Supporting Information

for

Asymmetric desymmetrization of *meso*-diols by C_2-symmetric chiral 4-pyrrolidinopyridines

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Experimental details and characterization data of new compounds, copies of ^{1}H NMR and ^{13}C NMR

Content:

Some of the results shown are already mentioned in the patent, JP2005132746.

General

NMR spectra were obtained with a Varian Gemini 200 (^{1}H NMR: 200 MHz, ^{13}C NMR: 50 MHz) or JEOL JMN 400 spectrometer (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz), chemical shifts being given in ppm units (tetramethylsilane or the solvent residual signal for CD_3OD as internal standard, indicating 0 and 3.30, respectively). IR spectra were recorded with a JASCO FT/IR-300 spectrometer. Specific rotation was measured with a Horiba SEPA-200 automatic digital polarimeter. MS spectra were recorded with a JEOL JMS-DX300 mass spectrometer or JEOL JMS–700 mass spectrometer. TLC analysis and preparative TLC were performed on commercial glass plates bearing a 0.25 mm layer and 0.5 mm layer of Merck Kiesel-gel 60 F_{254}, respectively. Silica gel chromatography was carried with Wakogel C-200, Fuji Silysia BW-1277H, or Nacalai Tesque Silica gel 60 (150–325 mesh). Dry solvents (THF, ether, hexane, dichloromethane, and toluene; <50 ppm water contents) were purchased from Kanto Chemical CO., Inc. and used without further treatment.

List of abbreviations

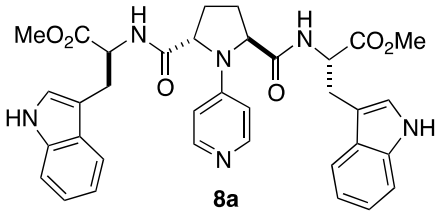
AcOEt	ethyl acetate
DCM	dichloromethane
DMAP	4-dimethylaminopyridine
DMF	dimethylformamide
EDCI	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride
HOBt	1-hydroxybenzotriazole
NMM	*N*-methylmorpholine
THF	tetrahydrofuran

General procedure for the preparation of C_2-symmetric catalysts

To a solution of (2*S*,5*S*)-1-(pyridin-4-yl)pyrrolidine-2,5-dicarboxylic acid [1] (130 mg, 0.55 mmol) and the corresponding amino acid or amino alcohol (1.6 mmol, 2.9 equiv) in DMF or DCM (10 mL) were added NMM (148 μl, 1.6 mmol, 2.9 equiv), EDCI (312 mg, 1.6 mmol, 2.9 equiv) and HOBt (222 mg, 1,6 mmol, 2.9 equiv). After stirring for 24 h, the mixture was evaporated and diluted with EtOAc (200 mL). The organic layer was washed with sat. aq. $NaHCO_3$, brine, dried over Na_2SO_4, filtered and evaporated in vacuo. The residue was purified by SiO_2 column chromatography or preparative TLC on silica gel, or recrystallization to give the corresponding C_2-symmetric catalyst.

Preparation of (2*S*,5*S*)-1-(pyridin-4-yl)pyrrolidine-2,5-dicarboxylic acid was previously reported [1].

(2*S*,5*S*)-2,5-Bis[(2*S*)-3-(1*H*-indol-3-yl)-1-(methyloxy)-1-oxopropan-2-ylamino]carbonyl]-1-(pyridin-4-yl)pyrrolidine (8a)

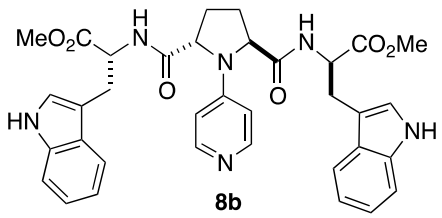


8a

According to the general procedure, **8a** was prepared with (*S*)-tryptophane methyl ester hydrochloride in DMF and purified by SiO_2 column chromatography (AcOEt/MeOH = 5/1) as a white powder in 46% yield.

M.p. 223–225 °C. $[\alpha]_D^{20}$ = –26 (*c* 0.5, DMSO). ^{1}H NMR (200 MHz, DMSO) δ 1.65–1.85 (m, 2H), 2.20 (br s, 2H), 3.05 (dd, *J* = 10.6, 14.6 Hz, 1H), 3.24 (dd, *J* = 4.2, 14.6 Hz, 1H), 4.22 (d, *J* = 7.8 Hz, 1H), 4.20–4.60 (m, 1H), 5.78 (d, *J* = 6.0 Hz, 1H), 6.90-7.16 (m, 2H), 7.21 (s, 1H), 7.38 (d, *J* = 8.0 Hz, H), 7.55 (d, *J* = 7.2 Hz, H), 7.74 (d, *J* = 5.0 Hz, 1H), 8.68 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (50 MHz, DMSO) δ 24.3, 26.6, 49.6, 50.4, 58.6, 104.9, 107.3, 109.0, 115.5, 116.0, 118.5, 121.3, 124.5, 133.7, 146.2, 147.5, 169.4, 169.7. IR (KBr) 3255, 1755, 1735, 1655, 1600 cm^{-1}. MS (FAB) *m/z* (rel intensity) 659 (MNa^+), 637 (MH^+). HRMS (FAB) calcd for $C_{35}H_{37}N_6O_6$ (MH): 637.2775, found, 637.2764. Anal calcd for $C_{35}H_{36}N_6O_6$: C, 66.03; H, 5.70; N, 13.20. Found C, 65.91; H, 5.79; N, 13.00.

(2*S*,5*S*)-2,5-Bis[(2*R*)-3-(1*H*-indol-3-yl)-1-(methyloxy)-1-oxopropan-2-ylamino]carbonyl]-1-(pyridin-4-yl)pyrrolidine (8b)

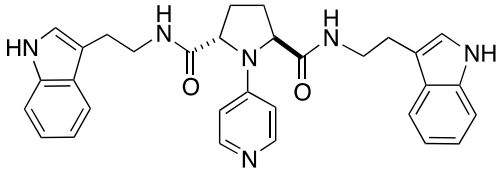


8b

According to the general procedure, **8b** was prepared with (*R*)-tryptophane methyl ester hydrochloride in DMF and purified by SiO_2 column chromatography (AcOEt/MeOH = 5/1)

in 34% yield as a crystalline powder.
M.p. 176–178 °C. $[\alpha]_D^{20}$ = –58 (c 0.5, DMSO). ^{1}H NMR (200 MHz, CD_3OD) δ 1.40–1.70 (m, 2H), 2.03 (br s, 2H), 3.12 (dd, *J* = 9.4, 14.6 Hz, 2H), 3.20–3.40 (m, 1H), 3.70 (s, 6H), 4.29 (d, *J* = 7.8 Hz, 2H), 4.75 (dd, *J* = 4.8, 9.2, 2H), 6.28 (d, *J* = 6.8 Hz, 2H), 6.80-7.20 (m, 8H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 7.4 Hz, 2H), 7.93 (d, *J* = 6.8 Hz, 2H). ^{13}C NMR (50 MHz, CD_3OD) δ 26.2, 28.4, 51.0, 52.5, 61.6, 107.9, 108.7, 110.5, 117.1, 118.0, 120.6, 122.4, 126.6, 136.1, 144.9, 151.7, 171.7, 172.0. IR (KBr) 3380, 3260, 1740, 1665, 1600 cm^{-1}. MS (FAB) *m/z* (rel intensity) 637 (MH^+). HRMS (FAB) calcd for $C_{35}H_{37}O_6N_4$ (MH): 637.2775, found, 637.2748.

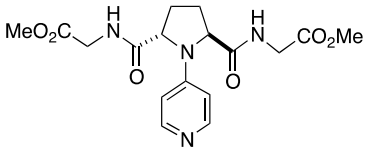
(2*S*,5*S*)-2,5-Bis[tryptamino]carbonyl]-1-(pyridin-4-yl)pyrrolidine (9)



9

According to the general procedure, **9** was prepared with tryptamin hydrochloride in DMF and purified by SiO_2 column chromatography (AcOEt/MeOH = 5/1) in 40% yield as a crystalline powder.
M.p. 140–145 °C. $[\alpha]_D^{20}$ = –36 (c 0.5 MeOH). ^{1}H NMR (200 MHz, CD_3OD) δ 1.70–1.90 (m, 2H), 2.10–2.40 (m, 2H), 2.91 (t, *J* = 7.6 Hz, 4H), 3.49 (dd, *J* = 7.0 Hz, 4H), 4.31 (d, *J* = 7.6 Hz, 2H), 6.16 (d, *J* = 6.6 Hz, 2H), 6.90–7.20 (m, 6H), 7.30–7.40 (m, 2H), 7.42–7.60 (m, 2H), 7.85 (d, 6.6, 2H). ^{13}C NMR (50 MHz, CD_3OD) δ 24.1, 28.7, 39.2, 61.8, 107.6, 110.4, 111.0, 117.4, 117.8, 120.5, 121.7, 126.9, 136.2, 147.3, 150.7, 172.4. IR (KBr) 3240, 1660, 1600, 1518 cm^{-1}. MS (FAB) *m/z* (rel intensity) 521 (MH^+). HRMS (FAB) calcd for $C_{31}H_{32}O_2N_6$ (MH): 521.2665, found, 521.2657.

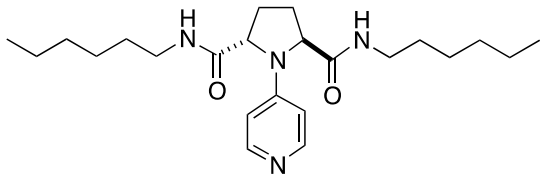
(2*S*,5*S*)-2,5-Bis[(2*S*)-3-(1-(methyloxy)-1-oxoethan-2-ylamino)carbonyl]-1-(pyridin-4-yl) pyrrolidine (10)



10

According to the general procedure, **10** was prepared with glycine methyl ester hydrochloride in 16% yield as a white powder.
M.p. 222–225 °C. $[\alpha]_D^{20}$ = –76 (c 0.25, CH_3OH). ^{1}H NMR (200 MHz, CD_3OD) δ 2.10–2.30 (m, 2H), 2.42–2.33 (m, 2H), 3.73 (s, 6H), 3.96 (d, *J* = 6.2 Hz, 4H), 4.59 (d, *J* = 8.2 Hz, 2H), 6.56 (d, *J* = 6.4 Hz, 2H), 8.14 (d, *J* = 6.4 Hz, 2H). ^{13}C NMR (50 MHz, CD_3OD) δ 28.7, 39.9, 50.7, 61.7, 108.1, 147.2, 150.8, 169.5, 173.4. IR (KBr) 3245, 1742, 1642, 1600, 1542, 1519 cm^{-1}. MS (FAB) *m/z* (rel intensity) 401 (MNa^+, 12), 379 (MH^+, 100), 262 (30). HRMS (FAB) calcd for $C_{17}H_{23}O_6N_4$ (MH): 379.1618, found, 379.1598.

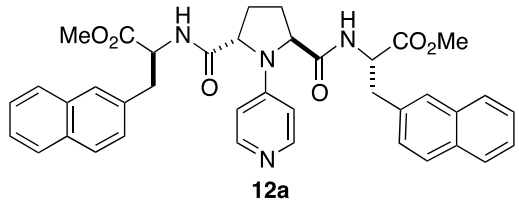
(2*S*,5*S*)-2,5-Bis[hexylamino]carbonyl]-1-(pyridin-4-yl)pyrrolidine (11)



11

According to the general procedure, **11** was prepared with *n*-hexylamine in DCM, purified by repeated preparative TLC (SiO_2, EtOAc/MeOH = 3 : 1 and $CHCl_3$/MeOH = 5 : 1) and recrystallization from EtOAc-CH_2Cl_2 to afford **11** in 54% yield as a colorless powder.
M.p. 222–223 °C. $[\alpha]_D^{20}$ = –86 (c 0.5, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.85 (t, *J* = 6.8 Hz, 6H), 1.10–1.35 (m, 12H), 1.35–1.50 (m, 4H), 2.10–2.30 (m, 2H), 2.30–2.60 (m, 2H), 3.10–3.40 (m, 4H), 4.42 (d, *J* = 7.6 Hz, 2H), 6.30–6.60 (m, 4H), 8.13 (dd, *J* = 1.4, 5.0 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.1, 22.7, 26.7, 29.6, 30.1, 31.6, 39.7, 62.4, 108.3, 149.0, 150.5, 172.3. IR (KBr) 3288, 2928, 1651, 1596, 1552, 1510 cm^{-1}. MS (FAB) *m/z* (rel intensity) 402 (M, 3), 274 (100), 145 (60). HRMS (FAB) calcd for $C_{23}H_{38}O_2N_4$ (M^+) 402.2995, found, 402.2974. Anal calcd for $C_{23}H_{38}N_2O_4$: C, 68.62; H, 9.51; N, 13.92. Found C, 68.35; H, 9.40; N, 13.93.

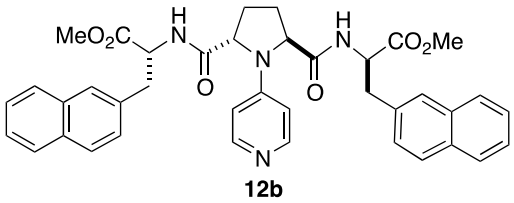
(2*S*,5*S*)-2,5-Bis[(2*S*)-3-(2-naphthylmethyl)-1-(methyloxy)-1-oxopropan-2-ylamino]carb onyl]-1-(pyridin-4-yl)pyrrolidine (12a)



12a

According to the general procedure, **12a** was prepared with (*S*)-naphtylalanine methyl ester hydrochloride in DMF in 41% yield as a white powder.
M.p. 225–228 °C. $[\alpha]_D^{20}$ = +39 (c 0.25, MeOH). ^{1}H NMR (200 MHz, DMSO) δ 1.50–1.65 (m, 2H), 2.09 (br s, 2H), 3.05 (t, *J* = 13.0 Hz, 2H), 3.20–3.50 (m, 2H), 3,63 (s, 6H), 4.10 (d, *J* = 7.2 Hz, 2H), 4.50–4.65 (m, 2H), 5.53 (d, *J* = 6.2 Hz, 2H), 7.10 (d, *J* = 5.8 Hz, 2H), 7.38-7.60 (m, 6H), 7.70–8.00 (m, 8H), 8.66 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (50 MHz, DMSO) δ 29.6, 37.1, 52.9, 53.7, 61.9, 108.0, 126.34, 126.8, 128.1, 128.3, 128.4, 132.6, 133.6, 135.9, 149.2, 150.4, 172.4, 172.5. IR (KBr) 3255, 1750, 1650, 1600 cm^{-1}. MS (FAB) *m/z* (rel intensity) 659 (MH^+). HRMS (FAB) calcd for $C_{39}H_{39}O_6N_4$ (MH): 659.2869, found, 659.2859.

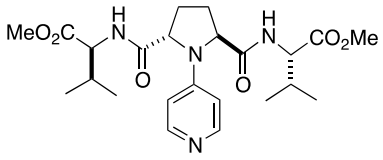
(2*S*,5*S*)-2,5-Bis[(2*R*)-3-(2-naphthylmethyl)-1-(methyloxy)-1-oxopropan-2-ylamino]carbonyl]-1-(pyridin-4-yl)pyrrolidine (12b)



12b

According to the general procedure, **12b** was prepared with (*R*)-naphtylalanine methyl ester hydrochloride in DMF and purified by SiO_2 column chromatography (SiO_2, AcOEt /MeOH = 4/1) in 53% yield as an amorphous powder.
M.p. 191–193 °C. $[\alpha]_D^{20}$ = –90 (c 0.5, MeOH). ^{1}H NMR (200 MHz, CD_3OD) δ 1.20–1.50 (m, 2 H), 1.87 (br s, 2 H), 3.05 (dd, *J* = 10.8, 13.9 Hz, 2 H), 3.41 (dd, *J* = 4.4, 13.9 Hz, 2H), 3.73 (s, 6H), 4.26 (d, *J* = 7.6 Hz, 2H), 4.83 (dd, *J* = 4.6, 10.8 Hz, 2H), 6.18 (d, *J* = 6.6 Hz, 2H), 7.25 (dd, *J* = 1.6, 8.4 Hz, 2H), 7.40–7.60 (m, 6H), 7.60–7.90 (m, 8H). ^{13}C NMR (100 MHz, CD_3OD) δ 28.4, 36.2, 51.1, 52.6, 61.4, 107.7, 124.9, 125.3, 126.2, 126.6, 126.7, 126.8, 127.2, 131.89, 132.9, 133.8, 146.7, 150.7, 171.3, 172.4. IR (KBr) 3280, 1740, 1657, 1600 cm^{-1}. MS *m/z* (FAB) (rel intensity) 659 (MH^+). HRMS (FAB) calcd for $C_{39}H_{39}O_6N_4$ (MH): 659.2869, found, 659.2859.

