Supporting Information:

General. Unless otherwise noted, all reactions were run under nitrogen atmosphere and distilled solvents were transferred by syringe. Tetrahydrofuran (THF) and ether were distilled from sodium/benzophenone immediately before use; 1,1,1,3,3,3-hexamethyldisilazane (HMDS) and CH_2Cl_2 were distilled from CaH_2; Et_3N was distilled from BaO. Final reaction mixture solutions were dried over Na_2SO_4. Chromatography was on 230-400 mesh silica gel; TLC on aluminum-backed silica plates. Melting points are uncorrected. Mass spectral data, HRMS (EI and FAB), were obtained by the Université de Montréal Mass Spec. facility. ^{1}H NMR (300/400 MHz) and ^{13}C NMR (75/100 MHz) spectra were recorded in $CDCl_3$. Chemical shifts are reported in ppm (δ units) downfield of internal tetramethylsilane ($(CH_3)_4Si$). Coupling constants are given in Hz. Chemical shifts for aromatic PhF carbons are not reported.

Methyl 5-Oxo-4-(methyloxycarbonyl)-2-[*N*-(PhF)amino]hexanoate (2a). Crude **2a** (MS: *m/e* 458.1(m+1)) was used directly in the next step.

Methyl 5-Oxo-4-(ethyloxycarbonyl)-2-[*N*-(PhF)amino]heptanoate (2b) was prepared from ethyl propionylacetate and isolated as an inseparable 1.1:1 mixture of diastereomers by chromatography on silica gel eluting with a gradient of 10-20% EtOAc in hexane in 82% yield: ^{1}H NMR δ 0.98 (t, 3 H, J = 7.2), 1.11 (t, 3 H, J = 7.2), 1.19 (t, 3 H, J = 7.2), 1.28 (t, 3 H, J = 7.2), 1.91-1.99 (m, 4 H), 2.32-2.39 (m, 2 H), 2.52-2.68 (m, 4 H), 3.24 (s, 3 H), 3.25 (s, 3 H), 3.67 (t, 1 H, J = 6.4), 3.89-4.10 (m, 3 H), 4.23 (dd, 2 H, J = 7.2, 14.1), 7.14-7.70 (m, 26 H); ^{13}C NMR δ 7.35, 7.59, 13.8, 13.9, 32.5, 32.7, 35.1, 35.3, 51.3, 51.6, 53.6, 54.1, 54.9, 55.6, 61.1, 61.4, 72.6, 72.7, 169.0, 169.7, 175.9, 176.0, 204.6, 205.5; HRMS calcd for $C_{30}H_{31}O_5NNa$ (M^++Na) 508.2100, found 508.2116.

Methyl 6,6-Dimethyl-5-oxo-4-(ethyloxycarbonyl)-2-[*N*-(PhF)amino]heptanoate (2c) was prepared from ethyl pivaloylacetate and isolated as an 1:1 mixture of diastereomers by chromatography on silica gel eluting with a gradient of 10-20% EtOAc in hexane in 63% yield: ^{1}H NMR δ 1.10 (s, 9 H), 1.13 (t, 3 H, J = 7.1), 1.27 (t, 3 H, J = 7.1), 1.31 (s, 9 H), 1.48 (m, 1 H), 1.58 (m , 1 H), 2.03 (m, 1 H), 2.33 (m, 1 H), 2.60 (m, 2 H), 3.26 (s, 6 H), 3.81-3.98 (m, 3 H), 4.24 (q, 2 H, J = 7.1), 4.45 (dd, 1 H, J = 2.4, 10.4), 7.14-7.71 (m, 26 H); ^{13}C NMR δ 13.7, 14.0, 26.0, 26.2, 33.5, 34.4, 45.3, 45.6, 47.9, 49.8,

51.5, 51.7, 53.6, 54.6, 60.8, 61.2, 72.6, 72.8, 168.9, 169.5, 175.4, 176.5, 209.9, 210.5; HRMS calcd for $C_{32}H_{35}O_5NNa$ (M^++Na) 536.2413, found 536.2392.

Methyl 5-Oxo-4-(methylcarbonyl)-2-[*N*-(PhF)amino]hexanoate (2d) was used directly in the next step. HRMS calcd for $C_{28}H_{28}O_4N$ (MH^+) 442.2018, found 442.2033.

Methyl 5-Oxo-4-(phenylcarbonyl)-2-[*N*-(PhF)amino]hexanoate (2e) was isolated by chromatography on silica gel eluting with a gradient of 10-20% EtOAc in hexane as a 1.1:1 mixture of diastereomers in 45% yield from 1-benzoyl acetone: ^{1}H NMR δ 2.00 (s, 3 H), 2.07 (m, 4 H), 2.17 (s, 3 H), 2.58 (m, 2 H), 3.26 (s, 3 H), 3.28 (s, 3 H), 4.78 (t, 1 H, J = 6.0), 4.83 (dd, 1 H, J = 4.8, 7.4), 6.70-8.26 (m, 36 H); ^{13}C NMR δ 28.0, 28.7, 33.0, 33.2, 51.69, 51.73, 53.8, 54.5, 59.1, 59.3, 72.7, 72.8, 176.0, 195.0, 196.1, 202.9, 203.6; HRMS calcd for $C_{33}H_{30}O_4N$ (MH^+) 504.2175, found 504.2153.

4-(Methyloxycarbonyl)-2-[*N*-(PhF)]glutamate Dimethyl Ester (2f) was isolated by chromatography on silica gel eluting with a gradient of 10-20% EtOAc in hexane in 65% yield: ^{1}H NMR δ 2.03 (m, 2 H), 2.61 (dd, 1 H, J = 4.7, 8.9), 3.20 (s, 3 H), 3.36 (s, 3 H), 3.57 (s, 3 H), 3.73 (m , 1 H), 7.11-7.67 (m, 13 H); ^{13}C NMR δ 33.3, 48.3, 51.5, 52.3, 52.5, 53.7, 72.6, 77.3, 166.8, 169.0, 169.8; HRMS calcd for $C_{28}H_{27}O_6NNa$ (M^++Na) 496.1736, found 496.1728.

Methyl 5-Oxo-2-[*N*-(PhF)amino]hexanoate (6a). Crude methyl 5-oxo-4-(methyloxycarbonyl)-2-[*N*-(PhF)amino]hexanoate (**2a**) was dissolved in EtOH (10 mL), treated with 1 N NaOH (10 mL), and heated at a reflux for 5 h. The mixture was cooled to room temperature and adjusted to pH 5 using 10% HCl. The solution was extracted with EtOAc (3 × 30 mL) and the combined organic phases were washed with brine (30 mL), dried, filtered, and evaporated to a residue that was dissolved in acetonitrile (20 mL), treated with K_2CO_3 (300 mg, 2.2 mmol) and MeI (0.3 mL, 4.8 mmol) and stirred at room temperature for 18 h. Brine (50 mL) was added to the reaction mixture, which was extracted with EtOAc (3 × 30 mL). The organic phases were combined, washed with 0.65 M sodium thiosulfate (50 mL) and brine (50 mL), dried, filtered and evaporated to a residue that was purified by chromatography on silica gel using a gradient of 10-20% EtOAc in hexane. Evaporation of the collected fractions gave 259 mg (71% overall from **1**) of **6a**: ^{1}H NMR δ 1.71 (m, 2 H), 2.11 (s, 3 H), 2.45-2.61 (m, 3 H), 3.29 (s, 3 H), 7.18-

7.73 (m, 13 H); ^{13}C NMR δ 28.6, 29.8, 39.6, 51.5, 54.6, 72.8, 176.3, 207.8; HRMS calcd for $C_{26}H_{26}O_3N$ (MH^+) 400.1913, found 400.1905.

***cis*-*N*-(BOC)-5-Methylproline Methyl Ester (*cis*-7a).** A solution of methyl 5-oxo-2-[*N*-(PhF)amino]hexanoate (**6a,** 400 mg, 1 mmol) and di-*tert*-butyldicarbonate (670 mg, 3 mmol) in MeOH (50 mL) was placed into a hydrogenation vessel and treated with palladium-on-carbon (10 wt %, 65 mg). The vessel was filled, vented and filled three times with hydrogen and the mixture was stirred under 4 atm of hydrogen for 48 h. The mixture was filtered on celite™ and washed with MeOH (50 mL). The combined organic phase was evaporated to a residue that was purified by chromatography on silica gel using a gradient of 10-15 % EtOAc in hexane. Evaporation of the collected fractions gave 225 mg (92 %) of *cis*-**7a** as an oil: ^{1}H NMR δ (showed a mixture of carbamate isomers) 1.24 (d, 6 H, J = 6.2), 1.38 (s, 9 H), 1.42 (s, 9 H), 1.58 (m, 2 H), 1.97 (m, 4 H), 2.14 (m, 2 H), 3.68 (s, 6 H), 3.86 (m, 1 H), 3.98 (m, 1 H), 4.16 (m, 1 H), 4.27 (m, 1 H); ^{13}C NMR δ (showed a mixture of carbamate isomers) 19.7, 20.5, 28.3, 28.7, 31.6, 32.4, 51.9, 53.9, 59.7, 60.0, 79.5, 158.2, 159.0, 173.0, 173.9; HRMS calcd for $C_{12}H_{22}O_4N$ (MH^+) 244.1549, found 244.1556.

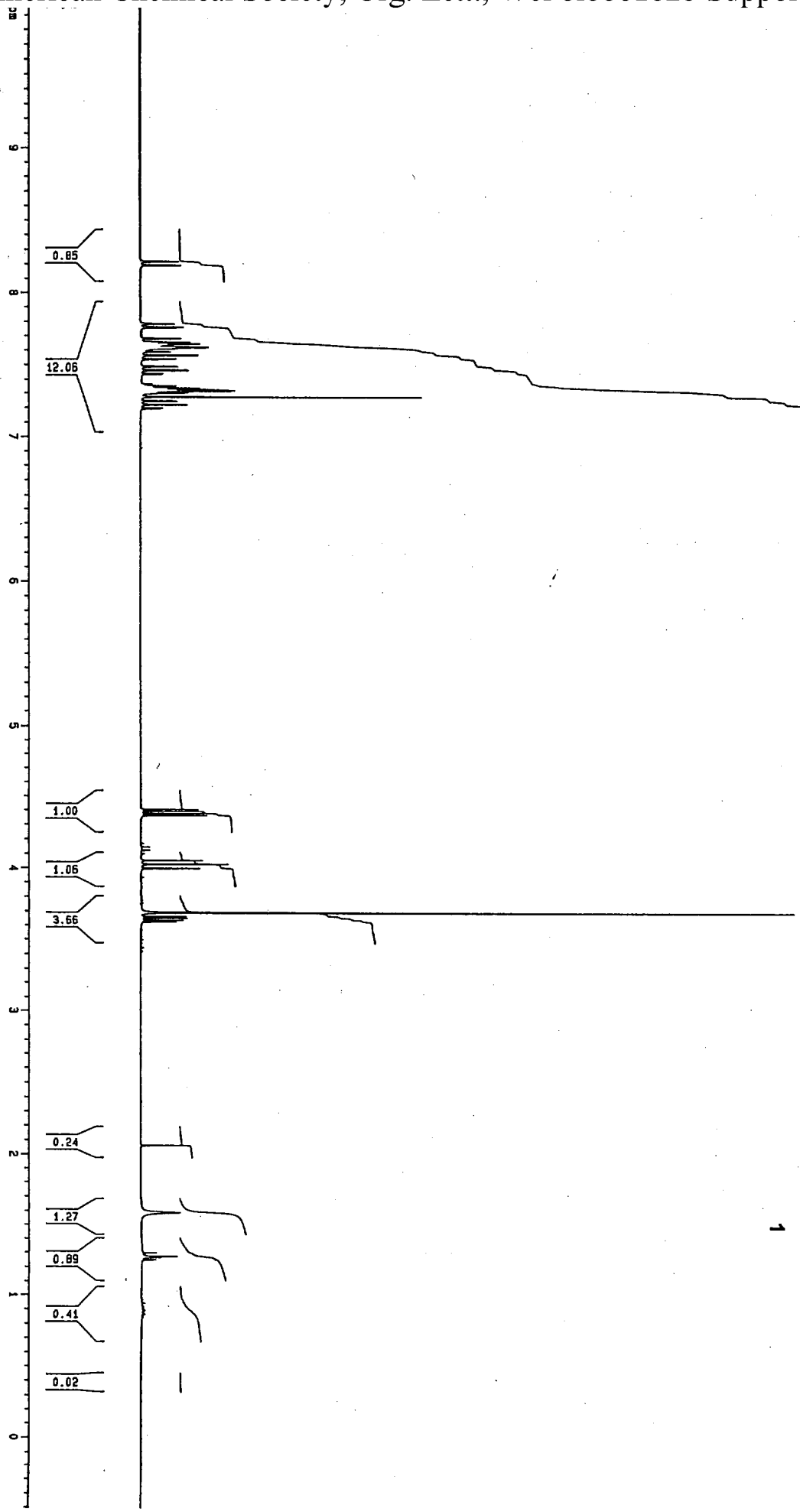
***cis*-*N*-(BOC)-5-Methylproline (*cis*-8a).** Methyl ester **7a** (110 mg, 0.45 mmol) was dissolved in 10 mL of Et_2O, treated with $KOSi(Me)_3$ (70 mg, 0.55 mmol) and stirred for 18 h at room temperature. The reaction mixture was extracted with water (5 × 20 mL), and the aqueous phases were combined, acidified with acetic acid to pH 2, saturated with NaCl, and extracted with EtOAc (3 × 30 mL). The organic phases were combined, dried, filtered and evaporated to give 99.4 mg (0.43 mmol, 96%) of *cis*-**8a**: ^{1}H NMR (CD_3OD) δ (showed a mixture of carbamate isomers) 1.27 (d, 3 H, J = 6.2), 1.42 (ds, 9 H), 1.65 (m, 1 H), 2.02 (m, 2 H), 2.23 (m, 1 H), 3.96 (m, 1 H), 4.18 (m, 1 H); ^{13}C NMR (CD_3OD) δ (showed a mixture of carbamate) isomers 20.1, 20.9, 28.6, 28.8, 29.3, 29.8, 32.7, 33.4, 49.6, 49.8, 55.4, 55.7, 61.2, 61.5, 81.2, 81.3, 155.4, 155.8, 176.6, 176.8; HRMS calcd for $C_{11}H_{20}O_4N$ (MH^+) 230.1392, found 230.1385.

