Electronic Supplementary Information (ESI)

Highly enantioselective hydrogenation and transfer hydrogenation of cycloalkyl and heterocyclic ketones catalysed by an iridium complex of a tridentate phosphine-diamine ligand.

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1. General Information

All manipulations were carried out under an inert nitrogen atmosphere using standard Schlenk techniques. Solvents were dried and degassed prior to use. Other reagents were purchased commercially and used as received. Ligands (*R*,*R*)-**3**[1] and (*R*,*R*),(S^P)-**4**[2] were prepared according to the literature. $[IrCl(COD)]_2$ and $[RhCl(COD)]_2$ were purchased from Strem and Aldrich and used as received. K^{t}BuO 1M solution in 2-methyl-2-propanol was purchased from Aldrich. Solvents were removed by rotary evaporation on a Heidolph labrota 4000. Flash column chromatography was performed on Davisil silica gel Fluorochem 60 Å, particle size 35-70 μm. NMR spectra were recorded on Bruker Avance 300 and 400 instruments. Proton chemical shifts are referenced to internal residual solvent protons. Proton signal multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad) or a combination of the above. Where appropriate, coupling constants (*J*) are quoted in Hz and are reported to the nearest 0.1 Hz. All spectra were recorded at room temperature and the solvent for a particular spectrum is given in parentheses. Carbon chemical shifts are referenced to the carbon signal of the deuterated solvents. Chemical ionisation mass spectroscopy and electron ionisation mass spectroscopy were performed on a Micromass GCT spectrometer. Electrospray mass spectroscopy was performed on a Micromass LCT spectrometer. All were operated by Mrs Caroline Horsburgh at St Andrews University, or at the ESPSRC National Mass Spectrometry Service Centre, Swansea University, using Waters ZQ4000, Thermofisher LTQ Orbitrap XL and Finnigan MAT 900 XLT Instruments. Only major peaks are reported, and intensities are quoted as percentages of the base peaks. Optical rotations were measured on a Perkin elmer 341 polarimeter using a 1 ml cell with a 1 dm path length at room temperature using the sodium D-line, and a suitable solvent that is reported along with the concentration (*c* = g/100ml). HPLC analysis has been determined using a Varian Prostar operated by Galaxie workstation PC software.

2. Hydrogenation Using $[IrCl(COD)]_2$ and (P^N^N)L Catalysts

A Biotage 5 ml microwave vial containing a stirring bar was charged with the appropriate amounts of substrate (1 mmol). The vial was sealed with a crimp cap, purged with three vacuum/argon cycles and left under argon atmosphere. 2-Propanol (3 mL total final volume), $[IrCl(COD)]_2$ (0.1 mol%) and ligand (0.1 mol%) were added using a syringe from stock solutions. Finally, potassium *tert*-butoxide (2 mol%) (1 M solution in 2-methyl-2-propanol) was added and then two needles were pierced into the vial and this was introduced into an autoclave, which had been previously purged with three vacuum/argon cycles. The autoclave was then purged three times with H_2, pressurised to 50 bar and

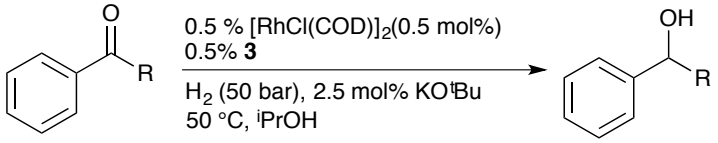
immersed into an oil bath preheated to the desired temperature. After the desired reaction time, the autoclave was cooled, depressurised and opened and the reaction mixture concentrated *in vacuo*. The conversion of substrate to product was calculated by ^{1}H NMR spectroscopy (In these experiments only starting material and product were observed, so an internal standard was generally not used). The products were isolated by column chromatography, or simple filtration through a 3 cm pad of silica with ethyl acetate eluent and characterised by comparison of NMR, MS and optical rotation with literature values. The enantiopurity of the product was determined using high performance liquid chromatography with the chiral stationary phase noted for each product.

3. Racemic Reduction with Sodium Borohydride

All alcohols produced were also reduced with sodium borohydride on a small scale to develop the HPLC method. To a solution of the substrate (1 equivalent) in absolute ethanol was added powdered sodium borohydride (3 equivalents) and the mixture stirred. The reaction was monitored by thin layer chromatography and upon completion quenched with 1M hydrochloric acid solution. The mixture was then extracted with dichloromethane and washed with water and brine before drying with magnesium sulfate, filtration and concentration *in vacuo* yielded the product. The HPLC and NMR data is in agreement with the products from the hydrogenation reactions.

4. Asymmetric hydrogenation of aryl ketones with $[RhCl(COD)]_2$ and ligand 3

Table S.1: Asymmetric hydrogenation of various ketones with a Rh(PNN) complex.



Entry	R=	Conversion	Enantioselectivity
1	Me	>99	50
2	*Iso*-propyl	58	45
3	*Tert*-butyl	79	55
4	Cyclohexyl	64	72

Reaction conditions used were: 0.3 mmols substrate, 3 ml *i*-PrOH, 1 hour

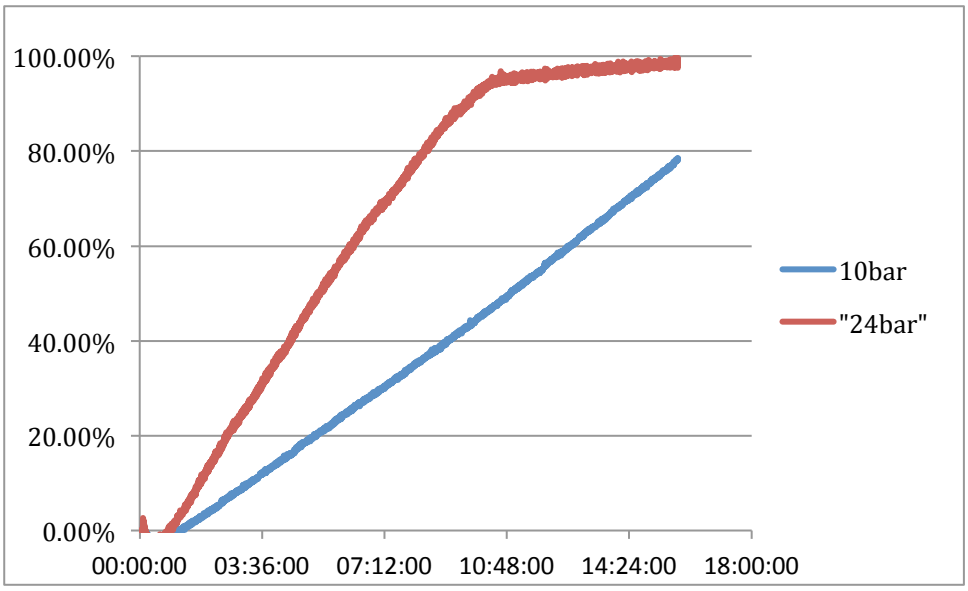
5. Kinetic data for the hydrogenation of cyclohexyl phenyl ketone using iridium catalyst 13

The following kinetics experiments were carried out using the complex [Ir(COD)(L**3**-H)] at 55 °C in Argonaut Endeavour multiwell autoclave with mechanical stirring, and continuously kept to the desired pressure by topping up from a ballast vessel. The catalyst, co-catalyst and substrate were all added to the reaction vial in air, and then the vessel was degassed with 3 purges with nitrogen gas. HPLC grade IPA (6 ml) was then added via a syringe and the system degassed by 3 further nitrogen purges, and 3 hydrogen purges. The reactions were carried out using 0.1 mol% catalyst, a substrate concentration of 0.606 M, and a base loading of 1.2%. Both reactions should differ only in the pressure of hydrogen applied. Whole gas uptake was monitored for 16 hours, the reactions were maintained under pressure of hydrogen for 19 hours.

10 bar reaction: >98% conversion, 60% e.e.

24 bar reaction: >99.5% conversion, 41% e.e.

Figure 1. Conversion against time at 10 and 24 bar of hydrogen pressure.



The results shown in Figure 1 are indicative of positive order in hydrogen, and zero or near zero order in substrate.

6. Asymmetric hydrogenation of cyclohexyl phenyl ketone. Effect of concentration and temperature on reaction rate and enantiomeric excess.

Table S.2: Asymmetric hydrogenation of cyclohexyl phenyl ketone using complex **13**, $[IrCl(COD)]_2$ and ligand **3**.

Entry[a]	Conc (M)	T (°C)	L mol%	M mol%	t min	Conv %	ee %
1	0.5	50		**13**, 0.1	180	98.5	64 (*S*)
2	0.5	45		**13**, 0.1	60	94	88 (*S*)
3	0.5	35		**13**, 0.1	30	90	90 (*S*)
4	0.5	21		**13**, 0.1	20	81	96 (*S*)
5	0.5	23		**13**, 0.1	5	19.4	94 (*S*)
6	0.25	50		**13**, 0.1	180	99.5	76 (*S*)
7	0.25	45		**13**, 0.1	60	97	87 (*S*)
8	0.25	35		**13**, 0.1	30	93	92 (*S*)
9	0.25	21		**13**, 0.1	20	85	97 (*S*)
10	0.25	23		**13**, 0.1	5	18.6	93 (*S*)
11[b]	0.33	50		**13**, 0.1	300	24	8 (*S*)
12[c]	0.33	50		**13**, 0.1	17 h	6	87 (*S*)
13	0.5	50	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	180	97.5	86 (*S*)
14	0.5	45	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	60	94	91 (*S*)
15	0.5	35	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	30	88	95 (*S*)
16	0.5	21	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	20	71	97 (*S*)
17	0.5	23	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	5	14	94 (*S*)
18	0.25	50	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	180	98.5	91 (*S*)
19	0.25	45	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	60	98	93 (*S*)
20	0.25	35	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	30	92	96 (*S*)
21	0.25	21	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	20	78	98 (*S*)
22	0.25	23	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	5	9.2	93 (*S*)
23[b]	0.33	50	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	300	74	12 (*S*)

[a] Reactions carried out using 2 mol% $KOBu^t$ co-catalyst in dry IPA at 50 bar initial hydrogen pressure, unless indicated otherwise. [b] Reaction carried out in Me-THF as solvent. [c] Reaction carried out without base ($KOBu^t$).

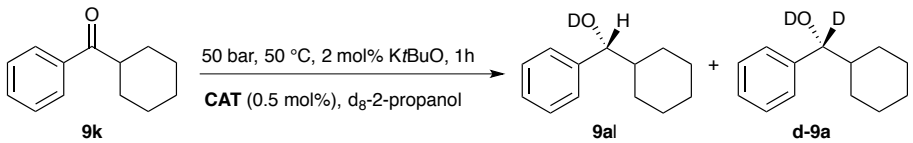
7. Asymmetric transfer hydrogenation

Table S.3: Asymmetric transfer hydrogenation of various ketones using complex **13**, $[IrCl(COD)]_2$ and ligand **3**.

Entry	Ketone	T (°C)	Conc (M)	L mol%	M mol%	t	Conv %	ee %
1	9k	50	0.5		**13**, 0.1	16 h	95	89 (*S*)
2	9k	50	0.33		**13**, 0.1	30 min	90	95 (*S*)
3						70 min	93	95 (*S*)
4						21 h	95	78 (*S*)
5	9k	19	0.33		**13**, 0.1	20 min	28	96 (*S*)
6						60 min	30	95 (*S*)
7						5 h	38	95 (*S*)
8						22 h	46	94 (*S*)
9	9k	50	0.5	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	16 h	95	87 (*S*)
10	9k	50	0.33	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	30 min	94	95 (*S*)
11						70 min	94	94 (*S*)
12						21 h	95	75 (S)
13	9k	19	0.33	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	20 min	50	95 (*S*)
14						60 min	63	95 (*S*)
15						5 h	80	95 (*S*)
16						22 h	85	94 (*S*)
17	10k	50	0.33		**13**, 0.1	3 h	74	80 (*S*)
18						21 h	86	74 (*S*)
19	10k	50	0.33	**3**, 0.1	$[Ir(COD)Cl]_2$, 0.1	3 h	96 (86)	83 (*S*)

[a] Reactions carried out using 2 mol% $KOBu^t$ co-catalyst in dry IPA, unless indicated otherwise.

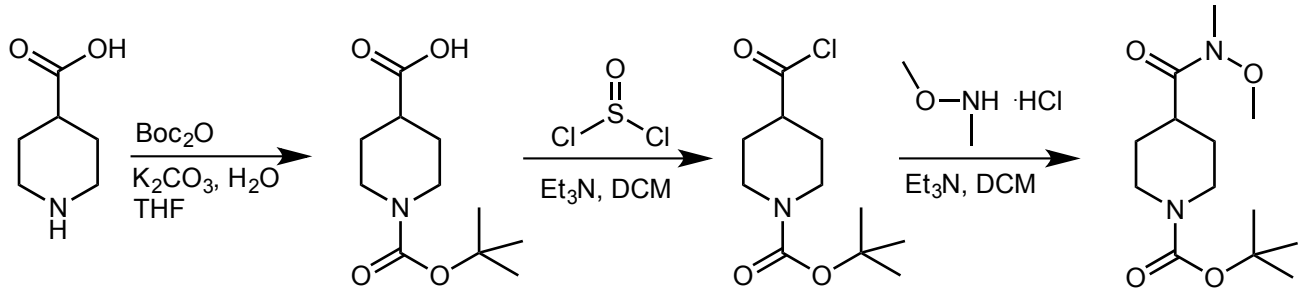
Deuterium labelling of ketone 9k



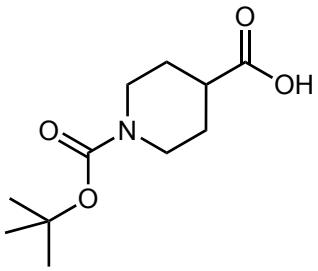
13, C= 97.5%, **d-9al/9al** 95 / 2.5
[IrCODCl]$_2$, 3, C= 98.7%, **d-9al/9al** 94.3 / 4.4

8. Synthesis of ketones

General Scheme for the preparation of Weinreb amides

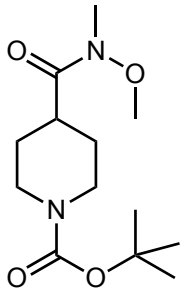


1-(*tert*-butoxycarbonyl)piperidine-4-carboxylic acid[3]



To a stirred solution of isonipecotic acid (38.7 mmol, 5.0 g) and potassium carbonate (77.4 mmol, 10.7 g) in water (75 mL) at 0 °C was added dropwise a solution of di-*tert*-butyl dicarbonate (38.7 mmol, 8.45 g) in THF (75 mL). The reaction mixture was gradually warmed to rt and stirred overnight. The solvents were evaporated, and the residue was dissolved in methylene chloride. The methylene chloride layer was washed with HCl (1N) (3 x 50 mL) and then water, dried over magnesium sulfate, and concentrated *in vacuo* to give pure *N*-Boc protected carboxylic acid as a white solid (28.8 mmol, 6.63 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.04-4.00 (m, 2H), 2.90-2.81 (m, 2H), 2.52-2.44 (m, 1H), 1.93-1.88 (m, 2H), 1.70-1.57 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.4 (O=C-OH), 154.9 (O=C-N), 79.9 (C), 43.1 (CH_2), 40.9 (CH), 28.6 ((CH_3)$_3$), 27.9 (CH_2).

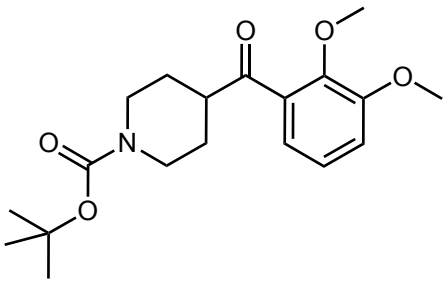
tert-Butyl 4-(methoxy(methyl)carbamoyl)piperidine-1-carboxylate[4]



To a stirred solution of the carboxylic acid prepared in the previous step (28.8 mmol, 6.63 g) in methylene chloride (80 mL) under N_2 and at rt was added thionyl chloride (57.6 mmol, 6.85 g) and triethyl amine (57.6 mmol, 5.83 g). The resulting suspension was stirred for 17 h. The solvents were evaporated and the resulting solid was dried under vacuum and use without further purification in the following step.

Diethylhydroxylamine hydrochloride salt (28.83 mmol, 2.81g) was suspended in methylene chloride (70 mL) and then triethylamine (57.6 mmol, 8.02 mL) was added and the mixture cooled down to 0 °C using an ice bath. The acid chloride obtained in the previous step was dissolved in methylene chloride and the resulting suspension was added slowly to the reaction mixture and stirred at rt for 6h. The resulting reaction mixture was washed with water (2 x 50 mL), HCl 0.1 M (1x 50 mL) and $NaHCO_3$ (aq) (1 x 50 mL). The organic layer was then dried over magnesium sulphate, and concentrated *in vacuo* to give to give a dark red syrup. The crude mixture was purified by chromatography on SiO_2 using EtOAc/hexane 2:1 as eluent to give the corresponding Weinreb amide as a White solid (13.3 mmol, 3.63 g, 46%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.11-4.06 (m, 2H), 3.66 (s, 3H), 3.13 (s, 3H), 2.77-2.67 (m, 3H), 1.68-1.57 (m, 4H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.6 (O=C-NOMe), 154.7 (O=C-N), 79.5 (C), 61.6 (MeO), 43.3 (CH_2), 38.1 (NMe), 32.3 (CH), 28.5 ((CH_3)$_3$), 28.0(CH_2); HRMS (ES)$^+$: 295.1622 $[M+Na]^+$, $C_{13}H_{24}N_2O_4Na$ requires 295.1628.

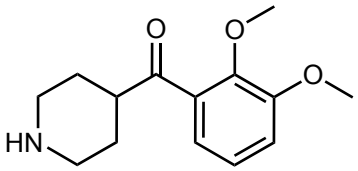
tert-Butyl 4-(2,3-dimethoxybenzoyl)piperidine-1-carboxylate, **6k**[5]



n-BuLi (4.49 mmol, 2.8 mL, 1.6 M in hexane) was added via syringe to a stirred solution of veratrole (4.62 mmol, 0.638 g) in anhydrous THF (7 mL) under N_2 at 0 °C. After 1 h, the ice bath was removed

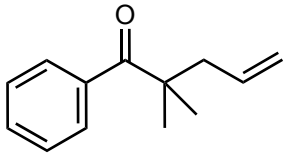
and the reaction mixture was allowed to stir for another 1h 45 min and then was transferred via cannula to a Schlenk flask containing a solution of Weinreb amide (3.30 mmol, 0.9 g) in anhydrous THF (3 mL) under N_2 at –20 °C. The reaction mixture was the allow to warm up to rt and to stir for 21 h. The reaction mixture was quenched with saturated aqueous NH_4Cl, the layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried with anhydrous magnesium sulfate, filtered, and evaporated to give a brown oil. The crude mixture was purified by chromatography on SiO_2 using Et_2O/hexane 1:2 as eluent to give the corresponding ketone **6k** as a colorless syrup (2.5 mmol, 0.87 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12-6.95 (m, 3H), 4.10-4.05 (m, 2H), 3.90 (s, 3H), 3.86 (s, 3H), 3.28-3.19 (m, 1H), 2.87-2.78 (m, 2H), 1.87-1.82 (m, 2H), 1.65-1.51 (m, 3H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.9, 154.7, 152.7, 146.9, 134.0, 124.3, 120.2, 114.9, 79.4, 61.7, 55.9, 48.0, 43.3, 28.4, 27.8; HRMS (ES)$^+$: 372.1773 $[M+Na]^+$, $C_{19}H_{27}NO_5Na$ requires 372.1781.

(2,3-dimethoxyphenyl)(piperidin-4-yl)methanone, **5k**[5]



tert-Butyl 4-(2,3-dimethoxybenzoyl)piperidine-1-carboxylate **6k** (0.93 mmol, 0.325 g) was placed in a round bottom flask. Methylene chloride (5 mL) and trifluoro acetic acid (1 mL) were added and the resulting solution was stirred at rt for 22 h. The solvents were then evaporated using a rotavapor. The reaction crude was dissolved again in methylene chloride (5 mL) and NaOH (1 M, 3 mL) were added until decidedly basic pH according to Litmus paper. The organic layer was separated and the aqueous layer was then extracted with Et_2O (3 x 5 mL) and methylene chloride (3 x 5 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and the final solution concentrated to dryness under vacuum. The residue consisted in the pure amine **5k** (0.72 mmol, 0.180 g, 77%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11-6.95 (m, 3H), 3.89 (s, 3H), 3.86 (s, 3H), 3.28-3.11 (m, 4H), 2.71 (td, J = 12.3, 2.8 Hz, 2H), 1.93-1.87 (m, 2H), 1.67-1.54 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.6, 153.2, 134.6, 124.9, 120.9, 115.4, 78.0, 77.6, 77.2, 62.3, 56.5, 48.5, 46.2, 29.0.
HRMS (ES)$^+$: 250.1435 $[MH]^+$, $C_{14}H_{20}NO_3$ requires 250.1438.

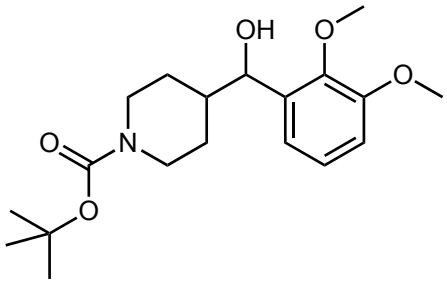
2, 2-Dimethyl-1-phenylpent-4-en-1-one **12k**[6]



Compound **12k** was prepared in a similar way as reported in the literature.[5] A mixture of isobutyrophenone (27.2 mmol, 4g), allyl bromide (31.4 mmol, 3.52g) and potassium *tert*butoxide (30 mmol, 3.36g) in *tert*butanol (40 mL) was heated at 90 °C for 5h. After cooling, water (40 mL) was added and the organic layer was extracted with diethyl ether (2 x 50 mL). The organic layers were then dried over magnesium sulphate, and concentrated *in vacuo* to give to give a colorless oil (3.7 g) containg a mixture of isobutyrophenone and the desired product (1.33: 1). The mixture was dissolved back in *tert*butanol (40 mL) and allyl bromide (31.4 mmol, 3.52g) and potassium *tert*butoxide (30 mmol, 3.36g) were added. And heated at 97 °C for 8h. The work up was done as above to afford a mixture of isobutyrophenone and the desired product (1:2). The crude mixture was purified by kugelrohr distillation (0.2 torr, 75 °C). Three different fractions were obtained containing different levels of isobutyrophenone. The fraction used in catalysis (1.47 g, 7.8 mmol, 29 %) containing 8.7% of isobutyrophenone. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.64 (m, 2H), 7.48-7.37 (m, 3H), 5.77-5.67 (m, 1H), 5.06-4.98 (m, 2H), 2.49 (dt, J = 7.3, 1.1 Hz, 1H), 1.32 (s, 6H).

