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X-ray Crystallographic and Spectroscopic Properties of Eight Schiff Bases as Evidence of the Proton Transfer Reaction. Role of the Intermolecular Hydrogen Bond.

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Supplementary Information

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General method for the synthesis of Schiff bases 1-8. Equimolar quantities of the corresponding salicylaldehyde and aminoalcohol were dissolved in methanol (50 mL) and heated under reflux from 45 min to 1.5 hr, using a Dean-Stark trap, until formation of a solid precipitate or a turbidity of the solution. Then, the reaction mixtures were left to evaporate at ambient temperature and suitable crystals for X-ray diffraction were obtained.

2,4-ditertbutyl-6-[(1-hydroxycyclohexylmethylimino)methyl]phenol **(1).** The title compound was prepared from 3,5-ditertbutylsalicylaldehyde 0.50 g (2.13 mmol) and 1-aminomethyl-1-cyclohexanol hydrochloride 0.35 g (2.13 mmol) under reflux for 30 min, to give 0.68 g (1.96 mmol, 92% yield) of **1**. m.p.: 98-100 °C. IR (KBr) $\bar{\nu}_{max}$: 3438 (OH), 2958, 2935, 2866, 1628 (C=N), 1596, 1474, 1441, 974, 887, 852, 715 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 13.59 (1H, br, OH), 8.37 (1H, s, H-8), 7.40 (1H, d, J = 2.3 Hz, H-4), 7.11 (1H, d, J = 2.3 Hz, H-6), 3.58 (2H, s, CH_2-10), 1.72-.1.47 [10H, m, (-CH_2-)$_5$], 1.45 [9H, s, -C(CH_3)$_3$], 1.31 [9H, s, -C(CH_3)$_3$]. ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.1 (C-8), 158.2 (C-2), 140.3 (C-5), 136.8 (C-3), 127.2 (C-4), 126.2 (C-6), 117.9 (C-7), 71.6 (C-11), 70.4 (C-10), 35.9 (C-12 and C-16), 35.1 (-**C**(CH_3)$_3$), 34.2 (-**C**(CH_3)$_3$), 31.6 (-C(**C**H_3)$_3$), 29.5 (-C(**C**H_3)$_3$), 26.0 (C-14), 22.0 (C-13 and C-15). HR-APCI-MS: *m/z* for $C_{22}H_{35}NO_2$ $[M + H]^+$ calc.: 346.2741, found: 346.2745.

2,4-ditertbutyl-6-[(2-hydroxymethylphenylimino)methyl]phenol **(2).** The title compound was prepared from 3,5-ditertbutylsalicylaldehyde 0.50 g (2.13 mmol) and 2-aminobenzylalcohol 0.26 g (2.13 mmol) under reflux for 1.5 h, to give 0.62 g (1.82 mmol, 86 %) of **2**. m.p.: 105-107 °C. IR (KBr) $\bar{\nu}_{max}$: 3315 (OH), 2956, 2868, 2355, 2350, 1614(C=N), 1569, 1464, 1436, 1360, 1247, 1168, 1038, 761 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 13.42 (1H, br, OH), 8.64 (1H, s, H-8), 7.53 (1H, d, J = 7.4 Hz, H-14), 7.50 (1H, d, J = 2.5 Hz, H-6), 7.39 (1H, t, J = 7.5 Hz, H-12), 7.31 (1H, t, J = 7.5, H-13), 7.27 (1H, d, J = 2.5 Hz, H-4), 7.14 (1H, d, J = 7.5 Hz, H-11), 4.90 (1H, s, H-16), 2.00 (1H, br, OH), 1.51 (9H, s, -C(CH_3)$_3$), 1.36 (9H, s, -C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 164.7 (C-8), 158.3 (C-2), 147.1 (C-10), 140.9 (C-5), 137.2 (C-3), 134.5 (C-15), 128.9 (C-12), 128.5 (C-6), 128.2 (C-14), 127.1 (C-4), 126.9 (C-13), 118.5 (C-7), 118.3 (C-11), 62.0 (C-16), 35.3 (-**C**(CH_3)$_3$), 34.3 (-**C**(CH_3)$_3$), 31.6 (-C(**C**H_3)$_3$), 29.6 (-C(**C**H_3)$_3$). HR-APCI-MS: *m/z* for $C_{22}H_{30}NO_2$ $[M + H]^+$ calc.: 340.2271, found: 340.2275.

(1R,2S)-2-[(2-hydroxy-1,2-diphenylethylimino)methyl]phenol **(3)**. The title compound was prepared from salicylaldehyde 0.15 g (1.23 mmol) and (1*S*,2*R*)-2-amino-1,2-diphenyletanol 0.26 g (1.23 mmol) under reflux for 45 min, to give 0.34 g (1.07 mmol, 87% yield) of **3**. m.p.: 129-131°C. IR

(KBr) $\bar{\nu}_{max}$: 3444 (OH), 3060, 3030, 2872, 1629 (C=N), 1579, 1497, 1454, 1425, 1277, 1054, 759, 710, 697 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ: 13.18 (1H, br, OH), 8.08 (1H, s, H-8), 7.43-7.20 (11H, m, H-4, H-13-H-17 and H-19-H-23), 7.08 (1H, d, J = 7.4 Hz, H-6), 6.95 (1H, d, J = 8.4, H-3), 6.82 (1H, t, J = 7.4, H-5), 5.04 (1H, d, J = 7.0 Hz, H-11), 4.53 (1H, d, J = 7.0 Hz, H-10), 2.20 (1H, br, OH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 166.0 (C-8), 161.0 (C-2), 140.3 (C_i), 139.6 (C_i), 132.6 (C-4), 131.8 (C-6), 128.9 (C_{o}-), 128.3 (C_{o}-), 128.2 (C_{p}-), 128.1 (C_{m}-), 127.3 (C_{m}-), 118.8 (C-5), 118.7 (C-7), 117.0 (C-3), 80.2 (C-11), 78.4 (C-10). HR-APCI-MS: *m/z* for $C_{21}H_{19}NO_2$ $[M + H]^+$ calc.: 318.1489, found: 318.1492.

***2-[{(1-hydroxylcyclohexyl)methylimino}methyl]phenol* (4).** The title compound was prepared from salicylaldehyde 0.20 g (1.64 mmol) and 1-aminomethyl-1-cyclohexanol hydrochloride 0.27 g (1.64 mmol) under reflux for 30 min, to give 0.36 g (1.55 mmol, 95% yield) of **4**. m.p.: 156-158 °C. IR (KBr) $\bar{\nu}_{max}$: 3221 (NH), 3050, 2925, 2850, 1644 (C=O), 1611 (C=N), 1524, 1288, 1146, 912, 742 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ: 13.41 (1H, br, OH), 8.35 (1H, s, H-8), 7.32-7.26 (2H, m, H-4 and H-6), 6.96-6.90 (1H, m, H-3), 6.89-6.86 (1H, m, H-5), 3.58 (2H, s, CH_2-10), 2.16 (1H, s, br, OH), 1.72-1.53 (8H, m, CH_2-12, CH_2-13, CH_2-15 and CH_2-16), 1.33-1.28 (2H, m, CH_2-14). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 166.9 (C-8), 161.3 (C-2), 132.5 (C-4), 131.5 (C-6), 118.9 (C-7), 118.7 (C-5), 117.2 (C-3), 71.5 (C-11), 70.2 (C-10), 35.8 (C-12 and C-16), 25.8 (C-14), 21.9 (C-13 and C-15). HR-APCI-MS: *m/z* for $C_{14}H_{19}NO_2$ $[M + H]^+$ calc.: 234.1489, found: 234.1491.

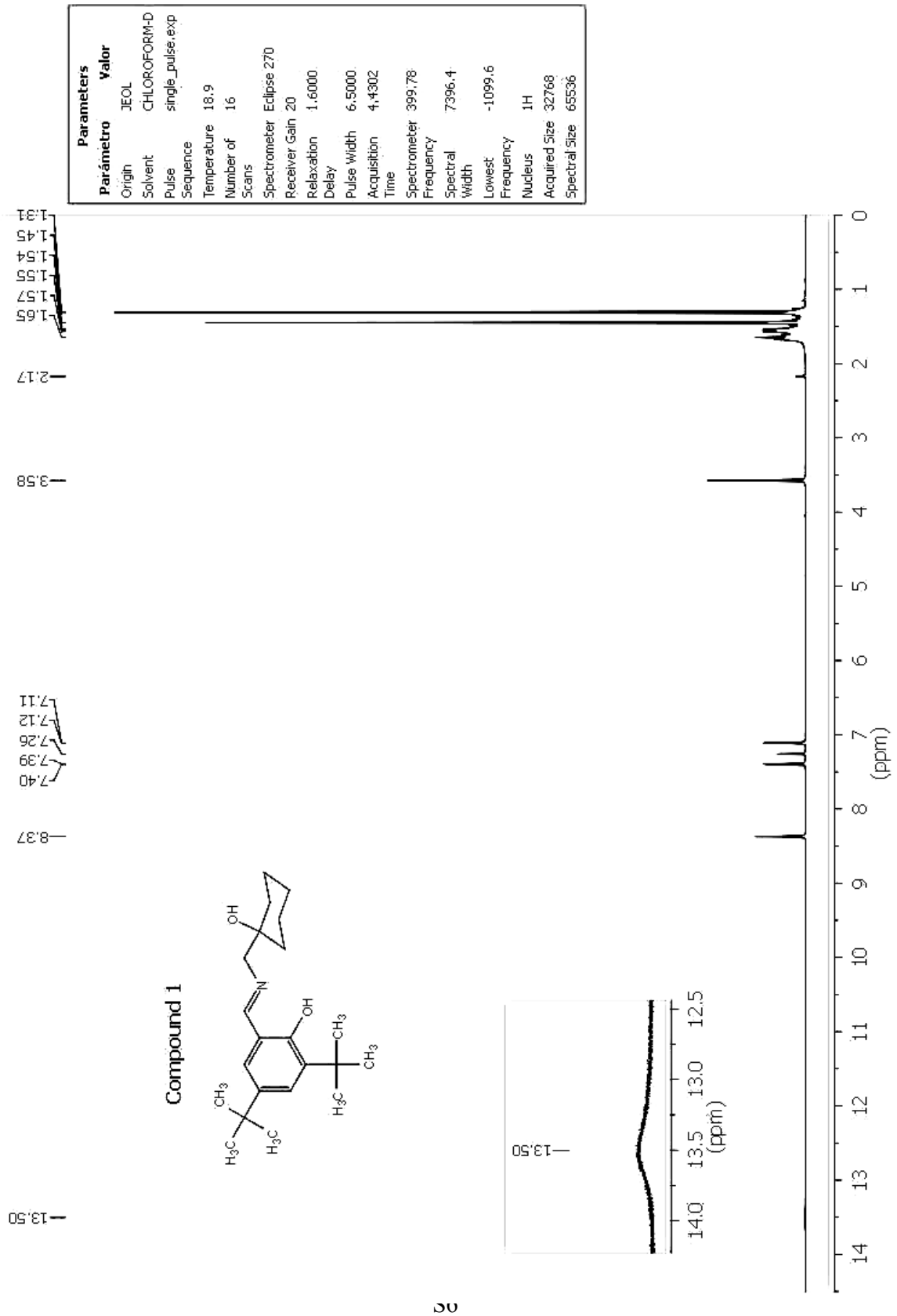
***2-[1-(2-hydroxyethylimino)ethyl]phenol* (5).** The title compound was prepared from 2′-hydroxyacetophenone 0.50 g (3.67 mmol) and ethanolamine 0.22 g (3.67 mmol) under reflux for 1 h, to give 0.63 g (3.52 mmol, 95% yield) of **5**. m.p.: 96-98 °C. IR (KBr) $\bar{\nu}_{max}$: 3170 (NH), 2923, 2866, 1607 (C=N), 1543, 1459, 1340, 1068, 772, 754 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ: 16.75 (1H, br, OH), 7.30 (1H, d, J = 8.1 Hz, H-6), 7.20 (1H, t, J = 7.2 Hz, H-4), 6.79 (1H, d, J = 8.1, H-3), 6.60 (1H, t, 7.2 Hz, H-5), 4.66 (1H, b, OH), 3.90 (2H, t, J = 5.1 Hz, -CH_2-O-), 3.63 (2H, t, J = 5.1 Hz, N-CH_2-), 2.22 (3H, s, CH_3-8). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 173.7 (C-8), 166.9 (C-2),133.4 (C-6), 128.5 (C-4), 119.9 (C-5), 118.2 (C-7), 116.1 (C-3), 61.6 (-CH_2-O-), 50.6 (N-CH_2-), 14.5 (CH_3). HR-APCI-MS: *m/z* for $C_{10}H_{13}NO_2$ $[M + H]^+$ calc.: 180.1019, found: 180.1023.

