Supporting Information

Direct Organocatalytic Asymmetric Aldol Reactions of α-Amino Aldehydes: Expedient Syntheses of Highly Enantiomerically Enriched *anti*-β-Hydroxy-α-Amino Acids

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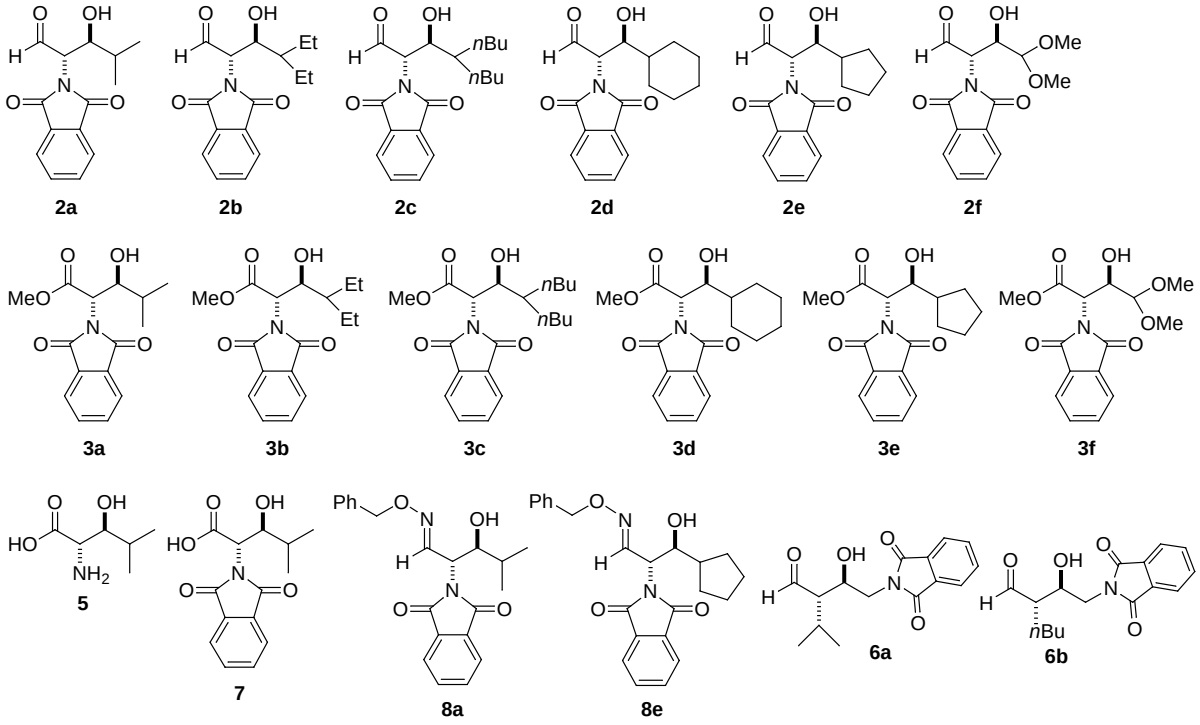
Phthalimidoacetaldehyde (1). To a stirred mixture of a solution of phthalic anhydride (25 g, 169 mmol) in DMF (100 mL) and molecular sieves 4A (5 g), allylamine (15 mL, 200 mmol) was slowly added at rt. The mixture was stirred at 100 °C for overnight.[S1] After cooling to rt, the mixture was filtered through celite and the filtrate was concentrated *in vacuo*. The residue was dissolved in EtOAc, washed with saturated aqueous NH_4Cl and with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2-MeOH (9:1, 500 ml) and ozone was bubbled through the solution at –78 °C for 5 h until a blue color persisted. The mixture was purged N_2 until the blue color disappeared at the same temperature. Dimethylsulfide (90 mL, 1.2 mol) was added and the mixture was allowed to warm to rt and stirred for 16 h at which point it was concentrated *in vacuo*. The residue was crystallized from CH_2Cl_2/hexanes to give **1**[S2] as colorless crystals (22 g, 68 %).

(2*S*,3*S*)-2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-4-methyl-pentanal (2a) (Table 1 entry 6). To a mixture of aldehyde **1** (378 mg, 2 mmol) and isobutyraldehyde (1.8 mL,

20 mmol) in NMP (1mL) was added L-proline (69 mg, 0.6 mmol) at 0 °C and the mixture was stirred at 4 °C. After 36 h, excess isobutyraldehyde was removed *in vacuo*, and EtOAc and saturated aqueous NH_4Cl were added to the residue. The organic layer was washed with brine, dried over $MgSO_4$, filtered, concentrated *in vacuo*, and flash chromatographed (silica gel, EtOAc/hexane = 20:80) to afford **2a** (454 mg, 87%, dr = >100:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H, C<u>H</u>O), 7.91-7.76 (m, 4H), 4.94 (d, *J* = 5.0 Hz, 1H, α-H), 4.15 (m, 1H), 3.67 (d, *J* = 3.5 Hz, 1H), 1.98 (m, 1H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H); (2*S**,3*R**)-isomer: 9.71 (s, C<u>H</u>O), 5.25 (d, *J* = 4.1 Hz, α-H).



(2*S*,3*S*)-2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-4-methyl-pentanal *O*-benzyl-oxime (8a). Aldehyde **2a** was transformed to oxime **8a** with *O*-benzylhydroxylamine hydrochloride according to the reported procedure.[S3] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.73 (m, 4H), 7.40-7.27 (m, 6H), 5.05-5.02 (2H), 4.06 (m, 1H), 3.32 (d, *J* = 3.8 Hz, 1H), 1.74 (m, 1H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H). HRMS (ESI-TOF): calcd for $C_{21}H_{23}N_2O_4$

(MH^+) 367.1652, found 367.1655. HPLC (Daicel Chiralcel OD-H, 2-PrOH/hexane = 10:90, flow rate 1.0 mL/min, 254 nm): (2*S*,3*S*) 19.8 min, (2*R*,3*R*) 38.9 min.

(2*S*,3*S*)-2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-4-methyl-pentanoic acid methyl ester (3a) (Table 1 entry 7). To a mixture of aldehyde **1** (378 mg, 2 mmol) and isobutyraldehyde (1.8 mL, 20 mmol) in NMP (1mL) was added L-proline (69 mg, 0.6 mmol) at 0 °C and the mixture was stirred at 4 °C. After 36 h, excess isobutyraldehyde was removed *in vacuo*, and EtOAc and saturated aqueous NH_4Cl were added to the residue. The organic layer was washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in *t*BuOH:H_2O (5:1, 24 mL) and to this solution was added successively NaH_2PO_4 (480 mg, 4.0 mmol), 2-methyl-2-butene (2M solution in THF, 6.8 mL, 13.6 mmol) and $NaClO_2$ (624 mg, 6.9 mmol).[S4] The reaction mixture was stirred at rt for 4 h. The volatile components were removed *in vacuo* and the residue was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in toluene (2 mL) and methanol (5 mL) and $TMSCHN_2$ (2M solution in hexane) was added by dropwise at –20 °C until the yellow color persisted. The solution was stirred for additional 10 min and quenched with a drop of acetic acid. The solvents were removed *in vacuo* and the residue was purified by silica gel flash column chromatography (EtOAc/hexane = 5:95–10:90) to afford **3a** (425 mg, 73% for 3 steps from **1**, dr = >100:1, >99.5% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92-7.77 (m, 4H), 4.95 (d, *J* = 6.8 Hz, 1H), 4.21 (m, 1H), 4.11 (d, *J* = 2.4 Hz, 1H), 3.75 (s, 3H), 1.81 (m, 1H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 167.7, 134.4, 131.6, 123.7, 74.2, 54.6, 52.6, 52.9, 29.6, 19.9, 15.9. IR (neat) 3537, 2960, 1710, 1383, 1249, 1208, 1173, 1086, 716 cm^{-1}. HRMS (ESI-TOF): calcd for $C_{15}H_{18}NO_5$ (MH^+) 292.1179, found 292.1177. HPLC (Daicel Chiralcel OD-H, 2-PrOH/hexane = 5:95, flow rate 1.0 mL/min, 254 nm): (2*S*,3*S*) 10.3 min, (2*R*,3*R*) 13.0 min. $[\alpha]^{24}_D$ +7.1 (c 1.0, $CHCl_3$).

(2*S*,3*S*)-2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-4-methyl-pentanoic acid (7). The aldol reaction of **1** and isobutyraldehyde and oxidation at Table 1 entry 7 was

performed using of **1** (2.00 g, 10.5 mmol) and the residue was purified by silica gel flash chromatography ($CHCl_3$/MeOH = 90:10) to afford **7** (1.92 g, 66%). ^{1}H NMR (400 MHz, CD_3OD) δ 7.86-7.77 (m, 4H), 4.57 (d, *J* = 9.4 Hz, 1H), 4.37 (dd, *J* = 2.4 Hz, 9.4 Hz, 1H), 1.60 (m, 1H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 177.1, 169.6, 135.5, 133.2, 124.3, 74.2, 56.1, 30.8, 20.3, 15.0. HRMS (ESI-TOF): calcd for $C_{14}H_{16}NO_5$ (MH^+) 278.1023, found 278.1025. This acid **7** (5 mg) was transformed to methyl ester **3a** as described above and the ee was determined to be >99.5% ee.

(2*S*,3*S*)-3-Hydroxyleucine (5). To a stirred solution of **7** (1.92 g, 6.93 mmol) in EtOH (100 mL), anhydrous hydrazine (35 mL) was added at rt and the mixture was refluxed for 2 h until a precipitate of phthalazone was formed.[S5] The mixture was cooled to rt and filtered, and the filtrate was concentrated *in vacuo*. The solid residue was dissolved in water and was washed with $CHCl_3$ (x 5). The aqueous layer was loaded to Dowex 50WX4-100 ion-exchange resin (H^+ form) and the resin was washed with water (1 L) then eluted with 2N pyridine.[S6] The eluted fractions were lyophilized to afford (2*S*,3*S*)-hydroxyleucine (**5**) (940 mg, 92% from **7**, 60% from **1**) as a colorless solid. ^{1}H NMR (400 MHz, D_2O) δ 3.78 (d, *J* = 3.2 Hz, 1H), 3.41 (dd, *J* = 3.2 Hz, 9.0 Hz, 1H), 1.82 (m, 1H), 0.86 (d, *J* = 6.4 Hz, 3H), 0.85 (d, *J* = 6.4 Hz, 3H). HRMS (ESI-TOF): calcd for $C_6H_{14}NO_3$ (MH^+) 148.0968, found 148.0966. $[\alpha]^{25}_D$ +27.6 (c 0.6, H_2O) [lit.[S6] $[\alpha]^{20}_D$ +20.9 (c 1.03, H_2O) as 98% ee; lit.[S7] $[\alpha]^{28}_D$ +37 (c 1.0, H_2O)].

