Electronic Supplementary Material (ESI) for Organdic and Biomolecular Chemistry

Supporting information

The importance of the N-H bond in Ru/TsDPEN complexes for asymmetric transfer hydrogenation of ketones and imines.

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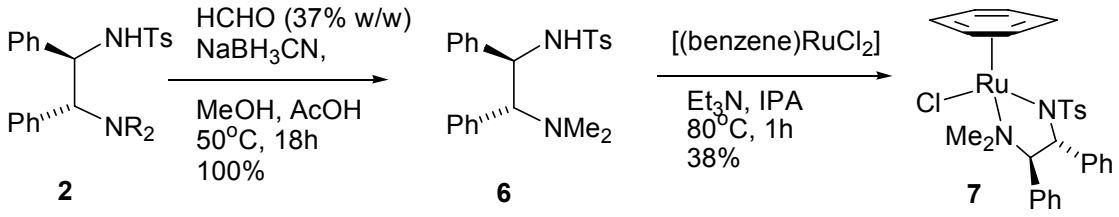
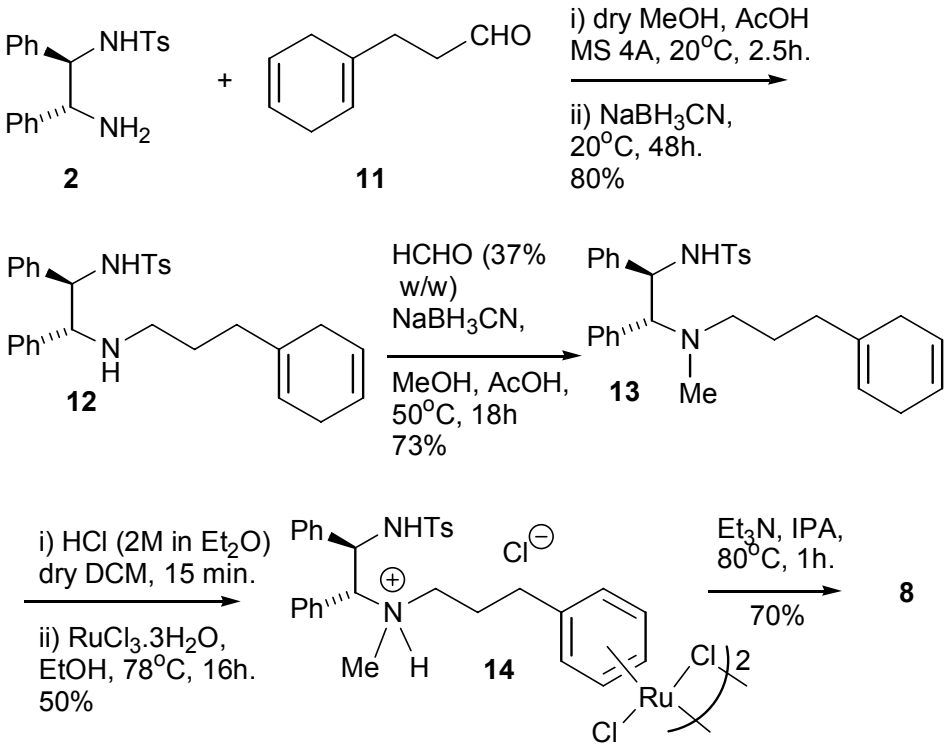
1. Synthesis of Ru metal complexes.

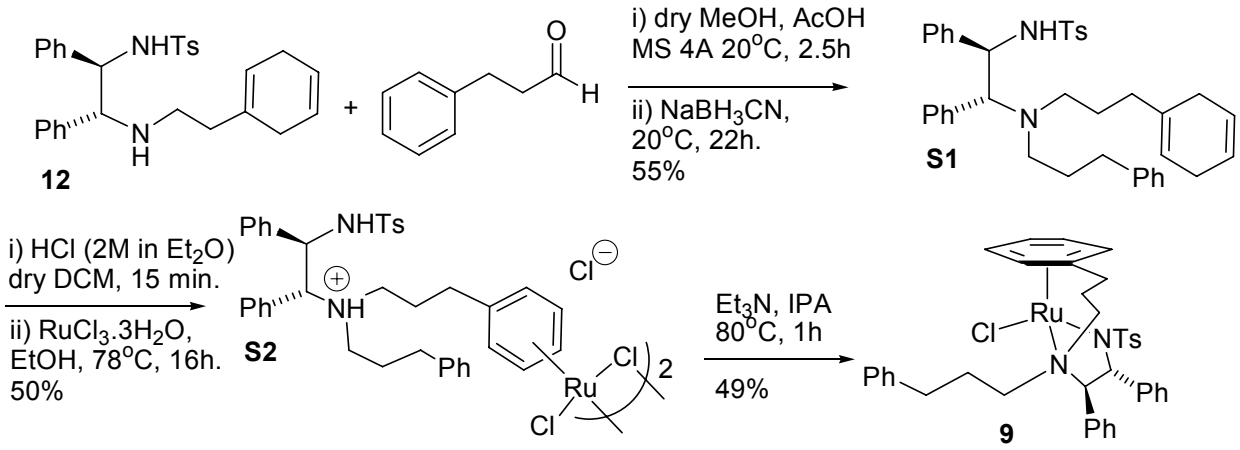
Complex **7** was synthesized from dimethyl Ts-DPEN **6**, itself prepared from Ts-DPEN **2**. Reductive amination was followed by complexation with the dimer of benzene ruthenium(II)dichloride.



Complex **8** was prepared by reductive amination of Ts-DPEN **2** with aldehyde **11** to give **12**, which was subjected to a second reductive amination with formaldehyde to give N-methyl derivative **13**. This was converted into a hydrochloride salt and reacted with ruthenium trichloride to give dimer **14**, which was converted into monomer **8** using triethylamine in IPA.



Complex **9** was synthesized by reductive amination of **12** with phenyl propionaldehyde to form **S1**. This was converted into a hydrochloride salt and reacted with ruthenium trichloride to give dimer **S2**, which was then converted into monomer **9** by using triethylamine in IPA.



2. Use of synthesized complexes in transfer hydrogenation; initial studies.

Transfer Hydrogenation: Neat formic acid: triethylamine (5:2) was used as source of hydrogen in transfer hydrogenation. The reduction of ketone **15**, imine **16** and imine salt **16H.X** were carried out in inert atmosphere at atmospheric pressures using complexes **7-9**.

ATH of ketone: Asymmetric transfer hydrogenation of acetophenone (Table 1) with complex **7** gave very low conversion under all conditions (entries 1-4), which confirms the necessity of NH for reduction of ketone group. Complexes **8** and **9** gave higher conversion (entries 6 and 7). The ee measurements on products of low conversions should be treated with caution as there is likely to be a high experimental error. It is unclear why (*S,S*)-**8** and (*R,R*)-**9** both gave products of *R* configuration; presumably the difference in steric bulk of the N-substituents contributes to the observed stereocontrol.

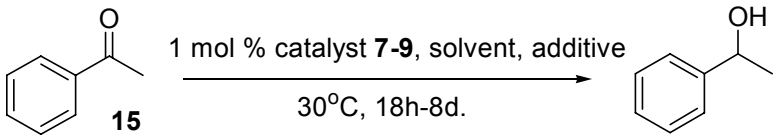


Table 1: Asymmetric transfer hydrogenation of acetophenone using complexes **7-9** and **14**.

Entry	Substrate	Catalyst	Additive[a]/ Solvent	Time	% Conv[b]	% ee[c]	Exp No.
1	C=O	(R,R)-NMe_2 **7**	$AgSbF_6$/ FA:TEA (5:2)	5 days	1.5%	17% (R)	287
2	C=O	(R,R)-NMe_2 **7**	FA:TEA (5:2)	6 days	1.7%	46% (R)	283
3	C=O	(R,R)-NMe_2 **7**	FA:TEA (5:2)	21h	0.6%	0%	328
				4days	1.1%	0%	
4	C=O	(R,R)-NMe_2 **7**	HCOONa/ IPA	4 days	0%		329
5	C=O	(S,S) teth-NMe **8**	FA:TEA (5:2)	18h	6%	73% (R)	358
6	C=O	(R,R) teth-$N(CH_2)_3Ph$ **9**	FA:TEA (5:2)	24h	11%	70% (R)	389
				4 days	17%	36% (R)	

[a] additive $AgSbF_6$ = 4 mol%, HCOONa = 3 eq. FA:TEA = 2M solution of substrate, [c] % conversion is calculated from chiral GC data, [c] The ee was calculated by chiral GC.

ATH of imine 16.

Asymmetric transfer hydrogenation of imine and its salt was carried out using complexes **7-9** (Table 2). Complex **7** did not give a high reduction of imine with sodium formate but gave very good conversion of the imine salt under the same conditions. This suggests that formation of salt is required for reduction of imine. Complex **7** was able to reduce the imine with formic acid : triethylamine(5:2) in 5 days to 91% conversion, but in the presence of solvent, the rate of reduction dropped. Complex **8** reduced imine faster than complex **7** even in different solvents. But complex **8** gave very low reduction of imine salt using sodium formate. Complex **9** gave good conversion for imine reduction compared to complex **7** but was not as high as as for **8**. (*R,R*)-Catalysts gave *S* configuration products in all cases, and vice-versa, however the low ees preclude any definitive prediction of transition state structure.

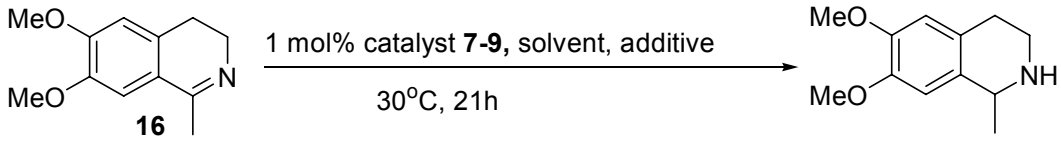


Table 2: Asymmetric transfer hydrogenation of imine and its salt using complexes **7-9**.

Entry	Substrate	Catalyst	Solvent	Time	% Conv	% ee	Exp No.
1	C=N	(R,R)-NMe_2 **7**	FA	21h	9%	19% (S)	313
2	C=N	(R,R)-NMe_2 **7**	HCOONa/ IPA	21h	2%	na	325
3	C=N. HCl	(R,R)-NMe_2 **7**	HCOONa/ IPA	19h	91%	0%	327
4	C=N	(R,R)-NMe_2 **7**	FA:TEA (5:2)	19h	36%	17% (S)	326
				45h	71%	24% (S)	
				5 days	91%	18% (S)	
5	C=N. HCl	(R,R)-NMe_2 **7**	FA:TEA (5:2)	4 days	12%	0%	330
7	C=N	(R,R)-NMe_2 **7**	FA:TEA	22h	7%	4% (S)	332

			(5:2)/ CH_3CN	3 days	9%	0%	
8	C=N	(R,R)-NMe_2 **7**	FA:TEA/ DCM	22h	8%	9% (S)	333
				3 days	12%	11% (S)	
9	C=N	(R,R)-NMe_2 **7**	FA:TEA (5:2)/ DMF	22h	12%	0%	334
				3 days	18%	15% (S)	
10	C=N	(R,R)-NMe_2 **7**	FA:TEA (5:2)/ MeOH	22h	6%	0%	335
				3 days	32%	0%	
11	C=N	(R,R)-NMe_2 **7**	FA:TEA/ IPA	22h	9%	11% (S)	336
				69h	16%	10% (S)	
12	C=N	(R,R)-NMe_2 **7**	FA:TEA (5:2)/ EtOAc	22h	16%	5% (S)	337
				69h	30%	0%	
13	C=N	(S,S) teth-NMe **8**	FA:TEA (5:2)	16.5h	95%	27% (R)	357
				20h	97%	24% (R)	
14	C=N	(R,R) teth-NMe **8**	FA:TEA (5:2) / MeOH	20h	95%	8% (S)	378
15	C=N	(R,R) teth-NMe **8**	FA:TEA (5:2)/CH_3 CN	20h	95%	21% (S)	379
16	C=N	(R,R) teth-NMe **8**	FA:TEA (5:2)/IPA	20h	97%	14% (S)	380
17	C=N. HCl	(R,R) teth-NMe **8**	FA:TEA (5:2)	22h	14%	0%	390
18	C=N. HCl	(R,R) teth-NMe **8**	HCOONa/ IPA	22h	37%	10% (S)	391
19	C=N	((R,R) teth-$N(CH_2)_3Ph$ **9**	FA:TEA (5:2)	24h	95%	7% (S)	388

[a] HCOONa = 3 eq. FA:TEA = 2M solution of substrate, [c] % conversion is calculated from chiral GC data, [c] The ee was calculated by chiral GC.

3. Graphical data for transfer hydrogenation reactions.

Reduction of imine 16 followed by chiral GC.

Reduction of imine **16** using complexes **7** ('NMe_2'), **8** ('teth-NMe') and **9** ('teth-$N(CH_2)_3Ph$') was repeated by analysing the reaction using chiral GC at different time intervals (Figure 1).

