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Supporting Information for

Enantioselective β-Amino Acid Synthesis Based on Catalyzed Asymmetric Acyl Halide-Aldehyde Cyclocondensation Reactions

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General Information: Optical rotations were measured on a Perkin-Elmer 241 digital polarimeter with a sodium lamp at ambient temperature and are reported as follows: $[\alpha]_\lambda$ (*c* g/100mL). Infrared spectra were recorded on a Nicolet Avatar 360 FT-IR spectrometer. ^{1}H NMR spectra were recorded on Bruker Avance-300 (300 MHz) or DMX-500 (500 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), integration, coupling constants (Hz), and assignment. ^{13}C NMR spectra were recorded on a Bruker Avance-300 (75 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (deuterochloroform: δ 77.0 ppm). Mass spectra were obtained on a VG-7070 or Fisons Autospec high resolution magnetic sector mass spectrometer.

Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Flash chromatography was performed as previously described on EM silica gel 60 (230-240 mesh).[1] Analytical gas liquid chromatography (GLC) was performed on a Hewlet-Packard 5890 Series II gas chromatograph with a flame ionization detector and split mode capillary injection system, using a Chiraldex™ G-TA column (20 m x 0.25 mm) (Advanced Separation Technologies Inc.). Hydrogen was used as the carrier gas at the indicated pressures. Analytical high performance liquid chromatograph (HPLC) was performed on a Hewlett Packard 1100 liquid chromatograph equipped with a variable wavelength UV detector (deuterium lamp, 190-600 nm), using a Daicel Chiralcel™ OD-H column (250 × 4.6 mm) (Daicel Inc.). HPLC grade isopropanol and hexanes were used as the eluting solvents.

All experiments were carried out under a nitrogen atmosphere in oven or flame-dried glassware using standard inert atmosphere techniques for introducing reagents and solvents. Tetrahydrofuran was distilled form potassium-benzophenone ketyl. Dichloromethane (CH_2Cl_2), dimethylsulfoxide (DMSO), and *N*, *N*-diisopropylethylamine (DIEA) were distilled from CaH_2 under N_2. The mono sodium salt of *o*-nitrosulfonamide was prepared by reacting the sulfonamide with NaH in THF. All other commercially obtained reagents were used as received.

The β-lactones **1** were prepared according to the published procedure.[2]

General procedure for S_N2 addition of NaN_3 to β-lactone 1. To a 50 °C solution of 72 mg of NaN_3 (2.0 mmols, 2.0 equiv) in 3.4 mL of anhydrous DMSO (0.3M in lactone) was added 176 mg of β-lactone **1** (1.0 mmol) via syringe. The resulting homogeneous solution was stirred until all the lactone had been consumed as monitored by TLC (~6 h). After cooling the reaction mixture to ambient temperature, 3 mL of saturated aqueous $NaHCO_3$ was added. The resulting heterogeneous mixture was triturated with water until all the

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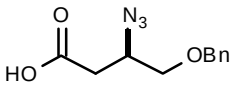
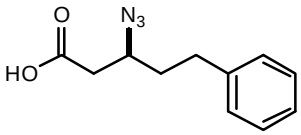
1 W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923-2925.

2 S. G. Nelsom, T. J. Peelen, Z. Wan, *J. Am. Chem. Soc.* **1999**, *121*, 9742-9743.

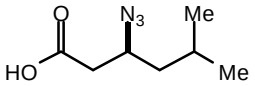
precipitated salts dissolved. The resulting mixture was extracted with ethyl acetate (2 x 5 mL) and the aqueous layer was separated and acidified with 1 M HCl. The acidic aqueous layer was extracted with ethyl acetate (3 x 5 mL) and the combined organic portions were washed with water (2 x 5 mL) and brine (2 x 5 mL). The organic portion was dried (Na_2SO_4) and evaporated in vacuo to afford the β-azido acid **4**.



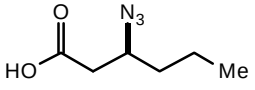
(*R*)-3-Azido-4-benzyloxybutanoic acid (**4a**): The general procedure was followed employing 192 mg of β-lactone **1a** (1.0 mmol). Extractive work-up gave 221 mg (94 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40-7.24 (m, 5H, Ph**H**), 4.59 (s, 2H, OC**H$_2$**Ph), 4.04 (m, 1H, C**H**N_3), 3.60 (d, 2H, J = 5.5 Hz, CHN_3C**H$_2$**O), 2.67 (dd, 1H, J = 16.6, 5.0 Hz, C**H$_a$**CO_2H), 2.54 (dd, 1H, J = 16.6, 8.4 Hz, C**H$_b$**CO_2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.8, 137.7, 128.7 (2C), 128.1, 127.8 (2C), 73.5, 71.8, 57.7, 36.1; IR (NaCl): 3089, 3065, 3034, 2927, 2863, 2673, 2127, 2095, 1711, 1414, 1267, 1093, 741, 701 cm^{-1}. MS (EI, 70 eV): *m/z* 207 $(M-N_2)^+$, 130, 91. MS (FAB, Na-ehtylene glycol): *m/z* 258 $(M+Na)^+$. $[\alpha]_D^{25}$ = +27.09^0 (*c* 5.5, CH_2Cl_2). Conversion of **4a** to the corresponding methyl ester (CH_2N_2, Et_2O) and separation of the enantiomers by chiral HPLC (Diacel Chiracel^{TM} OD-H column, flow rate 1.0 mL/min, 10% *i*-PrOH, 90% hexane, T_r 7.51 (*R*) and 8.35 (*S*) min) provided the enantiomer ratio: 4(*R*):4(*S*) = 96:4 (92%ee).



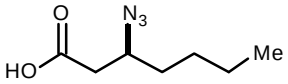
(*S*)-3-Azido-5-phenylpentanoic acid (4b): The general procedure was followed employing 176 mg of β-lactone **1b** (1.0 mmol). Extractive work-up gave 208 mg (95 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35-7.29 (m, 2H, Ph**H**), 7.25-7.20 (m, 3H, Ph**H**), 3.81 (m, 1H, C**H**N_3), 2.84 (m, 1H, C**H$_a$**CH_2Ph), 2.72 (m, 1H, C**H$_b$**CH_2Ph), 2.60 (d, 1H, J = 6.7 Hz, C**H$_a$**CO_2H), 1.89 (m, 2H, CH_2**C**H**$_2$**Ph); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.1, 140.4, 128.5 (2C), 128.3 (2C), 126.2, 58.0, 39.3, 36.0, 32.0; IR (NaCl): 3084, 3059, 3029, 2929, 2855, 2661, 2128, 2098, 1710, 1431, 1257, 749, 699 cm^{-1}. MS (FAB, Na-ehtylene glycol): *m/z* 242 $(M+Na)^+$. Anal. calcd. for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.98. Found: C, 60.35; H, 5.99. $[\alpha]_D^{25}$ = -3.00^0 (*c* 3.9, CH_2Cl_2). Conversion of **4b** to the corresponding methyl ester (CH_2N_2, Et_2O) and separation of the enantiomers by chiral HPLC (Diacel Chiracel^{TM} OD-H column, flow rate 1.0 mL/min, 10% *i*-PrOH, 90% hexane, T_r 7.05 (*S*) and 8.44 (*R*) min) provided the enantiomer ratio: 4(*S*):4(*R*) = 96.5:3.5 (93%ee).



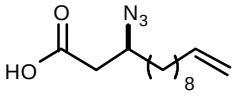
(S)-3-Azido-5-methylhexanoic acid (4c): The general procedure was followed employing 100 mg of β-lactone **1c** (0.78 mmol). Extractive work-up gave 126 mg (95 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.86 (m, 1H, C**H**N_3), 2.56 (d, 2H, J = 7.0 Hz, C**H$_2$**CO_2H), 1.81 (m, 1H, C**H**Me_2), 1.55 (ddd, 1H, J = 14.1, 9.5, 5.4 Hz, CHN_3C**H$_a$**CH), 1.33 (ddd, 1H, J = 13.7, 8.7, 4.8 Hz, CHN_3C**H$_b$**CH), 0.98 (d, 3H, J = 6.6 Hz, CH**Me$_a$**), 0.97 (d, 3H, J = 6.7 Hz, CH**Me$_b$**); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.2, 57.0, 43.3, 40.0, 25.0, 23.0, 21.8; IR (NaCl): 3029, 2954, 2925, 2880, 2870, 2666, 2108, 1710, 1431, 1262 cm^{-1}. MS (CI, methane): *m/z* 172 $(M+H)^+$. HRMS *m/z* cacld for $C_6H_{10}N_1O_2$ (M-CH_3, N_2): 128.0711. Found: 128.0713. $[\alpha]_D^{25}$ = +4.20^0 (*c* 4.8, CH_2Cl_2). Conversion of **4c** to the corresponding benzyl ester (BnOH, DCC, DMAP, CH_2Cl_2) and separation of the enantiomers by chiral HPLC (Diacel Chiracel^{TM} OD-H column, flow rate 1.0 mL/min, 3% *i*-PrOH, 97% hexane, T_r 5.45 (*R*) and 5.99 (*S*) min) provided the enantiomer ratio: 4(*S*):4(*R*) = 98.5:1.5 (97%ee).



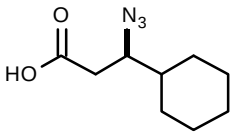
(*S*)-3-Azidohexanoic acid (4d): The general procedure was followed employing 250 mg of β-lactone **1d** (2.19 mmol). Extractive work-up gave 269 mg (78 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.80 (br s, 1H, CO_2**H**), 3.82 (m, 1H, C**H**), 2.59 (dd, 1H, J = 16.7, 5.9 Hz, C**H$_a$**CO_2H), 2.53 (dd, 1H, J = 16.4, 8.1 Hz, C**H$_b$**CO_2H), 1.65-1.37 (m, 4H, C**H$_2$**C**H$_2$**CH3), 0.98 (t, 3H, J = 7.2 Hz, CH_2C**H$_3$**); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.4, 58.5, 39.2, 36.3, 19.0, 13.5; IR (NaCl): 3049, 2962, 2935, 2875, 2665, 2123, 1715, 1434, 1263 cm^{-1}. MS (CI, isobutane): *m/z* 158 $(M+H)^+$. Anal. calcd. for $C_6H_{11}N_3O_2$: C, 45.85; H, 7.05. Found: C, 46.19; H, 7.11. $[\alpha]_D^{25}$ = +21.07^0 (*c* 4.3, CH_2Cl_2).



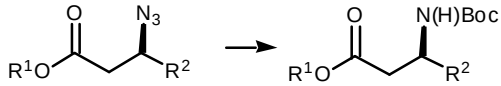
(*S*)-3-Azidoheptanoic acid (4e): The general procedure was followed employing 350 mg of β-lactone **1e** (2.73 mmol). Extractive work-up gave 387 mg (83 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.10 (br s, 1H, CO_2**H**), 3.80 (m, 1H, C**H**), 2.59 (dd, 1H, J = 16.3, 5.5 Hz, C$\mathbf{H_a}CO_2H$), 2.53 (dd, 1H, J = 16.4, 7.9 Hz, C$\mathbf{H_b}CO_2H$), 1.57 (m, 2H, $CHN_3C\mathbf{H_2}CH_2$), 1.49-1.30 (m, 4H, $CH_2C\mathbf{H_2}C\mathbf{H_2}CH3$), 0.94 (t, 3H, J = 7.0 Hz, $CH_2C\mathbf{H_3}$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.4, 58.7, 39.3, 33.9, 27.9, 22.2, 13.8; IR (NaCl): 3041, 2958, 2935, 2863, 2669, 2127, 2103, 1715, 1434, 1255 cm^{-1}. MS (CI, isobutane): *m/z* 172 $(M+H)^+$. HRMS *m/z* cacld for $C_6H_{10}N_1O_2$ (M-CH_2CH_3, N_2): 128.0711. Found: 128.0716. $[\alpha]_D^{25}$ = +20.41^0 (*c* 4.6, CH_2Cl_2).



(*S*)-3-Azido-12-tridecenoic acid (4f): The general procedure was followed employing 50 mg of β-lactone **1f** (0.24 mmol). Extractive work-up gave 52 mg (87 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.60 (br s, 1H, CO_2**H**), 5.82 (ddt, 1H, J = 17.0, 10.2, 6.6 Hz, $CH_2C\mathbf{H}CH_2$), 5.00 (ddd, 1H, J = 17.0, 3.3, 1.6 Hz, $CH_2CHC\mathbf{H_a}$), 4.94 (ddd, 1H, J = 8.9, 2.1, 1.0 Hz, $CH_2CHC\mathbf{H_b}$), 3.80 (m, 1H, C**H**N_3), 2.58 (dd, 1H, J = 16.7, 5.8 Hz, C$\mathbf{H_a}CO_2H$), 2.52 (dd, 1H, J = 16.4, 8.1 Hz, C$\mathbf{H_b}CO_2H$), 2.05 (dt, 2H, J = 8.2, 6.8 Hz, $CH_2C\mathbf{H_2}CHCH_2$), 1.57 (m, 2H, $CHN_3C\mathbf{H_2}CH_2$), 1.48-1.25 (m, 12H, alkyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 177.2, 139.2, 114.2, 58.9, 39.4, 34.4, 33.8, 29.4 (2C), 29.2, 29.1, 28.9, 25.9; IR (NaCl): 3074, 2925, 2855, 2666, 2103, 1715, 1426, 1262, 908 cm^{-1}. MS (CI, methane): *m/z* 254 $(M+H)^+$. Anal. calcd. for $C_{13}H_{23}N_3O_2$: C, 61.63; H, 9.15. Found: C, 62.12; H, 9.30. $[\alpha]_D^{25}$ = +15.00^0 (*c* 4.1, CH_2Cl_2).



(*R*)-3-Azido-3-cyclohexylpropanoic acid (4g): The general procedure was followed employing 200 mg of β-lactone **1g** (1.30 mmol). Extractive work-up gave 238 mg (93 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.08 (br s, 1H, CO_2**H**), 3.65 (m, 1H, C**H**N_3), 2.58 (dd, 1H, J = 16.3, 3.8 Hz, C$\mathbf{H_a}CO_2H$), 2.45 (dd, 1H, J = 16.4, 9.8 Hz, C$\mathbf{H_b}CO_2H$), 1.79-1.67 (m, 4H, Cyclohexyl), 1.48 (m, 1H, C**H**-Cyclohexyl), 1.29-1.00 (m, 6H, Cyclohexyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.0, 64.2, 42.0, 39.4, 36.7, 29.4, 28.2, 26.0, 25.8; IR (NaCl): 3007, 2929, 2853, 2617, 2121, 2085, 1716, 1450, 1271, 999 cm^{-1}. MS (CI, isobutane): *m/z* 198 $(M+H)^+$. HRMS *m/z* cacld for $C_9H_{15}N_1O_2$ (M- N_2): 169.1103. Found: 169.1107. $[\alpha]_D^{25}$ = +44.20^0 (*c* 4.9, CH_2Cl_2).



4b R^1=Me, R^2=CH_2CH_2Ph → **5b**
4c R^1=Me, R^2=CH_2CHMe_2 → **5c**
4d R^1=Me, R^2=^{n}Pr → **5d**
4e R^1=H, R^2=^{n}Bu → **i**

Stereochemical proofs for β-azido acids: The absolute configuration of β-azido acids **4b-d** was established by conversion to the corresponding *N*-Boc amino esters **5b-d** (i. CH_2N_2; ii. H_2, Boc_2O, Pd-C) and correlation of their optical rotation to those of authentic samples of known configuration: **5b** $[\alpha]_D^{25}$ = -5.76^0 (*c* 1.8, $CHCl_3$) [lit $[\alpha]_D^{25}$ = +7.2^0 (*R*) (*c* 1.8, $CHCl_3$)];[3] **5c** $[\alpha]_D^{25}$ = -25.8^0 (*c* 1.47, CH_3OH) [lit $[\alpha]_D^{25}$ = -22.8^0 (*c* 1.47, CH_3OH)];[4] **5d** $[\alpha]_D^{25}$ = -20.96^0 (*c* 1.9, $CHCl_3$) [lit $[\alpha]_D^{25}$ = +20.9^0 (*R*) (*c* 1.9, $CHCl_3$)]. The configuration of azido acid **4e** was established similarly by conversion to the corresponding *N*-Boc amino acid **i** (i. H_2, Pd-C; ii. Boc_2O, Et_3N): $[\alpha]_D^{25}$ = -1.02^0 (*c* 0.5, DMF) [lit $[\alpha]_D^{25}$ = -1.2^0 (*c* 0.5, DMF)].[5] The configuration of the remaining β-azido acids (**4a,f,g**) was assigned by analogy to these determinations.