Reactions in Table 2. Aldol reactions in Table 2 were performed using the same procedures as the procedures for Table 1 entry 7, but excess acceptor aldehydes were removed by fast silica gel column chromatography after work-up. The diastereomeric ratio of the aldol products decreased when they were stored or when they were purified by silica gel column chromatography. Attempts to obtain pure aldol products resulted lower yield and lower diasteromeric ratio. Thus, the chromatography was quickly performed to remove excess acceptor aldehyde instead of focusing to purify aldol product **2**. Oxidation and esterification were also performed using the same procedures for Table 1 entry 7 as described above. The column chromatography did not completely separate the *anti*- and *syn*-isomers of **3** each other.

(2*S*,3*S*)-2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-4-ethyl-3-hydroxy-hexanal (2b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H, C<u>H</u>O), 4.96 (d, J = 5.3 Hz, 1H, α-H). For (2*S**,3*R**)-isomer: 9.70 (s, 1H, C<u>H</u>O), 5.26 (d, α-H).

(2*S*,3*S*)-2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-4-ethyl-3-hydroxy-hexanoic acid methyl ester (3b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.76 (m, 4H), 4.99 (d, *J* = 6.8 Hz, 1H, α-H), 4.44 (m, 1H), 3.97 (d, *J* = 2.4 Hz, 1H), 3.75 (s, 3H), 1.64-1.18 (m, 5H), 0.88 (t, *J* = 7.5 Hz, 3H), 0.82 (t, *J* = 7.5 Hz, 3H); (2*S**,3*R**)-isomer: 5.26 (d, *J* = 4.1 Hz, α-H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.6, 167.6, 134.4, 131.6, 123.8, 70.9, 54.3, 52.9, 42.5, 22.2, 20.4, 11.6, 11.4. IR (neat) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 10:1] 3533, 2959, 2932, 2875, 1712, 1384, 1271, 1209, 1087, 1017, 717 cm^{-1}. HRMS (ESI-TOF): calcd for $C_{17}H_{21}NO_5Na$ (MNa^+) 342.1312, found 342.1318. HPLC (Daicel Chiralpak AS-H, 2-PrOH/hexane = 5:95, flow rate 1.0 mL/min, 254 nm): (2*S*,3*S*) 11.0 min, (2*R*,3*R*) 12.3 min. $[\alpha]^{24}_{D}$ –14.2 (C 1.0, $CHCl_3$) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 10:1, (2*S*,3*S*)-isomer 94% ee)].

(2*S*,3*S*)-4-Butyl-2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-octanal (2c). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H, C<u>H</u>O), 4.96 (d, *J* = 5.6 Hz, 1H, α-H); (2*S**,3*R**)-isomer: 5.23 (d, *J* = 5.2 Hz, 1H, α-H).

(2*S*,3*S*)-4-Butyl-2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-octanoic acid methyl ester (3c). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.76 (m, 4H), 4.98 (d, *J* = 7.4 Hz, 1H, α-H), 4.48 (m, 1H), 3.93 (d, *J* = 2.6 Hz, 1H), 3.74 (s, 3H), 1.53-0.82 (m, 19H); For (2*S**,3*R**)-isomer: 5.26 (d, *J* = 4.4 Hz, α-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 167.5, 134.4, 131.6, 123.7, 71.0, 54.2, 52.9, 39.3, 29.8, 29.6, 29.1, 27.8, 22.9, 14.1. IR (neat) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 7:1] 3541, 2954, 2928, 2859, 1713, 1384, 1262, 1210, 1085, 1018, 718 cm^{-1}. HRMS (ESI-TOF): calcd for $C_{21}H_{29}NO_5Na$ (MNa^+) 398.1938, found 398.1945. HPLC (Daicel Chiralpak AS-H, 2-PrOH/hexane = 5:95, flow rate 1.0 mL/min, 254 nm): (2*S*,3*S*) 7.1 min, (2*R*,3*R*) 7.8 min. $[\alpha]^{24}_{D}$ –30.7 (c 1.0, $CHCl_3$) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 7:1, (2*S*,3*S*)-isomer 93% ee)].

3-Cyclohexyl-2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-propionaldehyde

(2d). ^{1}H NMR (400 MHz, $CDCl_3$) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 5:1] δ 9.84 (s, 1H x 5/6), 9.70 (s, 1H x 1/6), 7.97-7.74 (m, 4H), 5.24 (d, *J* = 4.1 Hz, 1H x 1/6), 5.00 (d, *J* = 4.7 Hz, 1H x 5/6), 4.35 (d, *J* = 11.3 Hz, 1H x 1/6), 4.26 (m, 1H x 1/6), 4.11 (m, 1H x 5/6), 3.96 (brs, 1H x 5/6), 2.25-0.90 (m, 11H).

3-Cyclohexyl-2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-propionic acid methyl ester (3d). ^{1}H NMR (400 MHz, $CDCl_3$) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 5:1] δ 7.93-7.77 (m, 4H), 5.26 (d, *J* = 4.1 Hz, 1H x 1/6), 5.01 (d, *J* = 5.9 Hz, 1H x 5/6), 4.42 (d, *J* = 11.4 Hz, 1H x 1/6), 4.17-4.01 (m, 2H), 3.80 (s, 1H x 1/6). 3.75 (s, 3H x 5/6), 2.21 (m, 1H x 1/6), 1.89 (m, 1H x 5/6), 1.79-0.90 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$) [(2*S*,3*S*)-isomer] δ 170.0, 167.8, 134.4, 123.7, 74.3, 54.4, 52.8, 39.6, 30.0, 26.7, 26.2, 25.9. IR (neat) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 5:1] 3468, 2924, 2851, 1708, 1384, 1254, 1210, 1085, 1068, 1018, 719 cm^{-1}. HRMS (ESI-TOF): calcd for $C_{18}H_{21}NO_5Na$ (MNa^+) 354.1312, found 354.1323. HPLC (Daicel Chiralcel OD-H, 2-PrOH/hexane = 5:95, flow rate 1.0 mL/min, 254 nm): (2*S*,3*S*) 9.7 min, (2*R*,3*R*) 11.1 min. $[\alpha]^{24}_{D}$ –13.7 (c 0.75, $CHCl_3$) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 5:1, (2*S*,3*S*)-isomer = 98% ee)].

3-Cyclopentyl-2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-propionaldehyde (2e). ^{1}H NMR (400 MHz, $CDCl_3$) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 3:1] δ 9.85 (s, 1H x 3/4), 9.71 (s, 1H x 1/4), 7.93-7.70 (m, 4H), 5.16 (d, *J* = 2.1 Hz, 1H x 1/4), 4.96 (d, *J* = 3.0 Hz, 1H x 3/4), 4.35-4.33 (2H x 1/4), 4.12-4.09 (2H x 3/4), 2.40-1.20 (m, 9H).

(2*S*,3*S*)-3-Cyclopentyl-2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-propionic acid methyl ester (3e). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92-7.76 (m, 4H), 4.94 (d, *J* = 4.7 Hz, 1H, α-H), 4.32 (d, *J* = 2.9 Hz, 1H), 4.13 (m, 1H), 3.76 (s, 3H), 2.23 (m, 1H), 1.81-1.33 (m, 8H); (2*S**,3*R**)-isomer: 5.19 (d, *J* = 4.1 Hz, α-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 167.9, 134.5, 131.6, 123.8, 74.2, 56.5, 52.8, 42.1, 29.3, 28.0, 25.8. IR (neat) [(2*S*, 3*S*)-isomer:(2*S**,3*R**)-isomer = 16:1] 3469, 2951, 2867, 1708, 1384, 1250, 1208, 1085, 1019, 718. HRMS (ESI-TOF): calcd for $C_{17}H_{19}NO_5Na$ (MNa^+) 340.1155, found 340.1149. $[\alpha]^{24}_{D}$ +26.2 (c 1.0, $CHCl_3$) [(2*S*,3*S*)-isomer:(2*S**,3*R**)-isomer = 16:1].

3-Cyclopentyl-2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-propionaldehyde *O*-benzyl-oxime (8e). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.74 (m, 4H), 7.40-7.26 (6H), 5.07 (s, 2H), 3.99 (m, 1H), 3.74 (d, *J* = 2.9 Hz, 1H), 1.98 (m, 1H), 1.84-1.28 (m, 8H). HPLC (Daicel Chiralpak AD, 2-PrOH/hexane = 10:90, flow rate 1.0 mL/min, 254 nm): (2*S*,3*S*) 48.3 min, (2*R*,3*R*) 26.3 min.

2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-4,4-dimethoxy-butyraldehyde (2f). ^{1}H NMR (400 MHz, $CDCl_3$) [*anti*-(2*S*,3*R*)-isomer:*syn*-(2*S**,3*S**)-isomer = 5:1] δ 9.88 (s, 1H x 5/6), 9.73 (s, 1H x 1/6), 7.95-7.70 (m, 4H), 5.22 (d, *J* = 4.4 Hz, 1H x 5/6), 5.19 (d, *J* = 5.0 Hz, 1H x 1/6), 4.63 (m, 1H x 1/6), 4.58 (d, *J* = 5.9 Hz, 1H x 5/6), 4.37-4.25 (m, 1H), 3.52 (s, 3H x 5/6), 3.48 (s, 3H x 5/6), 3.45(s, 3H x 1/6), 3.41 (s, 3H x 1/6).

