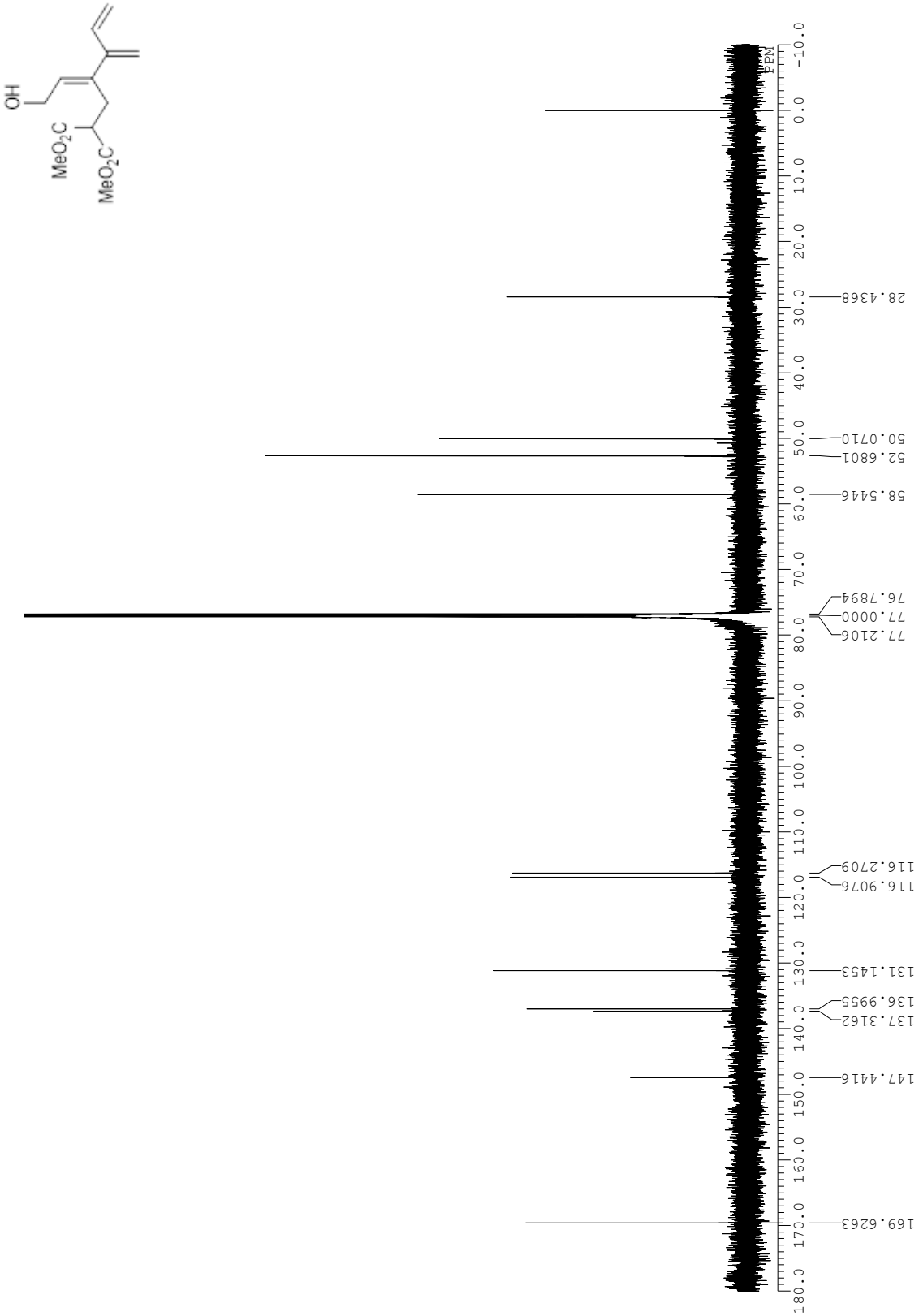
^{13}C NMR spectrum of **5bI**



^{1}H NMR spectrum of **10iG**



^{13}C NMR spectrum of **10iG**



NOESY spectrum of **10iG**