Enantiomeric Purity of *cis*-*N*-(BOC)-5-Methylproline (*cis*-8a). A room-temperature solution of *cis*-*N*-(BOC)-5-methylproline (*cis*-**8a**, 20 mg, 0.09 mmol) and either (*R*) or (*S*)-α-methylbenzylamine (28 µl, 0.22 mmol) in 1 mL of acetonitrile was treated with benzotriazol-1-yl-1,1,3,3-tetramethyluronium tetrafluoroborate (30 mg, 0.09 mmol) and stirred for 2 h when TLC showed complete disappearance of the starting acid.

Brine (2 mL) was added to the reaction mixture that was then extracted with EtOAc (2 × 3 mL). The combined organic phase was extracted with 2 N HCl (2 × 2 mL) and $NaHCO_3$ (2 × 2 mL), washed with H_2O (2 × 2 mL) and brine, dried, filtered, and evaporated to a residue that was dissolved in CH_2Cl_2 (5 mL), treated with 0.5 mL TFA, and stirred at room temperature for 1 h. The solution was concentrated, dried and directly examined by ^{1}H NMR spectroscopy. When (*S*)- and (*R*)-α-methylbenzylamine of 99% diastereomeric purity were used respectively, the same mixture of diastereomers were obtained. Examination of the methyl doublets at 1.50, 1.49, 1.46 and 1.42 ppm in the ^{1}H NMR spectra in $CDCl_3$ demonstrated **9a** to be of 1.1:1 mixture of diastereomers. Hence, *cis*-**8a** is presumed to be of 10% enantiomeric excess.

***N*-TFA-5-Methylproline *N*'-α-Methyl-benzylamide (9a)**: ^{1}H NMR (CD_3OD) δ 1.42 (d, 3 H, *J* = 6.6), 1.46 (d, 3 H, *J* = 6.6), 1.49 (d, 3 H, *J* = 7.0), 1.50 (d, 3 H, *J* = 7.0), 1.60 (m, 1 H), 1.73 (m, 1 H), 2.04 (m, 1 H), 2.19 (m, 3 H), 2.42 (m, 2 H), 3.74 (m, 2 H), 4.31 (m, 2 H), 5.04 (m, 2 H), 7.22-7.37 (m , 10 H).

Methyl 1-*N*-PhF-2-Methyl-3-[(methyloxy)carbonyl]-Δ^2-pyrroline (11). A solution of (4*S*)-methyl 2,2-dioxo-3-PhF-1,2,3-oxathiazolidine-4-carboxylate (**1**, 60 mg, 0.14 mmol) in 8 mL of DME was treated with NaH (40 mg, 1 mmol), stirred at room temperature for 30 min. (A 0.5 mL aliquot was taken, poured into 1 M KH_2PO_4 and extracted with EtOAc (2 × 10 mL). The combined organic fractions were concentrated, dried on vacuum, and examined directly by ^{1}H NMR spectroscopy which showed complete conversion to dehydroalanine **5**: ^{1}H NMR δ 3.76 (s, 3 H), 4.63 (brs, 1 H), 5.62 (brs, 1 H), 7.20-7.74 (m, 13 H)). In a separate flask, a solution of methyl acetoacetate (50 μL, 0.46 mmol) in 3 mL of DME was treated with NaH (25 mg, 0.6 mmol) and stirred at room temperature for 1 h. The enolate solution was then added to the remaining solution of dehydroalanine, stirred at a reflux for 18h, poured into 40 mL of 1 M KH_2PO_4 and extracted with EtOAc (3 × 30 mL). The combined organic phases were washed with brine (2 × 30 mL), dried, filled, and evaporated to a residue that was chromatographed on silica gel eluting with a gradient of 10-15% EtOAc in hexane. Concentrated of the collected fractions provided 49.6 mg (87%) of **11**: ^{1}H NMR δ 2.08 (s, 3 H), 2.48 (dd, 1 H, *J* = 6.8, 12.8), 2.82 (t, 1 H, *J* = 12.8), 3.47 (dd, 1 H, *J* = 6.8, 12.8), 3.48 (s, 3 H), 3.61 (s, 3 H), 7.12-7.77 (m, 13 H); ^{13}C NMR δ 13.4, 33.8, 50.8, 52.2, 61.9, 77.0, 103.5, 161.9, 166.7, 174.7, 174.8; MS: *m/e* 440.3 (m+1), 307.1, 241.2.



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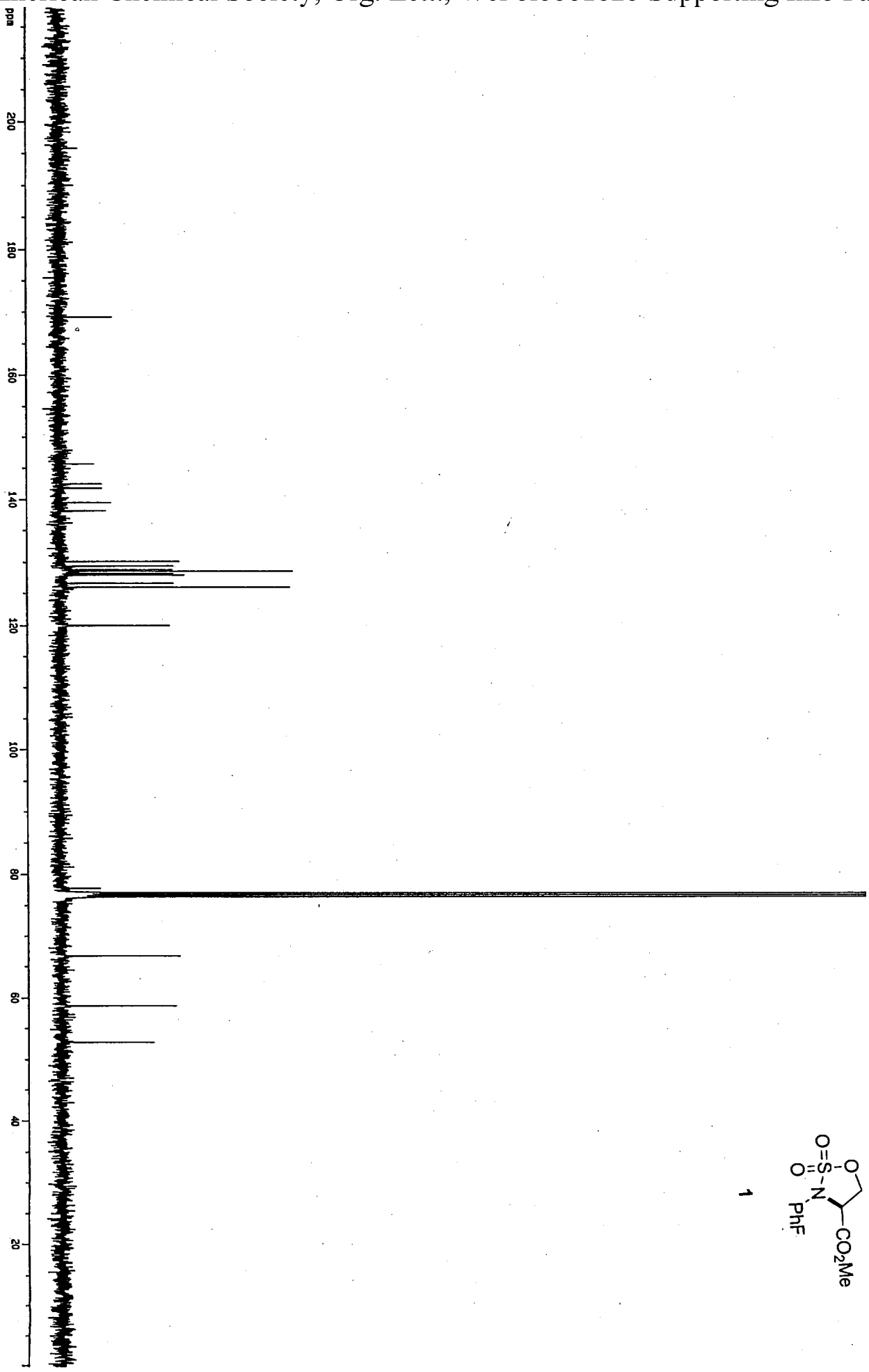
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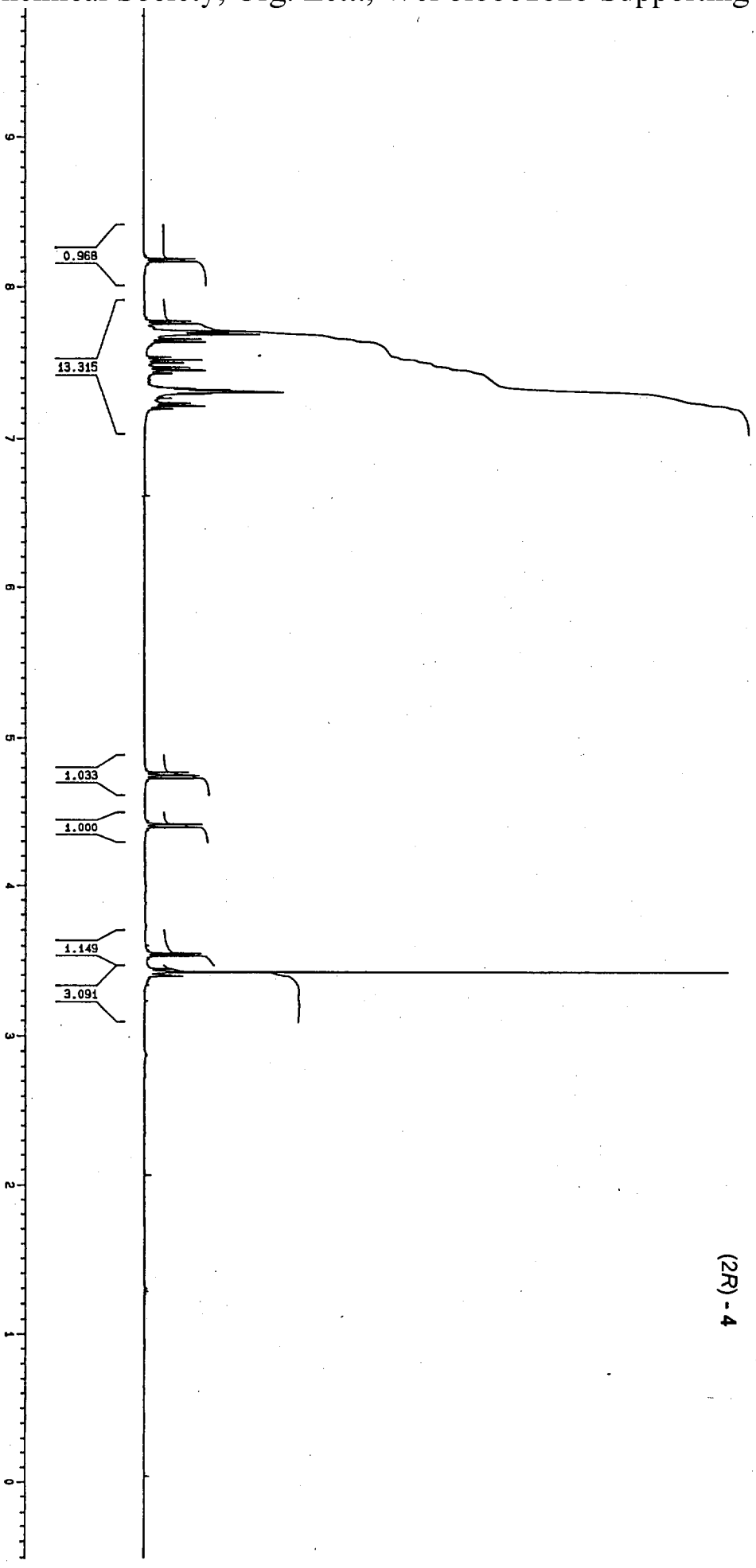
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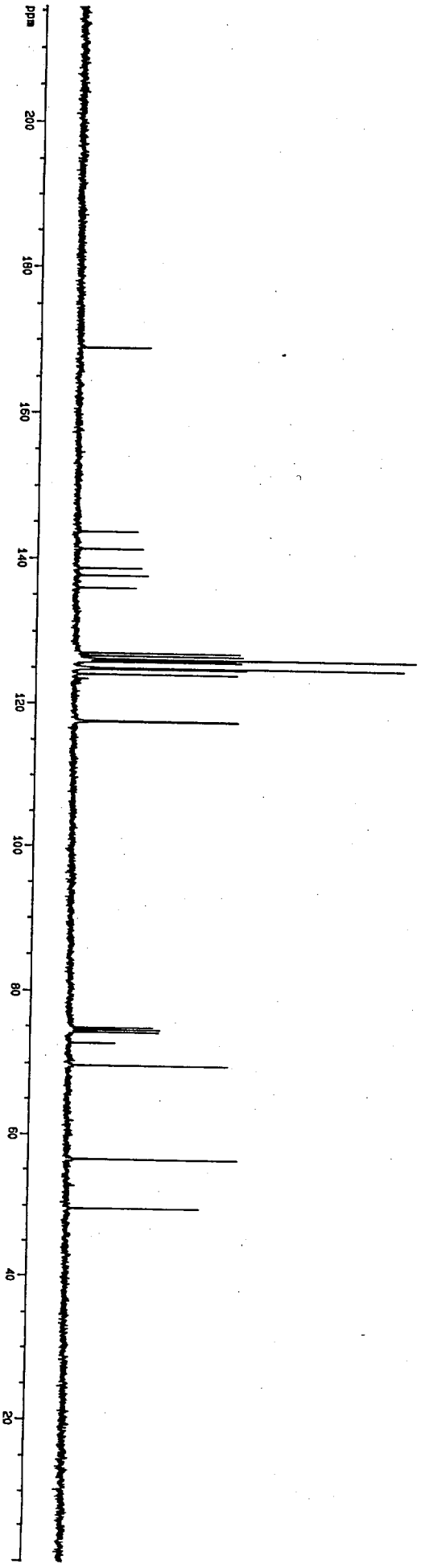

