A cascade Heck-Aldol-Heck reaction by a combination of transition-metal and aminocatalysis

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Electronic supplementary information

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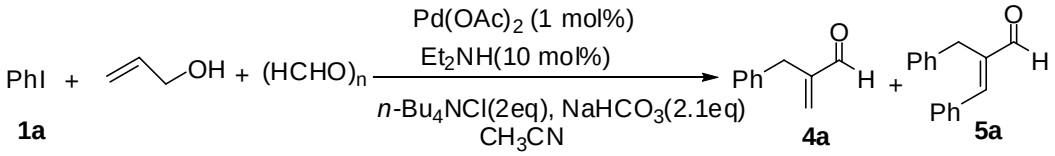
Experimental section

Part I. Optimization of reaction conditions and synthesis of starting materials

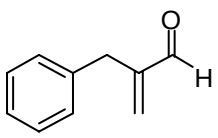
Table 1. Optimization of ratios of substrates[a]



entry	molar ratio **1a** : propenol	time (h)	yield (%)[b] **4a**:**5a**
1	1:1.1	10	45:13
2	1.5:1	12	38:21
3	2:1	12	0:54
4	1:2	10	56:3
5	1:2.5	10	58:0

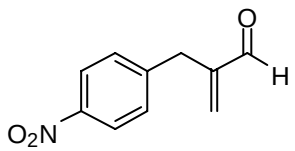
[a] The reaction of aryl iodide **1a**, propenol and paraformaldehyde (2.25 mmol) in acetonitrile (0.5 mL) was performed under the catalysis of $Pd(OAc)_2$ (0.0045 mmol, 1 mol%) and Et_2NH (0.045 mmol, 10 mol%) in the presence of *n*-Bu_4NCl (0.90 mmol) and $NaHCO_3$ (0.95 mmol) at 60℃ under nitrogen. [b]Isolated yields.

2-Benzylacrylaldehyde **4a**[1]



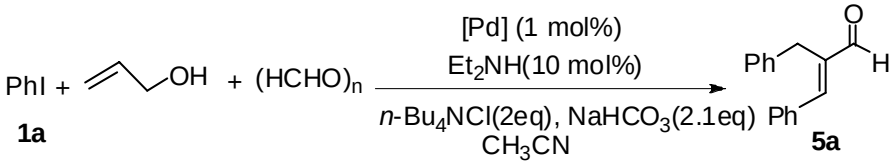
^{1}H NMR(300 MHz, $CDCl_3$), δ (ppm): 9.62 (s, 1 H), 7.36-7.17 (m, 5 H), 6.12 (s, 1 H), 6.07 (s,1 H), 3.59 (s, 2 H);

2-(4-Nitrobenzyl)acrylaldehyde



^{1}H NMR(300 MHz, $CDCl_3$), δ (ppm): 9.54 (s, 1 H), 8.60 (d, J=8.8Hz, 2 H), 7.31 (d, J=8.6 Hz, 2H), 6.21 (s, 1 H), 6.14 (s,1 H), 3.62 (s, 2 H); ^{13}C NMR(75 MHz, $CDCl_3$), δ (ppm): 193.51, 148.02, 146.67, 146.14, 136.05, 129.89, 123.73, 34.25; MS(EI) *m/z*: 191.1 (M^+,0.13), 174.0 (94.3), 145.0 (47.3), 144.0 (60.4), 115.0 (100.0).

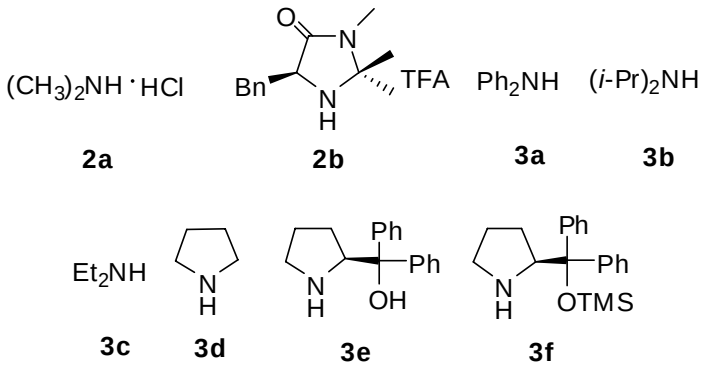
Table2. Screening of various transitional-metal catalysts[a]



1a **5a**

entry	transitional-metal catalyst	time (h)	yield (%)[b]
1	$Pd(OAc)_2$	12	54
2	$Pd(Ph_3P)_4$	16	0
3	$Pd(Ph_3P)_2Cl_2$	24	0
4	$PdCl_2$	24	43
5	$Pd[(PhCHCH)_2CO]_2$	16	40
6	CuI	24	0
7	—	24	0

[a] The reaction of aryl iodide **1a** (0.90 mmol), propenol (0.45 mmol) and paraformaldehyde (2.25 mmol) in acetonitrile (0.5 mL) was performed under the catalysis of transition-metal catalyst (0.0045 mmol, 1 mol%) and Et_2NH (0.045 mmol,10 mol%) in the presence of *n*-Bu_4NCl (0.90 mmol) and $NaHCO_3$ (0.95 mmol) at 60℃ under nitrogen. [b]Isolated yields of **5a**.

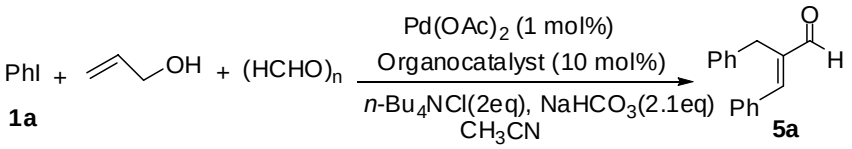


2a **2b** **3a** **3b**

3c **3d** **3e** **3f**

Scheme 1. Various organocatalysts

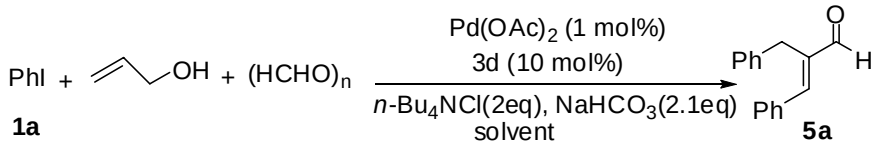
Table 3 Screening of various organocatalysts[a]



entry	organocatalyst	time (h)	yield (%)[b]
1	**2a**	12	52
2	**2b**	24	26
3	**3a**	12	56
4	**3b**	24	41
5	**3c**	12	54
6	**3d**	10	62
7	**3e**	10	50
8	**3f**	12	46

[a] The reaction of aryl iodide **1a** (0.90 mmol), propenol (0.45 mmol) and paraformaldehyde (2.25 mmol) in acetonitrile (0.5 mL) was performed under the catalysis of $Pd(OAc)_2$ (0.0045 mmol, 1 mol%) and organocatalyst (0.045 mmol,10 mol%) in the presence of *n*-Bu_4NCl (0.90 mmol) and $NaHCO_3$ (0.95 mmol) at 60℃ under nitrogen. [b]Isolated yields of **5a**.

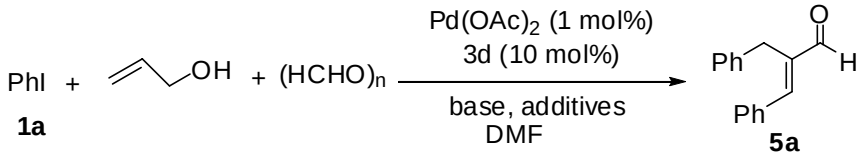
Table 4 Screening of various solvents[a]



entry	solvent	time (h)	yield[b] (%)
1	MeCN	10	62
2	NMP	8	60
3	THF	24	41
4	$CHCl_3$	24	45
5	1,4-Dioxane	16	51
6	DMF	8	70
7[c]	DMF	36	18
8[d]	DMF	8	68

[a] The reaction of aryl iodide **1a** (0.90 mmol), propenol (0.45 mmol) and paraformaldehyde (2.25 mmol) in a solvent (0.5 mL) was performed under the catalysis of $Pd(OAc)_2$ (0.0045 mmol, 1 mol%) and 3d (0.045 mmol,10 mol%) in the presence of *n*-Bu_4NCl (0.90 mmol) and $NaHCO_3$ (0.95 mmol) at 60℃ under nitrogen. [b] Isolated yields of **5a**. [c] In the absence of 3d. [d] The reaction of aryl iodide **1a** (10.00 mmol), propenol (5.00 mmol) and paraformaldehyde (25.00 mmol) in DMF (5.5 mL) was performed under the catalysis of $Pd(OAc)_2$ (0.05 mmol, 1 mol%) and pyrrolidine **3d** (0.5 mmol, 10 mol%) in the presence of *n*-Bu_4NCl (10.00 mmol) and $NaHCO_3$ (10.56 mmol) at 60℃ under nitrogen.

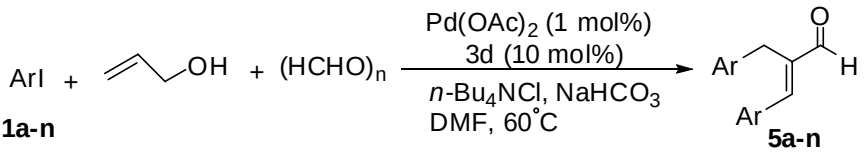
Table 5 Screening of various bases and additives[a]



entry	base	additive	t (℃)	time (h)	yield (%)[b]
1	Et_3N	-	60	12	42
2	*n*-Bu_3N	-	60	12	53
3	K_2CO_3	-	60	24	22
4	Na_2CO_3	-	60	24	12
5	$NaHCO_3$	-	60	24	10
6	K_2CO_3	*n*-Bu_4NCl	60	12	58
7	Na_2CO_3	*n*-Bu_4NCl	60	12	48
8	NaOAc	*n*-Bu_4NCl	60	12	54
9	$NaHCO_3$	*n*-Bu_4NCl	60	12	70
10	$NaHCO_3$	*n*-Bu_4NBr	60	24	41
11	$NaHCO_3$	*n*-Bu_4NI	60	24	32
12	$NaHCO_3$	*n*-Bu_4NCl	40	12	42
13	$NaHCO_3$	*n*-Bu_4NCl	80	12	50
14	$NaHCO_3$	*n*-Bu_4NCl	110	12	45

[a] The reaction of aryl iodide **1a** (0.90 mmol), propenol (0.45 mmol) and paraformaldehyde (2.25 mmol) in DMF (0.5 mL) was performed under the catalysis of $Pd(OAc)_2$ (0.0045 mmol, 1 mol%) and 3d (0.045 mmol,10 mol%) in the presence of a base (0.95 mmol) and an additive (0.90 mmol) at 60℃ under nitrogen. [b] Isolated yields of **5a**.

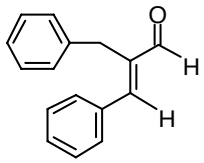
Part II. Cascade reaction by a combination of palladium(0) and aminocatalysis for the synthesis of (*E*)-trisubstituted alkenes



General procedure with one aryl iodide: The mixture of propenol (0.0261 g, 0.45 mmol), paraformaldehyde (0.0615 g, 2.05 mmol), $Pd(OAc)_2$ (1.0 mg,0.0045 mmol), *n*-Bu_4NCl (0.250 g, 0.90 mmol) and $NaHCO_3$ (0.0798 g, 0.95mmol) in DMF (0.5 mL) was stirred for 10 min at 60℃, and then aryl iodide **1a-n** (0.90 mmol) and pyrrolidine **3d** (3.20 mg, 0.045 mmol, 10 mol%) were added. The reaction mixture was stirred at 60℃ for the time indicated in Table 2 of the text under nitrogen. After the reaction was finished, EtOAc was added to the reaction system. The mixture

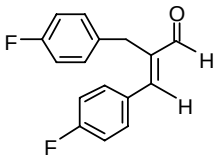
was filtered, and the filtrate was washed with water and brine, and dried over $MgSO_4$. After concentration, the residue was subjected to column chromatography (silica gel, petroleum ether / EtOAc as eluent) to give the desired trisubstituted alkene **5a-n**.

(*E*)-2-Benzyl-3-phenylacrylaldehyde **5a**[2]



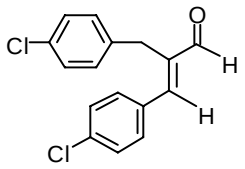
Yield: 70%. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.71 (s, 1 H), 7.54-7.35 (m, 6 H), 7.32-7.14 (m, 5 H), 3.96 (s, 2 H).

(*E*)-2-(4-Fluorobenzyl)-3-(4-fluorophenyl)acrylaldehyde **5b**



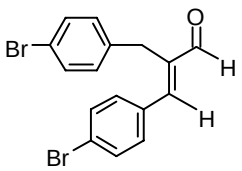
Yield: 81%. ^{1}H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.68 (s, 1 H), 7.52-7.40 (m, 3 H), 7.20-7.02 (m, 4 H), 7.00-6.90 (m, 2 H), 3.89 (s, 2 H); ^{13}C NMR(75 MHz, $CDCl_3$) δ (ppm): 194.9, 164.2 (d, *J*=155.3 Hz), 160.9 (d, *J*=146.8 Hz), 150.3, 140.1, 133.7 (d, *J*=3.0 Hz), 131.9 (d, *J*=8.6 Hz), 130.6 (d, *J*=3.8 Hz), 129.4 (d, *J*=8.0 Hz), 116.1 (d, *J*=21.2 Hz), 115.5 (d, *J*=20.2 Hz), 29.5; IR (film): 3091, 2960, 2829, 2795, 1696, 1640, 1583, 1505, 1231, 1151, 846, 774 cm^{-1}; MS (EI) *m/z*: 258.0 (M^+, 49.8), 228.0 (55.0), 134.0 (30.6), 133.0 (100.0), 109.0 (63.6).

(*E*)-2-(4-Chlorobenzyl)-3-(4-chlorophenyl)acrylaldehyde **5c**



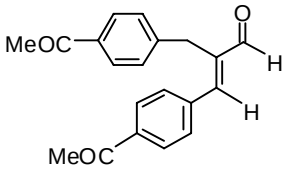
Yield: 75%. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.67 (s, 1 H), 7.46 (s, 1 H), 7.42-7.36 (m, 4 H), 7.27-7.19 (m, 2 H), 7.10-7.00 (m, 2 H), 3.87 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 194.68, 150.19, 140.43, 136.53, 136.24, 132.76, 132.22, 130.95, 129.29, 129.24, 128.83, 29.80; IR (film): 3066, 2928, 2826, 2817, 1686, 1632, 1590, 1491, 1146, 1092, 1013, 824, 804, cm^{-1}; MS (EI) *m/z*: 290.0 (M^+, 1.7), 255.0 (100.0), 149.0 (30.2), 143.0 (97.2), 125.0 (62.5), 115.0 (81.2).

(*E*)-2-(4-Bromobenzyl)-3-(4-bromophenyl)acrylaldehyde **5d**



Yield: 77%. ^{1}H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.68 (s, 1H), 7.60-7.48 (m, 2 H), 7.44(s, 1 H), 7.42-7.27 (m, 4 H), 7.10（d, *J*=8.7 Hz, 2 H）, 3.85 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 194.63, 150.22, 140.47, 137.03, 133.16, 132.23, 131.78, 131.10, 129.68, 124.68, 120.32, 29.89; IR (film): 3063, 2933, 2845, 2732, 1681, 1625, 1586, 1488, 1141, 1071, 1009, 818, 803 cm^{-1}; MS (EI) *m/z*: 379.9 [$(M+2)^+$, 3.0)], 301.0 (97.9), 298.0 (100.0), 191.1 (75.4), 189.0 (74.3), 168.9 (48.8), 143.0 (94.3), 115.0 (95.4).

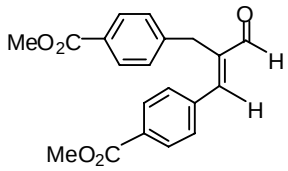
(*E*)-2-(4-Acetylbenzyl)-3-(4-acetylphenyl)acrylaldehyde **5e**



Yield: 73%. ^{1}H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.73(s, 1 H), 7.97 (d, *J*=8.4 Hz, 2 H), 7.87 (d, *J*=8.4 Hz, 2 H), 7.58 (s, 1 H), 7.51 (d, *J*=8.4 Hz, 2 H), 7.22 (d, *J*=8.4 Hz, 2 H), 3.97 (s, 2 H), 2.60 (s, 3 H), 2.56(s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 197.63, 197.15, 194.45, 150.07, 145.66, 143.71, 141.44, 138.60, 135.60, 129.66, 128.85,

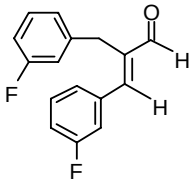
128.77, 128.17, 30.61, 26.68, 26.56; IR (film):3088, 2968, 2810, 2802, 1691, 1682, 1627, 1608, 1463, 1269, 1182, 1019, 833, 791 cm^{-1}; MS (ESI) *m/z* $[M+Na]^+$ Calcd for $C_{20}H_{18}NaO_3$: 329.13, found: 329.25.

(*E*)-2-(4-Methoxylcarbonylbenzyl)-3-(4-Methoxylcarbonylphenyl)acrylaldehyde **5f**



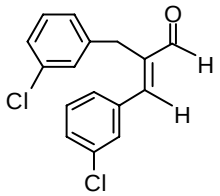
Yield: 78%. ^1H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.73(s, 1 H), 8.04 (d, *J*=8.4 Hz, 2 H), 7.93 (d, *J*=8.4 Hz, 2 H), 7.57 (s, 1 H), 7.47 (d, *J*=8.4 Hz, 2 H), 7.19(d, *J*=8.4 Hz, 2 H), 3.96 (s, 2 H), 3.92 (s, 3 H), 3.89 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 194.54, 166.89, 166.27, 150.26, 143.51, 141.42, 138.50, 131.16, 130.03, 129.40, 128.46, 128.00, 52.39, 52.07, 30.56; IR (film): 3041, 2954, 2841, 2728, 1724, 1674, 1623, 1565, 1434, 1285, 1187, 1108, 833, 810 cm^{-1} ; MS (ESI) *m/z* $[M+Na]^+$ Calcd for $C_{20}H_{18}NaO_5$: 361.12, found 361.17.

(*E*)-2-(3-Fluorobenzyl)-3-(3-fluorophenyl)acrylaldehyde **5g**



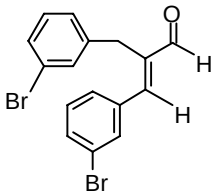
Yield: 78%. ^1H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.70 (s, 1 H), 7.49 (s, 1 H), 7.43-7.33 (m, 1 H), 7.30-7.19 (m, 2 H), 7.18-7.03 (m, 2 H), 7.00-6.79 (m, 3 H), 3.92 (s, 2 H); ^{13}C NMR(75 MHz, $CDCl_3$) δ (ppm): 194.6, 164.6 (d, *J*=21.2 Hz), 161.3 (d, *J*＝23.8 Hz), 150.1 (d, *J*=2.6 Hz), 140.9, 140.6 (d, *J*=6.5 Hz), 136.3 (d, *J*=7.4 Hz), 130.4 (d, *J*=8.3 Hz), 130.1 (d, *J*=9.0 Hz), 125.4 (d, *J*=2.6 Hz), 123.6 (d, *J*=2.8 Hz), 117.0 (d, *J*=20.9 Hz), 116.3 (d, *J*=22.4 Hz), 114.9 (d, *J*=20.8 Hz), 113.4 (d, *J*=20.6 Hz), 30.1 (d, *J*=1.9 Hz); IR (film): 3096, 2956, 2823, 2788, 1698, 1645, 1569, 1496, 1257, 1129, 850, 791, 750 cm^{-1}; MS (EI) *m/z*: 258.1 (M^+, 100.0), 228.1 (32.3), 149.0 (30.2), 133.0 (93.5), 109.0 (49.6).

(*E*)-2-(3-Chlorobenzyl)-3-(3-chlorophenyl)acrylaldehyde **5h**



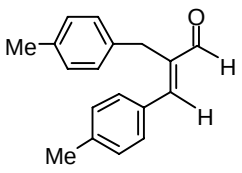
Yield: 74%. ^1H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.69 (s, 1 H), 7.48-7.27 (m, 5 H), 7.26-7.10 (m, 3 H), 7.05-6.95 (m, 1 H), 3.88 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 194.57, 149.94, 141.00, 140.13, 135.97, 134.91, 134.54, 130.19, 129.98, 129.93, 129.55, 128.13, 127.45, 126.71, 126.25, 30.12; IR (film):3077, 2881, 2822, 2813, 1688, 1636, 1575, 1478, 1264, 833, 750, 721 cm^{-1}; MS (EI) *m/z*: 290.0 (M^+,15.6), 255.0 (100.0), 149.0 (53.2), 143.0 (76.9), 115.0 (57.52).

(*E*)-2-(3-Bromobenzyl)-3-(3-bromophenyl)acrylaldehyde **5i**



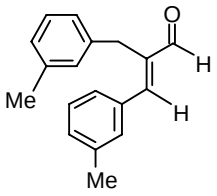
Yield: 76%. ^1H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.68 (s, 1 H), 7.62-7.40 (m, 3 H), 7.39-7.20 (m, 4 H), 7.19-7.00 (m, 2 H), 3.86 (s, 2 H); ^{13}C NMR(75 MHz, $CDCl_3$) δ (ppm): 194.53, 149.88, 141.04, 140.48, 136.23, 132.87, 132.46, 131.07, 130.43, 130.25, 129.64, 127.85, 126.72, 122.97, 122.85, 30.09; IR (film):3065, 2831, 2841, 2730, 1683, 1631, 1569, 1466, 1192, 827, 786, 707 cm^{-1}; MS (EI) *m/z*: 379.9 [$(M+2)^+$, 12.4], 300.9 (74.6), 298.9 (95.5), 191.0 (54.1), 143.0 (100.0), 115.0 (76.6).

(*E*)-2-(4-Methylbenzyl)-3-(4-methylphenyl)acrylaldehyde **5j**



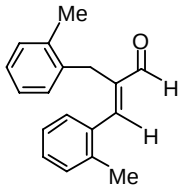
Yield: 69%. ^{1}H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.68 (s, 1 H), 7.55-7.37 (m, 3 H), 7.27-7.18 (m, 2 H), 7.08 (s, 4 H), 3.93 (s, 2 H), 2.38 (s, 3 H), 2.31 (s, 3 H); ^{13}C NMR(75 MHz, $CDCl_3$) δ (ppm): 195.33, 151.65, 140.53, 139.84, 135.70, 135.25, 131.82, 130.03, 129.63, 129.33, 127.86, 30.07, 21.49, 21.03; IR (film): 3044, 2963, 2827, 2734, 1689, 1629, 1606, 1577, 1450, 1209, 1159, 837, 810 cm^{-1}; MS (ESI) *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{18}NaO$: 273.14, found: 273.25.

