Transfer hydrogenation reduction of acetophenone catalyzed by Ru(II) and Rh(I) complexes with ligands derived from (1*R*,2*R*)-cyclohexane-1,2-diamine

Norma Aidé Cortez, Celia Z. Flores-López, Ramón Rodríguez-Apodaca, Lucía Z. Flores-López, Miguel Parra-Hake, and Ratnasamy Somanathan*

Centro de Graduados e Investigación, Instituto Tecnológico de Tijuana, Apartado Postal 11000, Tijuana, B.C. México
E-mail: somantha@sundown.sdsu.edu

Dedicated to Professor E. Juaristi on the occasion of his 55th birthday
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Abstract
A number of bidenate and tridentate ligands were synthesized from chiral mono sulfonamides, which were derived from cyclohexane-1,2-diamine. These ligands were tested with Ru(II) and Rh(I) for catalytic activity in the transfer hydrogenation reaction of ketone.

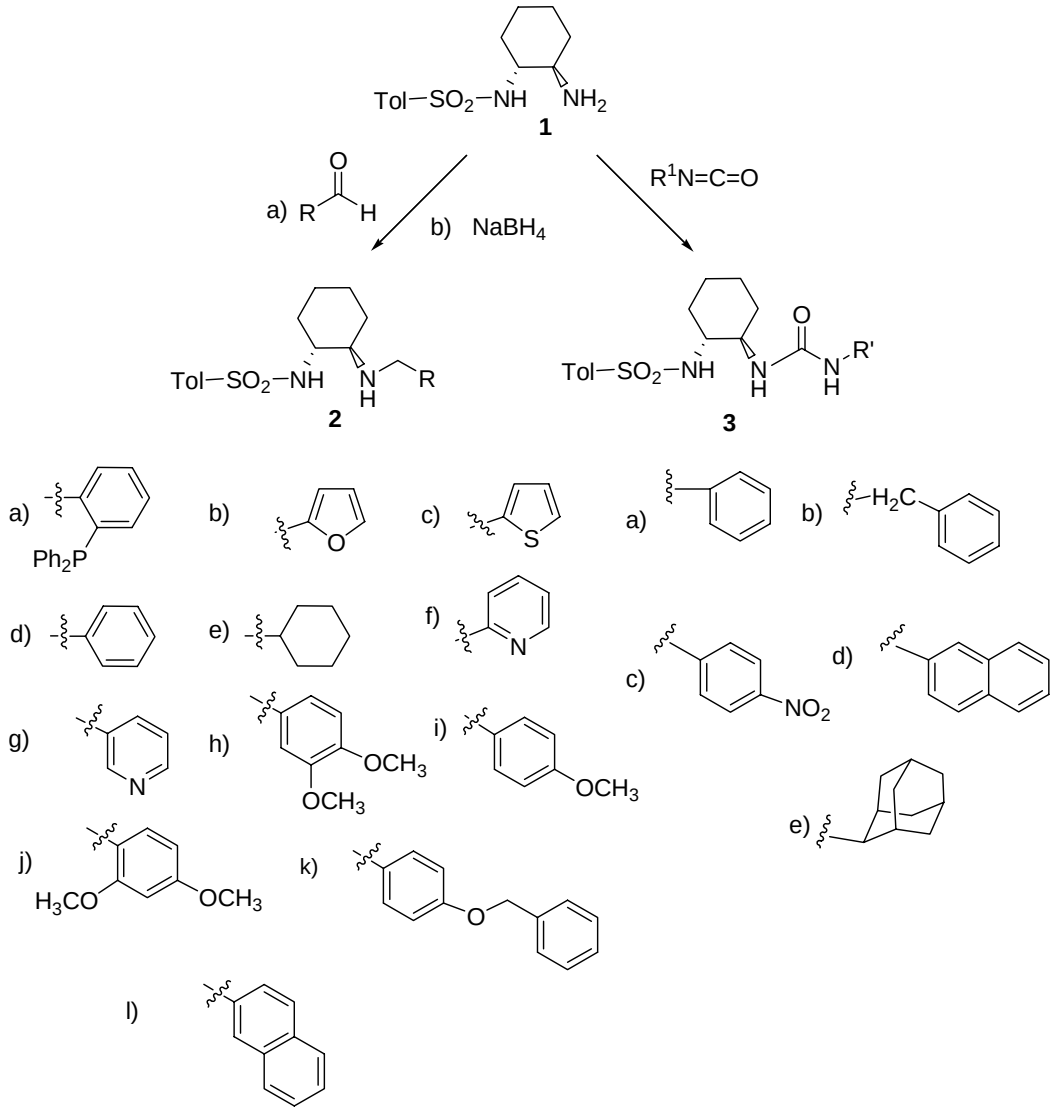
Keywords: Catalytic transfer hydrogenation, acetophenone reduction, Ru(II), Rh(I), chiral ligands, cyclohexane-1,2-diamine

