Supplementary Material (ESI) for Organic & Biomolecular Chemistry

A concise synthesis of enantiopure circumdatins E, H and J

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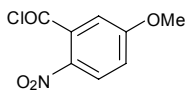
1. General information

Unless otherwise noted, reagents and solvents were used as received from commercial suppliers. All reactions were conducted under nitrogen. Proton and carbon nuclear magnetic resonance spectra were obtained on a Bruker AVANCE 300 spectrometer at 300 MHz for proton and 75 MHz for carbon, or on a Bruker AVANCE 500 spectrometer at 500 MHz for proton and 125 MHz for carbon. NMR chemical shifts (δ) are reported in ppm and coupling constants (*J*) are reported in Hertz. Tetramethylsilane was used as an internal standard for proton and carbon NMR spectra. Mass spectra were obtained on a Finnigan LCQ Duo LCMS ion trap electrospray ionization (ESI) mass spectrometer or a PESCiex API 150EX mass spectrometer using atmospheric chemical ionization (APCI). High resolution mass spectra were obtained on a TOF mass spectrometer using electrospray ionization at the Center for Functional Genomics, University at Albany (Albany, NY). Melting points were determined on an Electrothermal Mel-Temp apparatus and are uncorrected. All isolated compounds had purity greater than 95% (area percent) as judged by HPLC analysis area method.

2. Experimental procedures

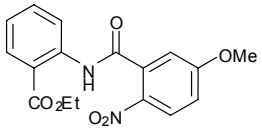
5-Methoxy-2-nitrobenzoyl chloride (11a)



5-Methoxy-2-nitrobenzoic acid (5.00 g, 25.4 mmol) was mixed with toluene (50 mL) and thionyl chloride (6.0 mL, 9.8 g, 82 mmol). DMF (0.1 mL) was added, and the reaction mixture was heated at reflux for 1 h. The reaction was concentrated under reduced

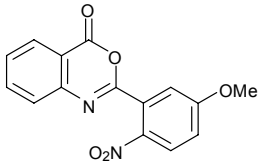
pressure at 50 °C to afford a quantitative yield (5.46 g) of 5-methoxy-2-nitrobenzoyl chloride as a dark brown oil. This material was used without further purification.

Ethyl 2-(5-methoxy-2-nitrobenzamido)benzoate (12)



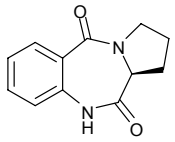
5-Methoxy-2-nitrobenzoyl chloride (5.46 g, 25.4 mmol) was dissolved in anhydrous THF (45 mL). *i*-Pr_2EtN (13.3 mL, 9.83 g, 76.2 mmol) and ethyl anthranilate (3.8 mL, 4.20 g, 25.4 mmol) were added at 0 °C. After stirring overnight at room temperature, the reaction mixture was concentrated, dissolved in CH_2Cl_2 (300 mL) and washed with 2M aqueous citric acid (100 mL). The residue obtained after concentrating the CH_2Cl_2 solution was purified by flash chromatography (hexanes/EtOAc gradient from 0 to 40% EtOAc) to afford an 83% yield (7.30 g) of **12** as a white solid: mp 85–86 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.00 (s, 1H), 8.24 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 9.0 Hz, 1H), 7.96 (dd, J = 7.9, 1.4 Hz, 1H), 7.69 (dt, J = 7.8, 1.5 Hz, 1H), 7.33–7.26 (m, 3H), 4.28 (q, J = 7.1 Hz, 2H), 3.95 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 164.7, 163.9, 141.2, 139.0, 135.8, 134.8, 130.9, 127.4, 123.3, 120.8, 115.7, 115.2, 113.6, 61.6, 56.2, 14.1; HRMS (ESI+) calcd for $C_{17}H_{17}N_2O_6$ $[M+H]^+$: 345.1086, found: 345.1083.

Isolation of 2-(5-methoxy-2-nitrophenyl)-4H-benzo[d][1,3]oxazin-4-one (13) from the reaction of 12 with thionyl chloride followed by addition of Boc-L-proline.



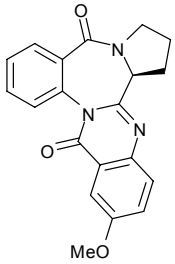
A mixture of **12** (516 mg, 1.50 mmol), toluene (5 mL), thionyl chloride (0.55 mL, 0.90 g, 7.56 mmol) and DMF (1 drop) was heated at reflux for 24 h and then evaporated to dryness. The residue was dissolved in CH_2Cl_2 (7 mL). The solution was cooled to 0 °, treated with *i*-Pr_2NEt (0.33 mL, 0.24 g, 1.9 mmol) and Boc-L-proline (322 mg, 1.50 mmol) and stirred for 1.5 h at room temperature. The mixture was then diluted with CH_2Cl_2 (10 ml) and washed with 10% aqueous citric acid (10 mL) followed by saturated aqueous $NaHCO_3$ (10 mL). After evaporating *in vacuo*, the residue was triturated with 3 mL of hexanes/EtOAc/CH_2Cl_2 (90:5:5) to afford a 67% yield (300 mg) of **13** as an off-white solid: mp 151–152 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.23 (m, 2H), 8.03 (td, J = 7.9, 1.4 Hz, 1H), 7.76–7.71 (m, 2H), 7.53 (d, J = 2.7 Hz, 1H), 7.38 (dd, J = 9.1, 2.8 Hz), 3.96 (s, 3H).); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1, 158.3, 155.2, 145.6, 139.9, 137.3, 129.5, 128.6, 128.2, 127.4, 126.8, 116.8, 116.5, 116.4, 56.6; HRMS (ESI+) calcd for $C_{15}H_{11}N_2O_5$ $[M+H]^+$: 299.0668, found: 299.0659.

(*S*)-2,3-Dihydro-1*H*-benzo[e]pyrrolo[1,2-a][1,4]diazepine-5,11(10*H*,11a*H*)-dione (10a)[1]



In a 100-mL round-bottomed flask, DMSO (11 mL) was added to a solid mixture of L-proline (12.7 g, 0.110 mol) and isatoic anhydride (16.3 g, 0.100 mol). The flask was placed into an oil bath, and the bath was heated to 140 °C. Vigorous evolution of CO_2 began at 120–130 °C, and the mixture liquefied. After heating at 140 °C for 2 h, the reaction was cooled to room temperature. The solid cake was crushed and stirred with water (35 mL) for 30 min. The suspension was filtered, and the filter cake was washed with water (20 mL), saturated aqueous $NaHCO_3$ (2 × 20 mL) and again with H_2O (3 ×20 mL) and dried under vacuum at 45 °C for 3 d to afford **10a** in 91% yield (19.6 g) as a gray powder: mp 202–203 °C (lit.[1] 209–210 °C); NMR data are consistent with literature:[1] ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.49 (s, 1H), 7.78 (d, J =7.7 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H), 7.13 (d, J = 8.1 Hz, 1H), 4.11 (d, J = 6.4 Hz, 1H), 3.63–3.56 (m, 1H), 3.50–3.40 (m, 1H), 2.45 (m, 1H, overlapped with DMSO peak), 2.02–1.72 (m, 3H).

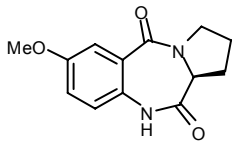
Circumdatin H (5)



Compound **10a** (500 mg, 2.31 mmol), DMAP (113 mg, 0.924 mmol) and Et_3N (0.64 mL, 470 mg, 4.62 mmol) were dissolved in anhydrous *N*,*N*-dimethylacetamide (5 mL), and the solution was cooled to -8 °C using an ice/acetone bath. Acid chloride **11a** (0.43 mL, 600 mg, 2.78 mmol) was added while keeping temperature below 0 °C, and the reaction mixture was stirred at 0 °C for 30 min. After this time, acetic acid (5 mL) was added, and the reaction mixture was cooled to -30 °C. Zinc dust (3.00 g, 46.2 mmol) was added, and the reaction was stirred at -20 °C for 1.5 h and then slowly warmed to -5 °C over 2 h. After this time, the reaction mixture was poured into 10% aqueous K_2CO_3 (60 mL), and extracted with EtOAc (2 × 100 mL). The organic extracts were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (hexanes/EtOAc gradient from 50 to 100% EtOAc) to

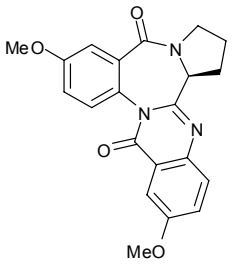
afford **5** in 72% yield (582 mg) as a yellow solid: mp 171–172 ºC; $[\alpha]_D^{25}$ -123.6° (c 0.8, MeOH) (lit.[2] $[\alpha]_D$ -26.3° (c 0.078, MeOH)). 97.9% *ee* was determined by HPLC analysis using Chiralpak AD-H column (4.6 × 250 mm, 60% heptane: 40% *i*-PrOH with 0.1% TFA at 1 mL/min, wavelength 235 nm), retention time: t_S= 12.7 min, and t_R= 15.6 min. NMR data are consistent with the literature:[2] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.68 (d, *J* = 2.9 Hz, 1H), 7.64 (d, *J* = 8.9 Hz, 1H), 7.60–7.55 (m, 2H), 7.52 (ddd, *J* = 7.8, 6.2, 2.5, 1H), 7.38 (dd, *J* = 8.0, 3.0 Hz, 1H), 4.54 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.93 (s, 3H), 3.79 (ddd, *J* = 11.5, 8.4, 2.7 Hz, 1H), 3.64–3.68 (m, 1H), 3.16 (m, 1H), 2.31 (sextet, *J* = 9.4 Hz, 1H), 2.18–2.12 (m, 1H), 2.11–2.03 (m, 1H).

(*S*)-7-Methoxy-2,3-dihydro-1H-benzo[e]pyrrolo[1,2-a][1,4]diazepine-5,11(10*H*,11a*H*)-dione (10b)



A 50-mL single-neck round-bottomed flask equipped with a magnetic stirrer and nitrogen inlet was charged with **15b** (2.00 g, 10.4 mmol), L-proline (1.19 g, 10.4 mmol) and DMSO (2 mL). After heating at 140 °C for 2 h, water (10 mL) was added, and the resulting suspension was filtered. The filter cake was washed with saturated aqueous sodium bicarbonate (10 mL) and water (5 mL) and dried under vacuum at 45 °C for 16 h to afford **10b** in 87% yield (2.24 g) as an off-white solid: mp 173–174 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.48 (d, *J* = 3.0 Hz, 1H), 7.04 (dd, *J* = 8.5, 3.0 Hz, 1H), 6.89 (t, *J* = 8.5 Hz, 1H), 4.07 (d, *J* = 7.1 Hz, 1H), 3.85 (s, 3H), 3.84–3.80 (m, 1H), 3.64–3.58 (m, 1H), 2.80–2.73 (m, 1H), 2.14–2.00 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 165.2, 156.8, 128.7, 128.3, 122.7, 120.3, 113.4, 56.7, 55.7, 47.4, 26.3, 23.5; HRMS (ESI+) calcd for $C_{13}H_{15}N_2O_3$ $[M+H]^+$: 247.1080, found: 247.1080.

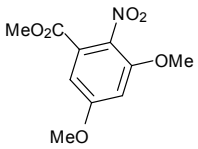
Circumdatin J (6)



Using the same general procedure as described for the preparation of circumdatin H (**5**), compound **10b** (500 mg, 2.03 mmol) was reacted with acid chloride **11a** (526 mg, 2.44 mmol). Purification by flash chromatography (CH_2Cl_2/MeOH gradient from 0 to 1.5% MeOH) followed by trituration with ether gave a 70% yield (536 mg) of **6** as an off-white

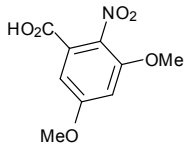
solid: mp 144–145 ºC; $[\alpha]_D^{25}$ -79.9° (c 1.18, 1:1 MeOH/CH_2Cl_2). 100% *ee* was determined by HPLC analysis using Chiralpak AD-H column (4.6 × 250 mm, 60% heptane: 40% *i*-PrOH with 0.1% TFA at 1 mL/min, wavelength 235 nm), retention time: t_S= 10.9 min, and t_R= 14.7 min. NMR data are consistent with the literature:[3] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 3.0 Hz, 1H), 7.63 (d, *J* = 8.9 Hz, 1H), 7.47 (d, *J* = 8.9 Hz), 7.46 (d, *J* = 2.6 Hz, 1H), 7.37 (dd, *J* = 8.9, 2.9 Hz, 1H), 7.10 (dd, *J* = 9.1, 3.1 Hz, 1H), 4.56 (dd, *J* = 8.0, 1.6 Hz, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.77 (ddd, *J* = 11.8, 8.4, 2.7 Hz, 1H), 3.62 (ddd, *J* = 11.9, 9.7, 7.1 Hz, 1H), 3.17 (ddt, *J* = 12.4, 6.8, 2.3 Hz, 1H), 2.30 (sextet, *J* = 9.6 Hz, 1H), 2.18–2.10 (m, 1H), 2.10–2.03 (m, 1H).

