Asymmetric Catalysis

DOI: 10.1002/anie.201209112

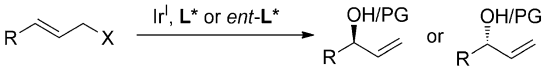
Cross-Metathesis/Iridium(I)-catalyzed Allylic Etherification Strategy: (Iterative) Catalytic Asymmetric Synthesis of *syn*- and *anti*-1,2-Diols**

*Dongeun Kim, Jae Seung Lee, Suk Bin Kong, and Hyunsoo Han**

1,2-Diol functional groups are common structures in many biologically active natural products[1] and "privileged" chiral catalysts/ligands.[2] Furthermore, 1,2-diols can serve as valuable synthetic precursors for the construction of a wide variety of other useful structures. 1,2-Diols can appear in many different forms depending on their protection state (diprotected, monoprotected, or free diol), as well as their absolute and relative stereochemistry (*syn* or *anti*). Thus, an ideal synthetic method/strategy for 1,2-diols would be one that can a) furnish any of the aforementioned 1,2-diol forms and b) control their absolute and relative stereochemistry by using a pair of enantiomeric ligands/catalysts, but such methodology is not currently available.

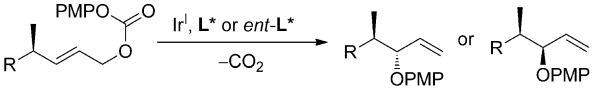
Despite tremendous methodological advancements, literature inspection surprisingly revealed that almost all prior asymmetric methods for the synthesis of 1,2-diols focused on controlling relative stereochemistry of 1,2-diols, thus giving either *syn*- or *anti*-1,2-diols, and employed chiral reagents and auxiliaries for stereochemical control.[3–8] In addition, they often suffered from a narrow substrate scope, low yields, and low stereoselectivities. To our knowledge, the only catalytic asymmetric method that met the above two criteria was recently reported by the McQuade group, who employed the copper-catalyzed asymmetric allylic boronation/cross-metathesis (AAB/CM) strategy.[9] Although highly selective formation of differentiated *syn*- and *anti*-1,2-diols could be achieved by using a pair of enantiomeric ligands, the strategy required two extra steps for the in situ oxidation of the boronate product of the AAB reaction and the subsequent alcohol protection, and the AAB reaction did not occur with a TBS protecting group, thus considerably limiting the generality and practicality of the strategy.

In recent years, iridium(I)-catalyzed allylic substitution reactions have emerged as a powerful tool for the enantioselective introduction of carbon–carbon and carbon–heteroatom bonds.[10] A distinct feature of iridium(I)-catalyzed allylic substitution reactions is the formation of chiral branched allylation products from achiral linear allyl substrates, which complements the more traditional palladium-catalyzed allylic substitution reactions which typically give rise to linear allylation products.[11] Iridium-catalyzed allylic etherification reactions have been shown to generate a wide range of protected and free chiral allylic alcohols in high yields at synthetically useful levels of stereoselectivity [Eq. (1); PG = protecting group].[12]



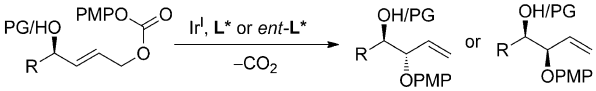
(1)

We recently demonstrated that iridium(I)-catalyzed decarboxylative allylic etherification exhibited much broader substrate scope and higher reaction yield than the corresponding intermolecular version, and that stereoselection in iridium(I)-catalyzed diastereoselective decarboxylative allylic etherification was controlled by the ligands/catalysts used [Eq. (2); PMP = *p*-methoxyphenyl].[13] Based on these

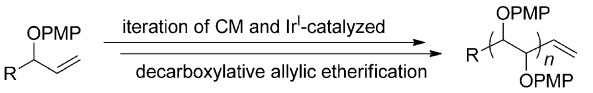


(2)

results, we envisioned that iridium(I)-catalyzed decarboxylative allylic etherification, coupled with olefin cross-metathesis,[14] could be used to synthesize any form of 1,2-diols with complete stereochemical control [Eq. (3)]. Also envisaged was that this strategy could be used in an iterative fashion to give poly-1,2-diols [Eq. (4)]. Herein we describe our success in developing these methodologies.