2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-4,4-dimethoxy-butyric acid methyl ester (3f). ^{1}H NMR (400 MHz, $CDCl_3$) [*anti*-(2*S*,3*R*)-isomer:*syn*-(2*S**,3*S**)-isomer = 1:1] δ 7.93-7.75 (m, 4H), 5.33 (d, *J* = 4.4 Hz, 1H x 1/2), 5.26 (d, *J* = 3.5 Hz, 1H x 1/2), 4/69 (d, *J* = 6.8 Hz, 1H x 1/2), 4.54 (m, 1H x 1/2), 4.45-4.25 (m, 2H), 3.79 (d, *J* = 4.7 Hz, 3H), 3.42 (d, *J* = 4.7 Hz, 3H), 3.41 (s, 3H x 1/2), 3.36 (s, 3H x 1/2). ^{13}C NMR (125 MHz, $CDCl_3$) [*anti*-isomer:*syn*-isomer = 1:1] δ 168.6, 168.5, 168.2, 168.0, 134.3, 131.7, 123.8, 123.7, 104.3, 103.9, 104.3, 103.9, 71.1, 70.3, 56.1, 55.3, 54.7, 54.6, 54.4, 53.9, 52.9, 52.8. IR (neat) [*anti*-isomer:*syn*-isomer = 1:1] 3436, 2953, 2835, 1746, 1705, 1387, 1264, 1193, 1114, 1063, 970, 718. HRMS (ESI-TOF): calcd for $C_{15}H_{17}NO_7Na$ (MNa^+) 346.0897, found 346.0899. HPLC (Daicel Chiralcel OD-H, 2-PrOH/hexane = 10:90, flow rate 1.0 mL/min, 254 nm): *anti*-isomers, (2*S*,3*R*) 44.7 min, (2*R*,3*S*) 72.6 min; *syn*-isomer, 36.8 min, 54.1 min. $[\alpha]^{24}_D$ +19.8 (c 1.0, $CHCl_3$) [*anti*-isomer:*syn*-isomer = 1:1, *anti*-isomer 86% ee, *syn*-isomer 68% ee].

4-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3-hydroxy-2-isopropyl-butyraldehyde (6a). ^{1}H NMR (400 MHz, $CDCl_3$) (anti:syn = 3:1) δ 9.90 (d, *J* = 2.3 Hz, 1H x 1/4), 9.87 (d, *J* = 3.0 Hz, 1H x 3/3), 7.89-7.70 (m, 4H), 4.31 (m, 1H x 1/4), 4.26 (m, 1H x 3/4), 3.91-3.81 (2H), 3.27 (brs, 1H x 3/4), 2.95 (brs, 1H x 1/4), 2.53-2.10 (m, 2H), 1.16 (d, *J* = 6.8 Hz, 3H x 1/4), 1.10 (d, *J* = 6.8 Hz, 3H x 3/4), 1.06 (d, *J* = 6.8 Hz, 3H x 1/4). 1.04 (d, *J* = 6.8 Hz, 3H x 1/4). ^{13}C NMR (125

MHz, $CDCl_3$) (*anti*-isomer) δ 206.0, 168.7, 134.1, 131.7, 123.4, 69.0, 60.6, 43.0, 27.0, 20.8, 19.7. HPLC (Daicel Chiralcel OD-H, 2-PrOH/hexane = 10:90, flow rate 1.0 mL/min, 254 nm): *anti*-isomer, major 17.0 min, minor 53.1 min.

2-[2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-1-hydroxy-ethyl]-hexanal (6b). ^1H NMR (400 MHz, $CDCl_3$) (anti:syn = 3:1) δ 9.83 (d, *J* = 1.4 Hz, 1H x 1/4), 9.77 (d, *J* = 2.9 Hz, 1H x 3/4), 7.90-7.75 (m, 4H), 4.26 (m, 1H x 1/4), 4.12 (m, 1H x 3/4), 3.96-3.86 (m, 2H), 3.10 (m, 1H x 3/4), 2.82 (m, 1H x 1/4), 2.57-0.90 (m, 9H). HPLC (Daicel Chiralcel OD-H, 2-PrOH/hexane = 10:90, flow rate 1.0 mL/min, 254 nm): *anti*-isomer, major 16.1 min, minor 36.3 min.

References

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(S2) Aldehyde **1** is commercially available in some countries.

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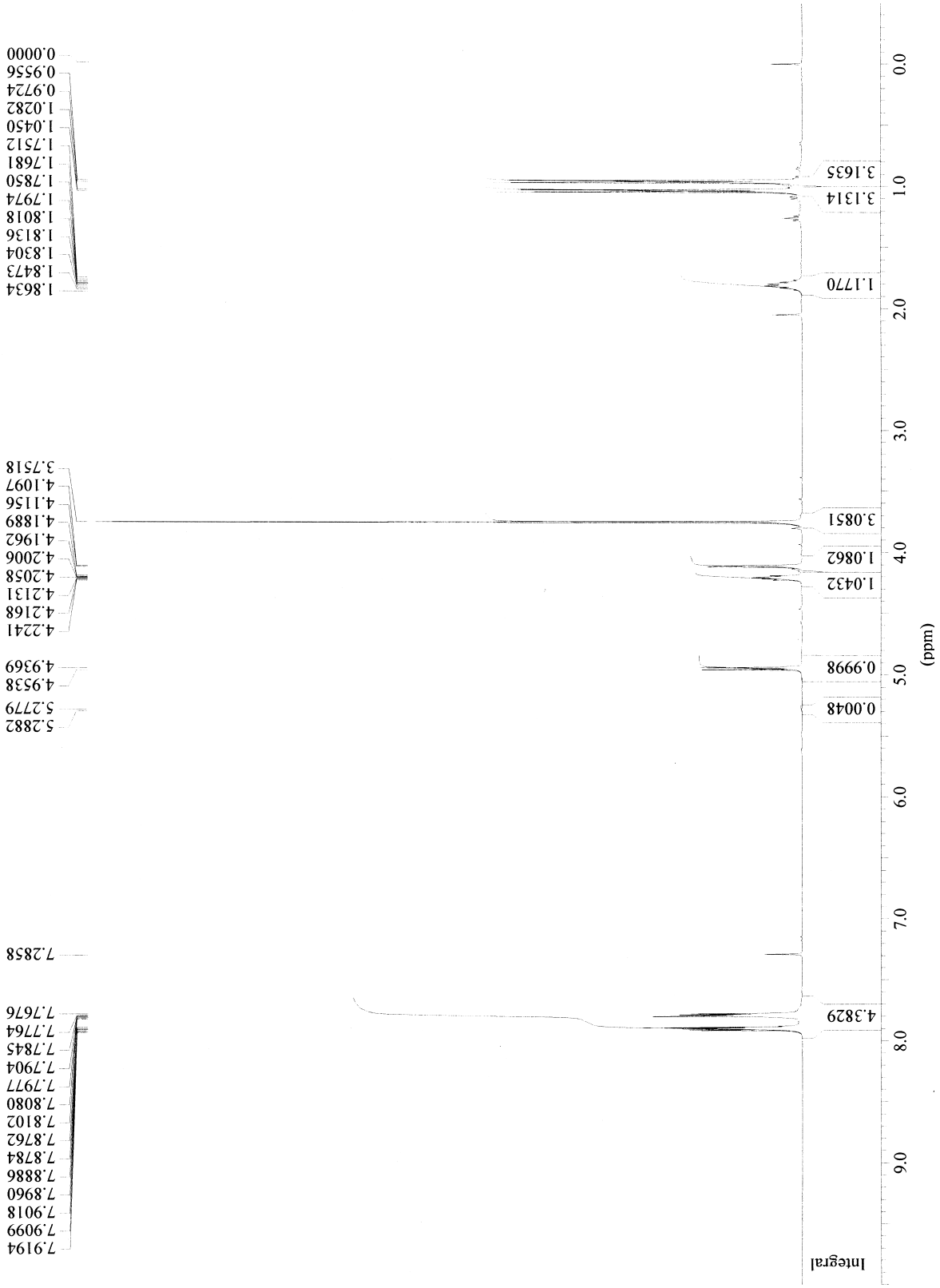
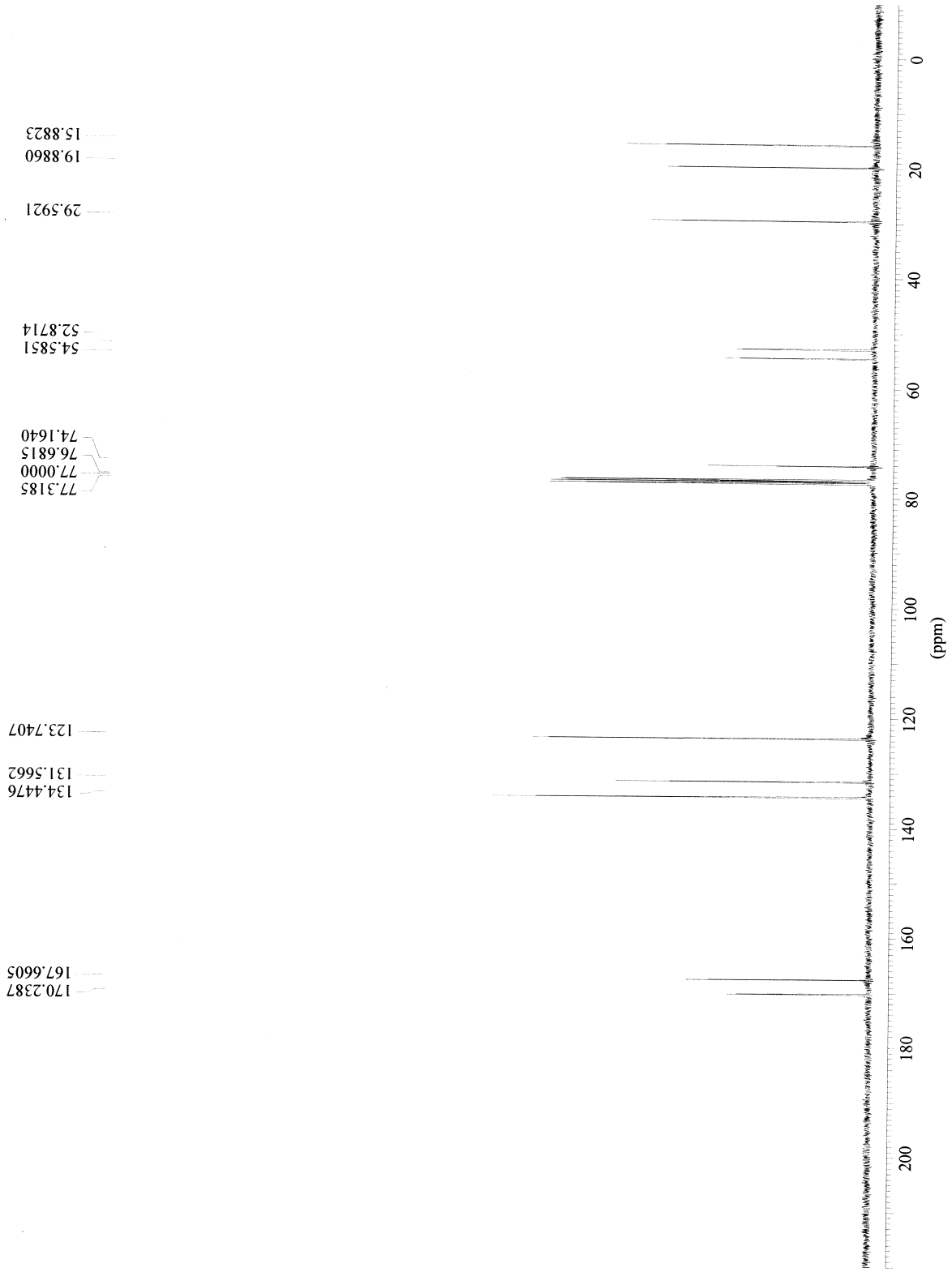
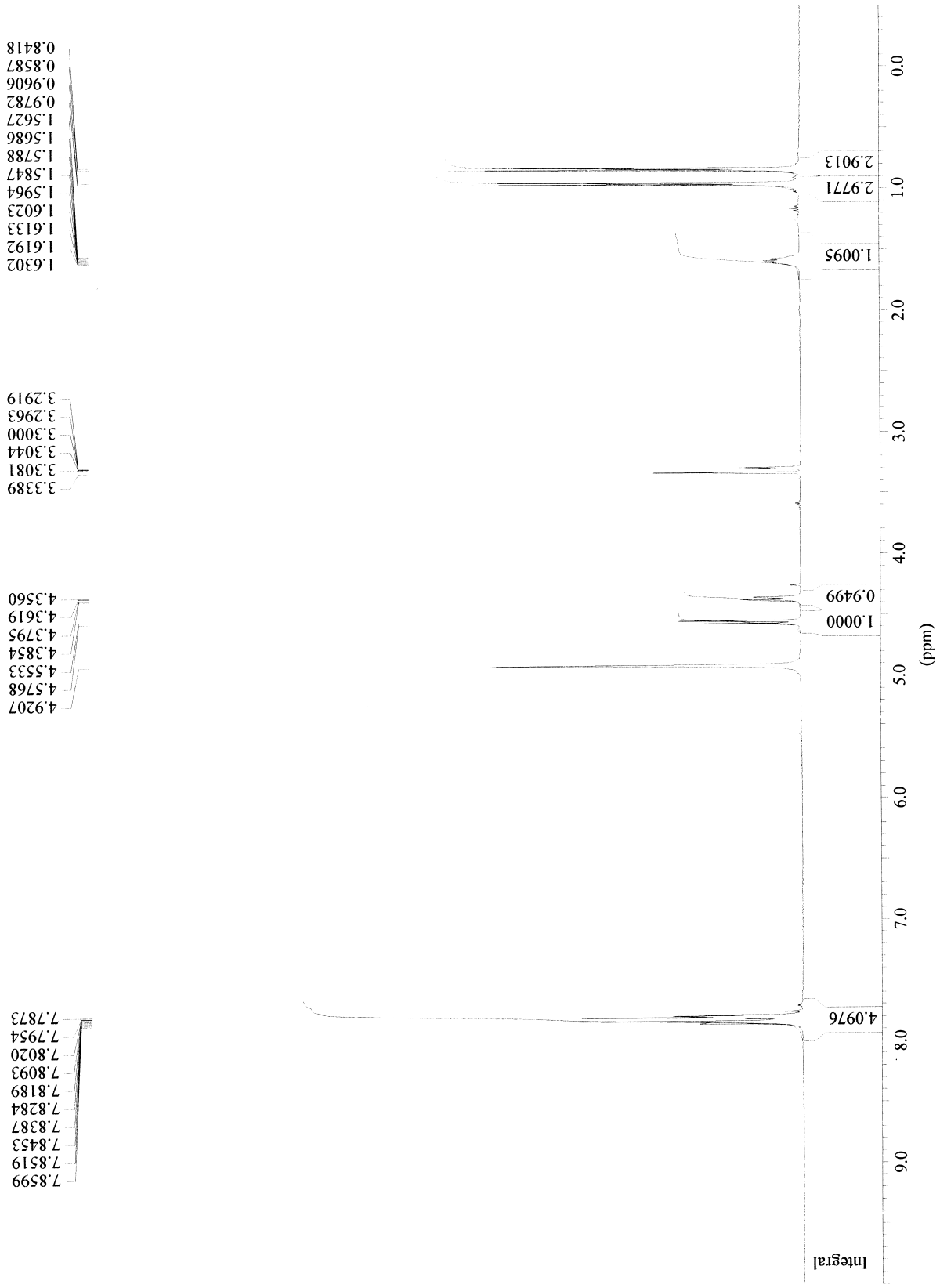
Compound **3a**, ^{1}H NMR (400 MHz, $CDCl_3$)



