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# The "Reverse-Tethered" Ruthenium (II) Catalyst for Asymmetric Transfer Hydrogenation: Further Applications

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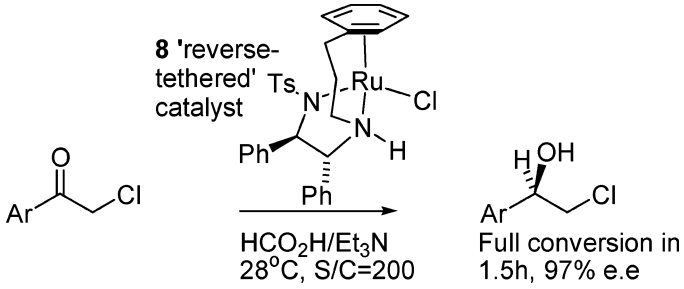


The attachment of a tethering group from the basic nitrogen atom to the arene ligand of a ruthenium(II) catalyst greatly improves its ability to catalyze asymmetric transfer hydrogenation (ATH) reactions. In this paper, we describe further applications of this versatile system to an extended substrate range.

## Introduction

Asymmetric transfer hydrogenation (ATH) is now firmly established as an excellent method for the asymmetric synthesis of enantiomerically pure alcohols.[1] One of the most significant reasons for this has been the introduction, by Noyori and co-workers, of powerful new catalyst systems based upon ruthenium (II) complexes of monotosylated diamines[2] and amino alcohols,[3] i.e., **1** and **2**, respectively. Diamine[4−6] and amino alcohol[7] based systems, as well as those based on other ligand combinations,[8−16] have been further developed and applied to numerous target syntheses by many research groups worldwide. In recent years, heterogeneous versions of the catalysts have been developed,[5] as has the application of ATH in aqueous solution.[6]

Several amino alcohol ligands have been reported for use in ATH[7] as have Ru(II) complexes of other ligand classes including

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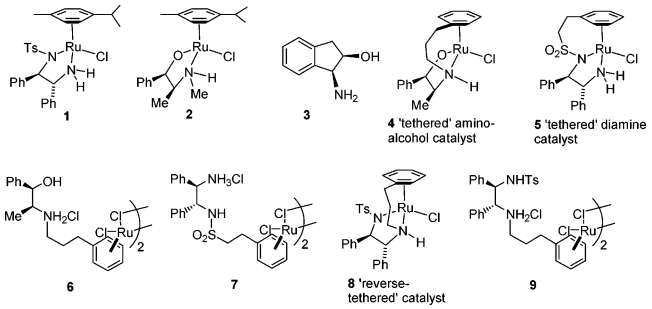


oxazolines,[8] diamines,[9] phosphine oxides,[10] amino acid derivatives,[11] tetradentate Salen-type ligands,[12] and derivatives of BINOL based phosphonites.[13] We ourselves contributed to this field through the introduction of *cis*-aminoindanol **3** as a ligand and also extension of the range of applications.[15] Recently, we reported the synthesis and applications to ketone reduction of a new series of Ru(II) catalysts in which the homochiral ligand is linked to the $\eta^6$-arene ring.[16] Representative examples are complexes **4** and **5**, which can either be isolated before use or (more conveniently) formed in situ by the treatment of dimers **6** and **7**, respectively, during the reduction of ketones in formic acid/triethylamine media. These complexes benefit from increased stability due to the "three point" attachment of the ligand to metal and also practical simplicity through the requirement for a single reagent in the reaction. A further benefit is the well-defined structures of the catalysts, which provide a basis for predictable modification toward particular substrate applications.

In our most recent studies, we discovered that the "tethered" catalyst based on monotosylated diamines, such as 1,2-diphenylethanediamine (DPEN), could be significantly improved by attaching the linking group from the "basic" amine rather than the sulfonyl group, i.e., as in **8**.[16a] Complex **8**, which we refer to as "reverse-tethered", can be prepared and isolated prior to

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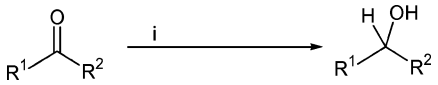
**SCHEME 1**[a]




[a] Reagents and conditions: (i) see Tables 1 and 4 for conditions and results.

use or, as for **4** and **5**, it can be formed in situ upon addition of the precursor dimer **9** to the reaction media. In this paper, we describe further applications of the "reverse-tethered" catalyst system **8** as well as the synthesis and applications to ketone reduction of a series of derivatives.

## Results and Discussion

In our preliminary paper,[16a] we decribed the synthesis and structural characterization of complex **8**, which demonstrated dramatically increased rates of ketone reduction (Scheme 1) and an expanded substrate scope relative to the untethered parent compound. Complex *RR*-**8** (used in the form of dimer *RR*-**9**) was initially evaluated for the reduction of three ketones: acetophenone, *c*-hexyl methyl ketone, and *c*-hexyl phenyl ketone (Table 1, entries 1−3). Employing the standard reduction conditions of 5:2 formic acid/triethylamine (FA/TEA), 0.5 mol % catalyst loading, a 2 M solution of ketone at 28 °C, and overnight reaction times, acetophenone (Entry 1) was completely reduced with an ee of 96% to the *R*-isomer consistent with the phenyl group of the ketone approaching adjacent to the arene ring of the catalyst. *c*-Hexyl methyl ketone (Entry 2) was again fully reduced with an ee of 69% (*S*), which coincidentally is the same ee obtained with the tethered $\beta$-amino alcohol catalyst **4**,[16c] with the catalyst directing the larger *c*-hexyl group away from the arene ring of the catalyst. *c*-Hexyl phenyl ketone (Entry 3) was also reduced in good ee (85%, *R*) although the conversion was rather low (23%).

Repeating the reductions of acetophenone and *c*-hexyl methyl ketone again, monitoring the extent of reaction more frequently via GC analysis, revealed that the activity of the catalyst was far greater than had been anticipated (Table 1, Entry 4). Reduction of acetophenone was complete in just 6 h in contrast to the usual overnight reaction times required with the untethered TsDPEN **1** systems[2a] or the sulfonamide tethered diamine catalyst **5**.[16b] Increasing the temperature to 40 °C reduced the reaction time to just 3 h with no loss of ee, whereas at 80 °C,

**TABLE 1. Initial Ketone Reductions Using Ruthenium Dimer *RR*-9**[a]

| entry | $R^1$ | $R^2$ | temp/°C | time (h) | conv. (%)[b] | ee (%)[c] | config[d] |
|---|---|---|---|---|---|---|---|
| 1 | Ph | Me | 28 | 24 | 100 | 96 | *R* |
| 2 | *c*-$C_6H_{11}$ | Me | 28 | 24 | 100 | 69 | *S* |
| 3 | Ph | *c*-$C_6H_{11}$ | 28 | 24 | 23 | 85 | *R* |
| 4 | Ph | Me | 28 | 6 | 100 | 96 | *R* |
| 5 | Ph | Me | 40 | 3 | 100 | 96 | *R* |
| 6 | Ph | Me | 80 | <0.33 | 100 | 94 | *R* |
| 7 | *c*-$C_6H_{11}$ | Me | 28 | 10 | 100 | 69 | *S* |
| 8 | *c*-$C_6H_{11}$ | Me | 14 | 24 | 88 | 72 | *S* |
| 9[e] | Ph | Me | 28 | 8 | 72 | 96 | *R* |
| 10 | Ph | Et | 28 | 6 | 100 | 95 | *R* |
| 11 | Ph | $^i$Pr | 28 | 24 | 57 | 86 | *R* |
| 12 | Ph | tBu | 28 | 24 | 56 | 78 | *R* |
| 13 | Ph | Et | 40 | 3 | 100 | 95 | *R* |
| 14 | Ph | $^i$Pr | 40 | 24 | 92 | 95 | *R* |
| 15 | Ph | tBu | 40 | 24 | 95 | 77 | *R* |
| 16 | Ph | *c*-$C_6H_{11}$ | 40 | 24 | 90 | 94 | *R* |
| 17 | Ph | *c*-$C_3H_5$ | 40 | 24 | 98 | 78 | *S*[f] |
| 18 | Ph | *c*-$C_4H_7$ | 40 | 22 | 100 | 87 | *S*[f] |
| 19 | Ph | *c*-$C_5H_9$ | 40 | 22 | 100 | 78 | *S*[f] |