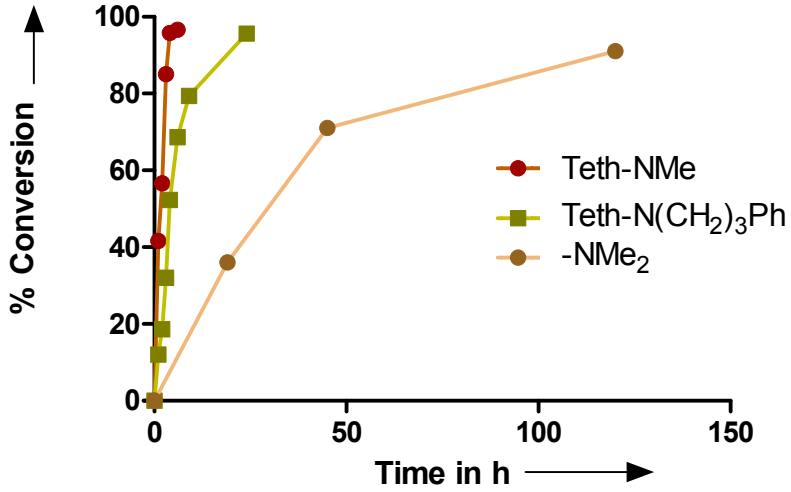


Figure 1: Reduction of imine **16** in ATH by catalysts **7-9**. **Conditions:** FA/TEA=5:2, [Imine]=0.5 M, 30 °C, S/C = 100. Followed by chiral GC. TethNMe= **8** (ex 382), Teth-$N(CH_2)_3Ph$ = **9** (ex 388), NMe_2= **7** (ex. 326).

The enantiomeric excesses were as follows:

For TethNMe (**8**); 1h; 3%, 2h; 8.5%, 3h; 12.6%, 4h; 12%, 5h; 13.4% (*S*). (*R,R*)-**8** used.

For Teth$N(CH_2)_3Ph$ (**9**); 1h; 10%, 2h; 14%, 3h; 15%, 4h; 14%, 6h; 10.5%, 9h; 10%, 24h; 7.8% (*S*). (*R,R*)-**9** used.

For NMe_2 (**7**); 19h; 17%, 45h; 24%, 5d; 18% *(S)*. (*R,R*)-**7** used.

Ketone and imine reductions followed by ^{1}H NMR.

On the basis of results obtained from asymmetric transfer hydrogenation of ketone and imine, further reactions were carried out in an NMR tube under varying conditions:

Ketone reduction: Complexes **1** ('NH2'), **5** ('NMe') and **7** ('NMe2') were compared for reduction of acetophenone using 400MHz NMR (Ozric) by taking ^{1}H-NMR at different time intervals. Complexes **10** ('teth-NH') and **8** ('teth-NMe') were faster than complex **7** for acetophenone reduction. Complexes **10** and **8** were also compared for reduction of acetophenone under similar conditions. Complex **10** was found to be much more active than complex **8** for acetophenone reduction.

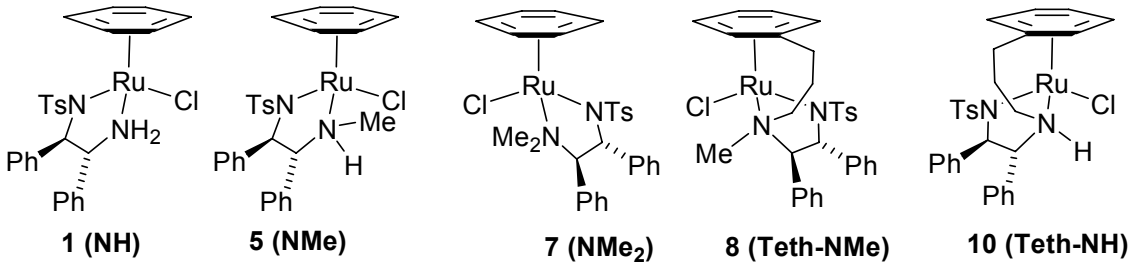


Figure 2: Catalysts used in comparative ^{1}H NMR studies.

The results of comparative reductions by the above complexes are illustrated in the graphs below:

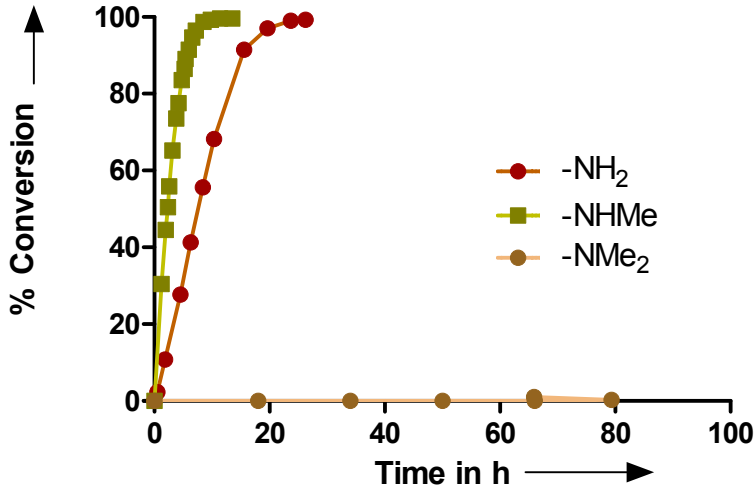


Figure 3: Reduction of acetophenone in ATH by catalysts **1**, **5** and **7**. *Conditions*: FA/TEA=5:2, [Ketone]=0.86 M, 25 ^{o}C, S/C = 100. Followed by ^{1}H-NMR (400 MHz). The NH and NHMe results were conducted by Jose E D Martins and are taken from a previous publication.[1] NMe_2 = **7** (ca 1% conversion at t=80h), the ee was not recorded.

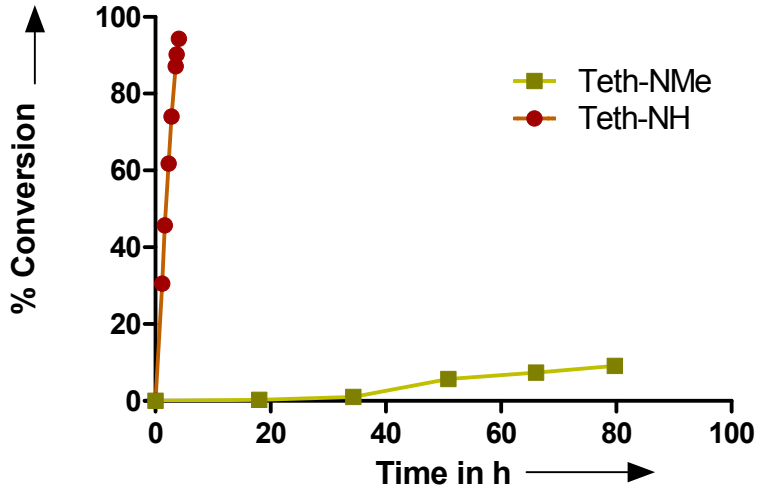


Figure 4: Reduction of Acetophenone in ATH by catalysts **8** and **10**. *Conditions*: FA/TEA=5:2, [Ketone]=0.86 M, 25 °C, S/C = 100. Followed by ^{1}H-NMR (400 MHz). Teth-NMe = **8** (ex. 399, ee at end not recorded), Teth-NH = **10** (ex. 400, ee at end; 96.5% (*R*) using (*R,R*) catalyst).

Imine reduction: Complexes **1**, **5** and **7** were compared for reduction of imine **16** by taking ^{1}H-NMR spectra at different time intervals. Complexes **1** and **5** were much faster than complex **7** (Figure 5). Complexes **8** and **10** were also compared for reduction of imine under the same conditions. Complex **10** was found to be much faster for imine reduction although complex **8** gave good conversion (Figure 6).

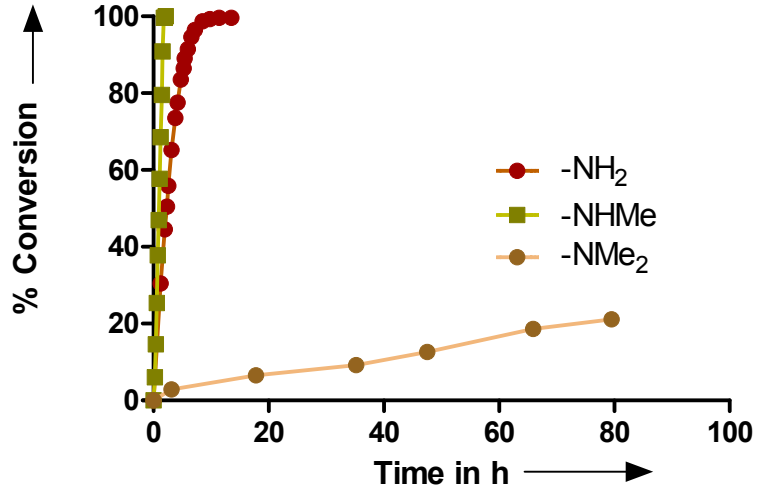


Figure 5: Reduction of imine **16** in ATH by catalysts **1**, **5** and **7**. *Conditions:* MeCN, FA/TEA=5:2, [Imine]=0.45 M, 25 °C, S/C = 100. Followed by ^{1}H-NMR (400 MHz). The

NH_2 result was conducted by Jose E D Martins and are taken from a previous publication.[1] NHMe = **5** (ex. 401, ee at end = 59% (*S*) using (*R,R*) catalyst), NMe_2 = **7** (ex. 395, ee at end not recorded).

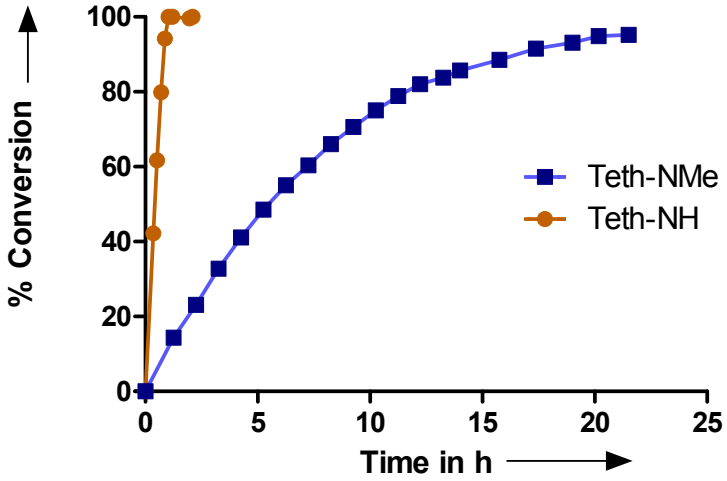


Figure 6: Reduction of imine **16** in ATH by catalysts **8** and **10**. *Conditions:* MeCN, FA/TEA=5:2, [Imine]=0.45 M, 25 °C, S/C = 100. Followed by ^{1}H-NMR (400 MHz). Teth-NMe = **8** (ex. 397, ee at end 21.8% (*S*) using (*R,R*) catalyst), Teth-NH = **10** (ex. 396, ee at end 34.5% (*S*) using (*R,R*) catalyst).

Imine reduction without solvent: To remove possible solvent effects, complexes **7** and **8** were used for imine reduction with 1 mol% and 3 mol% catalyst loading in FA:TEA without any solvent. These reactions were carried out in an NMR tube and monitored by ^{1}H-NMR. The level of Ru-H species was also monitored in these experiments. Complex **7** exhibited a very slow reaction with 1 mol% of catalyst loading compare to 3 mol%. A similar effect was observed with complex **8**, however the reduction is much more rapid than with **7**.

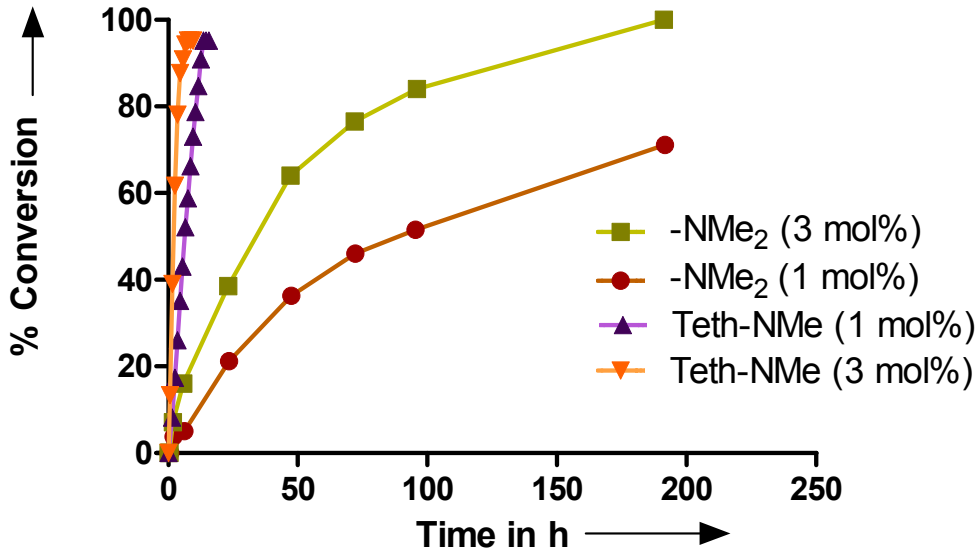


Figure 7: Reduction of imine **16** in ATH by catalysts **7** and **8**. *Conditions:* FA/TEA=5:2, [Imine]=0.50 M, 25 ^{o}C. Followed by ^{1}H-NMR (700 MHz). NMe_2 = **7** (3 mol% ex. 350, 1 mol% ex. 349), Teth-NMe = **8** (3 mol% ex. 443, 1 mol% ex. 444). Ees were not recorded for these reactions.

Monitoring Ru-H levels.

In the above ^{1}H NMR reactions with 3 mol% complexes **8** and **10**, the change in hydride formation was calculated using NMR data. At 1 mol% loading the hydride signal was very weak and could not be accurately integrated. Each complex exhibited different a pattern for hydride formation which may be one of the factors affecting their different rates of imine reduction. The level of Ru-H in the NMe_2 compound **7** appeared to decrease throughout the reaction, suggesting that the hydride may be unstable and is decomposing. In the case of teth-NMe **8**, the Ru-H peak remained stable throughout the time period of the imine reduction, suggesting that it is responsible for the observed reduction process. This difference in stability may account, at least in part, for the difference in imine reduction rates.

