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Selectivity in Metal-Catalyzed Carbon–Carbon Bond Cleavage of Alkylidenecyclopropanes

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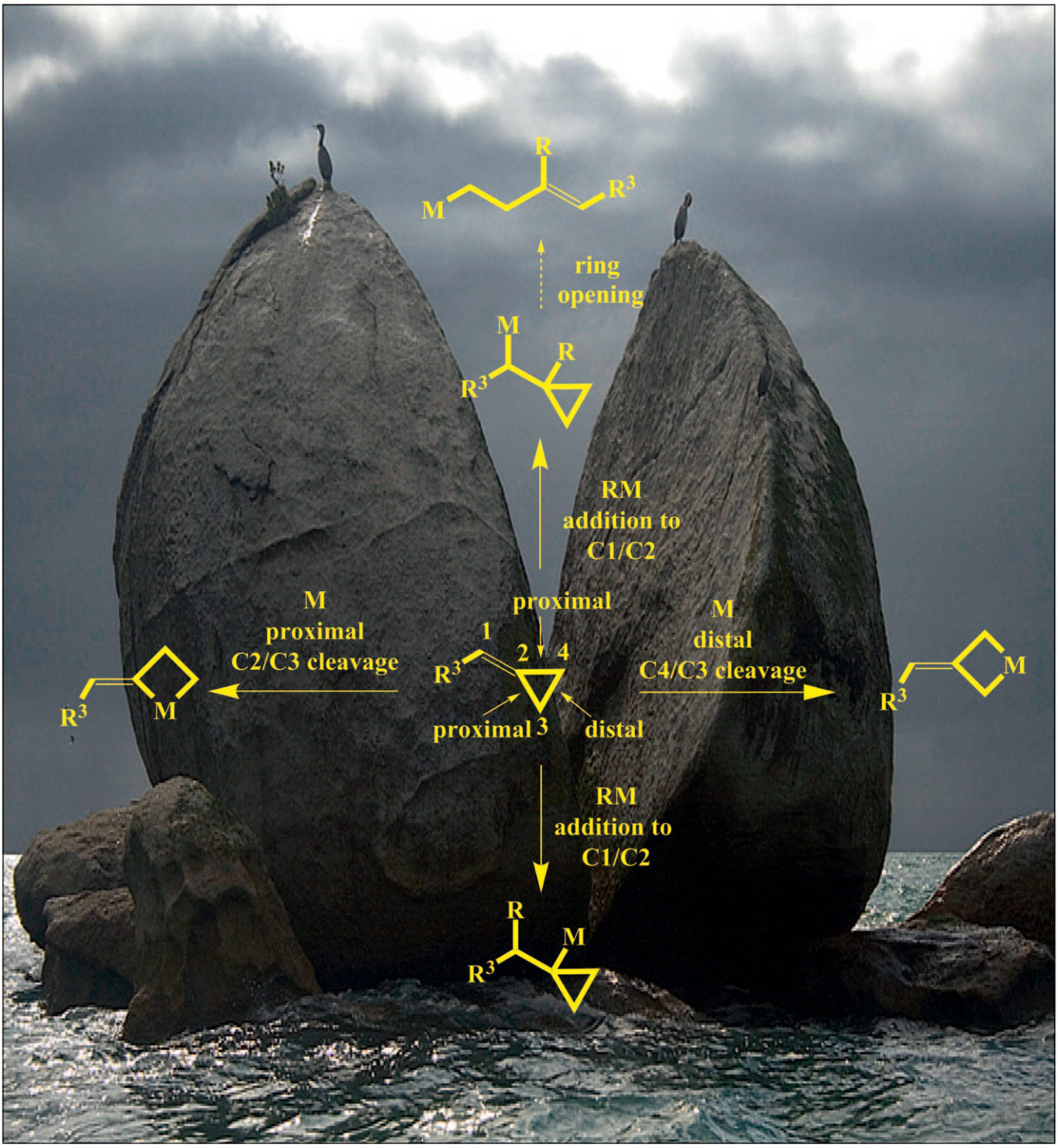
Dedicated to Professor José Barluenga on the occasion of his 70th birthday



Abstract: When more complex system leads to simpler reactivity profile; the ring-opening of strained three-membered rings such as methylene- and alkylidenecyclopropanes generally lead to several products. If one starts with more functionalized carbon skeletons, selective reactions are now observed and rationalization as well as synthetic applications are described in this concept article. This methodology could be used to the preparation of challenging structural motifs possessing quaternary carbon stereocenters in acyclic systems.

Keywords: alkylidenecyclopropane · insertion · quaternary stereocenters · ring-opening · selectivity

Introduction

Metal-catalyzed cleavage of carbon–carbon bonds is a field of major interest since it can lead to the design of new, selective and efficient processes for the functionalization of non-reactive hydrocarbons.[1] Following the original activation of C–C single bonds of cyclopropylcarbinyl Grignard reagents[2] and metal-promoted carbon–carbon activation of strained alkanes,[3] the carbon–carbon activation of methylenecyclopropanes (MCPs) and alkylidenecyclopropanes (ACPs),[4] through transition-metal catalysts, has emerged[5] and different reactivities could be observed and are summarized in Scheme 1. In a general approach, when the cyclopropane ring of MCP **1** reacts with transition-metal catalyst M, two different types of reaction patterns could be envisaged; 1) insertion of M into the distal (C3/C4) bond to give **2**; 2) insertion of M into the proximal (C2/C3) bond to provide **3**.[6] From the examples collected over the years, it has been established that cycloadditions catalyzed by "naked" nickel catalysts [Ni(cod)$_2$] favor the proximal ring-opening, whereas in the presence of phosphine or phosphite ligands, a preference for a cleavage of the distal bond is observed.[7] When the exomethylene part of **1** first reacts with an organometallic species RML$_n$, two different regioisomers could be formed during the carbometalation reaction;[8] the addition of RML$_n$ leading to metalated C1 gives the anti-Markovnikov adduct **4** that usually undergo a further ring-opening reaction whereas the Markovnikov addition leads to product **5**.[9] In all cases, functionalization of the carbon skeleton can be achieved by adding electrophiles to the resulting organometallic species.[10]

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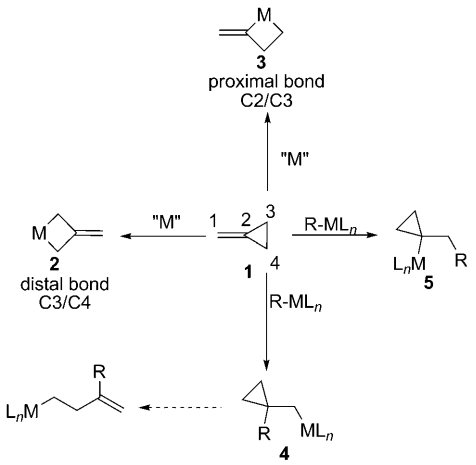


