Catalytic Asymmetric Cyclopropanation of Heteroaryldiazoacetates

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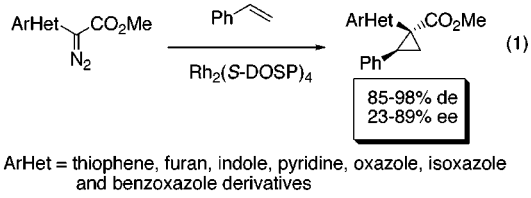
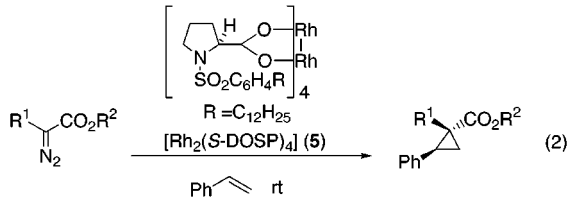
Rh_2(*S*-DOSP)$_4$-catalyzed decomposition of heteroaryldiazoacetates in the presence of styrene results in highly diastereoselective and enantioselective cyclopropanations. Heteroaryldiazoacetates containing both electron-rich and electron-deficient heterocycles, such as thiophene, furan, pyridine, indole, oxazole, isoxazole, and benzoxazole, are effective in this chemistry. These studies broaden the range of diazo compounds containing both electron-withdrawing and electron-donating groups, which undergo highly diastereoselective cyclopropanations.

New methods for the stereoselective synthesis of highly functionalized cyclopropanes have been extensively studied.[1] The metal-catalyzed decomposition of α-diazocarbonyl compounds in the presence of alkenes is a powerful method for the synthesis of highly functionalized cyclopropanes.[2] In this paper, we describe that various heteroaryldiazoacetates are capable of highly stereoselective cyclopropanations (eq 1), which greatly broadens the scope of this chemistry.



ArHet = thiophene, furan, indole, pyridine, oxazole, isoxazole and benzoxazole derivatives

The most widely utilized carbenoids that have been used for metal-catalyzed cyclopropanations are those derived from unsubstituted diazoacetates, such as ethyl diazoacetate (**1**).[2a] Even though various catalysts have been developed that are capable of highly enantioselective cyclopropanations of this class of metal-carbenoids, diastereocontrol has been a major challenge that has been successfully solved in only a few systems.[3] In contrast, diazo compounds containing both electron-withdrawing (EWG) and electron-donating groups (EDG) undergo highly diastereoselective and chemoselective cyclopropanations.[4] Examples of such systems are the phenyldiazoacetate **2**,[5] the vinyldiazoacetate **3**,[6] and the alkynyldiazoacetate **4**.[7] Furthermore, high asymmetric induction can be achieved for the transformations of **2**−**4**, when the reactions are catalyzed by the dirhodium catalyst Rh_2(*S*-DOSP)$_4$ (**5**),[5b,6c,7,8] again in marked contrast to the result with ethyl diazoacetate (**1**) (eq 2).[6b] Room temperature reactions of **2**−**4** in pentane result in cyclopropanation in around 90% ee, while the cyclopropanation of **3** at −78 °C occurs in 98% ee. Considering the impressive cyclopropanation stereoselectivity that is exhibited by diazo compounds **2**−**4**, the development of an even wider range of diazo compounds with the EWG−EDG group combination would be very worthwhile.



			CH_2Cl_2		pentane	
Diazo	R^1	R^2	de, %	ee, %	de, %	ee, %
1	H	Et	8	6	–	–
2	Ph	Me	96	69	94	91
3	CH=CHPh	Me	>96	74	>96	90
4	C≡CPh	Me	–	–	84	89

Even though a number of heteroaryldiazoacetates are known,[9] there are no previous reports to our knowledge

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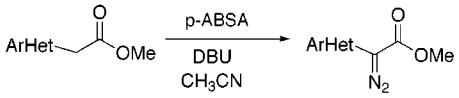
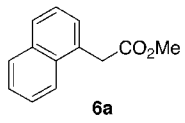
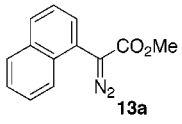
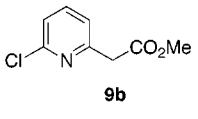
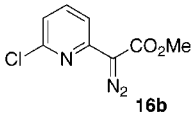
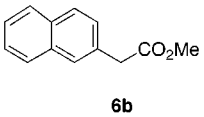
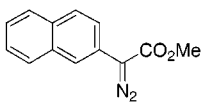
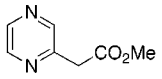
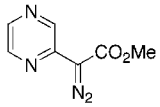
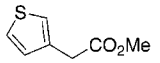
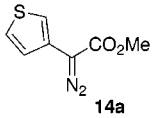
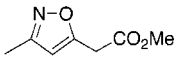
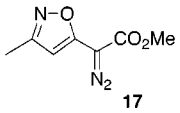
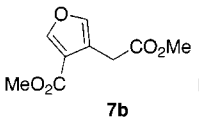
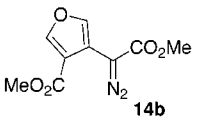
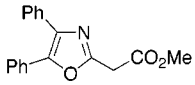
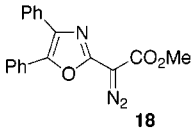
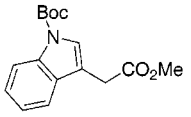
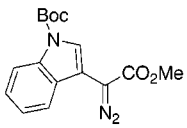
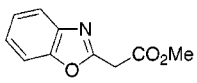
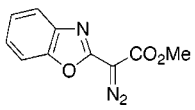
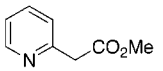
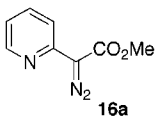
Table 1. Synthesis of Methyl Heteroaryldiazoacetates



Substrate	Product	Yield, %	Substrate	Product	Yield, %
 **6a**	 **13a**	84	 **9b**	 **16b**	89
 **6b**	 **13b**	84[a]	 **9c**	 **16c**	87
 **7a**	 **14a**	68	 **10**	 **17**	86
 **7b**	 **14b**	93	 **11**	 **18**	85
 **8**	 **15**	89	 **12**	 **19**	90
 **9a**	 **16a**	88			

[a] Reference 12.

of their use in metal-catalyzed intermolecular cyclopropanations. The metal-catalyzed reactions of heteroaryldiazoacetates are limited to intramolecular capture of the carbenoid by ylide formation,[9a−d,f,g,j,k,n,p−r] C−H insertion,[9e,l] N−H insertion,[9t] or cyclopropanation[9l] and intermolecular O−H insertion.[9u] The thermolysis of various heteroaryldiazoacetates has been examined.[9r,s,u] Heteroaryldiazoacetates substituted at the 2-position of electron-rich heteroaryl rings such as furan are of limited stability at room temperature,[9u] but other heteroaryldiazoacetates appear to have good stability and are easily handled.

In addition to the stereochemical issues, two other issues needed to be considered in extending the rhodium(II)-catalyzed cyclopropanation to representative heterocycles. First, Lewis basic sites on the heteroaryl ring systems may interfere with the chemistry either by complexation to the catalyst or by reaction with the highly electrophilic carbenoid. Highly electron-rich heterocycles may also react with the carbenoid.[10] Second, certain heteroaryldiazoacetates may not be sufficiently stable to be practical carbenoid precursors such as those substituted at the 2-position of electron-rich heteroaryl rings. Consequently, as the focus of this research is on the development of practical carbenoid precursors, the electron-rich heterocycles that were examined in this study were limited to 3-substituted derivatives.

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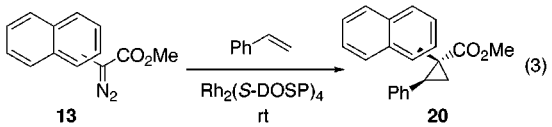
The methyl naphthyl- and heteroaryldiazoacetates **13**−**19** were readily prepared from the corresponding naphthyl and heteroarylacetates **6**−**12** by a diazo transfer reaction using *p*-acetamidobenzenesulfonyl azide (*p*-ABSA)[11] and DBU in acetonitrile at room temperature (Table 1). The methyl heteroarylacetates were synthesized by esterification of the corresponding substituted acetic acids. Some of these substituted acetic acids are commercially available or were readily formed by one-carbon homologation of methyl- or methanol-substituted heteroaryl ring compounds. Experimental procedures describing the preparation of heteroarylacetates **7**−**12** and heteroaryldiazoacetates **13**−**19** are given in the Supporting Information. All of the heteroaryldiazoacetates **13**−**19** were easily handled and could be stored for months at −10 °C without any apparent decomposition. Appropriate care, however, should be taken with any new diazo compound because many compounds of this class have the potential to be shock sensitive.

