Asymmetric synthesis of enantiopure pyrrolidines from N-allyl oxazolidines via hydrozirconation-cyclisation.

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All reactions were conducted under an atmosphere of argon using standard Schlenk techniques. Prior to use, tetrahydrofuran and Et_2O were distilled under argon from sodium benzophenone ketyl, NEt_3 and CH_2Cl_2 was distilled under argon from CaH_2, $Cp_2Zr(H)Cl$ was prepared according to known procedure,[1] reagents (Aldrich) were used as received. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Brucker AC-250. Mass spectra were recorded on a Micromass Q-TOF micro MS spectrometer.

(*R*) 2-(allylamino)-2-phenylethanol.[2]
Allyl bromide (6.35 mL, 73 mmol) was added dropwise to a solution of phenylglycinol (10 g, 72.9 mmol) and triethylamine (10.4 mL, 75 mmol) in THF (35 mL) and stirred at rt overnight. The white solide was filtered off, the filtrate was concentrated under vaccum and purified by column chromatography on silica gel using EtOAc : Petroleum ether (7 : 3) as eluant to give the title compound as a colorless oil (9.4 g, 79 %). $[\alpha]^D_{23}$ = -74.5 (*c* 1, CH_2Cl_2); ^1H NMR δ: 2.60 (br s, 2H), 2.98 (dd, *J* = 14.0, 7.6 Hz, 1H), 3.12 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.50 (dd, *J* = 10.6, 8.7 Hz, 1H), 3.63 (dd, *J* = 10.7, 4.3 Hz, 1H), 3.73 (dd, *J* = 8.7, 4.3, 1H), 5.00 (dd, *J* = 10.2, 1.4 Hz, 1H), 5.06 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.79 (dddd, *J* = 17.2, 10.2, 7.6, 5.6 Hz; 1H), 7.16-7.30 (m, 5H); ^{13}C NMR δ: 49.7, 63.7, 66.6, 116.1, 127.2, 127.6, 128.6, 136.5, 140.5.

(*R*)-2-Phenyl-2-[(*R*)-1-phenylallylamino]ethanol.[3]
To a solution of (*R*)-2-benzylideneamino-2-phenylethanol[4] (2.25 g, 10 mmol) in Et_2O (30 mL) was added dropwise a solution of vinyl magnesium bromide in THF (1N, 30 mL) at 0°C. The mixture was stirred at r.t. for 6h. Water was slowly added at 0°C, the aqueous layer was extracted with Et_2O (3 x 25 mL), the organics phases were combined, concentrated to 50 mL and extracted with an aqueous solution of HCl (1N, 2 x 25 mL). The aqueous layer was neutralized with a saturated aqueous solution of Na_2CO_3 and extracted with Et_2O (3 x 25 mL). The organic layers were combined, dried over Na_2SO_4 filtered and concentrated to give the title compound as a pale yellow oil (2.02 g, 80%). $[\alpha]^{25}_D$ -16.0 (*c* 1, CH_2Cl_2); ^1H NMR δ: 2.23 (br s, 2H), 3.55 (dd, *J* = 10.7, 8.7 Hz, 1H), 3.41 (dd, *J* = 10.7, 4.5 Hz, 1H), 3.98 (dd, *J* = 8.7, 4.5 Hz, 1H), 4.07 (d, *J* = 8.0 Hz, 1H), 5.11-5.19 (m, 2H), 5.86 (ddd, *J* = 17.0, 10.2, 8.0 Hz, 1H), 7.19-7.28 (m, 10H); ^{13}C NMR δ: 61.4, 62.6, 66.9, 116.5, 127.2, 127.4, 127.5, 127.7, 128.7, 128.8, 140.1, 140.7, 143.2; MS-ESI: *m/z* $[M+H]^+$ 254.

(*R*)-2-Phenyl-2-[(*R*)-1-(4-chloro-phenyl)allylamino]ethanol.
obtained as a yellow oil (39%) according to the above procedure. $[\alpha]^{25}_D$ -12.0 (*c* 1, CH_2Cl_2); ^1H NMR δ: 2.53 (br s, 2H), 3.52 (dd, *J* = 10.7, 8.8 Hz, 1H), 3.66 (dd, *J* = 10.7, 4.3 Hz, 1H), 3.93 (dd, *J* = 8.6, 4.3 Hz, 1H), 4.00 (d, *J* = 8.0 Hz, 1H), 5.13 (m, 2H), 5.77 (ddd, *J* = 17.1, 10.1, 8.0 Hz, 1H), 7.19-7.28 (m, 9H); ^{13}C NMR δ: 61.3, 61.6, 66.6, 116.7, 127.2, 127.5, 128.3, 128.45, 128.55, 132.7, 139.2, 140.2, 141.4; MS-ESI: *m/z* $[M+H]^+$ 288.

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[3] Scialdone, M. A. ; Meyers, A. I. *Tetrahedron Lett.* **1994**, *35*, 7533-7536.
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General procedure for the preparation of oxazolidines 1.
A solution of (*R*) 2-(allylamino)-2-phenylethanol (354 mg, 2 mmol) and the relevant aldehyde (2 mmol) in toluene (10 mL) was heated to reflux for 4h in a Dean-Stark apparatus. The solvent was removed under reduced pressure to give the oxazolidine which was used without purification in the next step.

(2*R*,4*R*) 3-allyl-2,4-diphenyloxazolidine 1a.
Yellow oil, $[\alpha]^{D}_{23}$ - 17.1 (*c* 1, CH_2Cl_2); ^{1}H NMR δ: 3.16 (dd, *J* = 6.7, 0.8 Hz, 2H), 3.88 (dd, *J* = 8.0, 7.6 Hz, 1H), 4.08 (dd, *J* = 8.0, 7.3 Hz, 1H), 4.27 (dd, *J* = 7.6, 7.3 Hz, 1H), 4.91 (dm, *J* = 8.4 Hz, 1H), 4.95 (dm, *J* = 10.0 Hz, 1H), 5.18 (s, 1H), 5.65 (m, 1H), 7.20-7.40 (m, 6H), 7.49 (d, *J* = 7.8 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR δ: 52.4, 66.7, 74.5, 96.7, 118.3, 128.2, 128.4, 128.7, 128.8129.0, 129.4, 134.0, 134.4, 137.1; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{18}H_{20}NO$: 266.1545; found : 266.1553.

(2*R*,4*R*) 3-allyl-2-(2-bromophenyl)-4-phenyloxazolidine.
Orange oil, $[\alpha]^{D}_{23}$ - 28.1 (*c* 1, CH_2Cl_2); ^{1}H NMR δ: 3.13 (dd, *J* = 14.2, 7.5 Hz, 1H), 3.23 (dd, *J*, = 14.2, 6.0 Hz, 1H), 3.84 (dd, *J* = 7.5, 7.2 Hz, 1H), 4.11 (dd, *J* = 8.2, 7.2 Hz, 1H), 4.28 (dd, *J* = 8.2, 7.5 Hz, 1H), 4.89 (dm, *J* = 10.0 Hz, 1H), 4.98 (dm, *J* = 17.0 Hz, 1H), 5.63 (m, 1H), 5.65 (s, 1H), 7.20 (m, 2H), 7.30-7.45 (m, 4H), 7.53 (t, *J* = 8.5 Hz, 2H), 7.95 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR δ: 52.4, 66.6, 73.9, 94.6, 118.0, 127.6, 127.6, 128.0 (2C), 128.7, 130.3, 132.9, 133.7, 138.9, 139.7, 1C is missing; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{18}H_{19}BrNO$: 344.0662; found : 344.0650.

(2*R*,4*R*) 3-allyl-4-(2-methoxyphenyl)-4-phenyloxazolidine.
Yellow oil, $[\alpha]^{D}_{23}$ - 22.2 (*c* 0.8, CH_2Cl_2); ^{1}H NMR δ: 3.07 (dd, *J* = 14.2, 7.0 Hz, 1H), 3.23 (dd, *J* = 14.2, 6.2 Hz, 1H), 3.76 (dd, *J* = 7.7, 7.2 Hz, 1H), 3.78 (s, 3H), 4.01 (dd, *J* = 8.0, 7.2 Hz, 1H), 4.18 (dd, *J* = 8.0, 7.7 Hz, 1H), 4.82 (dm, *J* = 9.0 Hz, 1H), 4.88 (dm, *J* = 15.2 Hz, 1H), 5.62 (m, 1H), 5.65 (s, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 7.12-7.32 (m, 3H), 7.44 (d, *J* = 7.0 Hz, 2H), 7.82 (dd, *J* = 7.5, 1.5 Hz, 1H), ^{13}C NMR δ: 52.5, 55.7, 66.5, 73.9, 89.7, 110.7, 117.6, 120.7, 120.7, 127.7, 128.1, 128.6, 128.8, 12.9.9, 134.1, 140.1, 158.5, 1C is missing; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{19}H_{22}NO_2$: 296.1651; found : 296.1651.

(2*R*,4*R*) 3-allyl-2-(2-furyl)-4-phenyloxazolidine.
Orange oil, Obtained after purification by column chromatography as a 4:1 mixture of diastereomers. Major isomer : ^{1}H NMR δ: 3.21 (dd, *J* = 14.2, 7.2 Hz, 1H), 3.33 (dd, *J* = 14.2, 4.7 Hz, 1H), 3.82 (dd, *J* = 8.7, 7.5 Hz, 1H), 4.04 (dd, *J* = 8.7, 6.7 Hz, 1H), 4.23 (dd, *J* = 7.5, 6.7 Hz, 1H), 4.97 (dm, *J* = 10.2 Hz, 1H), 5.03 (dm, *J* = 18.2 Hz, 1H), 5.35 (s, 1H), 5.71 (m, 1H), 6.37 (m, 1H), 6.54 (d, *J* = 3.2 Hz, 1H), 7.25-7.52 (m, 6H); ^{13}C NMR δ: 53.7, 66.9, 73.5, 89.8, 109.2, 110.2, 117.8, 127.9, 128.2, 128.6, 134.0, 139.2, 143.1, 153.8 ; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{16}H_{18}NO_2$: 256.1338; found : 256.1339.

