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Enantioselective C−C Bond Formation by Rhodium-Catalyzed Tandem Ylide Formation/[2,3]-Sigmatropic Rearrangement between Donor/Acceptor Carbenoids and Allylic Alcohols

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Abstract: The rhodium-catalyzed reaction of racemic allyl alcohols with methyl phenyldiazoacetate or methyl styryldiazoacetate results in a two-step process, an initial oxonium ylide formation followed by a [2,3]-sigmatropic rearrangement. This process competes favorably with the more conventional O−H insertion chemistry as long as donor/acceptor carbenoids and highly substituted allyl alcohols are used as substrates. When the reactions are catalyzed by Rh_2(*S*-DOSP)$_4$, tertiary α-hydroxycarboxylate derivatives with two adjacent quaternary centers are produced with high enantioselectivity (85−98% ee).

Introduction

Metal-catalyzed reactions of diazo compounds result in a variety of useful transformations such as cyclopropanations, C−H insertions, and various transformations that are initiated by reactions of carbenoids with heteroatoms to form ylides.[1] For some time we have been exploring the rhodium-catalyzed reactions of donor/acceptor carbenoids.[2] We have developed highly enantioselective processes for cyclopropanation and C−H insertion,[2] but the studies by us and others on enantioselective reactions involving ylide intermediates, have resulted in limited success. Chiral rhodium catalysts gave no asymmetric induction in O−H and N−H insertions of aryldiazoacetates.[3−6] Similarly, no asymmetric induction was obtained in rhodium-catalyzed epoxidation[7] or the three-component coupling between aryldiazoacetates, alcohols and aldehydes (or imines).[8,9] The only exception to date is the reaction of aryldiazoacetates with allyl aryl sulfides and propargyl aryl sulfides.[10,11] The resulting sulfur ylides undergo a [2,3]-sigmatropic rearrangement with moderate asymmetric induction (∼70% ee).

We hypothesized that in order to obtain high asymmetric inductions in ylide transformations of rhodium carbenoid **1**, two critical issues need to be controlled (Scheme 1). The first would be to avoid reactions in which the metal associated ylide **2** undergoes a proton transfer, since this would likely result in the formation of achiral enol intermediate **3** and consequent loss of any asymmetric induction.[12] The second would be to avoid

(1) (a) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263. (b) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylide*; Wiley: New York, 1998. (c) Lydon, K. M.; McKervey, M. A. *Compr. Asymmetric Catal. I-III*; Springer: Berlin, 1999; Vol. 2, p 539. (d) Davies, H. M. L. *Compr. Asymmetric Catal., Suppl.*; Springer: Berlin, 2004; Vol. 1, p 83. (e) Davies, H. M. L.; Walji, A. M. *Modern Rhodium-Catalyzed Organic Reactions*; Wiley: New York, 2005; p 301. (f) Wee, A. G. H. *Curr. Org. Synth.* **2006**, *3*, 499. (f) Zhang, Z.; Wang, J. *Tetrahedron* **2008**, *64*, 6577. (g) Padwa, A. *J. Org. Chem.* **2009**, *74*, 6421.

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(3) (a) Ferris, L.; Haigh, D.; Moody, C. J. *Tetrahedron Lett.* **1996**, *37*, 107. (b) Bulugahapitiya, P.; Landais, Y.; Parra-Rapado, L.; Planchenault, D.; Weber, V. *J. Org. Chem.* **1997**, *62*, 1630.

(4) For references on enantioselective O-H insertion via copper-catalyzed decomposition of diazo carbonyl compounds, see: (a) Maier, T. C.; Fu, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 4594. (b) Chen, C.; Zhu, S.-F.; Liu, B.; Wang, L.-X.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2007**, *129*, 12616. (c) Zhu, S.-F.; Chen, C.; Cai, Y.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2008**, *47*, 932.

(5) For references on enantioselective N−H insertion via copper-catalyzed decomposition of diazo carbonyl compounds, see: (a) Bachmann, S.; Fielenbach, D.; Jørgensen, K. A. *Org. Biomol. Chem.* **2004**, *2*, 3044. (b) Liu, B.; Zhu, S.-F.; Zhang, W.; Chen, C.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2007**, *129*, 5834. (c) Lee, E. C.; Fu, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 12066.

(6) Diastereoselective O−H and N−H insertions using dirhodium catalysis have been generally unsuccessful. For leading references see: (a) Aller, E.; Cox, G. G.; Miller, D. J.; Moody, C. J. *Tetrahedron Lett.* **1994**, *35*, 5949. (b) Aller, E.; Brown, D. S.; Cox, G. G.; Miller, D. J.; Moody, C. J. *J. Org. Chem.* **1995**, *60*, 4449. (c) Miller, D. J.; Moody, C. J.; Morfitt, C. N. *Aust. J. Chem.* **1999**, *52*, 97. (d) Doyle, M. P.; Yan, M. *Tetrahedron Lett.* **2002**, *43*, 5929. (e) Bolm, C.; Saladin, S.; Classen, A.; Kasyan, A.; Veri, E.; Raabe, G. *Synlett* **2005**, 461. (f) Im, C. Y.; Okuyama, T.; Sugimura, T. *Chem. Lett.* **2005**, *34*, 1328. (g) Im, C. Y.; Okuyama, T.; Sugimura, T. *Eur. J. Org. Chem.* **2008**, 285. (h) Davis, F. A.; Fang, T.; Goswami, R. *Org. Lett.* **2002**, *4*, 1599.

