Organocatalytic enantioselective conjugate addition of aldehydes to maleimides

Gui-Ling Zhao, Yongmei Xu, Henrik Sundén, Lars Eriksson, Mahmoud Sayah, and Armando Córdova*

The Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-10691Stockholm, Sweden

Supporting Information

General. Chemicals and solvents were either purchased *puriss p.A.* from commercial suppliers or purified by standard techniques. Catalyst **8** was synthesized according to litterature procedures.[1] For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot H_2O$ (10 g), conc. H_2SO_4 (60 mL), and H_2O (940 mL) followed by heating or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating. Flash chromatography was performed using silica gel Merck 60 (particle size 0.040-0.063 mm), ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian AS 400. Chemical shifts are given in δ relative to tetramethylsilane (TMS), the coupling constants *J* are given in Hz. The spectra were recorded in $CDCl_3$ as solvent at room temperature, TMS served as internal standard (δ = 0 ppm) for ^{1}H NMR, and $CDCl_3$ was used as internal standard (δ = 77.0 ppm) for ^{13}C NMR. HPLC was carried out using a Waters 2690 Millennium with photodiode array detector. Optical rotations were recorded on a Perkin Elemer 241 Polarimeter (λ = 589 nm, 1 dm cell). High-resolution mass spectra were recorded on a Bruker MicrOTOF spectrometer. The optical rotations were taken at the diastereomeric mixtures as shown in Table 2, since the minor diastereomer was not separable from the major one.

1. a) M. Marigo, T. C. Wabnitz, D. Fielenbach, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2005**, *44*, 794. b) M. Marigo, D. Fielenbach, A. Braunton, A. Kjaersgaard, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2005**, *44*, 3703. c) J. Franzén, M. Marigo, D. Fielenbach, T. C. Wabnitz, A. Kjaersgaard, K. A. Jørgensen, *J. Am. Chem. Soc.* **2005**, *127*, 18296. d) Y. Hayashi, H. Gotoh, T. Hayashi, M. Shoji, *Angew. Chem. Int. Ed.* **2005**, *44*, 4212. e) M. Marigo, J. Franzén, T. B. Poulsen, W. Zhuang, K. A. Jørgensen, *J. Am. Chem. Soc.* **2005**, *127*, 6964. g) H. Sundén, I. Ibrahem, A. Córdova, *Tetrahedron Lett.* **2006**, 47, 99. h) I. Ibrahem, A. Córdova, *Chem. Commun.* **2006**, 1760.

Experimental procedure for the preparation of catalyst **9**:

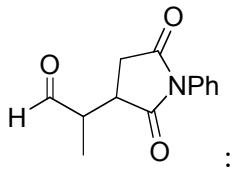
To a solution of (*R*)-(+)-2-Amino-1,1-diphenyl-1-propanol (2.22 mmol, 0.5 g) dissolved in $CHCl_3$ (10 mL) was added triethyl amine (2.88 mmol, 0.4 mL) followed by addition of trimethylsilyl tifluoro-methanesulfonate (2.88 mmol, 0.52 mL) at 0 ºC. The reaction mixture was stirred under Ar atmosphere for 16 h. Thereafter, water (10 mL) was added to quench the reaction and the organic layer was washed with saturated $NaHCO_3$ (3 x 7mL), the collected aqueous layer was extracted with $CHCl_3$ (3 x 20 mL) and the gathered organic layer was dried over Na_2SO_4 before the solvent removal under reduced pressure. Silica gel chromatography (pentane: EtOAC= 1:1) was performed to furnish 0.53 g (80 % yield) of the desired pure product.

$[\alpha]_D^{25}$ = +29.0 (c = 1.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41 (m, 10H), 3.92 (q, *J* = 6.1, 12.3 Hz, 1H), 0.95 (d, *J* = 6.6 Hz, 3H), -0.13 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz,) δ 143.5, 143.2, 128.8, 128.7, 127.5, 127.4, 127.3, 127.1, 84.8, 52.9, 18.4, 1.9.

General procedure for the condition screen of Michael addition of propionaldehyde to *N*-phenylmaleimide: To a stirred solution of the catalyst (10, 20 or 30 mol %) in solvent (1 mL) was added propionaldehyde (29 mg, 0.5 mmol) and *N*-phenylmaleimide (43 mg, 0.25 mmol) at the temperature given in Table 1. The reaction was vigorously stirred and monitored by TLC analysis. The reaction mixture was washed with water and extracted with EtOAc. The organic layer was separated, dried over Na_2SO_4 and the solvent was removed. The residue was purified by silica gel (pentane: ethyl acetate = 1:1) to give product **3a**.

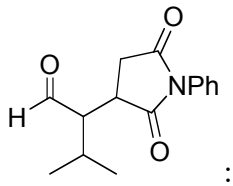
General procedure for Michael addition of unmodified aldehydes to *N*-phenylmaleimides: To a stirred solution of the catalyst **8** (10 mol %) in $CHCl_3$ (1 mL) was added aldehyde (0.5 mmol) and *N*-phenylmaleimide (43 mg, 0.25 mmol) at the temperature given in Table 2. The reaction was vigorously stirred and monitored by TLC analysis. The reaction mixture was washed with water and extracted with EtOAc. The organic layer

was separated, dried over Na_2SO_4 and the solvent was removed. The residue was purified by silica gel (pentane: ethyl acetate = 1:2-1:1) to give product **3**.



:

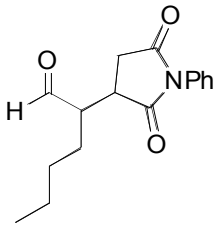
2-(2,5-Dioxo-1-phenyl-pyrrolidin-3-yl)-propionaldehyde **3a**: $[\alpha]_D^{25}$ = + 76.2 (c 1.0, $CHCl_3$). IR (KBr): 3469, 2974, 2881, 1776, 1712, 1598, 1500, 1387, 1187, 1028, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) major diastereomer: δ 9.72 (s, 1H), 7.50-7.24 (m, 5H), 3.44-3.36 (m, 1H), 3.18 (dq, *J* = 7.6, 3.6 Hz, 1H), 3.03 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.52 (dd, *J* = 18.4, 5.2 Hz, 1H), 1.33 (d, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.4, 177.7, 175.1, 131.8, 129.2, 128.7, 126.4, 47.0, 39.5, 31.6, 9.7; ^1H NMR ($CDCl_3$, 400 MHz) minor diastereomer: δ 9.62 (s, 1H), 7.50-7.28 (m, 5H), 3.26 (dq, *J* = 7.6, 3.6 Hz, 1H), 3.11-3.06 (m, 1H), 2.93 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.56 (dd, *J* = 18.4, 5.2 Hz, 1H), 1.39 (d, *J* = 7.6 Hz, 3H). The ee of the product was determined by chiral HPLC analysis (Chiralpak AD column, isohexane/2-propanol = 80/20, 0.5 mL/min, 210 nm, major diastereomer: t_R (minor) = 36.51 min, t_R (major) = 41.72 min; minor diastereomer: t_R (minor) = 31.95 min, t_R (major) = 56.14 min). HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{13}H_{13}NO_3Na$) requires *m/z* 254.0788, found *m/z* 254.0790.



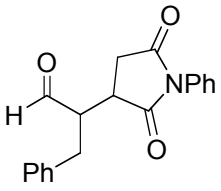
:

2-(2,5-Dioxo-1-phenyl-pyrrolidin-3-yl)-3-methyl-butyraldehyde **3b**: $[\alpha]_D^{25}$ = + 55.1 (c 1.0, $CHCl_3$). IR (KBr): 3584, 3020, 2969, 1777, 1713, 1600, 1501, 1388, 1216, 1187, 1046, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.89 (d, *J* = 1.2 Hz, 1H), 7.45 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 3.41-3.35 (m, 1H), 3.01 (dd, *J* = 18.4, 10.0 Hz, 1H), 2.69-2.64 (m, 1H), 2.56 (dd, *J* = 18.4, 6.0 Hz, 1H), 2.37-2.27 (m, 1H), 1.17 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 202.7, 177.6, 174.8, 131.9, 129.1, 128.6, 126.4, 59.0, 37.9, 33.3, 28.1, 21.7, 20.3; The

ee of the product was determined by chiral HPLC analysis (Chiralpak AD column, isohexane/2-propanol = 80/20, 0.5 mL/min, 230 nm, major diastereomer: t_R (minor) = 27.45 min, t_R (major) = 50.89 min; minor diastereomer: t_R (major) = 32.35 min, t_R (minor) = 38.32 min). HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{15}H_{17}NO_3Na$) requires *m/z* 282.1101, found *m/z* 282.1106.



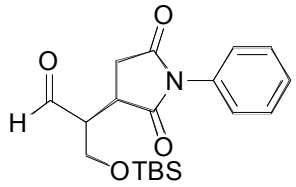
2-(2,5-Dioxo-1-phenyl-pyrrolidin-3-yl)-hexanal **3c**: $[\alpha]_D^{25}$ = + 70.2 (c 1.0, $CHCl_3$). IR (KBr): 3584, 3019, 2959, 2931, 2861, 1778, 1713, 1501, 1387, 1216, 1185, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.73 (s, 1H), 7.47 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 2H), 3.34-3.28 (m, 1H), 2.98-2.93 (m, 1H), 2.97 (dd, *J* = 18.4, 9.6 Hz, 1H), 2.53 (dd, *J* = 18.4, 5.6 Hz, 1H), 1.94-1.84 (m, 1H), 1.69-1.61 (m, 1H), 1.51-1.33 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.8, 177.9, 175.3, 132.2, 129.4, 128.9, 126.7, 52.9, 38.9, 32.6, 30.0, 26.2, 22.8, 14.0; The ee of the product was determined by chiral HPLC analysis (Agilent, Chiralpak AD column, hexane/2-propanol = 80/20, 0.5 mL/min, 210 nm, major diastereomer: t_R (minor) = 27.05 min, t_R (major) = 58.50 min, minor diastereomer: t_R (major) = 31.60 min, t_R (minor) = 34.27 min). HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{16}H_{19}NO_3Na$) requires *m/z* 296.1257, found *m/z* 296.1268.



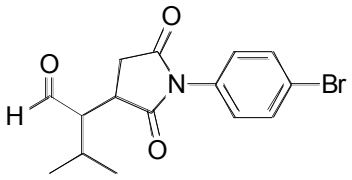
:

2-(2,5-Dioxo-1-phenyl-pyrrolidin-3-yl)-3-phenyl-propionaldehyde **3d**: $[\alpha]_D^{25}$ = - 9.4 (c 0.5, $CHCl_3$); IR (KBr): 3584, 3020, 2977, 2400, 1779, 1712, 1600, 1500, 1390, 1216, 1046, 759 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.76 (1H, s), 7.46 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.36-7.22 (m, 7H), 3.32-3.29 (m, 2H), 3.18-3.13 (m, 2H),

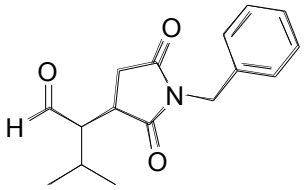
2.94 (dd, *J* = 18.4, 10.0 Hz, 1H), 2.57 (dd, *J* = 18.4, 6.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.1, 177.8, 175.1, 137.4, 132.1, 129.34, 129.27, 129.2, 128.8, 127.4, 126.7, 55.3, 37.4, 33.2, 32.7. The ee of the product was determined by chiral HPLC analysis (Chiralpak AD column, isohexane/2-propanol = 95/5, 0.5 mL/min, 210 nm, major diastereomer: t_R (minor) = 122.278 min, t_R (major) = 189.645 min, minor diastereomer: t_R (major) = 169.577 min, t_R (minor) = 234.860 min). HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{19}H_{17}NO_3Na$) requires *m/z* 330.1101, found *m/z* 330.1108.



3-(*tert*-Butyldimethylsilyloxy)-2-(2,5-dioxo-1-phenylpyrrolidin-3-yl)propanal **3e**: $[\alpha]_D^{25}$ = + 4.7 (c 1, $CHCl_3$); IR (KBr): 3474, 3104, 2954, 2929, 2857, 1771, 1722, 1714, 1598, 1504, 1457, 1392, 1385, 1146, 831, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ major diastereomer 9.70 (d, *J* = 1.5 Hz, 1H), 7.29- 7.51 (m, 5H), 4.30 (dd, *J* = 5.1, 10.8 Hz, 1H), 4.10 (dd, *J* = 3.9, 10.8 Hz, 1H), 3.35-3.40 (m, 1H), 3.12-3.20 (m, 1H), 3.03 (dd, *J* = 8.7, 12.3 Hz, 1H), 2.84-2.93 (m, 1H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); minor diastereomer 9.84 (d, *J* = 1.5 Hz, 1H), 7.29- 7.51 (m, 5H), 4.23 (dd, *J* = 5.7, 10.8 Hz, 1H), 4.15 (dd, *J* = 5.1, 10.8 Hz, 1H), 3.45-3.51 (m, 1H), 3.12-3.20 (m, 1H), 2.84-2.93 (m, 2H), 0.88 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ major diastereomer 200.9, 178.3, 175.9, 129.3, 128.8, 126.8, 126.2, 100.2, 61.4, 54.3, 39.1, 32.7, 25.9, -5.4, -5.5; minor diastereomer 201.0, 178.3, 175.9, 129.3, 128.7, 128.1, 126.5, 99.5, 60.4, 54.7, 37.6, 33.0, 25.9, -5.4, -5.5; The enantiomeric excess was determined by HPLC (Chiralpak ODH column, isohexane/2-propanol = 97/3, 0.5 mL/min, 230 nm, major diastereomer: t_R (minor) = 99.895 min, t_R (major) = 103.859 min; minor diastereomer: t_R (minor) = 121.895 min, t_R (major) = 127.034 min). HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{19}H_{27}NO_4SiNa$) requires *m/z* 384.1602, found *m/z* 384.1615.

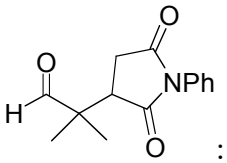


2-[1-(4-Bromo-phenyl)-2,5-dioxo-pyrrolidin-3-yl]-3-methyl-butyraldehyde **3f**: $[\alpha]_D^{25} = +43.2$ (c 1.0, $CHCl_3$). IR (KBr): 3479, 3020, 2965, 2928, 1780, 1714, 1491, 1388, 1215, 1184, 1071, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 9.89 (d, *J* = 1.5 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 2H), 3.33-3.40 (m, 1H), 3.02 (dd, *J* = 9.6, 18.0 Hz, 1H), 2.64-2.69 (m, 1H), 2.56 (dd, *J* = 6.0, 18.0 Hz, 1H), 2.31-2.39 (m, 1H), 1.19 (d, *J* = 6.9 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 202.8, 177.4, 174.7, 132.5, 131.0, 128.2, 122.6, 59.5, 37.9, 33.7, 28.3, 22.0, 20.6. The ee of the product was determined by chiral HPLC analysis (Agilent, Chiralpak AD column, hexane/2-propanol = 80/20, 0.5 mL/min, 230 nm, major diastereomer: t_R (minor) = 16.827 min, t_R (major) = 43.009 min; minor diastereomer: t_R (major) = 19.000 min, t_R (minor) = 31.488 min). HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{15}H_{16}NO_3BrNa$) requires *m/z* 360.0206, found $[M+2+Na]^+$ *m/z* 362.0197.



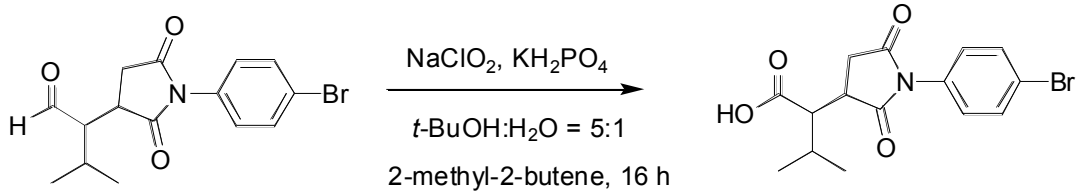
2-(1-Benzyl-2,5-dioxo-pyrrolidin-3-yl)-3-methyl-butyraldehyde **3g**: $[\alpha]_D^{25}$ = + 18.8 (c 1, $CHCl_3$); IR (KBr): 3459, 3033, 2966, 2876, 2339, 1776, 1732, 1714, 1699, 1683, 1497, 1434, 1403, 1348, 1169, 1083, 756 cm^{-1}; ^1H NMR (TMS, $CDCl_3$, 300 MHz) δ 9.82 (d, *J* = 2.6 Hz, 1H), 7.24- 7.39 (m, 5H), 4.65 (d, *J* = 4.1 Hz, 2H), 3.24 (m, 1H), 2.85 (dd, *J* = 10.0, 18.7 Hz, 1H), 2.53 (m, 1H), 2.44 (dd ,*J* = 6.0, 17.8 Hz, 1H), 2.19 (m, 1H), 1.08 (d, *J* = 6.9 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (TMS, $CDCl_3$, 75 MHz) δ 202.6, 178.2, 175.4, 135.5, 128.8, 128.6, 127.9, 58.4, 42.5, 38.1, 32.9, 28.0, 21.5, 19.9; The enantiomeric excess was determined by chiral HPLC analysis (Chiralpak ODH column, *iso*-hexane/2-propanol = 92:8, λ =210 nm, 0.5 mL/min), major diastereomer: t_R (major) =

73.408 min, t_R = (minor) 85.447 min,; minor diastereomer: t_R (minor) = 52.848 min, t_R (major) = 116.344 min). HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{16}H_{19}NO_3Na$) requires *m/z* 296.1257, found *m/z* 296.1271.



:

2-(2,5-Dioxo-1-phenyl-pyrrolidin-3-yl)-2-methyl-propionaldehyde **3h**: IR (KBr): 3340, 2934, 2650, 1773, 1710, 1667, 1597, 1477, 1396, 1183, 1159, 1149, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.52 (s, 1H), 7.47 (dd, *J* = 6.4, 7.2 Hz, 2H), 7.40 (t, *J* = 6.4 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 2H), 3.16 (dd, *J* = 5.6, 9.6 Hz, 1H), 2.99 (dd, *J* = 9.6, 18.0 Hz, 1H), 2.62 (dd, *J* = 5.6, 18.0 Hz, 1H), 1.34 (s, 3H), 1.29 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 202.9, 177.0, 174.9, 131.9, 129.3, 128.8, 126.6, 48.6, 45.1, 31.9, 20.4, 19.6; The ee of the product was determined by chiral HPLC analysis (Agilent, Chiralpak ODH column, hexane/2-propanol = 75/25, 0.5 mL/min, 210 nm, t_R (minor) = 42.881 min, t_R (major) = 52.803 min). HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{14}H_{15}NO_3Na$) requires *m/z* 268.0944, found *m/z* 268.0956.