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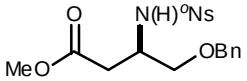
3 M. Alcón, M. Canas, M. Poch, A. Moyano, M. A. Pericás, A. Riera, *Tetrahedron Lett.* **1994**, *35*, 1589-1592.

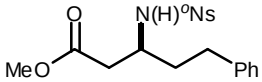
4 E. M. Gordon, J. D. Godfrey, N. G> Delaney, M. M. Asaad, A. Von Langen, D. W. Cushman, *J. Med. Chem.* **1988**, *31*, 2199-2211.

5 C. Mendre, M. Rodriguez, J. Laur, A. Aumelas, J. Martinez, *Tetrahedron* **1988**, *44*, 4415-4430.

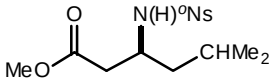
General procedure for S_N2 addition of *o*-nitrobenzenesulfonamide, mono sodium salt to β-lactone 1. To a 50 °C suspension of 700 mg of o-nitrobenzenesulfonamide, mono sodium salt (3.13 mmols, 2.0 equiv) and 200 mg of activated powdered 4 Å molecular seives in 5.2 mL of anhydrous DMSO (0.3 M in lactone) was added 200 mg of β-lactone **1** (1.56 mmols) via syringe. The resulting suspension was stirred until all the lactone had been consumed as monitored by TLC (~5 h). After cooling the reaction mixture to ambient temperature, 5 mL of 1 M aqueous HCl was added and the resulting mixture was extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were washed with water (2 x 5 mL) and brine (2 x 5 mL). The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo to afford a yellow solid. The solid was triturated with chloroform and the insoluble material (o-nitrosulfonamide) removed by filtration. The filtrate was concentrated in vacuo to afford the crude β-sulfonamido acid. The crude acid was dissolved in ethyl acetate and an ethereal solution of CH_2N_2 was added until a yellow color persisted. Glacial acetic acid was added to decolorize the reaction mixture and the volatiles were evaporated in vacuo to afford the β-sulfonamido ester **8** as a yellow oil that was purified by column chromatography (hexanes:ethyl acetate).



(*S*)-4-Benzyloxy-3-(*o*-nitrosulfonamido)butanoic acid, methy ester (8a): The general procedure was followed employing 200 mg of β-lactone **1a** (1.04 mmol). Extractive work-up gave 272 mg (64 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.13 (m, 1H, Ar**H**), 7.79 (m, 1H, Ar**H**), 7.67 (m, 2H, Ar**H**), 7.34-7.28 (m, 3H, Ph**H**), 7.16 (m, 2H, Ph**H**), 6.10 (d, 1H, J = 8.0 Hz, N**H**), 4.33 (s, 2H, OC**H$_2$**Ph), 4.02 (m, 1H, C**H**N), 3.60 (s, 3H, CO_2**Me**), 3.50 (dd, 1H, J = 9.8, 5.4 Hz, CHC**H$_a$**OBn), 3.42 (dd, 1H, J = 9.5, 5.0 Hz, CHC**H$_b$**OBn), 2.71 (dd, 1H, J = 16.4, 5.6 Hz, C**H$_a$**CO_2Me), 2.64 (dd, 1H, J = 16.5, 6.6 Hz, C**H$_b$**CO_2Me); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0, 147.4, 137.1, 134.4, 133.3, 132.7, 130.5, 128.2 (2C), 127.7 (2C), 127.6, 125.2, 73.0, 70.7, 51.7, 51.2, 36.6; IR (NaCl): 3335, 3089, 3061, 3030, 2950, 2867, 1735, 1541, 1366, 1164, 1121, 851, 784, 741, 697, 653 cm^{-1}. MS (EI, 70 eV): *m/z* 287 (M-CH_2OBn)$^+$, 222 [M-SO_2($C_6H_4NO_2$)]$^+$. HRMS *m/z* cacld for $C_{10}H_{11}N_2O_6S$ (M- CH_2OBn): 287.0338. Found: 287.0331. $[\alpha]_D^{25}$ = +71.51^0 (*c* 4.5, $CHCl_3$).

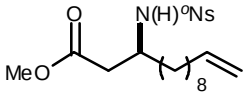


(*S*)-3-(*o*-nitrosulfonamido)-5-phenylpentanoic acid, methy ester (8b): The general procedure was followed employing 200 mg of β-lactone **1b** (1.14 mmol). Extractive work-up gave 322 mg (72 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.11 (m, 1H, Ar**H**), 7.88 (m, 1H, Ar**H**), 7.74 (m, 2H, Ar**H**), 7.29-7.11 (m, 3H, Ph**H**), 7.08 (m, 2H, Ph**H**), 5.93 (d, 1H, J = 8.6 Hz, N**H**), 3.85 (m, 1H, C**H**N), 3.61 (s, 3H, CO_2**Me**), 2.73-2.47 (m, 2H, C**H$_2$**CH_2Ph), 2.57 (dd, 1H, J = 16.3, 5.0 Hz, C**H$_a$**CO_2Me), 2.51 (dd, 1H, J = 16.3, 5.5 Hz, C**H$_b$**CO_2Me), 1.94-1.85 (m, 2H, CH_2C**H$_2$**Ph); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.0, 147.4, 140.5, 134.4, 133.5, 132.8, 130.3, 128.2 (2C), 128.1 (2C), 125.9, 125.0, 51.6, 51.2, 38.9, 36.2, 31.7; IR (NaCl): 3335, 3089, 3061, 3026, 2946, 2859, 1727, 1541, 1358, 1168, 848, 784, 741, 695, 653 cm^{-1}. MS (EI, 70 eV): *m/z* 287 (M-CH_2Bn)$^+$, 206 [M-SO_2($C_6H_4NO_2$)]$^+$. Anal. calcd. for $C_{18}H_{20}N_2O_6S$: C, 55.09; H, 5.14. Found: C, 55.07; H, 5.34. $[\alpha]_D^{25}$ = -4.63^0 (*c* 8.2, $CHCl_3$). The enantiomeric purity of the β-sufonamido ester **8b** was determined by the integration of the methyl ester portion (CO_2**Me**) of the crude (*S*)-α-methoxyphenylacetamides which provided the diastereomer ratio: 3(*S*):3(*R*) > 96.5:3.5. (93% de). ^{1}H NMR ($CDCl_3$, 500 MHz) [-CO_2**Me**] δ 3.70 (major), 3.59 (minor). The diastereomeric (*S*)-α-methoxyphenylacetamides were prepared from **8b** by sulfonamide deprotection (PhSH, K_2CO_3, DMF) followed by coupling the derived β-amino ester with (*S*)-α-methoxyphenylacetic acid (DCC, 5 mol% DMAP).

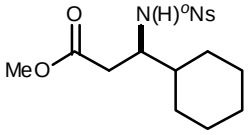


(*S*)-5-Methyl-3-(*o*-nitrosulfonamido)hexanoic acid, methy ester (8c): The general procedure was followed employing 200 mg of β-lactone **1c** (1.56 mmol). Extractive work-up gave 381 mg (74 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.18 (m, 1H, Ar**H**), 7.89 (m, 1H, Ar**H**), 7.75 (m, 2H, Ar**H**), 5.78 (d, 1H, J = 8.4 Hz, N**H**), 3.89 (m, 1H, C**H**N), 3.62 (s, 3H, CO_2**Me**), 2.55 (dd, 1H, J = 16.2, 4.9 Hz, C**H$_a$**CO_2Me), 2.48 (dd, 1H, J = 16.2, 5.6 Hz, C**H$_b$**CO_2Me), 1.58 (m, 1H, C**H**Me_2), 1.50 (m, 1H, CHC**H$_a$**CHMe), 1.30 (m, 1H, CHC**H$_b$**CHMe), 0.85 (d, 3H, J = 6.5 Hz,

CH**Me$_a$**), 0.77 (d, 3H, J = 6.4 Hz, CH**Me$_b$**); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.2, 147.5, 134.7, 133.5, 132.9, 130.3, 125.2, 51.6, 49.9, 43.8, 39.4, 24.3, 22.6, 21.4; IR (NaCl): 3331, 3093, 2958, 2867, 1735, 1537, 1362, 1160, 851, 780, 741, 653 cm^{-1}. MS (EI, 70 eV): *m/z* 344 (M+), 287 (M-CH_2CHMe_2)$^+$, 186 [$SO_2(C_6H_4NO_2)$]$^+$. HRMS *m/z* cacld for $C_{14}H_{20}N_2O_6S$ (M- CH_2OBn): 344.1042. Found: 344.1037. $[\alpha]_D^{25}$ = -14.70^0 (*c* 8.4, $CHCl_3$). The enantiomeric purity of the β-sufonamido ester **8c** was determined by the integration of the methyl ester portion (CO_2**Me**) of the crude (*S*)-α-methoxyphenylacetamides which provided the diastereomer ratio: 3(*S*):3(*R*) > 97.5:2.5. (95% de). ^{1}H NMR ($CDCl_3$, 500 MHz) [-CO_2**Me**] δ 3.70 (major), 3.57 (minor). The diastereomeric (*S*)-α-methoxyphenylacetamides were prepared from **8c** by sulfonamide deprotection (PhSH, K_2CO_3, DMF) followed by coupling the derived β-amino ester with (*S*)-α-methoxyphenylacetic acid (DCC, 5 mol% DMAP).

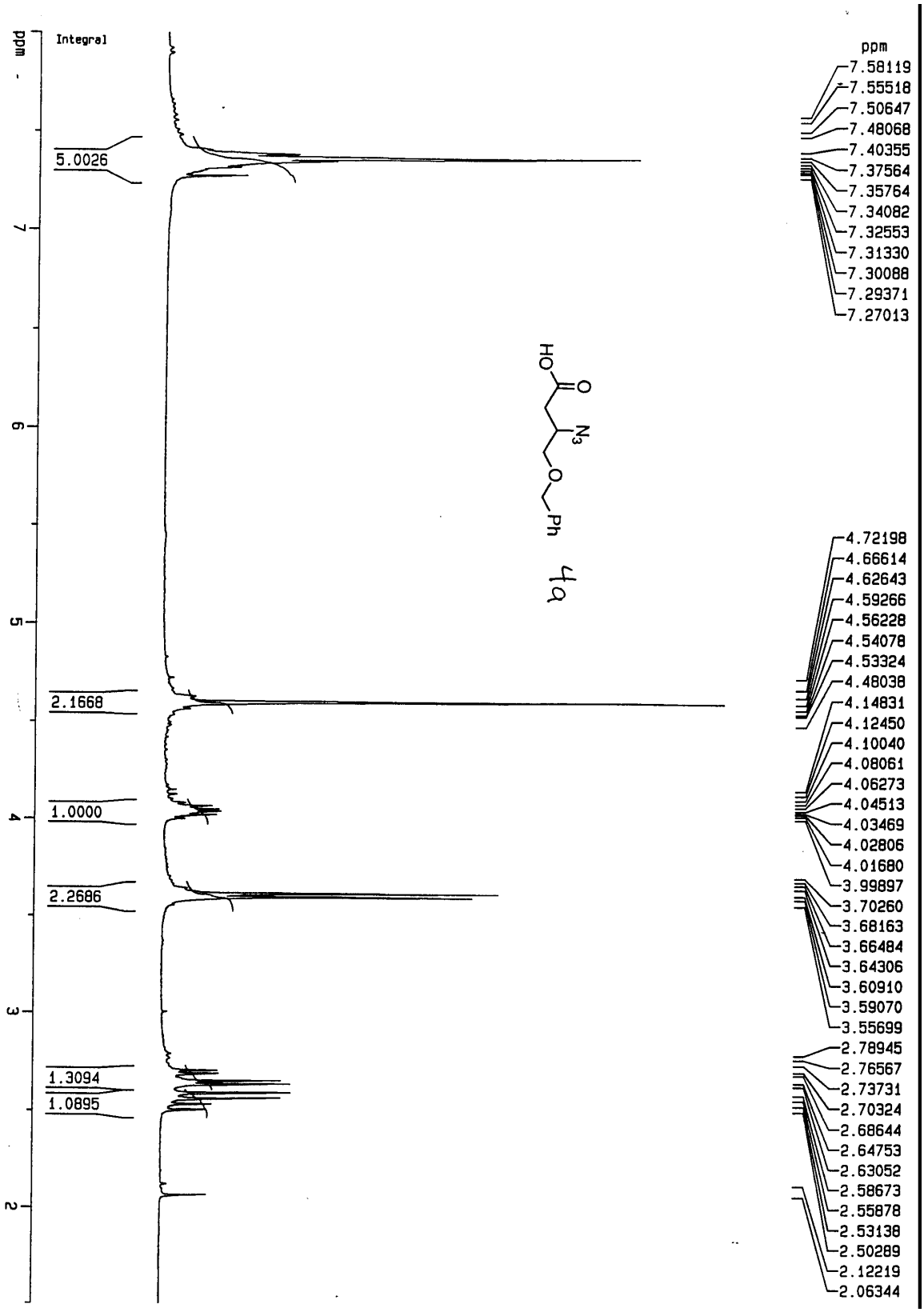


(*S*)-3-(*o*-nitrosulfonamido)-12-tridecenoic acid, methy ester (8f): The general procedure was followed employing 200 mg of β-lactone **1f** (0.95 mmol). Extractive work-up gave 337 mg (83 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.17 (m, 1H, Ar**H**), 7.88 (m, 1H, Ar**H**), 7.75 (m, 2H, Ar**H**), 5.81 (ddt, 1H, J = 16.9, 10.3, 6.7 Hz, CH_2C**H**CH_2), 5.78 (d, 1H, J = 8.2 Hz, N**H**), 5.00 (m, 1H, CH_2CHCH**H$_a$**), 4.94 (m, 1H, CH_2CHCH**H$_b$**), 3.80 (m, 1H, C**H**N), 3.61 (s, 3H, CO_2**Me**), 2.57 (dd, 1H, J = 16.2, 5.2 Hz, C**H$_a$**CO_2Me), 2.49 (dd, 1H, J = 16.3, 6.1 Hz, C**H$_b$**CO_2Me), 2.03 (m, 2H, CH_2C**H$_2$**$CHCH_2$), 1.54 (m, 2H, CHNC**H$_2$**CH_2), 1.37-1.15 (m, 12H, alkyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.2, 147.5, 138.9, 134.7, 133.4, 132.8, 130.3, 125.1, 114.0, 51.7, 51.6, 39.2, 34.6, 33.8, 29.1 (2C), 28.8, 28.7, 28.6, 25.5; IR (NaCl): 3331, 3073, 2927, 2855, 1735, 1541, 1358, 1168, 784, 741, cm^{-1}. MS (EI, 70 eV): *m/z* 353 (M-MeO_2CCH_2), 287 (M-$(CH_2)_8CHCH_2$)$^+$, 186 [$SO_2(C_6H_4NO_2)$]$^+$. HRMS *m/z* cacld for $C_{10}H_{11}N_2O_6S$ (M-$(CH_2)_8CHCH_2$): 287.0338. Found: 287.0330. $[\alpha]_D^{25}$ = +4.28^0 (*c* 3.9, $CHCl_3$).



