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Titanium (IV) Mediated Tandem Deprotection-Cyclodehydration of Protected Cysteine *N*-Amides: Biomimetic Syntheses of Thiazoline and Thiazole Containing Heterocycles

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Supporting Information

General Methods. Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purchased from Fisher and were dried prior to use. All other reagents were used without further purification. ^{1}H NMR spectra were measured at 500 MHz on a Bruker DRX spectrometer or at 600 MHz on a Bruker DRX spectrometer, and were referenced to internal TMS (0.0 ppm). ^{13}C spectra were performed at 125 MHz on a Bruker DRX-500 or at 150 MHz on a Bruker DRX-600 instrument and were referenced to $CDCl_3$. Thin-layer chromatographic analyses were performed on aluminum-backed thin-layer analytical plates (Kieselgel 60 F_{254}). Visualization was accomplished using 10% phosphomolybdic acid in ethanol. Flash chromatography was performed on silica gel 60 (230-400 mesh, E. Merck no. 9385).

Procedure A: Synthesis of Fully Protected Cysteine Derivatives. A solution of N^{α}-Fmoc-Cys(*S*-trityl)-OH (0.586 g, 1 mmol) in MeOH:Benzene (5 mL; 1:4) was treated with TMS-CHN_2 (600 µl of 2.0 M solution in hexanes, 1.2 mmol) at 25 °C and the reaction progress was monitored by TLC (usually complete after 0.5 h). The reaction mixture was concentrated in *vacuo* and the crude reaction mixture was used in the next step without purification.

Diethylamine (6 ml) was added to a solution of crude methyl ester in CH_3CN (6 ml) and the resulting mixture was stirred at 25 °C for 30 min to ensure complete removal of the Fmoc protecting group. After concentration in *vacuo*, the mixture was azeotroped to dryness with CH_3CN (2 x 6ml) and the reside was resuspended in CH_3CN (8 ml). The desired Carboxylic acid (1.1 mmol), HBTU (1.1 mmol) and DIEA (2.1 mmol) were sequentially added and the resulting mixture was stirred at 25 °C overnight (~10-12 h). Next, the reaction mixture was concentrated and the residue was dissolved in EtOAc and washed with $NaHCO_3$ (10% aqueous). The organic layer was dried over $MgSO_4$, filtered, concentrated and purified by flash chromatography (EtOAc/hexanes) to afford the title product.

Procedure B: Synthesis of thiazolines. A solution of fully protected cysteine *N*-Amide (0.125 mmol) in dry CH_2Cl_2 (2.5 ml) was treated with $TiCl_4$ (375 µL of a 1.0 M solution in CH_2Cl_2, 0.375 mmol) and stirred at 0°C for 18 h. The reaction mixture was quenched with cold saturated aqueous $NaHCO_3$ (2x). The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried over $MgSO_4$, filtered and concentrated. The resultant crude product was purified by flash chromatography using a mixture of EtOAc/hexanes.

***N*-Benzoyl-*S*-trityl-*L*-cysteine Methyl Ester (1).** Prepared from *N*-Fmoc-*S*-trityl-*L*-cysteine (1.96 g, 3.34 mmol), according to the procedure A, to afford **1** as a white solid (1.455 g,

3.02 mmol, 90%). Data for **1**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78-7.18 (m, 20H, Ar), 6.68 (br.d, 1H, *J*= 7.5 Hz, N*H*), 4.84 (dt of ABX, 1H, *J*= 7.5, 5.3, 4.8 Hz, C*H*-N),), 3.75 (s, 3H, O-CH_3),), 2.79 (ABX, 1H, J_{AB}= 12.3, J_{AX}= 5.3 Hz, C*H*-S), 2.74 (ABX, 1H, J_{AB}= 12.3, J_{BX}= 4.8 Hz, C*H*-S); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.0, 166.8, 144.2, 133.6, 132.0, 131.8, 129.4, 128.6, 128.0, 127.2, 126.8, 66.9, 52.8, 51.4, 34.0; mp 132-134 °C; HRMS (MALDI-FTMS) calcd. for $C_{30}H_{27}NO_3SNa$ (M+Na^+) 504.1604, found 504.1620.

4-Carbomethoxy-2-phenyl-Δ^2-thiazoline (2). Prepared from *N*-Benzoyl-*S*-trityl-*L*-cysteine Methyl Ester **1** (60.2 mg, 0.125 mmol), according to the procedure B, to give **2** a colorless oil (23.0 mg, 0.104 mmol, 83%). Data for **2**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.26 (m, 5H, Ar), 5.29 (ABX, 1H, J_{AX}= 9.0, J_{BX}= 9.4 Hz, C*H*-N), 3.84 (s, 3H, O-CH_3), 3.72 (ABX, 1H, J_{AB}= 11.2, J_{AX}= 9.0 Hz, C*H*-S), 3.64 (ABX, 1H, J_{AB}= 11.2, J_{BX}= 9.4 Hz, C*H*-S); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 171.0, 132.6, 131.7, 128.6, 128.5, 78.5, 52.8, 35.3; HRMS (MALDI-FTMS) calcd. for $C_{11}H_{12}NO_2S$ (M+H^+) 222.0589, found 222.0591.

***N*-Benzoyl-*S*-trityl-*L*-penicillamine Methyl Ester (3).** Prepared from *N*-Fmoc-*S*-trityl-*L*-penicillamine (614 mg, 1.00 mmol), according to the procedure A, to afford **3** as a white foam (408 mg, 0.800 mmol, 80%). Data for **3**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84-7.17 (m, 20H, Ar), 7.00 (br.d, 1H, *J*= 7.0 Hz, N*H*), 3.92 (d, 1H, *J*= 7.0 Hz, C*H*-N),), 3.72 (s, 3H, O-CH_3),), 1.17 (s, 3H, CH_3C-S), 1.09 (s, 3H, CH_3C-S); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.3, 167.0, 144.4, 133.8, 131.8, 129.8, 128.6, 127.7, 127.1, 126.8, 68.1, 61.0, 53.4, 52.1, 27.1, 27.0; mp 188-190 °C; HRMS (MALDI-FTMS) calcd. for $C_{32}H_{31}NO_3SNa$ (M+Na^+) 532.1917, found 532.1935.

***N*-(4-Nitrobenzoyl)-*S*-trityl-*L*-cysteine Methyl Ester (4).** Prepared from *N*-Fmoc-*S*-trityl-*L*-cysteine (0.294 g, 0.500 mmol), according to the procedure A, to furnish **4** as a white solid (0.244 g, 0.464 mmol, 93%). Data for **4**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32-7.18 (m, 19H, Ar), 6.68 (d, 1H, *J*= 7.5 Hz, N*H*), 4.80 (m, 1H), 3.78 (s, 3H, *O*-C*H*$_3$),), 2.84 (dd, 1H, J_{AB}= 12.6, J_{AX}= 5.5 Hz, C*H*-S), 2.77 (dd, 1H, J_{AB}= 12.6, J_{BX}= 4.6 Hz, C*H*-S); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.6, 164.8, 144.1, 139.2, 129.4, 128.4, 128.0, 127.0, 123.8, 66.9, 52.9, 51.7, 33.7; mp 162-164 °C; MS (ESI) calcd. for $C_{30}H_{27}NO_3SNa$ (M+Na$^+$) 549, found 549.

***N*-(4-Methoxybenzoyl)-*S*-trityl-*L*-cysteine Methyl Ester (5).** Prepared from *N*-Fmoc-*S*-trityl-*L*-cysteine (0.294 g, 0.500 mmol), according to the procedure A, to afford **5** as a white solid (0.211 g, 0.412 mmol, 82%). Data for **5**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74-6.93 (m, 19H, Ar), 6.61 (d, 1H, *J*= 7.5 Hz, N*H*), 4.82 (dt of AB<u>X</u>, 1H, *J*= 7.5, 5.3, 4.8 Hz, C*H*-N),), 3.86 (s, 3H, Ar-O-C*H*$_3$), 3.74 (s, 3H, COO-C*H*$_3$), 2.77 (<u>A</u>BX, 1H, J_{AB}= 12.2, J_{AX}= 5.3 Hz, C*H*-S), 2.72 (A<u>B</u>X, 1H, J_{AB}= 12.2, J_{BX}= 4.8 Hz, C*H*-S); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.1, 166.2, 162.4, 144.2, 129.4, 129.0, 128.0, 126.8, 125.9, 113.7, 66.5, 55.4, 52.7, 51.3, 34.1; mp 148-149 °C; HRMS (MALDI-FTMS) calcd. for $C_{31}H_{29}NO_4SNa$ (M+Na$^+$) 534.1709, found 534.1707.

***N*-Dihydrocinnamoyl-*S*-trityl-*L*-cysteine Methyl Ester (6).** Prepared from *N*-Fmoc-*S*-trityl-*L*-cysteine (0.300 g, 0.500 mmol), according to the procedure A, to give **6** as a white foam (0.205 g, 0.402 mmol, 80%). Data for **6**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.15 (m, 20H, Ar), 5.79 (br.d, 1H, *J*= 7.7 Hz, N*H*), 4.57 (dt, 1H, *J*= 7.7, 5.5 Hz, C*H*-N), 3.68 (s, 3H, O-C*H*$_3$), 2.93 (m, 2H, PhCH$_2$-C*H*$_2$CONH), 2.63 (d, 2H, *J*= 5.5, C*H*$_2$-S), 2.45 (t, 2H, *J*= 7.7, PhC*H*$_2$-CH$_2$CONH); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.6, 170.9, 144.4, 140.7, 129.5, 128.5, 128.3, 128.0, 126.9, 126.2, 67.0, 52.5, 51.1, 37.9, 33.8, 31.3.

4-Carbomethoxy-5,5-dimethyl-2-phenyl-Δ^2-thiazoline (7). Prepared from *N*-Benzoyl-*S*-trityl-*L*-penicillamine Methyl Ester **3** (64.0 mg, 0.125 mmol), according to the procedure B, to give **7** a colorless oil (30.0 mg, 0.120 mmol, 96%). Data for **7**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85-7.38 (m, 5H, Ar), 4.86 (s, 1H, C*H*-N), 3.82 (s, 3H, O-CH_3), 1.78 (s, 3H, C(CH_3)-S), 1.46 (s, 3H, C(CH_3)-S); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 170.0, 133.2, 131.6, 128.4, 128.4, 86.2, 60.6, 52.2, 28.5, 26.0; HRMS (MALDI-FTMS) calcd. for $C_{13}H_{16}NO_2S$ ($M+H^+$) 250.0896, found 250.0899.

4-Carbomethoxy-2-(4-nitrophenyl)-Δ^2-thiazoline (8). Prepared from *N*-(4-Nitrobenzoyl)-*S*-trityl-*L*-cysteine Methyl Ester **4** (65.8 mg, 0.125 mmol), according to the procedure B, to give **8** a white solid (25.8 mg, 0.097 mmol, 77%). Data for **8**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28-8.02 (m, 4H, Ar), 5.34 (AB<u>X</u>, 1H, J_{AX}= 9.2, J_{BX}= 9.5 Hz, C*H*-N), 3.86 (s, 3H, O-CH_3), 3.81 (<u>A</u>BX, 1H, J_{AB}= 11.2, J_{AX}= 9.2 Hz, C*H*-S), 3.72 (A<u>B</u>X, 1H, J_{AB}= 11.2, J_{BX}= 9.5 Hz, C*H*-S); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 169.0, 149.6, 138.0, 129.5, 123.7, 78.7, 52.9, 35.9; HRMS (MALDI-FTMS) calcd. for $C_{11}H_{11}N_2O_4S$ ($M+H^+$) 267.0439, found 267.0431.

4-Carbomethoxy-2-(4-methoxyphenyl)-Δ^2-thiazoline (9). Prepared from *N*-(4-Methoxybenzoyl)-*S*-trityl-*L*-cysteine Methyl Ester **5** (64.0 mg, 0.125 mmol), according to the procedure B, to give **9** a colorless oil (8.8 mg, 0.035 mmol, 28%). Data for **9**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82-6.89 (m, 4H, Ar), 5.25 (AB<u>X</u>, 1H, J_{AX}= 8.8, J_{BX}= 9.2 Hz, C*H*-N), 3.84 (s, 3H, O-CH_3), 3.83 (s, 3H, O-CH_3), 3.68 (<u>A</u>BX, 1H, J_{AB}= 11.0, J_{AX}= 8.8 Hz, C*H*-S), 3.62 (A<u>B</u>X, 1H, J_{AB}= 11.0, J_{BX}= 9.2 Hz, C*H*-S); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 170.2, 162.4, 130.4, 125.4, 113.8, 78.3, 55.4, 52.7, 35.4.

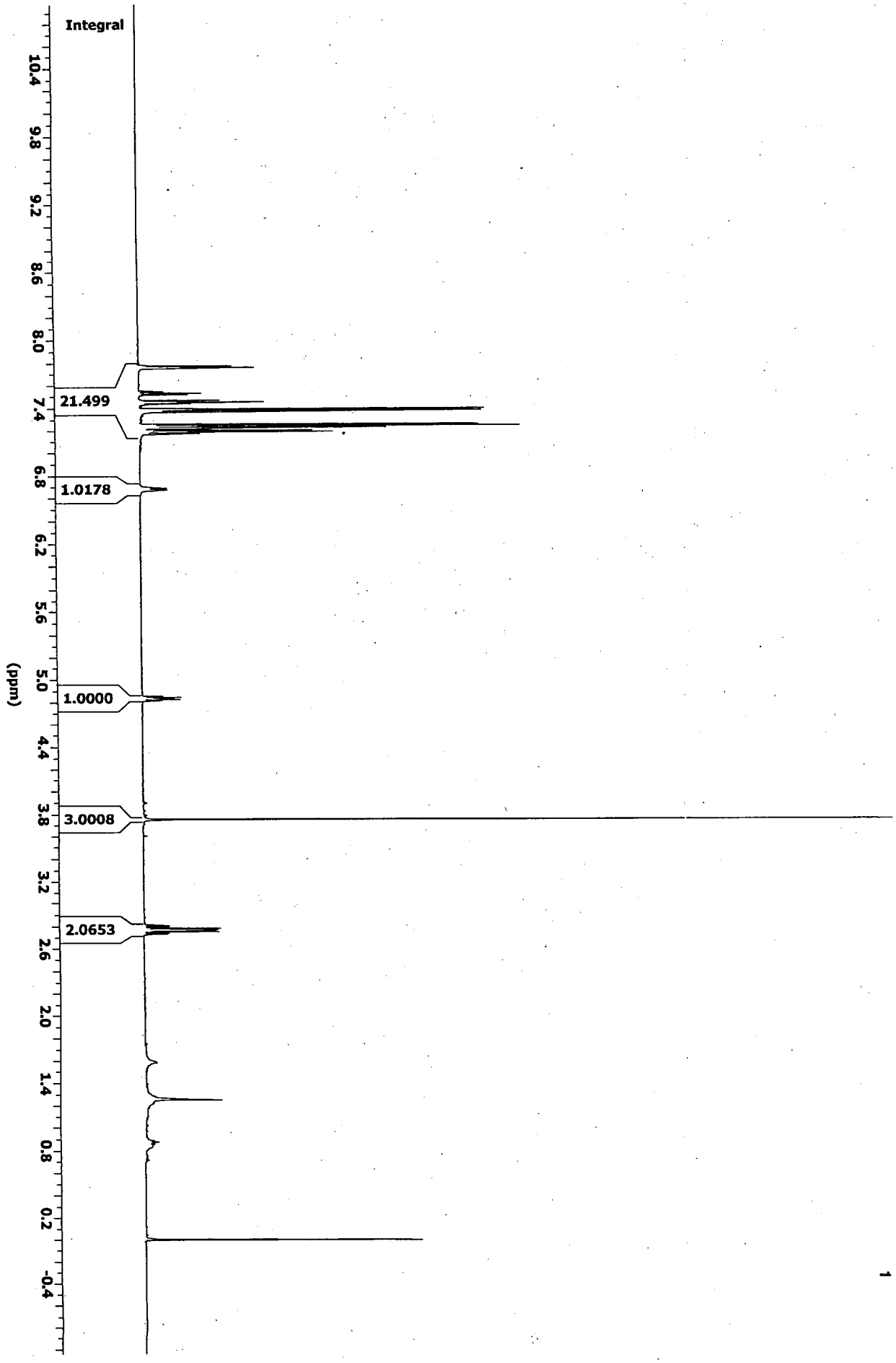
4-Carbomethoxy-2-(2-phenylethyl)-Δ^2-thiazoline (10). Prepared from *N*-Dihydrocinnamoyl-*S*-trityl-*L*-cysteine Methyl Ester **6** (51.0 mg, 0.100 mmol), according to the procedure B, to give **10** a colorless oil (15.2 mg, 0.061 mmol, 61%). Data for **10**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.18 (m, 5H, Ar), 5.07 (ABX, 1H, J_{AX}= 8.8, J_{BX}= 9.5 Hz, C*H*-N), 3.80 (s, 3H, O-CH_3), 3.60 (ABX, 1H, J_{AB}= 11.2, J_{AX}= 8.8 Hz, C*H*-S), 3.51 (ABX, 1H, J_{AB}= 11.2, J_{BX}= 9.5 Hz, C*H*-S), 2.99 (m, 2H, PhCH_2CH$_2$), 2.86 (m, 2H, PhCH$_2$CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 171.3, 140.2, 128.4, 128.3, 126.3, 77.9, 52.7, 36.0, 35.5, 33.6.