Introduction

Asymmetric reduction of ketones by transfer hydrogenation from isopropanol or using hydrogen gas is a useful technique, whereby a chiral center is introduced into the molecule in a single step.[1-6] Of these two techniques transfer hydrogenation has attracted much attention due to its simplicity of operation compared to the use of gaseous hydrogen reduction, which requires special apparatus and is usually carried out under high pressures. A tremendous number of chiral ligands of the type [NN], [NO], [NNP], [PNP], [NNNN] and [PNNP],[7-12] have been used as auxiliaries with metals such as Ru,[7-17] Rh,[18a-d] Ir,[19] Al[20] and Sm.[21] Recently we reported the use of chiral [NNP] ligands derived from cyclohexane-1,2-diamine in the enantioselective reduction of ketones.[22] These phosphorous containing ligands gave high enantioselectivities (80-99%) and low yields (20%) in the hydrogen transfer reduction of ketone. Continuing on the same lines, our objective was to synthesize new chiral ligands maintaining the cyclohexane 1,2-diamine as a backbone and test them in the transfer hydrogenation of ketone with metals such as Ru(II) and Rh(I).

Results and Discussion

The readily available monosulfonamide from cyclohexane-1,2-diamine[23] was converted into a library of over 80 of bidentate and tridentate ligands by reaction with aldehydes and isocyanates, synthesis of a selected few is shown in Scheme 1.

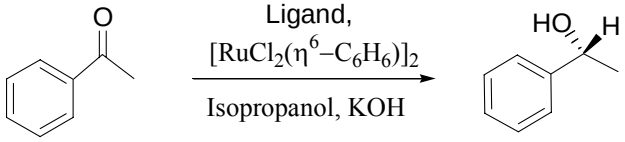


Scheme 1

These ligands were then screened for catalytic activity in the asymmetric hydrogen transfer reaction with Ru(II), Rh(I) complexes (Table 1). Ligands **2b-l** when used with $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$ and isopropanol gave the secondary alcohol with enantioselectivities from moderate to high (47-91% ee), but in low yields (20-30%) as shown in Table 1. A previous literature report has indicated that tridentate monourea substituted diamine ligands gave high enantioselectivities in

the transfer hydrogenation reduction.[24] Based on this we attempted the reduction of ketone with urea ligands derived from the monosulfonamides **3a-e** (Scheme 1), which resulted in low yields (20-30%) and low to moderate enantioselectivities (12-79%), when used with $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$. The low yields in these reactions suggest, either steric crowding around the metal center in the transition state, or more likely the tridentate ligands with additional heteroatom on these substituents binds to ruthenium leading to a catalytically inactive species (Figure 1). Ligands **4, 5** with *ortho* diphenylphosphine substituent reported previously (Scheme 2),[22] when used with $[RuCl_2(PPh_3)_3]$ gave high enantioselectivities (80-99%) and low yields, and failed to show any reaction with $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$. This strongly supports our assumption that the heteroatom (X, in Figure 1) is involved in binding with the metal, inhibiting the intermediate catalytic species. This could be the major factor, at least when $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$ is used in the reduction. Attempts to obtain X-ray quality crystals of the intermediate derived from **2a** failed.

Table 1. Asymmetric transfer hydrogenation of acetophenone using ligands derived from (1*R*,2*R*)-cyclohexane-1,2-diamine with $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$[a]



Entry	Ligand	% e.e. (Configuration)
1	2a	No reaction[b]
2	2b	87 (*R*)
3	2c	86 (*R*)
4	2d	83 (*R*)
5	2e	47 (*R*)
6	2f	73 (*R*)
7	2g	91 (*R*)
8	2h	73 (*R*)
9	2i	82 (*R*)
10	2j	63 (*R*)
11	2k	66 (*R*)
12	2l	70 (*R*)
13	3a	79 (*R*)
14	3b	14 (*R*)
15	3c	12 (*R*)
16	3d	39 (*R*)
17	3e	74 (*R*)

[a] Yields were between 20-30 %.
[b] Ref. 22.

