β, β -Disubstituted *C*- and *N*-Vinylindoles from one-step condensations of aldehydes and indole derivatives

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Supporting Information

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General information:
Unless otherwise noted all reactions were performed under an atmosphere of dry nitrogen or argon. Anhydrous solvents (acetonitrile and toluene) were obtained by passage through solvent filtration systems. Microwave experiments were performed using a Biotage Initiator Sixty reactor, which monitors the reaction mixture temperature using an IR sensor and increases the temperature in a rate of 2-5 °C/sec. The microwave experiments were performed in sealed reaction vessels. ^{1}H NMR spectra were measured in $CDCl_3$ or DMSO-d_6 at 300 or 400 MHz and referenced to internal tetramethylsilane (0.00 ppm) or $CHCl_3$ (7.26 ppm) or to residual CHD_2SOCD_3 (2.50 ppm), respectively. ^{13}C NMR spectra were measured in $CDCl_3$ or DMSO-d_6 at 75 or 100 MHz and referenced to 77.16 ppm or 39.52 ppm, respectively. In the case of particularly acid sensitive compounds (**1b** and **1e**) $CDCl_3$ was first filtered over anhydrous K_2CO_3. In the case of products **1e** and **2c** the *E* and *Z* isomers were characterized using NOESY experiments at 300, 500 or 700 MHz. Assignments of their ^{1}H and ^{13}C NMR signals were made possible using COSY, HMQC and DEPT experiments. Chromatography was performed using 230-400 mesh silica gel. In the case of particularly acid-sensitive compounds, silica gel was pre-treated with triethylamine as follows: silica was suspended in a solution of 5% triethylamine in hexanes and stirred for 30 minutes, the chromatography column was then packed and the silica rinsed with 3 column volumes of hexanes. Melting points were determined with a capillary melting point apparatus and are uncorrected. FT-IR spectra were taken using a FT-IR spectrophotometer. Accurate mass measurements (HRMS) were performed on a LC-MSD-Tof instrument using positive electrospray.

1,3-bis(2-methylprop-1-enyl)-1*H*-indole (5). A solution of indole (0.364 mmol) in neat isobutyraldehyde (17.84 mL) was placed in a 10-20 mL microwave (MW) flask and was treated with 300 mol % of TFA (0.273 mmol, 84 μL). The mixture (0.02 M) was flushed with argon, and the flask was immediately capped and heated to 140 °C using microwave irradiation for 2.5 h. The crude reaction mixture was diluted with EtOAc and was washed with a saturated solution of $NaHCO_3$. The aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated to dryness. Chromatography of the residue using a gradient of EtOAc in hexanes furnished bisvinylindole as a brown oil (43.4 mg, 53 %): R_f 0.27 (2 % EtOAc in hexanes). IR ($CHCl_3$) 3018, 2972, 2917, 1678, 1610, 1537, 1464, 1384, 1312, 1216 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 7.8 Hz, 1H), 7.24-7.21 (m, 2H), 7.14-7.11 (m, 1H), 7.06 (s, 1H), 6.58 (s, 1H), 6.41 (s, 1H), 1.98 (s, 3H), 1.93 (s, 3H), 1.92 (s, 3H), 1.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.2, 133.0, 132.0, 127.8, 126.0, 122.2, 120.0, 119.7, 119.2, 115.7, 114.1, 110.2, 27.0, 22.7, 20.5, 18.4. HRMS (*m/z*): calcd for $C_{16}H_{20}N$ $(M+H)^+$, 226.1590; found, 226.1586.

General procedure A: preparation of *C*-vinylindoles. A solution of 1-methylindole **3a** or 1-benzylindole **3b** (0.364 mmol) in acetonitrile (17.84 mL) was placed in a 10-20 mL microwave (MW) flask and was treated with aldehyde (1.092 mmol, 300 mol %) and 300 mol % of TFA (0.273 mmol, 84 μL). The mixture (0.02 M) was flushed with argon, and the flask was immediately capped and heated to 140 °C using microwave irradiation for 3 h. The crude reaction mixture was diluted with EtOAc and was washed with a saturated solution of $NaHCO_3$. The aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated to dryness to provide a residue that was purified by silica chromatography using a gradient of EtOAc or Et_2O in hexanes.

1-methyl-3-(2-methylprop-1-enyl)-1*H*-indole (1a). The title compound was prepared from indole **3a** and isobutyraldehyde using general procedure A. Chromatography using 5 % EtOAc in hexanes furnished 3-vinylindole **1a** as a brown oil (51.4 mg, 76 %): R_f 0.53 (1 % EtOAc in hexanes). IR ($CHCl_3$) 3018, 2975, 1702, 1611, 1522, 1473, 1421, 1375, 1216 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 7.9 Hz, 1H), 7.27-7.23 (m, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.01 (s, 1H), 6.40 (s, 1H), 3.77 (s, 3H), 1.97 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 132.3, 128.1, 126.7, 121.9, 119.3, 119.2, 115.8, 113.3, 109.1, 32.9, 27.0, 20.5. HRMS (*m/z*): calcd for $C_{13}H_{16}N$ $(M+H)^+$, 186.1277; found, 186.1271.

1-methyl-3-(2,2-diphenylvinyl)-1*H*-indole (1c). The title compound was prepared from indole **3a** and diphenylacetaldehyde using general procedure A. Chromatography using 2 % EtOAc in hexanes provided a crude product that was further purified by precipitation from hot *i*-PrOH to furnish 3-vinylindole **1c** as a yellow solid (28.3 mg, 25 %): mp 154-155 °C; R_f 0.33 (1 % EtOAc in hexanes). IR ($CHCl_3$) 3019, 2976, 1595, 1528, 1475, 1423, 1222, 1208 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* =7.8 Hz, 1H), 7.46-7.38 (m, 5H), 7.33-7.29 (m, 5H), 7.24-7-21 (m, 3H), 7.17-7-13 (m, 1H), 5.98 (s, 1H), 3.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 142.2, 137.3, 136.2, 130.2,

129.3, 128.5, 128.4, 128.35, 128.0, 127.4, 126.7, 122.1, 119.8, 118.8, 118.6, 112.6, 109.3, 33.0. HRMS (*m/z*): calcd for $C_{23}H_{20}N$ $(M+H)^+$, 310.15903; found, 310.15901.

1-benzyl-3-(2,2-diphenylvinyl)-1*H*-indole (1d). The title compound was prepared from indole **3b** and diphenylacetaldehyde using general procedure A. Chromatography using a gradient of 1-2 % EtOAc in hexanes provided a crude product that was further purified by precipitation from hot *i*-PrOH to furnish 3-vinylindole **1d** as a yellow solid (24.8 mg, 18 %): mp 140-141 °C; R_f 0.22 (2 % EtOAc in hexanes). IR ($CHCl_3$) 3019, 2977, 1601, 1528, 1496, 1468, 1422, 1216 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.76-7.72 (m, 1H), 7.41-7.16 (m, 17H), 6.98-6.95 (m, 2H), 6.07 (s, 1H), 5.04 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 142.1, 138.1, 137.0, 135.7, 130.2, 129.25, 129.17, 128.84, 128.81, 128.4, 127.8, 127.6, 127.4, 127.2, 126.8, 122.3, 120.0, 118.9, 118.6, 113.2, 109.9, 50.3. HRMS (*m/z*): calcd for $C_{29}H_{24}N$ $(M+H)^+$, 386.1903; found, 386.1892.

1-methyl-3-(2-phenylprop-1-enyl)-1*H*-indole (1e). The title compound was prepared from indole **3a** and 2-phenylpropionaldehyde using general procedure A and was obtained as a mixture of *E/Z* isomers (85/15) as indicated from comparison of the methyl protons signals at 2.4 ppm (*E*) and 2.2 ppm (*Z*) at the ^1H NMR spectra of the crude product taken in $CDCl_3$ at 400 MHz.
In order to facilitate purification, excess 2-phenylpropionaldehyde present in the crude mixture was reduced to its corresponding alcohol as follows: the crude mixture was dissolved in EtOH (15 mL), the resulting solution cooled to -20 °C and $LiBH_4$ (1000 mol %, 80 mg) was added. The mixture was allowed to reach room temperature with stirring for 40 minutes. The mixture was then diluted with EtOAc (50 mL) and washed with water (20 mL). The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic phases were washed with brine (50 mL), dried over anhydrous $MgSO_4$ and evaporated to dryness. Chromatography using triethylamine pre-treated silica and 1 % Et_2O in hexanes furnished 3-vinylindole **1e(*Z*)** (first to elute, 8 mg, 9%) and **1e(*E*)** (second to elute, 49 mg, 53%) as yellow oils (combined yield 62 %).
1e(*E*) was identified by the display of transfer of magnetization between the protons of the vinylic CH_3 (2.25 ppm) and the indolic proton at position 2 (7.45 ppm) in a NOESY correlation experiment (500 MHz, in MeCN at 5 °C, selected expansion of the correlation provided hereafter).
1e(*Z*) was identified by the display of transfer of magnetization between the vinylic proton (6.66 ppm) and the protons of the vinylic CH_3 (2.26 ppm) in a NOESY correlation experiment (300 MHz, in $CDCl_3$, selected expansion of the correlation provided hereafter).

1e(*E*) : R_f 0.20 (1 % EtOAc in hexanes). IR ($CHCl_3$) 3019, 1702,1612, 1529, 1493, 1474, 1424, 1377, 1336, 1216 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 7.5 Hz, 1H), 7.66-7.63 (m, 2H), 7.44 (t, J = 7.9 Hz, 2H), 7.41-7.29 (m, 3H), 7.28-7.22 (m, 2H), 7.13 (s, 1H), 3.87 (s, 3H), 2.44 (d, J = 0.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.5, 137.3, 134.1, 129.2 (2C), 128.3, 127.3, 126.7, 123.0, 120.4, 120.0, 119.3, 114.2, 110.1, 33.8, 19.6. HRMS (*m/z*): calcd for $C_{18}H_{18}N$ $(M+H)^+$, 248.1434; found, 248.1436.
1e(*Z*) : R_f 0.21 (1 % EtOAc in hexanes). IR ($CHCl_3$) 3018, 1685, 1613, 1525, 1498, 1469, 1415, 1375, 1332, 1217 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (td, J = 7.9 Hz, J = 0.9 Hz, 1H), 7.39-7.07 (m, 8H), 6.66 (s, 1H), 6.15 (s, 1H), 3.55 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.8, 136.9,135.4, 129.6, 128.8, 128.7, 127.7, 127.5, 122.4, 120.0, 119.6, 118.1, 112.9, 109.8, 33.5, 27.8. HRMS (*m/z*): calcd for $C_{18}H_{18}N$ $(M+H)^+$, 248.1434; found, 248.1433.

3-(cyclohexylmethyl)-1-methyl-1*H*-indole (6). The title compound was prepared from indole **3a** and cyclohexane carboxaldehyde using general procedure A. Chromatography using 1 % EtOAc in hexanes furnished 3-alkyllindole **1f** as a brown oil (17.4 mg, 21 %): R_f 0.73 (1 % EtOAc in hexanes). IR ($CHCl_3$) 3017, 2975, 2927, 1601, 1522, 1475, 1421, 1327, 1225, 1205 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 7.9 Hz, 1H), 7.28 (d, J = 8.3 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.80 (s, 1H), 3.74 (s, 3H), 2.60 (d, J = 6.9 Hz, 1H), 1.78-1.74 (m, 2H), 1.69-1.66 (m, 2H), 1.63-1.60 (m, 3H), 1.20-1.15 (m, 2H), 0.98-0.95 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.1, 128.6, 126.9, 121.4, 119.4, 118.5, 114.1, 109.1, 39.1, 33.7, 33.2, 32.7, 26.8, 26.5. HRMS (*m/z*): calcd for $C_{16}H_{22}N$ $(M+H)^+$, 228.1747; found, 228.1738.

General procedure B: preparation of *N*-vinylindoles. A solution of indole **4a-c** (0.364 mmol) in acetonitrile (17.84 mL) was placed in a 10-20 mL microwave (MW) flask, treated with aldehyde (3.64 mmol, 1000 mol %) and TFA (0.273 mmol, 84 μL, 300 mol %) and flushed with argon. The flask was immediately capped and heated to 140 °C using microwave irradiation for 1 h. The crude reaction mixture was diluted with EtOAc and was washed with a saturated solution of $NaHCO_3$. The aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated to dryness to provide a residue that was purified by silica chromatography using a gradient of EtOAc in hexanes. In the case of products **2e-h** crude reaction mixtures were evaporated to dryness without extractive work-up and purified by silica chromatography.

3-methyl-1-(2-methylprop-1-enyl)-1*H*-indole (2a). The title compound was prepared from indole **4a** and isobutyraldehyde using general procedure B. Chromatography using 2-5 % EtOAc in hexanes furnished 3-vinylindole **2a**

as a brown oil (27.3 mg, 40 %): R_f 0.80 (1 % EtOAc in hexanes). IR ($CHCl_3$) 3019, 2975, 2930, 1677, 1602, 1523, 1463, 1421, 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* =7.8 Hz, 1H), 7.21-7.20 (m, 2H), 7.12-7.10 (m, 1H), 6.88 (s, 1H), 6.53 (s, 1H), 2.33 (s, 3H), 1.90 (s, 3H), 1.72 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.8, 131.0, 128.4, 125.8, 121.8, 120.0, 119.2, 118.9, 111.3, 110.2, 22.7, 18.4, 9.8. HRMS (*m/z*): calcd for $C_{13}H_{16}N$ $(M+H)^+$, 186.1277; found, 186.1271.

3-methyl-1-(2,2-diphenylvinyl)-1*H*-indole (2b). The title compound was prepared from indole **4a** and diphenylacetaldehyde using general procedure B. Chromatography using a gradient of petroleum ether to 1 % EtOAc in petroleum ether furnished 3-vinylindole **2b** as a beige solid (72.0 mg, 64 %): mp 129-130 °C; R_f 0.71 (1 % EtOAc in hexanes). IR ($CHCl_3$) 3018, 2976, 2923, 1629, 1522, 1459, 1421, 1354, 1223, 1207 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.32-7.31 (m, 9H), 7.23-7.21 (m, 3H), 7.17 (t, *J* = Hz, 1H), 6.39 (s, 1H), 2.12 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.8, 138.9, 137.0, 130.5, 129.4, 129.1, 128.9, 128.5, 127.9, 127.8, 127.4, 124.5, 122.6, 121.7, 120.5, 119.1, 113.4, 109.9, 9.7. HRMS (*m/z*): calcd for $C_{23}H_{20}N$ $(M+H)^+$, 310.1590; found, 310.1588.

3-methyl-1-(2-phenylprop-1-enyl)-1*H*-indole (2c). The title compound was prepared from indole **4a** and 2-phenylpropionaldehyde using general procedure B and was obtained as a mixture of *E/Z* isomers (6/1) as indicated from comparison of the methyl protons signals at 2.49 ppm (*E*) and 2.25 ppm (*Z*) in the ^1H NMR spectrum of the crude product taken in $CDCl_3$ at 400 MHz. In order to facilitate the purification, excess 2-phenylpropionaldehyde present in the crude mixture was reduced to its corresponding alcohol as previously described for compound **1e**.
Chromatography using triethylamine pre-treated silica and 0.1% Et_2O in hexanes furnished 3-vinylindole **2c** as a yellow oil (57 mg, 65 %, *E/Z* = 6:1): R_f 0.48 (1 % EtOAc in hexanes). IR ($CHCl_3$) 3019, 2925, 2859, 1643, 1462, 1389, 1357, 1316, 1216 cm^{-1}.
(*E*)-2c was identified by the display of transfer of magnetization between the protons of the vinylic CH_3 (2.25 ppm) and the indolic proton at position 2 (7.16 ppm) in a NOESY correlation experiment (700 MHz, in $CDCl_3$, selected expansion of the correlation is provided hereafter).
(*Z*)-2c was identified by the display of transfer of magnetization between the vinylic proton (6.91 ppm) and the protons of the vinylic CH_3 (2.26 ppm) in a NOESY correlation experiment (700 MHz, in $CDCl_3$, selected expansion of the correlation is provided hereafter).

^1H NMR (700 MHz, $CDCl_3$, underlined data account for the minor *Z* isomer): δ 7.63 (d, *J* = 7.8 Hz, 1H), 7.57-7.44 (m, 2H), 7.54-7.52 (m, 1/6H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 7.6 Hz, 1/6H), 7.37 (tt, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H), 7.34, (d, *J* = 8 Hz, 1H), 7.30-7.24 (m, 1H + 4/6 H), 7.23-7.19 (m, 1H + 2/6 H), 7.18-7.16 (m, 1/6 H), 7.16 (q, *J* = 1.3 Hz, 1H), 7.11 (q, *J* = 1.0 Hz, 1H), 6.91 (q, *J* = 1.4 Hz, 1/6H), 6.43 (q, *J* = 1.0 Hz, 1/6H), 2.41(d, *J* = 1.0 Hz, 3H), 2.26 (d, *J* = 1.4 Hz, 3/6H), 2.25 (d, *J* = 1.3 Hz, 3H), 2.16 (d, *J* = 1.0 Hz, 3/6H).

