The use of a [4 + 2] cycloaddition reaction for the preparation of a series of 'tethered' Ru(II)–diamine and aminoalcohol complexes†

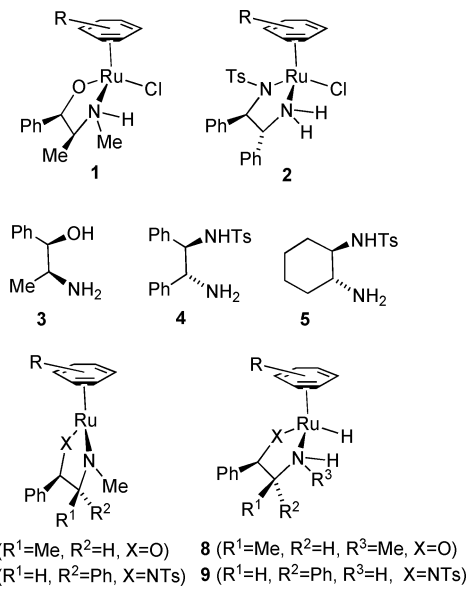
Fung Kei Cheung, Aidan M. Hayes, David J. Morris and Martin Wills*

Received 17th January 2007, Accepted 12th February 2007
First published as an Advance Article on the web 1st March 2007
DOI: 10.1039/b700744b

A series of catalysts have been prepared for use in the asymmetric transfer hydrogenation of ketones. The complexes were prepared using a [4 + 2] cycloaddition reaction at a key step in the reaction sequence. This provides a means for the synthesis of catalysts with modifications at specific sites.

Introduction

Recent research has led to the development of a number of highly active catalysts for asymmetric transfer hydrogenation (ATH) of ketones.[1–6] The popular Ru(II)–arene based catalysts **1** and **2** contain an η6-coordinated arene ring which occupies three vertices of an octahedrally-complexed metal.[2–5] An enantiomerically pure bidentate ligand, most commonly an amino alcohol[2] such as ephedrine **3** or a monotosylated diamine[3] such as *N*-tosyl-1,2-diphenylethane-1,2-diamine (TsDPEN) **4** or *N*-tosyl-1,2-diaminocyclohexane (TsDAC) **5**, and a chloride, complete the structure of the 'pre-catalyst' which may be isolated prior to use or formed *in situ*. Upon addition to the reaction, which typically consists of a solution of ketone substrate in either isopropanol–alkoxide or formic acid–triethylamine (FA–TEA), HCl is lost from the pre-catalyst to generate the 16-electron species **6** or **7**. This intermediate removes two hydrogen atoms from either isopropanol or formic acid to give hydride **8** or **9** which goes on to transfer these subsequently to the ketone substrate to form the product thereby regenerating **6**/**7** which re-enters the catalytic cycle.[4] Formic acid is generally preferred to isopropanol in this application because the reactions are essentially irreversible, and may be carried out at high concentrations. However this limits the ligand to the monotosylated diamines, since the Ru(II)–aminoalcohol complexes are not stable to formic acid conditions.



The asymmetry of the ketone reduction is controlled by the approach of the ketone to the hydrides **8** or **9**, which are known to be formed predominantly in the diastereoisomeric forms illustrated (supported by X-ray crystallography and molecular modeling studies).[4] Crucial to the high enantioselectivity is a favourable CH–π interaction between the hydrogen atoms of the η6-arene and the aryl ring of a substrate, such as an acetophenone derivative (illustrated for **9** in Fig. 1). This interaction accounts for the high degree of enantiocontrol observed for acetophenone derivatives. In contrast, substrates which contain a combination of two alkyl groups flanking the ketone are generally reduced in poor enantioselectivity, as the key stabilizing interaction does not exist. There is evidence that dispersion and steric effects[4e] also contribute to the enantiocontrol of the reduction process, however these forces are not by themselves sufficiently strong to effectively control the reduction of dialkyl ketones with high enantioselectivity.

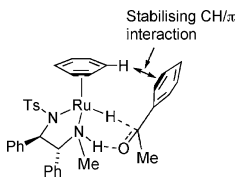


Fig. 1 Reduction of acetophenone derivatives by catalyst *RR*-**9**.

Some investigations into the modification of the η6-arene rings have been reported, although these have been largely limited to methyl substitution.[2a,3a,c,4] In the case of the amino alcohol complexes, it has been clearly demonstrated that the CH–π interaction can be productively extended through a methyl group on the arene ring, and indeed can even increase the enantioselectivity in some cases.[2a] However for the monotosylated diamine complexes, the situation is slightly more complicated. This is because an additional *N*-Ts–η6-arene nonbonded interaction results in a reduction of reaction rate,[4d] when hexamethylbenzene is used instead of benzene as the η6-arene component.

The Department of Chemistry, The University of Warwick, Coventry, UK CV4 7AL. E-mail: m.wills@warwick.ac.uk; Fax: 024 7652 3260; Tel: 024 7652 3260

† Electronic supplementary information (ESI) available: General experimental details, preparation of precursor molecules and ketone reductions, ^{1}H and ^{13}C-NMR of all new compounds lacking elemental analyses, and synthetic procedures. See DOI: 10.1039/b700744b

A comparison between the closely related Rh(III)–pentamethylcyclopentadienyl transfer hydrogenation catalysts is also of value.[7] Rhodium(III) catalysts offer advantages in the reduction of certain substrates, notably α-chloroacetophenones and related substrates, for which they appear to give better conversions and e.e. compared to the Ru(II) complexes.[7] For the Rh(III) complexes, however, the investigations have focused (with the exception of some of our own studies) on the pentamethylated complexes, which are widely assumed to operate through an analogous transition state to that illustrated in Fig. 1, again suggesting that the CH–π interaction works productively through methyl groups on the η5-coordinated ring. We are not aware of Rh(III) catalysts which lack the methyl groups on the Cp ring having been reported for ATH of ketones or imines, however this may be due to the increased stability of complexes containing Cp′ over Cp.

Results and discussion

In order to make the catalysts such as **1** and **2** effective at enantioreduction of dialkyl ketones, it would be desirable to be able to substitute the arene ring with large functional groups. A large group such as *t*-butyl, positioned in the region close to the substrate in the reduction, may be able to change the basis of enantiocontrol from primarily electronic to steric. A substrate such as acetocyclohexane, for example, might be expected to approach the catalyst in a manner that positions the larger substituent away from the bulky group on the arene, thus forcing delivery of hydrogen to predominantly one face of the carbonyl group (Fig. 2). One difficulty with this, however, is ensuring that the 'bulky' group is correctly positioned relative to the substrate; this is difficult to control due to the high conformational flexibility of the arene group.

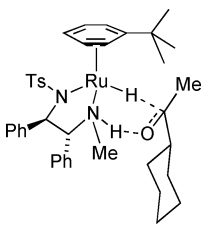
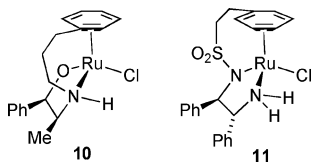


Fig. 2 Changing the basis of stereocontrol from electronic to steric.

In our research work on Ru(II) complexes, we have sought to address this problem by preparing modified catalysts which contain a 'tether' between the chiral ligand component and the arene.[8] This tether serves to increase the stability of the catalyst and to restrict the conformations available to the arene, thus permitting it to be selectively functionalized. Two of our 'tethered' catalysts, are **10** and **11**, containing an aminoalcohol and a sulfonylated diamine respectively.[8b] In order to prepare derivatives of these with functional groups on the arene ring, the conventional approach has been to use a Birch reduction to prepare the appropriate 1,4-cyclohexadiene precursor (*e.g.* **12**), coupling to the chiral ligand to give intermediate **13**, and finally complexation with ruthenium(III) chloride. However, this route is difficult to pursue on a large scale, and requires an appropriately-substituted aryl substrate, which may not be readily available.



In order to prepare derivatives of **10** and **11** on a larger scale and with substituents in specific positions, we chose to investigate an alternative approach based on a [4 + 2] cycloaddition strategy between a diene and a functionalized alkyne **14** (Fig. 3). If successful, this would permit the large scale synthesis of large quantities of the required functionalized catalysts.

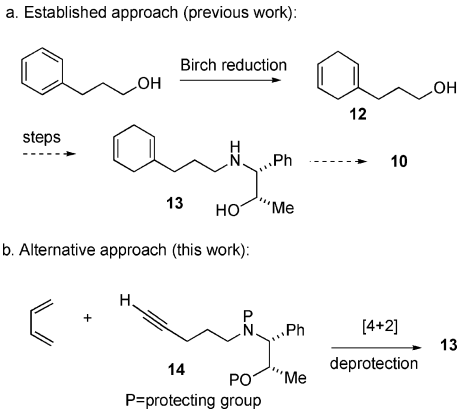
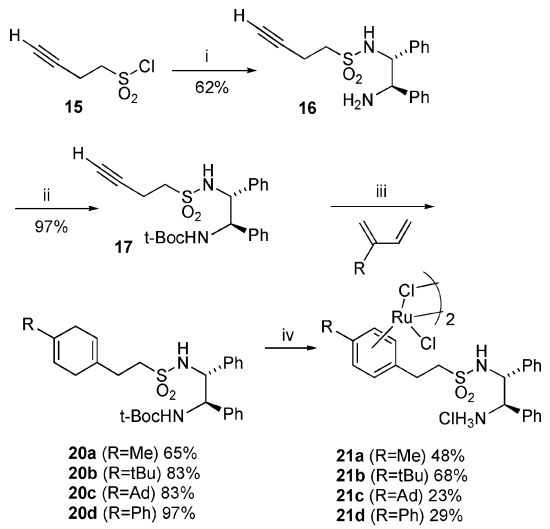


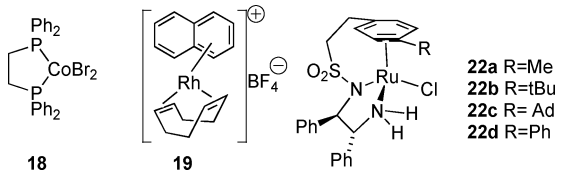
Fig. 3 Established and proposed alternative approaches to complex **10** and its derivatives.

We first examined the synthetic approach to derivatives of the monotosylated catalyst **11**, and our final route is shown in Scheme 1. Alkyne-containing sulfonyl chloride **15** was combined with *RR*-DPEN **4** to give sulfonamide **16** in 62% yield. Studies revealed that it was necessary to protect the free amine group in **16**, which was achieved by reaction with Boc_2O to give **17** in 97% yield. The cycloaddition reaction with isoprene required the use of a catalyst. In our studies we examined the use of two catalysts which have been reported for this application, the cobalt based **18** [9] and



Scheme 1 *Reagents and conditions:* i) **4**, Et_3N, DCM, 0 °C. ii) *t*Boc_2O, THF, rt. iii) Catalyst **19** (2 mol%), DCM, rt. iv) HCl, Et_2O, DCM, rt then $RuCl_3$, EtOH, reflux o/n.

the rhodium complex **19**.[10] In the event, only the Rh(I) complex **19** proved to be successful, yielding **20a** from the acetylene **17** in 65% isolated yield. Following the success of this protocol, a series of derivatives **20b–20d** were also prepared. In the cases of **20a–20c**, the products were formed predominantly as the 1,4-disubstituted dienes (1,4- : 1,3- *ca.* 5–6 : 1), however **20d** contained *ca.* 25% of the 1,3-isomer, which was not separable by flash chromatography. Each of these was converted into the dimeric catalyst precursors **21a–21d** in good yield through *t*Boc deprotection followed by complexation with $RuCl_3$. At the complexation stage, only the 1,4-disubstituted products were isolated, except for the case of **21d**, which retained *ca.* 25% of the 1,3- isomer. In the final step, yields were low to moderate, reflecting an incomplete crystallization of the product from solution rather than an inherently low yielding reaction. It is anticipated that these yields can be optimized through modification of our isolation procedure.



18 **19**

We have previously demonstrated that dimers such as **21a–d** are converted directly to the respective monomers **22a–d** *in situ* during the reaction in FA–TEA. This process involves neutralization of the salt, splitting of the dimer and 'wrapping' of the ligand around the metal. In practice, the dimers give identical results in reduction reactions to the monomers. We therefore employed **21a–21d** directly in reduction reactions without prior isolation of the monomers. Results of ketone reduction using our new catalysts are given in Table 1, with examples of reduction of both acetophenone **23** and acetocyclohexane **24**. The introduction of substituents results in the reduction of enantioselectivity and conversion for acetophenone reduction. It therefore appears that the substituents have an effect on the catalysts, but not a productive one. For the reduction of acetocyclohexane **24**, there is a more complex pattern. The parent catalyst **11** gave a reduction product of only 19% e.e., in 84% yield. The methyl-substituted derivative **21a** reduced the ketone in slightly higher e.e. (27%) but at a significantly reduced rate, only 20% yield after 166 hours. It appears that the new group has a significant effect on reactivity, possibly due to an overall increase of the steric hindrance around the metal. Alternatively the effect may be due to electronic factors. The complexes containing the larger groups, **21b** and **21c** gave products in even lower conversions, and *ca.* 17–18% e.e. The phenyl-substituted catalyst **21d** gave a product in the best observed e.e. of 36%, although only 50% conversion. The extra phenyl ring therefore appears to have a beneficial effect, although it is not clear which isomer of the catalyst may be giving the improved result, since the catalyst was a mixture of 1,3- and 1,4-disubstituted arene derivatives. This remains to be established.