(*R*)-3-Cyclohexyl-3-(*o*-nitrosulfonamido)propionic acid, methy ester (8g): The general procedure was followed employing 308 mg of β-lactone **1g** (2.0 mmol). Extractive work-up gave 309 mg (43 %) of the title compound. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.15 (m, 1H, Ar**H**), 7.87 (m, 1H, Ar**H**), 7.74 (m, 2H, Ar**H**), 5.77 (d, 1H, J = 8.8 Hz, N**H**), 3.66 (m, 1H, C**H**N), 3.56 (s, 3H, CO_2**Me**), 2.54 (dd, 1H, J = 16.2, 6.0 Hz, C**H$_a$**CO_2Me), 2.54 (dd, 1H, J = 16.1, 5.4 Hz, C**H$_b$**CO_2Me), 1.84-1.48 (m, 6H, cyclohexyl), 1.27-1.03 (m, 3H, cyclohexyl), 0.99-0.84 (m, 2H, cyclohexyl); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.5, 147.5, 134.9, 133.3, 132.8, 130.4, 125.1, 60.3, 56.6, 51.7, 41.4, 36.6, 29.2, 28.8, 25.9, 25.8; IR (NaCl): 3331, 3097, 2927, 2852, 1731, 1541, 1442, 1358, 1164, 852, 784, 733, 657 cm^{-1}. MS (EI, 70 eV): *m/z* 297 (M-MeO_2CCH_2), 287 (M-C_6H_{11})$^+$, 186 [$SO_2(C_6H_4NO_2)$]$^+$. HRMS *m/z* cacld for $C_{10}H_{11}N_2O_6S$ (M- C_6H_{11}): 287.0338. Found: 287.0326. Anal. calcd. for $C_{16}H_{22}N_2O_6S$: C, 51.88; H, 5.99. Found: C, 51.86; H, 6.05. $[\alpha]_D^{25}$ = -32.53^0 (*c* 1.9, $CHCl_3$). The enantiomeric purity of the β-sufonamido ester **8g** was determined by the integration of the methyl ester portion (CO_2**Me**) of the crude (*S*)-α-methoxyphenylacetamides which provided the diastereomer ratio: 3(*R*):3(*S*) > 98:2 (>95% de). ^{1}H NMR ($CDCl_3$, 500 MHz) [-CO_2**Me**] δ 3.70 (major), 3.52 (minor). The diastereomeric (*S*)-α-methoxyphenylacetamides were prepared from **8g** by sulfonamide deprotection (PhSH, K_2CO_3, DMF) followed by coupling the derived β-amino ester with (*S*)-α-methoxyphenylacetic acid (DCC, 5 mol% DMAP).

