Angewandte Chemie International Edition

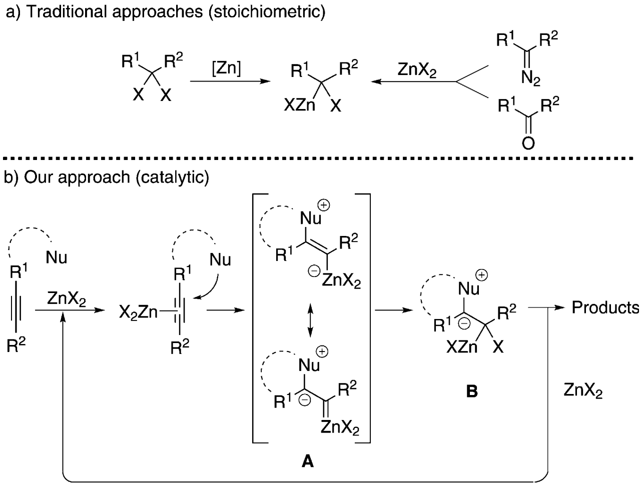
DOI: 10.1002/anie.201203914

Zinc Catalysis

Catalytic Generation of Zinc Carbenes from Alkynes: Zinc-Catalyzed Cyclopropanation and Si–H Bond Insertion Reactions**

Rubén Vicente, Jesús González, Lorena Riesgo, Javier González, and Luis A. López**

The preparation of zinc carbenoids and their applications in alkene cyclopropanations were reported by Simmons and Smith for the first time in 1958.[1] Even today, this synthetic methodology remains one of the most important ways to access relevant cyclopropane rings.[2] Despite the extensive studies on this process, the number of available precursors for the generation of zinc carbenoids still remains very limited (Scheme 1 a). In fact, more than fifty years after the seminal work of Simmons and Smith, diiodoalkanes remain the most common precursors of zinc carbenoids. Regarding the zinc source, subsequent developments enabled the replacement of the originally used Zn/Cu couple by alternative stoichiometric zinc precursors, which in a number of cases improved the efficiency or selectivity of the cyclopropanation reaction.[3] Elegant studies performed by Denmark et al. and Charette et al. support a halomethylzinc structure for these reagents.[4] Alternatively, zinc carbenoids can be generated by making use of diazo compounds and zinc salts as disclosed by Wittig and Schwarzenbach.[5] Moreover, Motherwell et al. described that carbonyl groups and acetals, upon treatment with zinc and chlorotrialkylsilanes, afford zinc carbenoids which can be additionally trapped.[6] It is noteworthy that all these approaches to zinc carbenoids are stoichiometric processes, with, to our knowledge, only one remarkable example of a catalytic transformation using phenyldiazomethane as the sole carbenoid source.[7] Consequently, the development of broadly applicable methodologies for the catalytic generation of zinc carbenoids is highly desirable.

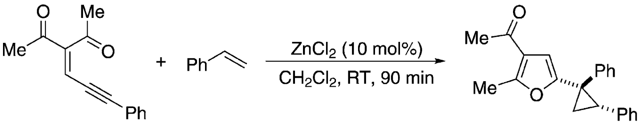


Scheme 1. Different approaches for the generation of zinc carbenoid species.

Additionally, zinc complexes proved capable of activating alkynes, both in a stoichiometric or catalytic fashion.[8] Interestingly, as early as 1976, Ohloff and co-workers reported a $ZnCl_2$-mediated rearrangement of propargyl acetates which afforded cyclopropane derivatives, albeit in a very low yield.[9] Despite these precedents, the catalytic generation of efficient cyclopropanating intermediates from alkynes and zinc salts has, to date, not evolved into a synthetically useful methodology. To achieve this goal, we hypothesized that a sequence involving initial coordination of the zinc to the alkyne and a subsequent nucleophilic attack, similar to that reported for other transition metals,[10] could afford intermediates such as **A** or **B**, which could be active in cyclopropanation reactions (Scheme 1 b).

Herein, we report the catalytic generation of zinc(II) furylcarbenes derived from carbonyl ene-yne compounds and zinc salts as well as their reactivity in addition and insertion processes. A theoretical study of the nature of the involved intermediates is also disclosed.