9. Experimental data for alcohols from catalysis

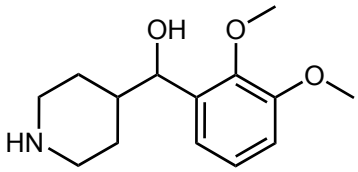
(*S*)-(+)-*tert*-Butyl 4-((2,3-dimethoxyphenyl)(hydroxy)methyl)piperidine-1-carboxylate, **6al**[7]



$[\alpha]_D^{20}$ +6.3 (*c* 3.2, $CHCl_3$, ee 75%); IR (KBr, cm^{-1}) 3446, 2975, 2936, 2856, 1692, 1586, 1475, 1430, 1366, 1264, 1131; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04-6.99 (m, 1H), 6.87-6.80 (m, 2H), 4.59 (d, J = 7.8 Hz, 1H), 4.14-3.99 (m, 2H), 3.83 (s, 3H), 3.83 (s, 3H), 2.66-2.49 (m, 2H), 2.38 (br s, 1H), 1.98-1.92 (m, 1H), 1.80-1.68 (m, 1H), 1.41 (s, 9H), 1.32-1.10 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.7, 152.4, 146.3, 136.1, 124.0, 119.5, 111.4, 79.2, 74.1, 60.8, 55.6, 43.7, 43.6, 43.1, 28.6, 28.4, 28.3; HRMS $(ES)^+$: 374.1927 $[M+Na]^+$, $C_{19}H_{29}NO_5Na$ requires 374.1938. The enantiomeric excess was determined by HPLC on a Chiralpak AD-H, 250 x 4.6 mm, 95:5 *n*-hexane: 2-propanol, 1 ml/min, 210 nm, t_R[(+)-(*S*), major][a] = 39.2 min, t_R[(–)-(*R*), minor] = 44.2 min.

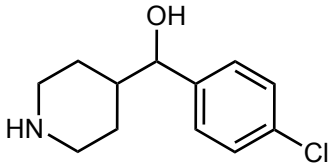
[a]Tentatively assigned as the *S* enantiomer based on the fact that (*R*,*R*) catalyst usually gives the *S* enantiomer.

(*S*)-(–)-(2,3-dimethoxyphenyl)(piperidin-4-yl)metanol, **5al**[8]



$[\alpha]_D^{20}$ –6.5 (*c* 0.8, MeOH, ee 80%) {lit:[9] $[\alpha]_D^{20}$ –7.1 (*c* 0.1 MeOH, ee >98%)}; IR (KBr, cm^{-1}) 3381, 3248, 2933, 2854, 1599, 1587, 1479, 1426, 1342, 1262; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04-6.99 (m, 1H), 6.88-6.79 (m, 2H), 4.58 (d, *J* = 7.9 Hz, 1H), 3.83 (s, 3H), 3.83 (s, 3H), 3.09-2.93 (m, 2H), 2.56-2.40 (m. 2H), 2.21 (br s, 2H), 1.99-1.95 (m, 1H), 1.77-1.67 (m, 1H), 1.31-1.12 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.4, 146.4, 136.5, 123.9, 119.6, 111.2, 74.3, 60.8, 55.7, 46.5, 46.4, 43.2, 29.9, 29.7; HRMS $(ES)^+$: 252.1581 $[M+H]^+$, $C_{14}H_{22}NO_3$ requires 252.1594. The enantiomeric excess was determined by HPLC on a Chiralpak AD-H, 250 x 4.6 mm, 90:10 *n*-hexane: 2-propanol (0.25% diethanolamine), 1 ml/min, 254 nm, t_R[(–)-(*S*), major] = 21.8 min, t_R[(+)-(*R*), minor] = 25.4 min.

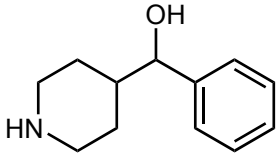
(*S*)-(–)-(4-Chlorophenyl)(piperidin-4-yl)methanol, **7al**[9]



$[\alpha]_D^{20}$ –4.1 (*c* 0.9, MeOH, ee 94%); IR (KBr, cm^{-1}) 3343, 2963, 2925, 2850, 1655, 1491, 1450, 1400, 1262; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.5 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 4.29 (d, *J* = 7.2 Hz, 1H), 3.08-2.94 (br m, 4H), 2.54-2.40 (m, 2H), 1.90-1.86 (m, 1H), 1.68-1.56 (m, 1H), 1.31-1.04 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.8, 133.1, 128.4, 127.9, 77.8, 46.0, 45.9, 43.4, 29.0, 28.7; HRMS $(ES)^+$: 226.0984 $[M+H]^+$, $C_{12}H_{17}ClNO$ requires 226.0993. The enantiomeric excess was determined by HPLC on a Chiralpak AD-H, 250 x 4.6 mm, 90:10 *n*-hexane: 2-propanol (0.25% diethanolamine), 0.5 ml/min, 230 nm, t_R[(–)-(*S*), major][a] = 25.1 min, t_R[(+)-(*R*), minor] = 31.1 min.

[a]Tentatively assigned as the *S* enantiomer based on the fact that (*R*,*R*) catalyst usually gives the *S* enantiomer.

(*S*)-(–)-Phenyl(piperidin-4-yl)metanol, **8al**[10]

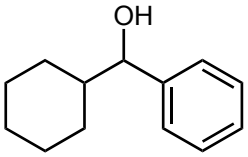


$[\alpha]_D^{20}$ –36.7 (*c* 0.45, $CHCl_3$, ee 96%) {lit:[10] $[\alpha]_{546}$ –36 (*c* 0.106 $CHCl_3$, ee 86%)}; IR (KBr, cm^{-1}) 3268, 3084, 2924, 2856, 1601, 1537, 1491, 1430, 1332, 1262, 1148; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28-7.16 (m, 5H), 4.21 (d, *J* = 7.5 Hz, 1H), 2.98-2.82 (m, 2H), 2.47-2.00 (m, 4H), 1.88-1.84 (m, 1H), 1.66-1.53 (m, 1H), 1.22-0.92 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 128.2, 127.5, 126.7, 78.7, 77.5, 77.1,

76.6, 46.4, 46.3, 43.6, 29.6; MS (GCMS) 191 (M^+). The enantiomeric excess was determined by HPLC on a Chiralpak AD-H, 250 x 4.6 mm, 90:10 *n*-hexane: 2-propanol (0.1% ethanolamine), 1 ml/min, 210 nm, t_R[(–)-(*S*), major][a] = 13.9 min, t_R[(+)-(*R*), minor] = 19.1 min.

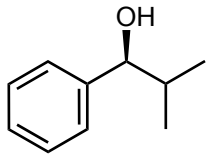
[a]Tentatively assigned as the *S* enantiomer based on the fact that (*R*,*R*) catalyst usually gives the *S* enantiomer.

(−)-(*S*)-Cyclohexyl(phenyl)methanol, **9al**[11(a)]



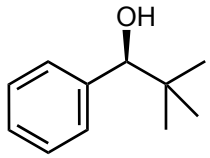
$[\alpha]_D^{20}$ –38.3 (*c* 1.0, $CHCl_3$, ee >99%) {lit[11(b)] $[\alpha]_D^{20}$ –22.2 (*c* 1.0 $CHCl_3$), ee 67%, lit:[11(c)] $[\alpha]_D^{23}$ +38 (*c* 0.4 $CHCl_3$), ee 96%, (*R*)-enantiomer}; ^{1}H NMR (400 MHz, $CDCl_3$) δ= 7.26-7.15 (5H, m, Ar *H*); 4.44 (1H, d, *J* 7.2, C*H*OH), 1.94 (1H, br s, O*H*), 1.91-0.78 (11H, m, C_6H_{11}); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 143.56 (Ar*C*), 128.08 (Ar*C*), 127.29 (Ar*C*), 126.58 (Ar), 79.27 (*C*HOH), 44.87 (*C*H), 29.23 (CH_2), 28.78 (CH_2), 26.37 (CH_2), 26.04(CH_2), 25.96 (CH_2); MS $(ES)^+$: 173.12 (12%), 213.05 ($[M+Na]^+$, 100). Enantioselectivity determined by HPLC, ChiralPak AD-H, 250 x 4.6 mm, 97:3 *n*-hexane: 2-propanol, 0.5 mL/min, 210 nm, t_R[(*S*)-(–), major] = 25.5 min, t_R[(*R*)-(+), minor] = 27.8 min.

(−)-(*S*)-2-Methyl-1-phenylpropanol, **10al**[11(a)]



$[\alpha]_D^{20}$ –37.6 (*c* 0.465, $CHCl_3$, ee 83%), $[\alpha]_D^{20}$ –43.3 (*c* 0.63, Et_2O, ee 83%), {lit[11(d)] $[\alpha]_D^{19}$ +11.3 (*c* 0.42, $CHCl_3$), ee 96%, (*R*)-enantiomer, lit:[11(e)] $[\alpha]_D^{23}$ –48.4 (*c* 1.34, Et_2O), ee 95%, (*S*)-enantiomer}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15-7.28 (m, 5H), 4.26 (d, *J* = 6.9 Hz, 1H), 1.95-1.79 (m and br s, 2H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 128.1, 127.3, 126.5, 80.0, 35.2, 19.0, 18.2; MS $(ES)^+$: 133.11 (40%), 173.1 ($[M+Na]^+$, 100). The enantiomeric excess was determined by HPLC on a Chiralcel OD-H, 250 x 4.6 mm, 98:2 *n*-hexane: 2-propanol, 0.5 ml/min, 210 nm, t_R[(*S*)-(–), major] = 25.7 min, t_R[(*R*)-(+), minor] = 27.7 min. HPLC data matches that reported previously.

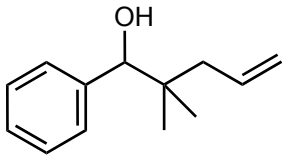
(−)-(*S*)-2,2-Dimethyl-1-phenylpropan-1-ol, **11al**[11(a)]



$[\alpha]_D^{20}$ –26.9 (*c* 0.84, $CHCl_3$, ee 67%), [{lit[11(f)] $[\alpha]_D^{19}$ –36.5 (*c* 0.30, $CHCl_3$), ee 99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.15 (m, 5H), 4.30 (s, 1H), 1.82 (s, 1H), 0.84 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.2, 127.6, 127.5, 124.7, 82.3, 35.6, 25.9; MS $(ES)^+$: 187.13 ($[M+Na]^+$, 100%).

The enantiomeric excess was determined by HPLC on a Chiralcel OD-H, 250 x 4.6 mm, 95:5 *n*-hexane: 2-propanol, 0.5 ml/min, 210 nm, t_R[(*S*)-(–), major] = 13.6 min, t_R[(*R*)-(+), minor] = 17.6 min. HPLC data matches that reported previously.

(*S*)-2, 2-dimethyl-1-phenylpent-4-en-1-ol, **12al**[12]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.20 (m, 5H), 5.91-5.81 (m, 1H), 5.05-4.99 (m, 2H), 4.40 (s, 1H), 2.15 (dd, *J* = 13.5, 7.6 Hz, 1H), 1.97 (dd, *J* = 13.5, 7.4 Hz, 2H), 1.89 (br s, 1H), 0.85 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 135.5, 127.9, 127.7, 127.4, 117.5, 81.1, 43.6, 38.6, 23.5, 22.4; HRMS $(ES)^+$: 213.1248 $[M+Na]^+$, $C_{13}H_{18}ONa$ requires 213.1250. The enantiomeric excess was determined by HPLC on a Chiralcel OD-H, 250 x 4.6 mm, 95:5 *n*-hexane: 2-propanol, 0.5 ml/min, 210 nm, t_R[(*S*), major][a] = 11.2 min, t_R[(*R*), minor] = 17.3 min. This compound was isolated containing (−)-(*S*)-2-Methyl-1-phenylpropanol as impurity (<8%, originated from the corresponding ketone present in the starting material).

[a]Tentatively assigned as the *S* enantiomer based on the fact that (*R*,*R*) catalyst usually gives the *S* enantiomer.

10. Preparation of complex 13

$[Ir(COD)Cl]_2$ (154 mg, 0.23 mmol) and NaOMe (37 mg, 0.69 mmol) were placed in a Schlenk flask under a nitrogen atmosphere. Hexane (6 mL) and methylene chloride (6 mL) were added and the mixture stirred at room temperature for 2 hours. The resulting suspension was filtered *via* cannula to another Schlenk flask and the solvent removed under reduced pressure. The resulting solid was disolved in methylene chloride (3 mL), added to a Schlenk flask containg ligand **3** (200 mg, 0.51 mmol) and stirred at room temperatura under a nitrogen atmosphere for 1 h. Diethyl ether was added to the resulting red-brown solution forming the desired product as a pale brown solid (187 mg, 0.27 mmol, 59 %). IR (KBr, cm^{-1}) 3386, 3131, 3053, 2934, 2859, 1623, 1587, 1480, 1448, 1435, 1320,

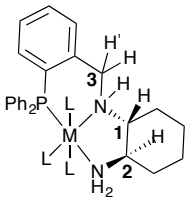
1299, 1157, 1090, 750, 697; ^{31}P NMR (161 MHz, CD_2Cl_2) δ +0.78 (s); ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.94-7.00 (m, 4H), 6.84 (br d, *J* = 9.1 Hz, 1H, N*H*), 4.99 (d, *J* = 14.6 Hz, 1H, ArC*H*$_2$-N), 4.72-4.67 (m, 1H, ArC*H*$_2$-N), 4.36 (br s, 1H, N*H*), 3.63-3.60 (m, 2H, COD C*H*), 3.42-3.37 (m, 2H, COD C*H*), 2.88-2.77 (m, 1H, C*H*), 2.54-0.61 (m, 17H, C*H*, COD CH_2, Cy CH_2); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 139.6 (d, $J_{C\text{-}P}$ = 17.9 Hz, Ar*C*), 134.9- 128.5 (14xArCH), 134.0 (d, $J_{C\text{-}P}$ = 46.5 Hz, Ar*C*), 133.3 (d, $J_{C\text{-}P}$ = 35.5 Hz, Ar*C*), 126.8 (d, $J_{C\text{-}P}$ = 34.5 Hz, Ar*C*), 65.9 (N-*C*H), 60.8 (COD *C*H), 60.6 (COD *C*H), 59.9 (COD 2x*C*H), 58.9 (NH_2-*C*H), 53.6 (d, $^{3}J_{C\text{-}P}$ = 10.0 Hz, Ar*C*H$_2$-N), 38.0 (CH_2), 37.9 (CH_2), 37.1 (CH_2), 28.0 (CH_2), 27.5 (2xCH_2), 24.3 (CH_2), 24.1 (CH_2); HRMS $(ES)^+$: 689.2631 $[M+H]^+$, $C_{33}H_{41}IrN_2P$ requires 689.2633.

11. Coordination Chemistry of Ligand 3

The reaction of $[Ir(COD)Cl]_2$ with 1.1 equivalents of ligand 3 in acetonotrile under nitrogen (r.t., 15 h) lead to a mixture of compounds. The ^{31}P-NMR spectrum of the reaction mixture displayed two singlets at +0.80 (major) and +6.78 ppm (minor) for the two main species in solution. A similar behaviour was observed when other solvents (DCM, THF) were used or when non-coordinating anions, such as $^{-}PF_6$, were employed. Any attempt of isolation and purification (precipitation, recrystallisation, chromatography, size exclusion chromatography) of the main species in solution failed or resulted in the formation of further decomposition products. The use of $[Ir(OMe)(COD)]_2$ afforded a similar crude NMR to that obtained with $[Ir(COD)Cl]_2$, but in this occasion a single species by ^{31}P NMR was isolated by precipitation with diethyl ether. Attempts to obtain suitable crystals for X-ray difraction were unsuccessful. The coordination geometry of the complex was therefore studied using NMR techniques. $[Ir(OMe)(COD)]_2$ has been used in the literature as an iridium precursor that leads to amido complexes when ligands containing a primary amine moiety are employed.[13] It is expected that when ligand **3** reacted with $[Ir(OMe)(COD)]_2$, deprotonation of the primary amine will lead to the formation of amido complex **13**. ^{1}H, ^{13}C NMR, HSQC and MS showed the presence of coordinated COD. This was also further confirmed by the reaction of complex **13** with hydrogen in deuterated dichloromethane (10 bar, rt, 17h). ^{1}H-NMR of the reaction crude showed the presence of cyclooctane (s, 1.53 ppm) and the formation of several unidentifiable species (–20.2 - –25.4 ppm) in the hydride región of the NMR. In any case, this further confirms the presence of COD in complex **13**.

The coordination mode of ligand **3** in complex **13** is tentatively assigned as tridentate, since ^{13}C and ^{1}H signals in α position to both the middle N and NH_2 function in the ligand shift downfield in complex **13**. The chemical shifts for these characteristic ^{13}C and ^{1}H for ligand 3, a known Ru complex with a tridentate coordination mode and complex **13** are collected in Table S.4 for comparation.

Table S.4: Characteristic chemical shifts in Ligand **3**[14], [Ru **3** DMSO Cl_2][15] and complex **13**.

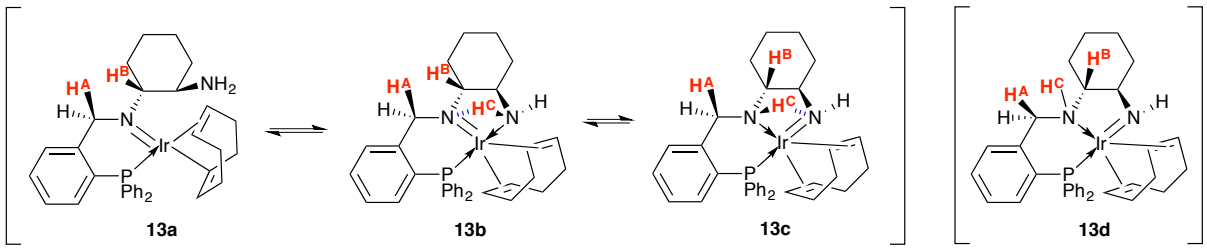


	δ_{C1}	δ_{C2}	δ_{C3}	δ_{HC1}	δ_{HC2}	δ_{HC3}	$\delta_{H'C3}$
3	63.6	55.3	49.4	2.3-1.9 (m, 2H)		4.1 (d, *J* 13 Hz)	3.9 (d, *J* 13 Hz)
M= Ru L= Cl, Cl, DMSO	62.7	56.1	51.5	3.3-3.2 (m)	3.2-3.0 (m)	4.4-3.9 (m, 2H)	
M= Ir L= COD	65.9	58.9	53.6	1.75 (m)	2.9-2.8 (m)	5.0 (d, *J* 14.6 Hz)	4.72-4.67 (m)

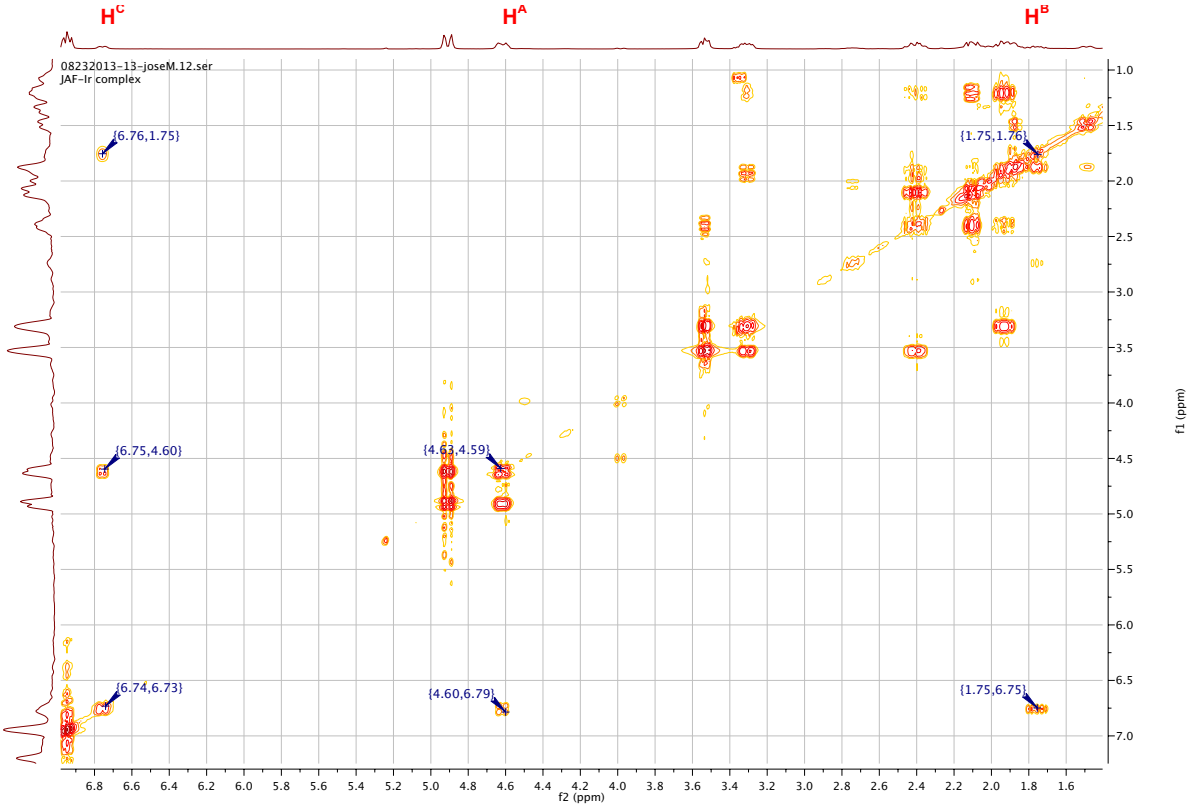
^{1}H NMR (300 MHz, $CDCl_3$), ^{13}C NMR (75 MHz, $CDCl_3$) for **3** and [Ru **3** DMSO Cl_2]. ^{1}H NMR (400 MHz, CD_2Cl_2), ^{13}C NMR (100 MHz, CD_2Cl_2) for complex **13**.

Of the tridentate complexes possible, a neutral mode with methoxide counter ion seems unlikely unless some ion exchange has occurred, and only two NH functions were located in the ^{1}H-NMR in $CDCl_2$ (and there is no evidence for deuterium exchange).

