SUPPORTING INFORMATION

Stereoselective Syntheses of L-Pipecolic Acid and (2*S*,3*S*)-3-Hydroxypipecolic Acid From a Chiral *N*-Imino-2-phenyl-1,2-dihydropyridine Intermediate.

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General information. Unless otherwise stated, reactions were run under argon atmosphere with rigid exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds.[1] All glassware were rinsed with a base bath, left to stand for 15 min., washed with water, then acetone and stored in the oven and/or were flame-dried under an argon atmosphere prior to use.Dichloromethane, diethyl ether, tetrahydrofuran and acetonitrile were obtained by filtration through drying columns. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel. Visualization of the developed chromatogram was performed by UV and aqueous potassium permanganate. Flash column chromatography was performed using 230-400 mesh silica. Melting points are uncorrected. Optical rotation data are reported as follows: $[\alpha]_D^{20}$ [observed rotation x volume (mL)]/[length (dm) x mass (g)]), concentration (*c* in g/100 mL), and solvent. Chemical shifts for ^{1}H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sx = sextet, h = heptet, o = octet, m = multiplet and br = broad), coupling constant in Hz, integration. Chemical shifts for ^{13}C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of the solvent resonance (deuterochloroform = 77.23 ppm) as the internal standard. All ^{13}C NMR spectra were obtained with complete proton decoupling. When ^{13}C-^{19}F couplings are present, data are reported as follow: chemical shift, multiplicity (q = quartet, m = multiplet), coupling constant in Hz. High resolution mass spectrometry (HRMS) was performed on a LC-MSD-TOF instrument with a metastable atom bombardment (MAB) source or an electrospray (ES) source. Low resolution mass spectrometry (LRMS) was performed on a LC-MSD instrument with an atmospheric pressure chemical ionization (APCI) source. HPLC or SFC separation data are reported as follow: column type, eluent, flow rate, and retention time (t_r). GC separation data are reported as follow: column type, colomn lenght, initial temperature, rate of heating, final temperature, flow rate, and retention time (t_r).

Reagents: Unless otherwise stated, commercial reagents were used without purification. Triflic anhydride was distilled over a small amount of P_2O_5. Pyridine was distilled over calcium hydride. Chiral amide **3**, and dihydropyridine **8** were prepared as reported in literature.[2] Tributyl[(methoxymethoxy)methyl]stannane ($MOMOCH_2SnBu_3$) was prepared as

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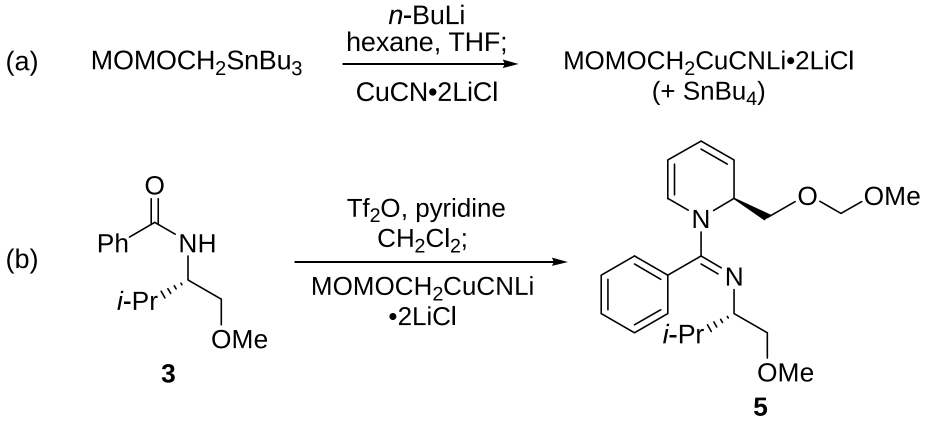
(1) Shriver, D. F.; Drezdzon, M. A. *The manipulation of air-sensitive compounds*; 2nd Edition ed.; Wiley: New York, 1986.

(2) Charette, A. B.; Grenon, M.; Lemire, A.; Pourashraf, M.; Martel, J. *J. Am. Chem. Soc.* **2001**, *123*, 11829.

reported in literature.[3] Dry copper cyanide and lithium chloride were weighed in a glove box under argon atmosphere.

N-[(1*E*)-[(2*S*)-2-[(Methoxymethoxy)methyl]pyridin-1(2*H*)-yl](phenyl)methylene]-*N*-[(1*S*)-1-(methoxymethyl)-2-methylpropyl]amine (5).



To a solution of pyridine (0.12 mL, 0.12 g, 1.5 mmol) and amide **3** (111 mg, 0.50 mmol) in dichloromethane (2.5 mL), cooled to -40 °C, was added Tf_2O (0.10 mL, 0.18 g, 0.65 mmol) dropwise. The mixture was warmed to room temperature and stirred for 3 hours. In a separate flask was added CuCN (141 mg, 1.58 mmol) and LiCl (134 mg, 3.16 mmol), in a glove box under argon atmosphere. The flask were removed from the glove box, salts were solubilized in THF (4.2 mL), the solution was cooled to -78 °C, then *i*-PrMgCl (0.055 mL of a 1.48 M solution in THF, 0.08 mmol) was added. In a third flask was added Bu_3SnCH_2OMOM (566 mg, 1.55 mmol), the tin reagent was solubilized in THF (2.2 mL) and the solution was cooled to -78 °C. *n*-Butyllithium (0.59 mL of a 2.5 M solution in hexane, 1.50 mmol) was added and the mixture was stirred for 6 minutes. The CuCN•2LiCl solution at -78 °C was then canulated over the $LiCH_2OMOM$ reagent at -78 °C. The solution was stirred for 35 minutes, then preformed pyridinium salt was transferred drop wise using a syringe. The mixture was stirred for 3 hours at -78 °C and was quenched with a saturated solution of aqueous ammonium chloride. The mixture was transferred to an extraction funel, phases were separated and the aqueous phase was extracted using dichloromethane. The combined organic phase was dried over magnesium sulfate, filtered and concentrated under

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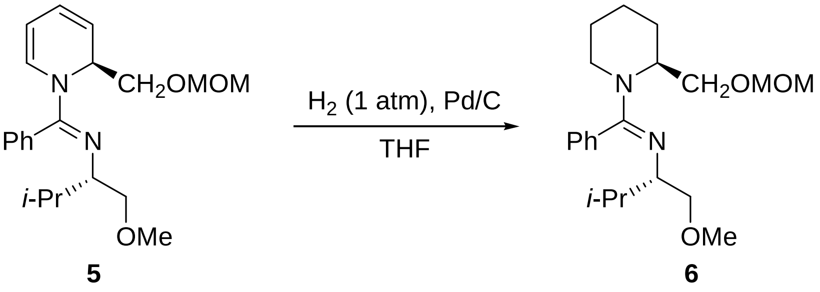
(3) (a) Johnson, C. R.; Medich, J. R. *J. Org. Chem.* **1988**, *53*, 4131. See also: (b) Danheiser, R. L.; Romines, K. R.; Koyama, H.; Gee, S. K.; Johnson, C. R.; Medich, J. R. *Org. Synth.* **1993**, *71*, 133. (c) Johnson, C. R.; Medich, J. R.; Danheiser, R. L.; Romines, K. R.; Koyama, H.; Gee, S. K.; *Org. Synth.* **1993**, *71*, 140.

reduced pressure. Oily residue (711 mg)[4] was purified over silica gel (gradient 0-10% EtOAc/hexane) to afford **5** (129 mg, 72%) as a yellow oil: R_f 0.20 (25% EtOAc/hexane); $[\alpha]_D^{20}$ = -469 (*c* 1.31, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) 7.45-7.35 (m, 3H), 7.29 (br s, 1H), 7.10 (br s, 1H), 5.98 (dd, *J* = 9.0, 5.4 Hz, 1H), 5.96 (br s, 1H), 5.55 (dd, *J* = 9.3, 5.8 Hz, 1H), 5.52 (br s, 1H), 4.87 (t, *J* = 6.5 Hz, 1H), 4.68 (d, *J* = 12.5 Hz, 1H), 4.66 (d, *J* = 12.5 Hz, 1H), 3.72 (dd, *J* = 9.3, 7.1 Hz, 1H), 3.66 (dd, *J* = 9.4, 4.6 Hz, 1H), 3.45 (dd, *J* = 9.4, 4.9 Hz, 1H), 3.37 (s, 3H), 3.31 (dd, *J* = 9.3, 7.5 Hz, 1H), 3.27 (s, 3H), 2.97 (dt, *J* = 7.5, 4.8 Hz, 1H), 1.65 (hd, *J* = 6.8, 4.7 Hz, 1H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.2 (C), 133.0 (C), 129.7 (CH), 129.2 (CH), 128.8 (2CH), 128.7 (CH), 128.6 (CH), 123.4 (CH), 118.3 (CH), 101.2 (CH), 96.6 (CH_2), 76.1 (CH_2), 66.8 (CH_2), 63.6 (CH), 59.1 (CH_3), 55.3 (CH_3), 51.4 (CH), 31.0 (CH), 20.2 (CH_3), 17.8 (CH_3); FTIR (film) 3078, 3052, 1629, 1599, 1567, 1336, 1151, 1040, 715, 703 cm^{-1}; HRMS (MAB) calc. for $C_{21}H_{30}N_2O_3$ $(M)^+$: 358.2256, found 358.2248.

N-[(1*E*)-{(2*S*)-2-[(Methoxymethoxy)methyl]piperidin-1-yl}(phenyl)methylene]-*N*-[(1*S*)-1-(methoxymethyl)-2-methylpropyl]amine (6).



To a solution of dihydropyridine **5** (68 mg, 0.19 mmol) in THF (2.3 mL) was added Pd/C (103 mg of Pd 10%/C, 0.097 mmol). The mixture was purged 3x under hydrogen atmosphere (water vacuum followed by hydrogen fill), then stirred for 18 hours under hydrogen atmosphere (1 atm). The mixture was filtered over Celite®, the solids were rinsed with dichloromethane and the filtrate was concentrated under reduced pressure. Oily residue was purified over silica gel (gradient 0-50% EtOAc/hexane containing 1% NEt_3) to afford **6** (43 mg, 63%) as a pale yellow oil: R_f 0.47 (10:10:80 AcOH:MeOH:CH_2Cl_2); $[\alpha]_D^{20}$ = -71 (*c* 2.2, $CHCl_3$); ^1H NMR (C_6D_6, 400 MHz) δ 7.35-7.28 (m, 3H), 7.15 (d, *J* = 7.7 Hz, 2H), 4.62

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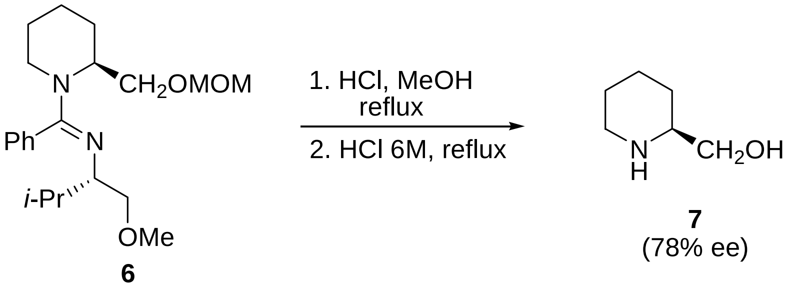
[4] Regiomeric ratio (**5** : 4-methoxymethyl-1,4-dihydropyridine) is 90:10 in the crude mixture by ^1H NMR analysis. Diastereomeric ratio at C-2 of 81:19 in the crude mixture. After purification, diastereomeric ratio could be enriched to 91:9. The minor regioisomer methyl signals on the isopropyl group of the chiral auxiliary are found at 1.04 ppm and 0.93 ppm and those of the minor diastereoisomer are found at 0.91 ppm and 0.82 ppm.

(d, *J* = 10.1 Hz, 1H), 4.60 (d, *J* = 10.2 Hz, 1H), 4.12 (br s, 1H), 3.76 (dd, *J* = 9.5, 6.0 Hz, 1H), 3.70-3.58 (m + dd, *J* = 9.2, 8.7 Hz, 2H), 3.37-3.33 (m, 1H), 3.34 (s, 3H), 3.19 (s, 3H), 3.16 (dd, *J* = 9.6, 6.9 Hz, 1H), 2.84 (dt, *J* = 6.7, 5.3 Hz, 1H), 2.72 (td, *J* = 12.8, 3.0 Hz, 1H), 1.75-1.35 (m, 7H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.74 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ 160.8 (C), 135.2 (C), 128.4 (2CH), 128.0 (2CH), 127.8 (CH), 96.2 (CH_2), 76.3 (CH_2), 64.4 (CH_2), 62.8 (CH), 58.8 (CH_3), 55.1 (CH_3), 50.5 (CH), 41.6 (CH_2), 30.7 (CH), 25.6 (CH_2), 25.4 (CH_2), 20.1 (CH_3), 20.0 (CH_2), 17.8 (CH_3); FTIR (film) 1616, 1597, 1113, 1046 cm^{-1}; HRMS (MAB) calc. for $C_{21}H_{34}N_2O_3$ $(M)^+$: 362.2569, found 362.2561.

(2*S*)-Piperidin-2-ylmethanol (7).



To a solution of piperidine **6** (43 mg, 0.12 mmol) in methanol (2.4 mL) was added concentrated hydrochloric acid (6 drops). The solution was heated under reflux for 13 hours. The mixture was then concentrated under reduced pressure, the residue was dissolved with a solution of aqueous potassium carbonate (1.0 M, 5 mL) and was transferred into a separatory funel. Aqueous phase was extracted with dichloromethane (3x10 mL), the combined organic layer was dried over potassium carbonate, filtered and concentrated under reduced pressure. The residue (28 mg) was then dissolved with hydrochloric acid (2.0 mL of a 6 M solution), and the solution was refluxed for 4 hours. The mixture was cooled to room temperature and transferred into a separatory funel. The aqueous phase was washed with dichloromethane (3x10 mL) and concentrated. The afforded residue was dissolved with aqueous sodium hydroxide (2 mL of a 2 M solution), dichloromethane was added (10 mL), the mixture was transfered into a separatory funel and the organic layer was collected. The aqueous phase was extracted using dichloromethane (3x10 mL), the combined organic layer was dried over potassium carbonate, filtered and concentrated under reduced pressure to afford **7** (7.2 mg, 63%) as a beige solid: Mp 66-68 °C, lit.[5] 68-70 °C (racemic); Rf 0.08 (10:10:80

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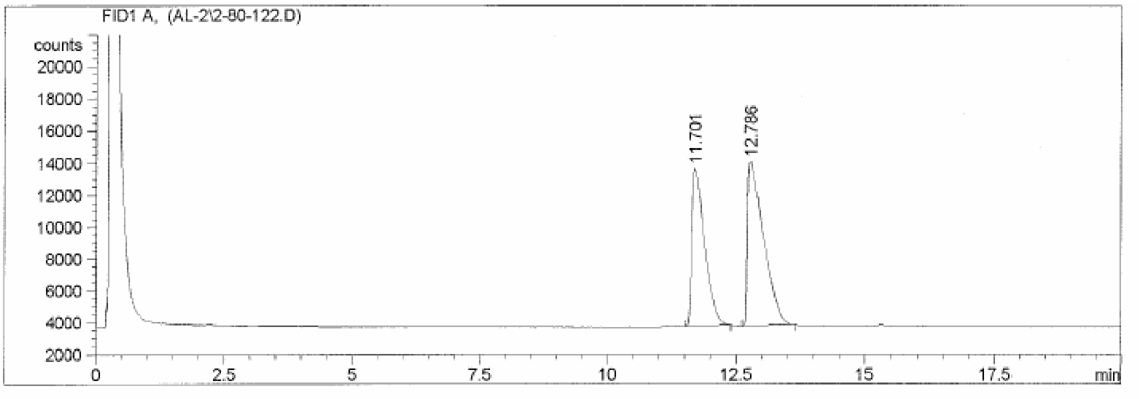
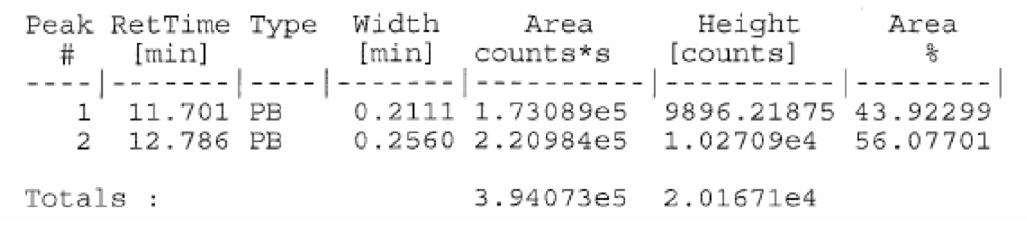
[5] Aldrich Catalogue Handbook of Fine Chemicals, Aldrich Chemical Company, Inc., Milwaukee, WI, É.-U.

AcOH:MeOH:CH_2Cl_2); $[\alpha]_D^{20}$ = 12 (*c* 0.55, EtOH), lit.[6a] 15.9 (*c* 2.50, EtOH), lit. (enantiomer of **7**)[6b] –13.5 (*c* 2.38, EtOH); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.70 (dd, *J* = 10.8, 3.7 Hz, 1H), 3.27 (dd, *J* = 10.8, 8.1 Hz, 1H), 3.20 (br s, 2H), 3.07 (br d, *J* = 11.9 Hz, 1H), 2.67-2.55 (m, 2H) 1,83-1.74 (m, 1H), 1.65-1.57 (m, 1H), 1.57-1.49 (m, 1H), 1.48-1.27 (m, 2H), 1.11 (qd, 12.0, 7.9 Hz, 1H). Optical purity of **7** was 77% *ee* by comparison of optical rotation with ref. 6a. Enantiomeric purity of **7** was 78% *e.e.* (89:11 *e.r.*) by GC analysis : sample (1 mg) was dissolved in dichloromethane (1 mL), TFAA (10 μL) was added to generate the bistrifluoroacetyl derivative; colomn Chiraldex G-TA; 25 psi (H_2); split 1/100; 80 °C for 1 minute, gradient 2 °C/minute up to 120 °C, kept for 10 minutes: (–)-**7** T_r, 12.0 min, (+)-**7** T_r, 13.0 min.