Methyl 3,5-dimethoxy-2-nitrobenzoate.[4]



A solution of methyl 3,5-dimethoxybenzoate (5.57 g, 28.4 mmol) in acetic anhydride (17 mL) was cooled to -20 °C. Carefully, dropwise fuming nitric acid (2.0 mL) was added, while the reaction temperature was maintained at -20–-10 °C. (CAUTION. The reaction is very exothermic. Dropwise addition of nitric acid, while ensuring adequate cooling is necessary.) Soon after the addition was completed, the product began precipitating. After an additional 20 minutes in the cooling bath, the mixture was transferred into excess 1M aqueous solution of K_2HPO_4. K_3PO_4 was further added to bring the pH to 6.5. The precipitate was filtered, washed with water and dried overnight *in vacuo* at 45 °C. The resulting crude material was heated to reflux with MeOH (30 mL), then cooled to room temperature and filtered. The filter cake was washed with MeOH (2 × 5 mL) and dried overnight *in vacuo* at 40 °C to afford an 82% yield (5.60 g) of methyl 3,5-dimethoxy-2-nitrobenzoate as a light yellow solid: mp 120–121 °C (lit.[4] 134–136 °C); NMR data are consistent with the literature:[4] ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.09 (d, *J* =2.5 Hz, 1H), 6.99 (d, *J* =2.4 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.82 (s, 3H).

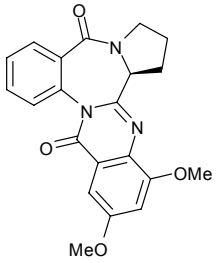
3,5-Dimethoxy-2-nitrobenzoic acid



Methyl 3,5-dimethoxy-2-nitrobenzoate (5.60 g, 23.2 mmol) was mixed with methanol (85 mL) and a solution of LiOH (1.61 g, 70.0 mmol) in water (15 mL). The resulting mixture was heated at reflux for 30 min, and then evaporated under reduced pressure on a rotary evaporator at 45 °C to dryness. The residue was mixed with water (30 mL), and the resulting suspension was acidified with 6 M hydrochloric acid to pH 3. The precipitate

was filtered and dried at 55 °C overnight in vacuo to afford an 87% yield (4.60 g) of 3,5-dimethoxy-2-nitrobenzoic acid as a light yellow solid: mp 217–218 °C (lit.[4] 248–250 °C); NMR data are consistent with the literature:[4] ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.04 (d, J =2.5 Hz, 1H), 6.97 (d, J =2.5 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H).

(5b*S*)-5b,6,7,8-Tetrahydro-2,4-dimethoxy-10*H*,16*H*-pyrrolo[2,1-c]quinazolino[3,2-a][1,4]benzodiazepine-10,16-dione (16)

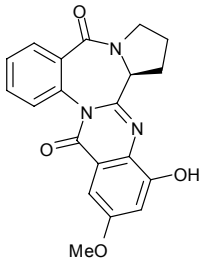


3,5-Dimethoxy-2-nitrobenzoyl chloride **11b** was prepared by reacting 3,5-dimethoxy-2-nitrobenzoic acid (681 mg, 3.00 mmol) with oxalyl chloride (451 mg, 3.60 mmol) and DMF (0.2 mL) in CH_2Cl_2 (8 mL). After stirring at room temperature for 12 h, the reaction mixture was concentrated to dryness and used directly in the following step.

Chloride **11b** (prepared above, 3.00 mmol) was added at 0 °C to a solution of **10a** (540 mg, 2.50 mmol), Et_3N (505 mg, 5.00 mmol) and DMAP (122 mg, 1.0 mmol) in anhydrous *N*,*N*-dimethylacetamide (10 mL). The reaction mixture was stirred at 0 ºC for 2 h. After this time, the reaction was warmed to room temperature, diluted with EtOAc (200 mL) and washed with water (3 × 100 mL). The organic layer was separated and dried over Na_2SO_4. The drying agent was removed by filtration, and the filtrate was concentrated under reduced pressure to afford the crude intermediate **9c** (1.10 g), which was used directly in following step.

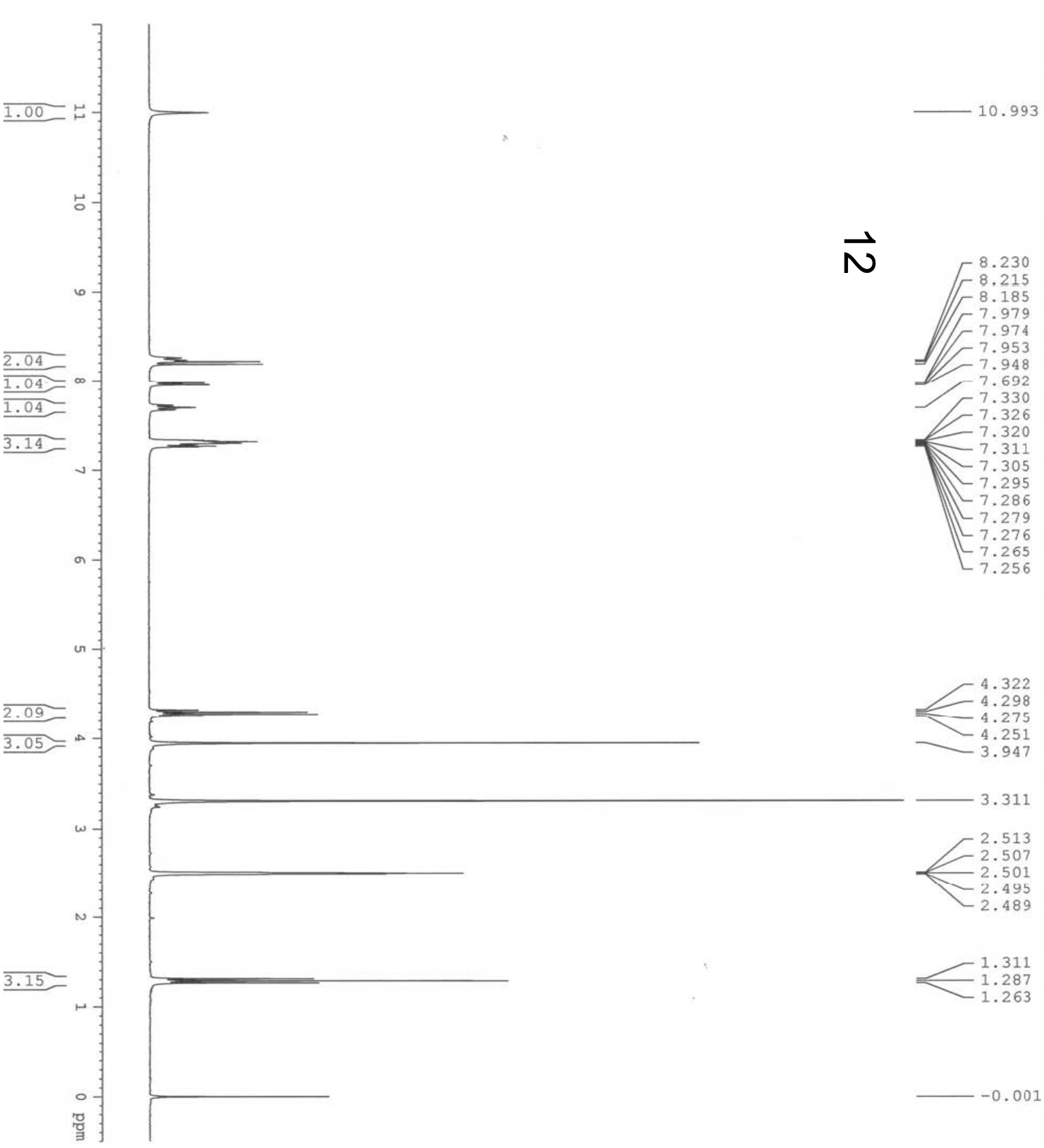
Intermediate **9c** (1.00 g, taken from the lot prepared above, 2.27 mmol) was dissolved in AcOH (10 mL) and THF (5 mL). The solution was cooled to 0 ºC, and zinc dust (3.05 g, 47 mmol) was added in portions. The reaction mixture was stirred at room temperature for 30 min, diluted with EtOAc (300 mL), filtered and washed with saturated aqueous $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification of the resulting residue by flash chromatography (CH_2Cl_2/MeOH gradient from 0 to 10% MeOH) afforded **16** in 50% yield (446 mg) as a yellow solid: mp 240–242 °C; $[\alpha]^{25}_D$ -148.5 (*c* 0.3, MeOH); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.83 (d, J = 6.6 Hz, 1H), 7.81-7.54 (m, 3H), 7.13 (d, J = 2.7 Hz, 1H), 7.02 (d, J = 2.7 Hz, 1H), 4.60 (d, J = 5.4 Hz, 1H), 3.95 (s, 3H), 3.87 (s, 3H), 3.57-3.46 (m, 2H), 2.95 (m, 1H), 2.11 (m, 2H), 1.96 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.5, 161.0, 158.9, 155.9, 150.9, 133.2, 132.2, 131.2, 130.5, 129.0, 128.9, 128.5, 122.7, 105.9, 97.9, 58.4, 56.4, 55.7, 46.0, 26.3, 23.3; HRMS (ESI+) calcd for $C_{21}H_{20}N_3O_4$ $[M + H]^+$: 378.1454, found 378.1461.

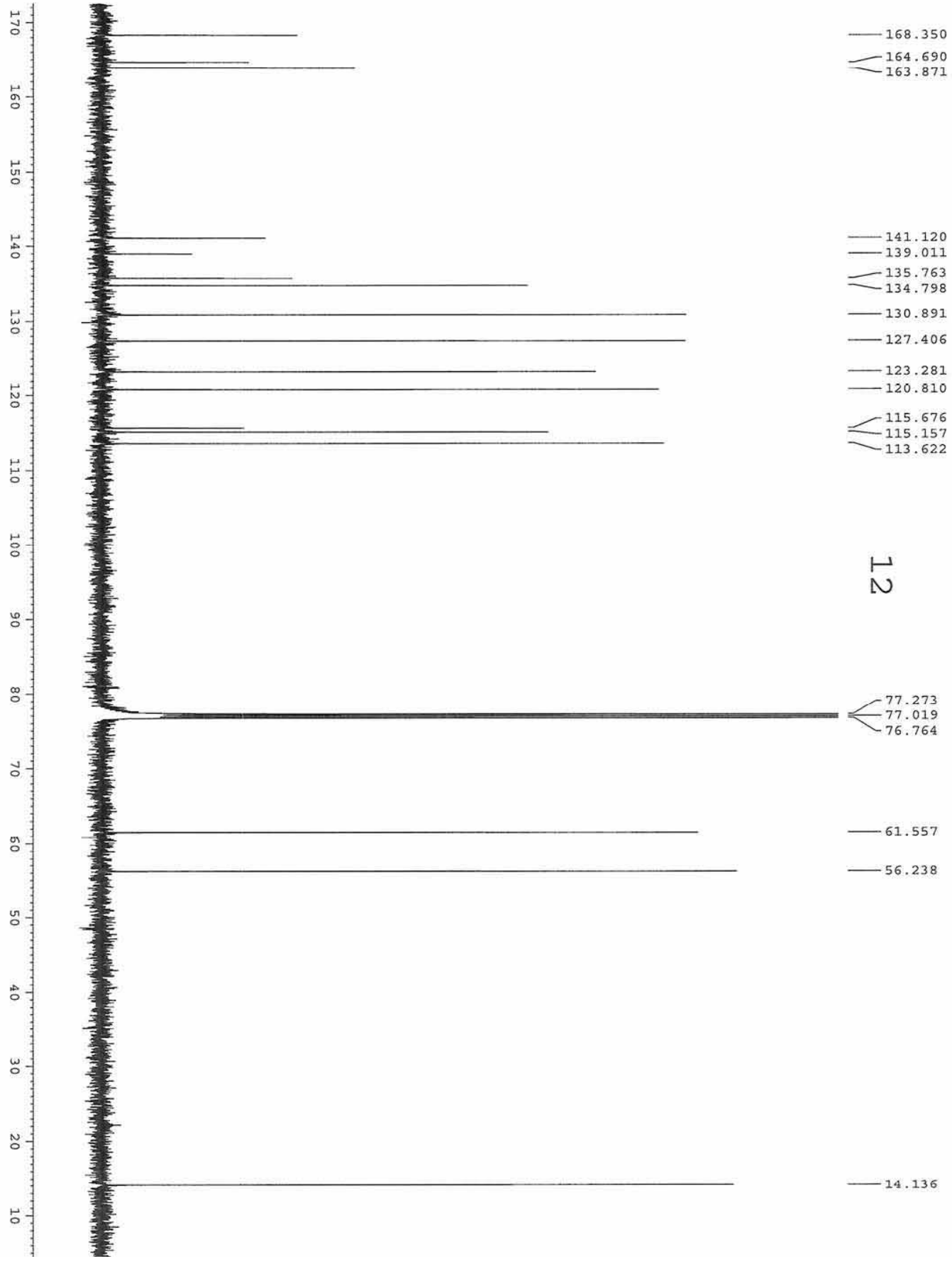
Circumdatin E (4)