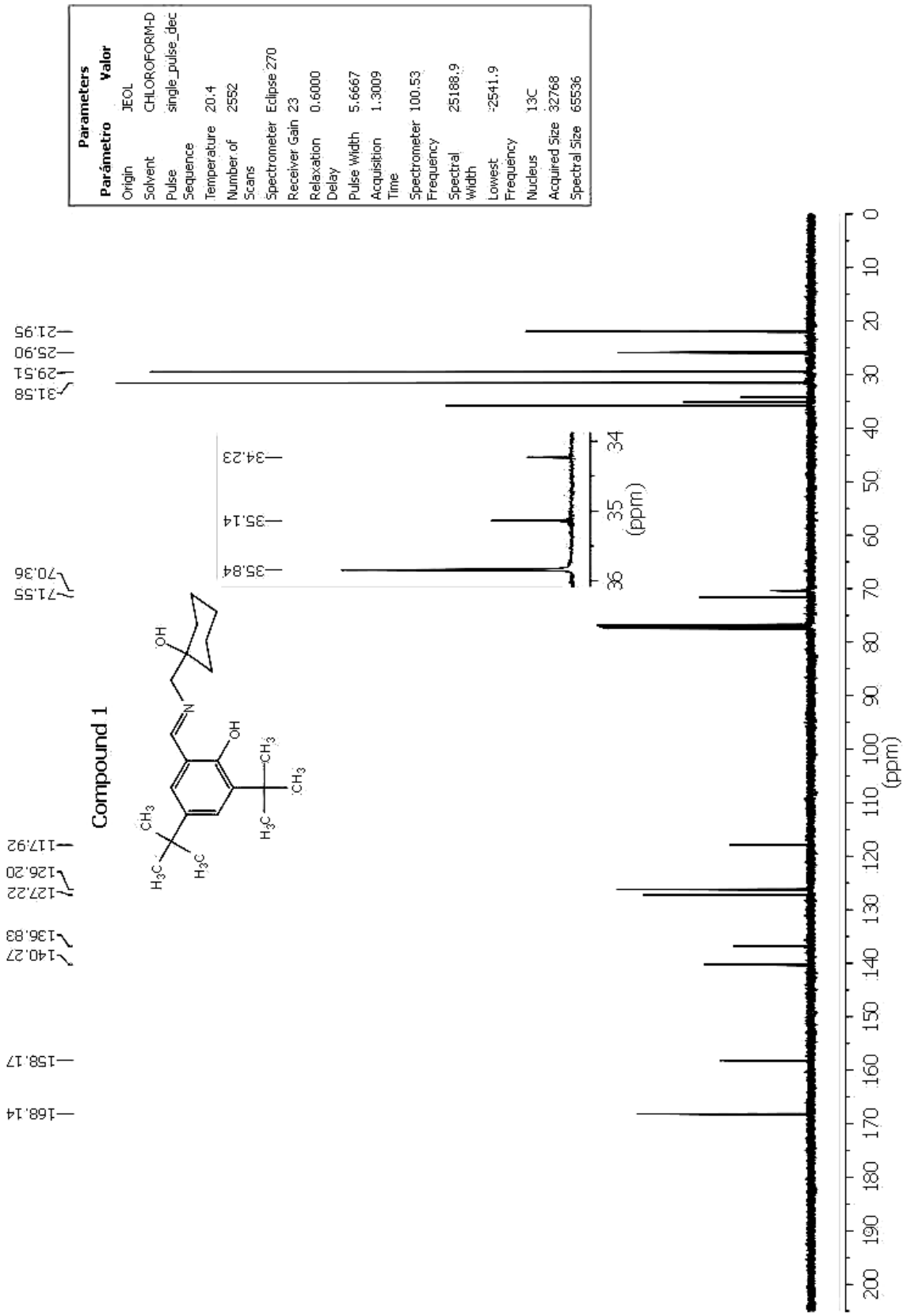
***2-[{(1S,2R)-1-hydroxy-1-phenylpropan-2-ylimino}methyl]-4-nitrophenol* (6).** The title compound was prepared from 2-hydroxy-5-nitrosalicyaldehyde 0.50 g (2.99 mmol) and (1*S*,2*R*)-norephedrine 0.45 g

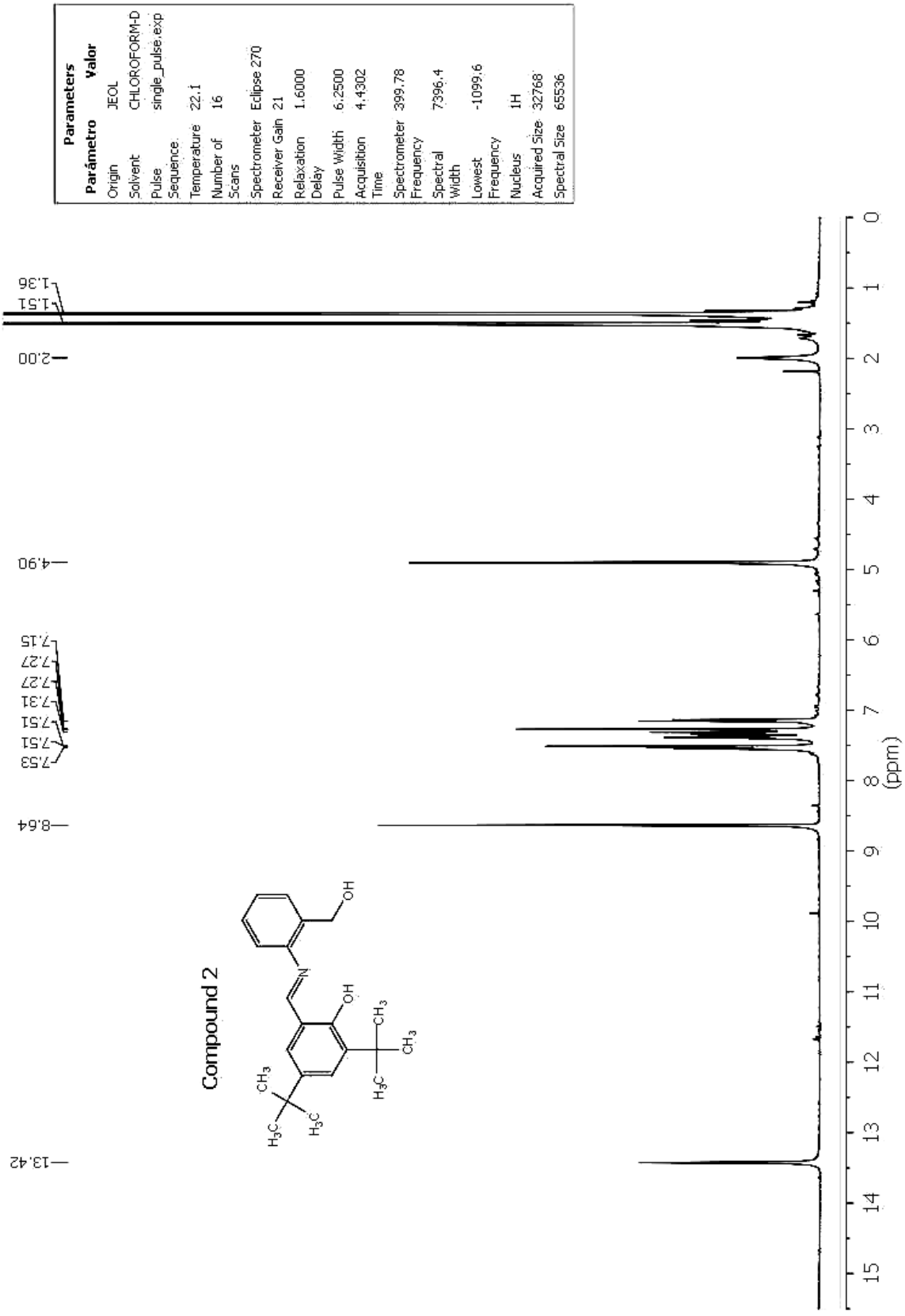
(2.99 mmol) under reflux for 1 h, to give 0.79 g (2.64 mmol, 88% yield) of **6**. m.p.: 169-171 °C. IR (KBr) $\bar{\nu}_{max}$: 3413 (O-H), 3257 (N-H), 3067, 2986, 1657 (C=O), 1612 (C=N), 1547, 1332, 1300, 1233, 702 ,754 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 14.55 (1H, br, OH), 8.19 (1H, d, J = 4.54 Hz, H-8), 8.18-8.15 (2H, m, H-4 and H-6), 7.38-7.25 (5H, m, H-13-H-17), 6.90-6.83 (1H, m, H-3), 4.85 (1H, d, J = 5.02 Hz, H-11), 3.86-3.80 (1H, m, H-10), 2.48 (1H, br, OH), 1.35 (3H, d, J = 6.21 Hz, CH_3-10). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 170.8 (C-2), 163.8 (C-8), 140.0 (C-5), 138.3 (C-12), 129.1 (C-4), 128.7 (C-6), 128.6 (C-13 and C-17), 128.5 (C-15), 126.8 (C-14 and C-16), 119.8 (C-3), 116.1 (C-7), 77.0 (C-11), 67.7 (C-10), 17.2 (CH_3). HR-APCI-MS: *m/z* for $C_{16}H_{17}N_2O_4$ $[M + H]^+$ calc.: 301.1183, found: 301.1186.