(3)



(4)

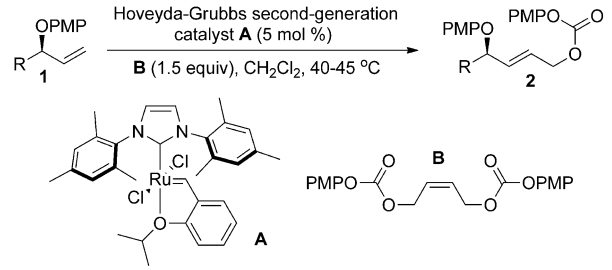
The PMP-protected allylic alcohols **1** were selected to represent a variety of allylic alcohols with simple linear alkyl, functionalized linear alkyl, branched/cyclic alkyl, and aromatic side chains, and prepared by iridium(I)-catalyzed enantioselective decarboxylative allylic etherification of PMP allyl carbonates.[13] As shown in Table 1, CM was explored by using **1a**, the Hoveyda–Grubbs second-genera-

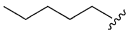
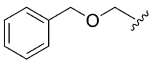
[*] Dr. D. Kim, Dr. J. S. Lee, Prof. Dr. H. Han
Department of Chemistry, University of Texas at San Antonio
1 UTSA Circle, San Antonio, TX 78249 (USA)
E-mail: Hyunsoo.Han@utsa.edu
Prof. Dr. S. B. Kong
Department of Chemistry, University of the Incarnate Word
4301 Broadway, San Antonio, TX 78209 (USA)

[**] Research reported in this publication was supported by the US National Science Foundation (CHE 0911134).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201209112.

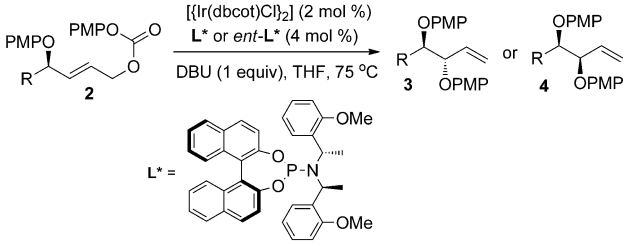
Table 1: Ruthenium-catalyzed cross-metathesis of the PMP-protected allylic alcohols **1** with (*Z*)-but-2-ene-1,4-diyl bis(4-methoxybenzoate) (**B**).

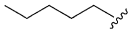
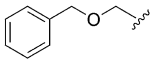


Entry	R	Product	Yield [%][a]	*E*/*Z*[b]
1		**2a**	84	>25:1
2		**2b**	78	>25:1
3		**2c**	81	>25:1
4		**2d**	76	>25:1

[a] Yield of the isolated product. [b] *E*/*Z* selectivities determined by the ^{1}H NMR spectroscopy of the reaction mixtures.

Table 2: Asymmetric synthesis of di-protected *syn*- and *anti*-1,2-diols by iridium(I)-catalyzed diastereoselective decarboxylative allylic etherification of **2**.



Entry	R	**2** *ee* [%][a]	Ligand	Product	Yield [%][b]	d.r.[c]
1		95	**L***	**3a**	92	>25:1
2			*ent*-**L***	**4a**	90	1:20
3		90	**L***	**3b**	91	20:1
4			*ent*-**L***	**4b**	94	1:18
5		95	**L***	**3c**	91	>25:1
6			*ent*-**L***	**4c**	93	1:>25
7		93	**L***	**3d**	84	20:1
8			*ent*-**L***	**4d**	86	1:19

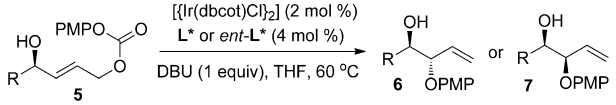
[a] Determined using precursors **1**. [b] Yield of the isolated product. [c] Determined by the ^{1}H NMR spectroscopy of the reaction mixtures. dbcot = dibenzocyclooctatetraene.