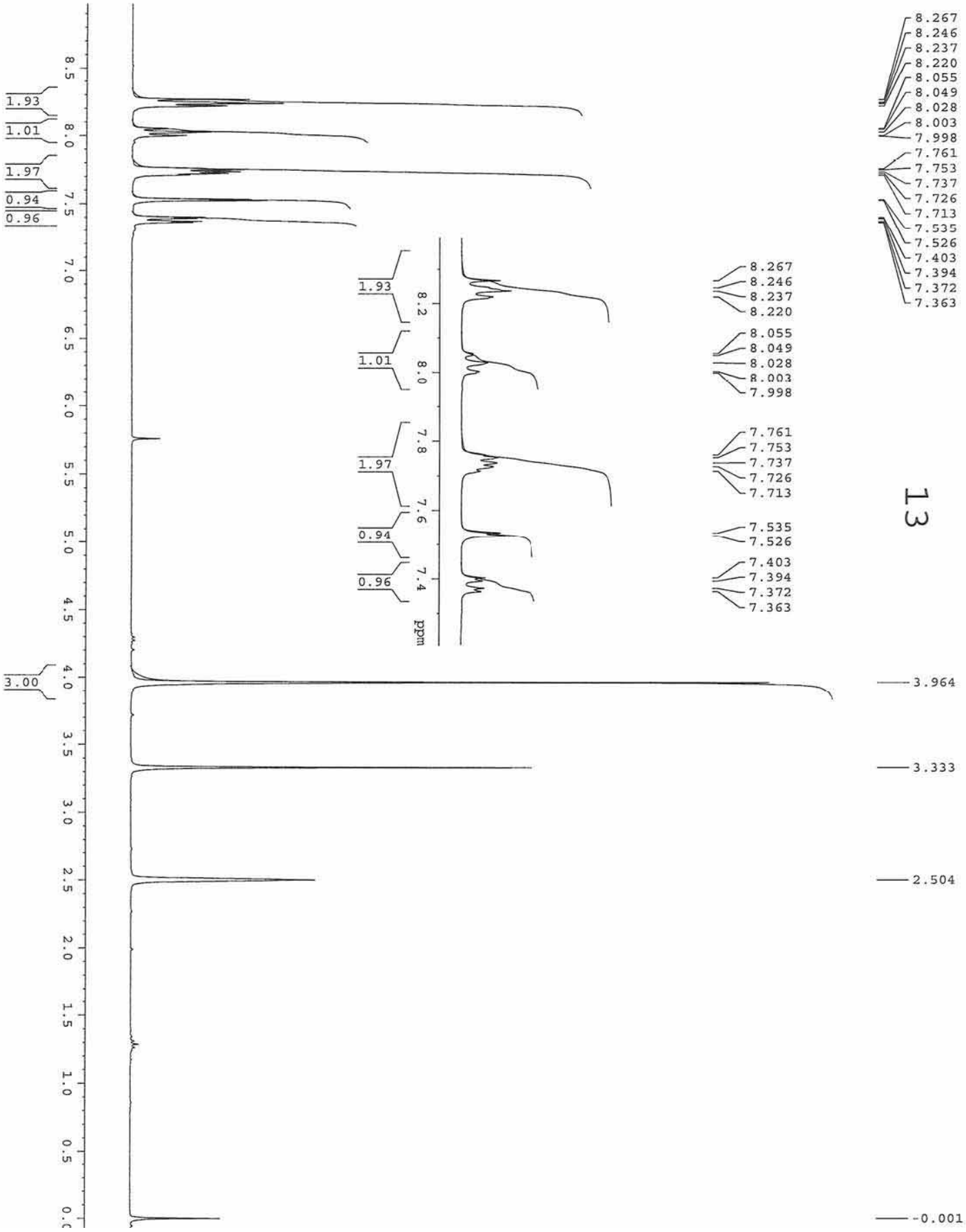


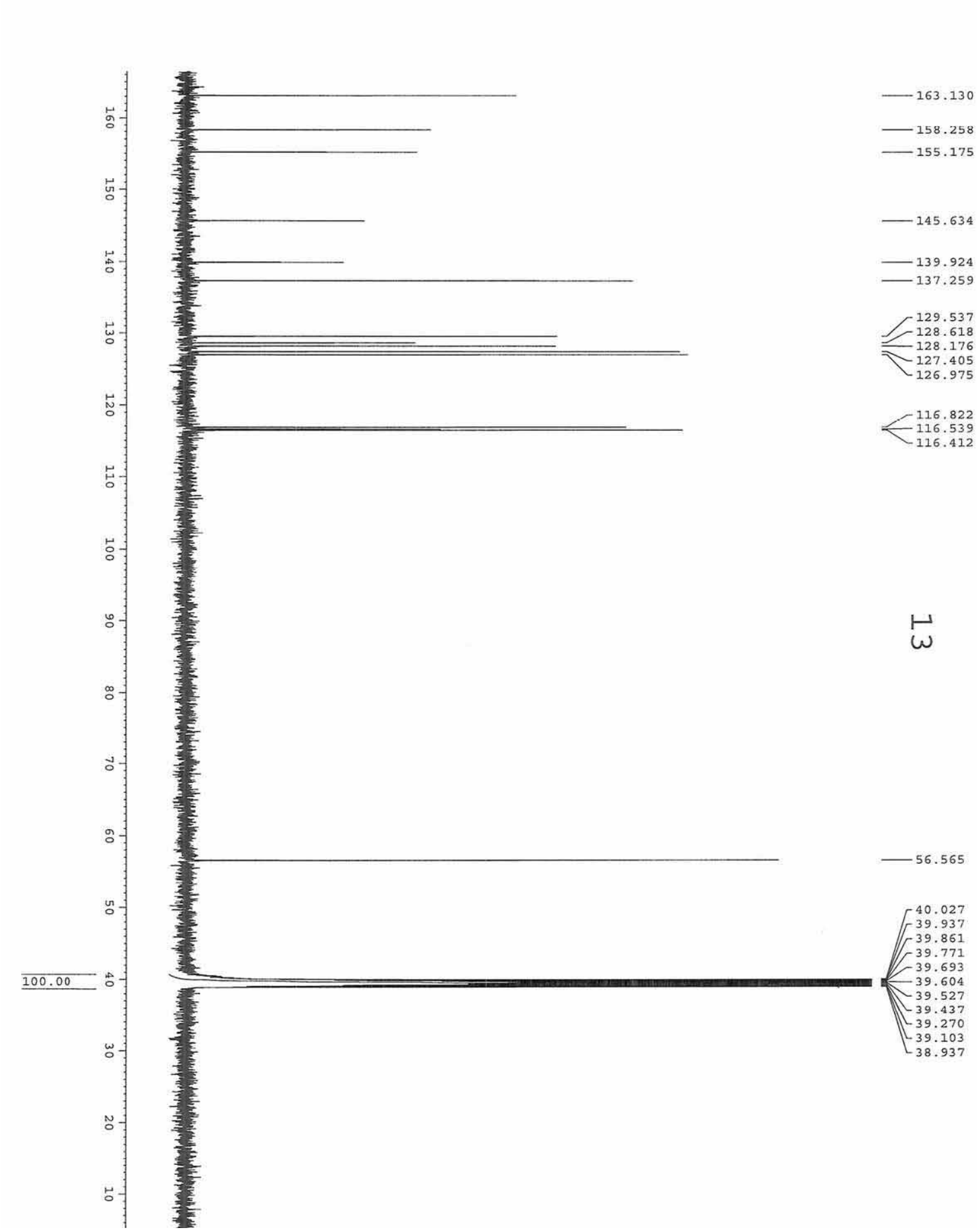
A solution of **16** (150 mg, 0.398 mmol) in CH_2Cl_2 (20 mL) was treated with BBr_3 (1 M in CH_2Cl_2, 0.45 mL, 0.45 mmol). The mixture was heated at reflux for 24 h. After this time, the reaction mixture was cooled to room temperature and MeOH (5 mL) was added. The mixture was concentrated under reduced pressure. The resulting residue was purified by flash chromatography. 23% (35.0 mg) of the starting material **16** was recovered. Taking into account the amount of **16** recovered, **4** was isolated in 46% yield (53.0 mg) as a white solid: mp 232–235 °C; $[\alpha]^{25}_D$ = -197.0 (*c* 0.3 in MeOH) (lit.[5] $[\alpha]_D^{25}$ -90° (c 0.007, MeOH)). 100% *ee* was determined by HPLC analysis using CHIRALCEL OJ column (4.6 × 250 mm, 40% heptane: 60% EtOH with 0.1% TFA at 1 mL/min, wavelength 245 nm), retention time: t_S= 29.9 min, and t_R= 13.3 min. NMR data are consistent with the literature:[5] ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.87 (s, 1H), 7.81 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.64 (td, *J* = 7.7, 1.7 Hz, 1H), 7.57 (m, 2H), 7.04 (d, *J* = 2.8 Hz, 1H), 6.89 (d, *J* = 2.8 Hz, 1H), 4.59 (dd, *J* = 7.9, 1.7 Hz, 1H), 3.83 (s, 3H), 3.60 (ddd, *J* = 11.2, 7.7, 2.7 Hz, 1H), 3.47–3.41 (m, 1H), 3.26–3.21 (m, 1H), 2.18–2.03 (m, 2H), 1.98–1.91 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.4, 161.1, 158.9, 154.2, 150.7, 133.3, 132.2, 130.5, 129.7, 128.97, 128.93, 128.4, 122.4, 107.7, 97.9, 58.5, 55.5, 46.0, 26.1, 23.4.