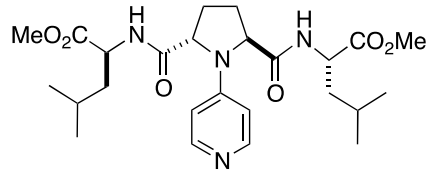
(2*S*,5*S*)-2,5-Bis[(2*S*)-3-(isopropyl)-1-(methyloxy)-1-oxopropan-2-ylamino]-carbonyl]-1-(pyridin-4-yl)pyrrolidine (13)



13

According to the general procedure, **13** was prepared with (*S*)-valine methyl ester hydrochloride in CH_2Cl_2 with preparative TLC (SiO_2, AcOEt /MeOH = 3/1) in 29% yield as a white powder.
M.p. 203–205 °C. $[\alpha]_D^{21}$ = –117 (c 0.5, MeOH). ^{1}H NMR (200 MHz, CD_3OD) δ 0.99–1.10 (m, 12H), 2.07–2.35 (m, 4H), 2.40–2.60 (m, 2H), 3.73 (s, 6H), 4.37 (d, *J* = 5.6 Hz, 2H), 4.66 (d, *J* = 7.6 Hz, 2H), 6.47 (d, *J* = 6.4 Hz, 2H), 8.09 (d, *J* = 6.4 Hz, 2H). ^{13}C NMR (50 MHz, CD_3OD) δ 16.7, 17.8, 28.7, 29.7, 50.6, 57.4, 61.2, 107.5, 147.3, 151.0, 171.3, 173.1. IR (KBr) 3255, 2880, 1740, 1655, 1600 cm^{-1}. MS (FAB) *m/z* (rel intensity) 462 (M, 7), 304 (55), 71 (100). HRMS (FAB) Calcd for $C_{23}H_{34}O_6N_4$ (M): 462.2478, found, 462.2490.

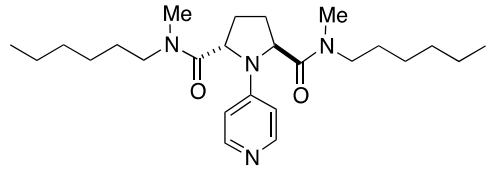
(2*S*,5*S*)-2,5-Bis[(2*S*)-3-(isobutyl)-1-(methyloxy)-1-oxopropan-2-ylamino]-carbonyl]-1-(pyridin-4-yl)pyrrolidine (14)



14

According to the general procedure, **14** was prepared with (*S*)-leucine methyl ester hydrochloride in CH_2Cl_2 with SiO_2 column chromatography ($CHCl_3$/MeOH = 6/1) and successive preparative TLC (SiO_2, $CHCl_3$ /MeOH = 6/1) in 71% yield as a white powder.
M.p. 187–189 °C. $[\alpha]_D^{20}$ = –133 (c 0.5, CH_3OH). ^{1}H NMR (200 MHz, CD_3OD) δ 0.93 (d, *J* = 5.8 Hz, 6H), 1.02 (d, *J* = 6.2 Hz, 6H), 1.50–1.90 (m, 4H), 2.10–2.30 (m, 2H), 2.35–2.60 (m, 2H), 3.70 (s, 6H), 4.20–4.60 (m, 4H), 6.46 (d, *J* = 5.5 Hz, 2H), 8.10 (d, *J* = 5.5 Hz, 2H). ^{13}C NMR (50 MHz, CD_3OD) δ 19.6, 21.6, 24.4, 28.6, 39.1, 50.2, 50.8, 61.4, 107.7, 147.1, 151.0, 172.2, 172.93. IR (KBr) 2880, 1745, 1660, 1600, 1545, 1518 cm^{-1}. MS (FAB) *m/z* (rel intensity) 490 (M, 4), 318 (100), 145 (40). HRMS (FAB) calcd for $C_{25}H_{38}O_6N_4$ (M): 490.2791, found, 490.2796.

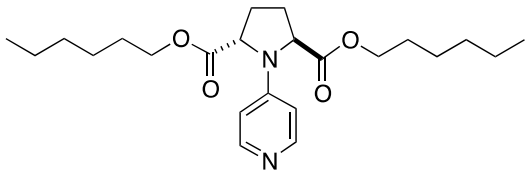
(2*S*,5*S*)-2,5-Bis[*N*-methyl-*N*-hexylamino]carbonyl]-1-(pyridin-4-yl)pyrrolidine (15)



15

According to the general procedure, **15** was prepared with *N*-methyl hexylamine in CH_2Cl_2 without addition of NMM and purified by preparative TLC (SiO_2, $CHCl_3$/MeOH = 5/1) in 42% yield as a white solid.
Decomposition. $[\alpha]_D^{20}$ = –28 (c 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, DMSO, 150 °C) δ 0.90 (t, *J* = 6.8 Hz, 6H), 1.20–1.40 (m, 12H), 1.45–1.65 (m, 4H), 1.80–1.95 (m, 2H), 2.40–3.15 (m, 2H), 3.04 (m, 6H), 3.38 (t, *J* = 6.8 Hz, 4H), 4.81 (d, *J* = 7.8 Hz, 2H), 6.12 (d, *J* = 6.2 Hz, 2H), 8.02 (d, *J* = 6.2 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.1, 22.7, 26.6, 26.8, 27.2, 28.5, 28.8, 29.2, 31.6, 33.9, 35.0, 48.4, 49.8, 59.2, 107.7, 149.6, 150.4, 171.1, 171.4. IR (KBr) 2931, 1650, 1603, 1513 cm^{-1}. MS (FAB) *m/z* (rel intensity) 430 (M, 4), 402 (2), 288 (92), 145 (100). HRMS (FAB) calcd for $C_{25}H_{42}O_2N_4$ (M): 430.3307, found, 430.3311.

(2*S*,5*S*)-Dihexyl 1-(pyridin-4-yl)pyrrolidine-2,5-dicarboxylate (16)

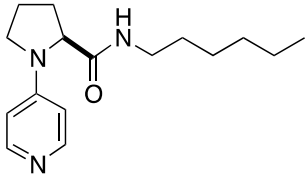


16

According to the general procedure, **16** was prepared with *n*-hexanol in CH_2Cl_2 without addition of NMM and purified by preparative TLC (SiO_2, Et_2O/MeOH = 10/1) in 38 % yield as a colorless oil.

$[\alpha]_D^{20}$ = –77 (c 0.25, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.6 Hz, 6H), 1.00–1.43 (m, 12 H), 1.43–1.70 (m, 4H), 2.10–2.30 (m, 2H), 2.40–2.65 (m, 2H), 4.00–4.20 (m, 4H), 4.48 (d, *J* = 8.2 Hz, 2H), 6.33 (dd, *J* = 1.6, 4.8 Hz, 2H), 8.24 (dd, *J* = 1.4, 4.8 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.1, 22.6, 25.6, 28.7, 29.1, 31.4, 60.9, 65.7, 107.8, 150.0, 150.4, 172.7. IR (film) 2956, 2858, 1743, 1595, 1510 cm^{-1}. MS (FAB) *m/z* (rel intensity) 404 (M, 7), 275 (100), 191 (12), 145 (30). HRMS (FAB) calcd for $C_{23}H_{36}O_4N_2$ (M): 404.2675, found, 404.2673.

4-Pyridinyl-L-proline 1'-hexylamide (17)



17

To a solution of *n*-hexylamine (87 μL, 0.66 mmol), *N*-(4-pyridyl)-L-proline hydrochloride (100 mg, 0.44 mmol) in DCM (10 mL) were added NMM (48 μl, 0.44 mmol), EDCI (125 mg, 0.66 mmol) and HOBt (89 mg, 0.66 mmol). After stirring for 24 h, the mixture was evaporated and diluted with EtOAc (200 mL). The organic layer was washed with sat. aq. $NaHCO_3$ (10 mL), brine (10 mL), dried over Na_2SO_4, filtered and evaporated in vacuo. The residue was purified by preparative TLC (SiO_2, $CHCl_3$/MeOH = 5/1) to give **17** (41 mg, 34%) as colorless needles.

M.p. 45 °C. $[\alpha]_D^{20}$ –110 (c 0.5, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.85 (t, *J* = 6.4 Hz, 3 H), 1.10–1.35 (m, 6 H), 1.42 (t, *J* = 6.6 Hz, 2 H), 1.90–2.20 (m, 2 H), 2.20–2.50 (m, 2 H), 3.17-3.40 (m, 3 H), 3.50–3.80 (m, 1 H), 4.10 (t, *J* = 5.4 Hz, 1 H), 6.24 (br s, 1 H), 6.46 (d, *J* = 5.9 Hz, 2H), 8.27 (d, *J* = 5.9 Hz, 2H). ^{13}C NMR (50 MHz, NMR ($CDCl_3$) δ 14.1, 22.6, 24.0, 26.6, 29.7, 31.4, 31.5, 39.5, 48.9, 63.5, 108.2, 150.0, 152.1, 172.0. IR (KBr) 3299, 2928, 1650, 1602, 1551, 1518 cm^{-1}. MS (FAB) *m/z* (rel intensity) 275 (M^+, 42), 147 (100), 105 (40), 78 (38). HRMS (FAB) Calcd for $C_{16}H_{25}ON_3$ 275.1998, found 275.1999.

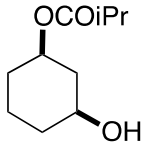
Typical procedure for asymmetric desymmetrization

To a solution of substrate (0.1 mmol), catalyst (5 mol %) and 2,4,6-collidine (0.14 mmol, 18.5 μL) in solvent (0.5 mL), isobutyric anhydride (0.13 mmol, 21.5 μL) was added. After the mixture was stirred, it was diluted with EtOAc and washed with 1 M aq. HCl, sat. aq. $NaHCO_3$ and brine. The organic layer was dried over Na_2SO_4, filtered and evaporated in vacuo. Yields of monoacylate, diacylate and recovered substrate were determined by ^{1}H NMR integration with dibenzyl ether as an internal standard.

Enantiomeric purities of 1,2- and 1,3-cyclohexanediol monoisobutyrate were determined by GLC analysis with beta-DEX 225 at 150 °C (Tables 1–5 in the manuscript).

Enantiomeric purities of *cis*-2,3-butanediol isobutyrate (**23a**) and hydrobenzoin isobutyrate (**23b**) were determined by GLC analysis with beta-DEX 225 at 90 °C and HPLC analysis with chiral stationary phase [column: CHIRALCEL OJ (4.6 mm x 25 cm), eluent: hexane–iPrOH (95:5), flow rate: 0.5 mL/min], respectively (Table 6 in the main manuscript).

1,3-Cyclohexanediol isobutyrate (**20**)



20

^{1}H-NMR (400 MHz, $CDCl_3$) δ: 4.65–4.54 (m, 1H), 3.61–3.50 (m, 1H), 3.28 (br s, 1H), 2.40 (sept, J = 7.1 Hz, 1H), 2.15–2.07 (m, 1H), 1.85–1.74 (m, 2H), 1.74–1.64 (m, 1H), 1.31–0.99 (m, 4H), 1.04 (d, J = 6.9 Hz, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 176.5, 70.6, 68.1, 40.4, 34.0, 33.9, 30.4, 19.9, 18.7. IR (neat) 3400, 2880, 2875, 2835, 1730, 1718 cm^{-1}; MS (EI) *m/z* (rel intensity) 186 (M^+, 0.15), 168 (5), 125 (10), 98 (80), 81 (100); HRMS (EI) calcd for $C_{10}H_{18}O_3$ (M^+), 186.1256, found 186.1248.

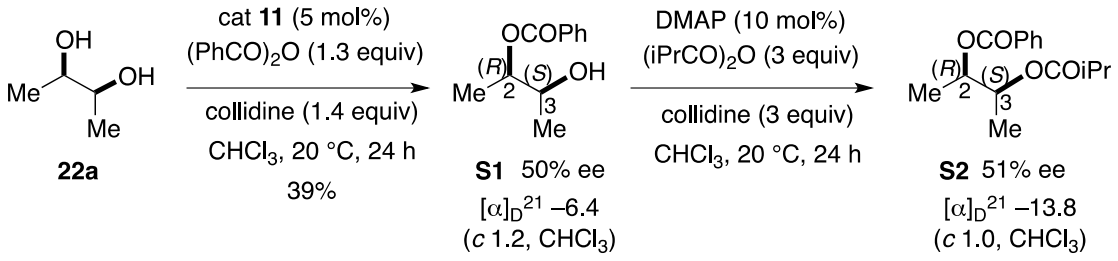
Acylative kinetic resolution of racemic-6 with catalyst 12b

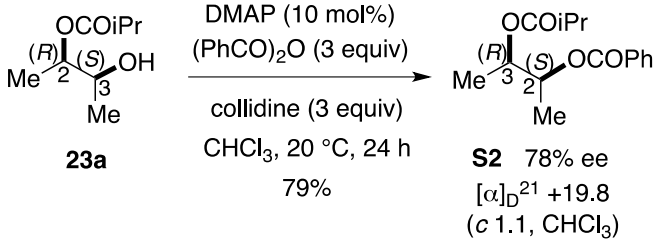
To a solution of racemic-**6** (18.6 mg, 0.1 mmol), catalyst **12b** (3.3 mg, 5 mol%) and 2,4,6-collidine (13.2 μL, 0.1 mmol) in $CDCl_3$ (0.7 mL), isobutyric anhydride (11.6 μL, 0.07 mmol) was added at 20 °C. After the mixture was stirred at 20 °C for 23 h, conversion of **6** was determined by ^{1}H NMR integration with dibenzyl ether as an internal standard. Then, the mixture was diluted with EtOAc and washed with 1 M aq. HCl, sat. aq. $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, filtered and evaporated in vacuo. Enantiomeric purity of (1*R*,2*S*)-**6** (67% ee) was determined by GLC analysis with beta-DEX 225 at 150 °C.

Determination of the absolute configuration of 2,3-butanediol isobutyrate (23a)

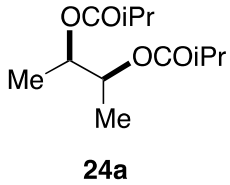
Asymmetric desymmetrization of 2,3-butanediol (**22a**) with benzoic anhydride in the presence of cat. **11**, according to the general procedure, afforded the monobenzoate (**S1**) in 50% ee in 39% yield (HPLC conditions: CHIRALPAK AD, *n*-hexane/2-propanol = 97:3, flow rate: 0.2 mL/min, t_R = 33 min, 37 min, Scheme I). The absolute configuration of **S1** was

determined to be (2*R*,3*S*) by comparison with the optical rotation of the literature data [2]. Monobenzoate (**S1**) was further converted to (2*R*,3*S*)-**S2** [$[\alpha]_D^{21}$ –13.8 (*c* 1.0, $CHCl_3$)]. On the other hand, 2,3-butanediol isobutyrate (**23a**) obtained in Table 5 was converted to the corresponding benzoate (**S2**), which was assigned to be (2*S*,3*R*) by comparison of the optical rotation of **S2** from Scheme I. Thus, the absolute configuration of **23a** was determined to be (2*R*,3*S*).





cis-2,3-Butanediol diisobutyrate (24a)



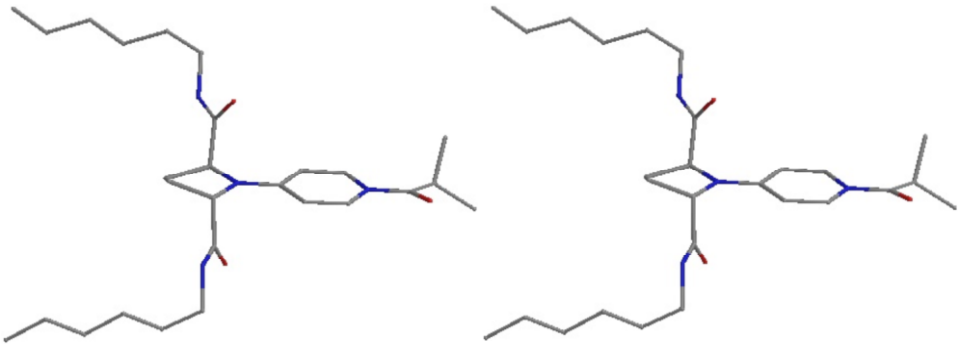
24a

^{1}H NMR (200 MHz, $CDCl_3$) δ 1.00-1.17 (m, 12H), 1.18 (d, *J* = 5.4 Hz, 6H), 2.40–2.62 (m, 2H), 4.90–5.10 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 176.1, 70.8, 34.0, 18.9, 18.7, 14.9. IR (film) 2890, 2870, 2840, 1730 cm^{-1}. MS *m/z* (rel intensity) 230 (M, 0.03), 215 (2), 142 (70), 115 (72), 89 (68), 71 (100), 55 (58). HRMS calcd for $C_{12}H_{22}O_4$ 230.1518, found 230.1521. HRMS calcd for $C_{11}H_{19}O_4$ (M–CH_3) 215.1284, found 215.1287.

