Synthetic Methods

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Synthesis of Functionalized Polycyclic Compounds: Rhodium(I)-Catalyzed Intramolecular Cycloaddition of Yne and Ene Vinylidenecyclopropanes**

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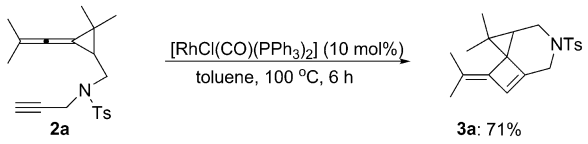
Herein we report that rhodium(I)-catalyzed intramolecular cycloadditions of yne and ene vinylidenecyclopropanes (VDCPs) can efficiently provide functionalized polycyclic compounds containing cyclobutene or aza-cyclooctene moieties in a highly regio- and diastereoselective manner with moderate to good yields under mild reaction conditions. The scope and limitations are disclosed and the plausible mechanisms are discussed given the results of a deuterium labeling experiment.

Organorhodium chemistry has now emerged as an important synthetic tool in organic chemistry and in other related areas.[1] Particularly, rhodium-catalyzed cycloadditions[2] and C–H bond activation reactions[3] have received considerable attention from the synthetic community because of their convenience, reduced environmental impact, and good atom economy. Polycyclic compounds containing cyclobutene units are often encountered in biologically significant molecules as well as in drug candidates,[4] such as 1-cyclobutenylmethylguanine, (+)-β-lumicolchicine, etc. The most efficient way of preparing these compounds is to employ a [2+2] cycloaddition between an alkene and alkyne directly. However, there have been only a few reports, mainly involving thermal, photochemical, and microwave reaction conditions, thus implying the difficulties and challenges of this strategy.[5] Recently, the rhodium-catalyzed [2+2] cycloaddition has been recognized as one of the most powerful and promising methodologies for the construction of cyclobutene units.[6] Meanwhile, the construction of polycyclic molecules containing a seven- or eight-membered ring (medium ring) system by using selective C–H bond activation is very difficult because of the numerous C–H bonds existing in the starting molecules. Therefore, the diastereoselective construction of such molecules is also a big challenge and must be considered carefully.[7] Because of these reasons, developing a mild and efficient way to synthesize the polycyclic compounds containing cyclobutene units and medium-sized ring systems using rhodium-catalyzed [2+2] cycloadditions and C–H bond activations is a very attractive option.[8]

VDCPs are highly strained but readily accessible molecules that serve as useful building blocks in organic synthesis. In the past several years, the chemistry of VDCPs has been extensively studied because of its unique structural and electronic properties.[9,10] During our ongoing studies of VDCP chemistry, we designed a series of novel vinylidenecyclopropanes tethered to alkyne and alkene moieties through a Mitsunobu reaction, and have successfully synthesized them in moderate to good yields (for the preparation of them, please see the Supporting Information). Herein, we report the rhodium(I)-catalyzed intramolecular cycloadditions of these yne and ene VDCPs through [2+2] cycloaddition and allylic C–H bond activation for the synthesis of polycyclic compounds having cyclobutene and aza-cyclooctene units, respectively.

We started our work by examining the intramolecular [2+2] cycloaddition of the yne VDCP **2a** in the presence of a rhodium(I) complex and found that the tricyclic adduct **3a** containing a cyclobutene unit was obtained (Scheme 1). The



Scheme 1. The optimal reaction conditions for the intramolecular [2 + 2] cycloaddition of the yne VDCP **2a**. Ts = 4-toluenesulfonyl.

structure of **3a** has been unambiguously determined by the X-ray diffraction and its CIF data are presented in the Supporting Information.[11] Screening of the reaction conditions revealed that using 10 mol% of $[RhCl(CO)(PPh_3)_2]$ as the catalyst and carrying out the reaction in toluene at 100 °C for 6 hours with a substrate concentration of 0.025 M were the best reaction conditions for this transformation, and the product **3a** was obtained in 71% yield (Scheme 1; see Table SI-1 in the Supporting Information for the details).

