Chemoenzymatic synthesis of optically active 2-(2- or 4-substituted-1*H*-imidazol-1-yl)cycloalcanols. Chiral additives for (L)-proline.

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Supporting information

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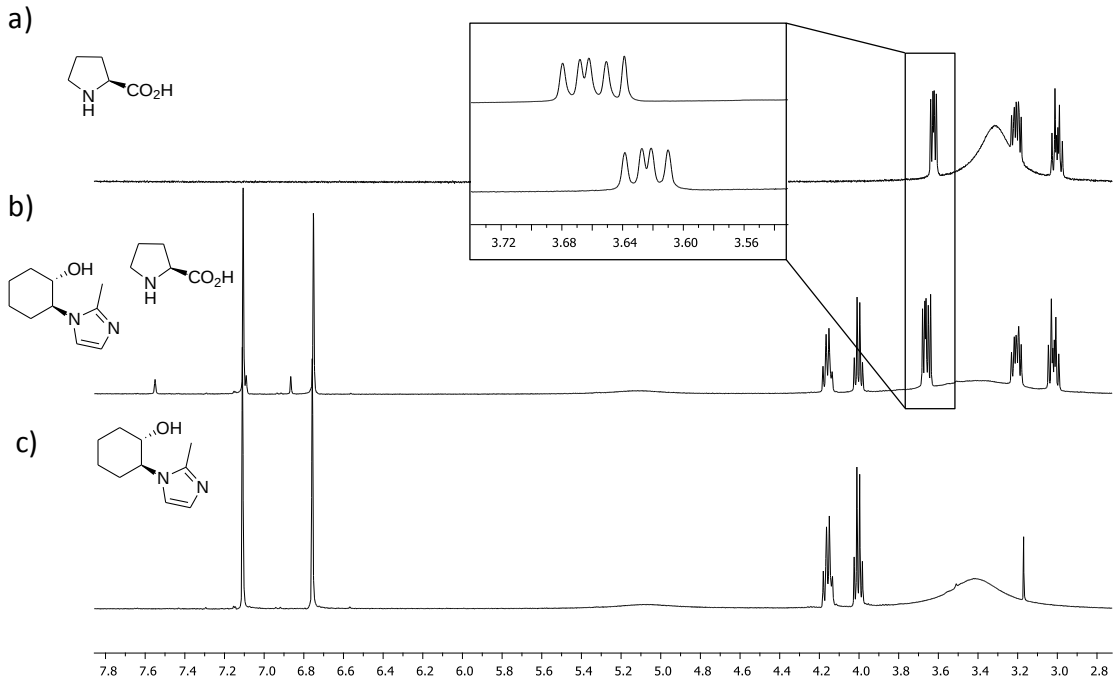


Figure S.I.1. ^{1}H-NMR spectra (DMSO) of a) (L)-proline, b) equimolecular mixture (L)-proline:**4d**, c) **4d**.

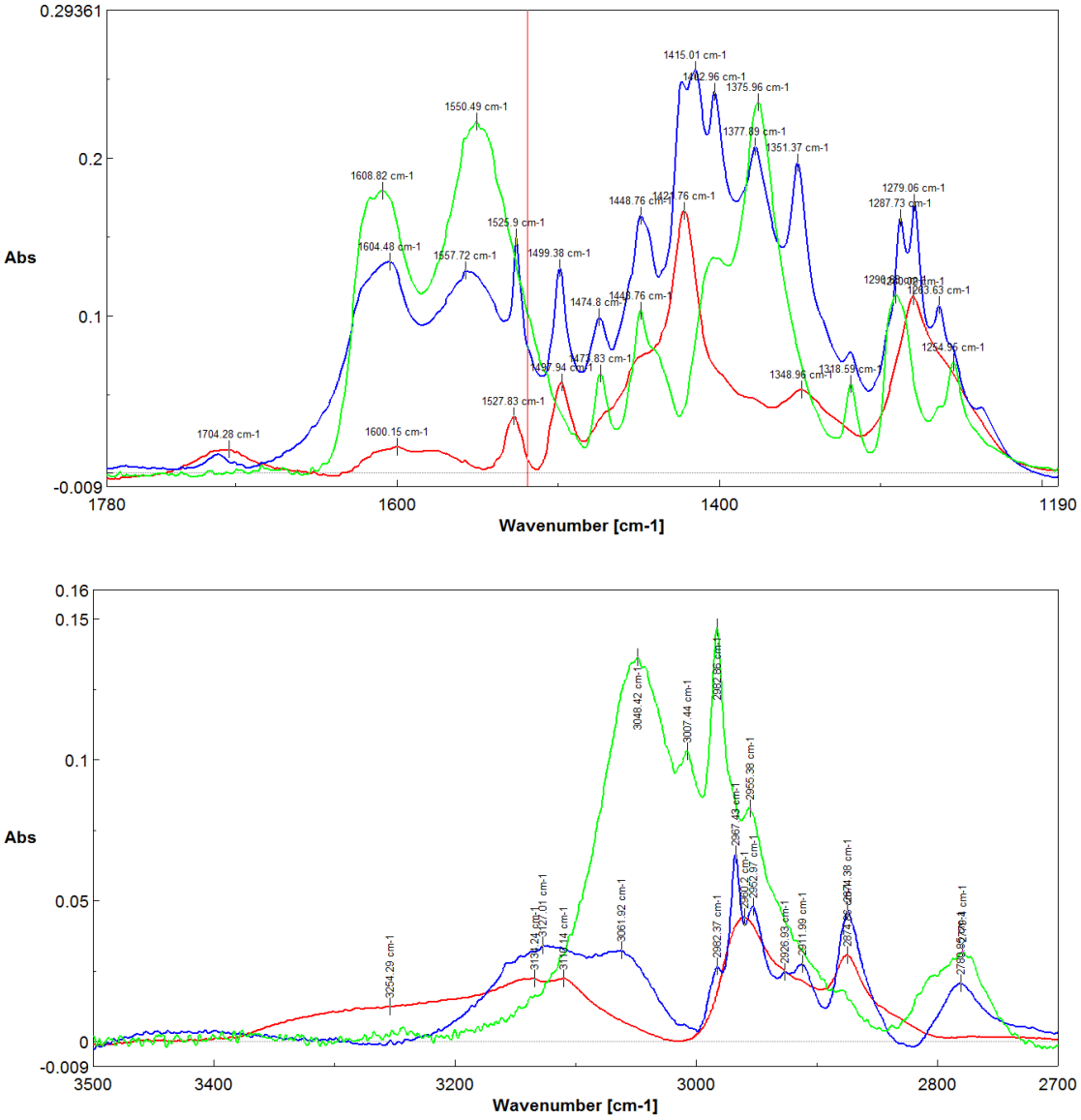


Figure S.I.2. FT-IR-ATR. Green: (L)-proline; Blue: equimolecular mixture (L)-proline:**4d**; Red: **4d**.

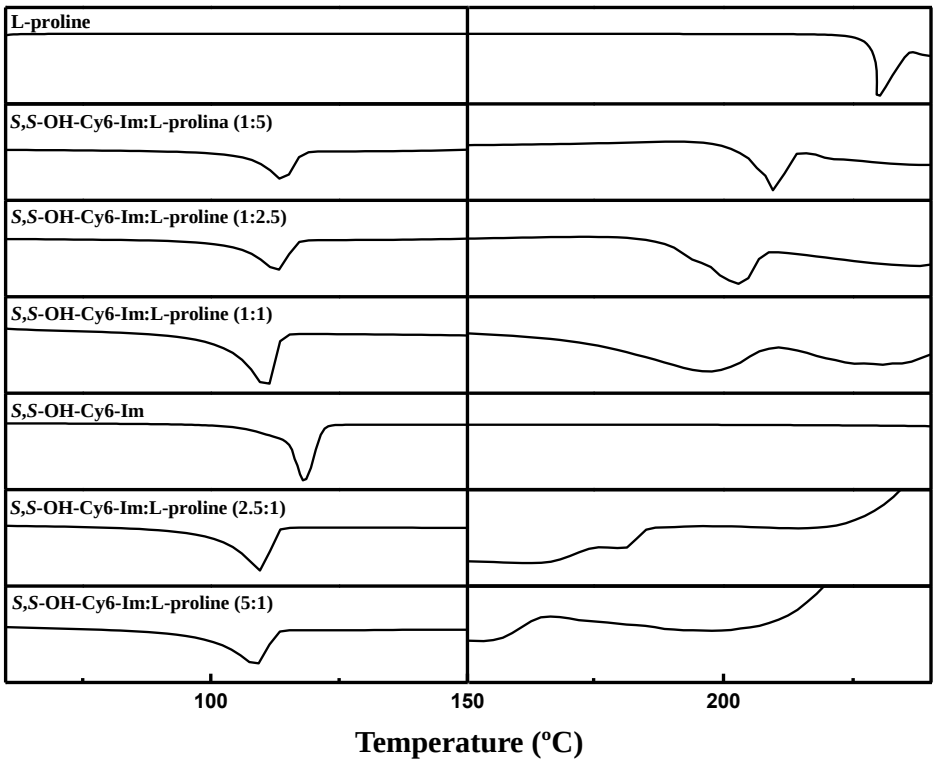


Figure S.I.3. DSC of different mixtures (*S*,*S*)-**4a**: (L)-proline.

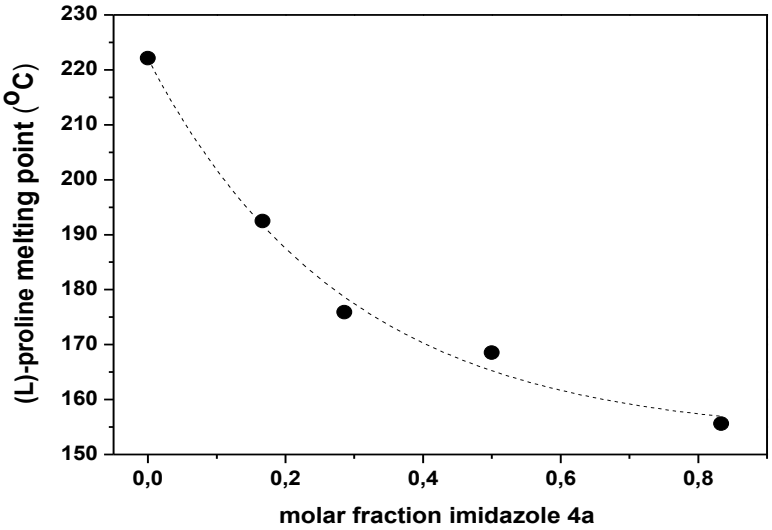


Figure S.I.4. (L)-proline melting temperature for a mixture of DSC of different mixtures (*S*,*S*)-**4a**: (L)-proline.

Table S.I.1. Melting temperatures of different complex (*S*,*S*)-**4a**: (L)-proline.

Entry	***S*,*S*-Cy6-OH-Im:L-proline**			
	Ratio	**Imidazole Molar fraction**	**T_m (ºC) imidazole[a]**	**T_m (ºC) L-proline[a]**
1	1:0	1	88.28	-
2	0:1	0	-	222.13
3	1:1	0.5	67.76	168.51
4	1:2.5	0.3	87.91	175.91
5	1:5	0.17	91.56	192.46
6	2.5:1	0.71	71.44	177.74
7	5:1	0.83	75.02	155.63

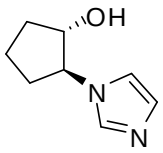
[a] The melting temperature (T_m) was determined as the onset of the transition.

Table S.I.2 Melting temperatures of different complexes formed by diverse imidazoles and (L)-proline with ratio 1:1.

Entry	-OX	R_1	R_2	Imidazole	Imidazole: (L)-proline (1:1)	
				T_m (ºC)[a]	**T_m (°C) imidazole[a]**	**T_m (°C) (L)-proline[a]**
1	*R*,*R*-OAc	H	H	-56	< -50	142
2	*S*,*S*-OH	H	H	88	86	166
3	*R*,*R*-OAc	CH_3	H	-48	-47	150
4	*S*,*S*-OH	CH_3	H	64	81	180
5	*S*,*S*-OH	H	Ph	173	179	195

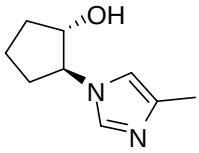
[a] The melting temperature (T_m) was determined as the onset of the transition.

Spectroscopical data of (1*S*,2*S*)-2-(1*H*-imidazol-1-yl)cyclopentanol (3a)



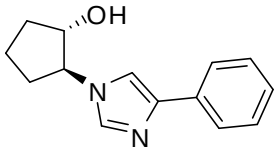
(1*S*,2*S*)-2-(1*H*-imidazol-1-yl)cylopentanol (3a). R_f (10% MeOH/$CHCl_3$): 0.22; Mp: 72-74 °C; IR (KBr): ν 3192, 3096, 2974, 2348, 1604, 1574, 1412, 1353, 1287, 1231, 1149, 1113, 1097, 1060 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.62-1.89 (m, 4H), 2.01-2.13 (m, 1H), 2.15-2.29 (m, 1H), 4.08-4.18 (m, 2H), 6.32 (brs, 1H), 6.83 (s, 1H), 6.89 (s, 1H), 7.26 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 20.3 (CH_2), 30.3 (CH_2), 32.2 (CH_2), 65.9 (CH), 77.9 (CH), 117.4 (CH), 128.7 (CH), 136.3 (CH); MS (ESI^+, *m/z*): 175 [$(M+Na)^+$, 100%], 153 [$(M+H)^+$, 35%]; (*S*,*S*)-**3a**: $[\alpha]^{20}_D$: +41.9 (*c* 1, $CHCl_3$), 99% *ee*; Analytical separation (HPLC): Chiralcel OB-H *n*-hexane/EtOH (97:3), 0.5 mL/min, 20 ºC, t_R (*R*,*R*)= 39.6 min, t_R (*S*,*S*)= 45.9 min.

Spectroscopical data of (1*S*,2*S*)-2-(4-methyl-1*H*-imidazol-1-yl)cyclopentanol (3b)



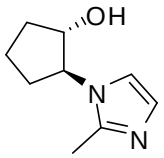
(1*S*,2*S*)-2-(4-methyl-1*H*-imidazol-1-yl)cyclopentanol (3b). R_f (10% MeOH/$CHCl_3$): 0.16; Mp: 95-97 °C; IR (KBr): ν 3112, 2964, 2859, 2763, 2362, 1602, 1561, 1497, 1356, 1322, 1227, 1171, 1114, 1070 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.65-1.90 (m, 5H), 2.05 (s, 3H), 2.21-2.33 (m, 1H), 4.01-4.10 (m, 1H), 4.17 (q, $^3J_{HH}$ = 7.5 Hz, 1H), 4.70 (brs, 1H), 6.61 (s, 1H), 7.18 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 13.2 (CH_3), 19.8 (CH_2), 29.8 (CH_2), 31.5 (CH_2), 65.6 (CH), 77.5 (CH), 122.9 (CH), 128.0 (C), 135.1 (CH); MS (ESI^+, *m/z*): 189 [$(M+Na)^+$, 20%], 167 [$(M+H)^+$, 100%]; (*S*,*S*)-**3b**: $[\alpha]^{20}_D$: +50.2 (*c* 1, $CHCl_3$), 99% *ee*; Analytical separation (HPLC) Chiralpak AS *n*-hexane/EtOH (96:4), 0.8 mL/min, 40 ºC, t_R (*S*,*S*)= 17.4 min, t_R (*R*,*R*)= 20.8 min.