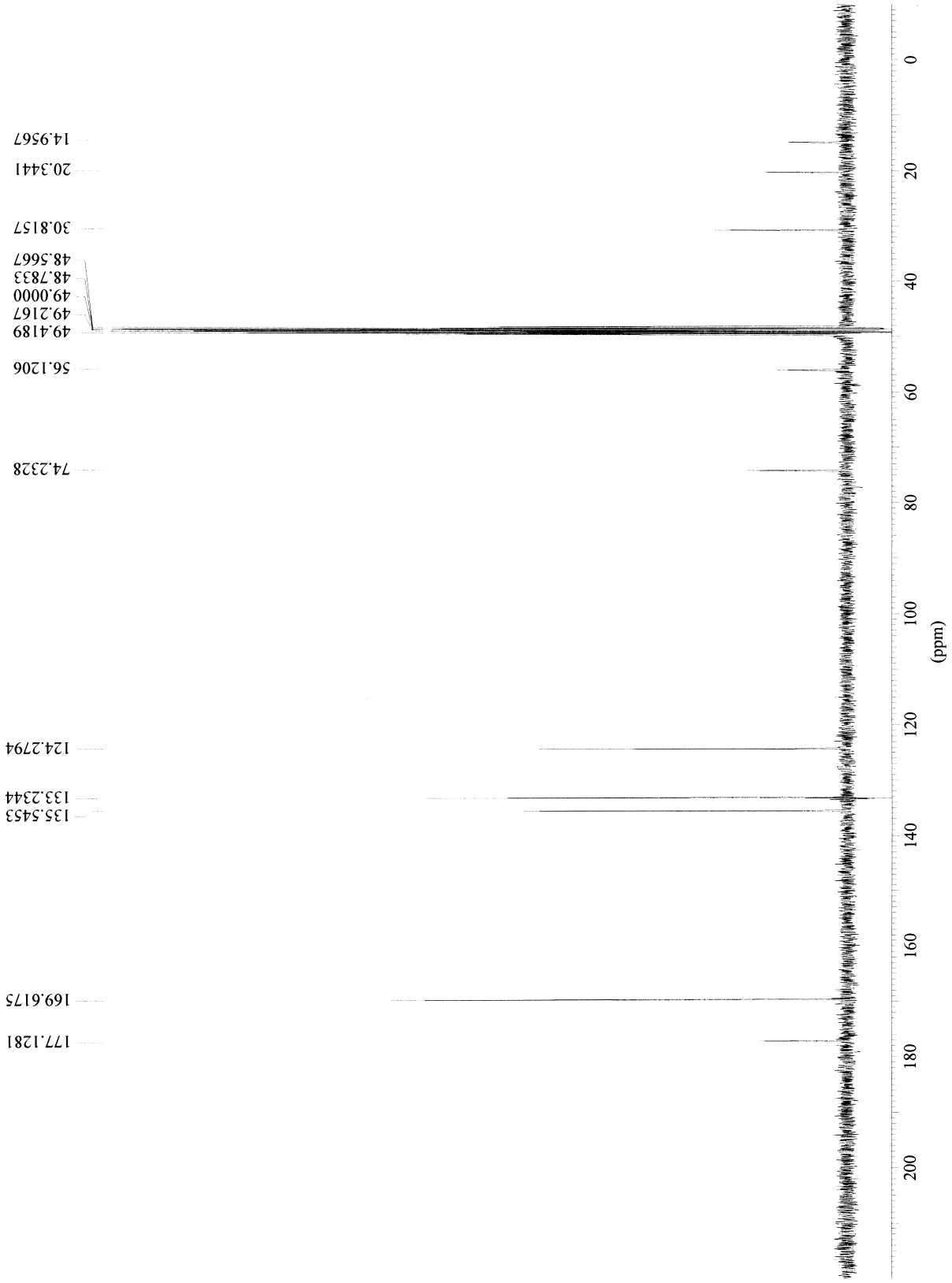
Compound **3a**, ^{13}C NMR (100 MHz, $CDCl_3$)



