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Catalytic asymmetric transfer hydrogenation of ketones using terpene-based chiral β-amino alcohols

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This paper is dedicated to the memory of Dr. Ronald Micetich

Abstract—Catalytic asymmetric transfer hydrogenations of aromatic alkyl ketones have been studied using $[RuCl_2(p\text{-cymeme})]_2$ and terpene-based β-amino alcohols. The limonene derived amino alcohol, (1*S*,2*S*,4*R*)-1-methyl-4-(1-methylethenyl)-2-(methylamino)cyclohexanol gave the most promising results. Chiral secondary alcohols were obtained in good to excellent yields and moderate enantioselectivities (up to 71%).

1. Introduction

The advantages of asymmetric transfer hydrogenation (ATH) using transition metal complexes as catalysts for a variety of substrates, have been well documented in the literature.[1] The development of new or improved asymmetric reduction methodologies is important for meeting the continuing need for enantiomerically pure secondary alcohols.[2] The catalysts used in asymmetric transfer hydrogenations are usually prepared from an achiral metal complex and a chiral auxiliary. In order to achieve the highest enantioselectivity possible, these catalysts should have ideal steric and electronic properties in relation to the substrate. In addition to chiral diamines,[1] β-amino alcohols are one of the most effective classes of chiral auxiliaries for asymmetric transfer hydrogenations.[3] A variety of β-amino alcohols have been successfully used to generate active catalysts in situ with $[RuCl_2(p\text{-cymene})]_2$, providing moderate to excellent catalytic activity in the ATH reduction of acetophenone. Patti et al. found that (*R*)-1-*N*-benzylamino-2-hydroxy-3-ferrocenylpropane **1** provided a 94% conversion and 70% ee (*R*) in 3 h at room temperature. Through optimization of the ligand structure, they were generally able to improve the reaction rate and asymmetric induction by increasing the steric bulk around the amine moiety via N-alkylation (Scheme 1).[3d]

While examining the chiral directive effects of several substituted 2-amino ethanol and norephedrine-based ligands in ATH reactions, van Leeuwen reported that (1*R*,2*S*)-*N*-benzyl-norephedrine **2** provided the highest asymmetric induction.[3i] Andersson et al. were successful in developing highly active and selective catalysts from 2-azanorbornyl derivative **3**.[4] Reductions using amino alcohol **3** were fast, providing 96% conversion to the alcohol and 96% ee with a S/C ratio of 5000 in 90 min. Amino alcohol (1*R*,2*S*)-*cis*-1-aminoindan-2-ol **4** was developed by Wills et al. and has been evaluated for its effectiveness in the reduction of various substrates.[5] It should be pointed out that when amino alcohols were used as chiral directors in ATH reactions, the best results were achieved using isopropanol as the hydride source. Several research groups have reported on the incompatability of amino alcohols with formic acid/triethylamine as the hydride source.[1c,d,4c,5e]

In a continuation of our interest in the development and use of terpenes in catalytic asymmetric methodology, we have synthesized several β-amino alcohols from limonene, pinene and carene.[6] Terpenes make ideal building blocks for the development of chiral auxiliaries, because they are naturally abundant, easily obtained and relatively

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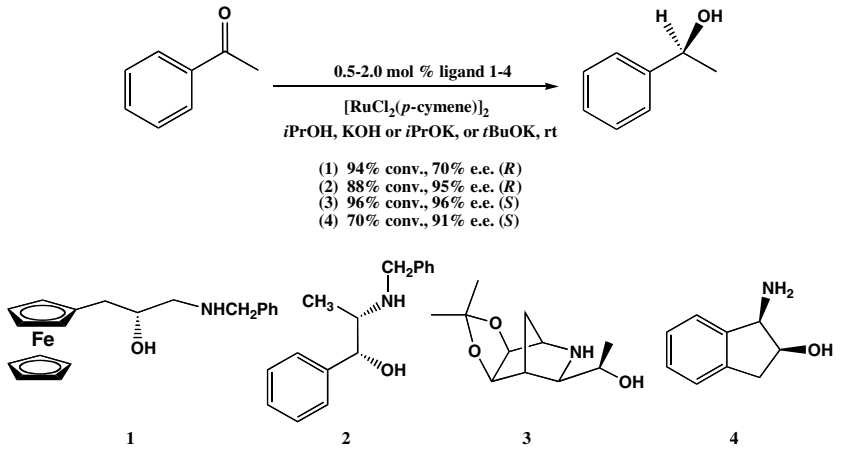