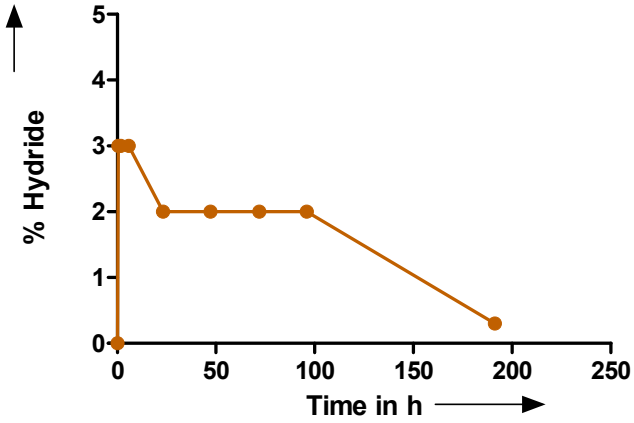


Figure 8: Change in hydride in reduction of imine **16** in ATH by catalyst **7**. *Conditions:* FA/TEA=5:2, [Imine]=0.50 M, 25 °C, 3 mol% catalyst used. Followed by ^{1}H-NMR (700 MHz). Experiment 350.

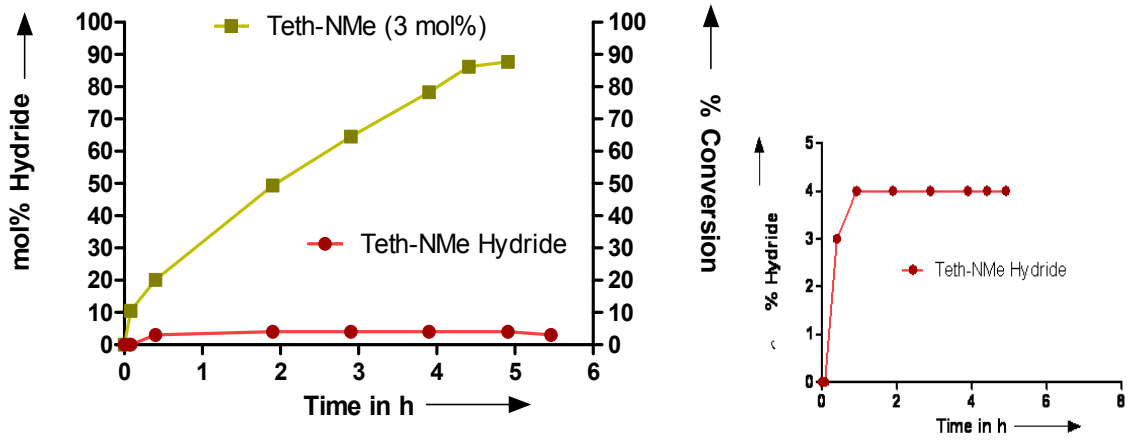


Figure 9: Change in hydride in reduction of imine **16** in ATH by catalyst **8** (red line) against conversion to amine (green line). *Conditions:* FA/TEA=5:2, [Imine]=0.50 M, 30 °C, 3 mol% catalyst used. Followed by ^{1}H-NMR (700 MHz). Experiment 417. The expanded graph of the % hydride for the same reaction is shown on the right.

4. Experimental, including X-ray crystallographic data.

General Experimental details:

All the air sensitive reactions were carried out in Argon atmosphere. NMR spectra were recorded on either a Bruker DPX 300, DPX 400, AV 400 or AV II-700 MHz spectrometers. All chemical shifts are reported in ppm downfield from TMS (Me_4Si). Coupling constants (*J*) are reported in Hz. Multiplicity in ^{1}H-NMR is reported as singlet (s), doublet (d), double doublet (dd), double triplet (dt), broad singlet (br s), broad doublet (br d),and multiplet (m). Mass spectra were recorded on Esquire 2000. High resolution mass spectra were recorded on Bruker Micro ToF. Infrared spectra were recorded on Avatar-320 FT-IR spectrometer. The optical rotations were measured on Polarimeter AA-1000. The Chiral HPLC measurements were carried out on Glison using CHIRAL PAK IB column. The chiral GC measurements were done on HEWLETT PACKARD 5890 or PERKIN-ELMER 8500 gas chromatography using Chrompak CP-Chirasil Dex Cβ column. Melting points were determined on a Stuart scientific melting point apparatus and are uncorrected. Purification of compounds was done by using Flash column chromatography using silica gel of mesh size 230-400.

Synthesis of Ru metal complexes.

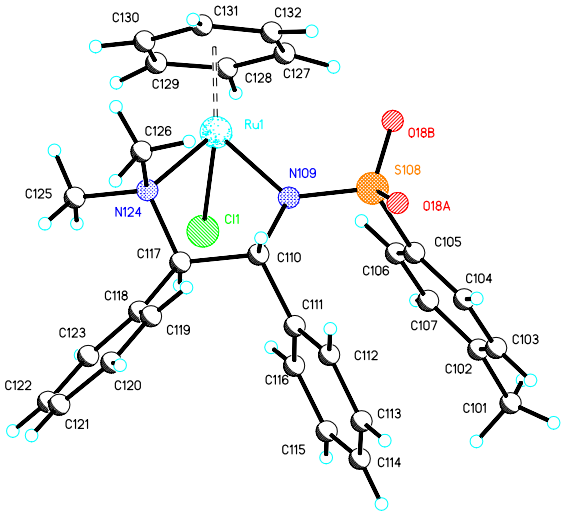
Synthesis of *N*-[(1*R*,2*R*)-2-(dimethylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide benzeneruthenium chloride 7.

*Preparation of N-[(1R,2R)-2-(dimethylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide **6**.*

To a solution of (*1R,2R*)-TsDPEN **2** (1.00 g, 2.73 mmol) in dry methanol (30 mL) was added 37% formaldehyde solution (1 mL, ~ 4.5 eq) and the mixture was stirred for 15 min at 21 ^oC under inert atmosphere. To this $NaBH_3CN$ (0.684 g, 10.88 mmol, 4.0 eq) was added slowly and the mixture was stirred for 15 min followed by addition of acetic acid (2 mL, ~12.5 eq). The reaction mixture was heated to 50 ^oC and stirred for 18 h, then cooled to room temperature and diluted with 2% MeOH in DCM (100 mL). The mixture was washed with 1M NaOH (3 x 100 mL), dried over anhydrous $MgSO_4$, filtered and the solvent removed on a rotavapor to give compound **6** as white solid (1.08 g, 2.73 mmol, 100%). m.p 102-104 ^oC; $[\alpha]_D^{24}$ = +54.9 (*c* = 0.570 in $CHCl_3$); ν_{max} = 1452, 1366, 1310, 1147, 1095, 1050, 937, 814,

700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.47 (2H, d, *J* = 8.3 Hz, *o*-CH of -$SO_2C_6H_4CH_3$), 7.18-7.14 (3H, m, ArH), 7.07 (2H, d, *J* = 8.2 Hz, *m*-CH of -$SO_2C_6H_4CH_3$), 6.96-6.88 (7H, m, ArH), 6.80 (1H, br s, NHTs), 4.61 (1H, d, *J* = 10.8 Hz, -C*H*N$(CH_3)_2$), 3.54 (1H, d, *J* = 11.1 Hz, -C*H*N), 2.33 (3H, s, CH_3), 2.06 (6H, s, -N$(CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 142.61, 137.95, 137.04, 130.89, 129.72, 128.87, 128.32, 127.59, 127.52, 127.23, 126.94, 73.33, 57.21, 40.06, 21.34; *m/z* ESI-MS $[M+H]^+$ 395.2; HRMS found 395.1791 ($C_{23}H_{26}N_2O_2S$ H+ requires 395.1788, error = -1.1 ppm).

X-ray crystal structure analysis of 7 (CCDC 793889).



(one of two nearly-identical molecules in unit cell)

The unit cell contains two crystallographically independent but nearly identical molecules of compound **7**. Two ethanol molecules of crystallisation were also found. The hydrogens on the ethanol OHs were located in a difference map and allowed to refine freely but given thermal parameters equal to 1.5 times the oxygen to which they were attached. They form short contacts to the sulphonamide oxygens as tabulated below.

Specified hydrogen bonds (with esds except fixed and riding H)

D-H	H...A	D...A	<(DHA)

0.89(4)	1.97(4)	2.830(2)	161(3)	O300-H300...O18A_$1
0.84(3)	1.98(3)	2.796(2)	163(3)	O400-H400...O28B_$2

The tosyl and first phenyl seem to form a pi stack in both complexes. These pi interactions are characterised by shortest atomic contact and angle between mean planes through the interacting pi systems. Shortest atomic contact 3.1388 (0.0031) C105 - C111. Angle between mean planes through C102 C103 C104 C105 C106 C107 to C111 C112 C113 c114 C115 C116 is 16.00 (0.14) degrees. Shortest atomic contact 3.1226 (0.0028) C205 - C212. Angle between mean planes through C202 C203 C204 C205 C206 C207 to C211 C212 C213 c214 C215 C216 is 23.70 (0.11) degrees. Symmetry operators used to define atoms in the above contacts were $1 x, y+1, z+1 and $2 x, y, z-1.

Crystal Data: $C_{31}H_{37}ClN_2O_3RuS$, M = 654.21, Triclinic, space group P1 a = 10.3603(2), b = 11.0519(3), c = 14.0747(3) Å , α = 90.6376(19)˚, β = 103.5283(17)˚, γ = 107.614(2)˚, U = 1487.56(6) $Å^3$ (by least squares refinement on 22067 reflection positions), T =100(2)K, λ = 0.71073 Å, Z = 2, D(cal) = 1.461 Mg/m^3, F(000) = 676. mu(MoK-α) = 0.721 mm^{-1}. Crystal character: orange block. Crystal dimensions 0.40 x 0.18 x 0.14 mm.

Synthesis of {*N*-[(1*R*,2*R*)-2-((3-cyclohexa-1,4-dienyl)propyl)(methyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide } ruthenium chloride monomer 8.

*Preparation of N-[(1R,2R)-2-(3-cyclohexa-1,4-dienylpropylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide **12**.*

To a solution of (*1R,2R*)-TsDPEN **2** (1.50 g, 4.09 mmol, 1.25 eq) in dry methanol (20 mL) was added solution of aldehyde **11** (0.445 g, 3.27 mmol, 1.0 eq) in dry methanol (10 mL) and MS 4Å (1.5 g) followed by acetic acid (3-4 drops) at 21 ^oC under an inert atmosphere. The resulting suspension was stirred for 2.5 h to form an imine. To this, $NaBH_3CN$ (0. 4 g, 6.54 mmol, 2.0 eq) was added slowly and resulting mixture was stirred for 48h at 22 ^oC. The reaction mixture was filtered and concentrated to give residue. The residue was dissolved in DCM (50 mL) and washed with 1M NaOH (2 x 50 mL), dried over anhydrous $MgSO_4$, filtered and evaporated on a rotavapor to give white solid. The crude compound was purified by flash column chromatography using hexane:EtOAc (8:2) to give compound **12** as a white solid (1.28 g, 2.63, 80%). m.p 106-108 ^oC; $[\alpha]_D^{24}$ = -10.35 (*c* = 0.285 in $CHCl_3$); ν_{max}=3294,

2819, 1454, 1430, 1333, 1129, 1060, 806, 699, 684 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.37 (2H, d, *J* = 8.1 Hz, *o*-CH of -$SO_2C_6H_4CH_3$), 7.16-7.10 (3H, m, ArH), 7.10-7.02 (5H, m, ArH), 6.98-6.88 (4H, m, ArH), 6.28 (1H, br s, NHTs), 5.70-5.64 (2H, m, -CH=CH), 5.32-5.28 (1H, m, -CH=), 4.24 (1H, d, *J* = 8.0 Hz, C*H*NH$(CH_2)_3$), 3.60 (1H, d, *J* = 8.0 Hz, C*H*NHTs), 2.64 (2H, m, NH(CH_2)), 2.51 (2H, m, -CH_2 of NH$(CH_2)_3$), 2.43-2.22 (2H, m, -CH_2 of CH_2CH=CH), 2.33 (3H, s, CH_3), 1.87 (2H, m, CH_2CH=CH), 1.70 (1H, br s, N*H*$(CH_2)_3$), 1.55-1.45 (2H, m, $CH_2CH_2CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 142.63, 139.31, 138.35, 137.01, 134.25, 129.04, 128.26, 127.88, 127.51, 127.33, 127.08, 124.21, 118.68, 67.75, 63.02, 46.64, 34.79, 28.77, 27.45, 26.70, 21.40; *m/z* ESI-MS $[M+H]^+$ 487.2; HRMS found 487.2427 ($C_{30}H_{34}N_2O_2S$ H+ requires 487.2414, error = -2.7 ppm).