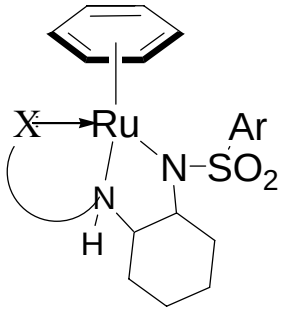
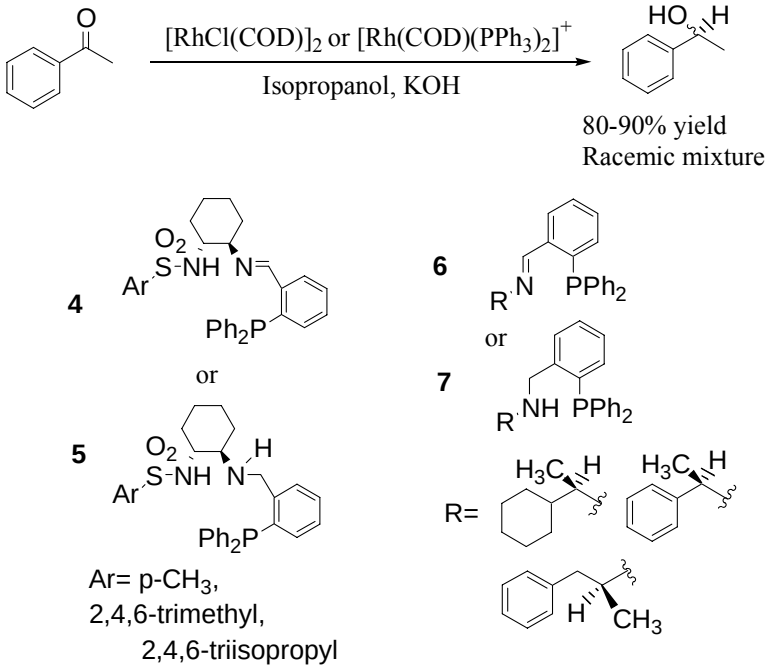


Figure 1

Interestingly, when ligands **4, 5** were used with $[RhCl(COD)]_2$ or $[Rh(COD)(PPh_3)_2]PF_6$ as 1:1 or 1:2 (metal:ligand) mixture as catalyst in the transfer hydrogenation reaction, excellent yields were obtained of the alcohol (80-90%), but as a racemic mixture (Scheme 2). This is in keeping with Lemaire's observation, where the ligand displaces only one of the COD ligands, and since the chiral center is far from the metal, it is unable to induce enantioselectivity in the formation of the alcohol.[25] Ligands **6, 7** reported previously gave similar results, a racemic mixture in 80-90% yield, suggesting that the ligands must be binding to rhodium in a bidentate fashion (Scheme 2).[22]



Scheme 2

Experimental Section

General Procedures. All experiments were carried out under inert atmosphere using standard Schlenk techniques. Solvents were dried and purified according to standard methods. All commercially available reagents were used as received. Starting monosulfonamide,[23] Schiffs bases,[26] their reduced derivatives,[22] and monourea derivatives[25] were prepared by previously reported methods.

***N*-((1R,2R)-2-(Furan-2-ylmethylamino)cyclohexyl)-4-methylbenzenesulfonamide (2b).** White solid; 1.30 g, 92% yield; mp 120-122 °C; $[\alpha]^{25}_{D}$= -49.6° (c 0.005, $CHCl_3$). IR (KBr) 3314, 3080, 2925, 2858, 1596, 1496, 1451, 1334, 1309, 1156, 1079, 1012, 906, 890, 818, 746, 675 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 2H)), 7.23-7.36 (m, 3H), 6.12 (d, *J* = 4.0 Hz, 1H), 5.29 (bs, 1H), 3.56-3.76 (m, 2H), 2.65 (bs, 1H), 2.40 (s, 3H), 2.20 (td, *J* = 7.0 and *J* = 3.4 Hz, 1H), 2.0 (s, 3H), 4.12-1.62 (m, 3H), 0.9-1.15 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) 153.1, 142.4, 136.6, 128.8, 126.5, 109.4, 105.9, 58.8, 56.6, 42.2, 31.9, 30.4, 23.7, 23.6, 20.6. HRMS-FAB (*m/z*): $[M + H]^+$ calculated for $C_{18}H_{24}N_2O_3S$, 348.15076; found, 348.15084.