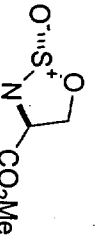

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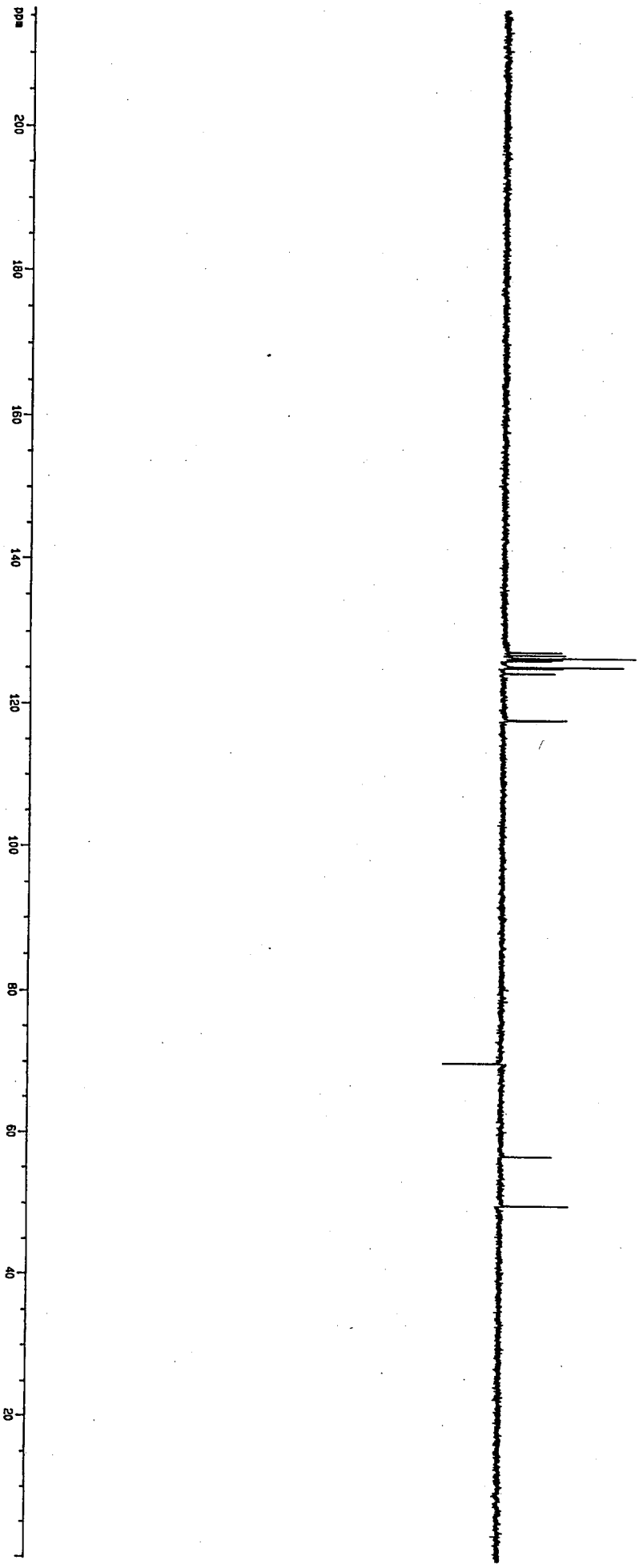

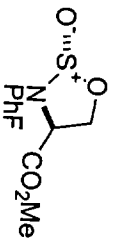

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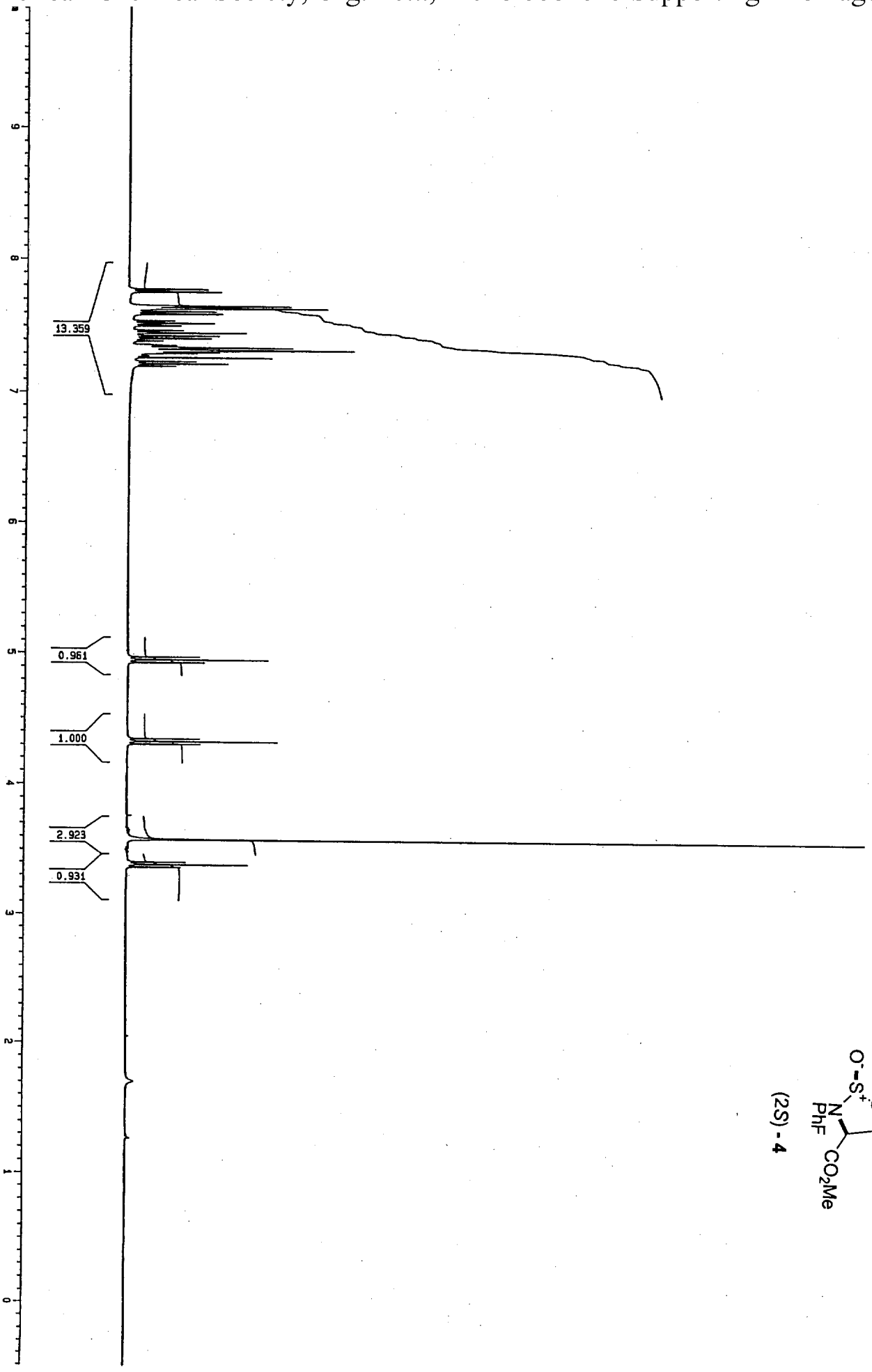

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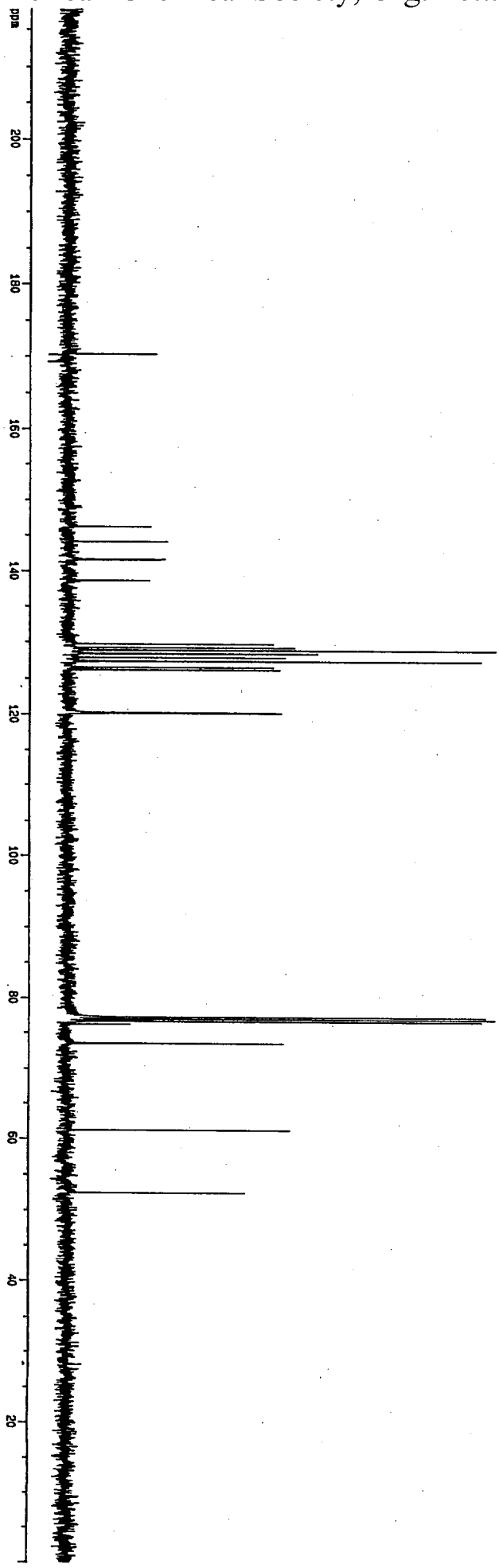