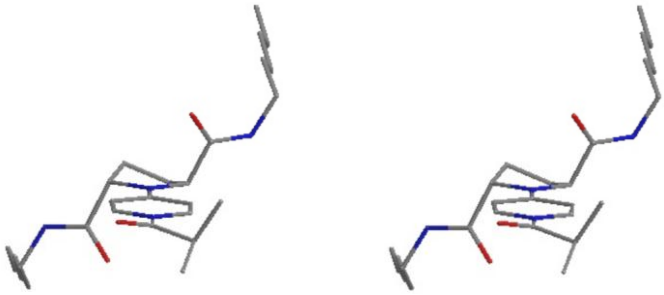
Conformation search of catalyst 11.

The most stable conformer of **11** was generated by a molecular modeling search with AMBER* force field with the GB/SA solvation model for chloroform using MacroModel V 9.0 (50,000 steps MCMM). Stereoview of the most stable conformation was shown below.

(a) side view

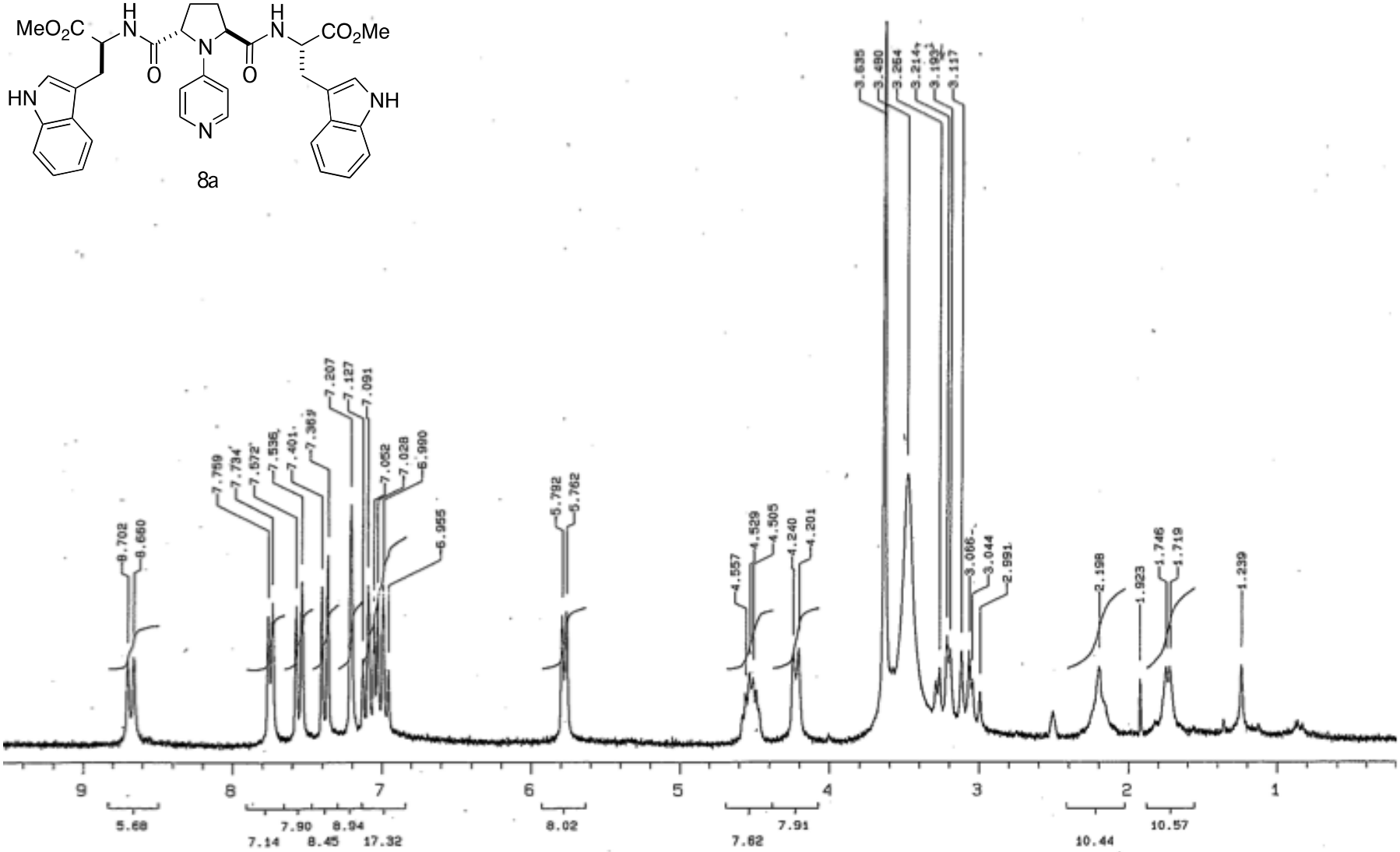


(b) front view



References

1. Kawabata, T.; Muramatsu, W.; Nishio, T.; Shibata, T.; Schedel, H. *J. Am. Chem. Soc.*, **2007**, *129*, 12890.
2. Mazet, C.; Köhler, V.; Pfaltz, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 4888.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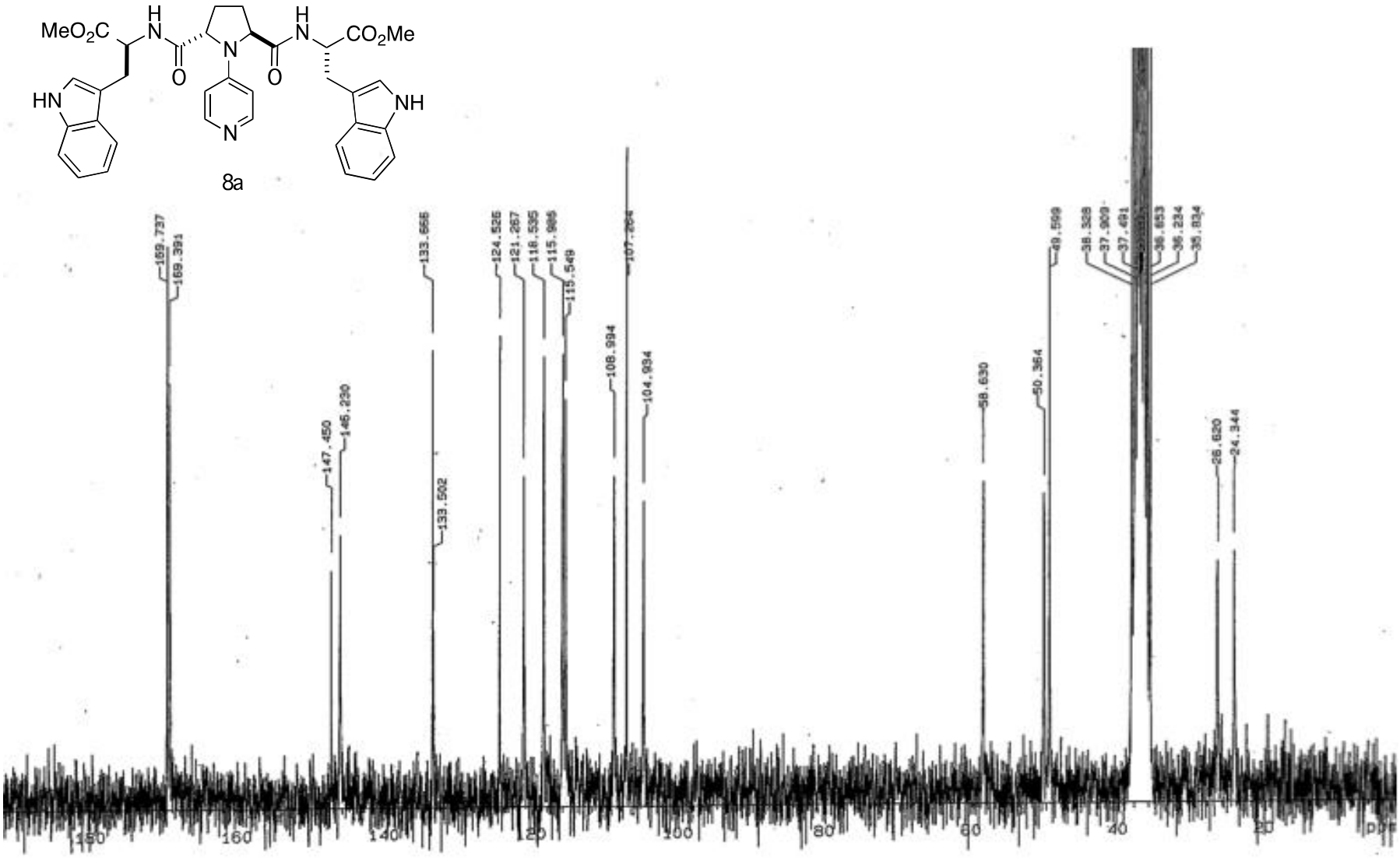
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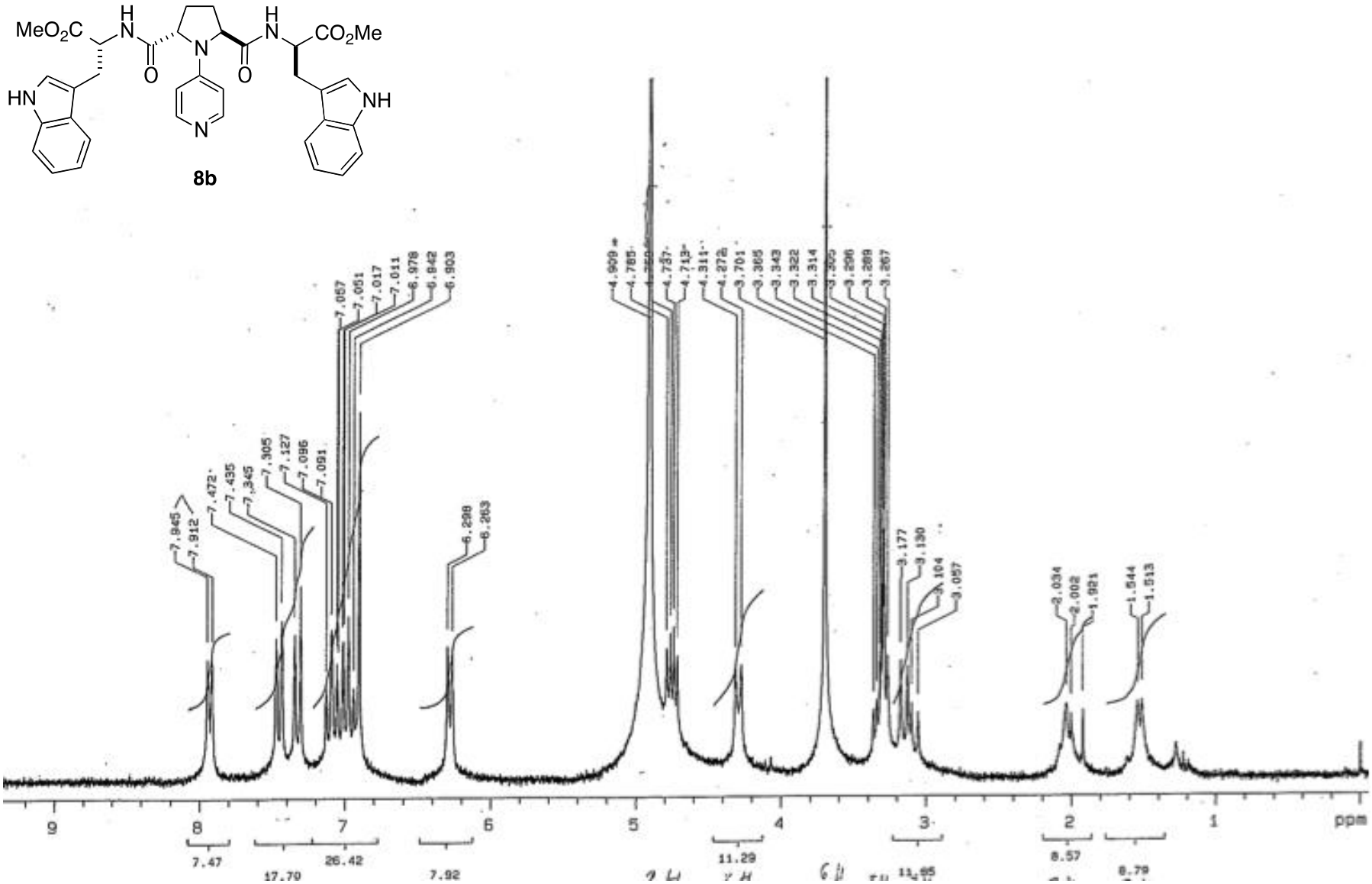