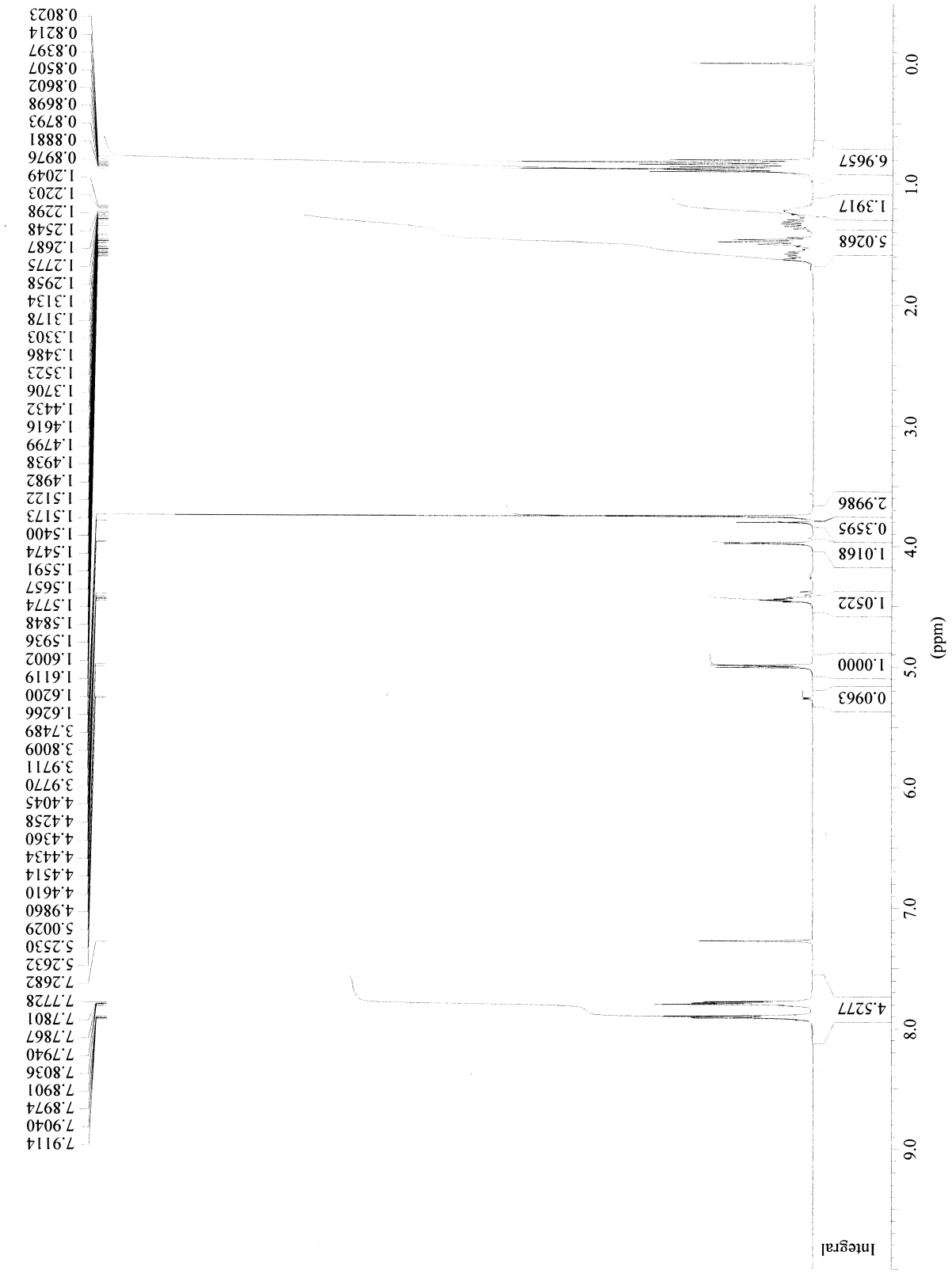
Compound **7**, ^{1}H NMR (400 MHz, CD_3OD)



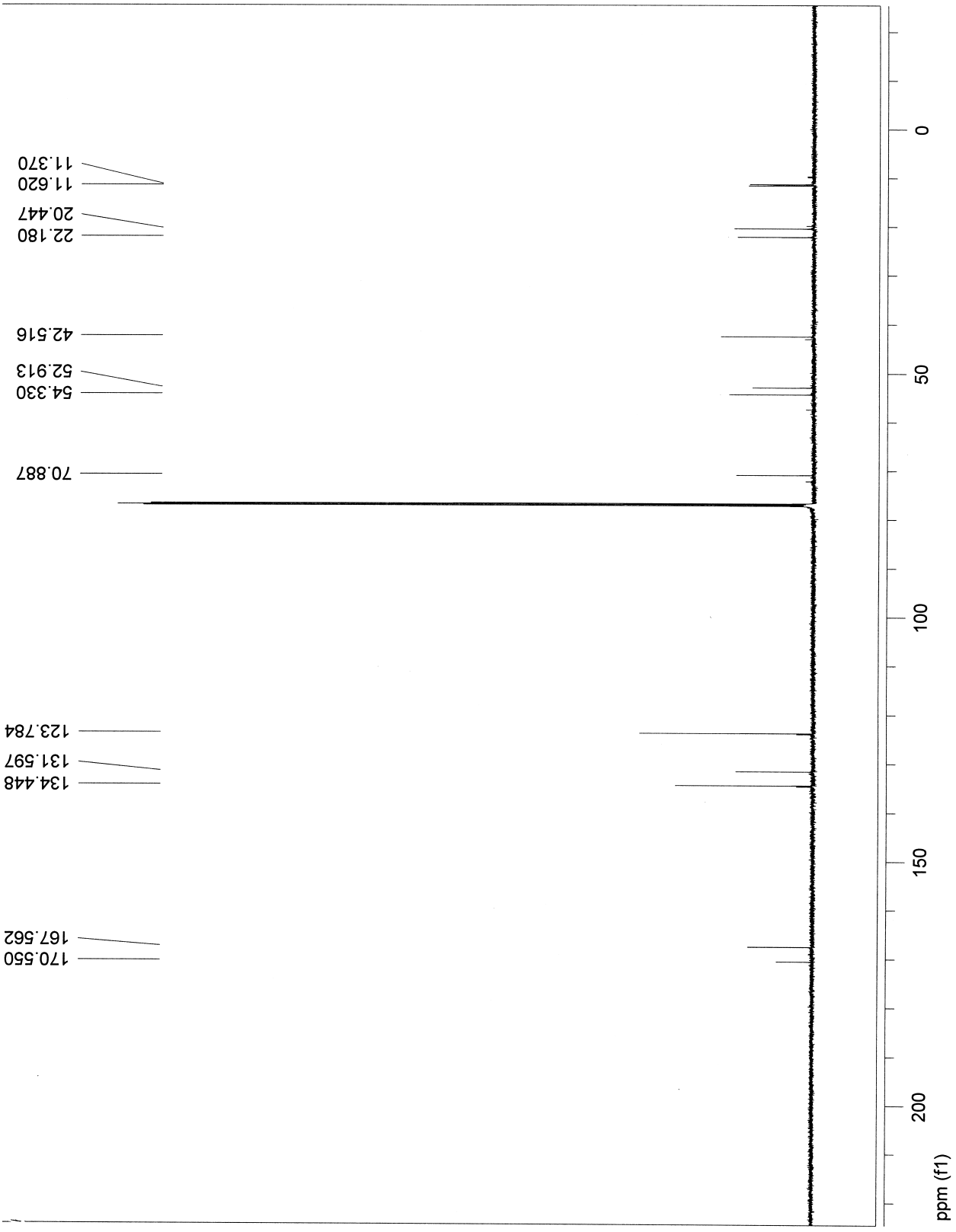
Compound **7**, ^{13}C NMR (100 MHz, CD_3OD)



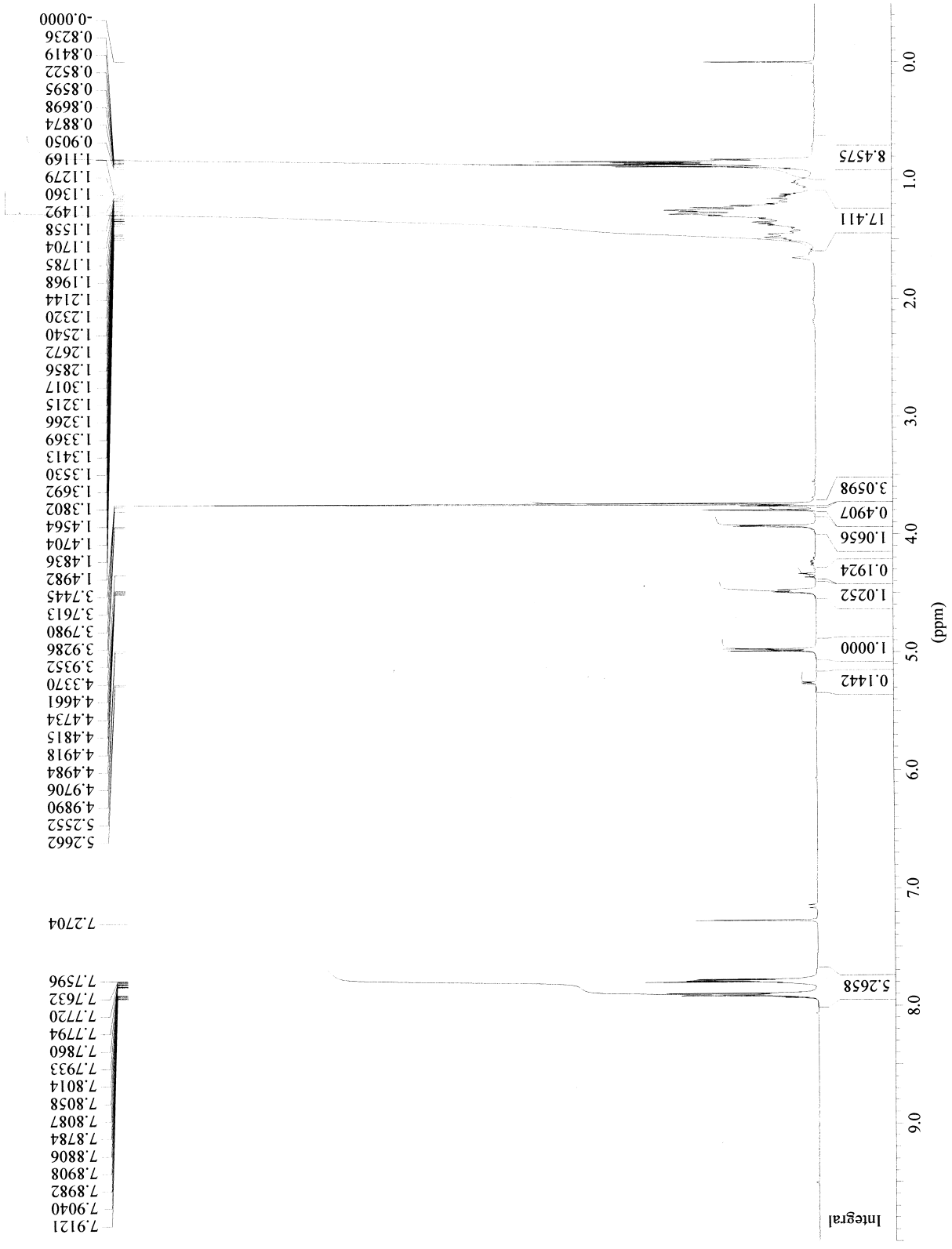
Compound **3b**, ^{1}H NMR (400 MHz, $CDCl_3$)