Stereochemical proofs for β-azido acids: The absolute configuration of β-sulfonamido acids **8b** and **8c** was established by conversion to the corresponding *N*-Boc amino methyl esters **5b** and **c** (i. CH_2N_2; ii. PhSH, K_2CO_3, DMF; iii. Boc_2O, Et_3N), respectively, and correlation of their optical rotation to those of authentic samples of known configuration: **5b** $[\alpha]_D^{25}$ = -6.38^0 (*c* 1.8, $CHCl_3$) [lit $[\alpha]_D^{25}$ = +7.2^0 (*R*) (*c* 1.8, $CHCl_3$)];[3] **5c** $[\alpha]_D^{25}$ = -28.7^0 (*c* 1.47, CH_3OH) [lit $[\alpha]_D^{25}$ = -22.8^0 (*c* 1.47, CH_3OH)];[4] The configuration of the remaining β-sulfonamido acids (**8a,f,g**) was assigned by analogy to these determinations.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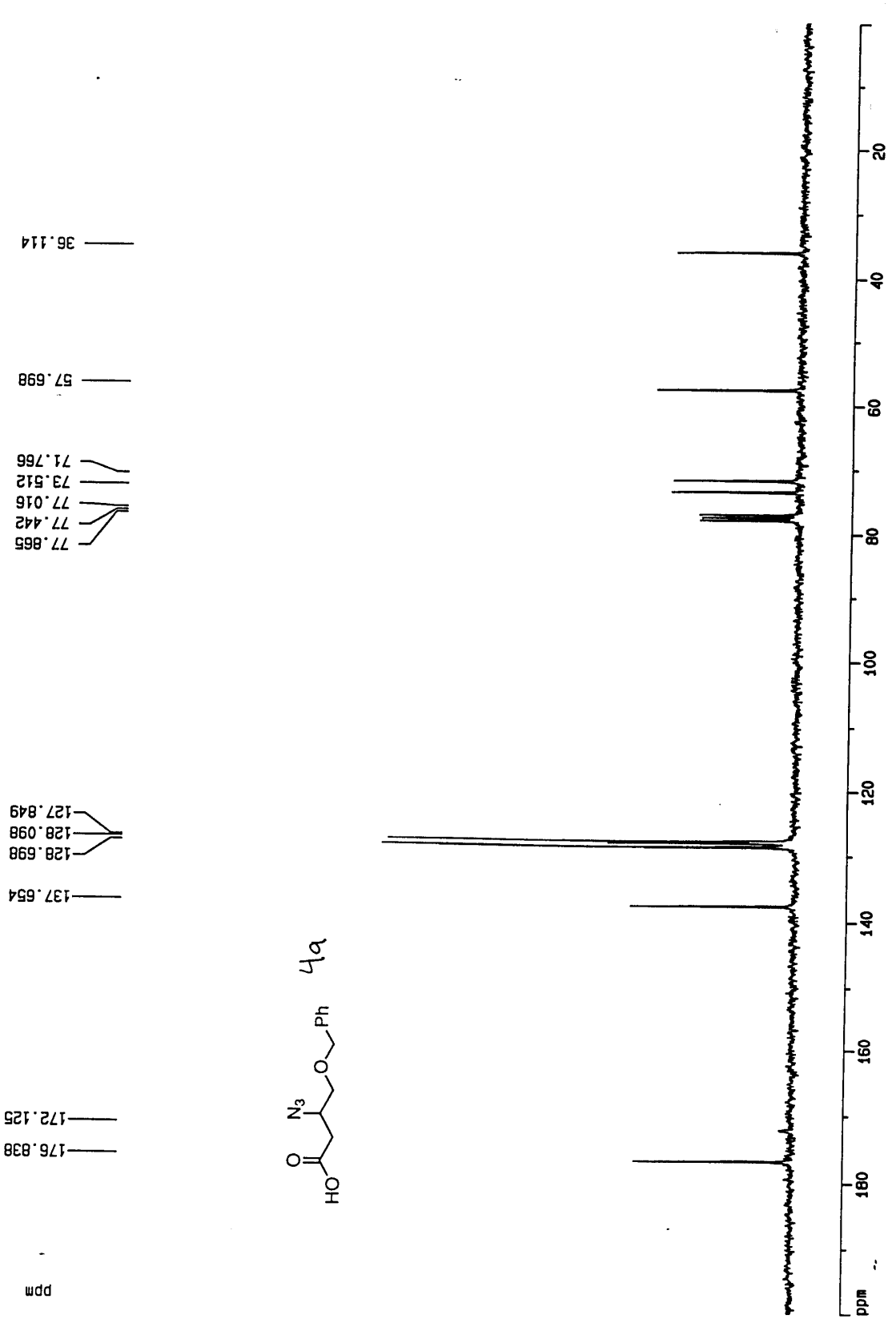
