Homogeneous Catalysis

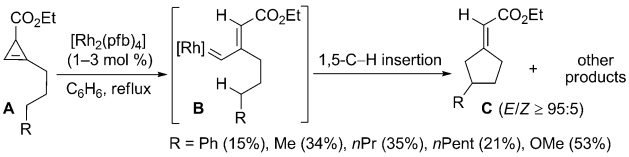
DOI: 10.1002/ange.201205913

Highly Efficient Stereoselective Catalytic C(sp^3)–H Insertions with Donor Rhodium Carbenoids Generated from Cyclopropenes**

Alexis Archambeau, Frédéric Miege, Christophe Meyer, and Janine Cossy**

Among the different methods that enable the formation of a C–C bond by catalytic functionalization of an unactivated C(sp^3)–H bond,[1] insertion of a transition-metal carbenoid constitutes a powerful approach.[2–4] Metal carbenoids are traditionally generated by decomposition of diazo compounds in the presence of transition-metal catalysts, and dirhodium(II) complexes are arguably the most useful catalysts.[2–4] The reactivity of rhodium carbenoids in C–H insertions markedly depends on the resonance effect of their substituents and, according to the classification of H. M. L. Davies, three major classes should be distinguished: acceptor/acceptor, acceptor, and donor/acceptor carbenoids.[2–4] The latter rhodium carbenoids display an appropriate balance between stability and reactivity, thereby leading to greater reaction effectiveness and the unique possibility to achieve challenging intermolecular C–H insertions.[4,5]

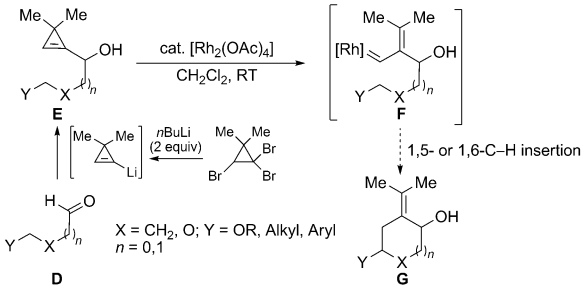
By contrast with these well-investigated classes, little is known on the reactivity of donor rhodium(II) carbenoids in C(sp^3)–H insertions, owing to the hazards associated with the preparation and handling of the required unstabilized diazo precursors.[2–4,6] Examples of intramolecular C(sp^3)–H insertions involving other donor metal carbenoids produced by alternative pathways have also been reported.[7–11] The ring opening of cyclopropenes in the presence of electrophilic transition-metal complexes is also an attractive strategy for the generation of alkenyl metal carbenoids.[12] These species can be involved in several transformations[12] but curiously, examples of C–H insertions have essentially only been disclosed with cyclopropenecarboxylates **A**.[13,14] These latter substrates, prepared by $[Rh_2(OAc)_4]$-catalyzed cyclopropenation of terminal alkynes with ethyl diazoacetate, underwent ring opening upon heating in refluxing benzene in the presence of the more electrophilic catalyst $[Rh_2(pfb)_4]$ (pfb = perfluorobutanoate; Scheme 1). Mixtures of products were obtained from which the alkylidenecyclopentanes **C**, resulting from 1,5-C–H insertions triggered by the rhodium carbenoids **B**, were isolated in low to moderate yields (15–53%). Büchner reactions (intermolecular reaction with C_6H_6 or intramolecular process when R = Ph) and polymerization also took place concurrently.[13] Although the dirhodium



Scheme 1. Previous work: C(sp^3)–H insertions involving rhodium carbenoids generated from cyclopropenecarboxylates.

complexes **B** should be classified as donor carbenoids,[4,15] they probably retain significant electrophilic character owing to the vinylogous ester moiety, which attenuates π donation from the olefin (Scheme 1).