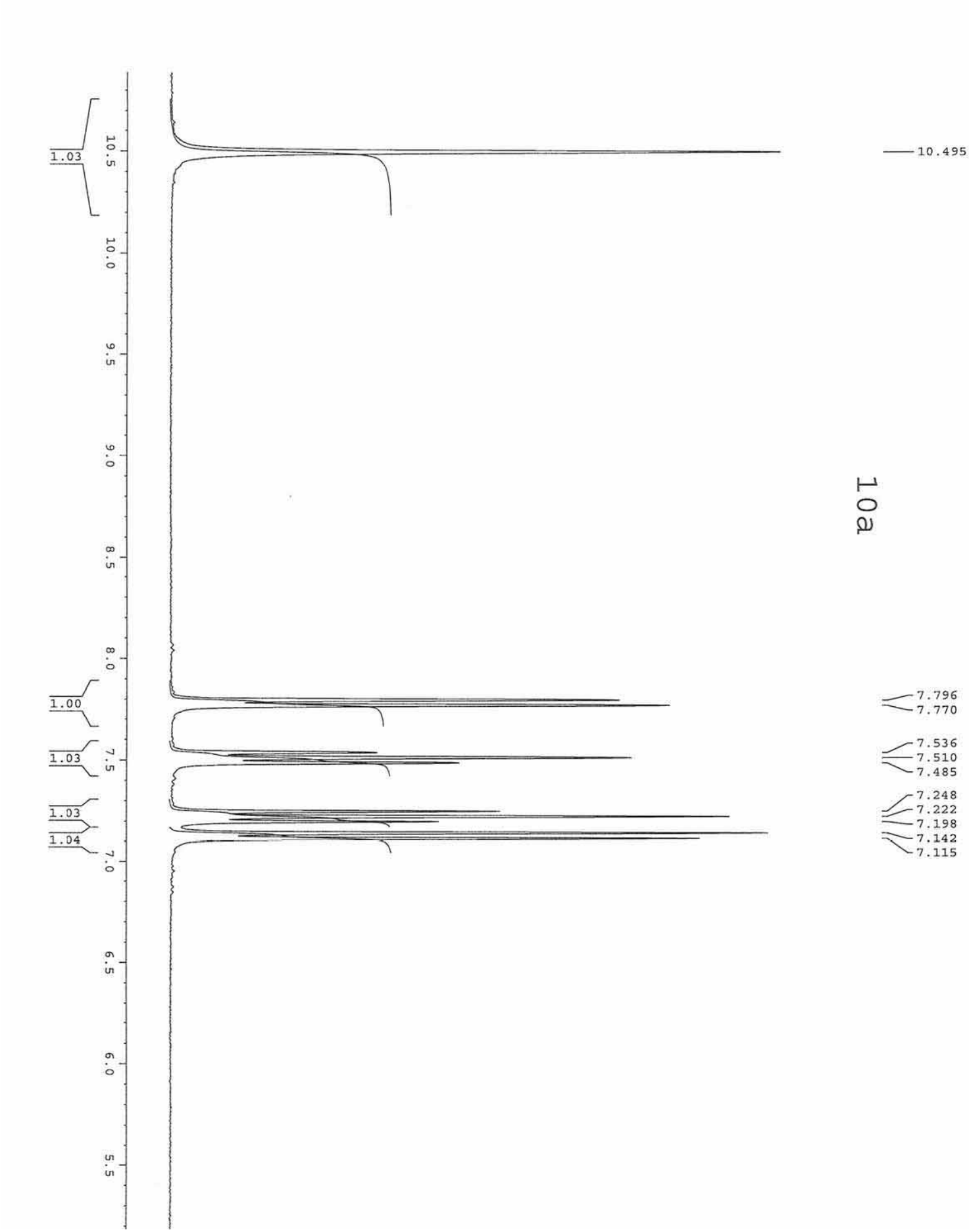
3. NMR Spectra

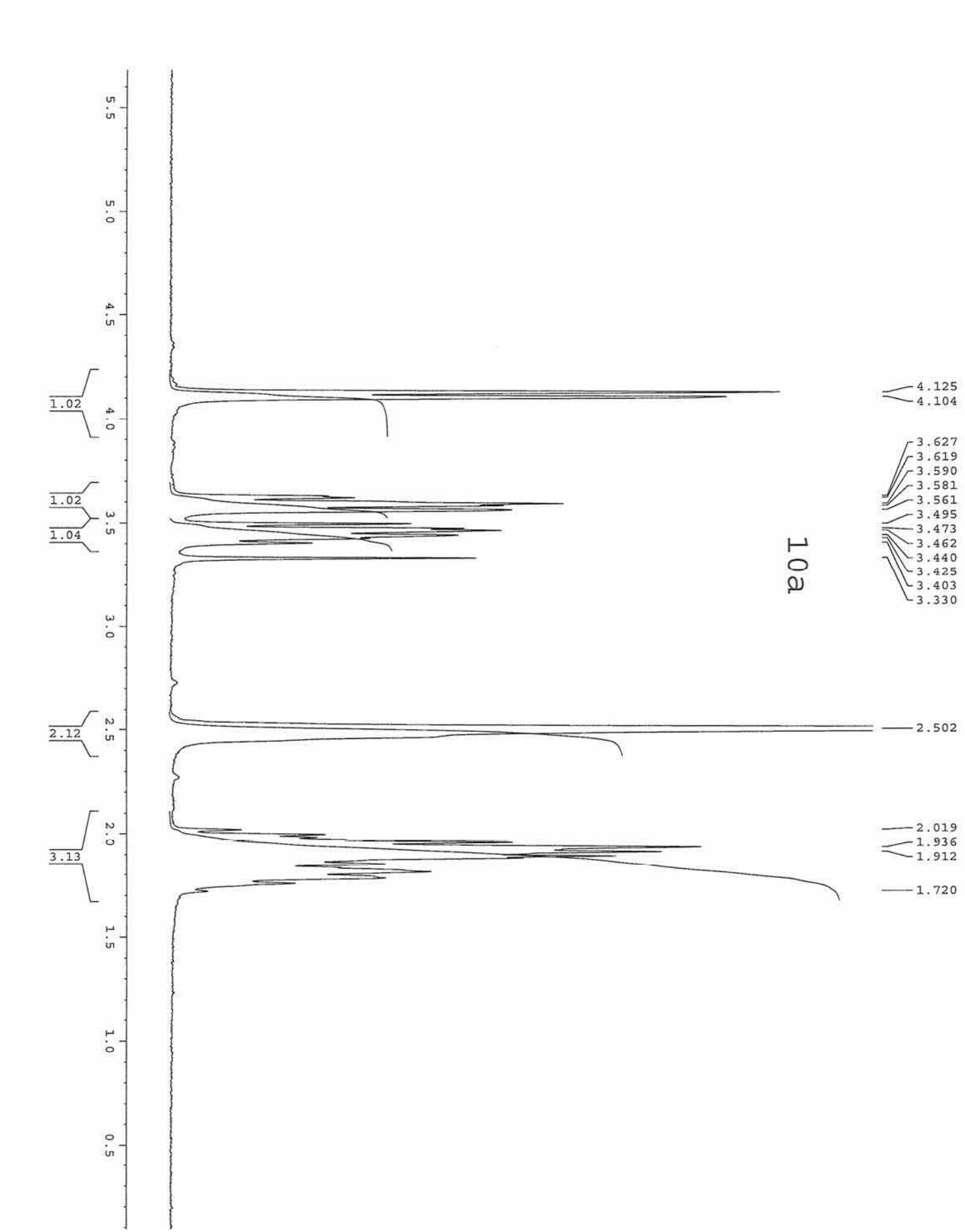


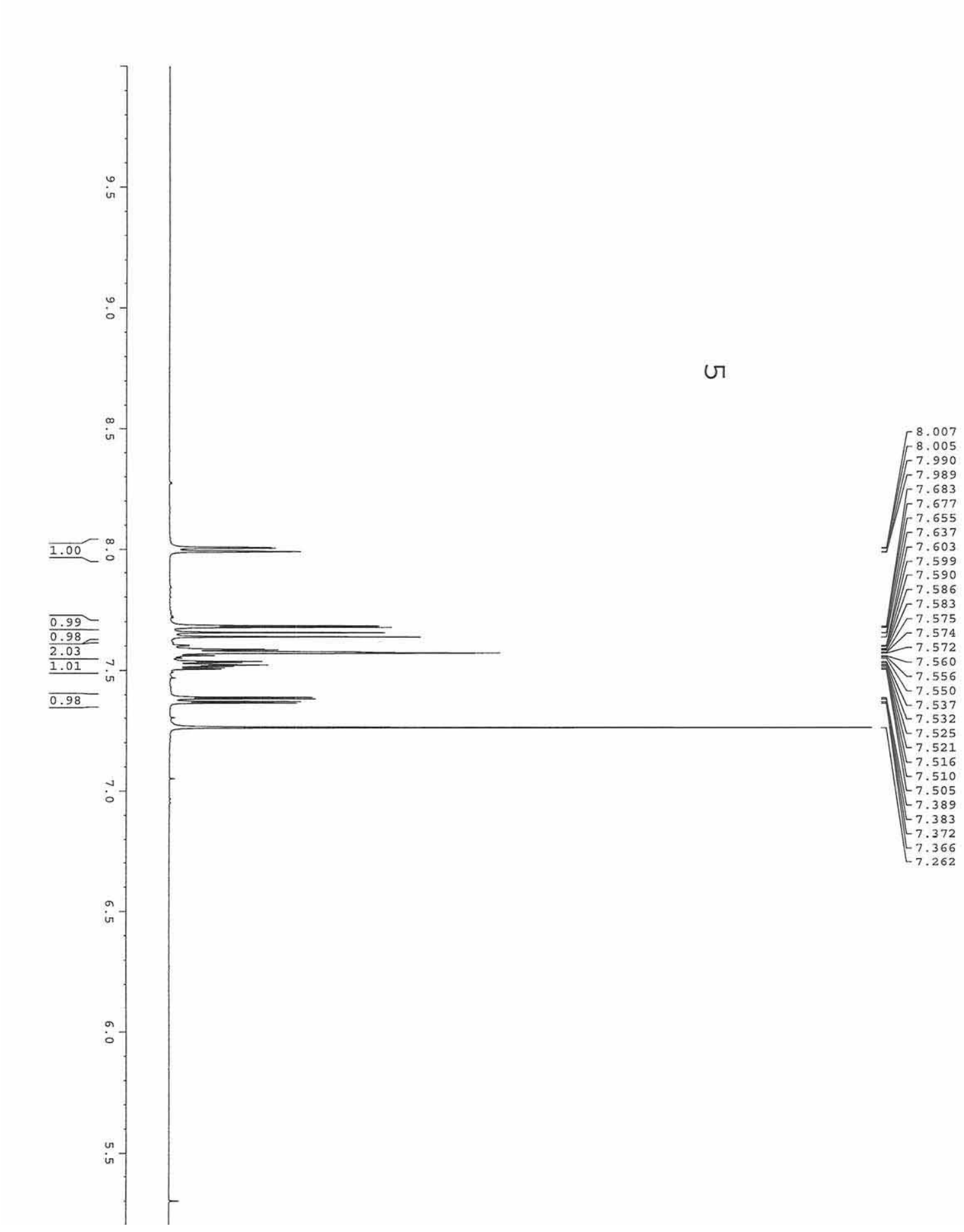


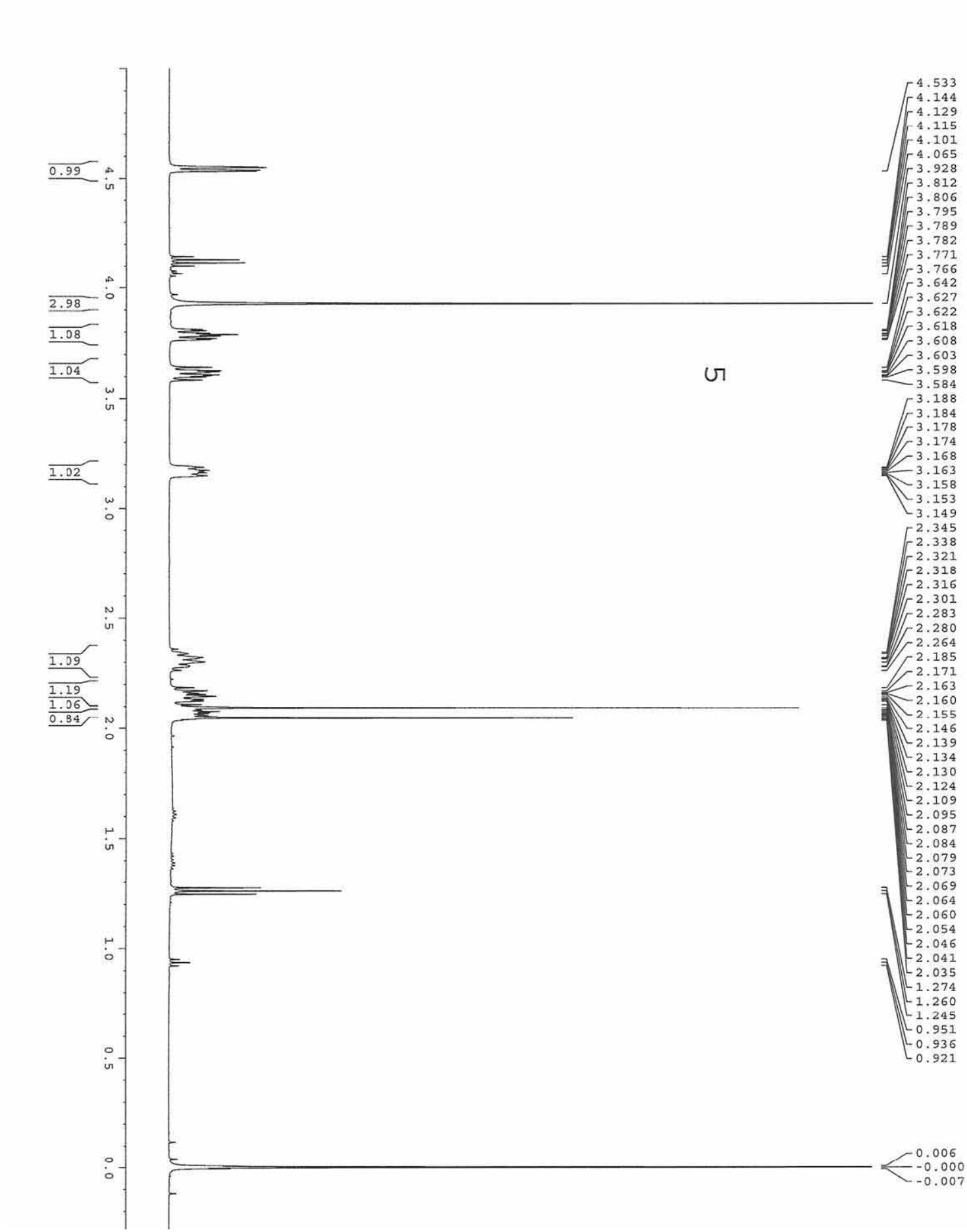








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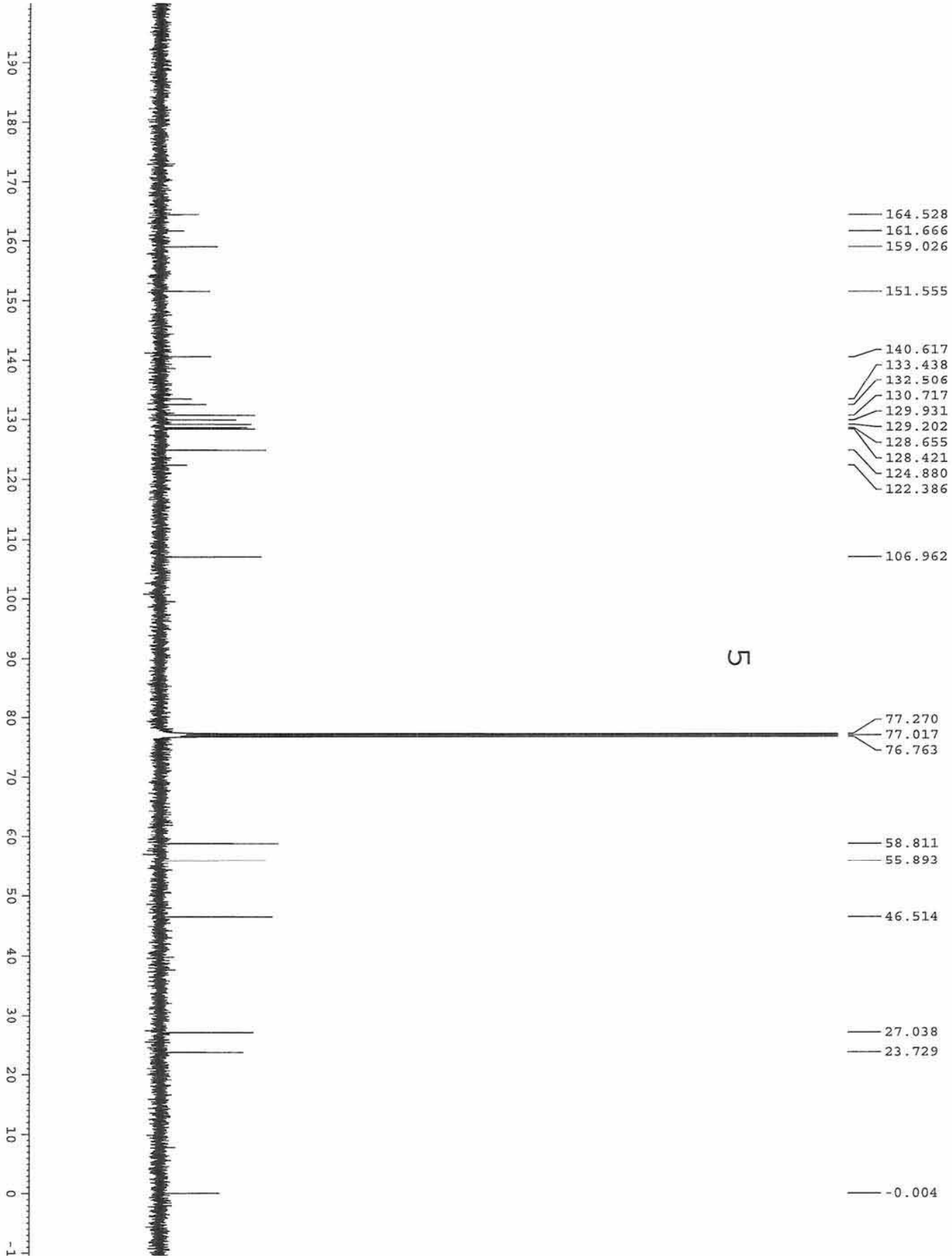