[a] Ruthenium dimer **9** (0.25 mol %) (200:1 S/C), 2 M solution of ketone in $HCO_2H/NEt_3$ (5:2). [b] Determined by GC or $^1$H NMR analysis. [c] Determined by GC analysis using a chrompac cyclodextrin-$\beta$-236M-19 50m column unless otherwise specified. [d] Determined from the sign of rotation of the isolated product. [e] Reduction carried out in $^i$PrOH/KOH rather than $HCO_2H$:$NEt_3$. [f] *SS* catalyst used.

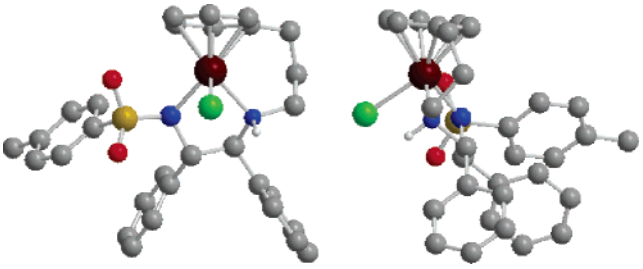


**FIGURE 1.** X-ray crystallographic structure of *SS*-**8**. The view on the right-hand side shows detail of tethering arm orientation in relation to the rest of the catalyst.

the reduction was complete in less than 20 min with just a 2% loss of ee (entries 5 and 6). The reduction of *c*-hexyl methyl ketone was also rapid, reaching full conversion in just 10 h at 28 °C. Lowering the temperature to 14 °C in an attempt to improve the ee resulted in a 3% improvement to 72%, although the reaction time was increased to 24 h to effect an 88% conversion. By way of a comparison, the reduction of acetophenone in 2-propanol using **9** was found to be far inferior to that in FA/TEA, with only 72% conversion reached after 8 h. The ee however, was unaffected and remained at 96% (Table 1, entry 9).

Although promising results were obtained using dimer **9,** we felt that a comparison with the monomer **8**, believed to be formed in-situ under the reaction conditions, should be undertaken. A sample of the *SS* enantiomer of **9** was refluxed with an excess of triethylamine in 2-propanol to form the monomer, which was first purified by flash column chromatography and then subsequently recrystallized from a mixture of dichloromethane and ethanol to give suitable crystals for X-ray analysis[16a] and testing in the reductions. The X-ray crystallographic structure of *SS*-**8** confirmed the correct structure and configuration of the catalyst as expected (Figure 1). The view of the catalyst on the right-hand side of Figure 1 seems to

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(16) (a) Hayes, A. M.; Morris, D. J.; Clarkson, G. J.; Wills, M. *J. Am. Chem. Soc.* **2005**, *127*, 7318. (b) Hannedouche, J.; Clarkson, G. J.; Wills, M. *J. Am. Chem. Soc.* **2004**, *126*, 986. (c) Cheung, F. K.; Hayes, A. M.; Hannedouche, J.; Yim, A. S. Y.; Wills, M. *J. Org. Chem.* **2005**, *70*, 3188.

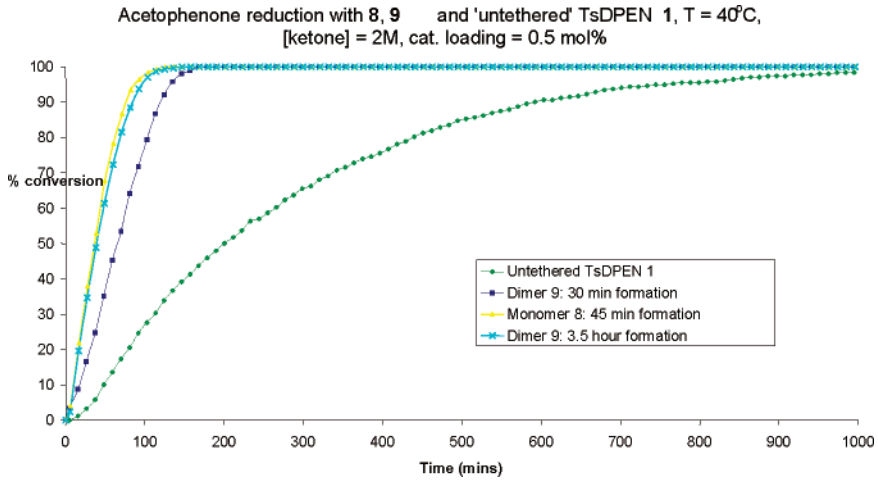


**FIGURE 2.** Conversion plotted against time for the reduction of acetophenone with dimer **9**, monomer **8**, and Ru(II)/TsDPEN complex **1**.

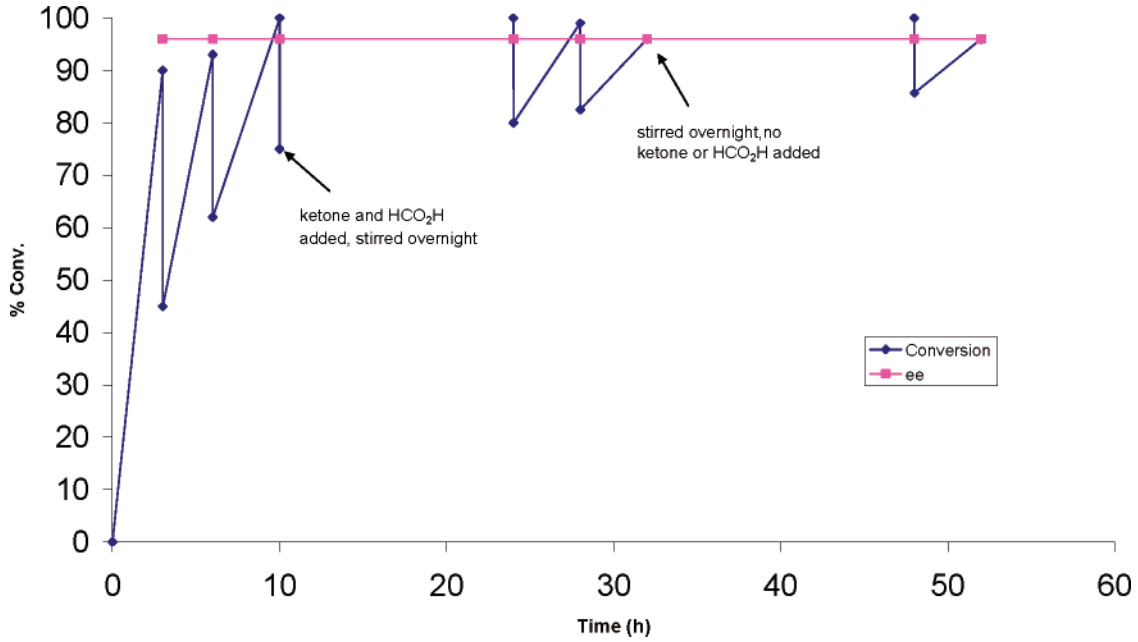


**FIGURE 3.** Repeated additions of acetophenone (200 equiv with respect to catalyst) along with additional formic acid to a solution of **8** in $HCO_2H/NEt_3$ (5:2) at 40 °C.

indicate that the tether is somewhat more remote from the area in which the substrate approaches the catalyst. It is therefore not immediately clear from the X-ray structure why the tether in *SS*-**8** increases the overall rate of reactions and in particular the enantioselectivity of reduction of alkyl/alkyl ketones.