Spectroscopical data of (1*S*,2*S*)-2-(4-phenyl-1*H*-imidazol-1-yl)cyclopentanol (3c)



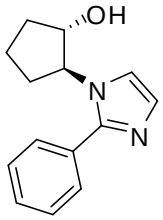
(1*S*,2*S*)-2-(4-phenyl-1*H*-imidazol-1-yl)cyclopentanol (3c). R_f (10% MeOH/$CHCl_3$): 0.23; Mp: 168-170 °C; IR (KBr): ν 3129, 2964, 2868, 2345, 2344, 1602, 1566, 1484, 1449, 1366, 1310, 1202, 1067 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.66-1.88 (m, 4H), 2.07-2.23 (m, 2H), 4.04-4.18 (m, 2H), 4.50 (brs, 1H), 6.99 (s, 1H), 7.31-7.42 (m, 4H), 7.56 (d, $^3J_{HH}$= 7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 19.4 (CH_2), 29.7 (CH_2), 31.2 (CH_2), 65.8 (CH), 77.4 (CH), 112.5 (CH), 124.5 (2CH), 126.7 (CH), 128.4 (2CH), 133.4 (C), 136.2 (CH), 141.3 (C); MS (ESI^+, *m/z*): 251 [$(M+Na)^+$, 20%], 229 [$(M+H)^+$, 100%]; (*S*,*S*)-**3c**: $[\alpha]^{20}_D$: +71.5 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC): Chiralpak AS *n*-hexane/EtOH (96:4), 0.8 mL/min, 40 ºC, t_R (*R*,*R*)= 19.9 min, t_R (*S*,*S*)= 24.6 min.

Spectroscopical data of (1*S*,2*S*)-2-(2-methyl-1*H*-imidazol-1-yl)cyclopentanol (3d)



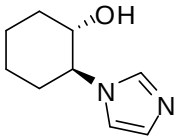
(1*S*,2*S*)-2-(2-methyl-1*H*-imidazol-1-yl)cyclopentanol (3d). R_f (10% MeOH/$CHCl_3$): 0.21; Mp: 72-74 ºC; IR (KBr): ν 3111, 2963, 2876, 2360, 2359, 1666, 1529, 1449, 1423, 1349, 1282, 1153, 1133, 1087, 1057, 990, 934, 907, 852, 729 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.63-1.90 (m, 4H), 1.98-2.18 (m, 2H), 2.20 (s, 3H), 4.09-4.19 (m, 2H), 6.63 (s, 1H), 6.73 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 13.1 (CH_3), 20.1 (CH_2), 29.9 (CH_2), 31.8 (CH_2), 63.9 (CH), 77.8 (CH), 114.9 (CH), 126.6 (CH), 145.1 (C); MS (ESI^+, *m/z*): 189 [$(M+Na)^+$, 20%], 167 [$(M+H)^+$, 100%]; (*S*,*S*)-**3d**: $[\alpha]^{20}_D$: +14.7 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC) Chiralcel OD *n*-hexane/EtOH (90:10), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 13.0 min, t_R (*R*,*R*)= 17.2 min.

Spectroscopical data of (1*S*,2*S*)-2-(2-phenyl-1*H*-imidazol-1-yl)cyclopentanol (3e)



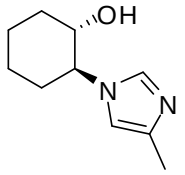
(1*S*,2*S*)-2-(2-phenyl-1*H*-imidazol-1-yl)cyclopentanol (3e). R_f (5% MeOH/$CHCl_3$): 0.17; Mp: 162-164 ºC; IR (KBr): ν 3404, 3144, 3109, 3061, 2957, 2873, 2771, 2360, 2341, 1602, 1468, 1444, 1422, 1352, 1331, 1300, 1280, 1202, 1157, 1131, 1105, 1069, 1022, 932, 775, 753, 719 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 1.57-1.80 (m, 4H), 1.99-2.12 (m, 2H), 4.24 (q, $^3J_{HH}$ = 7.6 Hz, 1H, H_2), 4.43 (q, $^3J_{HH}$ = 7.6 Hz, 1H), 6.88 (s, 2H), 7.31-7.34 (m, 3H), 7.54-7.56 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 19.8 (CH_2), 31.2 (CH_2), 31.9 (CH_2), 63.4 (CH), 78.2 (CH), 116.0 (CH), 128.2 (2CH), 128.5 (CH), 128.5 (CH), 129.5 (2CH), 130.1 (C), 148.4 (C); MS (ESI^+, *m/z*): 251 [$(M+Na)^+$, 32%], 229 [$(M+H)^+$, 100%]; (*S*,*S*)-**3e**: $[\alpha]^{20}_D$: -45.0 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC): Chiralcel OD *n*-hexane/EtOH (90:10), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 16.6 min, t_R (*R*,*R*)= 20.6 min.

Spectroscopical data of (1*S*,2*S*)-2-(1*H*-imidazol-1-yl)cyclohexanol (4a)



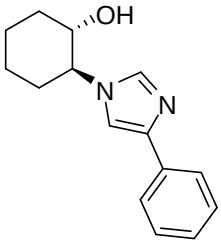
(1*S*,2*S*)-2-(1*H*-imidazol-1-yl)cyclohexanol (4a). R_f (10% MeOH/$CHCl_3$): 0.34; Mp: 132-133 ºC; IR (KBr): ν 3725, 2975, 1492, 1230, 1054, 1031 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 1.32-1.47 (m, 3H), 1.59-1.88 (m, 3H), 2.01-2.16 (m, 2H), 3.53-3.69 (m, 2H), 4.77 (s, 1H), 6.82 (s, 1H), 6.89 (s, 1H), 7.31 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 24.3 (CH_2), 25.0 (CH_2), 32.1 (CH_2), 34.2 (CH_2), 63.8 (CH), 72.8 (CH), 117.0 (CH), 128.0 (CH), 136.0 (CH); MS (ESI^+, *m/z*): 167 [$(M+H)^+$, 100%]; (*S*,*S*)-**4a**: $[\alpha]^{20}_D$: +12.1 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC) Chiralpak AS *n*-hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 21.9 min, t_R (*R*,*R*)= 30.3 min.

Spectroscopical data of (1*S*,2*S*)-2-(4-methyl-1*H*-imidazol-1-yl)cyclohexanol (4b)



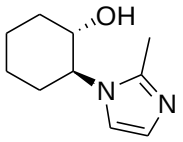
(1*S*,2*S*)-2-(4-methyl-1*H*-imidazol-1-yl)cyclohexanol (4b). R_f (10% MeOH/$CHCl_3$): 0.36; Mp: 89-91 ºC; IR (KBr): ν 3456, 2984, 1503, 1225, 1125, 1039 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.32-1.42 (m, 3H), 1.59-1.84 (m, 3H), 1.99-2.17 (m, 2H), 2.04 (s, 3H), 3.53-3.69 (m, 2H), 5.00 (s, 1H), 6.60 (s, 1H), 7.27 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 13.2 (CH_3), 24.3 (CH_2), 25.1 (CH_2), 32.0 (CH_2), 33.9 (CH_2), 64.0 (CH), 72.8 (CH), 113.3 (CH), 135.0 (CH), 136.8 (C); MS (ESI^+, *m/z*): 181 [$(M+H)^+$, 100%]; (*S*,*S*)-**4b**: $[\alpha]^{20}_D$: +20.5 (*c* 1, $CHCl_3$), 95% *ee*; Analytical separation (HPLC): Chiralcel OD *n*-hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 19.1 min, t_R (*R*,*R*)= 24.2 min.

Spectroscopical data of (1*S*,2*S*)-2-(4-phenyl-1*H*-imidazol-1-yl)cyclohexanol (4c)



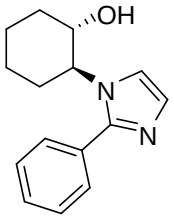
(1*S*,2*S*)-2-(4-phenyl-1*H*-imidazol-1-yl)cyclohexanol (4c). R_f (10% MeOH/$CHCl_3$): 0.35; Mp: 184-186 ºC; IR (KBr): ν 3200, 3123, 1575, 1503, 1324, 1021 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.25-1.40 (m, 3H), 1.54-1.79 (m, 3H), 1.93-2.18 (m, 2H), 3.53-3.63 (m, 1H), 5.90 (s, 1H), 6.97 (s, 1H), 7.18-7.28 (m, 4H), 7.48 (d, $^3J_{HH}$ = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 24.2 (CH_2), 24.9 (CH_2), 32.0 (CH_2), 34.0 (CH_2), 64.2 (CH), 72.6 (CH), 113.0 (CH), 124.4 (2CH), 126.3 (CH), 128.2 (2CH), 133.6 (C), 136.1 (CH), 140.6 (C); MS (ESI^+, *m/z*): 243 [$(M+H)^+$, 100%]; (*S*,*S*)-**4c**: $[\alpha]^{20}_D$: +31.5 (*c* 1, $CHCl_3$), 99% *ee*; Analytical separation (HPLC) Chiralcel OD *n*-hexane/2-propanol (80:20), 0.8 mL/min, 20 ºC, t_R (*R*,*R*)= 17.2 min, t_R (*S*,*S*)= 22.2 min.

Spectroscopical data of (1*S*,2*S*)-2-(2-methyl-1*H*-imidazol-1-yl)cyclohexanol (4d)



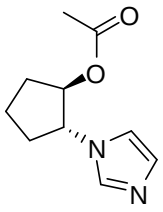
(1*S*,2*S*)-2-(2-methyl-1*H*-imidazol-1-yl)cyclohexanol (4d). R_f (10% MeOH/$CHCl_3$): 0.36; Mp: 137-139 ºC; IR (KBr): ν 3319, 2925, 1525, 1221, 1123 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.30-2.10 (m, 8H), 2.24 (s, 3H), 3.53-3.63 (m, 2H), 5.90 (s, 1H), 6.54 (s, 1H), 6.69 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 13.2 (CH_3), 24.2 (CH_2), 25.0 (CH_2), 32.0 (CH_2), 34.2 (CH_2), 61.8 (CH), 72.9 (CH), 114.4 (CH), 126.7 (CH), 145.0 (C); MS (ESI^+, *m/z*): 181 [$(M+H)^+$, 100%]; (*S*,*S*)-**4d**: $[\alpha]^{20}_D$: +11.3 (*c* 1, $CHCl_3$), 95% *ee*; Analytical separation (HPLC): Chiralcel OD *n*-hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 15.8 min, t_R (*R*,*R*)= 25.1 min.

Spectroscopical data of (1*S*,2*S*)-2-(2-phenyl-1*H*-imidazol-1-yl)cyclohexanol (4e)



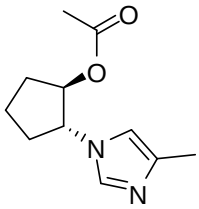
(1*S*,2*S*)-2-(2-phenyl-1*H*-imidazol-1-yl)cyclohexanol (4e). R_f (3% MeOH/$CHCl_3$): 0.30; Mp: 201-203 ºC; IR (KBr): ν 2953, 2924, 2854, 1465, 1377, 1265, 1090, 961 cm^{-1}; ^1H NMR (CD_3OD, 300.13 MHz): δ 1.40-2.29 (m, 8H), 3.98-4.20 (m, 2H), 7.27 (s, 1H), 7.55 (s, 1H), 7.66-7.85 (m, 5H); ^{13}C NMR (CD_3OD, 75.5 MHz): δ 26.6 (CH_2), 27.4 (CH_2), 35.7 (CH_2), 37.2 (CH_2), 64.7 (CH), 75.1 (CH), 119.6 (CH), 129.8 (CH), 130.9 (2CH), 131.5 (CH), 132.1 (2CH), 133.2 (C), 150.5 (C); MS (ESI^+, *m/z*): 243 [$(M+H)^+$, 100%]; Analytical separation (HPLC) Chiralpak IA *n*-hexane/2-propanol (90:10), 0.8 mL/min, 40 ºC, t_R (*S*,*S*)= 15.8 min, t_R (*S*,*S*)= 25.1 min.

Spectroscopical data of (1*S*,2*S*)-2-(1*H*-imidazol-1-yl)cyclopentyl acetate (5a)



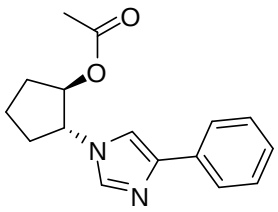
(1*R*,2*R*)-2-(1*H*-imidazol-1-yl)cyclopentyl acetate (5a). R_f (5% MeOH/$CHCl_3$): 0.30; IR (NaCl): ν 3433, 3116, 2970, 2880, 1738, 1502, 1375, 1241, 1084, 1050 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.65-1.76 (m, 1H), 1.86-1.98 (m, 3H), 2.00 (s, 3H), 2.17-2.38 (m, 2H), 4.44 (dt, $^3J_{HH}$ = 7.9, 5.6 Hz, 1H), 5.06 (dt, $^3J_{HH}$ = 7.4, 5.6 Hz, 1H), 6.97 (s, 1H), 7.06 (s, 1H), 7.64 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 20.9 (CH_2), 21.1 (CH_3), 29.9 (CH_2), 30.1 (CH_2), 62.5 (CH), 79.9 (CH), 117.3 (CH), 128.8 (CH), 136.0 (CH), 170.4 (C); MS (ESI^+, *m/z*): 217 [$(M+Na)^+$, 95%], 195 [$(M+H)^+$, 100%]; (*R*,*R*)-**5a**: $[\alpha]^{20}_D$: -61.8 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC): Chiralcel OB-H *n*-hexane/EtOH (95:5), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 20.8 min, t_R (*R*,*R*)= 24.0 min.

Spectroscopical data of (1*R*,2*R*)-2-(4-methyl-1*H*-imidazol-1-yl)cyclopentyl acetate (5b)



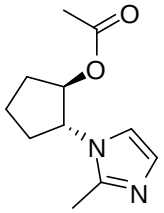
(1*R*,2*R*)-2-(4-methyl-1*H*-imidazol-1-yl)cyclopentyl acetate (5b). R_f (5% MeOH/$CHCl_3$): 0.31; IR (NaCl): ν 3129, 2969, 2879, 1737, 1498, 1475, 1374, 1240, 1046 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.60-1.75 (m, 1H), 1.87-2.01 (m, 3H), 2.01 (s, 3H), 2.03-2.35 (m, 2H), 4.38 (q, $^3J_{HH}$ = 6.07 Hz, 1H), 4.98-5.14 (m, 1H), 6.69 (s, 1H), 7.62 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 13.0 (CH_3), 20.1 (CH_2), 20.8 (CH_3), 29.9 (CH_2), 30.0 (CH_2), 62.5 (CH), 79.8 (CH), 113.6 (CH), 134.9 (CH), 137.6 (C), 170.4 (C); MS (ESI^+, *m/z*): 231 [$(M+Na)^+$, 100%], 209 [$(M+H)^+$, 45%]; (*R*,*R*)-**5b**: $[\alpha]^{20}_D$: -46.3 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC) Chiralcel OB-H *n*-hexane/EtOH (98:2), 0.8 mL/min, 20 ºC, t_R (*R*,*R*)= 39.9 min, t_R (*S*,*S*)= 46.8 min.

Spectroscopical data of (1*R*,2*R*)-2-(4-phenyl-1*H*-imidazol-1-yl)cyclopentyl acetate (5c)



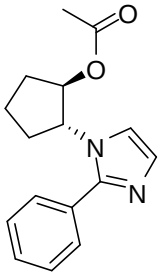
(1*R*,2*R*)-2-(4-phenyl-1*H*-imidazol-1-yl)cyclopentyl acetate (5c). R_f (5% MeOH/$CHCl_3$): 0.48; IR (NaCl): ν 2968, 1736, 1606, 1484, 1373, 1240, 1047, 749 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.74-1.85 (m, 1H), 1.93-2.05 (m, 3H), 2.07 (s, 3H), 2.24-2.34 (m, 1H), 2.40-2.46 (m, 1H), 4.56 (td, $^3J_{HH}$ = 7.9, 5.9 Hz, 1H), 5.15 (dt, $^3J_{HH}$ = 7.4, 5.7 Hz, 1H), 7.30-7.43 (m, 4H), 7.79 (d, $^3J_{HH}$ = 7.8 Hz, 2H), 8.11 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 20.9 (CH_2), 21.1 (CH_3), 30.0 (CH_2), 30.1 (CH_2), 63.5 (CH), 79.7 (CH), 113.1 (CH), 125.1 (2CH), 127.8 (CH), 128.7 (2CH), 135.7 (CH), 140.1 (C), 145.3 (C), 170.4 (C); MS (ESI^+, *m/z*): 293 [$(M+Na)^+$, 65%], 271 [$(M+H)^+$, 100%]; (*R*,*R*)-**5c**: $[\alpha]^{20}_D$: -54.5 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC): Chiralpak AS *n*-hexane/EtOH (96:4), 0.8 mL/min, 40 ºC, t_R (*R*,*R*)= 16.5 min, t_R (*R*,*R*)= 19.9 min.

