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# Asymmetric transfer hydrogenation of quinolines using tethered Ru(II) catalysts

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Dedicated to Professor H. B. Kagan on his 80th birthday

ABSTRACT

The first report of an asymmetric transfer hydrogenation, in formic acid/triethylamine, of quinolines is described. Using a Ru(II) catalyst containing a 4-carbon tether, products of up to 73% ee were formed, whilst a Rh(III)-tethered catalyst gave products of up to 94% ee.



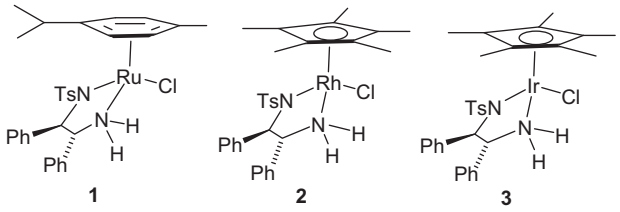
## 1. Introduction

The asymmetric reduction of C=N bonds is a valuable method for the asymmetric formation of chiral amines.[1] Whilst several methods exist for the asymmetric reduction of isolated C=N groups,[2] their reduction when they are a part of an aromatic ring represents a more challenging objective. The conversion of quinolines to tetrahydroquinolines is a useful direct method for the synthesis of chiral, non-racemic N-containing heterocycles from readily available starting materials. A number of reports on the pressure hydrogenation of quinolines have been published.[3–17]

## 2. Results and discussion

The first example of asymmetric quinoline hydrogenation employed chiral biaryldiphosphine ligands with an Ir(I) salt and gave products with ees of up to 94%. Iodine was found to be an essential additive.[3] Several other iridium/diphosphine complexes have given excellent results in this application.[4–10] Supported versions of these catalysts have been prepared and used successfully in recyclable catalyst systems.[11,12] The activation of quinolines with chloroformates has been reported to improve the rates of reactions.[13] Other ligands which have been used in Ir-catalysed quinoline hydrogenation include BINOL-derived diphosphonites[14] and ferrocenyloxazolines.[15]

The use of nitrogen-donor ligands, such as diamines, in this application is less developed. In a recent report, the use of a Ru/TsDPEN complex **1** as a catalyst for hydrogenation of 2-methylquinoline **4** in an ionic liquid gave excellent results.[16] In this process, the ionic liquid was essential—reactions in methanol proceeded with much lower activity. Switching to Rh(III) and Ir(III) as the metal, however, led to the development of catalysts **2** and **3** for hydrogenation of 2-methylquinoline **4** in organic solvents. Using the Ir(III) complex, 2-methyltetrahydroquinoline **5** was formed in up to 99% ee.[17] The use of an acidic additive was demonstrated to be important for optimal activity. These results suggested that the reduction of quinolines proceeds by an ionic mechanism in which N-protonation was required to activate the hydride addition process.[16,17]




**1** **2** **3**

In contrast, there are few reports on the use of asymmetric transfer hydrogenation, which can offer advantages in terms of practicality, in this particular application. Recently, Xiao et al. disclosed the use of Rh-based catalyst **2** in aqueous solution.[18] This gave impressive results and required careful control of pH for full reduction to occur. A racemic Ir(I)-catalysed transfer hydrogenation (using isopropanol as the hydrogen source) has been reported.[19] The closely related reduction of quinolines using Hantzsch esters as the source of hydrogen has, however, been reported to give excellent results in both the metal-free[20] and Ir/diphosphine-catalysed[21] methods.

We therefore instigated a series of studies on the asymmetric transfer hydrogenation for the asymmetric reduction of quinoline and isoquinoline rings. Given the success demonstrated by **1**–**3** in reduction by hydrogen gas and asymmetric transfer hydrogenation in water, it was considered that these might also prove successful in the closely related asymmetric transfer hydrogenation process in formic acid/triethylamine azeotrope (formic acid/TEA),[22] which

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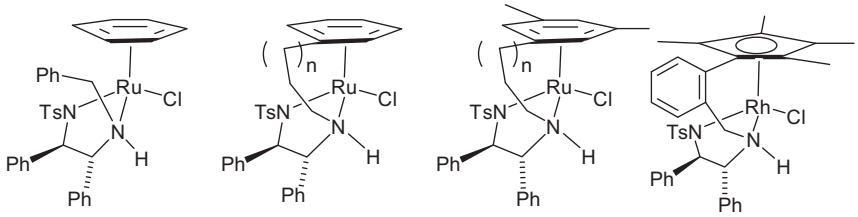
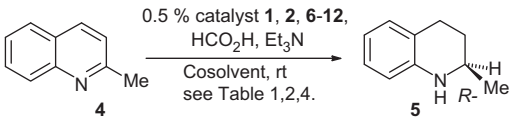
is known to work well with imines.[23] In addition, we wished to evaluate catalysts **6**–**12**, which have recently been developed in our group.[24,25] Initial studies of the reduction of 2-methylquinoline (Scheme 1) were carried out using the dropwise addition of formic acid, the method reported by Blackmond for imines, in methanol solvent.[26] These studies indicated that catalyst **9** was particularly active in this application (see SI). Further studies were conducted using the Noyori procedure (i.e., in which a 5:2 formic acid/TEA azeotrope is employed from the outset) and this was found to give similar results. Hence this method was selected for extended investigations.




**6** **7** (n=0) **9** (n=2) **11** (n=2) **12**
**8** (n=1) **10** (n=3)

In order to optimise the outcome of the reaction, systematic variation of the conditions was carried out using 2-methylquinoline **4** as a substrate and the 4C-tethered complex **9** as catalyst. The results of solvent variation are shown in Table 1. Of these, methanol gave the best result in terms of conversion and ee. A study of the effect of temperature revealed that (in methanol) the ee dropped only slightly at elevated temperature (to 43% at 60 °C).

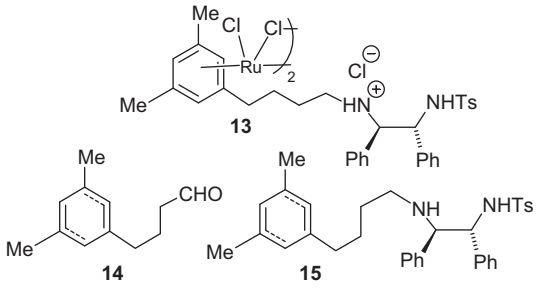



**4** **5**

**Scheme 1.**

Alternative Ru(II) catalysts were tested for comparison with **9** (Table 2) over a fixed 24-h reaction time. In the event, complex **1** proved to be capable of reducing 2-methylquinoline **4** in high ee but in very low conversion even after extended reaction times. The use of the N-benzylated TsDPEN ligand **6**[24] gave a product in higher conversion but lower ee. The tethered ligands **7**–**11** were tested next and, of these, **9** and **10** proved to be the most active.[25] In our previous studies, we have demonstrated that monomer catalysts **7–11** are formed in situ from their dimer precursors and both give identical results in asymmetric transfer hydrogenation reactions.[25] In the cases of **9** and **10**, the dimer catalyst precursors were, in practice, used directly in the experiments, although the corresponding monomers are illustrated for ease of structural comparison. The 3C-tethered complex **8** was used in both dimer and monomer forms to confirm reproducibility; both gave identical results within experimental error. All the catalysts were of (*R,R*)-configuration (illustrated) with respect to the diamine, with the exception of the dimer of **8**, which was of the (*S,S*)-configuration. Catalyst **9**, with a 4C tether, gave the highest conversion (24 h, rt). 2-Methylquinoline **4** was reduced to **5** in 96% conversion, with an ee of 43% (*R* configuration).