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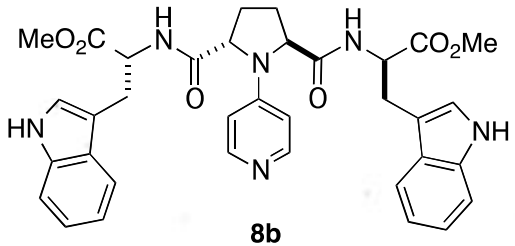
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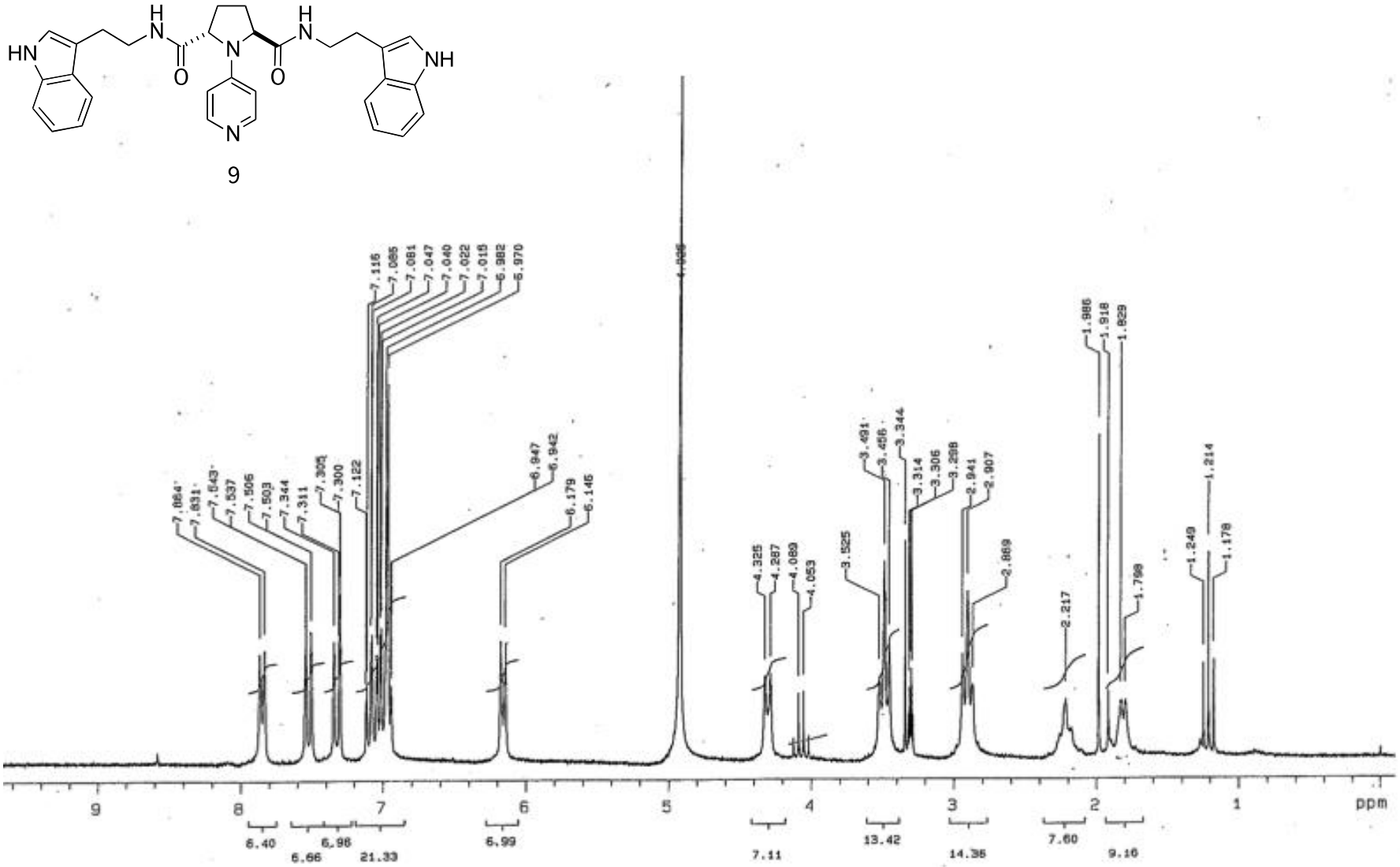
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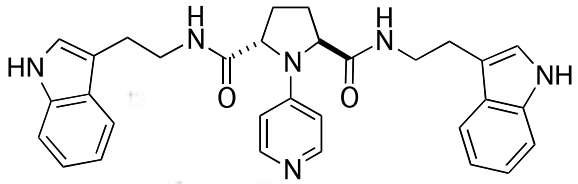
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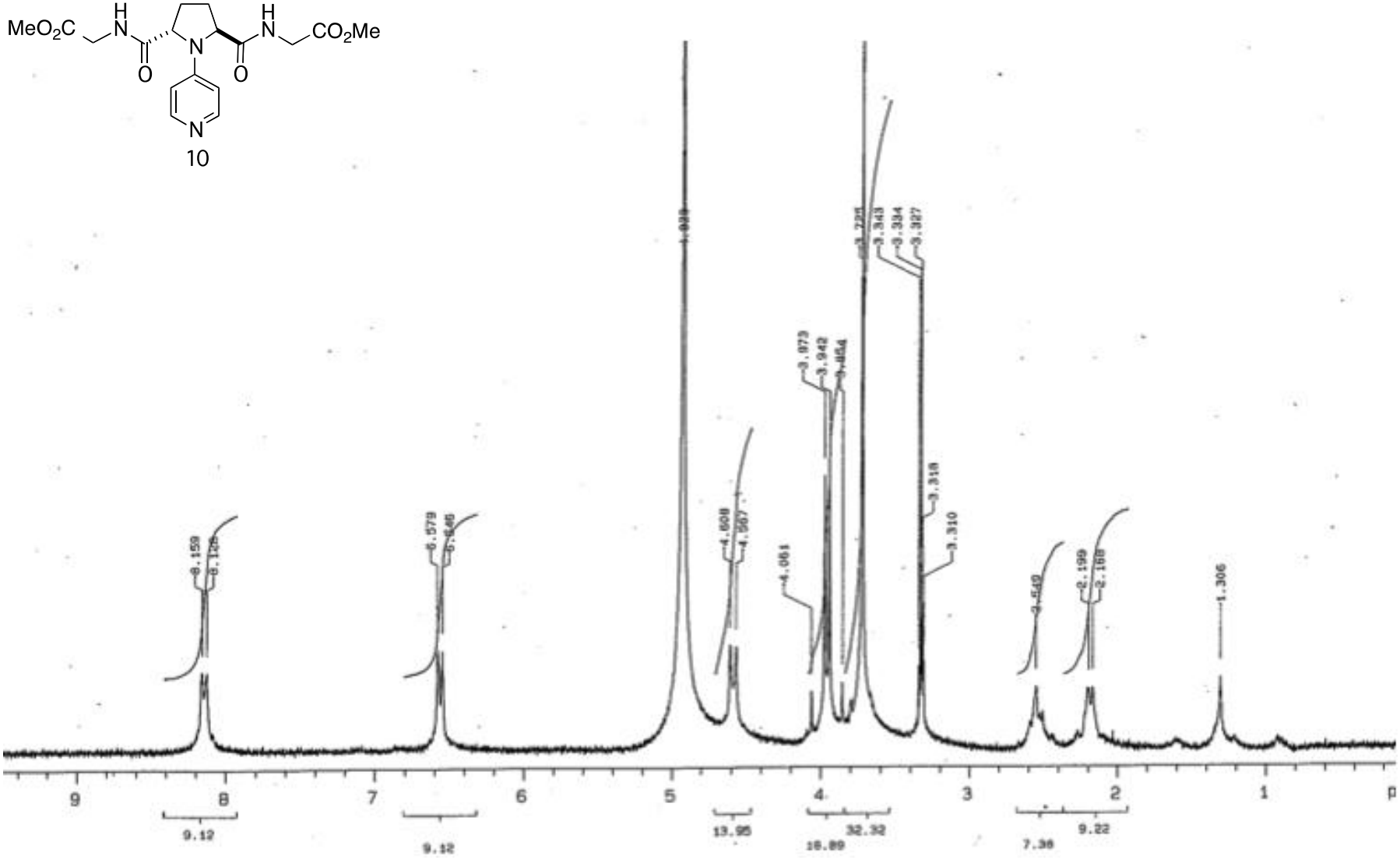
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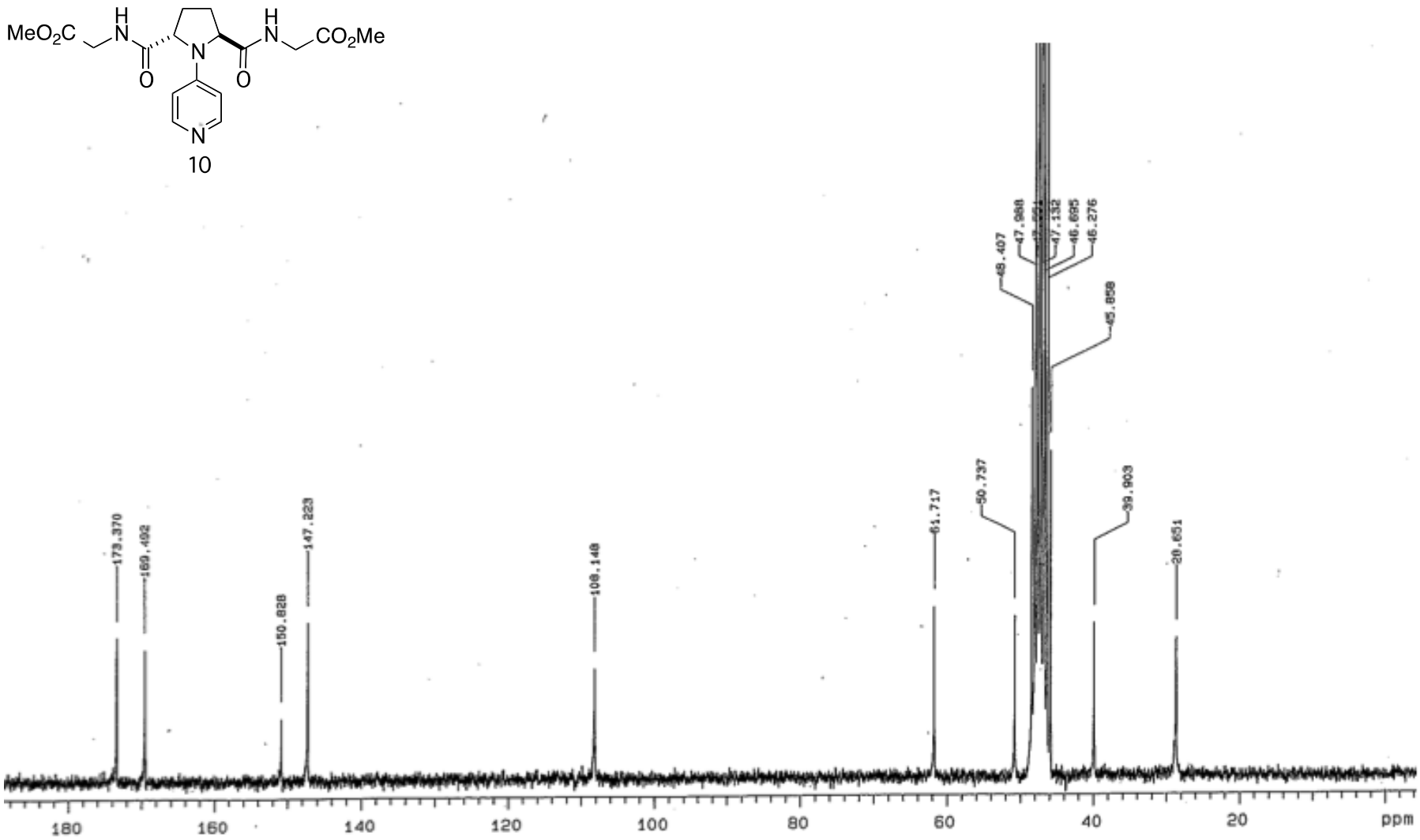
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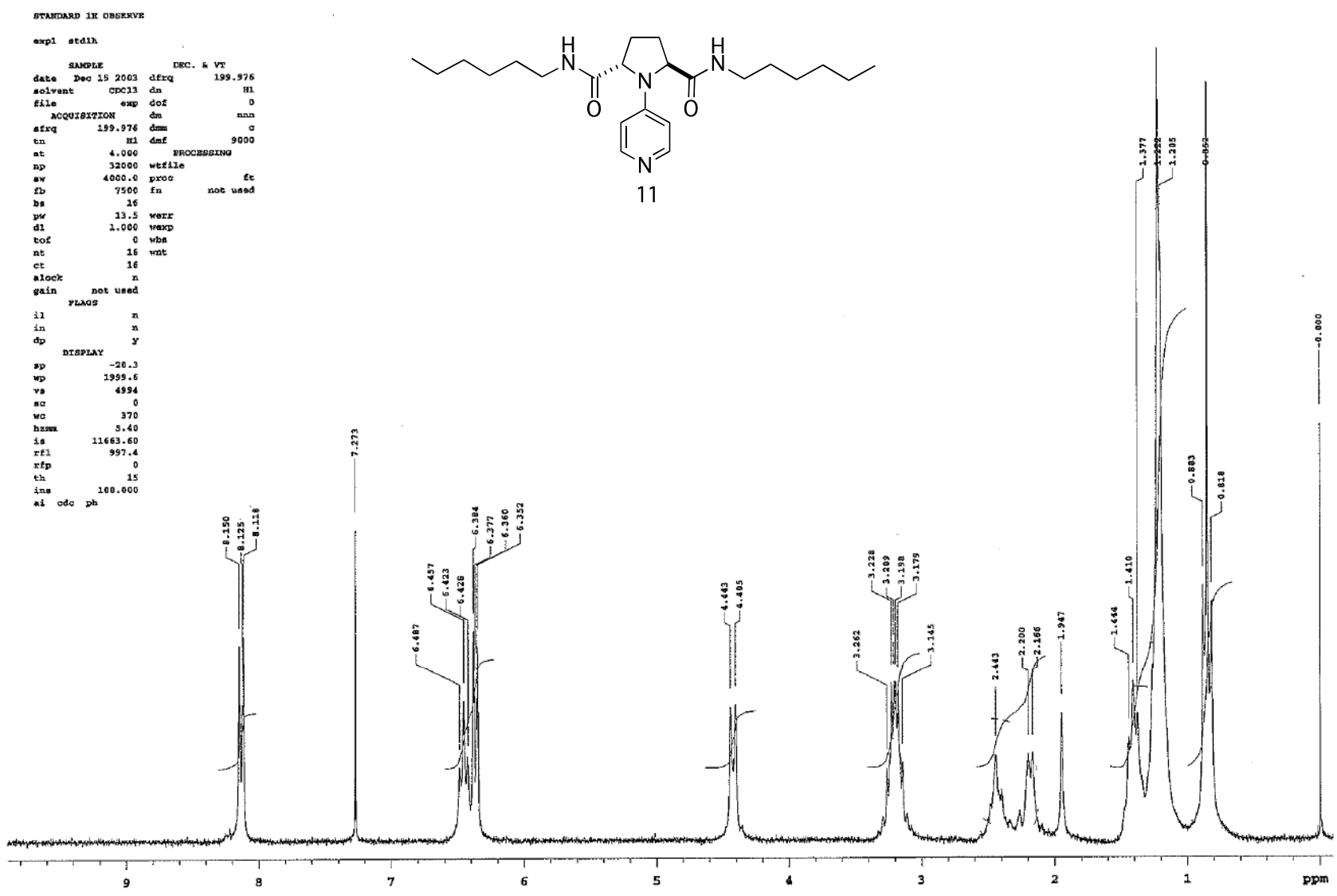
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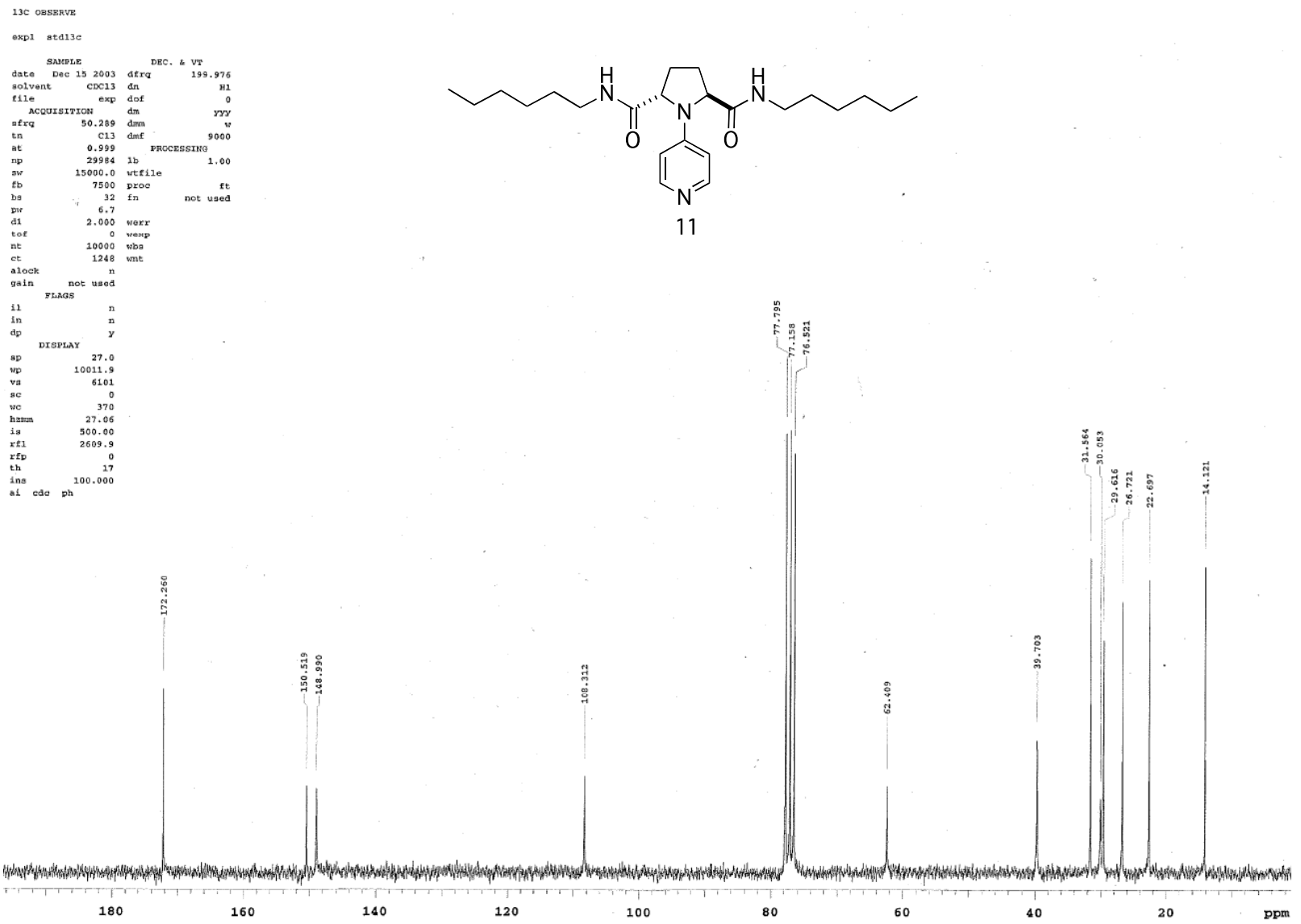
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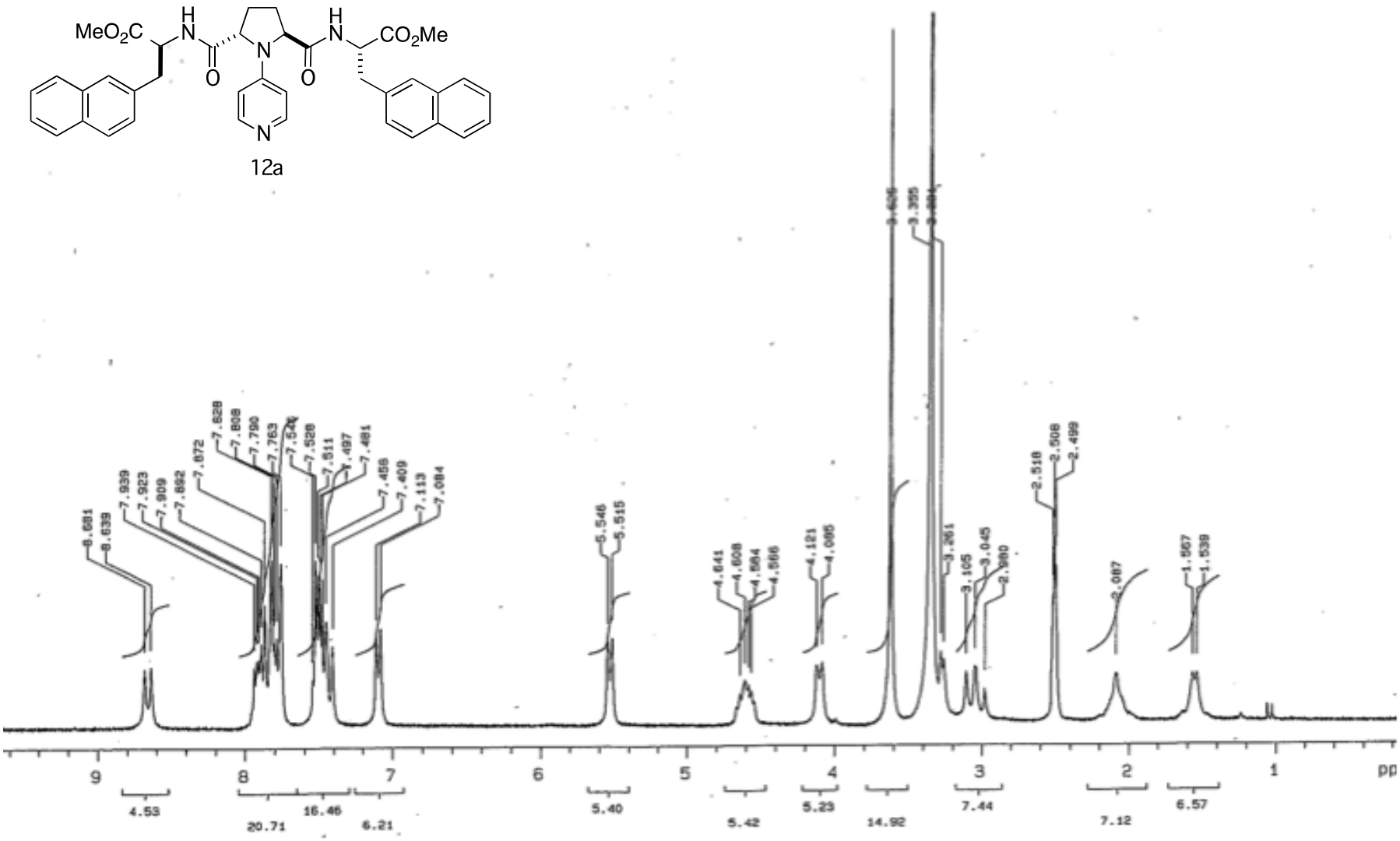