Spectroscopical data of (1*R*,2*R*)-2-(2-methyl-1*H*-imidazol-1-yl)cyclopentyl acetate (5d)



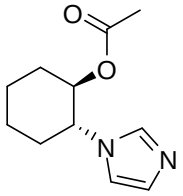
(1*R*,2*R*)-2-(2-methyl-1*H*-imidazol-1-yl)cyclopentyl acetate (5d). R_f (5% MeOH/$CHCl_3$): 0.29; IR (NaCl): ν 2972, 2881, 2487, 2361, 1959, 1793, 1528, 1498, 1422, 1374, 1240, 1152, 1048, 913, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.66-1.70 (m, 1H), 1.72-1.98 (m, 3H), 2.02 (s, 3H), 2.18-2.37 (m, 2H), 2.45 (s, 3H), 4.45 (q, $^3J_{HH}$ = 7.1 Hz, 1H), 5.04 (q, $^3J_{HH}$ = 7.1 Hz, 1H), 6.84 (s, 1H), 6.95 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 12.4 (CH_3), 20.5 (CH_2), 20.7 (CH_3), 29.6 (CH_2), 29.9 (CH_2), 60.5 (CH), 79.6 (CH), 114.9 (CH), 126.3 (CH), 144.6 (C), 169.8 (C); MS (ESI^+, *m/z*): 231 [$(M+Na)^+$, 30%], 209 [$(M+H)^+$, 100%]; (*R*,*R*)-**5d**: $[\alpha]^{20}_D$: +3.3 (*c* 1, $CHCl_3$), 95% *ee*; Analytical separation (HPLC) Chiralcel OD *n*-hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, t_R (*R*,*R*)= 13.0 min, t_R (*S*,*S*)= 18.1 min.

Spectroscopical data of (1*S*,2*R*)-2-(2-phenyl-1*H*-imidazol-1-yl)cyclopentyl acetate (5e)



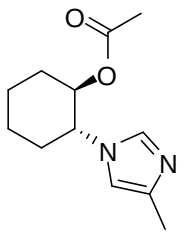
(1*R*,2*R*)-2-(2-phenyl-1*H*-imidazol-1-yl)cyclopentyl acetate (5e). R_f (5% MeOH/$CHCl_3$): 0.46; IR (NaCl): ν 3101, 2970, 2883, 2350, 1727, 1530, 1468, 1416, 1355, 1246, 1130, 1039, 918, 770, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.59-1.70 (m, 1H), 1.73-1.94 (m, 3H), 1.95 (s, 3H), 2.16-2.35 (m, 2H), 4.57 (q, $^3J_{HH}$ = 6.9 Hz, 1H), 5.16 (q, $^3J_{HH}$ = 6.9 Hz, 1H), 7.06 (d, $^3J_{HH}$ = 1.3 Hz, 1H), 7.18 (d, $^3J_{HH}$ = 1.3 Hz, 1H), 7.45-7.47 (m, 3H), 7.65-7.71 (m, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 20.9 (CH_2), 21.1 (CH_3), 30.0 (CH_2), 31.1 (CH_2), 62.8 (CH), 79.8 (CH), 116.2 (CH), 128.4 (2CH), 128.7 (CH), 129.2 (CH), 129.3 (2CH), 130.6 (C), 148.5 (C), 170.1 (C); MS (ESI^+, *m/z*): 293 [$(M+Na)^+$, 47%], 271 [$(M+H)^+$, 100%]; (*R*,*R*)-**5e**: $[\alpha]^{20}_D$: +44.6 (*c* 1, $CHCl_3$), 96% *ee*; Analytical separation (HPLC): Chiralcel OD *n*-hexane/2-propanol (90:10), 0.8 mL/min, 40 ºC, t_R (*S*,*S*)= 17.7 min, t_R (*R*,*R*)= 21.7 min.

Spectroscopical data of (1*R*,2*R*)-2-(1*H*-imidazol-1-yl)cyclohexyl acetate (6a)



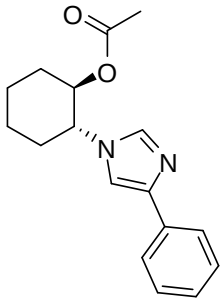
(1*R*,2*R*)-2-(1*H*-imidazol-1-yl)cyclohexyl acetate (6a). R_f (5% MeOH/$CHCl_3$): 0.25; IR (NaCl): ν 3390, 2942, 2864, 1734, 1499, 1376, 1329, 1083, 1053, 1031 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.33-1.52 (m, 3H), 1.70-1.96 (m, 6H), 2.07-2.23 (m, 2H), 3.87-4.10 (m, 1H), 4.79-4.94 (m, 1H), 6.96 (s, 1H), 7.05 (s, 1H), 7.74 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 20.6 (CH_3), 23.6 (CH_2), 24.5 (CH_2), 31.1 (CH_2), 32.1 (CH_2), 60.1 (CH), 74.3 (CH), 116.8 (CH), 127.9 (CH), 136.2 (CH), 169.7 (C); MS (ESI^+, *m/z*): 209 [$(M+H)^+$, 100%]; (*R*,*R*)-**6a**: $[\alpha]^{20}_D$: -6.5 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC) Chiralpak AS *n*-hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 20.7 min, t_R (*R*,*R*)= 30.9 min.

Spectroscopical data of (1*R*,2*R*)-2-(4-methyl-1*H*-imidazol-1-yl)cyclohexyl acetate (6b)



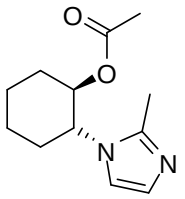
(1*R*,2*R*)-2-(4-methyl-1*H*-imidazol-1-yl)cyclohexyl acetate (6b). R_f (5% MeOH/$CHCl_3$): 0.27; IR (NaCl): ν 2965, 2910, 1737, 1525, 1501, 1365, 1331, 1089 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.31-1.46 (m, 3H), 1.75-1.90 (m, 6H), 2.11-2.19 (m, 5H), 3.80-3.89 (m, 1H), 4.80-4.89 (m, 1H), 6.62 (s, 1H), 7.36 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 13.6 (CH_3), 20.7 (CH_3), 23.8 (CH_2), 24.6 (CH_2), 31.2 (CH_2), 32.3 (CH_2), 59.6 (CH), 74.4 (CH), 112.8 (CH), 135.6 (CH), 138.1 (C), 169.8 (C); MS (ESI^+, *m/z*): 223 [$(M+H)^+$, 100%]; (*R*,*R*)-**6b**: $[\alpha]^{20}_D$: -9.4 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC): Chiralcel OD *n*-hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 12.0 min, t_R (*R*,*R*)= 14.0 min.

Spectroscopical data of (1*R*,2*R*)-2-(4-phenyl-1*H*-imidazol-1-yl)cyclohexyl acetate (6c)



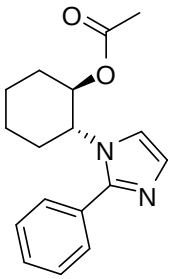
(1*R*,2*R*)-2-(4-phenyl-1*H*-imidazol-1-yl)cyclohexyl acetate (6c). R_f (5% MeOH/$CHCl_3$): 0.24; IR (NaCl): ν 2950, 2899, 1735, 1503, 1379, 1329, 1083, cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.42-1.51 (m, 3H), 1.80-1.95 (m, 6H), 2.20-2.25 (m, 2H), 3.93-4.00 (m, 1H), 4.92-4.98 (m, 1H), 7.23-7.38 (m, 4H), 7.55 (s, 1H), 7.76 (d, $^3J_{HH}$ = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 20.7 (CH_3), 23.8 (CH_2), 24.7 (CH_2), 31.3 (CH_2), 32.4 (CH_2), 60.0 (CH), 74.4 (CH), 112.4 (CH), 124.6 (2CH), 126.6 (CH), 128.5 (2CH), 134.0 (C), 136.7 (CH), 142.0 (C), 170.1 (C); MS (ESI^+, *m/z*): 285 [$(M+H)^+$, 100%]; (*R*,*R*)-**6c**: $[\alpha]^{20}_D$: -10.1 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC): Chiralcel OD *n*-hexane/2-propanol (80:20), 0.8 mL/min, 20 ºC, t_R (*R*,*R*)= 37.4 min, t_R (*S*,*S*)= 42.4 min.

Spectroscopical data of (1*R*,2*R*)-2-(2-methyl-1*H*-imidazol-1-yl)cyclohexyl acetate (6d)



(1*R*,2*R*)-2-(2-methyl-1*H*-imidazol-1-yl)cyclohexyl acetate (6d). R_f (5% MeOH/$CHCl_3$): 0.27; IR (NaCl): ν 2975, 2915, 1736, 1537, 1525, 1509, 1360, 1325 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.34-1.50 (m, 3H), 1.70-1.90 (m, 6H), 2.05-2.18 (m, 2H), 2.41 (s, 3H), 3.86-3.95 (m, 1H), 6.85 (s, 1H), 6.90 (s, 1H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 13.2 (CH_3), 20.7 (CH_3), 23.8 (CH_2), 24.8 (CH_2), 31.4 (CH_2), 32.4 (CH_2), 58.1 (CH), 74.8 (CH), 115.1 (CH), 127.3 (CH), 144.7 (C), 169.9 (C); MS (ESI^+, *m/z*): 223 [$(M+H)^+$, 100%]; (*R*,*R*)-**6d**: $[\alpha]^{20}_D$: -2.4 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC): Chiralcel OD *n*-hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, t_R (*S*,*S*)= 10.3 min, t_R (*R*,*R*)= 11.4 min.

Spectroscopical data of (1*R*,2*R*)-2-(2-phenyl-1*H*-imidazol-1-yl)cyclohexyl acetate (6e)



(1*R*,2*R*)-2-(2-phenyl-1*H*-imidazol-1-yl)cyclohexyl acetate (6e). R_f (5% MeOH/$CHCl_3$): 0.27; Mp: 114-116 ºC; IR (KBr): ν 2865, 1737, 1646, 1467, 1417, 1375, 1237, 1038 cm^{-1}; ^1H NMR ($CDCl_3$, 300.13 MHz): δ 1.26-1.46 (m, 3H), 1.73-1.85 (m, 6H), 2.00-2.14 (m, 2H), 4.17-4.27 (m, 1H), 4.98-5.07 (m, 1H), 7.07 (s, 1H), 7.13 (s, 1H), 7.44-7.49 (m, 5H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 20.6 (CH_3), 23.7 (CH_2), 24.5 (CH_2), 31.3 (CH_2), 33.2 (CH_2), 58.5 (CH), 74.6 (CH), 116.4 (CH), 128.5 (2CH), 128.6 (CH), 128.7 (CH), 129.1 (2CH), 130.6 (C), 148.1 (C), 169.6 (C); MS (ESI^+, *m/z*): 285 [$(M+H)^+$, 100%]; (*R*,*R*)-**6e**: $[\alpha]^{20}_D$: +91.0 (*c* 1, $CHCl_3$), >99% *ee*; Analytical separation (HPLC): Chiralcel OJ-H *n*-hexane/2-propanol (90:10), 0.8 mL/min, 40 ºC, t_R (*R*,*R*)= 8.0 min, t_R (*S*,*S*)= 8.8 min.

Chemoenzymatic Synthesis of Optically Active 2-(2- or 4-substituted-1*H*-imidazol-1-yl)cyloalcanols. Chiral additives for (L)-Proline

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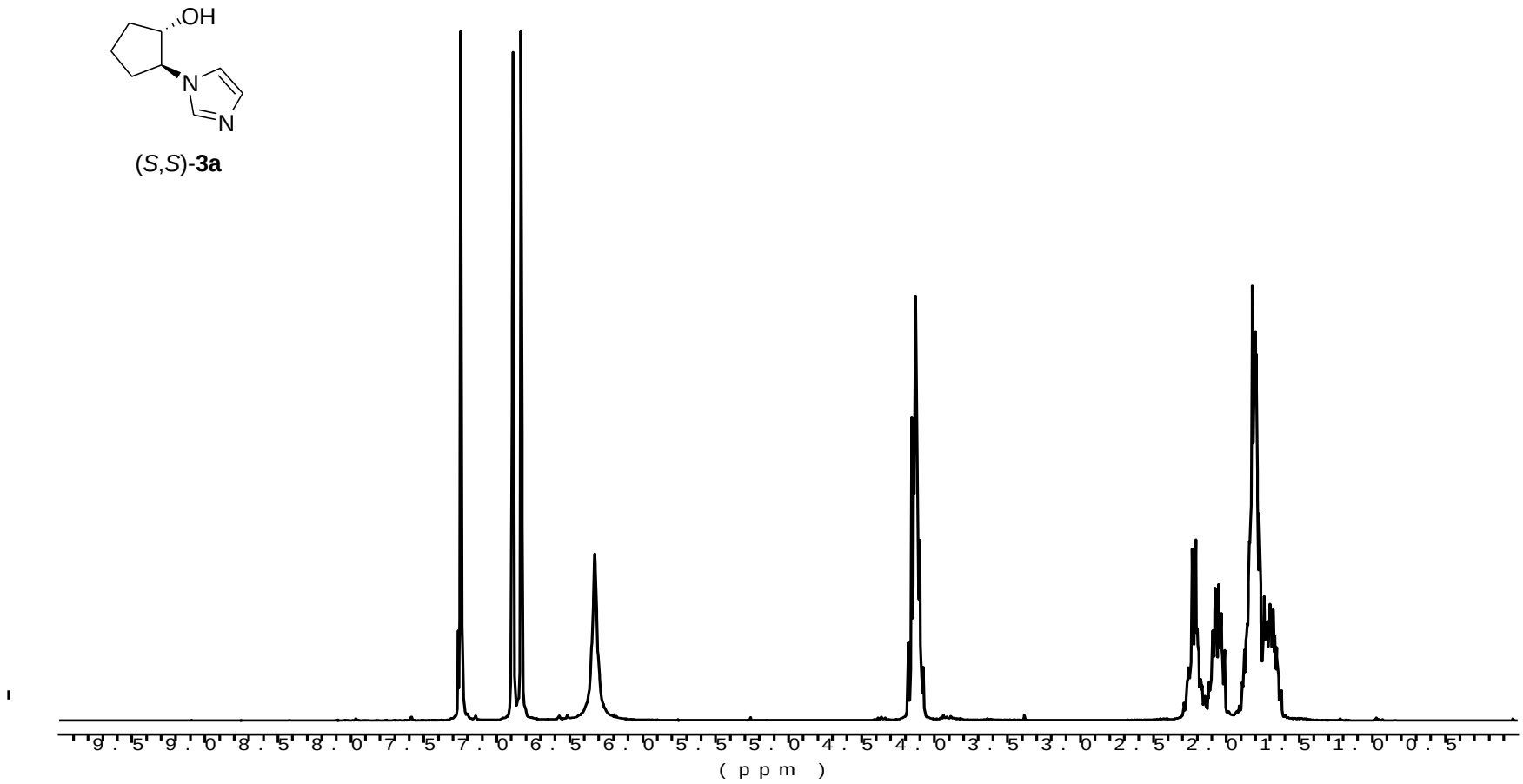
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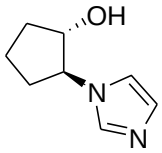
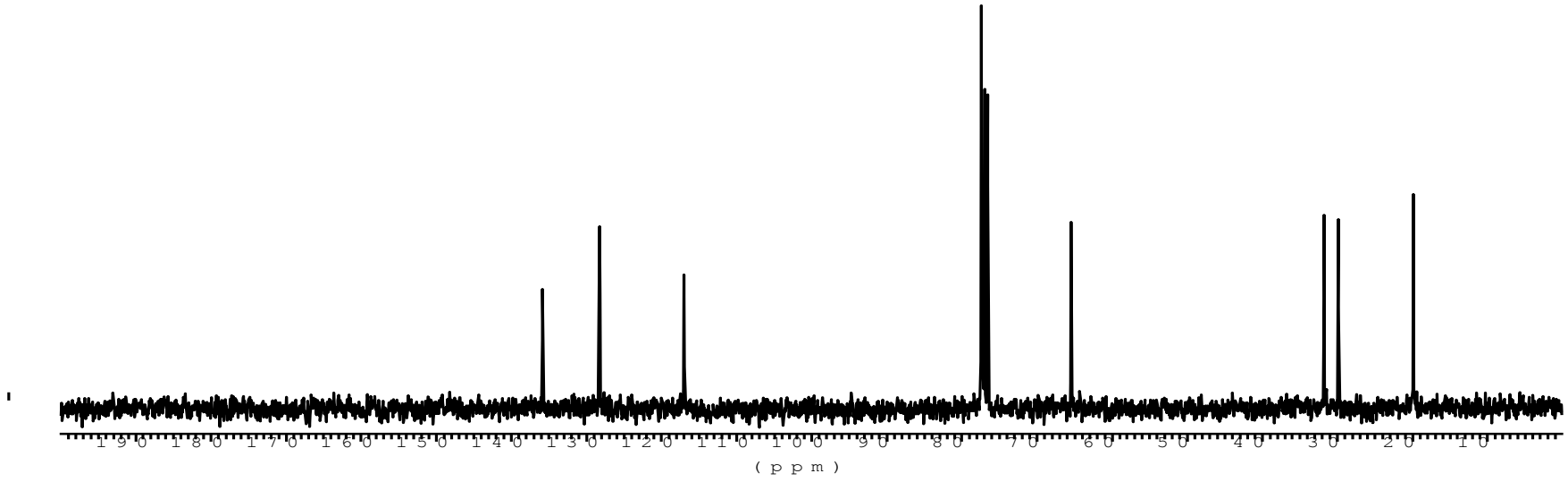
N
N
(S,S)-3a
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)