Chromatogram of (–/+) 7





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   2  12.786 PB    0.2560 2.20984e5  1.02709e4  56.07701

Totals :                  3.94073e5  2.01671e4
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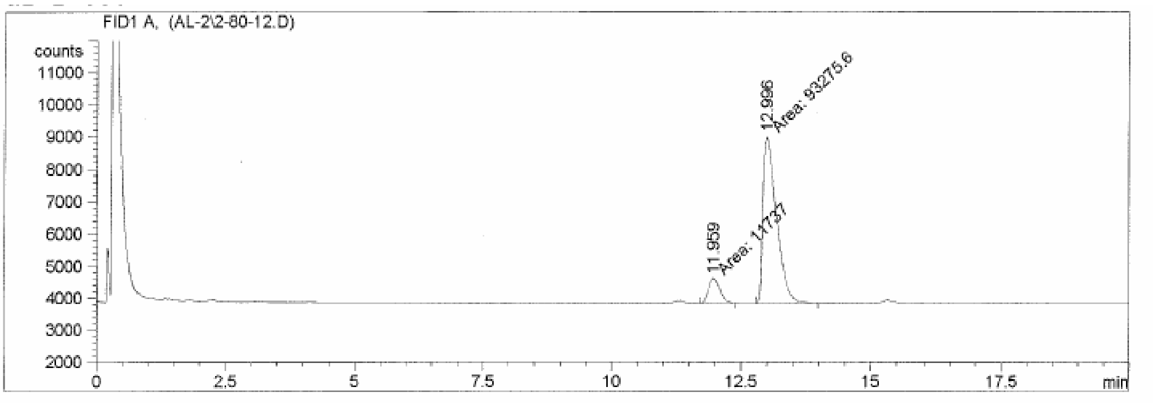
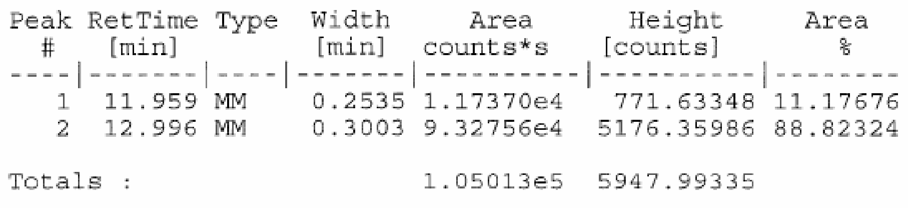
(6) (a) Segat-Dioury, F.; Lingibé, O.; Graffe, B.; Sacquet, M.-C.; Lhommet, G. *Tetrahedron* **2000**, *56*, 233. (b) Kawaguchi, M.; Hayashi, O.; Sakai, N.; Hamada, M.; Yamamoto, Y.; Oda, J.'i. *Agric. Biol. Chem.* **1986**, *50*, 3107.

Chromatogram of enantioenriched (+) 7





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Peak RetTime Type  Width     Area      Height     Area
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   2  12.996 MM    0.3003 9.32756e4 5176.35986 88.82324

Totals :                  1.05013e5 5947.99335
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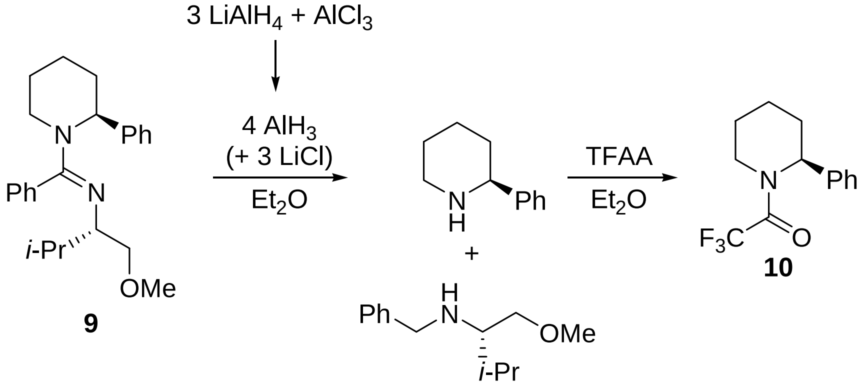
N-[(1*S*)-1-(Methoxymethyl)-2-methylpropyl]-*N*-{(1*E*)-phenyl[(2*S*)-2-phenylpiperidin-1-yl]methylene}amine (9).

The dihydropyridine derivative **8** (240 mg, 0.667 mmol) was charged in a small Parr bomb. Methanol (3.3 mL) was added, followed by the palladium catalyst (23 mg of 10 wt. % Pd/C, 0.022 mmol Pd). The Parr bomb was closed and the mixture purged three times with hydrogen atmosphere (pressurized to 250 psi followed by releasing pressure to atmospheric). Hydrogen (250 psi) was then introduced in the Parr bomb and the mixture was stirred for 50 hours at room temperature. The reaction mixture was then filtered through Celite®, the solids were rinsed with CH_2Cl_2 (50 mL) and the filtrate was concentrated under reduced pressure. Flash chromatography of the oily residue (25:75:0, then 25:74.5:0.5 to 50:49.5:0.5 EtOAc:hexane:NEt_3) afforded 194 mg of **9** (80%) as a colorless oil. R_f 0.40 (85:10:5 CH_2Cl_2:MeOH:AcOH); $[\alpha]_D^{20}$ = -124 (*c* 1.07, $CHCl_3$); ^{1}H NMR (C_6D_6, 300 MHz) δ 7.38 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.9 Hz, 2H), 7.26 (t, J = 7.9 Hz , 2H), 7.11 (t, J = 7.7 Hz, 3H), 7.03 (t, J = 7.4 Hz, 1H), 5.54 (br s, 1H), 3.82 (br d, J = 13.7 Hz, 1H), 3.44 (dd, J = 9.0, 5.1

Hz, 1H), 3.31 (t, *J* = 9.0 Hz, 1H), 3.18 (dt, *J* = 7.8, 5.1 Hz, 1H), 3.13 (s, 3H), 2.84 (dt, *J* = 14.6, 2.7 Hz, 1H), 2.02 (dq, *J* = 13.7, 2.0 Hz, 1H), 1.96-1.74 (m, 2H), 1.54-1.32 (m, 3H), 1.13-1.09 (m + d, *J* = 6.7 Hz, 4H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (C_6D_6, 75 MHz) δ 161.6 (C), 142.5 (C), 136.1 (C), 129.0 (2CH), 128.9 (2CH), 128.8 (2CH), 128.5 (CH), 127.9 (2CH), 126.6 (CH), 77.2 (CH_2), 64.0 (CH), 59.2 (CH_3), 54.3 (CH), 42.3 (CH_2), 31.8 (CH), 28.5 (CH_2), 26.3 (CH_2), 21.0 (CH_3), 20.9 (CH_2), 18.7 (CH_3); FTIR (neat) 3059, 1615, 1596, 1494, 1446, 1273, 1127, 1113, 701 cm^{-1}; HRMS (MAB) calcd. for $C_{24}H_{32}N_2O$ (M)+: 364.2515, found 364.2523. Anal. calcd. for $C_{24}H_{32}N_2O$: C, 79.08; H, 8.85; N, 7.68, found C, 79.13; H, 8.90; N, 7.58.

(2*S*)-2-Phenyl-1-(trifluoroacetyl)piperidine (10).



Lithium aluminum hydride (169 mg, 4.45 mmol) was suspended in Et_2O (5.4 mL) and cooled to 0-5 °C (ice bath cooling). A solution of aluminum chloride (197 mg, 1.48 mmol) in Et_2O (4.0 mL) was added and the mixture stirred for 15 minutes. A solution of the piperidine **9** (540 mg, 1.48 mmol) in Et_2O (4.4 mL) was added dropwise, the flask rinsed twice with Et_2O (1 mL) and the mixture was warmed to room temperature. After stirring for 2.5 hours, the reaction was quenched by slow addition of the resultant suspension to a heavily-stirred biphasic solution of Et_2O (30 mL), saturated aqueous sodium-potassium tartrate (30 mL) and 2.0 M aqueous NaOH (1.5 mL). After 1 hour of vigorous stirring, two clear phases were obtained and separated. The aqueous phase was extracted with CH_2Cl_2 (3x25 mL), organic phases were combined, dried over potassium carbonate, filtered and concentrated under reduced pressure which afforded 510 mg of a yellow oil. Flash chromatography of the oily residue with MeOH/CH_2Cl_2 (gradient from 1:99 to 10:90) afforded 196 mg (82%) of (*S*)-2-phenylpiperidine as a colorless oil.[7] R_f 0.31 (80:10:10 CH_2Cl_2:MeOH:AcOH); $[\alpha]_D^{20}$ = -30.3

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(7) (a) Vetuschi, C.; Ottolino, A.; Tortorella, V. *Gazz. Chim. Ital.* **1975**, *105*, 935. (b) Hattori, K.; Yamamoto, H. *Tetrahedron* **1993**, *49*, 1749. (c) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8952. (d) Poerwono, H.; Higashiyama, K.; Yamauchi, T.; Takahashi, H. *Heterocycles* **1997**, *46*, 385.

(*c* 0.27, MeOH), lit.[7d] –27.0 (*c* 0.43, MeOH), lit.[7a] (enantiomer) 35.3 (MeOH), lit.[7b] 27.6 (*c* 1.0, MeOH), lit.[7c] 49.5 (*c* 0.202, CH_2Cl_2). ^1H NMR (C_6D_6, 300 MHz) δ 7.41 (dtd, J = 8.2, 1.5, 0.5 Hz, 2H), 7.22 (tdd, J = 7.1, 2.7, 1.0 Hz, 2H), 7.13 (tt, J = 7.2, 2.3 Hz , 1H), 3.37 (dd, J = 10.8, 2.4 Hz, 1H), 2.92 (dddd, J = 11.2, 4.0, 2.4, 1.8 Hz, 1H), 2.47 (td, J = 11.3, 3.2 Hz, 1H), 1.72-1.62 (m, 2H), 1.58-1.38 (m, 3H), 1.29 (tt, J = 12.5, 4.0 Hz, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 147.0 (C), 128.9 (2CH), 127.5 (CH), 127.4 (2CH), 62.8 (CH), 48.0 (CH_2), 36.2 (CH_2), 26.4 (CH_2), 26.1 (CH_2); FTIR (neat) 3400-3100, 3062, 3026, 2932, 2851, 2788, 1602, 1491, 1453, 1441, 1325, 1109, 1020, 753, 699 cm^{-1}; LRMS (APCI) calcd. for $C_{11}H_{16}N$ $(M+H)^+$: 162.1, found 162.2.

From the same reaction mixture was isolated 214 mg *N*-benzyl-*N*-[(1*S*)-1-(methoxymethyl)-2-methylpropyl]amine[8] (*N*-benzyl-*O*-methylvalinol) (70%) as a colorless oil. R_f 0.51 (10:90 MeOH:CH_2Cl_2); $[\alpha]_D^{20}$ = -7.9 (*c* 2.0, MeOH), lit.[8a] -5.9 (*c* 1.0, MeOH); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.34-7.24 (m, 4H), 7.19 (tt, J = 6.8, 1.8 Hz, 1H), 3.76 (s, 2H), 3.41 (dd, J = 9.5, 4.1 Hz, 1H), 3.28 (dd, J = 9.3, 7.1 Hz, 1H), 3.28 (s, 3H), 2.54 (ddd, J = 6.9, 4.9, 4.2 Hz, 1H), 1.85 (hd, J = 6.9, 5.0 Hz, 1H), 1.58 (s, 1H), 0.91 (d, J = 7.6 Hz, 3H), 0.89 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 141.2 (C), 128.4 (2CH), 128.3 (2CH), 126.8 (CH), 72.8 (CH_2), 61.9 (CH), 59.0 (CH_3), 52.2 (CH), 28.9 (CH), 19.1 (CH_3), 18.3 (CH_3); FTIR (neat) 3332, 3064, 3028, 1604, 1495, 1454, 1116 cm^{-1}; LRMS (APCI) calcd. for $C_{13}H_{22}NO$ $(M+H)^+$: 208.2, found 208.3.

A solution of the (*S*)-2-phenylpiperidine (190 mg, 1.19 mmol) in ether (5.5 mL) was cooled at -20 °C, trifluoroacetic anhydride (0.34 mL, 0.50 g, 2.4 mmol) was added and the afforded solution was stirred for 30 minutes. The mixture was warmed to room temperature, stirred for 2 hours and then concentrated under reduced pressure, which afforded 331 mg of a yellow oil. Flash chromatography of the oily residue with EtOAc/hexane (gradient from 5:95 to 25:75) afforded 296 mg (96%) of **10** as a colorless oil. R_f 0.62 (25:75 EtOAc:hexane); $[\alpha]_D^{20}$ = -130 (*c* 3.26, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ (69:31 mixture of rotamers, * for the minor rotamer) 7.38 (t, J = 7.5 Hz, 2H + 2H*), 7.32-7.20 (m, 3H + 3H*), 5.90 (d, J = 4.3 Hz , 1H), 5.32 (br s, 1H*), 4.45 (d, J = 13.9 Hz, 1H*), 3,84 (d, J = 13.9 Hz, 1H), 3.10 (dt, J = 12.2, 2.8 Hz, 1H), 2.77 (t, J = 11.7 Hz, 1H*), 2.56 (d, J = 14.5 Hz, 1H*), 2.49 (d, J = 14.0 Hz, 1H), 2.02-1.90 (m, 1H + 1H*), 1.77-1.55 (m, 4H + 4H*); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (69:31 mixture of rotamers, * for the minor rotamer) 156.7 (q, J = 35.3 Hz, 1C +1C*), 137.4, (C), 137.2 (C*), 129.2 (2CH*), 129.1 (2CH), 127.5 (CH*), 127.3 (CH), 126.6 (2CH), 126.4

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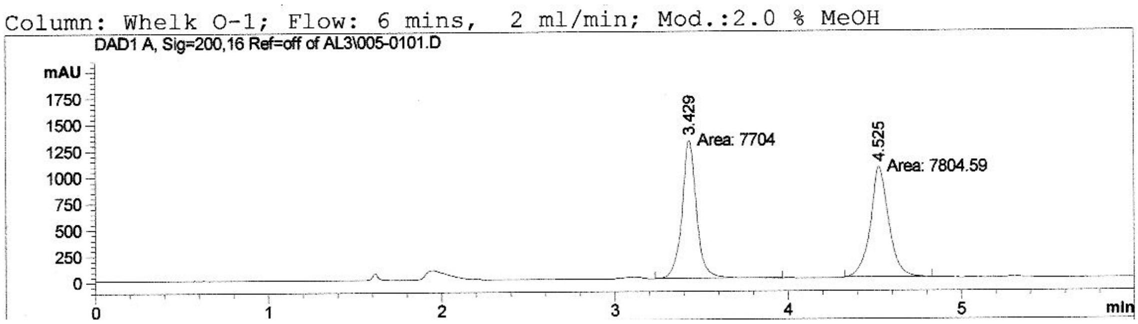
[8] (a) Ando, A.; Shioiri, T. *Tetrahedron* **1989**, *45*, 4969. (b) Yanada, R.; Negoro, N.; Okaniwa, M.; Miwa, Y.; Taga, T.; Yanada, K.; Fujita, T. *Synlett* **1999**, 537.

(2CH*), 117.0 (q, *J* = 286 Hz, 1C + 1C*), 55.9 (CH*), 52.9 (CH), 42.4 (CH_2), 39.9 (CH_2*), 28.5 (CH_2*), 27.0 (CH_2*), 26.3 (CH_2), 25.5 (CH_2*), 19.4 (CH_2), 19.3 (CH_2*); FTIR (neat) 3063, 1689, 1456, 1213, 1140, 1004 cm^{-1}; HRMS (MAB) calcd. for $C_{13}H_{14}F_3NO$ $(M)^+$: 257.1027, found 257.1025. Anal. calcd. for $C_{13}H_{14}F_3NO$: C, 60.70; H, 5.49; N, 5.44, found C, 60.55; H, 5.51; N, 5.24. Enantiomeric purity of **10** was 98.5% *e.e.* by SFC analysis (Whelk-01 column; 2% MeOH, 2 mL/min., 40 °C, 200 Bar, UV detector at 200 ηm): (–)-**10** T_r, 3.5 min, (+)-**10** T_r, 4.5 min.

Chromatogram of (–/+) 10



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Signal 1: DAD1 A, Sig=200,16 Ref=off

Peak     RT       Type    Width      Area          Height        Area
 #      [min]             [min]   [mAU*sec]        [mAU]           %
|----|---------|------|-------|------------|------------|-----------|
  1      3.429    MM     0.098    7704.00049   1309.91516     49.6757
  2      4.525    MM     0.124    7804.59180   1048.66687     50.3243

Totals :                         15508.59180   2358.58203
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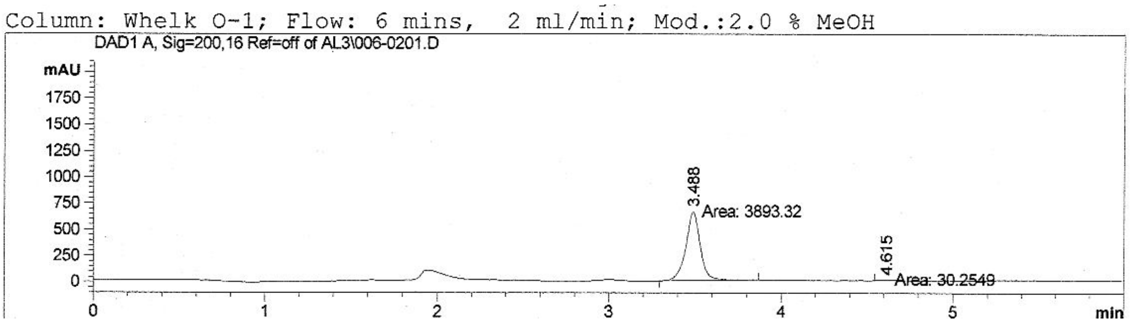
Chromatogram of enantioenriched (–) 10



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Signal 1: DAD1 A, Sig=200,16 Ref=off

Peak     RT       Type    Width      Area          Height        Area
 #      [min]             [min]   [mAU*sec]        [mAU]           %
|----|---------|------|-------|------------|------------|-----------|
  1      3.488    MM     0.099    3893.32031    656.53497     99.2289
  2      4.615    MM     0.084      30.25490      6.03427      0.7711

Totals :                          3923.57520    662.56921
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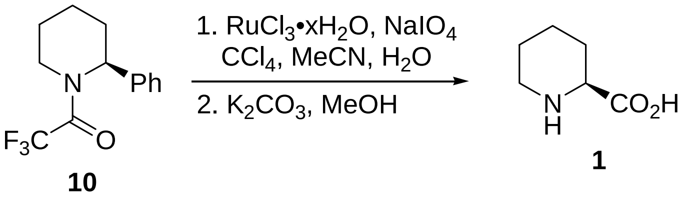
(2*S*)-Piperidine-2-carboxylic acid (L-pipecolic acid) (1).



