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Enantioselective Intramolecular Cyclopropanations of Allylic and Homoallylic Diazoacetates and Diazoacetamides Using Chiral Dirhodium(II) Carboxamide Catalysts

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Abstract: Diazo decomposition of allylic and homoallylic diazoacetates **10a–p** and **22a–j** catalyzed by chiral dirhodium(II) tetrakis[methyl 2-pyrrolidone-5(*S*)-carboxylate], Rh_2(5*S*-MEPY)$_4$ (**7**), and its enantiomer, Rh_2(5*R*-MEPY)$_4$ (**8**), produces the corresponding intramolecular cyclopropanation products **11a–p** and **23a–j** in good to excellent yields and with exceptional enantioselectivity. Higher enantiocontrol is observed with allylic diazoacetates than with their homoallylic counterparts, but allylic diazoacetates are subject to greater variations in enantioselectivities with changes in substitution patterns on the carbon–carbon double bond. For example, the enantioselectivities in the intramolecular cyclopropanations of 3-alkyl/aryl-2(*Z*)-alken-1-yl diazoacetates are generally ≥94%, whereas the cyclizations of the homologous 4-alkyl/aryl-3(*Z*)-alken-1-yl diazoacetates are typically in the range of 70–90% ee. The corresponding 3-alkyl/aryl-2(*E*)-alken-1-yl and 4-alkyl/aryl-3(*E*)-alken-1-yl diazoacetates undergo cyclization with slightly lower ee's (54–85%). Although the Rh_2(5*S*-MEPY)$_4$-catalyzed cyclization of the 2-methallyl diazoacetate **10c** proceeds with only 7% ee, alternative chiral dirhodium(II) catalysts, including those with methyl *N*-acylimidazolidin-2-one-4(*S*)-carboxylate ligands such as Rh_2(4*S*-MACIM)$_4$ (**14**) and Rh_2(4*S*-MPAIM)$_4$ (**15**), may be employed to increase the level of enantiocontrol to 78 and 65%, respectively. Some allylic diazoacetamides also undergo highly enantioselective cyclization to form cyclopropyl lactams as illustrated by the diazo decomposition of *N*-allyl diazoacetamide (**19**) in the presence of dirhodium(II) tetrakis[methyl 2-oxazolidinone-4(*S*)-carboxylate], Rh_2(4*S*-MEOX)$_4$, to give the 3-azabicyclo[3.1.0]hexan-2-one **20** in 98% ee. The absolute configuration and the level of enantiocontrol in these intramolecular cyclopropanations have been interpreted by a transition state model in which the important determinants are (i) the preferred conformation about the rhodium-carbon bond; (ii) the trajectory of approach of the double bond to the metallocarbene center; and (iii) the orientation of the double bond with respect to the chiral face of the catalyst.

Introduction

The importance of cyclopropanes in diverse areas of organic chemistry and biology is now well documented.[1–5] For example, cyclopropanes occur as structural subunits in biologically active natural and non-natural products, and they are frequently used as mechanistic probes to define specific details of reaction pathways. The availability of optically pure cyclopropanes is critical to many applications, and a number of useful methods for the enantioselective synthesis of cyclopropanes have been recently developed to meet this need.[6–30] For example, cyclopropanations of chiral bicyclic lactams lead to enantiomerically pure di- and trisubstituted cyclopropanes.[7] The Simmons–Smith cyclopropanation of allylic alcohols derivatized as ethers with chiral auxiliaries has been reported to be highly diastereoselective.[8] If the diethylzinc that is employed in the Simmons–Smith reactions of allylic alcohols is coordi-

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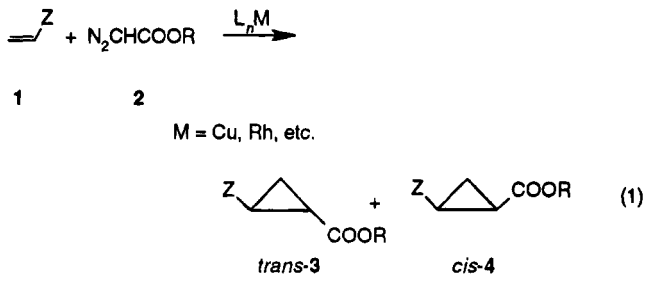
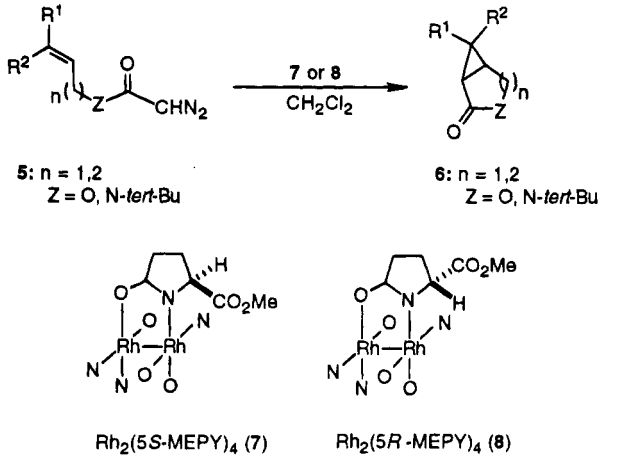
nated with chiral ligands, enantioselectivities as high as 83% ee may be observed.[9-11] Enzymatic methods have been used to prepare optically active cyclopropanes from *meso*-cyclopropanes by enantioselective hydrolysis, esterification, or oxidation.[12,13] The catalytic cyclopropanation of diazo compounds bearing chiral auxiliaries may result in high diastereoselectivity in selective cases.[14,15]

In the arena of asymmetric synthesis, those methods that use chiral catalysts to promote enantioselective transformations, especially carbon−carbon bond construction, are especially attractive. Thus, the catalytic asymmetric cyclopropanation of alkenes **1** with diazo carbonyl compounds **2** in the presence of chiral copper and rhodium catalysts offers significant potential as a general method for the synthesis of optically pure cyclopropanes **3** and **4** according to eq 1.[16] The first effective



chiral copper catalysts were developed by Aratani and coworkers and were derived from chiral 2-(salicylideneamino)-ethanol ligands.[17] More recently, copper catalysts bearing C_2-symmetric nitrogen ligands have been used to effect highly enantioselective intermolecular cyclopropanations of diazoacetate esters. These catalysts include the (semicorrinato)copper catalysts developed by Pfaltz,[18] the bisoxazoline copper catalysts independently reported by Evans,[19] Masamune,[20] and Pfaltz,[21] and the bipyridyl copper catalysts of Katsuki.[22] Rhodium

Scheme 1



catalysts that may be used in bimolecular asymmetric cyclopropanations include the chiral dirhodium(II) tetrakis(carboxamidates) developed by Doyle[23] or the *N*-(arenesulfonyl)-prolinates reported by McKervey[24] and the rhodium(III) porphyrin complexes designed by Kodadek.[25] Although these catalytic methods can provide substituted cyclopropanes with high levels of enantioselectivity, they suffer the major drawback that the reactions are not highly *diastereoselective*, and mixtures of *trans*- and *cis*-adducts **3** and **4** are generally produced. Only when sterically demanding ester substituents such as 2,6-di-*tert*-butyl-4-methylphenyl are employed can diastereoselectivity be influenced effectively.[19a,26]

Intramolecular cyclopropanations of unsaturated diazocarbonyl compounds can produce only one fused bicyclic cyclopropane because of geometric constraints. However, the cyclizations of a limited number of unsaturated diazoketones in the presence of the Aratani[27] or Pfaltz semicorrin[18a] catalysts proceeded with only modest to good levels of enantiocontrol. In contrast, we have discovered that allylic diazoacetates **5** ($n = 1$, Z = O) undergo highly enantioselective diazo decomposition and cyclization to give fused cyclopropyl lactones **6** ($n = 1$, Z = O) in the presence of the chiral dirhodium(II) carboxamide catalysts derived from methyl 2-oxapyrrolidine-5(*S* or *R*)-carboxylates, Rh_2(5*S*-MEPY)$_4$ (**7**) and Rh_2(5*R*-MEPY)$_4$ (**8**) (Scheme 1).[28] As seen by the partial structures depicted for **7** and **8**, these chiral dirhodium(II) carboxamide catalysts are structurally well defined with two oxygen and two nitrogen donor atoms bound to each rhodium so that the resulting configuration is (*cis*-2,2).[29] Moreover, moderate to high enantioselectivities were achieved using these catalysts with the homoallylic diazoesters **5** ($n = 2$, Z = O)[30] and *N*-*tert*-butyldiazoacetamides **5** ($n = 2$, Z = *N*-*t*-Bu).[31] We now present

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Table 1. Enantioselective Intramolecular Cyclopropanation Reactions of Allylic Diazoacetates **10a–p** Catalyzed by $Rh_2(5S\text{-MEPY})_4$ To Give Cyclopropyl Lactones **11a–p**[a]

entry	R^1	R^2	R^3	yield **11**, %[b]	ee, %	configuration[c]	ee method[d]
a	H	H	H	75	95	(1*R*, 5*S*)	A
b	CH_3	CH_3	H	89	98	(1*S*, 5*R*)	A
c	H	H	CH_3	72	7	(1*R*, 5*S*)	A
d	H	C_6H_5	H	70	≥94	(1*R*, 5*S*)	B
e	C_6H_5	H	H	78	68	(1*R*, 5*S*)	A
f	H	CH_3CH_2	H	88	≥94	(1*R*, 5*S*)	B
g	$CH_3CH_2CH_2$	H	H	93	85	(1*R*, 5*S*)	A
h	CH_3	$(CH_3)_2C{=}CH(CH_2)_2$	H	79	93	(1*S*, 5*R*)	A
i	$(CH_3)_2C{=}CH(CH_2)_2$	CH_3	H	88	95	(1*S*, 5*R*)	A
j	H	$C_6H_5CH_2$	H	80	≥94	(1*R*, 5*S*)	B
k	H	$(CH_3)_2CHCH_2$	H	73	≥94	(1*R*, 5*S*)	B
l	H	$(CH_3)_2CH$	H	85	≥94	(1*R*, 5*S*)	B
m	$(CH_3)_2CH$	H	H	71	54	(1*R*,5*S*)	B
n	H	(*n*-Bu)$_3$Sn	H	79	≥94	(1*R*, 5*S*)	B
o	H	I	H	78	≥94	(1*R*, 5*S*)	B
p	I	H	H	70	67	(1*R*, 5*S*)	B

[a] Reactions were performed in refluxing CH_2Cl_2 using 0.1–1.0 mol% $Rh_2(5S\text{-MEPY})_4$. Yields and enantiomeric excesses were reproducible (±3%) from duplicate runs. [b] Yield (unoptimized) of pure product isolated by distillation or chromatography. [c] Absolute configurations are as depicted for **11a–p**; change in notation results from change in priorities by substituents. [d] Method A: separation of peaks from individual enantiomers on cyclodextrin capillary GC columns and integration of peaks (±1%); method B: Lactones **11a–n** were treated with excess MeLi, and enantiomeric excesses of the derived diols, or the corresponding mono acetates (Ac_2O and DMAP in CH_2Cl_2), were determined by titration with the chiral shift reagent Eu(tfc)$_3$ or Eu(hfc)$_3$ in C_6D_6 and integration of suitable diastereotopic protons in the ^1H NMR spectrum (±3%).[37] Iodo lactones **11o,p** were reduced (Zn/HOAc) prior to reaction with excess MeLi. Control experiments were performed on racemates for each entry.

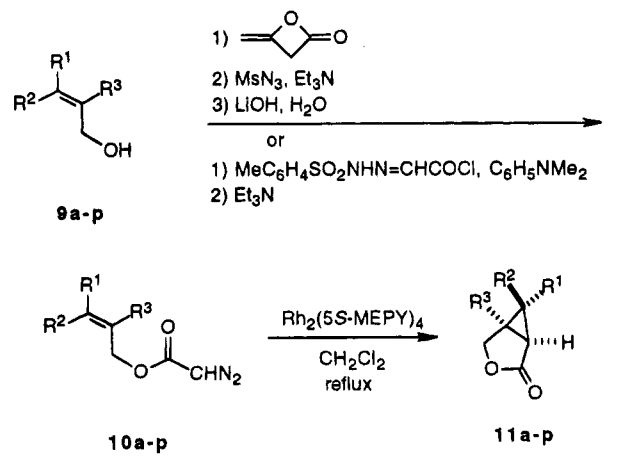
the synthetic and mechanistic details for these highly enantioselective intramolecular cyclopropanations and describe their scope and limitations together with the effects of varying the catalyst ligands.

Results

Cyclizations of Allylic Diazoacetates. In order to establish the efficacy of using the chiral dirhodium(II) catalysts $Rh_2(5S\text{-MEPY})_4$ (**7**) and $Rh_2(5R\text{-MEPY})_4$ (**8**) to induce the enantioselective cyclizations of allylic diazoacetates, we initiated a series of exploratory experiments. A representative series of allylic diazoacetates **10a–p** was first prepared from the corresponding allylic alcohols (Scheme 2). Diazoacetate **10a** was synthesized from glycine allyl ester hydrochloride.[32] One general procedure for preparing some of the requisite diazoacetates involved the transformation of the allylic alcohols **9b,c,e,g,h** into the corresponding acetoacetic esters by reaction with diketene[26] or the diketene equivalent, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one.[33] Subsequent diazo transfer followed by base-induced deacylation of the intermediate α-diazo acetoacetic ester then gave **10b,c,e,g,h**. Alternatively, the allylic alcohols **9d,f,i–p** were converted directly into the respective allylic diazoacetates **10d,f,i–p** by reaction with glyoxylic acid chloride *p*-toluenesulfonylhydrazone according to the procedure of Corey and Myers.[34]

Slow addition of solutions of the allylic diazoacetates **10a–p** to a solution of $Rh_2(5S\text{-MEPY})_4$ in refluxing dichloromethane then gave the cyclopropyl lactones **11a–p** with very good to excellent yields and enantioselectivities (Table 1). Generally 0.5–1.0 mol % of catalyst based on diazo compound was employed, but amounts of catalyst as low as 0.1 mol % have also proven effective (*e.g.*, with **10a**, 72–75% yield). Improved yields of cyclopropane products ordinarily accompany increases in mol % of the catalyst up to about 0.5 mol %. The absolute configurations of **11a**, **11b**, and **11g** were determined by correlation of the sign of rotation of polarized light with that of the known enantiomer. The absolute configurations of **11d** and **11l** were established by single crystal X-ray structures of their derivatives with *l*-(−)-menthol and a protected tyrosine derivative, respectively.[35,36] Other assignments are based upon analogy. Improvements in experimental procedures have resulted in enhancements of the observed enantioselectivities and yields reported for the formation of **11a**, **11b**, **11g**, and **11k** relative to that previously reported.[28]

Scheme 2



As is quickly evident from examination of the entries in Table 1, the method may be extended to the highly enantioselective cyclization of a diverse array of allylic diazoacetates substituted with aryl and alkyl substituents on the distal terminus of the double bond. However, substitution on the proximal position of the double bond appears to result in poor enantioselectivity as illustrated by the cyclization of **10c**. Higher enantioselectivities are generally observed in the cyclizations of *Z*-alkenes relative to their *E*-alkene counterparts as illustrated by comparison of the cyclizations of the diastereomeric pairs **10d/10e**, **10l/10m**, and **10o/10p**. However, very good enantioselectivities may be obtained with *E*-alkyl substitution on the double bond

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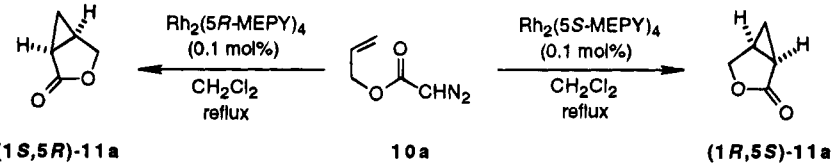
Scheme 3



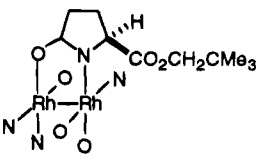
(1*S*,5*R*)-11a **10a** **(1*R*,5*S*)-11a**

as demonstrated by the cyclizations of **10b** and **10g–i**. The intramolecular cyclopropanations of the diazoacetates of nerol **10h** and geraniol **10i** reveal that γ-lactone formation is exclusive even when other double bonds are present in the substrate. The diazoacetates of allylic alcohols bearing vinylic trialkylstannyl and iodo substituents as **10n–p** also undergo cyclizations with good to excellent enantioselectivities to give cyclopropyl lactones that bear substituents on the cyclopropane ring that may be further elaborated by standard reactions.