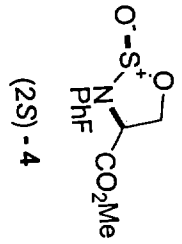

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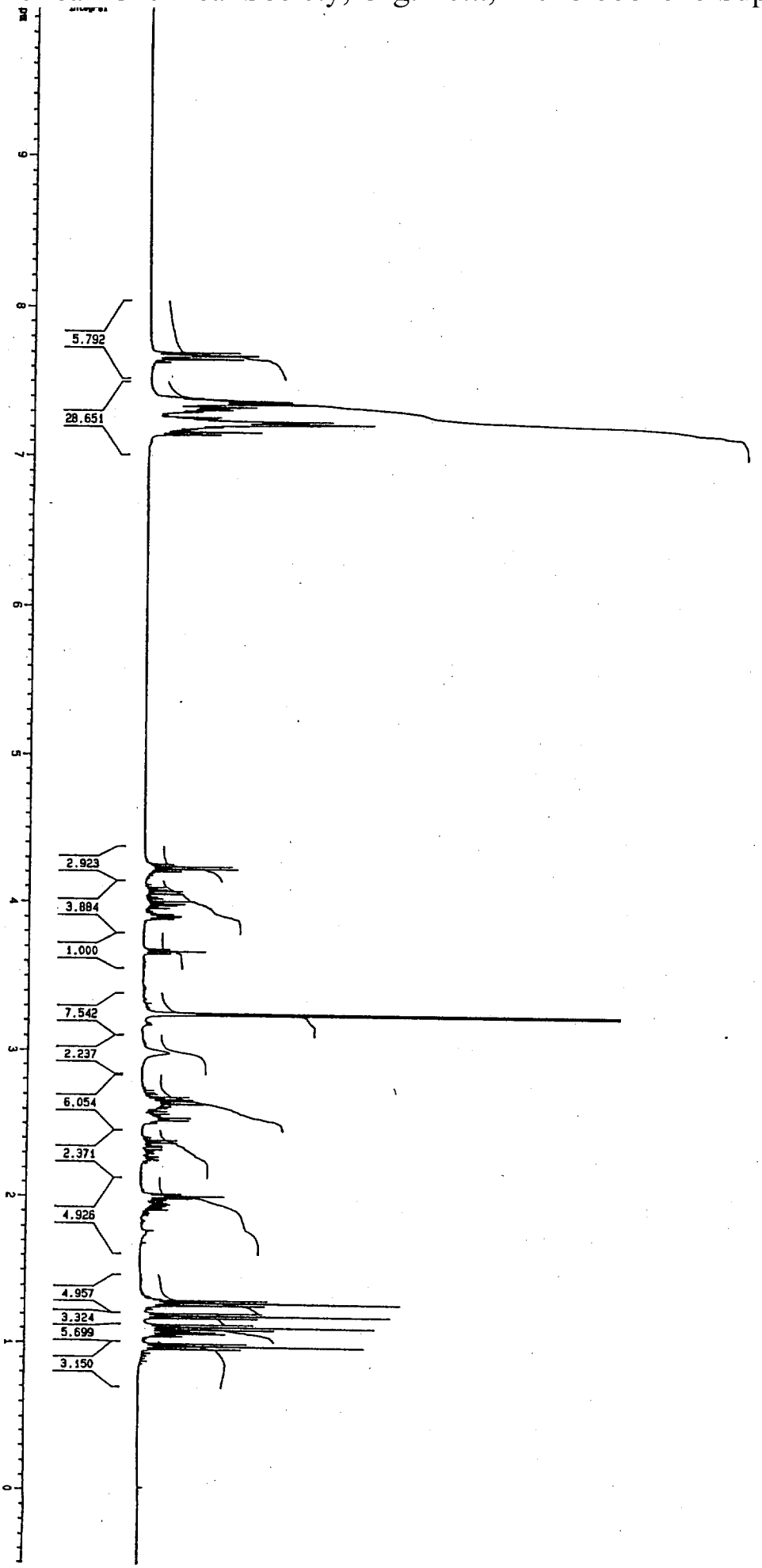
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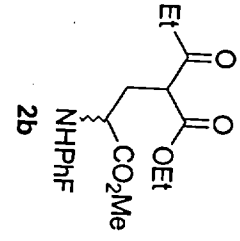
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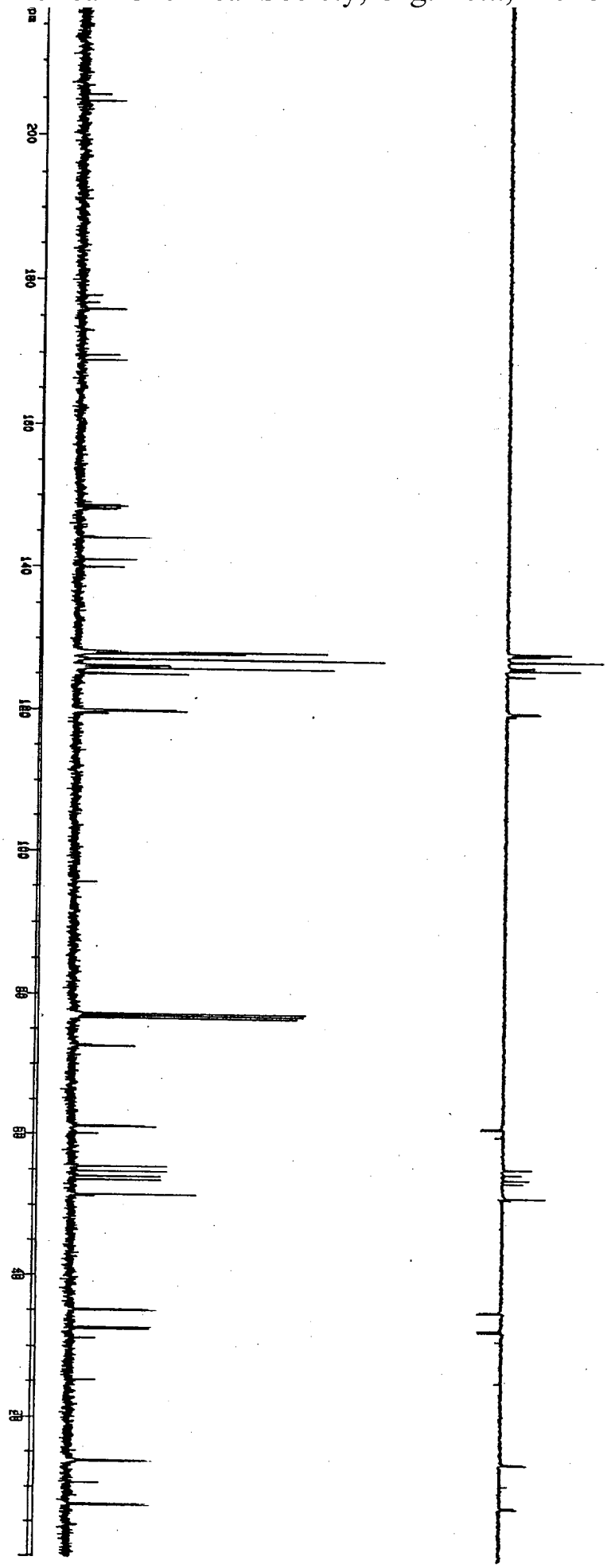

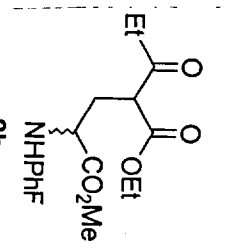

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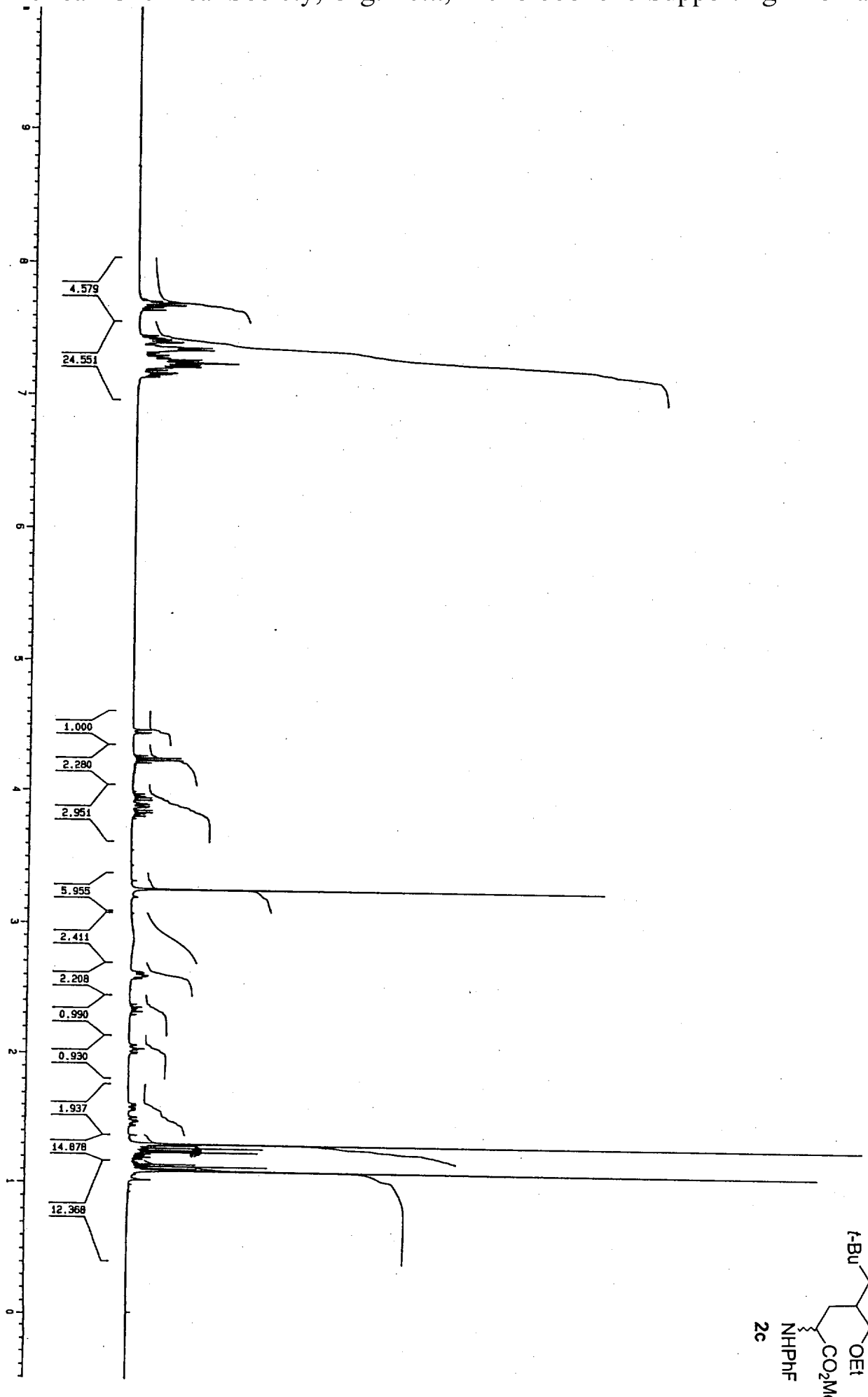
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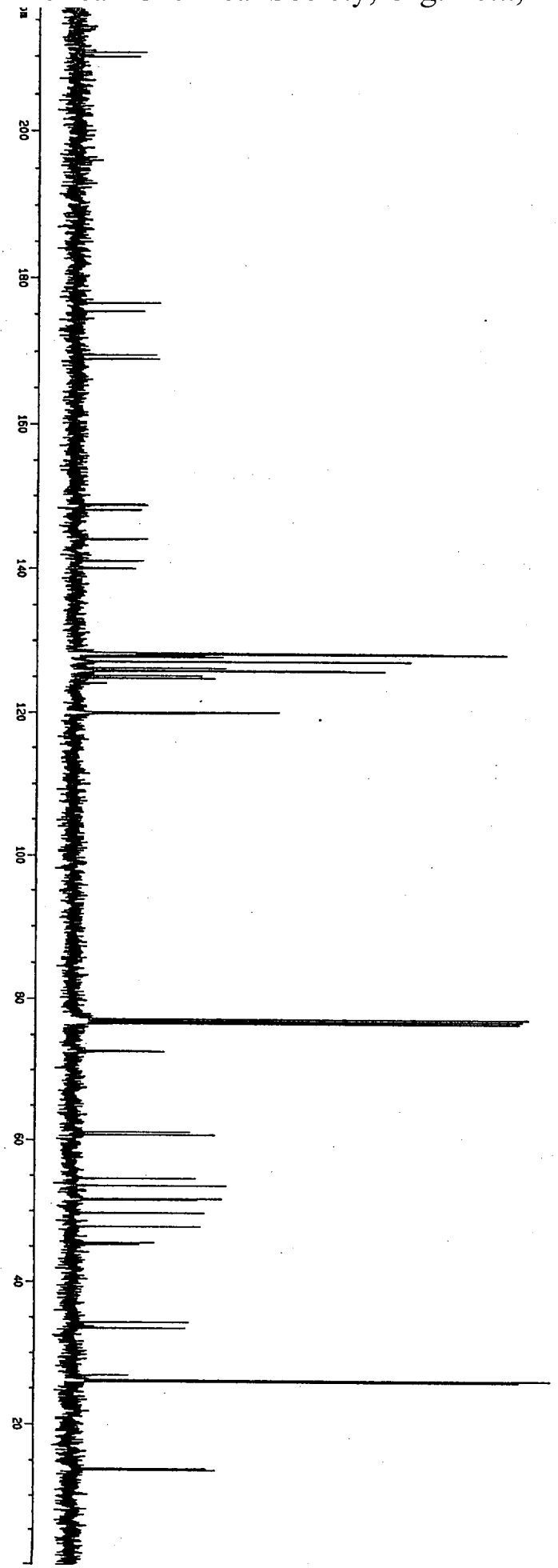