(*E*)-2-(3-Methylbenzyl)-3-(3-methylphenyl)acrylaldehyde **5k**



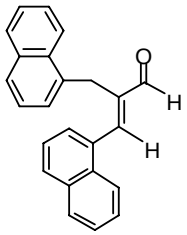
Yield: 68%. ^{1}H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.70 (s, 1 H), 7.48 (s, 1 H), 7.35-7.14 (m, 5 H), 7.03-6.95 (m, 3 H), 3.92 (s, 2 H), 2.36 (s, 3 H), 2.32 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 195.37, 151.85, 140.58, 138.54, 138.52, 138.20, 134.58, 130.82, 130.76, 128.90, 128.79, 128.53, 127.06, 126.87, 125.08, 30.49, 21.55, 21.43; IR (film): 3066, 2962, 2822, 2728, 1691, 1626, 1603, 1588, 1431, 1261, 1143, 829, 783, 686 cm^{-1}; MS (ESI) *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{18}NaO$: 273.14, found: 273.25.

(*E*)-2-(2-Methylbenzyl)-3-(2-methylphenyl)acrylaldehyde **5l**



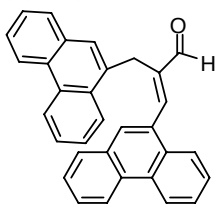
Yield: 67%. ^{1}H NMR(300 MHz, $CDCl_3$) δ (ppm): 9.74 (s, 1 H), 7.70 (s, 1 H), 7.24-7.18 (m, 2 H), 7.17-7.00 (m, 5 H), 6.94–6.82 (m, 1 H), 3.69 (s, 2 H), 2.35 (s, 3H), 2.23 (s, 3H); ^{13}C NMR(75 MHz, $CDCl_3$) δ (ppm): 194.94, 150.19, 141.44, 137.14, 136.87, 136.30, 133.71, 130.53, 130.18, 129.64, 128.20, 127.08, 126.25, 126.12, 126.09, 28.31, 20.05, 19.79; IR (film): 3041, 2926, 2856, 2733, 1697, 1623, 1605, 1573, 1438, 1211, 1150, 823, 754 cm^{-1}; MS (EI) *m/z*: 250.2 (M^+, 49.1), 235.1 (85.6), 145.1 (100.0), 129.1 (64.4), 115.1 (90.6), 105.1 (82.2), 91.1 (43.6).

(*E*)-3-(Naphthalen-1-yl)-2-(naphthalen-1-ylmethyl)acrylaldehyde **5m**



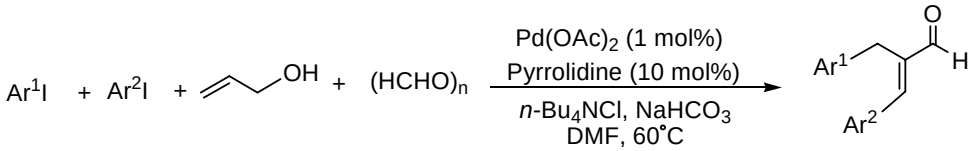
Yield: 66%. ^{1}H NMR($CDCl_3$) δ (ppm): 9.98 (s, 1 H), 8.32 (s, 1 H), 8.10-7.97 (m, 1 H), 7.95-7.80 (m, 4 H), 7.71 (d, *J*=8.1 Hz, 1 H), 7.65-7.55 (m, 2 H), 7.50-7.43 (m, 1 H), 7.40-7.25 (m, 4 H), 7.17 (d, *J*=7.2 Hz, 1 H), 4.28 (s, 1 H); ^{13}C NMR(75 MHz, $CDCl_3$) δ (ppm): 194.65, 149.49, 142.42, 134.28, 133.84, 133.52, 131.32, 131.23, 130.95, 130.11, 128.84, 128.70, 127.59, 127.04, 126.94, 126.42, 125.91, 125.60, 125.48, 125.35, 124.92, 123.90, 123.54, 28.56; IR (film): 3051, 2866, 2836, 2726, 1688, 1620, 1575, 1443, 1218, 1170, 825, 803, 772 cm^{-1}; MS (EI) *m/z*: 322.2 (M^+, 30.9), 303.1(16.2), 165.1 (100.0), 141.1 (49.4), 115.1 (17.7).

(*E*)-3-(Phenanthren-9-yl)-2-(phenanthren-9-ylmethyl)acrylaldehyde **5n**



Yield: 68%. ^{1}H NMR(300 MHz, $CDCl_3$) δ (ppm): 10.00 (s, 1 H), 8.75-8.42 (m, 4 H), 8.23 (s, 1 H), 7.96 (d, *J*=7.2 Hz, 1 H), 7.86 (d, *J*=8.1 Hz, 1 H), 7.70-7.41 (m, 8 H), 7.40-7.29 (m, 3 H), 7.26-7.18 (m, 1 H), 4.29 (s, 2 H); ^{13}C NMR(75 MHz, $CDCl_3$) δ (ppm): 194.67, 150.09, 146.34, 142.72, 132.72, 131.63, 131.06, 130.69, 130.38, 130.28, 130.00, 129.90, 129.78, 129.33, 128.99, 128.91, 128.34, 127.69, 127.07, 126.91, 126.62, 126.57, 126.34, 126.25, 126.08, 124.72,

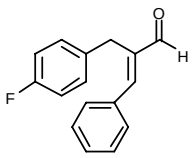
124.17, 123.27, 123.14, 122.46, 122.38, 28.95; IR (film): 3056, 2863, 2825, 2718, 1681, 1622, 1606, 1448, 1224, 1071, 841, 822, 751 cm^{-1}; MS (EI) *m/z*: 422.2 (M^+, 50.7), 244.0 (21.3), 216.0 (22.0), 215.0 (100.0) , 191.0 (58.9).



5o-r

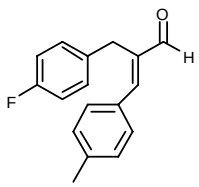
General procedure with two aryl iodides: The mixture of propenol (0.0261 g, 0.45 mmol), paraformaldehyde (0.0615 g, 2.05 mmol), $Pd(OAc)_2$ (1.0 mg,0.0045 mmol), *n*-Bu_4NCl (0.250 g, 0.90 mmol) and $NaHCO_3$ (0.0798 g, 0.95mmol) in DMF (0.5 mL) was stirred for 10 min at 60℃, and then Ar^1I (0.45 mmol), Ar^2I (0.45 mmol) and pyrrolidine **3d** (3.20 mg, 0.045 mmol, 10 mol%) were added. The reaction mixture was stirred at 60℃ for the time indicated in Table 3 of the text under nitrogen. A similar work-up to the above general procedure with one aryl iodide afforded the desired trisubstituted alkene **5o-r**.

(*E*)-2-(4-Fluorobenzyl)-3-phenylacrylaldehyde **5o**



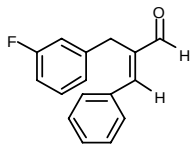
Yield: 63%. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.65 (s, 1 H), 7.60 -7.32 (m, 4 H), 7.30-6.82 (m, 6 H), 3.90 (d, *J*=8.1 Hz,2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 195.2, 165.2 (d, *J*=155.3 Hz), 151.8, 140.4, 134.5, 134.0 (d, *J*=3.9 Hz), 132.0 (d, *J*=8.3 Hz), 129.8, 128.8, 127.9, 116.1 (d, *J*=21.8 Hz), 30.3; IR (film): 3089, 2956, 2825, 2791, 1692, 1636, 1578, 1496, 1230, 1148, 829, 733 cm^{-1}; MS (EI) *m/z*: 240.0 (M^+, 62.9), 210.0 (59.4), 133.0 (54.9), 115.0 (46.8), 109.0 (100.0), 91.0 (95.9).

(*E*)-2-(4-Fluorobenzyl)-3-(4-tolyl)acrylaldehyde **5p**



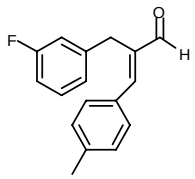
Yield: 58%. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.62 (d, *J*=5.7 Hz, 1 H), 7.52-7.30 (m, 3 H), 7.28-6.80 (m, 6 H), 3.87 (d, *J*=7.8 Hz, 2 H), 2.33 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 195.5, 164.2 (d, *J*=156.8 Hz), 152.3, 139.4, 135.0, 134.1 (d, *J*=2.8 Hz), 132.1 (d, *J*=8.5 Hz), 131.7, 130.1, 129.8, 116.1 (d, *J*=21.4 Hz) 29.9, 21.5; IR (film): 3091, 2949, 2819, 2769, 1691, 1630, 1569, 1489, 1228, 1141, 822, 730 cm^{-1}; MS (EI) *m/z*: 254.0 (M^+, 47.3), 239.0 (90.6), 143.0 (54.9), 133.0 (47.2), 115.0 (44.7), 109.0 (68.4), 105.0 (100.0), 91.0 (48.3).

(*E*)-2-(3-Fluorobenzyl)-3-phenylacrylaldehyde **5q**



Yield: 60%. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.68 (s, 1 H), 7.60-7.30 (m, 5 H), 7.26 (m, 3 H), 7. 00-6.80, 3.92 (s, 2 H), ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 195.1, 164.6 (d, *J*=22.5 Hz), 152.1, 141.1 (d, *J*=9.1 Hz), 139.8, 134.3, 130.5 (d, *J*=8.3 Hz), 129.8, 129.0, 128.0, 123.7 (d, *J*=2.7 Hz), 116.9 (d, *J*=21.6 Hz), 113.3 (d, *J*=21.7 Hz), 30.4; IR (film): 3092, 2952, 2822, 2783, 1693, 1633, 1573, 1492, 1229, 1140, 828, 753, 732 cm^{-1}; MS (EI) *m/z*: 240.0 (M^+, 100.0), 210.0 (79.2), 133.0 (66.1), 115.0 (66.1), 109.0 (43.8), 91.0 (51.2).

(*E*)-2-(3-Fluorobenzyl)-3-(4-tolyl)acrylaldehyde **5r**



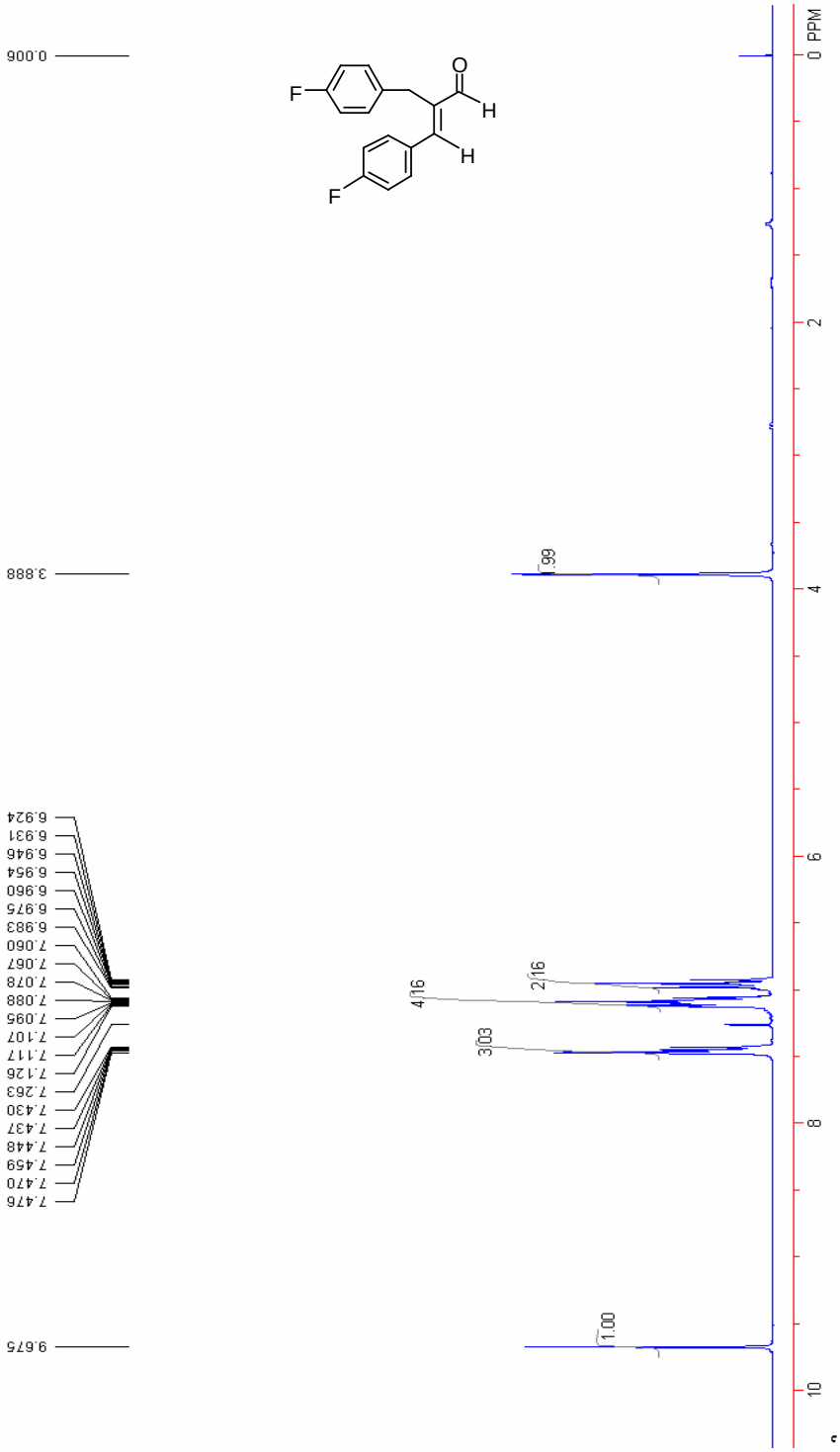
Yield: 56%. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 9.66 (d, *J*=3.9 Hz, 1 H), 7.54-7.30 (m, 2 H), 7.28-7.14 (m, 3 H), 7.12-6.80 (m, 4 H), 3.92 (d, *J*=10.2 Hz, 2 H), 2.36 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 195.1, 164.6 (d, *J*=23.3 Hz), 152.3, 141.1(d, *J*=7.7 Hz), 140.9, 138.9, 131.6, 130.5 (d, *J*=8.3 Hz), 130.0, 129.8, 123.7 (d, *J*=2.7 Hz), 116.8 (d, *J*=20.8 Hz), 113.2 (d, *J*=20.6 Hz), 30.0, 21.0; IR (film): 3088, 2946, 2818, 2772, 1688, 1632, 1576, 1493, 1228, 1146, 826, 751, 730 cm^{-1}; MS (EI) *m/z*: 254.0 (M^+, 66.0), 239.0 (100.0), 143.0 (42.8), 133.0 (59.4), 115.0 (31.1), 109.0 (19.2).

References

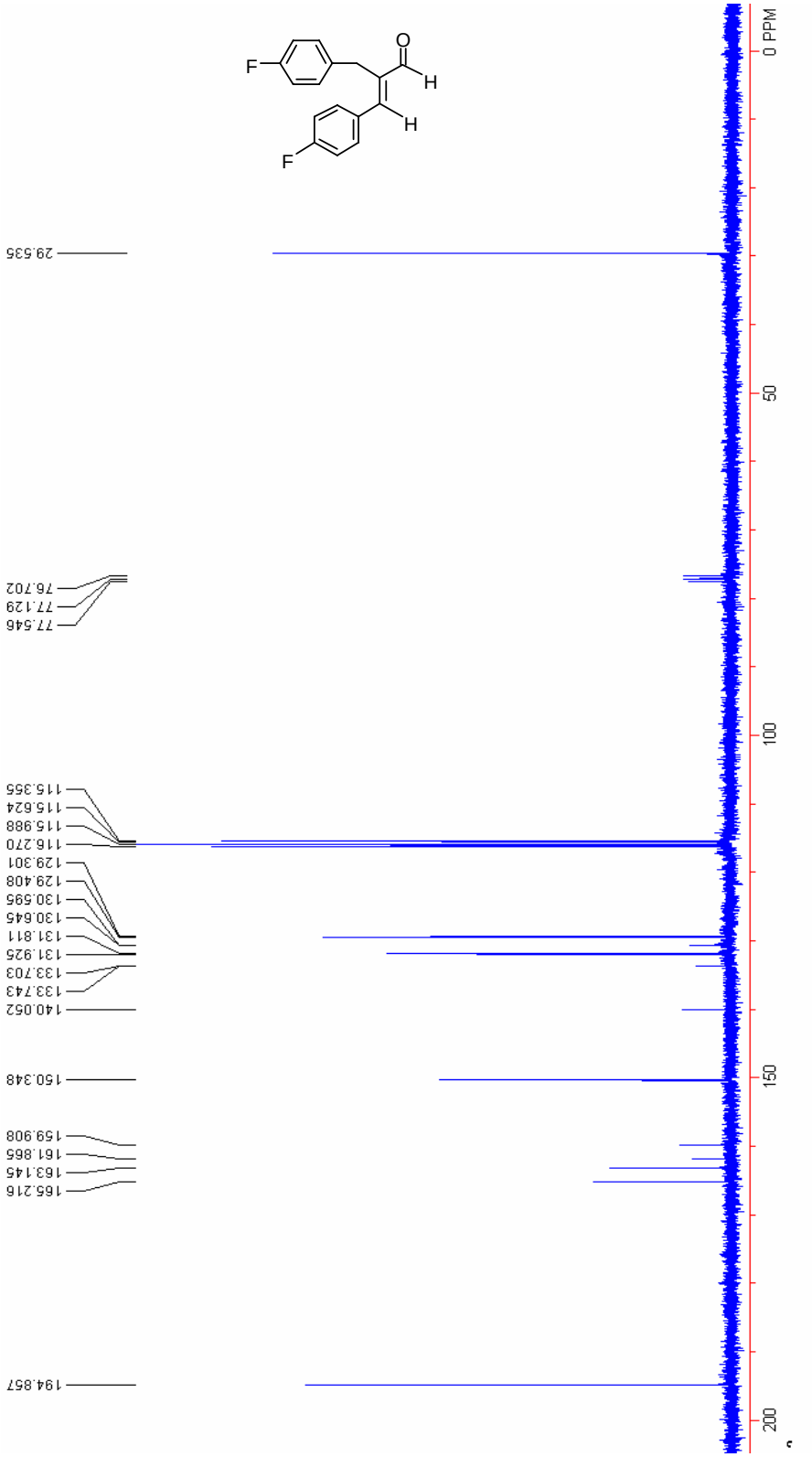
1. T. Yamada, S. Sakaguchi and Y. Ishii, *J. Org. Chem*., 2005, **70**, 5471.
2. S. Kiyooka, H. Fujimoto, M. Mishima, S. Kobayashi, K. M. Uddin and M. Fujio, *Tetrahedron Lett.*, 2003, **44**, 927.

Part III. Spectra of ^{1}H NMR, ^{13}C NMR and MS

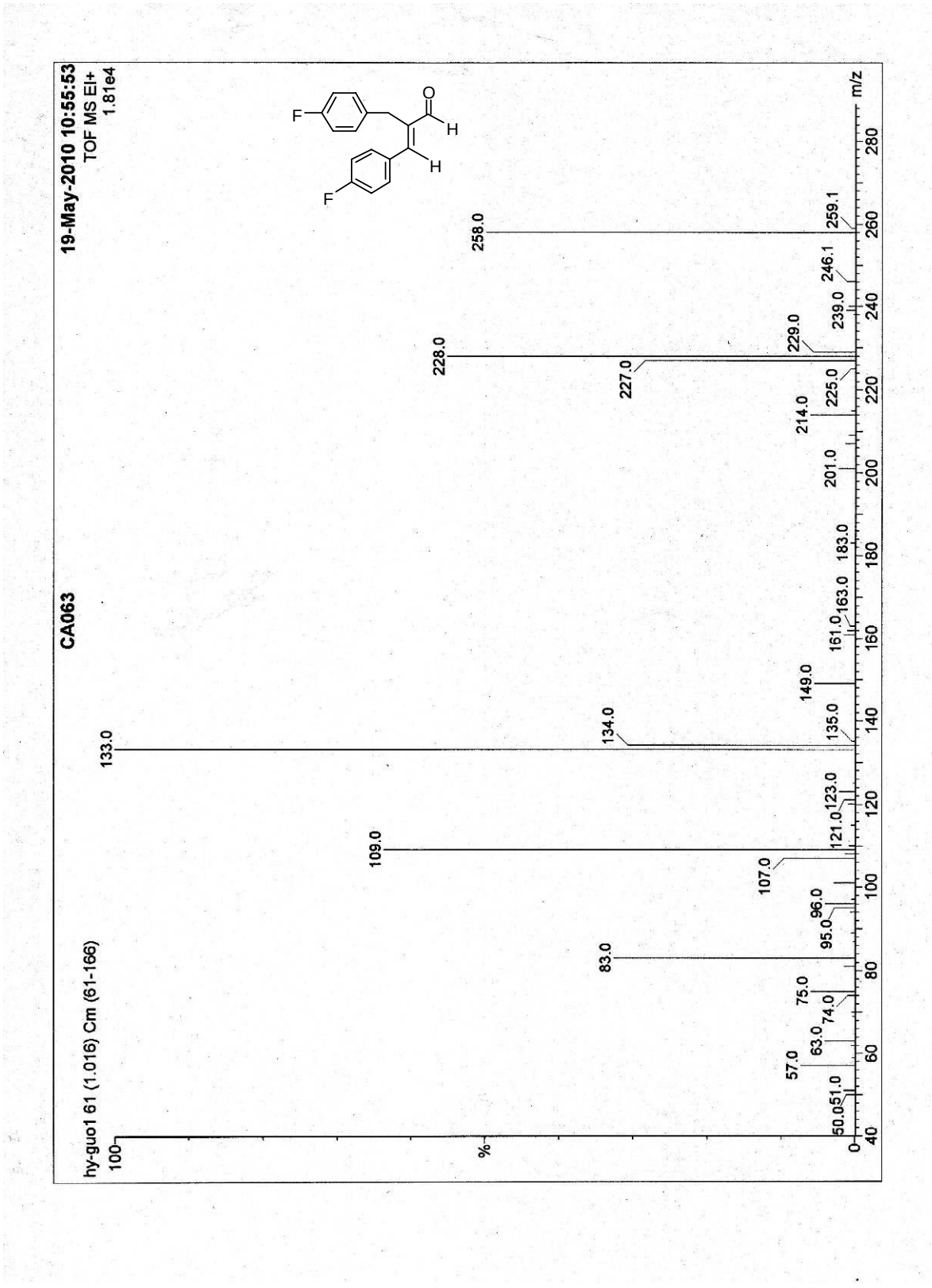
^{1}H NMR of (*E*)-2-(4-Fluorobenzyl)-3-(4-fluorophenyl)acrylaldehyde **5b**