tion catalyst **A**,[15] and (*Z*)-but-2-ene-1,4-diyl bis(4-methoxybenzoate) (**B**) in methylene chloride.[16] An initial attempt employing 3 mol% of **A** and 2 equivalents of **B** at room temperature gave rise to the desired CM product **2a** in 40% yield and with a greater than 25:1 *trans*/*cis* selectivity, and increasing the loadings of the catalyst did not improve the yields. During the course of further studies, it was observed that CM reactions did not proceed after the initial burst of product formation and **B** isomerized to the corresponding *trans* isomer at room temperature. Based on the reasoning that the *trans* isomer is the slower CM substrate and a higher temperature could make it participate more effectively in the CM reaction, the temperature was raised to 40–45 °C. Reaction yields improved to 60% with 3 mol% of **A** and 1 equivalent of **B**. When an additional 2 mol% of **A** and 0.5 equivalent of **B** were added, reaction yields increased to 84% (Table 1). Adding more **A** and **B** did not improve yields additionally. Under the optimized reaction conditions involving 5 mol% of **A** and 1.5 equivalents of **B** in methylene chloride at 40–45 °C, **2b–d** (entries 2–4) were obtained in good yields (≥76%) and with excellent *trans*/*cis* selectivities (>25:1).

Now the stage was set for the critical iridium(I)-catalyzed diastereoselective decarboxylative allylic etherification. When **2a** was subjected to the catalytic conditions employing [{Ir(dbcot)Cl}$_2$] (2 mol%), the phosphoramidite ligand **L*** (4 mol%), and DBU (1 equiv) in THF,[13] the desired decarboxylative allylic etherification reaction did not occur even after prolonged reaction times at room temperature. However, upon raising the temperature to 75 °C, the reaction took place cleanly to give the desired product **3a** with 92% yield and a greater than 25:1 diastereoselectivity (Table 2, entry 1). The use of the enantiomeric ligand *ent*-**L*** reversed the reaction stereochemistry to favor the formation of the corresponding diastereomeric product **4a** in 90% yield and with 20:1 diastereoselectivity (entry 2), thereby indicating that diastereoselectivity of the reactions was predominantly governed by the catalysts used, and the substrate stereochemistry had little effect on reaction stereochemistry (catalyst-controlled versus substrate-controlled).[17] To probe the generality of the reaction, other structurally diverse substrates with functionalized linear alkyl (entries 3 and 4), branched/cyclic alkyl (entries 5 and 6), and phenyl (entries 7 and 8) groups were studied, and uniformly good yields and high diastereoselectivities were obtained. In all cases studied, diastereoselectivities were dictated by the stereochemistry of the catalysts used, albeit the mismatched cases (entries 2, 4, 6, and 8) showed slightly lower diastereoselectivities than the matched ones. The results in Table 2 show that di-protected *syn*- and *anti*-1,2-diols can be prepared by CM of **1** with **B** followed by iridium(I)-catalyzed diastereoselective allylic etherification.

To study the functional group compatability of iridium(I)-catalyzed decarboxylative allylic etherification, the free alcohols **5** were prepared by CM of the corresponding allylic alcohol precursors with **B** in the presence of **A** (see the Supporting Information) and tested in the reaction.[18] If enabled, these reactions should provide monoprotected *syn*- and *anti*-1,2-diols with complete stereochemical control by the chiral ligands (**L*** and *ent*-**L***) used. As shown in Table 3, excellent reaction yields (≥84%) and diastereoselectivities (>25:1) were obtained in all examples, and the allylic hydroxy group was well tolerated in the reactions. Because of their tolerance of the hydroxy group, the use of CM and

Table 3: Asymmetric synthesis of monoprotected *syn*- and *anti*-1,2-diols by the iridium(I)-catalyzed diastereoselective decarboxylative allylic etherification of **5**.



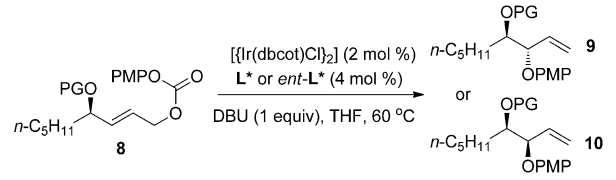
Entry	R	Ligand	Product	Yield [%][a]	d.r.[b]	*ee* [%][c]
1		**L***	**6a**	90	>25:1	>99
2		*ent*-**L***	**7a**	93	1:>25	>99
3[d]		**L***	*ent*-**7b**	90	>25:1[c]	>99
4[d]		***ent*-L***	***ent*-6b**	**91**	1:>25[c]	>99
5		**L***	**6c**	90	>25:1	–
6		*ent*-**L***	**7c**	92	1:>25	–
7[d]		**L***	*ent*-**7d**	87	>25:1[c]	99
8[d]		*ent*-**L***	*ent*-**6d**	84	1:16[c]	99