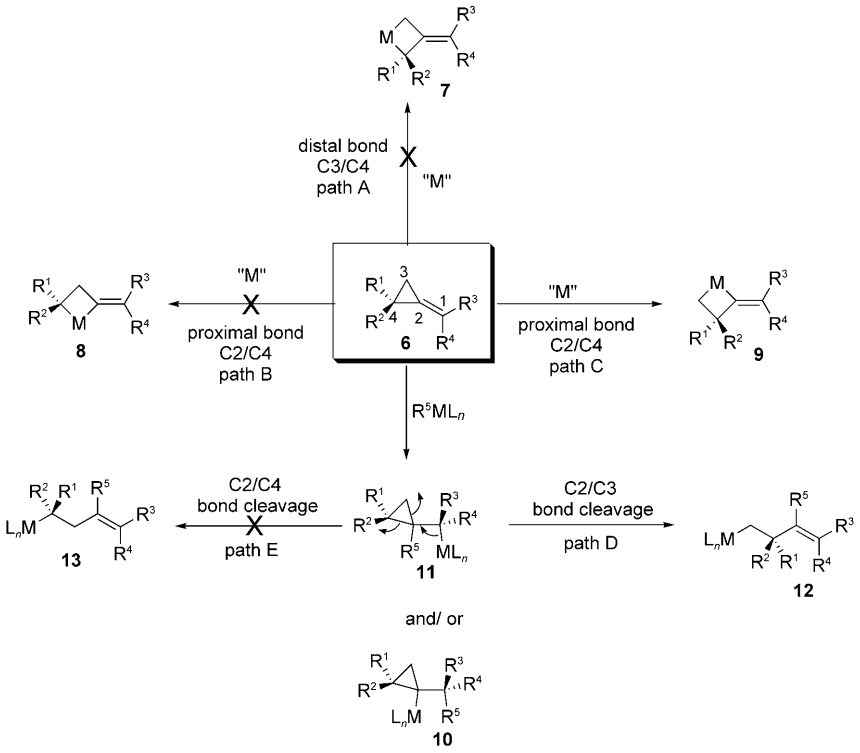
Scheme 1. General reactions of methylenecyclopropanes.

As can be seen from Scheme 1, the attractive but often troublesome feature of methylenecyclopropane is their multiform reactivities that may lead to the formation of a variety of products. A predictable control of the reactivity of MCPs and ACPs would be therefore synthetically important for the formation of a unique product. However, the control can't be achieved by adjusting reaction conditions but is inherent to the structure of the substrate. Thus, in order to control the reactivity and selectivity of such reactions, one has to design a substrate in which only a restricted numbers of possible reactions could occur.

Discussion

Our hypothesis was that adding complexity in the starting MCPs and ACPs (i.e., substituted ACPs) should lead to selective reactions. For instance, the distal insertion of a catalyst M to a more challenging ACPs **6**, possessing a quaternary stereocenter on the cyclopropyl ring, would lead to an unfavorable tertiary organometallic species **7** (path A, Scheme 2).[11] Therefore, products resulting from a distal insertion should not be formed in the reaction. If the proximal insertion of the catalyst M is now considered, two insertions are theoretically possible. The proximal insertion into the C2/C4 bond leads to a tertiary and vinyl organometallic **8** (path B, Scheme 2) whereas the proximal insertion into the C2/C3 bond would lead to a primary and vinyl organometallic species **9** (path C, Scheme 2). Here again, from these two possible reaction products, **9** should be preferentially formed (primary versus tertiary organometallic species).

If one considers the carbometalation of an organometallic species R^5-ML$_n$ to the *exo*-alkylidene moiety of **6**, the formation of either the Markovnikov or anti-Markovnikov adducts (**10** and **11**, respectively) should only be dependent of the nature of the substituents on the double bond (R^3 and R^4). Indeed, if the substituent R^3 is a hydrogen, alkyl or aryl



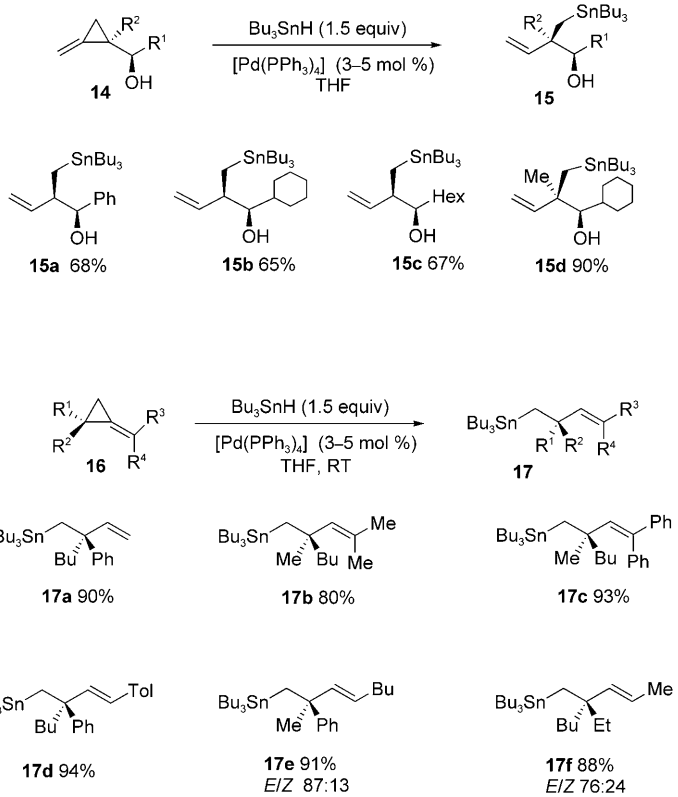
Scheme 2. Selectivity in the ring-opening of strained three-membered rings.

groups whereas R^4 is a hydrogen (or vice versa), the formation of the anti-Markovnikov adduct **11** should be preferred (primary and secondary organometallic adducts should be formed at the expense of tertiary cyclopropyl metal species). However, if the two substituents R^3 and R^4 are alkyl groups, we should reach the limit of the system and no selectivity should be expected.

If the carbometalation is performed on a properly substituted ACPs to give **11**, two possible ring-cleavage adducts could be obtained. If the carbon–carbon activation occurs through the C2/C3 bond, a primary acyclic organometallic species **12** would be obtained (path D, Scheme 2). On the other hand, if the ring opening occurs through the cleavage of the C2/C4 bond, the less stable trisubstituted organometallic species **13** would result (path E, Scheme 2). Based on the same assumption that primary organometallic is more stable than the tertiary one, we anticipated that only regioisomer **12** would be obtained in such a process (the isomerisation of alkylmetal species into π-allyl,[12] that is, palladium species, could not proceed if adjacent to quaternary stereocenter). Moreover, if the ring-opening indeed occurs through the C2/C3 bond, the organometallic species would be obtained potentially with a full preservation of the stereochemical information of the initial stereochemistry at the quaternary center. Therefore, as described previously, a more complex system leads to a simpler reactivity profile, and substituted MCPs and ACPs should lead to more selective transformations. The purpose of this concept article is to delineate the reactivity of substituted MCPs and ACPs with organometallic species RML_n (metal-catalyzed [3+2] cycloadditions were already treated in an excellent review and will not be discussed here).[4d]

