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Controlling Factors for C−H Functionalization versus Cyclopropanation of Dihydronaphthalenes

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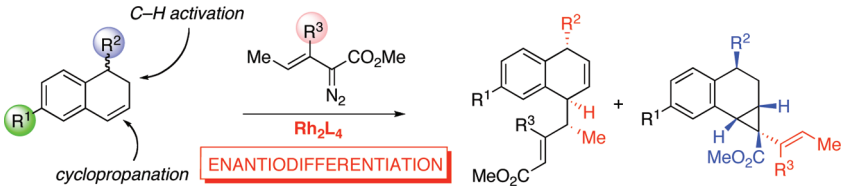
Received December 14, 2009



Rhodium(II)-catalyzed reactions of vinyldiazoacetates with dihydronaphthalenes were systematically studied. These substrates underwent cyclopropanantion and/or the combined C−H activation/Cope rearrangement in good overall yield and with good diastereo- and enantiocontrol. The selectivity of these reactions was profoundly influenced by the nature of the chiral catalyst, the vinyldiazoacetate, and the dihydronaphthalene. The best combinations for achieving the highest selectivity in the cyclopropanation and the combined C−H activation/Cope rearrangement of 1,2-dihydronaphthalenes are methyl 2-diazopent-3-enoate (**2a**)/Rh_2(*S*-DOSP)$_4$ and methyl 3-(*tert*-butyldimethylsilyloxy)-2-diazopent-3-enoate (**2b**)/Rh_2(*S*-PTAD)$_4$. These combinations are very effective at enantiodivergent reactions of 1-methyl-1,2-dihydronaphthalenes.

Introduction

The development of new synthetic methods that rely on C−H functionalization is an area of intense current research.[1−5] Two major strategies using organometallic complexes have been developed to achieve such transformations. The first relies on the classic "C−H activation" approach where a metal inserts into the C−H bond,[3] while the second is based upon the insertion of a transition metal-bound fragment, such as a carbene, nitrene, or oxo species, into the C−H bond.[4] Other elegant approaches have also been reported for C−H bond functionalization.[5] We have shown that metallocarbene intermediates, generated from the reaction between chiral rhodium(II) carboxylates and donor/acceptor-substituted diazo compounds, undergo highly diastereo- and enantioselective intermolecular insertions into C−H bonds.[2b,g] The presence of the donor group (typically vinyl or aryl) is crucial for these intermolecular reactions to occur in a selective fashion. A further advancement of this C−H

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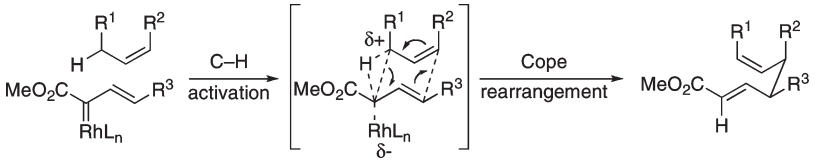
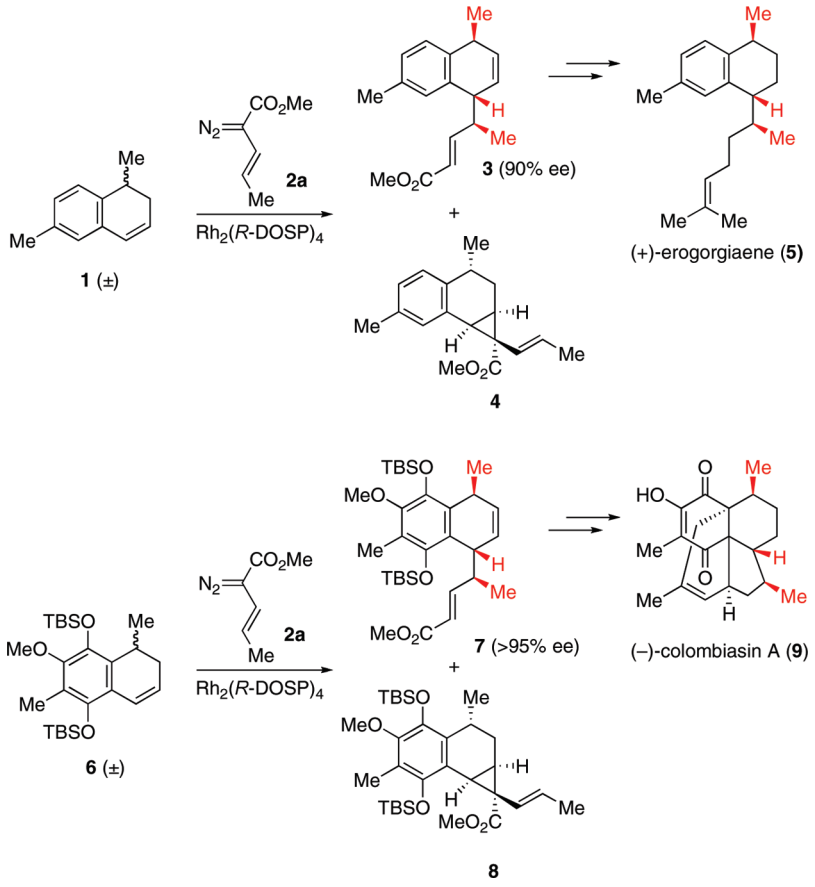
DOI: 10.1021/jo902644f Published on Web 02/19/2010

SCHEME 1. Combined C−H Activation/Cope Rearrangement



SCHEME 2. Synthesis of (+)-Erogorgiaene and (−)-Colombiasin A via an Enantiodivergent Process



functionalization chemistry is the discovery that when an allylic C−H bond is reacted with a vinylcarbenoid, the C−H insertion event is interrupted by a Cope rearrangement, generating products with two new stereocenters with exceptional stereocontrol (Scheme 1).[6]

The synthetic potential of the combined C−H activation/Cope rearrangement has been demonstrated by its use in the rapid assembly of natural products such as (+)-erogorgiaene (**5**)[7a] and (−)-colombiasin A (**9**).[7b] The challenging stereochemistry associated with these compounds is rapidly introduced by enantiodivergent reactions on racemic dihydronaphthalenes **1** and **6**. In the Rh_2(*R*-DOSP)$_4$-catalyzed reaction with vinyldiazoacetate **2a**, one enantiomer of the dihydronaphthalene undergoes the combined C−H activation/Cope rearrangement (to form either **3** or **7**), while the other undergoes cyclopropanation (to form either **4** or **8**) (Scheme 2). Both **3** and **7** have the

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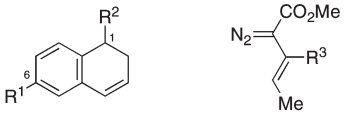
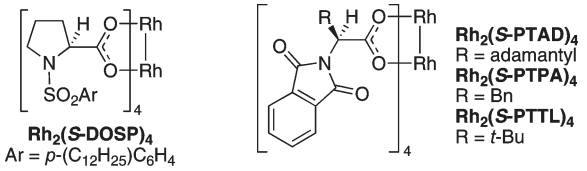


10 R^1 = H, R^2 = H
11 R^1 = OMe, R^2 = H
12 R^1 = H, R^2 = Me
13 R^1 = OMe, R^2 = Me

2a R^3 = H
2b R^3 = OTBS

FIGURE 1. Dihydronaphthalenes and diazo compounds being studied.



Rh_2(*S*-DOSP)$_4$
Ar = *p*-($C_{12}H_{25}$)C_6H_4

Rh_2(*S*-PTAD)$_4$
R = adamantyl
Rh_2(*S*-PTPA)$_4$
R = Bn
Rh_2(*S*-PTTL)$_4$
R = *t*-Bu

FIGURE 2. Chiral dirhodium catalysts.

three critical stereocenters of the natural products installed with the correct configuration and are readily converted to the natural products **5** and **9** in a concise fashion.[7] In spite of this success, as we began to extend this chemistry to more elaborate systems, we became aware that the factors controlling the selectivity were more subtle than we had observed in the natural product syntheses. Therefore, we decided to conduct a systematic study to better understand the controlling influences behind the selectivity of this chemistry, which would be needed to guide broader application of this methodology in total synthesis. The results of this study are presented in this paper.

One parameter to be evaluated was the substituent effect in the dihydronaphthalene substrate at positions C1 and C6 in order to determine to what extent the steric and electronic properties of the system influence the reaction (Figure 1). In parallel, the influence of the diazo compound structure was investigated. The vinyldiazoacetate used in the total syntheses of (+)-erogorgiaene and (−)-colombiasin A is the pentenoate **2a**.[7a,b] In recent years, however, β-silyloxyvinyldiazoacetates have been shown to be very versatile precursors to vinylcarbenoids.[8] Consequently, the studies were extended to include the silyloxy counterpart **2b**.

The chiral dirhodium tetracarboxylate Rh_2(*S*-DOSP)$_4$ is a well-established catalyst for asymmetric intermolecular C−H insertion reactions, generally resulting in high levels of asymmetric induction (Figure 2).[2g,9] Recently, the dirhodium tetracarboxylate catalyst, Rh_2(*S*-PTAD)$_4$, which is related to Hashimoto's catalysts, Rh_2(*S*-PTPA)$_4$ and Rh_2(*S*-PTTL)$_4$, has been developed for the reaction of donor/acceptor carbenoids. Rh_2(*S*-PTAD)$_4$ gives different product distributions and sometimes better enantioselectivity than Rh_2(*S*-DOSP)$_4$.[8c,10] Consequently both Rh_2(*S*-DOSP)$_4$ and Rh_2(*S*-PTAD)$_4$ were screened in this study.

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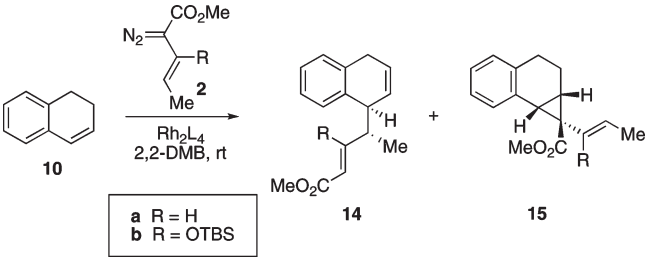
TABLE 1. Reaction of Dihydronaphthalene 10 with 2



entry[a]	R	2	catalyst	14:15[b]	ee (%)[c] 14	ee (%)[c] 15	combined yield (%)
1	H	**2a**	Rh_2(*S*-DOSP)$_4$	1.5:1	>99	52	49
2	H	**2a**	Rh_2(*S*-PTAD)$_4$	1:19	−84	−74	67
3	OTBS	**2b**	Rh_2(*S*-DOSP)$_4$	3:1	88	40	73
4	OTBS	**2b**	Rh_2(*S*-PTAD)$_4$	1:1	45	93	78

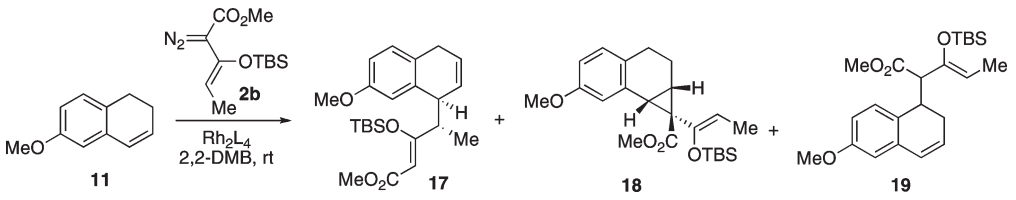
[a]Reaction conditions: (for entries 1 and 2) **10** (1 equiv), **2a** (2−3 equiv), Rh(II) catalyst (0.02 equiv), room temperature, 1.5−4 h; (for entries 3 and 4) **10** (3 equiv), **2b** (1 equiv), Rh(II) catalyst (0.01 equiv), room temperature, 18 h. 2,2-DMB = 2,2-dimethylbutane. [b]Ratio determined from the crude ^{1}H NMR. [c]Determined by chiral HPLC; a negative value represents the formation of the opposite enantiomer.