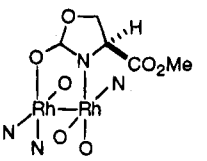
In order for a catalytic asymmetric process to be generally useful, it is essential that the method be readily applied to the preparation of both enantiomers of a product from a single achiral starting material. Indeed the enantiomeric catalyst Rh_2(5*R*-MEPY)$_4$ (**8**), which is easily prepared from methyl 5*R*-pyroglutamate, induces the cyclizations of allylic diazo esters with identical enantiocontrol as Rh_2(5*S*-MEPY)$_4$ (**7**) but in the opposite stereochemical sense. For example, the cyclization of 2-propen-1-yl diazoacetate (**10a**) with Rh_2(5*S*-MEPY)$_4$ gave **(1*R*,5*S*)-11a** (95% ee, 75% yield), whereas the use of Rh_2(5*R*-MEPY)$_4$ gave **(1*S*,5*R*)-11a** (95% ee, 72% yield) (Scheme 3).

Racemic products were obtained by diazo decomposition of the appropriate unsaturated diazoester using either dirhodium(II) tetraacetate, $Rh_2(OAc)_4$, or dirhodium(II) tetracaprolactamate, $Rh_2(cap)_4$, in refluxing dichloromethane, or with copper(II) bis(*N-tert*-butylsalicylaldimate), $Cu(TBS)_2$ in refluxing toluene. In virtually all cases lower yields of **11** accompanied the use of $Rh_2(OAc)_4$ relative to $Rh_2(cap)_4$, $Cu(TBS)_2$, Rh_2(5*S*-MEPY)$_4$ (**7**), Rh_2(5*R*-MEPY)$_4$ (**8**), and other chiral dirhodium(II) carboxamide catalysts. The intramolecular cyclopropanations catalyzed by $Rh_2(OAc)_4$ tended to be accompanied with larger quantities of byproducts including carbene dimers compared to those obtained from the use of dirhodium(II) carboxamide and $Cu(TBS)_2$ catalysts.

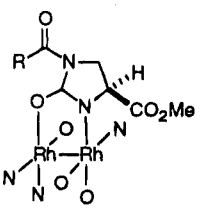
The intramolecular cyclopropanation of 2-methyl-2-propen-1-yl diazoacetate (**10c**) with Rh_2(5*S*-MEPY)$_4$ (**7**) stood as the lone example in which the product bicyclic lactone **11c** was obtained with poor enantioselectivity (7% ee). An extensive series of dirhodium(II) carboxamide catalysts derived from pyrrolidone (**12**),[38] oxazolidinone (**13**),[39] and imidazolidinone carboxylates (**14** and **15**)[40] was then examined to determine whether they might lead to improved enantiocontrol in this difficult case. Like Rh_2(5*S*-MEPY)$_4$ (**7**), each of the catalysts **12–15** possesses the (*cis*-2,2)-geometry and the *S*-absolute configuration at the stereogenic center in the chiral ligand. The X-ray crystal structures of Rh_2(5*R*-MEPY)$_4(CH_3CN)_2$[29] and Rh_2(4*S*-MEOX)$_4(C_6H_5CN)_2$[39b] have been determined, and their NMR spectra as well as those of **12–15** are consistent with the (*cis*-2,2)-geometry. The cyclizations of **10c** catalyzed by **12, 14,** and **15** proceeded in each case to give **(1*R*,5*S*)-11c**. Using **13** as the catalyst gave approximately equal amounts of **(1*R*,5*S*)-11c** and its enantiomer **(1*S*,5*R*)-11c**, the latter being favored by about 1%. A comparison of the enantioselectivities in these transformations is presented in Table 2. As is evident from the data, imidazolidinone-derived catalysts provide significant improvements in enantiocontrol, up to 78% ee with Rh_2(4*S*-MACIM)$_4$ (**15**), but the oxazolidinone-derived catalyst Rh_2(4*S*-MEOX)$_4$ (**13**) gives even lower enantiocontrol than Rh_2(5*S*-MEPY)$_4$ (**7**).



Rh_2(5*S*-NEPY)$_4$ (**12**)



Rh_2(4*S*-MEOX)$_4$ (**13**)



Rh_2(4*S*-MACIM)$_4$ (**14**): R = CH_3
Rh_2(4*S*-MPAIM)$_4$ (**15**): R = $PhCH_2$

The dramatic dependence of enantioselectivity observed in the cyclization of **10c** with the nature of the chiral ligand on rhodium suggested that the intramolecular cyclopropanations of **10e** and **10g** might be enhanced by using the dirhodium(II) catalysts **13–15**. However, the observed enantioselectivity in the cyclizations of **10e** and **10g** catalyzed by Rh_2(4*S*-MEOX)$_4$ (**13**) and Rh_2(4*S*-MACIM)$_4$ (**14**) either decreased or remained essentially unchanged (Table 2). On the other hand, when Rh_2-

Table 2. Effect of Different Catalysts upon the Cyclizations of Allylic Diazoacetates **10c**, **10e**, and **10g** To Give Cyclopropyl Lactones **11c**, **11e**, and **11g**

allylic diazoacetate	$Rh_2L^*_4$	yield, %	ee, %
10c	Rh_2(5*S*-MEPY)$_4$ (**7**)	72	7
	Rh_2(5*S*-NEPY)$_4$ (**12**)	49	29
	Rh_2(4*S*-MEOX)$_4$ (**13**)	84	1[a]
	Rh_2(4*S*-MACIM)$_4$ (**14**)	90	78
	Rh_2(4*S*-MPAIM)$_4$ (**15**)	57	65
10e	Rh_2(5*S*-MEPY)$_4$ (**7**)	78	68
	Rh_2(4*S*-MEOX)$_4$ (**13**)	89	50
	Rh_2(4*S*-MACIM)$_4$ (**14**)	70	82
	Rh_2(4*S*-MPAIM)$_4$ (**15**)	76	86
10g	Rh_2(5*S*-MEPY)$_4$ (**7**)	93	85
	Rh_2(4*S*-MEOX)$_4$ (**13**)	65	62
	Rh_2(4*S*-MACIM)$_4$ (**14**)	70	87
	Rh_2(4*S*-MPAIM)$_4$ (**15**)	87	90

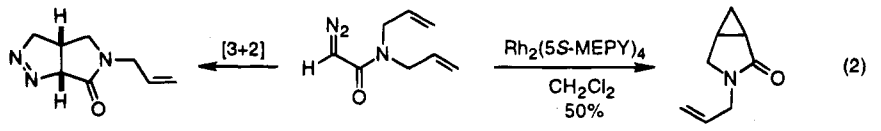
[a] The major product was ***ent*-11c** with an absolute configuration of (1*S*, 5*R*).

(37) This method is a modification of that reported by Jakovac, I. J.; Jones, J. B. *J. Org. Chem.* **1979**, *44*, 2165.

(38) Doyle, M. P.; van Oeveren, A.; Westrum, L. J.; Protopopova, M. N.; Clayton, T. W. Jr. *J. Am. Chem. Soc.* **1991**, *113*, 8982.

(39) (a) Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Daniel, K. L. *Tetrahedron Lett.* **1992**, *33*, 7819. (b) Doyle, M. P.; Dyatkin, A. B.; Protopopova, M. N.; Yang, C. I.; Miertschin, C. S.; Winchester, W. R. *Recl. Trav. Chim, Pays-Bas* **1995**, in press.

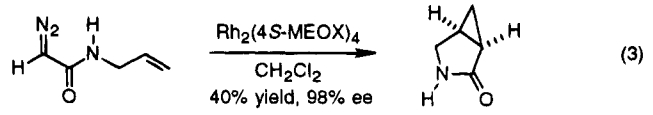
(40) Doyle, P.; Dyatkin, A. B.; Roos, G. H. P.; Cañas, F.; Pierson, D. A.; van Basten, A.; Müller, P.; Polleux, P. *J. Am. Chem. Soc.* **1994**, *116*, 4507.



18 **16** **17**

$(4S\text{-MPAIM})_4$ (**15**) was used to promote the cyclizations of both **10e** and **10g**, the enantioselectivity of the addition was improved, and **11e** and **11g** were formed with 86 and 90% ee, respectively.

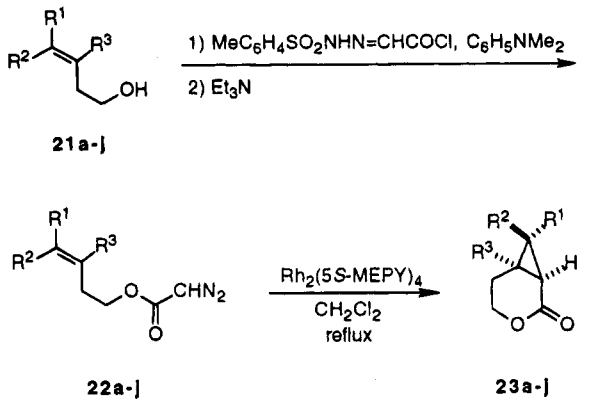
Cyclizations of *N*-Allylic Diazoacetamides. We recently reported that *N*,*N*-diallyl-α-diazoacetamide (**16**) underwent $Rh_2(5S\text{-MEPY})_4$-catalyzed diazo decomposition to form the corresponding *N*-allyl γ-lactam derivative **17** with 72% ee (eq 2).[31] Intramolecular [3 + 2] cycloaddition of **16** to give **18** was a facile competing reaction that limited the conversion of **16** to **17**, whose absolute configuration was inferred but not proven to be (1*R*,5*S*). Similar [3 + 2] cycloaddition reactions frustrated attempts to prepare *N*-allylic-*N*-*tert*-butyl, but not *N*-homoallylic-*N*-*tert*-butyl, analogues of **16**. However, we have prepared *N*-allyl diazoacetamide (**19**) from succinimidyl diazoacetate,[41] and this compound is relatively stable toward intramolecular [3 + 2] cycloaddition. Diazo decomposition of **19** catalyzed by $Rh_2(4S\text{-MEOX})_4$ produced bicyclic lactam **20** with exceptionally high enantiocontrol, albeit in modest yield (eq 3). The absolute configuration of the GABA derivative **20** formed by this cyclization was determined to be (1*R*,5*S*) by comparison of its sign of rotation with that of the Boc-derivative of **20** that was prepared independently in more than eight steps from (*R*)-2,3-*O*-isopropylidene glyceraldehyde.[42] With $Rh_2(5S\text{-MEPY})_4$ **20** was produced with 97% ee but in lower yield (23%). Carbene dimer formation from **19** was competitive with the formation of **20**, and efforts to reduce the occurrence of this side reaction by dilution or performing the diazo decomposition at a higher temperature were not successful. An examination of the reaction mixture provided no evidence for either intramolecular or intermolecular N−H insertion.[43] Although the *N*-allyl diazoacetamide **19** underwent intramolecular cyclopropanation, the dirhodium(II) catalyzed diazo decomposition of *N*-(2-methyl-2-propen-1-yl)diazoacetamide and *N*-(3-methyl-2-buten-1-yl)-diazoacetamide did not produce any significant amount of intramolecular cyclopropanation products.



19 **20**

Cyclization of Homoallylic Diazoacetates. The next extension of this methodology involved examination of the intramolecular cyclopropanations of homoallylic diazoacetates. Toward this end, the series of homoallylic alcohols **21a−j** were converted into the corresponding unsaturated diazo esters **22a−j** according to the method of Corey and Myers (Scheme 4).[34] Diazo decomposition of **22a−j** in the presence of $Rh_2(5S\text{-MEPY})_4$ (**7**) gave the respective cyclopropyl lactones **23a−j** in 71−90% enantiomeric excess (Table 3).[30] A comparison of the data summarized in Tables 1 and 3 for the cyclizations of allylic and homoallylic diazoacetates reveals that the lower degree of enantiocontrol that often accompanies an increase in the distance between two reacting centers is evident. One notable exception to this generalization is that the cyclization of the α-methyl allylic diazoacetate **10c** proceeded in only 7% ee, whereas the cyclization of corresponding homoallylic analogue **22c** gave **23c** in 83% ee. Although the enantioselectivity of the cyclization of **10c** was dramatically affected by the use of other chiral dirhodium(II) catalysts (Table 2), there was only a modest variation in yield (67−76%) and enantioselectivity (76−84% ee) when the series of catalysts $Rh_2(5S\text{-MEPY})_4$, $Rh_2(4S\text{-MEOX})_4$, and $Rh_2(4S\text{-MACIM})_4$ were utilized to promote the cyclization of **22c** to give **23c**.