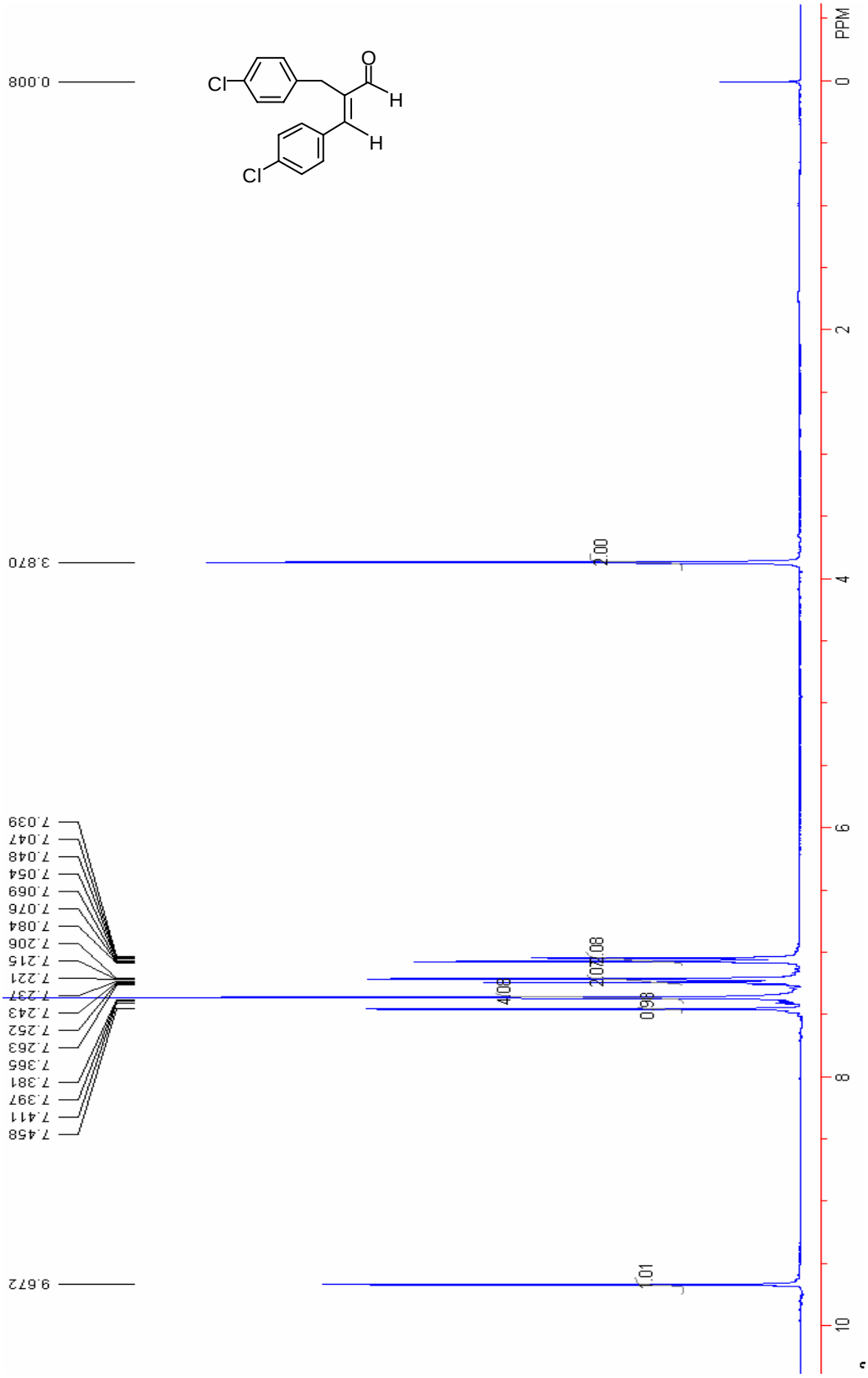
^{13}C NMR of (*E*)-2-(4-Fluorobenzyl)-3-(4-fluorophenyl)acrylaldehyde **5b**



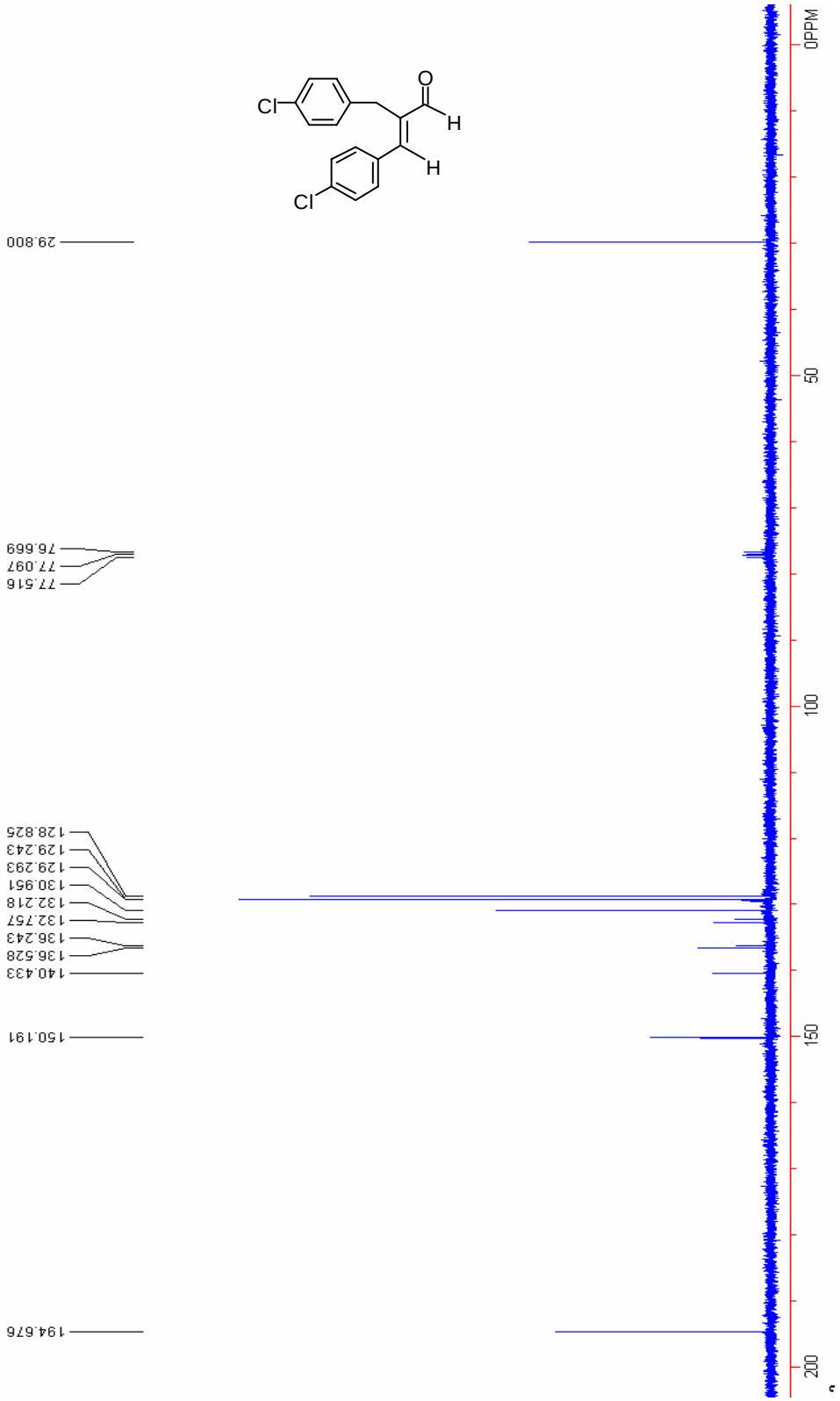
MS (EI) of (*E*)-2-(4-Fluorobenzyl)-3-(4-fluorophenyl)acrylaldehyde **5b**



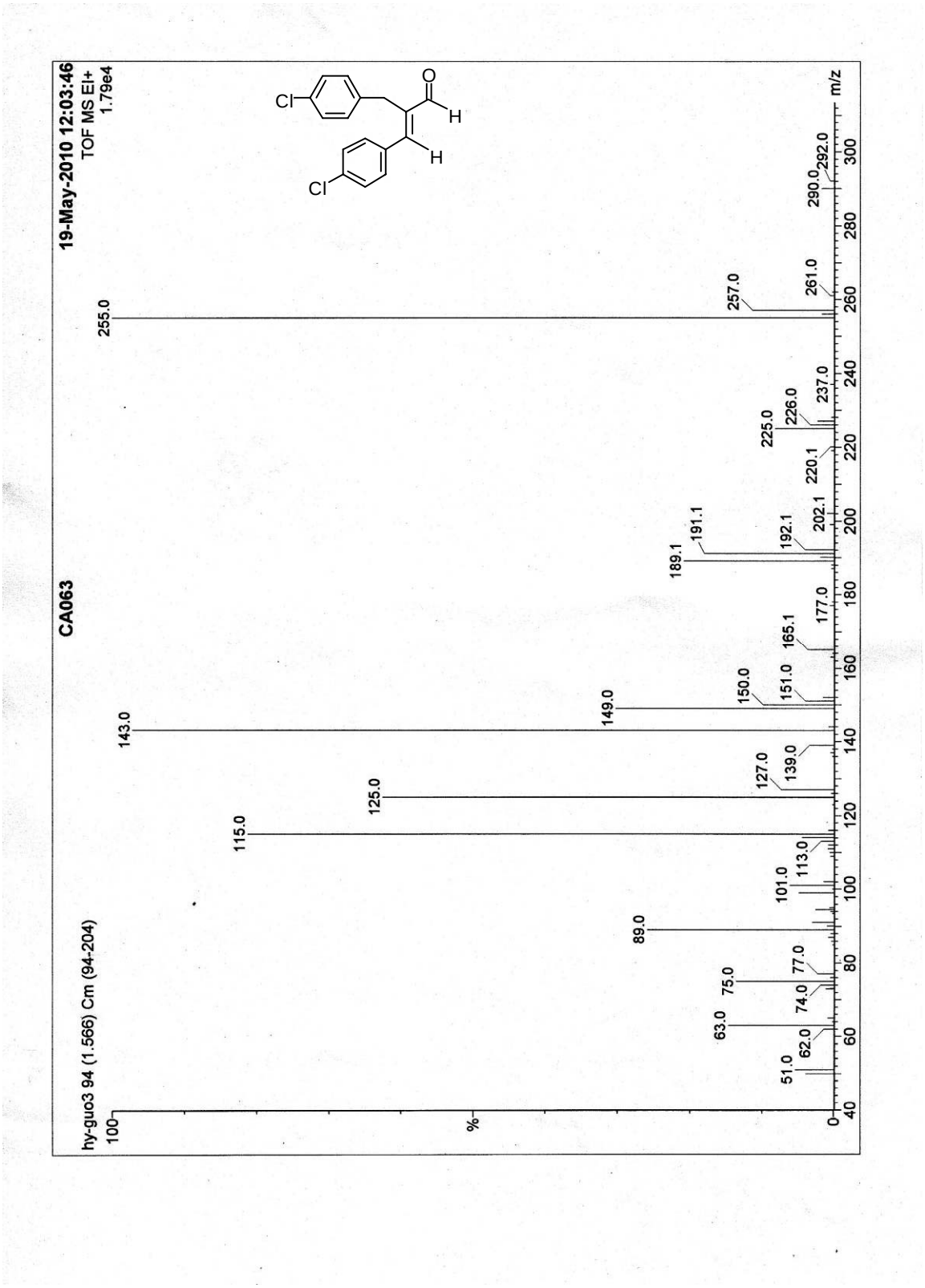
^{1}H NMR of (*E*)-2-(4-Chlorobenzyl)-3-(4-chlorophenyl)acrylaldehyde **5c**



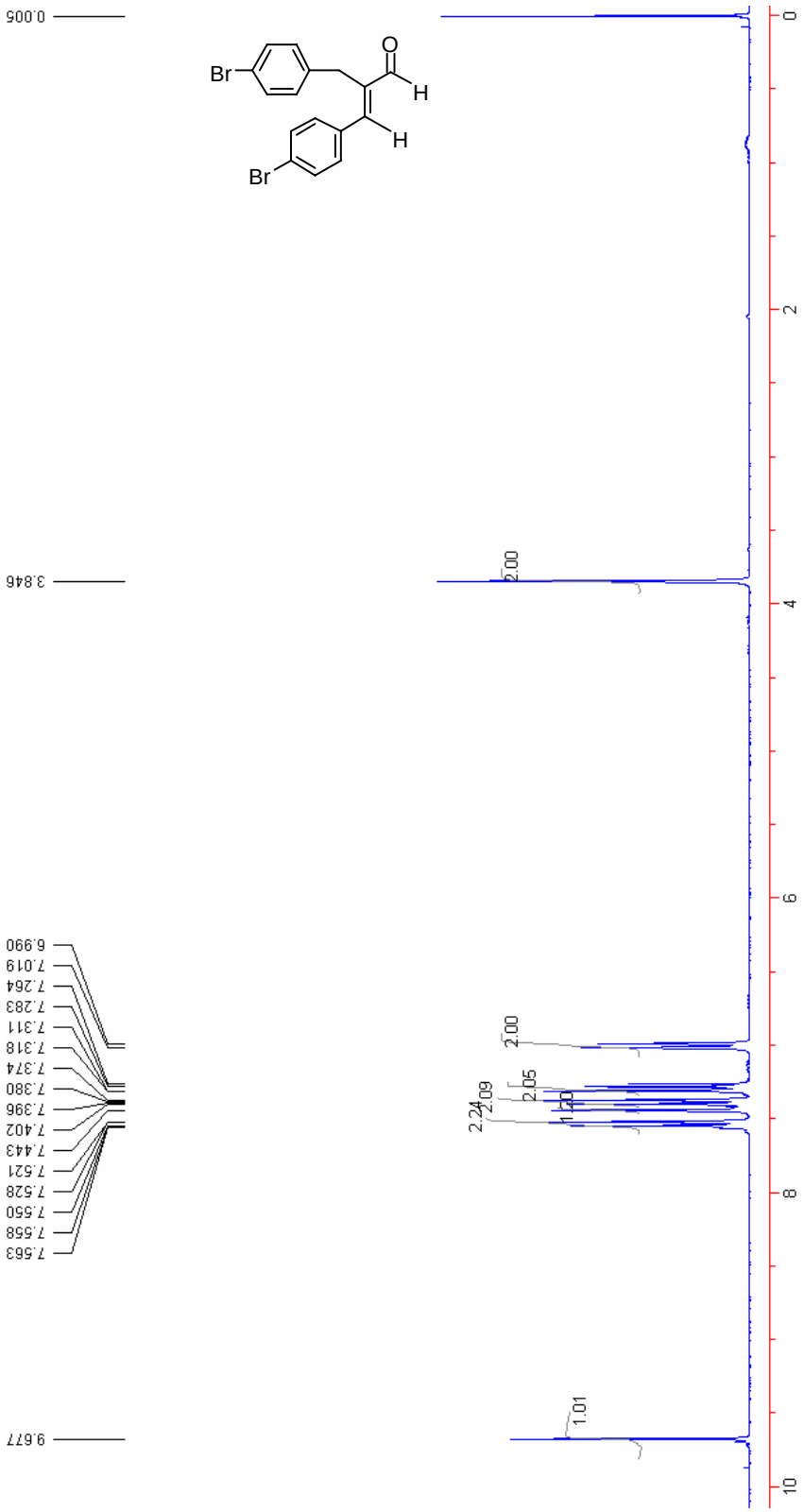
^{13}C NMR of (*E*)-2-(4-Chlorobenzyl)-3-(4-chlorophenyl)acrylaldehyde **5c**



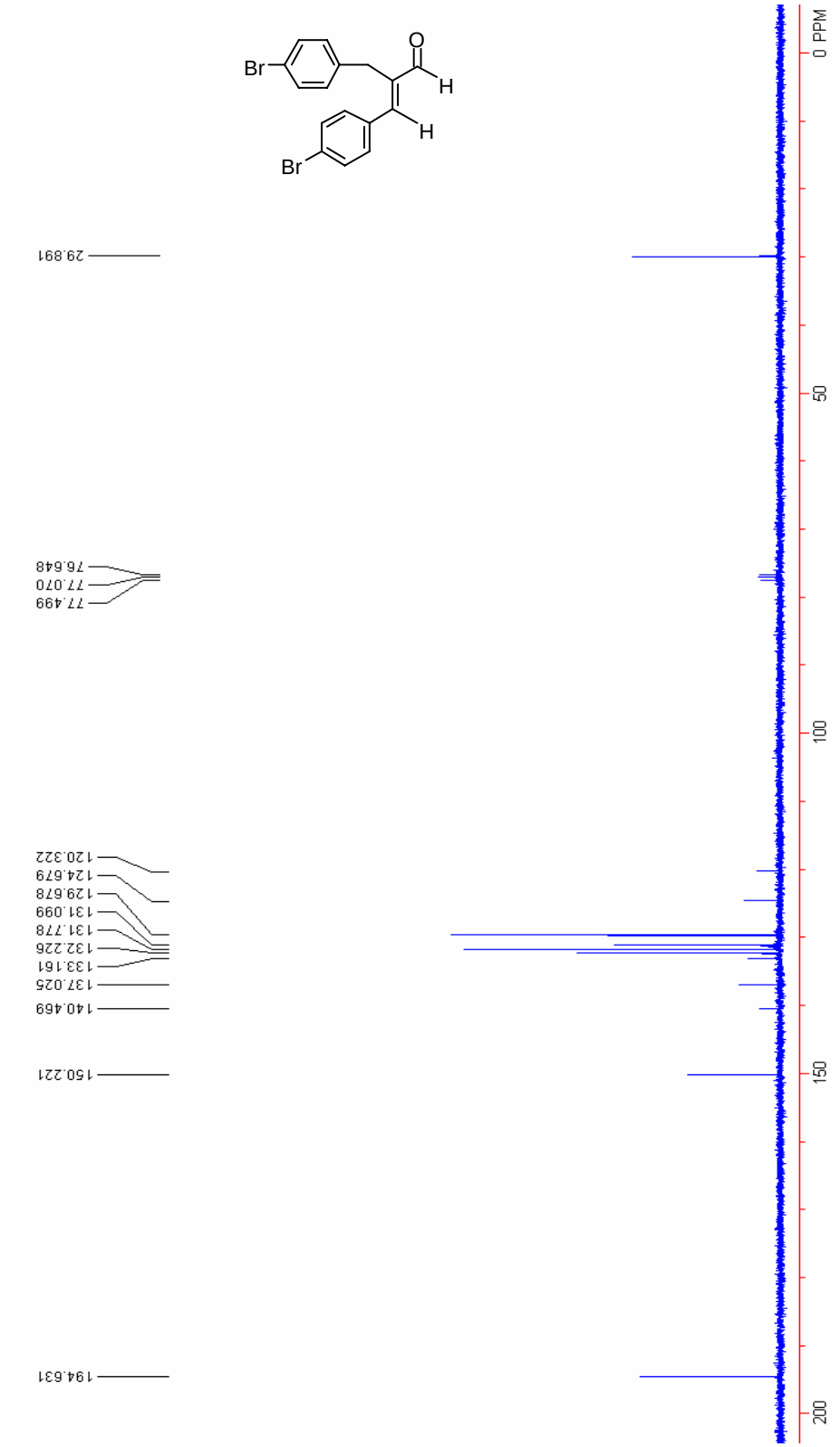
MS (EI) of (*E*)-2-(4-Chlorobenzyl)-3-(4-chlorophenyl)acrylaldehyde **5c**



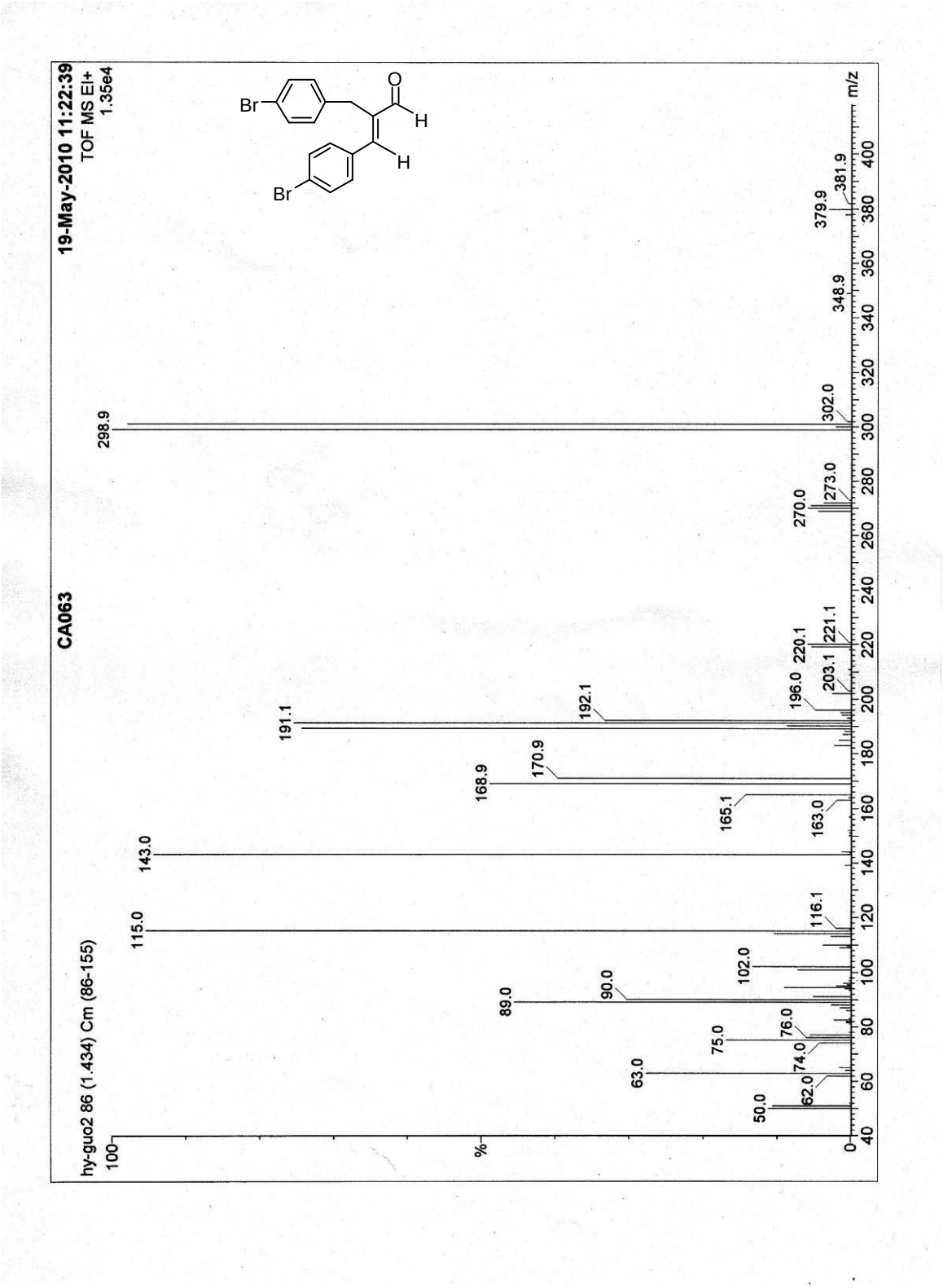
[1]H NMR of (*E*)-2-(4-Bromobenzyl)-3-(4-bromophenyl)acrylaldehyde **5d**