With the optimized reaction conditions being identified, we next examined the substrate scope of this highly regioselective intramolecular [2+2] cycloaddition of yne VDCPs and the results are summarized in Table 1. For substrates **2b**–**2f**, wherein $R^2 = CH_3$, $R^3 = H$, X = NTs, and R^1 is a either a noncyclic substituent (ethyl or butyl) or a cyclic substituent (cyclohexyl, cyclopentyl, or cycloheptyl), this rhodium(I)-

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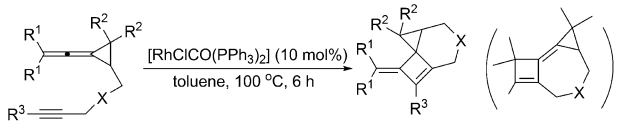
Table 1: Rhodium(I)-catalyzed [2+2] cycloaddition of the yne VDCPs **2** under the optimal reaction conditions.



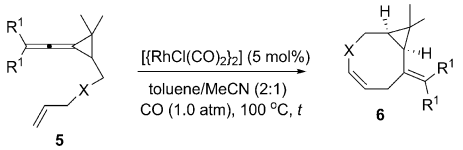
2 **3** **4a**

Entry[a]	**2**: R^1, R^1	R^2	R^3	X	Yield [%][b]
1	**2b**: C_2H_5, C_2H_5	CH_3	H	NTs	**3b**: 74
2	**2c**: C_4H_9, C_4H_9	CH_3	H	NTs	**3c**: 71
3	**2d**: $-(CH_2)_5-$	CH_3	H	NTs	**3d**: 77
4	**2e**: $-(CH_2)_4-$	CH_3	H	NTs	**3e**: 65
5	**2f**: $-(CH_2)_6-$	CH_3	H	NTs	**3f**: 68
6	**2g**: CH_3, CH_3	C_6H_5	H	NTs	**3g**: 78
7	**2h**: CH_3, CH_3	*p*-$CH_3C_6H_4$	H	NTs	**3h**: 69
8	**2i**: $-(CH_2)_5-$	*p*-ClC_6H_4	H	NTs	**3i**: 73
9[c]	**2j**: CH_3, CH_3	CH_3	H	NBs	**3j**: 64
10[c]	**2k**: C_4H_9, C_4H_9	CH_3	H	NBs	**3k**: 60
11[c]	**2l**: $-(CH_2)_5-$	CH_3	H	NBs	**3l**: 67
12[c]	**2m**: CH_3, CH_3	CH_3	CH_3	NNs	**3m**: 55
13[d,e]	**2n**: CH_3, CH_3	CH_3	CH_3	NNs	**3g**+**4a**: 52
14[f]	**2o**: CH_3, CH_3	CH_3	C_6H_5	NTs	complex mixture
15[f]	**2p**: CH_3, CH_3	CH_3	TMS	NTs	complex mixture
16[f]	**2q**: $-(CH_2)_5-$	CH_3	H	O	complex mixture

[a] All reactions were carried out using **2** (0.15 mmol) in the presence of $[RhClCO(PPh_3)_2]$ (10 mol%) in toluene (6.0 mL) at 100°C. [b] Yield of isolated product. [c] The reaction time is 10 h. [d] The reaction time is 14 h. [e] **3n**/**4a** = 1.2:1.0. [f] The reaction time is 24 h. Bs = 4-bromobenzenesulfonyl, Ns = 4-nitrobenzenesulfonyl, TMS = trimethylsilyl.

a mixed solvent of toluene and MeCN (2:1) at 100°C for 2.5 hours could produce the aza-cyclooctene derivative **6a** in 78% yield (see Table SI-2 in the Supporting Information for the details). These reaction conditions are the best for this rhodium(I)-catalyzed intramolecular cycloaddition and the generality of this reaction was examined using a variety of ene VDCPs (**5**). The results are shown in Table 2. Most of the reactions proceeded smoothly to give the corresponding aza-

Table 2: Rhodium(I)-catalyzed intramolecular cycloaddition of the ene VDCPs **5** under the optimal reaction conditions.