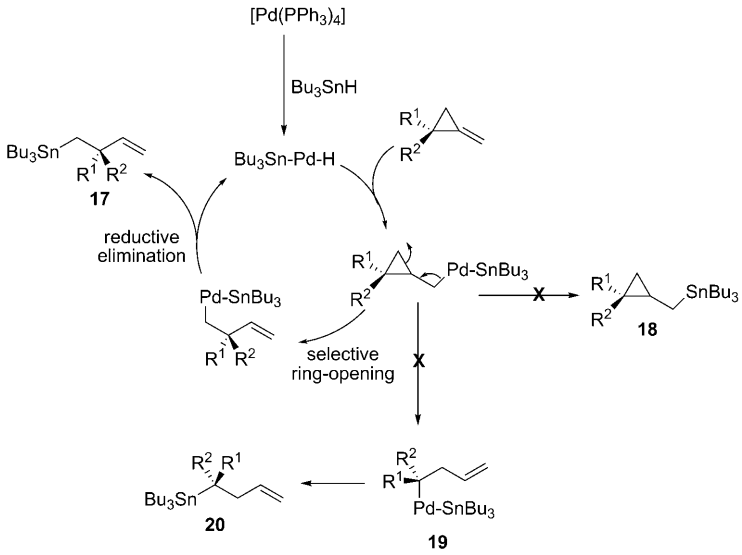
Pioneering results were obtained when (methylenecyclopropyl)carbinols **14** were treated with a slight excess of tributyltin hydride in THF in the presence of a catalytic amount of tetrakis(triphenylphosphine)-palladium (3–5 mol%). The corresponding ring-opened homoallylstannanes were obtained in good to excellent yields and as single diastereomers (Scheme 3).[13]

The relative stereochemistry of homoallylstannane **15** corresponds to that of the parent compound **14**, establishing that there is no loss of the stereochemical information initially present in the (methylenecyclopropyl)carbinol **14** throughout the course of the reaction. The same reaction could also be successfully applied to alkylidenecyclopropane derivatives



Scheme 3. Palladium-catalyzed hydrostanation of MCPs and ACPs.

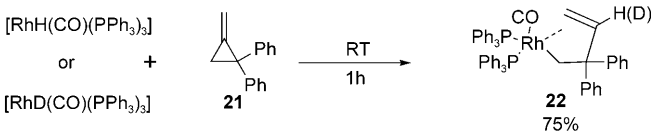
16 and selective ring-opening products **17** were obtained in all cases (Scheme 3).[14] The formation of the linear products could be rationalized through the following mechanism: Oxidative addition of a zero-valent palladium into the tin–hydrogen bond of tributyltin hydride first generates a stannylpalladium hydride species which hydropalladates the MCPs affording the (cyclopropylmethyl)palladium stannane. Importantly, the ring-opening is 1) faster then reductive elimination since no cyclopropylstannanes **18** were observed and 2) highly regioselective carbon–carbon activation is observed since primary homoallylpalladium stannane rather than a secondary or tertiary one were obtained. Even when potentially stable benzylpalladium species could be formed as intermediate (formation of **17a**,**d**,**e**), the ring opening product always leads to the primary adduct **17** and not **20** (Scheme 4).



Scheme 4. Mechanism of the Pd-catalyzed hydrostanation.

When 2,2-diphenyl-1-methylenecyclopropane (**21**) reacts with a stoichiometric amount of $[RhH(CO)(PPh_3)_3]$ at room temperature, the $[Rh(\eta^1{:}\eta^2\text{-}CH_2CPh_2CH{=}CH_2)(CO)(PPh_3)_2]$ (**22**) was isolated and fully characterized through a selective proximal carbon–carbon bond cleavage.[15] Use of $[D_{15}]$-$[RhD(CO)(PPh_3)_3]$ results in selective deuteration at the γ-position of the ligand. The carbon–carbon activation involves the initial insertion of the C=C double bond into the Rh–H bond and an ensuing β-alkyl elimination[16] of the resulting cyclopropylmethyl rhodium complex (Scheme 5).

The rhodium-catalyzed hydrosilylation of MCPs[17] and



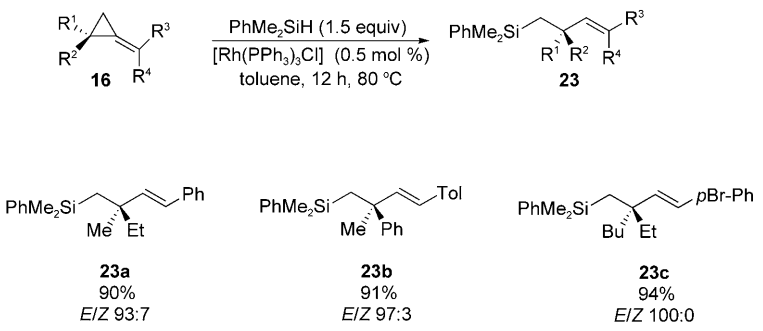
Scheme 5. Cyclopropylmethyl rhodium complex.

ACPs **16**[14] proceeds nicely, through a selective ring-opening, to give similarly a single isomer of the acyclic organosilanes **23** in good to excellent yields (Scheme 6).

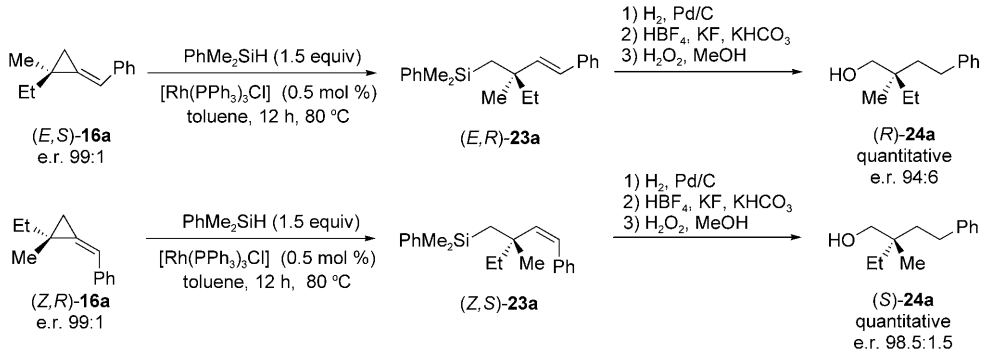
The reaction is stereoselective as the *E*/*Z* ratio of homoallylsilanes **23** correspond to the *E*/*Z* ratio of the initial alkylidenecyclopropanes **16**.[18] No traces of hydrosilylation of the *exo*-methylene double bond was detected suggesting that the ring-opening is again faster the reductive elimination. As the ring-cleavage always leads to the primary alkylsilane, the integrity of the quaternary stereogenic center should remain unaffected in the process. To confirm this assumption, several enantiomerically pure alkylidenecyclopropanes were prepared[18] and tested in those conditions. Accordingly, when the Rh-catalyzed hydrosilylation reaction of (*E*)-**16a** was performed, the (*E*)-homoallylsilane **23a** was obtained and directly subjected to hydrogenation of the double bond followed by the Tamao–Fleming oxidation reaction.[19] The corresponding saturated primary alcohol **24** was obtained with an enantiomeric ratio similar to the starting materials (Scheme 7).[14] The same trend was found for the *Z* isomer.[14]

The ring-opening process versus the reductive elimination to give the (2-silyl)-1,1-diphenylcyclopropane (**25**) is only dependent of the catalysts used. Indeed, the Wilkinson catalyst leads to homoallylsilanes **23** (Scheme 8), whereas platinum catalysts such as $[PtI_2(PPh_3)_2]$ only afford the silylmethyl cyclopropyl species **25** (Scheme 8).[20]

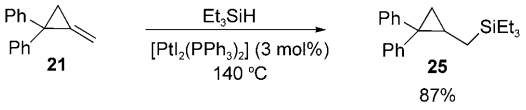
When MCPs and ACPs were subjected to the Rh-catalyzed hydroboration with pinocalborane at room temperature, a single boronate ester **26** was observed in all cases.[14] Here again, whatever MCPs and ACPs used, this reaction is a remarkable combination of several chemical steps that proceeds to give a unique ring-opened product (Scheme 9). Following oxidation with H_2O_2 and reduction of the double



Scheme 6. Rhodium-catalyzed hydrosilylation of MCPs and ACPs.