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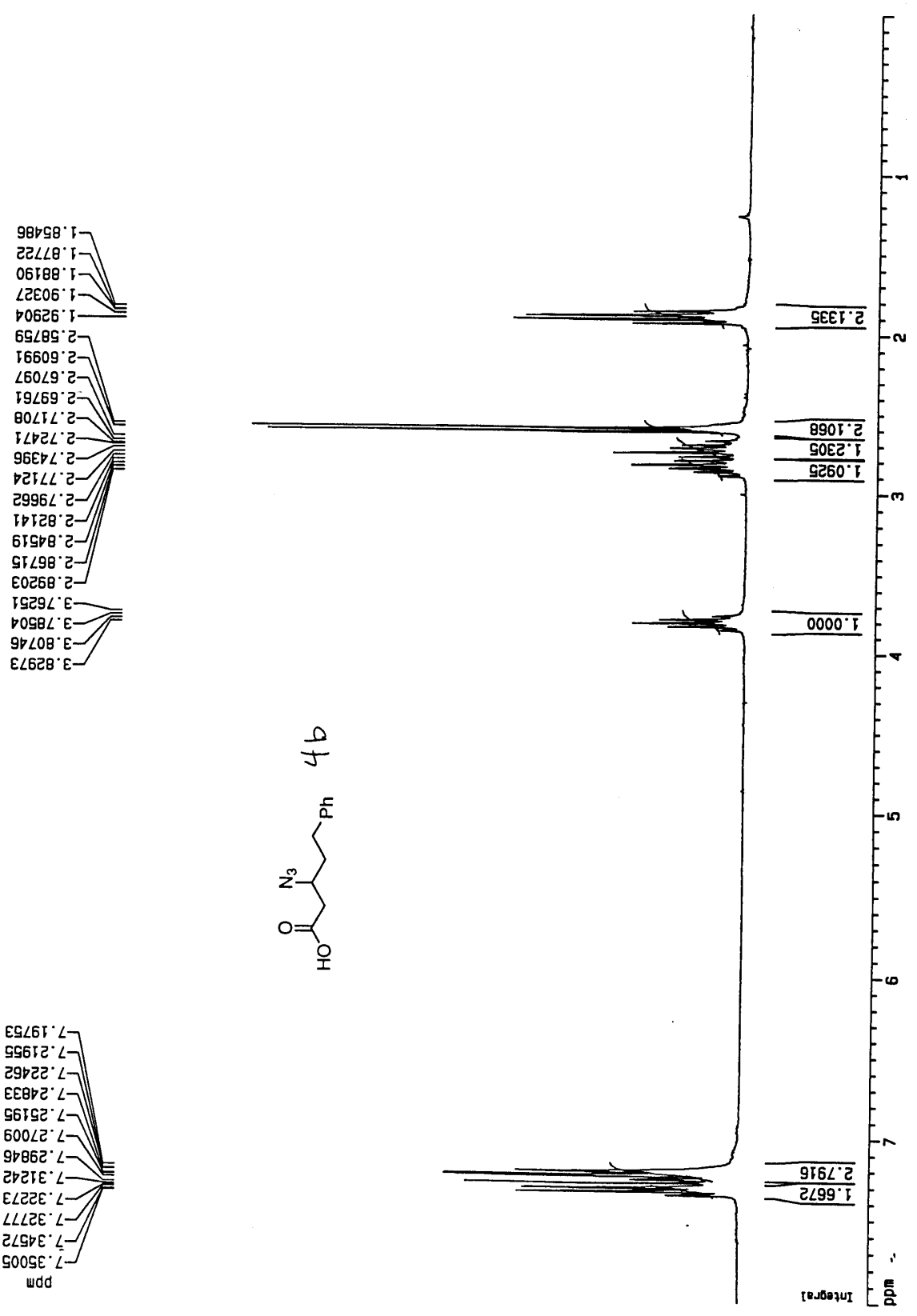
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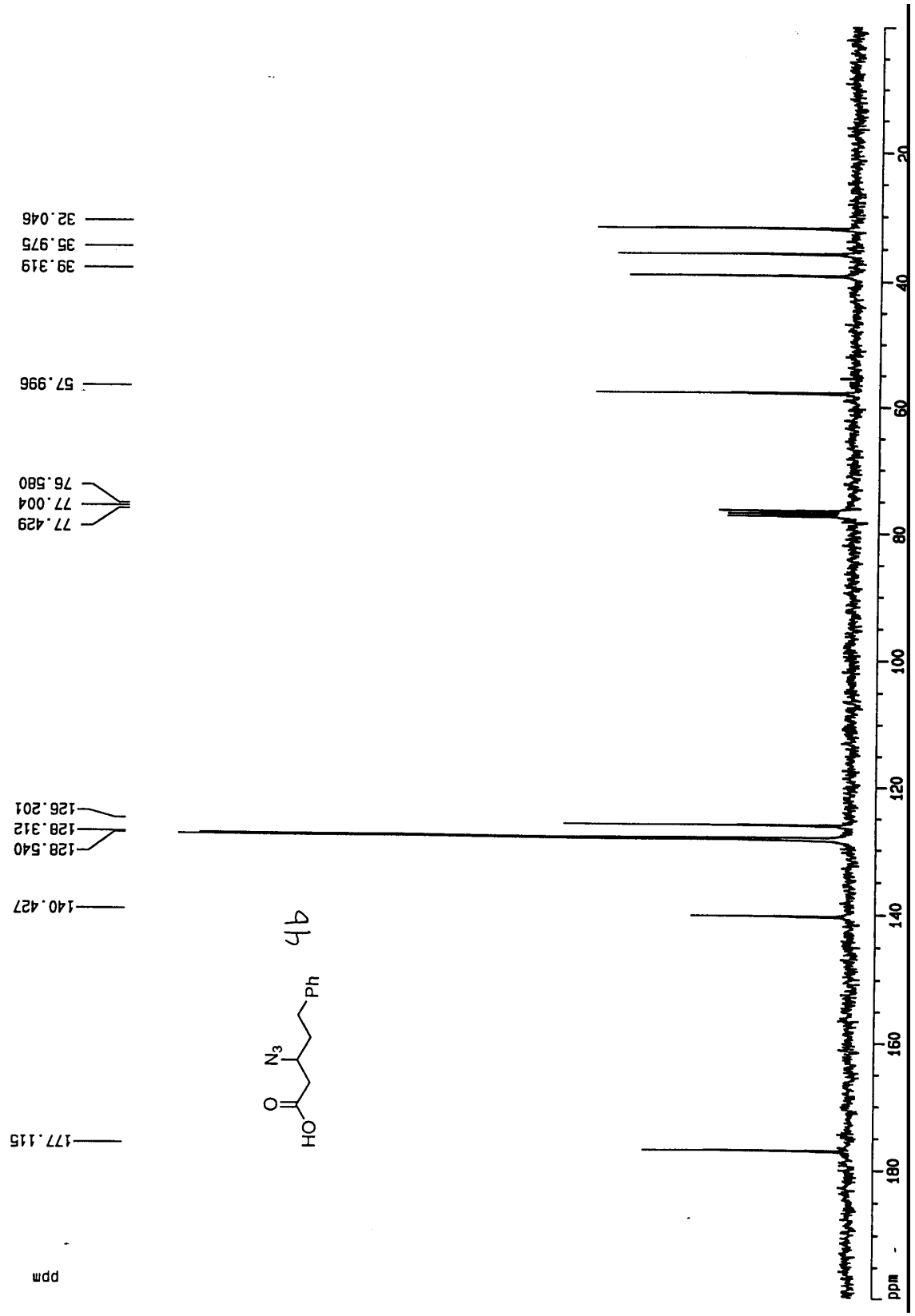
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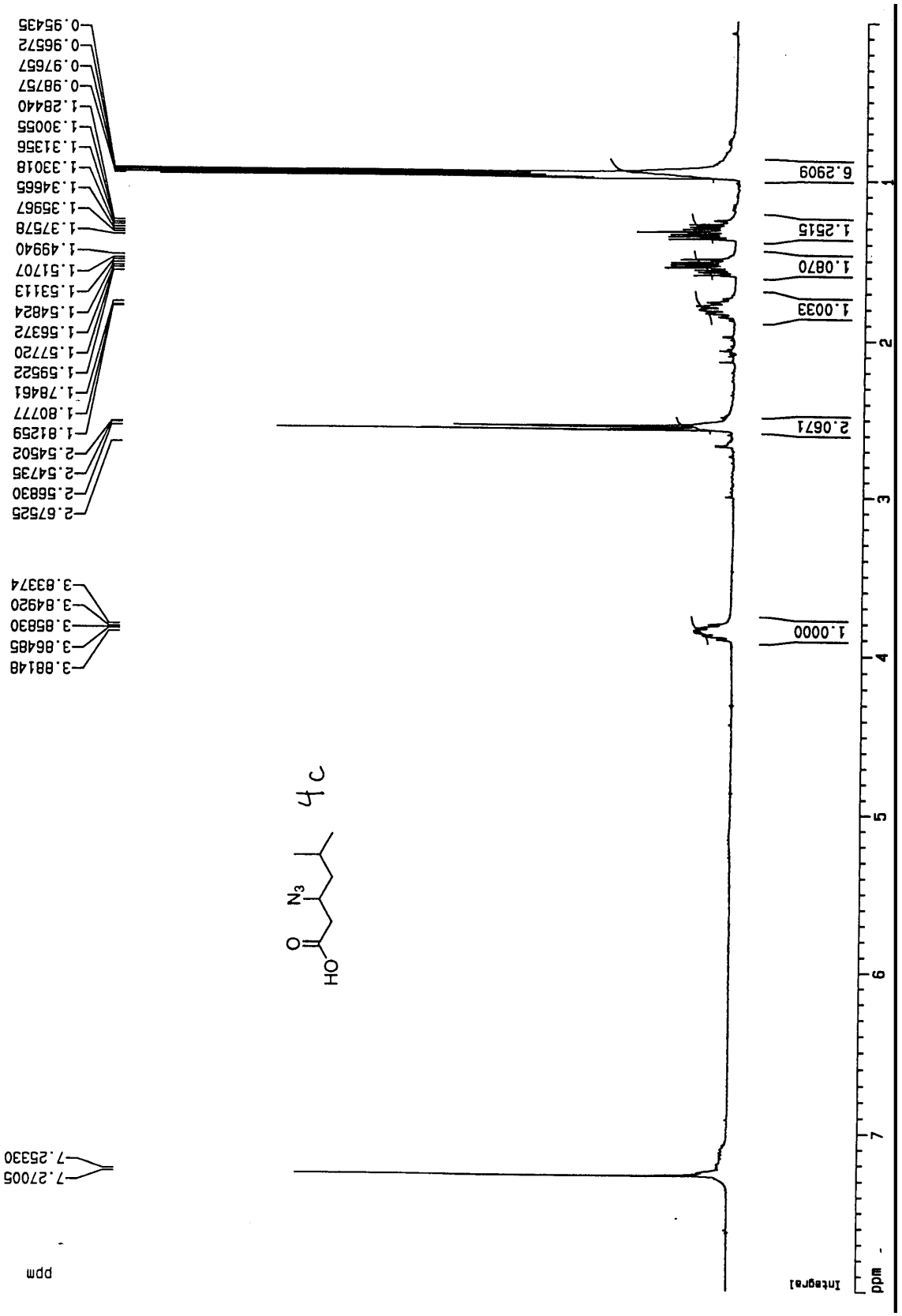
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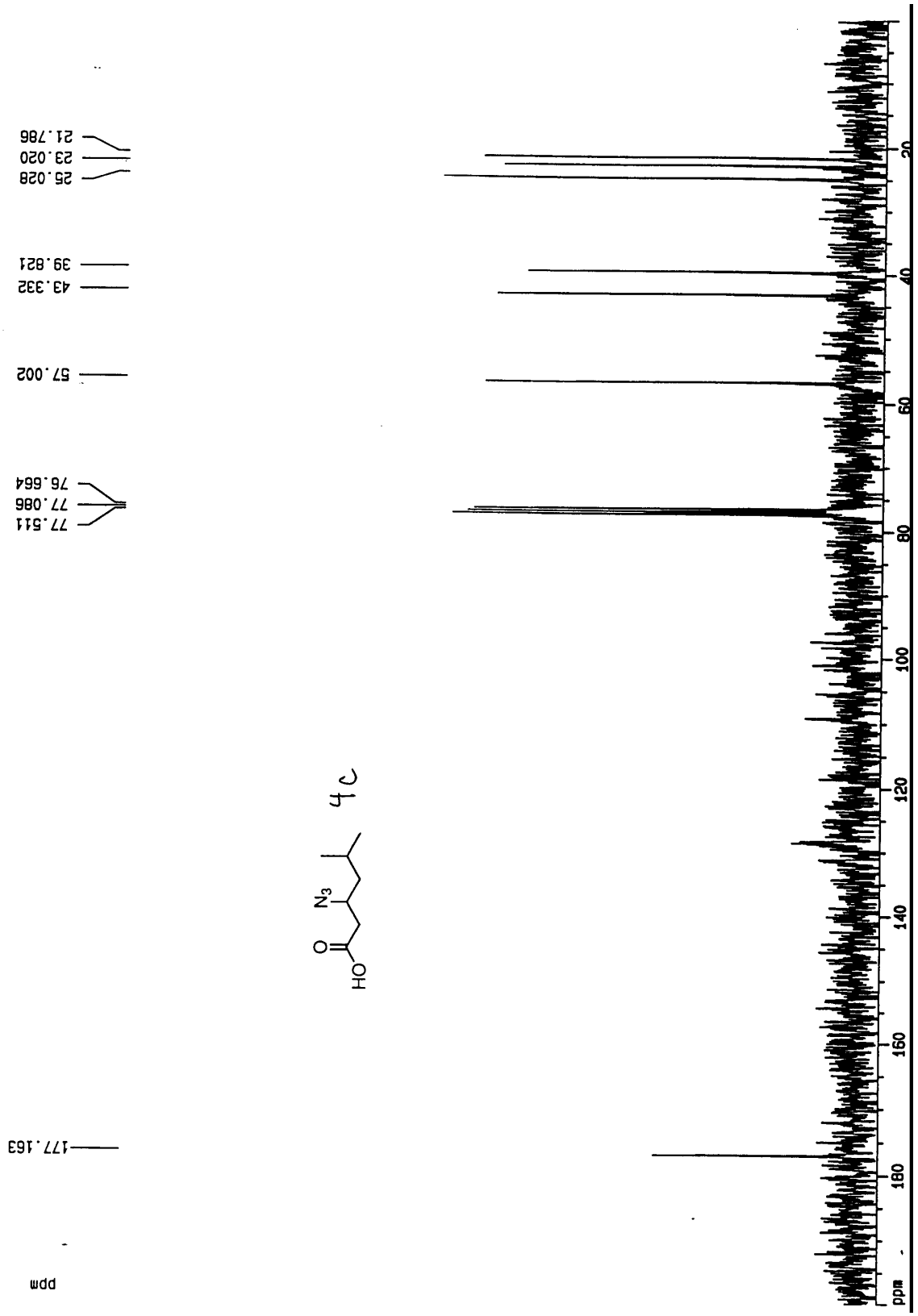
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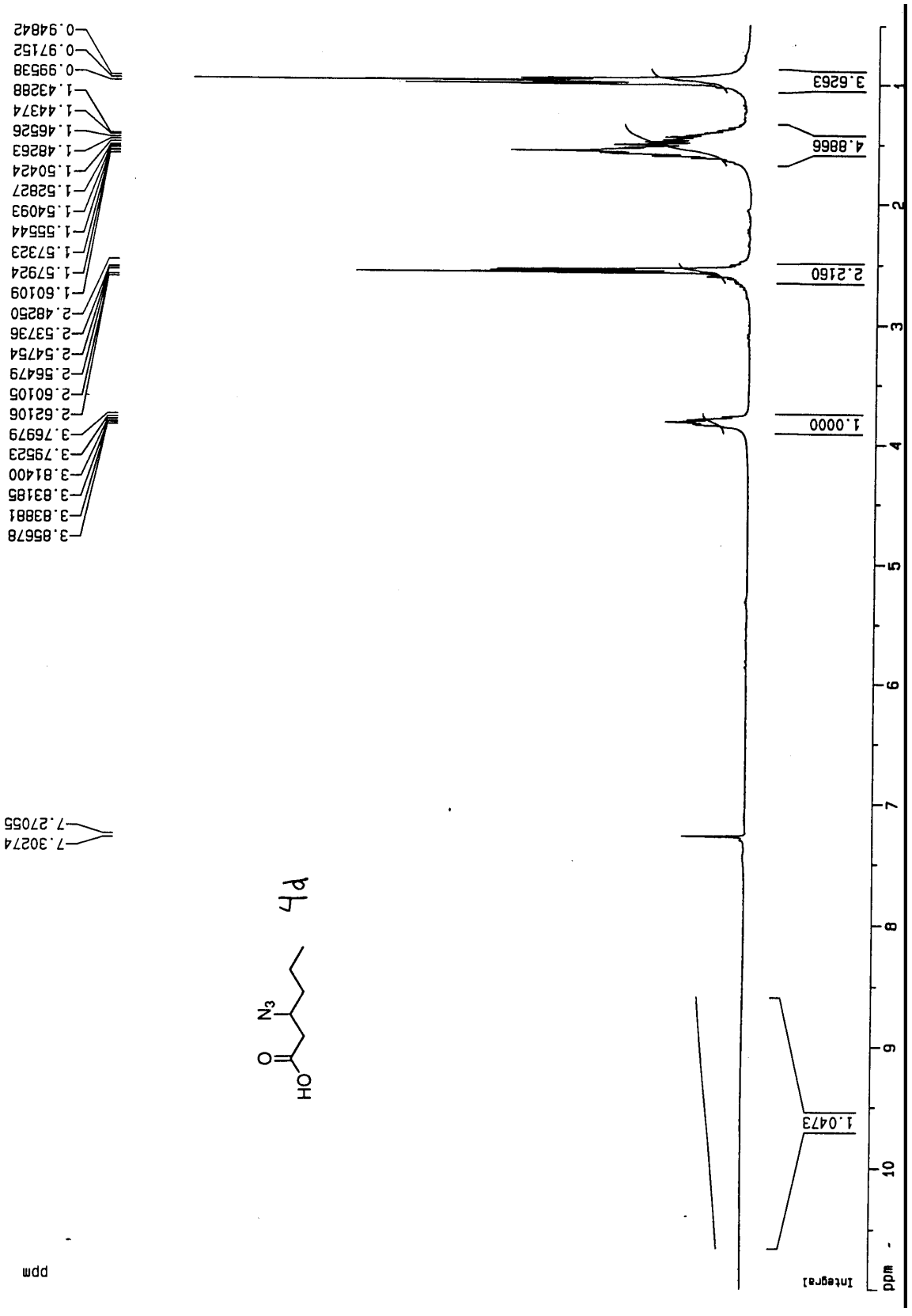
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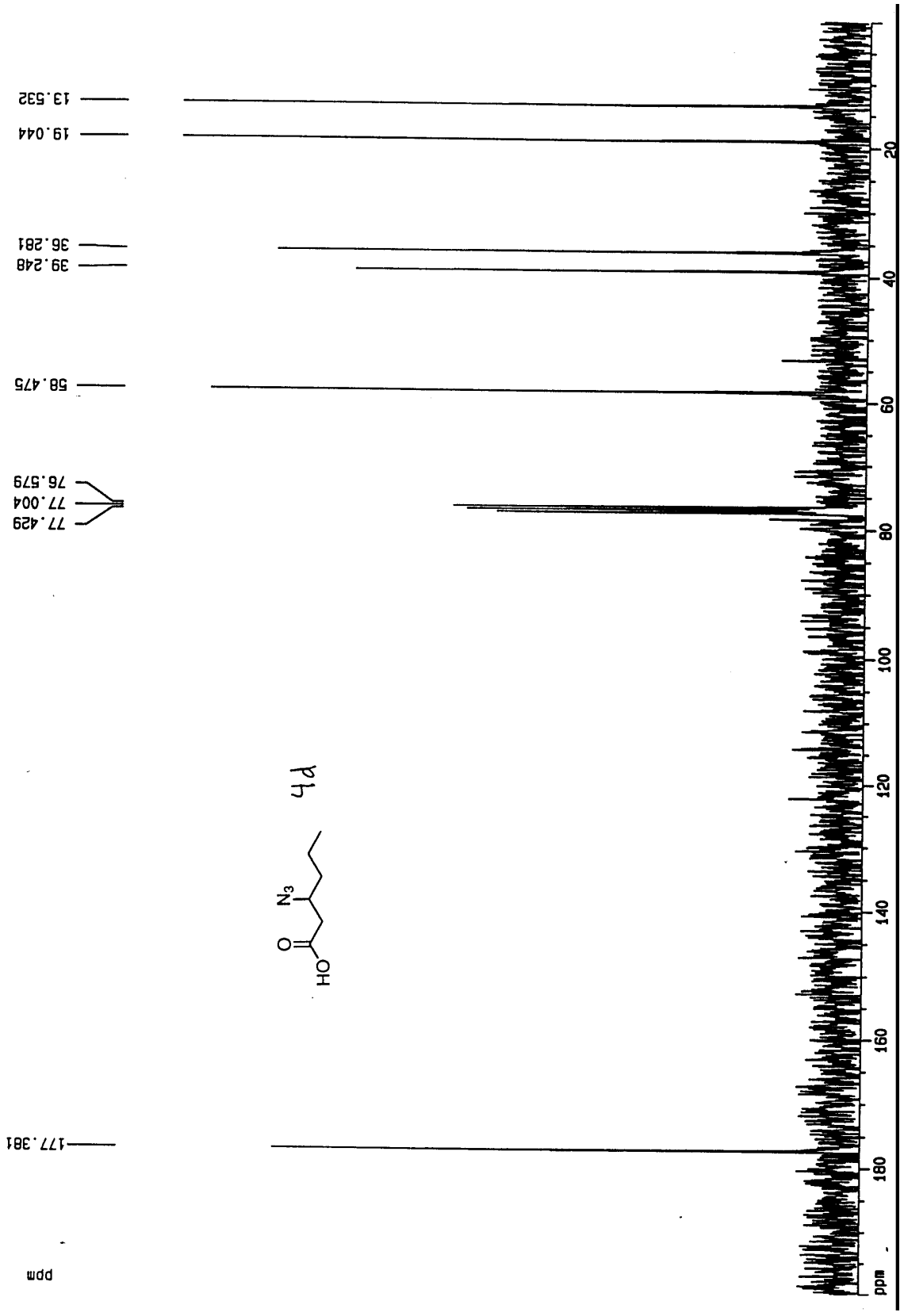
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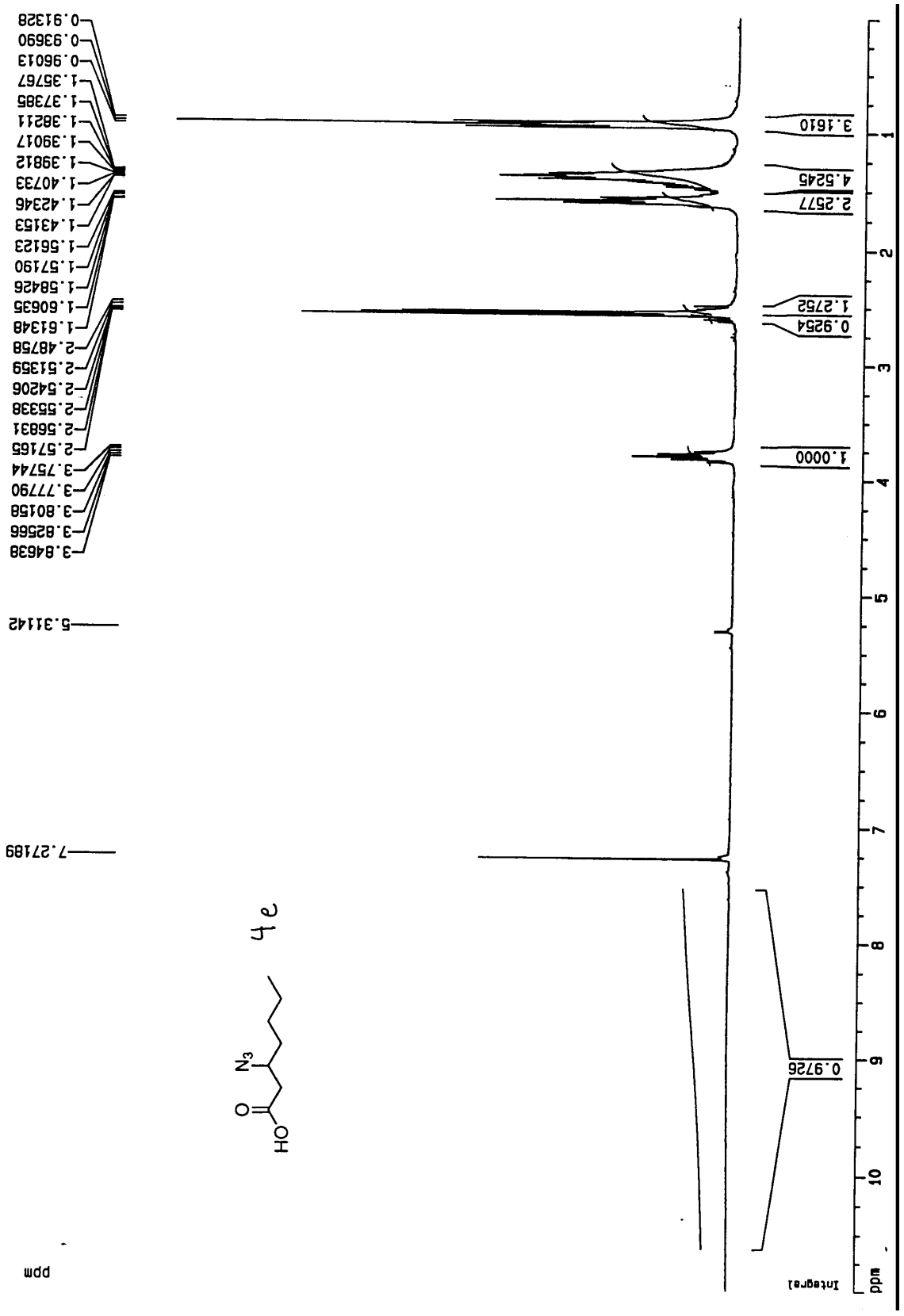
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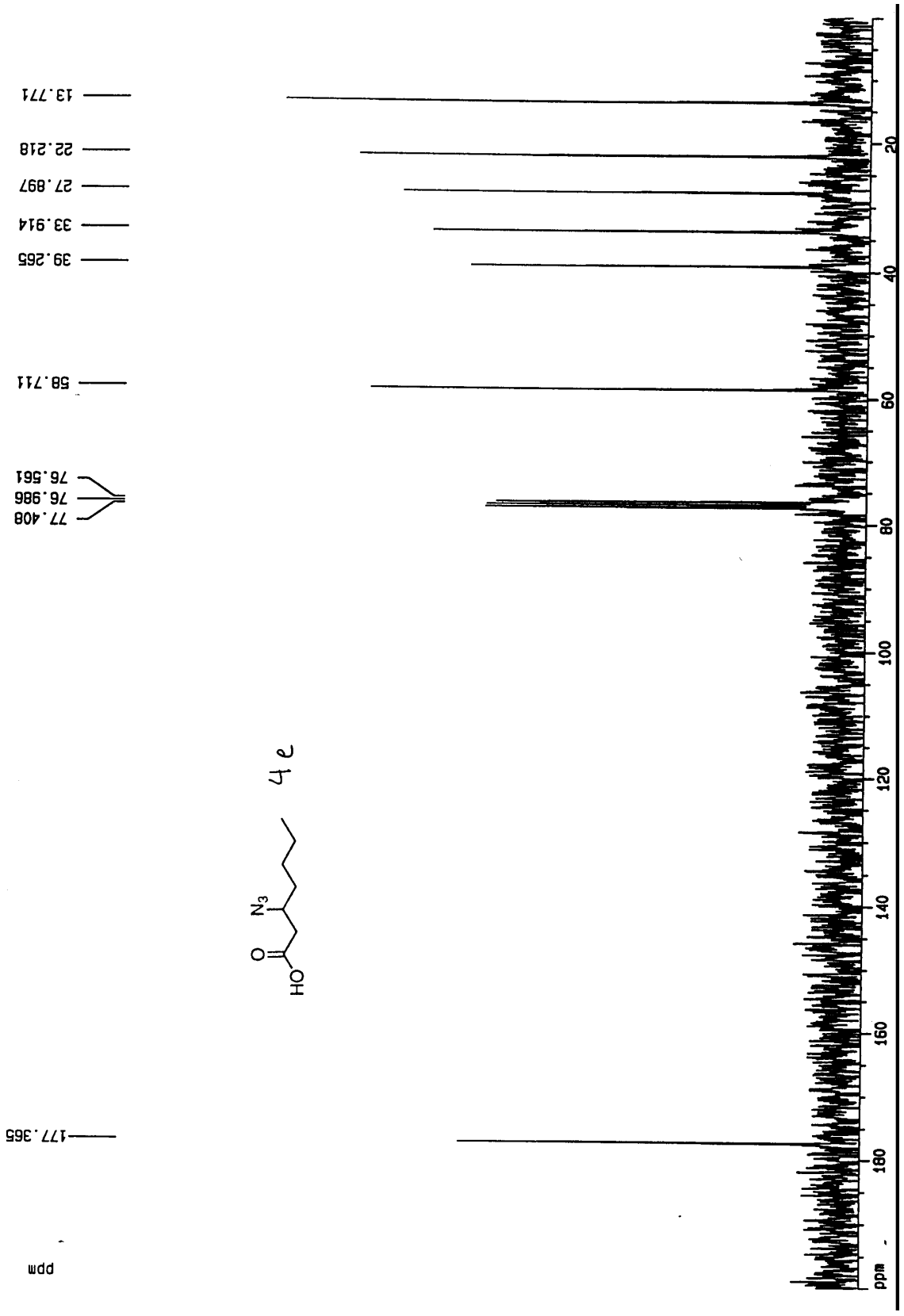