We could follow the reduction of acetophenone at 40 °C by $^1$H NMR by stirring a mixture of the catalyst in 5:2 formic acid/triethylamine for 20 min, adding it to an NMR tube along with a small amount of $d_6$-benzene to provide a signal for the machine to lock on to and then adding the required amount of acetophenone. Conversions were then simply calculated from the ratio of the integrals for the distinctly observable methyl signal of the starting material and the methine proton of the alcohol.

The results (Figure 2) clearly illustrate the dramatic rate enhancements that the tethered catalyst provides over the untethered equivalent. The untethered catalyst **1** takes ca. 18 h to achieve complete conversion whereas with the dimer **9**, reduction is complete after 3 h. If the monomeric species **8** is used directly, the reduction is even more rapid, reaching full conversion in only 110 minutes. A closer examination of the initial profile obtained with dimer **9** indicates an initial lag at the start of the reaction. This is most likely to be due to incomplete in situ interconversion of the dimeric species to the monomer in the 30 min catalyst formation period prior to the addition of ketone. Indeed, when the dimer was stirred in the 5:2 formic acid/triethylamine mixture for 3.5 h preceding the addition of ketone, the reduction was complete in 110 minutes, identical to the result obtained using the preformed monomer **8**.

Investigations as to the stability of catalyst **8** under the reaction conditions at a loading of 0.5 mol % were made by the repeated addition of an equivalent of acetophenone along with an equivalent of formic acid to replenish the hydrogen source at regular intervals once the reaction approached or reached 100% conversion (Figure 3). The drops in conversion seen on the graph are the points at which additional substrate was added to the reaction mixture. After seven cycles of ketone addition, the catalyst remained consistently active throughout

**TABLE 2. Reductions of Substituted Aromatic and Heteroaromatic Ketones Using Ruthenium Monomers-*SS*-8**[a]

| entry | reduction product | S/C | time (h) | conv. (%)[b] | ee (%)[c] | config[d] |
|---|---|---|---|---|---|---|
| 1 | **10** | 200 | 1.25 | 100 | 70 | *S* |
| 2 | **11** | 200 | 1 | 100 | 94 | *S* |
| 3 | **11** | 5000 | 20 | 100 | 94 | *S* |
| 4 | **12** | 200 | 1.67 | 100 | 94 | *S* |
| 5 | **13** | 200 | 6 | 100 | 92 | *S* |
| 6 | **14** | 200 | 16 | 100 | 93 | *S* |
| 7 | **15** | 200 | 20 | 100 | 91 | *S* |
| 8 | **16** | 200 | 20 | 100 | 65 | *S* |
| 9 | **17** | 200 | 1.17 | 100 | 83 | *S* |
| 10 | **18** | 200 | 1 | 100 | 72 | *S* |
| 11 | **19** | 200 | 0.5 | 100 | 94 | *S* |
| 12 | **19** | 5000 | 20 | 100 | 91 | *S* |
| 13 | **20** | 5000 | 1.17 | 100 | 98 | *S* |
| 14 | **21** | 200 | 1.5 | 100 | 97 | *S* |
| 15 | **22** | 200 | 22 | 59 | 89 | *S* |
| 16 | **22**[e] | 200 | 24 | 7 | – | – |
| 17 | **22**[f] | 200 | 18 | 54 | 96 | *S* |

[a] Monomer *SS*-**8** (0.5 mol %) (200:1 S/C), 2 M solution of ketone in $HCO_2H/NEt_3$ (5:2), 40 °C. [b] Determined by GC or $^1$H NMR analysis. [c] Determined by GC analysis using a chrompac cyclodextrin-$\beta$-236M-19 50m column unless otherwise specified. [d] Determined from the sign of rotation of the isolated product. [e] Solution (0.1 M ) of ketone in $^i$PrOH, 0.5 mol % KOH. [f] Solution (0.1 M ) of ketone in $^i$PrOH, 2.5 mol % KOH.

with no loss of ee. Leaving the reaction mixture overnight, either at full conversion or with another loading of ketone, did not affect the performance of the catalyst.

**Extended Studies of Ketone Reduction.** The notable result obtained previously in the reduction of *c*-hexyl phenyl ketone led us to study a range of acetophenone derivatives bearing alternative alkyl substitution at the 2-position (Table 1, entries 10−12). It has been reported that, for catalyst **1**, as the size of the substrate alkyl substituent increases, conversions and enantioselectivities decrease significantly to the point where no virtually no reduction of *tert*-butyl phenyl ketone is observed.[1b] In contrast, when dimer *RR*-**9** was evaluated in the reduction of these substrates at 28 °C, considerable improvements over the results obtained using untethered **1** were observed. All the ketones, including *tert*-butyl phenyl ketone, were converted to the corresponding alcohol products. The reductions were then repeated at 40 °C in an effort to improve the conversions (Table 1, entries 13−16). Pleasingly, all the ketones were reduced with a conversion of 90% or greater. The higher temperature had little effect on enantioselectivity and indeed increased the ee in some cases (entries 14 and 16).

A further set of phenyl-alkyl ketones containing cyclic alkyl groups were investigated (Table 1, Entries 17−19). Reactions were generally performed at 40 °C from this point onward in the study. The reductions of this series of ketones all proceeded in good yields, with conversions of greater than 90% observed again in all cases. The last three reductions in Table 1 were performed using *SS*-**9** as the catalyst. Using either the monomer **8** or the dimer precursor **9**, the reductions of ketones were complete in significantly shorter reaction times than for the untethered parent. For particularly challenging substrates, for example the *tert*-butyl substituted ketone, the tethered catalyst promotes reactions in cases where the untethered is much slower.[1b]

An extended range of more diverse substrates were then investigated (Table 2). The reduction products **10**−**22** obtained using monomer *SS*-**8** are illustrated in Figure 4.

The results obtained for a series of methoxy-substituted acetophenones revealed a clear trend. Substitution at either the 3′ or 4′-position (Entries 2−4) does not have an adverse effect on the ee obtained, whereas 2′-substitution (Entry 1) is detrimental to the ee. The reductions were rapid in each case, however, and complete reduction was observed in a shorter time than was required for acetophenone. The short reaction times permit the catalyst loading to be sharply reduced (Entry 3), as illustrated for product **11**. Although the reaction time is increased to 20 h (for 97% conversion), the extended time is not detrimental to the ee. Encouraged by the excellent result obtained for phenyl/cyclohexyl ketone reduction, we examined the synthesis of two related alcohols containing oxygen and nitrogen in the six-membered rings (Entries 5 and 6). Both products **13** and **14** were formed in excellent ee with full conversion. The ketone precursor to **14** was prepared simply by $^t$Boc protection of commercially available 4-benzoylpiperidine hydrochloride.[17] The ketone precursor to **13** was prepared in 3 steps from tetrahydro-4H-pyran-4-one.[18] Full details are given in the Supporting Information.