(2*R*,4*R*) 3-allyl-2-(3-furyl)-4-phenyloxazolidine.
Yellow oil, $[\alpha]^{D}_{23}$ - 15.0 (*c* 1, CH_2Cl_2);^{1}H NMR δ: 3.21 (d, *J* = 7.0 Hz, 2H), 3.80 (dd, *J* = 8.0, 7.7 Hz, 1H), 4.02 (dd, *J* = 8.0, 7.2 Hz, 1H), 4.22 (dd, *J* = 7.7, 7.2 Hz, 1H), 4.95 (dm, *J* = 9.2 Hz, 1H), 4.99 (dm, *J* = 17.0 Hz, 1H), 5.26 (s, 1H), 5.69 (m, 1H), 6.60 (s, 1H), 7.24-7.38 (m, 6H), 7.57 (s, 1H); ^{13}C NMR δ: 53.0, 66.6, 73.6, 89.5, 109.4, 117.8, 126.1, 127.8, 127.9, 128.6, 134.0, 140.0, 141.9, 143.6; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{16}H_{18}NO_2$: 256.1338; found : 256.1333.

(2*R*,4*R*) 3-allyl-2-pentyl-4-phenyloxazolidine.
Yellow oil, $[\alpha]^{D}_{23}$ - 90.5 (*c* 0.4, CH_2Cl_2); ^{1}H NMR δ: 0.91 (t, *J* = 6.8 Hz, 3H), 1.20-1.80 (m, 8H), 3.13 (dd, *J* = 14.2, 7.0 Hz, 1H), 3.27 (dd, *J* = 14.2, 6.0 Hz, 1H), 3.67 (dd, *J* = 7.9, 7.8 Hz, 1H), 3.89 (dd, *J* = 7.8, 7.3 Hz, 1H), 4.12 (dd, *J* = 7.9, 7.3 Hz, 1H), 4.33 (dd, *J* = 6.2, 2.7 Hz, 1H), 5.00 (dm, *J* = 10.2 Hz, 1H), 5.07 (dm, *J* = 17.2 Hz, 1H), 5.78 (m, 1H), 7.2-7.42 (m, 5H); ^{13}C NMR δ: 14.2, 22.8, 24.3, 32.1,

35.0, 54.1, 67.3, 73.2, 96.4, 117.2, 127.8, 128.5, 129.2, 135.3, 140.7; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{17}H_{26}ON$: 260.2014; found: 260.2019.

(2*R*,4*R*) 3-allyl-2-isopropyl-4-phenyloxazolidine.
Yellow oil, $[\alpha]^D_{23}$ - 10.5.1 (*c* 1, CH_2Cl_2);^{1}H NMR δ: 1.02 (d, *J* = 6.6 Hz, 6H), 1.89 (m, 1H), 3.14 (dd, *J* = 14.2, 7.2 Hz, 1H), 3.28 (dd, *J* = 14.2, 6.0 Hz, 1H), 3.61 (dd, *J* = 8.5, 7.0 Hz, 1H), 3.94 (dd, *J* = 8.5, 7.3 Hz, 1H), 4.14 (dd, *J* = 7.5, 7.0 Hz, 1H), 4.19 (d, *J* = 3.2 Hz, 1H), 4.99 (dm, *J* = 17.0 Hz, 1H), 5.04 (dm, *J* = 11.0 Hz, 1H), 5.79 (m, 1H), 7.15-7.45 (m, 5H); ^{13}C NMR δ: 15.9, 19.3, 32.2, 54.9, 67.7, 74.1, 100.6, 117.5, 127.9, 128.1, 128.6, 135.6, 140.8; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{15}H_{22}NO$: 232.1701; found : 232.1698.

General procedure for the preparation of oxazolidines 4.
A solution of aminoalcohol (1 mmol) and the relevant aldehyde (1 mmol) in toluene (5 mL) in the presence of PTSA (10 mg, 0.05 mmol) was heated to reflux for 24h in a Dean-Stark apparatus. The solvent was removed under reduced pressure to give the oxazolidine which was used without purification in the next step.

(2*R*,4*R*)-2,4-diphenyl 3-[(*R*) 1-phenylallyl]oxazolidine 4a.
Orange oil, $[\alpha]^D_{23}$ - 22.6 (*c* 1, CH_2Cl_2); ^{1}H NMR δ: 3.80 (dd, *J* = 7.7, 7.0 Hz, 1H), 4.13 (dd, *J* = 7.2, 7.0 Hz, 1H), 4.23 (dd, *J* = 7.7, 7.2 Hz, 1H), 4.41 (d, *J* = 8.7 Hz, 1H), 5.02 (dm, *J* = 10.2 Hz, 1H), 5.13 (dm, *J* = 17.2 Hz, 1H), 5.64 (s, 1H), 6.00 (m, 1H), 7.05-7.35 (m, 13H), 7.60 (d, *J* = 7.7 Hz, 2H); ^{13}C NMR δ: 66.7, 70.8, 73.5, 95.1, 117.1, 127.0, 127.2, 127.8, 127.9, 128.0, 128.10, 128.15, 128.20, 128.7, 138.7, 140.7, 141.6, 142.0; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{24}H_{24}NO$: 342.1858; found: 342.1857.

(2*R*,4*R*) 2,4-diphenyl-3-[(*R*) 1-(4-chlorophenyl)allyl]oxazolidine 4b.
Brown oil, $[\alpha]^D_{23}$ - 30.0 (*c* 0.12, CH_2Cl_2);^{1}H NMR δ: 3.82 (dd, *J* = 8.0, 7.5 Hz, 1H), 4.07 (dd, *J* = 7.5, 7.2 Hz, 1H), 4.24 (dd, *J* = 8.2, 7.2 Hz, 1H), 4.38 (d, *J* = 9.0 Hz, 1H), 5.06 (dm, *J* = 16.5 Hz, 1H), 5.14 (dm, *J* = 16.5 Hz, 1H), 5.61 (s, 1H), 5.95 (m, 1 H), 6.98-7.37 (m, 12 H), 7.57 (d, *J* = 7.7 Hz, 2H); ^{13}C NMR δ: 66.9, 69.9, 73.3, 94.8, 117.6, 127.0, 127.7, 127.9, 128.1, 128.1, 128.2, 129.8, 132.7, 137.8, 139.2, 141.3, 141.4; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{24}H_{23}ClNO$: 376.1468; found: 376.1467.

(2*R*,4*R*) 2-(4-chlorophenyl)-4-phenyl-3-[(*R*) 1-phenylallyl]oxazolidine 4c.
Orange oil, ^{1}H NMR δ: 3.71 (dd, *J* = 7.7, 7.1 Hz, 1H), 4.07 (dd, *J* = 7.1, 7.3 Hz, 1H), 4.16 (dd, *J* = 7.7, 7.3 Hz, 1H), 4.33 (d, *J* = 8.9 Hz, 1H), 5.00 (dm, *J* = 10.2 Hz 1H), 5.09 (dm, *J* = 17.1 Hz, 1H), 5.56 (s, 1H), 5.93 (m, 1H), 7.00-7.12 (m, 5H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), ^{13}C NMR δ: 66.7 (2C), 70.6, 73.4, 94.4, 117.6, 127.1, 127.4, 127.8, 128.2 (2C), 128.3, 128.7, 129.3, 133.9, 138.2, 140.4, 140.6, 141.6; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{24}H_{23}ClNO$: 376.1468; found: 376.1457.

General procedure for the preparation of pyrrolidines

Pyrrolidines 2.
To a solution of oxazolidine (0.5 mmol) in CH_2Cl_2 (2 mL) was added in one portion $Cp_2Zr(H)Cl$ (141 mg, 0.55 mmol) at r.t. The reaction was stirred until the suspension was completely soluble (c.a. 1-2h). The deep yellow solution was cooled to 0°C and the Lewis acid was added dropwise and the resulting mixture was stirred for two hours. Water (1 mL) was added the heterogenous mixture was stirred for one hour. The aqueous layer was extracted with CH_2Cl_2 (3x2 mL), the organic layers were combined, washed with water (2 mL), dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel using Petroleum ether : EtOAc : NEt_3 (80:20:1) as eluant to give the pyrrolidine as an oil.

(*R*) 2-phenyl-2-((*S*)-2-phenylpyrrolidin-1-yl]ethanol 2a.[5]
(yield 62%) $[\alpha]^{D}_{23}$ - 207 (*c* 1, CH_2Cl_2); ^{1}H NMR δ: 1.58-1.75 (m, 2H), 1.80-2.10 (m, 2H), 2.31 (q, *J* = 8.5 Hz, 1H), 3.13 (ddd, *J* = 8.7, 6.5, 2.2 Hz, 1H), 3.44 (t, *J* = 8.0 Hz, 1H), 3.50 (dd, *J* = 10.2, 5.0 Hz, 1H), 3.75 (dd, *J* = 10.5, 5.0 Hz, 1H), 3.97 (t, *J* = 10.2 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 2H), 7.28-7.42 (m, 8H); ^{13}C NMR δ: 22.2, 34.5, 45.2, 61.3, 61.9, 64.5, 127.3, 127.7, 127.8, 128.2, 128.8, 129.4, 134.5, 143.4; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{18}H_{22}ON$: 268.1701; found: 268.1699.

(*R*) 2-phenyl-2-[(*S*)-2-(2-bromo-phenyl)pyrrolidin-1-yl]ethanol 2b.
(yield 53%) $[\alpha]^{D}_{23}$ -116 (*c* 1, CH_2Cl_2); ^{1}H NMR δ: 1.52 (m, 1H), 1.66 (m, 1H), 1.84 (m, 1H), 2.14 (m, 1H),), 2.35 (q, *J* = 8.4 Hz, 1H), 2.67 (br s, 1H), 3.12 (td, *J* = 8.1, 1.8 Hz, 1H), 3.57 (dd, *J* = 10.2, 5.5 Hz, 1H), 3.75 (dd, *J* = 9.2, 5.5 Hz, 1H), 3.93-4.02 (m, 2H), 7.12-7.16 (m, 3H), 7.30-7.40 (m, 4H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR δ: 22.4, 32.9, 46.4, 62.2, 62.9, 63.7, 123.6, 127.8, 128.0, 128.2, 128.3, 129.5, 132.9, 133.8, 135.0, 142.9; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{18}H_{21}BrNO$: 346.0807; found: 346.0801.

(***R*) 2-phenyl-2-[(*S*)-2-(2-methoxyphenyl)pyrrolidin-1-yl)ethanol 2c.**
(yield 55%), $[\alpha]^{D}_{23}$ -149 (*c* 1, CH_2Cl_2); ^{1}H NMR δ: 1.57 (m, 1H,), 1.66 (m, 1H,), 1.84 (m, 1H,), 2.14 (m, 1H), 2.35 (q, *J* = 8.4 Hz, 1H), 2.52 (br s, 1H), 3.12 (td, *J* = 8.4, 1.8 Hz, 1H), 3.57 (dd, *J* = 10.2, 5.5 Hz, 1H), 3.75 (dd, *J* = 9.2, 5.5 Hz, 1H), 3.93-4.02 (m, 2H), 7.12-7.16 (m, 3H), 7.30-7.40 (m, 4H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR δ: 22.6, 32.6, 45.8, 55.7, 61.6, 62.8, 110.7, 121.0, 127.6, 127.9, 128.3, 129.4, 131.6, 135.4, 157.3; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{19}H_{24}BrNO_2$: 298.1807; found: 298.1803.

