

STERESELECTIVE CYCLOPROPANATIONS WITH VINYL CARBENOIDS

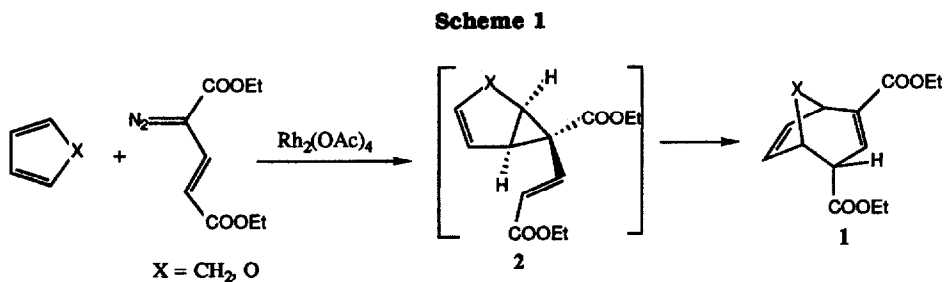
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Summary: Rhodium(III) acetate catalyzed decomposition of vinyl diazomethanes in the presence of alkenes results in cyclopropanation with a high degree of stereoselectivity.

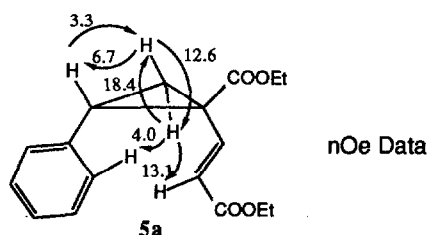
Considering that highly enantioselective cyclopropanations by keto-carbenoids have been developed¹ and ring opening of cyclopropanes can proceed in a stereodefined manner,² very valuable synthetic sequences would be possible if the original cyclopropanation was also diastereoselective. Intermolecular cyclopropanation of alkenes proceeds stereospecifically from the point of view of alkene geometry with most catalysts, but unfortunately, the stereoselectivity with respect to the arrangement of the alkene and carbenoid is generally rather moderate.³ Some notable exceptions have been the reactions with severely bulky diazoacetates.^{4,1c} Most of the mechanistic models for cyclopropanations with keto-carbenoids are based on these poorly selective reactions.^{3b} Consequently, further examination of the factors which cause this diastereoselection would be worthwhile, and in this paper we report our results on the cyclopropanation of simple alkenes with vinylcarbenoids.

We have recently reported that the reaction of vinylcarbenoids with furans and cyclopentadiene leads to [3.2.1]bicycloocta-2,6-dienes (**1**) by an apparent 3 + 4 cycloaddition, as illustrated in Scheme 1.⁵ The reaction has been shown to proceed by a two step sequence involving an initial cyclopropanation followed by a Cope rearrangement.^{5a} Considering that the reaction was carried out under rather mild conditions (40 °C), the clean formation of



bicyclic systems would suggest that the initial cyclopropanation must have been highly stereoselective producing exclusively *cis*-divinylcyclopropanes (**2**).

In order to determine the extent of this remarkable stereoselectivity, a series of reactions with simple alkenes was examined and the results are summarized in the Table. In a typical procedure, a solution of the vinyl diazomethane **4** (5 mmol) in dry dichloromethane (10 mL) was added over 10 min to a stirred mixture of rhodium(II) acetate (0.05 mmol) and the alkene **3** (25 mmol) in dry dichloromethane (25 mL), heated under reflux in an argon atmosphere. After heating for a further 10 min, the solvent was evaporated under reduced pressure. The isomeric ratio was calculated by NMR analysis of the crude reaction mixture while the yields represent isolated product purified by column chromatography on silica.⁶ The stereochemical assignment was readily determined through nOe difference analysis based on the very distinctive enhancements between the vinyl group and the cyclopropane protons as illustrated for **5a**.