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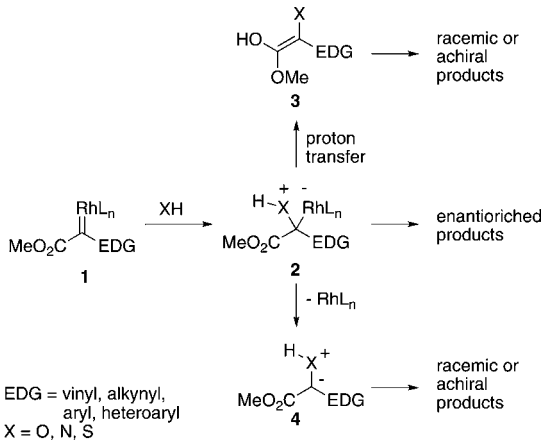
(9) Even though dirhodium catalysts gave no asymmetric induction in the three component coupling, excellent enantioselectivity was achieved with chiral phosphoric acid or Zr^{IV}/BINOL as co-catalyst. For references, see: (a) Hu, W.; Xu, X.; Zhou, J.; Liu, W.-J.; Huang, H.; Hu, J.; Yang, L.; Gong, L.-Z. *J. Am. Chem. Soc.* **2008**, *130*, 7782. (b) Zhang, X.; Huang, H.; Guo, X.; Guan, X.; Yang, L.; Hu, W. *Angew. Chem., Int. Ed.* **2008**, *47*, 6647.

(10) (a) Zhang, X.; Qu, Z.; Ma, Z.; Shi, W.; Jin, X.; Wang, J. *J. Org. Chem.* **2002**, *67*, 5621. (b) Liao, M.; Wang, J. *Green Chem.* **2007**, *9*, 184. (c) Zhang, X.; Ma, M.; Wang, J. *Tetrahedron: Asymmetry* **2003**, *14*, 891.

(11) A highly stereoselective [2,3]-sigmatropic rearrangement of sulfur ylide generated from aryldiazoacetate and allyl/propargyl sulfides was achieved with Cu(I) catalyst. For reference, see: Ma, M.; Peng, L.; Li, C.; Zhang, X.; Wang, J. *J. Am. Chem. Soc.* **2005**, *127*, 15016.

10.1021/ja9075293

Scheme 1



conditions that would favor dissociation of the rhodium catalyst from the metal associated ylide **2** to form the free ylide **4** prior to the subsequent reactions as this would likely cause erosion in asymmetric induction.[8] We proposed that the most favorable conditions for achieving such results would be to conduct the reactions in nonpolar solvents under the mildest conditions possible.[13] In this paper, we describe the discovery of highly enantioselective rhodium-catalyzed ylide transformations of donor/acceptor carbenoids.

Results and Discussion

The most promising system to date for enantioselective ylide transformations of donor/acceptor carbenoids has been the reaction of aryldiazoacetates with aryl allyl sulfides.[10] However, sulfides tend to poison the rhodium catalysts and consequently tend to require relatively forcing conditions. Furthermore, sulfur ylides are relatively stable; thus, dissociation of the rhodium complex from the ylide would be expected to be quite favorable. Therefore, we decided to explore the use of other allylic systems containing less nucleophilic heteroatoms. The reaction of allyl methyl ether **5** with methyl phenyldiazoacetate **6** was examined but this failed to give the desired [2,3]-sigmatropic rearrangement product (eq 1). Instead, it gave the C−H insertion product **7** as a 2:1 mixture of diastereomers.[14] Even though this was a failure in terms of the ylide chemistry, it is still a most compelling example of the complementary influence of steric and electronic effects on the regioselectivity of C−H functionalization.[2e] The allylic site is electronically highly activated, but, due to the overwhelming steric influence with

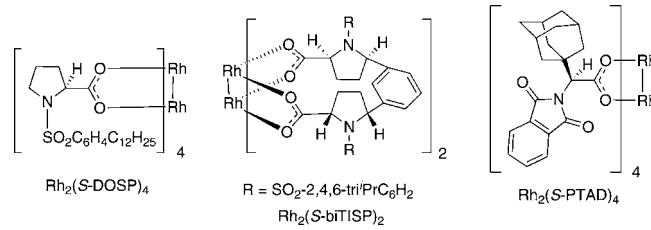
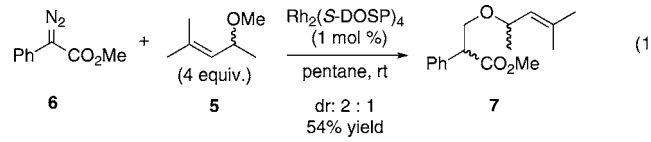


Figure 1. Structures of chiral dirhodium catalysts.

donor/acceptor carbenoids, C−H functionalization at the methyl group preferentially occurs.