5 **6**

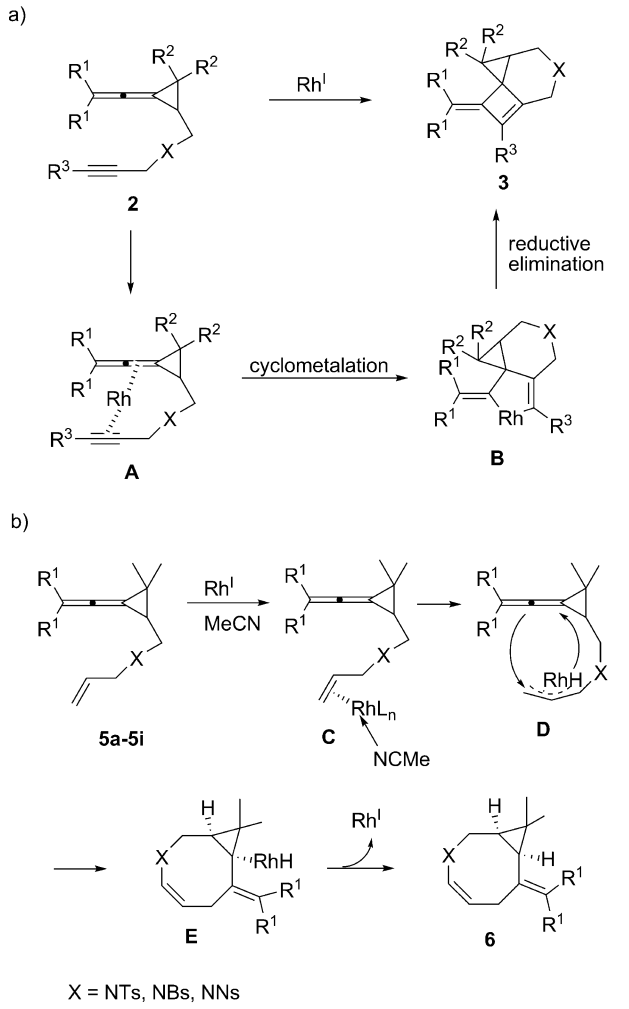
Entry[a]	**5**, R^1, R^1	X	*t* [h]	Yield [%][b]
1	**5b**: $-(CH_2)_5-$	NTs	2.5	**6b**: 77
2	**5c**: $-(CH_2)_4-$	NTs	2.5	**6c**: 69
3	**5d**: $-(CH_2)_6-$	NTs	2.5	**6d**: 80
4	**5e**: CH_3, CH_3	NBs	5	**6e**: 73
5	**5f**: $-(CH_2)_5-$	NBs	5	**6f**: 78
6	**5g**: C_4H_9, C_4H_9	NBs	5	**6g**: 70
7	**5h**: CH_3, CH_3	NNs	8	**6h**: 71
8	**5i**: $-(CH_2)_5-$	NNs	8	**6i**: 74
9	**5j**: $-(CH_2)_5-$	O	15	complex mixture

[a] All reactions were carried out using **5** (0.2 mmol) in the presence of $[\{RhCl(CO)_2\}_2]$ (5 mol%) in toluene/MeCN (2.0 mL/1.0 mL) under CO (1.0 atm). [b] Yield of isolated product.

catalyzed [2+2] cycloaddition proceeded smoothly to give the corresponding products **3b**–**3f** in yields within the range of 65–77% (Table 1, entries 1–5). Using the yne VDCP **2g** wherein R^2 is a phenyl group, the corresponding product **3g** was obtained in 78% yield (Table 1, entry 6). Moreover, adding moderately electron-donating or electron-withdrawing substituents onto the aromatic rings (substrates **2h** and **2i**) afforded the corresponding products **3h** and **3i** in 69% and 73% yields, respectively (Table 1, entries 7 and 8). Using the yne VDCPs **2j**–**2m** wherein X = NBs or NNs, the corresponding tricyclic adducts **3j**–**3m** containing cyclobutene units were formed in 55–67% yields a single regioisomer after a prolonged reaction time (10 h; Table 1, entries 9–12). The introduction of a methyl group at the terminus of the alkyne leads to a longer reaction time for this cycloaddition to go to completion, and affords the products **3n** and **4a** in 52% overall yield as a 1.2:1.0 regioisomeric mixture (Table 1, entry 13). However, when $R^3 = C_6H_5$ or trimethylsilyl (TMS), only complex product mixtures were formed, presumably as a result of the steric bulk (Table 1, entries 14 and 15). In the case of the oxygen-tethered yne VDCP **2q**, the reaction also afforded complex product mixtures (Table 1, entry 16).

