Enantiocontrolled Macrocycle Formation by Catalytic Intramolecular Cyclopropanation

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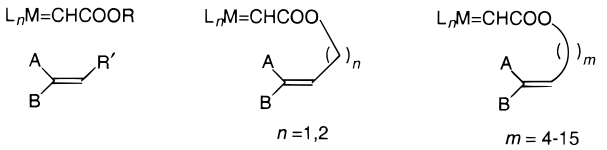
Abstract: Stereoselectivity in intramolecular cyclopropanation reactions resulting in cyclopropane fusion with ten- and larger-membered rings has been examined using chiral copper(I) and dirhodium(II) catalysts. The influence of alkene structure and catalyst has been obtained using the 1,2-benzenedimethanol linker between the allylic double bond and diazoacetate. Control features in the addition reaction, especially those for diastereoselectivity and enantioselectivity, have been elucidated, and they are associated with the metal itself or its attendant ligands that influence the trajectory of the alkene to the carbene center. The influence of ring size, from five- to twenty-membered rings, on stereoselectivity has been determined with selected copper(I) and dirhodium(II) catalysts, and the changes in stereocontrol as a function of ring size can be understood as being due to a change in the olefin trajectory to the carbene center. Hydride abstraction from a benzylic position accompanies addition when dirhodium catalysts are employed, and intramolecular C−H insertion into an allylic site to form a nine-membered ring has been observed as a major competing reaction but with negligible enantiocontrol. The use of 1,8-naphthalenedimethanol as a linker results in lower enantioselectivity than does use of 1,2-benzenedimethanol.

Carbene transfer from a transition metal via addition to a carbon−carbon double bond has been investigated in great detail, especially for catalytic reactions of diazo compounds.[1] In the intermolecular transformation both diastereocontrol and enantiocontrol are variables, and the factors that control them appear to act independently.[1−10] For intramolecular addition to form the favored five- or six-membered ring-fused cyclopropane, diastereocontrol is fixed, but enantiocontrol can vary widely.[1,8,11−14] The formation of macrocycles via intramolecular cyclopropanation[15,16] bridges the gap between intermolecular and intramolecular addition and provides us with the opportunity to probe more deeply those factors that control stereoselectivity.



Copper(I) and dirhodium(II) catalysts possessing chiral ligands have received the most attention and widespread use.[1,17−19] The data available suggest the validity of the generalization that enantiocontrol in intermolecular cyclopropanation is higher with chiral copper(I) bisoxazoline and semicorrinato complexes and that enantiocontrol for intramolecular cyclopropanation of allylic/homoallylic diazoacetates is highest when chiral dirhodium(II) carboxamidate catalysts are used. One might expect crossover of the optimal catalyst for enantioselective macrocyclization.[20]

Various mechanistic proposals have been advanced to account for the diastereocontrol observed in intermolecular cyclopropanation reactions,[1,17−19,21−23] but very few have confronted the

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Table 1. Enantioselective Cyclopropanation of **7a** and **7b** with Chiral Copper(I) and Dirhodium(II) Catalysts[a]

diazo compd	catalyst	yield, %, **8**[b,c]	% ee **8**[d]	% ee **11**
7a	**1**, Cu(bis-ox)PF_6	93	80 (1*R*,10*S*)	20[e] (1*R*,5*S*)
7a	**2**, Rh_2(5*S*-MEPY)$_4$	56	46 (1*S*,10*R*)	95[f] (1*R*,5*S*)
7a	**3**, Rh_2(4*S*-MEOX)$_4$	67	27 (1*S*,10*R*)	94 (1*R*,5*S*)
7a	**4**, Rh_2(4*S*-MPPIM)$_4$	67	26 (1*R*,10*S*)	87 (1*R*,5*S*)
7a	**5**, Rh_2(4*S*-IBAZ)$_4$	95	64 (1*S*,10*R*)	80 (1*R*,5*S*)
7a	**6**, Cu(BAZF)PF_6	71	53 (1*S*,10*R*)	66 (1*R*,5*S*)
7b	**1**, Cu(bis-ox)PF_6	82	90 (1*R*,10*S*)	87[g] (1*S*,5*R*)
7b	**2**, Rh_2(5*S*-MEPY)$_4$	81	45 (1*S*,10*R*)	7[f] (1*R*,5*S*)
7b	**3**, Rh_2(4*S*-MEOX)$_4$	78	38 (1*S*,10*R*)	1
7b	**4**, Rh_2(4*S*-MPPIM)$_4$	87	46 (1*S*,10*R*)	89[h] (1*S*,5*R*)
7b	**5**, Rh_2(4*S*-IBAZ)$_4$	87	60 (1*S*,10*R*)	28 (1*S*,5*R*)
7b	**6**, Cu(BAZF)PF_6	90	36 (1*S*,10*R*)	17 (1*S*, 5*R*)

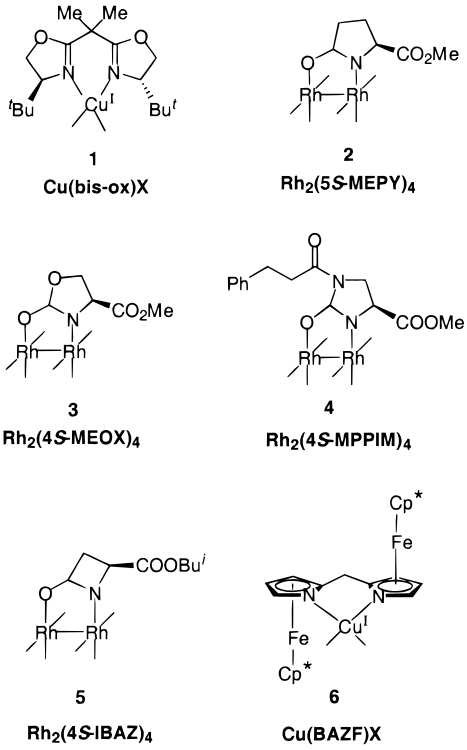
[a] Reactions were performed in refluxing dichloromethane using 1.0 mol % catalyst. [b] Product yield after chromatography. [c] Diastereomer ratio ≥98:2 obtained by GC using a SPB-5 column. [d] Obtained by GC with baseline separation using Chiraldex columns. [e] Reference 20. [f] Reference 11. [g] Reference 27. [h] Reference 28.

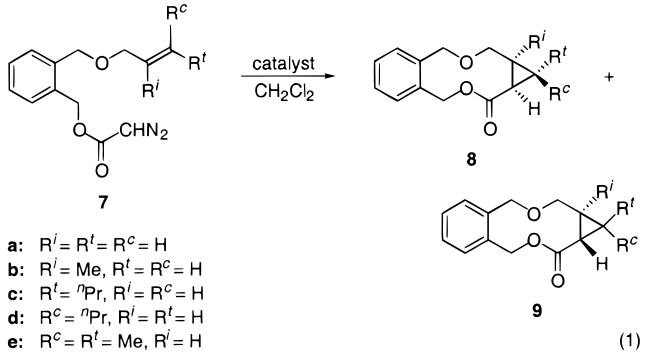
factors involved in enantiocontrol.[1,7,8,11] The reason for the relative absence of mechanistic models, which has contributed to the continued empiricism of catalyst design, is the lack of reliable data on enantiocontrol/diastereocontrol in cyclopropanation reactions as a function of alkene substituents and catalysts. Reissig and co-workers have reported extensive comparative data for intermolecular addition to vinyl ethers,[24−26] and we have communicated results for intramolecular allylic and homoallylic cyclopropanation.[11,27] We now report comparative data for cyclopropanation reactions as a function of alkene substituents, ring size, and catalysts, and from these data we are able to portray some of the limiting factors that define enantiocontrol.

Results

Although high enantiocontrol has been reported for the intermolecular cyclopropanation of monosubstituted and select 1,1-disubstituted alkenes,[1] there is generally a notable absence of enantioselectivity for addition to 1,2-disubstituted and trisubstituted alkenes using the same catalysts.[24−26] Yet for intramolecular cyclopropanation of allylic diazoacetates, chiral dirhodium(II) catalysts and conditions have been developed for uniformly high enantiocontrol, modestly dependent on the alkene substituent.[11,27,28] Extension to homoallylic diazoacetates produces a drop in enantiomeric excess by 10−20%, and extrapolation of these results to even larger rings leads to the prediction of progressively diminishing levels of enantiocontrol.

Among the chiral catalysts that have been employed for enantioselective cyclopropanation, C_2-symmetric bisoxazoline complexes of copper(I) (e.g., **1**) have given the highest % ee values in intermolecular reactions,[1,4,5] whereas Rh_2(5*S*-MEPY)$_4$ (**2**) represents a class of chiral dirhodium(II) carboxamidate catalysts that includes Rh_2(4*S*-MEOX)$_4$ (**3**),[29] Rh_2(4*S*-MPPIM)$_4$ (**4**),[30] and Rh_2(4*S*-IBAZ)$_4$ (**5**)[31] that are most effective for intramolecular cyclopropanation. In addition, a novel bisazoferrocene-derived catalyst **6**, recently reported by Fu and co-workers,[32] was chosen to ascertain the similarities and differences of its activities, especially compared with **1**. These are the catalysts that have been selected for evaluation of diastereocontrol/enantiocontrol in the intramolecular cyclopropanation of diazo esters **7** (eq 1) and related compounds.