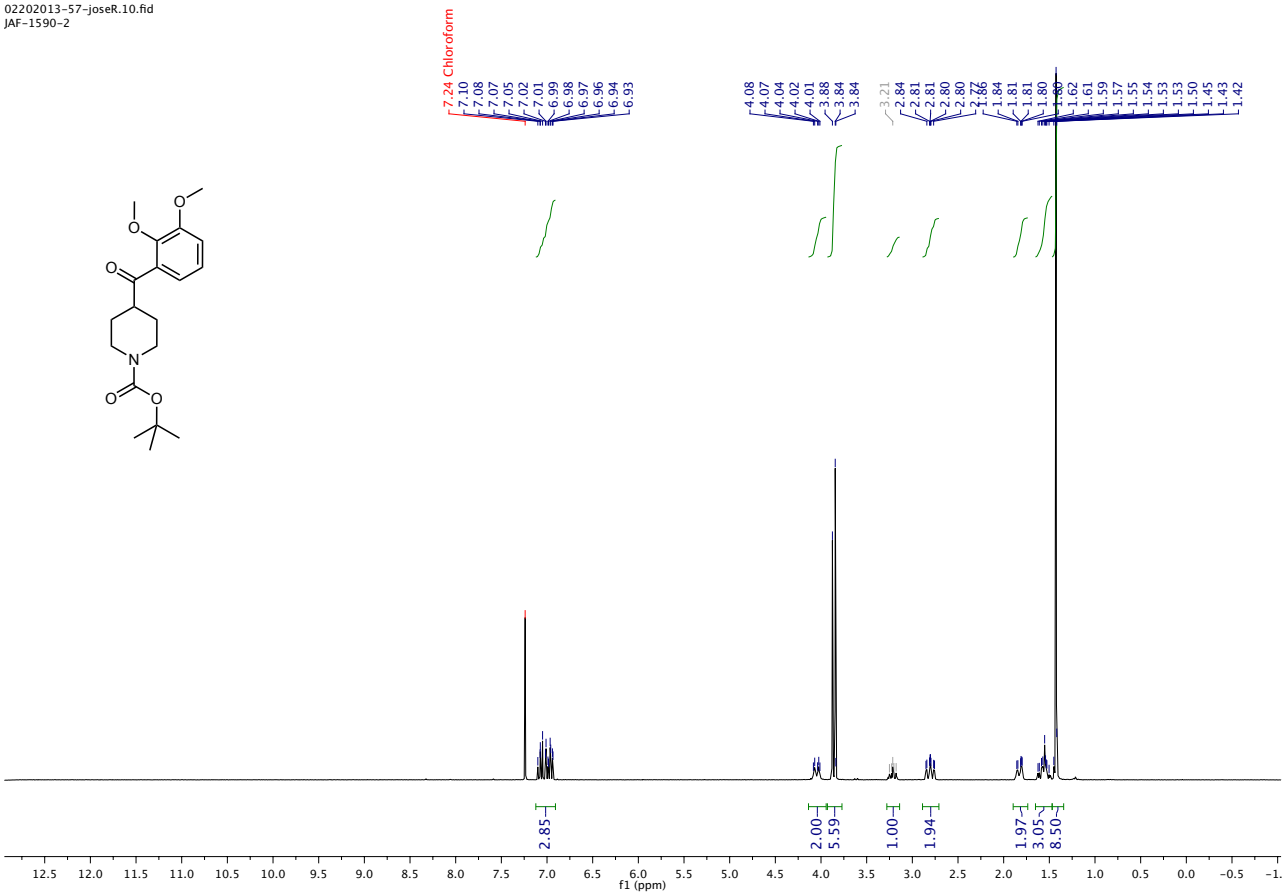
Close analysis of the COSY 2D NMR showed the coupling of a NH with H^A and also with one of the hydrogens in the cyclohexyl moiety, H^B. This coupling together with the high chemical shift of the signal points to the presence of a proton located close to the secondary amine/amido function. On the basis of this, complex **13** can either be a complex with the primary amine deprotonated and acting as an amido ligand (**13d**), or a complex where one of the NH functions is shared between each nitrogen (**13a-c**). It is perfectly plausible that these species, which only differ by a single hydrogen bond can interconvert in solution and can be treated as equivalent.

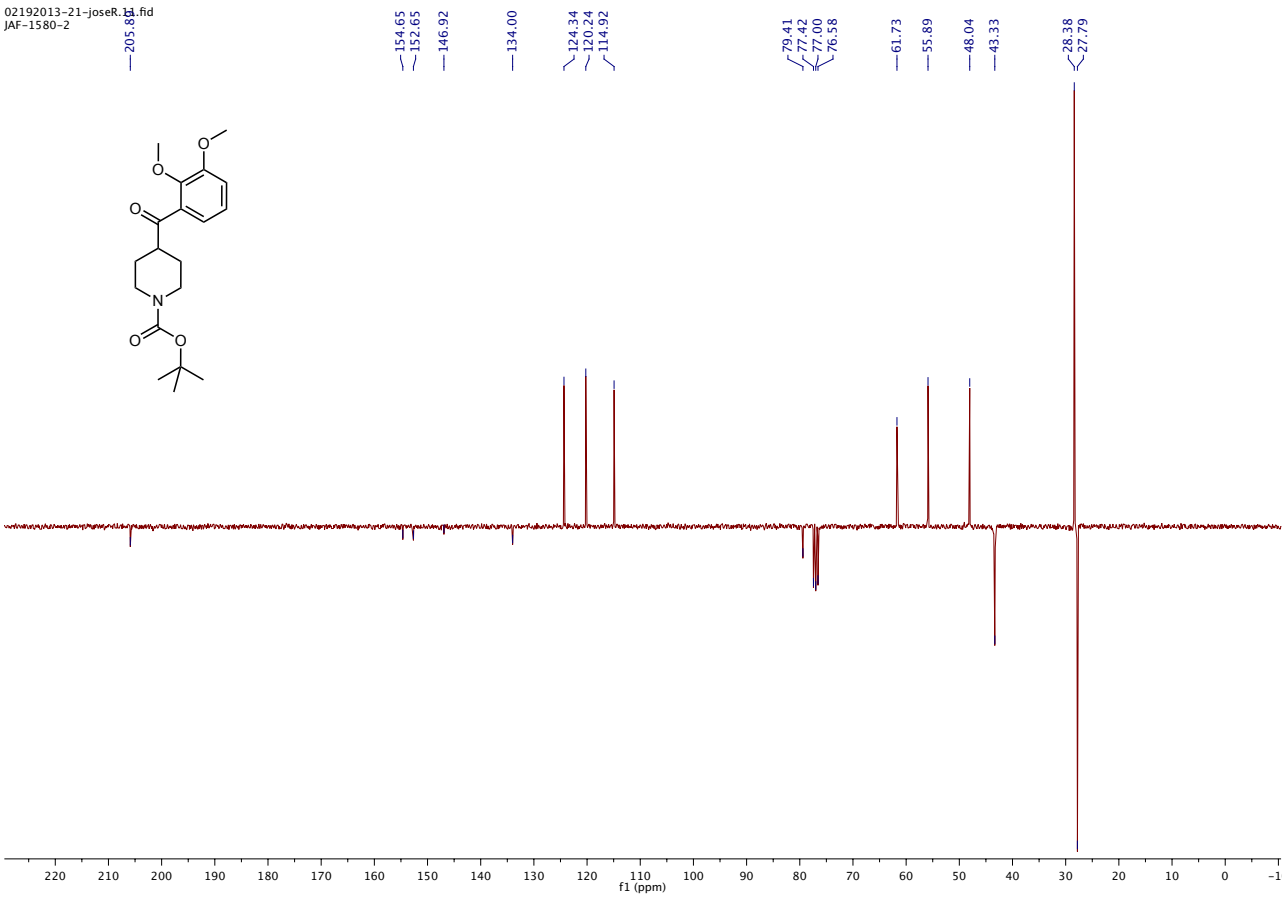


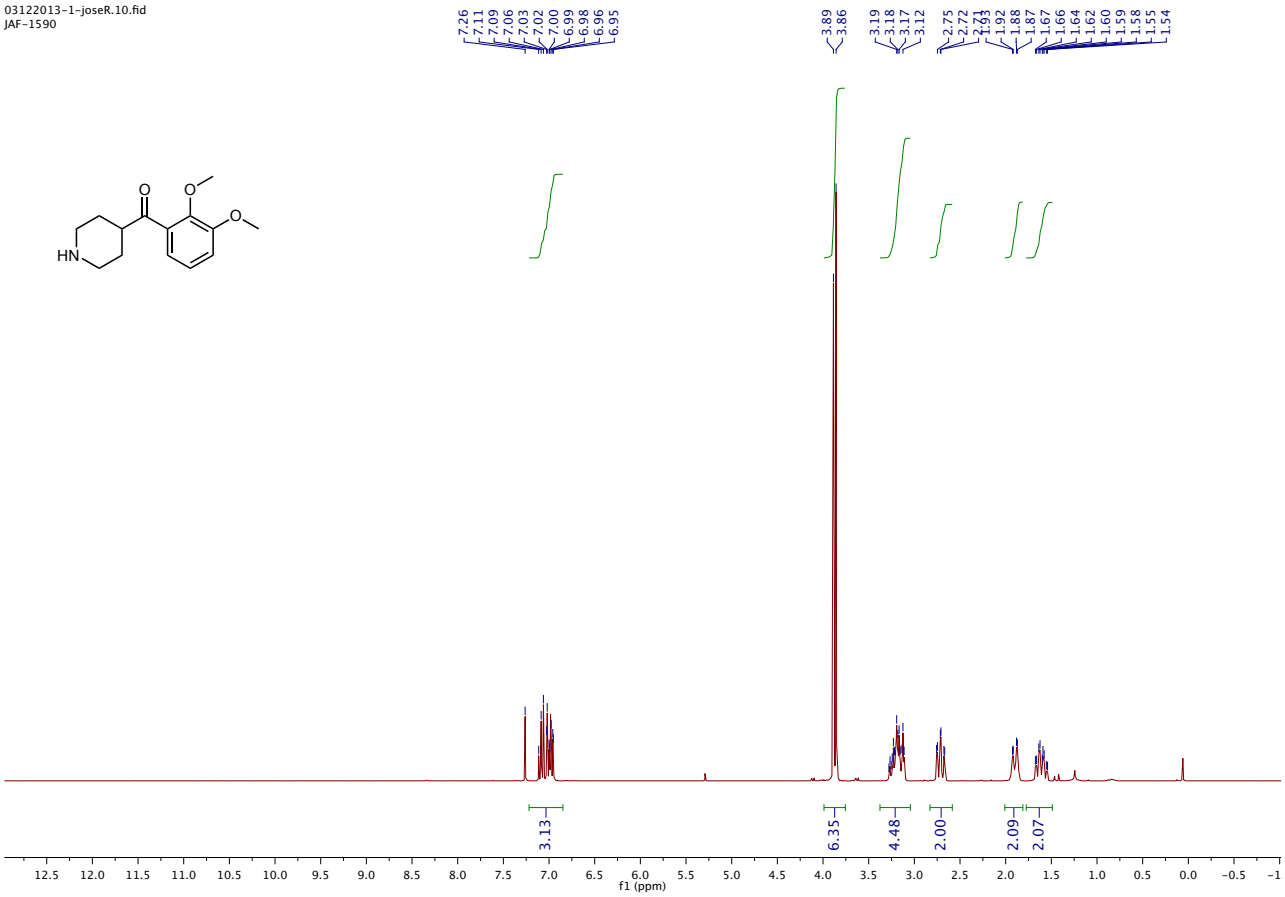
Expansion of the 2D ^{1}H, ^{1}H-COSY spectrum of complex **13** in CD_2Cl_2 showing correlations for H^A, H^B and H^C resonances in complex **13**.