Piperidine **10** (110 mg, 0.428 mmol) was diluted with CCl_4 (2.0 mL), acetonitrile (2.0 mL) and water (3.0 mL). To the biphasic mixture were added sequentially sodium periodate (1.42 g, 6.6 mmol) and ruthenium trichloride hydrate (5.0 mg, 0.021 mmol) under vigourous stirring. After 42 hours, dichloromethane was added, the mixture was filtrated over Celite®, the solids were rinsed with dichloromethane and the filtrate was dried over magnesium sulfate. The filtrate was concentrated under reduced pressure and the crude product showed 96% conversion by ^{1}H NMR analysis. The crude product was resubmitted to the oxidation conditions above (with 2.0 mL of CCl_4, 2.0 mL of acetonitrile and 3.0 mL of water) with 20% of the sodium periodate stoichiometry (248 mg, 1.3 mmol) and ruthenium trichloride hydrate (1.3 mg, 0.005 mmol) for 48 hours. The mixture was filtrated over Celite®, rinsed with dichloromethane and and the filtrate was dried over magnesium sulfate. The filtrate was concentrated under reduced pressure, the black residue was dissolved in ether (10 mL), filtrated over Celite®, and concentrated under reduced pressure, which afforded 100 mg of a black oil. The crude product showed complete conversion by ^{1}H NMR analysis. The crude product was dissolved in MeOH (5.2 mL), potassium carbonate (364 mg, 2.6 mmol) was added and the heterogeneous mixture was stirred for 48 hours. The mixture was concentrated under reduced pressure, dissolved in aqueous HCl (5 mL of a 1.2 M solution) and purified over ion exchange chromatography : Dowex 50WX8-200, 100-200 mesh (9.5 g), was pre-washed with water (30 mL), then 1.2 M HCl (30 mL); the HCl solution of the crude product was eluted with water (30 mL), 1.5 % NH_4OH (30 mL), 3% NH_4OH (30 mL) and 5% NH_4OH (30 mL). The ninhydrin containing fractions were evaporated under reduced pressure to afforde 41 mg of a yellow solid. The solid was diluted with water (20 mL), carbon black (1 g) was added and the mixture was refluxed for 15 minutes. The carbon black was removed by filtration over filter paper and the filtrate was concentrated under reduced pressure, which afforded 40 mg (72%) of **1** as a white solid. Mp >250°C, lit. 272 °C; $[\alpha]_D^{20}$ = -25.6 (*c* 1.2, H_2O), lit. -26.4 (*c* 1.0, H_2O), lit.[9] -25.5 (*c* 1.3, H_2O), lit.[10] -26.8 (*c* 0.5, H_2O). ^{1}H NMR (D_2O,

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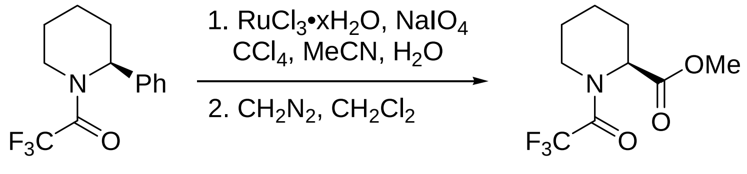
[9] Agami, C.; Kadouri-Puchot, C.; Kizirian, J. C. *Synth. Commun.* **2000**, *30*, 2565.
[10] Sánchez-Sancho, F. S.; Herradón, B. *Tetrahedron: Asymmetry* **1998**, *9*, 1951.

400 MHz) δ 3.52 (dd, *J* = 11.5, 3.2 Hz , 1H), 3.35 (br d, *J* = 12.7 Hz, 1H), 2.94 (tt, *J* = 12.2, 3.0 Hz, 1H), 2.16 (br dq, *J* = 13.8, 2.6 Hz, 1H), 1.86-1.75 (m, 2H), 1.66-1.46 (m, 3H).

(2*S*)-Methyl-1-(trifluoroacetyl)piperidine-2-carboxylate (11a).

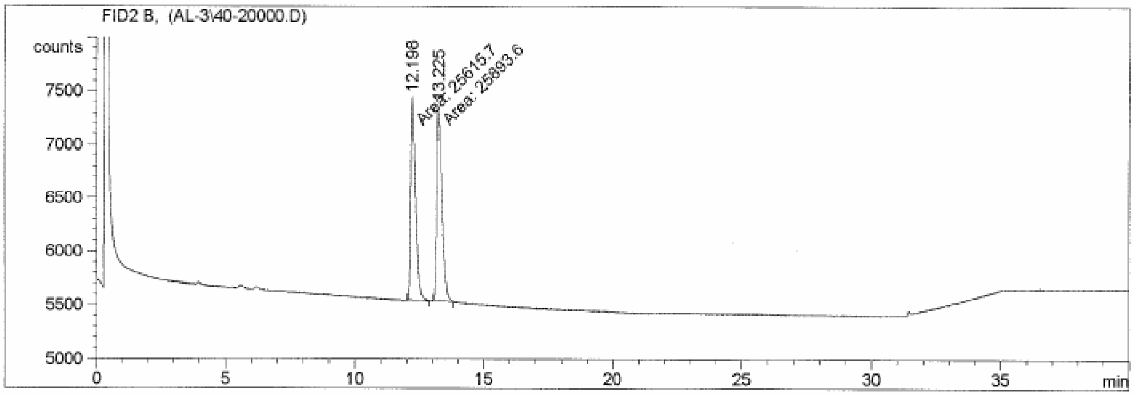


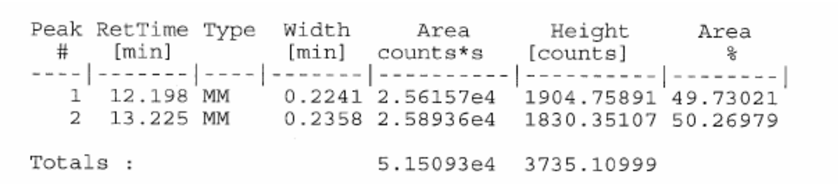
10 **11a**

Piperidine **10** (135 mg, 0.517 mmol) was diluted with CCl_4 (2.4 mL), acetonitrile (2.4 mL) and water (3.5 mL). To the biphasic mixture were added sequentially sodium periodate (1.66 g, 7.8 mmol) and ruthenium trichloride hydrate (6.1 mg, 0.026 mmol) upon stirring. After 22 hours, dichloromethane was added (10 mL), the mixture was filtrated over Celite®, the solids were rinsed with dichloromethane and the filtrate was dried over magnesium sulfate. The filtrate was concentrated under reduced pressure and the crude product showed 30% conversion by ^{1}H NMR analysis. The crude product was resubmitted to the same oxidation conditions as above for 48 hours and the mixture was filtrated over Celite®, the solids were rinsed with dichloromethane and the filtrate was dried over magnesium sulfate. The filtrate was concentrated under reduced pressure, the black residue was dissolved in ether (10 mL), charcoal (1 g) was added, followed by Celite® (3 g). The mixture was filtrated over Celite®, diazomethane (2.8 mL of a 0.2 M solution in dichloromethane, 1.2 mmol) was added, the yellow solution was stirred for 2 hours and then concentrated under reduced pressure, which afforded 96 mg of a pink oil. The crude product showed complete conversion by ^{1}H NMR analysis. Flash chromatography of the oily residue with EtOAc/hexane (gradient from 0:100 to 25:75) afforded 76 mg (62%) of **11a** as a colorless oil. R_f 0.36 (25:75 EtOAc:hexane); $[\alpha]_D^{20}$ = -51.1 (*c* 1.1, C_6H_6); ^{1}H NMR (C_6D_6, 400 MHz) *δ* (79:21 mixture of rotamers, * for the minor rotamer) 5.20 (d, *J* = 4.9 Hz , 1H), 4.50 (d, *J* = 4.3 Hz, 1H*), 4.39 (br d, *J* = 13.6 Hz, 1H*), 3,60 (br d, *J* = 13.6 Hz, 1H), 3.17 (s, 3H + 3H*), 3.01 (td, *J* = 13.0, 3.4 Hz, 1H), 2.69 (td, *J* = 13.4, 3.1 Hz, 1H*), 1.95-1.85 (m, 1H + 1H*), 1.12-0.85 (m, 5H + 5H*); ^{13}C NMR (C_6D_6, 75 MHz) *δ* (79:21 mixture of rotamers, * for the minor rotamer) 170.3 (C), 170.2 (C*), 157.3 (q, *J* = 35.8 Hz, 1C +1C*), 117.7 (q, *J* = 288 Hz, 1C + 1C*), 56.5 (CH*), 53.9 (CH), 52.4 (CH_3*), 52.3 (CH_3), 43.9 (q, *J* = 3.7 Hz, 1CH_2), 41.5 (CH_2*), 27.4 (CH_2*), 26.5 (CH_2), 25.1 (CH_2), 24.5 (CH_2*), 21.0 (CH_2), 20.5 (CH_2*); FTIR (neat) 2955, 1746, 1694, 1450, 1210, 1141, 1015 cm^{-1}; HRMS (ES) calcd. for $C_9H_{13}F_3NO_3$ $(M + H)^+$: 240.0842, found 240.0841. Enantiomeric purity of **11a** was 98.5% ee by chiral GC analysis (Chiraldex

G-TA; 25 psi (H_2); split 1/100; 80 °C for 1 minute, gradient 2 °C/minute up to 120 °C, kept 10 minutes): (–)-**11a** T_r, 12.2 min, (+)-**11a** T_r, 13.2 min.

Chromatogram of (+/–) 11a





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   2  13.225 MM    0.2358 2.58936e4  1830.35107 50.26979

Totals :                  5.15093e4  3735.10999
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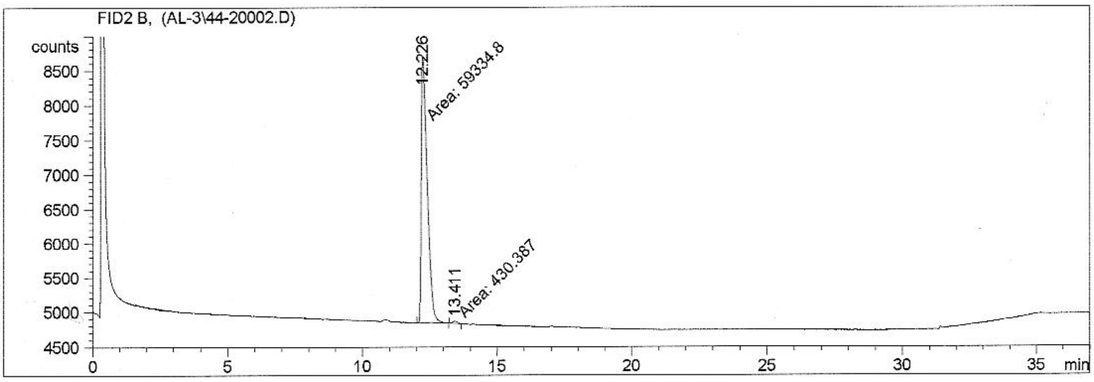
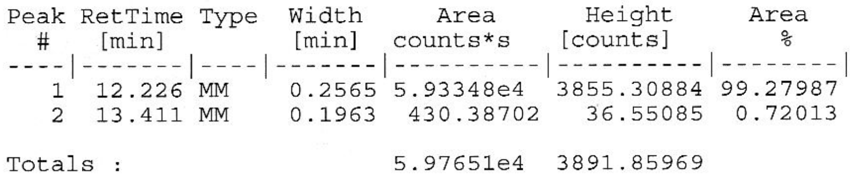
Chromatogram of enantioenriched (–) 11a





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Peak RetTime Type  Width    Area      Height     Area
  #   [min]        [min]  counts*s   [counts]     %
----|-------|----|-------|----------|----------|--------|
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   2  13.411 MM    0.1963  430.38702   36.55085  0.72013

Totals :                  5.97651e4  3891.85969
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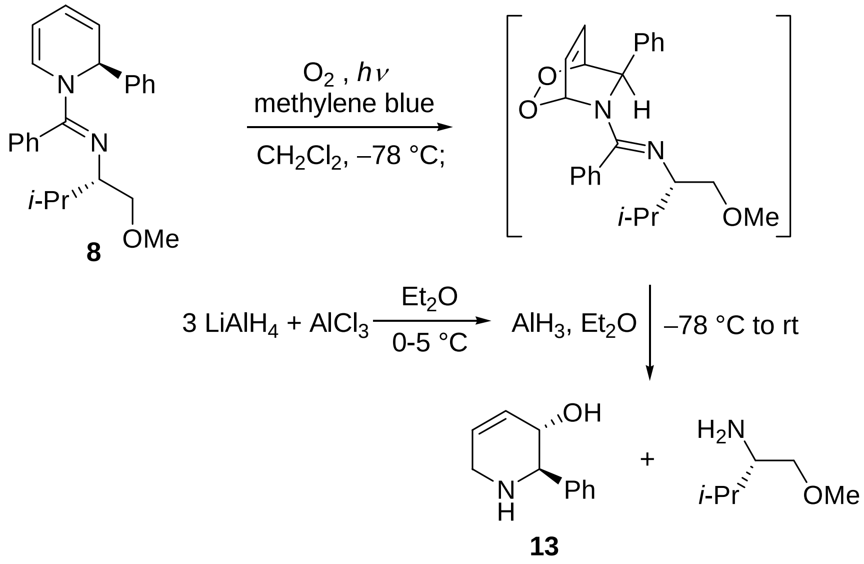
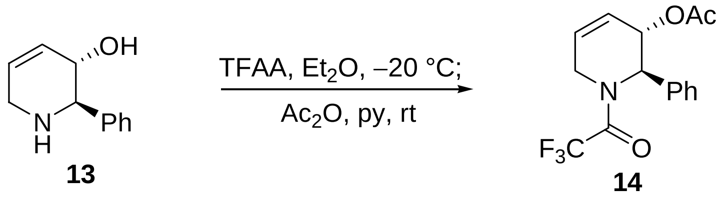
(2*R*,3*S*)-2-Phenyl-1,2,3,6-tetrahydropyridin-3-ol (13).



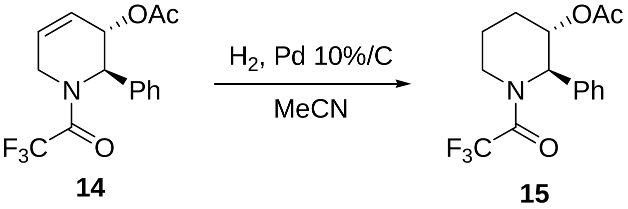
Methylene blue (26 mg, 0.070 mmol) and dihydropyridine **8** (143 mg, 0.398 mmol) were dissolved in dichloromethane (58 mL) and the blue solution was cooled at -78°C. Oxygen was bubbled through the solution with a needle and the solution was irradiated with a sunlamp (OSRAM Ultra-Vitalux 300W, 230V) placed at ca. 15 cm of the flask. The solution was irradiated for one hour with a constant oxygen flow. Completion of the hetero-Diels-Alder reaction was monitored by TLC. In a separate flask, lithium aluminum hydride (181 mg, 4.8 mmol) was suspended in ether (5.8 mL), cooled to 0-5 °C by means of an ice-water bath, followed by slow addition of aluminum chloride (4.3 mL of a 0.37 M solution in ether, 1.6 mmol) and the light grey suspension was stirred for 45 minutes. The freshly prepared AlH_3 suspension was cooled to –78 °C then the solution of endoperoxide cycloadduct at –78 °C was added to the alane suspension via a canula. The resultant suspension was then stirred at –78 °C for 12 hours, warmed to room temperature and stirred for 2 hours. The reaction was quenched by slow addition of the suspension to a well stirred biphasic solution of ether (50 mL), saturated aqueous sodium-potassium tartrate (50 mL) and 2.0 M aqueous sodium hydroxide (2 mL). After 1 hour of vigorous stirring, two clear phases were obtained and separated. The aqueous phase was extracted with ether, organic phases were combined and dried over potassium carbonate. Activated charcoal (1 g) was added to the blue solution, the afforded black mixture was stirred 5 minutes and Celite® (20 g) was added to the mixture. The suspension was filtered through Celite®, the solids were rinsed with dichloromethane and the filtrate was concentrated under reduced pressure to afford 177 mg of a yellow solid. Flash chromatography of the residue was performed using MeOH/CH$_2$Cl$_2$ (gradient 2:98-10:90) which afforded 43 mg of **13** (61%) as a white solid: Mp 139-140 °C; R_f 0.22 (10:90 MeOH:CH$_2$Cl$_2$); $[\alpha]_D^{20}$ = 58.7 (c 1.90, MeOH); ^{1}H NMR (CD$_3$OD, 400 MHz) δ 7.44 (br d, J = 7.1 Hz, 2H), 7.37 (td, J = 7.1, 1.6 Hz, 2H), 7.31 (tt, J = 7.2, 1.7 Hz, 1H), 5.91 (ddt, J = 10.2, 4.0, 1.8 Hz, 1H), 5.84 (dq, J = 10.2, 1.8 Hz, 1H), 4.24 (ddq, J = 8.6, 3.5, 2.0 Hz, 1H), 3.51 (ddt, J = 17.3, 3.5, 2.5 Hz, 1H), 3.49 (d, J = 8.5 Hz, 1H), 3.34 (ddt, J = 17.4, 3.6, 1.8 Hz, 1H); ^{13}C NMR (CD$_3$OD, 75 MHz) δ 143.1 (C), 132.0 (CH), 129.6 (2CH), 129.2 (2CH), 128.8 (CH), 128.5 (CH), 71.1 (CH), 66.2 (CH), 46.5 (CH$_2$); FTIR (neat) 3600-3000, 3584, 3269, 3091, 3030, 2898, 1649, 1586, 1491, 1288, 1088, 1044, 757, 702 cm^{-1}; LRMS (APCI) calcd for C$_{11}$H$_{14}$NO (M + H)$^+$: 176.1, found 176.1; Anal. calcd for C$_{11}$H$_{13}$NO: C, 75.40; H, 7.48; N, 7.99, found C, 75.08; H, 7.73; N, 7.82. From the same reaction mixture was isolated 55 mg (66%) of *N*-benzyl-*N*-[(1*S*)-1-(methoxymethyl)-2-methylpropyl]amine (*N*-benzyl-*O*-methylvalinol).

(2*R*,3*S*)-1-Trifluoroacetyl-2-phenyl-1,2,3,6-tetrahydropyridin-3-yl acetate (14).



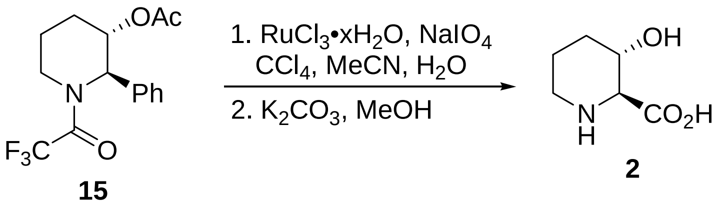
A suspension of the piperidine **13** (38 mg, 0.22 mmol) in ether (1.0 mL) was cooled to –20 °C, trifluoroacetic anhydride (0.12 mL, 0.18 g, 0.87 mmol) was added and the resulting solution was stirred for 30 minutes. The mixture was warmed to room temperature, stirred for 3 hours and the solution was concentrated under reduced pressure. The residue was dissolved in tetrahydrofuran (3.1 mL), pyridine (0.88 mL), sodium acetate (90 mg, 1.1 mmol), and acetic anhydride (0.41 mL, 4.3 mmol) were added. The mixture was stirred for 14 hours, cooled to 0-5 °C with an ice bath and saturated aqueous sodium bicarbonate (10 mL) was added. After stirring for 30 minutes, hexane (10 mL) was added, the mixture was transferred to a separatory funnel and the phases were separated. The aqueous phase was extracted using dichloromethane(3x10 mL), the combined organic phase was dried over magnesium sulfate, filtered and concentrated under reduced pressure, which afforded 78 mg of a yellow oil. Flash chromatography of the oily residue with EtOAc/hexane (gradient from 0:100 to 15:85) afforded 60 mg (89%) of **14** as a colorless oil: R_f 0.35 (25:75 EtOAc:hexane); $[\alpha]_D^{20}$ = +85.6 (*c* 5.03, C_6H_6); ^{1}H NMR (C_6D_6, 400 MHz) δ (51:49 mixture of rotamers, * for the minor rotamer) 7.09-7.06 (m, 1H + 1H*), 7.01-6.98 (m, 4H + 4H*), 6.26 (s, 1H), 5.81 (ddd, *J* = 9.9, 5.7, 2.7 Hz, 1H), 5.61-5.57 (m, 1H + 1H*), 5.52 (br d, *J* = 5.8 Hz, 1H*), 5.34 (s, 1H*), 5.18 (ddd, *J* = 10.0, 3.9, 2.4 Hz, 1H*), 5.11 (ddd, *J* = 10.1, 4.4, 2.0 Hz, 1H), 4.64 (ddd, *J* = 19.8, 3.7, 2.5 Hz, 1*H), 3.82 (br d, *J* = 18.7 Hz, 1H), 3.06 (ddd, *J* = 18.9, 4.1, 2.1 Hz, 1H), 3.02 (br d, *J* = 20.0 Hz, 1H*), 1.65 (s, 3H*), 1.60 (s, 3H); ^{13}C NMR (C_6D_6, 75 MHz) δ (51:49 mixture of rotamers, * for the minor rotamer) 170.3 (C + C*), 157.2 (q, *J* = 35.9 Hz, 1C + C*), 135.8 (C + C*), 130.4 (CH), 129.4 (2C + 2C*), 129.2 (CH*) 128.7 (CH + CH*), 127.8 (CH + CH*), 126.9 (CH + CH*), 123.1 (CH), 121.4 (CH*), 117.7 (q, *J* = 288 Hz, 1C*), 117.6 (q, *J* = 288 Hz, 1C), 67.2 (CH*), 66.9 (CH), 58.6 (CH*), 55.7 (CH), 41.4 (q, *J* = 4.2 Hz, 1CH_2), 40.6 (CH_2*), 20.7 (CH_3), 20.6 (CH_3*); FTIR (neat) 3063, 3035, 1739, 1694, 1667, 1452, 1234, 1203, 1141, 1023 cm^{-1}; HRMS (ES) calcd. for $C_{15}H_{14}F_3NO_3$ $(M+Ag)^+$: 419.9971, found 419.9963. Anal. calcd. for $C_{15}H_{14}F_3NO_3$: C, 57.51; H, 4.50; N, 4.47, found C, 57.24; H, 4.36; N, 4.50.