(1)

Influence of Catalysts and an Alkene Substituent. We previously reported results from reactions of allyl diazoacetate **7a** with chiral copper(I) catalyst **1** (X = PF_6^-) and of methallyl diazoacetate **7b** with **1** and **2** [Rh_2(5*S*-MEPY)$_4$].[20] In these cases only the *Z*-isomer **8** was reported, and product yields and % ee values were as listed in Table 1. The complete set of chiral dirhodium(II) catalysts and **6** have now been applied to these systems, and significant differences in enantiocontrol are evident. For comparison, catalyst-dependent enantioselectivity also

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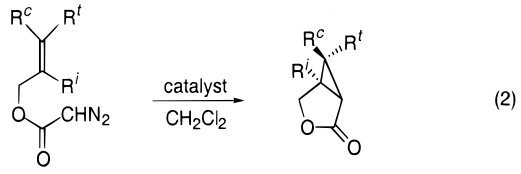
Table 2. Influence of Alkene Substituents in Enantioselective Cyclopropanation of **7c**−**7e** with Chiral Copper(I) and Dirhodium(II) Catalysts[a]

diazo compd	catalyst	isolated yield, %, **8**, **9**[b]	rel yield, %, **8** + **9** (**8**:**9**)[c]	rel yield, %, **12** + **13** (**12**:**13**)[c]	% ee **8**[d]	% ee **9**[d]	% ee **11**
7c	**1**, Cu(bis-ox)PF_6[e]	93 (55)	97 (>98:1)	3 (33:67)	84 (1*R*,10*S*,11*S*)		30[f]
7c	**2**, Rh_2(5*S*-MEPY)$_4$[e]	78 (17)	23 (>99:1)	77 (87:13)	72 (1*R*,10*S*,11*S*)		85[g]
7c	**3**, Rh_2(4*S*-MEOX)$_4$[e]	70 (18)	39 (94:6)	61 (70:30)	60 (1*R*,10*S*,11*S*)	*h*	62
7c	**5**, Rh_2(4*S*-IBAZ)$_4$[e]	77 (38)	57 (>99:1)	43 (58:42)	73 (1*R*,10*S*,11*S*)		44
7c	**6**, Cu(BAZF)PF_6[e]	88 (84)	98 (>99:1)	2 (50:50)	80 (1*S*,10*R*,11*R*)	*h*	44
7d	**1**, Cu(bis-ox)PF_6	77 (55)	94 (51:49)	6 (86:14)	17 (1*R*,10*S*,11*R*)	94	37[d]
7d	**2**, Rh_2(5*S*-MEPY)$_4$	80 (17)	22 (92:8)	78 (82:12)	19 (1*R*,10*S*,11*R*)	9	≥ 94[f]
7d	**3**, Rh_2(4*S*-MEOX)$_4$	78 (28)	51 (83:17)	49 (73:27)	6 (1*R*,10*S*,11*R*)	5	≥ 94
7d	**5**, Rh_2(4*S*-IBAZ)$_4$	80 (75)	>99 (98:2)	<1 (67:33)	85 (1*R*,10*S*,11*R*)	*h*	83
7d	**6**, Cu(BAZF)PF_6	82 (78)	98 (92:8)	2 (50:50)	6 (1*S*,10*R*,11*S*)	68	*h*
7e	**1**, Cu(bis-ox)PF_6	88 (70)	95 (92:8)	5 (80:20)	18 (1*S*,10*R*)	30	14[d]
7e	**2**, Rh_2(5*S*-MEPY)$_4$	82 (18)	26 (7:93)	74 (94:6)	62 (1*S*,10*R*)	3	98[f]
7e	**3**, Rh_2(4*S*-MEOX)$_4$	65 (24)	30 (15:85)	70 (74:26)	54 (1*S*,10*R*)	8	98
7e	**5**, Rh_2(4*S*-IBAZ)$_4$	78 (41)	76 (55:45)	24 (60:40)	63 (1*S*,10*R*)	2	89
7e	**6**, Cu(BAZF)PF_6	94 (90)	98 (96:4)	2 (50:50)	90 (1*R*,10*S*)	*h*	*h*

[a] Reactions were performed in refluxing dichloromethane using 1.0 mol % of catalyst. [b]Yield of products following separation of catalyst; isolated yield of pure **8** + **9** or only **8** is given in parantheses. [c]Product yield after chromatography; ratios of products were determined by GC analyses on a SPB-5 column. [d]Obtained by GC with baseline separation using Chiraldex columns. [e] Ratio of **8**:**14**: **1** (96:4), **2** (15:85), **3** (48:49), **5** (85:15), **6** (98:2). [f]ref 27. [g] ref 11. [h]Not determined.

characterized results with allylic diazoacetates **10** which produce cyclopropane-fused γ-lactones **11** (eq 2).[27] Representative results are reported in Table 1; product yields were consistently greater than 80%.

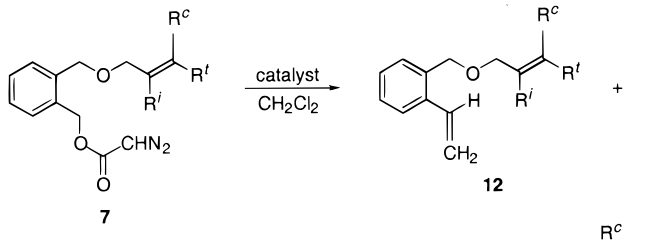


10 **11** (2)

a: $R^i = R^t = R^c = H$
b: R^i = Me, $R^t = R^c = H$
c: $R^t = {}^n$Pr, $R^i = R^c = H$
d: $R^c = {}^n$Pr, $R^i = R^t = H$
e: $R^c = R^t$ = Me, $R^i = H$

Product ratios were obtained on the product mixture prior to purification, but product yields were determined following chromatographic purification. High yields of cyclopropane product were obtained from reactions of **7a** and **7b**, and **8** was virtually the sole product. Trace amounts of diastereoisomer **9** (inferred) could be detected by GC/MS analysis from some of the reactions, but the **8**:**9** ratio was never less than 96:4. The absolute configurations of **8a** and **8b** were determined by hydrogenolysis of these products to **11a** and **11b**, respectively; comparison to known properties (GC and/or $[\alpha]_D$) defined their absolute configuration. The absolute configuration of the major enantiomer of **7a** formed from **1** is opposite that generated by any of the chiral dirhodium(II) carboxamidate catalysts **2**−**5** and, also, Cu(BAZF)PF_6 **6**.

Examination of results from **7c**, **7d**, and **7e**, however, portray a substantial divergence in results that are demonstrably catalyst dependent (Table 2). First, hydride abstraction from the benzylic position leading to both **12** and **13** (eq 3), a general process for benzyl and some allyl diazoacetates discovered only recently,[33] is competitive with intramolecular cyclopropanation for dirhodium(II) catalysts, but this process is relatively unimportant when the chiral copper catalysts are employed. Second, diastereoselectivity leading to **8** and **9** varies widely with the catalyst employed. For example, in reactions with **7d** the bisoxazoline copper(I) catalyst **1** provides a high preference for *trans*-fused



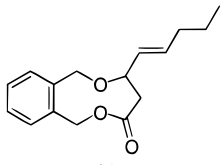
7 **12**

c: $R^t = {}^n$Pr, $R^i = R^c = H$
d: $R^c = {}^n$Pr, $R^i = R^t = H$
e: $R^c = R^t$ = Me, $R^i = H$

13 (3)

isomer **9d**, whereas Rh_2(5*S*-MEPY)$_4$ gives mainly the *cis*-fused isomer **8d**. Within the dirhodium(II) family of catalysts there is a discernible catalyst-dependent variation in diastereoselectivity, with the degree of change being dependent on the alkene substituents. That this is not merely a function of the difference between Cu(I) and Rh(II) can be seen from results with the achiral catalysts Cu(MeCN)$_4PF_6$ and $Rh_2(OAc)_4$, respectively; with product yields ≥85%, hydride abstraction was a negligible process (<1%) in all cases, and diastereocontrol favored **8** by 87:13 (from **7c**), 84:16 (from **7d**), and 95:5 (from **7e**) with only minor differences (±2%) between these achiral Cu(I) and Rh(II) catalysts.

For reactions of **7c** catalyzed by chiral dirhodium(II) carboxamidates, the nine-membered ring C−H insertion product **14** was produced in addition to **8c**, but instead of the *trans*-



14

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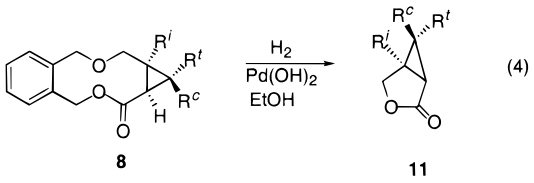
fused cyclopropane product **9c**. Insertion into a C−H bond resulting in the formation of a medium or large ring has been seen only once before,[16] but such products were not observed in reactions of **7a**,**b**,**d**,**e**. The low enantiocontrol that was found for **14** (37% with **1**, 12% with **2**, 12% with **3**, and 4% with **5**), especially in reactions catalyzed by chiral dirhodium(II) carboxamidates,[1] stands in marked contrast to that achieved in the synthesis of γ-lactones where enantiomeric excesses greater than 90% are common.

Product analyses were performed by initial NMR and GC determinations to provide relative product yields. Isolated yields were weight yields obtained following chromatographic removal of the catalyst, and % ee values were obtained by GC determinations on Chiraldex columns at this stage. Individual cyclopropane isomers were separated chromatographically, and especially when one diastereoisomer was dominant, the pure isomer was isolated. The *trans* stereochemistry of **9d** and **9e** was unambiguously established by chemical shifts and proton coupling constants, and by comparison with NMR data for the corresponding *cis*-isomers **8**. The absolute stereochemistries of **8c**, **8d**, and **8e** were determined by hydrogenolysis of an appropriate product mixture using $Pd(OH)_2$ in ethanol; under these conditions, **8** was converted to **11** (eq 4), and **11** was

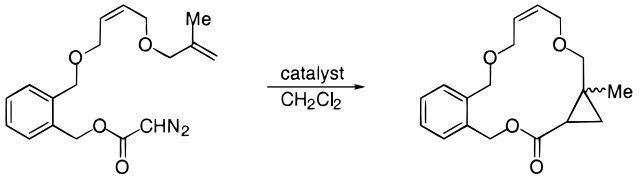


8 **11** (4)

analyzed chromatographically on a Chiraldex column relative to a sample of known configuration.[11] The reproducibility of results and match of % ee values for **8** and **11** suggested that isomerization did not occur under these conditions.

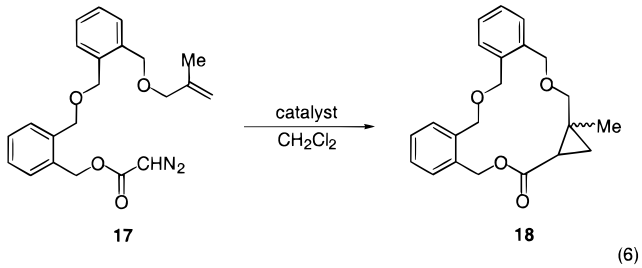
Enantioselectivities in the formation of **8** and **9** provided the greatest surprises. Although **1** is portrayed in intermolecular cyclopropanation reactions as consistently affording higher levels of enantiocontrol for the formation of the *trans*-isomer,[1,7,19] the data obtained for intramolecular cyclopropanation of **7c** and **7d** show that this is substituent dependent. Also, whereas chiral dirhodium(II) carboxamidates are generally exceptional for enantiocontrol in the intramolecular cyclopropanation of allylic diazoacetates **10**,[11,28] formation of both bicyclo[8.1.0] **8** and **9** occur with lower enantioselectivities than formation of bicyclo[3.1.0] **11**, and the % ee values for **8** are always higher than are those for **9**.