Given the promising result with **14**, we considered that catalyst **8** might be effective at the synthesis of the serotonin antagonist **16**[19,20] through reduction of ketone **24**, an approach which to the best of our knowledge has not been reported for this compound. We were anxious, however, that the ortho-methoxy substitutent might cause a reduction in enantioselectivity. We first examined the reduction of analogue **23** (prepared by the method illustrated in Scheme 4)[19] and obtained product **15** in full conversion in 91% ee (Entry 7), thereby confirming that the alkyl side chain was not detrimental to the reaction. Asymmetric reduction of **24** (preparation illustrated in Scheme 2) gave **16** in only 65% ee, however (Entry 8), which indicated that the proximal methoxy group was detrimental to the enantioselectivity of the reaction as previously observed for compound *S*-**10**.

Heteroaromatic substrates were also compatible with catalyst **8**. The reduction of a series of pyridine-containing alcohols **17**−**19** was successfully completed in short reaction times and, with the exception of **18**, in excellent ee (Entries 9−12). The reduction of 2′-acetylated pyridine was repeated at an increased S/C of 5000, resulting in complete reduction in 20 h, although in slightly reduced ee. Acetylfuran and thiophene were easily reduced to **20** and **21**, respectively, in excellent ee values of 98 and 97% respectively, the former at S/C of 5000.

The reduction of the $\alpha,\beta$-acetylene ketone **22**, following a process first reported by Noyori[2d] using **8**, was attempted (Table 2, entries 15−17). Using formic acid/triethylamine as the solvent (Entry 15), a good ee of 89% was obtained but the reaction appeared to stop at a conversion of 59%. Noyori reports a similar observation when using **1** in formic acid/triethylamine and comments that the reduction of this class of ketone works best in 2-propanol. Fortunately, due to the low oxidation potential of the ketone, the usual issue of reversibility when using

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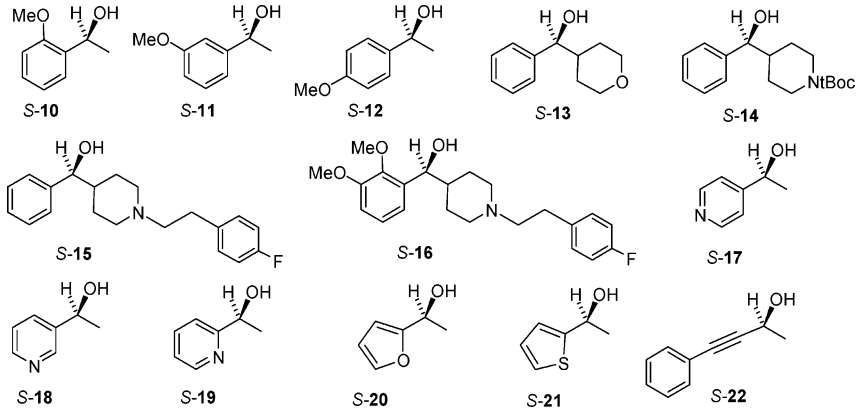
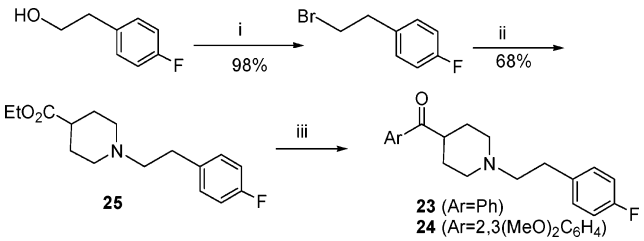


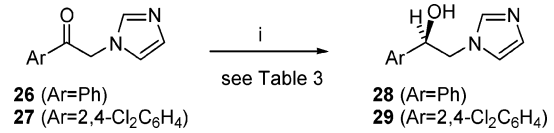

**FIGURE 4.** Products of reduction using monomer *SS*-**8**. Full details are summarized in Table 2.

**SCHEME 2**[a]



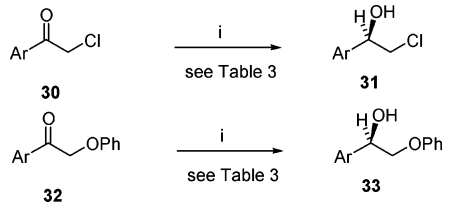

[a] Reagents and conditions: (i) $CBr_4$, $PPh_3$, DCM, rt, 98%. (ii) Ethyl isonipecotate, $K_2CO_3$, DMF, 90 °C, 68%. (iii) $NH(OCH_3)CH_3$.HCl, 1M EtMgBr, THF, −15 °C to 0 °C then either PhLi (for **23**) or veratrole, $^n$BuLi (prepared separately, for **24**), 0 °C to room temperature, 79% for **23**, 62% for **24**.

**SCHEME 3**[a]




[a] Reagents and conditions: (i) 0.5 mol % *SS*-**8**, 2M substrate in $HCO_2H$/$Et_3N$, 40 °C.

**SCHEME 4**[a]




[a] Reagents and conditions: (i) 0.5 mol % *SS*-**8**, 2M substrate in $HCO_2H$/$Et_3N$, 28 or 40 °C.

2-propanol is less of a problem. When reduction in 2-propanol with **8** was first attempted (Entry 16), using 0.5 equivalent of base (Noyori's conditions), only a poor conversion of 7% was obtained. Increasing the amount of base to 2.5 equiv (Entry 17) led to an improved conversion of 54% and 96% ee.

**α-Substituted Ketones.** Compounds containing a substituent at the position α to the ketone are particularly useful substrates because they act as precursors for a variety of synthetic intermediates, e.g., epoxide, diols, and amino alcohols. A recent report[4v] on the ATH of two α-imidazole substituted acetophenones, **26** and **27**, using **1**, prompted us to examine the application of **8** to these substrates (Scheme 3, Table 3).

**TABLE 3. Reductions of α-Substituted Ketones Using Ruthenium Monomer *SS*-8**[a]

| entry | reduction product | S/C | time (h) | conv (%)[b] | ee (%)[c] | config[d] |
|---|---|---|---|---|---|---|
| 1[e] | **28** | 200 | 18 | 100 | 99 | *R* |
| 2 | **28** | 200 | 24 | 43 | nd | − |
| 3[f] | **29** | 200 | 16 | 100 | 71 | *R* |
| 4[g] | **29** | 200 | 24 | 48 | 68 | *R* |
| 5[h] | **31** | 200 | 1.5 | 100 | 95 | *R* |
| 6[i] | **31** | 200 | 2 | 100 | 97 | *R* |
| 7[h] | **33** | 200 | 3 | 100 | 95 | *R* |

[a] Monomer *SS*-**8** (0.5 mol %) (200:1 S/C), 2 M solution of ketone in $HCO_2H/NEt_3$ (5:2), 40 °C. [b] Determined by GC or $^1$H NMR analysis. [c] Determined by GC analysis using a chrompac cyclodextrin-β-236M-19 50m column unless otherwise specified. [d] Determined from the sign of rotation of the isolated product. [e] [ketone] = 0.5 M. [f] [ketone] = 1.0 M. [g] DCM as cosolvent, 1:1 $HCO_2H/NEt_3$ (5:2). [h] 28 °C. [i] 28 °C, EtOAc as cosolvent, v/v 1.4:1.1 $HCO_2H/NEt_3$ (5:2).