[a] Yield of the isolated product. [b] Determined by the ^{1}H NMR spectroscopy of the reaction mixtures. [c] Determined by HPLC. [d] Used *ent*-**5**.

iridium(I)-catalyzed allylic etherification enabled the asymmetric synthesis of differentiated *syn*- and *anti*-1,2-diols without using protecting groups.

Next, the scope with respect to the alcohol protecting groups in the iridium(I)-catalyzed decarboxylative allylic etherification was studied with Me, Bn,[19] and TBS groups,[19] and the results are shown in Table 4. Both Me and Bn groups

Table 4: Asymmetric synthesis of orthogonally protected *syn*- and *anti*-1,2-diols by the iridium(I)-catalyzed decarboxylative allylic etherification of **8**.

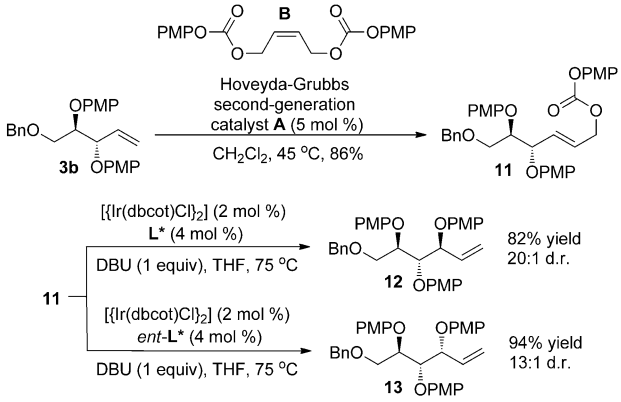


Entry	PG	Ligand	Product	Yield [%][a]	d.r.[b]
1	Me	**L***	**9a**	93	>25:1
2		*ent*-**L***	**10a**	95	1:>25
3	Bn	**L***	**9b**	91	>25:1
4		*ent*-**L***	**10b**	92	1:>25
5[c]	TBS	**L***	**9c**	82	12:1
6[c]		*ent*-**L***	**10c**	86	1:19

[a] Yield of the isolated product. [b] Determined by the ^{1}H NMR spectroscopy of the reaction mixtures. [c] Reaction ran at 75 °C.

worked well at 60 °C and proceeded with excellent yields and diastereoselectivities (entries 1–4). The TBS group required 75 °C, and exhibited a slightly reduced, but still synthetically useful yield and diastereoselectivity (entries 5 and 6). These results, taken together with those in Table 2 and Table 3, prove that the developed CM/iridium(I)-catalyzed decarboxylative allylic etherification strategy is a very efficient stereoselective synthetic route toward various 1,2-diol forms.

Finally, to highlight the powerful iteration of the CM/iridium(I)-catalyzed decarboxylative allylic etherification strategy, protected 1,2,3,4-tetraols were synthesized (Scheme 1). CM of the PMP-protected triol **3b** (entry 3 of



Scheme 1. Iteration of the iridium(I)-catalyzed decarboxylative allylic etherification and CM to synthesize PMP-protected 1,2,3,4-tetraols.

Table 2) with **B** generated **11** in 86% yield. Iridium(I)-catalyzed decarboxylative allylic etherification of **11** in the presence of **L*** at 75 °C gave the PMP-protected tetraol **12** in 82% yield and with a 20:1 diastereoselectivity. In contrast, the use of *ent*-**L*** generated the corresponding diastereomeric protected tetraol **13** in 94% yield and with 13:1 diastereoselectivity. Once again, diastereoselectivity was determined by the catalysts used.