(*R*) 2-phenyl-2[(*S*)-2-(2-furyl)pyrrolidin-1-yl]ethanol 2d.
(yield 41%), $[\alpha]^{D}_{23}$ -223 (*c* 0.15, CH_2Cl_2); ^{1}H NMR δ: 1.67 (m, 1H), 1.93 (m, 3H), 2.27 (q, *J* = 8.2 Hz, 1H), 2.48 (br s, 1H), 3.04 (td, *J* = 7.2, 2.2 Hz, 1H), 3.57 (dd, *J* = 10.0, 4.7 Hz, 1 H), 3.71 (t, *J* = 7.5 Hz, 1H), 3.80 (dd, *J*= 10.2, 4.7 Hz, 1H), 1H), 3.94 (t, *J* =10.0 Hz, 1H), 6.28 (d, *J* = 3.0 Hz, 1H), 6.36 (dd, *J* = 3.2, 3.0 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 2H), 7.30-7.40 (3H), 7.43 (m, 1H); ^{13}C NMR δ: 22.4, 30.4, 45.4, 57.8, 61.6, 62.8, 107.6, 110.2, 127.9, 128.3, 129.5, 142.02, 2C are missing, HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{16}H_{20}NO_2$: 258.1494; found: 258.1502.

(*R*) 2-phenyl-2-[(*S*)-2-(3-furyl)pyrrolidin-1-yl]ethanol 2e.
(yield 43%), $[\alpha]^{D}_{23}$ -175 (*c* 1, CH_2Cl_2); ^{1}H NMR δ: 1.68 (m, 2H), 1.92 (m, 2H), 2.25 (q, *J* = 8.4 Hz, 1H), 3.05 (ddt, *J* = 8.7, 7.2, 1.5 Hz, 1H), 3.10 (br s, 1H), 3.48 (t, *J* = 7.6 Hz, 1H), 3.56 (dd, *J* = 9.2, 4.2 Hz, 1H), 3.89 (dd, *J* = 10.7, 6.7 Hz, 1H), 3.97 (t, *J* = 10.5 Hz, 1H), 6.43 (s, 1H), 7.13 (dd, *J* = 7.5, 1.7 Hz, 2H), 7.30-7.37 (m, 3H), 7.44 (s, 2H); ^{13}C NMR δ: 22.0, 32.7, 44.8, 55.2, 61.2, 61.6, 108.9, 127.1, 127.7, 128.1, 129.4, 134.7, 140.2, 143.8; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{16}H_{20}NO_2$: 258.1494; found: 256.1490.

(*R*) 2-phenyl-2-[(*S*)-2-pentyl)pyrrolidin-1-yl]ethanol 2f.
(yield 52%), $[\alpha]^{D}_{23}$ -136 (*c* 0.35, CH_2Cl_2); ^{1}H NMR δ: 0.91 (t, *J* = 6.1 Hz, 3H), 1.20-1.88 (m, 12H), 2.16 (q, *J* = 8.5 Hz, 1H), 2.54 (m, 1H), 2.89 (ddd, *J* = 9.0, 6.5, 2.5, 1H), 3.20 (br s, 1H), 3.63 (dd, *J* = 9.5 , 4.5 Hz, 1H), 3.96 (dd, *J* = 10.7, 9.5 Hz, 1H), 4.06 (dd, *J* = 10.7, 4.5 Hz, 1H), 7.15 (dd, *J* = 7.7, 2.0 Hz, 2H), 7.29-7.36 (m, 3H); ^{13}C NMR δ: 14.0, 22.0, 22.7, 25.8, 29.7, 32.2, 34.0, 45.3, 59.0, 60.9, 62.0, 127.7, 128.0, 129.3, 135.2; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{17}H_{28}NO$: 262.2171; found: 262.2177.

(*R*) 2-phenyl-2-[(*S*)-2-isopropylpyrrolidin-1-yl]ethanol 2g.

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[5] L.E. Burgess, A. I. Meyers, *J. Org. Chem*, **1992**, *57*, 1656-1662.

(major isomer obtained using $TiCl_4$ as Lewis acid), (yield 49%), $[\alpha]^{D}_{23}$ -112 (*c* 0.13, CH_2Cl_2); ^{1}H NMR δ : 0.89 (d, *J* = 6.9 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 1.50 (m, 4H), 2.11 (m, 1H), 2.22 (q, *J* = 6.5 Hz, 1H), 2.59 (m, 1H), 3.35 (br s, 1H), 2.92 (m, 1H), 3.63 (dd, *J* = 16.5, 11.2 Hz, 1H), 4.05 (dd, *J* = 16.5, 11.2, 1H), 4.06 (t, *J* = 11.2 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.28-7.38 (m, 3H); ^{13}C NMR δ: 15.1, 20.5, 22.8, 23.8, 45.7, 61.2, 62.3, 63.5, 127.9, 128.2, 129.5, 135.1; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{15}H_{24}NO$: 234.1858; found: 234.1850.

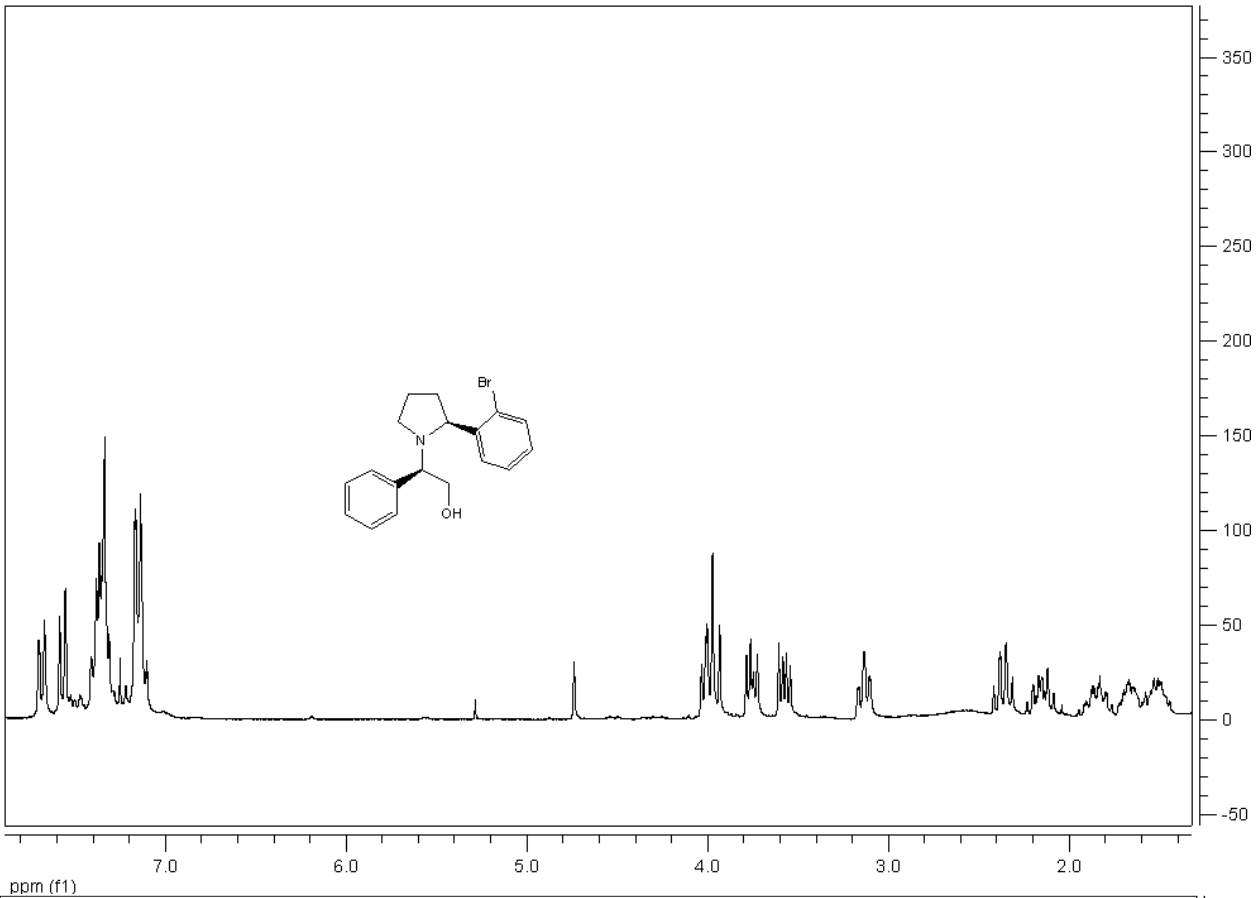
(*R*) 2-phenyl-2-[(*R*)-2-isopropylpyrrolidin-1-yl]ethanol.
(major isomer obtained using $BF_3{\cdot}OEt_2$ as Lewis acid),^{1}H NMR δ: 0.73 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H), 1.35-1.65 (m, 4H), 2.77 (m, 2H), 3.06 (m, 1H), 3.79-3.95 (m, 3H), 7.25-7.40 (m, 5H).

Pyrrolidines 5 were prepared according to the previous procedure using 2 equivalents of $Cp_2Zr(H)Cl$ with respect to the oxazolidines and $BF_3.OEt_2$ (1 equivalent) as Lewis acid.

***(R)* 2-phenyl-2[(2*R*,5*R*)-2,5-diphenylpyrrolidin-1-yl]ethanol 5a.**[4]
(yield 52%) $[\alpha]^{25}_{D}$ +41 (*c* 0.25, EtOH); ^{1}H NMR δ: 1.67 (m, 2H), 2.52 (m, 2H), 3.44 (m, 2H), 3.94 (t, *J* = 6.6 Hz, 1H), 4.40 (d, *J* = 7.0 Hz, 2H), 6.78 (d, *J* = 7.5 Hz, 2H), 6.90-7.50 (m, 13H); ^{13}C NMR δ : 33.8, 63.7, 63.8, 66.2, 128.6, 127.2, 127.7, 128.4, 129.6, 138.3, 146.7; HRMS-ESI: *m/z* $[M+H]^+$ calcd for $C_{24}H_{26}NO$: 344.2014; found: 344.2014.