Influence of Ring Size. Increasing the distance separation of the metal carbene from the alkene in intramolecular cyclopropanation provides a progression from intramolecular allylic cyclopropanation to intermolecular cyclopropanation. We previously reported results with **15** (eq 5) on which Cu(bis-ox)PF_6

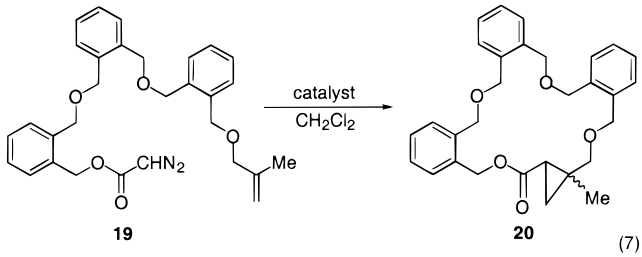


15 **16** (5)

(**1**) produced only the product from cyclopropanation of the remote methallyl double bond (61% yield, 90% ee)[20] without adding to the internal double bond.[34] With Rh_2(5*S*-MEPY)$_4$ **16** was formed in 66% yield with 36% ee, and, using Rh_2(4*S*-MEOX)$_4$, in 56% yield with 39% ee. We can now describe comparative results from intramolecular cyclopropanation of **17** (eq 6) and **19** (eq 7) which produce 15- and 20-membered ring-



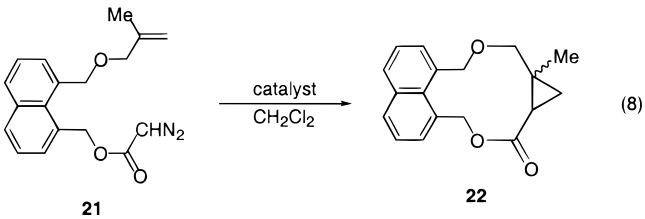
17 **18** (6)



19 **20** (7)

fused cyclopropane products, respectively (Table 3). Results from reactions of these same diazo compounds with the achiral catalysts Cu(MeCN)$_4PF_6$ (**18**, 64% yield, 80:20 *Z:E*; **20**, 42% yield, 72:28 *Z:E*) and $Rh_2(OAc)_4$ (**18**: 64% yield, 90:10 *Z:E*; **20**: 59% yield, 76:24 *Z:E*) have been reported,[15] and their diastereoselectivities are consistent with those in Table 3. In this comparison the most dramatic difference between catalysts in enantiocontrol is the virtually constant % ee values of the *cis*-cyclopropane isomer for copper catalyst **1** and the increasing % ee values, as a function of product ring size, with Rh_2(4*S*-MEOX)$_4$ and Rh_2(4*S*-IBAZ)$_4$. Enantioselectivities were determined following hydrogenolysis of the reaction mixture; the formation of **11** from the *cis*-cyclopropane isomer was monitored, and its % ee value was determined by GC.

Enantiocontrol as a Function of the Tether. If the geometry of the attached diazoacetate with respect to the alkene has a marked influence on enantioselectivity, the effect should be seen in the results from intramolecular cyclopropanation of **21** (eq 8) relative to those from cyclopropanation of **6b**. As can be



21 **22** (8)

seen from the data in Table 4, enantioselectivity in the formation of **22** is substantially lower than expected from Table 1, although the trend in stereoselectivity among catalysts is not significantly different. In contrast to reactions of **7b**, which were free of competing transformations, however, aromatic cycloaddition

(34) The product originally thought to be that from addition to the internal double bond was actually from oxonium ylide formation with [2,3]-sigmatropic rearrangement: Doyle, M. P.; Peterson, C. S. *Tetrahedron Lett.* **1997**, *38*, *5265*.

Table 3. Influence of Ring Size on Diastereoselectivity and Enantioselectivity in Catalytic Cyclopropanation Reactions[a]

diazo compd	catalyst	yield, %, cyclopropane[b]	*Z*:*E*[c]	% ee *Z*-isomer
17	Cu(bis-ox)PF_6	66 (**18**)	69:31	85 (1*R*,15*S*)
17	Rh_2(4*S*-MEOX)$_4$	56 (**18**)	80:20	39 (1*S*,15*R*)
17	Rh_2(4*S*-IBAZ)$_4$	78 (**18**)	79:21	62 (1*S*,15*R*)
19	Cu(bis-ox)PF_6	42 (**20**)	65:35	86 (1*R*,20*S*)
19	Rh_2(4*S*-MEOX)$_4$	46 (**20**)	75:25	65 (1*S*,20*R*)
19	Rh_2(4*S*-IBAZ)$_4$	64 (**20**)	78:22	69 (1*S*,20*R*)

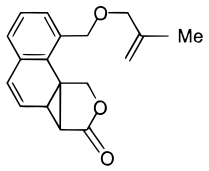
[a] Reactions were performed in refluxing dichloromethane using 1.0 mol % catalyst. [b]Product yield after chromatography. [c]Diastereomer ratio obtained by GC using a SPB-5 column.

Table 4. Enantioselectivity Cyclopropanation of 21 with Chiral Copper (I) and Dirhodium(II) Catalysts[a]

catalyst	yield, %[b]	**22**:**23**[c]	% ee **22**
1, Cu(bis-ox)PF_6	95	100:0	80 (1*R*,11*S*)
2, Rh_2(5*S*−MEPY)$_4$	86	100:0	10 (1*S*,11*R*)
3, Rh_2(4*R*−MEOX)$_4$	60	70:30	13 (1*R*,11*S*)
5, Rh_2(4*S*−IBAZ)$_4$	88	100:0	52 (1*S*,11*R*)

[a] Reactions were performed in refluxing dichloromethane using 1.0 mol % of catalyst. [b]Product yield after chromatography. [c]Diastereomer ratio obtained by GC using a SPB-5 column.

yielding **23** occurred in competition with cyclopropanation using Rh_2(MEOX)$_4$ catalysis.



23

Discussion

Tables 1−4 report results from six catalysts, two with chiral ligands for copper(I) and four with chiral carboxamidate ligands for rhodium(II). Data are compared from reactions with allylic diazoacetates producing fused cyclopropanes with ring sizes ranging from five to twenty. What is, perhaps, surprising is the virtual absence of correlations in stereoselectivities as a function of ring size on olefin substituents. Chiral dirhodium(II) carboxamidates, in particular, Rh_2(MEPY)$_4$, Rh_2(MEOX)$_4$, and Rh_2(MPPIM)$_4$ (**2**−**4**), are especially effective catalysts for intramolecular cyclopropanation with allylic diazoacetates (**11**), providing high product yields and enantiomeric excesses beyond 95%, but mixed effectiveness is achieved with macrocyclic cyclopropanation.

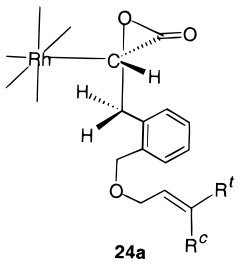
Dirhodium(II) carboxamidate catalysts promote unexpectedly diverse outcomes with **7**. First of all, and in contrast to the copper(I) catalysts, formation of the *trans*-cyclopropane isomer is a major process with **7d** and **7e**, although enantiocontrol in their formation is negligible. Macrocyclic C−H insertion resulting in **14** is a major competing reaction with **7c**. Last, hydride abstraction at an activated benzylic position becomes a major reaction process, although less so with Rh_2(4*S*-IBAZ)$_4$ and not in measurable quantities with diazo compounds **7a** and **7b**. The occurrence of hydride abstraction in intramolecular reactions of diazoacetates appended to benzylic ethers has been reported,[33] and the mechanism of the processes leading to alkene (with loss of carbon dioxide) and to carbonyl compound (with loss of ketene) has been established.

Why does hydride abstraction occur when addition to an inherently more nucleophilic center, a carbon−carbon double bond, is a competitive process? We believe that the answer lies in the orientation of the carbene appendage. As has been previously suggested from computational studies,[35] the carbonyl oxygen of the intermediate carbene is positioned to be as far away as possible from the rhodium catalyst face. Accordingly, both the benzylic C−H bond and the carbon−carbon double bond are positioned for reaction with the carbene center (Chart 1). If the formation of products **12** and **13** through **24a** is independent of the alkene, then the relative percentage of these products is a measure of the stereoelectronic factors involved in the cyclopropane-forming process. By this measure, substituents R^c and R^t both restrict access of the carbene center to the carbon−carbon double bond, but R^t is more restrictive than R^c.

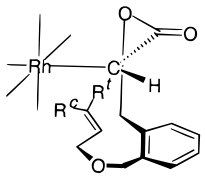
When the carbonyl oxygen of the intermediate metal carbene is positioned away from the catalyst face, as in **24a** or **24b**, the bulk of the reacting substrate is brought closer to the carbene center and is subject to enhanced stereocontrol. The corollary to this is that when the carbonyl group is oriented toward the catalyst face, the bulk of the reacting substrate is moved farther from the carbene center, and stereocontrol is minimized; this is the explanation given for the relative absence of enantioselectivity in dirhodium(II) carboxamidate catalyzed reactions of diazoketones.[36] We cannot rule out this alternative orientation as the cause for the minimal enantioselectivities in the formation of **9** or **14** with chiral dirhodium(II) carboxamidates.

Initial inspection of the C_2-symmetric structures for copper(I) catalysts **1** and **6** might suggest that enantioselectivity in product formation would be proportional but of opposite chirality. In fact, the configuration of the cyclopropane product is not a necessary function of the catalyst ligand configuration. Note that **1** and **6** have significant geometical differences (Chart 2),

Chart 1

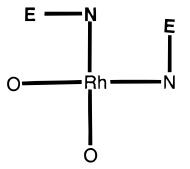


24a

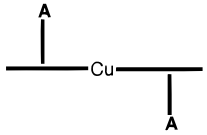


24b

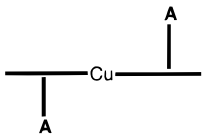
Chart 2



S-configuration
(E = COOMe,
[*cis*-2,2]-catalyst
configuration)



R-configuration
(A = *t*-Bu)

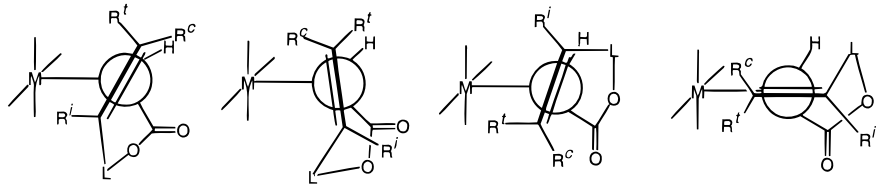


S-configuration
(A = FeCp*)

(35) Doyle, M. P.; Winchester, W. R.; Hoorn, J. A. A.; Lynch, V.; Simonsen, S. H. *J. Am. Chem. Soc*. **1993**, *115*, 9968−9978.

(36) Doyle, M. P.; Eismont, M. E.; Zhou, Q.-L. *Russ. Chem. Bull*. **1997**, *46*, 955.

