Highly Active Chiral Ruthenium Catalysts for Asymmetric Ring-Closing Olefin Metathesis

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Abstract: The synthesis of olefin metathesis catalysts containing chiral, monodentate *N*-heterocyclic carbenes and their application to asymmetric ring-closing metathesis (ARCM) are reported. These catalysts retain the high levels of reactivity found in the related achiral variants (**1a** and **1b**). Using the parent chiral catalysts **2a** and **2b** and derivatives that contain steric bulk in the meta positions of the *N*-bound aryl rings (catalysts **3**–**5**), five- through seven-membered rings were formed in up to 92% ee. The addition of sodium iodide to catalysts **2a**–**4a** (to form **2b**–**4b** in situ) caused a dramatic increase in enantioselectivity for many substrates. Catalyst **5a**, which gave high enantiomeric excesses for certain substrates without the addition of NaI, could be used in loadings of ≤1 mol %. Mechanistic explanations for the large sodium iodide effect as well as possible mechanistic pathways leading to the observed products are discussed.
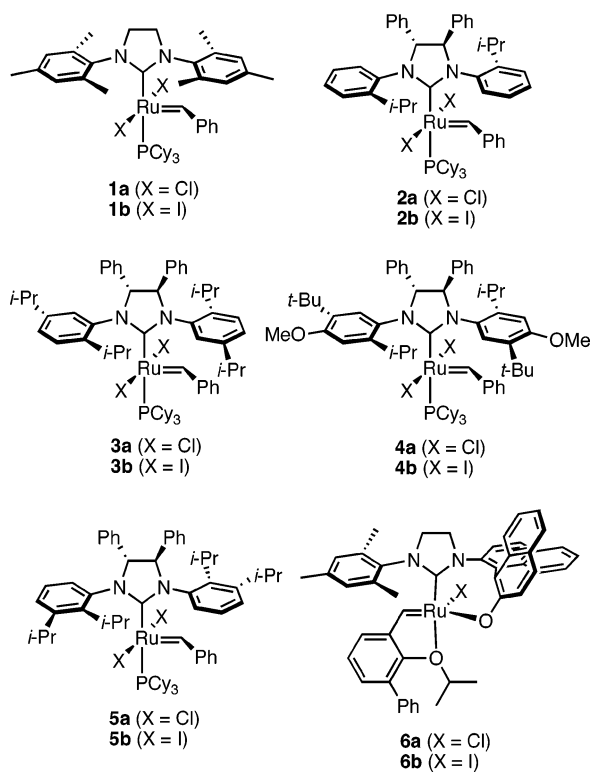
Introduction

The development of well-defined catalysts has made olefin metathesis an important, reliable, and widespread method for constructing carbon–carbon double bonds.[1] Since the initial report of asymmetric olefin metathesis for small molecule synthesis,[2] a variety of chiral, ruthenium- and molybdenum-based alkylidene catalysts have been developed.[3,4] The molybdenum catalysts have been shown to give excellent enantioselectivities in asymmetric ring-closing metathesis (ARCM), asymmetric ring-opening/ring-closing metathesis (ARORCM), and asymmetric ring-opening/cross metathesis (AROCM).[5,6] Our interest in ruthenium-based olefin metathesis catalysts stems from their increased functional group tolerance compared to the molybdenum systems, as well as their stability to air and moisture.[6b] Two classes of chiral ruthenium catalysts have been explored (Chart 1): those containing monodentate *N*-heterocyclic carbenes (NHCs) with chirality in the backbone of the carbene (**2a** and **2b**) developed in our laboratory[3c] and those containing chiral, bidentate NHC/binaphthyl ligands (**6a** and **6b**) developed by Hoveyda et al.[3a,b] While catalysts of the latter type gave good enantioselectivities and yields for AROCM reactions,[7] they exhibited reduced reactivity and selectivity toward ARCM relative to those of the former class.

The ruthenium catalysts containing monodentate, chiral NHCs (**2a** and **2b**) had the same air and moisture stability of the parent catalyst **1a**, as well as a similar level of reactivity.[8] Additionally, we achieved a single example of 90% ee using **2b**.[3c] On the basis of this initial discovery, and because ARCM remains challenging for **6a** and **6b**, we decided to modify **2a** and **2b** to enhance enantioselectivity and expand the substrate scope of ARCM. The synthesis of new chiral ruthenium catalysts for asymmetric olefin metathesis, as well as their reactivity and selectivity in expanding the scope of ARCM, is reported herein. Catalysts containing substitution on the aryl ring para to the *o*-isopropyl group (**3a**, **3b**, **4a**, and **4b**) showed enantioselec-

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(7) (a) Gillingham, D. G.; Kataoka, O.; Garber, S. B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 12288–12290. Also see: ref 7.