***N*-Bz-*L*-Cys(S-Trt)-*L*-Cys(S-Trt)-OMe (11).** Diethylamine (4 ml) was added to a solution of *N*-Fmoc-Cys(*S*-trityl)-OMe (0.300 g, 0.5 mmol) in CH_3CN (4 ml) and the resulting mixture was stirred at 25 °C for 30. After concentration in *vacuo*, the mixture was azeotroped to dryness with CH_3CN (2 x 4ml) and the residue was resuspended in DMF:CH_2Cl_2 (4 ml, 1:1). Next, *N*-Fmoc-Cys(*S*-trityl)-OH (0.322 g, 0.55 mmol), HBTU (0.209 g, 0.55 mmol), HOBT (0.074 g, 0.55 mmol) and collidine (140 µl, 1.05 mmol) were sequentially added, and the resulting mixture was stirred at 25 °C. After 10 h, the reaction mixture was concentrated and the residue was dissolved in EtOAc and washed with $NaHCO_3$ (10% aqueous). The organic layer was dried over $MgSO_4$, filtered, concentrated and purified by flash chromatography (30 % EtOAc/hexanes) to afford 0.402 g of the dipeptide (85%).

Diethylamine (3 ml) was added to a solution of Fmoc-*L*-Cys(S-Trt)-*L*-Cys(S-Trt)-OMe (0.4016 g, 0.425 mmol) in CH_3CN (3 ml) and the resulting mixture was stirred at 25 °C for 30. After concentration in *vacuo*, the mixture was azeotroped to dryness with CH_3CN (3 x 3ml) and the residue was resuspended in DMF (3 ml). Next, benzoic acid (0.057 g, 0.467 mmol), HBTU (0.177 g, 0.467 mmol) and DIEA (155 µl, 0.892 mmol) were sequentially added and the resulting mixture was stirred at 25 °C. After 8 h, the reaction mixture was concentrated and the

residue was dissolved in EtOAc and washed with $NaHCO_3$ (saturated aqueous). The organic layer was dried over $MgSO_4$, filtered, concentrated and purified by flash chromatography (40% EtOAc/hexanes) to furnish 0.305 g of compound **11** as a white foam (87%). Data for **11**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.14 (m, 35H, Ar), 6.54-6.53 (m, 2H, *J*= 7.9 Hz, N*H*), 4.43 (dt, 1H, *J*= 7.7, 5.5 Hz, C*H*-N), 4.33 (AB<u>X</u>, 1H, J_{AX}= 6.6, J_{BX}= 5.7 Hz, C*H*-N), 3.63 (s, 3H, *O*-CH_3), 2.84 (<u>A</u>BX, 1H, J_{AB}= 13.2, J_{AX}= 6.6 Hz, C*H*-S), 2.61 (A<u>B</u>X, 1H, J_{AB}= 13.2, J_{BX}= 5.7 Hz, C*H*-S), 2.59 (m, 2H, CH_2-S); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 169.6, 167.2, 144.3, 144.2, 133.7, 131.8, 129.5, 129.4, 128.5, 128.1, 128.0, 127.2, 126.8, 126.8, 67.1, 66.8, 52.5, 52.0, 51.4, 33.6, 33.5; mp 101-104 °C; HRMS (MALDI-FTMS) calcd. for $C_{52}H_{46}N_2O_4S_2Na$ ($M+Na^+$) 849.2791, found 849.2798.

4-Carbomethoxy-2-(4-(2-phenylthiazolyl))-Δ^2-thiazoline (12). Prepared from *N*-Bz-*L*-Cys(S-Trt)-*L*-Cys(S-Trt)-OMe **11** (0.138 g, 0.160 mmol), according to the procedure B (6 eq. $TiCl_4$, 25 °C), to give **12** a white solid (18.7 mg, 0.0614 mmol, 38%). Data for **12**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 1H, Thiazole), 8.00-7.44 (m, 5H, Ar), 5.32 (AB<u>X</u>, 1H, J_{AX}= 9.1, J_{BX}= 9.6 Hz, C*H*-N), 3.85 (s, 3H, O-CH_3), 3.71 (<u>A</u>BX, 1H, J_{AB}= 11.3, J_{AX}= 9.1 Hz, C*H*-S), 3.64 (A<u>B</u>X, 1H, J_{AB}= 11.3, J_{BX}= 9.6 Hz, C*H*-S); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 168.2, 166.1, 149.4, 132.8, 130.5, 129.0, 126.8, 120.7, 78.4, 52.8, 35.0; HRMS (MALDI-FTMS) calcd. for $C_{14}H_{13}N_2O_2S_2$ ($M+H^+$) 305.0413, found 305.0424.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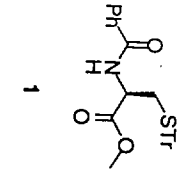
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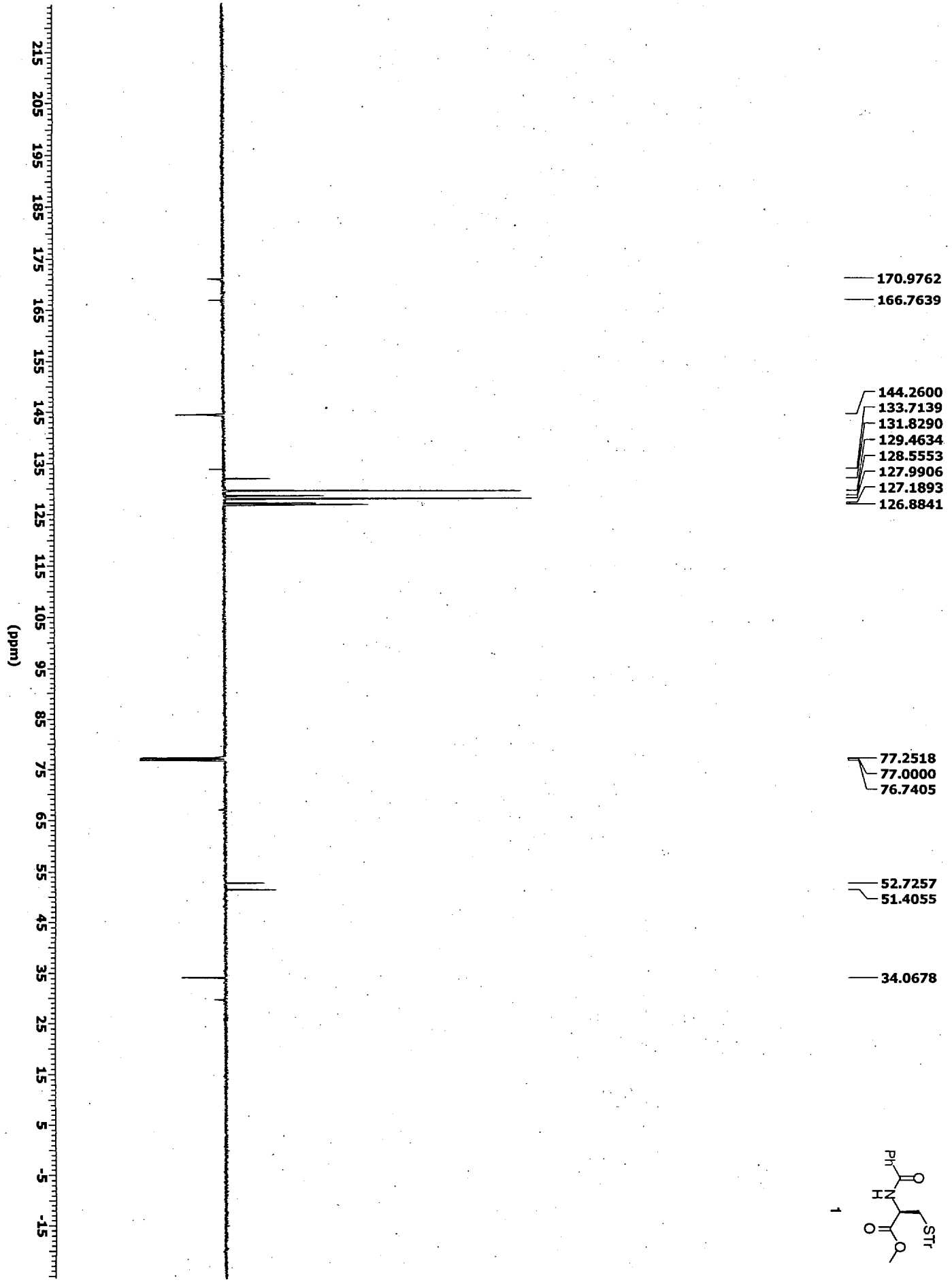