Preparation of N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(methyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide ***13****.*

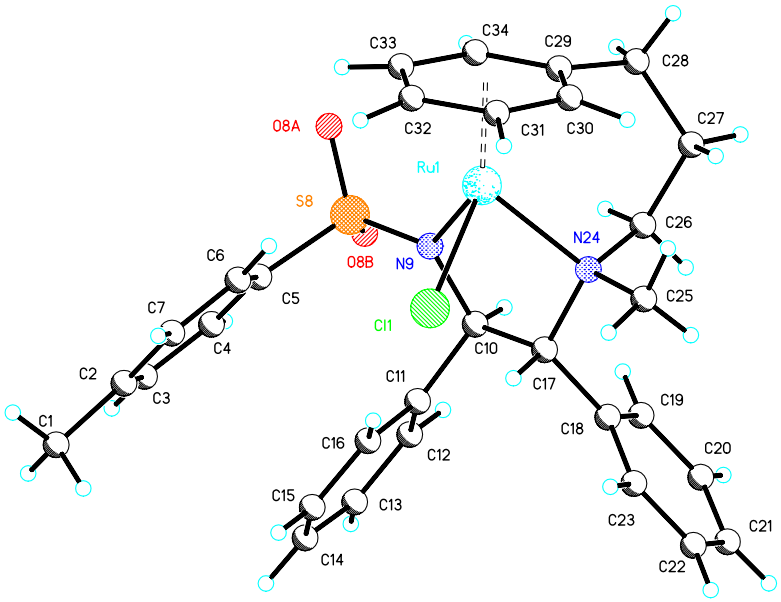
To a solution of *N*-[(1*R*,2*R*)-2-(3-cyclohexa-1,4-dienylpropylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide **12** (0.5 g, 1.03 mmol) in dry methanol (15 mL) was added 37% formaldehyde solution (0.251mL, 3.0 eq) and the mixture was stirred for 15 min at 21 ^oC under an inert atmosphere. To this, $NaBH_3CN$ (0.129 g, 2.06 mmol, 2.0 eq) was added slowly and the mixture stirred for 15 min followed by addition of acetic acid (2-3 drops). The reaction was heated to 50 ^oC and stirred for 16 h, then cooled to room temperature and diluted with 2% MeOH in DCM (50 mL). The mixture was washed with 1M NaOH (3 x 40 mL), dried over anhydrous $MgSO_4$, filtered and evaporated on a rotavapor to give crude product. The crude product was purified by flash column chromatography using Hexane:EtOAc (8.8:1.2) to give compound **13** as colourless oil (0.375 g, 0.748 mmol, 73%). $[\alpha]_D^{24}$ = +56.5 (*c* 0.115 in $CHCl_3$); ν_{max}= 3663, 3028, 2927, 2818, 1599, 1453, 13112, 1151, 1092, 932, 809, 699, 663 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.45 (2H, d, *J* = 8.1 Hz, *o*-CH of -$SO_2C_6H_4CH_3$), 7.18-7.14 (3H, m, ArH), 7.06 (2H, d, *J* = 8.1, *m*-CH of -$SO_2C_6H_4CH_3$), 6.96-6.90 (7H, m, ArH), 6.80 (1H, br s, NHTs), 5.75-5.71 (2H, m, -CH=CH), 5.50-5.46 (1H, m, -CH=), 4.67 (1H, d, *J* = 11.0 Hz, C*H*NH$(CH_2)_3$), 3.62 (1H, d, *J* = 11.0 Hz, C*H*NHTs), 2.76-2.68 (2H, m, -CH_2 of NHCH_2), 2.67-2.59 (2H, m, NHCH$_2$CH$_2$CH_2), 2.33 (3H, s, CH_3), 2.30-2.15 (2H, m, CH_2CH=CH), 2.03 (3H, s, NCH_3), 2.05-1.96 (2H, m, CH_2CH=CH), 1.70-1.55 (2H, m, -CH_2 of NH(CH$_2$CH_2CH$_2$); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 142.64, 138.13, 137.29, 134.41, 131.85, 129.74, 128.94, 128.40, 127.72, 127.65, 127.60, 127.27, 127.00, 124.28, 118.69, 72.67, 57.22, 56.06, 53.34, 36.04, 35.00, 29.00, 26.78, 25.50, 21.42; m/z

ESI-MS $[M+H]^+$ 501.2; HRMS found 501.2575 ($C_{31}H_{36}N_2O_2S$ H+ requires 501.2570, error = -1.0 ppm).

Preparation of {N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(methyl)ammonium chloride)-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride dimer ***14****.*

The preparation is described in the paper, however a note is added here. Protonation renders the basic nitrogen configurationally locked, hence two diastereoisomers may be formed with respect to the TsDPEN chirality. Since this is a dimer, the total no of diastereoisomers which may be formed is four, hence four brs peaks are observed at low field.

X-ray crystal structure analysis of 8 (CCDC 793888).



The asymmetric unit contains the complex. There is probably an intramolecular pi stacking interaction between the tosyl and the first phenyl of the chiral diamine. This is characterised as closest atomic contact and angle between mean planes through the interacting pi systems.

Closest atomic contact 3.1465 (0.0053) C5 - C11. Angle between mean planes for the tosyl C2 C3 C4 C5 C6 C7 to the phenyl C11 C12 C13 C14 C15 C16 is 8.91 (0.24) degrees. There are no other prominent features in the crystal packing.

Crystal Data : $C_{31}H_{33}ClN_2O_2RuS$, M = 634.17, Orthorhombic, space group P2(1)2(1)2(1) a = 8.39707(8), b = 9.14896(9), c = 35.0858(3) Å , α = 90˚, β = 90˚, γ = 90˚, U = 2695.44(4) $Å^3$ (by

least squares refinement on 7176 reflection positions), T =100(2)K, λ = 1.54184 Å, Z = 4, D(cal) = 1.563 Mg/m^3, F(000) = 1304. mu(MoK-α) = 6.436 mm^{-1}. Crystal character: orange block. Crystal dimensions 0.2108 x 0.1391 x 0.0319 mm

Synthesis of {*N*-[(1*R*,2*R*)-2-((3-cyclohexa-1,4-dienyl)propyl)(3-phenylpropyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride monomer 9.

Preparation of N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(3-phenylpropyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide ***S1****.*

To a solution of *N*-[(1*R*,2*R*)-2-(3-cyclohexa-1,4-dienylpropylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide **12** (0.275 g, 0.566 mmol, 1.0 eq) in dry methanol (24 mL) was added phenyl propionaldehyde (75 μL, 0.566 mmol, 1.0 eq) followed by acetic acid (3-4 drops) at 21 ^oC under inert atmosphere. The resulting suspension was stirred for 2.5 h to form the imine. To this, $NaBH_3CN$ (71.1 mg, 1.132 mmol, 2.0 eq) was added and resulting mixture was stirred at 50 ^oC for 22h. The reaction mixture was filtered and concentrated to give a residue. This was dissolved in DCM (20 mL) and washed with 1M NaOH (2 x 15 mL), dried over anhydrous $MgSO_4$, filtered and evaporated on a rotavapor to give the crude product which was purified by flash column chromatography using hexane:EtOAc (8.5:1.5) to give compound **S1** as an oil (0.190 g, 0.315 mmol, 55%). $[\alpha]_D^{24}$ = +18.54 (*c* = 0.240 in $CHCl_3$); ν_{max} =3676, 2972, 1600, 1453, 1347, 1151, 1076, 1057, 932, 810, 699, 663 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 7.40 (2H, d, *J* = 8.2 Hz, ArH), 7.36-7.22 (2H, m, ArH), 7.22-7.13 (6H, m, ArH), 7.02 (2H, d, *J*=8.1 Hz, *m*-CH of $-SO_2C_6H_4CH_3$), 6.95-6.85 (7H, m, ArH), 6.81 (1H, br s, NHTs), 5.76-5.70 (2H, m, -CH=CH), 5.48-5.42 (1H, m, -CH=), 4.74 (1H, d, *J* = 10.8 Hz, CH adjacent to NCH_2), 3.71 (1H, d, *J* = 7.8 Hz, C*H*NHTs), 2.79-2.47 (8H, m, CH_2), 2.31 (3H, s, CH_3), 2.16-1.81 (6H, m, CH_2), 1.68-1.58 (2H, m, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 142.54, 141.86, 138.15, 137.51, 134.36, 133.05, 129.70, 129.86, 128.38, 127.82, 127.63, 127.58, 127.19, 126.98, 125.86, 124.27, 118.64, 77.20, 69.31, 57.33, 49.11, 48.96, 35.12, 33.67, 30.06, 29.03, 26.75, 25.99, 21.39; m/z ESI-MS $[M+H]^+$ 605.3; HRMS found 605.3203 ($C_{39}H_{44}N_2O_2S$ H+ requires 605.3196, error = -1.0 ppm).

Preparation of {N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(3-phenylpropyl)ammonium chloride)-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride dimer ***S2****.*

To a solution of *N*-[(1*R*,2*R*)-2-((3-cyclohexa-1,4-dienyl)propyl)(3-phenylpropyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide **S1** (0.175 g, 0.290 mmol) in DCM (10 mL) was added a 2M solution of HCl in diethyl ether (0.44 mL, 0.869 mmol) and the mixture was stirred at 22 ^{o}C for 30 min under inert atmosphere. The solvents were removed under reduced pressure to give a residue. The residue was dissolved in ethanol (15 mL) and ruthenium trichloride trihydrate (61 mg, 0.232 mmol) was added. The resulting mixture was heated at 78 ^{o}C for 16 h. The reaction mixture was cooled, a solid separated out filtered and was washed with ethanol to give compound **S2** as green solid (0.158 g, 0.976 mmol, 67%), m.p > 300 ^{o}C; m/z ESI-MS $[M\text{-}Cl]^{+}$ 703.1 (monomer formed *in-situ*). This was used directly in the next step.

*Preparation of {N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(3-phenylpropyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride monomer **9**.*

A mixture of {*N*-[(1*R*,2*R*)-2-((3-cyclohexa-1,4-dienyl)propyl)(3-phenylpropyl)ammonium chloride)-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride dimer **S2** (0.100 mg, 0.062 mmol) and triethylamine (51.5 µL, 0.370 mmol, 6.0 eq) in IPA (10 mL) was heated at 80 ^{o}C for 1 h under inert atmosphere. The reaction mixture was cooled to room temperature and concentrated to give a residue. This was filtered and washed with water. The solid was purified by flash column chromatography on Florisil. The complex was eluted in hexane:EtOAc:MeOH (5:4:1) to give compound **9** as light brown solid (45 mg, 0.0610 mmol, 49%). Mp 156-158 ^{o}C with decomposition; $[\alpha]_D^{24}$ = +1525 (*c* = 0.004 in $CHCl_3$); ν_{max} =2972, 1600, 1494, 1453, 1259, 1131, 1086, 939, 842, 699, 664 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.45-7.35 (1H, m, ArH), 7.28-7.09 (7H, m, ArH), 7.00-6.90 (3H, m, ArH), 6.88-6.80 (2H, m, ArH), 6.70 (2H, d, *J*= 8.1 Hz, *m*-CH of $-SO_2C_6H_4CH_3$), 6.60-6.54 (2H, m, ArH), 6.52-6.44 (2H, m, ArH), 6.37 (1H, d, *J* = 5.2 Hz, *o*-CH of Ru-Ph), 6.32 (1H, t, *J* = 5.7 Hz, *o*-CH of Ru-Ph), 5.74 (1H, t, *J* = 5.8 Hz, *m*-CH of Ru-Ph), 5.36 (1H, t, *J* = 5.8 Hz, *m*-CH of Ru-Ph), 4.79 (1H, d, *J* = 6.0 Hz, C*H*N(CH_2)), 4.80-4.65 (2H, m, C*H*NHTs, *p*-CH of Ru-Ph), 3.62-3.50 (1H, dt, *J* = 13.6, 3.9 Hz, N(CH_2)), 3.46-3.23 (3H, m, CH_2), 2.82-2.76 (1H, m, CH_2), 2.30-2.10 (5H, m, CH_2), 2.15 (3H, s, CH_3), 1.55-1.45 (1H, m, CH_2), 1.08-0.95 (1H, m, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 141.68, 140.90, 139.60, 139.12, 134.09, 132.89, 130.18, 128.90, 128.72, 128.44, 128.38, 127.91, 127.43, 126.83, 126.26, 126.15, 125.08, 86.93, 86.91, 85.92, 85.62, 83.70, 78.25, 68.09, 60.82, 49.73, 33.04, 28.52, 26.79, 24.15, 21.14; m/z ESI-MS $[M\text{-}Cl]^{+}$ 703.1; HRMS found 703.1946 ($C_{39}H_{41}ClN_2O_2RuS$-Cl requires 703.1937, error = -1.3 ppm).

Use of synthesized complexes in transfer hydrogenation.

*Synthesis of dihydroisoquinoline **16**:*

*Preparation of hydrochloride salt of 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline **16**.*

To a solution of 3,4-dimethoxyphenethylamine (5.0 g, 27.6 mmol) in dry DCM (50 mL) was added acetic anhydride (2.61 mL, 27.6 mmol) at 18 ^{o}C under an inert atmosphere. The reaction mixture was stirred at 18-20 ^{o}C for 18 h. The reaction mixture was washed with saturated citric acid (10 mL), saturated $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was separated, dried over anhydrous $MgSO_4$, filtered and evaporated on a rotavapor to give a solid. The solid was scratched in hexane, filtered and dried to give compound the amide of 3,4-dimethoxyphenethylamine as a light brown solid (6.10 g, 27.2 mmol, 99%) m.p 100-102 ^{o}C; ν_{max} =3250, 3084, 2926, 2840, 1631, 1563, 1515, 1471, 1261, 1250, 1155, 1138, 1019, 814, 765 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 6.85-6.73 (1H, m, ArH), 6.72-6.68 (2H, m, ArH), 5.58 (1H, br s, NH), 3.87 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.54-3.46 (2H, m, C*H*$_2$NHCO), 2.76 (2H, t, *J* = 6.9 Hz, CH_2), 1.94 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 170.10, 147.68, 131.34, 120.60, 111.86, 111.34, 55.91, 55.87, 40.77, 35.18, 23.33; m/z ESI-MS $[M+H]^+$ 224, $[M+Na]^+$ 246. To a solution of the amide formed above (6.0 g, 26.90 mmol) in dry toluene (50 mL) was added $POCl_3$ (2.50 mL, 26.90 mmol) at 20 ^{o}C under inert atmosphere. The resulting mixture was refluxed at 111 ^{o}C for 2 h. The reaction mixture was cooled to room temperature and concentrated on a rotavapor to give a brown solid. The solid was scratched in diethyl ether, filtered and dried under vacuum to give compound **16H.Cl** as a light brown solid (6.5 g, 100%). m.p 128-130 ^{o}C with decomposition; ν_{max} 2778, 1664, 1602, 1562, 1514, 1426, 1343, 1274, 1296, 1216, 1163, 1104, 1010, 872, 816cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 13.43 (1H, br s, NH), 7.20 (1H, s, ArH), 6.86 (2H, m, ArH), 4.02 (3H, s, OCH_3), 3.96 (3H, s, OCH_3), 3.88 (2H, br t, *J* = 7.2 Hz, CH_2N), 2.76 (2H, t, *J* = 7.9 Hz, CH_2), 2.85 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 174.42, 156.64, 148.89, 133.15, 111.88, 111.34, 110.85, 56.61, 56.47, 41.12, 25.18, 20.00; m/z ESI-MS $[M+H]^+$ 206.