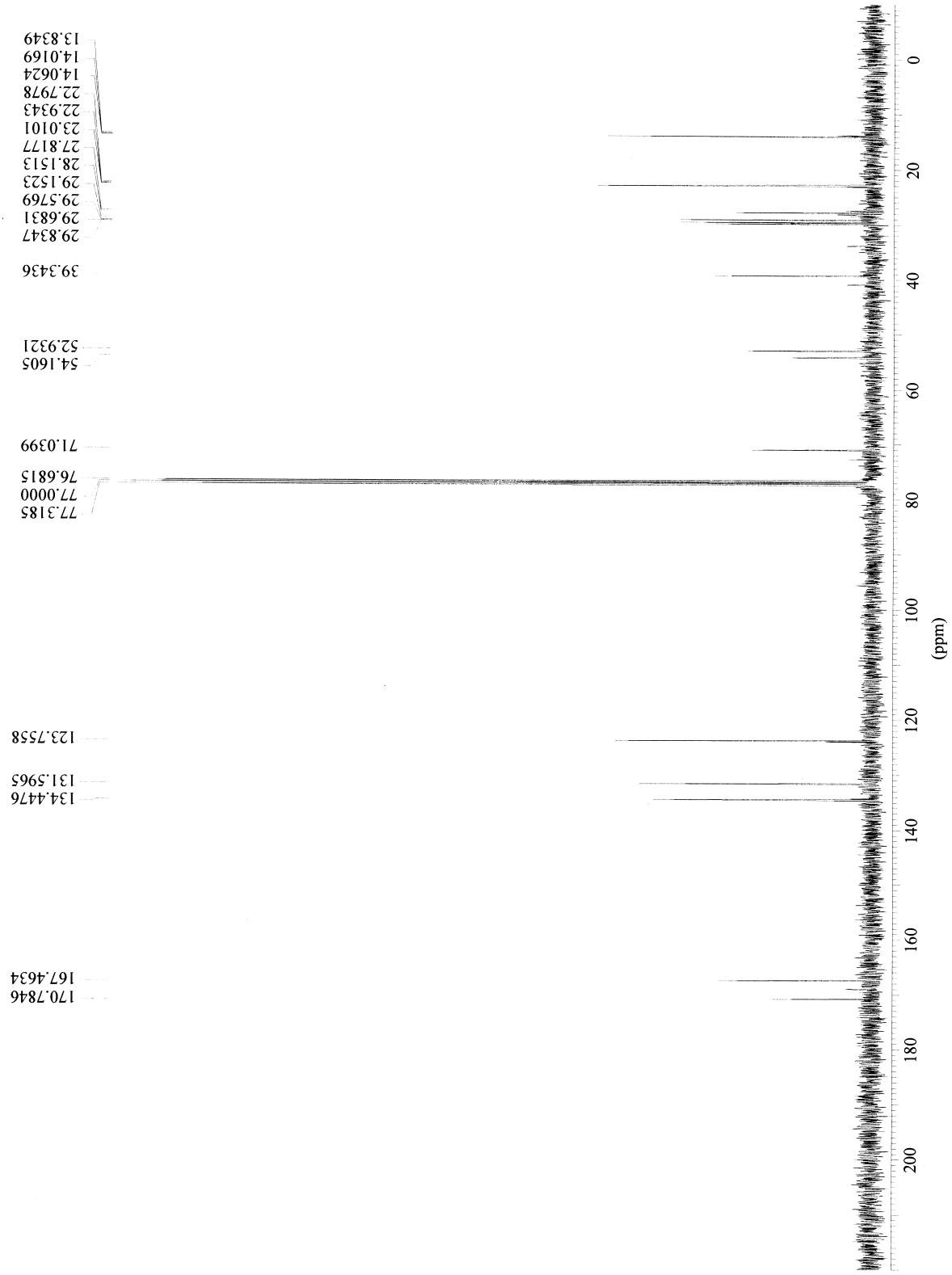
Compound **3b**, ^{13}C NMR (150 MHz, $CDCl_3$)



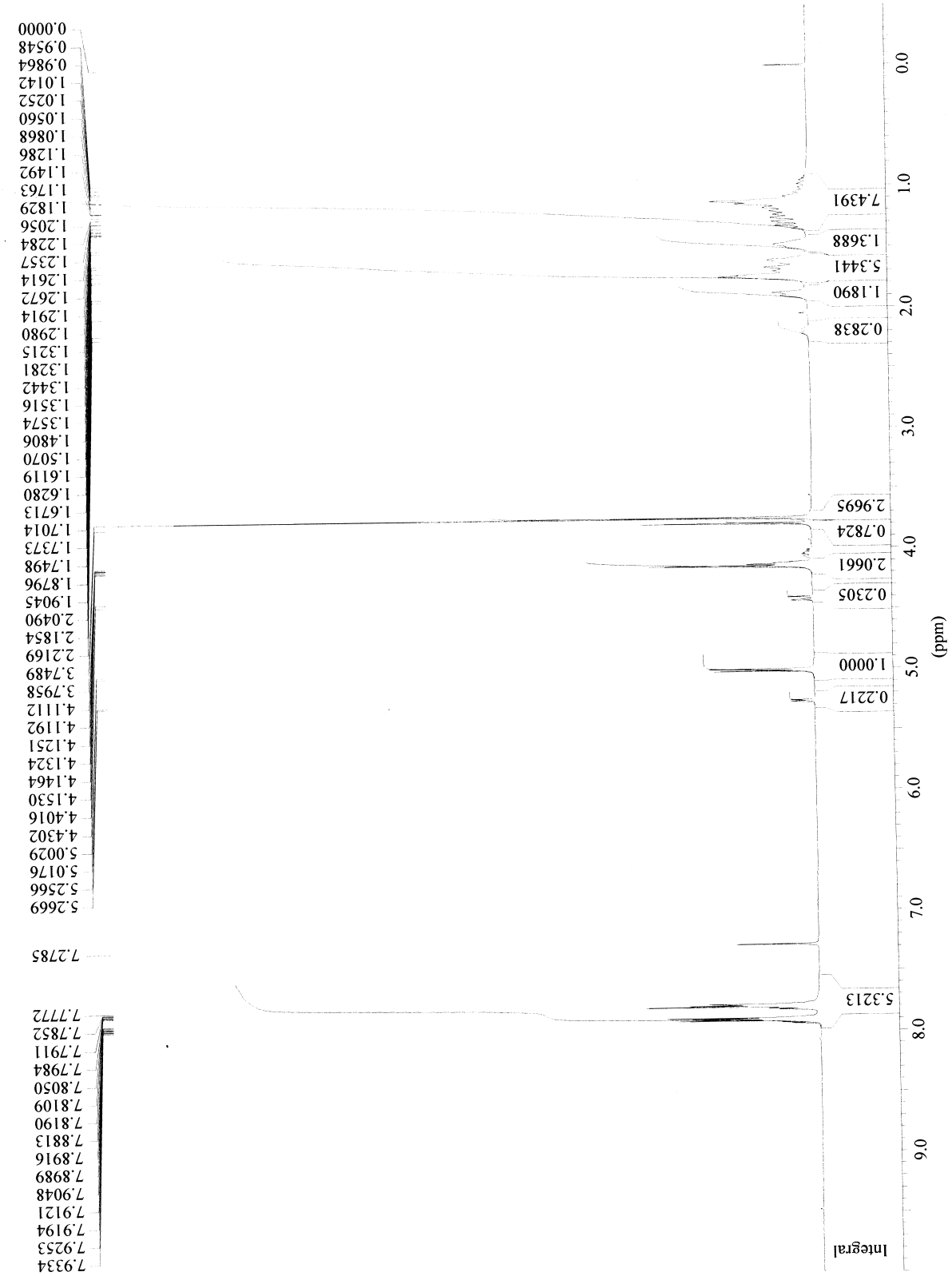
Compound **3c**, ^{1}H NMR (400 MHz, $CDCl_3$)



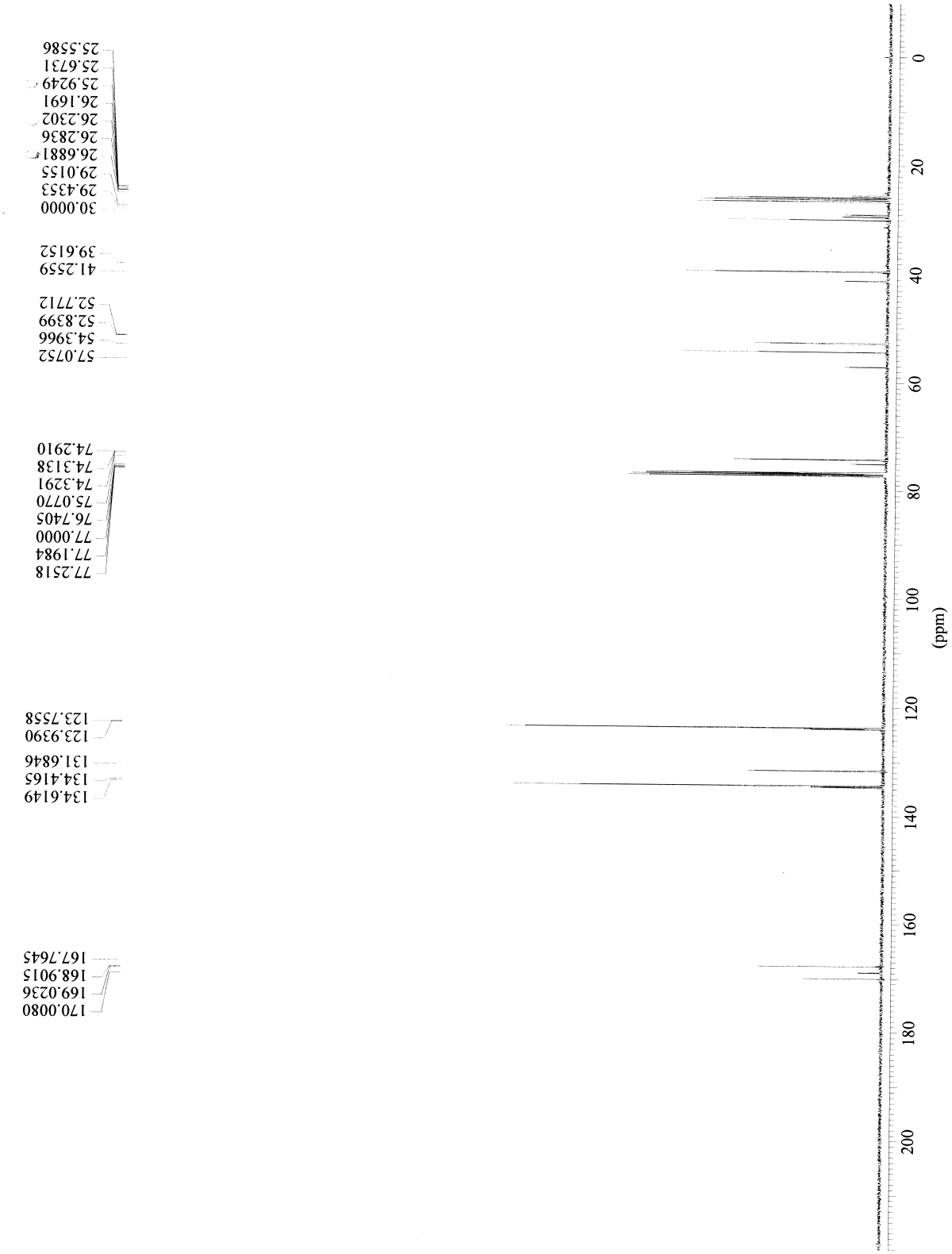
Compound **3c**, ^{13}C NMR (100 MHz, $CDCl_3$)