OH
N
N

(*S*,*S*)-**3a**


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
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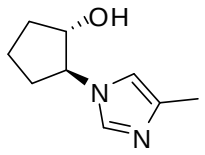
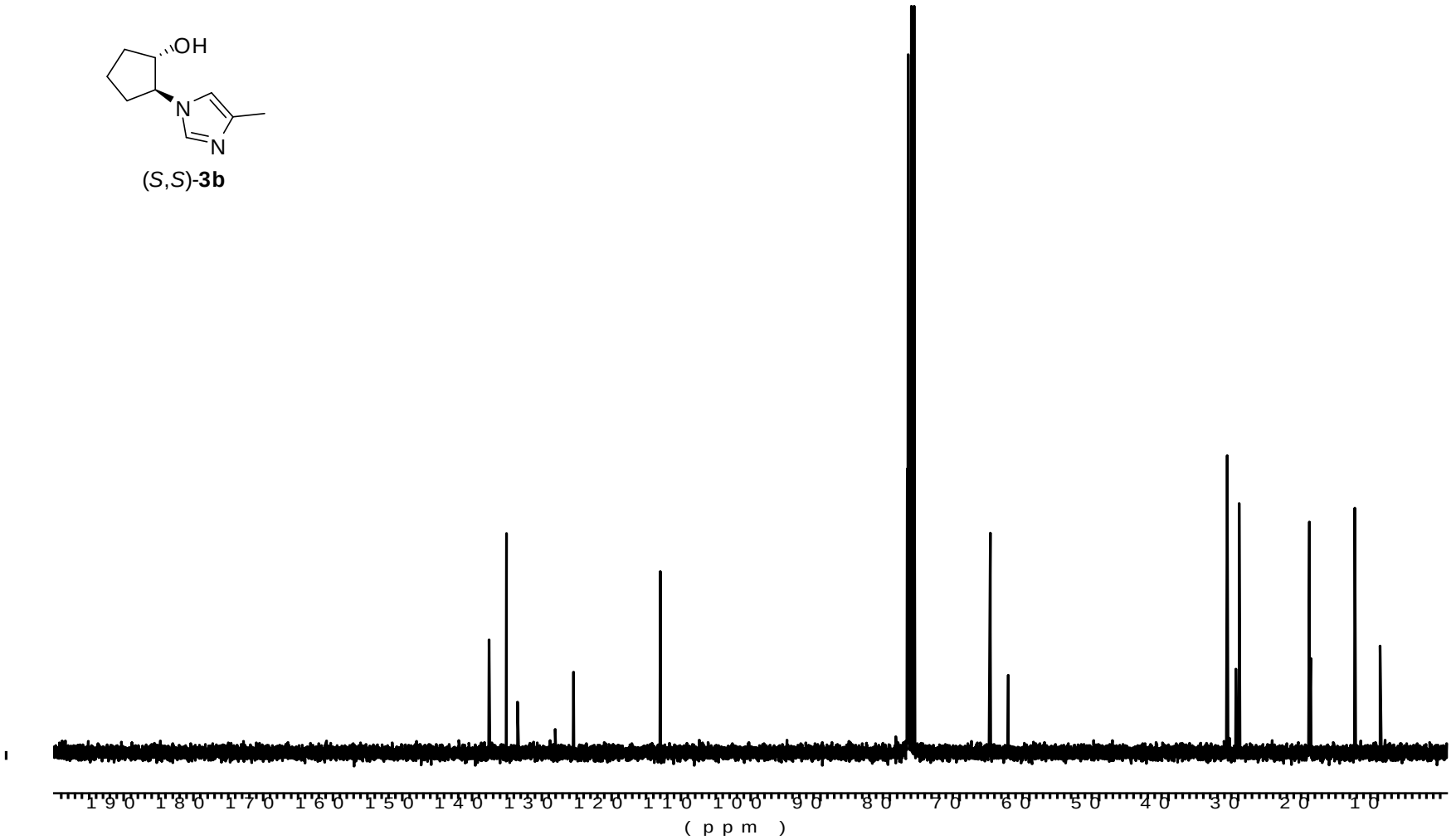


(*S*,*S*)-**3b**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N
N
(S,S)-3b
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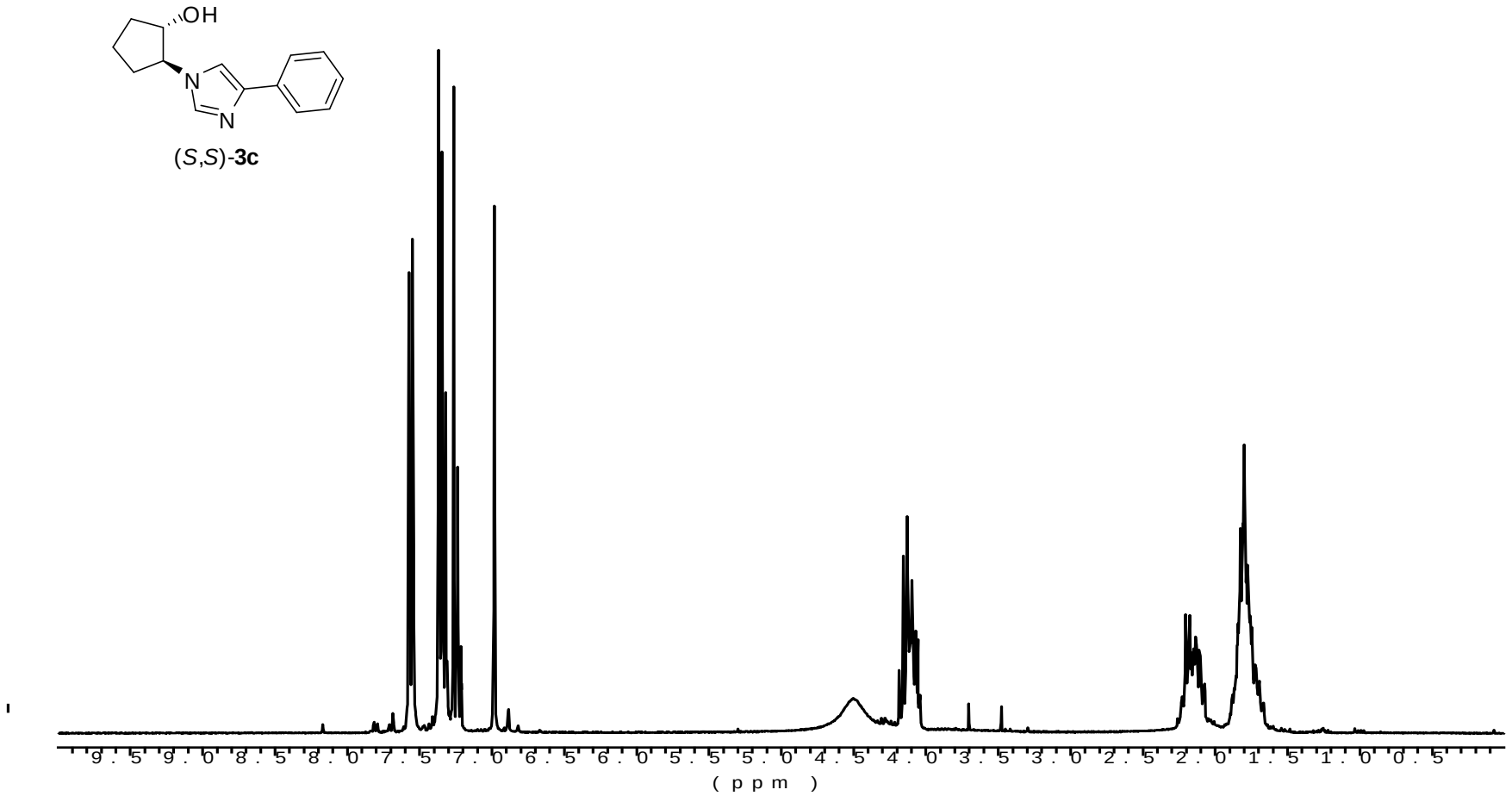
(ppm)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N
N
(S,S)-3c
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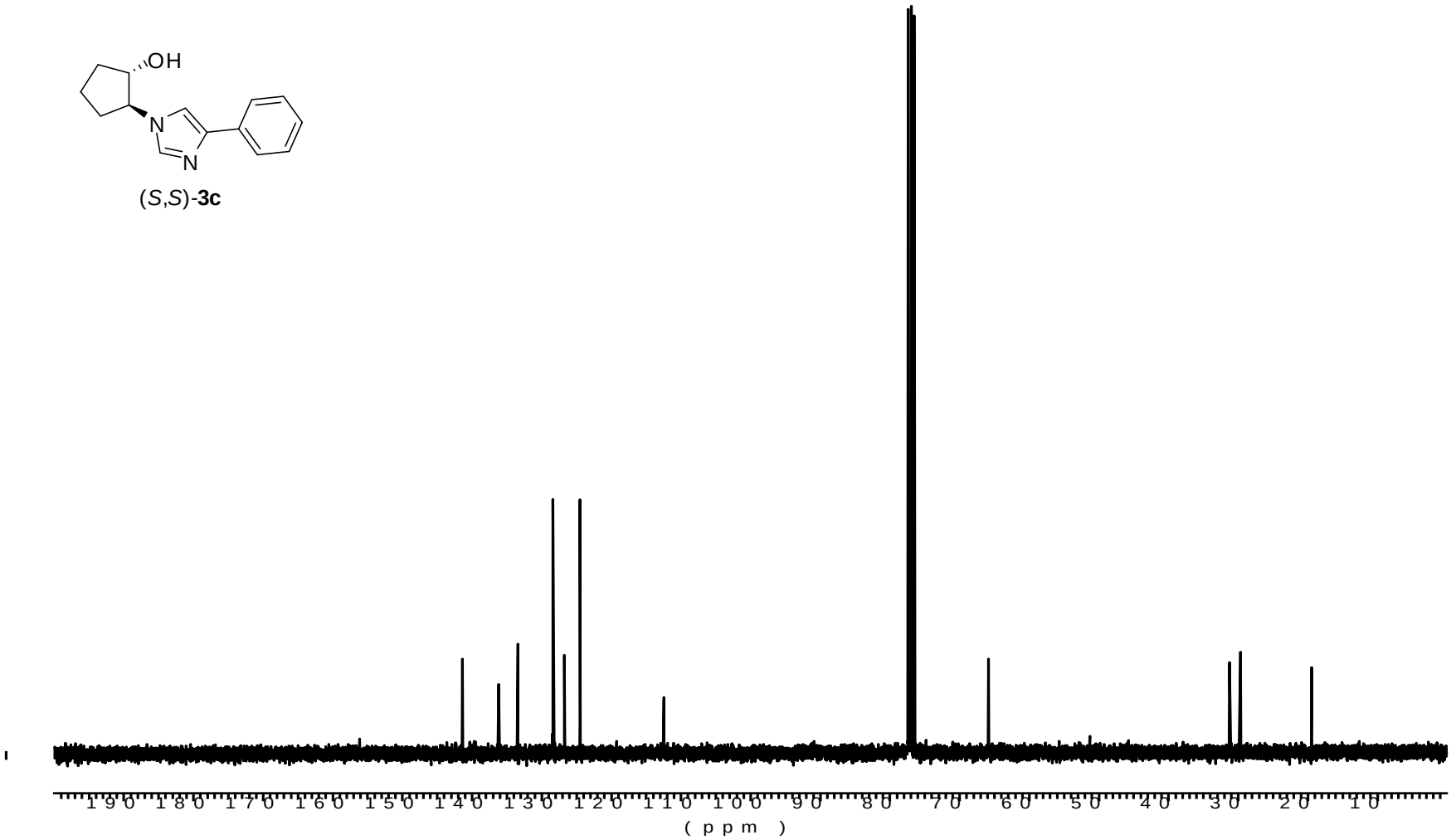
(ppm)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N
N
(S,S)-3c
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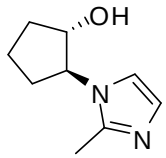
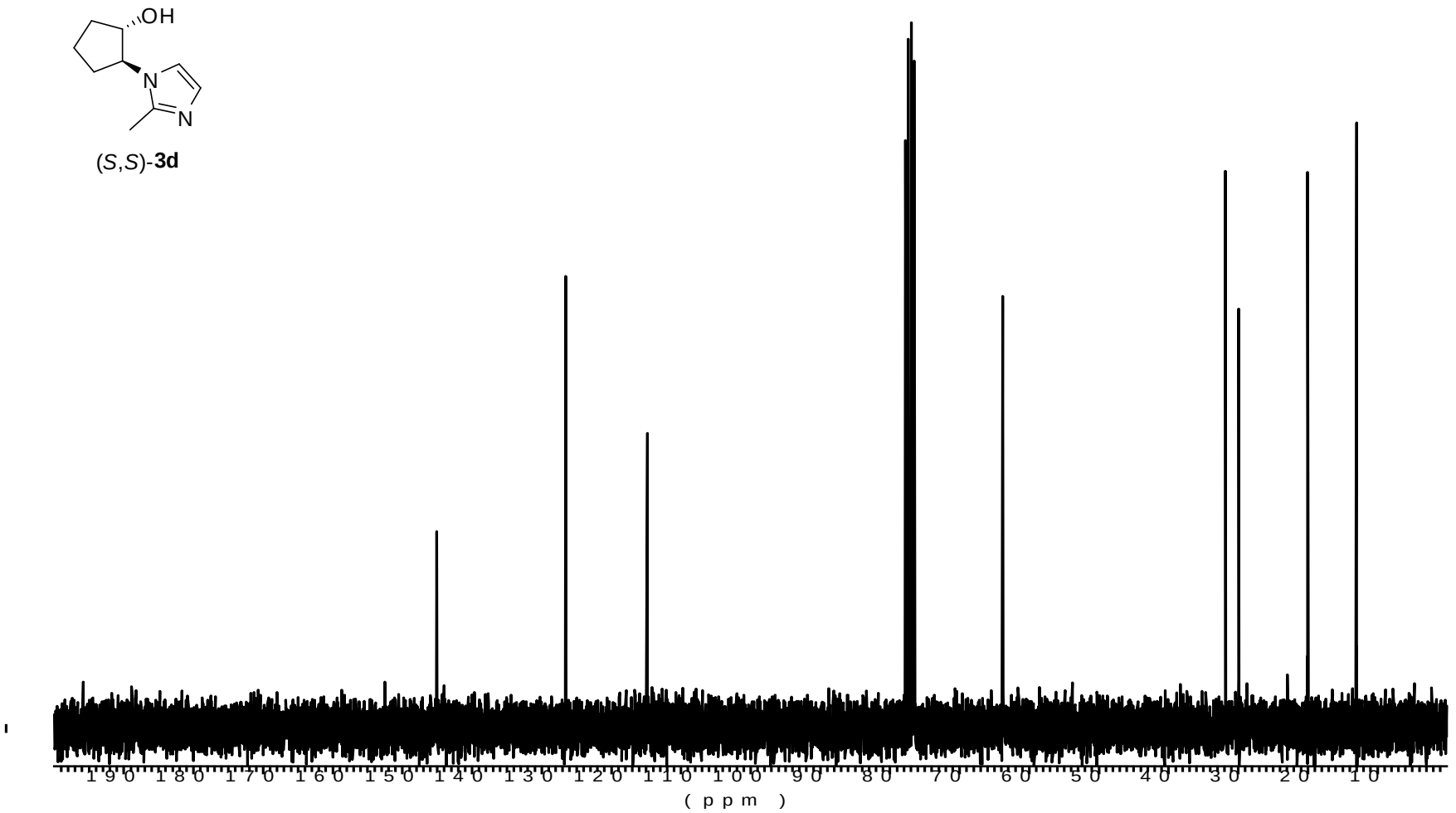
(ppm)