Scheme 4



21a-j **22a-j** **23a-j**

Table 3. Enantioselective Intramolecular Cyclopropanation Reactions of Homoallylic Diazoacetates **22a−j** Catalyzed by $Rh_2(5S\text{-MEPY})_4$ To Give Cyclopropyl Lactones **23a−j**[a]

entry	R^1	R^2	R^3	yield %[b]	ee, %	configuration[c]	ee method[d]
a	H	H	H	80	71	(1*R*, 6*S*)	B
b	CH_3	CH_3	H	74	77	(1*S*, 6*R*)	B
c[e]	H	H	CH_3	76	83	(1*R*, 6*S*)	A,B
d	H	C_6H_5	H	73	88	(1*S*, 6*R*)	C
e	C_6H_5	H	H	55	73	(1*S*, 6*R*)	B
f	H	CH_3CH_2	H	80	90	(1*S*, 6*R*)	B,C
g	CH_3CH_2	H	H	65	82	(1*S*, 6*R*)	B
h	H	*c*-$C_6H_{11}CH_2$	H	77	80	(1*S*, 6*R*)	C
i	H	$C_6H_5CH_2$	H	68	80	(1*S*, 6*R*)	B
j	H	$(CH_3)_3Si$	H	65	86	(1*S*, 6*R*)	C

[a] Reactions were performed in refluxing CH_2Cl_2 using 1.0 mol % $Rh_2(5S\text{-MEPY})_4$. [b] Isolated yield of purified product. [c] Absolute configurations are as depicted for **23a−j**; change in notation results from changes in priorities of substituent groups. [d] Method A: separation of enantiomers on cyclodextrin capillary GC columns (±1%); method B: integration of suitable diastereotopic protons using chiral shift reagent $Eu(tfc)_3$ (see Experimental Section); method C: integration of diastereomeric protons from (*R*)-(+)-α-methylbenzylamine derivative (see Experimental Section). [e] Using the catalysts **13** and **14**, **23c** was obtained in 72% yield (84% ee) and 67% yield (76% ee), respectively.

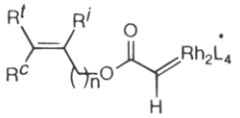
Discussion

The high enantiocontrol achieved for intramolecular cyclopropanation of allylic and homoallylic diazoacetate esters **10a−p** and **22a-j** (Tables 1−3) using $Rh_2(5S\text{-MEPY})_4$ and $Rh_2(5R\text{-MEPY})_4$ catalysts is exceptional.[16,43] This methodology may be extended to the cyclizations of unsaturated diazoacetates in

(41) Ouihia, A.; René, L.; Guilhem, J.; Pascard, C.; Badet, B. *J. Org. Chem.* **1993**, *58*, 1641.
(42) Morikawa, T.; Sasaki, H.; Hanai, R.; Shibuya, A.; Taguchi, T. *J. Org. Chem.* **1994**, *59*, 97.
(43) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091.

which the double bond is mono-, di-, and trisubstituted with alkyl, aryl, trialkylstannyl, and iodo groups. The reactions proceed in good to excellent yields, and there is a conspicuous absence of side products.

Examination of the results for the cyclizations of allylic and homoallylic diazoesters catalyzed by $Rh_2(5S\text{-MEPY})_4$ reveals some important insights regarding the steric influences of olefinic substituents on enantiocontrol in these intramolecular cyclopropanations. For example, comparison of the % ee's and product yields for the cyclizations in Table 1 suggests the following for the generalized substrate **24** ($n = 1$): (1) higher enantiocontrol is obtained when an aryl or alkyl group is present



24: n = 1, 2

at R^c rather than at R^t; (2) high enantioselectivities are obtained when substituents are present at both R^c and R^t, and this effect appears to be independent of the size of the two groups; and (3) a methyl group at R^i in allylic diazoesters virtually eliminates enantiocontrol.

These observations serve as the basis for developing an operational model to understand the absolute sense and level of the enantiocontrol in the $Rh_2(5S\text{-MEPY})_4$-catalyzed intramolecular cyclopropanations of allylic diazoacetates **10a−p**. It is now established by X-ray analysis that the chiral dirhodium(II) carboxamide catalysts are structurally well defined with two oxygen and two nitrogen donor atoms bound to each rhodium so that the resulting configuration is (*cis*-2,2).[29,39b] Although the stepwise mechanism of the reaction is not precisely known, available evidence suggests that the interaction of the rhodium catalyst with an unsaturated diazoester first affords an intermediate metallocarbene.[44,45] The diastereofacial selectivity in the ensuing intramolecular cyclopropanation is then determined by the interactions in the transition state between the chiral dirhodium(II) ligands and the substituents on the carbon−carbon double bond as it approaches the metallocarbene center. The magnitude of these interactions are primarily affected by (i) the conformation about the rhodium−carbon bond; (ii) the trajectory of approach of the double bond; and (iii) the orientation of the double bond with respect to the face of the catalyst.

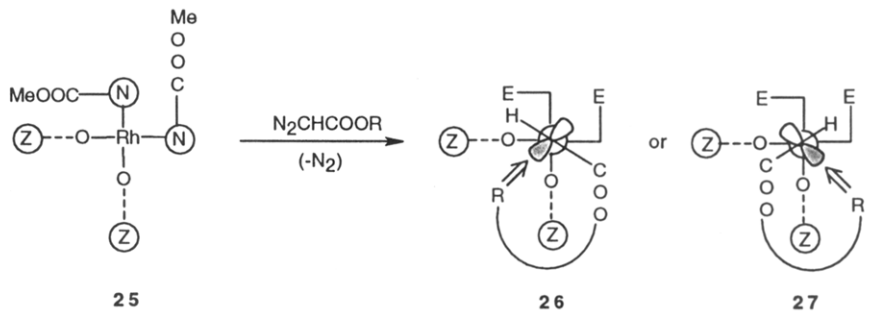
When viewed along the Rh−C bond axis of the presumed metallocarbene complex formed from the chiral dirhodium(II) catalyst **25**, the face of the catalyst can be divided into four quadrants, of which two are occupied by the pendant carboalkoxy group at the stereocenter of the ligands. A third quadrant is filled by the carboxylate group of the carbene leaving the fourth open for substrate approach to the carbene center. For a metallocarbene complex with $Rh_2(5S\text{-MEPY})_4$, calculations have shown that the preferred spatial orientation in the transition state for either an inter- or intramolecular cyclopropanation is that depicted by **26**.[29] In this array, the axis of the C−H bond of the metallocarbene bisects the O−Rh−N bond angle with the hydrogen atom in the sterically more congested quadrant, and the reacting double bond in R approaches the rhodium-bound electrophilic carbene from the less hindered *si* face of the double bond. A higher energy minimum was found for the alternative transition state geometry shown in **27** wherein the carbene bisects the N−Rh−N bond angle, and the double bond approaches from the less hindered *re* face. If the orientation of the double bond with respect to the face of the catalyst is the same in **26** and **27**, these two spatial arrangements necessarily lead to the formation of enantiomeric cyclopropyl lactones.

Since the double bond in a metallocarbene complex derived from $Rh_2(5S\text{-MEPY})_4$ approaches the electrophilic carbenoid center along the trajectory shown in **26**, steric constraints then dictate that the preferred orientation of the double bond in substrates lacking a substituent R^i is that depicted in **28**. This transition state geometry leads to the observed products generally represented by **30**, whereas the alternate rotamer about the allylic carbon−carbon bond depicted in **29** would form the enantiomeric adduct **31** (Scheme 6). An examination of this simple model suggests that the presence of a substituent R^t in **28** will sterically interact with the ester group on the ligand, thereby decreasing the energy difference between **28** and **29** and leading to reduced enantioselectivity. The R^c substituent is oriented away from the catalyst in **28** and should not affect the enantioselectivity of the cyclization.

These predictions are consistent with the experimental observations (Table 1) that the intramolecular cyclopropanations of the *E*-allylic diazoacetates **10e,g,m,p** (R^t = Ph, *n*-Pr, *i*-Pr, and I) proceed with 54−85% enantioselectivity (corresponding to a 0.7−1.5 kcal/mol energy difference between **28** and **29**), whereas the *Z*-allylic diazoacetates **10d,f,j,k,l,n,o** generally cyclize in ≥94% ee (≥2.2 kcal/mol energy difference between **28** and **29**). The enantioselectivity in the cyclizations of the *E*-allylic diazoacetates $R^t \neq H$ also decreases with the increasing size of R^t. With R^t and R^c = *n*-alkyl, there appears to be a subtle balance of interactions that again strongly favors the transition state arising from the geometry shown in **28**.

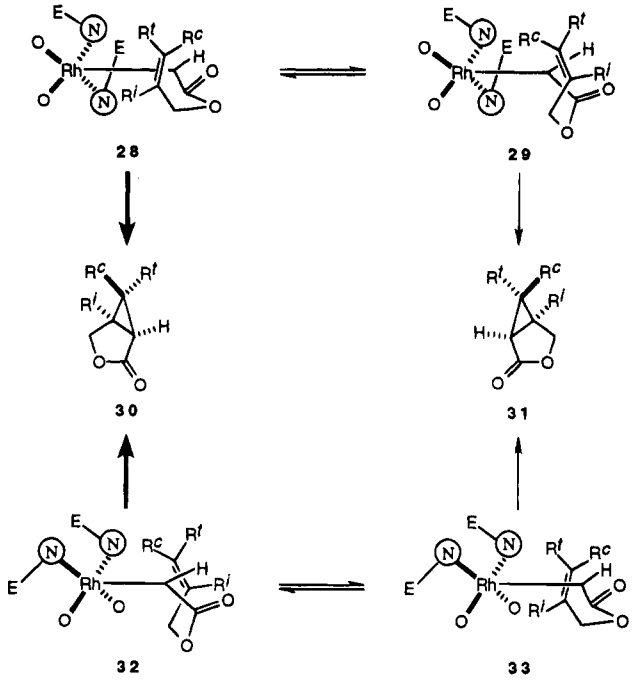
In the three-dimensional array **28**, the substituent R^i points directly toward the wall of the chiral dirhodium(II) catalyst. It is evident from the $Rh_2(5S\text{-MEPY})_4$-catalyzed cyclization of **10c** wherein $R^i = CH_3$ that this steric interaction is energetically unfavorable and results in the formation of the cyclopropane product **11c** with only 7% enantioselectivity. Cyclization via the conformation shown in **29** to give ***ent*-11c** presumably becomes competitive. The results shown in Table 2 reveal that cyclization of **10c** with the *N*-acyl imidazolidinone-derived catalysts **14** and **15** proceeded to give **11c** with 78 and 65% enantioselectivity, respectively. Since there would be significant steric repulsion between the *N*-acyl substituent on the imida-

Scheme 5

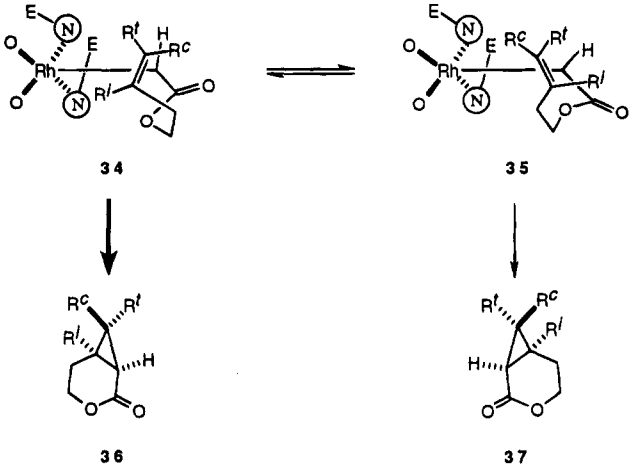


25 **26** **27**

Scheme 6



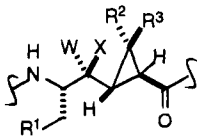
Scheme 7



zolidinone ring of the ligand and the methyl group at R^i on the approaching double bond in the transition state emanating from **28** (*cf.* the two R ↔ Z interactions in **26**), an alternative transition state model must obtain. The transition state shown in **29** is clearly not operative because it would lead to ***ent*-11c**. Examination of molecular models suggests that the metallocarbene produced from reaction of **10c** with **14** or **15** could cyclize via the N−Rh−N bisected conformer shown in **27** (Scheme 5) to minimize interactions between the internal vinyl methyl group and the *N*-acyl moiety on the catalyst. Such a cyclization must then proceed by the transition state depicted in **32** to give **11c**; the alternate arrangement illustrated in **33** would lead to ***ent*-11c**.

Thus, the stereochemical outcome of the intramolecular cyclopropanations of substituted allylic diazoacetates that are catalyzed by chiral dirhodium(II) carboxamide catalysts may be rationalized by considering the two possible transition states that emanate from each of the bisected carbene conformers **26** (*e.g.*, **28** and **29**) and **27** (*e.g.*, **32** and **33**). The transition state that seems to be preferred for these reactions is that depicted by **28**. The only exception to this trend observed thus far involves those cyclizations of internally substituted substrates, $R^i \neq H$, that are catalyzed by the *N*-acyl imidazolidinone-derived catalysts **14** and **15**. In these cases the alternate transition state depicted by **32** seems favored. These generalizations account for the stereoselectivities obtained and reported thus far, but they must be tested by further experiments.

Similar arguments pertain to the $Rh_2(5S\text{-MEPY})_4$-catalyzed cyclizations of homoallylic diazoacetates **22a−j**, which appear to undergo preferential cyclization via the trajectory depicted in **26** and by the transition state geometry shown in **34**. In general, the enantioselectivities in these intramolecular cyclopropanations are slightly lower than those of the allyl diazoacetates **10a−p** (*cf.* Schemes 1 and 3). The most significant difference between the allylic and homoallylic systems is that enantioselectivities of the latter cyclizations are less sensitive to the presence of a substituent R^i at the internal position on the double bond. This variation is strikingly exemplified by comparing the $Rh_2(5S\text{-MEPY})_4$-catalyzed cyclizations of the allylic diazoacetate **10c** and the homoallylic analogue **22c** to give their respective cyclopropanes **11c** (7% ee) and **23c** (83% ee). The introduction of the additional methylene group in the chain linking the double bond with the metallocarbene center as shown in **34** apparently introduces sufficient flexibility in the transition state for cyclization that there is reduced interaction of the olefinic substituent R^i with the face of the catalyst to give **36** as the major adduct (Scheme 7). The alternate transition state **35**, which would lead to the enantiomer **37**, is higher in energy partially because of interactions between the allylic CH_2 group at C(2) and the rhodium face. This increased flexibility also presumably accounts for the reduced enantioselectivity in these reactions.