12. NMR spectra of selected compounds



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1.88
1.87
1.67
1.66
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1.62
1.60
1.59
1.58
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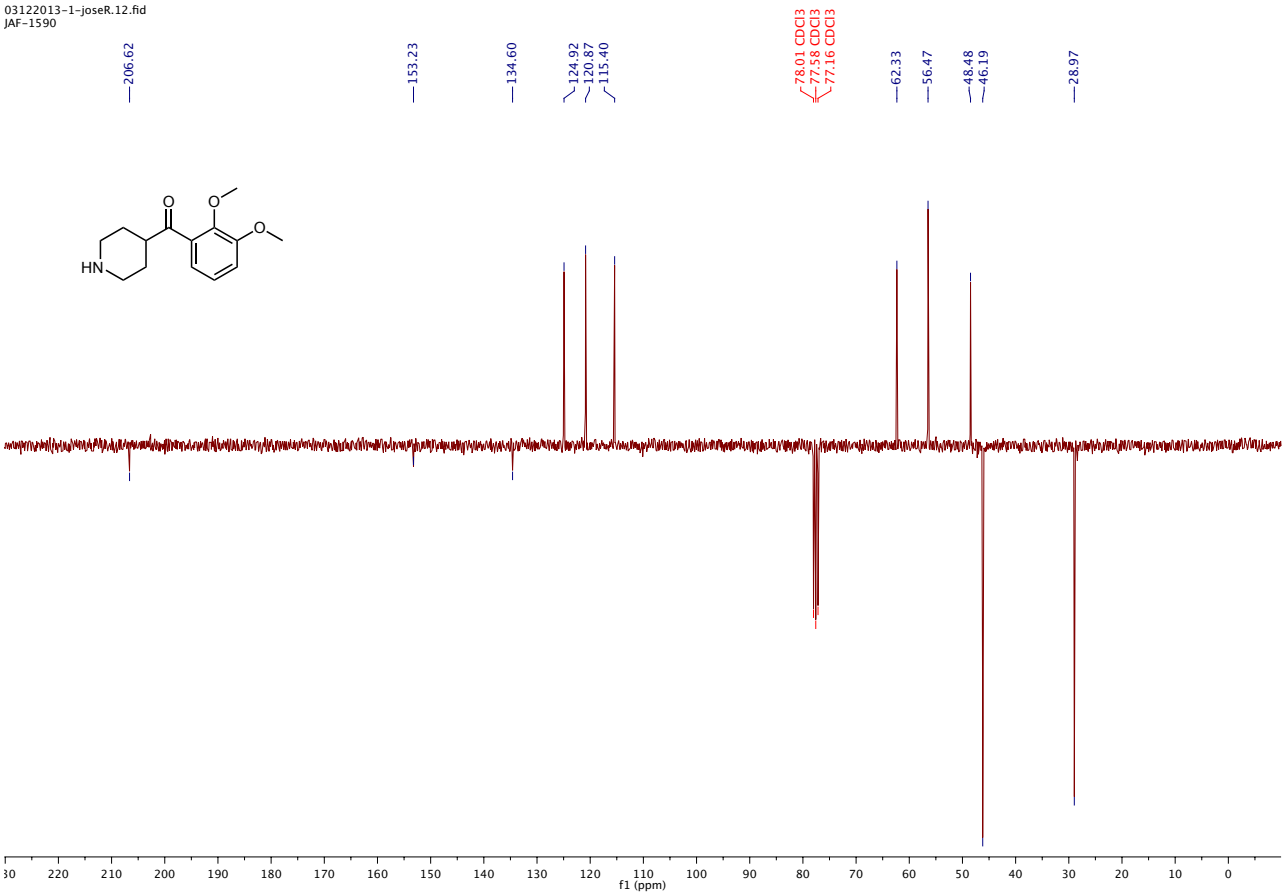
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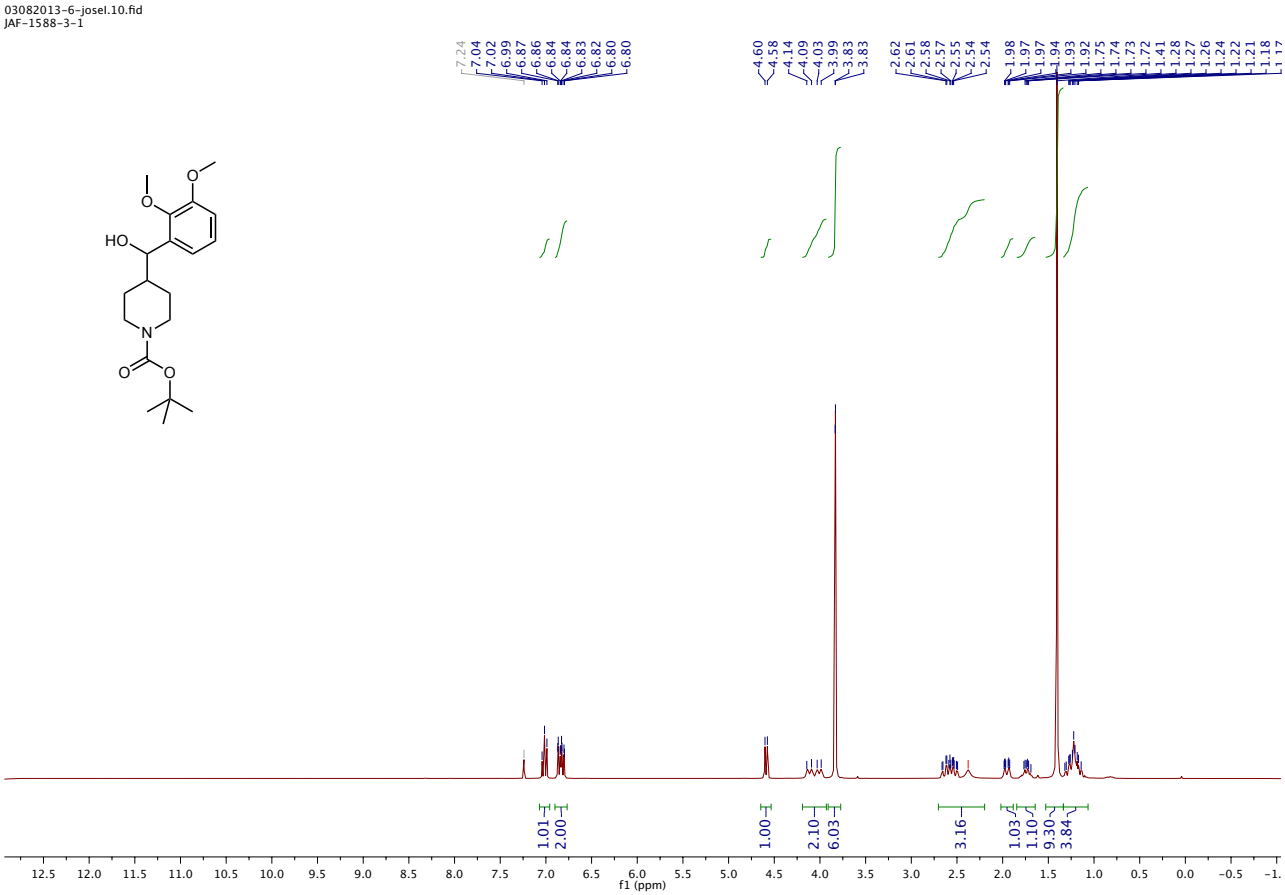
f1 (ppm)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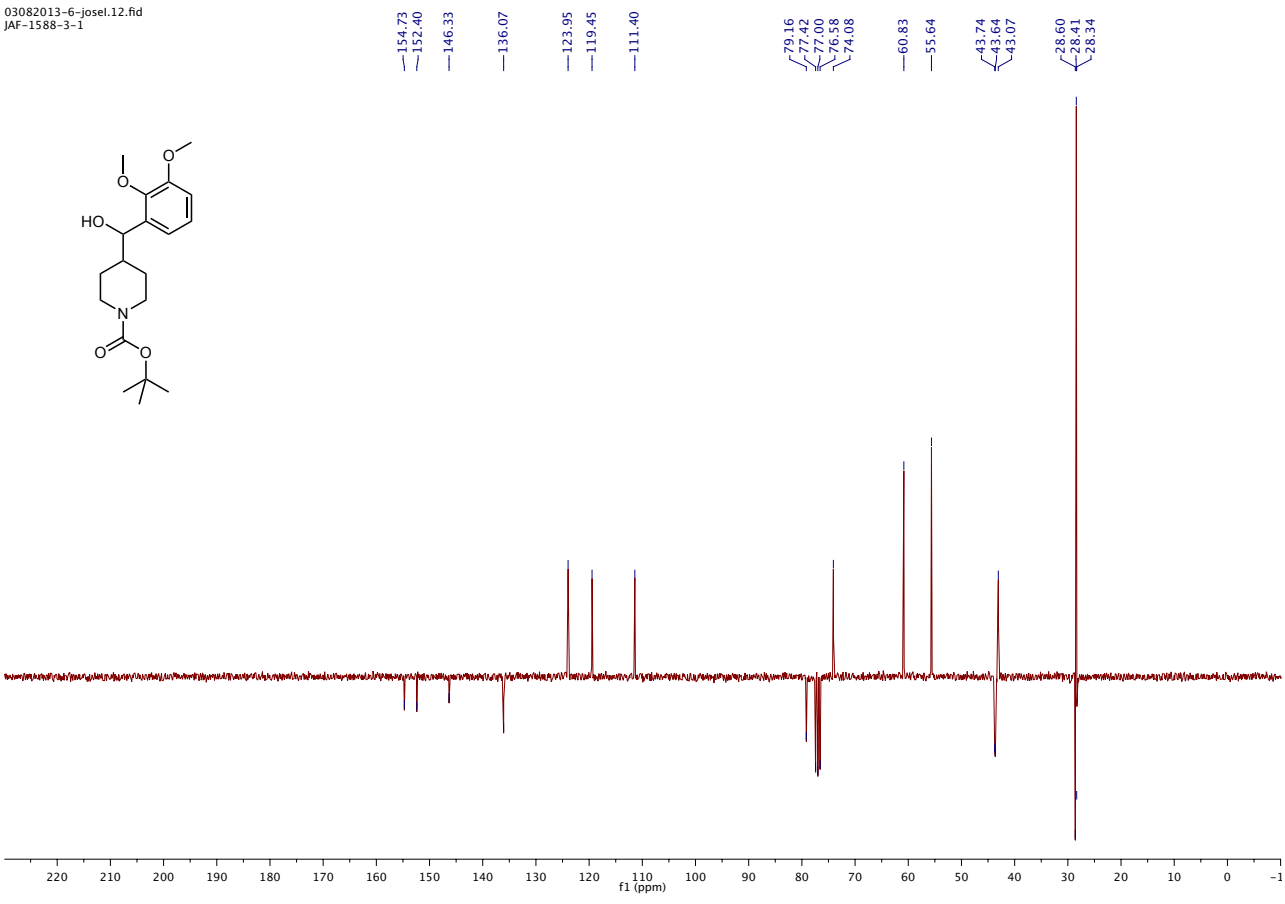
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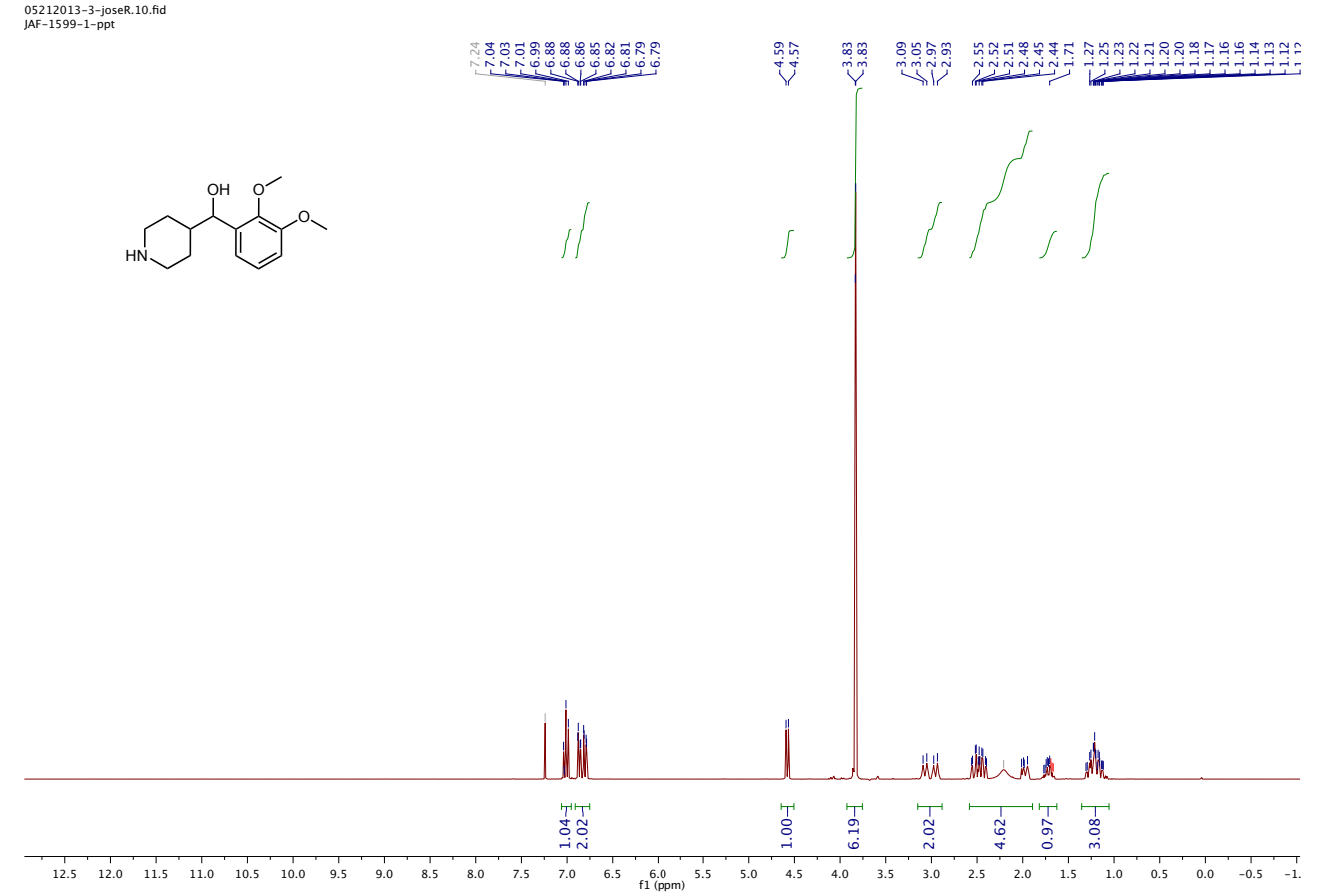
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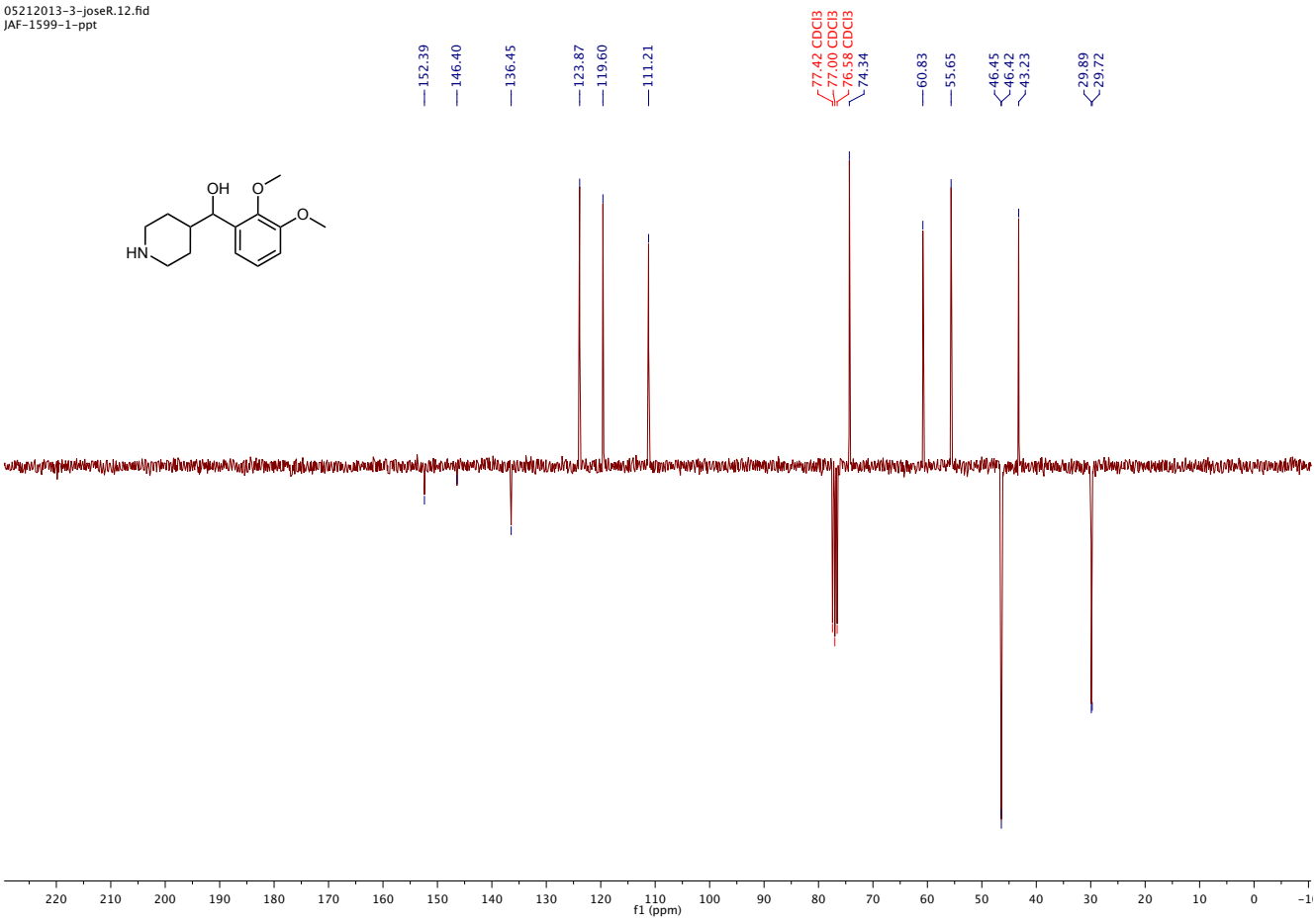
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43.23
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29.72
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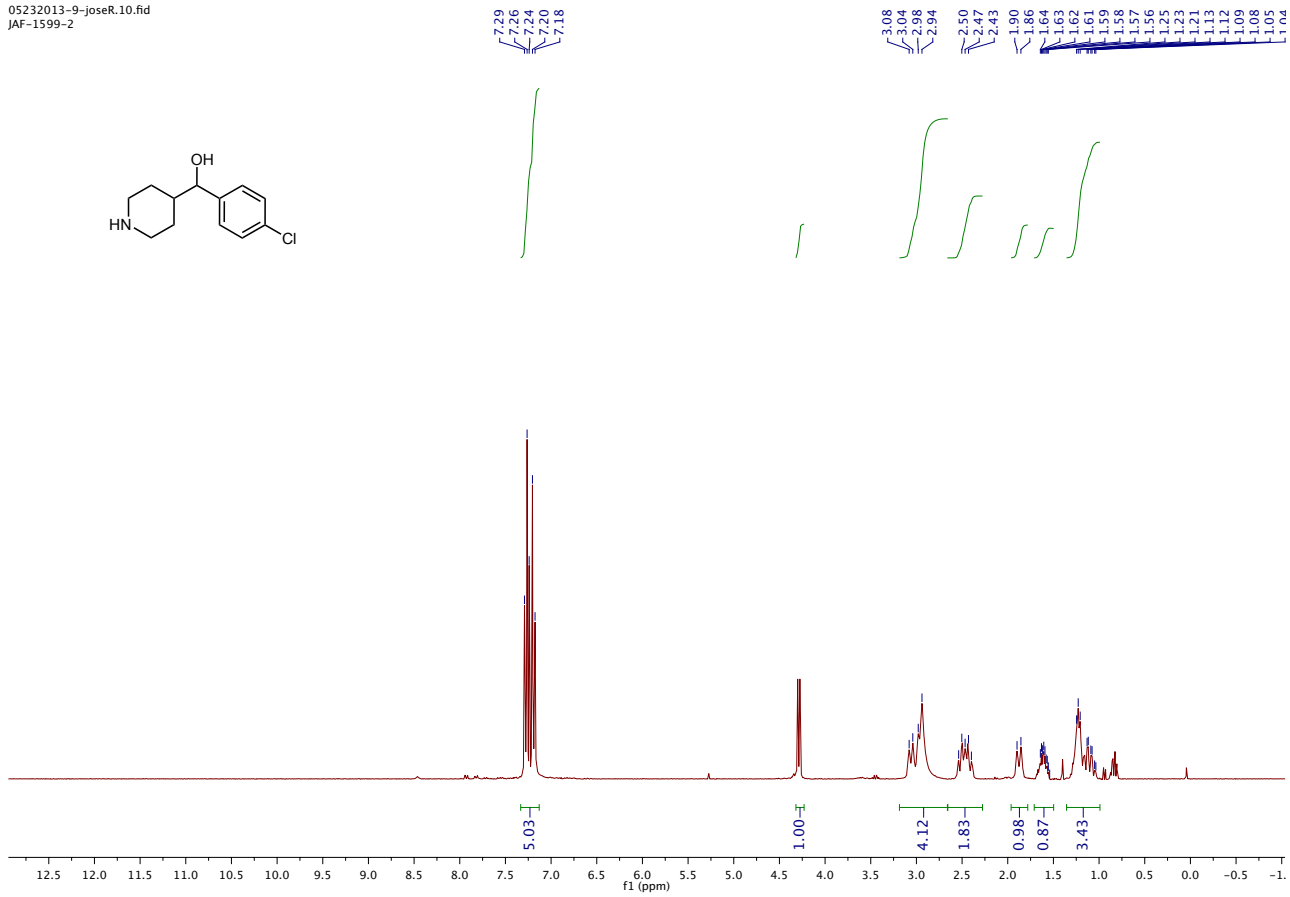
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2.43
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1.13
1.12
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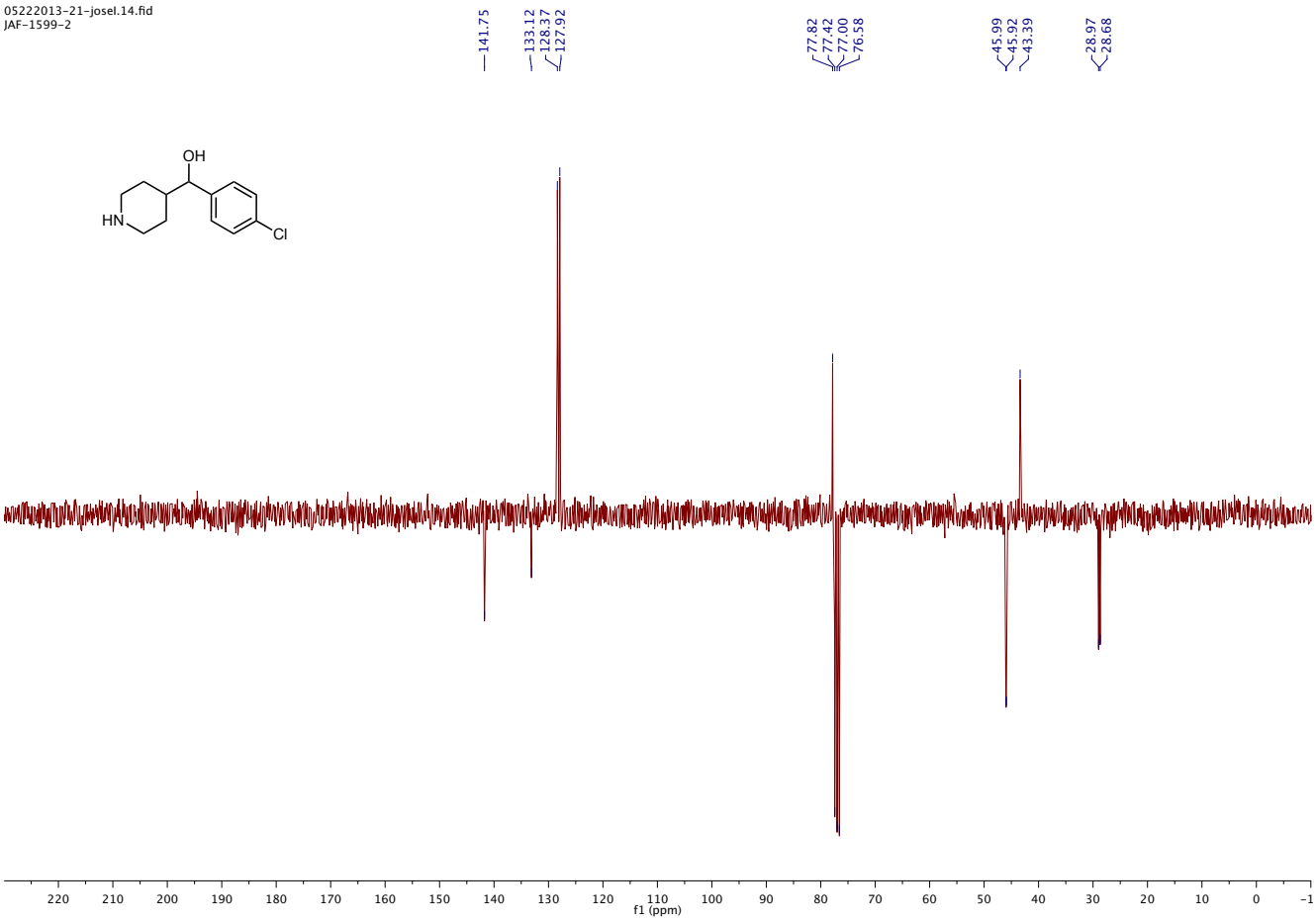
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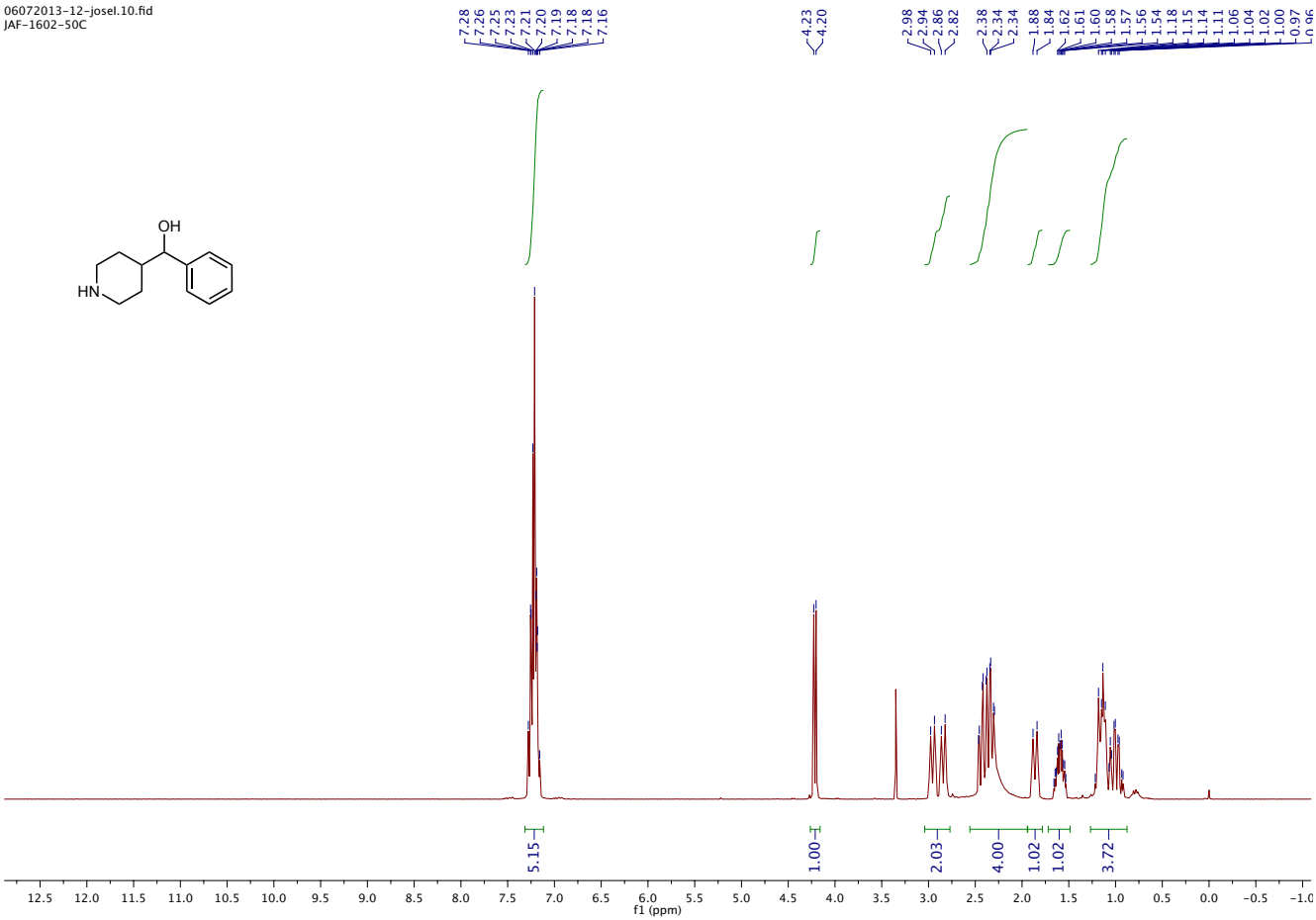