Scheme 1. Acetophenone reduction using amino alcohol ligands.

inexpensive. We reported that the cis- and trans-diastereomers of (*R*)-(+)-limonene oxide can be isolated in enantiomerically and diastereomerically pure forms from a commercially available (1:1) diastereomeric mixture of limonene oxides. Epoxide ring opening with a variety of amines allows the formation of β-amino alcohols from these chiral epoxides.[6d] Several of the amino alcohols we synthesized, were found to provide good yields and moderate enantioselectivities for the asymmetric addition of phenylacetylene to aldehydes promoted by diethyl zinc,[6a] as well as up to 87% ee for the diethyl zinc addition to aldehydes.[6b] Our recent encouraging results prompted us to further explore the scope of these amino alcohols in asymmetric catalysis. Herein, we report our results on the effectiveness of terpene-based β-amino alcohols as chiral auxiliaries for the catalytic asymmetric transfer hydrogenation of ketones.

2. Results and discussion

For our study we used the representative β-amino alcohols **5**–**10** (Fig. 1). The primary amine amino alcohol **5**, can be prepared from 3-carene oxide.[7] Ligands **6**–**10** were derived from *trans*-limonene oxide and were prepared as reported earlier.[6b]

Amino alcohols derived from terpenes have not been applied to asymmetric transfer hydrogenation as widely as other chiral ligands, such as those based on ephedrine or monotosylated diamines.[1,3] Most of the amino alcohols used for ATH have either primary or secondary alcohols, whereas amino alcohols **5**–**10** are unique in that they have tertiary hydroxyl groups. Under standard conditions, the chiral catalysts were prepared in situ by refluxing 0.25 mol % $[RuCl_2(p\text{-cymeme})]_2$ with 2.0 mol % of our amino alcohols in isopropanol at 80 °C for 1 h. The base was then added (2.5 mol %) and stirred for 30 min, before the addition of the substrate (0.1 M ketone). The reduction of acetophenone was carried out at 25 °C and the reaction progress monitored by TLC. The product alcohol was isolated and the enantiomeric excess determined by chiral GC or HPLC analysis.

Before screening our series of amino alcohols, we performed an initial study using ligand **6** and acetophenone

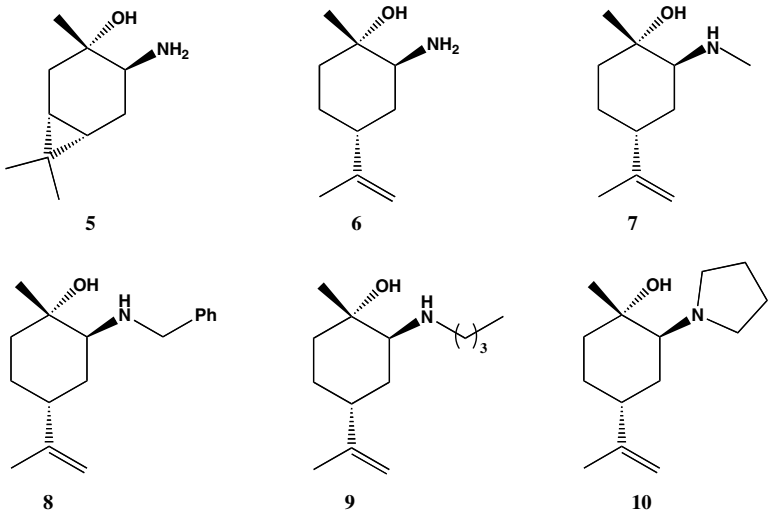


Figure 1. Terpene-based β-amino alcohols for use in Ru(II)-catalyzed transfer hydrogenation of acetophenone.