We also attempted to use the ene VDCP **5a** as a substrate to examine the reaction outcome under the above standard reaction conditions, but only complex product mixtures were produced. Further investigations revealed that using 5 mol% $[\{RhCl(CO)_2\}_2]$ as the catalyst and carrying out the reaction in cyclooctene derivatives **6** as single diastereoisomers in 69–80% yields, and the reaction outcomes are not influenced by the substituent on either the allene moiety or the nitrogen atom (Table 2, entries 1–8). The structure and the configuration of **6b** were unambiguously determined by the X-ray diffraction and its CIF data are presented in the Supporting Information.[12] Unfortunately, when using the oxygen-tethered ene VDCP **5j** as a substrate, the reaction system only gave complex product mixtures and no pure product could be isolated (Table 2, entry 9). Attempts to synthesize both ene VDCPs with two aryl groups on the cyclopropane and the carbon-tethered substrates failed to give the desired products (see the Supporting Information for the details).

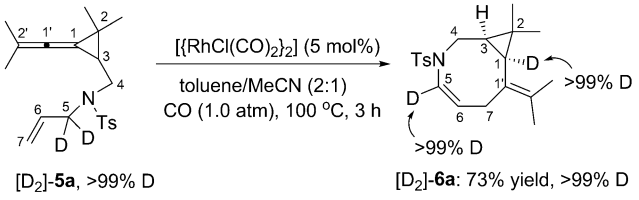
Plausible mechanisms for the formation of the polycyclic compounds **3** and **6** are outlined in Scheme 2. In the rhodium(I)-catalyzed [2+2] cycloaddition of the yne VDCPs **2**,[6a–c,f] selective coordination of the internal double bond of the allene and alkyne moiety by the rhodium(I) complex gives intermediate **A** (Scheme 2a). The corresponding polycyclic derivatives **3** containing a cyclobutene moiety can be afforded after cyclometalation/reductive elimination. In contrast, for the rhodium(I)-catalyzed intramolecular cycloaddition of the ene VDCPs **5**, acetonitrile and the tethered terminal alkene can coordinate to the rhodium(I) metal center to give intermediate **C**,[8k,13] which undergoes oxidative addition of the rhodium(I) catalyst onto the neighboring allylic C–H bond to give the π-allyl rhodium



Scheme 2. Plausible mechanisms for the formation of a) **3** and b) **6**.

hydrogen species **D** (Scheme 2b).[8,14] Next, intramolecular insertion to the internal double bond of the allene moiety leads to the rhodium hydrogen species **E**. Products **6** can be formed from intermediate **E** through reductive elimination along with the regeneration of rhodium(I) catalyst.

To verify the allylic C–H bond activation pathway from the ene VDCPs **5** to products **6**, we performed a deuterium labeling experiment using [D_2]-**5a** as the substrate (Scheme 3). When the ene VDCP [D_2]-**5a** [15] (>99% deuterium incorporation at the allylic C5 position, see the Supporting Information for the preparation) was used as the substrate under the standard reaction conditions, the corresponding deuterated product [D_2]-**6a** was exclusively formed in 73% yield (>99% deuterium incorporation at both C1 and C5 positions). This observation clearly suggested that one hydrogen atom at C5 position of [D_2]-**5a** was completely transferred to the C1 position of aza-cyclooctene derivative [D_2]-**6a** under the standard reaction conditions by the rhodium(I)-catalyzed C–H bond activation.