*Preparation of 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline **16**.*

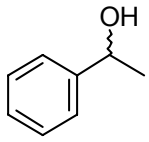
A solution of compound **16H.Cl** prepared above (6.0 g, 24.90 mmol) in DCM (70 mL) was washed with saturated K_2CO_3 (2 x 25 mL) and brine (20 mL). The organic layer was separated, dried over anhydrous Na_2SO_4, filtered and evaporated on a rotavapor to give a solid. The solid was scratched in cold diethyl ether, filtered and dried to give compound **11** as

a light yellow solid (4.60 g, 95%) m.p 124-126 ^{o}C; ν_{max} 2925, 1626, 1603, 1571, 1513, 1329, 1271, 1212, 1155, 1060, 871, 808 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 6.99 (1H, s, ArH), 6.69 (2H, m, ArH), 3.92 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 3.63 (2H, t, *J* = 7.5 Hz, CH_2N), 2.63 (2H, t, *J* = 7.5, CH_2), 2.36 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 163.54, 150.73, 147.36, 131.05, 122.43, 110.15, 108.92, 56.14, 55.89, 46.97, 25.68, 23.39; m/z ESI-MS $[M+H]^+$ 206.[2]

700 NMR reaction for hydride detection: To a 5 mm NMR tube were added the catalyst (3 mol%), and formic acid/triethylamine 5:2 complex (0.6 mL). After 30 minutes a solution of substrate in acetonitrile (0.8 cm^3) was added followed by 0.05 mL of C_6D_6. The reaction was followed by ^{1}H-NMR with hydride detection. The ^{1}H-NMR spectra of the reduction products matched that reported previously for this compound, as given below.

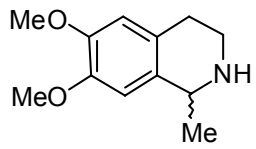
Characterisation data for reduction products: [1,3]

1-Phenylethanol:



Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 115 ^{o}C, P = 15 psi, gas H_2, Ketone 9.81 min, *R* isomer 15.32 min, *S* isomer 16.41 min). $[\alpha]_D^{22}$ + 53 (c 0.55 in $CHCl_3$) 98 % ee sample (*R*)[1] (lit.[4] $[\alpha]_D^{25}$ +49 (c 1.00 in $CHCl_3$) 95% ee (R)); ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 7.38-7.24 (5H, m, Ph), 4.87 (1H, q, *J* = 6.5, CH), 2.07 (1H, br s, OH), 1.48 (3H, d, *J* = 6.5, CH_3);

Salsolidine (6,7-Dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline) [2]*:*



Enantiomeric excess and conversion determined by GC analysis (Chrompac cyclodextrin-β-236M-19 50m, T = 170 ^{o}C, P = 15 psi, gas H_2, Imine 38.46 min, *S* isomer 35.12 min, *R* isomer 35.94 min). $[\alpha]_D^{22}$ = –40.1 (c 0.06 in $CHCl_3$) 94 % ee sample (*S*)[1] (lit.[5] $[\alpha]_D^{25}$ +56.5 (c 1.00 in $CHCl_3$) 91% ee (R)). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ 6.61 (1H, s, ArH), 6.57 (1H, s, ArH), 4.14 (1H, q, *J* = 6.6, CH), 3.85 (6H, s, 2 x OCH_3),

3.36 – 3.24 (1H, m, CH_2), 3.12 – 3.00 (1H, m, CH_2), 2.94 – 2.79 (1H, m, CH_2), 2.78 – 2.66 (1H, m, CH_2), 1.50 (3H, d, J = 6.6, CH_3).

5. References.

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4. J. E. D. Martins, D. J. Morris, B. Tripathi and M. Wills, *J. Organomet. Chem.* 2008, **693**, 3527 – 3532.
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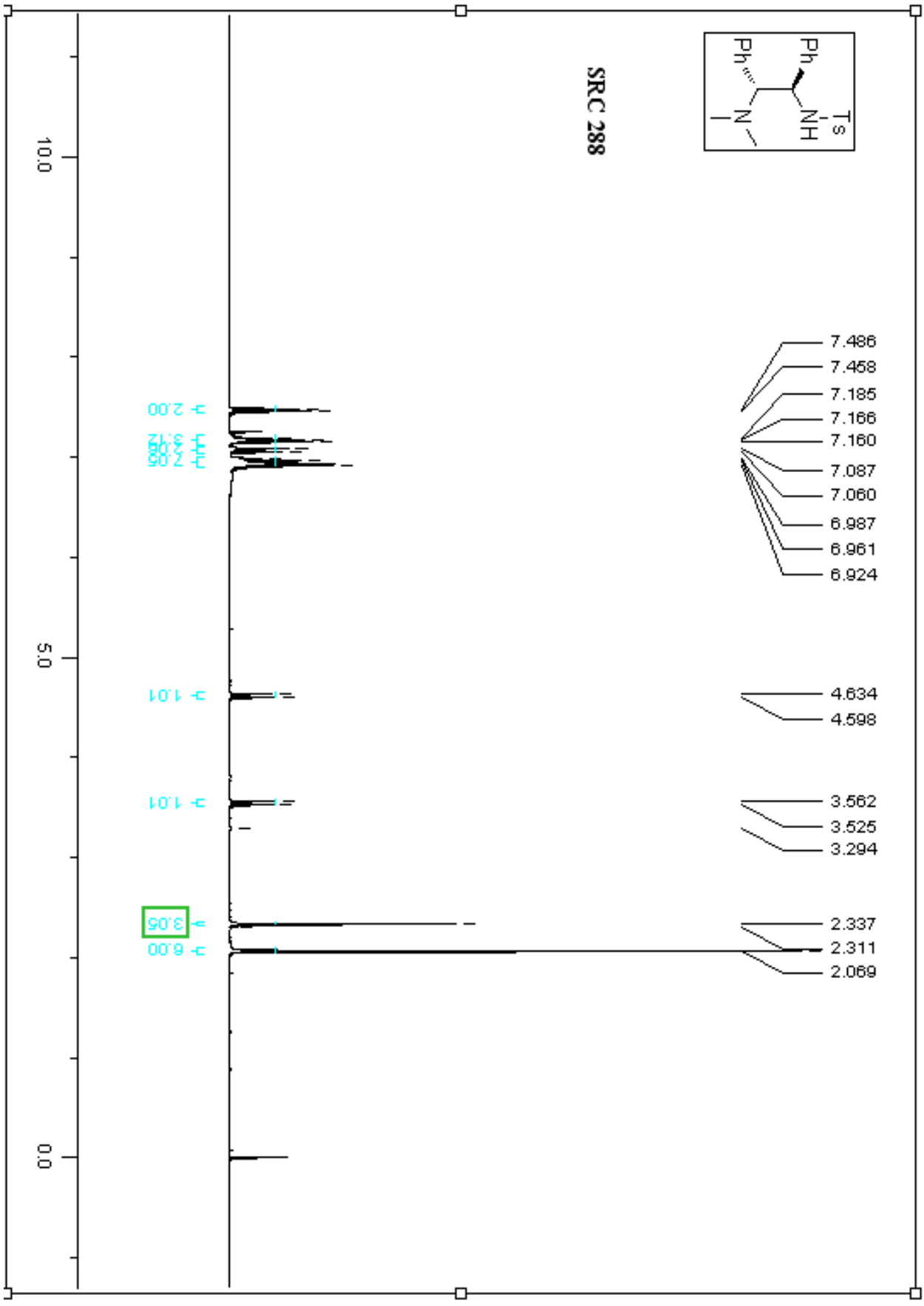
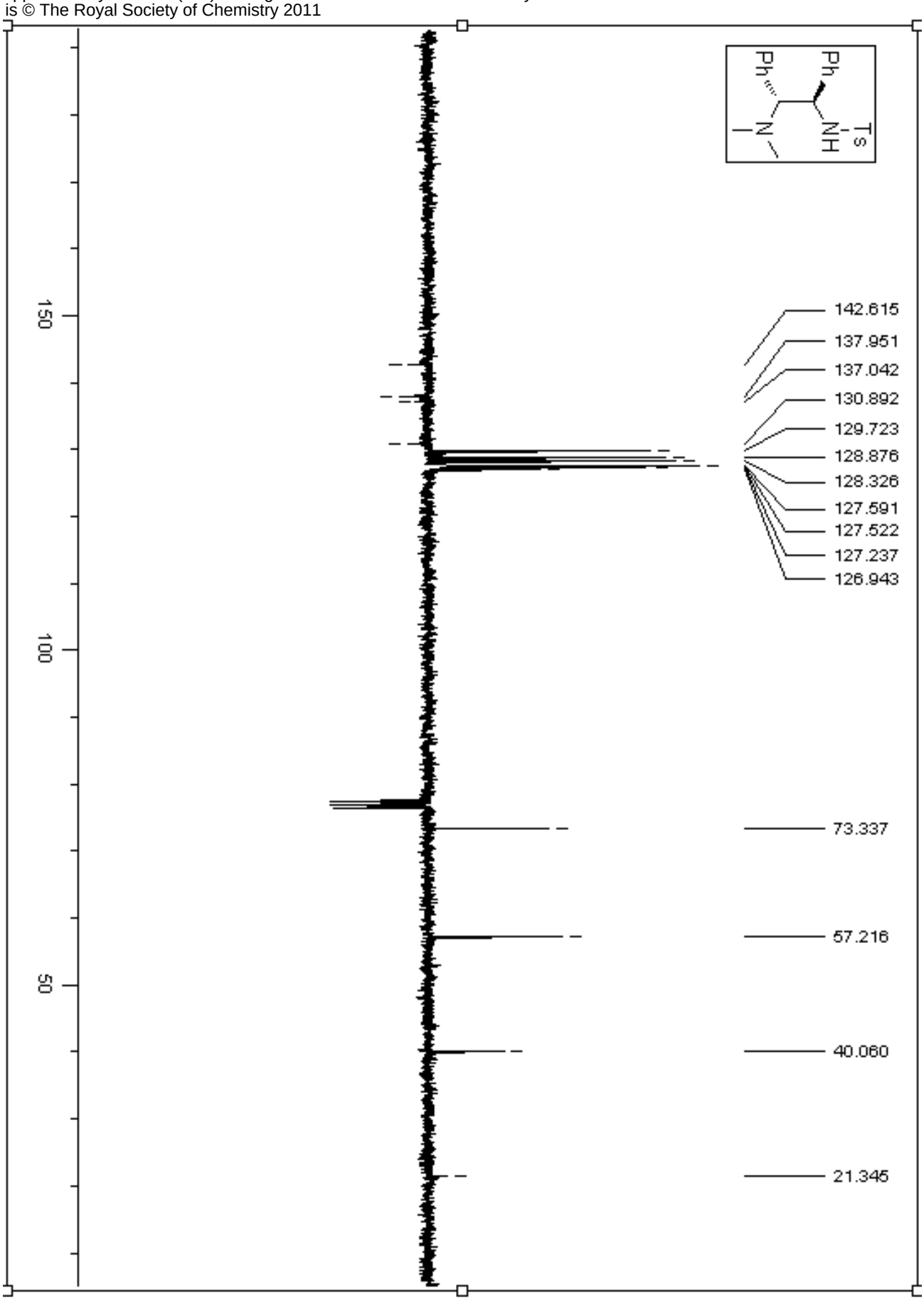
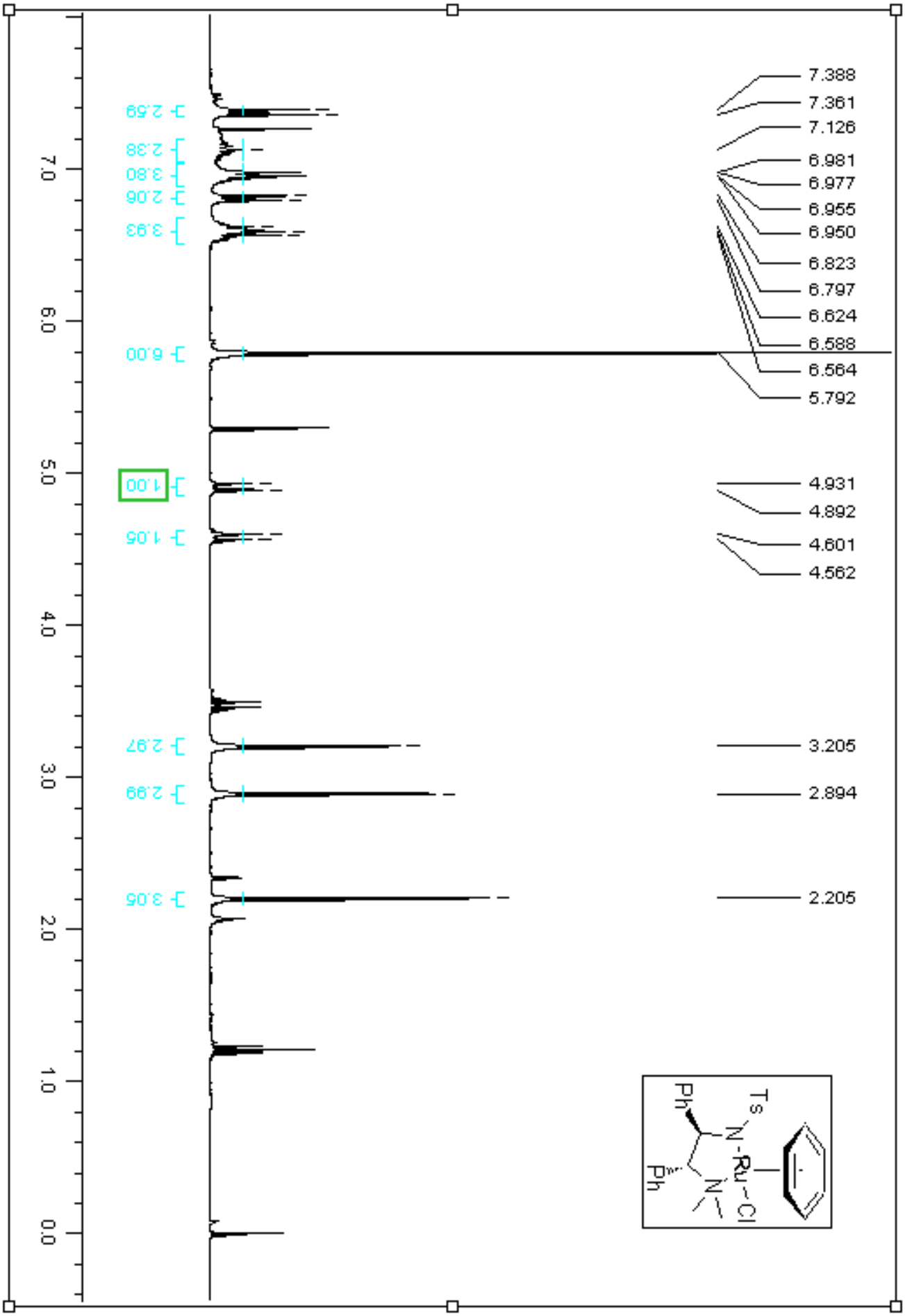
6. NMR data for catalysts and intermediates.