f1 (ppm)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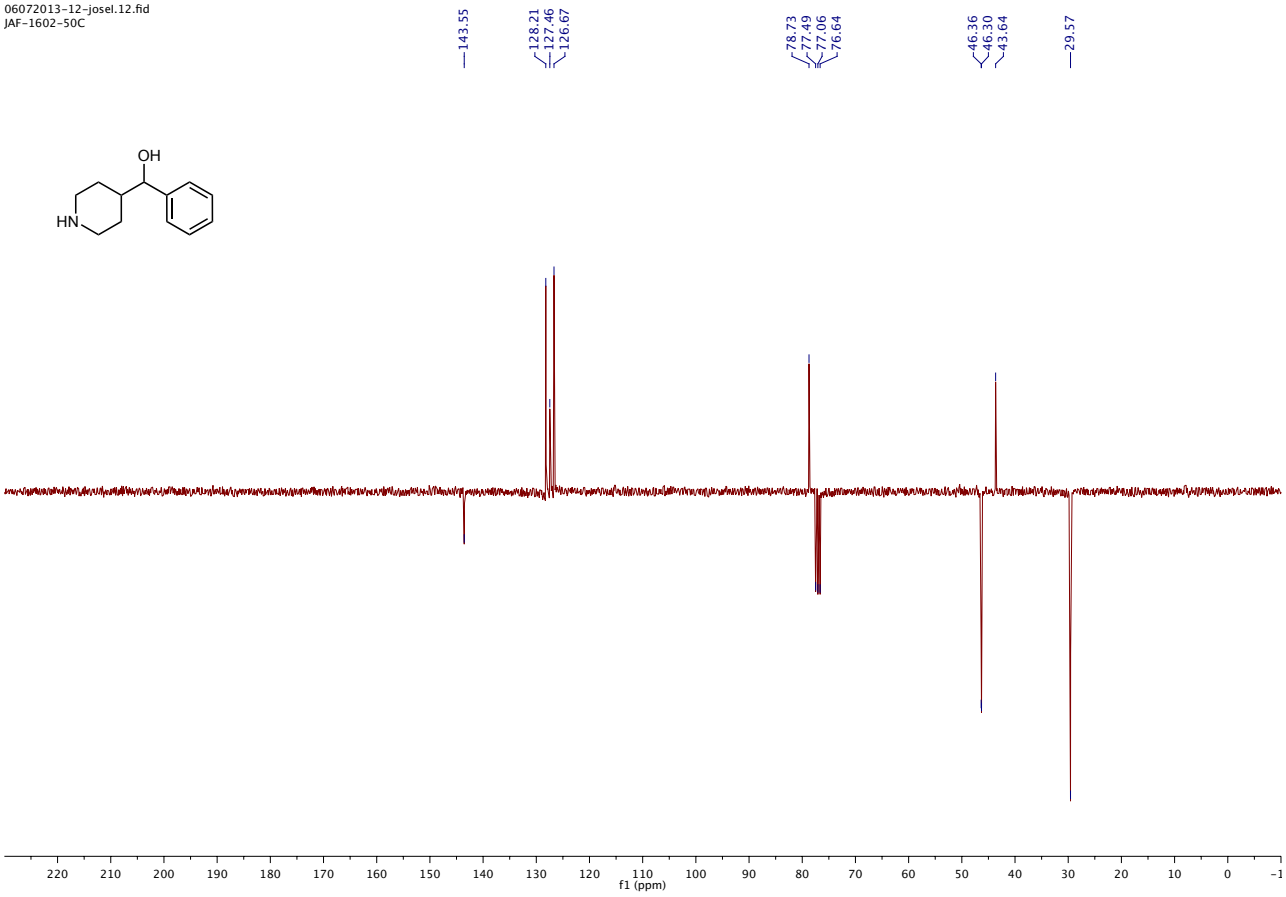
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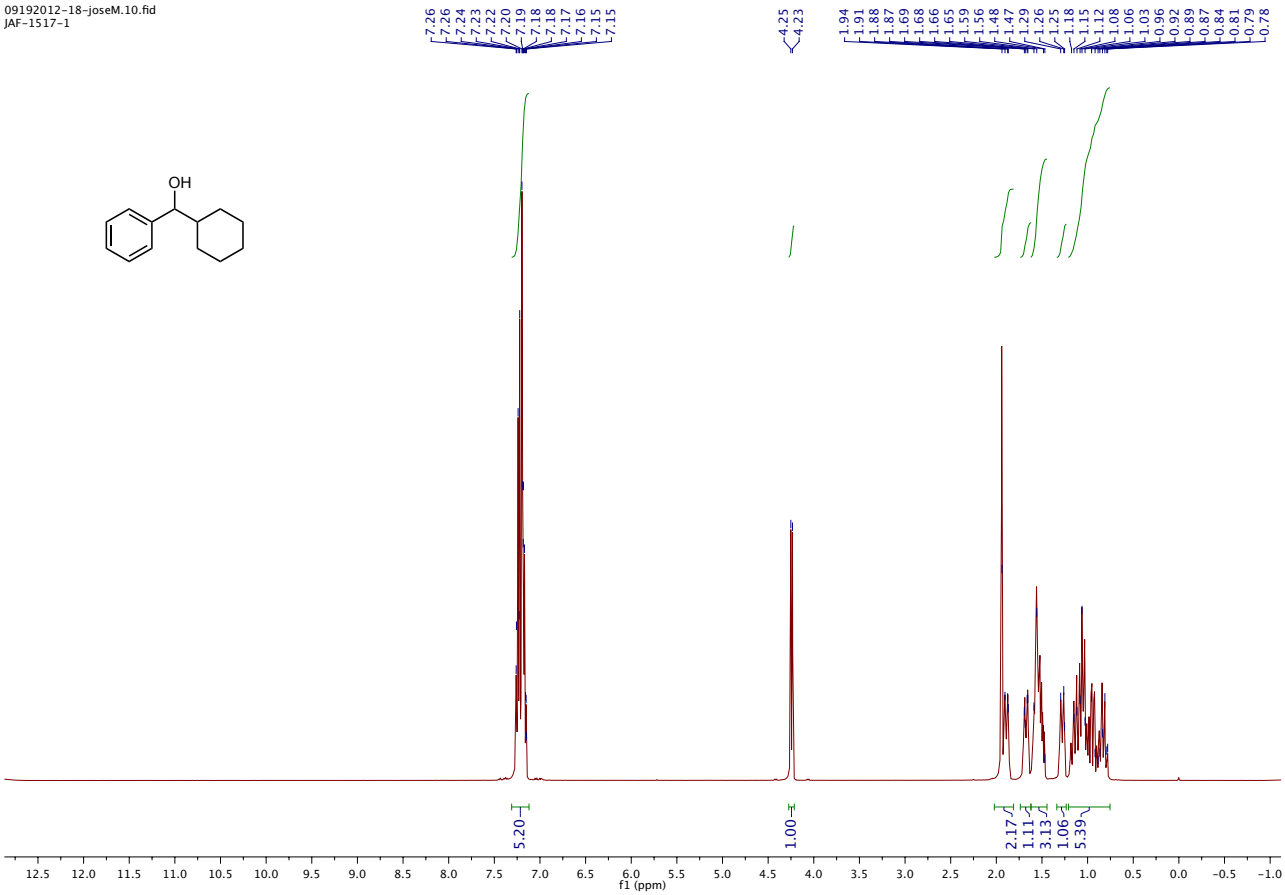
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4.23
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1.87
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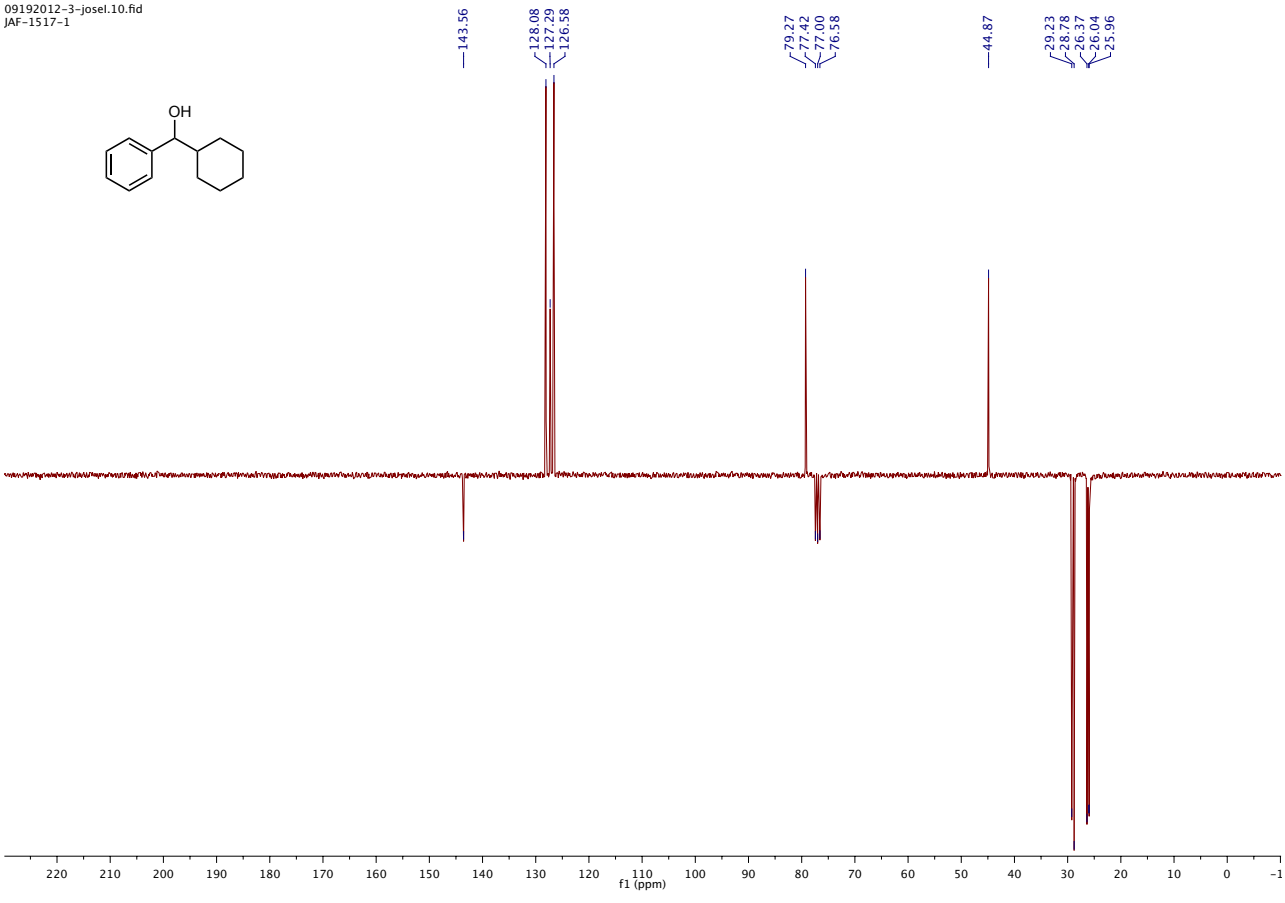
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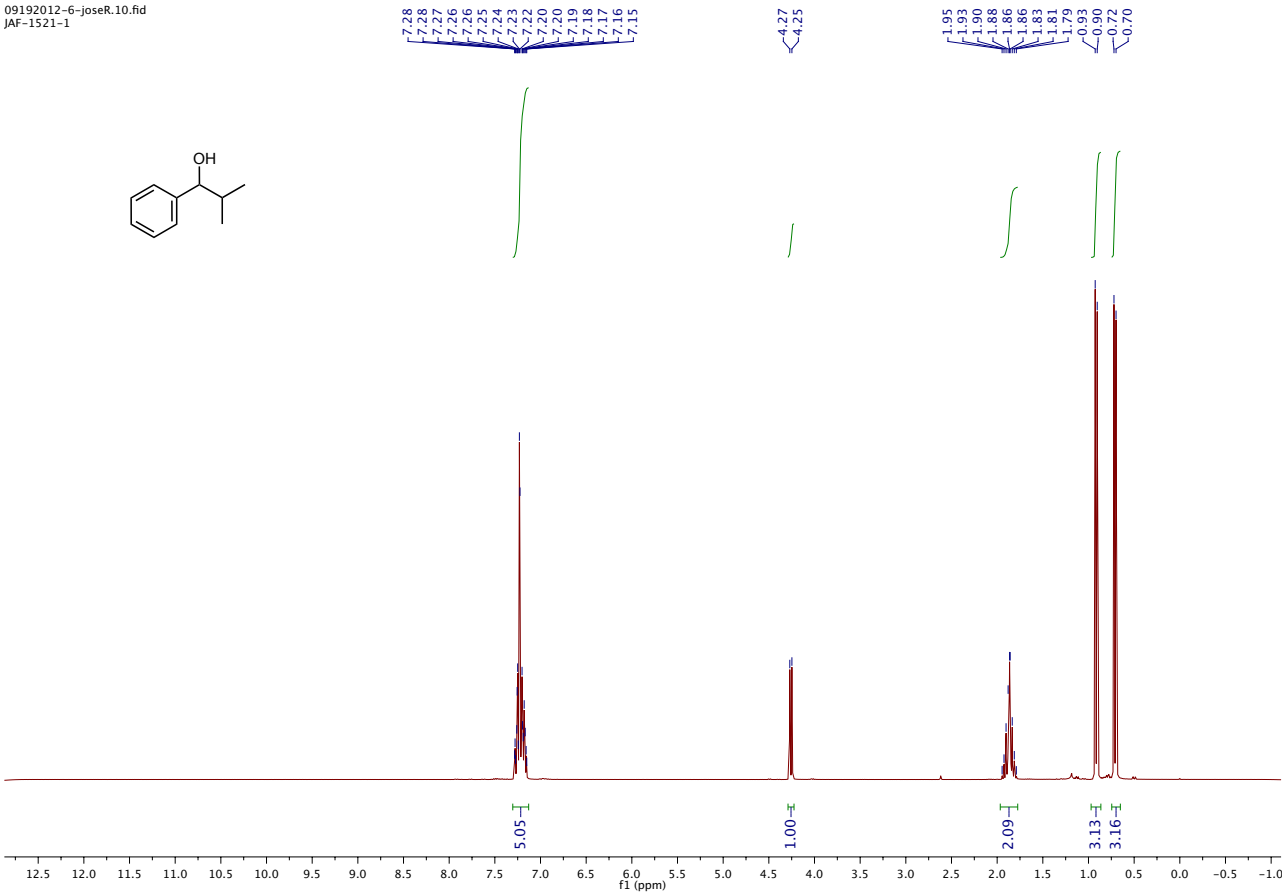
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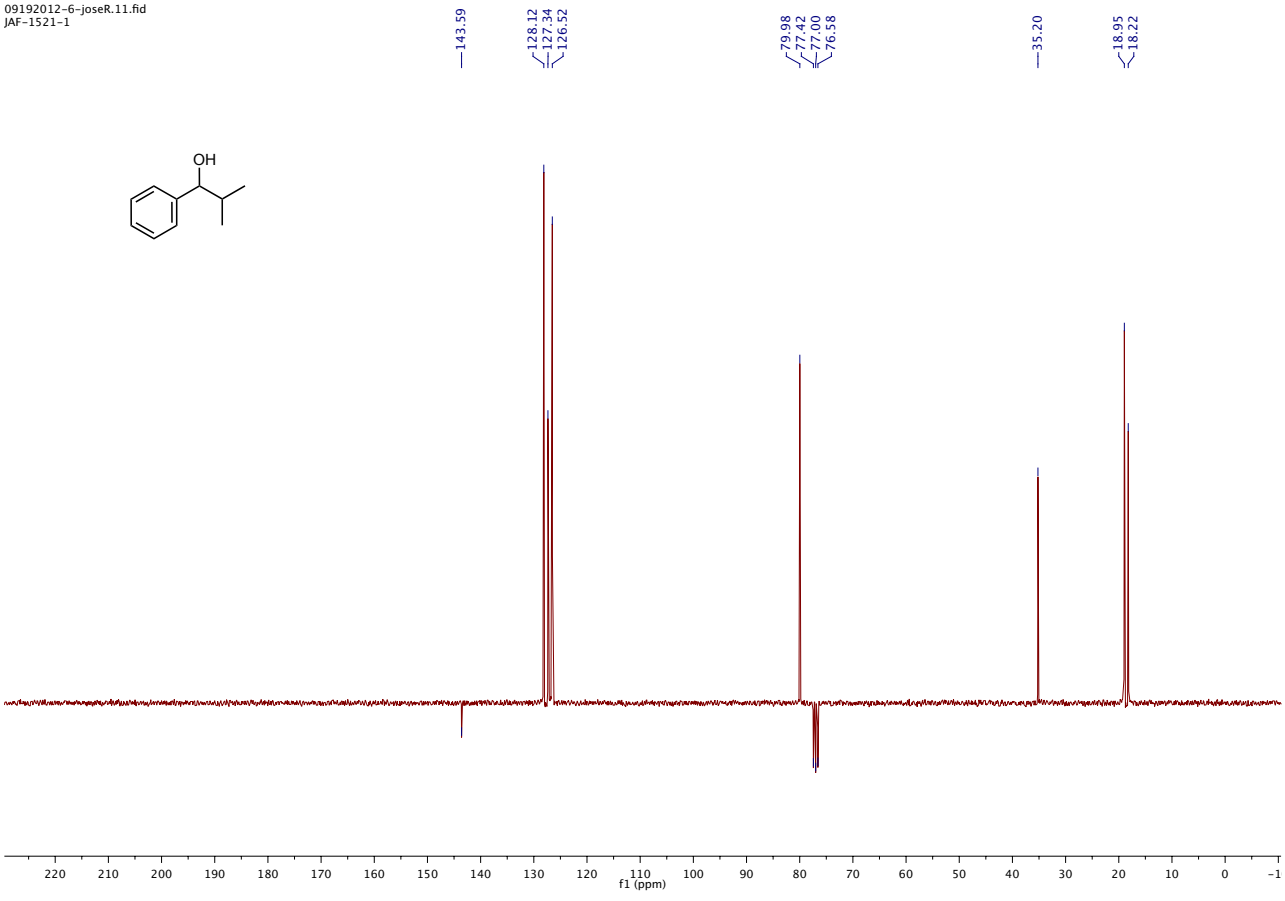
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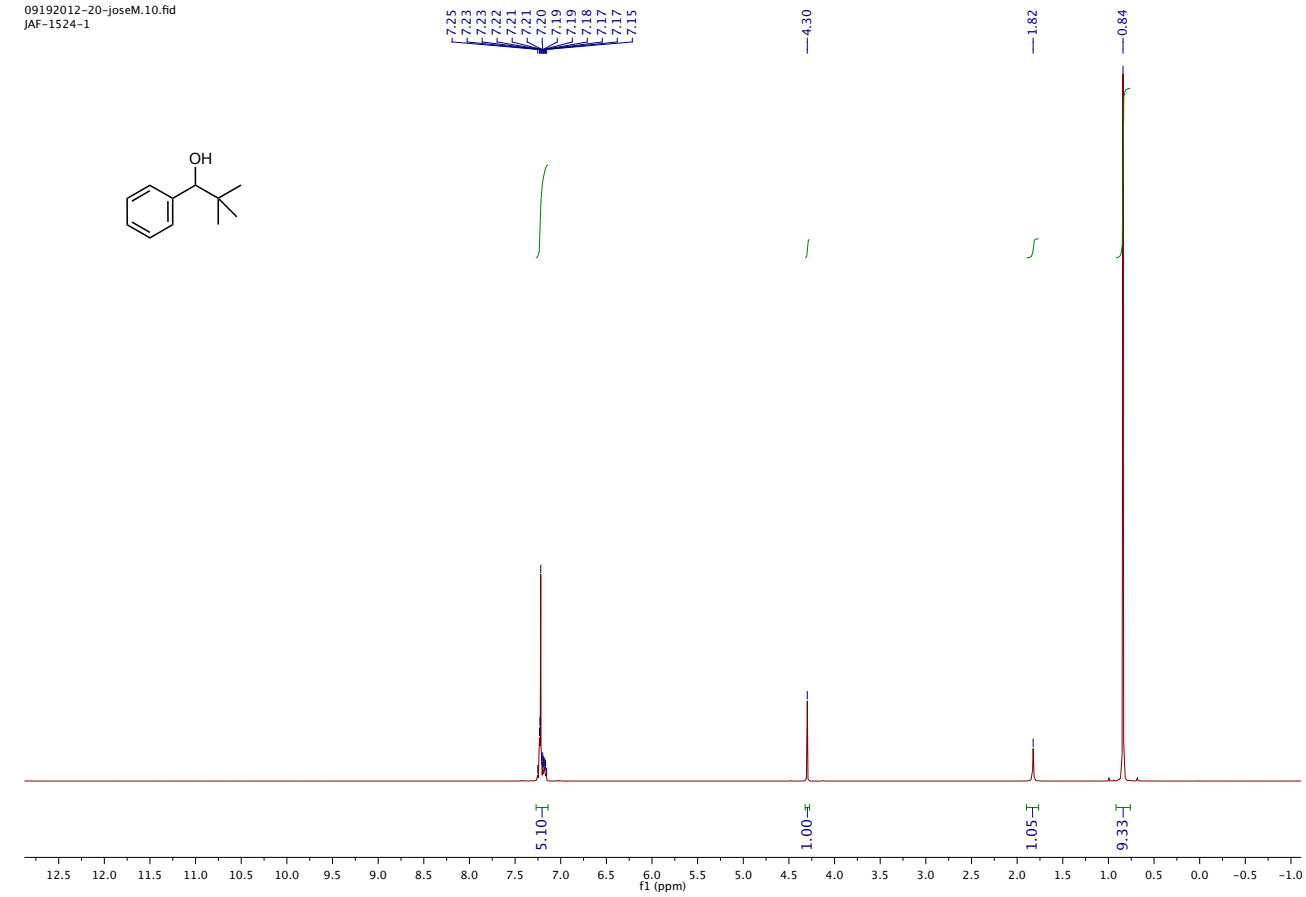
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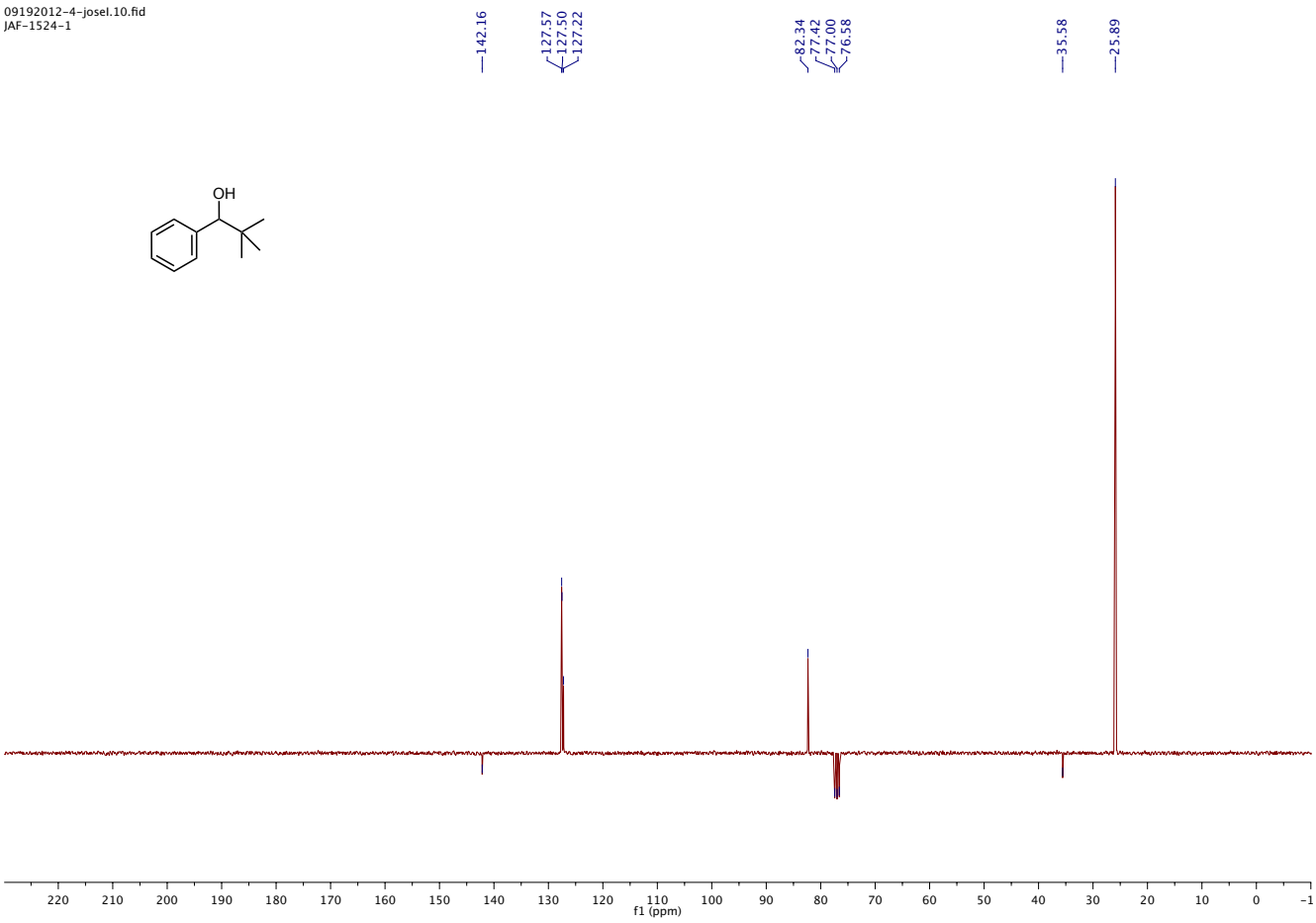
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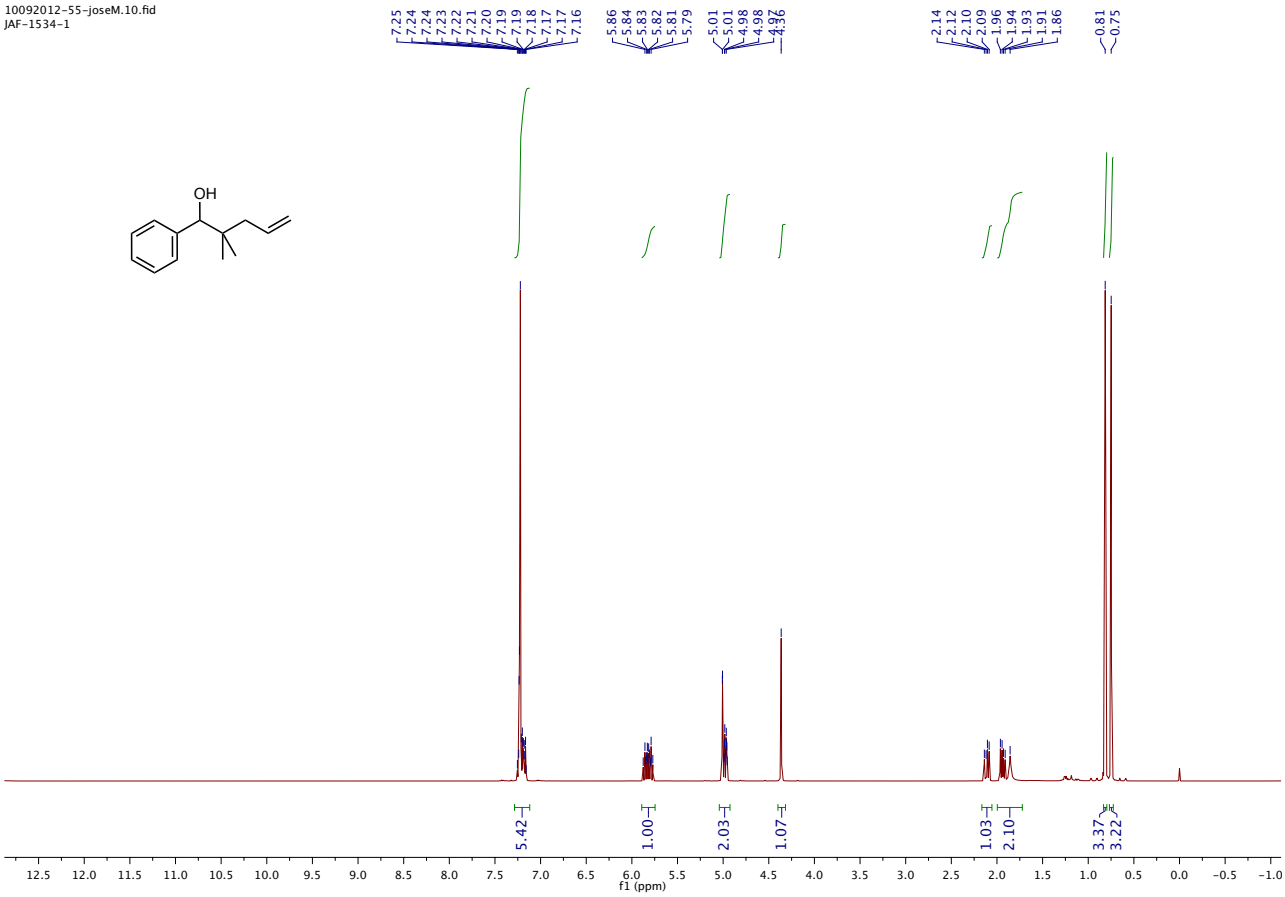
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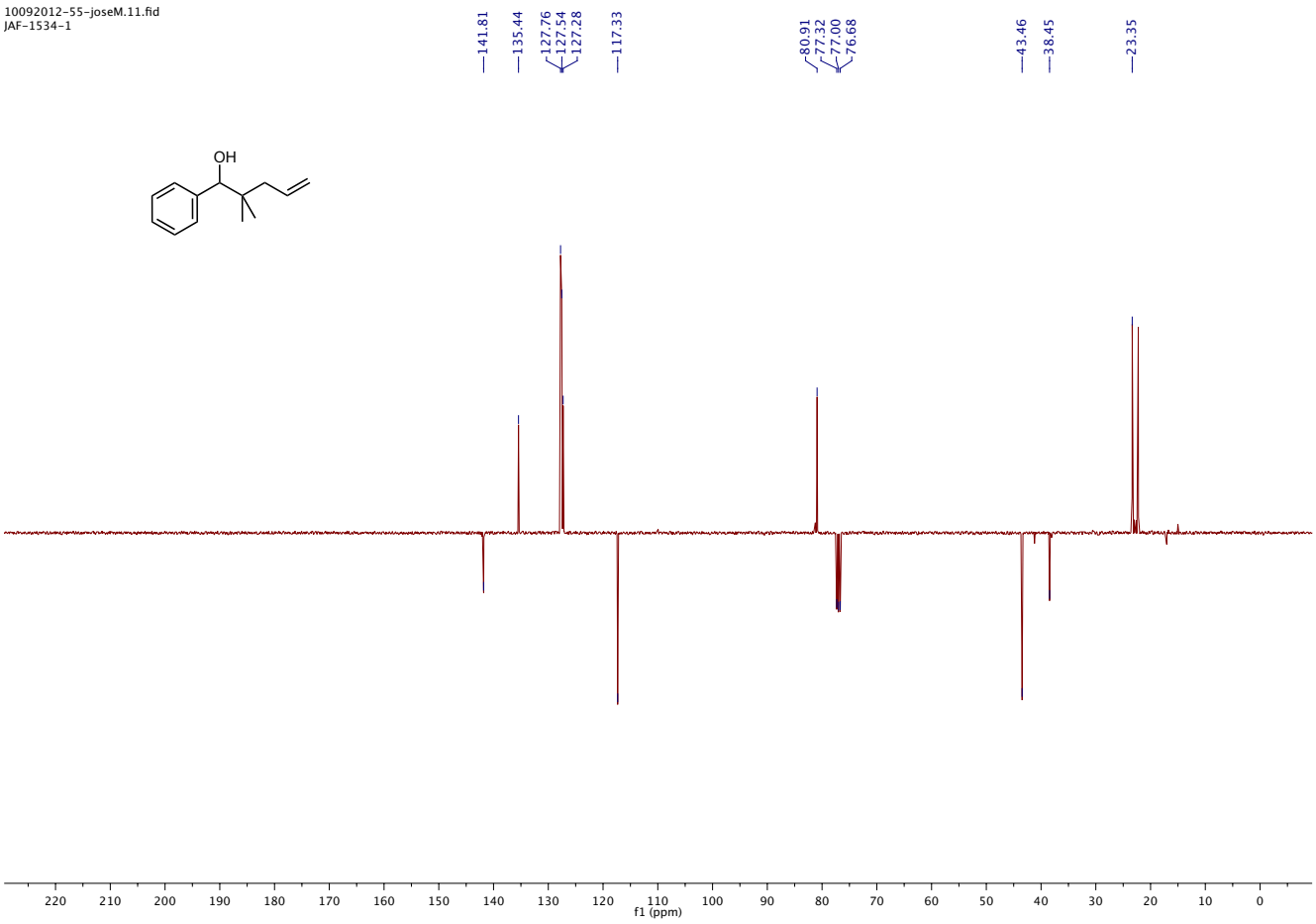
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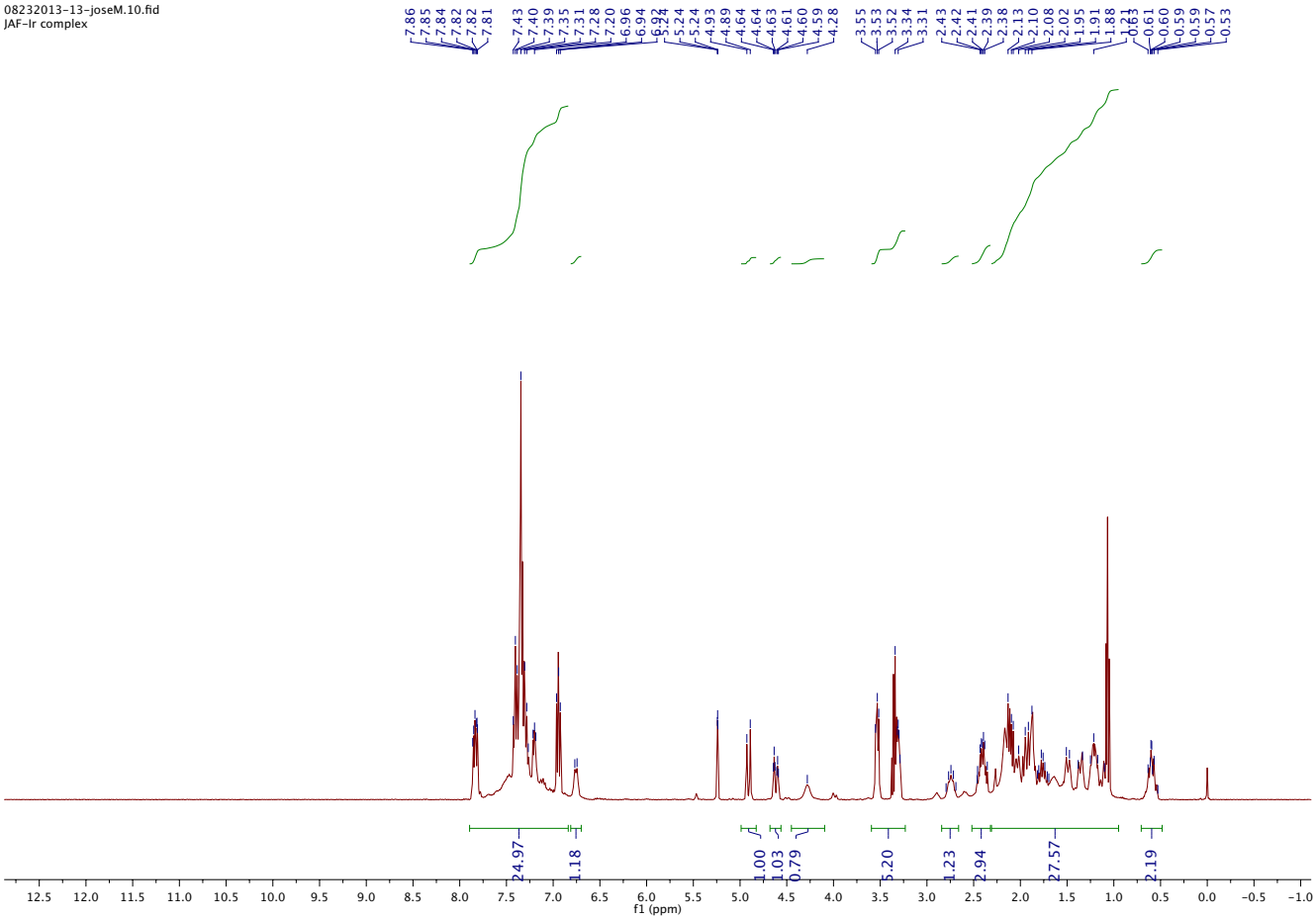
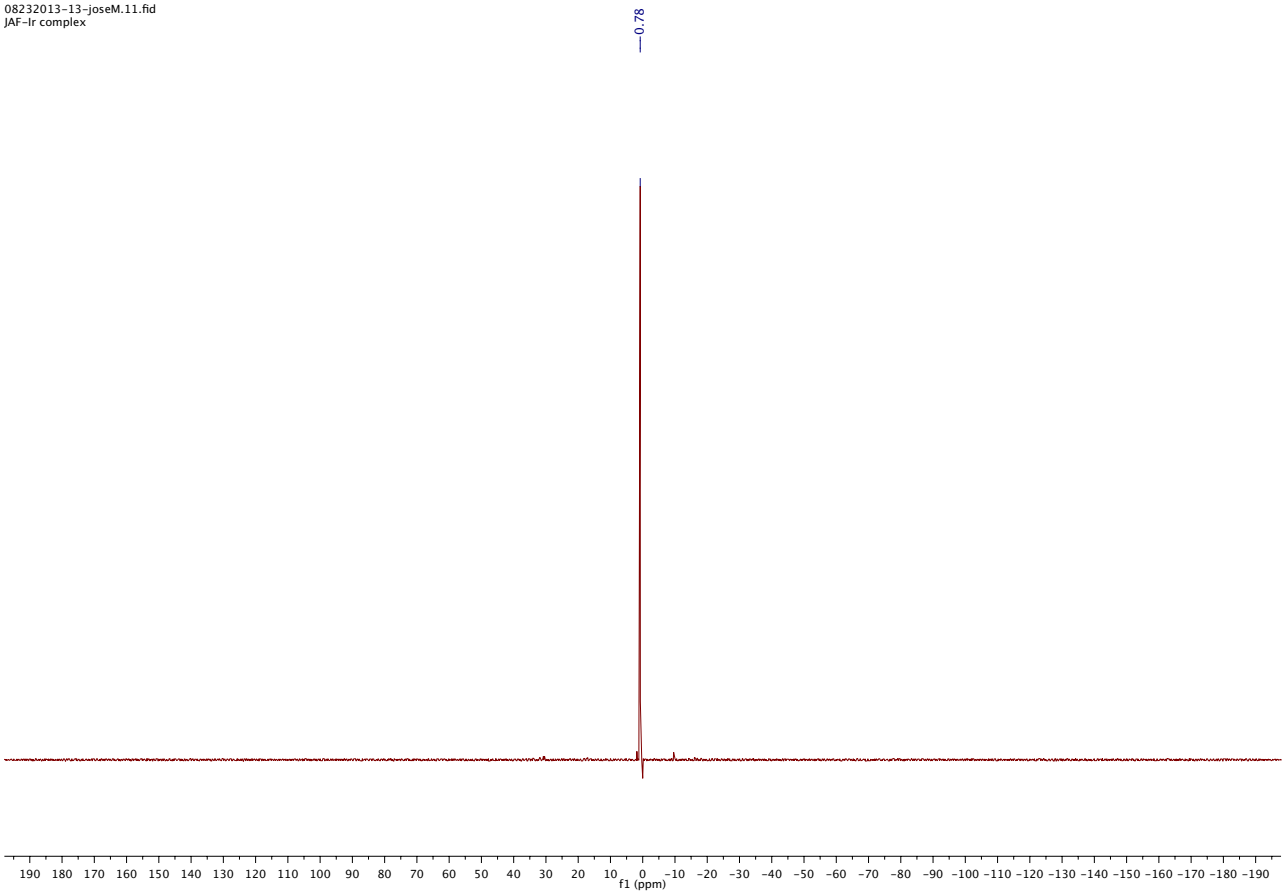
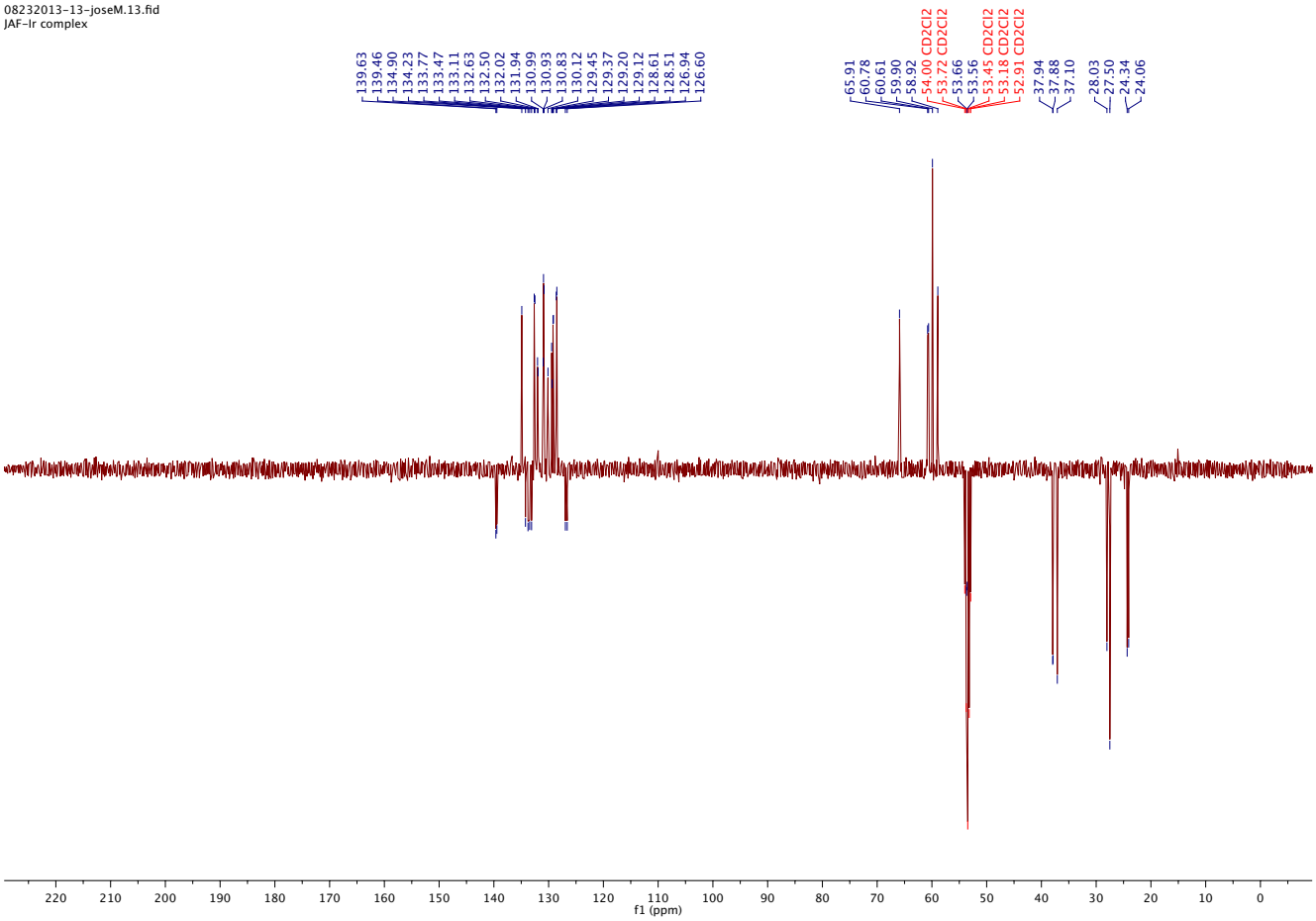
f1 (ppm)