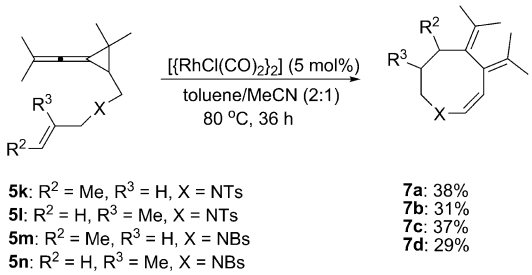


[D_2]-**5a**, >99% D

[D_2]-**6a**: 73% yield, >99% D

Scheme 3. Deuterium labeling experiment.

Unexpectedly, in the case of the ene VDCPs **5k** and **5m**, which have a methyl group at the terminal position of the alkene, and the ene VDCPs **5l** and **5n**, which bear a methyl group at the internal position of the alkene, different aza-cyclooctene derivatives (**7a**–**7d**) were obtained in yields within the range of 29–38% through the rhodium(I)-catalyzed sp^3 C–H bond activation along with a cyclopropane ring-opening process (Scheme 4). Some unidentified products were also obtained in the above reactions. The structures and



Scheme 4. Rhodium(I)-catalyzed sp^3 C–H bond activation of the ene VDCPs **5k**–**5n**.

configurations of **7b** and **7c** have been unambiguously determined by the X-ray diffraction and their CIF data, as well as a plausible reaction mechanism are presented in the Supporting Information.[16,17]

In summary, we have developed two interesting rhodium(I)-catalyzed intramolecular cycloadditions of yne and ene VDCPs which provide various functionalized polycyclic compounds in moderate to good yields and with high regio- and diastereoselectivity under mild reaction conditions. The polycyclic systems containing either a cyclobutene or an aza-cyclooctene are difficult to synthesize by other methods. Furthermore, a deuterium labeling experiment was conducted to confirm the mechanistic hypothesis of the rhodium(I)-catalyzed allylic C–H bond activation of ene VDCPs. Notably, using the ene VDCPs **5k**–**5n**, which have a methyl group at either the terminus or the internal position of the alkene, as the substrates produced aza-cyclooctene derivatives **7** after a cyclopropane ring-opening step. These interesting rhodoum(I)-catalyzed intramolecular cycloaddition reactions may be useful synthetic tools in the preparation of biologically active compounds. Additional efforts on the scope and mechanistic details of this reaction are currently ongoing in our laboratory.

Experimental Section

2a: Under an argon atmosphere, triphenylphosphine (110 mg, 0.42 mmol) and 4-methyl-*N*-(prop-2-ynyl)benzenesulfonamide

(92 mg, 0.44 mmol) were added into a Schlenk tube. Then 3.0 mL THF was added and the reaction solution was cooled to 0 °C. Vinylidenecyclopropane **1a** (61 mg, 0.4 mmol) which was dissolved in THF (1.0 mL) was added into the above Schlenk tube. Then diethyl azodicarboxylate (DEAD) (0.066 mL, 0.42 mmol) was added dropwise at 0 °C and warmed up to room temperature naturally. On reaction completion the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (silica gel. Eluent: EtOAc/petroleum ether = 1:30). Compound **2a** was isolated as a yellowish oil in 70% yield.

3a: Under an argon atmosphere, $[RhClCO(PPh_3)_2]$ (10 mg, 0.015 mmol), substrate **2a** (51 mg, 0.15 mmol), and toluene (6.0 mL) were added into a Schlenk tube. The reaction mixture was stirred at 100 °C until the reaction completed. Then, the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (silica gel. Eluent: EtOAc/petroleum ether = 1:20). Compound **3a** was isolated as a yellowish oil in 71% yield.

5a: Under an argon atmosphere, triphenylphosphine (110 mg, 0.42 mmol) and *N*-allyl-4-methylbenzenesulfonamide (93 mg, 0.44 mmol) were added into a Schlenk tube. Then 3.0 mL THF was added and cooled to 0 °C. Vinylidenecyclopropane **1a** (61 mg, 0.4 mmol) which dissolved in THF (1.0 mL) was added into the above Schlenk tube. Then diisopropyl azodicarboxylate (DIAD) (0.083 mL, 0.42 mmol) was added dropwise at 0 °C and warmed up to rt naturally. On completion the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (silica gel. Eluent: EtOAc/petroleum ether = 1:30). Compound **5a** was isolated as a yellowish oil in 59% yield.