38: W, X = H, OH, O

Conclusions

The utility of chiral dirhodium(II) carboxamide catalysts such as $Rh_2(5S\text{-MEPY})_4$ to promote highly enantioselective intramolecular cyclopropanations of primary allylic and homoallylic diazoacetates has been convincingly established. The effects of a full range of alkene substituents on enantioselectivity have been determined (Tables 1 and 3) including, for the first time, results from cyclization of neryl and geraneyl diazoacetates and methallyl and 3-iodo-2-propenyl diazoacetates and the first report of intramolecular cyclopropanation of *N*-allyldiazoacetamide. The remarkable influence of catalyst ligands on enantioselectivity is seen from results (Table 2) with dirhodium(II) carboxamide catalysts derived from pyrrolidone, oxazolidinone, and imidazolidinone carboxylates. Recently, we have discovered that the diazoacetates of chiral secondary allylic alcohols and prochiral divinyl carbinols also undergo cyclization with high enantioselectivities.[46] These discoveries set the stage for future investigations involving the intramolecular cyclopropanations of other unsaturated diazocarbonyl substrates. The practical utility of this methodology has been demonstrated by

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its successful application to the asymmetric synthesis of the novel cyclopropane-derived peptide mimics of the general type **38**. These peptide surrogates represent the first conformationally-restricted peptide isosteres that stabilize a β-strand conformation on a peptide backbone while directing the side chains to specific orientations.[47] Such replacements have already been incorporated in potent inhibitors of renin,[48] HIV-1 protease,[49] collagenase,[50] and stromelysin.[51] Applications to the field of natural product synthesis are in progress, and the results of these investigations will be reported in due course.

Experimental Section

General Methods. Dichloromethane was distilled from calcium hydride prior to use in catalytic reactions. Tetrahydrofuran was distilled from lithium aluminum hydride. Acetonitrile was distilled from calcium hydride and stored under nitrogen. ^{1}H NMR (300 MHz) and ^{13}C (75 MHz) NMR spectra were obtained as solutions in $CDCl_3$, unless indicated otherwise, and chemical shifts are reported in parts per million (ppm, δ) downfield from internal Me_4Si(TMS). Mass spectra were generally obtained using electron ionization. Infrared spectra were recorded either as a thin film on sodium chloride plates or as solutions as indicated, and absorptions are reported in wavenumbers (cm^{-1}). Elemental analyses were performed at Texas Analytical Laboratories, Inc. Methanesulfonyl azide was prepared from methanesulfonyl chloride and sodium azide.[52] The preparation of $Rh_2(5S\text{-MEPY})_4$ and $Rh_2(5R\text{-MEPY})_4$ by acetate displacement from $Rh_2(OAc)_4$ has been described,[29] and the synthesis and X-ray structure of $Rh_2(4S\text{-MEOX})_4$ is being separately reported. Diketene and its acetone adduct, 2,2,6-trimethyl-4H-1,3-dioxin-4-one, were distilled under reduced pressure prior to use. The *p*-toluenesulfonylhydrazone of glyoxylic acid chloride was prepared as a pale yellow crystalline solid in 80% yield.[53] The allylic alcohols **9d,j–p** and the homoallylic alcohols **21d,e,g,i,j** are known compounds and were generally prepared by the stereoselective semihydrogenation/hydride reduction of the corresponding acetylenes.[54–56]

2-Propen-1-yl diazoacetate (10a) was prepared from the glycine allyl ester hydrochloride salt in 70% isolated yield.[32] This diazoester, but not most of the others in this study, underwent polymerization over time, even when it was stored at 0 °C; consequently, only freshly distilled **10a** (Kugelrohr, lit.[32] bp 53 °C at 5 Torr) was employed for catalytic diazo decomposition reactions: ^{1}H NMR (300 MHz) δ 5.92 (ddt, J = 17.1, 10.4, 5.7 Hz, 1 H), 5.32 (dq, J = 17.1, 1.5 Hz, 1 H), 5.25 (dq, J = 10.4, 1.3 Hz, 1 H), 4.79 (br s, 1 H), 4.66 (dt, J = 5.7, 1.4 Hz, 2 H).

3-Methyl-2-buten-1-yl Diazoacetate (10b). Freshly distilled diketene (5.37 g, 63.9 mmol) in THF (10 mL) was added dropwise (20 min) to a stirred solution of 3-methyl-2-buten-1-ol (5.01 g, 58.0 mmol) and anhydrous NaOAc (0.31 g, 4.7 mmol) in refluxing, anhydrous THF (20 mL). The resulting solution was heated at reflux for 1 h. After cooling to room temperature, Et_2O (50 mL) and saturated NaCl solution (25 mL) were added, and the layers were separated. The aqueous layer was washed with Et_2O (2 × 50 mL). The combined organic fractions were washed with saturated aqueous NaCl (50 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the brown residue was distilled (64–70 °C, 0.10 Torr) to afford 6.33 g (70%) of 3-methyl-2-buten-1-yl acetoacetate as a colorless liquid: ^{1}H NMR δ 5.40–5.32 (m, 1 H), 4.64 (d, J = 7.3 Hz, 2 H), 3.45 (s, 2 H), 2.27 (s, 3 H), 1.79 (s, 3 H), and 1.72 (s, 3 H); enol form at 4.99 (s, 1 H) and 1.96 (s, 3 H).

A solution of methanesulfonyl azide (4.48 g, 39.1 mmol) in acetonitrile (40 mL) was added dropwise over 20 min to a stirred solution of 3-methyl-2-buten-1-yl acetoacetate (4.68 g, 30.0 mmol) and Et_3N (3.64 g, 36.0 mmol) in anhydrous acetonitrile (50 mL). The resulting yellow solution was maintained at room temperature for an additional 4 h, whereupon $LiOH{\cdot}H_2O$ (3.78 g, 90.1 mmol) in H_2O (25 mL) was added and stirring continued for 6 h. The resulting aqueous reaction solution was diluted with water and washed with Et_2O/EtOAc (3:1, 2 × 50 mL). The combined organic solution was then washed with saturated aqueous NaCl (25 mL) and dried ($MgSO_4$), and the solvent was removed under reduced pressure. The resulting orange liquid was purified by column chromatography on silica gel eluting with hexanes/EtOAc (10:1) to give 3.00 g (65%) of **10b** as a yellow oil: ^{1}H NMR δ 5.39–5.32 (m, 1 H), 4.74 (s, 1 H), 4.66 (d, J = 7.3 Hz, 2 H), 1.77 (s, 3 H), 1.72 (s, 3 H); ^{13}C NMR δ 166.8, 139.2, 118.4, 61.6, 46.0, 25.6, 17.8; IR (film) 2109, 1694 cm^{-1}.

2-Methyl-2-propen-1-yl Diazoacetate (10c) was prepared from 2-methyl-2-propen-1-ol in 39% overall yield by condensation with diketene, diazo transfer with methanesulfonyl azide, and deacylation according to the procedure described for the synthesis of **10b**: ^{1}H NMR δ 4.95 (d, J = 12.0 Hz, 2 H), 4.79 (br s, 1 H), 4.58 (s, 2 H), 1.76 (s, 3 H); ^{13}C NMR δ 166.8, 139.2, 118.4, 61.6, 46.0, 25.6, 17.8; IR (film) 2100, 1698, 1652 cm^{-1}.

***trans*-3-Phenyl-2-propen-1-yl diazoacetate (10e).** A solution of *trans*-cinnamyl alcohol (5.00 g, 37.3 mmol) and freshly distilled 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (5.30 g, 37.3 mmol) in xylene (15 mL) was heated with rapid stirring in a preheated oil bath at 150 °C for 30 min until the acetone that was produced had evaporated.[33] The xylene was removed by distillation, and the residue was purified by bulb-to-bulb distillation (120 °C, 0.05 Torr) to yield 6.84 g (89%) of *trans*-3-phenyl-2-propen-1-yl acetoacetate as a colorless liquid: ^{1}H NMR δ 7.41–7.24 (comp, 5 H), 6.68 (d, J = 15.9 Hz, 1 H), 6.28 (dt, J = 15.9, 6.5 Hz, 1 H), 4.80 (dd, J = 6.5, 1.3 Hz, 2 H), 3.50 (s, 2 H), 2.29 (s, 3 H); enol form at 5.04 (d, J = 0.5 Hz, 1 H) and 1.97 (d, J = 0.5 Hz, 3 H).

Diazo transfer and deacetylation were performed as described for **10b**. Diazo transfer was allowed to take place overnight, and hydrolysis occurred over 5 h to provide **10e** as a yellow oil in 54% overall yield after chromatographic purification on silica gel using hexanes/EtOAc (19:1). Slow decomposition of **10e** occurred over time: ^{1}H NMR δ 7.42–7.24 (comp, 5 H), 6.66 (d, J = 15.9 Hz, 1 H), 6.30 (dt, J = 15.9, 6.4 Hz, 1 H), 4.82 (dd, J = 6.4, 1.2 Hz, 2 H), 4.80 (br s, 1 H); ^{13}C NMR δ 166.4, 136.0, 134.1, 128.4, 127.9, 126.5, 123.0, 65.2, 46.1; IR (film) 2112, 1698 cm^{-1}. Anal. Calcd for $C_{11}H_{10}N_2O_3$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.43; H, 4.91; N, 13.84.

***trans*-2-Hexen-1-yl Diazoacetate (10g).** *trans*-2-Hexen-1-ol (3.74 g, 37.3 mmol) was employed in the same procedure as that used for **10e**, and the acetoacetate product was obtained in 90% yield: ^{1}H NMR δ 5.80 (dt, J = 15.3, 6.7 Hz, 1 H), 5.56 (dt, J = 15.3, 6.5 Hz, 1 H), 4.59 (dd, J = 6.5, 0.9 Hz, 2 H), 3.46 (s, 2 H), 2.27 (s, 3 H), 2.04 (q,

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J = 6.7 Hz, 2 H), 1.41 (sex, J = 7.0 Hz, 2 H), 0.90 (t, J = 7.3 Hz, 3 H); enol form at 5.00 (s) and 1.96 (s).

Diazo transfer and deacylation were performed as described for **10b** to produce **10g** in 67% overall yield after chromatographic purification; hexanes/EtOAc (19:1): ^{1}H NMR δ 5.80 (dt, J = 15.3, 6.6 Hz, 1 H), 5.57 (dt, J = 15.3, 6.4 Hz, 1 H), 4.75 (br s), 4.60 (dd, J = 6.4, 0.9 Hz, 2 H), 2.04 (q, J = 6.6 Hz, 2 H), 1.41 (sex, J = 7.3 Hz, 2 H), 0.90 (t, J = 7.1 Hz, 3 H); ^{13}C NMR δ 166.5, 136.5, 123.7, 65.5, 46.1, 34.2, 21.9, 13.5; IR (film) 2104, 1694 cm^{-1}. Anal. Calcd for $C_8H_{12}N_2O_2$: C, 57.13; H, 7.19; N, 16.66. Found: C, 56.98; H, 7.22; N, 16.71.

General Procedure for Forming the Diazoesters 10d,f,h−p and 22a−j. The *p*-toluenesulfonylhydrazone of glyoxylic acid chloride (1.2 equiv) was added to a solution of the appropriate allylic or homoallylic alcohol **9d,f,h−p** or **21a−j**, respectively, in dry CH_2Cl_2 (0.2 M) at 0 °C, and *N,N*-dimethylaniline (1.1 equiv) was added.[34] After stirring at 0 °C for 15 min, Et_3N (5.1 equiv) was added slowly. The resulting dark suspension was stirred for 15 min at 0 °C and then for 30 min at room temperature, whereupon an equal volume of water was added. The reaction mixture was extracted with Et_2O (3 × 1 volume), and the combined organic fractions were dried ($MgSO_4$) and concentrated *in vacuo*. The crude diazoesters thus obtained were purified by distillation or flash chromatography eluting with pentane/Et_2O mixtures (ratio given) to furnish pure **10d,f,h−p** and **22a−j** as yellow oils. Data for compounds **10d,f,j−l** have been recorded previously.[48,50]

***cis*-3,7-Dimethyl-2,6-octadien-1-yl diazoacetate (10h)** was prepared in 74% yield after column chromatography on silica gel using hexanes/EtOAc (9:1) and Kugelrohr distillation (95 °C at 0.25 Torr): ^{1}H NMR δ 5.36 (dt, J = 7.3, 1.4 Hz, 1 H), 5.13−5.06 (m, 1 H), 4.74 (br s, 1 H), 4.65 (dd, J = 7.3, 0.9 Hz, 2 H), 2.17−2.03 (comp, 4 H), 1.77 (dt, J = 1.2, 1.0 Hz, 3 H), 1.69 (d, J = 1.2 Hz, 3 H), 1.60 (s, 3 H); IR (film) 2119, 1702, 1608 cm^{-1}. Anal. Calcd for $C_{12}H_{18}N_2O_2$: C, 64.84; H, 8.16; N, 12.61. Found: C, 64.71; H, 8.25; N, 12.51.

***trans*-3,7-Dimethyl-2,6-octadien-1-yl diazoacetate (10i)** was prepared in 25% yield after Kugelrohr distillation (95° at 0.2 Torr): ^{1}H NMR δ 5.36 (tq, J = 7.2, 0.9 Hz, 1 H), 5.12−5.05 (m, 1 H), 4.76 (br s, 1 H), 4.69 (d, J = 7.2 Hz, 2 H), 2.17−2.02 (comp, 4 H), 1.72 (s, 3 H), 1.70 (s, 3 H), 1.61 (s, 3 H); IR (film) 2119, 1694 cm^{-1}. Anal. Calcd for $C_{12}H_{18}N_2O_2$: C, 64.84; H, 8.16; N, 12.61. Found: C, 64.78; H, 8.31; N, 12.56.

(*E*)-4-Methyl-2-pentenyl diazoacetate (10m) was prepared in 75% yield as a yellow oil: pentane/Et_2O (25:1); ^{1}H NMR δ 5.74 (dd, J = 15.5, 6.6 Hz, 1 H), 5.56−5.46 (m, 1 H), 4.75 (s, 1 H), 4.60 (d, J = 6.6 Hz, 2 H), 2.35−2.28 (m, 1 H), 1.00 (d, J = 6.7 Hz, 6 H); ^{13}C NMR δ 166.7, 143.4, 120.9, 65.7, 46.2, 30.7, 22.0; IR (neat) ν 2120, 1689 cm^{-1}; mass spectrum *m/z* 169.0975 (base) ($C_8H_{12}N_2O_2$ + H requires 169.0977), 141, 105.