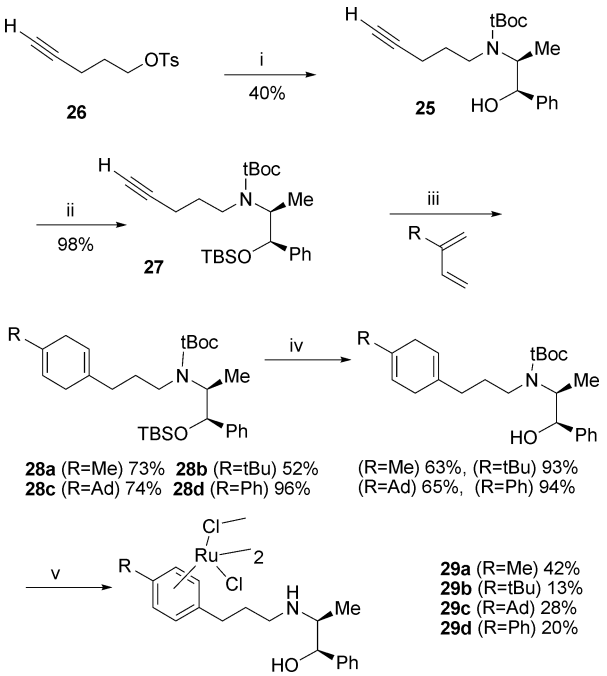
Table 1 Reductions of ketones using catalysts *RR*-**11** and **21a–d**[a]

Substrate	Catalyst	T/h	Conversion (%)[b]	Ee[c] (*R*/*S*)[d]
Acetophenone **23**	**11**	24	99	96 (*R*)
Acetophenone **23**	**21a**	96	88	63 (*R*)
Acetophenone **23**	**21b**	96	35	35 (*R*)
Acetophenone **23**	**21c**	96	44	25 (*R*)
Acetophenone **23**	**21d**	96	63	68 (*R*)
c-C_6H_{11}COMe **24**	**11**	63	84	19 (*R*)
c-C_6H_{11}COMe **24**	**21a**	166	20	27 (*R*)
c-C_6H_{11}COMe **24**	**21b**	72	10	17 (*R*)
c-C_6H_{11}COMe **24**	**21c**	91	< 10	18 (*R*)
c-C_6H_{11}COMe **24**	**21d**	72	50	36 (*R*)

[a] Monomer *RR*-**11**(0.5 mol%) or dimer **21a–d** (0.25 mol%) (200 : 1 S/C), 1 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 50 m column unless otherwise specified. [d] Determined from the sign of rotation of the isolated product.

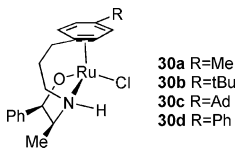
By way of literature comparison, the reduction of acetophenone under the same conditions with catalyst [(mesitylene)RuCl(*SS*-TsDPEN)] gives a product of 98% e.e. (*S* configuration) in >99% yield after 20 h at S/C = 200, 28 °C.[3a] Although no systematic comparison of [(benzene)RuCl(*SS*-TsDPEN)] against [(hexamethylbenzene)RuCl(*SS*-TsDPEN)] has been reported, it is known that the additional methyl groups in the latter complex reduce the reaction rate, in accord with our findings.

We also prepared a series of derivatives of the amino alcohol catalyst **10**, through the sequence in Scheme 2. The required alkyne **25** was prepared by the reaction of (1*R*, 2*S*)-norephedrine **3** with tosylate **26** followed by *N*-protection in 40% yield for the two steps. Experiments revealed that, as well as *N*-protection, it was also necessary to protect the oxygen atom of the norephedrine in order for the cycloaddition to be successful. This was achieved in 98% using TBDMSCl, to furnish **27**, which was subsequently reacted with a series of four dienes to give the predominantly 1,4-cyclodienes **28a–28d**. Following the precedent previously established, each of these complexes was deprotected and converted to the catalyst precursor dimers **29a–29d**. Diene **28a** and catalyst **29a** have been reported by us in an earlier publication, and the data obtained in this study matched that previously obtained.[8c] Again, since our



Scheme 2 *Reagents and conditions:* i) **3**, Et_3N, MeCN, rt, then *t*Boc_2O, THF, rt. ii) TBSCl, Im, DMF, rt. iii) Catalyst **19** (2 mol%), DCM, rt. iv) TBAF, THF, rt. v) HCl, Et_2O, DCM, rt, then $RuCl_3$, EtOH, reflux o/n.

previous studies had revealed that the dimers are converted to monomers **30a–30d** *in situ* in the reduction reactions,[8] complexes **29a–29d** were directly employed in the reduction of acetophenone and acetocyclohexane. For the aminoalcohol ligands, however, the reductions were carried out in isopropanol with 5 mol% KOH as base to form the activated catalysts. In contrast to the monotosylated diamines, the amino alcohol complexes do not appear to be stable to formic acid–triethylamine.



30a R=Me
30b R=tBu
30c R=Ad
30d R=Ph

All the complexes proved to be competent reduction catalysts (Table 2). In the case of acetophenone, the product e.e.s were similar or in some cases a little higher than that obtained using the parent complex **10**, however the conversions were lower, possibly due to increased steric hindrance. In the case of acetocyclohexane **24**, the e.e.s were slightly below that obtained using **10**, but in the same sense. Again the reactions proceeded at significantly reduced rates compared to the parent **10**, which suggests that the substituents are indeed in a position to influence the reaction, although not at present in a productive manner. A small series of dialkyl ketones were also reduced (Table 2) using **10** however in all cases the e.e.s were moderate or rather poor.

The results can be compared with published results obtained using the untethered [(benzene)RuCl(1*R*, 2*S*-*N*-methyl-1,2-diphenylaminoethanol)] and [(hexamethyl)RuCl(1*R*, 2*S*-*N*-methyl-1,2-diphenylaminoethanol)] complexes.[2a] In these systems, the more substituted complex gives an acetophenone reduction product of 13% e.e. in only 3% yield compared to 64% yield and 52% e.e. for the benzene complex. However this trend completely reverses when the (*S*,*S*)-aminoalcohol ligand is employed; the e.e. is 17% (91% yield) with the benzene complex and 92% (94% yield) with the hexamethylbenzene complex. In our own studies we have found that [(benzene)RuCl(1*R*, 2*S*-ephedrine)] reduces acetylhexane in only 6% e.e. under comparable conditions.[8c]

Table 2 Reductions of ketones using catalysts (1*R*, 2*S*)-**10** and **29a–d**[a]

Substrate	Catalyst	T/h	Conversion (%)[b]	Ee[c] (*R*/*S*)[d]
Acetophenone **23**	**10**	2	94	62 (*R*)
Acetophenone **23**	**29a**	2	56	72 (*R*)
Acetophenone **23**	**29b**	2	77	77 (*R*)
Acetophenone **23**	**29c**	2	64	64 (*R*)
Acetophenone **23**	**29d**	2	37	37 (*R*)
c-C_6H_{11}COMe **24**	**10**	2	78	69 (*S*)
c-C_6H_{11}COMe **24**	**29a**	2	22	62 (*S*)
c-C_6H_{11}COMe **24**	**29b**	2	15	45 (*S*)
c-C_6H_{11}COMe **24**	**29c**	2	12	54 (*S*)
c-C_6H_{11}COMe **24**	**29d**	2	43	16 (*S*)
*t*BuCOMe	**10**	2	100	63 (*S*)
AdCOMe	**10**	2	21	61 (*S*)
n-C_6H_{11}COMe	**10**	2	68	24 (*S*)
c-$C_6H_{11}COCH_2CH_3$	**10**	2	19	28 (*S*)

[a] Monomer (1*R*, 2*S*)-**10**(0.5 mol%) or dimer **29a–d** (0.25 mol%) (200 : 1 S/C), 0.1 M solution of ketone in iPrOH, 28 °C. [b] Determined by GC or ^{1}H NMR analysis. [c] Determined by GC analysis using a chrompac cyclodextrin-β-236M-19 50 m column unless otherwise specified. [d] Determined from the sign of rotation of the isolated product.

However, again caution should be maintained here before reading too much into the results, because the same reduction using pseudoephedrine is reported to give a product of 75% e.e.[3a]

The sense of the ketone reduction using **10** and **29a–d** is worthy of comment. In all the acetophenone reductions, the products of *R*-configuration were obtained, which matches that reported for these configurations of chiral ligand, thus suggesting that the CH–π interaction continues to dominate these (Fig. 1). In the case of the acetocyclohexane **24**, the product of *S*-configuration was obtained in every case, suggesting that the ketone is approaching the catalyst with the larger (cyclohexyl) substituent orientated away from the η6-arene ring. This appears to be in contrast to the mode of reduction operated by the sulfonylated diamine catalysts **11** and **21a–d** (Fig. 4). Although the reversed substrate approach to the aminoalcohol derivatives is what we had hoped to build into the catalyst design, it is surprising that the parent structure **10**, with no arene substituent, appears to enforce this approach most effectively. It appears that sterics are not the only factors here, but possibly also a combination of electronic effects from the various substituents which lead to subtle shifts in the enantiocontrol.

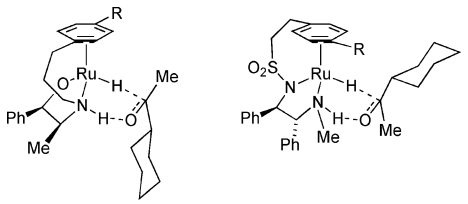


Fig. 4 Modes of asymmetric reduction of acetylcyclohexane.

Conclusion

In conclusion, we have developed a new approach to the synthesis of 'tethered' catalysts for ATH reductions of ketones using a variant of a [4 + 2] cycloaddition reaction to create the required 1,4-cyclohexadiene ring for complexation to ruthenium. This process provides a means for the preparation of Ru(II) catalysts on a larger scale than would be possible using the traditional approaches. Using this method, it was possible to prepare a small series of catalysts for evaluation in ATH of acetophenone derivatives and dialkyl ketones. In all cases, the sense of reduction for acetophenone was opposite to that for acetocyclohexane, however the conversions and e.e.s were lower for the derivatives than for the parent complexes, possibly reflecting the increased steric hindrance. We are currently investigating the development of 'tethered' catalysts in synthesis and are aided by the availability of this new method for their preparation.

Experimental

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. General experimental details are given in the ESI.† Compounds **28a**, **29a** and the desilylated derivative of **28a** have been reported in a previous publication.[8c]

Synthesis of but-3-yne-1-sulfonic acid ((*R*,*R*)-2-amino-1,2-diphenylethyl)-amide 16

To a stirred solution of *R*,*R*-diphenylethylene diamine **4** (0.795 g, 3.75 mmol) and triethylamine (0.757 g, 7.50 mmol) in DCM (20 cm^3) at 0 °C was added dropwise **15** (0.570 g, 3.75 mmol). The reaction mixture was stirred overnight at room temperature and concentrated under vacuum to give the crude product. The residue was purified by flash chromatography (20% EtOAc–hexane to 80% EtOAc–hexane) to give **16** (0.757 g, 62%) as a white solid (Found: C, 65.65; H, 6.1; N, 8.30. $C_{18}H_{20}N_2O_2S$ requires C, 65.85; H, 6.15; N, 8.55%); mp 148 °C (EtOH); $[a]_D^{24}$ +10.5 (*c* 1.25 in $CHCl_3$); ν_{max}/cm^{-1} (solid) 3352 (NH), 3310 (NH_2), 3145 (≡C–H), 1603 (NH_2), 1314 and 1133 (SO_2N), 767 and 697 (Ph); δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.93 (1 H, t, *J* 2.6, ≡CH), 2.35 (2 H, dt, *J* 8.3 and 2.6, ≡CCH_2), 2.49–2.66 (2 H, m, CH_2SO_2N), 2.85–4.05 (2 H, br s, NH_2), 4.28 (1 H, d, *J* 5.8, PhC*H*NH_2), 4.57 (1 H, d, *J* 5.8, PhC*H*NHTs), 7.21–7.40 (11 H, m, 2 × Ph and NH); δ_C (75.5 MHz; $CDCl_3$; Me_4Si) 14.1 (t), 52.0 (t), 60.6 (d), 63.0 (d), 70.4 (d), 80.4 (s), 127.1 (2 × d), 127.3 (2 × d), 128.4 (2 × overlapping s), 129.1 (2 × d), 129.2 (2 × d), 139.8 (s), 141.7 (s). Found (EI) 329.1321 $[MH]^+$, $C_{18}H_{21}N_2O_2S$ requires 329.1324 (0.9 ppm error); *m*/*z* (EI) 329 (MH+, 60%), 312 (30), 196 (30), 106 (100), 79 (40), 77 (30).