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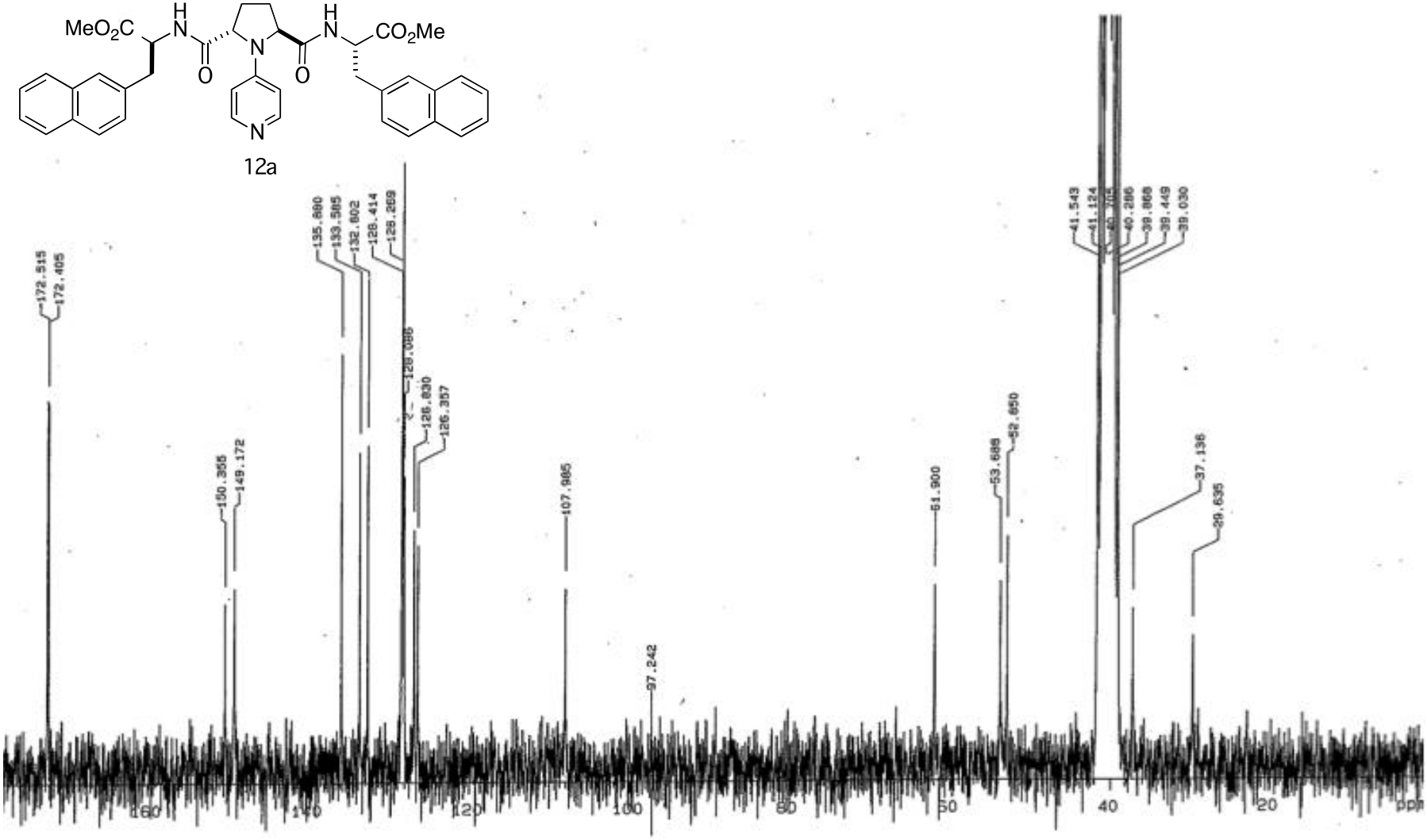
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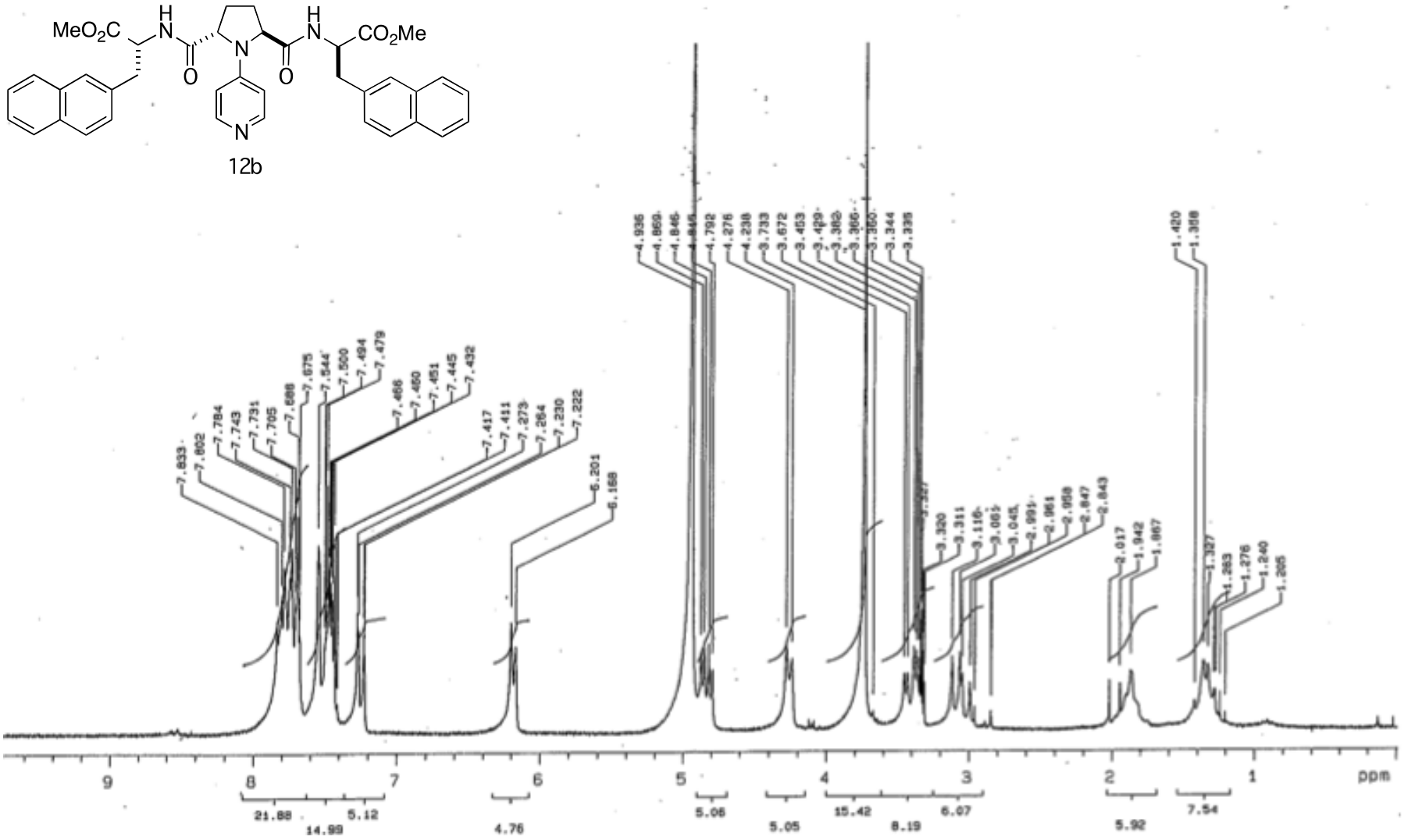
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7.411
7.273
7.264
7.230
7.222
6.201
6.168
4.936
4.869
4.846
4.792
4.276
4.238
3.733
3.672
3.453
3.429
3.382
3.366
3.350
3.344
3.338
3.320
3.311
3.116
3.065
3.045
2.991
2.961
2.958
2.847
2.843
2.017
1.942
1.867
1.420
1.388
1.327
1.283
1.276
1.240
1.205
9
8
7
6
5
4
3
2
1
ppm
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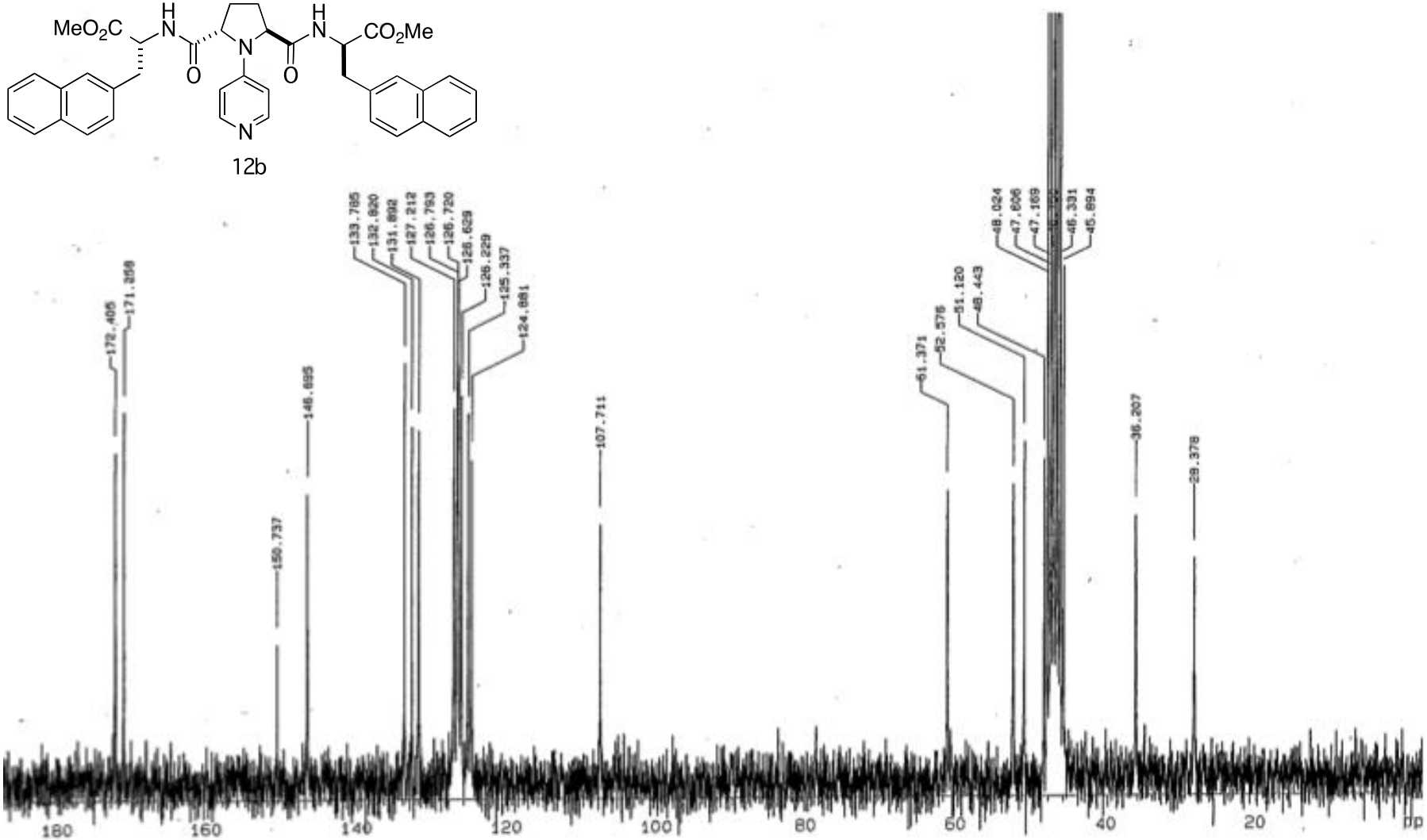
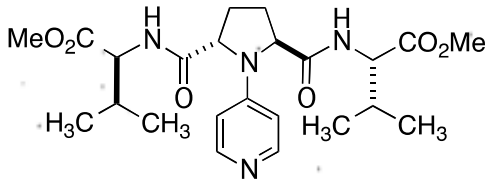
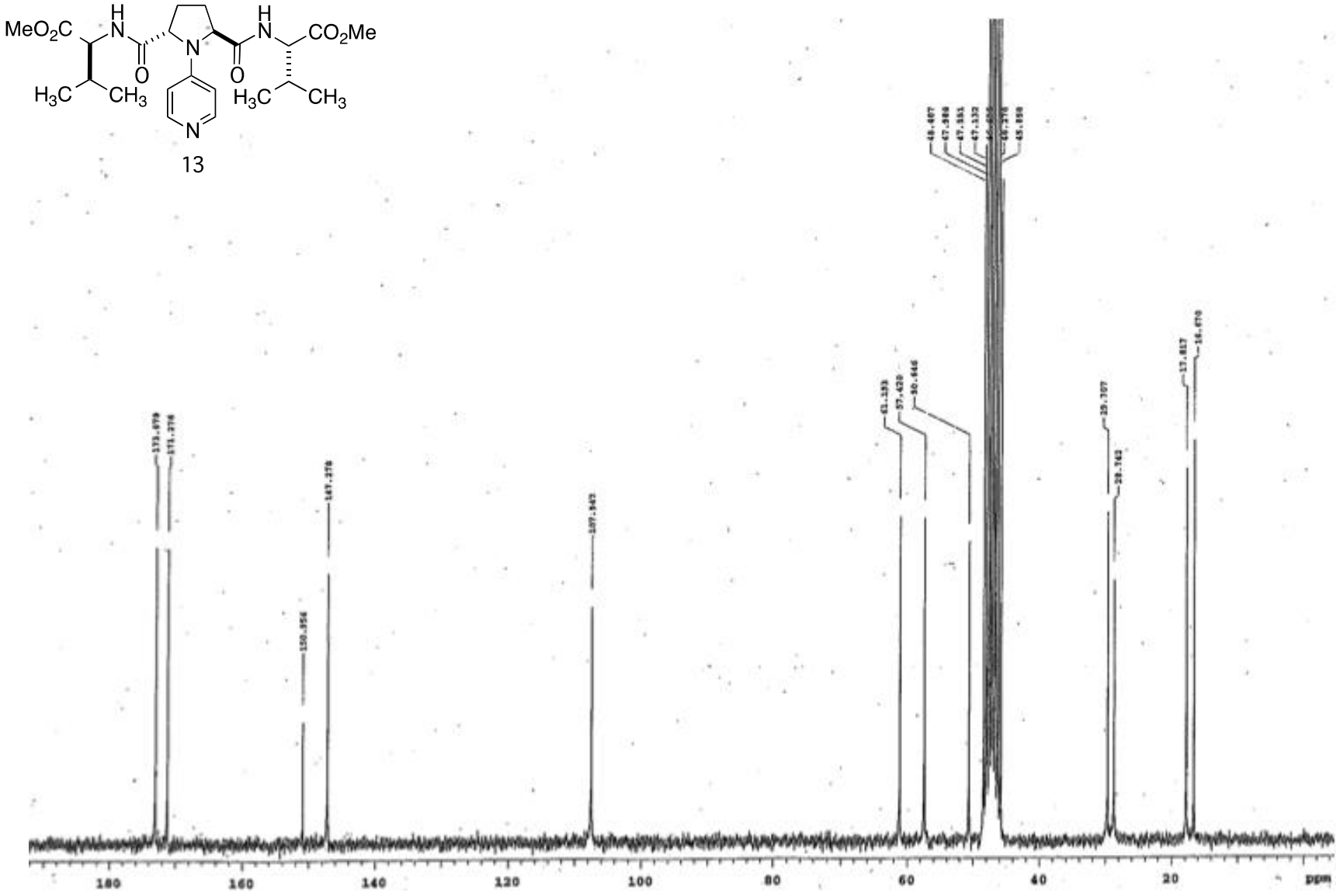
14.99
5.12
4.76
5.06
5.05
15.42
8.19
6.07
5.92
7.54