^{13}C NMR (75 MHz, $CDCl_3$, signals accounting for the minor *Z* isomer are written between brackets): δ 141.9 (140.6), 137.9 (137.3), 131.5 (131.5), 129.6 (129.3), 129.5 (128.8), 128.5 (128.2), (127.5) 127.0, 126.2 (125.9), 123.3 (122.9), 123.1 (121.1), 120.7 (120.6), 119.9 (119.7), 113.3 (113.1), 111.1 (110.6), (23.7) 17.5, 10.6 (10.4). HRMS (*m/z*): calcd for $C_{18}H_{18}N$ $(M+H)^+$, 248.1434; found, 248.1427.

1-(cyclohexylidenemethyl)-3-methyl-1*H*-indole (2d). The title compound was prepared from indole **4a** and cyclohexane carboxaldehyde using general procedure B. Chromatography using a gradient of 1-5 % EtOAc in hexanes furnished 3-vinylindole **2d** as a brown oil (13.2 mg, 16 %): R_f 0.51 (2 % EtOAc in hexanes). IR ($CHCl_3$) 3018, 2930, 2856, 1672, 1612, 1463, 1373, 1233, 1216 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.25-7.18 (m, 2H), 7.14-7.10 (m, 1H), 6.84 (s, 1H), 6.49 (s, 1H), 2.33 (s, 3H), 2.29 (t, *J* = 5.8 Hz, 2H), 2.18 (t, *J* = 5.9 Hz, 2H), 1.69-1.65 (m, 2H), 1.62-1.59 (m, 2H), 1.54-1.50 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.9, 137.0, 128.5, 126.2, 121.8, 119.2, 118.9, 117.0, 111.2, 110.3, 33.6, 28.7, 28.4, 27.6, 26.6, 9.8. HRMS (*m/z*): calcd for $C_{16}H_{20}N$ $(M+H)^+$, 226.1590; found, 226.1600.

2-(1-(2-methylprop-1-enyl)-1*H*-indol-3-yl)acetic acid (2e). The title compound was prepared from indole **4b** and isobutyraldehyde using general procedure B. Chromatography using a gradient of 30-50 % EtOAc in hexanes furnished 3-vinylindole **2e** as a brown oil (37.9 mg, 45 %): R_f 0.28 (30 % EtOAc in hexanes). IR (KBr) 2972, 2915, 2606, 1717, 1613, 1557, 1464, 1378, 1313, 1238 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.53 (d, *J* = 7.7 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.26 (s, 1H), 7.16 (t, *J* = 7.1 Hz, 1H), 7.08 (t, *J* = 7.0 Hz, 1H), 6.71 (s, 1H), 3.68 (s, 2H), 1.90 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 172.9, 136.1, 130.0, 127.3, 127.1, 121.8, 119.5, 119.3, 119.0, 110.2, 108.8, 30.8, 22.3, 18.1. HRMS (*m/z*): calcd for $C_{14}H_{16}NO_2$ $(M+H)^+$, 230.1176; found, 230.1159.

2-(5-methoxy-1-(2-methylprop-1-enyl)-1*H*-indol-3-yl)acetic acid (2g). The title compound was prepared from indole **4c** and isobutyraldehyde using general procedure B. Chromatography using 50 % EtOAc in hexanes furnished 3-vinylindole **2g** as a brown oil (29.2 mg, 31 %): R_f 0.19 (30 % EtOAc in hexanes). IR (KBr) 2971, 2941, 2592, 1716,

1620, 1581, 1485, 1456, 1388, 1226 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.23 (br s, 1H), 7.21 (s, 1H), 7.17 (d, J = 8.8 Hz, 1H), 7.03 (d, J = 2.1 Hz, 1H), 6.80 (dd, J = 8.8 Hz, 2.2 Hz, 1H), 6.67 (s, 1H), 3.76 (s, 3H), 3.64 (s, 2H), 1.88 (s, 3H), 1.68 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 173.0, 153.8, 131.3, 129.3, 127.7, 127.6, 119.6, 111.5, 111.0, 108.4, 101.1, 55.4, 30.7, 22.3, 18.1. HRMS (*m/z*): calcd for $C_{15}H_{18}NO_3$ $(M+H)^+$, 260.1281; found, 260.1282.

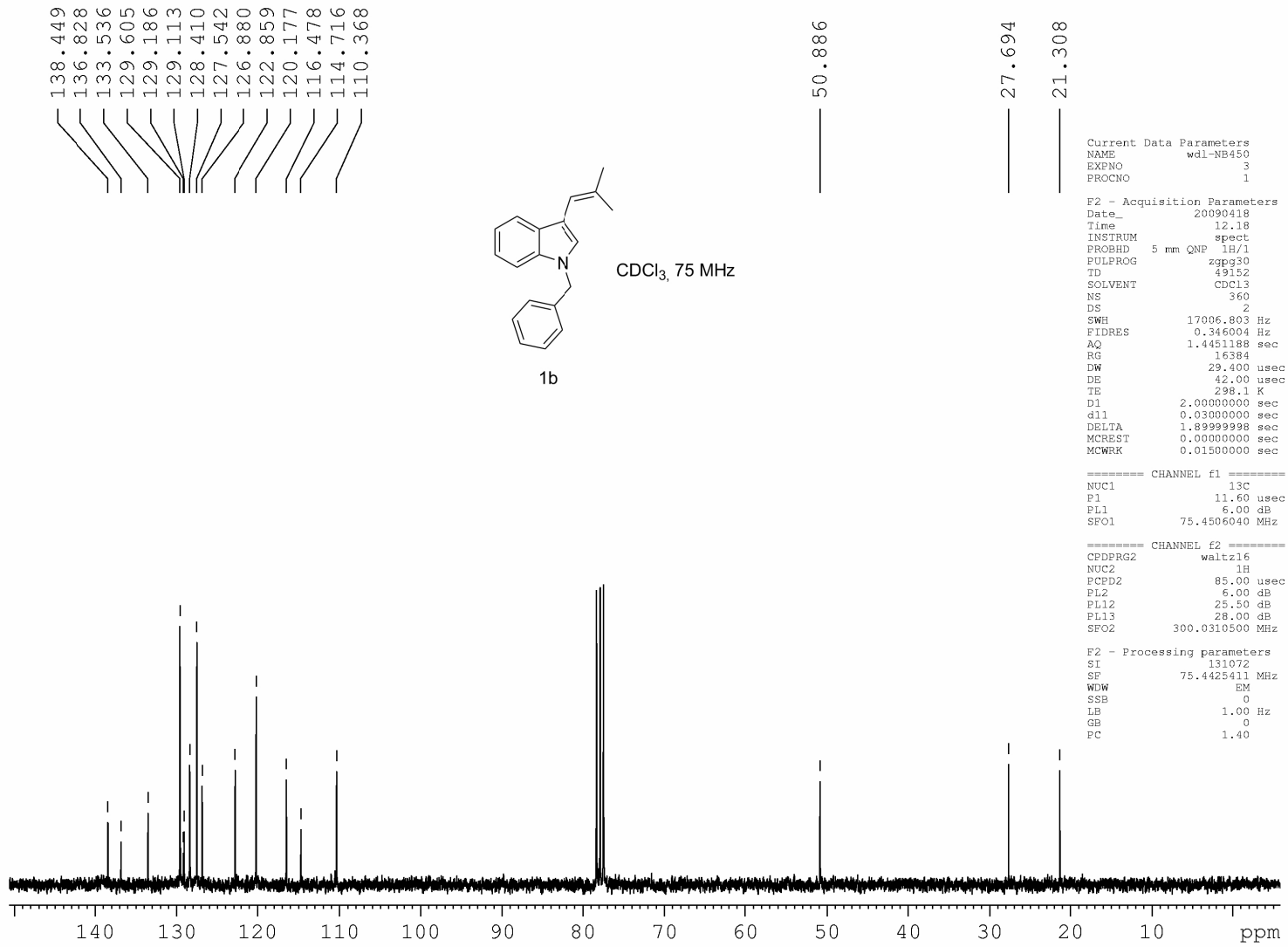
2-(5-methoxy-1-(2,2-diphenylvinyl)-1*H*-indol-3-yl)acetic acid (2h). The title compound was prepared from indole **4c** and diphenylacetaldehyde using general procedure B. Chromatography using a gradient of 20-50 % EtOAc in hexanes furnished 3-vinylindole **2h** as a beige solid (133.4 mg, 96 %): mp 105-106 °C; R_f 0.19 (30 % EtOAc in hexanes). IR (KBr) 2994, 2496, 1715, 1625, 1594, 1483, 1454, 1397, 1248, 1226 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 12.23 (br s, 1H), 7.56 (d, J = 8.9 Hz, 1H), 7.55 (s, 1H), 7.39-7.30 (m, 8H), 7.15 (d, J = 1.9 Hz, 1H), 7.13 (d, J = 1.4 Hz, 1H), 7.00 (d, J = 2.3 Hz, 1H), 6.83 (dd, J = 8.9 Hz, 2.4 Hz, 1H), 6.53 (s, 1H), 3.76 (s, 3H), 3.43 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4, 154.5, 140.8, 138.4, 131.4, 129.8, 129.0, 128.9, 128.5, 128.2, 127.9, 127.33, 127.3, 125.8, 121.7, 111.8, 111.4, 110.5, 101.4, 55.4, 30.6. HRMS (*m/z*): calcd for $C_{25}H_{22}NO_3$ $(M+H)^+$, 384.1594; found, 384.1588.

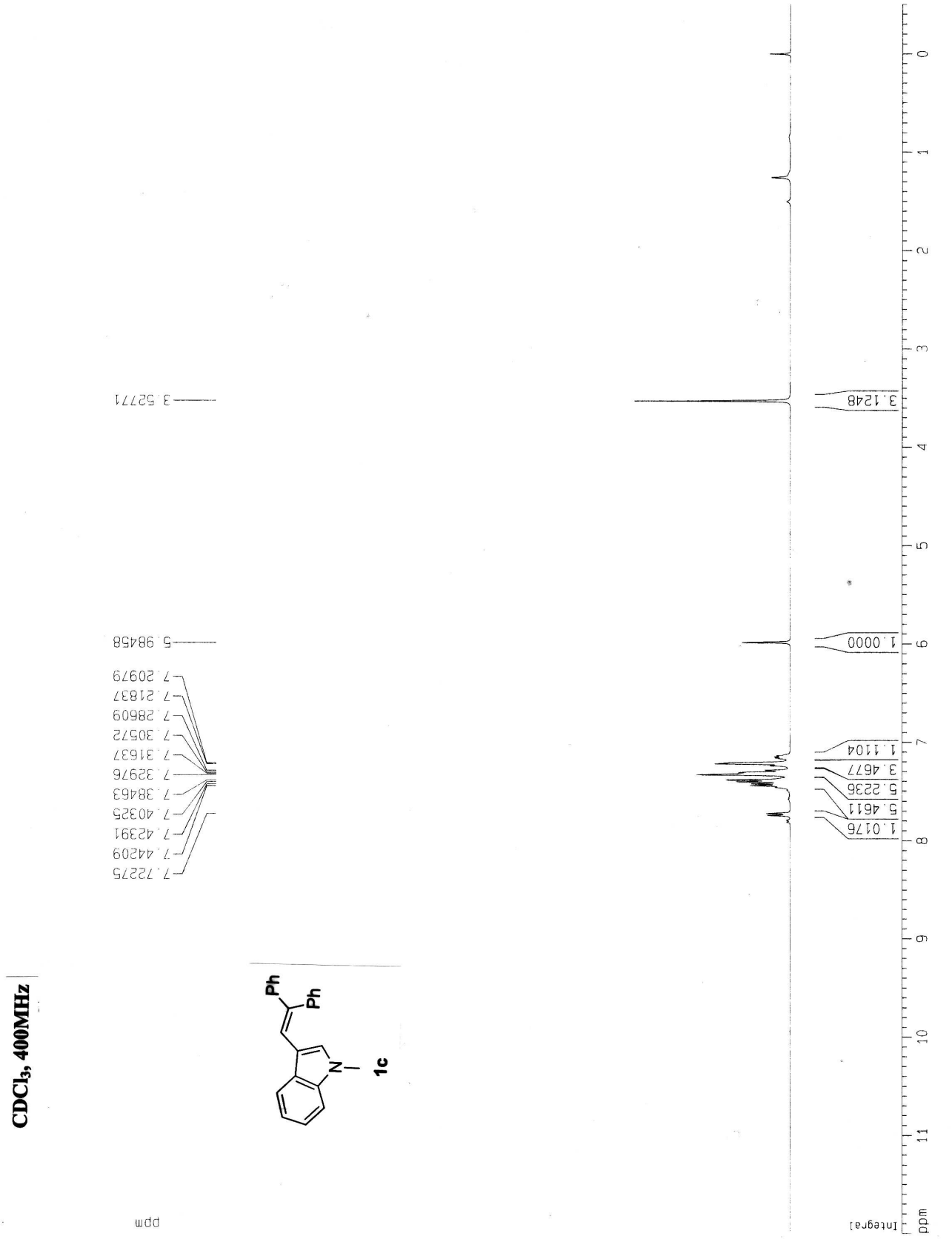
1-methyl-3-(2-methyl-1-(1-methyl-1*H*-indol-3-yl)propyl)-1*H*-indole (9). A solution of 1-methylindole **3a** (0.454 mmol) in neat isobutyraldehyde (4.48 mL) was placed in a 2-5 mL microwave (MW) flask and treated with 10 mol % of TFA (0.045 mmol, 3.5 μL). The mixture (0.1 M) was flushed with argon. The flask was immediately capped and heated to 140 °C using microwave irradiation for 10 minutes. The crude reaction mixture was diluted with EtOAc and washed with a saturated solution of $NaHCO_3$. The aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated to dryness. Chromatography of the residue using a gradient of EtOAc in hexanes furnished bisindolylalkane as a brown oil (51.7 mg, 72 %): R_f 0.24 (2 % EtOAc in hexanes). IR ($CHCl_3$) 3019, 2974, 1705, 1613, 1523, 1471, 1423, 1373, 1327, 1215 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 7.9 Hz, 2H), 7.23-7.13 (m, 4H), 7.03 (t, J = 7.4 Hz, 2H), 6.92 (s, 2H), 4.22 (d, J = 8.5 Hz, 2H), 3.66 (s, 6H), 2.61-2.59 (m, 1H), 1.00 (d, J = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.0, 128.3, 126.5, 121.2, 119.9, 118.6, 118.5, 109.1, 41.1, 33.4, 32.8, 22.1. HRMS (*m/z*): calcd for $C_{22}H_{25}N_2$ $(M+H)^+$, 317.2012; found, 317.2008.

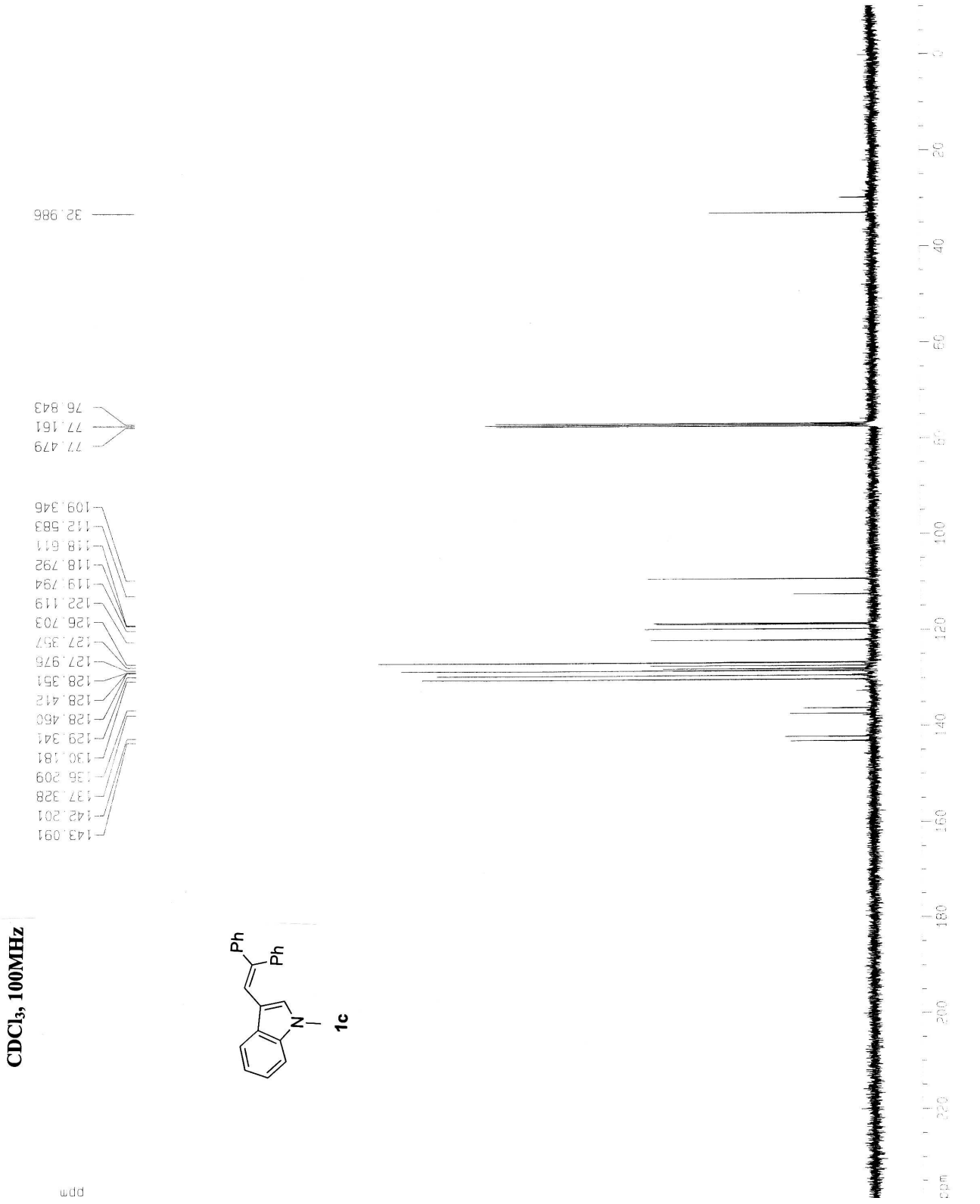
CDCl3, 400MHz
7.6529
7.6332
7.2721
7.2254
7.1200
7.0089
6.4006
3.7719
1.9721
1.9204
-0.0001
1a
ppm
Integral
1.0690
3.1281
1.4836
0.9994
1.0000
3.3143
3.1424
3.0833