Chart 3



	25a	**25b**	**26a**	**26b**
disfavored with:	R^i	R^c	R^t	R^c, R^t

but **11a** and **11b** produced with these catalysts have the same configurational preference. The same is not true for reactions of **7a**−**e** where **1** and **6** give preference to opposite enantiomers. Furthermore, enantioselectivity in product formation with **1** and **6** is not uniformly proportional with all substrates examined. With **7a**, **7b**, and **7d**, for example, catalyst **1** provides higher enantiocontrol than **6**. However, in reactions with **7c** and **7e**, catalyst **6** is comparable or superior to **1** in enantiocontrol. Similar comments can be offered for comparisons made between chiral rhodium(II) catalysts **2**−**5** and copper catalysts **1** and **6**. Whereas with **7a** and **7b**, enantiomer preferences for **1** and **2** are opposite, with **7c**−**e** they are the same but opposite to those produced with **6**. Clearly, broad generalizations cannot be made regarding catalyst-induced stereoselectivities on the basis of a limited number of results, and subtle structural changes in catalyst ligands and alkene structure can cause enormous changes in enantiocontrol. However, results from copper(I) and dirhodium(II) catalysts do conform to a significant geometrical difference between these two catalyst sets. The outcome is evident in results obtained as a function of ring size (Tables 1 and 3).

Figure 1 plots % ee versus ring size for catalysts **1**, **3**, and **5** operating on methallyl diazoacetates **7**, **10**, **17**, and **19**. With the copper(I) catalyst **1** there is virtually no change in enantiocontrol as a function of ring size, nor is a change in % ee apparent in reactions with **21**. With dirhodium(II) catalysts **3** and **5**, however, enantiocontrol increases substantially with ring size, reaching a plateau between ring sizes of 10 and 15 and rising again at 20. Data are included here for methallyl diazoacetate and the 1,2-benzenedimethanol-linked substrates, but there is no reason to expect that there is a smooth transition in % ee between ring sizes of 5 and 10.

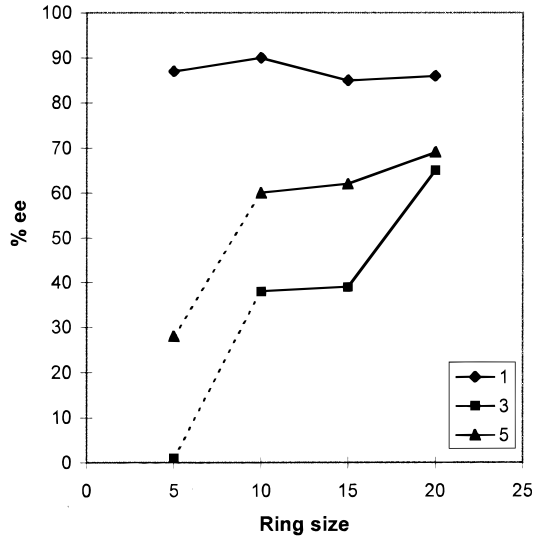


Figure 1. Ring size versus % ee for reactions of **7**, **10**, **17**, and **19** with catalysts **1** (◆), **3** (▲), and **5** (■).

Recently, we reported a comparative examination of enantiocontrol in intramolecular allylic cyclopropanation reactions and explained the results as being consistent with two limiting alkene trajectories, depicted in Chart 3 (L = linker = CH_2) by Newman projections **25a** and disfavored with R^i, R^c, R^t, R^c, and R^t **25b**, that produce mirror image isomers.[27] For **25a**, which models selectivity in reactions of **10** with dirhodium(II) carboxamidates, interaction of R^c with the catalyst face is the least pronounced and, appropriate to the high enantiocontrol observed with *cis*-disubstituted allylic diazoacetates, R^c is oriented away from the catalyst. In contrast, **25b** depicts a trajectory that suggests high enantiocontrol with methallyl diazoacetate, but not with *cis*-disubstituted allylic diazoacetates. We previously established that **25a** accounted for the results from chiral dirhodium(II) carboxamidate catalyzed reactions of allylic diazoacetates **10a,c**−**e**, and that **25b** could explain results obtained with methallyl-substituted **10b**. The presence of a substituent larger than H at R^i disfavors **25a** but is favored in **25b**. This explanation is also in accord with the influence of ring size on % ee; with Cu(bis-ox)PF_6 (**1**) the preferred trajectory remains constant (**25b**), while with chiral dirhodium(II) carboxamidates **2** and **3** the preferred trajectory moves from **25a** to **25b** as the size of the ring increases.

The importance of alternative structures **26a** and **26b** for product formation is revealed in the enantiomeric excess obtained with various chiral catalysts. For example, the outcome of reactions of allylic diazoacetates with Cu(bis-ox)PF_6 (**1**) in which only **10b** gave high enantiocontrol suggests that trajectory **26b** may be operative with this catalyst. The same trajectory appears to govern allylic cyclopropanation catalyzed by Cu(BAZF)PF_6. *cis*-Substituents disfavor **25b**, whereas *trans*-substituents disfavor **26a**. Structure **26b** is a preferred trajectory for formation of *trans*-cyclopropane isomers.

The naphthalene system **21** presents a geometry that is different from that of **7b**, and enantiocontrol is greatly influenced by this change, although less so with catalysis by **1**. Aromatic cycloaddition is competitive with cyclopropanation when the Rh_2(MEOX)$_4$ catalyst is employed. Such a competition was anticipated from recent studies,[37] and even the preference of Rh_2(MEOX)$_4$ for aromatic cycloaddition was expected.

Experimental Section

General Procedures. ^{1}H NMR (250, 300, 400, or 500 MHz) and ^{13}C NMR (62.5, 75, 100, or 125 MHz) 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. Infrared spectra were recorded in solution or as a thin film on sodium chloride plates, and absorptions are reported in wavenumbers (cm^{-1}). Mass spectra were obtained using electron ionization at 70 eV on a quadrupole instrument. High-resolution mass spectra were obtained using FAB ionization on a JEOL HX110A Sector instrument. Elemental

(37) Doyle, M. P.; Ene, D. G.; Forbes, D. C.; Pillow, T. *J. Chem. Soc., Chem. Commun.* **1999**, 1691.

analyses were performed at Texas Analytical Laboratories, Inc., or Atlantic Microlabs, Inc. Optical rotations were obtained on a digital polarimeter. Enantiomeric excesses of enriched samples were determined by gas chromatographic analyses with baseline separation using Chiraldex columns by comparison with racemic standards.

Methanesulfonyl azide was prepared from methanesulfonyl chloride, and sodium azide and was used without distillation.[38] Diketene was distilled before use. The preparation and characterization of Rh_2(4*S*-IBAZ)$_4$,[31] Rh_2(5*S*-MEPY)$_4$,[35] Rh_2(4*S*-MEOX)$_4$,[29] Rh_2(4*S*-MPPIM)$_4$,[30] 2,2-bis[2-[4(*S*)-*tert*-butyl-1,3-oxazolinyl]]propane corresponding to **1**,[39] bis-azaferrocene corresponding to **2**,[32] and Cu(MeCN)$_4$PF$_6$[40] have been previously reported. Preparation and spectral data for 1,2-benzenedimethanol, 2-(2-propen-1-yloxymethyl)benzyl diazoacetate (**7a**), 2-(2-methyl-2-propen-1-yloxymethyl)benzyl diazoacetate (**7b**), 5,6-benzo-3,8-dioxa-*cis*-bicyclo[8.1.0]undecan-2-one (**8a**), 5,6-benzo-3,8-dioxa-10-methyl-*cis*-bicyclo[8.1.0]undecan-2-one (**8b**), 2,3,7,8-bisbenzo-12-methyl-5,10-dioxa-12-tridecenyl diazoacetate (**17**), 2,3,7,8,12,13-trisbenzo-17-methyl-5,10,15-trioxa-17-octadecenyl diazoacetate (**19**), 5,6,10,11-bisbenzo-3,8,13-trioxa-15-methylbicyclo[13.1.0]hexadecan-2-one (**18**), and 5,6,10,11,15,16-trisbenzo-3,8,13,18-tetroxa-20-methylbicyclo[18.1.0]henicosan-2-one (**20**) have been previously reported.[15] Dichloromethane and hexanes were distilled from CaH_2. Tetrahydrofuran was distilled from sodium/benzophenone ketyl. 1,8-Naphthalenedimethanol was prepared by $LiAlH_4$ reduction of naphthalic anhydride and distilled under reduced pressure prior to use. All diazoesters were dried for 12 h under vacuum and KOH. Other reagents were used without further purification. All glassware and needles were oven dried at 130 °C for 12 h before use. Melting points are uncorrected.

Preparation of 2-[(*E*)-2-Hexen-1-yloxymethyl)]benzyl Diazoacetate (7c). Sodium hydride (0.935 g, 23.4 mmol, 60% dispersion in mineral oil) was washed with anhydrous hexanes (3 × 20 mL), then suspended in 250 mL of anhydrous THF, and cooled to 0 °C. To this solution was added 1,2-benzenedimethanol (9.69 g, 70.2 mmol) in 150 mL of anhydrous THF over 20 min. After addition was complete, the milky white suspension was removed from the ice bath, and stirring was continued for an additional 30 min, whereupon (*E*)-1-bromo-2-hexene (4.35 g, 26.9 mmol) was added dropwise via syringe. The solution was allowed to stir for 15 h at 23 °C, and the reaction was quenched by slow addition of 50 mL of H_2O. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 75 mL). The combined organic layer was washed with brine, and the solvent was evaporated under reduced pressure. Purification via column chromatography (7:3 hexanes/ethyl acetate) yielded 4.47 g (20.3 mmol, 87% yield) of 2-((*E*)-2-hexen-1-yloxymethyl)benzyl alcohol as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.22 (comp, 4H), 5.72 (dt, J = 15.4, 6.6 Hz, 1H), 5.59 (dt, J = 15.4, 6.2 Hz, 1H), 4.61 (d, J = 6.2 Hz, 2H), 4.56 (s, 2H), 3.99 (d, J = 6.3 Hz, 2H) 3.50 (t, J = 6.3 Hz, O*H*), 2.02 (dt, J = 6.6, 7.2 Hz, 2H), 1.42 (tq, J = 7.2, 7.4 Hz, 2H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDC1_3$) δ 140.6, 136.0, 135.8, 130.0, 129.7, 128.8, 127.8, 125.5, 71.0, 70.9, 63.7, 34.3, 22.1, 13.6; 1R (film) 3447 (OH), 1682 (C═C) cm^{-1}; mass spectrum, *m*/*e* (rel intens) 220 (0.01, M), 219 (0.02, M − 1), 120 (77), 119 (60), 104 (100), 91 (64). After isolation of the alcohol, a flush of the column with ethyl acetate yielded 6.63 g of 1,2-benezenedimethanol (97% recovery).