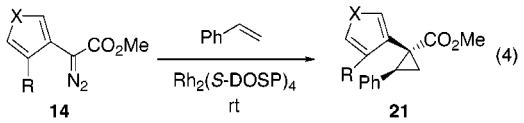
The cyclopropanation chemistry of aryldiazoacetates has been primarily focused on the parent methyl phenyldiazoacetate.[5] A range of substituted phenyldiazoacetates have been shown to be effective substrates for rhodium-catalyzed intermolecular cyclopropanations and C−H insertions.[12] Even though the phenyl ring was important for highly selective reactions, either electron donating or electron withdrawing groups could be tolerated on the ring. Thus, it was anticipated that electron-rich and electron-deficient heterocycles might be capable of undergoing highly stereoselective cyclopropanations. As an introduction to this study, the reaction of 1- and 2-naphthyldiazoacetates **13** was examined. The Rh_2(*S*-DOSP)$_4$-catalyzed cyclopropanation of styrene with the 1-naphthyldiazoacetate **13a** at room temperature was very effective. The reaction at room temperature in CH_2Cl_2 gave **20a** in 81% yield, 98% de, and 68% ee, while the reaction in hexane/toluene gave **20a** in 86% yield, 98% de, and 94% ee. Similarly impressive results were obtained with the 2-naphthyldiazoacetate **13b**. The relative stereochemistry of **20** is readily determined from the chemical shift for the methyl group in the ^{1}H NMR. In the minor diastereomer, the methyl signal is shielded by 0.3−0.5 ppm by the cis phenyl substituent. The improved enantioselectivity on using hexane/toluene instead of CH_2Cl_2 as solvent is characteristic of Rh_2(*S*-DOSP)$_4$-catalyzed cyclopropanations.[6c] Even higher enantioselectivity would be expected if the reaction was carried out at lower temperatures.[6c]



13 20 (3)

		solvent	yield, %	de, %	ee, %
a	1-naphthyl	CH_2Cl_2	81	98	68
a	1-naphthyl	hex/tol (5:1)	86	98	94
b	2-naphthyl	CH_2Cl_2	87	98	80
b	2-naphthyl	hex/tol (4:1)	78	90	90

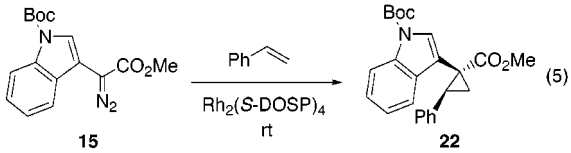
Diazo compounds **14**, containing an electron-rich heterocycle substituted at the 3-position, were then examined (eq 4). The thiophene derivative **14a** resulted in a highly efficient cyclopropanation to form **21a**, and once again, as is typical of Rh_2(*S*-DOSP)$_4$-catalyzed reactions, the highest enantioselectivity was obtained when the reaction was carried out in hydrocarbon solvent. The furan derivative **14b** containing an electron-withdrawing substituent also underwent a very effective cyclopropanation. Under the optimized conditions, **21b** was formed in 91% yield, 96% de, and 86% ee. No side reactions due to intramolecular ylide formation[13] were observed.



14 21 (4)

	X	R	solvent	yield, %	de, %	ee, %
a	S	H	CH_2Cl_2	85	95	78
a	S	H	hexane	87	96	89
b	O	CO_2Me	CH_2Cl_2	81	97	81
b	O	CO_2Me	hexane	91	96	86

The 3-indolyl derivative **15** was then examined. Rh_2(*S*-DOSP)$_4$-catalyzed cyclopropanation of **15** in CH_2Cl_2 to form **22** proceeded in good yield (67%) and diastereoselectivity (>96% de), but the enantioselectivity was very low (23% ee). No improvement in enantioselectivity was obtained when the reaction was carried out in hexane as solvent. The reason for the poor enantioselectivity with this substrate is not well understood but there may be interference due to the bulky *N*-BOC group.



15 22 (5)

solvent	yield, %	de, %	ee, %
CH_2Cl_2	67	97	23
hexane	82	94	12

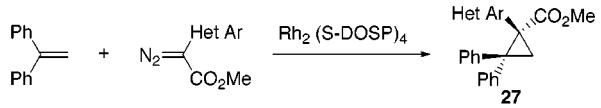
The next series of diazo compounds **16** contain electron-deficient heterocycles (eq 6). Furthermore, compounds **16** have Lewis basic sites that could coordinate to the catalyst or undergo reaction with the carbenoid. All three diazo compounds under the reaction conditions caused the color of the reaction to change from green to red, and such a color change is indicative of coordination of the heterocycle to the catalyst. In the reactions with CH_2Cl_2 at room temperature, only the 2-chloropyridin-6-yl systems **16b** resulted in cyclopropanation to form **23b**. The unsubstituted pyridin-2-yl system **16a**, however, did result in a low yield of cyclopropanation to form **23a** (59% yield) under refluxing conditions with 1,2-dichloroethane as solvent. Neither **16a** nor **16b** was sufficiently soluble in hexanes for the reaction to be carried out in that solvent. Both **23a** and **23b** were produced with high diastereoselectivity and moderate enantioselectivity. No cyclopropanation products were obtained in the reaction

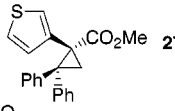
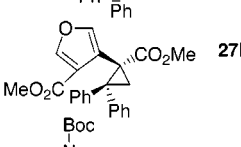
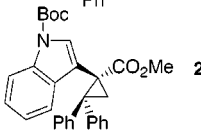
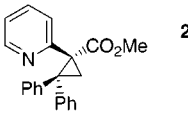
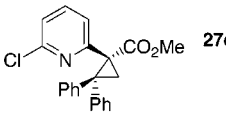
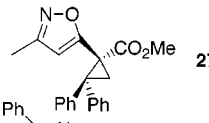
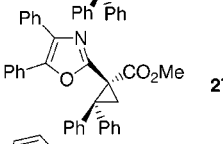
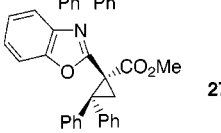
(11) Baum, J. S. S., D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, *17*, 1709.

(12) Davies, H. M. L.; Hansen, T.; Churchill, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 3063.

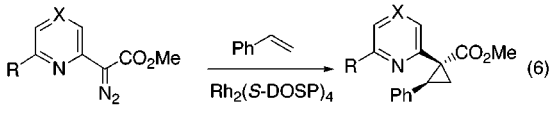
(13) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385.

Table 2. Asymmetric Cyclopropanation of 1, 1-diphyenylethylene



Substrate	Product		Conditions	%yield	%ee
14a		**27a**	hexanes, rt	72	97
14b		**27b**	hexanes:CH_2Cl_2 (4:1), rt	18	88
15		**27c**	hexanes, rt	79	67
16a		**27d**	$(CH_2Cl)_2$, 83°C	58	78
16b		**27e**	CH_2Cl_2:hexanes (2:1), rt	78	89
17		**27f**	hexanes, rt	91	95
18		**27g**	hexanes:PhMe (3:2), rt	88	92
19		**27h**	PhMe, reflux	73	70

with the pyrazine derivative **16c**. Even under forcing conditions, **16c** remained unchanged.

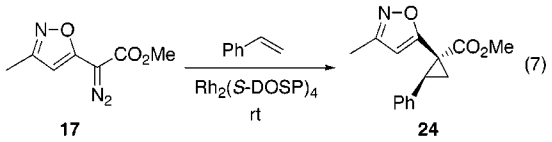


16 **23**

	X	R	conditions	yield, %	de, %	ee, %
a	CH	H	CH_2Cl_2, rt	no reaction		
a	CH	H	$(CH_2Cl)_2$, 83°C	59	91	47
b	CH	Cl	CH_2Cl_2, rt	91	97	69
b	CH	Cl	CH_2Cl_2/hex (2:1), rt	79	98	72
c	N	H	$ClCH_2CH_2Cl$, 83°C	no reaction		

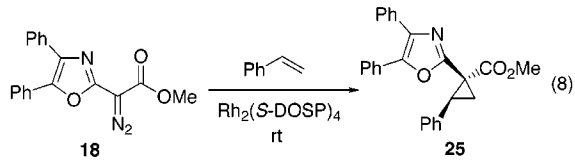
The final series of heteroaryldiazoacetates that were examined were the isoxazole **17**, oxazole **18**, and benzoxazole **19** derivatives. The isoxazole derivative **17** was an exceptional system, and under the optimized conditions, the cyclopropane **24** was formed in 84% yield, 93% de, and 86% ee (eq 7). The standard reaction for the oxazole in CH_2Cl_2 resulted in the formation of **25** in only 12% ee (eq 8). On changing the reaction solvent, however, to a toluene/hexane mixture **25** was formed in 81% yield, 96% de, and 71% ee. This represents another example of the remarkable solvent effect that is seen in Rh_2(*S*-DOSP)$_4$-catalyzed cyclopropanations. The color of the Rh_2(*S*-DOSP)$_4$-catalyzed reaction for the benzoxazole derivative **19** was red, indicating coordination of the heterocycle to the catalyst, and in the reaction in CH_2Cl_2 at room temperature, only a 10% yield of cyclopropane **26** was obtained (eq 9). On using more forcing conditions (refluxing toluene), the yield of **26** was improved to 68%. Even though the enantioselectivity was reasonable for such a high-temperature reaction (71% ee), the diastereoselectivity (88% de) was lower that for any of the other heteroaryldiazoacetates.