Herein, we report that "purely donor" rhodium carbenoids **F**, which are generated by ring opening of 3,3-dimethylcyclopropenylcarbinols **E**, can trigger highly efficient and diastereoselective intramolecular C(sp^3)–H insertions leading to a variety of functionalized carbocycles and oxygen heterocycles **G** under mild conditions (Scheme 2). The synthesis of compounds **E** is readily achieved by addition of 3,3-dimethylcyclopropenyllithium, which is generated in situ, to aldehydes **D**.[16,17]



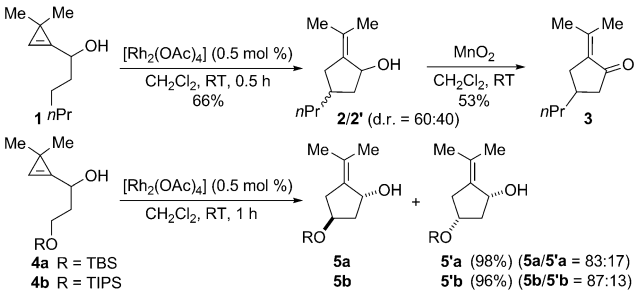
Scheme 2. This study: C(sp^3)–H insertions involving donor rhodium carbenoids **F** generated from 3,3-dimethylcyclopropenylcarbinols **E**.

The reactivity of cyclopropenylcarbinol **1**, derived from capronaldehyde, was investigated first. A rapid reaction occurred in the presence of $[Rh_2(OAc)_4]$ (0.5 mol%) under mild conditions (CH_2Cl_2, 0.1M, RT, 0.5 h) leading to a 60:40 mixture of cyclopentanols **2** and **2′** in 66% yield (Scheme 3). Oxidation of this mixture afforded a single enone **3** (53%), thus confirming that **2** and **2′** were diastereomers both arising from a ring opening/1,5-C–H insertion process. In the case of cyclopropenylcarbinols **4a** and **4b** bearing remote silyloxy groups, the rhodium-catalyzed reaction led to the five-membered diastereomeric compounds **5a**/**5′a** and **5b**/**5′b**, respectively, with higher levels of diastereoselectivity (d.r. = 83:17 and 87:13) and excellent yields (96–98%; Scheme 3).[18]

[*] A. Archambeau, Dr. F. Miege, Dr. C. Meyer, Prof. Dr. J. Cossy
Laboratoire de Chimie Organique
ESPCI ParisTech, CNRS (UMR 7084)
10 rue Vauquelin 75231 Paris Cedex 05 (France)
E-mail: christophe.meyer@espci.fr
janine.cossy@espci.fr

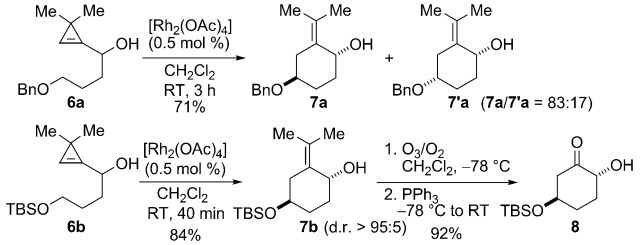
[**] A.A. thanks the MRES for a grant.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201205913.



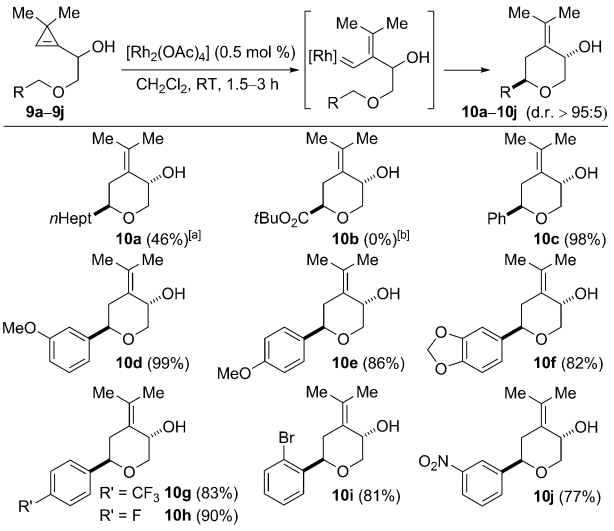
Scheme 3. 1,5-C–H insertions triggered by donor rhodium carbenoids generated from 3,3-dimethylcyclopropenylcarbinols. TBS = *tert*-butyldimethylsilyl, TIPS = triisopropylsilyl.