We started our investigation by using compound **1a** as the model substrate in the presence of styrene (**2a**), the carbenoid trapping reagent. Initial reactions were run at room temperature in dichloromethane by employing a series of zinc catalysts (10 mol%; Scheme 2; see the Supporting Information for a summary of the screening). To our delight, we found that $ZnCl_2$ produced the desired cyclopropane **3a** in nearly quantitative yield (99%) as a 3.5:1 mixture of diastereoiso-



1a **2a** **3a** (99%, d.r. = 3.5:1)

Scheme 2. Zinc-catalyzed reaction of **1a** and styrene (**2a**): initial finding.

---

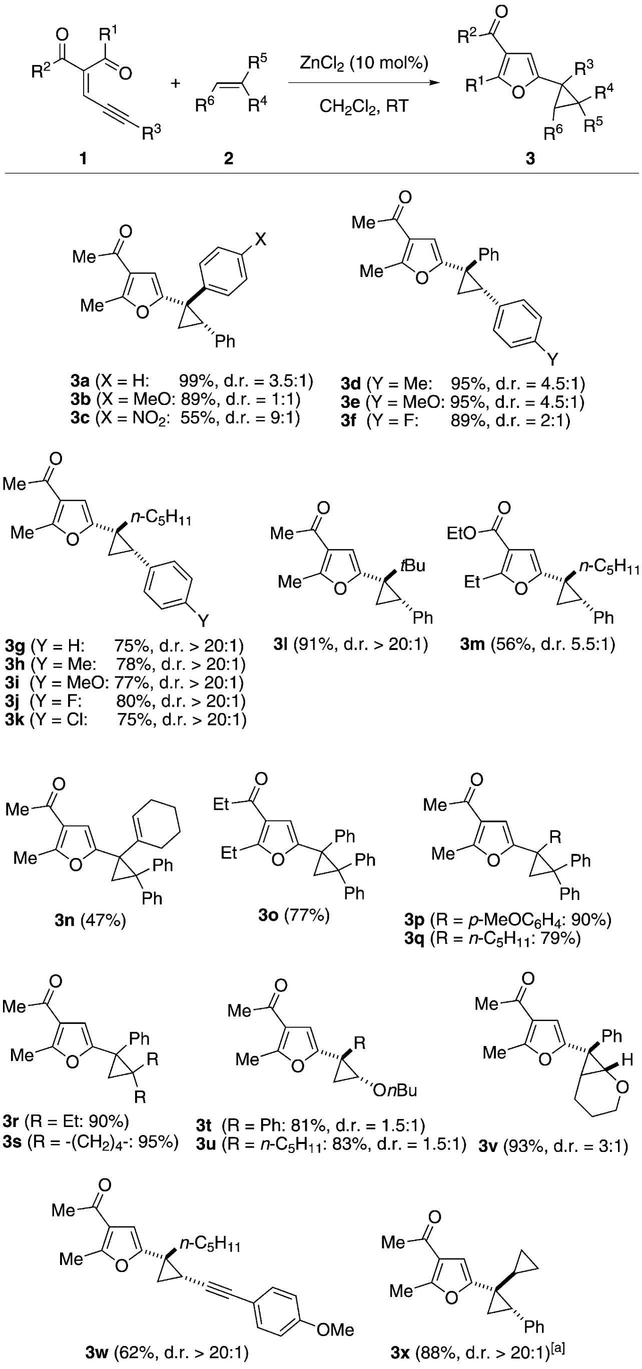
[*] Dr. R. Vicente, J. González, Dr. L. Riesgo, Dr. J. González, Dr. L. A. López
Departamento de Química Orgánica e Inorgánica e Instituto Universitario de Química Organometálica "Enrique Moles"
Universidad de Oviedo, c/Julián Clavería 8, 33007 Oviedo (Spain)
E-mail: vicenteruben@uniovi.es
lalg@uniovi.es

[**] We are grateful to the Ministerio de Economía y Competitividad of Spain (Grant CTQ2010-20517-C02-01) for funding. J.G. and L.R thank the MICINN and European Union (Fondo Social Europeo) for predoctoral grants. The calculations were carried out at the "Cluster de Modelización Científica" (Universidad de Oviedo). R.V. is a Ramón y Cajal Fellow. We thank Prof. J. Barluenga and Prof. M. Tomás for helpful discussions.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201203914.

mers after chromatographic purification ,[11] thus confirming that a zinc carbene was indeed generated.