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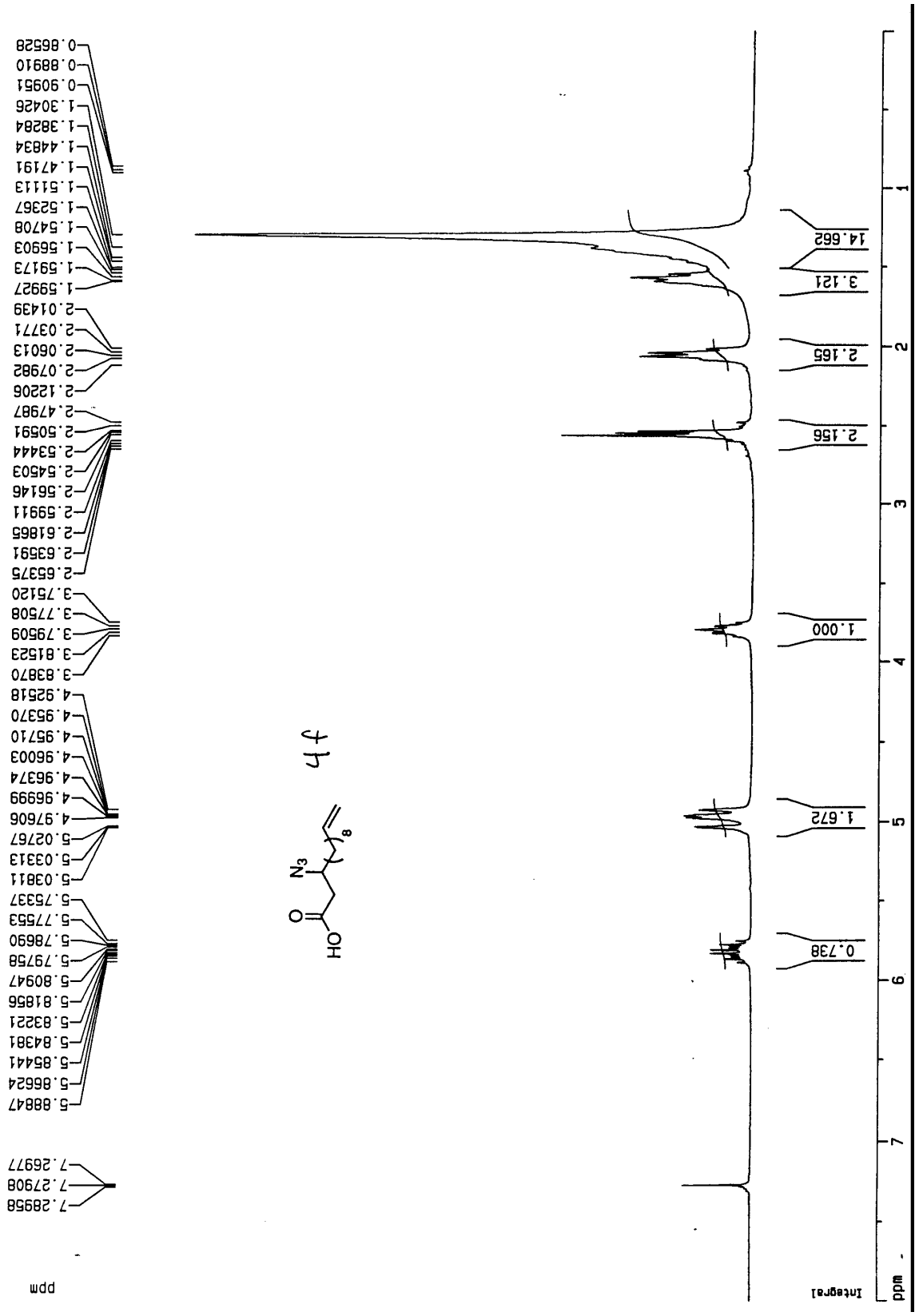
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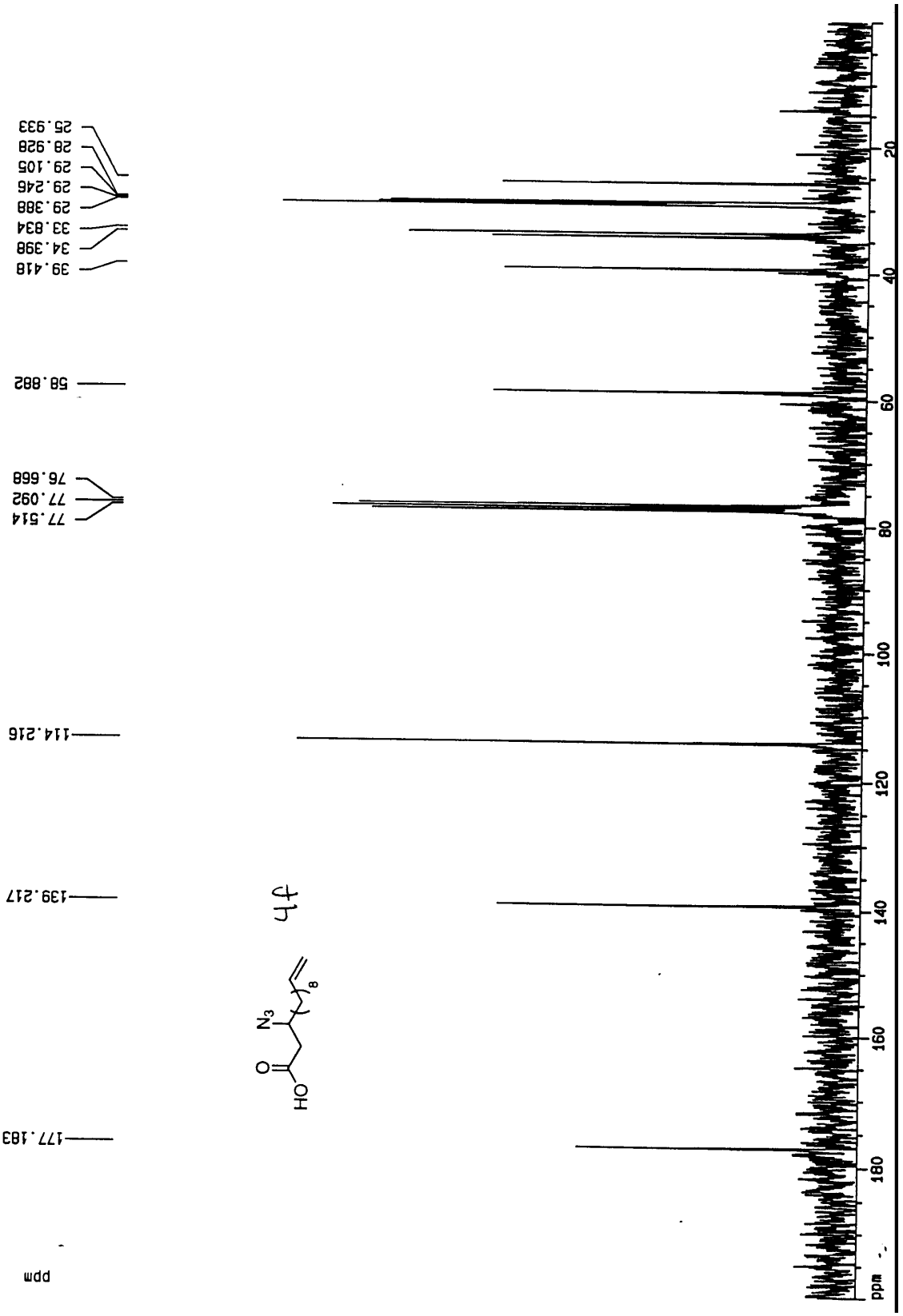
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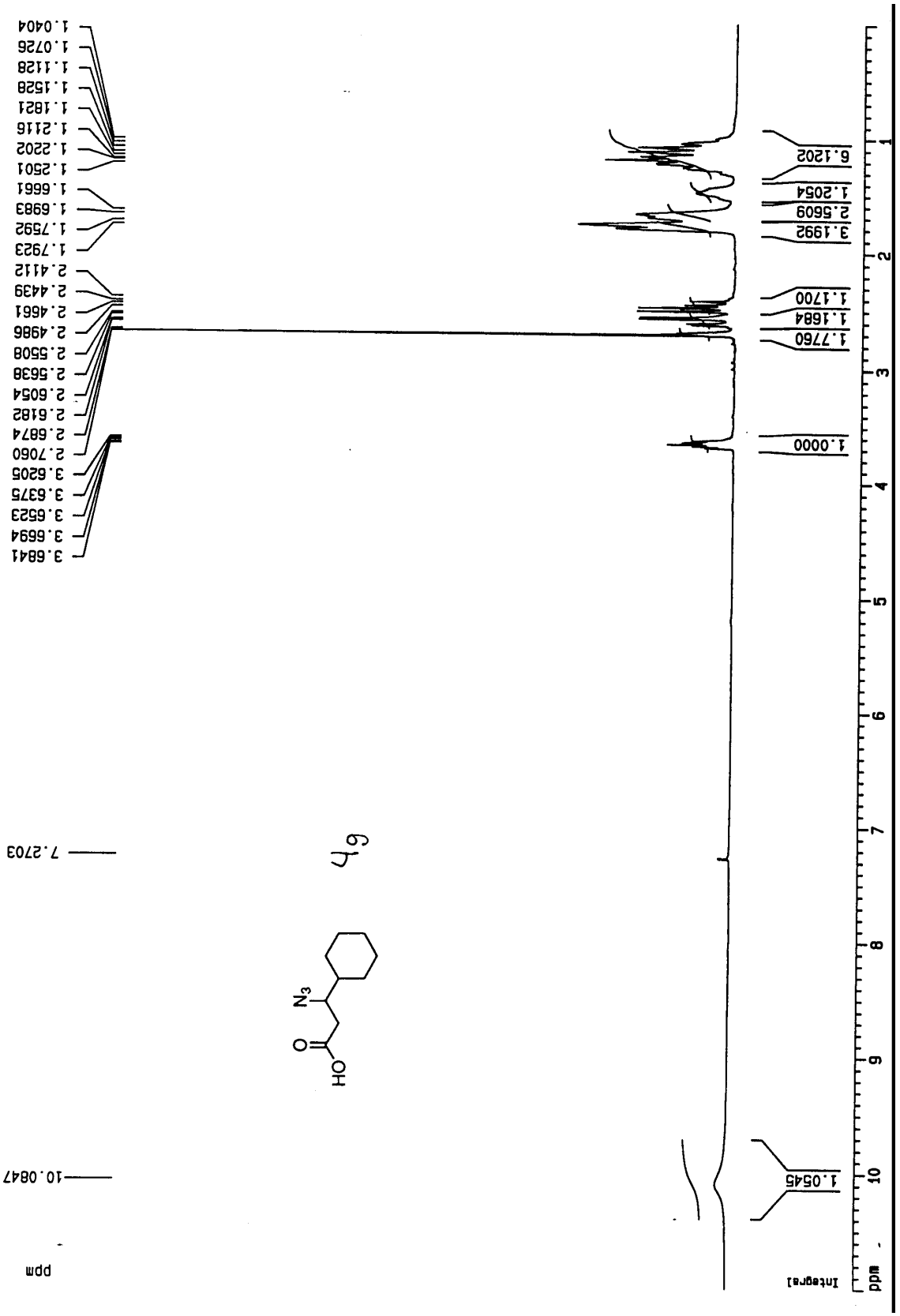
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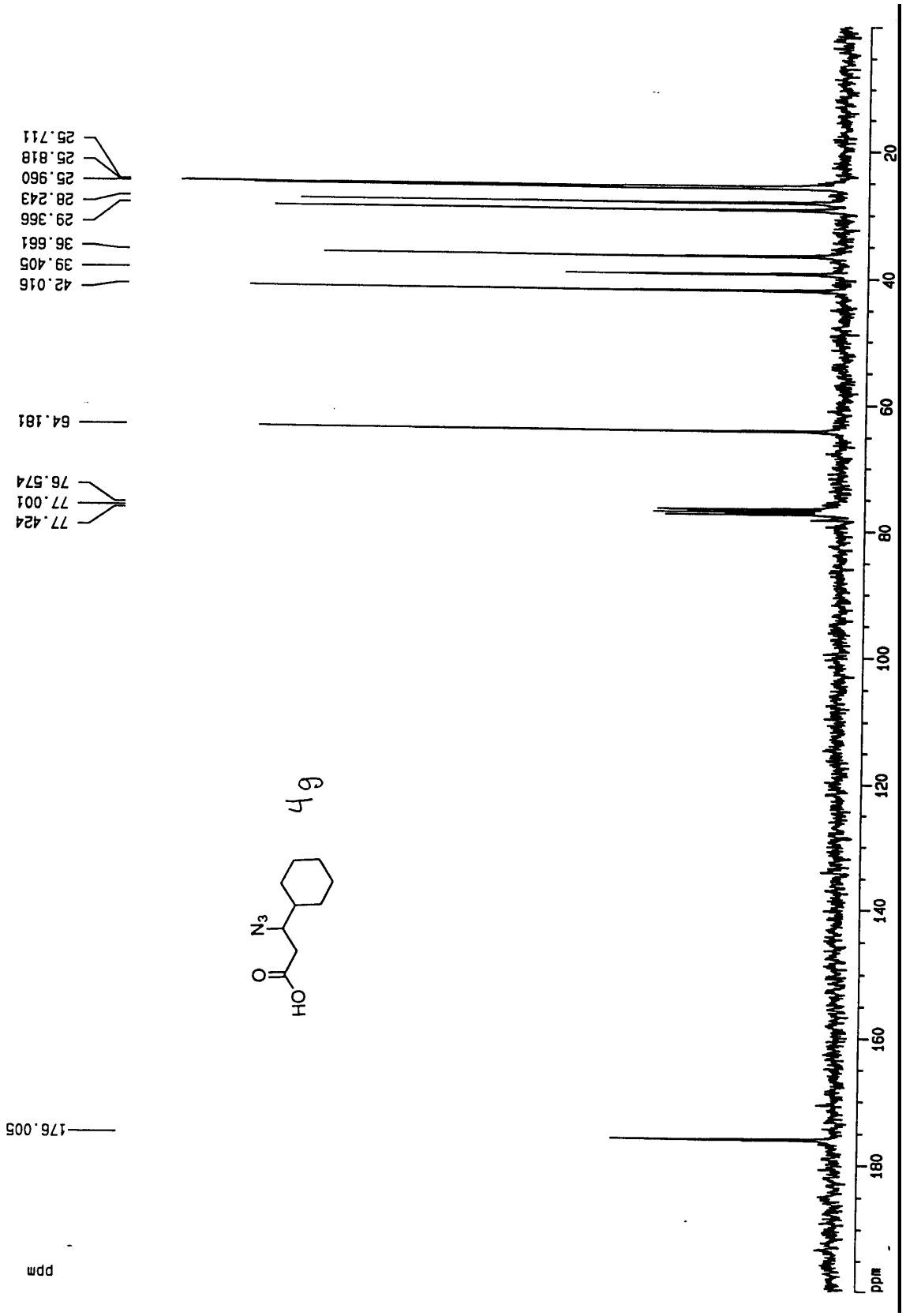
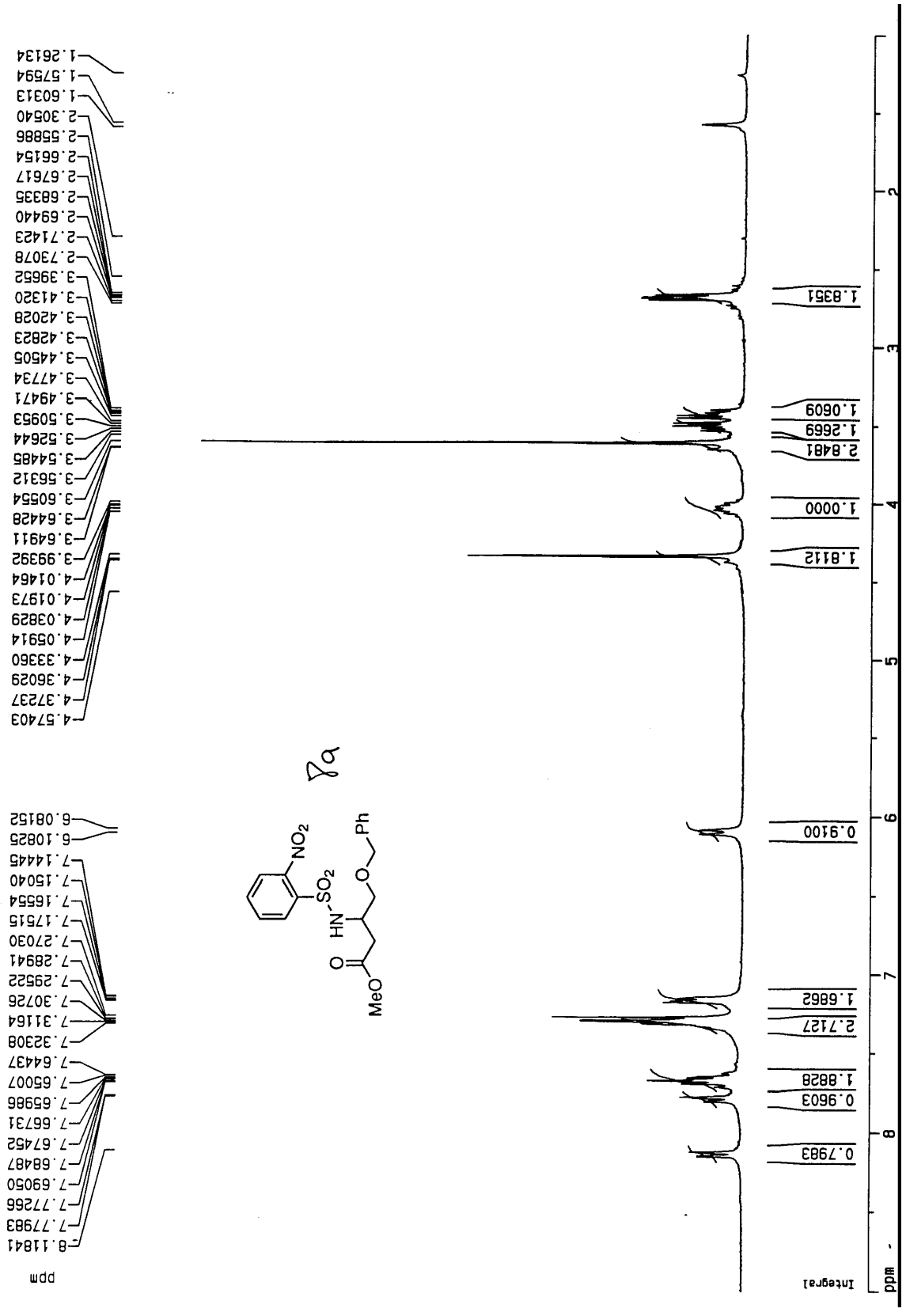
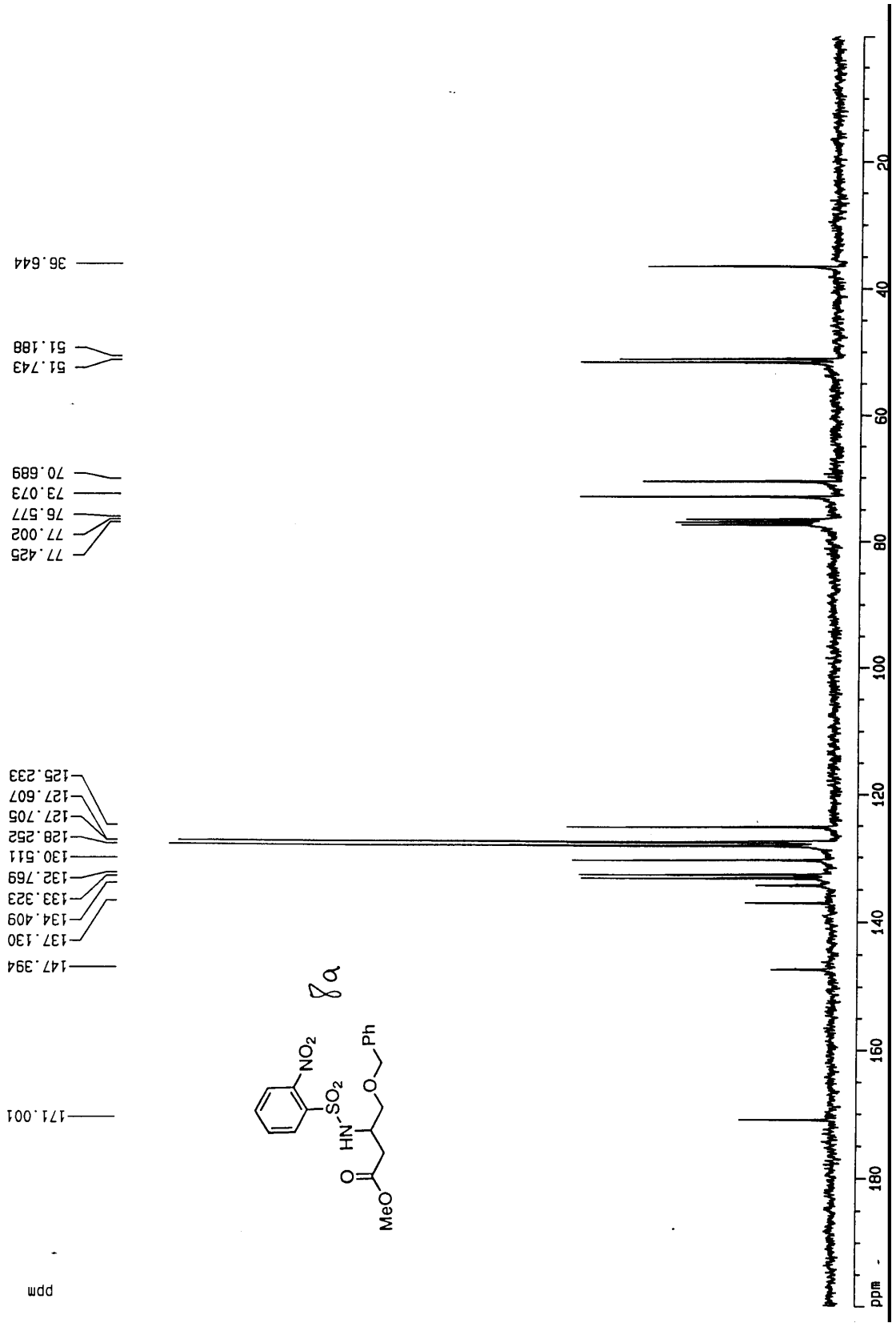
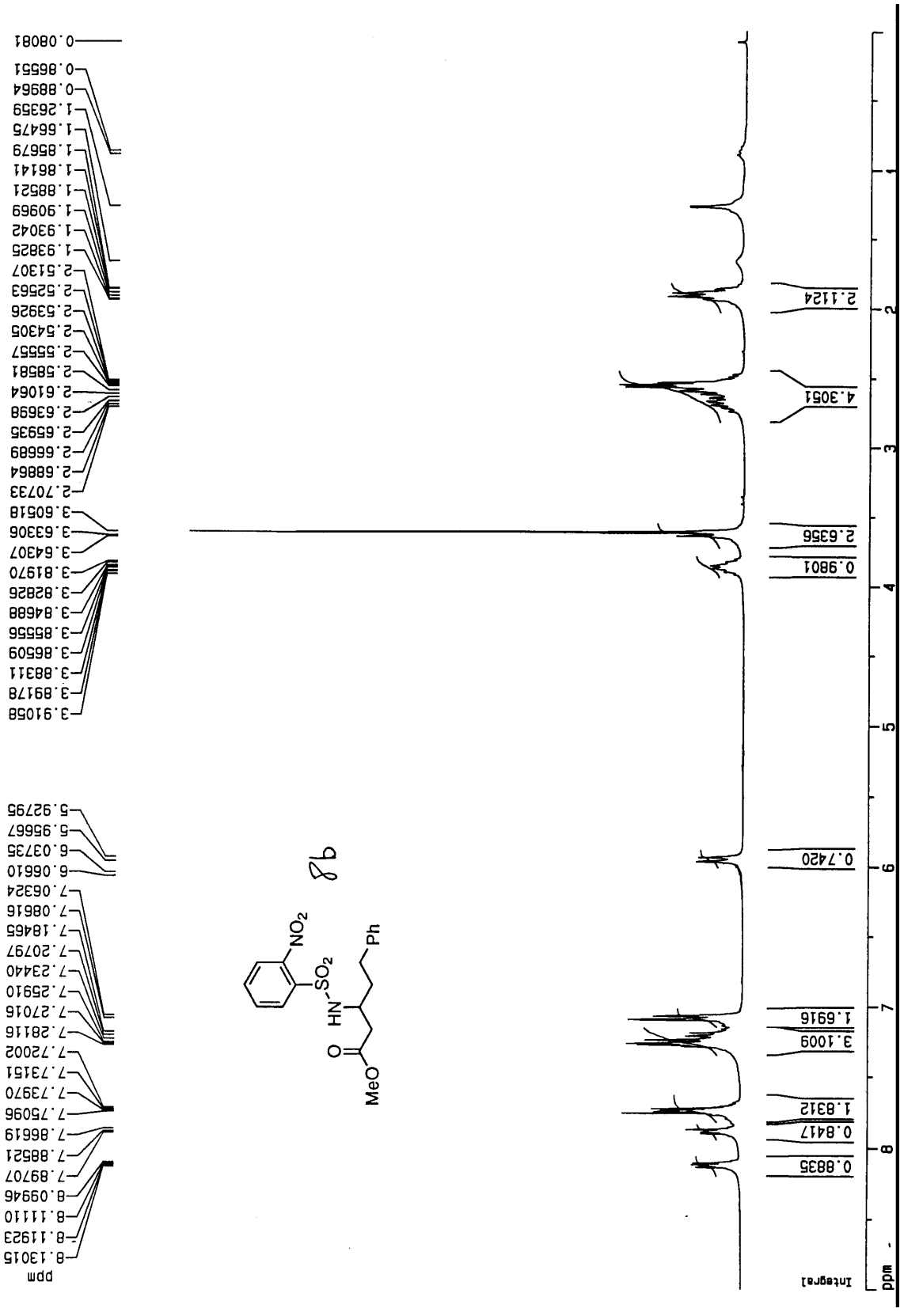
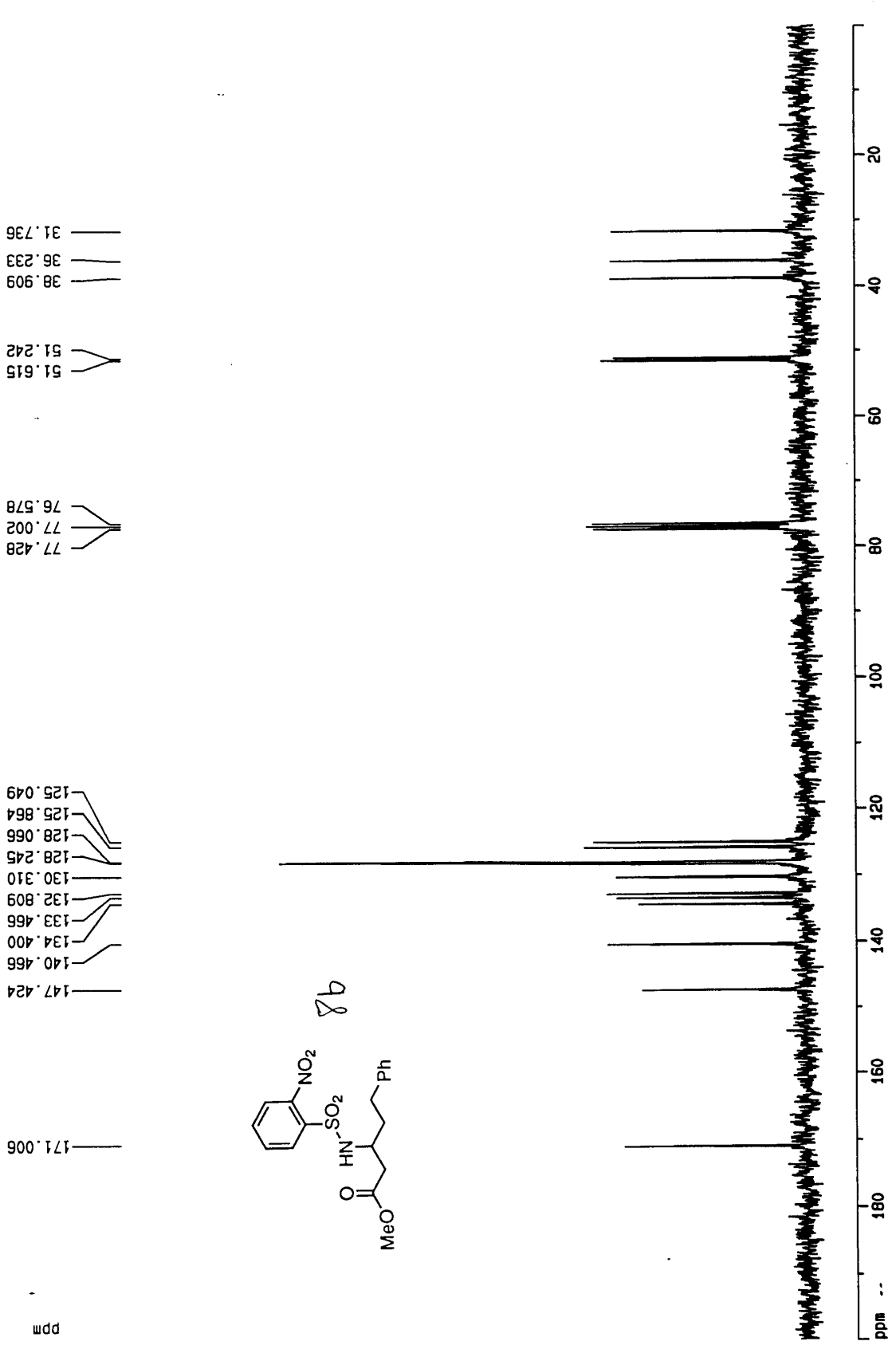
1.1128
1.1528
1.1821
1.2116
1.2202
1.2501
1.6661
1.6983
1.7592
1.7923
2.4112
2.4439
2.4661
2.4986
2.5508
2.5638
2.6054
2.6182
2.6874
2.7060
3.6205
3.6375
3.6523
3.6694
3.6841
7.2703
10.0847
ppm
6.1202
1.2054
2.5609
3.1992
1.1700
1.1684
1.7760
1.0000
1.0545
Integral
ppm
4g
N3
O
HO