The reduction of **26** was initially carried out at a lower ketone concentration of 0.5 M compared to the usual concentration of 2.0 M (Entry 1). A remarkable ee of in excess of 99% was obtained along with quantitative conversion to product **28**. When the reduction was repeated at the usual 2.0 M concentration of ketone, surprisingly a conversion of only 43% was obtained. Dichloro substituted **27** was then reduced, again at a lower concentration of ketone (1.0 M) using the standard 5:2 formic acid/triethylamine solvent system/hydrogen source (Entry 3). As with **26**, quantitative conversion was observed but a product of only of 71% ee was obtained. For the reduction of **27** with catalyst **1**, the authors reported an extended series of optimization studies, which revealed that DCM was an excellent cosolvent (100% conversion, 91% ee on 16 g scale at S/C of 1000).[4v] The reduction of **27** was then repeated using DCM cosolvent with **8** (Entry 4), however a slight drop in ee to 68% was noted along with a fall in the conversion. Further optimization work is required for our catalyst to compete with the best reported conditions for substrate **27**.

α-Chloroketones represent useful substrates, and particularly challenging ones for Ru(II) based ATH catalysts, because the best results have been to date obtained using Rh(III) catalysts,[21] including some of our own "tethered" variants.[22] For example, the asymmetric reduction of **30** by preformed **1** is reported to give a product of 91% ee in only 36% yield after 24h.[21f] In contrast the equivalent Rh(III) catalyst gives a product of 97% ee in 99% yield within 1 h. Using catalyst **8**, however, **30** was

**TABLE 4. Reductions of Dialkyl Ketones Using Ruthenium Dimer *SS*-9**[a]

| entry | $R^1$ | $R^2$ | time (h) | yield (%)[b] | ee (%)[c] | config[d] |
|---|---|---|---|---|---|---|
| 1 | *c*-$C_6H_{11}$ | Me | 10 | 100 | 69 | *S* |
| 2 | $^t$Bu | Me | 24 | 92 | 12 | *S* |
| 3 | Ad | Me | 24 | 48 | 37 | *S* |
| 4 | *n*-$C_6H_{11}$ | Me | 24 | 100 | 19 | *S* |
| 5 | *c*-$C_6H_{11}$ | Et | 24 | 55 | 26 | *S* |

[a] Ruthenium dimer (0.25 mol %) (200:1 S/C), 2 M solution of ketone in $HCO_2H/NEt_3$ (5:2), 28 °C. [b] Determined by GC or $^1$H NMR analysis. [c] Determined by GC analysis using a chrompac cyclodextrin-$\beta$-236M-19 50m column unless otherwise specified. [d] Determined from the sign of rotation of the isolated product.

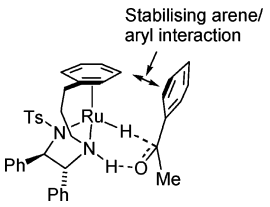



**FIGURE 5.** Reduction of aryl/alkyl ketones by catalyst *SS*-**8**.

fully reduced to a product of 95% ee within 1.5 h, reflecting the higher reactivity of this catalyst over the untethered version (Scheme 4). The ee could be improved to 97% without significant reduction in rate using a small amount of ethyl acetate cosolvent (Table 3, entry 6). For the first time, this represents the use of a Ru(II) ATH catalyst for the practical reduction of α−chloroketones, representing a viable alternative to Rh(III) catalysts[21,22] for this application. Finally, an equally useful reduction of α-phenoxy ketone **32** was achieved in 95% ee within 3 h using **8** (Table 3 entry 7).

**Studies on Alkyl/Alkyl Ketones.** The effectiveness of catalyst **8**(**9**) in the reduction of an extended range of dialkyl ketones was investigated. The results, (Scheme 1, Table 4) however, show that *SS*-**9** failed to give any reasonable enantioselection with pinacolone (Entry 2, 12% ee) or adamantyl methyl ketone (Entry 3, 37% ee). The reductions of *n*-hexyl methyl ketone and *c*-hexyl ethyl ketone failed to give notable selectivities.

**Mechanistic Discussion.** The promising results obtained with tethered monotosylated diamine complex **8** prompted further derivatization of the catalyst structures. The reduction of aryl/alkyl ketones (the majority of this study) indicated that the enantiocontrol arises from the well-established arene/aryl interaction in the reduction transition state (Figure 5; illustration for *R,R*- catalyst).[2g,2h,3b,7e,7s] In the case of the alkyl/alkyl ketone reduction, the reversed enantioselectivity suggested that the reduction was taking place through the alternative transition state illustrated in Figure 6.

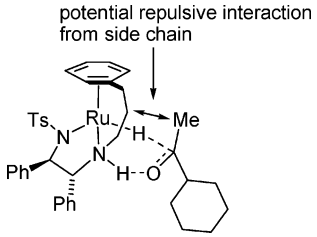



**FIGURE 6.** Reduction of alkyl/alkyl ketones by catalyst *SS*-**8**.

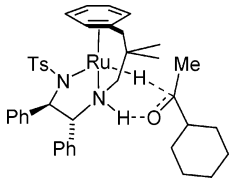



**FIGURE 7.** Speculated reduction of alkyl/alkyl ketones by proposed catalyst *SS*-**34**.

The tethering group has two important beneficial effects; it increases the rates of transfer hydrogenation in reactions in which it is used, and it gives improved enantioselectivities for alkyl/alkyl ketones over the untethered catalyst (although many substrates give rather poor results). The reason for the improved rates may be due to a superior "preorganization" toward hydride transfer imposed by the tether. Anderson et al have reported, for example, that the "H−Ru−N−H" torsion angle in Ru(II) ATH catalysts is important; the closer this is to zero then the higher the catalyst activity.[7e] In our catalyst, we have not yet calculated this angle, neither do we have an X-ray structure. However the "Cl−Ru−N−H" torsion angle in **8** is 4.5°. In the X-ray structure of **1**, the corresponding angle is higher at 18.2°, although this drops to 10.6° in the hydride.[2c] If this difference is reflected in the corresponding hydrides, it could hint at a reason for the higher reactivity of **8** over **1** and also provide a direction for further catalyst improvement. Molecular modeling studies are currently underway to determine the transition state structures through which our catalysts operate.

The reason for the effect of the tether on the reduction enantioselectivity for alkyl/alkyl ketones is less obvious. One speculation is that the tether may "lie" in the region occupied by a group on the ketone. If this is the case, then larger groups will be forced away from the chain and will occupy the area distant to the arene ring, as illustrated in Figure 6. To probe whether the chain proximity was an important factor, we elected to prepare complex **34**, in which a larger, dimethyl-substituted chain was incorporated. If this region of the chain is important for selectivity, we anticipated that we would see an effect in ketone reductions (Figure 7).

The synthesis of complex **34** is shown in Scheme 5. On the basis of a literature precedent,[23] commencing from 3-phenyl propionate, treatment of the ester with in-situ generated LDA from *n*-BuLi and diisopropylamine followed by quenching with iodomethane and repeating the process a second time gave dimethyl substituted ester **35** in moderate yield. Birch reduction of **35** achieved the desired transformation of the phenyl group to the cyclohexadiene but the ester group was also reduced to

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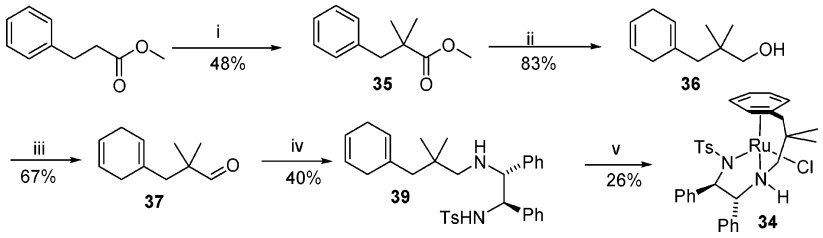
**SCHEME 5**[a]

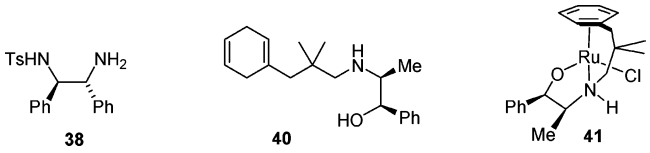



[a] Reagents and conditions: (i) $^{n}$BuLi, NH($^{i}$Pr)$_2$, MeI, THF (2 cycles), −60 °C, 48%. (ii) Na, $NH_3$, THF, EtOH, −78 °C, 83%. (iii) $COCl_2$, DMSO, $NEt_3$, DCM, −78 °C to room temperature, 67%. (iv) *RR*-TsDPEN **38**, 4A sieves, DCM, then $LiAlH_4$, THF, 40%. (v) HCl, ether then $RuCl_3$, EtOH, reflux followed by purification on alumina column, 26%.