4-Methyl-*N*-((1R,2R)-2-(thiophen-2-ylmethylamino)cyclohexyl)benzenesulfonami-de (2c). White solid; 0.60 g, 88% yield; mp 113-115 °C; $[\alpha]^{25}_{D}$= -49.6° (c 0.005, $CHCl_3$). IR (KBr) 3314, 3311, 3078, 2933, 2867, 2756, 1617, 1494, 1450, 1311, 1228, 1156, 1083, 1017, 7978, 917, 861, 817, 717, 656, 550, 527 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 2H)), 7.24 (d, *J* = 8.0 Hz, 2H), 7.22 (dd, *J* = 5.0 Hz and *J* = 5.0 Hz, 1H), 6.94 (dd, *J* = 5.0 and *J* = 5.0 Hz, 1H), 6.85 (dd, *J* = 2.0 and *J* = 2.5 Hz, 1H), 4.0 (d, *J* = 14.0 Hz, 1H), 3.80 (d, *J* = 14.0 Hz, 1H), 2.63 (td, *J* = 4.5 and *J* = 4.0 Hz, 1H), 2.40 (s, 3H), 2.27 (td, *J* = 4.0 and *J* = 4.0 Hz, 1H), 2.1-2.16 (m, 2H), 1.62-1.70 (m, 2H), 1.14-1.20 (m, 3H), 0.94-0.99 (m, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) 144.1, 143.1, 137.1, 129.5, 127.3, 126.6, 124.6, 124.4, 59.2, 57.4, 44.8, 32.8, 31.2, 24.6, 24.4, 21.5. HRMS-FAB (*m/z*): $[M + H]^+$ calculated for $C_{18}H_{24}N_2O_2S_2$, 364.12792; found, 364.12798.

***N*-((1R,2R)-2-(Benzylamino)cyclohexyl)-4-methylbenzenesulfonamide (2d)**. Yellow solid; 0.64 g, 96% yield; mp 77-79°C; $[\alpha]^{25}_{D}$= -16.2° (c 0.005, $CHCl_3$). IR (KBr) 3244, 2937, 2858, 1598, 1451, 1321, 1167, 1084, 1066, 900, 821, 748, 678, 667, 576 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.10-7.37 (m, 7H), 5.4 (bs, 1H), 3.56 (d, *J* = 5.2 Hz, 1H), 2.68-2.70 (m, 1H), 2.37 (s, 3H), 2.12-2.22 (m, 2H), 1.65 (d, *J* = 12.1 Hz, 2H), 0.99-1.20 (m, 5H). ^{13}C NMR (200 MHz, $CDCl_3$) 143.2, 140.2, 137.3, 129.6, 128.4, 127.2, 127.0, 59.7, 57.5, 50.0, 32.7, 31.2, 24.6, 24.4, 21.4.

***N*-((1R,2R)-2-(Cyclohexylmethylamino)cyclohexyl)-4-methylbenzenesulfonamide (2e)** Pale brown solid; 0.21 g, 80% yield; mp 80-82 °C; IR (KBr) 3265, 2923, 2852, 1598, 1448, 1326, 1161, 1093, 899, 813, 662 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 2.51-2.64 (m, 1H), 2.42 (s, 3H), 2.04-2.20 (m, 4H), 1.64 (bs, 7H), 1.10-0.98 (m, 12H). ^{13}C NMR (50 MHz, $CDCl_3$) 142.8, 137.5, 129.2, 127.8, 60.8, 57.8, 53.1, 38.9, 32.8, 31.4, 27.0, 26.6, 24.6, 24.4, 21.8. HRMS-FAB (*m/z*): $[M + H]^+$ calculated for $C_{20}H_{32}N_2O_2S$, 365.22627; found, 365.22621.