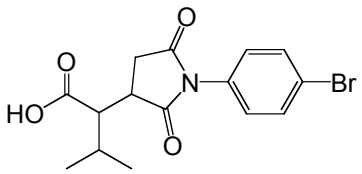


Yield: 94 %

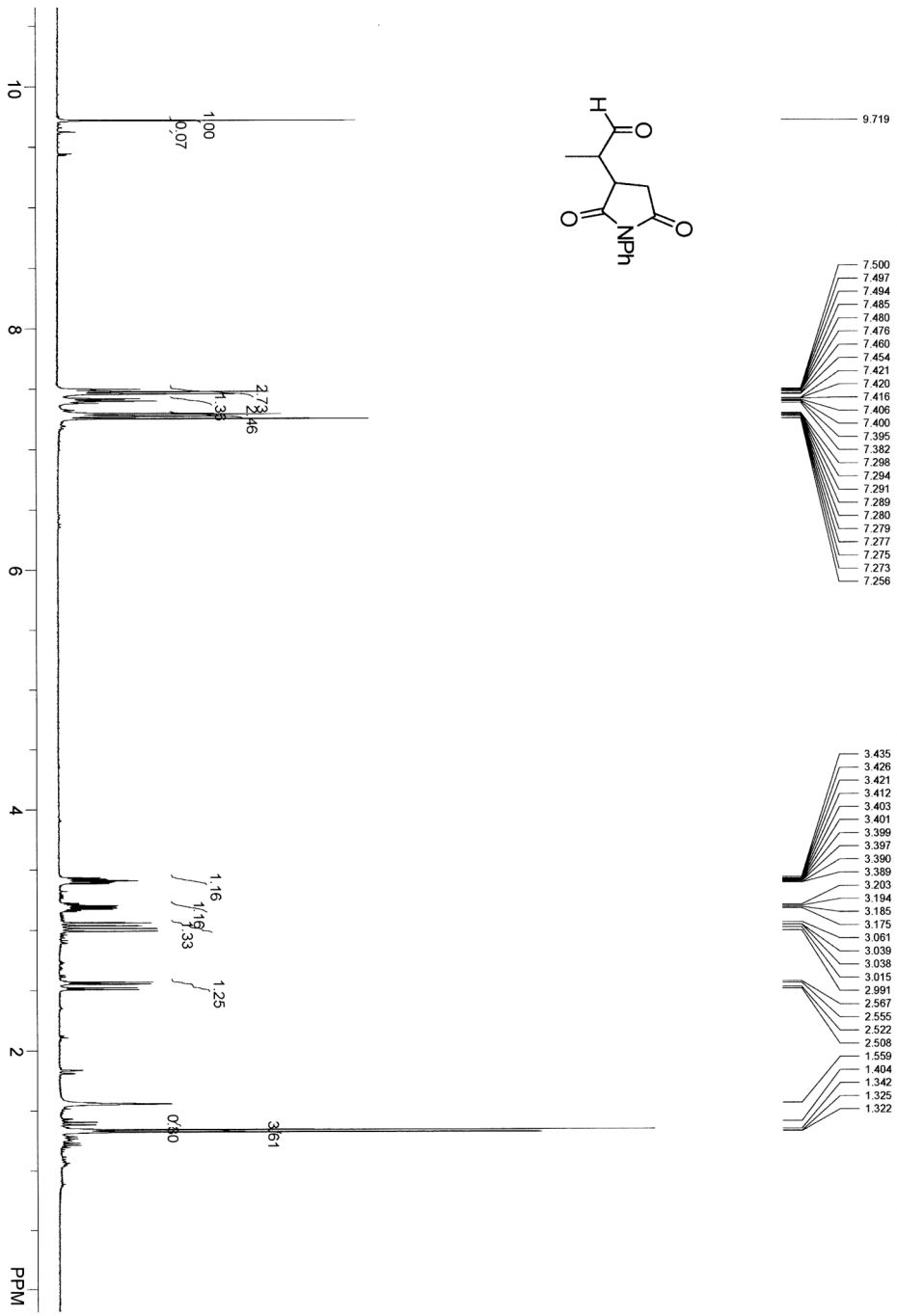
Reaction procedure for the oxidation of **3f**:

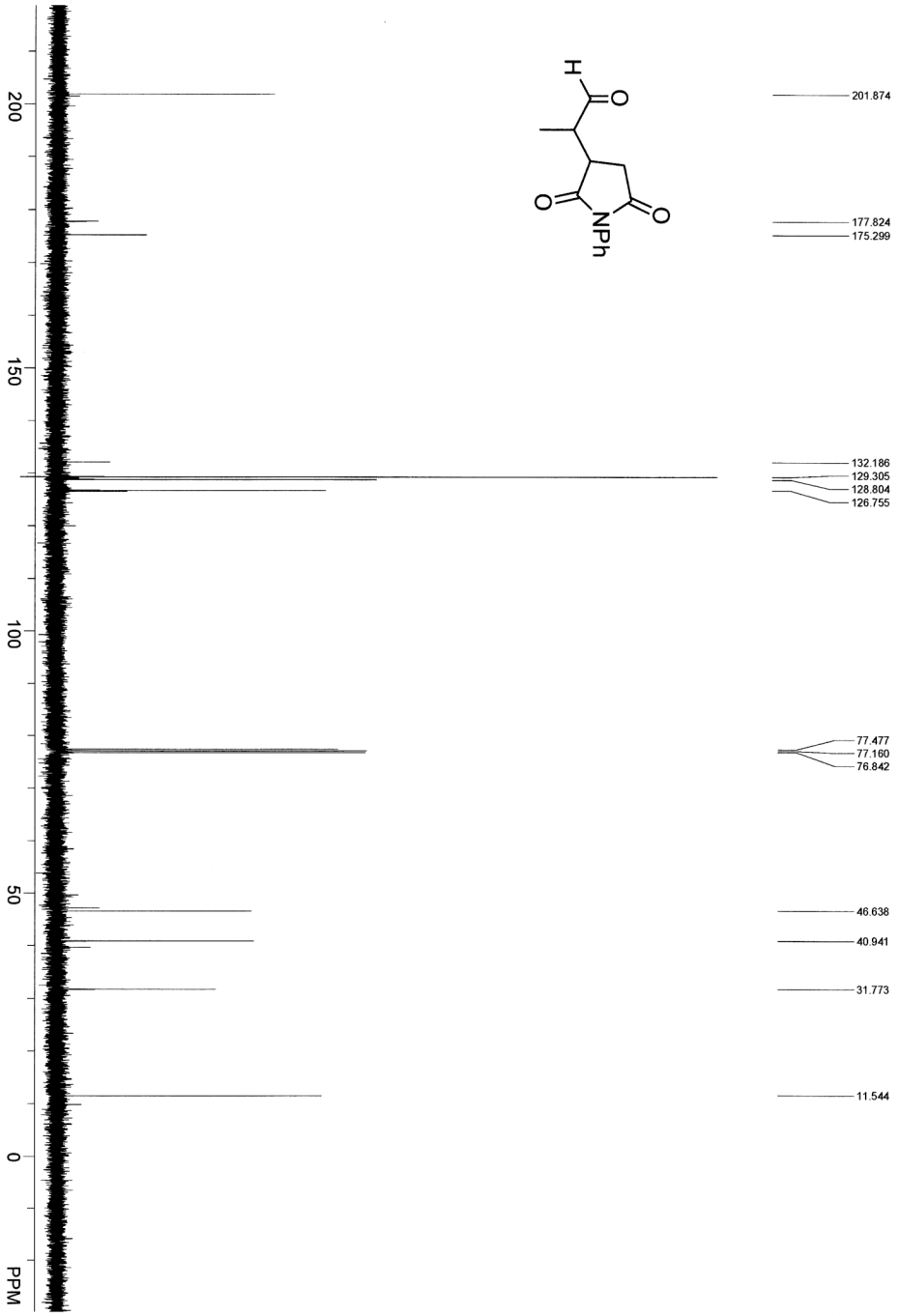
To a stirred solution of aldehyde **3f** (15 mg, 0.044 mmol) in *t*-BuOH/H_2O (5/1, 0.6 mL) were added KH_2PO_4 (12 mg, 0.088 mmol), 2-methyl-2-butene (24 mg, 0.35 mmol) and $NaClO_2$ (16 mg, 0.178 mmol). After stirring the mixture overnight the resulting yellow solution turned colorless. The solvent was removed and the residue was extracted with EtOAc, washed with H_2O, brine, dried over Na_2SO_4. The solvent was removed and the

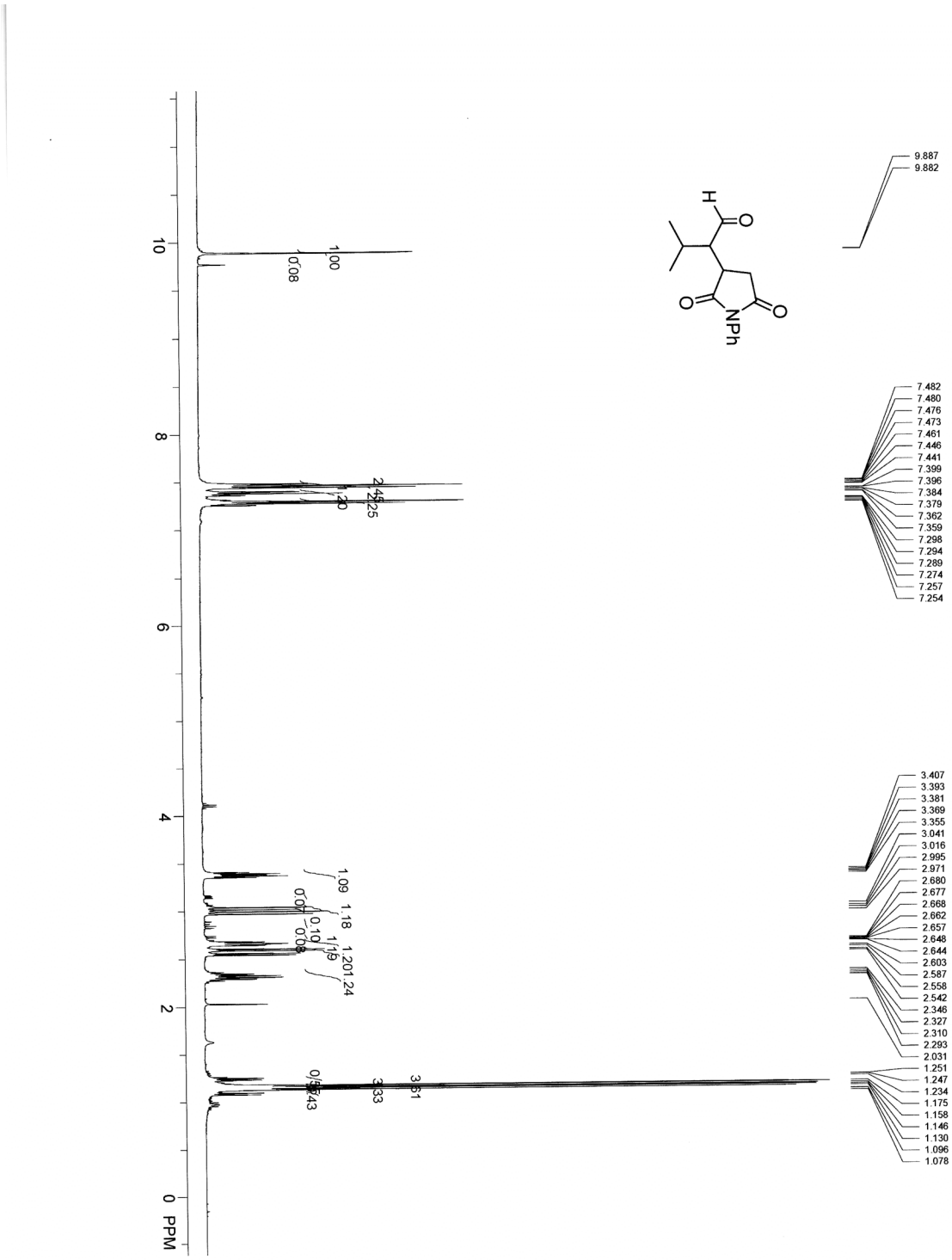
residue was purified by silica gel (pentane: ethyl acetate = 1:1) to give the product 15 mg (yield 94%).

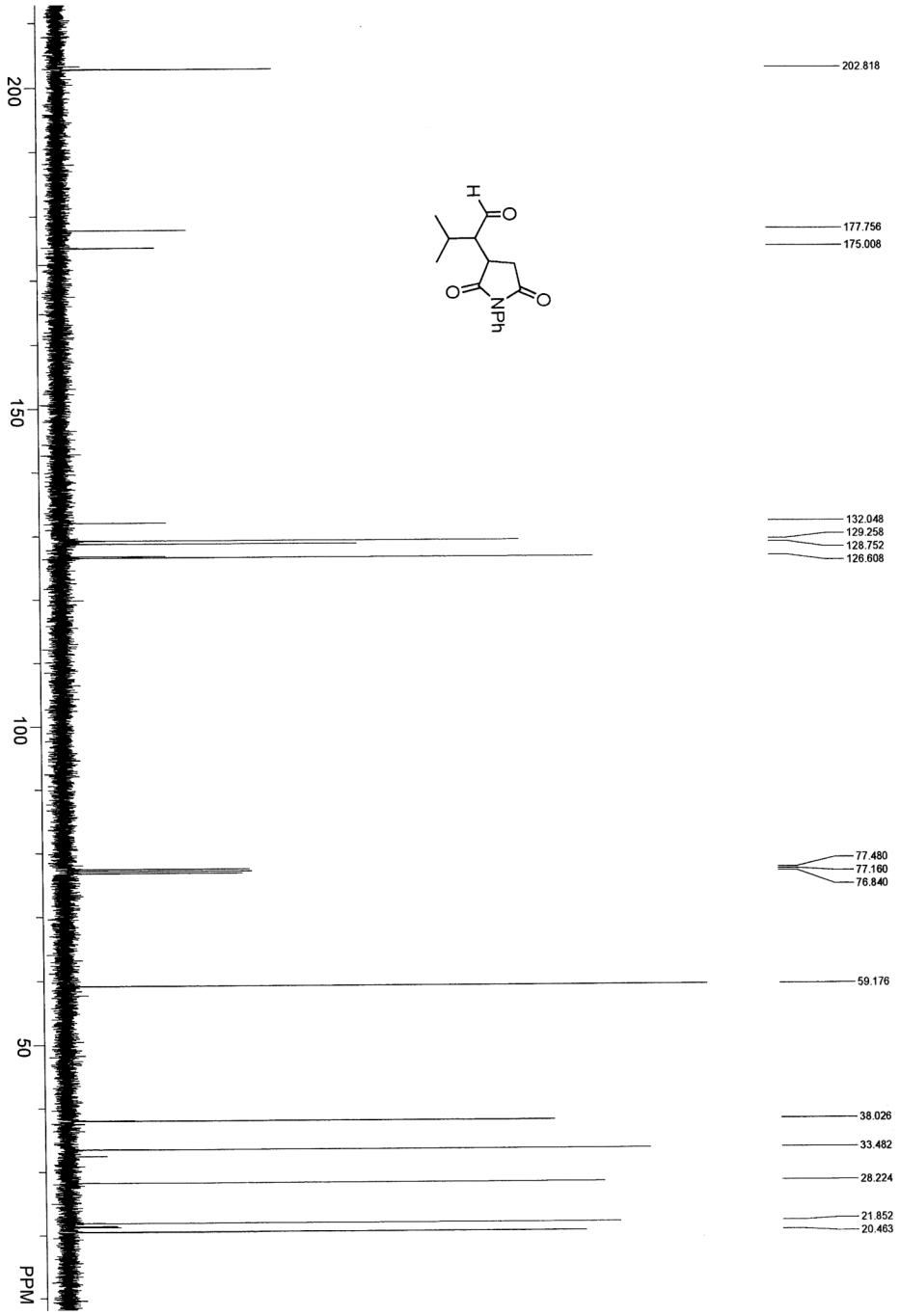


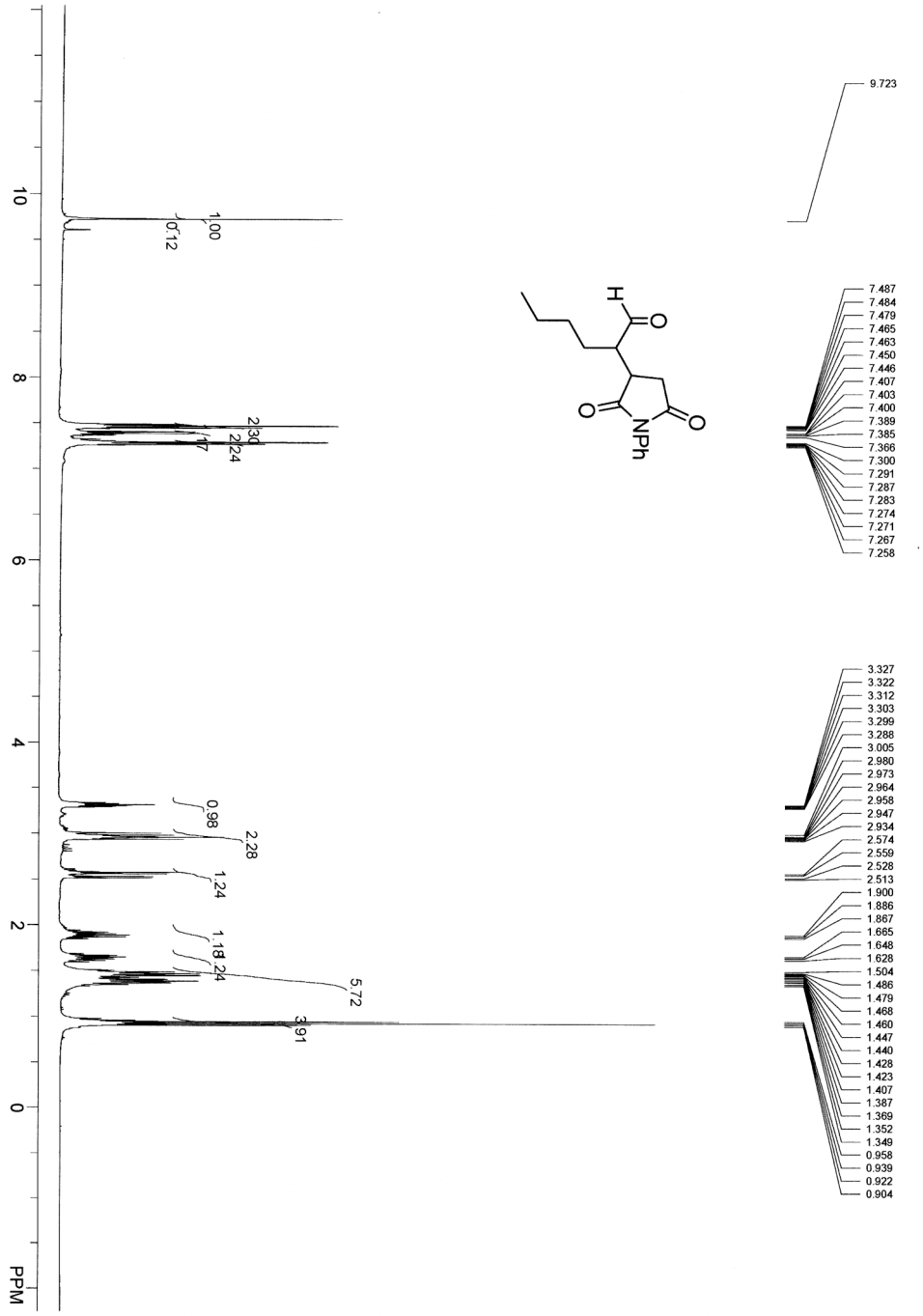
2-(1-(4-Bromophenyl)-2,5-dioxopyrrolidin-3-yl)-3-methylbutanoic acid **10**: $[\alpha]_D^{25}$ = + 11.4 (c 0.5, $CHCl_3$). IR (KBr): 3337, 2963, 2926, 1779, 1713, 1491, 1392, 1182, 1069, 1014 cm^{-1};^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H), 3.35-3.41 (m, 1H), 3.15-3.23 (m, 1H), 3.06 (dd, *J* = 9.6, 18.6 Hz, 1H), 2.96 (dd, *J* = 5.4, 9.6 Hz, 1H), 2.66 (dd, *J* = 6.0, 18.6 Hz, 1H), 2.28-2.37 (m, 1H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.3, 176.5, 174.5, 132.5, 130.9, 128.1, 122.7, 39.6, 33.3, 32.6, 28.3, 21.2, 20.1. HRMS(ESI) the exact mass calculated for $[M+Na]^+$ ($C_{15}H_{16}NO_4BrNa$) requires *m/z* 376.0155, found *m/z* 376.0169.