(*S*,*S*)-**3d**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N
N
(S,S)-3d
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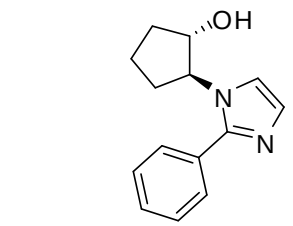
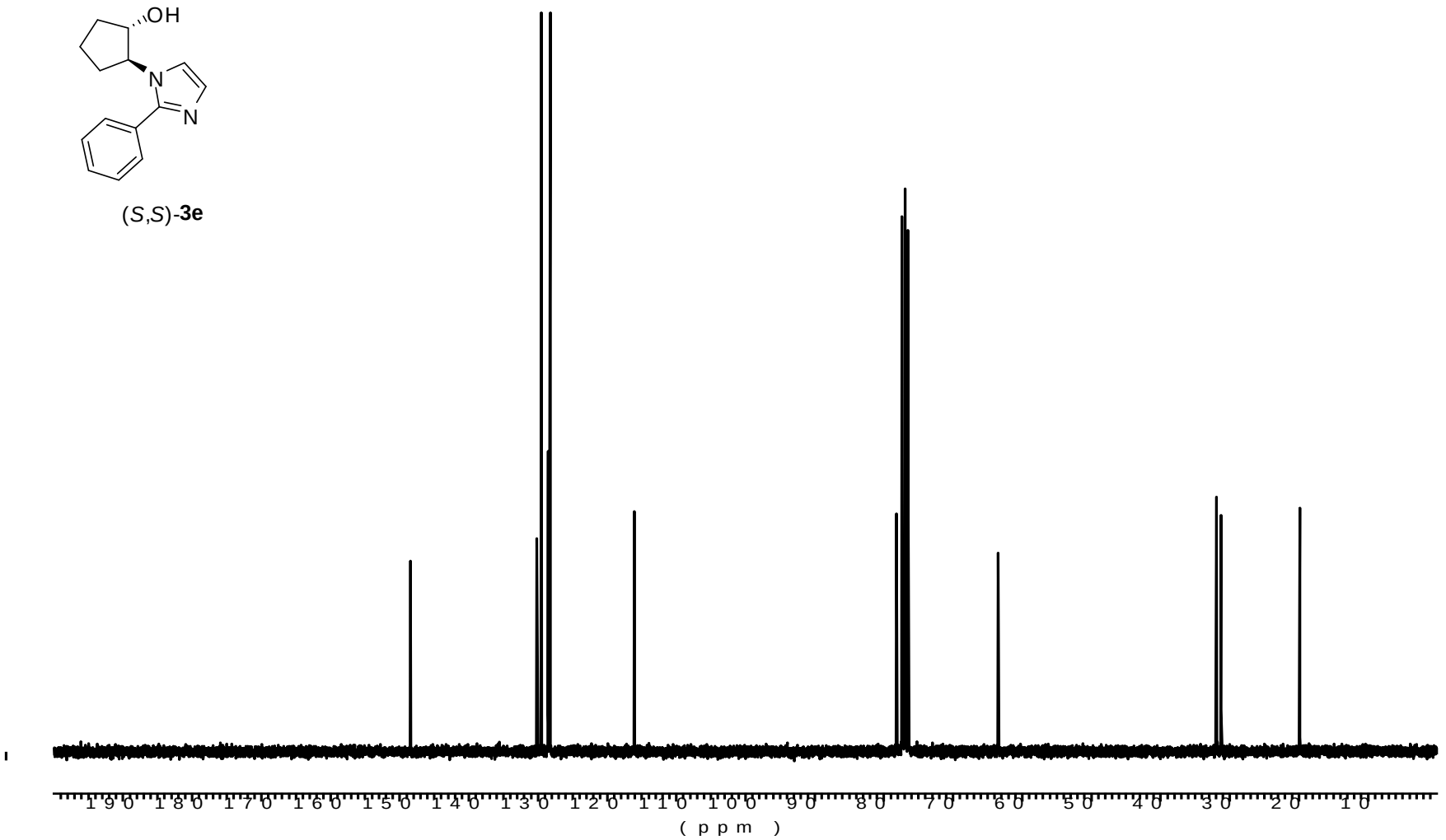
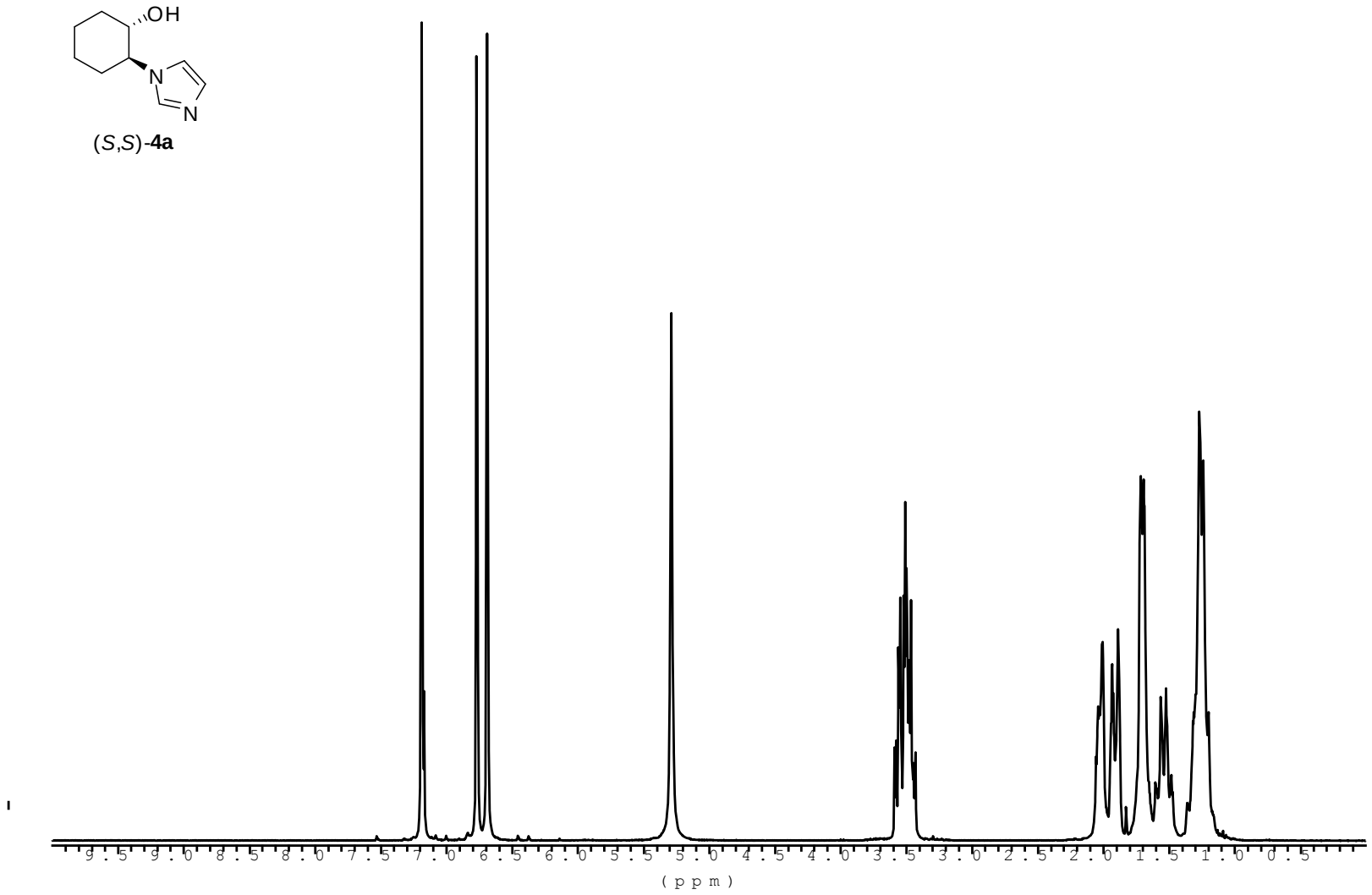
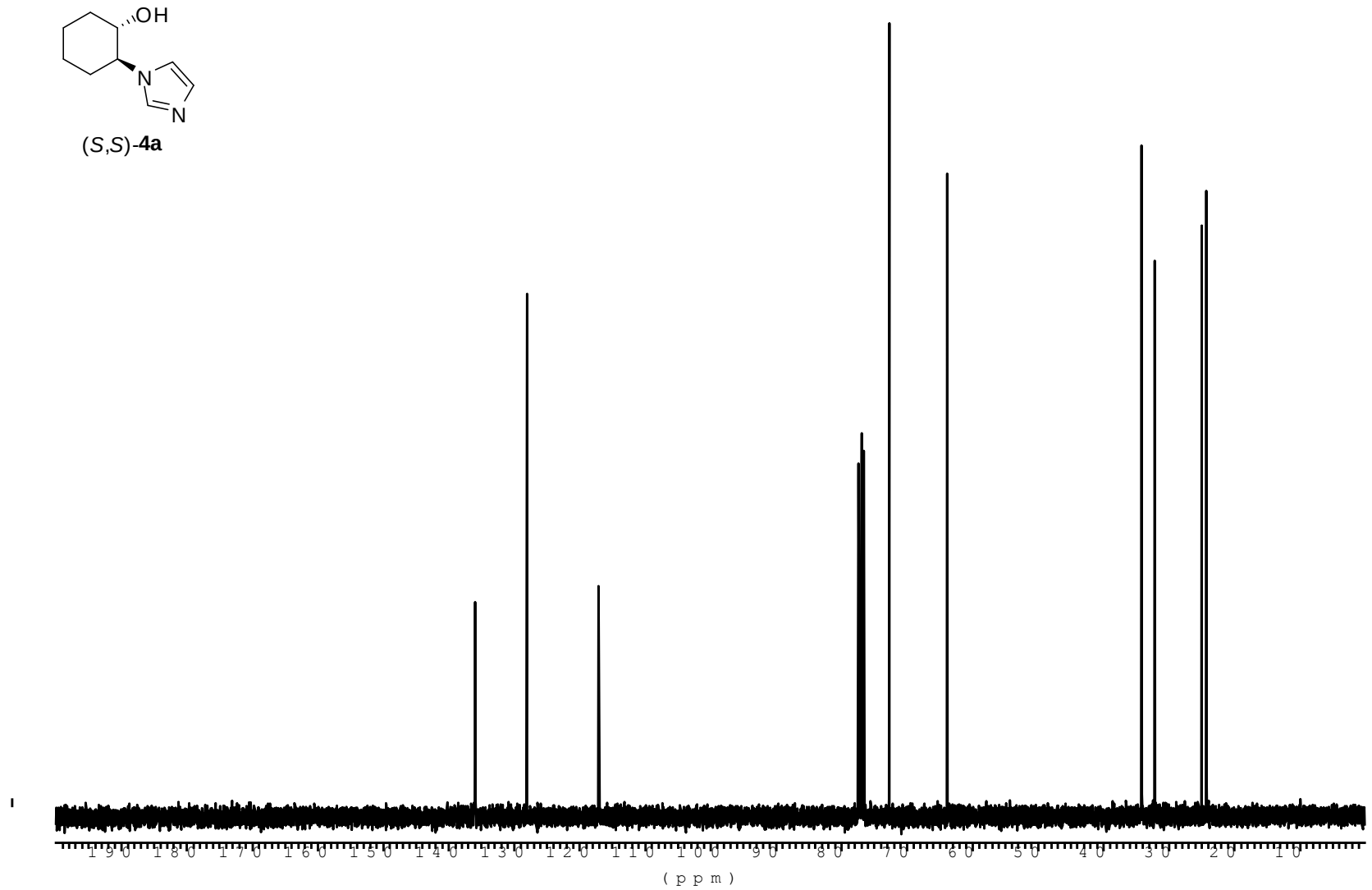
(ppm)

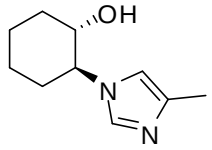


(*S*,*S*)-**3e**

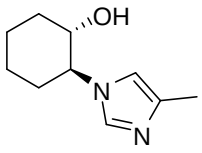

OH
N
N
(S,S)-3e
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)


OH
N
N
(S,S)-4a
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)