Synthesis of [(*R*,*R*)-2-(but-3-yne-1-sulfonylamino)-1,2-diphenylethyl]-*tert*-butyl carbamate 17

To a stirred solution of **16** (1.170 g, 3.57 mmol) in THF (20 cm^3) was added di-*tert*-butyl dicarbonate (0.770 g, 3.57 mmol). The reaction mixture was stirred overnight, diluted with 1 M potassium hydrogen sulfate (aq.) (50 cm^3) and extracted with DCM (2 × 75 cm^3). The combined extracts were dried ($MgSO_4$), filtered and concentrated under vacuum to give **17** (1.48 g, 97%) as a white solid; mp 161–162 °C (EtOH); $[a]_D^{24}$ +5.2 (*c* 0.90 in $CHCl_3$); ν_{max}/cm^{-1} (solid) 3385 (NH), 3304 (NH), 1684 and 1672 (C=O), 1323 and 1135 (SO_2N), 697 (Ph); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.47 (9 H, s, 3 × CH_3), 1.92 (1 H, t, *J* 2.5, ≡CH), 2.45 (2 H, dt, *J* 7.8 and 2.5, C*H*$_2CH_2SO_2$), 2.64–2.89 (2 H, m, CH_2SO_2), 4.71 (1 H, dd, *J* 10.0 and 6.8, PhC*H*$NHCO_2$), 4.86 (1 H, dd, *J* 10.0 and 8.0, PhC*H*$NHSO_2$), 5.30 (1 H, br s, $NHCO_2$), 6.28 (1 H, br s, $NHSO_2$), 7.02–7.20 (10 H, m, 2 × Ph); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 13.8 (t), 28.3 (3 × q), 52.1 (t), 60.1 (d), 64.4 (d), 70.7 (d), 79.8 (s), 81.1 (s), 127.4 (2 × overlapping (2 × d)), 128.1 (d), 128.2 (d), 128.6 (2 × d), 128.8 (2 × d), 137.9 (2 × overlapping s), 138.5 (s); Found (LSIMS) 429.1835 $[MH]^+$, $C_{23}H_{29}N_2O_4S$ requires 429.1848 (3.1 ppm error); *m*/*z* (EI) 329 ($[MH\text{-}CO_2C_4H_9]^+$, 5%), 222 (30), 206 (25), 150(50), 106 (100).

General procedure for the synthesis of compounds 20a–d

To a stirred solution of catalyst **19** (0.02 eq.) in DCM was added the required diene (2.00 eq.) followed by **17** (1.00 eq.). The reaction mixture was stirred for 2 hours and concentrated under vacuum to give the crude product. The residue was purified by flash chromatography (DCM to 2% DCM–MeOH) to give cyclohexadienes **20a–d**.

Synthesis of {(*R*,*R*)-2-[2-(4-methylcyclohexa-1,4-dienyl)-ethanesulfonylamino]-1,2-diphenylethyl} *tert*-butyl carbamate 20a

Catalyst **19** (0.005 g, 0.01 mmol), DCM (3 cm^3), isoprene (0.080 g, 1.17 mmol) and **17** (0.250 g, 0.58 mmol) were reacted according to the general procedure above to give **20a** (0.185 g, 65%) as a white solid; mp 158–166 °C (EtOH); $[a]_D^{24}$ +11.8 (*c* 0.9 in $CHCl_3$); ν_{max}/cm^{-1} (solid) 3300 (NH), 3262 (NH), 1686 (C=O), 1318 and 1145 (SO_2N), 756 and 696 (Ph); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.48 (9 H, s, $C(CH_3)_3$), 1.59 (0.5 H, s, CH_3 minor isomer), 1.61 (2.5 H, s, CH_3 major isomer), 2.08–2.29 (4 H, m, 2 × CH_2), 2.42–2.45 (2 H, m, CH_2), 2.54–2.62 (1 H, m, C$H_a$$H_b$$NHSO_2$), 2.70–2.77 (1 H, m, $CH_aH_b$$NHSO_2$), 4.69 (1 H, dd, *J* 10.3 and 6.8, PhC*H*$NHCO_2$), 4.84 (1 H, dd, *J* 10.3 and 10.0, PhC*H*$NHSO_2$), 5.16–5.33 (3 H, m, $NHCO_2$ and 2 × =CH), 6.03 (1 H, m, $NHSO_2$), 6.99–7.07 (4 H, m, Ph), 7.15–7.22 (6 H, m, Ph); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 22.9 (q, major isomer), 23.0 (q, minor isomer), 28.3 (3 × q), 29.4 (s), 30.6 (t), 31.4 (t), 52.3 (t), 60.0 (d), 64.0 (d), 80.8 (t), 118.0 (d, major isomer), 118.2 (d, minor isomer), 120.3 (d, minor isomer), 120.4 (d, major isomer), 127.4 (2 × d), 127.5 (2 × d), 127.9 (d), 128.0 (d), 128.6 (overlapping 2 × (2 × d)), 131.0 (overlapping 2 × s), 138.2 (s), 138.9 (s); Found (LSIMS) 495.2334 $[M\text{-}H]^+$, $C_{28}H_{35}N_2O_4S$ requires 495.2318 (3.4 ppm error); *m*/*z* (EI) 495 ($M\text{-}H^+$, 10%), 419 (100), 395 (75), 240 (75).

Synthesis of {(*R*,*R*)-2-[2-(4-*tert*-butylcyclohexa-1,4-dienyl)-ethanesulfonylamino]-1,2-diphenylethyl}-*tert*-butyl carbamate 20b

Catalyst **19** (0.006 g, 0.02 mmol), DCM (5 cm^3), 2-*t*Bu-butadiene (0.163 g, 1.48 mmol) and **17** (0.317 g, 0.74 mmol) were reacted according to the general procedure above to give **20b** (0.329 g, 83%) as a white solid; mp 99–100 °C; $[a]_D^{18}$ +15.3 (*c* 1.35 in $CHCl_3$); ν_{max}/cm^{-1} (solid) 3350 (NH), 3250 (NH), 1686 (C=O), 1319 and 1145 (SO_2N), 755 and 697 (Ph); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.90 (2.1 H, s, =$CC(CH_3)_3$ minor isomer), 0.98 (6.9 H, s, =$CC(CH_3)_3$ major isomer), 1.48 (9 H, s, $C(CH_3)_3$), 2.11–2.33 (4 H, m, 2 × CH_2), 2.53–2.63 (3 H, m, CH_2 and C$H_a$$H_b$$NHSO_2$), 2.69–2.79 (1 H, m, $CH_aH_b$$NHSO_2$), 4.70 (1 H, dd, *J* 10.0 and 6.8, PhC*H*$NHCO_2$), 4.84 (1 H, dd, *J* 10.0 and 10.0, PhC*H*$NHSO_2$), 5.18–5.42 (3 H, m, $NHCO_2$ and 2 × =CH), 6.03 (1 H, m, $NHSO_2$), 6.99–7.07 (4 H, m, Ph), 7.15–7.22 (6 H, m, Ph); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 28.7 (3 × q), 29.2 (3 × q, minor isomer), 29.3 (3 × q, major isomer), 30.1 (t), 30.9 (t), 31.3 (s), 35.2 (s), 52.7 (t), 60.5 (d), 64.6 (d), 81.3 (t), 115.1 (d, major isomer), 115.3 (d, minor isomer), 120.3 (d, minor isomer), 121.3 (d, major isomer), 127.8 (2 × d), 127.9 (2 × d), 128.3 (d), 128.4 (d), 128.9 (2 × d), 129.1 (2 × d), 130.9 (s), 135.1 (s), 139.2 (s), 142.8 (s); Found (LSIMS) 537.2769 $[M\text{-}H]^+$, $C_{31}H_{41}N_2O_4S$ requires 537.2787 (3.3 ppm error); *m*/*z* (LSIMS) 537 ($M\text{-}H^+$, 40%), 439 (80), 240 (65), 196 (90), 106 (100).

Synthesis of {(*R*,*R*)-2-[2-(4-adamantan-1-ylcyclohexa-1,4-dienyl)-ethanesulfonylamino]-1,2-diphenylethyl}-*tert*-butyl carbamate 20c

Catalyst **19** (0.009 g, 0.02 mmol), DCM (5 cm^3), 2-adamantyl-butadiene (0.404 g, 2.15 mmol) and **17** (0.460 g, 1.08 mmol) were reacted according to the general procedure above to give **20c** (0.550 g, 83%) as a white solid; mp 119–121 °C; $[a]_D^{24}$ +19.0 (*c* 1.4 in $CHCl_3$); ν_{max}/cm^{-1} (solid) 3340 (NH), 3268 (NH), 1682 (C=O), 1319 and 1146 (SO_2N), 755 and 698 (Ph); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.47 (9 H, s, $C(CH_3)_3$), 1.56–1.85 (12 H, m, adamantyl

6 × CH_2), 1.95–2.08 (3 H, m, adamantyl 3 × CH), 2.10–2.32 (4 H, m, 2 × CH_2), 2.52–2.95 (4 H, m, 2 × CH_2), 4.65–4.75 (1 H, m, PhC*H*$NHCO_2$), 4.83–4.91 (1 H, m, PhC*H*$NHSO_2$), 5.18 (0.1 H, m, =CH minor isomer), 5.21 (0.9 H, m, =CH major isomer), 5.31–5.41 (2 H, m, $NHCO_2$ and =CH), 6.08–6.24 (1 H, m, $NHSO_2$), 7.01–7.24 (10 H, m, Ph); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 24.8 (s), 28.4 (3 × q), 28.7 (3 × d), 29.8 (t), 30.5 (s), 37.1 (3 × t), 40.9 (3 × t), 43.2 (t), 52.4 (t), 60.2 (d), 64.2 (d), 80.9 (t), 114.9 (d, major isomer), 115.0 (d, minor isomer), 120.0 (d, minor isomer), 121.0 (d, major isomer), 127.4 (2 × d), 127.5 (2 × d), 128.0 (d), 128.1 (d), 128.6 (2 × d), 128.7 (2 × d), 130.6 (s), 138.9 (s), 143.0 (s); Found (LSIMS) 616.3287 $[M\text{-}H]^+$, $C_{36}{}^{13}CH_{47}N_2O_4S$ requires 616.3290 (0.5 ppm error); *m/z* (LSIMS) 615 (M^+, 3%), 559 (4), 515 (20), 408 (10), 240 (30), 196 (55).

Synthesis of {(*R*,*R*)-1,2-diphenyl-2-[2-(4-phenylcyclohexa-1, 4-dienyl)-ethanesulfonylamino]-ethyl}-*tert*-butyl carbamate 20d

Catalyst **19** (0.008 g, 0.02 mmol), DCM (5 cm^3), 2-phenylbutadiene (0.250 g, 1.92 mmol) and **17** (0.412 g, 0.96 mmol) were reacted according to the general procedure above to give **20d** (0.521 g, 97%) as a white solid (Found: C, 70.8; H, 6.8; N, 4.95. $C_{33}H_{38}N_2O_4S$ requires C, 70.95; H, 6.85; N, 5.0%); mp 164–168 °C (dec.); $[a]_D^{24}$ +23.7 (*c* 1.1 in $CHCl_3$); ν_{max}/cm^{-1} (solid) 3388 (NH), 3303 (NH), 1685 (C=O), 1320 and 1142 (SO_2N), 745 and 696 (Ph); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.47 (9 H, s, $C(CH_3)_3$), 2.16–2.39 (2 H, m, CH_2), 2.44–2.52 (1.5 H, m, CH_2), 2.57–2.68 (1.5 H, m, CH_2), 2.73–2.84 (1.5 H, m, CH_2), 2.94–3.00 (1.5 H, m, CH_2) (NB unable to determine major/minor isomers of CH_2 groups), 4.73 (1 H, dd, *J* 9.5 and 7.3, PhC*H*$NHCO_2$), 4.84 (1 H, dd, *J* 9.5 and 8.3, PhC*H*$NHSO_2$), 5.26–5.39 (2 H, m, $NHCO_2$ and CH_2C=C*H*), 5.97–6.01 (0.7 H, m, PhC=CH major isomer), 6.03–6.06 (0.3 H, m, PhC=CH minor isomer), 6.18 (1 H, m, $NHSO_2$), 7.01–7.37 (15 H, m, Ph); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 28.3 (3 × q), 28.7 (t), 30.0 (t), 30.5 (s), 52.3 (t), 60.1 (d), 64.3 (d), 81.0 (t), 119.9 (d, minor isomer), 120.5 (d, major isomer), 121.0 (d, major isomer), 121.3 (d, minor isomer), 124.9 (2 × d), 127.0 (d), 127.4 (2 × d), 127.5 (2 × d), 128.0 (d), 128.1 (d), 128.3 (2 × d), 128.6 (2 × d), 128.7 (2 × d), 130.6 (s), 131.2 (s), 133.3 (s, minor isomer), 133.6 (s, major isomer), 138.0 (s, minor isomer), 138.9 (s, major isomer), 141.0 (s); Found (LSIMS) 557.2471 $[M\text{-}H]^+$, $C_{33}H_{37}N_2O_4S$ requires 557.2474 (0.5 ppm error); *m/z* (LSIMS) 559 (MH^+, 5%), 503 (15), 459 (55), 351 (20), 240 (65), 196 (60).

General procedure for the synthesis of compounds 21a–d

To a stirred solution of cyclohexadiene **20a–d** (1.00 eq.) in DCM was added an excess of a 2 M solution of HCl in diethyl ether and the reactants stirred overnight. The solvent was removed from the resulting precipitate under vacuum, dissolved in ethanol and ruthenium trichloride trihydrate (typically 0.75 eq.) was added. The reaction mixture was heated at reflux overnight and then cooled to room temperature. The precipitate was collected by filtration and washed with ethanol (5 × 10 cm^3) to give ruthenium dimers **21a–d**.