**SCHEME 6**[a]


[a] Reagents and conditions: (i) see Table 5 for conditions and results.

the primary alcohol concurrently giving **36** in 83% yield. In the event, this was not problematic as the desired aldehyde **37** was obtained via Swern oxidation in 67% yield.




Reductive amination was employed using (*RR*)-TsDPEN **38** to generate **39** in a moderate yield of 40%. The complexation of **39** as the hydrochloric acid salts with ruthenium trichloride to give the corresponding dimer was attempted. Although the dimer appeared to be formed as evidenced by $^1$H NMR, it failed to precipitate from the reaction mixture. Efforts at recrystallizing the crude products was unsucessful, so flash column chromatography was attempted using alumina as the stationary phase. The major product eluted from the column was identified as ruthenium−chloride monomer, presumably formed while the dimer is in contact with the alumina while on the column. This led to the isolation of tethered dimethyl substituted monotosylated diamine **34** in only 26% yield. An opportunity was also taken to generate a comparison with the corresponding amino alcohol catalyst by preparing **41** from ephedrine via **40**. As was the case for **34**, the dimer was not isolated; instead, the monomer was isolated directly from the alumina column.

The effect of the introduction of the dimethyl substitution on the tethered monotosylated diamine in relation to the reduction of cyclohexyl/methyl ketone was a 5% improvement in ee over **8** to 74% when **34** was employed under identical conditions (Scheme 6, Table 5). However, the rate of reduction was significantly impaired with a conversion of only 48% achieved after 2 days. Raising the temperature to 40 °C provided an increase in rate with 60% conversion reached after 24 h with only a slight drop in ee to 73%. The reduction of acetophenone was also unsurprisingly slowed given the previous observation, and the ee was also lower than that obtained with **8**. Further evidence for the significant increase in steric interactions between the tether and the substrate as a result of the dimethyl substitution was provided with the reduction of pinacolone. The reduction using **34** at 40 °C failed to give any product although **8** had given a 92% conversion at 28 °C. The temperature had to be increased to 60 °C for **34** to effect any reduction.

**TABLE 5. Ketone Reductions Using Ruthenium Monomers *RR*-34 and *RR*-41**[a]

| entry | catalyst | $R^1$ | $R^2$ | temp (°C) | time (h) | yield (%)[b] | ee (%)[c] | config[d] |
|---|---|---|---|---|---|---|---|---|
| 1 | **34** | *c*-$C_6H_{11}$ | Me | 28 | 48 | 48 | 74 | *S* |
| 2 | **34** | *c*-$C_6H_{11}$ | Me | 40 | 24 | 60 | 73 | *S* |
| 3 | **34** | Ph | Me | 28 | 48 | 90 | 89 | *R* |
| 4 | **34** | Ph | Me | 40 | 24 | 93 | 90 | *R* |
| 5 | **34** | $^t$Bu | Me | 40 | 24 | 0 | − | − |
| 6 | **34** | $^t$Bu | Me | 60 | 18 | 10 | 49 | *S* |
| 7 | **34** | *n*-$C_6H_{11}$ | Me | 40 | 17 | 58 | 22 | *S* |
| 8 | **34** | Ph | $^t$Bu | 40 | 24 | 2 | 44 | *R* |
| 9 | **41** | *n*-$C_6H_{11}$ | Me | 28 | 2 | 26 | 48 | *S* |
| 10 | **41** | Ph | Me | 28 | 2 | 51 | 46 | *R* |

[a] Ruthenium monomer (0.5 mol %) (200:1 S/C), 2 M solution of ketone in $HCO_2H$/$NEt_3$ (5:2). [b] Determined by GC or $^1$H NMR analysis. [c] Determined by GC analysis using a chrompac cyclodextrin-$\beta$-236M-19 50m column unless otherwise specified. [d] Determined from the sign of rotation of the isolated product.

Conversions were still low at 10%, but an improvement in ee was noted in comparison to when **8** was used (49 vs 12%).

The trend for an improvement in ee for the reduction of dialkyl ketones with **34** was not seen with the corresponding $\beta$-amino alcohol **41**. The reduction of *c*-hexyl methyl ketone suffered both a drop in ee and conversion in comparison to the results seen with the parent tethered amino alcohol previously reported.[16c] The situation was the same with acetophenone: again, a drop in ee and conversion was noted. The effects of substitution on the tethering arm are significant and reveal that modification of the steric space in this region has a significant effect on enantioselectivity.

## Conclusions

In conclusion, we have demonstrated that a "tethered" catalyst for ATH reactions of ketones has broad application and significant advantages over the untethered variant. Particular advantages include increased rates, possibly due to better preorganization of the catalyst, and improved performance in the reduction of certain substrates such as hindered phenyl/tbutyl ketone and synthetically valuable α-chloro ketones.

## Experimental Section.

General experimental details have been given in a previous publication.[15g] The synthesis of dimer **9** and monomer **8** have been reported.[16a] Enantiomeric excesses were measured using chiral HPLC or chiral GC methods, details of which are given in the Experimental Section below. Absolute configurations were established by optical rotation and comparison to literature data. Racemic standards of all alcohol products were prepared by reduction of the precursor ketone with sodium borohydride.

**Synthesis of 2,2-Dimethyl-3-phenylpropionic Acid Methyl Ester 35.**[23] To a stirred solution of diisopropylamine (3.96 g, 39.1 mmol) in THF (100 $cm^3$) at −60 °C was added dropwise a solution of 2.5 M *n*-butyllithium (15.7 $cm^3$, 39.1 mmol) in hexane. The reaction mixture was stirred for 10 min, and then methyl 3-phenyl propionate (4.28 g, 26.1 mmol) was added. The reaction mixture was stirred for 10 min, and then methyl iodide (9.88 g, 69.6 mmol) was added, stirred for a further 15 min, and the reaction mixture was poured into a 1.2 M HCl solution (100 $cm^3$) and extracted with ether (2 × 100 $cm^3$). The combined extracts were dried ($MgSO_4$) and concentrated under vacuum to give the crude monomethylated product, which was then subjected to a second methylation cycle repeating the procedure described above. The resulting residue was purified by flash column chromatography (2% EtOAc/Hexane) to give **35** (2.42 g, 48%) as a colorless mobile liquid; $\nu_{max}/cm^{-1}$ (thin film) 1728 (C═O), 741 and 700 (Ph); $\delta_H$ (400 MHz; $CDCl_3$) 1.18 (6 H, s), 2.85 (2 H, s), 3.65 (3 H, s), 7.08−7.25 (5 H, m); $\delta_C$ (100.6 MHz; DMSO-$d_6$) 25.0 (2 × q), 43.7 (s), 46.4 (t), 51.7 (q), 126.5 (d), 128.0 (2 × d), 130.1 (2 × d), 137.9 (s), 177.9 (s). *m*/*z* (EI) 193 (M + $H^+$, 75%), 192 ($M^+$, 40), 133 (55), 132 (30), 91 (100).