To overcome the problem with competing C−H functionalization, we became intrigued with the possibility of using allyl alcohols as substrates. The missing methyl group would be expected to make the oxygen functionality more accessible for oxygen ylide formation and the favorable C−H functionalization site would no longer be present. However, allyl alcohols have not previously been used as substrates for [2,3]-sigmatropic rearrangements in carbenoid reactions because it is well established that alcohols undergo O−H insertion, by means of ylide formation followed by proton transfer.[1] To explore the feasibility of avoiding the O−H insertion process, the reaction of diazo compounds with racemic allyl alcohol **8** was examined using the established chiral catalyst Rh_2(*S*-DOSP)$_4$ (Figure 1).[2a] The reaction with ethyl diazoacetate **9** generated the O−H insertion product **10** in 67% yield without any evidence of a [2,3]-sigmatropic rearrangement product (eq 2). A more promising result was obtained with methyl diazomalonate **11**. Even though the O−H insertion product **12** still dominated, a significant amount of the [2,3]-sigmatropic rearrangement product **13** was also observed (eq 3). The outcome was quite different when the reaction was conducted with a donor/acceptor carbenoid. The reaction with phenyldiazoacetate **6** gave a 86% combined yield of products, in which the [2,3]-sigmatropic rearrangement product **14** was the major product favored over the O−H insertion product **15** by a ratio of 6:1 (eq 4). Promisingly, **14** was produced with good asymmetric induction (86% ee), even though the starting alcohol **8** was racemic.[15,16]

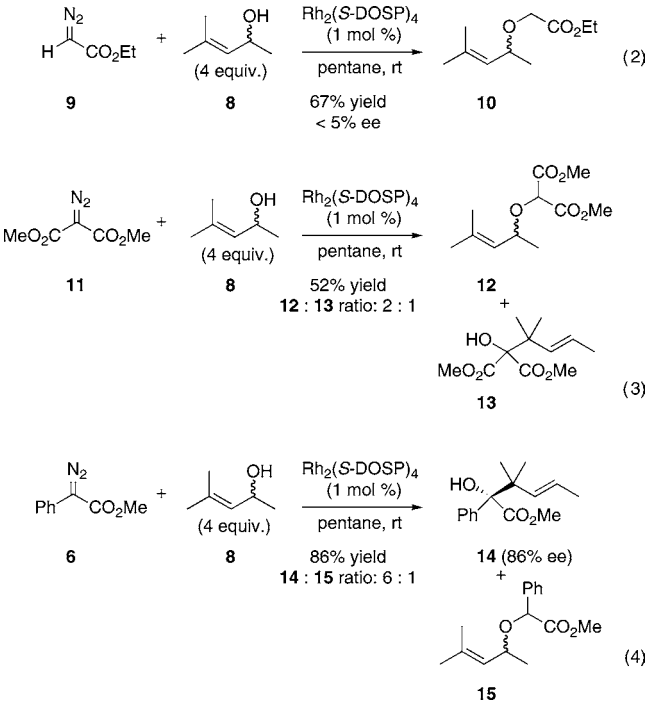
(12) Studies from the Wood group have shown that the reaction of α-diazoketones with propargylic or allylic alcohols proceeds through enol intermediates, which subsequently undergo a Claisen rearrangement. For references, see: (a) Wood, J. L.; Stoltz, B. M.; Dietrich, H.-J. *J. Am. Chem. Soc.* **1995**, *117*, 10413. (b) Wood, J. L.; Moniz, G. A.; Pflum, D. A.; Stoltz, B. M.; Holubec, A. A.; Dietrich, H.-J. *J. Am. Chem. Soc.* **1999**, *121*, 1748. (c) Wood, J. L.; Moniz, G. A. *Org. Lett.* **1999**, *1*, 371. (d) Moniz, G. A.; Wood, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 5095. (e) Drutu, I.; Krygowski, E. S.; Wood, J. L. *J. Org. Chem.* **2001**, *66*, 7025. It would be reasonable to propose that a similar enol mechanism routinely occurs in rhodium-catalyzed O−H insertions, but for simple alcohols the enol intermediates tautomerize to the isolated keto products.

(13) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6897–6907.

(14) The Rh_2(*S*-MEOX)$_4$-catalyzed reaction of cinnamyl methyl ether with ethyl diazoacetate results in ylide formation followed by a [2,3]-sigmatropic rearrangement with high asymmetric induction; see: Doyle, M. P.; Forbes, D. C.; Vasbinder, M. M.; Peterson, C. S. *J. Am. Chem. Soc.* **1998**, *120*, 7653.

(15) For reviews on the [2,3]-sigmatropic rearrangement of ylides, see: (a) Hodgson, D. M.; Pierard, F. Y. T. M.; Stupple, P. A. *Chem. Soc. Rev.* **2001**, *30*, 50. (b) Clark, J. S. in *Nitrogen, Oxygen and Sulfur Ylide Chemistry: A Practical Approach*; Oxford University Press: Oxford, 2002.