Synthesis of 2-*p*-tolyl-ethanesulfonic acid ((*R*,*R*)-2-amino-1, 2-diphenylethyl)-amide ammonium chloride ruthenium dimer 21a

Diene **20a** (0.170 g, 0.34 mmol), DCM (2 cm^3), 2 M solution of HCl in diethyl ether (8 cm^3, 8.00 mmol), ethanol (5 cm^3) and ruthenium trichloride trihydrate (0.065 g, 0.25 mmol) were reacted according to the general procedure above to give **21a** (0.098 g, 48%) as a dark green solid; mp >300 °C; ν_{max}/cm^{-1} (solid) 3442 (NH), 1602 and 1496 (NH_3^+), 1321 and 1137 (SO_2N), 764 and 699 (Ph); δ_H (400 MHz; DMSO-d_6) 2.07 (6 H, s, 2 × CH_3), 3.20–3.50 (8 H, m, 2 × CH_2CH_2SO_2 (peaks obscured by overlap with H_2O resonance)), 4.50 (2 H, m, 2 × PhC*H*NH_3^+), 4.70 (2 H, t, *J* 9.6, 2 × PhC*H*NH), 5.36 (2 H, d, *J* 6.0, 2 × ArH on Ru-Ph), 5.69 (2 H, d, *J* 6.0, 2 × ArH on Ru-Ph), 5.75 (4 H, d, *J* 6.0, 4 × ArH on Ru-Ph), 7.10–7.32 (20 H, m, 4 × Ph), 8.43 (2 H, d, *J* 9.6, 2 × NH), 8.65 (6 H, m, 2 × NH_3^+); δ_C (75.5 MHz; DMSO-d_6) 18.4 (2 × q), 26.4 (2 × t), 52.1 (2 × t), 58.7 (2 × d), 61.4 (2 × d), 86.1 (2 × d), 86.3 (2 × d), 88.6 (2 × d), 89.0 (2 × d), 96.7 (2 × s), 101.6 (2 × s), 128.3 (2 × (2 × d)), 128.4 (2 × d), 128.8 (2 × (2 × d)), 128.9 (overlapping 2 × (2 × d) and 2 × (2 × d)), 129.2 (2 × d), 134.7 (2 × s), 138.3 (2 × s). Found (LSIMS): 531.0440 (monomeric species formed *in situ*), $^{102}RuC_{23}H_{26}N_2O_2SCl$ requires 531.0447 (1.2 ppm error); *m/z* (LSIMS) 531 (monomer$^+$, 40%), 522 (60), 495 (M-HCl$^+$, 20), 397 (100), 196 (100).

Synthesis of 2-(4-*tert*-butyl-phenyl)-ethanesulfonic acid ((*R*,*R*)-2-amino-1,2-diphenylethyl)-amide ammonium chloride ruthenium dimer 21b

Diene **20b** (0.600 g, 1.12 mmol), DCM (10 cm^3), 1 M solution of HCl in diethyl ether (20 cm^3, 40.0 mmol), ethanol (10 cm^3) and ruthenium trichloride trihydrate (0.142 g, 0.55 mmol) were reacted according to the general procedure above to give **21b** (0.242 g, 68%) as a dark green solid; mp >300 °C; ν_{max}/cm^{-1} (solid) 3492 (NH), 1606 and 1496 (NH_3^+), 1319 and 1137 (SO_2N), 765 and 699 (Ph); δ_H (300 MHz; DMSO-d_6) 1.33 (18 H, s, 2 × $C(CH_3)_3$), 3.20–3.50 (8 H, m, 2 × CH_2CH_2SO_2 (peaks obscured by overlap with H_2O resonance)), 4.49 (2 H, m, 2 × PhC*H*NH_3^+), 4.70 (2 H, m, 2 × PhC*H*NH), 5.34 (2 H, d, *J* 5.8, 2 × ArH on Ru-Ph), 5.72 (2 H, d, *J* 6.0, 2 × ArH on Ru-Ph), 6.04 (4 H, m, 2 × (2 × ArH) on Ru-Ph), 7.10–7.36 (20 H, m, 4 × Ph), 8.45 (2 H, d, *J* 9.8, 2 × NH), 8.59–8.78 (6 H, m, 2 × NH_3^+); δ_C (125.8 MHz; DMSO-d_6) 27.0 (2 × t), 30.6 (2 × (3 × q)), 52.6 (2 × t), 59.2 (2 × d), 61.9 (2 × d), 84.1 (2 × overlapping 2 × d), 87.7 (2 × d), 87.9 (2 × d), 98.6 (2 × s), 112.5 (2 × s), 128.8 (2 × (2 × d)), 128.9 (2 × d), 129.3 (2 × (2 × d)), 129.4 (2 × overlapping 2 × (2 × d)), 129.7 (2 × d), 135.3 (2 × s), 138.9 (2 × s). Found (LSIMS): 573.0920 (monomeric species formed *in situ*), $^{102}RuC_{26}H_{32}N_2O_2SCl$ requires 573.0917 (0.6 ppm error); *m/z* (LSIMS) 573 (monomer$^+$, 40%), 551 (100), 537 (M-HCl$^+$, 50).

Synthesis of 2-(4-adamantan-1-yl-phenyl)-ethanesulfonic acid ((*R*,*R*)-2-amino-1,2-diphenylethyl)-amide ammonium chloride ruthenium dimer 21c

Diene **20c** (0.500 g, 0.81 mmol), DCM (5 cm^3), 2 M solution of HCl in diethyl ether (10 cm^3, 20.0 mmol), ethanol (12 cm^3) and ruthenium trichloride trihydrate (0.154 g, 0.59 mmol) were reacted according to the general procedure above to give **21c** (0.098 g, 23%) as a dark green solid; mp >300 °C; ν_{max}/cm^{-1} (solid) 3424 (NH), 1605 and 1495 (NH_3^+), 1318 and 1136 (SO_2N), 763 and 699 (Ph); δ_H (400 MHz; DMSO-d_6) 1.67–2.05 (30 H, m, 2 × adamantyl), 3.20–3.50 (8 H, m, 2 × CH_2CH_2SO_2 (peaks obscured by overlap with H_2O resonance)), 4.49 (2 H, m, 2 × PhC*H*NH_3^+), 4.71 (2 H,

m, 2 × PhC*H*NH), 5.30 (2 H, d, *J* 6.0, 2 × ArH on Ru-Ph), 5.68 (2 H, d, *J* 5.3, 2 × ArH on Ru-Ph), 6.07 (4 H, m, 4 × ArH on Ru-Ph), 7.09–7.35 (20 H, m, 4 × Ph), 8.44 (2 H, d, *J* 10.0, 2 × NH), 8.63–8.72 (6 H, m, 2 × NH_3^+); δ_C (125.8 MHz; DMSO-d_6) 26.7 (2 × t), 28.5 (2 × (3 × d)), 36.3 (2 × (3 × t)), 41.0 (2 × (3 × t)), 43.0 (2 × s), 52.0 (2 × t), 58.7 (2 × d), 61.4 (2 × d), 84.3 (2 × overlapping 2 × d), 85.9 (2 × d), 86.2 (2 × d), 128.3 (2 × d), 128.4 (2 × (2 × d)), 128.8 (2 × (2 × d)), 128.9 (2 × (2 × d)), 129.0 (2 × (2 × d)), 129.2 (2 × d), 134.6 (2 × s), 138.0 (2 × s) (NB not all quaternary carbons distinctly observed). Found (LSIMS): 652.1399 (monomeric species formed *in situ*), $^{102}RuC_{31}{}^{13}CH_{38}N_2O_2SCl$ requires 652.1420 (3.2 ppm error); *m/z* (LSIMS) 651 (monomer$^+$, 10%), 615 (M-HCl$^+$, 15), 515 (100), 196 (100).

Synthesis of 2-biphenyl-4-yl-ethanesulfonic acid ((*R*,*R*)-2-amino-1, 2-diphenylethyl)-amide ammonium chloride ruthenium dimer 21d

Diene **20d** (0.500 g, 0.90 mmol), DCM (5 cm^3), 2 M solution of HCl in diethyl ether (5 cm^3, 20.0 mmol), ethanol (15 cm^3) and ruthenium trichloride trihydrate (0.195 g, 0.75 mmol) were reacted according to the general procedure above to give **21d** (0.145 g, 29%) as a dark green solid; mp >300 °C; ν_{max}/cm^{-1} (solid) 3465 (NH), 1600 and 1495 (NH_3^+), 1321 and 1138 (SO_2N), 764 and 698 (Ph); δ_H (400 MHz; DMSO-d_6) 3.20–3.50 (8 H, m, 2 × CH_2C$H_2$$SO_2$ (peaks obscured by overlap with H_2O resonance)), 4.44–4.55 (2 H, m, 2 × PhC*H*NH_3^+), 4.73 (2 H, t, *J* 9.8, 2 × PhC*H*NH), 5.48 (1.5 H, d, *J* 6.2, 2 × ArH on Ru-Ph major isomer), 5.87 (1.5 H, d, *J* 6.2, 2 × ArH on Ru-Ph major isomer), 6.06–6.12 (1 H, m, 4 × ArH on Ru-Ph minor isomer), 6.26–6.29 (1 H, m, 4 × ArH on Ru-Ph minor isomer), 6.47 (3 H, d, *J* 6.2, 4 × ArH on Ru-Ph major isomer), 7.18–7.52 (30 H, m, 6 × Ph), 8.24 (0.5 H, d, *J* 9.8, 2 × NH minor isomer), 8.46 (1.5 H, d, *J* 9.8, 2 × NH major isomer), 8.60–8.72 (6 H, m, 2 × NH_3^+); δ_C (100.6 MHz; DMSO-d_6) 26.5 (2 × t), 51.8 (2 × t), 58.4 (2 × d), 61.0 (2 × d), 85.6 (2 × d), 85.8 (2 × d), 86.9 (2 × d), 87.0 (2 × d), 97.5 (2 × s), 101.8 (2 × s), 128.0 (2 × (2 × d)), 128.3 (2 × d), 128.5 (2 × (2 × d)), 128.7 (2 × (2 × d)), 128.8 (2 × (2 × d)), 128.9 (2 × (2 × d)), 129.0 (2 × (2 × d)), 129.1 (2 × d), 129.8 (2 × d), 133.2 (2 × s), 134.3 (2 × s), 137.7 (2 × s, major isomer), 137.8 (2 × s, minor isomer) (NB not all carbons of minor isomer distinctly observed). Found (LSIMS): 557.0841 (monomeric species formed *in situ*), $^{102}RuC_{28}H_{27}N_2O_2SCl$ requires 557.0837 (0.7 ppm error); *m/z* (LSIMS) 557 (monomer$^+$, 75%), 551 (90), 523 (100).

Note: the ^{1}H-NMR spectra for compounds containing *t*Boc protecting groups obtained at rt were subject to significant broadening due to restricted rotation effects. The data for these spectra have been quoted along with the best spectra obtained using elevated temperatures where this was possible.

Synthesis of *tert*-butyl (1*R*,2*S*)-1-hydroxy-1-phenylpropan-2-yl-(pent-4-ynyl) carbamate 25

To a solution of 1*R*,2*S*-norephedrine **3** (3.57 g, 23.6 mmol) and triethylamine (2.63 g, 26.0 mmol) in acetonitrile (70 cm^3) was added **26** (5.63 g, 23.6 mmol). The reaction mixture was refluxed overnight, cooled to room temperature and concentrated under vacuum. The residue was dissolved in DCM (150 cm^3), washed with sat. $NaHCO_3$ solution (100 cm^3) and the aqueous layer extracted with DCM (3 × 100 cm^3). The combined extracts were concentrated under vacuum, dissolved in THF (110 cm^3) and di-*tert*-butyl dicarbonate (3.65 g, 16.7 mmol) added. The mixture was stirred at room temperature overnight, diluted with 1 M $KHSO_4$ (220 cm^3) resulting in formation of a precipitate, to which water (500 cm^3) was added, extracted with DCM (2 × 500 cm^3) and the organic layers combined, dried ($MgSO_4$), filtered and concentrated under vacuum to give crude product. The residue was purified by flash column chromatography (5% EtOAc–hexane to 20% EtOAc–hexane) to give **25** (3.02 g, 40%) as a colourless oil; $[\alpha]_D^{27}$ +2.8 (*c* 2.1 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3427 (OH), 3306 (≡CH), 1664 (C=O), 770 and 701 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.27–1.30 (3 H, m, CH_3), 1.46 (9 H, s, $C(CH_3)_3$), 1.58–1.76 (2 H, m, C$H_2$$CH_2$C≡CH), 1.95–1.97 (1 H, m, ≡CH), 2.12–2.17 (2 H, m, CH_2C≡CH), 3.09–3.18 (2 H, m, NCH_2), 3.56 (1 H, br s, CH_3C*H*N), 4.58 (0.4 H, br s, PhCH rotamer A), 5.01 (0.6 H, br s, PhCH rotamer B), 7.10–7.41 (5 H, m, Ph); δ_H(400 MHz; DMSO-d_6; 373 K) 1.27 (3 H, d, *J* 7.0, CH_3), 1.38 (9 H, s, $C(CH_3)_3$), 1.47–1.65 (2 H, m, C$H_2$$CH_2$C≡CH), 2.05 (2 H, dt, *J* 7.0 and 2.6, CH_2C≡CH), 2.48–2.51 (1 H, m, ≡CH), 2.91–2.98 (1 H, m, NC$H_a$$H_b$), 3.05–3.12 (1 H, m, NCH_aH_b), 3.77 (1 H, apparent quintet, dq, *J* 7.0 and 7.0, CH_3C*H*), 4.72 (1 H, d, *J* 7.0, CHPh), 7.19–7.34 (5 H, m, Ph); δ_C(75.5 MHz; $CDCl_3$; Me_4Si) 10.8 (d), 14.2 (t), 26.6 (q), 27.4 (3 × q), 29.9 (d), 46.9 (t), 60.9 (d), 75.8 (t), 79.2 (s), 82.5 (s), 125.3 (2 × d), 126.3 (d), 127.1 (2 × d), 141.7 (s), 155.6 (s). Found (LSIMS) 318.2060 [MH]$^+$, $C_{19}H_{28}NO_3$ requires 318.2069 (2.8 ppm error); *m/z* (LSIMS) 318 (MH$^+$, 90%), 262 (65), 244 (100), 210 (75).