(8) Scholl, M.; Ding, S.; Less, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956.

Chart 1. Ruthenium Olefin Metathesis Catalysts

1a (X = Cl)
1b (X = I)

2a (X = Cl)
2b (X = I)

3a (X = Cl)
3b (X = I)

4a (X = Cl)
4b (X = I)

5a (X = Cl)
5b (X = I)

6a (X = Cl)
6b (X = I)

Table 1. Relative Reactivity and Selectivity of Asymmetric Ruthenium Catalysts

catalyst	11 to 12[a]		13 to 14[a]	
	ee[b] (%)	conv[c] (%)	ee[b] (%)	conv[c] (%)
2a	35	>98	83	>98
3a	31	>98	81	>98
4a	30	>98	75	>98
5a	46	>98	92	>98
2b	90	>98	86	68
3b	84	>98	90	>98
4b	87	>98	85	>98
5b	90	>98	92	58

[a] Reactions with **2a**−**5a** (2 mol %) run in CH$_2$Cl$_2$; catalysts **2b**−**5b** generated by stirring **2a**-**5a** (4 mol %) in THF with 25 equiv of NaI. [b] Enantiomeric excesses determined by chiral GC; see Supporting Information for chromatograms and proof of absolute stereochemistry. [c] Determined by ^{1}H NMR spectrum of crude reaction mixture.

tivities very similar to those of the parent chiral catalysts **2a** and **2b**. However, substitution on the same side of the ring as the *o*-isopropyl group (**5a** and **5b**) caused an increase in enantioselectivity to the extent that, in a number of substrates, the dichloride catalyst **5a** could be used at very low catalyst loadings to obtain high enantiomeric excesses and conversions.

Results and Discussion

Design and Synthesis of Chiral Ruthenium Catalysts. In our initial study we discovered that NHCs derived from enantioenriched 1,2-diamines could transfer the chirality of the backbone to the ortho-substituted *N*-aryl rings.[3c] This "gearing" effect, which results in the ortho-subtituent of the unsymmetrically substituted arene rings to reside on the face opposite to the phenyl groups on the backbone, has been shown to induce asymmetry in the ring-closing metathesis of prochiral trienes. Using the ring-closing metathesis of **11** to form **12** as a test reaction, we varied the backbone of the NHC as well as the substituent in the ortho-position of the *N*-aryl rings and discovered that **2b** was the most successful catalyst, forming dihydrofuran **12** in 90% ee. On the basis of the success of varying the ortho-substitution, we explored catalysts containing substitution in the meta-position of the *N*-bound aryl rings.

The synthesis of the chiral dihydroimidazolium salts (**9a**−**9d**) was straightforward and modular (Scheme 1). Pd$_2$(dba)$_3$/BINAP was used to couple the substituted aryl bromides (**7a**−**d**) to commercially available (1*R*,2*R*)-diphenylethylenediamine.[9,10] Compound **7b** was used as a mixture of aryl bromides; thus, the diamine coupling reaction was followed by a Pd-catalyzed reduction to yield **8b**. The *p*-methoxy group in aryl bromide **7c**

was present as a synthetic handle and was not expected to affect enantioselectivities due to its remote location relative to the Ru center. The chiral diamines were reacted with triethylorthoformate to form dihydroimidazolium BF$_4^-$ salts **9a**−**d** in good yields over two or three steps. Ligand substitution with bisphosphine compound **10** gave the desired chiral ruthenium benzylidenes as brown solids.[11] All of these ruthenium compounds were purified using silica gel chromatography with nondegassed solvents, and they were stored in air without significant decomposition over a period of at least 3 months. Conversions for the ligand substitution step were generally 90%, but challenging chromatographic separations gave varied isolated yields. The analogous catalysts with two iodides bound to the ruthenium (**2b**−**5b**) were generated in situ by dissolving the dichloride catalyst in THF in the presence of 25 equiv of NaI.

Enantioselectivities and Reactivities of Chiral Ru Catalysts for ARCM. In our previous study we discovered that substrate **11**, derived from (2*E*,5*E*)-3,5-dimethylhepta-2,5-dien-4-ol, gave the highest enantioselectivities and good conversions, so this substrate and a silyl ether analogue (**13**) were used to examine the reactivities and enantioselectivities of the new catalysts. The presence of trisubstituted alkenes was critical to obtaining high enantiomeric excess using catalyst **2b** with triene **11**. As can be seen in Table 1, catalysts **2a**−**4a** gave relatively similar enantioselectivities and conversions for substrate **11**. In all of these cases, the diiodide catalysts (**2b**−**4b**) caused dramatic increases in the enantioselectivity of the reaction (i.e. 35% ee with **2a**, 90% ee with **2b**). There is no simple pattern for selectivity based on the steric bulk in the meta-position for

(9) Wolfe, J. P.; Buchwald. S. L. *J. Org. Chem.* **2000**, *65*, 1144−1157.