Scheme 7. Preparation of quaternary carbon stereocenters in acyclic system.

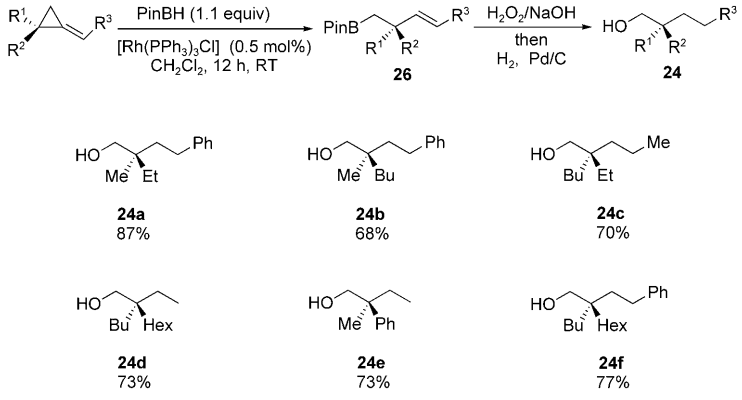


Scheme 8. Platinum-catalyzed hydrosilylation of MCPs.

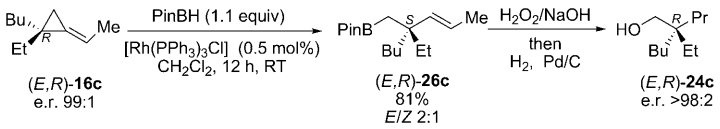
bond, the resulting saturated alcohols **24** were isolated in excellent yields.

When enantiomerically pure ACP **16c** was subjected to the Rh-catalyzed hydroboration, the obtained primary alkyl boronate ester **26c** is oxidized and reduced to give the homoallylic alcohol **24c** possessing a quaternary stereocenter with an enantiomeric ratio higher than 98:2, showing that the stereochemistry of the stereogenic center is unaffected during the whole process (Scheme 10).[14]

A very elegant illustration of the reactivity of ACP could be found in the combined C–H activation/cycloaddition

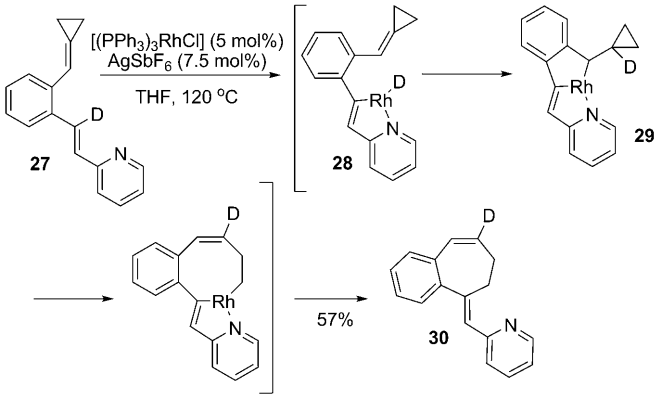


Scheme 9. Rhodium-catalyzed hydroboration of ACPs.



Scheme 10. Selective preparation of primary alkylboron species possessing a quaternary carbon stereocenter.

crossover.[21] When substrate **27** bearing an anchor group such as a pyridine ring to direct the C–H activation is subjected to the Wilkinson catalyst {[RhCl(PPh$_3$)$_3$], (5 mol%) and AgSbF$_6$ (7.5 mol%) in THF at 120°C}, the resulting vinyl metal hydride **28** undergo a carbometalation reaction on the alkylidenecyclopropane moiety to give metalacycle **29**. After ring-cleavage and reductive elimination, the functionalized cycloalkene **30** is formed (Scheme 11).

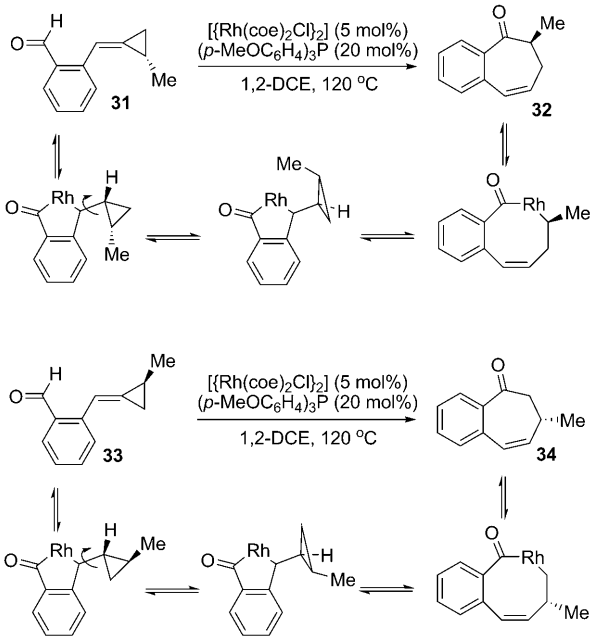


Scheme 11. Combined C–H activation/cycloaddition crossover.

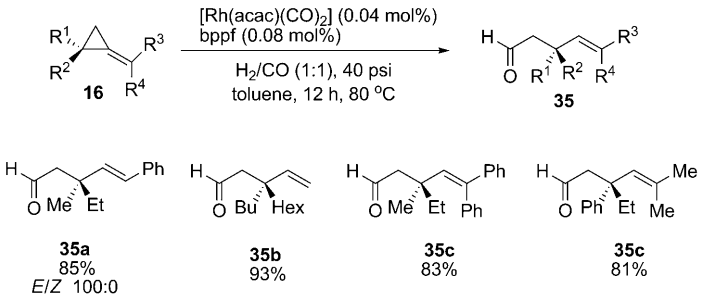
To extend the scope of this reaction, the 2-vinyl pyridine trigger was replaced by an aldehyde and these substrates convert into cycloheptenones on exposure to catalytic amounts of [Rh(coe)$_2$Cl]$_2$ (coe = cyclooctene) and (*p*-MeOC$_6$H$_4$)$_3$P at 80–120°C under ethylene atmosphere. However, under these conditions, the most substituted carbon–carbon bond is surprisingly cleaved in the process for only one isomer (Scheme 12). Indeed, when enantiomerically pure (*Z*,*S*)-alkylidenecyclopropane **31** is treated with the same catalytic system, ketone **32** is the only observed product. This result can be rationalized through the combined C–H bond insertion followed by the *syn*-addition of the resulting Rh–H species to the adjacent alkene, followed by a rotation to eclipse the C–Rh with the C–C bond of the cyclopropane, ring-opening and finally reductive elimination to give the ketone **32**. On the other hand, the analogous

transformation for the opposite isomer (*E*,*S*)-**33**, the ketone **34** in which the primary bond is cleaved is obtained. In both cases, the carbon–carbon bond of the cyclopropane that is *cis* relative to the C–Ar unit is broken during the cycloisomerization, independent of the degree of substitution. This discrepancy needs further investigations to be fully rationalized.