(16) For general references on the [2,3]-sigmatropic rearrangement of oxonium ylides formed by catalytic diazo decomposition, see: (a) Pirrung, M. C.; Werner, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 6060. (b) Roskamp, E. J.; Johnson, C. R. *J. Am. Chem. Soc.* **1986**, *108*, 6062. (c) Marmsater, F. P.; West, F. G. *J. Am. Chem. Soc.* **2001**, *123*, 5144. (d) Hodgson, D. M.; Petroliagi, M. *Tetrahedron: Asymmetry* **2001**, *12*, 877. (e) Marmsater, F. P.; Vanecko, J. A.; West, F. G. *Org. Lett.* **2004**, *6*, 1657. (f) Clark, J. S.; Fessard, T. C.; Wilson, C. *Org. Lett.* **2004**, *6*, 1773. (g) Quinn, K. J.; Biddick, N. A.; DeChristopher, B. A. *Tetrahedron Lett.* **2006**, *47*, 7281. (h) Clark, J. S.; Walls, S. B.; Wilson, C.; East, S. P.; Drysdale, M. J. *Eur. J. Org. Chem.* **2006**, 323. (I) Clark, J. S.; Fessard, T. C.; Whitlock, G. A. *Tetrahedron* **2006**, *62*, 73. (j) Clark, J. S.; Guerot, C.; Wilson, C.; Blake, A. *Chem. Commun.* **2007**, 4134. (k) Hodgson, D. M.; Angrish, D.; Erickson, S.; Kloesges, J.; Lee, C. H. *Org. Lett.* **2008**, *10*, 5553. (l) Shimada, N.; Nakamura, S.; Anada, M.; Shiro, M.; Hashimoto, S. *Chem. Lett.* **2009**, *38*, 488.



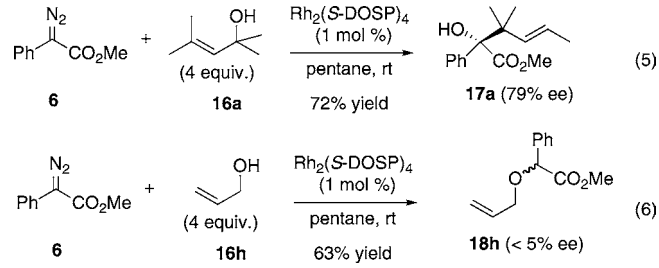
Having discovered that the ylide formed from the reaction of **6** with **8** is capable of undergoing a [2,3]-sigmatropic rearrangement, a systematic study was conducted to find the optimal conditions for this process. The effects of catalyst and solvent are summarized in Table 1. As the reaction between **6** and **8** appeared to be a very effective reaction, the optimization studies were conducted using just 2 equiv of the allyl alcohol **8**. The solvent had a significant effect on the amount of the [2,3]-sigmatropic rearrangement product **14** formed versus the O−H insertion product **15**. The reaction in pentane favored **14** over **15** by a 5:1 ratio, but in toluene the ratio was 3:1, and in dichloromethane the ratio had degraded to 1:1 (entries 1−3). The two other most prominent chiral rhodium catalysts for the reactions of aryldiazoacetates are Rh_2(*S*-PTAD)$_4$ and Rh_2(*S*-biTISP)$_2$ (Figure 1).[17,18] Neither of these catalysts were as effective as Rh_2(*S*-DOSP)$_4$ at favoring the formation of **14** over **15**, and both catalysts gave lower levels of asymmetric induction compared to Rh_2(*S*-DOSP)$_4$ (entries 4 and 5). Interestingly the common achiral dirhodium catalysts favored the formation of the O−H insertion product **15** (entries 6−9). The only exception was Du Bois' Rh_2(esp)$_2$ catalyst,[19] which gave a 2:1 preference of **14** over **15** (entry 10). From these results, it can be concluded that Rh_2(*S*-DOSP)$_4$ and nonpolar solvents are the optimal conditions for the selective formation of **14**.

Table 1. Effect of Dirhodium Catalysts and Solvent on the Ratio of **14/15**

entry	Rh(II)	solvent	**14**/**15**[b]	yield of (**14** + **15**), %[c]	ee of **14**, %[d]
1	Rh_2(*S*-DOSP)$_4$	pentane	5:1	94	84
2	Rh_2(*S*-DOSP)$_4$	toluene	3:1	75	83
3	Rh_2(*S*-DOSP)$_4$	CH_2Cl_2	1:1	65	74
4	Rh_2(*S*-biTISP)$_2$	CH_2Cl_2	1:1	69	−37
5	Rh_2(*S*-PTAD)$_4$	pentane	2:1	86	78
6	Rh_2(OAc)$_4$	pentane	1:6	82	
7	Rh_2(OOct)$_4$	pentane	1:5	94	
8	Rh_2(tfa)$_4$	pentane	1:4	92	
9	Rh_2(OPiv)$_4$	pentane	1:1	67	
10	Rh_2(esp)$_2$	pentane	2:1	49	

[a] All reactions were performed with **8** (1.0 mmol, 2 equiv) and Rh(II) (0.005 mmol, 1 mol %) in 1 mL of solvent under the addition of **6** (0.50 mmol) in 5 mL of solvent over 1 h at room temp. [b] Determined by crude ^{1}H NMR spectroscopy. [c] Isolated yield. [d] Determined by chiral HPLC.