(10) Both enantiomers of 1,2-diphenylethylenediamine are commercially available. See Supporting Information for the synthesis of the aryl bromides **7b**−**d** and other experimental details.

(11) Although we have been unable to obtain X-ray quality crystals of **2a**−**5b**, the carbene derived from chiral salt **9d** has been bound to [Rh(COD)Cl]$_2$, and an X-ray crystal structure of this complex shows that the isopropyl groups are oriented anti to the phenyl rings on the NHC backbone. See Supporting Information.

Scheme 1. Synthesis of Chiral Ruthenium Olefin Metathesis Catalysts
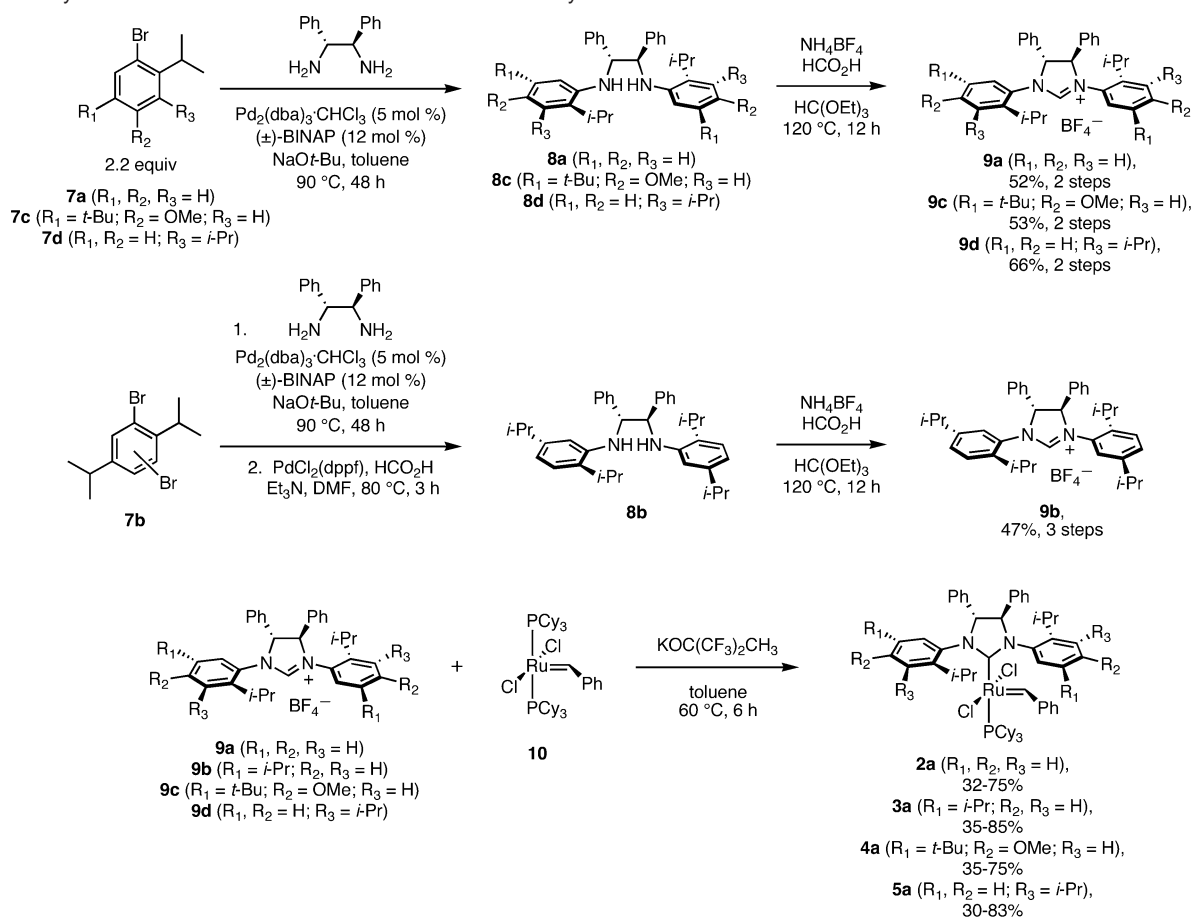
catalysts **2**−**4**: increasing the size of the meta group from H to *tert*-butyl caused a sequential decrease in the enantiomeric excess (**2a**−**4a**); but when NaI was added (**2b**−**4b**), it decreased for *m*-isopropyl but increased again when the larger *tert*-butyl group was in the meta-position. The largest difference in selectivity was seen when catalyst **5a** was used. An increase of 11% ee was observed relative to **2a**, and **5b** gave 90% ee just as **2b**. High conversions were obtained with all of the catalysts in 2 h at 40 °C.
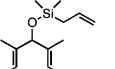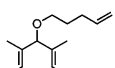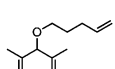
When **13** was reacted with these catalysts, higher enantio-selectivities were obtained without the need for NaI. As with substrate **11**, selectivity decreased as steric bulk in the meta-position increased (catalysts **2a**−**4a**). When the diiodide catalysts **2b**−**4b** were used, enantioselectivities increased for all of the reactions relative to those obtained using **2a**−**4a**. Introducing meta-substitut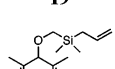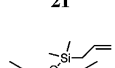ion adjacent to the *o*-isopropyl group (catalyst **5a**) resulted in a 92% ee for the ring closing of **13** without the need for NaI. This result was the highest enantiomeric excess for ring-closing metathesis we had observed. Moreover, since the dichloride catalysts are generally more reactive than the corresponding diiodide catalysts, complete conversion could be achieved with lower catalyst loadings of **5a**! Conversions with catalysts **2b** and **5b** decreased relative to the reactions with the dichloride catalysts when substitution was on just one side of the *N*-bound aryl rings. On the other hand, conversions remained high for catalysts **3b** and **4b**, which possess substitution on both sides of the aryl rings. This increase in conversion may be due to the substituent in the meta-position increasing the steric bulk