By using these reaction conditions [$ZnCl_2$ (10 mol%), CH_2Cl_2, room temperature] we explored the scope of this remarkable transformation (Scheme 3). We were pleased to find that the zinc(II)-catalyzed cyclization/cyclopropanation sequence tolerated a wide range of olefin substitutions including monosubstituted (see **3a**–**m**) and disubstituted (see **3n**–**s**) alkenes. Electron-rich olefins, such as *n*-butylvinylether or dihydropyran smoothly underwent the zinc-catalyzed cyclopropanation to afford the corresponding products **3t**–**v**. Interestingly, the reaction with 1-(4-methoxyphenyl)-3-buten-1-yne occurred with complete chemoselectivity, thus affording the corresponding alkynylcyclopropane **3w** in a respectable yield (62%). With regard to the substrate **1**, a variety of carbonyl ene-yne compounds derived either from 1,3-diketones or from β-ketoesters undergo this zinc-catalyzed process. Moreover, the reaction was found to tolerate a broad range of groups (R^3) on the alkyne terminus, including aryl, alkyl, and alkenyl groups. Interestingly, even R^3 = cyclopropyl is compatible with this catalytic process, thus affording the 1,1′-bi(cyclopropane) derivative **3x** in excellent yield. The diastereoselectivity of the cyclopropanation reaction was dependent upon the nature of both the alkyne and the olefin counterpart. In general, alkyl-substituted alkynes (R^3 = alkyl) produced cyclopropanes with higher diastereoselectivities.

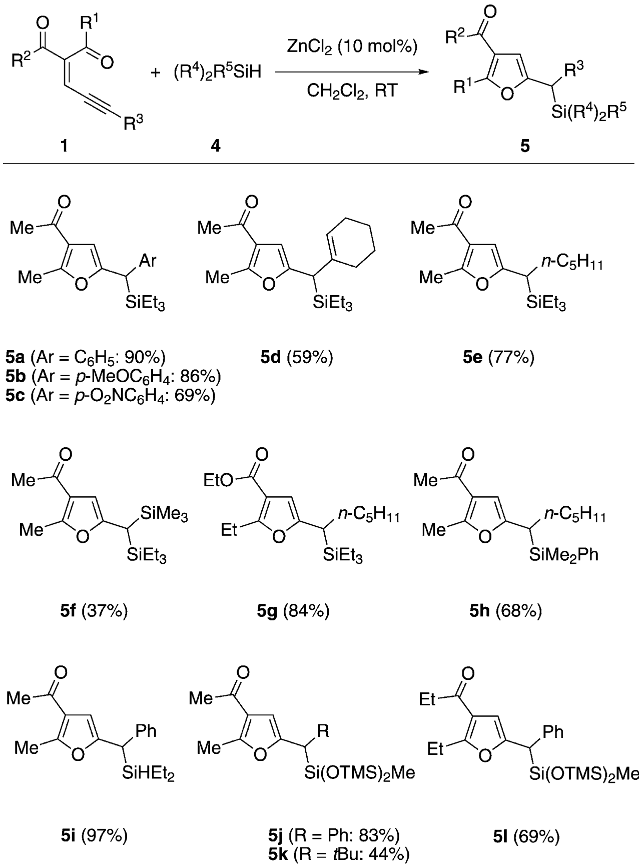


3a (X = H: 99%, d.r. = 3.5:1)
3b (X = MeO: 89%, d.r. = 1:1)
3c (X = NO_2: 55%, d.r. = 9:1)
3d (Y = Me: 95%, d.r. = 4.5:1)
3e (Y = MeO: 95%, d.r. = 4.5:1)
3f (Y = F: 89%, d.r. = 2:1)
3g (Y = H: 75%, d.r. > 20:1)
3h (Y = Me: 78%, d.r. > 20:1)
3i (Y = MeO: 77%, d.r. > 20:1)
3j (Y = F: 80%, d.r. > 20:1)
3k (Y = Cl: 75%, d.r. > 20:1)
3l (91%, d.r. > 20:1)
3m (56%, d.r. 5.5:1)
3n (47%)
3o (77%)
3p (R = *p*-MeOC_6H_4: 90%)
3q (R = *n*-C_5H_{11}: 79%)
3r (R = Et: 90%)
3s (R = -$(CH_2)_4$-: 95%)
3t (R = Ph: 81%, d.r. = 1.5:1)
3u (R = *n*-C_5H_{11}: 83%, d.r. = 1.5:1)
3v (93%, d.r. = 3:1)
3w (62%, d.r. > 20:1)
3x (88%, d.r. > 20:1)[a]