The next series of experiments explored the effect of the allyl alcohol structure on the outcome of this chemistry. These reactions were conducted in pentane with Rh_2(*S*-DOSP)$_4$ as catalyst. The reaction of the highly substituted allyl alcohol **16a** gave the [2,3]-sigmatropic rearrangement product **17a** in 72% yield and 79% ee (eq 5). No trace of the O−H insertion product was observed. In contrast the parallel reaction of the unsubstituted allyl alcohol **16h** with **6** gave the O−H insertion product **18h** as the only identifiable product in 63% yield (eq 6). As is typical of rhodium catalyzed O−H insertions, this material was formed without any asymmetric induction. The extension of this study to a range of methyl-substituted allyl alcohols is summarized in Table 2. As long as the allyl alcohols **16** are relatively highly substituted, the [2,3]-sigmatropic rearrangement products dominate (entries 1−4), but relatively less substituted allyl alcohols **16e**−**h** favor the O−H insertion products **18e**−**h** (entries 5−8).



One of the most unexpected features of the [2,3]-sigmatropic rearrangement was the high asymmetric induction obtained, even though the starting allyl alcohol was racemic. To explore this further, reactions were conducted in which a stoichiometric amount of the alcohol **8** was used. The reaction with racemic (*R*/*S*)-**8** with **6** gave a 69% isolated yield of the [2,3]-sigmatropic rearrangement product (*S*)-**14** in 88% ee (Table 3). The formation of **14** in >50% yield indicated that both enantiomers of **8** were capable of generating (*S*)-**14**. This was confirmed by conducting the reaction with enantioenriched allyl alcohol **8**. The reaction of (*R*)-**8** (83% ee) generated (*S*)-**14** in 59% isolated yield and 94% ee while the reaction with (*S*)-**8** (84% ee) gave (*S*)-**14** in 61% isolated yield and 85% ee. All the reactions went with high conversion and the moderate isolated yields are due to the slight difficulty in the chromatographic separation of **14** from the O−H insertion side-product, formed in 10−15% yield. The control reaction of (*R*/*S*)-**8** with Rh_2(*R*-DOSP)$_4$ as catalyst, inverted the asymmetric induction and (*R*)-**14** was obtained in

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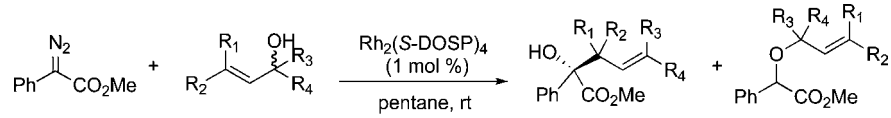
(19) (a) Zalatan, D. N.; Du Bois, J. *J. Am. Chem. Soc.* **2009**, *131*, 7558. (b) Trost, B. M.; Malhotra, S.; Olson, D. E.; Maruniak, A.; Du Bois, J. *J. Am. Chem. Soc.* **2009**, *131*, 4190. (c) Fiori, K. W.; Espino, C. G.; Brodsky, B. H.; Du Bois, J. *Tetrahedron* **2009**, *65*, 3042. (d) Olson, D. E.; Du Bois, J. *J. Am. Chem. Soc.* **2008**, *130*, 11248.

Table 2. Effect of Allyl Alcohols on the Formation of [2,3]-Sigmatropic Rearrangement Products[a]

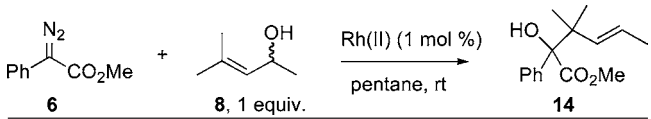


6 **16a-h,** 4 equiv. **17a-h** **18a-h**

entry	R_1	R_2	R_3	R_4	alcohol	**17**/**18**[b]	major product	yield, %[c]	ee, %[d]
1	Me	Me	Me	Me	**16a**	>20:1	**17a**	72	79
2[g]	Me	H	Me	Me	**16b**	>20:1	**17b**	79	88, 65[e,g]
3	H	H	Me	Me	**16c**	5: 1	**17c**	40	79
4	Me	H	H	Me	**16d**	4:1	**17d**	66	90, 85[f]
5	H	H	H	Me	**16e**	1:14	**18e**	61	<5
6	Me	Me	H	H	**16f**	1:16	**18f**	84	<5
7	H	Me	H	H	**16g**	1:>20	**18g**	72	<5
8	H	H	H	H	**16h**	1:>20	**18h**	63	<5

[a] All reactions were performed with **16a**−**h** (2.0 mmol, 4 equiv) and Rh_2(*S*-DOSP)$_4$ (0.005 mmol, 1 mol %) in 1 mL of pentane under the addition of **6** (0.50 mmol) in 5 mL of pentane over 1 h at room temp. [b] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture. [c] Isolated yield of major poduct. [d] Determined by chiral HPLC. [e] Ratio of 4:1 diastereomers. [f] Ratio of 1:1 diastereomers. [g] The reaction was performed at 40 °C.

