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ASYMMETRIC SYNTHESIS OF 1,4-CYCLOHEPTADIENES AND BICYCLO[3.2.1]OCTA-2,6-DIENES BY RHODIUM(II) N-(p-(*tert*-BUTYL)PHENYLSULFONYL)PROLINATE CATALYZED REACTIONS BETWEEN VINYLDIAZOMETHANES AND DIENES

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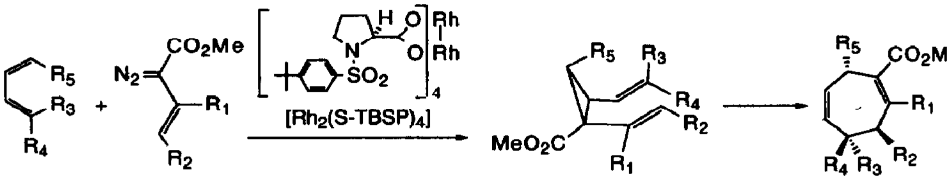
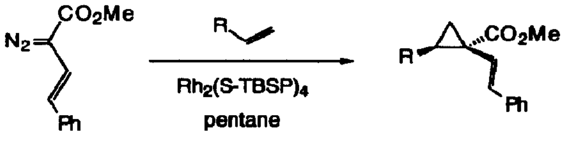
Abstract: Rhodium(II) (S)-(N-p-(*tert*butyl)phenylsulfonyl)prolinate catalyzed decomposition of vinyldiazomethanes in the presence of dienes results in a tandem cyclopropanation/Cope rearrangement, leading to a general and enantioselective approach for the construction of seven-membered carbocycles.

The rhodium(II) carboxylate catalyzed decomposition of vinyldiazomethanes in the presence of dienes is a general process for the construction of seven-membered carbocycles.[1] Excellent control of relative stereochemistry is possible because the reaction proceeds by a tandem cyclopropanation/Cope rearrangement. This paper focuses on extending this chemistry to the enantioselective construction of seven-membered carbocycles by incorporating an initial asymmetric cyclopropanation into the tandem cyclopropanation/Cope rearrangement sequence by using rhodium(II) (S)-N-(p-(*tert*-butyl)phenylsulfonyl)prolinate [Rh_2(S-TBSP)$_4$] as a chiral catalyst (eq. 1).



(1)

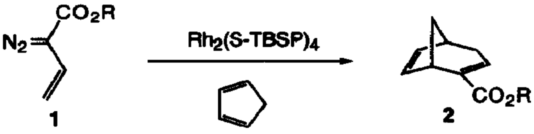
A number of excellent chiral copper[2] and rhodium(II) amide[3] catalysts have been developed for asymmetric cyclopropanations with diazoacetates. These catalysts do not appear to be useful for the decomposition of vinyldiazomethanes because they are not sufficiently active to compete with the tendency of vinyldiazomethanes to undergo electrocyclization to 3H-pyrazoles.[4] Although the kinetically more reactive rhodium(II) carboxylate catalysts are very effective at the decomposition of vinyldiazomethanes,[1] until recently chiral rhodium(II) carboxylate catalysts have had limited success in asymmetric cyclopropanations.[5,6] We have found, however, that $Rh_2(S\text{-}TBSP)_4$, a catalyst closely related to one developed by McKervey,[5a,6a] is an excellent catalyst for asymmetric cyclopropanations between 4-phenyl-2-diazobutenoates and alkenes (eq. 2).[7] The best enantioselectivities (90-95% ee) occurred when the vinylcarbenoid contained a small ester group, the alkenes were moderately electron rich and the solvent was non-polar.[8] Extension of this process to reactions between vinyldiazomethanes and dienes would lead to the enantioselective synthesis of seven-membered carbocycles.



(2)

R = alkyl, phenyl 90-95% ee

The first series of experiments focused on the reaction of 2-diazobutenoates with cyclopentadiene. $Rh_2(S\text{-}TBSP)_4$ catalyzed decomposition of the methyl ester **1a** in the presence of cyclopentadiene using pentane as solvent gave the bicyclo[3.2.1]octadiene **2a** in 63% ee (eq. 3).[9] The enantioselectivity of this process was determined by GC on a Chiraldex β-PH cyclodextrin column and confirmed by NMR using tris[3-(heptafluoropropylhydroxymethylene)-(-)-camphorato praseodymium(III) as a chiral shift reagent. A similar reaction with the *tert*-butyl ester **1b** gave the bicyclo[3.2.1]octadiene **2b** in only 5% ee. This dramatic drop in enantioselectivity parallels the results that were observed in the cyclopropanation of styrene.[7] The detrimental effect of a bulky ester group in this system is in contrast to the trend that is seen in chiral copper and rhodium amide catalyzed decomposition of diazoacetates where bulky esters strongly enhance asymmetric induction.[2,3]