to try and optimize the reaction conditions. Several different bases are currently in use by a number of research groups conducting research into ATH, including NaOH, KOH, *i*-PrONa, and *t*-BuOK.[1] Changing the base from *i*-PrONa to *t*-BuOK lead to an increase in asymmetric induction (Table 1, entries 1 and 2).

Table 1. Influence of the amount of base, ligand, and substrate on conversion and enantioselectivity for the reduction of acetophenone using ligand **6**

Entry	Molar ratio of M:L*:*t*-BuOK	Conv. [%]	ee [%]
1	1:8:10[a]	99	20
2	1:8:10	99	50
3	1:8:20	68	35
4	1:8:40	61	33
5	1:40:10[b]	92	27
6	1:8:10[c]	42	26

[a] *i*-PrONa was used for base.
[b] 10 mol % of ligand was used.
[c] Substrate concentration was 0.5 M.

We also studied the effect of base and amino alcohol concentration on the reduction of acetophenone. These results showed that increasing the amount of base in the reaction had a negative effect on the asymmetric induction of the product. The best molar ratio of Ru(II) to *t*-BuOK was 1:10 for our system (entry 2). Increasing the concentration of the ligand by a factor of 5 led to a slight drop in conversion, but a larger drop in enantioselectivity (entry 5). We also tried changing the molarity of the reaction solution by decreasing the amount of 2-propanol used for solvent. After 48 h, only a 42% conversion and 26% ee were noted when using a 0.5 M solution of ketone (entry 6). The reaction progressed much faster when the ketone concentration was 0.1 M (entry 2). This observation can be explained by a change in the isopropanol to acetone equilibrium, which is reversible.[1b,1c,1d] Decreasing the amount of 2-propanol would shift the equilibrium away from the acetone product back towards the 2-propanol reactant. With less 2-propanol being converted to acetone, the active catalyst cannot be formed as fast. Although the reduction itself can be carried out at room temperature, the pre-catalyst is formed during reflux at 80 °C. When the reaction temperature was changed from room temperature to 55 °C, over 90% of acetophenone was converted to 1-phenylethanol after 24 h, but the product was racemic. After our attempts at optimization we screened the rest of the amino alcohols under our standard conditions (Table 2).

Table 2. Asymmetric reduction of acetophenone using β-amino alcohols **5**–**10**[a]

Entry	β-Amino alcohol[b]	Time [h]	Conv. [%]	ee [%]
1	5	72	86	50 (*S*)
2	6	36	99	50 (*S*)
3	7	72	99	63 (*S*)
4	8	24	45	50 (*S*)
5	9	24	83	34 (*S*)
6	10	72	0	—

[a] 0.1 M ketone.
[b] Ketone–ligand:[$RuCl_2$(*p*-cymeme)]$_2$–*t*-BuOK = 100:2:0.5:5; 25 °C.

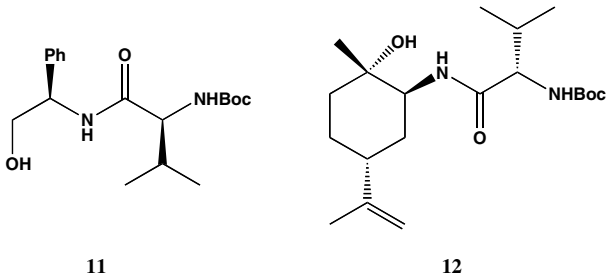
The terpene amino alcohols with primary amines, **5** and **6,** were both equally effective in terms of asymmetric induction for acetophenone. Limonene based ligand **6** has a slight advantage over carene based ligand **5** in that the catalyst derived from ligand **6** promoted a faster reaction (Table 2, entries 1 and 2). As the steric bulk increased on the amine with the addition of a methyl group in **7**, the enantioselectivity also increased slightly to 63% ee with 99% conversion after 72 h (entry 3). A further increase of the steric bulk around the amine lead to a decline in the asymmetric induction for ligands **8** and **9**, decreasing from 50% down to 33% (entries 4–6). Our attempt to use **10** as a ligand in the ATH reduction of acetophenone was unsuccessful due to the tertiary amine. Noyori and others have pointed out that ligands having a tertiary amine group were unable to catalyze the reduction of carbonyl compounds.[1b–d]