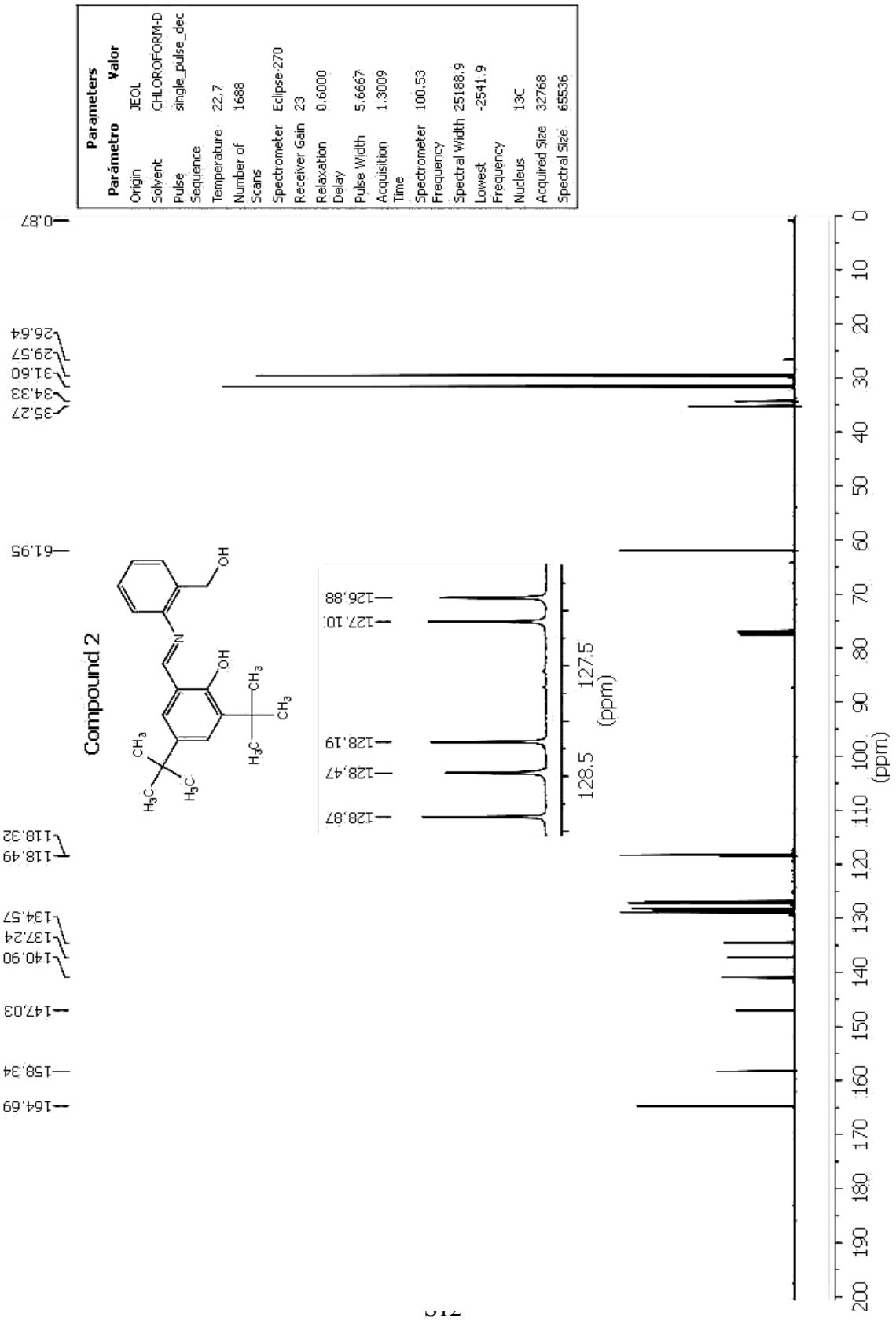
2-[{(1S,2R)-1-hydroxy-1-phenylpropan-2-ylimino}methyl]-4-bromophenol **(7).** The title compound was prepared from 5-bromosalicylaldehyde 0.33 g (1.65 mmol) and (1*S*,2*R*)-norephedrine 0.25 g (1.65 mmol) under reflux for 2 h, to give 0.45 g (1.47 mmol, 85% yield) of **7**. m.p.: 106-108 °C. IR (KBr) $\bar{\nu}_{max}$: 3053 (NH), 2975, 2849, 1645 (C=O), 1602 (C=N), 1495, 831, 750, 703 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ: 13.33 (1H, br, OH), 8.09 (1H, s, H-8), 7.40-7.25 (7H, m, H-4, H-6 and H-13-H-17), 6.80 (1H, d, J = 8.8 Hz, H-3), 4.74 (1H, d, J = 5.6 Hz, H-11), 3.64 (1H, quint, J = 6.3 Hz, H-10), 2.56 (1H, br, OH), 1.29 (3H, d, J = 6.3, CH_3-10). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 163.4 (C-8), 160.6 (C-2), 140.8 (C-12), 135.1 (C-4) 133.6 (C-6), 128.4 (C-13 and C-17), 128.1 (C-15), 127.0 (C-14 and C-16), 120.0 (C-7), 119.2 (C-3), 110.0 (C-5), 77.6 (C-11), 69.9 (C-10), 18.1 (CH_3). HR-APCI-MS: *m/z* for $C_{16}H_{16}BrNO_2$ $[M + H]^+$ calc.: 334.0437, found: 334.0433.

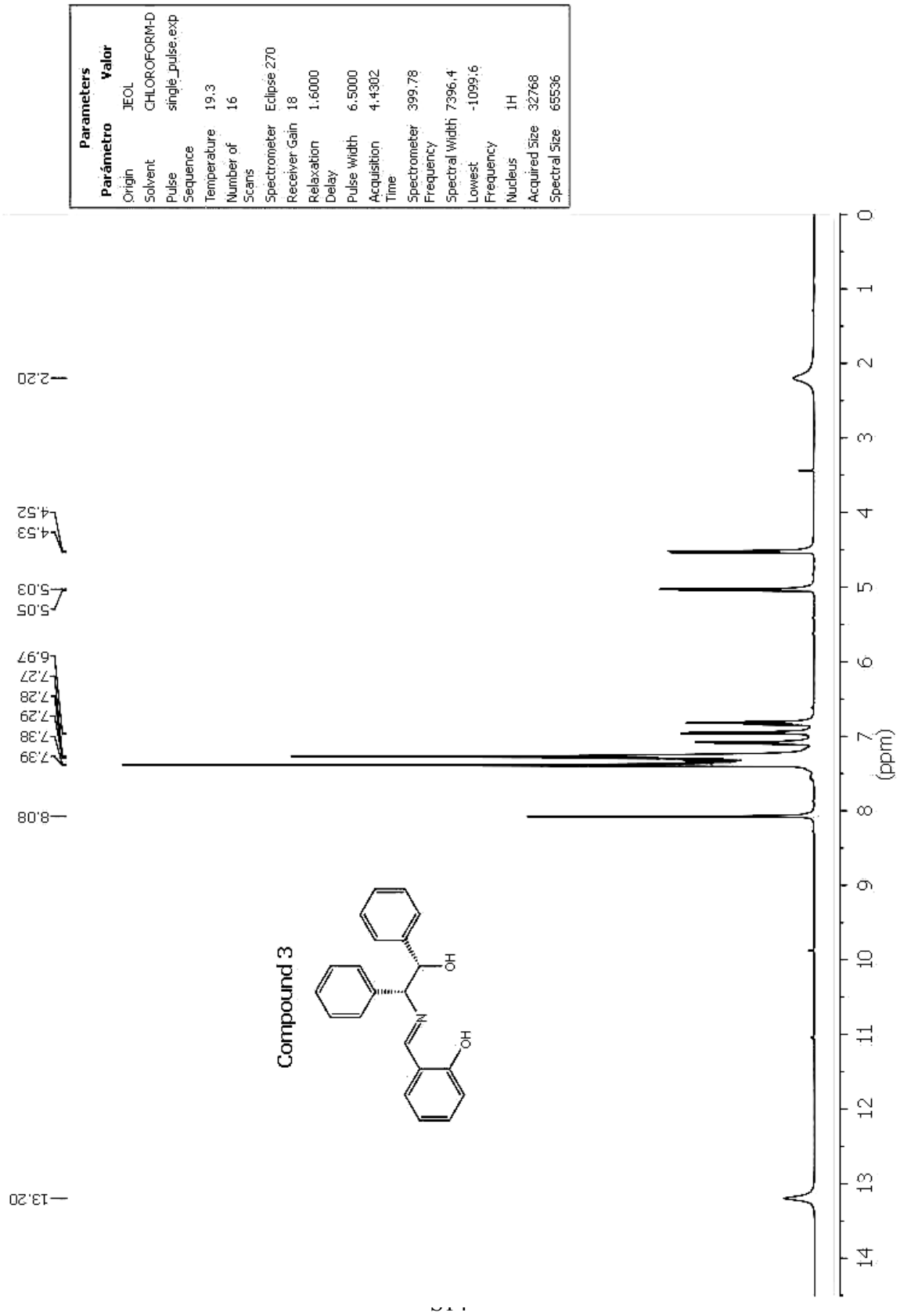
2-[(4-Chloro-2-hydroxymethylphenylimino)methyl]-5-diethylaminophenol **(8).** The title compound was prepared from 4-diethylaminosalicylaldehyde 1.00 g (5.17 mmol) and 2-amino-5-chlorobenzyl alcohol 0.82 g (5.17 mmol) under reflux of methanol for 2.0 h, to give 1.60 g (4.8 mmol, 93% yield) of **8**. m.p.: 115-117 °C. IR (KBr) $\bar{\nu}_{max}$: 3212 (OH, NH), 2971, 1610 (C=O, C=N), 1520, 1345, 1241, 1132, 1044, 785 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ: 13.63 (1H, br, OH), 8.28 (1H, s, H-8), 7.46 (1H, d, J = 2.3 Hz, H-14), 7.22 (1H, dd, J = 8.6, 2.3 Hz, H-12), 7.12 (1H, d, 8.8 Hz, H-6), 7.00 (1H, d, J = 8.6 Hz, H-11), 6.22 (1H, dd, J = 8.8, 2.3 Hz, H-5), 6.12 (1H, d, J = 2.3 Hz, H-3), 4.79 (2H, s, -CH_2-O), 3.38 (4H, q, J = 7.0 Hz, N-CH_2-), 3.0 (1H, b, OH), 1.19 (6H, t, J = 7.0 Hz, -CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 164.6 (C-2), 160.5 (C-8), 152.5 (C-4), 144.8 (C-10), 136.0 (C-15), 134.2 (C-6), 131.0 (C-13), 128.3 (C-14), 127.9 (C-12), 118.7 (C-11), 109.1 (C-7), 104.3 (C-5), 97.8 (C-3), 61.5 (C-16), 44.8 (N-CH_2-), 12.8 (-CH_3). HR-APCI-MS: *m/z* for $C_{18}H_{21}ClN_2O_2$ $[M + H]^+$ calc.: 333.1364, found: 333.1365