2-[(*E*)-2-Hexen-1-yloxymethyl)]benzyl alcohol (1.69 g, 7.7 mmol) was dissolved in 15 mL of THF, and cooled to 0 °C. Triethylamine (0.1 mL) was added rapidly, followed by dropwise addition of diketene (0.98 g, 11.6 mmol). The solution was allowed to stir at room temperature for 14 h, at which point ^{1}H NMR analysis of the crude reaction mixture indicated complete conversion of the starting alcohol to the desired acetoacetate. The solution was again cooled to 0 °C, whereupon triethylamine (1.17 g, 11.6 mmol) and methanesulfonyl azide (1.40 g, 11.6 mmol) were added sequentially. The solution was allowed to warm to room temperature, and stirring was continued for 10 h, at which time ^{1}H NMR analysis indicated that the diazo transfer reaction was complete. The solvent was removed under reduced pressure, and 50 mL of water and 75 mL of ethyl acetate were added. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 75 mL). The combined organic layer was washed with brine, and the solvent was evaporated under reduced pressure. The crude diazoacetoacetate was again dissolved in THF (10 mL), and H_2O (10 mL) was added. To this rapidly stirring bilayer was added solid LiOH·H_2O (1.29 g, 30.8 mmol). After 20 min, the layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 75 mL). The combined organic layer was washed with brine, and the solvent was evaporated under reduced pressure. Purification by column chromatography (9:1 hexanes/ethyl acetate) yielded 1.80 g (6.2 mmol, 81% yield) of **7c** as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.24 (comp, 4H), 5.78−5.68 (m, 1H), 5.63−5.54 (m, 1H), 5.29 (s, 2H), 4.76 (br s, 1H), 4.54 (s, 2H), 3.97 (dd, J = 0.9, 6.1 Hz, 2H), 2.03 (q, J = 7.4 Hz, 2H) 1.41 (hex, J = 7.4 Hz, 2H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 136.7, 135.0, 134.2, 129.2, 129.1, 128.4, 127.9, 126.1, 71.2, 69.4, 64.0, 46.2, 34.3, 22.1, 13.6; IR (film) 2116 (C═N_2), 1690 (C═O) cm^{-1}. Anal. Calcd for $C_{16}H_{20}N_2O_3$: C, 66.65; H, 6.99; N, 9.72. Found: C, 66.68; H, 6.93; N, 9.64

Preparation of 2-[(*Z*)-2-Hexen-1-yloxymethyl)]benzyl Diazoacetate (7d). Sodium hydride (0.45 g, 11 mmol, 60% dispersion in mineral oil) was washed with anhydrous hexanes (3 × 20 mL), then suspended in 100 mL of anhydrous THF, and cooled to 0 °C. To this solution was added 1,2-benzenedimethanol (4.63 g, 33.6 mmol) in 50 mL of anhydrous THF over 20 min. After addition was complete, the milky white suspension was removed from the ice bath, and stirring was continued for an additional 30 min, whereupon (*Z*)-1-bromo-2-hexene (2.18 g, 13.5 mmol) was added dropwise via syringe. The solution was allowed to stir for 16 h at 23 °C and then worked up as described for the preparation of **7c**. Purification via column chromatography (7:3 hexanes/ethyl acetate) yielded 2.10 g (9.52 mmol, 85% yield) of 2-[(*Z*)-2-hexen-1-yloxymethyl)]benzyl alcohol as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41−7.26 (comp, 4H), 5.66−5.50 (comp, 2H), 4.65 (s, 2H), 4.61 (s, 2H) 4.11 (d, J = 5.9 Hz, 2H), 3.08 (br s, 1H), 2.04 (dd, J = 7.3, 7.1 Hz, 2H),1.39 (hex, J = 7.3 Hz, 2H), 0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 136.0, 134.5, 129.9, 129.5, 128.7, 127.8, 125.2, 71.1, 65.8, 63.6, 29.5, 22.5, 13.6; IR (neat) 3448 (OH) cm^{-1}.

2-[(*Z*)-2-Hexen-1-yloxymethyl)]benzyl alcohol (2.10 g, 9.54 mmol) was dissolved in 20 mL of THF, and cooled to 0 °C. Triethylamine (0.1 mL) was added rapidly, followed by dropwise addition of diketene (1.20 g, 14.3 mmol). The solution was allowed to stir at room temperature for 6 h, at which time ^{1}H NMR analysis of the crude reaction mixture indicated complete conversion of the starting alcohol to the desired acetoacetate. The solution was again cooled to 0 °C, whereupon triethylamine (1.45 g, 14.3 mmol) and methanesulfonyl azide (1.73 g, 14.3 mmol) were added sequentially. The solution was treated as previously described for the preparation of **7c**. The crude diazoacetoacetate was again dissolved in THF (10 mL), and H_2O (10 mL) was added. To this rapidly stirring bilayer was added solid LiOH·H_2O (1.40 g, 33.4 mmol). After 40 min, the layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 75 mL). The combined organic layer was washed with brine, and the solvent was evaporated under reduced pressure. Purification by column chromatography (9:1 hexanes/ethyl acetate) yielded 2.30 g (8.0 mmol, 84% yield) of the title compound **7d** as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.28 (comp, 4H), 5.65−5.58 (comp, 2H), 5.31 (s, 2H), 4.78 (br s, 1H), 4.57 (s, 2H), 4.10 (d, J = 4.8 Hz, 2H), 2.02 (dd, J = 7.4, 7.1 Hz, 2H), 1.39 (hex, J = 7.4 Hz, 2H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 136.7, 134.2, 133.7, 129.2, 129.0, 128.3, 127.9, 125.9, 69.6, 65.9, 63.9, 46.1, 29.5, 22.5, 13.5; IR (neat) 2117 (C═N_2), 1694 (C═O) cm^{-1}. Anal. Calcd. for $C_{16}H_{20}N_2O_3$: C, 66.65; H, 6.99; N, 9.72. Found: C, 66.58; H, 7.03; N, 9.74.

Preparation of 2-(3-Methyl-2-buten-1-yloxymethyl)benzyl Diazoacetate (7e). Sodium hydride (0.60 g, 24 mmol, 60% dispersion in mineral oil) was washed with anhydrous hexanes (3 × 20 mL), then suspended in 300 mL of anhydrous THF, and cooled to 0 °C. To this solution was added 1,2-benzenedimethanol (7.20 g, 51.9 mmol) in 100 mL of anhydrous THF over 20 min. After addition was complete, the milky white suspension was removed from the ice bath, and stirring

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was continued for an additional 30 min, whereupon 1-bromo-3-methyl-2-butene (3.36 g, 17.3 mmol) was added dropwise via syringe. The solution was allowed to stir for 10 h at 23 °C and then worked up as described for the preparation of **7c**. Purification via column chromatography (7:3 hexanes/ethyl acetate) yielded 3.46 g (16.8 mmol, 97% yield) of 2-(3-methyl-2-buten-1-yloxymethyl)benzyl alcohol as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41−7.24 (comp, 4H), 5.37 (t of hept, J = 7.0, 1.2 Hz, 1H), 4.64 (d, J = 5.9 Hz, 2H), 4.59 (s, 2H), 4.05 (d, J = 7.0 Hz, 2H), 3.42 (br s, 1H), 1.75 (br s, 3H), 1.67 (br s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.6, 138.2, 136.2, 130.0, 129.7, 128.8, 127.9, 120.2, 71.2, 66.7, 63.8, 25.8, 18.0. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.73; H, 8.75. After isolation of the alcohol, the column was flushed with ethyl acetate to produce 4.64 g of 1,2-benezenedimethanol (97% recovery).

2-(3-Methyl-2-buten-1-yloxymethyl)benzyl alcohol (2.45 g, 11.9 mmol) was dissolved in 20 mL of THF, and cooled to 0 °C. Triethylamine (0.2 mL) was added rapidly, followed by dropwise addition of diketene (1.50 g, 17.9 mmol). The solution was allowed to stir at room temperature for 12 h, at which point ^{1}H NMR analysis of the crude reaction mixture indicated complete conversion of the starting alcohol to the desired acetoacetate. The solution was again cooled to 0 °C, whereupon triethylamine (1.81 g, 17.9 mmol) and methanesulfonyl azide (2.17 g, 17.9 mmol) were added sequentially. The solution was treated as previously described for the preparation of **7c**. The crude diazoacetoacetate was again dissolved in THF (12 mL), and H_2O (12 mL) was added. To this rapidly stirring bilayer was added solid $LiOH\cdot H_2O$ (2.50 g, 59.5 mmol). After 30 min, the layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 75 mL). The combined organic layer was washed with brine, and the solvent was evaporated under reduced pressure. Purification by column chromatography (9:1 hexanes/ethyl acetate) yielded 2.52 g (9.2 mmol, 77% yield) of the title compound **11** as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.26 (comp, 4H), 5.40 (t of hept, J = 7.0, 1.2 Hz, 1H), 5.30 (s, 2H), 4.78 (br s, 1H), 4.55 (s, 2H), 4.02 (d, J = 7.0 Hz, 2H), 1.76 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 137.3, 136.8, 134.3, 129.2, 129.1, 128.3, 127.9, 120.8, 69.5, 66.8, 63.9, 46.1, 25.7, 17.9; IR (neat) 2112 (C═N_2), 1706 (C═O) cm^{-1}. Anal. Calcd for $C_{15}H_{18}N_2O_3$: C, 65.68; H, 6.60; N, 10.21. Found: C, 65.62; H, 6.60; N, 10.05.

Preparation of 8-(2-Methyl-2-propen-1-yloxymethyl)naphthyl-1-methyl Diazoacetate (21). Sodium hydride (0.74 g, 31 mmol, 95%) was suspended in 200 mL of anhydrous THF and cooled to 0 °C. To this solution was added 1,8-naphthalenedimethanol (13.5 g, 72.1 mmol) in 300 mL of anhydrous THF over 20 min. After addition was complete, the milky white suspension was removed from the ice bath, and stirring was continued for an additional 30 min, whereupon 1-bromo-2-methyl-2-propene (2.78 g, 20.8 mmol) was added dropwise via syringe. The solution was then allowed to stir for 16 h at 23 °C. Diethyl ether (300 mL) was then added, and the solution was washed with 250 mL of water and 250 mL of saturated brine and then dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure yielded 4.53 g (18.9 mmol, 91% yield) of 8-(2-methyl-2-propen-1-yloxymethyl)-naphthyl-1-methyl alcohol as a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (dd, J = 6.8, 1.5 Hz, 1H), 7.85 (dd, J = 6.8, 1.2 Hz, 1H), 7.57 (dd, J = 7.0, 1.2 Hz, 1H), 7.51 (dd, J = 7.0, 1.3 Hz, 1H), 7.44 (dd, J = 6.8, 4.4 Hz, 1H), 7.42 (dd, J = 7.0, 4.4 Hz, 2H), 5.21 (d, J = 5.8 Hz, 2H), 5.13 (s, 2H), 5.00 (s, 1H), 4.93 (s, 1H), 3.95 (s, 2H), 3.34 (t, J = 5.8 Hz, 1H), 1.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7, 137.3, 135.9, 133.0, 131.7, 130.9, 130.7, 130.4, 128.6, 125.4, 124.8, 112.8, 73.8, 73.5, 66.4, 19.6. Analysis of the solid remaining from the filtration showed it to be 1,8-naphthalenedimethanol (8.15 g, 43.6 mmol, 82% recovery).