Synthesis of *tert*-butyl (1*R*,2*S*)–1-(*tert*-butyldimethylsilyloxy)-1-phenylpropan-2-yl (pent-4-ynyl)carbamate 27

To a solution of **25** (2.153 g, 6.79 mmol) and imidazole (0.740 g, 10.86 mmol) in anhydrous DMF (22 cm^3), was added *tert*-butyldimethylsilyl chloride (1.535 g, 10.19 mmol). The reaction mixture was stirred overnight, diluted with water (50 cm^3) and extracted with diethyl ether (2 × 100 cm^3). The combined extracts were dried ($MgSO_4$), filtered, and concentrated under vacuum to give the crude product. The residue was purified by flash chromatography (2% EtOAc–hexane to 4% EtOAc–hexane) to give **27** (2.856 g, 98%) as a colourless oil (Found: C, 69.5; H, 9.5, N, 3.05. $C_{25}H_{41}NO_3Si$ requires C, 69.55; H, 9.55, N, 3.25%); $[\alpha]_D^{27}$ +10.1 (*c* 1.45 in CH_2Cl_2); ν_{max}/cm^{-1} (thin film) 3250 (≡CH), 1688 (C=O), 1253 and 865 ($Si(CH_3)_2$), 774 and 701 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.25 (6 H, s, $Si(CH_3)_2$), 0.89 (9 H, s, $SiC(CH_3)_3$), 1.26–1.35 (3 H, m, CH_3CHN), 1.41 (9 H, s, $OC(CH_3)_3$), 1.45 (2 H, s, C$H_2$$CH_2$C≡CH), 1.92 (1 H, s, ≡CH), 1.95–2.10 (2 H, m, CH_2C≡CH), 2.91–3.07 (2 H, m, NCH_2), 3.64 (1 H, br s, CH_3C*H*N), 4.79 (0.4 H, br s, PhCH rotamer A), 4.98 (0.6 H, br s, PhCH rotamer B), 7.20–7.35 (5 H, m, Ph); δ_H(400 MHz; DMSO-d_6; 373 K) −0.24 (6 H, s, $Si(CH_3)_2$), 0.84 (9 H, s, $SiC(CH_3)_3$), 1.29 (3 H, d, *J* 7.0, CH_3CHN), 1.35 (9 H, s, $OC(CH_3)_3$), 1.45–1.55 (1H, m, ≡CH), 1.95–1.99 (2 H, m, C$H_2$$CH_2$C≡CH), 2.44–2.48 (2 H, m, CH_2C≡CH), 2.75–2.82 (1 H, m, NC$H_a$$H_b$), 2.92–2.99 (1 H, m, NCH_aH_b), 3.58 (1 H, apparent quintet, dq, *J* 7.3 and 7.0, CH_3C*H*), 4.88 (1 H, d, *J* 7.3, PhCH), 7.19–7.27 (5 H, m, Ph); δ_C(125.8 MHz; DMSO-d_6) −4.4 (2 × q), 15.6 (t), 18.1 (s), 26.0 (3 × q), 28.4 (3 × q), 40.4 (t), 55.3 (d), 71.5 (s), 71.6 (d), 76.3 (d), 78.7 (t), 79.1 (s), 84.1 (s), 126.7 (2 × d), 127.6 (d), 127.7 (2 × d), 143.1 (s),

154.5 (s) (NB signal due to CH_3CHN not observed possibly due to restricted rotation effects). Found (LSIMS): 432.2916 $[MH]^+$, $C_{25}H_{42}NO_3Si$ requires 432.2934 (4.2 ppm error); *m/z* (LSIMS) 432 (MH^+, 15%), 358 (25), 332 (65), 318 (50), 244 (100), 221 (75), 210 (60), 147 (55).

General procedure for the synthesis of compounds 28a–d

To a stirred solution of **19** (0.02 eq.) in DCM was added the appropriate diene (2.00 eq.) followed by **27** (1.00 eq.). The reaction mixture was stirred for 2 hours and concentrated under vacuum to give the crude product. The residue was purified by flash chromatography (2% EtOAc–hexane) to give cyclohexadienes **28a–d**.

Synthesis of [(1*S*,2*R*)-2-(*tert*-butyldimethylsilanyloxy)-1-methyl-2-phenylethyl]-[3-(4-methylcyclohexa-1,4-dienyl)-propyl]-*tert*-butyl carbamate 28a[7c]

Catalyst **19** (0.050 g, 0.12 mmol), DCM (30 cm^3), isoprene (0.317 g, 4.66 mmol) and **27** (1.00 g, 2.33 mmol) were reacted according to the general procedure above to give **28a** (0.853 g, 73%) as a thick colourless oil; $[\alpha]_D^{27}$ +5.9 (*c* 1.2 in DCM); ν_{max}/cm^{-1} (thin film) 1689 (C=O), 1252 and 865 ($Si(CH_3)_2$), 774 and 700 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.25 (6 H, s, $Si(CH_3)_2$), 0.88 (9 H, s, $SiC(CH_3)_3$), 1.19–1.29 (3 H, m, CH_3CHN), 1.40 (9 H, s, $OC(CH_3)_3$), 1.45 (2 H, m, CH_2CH_2N), 1.66 (3 H, s, CH_3C=), 1.82–1.85 (2 H, m, $CH_2CH_2CH_2N$), 2.22–2.27 (2 H, m, diene CH_2), 2.53 (2 H, m, diene CH_2), 2.80–3.00 (2 H, m, NCH_2), 3.63 (1 H, m, CH_3CHN), 4.79 (0.4 H, br s, PhCH rotamer A), 4.97 (0.6 H, br s, PhCH rotamer B), 5.35 (1 H, m, =CH), 5.39 (1 H, m, =CH), 7.00–7.20 (5 H, m, Ph); δ_H(500 MHz; DMSO-d_6; 373 K) −0.24 (6 H, s, $Si(CH_3)_2$), 0.84 (9 H, s, $SiC(CH_3)_3$), 1.27–1.29 (3 H, d, *J* 7.5, CH_3CHN), 1.36 (9 H, s, $OC(CH_3)_3$), 1.41–1.45 (2 H, m, CH_2CH_2N), 1.62 (3 H, s, CH_3C=), 1.77 (2 H, m, $CH_2CH_2CH_2N$), 2.16–2.39 (2 H, m, diene CH_2), 2.59–2.70 (2 H, m, diene CH_2), 2.89–2.94 (2 H, m, NCH_2), 3.56–3.61 (1 H, m, CH_3CHN), 4.88 (1 H, d, *J* 7.3, PhCH), 5.35 (1 H, m, =CH), 5.38 (1 H, m, =CH), 7.20–7.29 (5 H, m, Ph); δ_C(75.5 MHz; $CDCl_3$; Me_4Si) −4.9 (2 × q), 17.8 (s), 22.8 (q), 25.7 (3 × q), 28.3 (3 × q), 29.7 (t), 31.4 (t), 34.0 (t), 34.2 (t), 41.4 (t), 51.2 (d), 76.2 (d), 79.8 (s), 118.3 (d), 118.4 (d), 126.7 (2 × d), 127.0 (d), 127.6 (2 × d), 133.2 (s), 133.4 (s), 136.1 (s), 161.0 (s) (NB signal due to CH_3CHN not observed possibly due to restricted rotation effects). Found (LSIMS): 498.3415 $[M-H]^+$, $C_{30}H_{48}NO_3Si$ requires 498.3403 (2.4 ppm error); *m/z* (LSIMS) 498 ($M-H^+$, SS 5%), 426 (20), 400 (80), 312 (55), 222 (100), 178 (90).

Synthesis of [3-(4-*tert*-butyl-cyclohexa-1,4-dienyl)-propyl]-[(1*S*,2*R*)-2-(*tert*-butyldimethylsilanyloxy)-1-methyl-2-phenylethyl]-*tert*-butyl carbamate 28b

Catalyst **19** (0.009 g, 0.02 mmol), DCM (10 cm^3), 2-*t*Bu-butadiene (0.192 g, 1.75 mmol) and **27** (0.441 g, 1.53 mmol) were reacted according to the general procedure above to give **28b** (0.428 g, 52%) as a thick colourless oil; $[\alpha]_D^{25}$ +0.9 (*c* 0.95 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 1690 (C=O), 1253 and 865 ($Si(CH_3)_2$), 774 and 700 (Ph); δ_H(400 MHz; $CDCl_3$; Me_4Si) −0.27 (6 H, s, $Si(CH_3)_2$), 0.87 (9 H, s, $SiC(CH_3)_3$), 1.02 (9 H, s, $(CH_3)_3CC$=), 1.21–1.32 (3 H, m, CH_3CHN), 1.38 (9 H, s, $OC(CH_3)_3$), 1.44 (2 H, m, CH_2CH_2N), 1.78–1.83 (2 H, m, $CH_2CH_2CH_2N$), 2.52–2.56 (2 H, m, diene CH_2), 2.63–2.69 (2 H, m, diene CH_2), 2.85–2.97 (2 H, m, NCH_2), 3.63 (1 H, m, CH_3CHN), 4.79 (0.4 H, br s, PhCH rotamer A), 4.95 (0.6 H, br s, PhCH rotamer B), 5.34 (0.15 H, m, =CH minor isomer), 5.38 (0.85 H, m, =CH major isomer), 5.48 (1 H, m, =CH), 7.17–7.33 (5 H, m, Ph); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) −5.7 (2 × q), 13.1 (q), 17.0 (s), 24.9 (3 × q), 27.5 (3 × q), 27.9 (3 × q), 29.2 (t), 31.8 (t), 33.3 (t), 33.9 (t), 41.2 (t), 51.7 (d), 75.4 (d), 77.8 (s), 78.3 (s), 114.2 (d), 117.9 (d), 125.5 (2 × d), 125.9 (d), 126.6 (2 × d), 132.8 (s), 142.2 (s), 147.6 (s), 154.1 (s). Found (LSIMS): 540.3889 $[M-H]^+$, $C_{33}H_{54}NO_3Si$ requires 540.3873 (3.0 ppm error); *m/z* (LSIMS) 540 ($M-H^+$, 45%), 440 (95), 352 (60), 318 (55), 262 (100), 218 (85). A satisfactory ^{1}H-NMR to improve the resolution of peaks at elevated temperatures could not be obtained due to facile oxidation of the cyclohexadiene ring to the corresponding aromatic ring.

Synthesis of [3-(4-adamantan-1-ylcyclohexa-1,4-dienyl)-propyl]-[(1*S*,2*R*)–2-(*tert*-butyldimethylsilanyloxy)-1-methyl-2-phenyl-ethyl]-*tert*-butyl carbamate 28c

Catalyst **19** (0.034 g, 0.08 mmol), DCM (22 cm^3), 2-adamantyl-butadiene (0.600 g, 3.19 mmol) and **27** (0.685 g, 1.60 mmol) were reacted according to the general procedure above to give **28c** (0.730 g, 74%) as a thick colourless oil; $[\alpha]_D^{25}$ −15.4 (*c* 0.15 in DCM); ν_{max}/cm^{-1} (thin film) 1689 (C=O), 1251 and 864 ($Si(CH_3)_2$), 774 and 700 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.27 (6 H, s, $Si(CH_3)_2$), 0.86 (9 H, s, $SiC(CH_3)_3$), 1.21–1.23 (3 H, m, CH_3CHN), 1.28–1.83 (26 H, m, $OC(CH_3)_3$, 6 × adamantyl CH_2, 3 × adamantyl CH and CH_2CH_2N), 2.35–2.68 (4 H, m, 2 × diene CH_2), 2.86–2.92 (2 H, m, NCH_2), 3.61 (1 H, m, CH_3CHN), 4.77 (0.4 H, br s, PhCH rotamer A), 4.95 (0.6 H, br s, PhCH rotamer B), 5.32 (0.2 H, m, =CH minor isomer), 5.36 (0.8 H, m, =CH major isomer), 5.41 (1 H, m, =CH), 7.16–7.24 (5 H, m, Ph); δ_C(75.5 MHz; $CDCl_3$; Me_4Si) −4.2 (2 × q), 18.5 (s), 26.2 (t), 26.3 (3 × q), 29.2 (3 × q), 29.4 (3 × d), 30.6 (t), 33.2 (s), 34.7 (t), 37.0 (t), 37.2 (3 × t), 41.4 (3 × t), 43.6 (t), 58.0 (d), 76.8 (d), 79.2 (s), 115.7 (d), 119.4 (d), 126.9 (2 × d), 127.4 (d), 128.0 (2 × d), 134.2 (s), 134.4 (s), 143.6 (s), 154.1 (s) (NB signal due to CH_3CHN not observed possibly due to restricted rotation effects). Found (LSIMS): 618.4319 $[M-H]^+$, $C_{39}H_{60}NO_3Si$ requires 618.4342 (3.8 ppm error); *m/z* (LSIMS) 618 ($M-H^+$, 10%), 518 (65), 430 (40), 340 (75), 296 (100), 221 (55), 210 (60), 135 (50). A satisfactory ^{1}H-NMR to improve the resolution of peaks at elevated temperatures could not be obtained due to facile oxidation of the cyclohexadiene ring to the corresponding aromatic ring.