In summary, we have developed a very efficient CM/iridium(I)-catalyzed decarboxylative allylic etherification strategy for preparing 1,2-diols with complete control of absolute and relative stereochemistry, as well as the protecting group scheme. Iridium(I)-catalyzed diastereoselective decarboxylative allylic etherification is tolerable to free and Me-/Bn-/TBS-protected alcohol functionalities, and its diastereoselectivity is controlled by the stereochemistry of the ligands/catalysts used. Protected 1,2,3,4-tetraols have been synthesized by iterative applications of the strategy. Considering the ubiquitous presence of 1,2-diol functionalities in organic compounds, the strategy should find a wide range of applications in organic synthesis.

Experimental Section

General procedure for the ruthenium-catalyzed cross-metathesis of **1**: The Hoveyda–Grubbs second-generation catalyst **A** (12.5 mg, 0.020 mmol, 3 mol%) was added to a solution of **1** (0.640 mmol) and (*Z*)-but-2-ene-1,4-diyl bis(4-methoxyphenyl) dicarbonate **B** (250 mg, 0.640 mmol, 1 equiv) in CH_2Cl_2 (2.5 mL) at room temperature. After stirring for 6 h at 45 °C, an additional portion each of **A** (8.00 mg, 0.013 mmol, 2 mol%) and **B** (125 mg, 0.320 mmol, 0.5 equiv) in CH_2Cl_2 (2.0 mL) was added. The reaction mixture was stirred for 6 h at 45 °C. The reaction mixture was concentrated in

vacuo, and the residue was purified by flash chromatography using *n*-hexane/ethyl acetate as an eluent to give the desired product.

General procedure for the iridium(I)-catalyzed decarboxylative allylic etherification: A flame-dried 5 mL spherical flask was cooled under vacuum and flushed with N_2. [{Ir(dbcot)Cl}$_2$] (3.5 mg, 0.004 mmol, 2 mol%), phosphoramidite ligand **L*** (5.0 mg, 0.008 mmol, 4 mol%), and THF (1.0 mL) were added to this flask under N_2. The reaction mixture was stirred to obtain a homogenous orange solution. Upon addition of DBU (30.0 μL, 0.200 mmol, 1 equiv), the color of the solution was changed from orange to light yellow. A PMP allyl carbonate (**2**, **5**, or **8**; 0.200 mmol) in THF (2.0 mL) was added to this yellow solution, and then the resulting homogenous solution was stirred at 60 °C until the starting PMP carbonate disappeared on TLC. The reaction mixture was concentrated in vacuo, and the residue was purified by silica gel column chromatography using *n*-hexane/ethyl acetate as an eluent to give the desired product.

Received: November 14, 2012
Published online: January 15, 2013

Keywords: alcohols · allylation · asymmetric catalysis · metathesis · iridium

[1] a) G. Casiraghi, F. Zanardi, G. Rassu, P. Spanu, *Chem. Rev.* **1995**, *95*, 1677 – 1716; b) G. C. Fu in *Modern Carbonyl Chemistry* (Ed.: J. Otera), Wiley-VCH, Weinheim, **2000**, pp. 69 – 91.

[2] a) J. Seyden-Penn in *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*, Wiley-VCH, Weinheim, **1995**; b) Q.-L. Zhou in *Privileged Chiral Ligands and Catalysts*, Wiley-VCH, Weinheim, **2011**.

[3] For *syn*-1,2-diols, see: a) H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483 – 2547; b) J. Kister, A. C. DeBaillie, R. Lira, W. R. Roush, *J. Am. Chem. Soc.* **2009**, *131*, 14174 – 14175; c) E. Vedrenne, O. A. Wallner, M. Vitale, F. Schmidt, V. K. Aggarwal, *Org. Lett.* **2009**, *11*, 165 – 168; d) B. M. Trost, H. Ito, E. R. Silcoff, *J. Am. Chem. Soc.* **2001**, *123*, 3367 – 3368; e) P. Jiao, M. Kawasaki, H. Yamamoto, *Angew. Chem.* **2009**, *121*, 3383 – 3386; *Angew. Chem. Int. Ed.* **2009**, *48*, 3333 – 3336.