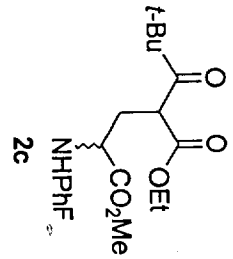

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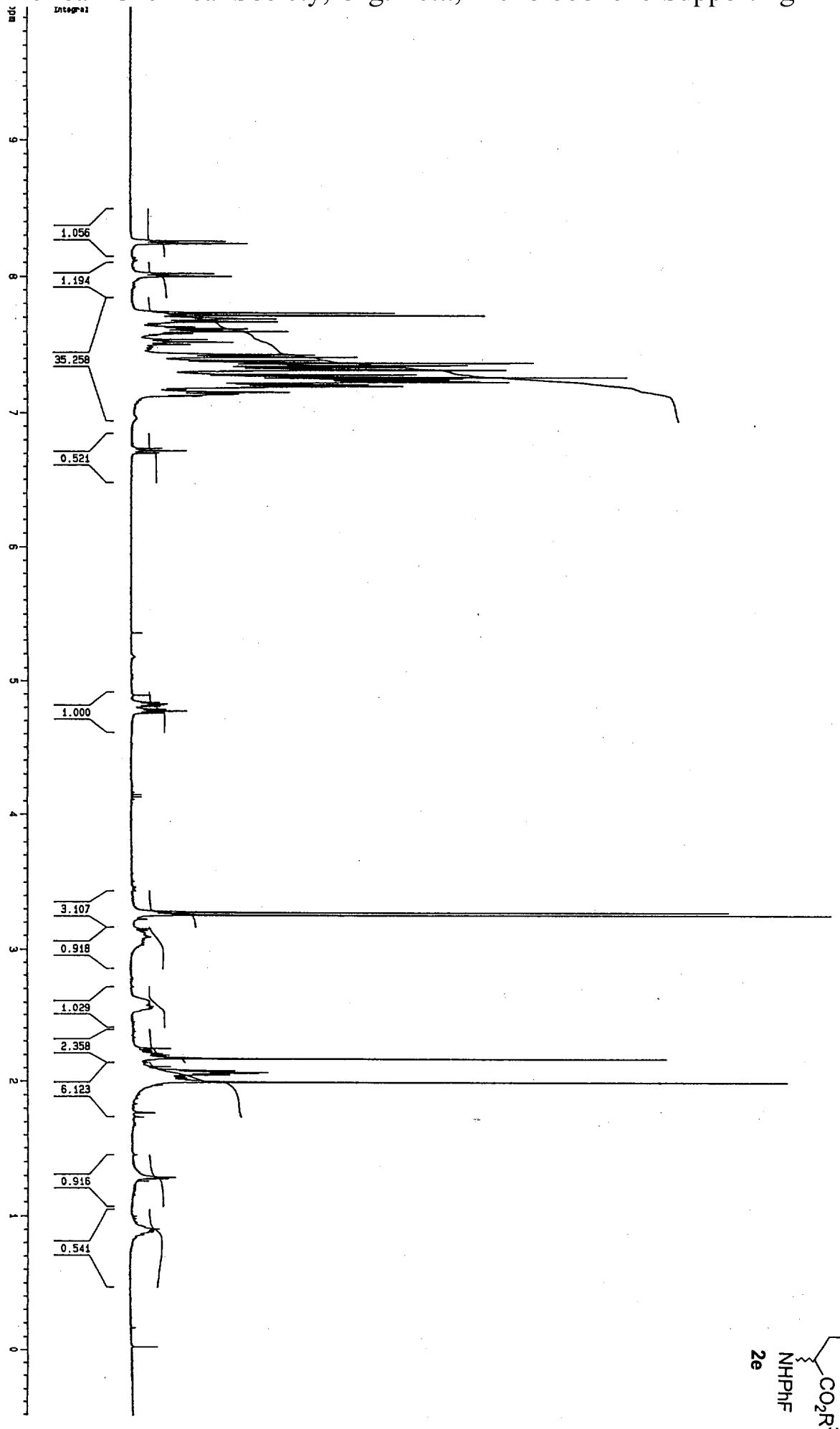
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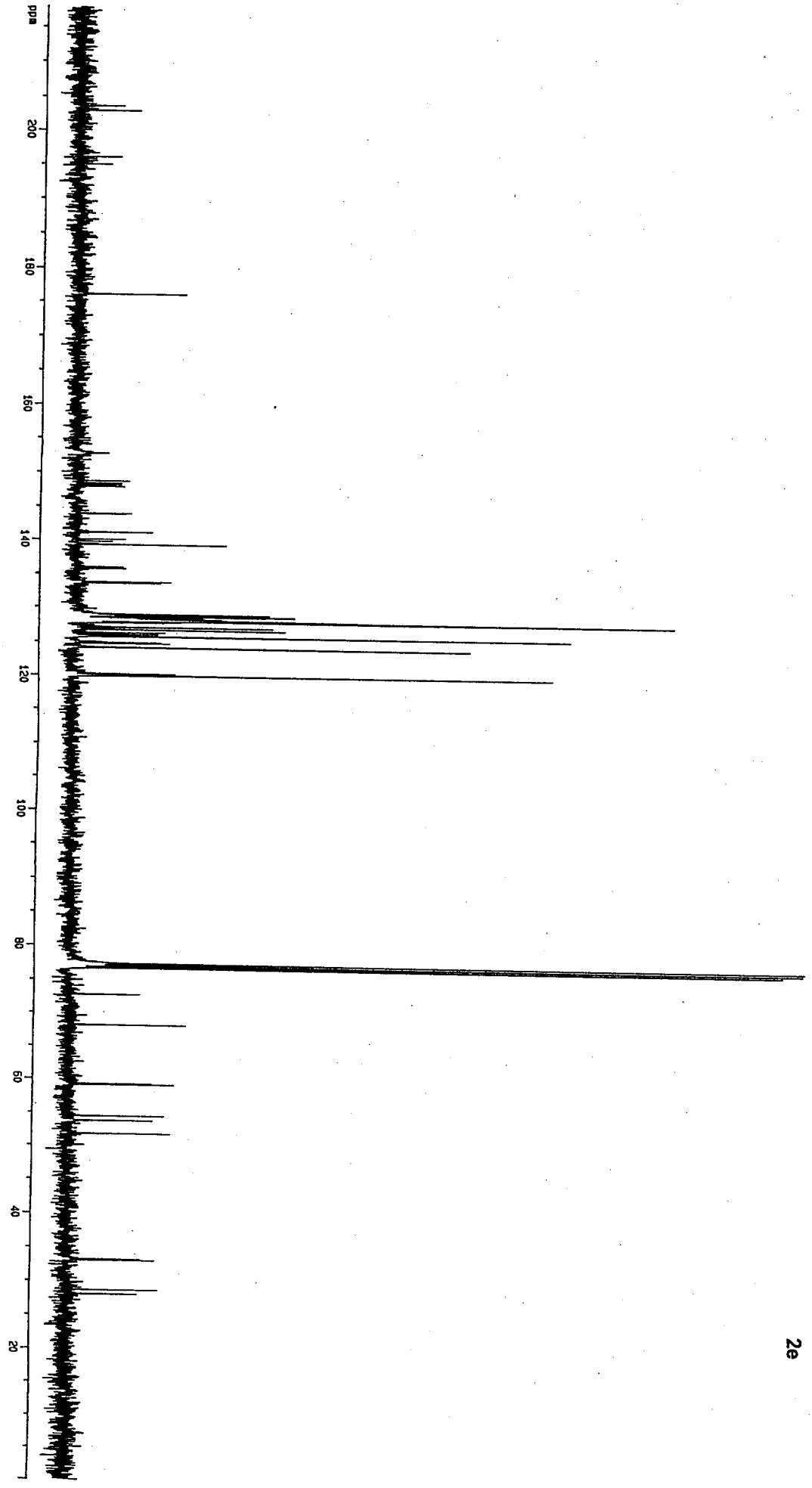

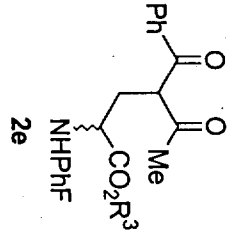

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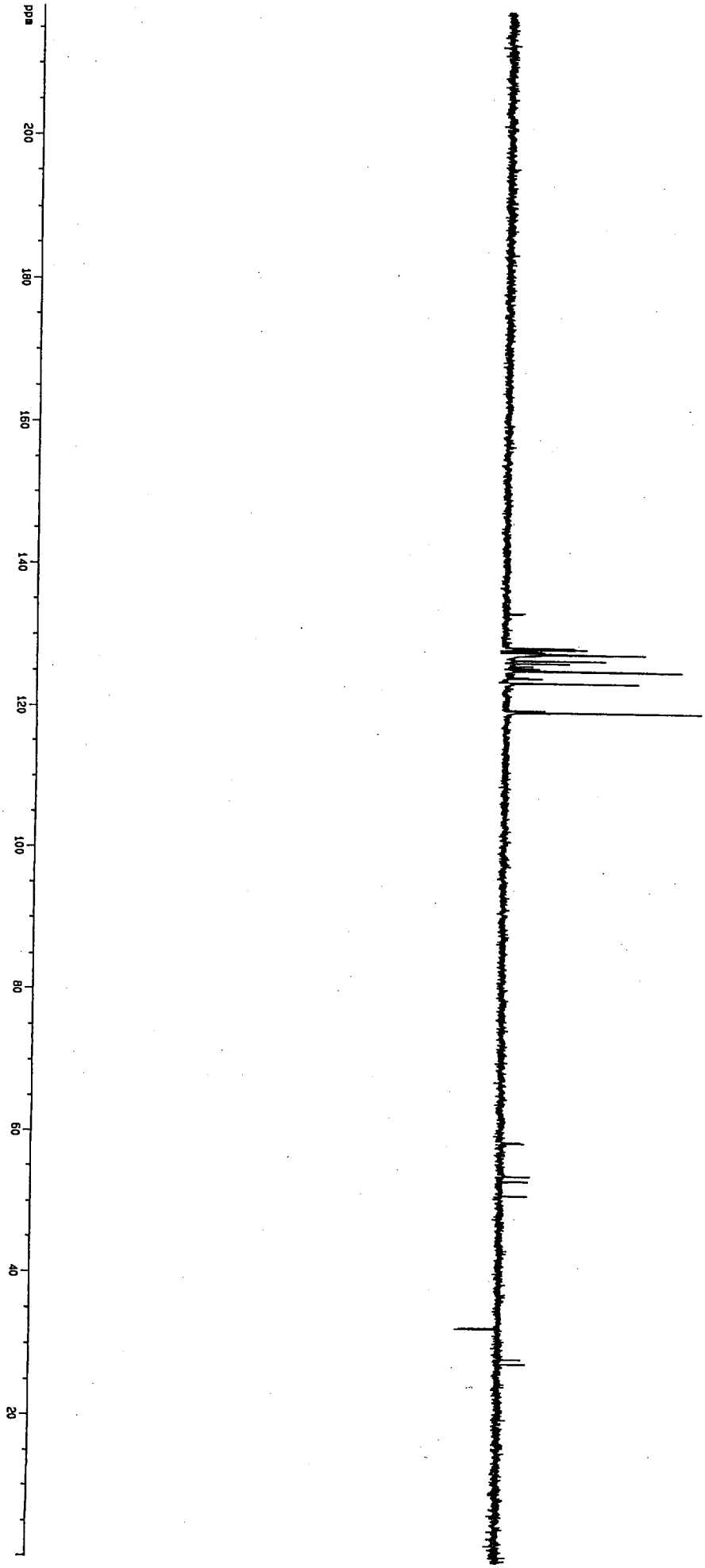