CDCl3, 100MHz
1a
20.529
26.986
32.921
76.848
77.166
77.367
77.483
109.125
113.314
115.768
119.151
119.336
121.896
126.730
128.063
132.342
136.417
ppm
0
20
40
60
80
100
120
140
160
180
200
220
ppm

7.733
7.719
7.718
7.716
7.714
7.379
7.357
7.352
7.347
7.335
7.332
7.321
7.317
7.309
7.305
7.291
7.284
7.273
7.257
7.249
7.246
7.232
7.229
7.226
7.212
7.208
7.199
7.196
7.188
7.182
7.180
7.177
7.170
7.165
7.160
7.155
7.149
7.139
7.136
7.134
7.119
7.117
7.114
7.099
7.097
6.487
6.484
6.482
6.479
5.365
2.035
2.033
1.967
1.966
CDCl3, 400MHz
1b
N
ppm
0
1
2
3
4
5
6
7
8
9
10
11
3.033
3.136
2.101
1.019
11.599
1.000

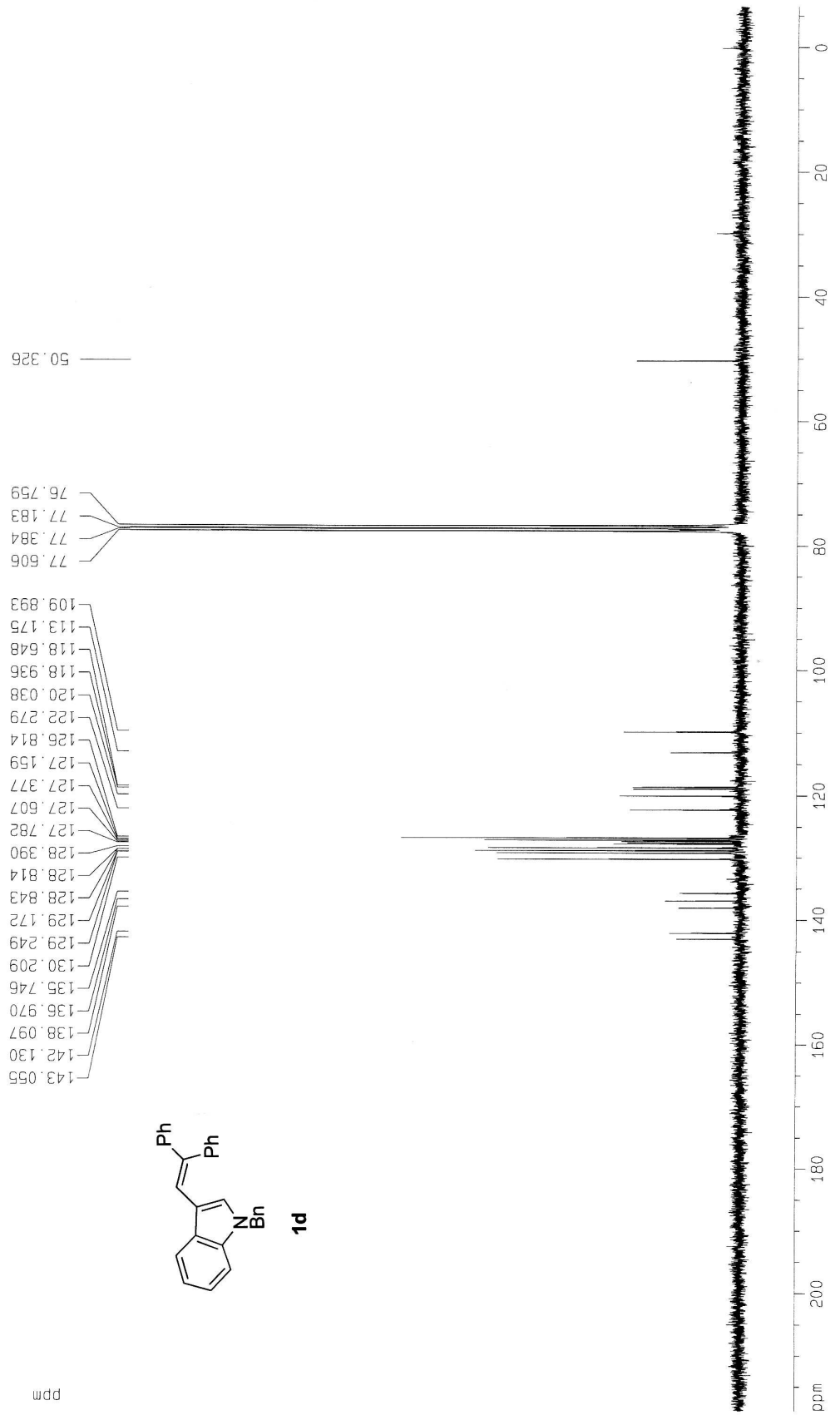

138.449
136.828
133.536
129.605
129.186
129.113
128.410
127.542
126.880
122.859
120.177
116.478
114.716
110.368
50.886
27.694
21.308
N
CDCl3, 75 MHz
1b
Current Data Parameters
NAME wdl-NB450
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090418
Time 12.18
INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 49152
SOLVENT CDCl3
NS 360
DS 2
SWH 17006.803 Hz
FIDRES 0.346004 Hz
AQ 1.4451188 sec
RG 16384
DW 29.400 usec
DE 42.00 usec
TE 298.1 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 11.60 usec
PL1 6.00 dB
SFO1 75.4506040 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 85.00 usec
PL2 6.00 dB
PL12 25.50 dB
PL13 28.00 dB
SFO2 300.0310500 MHz
F2 - Processing parameters
SI 131072
SF 75.4425411 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

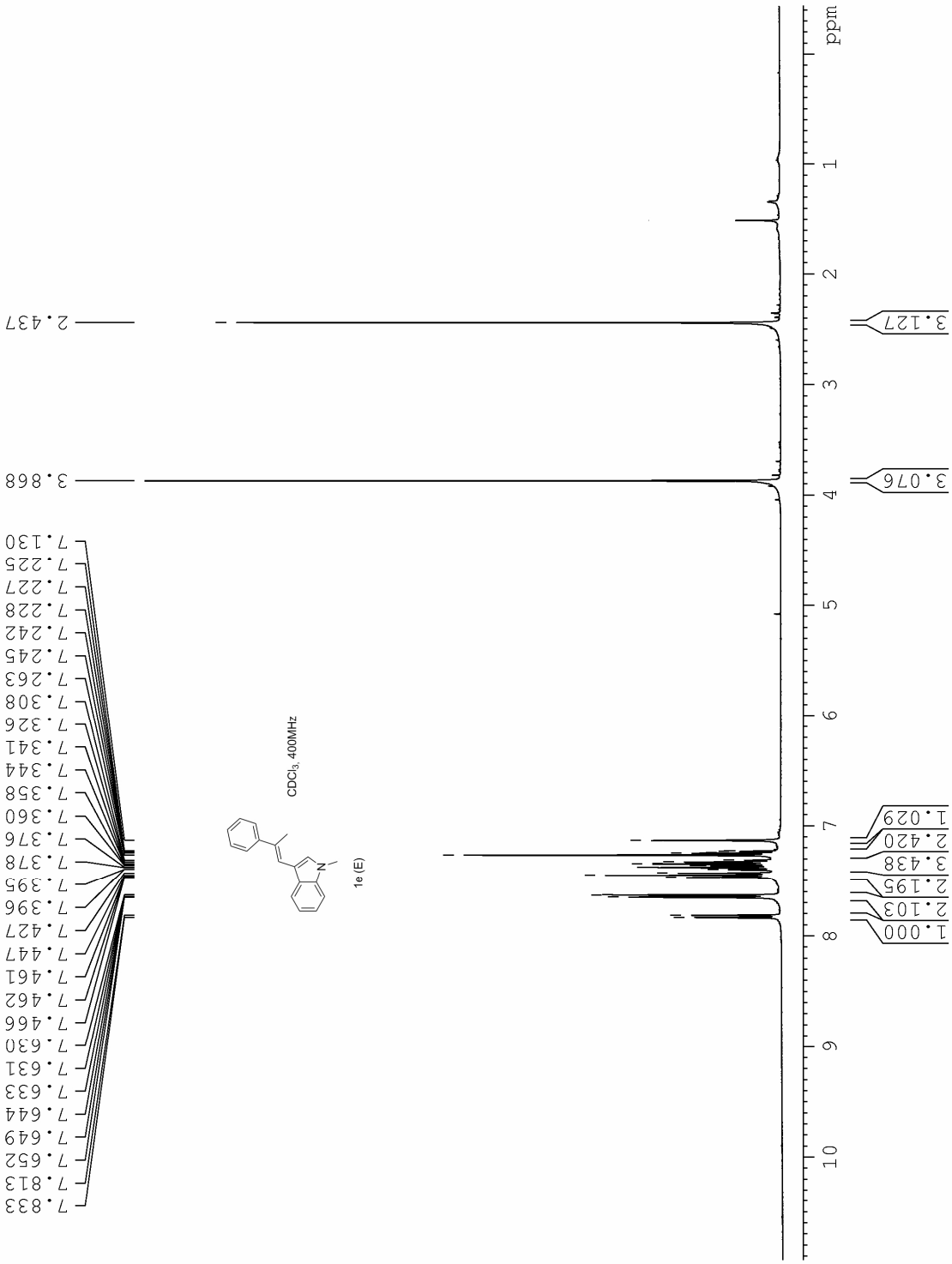

CDCl3, 400MHz
Ph
Ph
N
1c
7.72275
7.44209
7.42391
7.40325
7.38463
7.32976
7.31637
7.30572
7.28609
7.21837
7.20979
5.98458
3.52771
1.0176
5.4611
5.2236
3.4677
1.1104
1.0000
3.1248
Integral
ppm

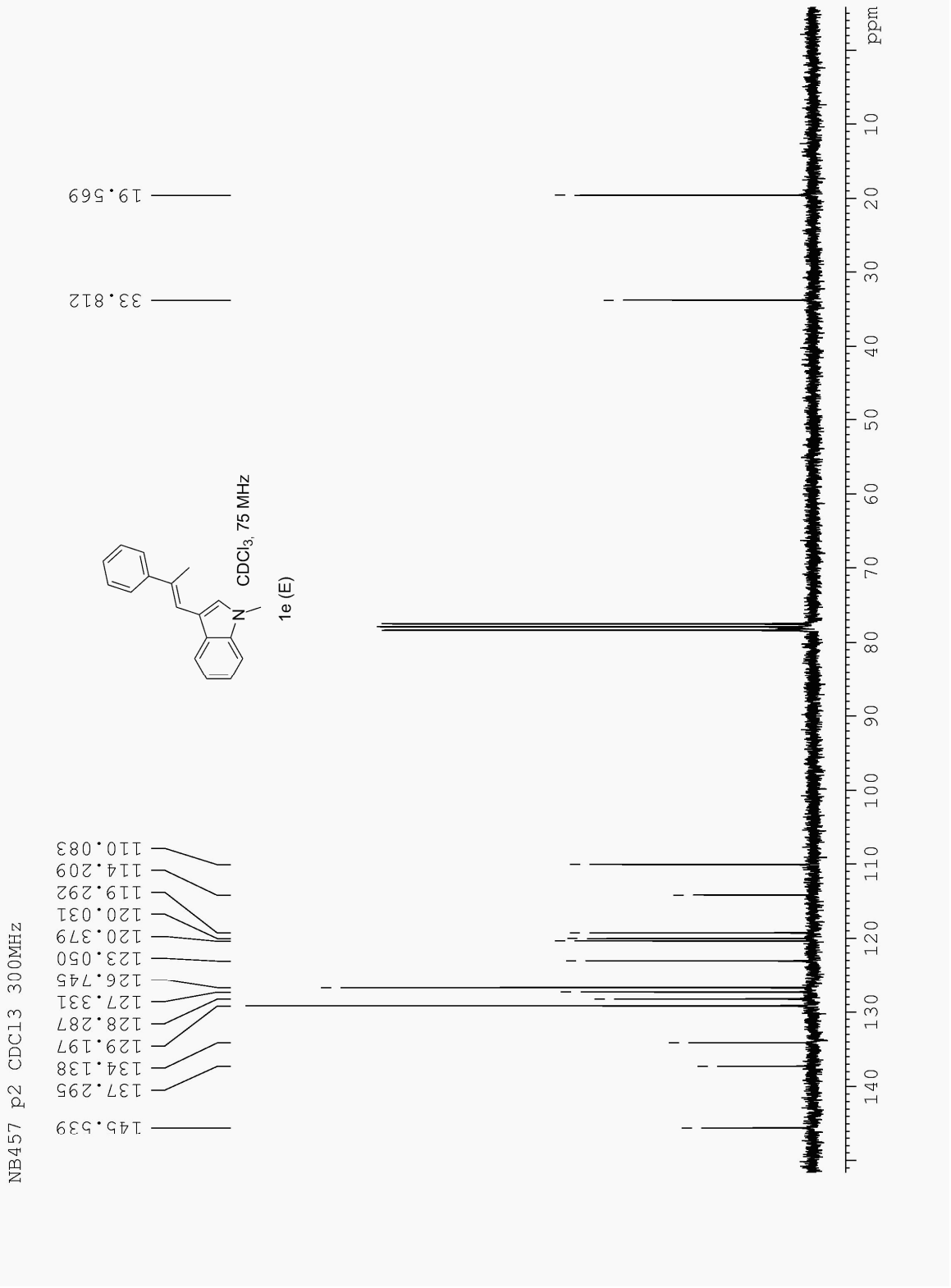

CDCl3, 100MHz
Ph
Ph
N
1c
32.986
76.843
77.161
77.479
109.346
112.583
118.611
118.792
119.794
122.119
126.703
127.357
127.976
128.351
128.412
128.460
129.341
130.181
136.209
137.328
142.201
143.091
ppm
0
20
40
60
80
100
120
140
160
180
200
220

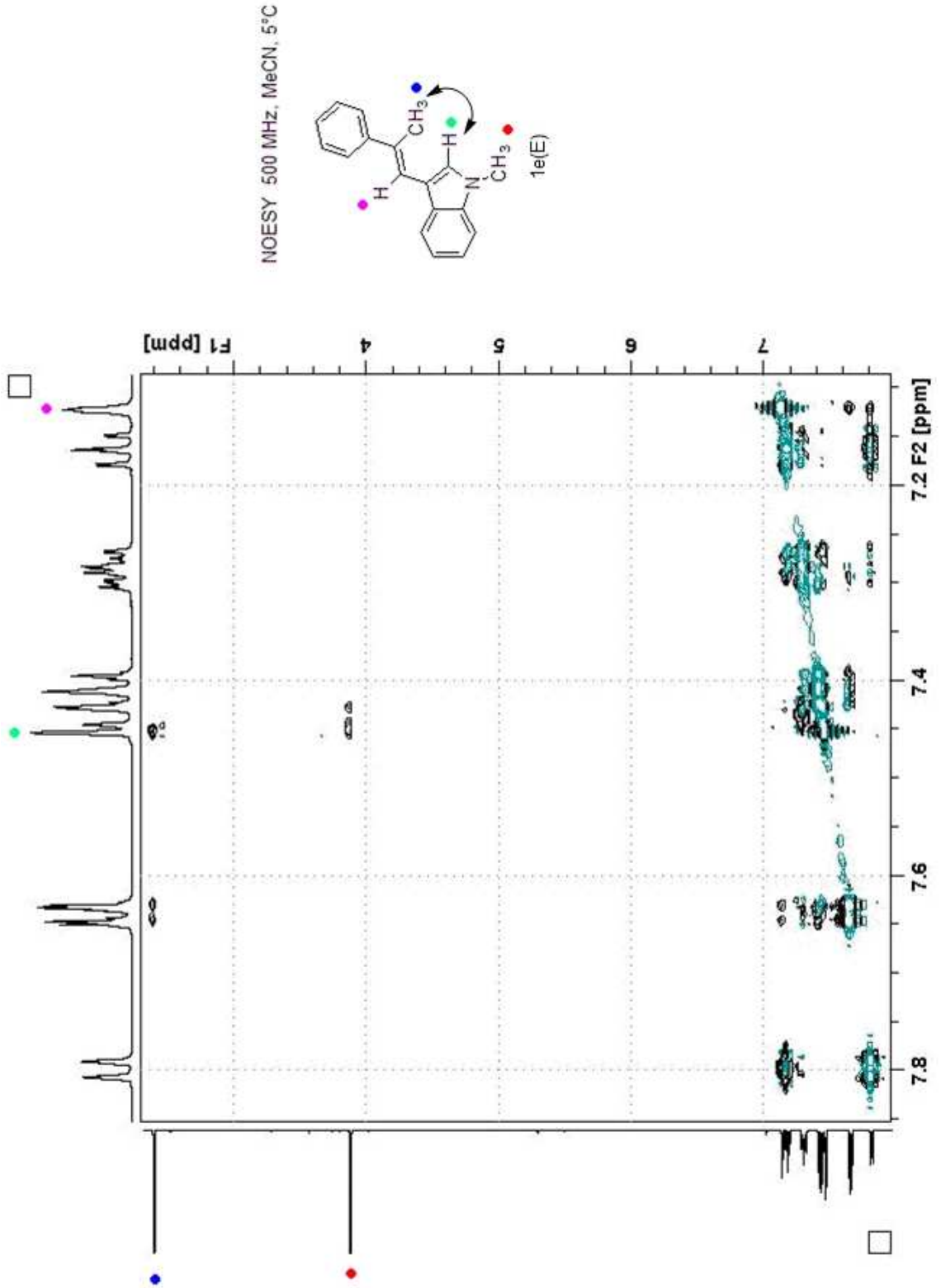
CDCl3, 400MHz
0.00019
1.25354
5.03621
6.06578
6.97959
7.15806
7.16194
7.17807
7.23221
7.24430
7.25794
7.28380
7.29298
7.30020
7.30386
7.31153
7.32259
7.34738
7.36591
7.38820
7.40742
7.75968
ppm
Ph
Ph
N
Bn
1d
1.944
0.955
2.000
18.501
0.960
Integral
ppm