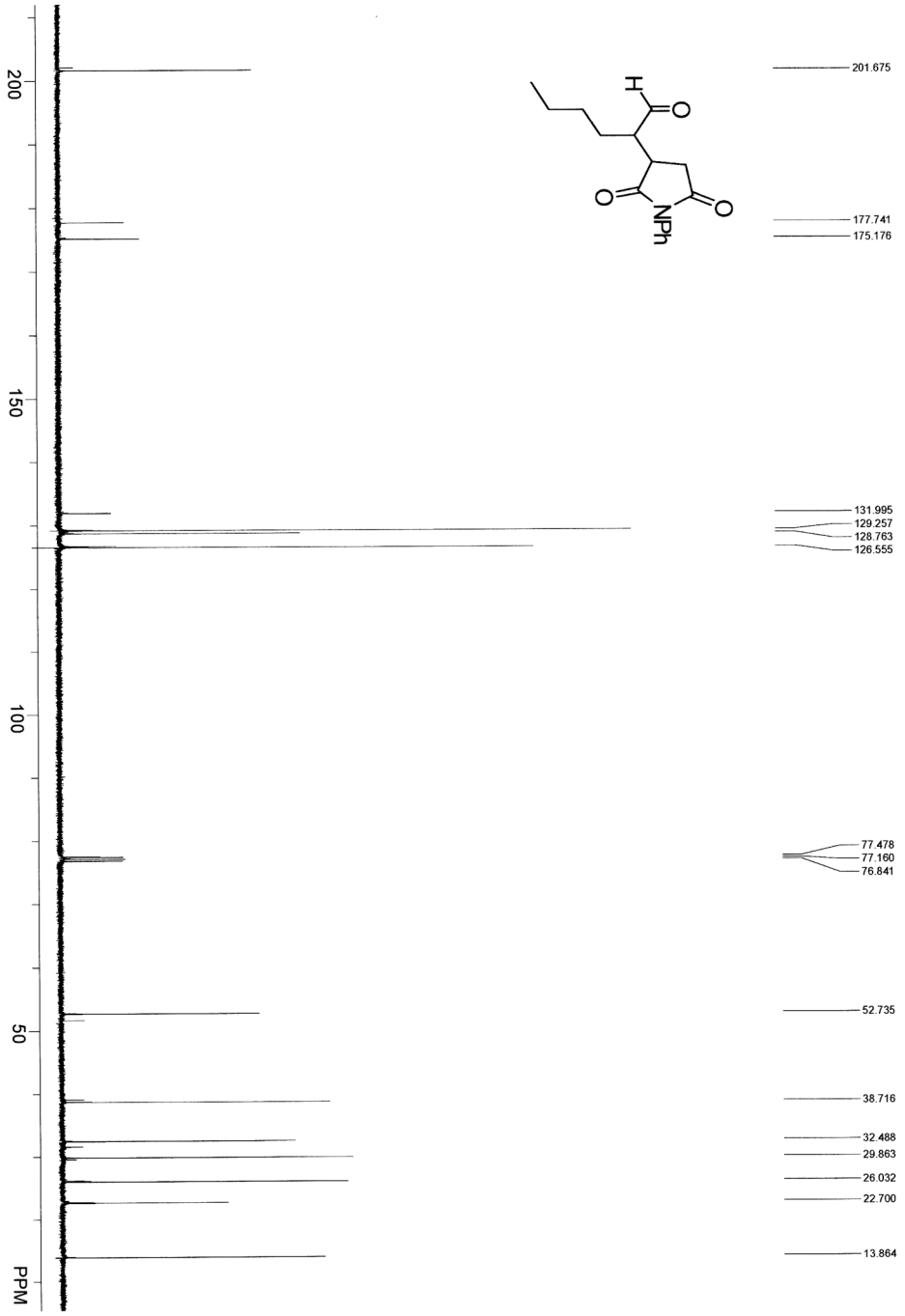

10
8
6
4
2
PPM
1.00
0.07
2.73
2.46
1.38
1.16
1.16
1.33
1.25
0.40
3.61
H
O
O
O
NPh
9.719
7.500
7.497
7.494
7.485
7.480
7.476
7.460
7.454
7.421
7.420
7.416
7.406
7.400
7.395
7.382
7.298
7.294
7.291
7.289
7.280
7.279
7.277
7.275
7.273
7.256
3.435
3.426
3.421
3.412
3.403
3.401
3.399
3.397
3.390
3.389
3.203
3.194
3.185
3.175
3.061
3.039
3.038
3.015
2.991
2.567
2.555
2.522
2.508
1.559
1.404
1.342
1.325
1.322

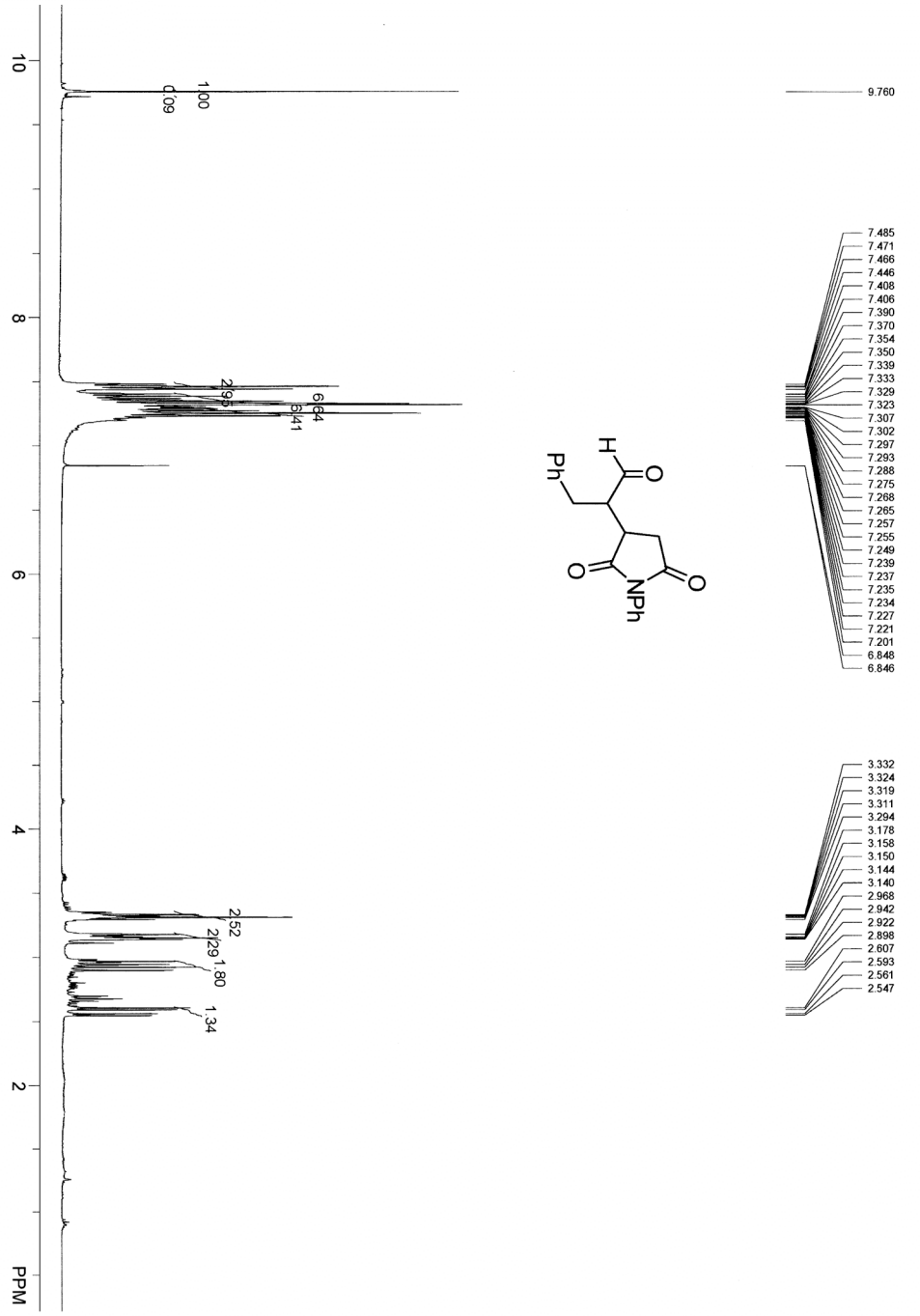

200
150
100
50
0
PPM
O
H
O
O
NPh
O
201.874
177.824
175.299
132.186
129.305
128.804
126.755
77.477
77.160
76.842
46.638
40.941
31.773
11.544

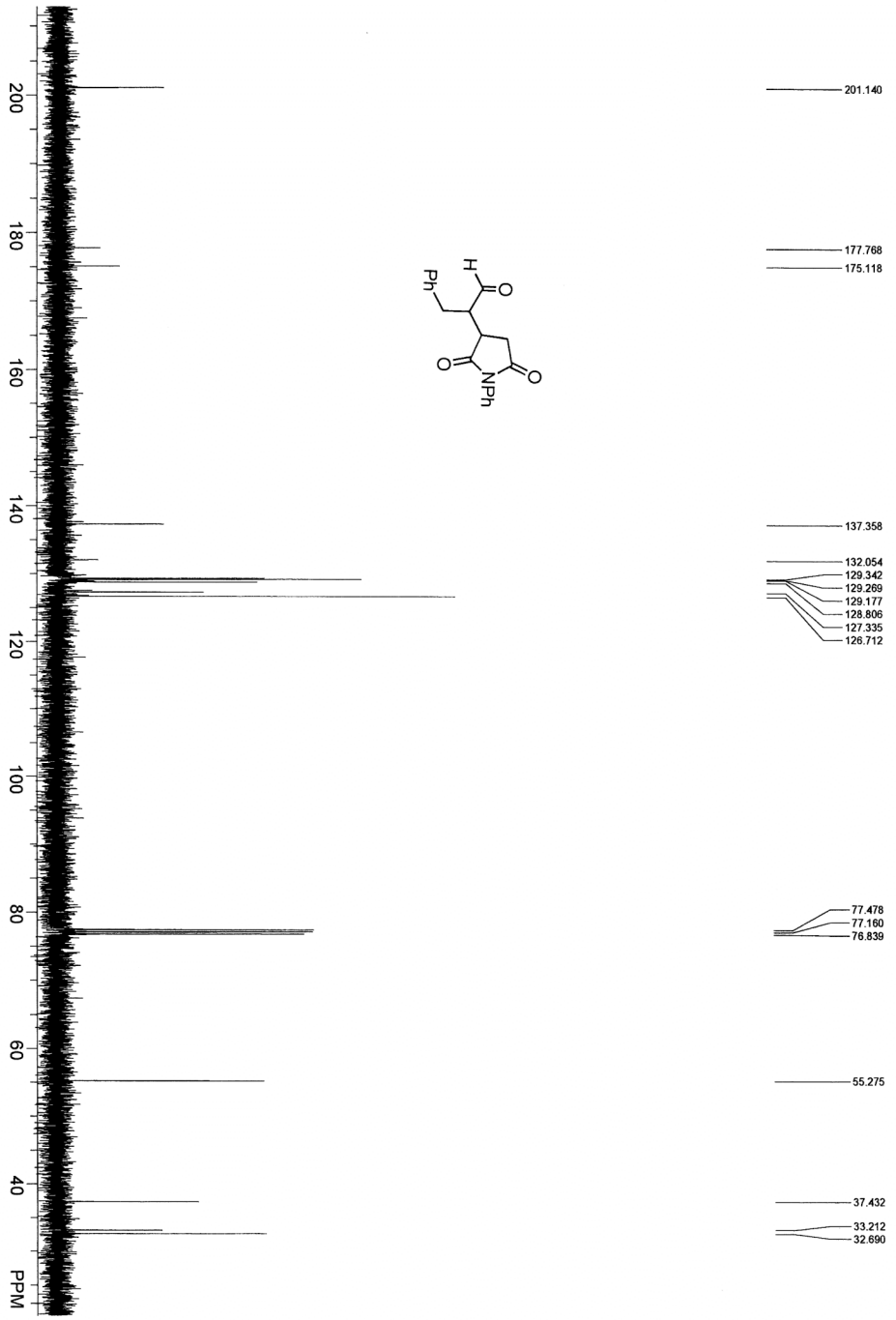

9.887
9.882
7.482
7.480
7.476
7.473
7.461
7.446
7.441
7.399
7.396
7.384
7.379
7.362
7.359
7.298
7.294
7.289
7.274
7.257
7.254
3.407
3.393
3.381
3.369
3.355
3.041
3.016
2.995
2.971
2.680
2.677
2.668
2.662
2.657
2.648
2.644
2.603
2.587
2.558
2.542
2.346
2.327
2.310
2.293
2.031
1.251
1.247
1.234
1.175
1.158
1.146
1.130
1.096
1.078
NPh
10
8
6
4
2
0 PPM

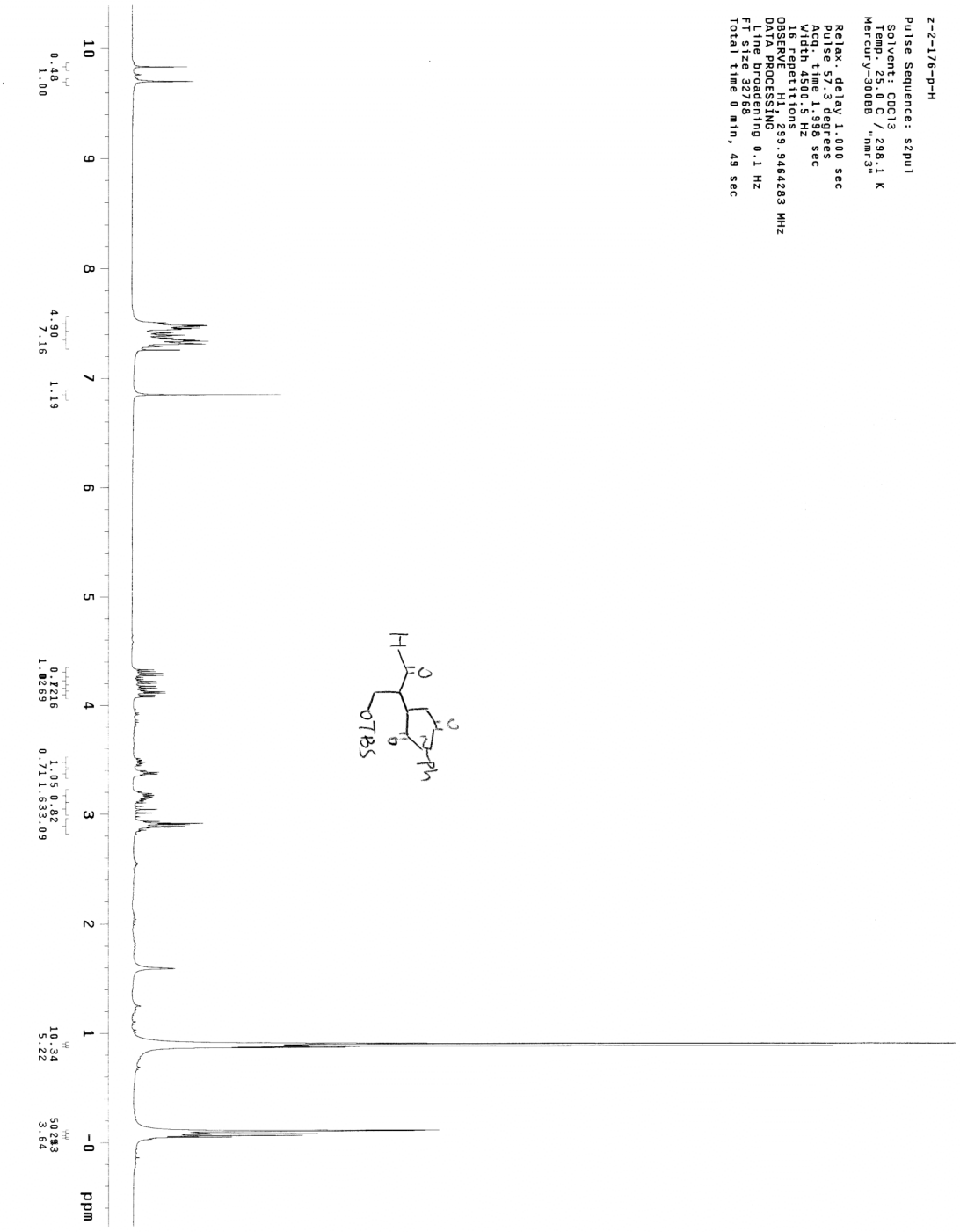

202.818
177.756
175.008
132.048
129.258
128.752
126.608
77.480
77.160
76.840
59.176
38.026
33.482
28.224
21.852
20.463
200
150
100
50
PPM
H
O
O
O
O
NPh

