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EFFECT OF DIAZOALKANE STRUCTURE ON THE STEREOSELECTIVITY OF RHODIUM(II) (*S*)-*N*-(ARYLSULFONYL)PROLINATE CATALYZED CYCLOPROPANATIONS

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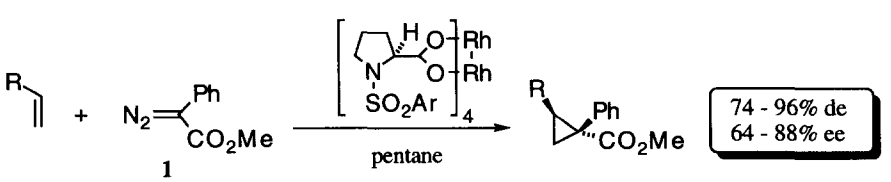
Summary: Rhodium(II) (S)-N-(arylsulfonyl)prolinate catalyzed decomposition of diazoalkanes containing a methyl ester and either a vinyl or a phenyl group in the presence of alkenes results in highly diastereoselective and enantioselective cyclopropanations. Copyright © 1996 Elsevier Science Ltd

For some time we have been interested in the development of new synthetic methodology based on the chemistry of rhodium(II)-stabilized vinylcarbenoid intermediates.[1] General methods for the stereoselective construction of three-,[2] five-[3] and seven-membered[4] rings have been achieved by means of combining vinylcarbenoid cyclopropanations with subsequent cyclopropane rearrangements. The success of the vinylcarbenoid chemistry is due to the fact that vinylcarbenoid intermediates undergo highly diastereoselective cyclopropanations.[2] Furthermore, when rhodium(II) (*S*)-*N*-(*tert*-butylphenyl)sulfonylprolinate is used as the catalyst, the reactions are also highly enantioselective.[5] The high diastereoselectivity of vinylcarbenoid cyclopropanations is in sharp contrast to the results obtained from the carbenoids derived from alkyl diazoacetates.[6] Alkyl diazoacetates have been extensively used as carbenoid precursors and highly enantioselective cyclopropanations are possible using chiral copper,[7] rhodium[8] and ruthenium[9] catalysts. In most cases, however, cyclopropanations with alkyl diazoacetates occur with low diastereoselectivity unless extremely bulky ester derivatives are used. The focus of this study was to determine what functionality on the carbenoid is needed for the occurrence of highly diastereoselective and enantioselective cyclopropanations. This led to the discovery that methyl phenyldiazoacetate (**1**) is an excellent carbenoid precursor for highly diastereoselective and enantioselective cyclopropanations as illustrated in Scheme 1.