With an increasing demand for environmentally friendly chemistry, asymmetric transfer hydrogenation performed in water has recently aroused great interest.[8] We decided to carry out a short investigation with our terpene-based amino alcohols following two procedures recently published in the literature, one taking place in water at 40 °C[8a] and the other at room temperature.[8b] Both of these procedures used sodium formate as the hydride source, which is preferable over 2-propanol due to its irreversible hydride delivery. In addition to [$RuCl_2$(*p*-cymene)]$_2$, we explored the use of [Cp^*RhCl_2]$_2$ and [Cp^*IrCl_2]$_2$ with ligands **6** and **7** under the reported conditions. Attempted use of ligands **6** and **7** under these conditions for ATH with acetophenone was unsuccessful.

While our work was in progress, Adolfsson reported an effective amino acid conjugate of an amino alcohol, **11**, as a chiral ligand in ATH reactions (Fig. 2).[9]

In order to explore the utility of an amino acid conjugate with our limonene amino alcohol system, we synthesized compound **12** by coupling Boc-L-valine with ligand **6**. Compound **12** was not effective for catalytic ATH under our reaction conditions. This could be attributed to the presence of the tertiary alcohol moiety in **12** as compared to the primary alcohol in **11**. We explored further the amide derivatives **13**–**15**, which were synthesized using ligand **6** (Fig. 3). However, none of the newly prepared compounds were effective as chiral directors in our ATH reactions.

Based on our initial results (Table 2) with acetophenone, we decided to explore the scope and limit of amino alcohols



11 **12**

Figure 2. Adolfsson's amino acid conjugate **11**, and a terpene-based conjugate of an amino alcohol **12**.

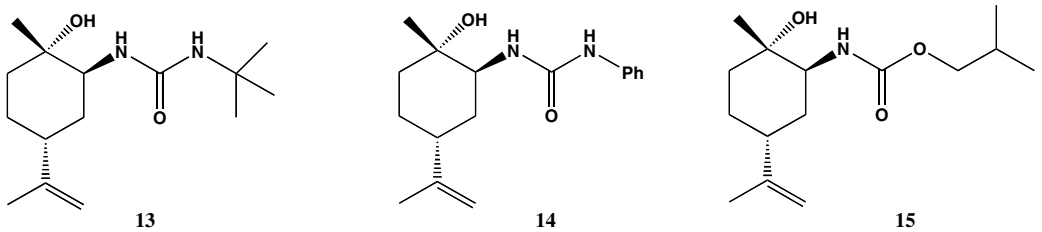
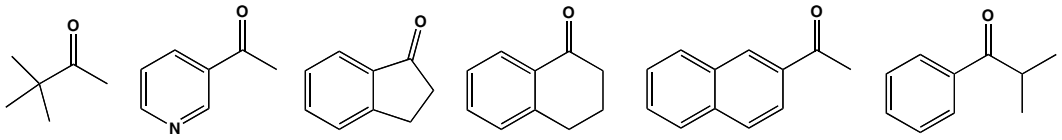


Figure 3. Terpene-based ligands containing amide moieties for ATH reduction of acetophenone.