The synthetically interesting hydroformylation of MCPs and ACPs **16** was recently disclosed and linear aldehydes **35** were obtained in good to excellent yields whatever the substituents on the starting materials (Scheme 13).[22]

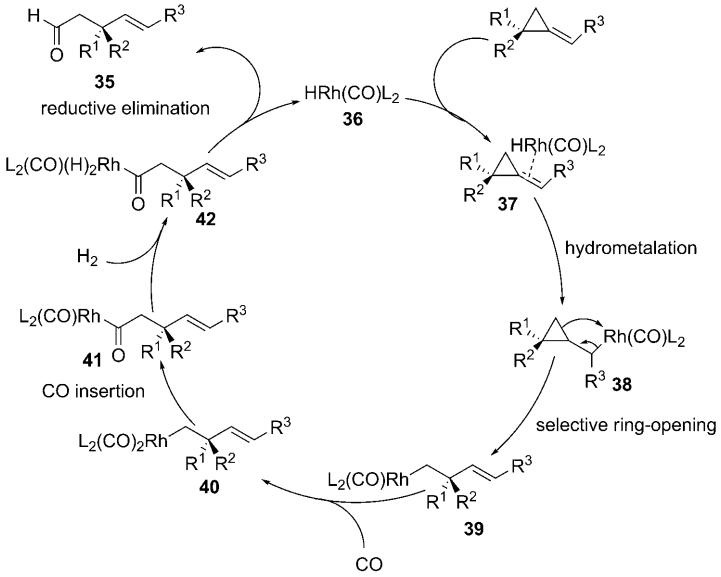


Scheme 12. Mechanistic hypothesis.



Scheme 13. Rhodium-catalyzed hydroformylation of ACPs.

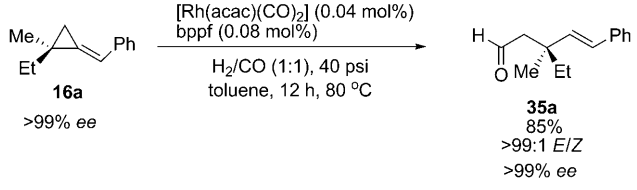
A postulated reaction pathway for the regioselective hydroformylation reaction of alkylidenecyclopropane is described in Scheme 14. A coordinatively unsaturated [$HRh(CO)L_2$] **36**, is in situ generated, forms a π-olefin–Rh complex **37** with ACPs that lead to Rh complex **38** via hydrometalation reaction. A selective ring-opening proceeds (selective cleavage of the primary bond). Carbon monoxide coordinates to **39** to form the saturated alkyl rhodium complex **40** and a migratory insertion takes place to give the unsaturated acyl–Rh **41**. Oxidative addition of molecular hydrogen to **41** gives the acyl–Rh dihydride **42** and after reductive elimination, the aldehyde **35** is produced and regenerate the active catalyst **36**.



Scheme 14. Mechanistic hypothesis for the rhodium-catalyzed hydroformylation of ACPs.

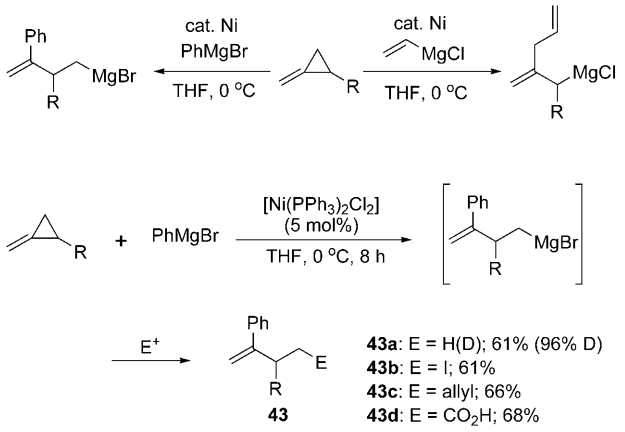
It is worth mentioning that the selective splitting of C–C bond is faster as compared to CO/H_2 insertion and reductive elimination since no cyclopropylcarboxaldehydes were detected. To further probe the utility of the hydroformylation reaction of alkylidenecyclopropanes in organic synthesis, the transformation of easily obtained enantiomerically pure alkylidenecyclopropane **16** into linear aldehyde **35** possessing the challenging enantiomeric enriched quaternary stereogenic carbon center[23] was achieved as described in Scheme 15.[22]

Nickel catalyst [$Ni(PPh_3)_2Cl_2$] could be used in combination with ArMgBr for the selective ring-opening of 2-phenyl-1-methylenecyclopropane as described in Scheme 16.[24] When the reaction mixture was quenched with electrophiles, functionalized adducts **43** were formed in moderate to good yields. However, surprisingly, the combination of vinyl Grignard derivatives and $NiCl_2$ as catalyst



Scheme 15. Selectivity in the carbon–carbon activation of ACPs.

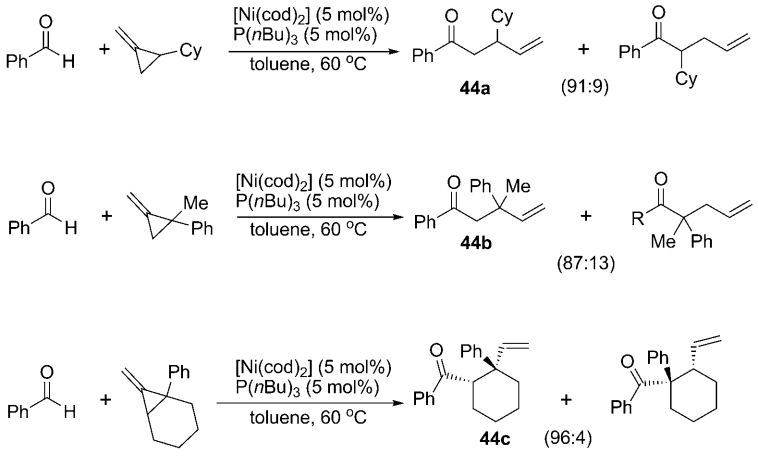
leads to a different chemical pathway and adducts from distal insertion were obtained.[24] The latter results show that a better understanding is still needed to predict reactivities of strained three-membered rings with different combination catalysts/nucleophiles.



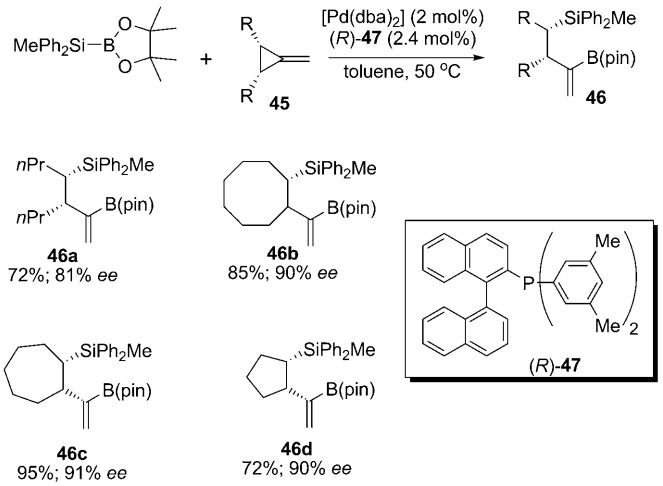
Scheme 16. Nickel-catalyzed ring-opening of ACPs.