[4] For differentiated *syn*-1,2-diols, see: a) G. R. Stanton, C. N. Johnson, P. J. Walsh, *J. Am. Chem. Soc.* **2010**, *132*, 4399 – 4408; b) D. R. Williams, A. A. Kiryanov, U. Emde, M. P. Clark, M. A. Berliner, J. T. Reeves, *Angew. Chem.* **2003**, *115*, 1296 – 1300; *Angew. Chem. Int. Ed.* **2003**, *42*, 1258 – 1262; c) D. Cartigny, K. Püntener, T. Ayad, M. Scalone, V. Ratovelomanana-Vidal, *Org. Lett.* **2010**, *12*, 3788 – 3791; d) S. Kobayashi, M. Horibe, *J. Am. Chem. Soc.* **1994**, *116*, 9805 – 9806; e) M. B. Andrus, J. Liu, Z. Ye, J. F. Cannon, *Org. Lett.* **2005**, *7*, 3861 – 3864; f) M. B. Andrus, B. B. V. Soma Sekhar, T. M. Truner, E. L. Meredith, *Tetrahedron Lett.* **2001**, *42*, 7197 – 7201; g) T. R. Hoover, S. R. Hitchcock, *Tetrahedron: Asymmetry* **2003**, *14*, 3233 – 3241.

[5] For *anti*-1,2-diols, see: a) T. Mukaiyama, N. Iwasawa, *Chem. Lett.* **1984**, 753 – 756; b) D. A. Evans, J. R. Gage, J. L. Leighton, A. S. Kim, *J. Org. Chem.* **1992**, *57*, 1961 – 1963; c) M. T. Crimmins, P. J. McDougall, *Org. Lett.* **2003**, *5*, 591 – 594; d) W. Notz, B. List, *J. Am. Chem. Soc.* **2000**, *122*, 7386 – 7387; e) A. B. Northrup, I. K. Mangion, F. Hettche, D. W. C. MacMillan, *Angew. Chem.* **2004**, *116*, 2204 – 2206; *Angew. Chem. Int. Ed.* **2004**, *43*, 2152 – 2154; f) A. B. Northrup, D. W. C. MacMillan, *Science* **2004**, *305*, 1752 – 1755; g) H. C. Brown, G. Narla, *J. Org. Chem.* **1995**, *60*, 4686 – 4687; h) T. Luanphaisarnnont, C. O. Ndubaku, T. F. Jamison, *Org. Lett.* **2005**, *7*, 2937 – 2940; i) K. Sa-ei, J. Montgomery, *Org. Lett.* **2006**, *8*, 4441 – 4443; j) B. M. Savall, N. A. Powell, W. R. Roush, *Org. Lett.* **2001**, *3*, 3057 – 3060; k) L. Albrecht, H. Jiang, G. Dickmeiss, B. Gschwend, S. G. Hansen, K. A. Jørgensen, *J. Am. Chem. Soc.* **2010**, *132*, 9188 – 9196; l) S. B. Han, H. Han, M. J. Krische, *J. Am. Chem. Soc.* **2010**, *132*, 1760 – 1761.

[6] For differentiated *anti*-1,2-diols, see: a) D. A. Evans, V. J. Cee, S. J. Siska, *J. Am. Chem. Soc.* **2006**, *128*, 9433 – 9441; b) S. M. Lim, N. Hill, A. G. Myers, *J. Am. Chem. Soc.* **2009**, *131*, 5763 – 5765; c) M. B. Andrus, B. B. V. Soma Sekhar, E. L. Meredith, N. K. Dalley, *Org. Lett.* **2000**, *2*, 3035 – 3037; d) Y. Zhao, A. W. Mitra, A. H. Hoveyda, M. L. Snapper, *Angew. Chem.* **2007**, *119*, 8623 – 8626; *Angew. Chem. Int. Ed.* **2007**, *46*, 8471 – 8474; e) Y. Zhao, J. Rodrigo, A. H. Hoveyda, M. L. Snapper, *Nature* **2006**, *443*, 67 – 70; f) N. Bajwa, M. P. Jennings, *J. Org. Chem.* **2008**, *73*, 3638 – 3641.

[7] For *syn*- and *anti*-1,2-diols, see: a) S. E. Denmark, W.-J. Chung, *Angew. Chem.* **2008**, *120*, 1916 – 1918; *Angew. Chem. Int. Ed.* **2008**, *47*, 1890 – 1892; b) S. Fanjul, A. N. Hulme, *J. Org. Chem.* **2008**, *73*, 9788 – 9791.