Table 3. Asymmetric reduction of several ketones using ligands **6** and **7**[a]



Entry	Ketone[b]	6			7		
		Time [h]	Conv. [%]	ee [%]	Time [h]	Conv. [%]	ee [%]
1	16	72	0	—	48	94	22 (*R*)
2	17	24	99	12 (*S*)	72	0	—
3	18	72	56	48 (*S*)	72	56	0
4	19	48	58	68 (*S*)	36	75	71 (*S*)
5	20	48	10	53 (*S*)	48	10	40 (*S*)
6	21	24	99	14 (*S*)	24	83	0

[a] Ketone–ligand:$[RuCl_2(p\text{-cymeme})]_2$–*t*-BuOK = 100:2:0.5:5, 25 °C.
[b] Substrate concentration was 0.1 M.

6 and **7**, which had provided the most encouraging results. Several representative aromatic alkyl ketones were reduced under our ATH conditions using ruthenium catalysts derived from primary amine **6**, and the *N*-methyl amine **7**. These results are summarized in Table 3.

The non-aromatic ketone pinacolone was not reduced in the presence of ligand **6**, but in the presence of ligand **7** was reduced in excellent conversion (94%). However, the asymmetric induction was poor (22% ee) (Table 3, entry 1).

Ligand **7** was unable to catalyze the reduction of heteroaromatic ketone, acetylpyridine, while ligand **6** provided an excellent conversion (99%) but poor induction (12%) (entry 2). It is possible that the pyridine ring is coordinating to the ruthenium thereby interfering with the asymmetric induction. In general, the primary amine containing limonene amino alcohol **6** was more effective for the ketones examined in our study compared to ligand **7** containing a secondary amine moiety (entries 3–6). However, both ligands provided their best catalytic activity in the reduction of tetralone (entry 4). The *N*-methyl limonene amino alcohol provided the highest asymmetric induction of 71% ee for tetralone, with **6** providing 68% ee for the same substrate.

3. Conclusion

The reduction of carbonyls under catalytic transfer hydrogenation conditions with 2-propanol as a hydrogen source is a mild and highly attractive route for the formation of secondary alcohols. We have shown that terpene-based β-amino alcohols can be used as ligands for catalytic ATH with moderate success. The reduction takes place with good to excellent conversion, and moderate asymmetric induction. This could be attributed to the presence of a tertiary hydroxyl group in the amino alcohol. Over the course of our investigation, we noted that our amino alcohols were not compatible with either the formic acid/triethylamine or sodium formate systems as hydrogen sources. The *N*-methyl limonene amino alcohol **7** catalyzed the reduction of tetralone to provide the corresponding secondary alcohol in 75% conversion and 71% enantiomeric excess for the (*S*)-enantiomer. This is the highest value reported for an amino alcohol containing a tertiary alcohol moiety. The terpene precursors of our chiral β-amino alcohols have the advantage of being abundant naturally occurring starting materials, which keeps the cost low.

4. Experimental

All reactions were carried out in oven-dried glassware under an inert atmosphere of argon. Bis-dichlororuthenium(II) *p*-cymene was obtained from Aldrich chemicals. Isopropanol was distilled over calcium hydride under argon and degassed using liquid N_2. Ketones, if necessary, were distilled over P_2O_5. Distillation, degassing and preparation of the base solution all took place immediately before the reaction in order to minimize the effects of air and water on the reaction. The NMR spectra were recorded on a Varian 500 MHz spectrometer and are

reported in parts per million (500 MHz for ^{1}H, 125 MHz for ^{13}C). High-resolution mass spectra were obtained via a positive ion ESI-TOF mass spectrometer. Optical rotations were recorded on a Jasco DIP-371 polarimeter. Conversion and enantiomeric excess of the product mixture was determined by either GC or HPLC analysis. GC analysis was accomplished with an HP 5890 gas chromatograph with a flame-ionization detector equipped with a Supelco β-cyclodextrin 120 chiral GC column (30 m × 0.25 mm). HPLC analysis was accomplished using the Beckman System Gold HPLC system equipped with a Daicel Chiralcel OD column. Elution took place with 5% *i*-PrOH in hexanes at 1.0 mL/min unless otherwise indicated, and detection was at 254 nm. Crude products were compared to the racemic alcohol, from the $NaBH_4$ reduction of the appropriate ketone. Product alcohols were also compared with literature references.