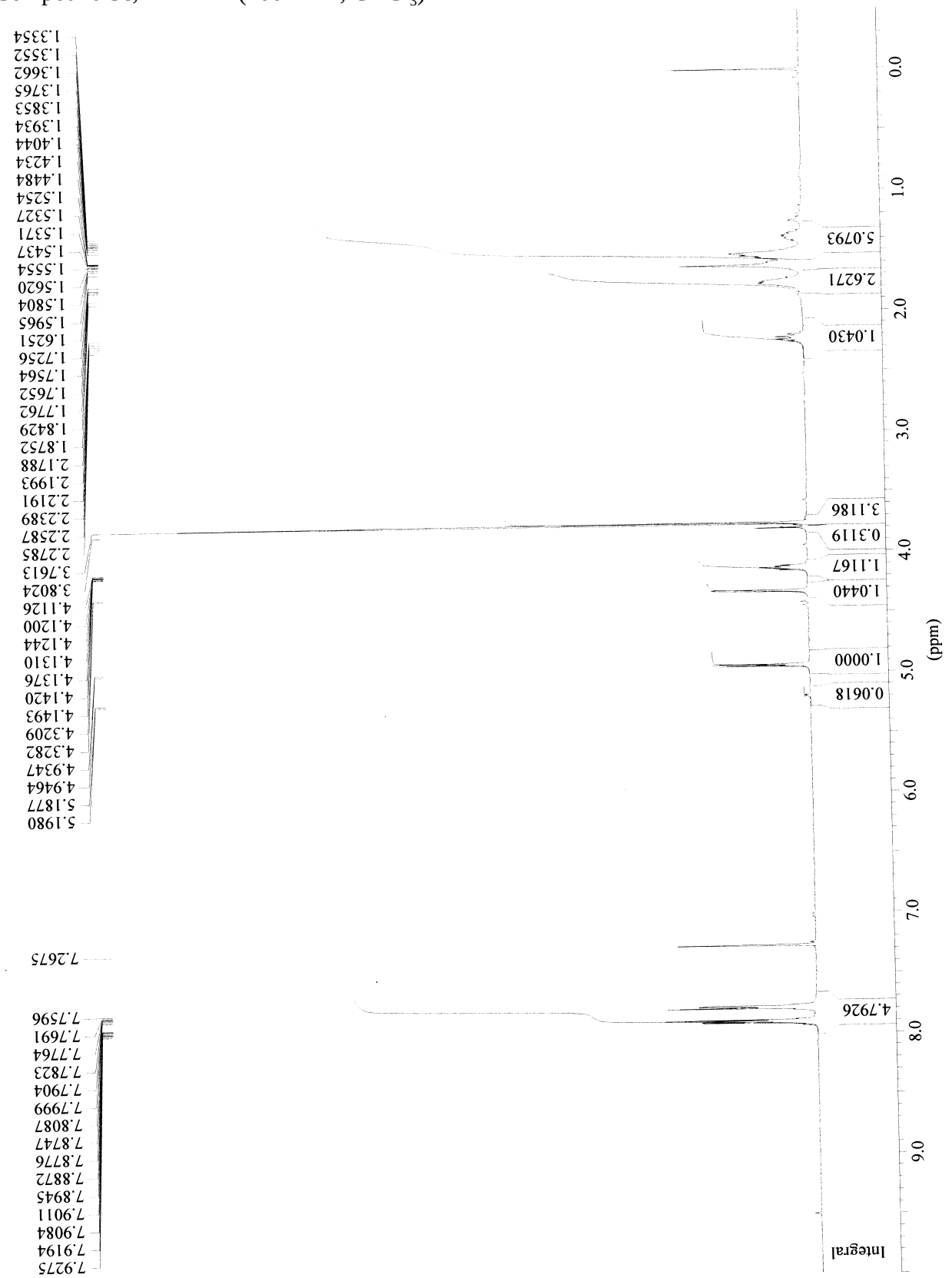
Compound **3d**, anti:syn = 5:1, ^{1}H NMR (400 MHz, $CDCl_3$)



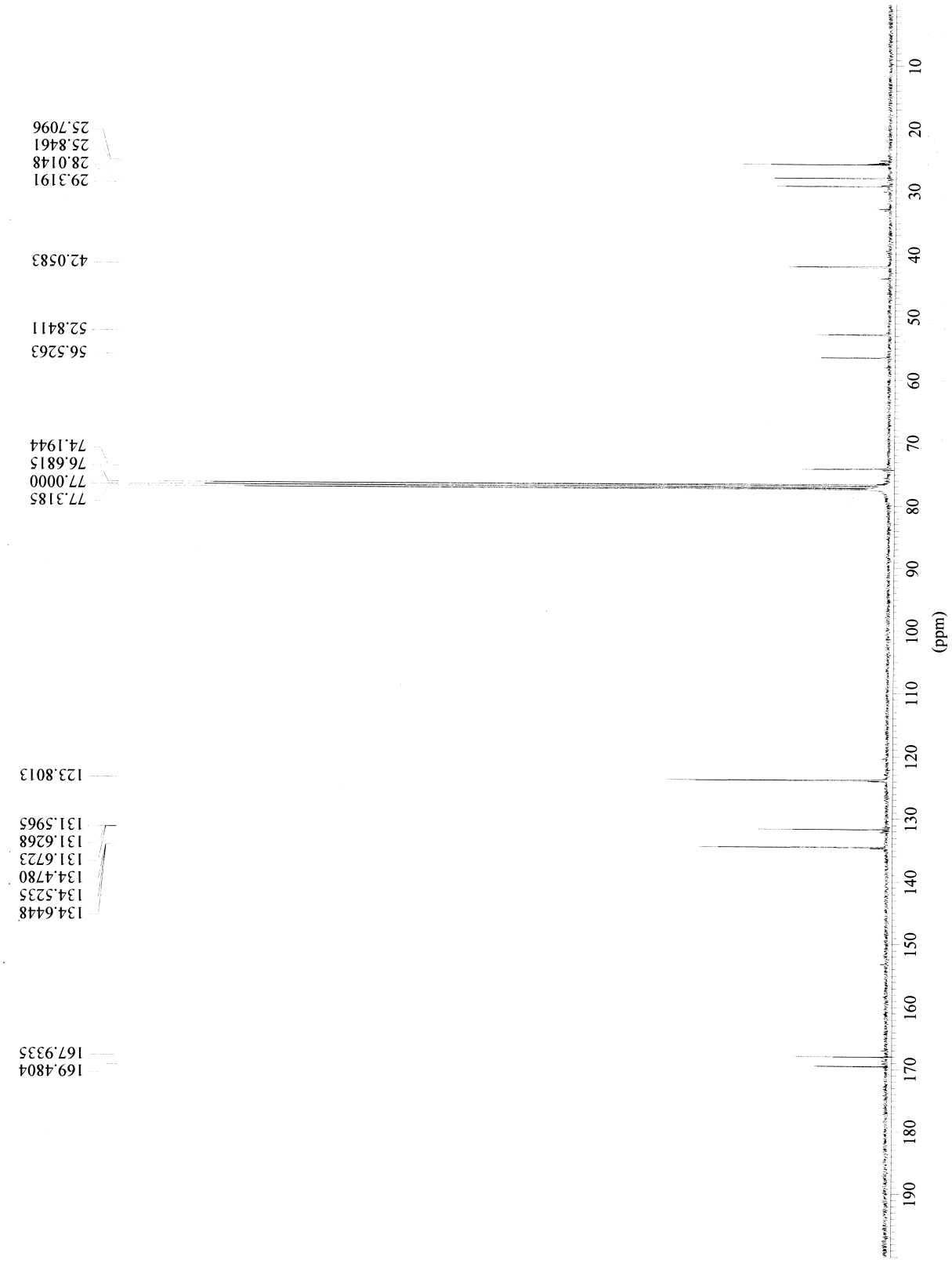
Compound **3d**, anti:syn = 5:1,^{13}C NMR (125 MHz, $CDCl_3$)