The cyclopropanation chemistry of the heteroaryldiazoacetates with 1,1-diphenylethylene was also examined, and the results are summarized in Table 2. For most of the monocyclic heterocyclic systems, high enantioselectivity (89−97% ee) was obtained. The enantioselectivity was slightly lower for the indole **27c** (67% ee), but a similar result was also seen in the cyclopropanation of styrene. Refluxing conditions were required for the decomposition of the pyridinyldiazoacetate **16a** and the benzoxazolyldiazoacetate **19**, and under these forcing conditions the cyclopropanes **27d** and **27h** were formed in 70−80% ee. Except for the furanyl derivative **27b**, the



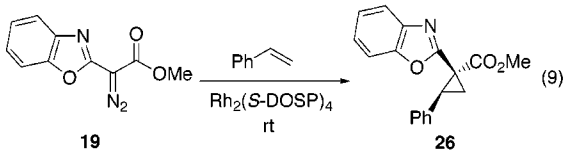
17 24

solvent	yield, %	de, %	ee, %
CH_2Cl_2	79	95	76
hexane	84	93	86



18 25

solvent	yield, %	de, %	ee, %
CH_2Cl_2	81	97	12
hex/tol (3: 2)	81	96	71



19 26

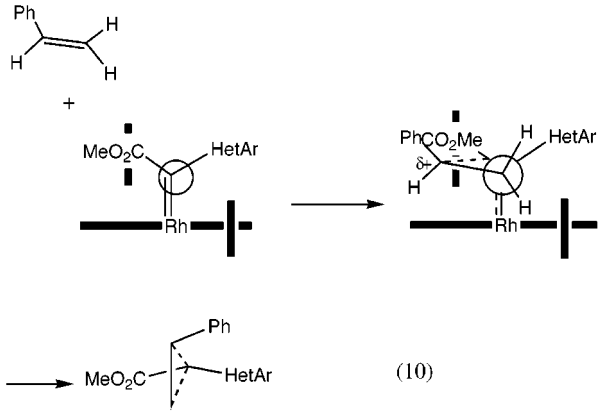
conditions	yield, %	de, %	ee, %
CH_2Cl_2, rt[a]	10	89	37
tol, 110 °C	68	85	71

a: Rh_2(*R*-DOSP)$_4$ was used as catalyst

desired cyclopropanes **27** were formed in moderate to good yields (58−91%).

These studies demonstrate that the carbenoids derived from methyl heteroaryldiazoacetates exhibit similar cyclopropanation stereoselectivity to other classes of carbenoids containing both donor and acceptor substituents. This stereoselectivity occurs when the heterocycle is either electron rich or electron deficient. A similar effect was seen with the substituted phenyldiazoacetates—the phenyl ring is a requirement but the effect on stereoselectivity of electron-donating or -withdrawing substituents is minimal. Presumably, the carbenoid center is so electron deficient that it can be stabilized by virtually any aromatic system, even those that would be formally considered as electron deficient. The most serious limitation with the heteroaryldiazoacetates is the use of heterocycles that are strongly Lewis basic. With these types of heteroaryldiazoacetates, the reactions are very slow or fail completely, presumably because the heterocycles coordinate strongly to the catalyst, inhibiting the coordination of the diazo function, which is a prerequisite step for the nitrogen extrusion and carbenoid formation.

The general model that has been used to explain the stereoselectivity in these reactions is illustrated in eq 10.[6c,8] The Rh_2(*S*-DOSP)$_4$ catalyst is viewed as if it has D_2 symmetry and can be simply considered as having two blocking groups represented by the thick vertical lines. The alkene approached the carbene side-on over the electron-withdrawing group in a concerted but nonsynchronous manner. Finally, rotation of the alkene away from the catalysts would lead to the cyclopropane where the alkene substituent is cis to the electron-donating group of the carbenoid. This relative stereochemistry is in agreement with that observed with the heteroaryldiazoacetates. This model has been an excellent predictor of the absolute stereochemistry that is obtained in these cyclopropanations.[6c,8] The drawn absolute stereochemistry for the cyclopropane products has not been determined but is that predicted from this model.



In summary, these studies demonstrate that a much wider range of carbenoid intermediates can be generated that contain both donor and acceptor groups. The cyclopropanation reactions of these carbenoids are highly diastereoselective and with Rh_2(*S*-DOSP)$_4$ as catalyst are highly enantioselective. Considering the aryldiazoacetates have been recently demonstrated to be highly effective in catalytic asymmetric C−H activation reactions,[12] it is reasonable to expect that many of the heteroaryldiazoacetates would also be effective in this chemistry. Thus the opportunity exists for the utilization of heteroaryldiazoacetates for the asymmetric synthesis of aromatic heterocycles containing side chains with multiple chiral centers.

Experimental Section

General Information. Reactions were performed using heat-gun-dried glassware under an atmosphere of argon. Tetrahydrofuran (THF) and hexanes were distilled from sodium benzophenone ketyl prior to use. Acetonitrile (CH_3CN), toluene, diisopropylamine, dichloromethane (CH_2Cl_2), and 1,2-dichloroethane ($ClCH_2CH_2Cl$) were distilled from calcium hydride. All reaction solvents were degassed by argon gas bubbling for about 30 min prior to use.

General Procedure for Methyl Heteroaryldiazoacetate Preparation. *p*-ABSA (10 mmol) was added to a solution of the heteroaryl acetate (5 mmol) and DBU (25 mmol) in CH_3CN (30 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature over 4 h and then concentrated in vacuo and diluted in CH_2Cl_2. The organic phase was washed with water, dried (Na_2SO_4), and concentrated in vacuo. Purification by silica gel chromatography (4:1 pentane/Et_2O) gave the methyl heteroaryldiazoacetate. The complete experimental for the preparation of the methyl heteroaryldiazoacetates and their precursors is given in the Supporting Information.

General Procedure for the Rhodium(II)-Catalyzed Decomposition of Heteroaryldiazoacetates in the Presence of Alkenes. A solution of diazo (1 equiv, 0.05−0.1 M) in hexanes, CH_2Cl_2, $ClCH_2CH_2Cl$, toluene, or some combination of these solvents was added dropwise over 20 min to 3 h to a stirred solution of alkene (5 equiv) in hexanes, CH_2Cl_2, $ClCH_2CH_2Cl$, or toluene at room temperature or heated at reflux. After 30 min to 22 h, the reaction mixture was concentrated in vacuo and the residue was purified by silica gel chromatography. The diastereomer ratio of the cyclopropane product was determined from the ^1H NMR spectra of the crude reaction mixture unless otherwise stated. The enantiomeric excess of

the cyclopropane product was determined by chiral HPLC using a Diacel Chiralcel-OD or (*R,R*)-Whelk-O1 analytical column.