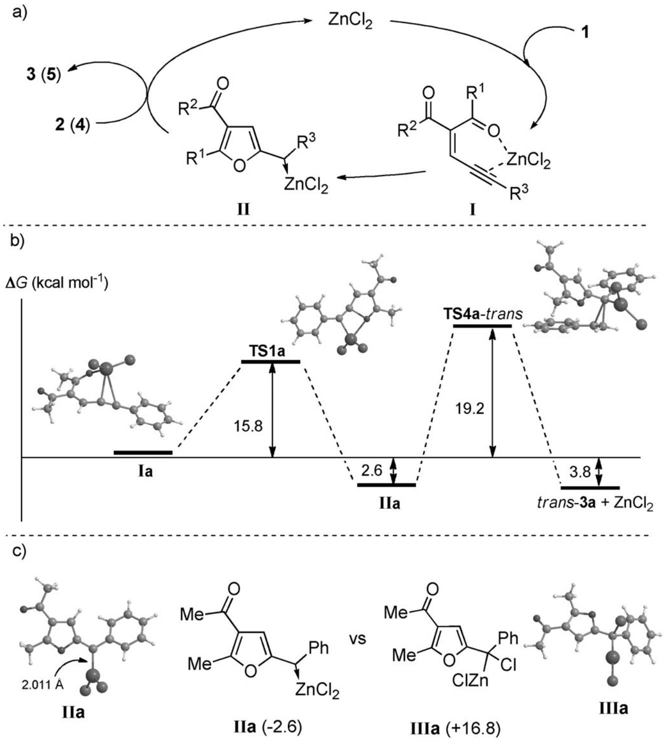
Scheme 3. Zinc(II)-catalyzed synthesis of cycloproplylfurans **3** from carbonyl ene-yne derivatives **1** and alkenes **2**. Reaction conditions: **1** (0.2 mmol), **2** (6 equiv), $ZnCl_2$ (10 mol%), CH_2Cl_2 (0.1 M), RT. Values in parentheses are the yields of the isolated products. The diastereoisomeric ratio was determined by ^1H NMR spectroscopy. [a] Reaction performed at 0°C.

Considering the feasibility of generating zinc carbenoid intermediates in this catalytic manner, we next decided to exploit this strategy in other processes with the aim to increase their synthetic potential. Thus, we turned our attention to the study of the insertion into a Si–H bond. Although metal carbenoid insertion into X–H bonds is a well-established process,[12] surprisingly, this methodology remains virtually unexplored in the case of zinc carbenoids.[13] Moreover, to the best of our knowledge zinc-catalyzed Si–H insertion reactions have not been yet reported. Thus, we decided to explore the viability of our system for this significant reaction class.[14] The results of our study involve a cyclization/Si–H bond insertion sequence as shown in Scheme 4. Again, different substitution patterns in compounds **1** proved to work satisfactorily (R^1 = Me, Et; R^2 = Me, Et, EtO; R^3 = aryl, alkenyl or alkyl), thus affording the corresponding silane derivatives **5a**–**g** in moderate to good yields. Regarding the silane, the reaction proceeded efficiently with various silanes (**4**), including trialkyl-, dialkylaryl-, and dialkylsilanes as well as 1,1,1,3,5,5,5-heptamethyltrisiloxane. Moreover, when using a silyl-substituted alkyne, a derivative bearing two different silyl groups, trimethylsilyl (TMS) and triethylsilyl (TES), at the same carbon atom was obtained (**5f**).

A mechanistic proposal to rationalize the obtained results is given in Scheme 5a. Initial coordination of the substrate to $ZnCl_2$ affords the intermediate **I**, where zinc is coordinated to a carbonyl group and the alkyne.[15] The complex **I** would then undergo an intramolecular 5-*exo*-dig cyclization by nucleophilic attack of the carbonyl oxygen atom onto the C4 carbon atom, thus affording the zinc complex **II**. Subsequent reaction of **II** with the alkenes **2** or silanes **4** would afford the final products **3** or **5**, respectively. The structure of the final products clearly suggests the participation of a zinc furyl carbene **II** as a key intermediate, which can be considered a vinylogous heteroatom-stabilized Fischer-type zinc(II) carbene complex. However, the participation of the classical Simmons–Smith carbenoid intermediate **III** (see Scheme 5c for structure) could not be ruled out.[16] For a better understanding of the nature of this species, a computational study of



Scheme 4. Zinc(II)-catalyzed synthesis of furan derivatives **5** from carbonyl ene-yne derivatives **1** and silanes **4**. Reaction conditions: **1** (0.2 mmol), **4** (6 equiv), ZnCl$_2$ (10 mol%), CH$_2$Cl$_2$ (0.1 M), RT. Values in parentheses are the yields of the isolated products.