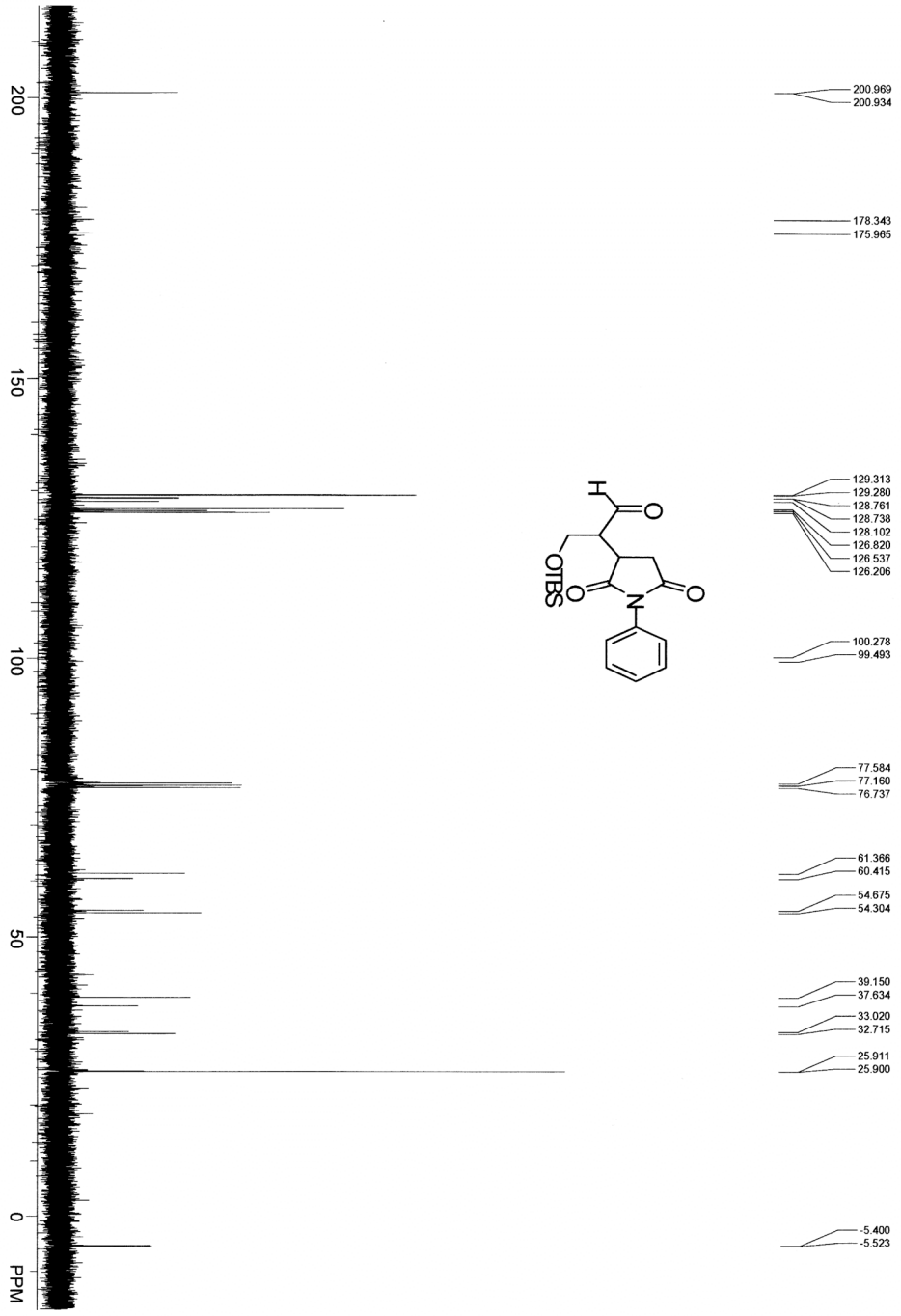

9.723
7.487
7.484
7.479
7.465
7.463
7.450
7.446
7.407
7.403
7.400
7.389
7.385
7.366
7.300
7.291
7.287
7.283
7.274
7.271
7.267
7.258
3.327
3.322
3.312
3.303
3.299
3.288
3.005
2.980
2.973
2.964
2.958
2.947
2.934
2.574
2.559
2.528
2.513
1.900
1.886
1.867
1.665
1.648
1.628
1.504
1.486
1.479
1.468
1.460
1.447
1.440
1.428
1.423
1.407
1.387
1.369
1.352
1.349
0.958
0.939
0.922
0.904
1.00
0.12
2.30
2.24
0.98
2.28
1.24
1.18
2.24
5.72
3.91
10
8
6
4
2
0
PPM
H
O
O
O
NPh

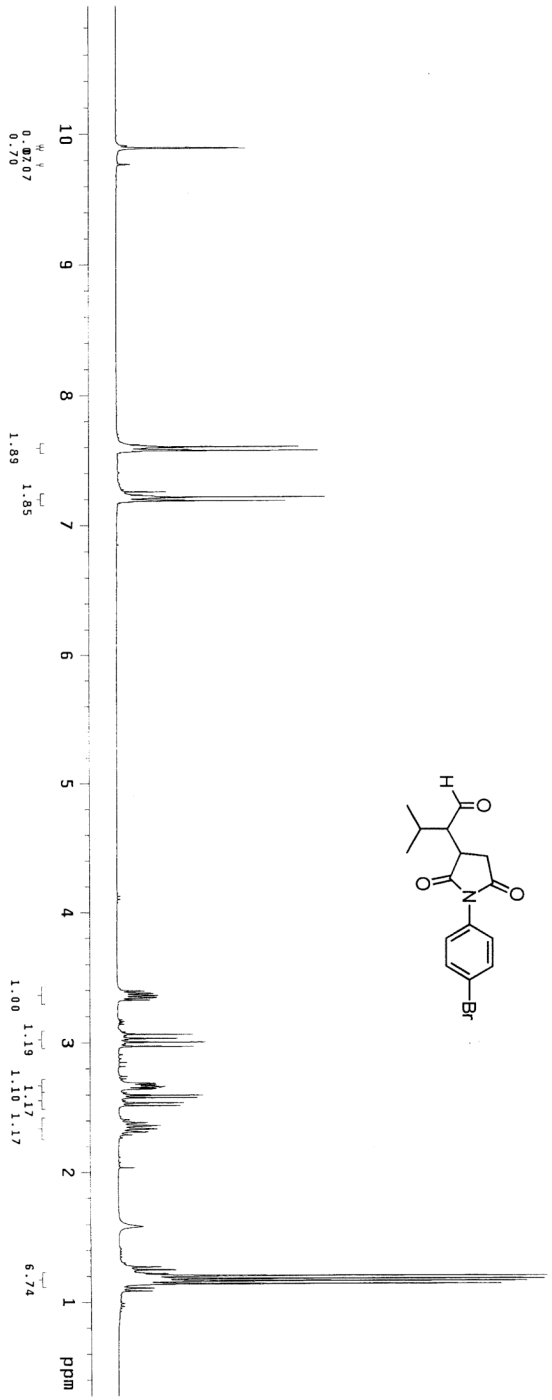

200
150
100
50
PPM
O
H
O
O
NPh
O
201.675
177.741
175.176
131.995
129.257
128.763
126.555
77.478
77.160
76.841
52.735
38.716
32.488
29.863
26.032
22.700
13.864

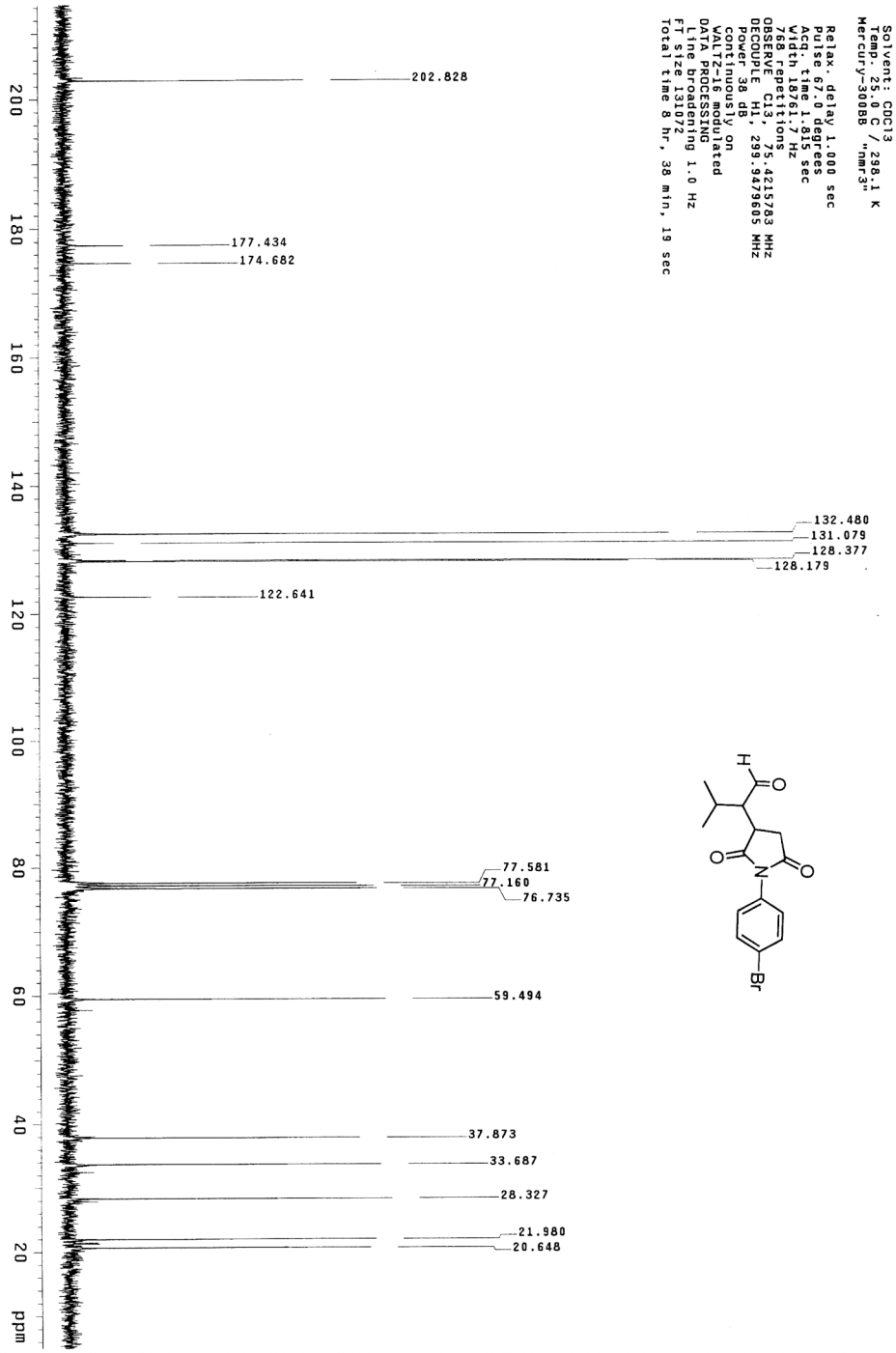

10
8
6
4
2
PPM
1.00
0.09
2.95
6.64
5.41
2.52
2.29
1.80
1.34
9.760
7.485
7.471
7.466
7.446
7.408
7.406
7.390
7.370
7.354
7.350
7.339
7.333
7.329
7.323
7.307
7.302
7.297
7.293
7.288
7.275
7.268
7.265
7.257
7.255
7.249
7.239
7.237
7.235
7.234
7.227
7.221
7.201
6.848
6.846
3.332
3.324
3.319
3.311
3.294
3.178
3.158
3.150
3.144
3.140
2.968
2.942
2.922
2.898
2.607
2.593
2.561
2.547
Ph
H
O
O
O
O
NPh

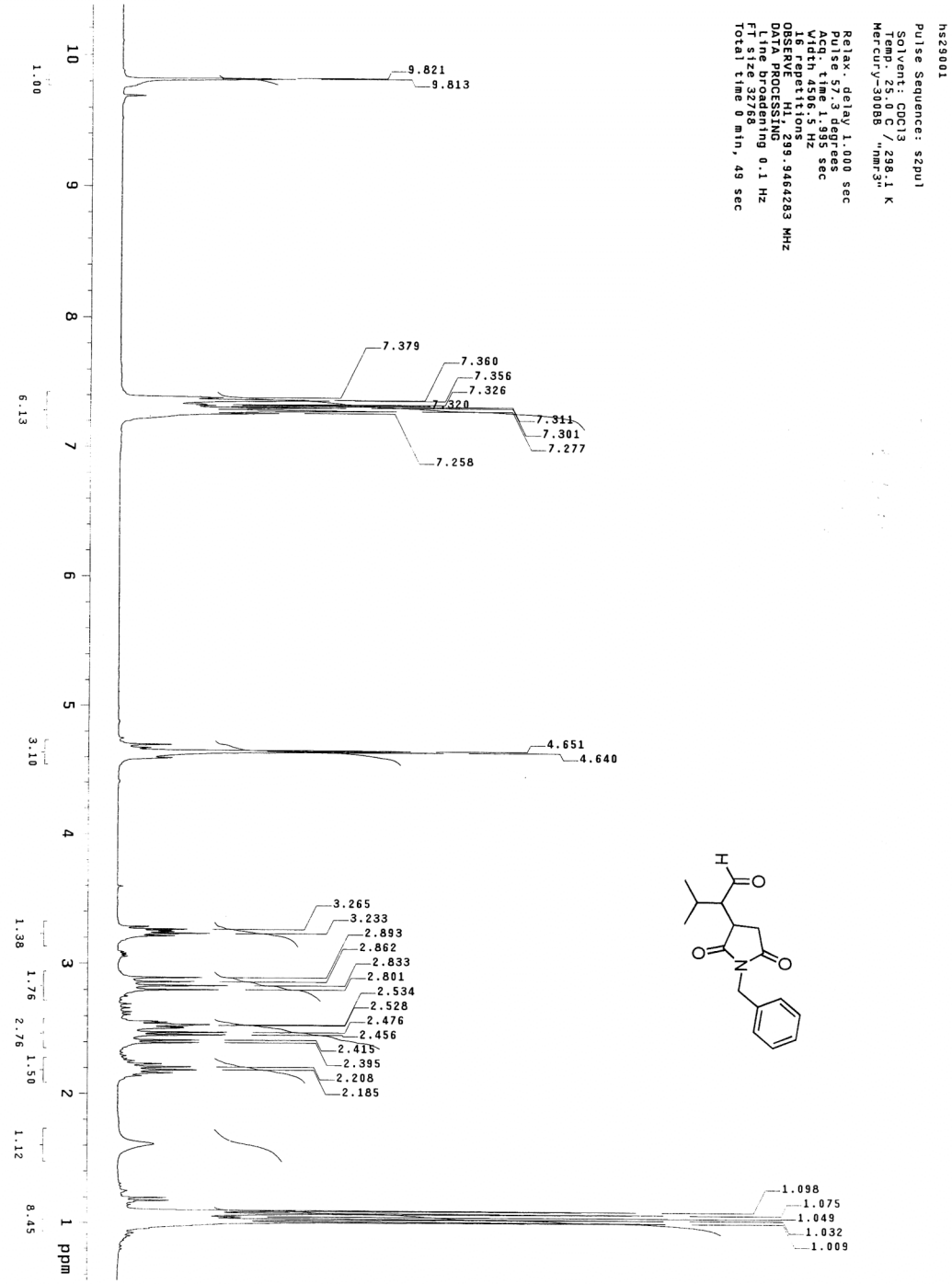

200
180
160
140
120
100
80
60
40
PPM
Ph
H
O
O
O
O
NPh
201.140
177.768
175.118
137.358
132.054
129.342
129.269
129.177
128.806
127.335
126.712
77.478
77.160
76.839
55.275
37.432
33.212
32.690

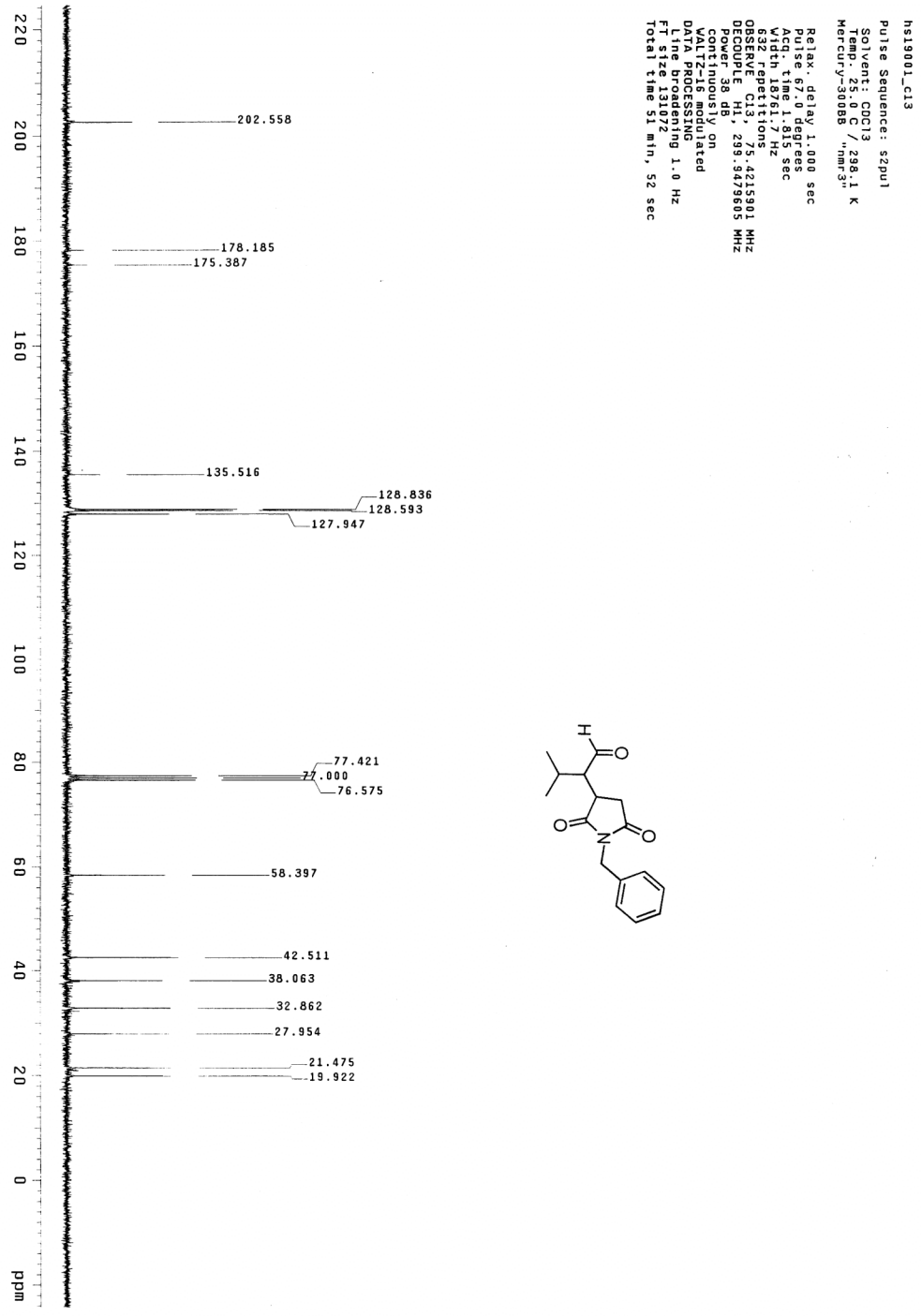

z-2-176-p-H
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Mercury-300BB "nmr3"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
16 repetitions
OBSERVE H1, 299.9464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 49 sec
OTBS
Ph
10
9
8
7
6
5
4
3
2
1
-0
ppm