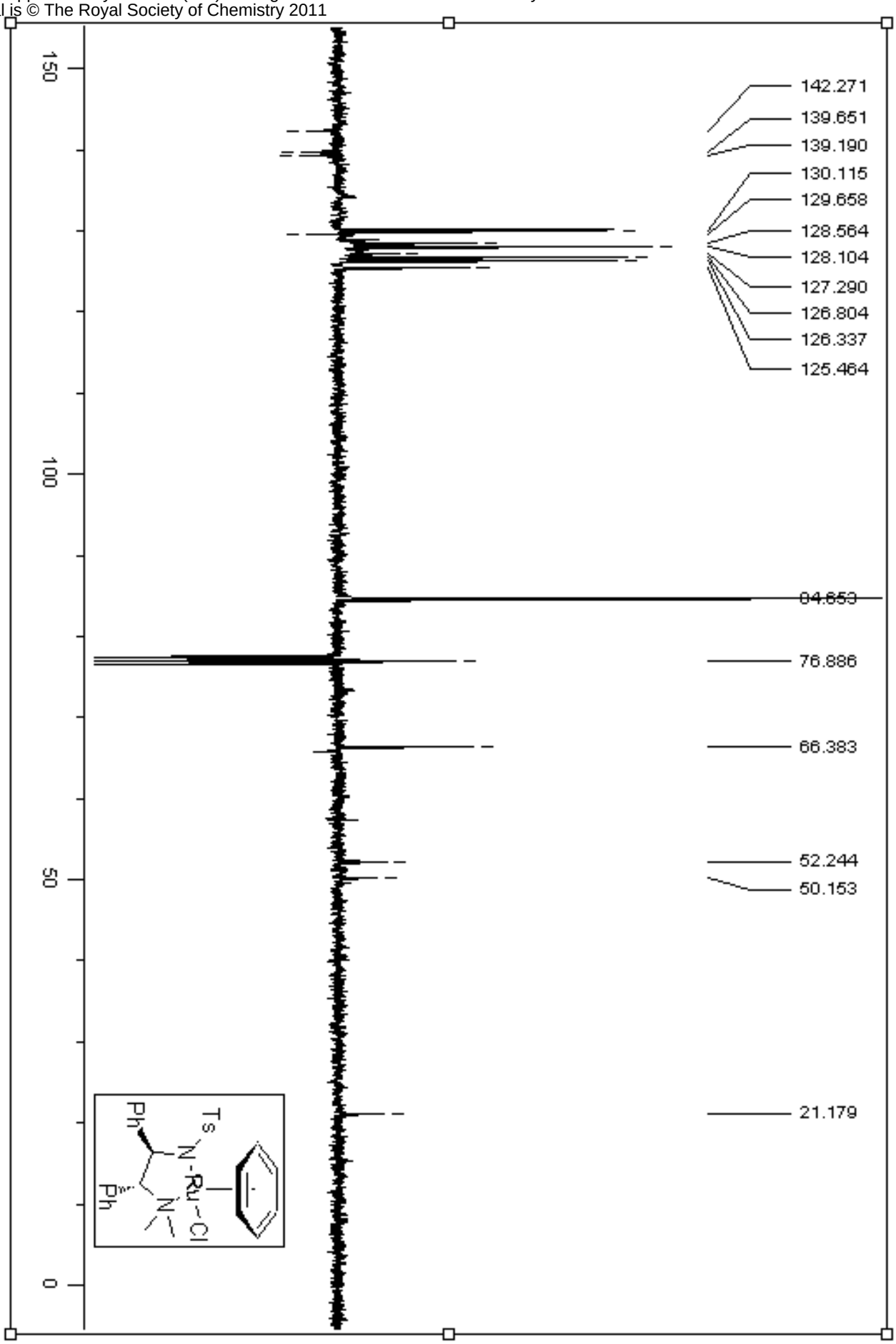
N-[(1R,2R)-2-(dimethylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide ***6***.



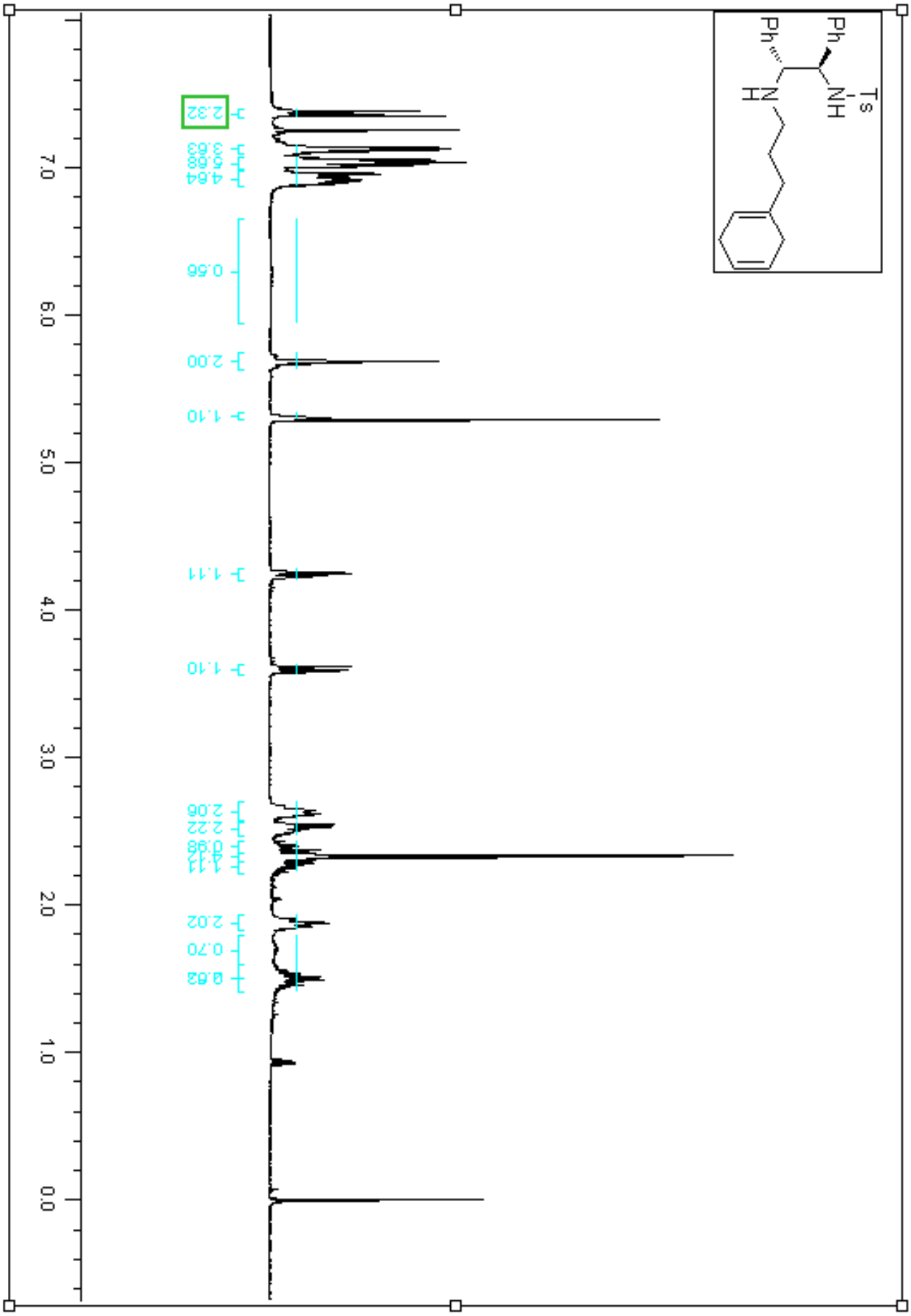


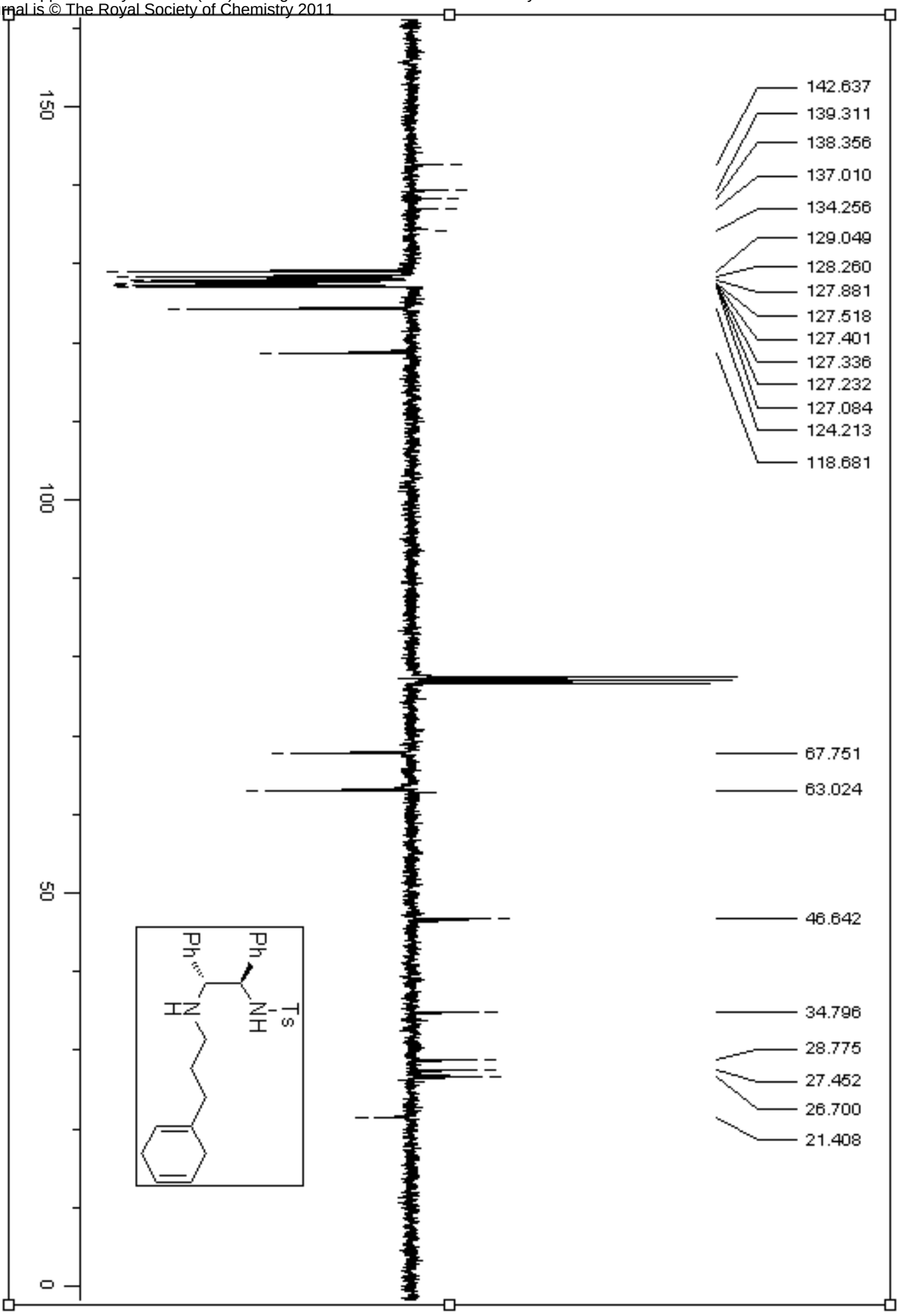
N-[(1R,2R)-2-(dimethylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide benzeneruthenium chloride 7.