Table 3. Reaction of Phenyldiazoacetate **6** with Chiral Allyl Alcohol **8**[a]



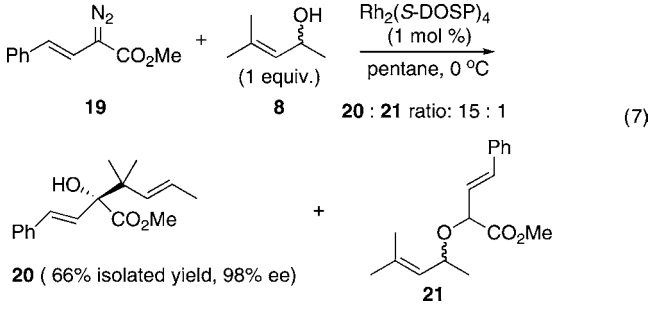
6 **8**, 1 equiv. **14**

entry	configuration of **8**	Rh(II)	configuration of **14**	yield, %[b]	ee, %[c]
1	(*R*/*S*)	Rh_2(*S*-DOSP)$_4$	(*S*)	69	88
2	(*S*) 84% ee	Rh_2(*S*-DOSP)$_4$	(*S*)	61	85
3	(*R*) 83% ee	Rh_2(*S*-DOSP)$_4$	(*S*)	59	94
4	(*R*/*S*)	Rh_2(*R*-DOSP)$_4$	(*R*)	74	87

[a] All reactions were performed with chiral allyl alcohol **8** (0.5 mmol, 1 equiv) and Rh(II) (0.005 mmol, 1 mol %) in 1 mL of pentane under the addition of **6** (0.5 mmol) in 5 mL of pentane over 1 h at room temp. [b] Isolated yield. [c] Determined by chiral HPLC.

74% yield with 87% ee. These studies indicate that the asymmetric induction is dominated by the influence of the chiral catalyst and both enantiomers of a racemic alcohol can lead to the preferential formation of the same enantiomer of the product.

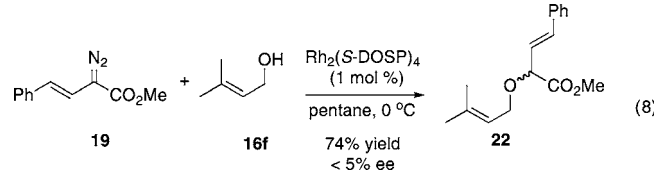
Having established the [2,3]-sigmatropic rearrangement of allyl alcohols with phenyldiazoacetate **6**, the studies were then broadened to include another type of donor/acceptor carbenoid. Vinyldiazoacetates are highly effective donor/acceptor carbenoid precursors, and on testing a typical system, the styryldiazoacetate **19**, it quickly became apparent that this system was even better than **6** (eq 7). The Rh_2(*S*-DOSP)$_4$ catalyzed reaction could be efficiently conducted with **19** using a single equivalent of the racemic alcohol **8**. The [2,3]-sigmatropic rearrangement product **20** was favored over the O−H insertion product **21** by a 15:1 ratio and **20** was formed with very high asymmetric induction (98% ee).



19 **8** **20** : **21** ratio: 15 : 1 (7)

20 (66% isolated yield, 98% ee) **21**

A relatively highly substituted allyl alcohol is still a requirement for the [2,3]-sigmatropic rearrangement to occur. For example, simply changing the substrate to allyl alcohol **16f**, caused a total change in the reaction, and O−H insertion product **22** was formed in 74% isolated yield (eq 8). Once again, the enantioselectivity for the O−H insertion is negligible (<5% ee)



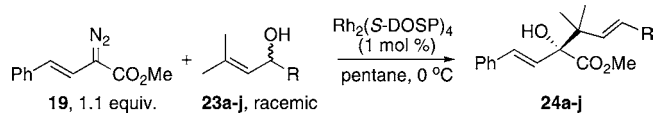
19 **16f** 74% yield, < 5% ee **22** (8)

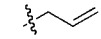
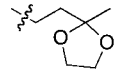
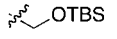
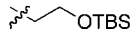
A variety of different racemic secondary allylic alcohols **23a**−**i** was reacted with styryldiazoacetate **19** and gave [2,3]-sigmatropic rearrangement products **24a**−**i** with excellent enantioselectivity (92−98% ee) (Table 4). A range of alkyl groups such as *iso*-propyl, *iso*-butyl, *tert*-butyl, and *n*-hexyl can be tolerated on the allyl alcohol. Other more functionalized groups such as ketal, TBS-protected alcohols, and trimethylsilyl are also compatible with this reaction. In all the cases, the [2,3]-sigmatropic rearrangement products dominated over the O−H insertion products by a ratio of 10:1 to >20:1. Even an allyl alcohol with an unencumbered terminal double bond (**23e**) is a suitable substrate, generating the [2,3]-sigmatropic rearrangement products **24e** in 69% yield with 95% ee.[20] A selective O−H insertion versus cyclopropanation has been observed previously with α-diazocarbonyl compounds.[21] The absolute configuration of **24c** was determined to be (*R*) by X-ray crystallography (see Supporting Information[22]). The drawn absolute configuration of the other products is the tentatively assigned stereochemistry, assuming that a similar mode of asymmetric induction occurs for all the substrates.