of the catalyst and therefore protecting it from various bi-molecular decomposition pathways.[12]

Expanded Substrate Scope for ARCM. The ability of the chiral ruthenium catalysts **2**−**5** to give high conversions and enantioselectivities for the ARCM reactions of **11** and **13** encouraged us to examine other substrates which afford five- to eight-membered rings upon ARCM. On the basis of the results from our initial screen, catalysts **2b** and **5a** were used. Two types of prochiral trienes were explored: alkenyl ethers and alkenyl silyl ethers (Table 2). Conversions >90 and 90% ees were obtained when generating five- and six-membered rings **12** and **16**. The isolated yields were moderately reduced due to the volatility of the products during the purification procedure. The synthesis of a seven-membered ring from **17** occurred in 85% ee when **2b** was used. Unfortunately the formation of the desired product was only ∼5%, with the major species being unreacted starting material and homocoupled product. The yield for the same reaction could be drastically increased when catalyst **5a** was used,[13] and because **5a** is more selective than the other catalysts in the absence of NaI (65% ee for **18** using **2a**), the desired product could be obtained in 92% yield and 76% ee. Synthesis of an eight-membered ring was more challenging, and **2b** catalyzed the ARCM reaction of **19** to **20** in 85% ee, but with only a ∼2% yield. Attempts to increase the yield using **5a** resulted in a similar yield and a reduced enantiomeric excess. This result was not surprising, as generating

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Table 2. ARCM Reactions with Chiral Ruthenium Catalysts[a]

triene	product	catalyst (mol %)	ee (%)[b]	conversion (%)[c]	yield (%)
11	**12**	**2b** (4)	90	>98	64
13	**14**	**5a** (0.8)	92	>98	77[f]
15	**16**	**2b** (4)	90	>98	77
17	**18**	**2b** (4)	85	5	nd
		5a (2)[d]	76	93	92
19	**20**	**2b** (4)	85	~2[e]	nd
21	**22**	**5a** (1)	92	65	64
23	**24**	**2b** (4)	78	>98	98

[a] Conditions for reactions with **2b**: NaI (25 equiv relative to catalyst) and **2a** in THF (0.055 M in triene) for 1 h at room temperature, then add triene, and stir for 2 h at 40 °C. Conditions for reactions with **5a**: triene, CH₂Cl₂ (0.055 M in triene), and **5a** for 2 h at 40 °C. [b] Enantiomeric excesses determined by chiral GC; see Supporting Information for chromatograms and proof of absolute stereochemistry. [c] Determined by ¹H NMR spectrum of crude reaction mixture. [d] See footnote 13. [e] Never isolated as a pure compound. [f] Reaction done on a 4 mmol (0.95 g) of **13** scale. nd = not determined.

eight-membered rings via ring-closing olefin metathesis is a challenging problem.