***(R)* 2-phenyl-2[(2*R*,5*R*)-2-(4-chlorophenyl)-5-phenylpyrrolidin-1-yl]ethanol 5b.**
(yield 48%) $[\alpha]^{25}_{D}$ +62 (*c* 0.15, EtOH); ^{1}H NMR δ: 1.68 (m, 1H), 1.75 (m, 1H), 2.05 (br s, 1H), 2.57 (m, 2H), 3.51 (dd, *J* = 10.7, 2.2 Hz, 1H), 3.59 (dd, *J* = 10.7, 6.2 Hz, 1H), 3.99 (t, *J* = 6.5 Hz, 1H), 4.42 (dd, *J* = 8.2, 2.2 Hz, 1H), 4.52 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.78 (d, *J* = 7.5 Hz, 2 H), 7.02-7.35 (m, 13 H); ^{13}C NMR δ: 33.2, 33.4, 63.5, 63.6, 65.2, 65.9, 127.0, 127.3, 127.5, 127.9, 128.5 (2C), 128.6, 132.3, 138.3, 145.9, 146.3; HRMS $[M+H]^+$ calcd for $C_{24}H_{25}ClNO$: 378.1628; found: 378.1625.

(2*R*) -2-pentyl-pyrrolidinium chloride.
A solution of pyrrolidine **2f** (125 mg, 0.48 mmol) in methanol (20 mL) with 10% Pd/C (25 mg) was charged with hydrogen at room temperature for 24 h. After filtration of the catalyst over a plug of celite, HCl (1N, 0.55 mL), was added to the filtrate. The solvent was removed under vaccum and the residue was heated at 60 °C at 0.1 mm Hg for 1h to give the title compound as a orange oil (65 mg, 76%). $[\alpha]^{25}_{D}$ –2.4 (*c* 1, MeOH); ^{1}H NMR δ: 0.82 (t, *J* = 6.7 Hz, 3H), 1.18-1.44 (m, 6H), 1.52-1.76 (m, 2H), 1.78-2.18 (m, 4H), 3.16-3.50 (m, 3H), 9.22 (br s, 1H), 9.88 (br s, 1H); ^{13}C NMR δ:14.4, 22.9, 23.9, 27.0, 30.7, 31.8, 32.6, 44.8, 60.8; HRMS-ESI: *m/z* $[M-Cl]^+$ calcd for $C_9H_{20}N^+$: 142.1596; found:142.1593.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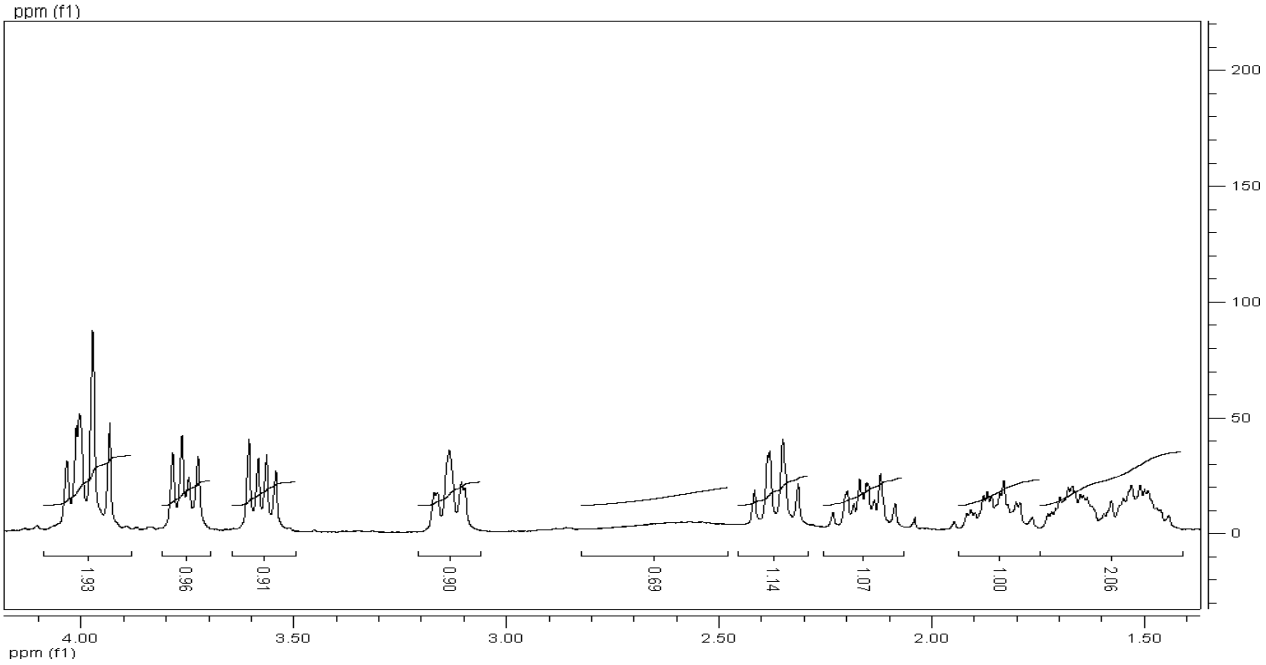
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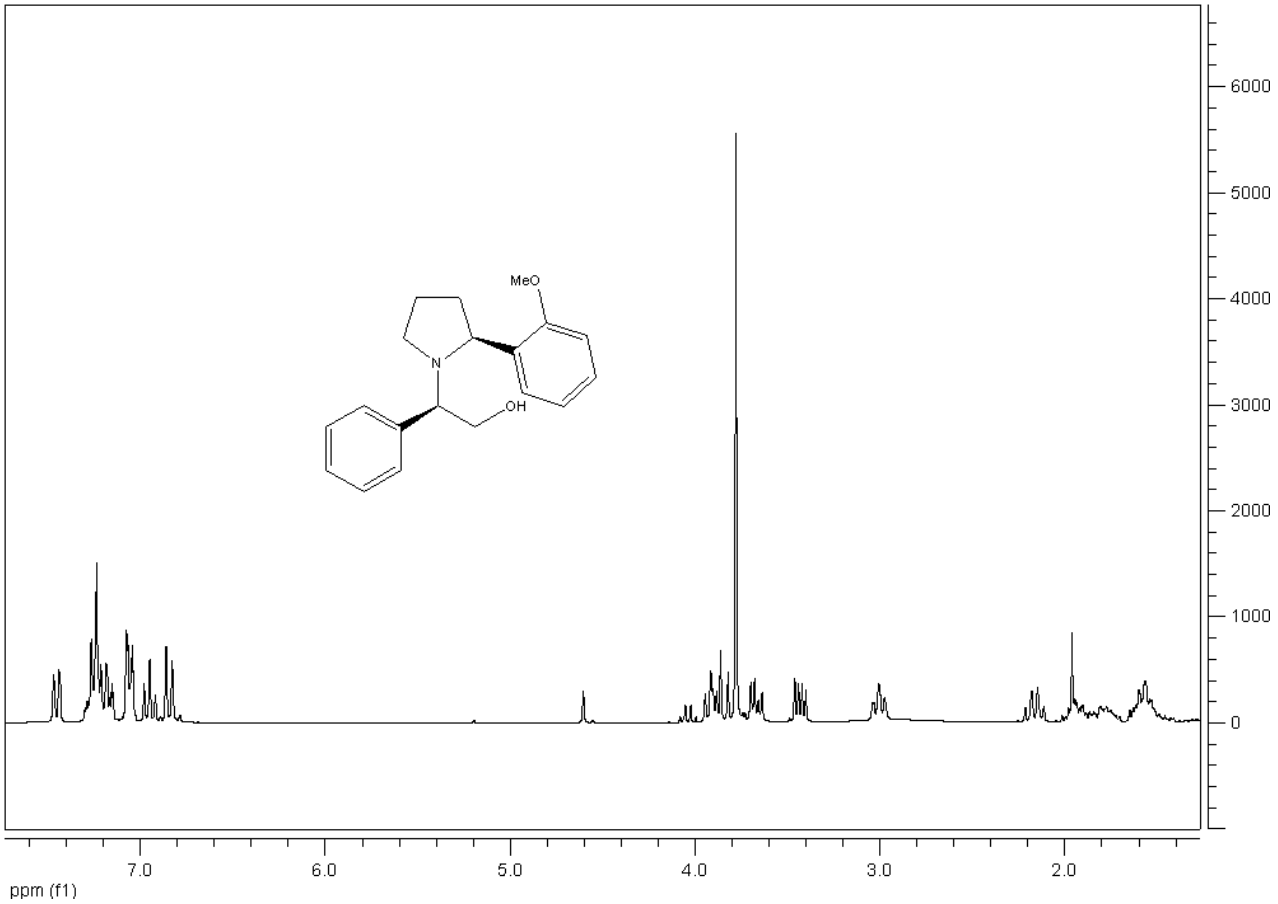
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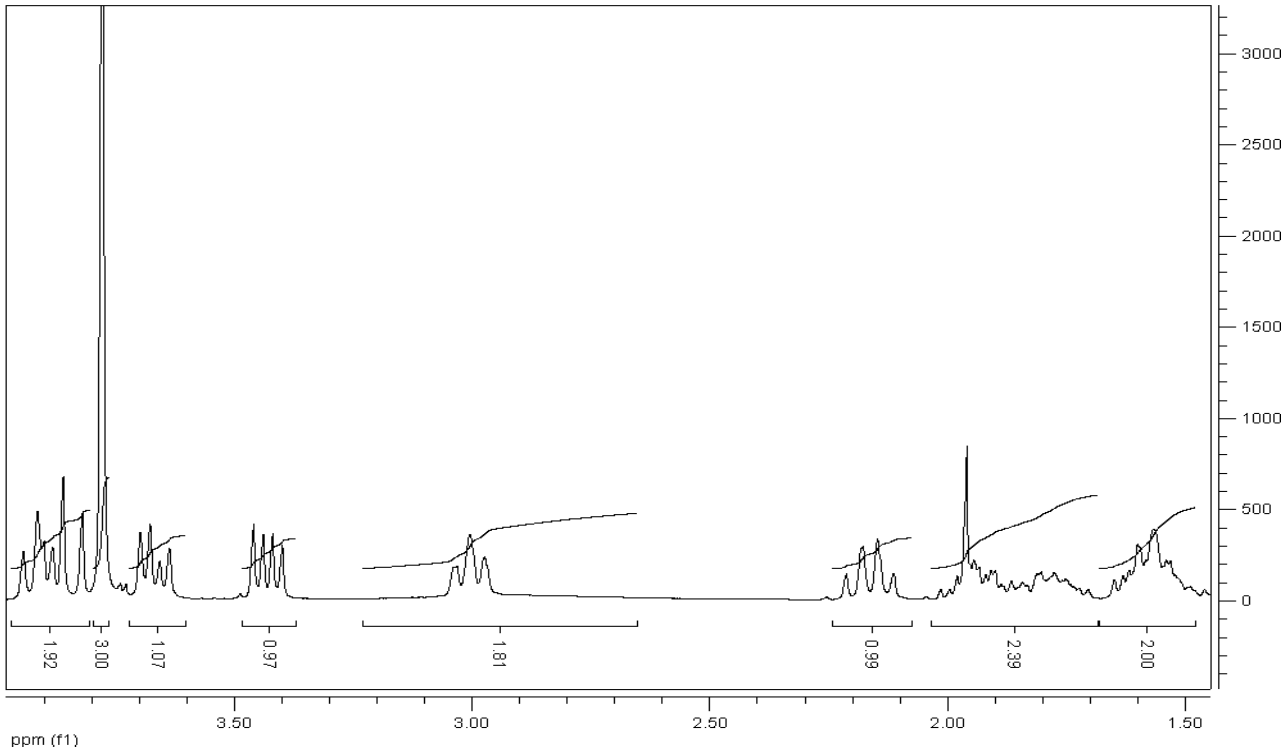