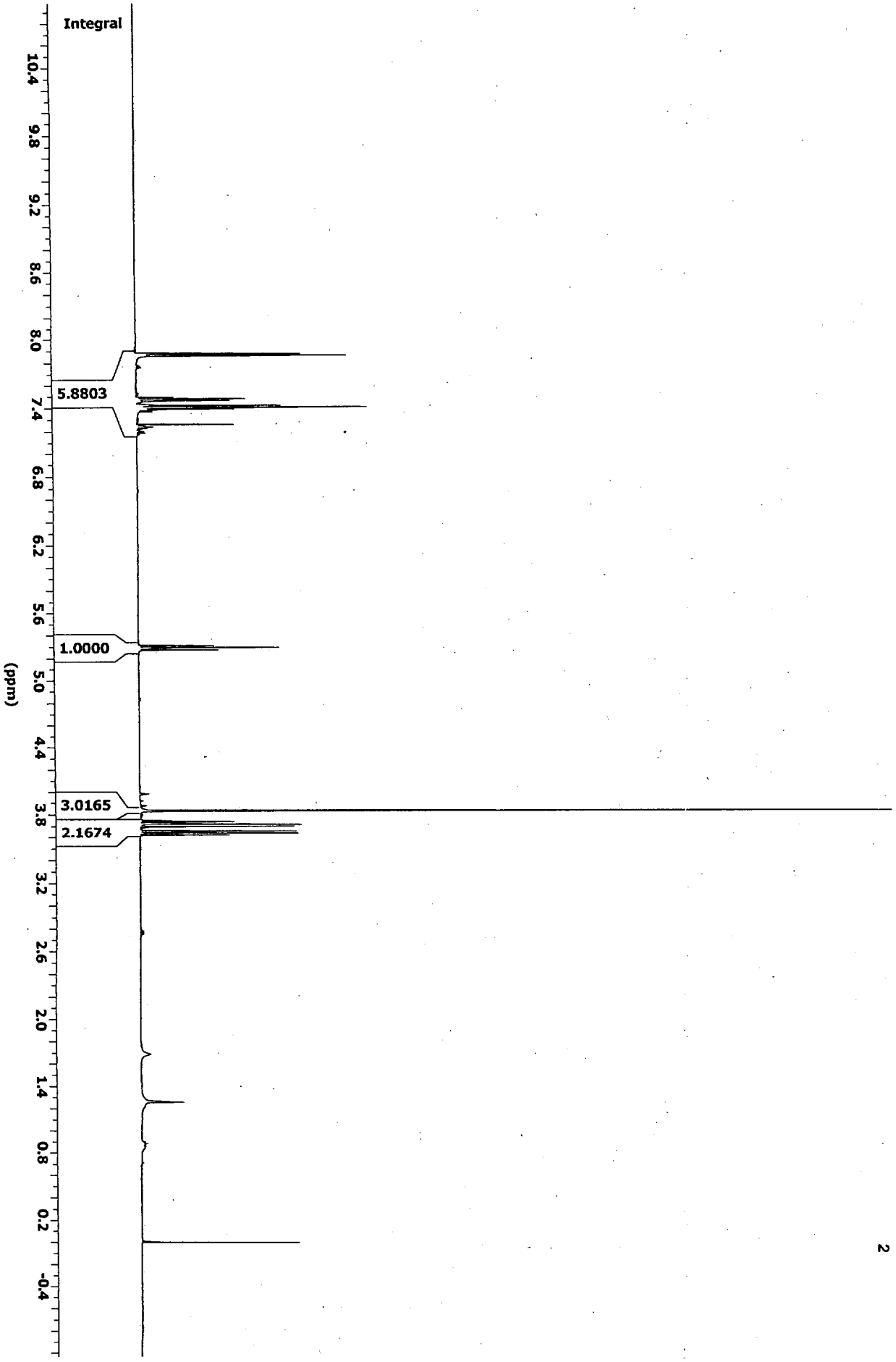
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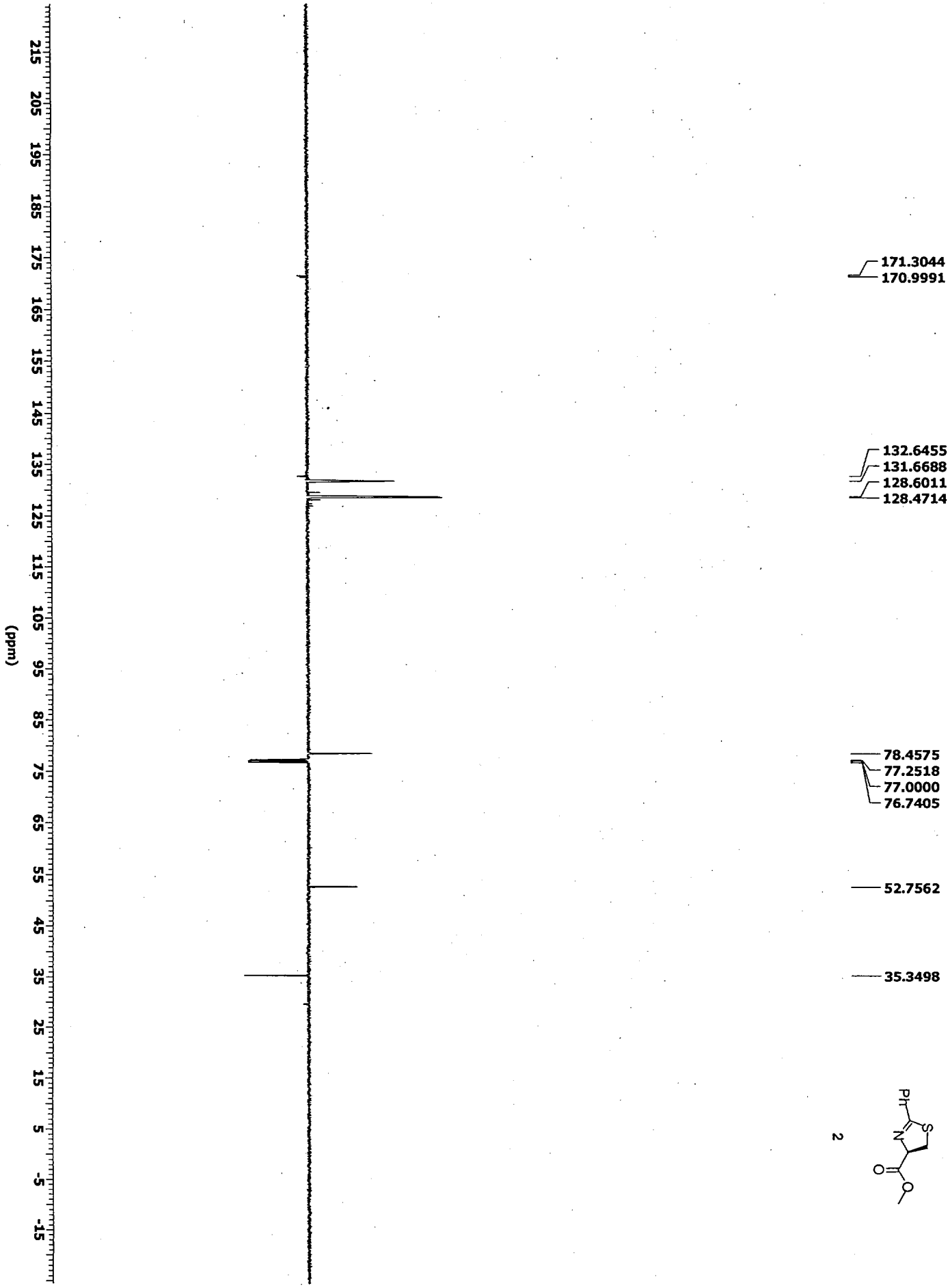
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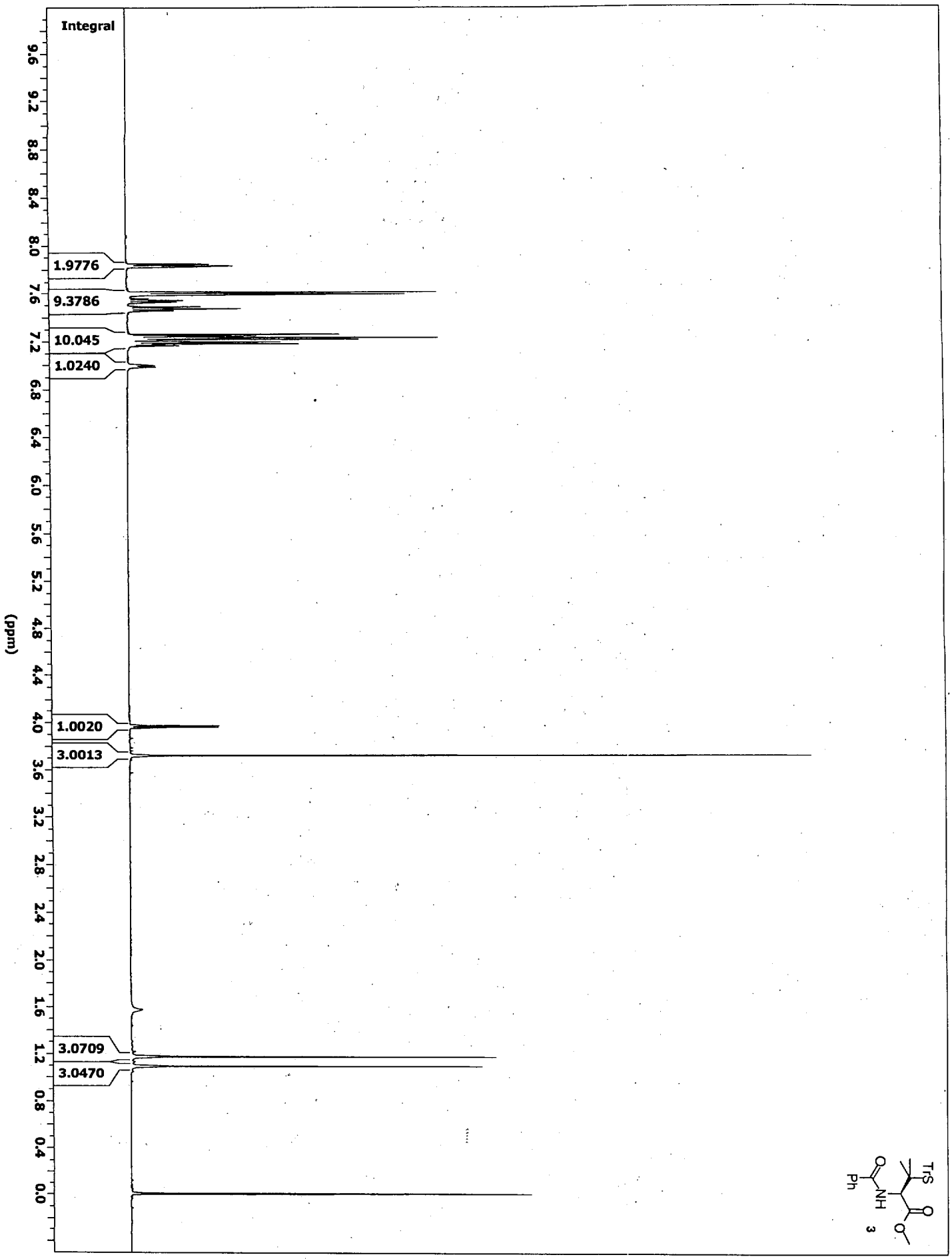
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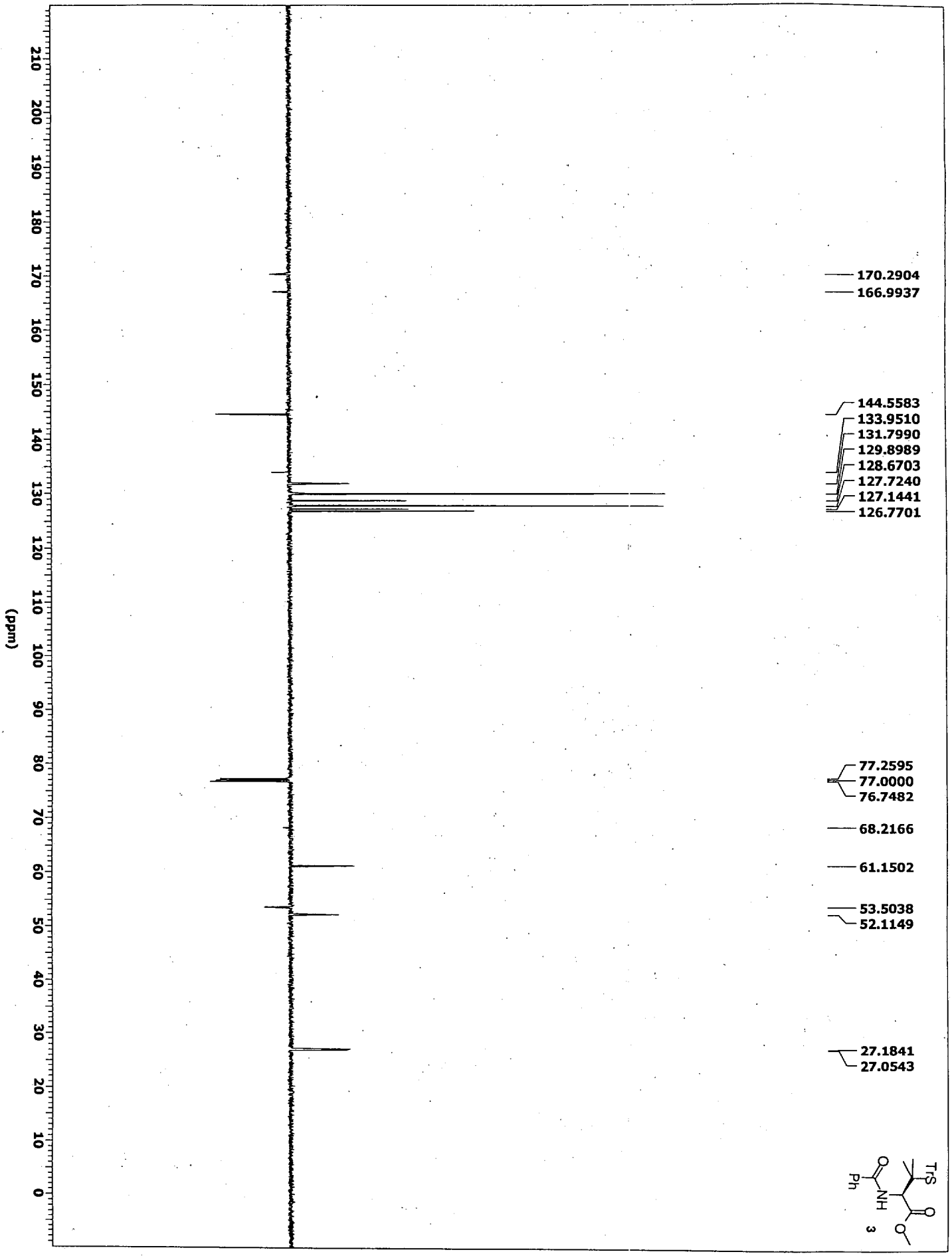
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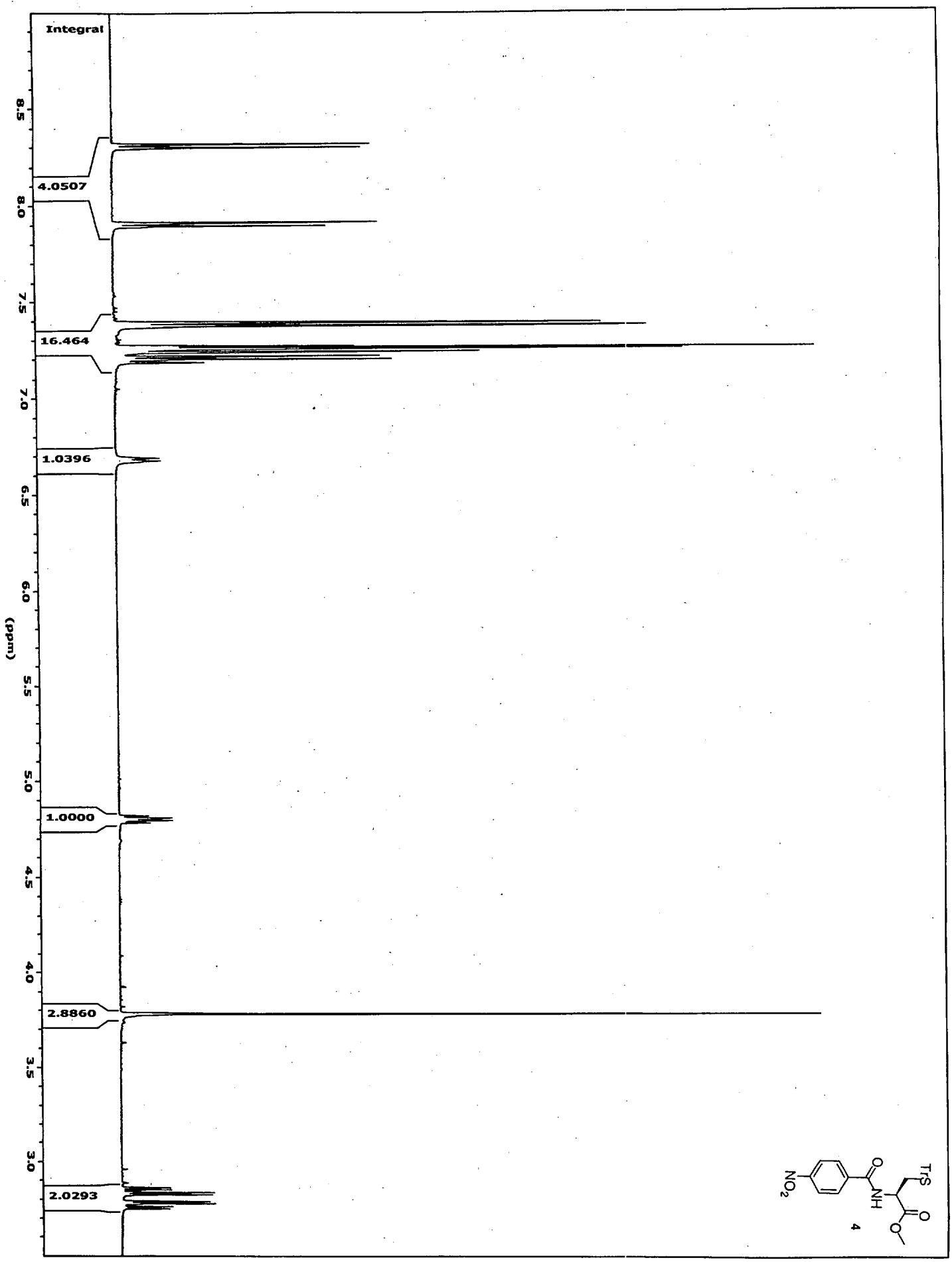
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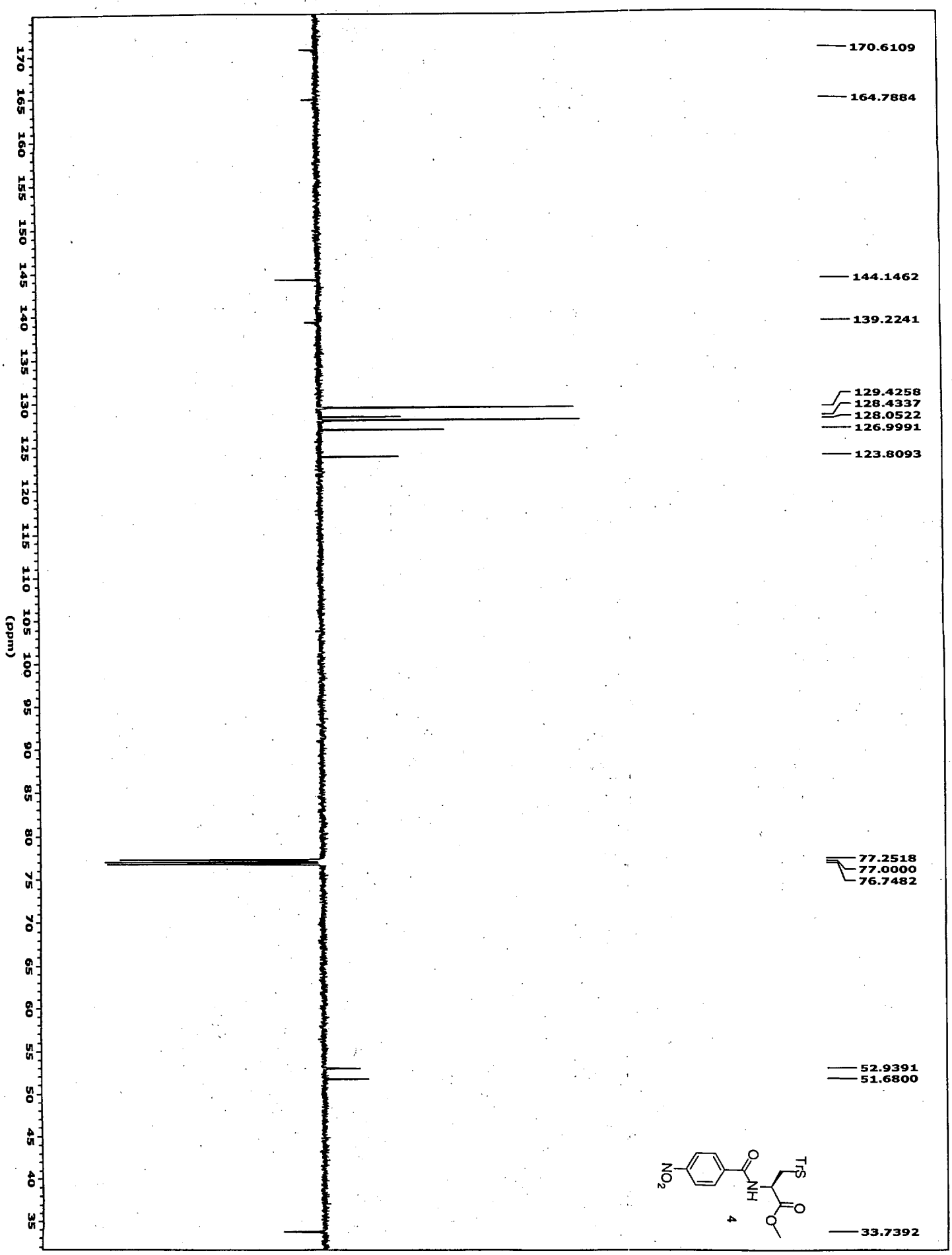
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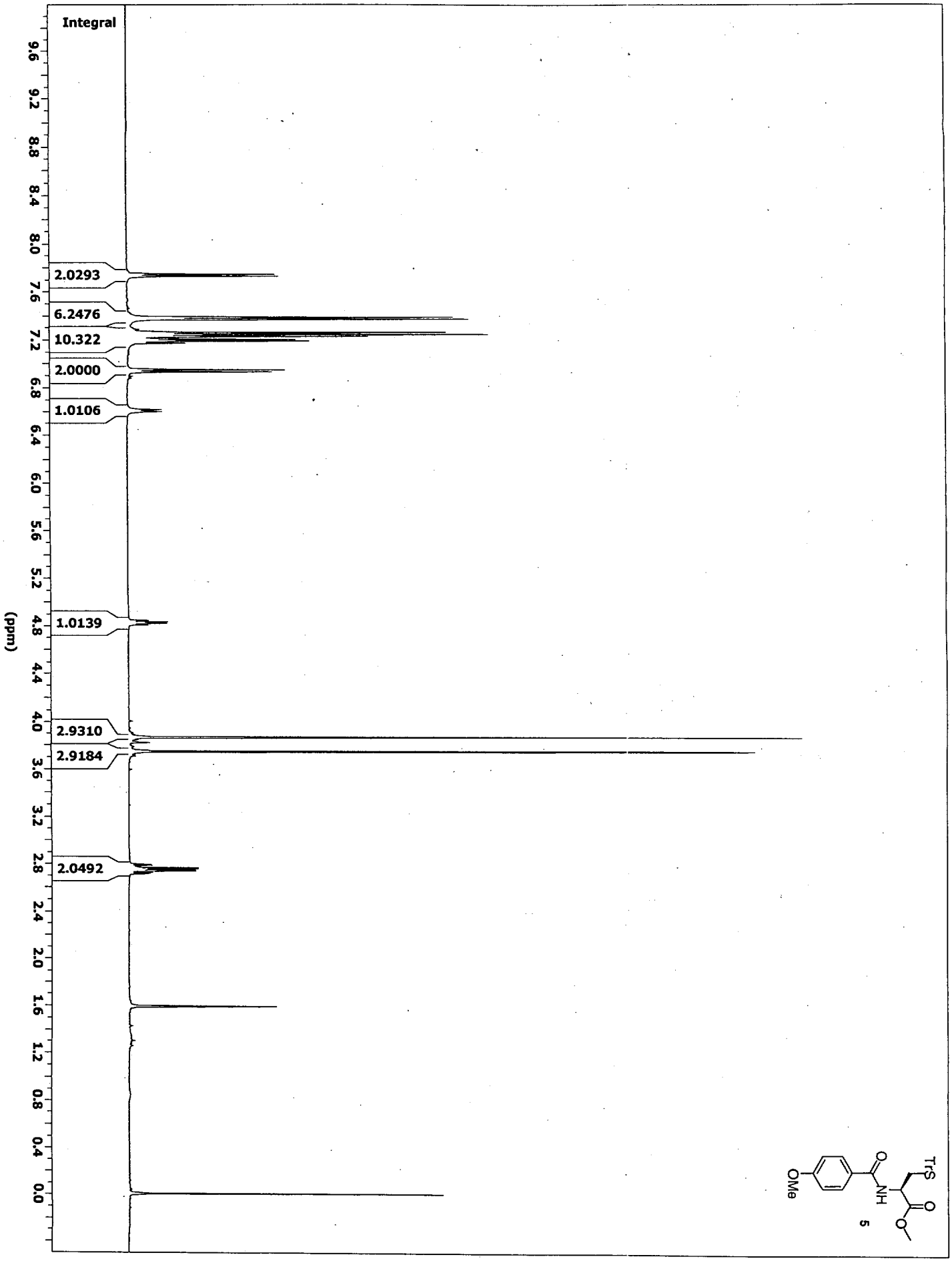
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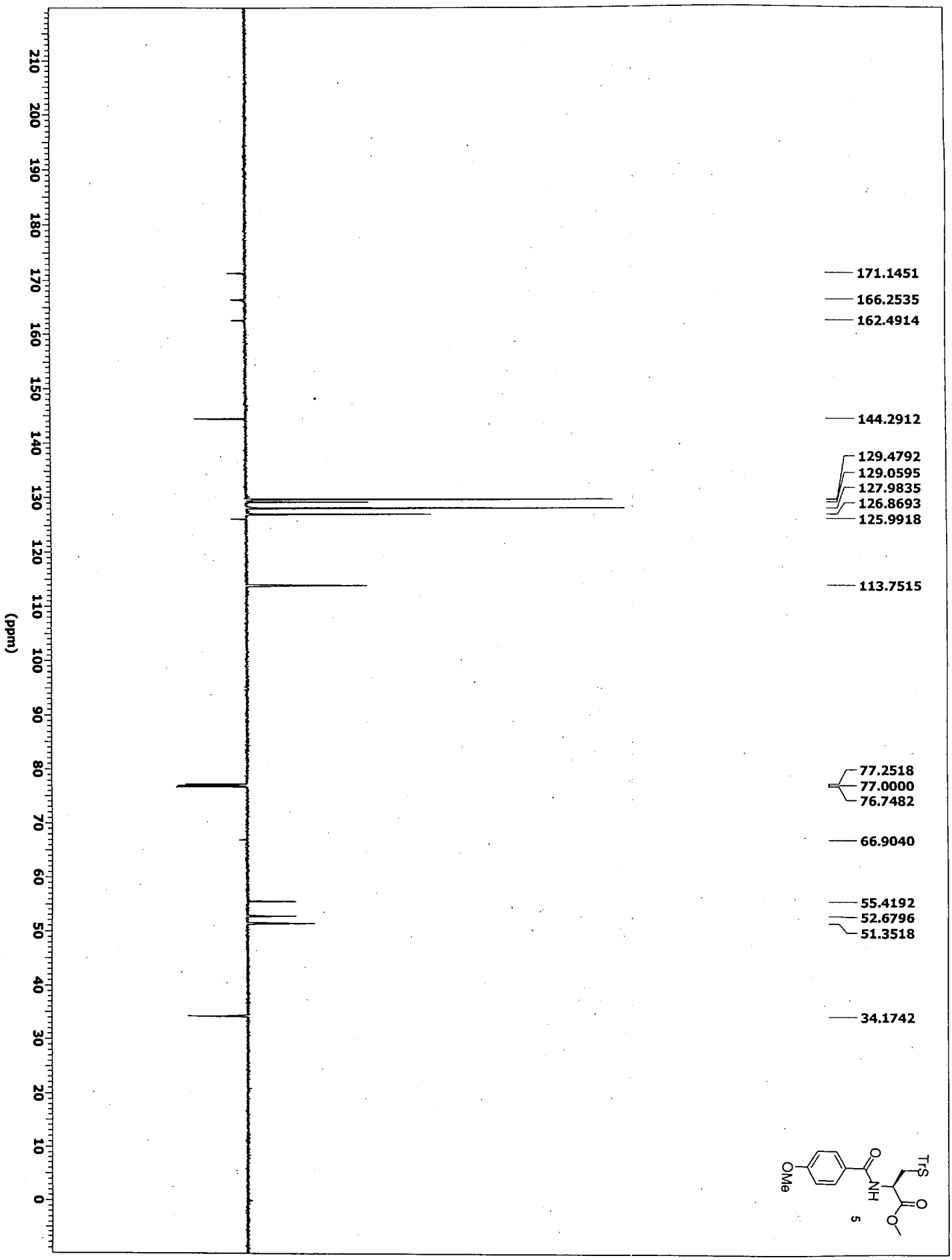
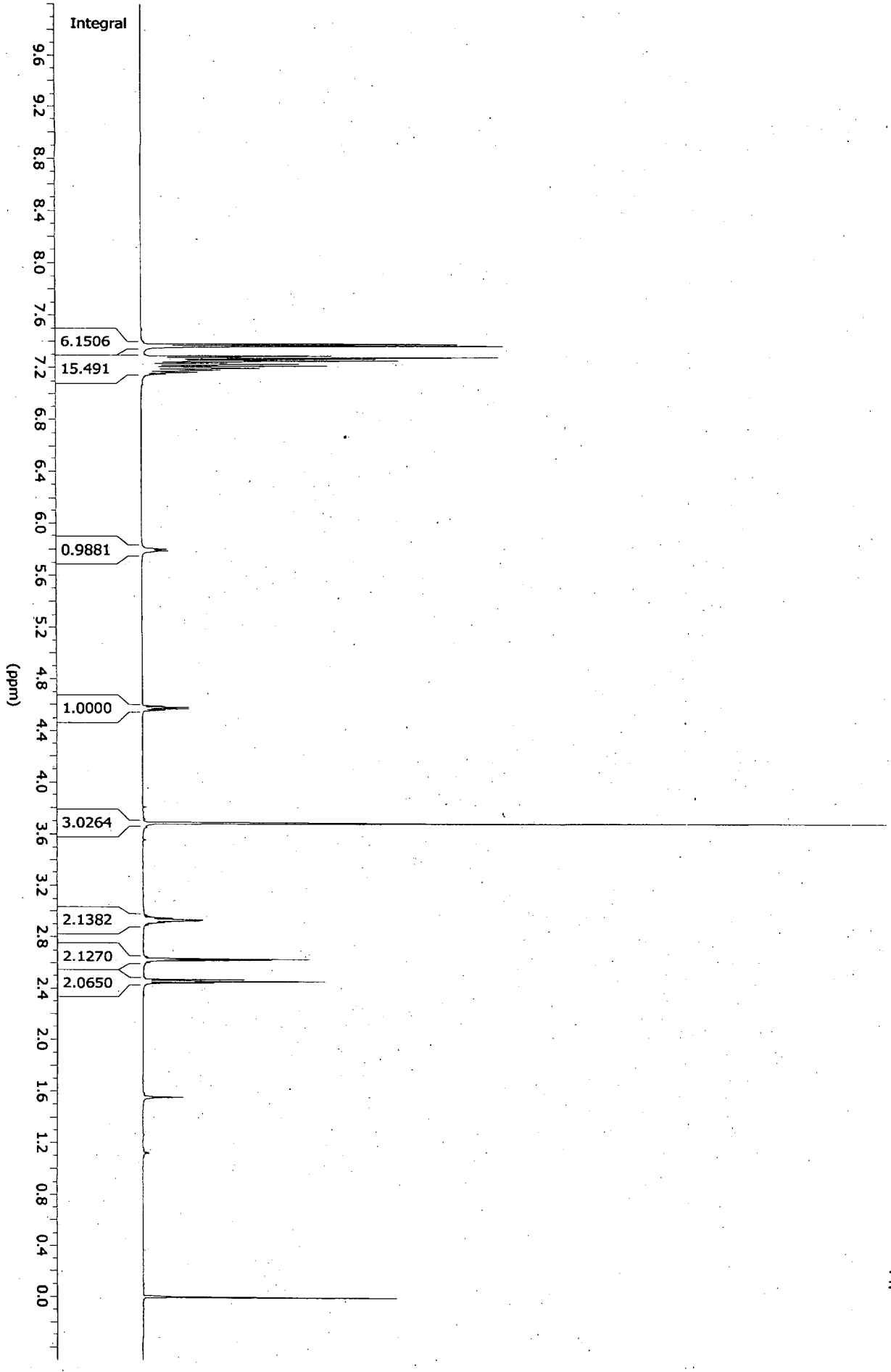
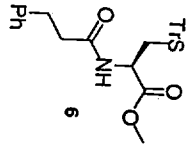
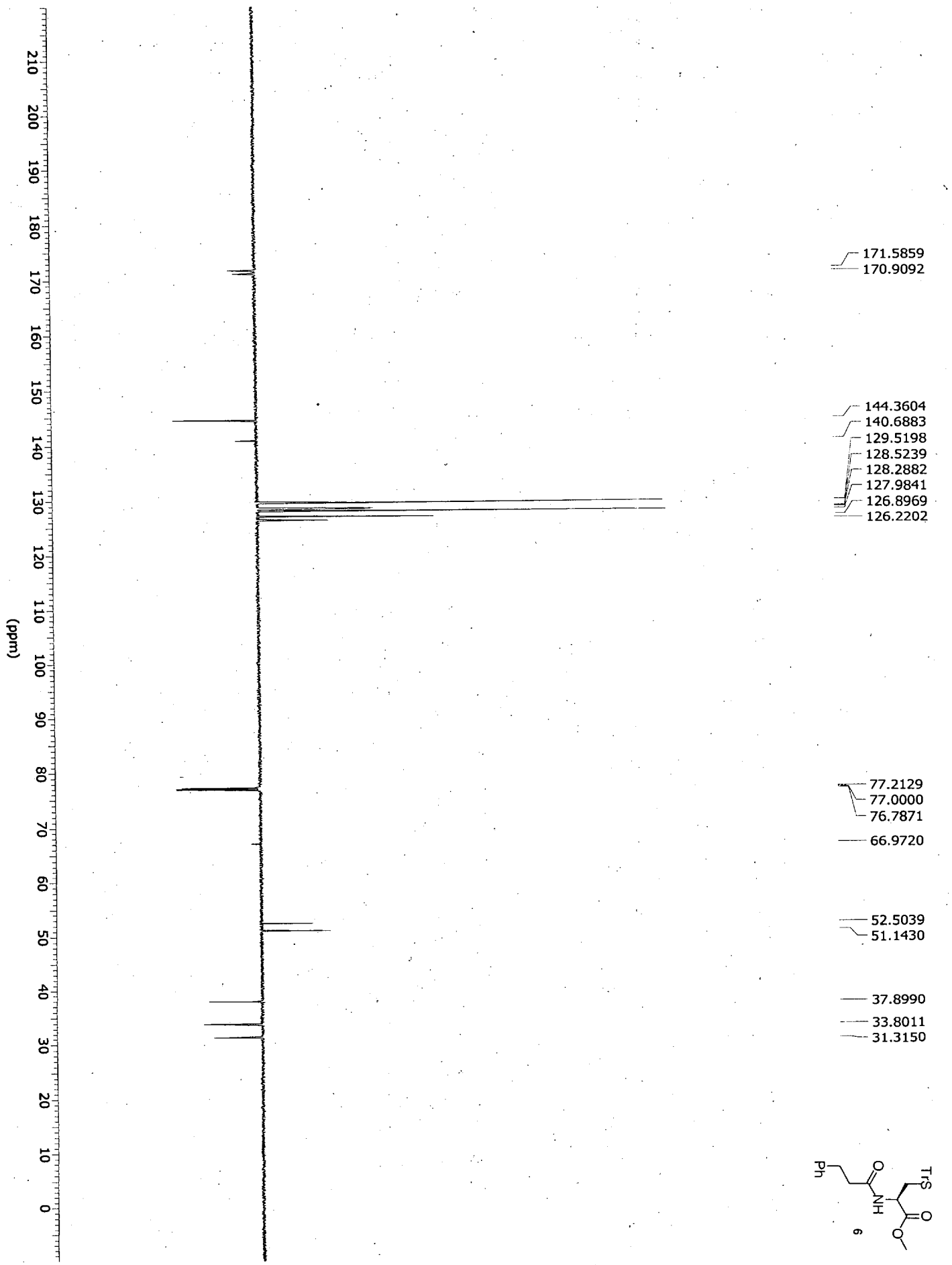
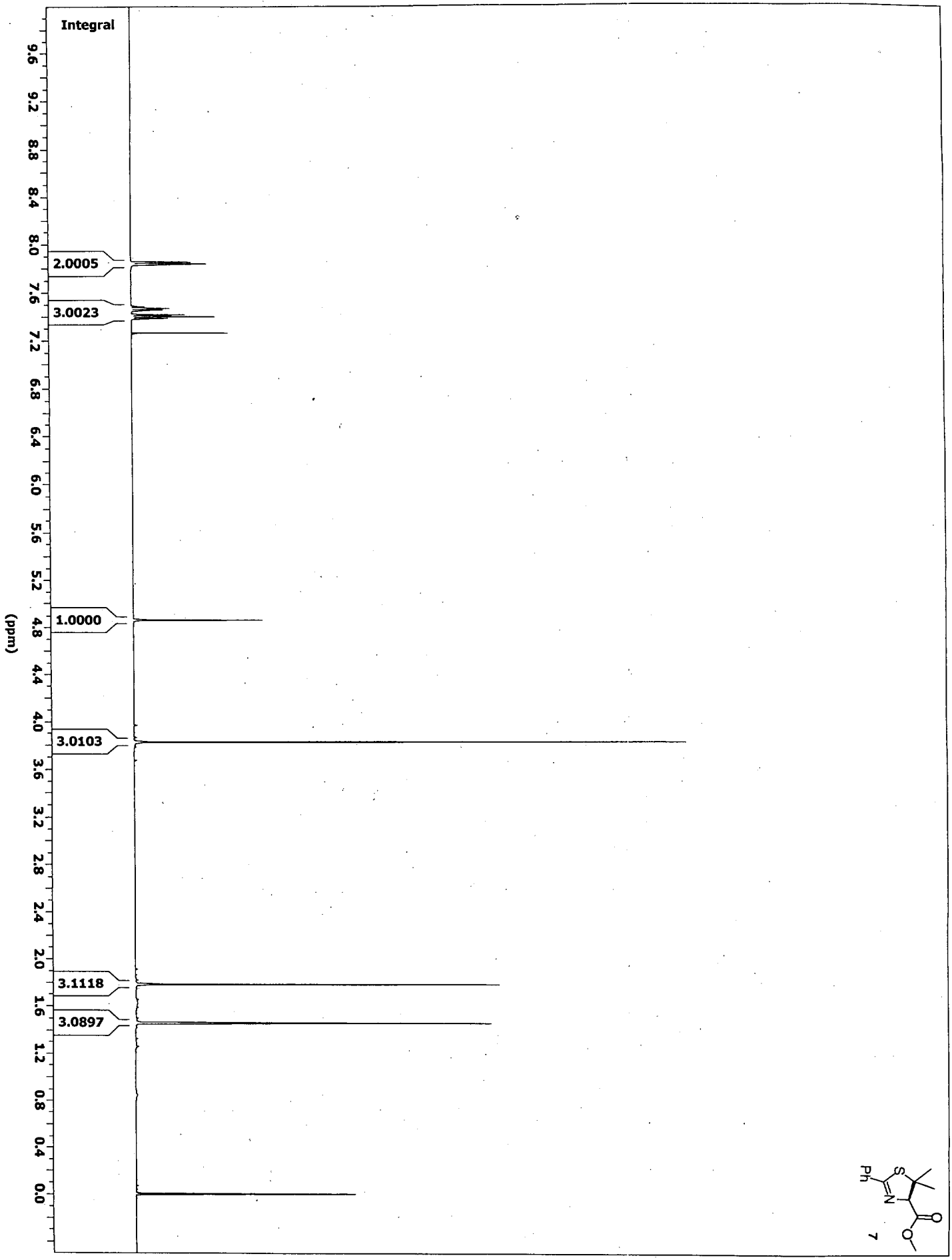
2.0293
6.2476
10.322
2.0000
1.0106
1.0139
2.9310
2.9184
2.0492
(ppm)
OMe
NH
TrS
5