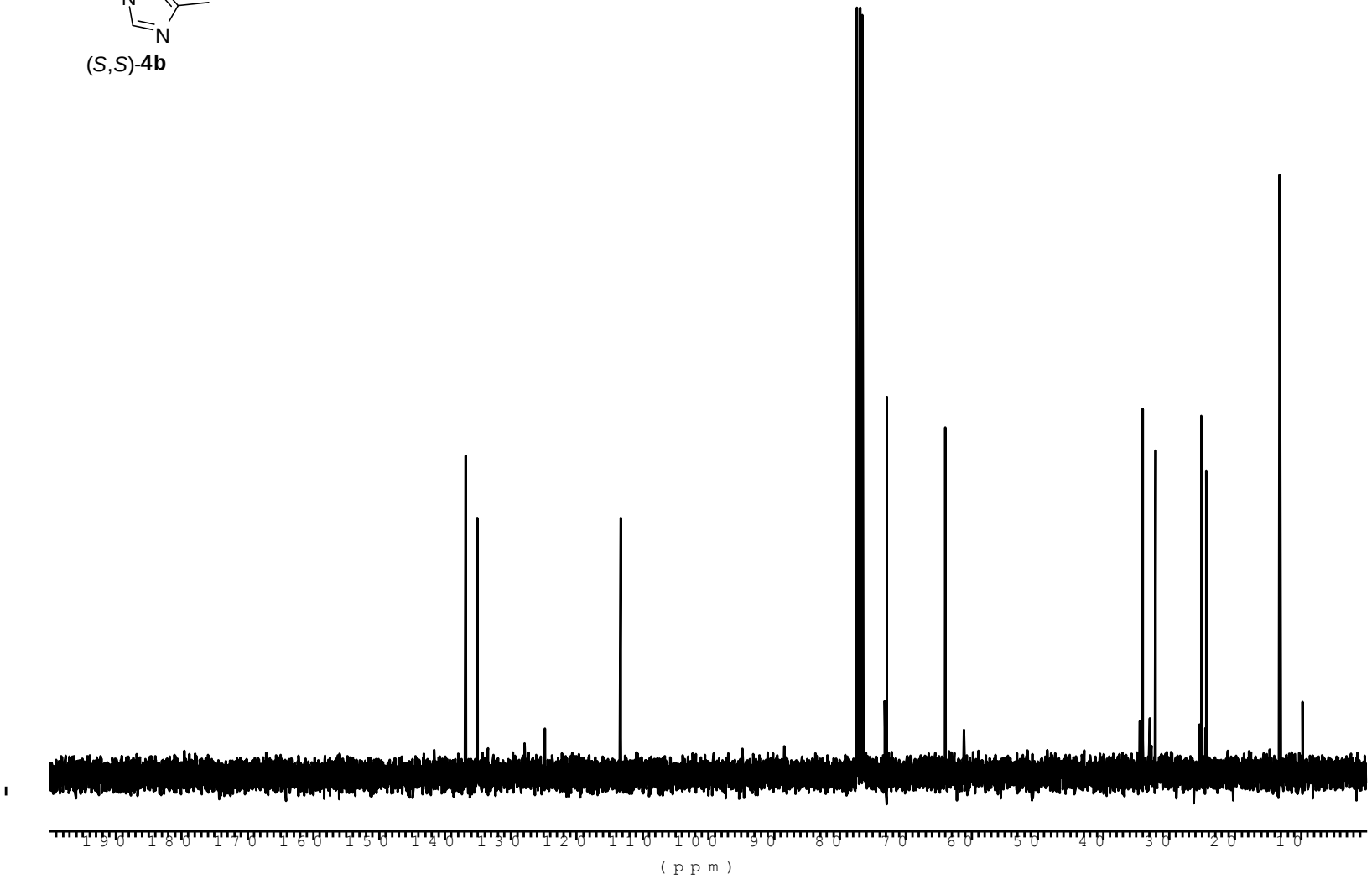

OH
N
N
(S,S)-4a
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

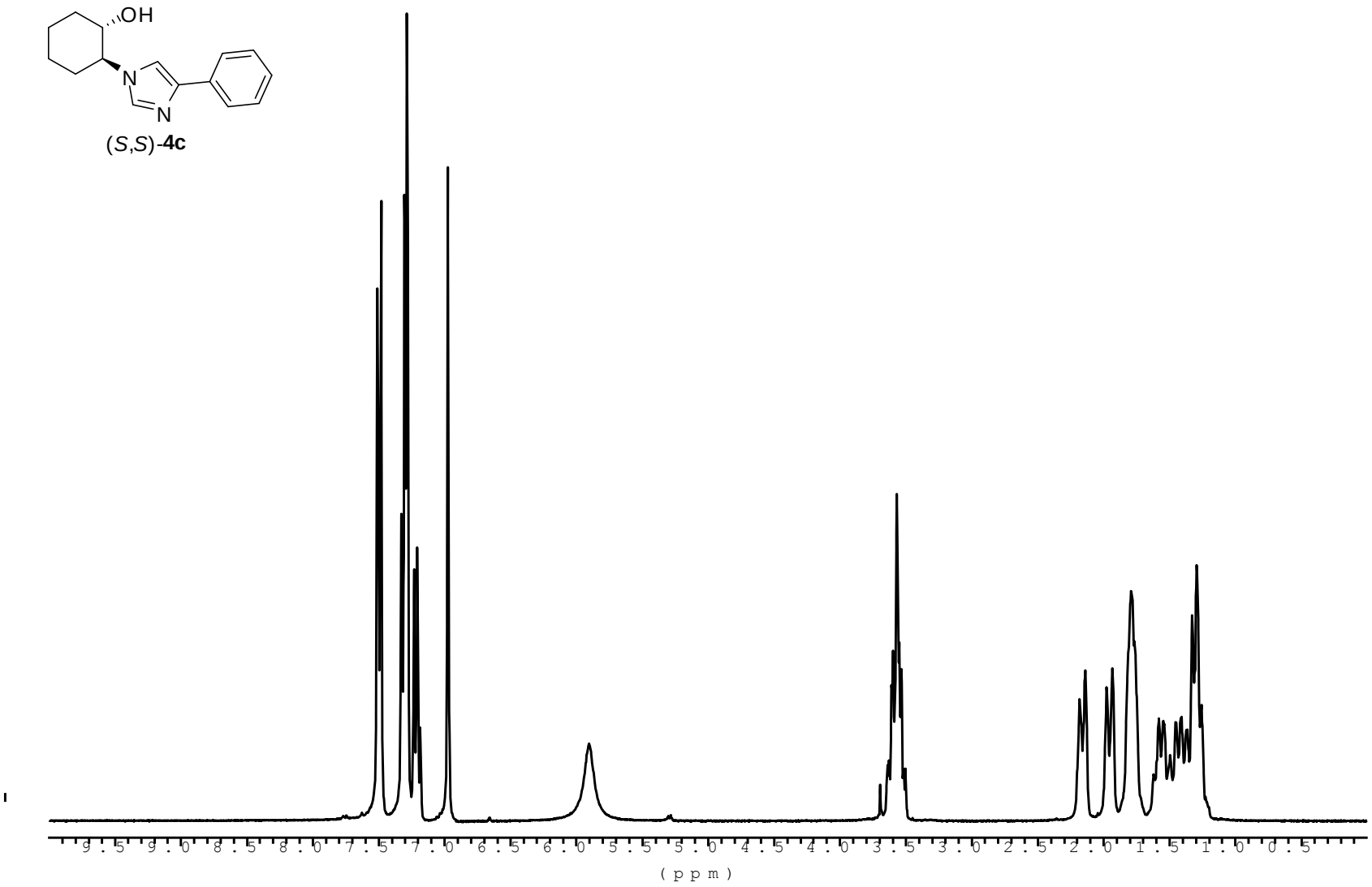


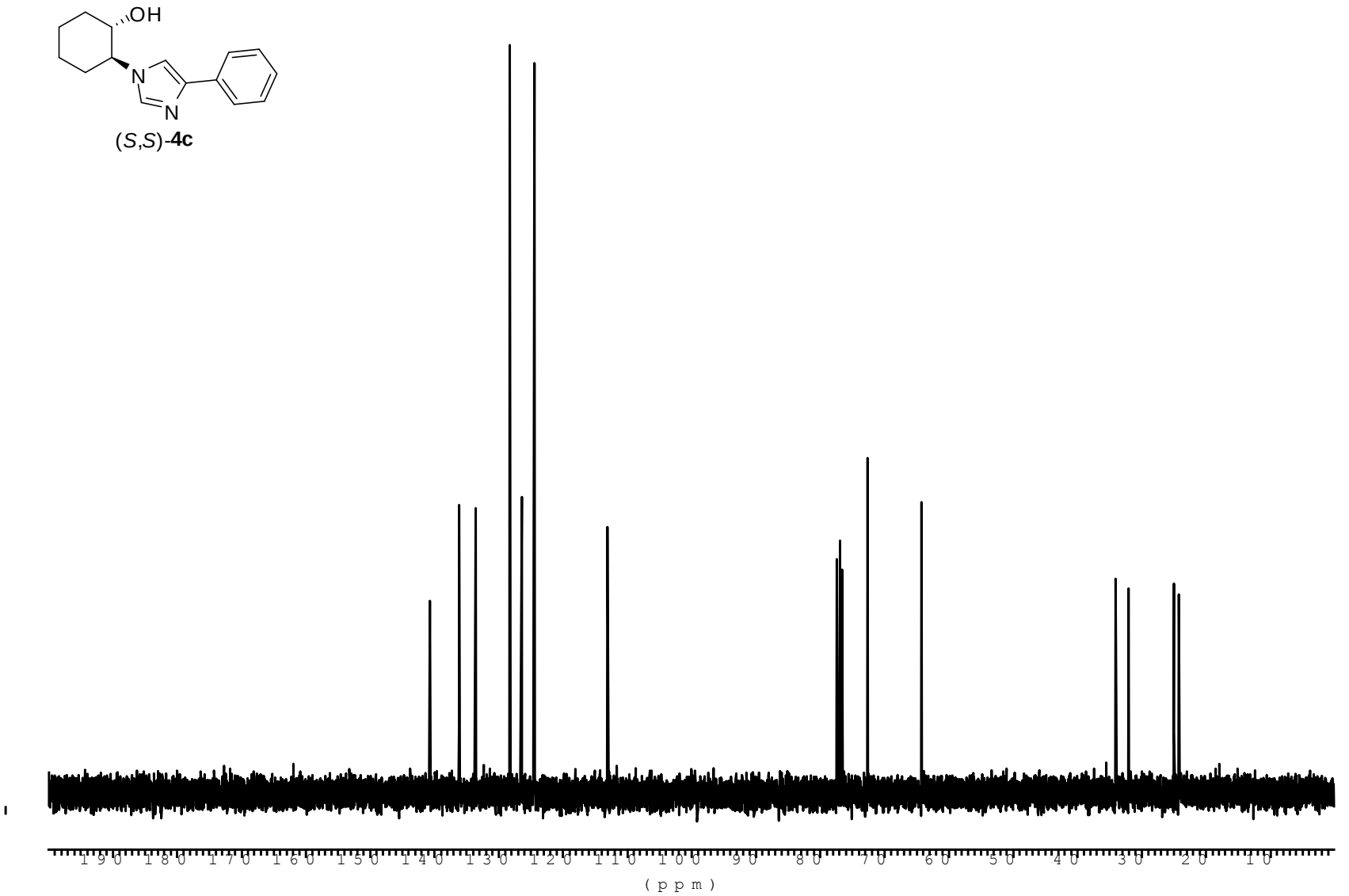
(*S*,*S*)-**4b**

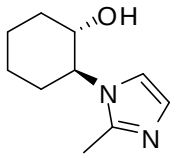

OH
N
N

(*S*,*S*)-**4b**

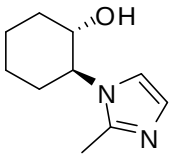

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)


OH
N
N
(S,S)-4c
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)


OH
N
N
(S,S)-4c
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

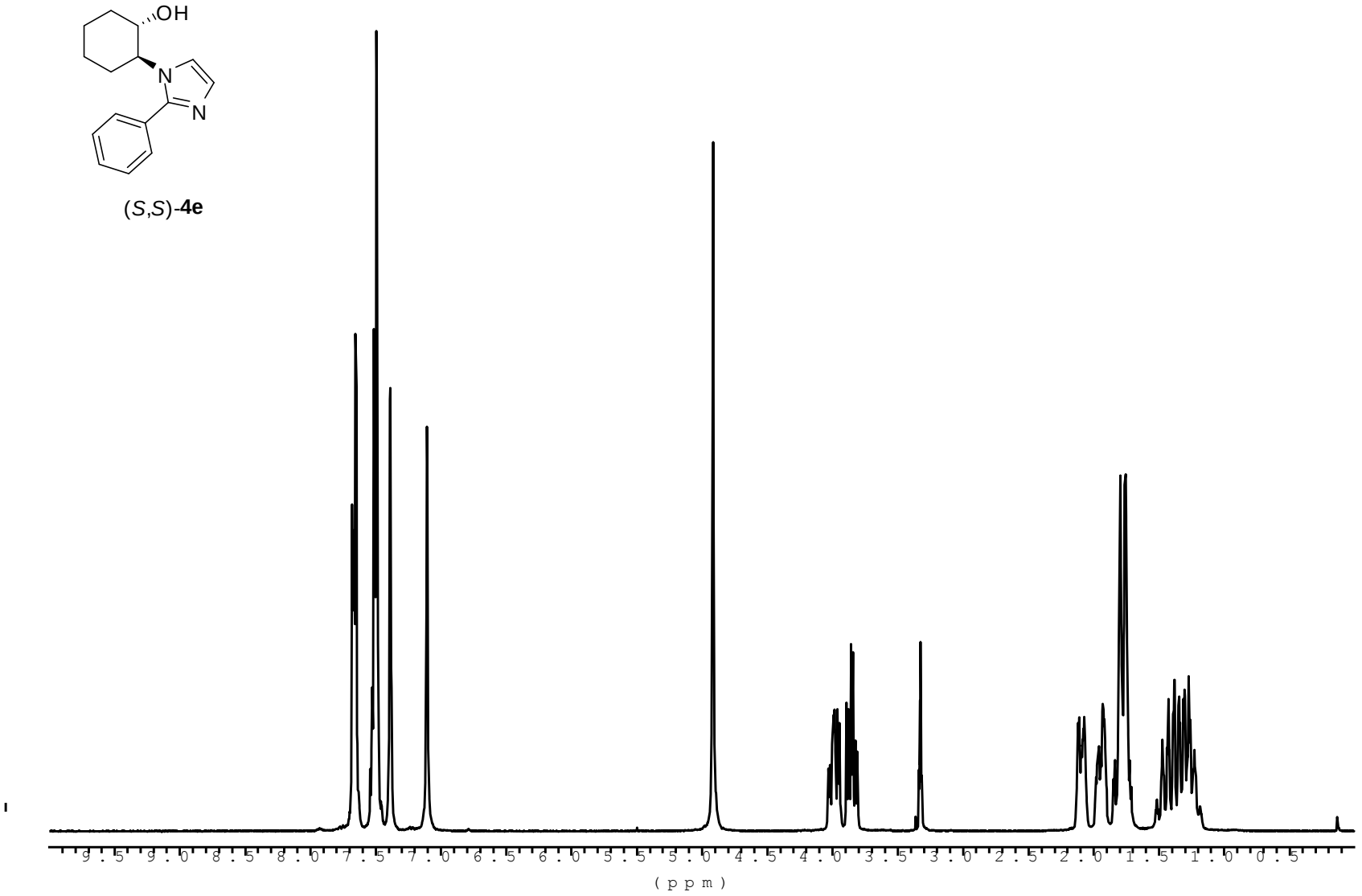


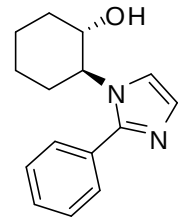
(*S*,*S*)-**4d**


OH
N
N

(*S*,*S*)-**4d**

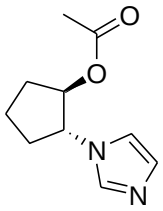
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)


OH
N
N
(S,S)-4e
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
(ppm)

