

EFFECT OF CARBENOID STRUCTURE ON THE REACTIVITY OF RHODIUM-STABILIZED CARBENOIDS

Huw M. L. Davies,* L. Mark Hodges, Julius J. Matasi, Tore Hansen and Douglas G. Stafford

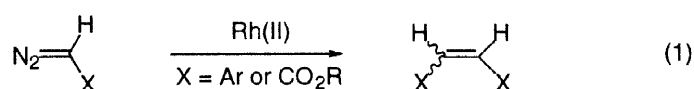
Department of Chemistry, State University of New York at Buffalo,

Buffalo, New York 14260-3000

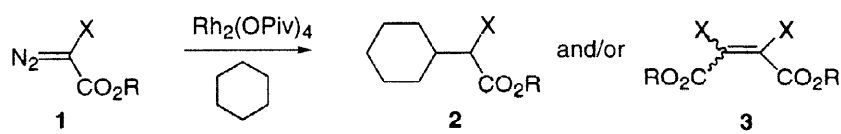
Received 3 March 1998; revised 13 April 1998; accepted 14 April 1998

Abstract: The outcome of rhodium(II) pivalate catalyzed decomposition of diazoacetates in the presence of cyclohexane is highly dependent on carbenoid structure. Carbenoids derived from phenyldiazoacetates or diazoketoesters undergo high yielding intermolecular C-H insertions while other carbenoid systems undergo rearrangements, dimerization or trimerization. © 1998 Elsevier Science Ltd. All rights reserved.

In recent years, considerable interest has been shown in the chemistry of rhodium-stabilized intermediates derived from vinyl diazoacetates¹ and phenyldiazoacetates.² A striking feature of the chemistry of these systems is the apparent lack of side products derived from carbene dimerization, although such dimerization is common for many carbenoid systems (eq 1).³ Consequently, the reactions of vinyl diazoacetates and phenyldiazoacetates can be used to achieve efficient cyclopropanation, O-H, N-H and Si-H insertion reactions^{1,2} without any need to use elaborate diazo addition conditions to avoid dimer formation.⁴ Recently, we have exploited this feature of vinyl- and phenyldiazoacetate chemistry to carry out high yielding asymmetric intermolecular C-H insertions.⁵ These results were counter to the general opinion that intermolecular C-H insertions were of limited synthetic utility.^{6,7} In this paper we describe what structural features of the carbenoid will enable efficient intermolecular insertions to occur and report on some unprecedented dimerizations and trimerizations that can occur with certain vinylcarbenoids.



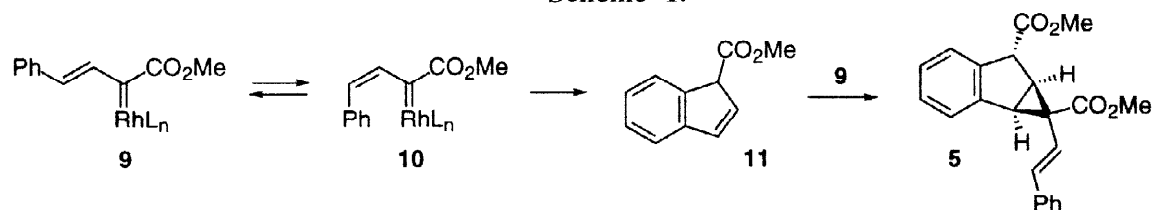
In order to directly compare the reactivity pathways of various carbenoid systems, each diazoacetate (**1a-h**) was examined under standard reaction conditions. A solution of the diazo compound (0.4 M in cyclohexane) was added dropwise over 5 min to a stirred solution of rhodium(II) pivalate (2 mol%) in an equal volume of cyclohexane, heated under reflux under an inert atmosphere. The diazo compounds **1a-c** all resulted in the formation of significant amounts of C-H insertion products **2** (Table 1). In the case of ethyl diazoacetate (**1d**), carbene dimerization predominates to give either fumarates or maleates (**3**). No dimerization products are formed in the reaction of the vinyl diazoacetate **1a**, phenyldiazoacetate **1b**, or the diazoketoester **1c**.