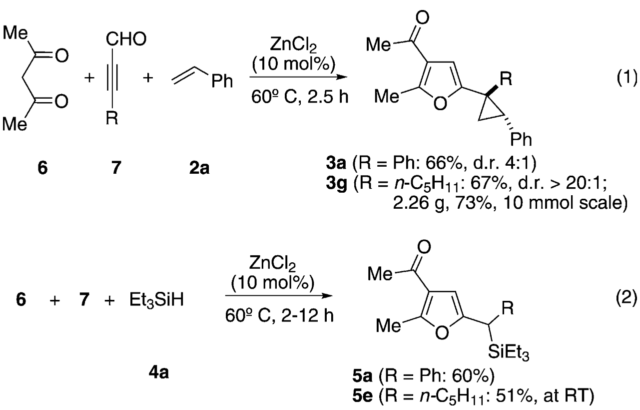


Scheme 5. Proposed mechanism for the zinc-catalyzed cyclization of compounds **1**. a) Catalytic cycle. b) Energy profile of the cyclopropanation of styrene. Computational study was performed with **1a**; ΔG_{rel} values in kcal mol^{-1} with respect to **Ia** are given in parentheses. c) Fischer-type zinc carbene (**IIa**) versus Simmons–Smith carbene (**IIIa**) intermediates.

this transformation was carried out.[17] Thus, the potential energy surface of the cyclization of the enyne **1a** in the presence of ZnCl$_2$ was explored (Scheme 5b). The calculations supported the participation of intermediates **Ia** (0.0 kcal mol^{-1}) and **IIa** (-2.6 kcal mol^{-1}) in the cyclization of **1a**. The predicted length of the C–Zn bond of **IIa** is 2.011 Å, which is similar to the one reported for related complexes.[18] According to our calculations, **IIa** is predicted to be more stable than **IIIa** by 16.8 kcal mol^{-1}.

The cyclopropanation reaction involving **II** was studied next.[19] The reaction with styrene (**2a**) occurred through a concerted, but asynchronous, transition structure, with **TS4a**-*trans* being favored over **TS4a**-*cis* (not shown, 21.8 versus 24.0 kcal mol^{-1}), as experimentally observed. Finally, the formation of *trans*-**3a** was predicted to be exothermic (-3.8 kcal mol^{-1}). Importantly, the potential energy surface for the cyclopropanation with the carbenoid intermediate **IIIa** was also explored. However, we did not find a first-order saddle point connecting **IIIa** and the reaction products. Accordingly, at this stage, we believe that the Fischer-type zinc carbene intermediate **II** is likely the active species. Likewise, the Si–H bond insertion took place via a concerted asynchronous transition structure (see the Supporting Information).[20]

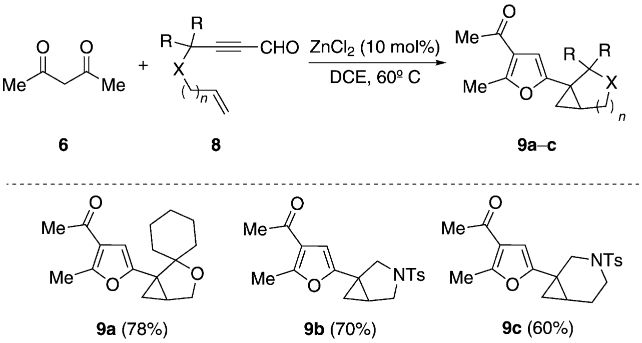
Next, considering the known ability of ZnCl$_2$ to catalyze some Knoevenagel reactions,[21] we decided to explore the feasibility of accessing compounds **3** and **5** in a straightforward manner through a multicomponent reaction. Indeed, we were pleased to find that heating a mixture of dione **6** (1.0 equiv), the corresponding 3-substituted prop-2-ynal **7** (1 equiv) and styrene (**2a**, 6.0 equiv) in the presence of ZnCl$_2$ (10 mol%) at 60 °C for 2 hours afforded the cyclopropylfurans **3a,g** in reasonable yields and with similar diastereoselectivities to those described above [Eq. (1); Scheme 6]. It is noteworthy



Scheme 6. Zinc(II)-catalyzed multicomponent synthesis of furans **3** and **5** (yields of isolated products given in parentheses).

that in this operationally simple protocol, three commercially available reagents were assembled through a condensation/cyclization/cyclopropanation sequence, in which three C–C bonds and one C–O bond were selectively created. Moreover, this protocol was accomplished on a multigram scale (10 mmol) with the same efficiency, as demonstrated for the cyclopropane **3g** (2.26 g, 73 %). Similarly, by replacing the olefin by triethylsilane (**4a**), under otherwise identical reaction conditions, this multicomponent approach proved also applicable to the synthesis of the furan derivatives **5a** and **5e** in good yields [Eq. (2); Scheme 6].