Thus, the ring opening of the more electron-rich 3,3-dimethylcyclopropenylcarbinols **E** proceeds smoothly in the presence of $[Rh_2(OAc)_4]$ compared to cyclopropenecarboxylates **A**, which required a more electrophilic catalyst and harsher conditions.[13] The regioselective formation of rhodium carbenoids **F** can be understood by preferential binding of the rhodium catalyst to the less-substituted cyclopropene carbon atom whilst a more stable tertiary cyclopropyl cation is generated and undergoes electrocyclic ring opening.[12,17] Despite their low electrophilic character, the high reactivity exhibited by these "purely donor" dirhodium carbenoids **F** (lacking any electron-withdrawing group on the alkene) in intramolecular $C(sp^3)$–H insertions is particularly noteworthy. To further explore the reactivity of these donor rhodium carbenoids, the behavior of cyclopropenylcarbinols **6a** and **6b** was examined with the hope that the location of the remote oxygen atom could bias the reaction in favor of a 1,6-C–H insertion process. Indeed, cyclopropenylcarbinol **6a** possessing a remote benzylic ether afforded the products **7a** and **7′a** containing six-membered rings with moderate diastereoselectivity (d.r. = 83:17, 71%), whereas the more sterically hindered TBS ether **6b** led to a single detectable diastereomer **7b** (d.r. > 95:5) in 84% yield (Scheme 4). Notably, oxidative cleavage of the isopropylidene group can be achieved by ozonolysis without epimerization, as illustrated by the formation of the α-hydroxycyclohexanone **8** from **7b** (92%; Scheme 4).[18]



Scheme 4. 1,6-C–H insertions triggered by donor rhodium carbenoids generated from 3,3-dimethylcyclopropenylcarbinols.

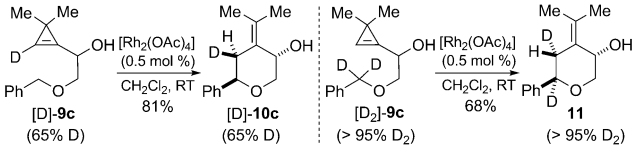
The remarkable ability of donor rhodium carbenoids generated from 3,3-dimethylcyclopropenylcarbinols to trigger 1,6-C–H insertions with high diastereoselectivity led us to investigate the application of this strategy to the synthesis of tetrahydropyrans. The requisite substrates **9a–j** were prepared by addition of 3,3-dimethyl-cyclopropenyllithium to the corresponding α-alkoxyacetaldehydes. Cyclopropene **9a**, in which the remote oxygen atom is substituted by an *n*-octyl chain, reacted slowly under standard conditions (CH_2Cl_2, RT, 8 h), and the reaction required a higher catalyst loading (1.5 mol%) to reach completion and eventually deliver the corresponding tetrahydropyran **10a** as a single detectable *anti* diastereomer in moderate yield (46%; Scheme 5). Formation of tetrahydropyran **10b** could not be observed from the corresponding cyclopropene **9b**, because 1,6-C–H insertion is probably retarded by the adjacent electron-withdrawing group (CO_2tBu). This result is in agreement with considerable positive charge build-up in the transition state at the carbon atom where C–H insertion occurs, as previously noted with the other classes of carbonyl-substituted acceptor rhodium carbenoids.[19] By contrast, cyclopropenylcarbinol **9c** reacted smoothly, since 1,6-C–H insertion involves a benzylic position, and the corresponding tetrahydropyran **10c** was obtained as a single *anti* diastereomer in excellent yield (98%).[18] The reaction was also applied to a variety of cyclopropenylcarbinols **9d–9j** bearing either electron-donating alkoxy substituents or electron-withdrawing groups (F, Br, CF_3, NO_2) on the aromatic ring. In all cases, the ring opening/1,6-C–H insertion sequence provided the corresponding 6-aryl-4-isopropylidenetetrahydropyran-3-ols **10d–10j** as single detectable diastereomers (d.r. > 95:5) in excellent yields (77–99%; Scheme 5).[18]



Scheme 5. Synthesis of substituted tetrahydropyrans from 3,3-dimethylcyclopropenylcarbinols by 1,6-C–H insertions. [a] With $[Rh_2(OAc)_4]$ (1.5 mol%), CH_2Cl_2, RT, 8 h. [b] No conversion observed.