Table 1. Decomposition of **1a-d** with by Rh₂(OPiv)₄ in Cyclohexane


Entry	Substrate	X	R	2, Yield, %	3, yield %
1	1a	CH=CHCO ₂ Et	Et	67	0
2	1b	Ph	Me	94	0
3	1c	COMe	Me	65	0
4	1d	H	Et	10	67

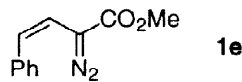
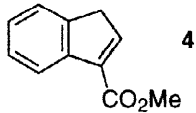
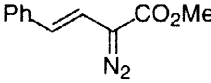
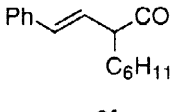
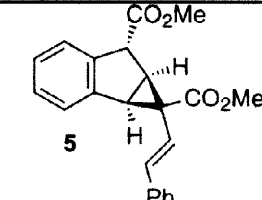
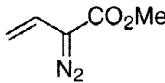
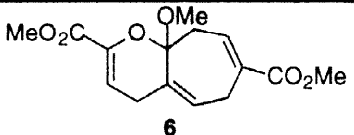
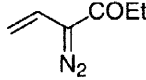
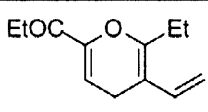
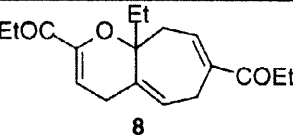
Extension of the reaction to vinyl diazoacetates **1e-h** led to some unprecedented carbenoid transformations (Table 2). Even though *cis*-vinyl diazomethanes have been reported to be excellent substrates for intermolecular Si-H insertions,⁵ the reaction of **1e** in cyclohexane solution led to the exclusive formation of indene **4**, presumably through an intramolecular reaction of the carbenoid with the proximal aromatic ring, followed by double bond migration. The reaction of the corresponding *trans*-isomer **1f** gave a mixture of the C-H insertion product **2f** (33% yield) and the cyclopropylindene derivative **5** in 22% yield. The most dramatic transformation was seen with the unsubstituted vinyl diazoacetate **1g** which results in the formation of the tetrahydrocyclohepta[b]pyran ring system (**6**)⁸ in 61% yield. The analogous reaction of the ketone derivative **1h** resulted in the formation of two compounds, the trimer **8** analogous to **6** as well as the dimer **7**.

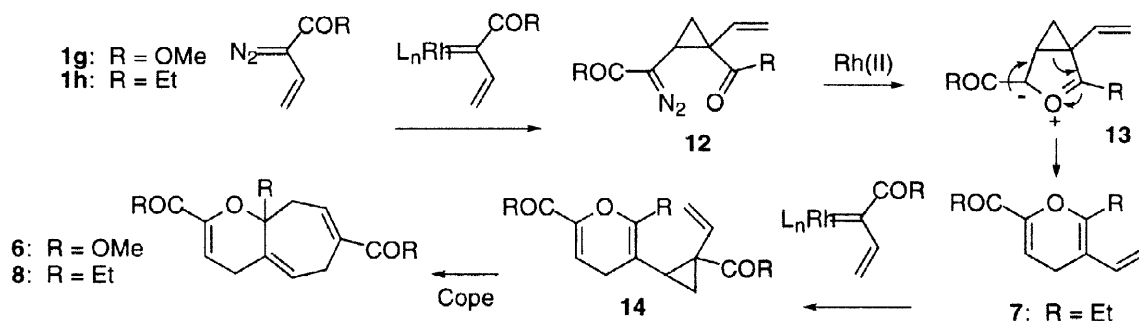
A plausible mechanism for the formation of the cyclopropanated indene derivative **5** is shown in Scheme 1. Rhodium-catalyzed decomposition of phenylvinyl diazoacetate **1f** results in the formation of the *trans*-carbenoid **9**. Unless the carbenoid is trapped quickly, isomerization can occur to give the corresponding *cis*-carbenoid **10**, which undergoes a facile intramolecular C-H insertion with the phenyl ring to give indene **11**.⁹ Cyclopropanation of **11** by the carbenoid **9** subsequently gives **5**.