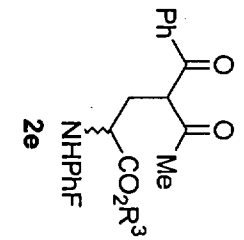

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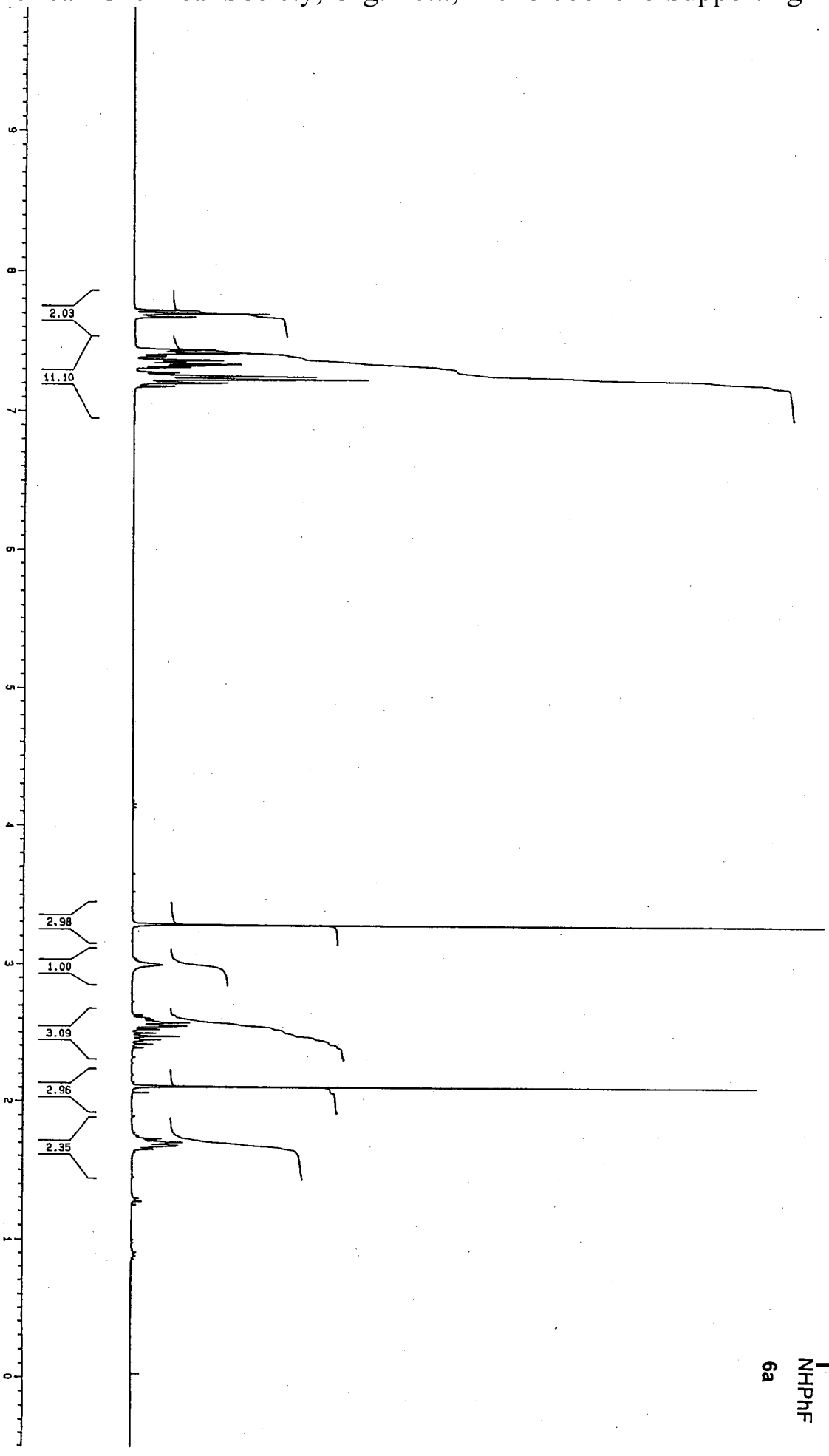

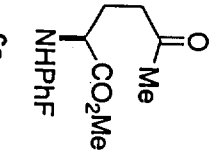

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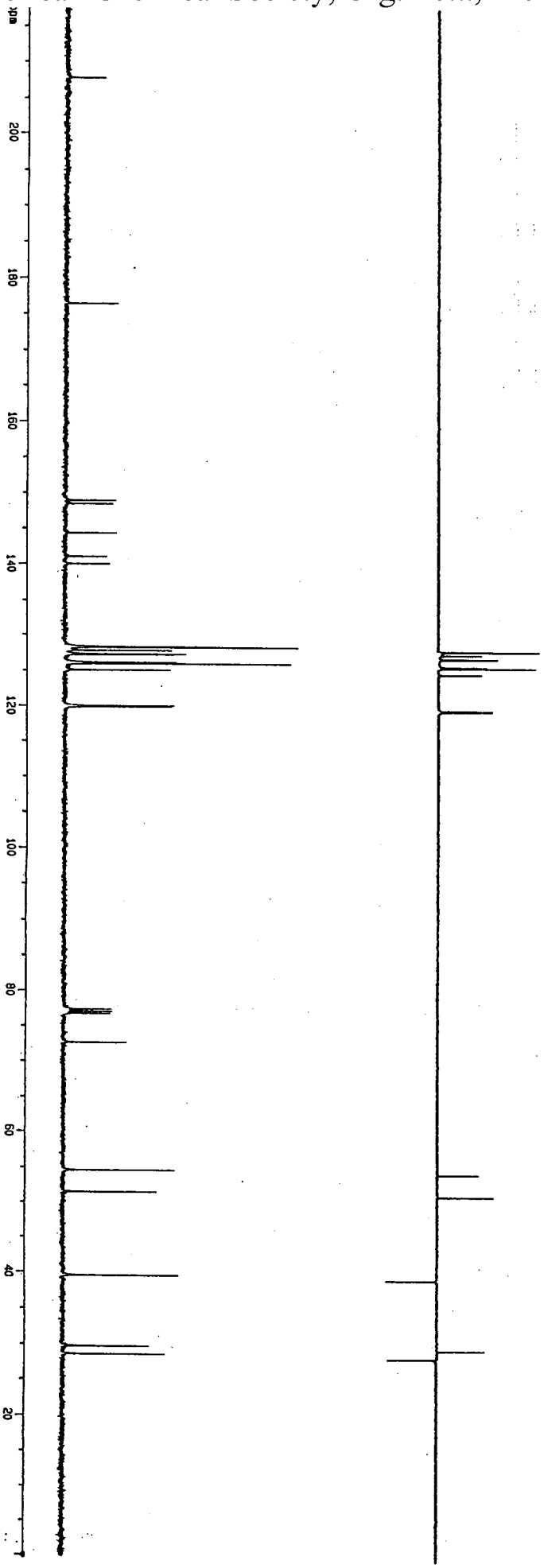

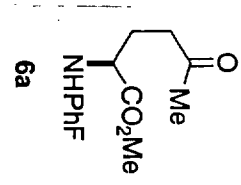

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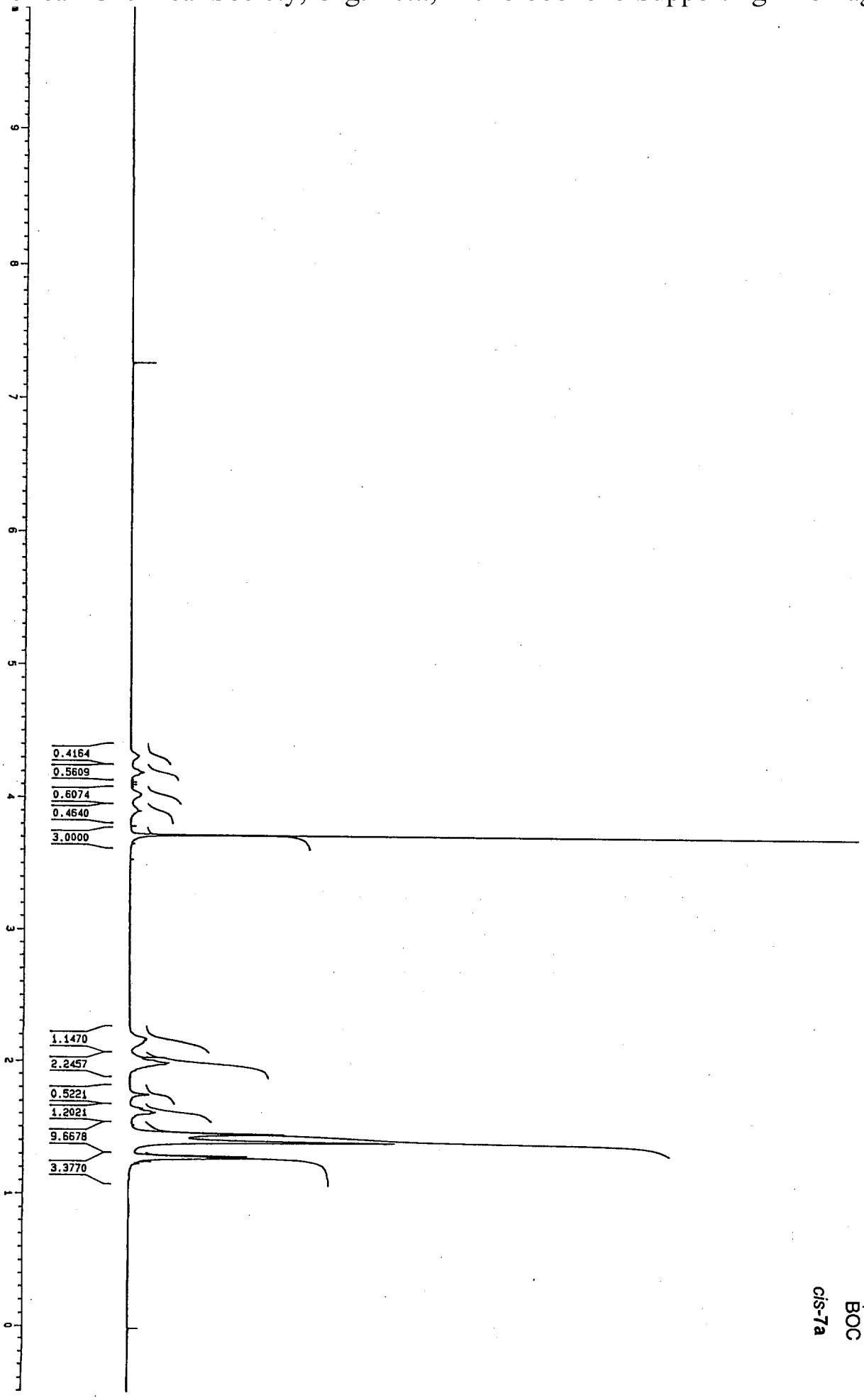
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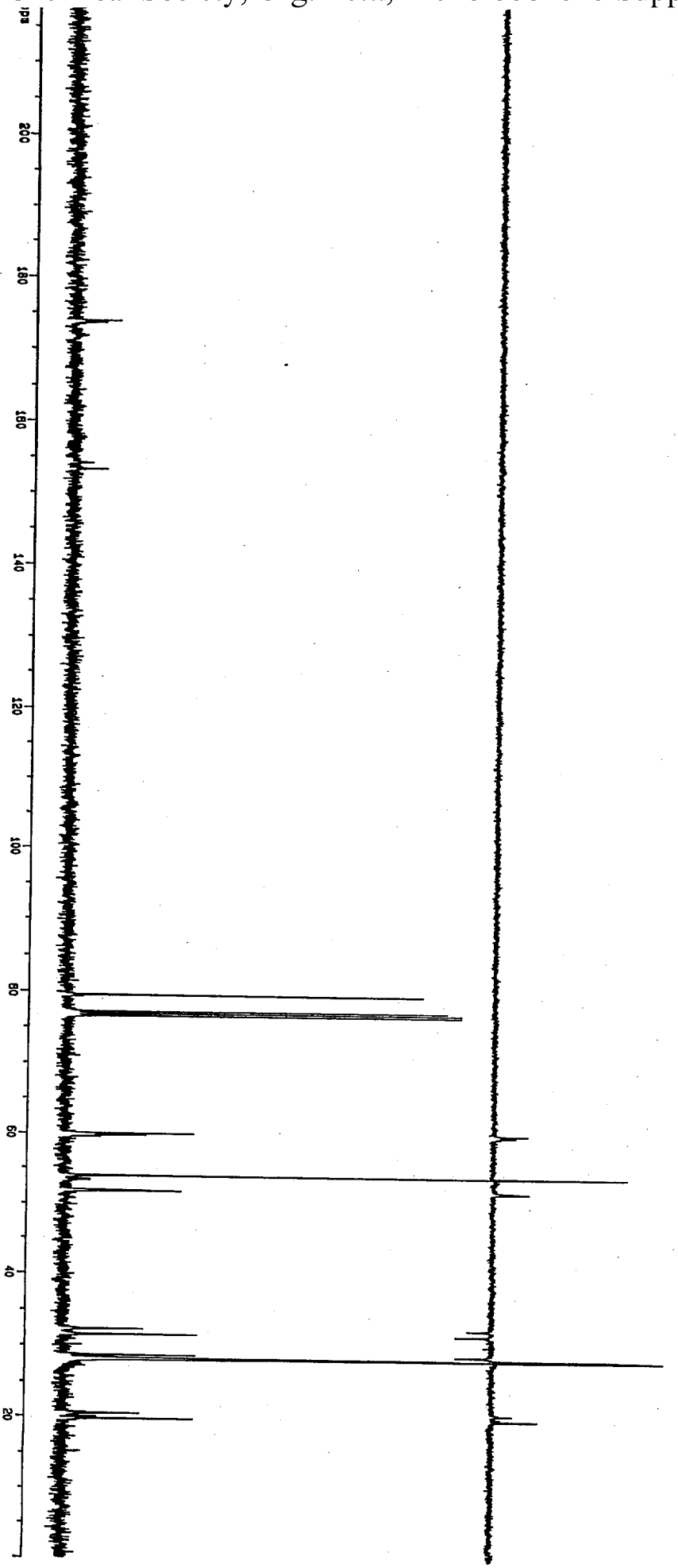
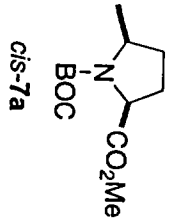
N
BOC
CO2Me
cis-7a