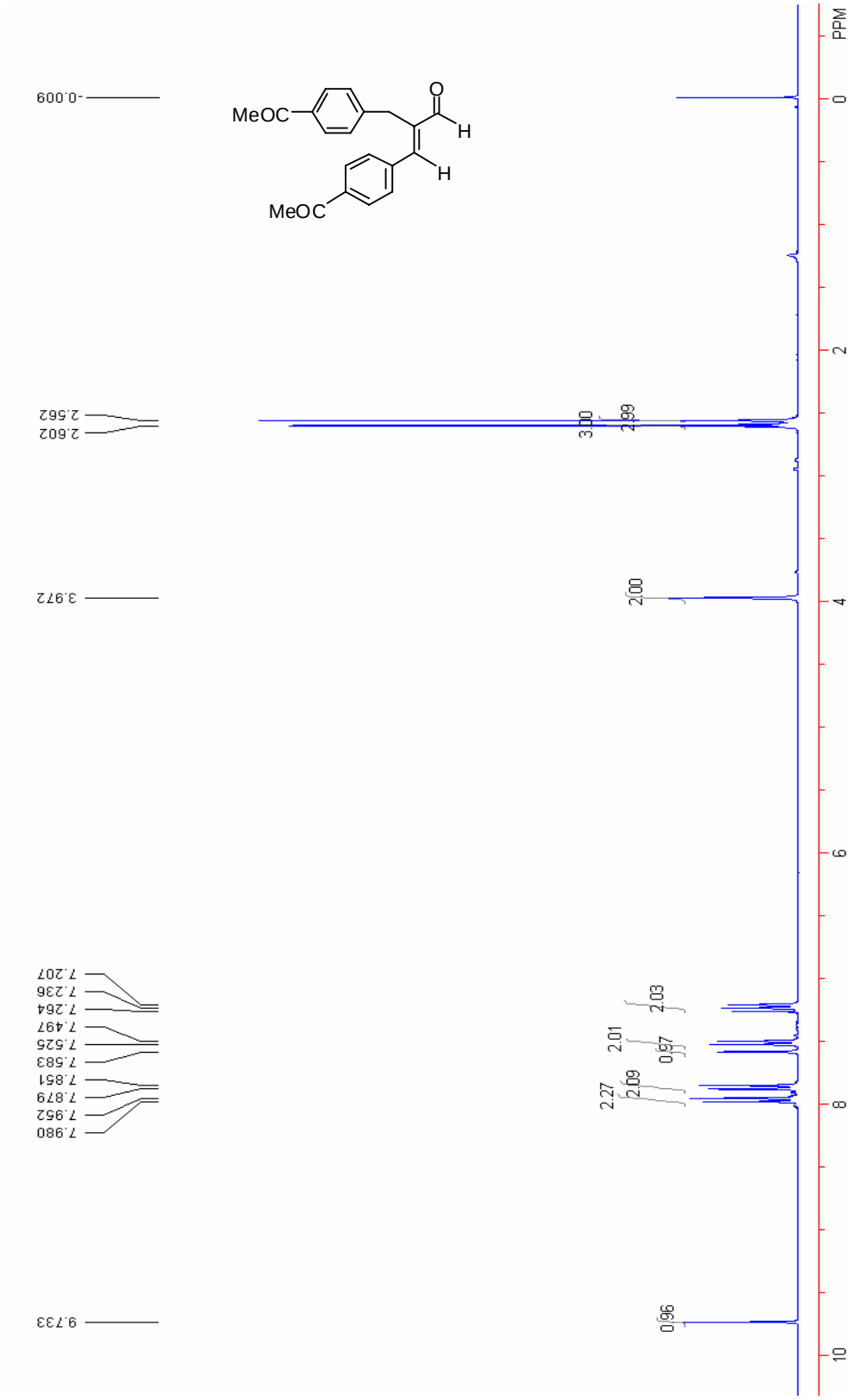
^{13}C NMR of (*E*)-2-(4-Bromobenzyl)-3-(4-bromophenyl)acrylaldehyde **5d**



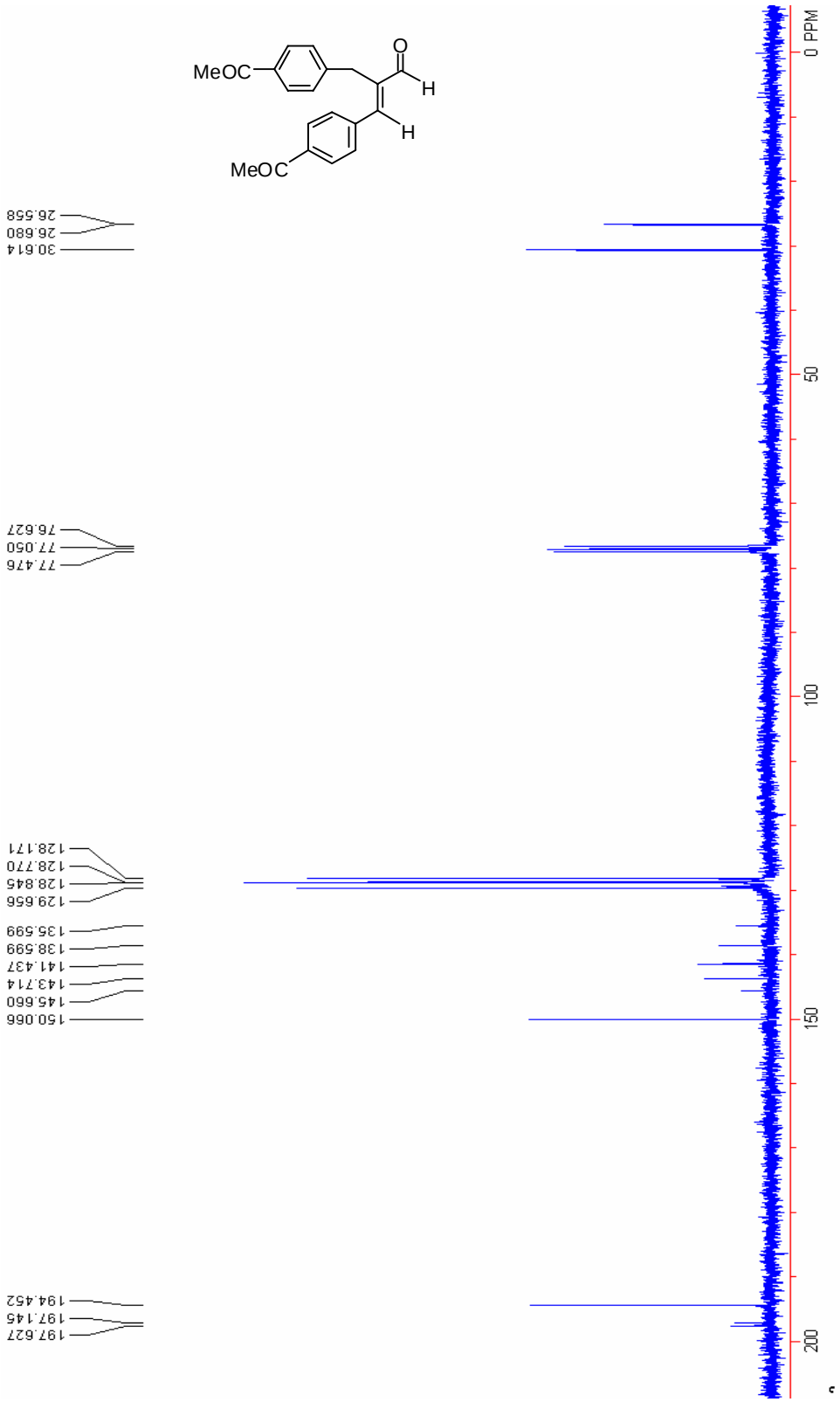
MS (EI) of (*E*)-2-(4-Bromobenzyl)-3-(4-bromophenyl)acrylaldehyde **5d**



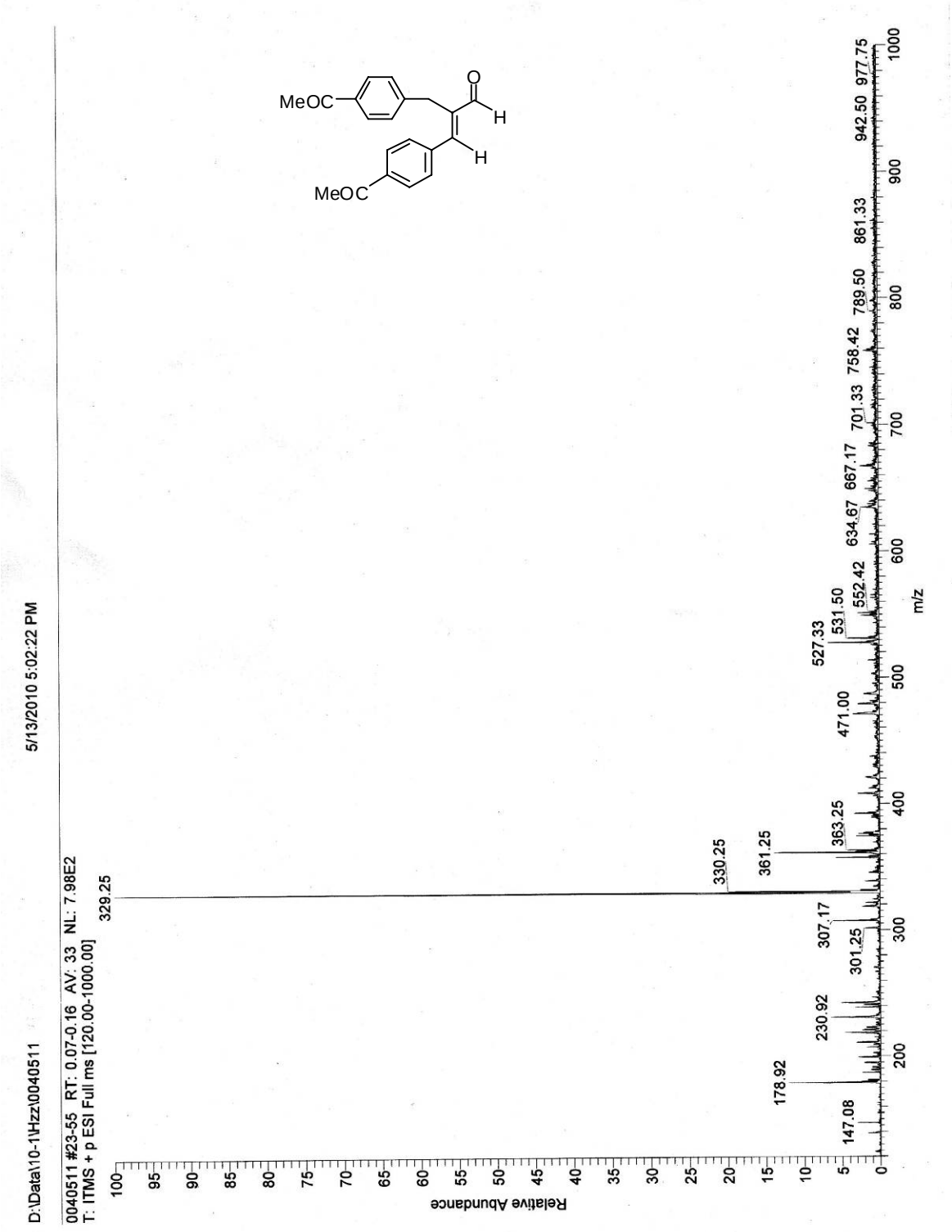
^{1}H NMR of (*E*)-2-(4-Acetylbenzyl)-3-(4-acetylphenyl)acrylaldehyde **5e**



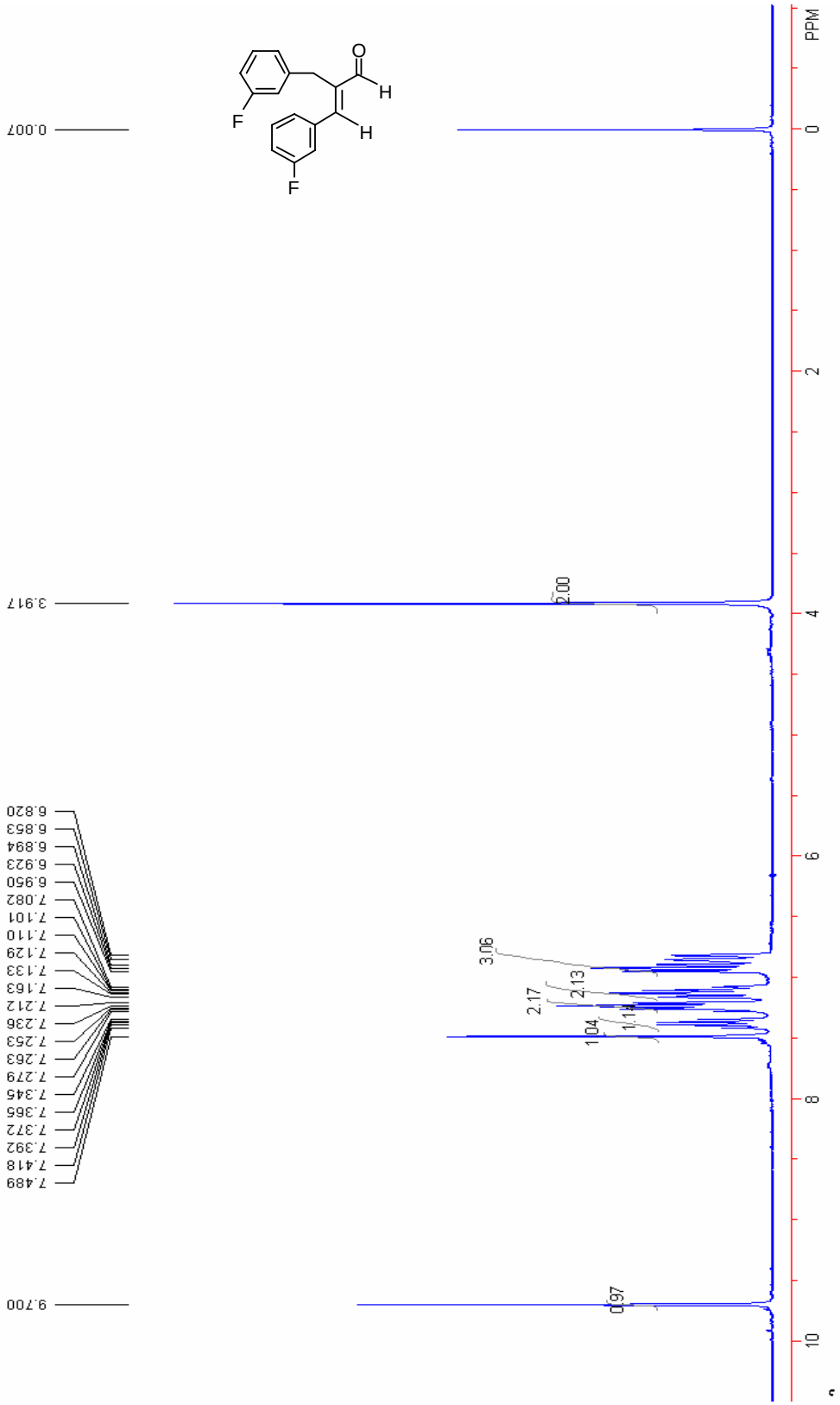
^{13}C NMR of (*E*)-2-(4-Acetylbenzyl)-3-(4-acetylphenyl)acrylaldehyde **5e**



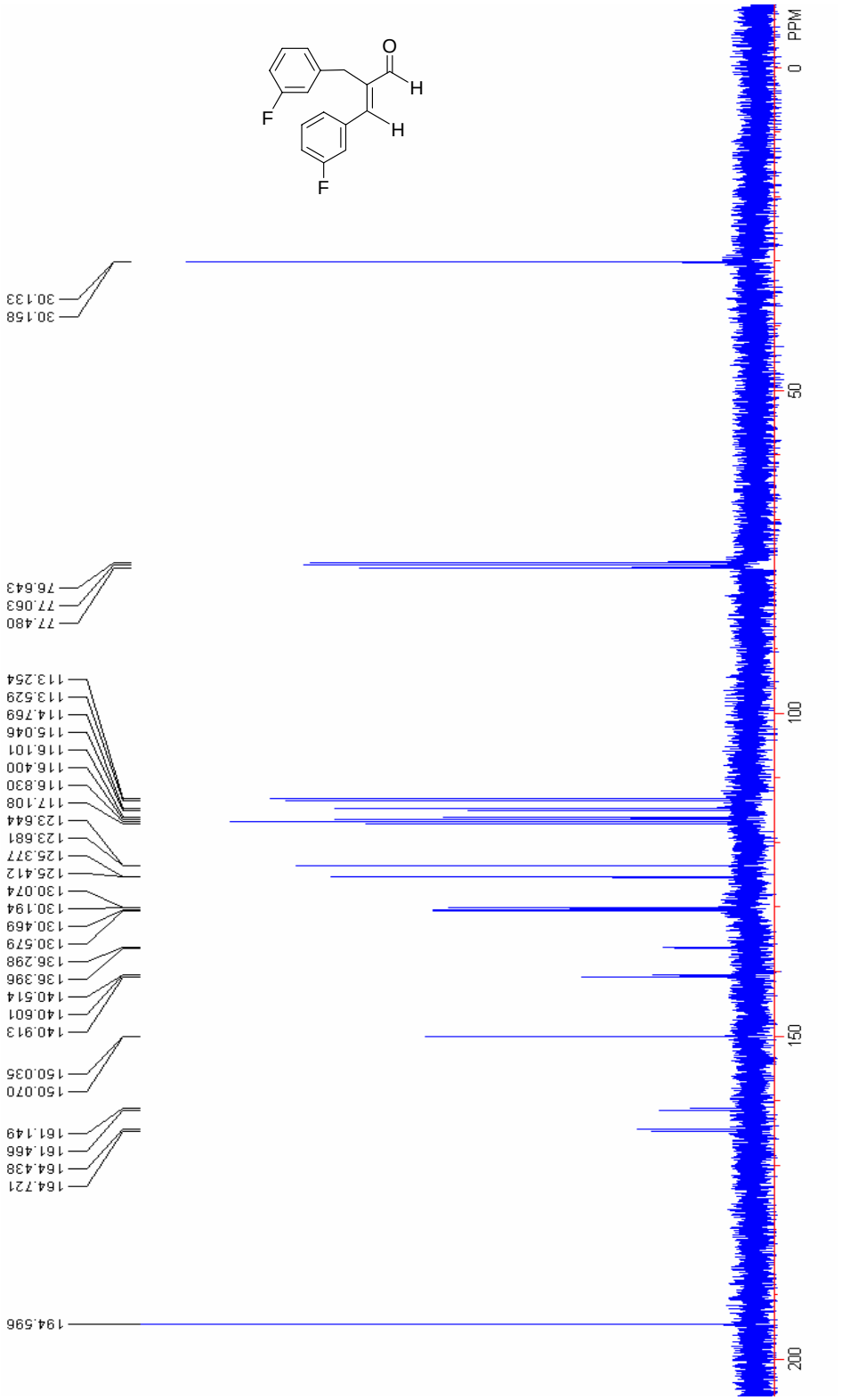
MS (ESI) of (*E*)-2-(4-Acetylbenzyl)-3-(4-acetylphenyl)acrylaldehyde **5e**



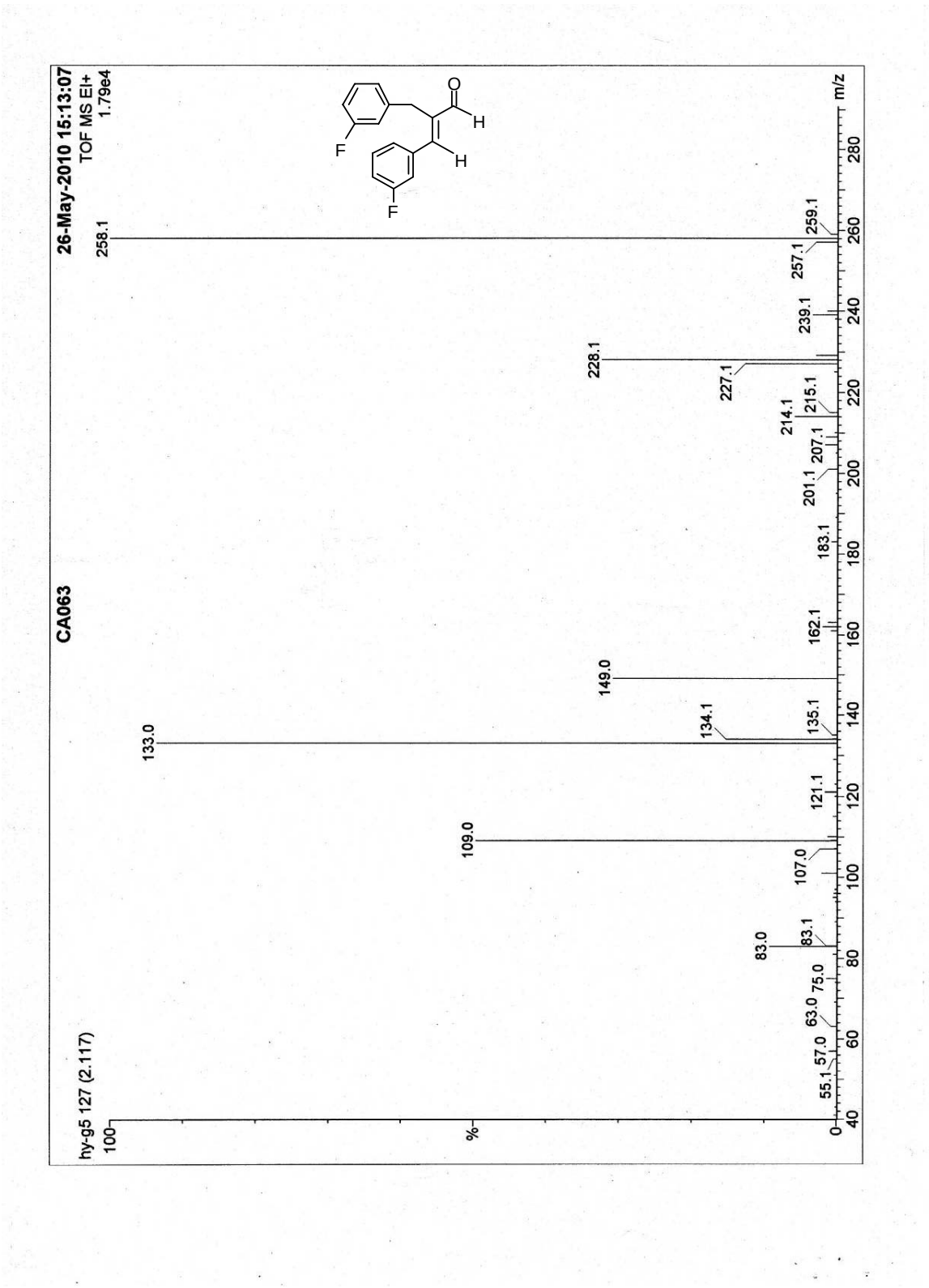
[1]H NMR of (*E*)-2-(3-Fluorobenzyl)-3-(3-fluorophenyl)acrylaldehydem **5g**