Results and Discussion

To determine a baseline for the influence of the catalyst and vinyldiazoacetate structure on the relative reactivity for C−H functionalization versus cyclopropanation, the first system to be studied was the unsubstituted dihydronaphthalene **10** (Table 1). The reaction could be carried out with either the vinyldiazoacetate or the dihydronaphthalene as the limiting reagent. 2,2-Dimethylbutane was used as an inert solvent, although test reactions indicated that pentane was similarly effective. When Rh_2(*S*-DOSP)$_4$ was used as catalyst, the reaction of **10** with vinyldiazoacetate **2a** afforded a 1.5:1 mixture of the C−H functionalization product **14a** and the cyclopropane **15a** (Table 1, entry 1). The C−H functionalization occurred with exceptionally high enantioselectivity (>99% ee), while the cyclopropane **15a** was obtained with moderate enantioselectivity (52% ee). The Rh_2(*S*-PTAD)$_4$-catalyzed reaction gave only a trace amount of the C−H functionalization product **14a** in −84% ee. The major product was the cyclopropane **15a**, which was formed with improved enantioselectivity (−74% ee) compared to the Rh_2(*S*-DOSP)$_4$-catalyzed reaction (Table 1, entry 2). The Rh_2(*S*-DOSP)$_4$- and Rh_2(*S*-PTAD)$_4$-catalyzed reactions gave rise to products of opposite asymmetric induction, consistent with previous observations.[10b,d]

The use of silyloxyvinyldiazoacetate **2b** with Rh_2(*S*-DOSP)$_4$ led to a similar result to that of **2a**, except that the C−H functionalization product **14b** was favored over the cyclopropane **15b** by a ratio of 3:1. Once again the C−H functionalization occurred with high enantioselectivity (88% ee), while the cyclopropane **15b** was formed with low enantioselectivity (40% ee) (Table 1, entry 3). Interestingly the use of Rh_2(*S*-PTAD)$_4$ gave a reversal in product enantioenrichement compared to the reaction with Rh_2(*S*-DOSP)$_4$. The reaction of **2b**, catalyzed by Rh_2(*S*-PTAD)$_4$, produced a 1:1 mixture of products consisting of a highly enantioenriched cyclopropane **15b** (93% ee) and a poorly enriched C−H activation/Cope rearrangement product **14b** (45% ee). It is noteworthy that in

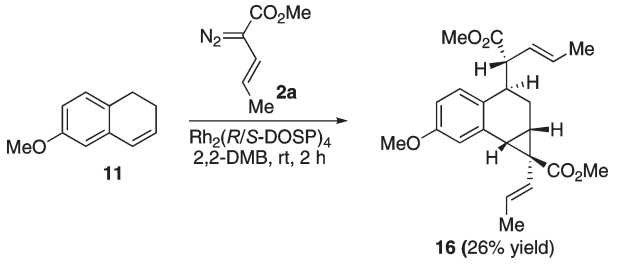
TABLE 2. Reaction of Dihydronaphthalene 11 with 2b



			ee (%)[c]			
entry[a]	catalyst	**17**:**18**:**19**[b]	**17**	**18**	**19**	combined yield (%)
1	Rh_2(*S*-DOSP)$_4$	2:0:1	90		90	90
2	Rh_2(*S*-PTAD)$_4$	1:1:0.2	33	95	45	82

[a]Reaction conditions: **11** (3 equiv), **2b** (1 equiv), Rh(II) catalyst (0.01 equiv), room temperature, 18 h. [b]Ratio determined from the crude ^{1}H NMR. [c]Determined by chiral HPLC.

SCHEME 3. Reaction of Dihydronaphthalene 11 with 2a



this case, Rh_2(*S*-DOSP)$_4$ and Rh_2(*S*-PTAD)$_4$ led to the selective formation of the same enantiomers of **14b** and **15b**. This behavior is characteristic for the Rh_2(*S*-DOSP)$_4$- and Rh_2(*S*-PTAD)$_4$-catalyzed reactions of silyloxyvinyldiazoacetate **2b**,[8c,d] however these two catalysts often give opposite asymmetric induction in the reactions of other types of donor/acceptor carbenoids. These studies show that Rh_2(*S*-DOSP)$_4$-catalyzed reactions have a greater preference for C−H functionalization compared to Rh_2(*S*-PTAD)$_4$-catalyzed reactions and silyloxyvinyldiazoacetate **2b** also has a greater preference for C−H functionalization compared to vinyldiazoacetate **2a**.

Many of the natural products accessible through this chemistry would require the use of electron-rich dihydronaphthalenes.[11] Therefore, as a test system, the reaction of 6-methoxydihydronaphthalene **11** was examined. In an attempt to obtain racemic material, the reaction of **11** with an excess of **2a** (3 equiv) in a Rh_2(*R*/*S*-DOSP)$_4$-catalyzed process led to a complex mixture of C−H insertion and cyclopropanation products, from which was isolated **16** as a single diastereomer, resulting from the double functionalization of **11** (Scheme 3). The relative configuration of **16** was determined by X-ray crystallography (see the Supporting Information).[12] When the same reaction was conducted with an excess of dihydronaphthalene **11** (3 equiv), a complex mixture was obtained, but still, a trace amount of **16** was observed. Similar mixtures were obtained with Rh_2(*S*-PTAD)$_4$. Such insertions at activated benzylic positions are well documented in the literature.[13] These results demonstrate that in this electronically activated system, benzylic C−H insertion is competing with the cyclopropanation and the combined C−H activation/Cope rearrangement, and with vinyldiazoacetate **2a**, the reaction cannot be effectively controlled.

The reaction of **11** with silyloxyvinyldiazoacetate **2b** gave a much cleaner reaction than that with **2a**, but the benzylic C−H insertion was still a competing pathway. However, the nature of the catalysts had a major influence on the product distribution. The reaction of **11** with **2b** catalyzed by Rh_2(*S*-DOSP)$_4$ afforded the rearrangement product **17** as the major product, but the minor product was the benzylic C−H insertion product **19** (2:1 ratio) (Table 2, entry 1). None of the cyclopropane **18** or double functionalized adducts were observed. Both products were obtained with high enantioselectivity (90% ee for both **17** and **19**). When Rh_2(*S*-PTAD)$_4$ was used as catalyst, only traces of the benzylic C−H insertion product **19** were observed (Table 2, entry 2). The major products were a 1:1 mixture of the C−H functionalization product **17** and the cyclopropane **18**. The cyclopropane was formed with very high enantioselectivity (95% ee) but the C−H activation/Cope rearrangement product was afforded with low enantioselectivity (33% ee). These results indicate that the carbenoid derived from silyloxyvinyldiazoacetate **2b** is more selective than the carbenoid derived from **2a**, and in the reaction of **2b**, Rh_2(*S*-PTAD)$_4$ equally favors the C−H functionalization product **17** and the cyclopropane **18**.

An intriguing aspect of the reaction of dihydronaphthalenes is the possibility for enantiomer differentiation when 1-substituted dihydronaphthalenes are used as substrates.[7] This was tested in the reaction with 1-methyl-1,2-dihydronaphthalene (**12**). The Rh_2(*S*-DOSP)$_4$-catalyzed reaction of racemic **12** with **2a** afforded a 1:1 mixture of C−H activation/Cope rearrangement product **20a** and cyclopropane **21a** in which **20a** was obtained with excellent enantioselectivity (91% ee) (Table 3, entry 1). The enantioselectivity for **20a** could be further improved to 96% ee when the same reaction was conducted at 0 °C. The cyclopropane **21a** was obtained as a 4:1 mixture of diastereomers and with moderate enantioselectivity (74% ee for the major and 50% ee for the minor). These conditions are similar to those used in the total synthesis of (+)-erogorgiaene (**5**) and (−)-colombiasin A

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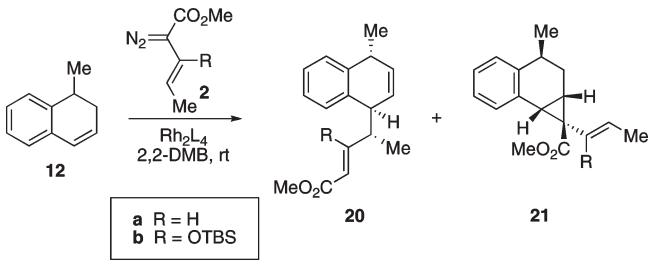
(12) The crystal structures of **16** and **21b** have been deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K. [fax: +44(0) 1223 336033 or e-mail deposit@ccdc.cam.ac.uk], under CCDC reference nos. CCDC 757794 and CCDC 757795.

(13) (a) Davies, H. M. L.; Hedley, S. J.; Bohall, B. R. *J. Org. Chem.* **2005**, *70*, 10737–10742. (b) Davies, H. M. L.; Loe, Ø. *Synthesis* **2004**, 2595–2608. (c) Davies, H. M. L.; Jin, Q. *Tetrahedron: Asymmetry* **2003**, *14*, 941–949. (d) Davies, H. M. L.; Jin, Q.; Ren, P.; Kovalevsky, A. Y. *J. Org. Chem.* **2002**, *67*, 4165–4169.

TABLE 3. Reaction of Dihydronaphthalene 12 with 2



entry[a]	R	2	catalyst	20:21[b]	ee (%)[c] 20	ee (%)[c] 21	combined yield (%)
1	H	**2a**	Rh_2(*S*-DOSP)$_4$	1:1	91(96)[d]	74[e]	72
2	H	**2a**	Rh_2(*S*-PTAD)$_4$	1:7	−40	−34[f]	42
3	OTBS	**2b**	Rh_2(*S*-DOSP)$_4$	3:1	86	53	58
4	OTBS	**2b**	Rh_2(*S*-PTAD)$_4$	1:1	88	96	90

[a]Reaction conditions: (for entries 1 and 2) **12** (1 equiv), **2a** (2−3 equiv), Rh(II) catalyst (0.02 equiv), room temperature, 3−16 h; (for entries 3 and 4) **12** (1 equiv), **2b** (4 equiv), Rh(II) catalyst (0.01 equiv), room temperature, 18 h. [b]Ratio determined from the crude ^{1}H NMR. [c]Determined by chiral HPLC; a negative value represents the formation of the opposite enantiomer. [d]Reaction at 0 °C. [e]dr = 4:1. The major diastereomer is 74% ee. The minor diastereomer is 50% ee. [f]dr = 2.3:1. The major diastereomer is −34% ee. The minor diastereomer is −78% ee.

(**9**), except Rh_2(*R*-DOSP)$_4$ was used as the catalyst in these cases.[7a,b] The same reaction catalyzed by Rh_2(*S*-PTAD)$_4$ afforded the cyclopropane **21a** as the major product in a 2.3:1 mixture of diastereomers (−34% ee for the major, −78% ee for the minor) along with recovered starting material and a minimal amount of the C−H activation product (Table 3, entry 2).

The reaction of silyloxyvinyldiazoacetate **2b** with **12** was quite different from the reaction of **2a**. The Rh_2(*S*-DOSP)$_4$-catalyzed reaction of **2b** with **12** generated a 3:1 mixture of **20b** and **21b** in a 58% combined yield (Table 3, entry 3). The C−H activation/Cope rearrangement showed a high level of enantioinduction (86% ee) but the cyclopropane **21b** was obtained with low enantioselectivity (53% ee). In contrast, the Rh_2(*S*-PTAD)$_4$-catalyzed reaction of **2b** with **12** went very smoothly, affording a 1:1 mixture of **20b** and **21b**, both of which were formed with excellent enantioinduction (88% ee and 96% ee, respectively) (Table 3, entry 4). These studies indicate that Rh_2(*S*-DOSP)$_4$ is the best catalyst for enantiodifferentiation of **12** with use of **2a** as the carbenoid precursor, while Rh_2(*S*-PTAD)$_4$ is the best catalyst when **2b** is used as the carbenoid precursor.