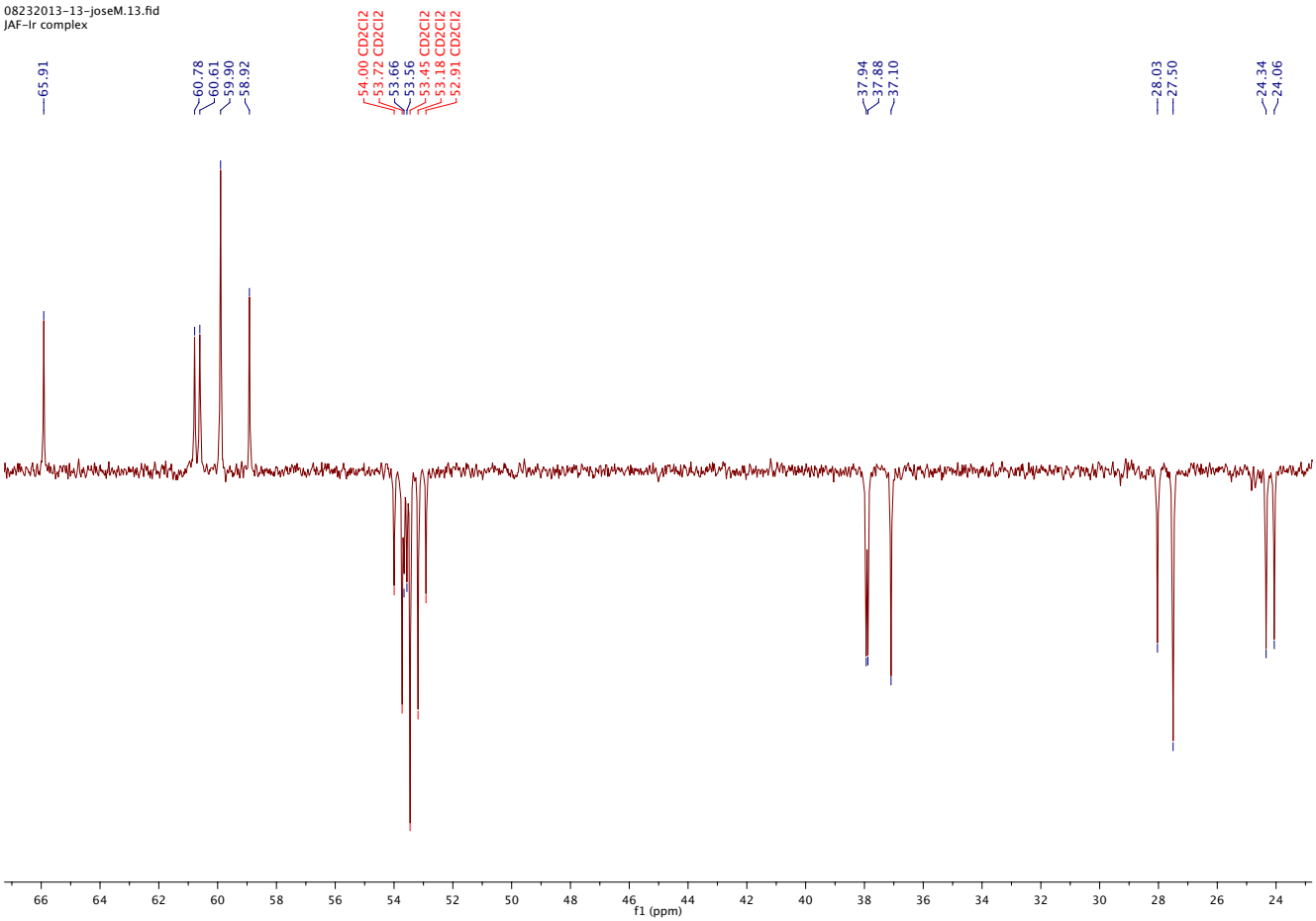
^{1}H-NMR and ^{31}P-NMR spectra for complex **13**