Synthesis of [(1*S*,2*R*)-2-(*tert*-butyldimethylsilanyloxy)-1-methyl-2-phenylethyl]-[3-(4-phenylcyclohexa-1,4-dienyl)-propyl]-*tert*-butyl carbamate 28d

Catalyst **19** (0.02 g, 0.04 mmol), DCM (30 cm^3), 2-phenyl-butadiene (0.579 g, 4.46 mmol) and **27** (1.00 g, 2.23 mmol) were reacted according to the general procedure above to give **28d** (1.20 g, 96%) as a thick colourless oil; $[\alpha]_D^{25}$ −2.7 (*c* 0.15 in DCM); ν_{max}/cm^{-1} (thin film) 1688 (C=O), 1252 and 864 ($Si(CH_3)_2$), 775 and 698 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.26 (6 H, s, $Si(CH_3)_2$), 0.86 (9 H, s, $SiC(CH_3)_3$), 1.23–1.26 (3 H, m, CH_3CHN),

1.39 (9 H, s, $OC(CH_3)_3$), 1.48 (2 H, m, CH_2CH_2N), 1.83–1.88 (2 H, m, $CH_2CH_2CH_2N$), 2.72–2.88 (4 H, m, 2 × diene CH_2), 3.01–3.05 (2 H, m, NCH_2), 3.62 (1 H, m, CH_3CHN), 4.70 (0.4 H, br s, PhCH rotamer A), 4.97 (0.6 H, br s, PhCH rotamer B), 5.41 (0.3 H, m, =CH α to Ph, minor isomer), 5.48 (0.7 H, m, =CH α to Ph, major isomer), 6.09 (1 H, m, =CH β to Ph), 7.16–7.40 (10 H, m, 2 × Ph); δ_H(400 MHz; DMSO-d_6; 373 K) −0.25 (6 H, s, $Si(CH_3)_2$), 0.84 (9 H, s, $SiC(CH_3)_3$), 1.30 (3 H, d, *J* 7.0, CH_3CHN), 1.37 (9 H, s, $OC(CH_3)_3$), 1.42–1.50 (2 H, m, CH_2CH_2N), 1.82–1.86 (2 H, m, $CH_2CH_2CH_2N$), 2.69–2.74 (4 H, m, 2 × diene CH_2), 2.97 (2 H, m, NCH_2), 3.58 (1 H, dq (app. quintet), *J* 7.7 and 7.0 CH_3CHN), 4.90 (1 H, d, *J* 7.7, PhC*H*), 5.40 (0.3 H, m, =CH α to Ph, minor isomer), 5.47 (0.7 H, m, =CH α to Ph, major isomer), 6.09 (1 H, m, =CH β to Ph), 7.16–7.39 (10 H, m, 2 × Ph); δ_C(75.5 MHz; $CDCl_3$; Me_4Si) −4.8 (2 × q), 13.9 (q), 17.9 (s), 25.7 (3 × q), 27.1 (t), 28.5 (3 × q), 28.6 (t), 30.1 (t), 31.0 (t), 34.1 (t) 53.2 (d), 76.2 (d), 78.7 (s), 118.3 (d), 121.5 (d), 124.8 (2 × d), 126.3 (2 × d), 126.8 (d), 127.4 (2 × d), 127.7 (d), 128.064 (2 × d), 133.6 (s), 134.1 (s), 141.2 (s), 143.0 (s), 154.8 (s). Found (LSIMS): 560.3554 $[M\text{-}H]^+$, $C_{35}H_{50}NO_3Si$ requires 560.3560 (1.0 ppm error); *m/z* (LSIMS) 560 ($M\text{-}H^+$, 30%), 460 (70), 372 (60), 338 (40), 282 (95), 238 (100), 221 (50), 136 (65).

General procedure for the desilylation of compounds 28a–d

To a stirred solution of **28a–d** (1.00 eq.) in THF was added a 1 M solution of TBAF in THF (1.50 eq.). The reaction mixture was stirred overnight, diluted with water, extracted with EtOAc, dried ($MgSO_4$) and concentrated under vacuum to give the crude product. The residue was purified by flash chromatography (2.5% to 20% EtOAc–hexane) to give the corresponding alcohols.

Synthesis of ((1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl)-[3-(4-methylcyclohexa-1,4-dienyl)-propyl]-*tert*-butyl carbamate[7c]

Diene **28a** (0.800 g, 1.60 mmol), THF (8 cm^3), and a 1 M solution of TBAF in THF (2.4 cm^3) were reacted according to the general procedure above to give the product (0.386 g, 63%) as a thick colourless oil; $[\alpha]_D^{27}$ +14.3 (*c* 1.05 in DCM); ν_{max}/cm^{-1} (thin film) 3391 (OH), 1664 (C=O), 759 and 700 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.22–1.26 (3 H, m, CH_3CHN), 1.45 (9 H, s, $OC(CH_3)_3$), 1.52–1.64 (2 H, m, CH_2CH_2N), 1.67 (3 H, s, CH_3), 1.88–1.91 (2 H, m, $CH_2CH_2CH_2N$), 2.49–2.62 (4 H, m, 2 × diene CH_2), 2.93–2.98 (2 H, m, NCH_2), 3.49 (1 H, m, CH_3CHN), 4.87 (0.4 H, br s, PhCH rotamer A), 4.99 (0.6 H, br s, PhCH rotamer B), 5.40 (2 H, m, 2 × =CH), 7.25–7.37 (5 H, m, Ph); δ_H(400 MHz; DMSO-d_6; 363 K) 1.20 (3 H, d, *J* 6.6, CH_3CHN), 1.34 (9 H, s, $OC(CH_3)_3$), 1.34–1.53 (2 H, m, CH_2CH_2N), 1.59 (3 H, s, CH_3), 1.79 (2 H, t, *J* 6.4, $CH_2CH_2CH_2N$), 2.55–2.62 (4 H, m, 2 × diene CH_2), 2.88–2.95 (2 H, m, NCH_2), 3.68 (1 H, dq (app. quintet), *J* 6.6 and 5.8, CH_3CHN), 4.66 (1 H, t, *J* 5.8 and 4.8), 4.99 (1 H, d, *J* 4.8, OH), 5.31–5.38 (2 H, m, 2 × =CH), 7.12–7.28 (5 H, m, Ph); δ_C(125.8 MHz; DMSO-d_6) 13.9 (q), 23.3 (q), 27.5 (3 × q), 29.7 (t), 31.4 (t), 34.3 (t), 40.4 (t), 45.9 (t), 58.6 (d), 75.0 (d), 78.4 (s), 118.2 (d), 118.8 (d), 126.7 (2 × d), 127.9 (d), 128.4 (2 × d), 131.1 (s), 134.2 (s), 144.5 (s), 154.4 (s). Found (LSIMS): 384.2520 $[M\text{-}H]^+$, $C_{24}H_{34}NO_3$ requires 384.2539 (4.9 ppm error); *m/z* (LSIMS) 384 ($M\text{-}H^+$, 25%), 330 (45), 312 (95), 310 (90), 242 (65), 222 (80), 220 (60), 178 (100), 176 (60).

Synthesis of [3-(4-*tert*-butylcyclohexa-1,4-dienyl)-propyl]-((1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl)-*tert*-butyl carbamate

Diene **28b** (0.400 g, 0.74 mmol), THF (6 cm^3), and a 1 M solution of TBAF in THF (1.1 cm^3) were reacted according to the general procedure above to give the alcohol (0.283 g, 90%) as a thick colourless oil; $[\alpha]_D^{21}$ +6.1 (*c* 0.95 in $CHCl_3$); ν_{max}/cm^{-1} (thin film) 3440 (OH), 1665 (C=O), 760 and 701 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.04 (9 H, s $(CH_3)_3CC$=), 1.22–1.28 (3 H, m, CH_3CHN), 1.45 (9 H, s, $OC(CH_3)_3$), 1.48–1.68 (2 H, m, CH_2CH_2N), 1.88–1.93 (2 H, m, $CH_2CH_2CH_2N$), 2.48–2.72 (4 H, m, 2 × diene CH_2), 2.95–3.08 (2 H, m, NCH_2), 3.50 (1 H, m, CH_3CHN), 5.00 (PhCH), 5.39 (0.15 H, m, =CH minor isomer), 5.44 (0.85 H, m, =CH major isomer), 5.51 (1 H, m, =CH), 7.21–7.40 (5 H, m, Ph); δ_C(125.8 MHz; $CDCl_3$; Me_4Si) 14.2 (q), 25.6 (t), 29.0 (3 × q), 29.0 (t), 31.4 (t), 31.6 (3 × q), 32.2 (t), 48.9 (t), 49.1 (s), 62.1 (d), 77.4 (d), 80.1 (s), 115.2 (d), 119.2 (d), 125.3 (d), 126.4 (2 × d), 127.9 (2 × d), 138.4 (s), 142.5 (s), 148.8 (s), 156.8 (s). Found (LSIMS): 426.2997 $[M\text{-}H]^+$, $C_{27}H_{40}NO_3$ requires 426.3008 (2.7 ppm error); *m/z* (LSIMS) 426 ($M\text{-}H^+$, 50%), 370 (40), 352 (80), 318 (50), 262 (100), 218 (85). A satisfactory ^{1}H-NMR to improve the resolution of peaks at elevated temperatures could not be obtained due to facile oxidation of the cyclohexadiene ring to the corresponding aromatic ring.

Synthesis of [3-(4-adamantan-1-yl-cyclohexa-1,4-dienyl)-propyl]-((1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl)-*tert*-butyl carbamate

Diene **28c** (0.730 g, 1.18 mmol), THF (10 cm^3), and a 1 M solution of TBAF in THF (1.8 cm^3) were reacted according to the general procedure above to give the alcohol (0.450 g, 65%) as a thick colourless oil; $[\alpha]_D^{25}$ +2.9 (*c* 0.1 in DCM); ν_{max}/cm^{-1} (thin film) 3441 (OH), 1665 (C=O), 758 and 700 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.15–1.17 (3 H, m, CH_3CHN), 1.34 (9 H, s, $OC(CH_3)_3$), 1.57–2.05 (19 H, m, $CH_2CH_2CH_2N$, 6 × adamantyl CH_2 and 3 × adamantyl CH), 2.38–2.61 (4 H, m, 2 × diene CH_2), 2.84–3.01 (2 H, m, NCH_2), 3.41 (1 H, m, CH_3CHN), 4.77 (0.4 H, br s, PhCH rotamer A), 4.99 (0.6 H, br s, PhCH rotamer B), 5.35–5.38 (2 H, m, 2 × =CH), 7.02–7.24 (5 H, m, Ph); δ_C(75.5 MHz; $CDCl_3$; Me_4Si) 11.3 (q), 24.6 (t), 28.3 (3 × q), 28.8 (3 × d), 30.0 (t), 32.5 (s), 34.0 (t), 36.6 (t), 36.9 (3 × t), 40.7 (3 × t), 43.0 (t), 61.9 (d), 77.2 (d), 79.9 (s), 115.0 (d), 119.0 (d), 125.9 (2 × d), 127.0 (d), 127.9 (2 × d), 133.4 (s), 142.6 (s), 143.0 (s), 155.4 (s). Found (LSIMS): 504.3460 $[M\text{-}H]^+$, $C_{33}H_{46}NO_3$ requires 504.3478 (3.5 ppm error); *m/z* (LSIMS) 432 ($M\text{-}H^+$, 45%), 430 (70), 396 (30), 340 (90), 296 (100). A satisfactory ^{1}H-NMR to improve the resolution of peaks at elevated temperatures could not be obtained due to facile oxidation of the cyclohexadiene ring to the corresponding aromatic ring.