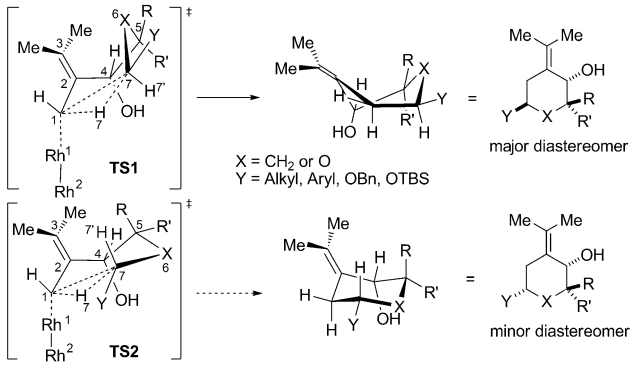
To gain further insight into the stereochemical issues of this transformation, deuterium labeling experiments were carried out. Cyclopropene [D]-**9c** (65% D) was prepared by treatment of **9c** with lithium diisopropylamide (LDA) (2.5 equiv, THF, −40 °C to −20 °C) and subsequent quenching with CD_3OD. Treatment with $[Rh_2(OAc)_4]$ (0.5 mol%,

CH_2Cl_2, RT) afforded tetrahydropyran [D]-**10c** (81%), in which 65% of the pro-(*S*) diastereotopic allylic proton in **10c** has been stereoselectively replaced by a deuterium atom (Scheme 6). Conversely, under the same conditions, cyclopropenylcarbinol [D_2]-**9c**, dideuterated at the benzylic position, led to the dideuterated tetrahydropyran **11** (d.r. > 95:5, 68%), in which the pro-(*R*) diastereotopic allylic proton has been exchanged to a deuterium.[18] Thus, C–H insertions mediated by donor rhodium carbenoids derived from 3,3-dimethylcyclopropenes, involve a stereospecific process at the carbenoid carbon atom, in agreement with a concerted mechanism.[19,20]



Scheme 6. Deuterium labeling experiments.

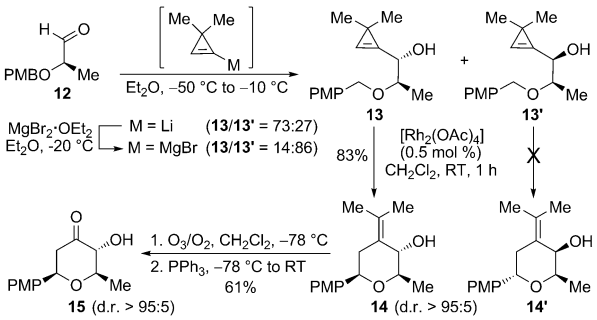
For C–H insertions mediated by dirhodium carbenoids generated from α-diazocarbonyl compounds, computational studies revealed that a concerted nonsynchronous process with a significant hydride transfer component was involved and that the more stabilized donor/acceptor carbenoids led to relatively late transition states.[19] By analogy with these results, in the absence of computational studies at this stage, we have devised empirical models to rationalize the diastereoselectivities observed in C–H insertions mediated by rhodium carbenoids generated from 3,3-dimethylcyclopropenylcarbinols. Although in the initially generated dirhodium carbenoids, the C2–C3 alkene bond should be parallel to the C1–Rh1 bond, this may no longer be the case in the transition state, if formation of the C1–H7 bond (hydride transfer component) is well-advanced (Scheme 7). Moreover, the conformation around the C2–C1 and C2–C4 bonds should result from minimization of $A^{1,3}$ strain (1,3-allylic strain).[21] If the forming C1–H7 bond is orthogonal to the C1–Rh1 bond,[19] then the four atoms H7, C1, C2, and C4 should be almost coplanar. Thus, for 1,6-C–H insertions, two seven-membered cyclic transition-state models **TS1** and **TS2**



Scheme 7. Empirical transition-state models for 1,6-C–H insertions (ligands on rhodium are omitted for the sake of clarity).

of boat and chair conformations, respectively,[22] in which the hydroxy group lies in the axial position and the substituent at C7 preferentially occupies an equatorial position, could be initially considered. However, only the boat transition-state model **TS1** can account for the observed 1,4-*anti* relative orientation between the hydroxy group and the Y substituent in the resulting six-membered products (Scheme 7).[23]