4-Methyl-*N*-{2-[(pyridin-2-ylmethyl)-amino]-cyclohexyl}-benzenesulfonamide (2f). Yellow oil; 0.25 g, 78% yield; $[\alpha]^{25}_{D}$= -25° (c 0.0053, CH_2Cl_2). IR (KBr) 3255, 3056, 2935, 2857, 1595, 1578, 1499, 1320, 1157, 1088, 809, 705 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.0 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 2H), 7.62-7.72 (m, 2H), 7.16-7.24 (m, 3H), 3.76 (d, *J* = 14.0 Hz, 1H), 3.92 (d, *J* = 13.8 Hz, 1H), 2.64-2.78(m, 1H), 2.38 (s, 3H), 1.98-2.30 (m, 3H), 1.56-1.70 (m, 3H), 0.98-1.24(m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$) 159.8, 149.1, 144.1, 136.8, 136.5. 129.5, 127.5, 122.4, 60.1, 57.8, 51.2, 33.8, 32.2, 24.4, 24.2, 21.8. HRMS-FAB (*m/z*): $[M + H]^+$ calculated for $C_{19}H_{25}N_3O_2S$, 360.17457; found, 360.17451.

4-Methyl-*N*-{2-[(pyridin-3-ylmethyl)-amino]-cyclohexyl}-benzenesulfonamide (2g). Yellow oil; 0.41 g, 67% yield; IR (KBr) 3585, 3268, 3057, 2933, 2854, 1599, 1572, 1449, 1322, 1154, 899, 815, 710, 661 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 8.46 (d, *J* = 15.1 Hz, 2H) 7.73 (d, *J* = 8.3 Hz, 2H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.23-7.29 (m, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 3.79 (d, *J* = 13.3 Hz, 1H), 3.61 (d, *J* = 13.4 Hz, 1H), 2.78-2.83 (m, *J* = 4.4 Hz, 1H), 2.37 (s, 3H), 2.3 (td, *J* = 4.1 and *J* = 6.5 Hz, 1H), 1.90-2.16 (m, 4H), 1.10-1.70(m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) 21.5, 24.5, 24.6, 31.2, 32.8, 47.5, 57.4, 60.1, 127.1, 129.6, 135.6, 135.84, 137.6, 143.3, 148.4, 149.39.

***N*-[2-(3,4-Dimethoxy-benzylamino)-cyclohexyl]-4-methyl-benzenesulfonamide (2h)**. Yellow oil; 0.18 g, 81% yield; $[\alpha]^{25}_{D}$= -13° (*c* 0.0061, CH_2Cl_2). IR (KBr) 3264, 2926, 2848, 1591, 1509, 1453, 1320, 1260, 1153, 1088, 1024, 809, 662 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.72(d, *J* = 8.7 Hz, 2H), 7.22(d, *J* = 8.9 Hz, 2H), 6.85(s, 1H), 6.76-6.87(m, 3H), 3.90 (s, 3H), 3.87 (s, 3H), 3.74(d, *J* = 13.2 Hz, 1H), 3.52 (d, *J* = 12.3 Hz, 1H), 2.60-2.78 (m, 2H), 2.38 (s, 3H), 2.0-2.28 (m, 2H), 1.60 (bs, 4H), 0.8-1.15 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) 149.1, 148.2, 143.5, 132.3, 129.5, 127, 120.1, 110.2, 110.2, 110.2, 59.2, 57.5, 56.5, 49.5. HRMS-FAB (*m/z*): $[M + H]^+$ calc. for $C_{22}H_{30}N_2O_4S$. 419.20045. Found: 419.20040.

***N*-[2-(4-Methoxy-benzylamino)-cyclohexyl]-4-methyl-benzenesulfonamide (2i).** Yellow oil; 0.27 g, 73% yield; $[\alpha]^{25}_{D}$ = -5° (*c* 0.0043, CH_2Cl_2). IR (KBr) 3272, 3062, 2935, 2857, 1613, 1509, 1449, 1325, 1243, 1157, 1088, 1033, 899, 809, 667 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 3.80 (s, 3H), 3.69 (d, *J* = 12.8 Hz, 1H), 3.50 (d, *J* = 12.8 Hz, 1H), 2.64-2.7 (m, 1H), 2.38 (s, 3H), 2.2-2.26 (m, 1H), 2.06-2.14 (m, 2H), 1.58-1.7 (m, 3H), 1.12-1.20 (m, 3H), 0.90-1.02 (m, 1H) ^{13}C NMR (125 MHz, $CDCl_3$) 148.7, 143.15, 137.3, 132.25, 129.5, 129.1, 127.2, 113.8, 59.6, 57.5, 55.3, 49.5, 32.8, 31.2, 24.7, 24.5, 21.5. HRMS-FAB (*m/z*): $[M + H]^+$ calculated for $C_{21}H_{28}N_2O_3S$, 389.53264; found, 389.53261.