Silyl ethers proved to be excellent substrates, as both six- and seven-membered rings (**14** and **22**) formed in good conversions and 92% ee with **5a**. Catalyst loadings of 1 mol % or less could be used in these reactions. The ring-closing of **13** illustrated that the high yield and enantiomeric excess were maintained when the reaction was scaled up to almost 1 g of substrate. Using the analogous diiodide catalyst **5b** for ARCM of **13** and **21** resulted in six- and seven-membered rings with the same enantiomeric excesses but lower conversions than with the dichloride catalyst **5a**. Substrate **23**, which placed the prochiral center further from the trisubstituted olefins, also underwent ARCM to form a seven-membered ring in good enantiomeric excess and excellent yield with a substitution pattern different from that of **22**.

Table 2 provides the best results between catalysts **2b** and **5a**. In most reactions (ARCM of **11**, **13**, **15**, **21**, and **23**), the yields and enantioselectivities are very similar whether catalyst **2b**, **5a**, or **5b** is used. Because both **2b** and **5a** promote the ARCM of five- to seven-membered rings, there is no need for specific catalyst/substrate matching.

Trienes other than those discussed above were also examined in the ARCM reactions (Table 3). Substrates analogous to **13** and **23**, but lacking a terminal methyl group on the olefin (**25** and **27**), formed cyclic products **26** and **28** in reduced enantio-selectivities and conversions. When the diiodide catalysts were used, conversions were <20%. The lower conversions using **25** and **27** relative to **11** and **23** may be due to the formation of a ruthenium methylidene versus a ruthenium ethylidene, respectively. Ruthenium methylidenes are known to decompose more rapidly than other ruthenium alkylidenes, and in these cases decomposition may have occurred more quickly than the cross-metathesis that introduces the ring-closing substrate to the catalyst.[14]

A number of variables other than catalyst and substrate in the ARCM reactions were examined. Using a variety of solvents typical for olefin metathesis, such as CH₂Cl₂, tetrahydrofuran
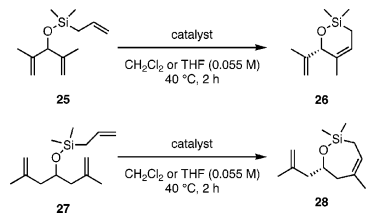
(13) A 1 mol % amount of **5a** is added at the beginning of the reaction, and then another 1 mol % is added after 2 h, and the seven-membered ring **18** is isolated in 92% yield with a 76% ee. When 2 mol % catalyst **5a** is used at the beginning of the reaction, a 74% yield is obtained. Presumably all of the starting material is homocoupled first, and then a second metathesis reaction forms the ruthenium alkylidene that leads to product. The homocoupling reaction forms a ruthenium methylidene, which may decompose at roughly the same rate as it performs the desired olefin metathesis reaction. Adding fresh catalyst allows most of the remaining unreacted starting material and homocoupled product to proceed to the desired seven-membered ring.

(14) (a) Ulman, M.; Grubbs, R. H. *J. Org. Chem.* **1999**, *64*, 7202−7207. (b) Sanford, M. S.; Love, J. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 6543−6554. (c) Reference 12.

Table 3. Challenging ARCM Substrates

	25 to 26[a]		27 to 28[a]	
catalyst	ee[b] (%)	conv[c] (%)	ee[b] (%)	conv[c] (%)
2a	16	72	-5	>98
3a	45	92	-5	>98
5a	30	93	-8	>98
2b	nd	<2	3	15
3b	nd	6	15	18

[a] Reactions with **2a**–**5a** (2 mol %) run in CH$_2$Cl$_2$; catalysts **2b** and **3b** generated by stirring **2a** and **3a** (4 mol %) in THF with 25 equiv of NaI. [b] Enantiomeric excesses determined by chiral GC; see Supporting Information for chromatograms and proof of absolute stereochemistry. [c] Determined by ^{1}H NMR spectrum of crude reaction mixture. nd = not determined.

CH$_2$Cl$_2$	**92% ee**, >98% conv
benzene	**88% ee**, >98% conv
THF	**92% ee**, >98% conv
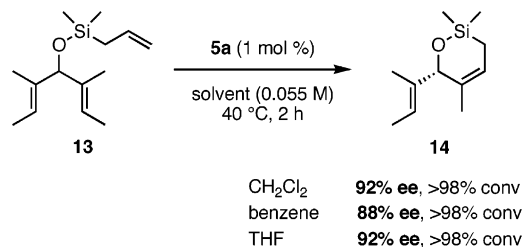
Figure 1. Solvent effect on enantioselectivity of ARCM.