Finally, we decided to apply this zinc-catalyzed one-pot procedure to the preparation of polycyclic compounds through an intramolecular cyclopropanation. Thus, the treatment of 2,4-pentanedione (**6**) with an equimolecular amount of the corresponding enynal **8** (dichloroethane, 60 °C, 2–4 h) in the presence of ZnCl$_2$ (10 mol %) gave rise to synthetically relevant 3-oxa- and 3-azabicyclo[*n*.1.0]alkane derivatives **9a–c** in good yields (Scheme 7).[22]



Scheme 7. Zinc(II)-catalyzed synthesis of polycyclic compounds **9** (yields of isolated products given in parentheses). Ts = 4-toluenesulfonyl.

In conclusion, we have disclosed a novel approach to the catalytic generation of synthetically valuable zinc carbenes by using alkynes and zinc salts. These new zinc carbenes have been employed in cyclopropanation and Si–H bond insertion reactions, which can now be accomplished in a catalytic manner. The overall process enabled an efficient synthesis of highly substituted furans, thus making use of easily available materials and inexpensive ZnCl$_2$, having low toxicity, as the catalyst.[23] Moreover, we have combined this methodology with known Knoevenagel condensations to develop convenient selective multicomponent or intramolecular reactions. A computational study indicates the participation of a 2-furyl zinc(II) Fischer-type carbene complex, whose structure is different to those previously proposed for Simmons–Smith reactions. Further investigations directed at the development of other sustainable and environmentally friendly synthetic protocols based on this unprecedented approach to zinc(II) carbenes, as well as the isolation of these intermediates are currently underway in our group.

Experimental Section

Representative procedure (**3a**; Scheme 3): ZnCl$_2$ (2.7 mg, 0.02 mmol, 10 mol %) was added to a solution of the enyne **1a** (42 mg, 0.2 mmol) and styrene (**2a**) (125 mg, 1.2 mmol, 6.0 equiv) in CH$_2$Cl$_2$ (2 mL). The mixture was stirred at room temperature until the disappearance of **1a** (monitored by TLC; 1.5 h). The solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (SiO$_2$, *n*-hexane/EtOAc 20:1) to yield **3a** (63 mg, 99 %, d.r. = 3.5:1) as a pale yellow oil.

Received: May 21, 2012

Keywords: carbenes · heterocycles · insertion · small ring systems · zinc

---

[1] a) H. E. Simmons, R. D. Smith, *J. Am. Chem. Soc.* **1958**, *80*, 5323; b) H. E. Simmons, R. D. Smith, *J. Am. Chem. Soc.* **1959**, *81*, 4256.

[2] Selected reviews on cyclopropanes: a) W. A. Donaldson, *Tetrahedron* **2001**, *57*, 8589; b) H. Lebel, J.-F. Marcoux, C. Molinaro, A. B. Charette, *Chem. Rev.* **2003**, *103*, 977; c) H.-U. Reissig, R. Zimmer, *Chem. Rev.* **2003**, *103*, 1151; d) F. Brackmann, A. de Meijere, *Chem. Rev.* **2007**, *107*, 4493; e) H. Pellissier, *Tetrahedron* **2008**, *64*, 7041.

[3] For a selection of modified protocols for the preparation of cyclopropanating reagents from CH$_2$I$_2$, see: a) J. Furukawa, N. Kawabata, J. Nishimura, *Tetrahedron Lett.* **1966**, *7*, 3353; b) J. Furukawa, N. Kawabata, J. Nishimura, *Tetrahedron* **1968**, *24*, 53; c) S. E. Denmark, J. P. Edwards, *J. Org. Chem.* **1991**, *56*, 6974; d) Z. Yang, J. C. Lorenz, Y. Shi, *Tetrahedron Lett.* **1998**, *39*, 8621; e) A. B. Charette, S. Francoeur, J. Martel, N. Wilb, *Angew. Chem.* **2000**, *112*, 4713; *Angew. Chem. Int. Ed.* **2000**, *39*, 4539; f) A. B. Charette, C. Molinaro, C. Brochu, *J. Am. Chem. Soc.* **2001**, *123*, 12160; g) A. B. Charette, A. Beauchemin, S. Francoeur, *J. Am. Chem. Soc.* **2001**, *123*, 8139.