6a: Under an argon atmosphere, $[\{RhCl(CO)_2\}_2]$ (4 mg, 0.01 mmol) was added into a Schlenk tube. Then the atmosphere was pumped off and a balloon filled with CO was connected to the reaction flask. A solution of substrate **5a** (70 mg, 0.2 mmol) in toluene/MeCN (2.0 mL/1.0 mL) was added into the Schlenk tube. The reaction mixture was stirred at 100 °C until the reaction completed. Then, the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (silica gel. Eluent: EtOAc/petroleum ether = 1:20). Compound **6a** was isolated as a colorless solid in 78% yield.

7a: Under an argon atmosphere, $[RhCl(CO)_2]_2$ (4 mg, 0.01 mmol) was added into a Schlenk tube. Then the solution of substrate **5k** (72 mg, 0.2 mmol) in toluene/MeCN (2.0 mL/1.0 mL) was added into the Schlenk tube. The reaction mixture was stirred at 80 °C until the reaction completed. Then, the solvent was removed under reduced pressure and the residue was purified by a flash column chromatography (silica gel. Eluent: EtOAc/petroleum ether = 1:30). Compound **7a** was isolated as a colorless solid in 38% yield.

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[1] For selected reviews, see: a) I. Ojima, A. T. Vu, D. Bonafoux, *Organometallic Complexes of Rhodium*, Thieme, Stuttgart, **2001**; b) P. van Leeuwen, C. Claver, *Rhodium Catalyzed Hydroformylation*; Springer, Berlin, **2002**; c) P. A. Evans, *Modern Rhodium-Catalyzed Organic Reactions*, VCH, Weinheim, **2005**; d) C. Aubert, L. Fensterbank, P. Garcia, M. Malacria, A. Simonneau, *Chem. Rev.* **2011**, *111*, 1954 – 1993.

[2] For selected reviews, see: a) M. Lautens, W. Klute, W. Tam, *Chem. Rev.* **1996**, *96*, 49 – 92; b) J. A. Varela, C. Saá, *Chem. Rev.* **2003**, *103*, 3787 – 3802; c) K. Tanaka, *Synlett* **2007**, 1977 – 1993; d) T. Shibata, K. Tsuchikama, *Org. Biomol. Chem.* **2008**, *6*, 1317 – 1323; e) S. Perreault, T. Rovis, *Chem. Soc. Rev.* **2009**, *38*, 3149 – 3159.

[3] For recent reviews, see: a) C. Slugovc, I. Padilla-Martínez, S. Sirol, E. Carmona, *Coord. Chem. Rev.* **2001**, *213*, 129 – 157; b) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev.* **2002**, *102*, 1731 – 1770; c) H. M. L. Davies, R. E. J. Beckwith, *Chem. Rev.* **2003**, *103*, 2861 – 2904; d) H. M. L. Davies, Ø. Loe, *Synthesis* **2004**, 2595 – 2608; e) P. M. P. Gois, C. A. M. Afonso, *Eur. J. Org. Chem.* **2004**, 3773 – 3788; f) H. M. L. Davies, J. Nikolai, *Org. Biomol. Chem.* **2005**, *3*, 4176 – 4187; g) A. G. H. Wee, *Curr. Org. Synth.* **2006**, *3*, 499 – 555; h) Y. J. Park, J.-W. Park, C.-H. Jun, *Acc. Chem. Res.* **2008**, *41*, 222 – 234; i) J. C. Lewis, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2008**, *41*, 1013 – 1025; j) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624 – 655; k) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212 – 11222; l) M. P. Doyle, R. Duffy, M. Ratnikov, L. Zhou, *Chem. Rev.* **2010**, *110*, 704 – 724; m) C. N. Slattery, A. Ford, A. R. Maguire, *Tetrahedron* **2010**, *66*, 6681 – 6705.