2a	**88% ee**, 39% conv (83% ee at 40 °C)
2b	**90% ee**, 40% conv (86% ee at 40 °C)
3b	**88% ee**, 29% conv (90% ee at 40 °C)
5a	**87% ee**, 25% conv (92% ee at 40 °C)
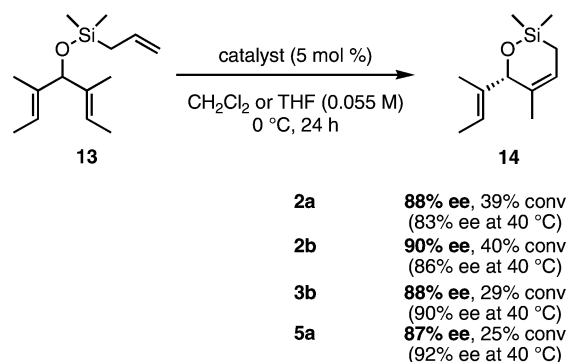
Figure 2. Temperature effect on enantioselectivity of ARCM.

(THF), and benzene, had very little affect on the conversions and enantiomeric excesses (Figure 1). The slight reduction in selectivity for ARCM reactions in benzene suggests that solvent coordination to the catalyst is not involved as in the molybdenum systems.[15] Lowering the temperature of the reactions to 0 °C led to a small increase (4−5%) in enantiomeric excesses when **2a** and **2b** were used, but catalysts **3b** and **5a** formed the product with slightly reduced (2−3%) enantioselectivities (Figure 2). In all cases, the conversions were reduced to no greater than 40% even when 5 mol % of the catalyst was used and the reaction was allowed to proceed for 24 h. The reactions which used I⁻ to form the diiodide catalysts had the best enantiose-lectivities when NaI in THF was used; NaI in CH$_2$Cl$_2$ and [Bu$_4$N]I in either THF or CH$_2$Cl$_2$ resulted in reduced enantio-

(15) Teng, X.; Cefalo, D. R.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 10779−10784.
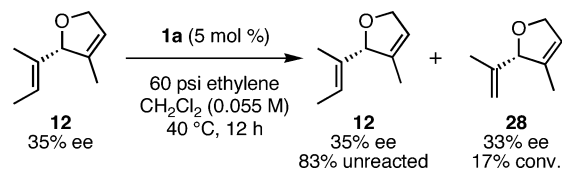
Figure 3. Ethenolysis of **12**.

meric excesses and reduced yields. No difference in enantio-selectivity or conversion was observed when dry NaI was used in place of ACS-grade NaI stored on the benchtop. This fact is a testament to the moisture stability of these ruthenium-based catalysts.

Mechanistic Considerations in Model Determination. To rationally design more reactive and selective chiral ruthenium catalysts for olefin metathesis, we must first develop a model which explains the enantioselectivity in these reactions. If the ARCM reaction has a degree of reversibility, a decrease in enantiomeric excesses over time would be expected. Although this was not observed, further experiments were performed to support the irreversibility of this reaction. When enantioenriched **14** was exposed to achiral catalyst **1a**, no erosion of the enantiomeric excess was observed, which suggests that once the ring is formed, it does not undergo a secondary ring-opening/ring-closing process. The same conclusion was drawn when enantioenriched **12** was heated under 60 psi of ethylene in the presence of **1a** (Figure 3). Under these forcing conditions, the enantiomeric excess of unreacted **12** did not erode, and the ethenolysis product **28** also retained the stereochemistry from the ARCM reaction.[16]