In all the reactions examined, considerable preference for the isomer with a *cis* arrangement between the vinyl group and the alkene substituent was observed. This was particularly so for oxygenated alkenes and also in the reaction of styrene with the vinyl diazomethanes **4b** and **4c**. Similar though less pronounced selectivity was also observed with alkyl substituted alkenes, which would indicate that the selectivity is not primarily due to secondary orbital interactions during the cyclopropanation process.

The reactions with allyl bromide and allyl vinyl ether were complicated by the formation of side-products (**7**). These arose by capture of the carbenoid by the heteroatoms to form ylides (**8**), which then underwent a 2,3-sigmatropic rearrangement to **7**. Similar reactions with ethyl diazoacetate have been examined in detail by Doyle and co-workers,⁷ and the extent of ylide formation was found to be much greater than was observed in this study.

Scheme 2

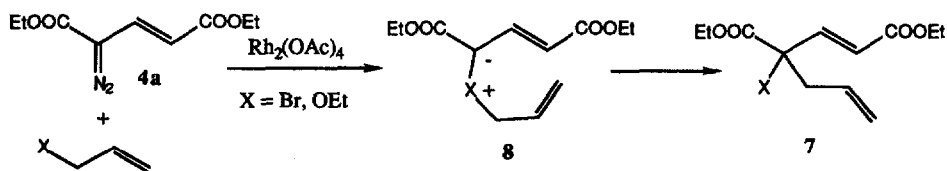
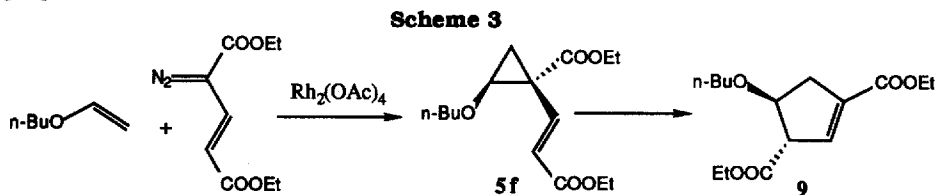


Table: Rhodium(III) acetate catalyzed decomposition of vinyl diazomethanes in the presence of alkenes.

R	4	X	Y	5,6	Yield,%	Ratio 5 : 6
Ph	a	COOEt	COOEt	a	96	8.3 : 1
Ph	b	COOMe	Ph	b	94	>20 : 1
Ph	c	COOEt	CH=CHPh	c	94	>20 : 1
4-(MeO)C ₆ H ₄	a	COOEt	COOEt	d	80	18 : 1
AcO	a	COOEt	COOEt	e	79	>20 : 1
BuO	a	COOEt	COOEt	f	(61) ^a	>20 : 1
cycloC ₆ H ₁₁	a	COOEt	COOEt	g	83	5.2 : 1
(CH ₃) ₃ C	a	COOEt	COOEt	h	72	3.5 : 1
PhCH ₂	a	COOEt	COOEt	i	68	8.1 : 1
CH ₃ (CH ₂) ₃	a	COOEt	COOEt	j	92	5.7 : 1
ClCH ₂	a	COOEt	COOEt	k	70	5.5 : 1
BrCH ₂	a	COOEt	COOEt	l	55 ^b	3.1 : 1
EtOCH ₂	a	COOEt	COOEt	m	35 ^c	12 : 1

^a Yield of **9** formed during attempted purification of **5f**. ^b **7** (X = Br) was also isolated in 11% yield. ^c **7** (X = OEt) was also isolated in 11% yield.