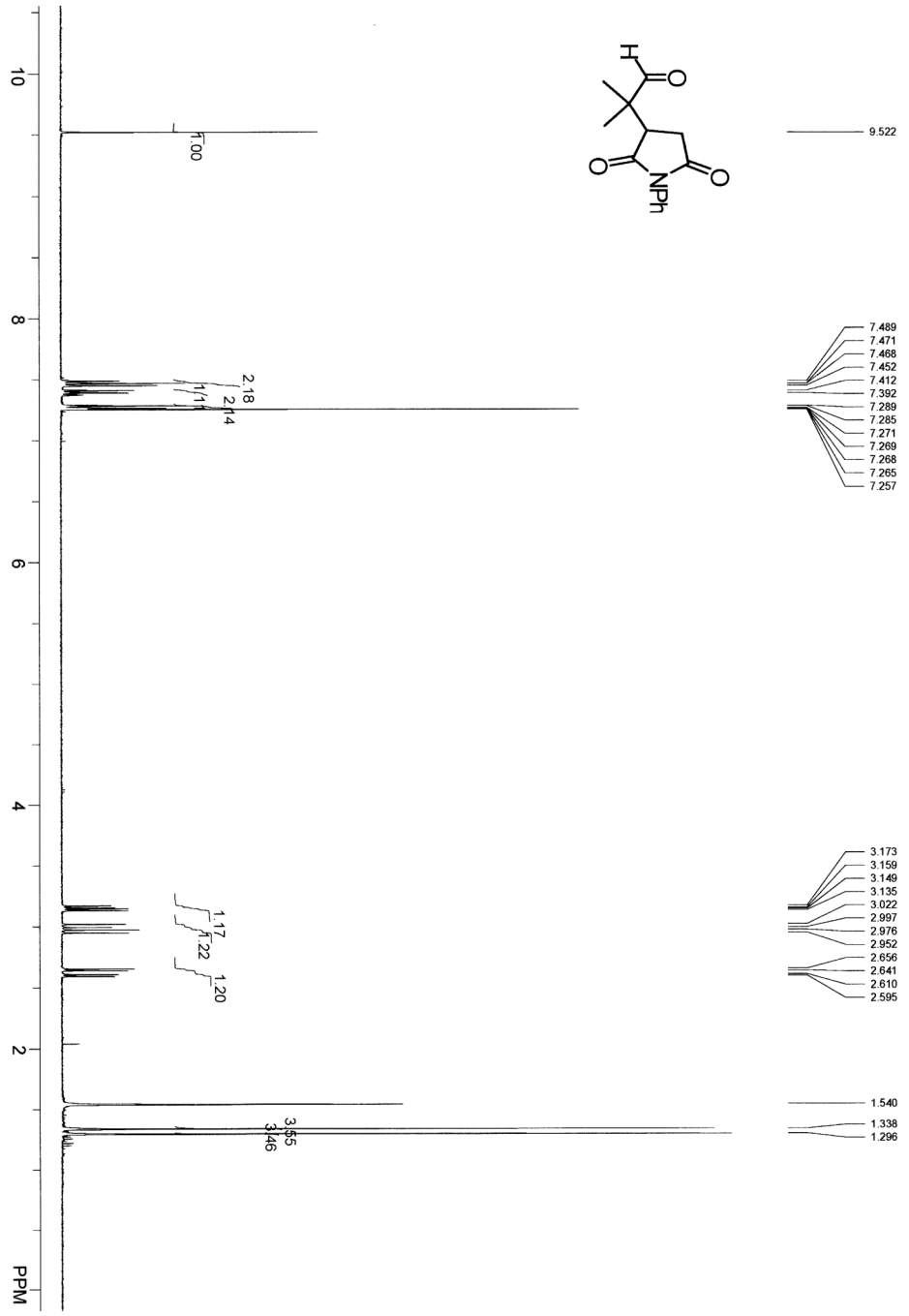

200
150
100
50
0
PPM
200.969
200.934
178.343
175.965
129.313
129.280
128.761
128.738
128.102
126.820
126.537
126.206
100.278
99.493
77.584
77.160
76.737
61.366
60.415
54.675
54.304
39.150
37.634
33.020
32.715
25.911
25.900
-5.400
-5.523
H
O
OTBS
O
O
N

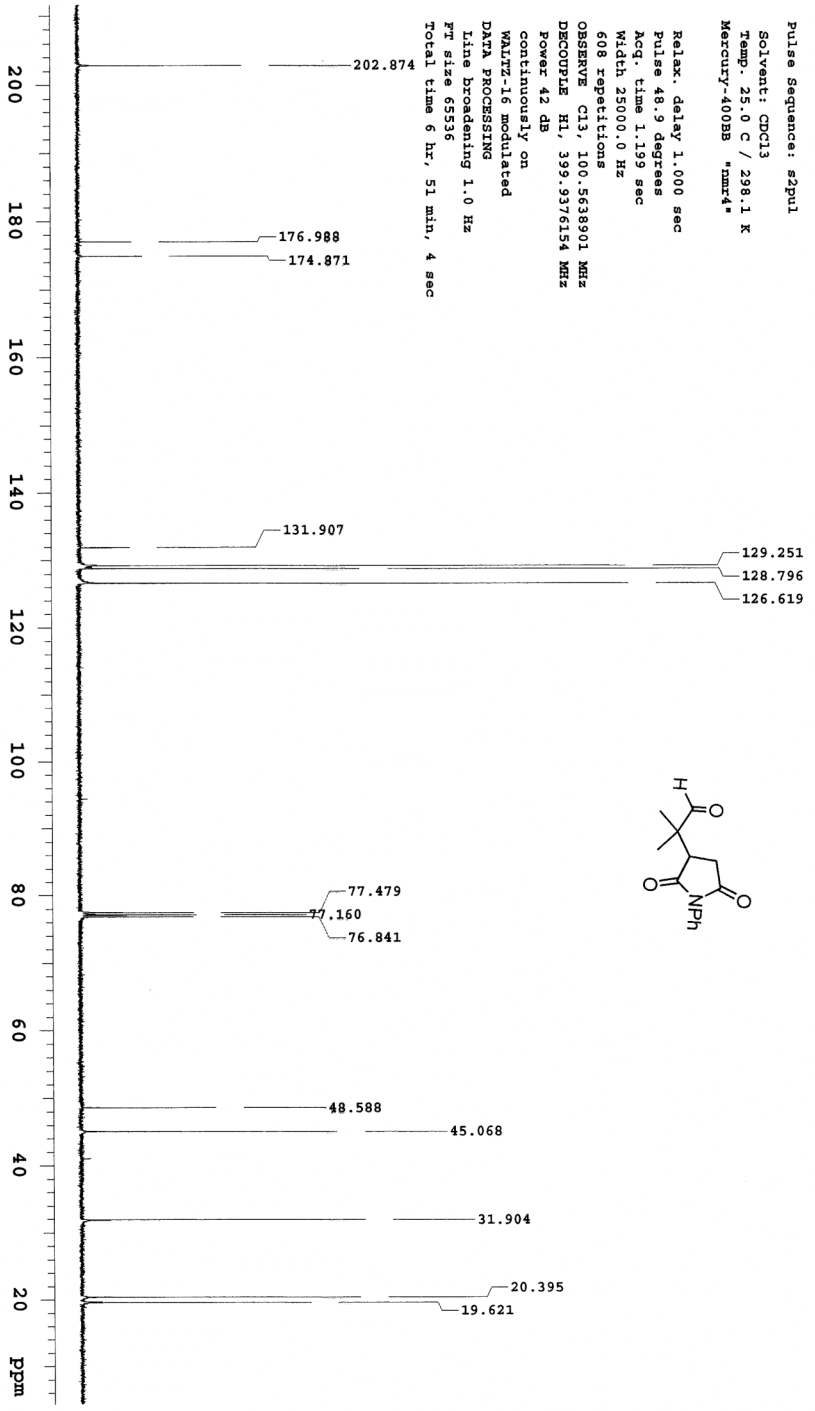

z-Hsz28002-H
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Mercury-300BB "nmr3"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
16 repetitions
OBSERVE H1, 299.9464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 49 sec
0.70
0.70
1.89
1.85
1.00
1.19
1.17
1.10
1.17
6.74
ppm

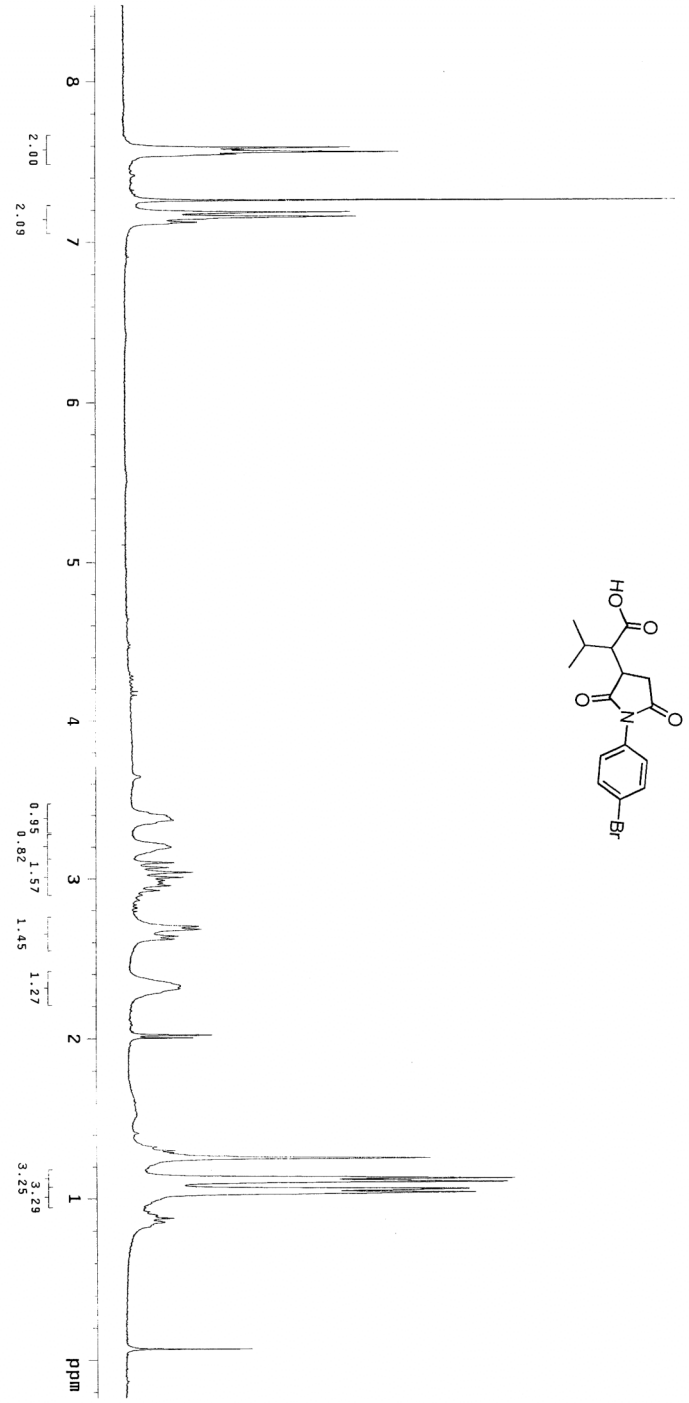

z-Hs28002-C
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Mercury-300BB "nmr3"
Relax. delay 1.000 sec
Pulse 67.0 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
76 repetitions
OBSERVE C13, 75.4215783 MHz
DECOUPLE H1, 299.9479605 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 8 hr, 38 min, 19 sec
202.828
177.434
174.682
132.480
131.079
128.377
128.179
122.641
77.581
77.160
76.735
59.494
37.873
33.687
28.327
21.980
20.648
200
180
160
140
120
100
80
60
40
20
ppm
H
O
O
N
O
Br

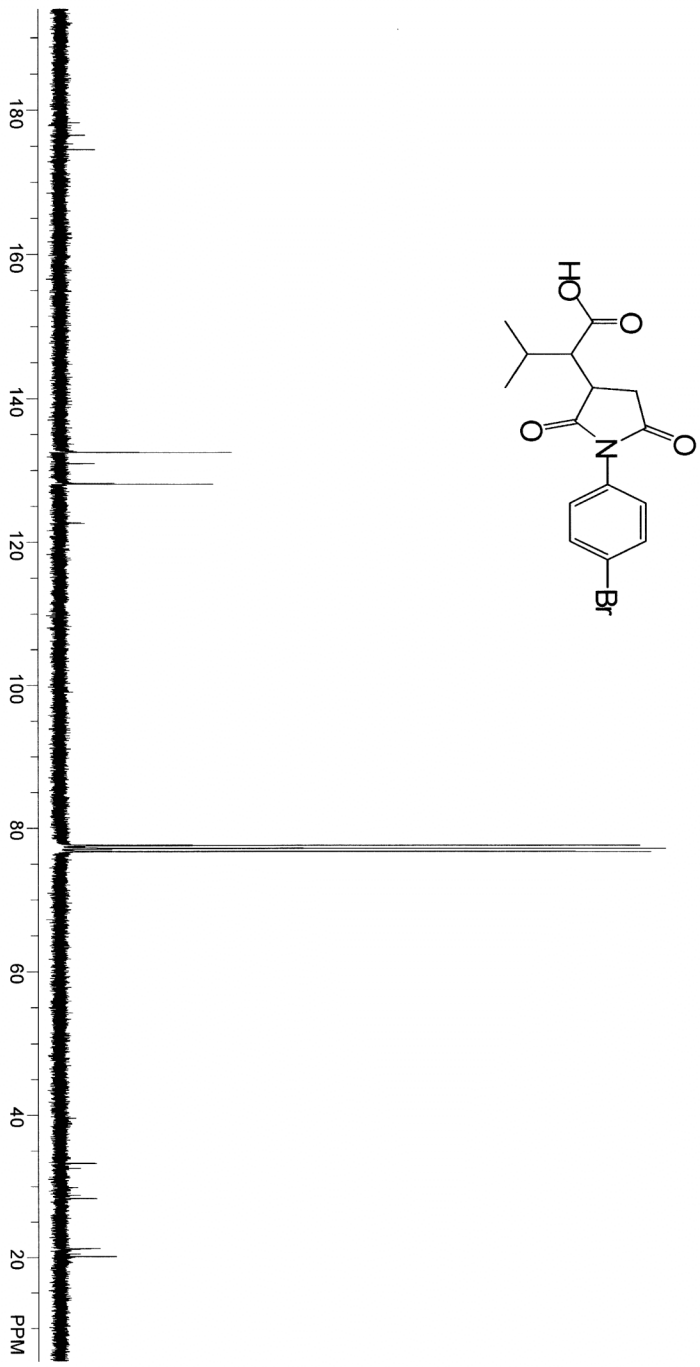

hs29001
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Mercury-300BB "nmr3"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
16 repetitions
OBSERVE H1, 299.9464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 0 min, 49 sec
9.821
9.813
7.379
7.360
7.356
7.326
7.320
7.311
7.301
7.277
7.258
4.651
4.640
3.265
3.233
2.893
2.862
2.833
2.801
2.534
2.528
2.476
2.456
2.415
2.395
2.208
2.185
1.098
1.075
1.049
1.032
1.009
1.00
6.13
3.10
1.38
1.76
2.76
1.50
1.12
8.45
10
9
8
7
6
5
4
3
2
1
ppm
H
O
O
O
N

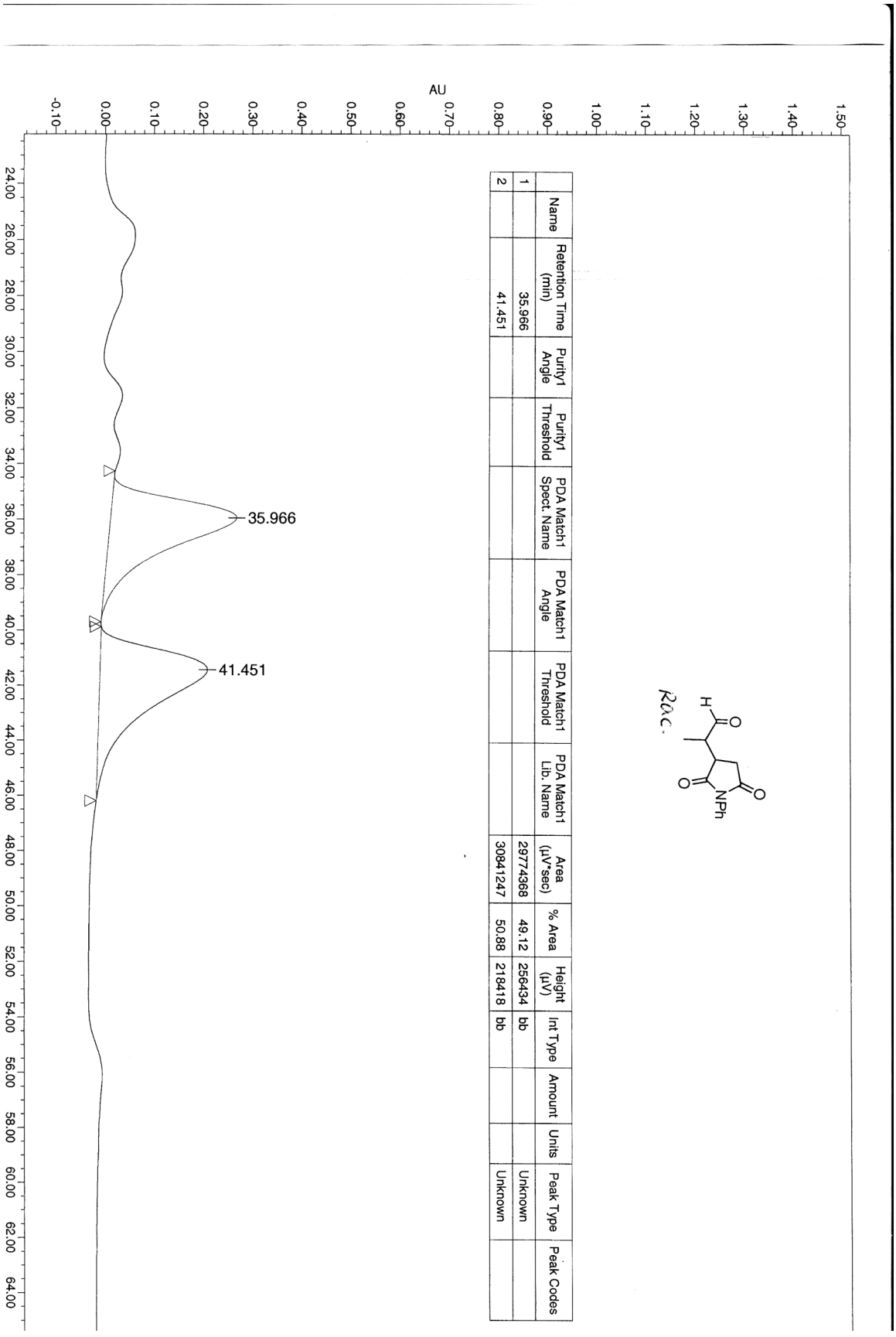

hs19001_c13
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Mercury-300BB "nmr3"
Relax. delay 1.000 sec
Pulse 67.0 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
632 repetitions
OBSERVE C13, 75.4215901 MHz
DECOUPLE H1, 299.9479605 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING 1.0 Hz
FT size 131072
Total time 51 min, 52 sec
202.558
178.185
175.387
135.516
128.836
128.593
127.947
77.421
77.000
76.575
58.397
42.511
38.063
32.862
27.954
21.475
19.922
220
200
180
160
140
120
100
80
60
40
20
0
ppm