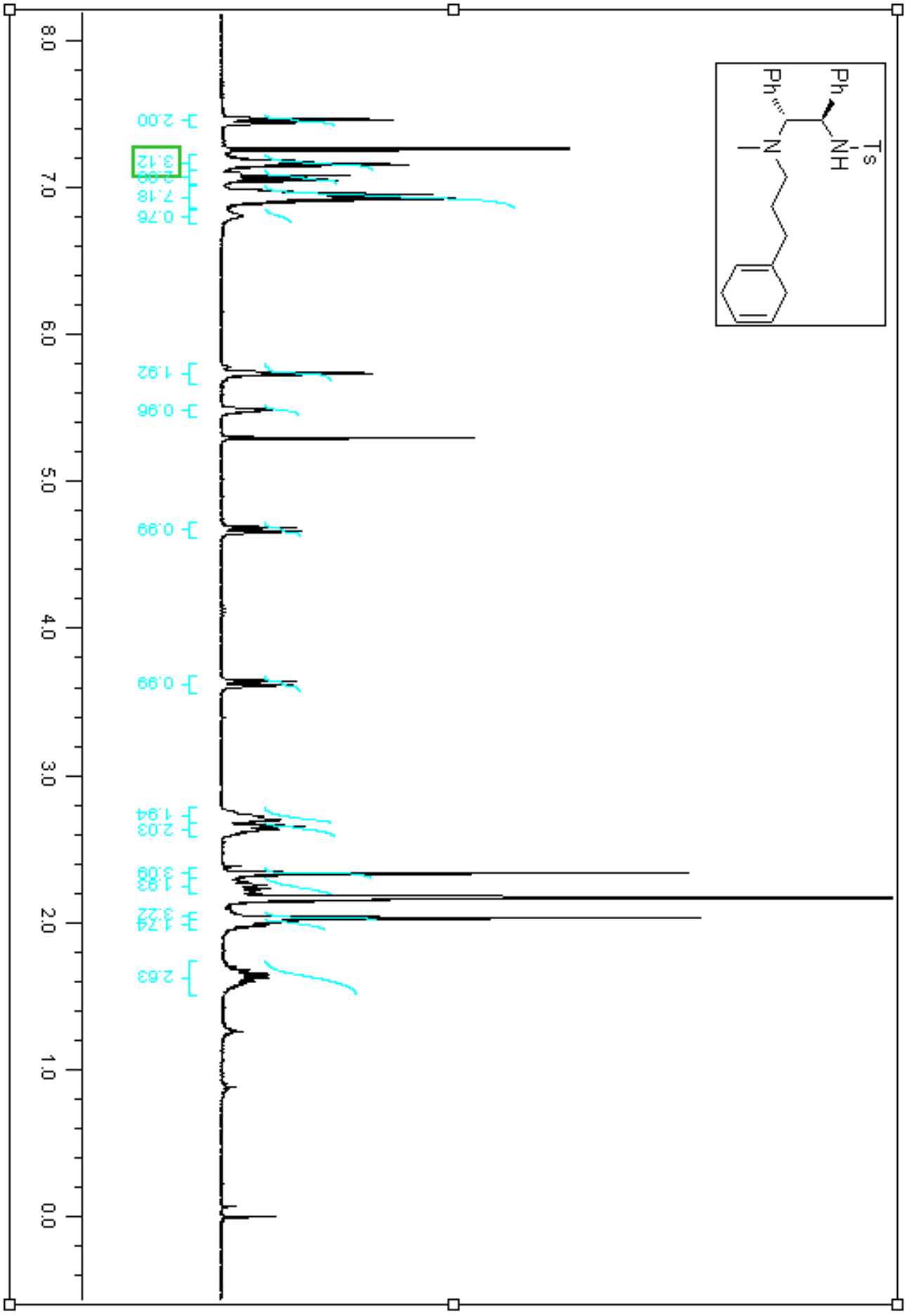


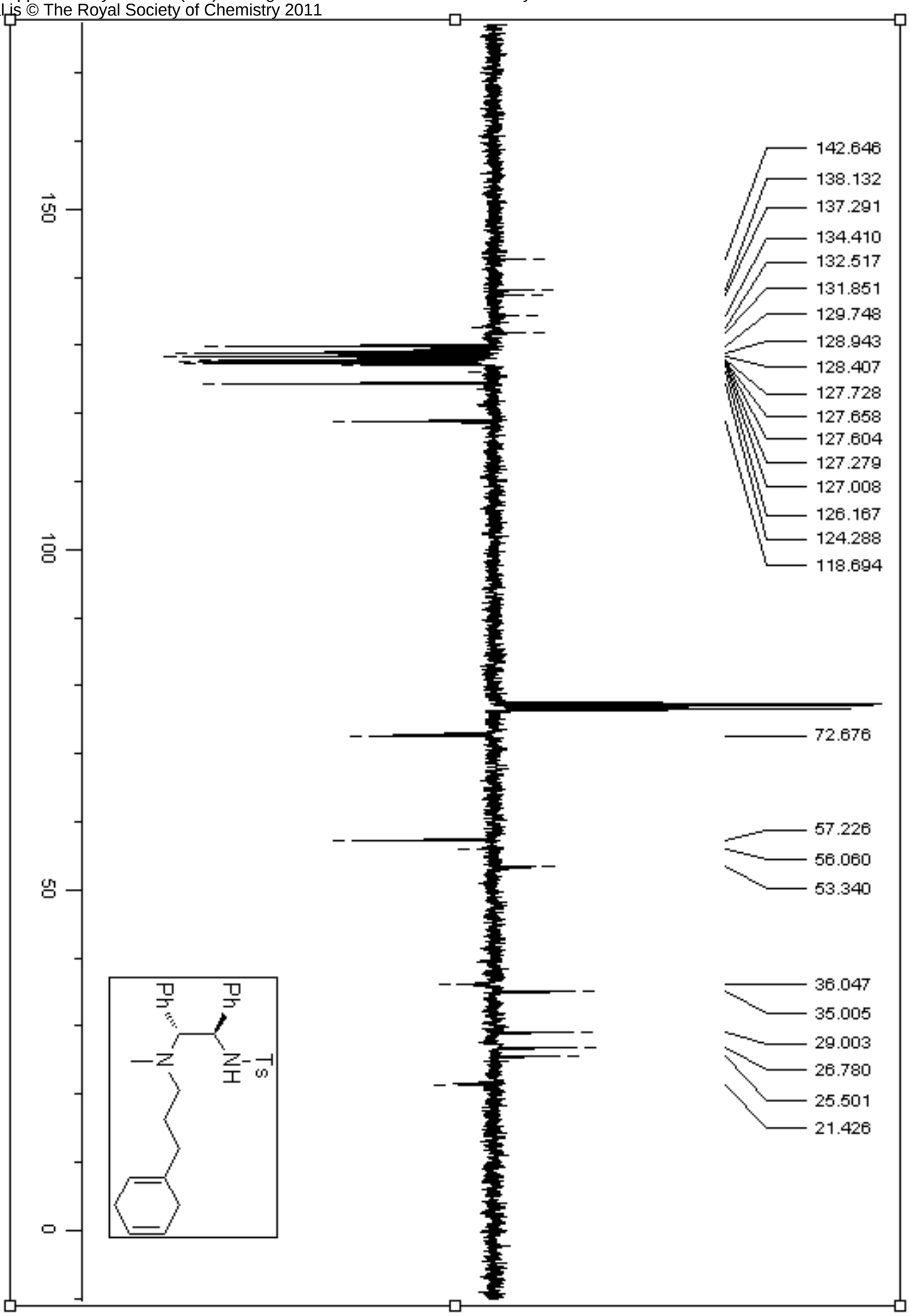
N-[(1R,2R)-2-(3-cyclohexa-1,4-dienylpropylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide ***12***.



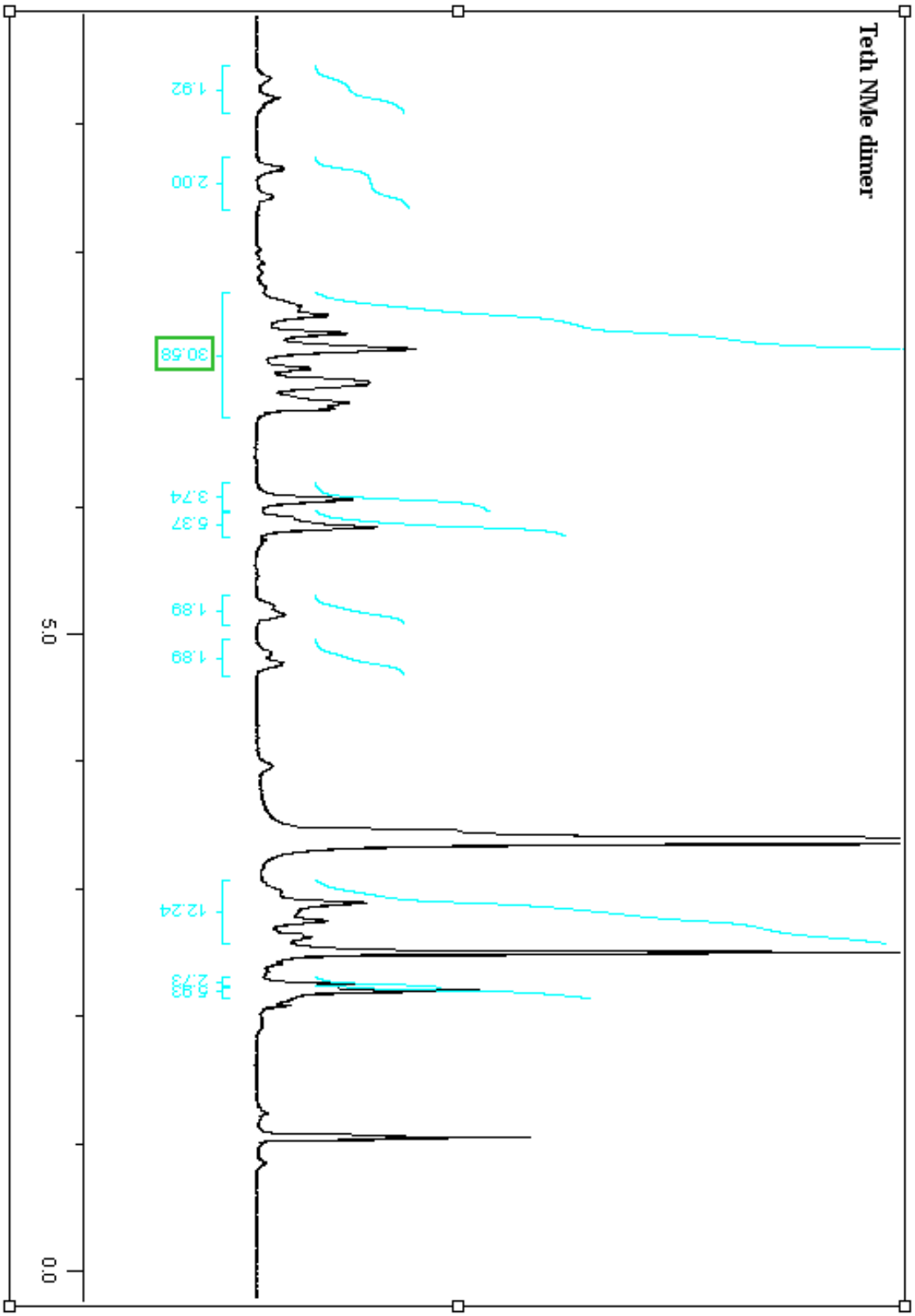


N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(methyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide ***13***.