8-(2-Methyl-2-propen-1-yloxymethyl)naphthyl-1-methyl alcohol (3.87 g, 16.0 mmol) was dissolved in 20 mL of THF, and cooled to 0 °C. Triethylamine (0.2 mL) was added rapidly, followed by dropwise addition of diketene (2.71 g, 32 mmol). The solution was allowed to stir at room temperature for 7 h, at which point ^{1}H NMR analysis of the crude reaction mixture indicated complete conversion of the starting alcohol to the desired acetoacetate. The solution was again cooled to 0 °C, whereupon triethylamine (3.27 g, 32 mmol) and methanesulfonyl azide (3.88 g, 32 mmol) were added sequentially. The solution was treated as previously described for the preparation of **7c**. The crude diazoacetoacetate was again dissolved in THF (7 mL), and H_2O (7 mL) was added. To this rapidly stirring bilayer was added solid $LiOH\cdot H_2O$ (3.36 g, 80 mmol). After 25 min, the layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 75 mL). The combined organic layer was washed with brine, and the solvent was evaporated under reduced pressure. Purification by column chromatography (9:1 hexanes/ethyl acetate) yielded 3.95 g (12.8 mmol, 80% yield) of the title compound **21** as a yellow solid (mp 38−40 °C): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (dd, J = 8.1, 1.4 Hz, 1H), 7.88 (dd, J = 8.1, 1.4 Hz, 1H), 7.66 (dd, J = 7.1, 1.4 Hz, 1H), 7.58 (dd, J = 7.1, 1.4 Hz, 1H), 7.47 (dd, J = 7.1, 2.4 Hz, 1H), 7.46 (dd, J = 7.1, 2.4 Hz, 1H), 5.87 (s, 2H), 5.01 (s, 1H), 4.93 (s, 2H), 4.92 (s, 1H), 4.73 (br s, 1H) 3.96 (s, 2H), 1.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 141.9, 135.6, 133.1, 131.6, 131.5, 131.3, 131.2, 131.0, 130.6, 125.0, 112.4, 73.6, 72.5, 67.2, 46.3, 19.6; IR (neat) 2115 (C═N_2), 1689 (C═O) cm^{-1}. Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.52; H, 5.87; N, 9.12

General Procedure for Diazo Decomposition of 7a. The procedure for diazo decomposition with $Rh_2(4S\text{-MPPIM})_4$ is representative. Diazoacetate **7a** (100 mg, 0.40 mmol) was dissolved in 4 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 4 h to a solution of $Rh_2(4S\text{-MPPIM})_4$ (6 mg, 1.0 mol %) in 4 mL of refluxing CH_2Cl_2. After the addition was complete, the solution was passed through a plug of a silica gel to remove the catalyst, and the silica was washed with 50 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure, and the crude reaction mixture was purified by column chromatography (8:2 hexanes/ethyl acetate) to yield 59 mg (0.27 mmol, 67% yield) of (1*R*,10*S*)-5,6-benzo-3,8-dioxabicyclo[8.1.0]-undecan-2-one (**8a**) as a white solid spectroscopically and chromatographically identical to known material.[8] Enantiomeric separation was achieved on a 30 m Chiraldex B-DM column operated at 165 °C: 37.6 min for the (1*S*,10*R*)-enantiomer (major isomer from reaction catalyzed by **5**), 38.9 min for the (1*R*,10*S*)-enantiomer. $[\alpha]^{23}_D$ = −23.8° (c = 3.69, $CHCl_3$) for 53% ee (from **6**). A small sample of **8a** (from **6**) was then subjected to hydrogenolysis [$Pd(OH)_2$, H_2 (1 atm) in EtOH, 24 h] to give (1*S*,5*R*)-3-oxabicyclo[3.1.0]hexan-2-one whose absolute configuration was determined by comparison of its elution order on a 30 m Chiraldex A-DA column [110 °C: 27.5 min for (1*R*,5*S*), 28.4 min for (1*S*,5*R*)] versus a sample of known absolute stereochemistry[10] prepared directly from 2-propenyl diazoacetate catalyzed by $Rh_2(5R\text{-MEPY})_4$.

General Procedure for Diazo Decomposition of 7b. The procedure for diazo decomposition with $Rh_2(4S\text{-IBAZ})_4$ is representative. Diazoacetate **7b** (65 mg, 0.25 mmol) was dissolved in 2.5 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 2.5 h to a solution of $Rh_2(4S\text{-IBAZ})_4$ (2.2 mg, 1.0 mol %) in 2.5 mL of refluxing CH_2Cl_2. After the addition was complete, the solution was passed through a plug of silica gel to remove the catalyst, and the silica was washed with 50 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure, and the crude reaction mixture was purified by column chromatography to yield 50 mg (0.22 mmol, 87% yield) of (1*S**,10*R**)-5,6-benzo-3,8-dioxa-10-methylbicyclo[8.1.0]undecan-2-one (**8b**) as a white solid, spectroscopically identical to known material.[8] Enantiomeric separation was achieved on a 30 m Chiraldex G-TA column operated at 135 °C: 92.6 min for the (1*S*,10*R*)-enantiomer (major isomer from reaction catalyzed by **5**), 94.1 min for the (1*R*,10*S*)-enantiomer (minor). $[\alpha]^{23}_D$ = +3.04° (c = 2.88, $CHCl_3$) for 36% ee (from **6**). A small sample of **8b** (from **6**) was then subjected to hydrogenolysis [$Pd(OH)_2$, H_2 (1 atm) in EtOH, 24 h) to give (1*S*,5*R*)-5-methyl-3-oxabicyclo[3.1.0]hexan-2-one whose absolute configuration was determined by comparison of its elution order on a 30 m Chiraldex G-TA column [120 °C: 12.2 min for (1*R*,5*S*), 12.5 min for (1*S*,5*R*)] versus a sample of known absolute stereochemistry[10] prepared directly from 2-methyl-2-propenyl diazoacetate catalyzed by $Rh_2(4S\text{-MPPIM})_4$.

General Procedure for Diazo Decomposition of 7c. The procedure for diazo decomposition with **1** (X = PF_6^-) is representative. Diazoacetate **7c** (288 mg, 1.00 mmol) was dissolved in 10 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 10 h to a solution of $Cu(MeCN)_4PF_6$ (8 mg, 1.0 mol %) and the bisoxazoline corresponding to **1** (10 mg, 1.2 mol %) in 10 mL of refluxing CH_2Cl_2. After the

addition was complete, the solution was passed through a plug of silica gel to remove the catalyst, and the silica was washed with 50 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure. GC and NMR analysis of the reaction mixture revealed the presence of a single major compound **8c**. Purification by column chromatography gave 192 mg (0.74 mmol, 74% yield) of the cyclopropane **8c** as a white solid (mp 47−49 °C).

When diazo decomposition was performed using 146 mg (0.50 mmol) of diazoacetate **7c** catalyzed by Rh_2(4*S*-MEOX)$_4$, GC and NMR analysis of the reaction mixture revealed, in addition to cyclopropane **8c** and C−H insertion product **14**, two other compounds, **12c** and **13c**. Purification by column chromatography yielded 30 mg (0.14 mmol, 27% yield) of alkene **12c**, 7 mg (0.03 mmol, 6% yield) of aldehyde **13c**, and 24 mg (0.09 mmol, 18% yield) of cyclopropane **8c**, and C−H insertion product **14** in a 1:1 ratio.

(1*R*,10*S*,11*S*)-5,6-Benzo-3,8-dioxa-11-propylbicyclo[8.1.0]-undecan-2-one (8c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.24 (comp, 4H), 5.33 (d, J = 12.0 Hz, 1H), 5.07 (d, J = 12.0 Hz, 1H), 4.73 (d, J = 11.8 Hz, 1H), 4.25 (d, J = 11.8 Hz, 1H), 4.02 (dd, J = 10.6, 6.1 Hz, 1H), 3.17 (dd, J = 10.6, 9.0 Hz, 1H), 1.67−1.57 (comp, 2H), 1.48 (dddd, J = 9.0, 8.9, 6.1, 5.9 Hz, 1H), 1.37 (hex, J = 7.1 Hz, 2H), 1.25 (q, J = 6.8 Hz, 2H), 0.88 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 136.9, 135.8, 131.0, 130.9, 128.9, 128.5, 72.6, 68.3, 66.5, 34.4, 28.3, 27.8, 26.9, 21.9, 13.7; IR (CH_2Cl_2) 1716 cm^{-1}; mass spectrum, *m*/*z* (rel intens) 260 (M, 0.03), 217 (0.4), 141 (52), 121 (11), 120 (88), 119 (30), 105 (23), 104 (100), 95 (63), 91 (46). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.76; H, 7.72.

***trans*-4-(Pent-1-en-1-yl)-1,5-dioxa-7,8-benzocyclononen-2-one (14):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45−7.20 (comp, 4H), 5.71 (dt, J = 14.5, 7.1 Hz, 1H), 5.68 (d, J = 13.6 Hz, 1H), 5.50 (dd, J = 14.5, 8.3 Hz, 1H), 5.22 (d, J = 13.6 Hz, 1H), 4.78 (d, J = 10.9 Hz, 1H), 4.53 (d, J = 10.9 Hz, 1H), 4.52 (ddd, J = 10.7, 8.3, 4.0 Hz, 1H), 2.62 (dd, J = 13.3, 4.0 Hz, 1H), 2.52 (dd, J = 13.3, 10.7 Hz, 1H), 2.02 (q, J = 7.1 Hz, 2H), 1.40 (hex, J = 7.1 Hz, 2H), 0.90 (t, J = 7.1, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (C=O not observed), 136.7, 136.4, 132.6, 132.2, 129.7, 128.6, 128.5, 128.4, 81.9, 74.3, 67.2, 42.7, 34.4, 34.2, 22.1, 13.7; IR (neat) 1743 cm^{-1} (C=O); HRMS (FAB$^+$) calcd 261.1491, found 261.1498.