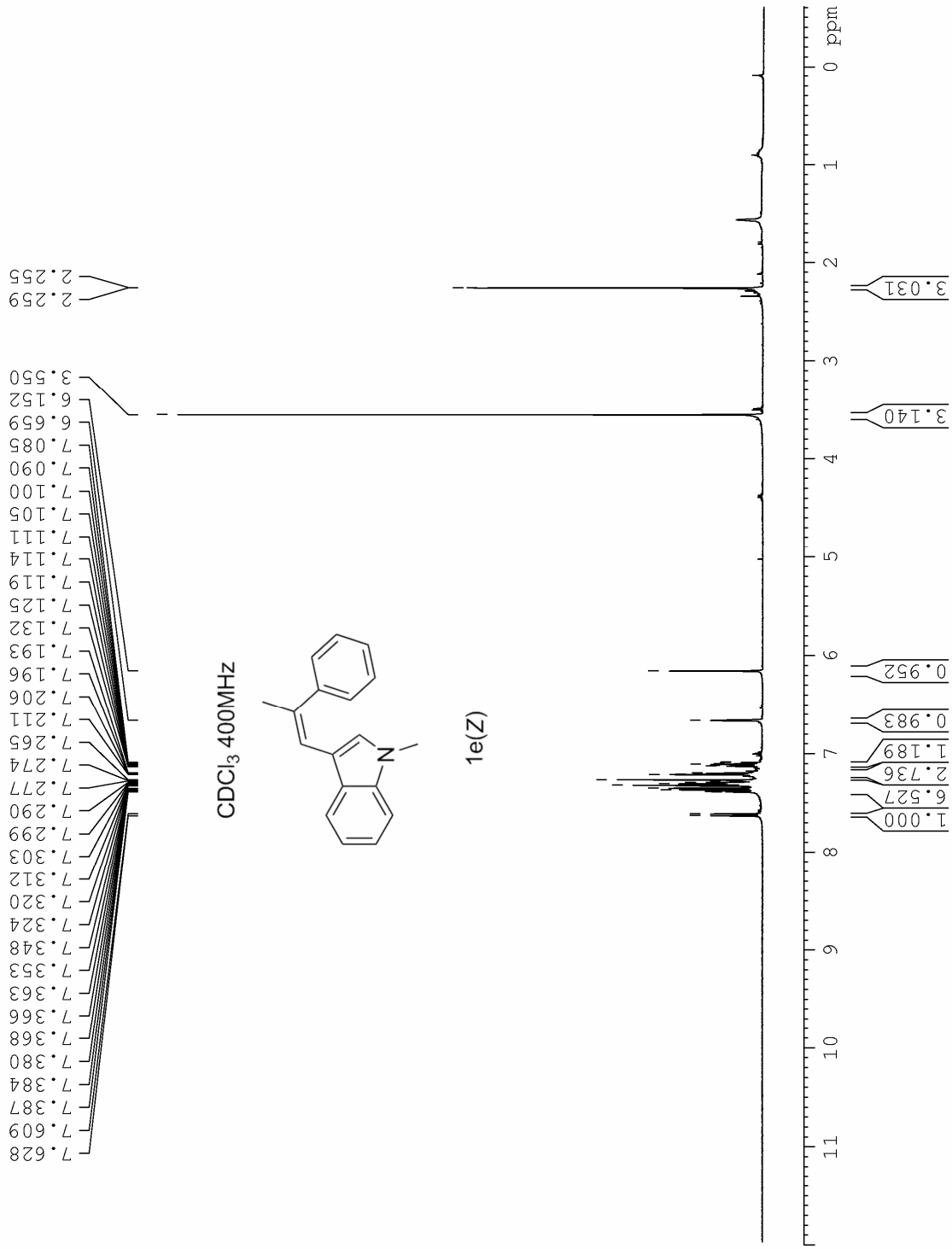
$CDCl_3$, 75MHz

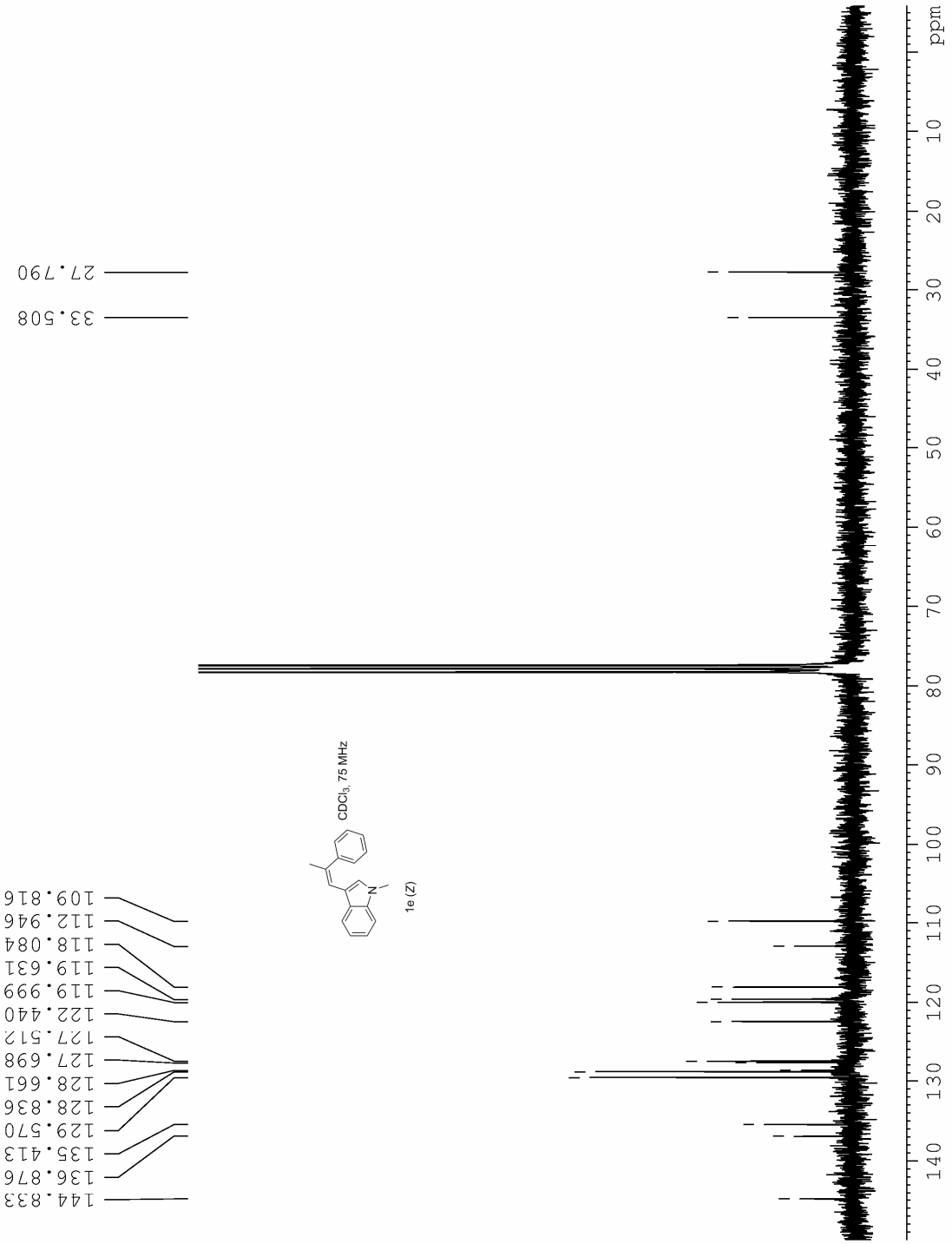

50.326
76.759
77.183
77.384
77.606
109.893
113.175
118.648
118.936
120.038
122.279
126.814
127.159
127.377
127.607
127.782
128.390
128.814
128.843
129.172
129.249
130.209
135.746
136.970
138.097
142.130
143.055
Ph
Ph
N
Bn
1d
ppm
0
20
40
60
80
100
120
140
160
180
200

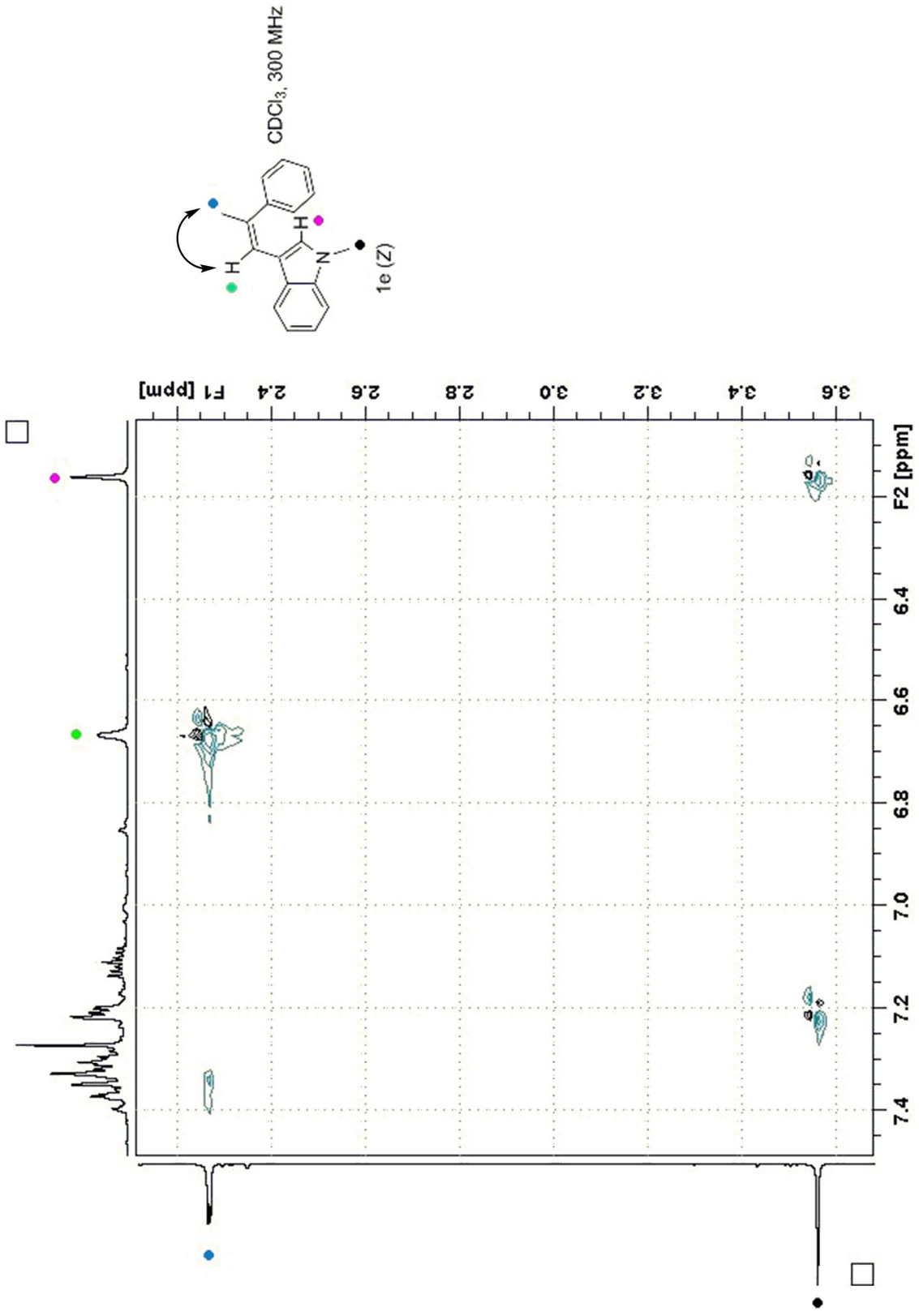

ppm
1
2
3
4
5
6
7
8
9
10
2.437
3.868
7.130
7.225
7.227
7.228
7.242
7.245
7.263
7.308
7.326
7.341
7.344
7.358
7.360
7.376
7.378
7.395
7.396
7.427
7.447
7.461
7.462
7.466
7.630
7.631
7.633
7.644
7.649
7.652
7.813
7.833
CDCl3, 400MHz
1e (E)
3.127
3.076
1.029
2.420
3.438
2.195
2.103
1.000


NB457 p2 CDCl3 300MHz
145.539
137.295
134.138
129.197
128.287
127.331
126.745
123.050
120.379
120.031
119.292
114.209
110.083
33.812
19.569
CDCl3, 75 MHz
1e (E)
N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140

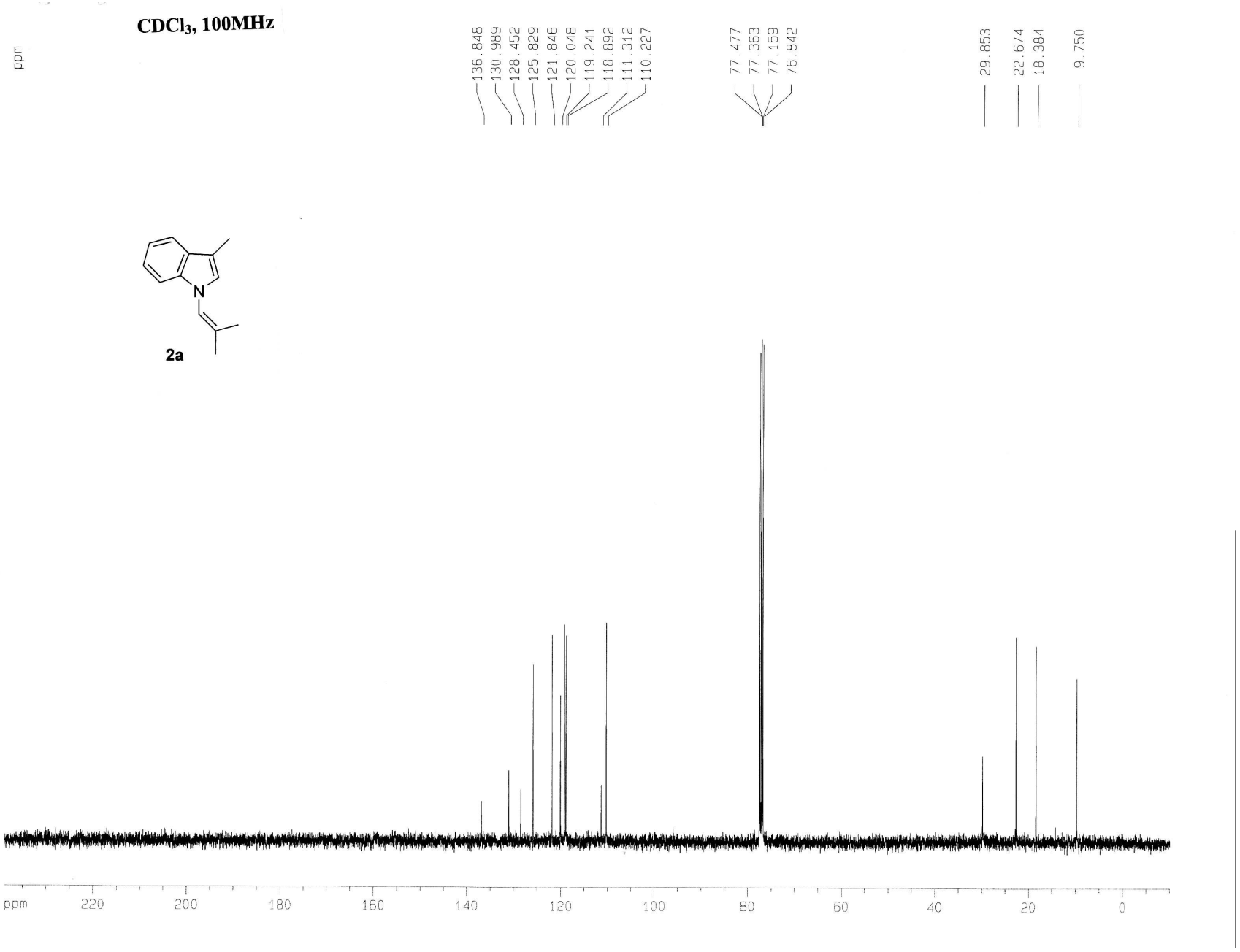

NOESY 500 MHz, MeCN, 5°C
CH3
H
H
N
CH3
1e(E)
F1 [ppm]
4
5
6
7
7.2 F2 [ppm]
7.4
7.6
7.8