10
8
6
4
2
PPM
1.00
2.18
2.14
1.17
1.22
1.20
3.55
3.46
9.522
7.489
7.471
7.468
7.452
7.412
7.392
7.289
7.285
7.271
7.269
7.268
7.265
7.257
3.173
3.159
3.149
3.135
3.022
2.997
2.976
2.952
2.656
2.641
2.610
2.595
1.540
1.338
1.296
O
H
O
O
NPh
O

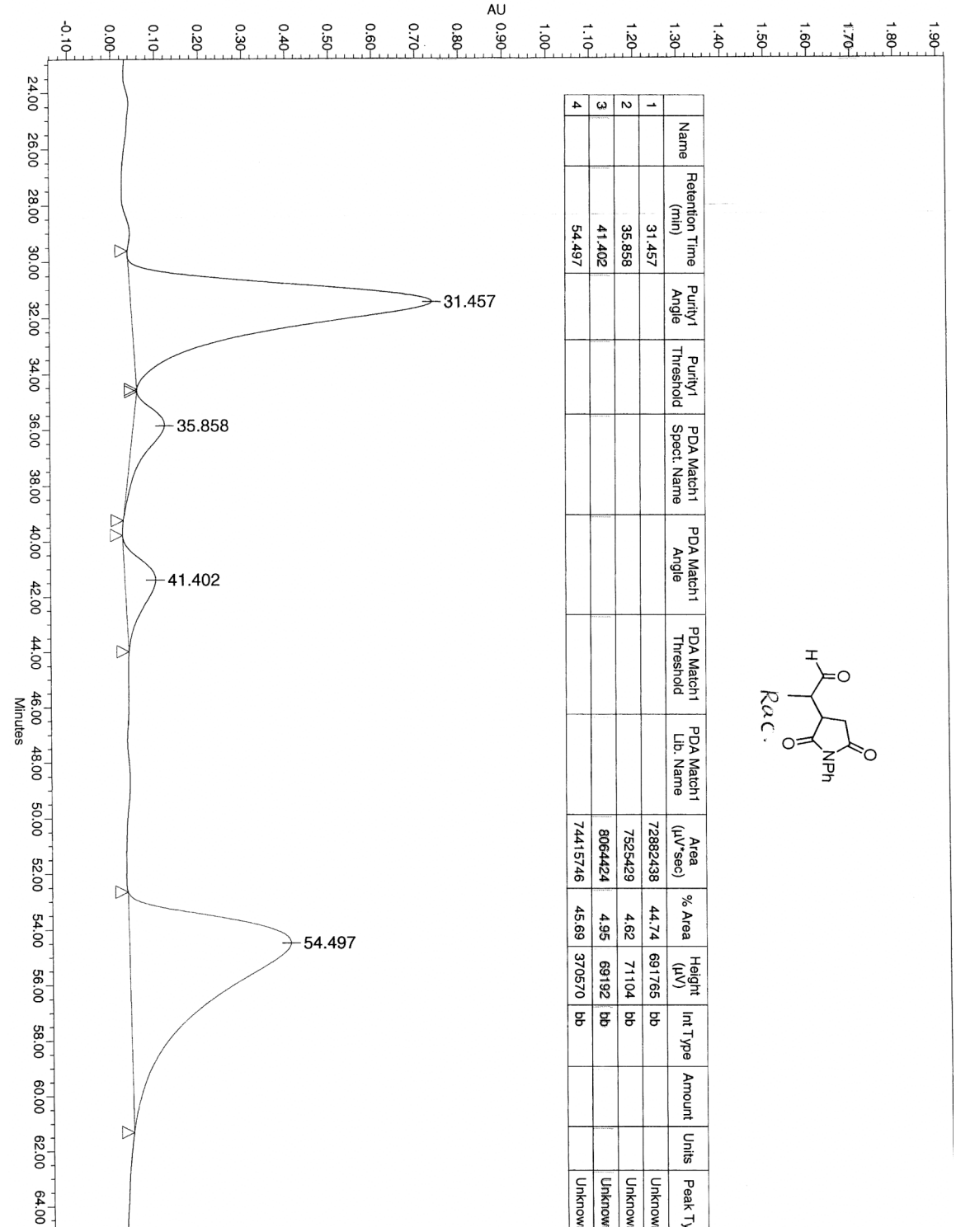

z-3-44-1-C
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Mercury-400BB "nmr4"
Relax. delay 1.000 sec
Pulse 48.9 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
608 repetitions
OBSERVE C13, 100.5638901 MHz
DECOUPLE H1, 399.9376154 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 6 hr, 51 min, 4 sec
202.874
176.988
174.871
131.907
129.251
128.796
126.619
77.479
77.160
76.841
48.588
45.068
31.904
20.395
19.621
200
180
160
140
120
100
80
60
40
20
ppm
H
O
O
NPh
O


z-2-199-H
Pulse Sequence: s2pul
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
Mercury-300BB "nmr3"
Relax. delay 1.000 sec
Pulse 57.3 degrees
Acq. time 1.998 sec
Width 4500.5 Hz
1 repetitions
OBSERVE H1, 299.9464283 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 51 min, 52 sec
HO
O
O
N
O
Br
8
7
6
5
4
3
2
1
ppm
2.00
2.09
0.95
1.57
0.82
1.45
1.27
3.29
3.25

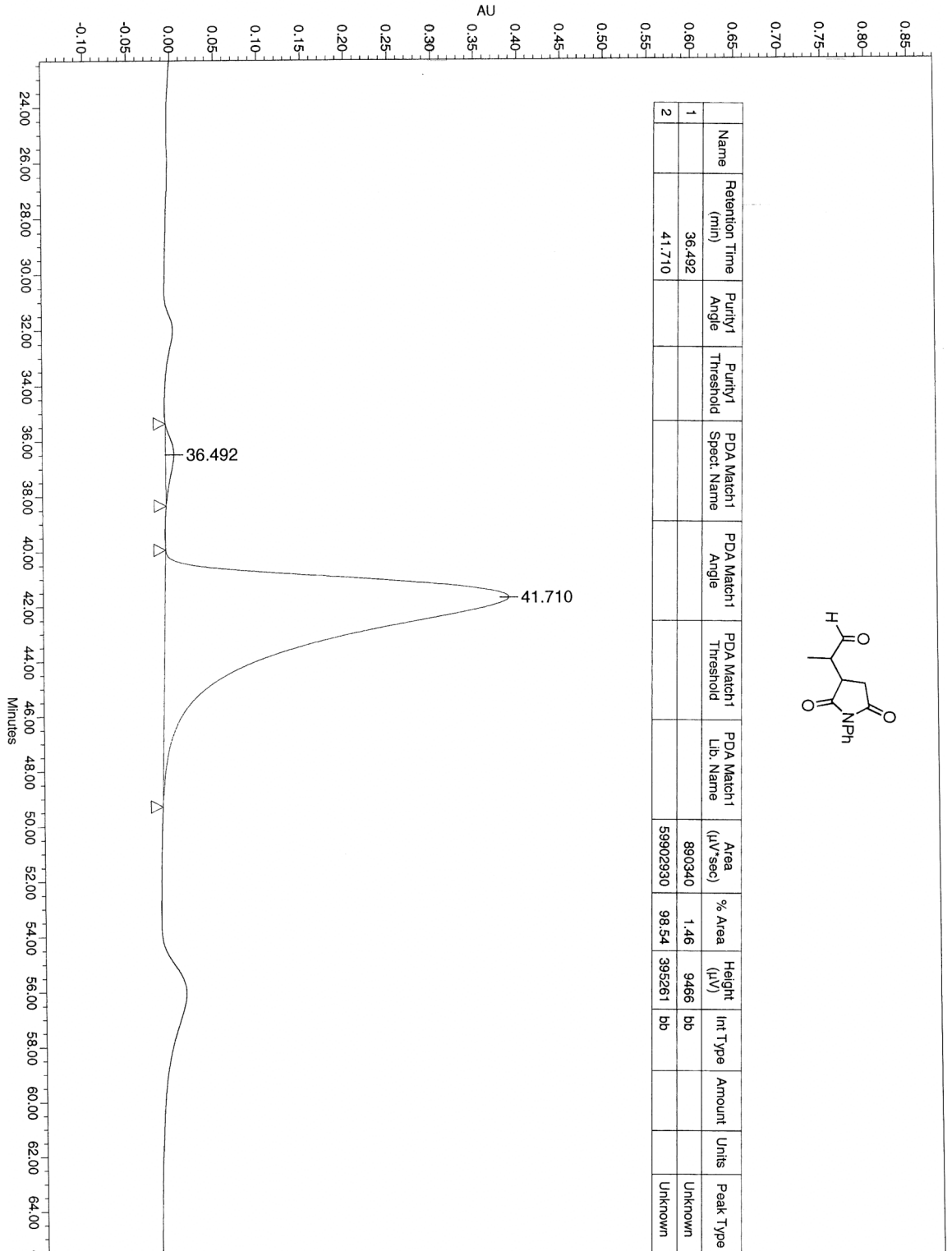

180
160
140
120
100
80
60
40
20
PPM
HO
O
O
N
O
Br



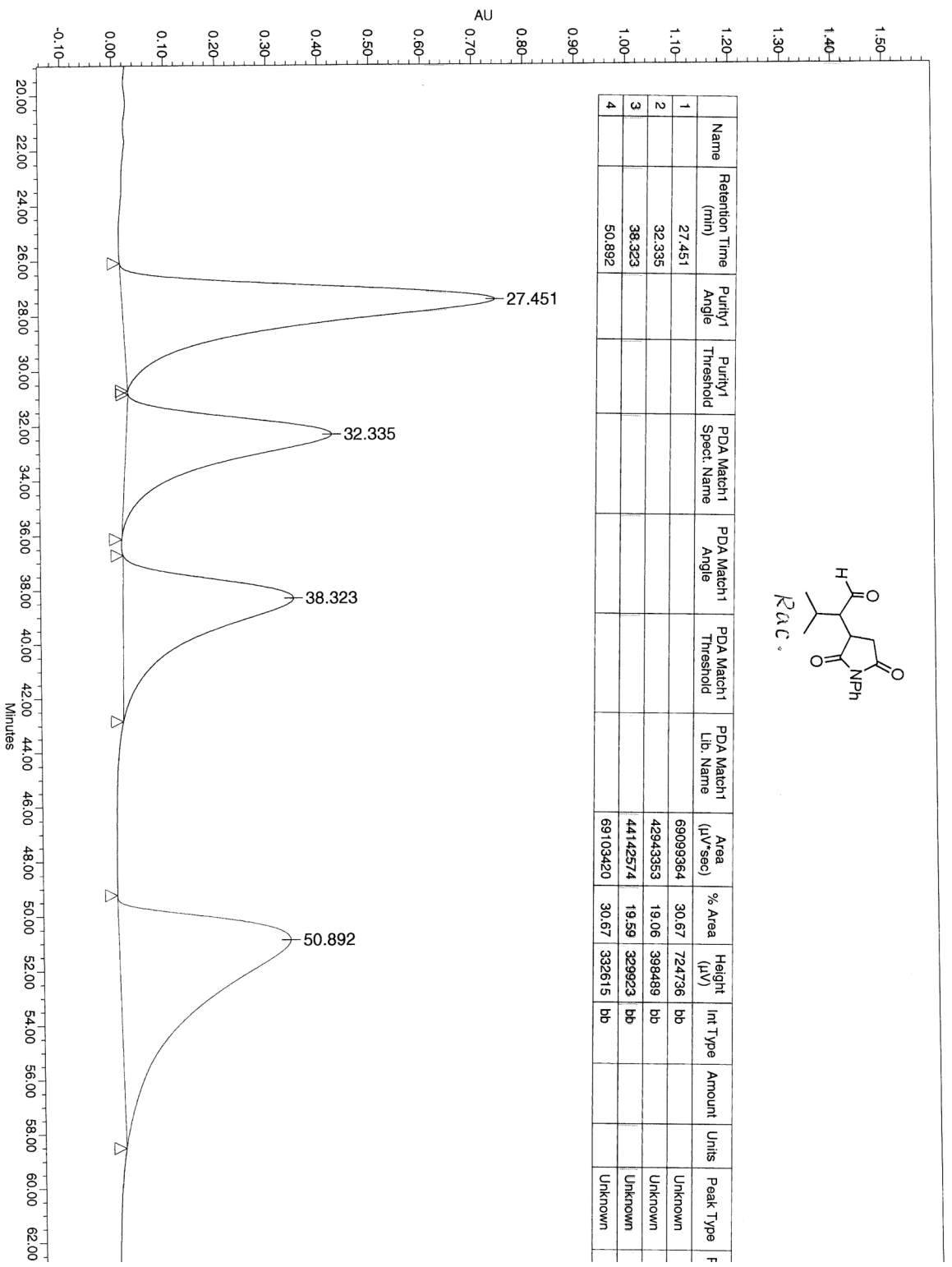
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		35.966							29774368	49.12	256434	bb			Unknown	
2		41.451							30841247	50.88	218418	bb			Unknown	



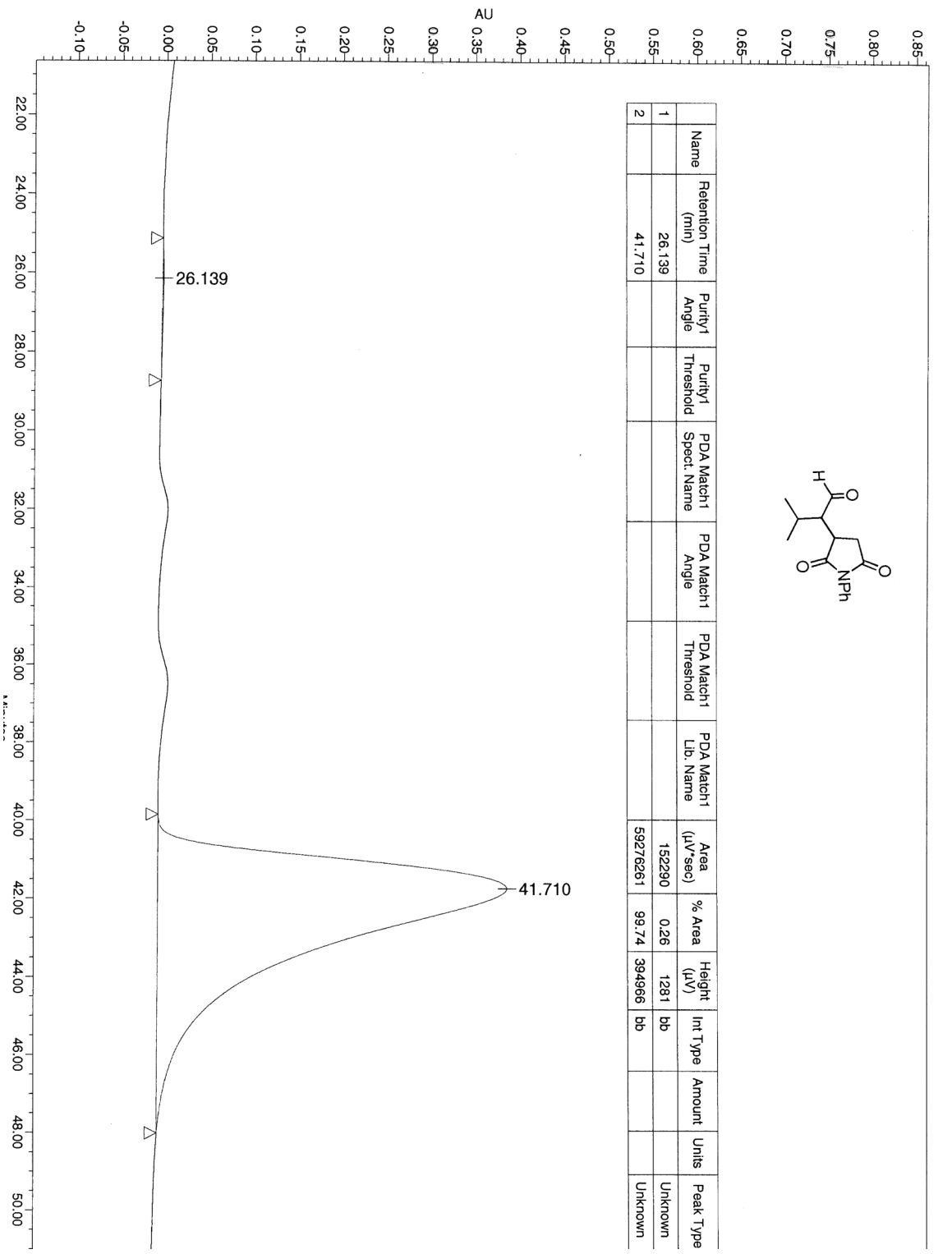
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Ty
1		31.457							72882438	44.74	691765	bb			Unknow
2		35.858							7525429	4.62	71104	bb			Unknow
3		41.402							8064424	4.95	69192	bb			Unknow
4		54.497							74415746	45.69	370570	bb			Unknow