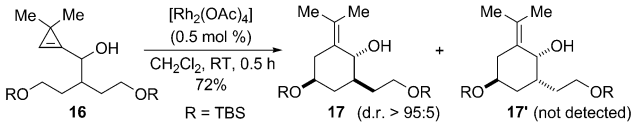
By considering the transition-state model **TS1**, we surmised that 1,6-C–H insertions should proceed at significantly different rates for diastereomeric substrates bearing one substituent at C5 (R or R′ ≠ H), owing to the eclipsed conformation around the C4–C5 bond and the axial orientation of the hydroxy group at C4. To verify this experimentally, the epimeric cyclopropenylcarbinols **13** and **13'** were synthesized from α-alkoxyaldehyde **12** (Scheme 8). Addition of 3,3-dimethylcyclopropenyllithium led to a 73:27 mixture of the (separable) diastereomeric alcohols **13** and **13′**, as a result of a moderate Felkin–Anh stereocontrol.[24a] As expected, addition of the Grignard reagent (generated by transmetalation with $MgBr_2{\cdot}OEt_2$) reversed the diastereoselectivity in favor of **13′** (**13**/**13′** = 14:86) owing to a chelation-controlled nucleophilic addition.[24] Upon treatment with [$Rh_2(OAc)_4$] (0.5 mol%) under standard conditions (CH_2Cl_2, RT), only cyclopropenylcarbinol **13** underwent a smooth and highly diastereoselective conversion to tetrahydropyran **14** (d.r. > 95:5), which was isolated in 83% yield. Ozonolysis of **14** provided the trisubstituted pyranone **15** (61%) without epimerization.[18] By contrast, in agreement with our hypothesis, the epimeric alcohol **13′** did not react even if a higher catalyst loading or harsher conditions (reflux) were used but underwent decomposition (Scheme 8).



Scheme 8. Different behavior of epimeric cyclopropenylcarbinols **13** and **13′**. PMB = *p*-methoxybenzyl, PMP = *p*-methoxyphenyl.

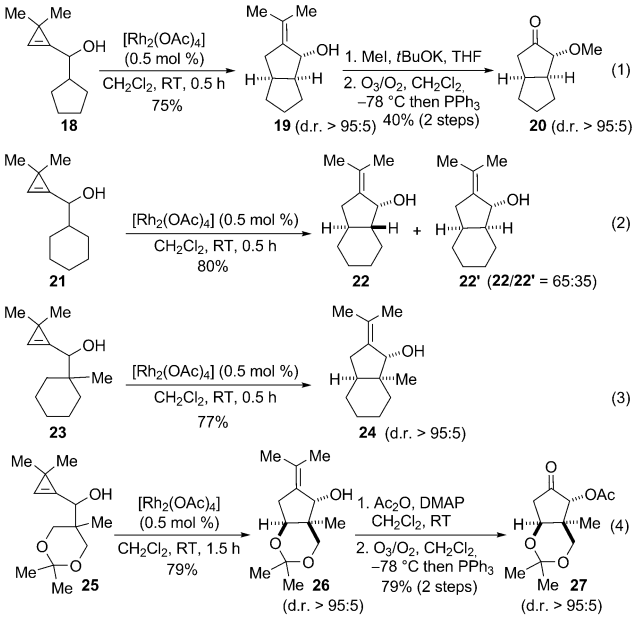
The different behavior of the epimers **13** and **13′** suggested that in C–H insertions it may be possible to differentiate C–H bonds belonging to two diastereotopic methylene groups. An interesting illustration is the rhodium-catalyzed reaction of cyclopropenylcarbinol **16**; of the four possible diastereomers this reaction selectively afforded **17** (72%), which is one of the two diastereomers (**17** and **17′**) that possess a 1,4-*anti* relative orientation between the hydroxy and the silyloxy groups (Scheme 9).[18]

Differentiation between two diastereotopic methylene units was also exploited to devise a straightforward access to bicyclic compounds, by using 3,3-dimethylcyclopropenyl-



Scheme 9. Differentiation of diastereotopic groups by diastereoselective 1,6-C–H insertion.

carbinols derived from cyclic aldehydes. Cyclopropenylcarbinol **18** was converted to a single bicyclo[3.3.0]octan-2-ol **19** (75%), the relative configuration of which was assigned after conversion to the known bicylic ketone **20** [Eq. (1), Scheme 10].[25] However, in the case of cyclopropenylcarbinol **21**, a 65:35 mixture of the separable epimeric *trans*- and *cis*-hydrindanols **22** and **22′**,[18] respectively, was obtained (80%) [Eq. (2), Scheme 10]. The diastereomeric ratio, which closely parallels the known relative stabilities of *trans*- and *cis*-hydrindanes,[26] may be a consequence of the late (product-like) transition state involved in C–H insertions with donor rhodium carbenoids.