(2*R*,3*S*)-2-Phenyl-1-(trifluoroacetyl)piperidin-3-yl acetate (15).



To a solution of the tetrahydropyridine **14** (47 mg, 0.15 mmol) in acetonitrile (1.5 mL) was added palladium catalyst (4.3 mg of Pd/C (10 wt% Pd), 0.0041 mmol Pd). The mixture (purged three times with water vacuum then hydrogen atmosphere) was stirred under hydrogen atmosphere (1 atm) for 15 h at room temperature. The reaction mixture was then filtered through Celite®, the solids were rinsed with dichloromethane and the filtrate was concentrated under reduced pressure, which afforded 48 mg of a colorless oil. Flash chromatography of the oily residue with EtOAc/hexane (gradient from 0:100 to 15:85) afforded 44 mg (93%) of **15** as a colorless oil. R_f 0.35 (25:75 EtOAc:hexane); $[\alpha]_D^{20}$ = -42.8 (*c* 0.975, C_6H_6); ^{1}H NMR (C_6D_6, 400 MHz) δ (55:45 mixture of rotamers, * for the minor rotamer) 7.06-6.88 (m, 5H + 5H*), 6.14 (s, 1H), 5.53 (q, *J* = 2.6 Hz, 1H), 5.43 (q, *J* = 2.5 Hz, 1H*), 5.26 (s, 1H*), 4.38 (br d, *J* = 13.4 Hz, 1H*), 3.51 (d, *J* = 14.2 Hz, 1H), 2.62 (td, *J* = 14.0, 2.6 Hz, 1H), 2.36 (td, *J* = 13.4, 2.7 Hz, 1H*), 1.67 (s, 3H*), 1.65 (s, 3H), 1.64 (qt, *J* = 13.4, 4.2 Hz, 1H + 1H*), 1.45 (br d, *J* = 14.9 Hz, 1H), 1.35 (br d, *J* = 14.1 Hz, 1H*), 1.23 (tdd, *J* = 13.9, 4.4, 2.7 Hz, 1H), 1.08 (tdd, *J* = 14.0, 4.3, 2.7 Hz, 1H*), 0.78 (br d, *J* = 12.4 Hz, 1H*), 0.74 (br d, *J* = 11.2 Hz, 1H); ^{13}C NMR (C_6D_6, 75 MHz) δ (55:45 mixture of rotamers, * for the minor rotamer) 170.1 (C*), 170.0 (C), 157.8 (q, *J* = 35.6 Hz, 1C + 1C*), 135.7 (C), 135.6 (C*), 129.7-126.6 (5CH + 5CH*), 117.9 (q, *J* = 289 Hz, 1C + 1C*), 69.4 (CH*), 69.1 (CH), 59.5 (CH*), 56.7 (CH), 42.1 (q, *J* = 3.6 Hz, CH_2*), 39.6 (CH_2), 24.3 (CH_2), 24.0 (CH_2*), 21.1 (CH_2), 20.8 (CH_3), 20.7 (CH_3*), 19.9 (CH_2*); FTIR (neat) 3065, 2960, 1739, 1692, 1452, 1238, 1143, 1001 cm^{-1}; HRMS (ES) calcd. for $C_{15}H_{17}F_3NO_3$ $(M+H)^+$: 316.1155, found 316.1145. Anal. calcd. for $C_{15}H_{16}F_3NO_3$: C, 57.14; H, 5,12; N, 4.44, found C, 57.55; H, 5.29; N, 4.48.

(2*S*,3*S*)-3-hydroxypiperidine-2-carboxylic acid (2).



Piperidine **15** (71 mg, 0.23 mmol) was diluted with CCl_4 (1.0 mL), acetonitrile (1.0 mL) and water (1.5 mL). To the biphasic mixture were added sequentially sodium periodate (724 mg, 3.4 mmol) and ruthenium trichloride hydrate (2.6 mg, 0.011 mmol) under vigourous stirring. After 119 hours, dichloromethane was added, the mixture was filtrated over Celite®, the solids were rinsed with dichloromethane and the filtrate was dried over magnesium sulfate. The filtrate was concentrated under reduced pressure and the crude product showed 92% conversion by ^{1}H NMR analysis. The crude product was resubmitted to the oxidation conditions above (with 1.0 mL of CCl_4, 1.0 mL of acetonitrile and 1.5 mL of water) with 50% of the sodium periodate stoichiometry (362 mg, 1.7 mmol) and ruthenium trichloride hydrate (1.3 mg, 0.005 mmol) for 96 hours and the mixture was filtrated over Celite®. The solids were rinsed with dichloromethane, the filtrate was dried over magnesium sulfate and concentrated under reduced pressure. The crude product was dissolved in methanol (2.5 mL), potassium carbonate (188 mg, 1.36 mmol) was added and the heterogeneous mixture was stirred for 48 hours. The mixture was diluted with methanol (10 mL), activated charcoal (1 g) was added and the black suspension was heated to reflux 15 minutes. The suspension was filtrated over Celite, the solids were rinsed with methanol and the filtrate was concentrated under reduced pressure. The residue was dissolved in aqueous HCl (5 mL of a 1.2 M solution) and purified over ion exchange chromatography : Dowex 50WX8-200, 100-200 mesh (9.5 g) was pre-washed with water (30 mL), then 1.2 M HCl (30 mL); the HCl solution of the crude product was eluted with water (30 mL), 1.5 % NH_4OH (30 mL), 3% NH_4OH (30 mL) and 5% NH_4OH (30 mL). The ninhydrin containing fractions were evaporated under reduced pressure to afford 20 mg (60%) of **2** as a white solid: M_p 230 °C (dec), lit.[11] 232-236 °C, lit.[12] 232 °C (dec), lit.[13] 230-238 °C (dec); $[\alpha]_D^{20} = 13$ (*c* 0.49, HCl 10% aq.), lit. 13.5 (*c*

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[11] Kumar,P.; Bodas, M. S. *J. Org. Chem.* **2005**, *70*, 360.

[12] Haddad, M.; Larchevêque, M. *Tetrahedron Lett.* **2001**, *42*, 5223.

0.2, HCl 10% aq.), lit. 12.9 (*c* 0.23, HCl 10% aq.), lit.[14] 15 (*c* 0.5, HCl 10% aq.), lit. (enantiomer of **2**) -13 (*c* 0.45, HCl 10% aq.). ^{1}H RMN (D_2O, 400 MHz)[15] δ 4.12 (ddd, J = 10.4, 7.3, 3.0 Hz, 1H), 3.58 (d, *J* = 7.0 Hz, 1H), 3.36-3.27 (m, 1H), 3.10-3.03 (m, 1H), 2.04-1.85 (m, 2H), 1.75-1.60 (m, 2H).

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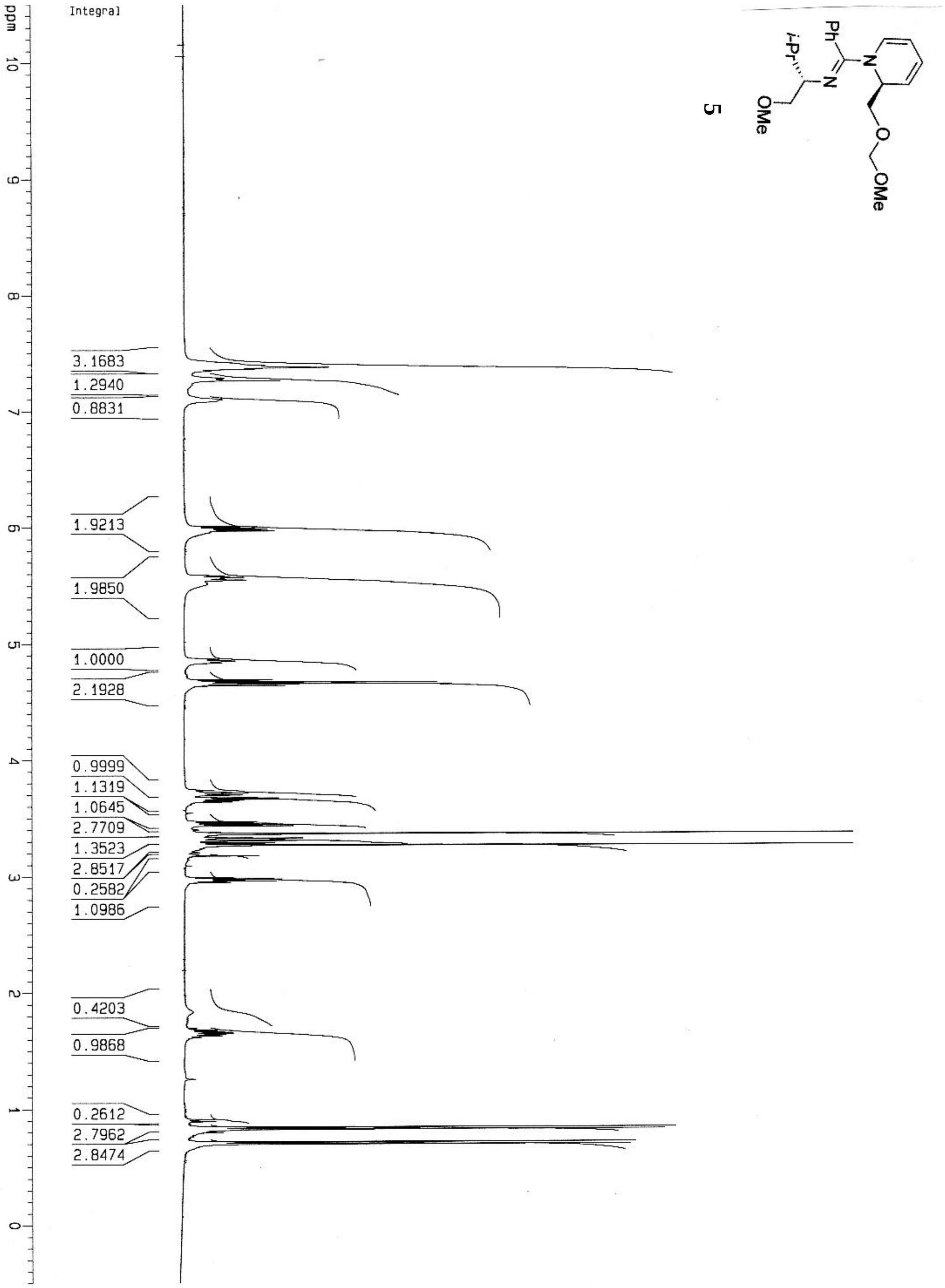
(13) Battistini, L.; Zanardi, F.; Rassu, G.; Spanu, P.; Pelosi, G.; Fava, G. G.; Ferrari, M. B.; Casiraghi, G. *Tetrahedron: Asymmetry* **1997**, *8*, 2975.

(14) Greck, C.; Ferreira, F.; Genêt, J. P. *Tetrahedron Lett.* **1996**, *37*, 2031.

(15) We found that diffecrent chemical shifts description are reported for most precedent syntheses of **2**. Ours correlate to thoses: (a) Roemmele, R. C.; Rapoport, H. *J. Org. Chem.* **1989**, *54*, 1866. (b) Ref. 13.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1.0000
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0.9999
1.1319
1.0645
2.7709
1.3523
2.8517
0.2582
1.0986
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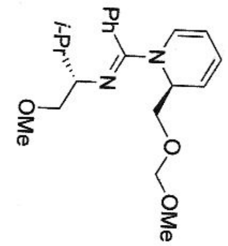
Ph
N
N
i-Pr
OMe
O
OMe
5



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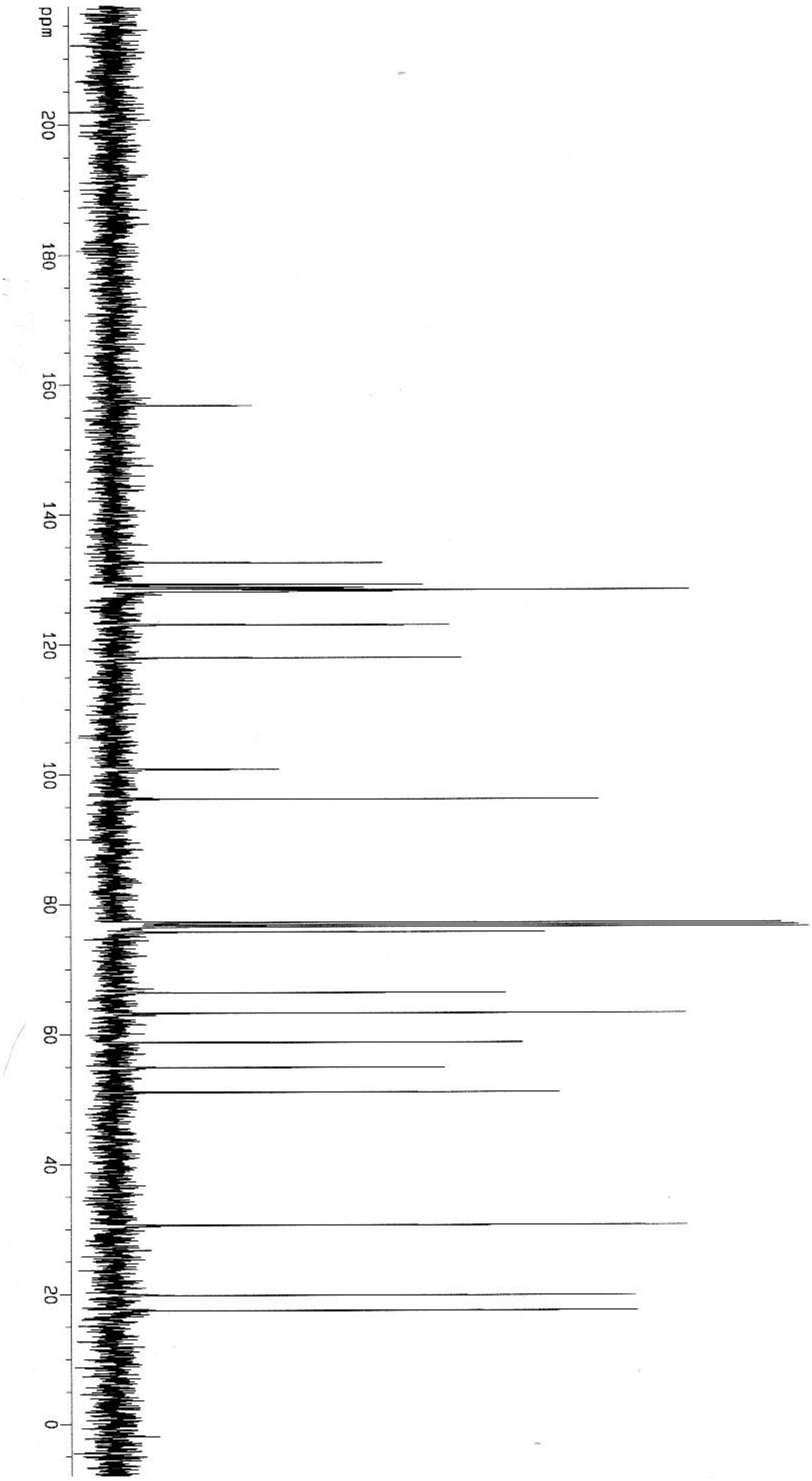

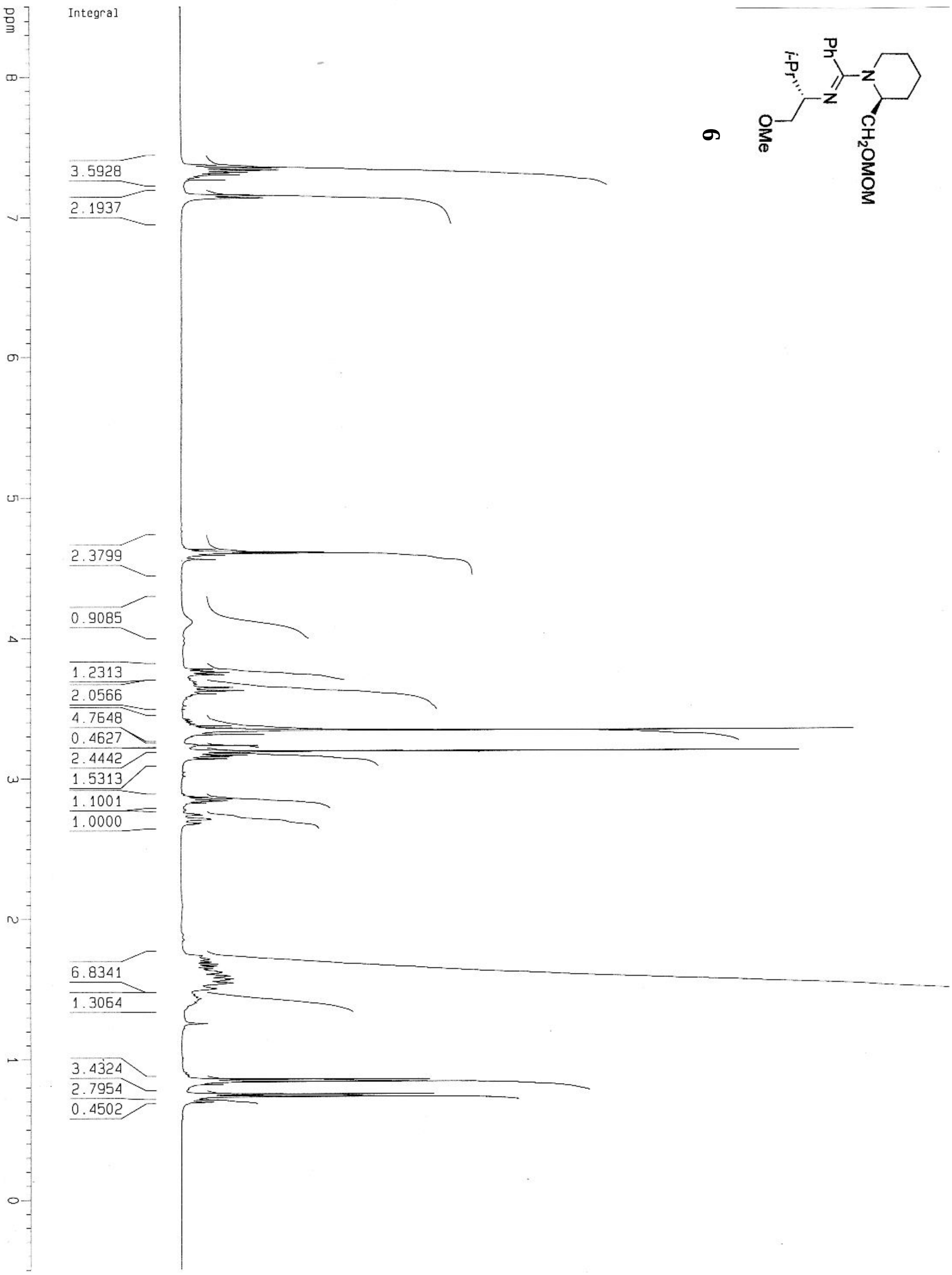
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4.7648
0.4627
2.4442
1.5313
1.1001
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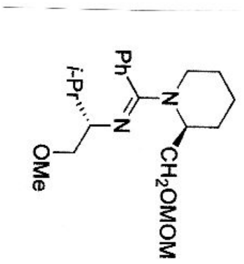
Ph
N
N
CH2OMOM
i-Pr
OMe