(1*R*,2*S*)-Methyl 1-(Naphth-1-yl)-2-phenylcyclopropanecarboxylate (20a). A solution of **13a** (0.205 g, 0.906 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 2.5 h to a solution of Rh_2(*S*-DOSP)$_4$ (20 mg, 11 μmol) and styrene (0.47 g, 0.52 mL, 4.5 mmol) in CH_2Cl_2 (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 12 h and then concentrated in vacuo to give **20a** (98% de, determined by GC−MS). Purification by silica gel chromatography (97:3 pentane/Et_2O) gave the major diastereomer **20a** (0.22 g, 81%): R_f 0.39 (9:1 pentane/Et_2O); 68% ee (Chiralcel-OD, 1 mL/min, 1.2% *i*-PrOH/hexanes, t_R = 13.3 and 15.4 min); $[\alpha]^{25}_D$ −98.2° (*c* 1.2, $CHCl_3$); IR (film) 3040, 2949, 2918, 2849, 1716, 1598, 1502 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$, −20 °C) δ (3.6:1 mixture of rotamers) 8.21 (d, 1H, *J* = 8.0 Hz, minor), 7.87 (d, 1H, *J* = 8.0 Hz, minor), 7.70 (d, 1H, *J* = 8.0 Hz, major), 7.65−7.5 (m, 3H + 1H major), 7.46 (t, 1H, *J* = 7.6 Hz, major), 7.26−7.10 (m, 2H), 7.04 (t, 1H, *J* = 7.6 Hz, minor), 6.8−6.7 (m, 3H+1H minor), 6.59 (d, 1H, *J* = 6.8 Hz, minor), 3.57 (s, 3H, minor), 3.55 (s, 3H, major), 3.47 (dd, 1H, *J* = 7.6, 9.2 Hz, major), 3.23 (app t, 1H, *J* = 8.8 Hz, minor), 2.60 (dd, 1H, *J* = 4.8, 9.6 Hz, minor), 2.20 (dd, 1H, *J* = 4.8, 9.2 Hz, major), 2.11 (app t, 1H, *J* = 6.8 Hz, major), 1.84 (dd, 1H, 1H, *J* = 4.8, 7.2 Hz, minor); ^{13}C NMR (125 MHz; $CDCl_3$, 0 °C) δ (3.6:1 mixture of rotamers) 174.5, 136.7, 135.5, 133.5, 132.7, 131.6, 131.3, 129.8, 128.7, 128.4, 128.0, 127.7, 127.6, 126.9, 126.3, 125.8, 124.8, 124.3, 52.5, 34.0 (minor), 32.8 (major), 23.3 (minor), 21.5 (major); MS *m*/*z* (relative intensity) 302 (100, M^+), 270 (52), 240 (65), 165 (77); HRMS-EI calcd for $C_{21}H_{18}O_2$ 302.1307, found 302.1313.

A solution of **13a** (0.214 g, 0.946 mmol) in hexanes/toluene (10 mL, 4:1) was added dropwise over 2.5 h to a solution of Rh_2(*S*-DOSP)$_4$ (35 mg, 18.9 μmol) and styrene (0.49 g, 0.54 mL, 4.7 mmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 12 h and then concentrated in vacuo to give **20a** (98% de, determined by GC−MS). Purification by silica gel chromatography (97:3 pentane/Et_2O) gave the major diastereomer **20a** (0.25 g, 86%): 94% ee; $[\alpha]^{25}_D$ −134° (*c* 1.46, $CHCl_3$).

(1*R*,2*S*)-Methyl 1-(Naphth-2-yl)-2-phenylcyclopropanecarboxylate (20b). A solution of **13b** (0.139 g, 0.614 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 1.5 h to a solution of Rh_2(*S*-DOSP)$_4$ (23 mg, 9.8 μmol) and styrene (0.32 g, 0.35 mL, 3.1 mmol) in CH_2Cl_2 (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 10 h and then concentrated in vacuo to give **20b** (98% de). Purification by silica gel chromatography (97:3 pentane/Et_2O) gave the major diastereomeric cyclopropane **20b** (0.16 g, 87%): R_f 0.29 (9:1 pentane/Et_2O); 80% ee (Chiralcel-OD, 0.8 mL/min, 0.3% *i*-PrOH/hexanes, t_R = 28.3 and 31.7 min); $[\alpha]^{25}_D$ +73.6° (*c* 1.62, $CHCl_3$); IR (film) 3055, 3025, 2950, 1717, 1602, 1500 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.70 (dd, 2H, *J* = 9.5, 5.5 Hz), 7.60 (s, 1H), 7.53 (d, 1H, *J* = 9.0 Hz), 7.41 (dd, 1H, *J* = 9.5, 5.0 Hz), 7.39 (dd, 1H, *J* = 9.5, 4.5 Hz), 7.02 (dd, 1H, *J* = 8.0, 1.0 Hz), 6.99 (m, 3H), 6.80 (dd, 2H, *J* = 6.5, 3.0 Hz), 3.18 (dd, 1H, *J* = 9.0, 7.5 Hz), 2.21 (dd, 1H, *J* = 9.0, 5.0 Hz), 2.01 (dd, 1H, *J* = 7.5, 5.0 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 174.4, 136.1, 132.9, 132.6, 132.4, 130.5, 130.1, 128.0, 127.7, 127.6, 127.5, 127.0, 126.3, 125.8, 125.7, 52.6, 37.5, 33.2, 20.6; MS *m*/*z* (relative intensity) 302 (100, M^+), 270 (95), 241 (90), 165 (86); HRMS-EI calcd for $C_{21}H_{18}O_2$ 302.1307, found 302.1333.

A solution of **13b** (0.102 g, 0.451 mmol) in hexanes/toluene (10 mL, 4:1) was added dropwise over 1.5 h to a solution of Rh_2(*S*-DOSP)$_4$ (18 mg, 9.8 μmol) and styrene (0.24 g, 0.26 mL, 2.3 mmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 12 h and then concentrated in vacuo to give **20b** (90% de). Purification by silica gel chromatography (97:3 pentane/Et_2O) gave the major diastereomer **20b** (0.106 g, 78%): 90% ee; $[\alpha]^{25}_D$ +100° (*c* 1.4, $CHCl_3$).

(1*R*,2*S*)-Methyl 2-Phenyl-1-(thiophen-3-yl)cyclopropanecarboxylate (21a). A solution of **14a** (0.110 g, 0.387 mmol) in CH_2Cl_2 (12 mL) was added dropwise over 20 min to a solution of styrene (0.31 g, 0.35 mL, 3.0 mmol) and Rh_2(*S*-DOSP)$_4$ (23 mg, 12 μmol) in CH_2Cl_2 (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h and then concentrated in vacuo to give **21a** (95% de). Purification by silica gel chromatography (97:3 pentane/Et_2O) gave the major diastereomer **21a** (0.133 g, 85%): R_f 0.24 (9:1 pentane/Et_2O); 78% ee (Chiralcel-OD, 0.8 mL/min, 0.6% *i*-PrOH/hexanes, t_R = 18.2 and 19.6 min); $[\alpha]^{25}_D$ −12.7° (*c* 1.04, $CHCl_3$); mp 81−83 °C; IR (film) 3105, 3028, 2950, 2847, 1717, 1499 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.08 (m, 3H), 7.01 (dd, 1H, *J* = 5.0, 3.0 Hz), 6.90 (dd, 1H, *J* = 3.0, 1.0 Hz), 6.85 (m, 2H), 6.67 (dd, 1H, *J* = 5.0, 1.0 Hz), 3.69 (s, 3H), 3.05 (dd, 1H, *J* = 9.0, 7.0 Hz), 2.12 (dd, 1H, *J* = 9.0, 5.0 Hz), 1.88 (dd, 1H, *J* = 7.0, 5.0 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 173.9 (s), 136.1 (s), 135.6 (s), 130.3 (d), 127.9 (d), 127.7 (d), 126.4 (d), 125.2 (d), 124.3 (d), 52.5 (q), 33.4 (d), 32.4 (s), 20.5 (t); MS *m*/*z* (relative intensity) 258 (47, M^+), 226 (100), 197 (53), 165 (46), 115 (86); HRMS-EI (calcd for $C_{15}H_{14}O_2S$) 258.0714, found 258.0730. Anal. Calcd for $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46. Found: C, 69.64; H, 5.64.

A solution of **14a** (49.5 mg, 0.271 mmol) in hexanes (4 mL) was added dropwise over 20 min to a solution of styrene (0.14 g, 0.16 mL, 1.4 mmol) and Rh_2(*S*-DOSP)$_4$ (10 mg, 5.4 μmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h and then concentrated in vacuo to give **21a** (96% de). Purification by silica gel chromatography (95:5 pentane/Et_2O) gave the major diastereomeric **21a** (61 mg, 87%): 89% ee; $[\alpha]^{25}_D$ −13.2° (*c* 1.75, $CHCl_3$).