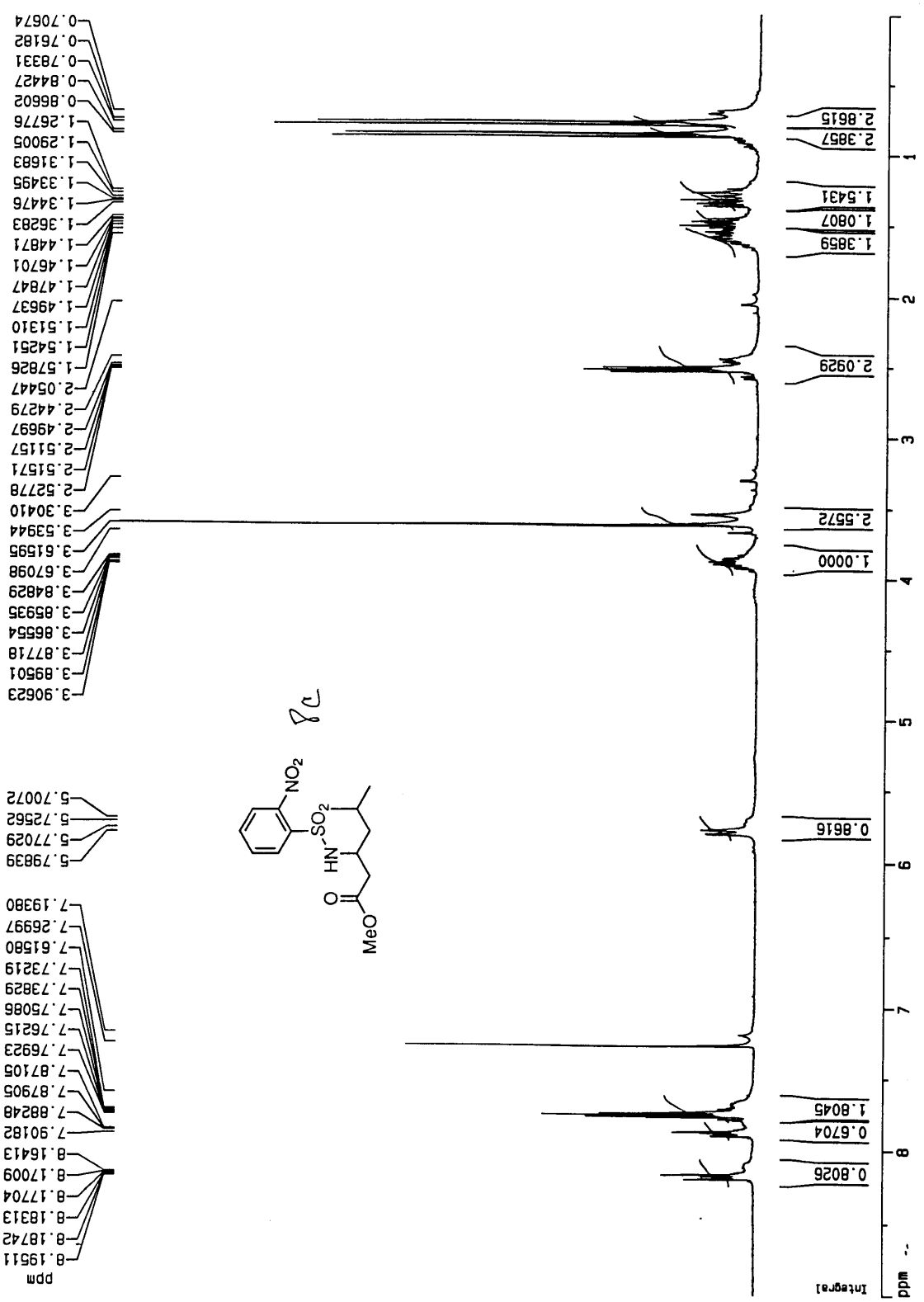

25.711
25.818
25.960
28.243
29.366
36.661
39.405
42.016
64.181
76.574
77.001
77.424
176.005
4g
N3
O
HO
ppm

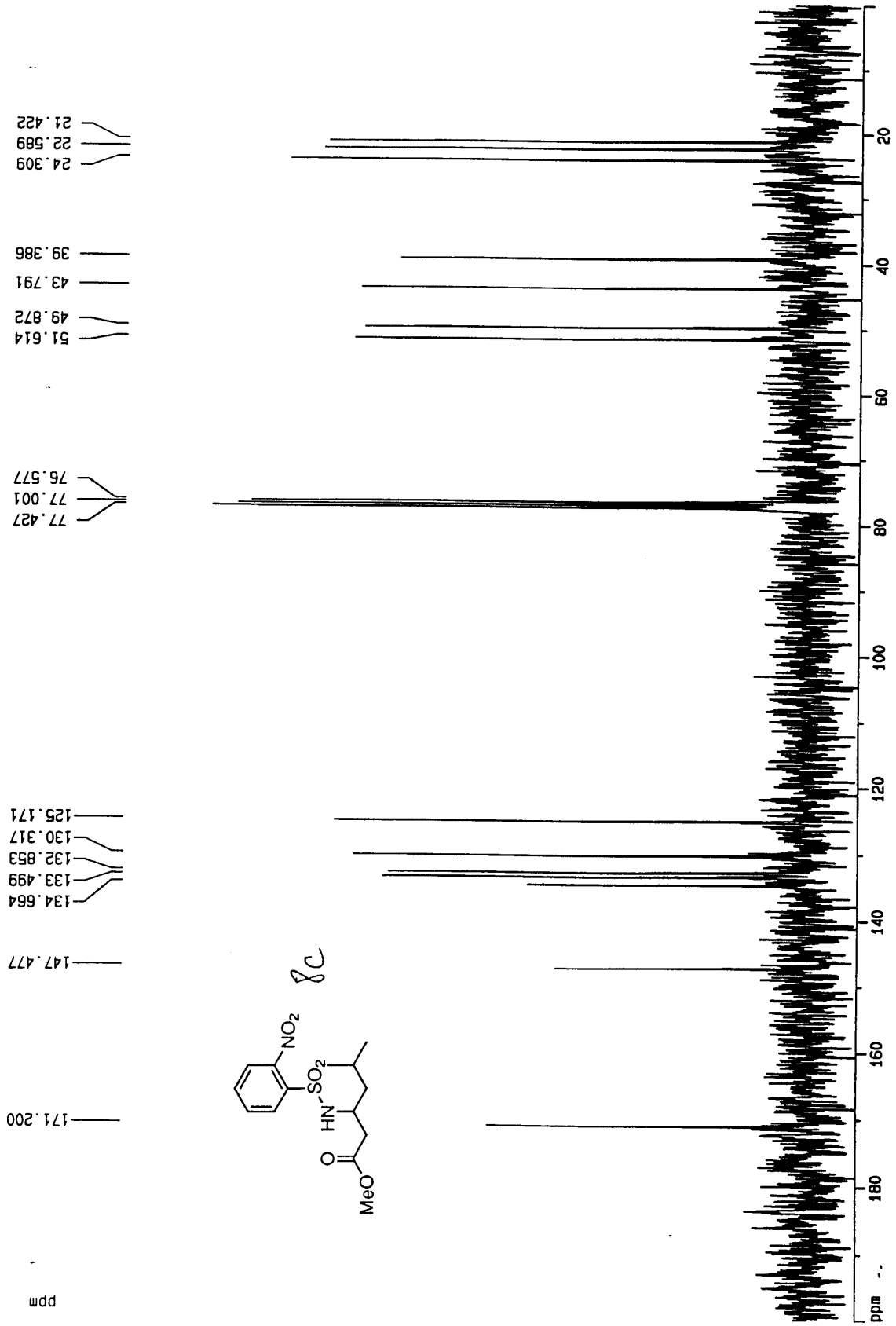

ppm
Integral
1.261
1.576
1.603
2.305
2.559
2.662
2.676
2.683
2.694
2.714
2.730
3.397
3.413
3.421
3.428
3.447
3.495
3.510
3.526
3.545
3.563
3.606
3.644
3.649
3.994
4.015
4.020
4.038
4.059
4.334
4.360
4.372
4.574
8.118
7.780
7.773
7.691
7.685
7.674
7.659
7.650
7.644
7.323
7.312
7.307
7.295
7.289
7.270
7.176
7.166
7.150
7.145
6.108
6.082
0.960
1.883
2.713
1.686
0.910
1.841
1.000
2.848
1.267
1.060
1.835
0.798
NO2
SO2
HN
O
MeO
Ph
O
7a

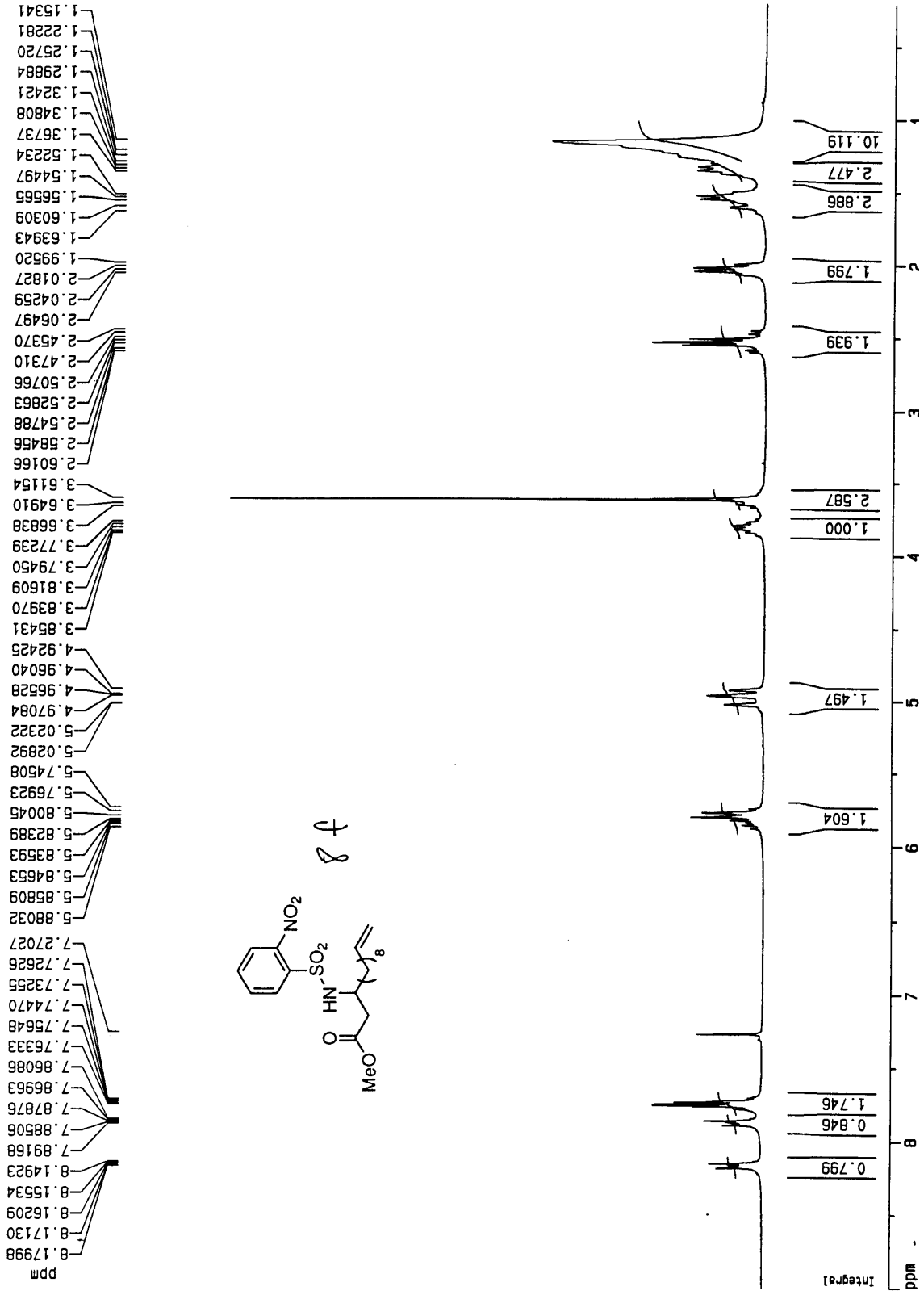

ppm
171.001
147.394
137.130
134.409
133.323
132.769
130.511
128.252
127.705
127.607
125.233
77.425
77.002
76.577
73.073
70.689
51.743
51.188
36.644
NO2
SO2
HN
O
MeO
Ph
O
8a