6



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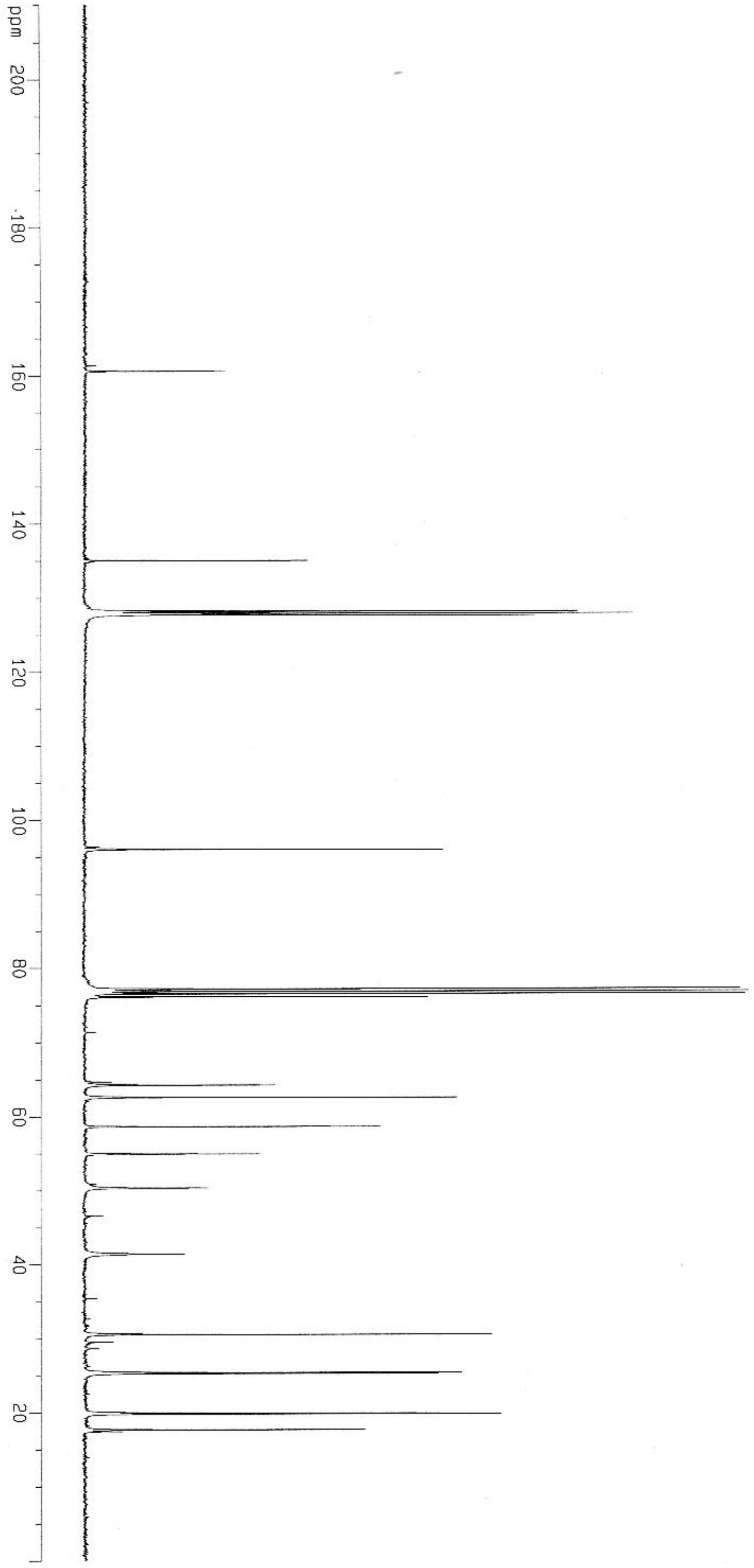

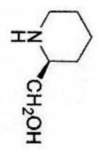
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H
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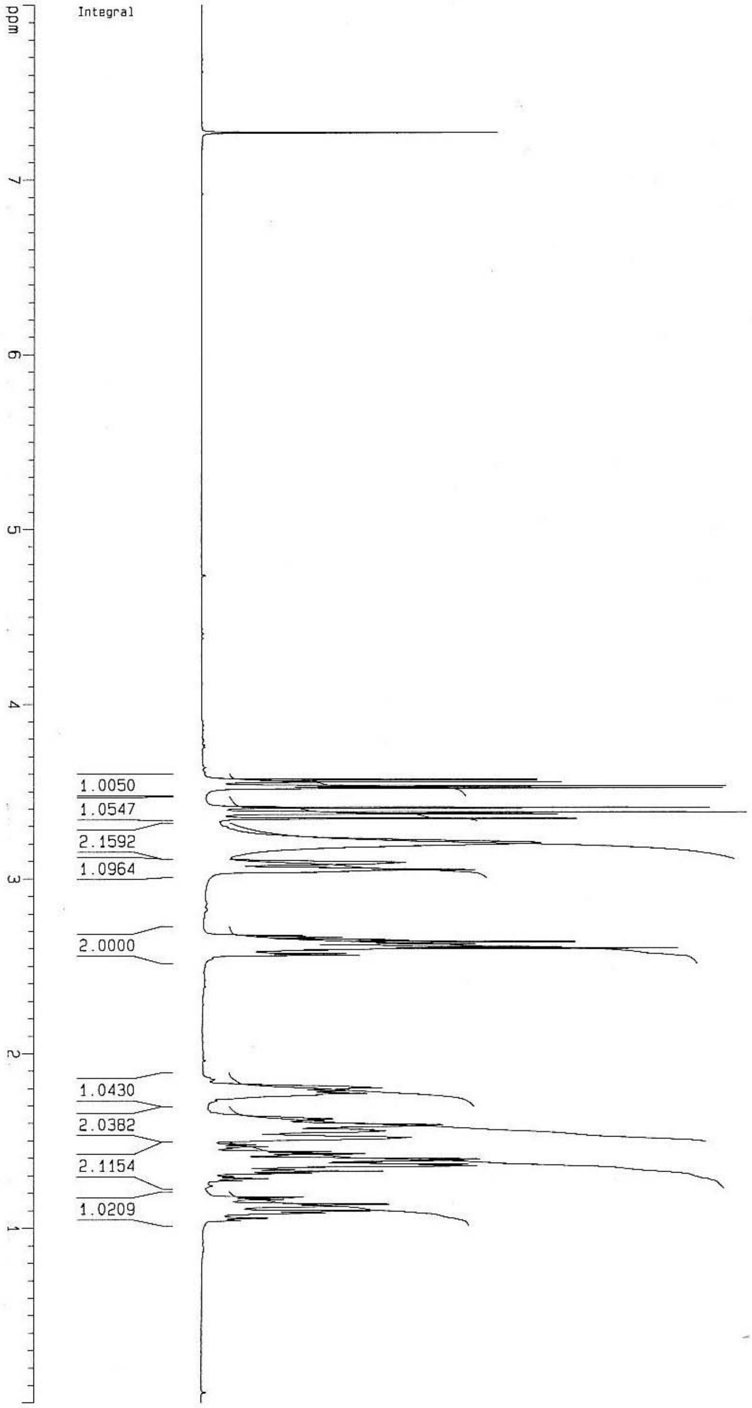
7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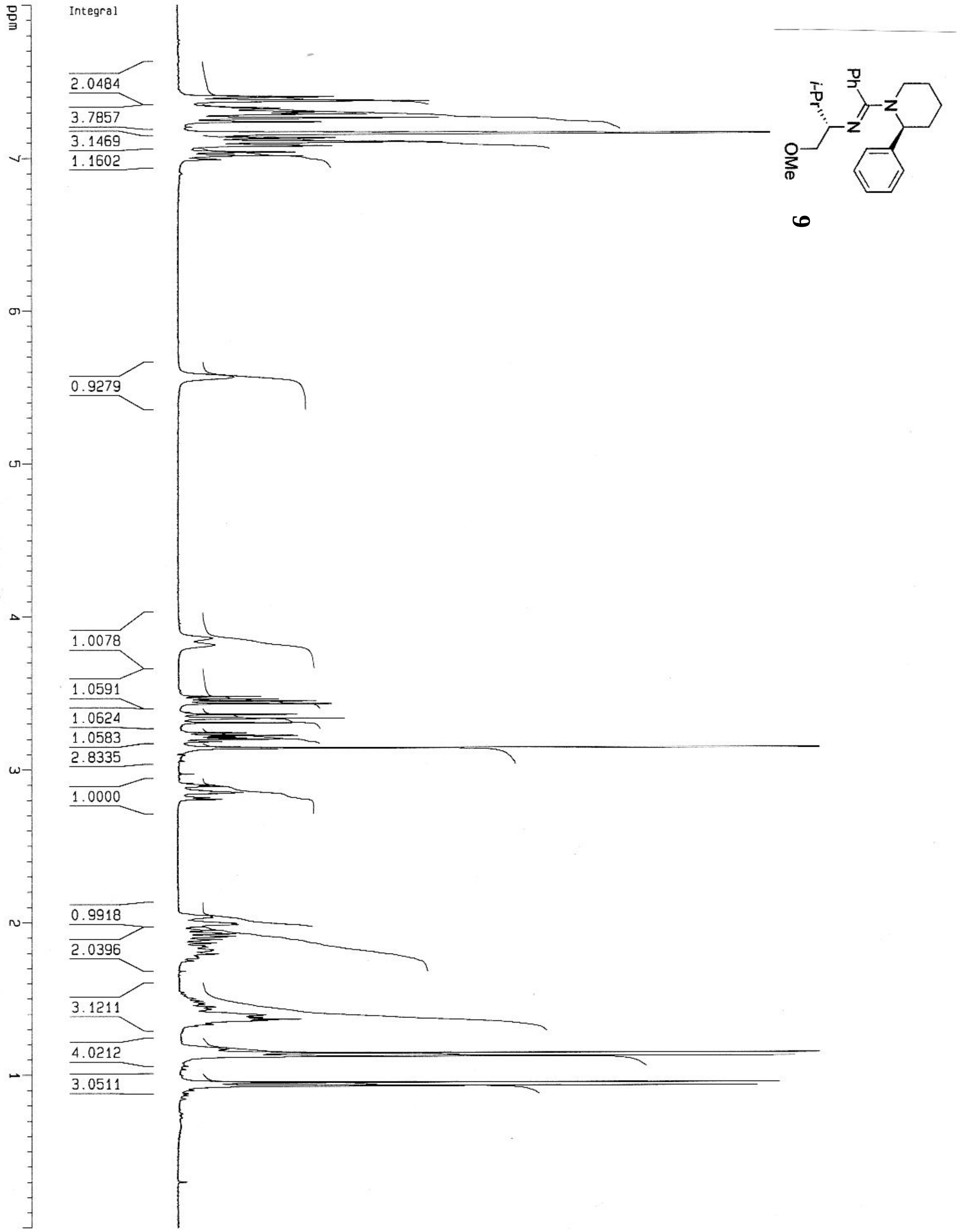
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1.0000
0.9918
2.0396
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5
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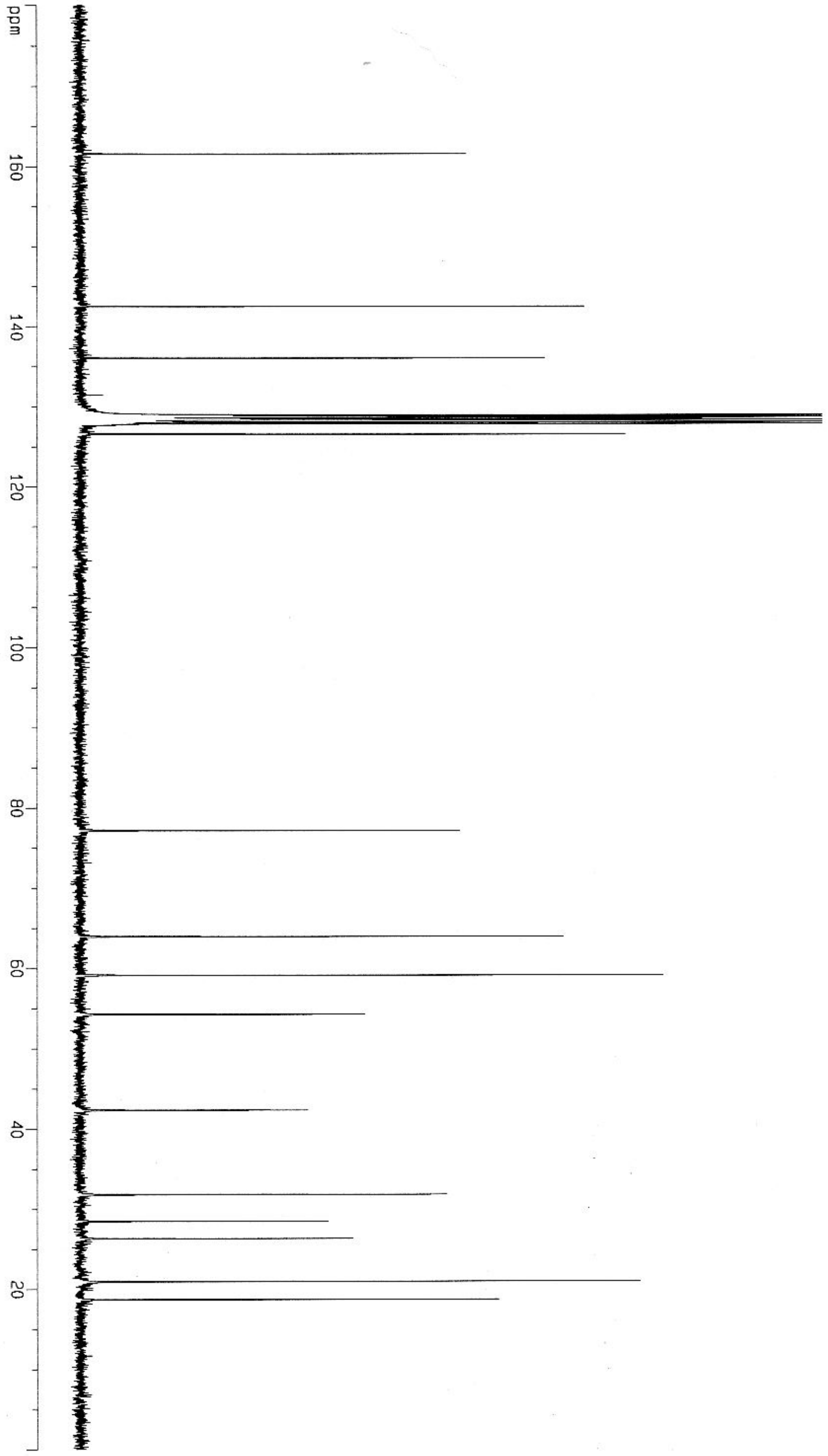
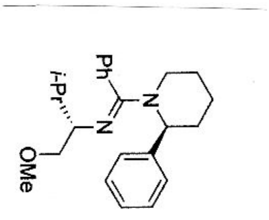
3
2
1
Ph
N
N
i-Pr
OMe

9





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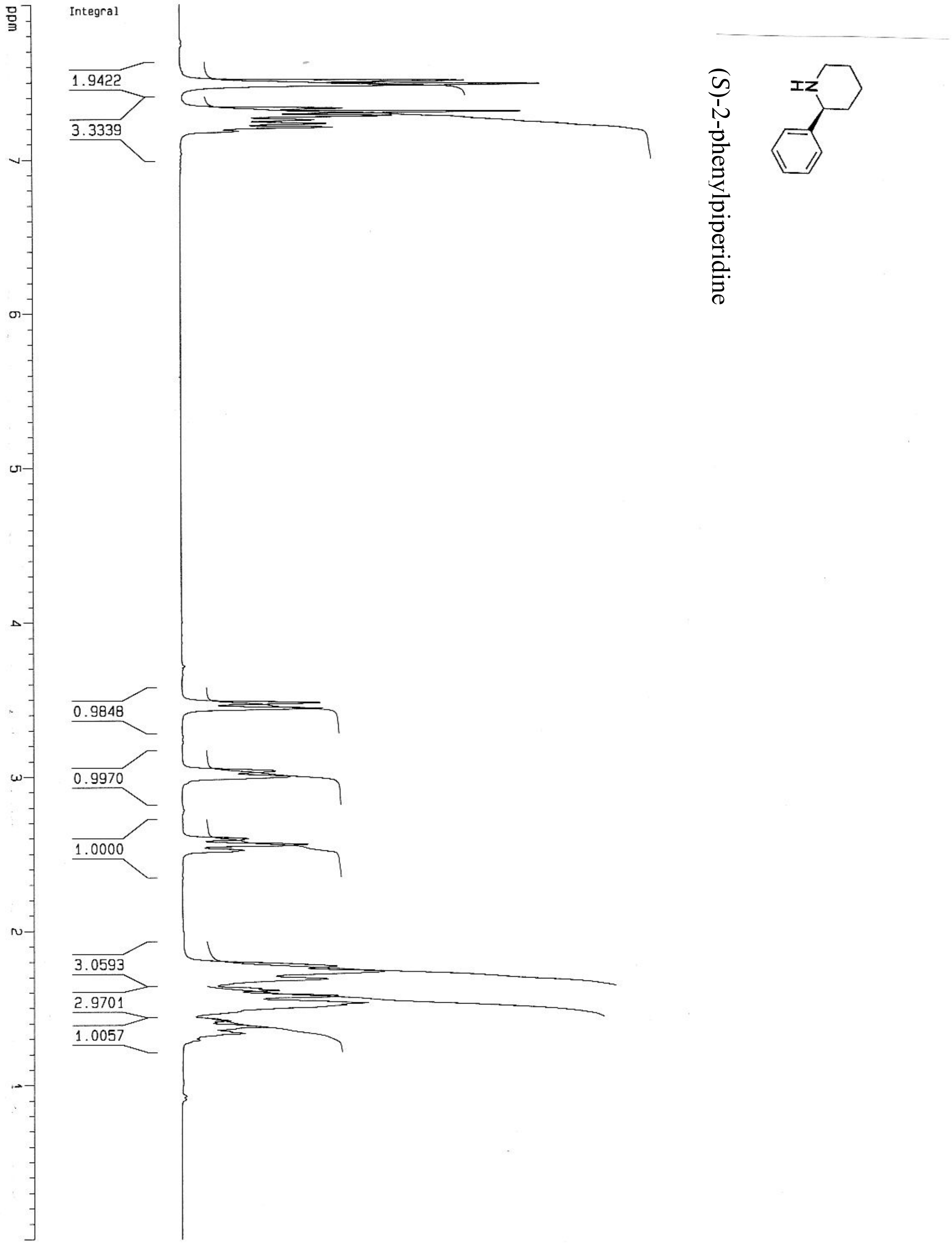