**Synthesis of 3-Cyclohexa-1,4-dienyl-2,2-dimethylpropan-1-ol 36.** Ammonia (50 $cm^3$) was condensed into a round-bottomed flask, which had been cooled to −78 °C and equipped with an acetone/$CO_2$ condenser. **35** (1.70 g, 8.84 mmol) was dissolved in ethanol (5 $cm^3$) and slowly added to the ammonia. THF (16 $cm^3$) was added to aid dissolving the substrate, and then sodium metal was added portionwise along with regular addition of ethanol to keep the solution homogeneous. Addition was continued until the solution remained blue for more than 30 min, and the reaction mixture was then allowed to warm to room-temperature overnight, saturated ammonium chloride solution was added (50 $cm^3$) and extracted with dichloromethane (3 × 50 $cm^3$). The combined extracts were dried ($MgSO_4$) and concentrated under vacuum to give **36** (1.22 g, 83%) as a colorless mobile liquid; $\nu_{max}/cm^{-1}$ (thin film) 3337 (OH), 1037 (C−O); $\delta_H$ (400 MHz; $CDCl_3$) 0.91 (6 H, s), 1.40 (1 H, t, *J* 5.3), 1.65 (2 H), 2.69−2.71 (4 H, m), 3.35 (2 H, d, *J* 5.3), 5.45 (1 H, m), 5.69 (2 H, m); $\delta_C$ (100.6 MHz; $CDCl_3$) 24.8 (2 × q), 27.0 (t), 31.7 (t), 46.3 (t), 69.0 (s), 72.0 (t), 122.7 (d), 124.0 (d), 124.6 (d), 132.8 (s). Found (EI) 166.1357 $[M]^+$, $C_{11}H_{18}O$ requires 166.1358 (0.5 ppm error); *m*/*z* (EI) 166 ($M^+$, 15%), 119 (20), 94 (55), 92 (90), 91 (95), 79 (100).

**Synthesis of 3-Cyclohexa-1,4-dienyl-2,2-dimethylpropional-dehyde 37.** To a 2 M solution of oxalyl chloride (3.75 $cm^3$, 7.52 mmol) at −78 °C was slowly added a solution of DMSO (1.174 g, 15.03 mmol) in dichloromethane (14 $cm^3$). The reaction mixture was stirred for 15 min, and then a solution of **36** (1.000 g, 6.01 mmol) was added dropwise. After stirring for a further 50 min, triethylamine (3.640 g, 36.08 mmol) was added and the reaction mixture was allowed to warm to room temperature, diluted with water (30 $cm^3$), and extracted with dichloromethane (3 × 50 $cm^3$). The combined extracts were dried ($MgSO_4$), concentrated under vacuum, dissolved in ether (50 $cm^3$), washed with water (2 × 25 $cm^3$), dried ($MgSO_4$), and concentrated under vacuum to give **37** (0.657 g, 67%) as a colorless oil; $\nu_{max}/cm^{-1}$ (thin film) 1724 (C═O); $\delta_H$ (400 MHz; $CDCl_3$) 1.06 (6 H, s), 2.20 (2 H, s), 2.46−2.51 (2 H, m), 2.65−2.71 (2 H, m), 5.43 (1 H, m), 5.65 (2 H, m) 9.55 (1 H, s); $\delta_C$ (100.6 MHz; $CDCl_3$) 21.9 (2 × q), 26.8 (t), 30.7 (t), 45.6 (t), 46.2 (s), 123.2 (d), 123.9 (d), 124.0 (d), 131.1 (s), 206.4 (d). *m*/*z* (EI) 133 (25%), 93 (50), 91 (100), 77 (25).

**Synthesis of *N*-[(1*R*,2*R*)-2-(3-Cyclohexa-1,4-dienyl-2,2-dimethylpropylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide 39.** To a suspension of 4 Å molecular sieves (0.349 g) in dichloromethane (5.5 $cm^3$) was added **37** (0.300 g, 1.83 mmol) followed by (*RR*)-TsDPEN **38** (1.00 g, 2.73 mmol). The reaction mixture was stirred overnight, filtered, concentrated under vacuum, dissolved in THF (7 $cm^3$), and slowly added to a suspension of lithium aluminum hydride (0.139 g, 3.66 mmol) in THF (7 $cm^3$). The reactants were stirred for 1 h and then water (0.15 $cm^3$), 15% NaOH solution (aq) (0.15 $cm^3$), and further water (0.45 $cm^3$) were added successively, filtered (Celite), washed (DCM), and concentrated under vacuum to give the crude product. The residue was purified by column chromatograhy (2.5% EtOAc/Hexane to 20% EtOAc/Hexane) to give **39** (0.377 g, 40%) as a thick colorless oil; $[\alpha]_D^{20}$ −36.8 (c 1.65 in $CHCl_3$); $\nu_{max}/cm^{-1}$ (thin film) 3265 (NH), 1647 and 1600 (diene C═C), 1325 and 1153 ($SO_2N$), 767 and 698 (Ph); $\delta_H$ (400 MHz; $CDCl_3$; $Me_4Si$) 0.83 (3 H, s), 0.85 (3 H), 1.26 (1 H, br s), 1.79 (1 H, d, *J* 15.4), 1.87 (1 H, d, *J* 15.4), 1.99 (1 H, d, *J* 11.6), 2.15 (1 H, d, *J* 11.6), 2.33 (3 H, s), 2.46−2.52 (2 H, m), 2.59−2.65 (2 H, m), 3.54 (1 H, d, *J* 7.8), 4.25 (1 H, d, *J* 7.8), 5.20 (1 H, m), 5.57−5.68 (2 H, m), 6.88−7.13 (12 H, m), 7.39 (2 H, d, *J* 8.3); $\delta_C$ (100.6 MHz; $CDCl_3$; $Me_4Si$) 21.5 (q), 26.5 (2 × q), 27.0 (t), 31.6 (t), 35.2 (s), 47.4 (t), 58.0 (t), 63.3 (d), 68.6 (d), 122.7 (d), 123.9 (d), 124.6 (d), 127.1 (2 × d), 127.3 (overlapping d and 2 × d), 127.4 (2 × d), 127.5 (2 × d), 128.0 (2 × d), 128.3 (2 × d), 129.2 (2 × d), 132.4 (s), 137.0(s), 138.6 (s), 139.4 (s), 142.8 (s). Found (LSIMS) 515.2743 $[MH]^+$, $C_{32}H_{39}N_2O_2S$ requires 515.2732 (2.0 ppm error); *m*/*z* (LSIMS) 515 ($MH^+$, 100%), 254 (50).