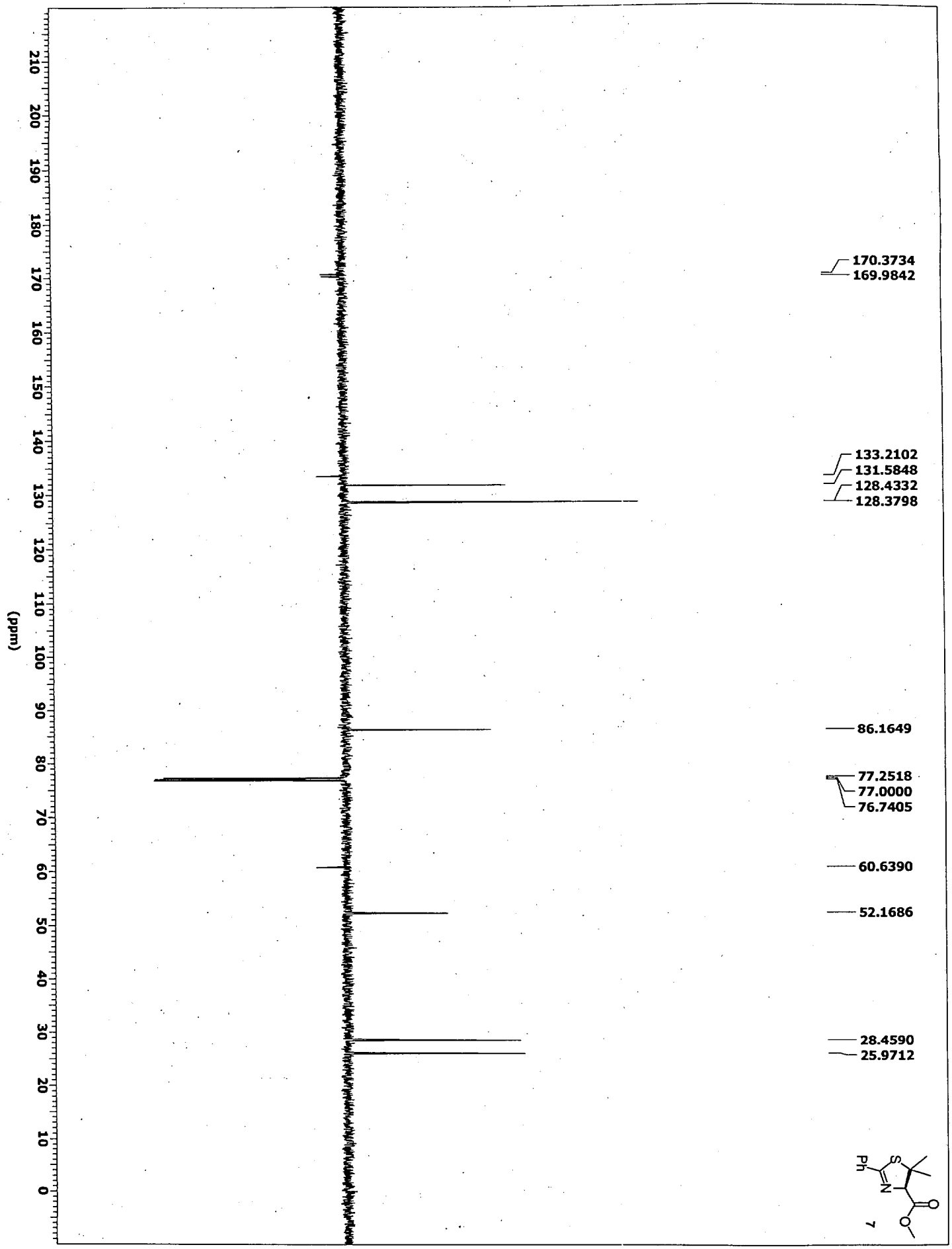

171.1451
166.2535
162.4914
144.2912
129.4792
129.0595
127.9835
126.8693
125.9918
113.7515
77.2518
77.0000
76.7482
66.9040
55.4192
52.6796
51.3518
34.1742
(ppm)
OMe
NH
TrS
5