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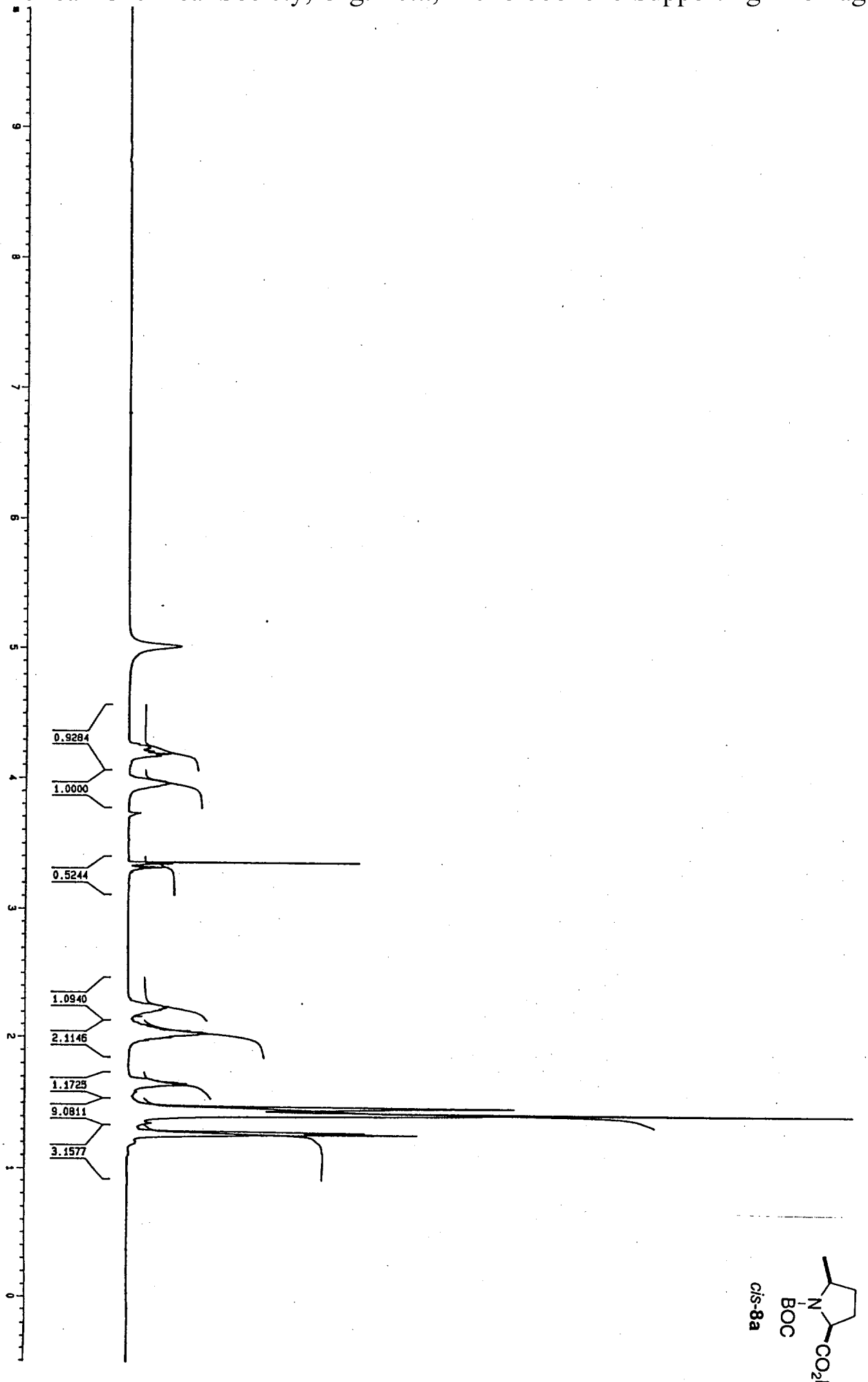