***N*-((1R,2R)-2-(2,4-Dimethoxybenzylamino)cyclohexyl)-4-methylbenzenesulfona-mide (2j)**. Yellow oil; 0.195 g, 80% yield; IR (KBr) 3264, 2926, 2857, 1608, 1587, 1453, 1320, 1286, 1200, 1157, 1057, 1032, 903, 813, 658 cm^{-1}. ^1H RMN (200 MHz, $CDCl_3$) δ 7.70(d, *J* = 8.2 Hz, 2H), 7.20 (d. *J* = 8.2 Hz, 2H), 7.03 (d, *J* = 8.2 Hz 1H), 6.44-6.47 (m, 2H), 3.84 (s, 3H), 3.81 (s, 3H), 3.78 (d, *J* = 11.8 Hz, 1H), 3.55 (d, *J* = 12.6 Hz, 1H), 2.60-2.76 (m, 1H), 2.38 (s, 3H), 1.96-2.18 (m, 3H), 1.56-1.74 (m, 3H), 1.06-1.22 (m, 4H). ^{13}C RMN (125 MHz, $CDCl_3$) 160, 158.3, 142.7, 136.9, 130, 129.2, 126.9, 103.5, 98.3, 59.8, 57.1, 55.3, 45.6, 32.5, 30.8, 24.6, 24.4, 21.5.

***N*-((1R,2R)-2-(4-(Benzyloxy)benzylamino)cyclohexyl)-4-methylbenzene-sulfonamide (2k).** **W**hite solid; 0.132 g, 71% yield; mp 125-127 °C; $[\alpha]^{25}_D$= +7° (c 0.0039, CH_2Cl_2); IR (KBr) 3264, 3030, 2926, 2857, 1608, 1509, 1449, 1320, 1243, 1153, 1084, 1019, 899, 813, 735, 662 cm^{-1}. ^1H RMN (200 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.32-7.45 (m, 5H), 7.19 (d, *J* = 7.9 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 5.0 (s, 2H), 3.69 (d, *J* = 12.8 Hz, 1H), 3.50 (d, *J* = 12.7 Hz, 1H), 2.69 (sext *J* = 4.3 Hz, 1H), 2.36 (s, 3H), 2.25 (td, *J* = 3.9 and *J* = 7.0 Hz, 1H), 2.1 (m, 2H), 1.61-1.69 (m, 2H), 1.15-1.16(m, 3H), 0.94-1.02 (m, 1H), ^{13}C RMN (125 MHz, $CDCl_3$) 157.9, 143.1, 137.1, 137.3, 132.33, 127.2, 127.4, 127.9, 128.6, 129.2, 129.5, 70.1, 59.5, 57.4, 49.3, 32.7, 31.1, 24.7, 24.5, 21.5.

4-Methyl-*N*-{2-[(naphthalen-2-ylmethyl)-amino]-cyclohexyl}-benzenesulfonamide (2l). Yellow oil, 0.165 g, 83% yield; $[\alpha]^{25}_D$ = +26° (c 0.0044, CH_2Cl_2); IR (KBr) 3262, 2931, 2855, 1598, 1507, 1448, 1325, 1161, 1092, 897, 814, 749, 663 cm^{-1}. ^1H NMR δ 7.82 (m, 3H), 7.71 (d, *J* = 8.3, 2H), 7.65 (s, 1H), 7.44-7.50 (m, 2H), 7.38 (m, 1H), 7.11 (d, *J* = 7.9, 2H), 3.90 (d, *J* = 13.2, 1H), 3.72 (d, *J* = 13.1, 1H), 2.74 (td, *J* = 4.5 and *J* = 5.7 Hz, 1H), 2.27 (s, 3H), 2.1-2.18 (m, 2H), 1.60-1.7 (m, 3H), 1.14-1.2 (m, 3H), 1.0-1.03 (m, 1H), 0.85-0.89 (m, 1H).^{13}C NMR (50 Mz, $CDCl_3$) 143.1, 137.6, 137.3, 133.4, 132.7, 129.5, 128.2, 127.7, 127.1, 126.4, 126.3, 126.1, 125.7, 59.8, 57.6, 50.2, 32.9, 31.3, 24.7, 24.5, 21.4.