2.259
2.255
3.550
6.152
6.659
7.085
7.090
7.100
7.105
7.111
7.114
7.119
7.125
7.132
7.193
7.196
7.206
7.211
7.265
7.274
7.277
7.290
7.299
7.303
7.312
7.320
7.324
7.348
7.353
7.363
7.366
7.368
7.380
7.384
7.387
7.609
7.628
CDCl3 400MHz
1e(Z)
3.031
3.140
0.952
0.983
1.189
2.736
6.527
1.000
ppm


144.833
136.876
135.413
129.570
128.836
128.661
127.698
127.512
122.440
119.999
119.631
118.084
112.946
109.816
CDCl3, 75 MHz
1e (Z)
33.508
27.790
ppm

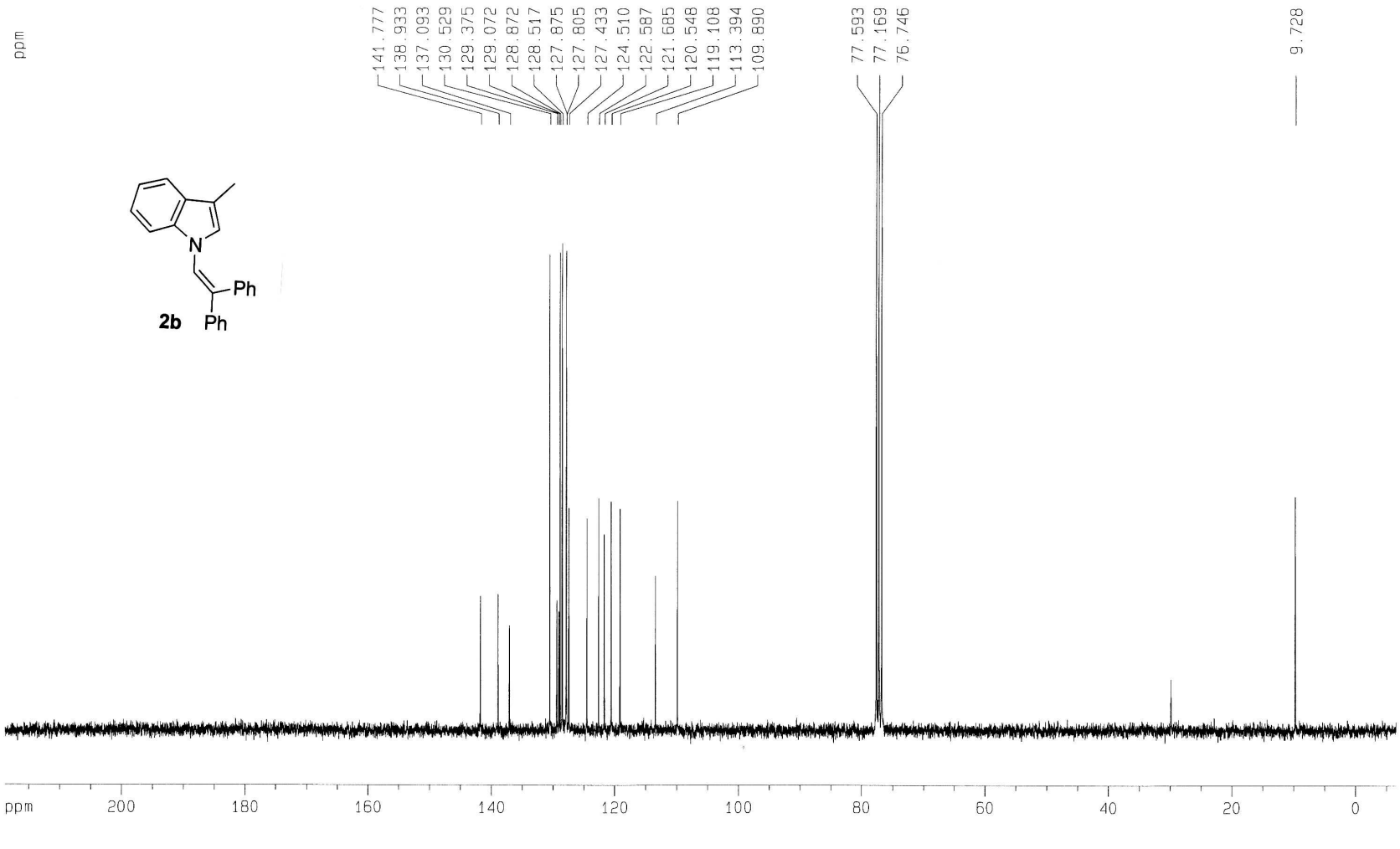

CDCl3, 300 MHz
1e (Z)
F1 [ppm]
F2 [ppm]

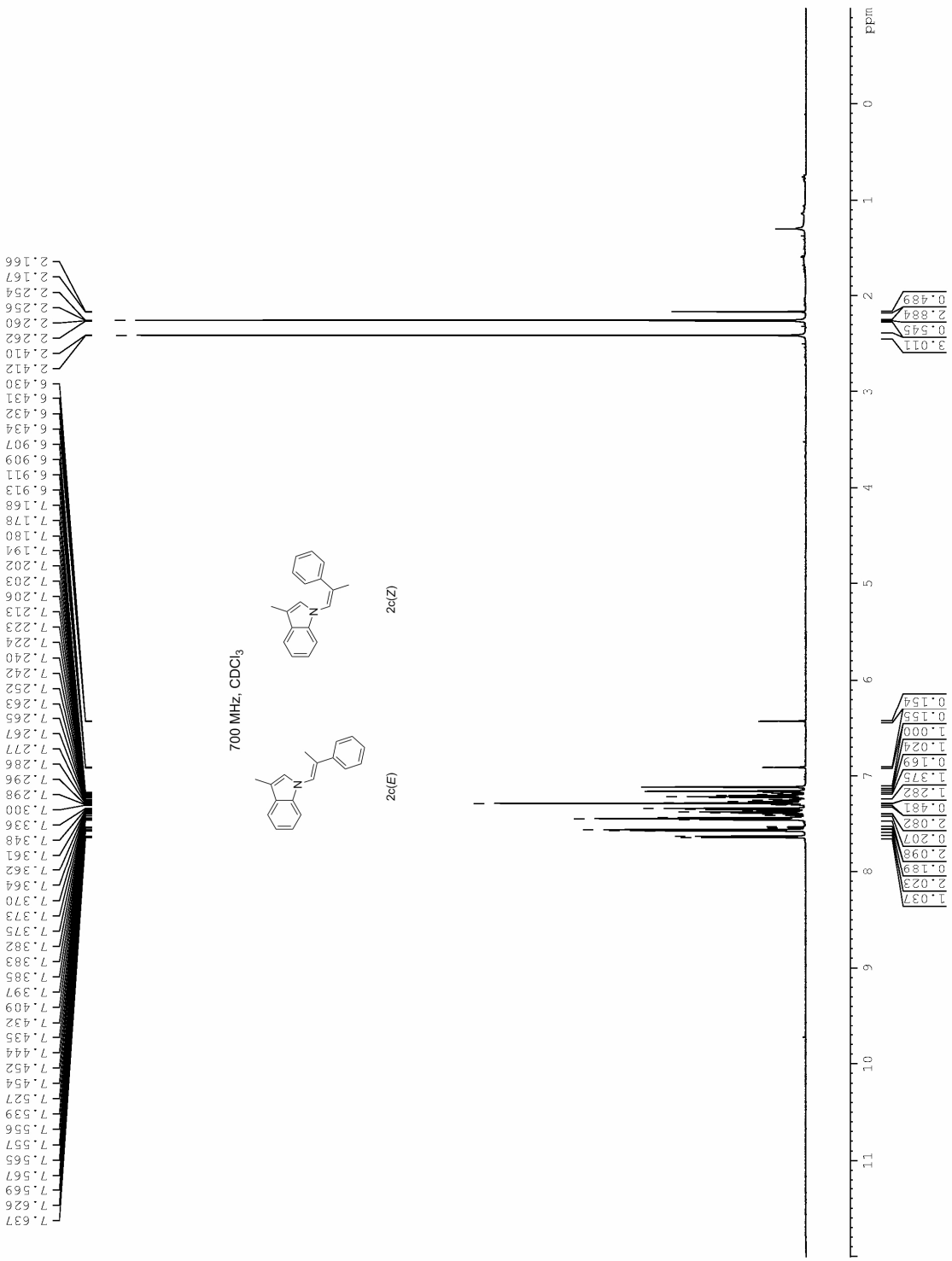
CDCl3, 400MHz
7.56675
7.54729
7.24115
7.20880
7.19529
7.12010
6.87861
6.53053
2.33419
1.90151
1.71656
1.25438
3.0412
3.1134
3.0363
1.0000
1.0296
1.2259
1.8153
1.0103
Integral
ppm
2a

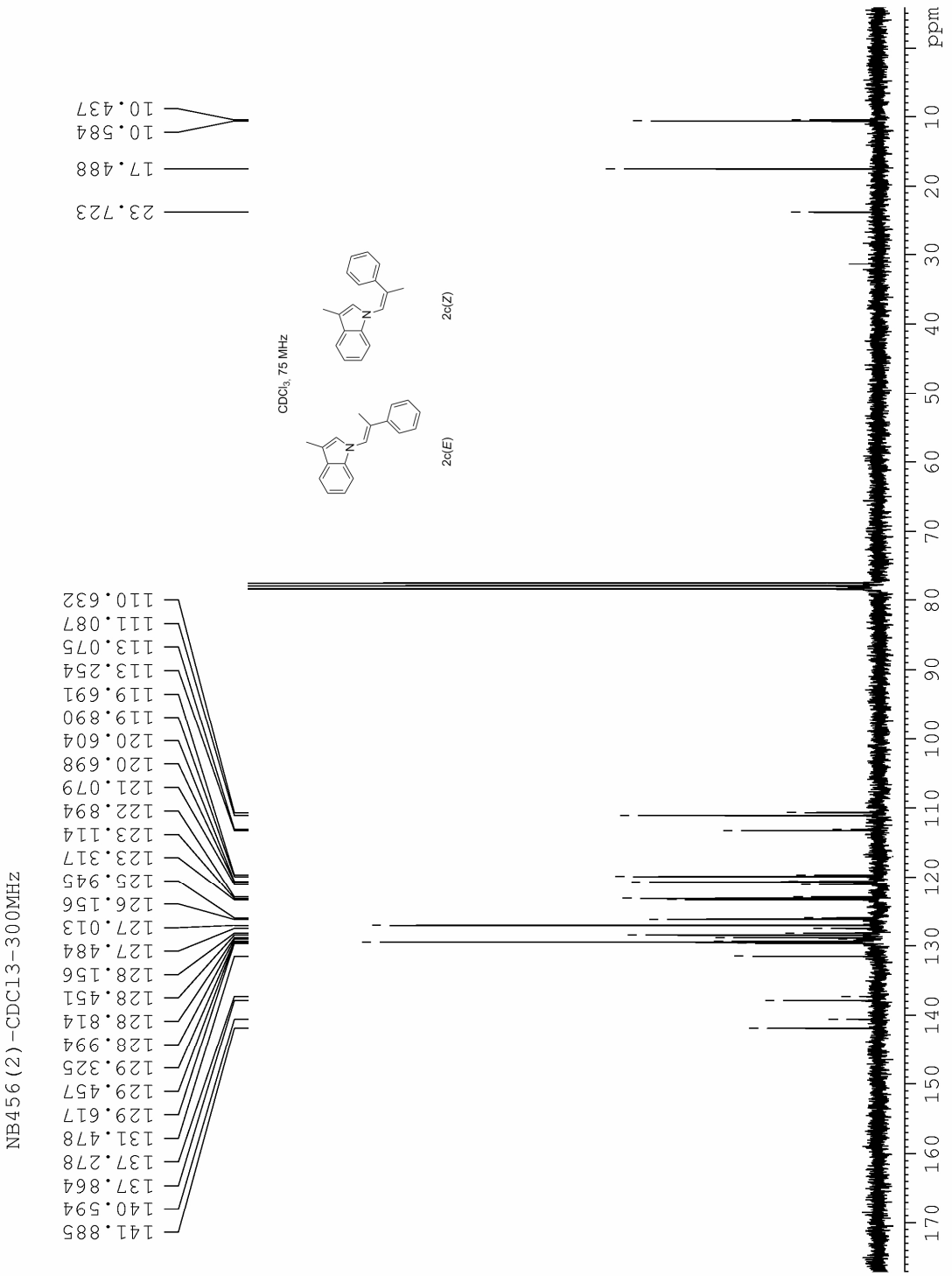

CDCl3, 100MHz
ppm
136.848
130.989
128.452
125.829
121.846
120.048
119.241
118.892
111.312
110.227
77.477
77.363
77.159
76.842
29.853
22.674
18.384
9.750
N
2a
ppm
220
200
180
160
140
120
100
80
60
40
20
0

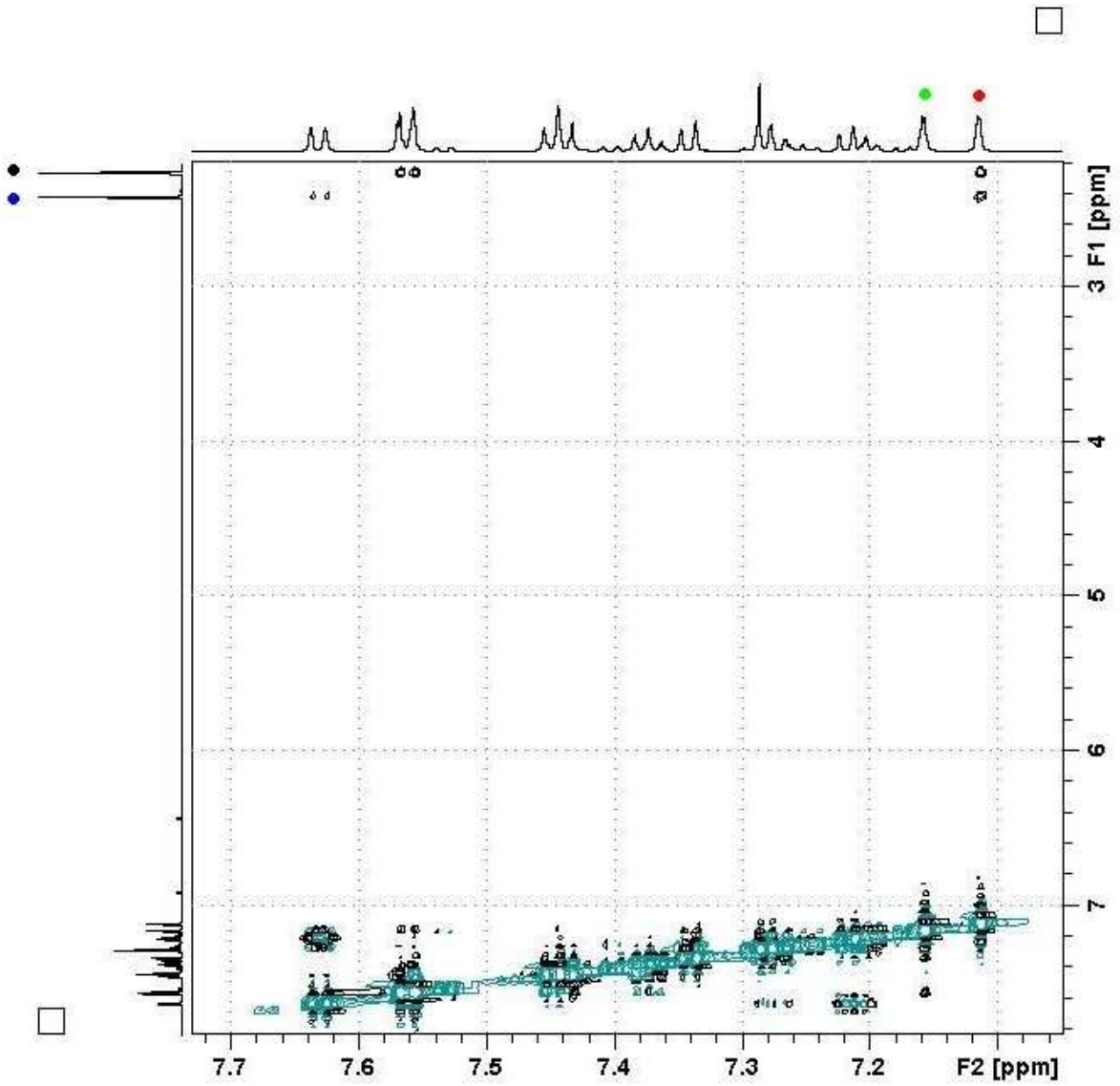
CDCl3, 400MHz
2b
Ph
Ph
N
ppm
Integral
1.25690
2.11559
6.39084
7.16255
7.18124
7.20774
7.21799
7.22543
7.23272
7.31239
7.31729
7.40767
7.42788
7.48971
7.50883
3.1923
1.0000
1.1544
3.0845
9.5696
1.1503
1.1439