(1*R*,2*S*)-Methyl 1-(3-Methoxycarbonylfuran-4-yl)-2-phenylcyclopropanecarboxylate (21b). A solution of **14b** (0.101 g, 0.451 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 1 h to a solution of styrene (0.23 g, 0.26 mL, 2.3 mmol) and Rh_2(*S*-DOSP)$_4$ (17 mg, 9.0 μmol) in CH_2Cl_2 (1 mL) containing 4 Å molecular sieves (0.5 g) at room temperature. The reaction mixture was stirred at room temperature for 8 h and then concentrated in vacuo to give **21b** (97% de). Purification by silica gel chromatography (4:1 pentane/Et_2O) gave the major diastereomer **21b** (0.109 g, 81%): R_f 0.31 (1:1 pentane/Et_2O); 81% ee (Chiralcel-OD, 1 mL/min, 1.2% *i*-PrOH/hexanes, t_R = 22.5 and 42.0 min); $[\alpha]^{25}_D$ −129° (*c* 0.65, $CHCl_3$); IR (film) 3147, 3086, 3028, 2951, 2852, 1724, 1602, 1549, 1500 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.72 (s, 1H), 7.11 (m, 3H), 7.02 (br s, 1H), 6.97 (m, 2H), 3.71 (s, 3H), 3.68 (s, 3H), 3.29 (dd, 1H, *J* = 9.0, 7.5 Hz), 1.96 (dd, 1H, *J* = 9.0, 5.0 Hz), 1.80 (dd, 1H, *J* = 7.5, 5.0 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 173.4 (s), 162.9 (s), 148.4 (d), 143.3 (d), 135.6 (s), 128.3 (d), 127.6 (d), 126.6 (d), 120.6 (s), 119.1 (s), 52.4 (q), 51.2 (q), 31.9 (d), 27.7 (s), 19.7 (t); MS *m*/*z*(relative intensity) 300 (1, M^+), 268 (16), 236 (100); HRMS-EI (calcd for $C_{17}H_{16}O_5$) 300.0998, found 300.1003. Anal. Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 67.96; H, 5.49.

A solution of **14b** (0.105 g, 0.468 mmol) in hexanes/CH_2Cl_2 (9 mL, 8:1) was added dropwise over 20 min to a solution of styrene (0.24 g, 0.27 mL, 2.3 mmol) and Rh_2(*S*-DOSP)$_4$ (18 mg, 9.4 μmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h and then concentrated in vacuo to give **21b** (96% de). Purification by silica gel chromatography (4:1 pentane/Et_2O) gave the major diastereomer **21b** (0.128 g, 91%): 86% ee; $[\alpha]^{25}_D$ −126° (*c* 1.6, $CHCl_3$).

(*1R,2S*)-Methyl 1-(1-*tert*-Butyloxycarbonylindol-3-yl)-2-phenylcyclopropanecarboxylate (22). A solution of **15** (0.122 g, 0.387 mmol) in CH_2Cl_2 (6 mL) was added dropwise over 20 min to a solution of styrene (0.20 g, 0.22 mL, 1.9 mmol) and Rh_2(*S*-DOSP)$_4$ (15 mg, 7.7 μmol) in CH_2Cl_2 (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h and then concentrated in vacuo to give **22** (97% de). Purification by silica gel chromatography (97:3 pentane/Et_2O) gave the major diastereomer **22** (0.102 g, 67%): R_f 0.19 (9:1 pentane/Et_2O); 23% ee (Chiralcel-OD, 0.8 mL/min, 0.6% *i*-PrOH/hexanes, t_R = 17.2 and 28.4 min); $[\alpha]^{25}_D$ +4.22° (*c* 1.66, $CHCl_3$); IR (film) 3061, 2977, 2854, 1726, 1607 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.99 (br m, 1H), 7.32 (d, 1H, *J* = 10.0 Hz), 7.19 (dd, 1H, *J* = 9.5, 9.5 Hz), 7.09 (dd, 1H, *J* = 9.0, 9.0 Hz), 7.05−6.95 (m, 6H), 3.65 (s, 3H), 3.23 (dd, 1H,

J = 12.0, 9.0 Hz), 2.18 (dd, 1H, J = 9.0, 6.0 Hz), 1.87 (dd, 1H, J = 9.0, 6.0 Hz), 1.58 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 174.1 (s), 149.4 (s), 136.1 (s), 135.0 (s), 130.9 (s), 128.3 (d), 127.7 (d), 126.6 (d), 126.5 (d), 124.1 (d), 122.3 (d), 119.7 (d), 115.2 (s), 114.9 (d), 83.4 (s), 52.6 (q), 32.9 (d), 28.3 (s), 28.1 (q), 20.2 (t); MS m/z (relative intensity) 391 (11, M^+), 335 (20), 291 (39), 259 (66); HRMS-EI (calcd for $C_{24}H_{25}NO_4$) 391.1784, found 391.1768. Anal. Calcd for $C_{24}H_{25}NO_4$: C, 73.64; H, 6.44; N, 3.58. Found: C, 73.41; H, 6.66; N, 3.39.

A solution of **15** (71 mg, 0.23 mmol) in hexanes (6 mL) was added dropwise over 20 min to a solution of styrene (0.12 g, 0.13 mL, 1.1 mmol) and Rh_2(*S*-DOSP)$_4$ (9 mg, 5 μmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 12 h and then concentrated in vacuo to give **22** (94% de). Purification by silica gel chromatography (97:3 pentane/Et_2O) gave the major diastereomer **22** (74 mg, 82%): 12% ee; $[\alpha]^{25}_D$ −2.77° (*c* 0.65, $CHCl_3$).

(1*R*,2*S*)-Methyl 2-Phenyl-1-(pyridin-2-yl)cyclopropanecarboxylate (23a). A solution of **16a** (56 mg, 0.32 mmol) in $ClCH_2CH_2Cl$ (6 mL) was added dropwise over 2.5 h to a solution of styrene (0.21 g, 0.23 mL, 2.0 mmol) and Rh_2(*S*-DOSP)$_4$ (12 mg, 8.1 μmol) in $ClCH_2CH_2Cl$ (1 mL) heated at reflux. The reaction mixture was heated at reflux for 22 h and then concentrated in vacuo to give **23a** (91% de). Purification by silica gel chromatography (3:1 pentane/EtOAc) gave the major diastereomer **23a** (47 mg, 59%) and recovered **16a** (5 mg, 9% recovery). **23a**: R_f 0.31 (2:1 pentane/EtOAc); 47%ee (Chiralcel-OD, 1 mL/min, 1.2% *i*-PrOH/hexanes, t_R = 16.6 and 26.1 min). $[\alpha]^{25}_D$ −17.0° (*c* 1.05, $CHCl_3$); IR (film) 3056, 3022, 2951, 2852, 1720, 1589 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 8.44 (d, 1H, J = 5.5 Hz), 7.34 (ddd, 1H, J = 9.5, 9.5, 1.5 Hz), 7.03 (m, 4H), 6.90 (d, 1H, J = 10.5 Hz), 6.80 (m, 2H), 3.68 (s, 3H), 3.23 (dd, 1H, J = 11.5, 9.5 Hz), 2.36 (dd, 1H, J = 9.5, 6.5 Hz), 2.13 (dd, 1H, J = 11.5, 6.5 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 173.4, 154.2, 148.5, 135.9, 135.4, 127.9, 127.7, 127.5, 126.4, 121.9, 52.6, 39.2, 33.8, 19.4; MS m/z(relative intensity) 253 (51, M^+), 222 (8), 193 (100); HRMS-EI (calcd for $C_{16}H_{15}NO_2$) 253.1103, found 253.1113.

(1*R*,2*S*)-Methyl 1-(2-Chloropyridin-6-yl)-2-phenylcyclopropanecarboxylate (23b). A solution of diazo **16b** (0.100 g, 0.473 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 1 h to a solution of styrene (0.25 g, 0.27 mL, 2.4 mmol) and Rh_2(*S*-DOSP)$_4$ (18 mg, 9.5 μmol) in CH_2Cl_2 (2 mL) containing 4 Å molecular sieves (0.5 g) at room temperature. The reaction mixture was stirred at room temperature for 2 h and then concentrated in vacuo to give **23b** (97% de). Purification by silica gel chromatography (4:1 pentane/Et_2O) gave the major diastereomer **23b** (0.12 g, 91%): R_f 0.69 (2:1 pentane/EtOAc); 69% ee (Chiralcel-OD, 1 mL/min, 0.8% *i*-PrOH/hexanes, t_R = 10.4 and 14.4 min); $[\alpha]^{25}_D$ +63.0° (*c* 1.08, $CHCl_3$); IR (film) 3062, 3029, 2951, 1723, 1583, 1557 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.33 (dd, 1H, J = 7.7, 7.7 Hz), 7.08 (m, 4H), 6.86 (m, 3H), 3.72 (s, 3H), 3.27 (dd, 1H, J = 9.2, 7.6), 2.41 (dd, 1H, J = 7.6, 5.5 Hz), 2.16 (dd, 1H, J = 9.2, 5.5 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 172.8 (s), 155.1 (s), 149.9 (s), 138.0 (d), 135.4 (s), 127.9 (d), 127.8 (d), 126.3 (d), 126.0 (d), 122.4 (d), 52.6 (q), 38.8 (s), 34.2 (d), 19.4 (t); MS m/z (relative intensity) 287 (50, M^+), 255 (25), 227 (100), 191 (20); HRMS-EI (calcd for $C_{16}H_{14}ClNO_2$) 211.0149, found 211.0135; Anal. Calcd for $C_{16}H_{14}ClNO_2$: C, 66.79; H, 4.90, N, 4.87. Found: C, 67.11; H, 5.00; N, 4.83.