The final system to be examined was **13**, an electron-rich 1-substituted dihydronaphthalene. The Rh_2(*R*-DOSP)$_4$-catalyzed reaction yielded a nearly equimolar mixture of the C−H activation/Cope rearrangement product **22a** and cyclopropane **23a** while small amounts of benzylic C−H insertion product **24a** were also observed.[14] Cyclopropane **23a** was obtained as a 9:1 mixture of diastereomers; however, **22a** and **24a** were single diastereomers and were obtained in −81% and 98% ee, respectively. Interestingly, when the reaction was catalyzed by Rh_2(*S*-PTAD)$_4$, the C−H activation/Cope rearrangement product **22a** was obtained as a minor product and with low enantioinduction, with the major products being the cyclopropane **23a** and the benzylic C−H insertion product **24a**. The cyclopropane **23a** was again a 9:1 mixture of diastereomers while the C−H functionalization products **22a** and **24a** were produced as single diastereomers. However, the diastereomer of **24a** formed in the Rh_2(*S*-PTAD)$_4$-catalyzed reaction was different from that obtained from the Rh_2(*R*-DOSP)$_4$-catalyzed reaction. The competing C−H insertion at a benzylic tertiary position is relatively unusual because such sites are generally not particularly reactive toward donor/acceptor carbenoids due to steric hindrance and typically more forcing reaction conditions would be required.[15]

The reactions of silyloxyvinyldiazoacetate **2b** with **13** were much cleaner, as there was no competing benzylic C−H insertion. The outcome of the reactions was very similar to the results obtained in the reactions of dihydronaphthalene **12**. The Rh_2(*S*-DOSP)$_4$-catalyzed reaction favored the C−H activation/Cope rearrangement, while Rh_2(*S*-PTAD)$_4$ afforded a 1:1 mixture of the C−H activation/Cope rearrangement product **22b** (88% ee) and the cyclopropane **23b** (96% ee) with excellent enantiodifferentiation (Table 4, entries 3 and 4). These results confirm the trend that the carbenoid derived from silyloxyvinyldiazoacetate **2b** is more selective than the carbenoid derived from **2a**, and in the reaction of **2b**, Rh_2(*S*-PTAD)$_4$ equally favors the C−H functionalization product **22** and the cyclopropane **23**. Additionally, direct C−H insertion at the electronically activated tertiary benzylic site in **13** is less prevalent than the direct C−H insertion into the secondary benzylic site in **11**. This is another example of how steric hindrance can protect an electronically activated site from C−H insertion by donor/acceptor carbenoids.

The absolute configuration of the C−H functionalization products **14a**, **20a**, and **22a** derived from vinyldiazoacetate **2a** was tentatively assigned on the basis of the known absolute configuration of analogous products obtained in model studies or natural products syntheses, which were unambiguously determined by X-ray crystallography and/or conversion to natural products.[7] The absolute configuration of **20b**, derived from the silyloxyvinyldiazoacetate **2b**, was established via derivatization (Scheme 4). Reaction of **12** with **2b** in the presence of Rh_2(*S*-DOSP)$_4$ afforded a mixture of C−H activation/Cope rearrangement and cyclopropanation products which was then treated with TBAF. Further reaction with $PhNTf_2$ afforded vinyl triflate **25**, which was then hydrogenated to give **26**.[16] The same product was prepared in a similar sequence from **12** and **2a** via hydrogenation of **20a**.[7] It was found that the same enantiomer of **26** was obtained in both cases, showing that diazo compounds **2a** and **2b** led to C−H activation/Cope rearrangement products with the same sense of enantioinduction in Rh_2(*S*-DOSP)$_4$-catalyzed reactions. The relative and absolute configurations of the direct benzylic C−H insertion products **19** and **24** were not determined.

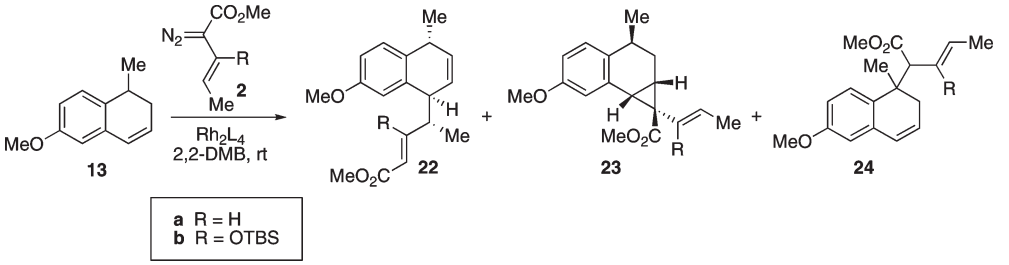
The relative configuration of the cyclopropanes **15**, **18**, **21**, and **23** was determined on the basis of the distinctive chemical shift for the methyl ester and NOE experiments on cyclopropane **21a** (see the Supporting Information). The absolute

(14) The reaction of vinyldiazoacetate **2a** with **13** was conducted with the enantiomeric catalyst Rh_2(*R*-DOSP)$_4$ as this simplified the chiral HPLC analysis.

(15) Nadeau, E.; Li, Z.; Morton, D.; Davies, H. M. L. *Synlett* **2009**, 151–154.

(16) (a) Jigajinni, V. B.; Wightman, R. H. *Tetrahedron Lett.* **1982**, *23*, 117–120. (b) Martínez, A. G.; Alvarez, R. M.; Casado, M. M.; Subramanian, L. R.; Hanack, M. *Tetrahedron* **1987**, *43*, 275–279. (c) Comins, D. L.; Benjelloun, N. R. *Tetrahedron Lett.* **1994**, *35*, 829–832.

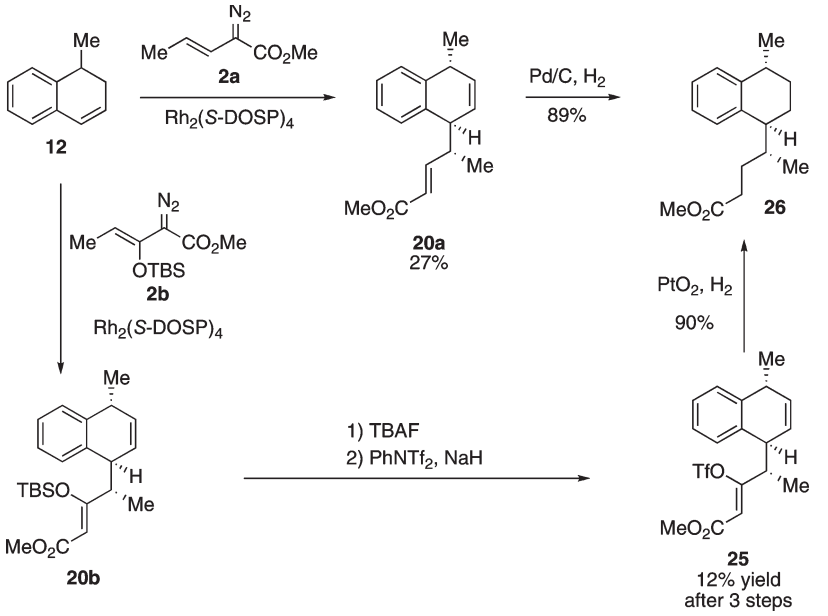
TABLE 4. Reaction of Dihydronaphthalene 13 with 2



					ee (%)[c]			
entry[a]	R	2	catalyst	22:23:24[b]	22	23	24	combined yield (%)
1	H	**2a**	Rh_2(*R*-DOSP)$_4$	0.9:1:0.1	−81[d]	ND[e]	98[f]	84
2	H	**2a**	Rh_2(*S*-PTAD)$_4$	0.1:1:0.7	−36	ND[e]	ND	75
3	OTBS	**2b**	Rh_2(*S*-DOSP)$_4$	5:1:0	85	59		55
4	OTBS	**2b**	Rh_2(*S*-PTAD)$_4$	1:1:0	88	96		90

[a]Reaction conditions: (for entries 1 and 2) **13** (1 equiv), **2a** (2−3 equiv), Rh(II) catalyst (0.02 equiv), room temperature, 1.5−2 h; (for entries 3 and 4) **13** (1 equiv), **2b** (3 equiv.), Rh(II) catalyst (0.01 equiv), room temperature, 18 h. [b]Ratio determined from the crude ^{1}H NMR. [c]Determined by chiral HPLC; a negative value represents the formation of the opposite enantiomer. [d]Determined after hydrogenation and reduction of the ester. [e]dr = 9:1. [f]Determined after hydrogenation.

SCHEME 4. Confirmation of Absolute Stereochemistry



configuration was tentatively assigned based on the established predictive model for Rh_2(*S*-DOSP)$_4$-catalyzed cyclopropanations.[17] For cyclopropane **21b** (Table 3, entry 4), the absolute stereochemistry was unambiguously assigned by X-ray crystallography (see the Supporting Information).[12]

Excellent predictive models have been developed for both the Rh_2(*S*-DOSP)$_4$-catalyzed C−H activation/Cope rearrangement[6b] and cyclopropanation.[17] The chiral catalyst is considered to adopt a D_2 symmetric arrangement (in nonpolar solvents) and can be viewed simply as having a blocking group in the front and another in the back.[2g,18] Applying these models to chiral dihydronaphthalenes (**12** and **13**) shows that an enantiodivergent process can take place in which one enantiomer is matched for a C−H activation/Cope rearrangement while the other enantiomer prefers a matched cyclopropanation.[7] C−H activation is considered to occur by approach of the substrate from the front face of the vinylcarbenoid and is interrupted by the interaction of the alkene in the dihydronaphthalene, which triggers the Cope rearrangement (Figure 3).[6,7] In the case of the (*R*)-enantiomer of the substrate, the C1 methyl group is pointing forward away from the carbenoid (TS-1) and thus the C−H functionalization is favored. The (*S*)-enantiomer of the substrate is unable to approach the vinylcarbenoid due to steric interaction by the C1 methyl group (TS-2) thereby inhibiting the C−H transformation.

In the case of the cyclopropanation reaction, the (*S*)-enantiomer of the dihydronaphthalene gives the matched

(17) Nowlan, D. T. III; Gregg, T. M.; Davies, H. M. L.; Singleton, D. A. *J. Am. Chem. Soc.* **2003**, *125*, 15902–15911.

(18) (a) Hansen, J.; Davies, H. M. L. *Coord. Chem. Rev.* **2008**, *252*, 545–555. (b) Hansen, J.; Autschbach, J.; Davies, H. M. L. *J. Org. Chem.* **2009**, *74*, 6555–6563.

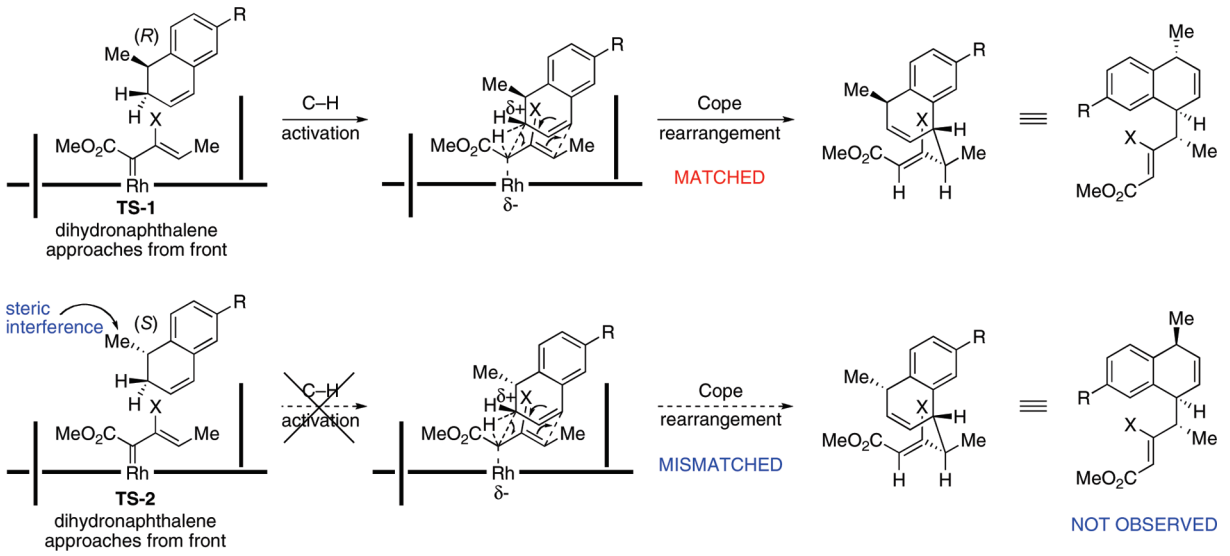


FIGURE 3. Rh_2(*S*-DOSP)$_4$ predictive model for the combined C−H activation/Cope rearrangement (X = H, OTBS).