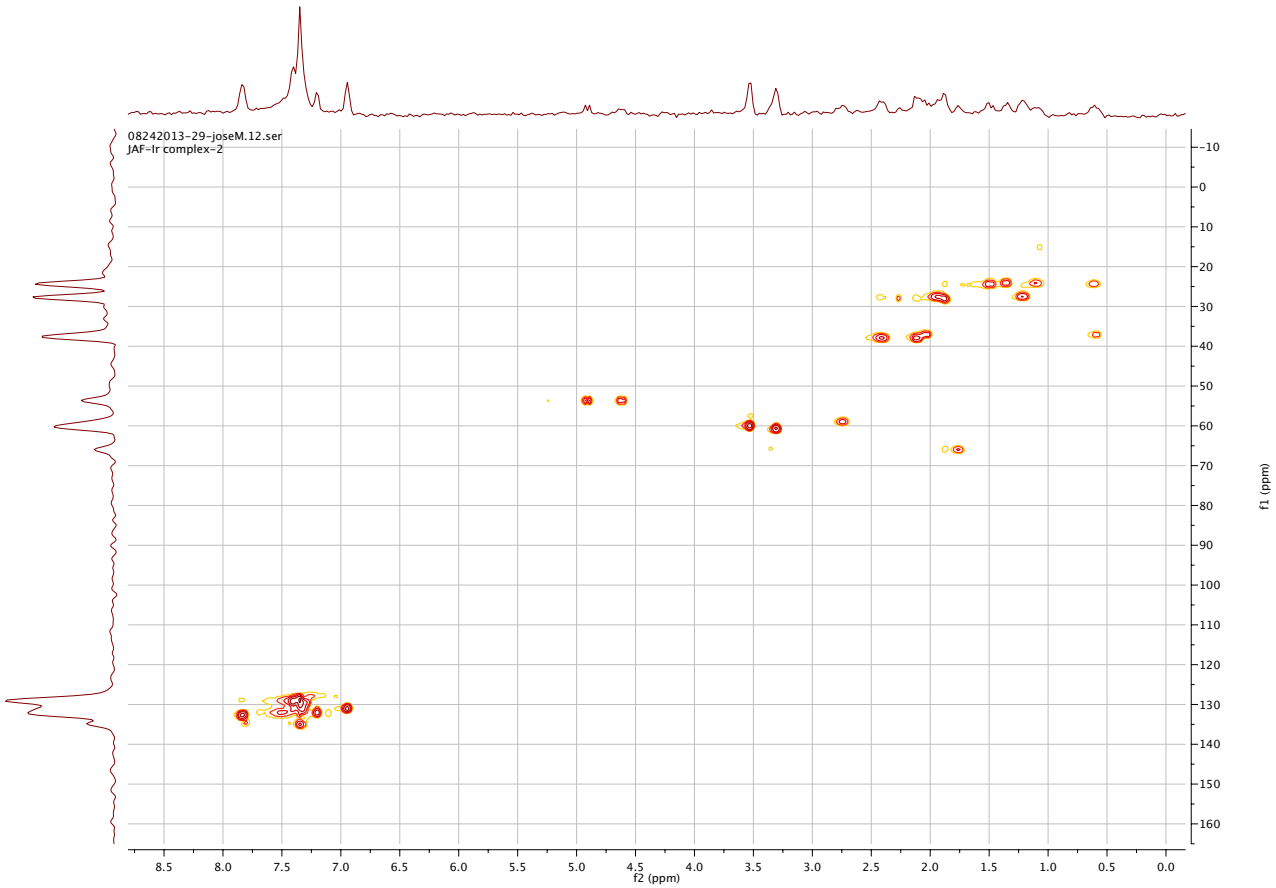


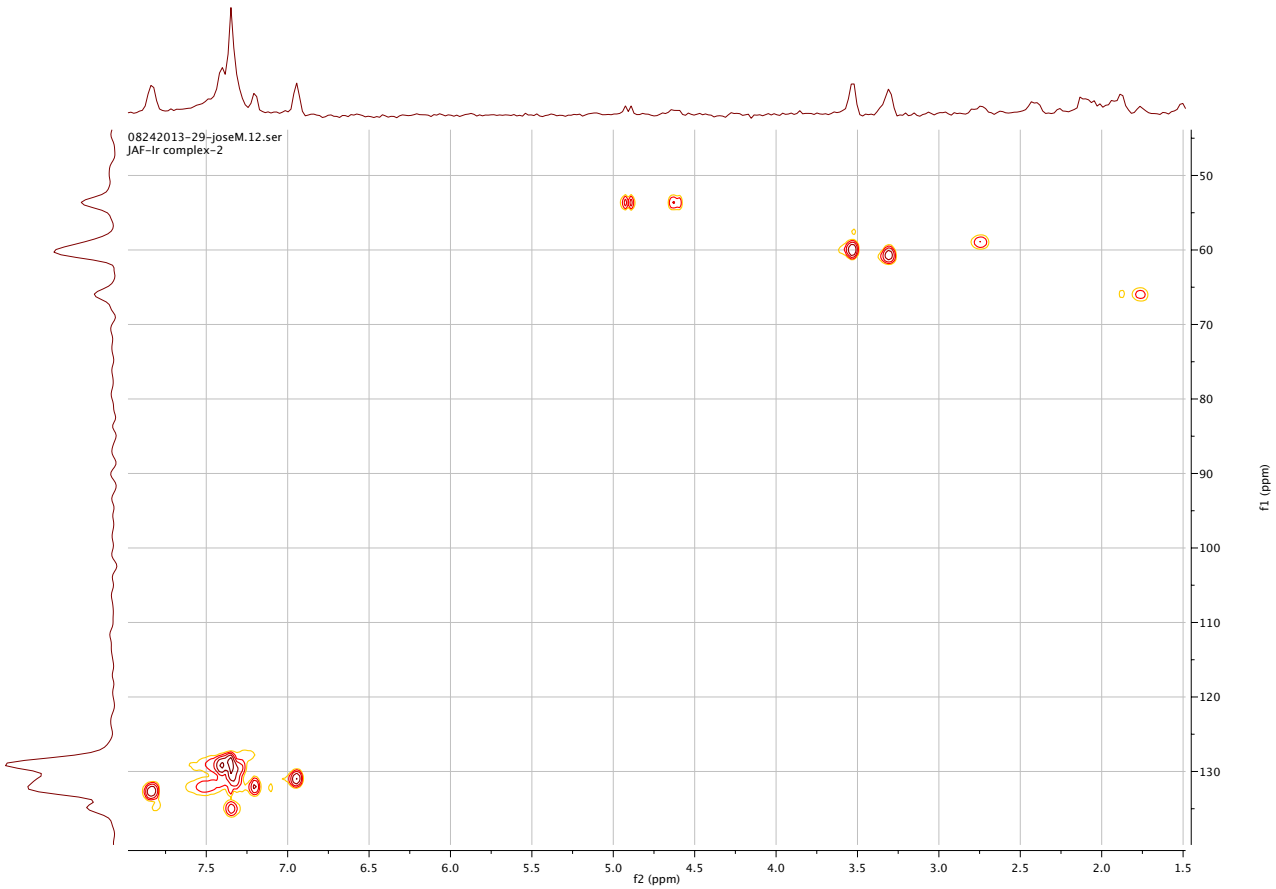
^{13}C-NMR spectrum and expansion showing COD and cyclohexyl signals in complex **13**



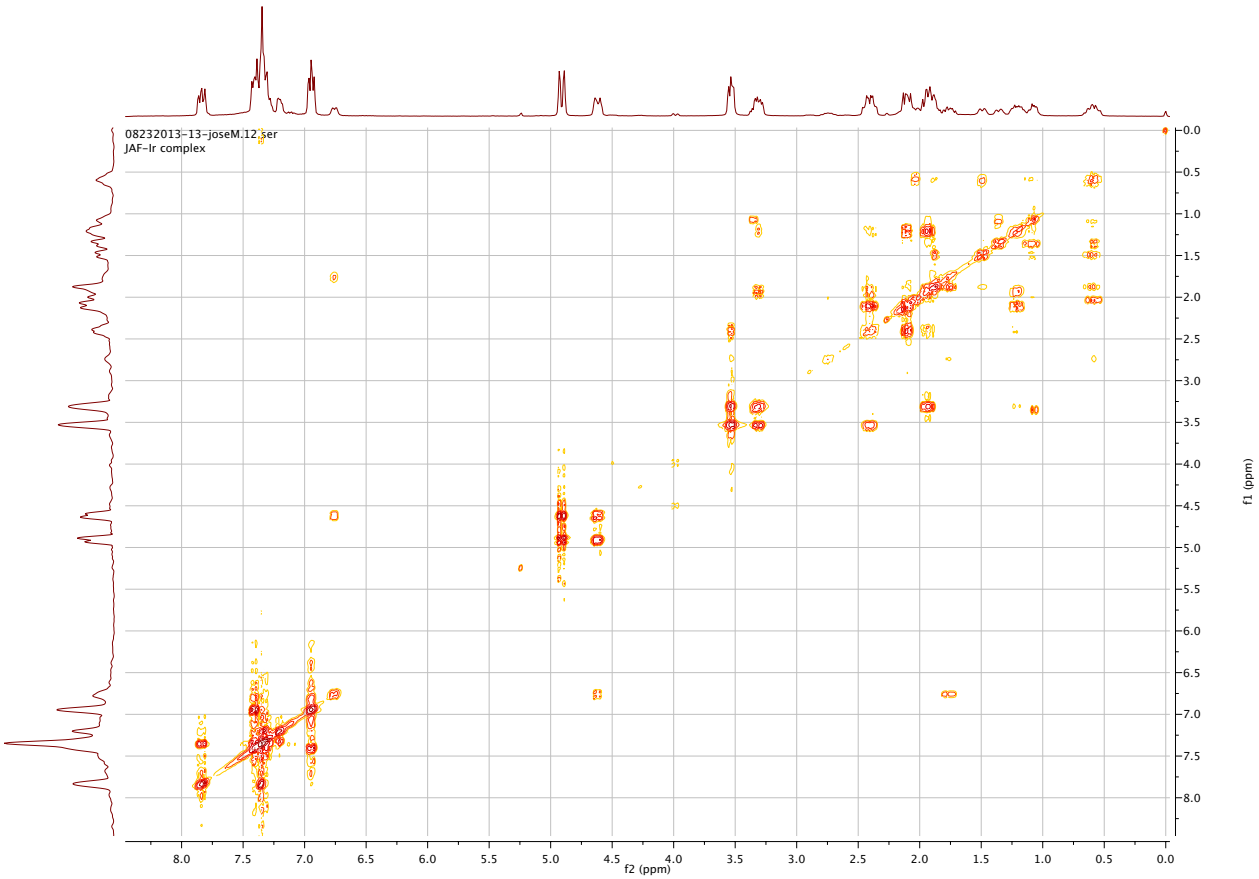


2D HSQC spectrum and expansion showing correlations for characteristic resonances in complex **13**

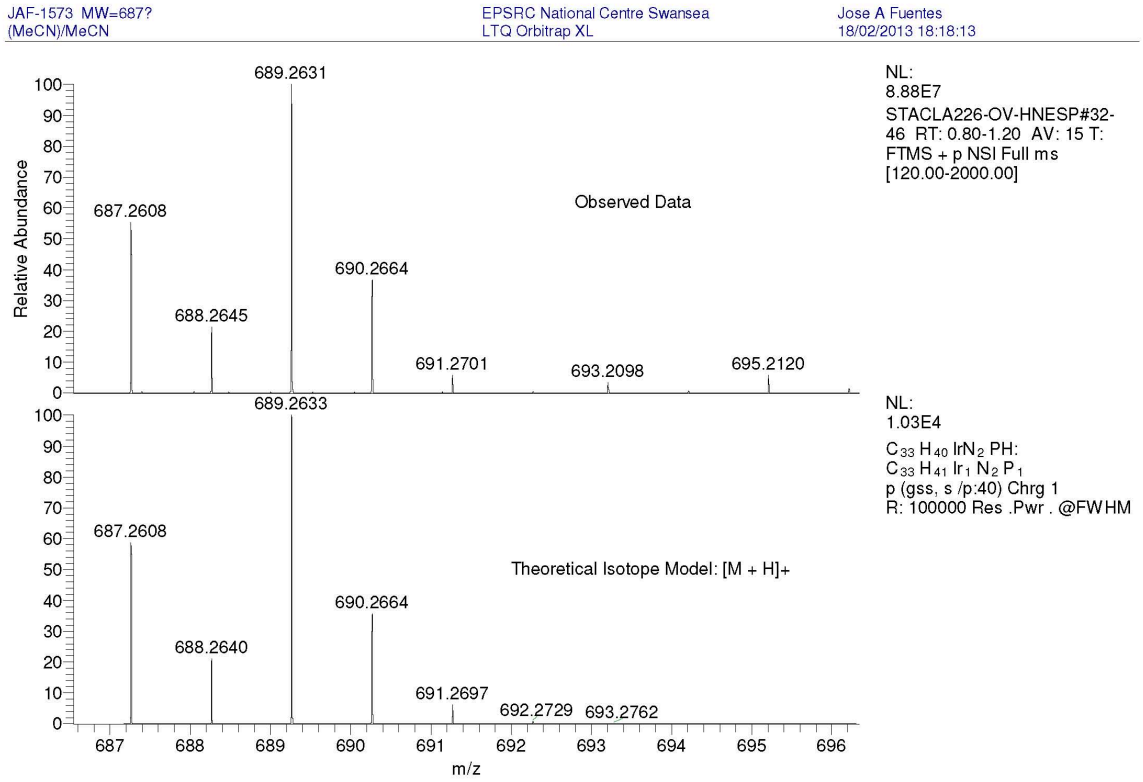




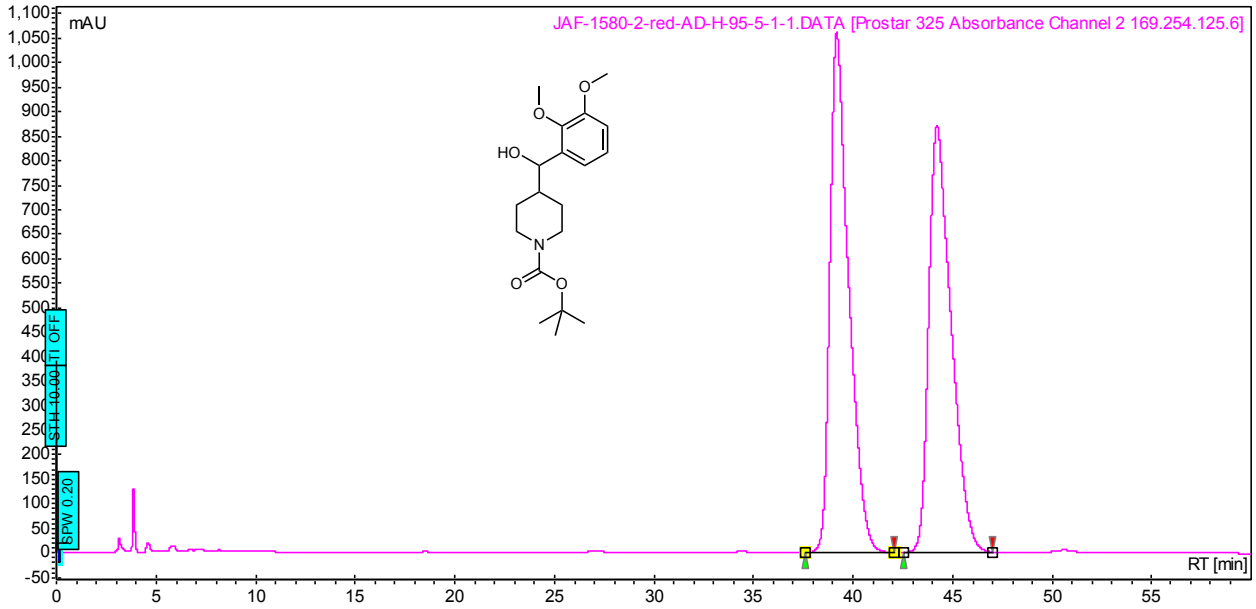
2D ^{1}H, ^{1}H-COSY spectrum for complex **13**



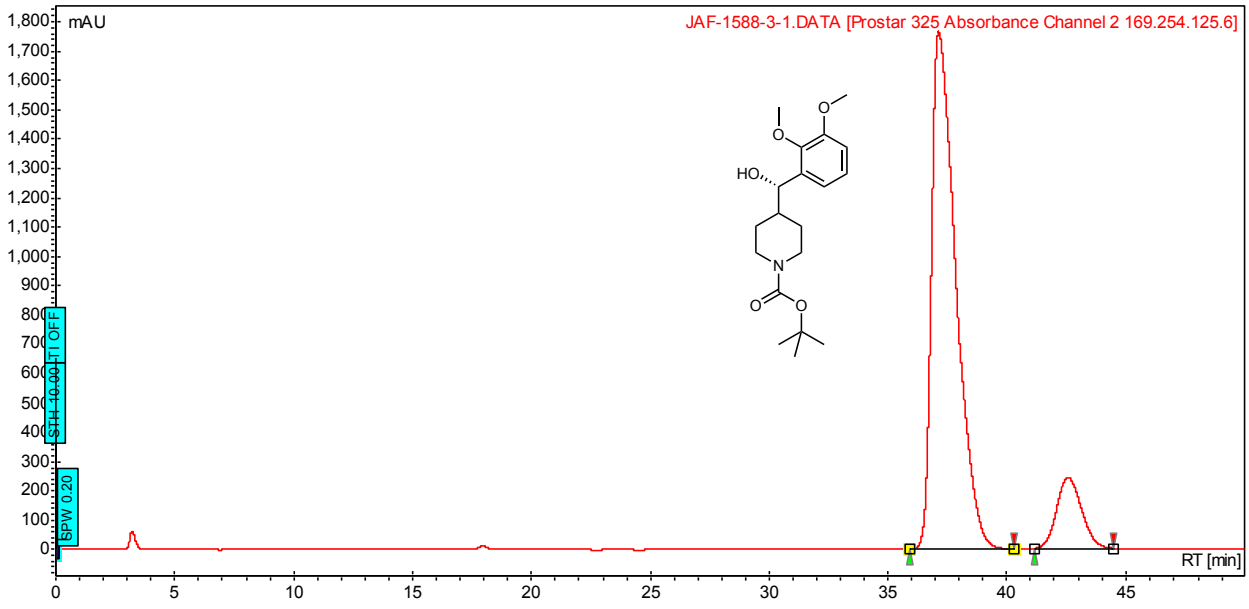
Theoretical isotope model and observed data for complex **13**



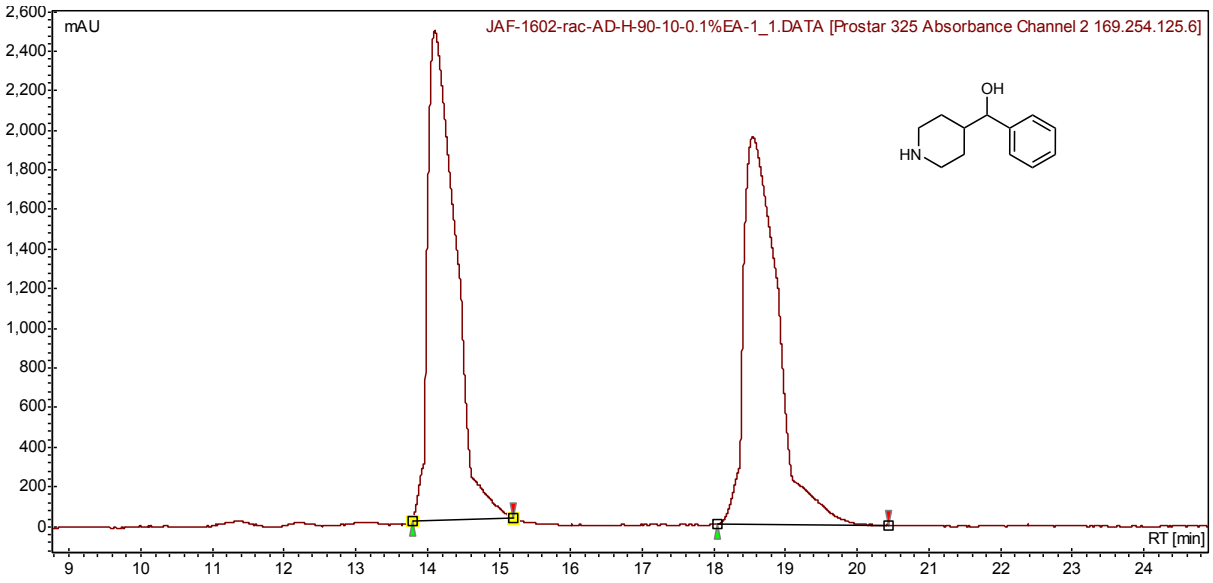
13. HPLC chromatograms for selected racemic alcohols and catalysis products



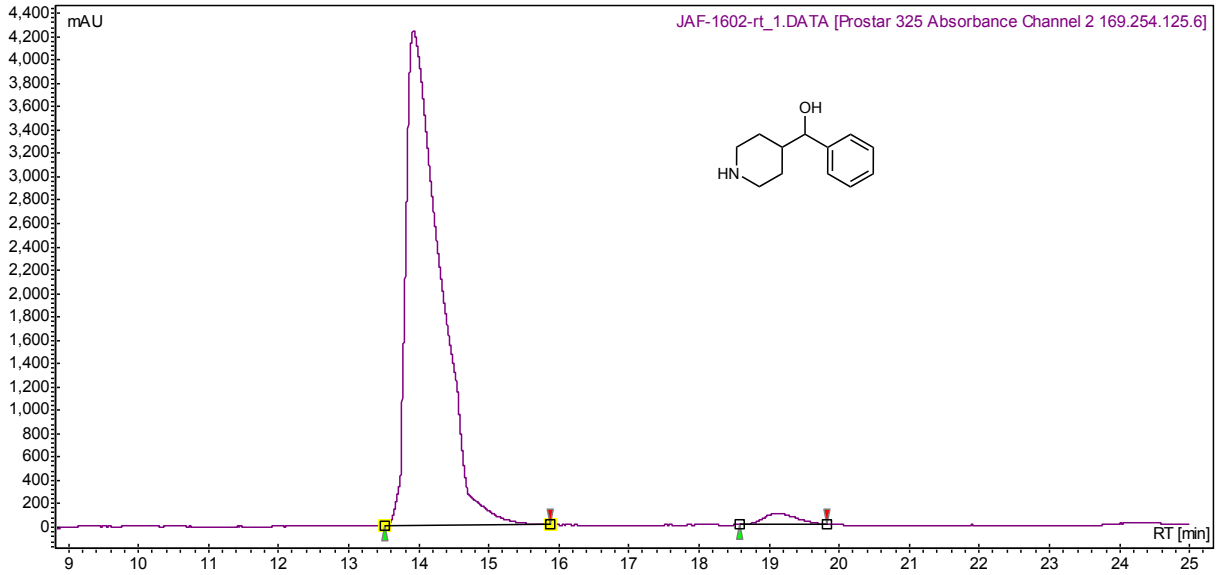
#	Name	Time [Min]	Quantity	[% Area]	Height [mAU]	Area [mAU.Min]
1	UNKNOWN	39.18	50.48	1060.3	1153.8	50.480
2	UNKNOWN	44.22	49.52	870.6	1131.9	49.520
Total			100.00	1930.9	2285.7	100.000