Nickel catalyst {[Ni(cod)$_2$] (5 mol%) combined with PBu$_3$ (5 mol%)} could also be used for hydroacylation reaction of substituted MCPs. As expected, when non-symmetrical MCPs were used, a selective cleavage of the less hindered carbon–carbon bond occurs to give the corresponding ketones **44** in good yields (Scheme 17).[25]

When symmetrically substituted (*meso*) MCPs **45** are subjected to catalytic silaboration,[26] the cyclopropane ring is cleaved to give homoallylsilane **46**. The stereochemically determining step is the desymmetrizing carbon–carbon bond cleavage and dictates the configuration of the final enantiomer (Scheme 18).[27] With MePh$_2$SiB(pin) as the silylboron reagent and chiral ligand **47**, both cyclic and acyclic MCPs are converted to the ring-opened products in high enantioselectivity.



Scheme 17. Nickel-catalyzed hydroacylation of MCPs.

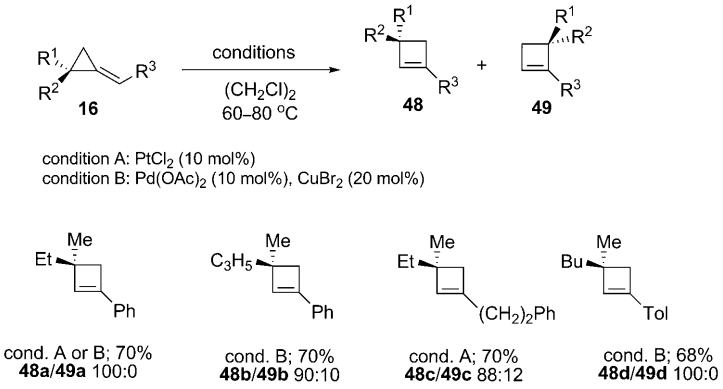


Scheme 18. Desymmetrization of MCPs.

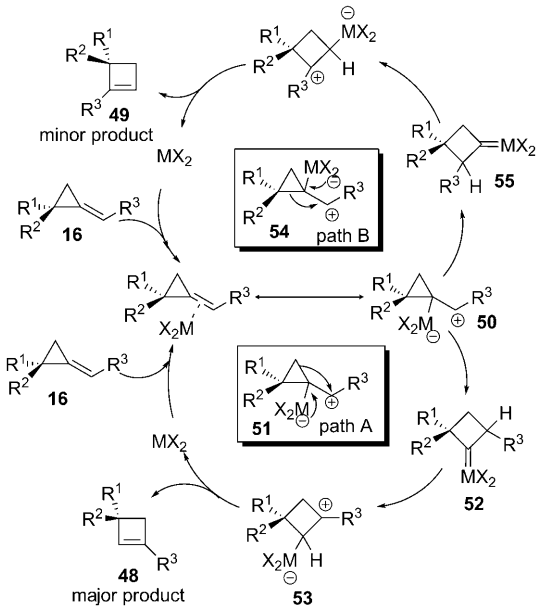
Even more challenging is the kinetic resolution of racemic 1-alkyl-2-methylenecyclopropanes and recent reports on the silaborative carbon–carbon cleavage catalyzed by a palladium complex bearing a chiral phosphoramidite ligand could illustrate the concept.[28] ACPs can be ring-expanded into cyclobutenes through the use of Pt^{II}[29] or Pd^{II}[30] catalysts. In the context of this concept article, it was of interest to investigate the regioselectivity of the ring-expansion using substituted ACPs such as **16**. When **16** (R^4=H) was treated with either Pt^{II} or Pd^{II}, cyclobutene **48** was formed at the expenses of its isomer **49** (Scheme 19).[31]

The selective ring expansion can be rationalized by the following mechanistic hypothesis (Scheme 20). Coordination of the transition metal MX$_2$ to the alkylidenecyclopropane **16** generates the corresponding cyclopropylmethyl cation **50** that may undergo two different ring expansions. In path A, the unsubstituted carbon center migrates (as described in **51**) to give the corresponding metal carbene **52**. Subsequent 1,2-hydrogen shift (formation of **53**) and elimination forms the corresponding cyclobutene **48**. On the other hand, when the tertiary alkyl group migrates as depicted in **54**, the metal carbene **55** is formed and after the same 1,2-hydrogen shift and elimination, the isomeric cyclobutene **49** could be obtained. The migrating carbon acquires a carbanion-like character in the transition state in a way that the most stable carbanions should migrate faster.

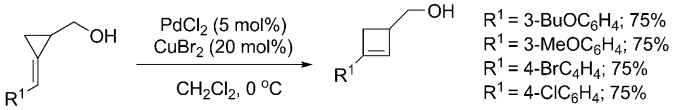
In the presence of Pd^{II} catalyst with excess of copper(II) bromide, 2-(arylmethylene)cyclopropylcarbinols undergo similar selective ring enlargement to deliver (arylcyclobutenyl)carbinols as described in Scheme 21.[33]



Scheme 19. Ring-expansion of ACPs to substituted cyclobutenes.



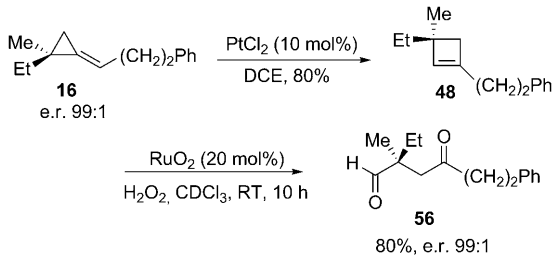
Scheme 20. Possible mechanisms for the ring-expansion.



Scheme 21. Palladium-catalyzed ring-expansion of methylenecyclopropanol.

As the primary alkyl group preferentially migrates in all examined cases, the integrity of the quaternary stereogenic center should remain unaffected in the process. When **16** (enantiomeric ratio 99:1) was submitted to the Pt^{II}-catalyzed ring expansion, the cyclobutene **48c** was obtained with the same enantiomeric ratio (e.r. 99:1) as determined by chiral HPLC after transformation into the linear dicarbonyl species **56** (Scheme 22).[31]

Recent studies on the ring-opening of monoactivated MCPs led to efficient preparations of various heterocyclic