Synthesis of ((1*S*,2*R*)-2-hydroxy-1-methyl-2-phenylethyl)-[3-(4-phenylcyclohexa-1,4-dienyl)-propyl]-*tert*-butyl carbamate

Diene **28d** (1.00 g, 1.79 mmol), THF (10 cm^3), and a 1 M solution of TBAF in THF (2.7 cm^3) were reacted according to the general procedure above to give the alcohol (0.740 g, 94%) as a thick colourless oil; $[\alpha]_D^{25}$ +9.7 (*c* 0.1 in DCM); ν_{max}/cm^{-1} (thin film) 3434 (OH), 1662 (C=O), 756 and 698 (Ph); δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.24–1.28 (3 H, m, CH_3CHN), 1.43 (9 H, s, $OC(CH_3)_3$), 1.52–1.64

(2 H, m, CH_2CH$_2$N), 1.98–2.03 (2 H, m, CH$_2$CH_2CH$_2$N), 2.56–3.07 (6 H, m, 2 × diene CH$_2$ and NCH$_2$), 3.48 (1 H, m, CH$_3$CHN), 4.77 (0.4 H, br s, PhCH rotamer A), 4.99 (0.6 H, br s, PhCH rotamer B), 5.38 (0.3 H, m, =CH α to Ph, minor isomer), 5.44 (0.7 H, m, =CH α to Ph, major isomer), 6.06 (1 H, m, =CH β to Ph), 7.24–7.48 (10 H, m, 2 × Ph); δ_C(75.5 MHz; CDCl$_3$; Me$_4$Si) 12.1 (q), 27.9 (t), 28.9 (3 × q), 31.3 (t), 33.3 (t), 33.8 (t), 47.0 (t), 57.5 (d), 77.8 (d), 80.6 (s), 120.8 (d), 125.4 (d), 126.6 (2 × d), 127.4 (2 × d), 127.6 (2 × overlapping d), 128.6 (2 × d), 129.2 (2 × d), 137.8 (s), 141.4 (s), 143.1 (s) (NB not all quaternary carbons distinctly observed). Found (LSIMS): 446.2711 [M-H]$^+$, $C_{29}H_{36}NO_3$ requires 446.2695 (3.5 ppm error); *m/z* (LSIMS) 446 (M-H$^+$, 30%), 372 (100), 318 (30), 282 (85), 238 (95). A satisfactory ^{1}H-NMR to improve the resolution of peaks at elevated temperatures could not be obtained due to facile oxidation of the cyclohexadiene ring to the corresponding aromatic ring.

General procedure for the synthesis of compounds 29a–d

To a stirred solution of the precursor alcohol prepared as described above (1.00 eq.) in DCM was added an excess of a 2 M solution of HCl in diethyl ether and the reactants stirred overnight. The solvent was removed from the resulting precipitate under vacuum, dissolved in ethanol and ruthenium trichloride trihydrate (typically 0.75 eq.) was added. The reaction mixture was heated at reflux overnight and then cooled to room temperature. The precipitate was collected by filtration and washed with ethanol (5 × 10 cm^3) to give ruthenium dimers **29a–d**.

Synthesis of (1*R*,2*S*)-1-phenyl-2-(3-*p*-tolylpropylamino)-propan-1-ol ruthenium dimer 29a[7c]

The precursor alcohol (0.350 g, 0.94 mmol), DCM (10 cm^3), 2 M solution of HCl in diethyl ether (15 cm^3, 30.00 mmol), ethanol (15 cm^3) and ruthenium trichloride trihydrate (0.196 g, 0.75 mmol) were reacted according to the general procedure above to give **29a** (0.182 g, 42%) as a dark green solid; ν_{max}/cm^{-1} (thin film) 3422 (OH), 1602 (NH$_2^+$), 749 and 703 (Ph); δ_H(400 MHz; DMSO-d$_6$) 0.93 (6 H, d, *J* 6.3, 2 × CH_3CHN), 2.00–2.03 (4 H, m, 2 × CH_2CH$_2$N), 2.13 (6 H, s, 2 × ArCH$_3$), 2.53–2.58 (4 H, m, 2 × CH_2CH$_2$CH$_2$N), 3.07–3.15 (4 H, m, 2 × NCH_2), 3.45 (2 H, m, 2 × CH$_3$CHN), 5.11 (2 H, m, 2 × PhCH), 5.84–5.88 (8 H, m, 2 × (4 × ArH on Ru-arene)), 6.13 (2 H, br s, 2 × OH), 7.29–7.45 (10 H, m, 2 × Ph), 8.50 (2 H, m, 2 × NH_aH$_b^+$), 8.56 (2 H, m, 2 × NH$_a$$H_b^+$); δ_C(100.6 MHz; DMSO-d$_6$) 9.8 (2 × q), 18.6 (2 × q), 25.8 (2 × t), 29.1 (2 × t), 45.0 (2 × t), 58.3 (2 × d), 69.7 (2 × d), 87.4 (2 × (2 × d)), 88.2 (2 × (2 × d)), 99.8 (2 × s), 100.4 (2 × s), 126.2 (2 × (2 × d)), 127.5 (2 × d), 128.4 (2 × (2 × d)), 141.0 (2 × s). Found (LSIMS): 420.0670 (monomeric species formed *in situ*), ^{102}RuC$_{19}$H$_{25}$NOCl requires 420.0668 (0.5 ppm error); *m/z* (LSIMS) 420 (monomer$^+$, 100%).

Synthesis of (1*R*,2*S*)-2-[3-(4-*tert*-butylphenyl)-propylamino]-1-phenylpropan-1-ol ruthenium dimer 29b

The precursor alcohol (0.235 g, 0.58 mmol), DCM (10 cm^3), 2 M solution of HCl in diethyl ether (15 cm^3, 30.00 mmol), ethanol (10 cm^3) and ruthenium trichloride trihydrate (0.125 g, 0.48 mmol) were reacted according to the general procedure above to give **29b** (0.038 g, 13%) as a dark green solid; ν_{max}/cm^{-1} (thin film) 3354 (OH), 1603 (NH$_2^+$), 745 and 701 (Ph); δ_H(400 MHz; DMSO-d$_6$) 0.94 (6 H, d, *J* 6.0, 2 × CH_3CHN), 1.39 (18 H, s, 2 × ArC(CH$_3$)$_3$), 1.96–2.03 (4 H, m, 2 × CH_2CH$_2$N), 2.53–2.58 (4 H, m, 2 × CH_2CH$_2$CH$_2$N), 3.08–3.17 (4 H, m, 2 × NCH_2), 3.48 (2 H, m, 2 × CH$_3$CHN), 5.10 (2 H, m, 2 × PhCH), 5.86 (4 H, d, *J* 6.0, 2 × (2 × ArH on Ru-arene)), 6.14 (4 H, d, *J* 6.0, 2 × (2 × ArH on Ru-arene)), 7.33 (2 H, br s, 2 × OH), 7.38–7.45 (10 H, m, 2 × Ph), 8.41–8.68 (4 H, m, 2 × NH$_2^+$); δ_C(100.6 MHz; DMSO-d$_6$) 9.8 (2 × q), 25.8 (2 × t), 29.5 (2 × t), 30.3 (2 × (3 × q)), 34.8 (s), 44.7 (2 × t), 58.5 (2 × d), 69.9 (2 × d), 84.7 (2 × (2 × d)), 86.1 (2 × (2 × d)), 101.7 (2 × s), 111.1 (2 × s), 126.3 (2 × (2 × d)), 127.8 (2 × d), 128.6 (2 × (2 × d)), 141.5 (2 × s). Found (LSIMS): 462.1148 (monomeric species formed *in situ*), ^{102}RuC$_{22}$H$_{31}$NOCl requires 462.1138 (2.1 ppm error); *m/z* (LSIMS) 462 (monomer$^+$, 30%), 326 (100), 232 (80).

Synthesis of (1*R*,2*S*)-2-[3-(4-adamantan-1-yl-phenyl)-propylamino]-1-phenylpropan-1-ol ruthenium dimer 29c

The precursor alcohol (0.450 g, 0.90 mmol), DCM (10 cm^3), 2 M solution of HCl in diethyl ether (15 cm^3, 30.00 mmol), ethanol (12.5 cm^3) and ruthenium trichloride trihydrate (0.157 g, 0.60 mmol) were reacted according to the general procedure above to give **29c** (0.149 g, 28%) as a dark green solid; ν_{max}/cm^{-1} (thin film) 3396 (OH), 1602 (NH$_2^+$), 746 and 701 (Ph); δ_H(300 MHz; DMSO-d$_6$) 0.92 (6 H, m, 2 × CH_3CHN), 1.60–2.05 (34 H, m, 2 × (CH_2CH$_2$N, 6 × adamantyl CH$_2$ and 3 × adamantyl CH)), 2.48–2.53 (4 H, m, 2 × CH_2CH$_2$CH$_2$N), 3.08–3.19 (4 H, m, 2 × NCH_2), 3.50 (2 H, m, 2 × CH$_3$CHN), 5.10 (2 H, m, 2 × PhCH), 5.81 (4 H, m, 2 × (2 × ArH on Ru-arene)), 6.05–6.18 (6 H, m, 2 × (2 × ArH on Ru-arene) and 2 × OH), 7.31–7.43 (10 H, m, 2 × Ph), 8.38–8.61 (4 H, m, 2 × NH$_2^+$); δ_C(125.8 MHz; DMSO-d$_6$) 9.9 (2 × q), 25.7 (2 × t), 28.5 (2 × (3 × d)), 29.7 (2 × t), 36.6 (2 × (3 × t)), 41.2 (2 × (3 × t)), 43.1 (2 × s), 44.8 (2 × t), 58.4 (2 × d), 70.0 (2 × d), 81.8 (2 × d), 84.6 (2 × d), 85.0 (2 × d), 85.5 (2 × d), 103.2 (2 × s), 109.7 (2 × s), 126.3 (2 × (2 × d)), 127.8 (2 × d), 128.6 (2 × (2 × d)), 141.4 (2 × s). Found (LSIMS): 540.1599 (monomeric species formed *in situ*), ^{102}RuC$_{28}$H$_{37}$NOCl requires 540.1607 (1.6 ppm error). *m/z* (LSIMS) 510 (monomer$^+$, 75%), 504 (M-HCl$^+$, 100).

Synthesis of (1*R*,2*S*)-2-(3-biphenyl-4-yl-propylamino)-1-phenylpropan-1-ol ruthenium dimer 29d

The precursor alcohol (0.600 g, 1.35 mmol), DCM (10 cm^3), 2 M solution of HCl in diethyl ether (2 cm^3, 4.00 mmol), ethanol (15 cm^3) and ruthenium trichloride trihydrate (0.186 g, 0.712 mmol) were reacted according to the general procedure above to give **29d** (0.180 g, 20%) as a dark green solid; ν_{max}/cm^{-1} (thin film) 3403 (OH), 1601 (NH$_2^+$), 764 and 699 (Ph); δ_H(400 MHz; DMSO-d$_6$) 0.95 (6 H, d, *J* 6.3, 2 × CH_3CHN), 1.31 (2 H, d, *J* 6.0, 2 × OH), 2.06–2.10 (4 H, m, 2 × CH_2CH$_2$N), 2.60–2.63 (4 H, m, 2 × CH_2CH$_2$CH$_2$N), 3.06–3.19 (4 H, m, 2 × NCH_2), 3.46 (2 H, m, 2 × CH$_3$CHN), 5.13 (2 H, m, 2 × PhCH), 5.99–6.02 (4 H, m, 2 × (2 × ArH on Ru-arene)), 6.15 (2 H, m, 2 × ArH on Ru-arene), 6.54 (2 H, d, *J* 5.8, 2 × ArH on Ru-arene), 7.36–7.84 (20 H, m, 2 × (2 × Ph)), 8.43–8.64 (4 H, m, 2 × NH$_2^+$); δ_C(100.5 MHz; DMSO-d$_6$) 9.1 (2 × q), 25.8 (2 × t), 29.8 (2 × t), 45.2 (2 × t), 58.4 (2 × d), 69.7 (2 × d), 84.8 (2 × (2 × d)),

85.3 (2 × (2 × d)), 96.6 (2 × s), 105.3 (2 × s), 124.8 (2 × (2 × d)), 127.5 (2 × d), 128.4 (2 × (2 × d)), 129.0 (2 × overlapping (2 × (2 × d))), 129.8 (2 × d), 141.1 (2 × s). Found (LSIMS): 482.0826 (monomeric species formed *in situ*), $^{102}RuC_{24}H_{27}NOCl$ requires 482.0825 (0.3 ppm error); *m*/*z* (LSIMS) 482 (monomer$^+$, 30%), 446 (M-HCl$^+$,15), 346 (100).

Acknowledgements

We thank the EPSRC for postdoctoral fellowship support (to DJM) and Warwick University for the award of a Warwick Postgraduate Research Fellowship (to AMH). We thank Dr B. Stein of the EPSRC National Mass Spectrometry Service Centre (Swansea) for HRMS analysis of certain compounds, Johnson-Matthey Ltd for loans of ruthenium salts and Arran chemical (Ireland) for generous donation of enantiopure diamines. We acknowledge the use of the EPSRC's Chemical Database Service at Daresbury.[11]

Notes and references

1 (*a*) M. Palmer and M. Wills, *Tetrahedron: Asymmetry*, 1999, **10**, 2045; (*b*) R. Noyori and S. Hashiguchi, *Acc. Chem. Res.*, 1997, **30**, 97; (*c*) S. E. Clapham, A. Hadzovic and R. H. Morris, *Coord. Chem. Rev.*, 2004, **248**, 2201; (*d*) S. Gladiali and E. Alberico, *Chem. Soc. Rev.*, 2006, **35**, 226; (*e*) T. Ikariya, K. Murata and R. Noyori, *Org. Biomol. Chem.*, 2006, **4**, 393.