**Synthesis of (1*R*,2*S*)-2-(3-Cyclohexa-1,4-dienyl-2,2-dimethylpropylamino)-1-phenylpropan-1-ol 40.** To a suspension of 4 Å molecular sieves (0.313 g) in dichloromethane (5 $cm^3$) was added **37** (0.270 g, 1.64 mmol) followed by (1*R*,2*S*)-norephedrine (0.248 g, 1.64 mmol). The reaction mixture was stirred overnight, filtered, and concentrated under vacuum. The residue was dissolved in methanol (10 $cm^3$), sodium borohydride (0.186 g, 4.91 mmol) added, stirred for 1 h, diluted with water (10 $cm^3$), and extracted with dichloromethane (3 × 20 $cm^3$). The combined extracts were dried ($MgSO_4$), filtered, and then concentrated under vacuum. The residue was purified by flash column chromatograhy (10% EtOAc/Hexane to 20% EtOAc/Hexane) to give **40** (0.178 g, 37%) as a thick colorless oil; $[\alpha]_D^{20}$ −4.8 (c 0.45 in $CHCl_3$); $\nu_{max}/cm^{-1}$ (thin film) 3420 (OH), 3026 (NH), 1646 and 1604 (diene C═C), 738 and 700 (Ph); $\delta_H$ (400 MHz; $CDCl_3$; $Me_4Si$) 0.80 (3 H, d, *J* 6.5), 0.94 (3 H, s), 0.95 (3 H, s), 1.95 (2 H, s), 2.41 (1 H, d, *J* 11.3), 2.56 (1 H, d, *J* 11.3), 2.63−2.74 (4 H, m), 2.82−2.89 (1 H, dq, *J* 6.5 and 3.8), 3.90 (1 H, br s), 4.72 (1 H, d, *J* 3.8), 5.41 (1 H, m), 5.68 (2 H, m), 7.22−7.36 (5 H, m); $\delta_C$ (100.6 MHz; $CDCl_3$; $Me_4Si$) 15.1 (q), 26.4 (q), 26.5 (q), 27.0 (t), 31.8 (t), 35.2 (s), 47.8 (t), 58.3 (t), 59.0 (d), 72.8 (d), 122.7 (d), 124.0 (d), 124.6 (d), 126.0 (2 × d), 126.9 (d), 128.0 (2 × d), 132.7 (s), 141.4 (s). Found (EI) 298.2185 $[M - H]^+$, $C_{20}H_{28}NO$ requires 298.2171 (4.8 ppm error); *m*/*z* (EI) 299 ($M^+$, 25%), 279 (40), 191 (100), 145 (35), 104 (50), 90 (55), 83 (40).

**Synthesis of *N*-[(1*R*,2*R*)-2-(2,2-Dimethyl-3-phenylpropylamino)-1,2-diphenylethyl]-4-methylbenzenesulfonamide Ruthenium Monomer 34.** To a stirred solution of **39** (0.300 g, 0.58 mmol) in dichloromethane (7.5 $cm^3$) was added a 1 M solution of HCl in diethyl ether (1.8 $cm^3$, 1.80 mmol), and the reactants were stirred for 30 min. The solvent was removed from the resulting precipitate under vacuum, dissolved in ethanol (20 $cm^3$), and ruthenium trichloride trihydrate (0.107 g, 0.41 mmol) was added. The reaction mixture was heated at reflux overnight, cooled to room temperature, and concentrated under vacuum to give the crude product. The residue was purified by column chromatography on alumina (0.1% MeOH/DCM to 2% MeOH/DCM) to give **34** (0.070 g, 26%) as an orange solid; mp > 300 °C; $\nu_{max}/cm^{-1}$ (solid) 3442 (NH), 1588 and 1495 ($NH_3^+$), 1332 and 1154 ($SO_2N$), 764 and 697 (Ph); $\delta_H$ (300 MHz; $CDCl_3$; $Me_4Si$) 0.95 (3 H, s), 1.15 (3 H, s), 2.07 (1 H, d, *J* 13.4), 2.18 (1 H, d, *J* 13.4), 2.21 (3 H, s), 2.32−2.50 (2 H, m), 3.37 (1 H, dd (app. t), *J* 11.3 and 11.1), 3.91−4.00 (2 H, m), 4.90 (1 H, d, *J* 5.7), 5.03 (1 H, d, *J* 5.7), 5.96 (1 H, dd (app. t), *J* 5.7 and 5.5), 6.03 (1 H, dd (app. t), *J* 6.0 and 5.7), 6.37 (1 H, dd (app. t), *J* 6.0 and 5.5), 6.55−7.20 (14 H, m); $\delta_C$ (100.6 MHz; $CDCl_3$; $Me_4Si$) 21.3 (q), 23.4 (q), 31.0 (q), 38.6 (t), 40.8 (s), 60.9 (t), 63.3 (d), 69.1 (d), 75.5 (d), 81.0 (d), 85.4 (d), 88.5 (d), 90.6 (d), 97.0 (s), 126.2 (d), 126.7 (2 × d), 127.2 (2 × d), 127.4 (d), 128.0 (2 × d), 128.1 (2 × d), 128.6 (2 × d), 129.4 (2 × d), 137.8 (s), 139.1

(s), 139.3 (s), 142.3 (s). Found (LSIMS): 613.1449 (M-Cl), $^{102}RuC_{32}H_{35}N_2O_2S$ requires 613.1463 (2.2 ppm error); *m*/*z* (LSIMS) 648 ($M^+$, 10%), 613 (M-$Cl^+$, 100), 515 (50), 352 (40).

**Synthesis of (1*R*,2*S*)-2-(2,2-Dimethyl-3-phenylpropylamino)-1-phenylpropan-1-ol Ruthenium Monomer 41.** To a stirred solution of **40** (0.140 g, 0.47 mmol) in ether (4 $cm^3$) was added a 1 M solution of HCl diethyl ether (1.4 $cm^3$, 1.40 mmol), and the reactants were stirred for 30 min. The solvent was removed from the resulting precipitate under vacuum, dissolved in ethanol (10 $cm^3$), and ruthenium trichloride trihydrate (0.086 g, 0.33 mmol) was added. The reaction mixture was heated at reflux overnight, cooled to room temperature, and concentrated under vacuum to give the crude product. The residue was purified by column chromatograhy on alumina (2% MeOH/DCM) to give **41** (0.056 g, 39%) as an orange solid; mp > 300 °C (decomp); $\nu_{max}/cm^{-1}$ (solid) 3419 (NH), 746 and 702 (Ph); $\delta_H$ (300 MHz; $CDCl_3$; $Me_4$-Si) 0.68 (3 H, d, *J* 6.4), 1.22 (3 H, s), 1.49 (3 H, s), 2.15 (1 H, d, *J* 13.7), 2.27 (1 H, d, *J* 13.7), 2.54−2.67 (2 H, m), 2.70−2.78 (1 H, m, C*H*NH), 2.91 (1 H, dd (app. t), *J* 12.8 and 12.6), 4.0 ppm unknown doublet, 4.69 (1 H, d, *J* 3.0), 4.83 (1 H, d, *J* 5.3), 4.86 (1 H, d, *J* 5.5), 5.39 (1 H, dd (app. t), *J* 5.5 and 4.3), 5.80−5.88 (2 H, m), 7.10−7.41 (5 H, m); $\delta_C$ (100.6 MHz; $CDCl_3$; $Me_4Si$) 9.0 (q), 23.5 (q), 31.3 (q), 39.1 (s), 41.3 (t), 57.3 (t), 63.9 (d), 75.5 (d), 77.0 (d), 79.8 (d), 81.3 (d), 86.3 (d), 91.2 (d), 92.7 (d), 126.1 (d), 127.0 (2 × d), 127.5 (2 × d), 142.6 (s). Found (LSIMS): 434.0816 ($M^+$), $^{102}RuC_{20}H_{27}NOCl$ requires 434.0825 (1.9 ppm error); *m*/*z* (LSIMS) 434 ($M^+$, 100%), 398 (M-HCl, 30), 298 (100).

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**Supporting Information Available:** General experimental details, $^1H$ and $^{13}C$ NMR of all new compounds lacking elemental analyses, and details of ketone preparations and reductions. This material is free of charge via the Internet at http://pubs.acs.org.

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