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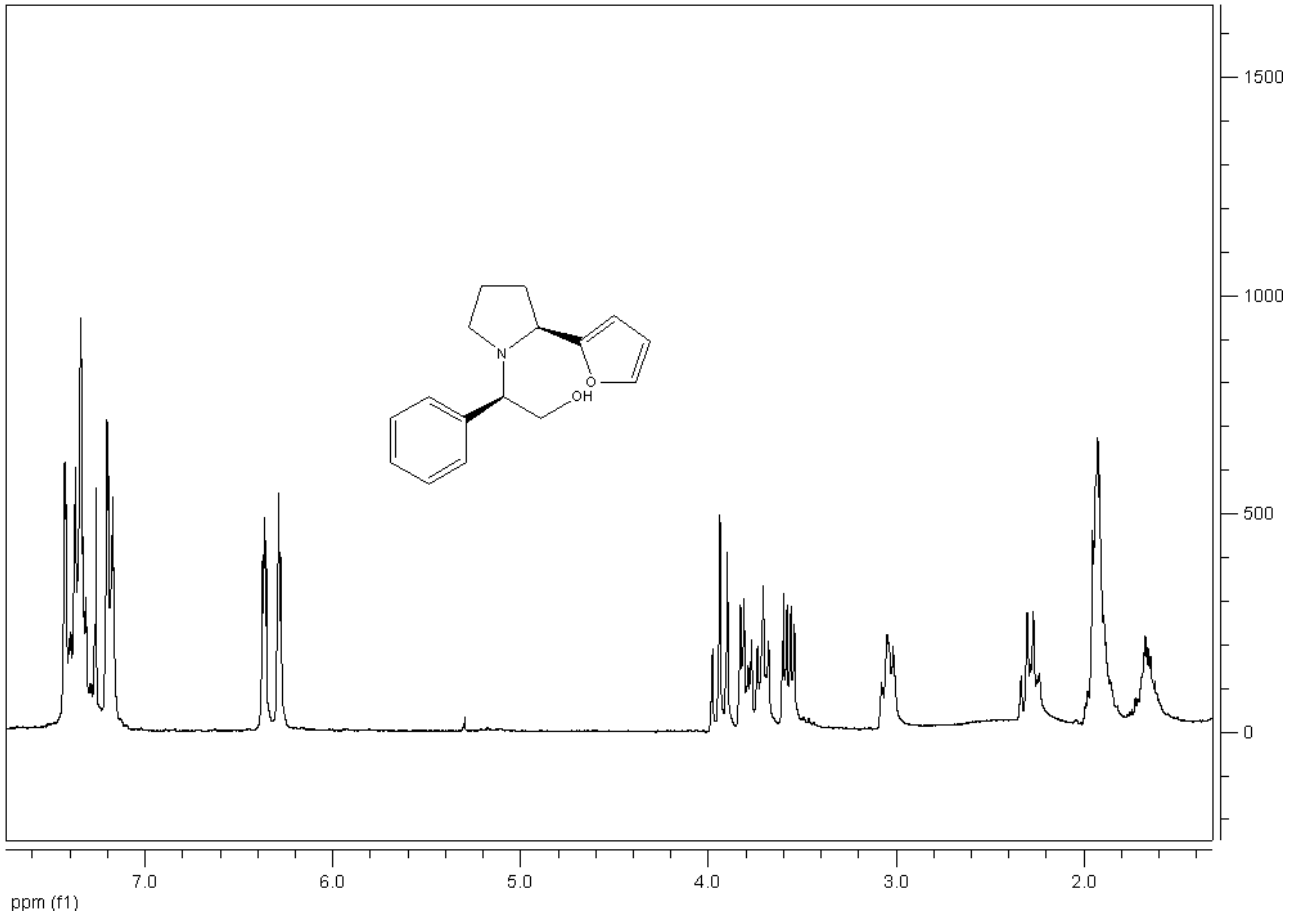
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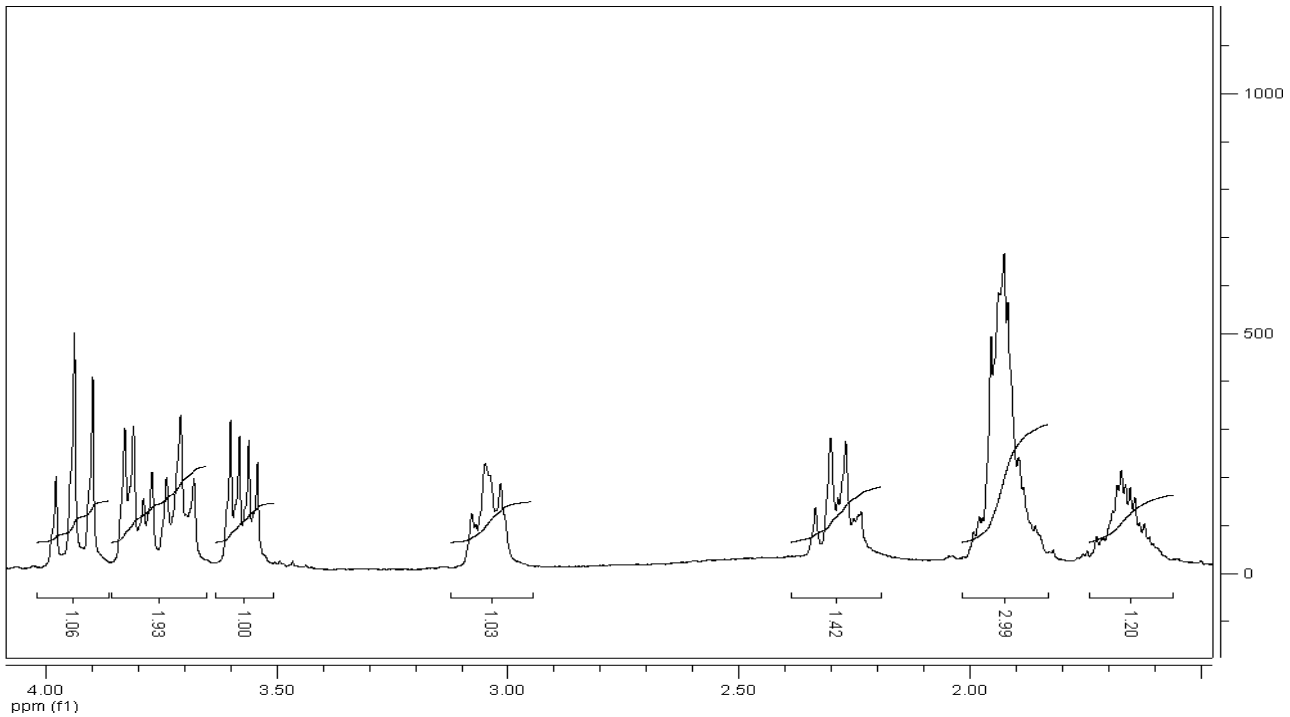
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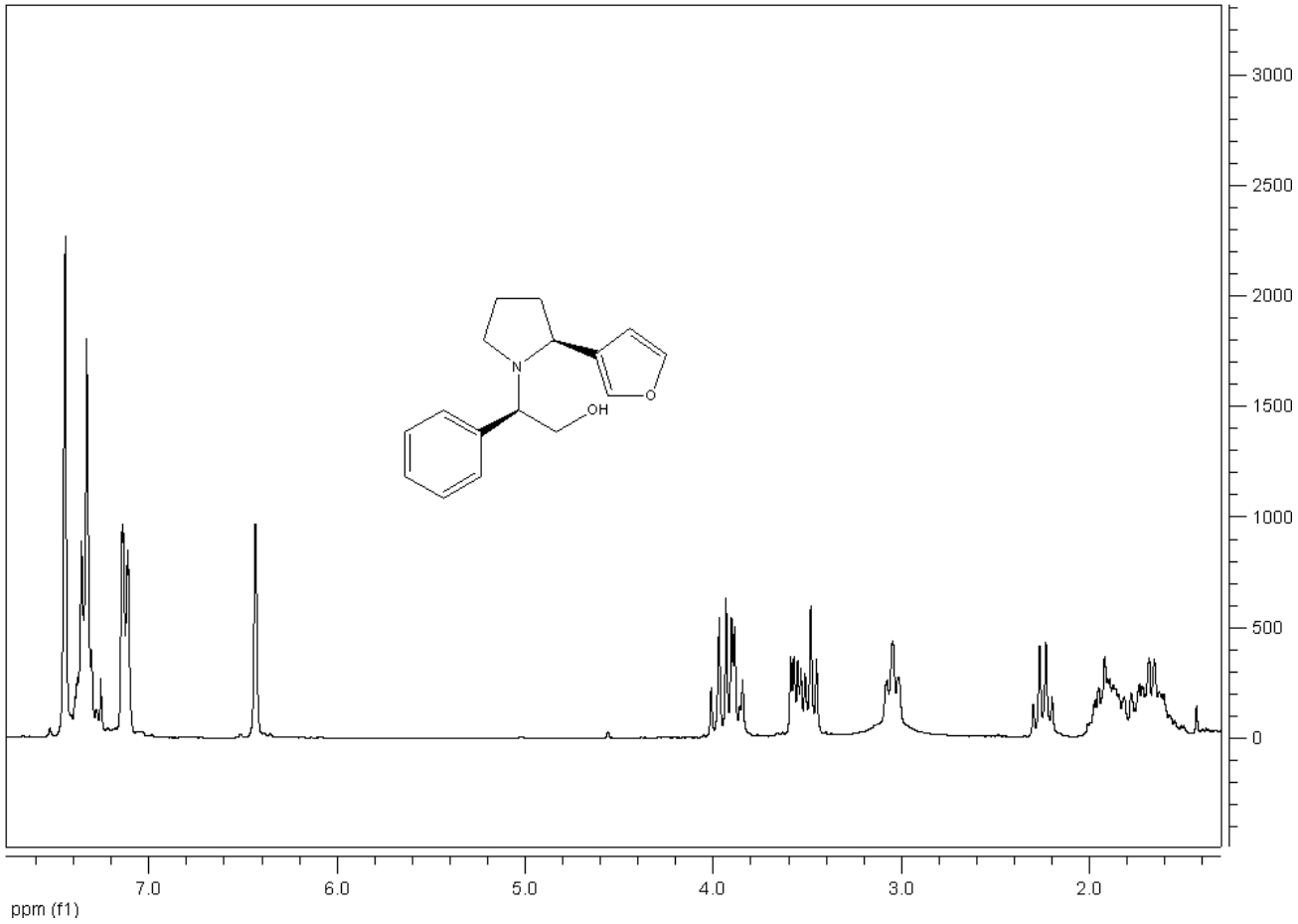
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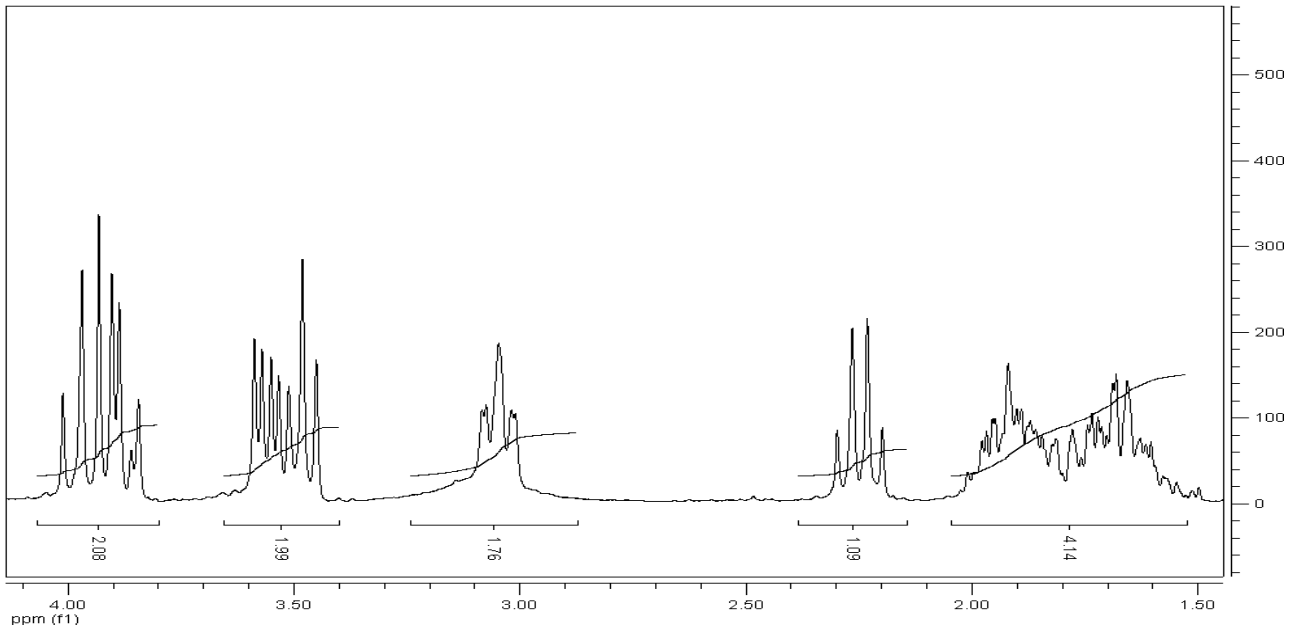
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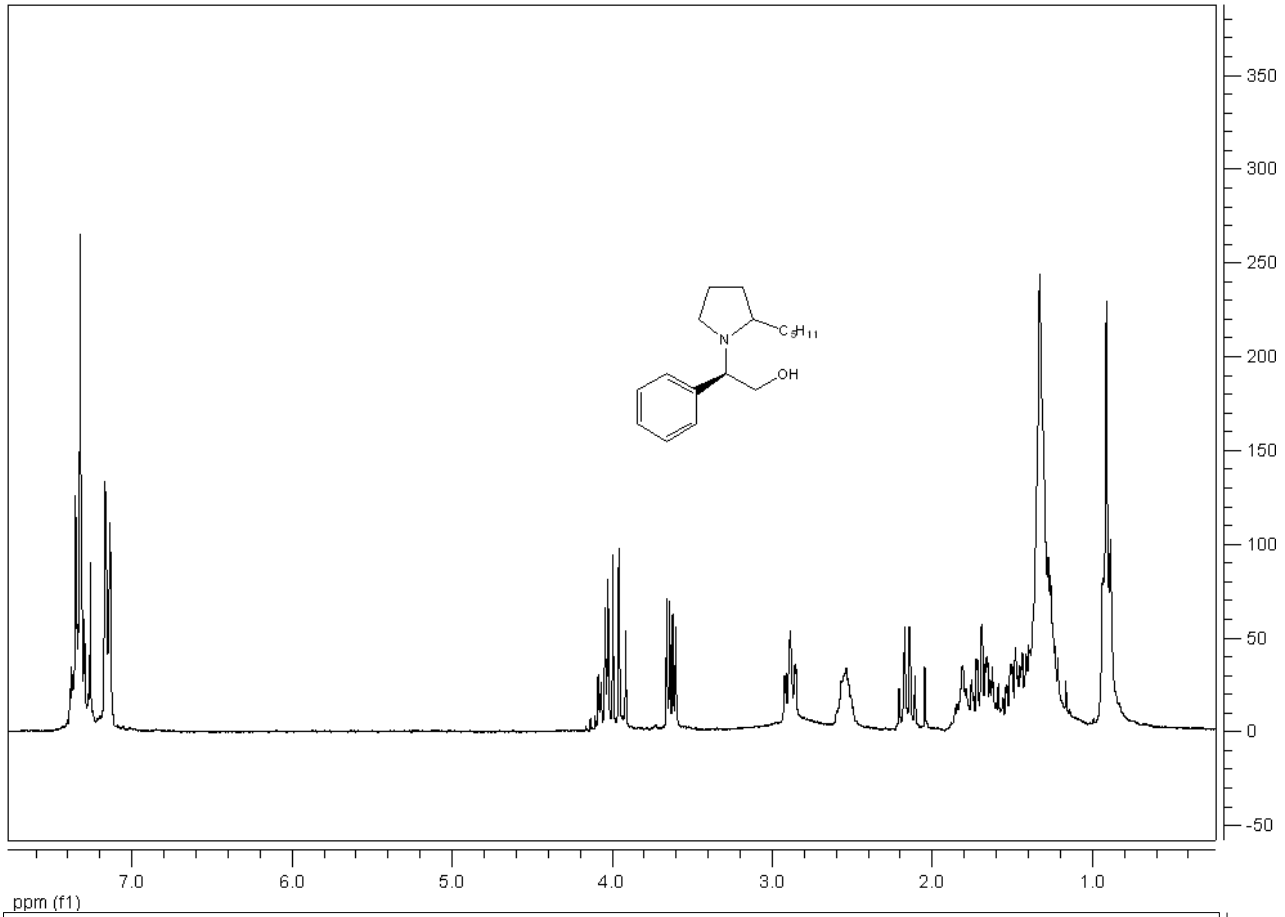
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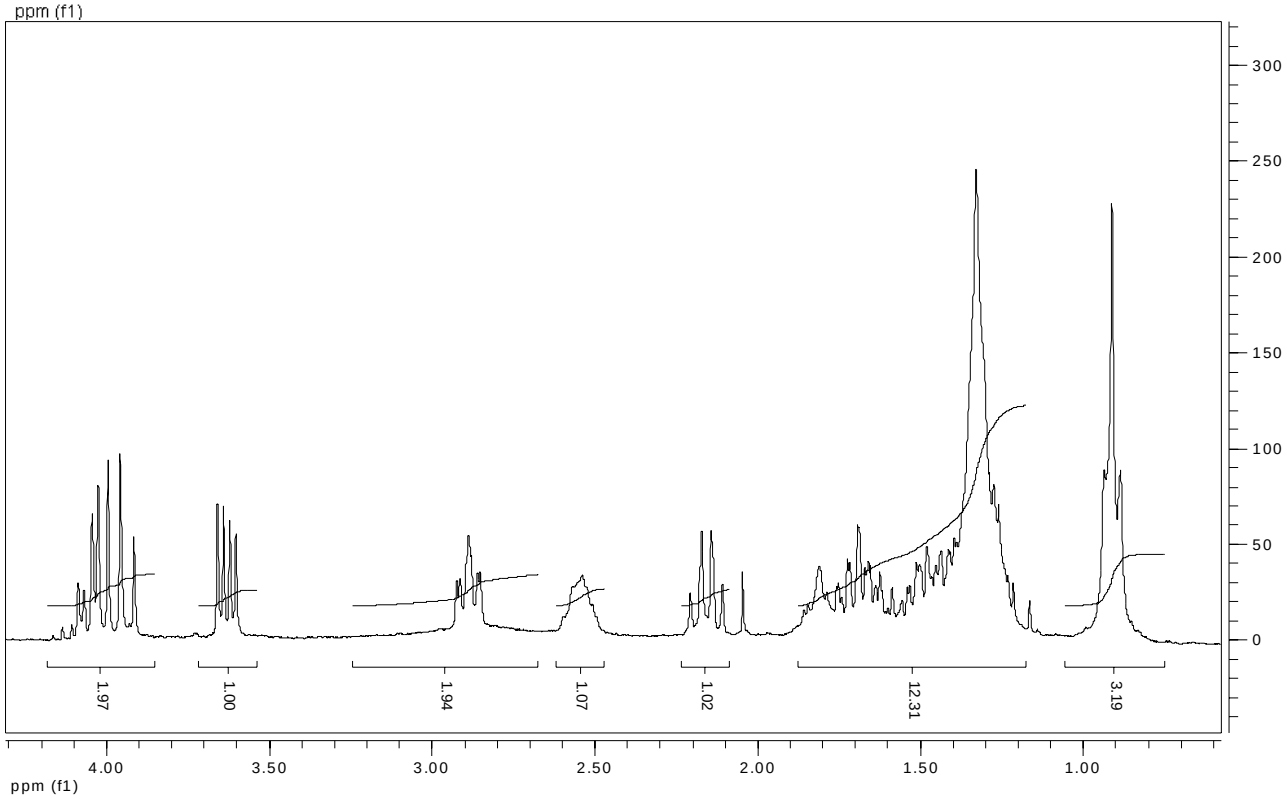