Catalysts **6–10** have already been reported,[24,25] however, **11** was prepared specifically for use in this project and is new. In view of the high conversion in reduction of **4** achieved using the 4C-tethered complex **9**, but the highest ee of 80% seen using the *p*-cymene containing untethered complex **1**, we sought to design a catalyst which contained elements of both **1** and **9** in order to achieve both high activity and ee, that is, **11**.




**13** **14** **15**

**Table 1**
Asymmetric transfer hydrogenation of 2-methylquinoline **4** to tetrahydroquinoline **5** (Scheme 1) using catalyst **9**; variation of solvent[a]

| Entry | Solvent | Conversion/% | ee[b]/% (*R*/*S*) |
|---|---|---|---|
| 1 | MeOH | 96 | 46 (*R*) |
| 2 | MeCN | 79 | 36 (*R*) |
| 3 | $H_2O$ | 23 | 32 (*R*) |
| 4 | EtOH | 96 | 37 (*R*) |
| 5 | DCM | 92 | 25 (*R*) |
| 6 | $Et_2O$ | 98 | 17 (*R*) |
| 7 | Acetone | 8 | 8 (*R*) |
| 8 | Toluene | 73 | 22 (*R*) |
| 9 | *i*PrOH | 98 | 31 (*R*) |
| 10 | EtOAc | 75 | 18 (*R*) |
| 11 | None[c] | 61 | 46 (*R*) |

[a] Conditions: 0.5 mol % of catalyst **9** (dimer precursor used). [quinoline] = 0.45 M, 28 °C, 24 h, 5:2 formic acid/TEA azeotrope.
[b] ee determined by chiral GC (see SI).
[c] Neat formic acid/TEA used.

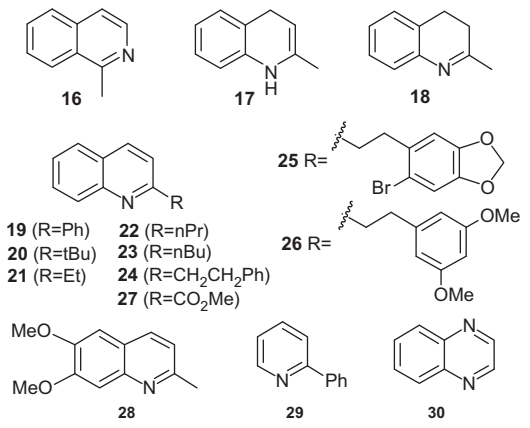
**Table 2**
Asymmetric transfer hydrogenation of 2-methylquinoline **4** to tetrahydroquinoline **5** (Scheme 1); variation of catalyst[a]

| Entry | Catalyst | Conversion/% | ee[b]/% (*R*/*S*) |
|---|---|---|---|
| 1 | **1** (monomer) | 17 | 80 (*R*) |
| 2 | **6** (monomer) | 66 | 29 (*R*) |
| 3 | **7** (monomer) | 27 | 68 (*R*) |
| 4 | **8** (dimer) | 63 | 43 (*S*)[c] |
| 5 | **8** (monomer) | 59 | 43 (*R*) |
| 6 | **9** (dimer) | 96 | 43 (*R*) |
| 7 | **10** (dimer) | 87 | 44 (*R*) |
| 8 | **11** (dimer) | 29 | 42 (*R*) |

[a] Conditions: 0.5 mol % of catalysts **6**–**11** wrt monomer form (i.e. 0.5 mol % of Ru(II)). [quinoline] = 0.45 M, 60 °C, 24 h, MeOH solvent, 5:2 formic acid/TEA azeotrope.
[b] ee determined by chiral GC (see SI).
[c] (*S,S*)-Catalyst used.

The synthetic approach to **11** required the synthesis of the dimer precursor **13** (converted in situ to **11** during asymmetric transfer hydrogenation reactions). To achieve this, **14** (mixture of regioisomers) was first prepared through Br/Li exchange on 3,5-dimethylbromobenzene and reaction with $Br(CH_2)_4OTBDPS$, then deprotection, Birch reduction and oxidation. Reductive amination of **14** with (*R*,*R*)-TsDPEN gave **15**, which was reacted with $RuCl_3$ to form the salt **13**. Unfortunately **11** did not give superior results. In the reduction of ketones, however, catalyst **11** was very efficient. Acetophenone was reduced in 97% ee (*R*) and acetylcyclohexane in 74% ee (*S*) using 0.5 mol % (wrt Ru(II)) of **11** (28 °C, 5:2 formic acid/TEA).

Other substrates were then examined including 1-methylisoquinoline **16**, which was not reduced under these conditions. This result suggests that the reduction mechanism of **4** may involve an initial 1,4-addition of hydrogen to the protonated heterocycle to give **17**, followed by isomerisation to the imine **18**, which is then reduced enantioselectively to the observed product. This sequence, which has previously been proposed for the closely related hydrogenation of **4** in an ionic liquid,[16] would not be applicable to isomeric heterocycle **16**.




The reduction of a series of further quinolines **19–28** was examined using tethered catalyst **9** (Table 3).

Of these, the phenyl-substituted substrate **19** was reduced in the highest ee of the series, whilst the *t*Bu derivative **20** was successfully reduced but only in racemic form. Other isoquinolines were reduced in high conversion but only moderate-good ee. The ester-substituted compound **27** was not reduced under the conditions used. Heterocycles **29** (0% conversion) and **30** (17% conversion) also proved resistant to reduction.

**Table 3**
Asymmetric transfer hydrogenation of 2-substituted quinolines to tetrahydroquinolines using catalyst **9**[a]

| Entry | Substrate | Time/h | Conversion/% | ee[b]/% (*R*/*S*) |
|---|---|---|---|---|
| 1 | **19** | 168 | 68 | 73 (*S*) |
| 2 | **20** | 48 | 57 | 0 (-) |
| 3 | **21** | 30 | 95 | 41 (*R*) |
| 4 | **22** | 144 | 94 | 42 (*R*) |
| 5 | **23** | 144 | 93 | 41 (*R*) |
| 6 | **24** | 48 | 90 | 50 (*R*) |
| 7 | **25** | 48 | 86 | 47 (*R*) |
| 8 | **26** | 48 | 93 | 67 (*R*) |
| 9 | **27** | 48 | 0 | - |
| 10 | **28** | 24 | 46 | 50 (*R*) |

[a] Conditions: 0.5 mol % of catalyst **9** wrt monomer form (i.e., 0.5 mol % of Ru(II)). [quinoline] = 0.45 M, 28 °C, MeOH solvent, 5:2 formic acid/TEA azeotrope.
[b] ee determined by chiral GC or HPLC (see SI).