(*Z*)-3-Tributylstannyl-2-propenyl diazoacetate (10n) was prepared in 51% yield as a yellow oil: hexane/EtOAc (50:1); ^{1}H NMR δ 6.62 (dt, J = 13.2, 6.5 Hz, 1 H), 6.23 (d, J = 13.2 Hz, 1 H), 4.77 (s, 1 H), 4.58 (d, J = 6.5 Hz, 2 H), 1.63−1.42 (comp, 6 H), 1.39−1.24 (comp, 6 H), 0.98−0.87 (comp, 15 H); ^{13}C NMR δ 165.8, 141.3, 135.8, 67.6, 46.1, 29.0, 27.2, 13.6, 10.3; IR (neat) ν 2920, 2230, 1710, 1400, 1360 1190 cm^{-1}; mass spectrum *m/z* 416.1468 ($C_{17}H_{32}N_2O_2Sn$ requires 416.1486), 358 (base), 358, 357, 356, 355, 303, 301, 291, 289, 177.

(*Z*)-3-Iodo-2-propenyl diazoacetate (10o) was prepared in 73% yield as a yellow oil: hexanes/EtOAc (15:1); ^{1}H NMR δ 6.55−6.46 (comp, 2 H), 4.82 (s, 1 H), 4.77 (d, J = 5.4 Hz, 2 H); ^{13}C NMR δ 166.3 , 135.5, 84.9, 67.1, 46.2; IR (CCl_4) ν 3115, 2935, 2110, 1685, 1020 cm^{-1}; mass spectrum, *m/z* 252.9481 ($C_5H_5N_2O_2I$ + H requires 252.9474), 236, 225, 207, 183, 167 (base), 125.

(*E*)-3-Iodo-2-propenyl diazoacetate (10p) was prepared in 65% yield as a yellow oil: hexanes/EtOAc (15:1); ^{1}H NMR δ 6.59 (dt, J = 6.0, 14.7 Hz, 1 H), 6.48 (d, J = 14.7 Hz, 1 H), 4.77 (s, 1 H), 4.52 (d, J = 5.9 Hz, 2 H); ^{13}C NMR δ 165.9 , 139.4, 81.1, 65.6, 46.1; IR (CCl_4) ν 3115, 2935, 2925, 2110, 1685, 1015 cm^{-1}; mass spectrum, *m/z* 252.9479 ($C_5H_5N_2O_2I$ + H requires 252.9474), 236, 225, 207, 183, 167 (base), 125.

***N*-(2-Propen-1-yl)diazoacetamide (19).** To *N*-allylamine (1.25 g, 21.9 mmol) in anhydrous THF (10 mL) was added succinimidyl diazoacetate[41] (1.83 g, 10.0 mmol) in THF (20 mL), and the resulting solution was stirred for 1 h. The solid was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with hexane/EtOAc (1:1) to provide 1.17 g (94%) of a yellow liquid that solidified upon cooling: mp 38−41 °C; ^{1}H NMR δ 5.84 (ddt, J = 17.0, 10.2, 5.5 Hz, 1 H), 5.62 (br s, 1 H), 5.19 (dq, J = 17.0, 1.4 Hz, 1 H), 5.14 (dd, J = 10.2, 1.4 Hz, 1 H), 4.84 (s, 1 H), 3.91 (m, 2 H); ^{13}C NMR δ 166.0, 134.4, 116.1, 47.0, 42.3; IR (film) 3447, 3326, 2114, 1638, 1518 cm^{-1}. Anal. Calcd for $C_5H_7N_3O$: C, 47.99; H, 5.64; N, 33.58. Found: C, 48.07; H, 5.64; N, 33.58.

5-Cyclohexyl-3-pentyn-1-ol. A solution of cyclohexyl bromide (3.34 g, 18.9 mmol) in anhydrous Et_2O (20 mL) was added dropwise over 20 min to a suspension of Mg (0.50 g, 20.8 mmol) in dry Et_2O (2 mL) while heating gently to initiate formation of the Grignard reagent; the mixture was then stirred for 1 h at room temperature. The reaction was then cooled to −30 °C, and THF (5 mL) and Me_2S (2.2 mL) were added. CuBr (2.10 g, 9.45 mmol) was then added in two portions over 5 min, and the reaction was cooled to −45 °C and stirred for 15 min. A solution of the 4-bromo-3-butyn-1-(-2′-tetrahydropyranyl) ether[57] (2.2 g, 9.45 mmol) in THF (15 mL) was added slowly over 10 min, and the reaction was stirred at −30 °C for 2 h. After warming to room temperature, saturated aqueous NH_4Cl (20 mL) was added, and the aqueous layer was washed with Et_2O (3 × 30 mL). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was dissolved in MeOH (20 mL) containing PTSA (0.10 g, 0.4 mmol), and the mixture was stirred at room temperature for 12 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography eluting with hexanes/EtOAc (5:1) to afford 0.78 g (50%) of 5-cyclohexyl-3-pentyn-1-ol: ^{1}H NMR δ 3.65−3.62 (comp, 2 H), 2.45−3.39 (comp, 2 H), 2.06−2.02 (comp, 2 H), 1.80−1.62 (comp, 5 H), 1.49−1.26 (m, 1 H), 1.25−0.89 (comp, 5 H); ^{13}C NMR δ 81.0, 77.1, 61.2, 37.3, 32.5, 26.4, 26.1, 26.0, 22.9; IR (CH_2Cl_2) ν 3621 cm^{-1}; mass spectrum *m/z* 167.1422 ($C_{11}H_{18}O$ + H requires 167.1435), 167, 149 (base), 121.

(*Z*)-5-Cyclohexyl-3-penten-1-ol (21h). A solution of 5-cyclohexyl-3-pentyn-1-ol (0.35 g, 2.11 mmol) in EtOH (3 mL) containing 5% Pd−$BaSO_4$ (50 mg) and 1 drop of quinoline was stirred under H_2 (1 atm) until 1 equiv of H_2 had been absorbed. The catalyst was removed by filtration through Celite, and the Celite was washed with EtOAc (10 mL). The combined filtrates were concentrated under reduced pressure, and the crude product was purified by flash chromatography eluting with hexanes/EtOAc (5:1) to afford 0.33g (93%) of **21h** as a colorless oil: ^{1}H NMR δ 5.62−5.53 (m, 1 H), 5.44−5.38 (m, 1 H), 3.63 (t, J = 6.4 Hz, 2 H), 2.35−2.23 (comp, 2 H), 1.98−1.94 (comp, 2 H), 1.72−1.74 (comp, 5 H), 1.33−1.10 (comp, 5 H), 0.96−0.84 (comp, 2 H); ^{13}C NMR δ 132.0, 125.5, 62.4, 38.2, 35.1, 33.2, 26.5, 26.4; IR (CH_2Cl_2) ν 3621 cm^{-1}; mass spectrum *m/z* 169.1587 ($C_{11}H_{20}O$ + H requires 169.1592), 169, 151 (base).

3-Butenyl diazoacetate (22a) was prepared in 68% yield as a yellow oil: pentane/Et_2O (15:1); ^{1}H NMR δ 5.84−5.70 (m, 1 H), 5.14−5.05 (comp, 2 H), 4.73 (s, 1 H), 4.20 (t, J = 6.7 Hz, 2 H), 2.39 (m, 2 H); ^{13}C NMR δ 166.8, 133.7, 117.3, 63.8, 46.1, 33.2; IR (neat) ν 2112, 1686 cm^{-1}; mass spectrum *m/z* 141.0665 (base) ($C_6H_8N_2O_2$ + H requires 141.0664), 113, 109.

4-Methyl-3-pentenyl diazoacetate (22b) was prepared in 82% yield from 4-methyl-3-penten-1-ol as a yellow oil: hexanes/EtOAc (15:1); ^{1}H NMR δ 5.09−5.04 (m, 1 H), 4.71 (s, 1 H), 4.10 (t, J = 7.0 Hz, 2 H), 2.67−2.34 (m, 2 H), 1.69 (s, 3 H) 1.52 (s, 3 H); ^{13}C NMR δ 166.8, 134.8, 119.0, 64.5, 46.1, 27.8, 25.7, 17.7; IR (CH_2Cl_2) ν 2113, 1692 cm^{-1}; mass spectrum *m/z* 169.0989 ($C_8H_{13}N_2O_2$ + H requires 169.0977), 169, 154 (base), 137, 111.

3-Methyl-3-butenyl diazoacetate (22c) was prepared in 80% yield as a yellow oil: pentane/Et_2O (15:1); ^{1}H NMR d 4.80 (s, 1 H), 4.73 (s, 2 H), 4.26 (t, J = 6.9 Hz, 2 H), 2.34 (t, J = 6.9 Hz, 2 H), 1.75 (s, 3 H); ^{13}C NMR δ 166.7, 141.5, 112.3, 62.9, 46.1, 36.9, 22.4; IR (neat) ν 2112, 1694 cm^{-1}; mass spectrum *m/z* 155.0823 ($C_7H_{10}N_2O_2$ + H requires 155.0821), 127 (base), 109.

(*Z*)-4-Phenyl-3-butenyl diazoacetate (22d) was prepared in 72% yield as a yellow oil: pentane/Et_2O (15:1); ^{1}H NMR δ 7.31−7.15 (comp, 5 H), 6.52 (d, J = 11.7 Hz, 1 H), 5.61 (dt, J = 11.7, 7.3 Hz, 1 H), 4.68 (s, 1 H,), 4.21 (t, J = 6.7 Hz, 2 H), 2.68−2.60 (m, 2 H); ^{13}C NMR δ 166.4, 136.8, 131.2, 128.4, 128.0, 126.9, 126.6, 63.8, 45.9, 28.1; IR (neat) ν 2108, 1699 cm^{-1}; mass spectrum *m/z* 217.0963 ($C_{12}H_{12}N_2O_2$ + H requires 217.0977) 189, 160, 147, 131 (base).

(*E*)-4-Phenyl-3-butenyl diazoacetate (22e) was prepared in 82% yield as a yellow oil: hexanes/EtOAc (15:1); ^{1}H NMR δ 7.34−7.16 (comp, 5 H), 6.44 (d, J = 15.8 Hz, 1 H), 6.13 (ddd, J = 15.8, 15.6, 14.0 Hz, 1 H) 4.71 (s, 1 H), 4.25 (t, J = 6.7 Hz, 2 H), 2.57−2.50 (m, 2 H); ^{13}C NMR δ 166.7, 137.2, 132.6, 128.5, 127.3, 126.1, 125.4, 64.0, 46.2, 32.6; IR (CH_2Cl_2) ν 2115, 1690 cm^{-1}; mass spectrum m/z 217.0957 ($C_{12}H_{12}N_2O_2$ + H requires 219.0977), 217, 189, 131(base), 117.

(*Z*)-3-Hexenyl diazoacetate (22f) was prepared in 82% yield as a yellow oil: pentane/Et_2O (20:1); ^{1}H NMR δ 5.54−5.46 (m, 1 H), 5.33−5.25 (m, 1 H), 4.72 (s, 1 H), 4.14 (t, J = 6.9 Hz, 2 H), 2.41−2.34 (m, 2 H), 2.09−2.02 (m, 2 H), 0.95 (t, J = 7.5 Hz, 3 H); ^{13}C NMR δ 166.7, 134.6, 123.4, 64.3, 46.1, 26.9, 20.6, 14.1; IR (neat) ν 2112, 1698 cm^{-1}; mass spectrum m/z 169.0977 ($C_8H_{12}N_2O_2$ + H requires 169.0977), 141 (base), 123, 111.

(*E*)-3-Hexenyl diazoacetate (22g) was prepared in 77% yield as a yellow oil: pentane/Et_2O (20:1); ^{1}H NMR δ 5.59−5.50 (m, 1 H), 5.39−5.29 (m, 1 H), 4.72 (s, 1 H), 4.14 (t, J = 6.8 Hz, 2 H), 2.34−2.28 (m, 2 H), 2.04−1.95 (m, 2 H), 0.95 (t, J = 7.5 Hz, 3 H); ^{13}C NMR δ 166.7, 135.2, 123.7, 64.4, 46.1, 32.1, 25.6, 13.6; IR (neat) ν 2109, 1698 cm^{-1}; mass spectrum m/z 169.0975 ($C_8H_{12}N_2O_2$ + H requires 169.0977), 141 (base), 123, 111.

(*Z*)-5-Cyclohexyl-3-pentenyl diazoacetate (22h) was prepared in 81% yield as a yellow oil: hexanes/EtOAc (15:1); ^{1}H NMR δ 5.55−5.46 (m, 1 H), 5.40−5.33 (m, 1 H), 4.71 (s, 1 H), 4.14 (t, J = 7.4 Hz, 2 H), 2.40−2.33 (m, 2 H,), 1.94−1.90 (m, 2 H) 1.66−1.61 (m, 4 H), 1.30−1.09 (m, 4 H), 0.95−0.83 (m, 2 H); ^{13}C NMR δ 166.7, 131.6, 124.6, 64.3, 46.1, 38.1, 35.0, 33.1, 27.1, 26.5, 26.3; IR (CH_2Cl_2) ν 2113, 1691 cm^{-1}; mass spectrum m/z 237.1592 ($C_{13}H_{21}N_2O_2$ + H requires 237.1603), 237, 209 (base), 149, 109.

(*Z*)-5-Phenyl-3-pentenyl diazoacetate (22i) was prepared in 86% yield from 5-phenyl-3-penten-1-ol as a yellow oil: hexanes/EtOAc (15:1); ^{1}H NMR δ 7.29−7.14 (comp, 5 H), 5.71−5.64 (m, 1 H), 5.51−5.46 (m, 1 H), 4.70 (s, 1 H), 4.19 (t, J = 6.8 Hz, 2 H), 3.38 (d, J = 7.4 Hz, 2 H), 2.52−2.46 (m, 2 H); ^{13}C NMR d 166.7, 140.5, 131.05, 128.4, 128.2, 125.9, 125.3, 64.1, 46.1, 33.5, 27.0; IR (CH_2Cl_2) ν 2114, 1693 cm^{-1}; mass spectrum m/z 231.1129 ($C_{13}H_{15}N_2O_2$ + H requires 231.1133), 231 (base), 194, 154.

(*Z*)-4-Trimethylsilyl-3-butenyl diazoacetate (22j) was prepared in 80% yield from 4-trimethylsilyl-3-buten-1-ol as a yellow oil: pentane/Et_2O (20:1); ^{1}H NMR δ 6.29−6.19 (m, 1 H), 5.64 (d, J = 14.1 Hz, 1 H), 4.73 (s, 1 H), 4.19 (t, J = 6.7 Hz, 2 H), 2.50−2.42 (m, 2 H), 0.12 (s, 9 H); ^{13}C NMR δ 166.7, 143.0, 132.6, 64.1, 46.1, 32.9, 0.08; IR (CH_2Cl_2) ν 2115, 1689 cm^{-1}; mass spectrum m/z 213.1051 ($C_9H_{16}N_2O_2$-Si + H requires 213.1059), 213 (base), 159, 102.