$CDCl_3$, 75MHz

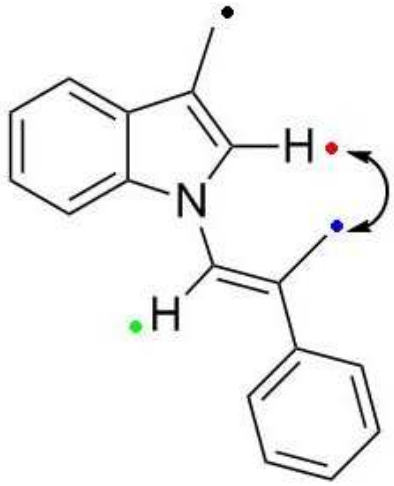

ppm
141.777
138.933
137.093
130.529
129.375
129.072
128.872
128.517
127.875
127.805
127.433
124.510
122.587
121.685
120.548
119.108
113.394
109.890
77.593
77.169
76.746
9.728
N
Ph
Ph
2b
ppm
200
180
160
140
120
100
80
60
40
20
0


700 MHz, CDCl3
2c(Z)
2c(E)
ppm

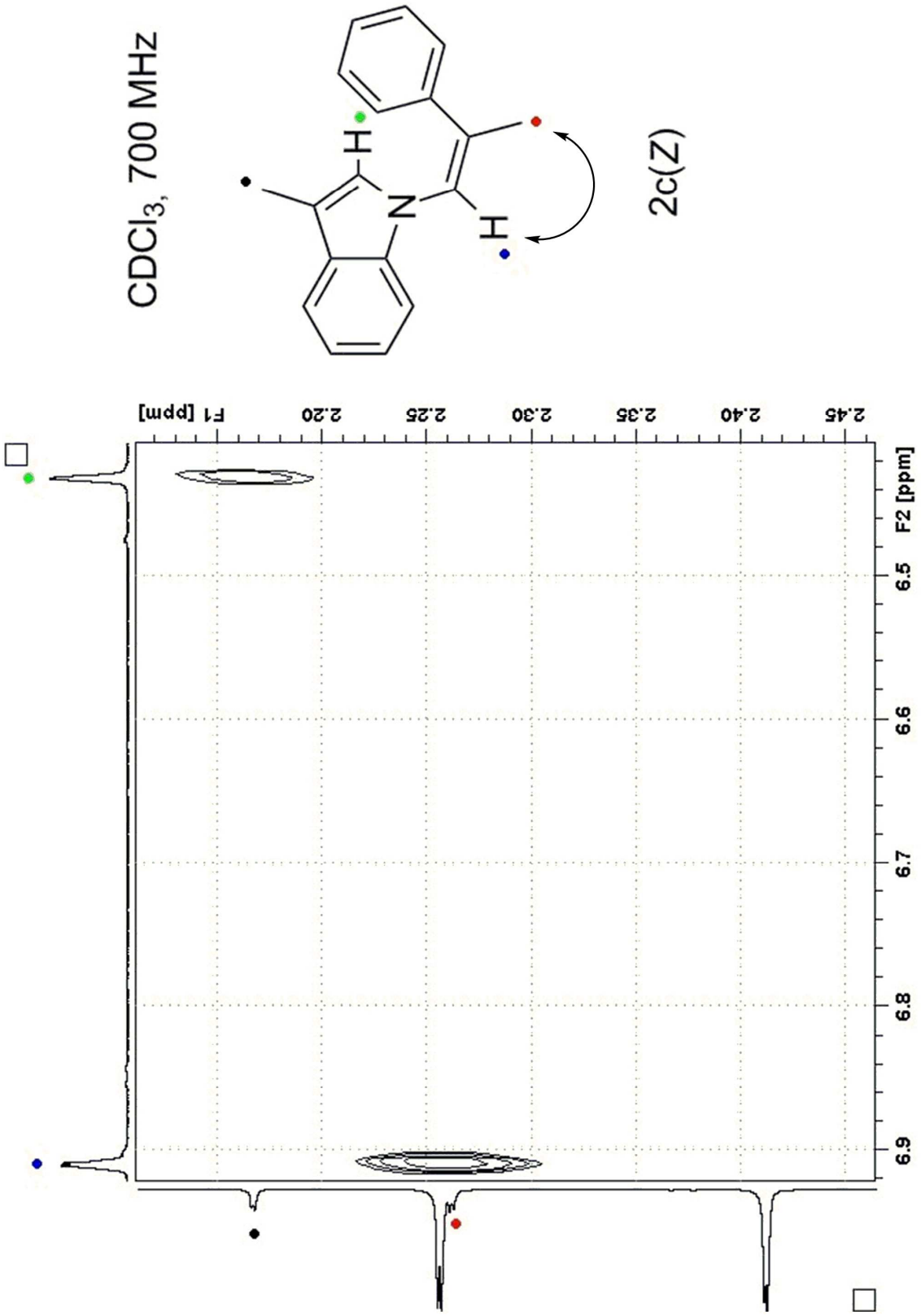

NB456(2)-CDC13-300MHz
141.885
140.594
137.864
137.278
131.478
129.617
129.457
129.325
128.994
128.814
128.451
128.156
127.484
127.013
126.156
125.945
123.317
123.114
122.894
121.079
120.698
120.604
119.890
119.691
113.254
113.075
111.087
110.632
23.723
17.488
10.584
10.437
CDCl3, 75 MHz
2c(Z)
2c(E)
ppm



$CDCl_3$, 700 MHz

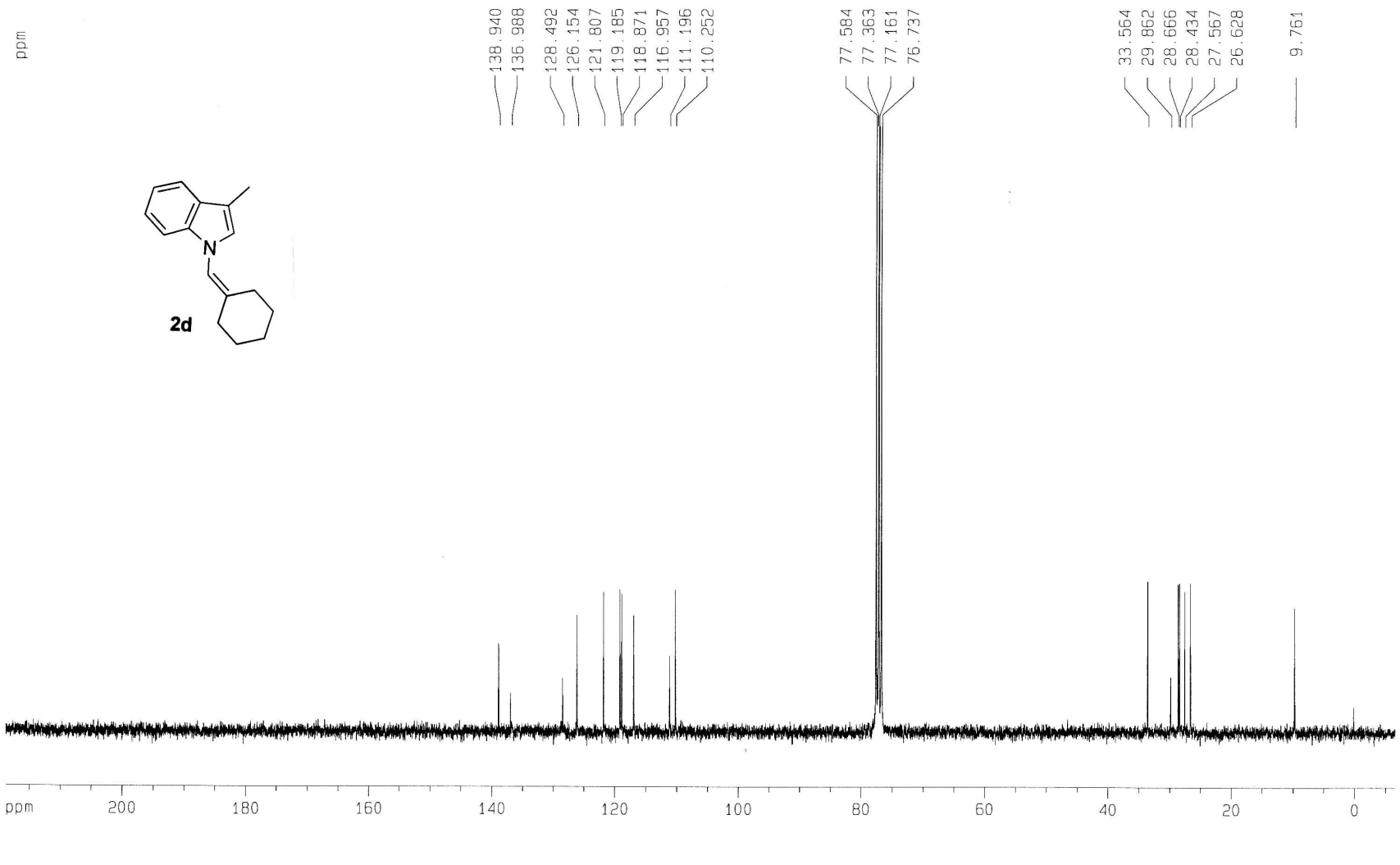


2c(*E*)


CDCl3, 700 MHz
H
N
H
2c(Z)
F1 [ppm]
2.45
2.40
2.35
2.30
2.25
2.20
F2 [ppm]
6.5
6.6
6.7
6.8
6.9

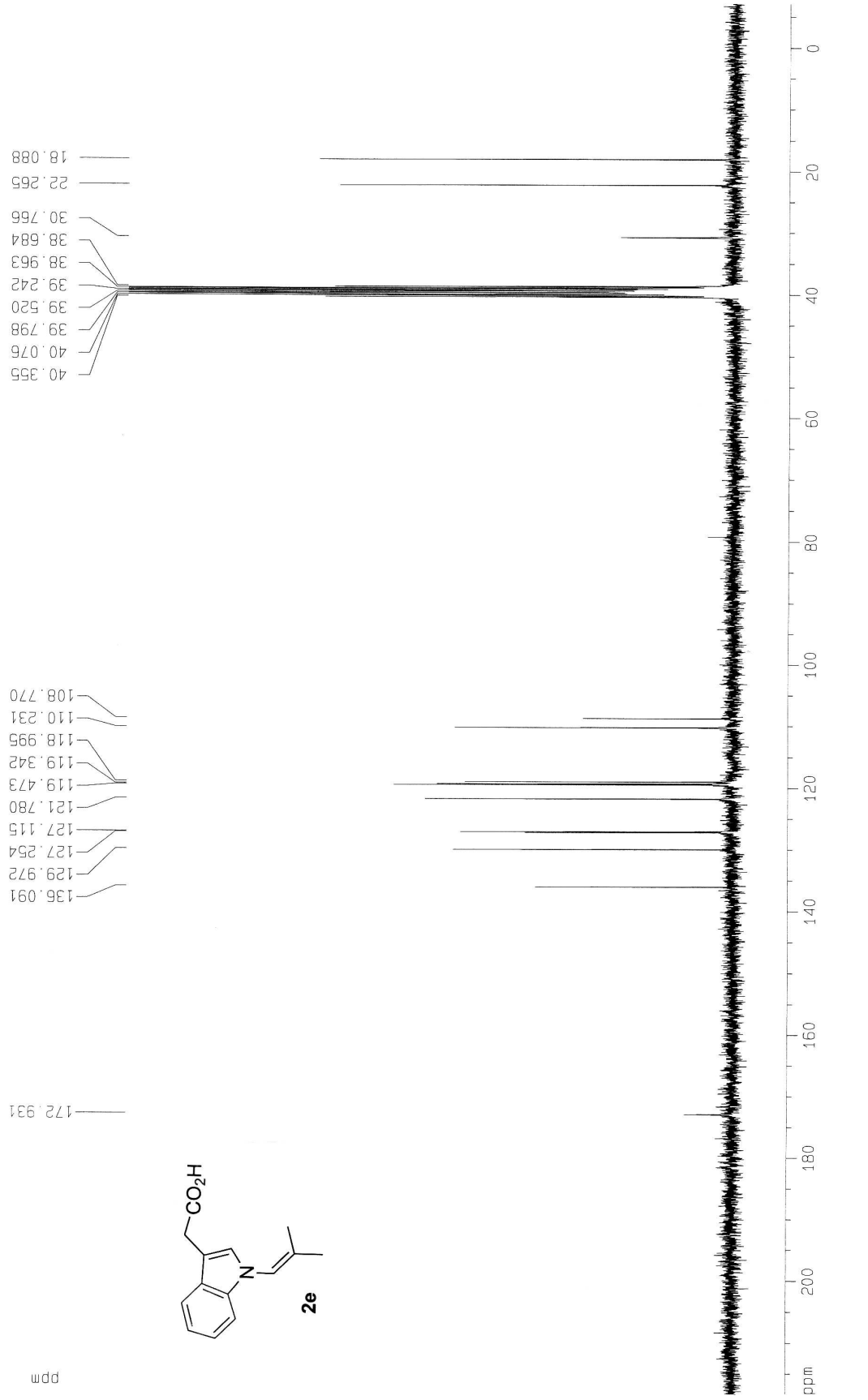
CDCl3, 400MHz
2d
ppm
Integral
0.00139
1.25632
1.49998
1.51456
1.52851
1.54363
1.59272
1.60783
1.61555
1.62376
1.64970
1.66557
1.67932
1.69409
2.16984
2.18445
2.19934
2.27406
2.28916
2.30316
2.33232
7.56314
7.54367
7.52474
7.52914
7.52319
7.51904
7.51743
7.51636
7.51376
7.51689
7.51002
7.50769
6.84145
6.84362
0.9893
2.5707
1.0098
0.9864
1.0000
3.0927
2.1230
2.1002
2.1647
2.2240
2.6064

$CDCl_3$, 75MHz

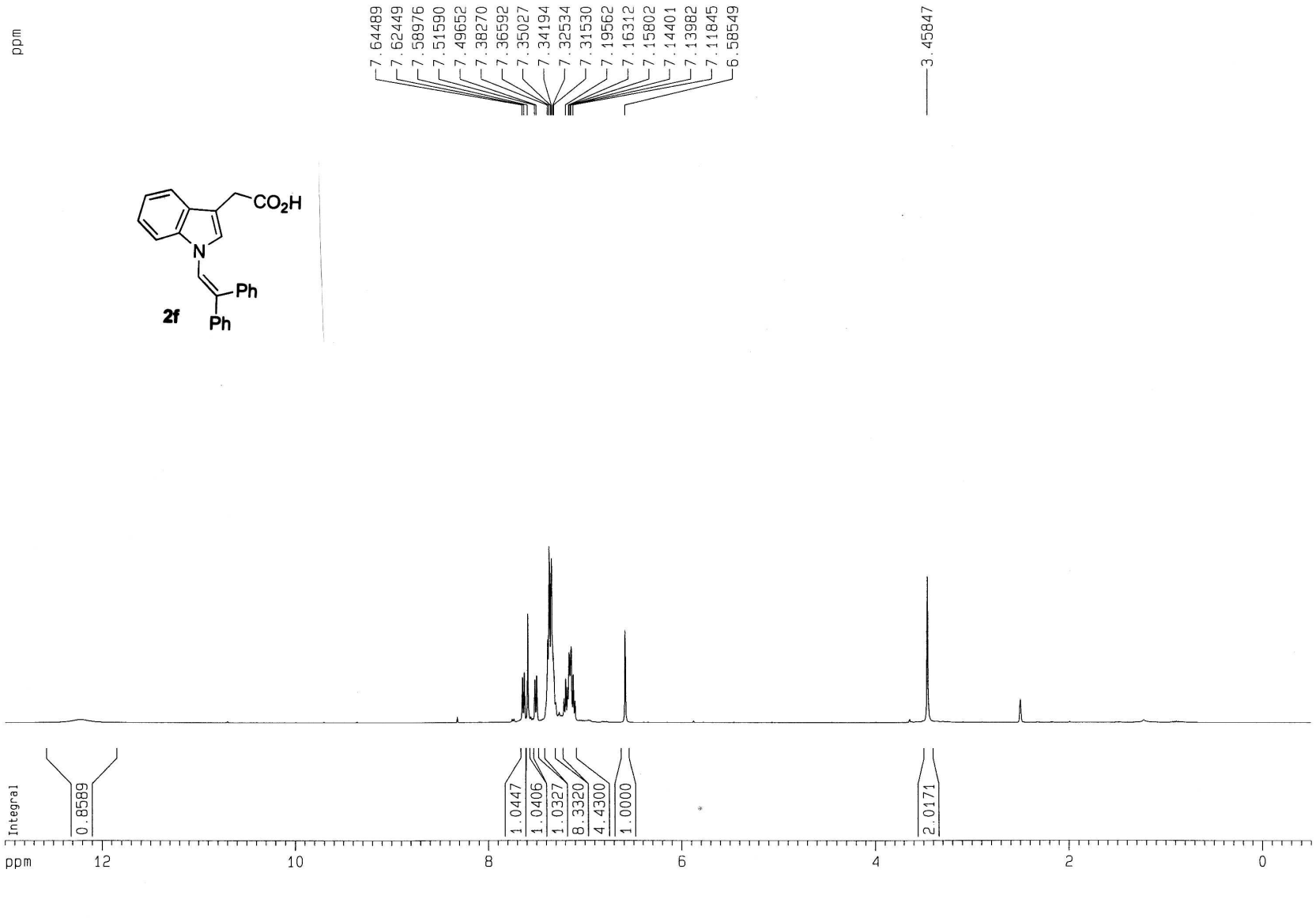

ppm
138.940
136.988
128.492
126.154
121.807
119.185
118.871
116.957
111.196
110.252
77.584
77.363
77.161
76.737
33.564
29.862
28.666
28.434
27.567
26.628
9.761
N
2d
ppm
200
180
160
140
120
100
80
60
40
20
0