4-Methyl-*N*-[2-(3-phenyl-ureido)-cyclohexyl]-benzenesulfonamide (3a). Brown solid; 0.2 g, 97% yield; mp 196-197 °C; $[\alpha]^{25}_D$= +29° (c 0.027, CH_2Cl_2) IR (KBr) 3394, 3095, 2927, 2855, 1665, 1597, 1440, 1316, 1154, 1087, 899, 749 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.20-7.27 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.85 (s, 1H), 4.89(d, 2H), 3.40-3.42 (m, 2H), 2.80-3.0 (m, 2H), 2.36 (s, 3H), 2.82-2.0 (m, 2H), 1.56-1.63 (m, 2H), 1.0-1.38 (m, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) 156.6, 142.9, 138.6, 138.4, 129.6, 129.1, 126.8, 123.4, 120.3, 59.7, 52.9, 34.1, 32.7, 24.7, 24.5, 21.4. Anal. calc. for $C_{20}H_{25}N_3O_3S$: C, 61.99; H, 7.92. Found: C, 62.24; H, 7.80.

1-Benzyl-3-((1R,2R)-2-(4-methylphenylsulfonamido)cyclohexyl)urea (3b). Brown solid; 0.178 g, 95% yield; mp 124-126 °C; $[\alpha]^{25}_D$= +27° (c 0.0052, CH_2Cl_2). IR (KBr) 3376, 3038, 2935, 2848, 1630, 1561, 1449, 1307, 1260, 1157, 1088, 800, 650 cm^{-1}. ^1H RMN (200 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.26-7.32 (m, 5H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.25 (bs, 1H), 4.86(bs, 1H), 4.33 (dd, *J* = 5.8 Hz, *J*= 5.4 Hz, 1H), 4.17 (dd, *J* = 5.6 Hz, *J*= 5.8 Hz, 1H), 3.46 (m, 1H), 2.37 (s, 3H), 2.75-2.92 (m, 1H), 1.50-1.98 (m, 5H), 0.98-1.36 (m, 4H). ^{13}C (200 MHz, $CDCl_3$) 157.7, 141.4, 137.6, 137, 128.1, 127.3, 126.1, 125.9, 125.5, 58.4, 51.9, 43.2, 32.6, 31.7, 23.6, 23.4, 20.4.

4-Methyl-*N*-{2-[3-(4-nitro-phenyl)-ureido]-cyclohexyl}-benzenesulfonamide (3c). Yellow solid; 92% yield; mp 116-118 °C; $[\alpha]^{25}_D$= +103° (c 0.0027, CH_2Cl_2); IR (KBr) 3366. 2926, 2853, 1883, 1605, 1550, 1495, 1321, 1151, 1105 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.91 (d, *J* = 9.2 Hz, 2H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 9.2 Hz, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 6.22(bs, 1H), 5.85(bs, 1H), 3.60(bs, 1H), 3.20(bs, 1H), 2.36(s, 3H), 2.0(bs, 2H), 1.77-1.66(m, 3H), 1.20-1.40(m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$) 155.7, 145.9, 143.7, 141.6, 138.4, 129.8,

126.5, 124.8, 117.5, 59.9, 53.1, 33.6, 32.5, 24.7, 24.6, 21.5. Anal. calc. for $C_{20}H_{24}N_4O_5S$: C, 55.54; H, 5.59. Found: C, 55.40; H, 5.45.