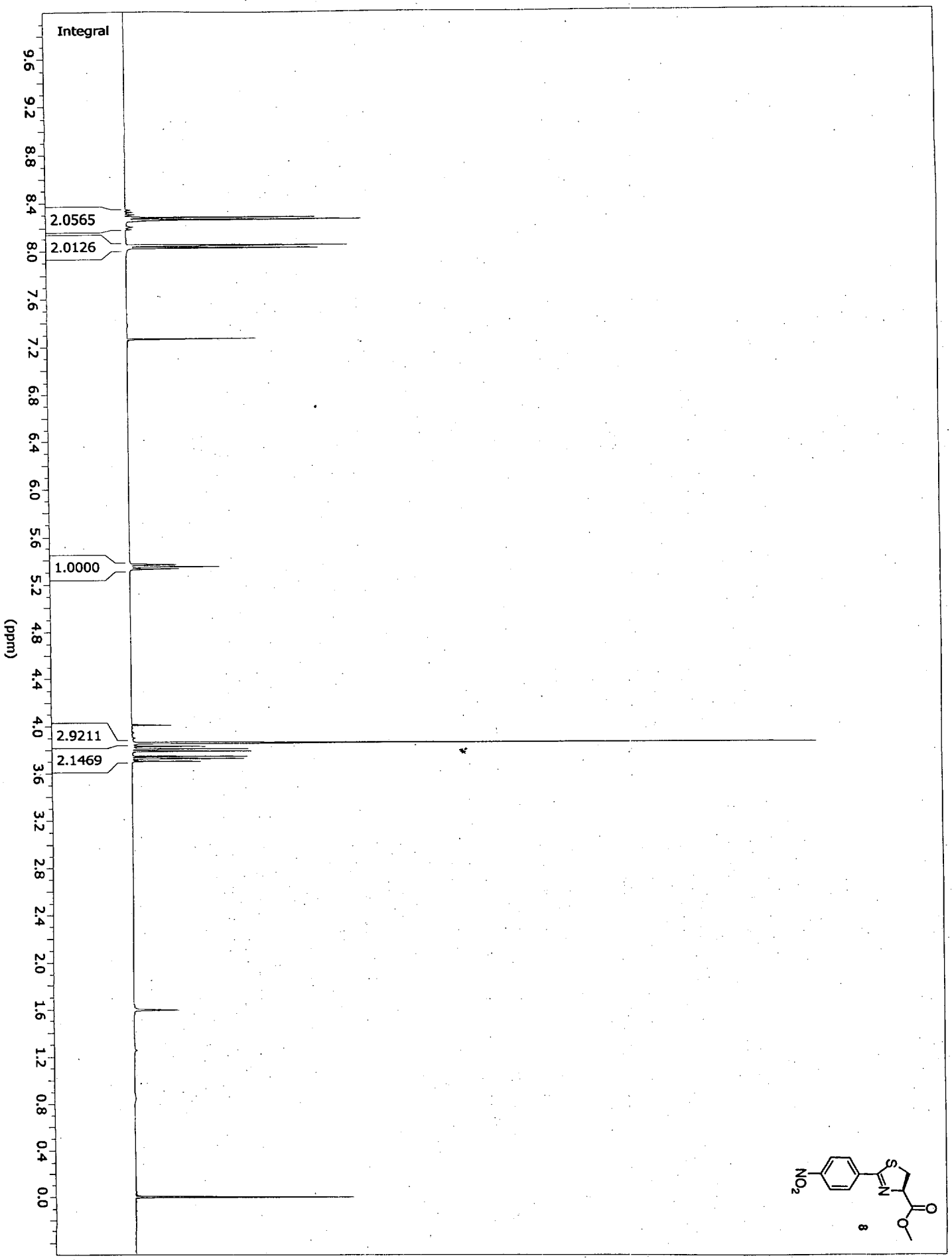

Integral
6.1506
15.491
0.9881
1.0000
3.0264
2.1382
2.1270
2.0650
(ppm)
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0

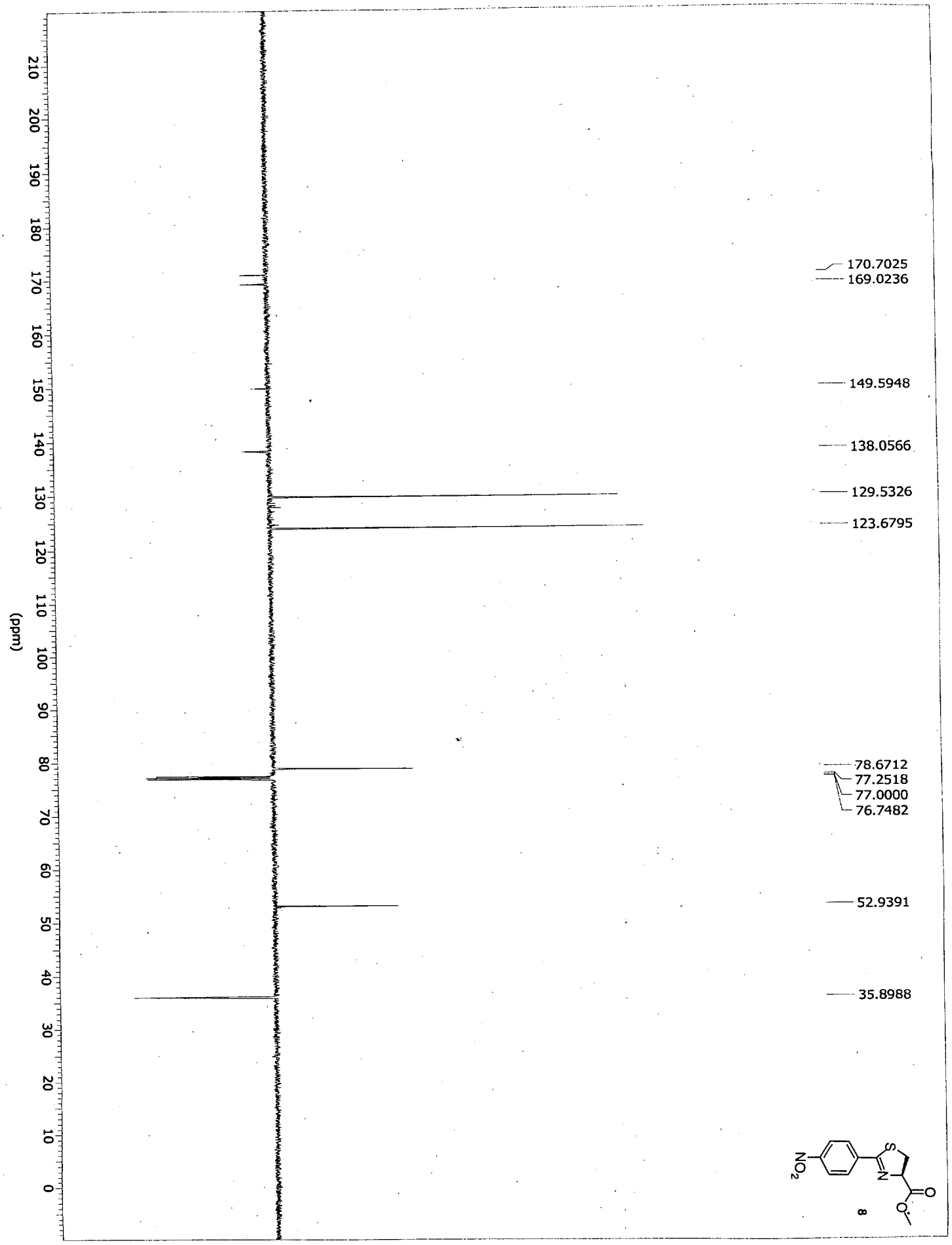

Ph
O
NH
TrS
O
O
6

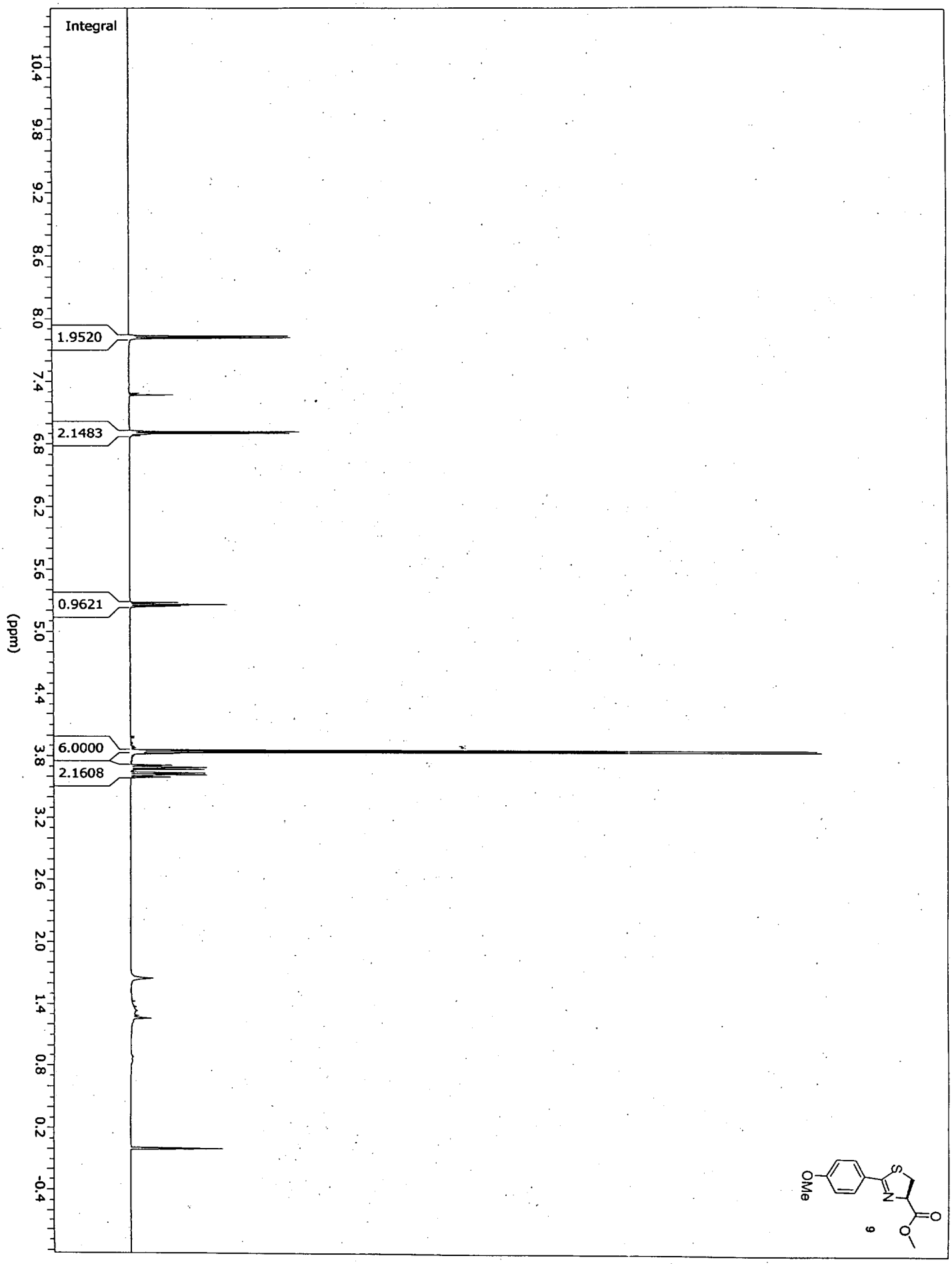

171.5859
170.9092
144.3604
140.6883
129.5198
128.5239
128.2882
127.9841
126.8969
126.2202
77.2129
77.0000
76.7871
66.9720
52.5039
51.1430
37.8990
33.8011
31.3150
(ppm)
Ph
NH
TrS
6

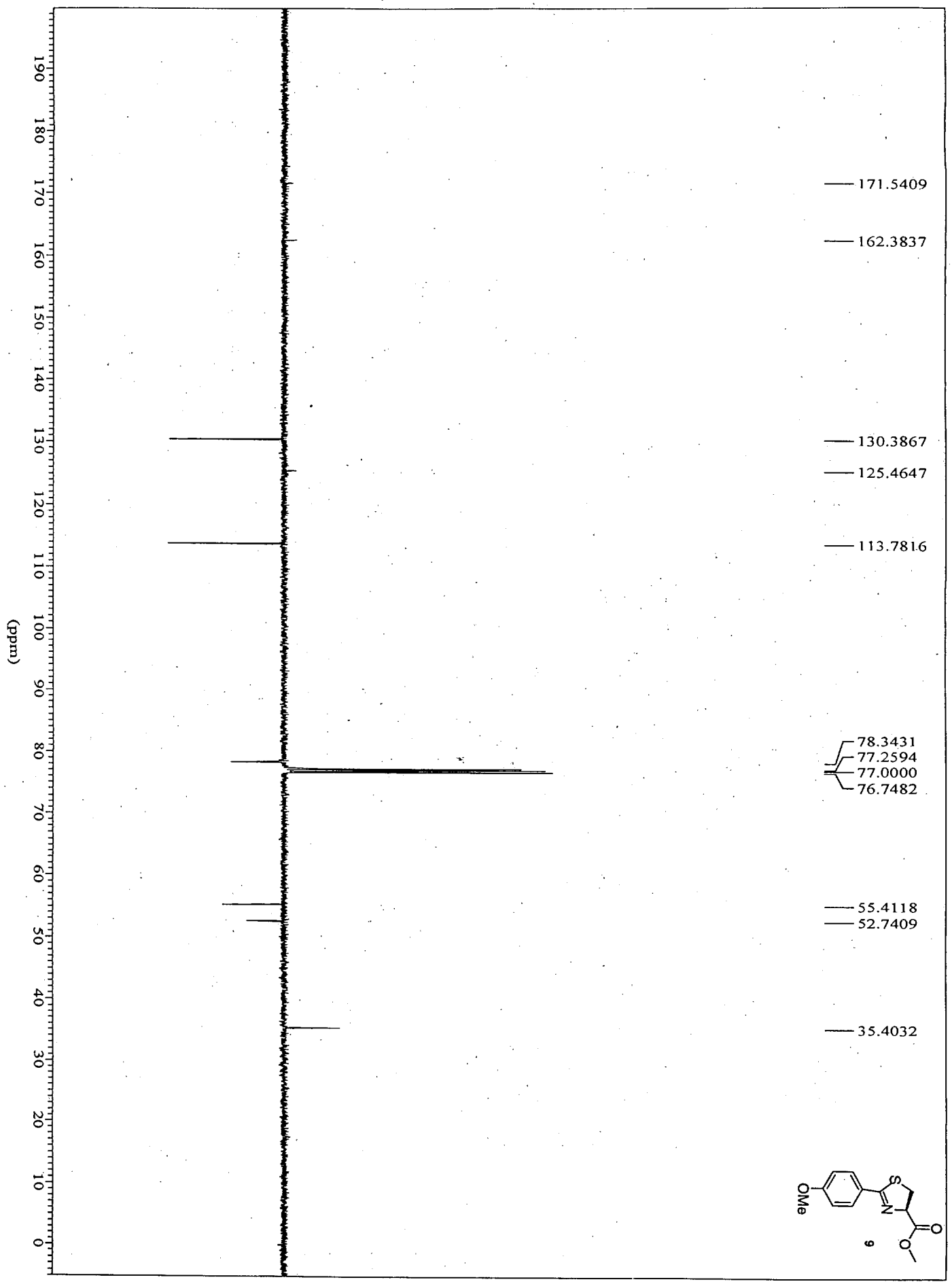

Integral
2.0005
3.0023
1.0000
3.0103
3.1118
3.0897
(ppm)
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0
Ph
S
N
O
O
7