Scheme 1.

A reasonable mechanism for the formation of the trimeric products is shown in Scheme 2. As the vinyl diazoacetates that lead to the trimers have mono-substituted vinyl groups, a reasonable first step is cyclopropanation of a vinyl diazoacetate by the vinylcarbenoid to give **12**. It is well established that vinylcarbenoids will not cyclopropanate *trans*-alkenes, which explains why **1a** and **1f** do not undergo this type of reaction. Decomposition of the diazocyclopropane **12** would lead to an oxonium intermediate (**13**),¹⁰ which would subsequently ring expand to give vinyl dihydropyran dimer. In the case of the ethyl ketone-substituted vinyl diazoacetate **1h**, this dimeric product (**7**) was isolable. Cyclopropanation of the dimer would then lead to the divinylcyclopropane **14** which would be expected to undergo a Cope rearrangement to give the trimer.

Table 2. Formation of Polycyclic Products from the Decomposition of Vinyl diazomethanes **1e-h**.

Substrate	Product(s)	Yield, %
		86
	 + 	2f (33) 5 (22)
		61
	 + 	7 (29) 8 (35)

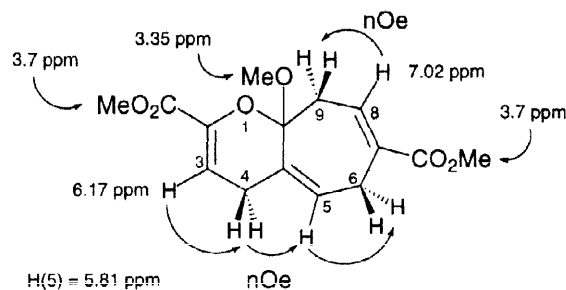
Scheme 2.

On the basis of these studies, it can be concluded that the structure of the carbenoid has a major effect on the products formed. A carbenoid with a single substituent is prone to dimerize and form alkenes, but such dimerizations were not observed by the disubstituted carbenoids that were studied here. The most spectacular reaction for the vinylcarbenoids was the formation of oxabicyclic and oxatricyclic products from vinylcarbenoids with a mono-substituted vinyl group (**1g** and **1h**). A second interesting feature is that even though vinylcarbenoid transformations generally occur with retention of vinyl group geometry,¹ the formation of **5** from **1f** indicates that equilibration of vinylcarbenoid geometry can occur. As it has been established that carbenoids containing both donor and acceptor groups are required for high asymmetric induction in the asymmetric intermolecular C-H insertions,⁵ it would seem that the phenyldiazoacetates are the optimum carbenoid precursors for this chemistry.

Acknowledgment: Financial support of this work by the National Science Foundation (CHE 9726124) and the National Institute on Drug Abuse (DA-06301, DA-06634). LMH thanks the National Institute of Drug Abuse (DA-05732) for a research fellowship.