In the ARCM reactions of the trienes described above, most likely a ruthenium alkylidene derived from the least-substituted olefin initially forms. This species binds one of the diastereotopic olefins and, through a metallacyclobutane intermediate/transition state, forms the ring-closed product. Our initial model[3c] assumed olefin coordination occurred cis to the NHC (Scheme 2, lower pathway), on the face opposite the isopropyl group (structure **30**), and that interaction determined the absolute stereochemistry of the product. The interaction of a halide ligand with a substituent on the ring of the cyclic intermediate was also proposed to be an important, stereodefining interaction.[17] The actual position of the coordinating olefin relative to the NHC is unclear; experimental evidence exists to support olefin binding both cis and trans to the NHC (Scheme 2).[18] In the most recent report on this issue,[18c] Piers and co-workers provide compelling evidence for the observation of a 14-electron ruthenacyclobutane trans to the NHC. Computational studies support olefin binding trans to the NHC,[19] and a recent computational study of **2b** reacting with **11** calculated that the diastereotopic olefin coordinated trans to the NHC (Scheme 2, upper pathway).[19a]
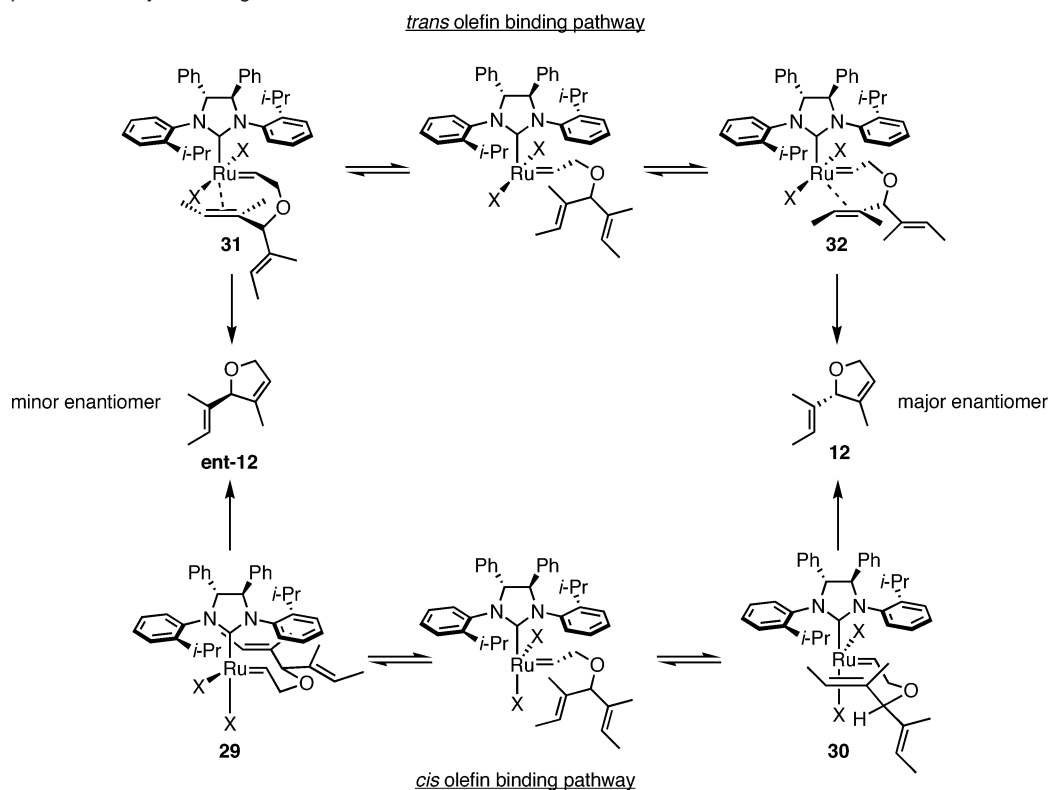
(16) See Supporting Information for more details.
(17) Allowing the hydrogen instead of the nonmetal bound vinyl group to interact with the iodide also puts the vinyl group in the pseudoequatorial position of the ring (see **30**).
(18) Evidence for cis-coordination: (a) Trnka, T. M.; Day, M. W.; Grubbs, R. H. *Organometallics* **2001**, *20*, 3845−3847. Evidence for trans-coordination: (b) Tallarico, J. A.; Bonitatebus, P. J., Jr.; Snapper, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 7157−7158. (c) Romero, P. E.; Piers, W. E. *J. Am. Chem. Soc.* **2005**, *127*, 5032−5033.
(19) (a) Costabile, C.; Cavallo, L. *J. Am. Chem. Soc.* **2004**, *126*, 9592−9600. (b) Adlhart, C.; Chen, P. *J. Am. Chem. Soc.* **2004**, *126*, 3496−3510. (c) Fomine, S.; Vargas, S. M.; Tlenkopatchev, M. A. *Organometallics* **2003**, *22*, 93−99. (d) Cavallo, L. *J. Am. Chem. Soc.* **2002**, *124*, 8965−8973. (e) Vyboishchikov, S. F.; Bühl, M.; Thiel, W. *Chem. Eur. J.* **2002**, *8*, 3962−3975.

Scheme 2. Proposed Pathways Leading to the Desired Product

trans olefin binding pathway

minor enantiomer

ent-12

major enantiomer

12

cis olefin binding pathway

Due to the tilt of the ortho-substituted *N*-bound aryl ring,[20] the alkylidene is positioned underneath the isopropyl group (structure **32**), which was found to be the "smaller" side of the aryl ring (Figure 4), instead of underneath the ortho C−H bond (structure **31**). In addition to the position of the alkylidene determining the absolute stereochemistry of the product, the cyclic intermediate formed upon olefin binding is also important. The pendent olefin not involved in the ring-closing reaction prefers to be in the pseudoequatorial position of the forming ring. Although the discussion presented here focuses on a substrate that forms a five-membered ring, substrates that form other ring sizes presumably have an energetically favored ring conformation once olefin binding occurs. Therefore the topics mentioned above can be extended to other ring-closing substrates. The importance of the position of the substituents on the ring in the cyclic transition state could explain the higher enantioselectivities observed for the substrates containing dimethylsilyl groups: there are more non-hydrogen substituents on the ring, and therefore the energy differences for various ring conformations are greater than those for substrates with only methylenes in the ring.