A solution of **16b** (28 mg, 0.13 mmol) in CH_2Cl_2/hexanes (2.25 mL, 2:1) was added dropwise over 20 min to a solution of styrene (69 mg, 76 μL, 0.66 mmol) and Rh_2(*S*-DOSP)$_4$ (5.0 mg, 2.6 μmol) in hexanes (0.5 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h and then concentrated in vacuo to give **23b** (98% de). Purification by silica gel chromatography (9:1 pentane/EtOAc) gave the major diastereomer **23b** (30 mg, 79%): 72% ee; $[\alpha]^{25}_D$ +64.2° (*c* 1.3, $CHCl_3$).

Attempted Cyclopropanation of Methyl (Pyrazin-2-yl)-diazoacetate (16c). A solution of **16c** (4 mg, 22.5 μmol) in $ClCH_2CH_2Cl$ (2 mL) was added dropwise over 20 min to a solution of styrene (47 mg, 52 μL, 0.45 mmol) and Rh_2(*S*-DOSP)$_4$ (1 mg, 0.45 μmol) in $ClCH_2CH_2Cl$ (0.5 mL) heated at reflux. The reaction mixture was heated at reflux for 12 h and then cooled and concentrated in vacuo. Peaks that would be characteristic of **23c** were not evident in the ^{1}H NMR spectrum of the crude reaction mixture.

(1*R*,2*S*)-Methyl 1-(3-Methylisoxazol-5-yl)-2-phenylcyclopropanecarboxylate (24). A solution of **17** (90 mg, 0.50 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 30 min to a solution of styrene (0.26 g, 0.28 mL, 2.5 mmol) and Rh_2(*S*-DOSP)$_4$ (18 mg, 9.9 μmol) in CH_2Cl_2 (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h and then concentrated in vacuo to give **24** (95% de). Purification by silica gel chromatography (9:1 hexanes/Et_2O) gave the major diastereomer **24** (0.12 g, 79%): R_f 0.34 (1:1 pentane/Et_2O); 76% ee (Chiralcel-OD, 0.8 mL/min, 0.6% *i*-PrOH/hexanes, t_R = 37.5 and 39.5 min); $[\alpha]^{25}_D$ −63.5° (*c* 1.62, $CHCl_3$); mp 70−71 °C; IR (film) 3025, 2953, 1726, 1611, 1434 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.15 (m, 3H), 7.02 (m, 2H), 5.73 (s, 1H), 3.75 (s, 3H), 3.23 (dd, 1H, J = 8.6, 8.4 Hz), 2.17 (m, 2H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 171.1 (s), 166.0 (s), 159.4 (s), 128.2 (d), 128.1 (d), 127.3 (d), 106.4 (d), 52.8 (q), 34.6 (d), 29.1 (s), 19.8 (t), 11.3 (q). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88, N, 5.44. Found: C, 70.08; H, 5.79; N, 5.50. A solution of **17** (0.101 g, 0.558 mmol) in hexanes (10 mL) was added dropwise over 1 h to a solution of styrene (0.29 g, 0.32 mL, 2.8 mmol) and Rh_2(*S*-DOSP)$_4$ (21 mg, 11 μmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 3 h and then concentrated in vacuo to give **24** (93% de). Purification by silica gel chromatography (9:1 hexanes/Et_2O) gave the major diastereomer **24** (0.12 g, 84%): 86% ee; $[\alpha]^{25}_D$ −74.4° (*c* 1.3, $CHCl_3$).

(1*R*,2*S*)-Methyl 1-(4,5-Diphenyloxazol-2-yl)-2-phenylcyclopropanecarboxylate (25). A solution of **18** (0.135 g, 0.423 mmol) in CH_2Cl_2 (8 mL) was added dropwise over 1 h to a solution of styrene (0.22 g, 0.24 mL, 2.1 mmol) and Rh_2(*S*-DOSP)$_4$ (16 mg, 8.5 μmol) in CH_2Cl_2 (1 mL) containing 4 Å molecular sieves (0.5 g) at room temperature. The reaction mixture was stirred at room temperature for 1 h and then concentrated in vacuo to give **25** (97% de). Purification by silica gel chromatography (4:1 pentane/Et_2O) gave the major diastereomer **25** (0.136 g, 81%): R_f 0.47 (1:1 pentane/Et_2O); 12% ee (Chiralcel-OD, 0.8 mL/min, 0.6% *i*-PrOH/hexanes, t_R = 18.8 and 21.7 min) $[\alpha]^{25}_D$ −13.1° (*c* 1.22, $CHCl_3$); IR (film) 3060, 3031, 2952, 2850, 1731, 1604, 1500, 1435, 1435 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.49 (d, 2H, J = 7.0 Hz), 7.35−7.08 (br m, 13H), 3.76 (s, 3H), 3.32 (dd, 2H, J = 8.0, 9.1 Hz), 2.51 (dd, 1H, J = 8.0, 5.3 Hz), 2.19 (dd, 1H, J = 9.1, 5.3 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 171.2 (s), 157.4 (s), 146.2 (s), 134.8 (s), 134.6 (s), 128.7 (s), 128.3 (d), 128.0 (d), 127.9 (d), 127.8 (d), 127.7 (d), 127.1 (d), 126.6 (d), 52.8 (q), 34.0 (d), 31.0 (s), 20.7 (t); MS m/z (relative intensity) 395 (100, M^+), 363 (73), 335 (17), 258 (39); HRMS-EI (calcd for $C_{26}H_{21}NO_3$) 395.1521, found 395.1515. Anal. Calcd for $C_{26}H_{21}NO_3$: C, 78.97; H, 5.35, N, 3.54. Found: C,79.01; H, 5.55; N, 3.46.

A solution of **18** (45.9 mg, 0.144 mmol) in hexanes/toluene (2.5 mL, 3:2) was added dropwise over 20 min to a solution of styrene (0.15 g, 0.16 mL, 1.4 mmol) and Rh_2(*S*-DOSP)$_4$ (9.0 mg, 4.8 μmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 14 h and then concentrated in vacuo to give **25** (96% de). Purification by silica gel chromatography (4:1 pentane/Et_2O) gave the major diastereomer **25** (46 mg, 81%): 71% ee; $[\alpha]^{25}_D$ −76.1° (*c* 0.92, $CHCl_3$).

(1*R*,2*S*)-Methyl 1-(Benzoxazol-2-yl)-2-phenylcyclopropanecarboxylate (26). A solution of **19** (60 mg, 0.28 mmol) in CH_2Cl_2 (5 mL) was added dropwise over 20 min to a solution of styrene (0.14 g, 0.16 mL, 1.4 mmol) and Rh_2(*R*-DOSP)$_4$ (10 mg, 5.5 μmol) in CH_2Cl_2 (2 mL) at room temperature. The reaction mixture was stirred at room temperature for 18 h and then concentrated in vacuo to give **26** (89% de). Purification by silica gel chromatography (95:5 pentane/EtOAc) gave the major diastereomer **26** (7 mg, 10%) and recovered **19** (40 mg, 67% recovery). **26**: R_f 0.49 (2:1 pentane/EtOAc); 37% ee (Chiralcel-OD, 0.8 mL/min, 0.6% *i*-PrOH/hexanes, t_R = 26.5 and 29.9 min); $[\alpha]^{25}_D$ +22.0° (*c* 0.6, $CHCl_3$); IR (film) 3089, 3061, 3031, 2953, 1732, 1613, 1573 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.60 (m, 1H), 7.30 (m, 1H), 7.06 (m, 5H), 3.76 (s, 3H),

3.38 (dd, 1H, J = 9.1, 8.2 Hz), 2.58 (dd, 1H, J = 9.1, 5.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 170.7, 160.8, 151.1, 140.4, 134.2, 128.0, 127.7, 127.2, 124.8, 123.9, 119.8, 110.2, 82.9, 34.3, 31.9, 20.7; MS m/z (relative intensity) 293 (9, M^+), 261 (14), 233 (12), 204 (7), 181 (9); HRMS-EI (calcd for $C_{18}H_{15}NO_3$) 293.1052, found 293.1061. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15, N, 4.78. Found: C, 73.58; H, 5.36; N, 4.77.

A solution of **19** (99.5 mg, 0.459 mmol) in toluene (6 mL) was added dropwise over 40 min to a solution of styrene (0.24 g, 0.26 mL, 2.3 mmol) and Rh_2(*S*-DOSP)$_4$ (17 mg, 9.2 μmol) in toluene (2 mL) heated at reflux. The reaction mixture was heated at reflux for 6 h and then concentrated in vacuo to give **26** (85% de). Purification by silica gel chromatography (95:5 pentane/EtOAc) gave the major diastereomer **26** (93 mg, 68%): 71% ee; $[\alpha]^{25}_D$ −69.8° (*c* 2.15, $CHCl_3$).