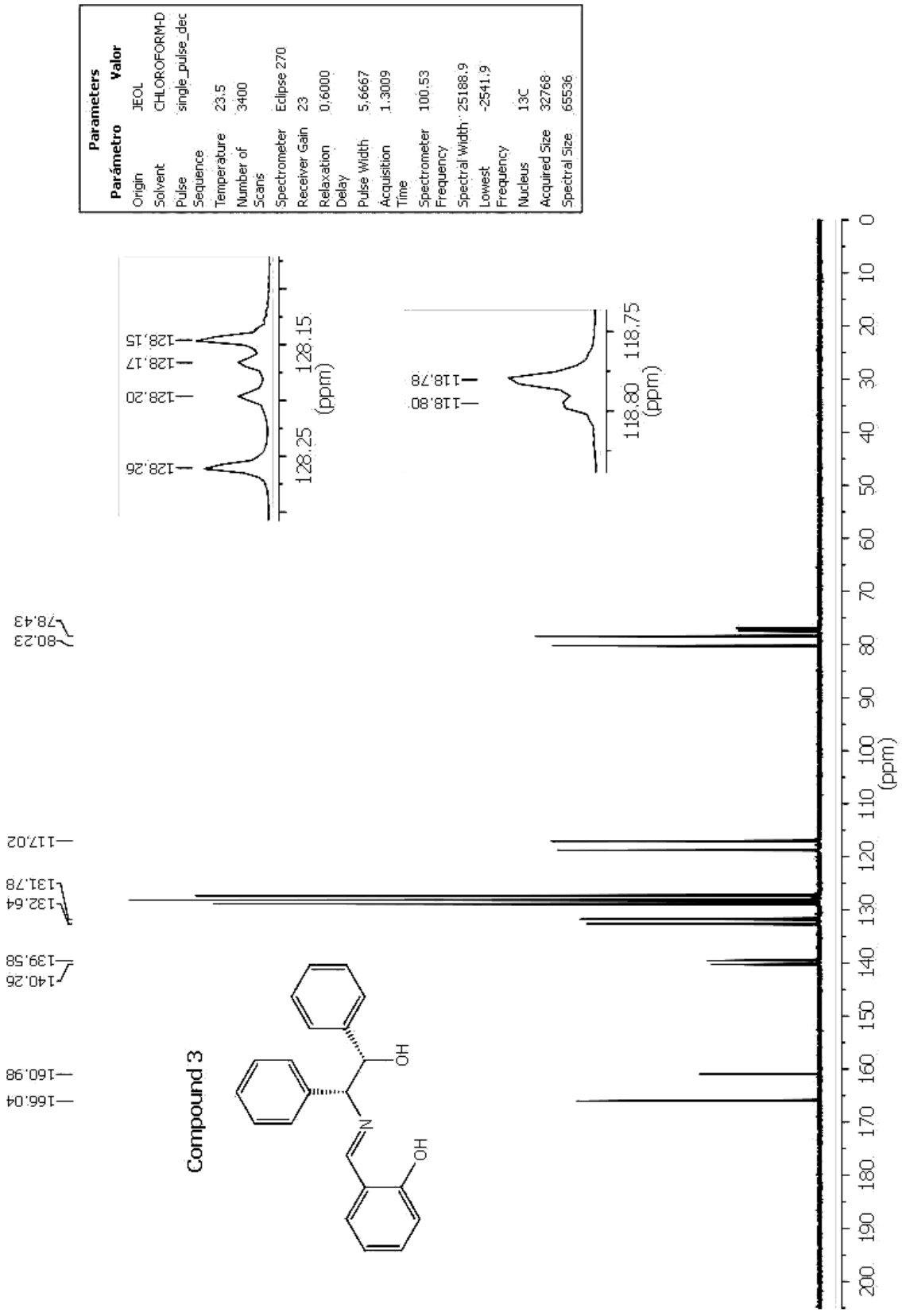


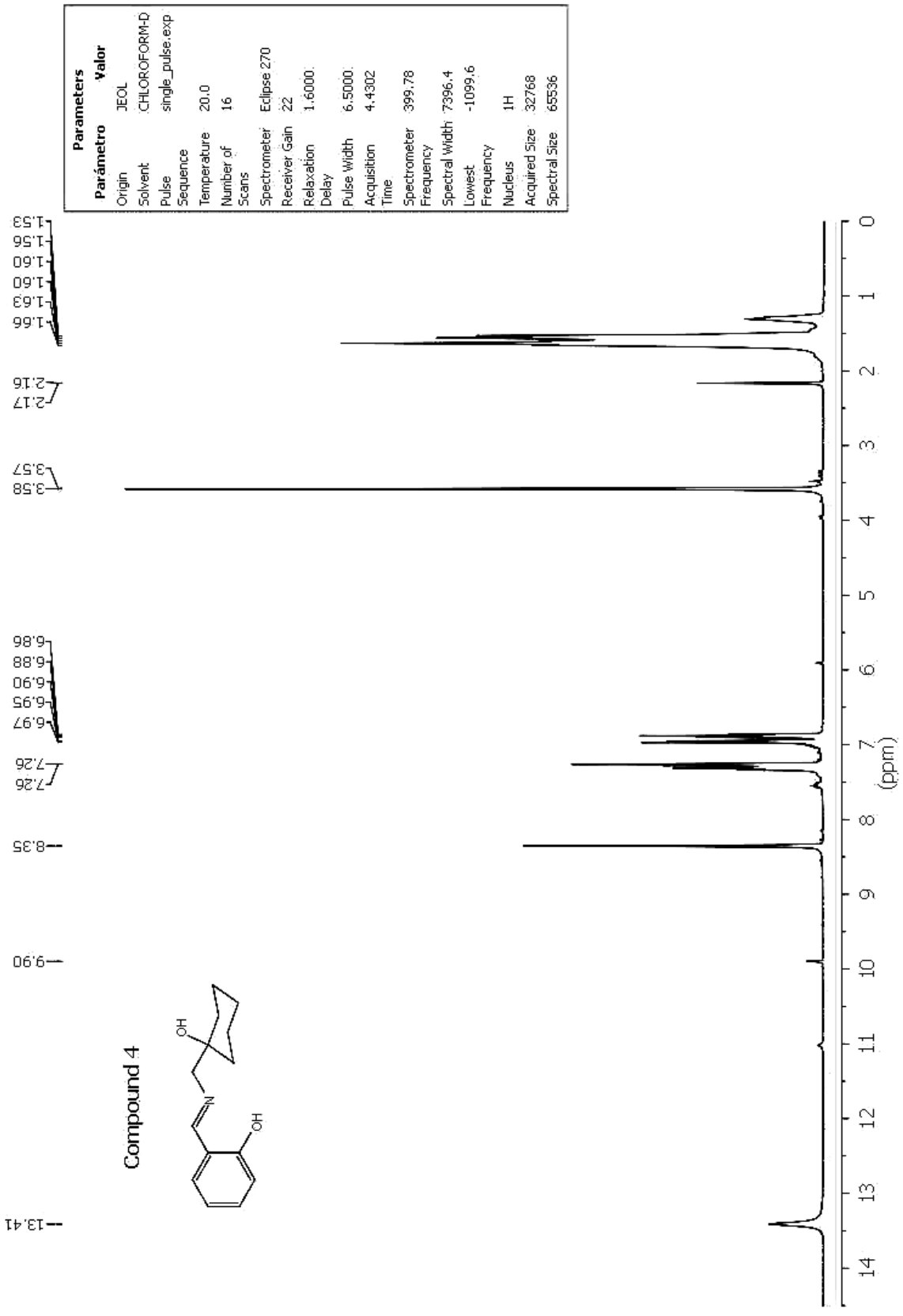


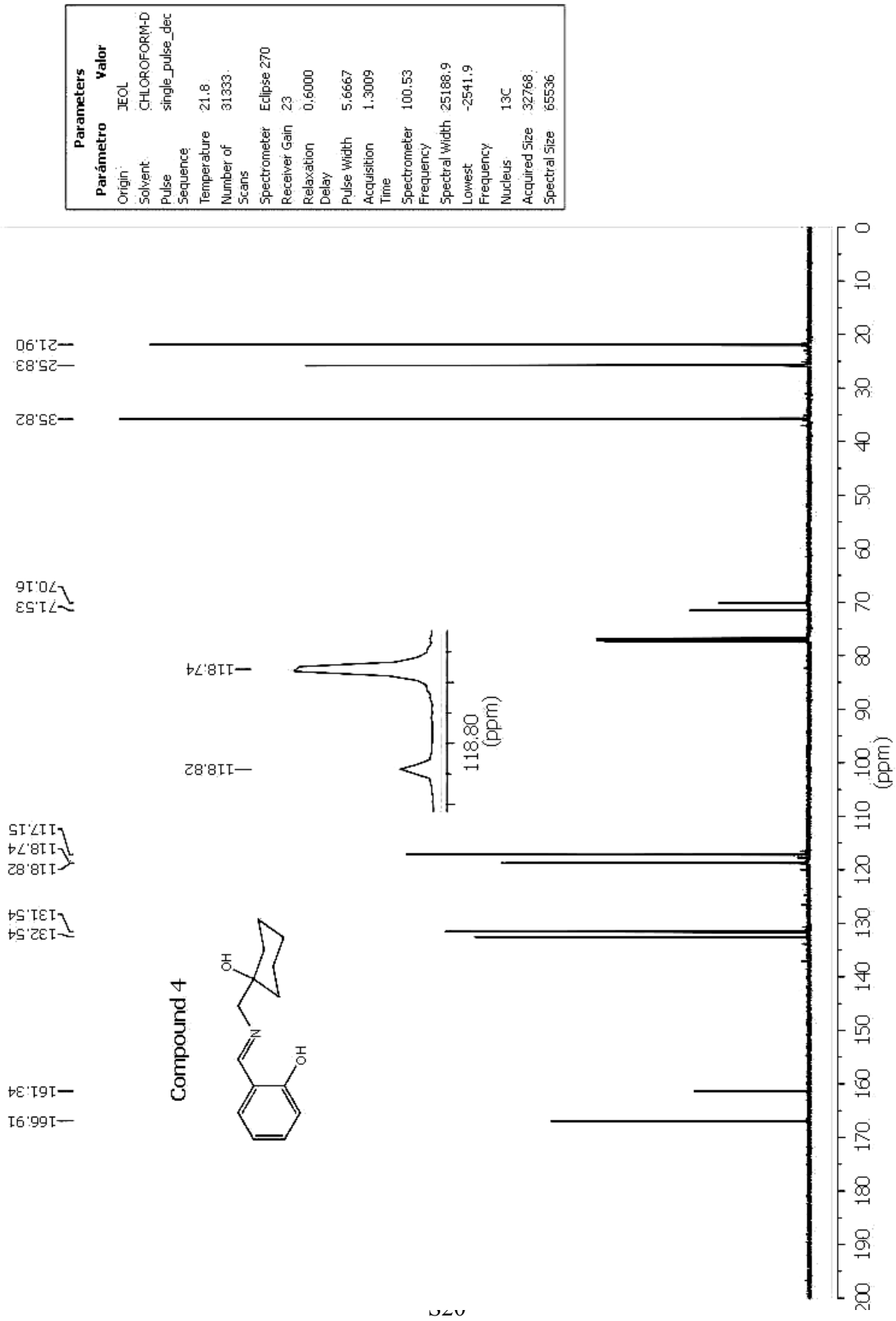