Scheme 10. Synthesis of bicyclic compounds. DMAP = *N*,*N*-dimethylaminopyridine.

As *cis*-hydrindanes are known to be more stable than the *trans* isomers when a methyl substituent is present at the ring junction,[26] the rhodium-catalyzed reaction of cyclopropenylcarbinol **23** was investigated. Rewardingly, hydrindanol **24** having a *cis* ring junction was obtained as a single diastereomer in good yield (77%) [Eq. (3), Scheme 10]. The same high diastereoselectivity was observed in the rhodium-catalyzed reaction of cyclopropenylcarbinol **25** possesing a cyclic ketal, which afforded the bicyclic compound **26** (79%, d.r. > 95:5). Acetylation of the alcohol and ozonolysis delivered the highly substituted bicyclic ketone **27** (79%), possessing a quaternary center at the β-position of the carbonyl group (ring junction) [Eq. (4), Scheme 10].[18]

In conclusion, donor rhodium carbenoids, generated by ring opening of 3,3-dimethylcyclopropenylcarbinols in the presence of $[Rh_2(OAc)_4]$, display a high reactivity in intramolecular C–H insertions. The substrates are readily prepared by addition of 3,3-dimethylcyclopropenyllithium to aldehydes, the C–H insertions proceed under mild conditions and tolerate the presence of the free hydroxy group. High levels of diastereoselectivity can be observed for a wide range of substrates. Since subsequent ozonolysis of the isopropylidene group in the resulting cyclic compounds can be achieved, this study illustrates that 3,3-dimethylcyclopropenes can also behave as surrogates for α-diazoketones in C–H insertions. We are currenty exploring the reactivity of such donor rhodium carbenoids in intermolecular and enantioselective C–H insertions.

Received: July 24, 2012
Published online: October 9, 2012

Keywords: carbenoids · C–H insertion · cyclopropenes · diastereoselectivity · rhodium catalysis

[1] a) *Handbook of C-H Transformations* (Ed.: G. Dyker), Wiley-VCH, Weinheim, **2005**; b) *C-H Activation* (Eds.: J.-Q. Yu, Z. Shi), *Topics in Current Chemistry, Vol. 292*, Springer, Berlin, **2010**; c) R. Jazzar, J. Hitce, A. Renaudat, J. Sofack-Kreutzer, O. Baudoin, *Chem. Eur. J.* **2010**, *16*, 2654–2672, and references therein.

[2] a) M. P. Doyle, *Chem. Rev.* **1986**, *86*, 919–939; b) M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, *98*, 911–936; c) M. P. Doyle, R. Duffy, M. Ratnikov, L. Zhou, *Chem. Rev.* **2010**, *110*, 704–724; d) M. P. Doyle, M. Ratnikov, Y. Liu, *Org. Biomol. Chem.* **2011**, *9*, 4007–4016.

[3] a) M. P. Doyle, M. A. McKervey, T. Ye in *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*, Wiley, New York, **1998**; b) A. G. H. Wee, *Curr. Org. Synth.* **2006**, *3*, 499–555; c) *Modern Rhodium-Catalyzed Organic Reactions* (Ed.: P. A. Evans), Wiley-VCH, Weinheim, **2005**.

[4] a) H. M. L. Davies, E. G. Antoulinakis, *J. Organomet. Chem.* **2001**, *617–618*, 47–55; b) H. M. L. Davies, R. E. J. Beckwith, *Chem. Rev.* **2003**, *103*, 2861–2904; c) H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417–424; d) H. M. L. Davies, J. R. Denton, *Chem. Soc. Rev.* **2009**, *38*, 3061–3071; e) H. M. L. Davies, D. Morton, *Chem. Soc. Rev.* **2011**, *40*, 1857–1869.

[5] For a recent report on C–H insertions of (donor/acceptor) rhodium(II) azavinylcarbenes, see: S. Chuprakov, J. A. Malik, M. Zibinsky, V. V. Fokin, *J. Am. Chem. Soc.* **2011**, *133*, 10352–10355.