[4] a) J. C. Namyslo, D. E. Kaufmann, *Chem. Rev.* **2003**, *103*, 1485 – 1537; b) R. J. Griffin, C. E. Arris, C. Bleasdale, F. T. Boyle, A. H. Calvert, N. J. Curtin, C. Dalby, S. Kanugula, N. K. Lembicz, D. R. Newell, A. E. Pegg, B. T. Golding, *J. Med. Chem.* **2000**, *43*, 4071 – 4083; c) N. Butta, A. Martin-Requero, E. Urcelay, R. Parrilla, M. S. Ayuso, *J. Pharmacol.* **1996**, *118*, 1797 – 1805.

[5] B. Alcaide, P. Almendros, C. Aragoncillo, *Chem. Soc. Rev.* **2010**, *39*, 783 – 816, and references therein.

[6] For recent reviews, see: a) W. Tam, J. Goodreid, N. Cockburn, *Curr. Org. Synth.* **2009**, *6*, 219 – 238. For selected examples, please see: b) T. Shibata, K. Takami, A. Kawachi, *Org. Lett.* **2006**, *8*, 1343 – 1345; c) R. E. Forslund, J. Cain, J. Colyer, M. P. Doyle, *Adv. Synth. Catal.* **2005**, *347*, 87 – 92; d) J. M. Joo, Y. Yuan, C. Lee, *J. Am. Chem. Soc.* **2006**, *128*, 14818 – 14819; e) H. Kim, C. Lee, *J. Am. Chem. Soc.* **2005**, *127*, 10180 – 10181; f) P. A. Wender, M. P. Croatt, B. Kühn, *Organometallics* **2009**, *28*, 5841 – 5844; g) R. S. Jolly, G. Luedtke, D. Sheehan, T. Livinghouse, *J. Am. Chem. Soc.* **1990**, *112*, 4965 – 4966; h) G. Hilt, A. Paul, J. Treutwein, *Org. Lett.* **2010**, *12*, 1536 – 1539.

[7] B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921 – 2944.

[8] For examples about rhodium-catalyzed allylic C–H bond activation, see: a) H. M. L. Davies, P. Ren, Q. Jin, *Org. Lett.* **2001**, *3*, 3587 – 3590; b) H. M. L. Davies, R. E. J. Beckwith, *J. Org. Chem.* **2004**, *69*, 9241 – 9247; c) T. Makino, K. Itoh, *J. Org. Chem.* **2004**, *69*, 395 – 405; d) K. M. Brummond, H. Chen, B. Mitasev, A. D. Casarez, *Org. Lett.* **2004**, *6*, 2161 – 2163; e) H. M. L. Davies, Q. Jin, *Org. Lett.* **2005**, *7*, 2293 – 2296; f) H. M. L. Davies, M. G. Coleman, D. L. Ventura, *Org. Lett.* **2007**, *9*, 4971 – 4974; g) D. N. Zalatan, J. D. Bois, *J. Am. Chem. Soc.* **2008**, *130*, 9220 – 9221; h) E. Nadeau, D. L. Ventura, J. A. Brekan, H. M. L. Davies, *J. Org. Chem.* **2010**, *75*, 1927 – 1939; i) Q. Li, Z.-X. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 4542 – 4543; j) S. Rakshit, F. W. Patureau, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 9585 – 9587; k) W. Li, W. Yuan, M. Shi, E. Hernandez, G. Li, *Org. Lett.* **2010**, *12*, 64 – 67; l) Q. Li, Z.-X. Yu, *Angew. Chem.* **2011**, *123*, 2192 – 2195; *Angew. Chem. Int. Ed.* **2011**, *50*, 2144 – 2147.

[9] For the synthesis of VDCPs, see: a) K. Isagawa, K. Mizuno, H. Sugita, Y. Otsuji, *J. Chem. Soc. Perkin Trans. 1* **1991**, 2283 – 2285, and references therein; b) A. R. Al Dulayymi, M. S. Baird, *J. Chem. Soc. Perkin Trans. 1* **1994**, 1547 – 1548.