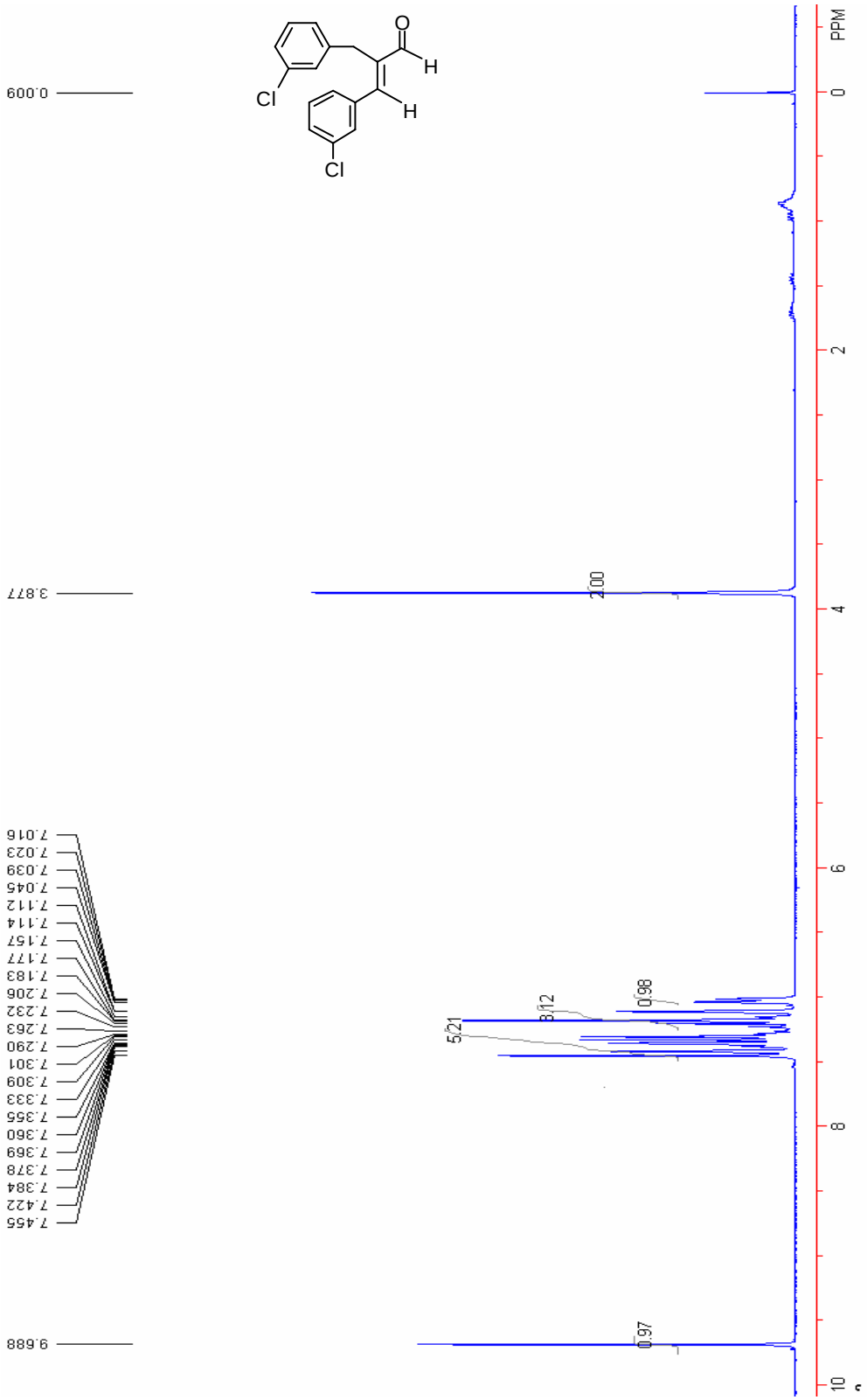
^{13}C NMR of (*E*)-2-(3-Fluorobenzyl)-3-(3-fluorophenyl)acrylaldehydem **5g**



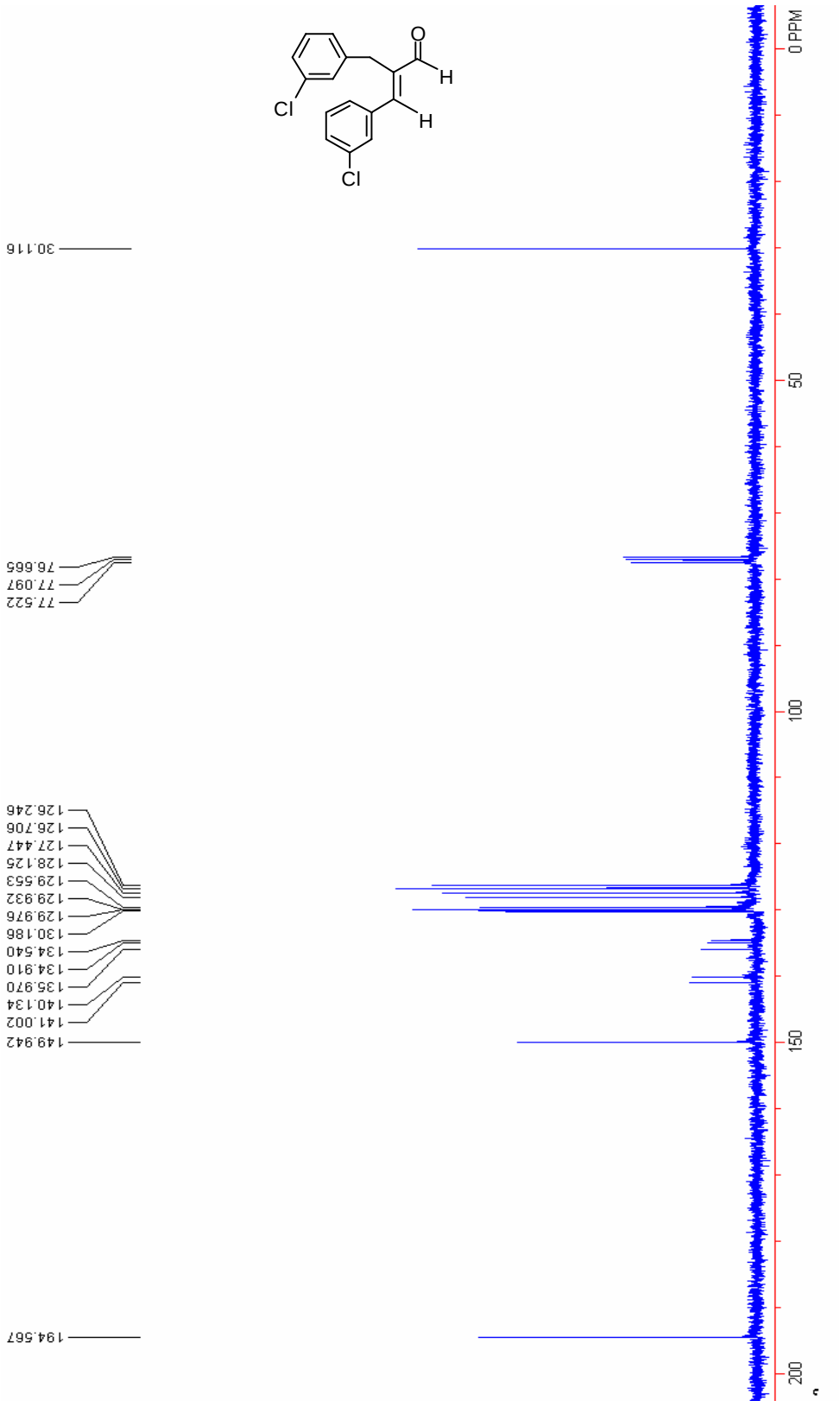
MS (EI) of (*E*)-2-(3-Fluorobenzyl)-3-(3-fluorophenyl)acrylaldehydem **5g**



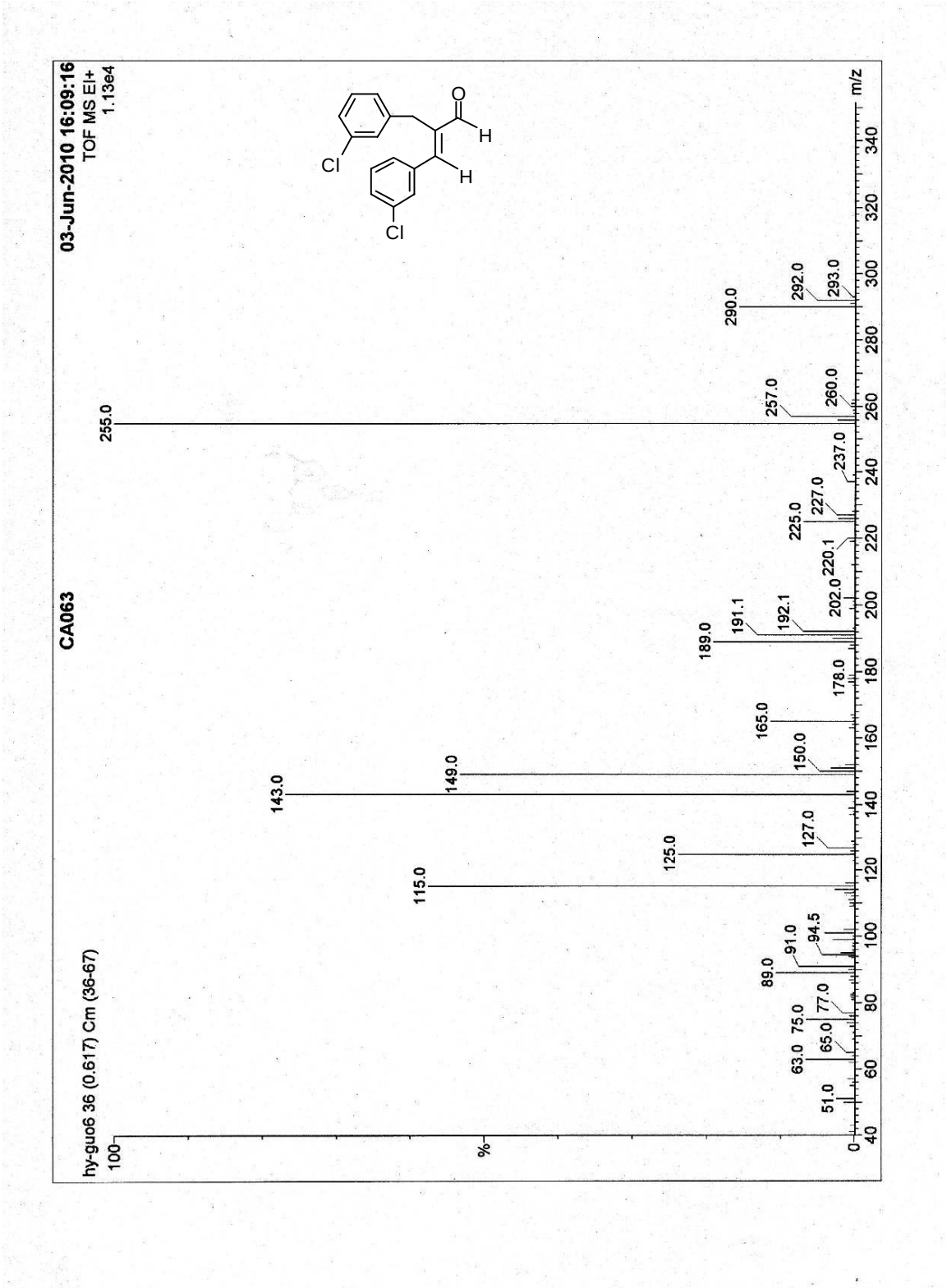
^{1}H NMR of (*E*)-2-(3-Chlorobenzyl)-3-(3-chlorophenyl)acrylaldehyde **5h**



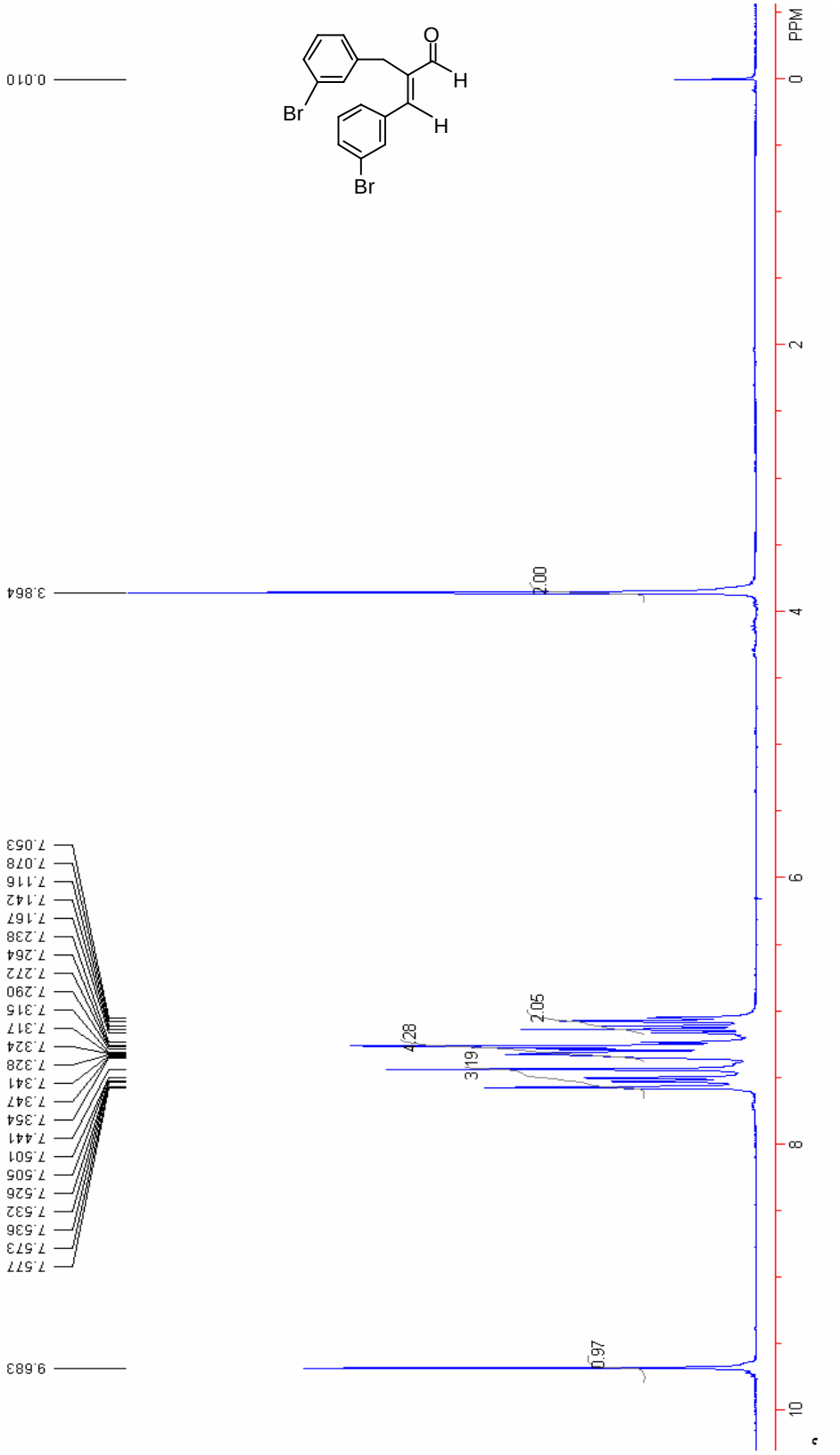
^{13}C NMR of (*E*)-2-(3-Chlorobenzyl)-3-(3-chlorophenyl)acrylaldehyde **5h**



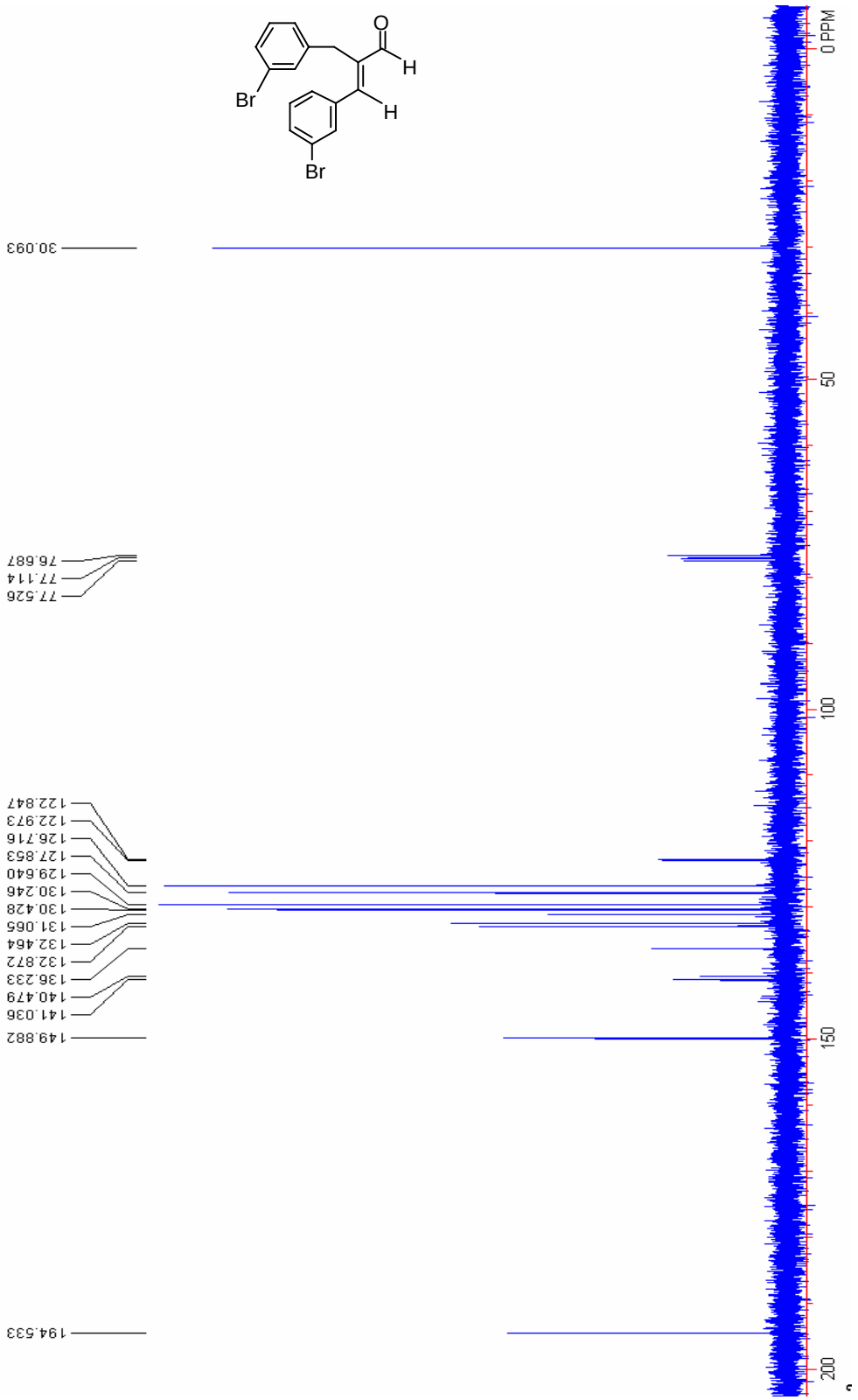
MS (EI) of (*E*)-2-(3-Chlorobenzyl)-3-(3-chlorophenyl)acrylaldehyde **5h**



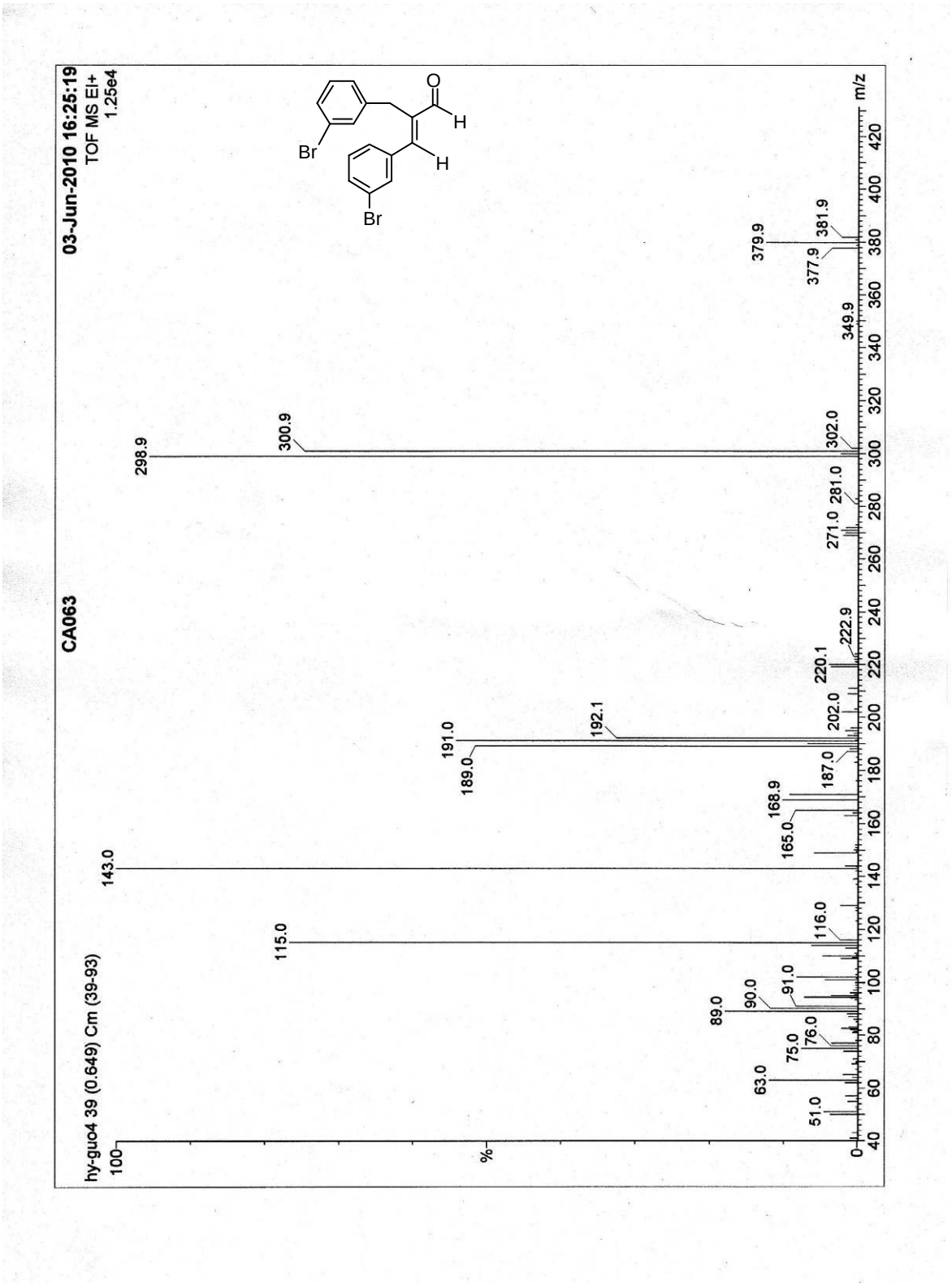
^{1}H NMR of (*E*)-2-(3-Bromobenzyl)-3-(3-bromophenyl)acrylaldehyde **5i**