Scheme 1

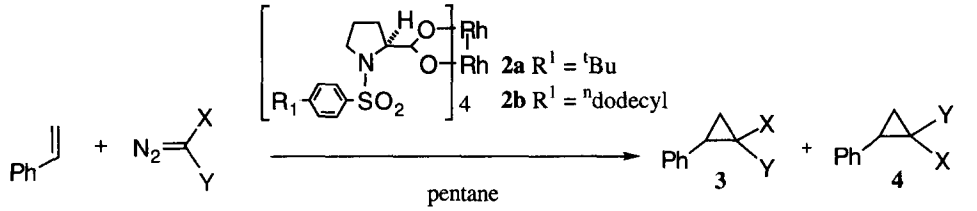


In order to probe what functionality on the carbenoid is necessary for highly stereoselective cyclopropanations catalyzed by rhodium(II) prolinates, the cyclopropanation of styrene using a series of methyl diazoacetate derivatives was examined, and the results are summarized in Table 1. All the reactions were carried out at room temperature in pentane as the use of a non-polar solvent has a very positive effect on the asymmetric induction.[5] Comparable levels of stereoselectivity were obtained with either the (*N*-(*tert*-butylphenyl)sulfonyl)-(**2a**)[5] or the more soluble (*N*-(*n*-dodecylphenyl)sulfonyl)prolinate (**2b**) catalysts (entries 1 and 2). The dramatic difference between the vinyldiazoacetate and the traditional diazoacetate systems is seen by comparing entries 1 and 3. Unlike the excellent stereoselectivity observed in entry 1, cyclopropanation with ethyl diazoacetate occurred with low diastereoselectivity and enantioselectivity (entry 3).[5] Carbenoids containing two electron withdrawing groups also resulted in cyclopropanation with low diastereoselectivity (entry 4) and enantioselectivity (<10% ee, entries 4 and 5). Cyclopropanation with methyl diazopropionate (entry 6) occurred with moderate diastereoselectivity (60% de), and the minor diastereomer was formed with moderate enantioselectivity (58% ee). In sharp contrast, cyclopropanation with methyl phenyldiazoacetate occurred with excellent stereoselectivity and the (*1R,2S*) isomer was preferentially formed in 96% de and 87% ee (entry 7). The importance of the ester functionality was clearly seen in the reactions of the unsubstituted vinyldiazomethane and the phenyldiazomethane (entries 8 and 9), which occurred with very low stereoselectivity. On the basis of these studies, it is clear that the structure of the carbenoid has a critical effect on both the diastereoselectivity and enantioselectivity of rhodium(II) prolinate catalyzed cyclopropanations. The combination of an ester and either a vinyl or an aryl functionality on the carbenoid is ideally suited for highly stereoselective cyclopropanations.

As methyl phenyldiazoacetate resulted in such a highly stereoselective cyclopropanation with styrene, the reaction was extended to a series of alkenes as shown in Table 2. High stereoselectivity was observed in most cases, with the diastereoselectivity ranging from 74-96% de and the enantioselectivity ranging from 66-88% ee. The general trends seen with phenyldiazoacetate are similar but not identical with those that have been previously reported for the vinyldiazoacetate system.[5] In the case of the vinyldiazoacetate system, the highest diastereoselectivity occurred in reactions with electron rich alkenes, while the highest enantioselectivity occurred in reactions with electron neutral alkenes. In the phenyldiazoacetate system, the highest diastereoselectivity occurs in reactions with electron rich alkenes such as the styrenes and vinyl ethers (entries 1-5), while the enantioselectivity is highest in reactions with styrenes (entries 1-3).

A key requirement for high stereoselectivity in these rhodium(II) prolinate catalyzed cyclopropanations is the presence of both acceptor (ester) and donor (vinyl or phenyl) groups on the carbenoid. The accompanying paper by Doyle and McKervey clearly demonstrates that, of the commonly available chiral catalysts, the prolinate catalyst **2a** is the best for enantioselective cyclopropanations by methyl phenyldiazoacetate. In our studies, we show that the *n*-dodecylphenylsulfonyl derivative **2b** is also an excellent catalyst and offers the advantage of being very soluble in non-polar solvents. One of the most distinctive features of vinylcarbenoid intermolecular cyclopropanations is the total lack of reactivity towards *trans*-alkenes. This suggests that the alkene approaches the carbenoid complex in a side-on approach analogous to the proposed trajectory for the attack of alkenes to metal oxo complexes.[11] The necessity of a specific alkene approach may be the key difference between the stereoselectivity of cyclopropanations by donor/acceptor substituted carbenoids and simpler carbenoids. Further studies are in progress to test this working hypothesis and to determine the critical stereocontrol elements of the

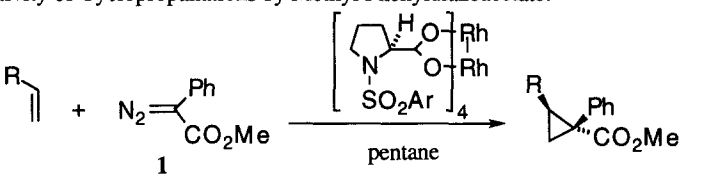
Table 1. Effect of Carbenoid Structure on Cyclopropanation Stereoselectivity.