**Table 4**
Asymmetric transfer hydrogenation of 2-substituted quinolines to tetrahydroquinolines using catalyst **12**[a]

| Entry | Substrate | Time/h | Conversion[c]/% | ee[b]/% (*R*/*S*) |
|---|---|---|---|---|
| 1 | **4** | 24 | 68 (85) | 93 (*R*) |
| 2 | **19** | 48 | 68 (35) | 86 (*S*) |
| 3 | **20** | 48 | 16 (43) | 0 (–) |
| 4 | **21** | 48 | 67 (76) | 91 (*R*) |
| 5 | **22** | 48 | 65 (73) | 90 (*R*) |
| 6 | **23** | 48 | 64 (76) | 92 (*R*) |
| 7 | **24** | 48 | 57 (65) | 93 (*R*) |
| 8 | **25** | 48 | 30 (29) | 81 (*R*) |
| 9 | **26** | 48 | 58 (69) | 94 (*R*) |

[a] Conditions: 0.5 mol % of catalyst **12** wrt monomer form (i.e., 0.5 mol % of Rh(III)). [quinoline] = 0.45 M, 28 °C, 24 h, MeOH solvent, 5:2 formic acid/TEA azeotrope.
[b] ee determined by chiral GC or HPLC (see SI).
[c] Figures in parenthesis are those obtained with 2 mol % of catalyst **12**.

Better results, in terms of enantioselectivity, in several cases exceeding 90% ee, were achieved using the rhodium-tethered catalyst **12**, which has previous been used for ketone and imine reductions (Table 4). Using 0.5 mol % of **12**, the reactions did not go to full conversion after 48 h, although the use of a higher loading (2 mol %) of catalyst increased the conversions in most cases. Further work is required to optimise the reductions by these catalysts.

## 3. Conclusion

In conclusion, we have demonstrated that tethered Ru(II) and Rh(III) complexes are effective catalysts for the asymmetric transfer hydrogenation of substituted quinolines, which are generally regarded as challenging substrates for this application. To the best of our knowledge, this is the first report of the use of such catalysts in a solution of formic acid/triethylamine/methanol. As has been observed in ketone reduction, the increased reactivity of tethered complexes over the untethered ones appears to be key to their capacity to work as effective catalysts in this application.

## 4. Experimental

### 4.1. (4-Bromobutoxy)(*tert*-butyl)diphenylsilane[27]

*tert*-Butyl-chlorodiphenylsilane (7.96 g, 7.53 ml, 28.97 mmol) was added to a stirred solution of 4-bromo-1-butanol (4.03 g, 26.34 mmol) and imidazole (3.95 g, 57.95 mmol) in THF (150 ml) under an argon atmosphere. The resulting mixture was stirred for 72 h at rt and the reaction was quenched with water (150 ml) followed by the addition of diethyl ether (150 ml). After phase separation and extraction of the aqueous phase with diethyl ether ($3 \times 150$ ml), the combined organic phases were dried ($MgSO_4$), concentrated and purified by flash chromatography (hexane/EtOAc 9:1) to afford the silyl alcohol as a colourless oil (3.23 g, 31%). $^1$H NMR (300 MHz; $CDCl_3$) $\delta$ 7.52–7.51 (m, 4H), 7.45–7.30 (m, 6H), 3.75 (t, $J$ = 6.1 Hz, 2H), 3.50 (t, $J$ = 6.8 Hz, 2H), 2.00 (m, 2H), 1.70 (m, 2H), 1.09 (s, 9H); $^{13}$C NMR (300 MHz; $CDCl_3$) $\delta$ 135.6, 133.8, 129.7, 127.7, 62.9, 34.0, 31.1, 29.5, 26.9, 20.0.

### 4.2. *tert*-Butyl(4-(3,5-dimethylphenyl)butoxy)diphenylsilane

A Schlenk tube was dried with a heat gun under vacuum and flushed with argon. 5-Bromo-m-xylene (1.53 g, 1.12 ml, 8.25 mmol) was injected into the tube followed by freshly distilled THF (16.5 ml). The tube was then degassed three times. *t*BuLi (1.7 M in pentane, 12.14 ml, 20.63 mmol) was added dropwise at −78 °C and the tube was again degassed and flushed with argon.

The mixture was stirred at rt for 1 h and then re-cooled to −78 °C. (4-Bromobutoxy)(*tert*-butyl)diphenylsilane (3.23 g, 8.25 mmol) was added dropwise to the reaction mixture and then degassed and flushed with argon. The solution was heated to 40 °C and allowed to stir at this temperature for 4 days. The mixture was allowed to cool to rt and then partitioned between diethyl ether (33 ml) and water (25 ml). The aqueous phase was extracted with diethyl ether (2 × 16.5 ml) and then the combined organic phases were dried over $MgSO_4$, filtered and then evaporated in vacuo to give a light yellow oil (2.4 g, 70%). $\nu_{max}/cm^{-1}$ (thin film) 3071, 2931, 2858, 1606, 1472, 1462, 1428, 1390, 1361, 1261, 1189, 1105, 1008, 998, 975, 939, 846, 822, 739, 699; $^1H$ NMR (400 MHz; $CDCl_3$) $\delta$ 7.70–7.62 (m, 4H), 7.45–7.30 (m, 6H), 6.85 (s, 1H), 6.80 (s, 2H), 3.65 (t, $J$ = 6.2 Hz, 2H), 2.53 (t, $J$ = 7.8 Hz, 2H), 2.25 (s, 6H), 1.70 (m, 2H), 1.60 (m, 2H), 1.05 (s, 9H); $^{13}C$ NMR (400 MHz; $CDCl_3$) $\delta$ 142.6, 137.7, 136.8, 136.6, 135.6, 134.2, 134.1, 131.0, 129.5, 129.1, 127.6, 127.3, 126.3, 63.8, 35.5, 32.3, 29.5, 29.0, 27.6, 26.9, 21.3. *m/z* (ESI) 439 (M+Na); HRMS Found (ESI): [$M^+$+Na] 439.2419, $C_{28}H_{36}NaOSi$ requires 439.2428 (1.86 ppm error).

### 4.3. 4-(3,5-Dimethylphenyl)butan-1-ol

Tetrabutylammonium fluoride (1 M solution in THF) (24 ml) was added to a solution of *tert*-butyl(4-(3,5-dimethylphenyl)butoxy)diphenylsilane (2.0 g, 4.8 mmol) in THF (65 ml). The mixture was allowed to stir for 3 days at 23 °C and the conversion was checked by TLC. The crude mixture was purified by flash chromatography (9:1 hexane:EtOAc to 5:5 hexane:EtOAc) to afford the product as a colourless oil (776 mg, 91%). $\nu_{max}/cm^{-1}$ (thin film) 3326, 3014, 2928, 2860, 1606, 1459, 1377, 1060, 1036, 985, 933, 894, 843, 700; $^1H$ NMR (400 MHz; $CDCl_3$) $\delta$ 6.82 (s, 1H), 6.80 (s, 2H), 3.65 (t, $J$ = 6.2 Hz, 2H), 2.59 (t, $J$ = 7.6 Hz, 2H), 2.30 (s, 6H), 1.75–1.55 (m, 4H), 1.35 (br s, 1H); $^{13}C$ NMR (400 MHz; $CDCl_3$) $\delta$ 142.3, 137.8, 127.4, 126.3, 62.9, 35.5, 32.5, 27.6, 21.3; *m/z* (ESI) 201 (M+Na), 161, 102; HRMS found (ESI): [$M^+$ +Na] 201.1247, $C_{12}H_{18}NaO$ requires 201.1250 (1.5 ppm error).