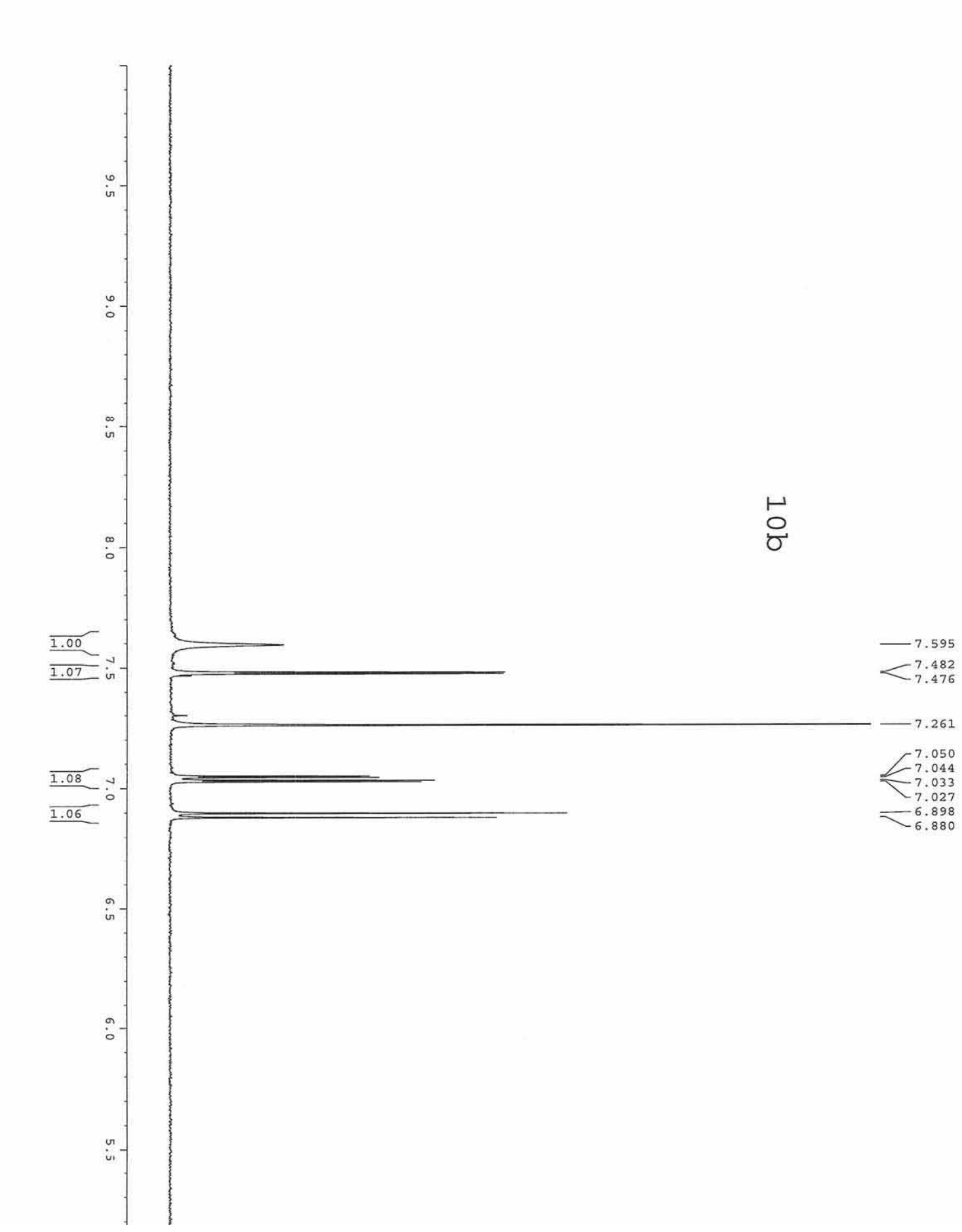

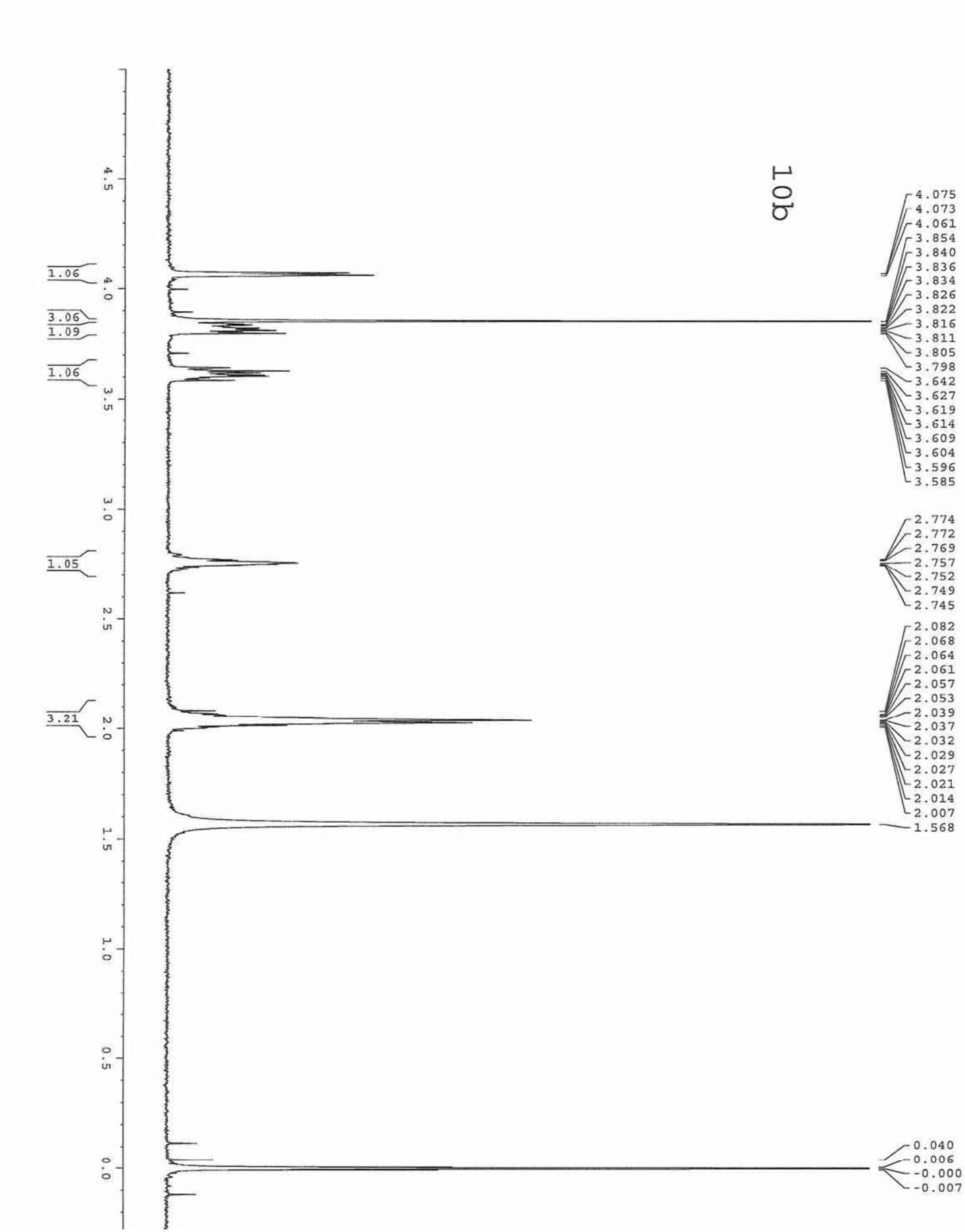

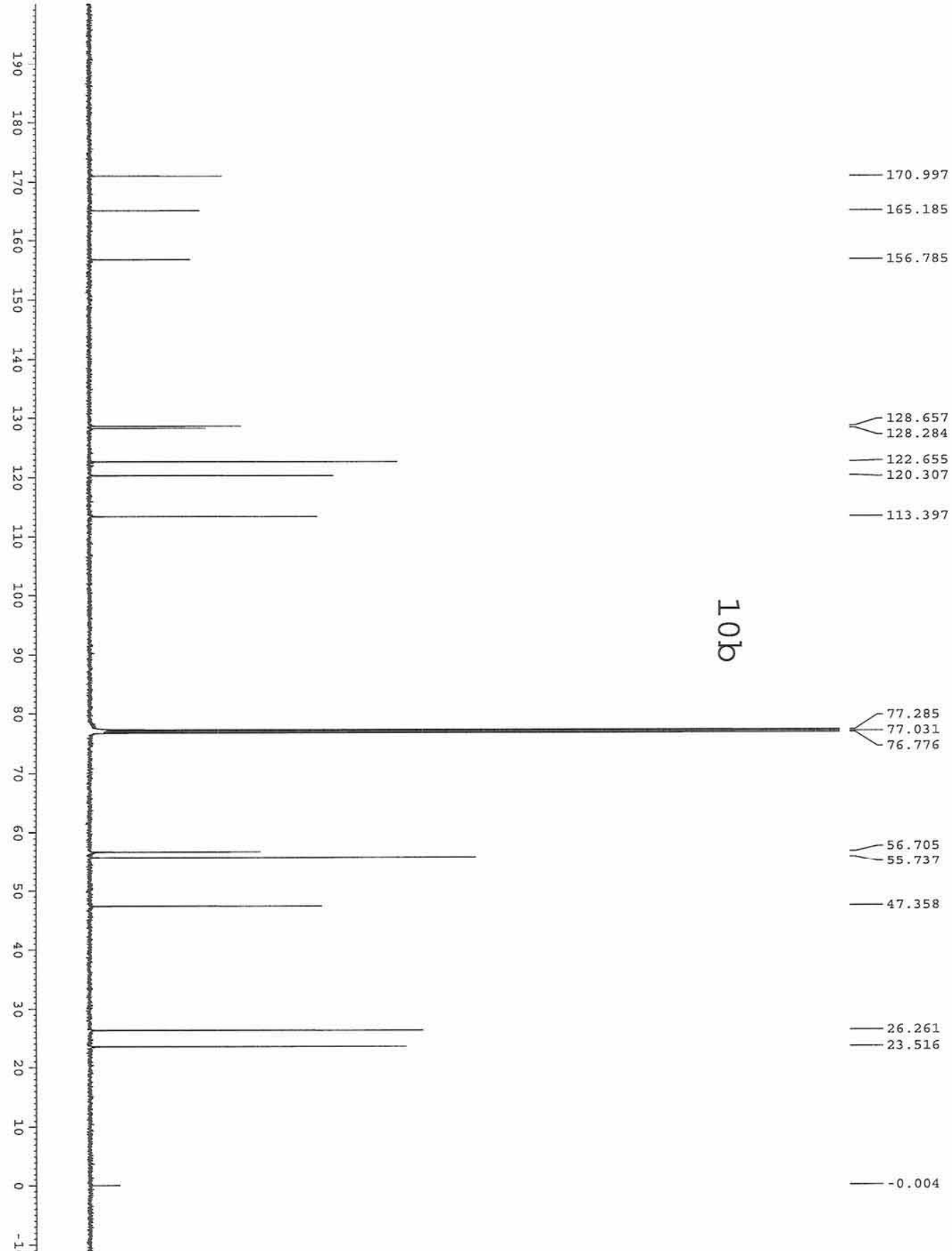