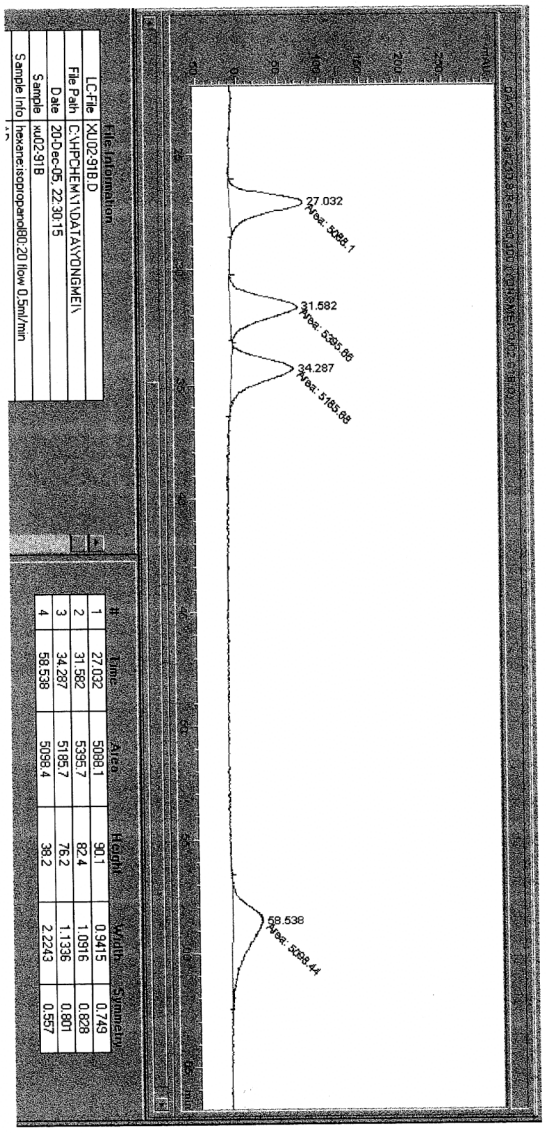
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		36.492							890340	1.46	9466	bb			Unknown
2		41.710							59902930	98.54	395261	bb			Unknown

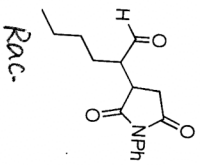


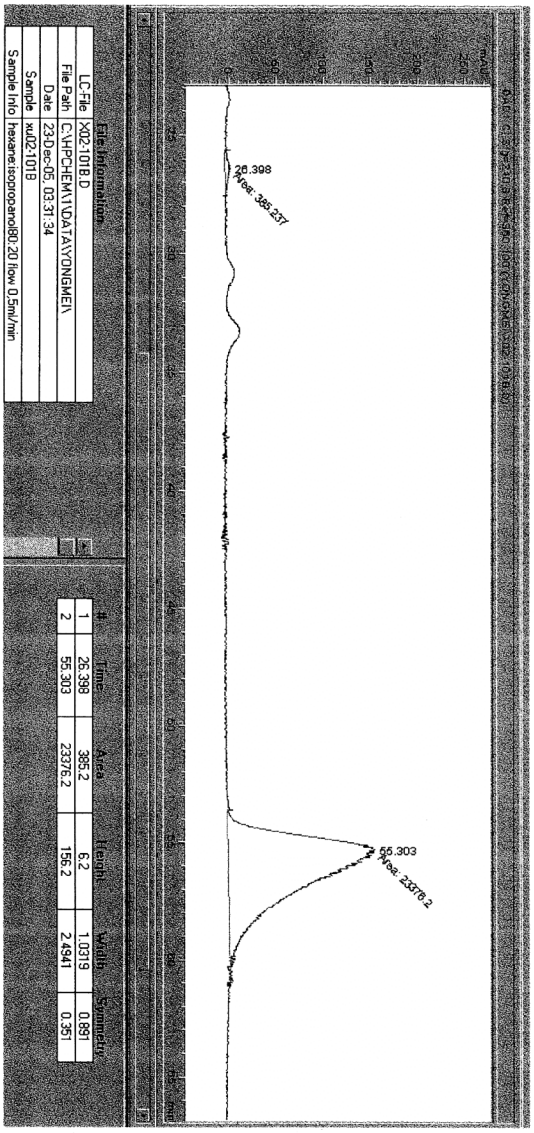
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		27.451							69099364	30.67	724736	bb			Unknown
2		32.335							42943353	19.06	398489	bb			Unknown
3		38.323							44142574	19.59	329923	bb			Unknown
4		50.892							69103420	30.67	332615	bb			Unknown

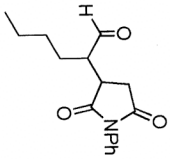


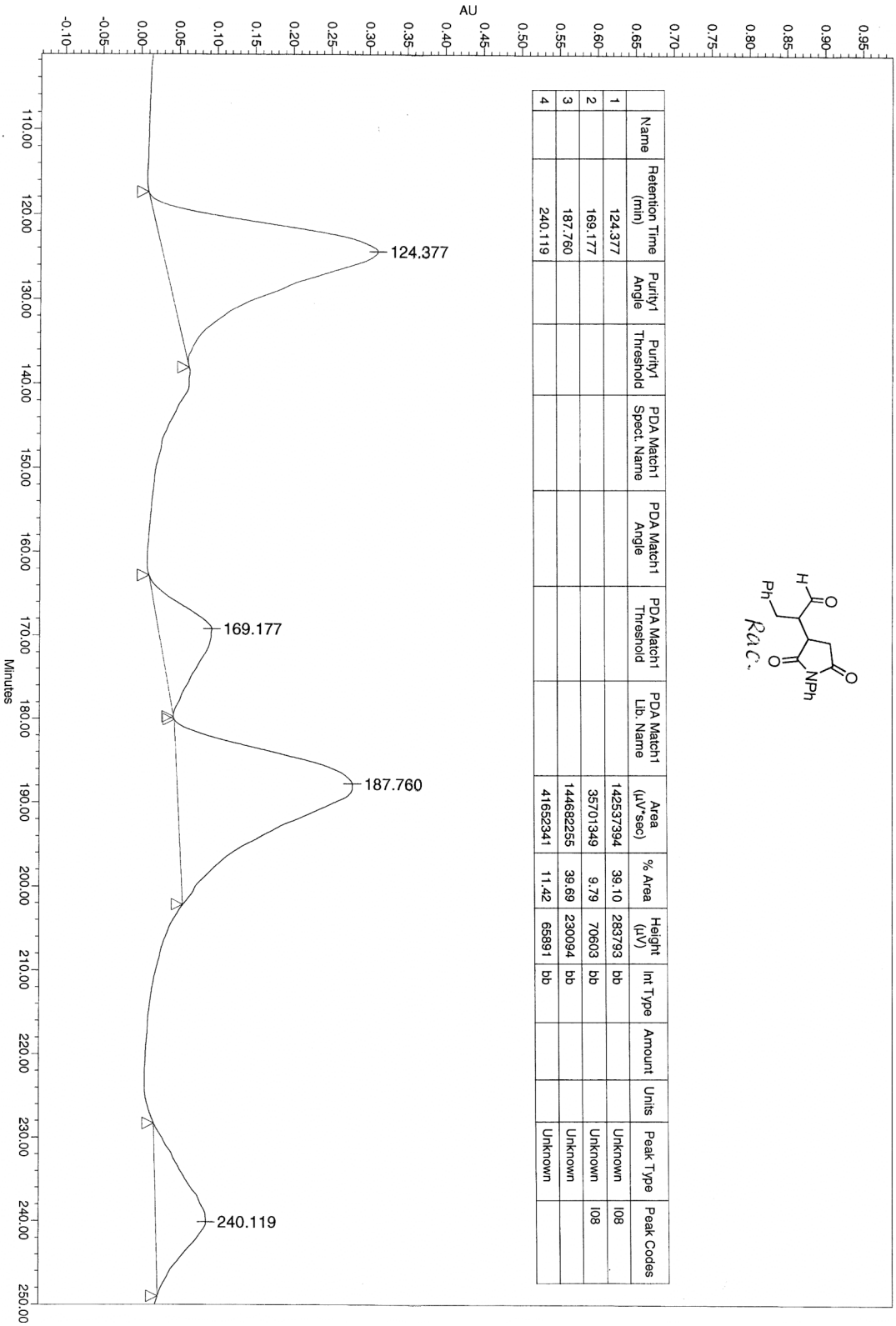
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type
1		26.139							152290	0.26	1281	bb			Unknown
2		41.710							59276261	99.74	394966	bb			Unknown


27.032
Area: 5088.1
31.582
Area: 5395.86
34.287
Area: 5185.68
58.536
Area: 5098.44
File Information
LC File: XJ02-91B.D
File Path: C:\HPCHEM\1\DATA\YONGMEI\
Date: 20-Dec-05, 22:30:15
Sample: xj02-91B
Sample Info: hexane:isopropanol80:20 flow 0.5ml/min
| Time | Area | Height | Width | Symmetry
1 | 27.032 | 5088.1 | 90.1 | 0.9415 | 0.749
2 | 31.582 | 5395.7 | 82.4 | 1.0916 | 0.828
3 | 34.287 | 5185.7 | 76.2 | 1.1336 | 0.801
4 | 58.536 | 5098.4 | 38.2 | 2.2243 | 0.557

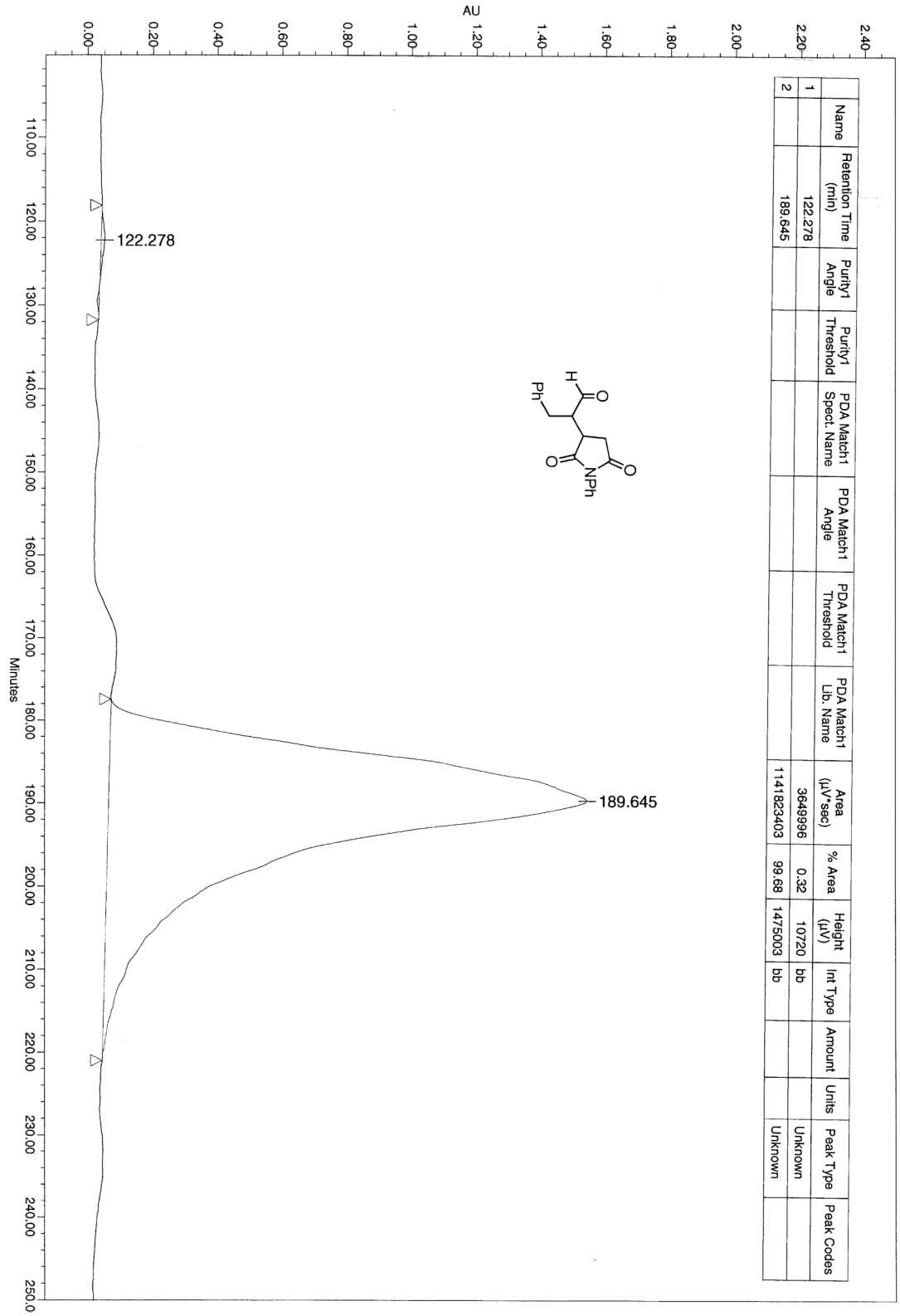

Rac-
H
O
O
O
NPh


26.398
Area: 385.237
55.303
Area: 23376.2
File Information
LC File: XD2-101B.D
File Path: C:\HPCHEM\1\DATA\YONGMEI\
Date: 23-Dec-05, 03:31:34
Sample: xu02-101B
Sample Info: hexane:isopropanol80:20 flow 0.5ml/min
| Time | Area | Height | Width | Symmetry
1 | 26.398 | 385.2 | 6.2 | 1.0319 | 0.891
2 | 55.303 | 23376.2 | 156.2 | 2.4941 | 0.351

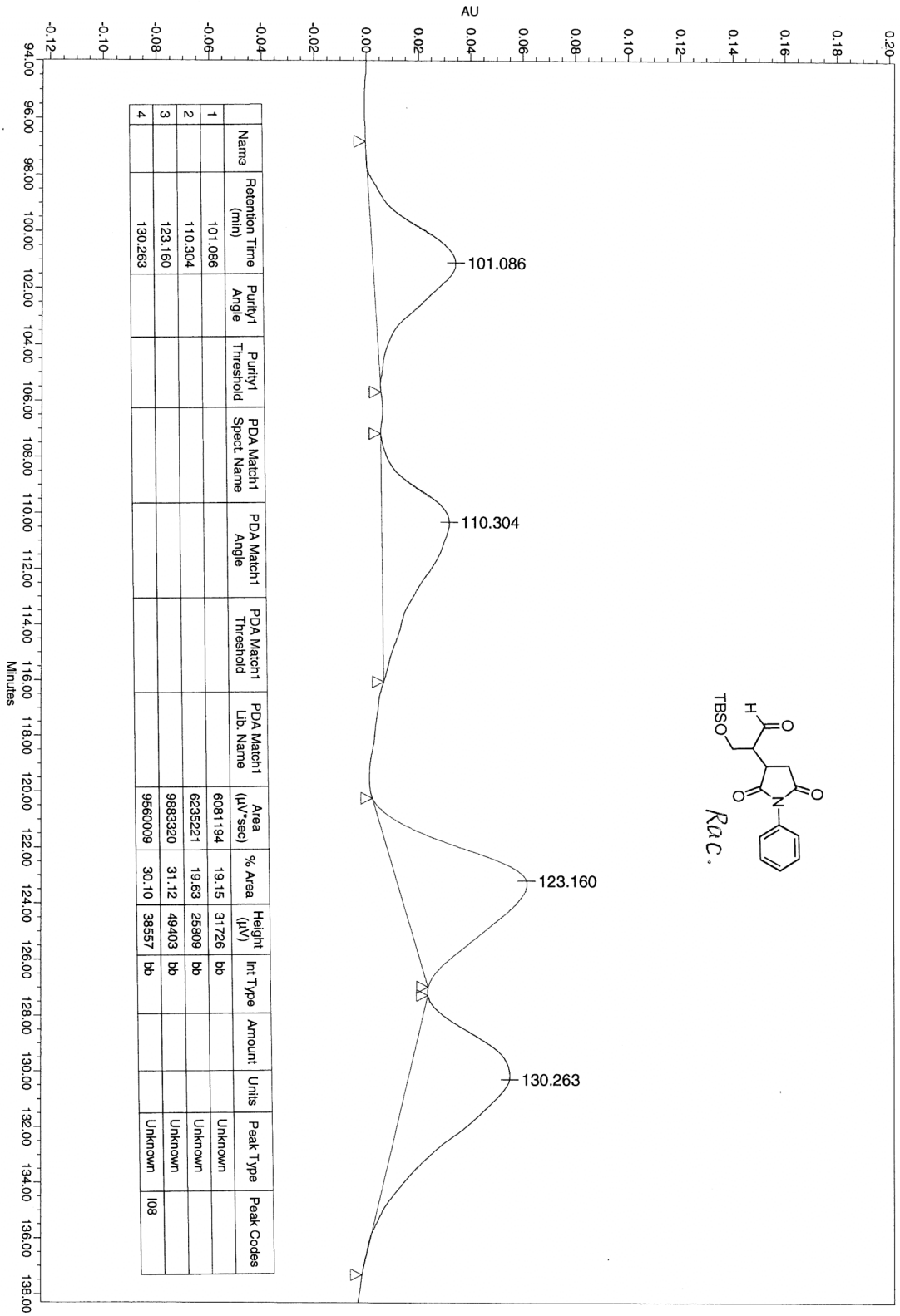

H
O
O
O
NPh



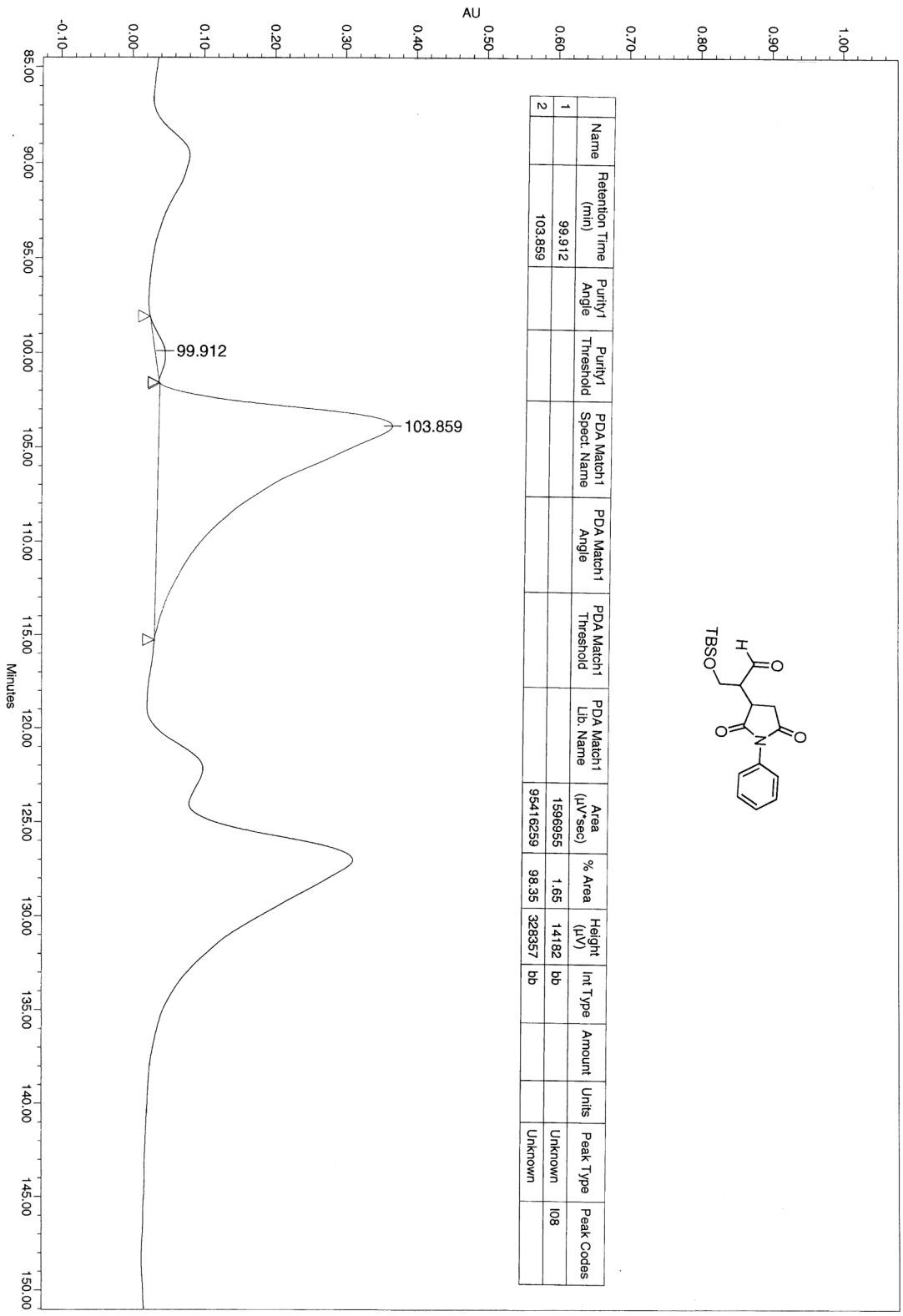
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		124.377							142537394	38.10	283793	bb			Unknown	I08
2		169.177							35701349	9.79	70603	bb			Unknown	I08
3		187.760							144682255	39.69	230094	bb			Unknown	
4		240.119							41652341	11.42	65891	bb			Unknown	