### 4.4. 4-(3,5-Dimethylcyclohexa-1,4-dienyl)butan-1-ol

A solution of 4-(3,5-dimethylphenyl)butan-1-ol (513 mg, 2.8 mmol) in ethanol (2.5 ml) was slowly added to a refluxing solution of ammonia (50 ml) containing ethanol (10 ml) at −78 °C while stirring. Small sodium pieces were added to the reaction mixture until the blue colour persisted. After the addition of sodium over the course of 7 h with regular additions of ethanol (2.5 ml), the reaction mixture was left overnight to evaporate ammonia. The reaction was quenched carefully with ammonium chloride (satd, 20 ml) and extracted by DCM (3 × 6 ml). The combined organic layer was dried over magnesium sulfate, filtered and concentrated under reduced pressure to afford crude 4-(3,5-dimethylcyclohexa-1,4-dienyl)butan-1-ol as an orange red oil (374 mg, 90%) which appeared to be a ca. 1:1 mixture of diene isomers. $^1H$ NMR (300 MHz; $CDCl_3$) $\delta$ 5.32 (br s, 2H), 3.60–3.55 (m, 2H), 2.71 (br s, 1H), 2.35–2.25 (m, 2H), 2.00–1.92 (m, 1H), 1.65 (br s, 4.5H), 1.50–1.20 (m, 6H), 0.95 (d, $J$ = 7.6 Hz, 1.5H). This material was directly used in the next step.

### 4.5. 4-(3,5-Dimethylcyclohexa-1,4-dienyl)butanal 14

A solution of oxalylchloride (2 M in DCM, 1.35 ml, 2.69 mmol) in anhydrous DCM (3 ml) was cooled to −78 °C and was slowly added to a solution of dimethylsulfoxide (0.38 ml, 5.38 mmol) in DCM (1.5 ml) by a syringe. The solution was stirred for 30 min at −78 °C before a solution of 4-(3,5-dimethylcyclohexa-1,4-dienyl)butan-1-ol (375 mg, 2.07 mmol) in DCM (5 ml) was slowly added at the same temperature. After stirring for 45 min at −78 °C, triethylamine (1.73 ml, 12.40 mmol) was added and the reaction mixture was allowed to warm up to rt. After 60 min, water (10 ml) was added and the mixture was extracted with DCM (3 × 5 ml). The combined organic layers were dried over magnesium sulfate, filtered and concentrated under reduced pressure to give crude 4-(3,5-dimethylcyclohexa-1,4-dienyl)butanal as a light orange oil (355 mg, 96%) which appeared to be a ca. 1:1 mixture of isomers **14a** and **14b**. $^1H$ NMR (400 MHz; $CDCl_3$) $\delta$ 9.88 (s, 0.5H), 9.85 (s, 0.5H), 5.30–5.20 (m, 2H), 2.80–2.76 (br s, 1H), 2.40–2.30 (m, 3H), 2.03–1.95 (m, 0.5H), 1.80–1.70 (m, 0.5H), 1.68 (br s, 4.5H), 1.30–1.20 (m, 3H), 1.01 (d, $J$ = 7.7 Hz, 1.5H). This material was directly used in the next step.

### 4.6. *N*-((1*R*,2*R*)-2-(4-(3,5-Dimethylcyclohexa-1,4-dienyl)-butylamino)-1,2-diphenylethyl)-4-methylbenzene-sulfonamide 15

To a suspension of powdered molecular sieves (4 Å, 0.50 g) in dry methanol (30 ml) were added 4-(3,5-dimethylcyclohexa-1,4-dienyl)butanal **14** (355 mg, 2.00 mmol), (*R*,*R*)-TsDPEN (806 mg, 2.20 mmol) and glacial acetic acid (4 drops). The reaction mixture was stirred at rt and monitored by TLC. After leaving for 2 h, the imine had formed and sodium cyanoborohydride (590 mg, 9.38 mmol) was added. The reaction was left overnight at rt. The molecular sieves were removed by filtration and the solution was concentrated under reduced pressure. The residue was re-dissolved in DCM (40 ml). The organic phase was washed with $NaHCO_3$ (satd, 40 ml) and brine (40 ml), dried over magnesium sulfate and concentrated. The resulting residue was purified by flash chromatography to afford *N*-((1*R*,2*R*)-2-(4-(3,5-dimethylcyclohexa-1,4-dienyl)butylamino)-1,2-diphenylethyl)-4-methylbenzene-sulfonamide **15** as a white oil (390 mg, 37% yield); $[\alpha]_D^{35} = -5.3$ (*c* 0.5 $CHCl_3$). $\nu_{max}/cm^{-1}$ (thin film) 3299, 3030, 2926, 2856, 2257, 1600, 1495, 1455, 1433, 1380, 1352, 1327, 1305, 1184, 1160, 1119, 1093, 1054, 1020, 909, 846, 807, 755, 731, 698, 667; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.38 (d, $J$ = 11.2 Hz, 2H), 7.15–7.10 (m, 3H), 7.05–7.00 (m, 5H), 6.95–6.85 (m, 4H), 6.40–6.20 (br s, 1H), 5.35–5.25 (m, 2H), 4.25 (m, 1H), 3.60 (m, 1H), 2.77–2.60 (m, 1H), 2.35 (s, 3H), 2.45–2.25 (m, 3H), 1.92 (m, 1H), 1.70 (s, 4.5H), 1.45–1.20 (m, 6H), 1.05 (d, $J$ = 7.2 Hz, 1.5H); $^{13}C$ NMR (400 MHz, $CDCl_3$) $\delta$ 142.7, 139.4, 138.4, 137.0, 131.1, 129.1, 128.0, 127.6, 127.4, 127.3, 127.2, 125.2, 125.0, 123.4, 67.9, 63.1, 47.1, 36.8, 36.5, 34.0, 30.4, 29.6, 24.9, 23.1, 21.5. *m/z* 529 (M+H), 350; HRMS found (EI): $[M-H]^+$ 529.2899, $C_{33}H_{41}N_2O_2S$ requires 529.2883 (−2.9 ppm error).

