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ENANTIOSELECTIVE SYNTHESIS OF VINYLCYCLOPROPANES BY RHODIUM(II) CATALYZED DECOMPOSITION OF VINYLDIAZOMETHANES IN THE PRESENCE OF ALKENES

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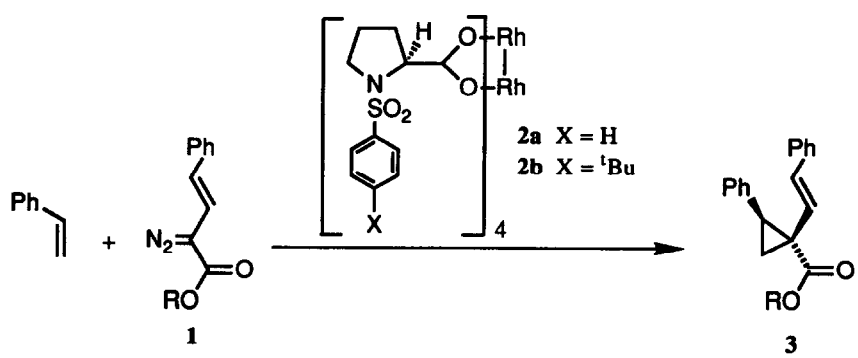
Summary: Rhodium(II) N-(arenesulfonyl)prolinate catalyzed decomposition of vinyldiazomethanes in the presence of alkenes resulted in highly diastereoselective and enantioselective cyclopropanations.

A number of very effective chiral catalysts have been developed in recent years for the asymmetric cyclopropanation of alkenes by diazoacetates.[1,2] One of the drawbacks with the use of diazoacetates, however, is that a mixture of cis and trans cyclopropanes are formed unless very bulky derivatives of diazoacetate are used.[3] Our observations that the metal catalyzed decomposition of vinyldiazomethanes results in highly diastereoselective cyclopropanations[4] has prompted us to extend this chemistry into enantioselective transformations. We have reported that vinyldiazomethanes containing α-hydroxyesters as chiral auxiliaries are very effective in asymmetric cyclopropanations.[5] In this communication, we present our results on enantioselective cyclopropanations with vinyldiazomethanes using a chiral catalyst as illustrated in Scheme 1.

Scheme 1



a: R = Me; **b**: R = Et; **c**: R = ^{i}Pr; **d**: R = ^{t}Bu

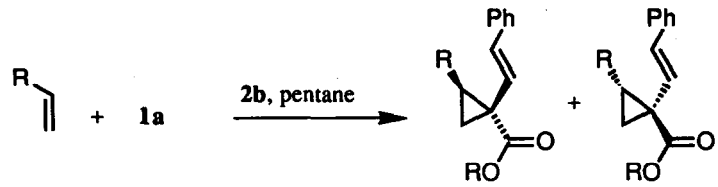
Table 1. Effect of catalyst, solvent and ester functionality on the enantioselectivity in Scheme 1.

Entry	Substrate	R	Catalyst	Solvent	%ee
1	**1a**	Me	**2a**	CH_2Cl_2	74
2	**1b**	Et	**2a**	CH_2Cl_2	68
3	**1c**	^{i}Pr	**2a**	CH_2Cl_2	43
4	**1d**	^{t}Bu	**2a**	CH_2Cl_2	9
5	**1a**	Me	**2a**	benzene	87
6	**1d**	^{t}Bu	**2a**	benzene	28
7	**1a**	Me	**2b**	CH_2Cl_2	74
8	**1a**	Me	**2b**	benzene	86
9	**1a**	Me	**2b**	pentane	90
10	**1b**	Et	**2b**	pentane	84
11	**1c**	^{i}Pr	**2b**	pentane	76
12	**1d**	^{t}Bu	**2b**	pentane	50

A very active catalyst is required to decompose vinyldiazomethanes to vinylcarbenoids or the vinyldiazomethanes will preferentially cyclize to 3*H*-pyrazoles. For example, Doyle's MEPY catalyst[2a-d] which has been very succesful in many asymmetric carbenoid transformations is a relatively unreactive catalyst and was ineffective at decomposition of the vinyldiazomethane **1a**.[5b] Consequently, we examined the (S)-*N*-(benzenesulfonyl)prolinate catalyst **2a** developed by McKervey[2e,f] as this appears to be the best rhodium carboxylate based catalyst that has been developed so far for asymmetric cyclopropanations. Decomposition of the methyl ester **1a** by **2a** in the presence of styrene proceeded very smoothly to generate the *E* cyclopropane **3a** in good yield. The NMR of the crude reaction mixture after removal of styrene showed no indication for the formation of the *Z* isomer of **3a**. The degree of asymmetric induction was readily determined to be 74% ee by NMR analysis using the chiral shift reagent $Pr(hfc)_3$, and the absolute configuration of the major enantiomer was shown to be (1S,2S) by comparing the optical rotation (-117.4 ° ($CHCl_3$, c 1.1)) with that of material of known absolute configuration (+157.1 ° ($CHCl_3$, c 1.1)).[5]