[4] a) S. E. Denmark, J. P. Edwards, S. R. Wilson, *J. Am. Chem. Soc.* **1991**, *113*, 723; b) S. E. Denmark, J. P. Edwards, S. R. Wilson, *J. Am. Chem. Soc.* **1992**, *114*, 2592; c) A. B. Charette, J.-F. Marcoux, *J. Am. Chem. Soc.* **1996**, *118*, 4539; d) A. B. Charette, J.-F. Marcoux, F. Bélanger-Gariépy, *J. Am. Chem. Soc.* **1996**, *118*, 6792; e) A. B. Charette, J.-F. Marcoux, C. Molinaro, A. Beauchemin, C. Brochu, E. Isabel, *J. Am. Chem. Soc.* **2000**, *122*, 4508.

[5] a) G. Wittig, K. Schwarzenbach, *Angew. Chem.* **1959**, *71*, 652. For other contributions on the use of diazo reagent and zinc salts in cyclopropanation reactions, also see: b) S. H. Goh, L. E. Closs, G. L. Closs, *J. Org. Chem.* **1969**, *34*, 25; c) L. J. Altman, R. C. Kowerski, H. C. Rilling, *J. Am. Chem. Soc.* **1971**, *93*, 1782; d) L. J. Altman, R. C. Kowerski, D. R. Laungani, *J. Am. Chem. Soc.* **1978**, *100*, 6174.

[6] a) W. B. Motherwell, L. R. Roberts, *J. Chem. Soc. Chem. Commun.* **1992**, 1582; b) R. J. Fletcher, W. B. Motherwell, M. E. Popkin, *Chem. Commun.* **1998**, 2191; c) W. B. Motherwell, *J. Organomet. Chem.* **2001**, *624*, 41; d) W. B. Motherwell, *Pure Appl. Chem.* **2002**, *74*, 135; e) G. Bégis, D. E. Cladingboel, W. B. Motherwell, *Chem. Commun.* **2003**, 2656; f) W. B. Motherwell, G. Bégis, D. E. Cladingboel, L. Jerome, T. D. Sheppard, *Tetrahedron* **2007**, *63*, 6462.

[7] S. R. Goudreau, A. B. Charette, *J. Am. Chem. Soc.* **2009**, *131*, 15633. For a seminal study on catalytic Simmons–Smith reactions, see Ref. [5b].

[8] For selected examples, see: a) A. Zulys, M. Dochnahl, D. Hollmann, K. Löhnwitz, J.-S. Herrmann, P. W. Roesky, S. Blechert, *Angew. Chem.* **2005**, *117*, 7972; *Angew. Chem. Int. Ed.* **2005**, *44*, 7794; b) A. Sniady, A. Durham, M. S. Morreale, K. A. Wheeler, R. Dembisky, *Org. Lett.* **2007**, *9*, 1175; c) K.

Alex, A. Tillack, N. Schwarz, M. Beller, *Angew. Chem.* **2008**, *120*, 2337; *Angew. Chem. Int. Ed.* **2008**, *47*, 2304; d) J.-W. Pissarek, D. Schlesiger, P. W. Roesky, S. Blechert, *Adv. Synth. Catal.* **2009**, *351*, 2081; e) C.-L. Deng, R.-J. Scong, Y.-L. Liu, J.-H. Li, *Adv. Synth. Catal.* **2009**, *351*, 3096; f) X. Zhao, X.-G. Zhang, R.-Y. Tang, C.-L. Deng, J.-H. Li, *Eur. J. Org. Chem.* **2010**, 4211; g) T. Sugiishi, H. Nakamura, *J. Am. Chem. Soc.* **2012**, *134*, 2504.

[9] H. Strickler, J. B. Davis, G. Ohloff, *Helv. Chim. Acta* **1976**, *59*, 1328.