General Procedure for Cyclopropanation of Allylic and Homoallylic Diazoacetates 10a,b,d−p and 22a−j in the Presence of Rh_2(*S*-MEPY)$_4$ (5). A solution of the appropriate diazoester **10a,b,d−p** and **22a−j** in dry CH_2Cl_2 (1.0×10^{-2} M) was added *via* syringe pump to a refluxing solution of the chiral rhodium catalyst **5** in CH_2Cl_2 (1.0×10^{-2} equiv, ca. $1.0-10.0 \times 10^{-4}$ M) over a period of 12−18 h. The initial blue color had turned to olive by the end of the addition. The reaction was cooled to room temperature, and the solvents were removed by distillation at atmospheric pressure. The crude product was purified either by flash chromatography eluting with pentane/Et_2O mixtures (ratios given) or by filtration through a plug of alumina using CH_2Cl_2 as the eluent followed by Kugelrohr distillation to give the cyclopropyl lactones. Data for compounds **11d,f,j−l** have been recorded previously.[48,50]

(1*R*,5*S*)-3-Oxabicyclo[3.1.0]hexan-2-one (11a) was obtained in 75% yield; bp 80 °C (5 Torr); lit.[12b] bp 60 °C (1 Torr). Enantiomer separation on a 30 m Chiraldex G-TA column operated at 80 °C for 2 min and then programmed to 150 °C at 1°/min: 44.4 min for **(1*R*,5*S*)-11a** enantiomer, 46.0 min for **(1*S*,5*R*)-11a** enantiomer; 95% ee; $[\alpha]^{23}_D$ = +60.2° (*c* 1.01, $CHCl_3$); 97% ee based on the specific rotation of optically pure **(1*R*,5*S*)-11a**, $[\alpha]^{20}_D$ = +62.0 (*c* 2.5, $CHCl_3$),[13a] or 88% ee based on a report of $[\alpha]^{25}_D$ = +68.7 (*c* 4.6, $CDCl_3$);[58] ^{1}H NMR δ 4.37 (dd, J = 9.2, 4.9 Hz, 1 H), 4.25 (dd, J = 9.2, 1.0 Hz, 1 H), 2.26 (ddd, J = 9.7, 7.5, 4.6 Hz, 1 H), 2.09 (dddd, J = 9.7, 4.6, 3.4, 1.0 Hz, 1 H), 1.29 (ddd, J = 8.8, 7.7, 4.9 Hz, 1 H), and 0.90 (dt, J = 4.6, 3.4 Hz, 1 H).

(1*S*,5*R*)-6,6-Dimethyl-3-oxabicyclo[3.1.0]hexan-2-one (11b) was obtained in 89% yield; bp 120 °C (15 Torr); lit.[12b] bp 105 °C (10 Torr). Enantiomer separation on a Chiraldex G-TA column operated at 140 °C: 13.8 min for **(1*S*,5*R*)-11b** enantiomer, 19.8 min for **(1*R*,5*S*)-11b** enantiomer; 98% ee; $[\alpha]^{23}_D$ = +85.0° (*c* 1.96, $CHCl_3$); 95% ee based on 81% optically pure **(1*R*,5*S*)-11b**, $[\alpha]^{25}_D$ = −72.8° (*c* 1.4, $CHCl_3$);[59] ^{1}H NMR δ 4.36 (dd, J = 9.8, 5.5 Hz, 1 H), 4.15 (d, J = 9.8 Hz, 1 H), 2.04 (dd, J = 6.2, 5.5 Hz, 1 H), 1.95 (d, J = 6.2 Hz, 1 H), 1.18 (s, 3 H), 1.17 (s, 3 H).

(1*R*,5*S*)-5-Methyl-3-oxabicyclo[3.1.0]hexan-2-one (11c) was obtained from Rh_2(4*S*-MACIM)$_4$ (1.0 mol%) catalyzed diazodecomposition of **10c** in 90% yield after Kugelrohr distillation: lit.[60] bp 107−110 °C (4 Torr). Enantiomer separation on a 30 m Chiraldex G-TA column operated at 120 °C: 24.9 min for the **(1*S*,5*R*)-11c** enantiomer, 25.7 min for the **(1*R*,5*S*)-11c** enantiomer; 78% ee. By washing the oily solid twice with cold pentane (2 mL/50 mg **11c**) a white solid, mp 44 °C, was obtained whose optical purity was 93% ee. A subsequent wash of this white solid with pentane gave a solid material, >99.5% ee by GC analysis on the Chiraldex G-TA column, whose optical rotation was $[\alpha]^{23}_D$ = −53.0° (*c* 0.91, $CHCl_3$); ^{1}H NMR δ 4.19 (d, J = 9.2 Hz, 1 H), 4.05 (dd, J = 9.2, 0.9 Hz, 1 H), 1.81 (ddd, J = 9.1, 3.2, 0.9 Hz, 1 H), 1.36 (s, 3 H), 1.16 (dd, J = 9.2, 4.7 Hz, 1 H), 0.99 (dd, J = 4.7, 3.2 Hz, 1 H); IR (film) 1779 cm^{-1}.

[1*R*-(1α,5α,6β)]-6-Phenyl-3-oxabicyclo[3.1.0]hexan-2-one (11e) was obtained in 78% yield. Enantiomer separation on a 30 m Chiraldex G-TA column operated at 150 °C: 72.9 min for **(1*S*)-11e** enantiomer, 79.6 min for **(1*R*)-11e** enantiomer; 68% ee. Lactone was purified on a chromatotron (hexanes/EtOAc, 1:1) and recrystallized until constant $[\alpha]_D$ (2×): mp 106 °C; $[\alpha]^{23}_D$ of recrystallized (hexanes/EtOAc), enantiomerically pure **11e** = +130° (*c* 0.29, $CHCl_3$); ^{1}H NMR δ 7.32−7.25 (comp, 3 H), 7.09 (dt, J = 6.7, 2.0 Hz, 2 H), 4.48 (dd, J = 9.5, 4.6 Hz, 1 H), 4.42 (d, J = 9.5 Hz, 1 H), 2.55−2.51 (m, 1 H), 2.37−2.32 (comp, 2 H). ^{13}C NMR δ 168.3, 138.2, 129.8, 128.2, 127.0, 70.7, 30.4, 28.4, and 27.1. Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.86; H, 5.74. Found: C, 75.66; H, 5.71. Lactone **(1*S*)-11e** (25 mg, 0.12 mmol) was hydrolyzed with 4% KOH (8 mL) and THF (2 mL) (room temperature, 36 h). The mixture was carefully acidified with concentrated HCl, and the hydroxy acid was extracted with Et_2O. The combined Et_2O extracts were dried ($MgSO_4$) and evaporated, and the *l*-menthyl esters were formed using a catalytic amount of $SOCl_2$ and *l*-(−)-menthol; GC baseline separation of the diastereomeric esters on a phenylsilicone column suggested 65% de.

[1*R*-(1α,5α,6β)]-6-*n*-Propyl-3-oxabicyclo[3.1.0]hexan-2-one (11g) was obtained in 93% yield: bp 130 °C (5 Torr); $[\alpha]^{23}_D$ = +51.6° (*c* 0.736, $CHCl_3$) (85% ee). Enantiomer separation on a 30 m Chiraldex G-TA column operated at 120 °C for 20 min then programmed to 150 °C at 10°/min: 35.0 min for **(1*S*)-11g** enantiomer, 37.7 min for **(1*R*)-11g**; 85% ee; ^{1}H NMR δ 4.30 (dd, J = 9.2, 4.8 Hz, 1 H), 4.23 (dt, J = 9.2, 0.8 Hz, 1 H), 2.05−1.95 (m, 1 H), 1.85 (ddd, J = 5.8, 2.6, 0.8 Hz, 1 H), 1.55−1.40 (comp, 2 H), 1.40−1.30 (comp, 2 H), 1.25−1.18 (m, 1 H), and 0.96 (t, J = 7.1 Hz, 3 H); ^{13}C NMR δ 175.1, 68.5, 32.2, 25.2, 23.0, 22.9, 20.9, 12.7; IR (film) 3032, 2971, 2933, 2880, 1768 cm^{-1}; mass spectrum, m/z 140, 139, 98, 95, 86, 85 (base), 81, 67, 56, 55, 54, 53. Anal. Calcd for $C_8H_{12}O_2$: C, 68.57; H, 8.57. Found: C, 68.34; H, 8.68. Lactone **(1*S*)-11g** (50 mg, 0.36 mmol) was hydrolyzed with 4% KOH solution in THF (room temperature, 14 h). The mixture was carefully acidified with concentrated HCl, and the hydroxy acid was extracted with Et_2O. The combined Et_2O extracts were dried ($MgSO_4$) and evaporated, and the (*S*)-1-phenyl-1-butyl esters were formed using a catalytic amount of $SOCl_2$ and (*S*)-(−)-1-phenyl-1-butanol; GC baseline separation of the diasteromeric esters on a phenylsilicone column suggested 75% de, but some racemization of the alcohol, as evidenced by the concurrent formation of 1-phenyl-1-butyl ether, may have occurred during the acid catalyzed esterification.

[1*S*-(1α,5α)]-6β-Methyl-6α-(4-methyl-3-penten-1-yl)-3-oxabicyclo-[3.1.0]hexan-2-one (11h) was obtained in 79% yield after chromatography on silica gel eluting with hexane/EtOAc (gradient 8:1 → 5:1) followed by Kugelrohr distillation (bp 100 °C at 0.25 Torr). Enantiomer separation on a 30 m Chiraldex G-TA column operated at 150 °C: 33.2 min for the **(1*S*)-11h** enantiomer, 38.4 min for the **(1*R*)-11h** enantiomer; 93% ee; $[\alpha]^{23}_D$ = +40.2° (*c* 1.74, $CHCl_3$) for 93% ee; ^{1}H NMR δ 5.12 (t of hept, J = 7.2, 1.4 Hz, 1 H), 4.36 (dd, J = 9.9, 5.6 Hz, 1 H), 4.16 (dt, J = 9.9, 1.1 Hz, 1 H), 2.14 (q, J = 7.7 Hz, 2 H),

2.07 (dt, J = 6.3, 1.0 Hz, 1 H), 1.96 (dd, J = 6.3, 1.0 Hz, 1 H), 1.68 (d, J = 1.0 Hz, 3 H), 1.61 (s, 3 H), 1.54−1.36 (comp, 2 H), 1.16 (s, 3 H); ^{13}C NMR δ 174.9, 132.4, 123.4, 66.5, 30.9, 30.8, 28.4, 27.0, 25.7, 24.9, 22.6, 17.6; IR (film) 1770, 1685, 1642 cm^{-1}; mass spectrum, *m/z* 195 (M + 1), 194 (M), 179, 163, 126, 112, 111, 110, 109, 107, 95, 93, 85, 81, 79, 69 (base), 67, 55, 53. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.23; H, 9.40. Use of Rh_2(5*R*-MEPY)$_4$ gave (**1*R*)-11h** with 93% ee; the racemic **11h** was formed in 37% isolated yield from Rh_2(cap)$_4$ catalyzed diazodecomposition of **10h**.

[1*S*-(1α,5α)]-6a-Methyl-6b-(4-methyl-3-penten-1-yl)-3-oxabicyclo-[3.1.0]hexan-2-one (11i) was obtained in 88% yield after Kugelrohr distillation (bp 100 °C at 0.15 Torr). Enantiomer separation on a 30 m Chiraldex G-TA column operated at 150 °C: 54.1 min for the **(1*S*)-11i** enantiomer, 57.9 min for the **(1*R*)-11i** enantiomer; 95% ee; $[\alpha]^{24}_D$ = +56.1° (*c* 1.44, $CHCl_3$) for 95% ee; ^{1}H NMR δ 5.06 (t of hept, J = 7.1, 1.4 Hz, 1 H), 4.38 (dd, J = 9.9, 5.5 Hz, 1 H), 4.15 (dt, J = 9.9, 1.0 Hz, 1 H), 2.09 (q, J = 7.7 Hz, 2 H), 2.06 (dt, J = 6.4, 1.0 Hz, 1 H), 1.96 (dd, J = 6.4, 0.9 Hz, 1 H), 1.68 (s, 3 H), 1.61 (s, 3 H), 1.43−1.23 (comp, 2 H), 1.17 (s, 3 H); ^{13}C NMR δ 175.0, 132.4, 123.2, 66.5, 39.3, 29.8, 29.4, 26.7, 25.7, 25.0, 17.7, 11.7; IR (film) 1770, 1677 cm^{-1}; mass spectrum, *m/z* 195 (M + 1), 194 (M), 179, 163, 126, 112, 111, 110, 109, 107, 95, 93, 85, 81, 79, 69 (base), 67, 55, 53. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.13; H, 9.30. The racemic **11i** was formed in 55% isolated yield from Rh_2(cap)$_4$ catalyzed diazodecomposition of **10i.**

[1*R*-(1α,5α,6β)]-6-(2′-Propyl)-3-oxabicyclo[3.1.0]hexan-2-one (11m) was prepared in 71% yield as a colorless oil: pentane/Et_2O (5:1). The enantiomeric purity was determined to be 54% according to method B: ^{1}H NMR δ 4.30 (dd, J = 9.3, 4.8 Hz, 1 H), 4.20 (d, J = 9.3 Hz, 1 H), 2.36−2.29 (m, 1 H), 2.18 (dd, J = 6.0, 3.8 Hz, 1 H), 1.35−1.16 (comp, 2 H), 1.02 (d, J = 5.9 Hz, 6 H); ^{13}C NMR δ 171.1, 69.5, 33.8, 30.6, 23.2, 23.0, 21.5; IR ($CHCl_3$) ν 1766 cm^{-1}; mass spectrum, *m/z* 141.0923 (base) ($C_8H_{12}O_2$ + H requires 141.0916), 139, 123.