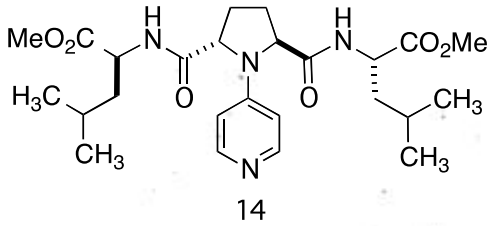

MeO2C
H
N
O
N
H
N
O
CO2Me
N
12b
172.405
171.359
150.737
148.695
133.785
132.820
131.892
127.212
126.793
126.720
126.629
126.229
125.337
124.881
107.711
61.371
52.576
51.120
48.443
48.024
47.606
47.169
46.331
45.894
36.207
29.378
180
160
140
120
100
80
60
40
20
ppm


MeO2C
H
N
O
H3C
CH3
N
N
O
H
N
CO2Me
H3C
CH3

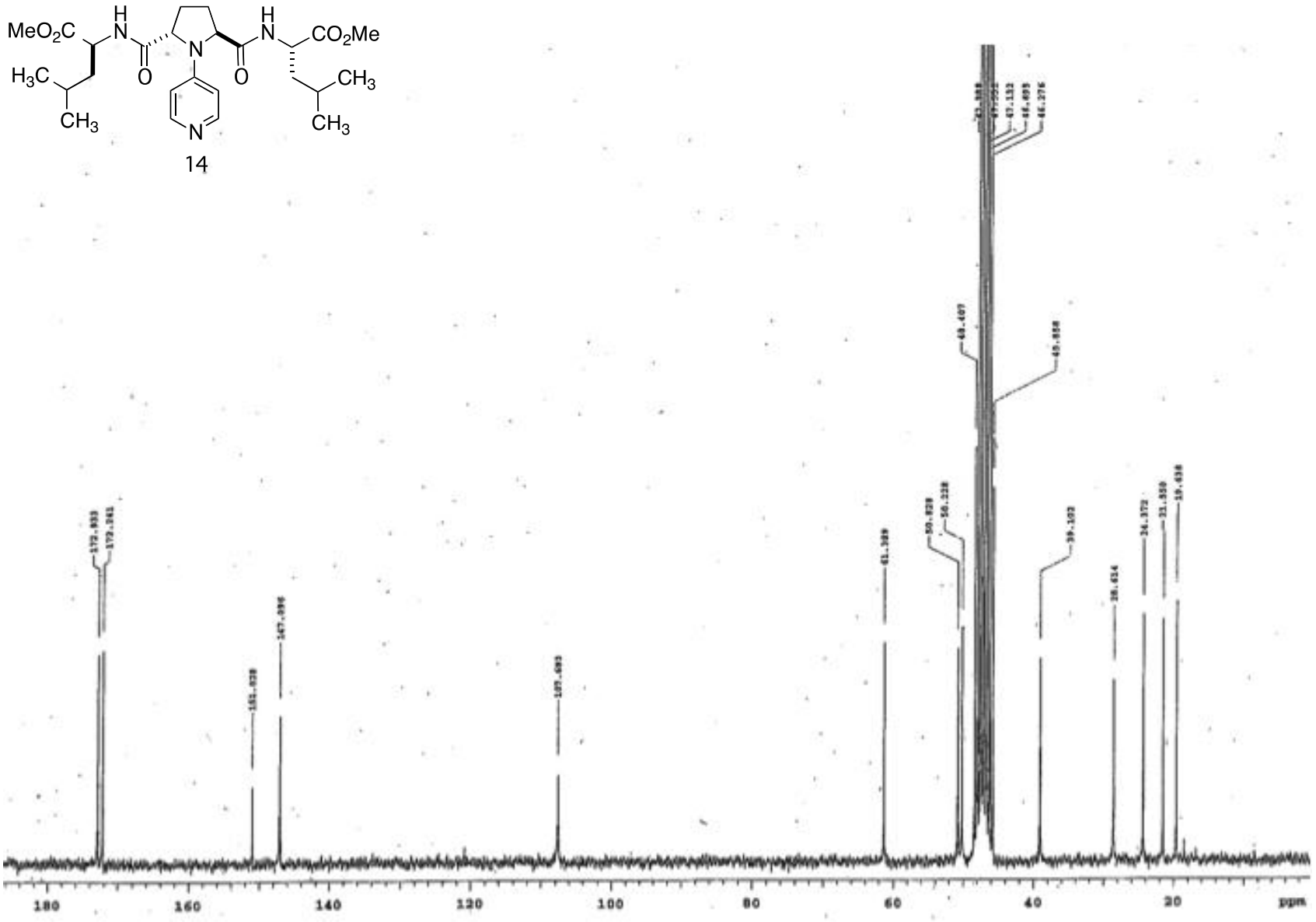
13

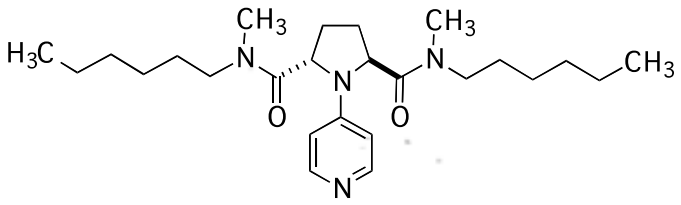
9
8
7
6
5
4
3
2
1
ppm
5.87
5.74
6.46
6.36
17.75
37.92
39.90


MeO2C
H
N
O
N
H
N
CO2Me
O
H3C
CH3
H3C
CH3
N
13
173.679
171.376
150.956
147.378
107.843
61.253
57.420
50.644
48.487
47.988
47.551
47.132
45.858
35.707
28.762
17.817
16.679
180
160
140
120
100
80
60
40
20
ppm



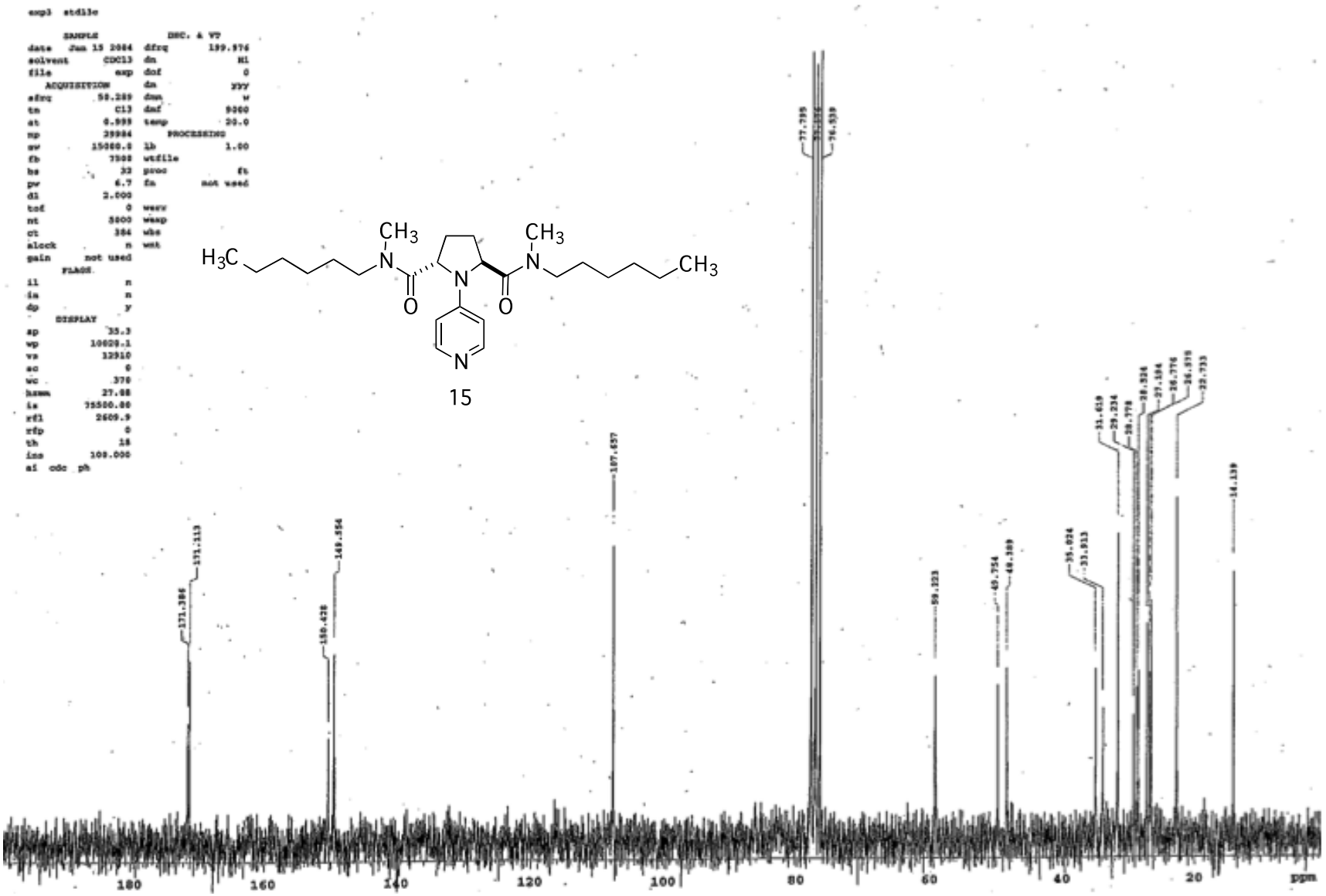
14


MeO2C
H3C
CH3
H
N
O
N
O
H
N
CO2Me
CH3
CH3
N
14
180
160
140
120
100
80
60
40
20
ppm


H3C
CH3
N
O
N
N
O
CH3
N
CH3

15

1.0486
0.0387
1.0000
1.0330
1.9136
4.0052
0.8970
1.0505
1.9059
6.1939
3.1939
2H
1
1
2
6
3
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


