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Effect of carbenoid structure on the reactions of rhodium-stabilized carbenoids with cycloheptatriene

Huw M. L. Davies,* Douglas G. Stafford, Tore Hansen, Melvyn Rowen Churchill and Kim M. Keil

Department of Chemistry, State University of New York at Buffalo, Buffalo, NY 14260-3000, USA

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Abstract

Rhodium prolinate catalyzed reactions of diazocarbonyls with cycloheptatriene are very dependent on the carbenoid structure and can result in either cyclopropanation, C–H insertion or a combined C–H insertion Cope rearrangement.

Metal catalyzed decomposition of diazo compounds is a general method to prepare metal stabilized carbenoids, which are versatile intermediates for organic synthesis. The most commonly used carbenoid intermediates are those derived from diazoacetates (**1a**).[1] For some time we have explored the synthetic utility of rhodium carbenoids derived from vinyldiazoacetates (**1b**) and aryldiazoacetates (**1c**).[2] These carbenoids, containing donor and acceptor groups, display remarkable differences in reactivity compared to carbenoids derived from diazoacetates. Alkene cyclopropanations with either vinyldiazoacetates or phenyldiazoacetates are highly diastereoselective[3,4] and very sensitive to alkene geometry.[5] On using dirhodium tetraprolinates such as $Rh_2(S\text{-DOSP})_4$ (**2**) as catalysts, the cyclopropanations are also highly enantioselective[6] even though the dirhodium tetraprolinates are poor chiral catalysts for diazoacetate cyclopropanations.[6,7] More recently, we have demonstrated that aryl diazoacetates are capable of highly enantioselective and diastereoselective intermolecular C–H insertions,[8] reactions that were not considered to be of significant practical utility with carbenoids derived from diazoacetates.[9] In this communication we describe the reactions of rhodium-stabilized carbenoids with cycloheptatriene (**3**), which illustrates the remarkable influence of carbenoid structure on the reaction outcome.

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[*] Corresponding author.

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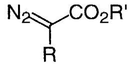
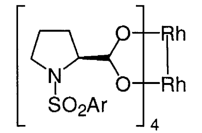
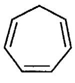


1a: R = H
1b: R = vinyl
1c: R = aryl



Ar = p-($C_{11\text{-}13}H_{23\text{-}27}$)$C_6H_4$
Rh_2(*S*-DOSP)$_4$
2



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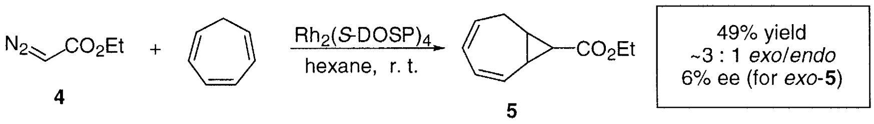
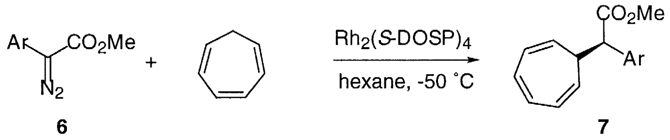
The reaction between cycloheptatriene and ethyl diazoacetate (**4**) is well established.[10] Rhodium(II) acetate catalyzed decomposition of ethyl diazoacetate in the presence of cycloheptatriene results in the formation of a mixture of mono-, di- and tricyclopropanated materials. When 5 equivalents of cycloheptatriene is used, the monocyclopropanated product **5** dominates. Similar reactivity is exhibited by the carbenoid derived from a diazoketone.[10b] As a control experiment, the reaction of ethyl diazoacetate catalyzed by Rh_2(*S*-DOSP)$_4$ was examined and similarly, the monocyclopropanated product **5** was formed in 49% yield as a 3:1 mixture of *exo*/*endo* isomers (Scheme 1). As is typical for ethyl diazoacetate cyclopropanations with Rh_2(*S*-DOSP)$_4$, the enantioselectivity was very low (6% ee for *exo*-**5**).



Scheme 1.

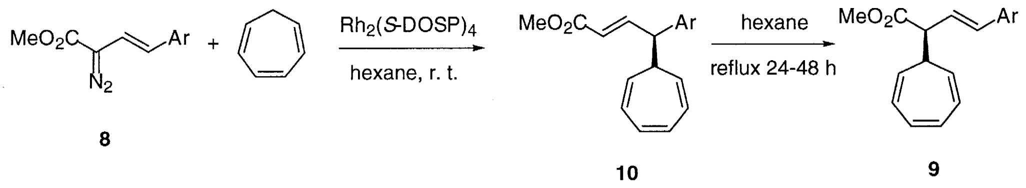
The reaction of methyl phenyldiazoacetate (**6a**) with cycloheptatriene resulted in an entirely different reaction pathway compared to the ethyl diazoacetate chemistry. Less than 5% of the cyclopropanation product was observed in the NMR of the crude reaction mixture and instead the C–H insertion product **7a** was formed in 55% yield and 95% ee (Scheme 2). The absolute stereochemistry of **7a** was determined to be of (*R*)-configuration by catalytic hydrogenation of **7a** to the known cycloheptane derivative.[8a] This reaction is applicable to aryldiazoacetates **6b**–**d** and the C–H insertion products **7b**–**d** were formed in greater than 90% ee.