[1*R*-(1α,5α,6α)]-6-Tributylstannyl-3-oxabicyclo[3.1.0]hexan-2-one (11n) was prepared in 79% yield as a colorless oil: hexanes/EtOAc (10:1). The enantiomeric purity was determined to be ≥94% according to method B: $[\alpha]^{21}_D$ +3.7° (*c* 0.86, $CHCl_3$); ^{1}H NMR δ 4.30 (dd, J = 4.8, 9.4 Hz, 1 H), 4.05 (d, J = 9.4 Hz, 1 H), 2.43 (ddd, J = 4.8, 5.6, 9.1 Hz, 1 H), 2.20 (dd, J = 5.6, 9.1 Hz, 1 H), 1.58−1.43 (comp, 6 H), 1.40−1.21 (comp, 6 H), 0.97 (dd, J = 7.1, 9.0 Hz, 6 H), 0.90 (t, J = 7.2 Hz, 9 H), 0.16 (t, J = 9.1 Hz, 1 H); ^{13}C NMR δ 177.5, 69.6, 28.9, 27.2, 21.4, 20.4, 13.6, 9.9, 9.3; IR (neat) ν 2950, 1780, 1040, 1000, 980, 760 cm^{-1}; mass spectrum, *m/z* 387.1354 ($C_{17}H_{31}O_2Sn$ requires 387.1346), 331 (base), 329, 327.

1*R*-(1α,5α,6α)]-6-Iodo-3-oxabicyclo[3.1.0]hexan-2-one (11o) was prepared in 78% yield as a pale yellow solid: hexanes/EtOAc (3:1); mp 77−78 °C. The enantiomeric purity was determined to be ≥94% according to method B; The reaction mixture was cooled to room temperature and concentrated in vacuo; ^{1}H NMR δ 4.55 (dd, J = 5.2, 10.1 Hz, 1 H), 4.00 (d, J = 10.1 Hz, 1 H), 3.39 (t, J = 7.4 Hz, 1 H), 2.62 (t, J = 6.9 Hz, 1 H), 2.38 (dd, J = 6.1, 12.4 Hz, 1 H); ^{13}C NMR δ 172.7, 69.9, 25.6, 22.9, −5.1; IR ($CHCl_3$) ν 2960, 1780, 1470, 1380, 1240, 1180, 1040 cm^{-1}; mass spectrum, *m/z* 224.9426 (C_5H_5IO + H requires 224.9413), 207, 180, 111.

[1*S*-(1α,5α,6β)]-6-Iodo-3-oxabicyclo[3.1.0]hexan-2-one (11p) was prepared in 70% yield as a pale yellow solid: hexanes/EtOAc (3:1); mp 76−77 °C. The enantiomeric purity was determined to be 67% according to method B; ^{1}H NMR δ 4.33 (d, J = 9,5 Hz, 1 H), 4.27 (dd, J = 4.9, 9.1 Hz, 1 H), 2.60 (m, 1 H), 2.58 (m, 1 H), 2.42 (dd, J = 2.3, 6.1 Hz, 1 H); ^{13}C NMR δ 172.3, 69.1, 28.6, 28.0, −17.4; IR ($CHCl_3$) ν 2975, 1765, 1480, 1175, 1085 cm^{-1}; mass spectrum, *m/z* 224.9406 (C_5H_5IO + H requires 224.9413), 207, 180, 111.

3-Benzyloxycarbonylimidazolidin-2-one-4(*S*)-carboxylic Acid. To a solution of NaOH (9.01 g, 225 mmol) in H_2O (200 mL), cooled to 0 °C in an ice-bath, was added dropwise bromine (13.21 g, 82.6 mmol) in H_2O (5 mL) from an addition funnel, maintaining a temperature of 0−5 °C. *N*-Benzyloxycarbonyl-L-asparagine (20.00 g, 75.1 mmol) was added rapidly to this yellow-brown solution at 0 °C. The resulting pale-yellow reaction mixture was heated at 50 °C for 3 h, then cooled, $Na_2S_2O_3$ crystals (~0.05 g) were added, and the resulting solution was washed with ether (2 × 50 mL) and then acidified to pH 2 with 6 N HCl. The cloudy aqueous mixture was allowed to crystallize overnight in a refrigerator, yielding white flakes which were recrystallized from H_2O to give 16.2 g (81%) of a white, crystalline product: mp 160 °C (lit.[61] mp 164 °C), $[\alpha]^{25}_D$ = −62.2° (*c* 0.51, MeOH); ^{1}H NMR (DMSO-d_6) δ 13.27 (s, 1 H), 7.57 (s, 1 H), 7.37−7.30 (comp, 5 H), 5.17 (s, 2 H), 4.67 (dd, J = 10.2, 2.0 Hz, 1 H), 3.67−3.61 (m, 1 H), 3.23−3.19 (m, 1 H); ^{13}C NMR (DMSO-d_6) δ 172.8, 154.9, 152.1, 136.9, 129.3, 128.9, 128.4, 67.6, 56.1.

Methyl 3-Benzyloxycarbonylimidazolidin-2-one-4(*S*)-carboxylate. To a rapidly stirred suspension of 3-benzyloxycarbonylimidazolidin-2-one-4(*S*)-carboxylic acid (10.0 g, 37.8 mmol) in methanol (100 mL) was added dropwise $SOCl_2$ (4.95 g, 41.6 mmol) at room temperature, and the mixture was stirred for 24 h. The solvent was removed under reduced pressure, and the residual white powder was dissolved in excess boiling EtOAc (~300 mL). The solution was cooled, washed with 5% aqueous $NaHCO_3$ (30 mL), dried ($MgSO_4$), filtered, and concentrated. The resulting white solid was recrystallized from EtOAc/hexane and dried *in vacuo* to give 9.67 g (92% yield) of white, flakey crystals: mp 142 °C (lit.[62] mp = 139−140 °C); $[\alpha]^{25}_D$ = −68.1° (*c* 0.36, CH_2Cl_2); ^{1}H NMR δ 7.39−7.31 (comp, 5 H), 6.65 (s, 1 H), 5.34 (d, J = 12.4 Hz, 1 H), 5.20 (d, J = 12.4 Hz, 1H), 4.75 (dd, J = 10.1, 3.6 Hz, 1 H), 3.77−3.70 (m, 1 H), 3.67 (s, 3 H), 3.41 (dd, J = 9.8, 3.6 Hz, 1 H); ^{13}C NMR δ 170.5, 155.2, 151.4, 135.5, 129.1, 124.4, 123.4, 68.5, 56.1, 53.2, 40.8.

General Procedure for the *N*-Acylation of Methyl 3-Benzyloxycarbonylimidazolidin-2-one-4(*S*)-carboxylate. To a stirred solution of methyl 3-benzyloxycarbonylimidazolidin-2-one-4(*S*)-carboxylate (5.0 g, 18.0 mmol), 4-dimethylaminopyridine (0.33 g, 2.70 mmol), and anhydrous pyridine (2.13 g, 27.0 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0 °C under nitrogen was added dropwise the given acylating agent (36.0 mmol) as either the acid anhydride or acid chloride. The reaction mixture was then refluxed until TLC indicated 100% conversion (time given). The reaction mixture was then cooled and washed with saturated aqueous NaCl (2 × 30 mL), 1% aqueous HCl (3 × 30 mL), saturated aqueous Na_2CO_3 (3 × 30 mL), and H_2O (2 × 30 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a pale yellow solid that was purified by column chromatography (eluting solvent given) to give the desired product as a white crystalline solid.

Methyl 1-acetyl-3-benzyloxycarbonylimidazolidin-2-one-4(*S*)-carboxylate was prepared in 90% yield as a white, crystalline solid using the above procedure: acetic anhydride; 20 h; 50% EtOAc/hexanes; mp 110−111°C; $[\alpha]^{25}_D$ = −14.1° (*c* 0.23, CH_2Cl_2); ^{1}H NMR δ 7.42−7.34 (comp, 5 H), 5.36 (d, J = 12.2 Hz, 1 H), 5.25 (d, J = 12.2 Hz, 1 H), 4.71 (dd, J = 9.9, 3.8 Hz, 1 H), 3.97−3.86 (comp, 2 H), 3.72 (s, 3 H), 2.54 (s, 3 H); ^{13}C NMR δ 170.5, 169.4, 150.7, 149.2, 134.6, 128.8, 128.6, 128.2, 68.8, 53.0, 52.1, 42.1, 23.8. Anal. Calcd for $C_{15}H_{16}N_2O_6$: C, 56.25; H, 5.03; N, 8.75. Found: C, 56.20; H, 5.10; N, 8.76.

Methyl 1-phenylacetyl-3-benzyloxycarbonylimidazolidin-2-one-4(*S*)-carboxylate was prepared as a solid in 51% yield and 90−92% purity using the above procedure: phenylacetyl chloride. Attempts to obtain >95% purity were not successful: ^{1}H NMR δ 7.38−7.25 (comp, 10 H), 5.37 (d, J = 12.2 Hz, 1 H), 5.25 (d, J = 12.2 Hz, 1 H), 4.68 (dd, J = 9.8, 3.9 Hz, 1 H), 4.33 (d, J = 15.9 Hz, 1 H), 4.24 (d, J = 15.9 Hz, 1 H), 3.98−3.85 (comp, 2 H), 3.68 (s, 3 H); ^{13}C NMR δ 171.0, 169.4, 150.6, 149.1, 134.6, 133.3, 130.4, 128.8, 128.6, 128.4, 128.3, 127.1, 68.9, 53.1, 52.2, 42.4, 41.8.

General Procedure for Hydrogenolysis of the *N*-Benzyloxycarbonyl Group. A solution of methyl 1-acyl-3-benzyloxycarbonylimidazolidin-2-one-4(*S*)-carboxylate (7.0 g) containing 5% Pd/C (0.14 g) in MeOH (140 mL) was shaken in a Parr hydrogenator under hydrogen (2 atm) until hydrogen uptake ceased and TLC indicated 100% conversion. The Pd/C catalyst was removed by filtration through a Celite plug, and the filtrate was concentrated to give a clear oil that was purified by column chromatography on silica gel (solvent given).

Methyl 1-acetylimidazolidin-2-one-4(*S*)-carboxylate was prepared in 94% yield as a colorless oil that solidified overnight after pumping at 0.5 Torr to give a white crystalline solid: EtOAc; mp 43−45 °C; $[\alpha]^{23}_D$ −43.8° (*c* 3.20, CH_2Cl_2); ^{1}H NMR δ 6.38 (s, 1 H), 4.33−4.28 (m, 1 H), 4.18−4.08 (comp, 2 H), 3.82 (s, 3 H), 2.49 (s, 3 H); ^{13}C NMR δ 170.9, 170.5, 155.5, 53.0, 49.5, 44.8, 23.3. Anal. Calcd for

$C_7H_{10}N_2O_4$: C, 45.16; H, 5.41; N, 15.05. Found: C, 45.08; H, 5.46; N, 15.03.

Methyl 1-phenylacetylimidazolidin-2-one-4(*S*)-carboxylate was prepared in 78% yield as a colorless oil: hexanes/EtOAc (1:1); ^{1}H NMR δ 7.35−7.20 (m, 5 H), 5.92 (s, 1 H), 4.32 (d, J = 15.5 Hz, 1 H), 4.23 (d, J = 15.5 Hz, 1 H), 4.30−4.16 (m, 1 H), 4.15−4.04 (comp, 2 H), 3.80 (s, 3 H); ^{13}C NMR δ 171.3, 170.7, 155.2, 134.2, 129.7, 128.4, 126.9, 53.1, 49.5, 45.2, 41.3.

Dirhodium(II) Tetrakis[methyl 1-acetylimidazolidin-2-one-4(*S*)-carboxylate], Rh_2(4*S*-MACIM)$_4$ (14). A mixture of rhodium(II) acetate (525 mg, 1.2 mmol), methyl 1-acetylimidazolidin-2-one-4(*S*)-carboxylate (3.33 g, 17.8 mmol), anhydrous benzonitrile (3 mL), and anhydrous chlorobenzene (25 mL) was heated at reflux under nitrogen in a round-bottom flask fitted with a small Soxhlet extractor that held a cellulose thimble containing an oven-dried mixture (1:1, 4 g) of Na_2CO_3 and sand on top of activated, powdered 4 Å molecular sieves (0.5 g). The rate of reflux was maintained to allow Soxhlet cycling once every 40 s. Reflux was continued for 8 h, at which stage HPLC analysis (μ-Bondapak-CN reverse-phase column, MeOH) showed the reaction to be complete. After cooling, the solvent was removed *in vacuo*, and the remaining purple oil was purified by column chromatography on reverse phase silica (BAKERBOND Cyano 40 μm prep LC packing) eluting with methanol. The first purple band was collected, anhydrous acetonitrile was added to give a red-orange solution of the acetonitrile adduct, and the solvent was evaporated to yield 0.78 g (63%) of Rh_2(4*S*-MACIM)$_4$(CH_3CN)$_2$ as a reddish powder (>99.9% purity by HPLC). Excess ligand was reclaimed after concentration of the eluent and column chromatography of the subsequent clear oil on a 5 cm silica-gel plug eluting with EtOAc: $[\alpha]^{22}_D$ = −325° (*c* 0.104, CH_3CN); ^{1}H NMR (acetone-d_6) δ 4.13−4.03 (comp, 4 H), 3.93−3.85 (comp, 4 H), 3.79 (dd, J = 7.6, 2.9 Hz, 2 H), 3.78 (s, 6 H), 3.56−3.51 (comp, 2 H), 3.56 (s, 6 H), 2.26 (s, 6 H), 2.21 (s, 6 H), 2.05 (s, 6 H); ^{13}C NMR (acetone-d_6) δ 174.7, 173.5, 168.3, 168.2, 165.5, 165.2, 117.6, 58.4, 52.5, 51.8, 47.7, 47.4, 23.5, 1.2. Anal. Calcd for $C_{32}H_{42}N_{10}O_{16}Rh_2$: C, 37.37; H, 4.12; N, 13.62. Found: C, 37.29; H, 4.20; N, 13.56.

Dirhodium(II) Tetrakis[methyl 1-phenylacetylimidazolidin-2-one-4(*S*)-carboxylate], Rh_2(4*S*-MPAIM)$_4$ (15). A mixture of rhodium-(II) acetate (160 mg, 0.36 mmol), methyl 1-phenylacetylimidazolidin-2-one-4(*S*)-carboxylate (1.30 g, 4.94 mmol), and anhydrous chlorobenzene (20 mL) was heated at reflux under nitrogen in a round-bottom flask fitted with a small Soxhlet extractor that held a cellulose thimble containing an oven-dried mixture (2:1, 5 g) of Na_2CO_3 and sand. Reflux was continued for 8 h, at which stage HPLC analysis (μ-Bondapak-CN reverse-phase column, MeOH) showed the reaction to be complete. After cooling, the solvent was removed under reduced pressure, and the residue was chromatographed on a column of reverse phase silica gel (BAKERBOND Cyano 40 μm prep LC packing) eluting with methanol. The center rose colored band was collected, and the solvent was evaporated to yield 0.21 g (44%) of Rh_2(4*S*-MPAIM)$_4$ as a red powder (>99.9% purity by HPLC): $[\alpha]^{23}_D$ = −385° (*c* 0.110, CH_3CN); ^{1}H NMR δ 7.37−7.21 (comp, 20 H), 4.65 (d, J = 14.0 Hz, 2 H), 4.10−3.70 (comp, 16 H), 3.62 (s, 6 H), 3.57 (s, 6 H); ^{13}C NMR δ 173.2, 172.9, 169.2, 168.8, 164.7, 164.6, 135.4, 129.7, 129.2, 128.2, 126.8, 126.7, 59.3, 58.8, 52.2, 52.0, 47.1, 46.9, 41.3, 40.9. Anal. Calcd for $C_{52}H_{52}N_8O_{16}Rh_2$: C, 49.93; H, 4.19. Found: C, 49.13; H, 4.36.