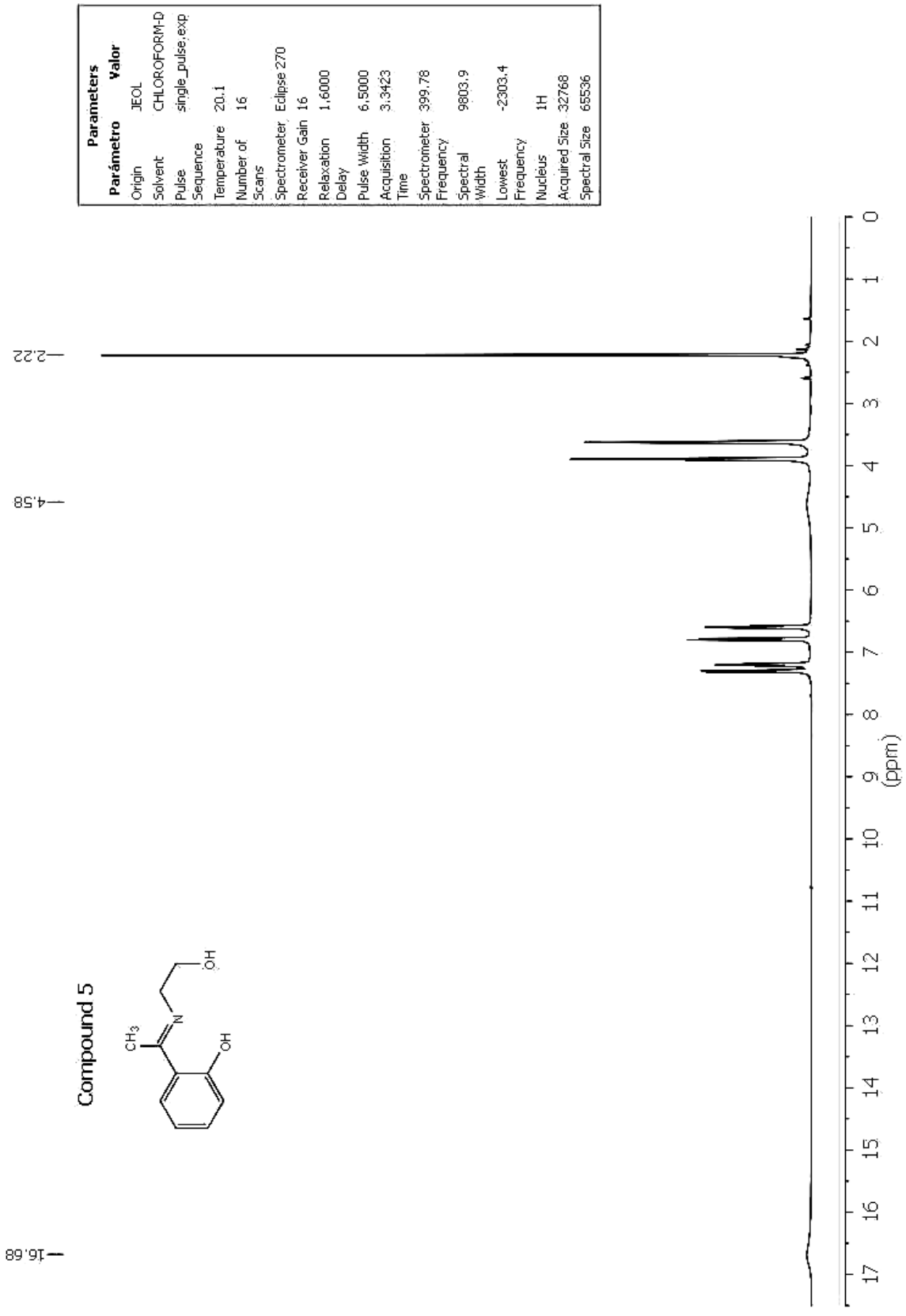


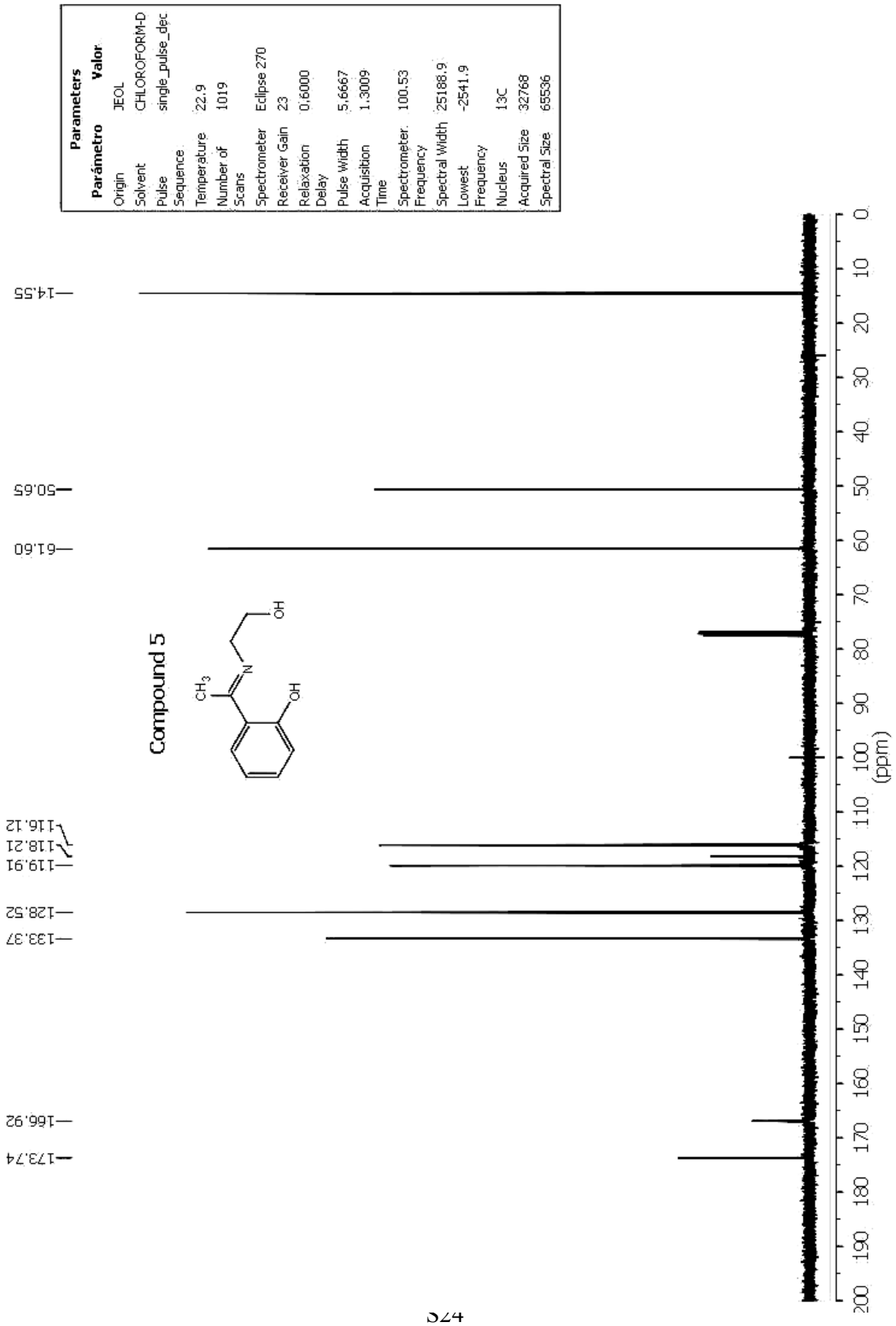


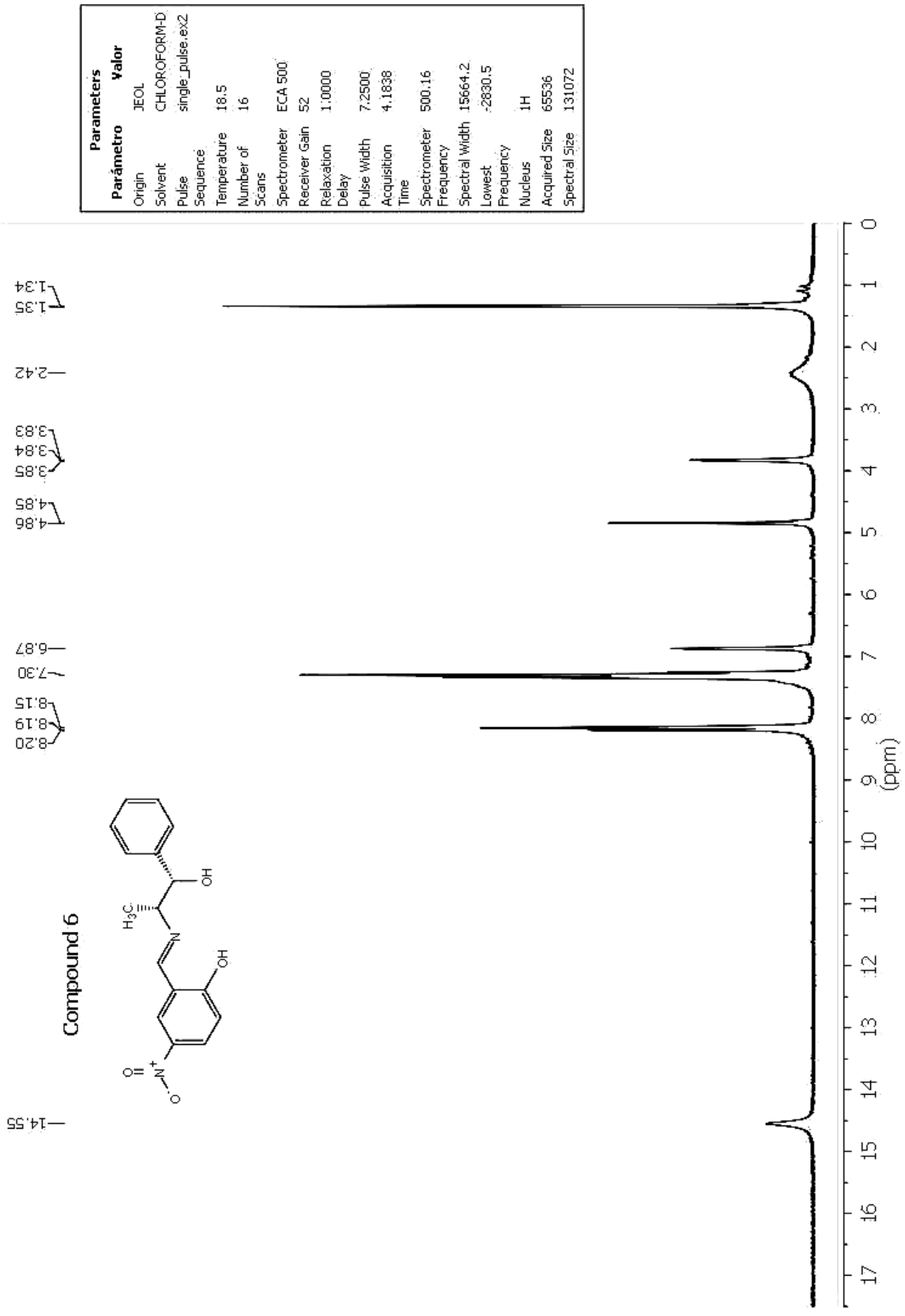


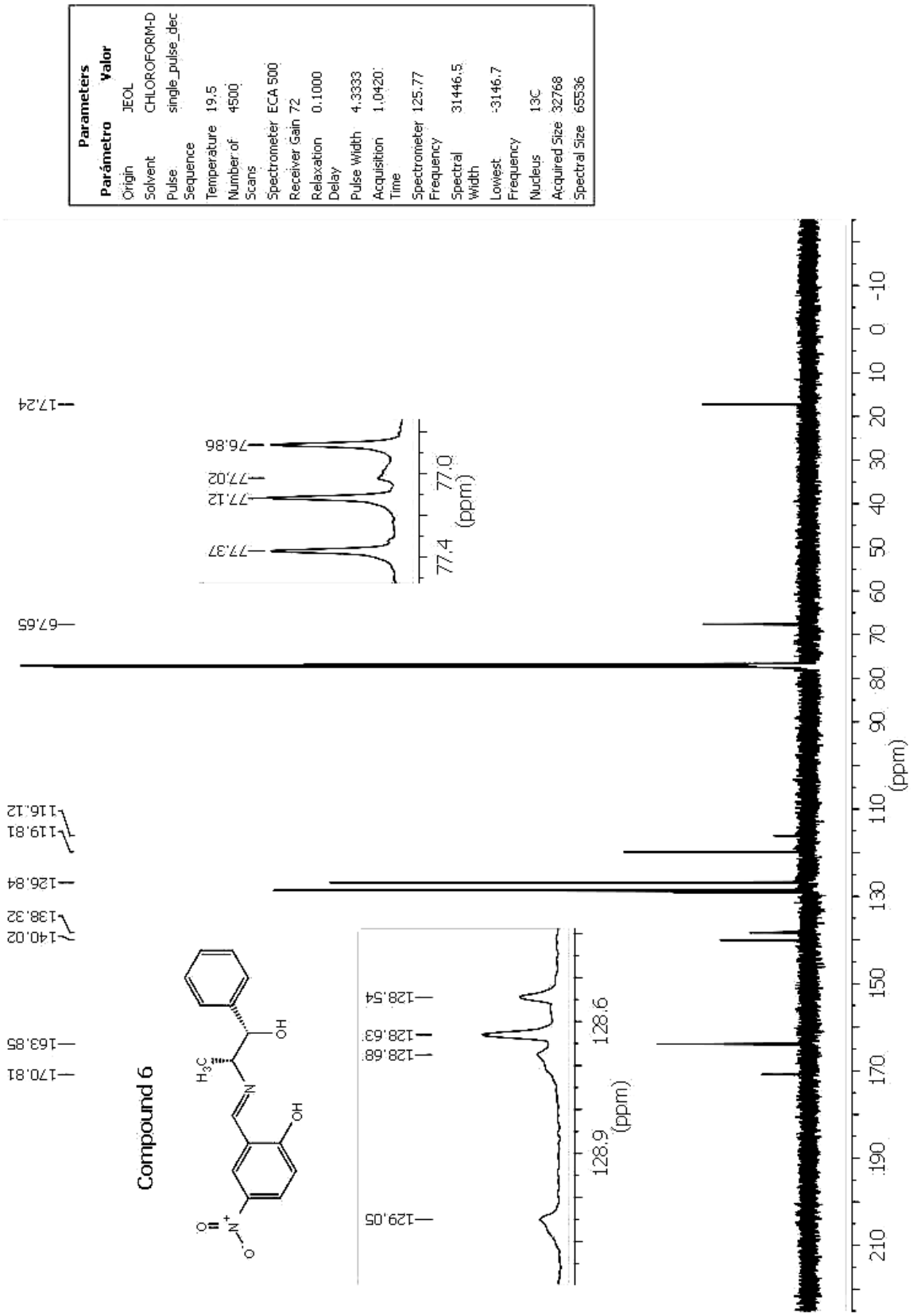