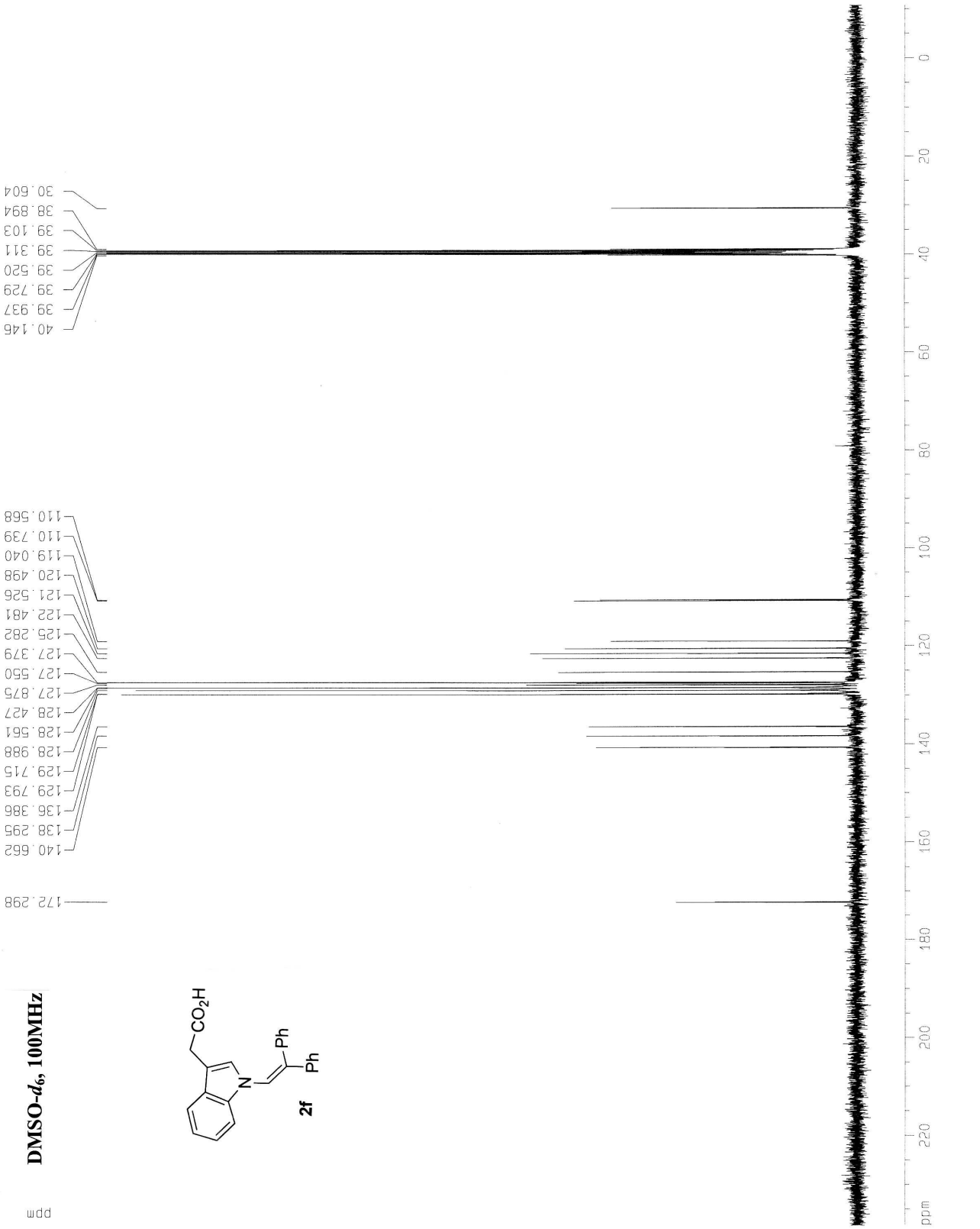
DMSO-d_6, 300MHz
CO_2H
N
2e
7.54706
7.52124
7.28378
7.25589
7.15943
7.08956
7.06606
6.70565
3.67789
2.50561
2.49992
2.49425
1.89572
1.68701
1.68493
1.06320
2.10560
1.13420
1.15140
1.00000
2.07350
3.13920
3.07130
Integral
ppm
0
2
4
6
8
10
12

DMSO-d_6, 75MHz

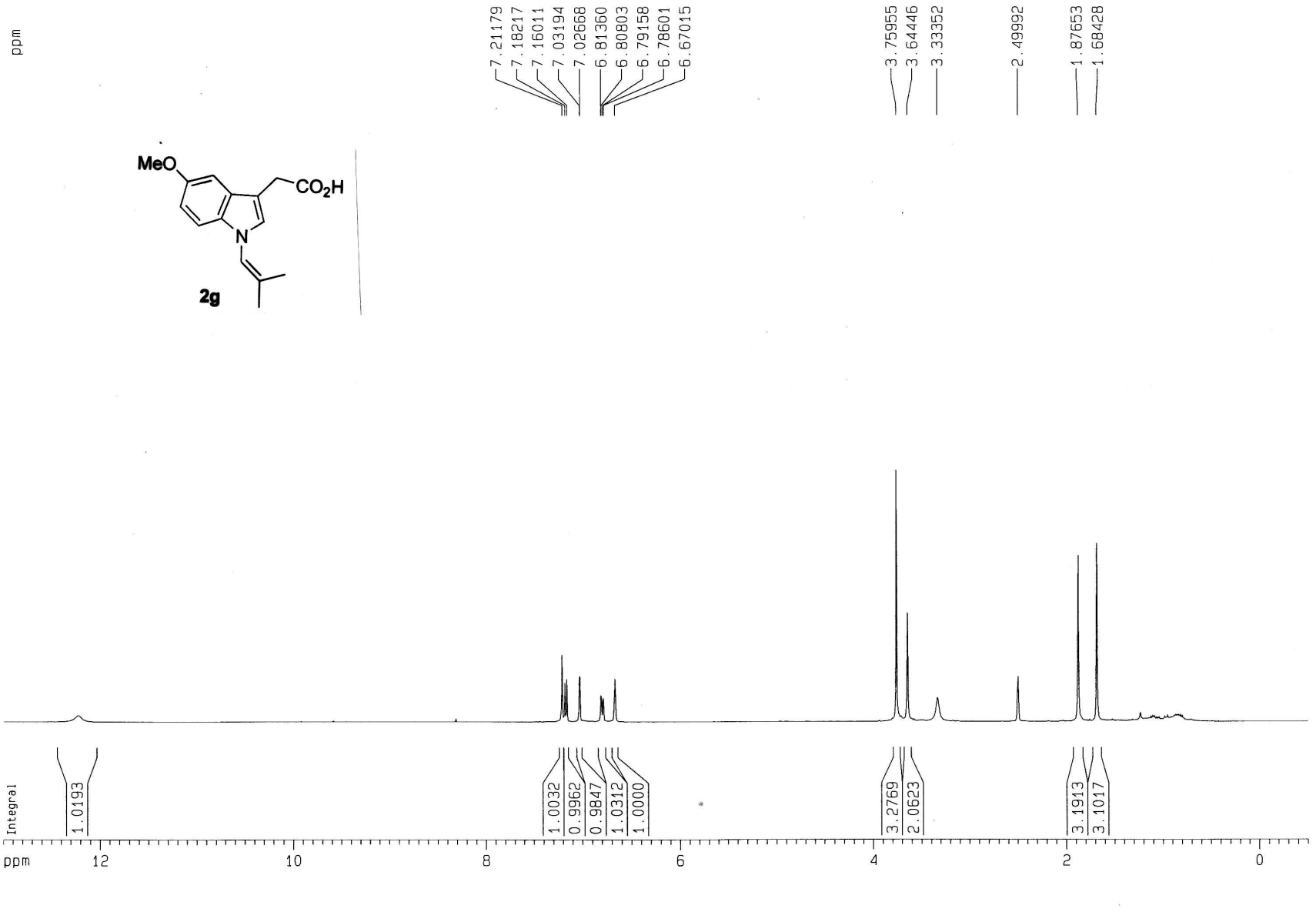


DMSO-d_6, 400MHz

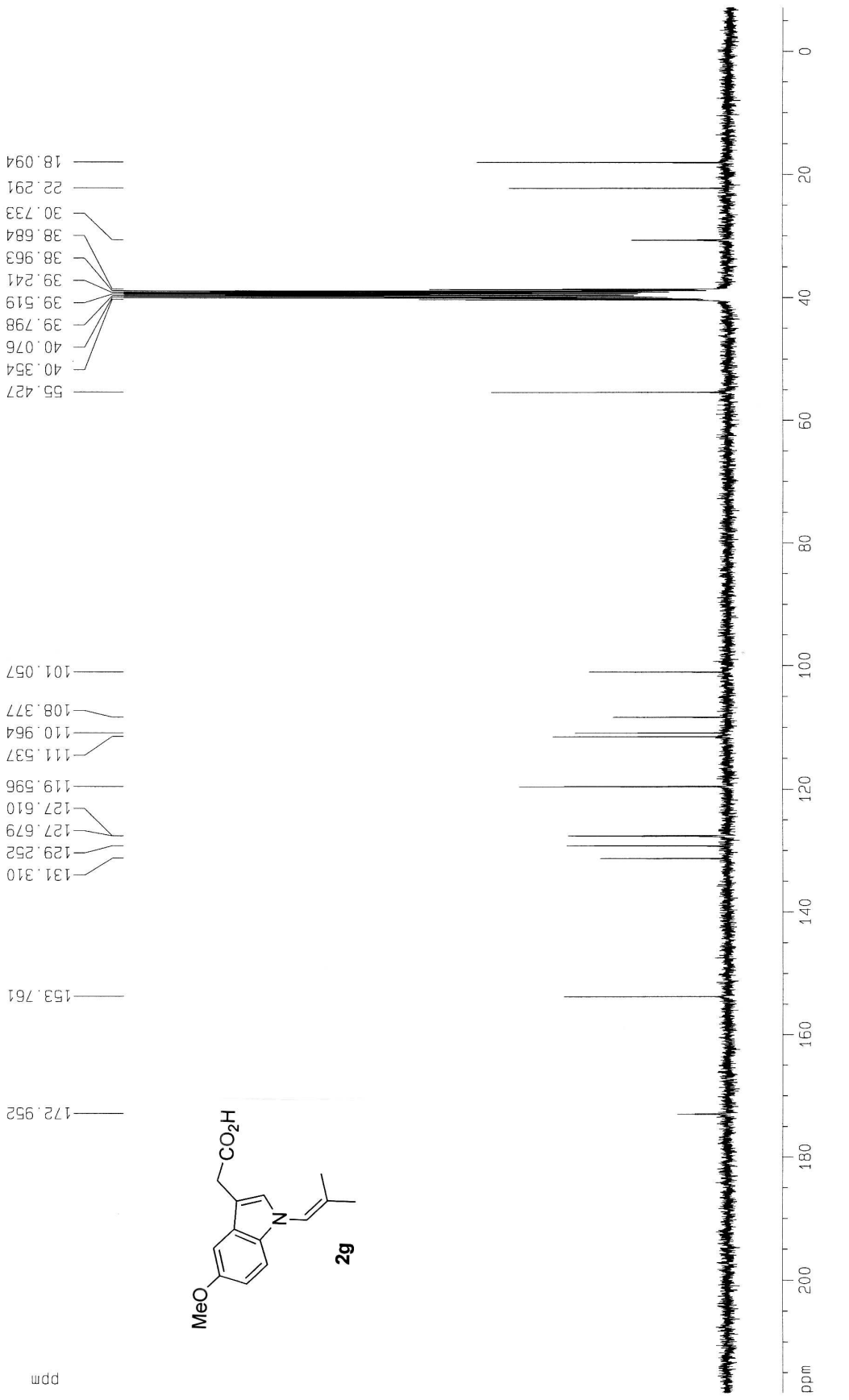



DMSO-d_6, 100MHz
2f
CO_2H
Ph
Ph
N
ppm
0
20
40
60
80
100
120
140
160
180
200
220
30.604
38.894
39.103
39.311
39.520
39.729
39.937
40.146
110.568
110.739
119.040
120.498
121.526
122.481
125.282
127.379
127.550
127.875
128.427
128.561
128.988
129.715
129.793
136.386
138.295
140.662
172.298