(1*R*)-Methyl 2,2-Diphenyl-1-(thiophen-3-yl)cyclopropanecarboxylate (27a). A solution of **14a** (46 mg, 0.25 mmol) in hexanes (4 mL) was added dropwise over 20 min to a solution of Rh_2(*S*-DOSP)$_4$ (9.5 mg, 5.0 μmol) and 1,1-diphenylethylene (0.23 g, 0.22 mL, 1.3 mmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 10 h and then concentrated in vacuo. Purification by silica gel chromatography (4:1 pentane/EtOAc) gave **27a** (61 mg, 72%): R_f 0.25 (9:1 pentane/Et_2O); 97% ee (Chiralcel-OD, 0.8 mL/min, 0.8% *i*-PrOH/hexanes, t_R = 11.7 and 14.2 min); $[\alpha]^{25}_D$ +114° (*c* 1.04, $CHCl_3$); IR (film) 3104, 3084, 3057, 3024, 2999, 2948, 2926, 2852, 1725, 1598 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.48 (d, 2H, J = 7.5 Hz), 7.27 (dd, 2H, J = 7.5, 7.5 Hz), 7.18 (t, 1H, J = 7.5 Hz), 7.13 (d, 2H, J = 7.5 Hz), 7.07−7.00 (m, 5H), 6.98 (app t, 1H, J = 7.5 Hz), 3.33 (s, 3H), 2.70 (d, 1H, J = 5.5 Hz), 2.32 (d, 1H, J = 5.5 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 170.9, 141.9, 140.1, 136.6, 130.1, 129.3, 129.0, 128.3, 127.7, 126.8, 126.3, 124.3, 124.0, 51.9, 45.5, 38.1, 23.1; MS m/z (relative intensity) 334 (10, M^+), 302 (36), 275 (100); HRMS-EI (calcd for $C_{21}H_{18}O_2S$) 334.1028, found 334.1040. Anal. Calcd for $C_{21}H_{18}O_2S$: C, 75.42; H, 5.42. Found: C, 75.42; H, 5.78.

(1*R*)-Methyl 2,2-Diphenyl-1-(3-methoxycarbonylfuran-4-yl)cyclopropanecarboxylate (27b). A solution of **14b** (94 mg, 0.42 mmol) in hexanes/CH_2Cl_2 (10 mL, 4:1) was added dropwise over 1 h to a solution of Rh_2(*S*-DOSP)$_4$ (17 mg, 8.4 μmol) and 1,1-diphenylethylene (0.38 g, 0.37 mL, 2.1 mmol) in hexanes (2 mL) at room temperature. The reaction mixture was stirred at room temperature for 8 h and then concentrated in vacuo. Purification by silica gel chromatography (4:1 pentane/Et_2O) gave **27b** (28 mg, 18%): R_f 0.31 (1:1 pentane/Et_2O); 88% ee ((*R*,*R*)-Whelk-O1, 1 mL/min, 2% *i*-PrOH/hexanes, t_R = 12.9 and 18.3 min); $[\alpha]^{25}_D$ +133° (*c* 1.1, $CHCl_3$); mp 156−158 °C; IR (film) 3150, 3059, 3025, 2950, 2838, 1725, 1599, 1545 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.76 (d, 1H, J = 2.0 Hz), 7.63 (app d, 2H, J = 7.0 Hz), 7.30 (dd, 2H, J = 7.5, 7.5 Hz), 7.27 (m, 2H), 7.20 (m, 1H), 7.08−7.00 (m, 3H), 6.88 (d, 1H, J = 1.5 Hz), 3.85 (s, 3H), 3.38 (s, 3H), 2.51 (d, 1H, J = 5.5 Hz), 2.27 (d, 1H, J = 5.5 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 171.2, 163.4, 148.5, 143.3, 142.2, 140.3, 129.7, 128.9, 128.1, 127.7, 126.6, 126.5, 122.0, 119.5, 51.9, 51.3, 46.1, 32.4, 24.6; MS m/z (relative intensity) 376 (1, M^+), 344 (27), 312 (100); HRMS-EI (calcd for $C_{23}H_{20}O_5$) 376.1311, found 376.1299. Anal. Calcd for $C_{23}H_{20}O_5$: C, 73.39; H, 5.36. Found: C, 73.49; H, 5.70.

(1*R*)-Methyl 1-(1-*tert*-Butyloxycarbonylindol-3-yl)-2-diphenylcyclopropanecarboxylate (27c). A solution of **15** (0.121 g, 0.384 mmol) in hexanes (6 mL) was added dropwise over 30 min to a solution of Rh_2(S-DOSP)$_4$ (15 mg, 7.7 μmol) and 1,1-diphenylethylene (0.35 g, 0.34 mL, 1.9 mmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 1 h and then concentrated in vacuo. Purification by silica gel chromatography (9:1 pentane/Et_2O) gave **27c** (0.142 g, 79%): R_f 0.66 (1:1 pentane/Et_2O); 67% ee (Chiralcel-OD, 0.8 mL/min, 0.6% i-PrOH/hexanes, t_R = 17.8 and 27.7 min); $[\alpha]^{25}_D$ +161° (*c* 0.84, $CHCl_3$); IR (film) 3055, 3025, 2979, 2947, 1730, 1603, 1494 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 8.01 (br s, 1H), 7.74 (d, 1H, J = 7.0 Hz), 7.55 (m, 2H), 7.34 (app t, 2H, J = 7.5 Hz), 7.26−7.18 (m, 5H), 7.10 (br s, 1H), 7.00−6.93 (br m, 3H); 3.38 (s, 3H), 2.72 (d, 1H, J = 5.0 Hz), 2.34 (d, 1H, J = 5.0 Hz), 1.57 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 171.4, 149.3, 142.0, 139.8, 135.0, 130.8, 129.8, 128.8, 128.4, 127.6, 127.0, 126.7, 126.5, 124.1, 122.4, 120.5, 116.7, 114.9, 83.4, 52.2, 44.8, 34.4, 28.1, 23.4; MS m/z (relative intensity) 467 (10, M^+), 411 (8), 367 (36), 335 (54), 306 (41); HRMS-EI (calcd for $C_{30}H_{29}NO_4$) 467.2096 found 467.2051.

(1*R*)-Methyl 2,2-Diphenyl-1-(pyridin-2-yl)cyclopropanecarboxylate (27d). A solution of **16a** (56 mg, 0.32 mmol) in $ClCH_2CH_2Cl$ (6 mL) was added dropwise over 2.5 h to a solution of Rh_2(*S*-DOSP)$_4$ (12 mg, 6.3 μmol) and 1,1-diphenylethylene (0.29 g, 0.28 mL, 1.6 mmol) in $ClCH_2CH_2Cl$ (1 mL) heated at reflux. The reaction mixture was heated at reflux for 22 h and then concentrated in vacuo. Purification by silica gel chromatography (2:1 pentane/EtOAc) gave **27d** (59 mg, 58%) and recovered **18a** (1 mg, 2% recovery). **27d**: R_f 0.53 (2:1 pentane/EtOAc); 78% ee ((*R*,*R*)-Whelk-O1, 1 mL/min, 2.0% *i*-PrOH/hexanes, t_R = 15.0 and 30.7 min); $[\alpha]^{25}_D$ +195° (*c* 0.82, $CHCl_3$); mp 138−139 °C; IR (film) 3083, 3057, 3024, 2948, 2928, 2850, 1720, 1588, 1567 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 8.35 (d, 1H, J = 4.0 Hz), 7.58 (d, 1H, J = 8.0 Hz), 7.50 (d, 2H, J = 7.5 Hz), 7.42 (ddd, 1H, J = 7.5, 7.5, 1.0 Hz), 7.31 (dd, 2H, J = 8.0, 8.0 Hz), 7.23 (dd, 1H, J = 7.0, 5.0 Hz), 7.04 (d, 2H, J = 8.0 Hz), 6.95 (m, 4H), 3.32 (s, 3H), 2.95 (d, 1H, J = 5.0 Hz), 2.70 (d, 1H, J = 5.0 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 170.8 (s), 154.7 (s), 148.1 (d), 141.9 (s), 139.5 (s), 135.1 (d), 129.5 (d), 128.7 (d), 128.3 (d), 128.0 (d), 127.6 (d), 126.8 (d), 126.1 (d), 121.7 (d), 51.9 (q), 46.2 (s), 44.1 (s), 21.9 (t); MS m/z (relative intensity) 329 (77, M^+), 297 (14), 268 (100); HRMS-EI (calcd for $C_{22}H_{19}NO_2$) 329.1416, found 329.1425.