### 4.7. *N*-((1*R*,2*R*)-2-(4-(3,5-Dimethylphenyl)butylamino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide ammonium chloride dimer 13

To a stirred solution of *N*-((1*R*,2*R*)-2-(4-(3,5-dimethylcyclohexa-1,4-dienyl)-butylamino)-1,2-diphenylethyl)-4-methylbenzene-sulfonamide **15** (200 mg, 0.38 mmol) in anhydrous DCM (5.5 ml) was added hydrochloric acid (2 M in diethyl ether, 0.57 ml, 1.14 mmol) at 0 °C. The reaction mixture was stirred at rt for 20 min and subsequently concentrated under reduced pressure to give a white residue. To a suspension of the residue in ethanol (7.2 ml) was added hydrate ruthenium(III) trichloride hydrate (62 mg, 0.30 mmol). The reaction mixture was refluxed overnight. The precipitate was collected by filtration and washed with ethanol to give *N*-((1*R*,2*R*)-2-(4-(3,5-dimethylphenyl)butylamino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide ammonium chloride dimer **13** (54 mg, 25%) as black crystals. The compound was too dark to obtain optical rotation measurement. Mp 240–250 °C (dec.); $\nu_{max}/cm^{-1}$ (thin film) 3054, 1597, 1456, 1323, 1156, 1091,

1030, 925, 813, 763, 700, 669; $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.85 (br s, 2H), 9.85 (br s, 2H), 8.95 (br s, 2H), 8.55 (d, $J$ = 8.5 Hz, 2H), 7.40–6.70 (m, 28H), 5.59–5.51 (m, 6H), 4.74–4.66 (m, 2H), 4.50–4.40 (m, 2H), 2.80–2.70 (m, 4H), 2.55 (br s, 12H), 2.40–2.35 (m, 4H), 2.20 (s, 6H), 1.83–1.50 (m, 8H); $^{13}$C NMR (400 MHz, DMSO-$d_6$) $\delta$ 142.3, 137.5, 135.4, 131.4, 129.2, 129.1, 128.9, 128.7, 127.7, 127.6, 127.2, 126.4, 126.1, 107.1, 104.1, 82.8, 82.2, 82.1, 64.4, 60.5, 56.0, 45.4, 31.6, 25.1, 24.5, 20.9, 18.6, 18.3. *m/z* 1321, 1307, 627 (0.5 M-2HCl-Cl), 353 (molecular ion not observed; fragmentation ions with Ru isotope patterns observed). HRMS found (EI): 627.1631; $C_{33}H_{37}N_2O_2RuS$ requires 627.1622 (1.4 ppm error), 314.0841, $C_{33}H_{38}N_2O_2RuS(2+)$ requires 314.0847 (1.9 ppm error).

### 4.8. General procedure for quinoline synthesis

2-Methylquinoline and 2-phenylquinoline were purchased from Sigma–Aldrich and Alfa Aesar.

#### 4.8.1. 2-*tert*-Butylquinoline 20[28]

To a solution of 6-nitrobenzaldehyde (3.02 g, 20 mmol) in ethanol (60 ml) was added iron power (<10 μm, aldrich, 4.47 g, 80 mmol) followed by 0.1 N aq HCl (10 ml, 1 mmol) and the resulting mixture was vigorously stirred at 95 °C (oil bath) for 2 h. TLC analysis revealed that the reduction reaction was complete and so 3,3-dimethyl-2-butanone (2.0 g, 2.5 ml, 20 mmol) and powdered KOH (1.35 g, 24 mmol) were added successively in portions (caution! potential exotherm; add KOH slowly). The reaction mixture was stirred at 95 °C, then cooled to rt, diluted with DCM (600 ml) and filtered through a Celite pad. The filtrate was washed with water (100 ml) and the aqueous phase was back-extracted with DCM (2 × 40 ml). The combined organic phases were dried over $MgSO_4$, filtered and concentrated in vacuo to give 2-*tert*-butylquinoline **20** as an orange red oil (3.7 g, 100%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.03 (d, $J$ = 8.6 Hz, 2H), 7.73 (d, $J$ = 7.5 Hz, 1H), 7.65 (t, $J$ = 7.0 Hz, 1H), 7.50 (d, $J$ = 8.7 Hz, 1H), 7.45 (t, $J$ = 7.1 Hz, 1H), 1.49 (s, 9H); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 169.3, 147.5, 135.9, 129.5, 129.0, 127.2, 126.5, 125.6, 118.2, 38.2, 30.2.

#### 4.8.2. 6,7-Dimethoxy-2-methylquinoline 28[28]

To a solution of 6-nitroveratraldehyde (2.11 g, 10 mmol) in ethanol (30 ml) was added iron power (<10 μm, aldrich, 2.23 g, 40 mmol) followed by 0.1 N aq HCl (5 ml, 0.5 mmol) and the resulting mixture was vigorously stirred at 95 °C (oil bath) for 2 h. TLC analysis revealed that the reduction reaction was complete and so acetone (0.58 g, 0.73 ml, 10 mmol) and powdered KOH (0.67 g, 12 mmol) were added successively in portions (caution! potential exotherm; add KOH slowly). The reaction mixture was stirred at 95 °C, then cooled to rt, diluted with DCM (300 ml) and filtered through a Celite pad. The filtrate was washed with water (50 ml) and the aqueous phase was back-extracted with DCM (2 x 20 ml). The combined organic phases were dried over $MgSO_4$, filtered and concentrated in vacuo to give 6,7-dimethoxy-2-methylquinoline **28** as brown crystals (1.55 g, 76 %). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.88 (d, $J$ = 8.3 Hz, 1H), 7.38 (s, 1H), 7.10 (d, $J$ = 8.3 Hz, 1H), 6.95 (s, 1H), 4.01 (s, 3H), 3.99 (s, 3H), 2.70 (s, 3H); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 156.5, 152.3, 149.1, 144.8, 134.5, 121.7, 120.1, 107.5, 105.1, 56.1, 56.0, 25.0.

#### 4.8.3. 2-Ethylquinoline 21[29]

2-Methylquinoline (2.50 g, 17.5 mmol) **5** was dissolved in dry THF (35 ml). The reaction vessel was cooled to −78 °C and *n*-butyllithium in hexanes (1.6 M, 10.9 ml, 17.5 mmol) was added. After 30 min, methyliodide (3.26 g, 1.43 ml, 23 mmol) was added via a syringe. The mixture was allowed to gradually warm to rt while being stirred overnight. The resulting light yellow solution was concentrated, diluted with water (75 ml) and brine (25 ml) and extracted thrice with 75 ml portions of dichloromethane. The combined organic layers were dried over $MgSO_4$, and after concentration yielded a yellow oil (1.90 g, 69%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.99 (m, 2H), 7.70 (d, $J$ = 8.1 Hz, 1H), 7.61 (dtd, $J$ = 1.4, 1.5, 1.4 Hz, 1H), 7.39 (dmd, $J$ = 1.0, 1.0 Hz, 1H), 7.25 (d, $J$ = 8.5 Hz, 1H), 2.88 (q, $J$ = 7.6 Hz, 2H), 1.30 (t, $J$ = 7.7 Hz, 3H); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 163.4, 147.2, 135.8, 128.8, 128.2, 126.9, 126.1, 125.1, 120.3, 31.7, 13.0.

#### 4.8.4. 2-Propylquinoline 22[29]

Prepared as for 2-ethylquinoline **21** as a yellow oil (1.83 g, 61%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.05 (dd, $J$ = 3.6, 3.7 Hz, 2H), 7.78 (d, $J$ = 8.1 Hz, 1H), 7.68 (dtd, $J$ = 1.4, 1.5, 1.4 Hz, 1H), 7.49 (dmd, $J$ = 1.0, 1.0 Hz, 1H), 7.25 (d, $J$ = 8.5 Hz, 1H), 2.99 (sts, $J$ = 1.6 Hz, 2H), 1.90 (m, 2H), 1.05 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 163.0, 148.0, 136.2, 129.3, 128.9, 127.5, 126.8, 125.7, 121.4, 41.3, 23.3, 14.0.