Enantiomer separation for **8c** was achieved on a 30 m Chiraldex G-TA column operated at 165 °C: 100.4 min for the (1*S*,10*R*,11*R*)-enantiomer, 102.4 min for the (1*R*,10*S*,11*S*)-enantiomer (major isomer from reactions catalyzed by **1**−**5**). $[\alpha]^{23}_D = -35.7°$ (c = 4.11, $CHCl_3$) for 84% ee (from **1**, X = PF_6^-), and $[\alpha]^{23}_D = +35.8°$ (c = 1.73, $CHCl_3$) for 80% ee (from **6**, X = PF_6^-). A small sample of **8c** (from **6**, X = PF_6^-) was then subjected to hydrogenolysis [$Pd(OH)_2$, H_2 (1 atm) in EtOH, 24 h] to give (1*S*,5*R*,6*R*)-3-oxa-6-propylbicyclo[3.1.0]hexan-2-one whose absolute configuration was determined by comparison of the elution order on a 30 m Chiraldex B-TA column [140 °C, 9.5 min for the (1*R*,5*S*,6*S*)-isomer (minor), 12.3 min for the (1*S*,5*R*,6*R*)-isomer (major)] versus a sample of known absolute stereochemistry[10] prepared directly from (*E*)-2-hexenyl diazoacetate catalyzed by Rh_2(5*S*-MEPY)$_4$. Enantiomer separation for **14** was achieved on a 30 m Chiraldex G-TA column operated at 165 °C: 78.0 and 79.6 min for two enantiomers.

General Procedure for Diazo Decomposition of 7d. The procedure for diazo decomposition with Rh_2(4*S*-IBAZ)$_4$ is representative. Diazoacetate **7d** (72 mg, 0.25 mmol) was dissolved in 2.5 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 2.5 h to a solution of Rh_2(4*S*-IBAZ)$_4$ (2.1 mg, 1.0 mol %) in 2.5 mL of refluxing CH_2Cl_2. After the addition was complete, the solution was passed through a plug of silica gel to remove the catalyst, and the silica was washed with 50 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure. GC and NMR analysis revealed the presence of a single major compound, cyclopropane **8d**. Purification by column chromatography gave cyclopropane **8d** (49 mg, 0.19 mmol, 75%) as a white solid (mp 69−71 °C).

When diazo decomposition was performed using 135 mg (0.47 mmol) of diazoacetate **7d** catalyzed by **1** (X = PF_6^-), GC and NMR analysis of the reaction mixture revealed the presence of a second cyclopropane, **9d**, in a 1:1 ratio with cyclopropane **8d**. Purification by column chromatography gave 67 mg (0.26 mmol, 55% yield) of the two diastereomeric cyclopropanes as an inseparable mixture. Radial chromatography allowed isolation of 24 mg (0.09 mmol, 20% yield) of the second cyclopropane **9d** as a white solid (mp 91−93 °C).

When diazo decomposition was performed using 73 mg (0.25 mmol) of diazoacetate **7d** catalyzed by Rh_2(4*S*-MEOX)$_4$, GC and NMR analysis of the reaction mixture revealed in addition to the cyclopropane products two other major compounds, **12d** and **13d**. Purification by column chromatography yielded 18 mg (0.07 mmol, 30% yield) of alkene **12d**, 4.4 mg (0.02 mmol, 8% yield) of aldehyde **13d**, and 18 mg (0.07 mmol, 28% yield) of cyclopropanes **8d** and **9d** in a 87:13 ratio.

(1*R*,10*S*,11*R*)-5,6-Benzo-3,8-dioxa-11-propylbicyclo[8.1.0]undecan-2-one (8d): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.25 (comp, 4H), 5.31 (d, J = 12.2 Hz, 1H), 5.13 (d, J = 12.2 Hz, 1H), 4.79 (d, J = 11.4 Hz, 1H), 4.27 (d, J = 11.4 Hz, 1H), 4.05 (dd, J = 10.4, 6.2 Hz, 2H), 3.38 (t, J = 10.4 Hz, 1H) 1.82 (q, J = 8.6 Hz, 1H) 1.80−1.71 (comp, 2H) 1.68−1.59 (m, 1H) 1.46−1.27 (comp, 3H), 0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 136.8, 135.9, 131.0, 130.6, 128.7, 128.4, 73.0, 66.4, 65.3, 26.3, 25.4, 24.5, 23.7, 23.0, 13.7; IR (film) 1740, 1099 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.85; H, 7.68.

Enantiomeric excess was determined on a 30 m Chiraldex B-DM operated at 165 °C: 75.4 min for the (1*R*,10*S*,11*R*)-isomer (major isomer from reactions catalyzed by **1**−**5**), 76.6 min for the (1*S*,10*R*,11*S*)-isomer. $[\alpha]^{23}_D = -6.83°$ (c = 1.82, $CHCl_3$) for 85% ee from Rh_2(4*S*-IBAZ)$_4$. A small sample of **8d** (from **1**, X = PF_6^-) was then subjected to hydrogenolysis [$Pd(OH)_2$, H_2 (1 atm) in EtOH, 24 h] to give (1*R*,5*S*,6*R*)-3-oxa-6-propylbicyclo[3.1.0]hexan-2-one whose absolute configuration was determined by comparison of the elution order on a 30 m Chiraldex G-TA column [140 °C, 9.1 min for (1*S*,5*R*,6*S*), 9.3 min for (1*R*,5*S*,6*R*)] versus a sample of known absolute stereochemistry[10] prepared directly from (*Z*)-2-hexenyl diazoacetate catalyzed by Rh_2(5*S*-MEPY)$_4$.

(1*R,10*R**,11*S**)-5,6-Benzo-3,8-dioxa-11-propylbicyclo[8.1.0]-undecan-2-one (9d):** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 7.6 Hz, 1H), 7.38−7.30 (comp, 3H), 6.03 (d, J = 13.3 Hz, 1H), 5.17 (d, J = 13.3 Hz, 1H), 4.88 (d, J = 13.1 Hz, 1H), 4.58 (d, J = 13.1 Hz, 1H), 4.00 (dd, J = 13.1, 5.2 Hz, 1H), 3.37 (dd, J = 13.1, 9.7 Hz, 1H), 1.73 (t, J = 5.4 Hz, 1H), 1.57−1.51 (m, 1H), 1.40−1.23 (comp, 4H), 0.90 (t, J = 7.1 Hz, 3H), 0.74 (hept, J = 4.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 136.2, 135.8, 130.6, 130.5, 129.0, 128.6, 71.5, 67.8, 65.8, 29.0, 26.1, 26.0, 23.5, 22.5, 13.8; IR (film) 1735 (C=O) cm^{-1}; mass spectrum, *m*/*z* (rel intens) 141 (25), 129 (18), 120 (33), 119 (21), 116 (7), 105 (24), 104 (100), 103 (16), 91 (28), 81 (26), 78 (16). Enantiomeric excess determined on a 30 m Chiraldex B-DM column operated at 180 °C: 54.7 min for the (1*R**,10*R**,11*S**)-isomer, 56.0 min for the (1*S**,10*S**,11*R**)-isomer. $[\alpha]^{23}_D = +113.8°$ (c = 0.47, $CHCl_3$) for 92% ee (from **1**, X = PF_6^-), and $[\alpha]^{23}_D = -83.7°$ (c = 0.37, $CHCl_3$) for 67% ee (from **6**, X = PF_6^-).

General Procedure for Diazo Decomposition of 7e. The procedure for diazo decomposition with **1** (X = PF_6^-) is representative. Diazoacetate **7e** (274 mg, 1.0 mmol) was dissolved in 10 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 10 h to a solution of $Cu(MeCN)_4PF_6$ (3.7 mg, 1.0 mol %) and the bisoxazoline corresponding to **1** (3.5 mg, 1.2 mol %) in 10 mL of refluxing CH_2Cl_2. After the addition was complete, the solution was passed through a plug of silica gel to remove the catalyst, and the silica was washed with 50 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure. GC and NMR analysis of the reaction mixture revealed the presence of two cyclopropanes, **8e** and **9e**, in a 92:8 ratio. Purification by column chromatography gave 214 mg (0.87 mmol, 87% yield) of the cyclopropanes as an inseparable mixture. Radial chromatography allowed isolation of **8e** (172 mg, 0.70 mmol, 70% yield) as a white solid (mp 80−82 °C) and **9e** (13 mg, 0.05 mmol, 5% yield) as a colorless oil.

When diazo decomposition was performed using 275 mg (1.0 mmol) of diazoacetate **7e** catalyzed by Rh_2(5*S*-MEPY)$_4$, GC and NMR analysis of the reaction mixture revealed, in addition to the cyclopropanes, two other major compounds, **12e** and **13e**. Purification by column chromatography yielded 82 mg (0.40 mmol, 40% yield) of alkene **12e**, 10 mg (0.05 mmol, 5% yield) of aldehyde **13e**, and 44 mg (0.18 mmol, 18% yield) of cyclopropanes **8e** and **9e** in a 7:93 ratio.

(1*S*,10*R*)-5,6-Benzo-3,8-dioxa-11,11-dimethylbicyclo[8.1.0]undecan-2-one (8e): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.38−7.25 (comp, 4H), 5.31 (d, J = 12.1 Hz, 1H), 5.10 (d, J = 12.1 Hz, 1H), 4.78 (d, J = 11.3 Hz, 1H), 4.27 (d, J = 11.3 Hz, 1H), 4.05 (dd, J = 11.0, 6.4 Hz, 1H), 3.38 (dd, J = 11.0, 9.5 Hz, 1H), 1.64 (d, J = 9.3 Hz, 1H), 1.58 (ddd, J = 9.5, 9.3, 6.4 Hz, 1H), 1.32 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 136.9, 136.0, 131.1, 130.7, 128.8, 128.5, 73.0, 66.5, 66.0, 33.3, 32.1, 29.2, 26.8, 15.8. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37 Found: C, 73.14; H, 7.38.

Enantiomeric separation was achieved on a 30 m Chiraldex B-DM column operated at 145 °C: 87.6 min for the (1*S*,10*R*)-enantiomer, 89.4 min for the (1*R*,10*S*)-enantiomer. $[\alpha]^{23}_D$ = +1.54° (c = 3.6, $CHCl_3$) for 63% ee [from Rh_2(4*S*-IBAZ)$_4$]. A small sample of **8e** (from **1**, X = PF_6^-) was then subjected to hydrogenolysis [$Pd(OH)_2$, H_2 (1 atm) in EtOH, 24 h] to give (1*S*,5*R*)-6,6-dimethyl-3-oxabicyclo[3.1.0]-hexan-2-one whose absolute configuration was determined by comparison of its elution order on a 30 m Chiraldex G-TA column [110 °C: 18.9 min for (1*R*,5*S*), 23.3 min for (1*S*,5*R*)] versus a sample of known absolute stereochemistry[10] prepared directly from 3-methyl-2-butenyl diazoacetate catalyzed by Rh_2(5*S*-MEPY)$_4$.