The stereoselective cyclopropanations reported here have potential for the synthesis of other structures through further transformation of the labile cyclopropanes. As many of the cyclopropanes have both donor and acceptor groups further reactions should occur under mild conditions.⁸ An example of this is shown for **5f**, which was unstable to chromatography and on attempted kugelrohr distillation underwent a clean rearrangement to the cyclopentene **9** in 61% overall yield. The stereochemistry of **9** was assigned based on the coupling constants for $\text{CH}^{\text{H}}\text{OBu}$ ($J = 6.3, 3.8, 3.8 \text{ Hz}$),⁹ which indicates the presence of only one *syn* proton on the adjacent carbons. The mild heating required for this transformation may be contrasted to the harsh flash vacuum pyrolysis conditions (500-600 °C) that are often employed to rearrange vinylcyclopropanes.^{10,11}



In summary, cyclopropanations with vinylcarbenoids show much greater stereoselectivity than with simple carbenoids. Extremely high selectivity is observed with styrenes. These results support the tandem cyclopropanation/Cope rearrangement mechanism proposed for the reaction of vinylcarbenoids with furan or cyclopentadiene.⁵ The much greater selectivity observed in these reactions may enable more definitive models for the cyclopropanation mechanism to be developed and we are currently pursuing this goal.

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References

1. (a) Fritschl, H.; Leutenegger, U.; Pfaltz, A. *Helv. Chim. Acta* 1988, **71**, 1553; (b) Matlin, S. A.; Lough, W. J.; Chan, L.; Abram, D. M. H.; Zhou, Z. *J. Chem. Soc., Chem. Commun.* 1984, 1038; (b) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* 1977, 2599.
2. (a) Reissig, H. -U. "The Chemistry of the Cyclopropyl Group"; Rappoport, Z., Ed.; John Wiley & Sons, Ltd., 1987; part 1, p. 375; (b) Vehre, R.; De Kimpe, N. "The Chemistry of the Cyclopropyl Group"; Rappoport, Z., Ed.; John Wiley & Sons, Ltd., 1987; part 1, p. 445; (c) Reissig, H. -U. *Topics Curr. Chem.* 1988, **144**, 73.
3. (a) Maas, G. A. *Topics Curr. Chem.* 1987, **137**, 75; (b) Doyle, M. P. *Chem. Rev.* 1986, **86**, 919.
4. Doyle, M. P.; Loh, K. -L.; DeVries, K. M.; Chinn, M. S. *Tetrahedron Lett.* 1987, **28**, 833.
5. (a) Davies, H. M. L.; Smith, H. D.; Korkor, O. *Tetrahedron Lett.* 1987, **28**, 1853; (b) Davies, H. M. L.; D. Clarke, D. M.; Smith, T. K. *Tetrahedron Lett.*, 1985, **26**, 5659 (c) Davies, H. M. L.; Clarke, D. M.; Allgood, D. B.; Eiband, G. R. *Tetrahedron* 1987, **17**, 1709.
6. All new compounds were fully characterized by proton and carbon NMR, IR, molecular analysis and/or high resolution MS.
7. (a) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* 1981, **46**, 5094; (b) Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; van Leusen, D. *J. Org. Chem.* 1984, **49**, 1917. (c) Doyle, M. P.; Bagheri, V.; Harn, N. K. *Tetrahedron Lett.* 1988, **29**, 5119.
8. Reissig, H. -U. *Top. Curr. Chem.* 1988, **144**, 73.
9. For cyclopentenes, $J_{(syn)}$ is usually larger than $J_{(anti)}$ although exceptions are known. For a discussion on this, see (a) Hunter, G.; Miller, J. A.; Moore, M.; Ullah, G. M. *Org. Mag. Res.* 1983, **21**, 275; (b) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* 1981, **103**, 5969; (c) Burgess, K.; *J. Org. Chem.* 1987, **52**, 2046; (d) Partridge, J. J.; Chadha, N. K.; Uskokovic, M. R. *J. Am. Chem. Soc.* 1973, **95**, 532.
10. (a) Hudlicky, T; Kutchan, T. M.; Naqui, S. M. *Org. React.* 1985, **33**, 247; (b) Goldschmidt, Z.; Crammer, B. *Chem. Soc. Rev.* 1988, **17**, 229.
11. Very mild conditions for rearrangement of vinylcyclopropanes have been reported: Danheiser, R. L.; Bronson, J. J.; Okano, K.; *J. Am. Chem. Soc.* 1985, **107**, 4579.

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