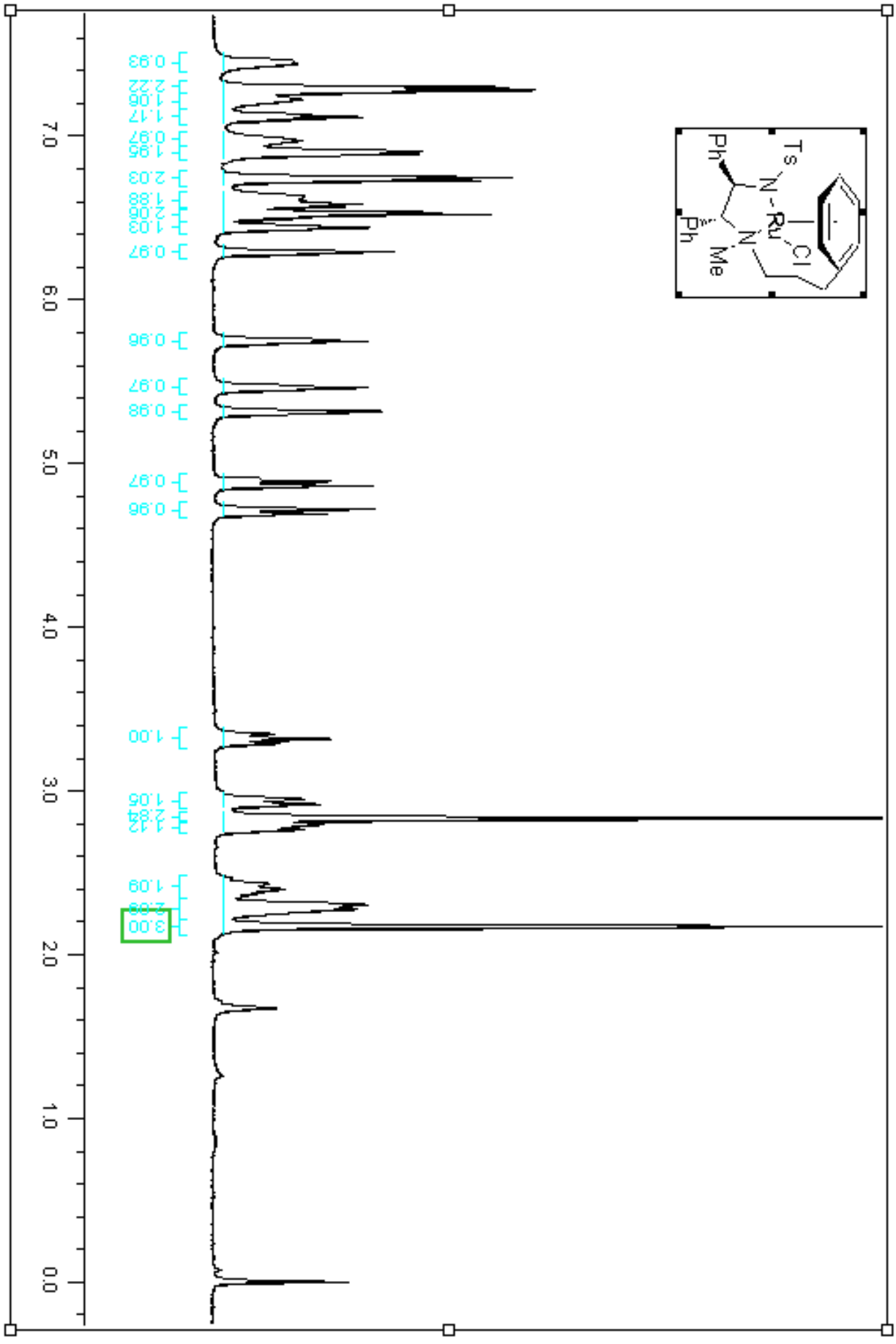


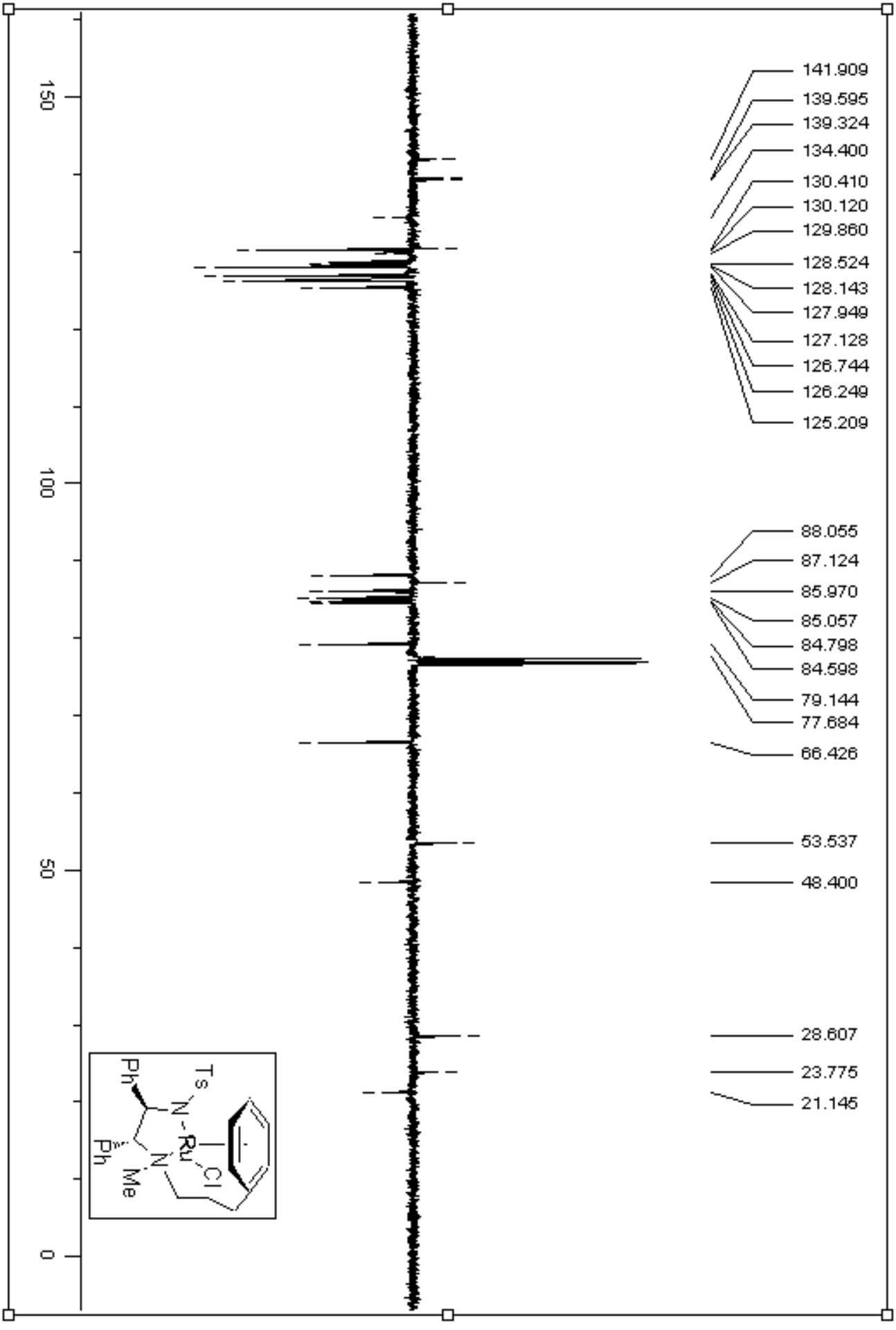


{N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(methyl)ammonium chloride)-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride dimer ***14***.

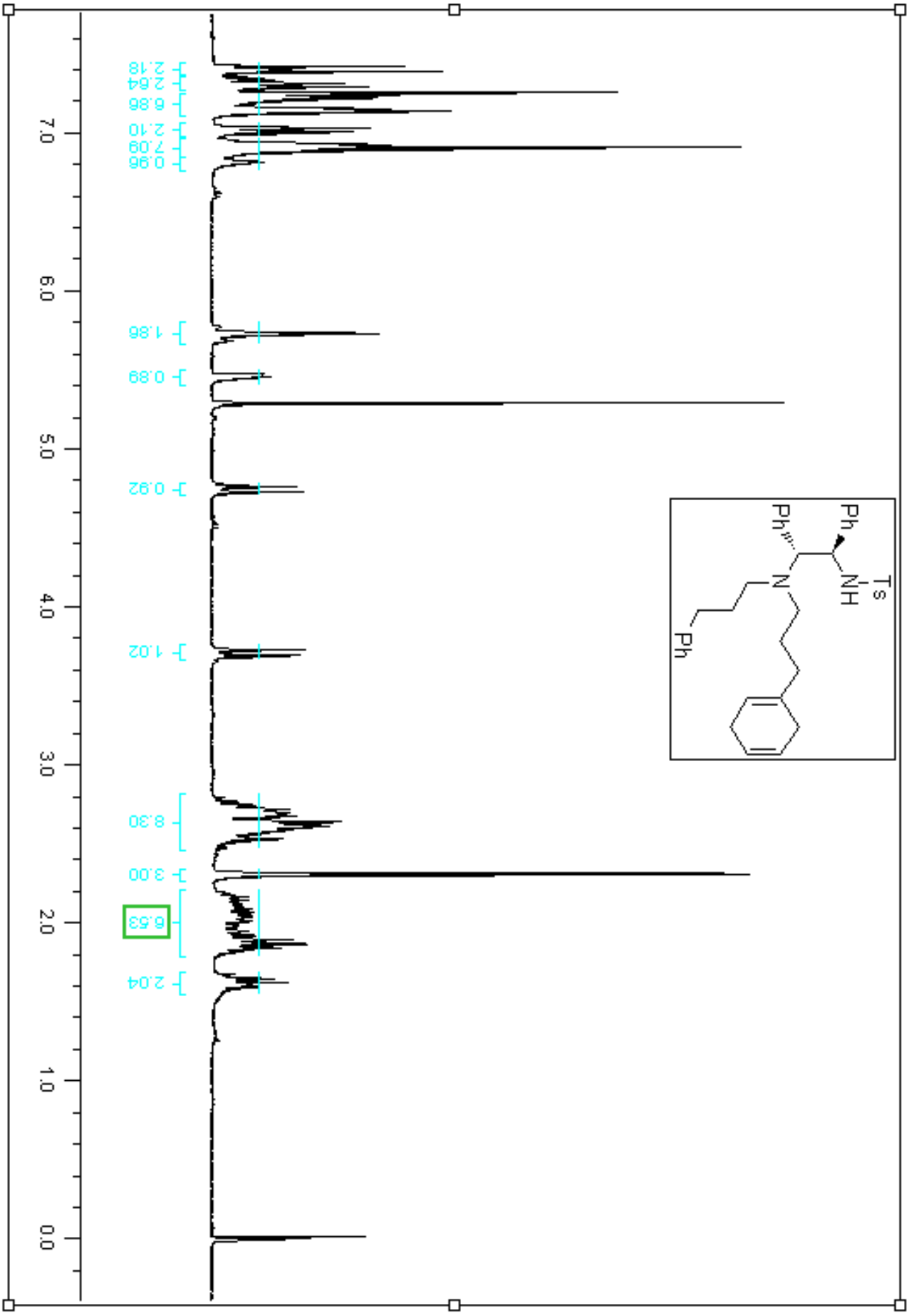


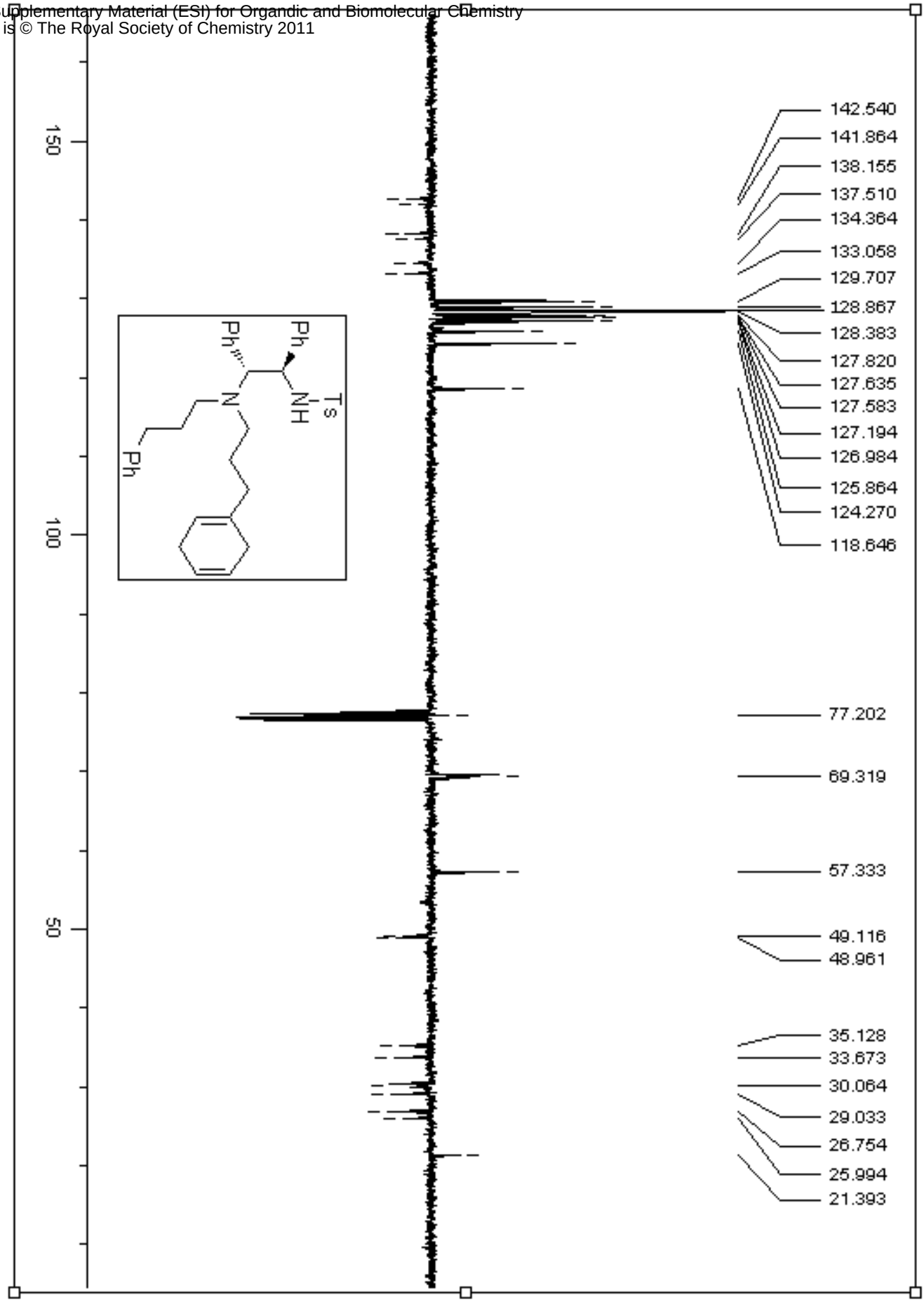
{N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(methyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride monomer ***8***.





N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(3-phenylpropyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide ***S1***.





{N-[(1R,2R)-2-((3-cyclohexa-1,4-dienyl)propyl)(3-phenylpropyl)amino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide} ruthenium chloride monomer ***9****.*