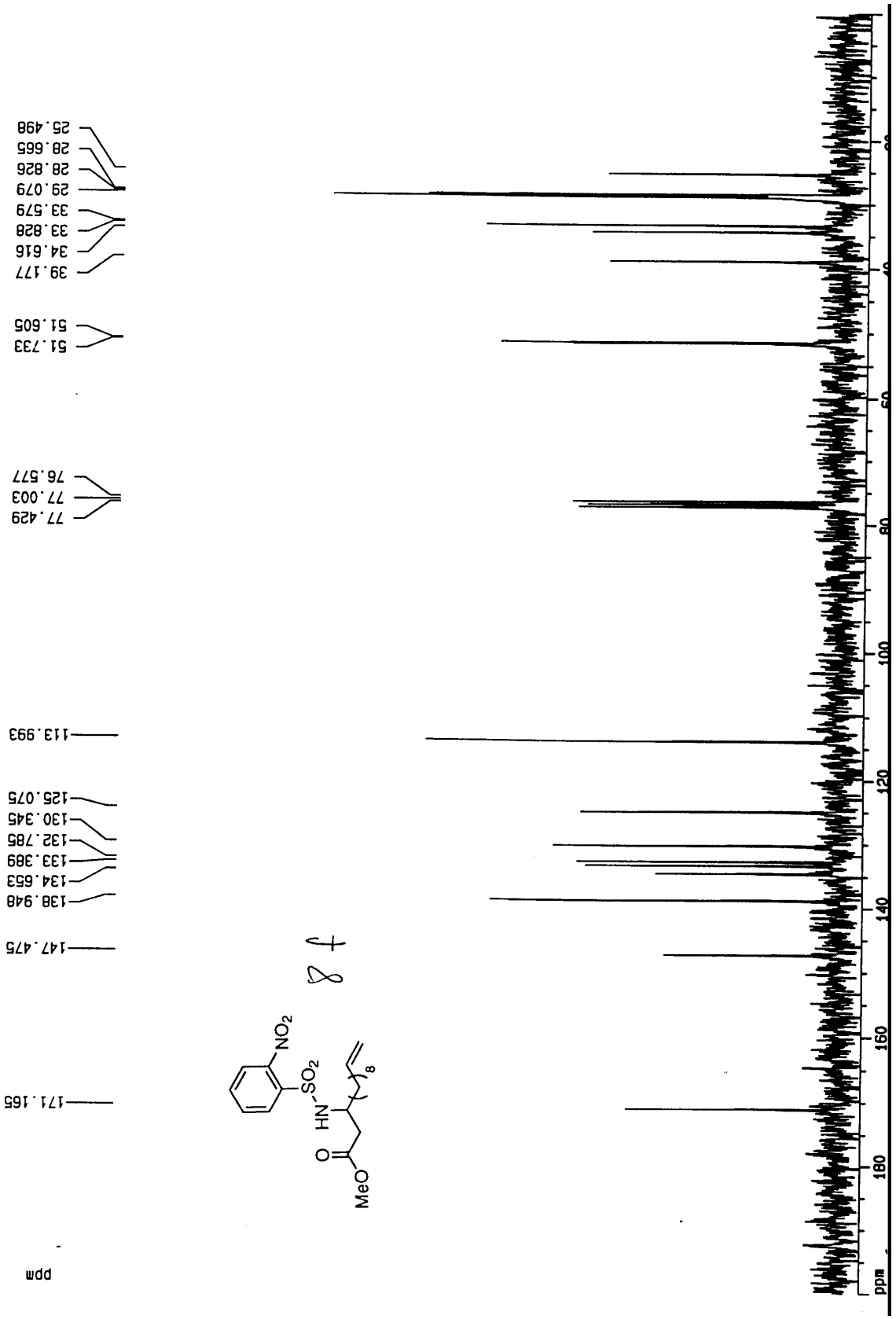

8b
NO2
SO2
HN
O
MeO
Ph
ppm
Integral
2.1124
4.3051
2.6356
0.9801
0.7420
1.6916
3.1009
1.8312
0.8417
0.8835

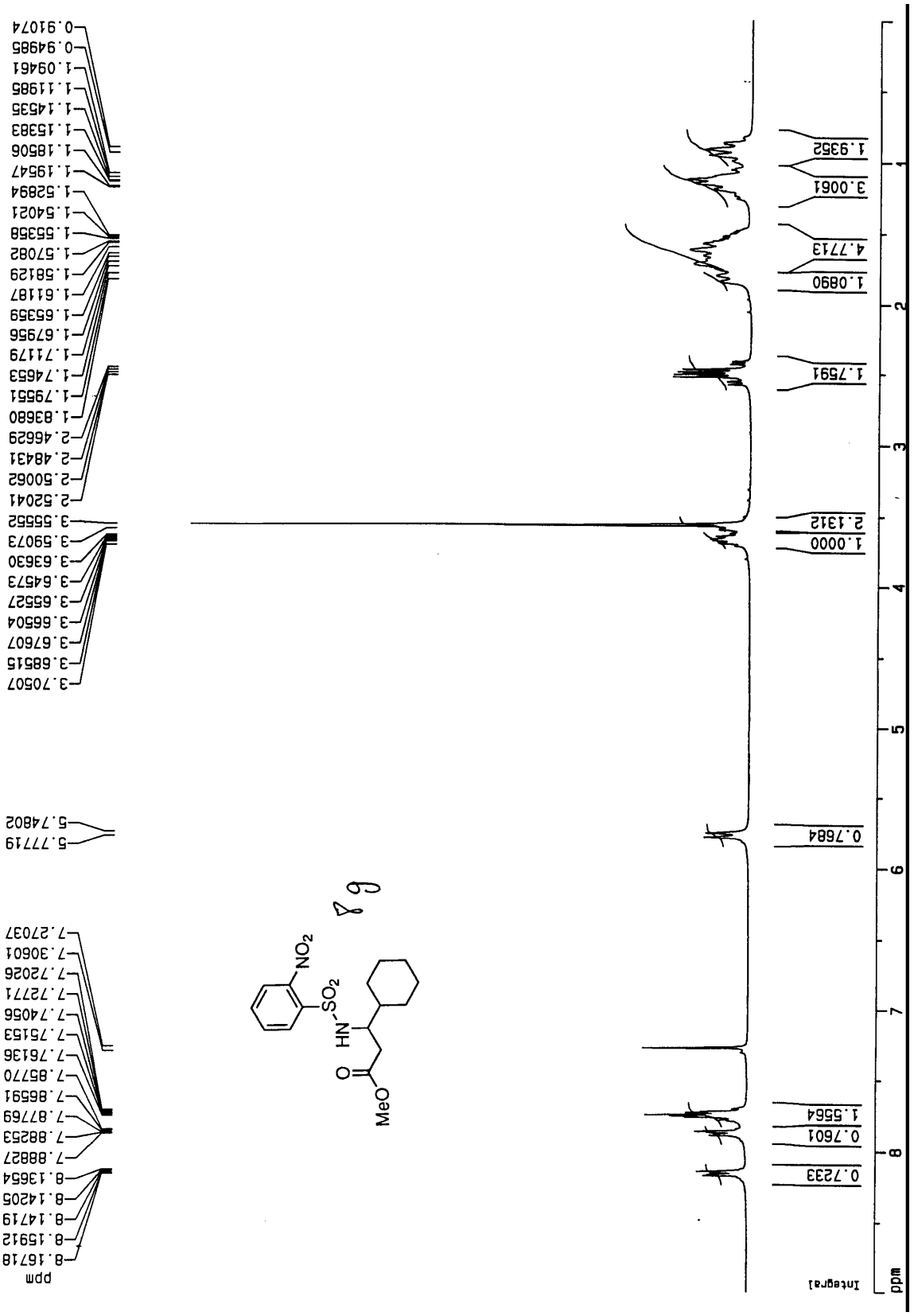

ppm
171.006
147.424
140.466
134.400
133.466
132.809
130.310
128.245
128.066
125.864
125.049
77.428
77.002
76.578
51.615
51.242
38.909
36.233
31.736
ppm
20
40
60
80
100
120
140
160
180
NO2
SO2
HN
O
MeO
Ph
8b

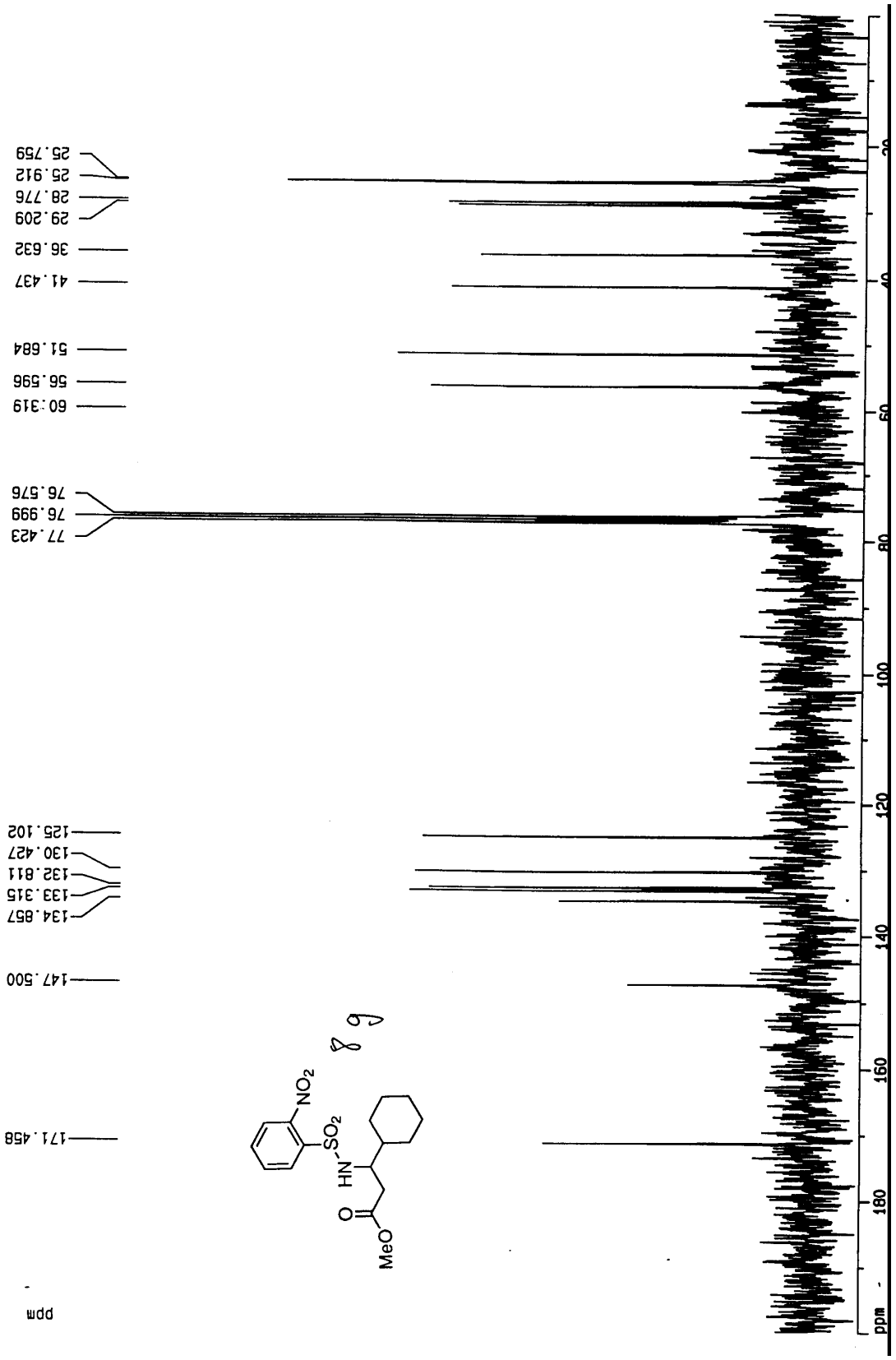

0.70674
0.76182
0.78331
0.84427
0.86602
1.26776
1.29005
1.31683
1.33495
1.34476
1.36283
1.44871
1.46701
1.47847
1.49637
1.51310
1.54251
1.57826
2.05447
2.44279
2.49697
2.51157
2.51571
2.52778
3.30410
3.53944
3.61595
3.67098
3.84829
3.85935
3.86554
3.87718
3.89501
3.90623
5.70072
5.72562
5.77029
5.79839
7.19380
7.26997
7.61580
7.73219
7.73829
7.75086
7.76215
7.76923
7.87105
7.87905
7.88248
7.90182
8.16413
8.17009
8.17704
8.18313
8.18742
8.19511
ppm
Integral
2.8615
2.3857
1.5431
1.0807
1.3859
2.0929
2.5572
1.0000
0.8616
1.8045
0.6704
0.8026
1
2
3
4
5
6
7
8
ppm
NO2
SO2
HN
O
MeO


21.422
22.589
24.309
39.386
43.791
49.872
51.614
76.577
77.001
77.427
125.171
130.317
132.853
133.499
134.664
147.477
171.200
ppm
20
40
60
80
100
120
140
160
180
ppm
8C
NO2
SO2
HN
O
MeO


8.17998
8.17130
8.16209
8.15534
8.14923
7.89168
7.88506
7.87876
7.86963
7.86086
7.76333
7.75648
7.74470
7.73255
7.72626
7.27027
5.88032
5.85809
5.84653
5.83593
5.82389
5.80045
5.76923
5.74508
5.02892
5.02322
4.97084
4.96528
4.96040
4.92425
3.85431
3.83970
3.81609
3.79450
3.77239
3.66838
3.64910
3.61154
2.60166
2.58456
2.54788
2.52863
2.50766
2.47310
2.45370
2.06497
2.04259
2.01827
1.99520
1.63943
1.60309
1.56565
1.54497
1.52234
1.36737
1.34808
1.32421
1.29884
1.25720
1.22581
1.15341
ppm
Integral
10.119
2.477
2.886
1.799
1.939
2.587
1.000
1.497
1.604
0.799
0.846
1.746
8f
NO2
SO2
HN
O
MeO
8
1
2
3
4
5
6
7
8


25.498
28.665
28.826
29.079
33.579
33.828
34.616
39.177
51.605
51.733
76.577
77.003
77.429
113.993
125.075
130.345
132.785
133.389
134.653
138.948
147.475
171.165
ppm
NO2
SO2
HN
O
MeO
8
8 et


δ9
NO2
SO2
HN
O
MeO
ppm
Integral
1.9352
3.0061
4.7713
1.0890
1.7591
2.1312
1.0000
0.7684
1.5564
0.7601
0.7233


25.759
25.912
28.776
29.209
36.632
41.437
51.684
56.596
60.319
76.576
76.999
77.423
125.102
130.427
132.811
133.315
134.857
147.500
171.458
ppm
NO2
SO2
HN
O
MeO
8g