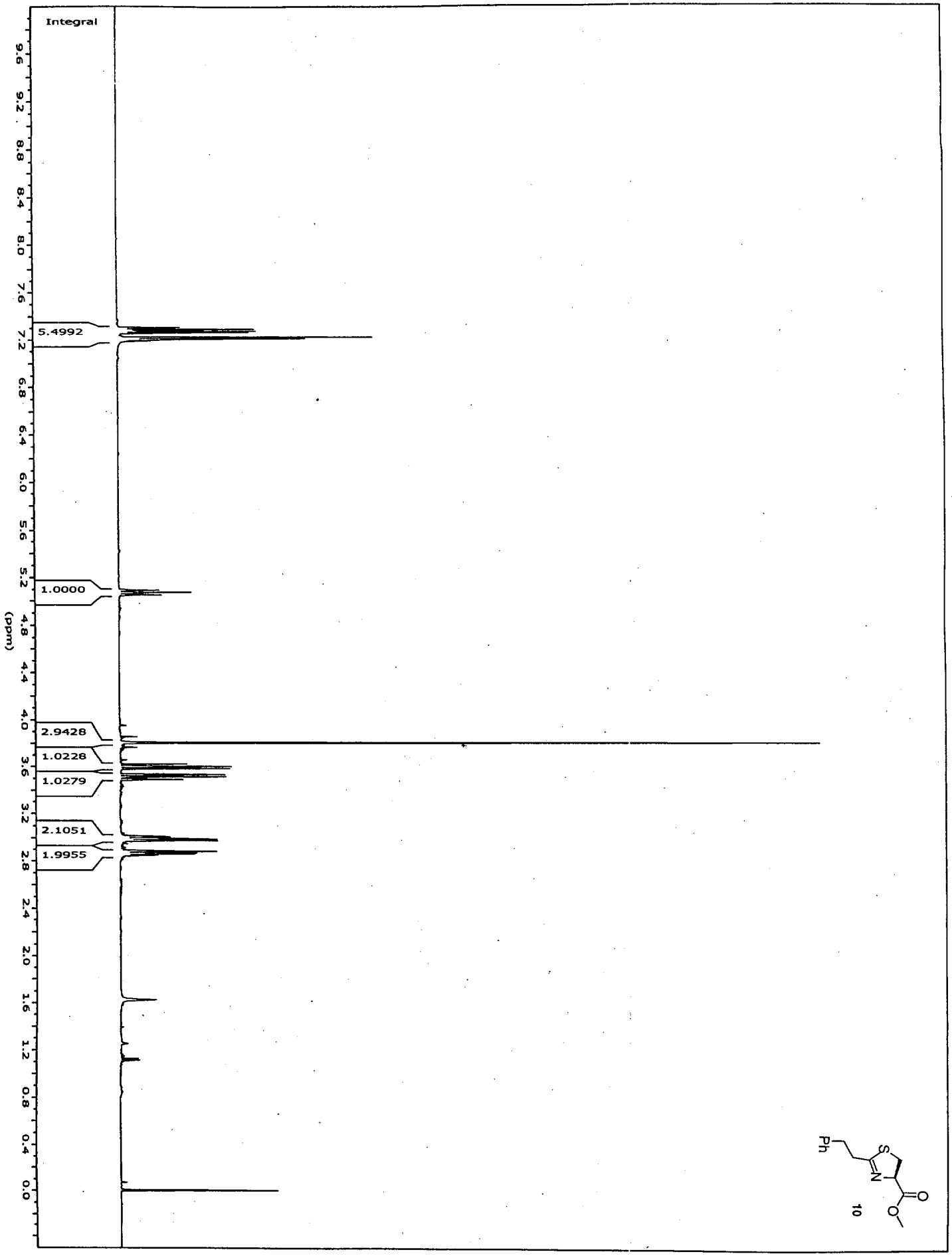

170.3734
169.9842
133.2102
131.5848
128.4332
128.3798
86.1649
77.2518
77.0000
76.7405
60.6390
52.1686
28.4590
25.9712
(ppm)
Ph
S
N
O
O
7

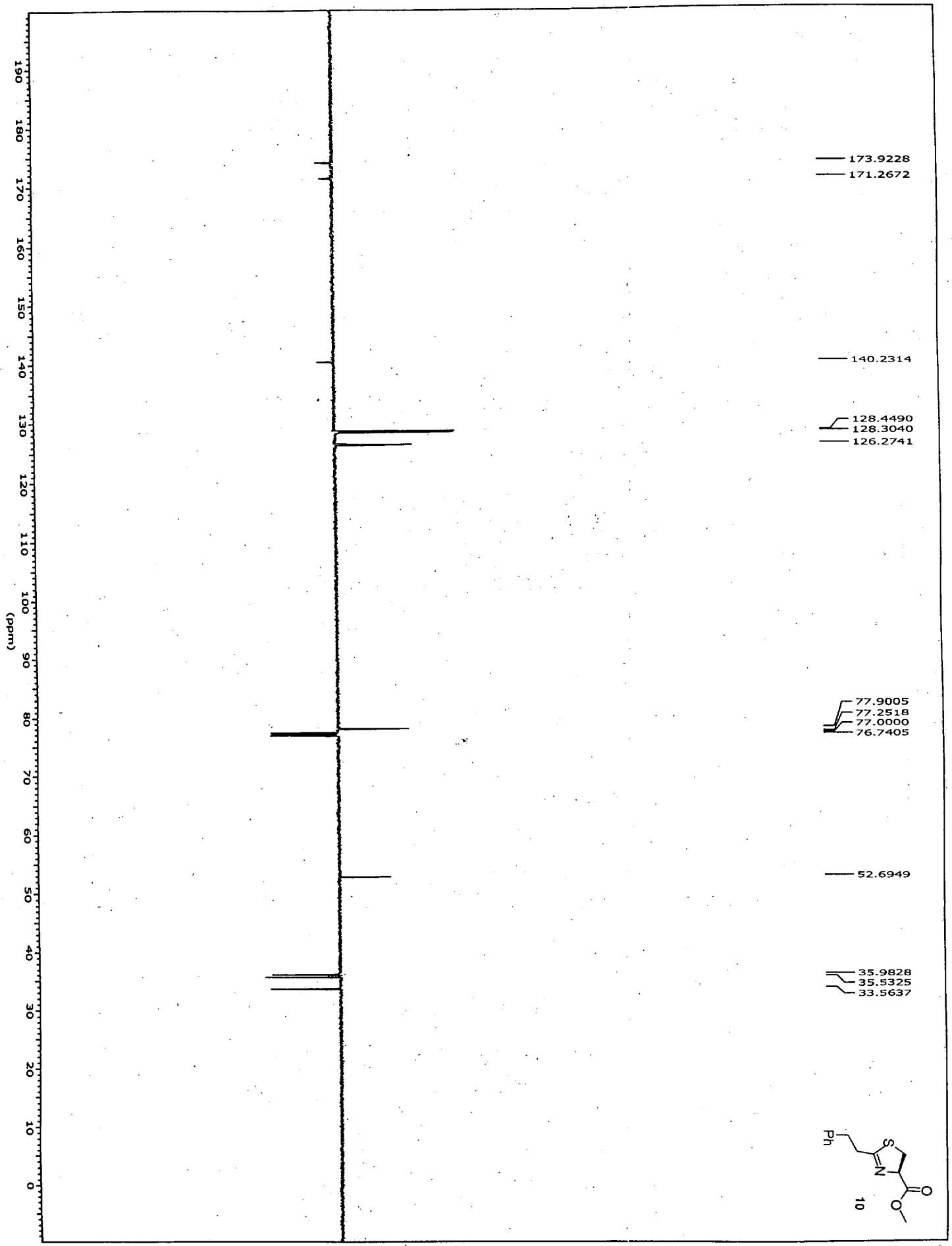

Integral
2.0565
2.0126
1.0000
2.9211
2.1469
(ppm)
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0.0
NO2
S
N
O
O
8

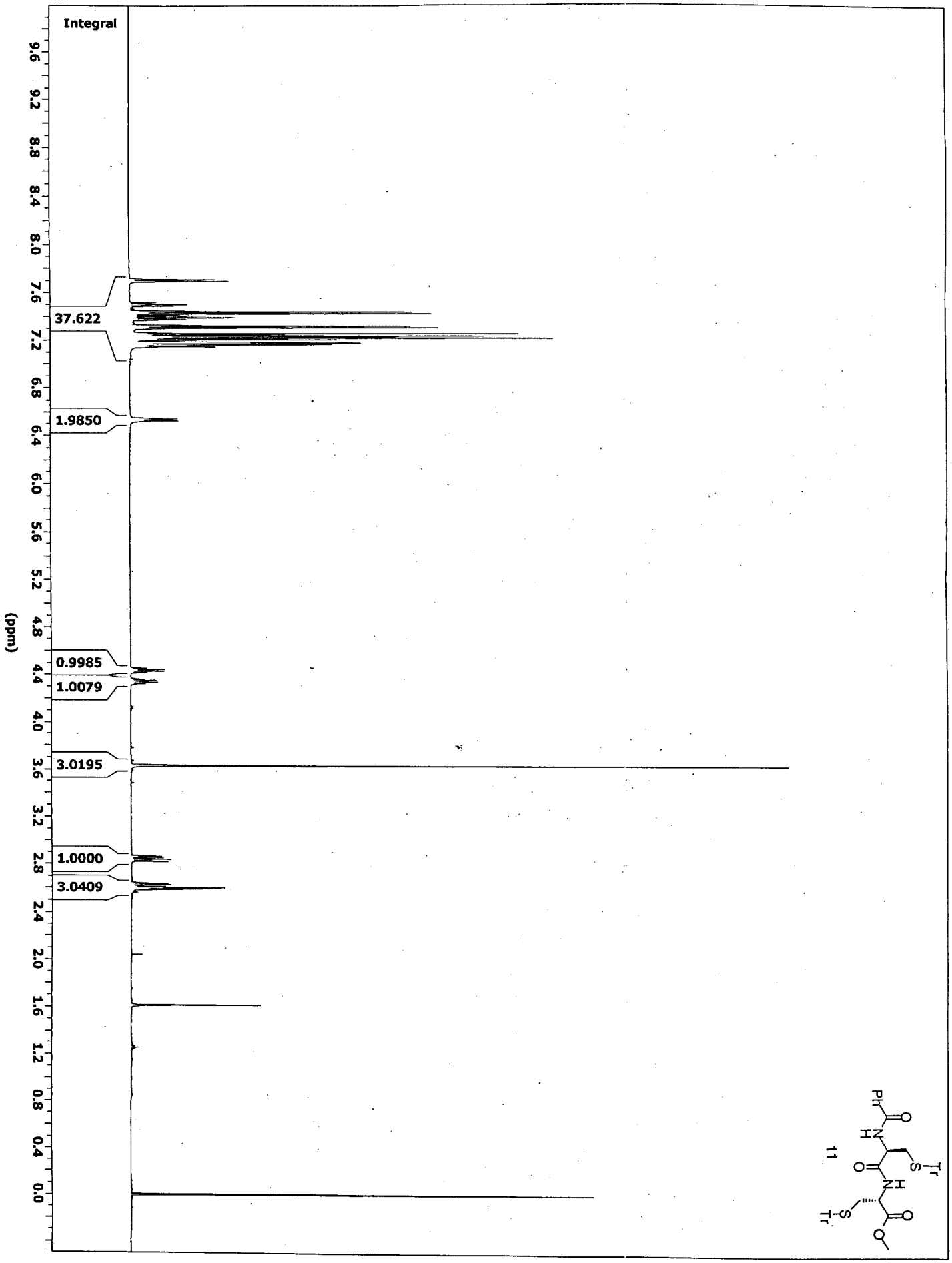

170.7025
169.0236
149.5948
138.0566
129.5326
123.6795
78.6712
77.2518
77.0000
76.7482
52.9391
35.8988
(ppm)
NO2
S
N
O
O
8

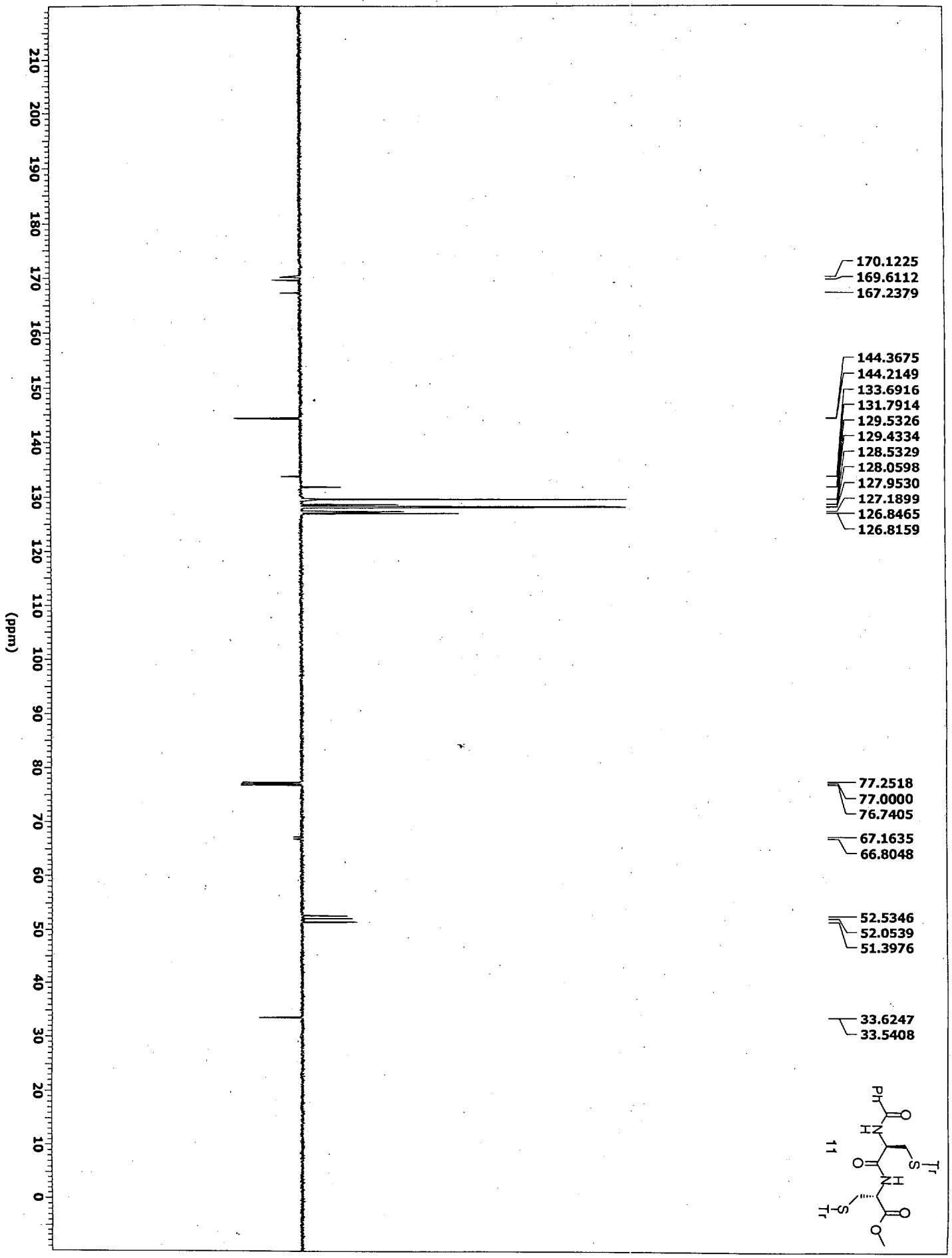

Integral
1.9520
2.1483
0.9621
6.0000
2.1608
(ppm)
10.4
9.8
9.2
8.6
8.0
7.4
6.8
6.2
5.6
5.0
4.4
3.8
3.2
2.6
2.0
1.4
0.8
0.2
-0.4
OMe
S
N
O
O
9

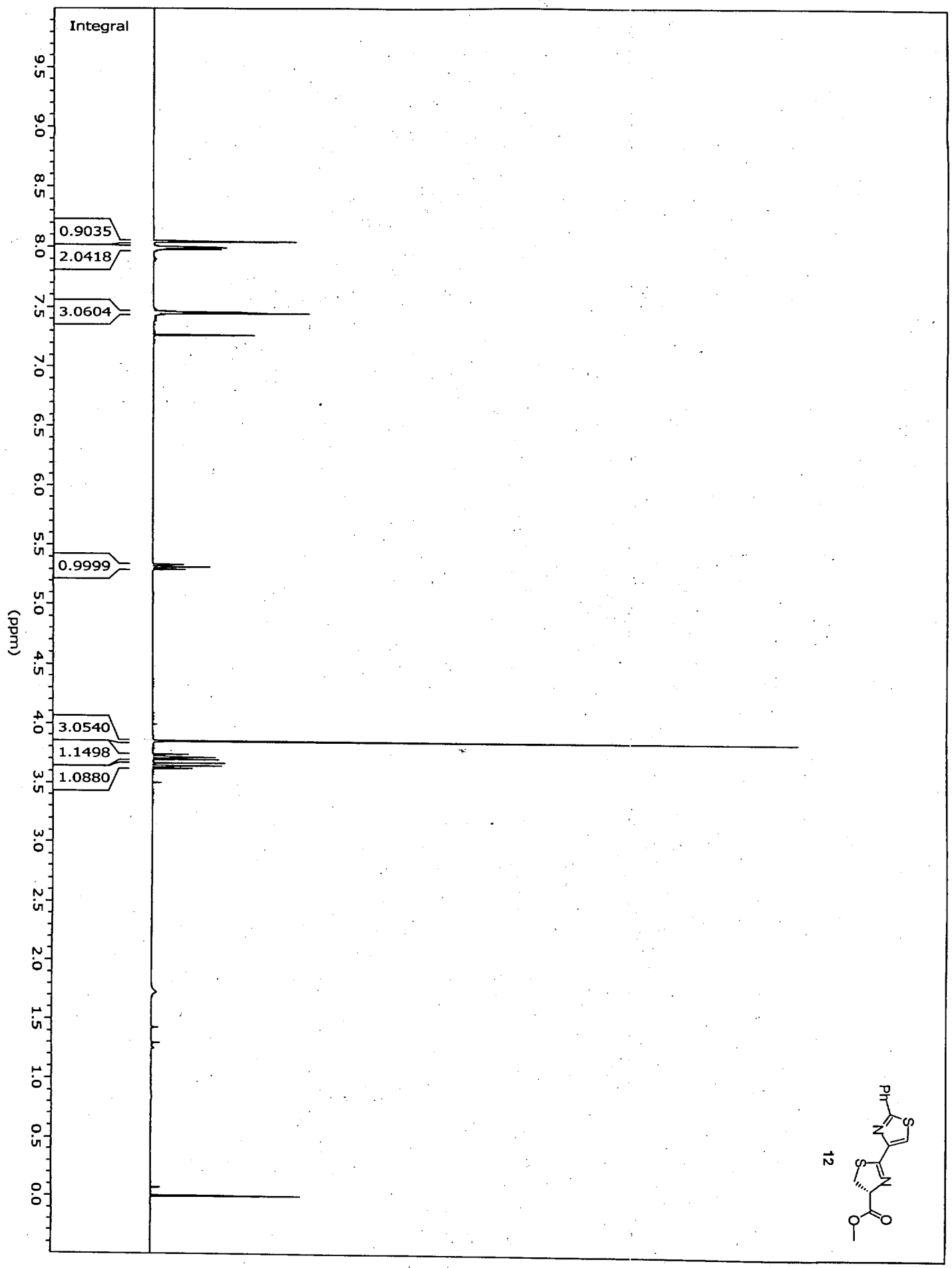

171.5409
162.3837
130.3867
125.4647
113.7816
78.3431
77.2594
77.0000
76.7482
55.4118
52.7409
35.4032
(ppm)
OMe
S
N
O
O
9