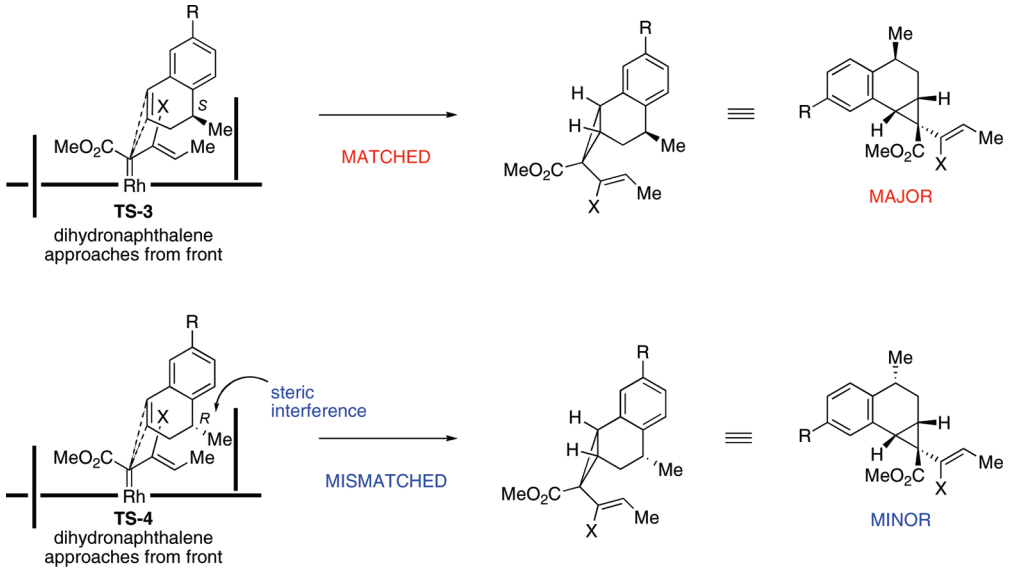


FIGURE 4. Rh_2(*S*-DOSP)$_4$ predictive model for the cyclopropanation reaction (X = H, OTBS).

reaction (TS-3), while the (*R*)-enantiomer gives the mismatched reaction (TS-4), as illustrated in Figure 4. The influence of the C1 methyl group in the cyclopropanation is not as dominating as it is in the C−H functionalization, as it is further away from the site of attack. In the case of the unsubstituted vinyldiazoacetate (X = H), a mixture of diastereomeric cyclopropanes is formed, but with the more sterically demanding silyloxyvinyldiazoacetate (X = OTBS), only the matched reaction is observed.

The reactions catalyzed by Rh_2(*S*-PTAD)$_4$ also undergo an enantiodivergent process, which is similar to the enantiodivergent step catalyzed by Rh_2(*S*-DOSP)$_4$. Hashimoto reported that the crystal structure of the chiral dirhodium tetracarboxylate Rh_2(*S*-PTPA)$_4$ adopts a C_2 symmetrical arrangement, in which two adjacent phthalimido groups are positioned on the top face of the complex, while the next two are positioned on the bottom face. This structure was used to develop a predictive model for the stereoselection of intramolecular C−H

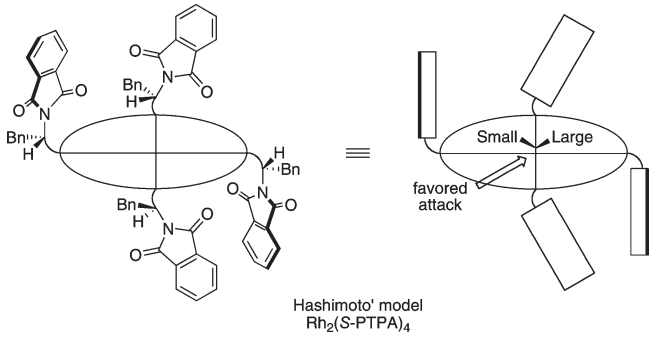


FIGURE 5. C_2 symmetrical Rh_2(*S*-PTPA)$_4$ predictive model.

insertion reactions (Figure 5).[19] Two possible orientations of the carbenoid are possible and the preferred orientation would place the smaller group pointing toward the phthalimido

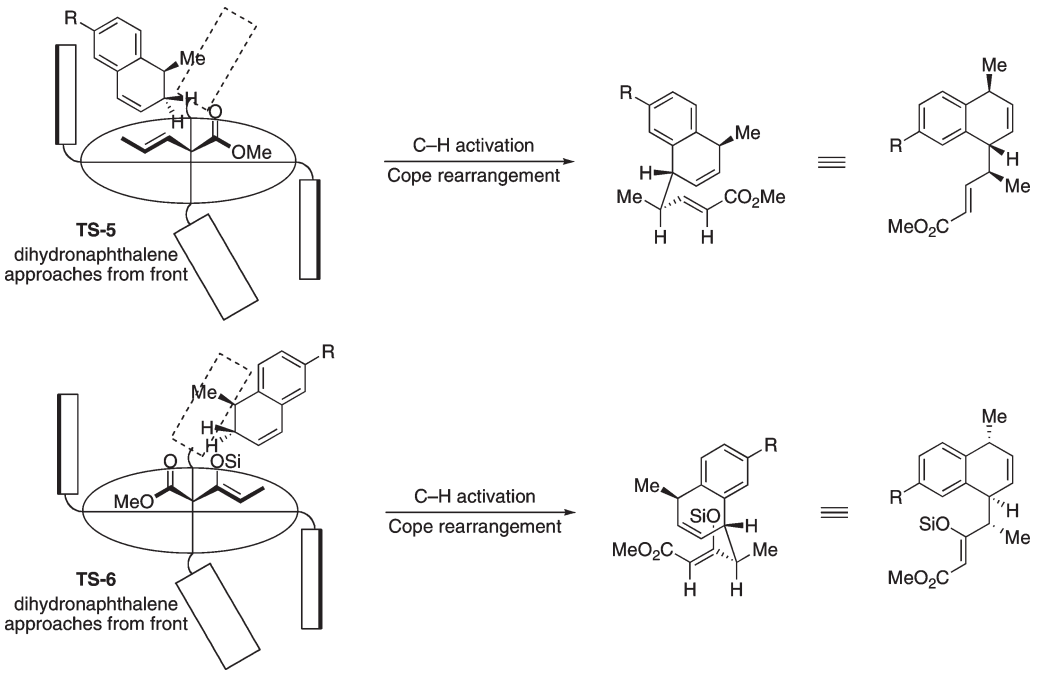


FIGURE 6. Rh_2(*S*-PTAD)$_4$ predictive model for the combined C−H activation/Cope rearrangement with vinylcarbenoids derived from diazo compounds **2a** (TS-5) and **2b** (TS-6).

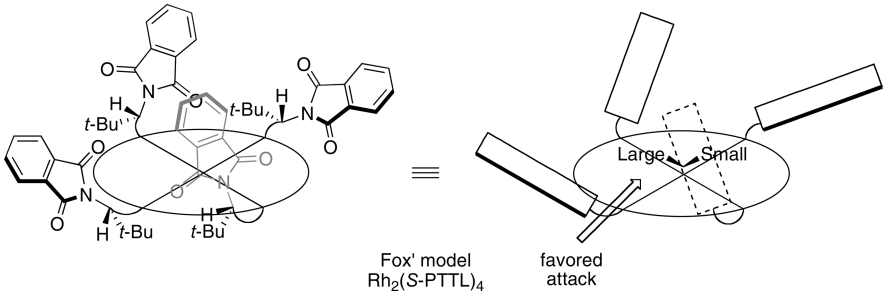


FIGURE 7. Rh_2(*S*-PTTL)$_4$ predictive model.

group. The two adjacent phthalimido groups would then block the attack to one of the two faces of the carbenoid.

Application of the Hashimoto model to rationalize the Rh_2(*S*-PTAD)$_4$-catalyzed reactions with dihydronaphthalenes is shown in Figure 6.[8d] In this model, the back-face of the vinylcarbenoid is blocked by the two adjacent phthalimide groups. With the unsubstituted vinyldiazoacetate **2a**, it is assumed that the methylvinyl moiety is small enough to fit in the most encumbered pocket of the catalyst. Approach of the substrate from the front, with the C1 methyl group pointing away from the blocking groups, would lead to the opposite enantiomer to the one obtained from a Rh_2(*S*-DOSP)$_4$-catalyzed reaction, which is in accordance with experimental data (Figure 6, TS-5). With silyloxyvinyldiazoacetate **2b**, the electron-donating group of the carbenoid is significantly larger, and therefore, it prefers an orientation in which the bulky silyl group is away from the blocking groups (Figure 6, TS-6). Hence, unlike **2a**, the silyloxyvinyldiazoacetate **2b** generates products of the same overall asymmetric induction with both Rh_2(*S*-PTAD)$_4$ and Rh_2(*S*-DOSP)$_4$.

Recently, Fox[20] and Charette[21] independently reported the crystal structure of chiral dirhodium tetracarboxylate Rh_2(*S*-PTTL)$_4$ and other phthalimido-derived catalysts, which are closely related to Rh_2(*S*-PTAD)$_4$. Interestingly, they found that their structure is considerably different from that of Rh_2(*S*-PTPA)$_4$. Indeed, the four phthalimide groups were found to be orientated on the same face of the catalyst, providing a "chiral crown" environment.[20] For Rh_2(*S*-PTTL)$_4$, Fox suggested that two opposite groups are acting as blocking groups, while the two others are slightly tilted, thus leading to a cavity with narrow (∼11 Å) and wide (∼15 Å) dimensions.[20] From this structure, a model was proposed to explain highly enantioselective cyclopropanation reactions of alkyldiazoacetates (Figure 7).

The Fox model was applied to our reactions with dihydronaphthalenes, but the current version of the model predicted the opposite asymmetric induction to what was observed. As shown in Figure 8 for the reaction with silyloxyvinyldiazoacetate **2b**, the bulky silyloxyvinyl group should be located in

(19) (a) Hashimoto, S.; Watanabe, N.; Sato, T.; Shiro, M.; Ikegami, S. *Tetrahedron Lett*. **1993**, *34*, 5109–5112. (b) Watanabe, N.; Ohtake, Y.; Hashimoto, S.; Shiro, M.; Ikegami, S. *Tetrahedron Lett*. **1995**, *36*, 1491–1494.

(20) DeAngelis, A.; Dmitrenko, O.; Yap, G. P. A.; Fox, J. M. *J. Am. Chem. Soc*. **2009**, *131*, 7230–7231.

(21) Lindsay, V. N. G.; Lin, W.; Charette, A. B. *J. Am. Chem. Soc*. **2009**, *131*, 16383–16385.

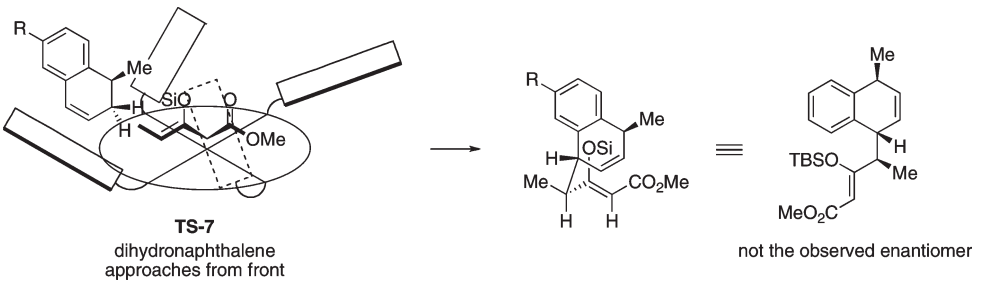


FIGURE 8. Alternative Rh_2(*S*-PTAD)$_4$ predictive model for the combined C−H activation/Cope rearrangement with vinylcarbenoid derived from diazo compound **2b**.

the less hindered quadrant of the catalyst cavity and the dihydronaphthalene should approach from the front, over the tilted phthalimide group (TS-7). However, this model predicts the wrong absolute stereochemistry of the reaction. Recent studies by Charette suggest that Rh_2(*S*-PTTL)$_4$ may be conformationally mobile in solution and not locked in the "chiral crown" configuration.[21] Further studies will be necessary to determine if there is a defined orientation for the Hashimoto catalysts including Rh_2(*S*-PTAD)$_4$, which can rationalize all the types of asymmetric transformations that have been achieved with these catalysts.