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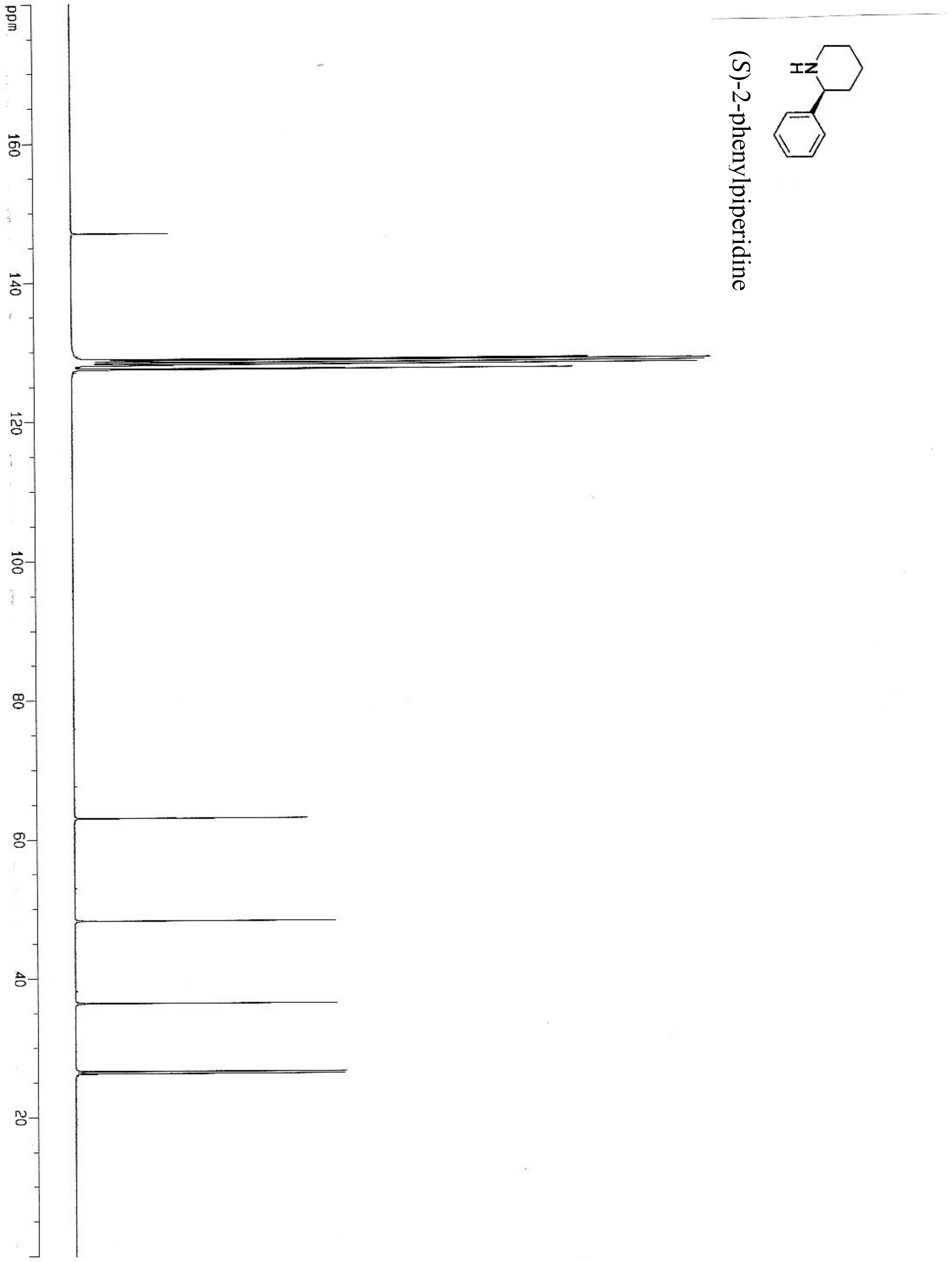
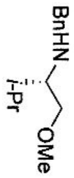


(S)-2-phenylpiperidine



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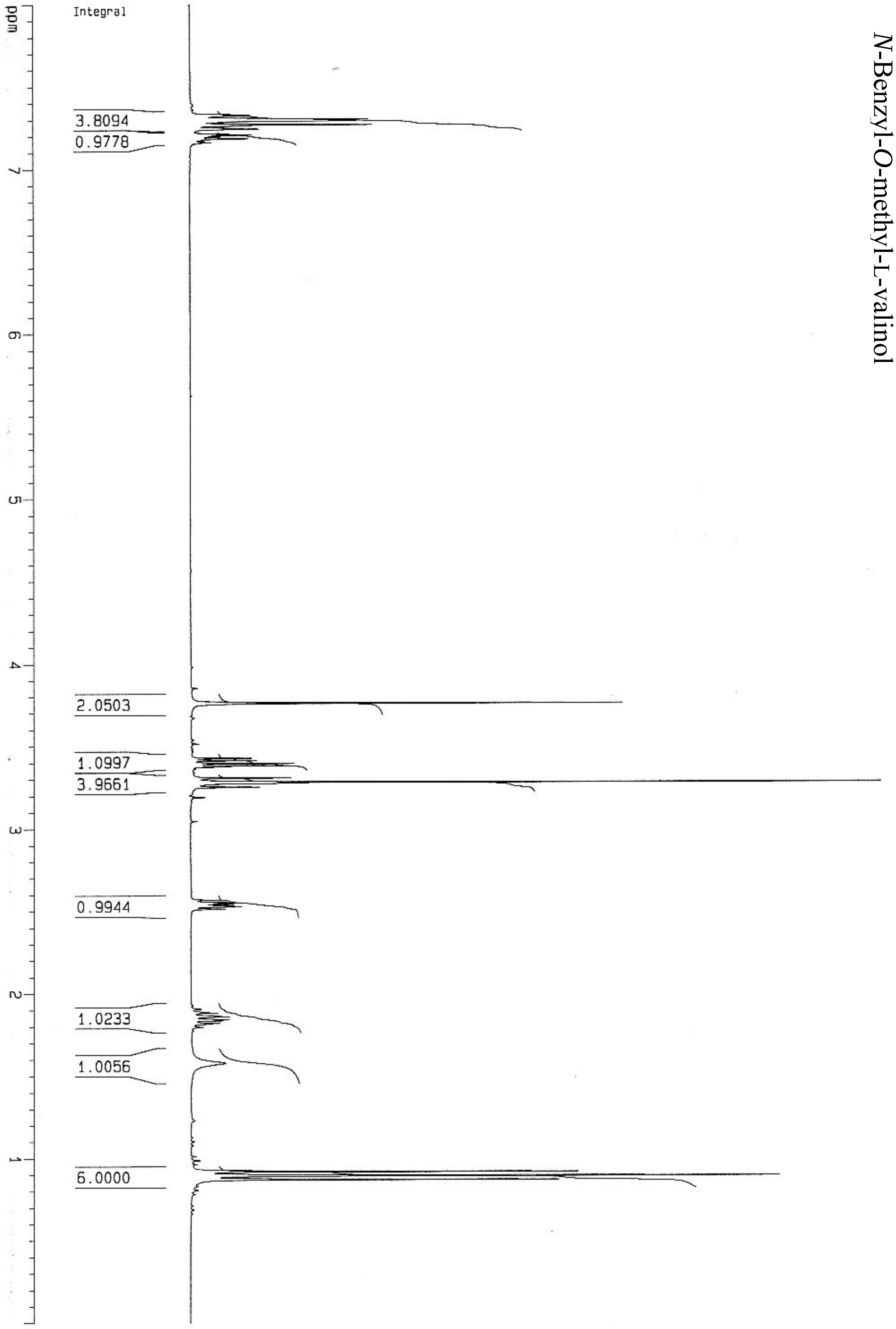

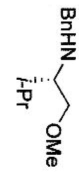

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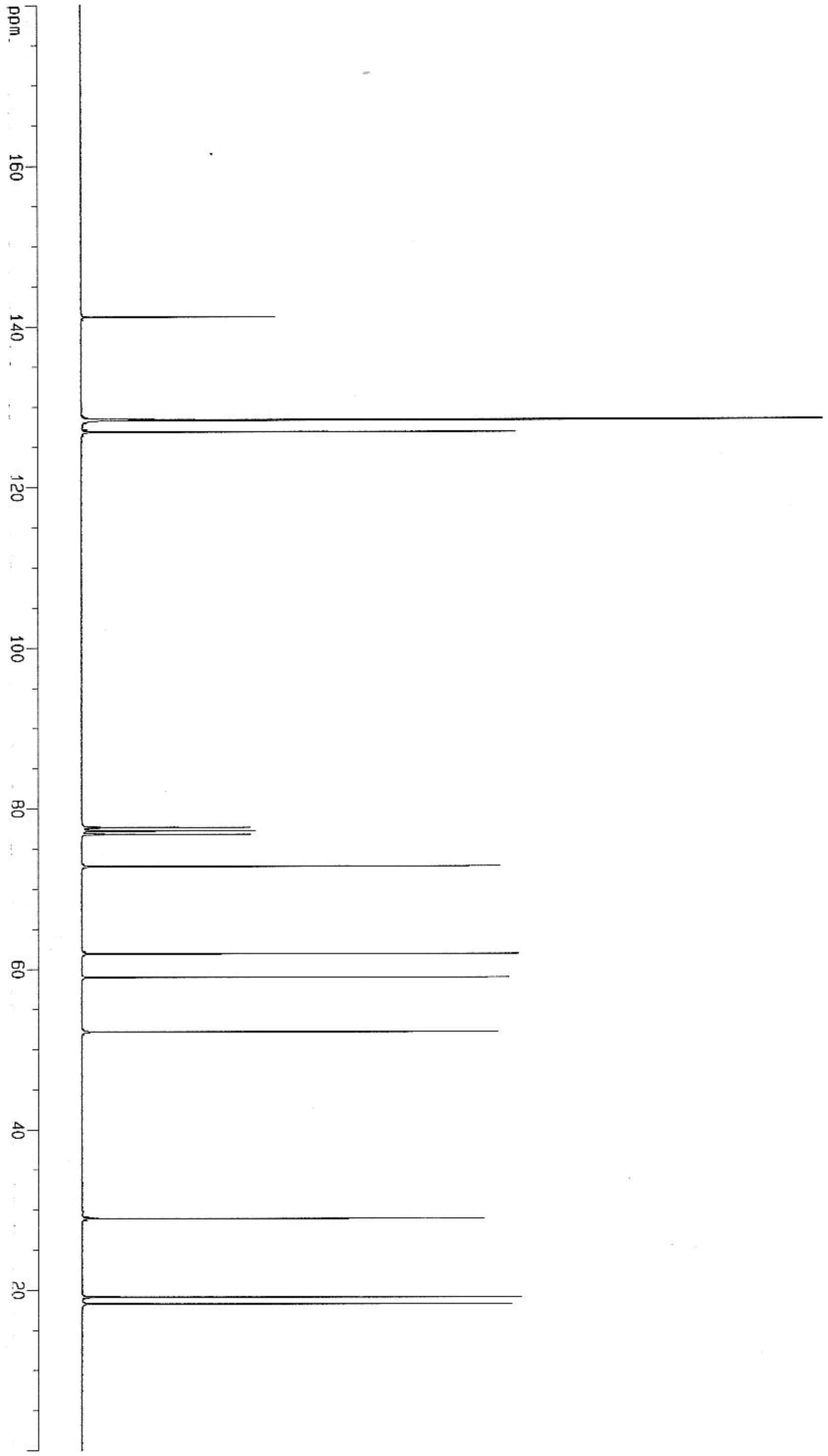

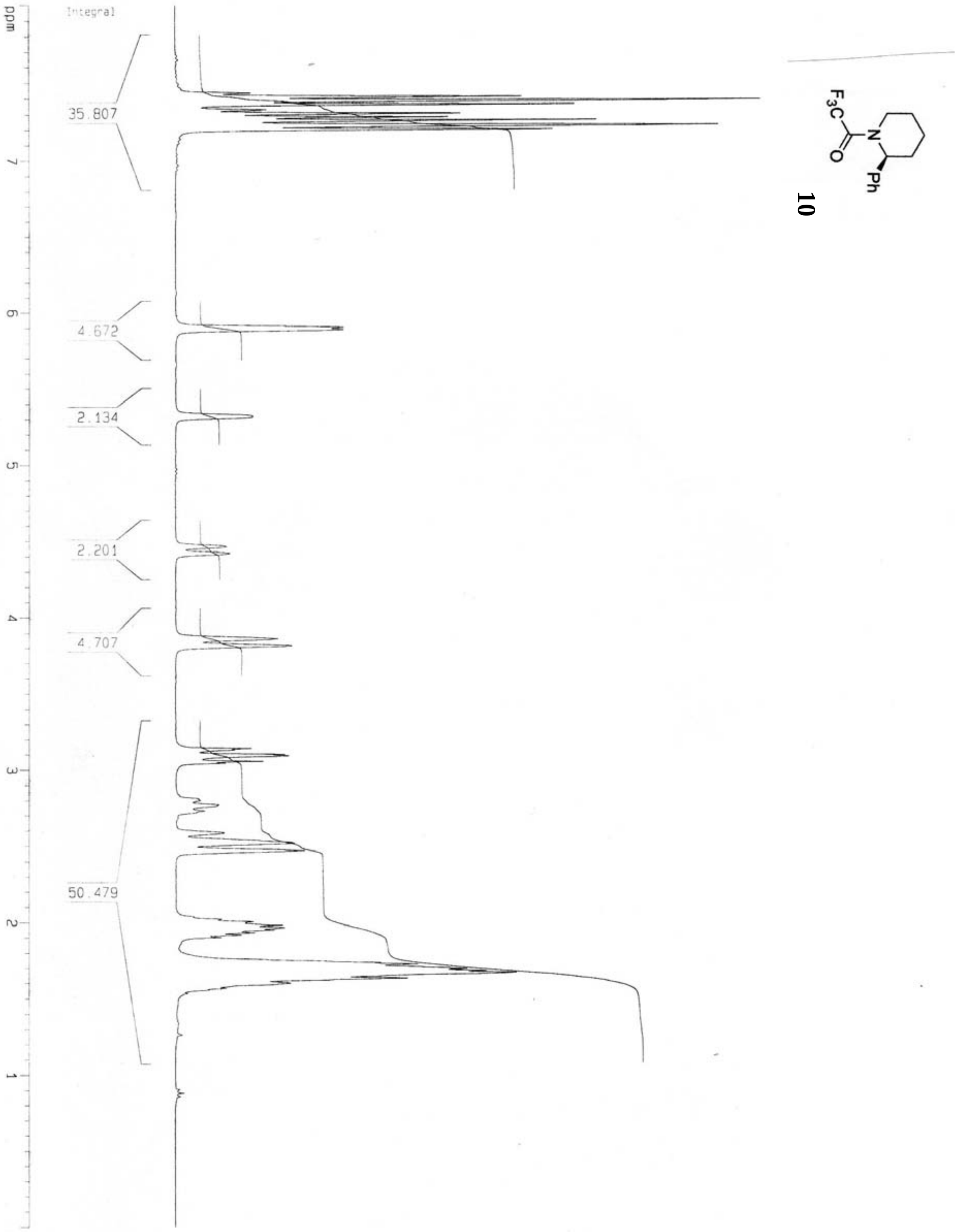
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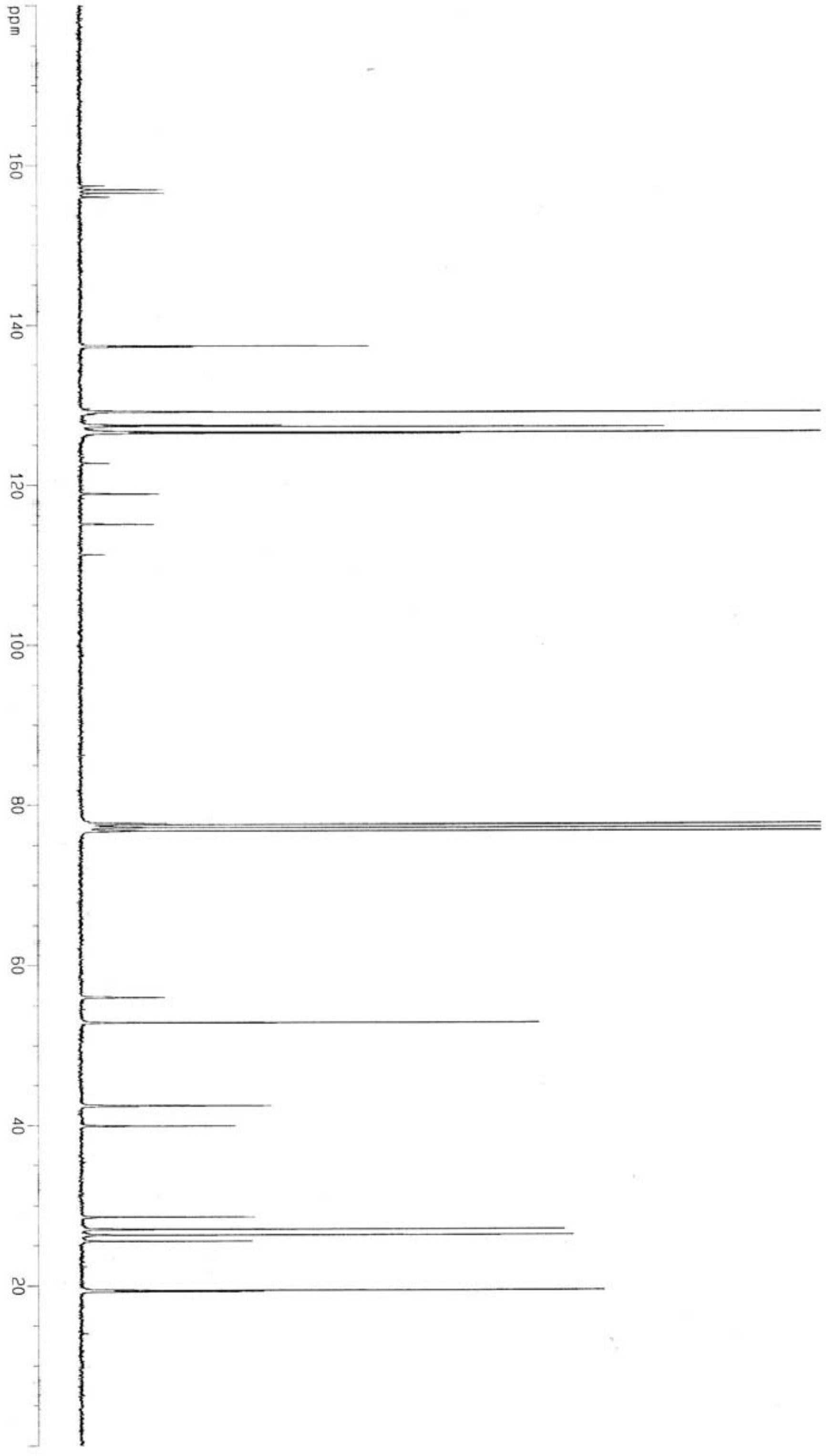
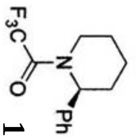
O
N
Ph