2 (*a*) J. Takehara, S. Hashiguchi, A. Fujii, S.-I. Inoue, T. Ikariya and R. Noyori, *Chem. Commun.*, 1996, 233; (*b*) M. Palmer, T. Walsgrove and M. Wills, *J. Org. Chem.*, 1997, **62**, 5226; (*c*) D. A. Alonso, S. J. Nordin, P. Roth, T. Tarnai and P. G. Andersson, *J. Org. Chem.*, 2000, **65**, 3116; (*d*) K. Everaere, A. Mortreaux and J.-F. Carpentier, *Adv. Synth. Catal.*, 2003, **345**, 67; (*e*) S. J. M. Nordin, P. Roth, T. Tarnai, D. A. Alonso, P. Brandt and P. G. Andersson, *Chem.–Eur. J.*, 2001, **7**, 1431; (*f*) D. G. I. Petra, J. N. H. Reek, J.-F. Handgraaf, E.-J. Meijer, P. Dierkes, P. C. J. Kamer, J. Brussee, H. E. Schoemaker and P. W. N. M. van Leeuwen, *Chem.–Eur. J.*, 2000, **6**, 2818; (*g*) A. Hage, D. G. I. Petra, J. A. Field, D. Schipper, J. B. P. A. Wijnberg, P. C. J. Kamer, J. N. H. Reek, P. W. N. M. van Leeuwen, R. Wever and H. E. Schoemaker, *Tetrahedron: Asymmetry*, 2001, **12**, 1025; (*h*) M. Hennig, K. Püntener and M. Scalone, *Tetrahedron: Asymmetry*, 2000, **11**, 1849; (*i*) K. Everaere, A. Mortreux, M. Bulliard, J. Brussee, A. van der Gen, G. Nowogrocki and J. F. Carpentier, *Eur. J. Org. Chem.*, 2001, 275; (*j*) J. W. Faller and A. R. Lavoie, *Org. Lett.*, 2001, **3**, 3703; (*k*) J. W. Faller and A. R. Lavoie, *Organometallics*, 2002, **21**, 2010; (*l*) M. A. Evans and J. P. Morken, *J. Am. Chem. Soc.*, 2002, **124**, 9020; (*m*) K. B. Hansen, J. R. Chilenski, R. Desmond, P. N. Devine, E. J. J. Grabowski, R. Heid, M. Kubryk, D. J. Mathre and R. Varsolona, *Tetrahedron: Asymmetry*, 2003, **14**, 3581; (*n*) P. N. Liu, Y. C. Chen, X. Q. Li, Y. Q. Tu and J. G. Deng, *Tetrahedron: Asymmetry*, 2003, **14**, 2481; (*o*) I. Schiffers, T. Rantanen, F. Schmidt, W. Bergmans, L. Zani and C. Bolm, *J. Org. Chem.*, 2006, **71**, 2320; (*p*) R. V. Wisman, J. G. de Vries, B.-J. Deelman and H. J. Heeres, *Org. Process Res. Dev.*, 2006, **10**, 423; (*q*) J. Hannedouche, J. A. Kenny, T. Walsgrove and M. Wills, *Synlett*, 2002, 263; (*r*) S. Bastin, R. J. Eaves, C. W. Edwards, O. Ichihara, M. Whittaker and M. Wills, *J. Org. Chem.*, 2004, **69**, 5405.

3 (*a*) A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya and R. Noyori, *J. Am. Chem. Soc.*, 1996, **118**, 2521; (*b*) S. Hashiguchi, A. Fujii, J. Takehara, T. Ikariya and R. Noyori, *J. Am. Chem. Soc.*, 1995, **117**, 7562; (*c*) K. J. Haack, S. Hashiguchi, A. Fujii, T. Ikariya and R. Noyori, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 285; (*d*) K. Matsumura, S. Hashiguchi, T. Ikariya and R. Noyori, *J. Am. Chem. Soc.*, 1997, **119**, 8738; (*e*) K. Okano, K. Murata and T. Ikariya, *Tetrahedron Lett.*, 2000, **41**, 9277; (*f*) M. Watanabe, K. Murata and T. Ikariya, *J. Org. Chem.*, 2002, **67**, 1712; (*g*) M. Li and G. A. O'Doherty, *Tetrahedron Lett.*, 2004, **45**, 6407; (*h*) J. A. Marshall and K. Ellis, *Tetrahedron Lett.*, 2004, **45**, 1351; (*i*) H. Yamashita, T. Ohtani, S. Morita, K. Otsubo, K. Kan, J. Matsubara, K. Kitano, Y. Kawano, M. Uchida and F. Tabusa, *Heterocycles*, 2002, **56**, 123; (*j*) M. Miyagi, J. Takehara, S. Collet and K. Okano, *Org. Process Res. Dev.*, 2000, **4**, 346; (*k*) K. Tanaka, M. Katsurada, F. Ohno, Y. Shiga, M. Oda, M. Miyago, J. Takehara and K. Okano, *J. Org. Chem.*, 2000, **65**, 432; (*l*) Y. Yamano, Y. Watanabe, N. Watanabe and M. Ito, *J. Chem. Soc., Perkin Trans. 1*, 2002, 2833; (*m*) J. Cossrow and S. D. Rychnovsky, *Org. Lett.*, 2002, **4**, 147; (*n*) Y. Yamano, Y. Shimizu and M. Ito, *Chem. Pharm. Bull.*, 2003, **51**, 878; (*o*) J. Hannedouche, P. Peach, D. J. Cross, J. A. Kenny, I. Mann, I. Houson, L. Campbell, T. Walsgrove and M. Wills, *Tetrahedron*, 2006, **62**, 1864; (*p*) M. Mogi, K. Fuji and M. Node, *Tetrahedron: Asymmetry*, 2004, **15**, 3715; (*q*) K. Vandyck, B. Matthys and J. Van der Eycken, *Tetrahedron Lett.*, 2005, **46**, 75; (*r*) N. Bogliotti, P. I. Dalko and J. Cossy, *Tetrahedron Lett.*, 2005, **46**, 6915; (*s*) K. Maki, R. Motoki, K. Fujii, M. Kanai, T. Kobayashi, S. Tamura and M. Shibasaki, *J. Am. Chem. Soc.*, 2005, **127**, 17111; (*t*) A. Ros, A. Magriz, H. Dietrich, R. Fernández, E. Alvarez and J. M. Lassaletta, *Org. Lett.*, 2006, **8**, 127; (*u*) B. Mohar, A. Valleix, J.-R. Desmurs, M. Felemez, A. Wagnet and C. Mioskowski, *Chem. Commun.*, 2001, 2572; (*v*) I. C. Lennon and J. A. Ramsden, *Org. Process Res. Dev.*, 2005, **9**, 110; (*w*) A. Hayes, G. Clarkson and M. Wills, *Tetrahedron: Asymmetry*, 2004, **15**, 2079.

4 (*a*) D. A. Alonso, P. Brandt, S. J. M. Nordin and P. G. Andersson, *J. Am. Chem. Soc.*, 1999, **121**, 9580; (*b*) M. Yamakawa, H. Ito and R. Noyori, *J. Am. Chem. Soc.*, 2000, **122**, 1466; (*c*) R. Noyori, M. Yamakawa and S. Hashiguchi, *J. Org. Chem.*, 2001, **66**, 7931; (*d*) M. Yamakawa, I. Yamada and R. Noyori, *Angew. Chem., Int. Ed.*, 2001, **40**, 2818; (*e*) P. Brandt, P. Roth and P. G. Andersson, *J. Org. Chem.*, 2004, **69**, 4885.

5 (*a*) Y.-C. Chen, T.-F. Wu, L. Jiang, J.-G. Deng, H. Liu, J. Zhu and Y.-Z. Jiang, *J. Org. Chem.*, 2005, **70**, 1006; (*b*) W. Liu, X. Cui, L. Cun, J. Zhu and J. G. Deng, *Tetrahedron: Asymmetry*, 2005, **16**, 2525; (*c*) S. B. Wendicke, E. Burri, R. Scopelliti and K. Severin, *Organometallics*, 2003, **22**, 1894; (*d*) P.-N. Liu, P.-M. Gu, J. G. Deng, Y.-Q. Tu and Y.-P. Ma, *Eur. J. Org. Chem.*, 2005, **70**, 3221; (*e*) X. Li, W. Chen, W. Hems, F. King and J. Xiao, *Tetrahedron Lett.*, 2004, **45**, 951; (*f*) Y. Arakawa, N. Haraguchi and S. Itsuno, *Tetrahedron Lett.*, 2006, **47**, 3239; (*g*) K. Severin and K. Polborn, *Chem.–Eur. J.*, 2000, **6**, 4604; (*h*) Y. Li, Z. Li, F. Li, Q. Wang and F. Tao, *Org. Biomol. Chem.*, 2005, **3**, 2513; (*i*) X. Wu, X. Li, F. King and J. Xiao, *Angew. Chem., Int. Ed.*, 2005, **44**, 3407; (*j*) P. N. Liu, J. G. Deng, Y. Q. Tu and S. H. Wang, *Chem. Commun.*, 2004, 2070; (*k*) X. Wu, D. Vinci, T. Ikariya and J. Xiao, *Chem. Commun.*, 2005, 4447; (*l*) T. Thorpe, J. Blacker, S. M. Brown, C. Bubert, J. Crosby, S. Fitzjohn, J. P. Muxworthy and J. M. J. Williams, *Tetrahedron Lett.*, 2001, **42**, 4041; (*m*) J. Mao, B. Wan, F. Wu and S. Lu, *Tetrahedron Lett.*, 2005, **46**, 7341; (*n*) J. Canivet, G. Labat, H. Stoeckli-Evans and G. Suss-Fink, *Eur. J. Inorg. Chem.*, 2005, 4493; (*o*) X. Wu, X. Li, M. McConville, O. Saidi and J. Xiao, *J. Mol. Catal. A: Chem.*, 2006, **247**, 153; (*p*) X. Li, J. Blacker, I. Houson, X. Wu and J. Xiao, *Synlett*, 2006, 1155.

6 (*a*) R. Guo, C. Elphelt, X. Chen, D. Song and R. H. Morris, *Chem. Commun.*, 2005, 3050; (*b*) M. T. Reetz and X. Li, *J. Am. Chem. Soc.*, 2006, **128**, 1044; (*c*) P. Vastilla, J. Wettergren and H. Adolfsson, *Chem. Commun.*, 2005, 4039; (*d*) W. Baratta, G. Chelucci, S. Gladiali, K. Siega, M. Toniutti, M. Zanette, E. Zangrando and P. Rigo, *Angew. Chem., Int. Ed.*, 2005, **44**, 6214; (*e*) Y.-Y. Li, H. Zhang, J.-S. Chen, X.-L. Liao, Z.-R. Dong and J.-X. Gao, *J. Mol. Catal. A: Chem.*, 2004, **218**, 153.

7 (*a*) K. Mashima, T. Abe and K. Tani, *Chem. Lett.*, 1998, 1199; (*b*) K. Murata, T. Ikariya and R. Noyori, *J. Org. Chem.*, 1999, **64**, 2186; (*c*) K. Mashima, T. Abe and K. Tani, *Chem. Lett.*, 1998, 1201; (*d*) D. J. Cross, J. A. Kenny, I. Houson, L. Campbell, T. Walsgrove and M. Wills, *Tetrahedron: Asymmetry*, 2001, **12**, 1801; (*e*) T. Hamada, T. Torii, K. Izawa, R. Noyori and T. Ikariya, *Org. Lett.*, 2002, **4**, 4373; (*f*) T. Hamada, T. Torii, K. Izawa and T. Ikariya, *Tetrahedron*, 2004, **60**, 7411; (*g*) T. Hamada, T. Torii, T. Onishi, K. Izawa and T. Ikariya, *J. Org. Chem.*, 2004, **69**, 7391; (*h*) D. S. Matharu, D. J. Morris, A. M. Kawamoto, G. J. Clarkson and M. Wills, *Org. Lett.*, 2005, **7**, 5489.

8 (*a*) A. M. Hayes, D. J. Morris, G. J. Clarkson and M. Wills, *J. Am. Chem. Soc.*, 2005, **127**, 7318; (*b*) J. Hannedouche, G. J. Clarkson and M. Wills, *J. Am. Chem. Soc.*, 2004, **126**, 986; (*c*) F. K. Cheung, A. M. Hayes, J. Hannedouche, A. S. Y. Yim and M. Wills, *J. Org. Chem.*, 2005, **70**, 3188; (*d*) D. J. Morris, A. M. Hayes and M. Wills, *J. Org. Chem.*, 2006, **71**, 7035–7044.

9 (*a*) G. Hilt and F.-X. du Mesnil, *Tetrahedron Lett.*, 2000, **41**, 6757; (*b*) G. Hilt and S. Lüers, *Synthesis*, 2002, **5**, 609.

10 S.-J. Paik, S. U. Son and Y. K. Chung, *Org. Lett.*, 1999, **1**, 2045.

11 D. A. Fletcher, R. F. McMeeking and D. Parkin, *J. Chem. Inf. Comput. Sci.*, 1996, **36**, 746.