[8] For differentiated *syn*- and *anti*-1,2-diols, see: a) K. Soai, C. Shimada, M. Takeuchi, M. Itabashi, *J. Chem. Soc. Chem. Commun.* **1994**, 567 – 568; b) E. El-Sayed, N. K. Anand, E. M. Carreira, *Org. Lett.* **2001**, *3*, 3017 – 3020; c) Y. Georges, X. Ariza, J. Garcia, *J. Org. Chem.* **2009**, *74*, 2008 – 2012; d) K. Rohr, R. Mahrwald, *Org. Lett.* **2012**, *14*, 2180 – 2183; e) Z. Li, R. Wu, R. Michalczyk, R. B. Dunlap, J. D. Odom, L. A. P. Silks III, *J. Am. Chem. Soc.* **2000**, *122*, 386 – 387; f) J. A. Marshall, P. Eidam, *Org. Lett.* **2004**, *6*, 445 – 448.

[9] J. K. Park, D. T. McQuade, *Angew. Chem.* **2012**, *124*, 2771 – 2775; *Angew. Chem. Int. Ed.* **2012**, *51*, 2717 – 2721.

[10] a) P. Tosatti, A. Nelson, S. P. Marsden, *Org. Biomol. Chem.* **2012**, *10*, 3147 – 3163; b) J. F. Hartwig, M. J. Pouy, *Top. Organomet. Chem.* **2011**, *34*, 169 – 208; c) G. Helmchen, A. Dahnz, P. Düebon, M. Schelwies, R. Weihofen, *Chem. Commun.* **2007**, 675 – 691; d) R. Takeuchi, S. Kezuka, *Synthesis* **2006**, 3349 – 3366.

[11] a) B. M. Trost, M. L. Crawley, *Top. Organomet. Chem.* **2011**, *38*, 321 – 340; b) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921 – 2943.

[12] a) M. Roggen, E. M. Carreira, *Angew. Chem.* **2011**, *123*, 5683 – 5686; *Angew. Chem. Int. Ed.* **2011**, *50*, 5568 – 5571; b) S. Ueno, J. F. Hartwig, *Angew. Chem.* **2008**, *120*, 1954 – 1957; *Angew. Chem. Int. Ed.* **2008**, *47*, 1928 – 1931; c) F. López, T. Ohmura, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 3426 – 3427; d) M. Gärtner, S. Mader, K. Seehafer, G. Helmchen, *J. Am. Chem. Soc.* **2011**, *133*, 2072 – 2075.

[13] D. Kim, S. Reddy, O. V. Singh, J. S. Lee, S. B. Kong, H. Han, *Org. Lett.* **2013**, *15*, DOI: 10.1021/ol033237.

[14] a) J. Tornatzky, A. Kannenberg, S. Blechert, *Dalton Trans.* **2012**, *41*, 8215 – 8225; b) G. C. Vougioukalakis, R. H. Grubbs, *Chem. Rev.* **2010**, *110*, 1746 – 1787.

[15] a) J. S. Kingsbury, J. P. A. Harrity, P. J. Bonitatebus, Jr., A. H. Hoveyda, *J. Am. Chem. Soc.* **1999**, *121*, 791 – 799; b) S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000**, *122*, 8168 – 8179.

[16] For cross-metathesis of (protected)allylic alcohols, see: I. C. Stewart, C. J. Douglas, R. H. Grubbs, *Org. Lett.* **2008**, *10*, 441 – 444.

[17] S. Masamune, W. Choy, J. S. Petersen, L. R. Sita, *Angew. Chem.* **1985**, *97*, 1 – 31; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1 – 30.

[18] Although the free alcohols **5** were prepared by other routes, they can in principle be more efficiently prepared by iridium(I)-catalyzed allylic hydroxylation (Ref. [12d]) followed by CM with **B** (see the preparation of **5c** in the Supporting Information). The allylic hydroxy group is known to facilitate CM: A. H. Hoveyda, P. J. Lombardi, R. V. O'Brien, A. R. Zhugralin, *J. Am. Chem. Soc.* **2009**, *131*, 8378 – 8379.

[19] The TBS- and Bn-protected **8** can in principle be more efficiently prepared by iridium(I)-catalyzed allylic etherification (Ref. [12a] for the TBS-protected **8** and Ref. [12b] for the Bn-protected **8**) followed by CM with **B**.