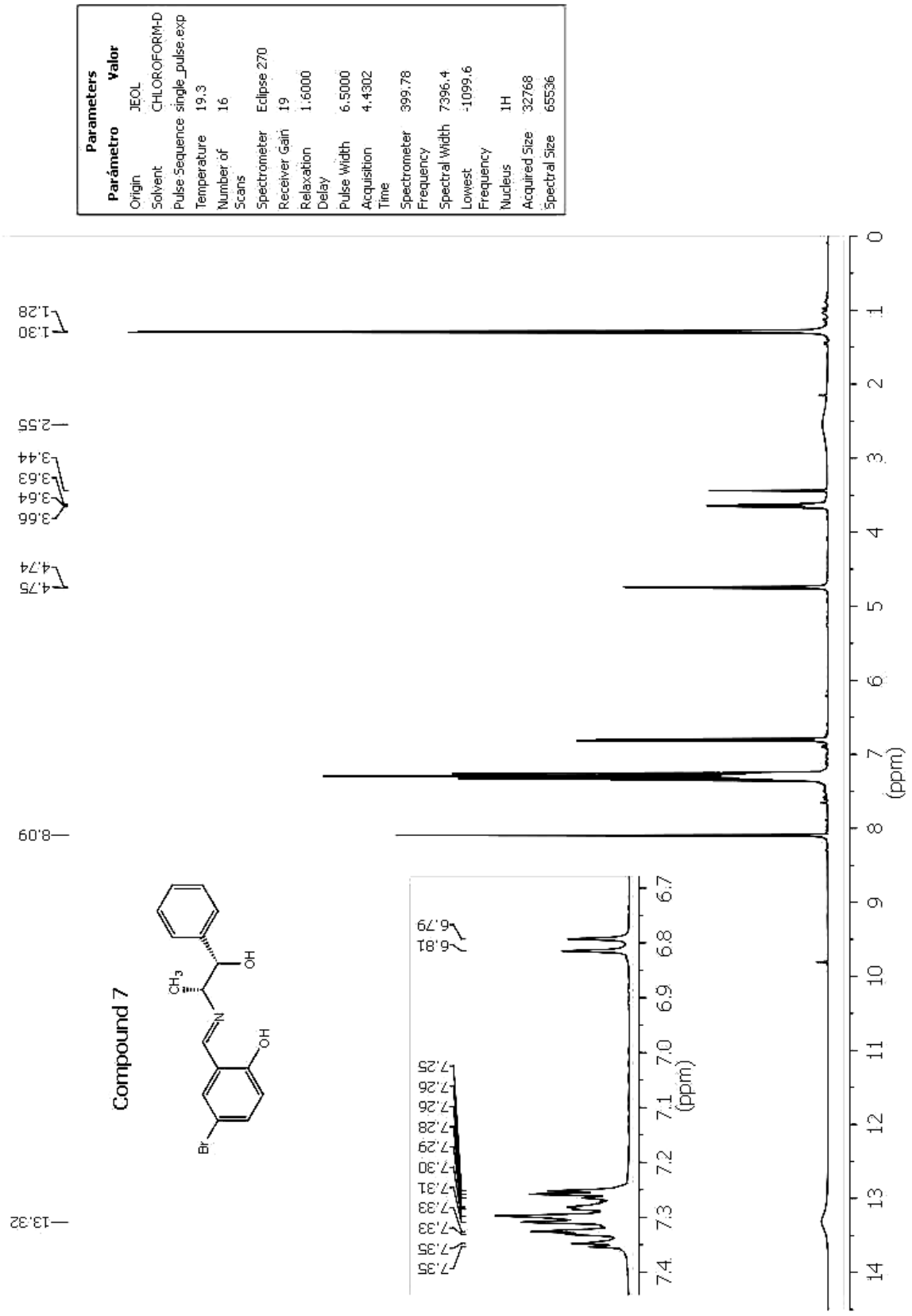


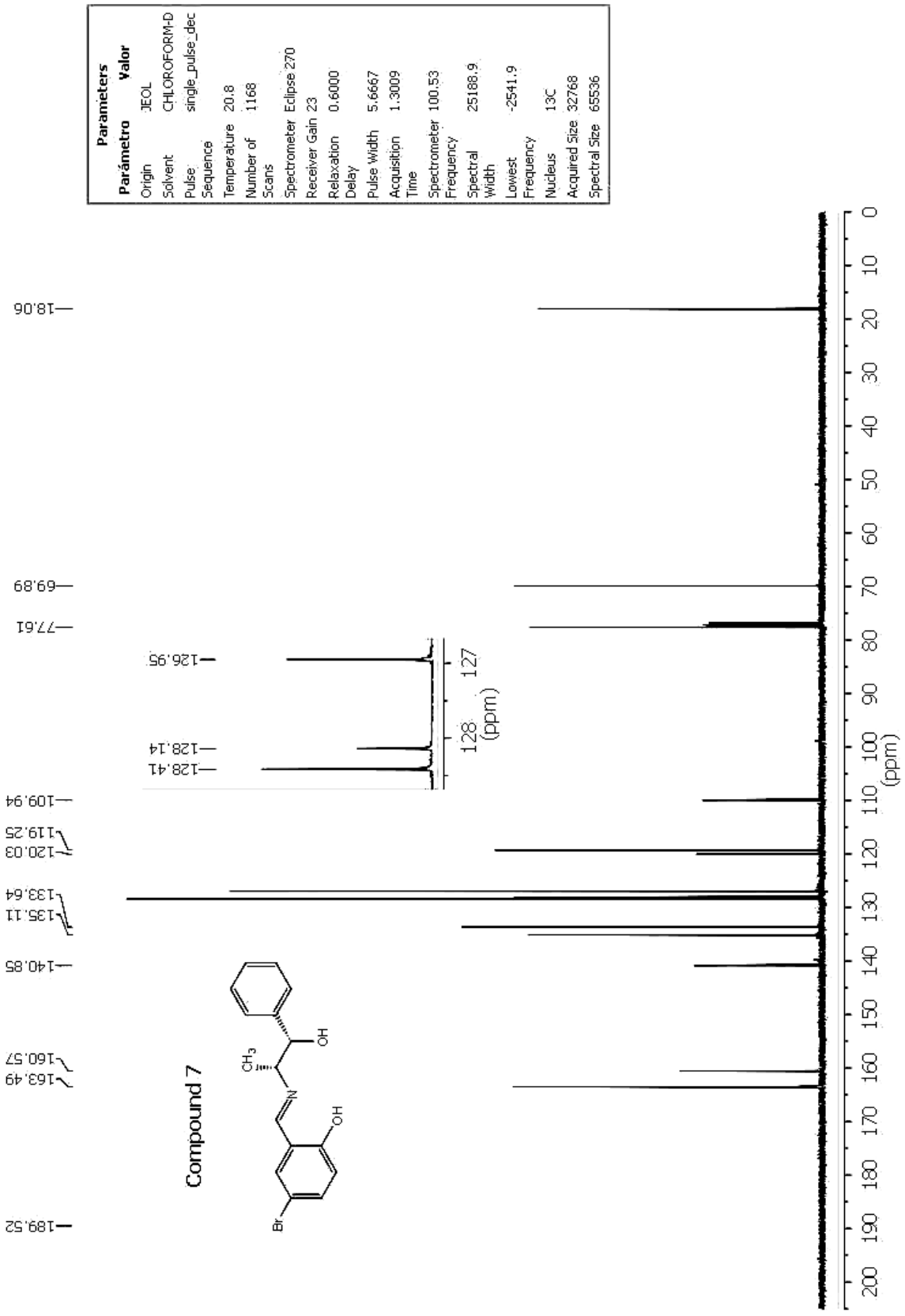


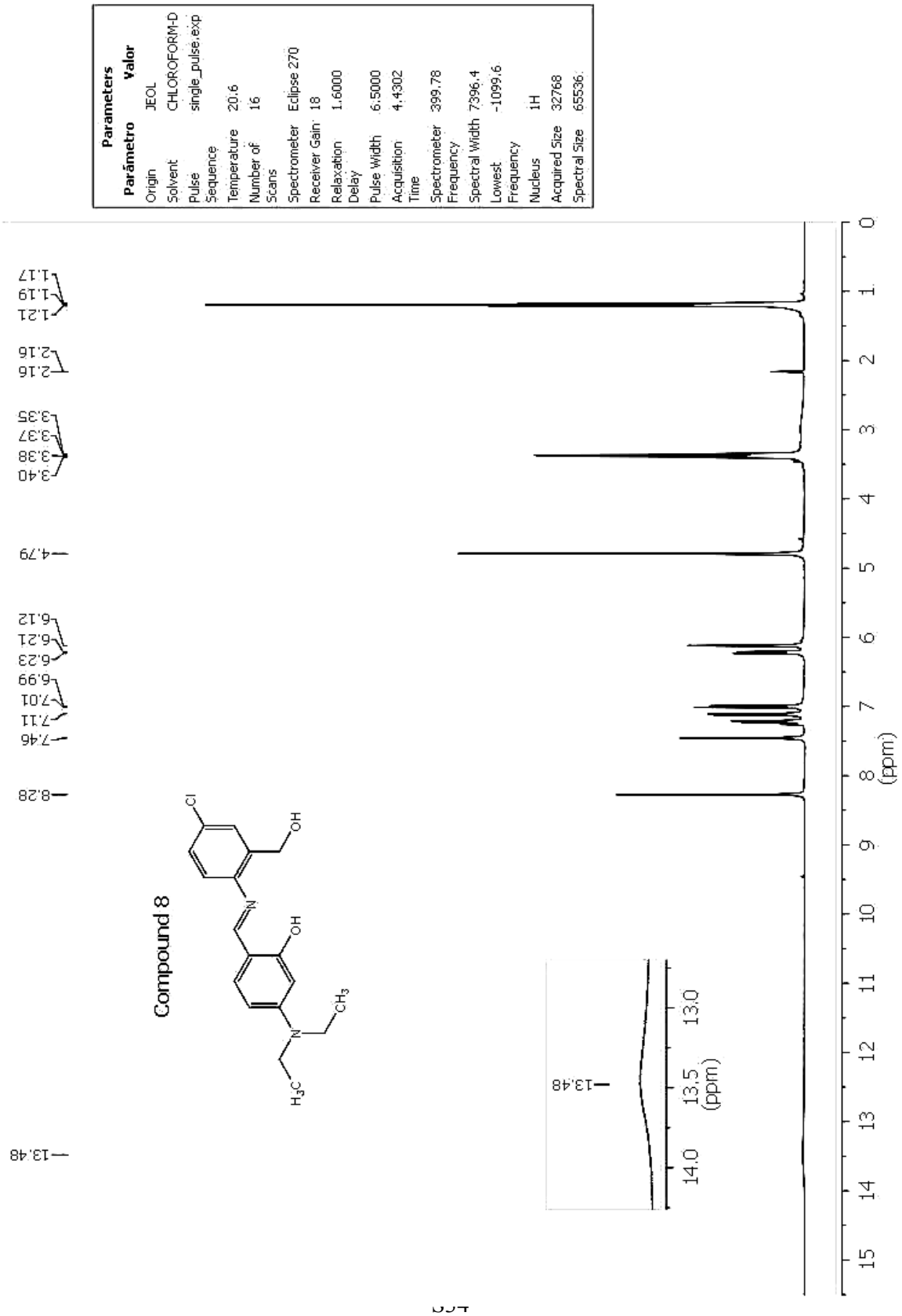