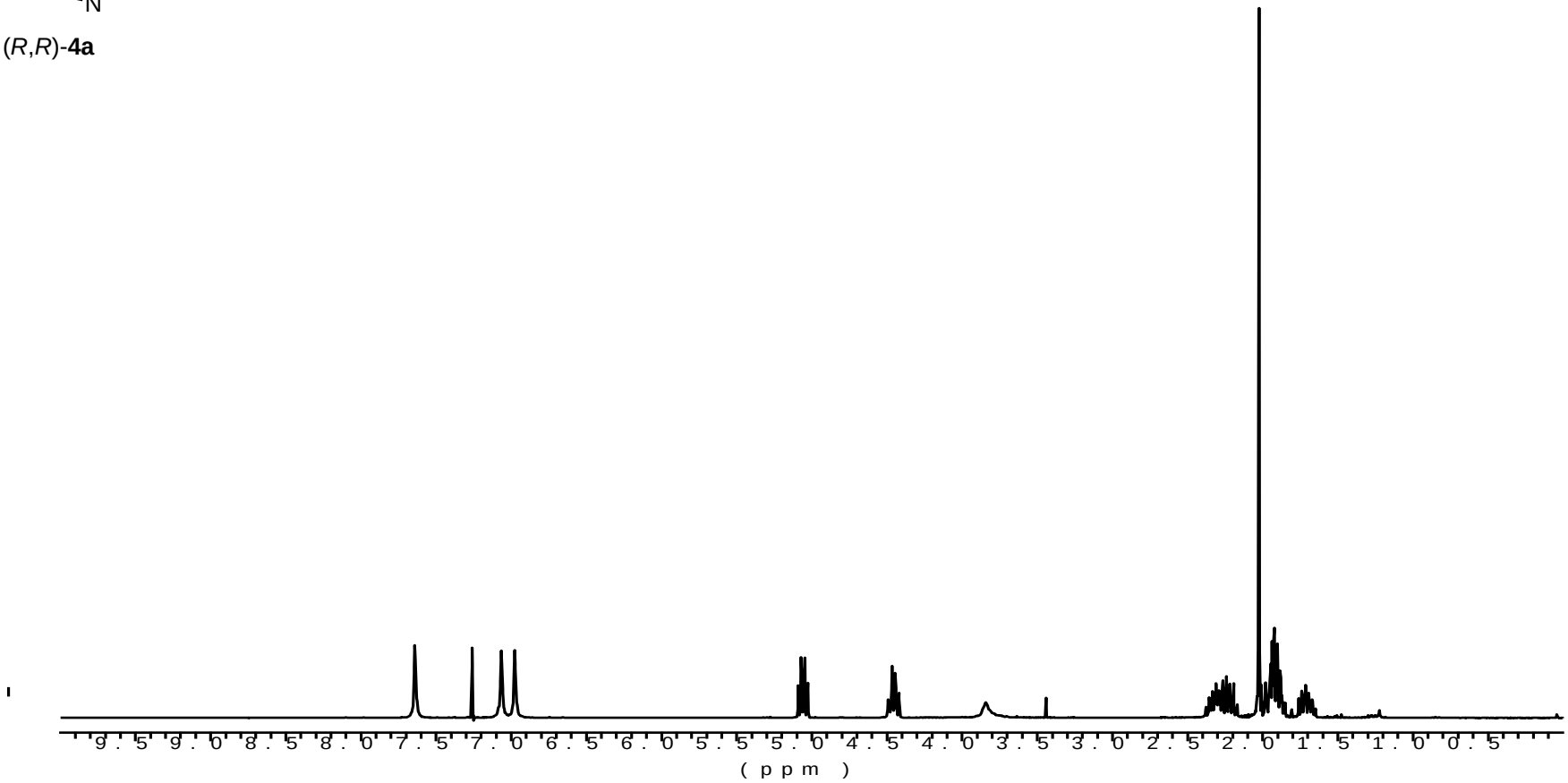

OH
N
N

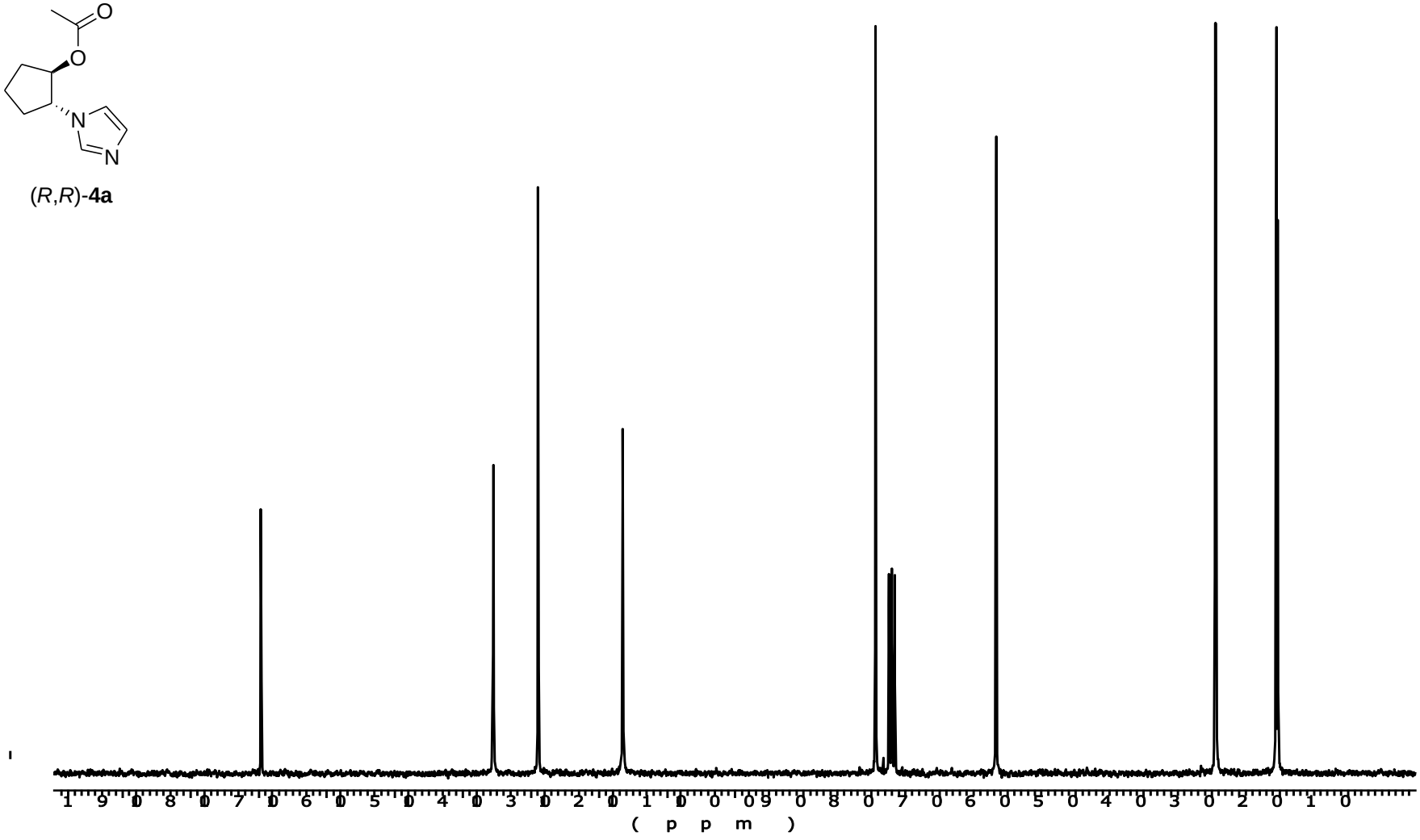
(*S*,*S*)-**4e**

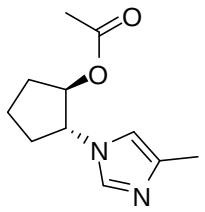
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)



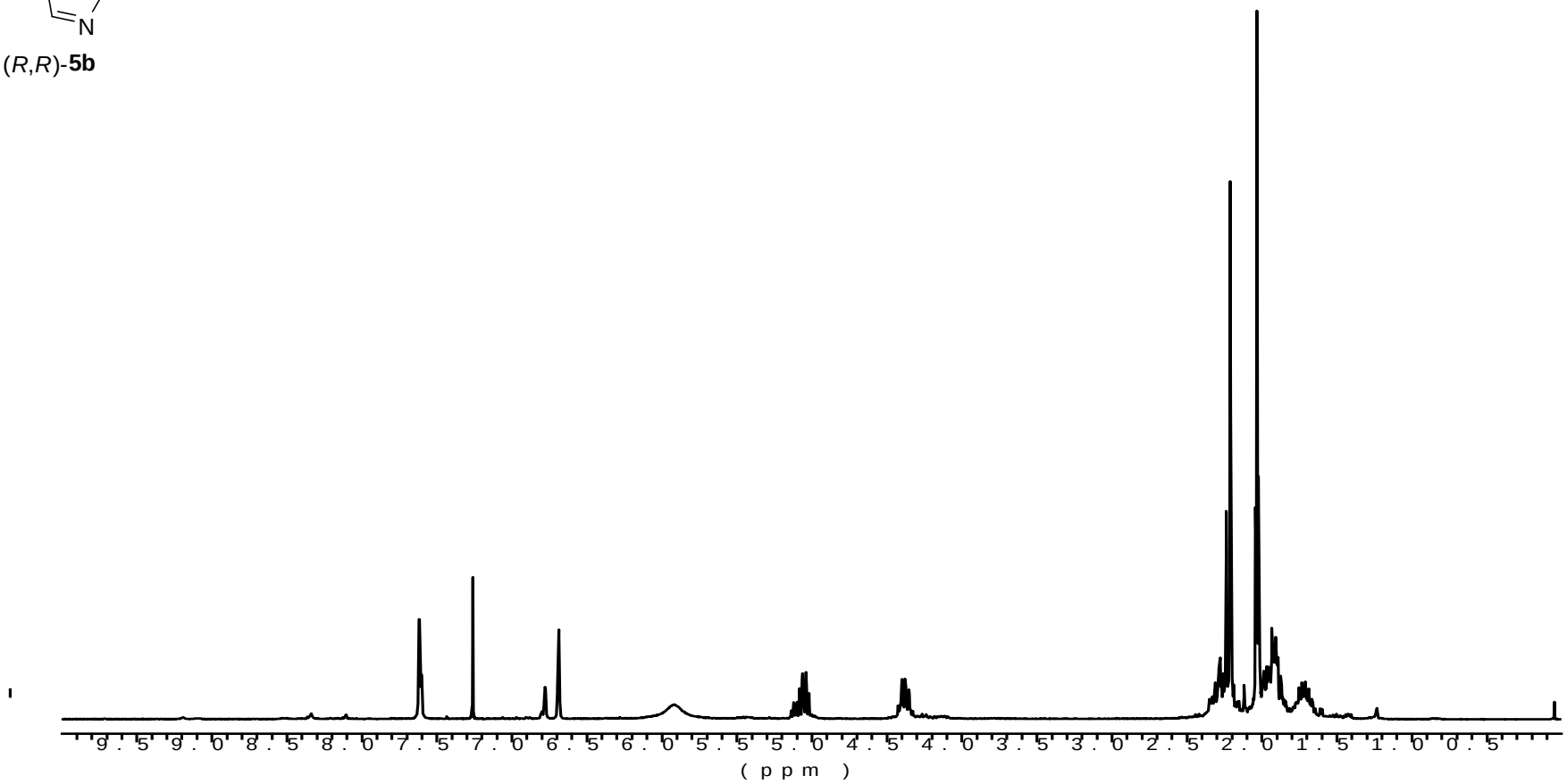
(*R*,*R*)-**4a**

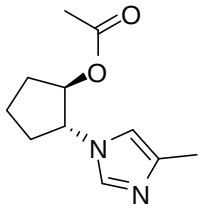



O
O
N
N
(R,R)-4a
1 9 0 8 0 7 0 6 0 5 0 4 0 3 0 2 0 1 0 0 0 9 0 8 0 7 0 6 0 5 0 4 0 3 0 2 0 1 0
(p p m)

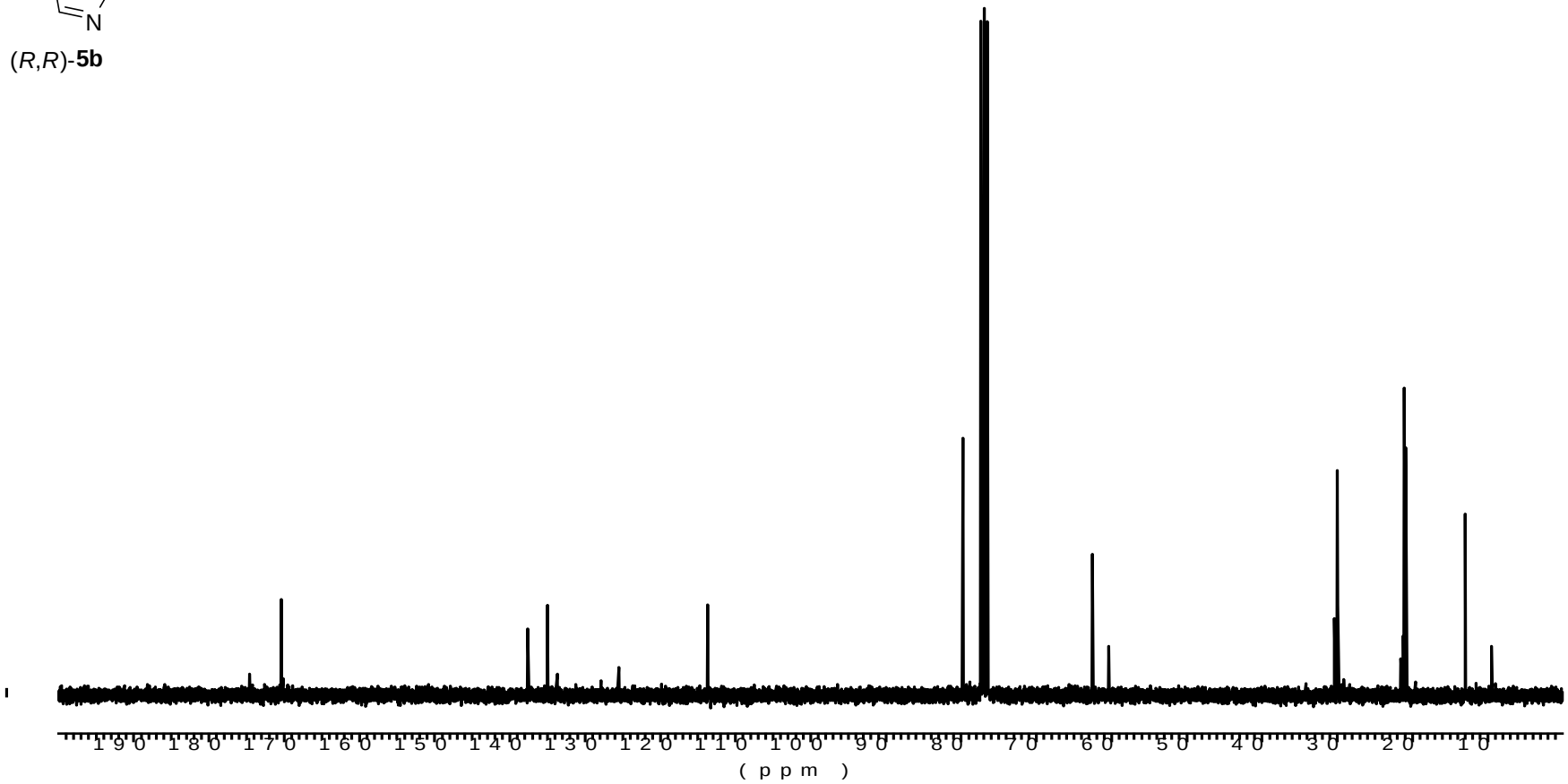


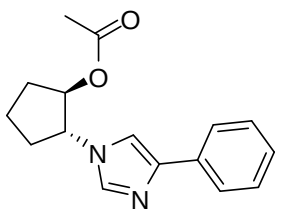
(*R*,*R*)-**5b**



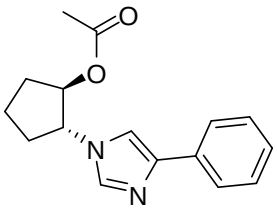

O
O
N
N

(*R*,*R*)-**5b**


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(p p m)