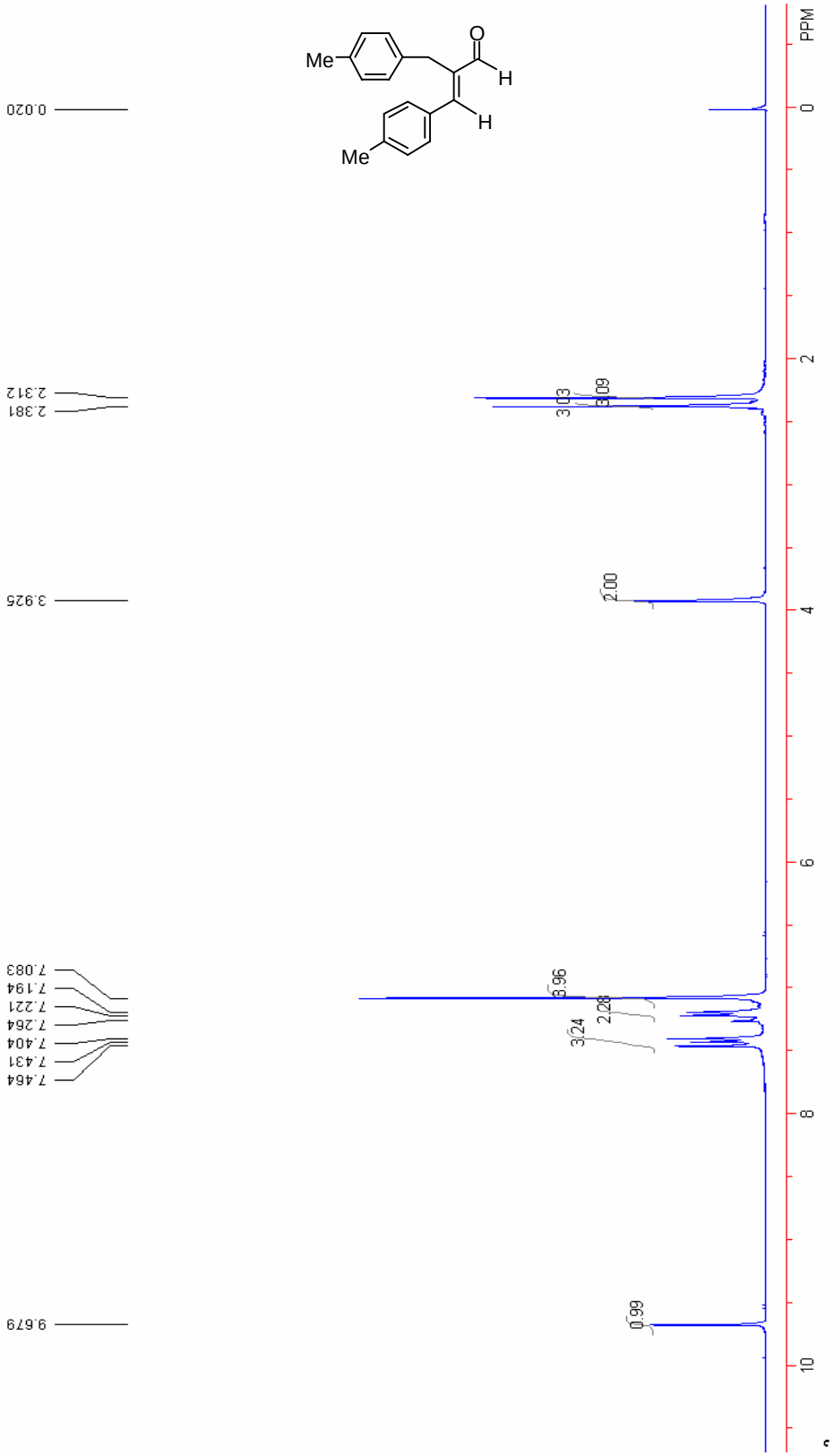
^{13}C NMR of (*E*)-2-(3-Bromobenzyl)-3-(3-bromophenyl)acrylaldehyde **5i**



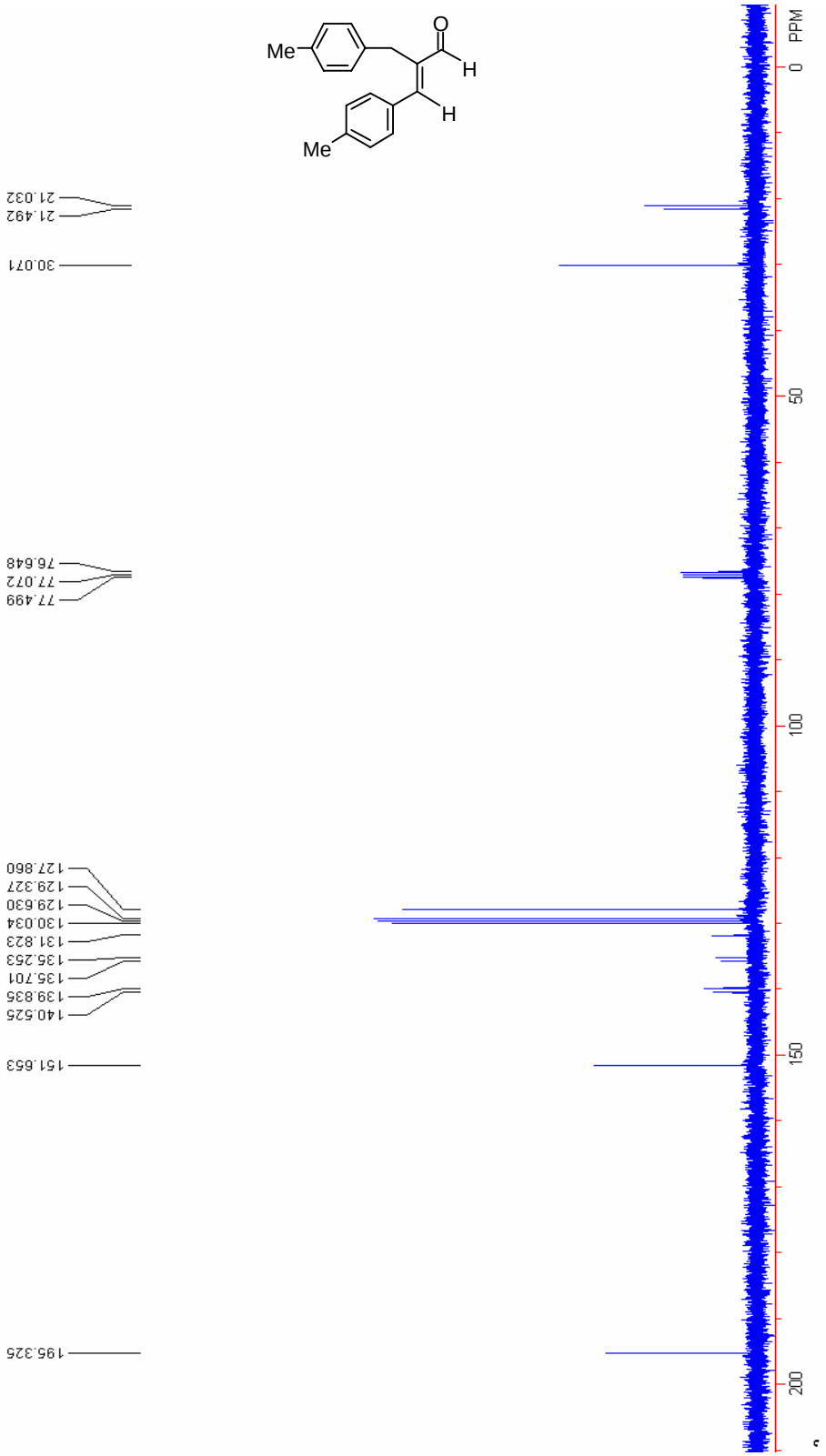
MS (EI) of (*E*)-2-(3-Bromobenzyl)-3-(3-bromophenyl)acrylaldehyde **5i**



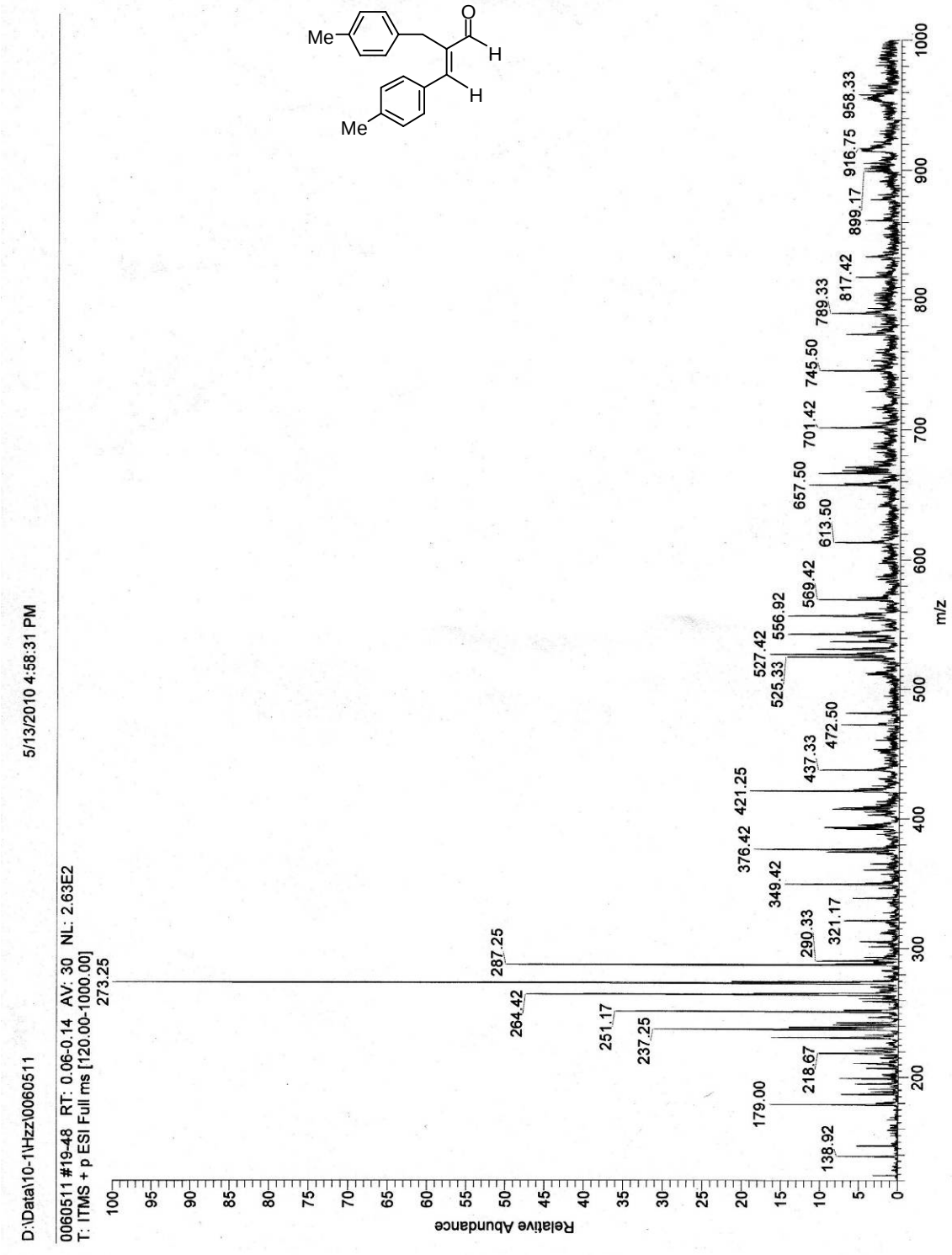
^{1}H NMR of (*E*)-2-(4-Methylbenzyl)-3-(4-methylphenyl)acrylaldehyde **5j**



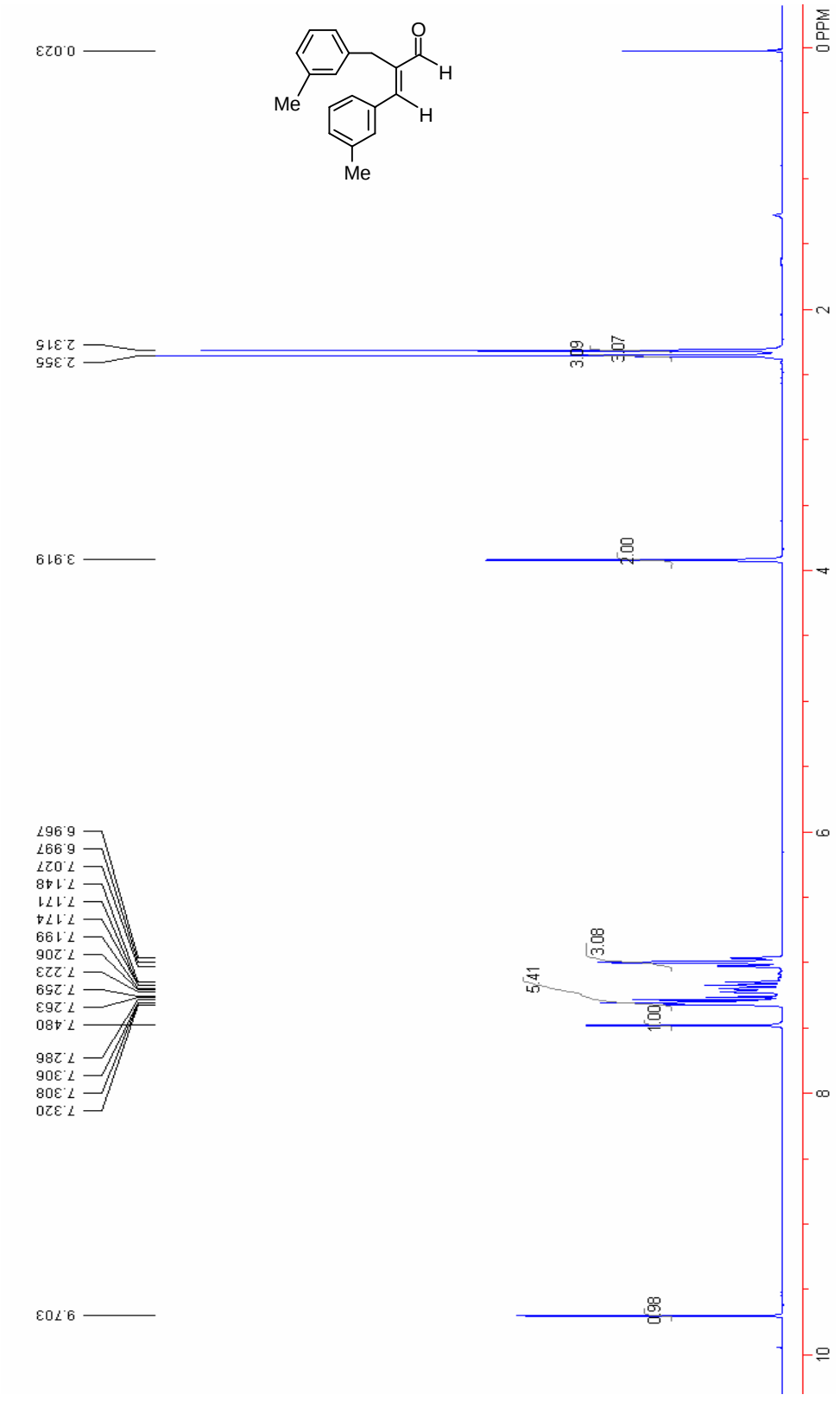
^{13}C NMR of (*E*)-2-(4-Methylbenzyl)-3-(4-methylphenyl)acrylaldehyde **5j**



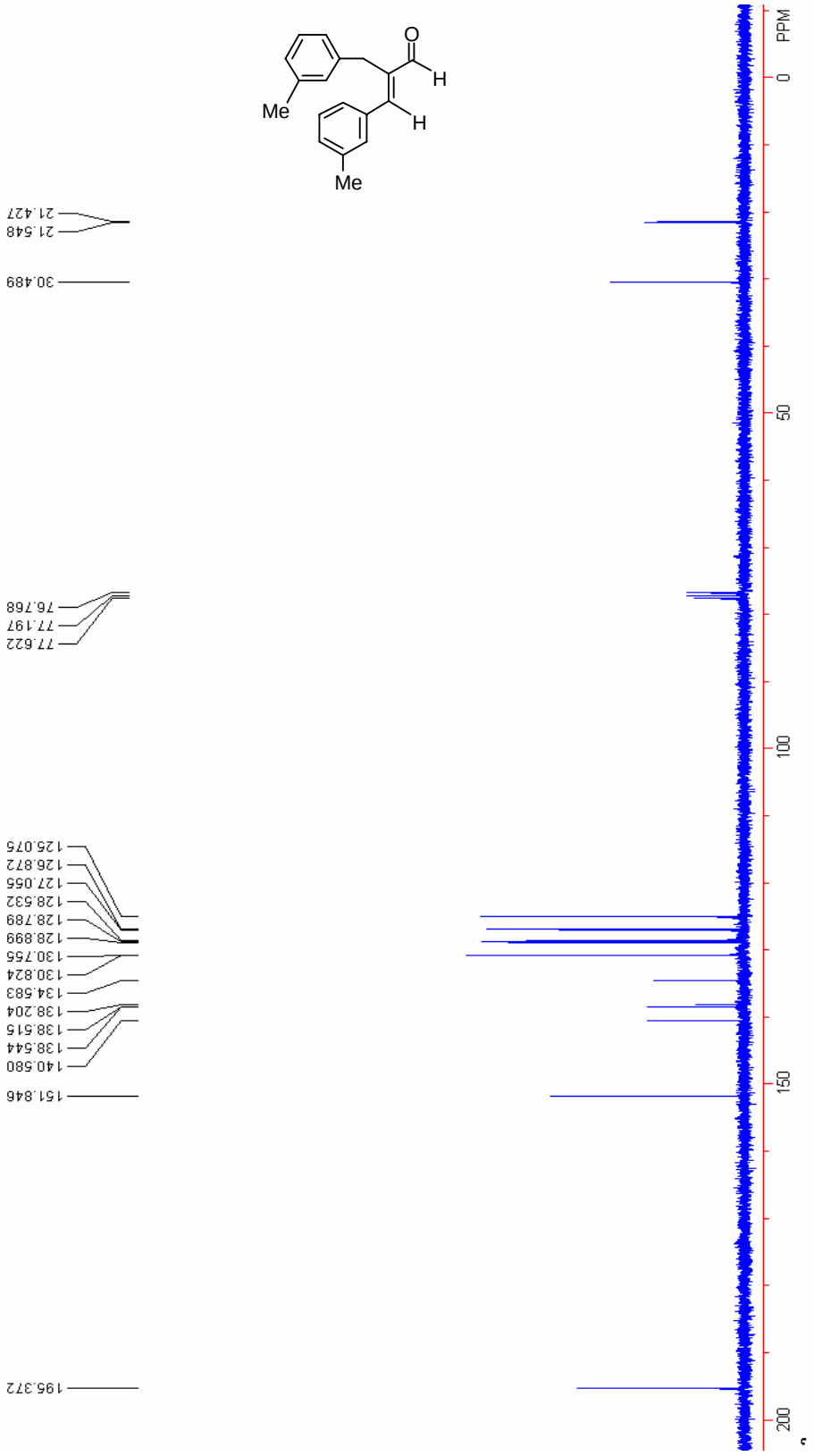
MS (ESI) of (*E*)-2-(4-Methylbenzyl)-3-(4-methylphenyl)acrylaldehyde **5j**