(1*R*,5*S*-)-3-Azabicyclo[3.1.0]hexan-2-one (20). To a solution of Rh_2(4*S*-MEOX)$_4$ (8.6 mg, 0.01 mmol) in refluxing CH_2Cl_2 (50 mL) was added *N*-allyldiazoacetamide (0.125 g, 1.00 mmol) in CH_2Cl_2 (5.0 mL) via a syringe pump (0.25 mL/h) over a period of 20 h. The resulting solution was refluxed for 1 h and then filtered through silica. The solvent was evaporated, and the residue was distilled (Kugelrohr) at 100−115 °C (0.5 Torr) to give 39 mg (40%) of **20** as a white crystalline solid: mp 118−119 °C; lit.[63] mp 91−93 °C. Enantiomer separation on a Chiraldex G-TA column operated at 100 °C for 5 min and then programmed to 150 °C at 5°/min: 26.0 min for **(1*R*,5*S*)-20** enantiomer, 28.5 min for **(1*S*,5*R*)-20** enantiomer; 98% ee; $[\alpha]^{22}_D$ = +68.4° (*c* 1.22, $CHCl_3$); ^{1}H NMR δ 6.28 (br s, 1 H), 3.53 (dd, J = 10.1, 5.8 Hz, 1 H), 3.35 (dd, J = 10.1, 1.0 Hz, 1 H), 2.00−1.90 (m, 1 H), 1.85−1.75 (m, 1 H), 1.11 (ddd, J = 8.2, 7.6, 4.6 Hz, 1 H), 0.67 (q, J = 4.4 Hz, 1 H); ^{13}C NMR δ 179.1, 44.3, 19.4, 14.8, 12.3; mass spectrum, *m/z* 98 (M + 1), 97 (M), 82, 78, 69, 68 (base); IR (film) ν 3455, 3244, 1693 cm^{-1}; Anal. Calcd for C_5H_7NO: C, 61.83; H, 7.27; N, 14.42. Found: C, 61.76; H, 7.38; N, 14.46.

[1*R*-(1α,6α)]-3-Oxabicyclo[4.1.0]heptan-2-one (23a) was prepared in 80% yield as a colorless oil: pentane/Et_2O (2:1). The enantiomeric purity was determined to be 71% by method A: ^{1}H NMR δ 4.27−4.20 (m, 1 H), 4.14−4.04 (m, 1 H), 2.26−2.14 (m, 1 H), 2.01−1.76 (comp, 3 H), 1.50−1.45 (m, 1 H), 1.19−1.11 (m, 1 H); ^{13}C NMR δ 171.4, 63.6, 20.5, 15.8, 14.6, 7.7; IR ($CHCl_3$) ν 1721 cm^{-1}; mass spectrum *m/z* 112.0532 ($C_6H_8O_2$ requires 112.0524) 82, 67, 54, 39.

[1*R*-(1α,6α)]-7,7-Dimethyl-3-oxabicyclo[4.1.0]heptan-2-one (23b) was prepared in 74% yield as a colorless oil: hexanes/EtOAc (5:1). The enantiomeric purity was determined to be 77% by method B: ^{1}H NMR δ 4.17−4.4.13 (comp, 2 H), 2.02−1.93 (m, 1 H), 1.82−1.72 (m, 1 H), 1.55−1.42 (comp, 2 H), 1.16 (s, 3 H), 1.09 (s, 3 H); ^{13}C NMR δ 170.9, 69.3, 27.4, 25.1, 24.9, 23.8, 19.2, 16.3; IR ($CDCl_3$) ν 1728 cm^{-1}; mass spectrum *m/z* 141.0912 ($C_8H_{12}O_2$ + H requires 141.0915), 141 (base), 125, 111.

[1*R*-(1α,6α)]-6-Methyl-3-oxabicyclo[4.1.0]heptan-2-one (23c) was prepared in 76% yield as a colorless oil: pentane/Et_2O (2:1). The enantiomeric purity was determined to be 83% by methods A and B: ^{1}H NMR δ 4.25−4.19 (m, 1 H), 4.08−3.98 (m, 1 H), 2.08−1.97 (m, 1 H), 1.93−1.87 (m, 1 H), 1.67−1.64 (m, 1 H), 1.63−1.57 (m, 1 H), 1.27 (s, 3 H), 0.97 (dd, J = 9.3, 5.7 Hz, 1H); ^{13}C NMR δ 171.7, 64.6, 27.1, 23.8, 23.4, 21.8, 15.4; IR ($CHCl_3$) ν 1717 cm^{-1}; mass spectrum *m/z* 127.0774 (base) ($C_7H_{10}O_2$ + H requires 127.0759), 109.

[1*R*-(1α,6α,7α)]-7-Phenyl-3-oxabicyclo[4.1.0]heptan-2-one (23d) was prepared in 73% yield as a white solid: pentane/Et_2O (2:1); mp 120−122 °C. The enantiomeric purity was determined to be 88% by method C: ^{1}H NMR δ 7.37−7.25 (comp, 5 H), 3.93−3.82 (m, 1 H), 2.95 (m, 1 H), 2.81 (m, 1 H), 2.37−2.22 (comp, 2 H), 2.08−1.95 (comp, 2 H); ^{13}C NMR δ 171.0, 135.7, 129.1, 128.6, 127.5, 65.5, 28.4, 19.6, 19.3, 18.5; IR ($CHCl_3$) ν 1709 cm^{-1}; mass spectrum *m/z* 189.0919 ($C_{12}H_{12}O_2$ + H requires 189.0916) 143, 129 (base), 115.

[1*R*-(1α,6α,7β)]-7-Phenyl-3-oxabicyclo[4.1.0]heptan-2-one (23e) was prepared in 55% yield as a colorless oil: hexanes:EtOAc (3:1). The enantiomeric purity was determined to be 73% by method B: ^{1}H NMR δ 7.31−7.16 (comp, 3 H), 4.35−4.19 (comp, 2 H), 2.91−2.88 (ap. t, J = 4.3 Hz, 1 H), 2.30−2.09 (comp, 4 H); ^{13}C NMR δ 169.5, 138.0, 128.7, 127.0, 126.2, 64.5, 26.6, 25.0, 23.7, 20.4; IR ($CDCl_3$) ν 1723 cm^{-1}; mass spectrum *m/z* 189.0918 ($C_{12}H_{12}O_2$ + H requires 189.0915), 189 (base), 144, 115.

[1*R*-(1α,6α,7α)]-7-Ethyl-3-oxabicyclo[4.1.0]heptan-2-one (23f) was prepared in 80% yield as a colorless oil: pentane/Et_2O (2:1). The enantiomeric purity was determined to be 90% by methods B and C: ^{1}H NMR δ 4.21−4.08 (comp, 2 H), 2.00−1.92 (m, 1 H), 1.73−1.64 (comp, 3 H), 1.44−1.16 (comp, 3 H), 0.95 (t, 3 H); ^{13}C NMR δ 170.9, 69.1, 25.3, 18.1, 17.9, 16.4, 15.8, 12.6; IR ($CHCl_3$) ν 1724 cm^{-1}; mass spectrum *m/z* 141.0920 ($C_8H_{12}O_2$ + H requires 141.0916).

[1*R*-(1α,6α,7β)]-7-Ethyl-3-oxabicyclo[4.1.0]heptan-2-one (23g) was prepared in 65% yield as a colorless oil: pentane/Et_2O (2:1). The enantiomeric purity was determined to be 82% by method A: ^{1}H NMR δ 4.21−4.4.08 (comp, 2 H), 2.00−1.92 (m, 1 H), 1.73−1.64 (comp, 3 H), 1.44−1.16 (comp, 3 H), 0.95 (t, 3 H); ^{13}C NMR δ 170.9, 69.1, 25.3, 18.1, 17.9, 16.4, 15.8, 12.6; IR ($CHCl_3$) ν 1724 cm^{-1}; mass spectrum *m/z* 141.0920 ($C_8H_{12}O_2$ + H requires 141.0916).

[1*R*-(1α,6α,7α)]-7-Cyclohexylmethyl-3-oxabicyclo[4.1.0]heptan-2-one (23h) was prepared in 77% yield as a white solid: hexanes/EtOAc (3:1); mp 61−62 °C. The enantiomeric purity was determined to be 80% by method C: ^{1}H NMR δ 4.24−4.4.17 (comp, 2 H), 2.06−1.99 (m, 1 H), 1.98−1.41 (comp, 8 H,), 1.39−1.10 (comp, 7 H), 0.99−0.96 (m, 2 H); ^{13}C NMR δ 171.2, 69.2, 37.6, 33.2, 33.0, 32.2, 26.5, 26.3, 26.2, 22.2, 18.5, 16.9, 16.1; IR ($CDCl_3$) ν 1729 cm^{-1}; mass spectrum *m/z* 209.1540 ($C_{13}H_{20}O_2$ + H requires 209.1541), 209 (base), 163.

[1*R*-(1α,6α,7α)]-7-Methylphenyl-3-oxabicyclo[4.1.0]heptan-2-one (23i) was prepared in 68% yield as a white solid: hexanes/EtOAc (3:1); mp 112−114 °C. The enantiomeric purity was determined to be 80% by method B: ^{1}H NMR δ 7.31−7.17 (comp, 5 H), 4.35−4.21 (comp, 2 H), 2.90 (dd, J = 15.8, 6.2 Hz, 1 H), 2.60 (dd, J = 15.8, 8.5 Hz, 1 H), 2.09−1.99 (m, 1 H), 1.89−1.70 (comp, 3 H), 1.68−1.55 (m, 1 H); ^{13}C NMR δ 170.7, 139.5, 128.6, 128.1, 126.4, 69.3, 30.5, 24.2,

18.5, 17.0, 16.3; IR ($CDCl_3$) ν 1728 cm^{-1}; mass spectrum *m/z* 203.1078 ($C_{13}H_{14}O_2$ + H requires 203.1072), 203 (base), 157, 104.

[1*R*-(1α,6α,7α)]-7-Trimethylsilyl-3-oxabicyclo[4.1.0]heptan-2-one (23j) was prepared in 65% yield as a white solid: hexanes/EtOAc (3:1); mp 53−55 °C. The enantiomeric purity was determined to be 86% by method C: ^1H NMR δ 4.29−4.20 (m, 1 H), 4.14−4.05 (m, 1 H), 2.18−2.02 (m, 1 H), 1.98−1.84 (comp, 3 H), 0.36 (dd, J = 10.8, 9.5 Hz, 1 H), 0.14 (s, 3 H); ^{13}C NMR δ 172.4, 66.7, 21.3, 18.1, 16.9, 12.9, −0.31; IR ($CDCl_3$) ν 1723 cm^{-1}; mass spectrum *m/z* 185.1003 ($C_9H_{16}O_2Si$ + H requires 185.0997), 185, 169 (base) 111.

General Procedure for Determination of the Enantiomeric Purity of Lactones 11 and 23 (Method B). Methyllithium (3.0 equiv in Et_2O) was slowly added to a stirring solution of the appropriate lactone (1.0 equiv) in THF (1.0 × 10^{-2} M) at 0 °C. The reaction mixture was stirred for 1 h at room temperature and then quenched by the addition of an equal volume of water. The resulting mixture was then extracted with Et_2O (3 × 2 volumes), and the combined ether extracts were dried ($MgSO_4$) and concentrated under reduced pressure. A solution of the resulting diol in CH_2Cl_2 (0.1 M) was then treated with Ac_2O (1.0 equiv) and DMAP (0.1 equiv). After 1 h, the reaction was quenched by the addition of water (1 volume) and then extracted with CH_2Cl_2 (3 × 1 volume). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure, and purified by flash chromatography eluting with hexane/Et_2O mixtures to give the corresponding mono acetates in 65−86% yield. The enantiomeric purities of the intermediate diols (for **11d,f,j,l**) or the monoacetates (for **11k,m−p** and **12a−c,e−g,i**) were then determined by ^1H NMR spectroscopy in C_6D_6 in the presence of the chiral shift reagents Eu(tfc)$_3$ or Eu(hfc)$_3$ (0.1−0.4 equiv). The relative amounts of the two enantiomers were typically established by integration of the signals of the diastereotopic protons of the geminal dimethyl groups of the dimethyl carbinol moiety. In all cases, control experiments were performed on racemic materials. The spectral data for the diols or their derived monoacetates for compounds **11d,f,j,k** have been recorded previously,[48] and those for **11l−p** and **23a−c,e−g,i** are included in the supplementary material.

General Procedure for Determining Enantiomeric Purity of Lactones 23d,f,h,j by Derivativization with (*R*)-(+)-α-Methylbenzylamine. A 2.0 M solution of $AlMe_3$ (3.0 equiv) in hexanes was added with stirring to a solution of (*R*)-(+)-α-methylbenzylamine (3.0 equiv) in CH_2Cl_2 (0.2 M) at 0 °C. The reaction was allowed to warm to room temperature over 30 min, and the appropriate lactone **23d,f,h,j** (1.0 equiv) was added in one portion. The reaction mixture was heated at reflux for 16 h and then cooled to 0 °C. The reaction was then quenched by the careful addition of 5% aqueous HCl (1 volume), and the resulting mixture was extracted with CH_2Cl_2 (3 × 1 volume). The combined organic layers were then washed with H_2O (2 × 1 volume), dried ($MgSO_4$), and evaporated at reduced pressure. The mixture was then analyzed by HPLC eluting with hexanes/EtOAc (1:2) to determine the relative amounts of the two diastereomers. In all cases, control experiments were performed on racemic materials. The spectral data for the amides derived from **23d,f,h,j** are in the supplementary material.

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Supplementary Material Available: Spectral data for the cyclopropyl diols, hydroxy acetates, and chiral amides derived from **11k−p** and **23a−j** that were used to determine the optical purities and copies of ^1H NMR spectra of **10b,m−p**, **11m−p**, **22a−j**, **23a−j**, and other relevant new compounds and ^1H and ^{13}C NMR spectra of the MPAIMH ligand and **15** (61 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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