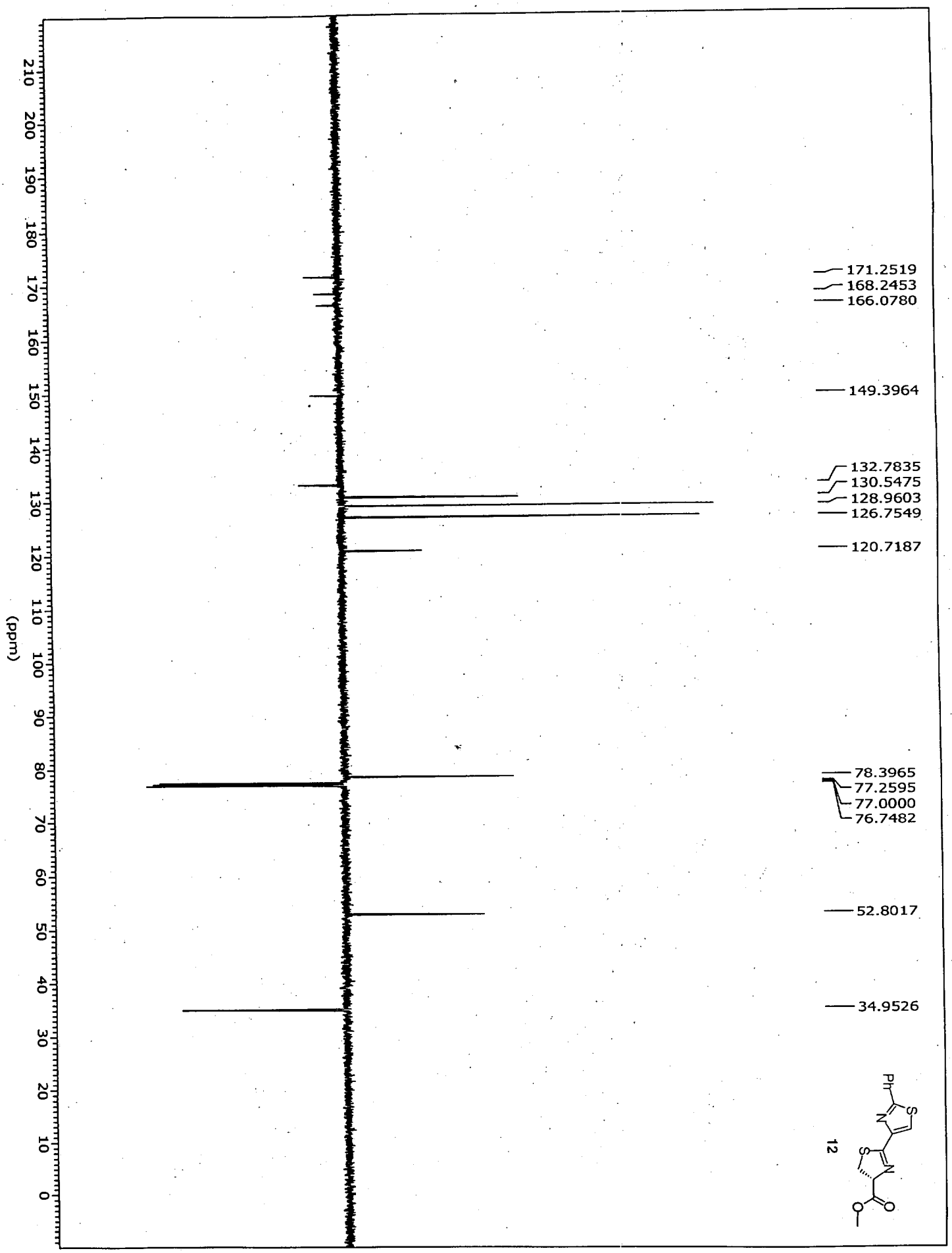


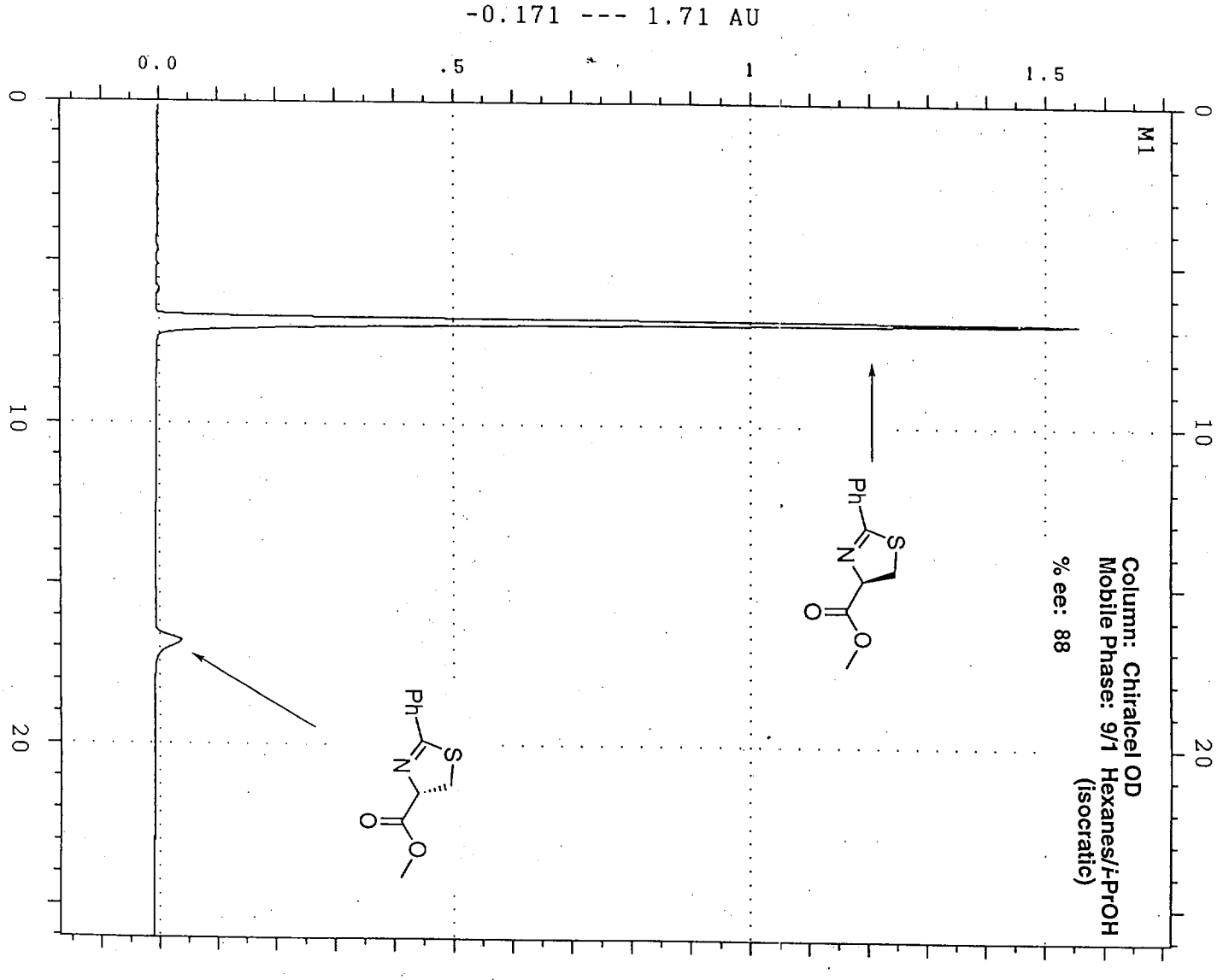

173.9228
171.2672
140.2314
128.4490
128.3040
126.2741
77.9005
77.2518
77.0000
76.7405
52.6949
35.9828
35.5325
33.5637
(ppm)
Ph
S
N
O
O
10

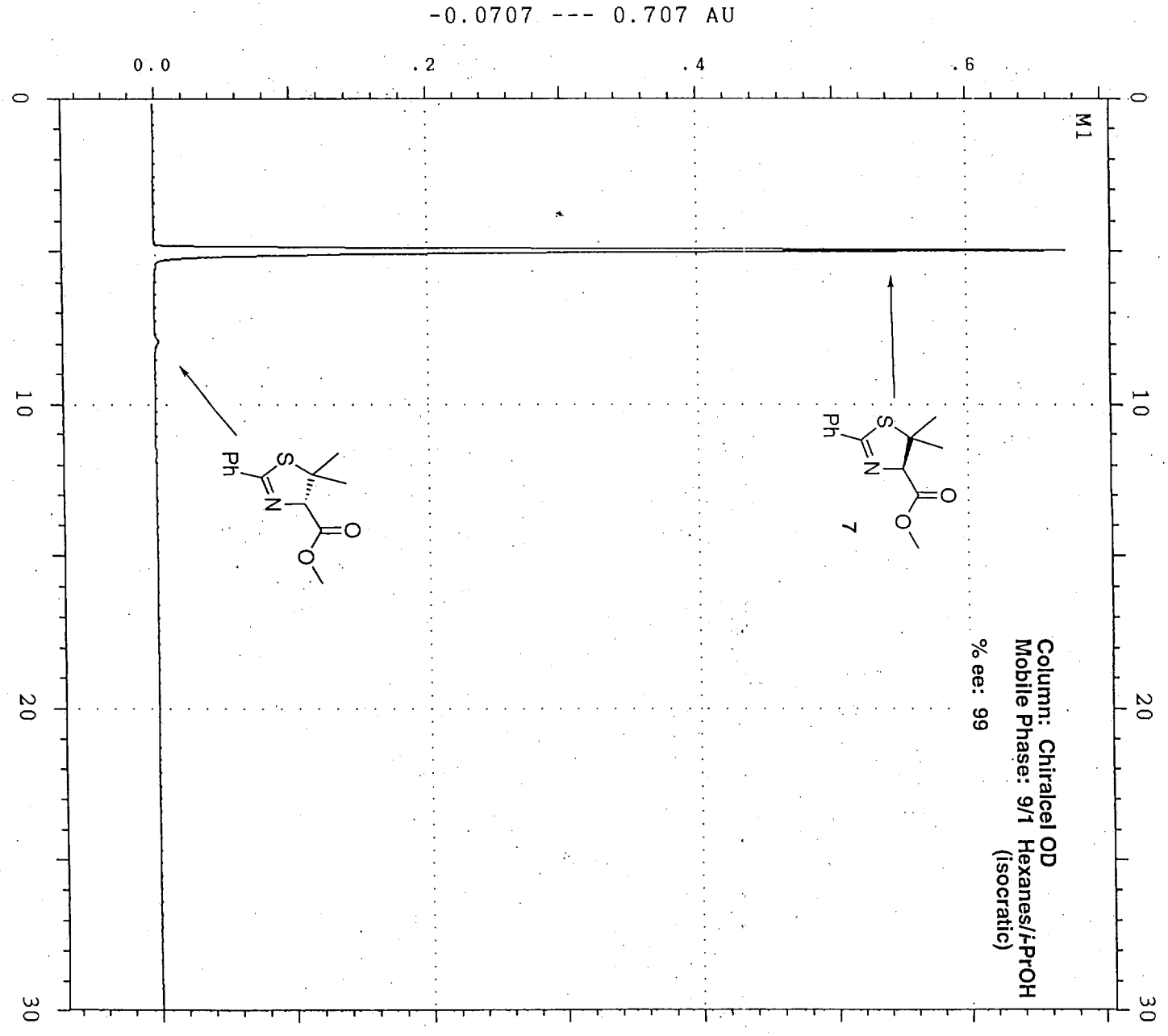


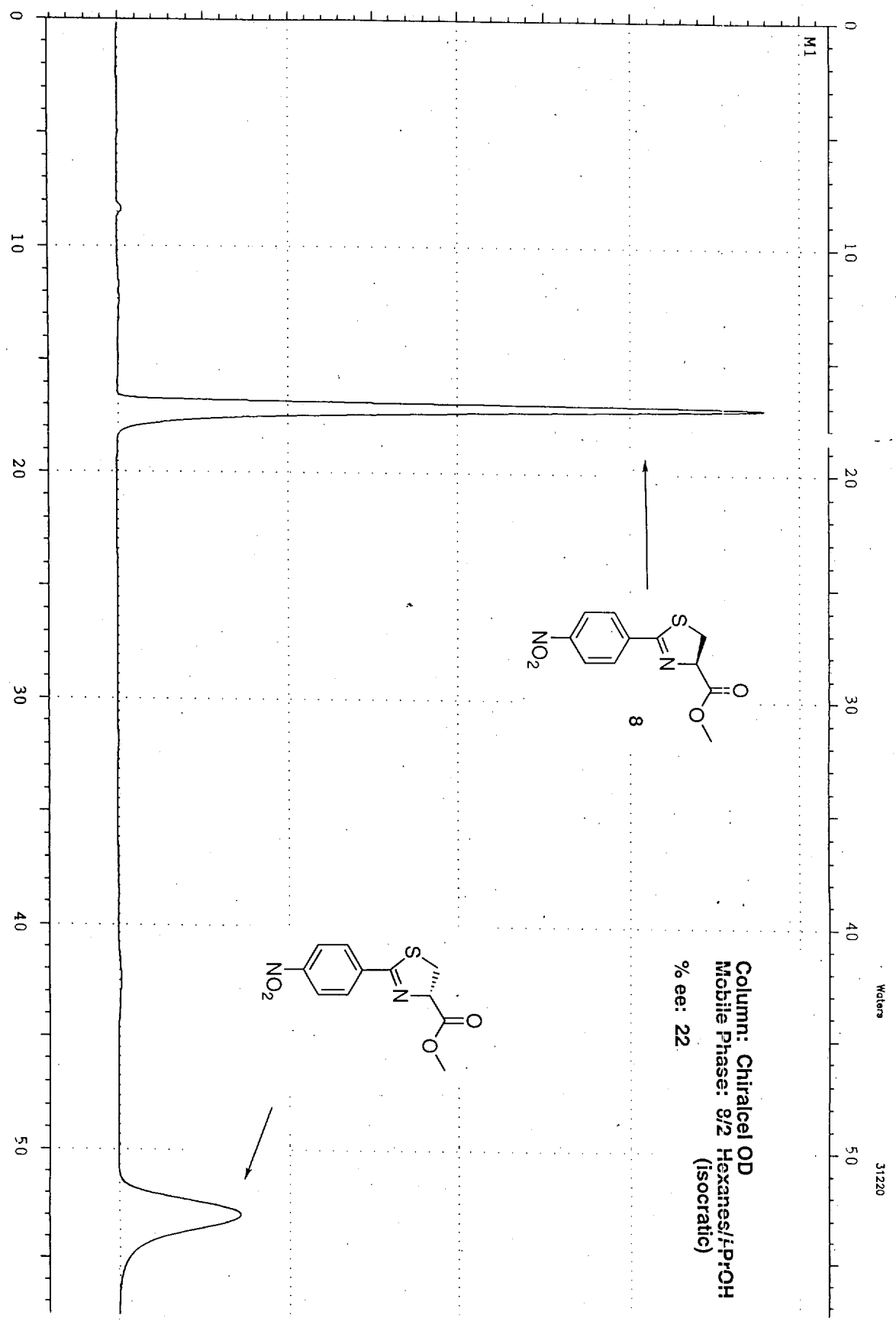

170.1225
169.6112
167.2379
144.3675
144.2149
133.6916
131.7914
129.5326
129.4334
128.5329
128.0598
127.9530
127.1899
126.8465
126.8159
77.2518
77.0000
76.7405
67.1635
66.8048
52.5346
52.0539
51.3976
33.6247
33.5408
(ppm)
11