In summary, these studies demonstrate that **2a**/Rh_2(*S*-DOSP)$_4$ and **2b**/Rh_2(*S*-PTAD)$_4$ are the best combinations for achieving high selectivity in the cyclopropanation and the combined C−H activation/Cope rearrangement of 1,2-dihydronaphthalenes, and hence are the most effective for enantiodivergent reactions in these systems. The **2a**/Rh_2(*S*-PTAD)$_4$ combination strongly favors cyclopropanation, while the **2b**/Rh_2(*S*-DOSP)$_4$ combination strongly favors the combined C−H activation/Cope rearrangement. The **2a**/Rh_2(*S*-DOSP)$_4$ combination gives high enantioselectivity for the combined C−H activation/Cope rearrangement with achiral substrates and substrates capable of enantiodivergent reactions. In contrast, the **2b**/Rh_2(*S*-PTAD)$_4$ combination gives high enantioselectivity only with substrates capable of enantiodivergent reactions. With chiral dihydronaphthalenes, **2b**/Rh_2(*S*-PTAD)$_4$ is generally more selective than **2a**/Rh_2(*S*-DOSP)$_4$, and therefore, it is a good backup system when the **2a**/Rh_2(*S*-DOSP)$_4$ fails to give a clean enantiomer differentiation.

Experimental Section

General Considerations. All reactions were conducted in flame-dried glassware under an inert atmosphere of dry argon. All reagents were used as received from commercial suppliers unless otherwise stated. 2,2-Dimethylbutane (2,2-DMB) was distilled from sodium metal. Pentane, tetrahydrofuran, and toluene were obtained through drying columns. All solvents used for C−H functionalization reactions were degassed by bubbling argon through the solvent for 15 min prior to use. Diastereomeric ratios were determined by values derived from the ^{1}H NMR spectra of the crude reaction mixtures. Enantiomeric excess was determined by high performance liquid chromatography (HPLC), using chiral analytical columns with 2-propanol in hexane as eluant.

(*R*,*E*)-Methyl 4-((*S*)-1,4-Dihydronaphthalen-1-yl)pent-2-enoate (14a) and (1*R*,1a*S*,7b*S*)-Methyl 1-((*E*)-Prop-1-enyl)-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (15a). Table 1, entry 1: 2a (210 mg, 1.5 mmol, 3 equiv) in 4.5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **10** (65 mg, 0.5 mmol, 1 equiv) and Rh_2(*S*-DOSP)$_4$ (19 mg, 0.01 mmol, 0.02 equiv) in 5.5 mL of 2,2-DMB. After 0.5 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2) to afford **14a** and **15a** (59 mg, 49% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% $AgNO_3$[22] (hexane:ether). **Table 1, entry 2: 2a** (140 mg, 1 mmol, 2 equiv) in 4.5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **10** (65 mg, 0.5 mmol, 1 equiv) and Rh_2(*S*-PTAD)$_4$ (16 mg, 0.01 mmol, 0.02 equiv) in 5.5 mL of 2,2-DMB. After 3 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2) to afford **14a** and **15a** (81 mg, 67% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% $AgNO_3$ (hexane:ether).

14a: colorless oil; R_f 0.57 (hexane:ethyl acetate 80:20); IR (neat) ν 3028, 2966, 2872, 1720; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.15−7.21 (3H, m), 7.13 (1H, d, J = 7.1 Hz), 7.09 (1H, dd, J = 15.9, 6.9 Hz), 6.07−6.10 (1H, m), 5.82 (1H, d, J = 15.9 Hz), 5.74−5.78 (1H, m), 3.75 (3H, s), 3.62 (1H, ddd, J = 8.0, 3.9, 3.9 Hz), 3.27−3.40 (2H, m), 2.77−2.84 (1H, m), 0.84 (3H, d, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 152.7, 136.4, 135.4, 128.2, 128.0, 127.4, 126.1(2C), 125.4, 120.3, 51.5, 44.1, 43.8, 30.2, 13.2; HRMS (APCI) calcd for $C_{16}H_{19}O_2$ (MH^+) 243.1380, found 243.1379; $[\alpha]^{20}_D$ −172.7 (*c* 0.7, $CHCl_3$) for 99% ee; HPLC anal. 99% ee with Rh_2(*S*-DOSP)$_4$ and −84% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm, t_R = 8.97, 10.63 min).

15a: white solid; mp 33−34 °C; R_f 0.57 (hexane:ethyl acetate 80:20); IR (neat) ν 3021, 2926, 1713, 1232; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.32 (1H, m), 7.10−7.18 (2H, m), 6.98−7.02 (1H, m), 5.21−5.33 (2H, m), 3.70 (3H, s), 2.81 (1H, d, J = 9.1 Hz), 2.62 (1H, ddd, J = 16.6, 7.0, 4.1 Hz), 2.44 (1H, ddd, J = 16.6, 9.8, 7.3 Hz), 2.23 (1H, ddd, J = 9.1, 5.7, 2.9 Hz), 1.92−2.08 (2H, m), 1.48 (3H, d, J = 4.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.3, 135.7, 133.1, 132.2, 130.2, 128.3, 126.3, 125.9, 121.7, 52.3, 35.6, 29.9, 27.8, 26.6, 18.4, 17.9; HRMS (APCI) calcd for $C_{16}H_{19}O_2$ (MH^+) 243.1380, found 243.1380; $[\alpha]^{20}_D$ +3.2 (*c* 2.5, $CHCl_3$) for −74% ee; HPLC anal. 48% ee with Rh_2(*S*-DOSP)$_4$ and −74% ee with Rh_2(*S*-PTAD)$_4$ ((*S*,*S*)-Whelk-O 1, 0.5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm, t_R = 13.24, 14.47 min).

(1*R*,1a*S*,3*R*,7b*S*)-Methyl 6-Methoxy-3-((*R*,*E*)-1-methoxy-1-oxopent-3-en-2-yl)-1-((*E*)-prop-1-enyl)-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (16) (Scheme 3). 2a (315 mg, 2.25 mmol, 3 equiv) in 7 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **11** (120 mg, 0.75 mmol, 1 equiv) and Rh_2(*R*/*S*-DOSP)$_4$ (28 mg, 0.015 mmol, 0.02 equiv) in 8 mL of 2,2-DMB. After 1 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2−80:20). **16** was

(22) Li, T.-S.; Li, J.-T.; Li, H.-Z. *J. Chromatogr., A* **1995**, *715*, 372–375.

further purified by recrystallization from hexane to afford 76 mg (26%) of **16**.

16: white solid; mp 108−109 °C; R_f 0.36 (hexane:ethyl acetate 80:20); IR (neat) ν 2949, 1716, 1193, 1158; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (1H, d, J = 8.5 Hz), 6.78 (1H, d, J = 2.6 Hz), 6.61 (1H, dd, J = 8.5, 2.6 Hz), 5.69 (1H, dq, J = 15.2, 6.4 Hz), 5.51 (1H, ddq, J = 15.2, 9.5, 1.6 Hz), 5.44 (1H, dq, J = 15.9, 6.6 Hz), 4.86 (1H, dq, J = 15.9, 1.7 Hz), 3.76 (3H, s), 3.72 (3H, s), 3.43 (3H s), 3.24 (1H, dd, J = 10.0, 10.0 Hz), 2.77−2.82 (1H, m), 2.77 (1H, d, J = 8.9 Hz), 2.22 (1H, ddd, J = 14.5, 9.1, 2.2 Hz), 2.08 (1H, ddd, J = 9.1, 9.1, 6.4 Hz), 1.73 (3H, dd, J = 6.4, 1.6 Hz), 1.56−1.62 (1H, m), 1.55 (3H, dd, J = 6.6, 1.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 174.1, 158.4, 133.7, 132.8, 131.8, 129.7, 129.2, 127.8, 121.9, 115.5, 112.6, 55.8, 55.1, 52.3, 51.3, 40.6, 35.8, 28.6, 23.2, 21.6, 18.8, 17.9; HRMS (APCI) calcd for $C_{23}H_{29}O_5$ (MH^+) 385.2010, found 385.2012.

(*R*,*E*)-Methyl 4-((1*S*,4*R*)-4-Methyl-1,4-dihydronaphthalen-1-yl)-pent-2-enoate (20a) and (1*R*,1a*S*,3*S*,7b*S*)-Methyl 3-Methyl-1-((*E*)-prop-1-enyl)-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (21a). Table 3, entry 1: 2a (210 mg, 1.5 mmol, 3 equiv) in 4.5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **12** (72 mg, 0.5 mmol, 1 equiv) and Rh_2(*S*-DOSP)$_4$ (19 mg, 0.01 mmol, 0.02 equiv) in 5.5 mL of 2,2-DMB. After 2 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2) to afford **20a** and **21a** (92 mg, 72% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% $AgNO_3$ (hexane:ether). **Table 3, entry 2: 2a** (140 mg, 1 mmol, 2 equiv) in 4.5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **12** (72 mg, 0.5 mmol, 1 equiv) and Rh_2(*S*-PTAD)$_4$ (16 mg, 0.01 mmol, 0.02 equiv) in 5.5 mL of 2,2-DMB. After 15 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 98:2) to afford **20a** and **21a** (54 mg, 42% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% $AgNO_3$ (hexane:ether).

20a: colorless oil; R_f 0.63 (hexane:ethyl acetate 80:20); IR (neat) ν 3024, 2966, 2872, 1721, 1271, 1173; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.31 (1H, m), 7.19−7.24 (3H, m), 7.13 (1H, dd, J = 15.8, 6.5 Hz), 5.91 (1H, ddd, J = 10.2, 2.6, 1.3 Hz), 5.84 (1H, dd, J = 15.8, 1.6 Hz), 5.67 (1H, ddd, 10.2, 4.4, 2.5 Hz), 3.75 (3H, s), 3.61−3.65 (1H, m), 3.36−3.44 (1H, m), 2.81−2.89 (1H, m), 1.36 (3H, d, J = 7.3 Hz), 0.78 (3H, d, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 153.2, 140.8, 136.1, 134.4, 127.7, 127.2, 126.5, 126.3, 123.7, 120.5, 51.7, 43.9, 43.5, 32.8, 23.1, 13.0; HRMS (APCI) calcd for $C_{17}H_{21}O_2$ (MH^+) 257.1536, found 257.1540; $[\alpha]^{20}_D$ −189.2 (*c* 0.3, $CHCl_3$) for 91% ee; HPLC anal. 91% ee with Rh_2(*S*-DOSP)$_4$ and −40% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm, t_R = 7.57, 8.37 min).

21a: major/minor = 80:20; colorless oil; R_f 0.63 (hexane:ethyl acetate 80:20); IR (neat) ν 3021, 2954, 1715, 1233; major: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.29 (1H, m), 7.09−7.19 (3H, m), 5.33 (1H, dq, J = 15.9, 6.5 Hz), 5.10 (1H, dq, J = 15.9, 1.7 Hz), 3.71 (3H, s), 2.82 (1H, d, J = 9.5 Hz), 2.58−2.67 (1H, m), 2.21 (1H, ddd, J = 9.5, 7.3, 4.4 Hz), 1.95 (1H, ddd, J = 14.4, 5.8, 4.4 Hz), 1.81 (1H, ddd, J = 14.4, 7.3, 6.4 Hz), 1.50 (3H, dd, J = 6.5, 1.7 Hz), 1.27 (3H, d, J = 7 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.6, 142.3, 132.8, 132.1, 130.6, 126.6, 126.0, 122.1, 52.3, 35.6, 31.6, 29.4, 26.6, 25.3, 22.2, 18.6; HRMS (APCI) calcd for $C_{17}H_{21}O_2$ (MH^+) 257.1536, found 257.1539; HPLC anal. major diastereomer 74% ee with Rh_2(*S*-DOSP)$_4$ and −34% ee with Rh_2(*S*-PTAD)$_4$ ((*S*,*S*)-Whelk-O 1, 100% hexane, 0.5 mL/min, λ = 254 nm, t_R = 13.55, 14.93 min), minor diastereomer 50% ee with Rh_2(*S*-DOSP)$_4$ and −78% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm, t_R = 5.84, 6.58 min).