Our initial cis-binding hypothesis was supported by the fact that when a larger halide ligand was present, the enantiomeric

excess of the product increased. With recent experimental and computational studies providing evidence for olefin binding trans to the NHC, we sought to relate our experimental data to the suggested trans-binding mechanism. If olefin binding occurs trans to the NHC, exchanging the chloride ligands for iodides should not have a major steric impact on the transition state.[21] Instead, the iodide ligands may have an electronic effect. When the chlorides in **1a** were exchanged for iodides (**1b**), phosphine dissociation occurred more rapidly, but the reactivity of the active species did not increase.[14b] In the case of the chiral catalysts **2b**−**4b**, a lower reactivity could increase the enantioselectivity by causing the reaction to proceed through a late, more product-like transition state.[22] The added steric bulk in **5a** may hamper its reactivity enough to mimic the electronic deactivation present in the diiodide catalysts **2b**−**4b**, resulting in a late transition state and higher degree of stereochemical communication between the catalyst and the substrate. Substrates **25** and **27**, which have alkenes with less steric hindrance compared to substrates **13** and **23**, may form products in lower enantiomeric excess due to a higher reactivity with the catalyst. Although recent studies suggest olefin binding occurs trans to the NHC, and the observed absolute stereochemistry can be justified using a proposed model based on trans binding, the

trans olefin binding   alkylidene under *i*-Pr group
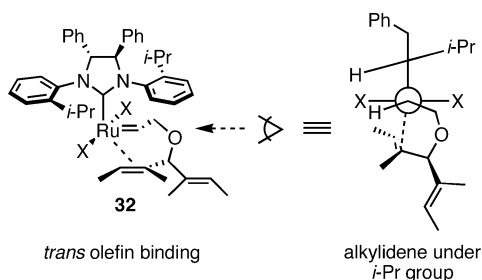
Figure 4. Suggested alkylidene position in trans-binding transition state.

(20) The X-ray crystal structure of an analogue of **2a** in ref 3c shows that the plane of the *N*-bound aryl ring is not orthogonal to the plane of the NHC. QM/MM calculations in ref 19a concluded that the *N*-bound aryl rings of a substrate-bound ruthenium alkylidene also are not orthogonal to the plane of the NHC.
(21) Computations suggest that as the halide ligand increases in size (van der Waals radii) from Cl⁻ to I⁻, the X−Ru−X bond angle also increases. A larger bond angle positions the halides closer to the Ru═CHR moiety (a smaller angle means the halides are pulled away from the alkylidene), which puts the halides in closer proximity to the reacting olefin, creating a smaller pocket, and therefore a more selective reaction. See ref 19a.
(22) Palucki, M.; Finney, N. S.; Pospisil, P. J.; Güler, M. L.; Ishida, T.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 948−954.

experimental data do not provide enough support to rule out a cis-binding mechanism.

Conclusions

We have synthesized novel asymmetric olefin metathesis catalysts, which contain chiral, monodentate NHC ligands and have shown their use in asymmetric ring-closing metathesis of prochiral trienes containing trisubstituted alkenes. Adding substitution to the position para to the *o*-isopropyl group of the *N*-bound aryl rings (**3a** and **4a**) of the parent compound **2a** had a relatively small effect on the enantioselectivities of the ARCM reactions. By exchanging the chloride ligands for iodides, an increase in enantioselectivity was observed for catalysts **2b**–**4b** relative to **2a**–**4a**. In the case of catalyst **5a**, substitution on the same side of the aryl ring results in enantiomeric excesses in up to 92% and very high conversions with low catalyst loadings (less than 1 mol %). Two proposed models for the formation of the observed products have been discussed: if the incoming olefin binds cis to the NHC, the stereodefining interaction is the face of the ruthenium to which the olefin binds; if the incoming olefin binds trans to the NHC, the stereodefining interaction is the position of the alkylidene under the *N*-bound aryl ring. In both cases, the position of the pendent olefin in the forming ring also plays an important role in the transition state.

The general interest in developing ruthenium olefin metathesis catalysts stems from their ease of handling and their different functional group tolerance relative to that of the molybdenum catalysts. Catalysts **2a**–**5b**, much like the achiral analogues, are also stable to air and moisture, making them simple to use. The synthesis of enantioenriched five- to seven-membered rings has been illustrated, and although further development is needed to expand the substrate scope of ruthenium-catalyzed ARCM, catalysts containing chiral, monodentate NHC ligands are promising due to their high activity, low catalyst loadings, and ease of handling.

Supporting Information Available: Experimental procedures and spectral data for catalysts, substrates, and products (pdf). This material is available free of charge via the Internet at http://pubs.acs.org.

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