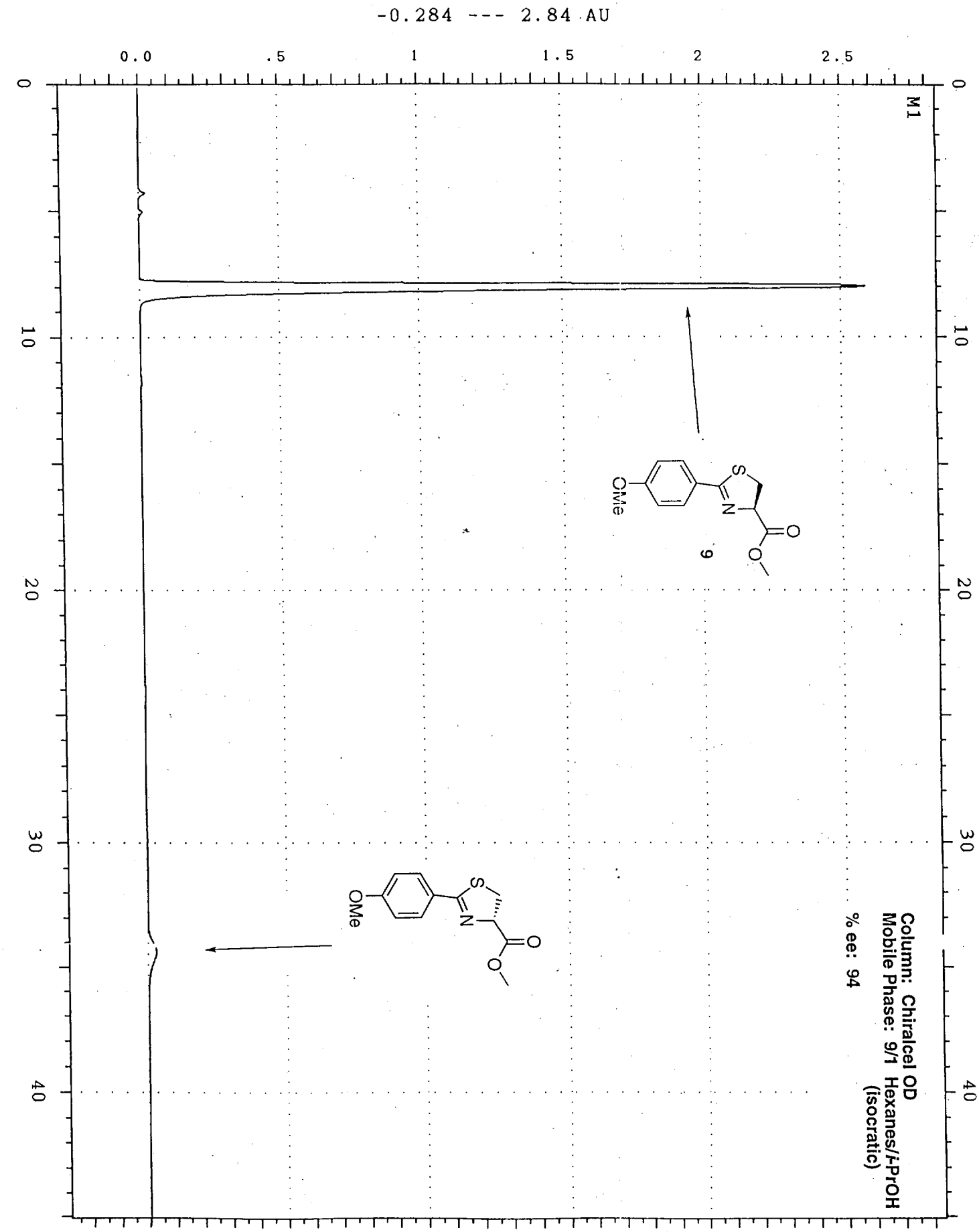

Integral
0.9035
2.0418
3.0604
0.9999
3.0540
1.1498
1.0880
(ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Ph
S
N
S
N
O
O
12

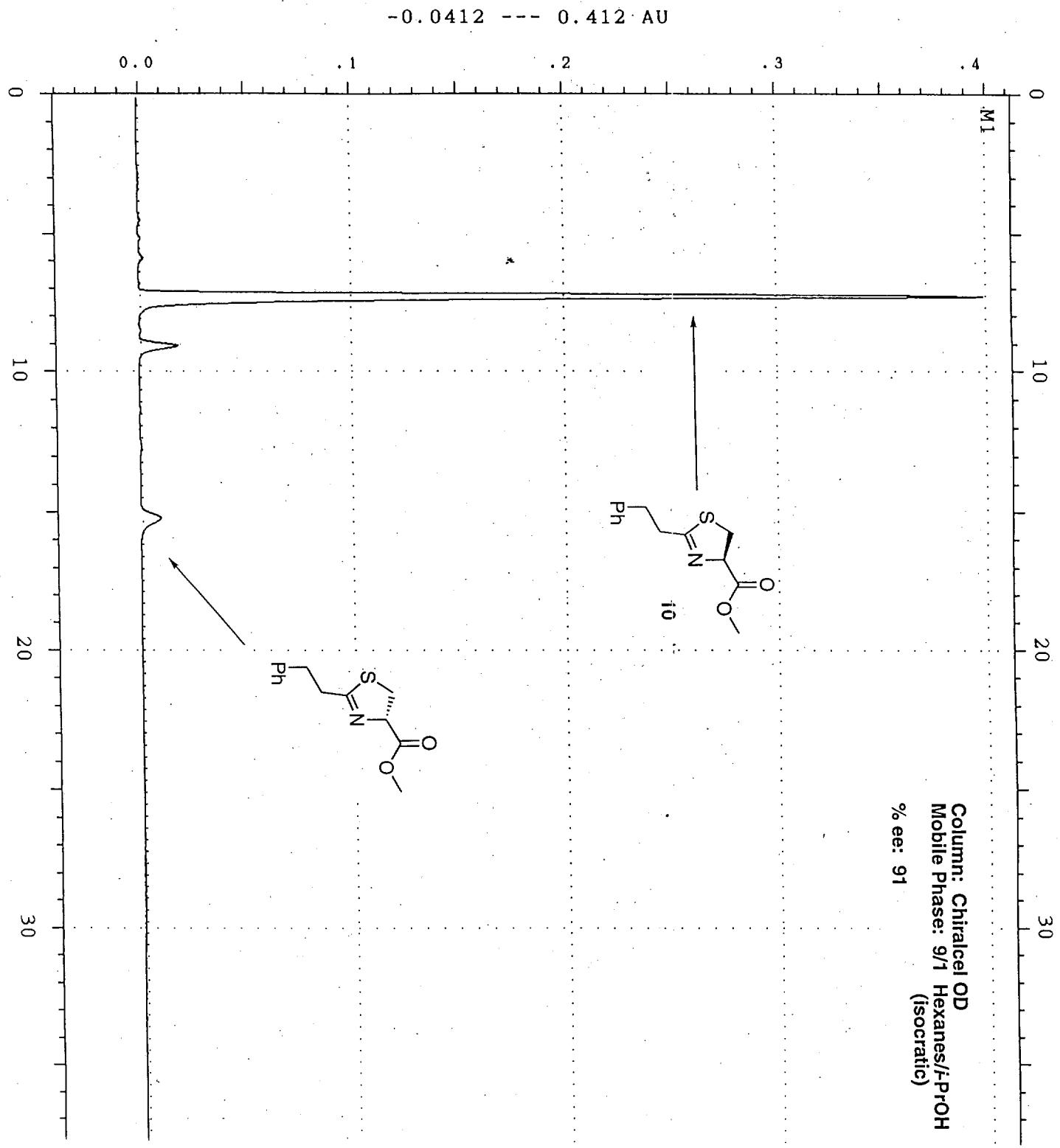

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)
171.2519
168.2453
166.0780
149.3964
132.7835
130.5475
128.9603
126.7549
120.7187
78.3965
77.2595
77.0000
76.7482
52.8017
34.9526
Ph
S
N
S
N
O
O
12

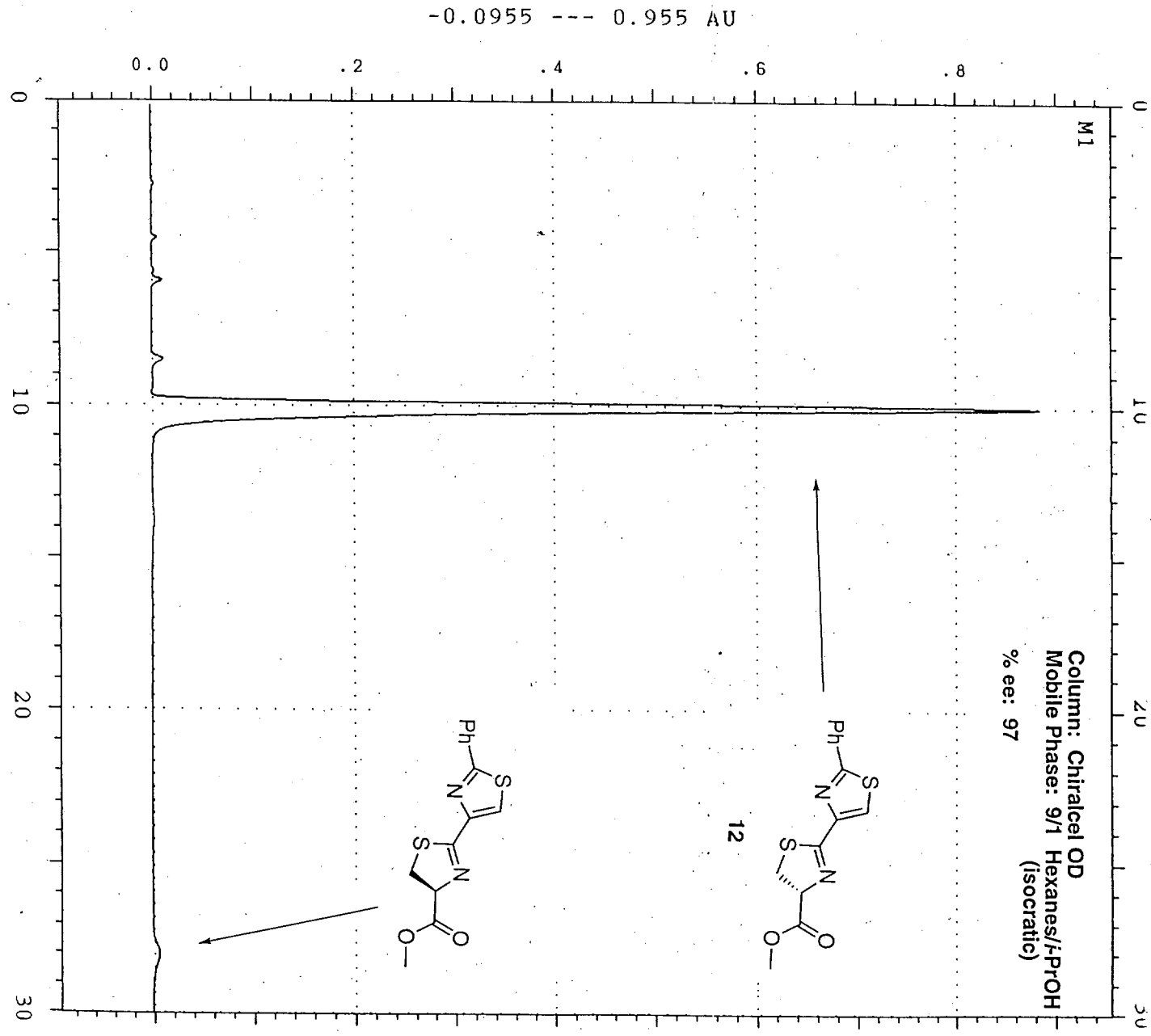

-0.171 --- 1.71 AU
0.0
.5
1
1.5
0
10
20
M1
Column: Chiralcel OD
Mobile Phase: 9/1 Hexanes/i-PrOH
(isocratic)
% ee: 88
Ph
S
N
O
O


-0.0707 --- 0.707 AU
0.0
.2
.4
.6
M1
0
10
20
30
Column: Chiralcel OD
Mobile Phase: 9/1 Hexanes/i-PrOH
(isocratic)
% ee: 99
Ph
S
N
O
O
7




-0.284 --- 2.84 AU
0.0
.5
1
1.5
2
2.5
M1
0
10
20
30
40
OMe
S
N
O
O
9
OMe
S
N
O
O
Column: Chiralcel OD
Mobile Phase: 9/1 Hexanes/i-PrOH
(isocratic)
% ee: 94


-0.0412 --- 0.412 AU
0.0
.1
.2
.3
.4
M1
0
10
20
30
Ph
S
N
O
O
10
Column: Chiralcel OD
Mobile Phase: 9/1 Hexanes/i-PrOH
(isocratic)
% ee: 91


-0.0955 --- 0.955 AU
0.0
.2
.4
.6
.8
M1
0
10
20
30
Column: Chiralcel OD
Mobile Phase: 9/1 Hexanes/i-PrOH
(isocratic)
% ee: 97
12
Ph
S
N
S
N
O
O

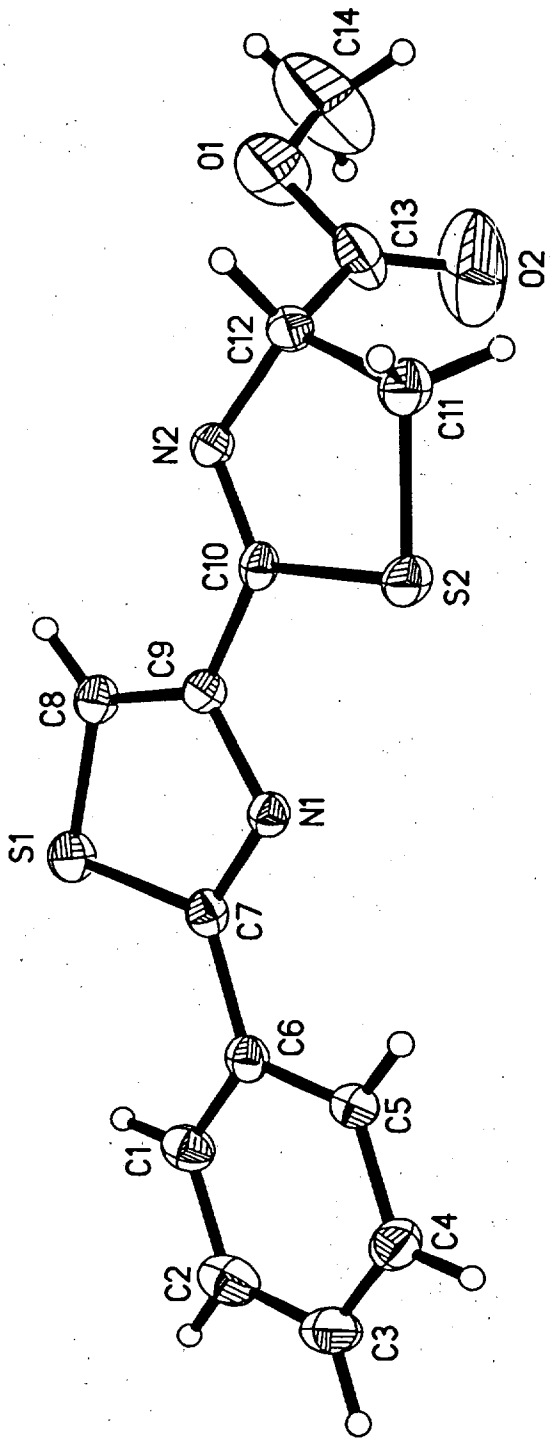
X-ray Structure Report

For

Hossein Razavi & Kelly

X-Ray Facility Reference Number: /HOS2/HOS21m

Raj K. Chadha
Director, X-Ray Facility
Chemistry Department, BCC-159
The Scripps Research Institute
10550 N. Torrey Pines Rd.
La Jolla, CA 92037


C14
O1
C13
O2
C12
C11
N2
C10
S2
C9
C8
N1
S1
C7
C6
C5
C1
C4
C2
C3

Experimental

A colorless, prism-shaped crystal (0.08x0.16x0.32 mm) was mounted alongwith the largest dimension and data were collected with a Bruker SMART APEX diffractometer equipped with a molybdenum sealed tube and a highly oriented graphite monochromator. The frame data are acquired with SMART software using a three axis stage. The chi-axis on this stage is fixed at 54.74°, and the CCD detector is maintained at -40 °C. Cell constants are determined from 20 10s frames. A complete hemisphere of data is scanned on ω (0.3°) with a run time of 10 s per frame at the detector resolution of 512x512 pixels. A total of 1100 frames are collected in three sets and a final set 50 frames, identical to first 50 frames are also scanned to determine crystal decay. The frames are then processed on a IBM compatible PC by using SAINT+ software to give the hkl file corrected for Lp/decay and absorption. See Table 1 for cell parameters and other relevant data.

The systematic absences (0k0, k=2n+1) indicated the space group $P2_1$ or $P2_1/m$. The former space group was chosen based on the fact that the compound is a single enantiomer. The structure was solved by direct methods using SHELXTL-PC. All non-hydrogen atoms were refined anisotropically by the full matrix least-squares method. The function minimized was $\sum w(\|Fo\|-\|Fc\|)^2$. Hydrogen atoms were included in the ideal positions with fixed isotropic U values equal to 1.2 times that of the atom they are attached to. A weighting scheme of the form $w=1/[\sigma^2(Fo^2)+(aP)^2)+bP]$ with a=0.03 and b=0.00 was used.(P is defined as $Max(Fo^2,0)+2F_c^2)/3$.) There was no evidence of secondary extinction; therefore it was not applied. The refinement converged to the R indices given in the Table 1 which also includes the the largest difference peak and the hole in the last cycles of refinement. The final difference map was devoid of significant features.

All calculations were done on an IBM compatible PC with PentiumIII chip and Windows-NT operating system. The programs used were SAINT+ (data reduction), SADABS (absorption correction), SHELXTL-PC (XS for solution, XL for refinement, XP for plotting and XCIF for tables). Final atomic coordinates are listed in Table 2 and selected bond lengths and bond angles in Table 3.