Attempts were then made to optimize the asymmetric induction by varying the vinyldiazomethane and the solvent and the results are summarized in Table 1. As can be seen in entries 1-4, increasing the size of the ester group from Me, Et, ^{i}Pr to ^{t}Bu (**1a-d**) had a deterimental effect on asymmetric induction, leading to a steady drop in enantioselectivity from 74% to 9% ee. The reactions with the Me and ^{t}Bu derivatives (**1a** and **1d**) were repeated in benzene as solvent and this resulted in a significant improvement in asymmetric induction to 87 and 28% ee, respectively (entries 5 and 6). In order to further explore the effect of non-polar solvents the (S)-*N*-(*tert*-butylbenzenesulfonyl)prolinate catalyst **2b** (Rh_2(S-TBSP)$_4$)was prepared as it was expected to have greater solubility in non polar solvents than **2a**. As can be seen in entries 7 and 8, the extent of asymmetric induction by Rh_2(S-TBSP)$_4$ was very similar to **2a** in either CH_2Cl_2 or benzene as solvent. However, Rh_2(S-TBSP)$_4$ was sufficiently soluble to be used in pentane and this solvent gave even higher levels of asymmetric induction. Again, as one continues through the series of Me, Et, ^{i}Pr to ^{t}Bu a steady decline in enantioselectivity was observed going from 90% to 50% ee (entries 9-12), but in each case, the asymmetric induction was higher than the values obtained using **1a** and CH_2Cl_2 as solvent (entries 1-4).

Table 2. Cyclopropanation of alkenes on Rh_2(S-TBSP)$_4$-catalyzed decomposition of **1a** in pentane.

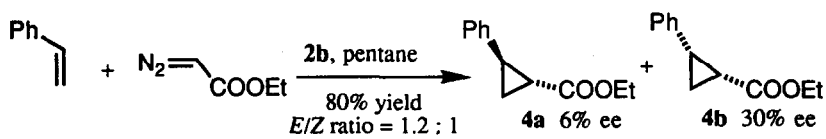


Entry	Alkene	ee, %	Yield, %
1	$PhCH=CH_2$	90	63
2	$pClC_6H_4CH=CH_2$	89	91
3	$pMeOC_6H_4CH=CH_2$	83	87
4	$AcOCH=CH_2$	76	40
5	$EtOCH=CH_2$	59	83
6	$nBuCH=CH_2$	>90	63
7	$EtCH=CH_2$	>95	65
8	$^iPrCH=CH_2$	95	58

Having developed the optimum conditions for asymmetric cyclopropanation, Rh_2(S-TBSP)$_4$ catalyzed decomposition of the methyl ester **1a** using pentane as solvent in the presence of a variety of alkenes was examined, and the results are summarized in Table 2. For entires 1-5, the crude NMR of the reaction mixtures after removal of solvent and alkene showed no evidence for the formation of Z isomers of the cyclopropanes, although E/Z ratios ranging from 16 : 1 to 8 : 1 were observed for simple alkenes (entries 6-8). The reaction is quite general and impressive levels of asymmetric induction were observed.[6] The best levels of asymmetric induction were obtained with styrenes and simple alkenes while a drop in enantioselectivity was observed when the more electron rich alkenes such as vinyl acetate and ethyl vinyl ether were used.

The vinylcarbenoid structure appears to be a critical factor for the high levels of asymmetric induction observed in these cyclopropanations. This was clearly seen in comparison of the results of **1a** with those from the asymmetric cyclopropanation of styrene by ethyl diazoaceate using Rh_2(S-TBSP)$_4$ as catalyst. As is typical of cyclopropanations with ethyl diazoacetate, a poor *E/Z* ratio (1.2 : 1) of cyclopropanes **4** was obtained. Furthermore, the enantioselectivity for the formation of either diastereomer was rather moderate (6% ee for the 1R,2R isomer **4a**, 30% ee for the 1R,2S isomer **4b**).[7] A similar positive effect on enantioselectivity by using vinyldiazomethanes instead of diazoacetates as substrates was seen by us in asymmetric cyclopropanations using (R)-pantolactone as a chiral auxiliary on the carbenoid.[5,8]

Scheme 2



In summary, McKervey's complex **2a** and Rh_2(S-TBSP)$_4$ have been found to be excellent catalysts for asymmetric cyclopropanations with vinyldiazomethanes.[9] The level of asymmetric induction is strongly enhanced by the use of non-polar solvents while increasing the size of the ester on the carbenoid results in a significant drop in enantioslelectivity. Further extension of this reaction to the asymmetric synthesis of more elaborate cyclopropanes is now under active investigation.

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6. The degree of asymmetric induction was readily determined by NMR analysis (200 MHz for entries 1-5, 500 MHz for entries 6-8) using the chiral shift reagent Pr(hfc)$_3$.

7. Enantiomeric excesses and absolute stereochemistry were determined by conversion of **4** to the (-)-menthyl esters followed by GC and NMR analysis as described by Pfaltz (Ref. 1c).

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9. The arrangements of the ligands in **2a** and **2b** is considered to result in complexes with D_2 symmetry, which are capable of effectively blocking one face of the carbenoid.

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