4.1. Preparation of β-amino alcohol derivatives

4.1.1. {(*S*)-1-[(1*S*,2*S*,5*R*)-2-Hydroxy-2-methyl-5-(1-methylethenyl)cyclohexylcarbamoyl]-2-methylpropyl}-carbamic acid *tert*-butyl ester, 12. Boc protected valine (0.534 g, 2.5 mmol) was dissolved in THF (10 mL) along with carbonyldiimidazole (0.524 g, 3.3 mmol) and stirred at reflux for 5 h. (1*S*,2*S*,4*R*)-2-Amino-1-methyl-4-(methylethenyl)cyclohexanol (0.380 g, 2.2 mmol) in THF was added dropwise to the solution over 10 min. The reaction mixture was held at reflux for another 18 h, after which the solvent was evaporated, to give an oil (0.838 g). The oil was dissolved in diethyl ether and washed with satd $NaHCO_3$ solution and brine. After $MgSO_4$ and filtration, evaporation of the solvent gave an off-white solid (0.838 g) of which 490 mg was recrystallized from diethyl ether and dried on a high vac for 24 h to give 0.398 g of a sticky white crystalline solid. A second batch (0.348 g) was recrystallized from diethyl ether to give 0.324 g (total: 0.722 g, 89% yield) of the sticky white crystalline solid. Mp = 82–84 °C; $[\alpha]_D^{28} = +18.1$ (*c* 2.0, methanol); ^{1}H NMR (500 MHz, $CDCl_3$) $\delta = 0.94$–1.00 (dd, 6H), 1.20 (s, 3H), 1.45 (s, 9H), 1.47–1.71 (m, 6H), 1.73 (s, 3H), 2.00 (dd, 1H), 2.19 (m, 1H), 3.81 (t, 1H), 4.07 (dd, 1H), 4.76 (s, 1H), 4.77 (s, 1H), 5.01 (br s, OH), 6.24 (d, NH); ^{13}C NMR (125.6 MHz, $CDCl_3$) $\delta = 17.8$, 19.4, 21.1, 25.9, 27.4, 28.3, 30.1, 31.8, 34.7, 38.7, 53.2, 60.7, 70.9, 109.6 148.4, 163.3, 171.6; HRMS (EI) $(M+H)^+$ calcd for $C_{20}H_{37}N_2O_4$ 369.27524, found 369.27478.

4.1.2. 1-*tert*-Butyl-3-[(1*S*,2*S*,5*R*)-2-hydroxy-2-methyl-5-(1-methylethenyl)cyclohexyl]urea, 13. To a solution of *tert*-butylisocyanate (0.35 mL, 3 mmol) in toluene (20 mL, 0.15 M), a solution of (1*S*,2*S*,4*R*)-2-amino-1-methyl-4-(1-methylethenyl)cyclohexanol (0.500 g, 2.95 mmol) in dry toluene (15 mL) was added dropwise at 80 °C. After 24 h, the product was extracted by adding water and ethyl ether to the toluene. The organic layer was dried, filtered, and was evaporated to give 0.715 g (90% yield) of a white solid (powder) after 24 h on the high vac. Mp: 144–145 °C; $[\alpha]_D^{28} = +22.4$ (*c* 2.0, methanol); ^{1}H NMR (500 MHz, $CDCl_3$) $\delta = 1.21$ (s, 3H), 1.36 (dd, 9H), 1.49–1.66 (m, 6H), 1.72 (s, 3H), 2.06 (m, 1H), 3.75 (m, 1H), 4.21 (d, NH), 4.37 (s, OH), 4.79 (d, 2H); ^{13}C NMR (125.6 MHz, $CDCl_3$) $\delta = 21.5$, 25.8, 29.6, 32.4, 34.8, 38.8, 50.4, 53.8, 72.2, 110.0, 147.9, 157.8; HRMS (EI) $(M+H)^+$ calcd for $C_{15}H_{29}N_2O_2$ 269.22420, found 269.22235.