#### 4.8.5. 2-Butylquinoline 23[29]

Prepared as for 2-ethylquinoline **21** as a yellow oil (1.70 g, 92%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.06 (d, $J$ = 8.5 Hz, 1H), 7.99 (d, $J$ = 8.4 Hz, 1H), 7.71 (d, $J$ = 8.1 Hz, 1H), 7.64 (t, $J$ = 7.0 Hz, 1H), 7.43 (t, $J$ = 7.1 Hz, 1H), 7.23 (d, $J$ = 8.4 Hz, 1H), 2.98–2.94 (m, 2H), 1.83–1.75 (m, 2H), 1.43 (h, $J$ = 7.4 Hz, 2H), 0.95 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 163.1, 147.9, 136.1, 129.3, 128.8, 126.7, 125.6, 121.3, 39.1, 32.2, 22.7, 14.0.

#### 4.8.6. 2-Phenylethylquinoline 24[29]

Prepared as for 2-ethylquinoline **21** as a yellow oil (3.02 g, 74%).$^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.23 (d, $J$ = 8.4 Hz, 1H), 7.97 (d, $J$ = 8.4 Hz, 1H), 7.73 (m, 2H), 7.49 (t, $J$ = 7.8 Hz, 1H), 7.37–7.24 (m, 5H), 7.18 (d, $J$ = 8.4 Hz, 1H), 3.38–3.34 (m, 2H), 3.26–3.22 (m, 2H); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 161.8, 148.1, 141.6, 136.2, 129.0, 128.6, 128.6, 126.9, 126.2, 125.9, 121.6, 41.1, 36.0.

#### 4.8.7. 2-(3,5-Dimethoxyphenethyl)quinoline 26[29]

Prepared as for 2-ethylquinoline **21** as an orange oil (2.29 g, 78%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.05 (t, $J$ = 8.5 Hz, 2H), 7.77 (dd, $J$ = 8.1, 1.2 Hz, 1H), 7.69 (t, $J$ = 6.9 Hz, 1H), 7.49 (t, $J$ = 7.0 Hz, 1H), 7.24 (d, $J$ = 8.3 Hz, 1H), 6.43 (d, $J$ = 2.3 Hz, 2H), 6.32 (t, $J$ = 2.3 Hz, 1H), 3.74 (s, 6H), 3.31–3.26 (m, 2H), 3.12–3.07 (m, 2H); $\nu_{max}$/cm$^{-1}$ (thin film) 3057, 2998, 2935, 2837, 1735, 1594, 1563, 1504, 1459, 1427, 1349, 1310, 1295, 1204, 1147, 1115, 1065, 826, 750, 690; $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 161.1, 160.2, 147.4, 143.3, 135.6, 135.5, 128.8, 128.2, 126.9, 126.2, 125.2, 121.0, 105.9, 97.6, 54.6, 40.2, 35.6. *m/z* (ESI) 294 (M+H). HRMS Found (EI): [M$^+$+H] 294.1486, $C_{19}H_{20}NO_2$ requires 294.1489 (1.0 ppm error).

#### 4.8.8. 2-(2-(6-Bromobenzo[*d*][1,3]dioxol-5-yl)ethyl)quinoline 25[29,30]

Prepared as for 2-ethylquinoline **21** as white crystals (1.65 g, 46%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.05 (d, $J$ = 8.3 Hz, 2H), 7.77 (dd, $J$ = 8.2, 1.5 Hz, 1H), 7.68 (t, $J$ = 6.9 Hz, 1H), 7.48 (t, $J$ = 6.9 Hz, 1H), 7.27 (d, $J$ = 8.4 Hz, 1H), 7.00 (s, 1H), 6.72 (s, 1H), 5.91 (s, 2H), 3.24–3.15 (m, 4H); $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 135.7, 128.8, 128.3, 126.9, 125.2, 121.0, 112.1, 109.6, 100.9, 38.7, 35.5.

### 4.9. General procedure for the asymmetric transfer hydrogenation of ketones[25d]

A solution of ruthenium dimer (0.0025 mmol) in formic acid/triethylamine (5:2) azeotrope (0.5 ml) was stirred in a flame-dried schlenk tube at 28 °C for 30 min. Ketone (1 mmol) was added. The reaction mixture was stirred at 28 °C and monitored by TLC. After the starting material was consumed, the reaction mixture

was diluted by DCM (6.7 ml) and washed with $NaCO_3$ solution (3 × 5 ml). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure.

#### 4.9.1. Reduction of acetophenone using catalyst 11

Enantiomeric excess and conversion by GC analysis: 97% ee (*R*) (Chrompac cyclodextrin-β-236M-19 50 m, $T$ = 115 °C, $P$ = 15 psi, ketone 22.2 min, *R* isomer 33.5 min, *S* isomer 36.7 min); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.34–7.21 (m, 5H), 4.79 (q, $J$ = 6.5, 1H), 2.62 (s, 1H), 1.44 (d, $J$ = 6.5, 3H); $\delta_C$ (300 MHz; $CDCl_3$) 145.9, 128.5, 127.4, 125.5, 70.3, 25.2.

#### 4.9.2. Reduction of acetylcyclohexane using catalyst 11

Enantiomeric excess and conversion by GC analysis: 74% ee (*S*) (Chrompac cyclodextrin-β-236 M-19 50 m, $T$ = 115 °C, $P$ = 15 psi, ketone 18.8 min, *R* isomer 28.1 min, *S* isomer 31.0 min); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.59–3.51 (m, 1H), 1.88–1.62 (m, 5H), 1.37 (br s, 1H), 1.15 (d, $J$ = 6.3 Hz, 3H), 0.91–1.31 (m, 6H); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 72.2, 45.1, 28.7, 28.4, 26.5, 26.2, 26.1, 20.4.

### 4.10. General procedure for the asymmetric transfer hydrogenation of Quinolines[22a]

A solution of ruthenium dimer (0.0025 mmol) and imine (1 mmol) in Methanol (1.6 ml) was stirred in a flame-dried Schlenk tube at 28 °C for 10 min. Formic acid/triethylamine (5:2) azeotrope (0.5 ml) was then added. The reaction mixture was stirred at 28 °C and monitored by TLC. After the starting material was consumed, $NaHCO_3$ solution (5 ml) was added and was extracted with DCM (3 × 6.7 ml). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure.

### 4.11. General procedure for the racemic standards[3b]

To reaction bottle (A) were added [Ru(*p*-cymene)$Cl_2$]$_2$ (0.0028 g, 0.0045 mmol) and undistilled THF (2 ml). The mixture was stirred until the solution was homogeneous. At the same time, to the reaction bottle (B) were added quinoline (0.13 g, 0.12 ml, 0.89 mmol) and $I_2$ (0.012 g, 0.045 mmol) followed by THF (1 ml). The mixture was stirred until the iodine was dissolved. Then to the reaction bottle (B) was added the solution of [Ru(*p*-cymene)$Cl_2$]$_2$ of THF in bottle (A). The final mixture was pressurised to 600 psi hydrogen and stirred at 20 °C for 20 h. The reaction mixture was concentrated to afford the crude product and a sample was taken for GC analysis.