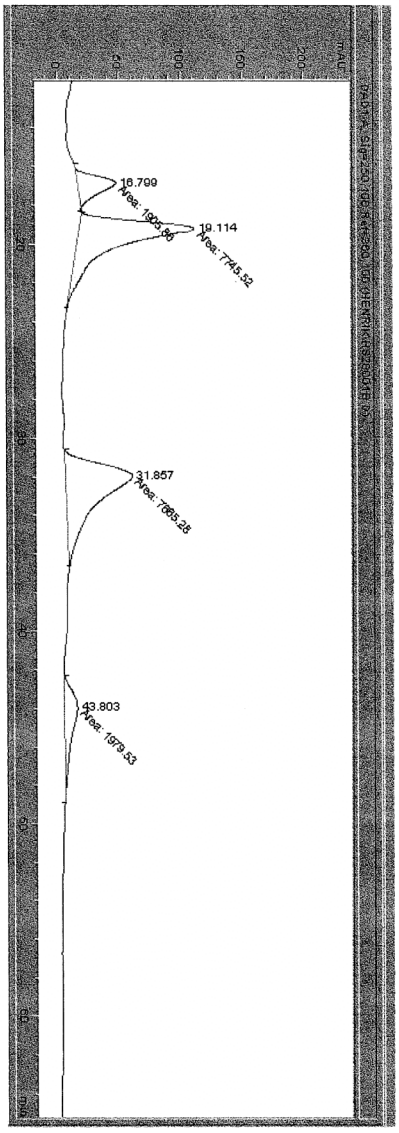
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		122.278							3649996	0.32	10720	bb			Unknown	
2		189.645							1141823403	99.68	1475003	bb			Unknown	



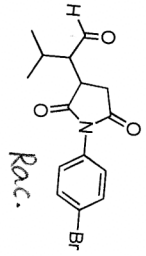
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		101.086							6081194	19.15	31726	bb			Unknown	
2		110.304							6235221	19.63	25809	bb			Unknown	
3		123.160							9883320	31.12	49403	bb			Unknown	
4		130.263							9560009	30.10	38557	bb			Unknown	I08



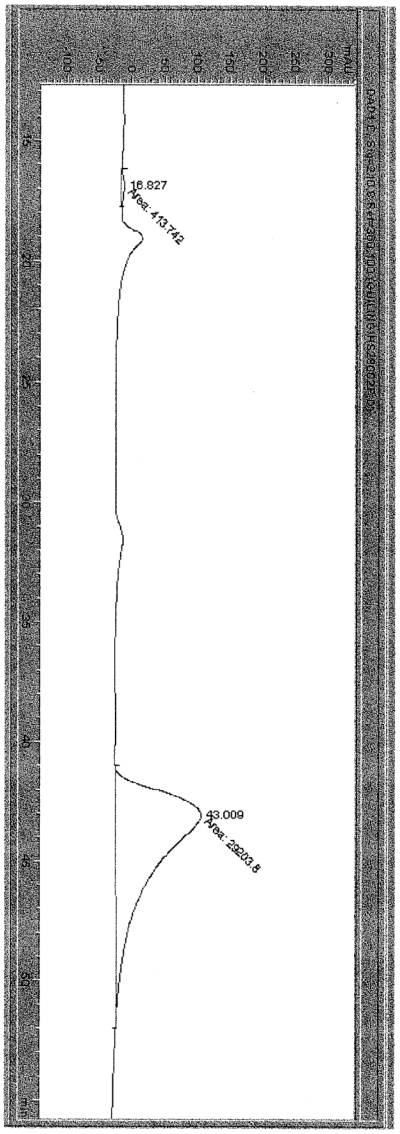
	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		99.912							1596955	1.65	14182	bb			Unknown	I08
2		103.859							95416259	98.35	328357	bb			Unknown	



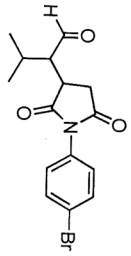
#	Time	Area	Height	Width	Symmetry
1	16.799	1905.9	32	0.9917	0.659
2	19.114	7745.5	93.8	1.376	0.412
3	31.857	7665.3	54.7	2.3349	0.427
4	43.803	1979.5	10.9	3.0138	0.467

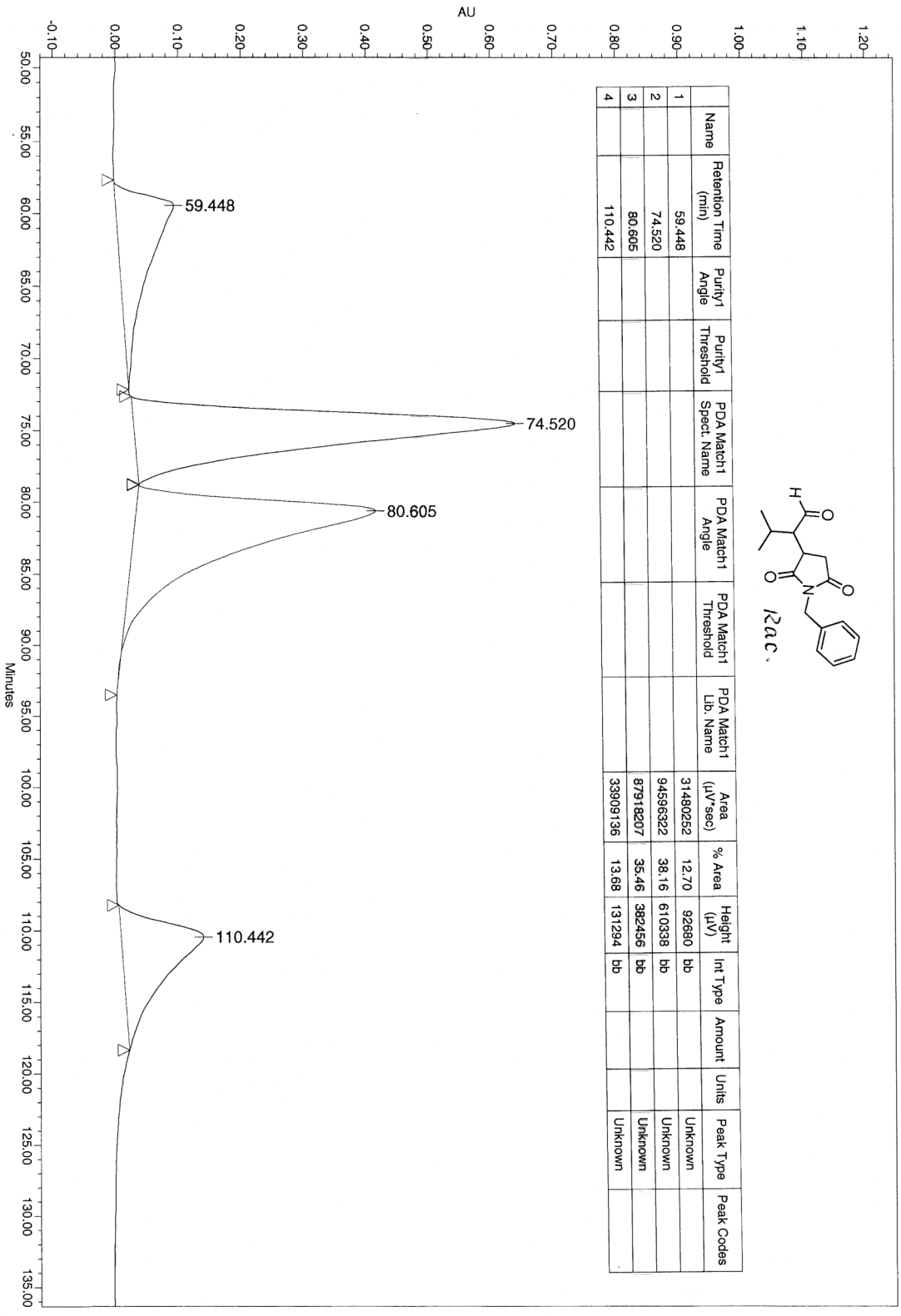


Rac.

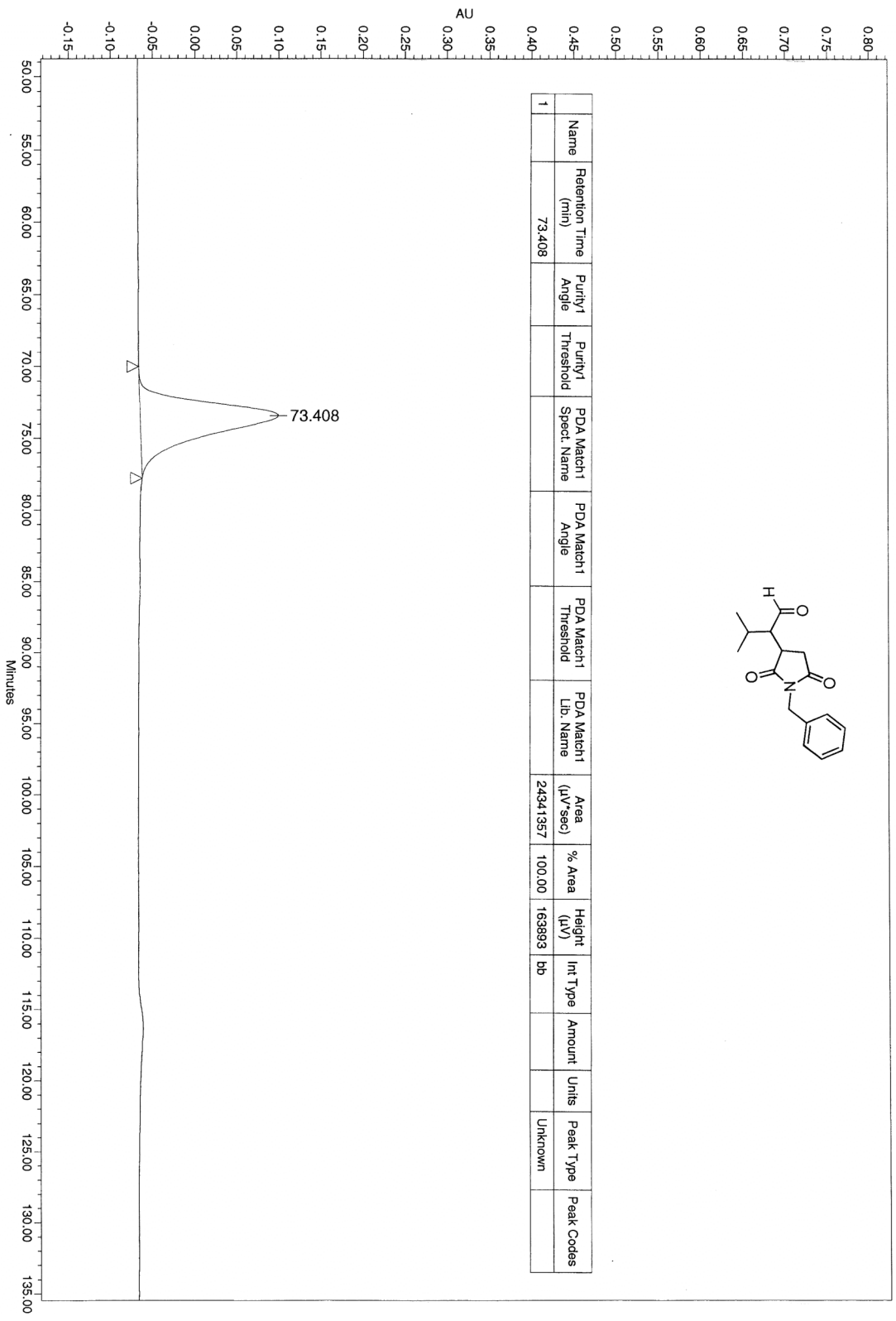


#	Time	Area	Height	Width	Symmetry
1	16.827	413.7	6.2	1.106	0.54
2	43.009	29203.8	131.8	3.6928	0.39

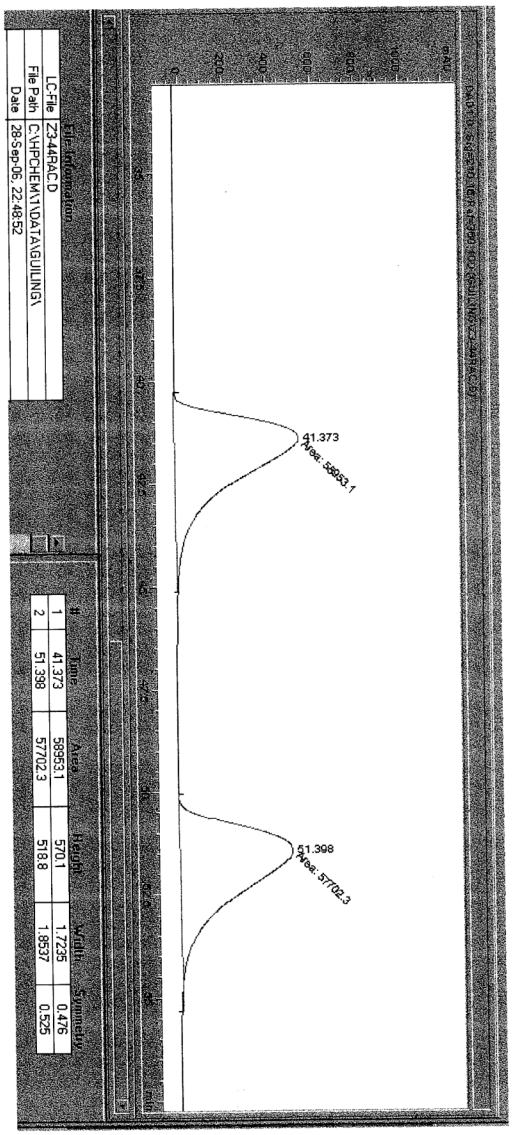


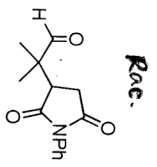


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		59.448							31480252	12.70	92680	bb			Unknown	
2		74.520							94596322	38.16	610338	bb			Unknown	
3		80.605							87918207	35.46	382456	bb			Unknown	
4		110.442							33909136	13.68	131294	bb			Unknown	

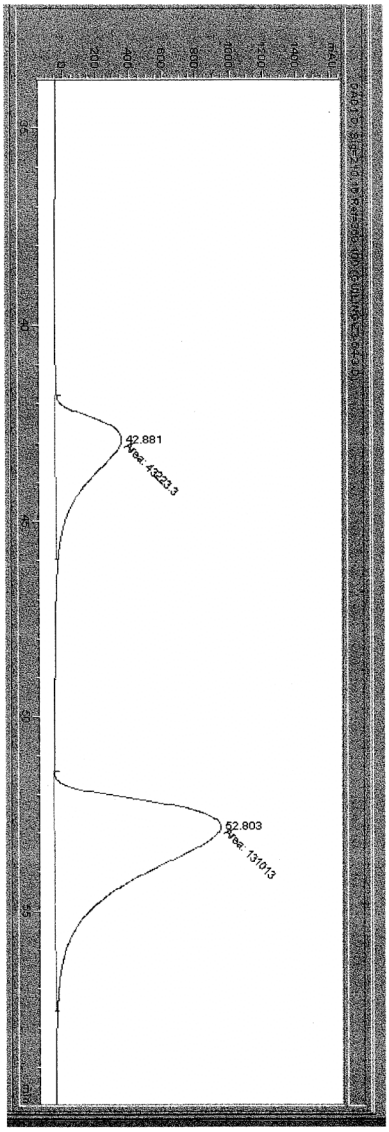


	Name	Retention Time (min)	Purity1 Angle	Purity1 Threshold	PDA Match1 Spect. Name	PDA Match1 Angle	PDA Match1 Threshold	PDA Match1 Lib. Name	Area (µV*sec)	% Area	Height (µV)	Int Type	Amount	Units	Peak Type	Peak Codes
1		73.408							24341357	100.00	163893	bb			Unknown	


41.373
Area: 58953.1
51.398
Area: 57702.3
File Information
LC File: Z3-44RAC.D
File Path: C:\HPCHEM\1\DATA\GUILING\
Date: 28-Sep-06, 22:48:52
| Time | Area | Height | Width | Symmetry
1 | 41.373 | 58953.1 | 570.1 | 1.7235 | 0.476
2 | 51.398 | 57702.3 | 518.8 | 1.8537 | 0.525


H
O
O
O
NPh

Rac.



#	Time	Area	Height	Width	Symmetry
1	42.881	43223.3	399.9	1.8012	0.505
2	52.803	131012.9	998.2	2.1875	0.474