4.1.3. 1-[(1*S*,2*S*,5*R*)-2-Hydroxy-2-methyl-5-(1-methylethenyl)cyclohexyl]-3-phenylurea, 14. To a solution of phenylisocyanate (0.31 mL, 2.8 mmol) in toluene (15 mL, 0.2 M), a solution of (1*S*,2*S*,4*R*)-2-amino-1-methyl-4-(methylethenyl)cyclohexanol (0.500 g, 2.95 mmol) in dry toluene (15 mL) was added dropwise at 80 °C. After 1 h, the toluene was evaporated and the product dissolved in chloroform/methanol 2:1 (30 mL) to be poured into acetone/acetonitrile 3:1 (200 mL). No precipitate formed at this point. The solution was cooled overnight in a refrigerator but no precipitate was observed. The solvent was removed by rotary evaporation to give a clear yellow oil. The oil was put under house vacuum overnight, but no change was observed the next day. The oil was put under high vacuum (100 mTorr) and the next day a highly bubbled solid had formed. This was broken up to give 0.744 g of the title compound (crude yield, 92%) as an off-white solid. The compound was dissolved in a minimal amount of EtOAc/hex for recrystallization and left at 0 °C overnight. No crystals had formed by the next day. The solvent was removed and the oil dried on high vacuum over several days, giving an off-white solid (88% yield). Mp = 73–76 °C; $[\alpha]_D^{28} = +9.7$ (*c* 2.0, methanol); ^{1}H NMR (250 MHz, $CDCl_3$) $\delta = 1.23$ (s, 3H), 1.46 (s, 3H), 1.48–1.66 (m, 6H), 2.02–2.06 (m, 1H), 3.92 (m, 1H), 4.77–4.78 (d, 2H), 7.00 (m, 1H), 7.23 (m, 4H); ^{13}C NMR (62.5 MHz, $CDCl_3$) $\delta = 21.4$, 25.7, 32.4, 35.0, 38.8, 41.5, 54.2, 72.4, 110.0, 120.9, 121.6, 123.4, 129.4, 129.5, 138.6, 147.7, 156.1; HRMS (EI) $(M+H)^+$ calcd for $C_{17}H_{25}N_2O_2$ 289.19112, found 289.19106.

4.1.4. [(1*S*,2*S*,5*R*)-2-Hydroxy-2-methyl-5-(1-methylethenyl)cyclohexyl]carbamic acid isobutyl ester, 15. To a solution of (1*S*,2*S*,4*R*)-2-amino-1-methyl-4-(1-methylethenyl)-cyclohexanol (1.132 g, 7.0 mmol) in dry THF (20 mL), isobutylchloroformate (0.95 mL, 7.3 mmol) was added dropwise via syringe at −15 °C. The reaction mixture was warmed to room temperature and was stirred for a total of 18 h. Water (50 mL) was added to the reaction mixture and the product was extracted with ethyl ether (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent removed by roto-evaporation to give 1.403 g (78% yield) of a viscous colorless oil. $[\alpha]_D^{28} = +13.5$ (*c* 1.0, methanol); ^{1}H NMR (500 MHz, $CDCl_3$) $\delta = 0.94$ (dd, 6H), 1.24 (s, 3H), 1.41–1.69 (m, 6H), 1.74 (s, 3H), 1.92 (m, 1H), 2.0 (dd, 1H), 3.80–3.90 (m, 3H), 4.76–4.77 (d, 2H); ^{13}C NMR (125.6 MHz, $CDCl_3$) $\delta = 19.1$, 21.1, 25.9, 28.1, 32.0, 34.7, 38.8, 54.8, 68.0, 71.3, 109.7, 148.5, 163.3; HRMS (EI) $(M+H)^+$ calcd for $C_{15}H_{28}NO_3$ 270.20826, found 270.20637.