DMSO-d_6, 400MHz

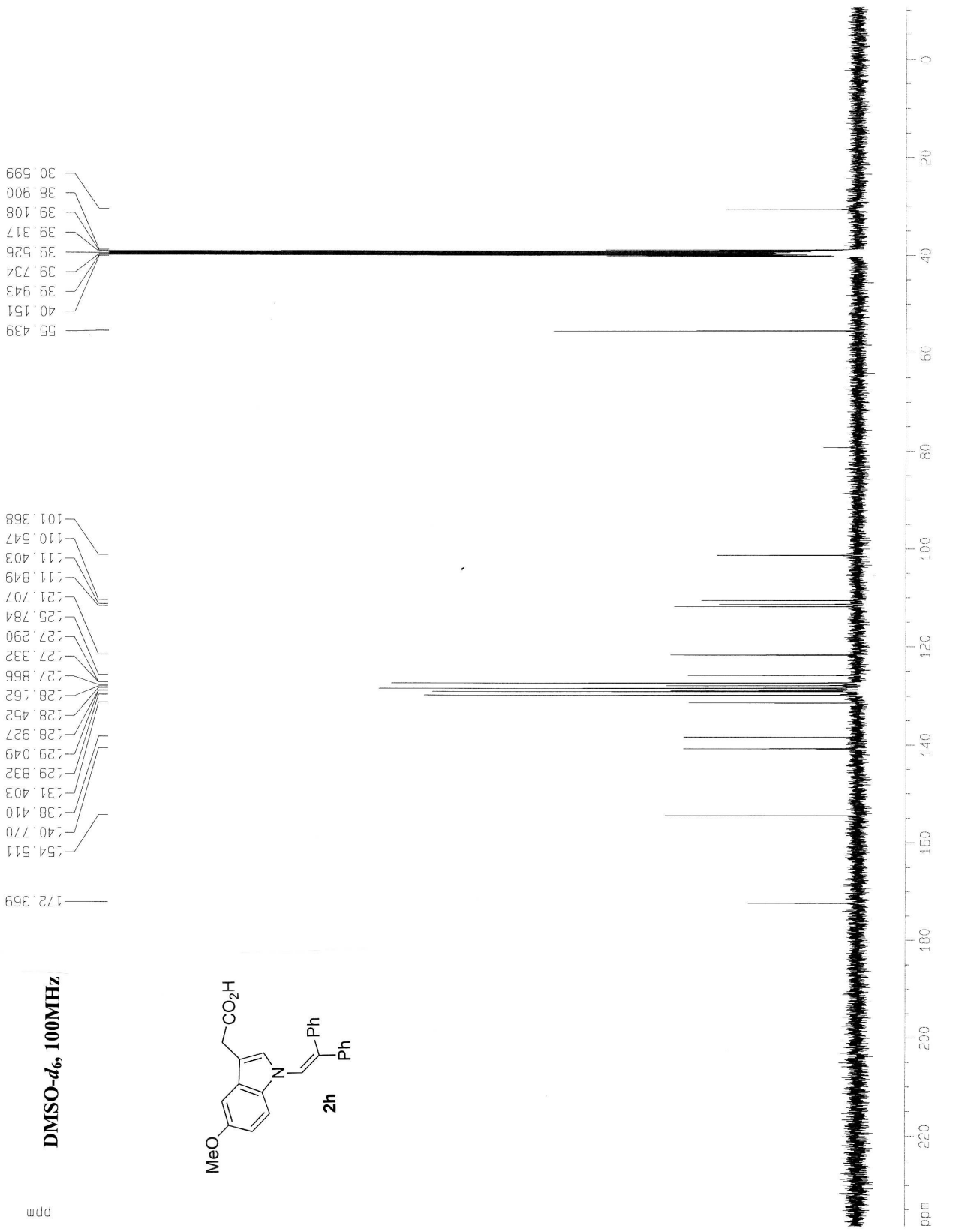


DMSO-d_6, 75MHz



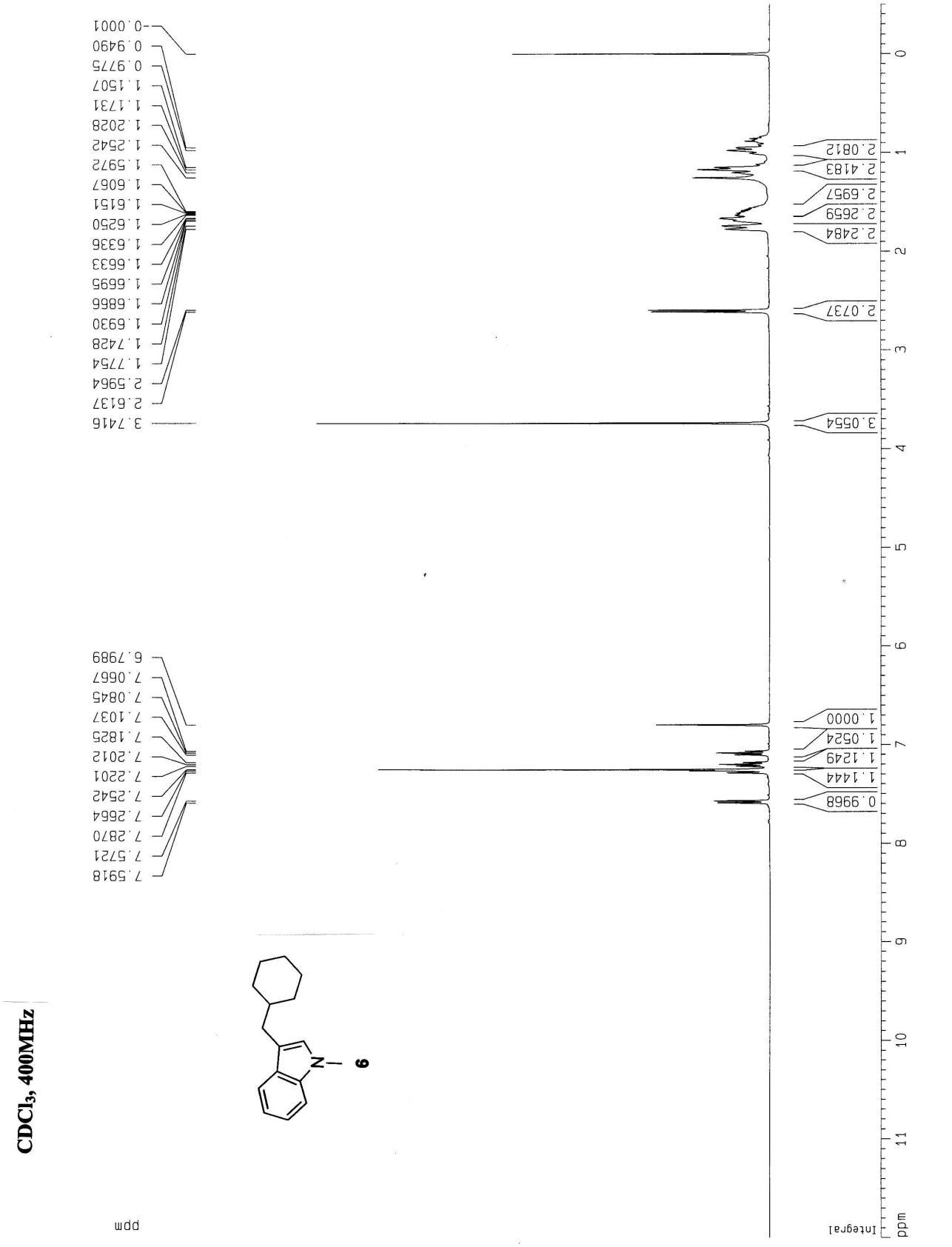
2g

DMSO-d_6, 400MHz
2h
MeO
CO_2H
Ph
Ph
N
ppm
Integral
0.9373
2.0762
8.7970
1.1102
0.9936
1.0256
1.0336
1.0000
2.2809
3.0557
2.50009
3.42815
3.75781
7.56255
7.54784
7.54032
7.38580
7.36752
7.36257
7.35953
7.35468
7.34080
7.32238
7.30878
7.30465
7.15308
7.14835
7.13356
7.00852
7.00272
6.83352
6.53110

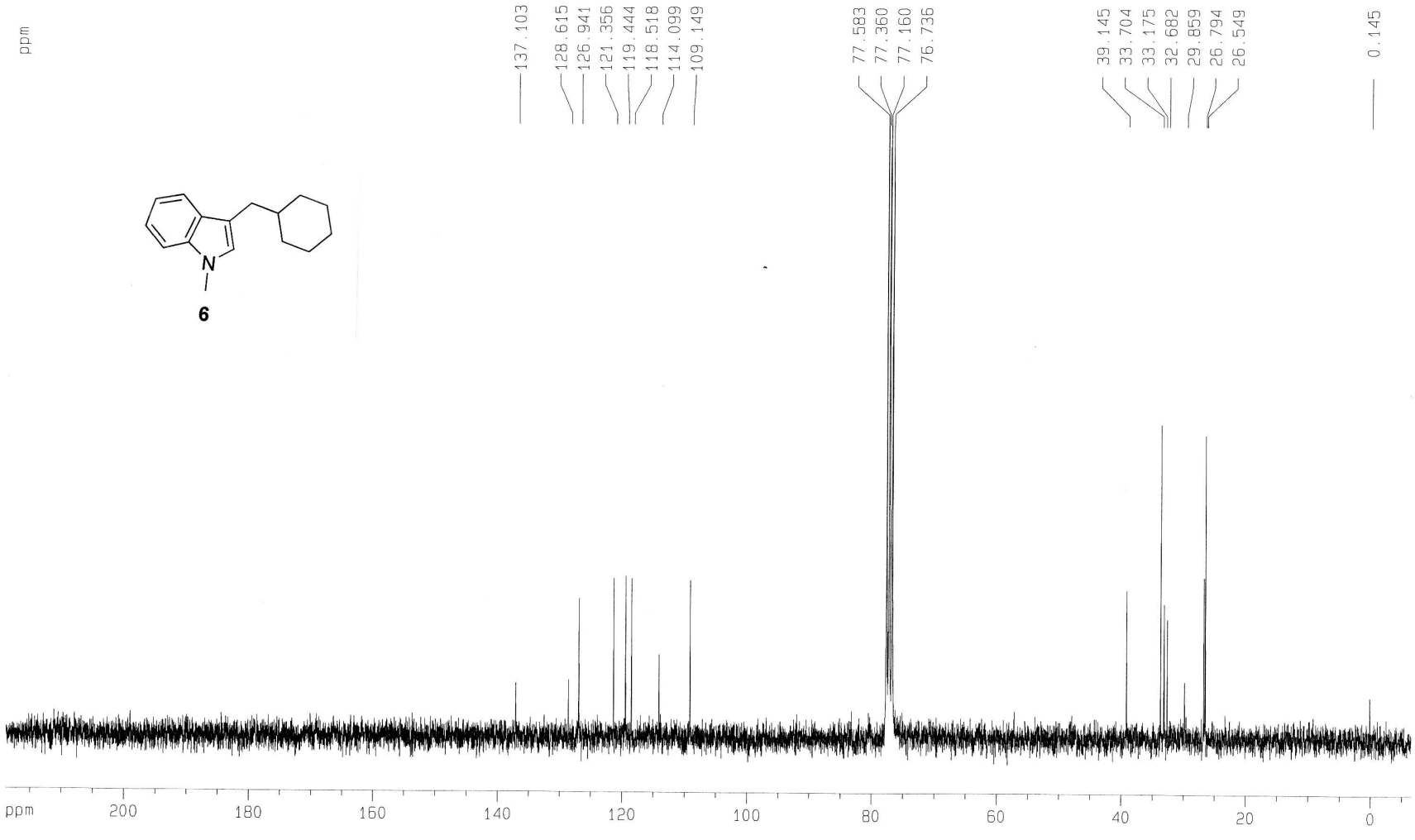

DMSO-d_6, 100MHz
MeO
CO_2H
Ph
Ph
N
2h
ppm
0
20
40
60
80
100
120
140
160
180
200
220
30.599
38.900
39.108
39.317
39.526
39.734
39.943
40.151
55.439
101.368
110.547
111.403
111.849
121.707
125.784
127.290
127.332
127.866
128.162
128.452
128.927
129.049
129.832
131.403
138.410
140.770
154.511
172.369

CDCl3, 400MHz
7.65048
7.63096
7.23502
7.22622
7.22050
7.21278
7.14005
7.06203
6.57751
6.41294
1.98466
1.93256
1.92366
1.73130
ppm
5
Integral
0.9912
2.1808
1.1332
1.0440
1.0000
1.0162
3.1347
3.4896
3.3544
3.0046
ppm

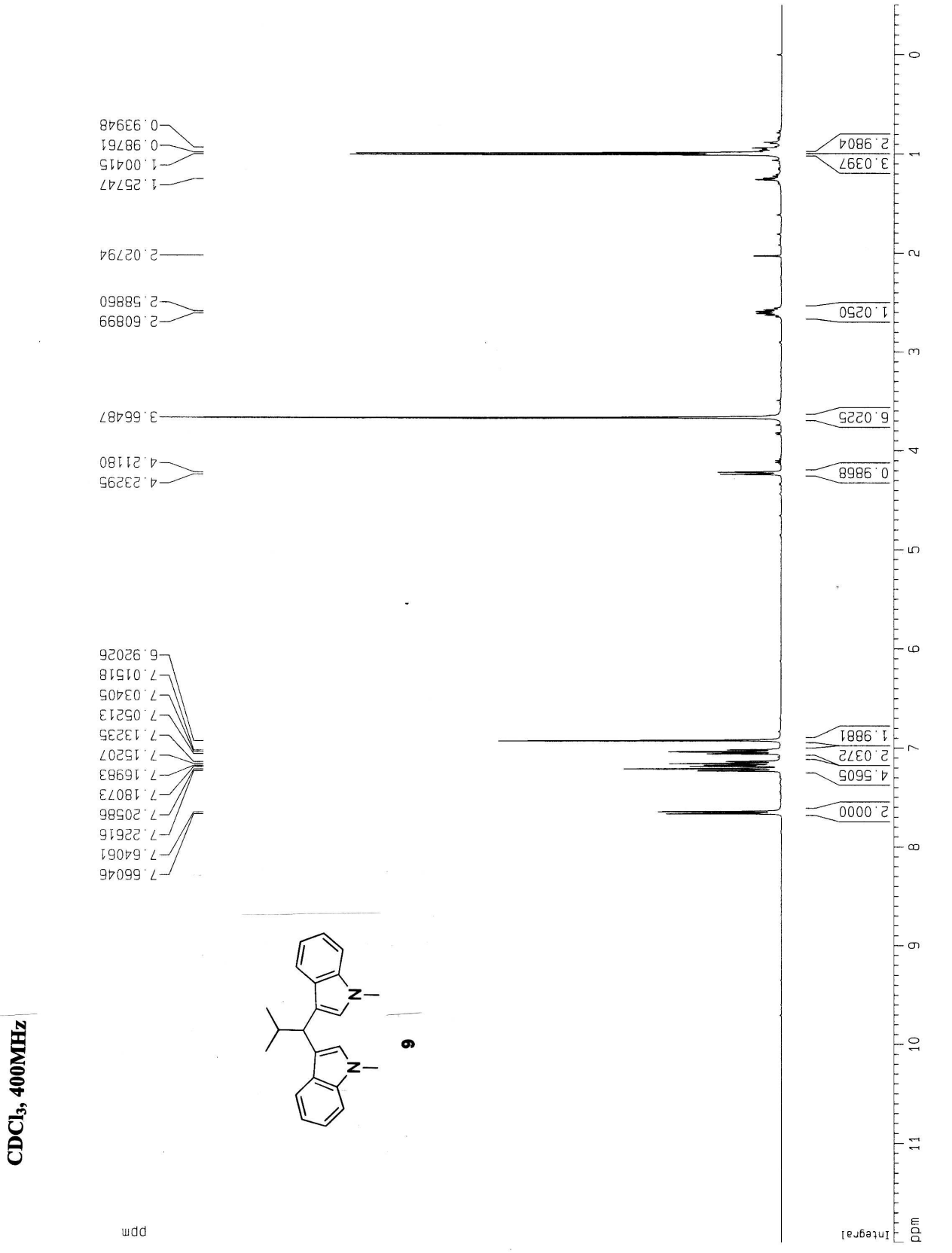
18.387
20.545
22.689
27.005
76.842
77.160
77.478
110.228
114.131
115.653
119.164
119.723
119.979
122.185
125.985
127.756
132.009
132.984
136.216
CDCl3, 100MHz
5
ppm
0
20
40
60
80
100
120
140
160
180
200
220
ppm


CDCl3, 400MHz
6
ppm
Integral

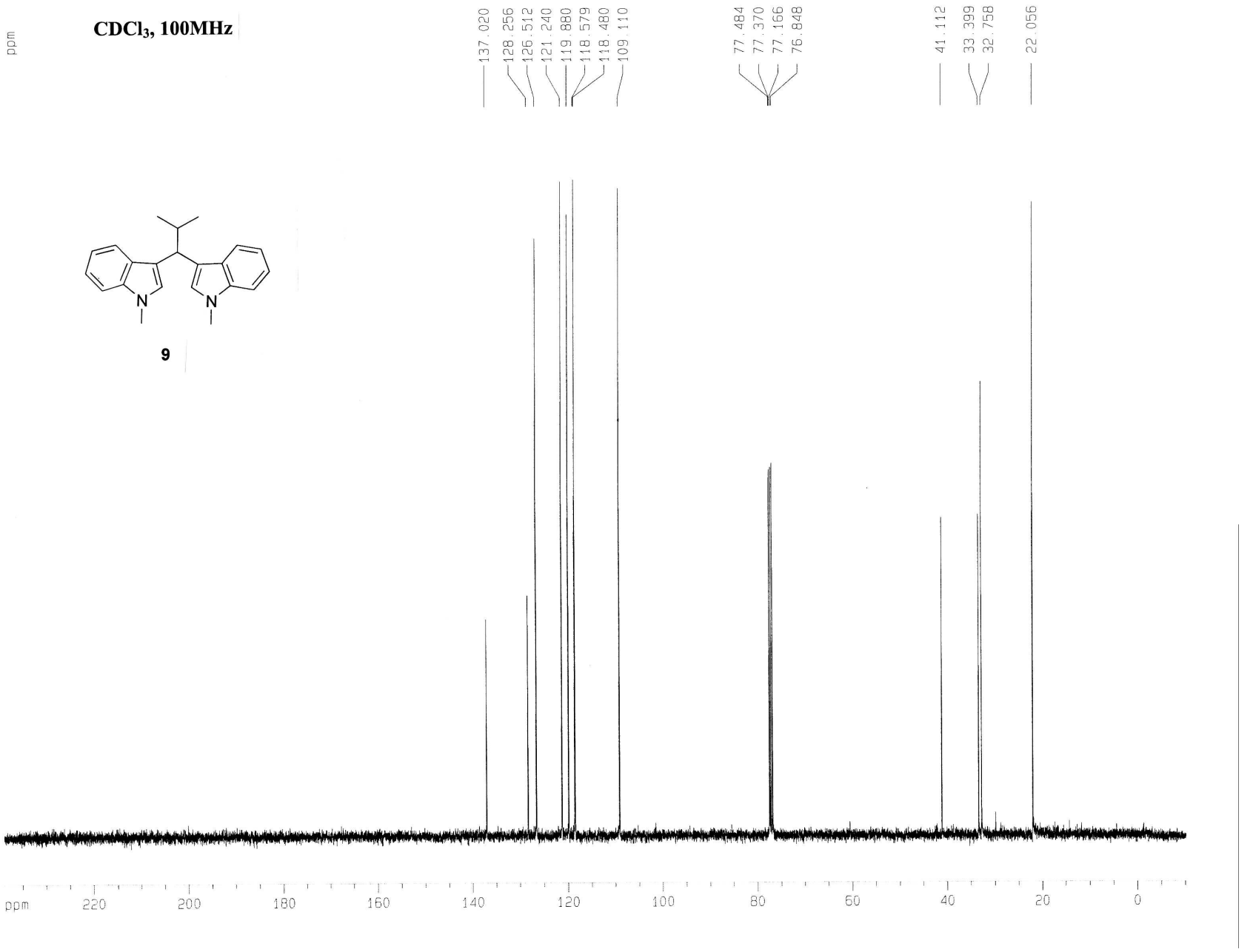
$CDCl_3$, 75MHz


ppm
137.103
128.615
126.941
121.356
119.444
118.518
114.099
109.149
77.583
77.360
77.160
76.736
39.145
33.704
33.175
32.682
29.859
26.794
26.549
0.145
N
6
ppm
200
180
160
140
120
100
80
60
40
20
0

$CDCl_3$, 400MHz



9


CDCl3, 100MHz
ppm
137.020
128.256
126.512
121.240
119.880
118.579
118.480
109.110
77.484
77.370
77.166
76.848
41.112
33.399
32.758
22.056
N
N
9
ppm
220
200
180
160
140
120
100
80
60
40
20
0