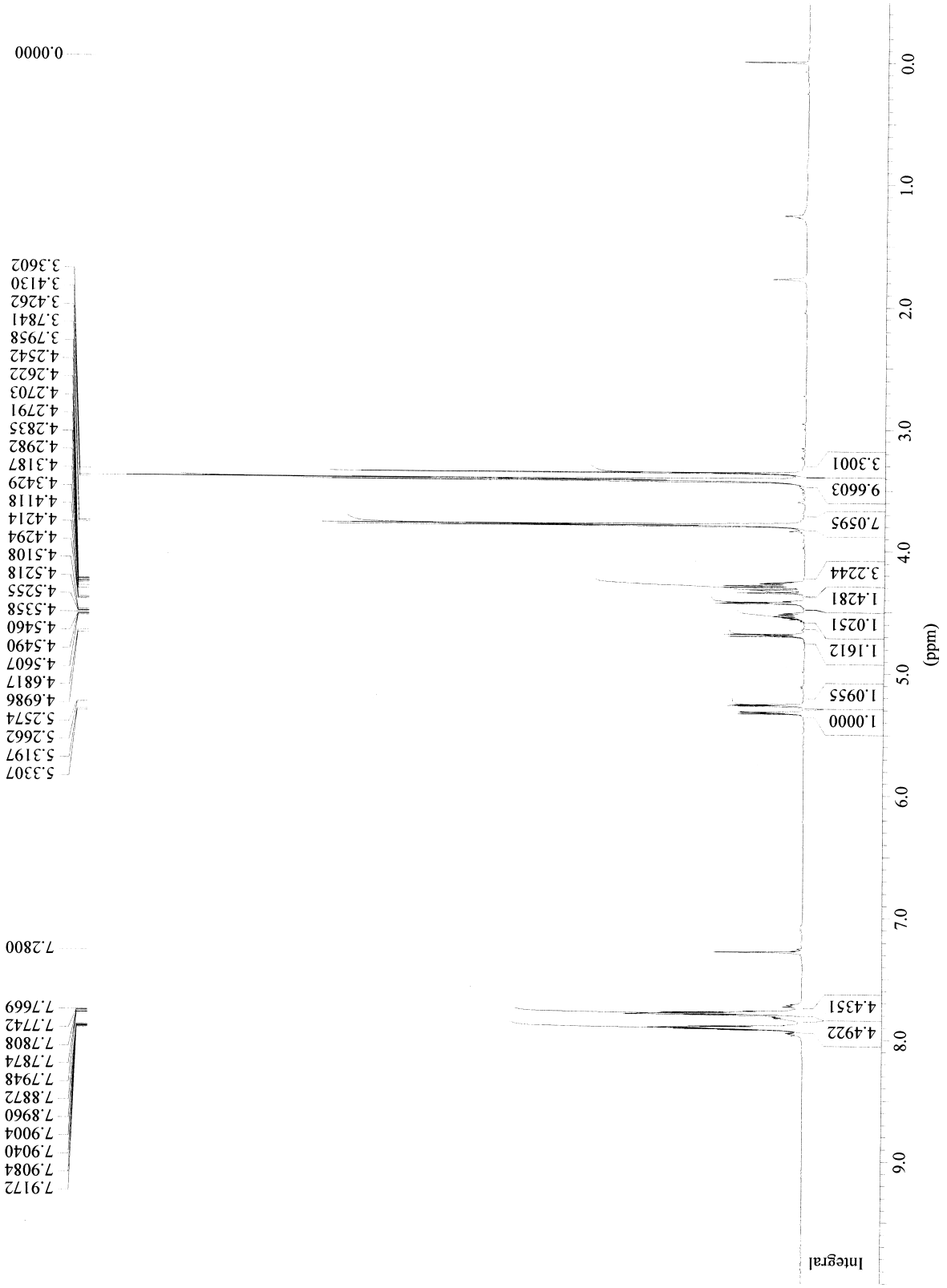
Compound **3e**, ^{1}H NMR (400 MHz, $CDCl_3$)



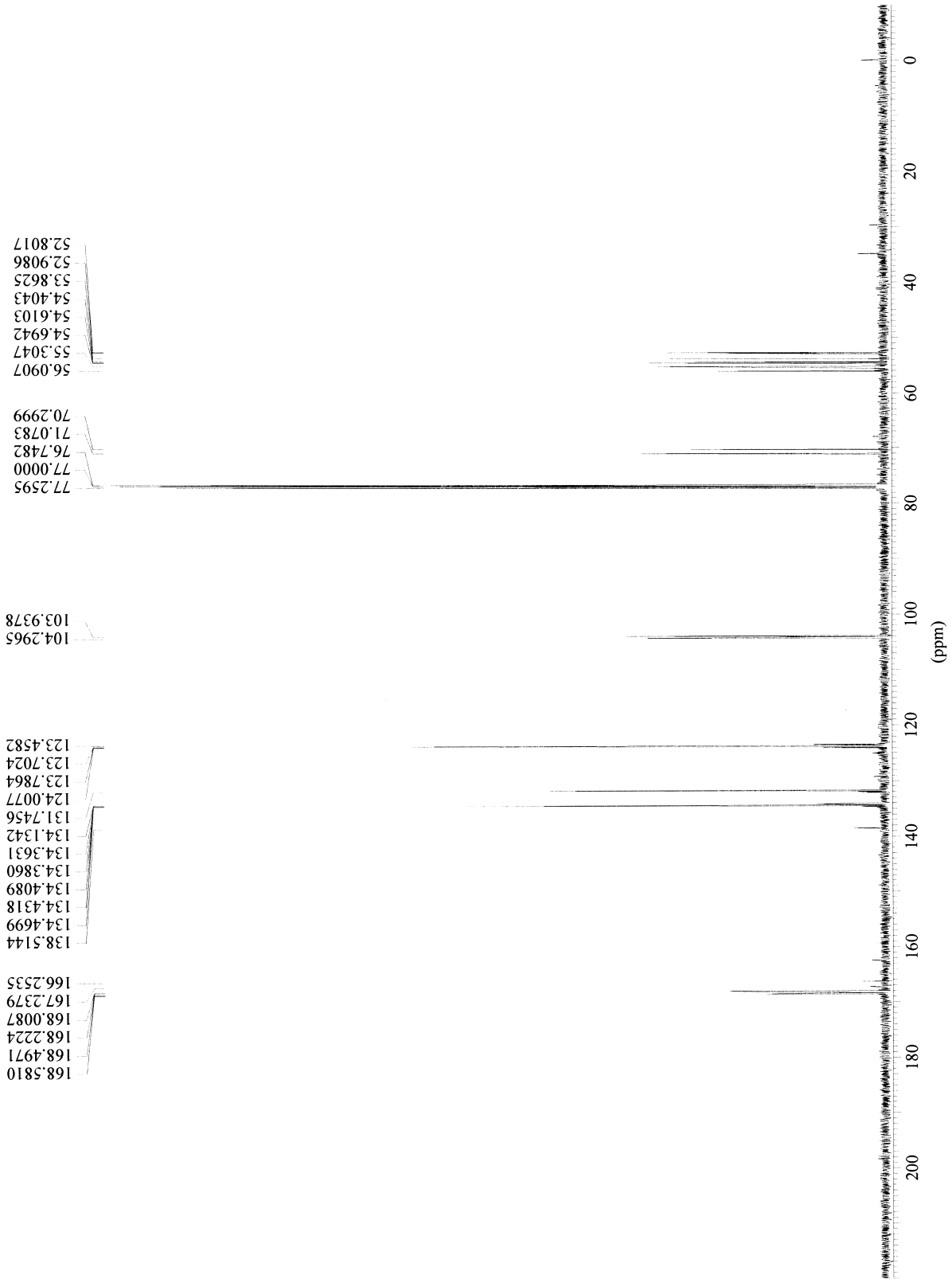
Compound **3e**, ^{13}C NMR (100 MHz, $CDCl_3$)



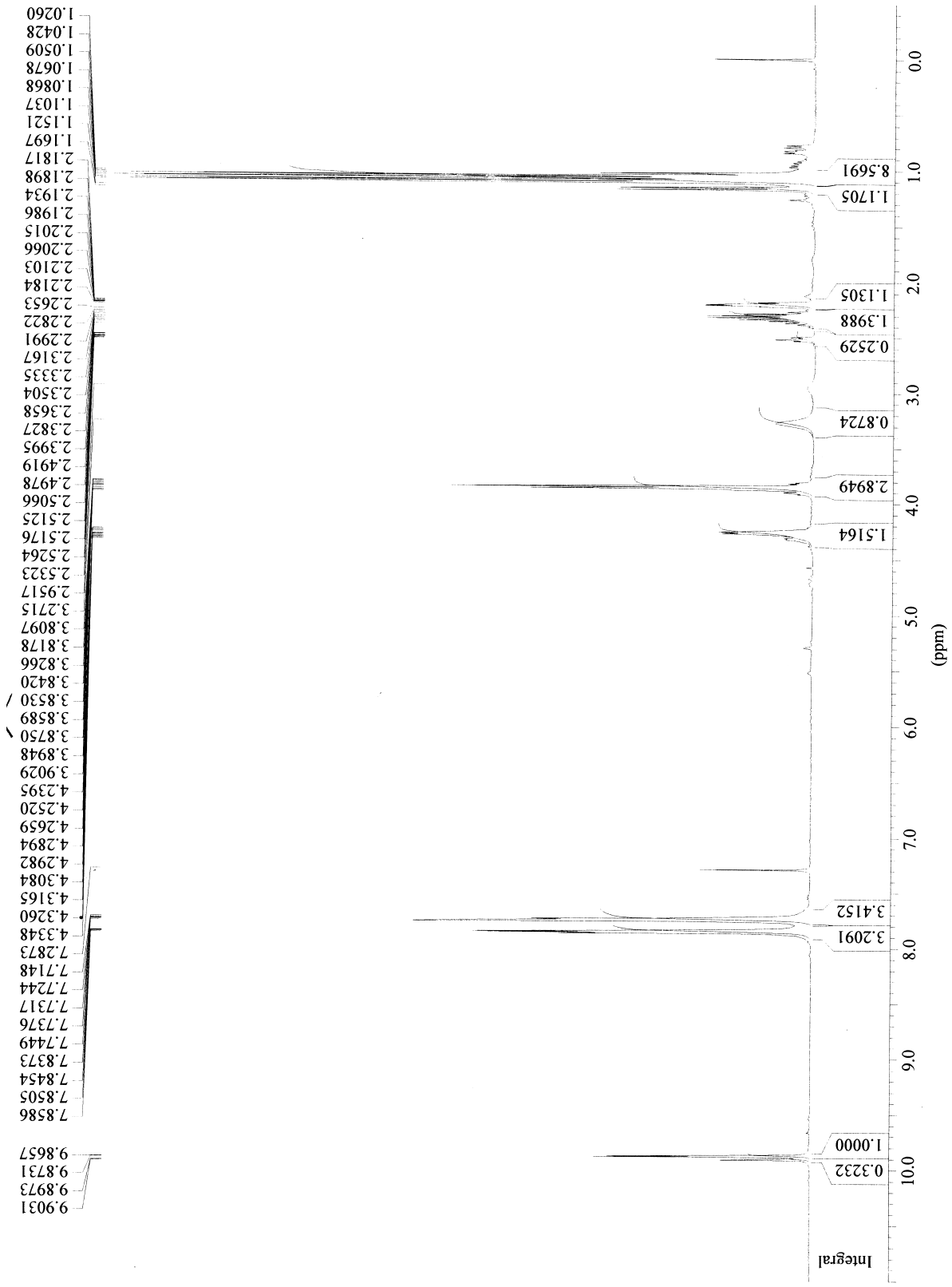
Compound **3f**, anti:syn = 1:1, ^{1}H NMR (400 MHz, $CDCl_3$)



Compound **3f**, anti:syn = 5:1, ^{13}C NMR (125 MHz, $CDCl_3$)



Compound**6a**, ^{1}H NMR (400 MHz, $CDCl_3$)



Compound **6a**, ^{13}C NMR (125 MHz, $CDCl_3$)