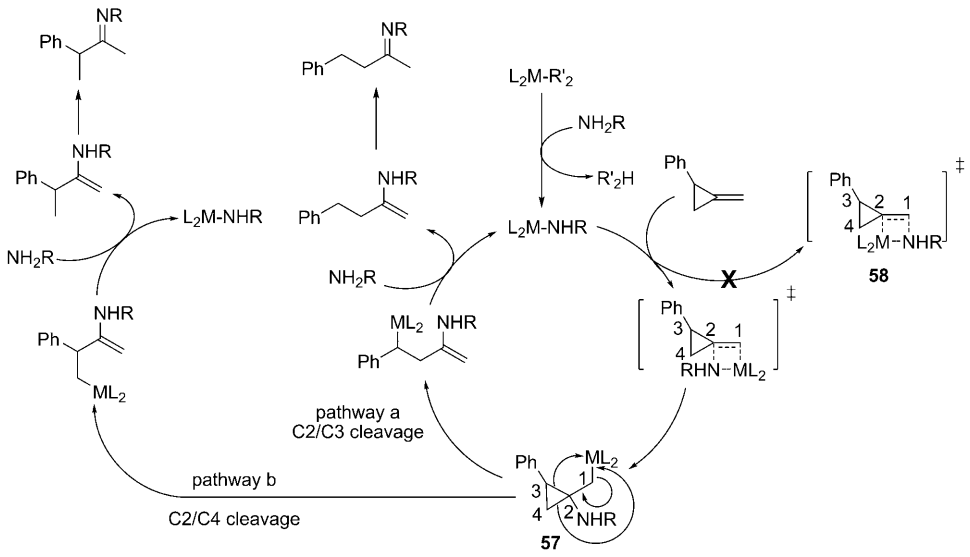
Scheme 22. Preparation of enantiomerically pure dicarbonyl species possessing quaternary carbon stereocenter.

structures, but as the selectivity of the ring-opening is either dictated by the presence of the activating group (Michael-type addition),[34] or by the ring-opening of bicyclic carbocation intermediates,[35] it will not be treated in details here. Finally, organolanthanide-[36] as well as titanium-mediated[37] intermolecular hydroamination reactions of MCPs represent an important class of transformation. When unsymmetrical phenylmethylenecyclopropane is treated with various amines in the presence of organolanthanide complexes [[$Cp^*_2LnCH(SiMe_3)_2$], Ln = La, Sm][36] or octahedral titanium catalyst [$Ti(Ph_2\text{-}PNpy)_2(NEt_2)_2$],[37] the 1,2-addition **57** is initially observed (no traces of 2,1-addition adducts **58** was detected) ensuing β-alkyl eliminative cyclopropane ring-opening of the Ln–alkyl cyclopropane species **57** to afford mainly the linear imine products after protonolysis and tautomerization (Scheme 23).[36,37]

This observed selectivity is opposite to all the ones discussed previously (and is identical to ring-opening reaction of radical species)[38] and could be understood on the basis of a weak coordination of the metal by the adjacent π-electrons of the arene ring. Such interactions would favor a *syn*-orientation of M-C and C2/C3 bonds, which would lead to preferential C2/C3 cleavage. Whereas many amines were tested in these reactions, no examples of alkyl-substituted methylene or alkylidenecyclopropane derivatives were tested to validate this hypothesis.

Summary and Outlook

By slightly increasing the structural complexity of methylene- and alkylidenecyclopropanes through judicious addition of substituents on its cyclopropyl core, the multiform reactivity of ACPs is now transformed into selective reaction. In this article, we are concentrating on the reactivity of MCPs and APCs via an initial addition reaction on the strained *exo*-alkylidene double bond followed by selective carbon–carbon bond activation. This concept could be used to the preparation of challenging structural motifs possessing quaternary carbon stereocenters in acyclic systems. New and efficient routes to enantiomerically enriched MCPs and ACPs are still in needs to fully exploit the rich and selective metal-catalyzed ring-opening reactions.



Scheme 23. Hydroamination reaction of MCPs.