(1*R,10*S**,11*R**)-5,6-Benzo-3,8-dioxa-11,11-dimethylbicyclo[8.1.0]-undecan-2-one (9e):** ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.54 (d, J = 7.2 Hz, 1H), 7.42−7.24 (comp, 3H), 5.95 (d, J = 13.2 Hz, 1H), 5.31 (d, J = 13.2 Hz, 1H), 4.88 (d, J = 12.8 Hz, 1H), 4.51 (d, J = 12.8 Hz, 1H), 3.95 (dd, J = 13.0, 5.8 Hz, 1H), 3.39 (dd, J = 13.0, 9.5 Hz, 1H), 1.51 (d, J = 6.0 Hz, 1H), 1.16 (s, 3H), 1.05 (s, 3H), 0.70 (dt, J = 9.5, 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 137.4, 135.5, 130.5, 129.5, 129.1, 128.3, 72.2, 67.4, 65.8, 30.5, 25.8, 22.7, 21.0, 18.1; mass spectrum, *m*/*z* (rel intens) 246 (M, 1), 163 (42), 162 (81), 119 (55), 117 (37), 104 (78), 92 (100), 91 (73). Enantiomeric separation was achieved on a 30 m Chiraldex B-DM column operated at 145 °C: 91.4 min for the (1*R**,10*S**)-enantiomer, 93.4 min for the (1*S**,10*R**)-enantiomer. $[\alpha]^{23}_D$ = +28.9° (c = 2.62, $CHCl_3$) for 30% ee (from **1**, X = PF_6^-).

General Procedure for Diazo Decomposition of 17. The procedure for diazo decomposition with **1** (X = PF_6^-) is representative. Diazoacetate **7** (390 mg, 1 mmol) was dissolved in 10 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 5 h to a solution of Cu(MeCN)$_4$$PF_6$ (4.0 mg, 1.0 mol %) and the bisoxazoline corresponding to **1** (4.2 mg, 1.3 mol %) in 10 mL of refluxing CH_2Cl_2. After the addition was complete, the solution was passed through a plug of silica gel to remove the catalyst, and the silica was washed with 50 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure. GC and NMR analysis revealed the presence of two diastereomeric cyclopropanes, **18a** and **18b**, in a 69:31 ratio. Purification by column chromatography (10:1 hexanes/ethyl acetate) gave 156 mg of (1*R*,15*S*)-5,6,10,11-bisbenzo-3,8,3-trioxa-15-methylbicyclo[13.1.0]-hexadecan-2-one (**18a**; 0.44 mmol, 44%) followed by 69 mg of (1*S**,15*S**)-5,6,10,11-bisbenzo-3,8,13-trioxa-15-methylbicyclo[13.1.0]-hexadecan-2-one (**18b**; 0.20 mmol, 20%). Enantiomeric separation was achieved for **18a** on a 30 m Chiraldex B-DM column operated at 200 °C: 119.3 min for the (1*R*,15*S*)-enantiomer, 121.6 min for the (1*S*,15*R*)-enantiomer. A small sample of **18a** (from Rh_2(4*S*-IBAZ)$_4$) was then subjected to hydrogenolysis [$Pd(OH)_2$, H_2 (1 atm) in EtOH, 24 h] to give (1*S*,5*R*)-5-methyl-3-oxabicyclo[3.1.0]hexan-2-one whose absolute configuration was determined by comparison of its elution order on a 30 m Chiraldex G-TA column [120 °C, 12.2 min for (1*R*,5*S*), 12.5 min for (1*S*,5*R*)] versus a sample of known absolute stereochemistry[10] prepared directly from 2-methyl-2-propenyl diazoacetate catalyzed by Rh_2(4*S*-MPPIM)$_4$.

General Procedure for Diazo Decomposition of 19. The procedure for diazo decomposition with Rh_2(4*S*-MEOX)$_4$ is representative. Diazoacetate **19** (215 mg, 0.43 mmol) was dissolved in 5 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 5 h to a solution of Rh_2(4*S*-MEOX)$_4$ (3.4 mg, 1.0 mol %) in 5 mL of refluxing CH_2Cl_2. After the addition was complete, the solution was passed through a plug of silica gel to remove the catalyst, and the silica was washed with 50 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure. GC and NMR analysis revealed the presence of two diastereomeric cyclopropanes, **20a** and **20b**, in a 75:25 ratio. Purification by column chromatography (8:2 hexanes/ethyl acetate) gave (1*R*,20*S*)-5,6,10,11,15,16-trisbenzo-3,8,13,18-tetroxa-20-methylbicyclo-[18.1.0]henicosan-2-one (**20a**) and (1*S**,20*S**)-5,6,10,11,15,16-trisbenzo-3,8,13,18-tetroxa-20-methylbicyclo[18.1.0]henicosan-2-one (**20b**) as an inseparable mixture by column or radial chromatography (94.3 mg, 0.20 mmol, 46%). Enantiomeric excess and absolute configuration were determined for the (1*S**,20*R**) compound by hydrogenolysis [Pd-$(OH)_2$, H_2 (1 atm) in EtOH, 24 h] to give (1*R*,5*S*)-5-methyl-3-oxabicyclo-[3.1.0]hexan-2-one. Absolute configuration was determined by comparison of the elution order on a 30 m Chiraldex G-TA column [120 °C, 12.2 min for (1*R*,5*S*), 12.5 min for (1*S*,5*R*)] versus a sample of known absolute stereochemistry[10] prepared directly from 2-methyl-2-propenyl diazoacetate catalyzed by Rh_2(4*S*-MPPIM)$_4$.

General Procedure for Diazo Decomposition of 21. The procedure for diazo decomposition with **1** (X = PF_6^-) is representative. Diazoacetate **21** (87 mg, 0.28 mmol) was dissolved in 3 mL of freshly distilled CH_2Cl_2 and added via syringe pump over 3 h to a solution of Cu(MeCN)$_4$$PF_6$ (1 mg, 1.0 mol %) and the bisoxazoline corresponding to **1** (1 mg, 1.2 mol %) in 3 mL of refluxing CH_2Cl_2. After the addition was complete, the solution was passed through a plug of silica gel to remove the catalyst, and the silica was washed with 50 mL of 30% ethyl acetate in hexanes. The solvent was removed under reduced pressure. GC and NMR analysis revealed the presence of a single major compound. Purification by column chromatography (8:2 hexanes/ethyl acetate) gave cyclopropane **22** (75 mg, 0.27 mmol, 95% yield) as a white solid (mp 88−90 °C).

When diazo decomposition was performed using 79 mg (0.25 mmol) of diazoacetate **21** catalyzed by Rh_2(4*R*-MEOX)$_4$, GC and NMR analysis of the reaction mixture revealed the presence of a second compound, **23**, in a 3:7 ratio with cyclopropane **22**, Purification by radial chromatography gave 43 mg (0.15 mmol, 60% yield) of the cyclopropane **22**, and 17 mg (0.06 mmol, 24% yield) of aromatic cycloaddition product **23**.

(1*R*,11*S*)-11-Methyl-5,6,7[*i*,*j*]naphthobicyclo[9.1.0]dodecan-2-one (22): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dd, J = 8.1, 1.3 Hz, 1H), 7.89 (dd, J = 8.1, 1.3 Hz, 1H), 7.62 (dd, J = 7.0, 1.4 Hz, 1H), 7.52 (dd, J = 7.0, 1.4 Hz, 1H), 7.47 (dd, J = 8.1, 7.0 Hz, 1H), 7.41 (dd, J = 8.1, 7.0 Hz, 1H), 5.50 (br s, 2H), 4.86−4.76 (comp, 2H), 3.79 (d, J = 11.0 Hz, 1H), 3.38 (d, J = 11.0 Hz, 1H) 1.65 (dd, J = 7.8, 5.6 Hz, 1H), 1.35 (t, J = 5.4 Hz, 1H), 1.22 (s, 3H), 0.81 (dd, J = 7.8, 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 135.8, 133.8, 133.0, 131.8, 131.7, 131.6, 131.5, 131.0, 130.7, 125.3, 124.7, 73.3, 72.3, 69.9, 26.1, 23.2, 18.7. Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.58; H, 6.42. Found: C, 76.69; H, 6.45. Enantiomer separation was achieved on a 30 m Chiraldex B-DM column operated at 160 °C for 60 min and then heated at 0.2 °C/min to 220 °C: 186.8 min for the (1*R*,11*S*)-enantiomer, 188.8 min for the (1*S*,10*R*)-enantiomer. $[\alpha]^{23}_D$ = +25.1° (c = 10.4, $CHCl_3$) for 80% ee (from **1**, X = PF_6^-). A small sample of **22** (from **1**) was then subjected to hydrogenolysis [$Pd(OH)_2$, H_2 (1 atm) in EtOH, 24 h] to give (1*R*,5*S*)-5-methyl-3-oxabicyclo[3.1.0]hexan-2-one whose absolute configuration was determined by comparison of the elution order on a 30 m Chiraldex G-TA column [(120 °C, 12.2 min for (1*R*,5*S*), 12.5 min for (1*S*,5*R*)] versus a sample of known absolute stereochemistry[10] prepared directly from 2-methyl-2-propenyl diazoacetate catalyzed by Rh_2(4*S*-MPPIM)$_4$.

6,7-[2-(2-Methyl-2-propen-1-yloxymethyl)benzo]-3-oxatricyclo-[4,3,0^{1,5}.0^{5,10}]-(*Z*)-8-decene-2-one (23): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27−7.20 (comp, 2H), 7.12 (dd, J = 6.9, 2.0 Hz, 1H), 6.48 (d, J = 9.6 Hz, 1H), 6.26 (dd, J = 9.6, 4.5 Hz, 1H), 5.23 (d, J = 9.6 Hz, 1H), 4.97 (s, 1H), 4.93 (s, 1H), 4.67 (d, J = 11.9 Hz, 1H), 4.59 (d, J = 11.9 Hz, 1H), 4.22 (d, J = 9.6 Hz, 1H), 3.93 (s, 2H), 2.27 (dd, J = 4.5, 3.4 Hz, 1H), 1.76 (s, 3H), 1.18 (d, J = 3.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$ δ 177.2, 141.3, 136.7, 131.8, 129.4, 128.7, 127.5, 125.1, 123.2, 113.1, 112.5, 74.3, 73.4, 71.5, 32.8, 32.6, 19.6, 19.2. Enantiomeric separation was achieved on a 30 m Chiraldex B-DM column operated at 160 °C for 60 min and then heated at 0.2 °C/min to 220 °C: 201.9 min for the (1*R**,5*S**)-enantiomer, 203.0 min for the (1*S**,5*R**)-enantiomer.

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Supporting Information Available: Characterization of compounds **12** and **13** (PDF). This information is available free of charge via the Internet at http://pubs.acs.org.

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