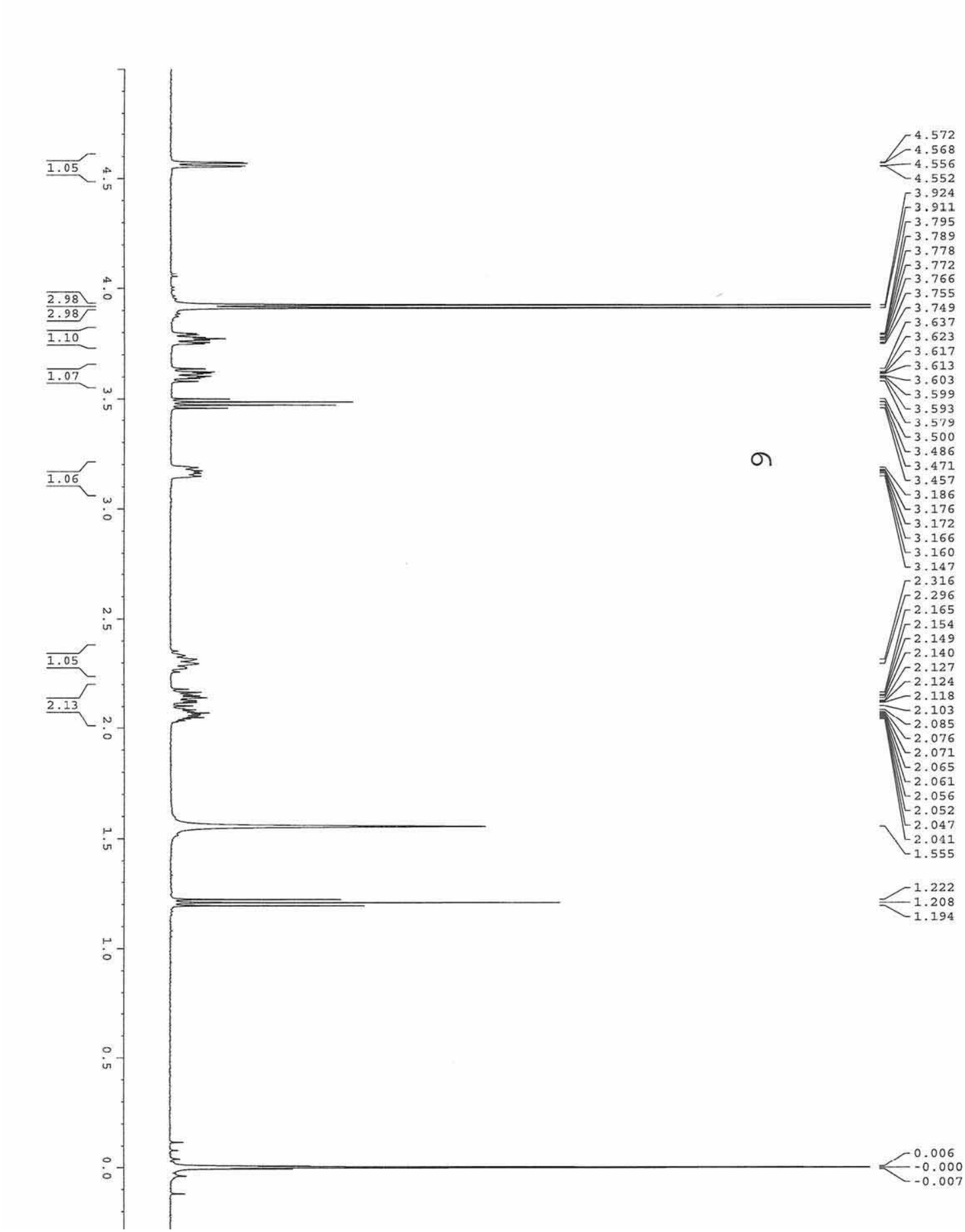
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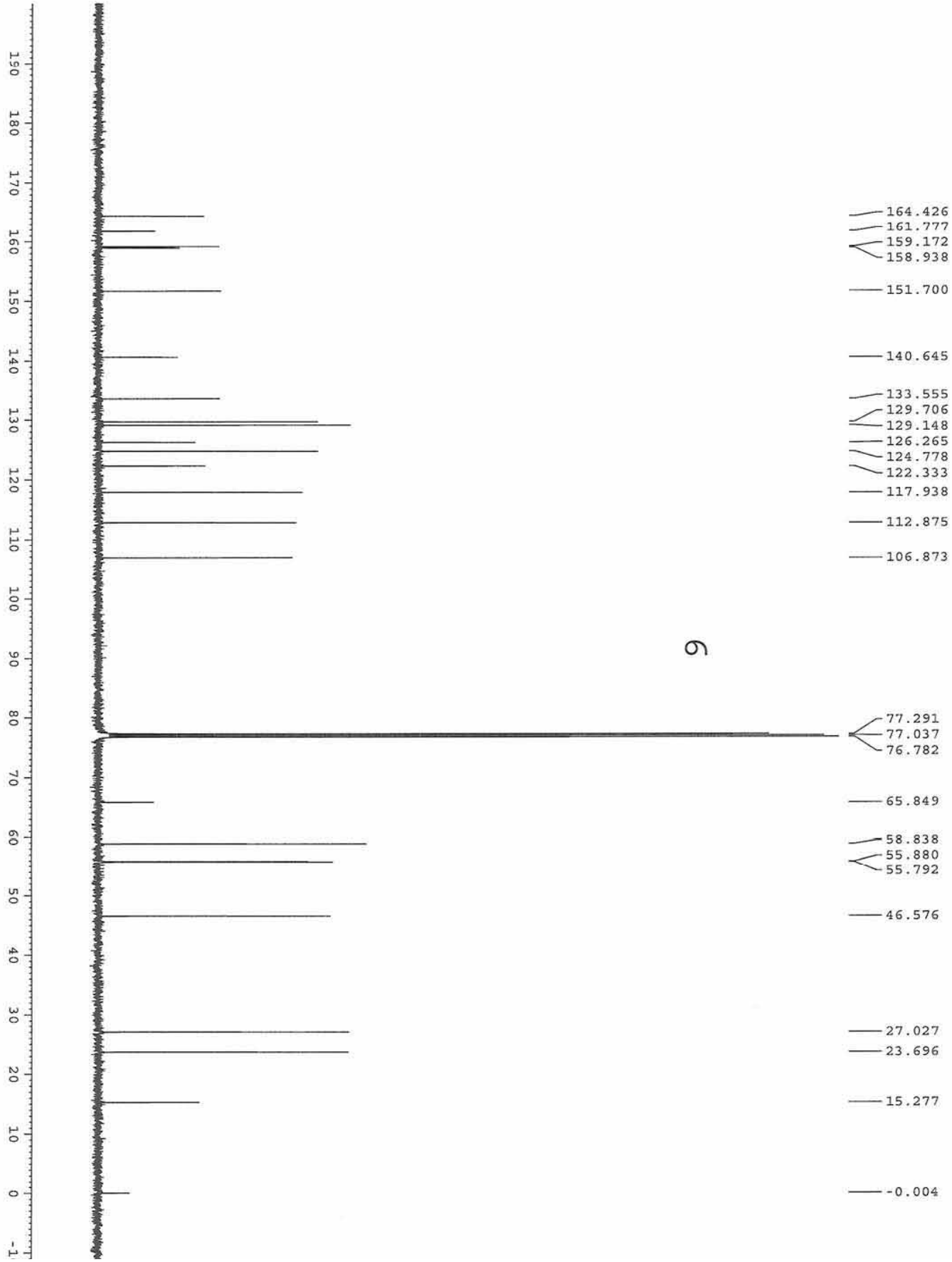