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[1] B. Rybtchinski, D. Milstein, *Angew. Chem.* **1999**, *111*, 918; *Angew. Chem. Int. Ed.* **1999**, *38*, 870.
[2] a) J. D. Roberts, R. H. Mazur, *J. Am. Chem. Soc.* **1951**, *73*, 2509; b) M. S. Silver, P. R. Shafer, J. E. Nordlander, C. Rüchardt, J. D. Roberts, *J. Am. Chem. Soc.* **1960**, *82*, 2646; c) D. J. Patel, C. L. Hamilton, J. D. Roberts, *J. Am. Chem. Soc.* **1965**, *87*, 5144; d) A. Maercker, J. D. Roberts, *J. Am. Chem. Soc.* **1966**, *88*, 1742.
[3] a) D. M. Adams, J. Chatt, R. G. Guy, N. Sheppard, *J. Chem. Soc.* **1961**, 738; b) K. C. Bishop III, *Chem. Rev.* **1976**, *76*, 461; c) P. W. Jennings, L. L. Johnson, *Chem. Rev.* **1994**, *94*, 2241.
[4] a) I. A. Brandi, S. Cicchi, F. M. Cordero, A. Goti, *Chem. Rev.* **2003**, *103*, 1213; b) M. Rubin, M. Rubina, V. Gevorgyan, *Chem. Rev.* **2007**, *107*, 3117; c) A. Goti, F. M. Cordero, A. Brandi, *Top. Curr. Chem.* **1996**, *178*, 1; d) M. Lautens, W. Klute, W. Tam, *Chem. Rev.* **1996**, *96*, 49; e) A. de Meijere, S. I. Kozhushkov, A. F. Khlebnikov, *Top. Curr. Chem.* **2000**, *207*, 89; f) P. Binger, U. Schuchardt, *Chem. Ber.* **1981**, *114*, 3313; g) I. Marek, S. Simaan, A. Masarwa, *Angew. Chem.* **2007**, *119*, 7508; *Angew. Chem. Int. Ed.* **2007**, *46*, 7364; h) G. Audran, H. Pelissier, *Adv. Synth. Catal.* **2010**, *352*, 575.
[5] I. Nakamura, Y. Yamamoto, *Adv. Synth. Catal.* **2002**, *344*, 111.
[6] a) R. García-Fandiño, M. Gulías, L. Castedo, J. R. Granja, J. L. Mascareñas, D. J. Cárdenas, *Chem. Eur. J.* **2008**, *14*, 272; b) M. Lautens, Y. Ren, P. H. M. Delanghe, *J. Am. Chem. Soc.* **1994**, *116*, 8821; c) M. Lautens, Y. Ren, *J. Am. Chem. Soc.* **1996**, *118*, 9597; d) H. Corlay, R. T. Lewis, W. B. Motherwell, M. Shipman, *Tetrahedron* **1995**, *51*, 3303; e) A. Delgado, J. R. Rodríguez, L. Castedo, J. L. Mascareñas, *J. Am. Chem. Soc.* **2003**, *125*, 9282; f) R. Castro-Rodrigo, R. M. A. Esteruelas, A. M. López, F. Lóópez, J. L. Mascareñas, M. Oliván, E. Oñate, L. Saya, L. Villarino, *J. Am. Chem. Soc.* **2010**, *132*, 454, and references therein.
[7] T. Chevtchouk, J. Ollivier, J. Salaün, *Top. Curr. Chem.* **1987**, *135*, 77.
[8] For reviews on carbometalation reactions, see: a) I. Marek, N. Chinkov, D. Banon-Tenne in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, A. de Meijere), Wiley-VCH, Weinheim, **2004**, p. 395; b) I. Marek, *J. Chem. Soc. Perkin Trans. 1* **1999**, 535; c) J. F. Normant, A. Alexakis, *Synthesis* **1981**, 841; d) N. Chinkov, H. Chechik, S. Majumbar, A. Liard, I. Marek, *Synthesis* **2002**, 2473; e) N. Chinkov, S. Majumdar, I. Marek, *J. Am. Chem. Soc.* **2002**, *124*, 10282; f) N. Chinkov, S. Majumdar, I. Marek, *J. Am. Chem. Soc.* **2003**, *125*, 13258.
[9] F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079.
[10] For recent metal-catalyzed reactions of MCPs and ACPs, see: a) S. I. Kozhushkov, D. S. Yufit, L. Ackermann, *Org. Lett.* **2008**, *10*, 3409; b) P. A. Evans, P. A. Inglesby, *J. Am. Chem. Soc.* **2008**, *130*, 12838; c) A. I. Siriwardana, I. Nakamura, Y. Yamamoto, *J. Org. Chem.* **2004**, *69*, 3202; d) M. Shi, B.-Y. Wang, J.-W. Huang, *J. Org. Chem.* **2005**, *70*, 5606; e) S. Ma, J. Zhang, *Angew. Chem.* **2003**, *115*, 193; *Angew. Chem. Int. Ed.* **2003**, *42*, 184; f) D. H. Camacho, I. Nakamura, S. Saito, Y. Yamamoto, *J. Org. Chem.* **2001**, *66*, 270.
[11] *Organometallics in Synthesis A Manual* (Ed.: M Schlosser), Wiley, New York, **1994**.
[12] R. C. Larock, S. Varaprath, *J. Org. Chem.* **1984**, *49*, 3432; G. Fournet, G. Balme, J. Gore, *Tetrahedron* **1988**, *44*, 5809.
[13] M. Lautens, C. Meyer, A. Lorenz, *J. Am. Chem. Soc.* **1996**, *118*, 10676.
[14] S. Simaan, A. F. G. Goldberg, S. Rosset, I. Marek, *Chem. Eur. J.* **2010**, *16*, 774.
[15] Y. Nishihara, C. Yoda, K. Osakada, *Organometallics* **2001**, *20*, 2124.
[16] a) J. F. Hartwig, R. A. Andersen, R. G. Bergman, *J. Am. Chem. Soc.* **1989**, *111*, 2717; b) K. McNeill, R. A. Andersen, R. G. Bergman, *J. Am. Chem. Soc.* **1997**, *119*, 11244; c) B. Rybtchinski, A. Vigalok, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **1996**, *118*, 12406.
[17] A. G. Bessmertnykh, K. A. Blinov, Yu. K. Grishin, N. A. Donskaya, E. V. Tveritinova, N. M. Yur′eva, I. P. Beletskaya, *J. Org. Chem.* **1997**, *62*, 6069.
[18] a) S. Simaan, A. Masarwa, P. Bertus, I. Marek, *Angew. Chem.* **2006**, *118*, 4067; *Angew. Chem. Int. Ed.* **2006**, *45*, 3963; b) A. Masarwa, A. Stanger, I. Marek, *Angew. Chem.* **2007**, *119*, 8185; *Angew. Chem. Int. Ed.* **2007**, *46*, 8039; c) S. Simaan, I. Marek, *Org. Lett.* **2007**, *9*, 2569; d) S. Simaan, I. Marek, *Chem. Commun.* **2009**, 292; e) S. Simaan, A. Masarwa, E. Zohar, A. Stanger, P. Bertus, I. Marek, *Chem. Eur. J.* **2009**, *15*, 8449.
[19] I. Fleming, R. Henning, D. C. Parker, H. E. Plaut, P. E. J. Sanderson, *J. Chem. Soc. Perkin Trans. 1* **1995**, 317.
[20] a) Y. Nishihara, M. Itazaki, K. Osakada, *Tetrahedron Lett.* **2002**, *43*, 2059; b) M. Itazaki, Y. Nishihara, K. Osakada, *J. Org. Chem.* **2002**, *67*, 6889; c) Y. Nishihara, C. Yoda, M. Itazaki, K. Osakada, *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1469.
[21] C. Aïssa, A. Fürstner, *J. Am. Chem. Soc.* **2007**, *129*, 14836.
[22] S. Simaan, I. Marek, *J. Am. Chem. Soc.* **2010**, *132*, 4066.
[23] a) J. P. Das, H. Chechik, I. Marek, *Nat. Chem.* **2009**, *1*, 128; b) I. Marek, *Chem. Eur. J.* **2008**, *14*, 7460; c) I. Marek, G. Sklute, *Chem. Commun.* **2007**, 1683; d) G. Kolodney, G. Sklute, S. Perrone, P. Knochel, I. Marek, *Angew. Chem.* **2007**, *119*, 9451; *Angew. Chem. Int. Ed.* **2007**, *46*, 9291; e) G. Sklute, I. Marek, *J. Am. Chem. Soc.* **2006**, *128*, 4642; f) G. Sklute, D. Amsallem, A. Shibli, J. P. Varghese, I. Marek, *J. Am. Chem. Soc.* **2003**, *125*, 11776.
[24] J. Terao, M. Tomita, S. P. Singh, N. Kambe, *Angew. Chem.* **2010**, *122*, 148; *Angew. Chem. Int. Ed.* **2010**, *49*, 144.

[25] H. Taniguchi, T. Ohmura, M. Suginome, *J. Am. Chem. Soc.* **2009**, *131*, 11298.
[26] H. E. Burks, J. P. Morken, *Chem. Commun.* **2007**, 4717.
[27] T. Ohmura, H. Taniguchi, Y. Kondo, M. Suginome, *J. Am. Chem. Soc.* **2007**, *129*, 3518.
[28] T. Ohmura, H. Taniguchi, M. Suginome, *Org. Lett.* **2009**, *11*, 2880.
[29] A. Fürstner, C. Aïssa, *J. Am. Chem. Soc.* **2006**, *128*, 6306.
[30] M. Shi, L.-P. Liu, J. Tang, *J. Am. Chem. Soc.* **2006**, *128*, 7430.
[31] A. Masarwa, A. Fürstner, I. Marek, *Chem. Commun.* **2009**, 5760.
[32] T. Irshaidat, *Tetrahedron Lett.* **2008**, *49*, 5894.
[33] G.-Q. Tian, Z.-L. Yuan, Z.-B. Zhu, M. Shi, *Chem. Commun.* **2008**, 2668.
[34] a) M. Lautens, W. Han, *J. Am. Chem. Soc.* **2002**, *124*, 6312; b) M. Lautens, W. Han, J. H.-C. Liu, *J. Am. Chem. Soc.* **2003**, *125*, 4028; c) C. Taillier, M. Lautens, *Org. Lett.* **2007**, *9*, 591; d) M. E. Scott, W. Han, M. Lautens, *Org. Lett.* **2004**, *6*, 3309; e) M. E. Scott, M. Lautens, *Org. Lett.* **2005**, *7*, 3045; f) M. E. Scott, M. Lautens, *J. Org. Chem.* **2008**, *73*, 8154.
[35] X. Huang, M. Miao, *J. Org. Chem.* **2008**, *73*, 6884; G.-Q. Tian, M. Shi, *Org. Lett.* **2007**, *9*, 2405.
[36] J.-Sang. Ryu, G. Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **2003**, *125*, 12584.
[37] E. Smolensky, M. Kapon, M. S. Eisen, *Organometallics* **2007**, *26*, 4510.
[38] N. Hayashi, Y. Hirokawa, I. Shibata, M. Yasuda, A. Baba, *J. Am. Chem. Soc.* **2008**, *130*, 2912.

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