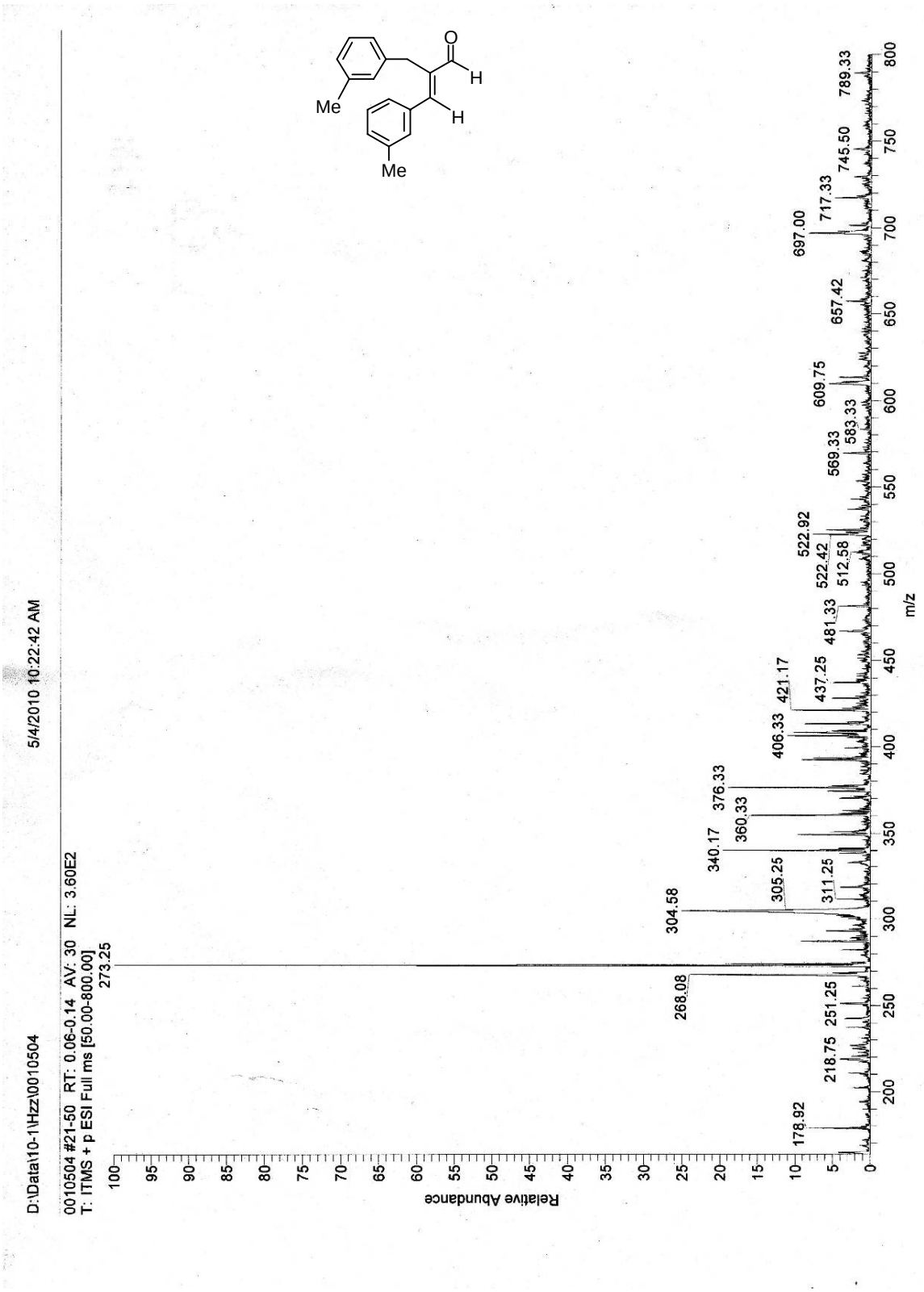
^{1}H NMR of (*E*)-2-(3-Methylbenzyl)-3-(3-methylphenyl)acrylaldehyde **5k**



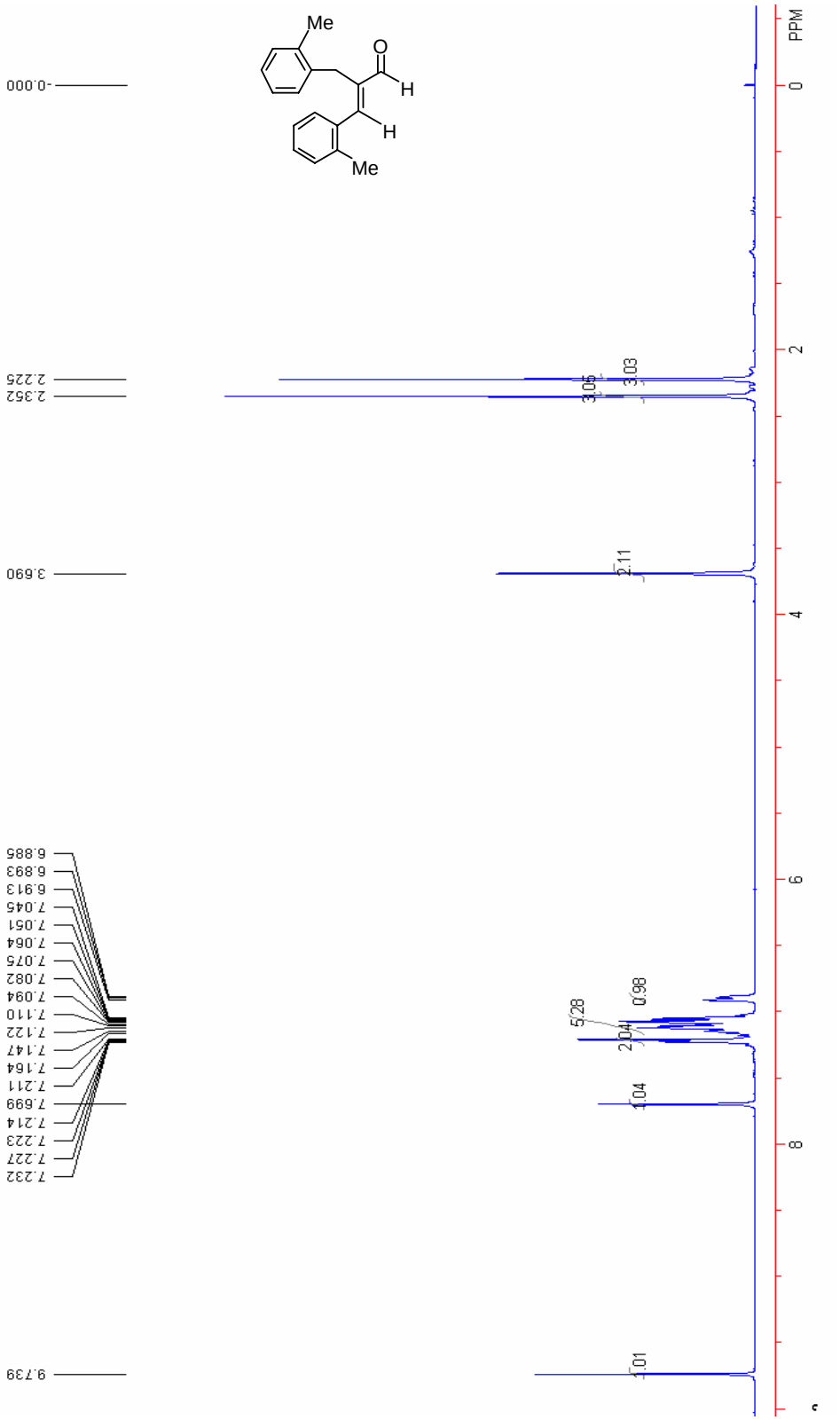
^{13}C NMR of (*E*)-2-(3-Methylbenzyl)-3-(3-methylphenyl)acrylaldehyde **5k**



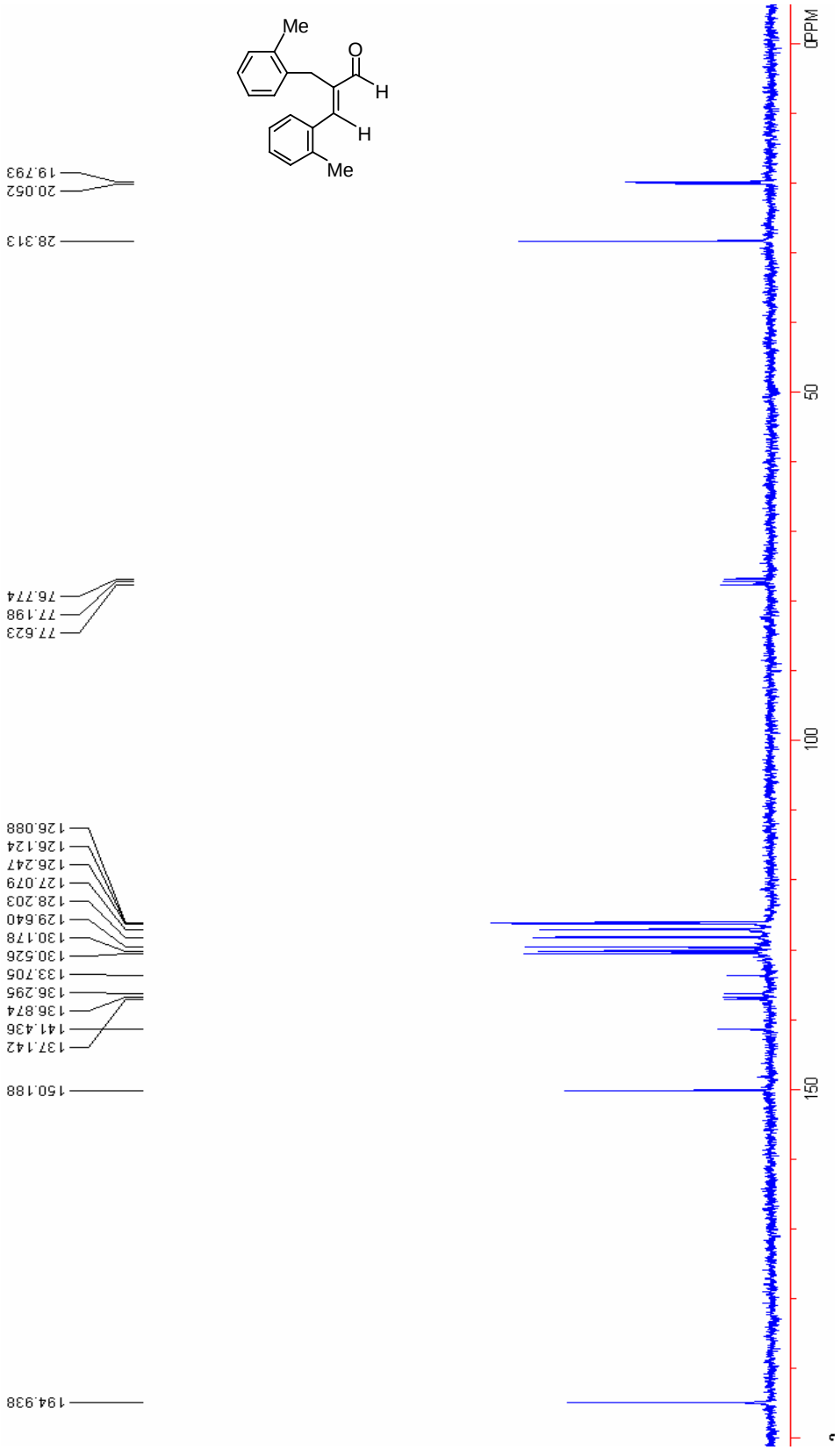
MS (ESI) of (*E*)-2-(3-Methylbenzyl)-3-(3-methylphenyl)acrylaldehyde **5k**



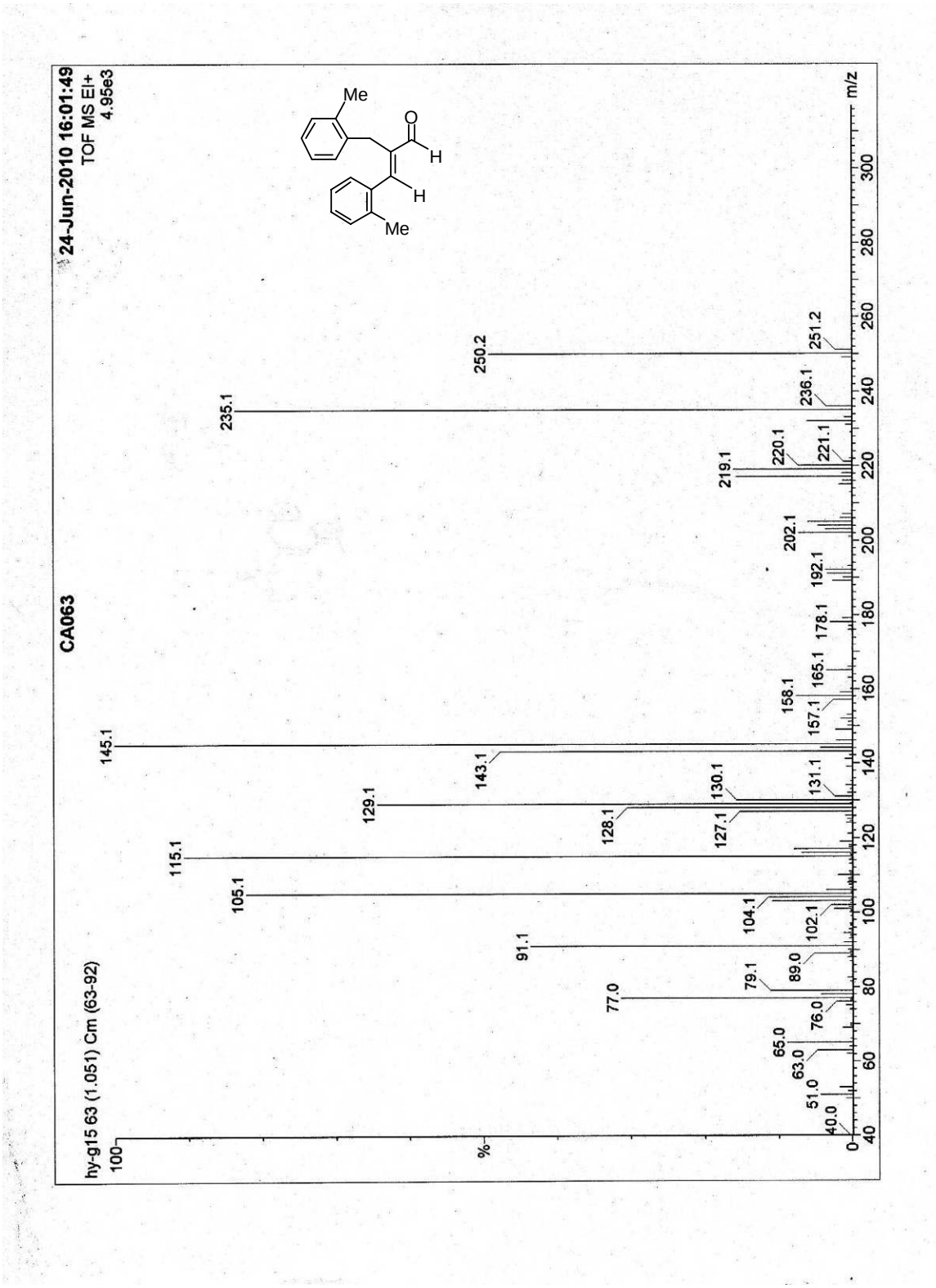
^{1}H NMR of (*E*)-2-(2-Methylbenzyl)-3-(2-methylphenyl)acrylaldehyde **5l**



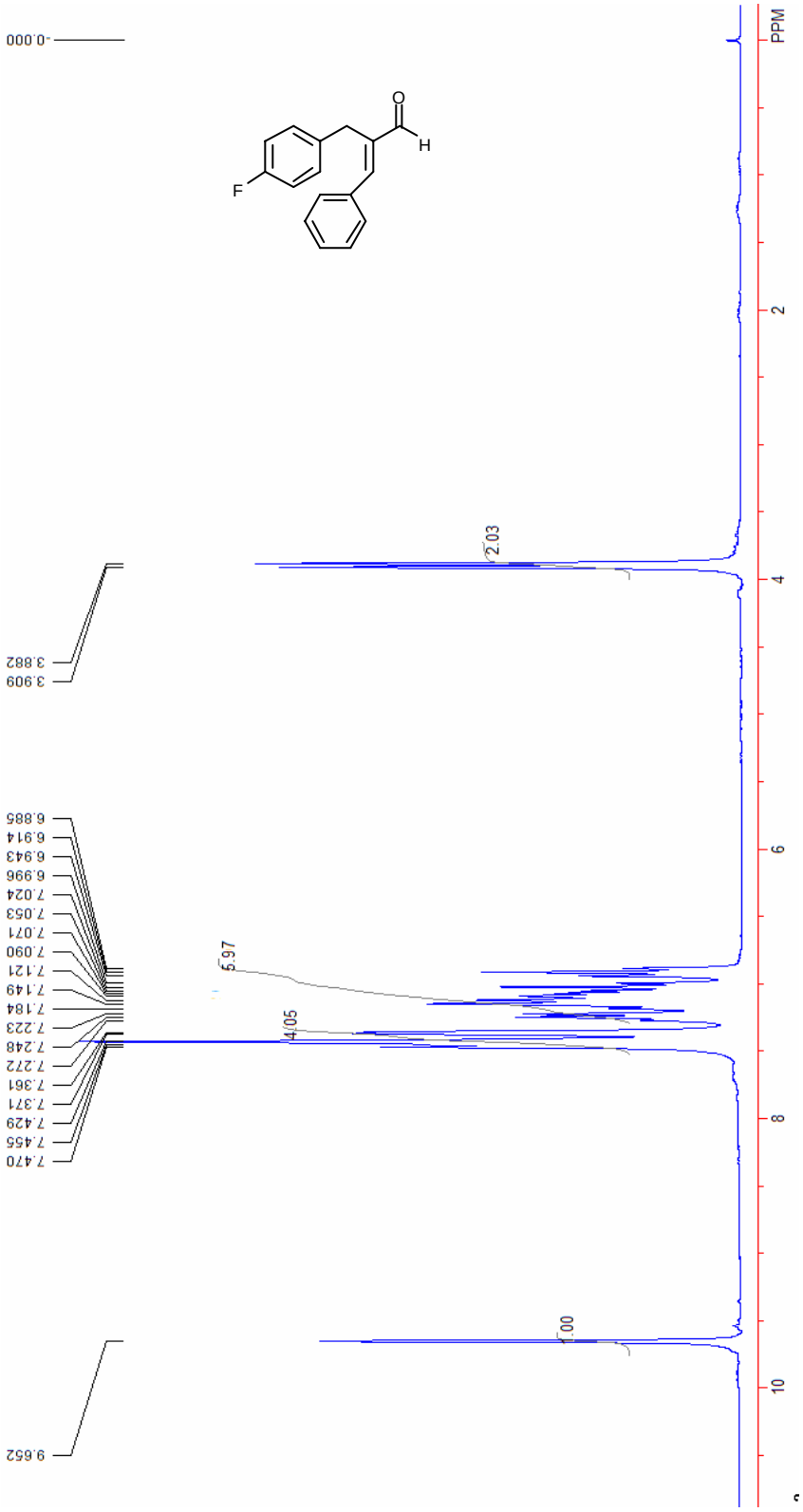
^{13}C NMR of (*E*)-2-(2-Methylbenzyl)-3-(2-methylphenyl)acrylaldehyde **5l**



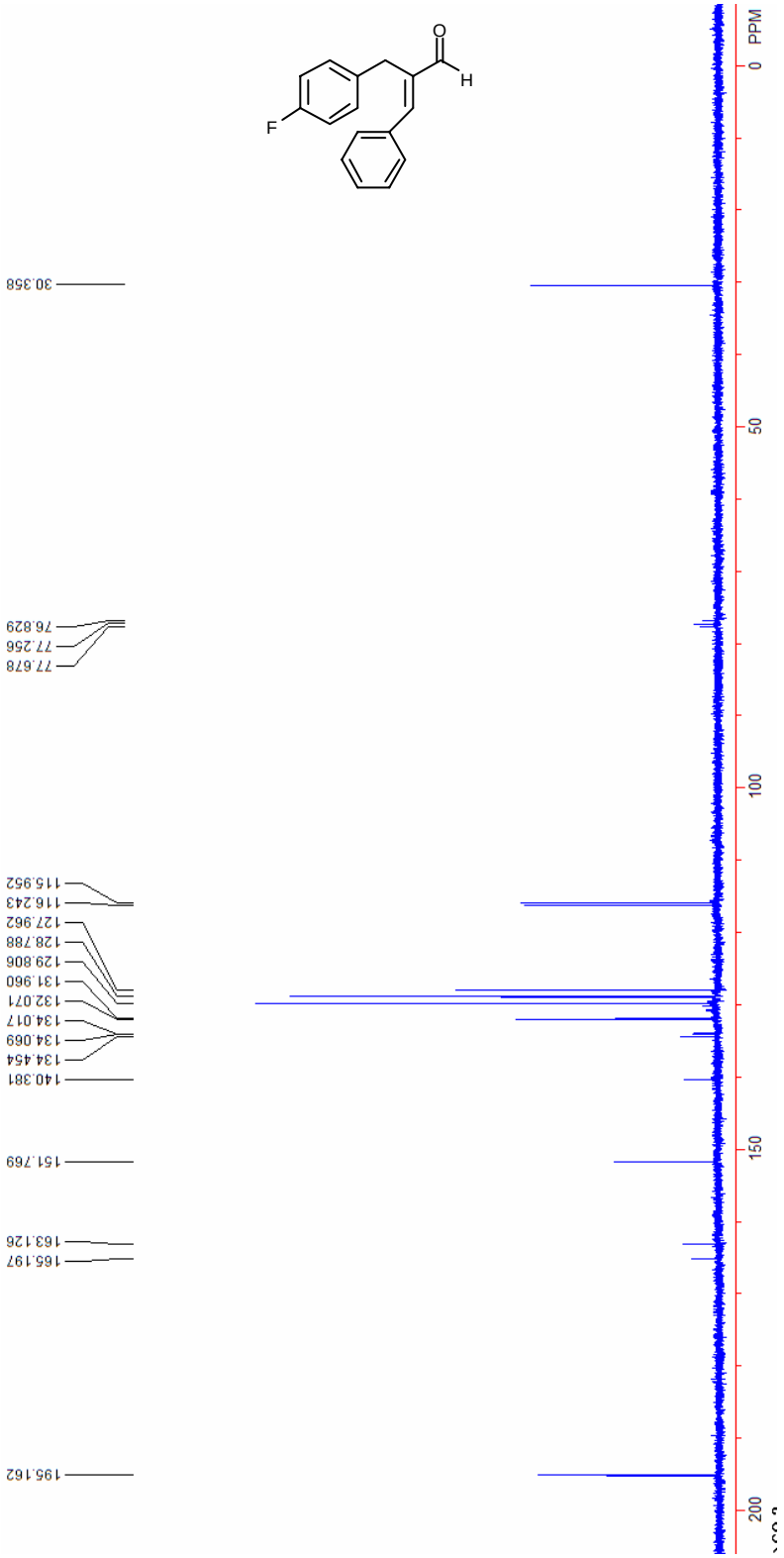
MS (EI) of (*E*)-2-(2-Methylbenzyl)-3-(2-methylphenyl)acrylaldehyde **5l**