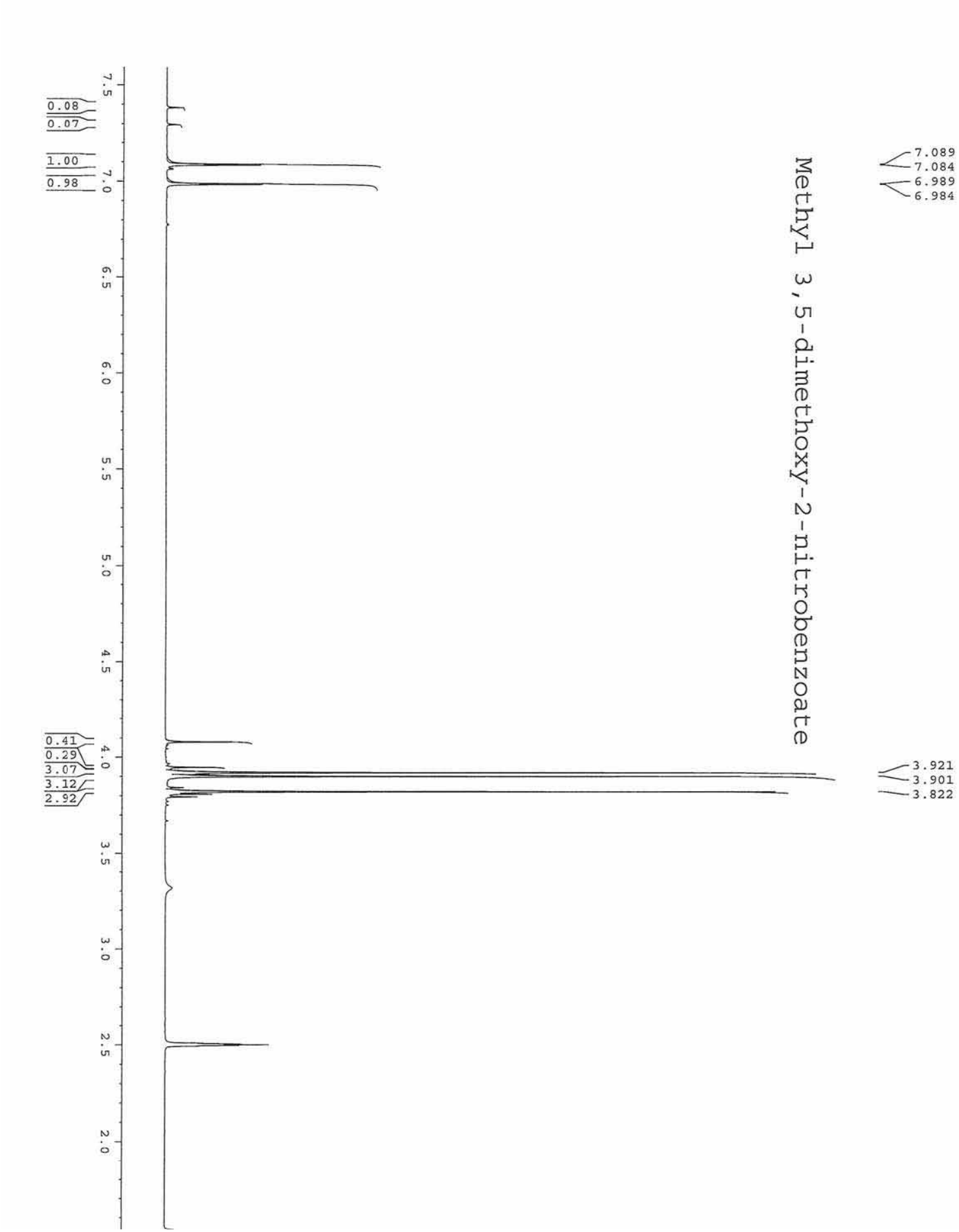

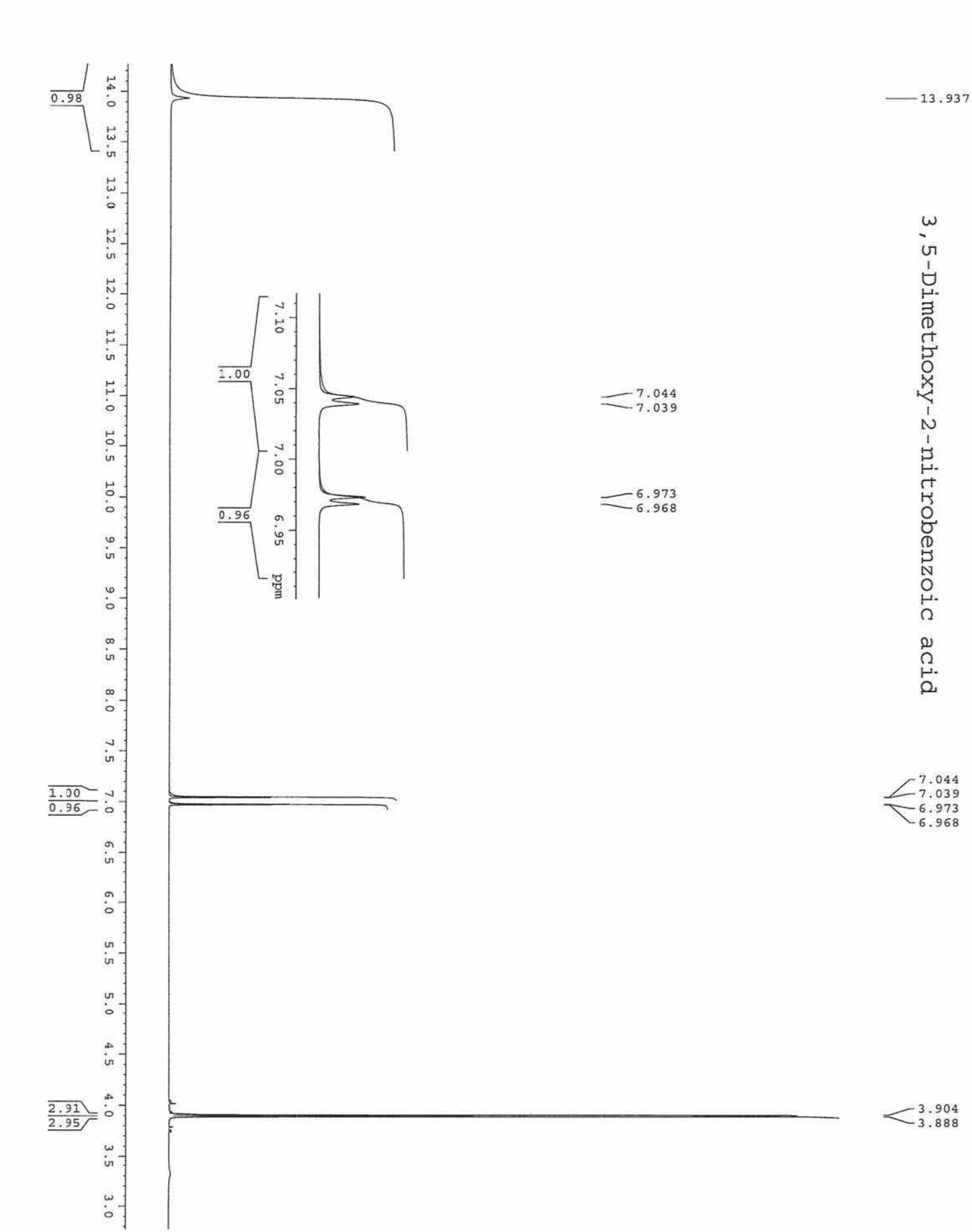

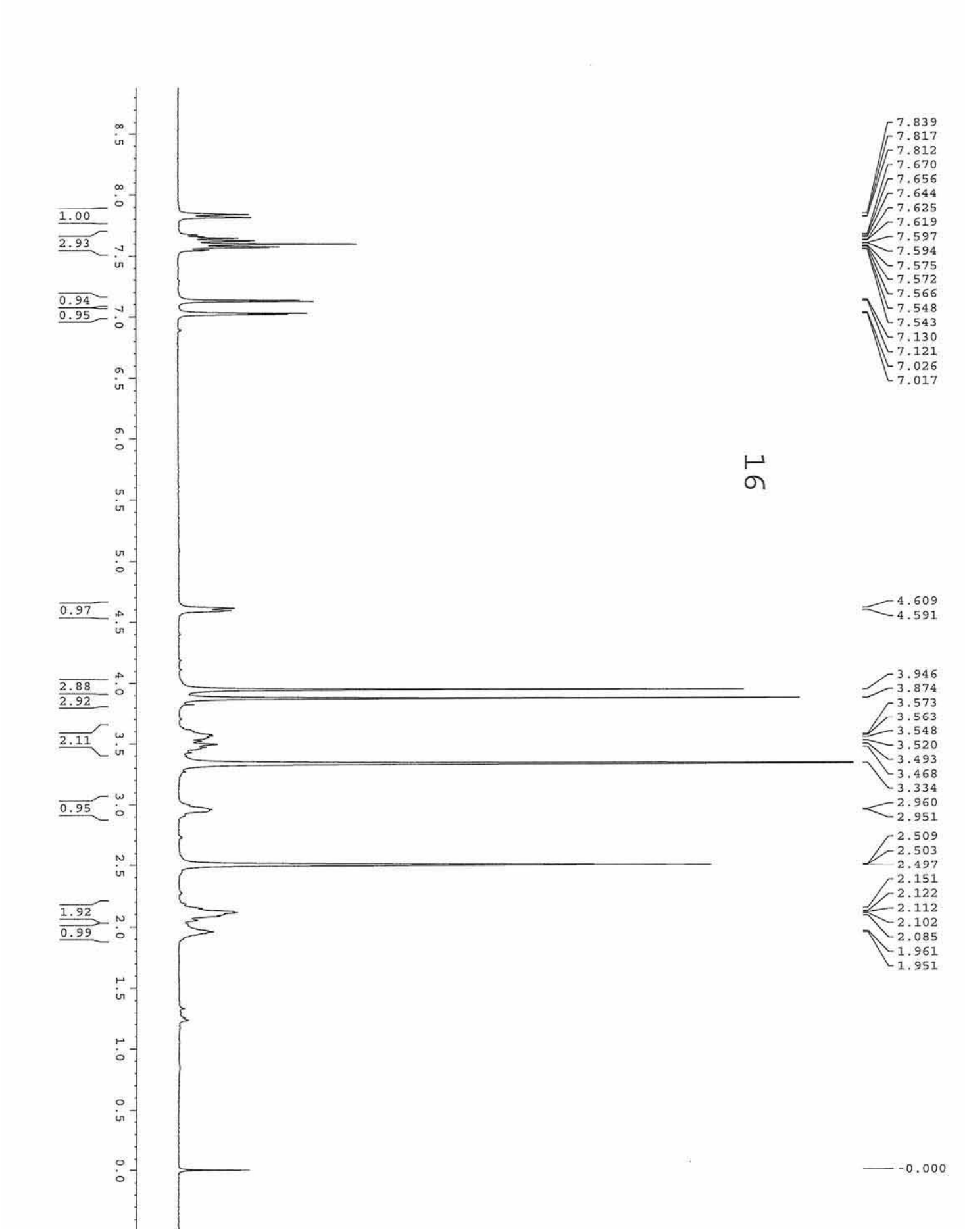

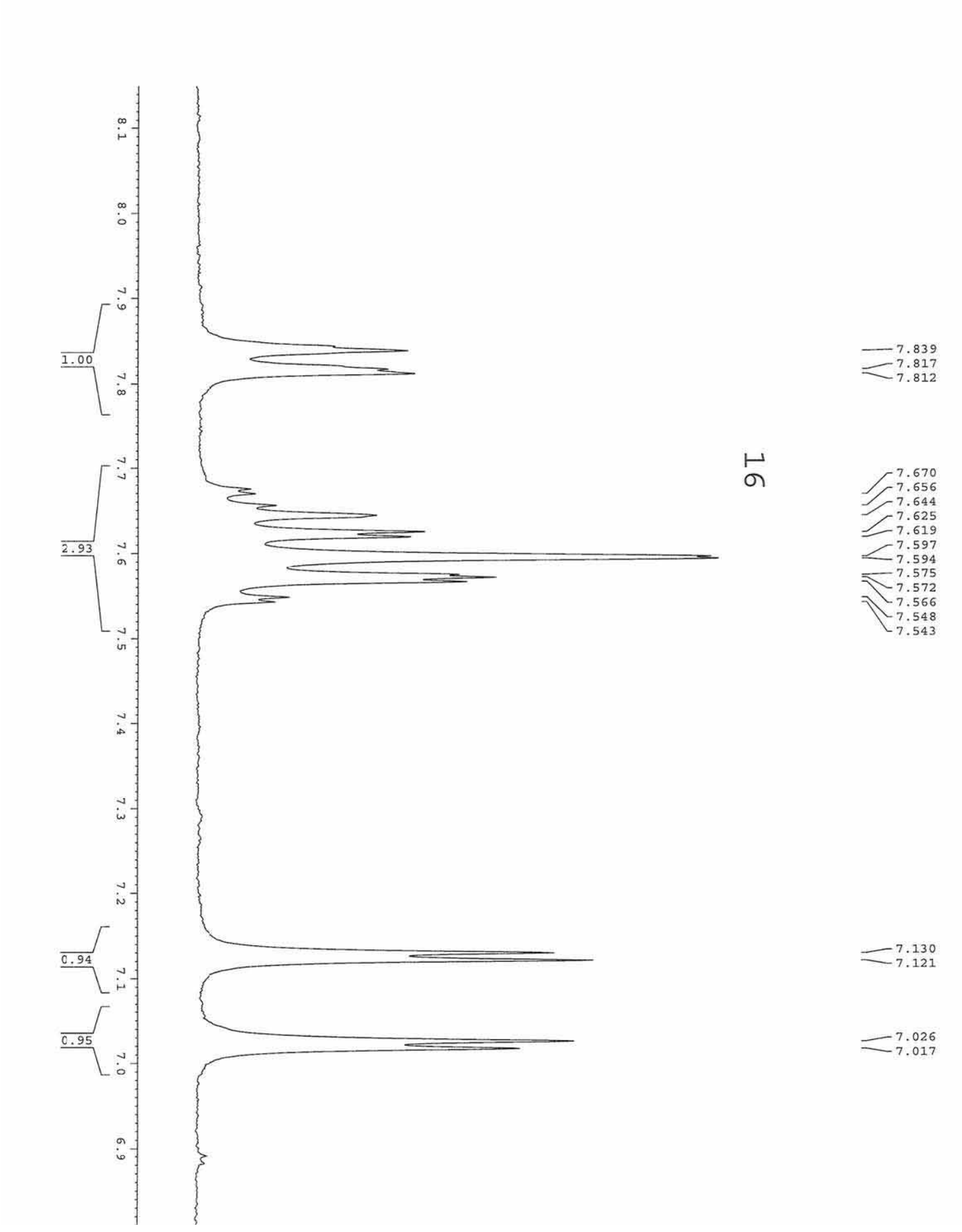

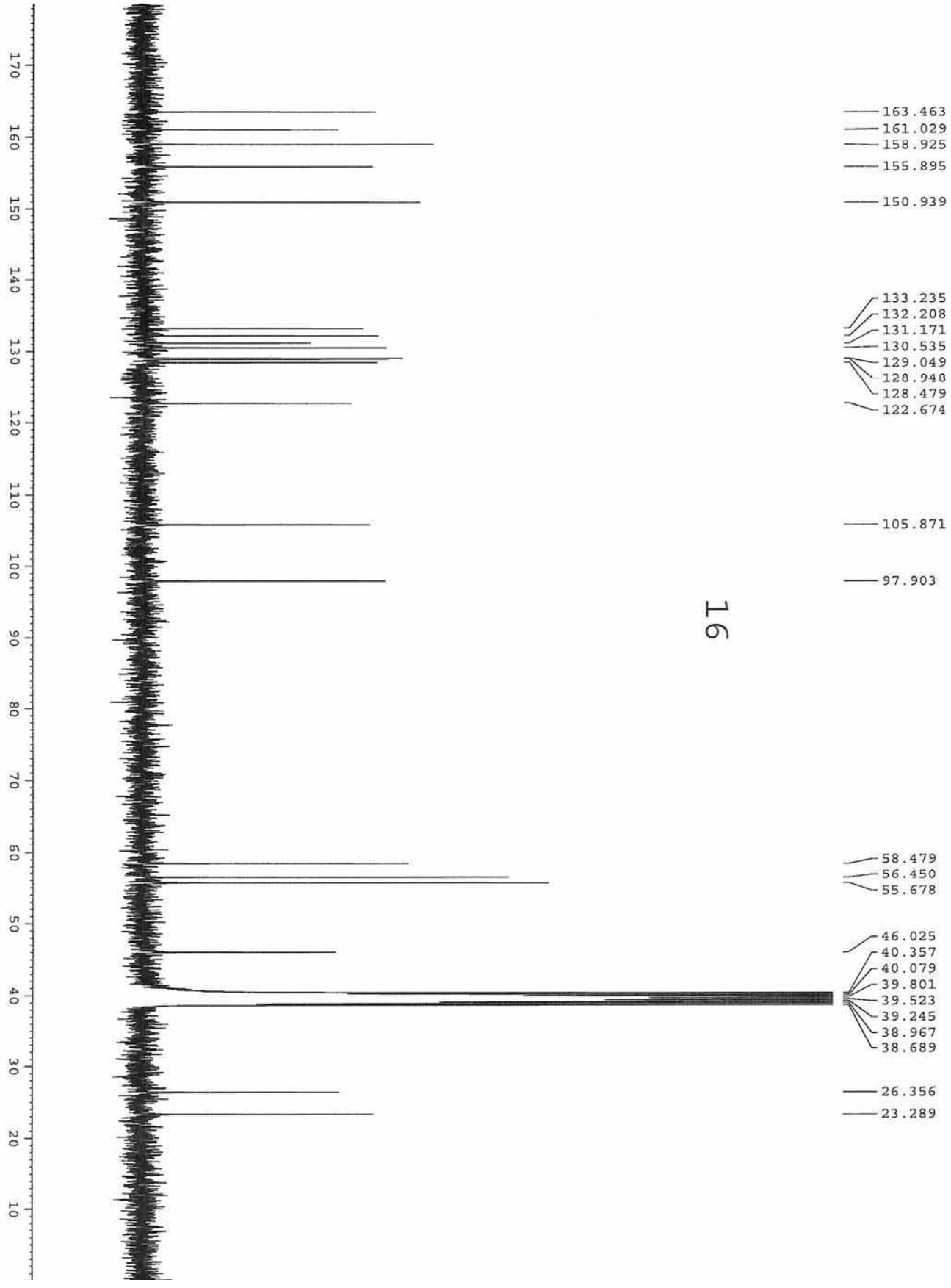

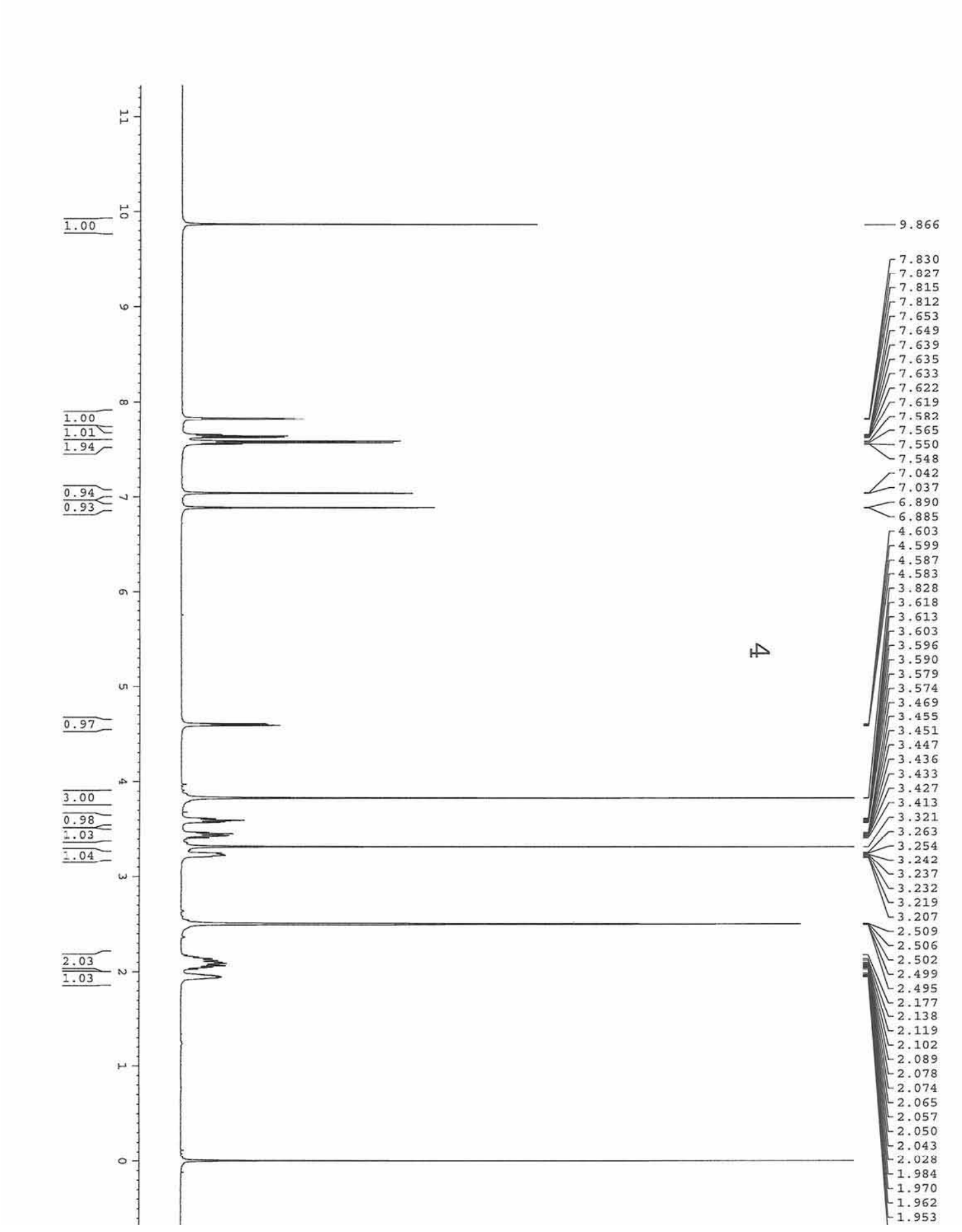

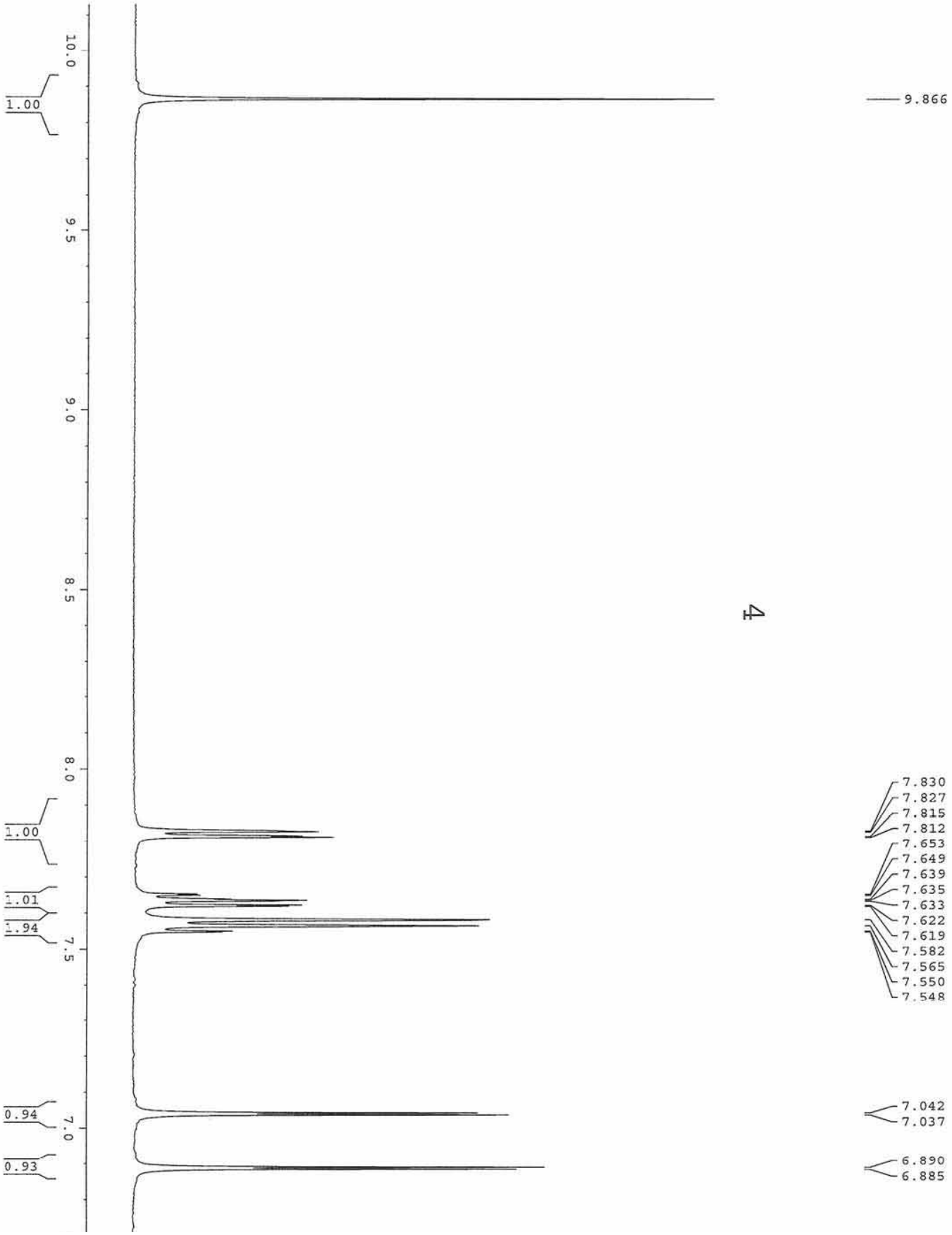
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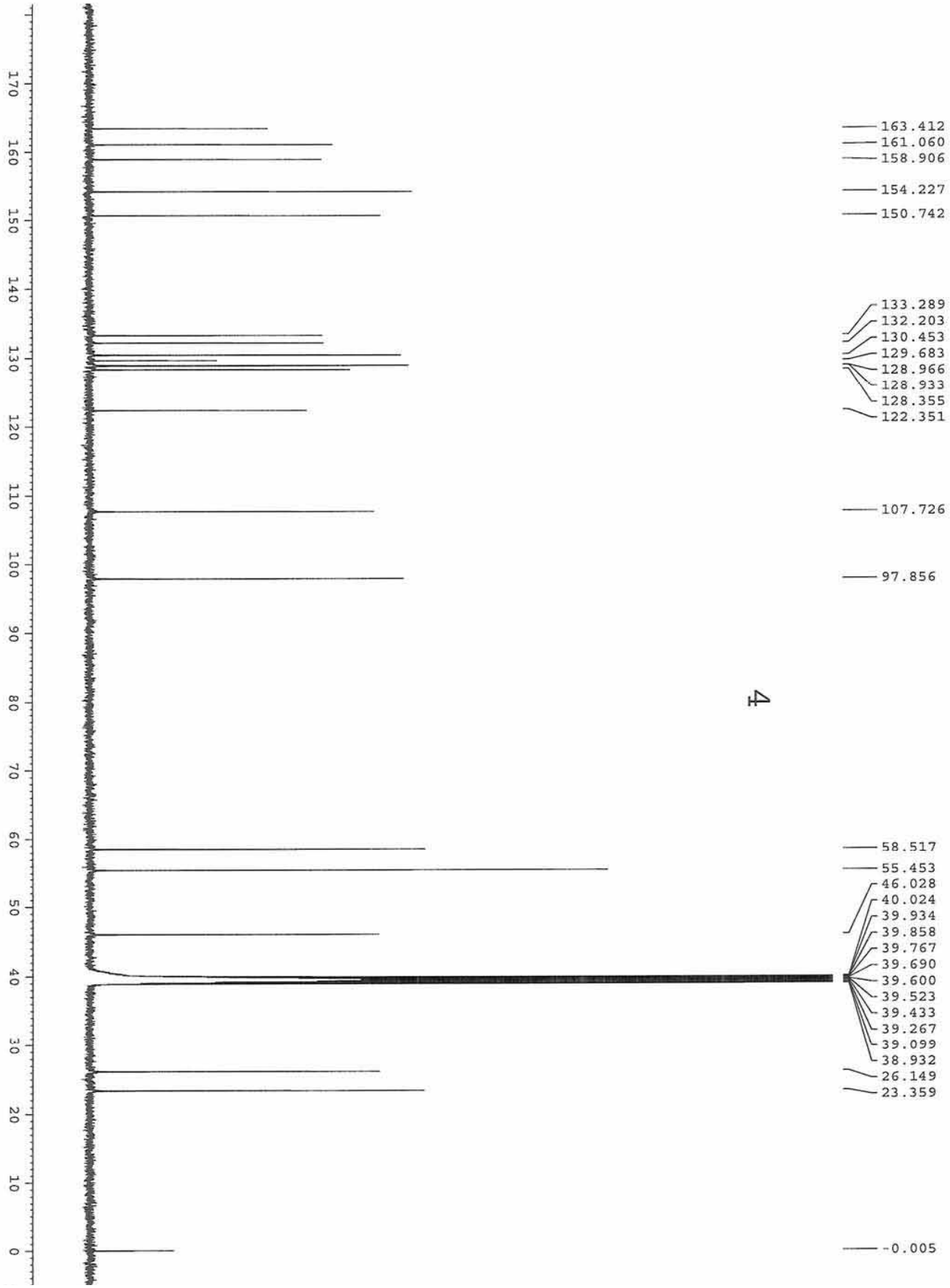

4. References

[1] R. L. Clark, K. C. Carter, A. B. Mullen, G. D. Coxon, G. Owusu-Dapaah, E. McFarlane, M. D. D. Thi, M. H. Grant, J. N. A. Tettey and S. P. Mackay, *Bioorg. Med. Chem. Lett.*, 2005, **17**, 624.
[2] M. P. Lopez-Gresa, M. C. Gonzalez, J. Primo, P. Moya, V. Romero and E. Estornell, *J. Antibiot.*, 2005, **58**, 416.
[3] R. Ookura, K. Kito, T. Ooi, M. Namikoshi and T. Kusumi, *J. Org. Chem.*, 2008, **73**, 4245.
[4] F. Roblot, R. Hocquemiller and A. Cavé, *Bull. Soc. Chim. Fr.*, 1990, **127**, 258.
[5] L. Rahbæk and J. Breinholt, *J. Nat. Prod.*, 1999, **62**, 904.