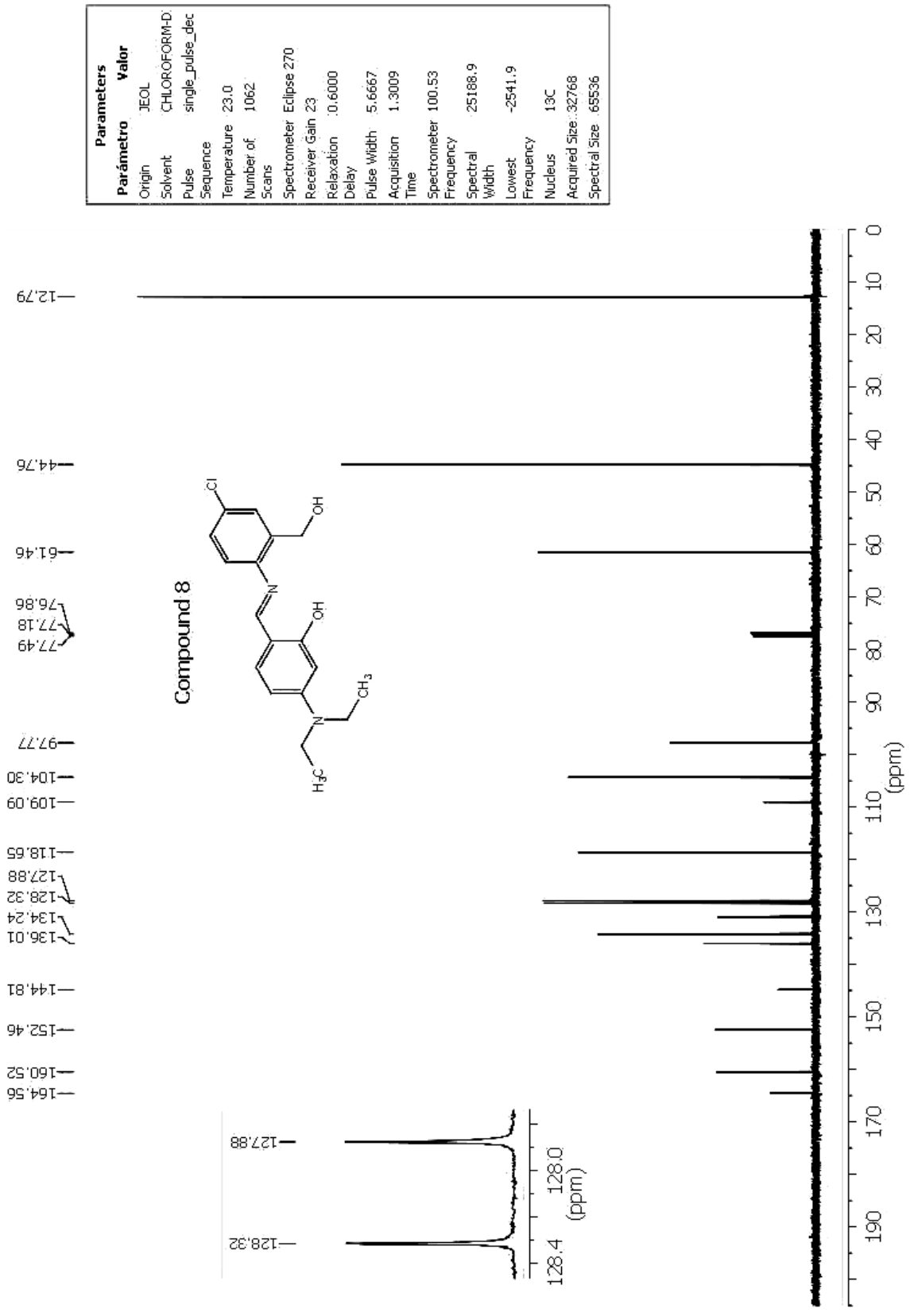












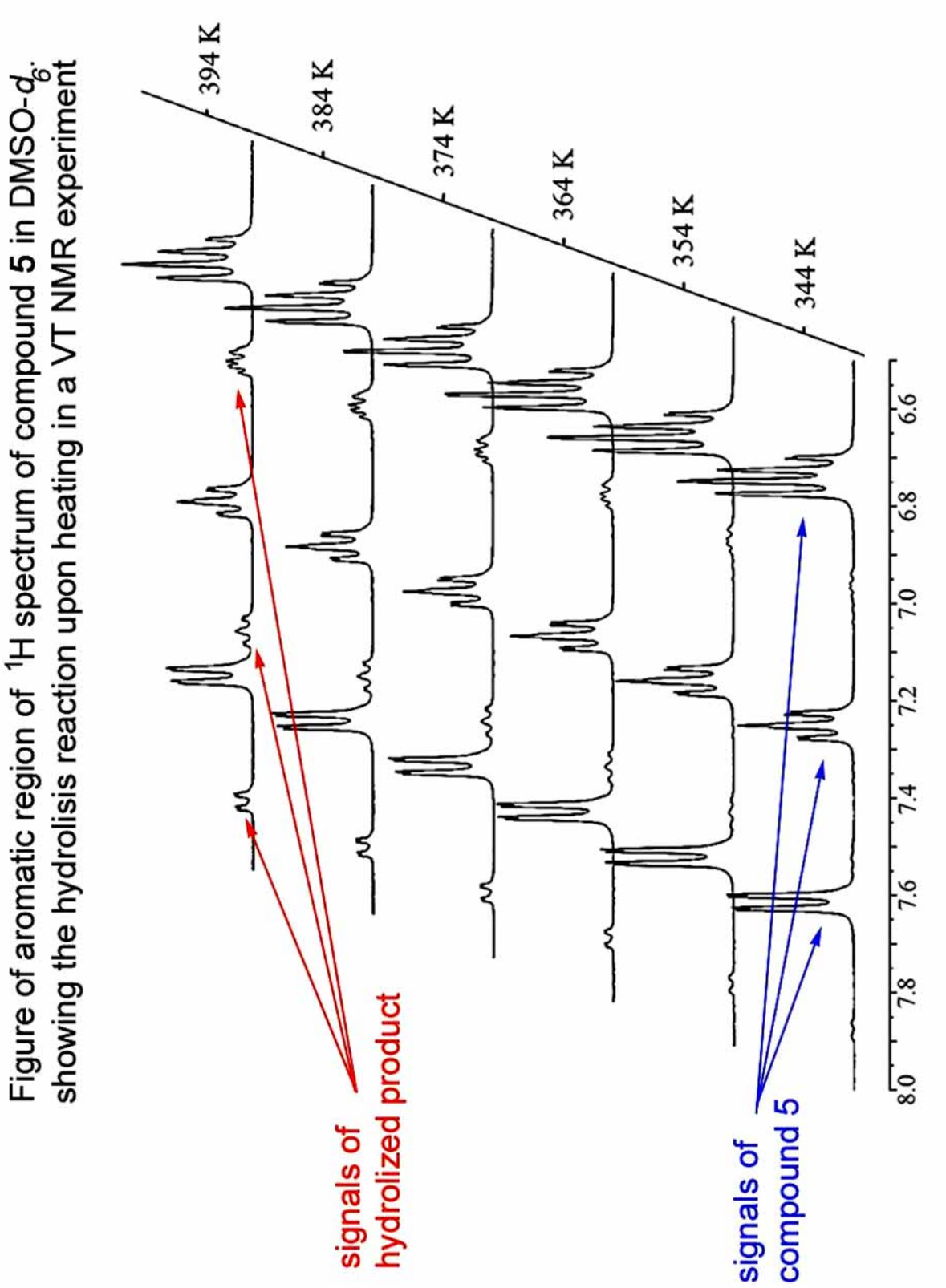
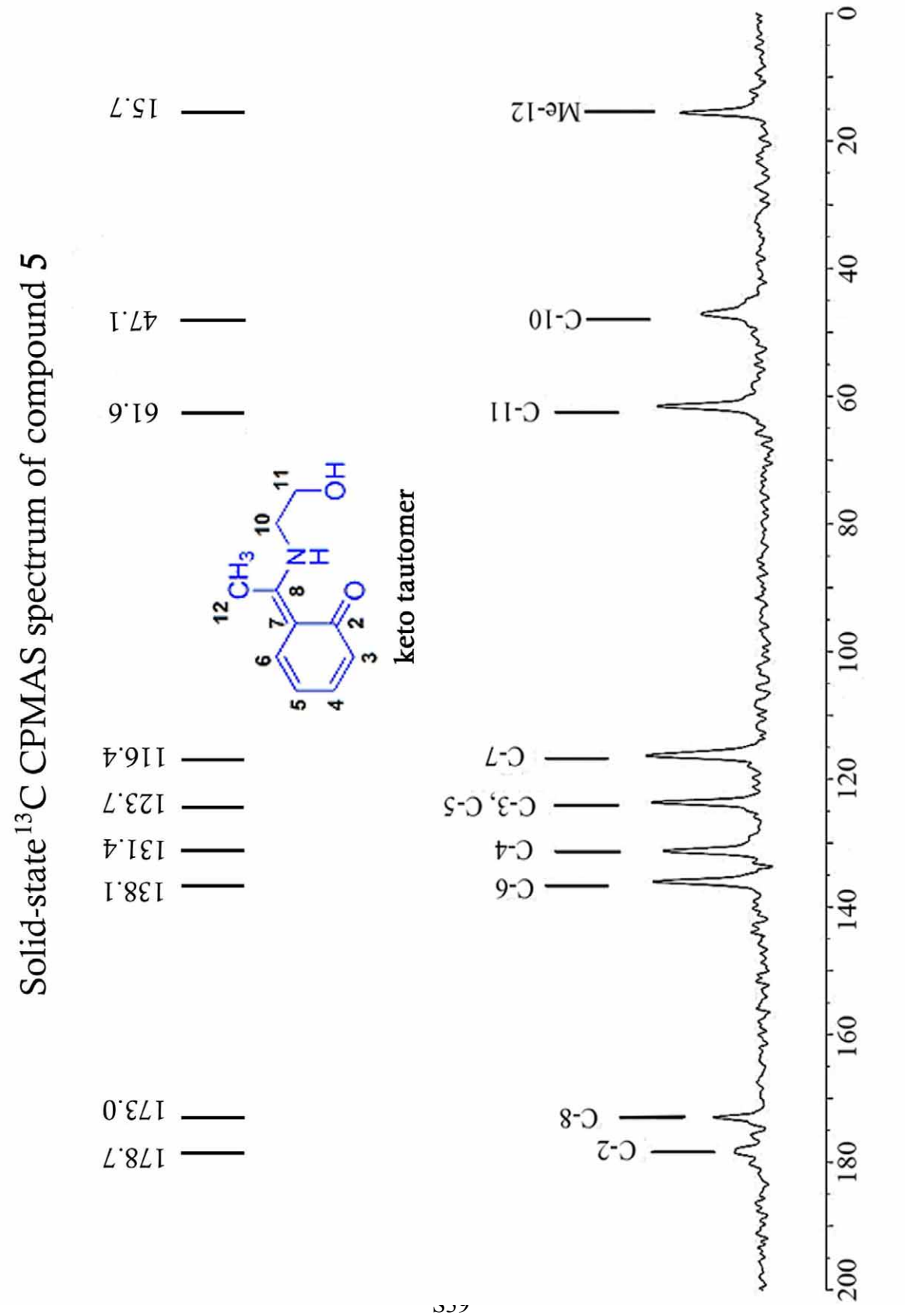