10





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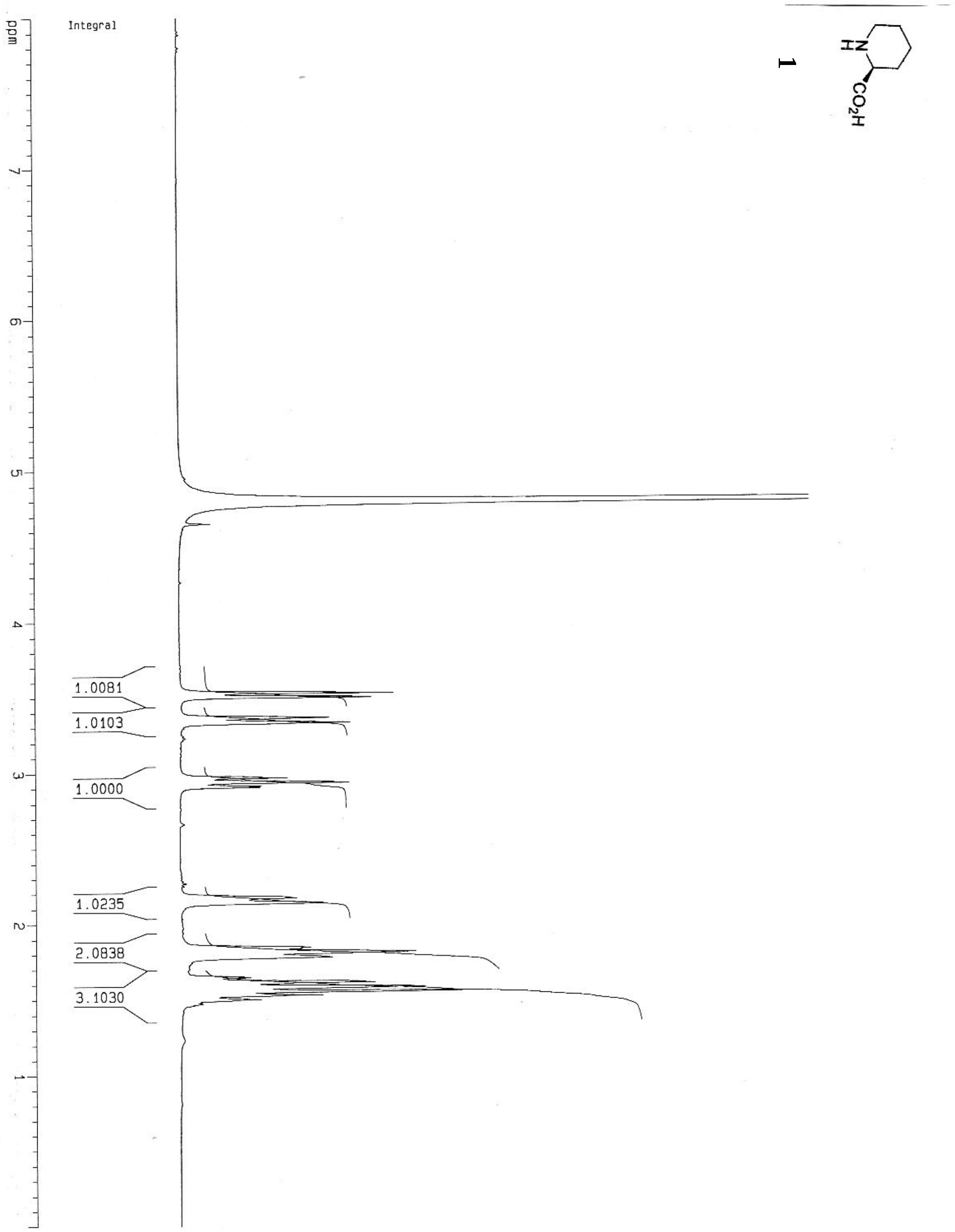
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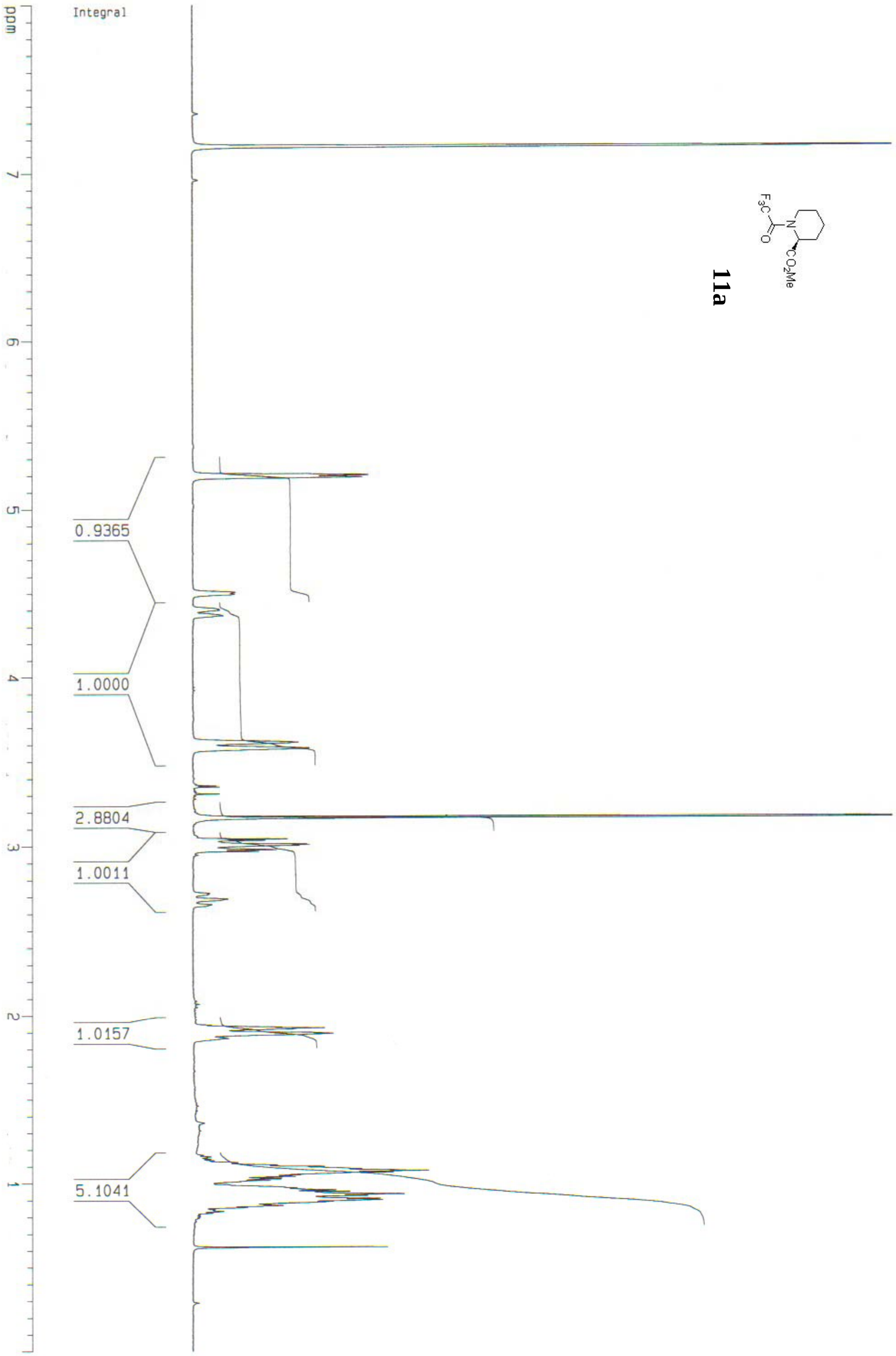
N
H
CO2H
1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4
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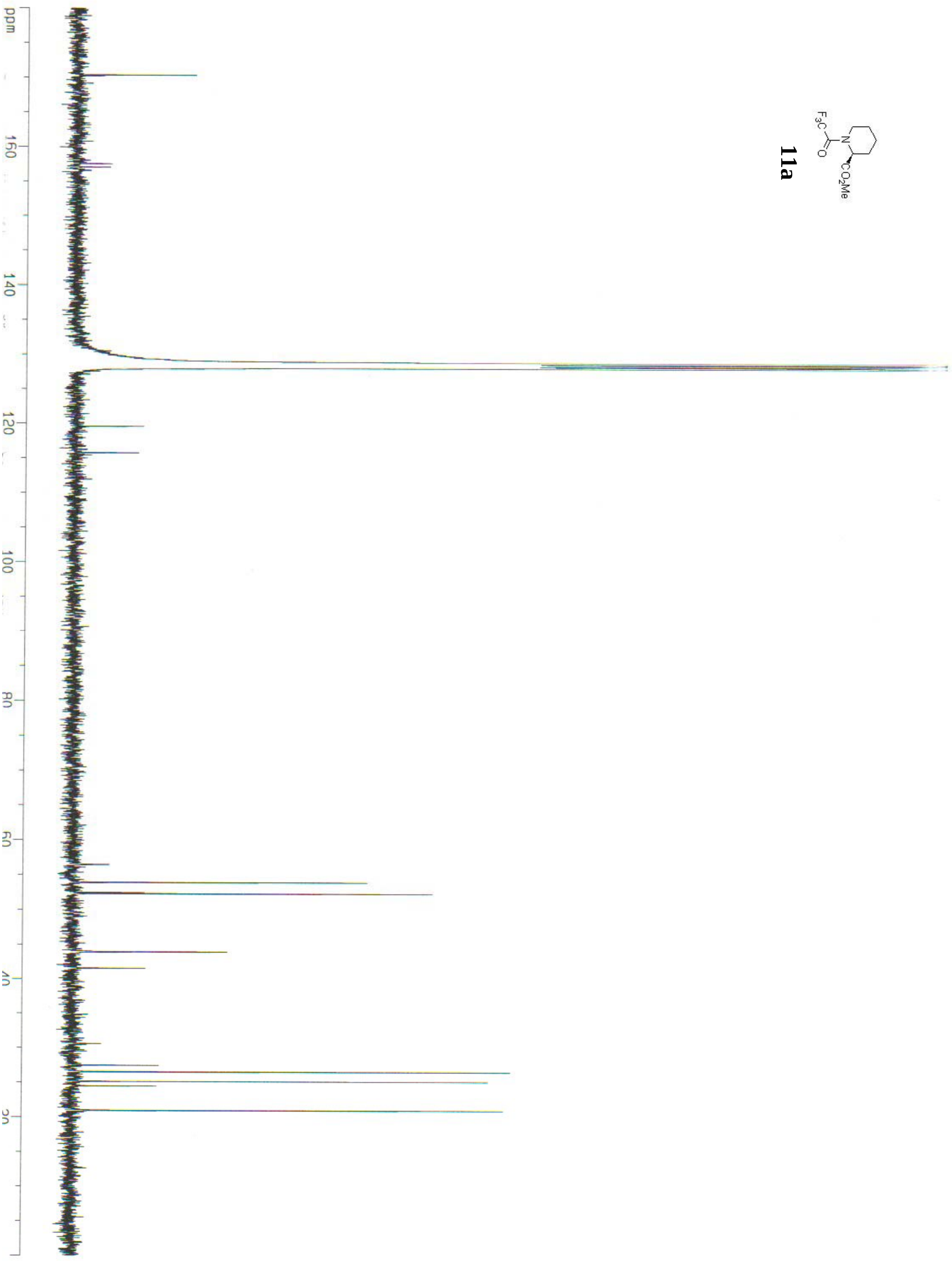
O
N
CO2Me

11a



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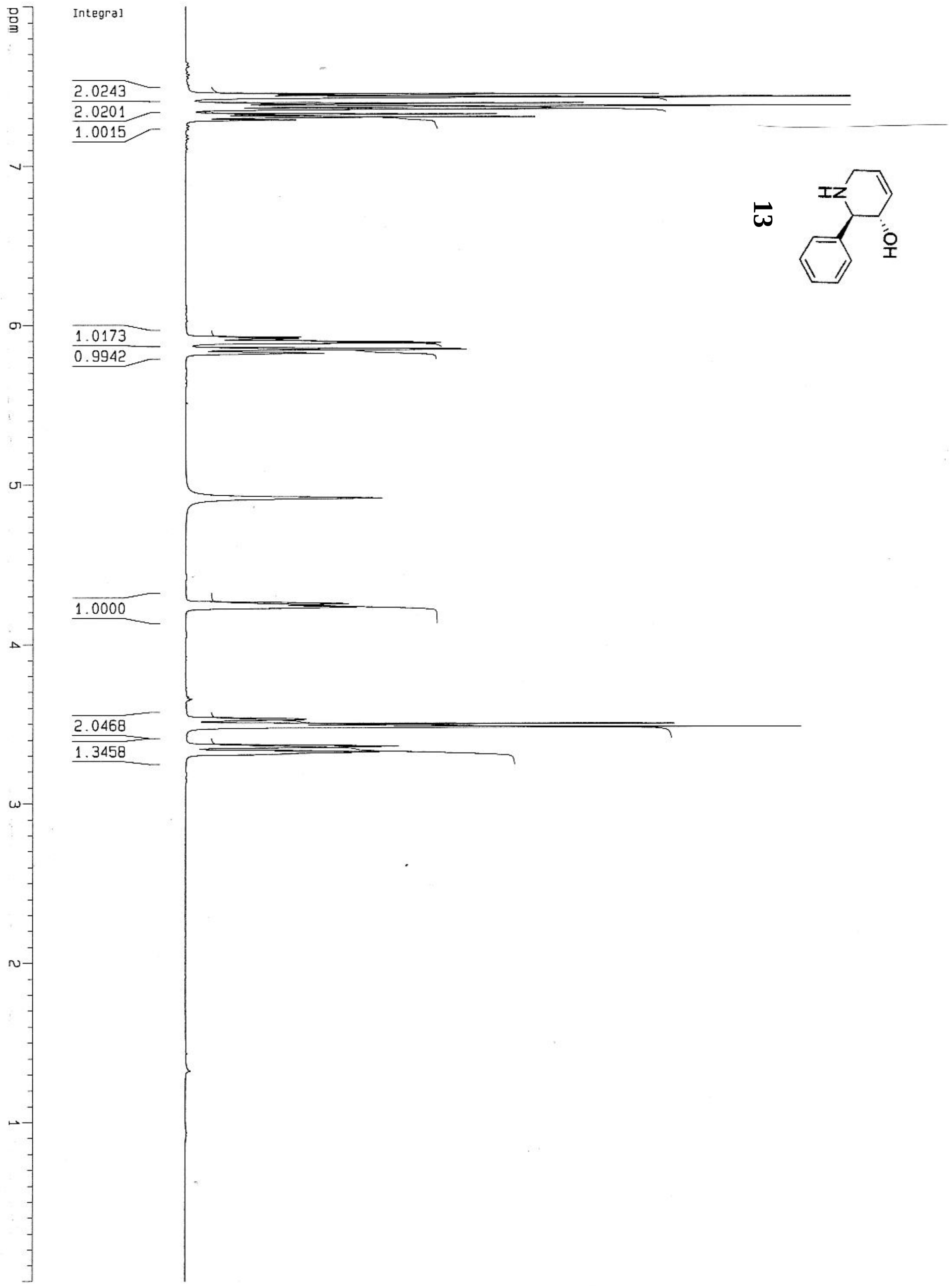
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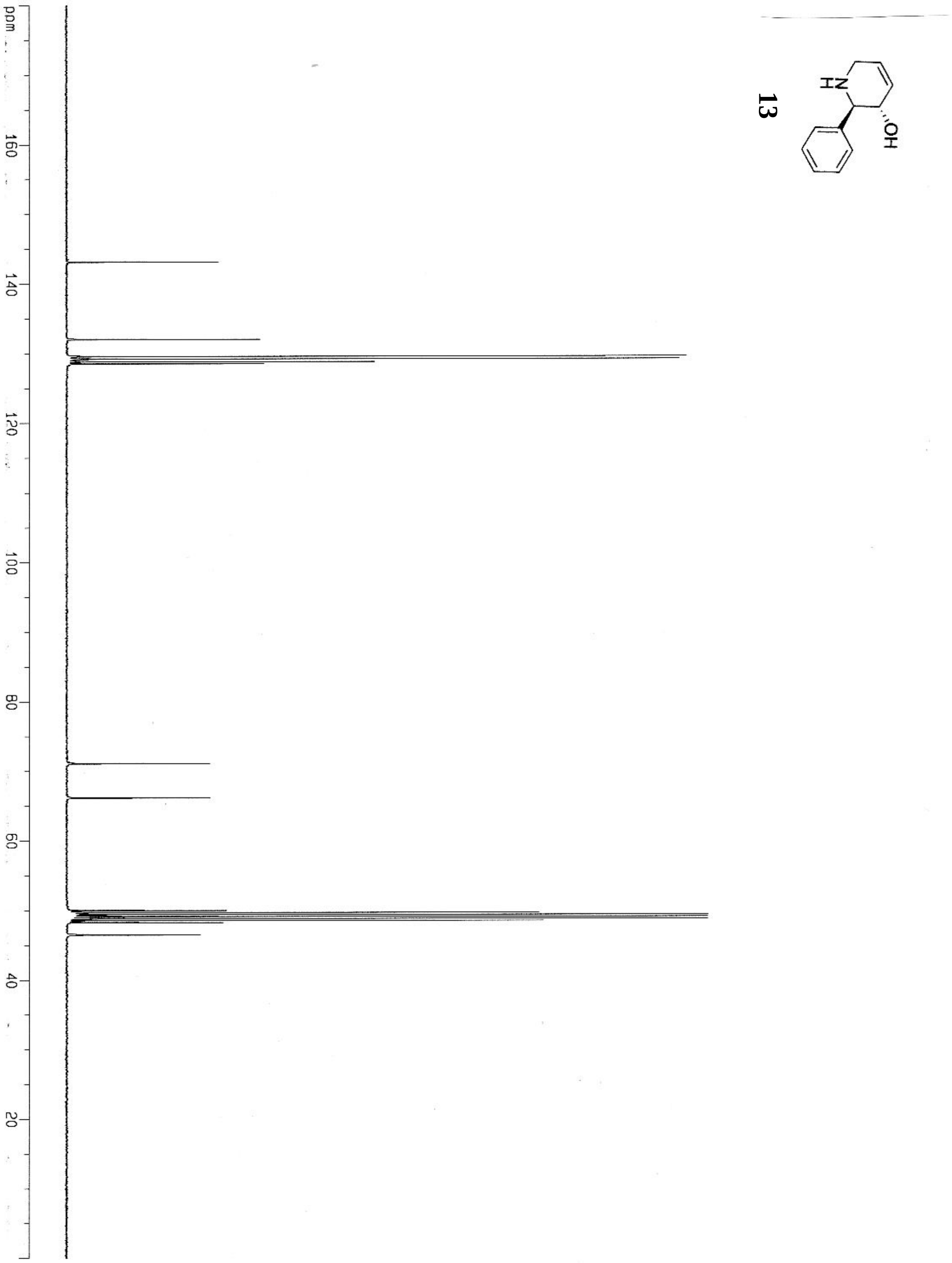
H
OH