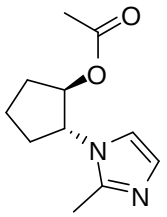


(*R*,*R*)-**5c**

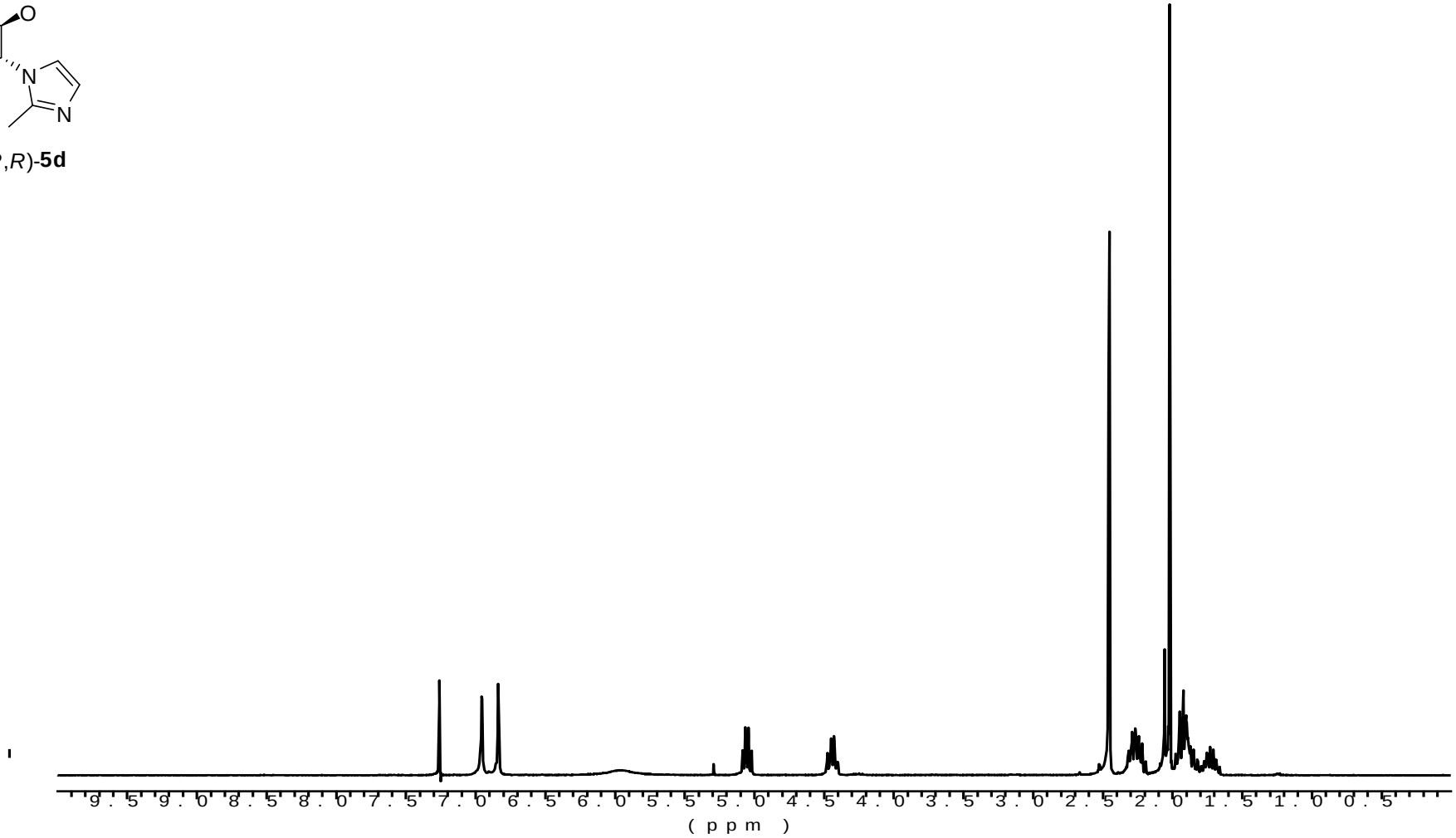

O
O
N
N

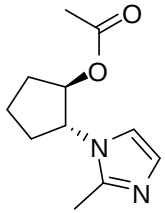
(*R*,*R*)-**5c**

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(p p m)



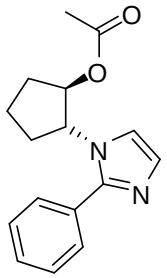
(*R*,*R*)-**5d**



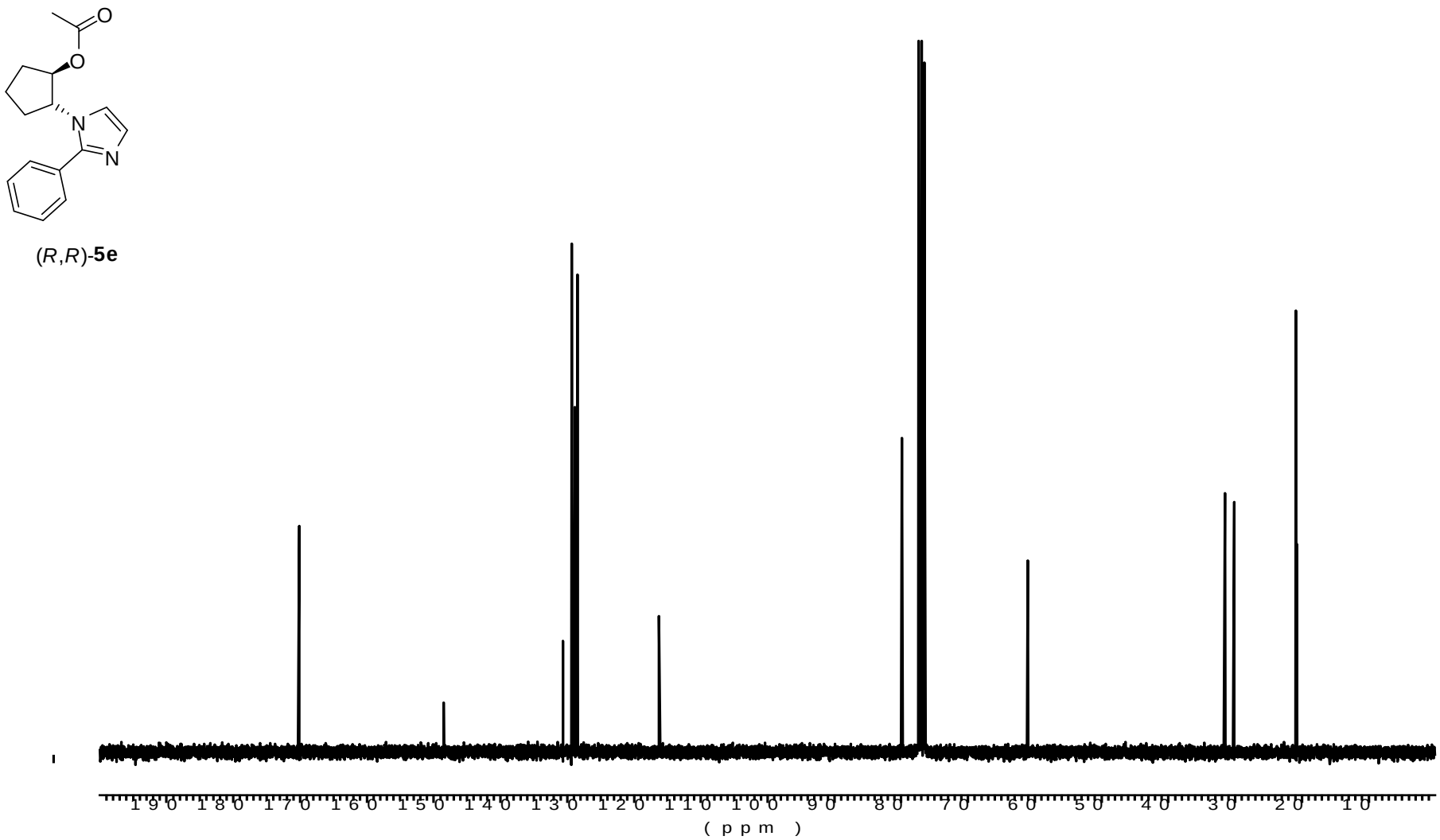

O
O
N
N

(*R*,*R*)-**5d**

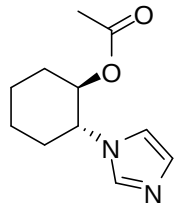
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(p p m)



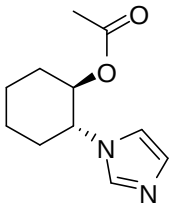
(*R*,*R*)-**5e**


O
O
N
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(p p m)

(*R*,*R*)-**5e**

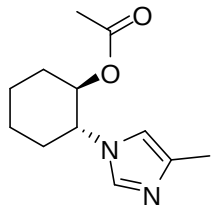


(*R*,*R*)-**6a**

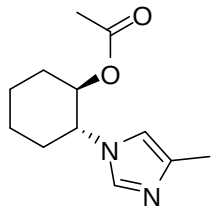

O
O
N
N

(*R*,*R*)-**6a**

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

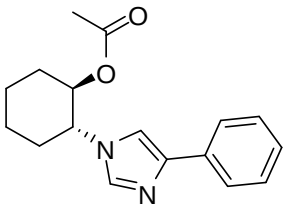


(*R*,*R*)-**6b**

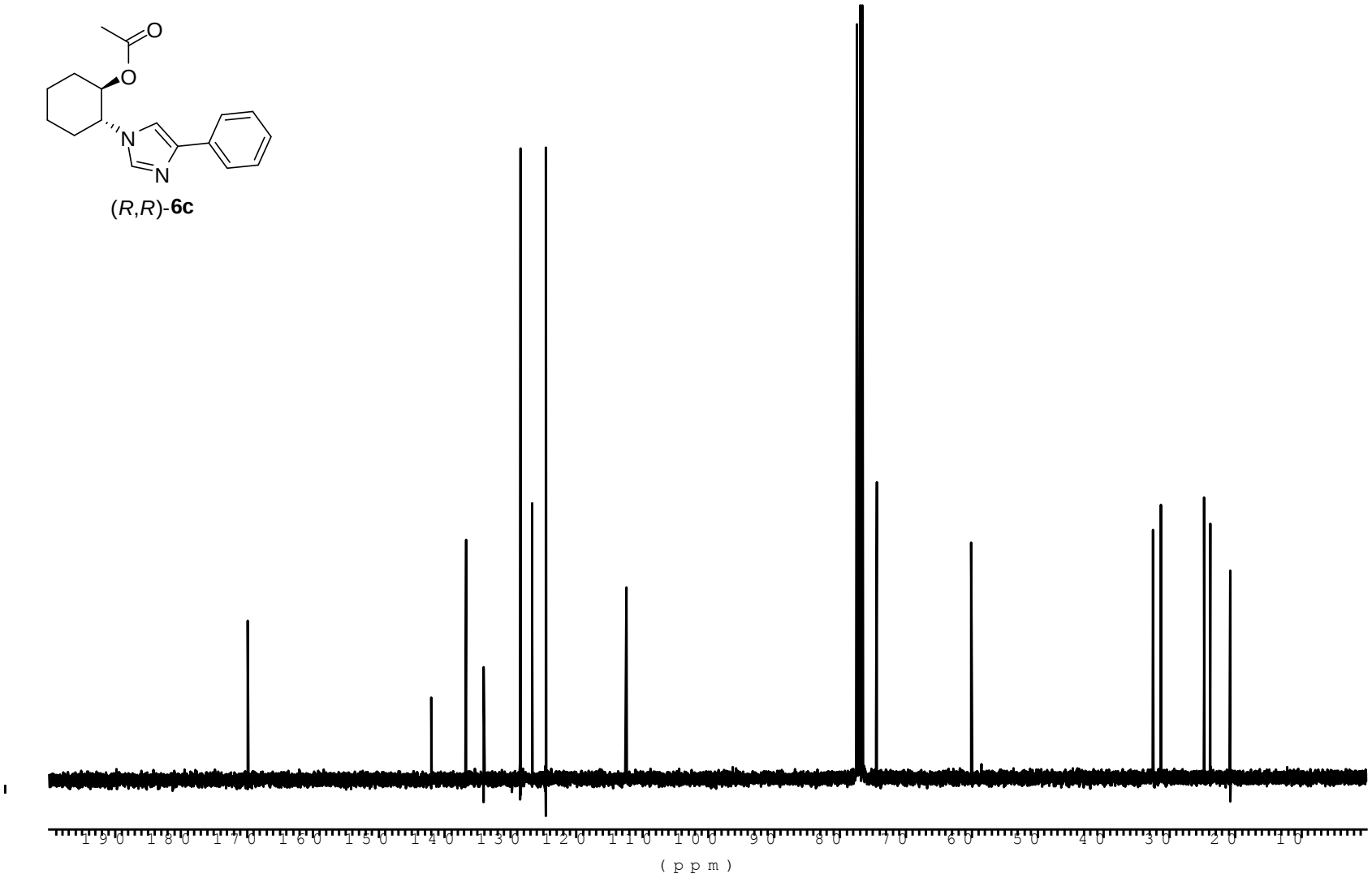

O
O
N
N

(*R*,*R*)-**6b**

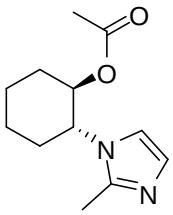
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)



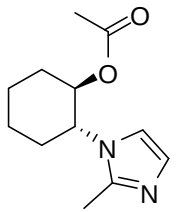
(*R*,*R*)-**6c**


O
O
N
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

(*R*,*R*)-**6c**

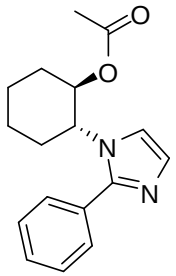


(*R*,*R*)-**6d**

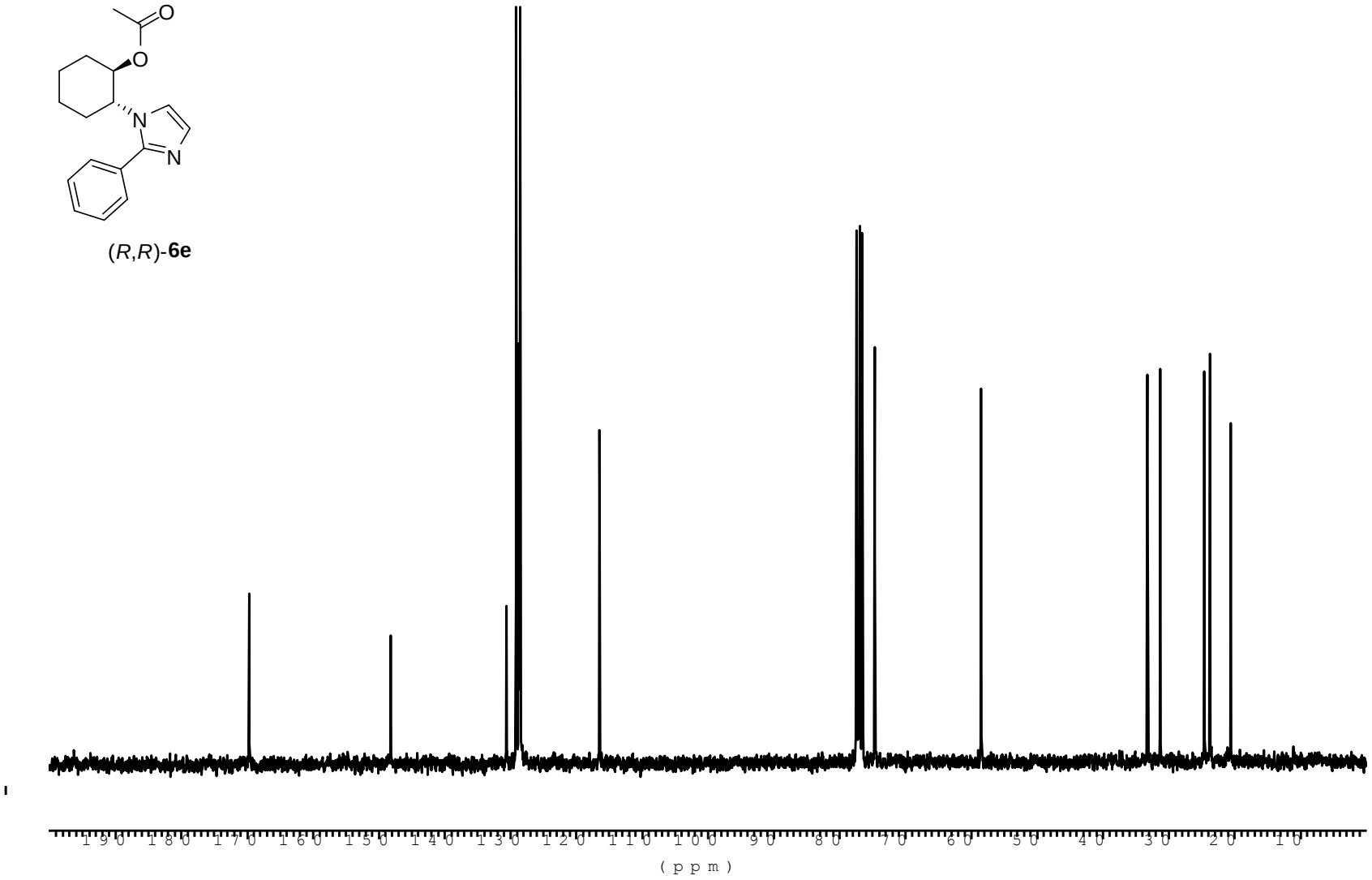

O
O
N
N

(*R*,*R*)-**6d**

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)



(*R*,*R*)-**6e**


O
O
N
N
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

(*R*,*R*)-**6e**