#### 4.11.1. (*R*)-2-Methyl-1,2,3,4-tetrahydroquinoline 5

Reduction of **4** using catalyst **9;** 46% ee and 96% conversion, reduction of **4** using catalyst **12**; 93% ee and 68% conversion: Enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236M-19 50 m, $T$ = 125 °C, $P$ = 15 psi, gas He. imine 43.9 min, *S* isomer 67.5 min (minor), *R* isomer 68.6 min (major); $^*[\alpha]_D^{27}$ = +46.7 (*c* 0.5, $CHCl_3$) 43% ee (*R*) (lit.[31] $[\alpha]_D^{25}$ = −78.3 (*c* 0.76, $CHCl_3$) 91% ee (*S*); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.98–6.95 (m, 2H), 6.61 (t, $J$ = 7.2 Hz, 1H), 6.48 (d, $J$ = 8.1 Hz, 1H), 3.70 (br s, 1H), 3.44–3.38 (m, 1H), 2.85–2.74 (m, 2H), 1.94–1.91 (m, 1H), 1.64–1.55 (m, 1H), 1.22 (d, $J$ = 6.3 Hz, 3H); $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 144.2, 128.7, 126.1, 120.5, 116.4, 113.4, 46.6, 29.5, 26.0, 22.0. $^*[\alpha]_D$ determined on sample with 43% ee.

#### 4.11.2. (*R*)-2-Ethyl-1,2,3,4-tetrahydroquinoline

Reduction of **21** using catalyst **9;** 41% ee and 95% conversion: enantiomeric excess and conversion by GC analysis (Chrompac cyclodextrin-β-236 M-19 50 m, $T$ = 115 °C, $P$ = 15 psi, gas He. imine 94.6 min, *S* isomer 174.0 min (minor), *R* isomer 176.4 min (major); $[\alpha]_D^{28}$ = +35.6 (*c* 0.5, $CHCl_3$) 41% ee (*R*) (lit.[31] $[\alpha]_D^{25}$ = −73.2 (*c* 0.24, $CHCl_3$) 91% ee (*S*); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.98–6.94 (m, 2H), 6.60 (td, $J$ = 7.4, 1.1 Hz, 1H), 6.47 (dd, $J$ = 8.6, 1.3 Hz, 1H), 3.77 (br s, 1H), 3.19–3.13 (m, 1H), 2.85–2.69 (m, 2H), 2.00–1.94 (m, 1H), 1.63–1.48 (m, 3H), 0.98 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 144.1, 128.6, 126.1, 120.8, 116.3, 113.4, 52.4, 28.8, 27.0, 25.8, 9.5. Reduction of **21** using catalyst **12**; 91% ee and 67% conversion: enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane/isopropanol = 90:10, flow rate 0.2 ml/min, 254 nm, 17.0 °C): $t_R$ = 26.8 min (major), $t_S$ = 30.5 (minor).

#### 4.11.3. (*R*)-2-Propyl-1,2,3,4-tetrahydroquinoline

Reduction of **22** using catalyst **9**; 42% ee and 94% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD, hexane/isopropanol = 90:10, flow rate 0.2 ml/min, 254 nm, 18.0 °C): $t_R$ = 23.6 min (major), $t_S$ = 26.8 (minor); $[\alpha]_D^{24}$ = +54.1 (*c* 0.5, $CHCl_3$) 42% ee (*R*) (lit.[32] $[\alpha]_D^{21}$ = −70.8 (*c* 1.1, $CHCl_3$) 80% ee (*S*); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.97–6.94 (m, 2H), 6.59 (t, $J$ = 7.3 Hz, 1H), 6.47 (d, $J$ = 8.0 Hz, 1H), 3.76 (br s, 1H), 3.28–3.21 (m, 1H), 2.85–2.69 (m, 2H), 1.98–1.92 (m, 1H), 1.64–1.54 (m, 1H), 1.51–1.39 (m, 4H), 0.96 (t, $J$ = 6.6 Hz, 3H); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 144.8, 129.3, 126.7, 121.4, 116.9, 114.1, 51.3, 38.9, 28.2, 26.5, 19.0, 14.3. Reduction of **22** using catalyst **12**; 90% ee and 65% conversion: enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane/isopropanol = 90:10, flow rate 0.2 ml/min, 254 nm, 14.5 °C): $t_R$ = 24.5 min (major), $t_S$ = 28.1 (minor).

#### 4.11.4. (*R*)-2-Butyl-1,2,3,4-tetrahydroquinoline

Reduction of **23** using catalyst **9**; 41% ee and 93% conversion: enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD, hexane:isopropanol = 90:10, flow rate 0.2 ml/min, 254 nm, 18.5 °C): $t_R$ = 21.8 min (major), $t_S$ = 24.4 (minor); $[\alpha]_D^{26}$ = +46.6 (*c* 0.5, $CHCl_3$) 41% ee (*R*) (lit.[31] $[\alpha]_D^{25}$ = −78.2 (*c* 0.53, $CHCl_3$) 89% ee (*S*); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.96–6.93 (m, 2H), 6.59 (t, $J$ = 7.4 Hz, 1H), 6.46 (d, $J$ = 8.3 Hz, 1H), 3.72 (br s, 1H), 3.24–3.18 (m, 1H), 2.84–2.68 (m, 2H), 1.98–1.91 (m, 1H), 1.63–1.53 (m, 1H), 1.51–1.45 (m, 2H), 1.41–1.32 (m, 4H), 0.94–0.91 (m, 3H); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 144.8, 129.3, 126.7, 121.4, 116.9, 114.1, 51.6, 36.5, 28.2, 28.0, 26.5, 22.9, 14.1. Reduction of **23** using catalyst **12**; 92% ee and 64% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane/isopropanol = 90:10, flow rate 0.2 ml/min, 254 nm, 14.0 °C): $t_R$ = 22.8 min (major), $t_S$ = 25.6 (minor).

#### 4.11.5. (*S*)-2-Phenyl-1,2,3,4-tetrahydroquinoline

[21] Reduction of **19** using catalyst **9**; 73% ee and 68% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD, hexane/isopropanol = 90:10, flow rate 0.5 ml/min, 254 nm, 21.0 °C): $t_S$ = 17.0 min (major), $t_R$ = 21.1 (minor); $[\alpha]_D^{27}$ = −31.3 (*c* 0.5, $CHCl_3$) 73% ee (*S*) (lit.[31] $[\alpha]_D^{25}$ = +71.2 (*c* 1.0, $CHCl_3$) 72% ee (*R*); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.40–7.26 (m, 5H), 7.00 (m, 2H), 6.65 (t, $J$ = 6.7 Hz, 1H), 6.55 (d, $J$ = 7.7 Hz, 1H), 4.43 (dd, $J$ = 3.3, 3.3 Hz, 1H), 4.04 (br s, 1H), 2.97–2.88 (m, 1H), 2.73 (tt, $J$ = 4.8, 4.8 Hz, 1H), 2.15–2.09 (m, 1H), 2.04–1.94 (m, 1H); $^{13}$C NMR (400 MHz, $CDCl_3$) $\delta$ 144.8, 144.7, 129.3, 128.6, 127.5, 126.9, 126.6, 120.9, 117.2, 114.0, 56.3, 31.0, 26.4. Reduction of **19** using catalyst **12**; 86% ee and 30% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane/isopropanol = 90:10, flow rate 0.5 ml/min, 254 nm, 19.0 °C): $t_S$ = 17.1 min (major), $t_R$ = 21.5 (minor).