4.2. Typical procedure for the catalytic asymmetric transfer hydrogenation of ketones

An oven-dried Schlenk-type flask with a magnetic stirrer bar was cooled under argon and then charged with bis-ruthenium dichloro-*p*-cymene (7.7 mg, 12.5 μmol) followed by amino alcohol (100 μmol). Freshly distilled 2-propanol

(10 mL) was added via cannula. The contents of the flask were degassed with liquid N_2 (3 freeze–thaw cycles) and flushed with argon. The reaction mixture was refluxed for 1 h during which time the color of the solution changed depending on the ligand used. The solution was cooled to room temperature and freshly prepared base, potassium tertiary butoxide (0.5 mL, 0.25 M in 2-propanol) was added. The solution was stirred for an additional 30 min. 2-Propanol (40 mL) and then ketone (5 mmol) were added and the solution stirred at room temperature. The reaction progress was monitored by TLC. After a significant amount of alcohol could be seen (compared to ketone), the contents of the flask were transferred to a separatory funnel and hydrochloric acid (20 mL, 1 M) was added. The aqueous layer was extracted with diethyl ether (150 mL). The combined organic extracts were washed with sodium bicarbonate (75 mL), brine (75 mL) and dried over magnesium sulfate and filtered. The solvent was removed by rotary evaporation leaving a crude oil, which was passed through a small plug of silica gel to remove any remaining transition metal. The resulting product was concentrated and analyzed by either chiral HPLC or chiral gas chromatography.

4.2.1. (*S*)-1-Phenylethanol.[1r] Table 2, entry 3 product: 99% conversion, 63% ee (*S*) by HPLC (hexane/*i*-PrOH = 90:10, 1.0 mL/min; t_R(*R* isomer) = 7.5 min, t_R(*S* isomer) = 8.3 min).

4.2.2. (*R*)-3,3-Dimethylbutan-2-ol, 16.[1g] Table 3, entry 1 product: 94% conv., 22% ee (*S*) by GC (70 °C, 20 min; t_R(*R* isomer) = 13.1 min, t_R(*S* isomer) = 13.7 min).

4.2.3. (*S*)-1-(3-Pyridyl)ethanol, 17.[1x] Table 3, entry 2 product: 99% conv., 12% ee (*S*) by GC (140 °C, 25 min; t_R(*R* isomer) = 19.5 min, t_R(*S* isomer) = 20.3 min).

4.2.4. (*S*)-2,3-Dihydro-1*H*-inden-1-ol, 18.[1r] Table 3, entry 3 product: 56% conv., 48% ee (*S*) by GC (118 °C, 60 min; t_R(*R* isomer) = 53.3 min, t_R(*S* isomer) = 52.4 min).

4.2.5. (*S*)-1,2,3,4-Tetrahydronaphthealen-1-ol, 19.[1r] Table 3, entry 4 product: 75% conv., 71% ee (*S*), by GC (135 °C, 50 min; t_R(*R* isomer) = 47.8 min, t_R(*S* isomer) = 46.8 min).

4.2.6. (*S*)-1-(2-Naphthyl)ethanol, 20.[1r] Table 3, entry 5 product: 10% conv., 53% ee (*S*), by HPLC (hexane/*i*-PrOH = 95:5, 1.0 mL/min, t_R(*R* isomer) = 24.1 min, t_R(*S* isomer) = 12.4 min).

4.2.7. (*S*)-1-Phenylpropanol, 21.[1r] Table 3, entry 5 product: 99% conv., 14% ee (*S*), HPLC (hexane/*i*-PrOH = 95:5, 1.0 mL/min; t_R(*R* isomer) = 39.3 min, t_R(*S* isomer) = 40.6 min).

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