4-Methyl-*N*-[2-(3-naphthalen-1-yl-ureido)-cyclohexyl]-benzenesulfonamide (3d). Brown solid, 0.174 g, 95% yield; mp 175-177 °C; $[\alpha]^{25}_D$ = +57° (c 0.0052, CH_2Cl_2); IR (KBr) 3376, 3038, 2935, 2848, 1630, 1561, 1449, 1307, 1260, 1157, 1088, 80, 650 cm^{-1}.. ^1H NMR (200 MHz, $CDCl_3$) δ 7.78-8.0 (m, 1H), 7.82-7.80 (m, 1H), 7.70-7.69 (d, *J* = 8.3 Hz, 2H), 7.65-7.63 (d, *J* = 8.2 Hz, 1H), 7.51-7.53 (m, 1H), 7.45-7.47 (m, 2H), 7.37 (t, *J* = 7.7 and *J* = 8.1 Hz, 1H), 7.08-7.10 (d, *J* = 7.9 Hz, 2H), 6.58 (bs, 1H), 5.12 (d, 1H), 3.50 (bs, 1H), 2.79-2.87 (td, *J* = 4.2 and *J* = 7.0 Hz, 1H), 2.23 (s, 3H), 1.77-1.87 (m, 3H), 1.53-1.50 (d, *J* = 12.0 Hz, 2H), 0.9-1.20 (m, 4H). ^{13}C RMN (125 MHz, $CDCl_3$) 157.9, 142.8, 138.6, 138.5, 134.4, 133.2, 129.5, 128.4, 128.3, 126.8, 126.4, 126.2, 125.8, 125.7,121.9, 121.7, 59.4, 53.1, 33.8, 32.6, 24.6, 24.4, 21.3. Anal. calc. for $C_{24}H_{27}N_3O_3S$: C, 65.88; H, 6.22. Found: C, 65.79; H, 6.00.

N-[2-(3-Adamantan-2-yl-ureido)-cyclohexyl]-4-methyl-benzenesulfonamide (3e). White solid; 0.174 g, 95% yield; mp = 225-227 °C $[\alpha]^{25}_D$= +47° (c 0.0025, CH_2Cl_2); IR (KBr) 3408, 2905, 2850, 1643, 1552, 1492, 1449, 1304, 1157, 1089, 812, 665 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 6.48 (s, 1H), 4.26 (bs, 2H), 3.40 (t, *J*= 9.4 Hz, 1H), 2.78 (td, J = 4.2 y J = 6.8 Hz, 1H), 2.42 (s, 3H), 2.06 (s, 3H), 1.88-2.0 (m, 8H), 1.58-1.68 (m, 7H), 1.04-1.3 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$) 158.1, 142.7, 138.6, 129.4, 127.1, 60.0, 52.7, 51.2, 42.4, 36.4, 33.9, 29.6, 33.0, 24.9, 24.5, 21.5. Anal. calc. for $C_{24}H_{35}N_3O_3S$: C, 64.69; H, 7.92. Found: C, 64.66; H, 7.80.

General method for reduction of acetophenone

A mixture of $[RuCl_2(\eta^6\text{-}C_6H_6)]_2$ (0.015 mmol) and the chiral ligand (0.03 mmol) was placed in freshly distilled propan-2-ol (5mL). The solution was stirred at 80°C for 20 min. After being cooled to room temperature, additional propan-2-ol (10 mL) was added followed by the addition of KOH (1.5 mL, 0.1M in propan-2-ol) followed by acetophenone (1.5 mmol) in propan-2-ol. The mixture was stirred at room temperature for 20 h. The final mixture was concentrated under reduced pressure and the product purified by flash chromatography (silica gel-CH_2Cl_2/MeOH 9:1). The solvent was removed under reduced pressure to give an oily residue. The residue containing the alcohol was derivatized using acetic anhydride (0.5 mL). Enantiomeric excesses were determined by GC using a Hewlett-Packard 5890 chromatograph with a chiral β-DEX™ 120, 30 m, x 0.25 mm x 0.25μm column. The GC conditions were: oven temperature 110°C, flow rate 1.33 mL/min. The retention time for (*S*) acetate is 18.5 min, and for (*R*) acetate is 19.7 min.

Conclusions

We have synthesized a number of bidentate and tridentate ligands derived from chiral cyclohexane monosulfonamide. These ligands were found to assist the transfer hydrogenation of ketone in moderate to good enantioselectivities, but in poor yields. The low yields are probably due to steric crowding at the metal center, or due to the formation of a catalytically inactive species through heteroatom-ruthenium interaction. Further modification of the chiral diamine and its application in the transfer hydrogenation of ketone is under investigation.

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