Figure of aromatic region of ^{1}H spectrum of compound **5** in DMSO-d_6. showing the hydrolisis reaction upon heating in a VT NMR experiment



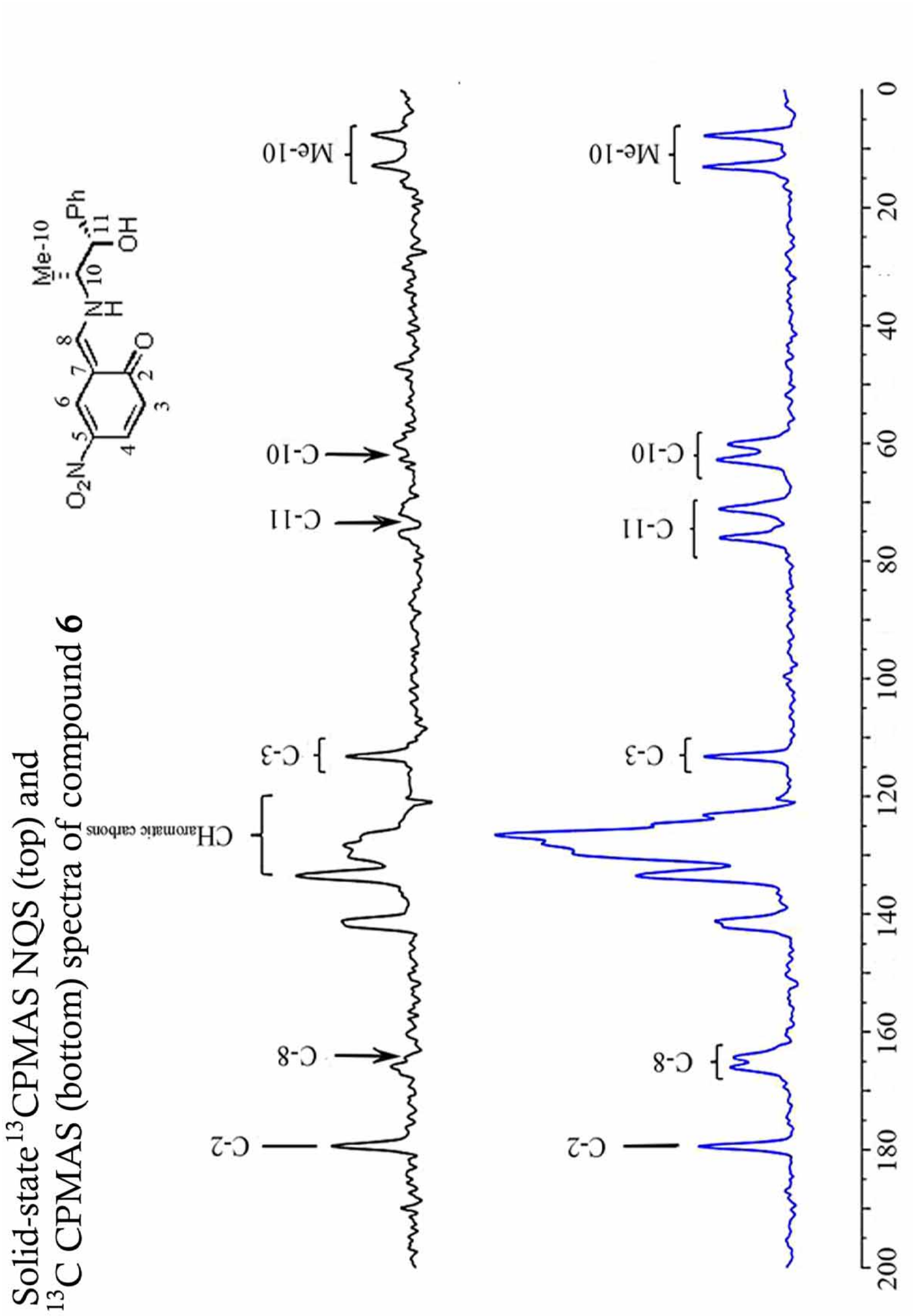

Solid-state ^{13}C CPMAS NQS (top) and
^{13}C CPMAS (bottom) spectra of compound 6
C-2
C-8
CH aromatic carbons
C-3
C-11
C-10
Me-10
0
20
40
60
80
100
120
140
160
180
200

Table 4. Hydrogen-bonding and short intermolecular contact geometry in the crystal structures of compounds **1-8**

	***D*−H···*A* [Å]**	***D*−H [Å]**	**H···*A* [Å]**	***D*−*A* [Å]**	**∠ *D*−H···*A* [º]**
1a	O1A−H1A···N9A	0.94(2)	1.72(2)	2.578(2)	150(2)
	O2A−H2A···O2B^{i}	0.88(3)	2.13(3)	3.003(2)	173(3)
	C22A-H22C···O1A	0.96	2.35	2.993(2)	124
	C23A-H23A···O1A	0.96	2.35	3.005(3)	125
1b	O1B−H1B···N9B	1.00(3)	1.63(3)	2.583(2)	156(2)
	O2B−H2B···O2A^{ii}	0.87(3)	2.19(3)	3.039 (2)	168(2)
	C15B-H15F···O1B^{iii}	0.97	2.59	3.455 (3)	149
	C22B-H22F···O1B	0.96	2.38	3.005(3)	122
	C23B-H23E···O1B	0.96	2.36	3.012(3)	125
2a	O1A−H1A···N9A	0.87(3)	1.78(3)	2.591(2)	155(3)
	O2A−H2A···O2B^{iv}	0.82	2.03	2.764(5)	149
	C23A−H23A···O1A	0.96	2.36	3.000(3)	124
	C24A−H24C···O1A	0.96	2.34	2.985(3)	124
2b	O1B−H1B···N9B	0.99(3)	1.65(3)	2.587(2)	157(3)
	O2B−H2B···O2A^{v}	0.82	1.86	2.622(6)	155
	C22B−H22D···O1B	0.96	2.33	2.976(3)	125
	C23B−H23F···O1B	0.96	2.33	2.984(4)	124
3	O1−H1···N9	0.88(3)	1.77(3)	2.553(4)	147(4)
	O2−H2···O1^{vi}	0.83(4)	2.04(4)	2.866(3)	176(5)
4	N9−H9···O1	0.85(5)	1.88(5)	2.578(3)	139(4)
	O2−H2···O1^{vii}	0.76(4)	2.01(4)	2.752(3)	165(4)
	C10−H10B···O2^{viii}	0.97	2.56	3.445(4)	151
5	N9−H9···O1	0.99(2)	1.60(2)	2.512(2)	152(2)
	O2−H2···O1^{ix}	0.83(2)	1.93(2)	2.750(2)	173(2)
	C6−H6···O1^{iii}	0.93	2.60	3.462(2)	155
	C12−H12F···O2	0.96	2.45	3.194(2)	134
6a	N9A−H9A···O1A	0.87(3)	1.82(3)	2.583(5)	145(4)
	O2A−H2A···O1B	0.85(7)	1.90(7)	2.728(5)	168(7)
	C6A−H6A···O3B^{x}	0.93	2.55	3.300(5)	138
	C8A−H8A···O3B^{x}	0.93	2.58	3.300(5)	134
	C16A−H16A···O3A^{xi}	0.93	2.49	3.330(5)	151
6b	N9B−H9B···O1B	0.89(6)	1.85(5)	2.593(5)	140(4)
	O2B−H2B···O1A	0.78(7)	1.95(7)	2.725(4)	175(10)

7a	N9A−H9A···O1A	0.92(12)	1.86(10)	2.549(4)	130(13)
	O2A−H2A···O1B^{vii}	0.87(6)	1.86(6)	2.721(5)	169(7)
7b	N9B−H9B···O1B	0.91(9)	1.80(9)	2.543(5)	137(10)
	O2B−H2B···O1A^{iv}	0.79(6)	1.93(7)	2.719(5)	171(6)
	C10B−H10B···Br1A^{xii}	0.98	2.87	3.692(6)	142
	C11B−H11B···Br1A^{xiii}	0.98	2.86	3.572(4)	130
	C14B−H14B···O2A^{xiv}	0.93	2.45	3.321 (7)	157
8a	O1A−H1A···N9A	0.86(3)	1.79(4)	2.588(4)	154(4)
	O2A−H2A···O1B^{xv}	0.79(4)	1.96(4)	2.735(4)	169(4)
8b	N9B−H9B···O1B	0.85(4)	1.85(3)	2.622(3)	151(4)
	O2B−H2B···O1B^{xvi}	0.78(5)	1.93(5)	2.702(4)	175(4)
	C8B−H8B···O2A^{xvii}	0.93	2.47	3.287(4)	147

Symmetry code: (i) 1+x, 1/2-y, -1/2+z; (ii) -1+x, y, z; (iii) x, 1/2-y, 1/2+z; (iv) x, -1+y, z; (v) 2-x, 1-y, -z; (vi) -1+x, y, z; (vii) x, 1+y, z; (viii) -1/2+x, 1-y, z; (ix) -x,-1/2+y,1/2-z; (x) 1+x, y, -1+z; (xi) x, 1+y, 1+z; (xii) 1+x, -2+y, z; (xiii) x, -2+y, z; (xiv) x, -1+y, -1+ z; (xv) 1+x, y, 1+z; (xvi) -x, -y, -z; (xvii) 2-x, -y, 1-z;

Figure of the C=O···Br and C-H··· Br contacts in compound **7**