[10] a) M. L. Poutsma, P. A. Ibarbia, *J. Am. Chem. Soc.* **1971**, *93*, 440 – 450; b) W. Smadja, *Chem. Rev.* **1983**, *83*, 263 – 320; c) H. Sugita, K. Mizuno, T. Saito, K. Isagawa, Y. Otsuji, *Tetrahedron Lett.* **1992**, *33*, 2539 – 2542; d) K. Mizuno, H. Sugita, T. Kamada, Y. Otsuji, *Chem. Lett.* **1994**, 449 – 452, and references therein; e) L. K. Sydnes, *Chem. Rev.* **2003**, *103*, 1133 – 1150; f) K. Mizuno, H. Sugita, K. Isagawa, M. Goto, Y. Otsuji, *Tetrahedron Lett.* **1993**, *34*, 5737 – 5738; g) K. Mizuno, H. Sugita, T. Hirai, H. Maeda, *Chem. Lett.* **2000**, 1144 – 1145; h) K. Mizuno, H. Maeda,

H. Sugita, S. Nishioka, T. Hirai, A. Sugimoto, *Org. Lett.* **2001**, *3*, 581 – 584; i) H. Maeda, K. Mizuno, *J. Synth. Org. Chem. Jpn.* **2004**, *62*, 1014 – 1025; j) M. Shi, L.-X. Shao, J.-M. Lu, Y. Wei, K. Mizuno, H. Maeda, *Chem. Rev.* **2010**, *110*, 5883 – 5913; k) G.-C. Xu, L.-P. Liu, J.-M. Lu, M. Shi, *J. Am. Chem. Soc.* **2005**, *127*, 14552 – 14553; l) J.-M. Lu, M. Shi, *Org. Lett.* **2007**, *9*, 1805 – 1808; m) J.-M. Lu, Z.-B. Zhu, M. Shi, *Chem. Eur. J.* **2009**, *15*, 963 – 971; n) L.-F. Yao, M. Shi, *Chem. Eur. J.* **2009**, *15*, 3875 – 3881; o) W. Li, W. Yuan, M. Shi, E. Hernandez, G.-G. Li, *Org. Lett.* **2010**, *12*, 920 – 923; p) L. Wu, M. Shi, *Chem. Eur. J.* **2010**, *16*, 1149 – 1152; q) J.-M. Lu, M. Shi, *Org. Lett.* **2006**, *8*, 5317 – 5320; r) J.-M. Lu, M. Shi, *Org. Lett.* **2008**, *10*, 1943 – 1946; s) L. Wu, M. Shi, *J. Org. Chem.* **2010**, *75*, 2296 – 2301; t) L. Wu, M. Shi, *Eur. J. Org. Chem.* **2011**, 1099 – 1105; u) W. Yuan, M. Shi, *Tetrahedron* **2010**, *66*, 7104 – 7111; v) B.-L. Lu, Y. Wei, M. Shi, *Chem. Eur. J.* **2010**, *16*, 10975 – 10979; w) B.-L. Lu, M. Shi, *Eur. J. Org. Chem.* **2011**, 243 – 248.

[11] CCDC 791963 (**3a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[12] CCDC 816150 (**6b**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[13] a) M. E. Prater, L. E. Pence, R. Clérac, G. M. Finniss, C. Campana, P. Auban-Senzier, D. Jérome, E. Canadell, K. R. Dunbar, *J. Am. Chem. Soc.* **1999**, *121*, 8005 – 8016; b) F. L. Taw, P. S. White, R. G. Bergman, M. Brookhart, *J. Am. Chem. Soc.* **2002**, *124*, 4192 – 4193.

[14] a) Z.-X. Yu, P. H.-Y. Cheong, P. Liu, C. Y. Legault, P. A. Wender, K. N. Houk, *J. Am. Chem. Soc.* **2008**, *130*, 2378 – 2379; b) S. Mao, D. Probst, S. Werner, J. Chen, X. Xie, K. M. Brummond, *J. Comb. Chem.* **2008**, *10*, 235 – 246.

[15] a) R. D. Schuetz, F. W. Millard, *J. Org. Chem.* **1959**, *24*, 297 – 300; b) K.-T. Yip, J.-H. Li, O.-Y. Lee, D. Yang, *Org. Lett.* **2005**, *7*, 5717 – 5719.

[16] CCDC-830623 (**7b**) CCDC 6.. contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[17] CCDC-828941 (**7c**) CCDC 6.. contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