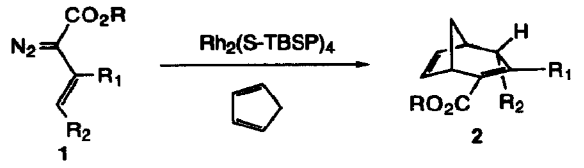


(3)

a: R = Me 63% ee; b: R = ^{t}Bu 5% ee

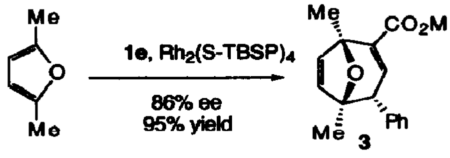
The studies were then focused on the effect of structural variations within the vinylcarbenoid upon the level of asymmetric induction. The results of these studies are summarized in Table 1. The exclusive formation of the *endo* relative stereochemistry for the bicyclo[3.2.1]octadienes **2c-g,j** was readily established on the basis of the coupling constants at the bridgehead proton and is fully consistent with the boat transition state required for the Cope rearrangement of divinylcyclopropanes.[10] Several modifications to the vinyldiazomethanes at either of the vinyl positions were tolerated as seen for **1c-1h** (64-91% ee). Introduction of vinyl, phenyl or methyl functionality at the vinyl terminus (**1c-e**) resulted in significantly higher levels of asymmetric induction. However, the presence of a siloxy group adjacent to the carbenoid (**1i**, 42% ee) or a strongly electron withdrawing group at the vinyl terminus (**1j**, 10% ee) resulted in a large decrease in asymmetric induction.

Table 1: $Rh_2(S\text{-}TBSP)_4$ catalyzed decomposition of vinyldiazomethanes **1** in the presence of cyclopentadiene

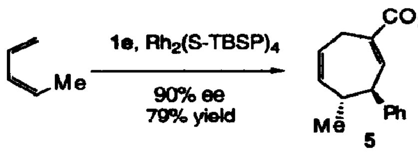


compound	R	R_1	R_2	ee, %	yield, %
a	Me	H	H	63	76
b	tBu	H	H	5	50
c	Me	H	$CH=CH_2$	91	64
d	Me	H	Me	83	75
e	Me	H	Ph	75	92
f	Me	cyclo$(CH_2)_3$		68	68
g	Me	cyclo$(CH_2)_4$		69	70
h	Me	Me	H	64	66
i	Me	OTBDMS	H	42	66
j	Et	H	CO_2Et	10	98

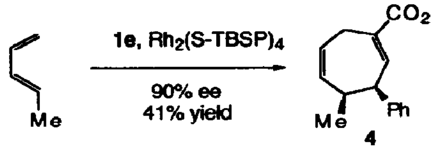
The wider application of $Rh_2(S\text{-}TBSP)_4$ for the enantioselective formation of seven-membered carbocycles has been established through the reaction of the vinyldiazomethane **1e** with a variety of dienes (eqs. 4-7). With 2,5-dimethylfuran, reaction of **1e** gave **3** in 86% ee.[9] Such high levels of asymmetric induction were repeated with acyclic dienes. For example, reaction of **1e** with *trans*-piperylene resulted in the formation of the *cis*-cycloheptadiene **4** in 90% ee. In addition to the absolute stereocontrol, this reaction proceeds with excellent control of regiochemistry and relative stereochemistry. Cyclopropanation occurs exclusively at the least substituted double bond and the relative stereochemistry is fixed by the demands of the boat transition state for the Cope rearrangement. The enantioselectivity of this reaction was repeated for the corresponding conversion of *cis*-piperylene to the *trans*-cycloheptadiene **5**, and the reaction of **1e** with *trans*-1-(*tert*-butyldimethylsiloxy)butadiene led to the formation of *cis*-cycloheptadiene **6** in 85% ee.



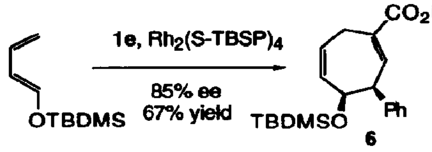
(4)



(6)



(5)



(7)

In summary, $Rh_2(S\text{-}TBSP)_4$ catalyzed decomposition of vinyldiazomethanes in the presence of dienes results in a general and enantioselective entry to seven-membered carbocycles. The utility of this process is underscored by the high enantioselectivity observed in these studies combined with the predictable control of regiochemistry and diastereoselectivity of the tandem cyclopropanation/Cope rearrangement.

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9. The depicted absolute stereochemistries of the products are based on the assumption that the face selectivity of the carbenoid in these reactions is the same as was observed in the $Rh_2(S\text{-}TBSP)_4$ catalyzed reaction of **1e** with styrene described in Ref. 7. It is also assumed that the non-synchronous cyclopropanation occurs with greater initial bonding at the vinyl terminus of dienes and at the 3-position of 2,5-dimethylfuran. For discussions on the mechanism of vinylcarbenoid cyclopropanations, see Refs. 1 and 10.
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