exp3 stdlic
SAMPLE
date Jun 15 2004
solvent CDCl3
file exp
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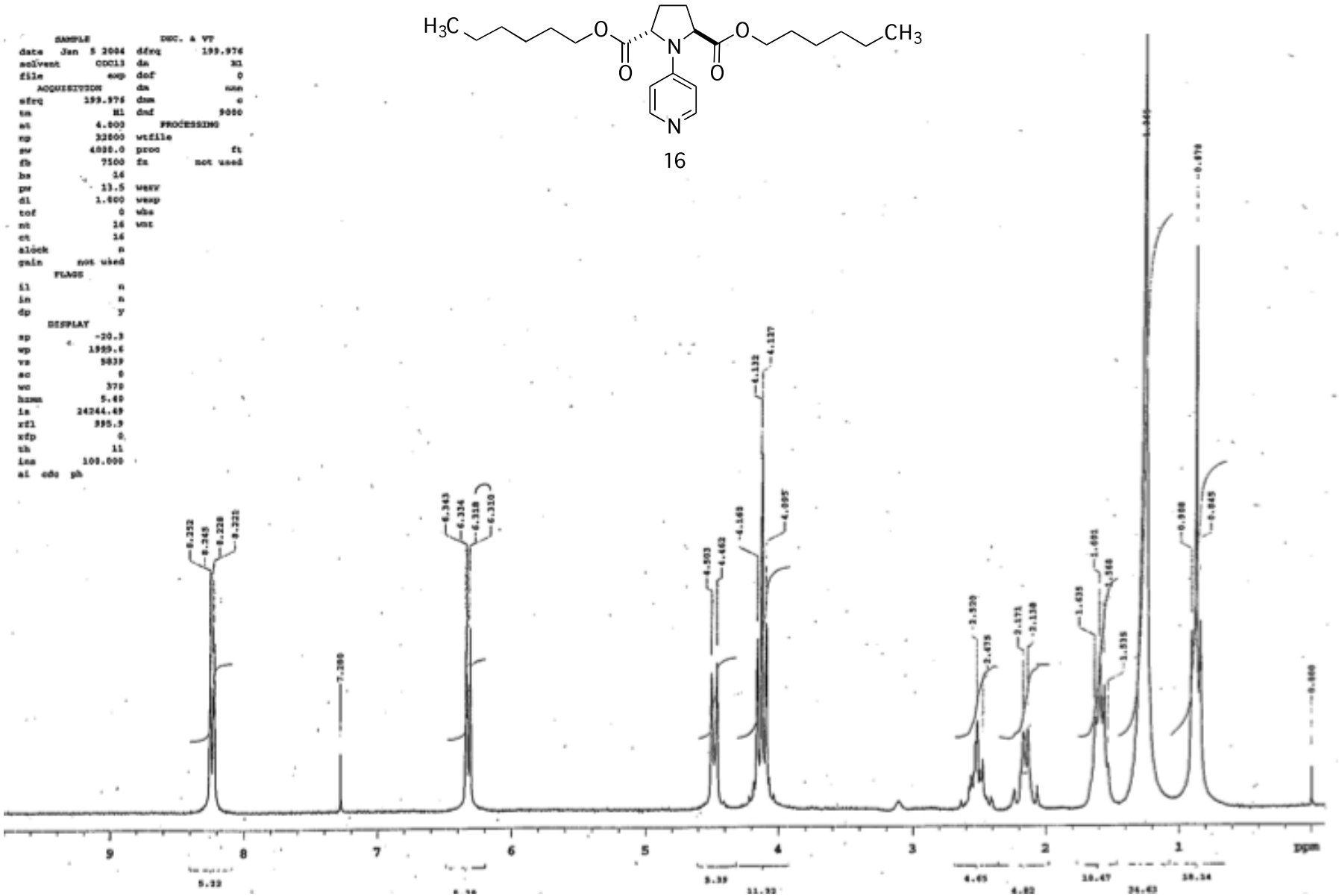
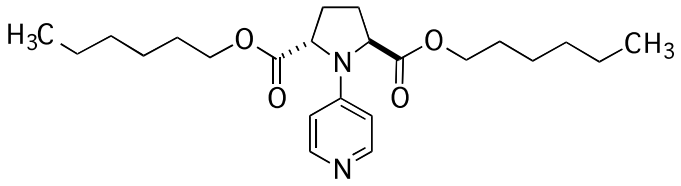
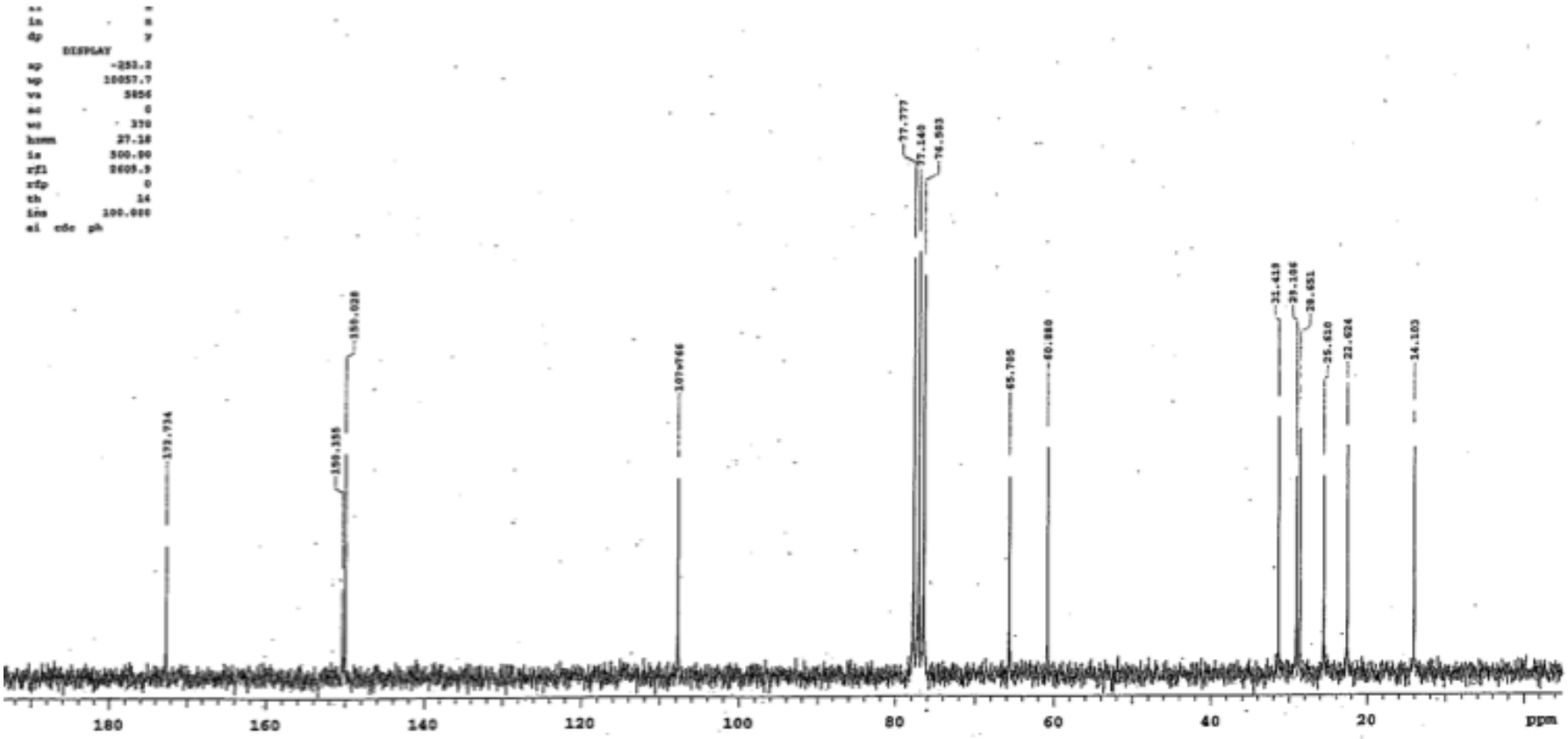
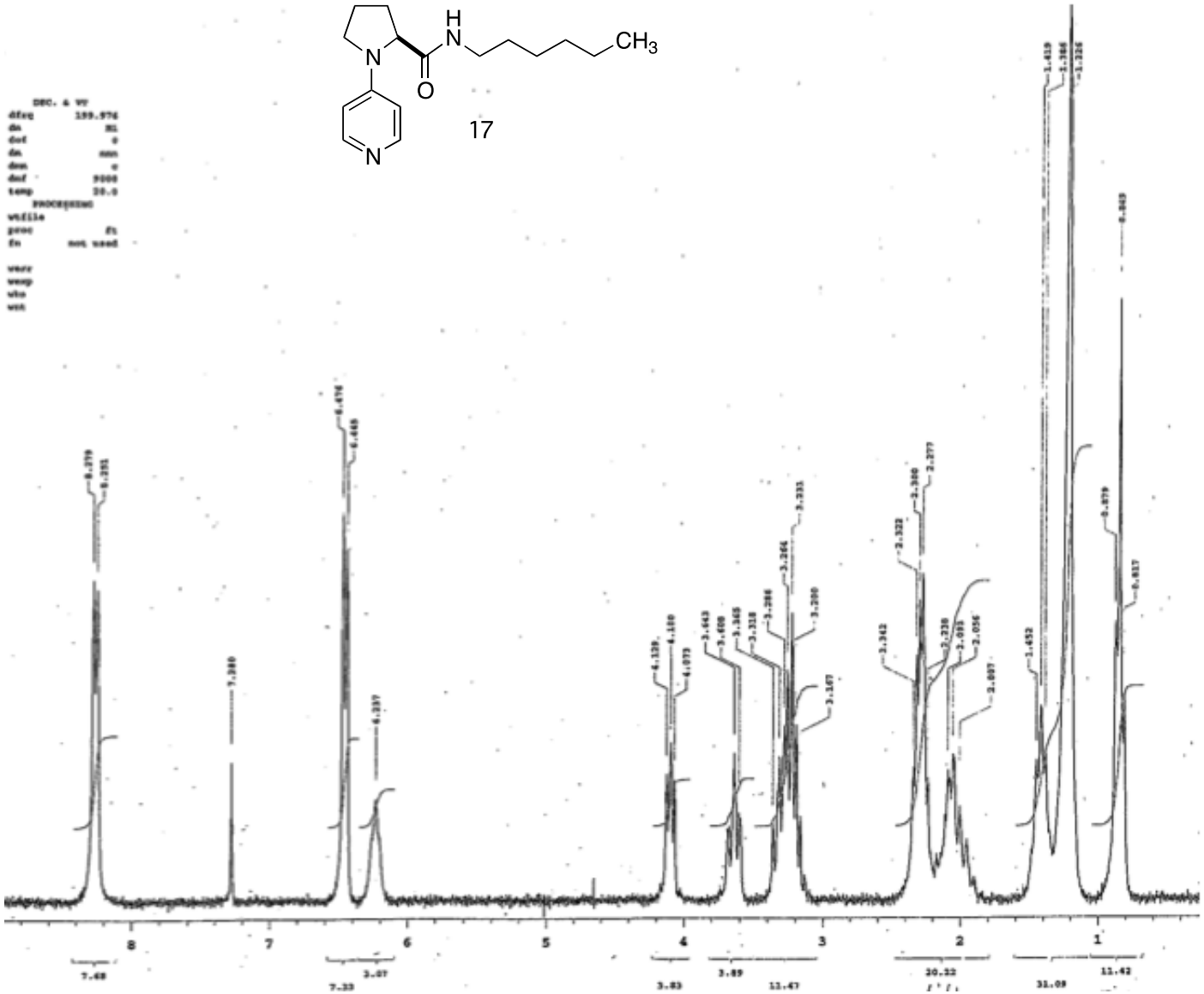
tn C13
at 0.999
np 29984
sw 15060.5
fb 7508
bs 32
pw 6.7
d1 2.000
tof 0
nt 5600
ct 384
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp 35.3
wp 10028.1
vs 12910
sc 0
wc 370
hzmm 27.88
is 75500.00
rfl 2609.9
rfp 0
th 18
ins 109.000
ai cdc ph
DEC. & VT
dfrq 199.976
dn H1
dof 0
dm yyy
dmm w
dmf 9200
temp 20.0
PROCESSING
lb 1.00
wtfile
proc ft
fn not used
wexv
wexp
whe
wnt
15
171.113
171.386
149.354
149.428
107.657
77.395
59.323
49.754
49.389
35.024
31.913
31.619
29.234
28.778
28.534
27.184
26.776
26.939
22.733
14.139
180
160
140
120
100
80
60
40
20
ppm

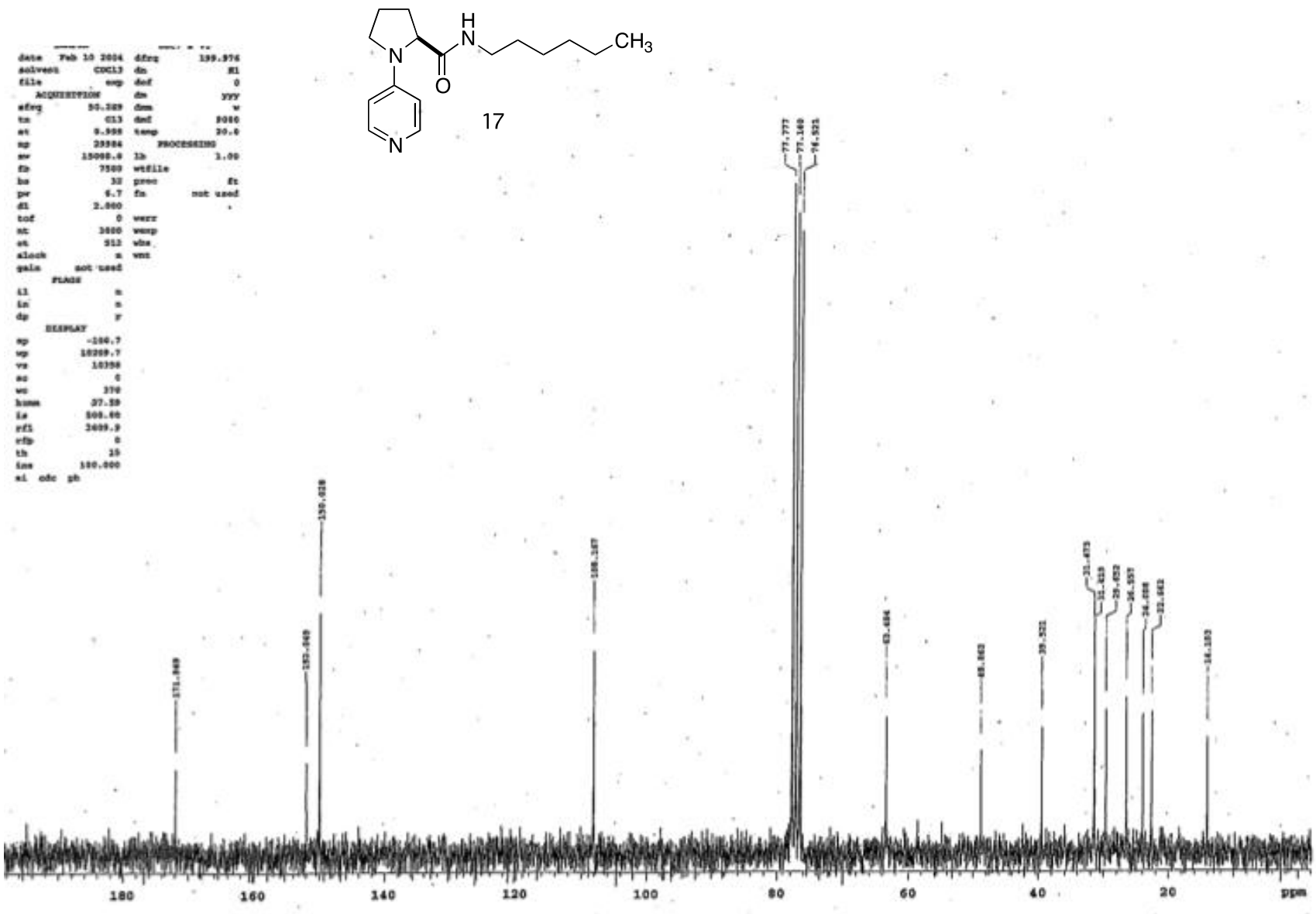

H3C
CH3
O
O
O
O
N
N
16
SAMPLE
date Jan 5 2004
solvent CDCl3
file exp
ACQUISITION
sfrq 199.976
tn H1
at 4.000
np 32800
sw 4032.0
fb 7500
bs 16
pw 13.5
d1 1.000
tof 0
nt 16
ct 16
alock n
gain not used
FLAGS
il n
in n
dp y
DISPLAY
sp -20.3
wp 1959.6
vs 5039
sc 0
wc 379
hzmm 5.49
is 24244.49
rfl 395.9
rfp 0
th 11
ins 100.000
ai cdc ph
DEC. & VT
dfrq 199.976
dn H1
dof 0
dm nnn
dmm c
dmf 9000
PROCESSING
wtfile
proc ft
fn not used
wexv
wexp
wbs
wnt
7.280
ppm
5.33
11.33
4.65
4.82
10.47
24.63
10.14