[6] The intramolecular 1,5-C–H insertion of a noncarbonyl stabilized rhodium carbenoid (generated from a *N*-aziridinyl imine) was used recently as an elegant route toward *N*-fused indolines, see: S. J. Mahoney, E. Fillion, *Chem. Eur. J.* **2012**, *18*, 68–71.

[7] For gold- or platinum-catalyzed reactions involving enynes, see: a) Y. Horino, T. Yamamoto, K. Ueda, S. Kuroda, F. D. Toste, *J. Am. Chem. Soc.* **2009**, *131*, 2809–2811; b) A. Escribano-Cuesta, V. López-Carrillo, D. Janssen, A. M. Echavarren, *Chem. Eur. J.* **2009**, *15*, 5646–5650; c) Y. Liu, D. Zhang, J. Zhou, C. Liu, *J. Phys. Chem. A* **2010**, *114*, 6164–6170; d) C. H. Oh, J. H. Lee, S. M. Lee, H. J. Yi, C. S. Hong, *Chem. Eur. J.* **2009**, *15*, 71–74.

[8] For gold-catalyzed reactions involving vinylallenes, see: a) H. Funami, H. Kusama, N. Iwasawa, *Angew. Chem.* **2007**, *119*, 927–929; *Angew. Chem. Int. Ed.* **2007**, *46*, 909–911; b) G. Lemière, V.

Gandon, K. Cariou, A. Hours, T. Fukuyama, A.-L. Dhimane, L. Fensterbank, M. Malacria, *J. Am. Chem. Soc.* **2009**, *131*, 2993 – 3006; c) S. Bhunia, R.-S. Liu, *J. Am. Chem. Soc.* **2008**, *130*, 16488 – 16489.

[9] For a review on gold-mediated C–H activation processes, see: T. de Haro, C. Nevado, *Synthesis* **2011**, 2530 – 2539.

[10] One example of C–H insertion with a gold carbenoid generated by retro-Büchner reaction has been reported, see: C. R. Solorio-Alvarado, Y. Wang, A. M. Echavarren, *J. Am. Chem. Soc.* **2011**, *133*, 11952 – 11955.

[11] For a ruthenium-catalyzed reaction between trimethylsilyl diazomethane and terminal alkynes, see: F. Cambeiro, S. López, J. A. Varela, C. Saá, *Angew. Chem.* **2012**, *124*, 747 – 751; *Angew. Chem. Int. Ed.* **2012**, *51*, 723 – 727.

[12] For reviews, see: a) P. Binger, H. M. Büch, *Top. Curr. Chem.* **1987**, *135*, 77 – 151; b) M. Rubin, M. Rubina, V. Gevorgyan, *Chem. Rev.* **2007**, *107*, 3117 – 3179; c) Z.-B. Zhu, Y. Wei, M. Shi, *Chem. Soc. Rev.* **2011**, *40*, 5534 – 5563; d) F. Miege, C. Meyer, J. Cossy, *Beilstein J. Org. Chem.* **2011**, *7*, 717 – 734.

[13] a) P. Müller, N. Pautex, M. P. Doyle, V. Bagheri, *Helv. Chim. Acta* **1990**, *73*, 1233 – 1241; b) P. Müller, C. Gränicher, *Helv. Chim. Acta* **1993**, *76*, 521 – 534; c) P. Müller, C. Gränicher, *Helv. Chim. Acta* **1995**, *78*, 129 – 144.

[14] In the presence of a rhodium(II) catalyst, ω-alkynyl diazoketones can cyclise (not necessarily through cyclopropenylketones) to alkenyl rhodium carbenoids (with a vinylogous acceptor keto group). One example of 1,5-C–H insertion has been reported: a) A. Padwa, U. Chiacchio, Y. Garreau, J. M. Kassir, K. E. Krumpe, A. M. Schoffstall, *J. Org. Chem.* **1990**, *55*, 414 – 416; b) A. Padwa, K. E. Krumpe, J. M. Kassir, *J. Org. Chem.* **1992**, *57*, 4940 – 4948; see also: c) T. R. Hoye, C. J. Dinsmore, *J. Am. Chem. Soc.* **1991**, *113*, 4343 – 4345.

[15] H. T. Bonge, T. Hansen, *Tetrahedron Lett.* **2010**, *51*, 5378 – 5381, and references therein.