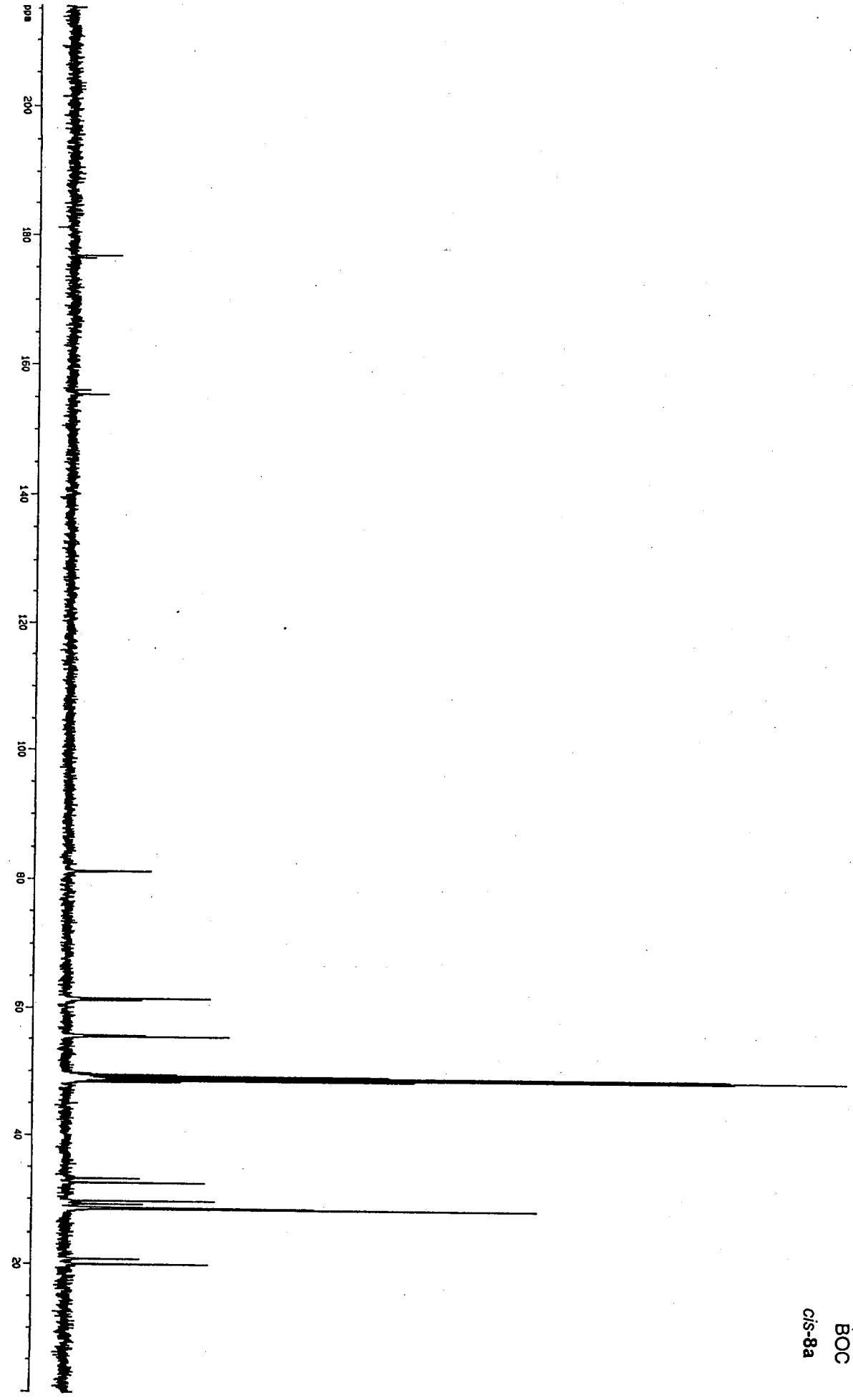

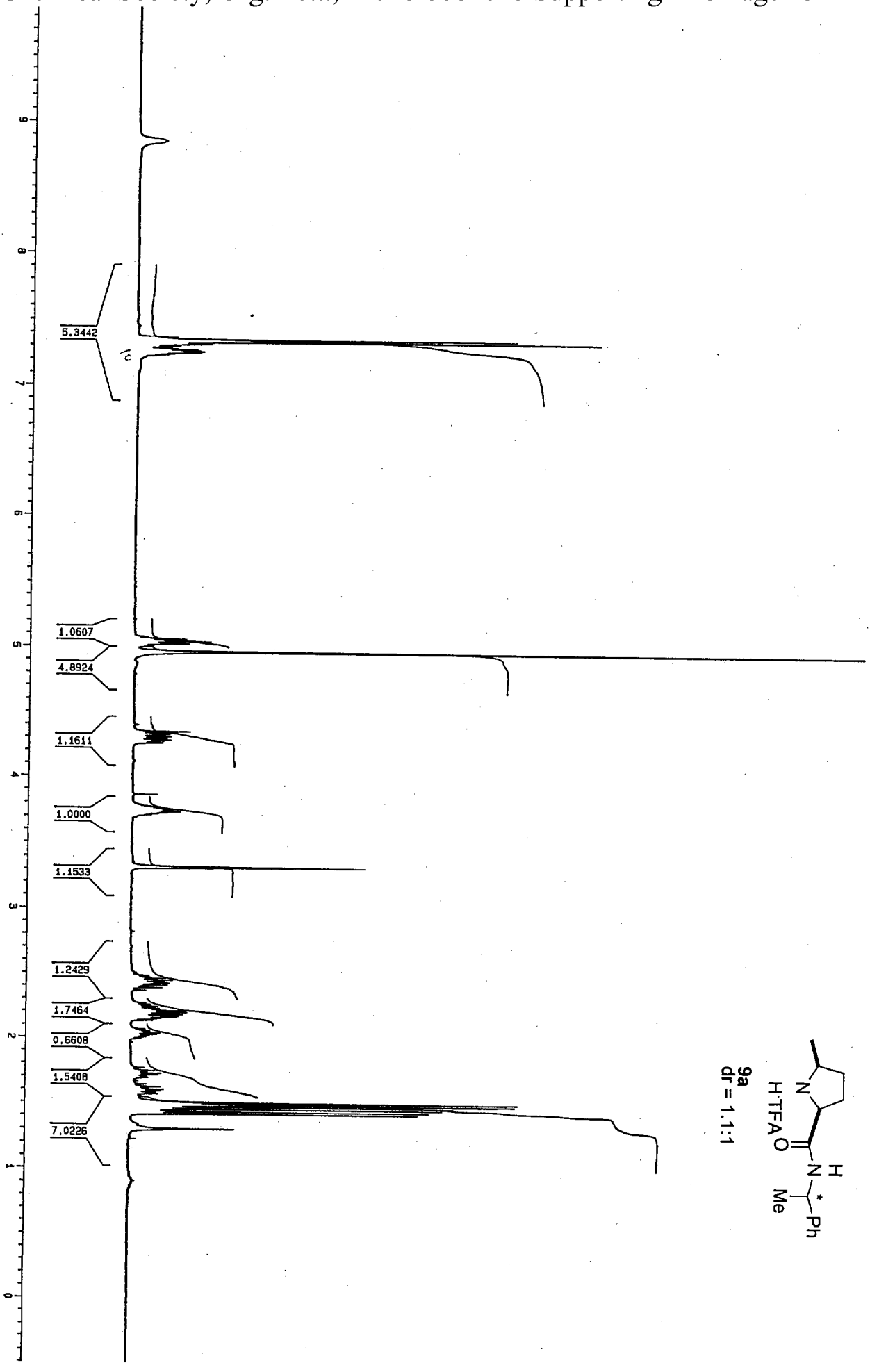

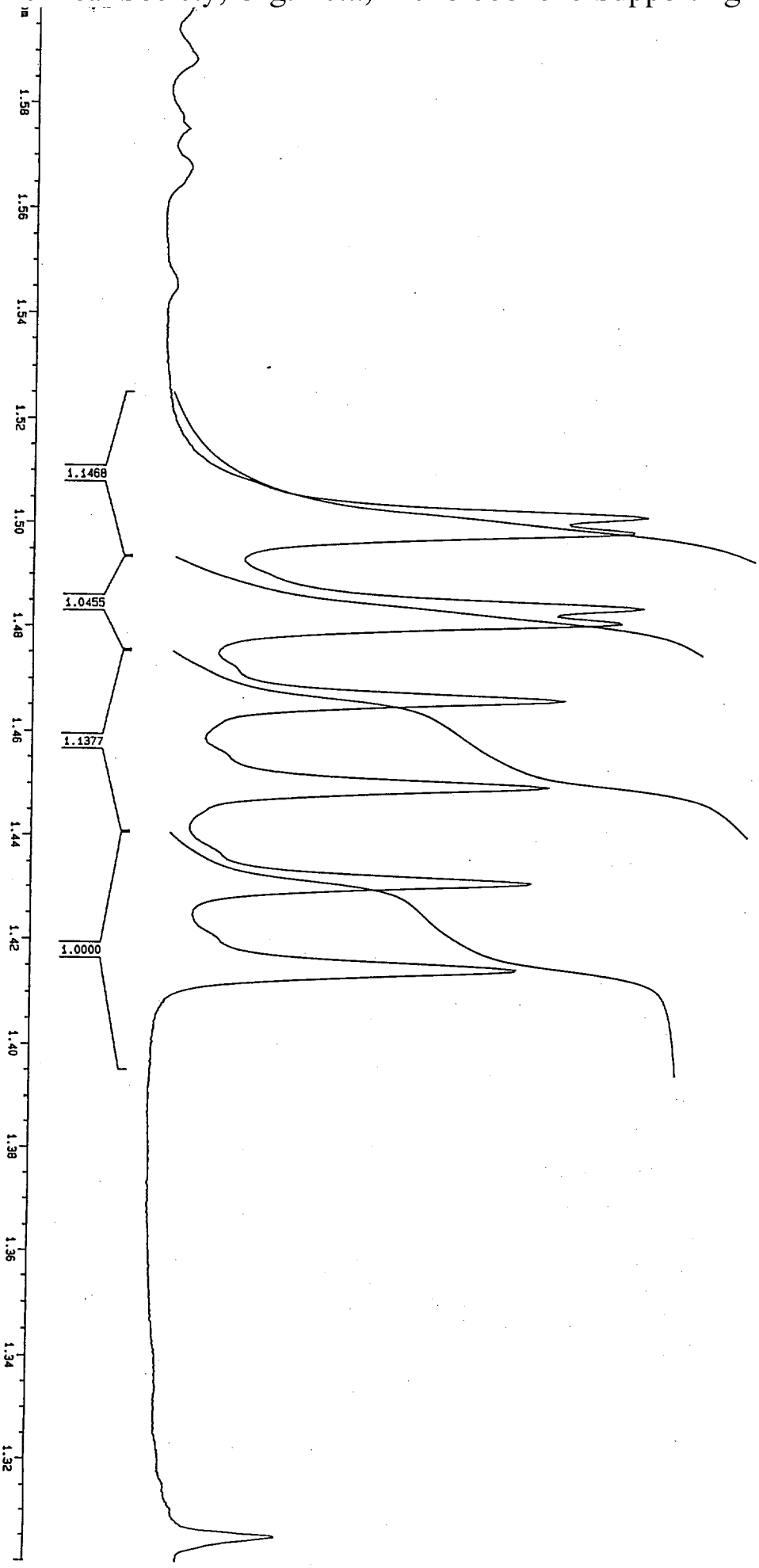

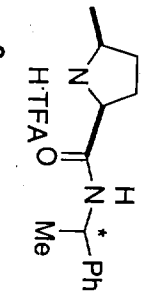

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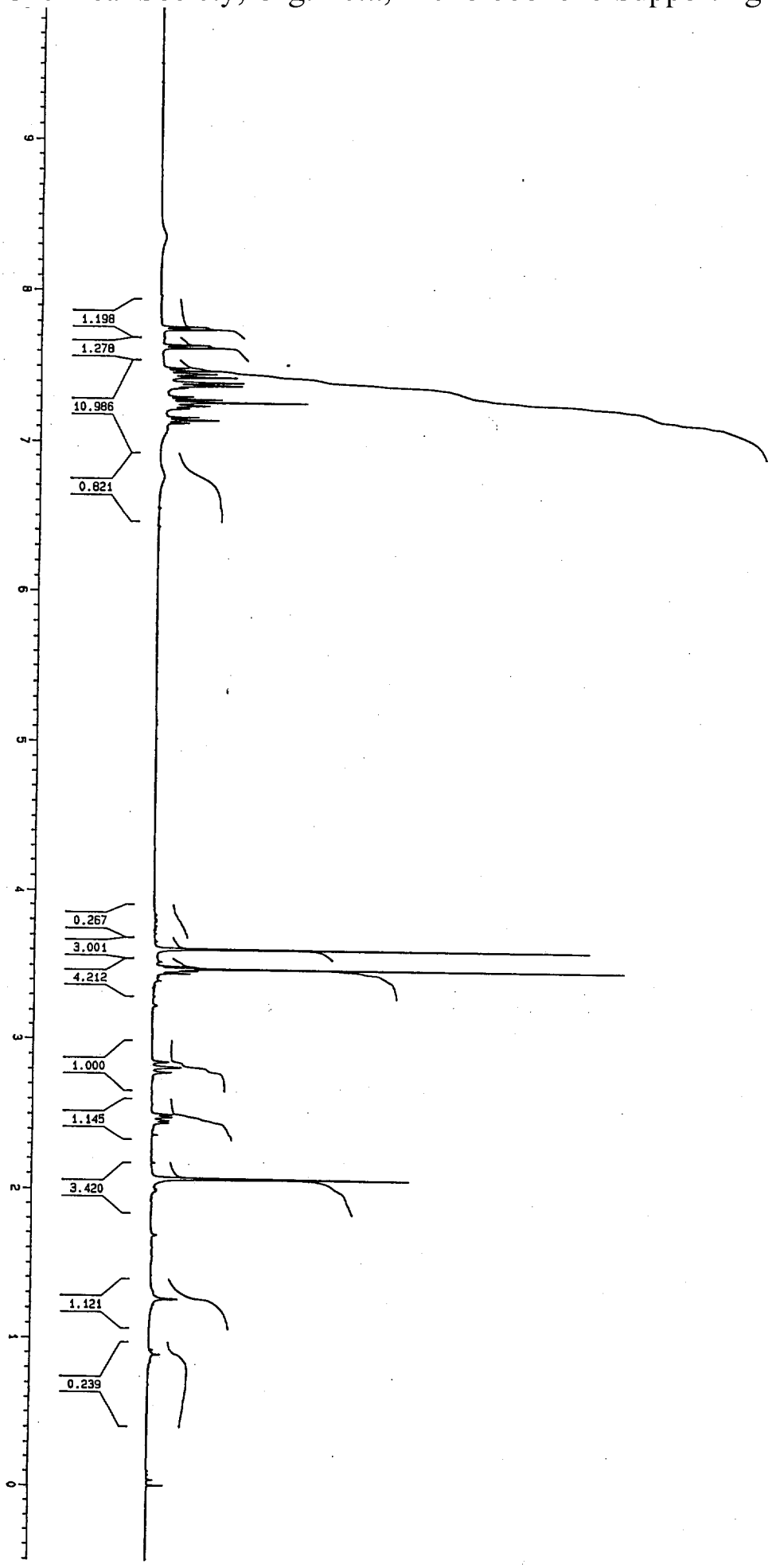

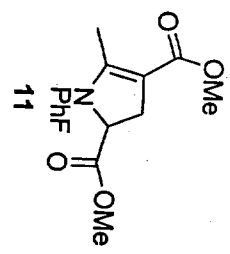

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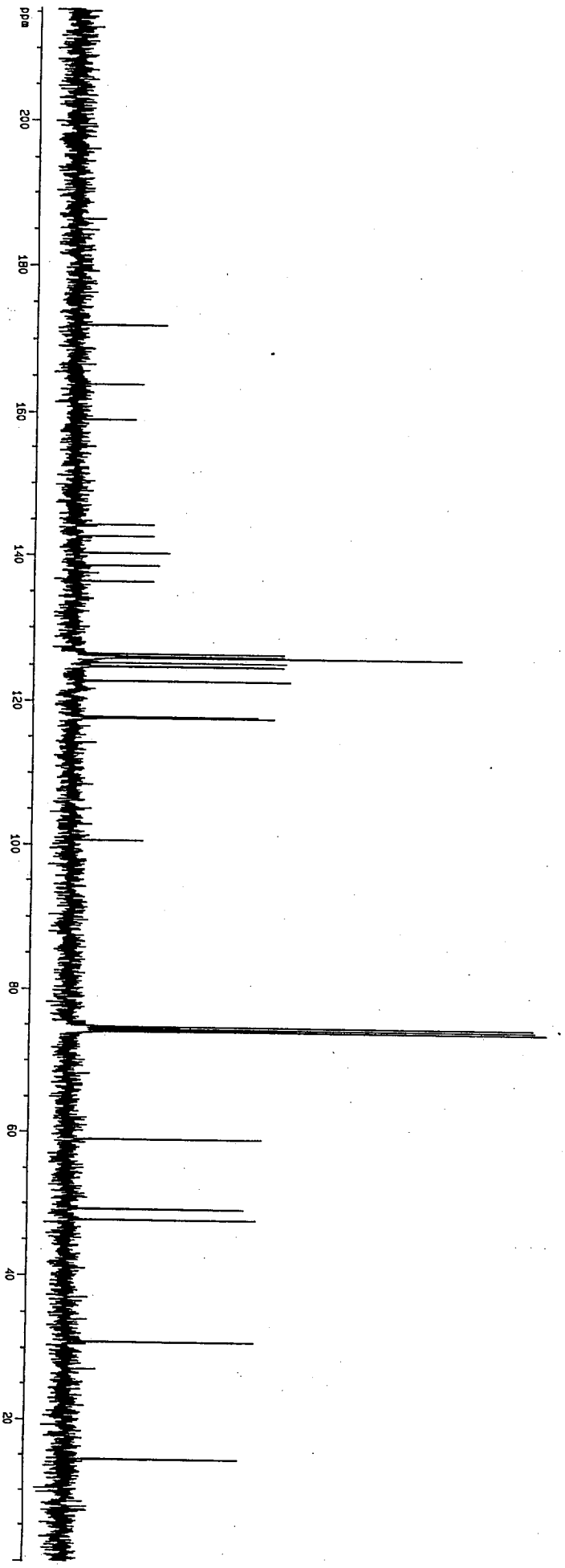

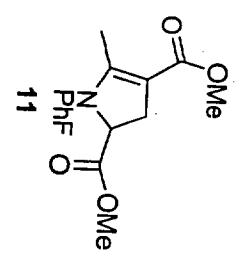

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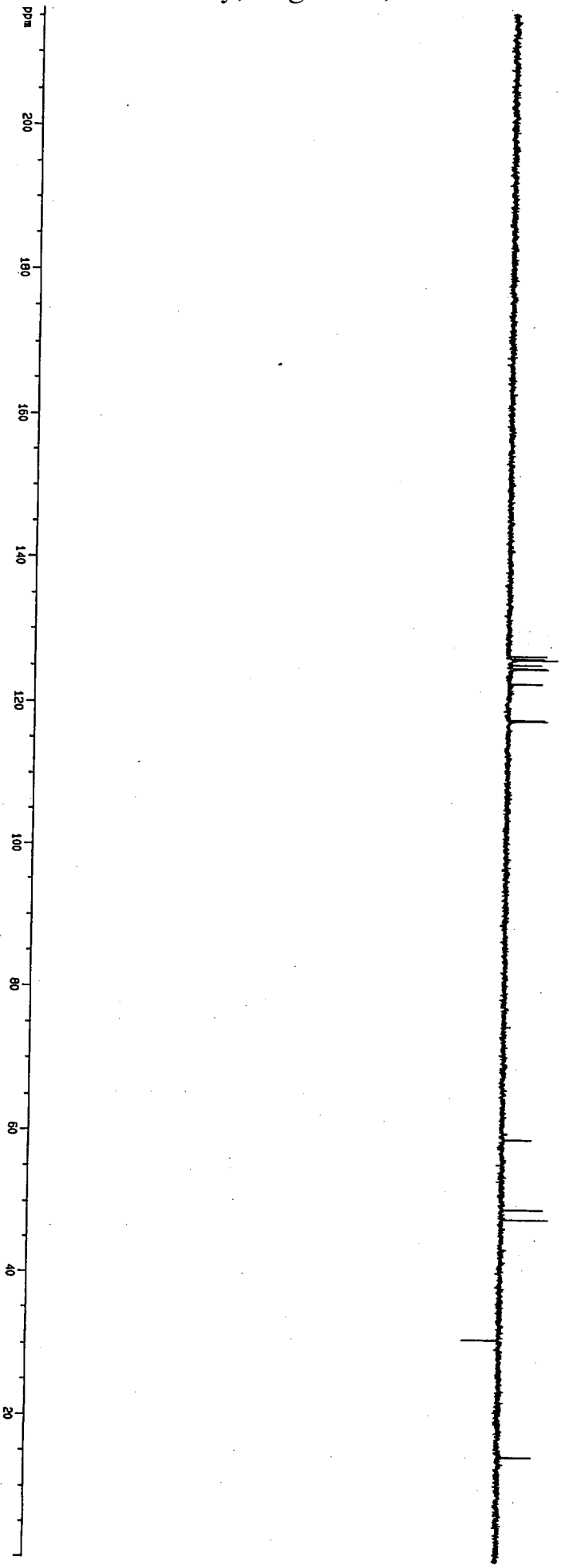
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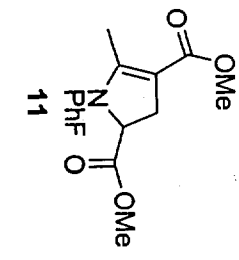
OMe
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11