	Ar	Yield, %	ee, %
a	phenyl	55	95
b	*p*-chlorophenyl-	64	95
c	*p*-methylphenyl-	60	94
d	2-napthyl-	53	91

Scheme 2.

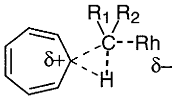
The reaction of vinyldiazoactetate **8a** with cycloheptatriene resulted in less than 5% of cyclopropanation. In this case, however, only a trace of the C–H insertion product **9a** was formed and the major product was the isomeric structure **10a** (56% yield, 99% ee) (Scheme 3). The formation of a product similar to **10a** has been observed in the reaction of vinyldiazoacetates with 1,3-cyclohexadiene.[8b] The mechanism of the reaction is considered to be a combined C–H insertion/Cope rearrangement rather than a two step process because the direct C–H insertion product is the thermodynamically most favored product. A similar behavior was seen with **10a** because on heating it underwent a Cope rearrangement back to the formal C–H insertion product **9a** (84% conversion, 68% isolated yield, 99% ee). Similar chemistry was possible with the bromo derivative **8b** and the absolute stereochemistry of **9b** and **10b** was determined by X-ray crystallography to be of (*S*) and (*R*) configuration, respectively.[11]



	Ar	**10**, yield, %	**10**, ee, %	**9**, yield, %	**9**, ee, %
a	phenyl-	56	99	68	99
b	*p*-bromophenyl-	67	99	86	>98

Scheme 3.

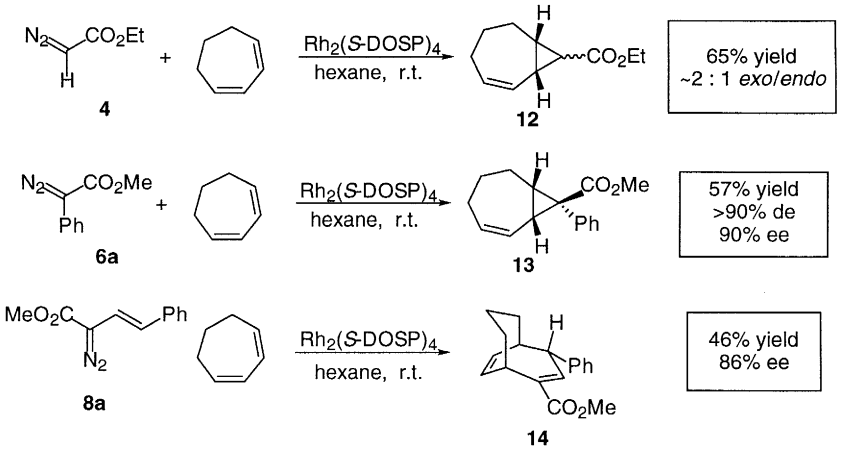
The reaction of vinyl- and aryldiazoacetates towards cycloheptatriene is very different from that of diazoacetates and diazoketones. Two explanations are possible to rationalize this result. It is well established that cyclopropanation with vinyldiazoacetates is much more sensitive to steric effects than cyclopropanation with diazoacetate,[5] and so, it is conceivable that cyclopropanation of cycloheptatriene by **6** and **8** is not favorable. Alternatively, the C–H insertions by vinyl- and aryldiazoacetates preferentially occur at sites that would stabilize positive charge during the concerted but non-synchronous insertion.[8c,d] It has also been established, at least for the cyclopropanation reaction, that considerably greater charge build-up occurs in the transition state of reactions of vinyl- and aryldiazoacetates compared to diazoacetates.[12] Consequently, cycloheptatriene may be an exceptional substrate for C–H insertion because the positive charge build-up in this reaction would be favorable due to homoaromatic stabilization as shown in structure **11**.



11

In order to explore which explanation is the most reasonable, the reaction of the three types of carbenoids with 1,3-cycloheptadiene was examined. Both ethyl diazoacetate (**4**) and methyl phenyldiazoacetate (**6a**) resulted in the predominant formation of the cyclopropanation products **12**[13] and **13** (Scheme 4). As expected, poor stereocontrol was observed in the formation of **12**, while **13**[14] was formed in >90% de and 90% ee. Less than 5% of the C–H insertion product was observed in the reaction of cycloheptadiene with **6a**. Similarly, the reaction of 1,3-cycloheptatriene with the vinyldiazoacetate **8a** gave only trace amounts (<5%) of C–H insertion products. The major product that was formed was the bicyclic system **14**[14] (46% yield, 86% ee), derived from a tandem cyclopropanation Cope rearrangement. As all three carbenoid systems initially form cyclopropanation products with 1,3-cycloheptadiene, it would appear that the reactivity difference for the cycloheptatriene system is due to special stabilization of the C–H insertion transition state associated with this system, as illustrated in structure **11**.

In summary these studies demonstrate that the structure of rhodium carbenoids has a profound influence on the outcome of their chemistry. Furthermore, these studies underscore the effectiveness of $\mathrm{Rh_2}$(*S*-DOSP)$_4$ as a chiral catalyst for vinyl- and aryldiazoacetate reactions even though it is very poor for diazoacetate reactions.



Scheme 4.

Acknowledgements

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