(1*R*)-Methyl 1-(2-Chloropyridin-6-yl)-2,2-diphenylcyclopropane carboxylate (27e). A solution of **16b** (50 mg, 0.24 mmol) in CH_2Cl_2/hexanes (4.5 mL, 2:1) was added dropwise over 20 min to a solution of Rh_2(*S*-DOSP)$_4$ (8.9 mg, 4.7 μmol) and 1,1-diphenylethylene (0.23 g, 0.22 mL, 1.3 mmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h and then concentrated in vacuo. Purification by silica gel chromatography (4:1 pentane/EtOAc) gave **27e** (67 mg, 78%): 89% ee (Chiralcel-OD, 1 mL/min, 0.8% *i*-PrOH/hexanes, t_R = 11.6 and 12.5 min); $[\alpha]^{25}_D$ +284° (*c* 1.14, $CHCl_3$); IR (film) 3058, 3025, 2949, 2926, 2842, 1722, 1580, 1439 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.59 (d, 1H, J = 7.5 Hz), 7.48 (d, 2H, J = 7.5 Hz), 7.39 (t, 1H, J = 7.5 Hz), 7.32 (t, 2H, J = 7.5 Hz), 7.25 (dd, 1H, J = 7.5, 6.0 Hz), 7.08 (d, 2H, J = 8.5 Hz), 7.01−6.98 (m, 3H), 6.95 (t, 1H, J = 7.0 Hz), 3.0 (d, 1H, J = 6.0 Hz), 2.68 (d, 1H, J = 6.0 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 170.5, 155.7, 149.4, 139.1, 137.8, 129.5, 128.7, 128.3, 127.8, 127.0, 126.6, 126.4, 122.1, 52.0, 47.0, 43.6, 22.2; MS m/z (relative intensity) 363 (11, M^+), 331 (100), 303 (21), 267 (11); HRMS-EI (calcd for $C_{16}H_{14}ClNO_3$) 287.0713, found 287.0712. Anal. Calcd for $C_{22}H_{18}ClNO_2$: C, 72.62; H, 4.99; N, 3.85. Found: C, 72.39; H,5.16; N, 3.63.

(1*R*)-Methyl 2,2-Diphenyl-1-(3-methylisoxazol-5-yl)cyclopropanecarboxylate (27f). A solution of **17** (0.113 g, 0.624 mmol) in hexanes (10 mL) was added dropwise over 30 min to a solution of Rh_2(S-DOSP)$_4$ (24 mg, 13 μmol) and 1,1-diphenylethylene (0.56 g, 0.55 mL, 3.1 mmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 2 h and then concentrated in vacuo. Purification by silica gel chromatography (4:1 pentane/Et_2O) gave **27f** (0.189 g, 91%): R_f 0.41 (1:1 pentane/Et_2O); 95% ee (Chiralcel-OD, 0.8 mL/min, 0.6% *i*-PrOH/hexanes, t_R = 35.7 and 44.7 min); $[\alpha]^{25}_D$ +60.5° (*c* 1.58, $CHCl_3$); mp 136−137 °C; IR (film) 3114, 3083, 3059, 3024, 2957, 2848, 1953, 1884, 1731, 1688, 1607, 1581 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.44 (d, 2H, J = 7.5 Hz), 7.28−7.25 (m, 4H), 7.18 (t, 1H, J = 7.5 Hz), 7.12 (t, 2H, J = 7.0 Hz), 7.07 (t, 1H, J = 7.0 Hz), 6.31 (s, 1H), 3.39 (s, 3H), 2.76 (d, 1H, J = 5.5 Hz), 2.64 (d, 1H, J = 5.5 Hz), 2.15 (s, 3H); ^{13}C NMR (125 MHz; $CDCl_3$) δ 168.2, 166.3, 159.4, 140.9, 139.5, 128.6, 128.5, 128.3, 128.0, 127.0, 105.0, 52.1, 48.0, 34.9, 22.8; MS m/z (relative intensity) 333 (8, M^+), 304 (16), 274 (44), 250 (50), 233 (100); HRMS-EI (calcd for $C_{21}H_{19}NO_3$) 333.1365, found 333.1391. Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.95; H, 5.80; N, 4.26.

(1*R*)-Methyl 2,2-Diphenyl-1-(4,5-diphenyloxazol-2-yl)-cyclopropanecarboxylate (27g). A solution of **18** (54.2 mg, 0.166 mmol) in hexanes/toluene (2 mL, 3:2) was added drop-

wise over 20 min to a solution of Rh_2(*S*-DOSP)$_4$ (8.0 mg, 3.3 μmol) and 1,1-diphenylethylene (0.30 g, 0.15 mL, 1.7 mmol) in hexanes (1 mL) at room temperature. The reaction mixture was stirred at room temperature for 16 h and then concentrated in vacuo. Purification by silica gel chromatography (4:1 pentane/Et_2O) gave **27g** (72 mg, 88%): R_f 0.38 (1:1 pentane/Et_2O); 92% ee (Chiralcel-OD, 0.8 mL/min, 0.6% *i*-PrOH/hexanes, t_R = 26.2 and 30.3 min); $[\alpha]^{25}_D$ +49.6° (*c* 1.22, $CHCl_3$); mp 160−161 °C; IR (film) 3082, 3058, 3020, 2949, 2927, 2852, 1954, 1890, 1735, 1604, 1561 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.52 (d, 2H, J = 6.5 Hz), 7.40−7.30 (m, 6H), 7.31−7.26 (m, 8H, 7.21 (t, 1H, J = 7.0 Hz), 7.10 (t, 2H, J = 7.0 Hz), 7.02 (t, 1H, J = 7.0 Hz), 3.50 (s, 3H), 2.91 (d, 1H, J = 5.5 Hz), 2.76 (d, 1H, J = 5.5 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 168.4, 157.8. 146.5, 140.5, 139.7, 134.8, 132.3, 129.1, 128.8, 128.7, 128.4, 128.3, 127.9, 127.9, 127.2, 127.0, 126.6, 52.5, 48.0, 36.2, 24.2; MS *m*/*z* (relative intensity) 395 (100, M^+), 363 (73), 335 (17), 258 (39); HRMS-EI (calcd for $C_{26}H_{21}NO_3$) 395.1521, found 395.1515. Anal. Calcd for $C_{32}H_{25}NO_3$: C, 81.51; H, 5.34; N, 2.97. Found: C, 81.40; H, 5.57; N, 3.01.

(1*R*)-Methyl 1-(Benzoxazol-2-yl)-2,2-diphenylcyclopropanecarboxylate (27h). A solution of **19** (74.9 mg, 0.345 mmol) in toluene (6 mL) was added dropwise over 20 min to a solution of Rh_2(*S*-DOSP)$_4$ (13 mg, 7.1 μmol) and 1,1-diphenylethylene (0.31 g, 0.30 mL, 1.7 mmol) in toluene (1 mL) heated at reflux. The reaction mixture was heated at reflux for 2 h, allowed to cool to room temperature, and concentrated in vacuo. Purification by silica gel chromatography (4:1 pentane/Et_2O) gave **27h** (93 mg, 73%): R_f 0.60 (2:1 pentane/Et_2O); 70% ee (Chiralcel-OD, 0.8 mL/min, 0.6% *i*-PrOH/hexanes, t_R = 35.0 and 45.9 min); $[\alpha]^{25}_D$ +54.8° (*c* 1.42, $CHCl_3$); mp 160−161 °C; IR (film) 3084, 3058, 3026, 2950, 1736, 1611, 1564, 1494, 1454 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ 7.55 (t, 3H), 7.42 (d, 1H J = 7.5 Hz), 7.36 (d, 2H, J = 7.5 Hz), 7.31 (t, 2H, J = 7.5 Hz), 7.26−7.20 (m, 3H), 7.0 (t, 2H, J = 7.0 Hz), 6.91 (t, J = 7.0 Hz), 3.50 (s, 3H), 2.96 (d, 1H, J = 5.5 Hz), 2.83 (d, 1H, J = 5.5 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ 169.7, 161.3, 150.9, 140.5, 139.3, 128.8, 128.4, 127.9, 127.3, 127.0, 124.8, 124.0, 52.5, 48.6, 36.5, 24.2; MS *m*/*z* (relative intensity) 369 (35, M^+), 337 (55), 310 (29); HRMS-EI (calcd for $C_{24}H_{19}NO_3$) 369.1365, found 369.1359.

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Supporting Information Available: Experimental data for the preparation of **6**−**19**. This material is available free of charge via the Internet at http://pubs.acs.org.

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