13



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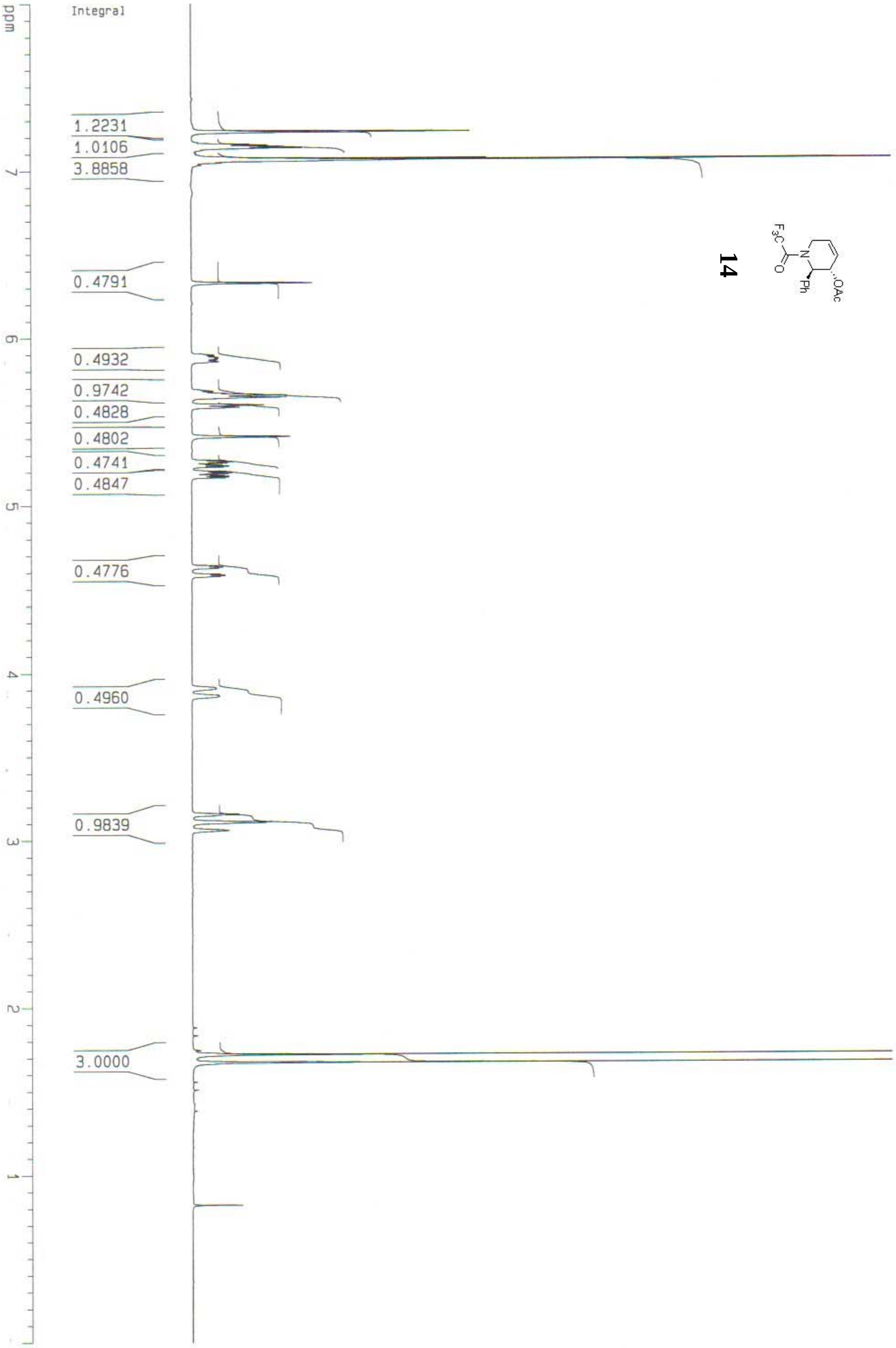
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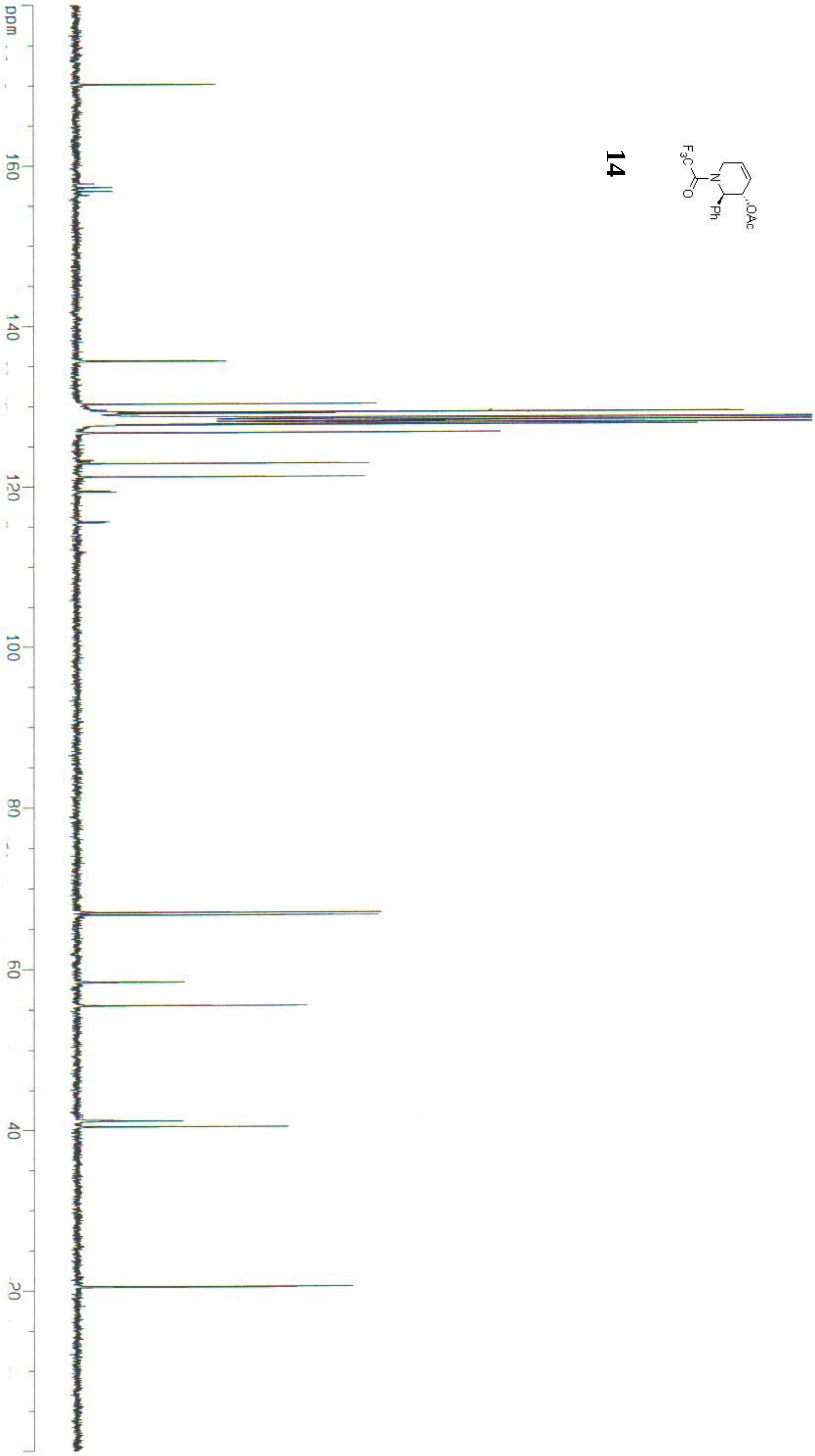
Ph
OAc

14



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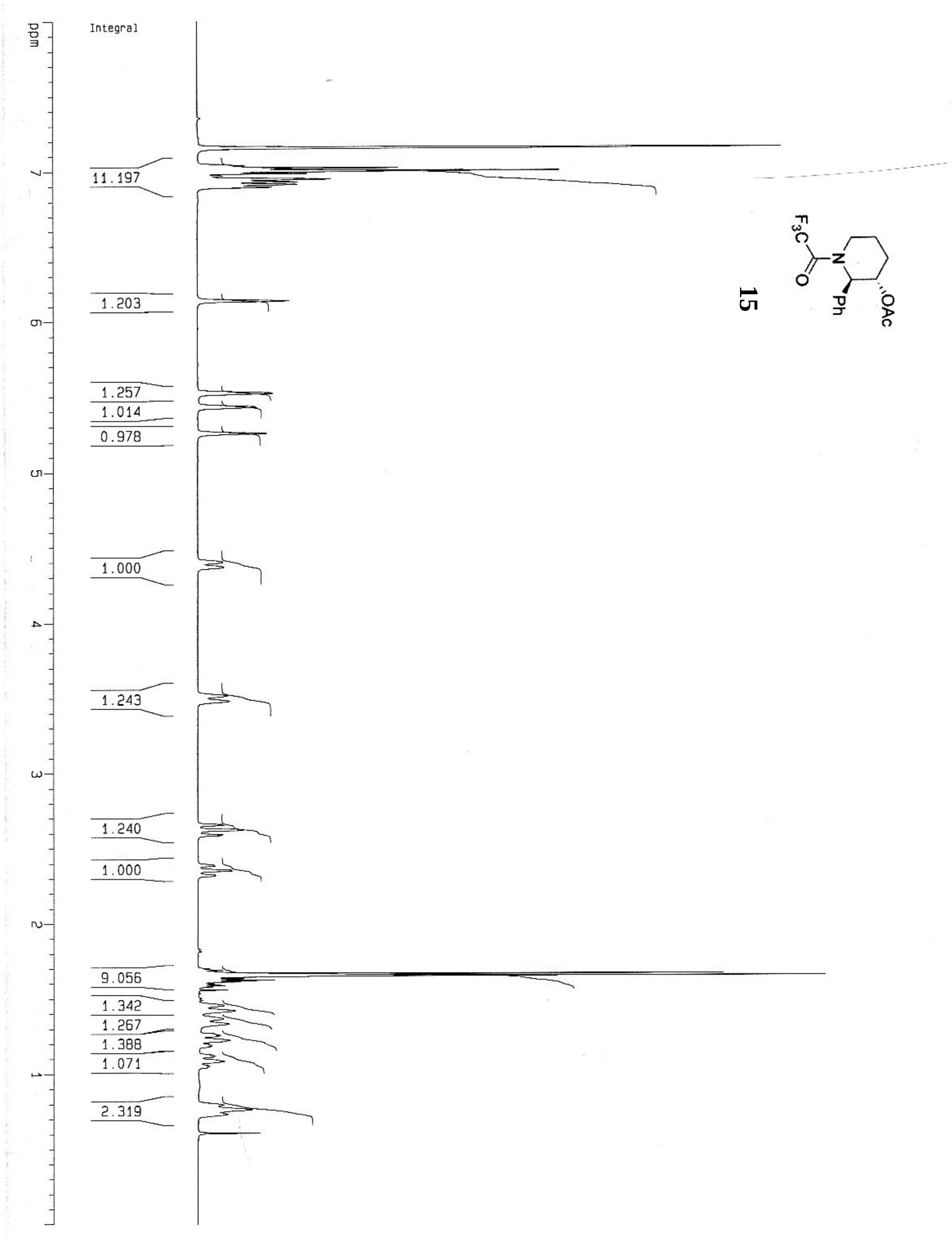
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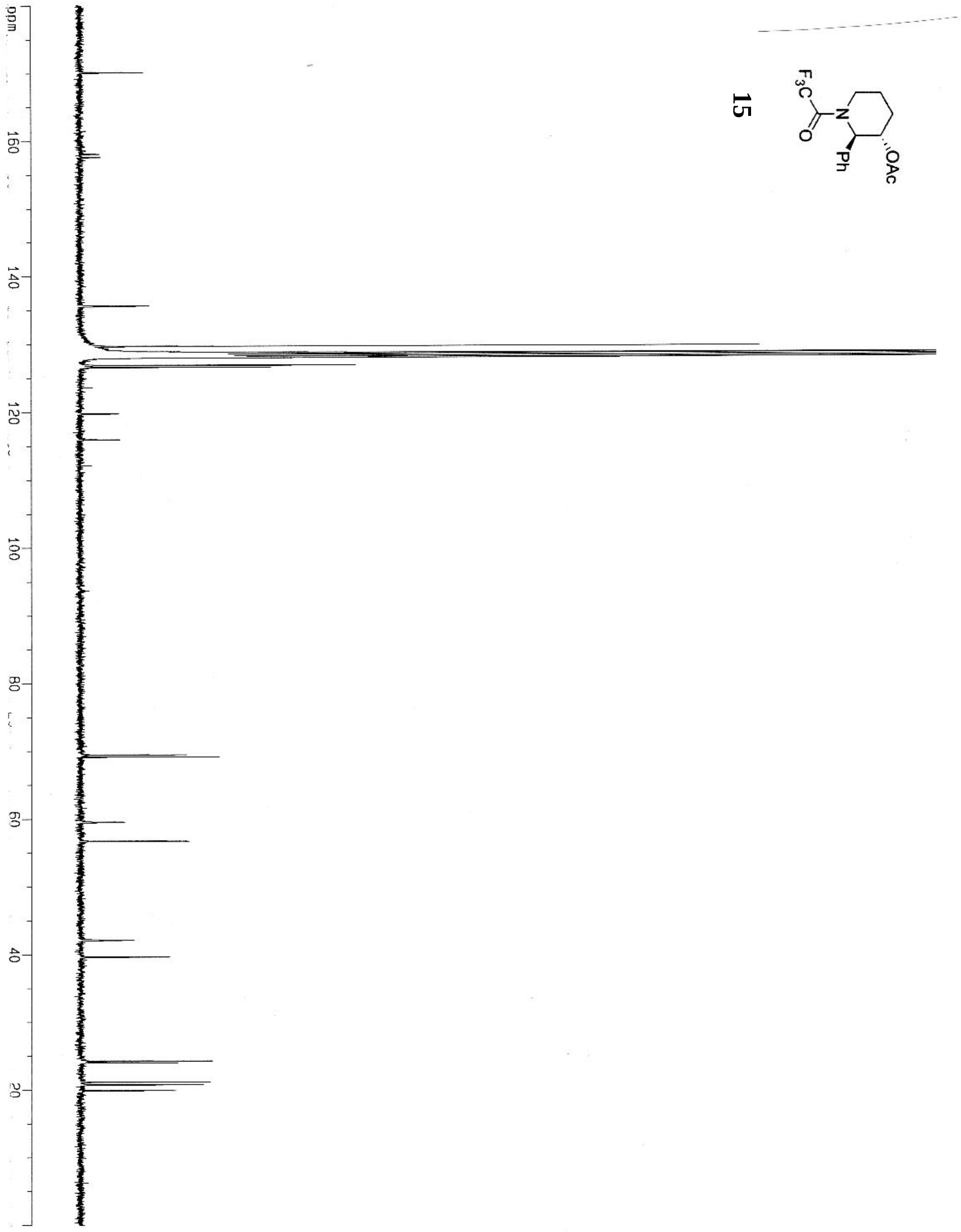
OAc
15



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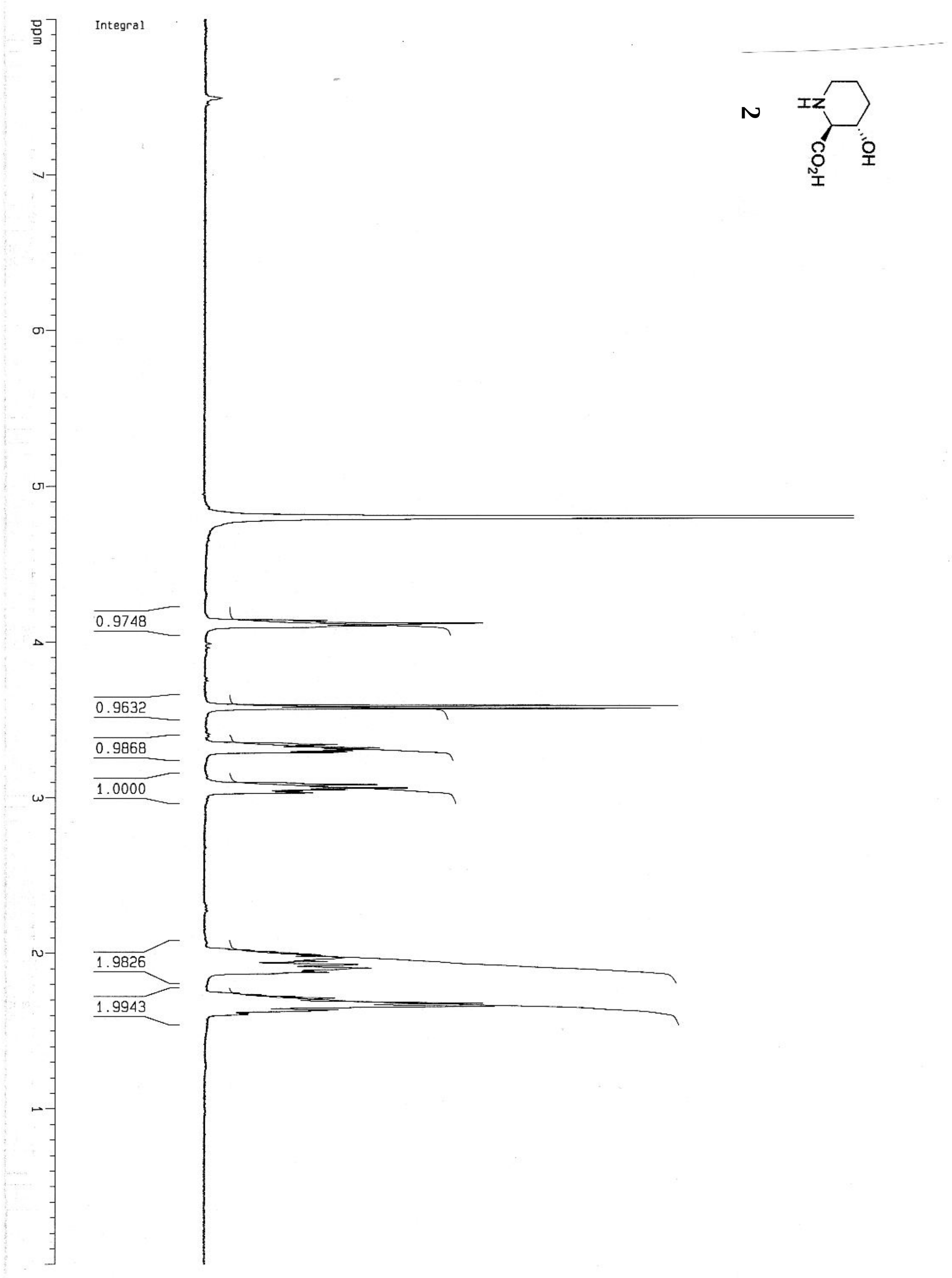
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1.9943
OH
N
H
CO$_2$H
2