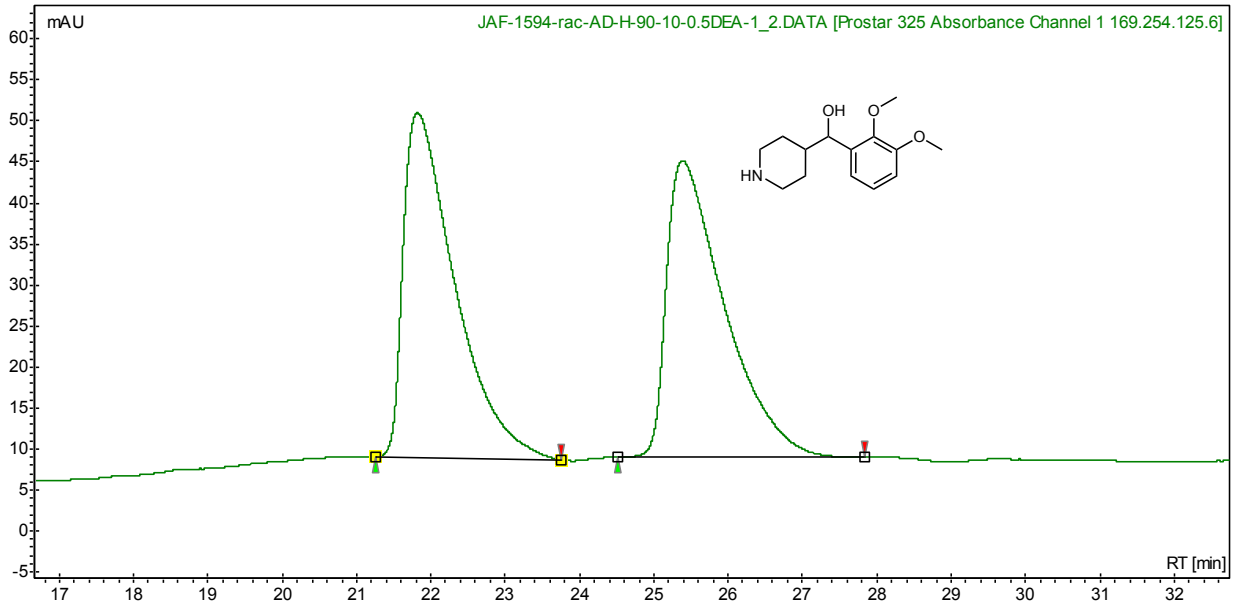
#	Name	Time [Min]	Quantity	[% Area]	Height [mAU]	Area [mAU.Min]
1	UNKNOWN	37.13	87.66	1765.4	2086.7	87.657
2	UNKNOWN	42.57	12.34	242.0	293.8	12.343
Total			100.00	2007.4	2380.5	100.000



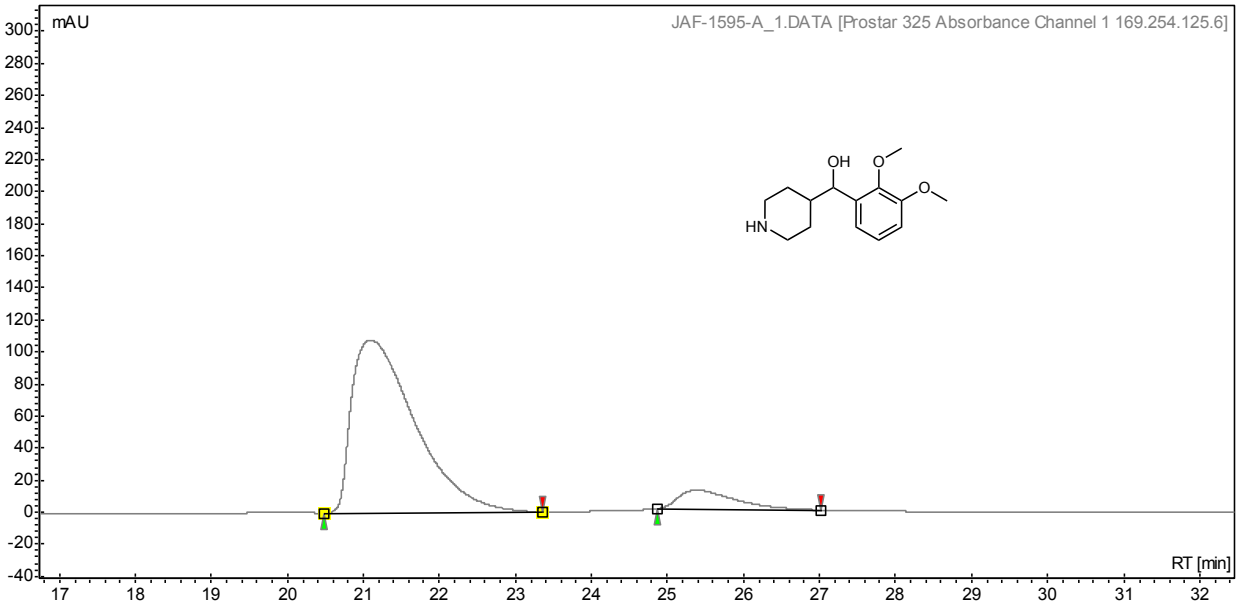
#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	14.10	50.54	2469.6	1106.7	50.536
2	UNKNOWN	18.54	49.46	1960.2	1083.2	49.464
	Total		100.00	4429.8	2189.9	100.000



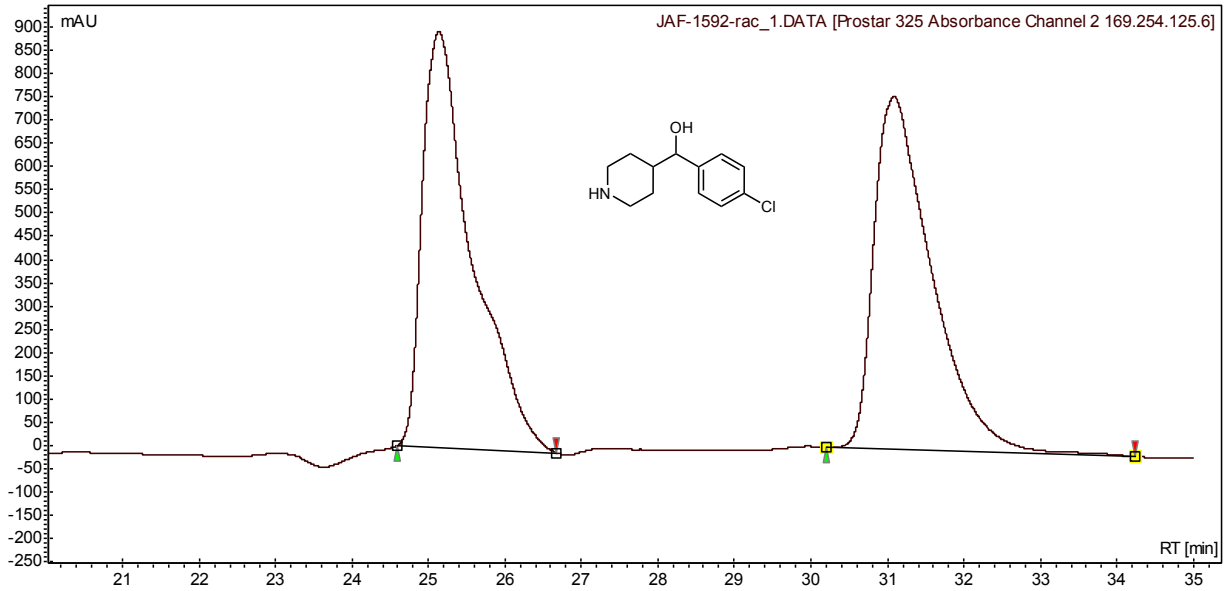
#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	13.92	97.82	4236.5	2373.6	97.823
2	UNKNOWN	19.11	2.18	94.1	52.8	2.177
	Total		100.00	4330.6	2426.4	100.000



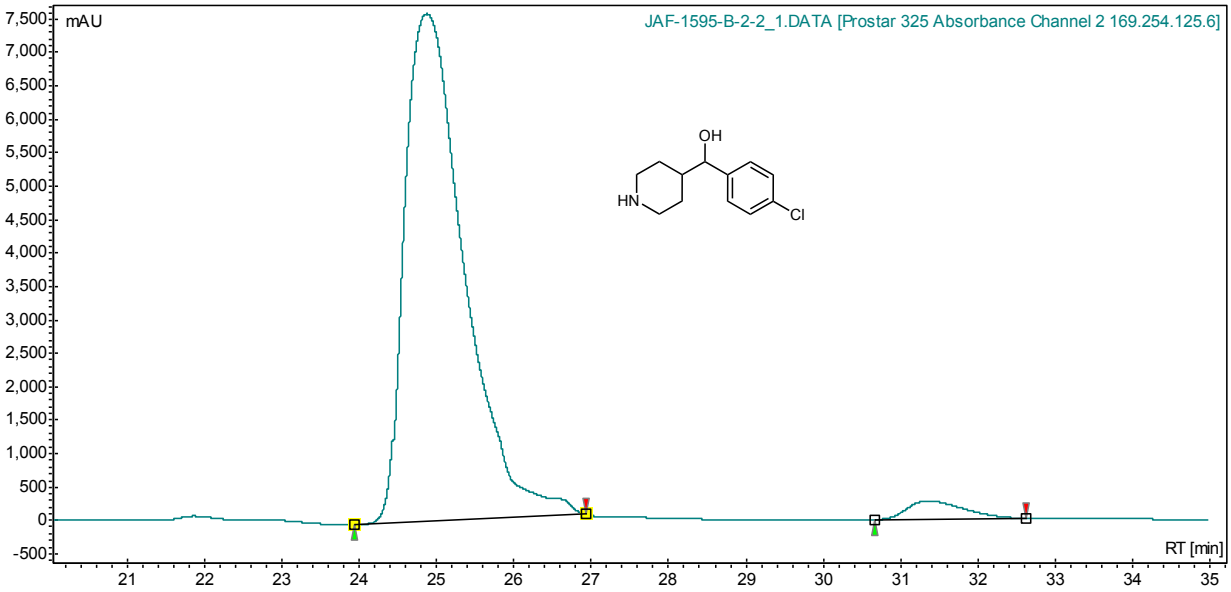
#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area %
1	UNKNOWN	21.82	50.93	42.1	33.9	50.930
2	UNKNOWN	25.39	49.07	36.2	32.6	49.070
Total			100.00	78.2	66.5	100.000



#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	21.10	91.02	107.9	104.4	91.018
2	UNKNOWN	25.39	8.98	12.0	10.3	8.982
Total			100.00	119.9	114.7	100.000

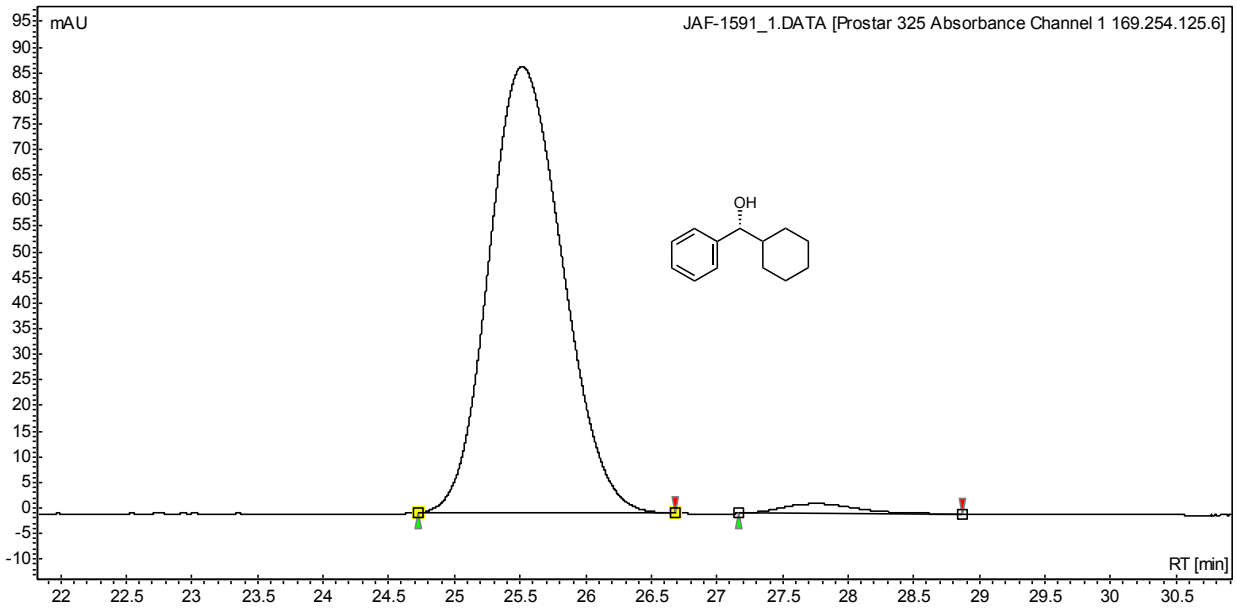


#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
2	UNKNOWN	25.14	50.50	895.1	677.9	50.500
1	UNKNOWN	31.08	49.50	758.5	664.5	49.500
Total			100.00	1653.7	1342.4	100.000

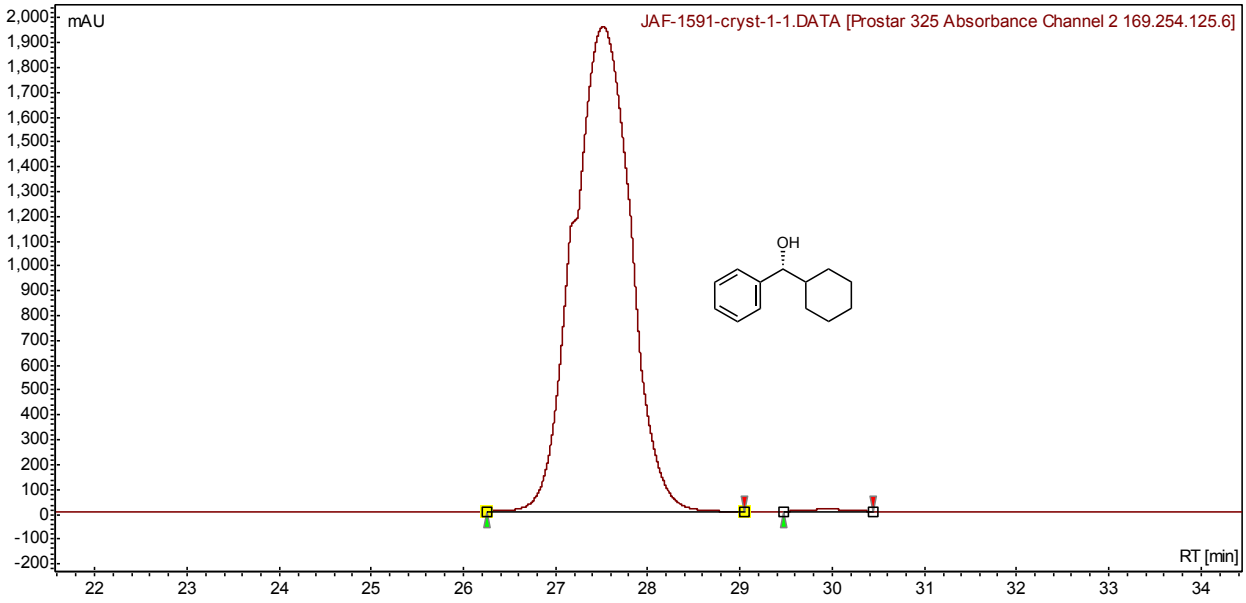


#	Name	Time [Min]	Quantity [% Area]	Height [mAU]	Area [mAU.Min]	Area % [%]
1	UNKNOWN	24.87	96.66	7586.9	6797.6	96.658
2	UNKNOWN	31.37	3.34	276.6	235.0	3.342
Total			100.00	7863.5	7032.6	100.000

Chromatograms of alcohol **9al** showing a 95% ee (top) and a >99% ee after a single recrystallization.

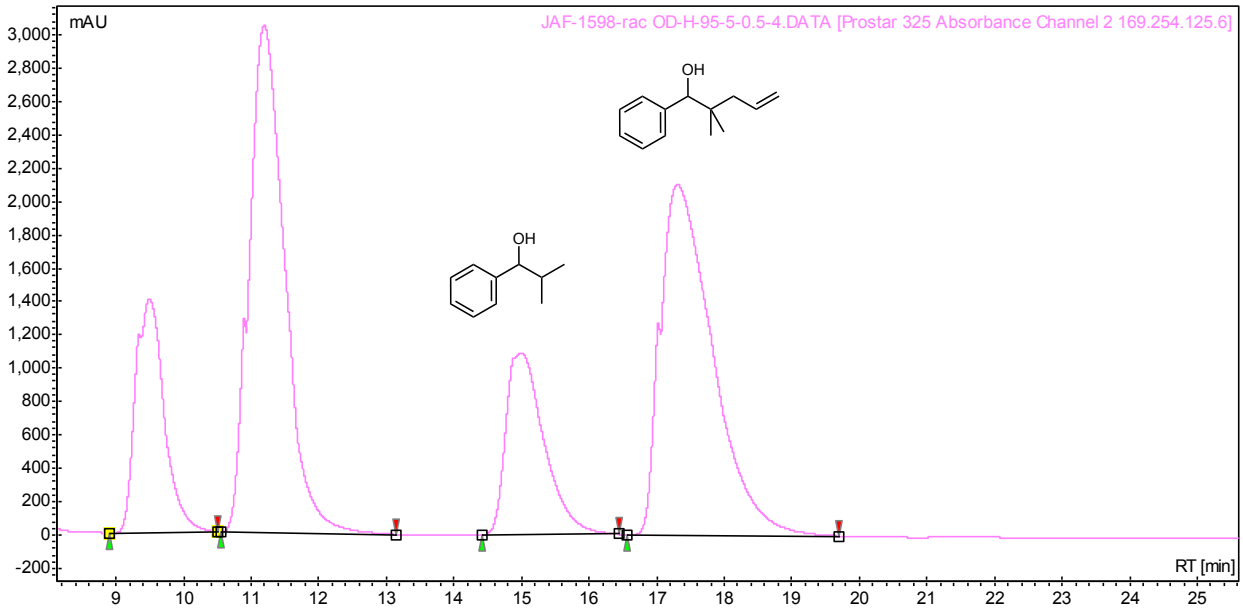


#	Name	Time [Min]	Quantity	[% Area]	Height [mAU]	Area [mAU.Min]
1	UNKNOWN	25.52	97.77	87.2	56.8	97.768
2	UNKNOWN	27.77	2.23	2.0	1.3	2.232
Total			100.00	89.2	58.1	100.000

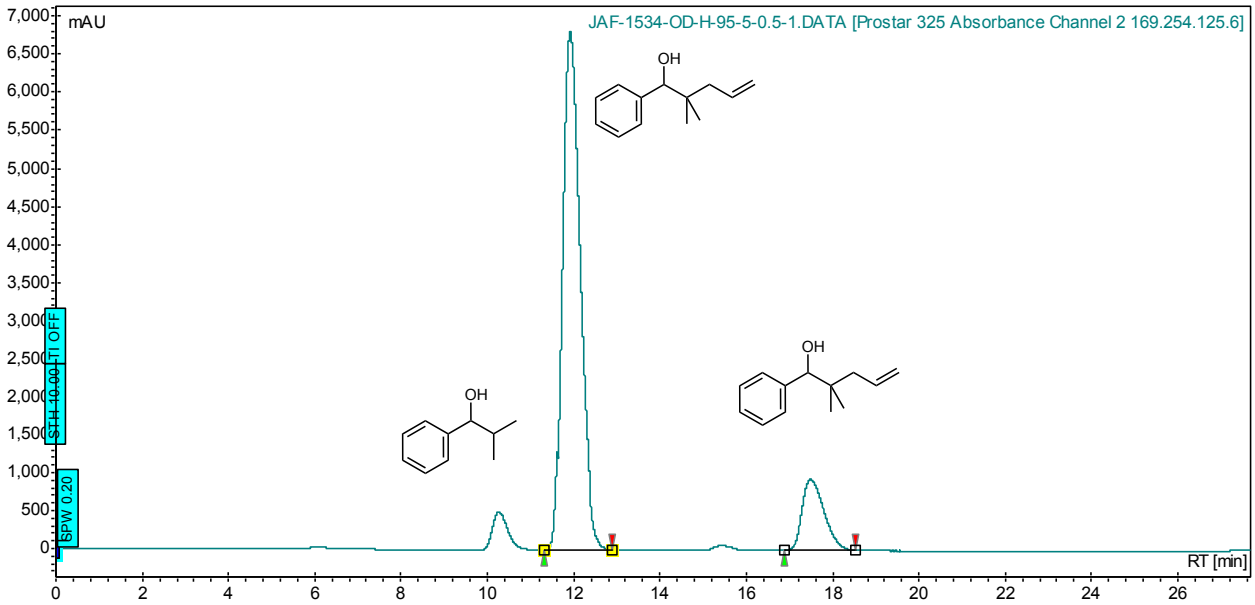


#	Name	Time [Min]	Quantity	[% Area]	Height [mAU]	Area [mAU.Min]
1	UNKNOWN	27.51	99.68	1953.8	1408.9	99.676
2	UNKNOWN	29.94	0.32	8.3	4.6	0.324
Total			100.00	1962.1	1 413.4	100.000

Ketone **12k** was used in catalysis containing a small amount of ketone **10k** (c.a. 8%), For this reason HPLC methods were developed using racemic mixtures of alcolhols **12al** and **10al**.



#	Name	Time [Min]	Quantity	[% Area]	Height [mAU]	Area [mAU.Min]
1	UNKNOWN	9.50	13.44	1407.8	692.5	13.436
2	UNKNOWN	11.19	36.03	3049.2	1857.1	36.034
3	UNKNOWN	15.00	13.90	1089.7	716.3	13.899
4	UNKNOWN	17.31	36.63	2106.8	1887.9	36.631
Total			100.00	7653.5	5153.8	100.000



#	Name	Time [Min]	Quantity	[% Area]	Height [mAU]	Area [mAU.Min]
1	UNKNOWN	11.92	85.44	6803.0	3249.3	85.444
2	UNKNOWN	17.48	14.56	932.1	553.5	14.556
Total			100.00	7735.1	3802.9	100.000

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