Entry	X	Y	Catalyst	Yield, %	3 : 4 ratio	ee of 3, %	ee of 4, %
1[a]	CO_2Me	CH=CHPh	**2a**	91	**98 : 2**	**90**	-[b]
2	CO_2Me	CH=CHPh	**2b**	91	**98 : 2**	**94**	-[b]
3[a]	CO_2Me	H	**2a**	80	55 : 45	6	30
4	CO_2Me	COMe	**2a**	57	75 : 25	5	8
5	CO_2Me	CO_2Me	**2a**	63	-[c]	7[c]	-[c]
6	CO_2Me	Me	**2b**	45	80 : 20	12	58
7	CO_2Me	Ph	**2a**	90	**98 : 2**	**87**	-[b]
8	H	$CH=CH_2$	**2b**	<10	31 : 69	<5	17
9	H	Ph	**2b**	<10	35 : 65	<5	-[d]

a: Ref. 5; b: not determined; c: only one possible diastereomer; d: meso compound.

Table 2. Stereoselectivity of Cyclopropanations by Methyl Phenyldiazoacetate.



Entry	R	Catalyst	Yield, %	E/Z ratio	ee[a] of Z, %
1[a]	Ph	**2a**	90	98 : 2	87
2	*p*-(OMe)Ph	**2a**	82	98 : 2	88
3[a]	*p*-(Cl)Ph	**2a**	84	98 : 2	85
4	OEt	**2b**	88	97 : 3	66
5	OBu	**2b**	84	97 : 3	64
6	Et	**2b**	86	93 : 7	80
7	Bu	**2b**	86	93 : 7	77
8	*i*Pr	**2b**	63	87 : 13	74
9	CH_2OAc	**2b**	85	97 : 3	80

a: Enantiomeric excesses (% ee) were determined either by ^1H NMR using tris[3-(heptafluoropropyl-hydroxymethylene)-(-)-camphorato]praseodymium(III) as a chiral shift reagent, or by HPLC using a Diacel Chiralcel OJ analytical column. The absolute configurations are tentatively assigned assuming a similar asymmetric induction that was observed in the vinylcarbenoid cyclopropanations (ref. 5).

prolinate catalyst through examination of other donor/acceptor substituted carbenoids and conformationally constrained rhodium(II) prolinate catalysts.

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References and Notes

1. Davies, H. M. L. *Tetrahedron*, **1993**, *49*, 5203.
2. Davies, H. M. L.; Clark, T. J.; Church, L. A. *Tetrahedron Lett.* **1989**, *30*, 5057.
3. Davies, H. M. L.; Hu. B. *J. Org. Chem.* **1992**, *57*, 3186.
4. Davies, H. M. L.; Clark, T. J.; Smith, H. D. *J. Org. Chem.* **1991**, *56*, 3817.
5. (a) Davies, H. M. L.; Hutcheson, D. K. *Tetrahedron Lett.* **1993**, *34*, 7243. (b) Davies, H. M. L.; Peng, Z. -Q.; Houser, J. H. *Tetrahedron Lett.* **1994**, *35*, 8939.
6. Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometallics* **1984**, *3*, 53.
7. (a) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Helv. Chim. Acta* **1988**, *71*, 1553. (b) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005. (c) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 736. (d) Ito, K.; Katsuki, T. *Tetrahedron Lett.* **1993**, *34*, 2661.
8. Doyle, M. P. *Recl. Trav. Chim. Pays-Bas* **1991**, *110*, 305.
9. Nishiyama, H.; Itoh, Y.; Sugawar, Y.; Matsumoto, H.; Aoki, K.; Itoh, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1247.
10. Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K. L. *J. Am. Chem. Soc.* **1990**, *112*, 1906.
11. Jacobsen, E. N., *Catalytic Asymmetric Synthesis*, Ojima, I., Ed., VCH Publishers, 1993, pp 159-202.

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