(*R*,*E*)-Methyl 4-((1*S*,4*R*)-7-Methoxy-4-methyl-1,4-dihydronaphthalen-1-yl)pent-2-enoate (22a) and (1*R*,1a*S*,3*S*,7b*S*)-Methyl 6-Methoxy-3-methyl-1-((*E*)-prop-1-enyl)-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (23a). Table 4, entry 1: 2a (4.80 g, 34.4 mmol, 2 equiv) in 20 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **13** (3.00 g, 17.2 mmol, 1 equiv) and Rh_2(*R*-DOSP)$_4$ (650 mg, 0.344 mmol, 0.02 equiv) in 60 mL of 2,2-DMB. After 0.5 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ethyl acetate 90:10) to afford **22a**, **23a**, and **24a** (4.14 g, 84% combined yield). **Table 4, entry 2: 2a** (168 mg, 1.2 mmol, 2 equiv) in 5 mL of 2,2-DMB was added by syringe pump over 1 h to a solution of dihydronaphthalene **13** (105 mg, 0.6 mmol, 1 equiv) and Rh_2(*S*-PTAD)$_4$ (19 mg, 0.012 mmol, 0.02 equiv) in 7 mL of 2,2-DMB. After 1 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (hexane:ether 95:5−80:20) to afford **22a**, **23a**, and *epi*-**24a** (129 mg, 75% combined yield). Analytically pure products were obtained by purification on silica gel impregnated with 5% $AgNO_3$ (hexane:ether).

22a: colorless oil; R_f 0.53 (hexane:ethyl acetate 80:20); IR (neat) ν 3024, 2963, 2871, 2836, 1720; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (1H, d, J = 8.6 Hz), 7.13 (1H, dd, J = 15.7, 6.5 Hz), 6.80 (1H, dd, J = 8.6, 2.5 Hz), 6.72 (1H, d, J = 2.5 Hz), 5.89 (1H, ddd, J = 10.2, 2.7, 1.1 Hz), 5.85 (1H, dd, J = 15.7, 1.7 Hz), 5.64 (1H, ddd, J = 10.2, 4.1, 2.5 Hz), 3.81 (3H, s), 3.75 (3H, s), 3.56−3.62 (1H, m), 3.30−3.38 (1H, m), 2.80−2.88 (1H, m), 1.33 (3H, d, J = 7.3 Hz), 0.78 (3H, d, J = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 158.0, 153.1, 137.4, 134.7, 133.2, 128.2, 123.3, 120.5, 112.6, 112.5, 55.4, 51.7, 44.3, 43.6, 32.2, 23.2, 12.9; HRMS (APCI) calcd for $C_{18}H_{23}O_3$ (MH^+) 287.1647, found 287.1643; HPLC anal. −36% with Rh_2(*S*-PTAD)$_4$ ((*S*,*S*)-Whelk-O 1, 0.5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm, t_R = 22.52, 26.51 min).

23a: major/minor = 90:10; colorless oil; R_f 0.53 (hexane:ethyl acetate 80:20); IR (neat) ν 3021, 2952, 1713, 1230; major: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (1H, d, J = 8.3 Hz), 6.83 (1H, d, J = 2.9 Hz), 6.71 (1H, dd, J = 8.3, 2.9 Hz), 5.35 (1H, dq, J = 15.7, 6.5 Hz), 5.11 (1H, dq, 15.7, 1.6 Hz), 3.79 (3H, s), 3.71 (3H, s), 2.79 (1H, d, J = 9.2 Hz), 2.52−2.61 (1H, m), 2.19 (1H, ddd, J = 9.2, 7.0, 4.3 Hz), 1.94 (1H, ddd, J = 14.4, 6.0, 4.3 Hz), 1.78 (1H, ddd, J = 14.4, 7.0, 7.0 Hz), 1.51 (3H, dd, J = 6.7, 1.6 Hz), 1.24 (3H, d, J = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 157.7, 134.4, 133.3, 132.7, 127.5, 122.0, 115.1, 112.8, 55.2, 52.3, 35.6, 30.7, 29.8, 26.9, 25.6, 22.3, 18.6; HRMS (APCI) calcd for $C_{18}H_{23}O_3$ (MH^+) 287.1642, found 287.1643.

(*S*)-4-((1*R*,4*S*)-7-Methoxy-4-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)pentan-1-ol.[7a] The purified mixture of **22a**, **23a**, and **24a** (4.14 g, from the Rh_2(*R*-DOSP)$_4$-catalyzed reaction, Table 4, entry 1) was taken up in 100 mL of ethyl acetate and transferred to a Parr hydrogenation bottle containing 5% Pd/C (1.80 g, 90 mg of Pd, 0.85 mmol). The vessel was purged with H_2. The reaction was shaken under H_2 atmosphere (35 psi) for 12 h at rt, then filtrated on a short plug of silica gel. The plug was washed with ethyl acetate and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane:ethyl acetate 95:5) to yield 1.38 g (28% over 2 steps from **13**) of the C−H activation/Cope rearrangement product. The latter (200 mg, 0.7 mmol) was dissolved in 5 mL of THF and cooled to 0 °C. The reaction vessel was purged with argon and $LiAlH_4$ (50 mg, 1.4 mmol) was added portionwise to the stirring solution against positive argon pressure. The reaction was stirred for 0.5 h, quenched slowly with H_2O (10 mL), followed by 10% HCl (5 mL). The aqueous layer was extracted with ether (3 × 10 mL). The organic extracts were combined and dried with $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was purified on silica gel (hexane:ethyl acetate 60:40) to give 160 mg (87%) of the titled compound. Colorless oil; IR (neat) ν 2927, 1607, 1491, 1279, 1237, 1051, 804; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 7.17 (1H, d, J = 8.5 Hz), 6.77 (1H, d, J = 2.5 Hz), 6.71 (1H, dd, J = 8.5, 2.5 Hz), 3.79 (3H, s), 3.69 (2H, t, J = 6.5 Hz), 2.86−2.92 (1H, m), 2.65−2.74 (1H, m), 2.08−2.16 (1H, m), 1.89−1.95 (1H, m), 1.78−1.84 (1H, m), 1.60−1.73 (2H, m), 1.44−1.58 (3H, m), 1.28−1.41 (2H, m), 1.26 (3H, d, J = 6.5 Hz), 0.66 (3H, d, J = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.5, 141.2, 135.9, 127.5, 112.9, 110.8, 63.3, 55.2, 42.1, 37.3, 32.5, 31.8, 31.2(2C), 21.9, 21.6, 14.5; HRMS (EI) calcd for $C_{17}H_{26}O_2$ (M^+) 262.1927, found 262.1937; $[\alpha]^{20}_D$ +76.7 (c 1.1, $CHCl_3$); HPLC anal. 81% ee (Chiralcel OJ, 0.5% i-PrOH in hexane, 0.8 mL/min, λ = 254 nm, t_R = 29.9, 47.9 min).

Methyl 2-(6-Methoxy-1-methyl-1,2,3,4-tetrahydronaphthalen-1-yl)-pentanoate (27). Typical experimental procedure for hydrogenation of 24a epimers: In a Parr hydrogenation bottle was added *epi*-**24a** (Table 4, entry 2) (29 mg, 0.1 mmol), 30 mL of ethyl acetate, and 5% Pd/C (32 mg, 1.6 mg of Pd, 0.015 mmol). The vessel was purged with H_2. The reaction mixture was shaken under H_2 atmosphere (40 psi) for 18 h, then filtrated on a short plug of silica gel. The plug was washed with ethyl acetate and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane:ether 98:2−96:4) to yield 18 mg (62%) of the titled compound.

epi-**27** (Table 4, entry 2): 62% yield (18 mg); colorless oil; R_f 0.58 (hexane:ethyl acetate 80:20); IR (neat) ν 2956, 2933, 2871, 1730; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (1H, d, J = 8.7 Hz), 6.69 (1H, dd, J = 8.7, 2.9 Hz), 6.54 (1H, d, J = 2.9 Hz), 3.76 (3H, s), 3.37 (3H, s), 2.77 (1H, dd, J = 12.1, 2.9 Hz), 2.62−2.74 (2H, m), 2.19 (1H, ddd, J = 13.5, 10.8, 3.0 Hz), 1.88−1.96 (1H, m), 1.62−1.77 (2H, m), 1.54−1.61 (1H, m), 1.43−1.52 (1H, m), 1.31 (3H, s), 1.14−1.30 (2H, m), 0.90 (3H, t, J = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 157.3, 138.8, 135.2, 129.1, 113.3, 111.7, 55.6, 55.3, 50.9, 39.1, 33.2, 30.8, 30.1, 28.4, 22.0, 19.6, 14.3; HRMS (APCI) calcd for $C_{18}H_{27}O_3$ (MH^+) 291.1955, found 291.1956.

27 (Table 4, entry 1): 5% yield (250 mg) (yield over 2 steps from **13**); colorless oil; R_f 0.57 (hexane:ethyl acetate 80:20); IR (neat) ν 2957, 2871, 2837, 1732, 1501; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (1H, d, J = 8.9 Hz), 6.71 (1H, dd, J = 8.9, 2.4 Hz), 6.58 (1H, d, J = 2.4 Hz), 3.77 (3H, s), 3.65 (3H, s), 2.85 (1H, dd, J = 11.8, 2.3 Hz), 2.65−2.76 (2H, m), 2.00 (1H, ddd, J = 13.6, 10.9, 2.9 Hz), 1.80−1.87 (1H, m), 1.64−1.74 (2H, m), 1.58 (1H, ddd, J = 13.6, 6.6, 2.6 Hz), 1.28 (3H, s), 1.15−1.24 (1H, m), 1.04−1.14 (1H, m), 0.93−1.02 (1H, m), 0.79 (3H, t, J = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.7, 157.1, 138.9, 135.1, 127.3, 113.3, 112.3, 55.7, 55.0, 51.0, 39.2, 32.3, 30.9, 30.1, 29.3, 21.6, 19.5, 13.8; HRMS (EI) calcd for $C_{18}H_{26}O_3$ (M^+) 290.1876, found 290.1880; $[\alpha]^{20}_D$ −14.8 (c 3.09, $CHCl_3$); HPLC anal. 98% ee (Chiralcel OJ, 0.4% i-PrOH in hexane, 0.4 mL/min, λ = 254 nm, t_R = 15.10, 17.12 min).

(*S*,*Z*)-Methyl 3-(*tert*-Butyldimethylsilyloxy)-4-((*S*)-1,4-dihydronaphthalen-1-yl)pent-2-enoate (14b) and (1*R*,1a*S*,7b*S*)-Methyl 1-((*Z*)-1-(*tert*-Butyldimethylsilyloxy)prop-1-enyl)-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[a]naphthalene-1-carboxylate (15b). Table 1, entry 3: 2b (270 mg, 1 mmol, 1 equiv) in 5 mL of 2,2-DMB was added by syringe pump over 2 h to a solution of dihydronaphthalene **10** (390 mg, 3 mmol, 3 equiv) and Rh_2(*S*-DOSP)$_4$ (19 mg, 0.01 mmol, 0.01 equiv) in 5 mL of 2,2-DMB. After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 99.5:0.5) to afford **14b** and **15b** (272 mg, 73% combined yield). **Table 1, entry 4: 2b** (270 mg, 1 mmol, 1 equiv) in 5 mL of 2,2-DMB:toluene (5:1) was added by syringe pump over 2 h to a solution of dihydronaphthalene **10** (390 mg, 3 mmol, 3 equiv) and Rh_2(*S*-PTAD)$_4$ (16 mg, 0.01 mmol, 0.01 equiv) in 5 mL of 2,2-DMB:toluene (5:1). After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 99.5:0.5) to afford **14b** and **15b** (291 mg, 78% combined yield).