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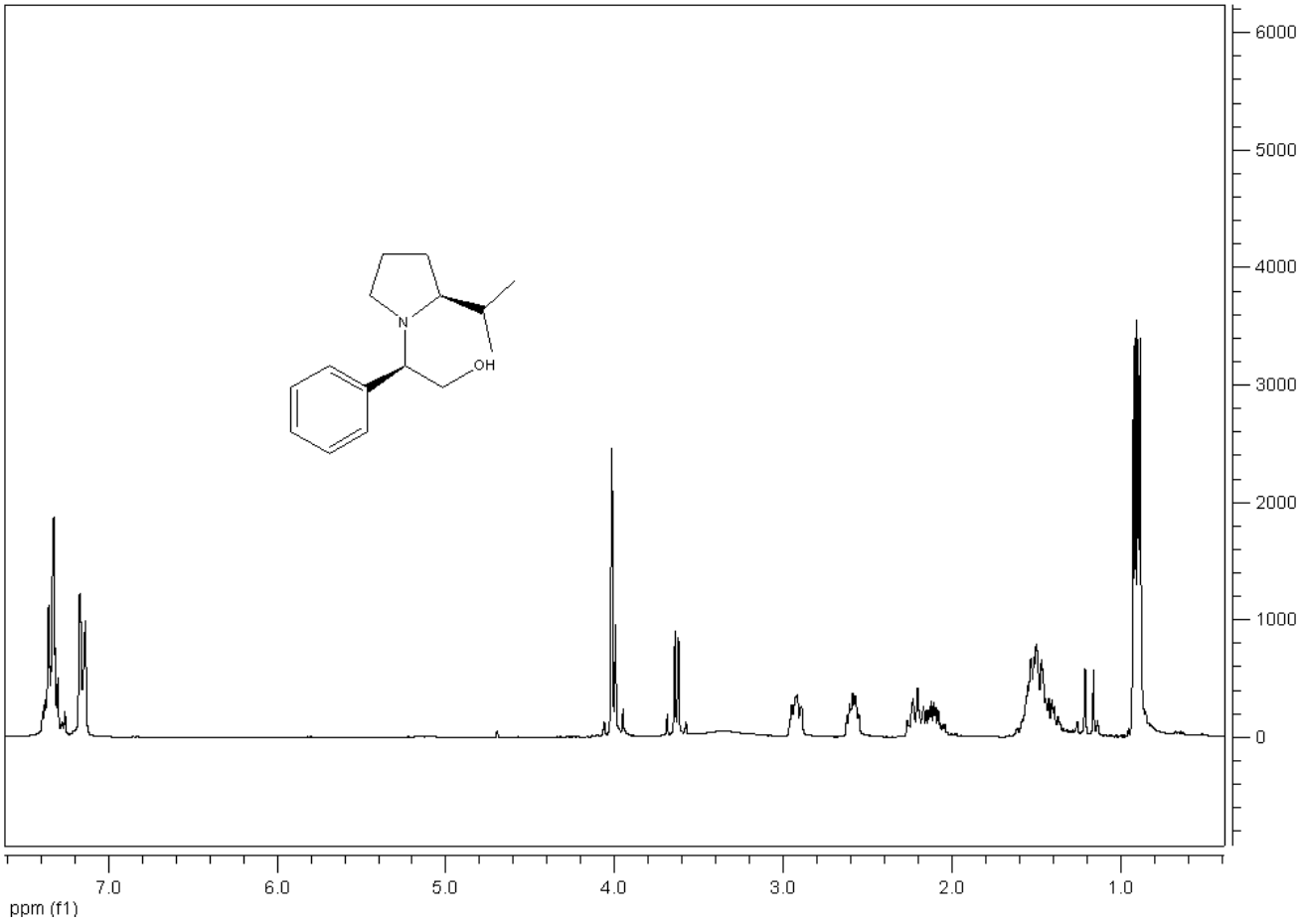
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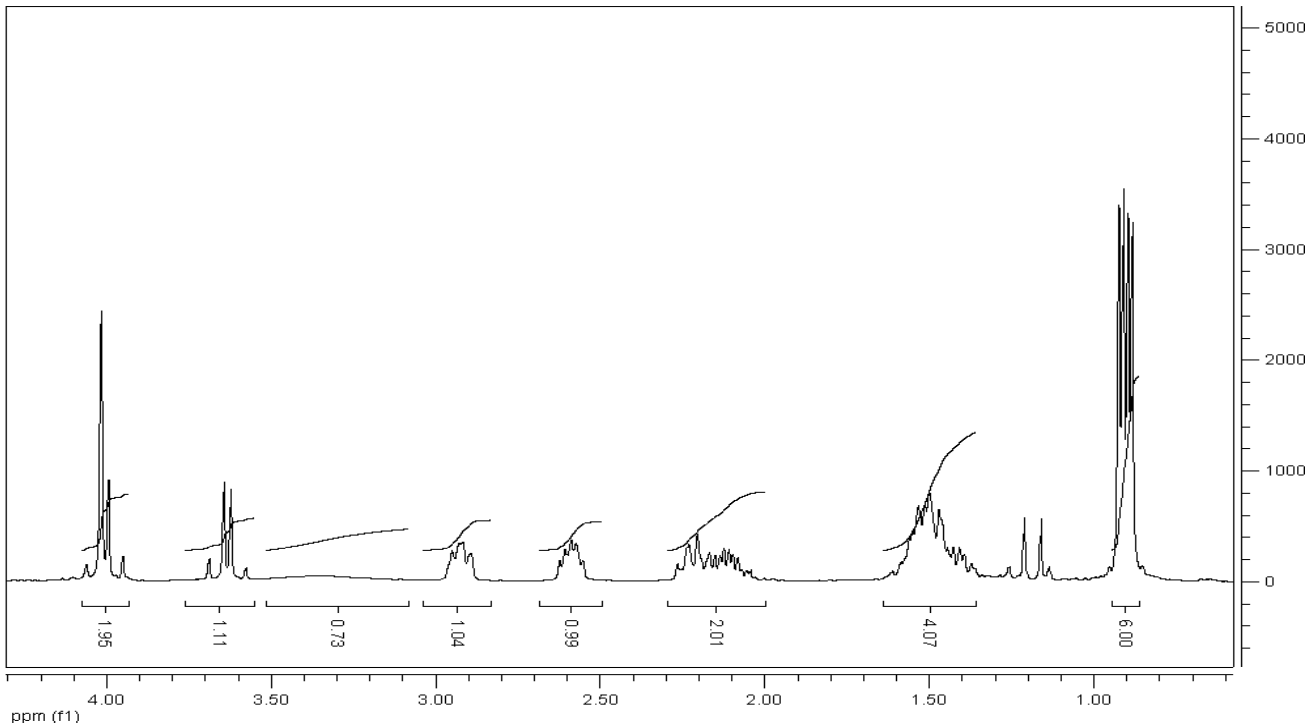
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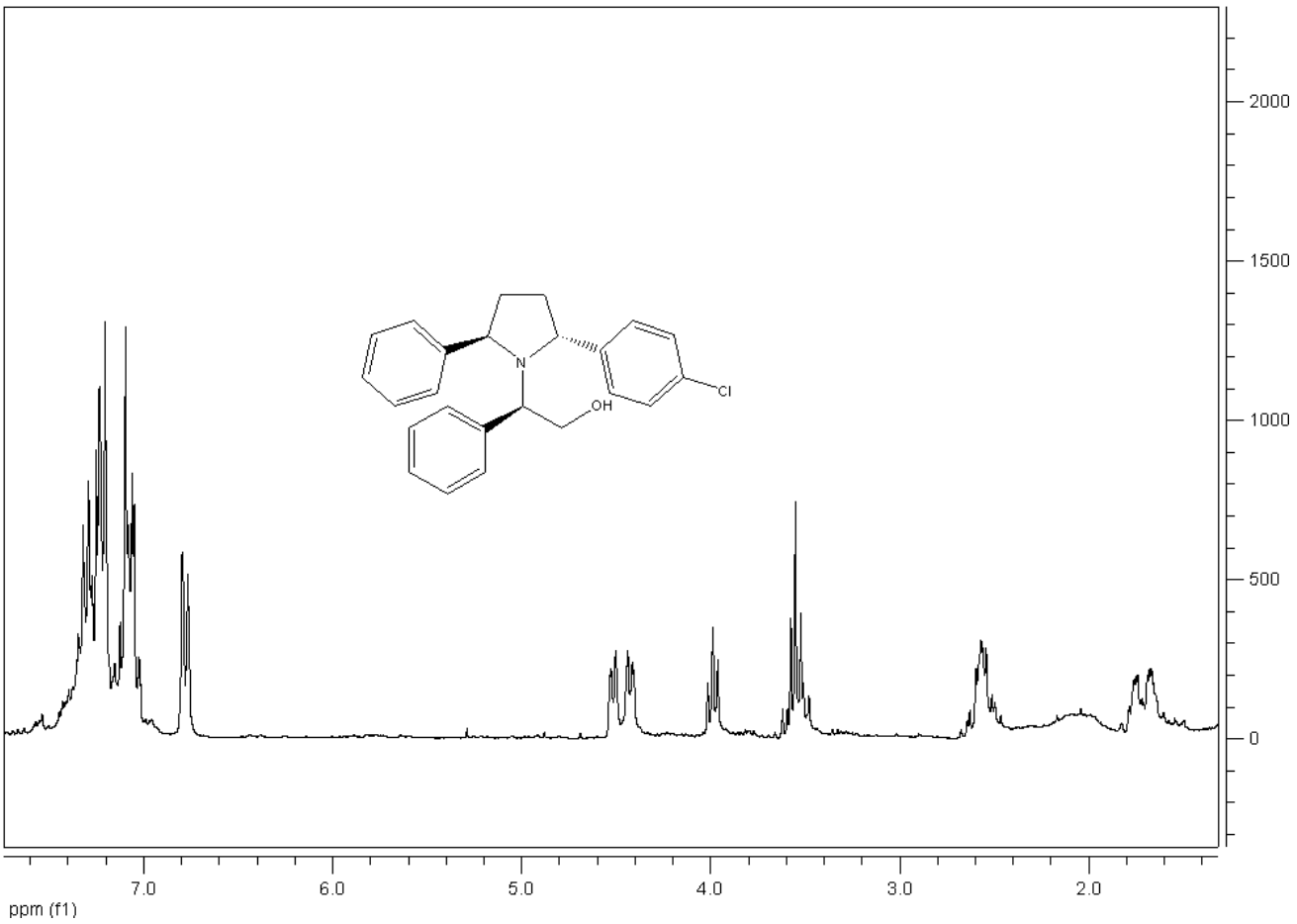
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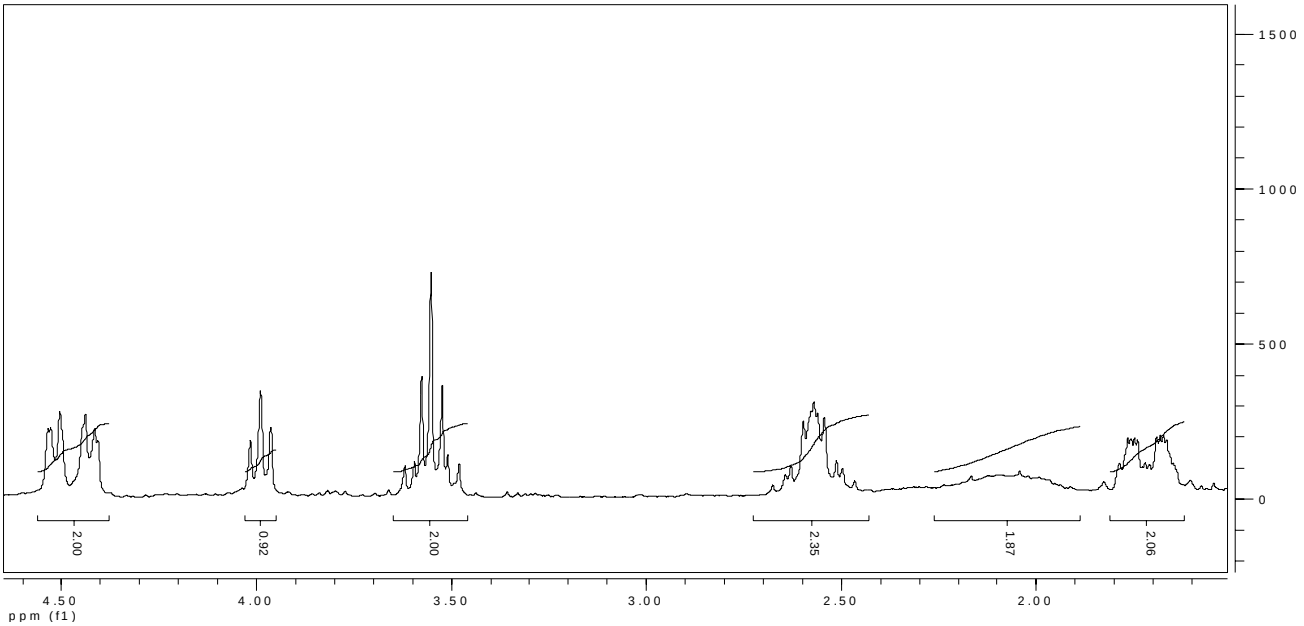
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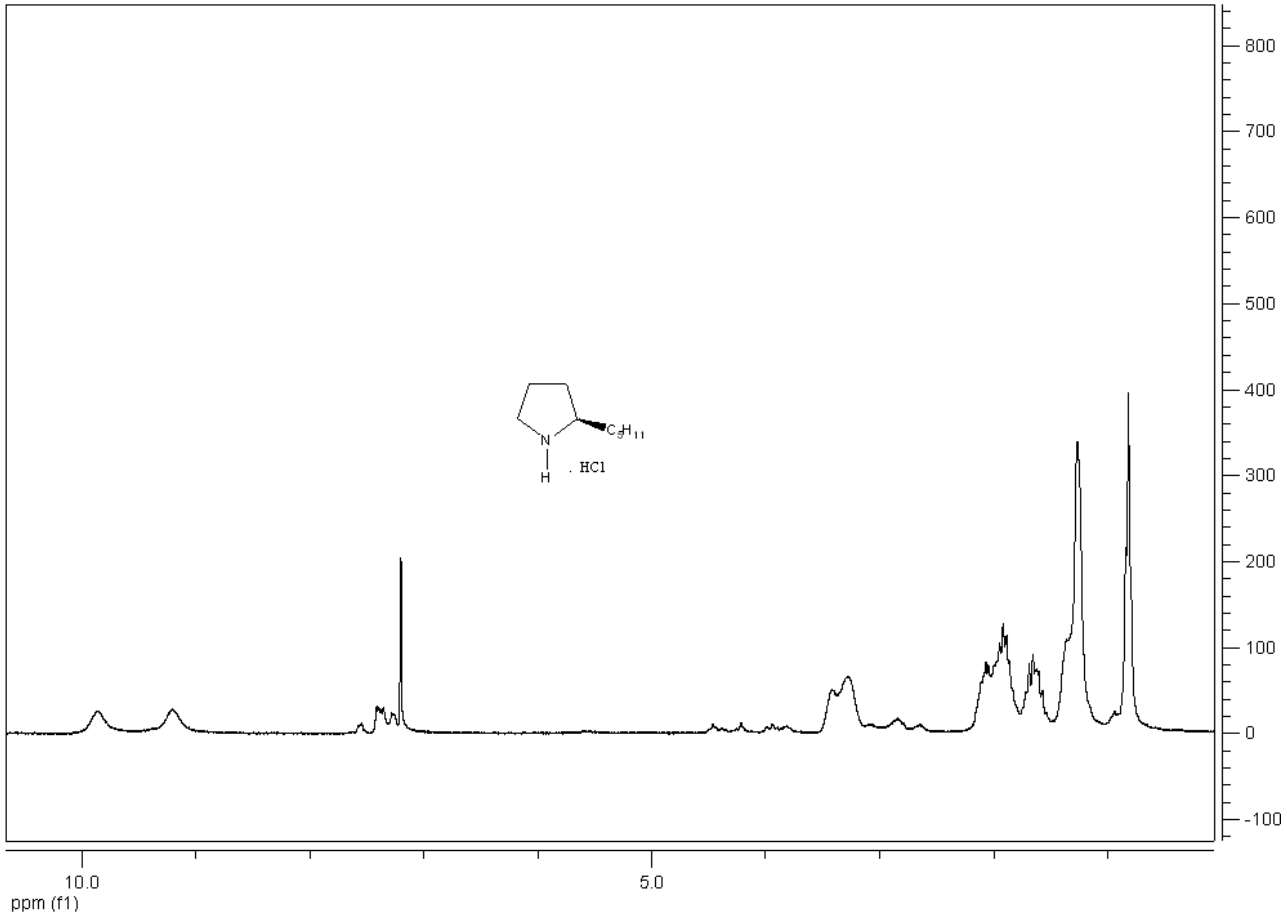
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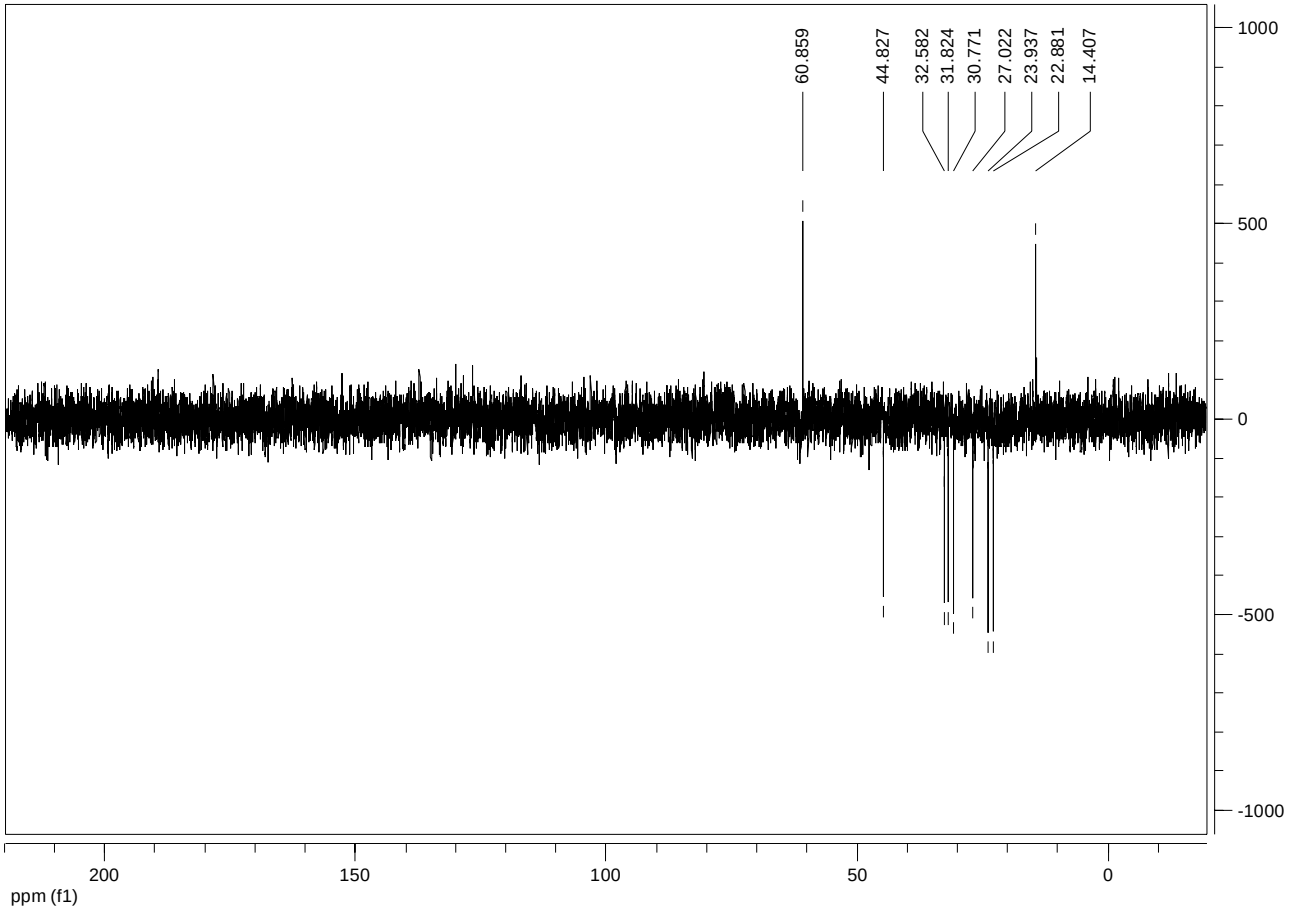
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