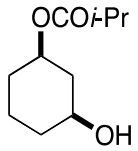

H3C
O
O
N
O
O
CH3
N

16

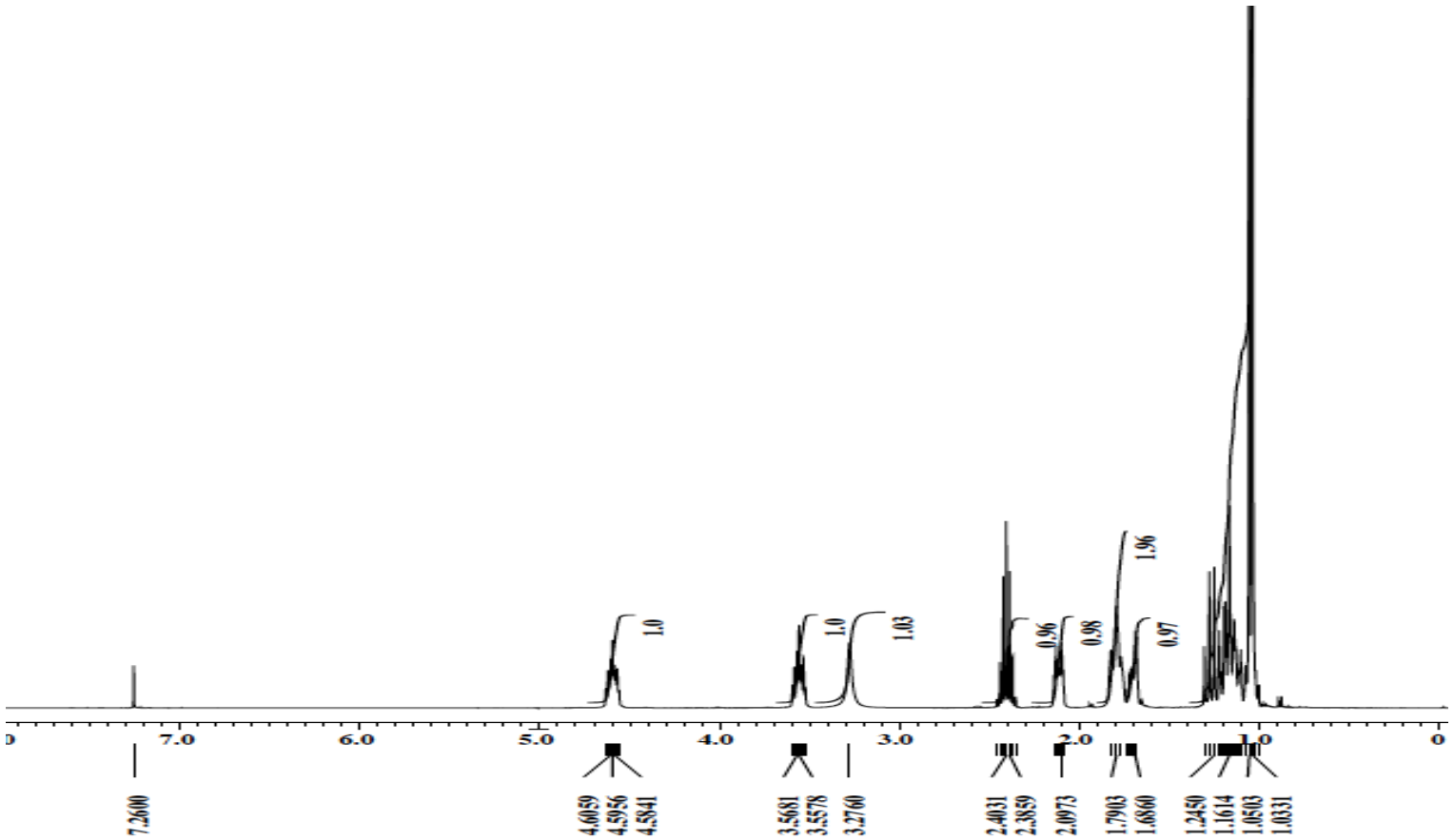

DISPLAY
173.734
159.355
159.028
107.766
77.777
77.140
76.503
65.705
60.880
31.419
29.186
28.651
25.610
22.624
14.103
180
160
140
120
100
80
60
40
20
ppm

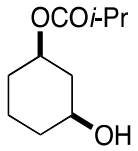

H
N
CH3
N
O
N
17


17
CH3
ppm

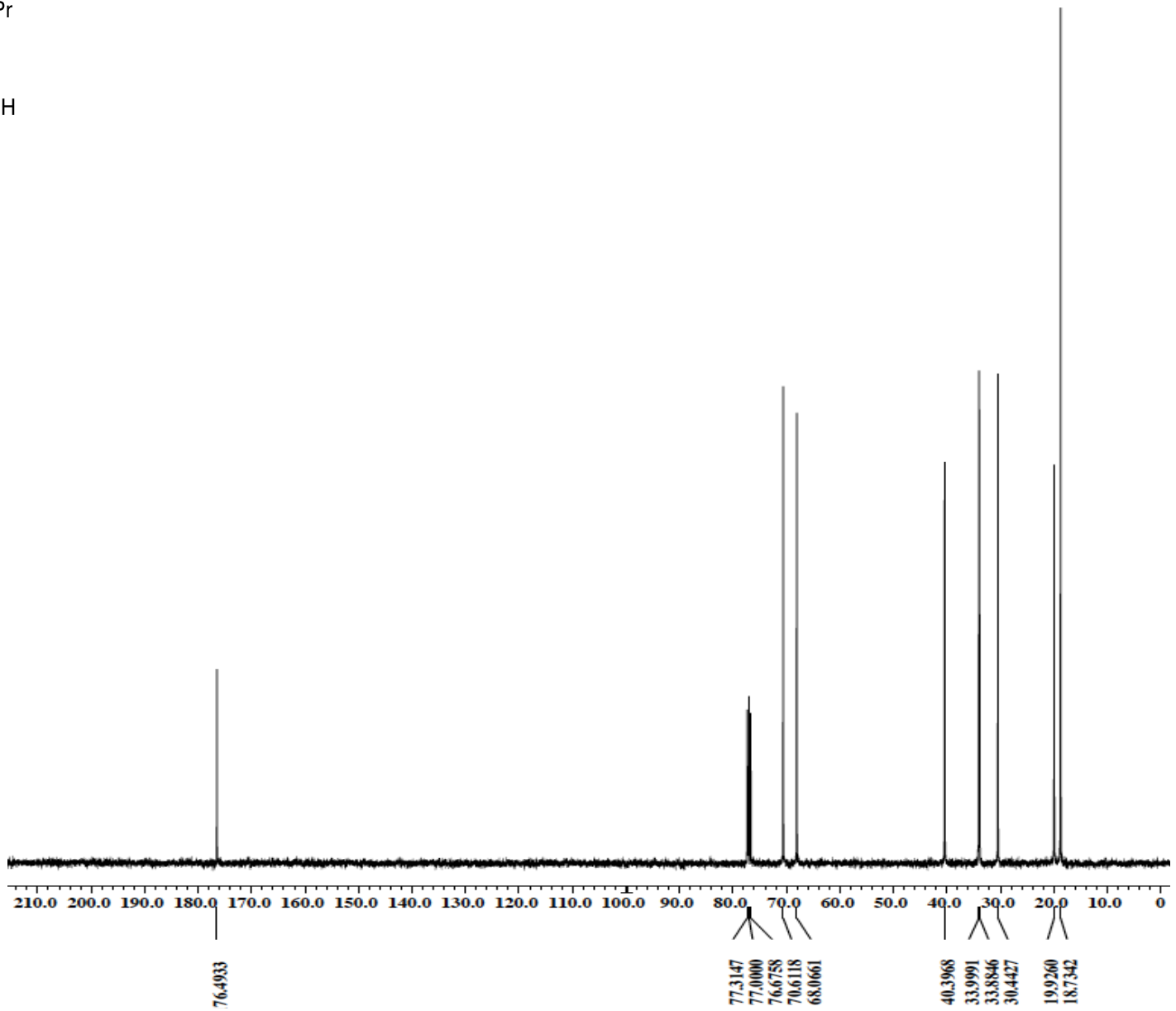

OCOi-Pr
OH

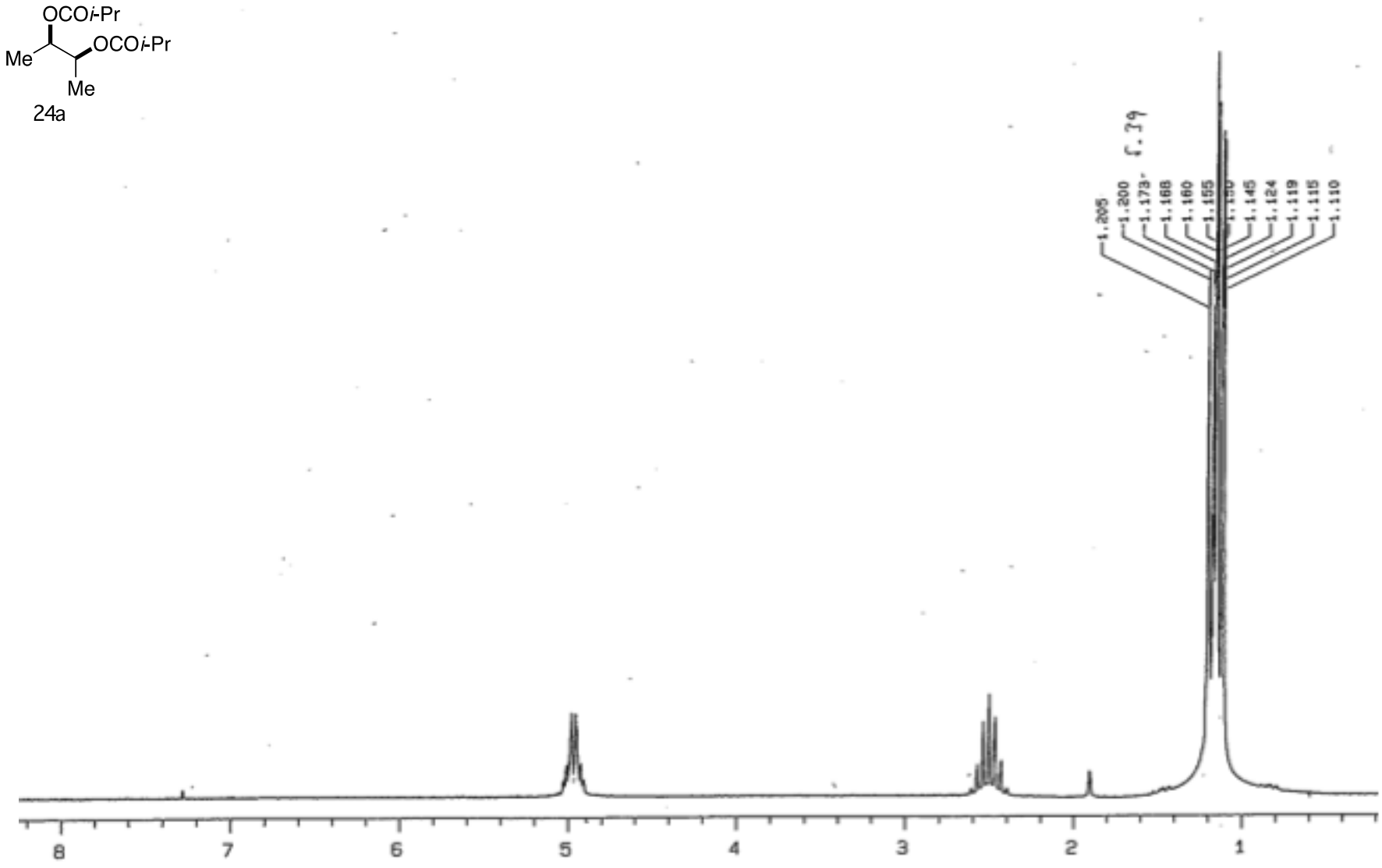
20

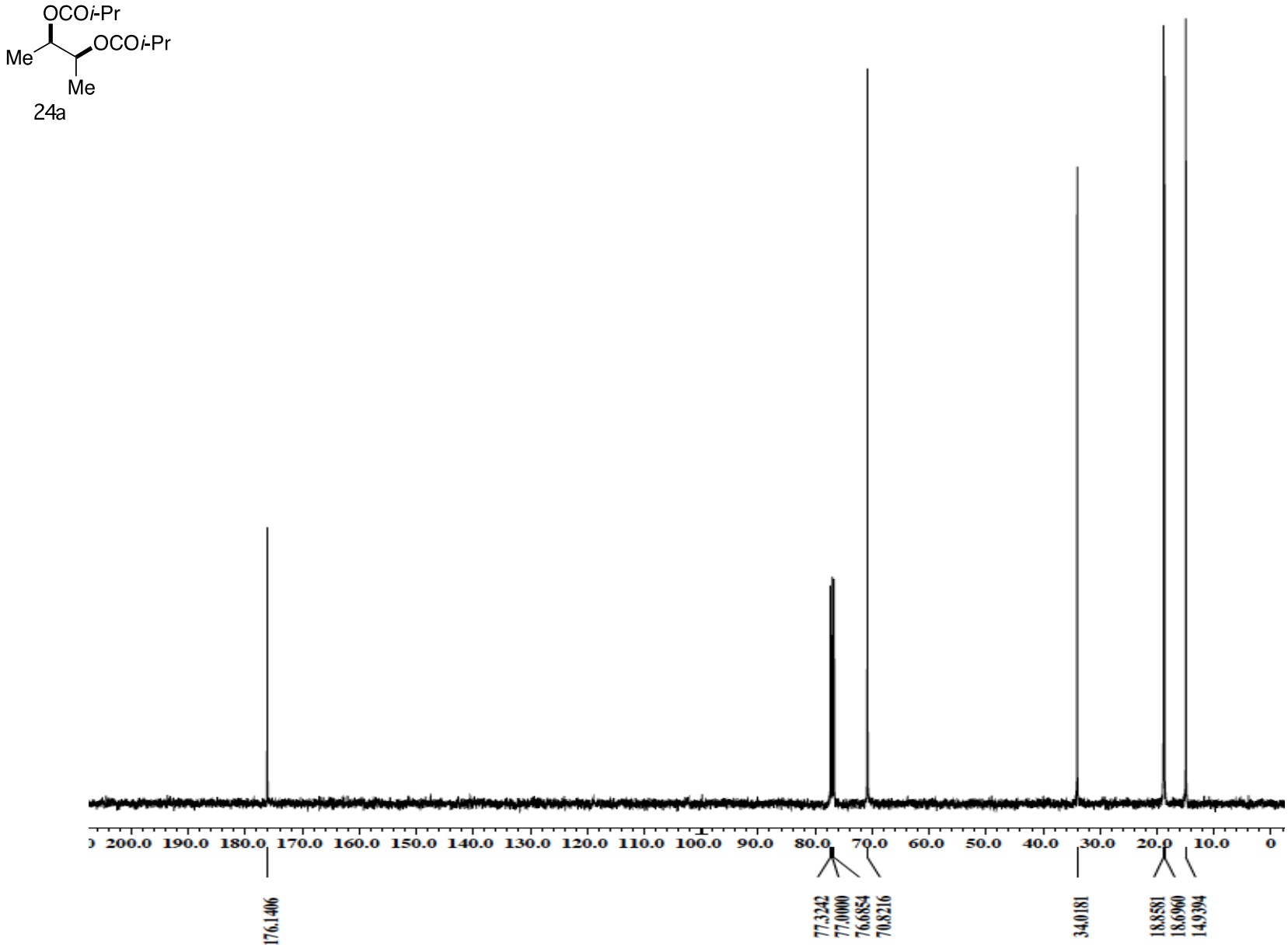

1.0
1.0
1.03
0.96
0.98
1.96
0.97
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2600
4.6059
4.5956
4.5841
3.5681
3.5578
3.2760
2.4031
2.3859
2.0973
1.7903
1.6860
1.2450
1.1614
1.0503
1.0331


OCO*i*-Pr
OH

20


210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
76.4933
77.3147
77.0000
76.6758
70.6118
68.0661
40.3968
33.9991
33.8846
30.4427
19.9260
18.7342


OCO*i*-Pr
Me
OCO*i*-Pr
Me
24a
1.205
1.200
1.173
1.168
1.160
1.155
1.145
1.124
1.119
1.115
1.110
8
7
6
5
4
3
2
1


OCOi-Pr
OCOi-Pr
Me
Me
24a
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
176.1406
77.3242
77.0000
76.6854
70.8216
34.0181
18.8581
18.6960
14.9394