14b: colorless oil; R_f 0.56 (pentane:ether 80:20); IR (neat) ν 1723, 1626, 1201, 1161, 1080, 839, 825, 782, 747; ^{1}H NMR (500 MHz, C_6D_6) δ 7.31 (1H, d, J = 7.5 Hz), 7.10 (1H, t, J = 7.5 Hz), 7.04 (1H, t, J = 7.0 Hz), 6.91 (1H, d, J = 7.5 Hz), 5.80 (2H, s), 5.33 (1H, s), 4.12−4.18 (1H, m), 3.44 (3H, s), 2.98−3.13 (2H, m), 2.71−2.73 (1H, m), 1.08 (9H, s), 0.64 (3H, d, J = 7.0 Hz), 0.45 (3H, s), 0.30 (3H, s); ^{13}C NMR (75 MHz, C_6D_6) δ 169.1, 164.9, 136.8, 135.0, 128.0, 126.8, 126.7, 125.9, 125.6, 124.1, 98.3, 49.4, 48.4, 40.6, 29.5, 25.5, 18.3, 10.8, −4.2, −4.4; HRMS (ESI) calcd for $C_{22}H_{33}O_3Si$ (MH^+) 373.2193, found 373.2196; $[\alpha]^{20}_D$ −92.1 (c 1.12, $CHCl_3$) for 88% ee; HPLC anal. 88% ee with Rh_2(*S*-DOSP)$_4$ and 45% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.2% i-PrOH in hexane, 0.5 mL/min, λ = 254 nm, t_R = 10.3 (major), 12.2 min (minor)).

15b: colorless oil; R_f 0.52 (pentane:ether 80:20); IR (neat) ν 1721, 1675, 1494, 1472, 1462, 1435, 1334, 1305, 1239, 1203, 1160, 1076, 874, 837, 799, 779, 753; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21−7.23 (1H, m), 7.07−7.12 (2H, m), 6.95−6.97 (1H, m), 3.98 (1H, br s), 3.70 (3H, s), 2.78 (1H, d, J = 9.0 Hz), 2.57−2.64 (1H, m), 2.50 (1H, dd, J = 16.5, 7.0 Hz), 2.25−2.31 (2H, m), 1.88−1.95 (1H, m), 1.25 (3H, d, J = 6.0 Hz), 0.91 (9H, br s), 0.14 (3H, s), 0.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 143.1, 136.4, 133.1, 129.9, 128.0, 126.2, 125.6, 110.7, 52.0, 38.9, 33.4, 28.3, 25.8, 25.6, 18.5, 18.4, 11.1, −4.3, −4.8; HRMS (EI) calcd for $C_{22}H_{32}O_3Si$ (M^+) 372.2115, found 372.2113; $[\alpha]^{20}_D$ −22.6 (c 0.72, $CHCl_3$) for 93% ee; HPLC anal. 40% ee with Rh_2(*S*-DOSP)$_4$ and 93% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 100% hexane, 0.8 mL/min, λ = 230 nm, t_R = 11.8 (major), 14.3 min (minor)).

(*S*,*Z*)-Methyl 3-(*tert*-Butyldimethylsilyloxy)-4-((*S*)-7-methoxy-1,4-dihydronaphthalen-1-yl)pent-2-enoate (17), (1*R*,1a*S*,7b*S*)-Methyl 1-((*Z*)-1-(*tert*-Butyldimethylsilyloxy)prop-1-enyl)-6-methoxy-1a,2,3,7b-tetrahydro-1*H* cyclopropa[*a*]naphthalene-1-carboxylate (18), and (*Z*)-Methyl 3-(*tert*-Butyldimethylsilyloxy)-2-(6-methoxy-1,2-dihydronaphthalen-1-yl)pent-3-enoate (19). Table 2, entry 1: 2b (270 mg, 1 mmol, 1 equiv) in 5 mL of 2,2-DMB was added by syringe pump over 2 h to a solution of dihydronaphthalene **11** (480 mg, 3 mmol, 3 equiv) and Rh_2(*S*-DOSP)$_4$ (19 mg, 0.01 mmol, 0.01 equiv) in 5 mL of 2,2-DMB. After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 98:2) to afford **17**, **18**, and **19** (362 mg, 90% combined yield). **Table 2, entry 2: 2b** (270 mg, 1 mmol, 1 equiv) in 5 mL of 2,2-DMB:toluene (5:1) was added by syringe pump over 2 h to a solution of dihydronaphthalene **11** (480 mg, 3 mmol, 3 equiv) and Rh_2(*S*-PTAD)$_4$ (16 mg, 0.01 mmol, 0.01 equiv) in 5 mL of 2,2-DMB:toluene (5:1). After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 98:2) to afford **17**, **18**, and **19** (330 mg, 82% combined yield).

17: colorless oil; R_f 0.57 (pentane:ether 80:20); IR (neat) ν 1722, 1624, 1503, 1464, 1434, 1370, 1277, 1254, 1239, 1201, 1160, 1081, 1042, 968, 895, 837, 810, 782; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (1H, d, J = 8.0 Hz), 6.74−6.76 (2H, m), 6.07−6.09 (1H, m), 5.70−5.72 (1H, m), 5.11 (1H, s), 3.92−3.96 (1H, m), 3.78 (3H, s), 3.67 (3H, s), 3.23−3.34 (2H, m), 2.64−2.70 (1H, m), 1.05 (9H, s), 0.72 (3H, d, J = 7.0 Hz), 0.32 (3H, s), 0.28 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 166.0, 158.0, 138.1, 129.2, 127.6, 127.5, 124.0, 112.6, 111.6, 98.7, 55.1, 50.5, 48.8, 41.1, 29.3, 26.0, 18.7, 11.4, −3.8, −4.0; HRMS (EI) calcd for $C_{23}H_{34}O_4Si$ (M^+) 402.2221, found 402.2219; $[\alpha]^{20}_D$ −53.2 (c 0.54, $CHCl_3$) for 33% ee; HPLC anal. 90% ee with Rh_2(*S*-DOSP)$_4$ and 33% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.4% i-PrOH in hexane, 0.5 mL/min, λ = 254 nm, t_R = 10.6 (major), 12.1 min (minor)).

18: colorless oil; R_f 0.51 (pentane:ether 80:20); IR (neat) ν 1720, 1676, 1610, 1505, 1463, 1435, 1334, 1304, 1238, 1193, 1167, 1113, 1076, 1040, 866, 837, 779; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (1H, d, J = 8.0 Hz), 6.79 (1H, d, J = 2.5 Hz), 6.65 (1H, dd,

J = 8.0, 2.5 Hz), 4.02 (1H, br s), 3.79 (3H, s), 3.70 (3H, s), 2.72 (1H, d, J = 9.0 Hz), 2.40−2.55 (2H, m), 2.24−2.30 (2H, m), 1.85−1.92 (1H, m), 1.26 (3H, br s), 0.91 (9H, br), 0.14 (3H, s), 0.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 157.5, 143.1, 134.1, 128.8, 128.6, 115.0, 112.2, 110.4, 55.2, 52.0, 38.9, 33.6, 28.3, 25.7, 24.7, 18.8, 18.5, 11.1, −4.3, −4.7; HRMS (EI) calcd for $C_{23}H_{34}O_4Si$ (M^+) 402.2221, found 402.2228; $[\alpha]^{20}_D$ +26.0 (c 0.64, $CHCl_3$) for 95% ee; HPLC anal. 95% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.2% *i*-PrOH in hexane, 0.5 mL/min, λ = 230 nm, t_R = 18.6 (major), 21.2 min (minor)).

19: colorless oil; R_f 0.56 (pentane:ether 80:20); IR (neat) ν 1738, 1668, 1603, 1572, 1496, 1432, 1344, 1261, 1204, 1186, 1146, 1091, 1048, 880, 837, 778, 704; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.05 (1H, d, J = 8.6 Hz), 6.59−6.64 (2H, m), 6.44 (1H, dd, J = 9.3, 2.9 Hz), 5.93 (1H, ddd, J = 9.3, 6.4, 2.5 Hz), 4.93 (1H, q, J = 6.7 Hz), 3.77 (3H, s), 3.43 (3H, s), 3.14−3.19 (2H, m), 2.52 (1H, dd, J = 16.9, 6.4 Hz), 2.35−2.41 (1H, m), 1.59 (3H, d, J = 6.7 Hz), 0.96 (9H, s), 0.13 (3H, s), 0.12 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 158.7, 147.4, 134.4, 129.6, 128.3, 127.6, 127.3, 111.74, 111.71, 104.6, 55.2, 54.6, 51.4, 38.8, 26.2, 25.9, 18.3, 11.1, −3.9, −4.2; HRMS (ESI) calcd for $C_{23}H_{34}O_4SiNa$ (MNa^+) 425.2119, found 425.2122; $[\alpha]^{20}_D$ +16.9 (c 0.10, $CHCl_3$) for 90% ee; HPLC anal. 90% ee with Rh_2(*S*-DOSP)$_4$ and 45% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.1% *i*-PrOH in hexane, 0.5 mL/min, λ = 254 nm, t_R = 48.4 (major), 65.6 min (minor)).

(*S*,*Z*)-Methyl 3-(*tert*-Butyldimethylsilyloxy)-4-((1*S*,4*R*)-4-methyl-1,4-dihydronaphthalen-1-yl)pent-2-enoate (20b) and (1*R*,1a*S*,3*S*,7b*S*)-Methyl 1-((*Z*)-1-(*tert*-Butyldimethylsilyloxy)prop-1-enyl)-3-methyl-1a,2,3,7b-tetrahydro-1*H* cyclopropa[*a*]naphthalene-1-carboxylate (21b). Table 3, entry 3: 2b (540 mg, 2 mmol, 4 equiv) in 5 mL of 2,2-DMB was added by syringe pump over 2 h to a solution of dihydronaphthalene **12** (73 mg, 0.5 mmol, 1 equiv) and Rh_2(*S*-DOSP)$_4$ (9 mg, 0.005 mmol, 0.01 equiv) in 5 mL of 2,2-DMB. After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 99.5:0.5) to afford **20b** and **21b** (112 mg, 58% combined yield). **Table 3, entry 4: 2b** (540 mg, 2 mmol, 4 equiv) in 5 mL of 2,2-DMB:toluene (5:1) was added by syringe pump over 2 h to a solution of dihydronaphthalene **12** (73 mg, 0.5 mmol, 1 equiv) and Rh_2(*S*-PTAD)$_4$ (8 mg, 0.005 mmol, 0.01 equiv) in 5 mL of 2,2-DMB:toluene (5:1). After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 99.5:0.5) to afford **20b** and **21b** (174 mg, 90% combined yield).

20b: colorless oil; R_f 0.67 (pentane:ether 80:20); IR (neat) ν 1721, 1624, 1250, 1202, 838, 778; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.31 (1H, m), 7.18−7.24 (3H, m), 5.91 (1H, ddd, J = 10.2, 2.9, 1.6 Hz), 5.67 (1H, ddd, J = 10.2, 4.0, 2.4 Hz), 5.12 (1H, s), 3.95−3.99 (1H, m), 3.68 (3H, s), 3.37−3.45 (1H, m), 2.72 (1H, dq, J = 7.0, 4.1 Hz), 1.35 (3H, d, J = 7.3 Hz), 1.04 (9H, s), 0.66 (3H, d, J = 7.0 Hz), 0.31 (3H, s), 0.29 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 166.0, 140.8, 136.4, 133.8, 127.3, 126.7, 126.3, 126.2, 122.7, 98.9, 50.6, 48.2, 40.2, 32.7, 26.0, 23.2, 18.7, 11.4, −3.7, −3.8; HRMS (EI) calcd for $C_{23}H_{34}O_3Si$ (M^+) 386.2272, found 386.2283; $[\alpha]^{20}_D$ +70.8 (c 0.68, $CHCl_3$) for 88% ee; HPLC anal. 86% ee with Rh_2(*S*-DOSP)$_4$ and 88% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 100% hexane, 0.25 mL/min, λ = 254 nm, t_R = 27.7 (major), 33.0 min (minor)).