Excellent chemo- and enantioselectivities were also observed in the reactions of the tertiary allyl alcohols **16a** and **16c** (Table 5). The reaction with alcohol **16c** illustrates the enhanced selectivity of styryldiazoacetate **19** compared to phenyldiazoacetate **6**. The reaction of **19** with **16c** showed no evidence of

(20) When 1 equiv of allyl alcohol **24e** was used, the isolated yield of product **25e** decreased to 32% but the enantioselectivity increased to 97% ee.
(21) Shi, G.-Q.; Cao, Z.-Y.; Cai, W.-l. *Tetrahedron* **1995**, *5*, 5011.
(22) The X-ray crystallographic data has been deposited in the Cambridge Crystallographic Database.

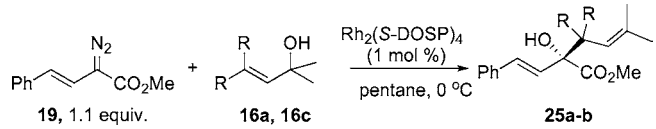
Table 4. Reaction of Styryldiazoacetate **19** with Racemic Allyl Alcohols[a]



entry	R	alcohol	[2,3]-sigmatropic rearrangement/ O-H insertion [b]	product	yield, %[c]	ee, %[d]
1	*i*-Pr	**23a**	> 20 :1	**24a**	68	97
2	*i*-Bu	**23b**	> 20 :1	**24b**	66	96
3	*t*-Bu	**23c**	> 20 :1	**24c**	71	94
4	*n*-Hex	**23d**	10 : 1	**24d**	73	96
5[e]		**23e**	10 : 1	**24e**	69	95
6		**23f**	20 : 1	**24f**	69	95
7		**23g**	10 : 1	**24g**	50	98
8		**23h**	10 : 1	**24h**	70	97
9		**23i**	> 20 :1	**24i**	69	92

[a] All reactions were performed with **23a**−**j** (0.5 mmol, 1.0 equiv) and Rh_2(*S*-DOSP)$_4$ (0.005 mmol, 1 mol %) in 1 mL of pentane under the addition of **19** (0.55 mmol, 1.1 equiv) in 5 mL of pentane over 1 h at 0 °C. [b] Determined by crude ^{1}H NMR spectroscopy. [c] Isolated yield of **24**. [d] Determined by chiral HPLC. [e] A total of 4 equiv alcohol **23e** was used.

Table 5. Reactions of Styryldiazoacetate **19** with Tertiary Allyl Alcohols[a]



entry	R	alcohol	[2,3]-sigmatropic rearrangement/O−H insertion[b]	product	yield, %[c]	ee, %[d]
1	Me	**16a**	>20:1	**25a**	62	93
2	H	**16c**	>20:1	**25b**	45	96

[a] All reactions were performed with **16a** and **16c** (0.5 mmol, 1.0 equiv) and Rh_2(*S*-DOSP)$_4$ (0.005 mmol, 1 mol %) in 1 mL of pentane under the addition of **19** (0.55 mmol, 1.1 equiv) in 5 mL of pentane over 1 h at 0 °C. [b] Determined by ^{1}H NMR of the crude reaction mixture. [c] Isolated yield of 25. [d] Determined by chiral HPLC.

an O−H insertion product, while the reaction of **6** with **16c** generated only a 5:1 ratio of the [2,3]-sigmatropic rearrangement versus O−H insertion (Table 3).

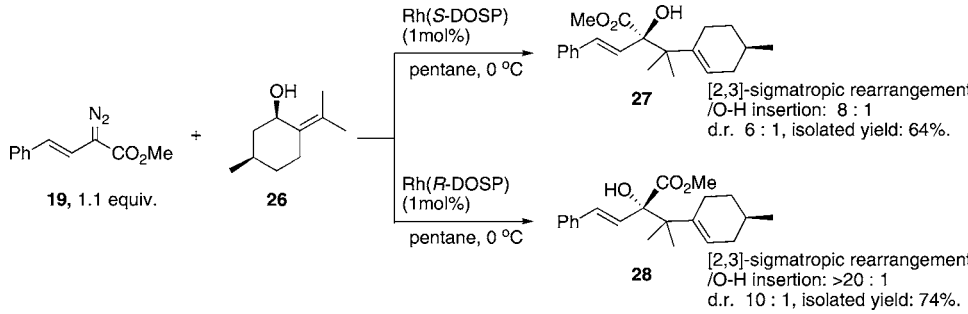
To showcase the synthetic potential of the ylide formation/[2,3]-sigmatropic rearrangement, the effect of the chiral catalyst was examined on the reaction of styryldiazoacetate **19** with the commercially available monoterpene, *cis*-(1*R*,5*R*)-(−)-pulegol **26**.[23] When Rh_2(*S*-DOSP)$_4$ was used as catalyst, the reaction gave a 6:1 diastereomeric mixture of [2,3]-sigmatropic rearrangement products as the major products, from which the major diastereomer **27** was selectively recrystallized from hexanes. Both its relative and absolute configuration was determined by X-ray crystallography (see Supporting Information[22]). The observed (*R*) configuration at the tertiary alcohol carbon in **27** is consistent with the (*R*) configuration determined for **24c**, supporting the assumption that a similar mode of asymmetric induction occurs for all the substrates. The reaction of **19** and **26** with Rh_2(*R*-DOSP)$_4$ as catalyst gave a 10:1 diastereomeric mixture of [2,3]-sigmatropic rearrangement products, without any evidence of O−H insertion. The major diastereomer formed in this case was **28**, in which the tertiary alcohol carbon has the (*S*) configuration. This study illustrates that the chirailty of the catalyst is the dominant influence of the asymmetric induction in this chemistry.