[10] For representative reviews, see: a) K. Miki, S. Uemura, K. Ohe, *Chem. Lett.* **2005**, *34*, 1068; b) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478; *Angew. Chem. Int. Ed.* **2007**, *46*, 3410; c) L. Zhang, J. Sun, S. A. Kozmin, *Adv. Synth. Catal.* **2006**, *348*, 2271; d) E. Jiménez-Núñez, A. Echavarren, *Chem. Rev.* **2008**, *108*, 3326; e) M. Marion, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 2806; *Angew. Chem. Int. Ed.* **2007**, *46*, 2750.

[11] A lower catalyst loading (5.0 mol%) gave rise to a similar yield (93%), however, a longer reaction time was required (24 h). Moreover, the AuCl$_3$-catalyzed reaction of compound **1a** with styrene (**2a**) afforded the cyclopropane **3a**, but with lower efficiency and selectivity. See: T. Wang, J. Zhang, *Dalton Trans.* **2010**, *39*, 4270.

[12] *Metal Carbenes in Organic Synthesis* (Ed.: K. H. Dötz), Springer, New York, **2004**.

[13] Only two examples of stoichiometric Si−H bond insertion reactions of zinc carbenoids have been reported: a) J. Nishimura, J. Furukawa, N. Kawabata, *J. Organomet. Chem.* **1971**, *29*, 237; b) H. Kondo, Y. Yamanoi, H. Nishihara, *Chem. Commun.* **2011**, *47*, 6671.

[14] Organosilanes are versatile compounds in both synthetic and materials chemistry. For representative reviews, see: a) L. Nicole, C. Boissier, D. Grosso, A. Quach, C. Sánchez, *J. Mater. Chem.* **2005**, *15*, 3598; b) A. Hosomi, K. Miura, *Bull. Chem. Soc. Jpn.* **2004**, *77*, 835.

[15] A related coordination mode has been proposed recently in zinc(II)-catalyzed Conia-ene reactions: a) W. Hess, J. W. Burton, *Adv. Synth. Catal.* **2011**, *353*, 2966; b) S. Yamazaki, *Chem. Eur. J.* **2008**, *14*, 6026.

[16] For a theoretical study on the metal carbene versus carbenoid complex preference of some transition-metal catalysts, see: F. Bernardi, A. Bottoni, G. P. Miscione, *Organometallics* **2000**, *19*, 5529.

[17] This study was performed with the density functional theory, using the hybrid functional B3LYP and the 6-31G(d) basis set and employing Gaussian03, see the Supporting Information for details. M. J. Frisch et al. Gaussian 03, revision C.02; Gaussian, Inc., Wallingford, CT, **2009**.

[18] a) T. R. Jensen, C. P. Schaller, M. A. Hillmyer, W. B. Tolman, *J. Organomet. Chem.* **2005**, *690*, 5881; b) D. Wang, K. Wurst, M. Buchmeiser, *J. Organomet. Chem.* **2004**, *689*, 2123.

[19] For computational studies on the Simmons–Smith reaction, see: a) F. Bernardi, A. Bottoni, G. P. Miscione, *J. Am. Chem. Soc.* **1997**, *119*, 12300; b) W. H. Fang, D. L. Phillips, D. Wang, Y.-L. Li, *J. Org. Chem.* **2002**, *67*, 154.

[20] A concerted pathway has also been proposed for Si−H bond insertions of electrophilic rhodium carbenoids: Y. Landais, L. Parra-Rapado, D. Planchenault, V. Weber, *Tetrahedron Lett.* **1997**, *38*, 229.

[21] P. S. Rao, R. V. Venkataratnam, *Tetrahedron Lett.* **1991**, *32*, 5821.

[22] The bicyclo[*n*.1.0]alkane core is present in many natural products and bioactive substances. See, for example: a) K. S. MacMillan, T. Nguyen, I. Hwang, D. L. Boger, *J. Am. Chem. Soc.* **2009**, *131*, 1187; b) F. Micheli, D. Hamprecht, G. Bonanomi, R. Di Fabio, D. Donati, G. Gentile, C. Heidbreder, A. Prandi, L. Tarsi, S. Terreni, *Bioorg. Med. Chem. Lett.* **2009**, *19*, 5056.

[23] Prices of commonly used transition-metal salts (related to 10 mmol at $>$99.9% purity, Sigma–Aldrich, 1.05.2012): ZnCl$_2$: 11.0 €; FeCl$_3$: 29.6 €; CuCl$_2$: 22.1 €; PdCl$_2$: 128.0 €; AuCl: 358.1 €; AuCl$_3$: 609.1 €; PtCl$_2$: 490.4 €; RhCl$_3$: 1045.8 €.