21b: white solid; mp 100−102 °C; R_f 0.63 (pentane:ether 80:20); IR (neat) ν 1721, 1675, 1462, 1434, 1332, 1305, 1239, 1165, 1124, 1076, 837, 777, 755; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (1H, d, J = 7.1 Hz), 7.10−7.19 (3H, m), 4.06 (1H, br s), 3.71 (3H, s), 2.79 (1H, d, J = 9.1 Hz), 2.64−2.72 (1H, m), 2.24−2.28 (2H, m), 1.66 (1H, ddd, J = 14.6, 10.4, 4.6 Hz), 1.26 (3H, d, J = 6.7 Hz), 1.24 (3H, d, J = 6.7 Hz), 0.91 (9H, s), 0.14 (3H, s), 0.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.0, 143.1, 141.3, 132.8, 130.2, 126.5, 125.5, 125.3, 110.8, 52.0, 39.2, 33.8, 28.7, 28.2, 27.3, 25.7, 20.1, 18.4, 11.0, −4.3, −4.7; HRMS (EI) calcd for $C_{23}H_{34}O_3Si$ (M^+) 386.2272, found 386.2266; $[\alpha]^{20}_D$ −12.1 (c 0.32, $CHCl_3$) for 96% ee; HPLC anal. 53% ee with Rh_2(*S*-DOSP)$_4$ and 96% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 100% hexane, 0.25 mL/min, λ = 254 nm, t_R = 39.5 (major), 44.0 min (minor)).

(*S*,*Z*)-Methyl 3-(*tert*-Butyldimethylsilyloxy)-4-((1*S*,4*R*)-7-methoxy-4-methyl-1,4-dihydronaphthalen-1-yl)pent-2-enoate (22b) and (1*R*,1a*S*,6*S*,7a*S*,*Z*)-Methyl 1-(1-(*tert*-Butyldimethylsilyloxy)prop-1-enyl)-3-methoxy-6-methyl-1a,6,7,7a-tetrahydro-1*H* cyclopropa-[*a*]naphthalene-1-carboxylate (23b). Table 4, entry 3: 2b (811 mg, 3 mmol, 3 equiv) in 5 mL of 2,2-DMB was added by syringe pump over 2 h to a solution of dihydronaphthalene **13** (174 mg, 1 mmol, 1 equiv) and Rh_2(*S*-DOSP)$_4$ (19 mg, 0.01 mmol, 0.01 equiv) in 5 mL of 2,2-DMB. After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 98:2) to afford **22b** and **23b** (229 mg, 55% combined yield). **Table 4, entry 4: 2b** (811 mg, 3 mmol, 3 equiv) in 5 mL of 2,2-DMB:toluene (5:1) was added by syringe pump over 2 h to a solution of dihydronaphthalene **13** (174 mg, 1 mmol, 1 equiv) and Rh_2(*S*-PTAD)$_4$ (16 mg, 0.01 mmol, 0.01 equiv) in 5 mL of 2,2-DMB:toluene (5:1). After 16 h of additional stirring, the solvent was removed under vacuum and the remaining residue was purified on silica gel (pentane:ether 98:2) to afford **22b** and **23b** (375 mg, 90% combined yield).

22b: colorless oil; R_f 0.61 (pentane:ether 80:20); IR (neat) ν 1723, 1625, 1253, 1202, 1163, 826, 781; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (1H, d, J = 8.5 Hz), 6.79 (1H, dd, J = 8.5, 2.5 Hz), 6.74 (1H, d, J = 2.5 Hz), 5.90 (1H, d, J = 10.0 Hz), 5.65−5.63 (1H, m), 5.11 (1H, s), 3.92−3.94 (1H, m), 3.79 (3H, s), 3.68 (3H, s), 3.30−3.40 (1H, m), 2.68−2.72 (1H, m), 1.32 (3H, d, J = 7.0 Hz), 1.05 (9H, s), 0.67 (3H, d, J = 6.5 Hz), 0.32 (3H, s), 0.28 (3H, s); ^{13}C NMR (75 MHz, C_6D_6) δ 169.8, 165.6, 158.6, 137.9, 134.5, 133.2, 128.6, 122.7, 113.1, 111.7, 99.0, 54.7, 50.2, 48.9, 41.2, 32.5, 26.3, 23.5, 19.0, 11.4, −3.4, −3.9; HRMS (EI) calcd for $C_{24}H_{36}O_4Si$ (M^+) 416.2377, found 416.2379; $[\alpha]^{20}_D$ −18.0 (c 1.2, $CHCl_3$) for 88% ee; HPLC anal. 85% ee with Rh_2(*S*-DOSP)$_4$ and 88% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.2% *i*-PrOH in hexane, 0.5 mL/min, λ = 254 nm, t_R = 11.7 (major), 16.5 min (minor)).

23b: colorless oil; R_f 0.47 (pentane:ether 80:20); IR (neat) ν 1720, 1500, 1464, 1434, 1332, 1306, 1237, 1218, 1168, 1070, 1048, 860, 837, 800; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (1H, d, J = 8.5 Hz), 6.82 (1H, d, J = 2.5 Hz), 6.72 (1H, dd, J = 8.5, 2.5 Hz), 4.12 (1H, br s), 3.79 (3H, s), 3.72 (3H, s), 2.77 (1H, d, J = 9.0 Hz), 2.60−2.67 (1H, m), 2.24−2.30 (2H, m), 1.63 (1H, ddd, J = 14.2, 10.7, 5.2 Hz), 1.27 (3H, d, J = 6.5 Hz), 1.24 (3H, d, J = 7.0 Hz), 0.93 (9H, s), 0.17 (3H, s), 0.10 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.9, 157.2, 143.0, 134.0, 133.4, 126.1, 115.1, 112.1, 110.5, 55.0, 51.9, 39.1, 34.0, 28.5, 27.8, 27.5, 25.6, 20.1, 18.3, 11.0, −4.3, −4.8; HRMS (EI) calcd for $C_{24}H_{36}O_4Si$ (M^+) 416.2377, found 416.2382; $[\alpha]^{20}_D$ +22.8 (c 1.3, $CHCl_3$) for 96% ee; HPLC anal. 59% ee with Rh_2(*S*-DOSP)$_4$ and 96% ee with Rh_2(*S*-PTAD)$_4$ (Chiralcel OD-H, 0.1% *i*-PrOH in hexane, 0.8 mL/min, λ = 235 nm, t_R = 24.1 (minor), 34.8 min (major)).

(*S*,*Z*)-Methyl 4-((1*S*,4*R*)-4-Methyl-1,4-dihydronaphthalen-1-yl)-3-(trifluoromethylsulfonyloxy)pent-2-enoate (25).[16] Diazo compound **2b** (1.08 g, 4 mmol, 4 equiv) in 10 mL of 2,2-DMB was added dropwise by syringe pump over 2 h to a solution of 1-methyl-1,2-dihydronaphthalene **12** (0.144 g, 1 mmol, 1 equiv) and Rh_2(*S*-DOSP)$_4$ (0.038 g, 0.02 mmol, 0.02 equiv) in 10 mL of 2,2-DMB. The reaction mixture was stirred for an additional 14 h, then concentrated in vacuo. The crude was quickly purified by flash chromatography (hexane:ether 99:1 to 98:2) to yield 217 mg of a mixture of **20b** and **21b**. This mixture was dissolved in 10 mL of THF and cooled to 0 °C. TBAF (211 mg, 0.67 mmol, 1.2 equiv) was added to the solution in one portion. After 0.7 h, the reaction was diluted with 30 mL of ether and 10 mL of distilled water. The aqueous layer was extracted with ether (3 × 30 mL). The organic extracts were combined and washed with

10 mL of distilled water and 10 mL of saturted aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude was quickly purified by flash chromatography (hexane:ether 95:5 to 93:7) to yield 88 mg of a mixture of C−H activation/Cope rearrangement product and cyclopropane. The mixture was dissolved in 3 mL of dry THF and cooled to 0 °C. NaH (23 mg, 0.96 mmol) was added to the solution, followed 5 min later by $PhNTf_2$ (229 mg, 0.64 mmol). After 1 h, the cold bath was removed and the reaction allowed to reach rt. After 6 h, the reaction was diluted with 30 mL of ether and 10 mL of distilled water. The aqueous layer was extracted with ether (2 × 30 mL). The organic extracts were combined and washed with 5 mL of distilled water and 5 mL of saturted aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude was purified by flash chromatography (hexane:ether 95:5 to 90:10) to yield 25 mg (12%, theorical yield from *R*-**12**) of vinyl triflate **25**.

25: white solid; mp 83−85 °C; R_f 0.60 (hexane:ethyl acetate 80:20); IR (neat) ν 3027, 2977, 2959, 2932, 1739, 1430, 1207; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.32 (1H, m), 7.20−7.25 (2H, m), 7.14−7.17 (1H, m), 6.00 (1H, ddd, J = 10.3, 2.9, 1.4 Hz), 5.75 (1H, d, J = 1.3 Hz), 5.57 (1H, ddd, J = 10.3, 4.1, 2.4 Hz), 3.94−3.98 (1H, m), 3.82 (3H, s), 3.38−3.46 (1H, m), 3.02−3.08 (1H, m), 1.37 (3H, d, J = 7.3 Hz), 0.75 (3H, d, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 161.3, 140.5, 135.5, 134.5, 127.4, 126.8, 126.7 (2C), 120.8, 118.5 (q, J = 320 Hz), 111.6, 52.1, 45.7, 39.6, 32.6, 23.1, 11.2; ^{19}F NMR (375 MHz, $CDCl_3$) δ −74.6; HRMS (APCI) calcd for $C_{18}H_{20}O_5F_3S$ (MH^+) 405.0978, found 405.0979.

(*R*)-Methyl 4-((1*S*,4*R*)-4-Methyl-1,2,3,4-tetrahydronaphthalen-1-yl)pentanoate (26).[16] **From vinyl triflate 25:** In a Parr hydrogenation bottle was added vinyl triflate **25** (7 mg, 0.017 mmol), 20 mL of MeOH, PtO_2 (1.2 mg, 0.0051 mmol), and Li_2CO_3 (2.5 mg, 0.034 mmol). The vessel was purged with H_2. The mixture was shaken under H_2 atmosphere (30 psi) for 14 h at rt, then diluted with 40 mL of ether and 20 mL of distilled water. The aqueous layer was extracted with ether (3 × 40 mL). The combined organic extracts were washed with 10 mL of distilled water and 10 mL of saturated aqueous NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane:ether 99:1) to yield 4 mg (90%) of **26**.

From 20a:[16] In a Parr hydrogenation bottle was added **20a** (14 mg, 0.055 mmol), 30 mL of ethyl acetate, and 5% Pd/C (24 mg, 1.2 mg of Pd, 0.011 mmol). The vessel was purged with H_2. The mixture was shaken under H_2 atmosphere (30 psi) for 13 h at rt, then filtrated on a short plug of silica gel. The plug was washed with ethyl acetate and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (hexane:ether 99:1) to yield 12.5 mg (89%) of **26**.

26: colorless oil; R_f 0.62 (hexane:ethyl acetate 80:20); IR (neat) ν 3022, 2954, 2930, 2869, 1738, 1168; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23−7.26 (1H, m), 7.17−7.21 (1H, m), 7.11−7.15 (2H, m), 3.70 (3H, s), 2.90−2.94 (1H, m), 2.74−2.81 (1H, m), 2.34−2.46 (2H, m), 2.10−2.18 (1H, m), 1.92−1.98 (1H, m), 1.75−1.87 (2H, m), 1.62−1.69 (1H, m), 1.52−1.59 (1H, m), 1.32−1.39 (1H, m), 1.29 (3H, d, J = 6.7 Hz), 0.66 (3H, d, J = 6.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 143.3, 139.4, 127.4, 126.7, 125.5, 125.3, 51.6, 41.6, 36.9, 33.1, 32.6, 31.4, 30.2, 21.8, 21.5, 14.2; HRMS (APCI) calcd for $C_{17}H_{25}O_2$ (MH^+) 261.1849, found 261.1849; $[\alpha]^{20}_D$ −36.5 (*c* 0.97, $CHCl_3$); HPLC anal. 93% ee ((*S*,*S*)-Whelk-O 1, 0.5% *i*-PrOH in hexane, 1 mL/min, λ = 254 nm, t_R = 11.04, 12.56 min).

Acknowledgment. This research was supported by the National Institutes of Health (GM080337). E.N. thanks the Fonds Québécois de la Recherche sur la Nature et les Technologies (FQRNT, Québec, Canada) for a postdoctoral research fellowship.

Supporting Information Available: Detailed experimental procedures, full characterization, and spectra for all new compounds, and crystallographic data for compounds **16** and **21b** (CIFs). This material is available free of charge via the Internet at http://pubs.acs.org.