[16] a) M. S. Baird, H. H. Hussain, W. Nethercott, *J. Chem. Soc. Perkin Trans. 1* **1986**, 1845 – 1853; enantiomerically enriched cyclopropenylcarbinols can be obtained by Sharpless kinetic resolution, see: b) S. Simaan, A. Masarwa, P. Bertus, I. Marek, *Angew. Chem.* **2006**, *118*, 4067 – 4069; *Angew. Chem. Int. Ed.* **2006**, *45*, 3963 – 3965.

[17] For our previous contributions on gold- and rhodium-catalyzed cycloisomerizations of 3,3-dimethylcyclopropene-enes, see: a) F. Miege, C. Meyer, J. Cossy, *Org. Lett.* **2010**, *12*, 4144 – 4147; b) F. Miege, C. Meyer, J. Cossy, *Chem. Eur. J.* **2012**, *18*, 7810 – 7822; c) F. Miege, C. Meyer, J. Cossy, *Angew. Chem.* **2011**, *123*, 6054 – 6059; *Angew. Chem. Int. Ed.* **2011**, *50*, 5932 – 5937.

[18] The diastereomeric ratios were determined in all cases by analysis of the crude products by ^{1}H NMR spectroscopy. For the assignment of the relative configuration of the cyclic products by chemical correlations and NMR spectroscopy, see the Supporting Information.

[19] a) N. Yoshikai, E. Nakamura, *Adv. Synth. Catal.* **2003**, *345*, 1159 – 1171; b) E. Nakamura, N. Yoshikai, M. Yamanaka, *J. Am. Chem. Soc.* **2002**, *124*, 7181 – 7192; c) J. Hansen, J. Autschbach, H. M. L. Davies, *J. Org. Chem.* **2009**, *74*, 6555 – 6563.

[20] A scenario involving hydride transfer followed by cyclization of the resulting allylic rhodium(II) species onto the oxycarbenium ion could be considered, by analogy with the formation of abnormal products from carbonyl-substituted acceptor rhodium carbenoids, see: a) J. D. White, P. Hrnciar, *J. Org. Chem.* **1999**, *64*, 7271 – 7273; b) M. O. Erhunmwunse, P. G. Steel, *Tetrahedron Lett.* **2009**, *50*, 3568 – 3570; c) J. S. Clark, Y.-S. Wong, R. J. Townsend, *Tetrahedron Lett.* **2001**, *42*, 6187 – 6190, and references therein. However, this scenario would imply that the allylic rhodium(II) species, generated after hydride (or deuteride) transfer, reacts with complete regio- and stereoselectivity with the oxycarbenium ion. Additionally, no significant rate differences were observed whether the insertion proceeds at an adjacent position of a carbon or an oxygen atom.

[21] a) F. Johnson, S. K. Malhotra, *J. Am. Chem. Soc.* **1965**, *87*, 5492 – 5493; for a review, see: b) R. W. Hoffmann, *Chem. Rev.* **1989**, *89*, 1841 – 1860.

[22] a) D. F. Bocian, H. M. Pickett, T. C. Rounds, H. L. Strauss, *J. Am. Chem. Soc.* **1975**, *97*, 687 – 695; b) K. B. Wiberg, *J. Org. Chem.* **2003**, *68*, 9322 – 9329; c) C. P. A. Anconi, C. S. Nascimento, Jr., H. F. Dos Santos, W. B. DeAlmeida, *Chem. Phys. Lett.* **2006**, *418*, 459 – 466.

[23] Transition-state models have also been proposed for 1,5-C–H insertions, see the Supporting Information.

[24] a) For a review, see: A. Mengel, O. Reiser, *Chem. Rev.* **1999**, *99*, 1191 – 1224; b) M. T. Reetz, *Acc. Chem. Res.* **1993**, *26*, 462 – 468.

[25] H. Finch, A. M. M. Mjalli, J. G. Montana, S. M. Roberts, R. J. K. Taylor, *Tetrahedron* **1990**, *46*, 4925 – 4950.

[26] a) *Stereochemistry of Organic Compounds* (Eds.: E. L. Eliel, S. H. Wilen, L. N. Mander), Wiley, New York, **1993**; see also: b) H. L. Gordon, S. Freeman, T. Hudlicky, *Synlett* **2005**, 2911 – 2914.