Conclusion

A novel oxonium ylide/[2,3]-sigmatropic rearrangement reaction of racemic allyl alcohols with methyl phenyldiazoacetate or methyl styryldiazoacetate was discovered. This process competes favorably with the more conventional O−H insertion chemistry when donor/acceptor carbenoids and highly substituted allyl alcohols are used as substrates. When the reactions are catalyzed by Rh_2(*S*-DOSP)$_4$, tertiary α-hydroxycarboxylate derivatives with two adjacent quaternary centers are produced with high enantioselectivity. The reaction is presumed to occur via a rhodium-associated oxonium ylide intermediate, which undergoes the [2,3]-sigmatropic rearrangement with effective transfer of chirality. In systems capable of double stereodifferentiation, the asymmetric induction by the catalyst dominates over the chirality of the substrate. These studies demonstrate

(23) Dams, I.; Bialonska, A.; Ciunik, Z.; Wawrzenczyk, C. *Eur. J. Org. Chem.* **2004**, 2662.

Scheme 2. Reaction of Styryldiazoacetate **19** with *cis*-(1*R*,5*R*)-(−)-Pulegol **26**



that the intermolecular ylide chemistry of rhodium carbenoids is capable of highly enantioselective reactions.

Experimental Section

Representative Example. A solution of Rh_2(*S*-DOSP)$_4$ (10 mg, 0.005 mmol, 1 mol %) and allyl alcohol **23a** (64 mg, 0.5 mmol) in 1 mL of degassed pentane was cooled to 0 °C with ice bath under argon. Styryldiazoacetate **19** (113 mg, 0.55 mmol, 1.1 equiv) in 5 mL of degassed pentane was added by syringe pump over 1 h. The syringe was rinsed with another 1 mL of degassed pentane and added to the reaction mixture. After addition, the solution was stirred for 30 min at 0 °C, then concentrated under vacuum. The crude material was purified by flash chromatography on silica gel eluting with pentane/diethyl ether (20:1) to give compound **24a** as a clear oil (0.103 g, 68% yield). $[\alpha]^{20}_D$ −26.3° (*c* 1.0, $CHCl_3$). R_f, 0.33 (pentane/diethyl ether 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (2H, d, J = 7.2 Hz), 7.33 (2H, t, J = 7.2 Hz), 7.27−7.23 (1H, m), 6.84 (1H, d, J = 16.0 Hz), 6.50 (1H, d, J = 16.0 Hz), 5.55 (1H, dd, J = 16.0, 1.2 Hz), 5.40 (1H, dd, J = 16.0, 9.2 Hz), 3.80 (3H, s), 3.45 (1H, s), 2.33−2.28 (1H, m), 1.15 (3H, s), 1.07 (3H, s), 1.00 (3H, d, J = 6.8 Hz), 0.99 (3H, d, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2 (C), 137.0 (C), 136.9 (CH), 132.5 (CH), 130.9 (CH), 128.7 (CH), 127.8 (CH), 127.4 (CH), 126.8 (CH), 81.9 (C), 52.9 (CH_3), 44.1 (C), 31.6 (CH), 23.0 (CH_3), 22.9 (CH_3). IR (neat): 3511, 1722, 1237, 1135, 974, 755, 740, 692 cm^{-1}. HRMS (+APCI) Calcd for $C_{19}H_{25}O_2$ ([M−OH]$^+$): 285.1849. Found: 285.1850. Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.25; H, 8.73. HPLC analysis: 97% ee, CHIRALCEL OD-H, 0.3% isopropanol/hexanes, 1.0 mL/min. UV: 254 nm. t_R: 14.7 min (major), 16.1 min (minor).

Acknowledgment. Support of this work by the National Science Foundation (CHE-07502730) is gratefully acknowledged. We thank Ken Hardcastle for the X-ray crystallographic structural determination.

Supporting Information Available: Full experimental and X-ray data for **24c** and **27**. This material is available free of charge via the Internet at http://pubs.acs.org.

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