References and Notes

- (1) For representative examples of vinylcarbenoid transformations, see: (a) Davies, H. M. L. *Aldrichimica Acta* **1997**, *30*, 107. (b) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6897. (c) Bulugahapitiya, P.; Landais, Y.; Parra-Rapado, L.; Planchenault, D.; Weber, V. *J. Org. Chem.* **1997**, *62*, 1630. (d) Davies, H. M. L.; Hansen, T.; Rutberg, J.; Bruzinski, P. R. *Tetrahedron Lett.* **1997**, *38*, 1741.
- (2) For representative examples of phenylcarbenoid transformations, see: (a) Davies, H. M. L.; Bruzinski, P. R.; Fall, M. J. *Tetrahedron Lett.* **1996**, *37*, 4133. (b) Doyle, M. P.; Zhou, Q. -L.; Charnsangavej, C.; Longoria, M. A.; McKerver, M. A.; Garcia, C. F. *Tetrahedron Lett.* **1996**, *37*, 4129. (c) Buck, R. T.; Doyle, M. P.; Drysdale, M. J.; Ferris, L.; Forbes, D. C.; Haigh, D.; Moody, C. J.; Pearson, N. D.; Zhou, Q. -L. *Tetrahedron Lett.* **1996**, *37*, 7631. (d) Paulini, K.; Reissig, H. -U. *J. Prakt. Chem.* **1995**, *337*, 55. Aller, E.; Cox, G. G.; Miller, D. J.; Moody, C. J. *Tetrahedron Lett.* **1994**, *35*, 5949.
- (3) (a) Wulfman, D. S.; Pearce, B. W.; McDaniel Jr., R. S. *Tetrahedron* **1976**, *32*, 1251. (b) Kulkowit, S.; McKerver, M. A. *J. Chem. Soc., Chem. Commun.* **1983**, 1069.
- (4) Doyle, M. P.; van Leusen, D.; Tamblyn, W. H. *Synthesis* **1981**, 787.
- (5) Davies, H. M. L.; Hansen, T. *J. Am. Chem. Soc.* **1997**, *119*, 9075.
- (6) For earlier examples of intermolecular C-H insertions, see: (a) Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *J. Chem. Soc., Chem. Commun.* **1981**, 688. (b) Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *J. Bull. Soc. Chim. Belg.* **1984**, *93*, 945. (c) Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *J. Mol. Catal.* **1988**, *49*, L13. (d) Scott, L. T.; DeCicco, G. J. *J. Am. Chem. Soc.* **1974**, *96*, 322. (e) Ambramovitch, R. A.; Roy, J. *J. Chem. Soc., Chem. Commun.* **1965**, 542. (f) Adams, J. Poupart, M. A.; Greiner, L.; Schaller, C.; Quimet, N.; Frenette, R. *Tetrahedron Lett.* **1989**, *30*, 1749.
- (7) For recent reviews that discuss the status of intermolecular C-H insertions, see: (a) Ye, T.; McKerver, M. A. *Chem. Rev.* **1994**, *94*, 1091. (b) Doyle, M. P.; McKerver, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons, Inc.: New York, **1997**, pp 115.
- (8) The structure of trimer **6** was assigned on the basis of ^{13}C , DEPT, and extensive ^1H NMR data. The 500 MHz ^1H NMR spectrum of **6** is characterized by two downfield methoxy resonances (3.79, 3.74) as well as an upfield methoxy resonance assigned for the methyl ether group at C(9a). Also present are three vinyl resonances at 7.02, 6.17 and 5.81 ppm, assigned to the C(8), C(3) and C(5) protons, respectively. Each of these protons is coupled to two diastereotopic protons on the neighboring methylene units (^1H - ^1H COSY, ^1H -decoupling experiments). Furthermore, irradiation of one of the C(4) protons (2.60 ppm) results in an nOe enhancement of the C(5) proton (5.81 ppm); irradiation of this C(5) proton results in enhancement of the same C(4) proton resonance. Additional nOe enhancements were observed between the C(3) and the C(4) protons, the C(5) and one of the C(6) protons, and the C(8) and one of the C(9) protons.



- (9) (a) Muller, P.; Pautex, N.; Doyle, M. P.; Bagheri, V. *Helv. Chim. Acta* **1990**, *73*, 1233. (b) Muller, P.; Granicher, C. *Helv. Chim. Acta* **1993**, *76*, 521.
- (10) Padwa, A. *Acc. Chem. Res.* **1991**, *24*, 22.