#### 4.11.6. (*R*)-2-Phenethyl-1,2,3,4-tetrahydroquinoline

Reduction of **24** using catalyst **9**; 50% ee and 90% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD, hexane:isopropanol = 90:10, flow rate

0.5 ml/min, 254 nm, 20.0 °C): $t_R$ = 17.8 min (major), $t_S$ = 19.5 (minor); $[\alpha]_D^{25} = +45.5$ (*c* 0.5, $CHCl_3$) 50% ee (*R*) (lit.[31] $[\alpha]_D^{25} = -73.1$ (*c* 0.55, $CHCl_3$) 92% ee (*S*); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.30–7.16 (m, 5H), 6.97–6.92 (m, 2H), 6.59 (td, *J* = 7.4, 1.1 Hz, 1H), 6.42 (dd, *J* = 8.6, 1.3 Hz, 1H), 3.80 (br s, 1H), 3.31–3.22 (m, 1H), 2.85–2.66 (m, 4H), 2.01–1.92 (m, 1H), 1.84–1.77 (m, 2H), 1.71–1.59 (m, 1H); $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 143.9, 141.3, 128.7, 127.9, 127.8, 126.1, 125.4, 120.7, 116.4, 113.5, 50.5, 37.7, 31.6, 27.4, 25.6. Reduction of **24** using catalyst **12**; 93% ee and 57% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane/isopropanol = 90:10, flow rate 0.5 ml/min, 254 nm, 15.0 °C): $t_R$ = 19.7 min (major), $t_S$ = 21.7 (minor).

#### 4.11.7. 2-*tert*-Butyl-1,2,3,4-tetrahydroquinoline

Reduction of **20** using catalyst **9**; 0% ee and 57% conversion: enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane/isopropanol = 90:10, flow rate 0.5 ml/min, 254 nm, 15.0 °C): $t_R$ = 20.5 min, $t_S$ = 27.5; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.98–6.94 (m, 2H), 6.52 (td, *J* = 7.4, 1.1 Hz, 1H), 6.45 (d, *J* = 7.7 Hz, 1H), 3.78 (br s, 1H), 3.00–2.96 (m, 1H), 2.83–2.70 (m, 2H), 2.00–1.95 (m, 1H), 1.60–1.55 (m, 1H), 0.98 (s, 9H); $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 144.8, 128.4, 126.1, 120.9, 116.1, 113.4, 60.3, 32.8, 26.8, 25.4, 22.5. Reduction of **20** using catalyst **12**; 0% ee and 16% conversion; HPLC (Chiralcel OD-H, hexane/isopropanol = 90:10, flow rate 0.2 ml/min, 254 nm, 14.0 °C): $t_R$ = 20.6 min, $t_S$ = 27.9.

#### 4.11.8. (*R*)-2-(3,5-Dimethoxyphenethyl)-1,2,3,4-tetrahydroquinoline

Reduction of **26** using catalyst **9**; 67% ee and 93% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane:isopropanol = 80:20, flow rate 0.6 ml/min, 254 nm, 18.0 °C): $t_R$ = 28.1 min (major), $t_S$ = 36.8 (minor); $^*[\alpha]_D^{24} = +39.5$ (*c* 0.5, $CHCl_3$) 67% ee (*R*); $\nu_{max}/cm^{-1}$ (thin film) 3675, 3396, 2935, 2838, 1594, 1460, 1428, 1351, 1309, 1276, 1254, 1203, 1148, 1114, 1056, 924, 830, 746, 718, 696, 667; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 6.98–6.90 (m, 2H), 6.60 (td, *J* = 7.4, 1.1 Hz, 1H), 6.45 (dd, *J* = 8.2, 1.4 Hz, 1H), 6.38–6.35 (m, 2H), 6.32–6.28 (m, 1H), 3.77 (s, 6H), 3.34–3.25 (m, 1H), 2.81–2.72 (m, 2H), 2.69–2.63 (m, 2H), 2.2–1.94 (m, 1H), 1.85–1.75 (m, 2H), 1.72–1.60 (m, 1H). $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 160.9, 144.3, 129.3, 126.8, 121.3, 117.0, 114.2, 106.5, 97.9, 55.3, 51.1, 38.0, 32.5, 28.0, 26.2. HRMS Found (EI): $[M^+ + H]$ 298.1798, $C_{19}H_{24}NO_2$ requires 298.1802 (1.3 ppm error). Reduction of **26** using catalyst **12**; 94% ee and 58% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane:isopropanol = 80:20, flow rate 0.6 ml/min, 254 nm, 19.0 °C): $t_R$ = 27.4 min (major), $t_S$ = 35.9 (minor). *The absolute configuration has not been determined, but can be compared with the reduction product of substrate **27**.

#### 4.11.9. (*R*)-2-(2-(6-Bromobenzo[d][1,3]dioxol-5-yl)ethyl)-1,2,3,4-tetrahydroquinoline

Reduction of **25** using catalyst **9**; 47% ee and 86% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane/isopropanol = 80:20, flow rate 0.6 ml/min, 254 nm, 19.0 °C): $t_S$ = 21.2 min (major), $t_R$ = 29.2 (minor); $^*[\alpha]_D^{25} = +25.6$ (*c* 0.5, $CHCl_3$) 47% ee (*R*); $\nu_{max}/cm^{-1}$ (thin film) 3664, 3410, 2912, 1606, 1585, 1500, 1473, 1434, 1408, 1353, 1309, 1275, 1227, 1111, 1066, 1035, 964, 931, 858, 832, 746, 718, 657; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.02–6.92 (m, 3H), 6.70 (s, 1H), 6.59 (td, *J* = 7.4, 1.2 Hz, 1H), 6.45 (dd, *J* = 8.3, 1.3 Hz, 1H), 5.90 (s, 2H), 3.84 (br s, 1H), 3.38–3.30 (m, 1H), 2.88–2.72 (m, 4H), 2.10–2.00 (m, 1H), 1.88–1.72 (m, 2H), 1.60 (s, 1H); $^{13}$C NMR (300 MHz, $CDCl_3$) $\delta$ 146.8, 143.9, 133.5, 128.6, 126.1, 120.7, 116.5, 113.6, 112.7, 112.1, 109.1, 101.0, 50.3, 36.4, 31.6, 27.2, 25.6. HRMS Found (EI): $[M^+ + H]$ 360.0596, $C_{18}H_{19}BrNO_2$ requires 360.0594 (-0.7 ppm error). Reduction of **25** using catalyst **12**; 81% ee and 30% conversion: Enantiomeric excess by HPLC analysis and conversion by NMR analysis (Chiralcel OD-H, hexane/isopropanol = 80:20, flow rate 0.6 ml/min, 254 nm, 19.0 °C): $t_S$ = 21.1 min (major), $t_R$ = 29.1 (minor). *The absolute configuration has not been determined, but can be compared with the reduction product of substrate **24**.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