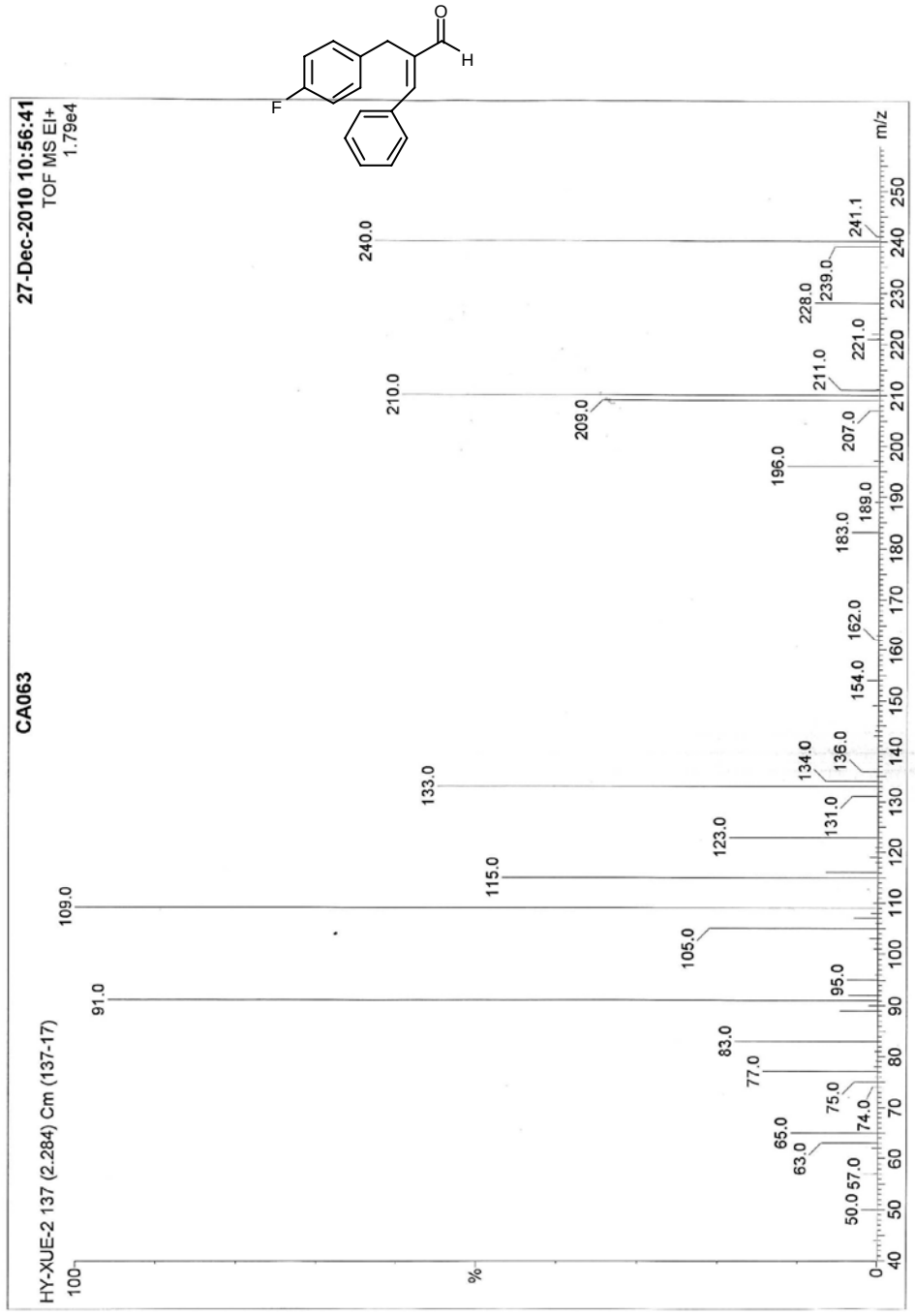
^{1}H NMR of (*E*)-2-(4-Fluorobenzyl)-3-phenylacrylaldehyde **5o**



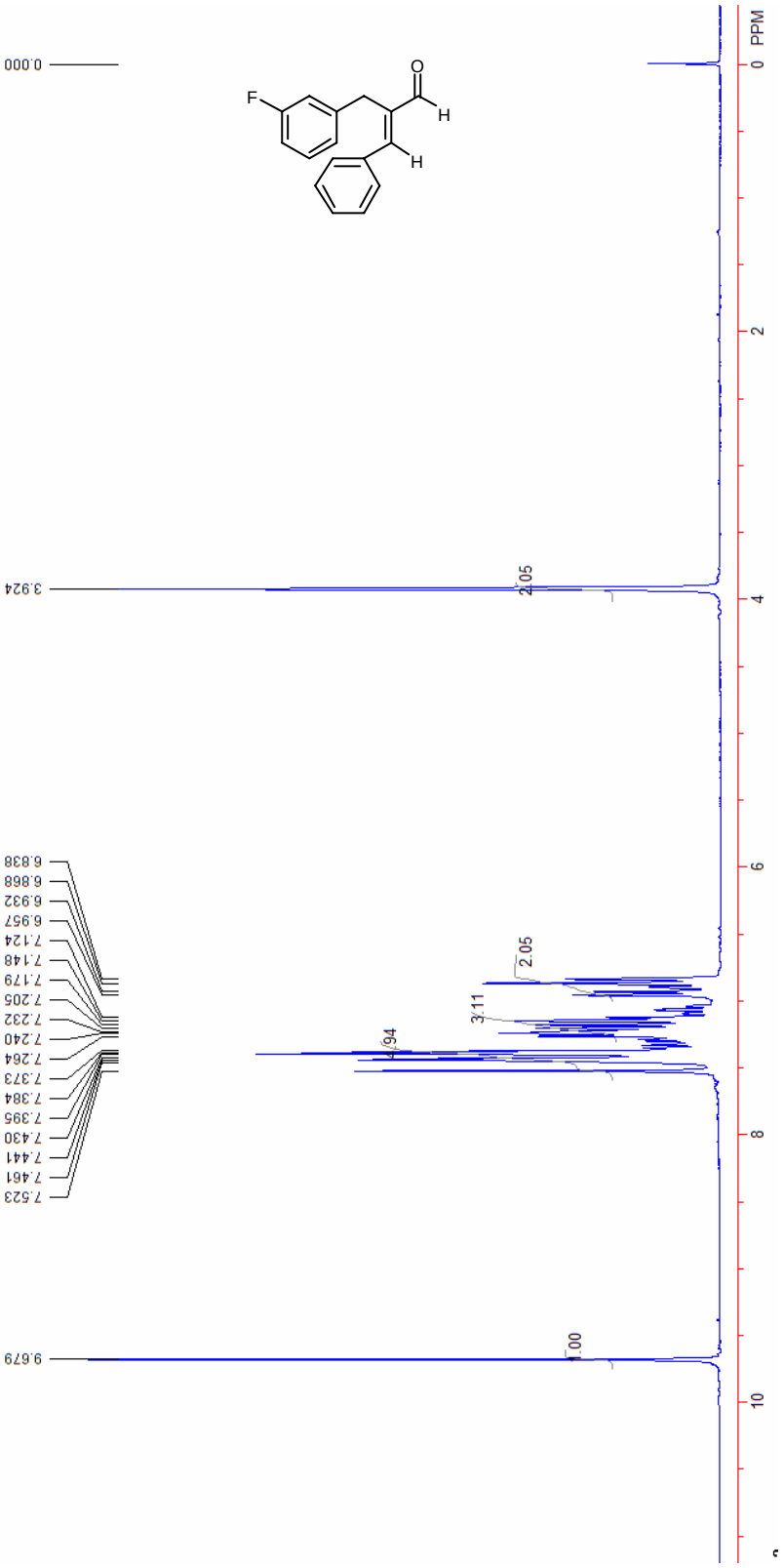
^{13}C NMR of (*E*)-2-(4-Fluorobenzyl)-3-phenylacrylaldehyde **5o**



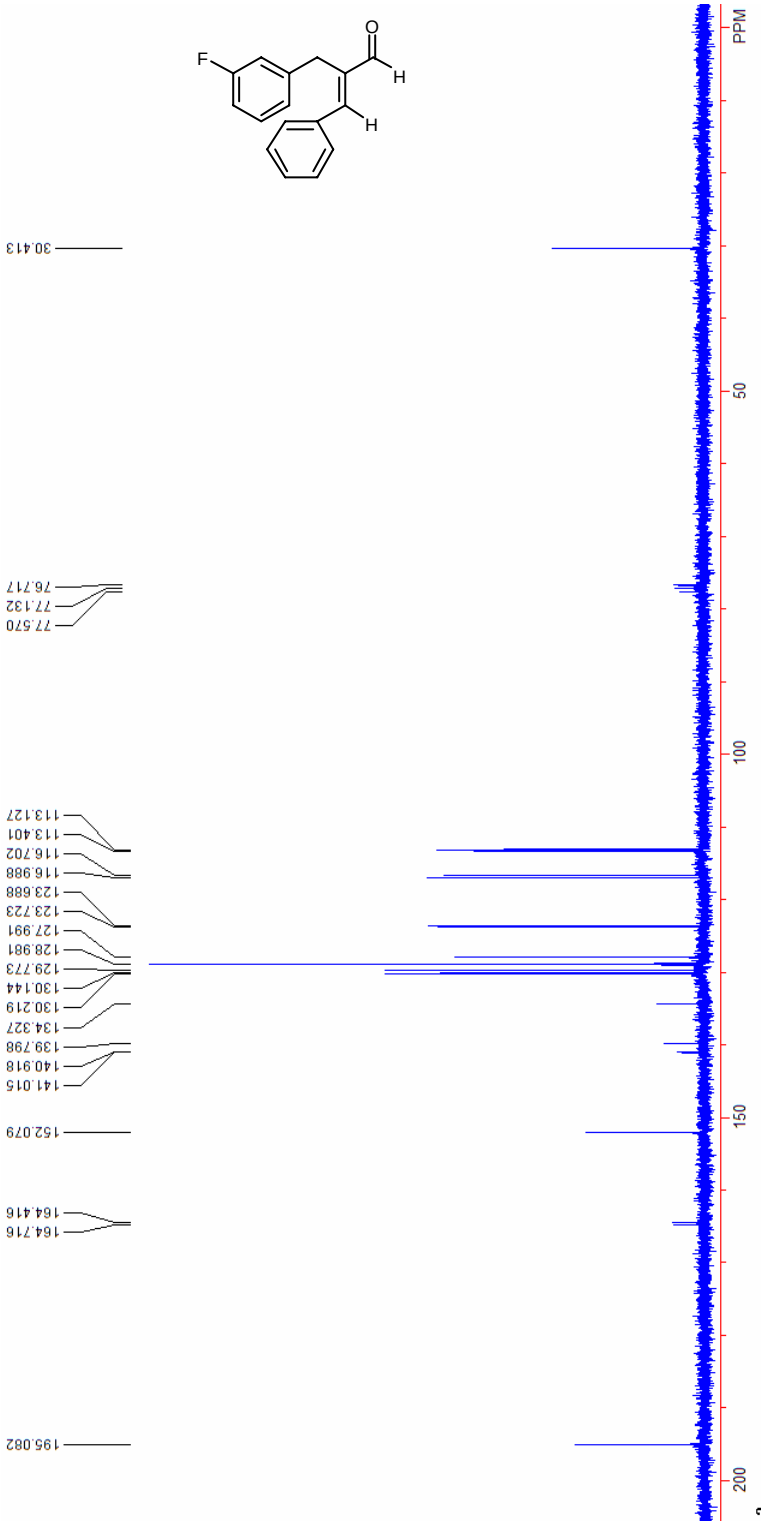
MS (EI) of (*E*)-2-(4-Fluorobenzyl)-3-phenylacrylaldehyde **5o**



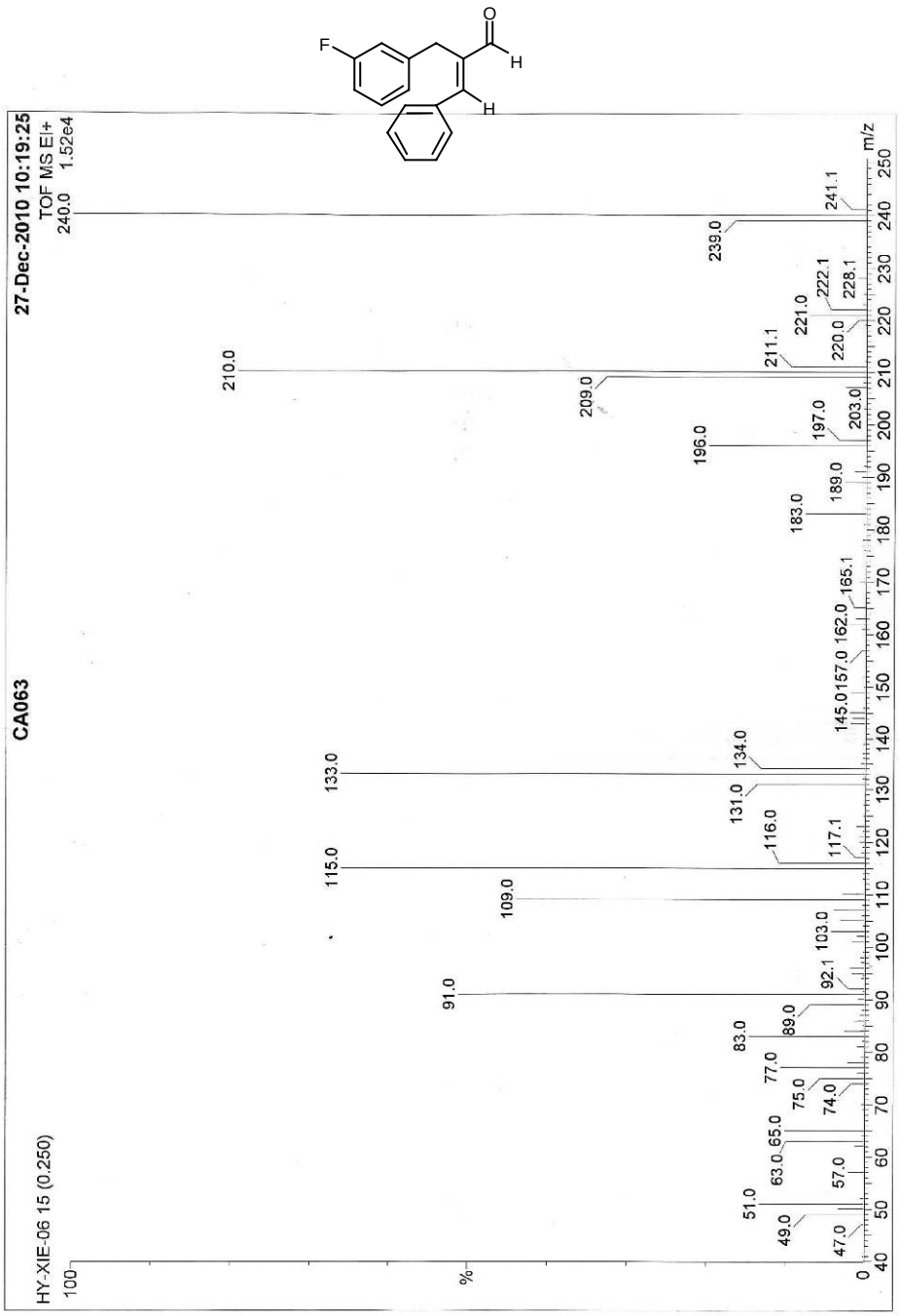
[1]H NMR of (*E*)-2-(3-Fluorobenzyl)-3-phenylacrylaldehyde **5q**



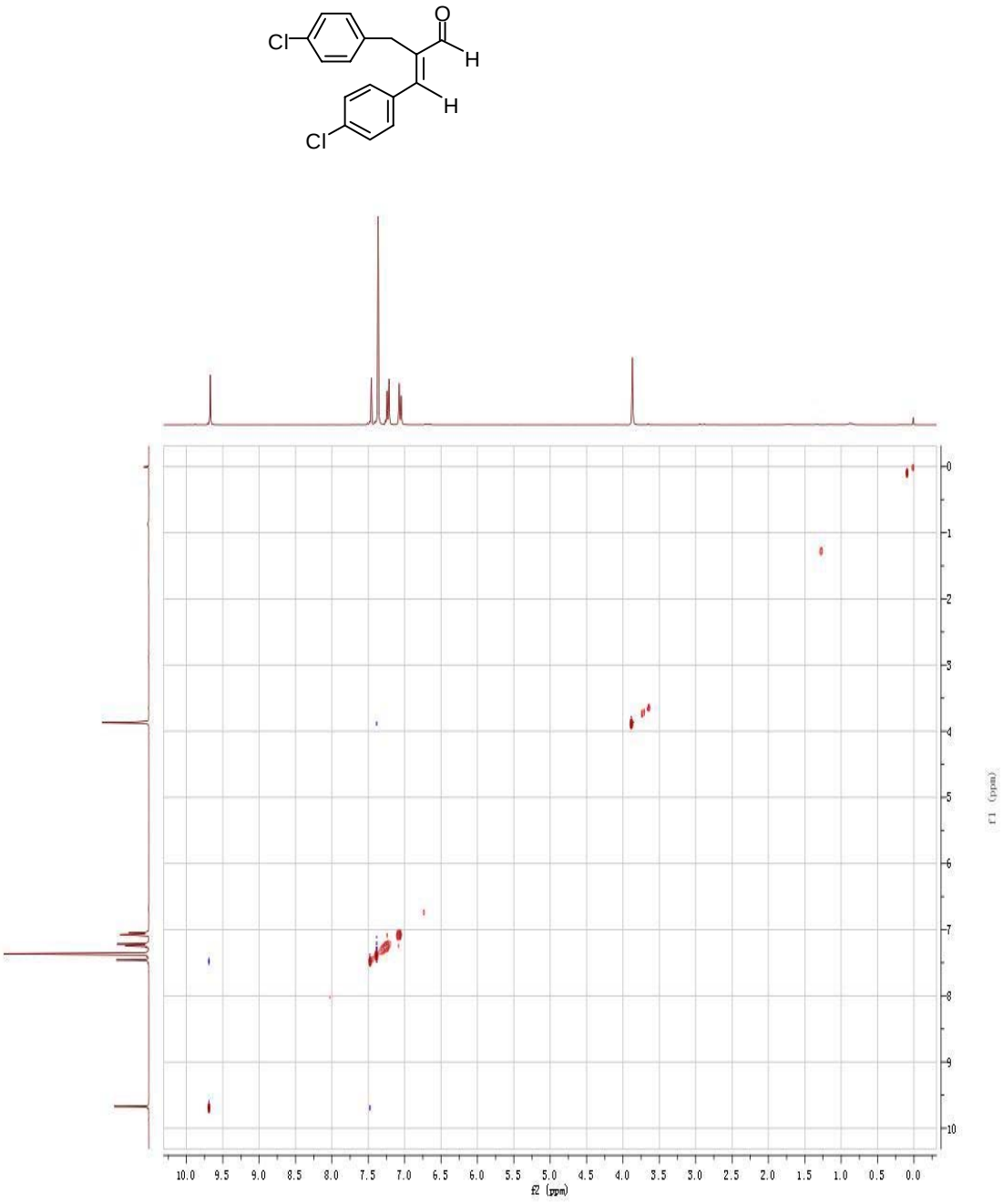
^{13}C NMR of (*E*)-2-(3-Fluorobenzyl)-3-phenylacrylaldehyde **5q**



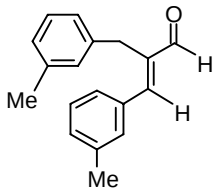
MS (EI) of (*E*)-2-(3-Fluorobenzyl)-3-phenylacrylaldehyde **5q**

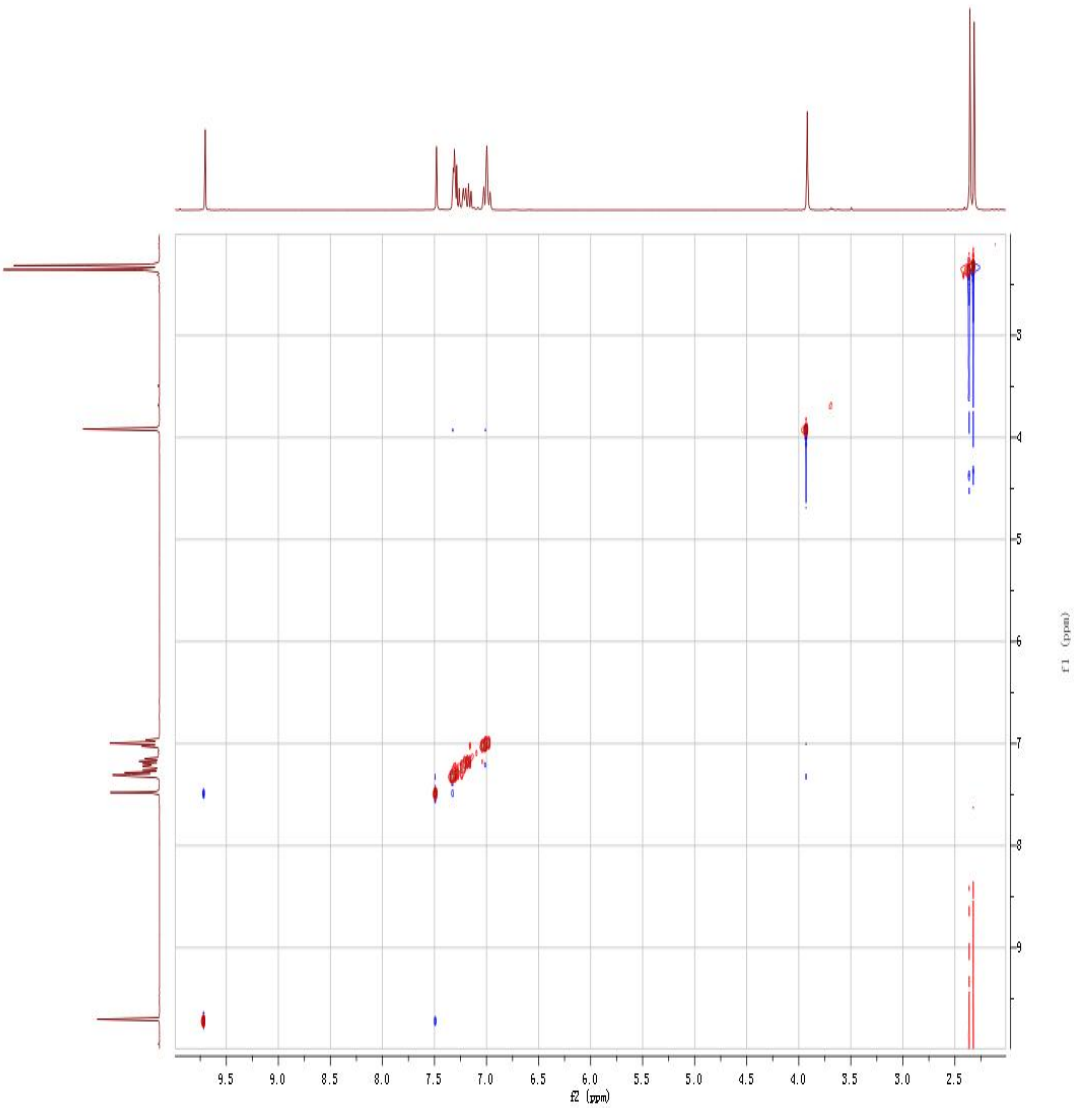


NOESY spectrum ($CDCl_3$) of (*E*)-2-(4-Chlorobenzyl)-3-(4-chlorophenyl)acrylaldehyde **5c**



NOESY spectrum ($CDCl_3$) of (*E*)-2-(3-Methylbenzyl)-3-(3-methylphenyl)acrylaldehyde **5k**





NOESY spectrum ($CDCl_3$) of (*E*)-2-(2-Methylbenzyl)-3-(2-methylphenyl)acrylaldehyde **5l**