DOI: 10.1002/adsc.201100262

sp^3-sp^2 C-C Bond Formation *via* Brønsted Acid Trifluoromethanesulfonic Acid-Catalyzed Direct Coupling Reaction of Alcohols and Alkenes

Hui-Lan Yue,[a,b] Wei Wei,[a,b] Ming-Ming Li,[a,b] Yong-Rong Yang,[a,b] and Jian-Xin Ji[a,*]

[a] Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, People's Republic of China
Fax: (+86)-28-8285-5223; e-mail: jijx@cib.ac.cn
[b] Graduate University of the Chinese Academy of Sciences, Beijing 100049, People's Republic of China

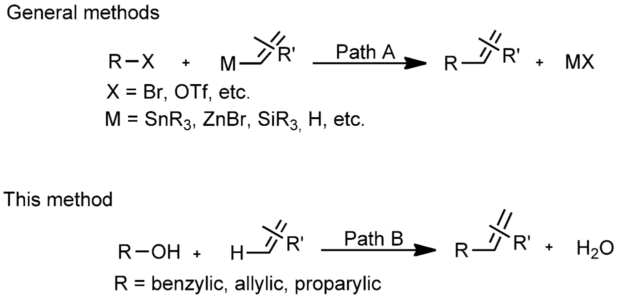
Received: April 7, 2011; Revised: July 27, 2011; Published online: November 16, 2011

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adcs.201100262.

Abstract: A novel and efficient trifluoromethanesulfonic acid-catalyzed sp^3-sp^2 C–C bond formation reaction through the direct coupling of alcohols with alkenes has been realized under mild conditions. The present protocol provides an attractive approach to a diverse range of polysubstituted olefins in good to excellent yields with high stereo- and regioselectivities.

Keywords: alcohols; alkenes; Brønsted acids; C–C bond formation; homogeneous catalysis; trifluoromethanesulfonic acid

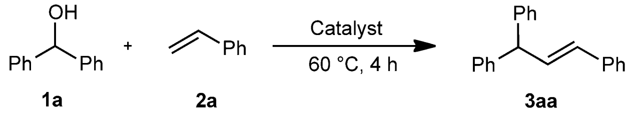
The efficient and selective creation of sp^3-sp^2 C–C bonds is one of the most important subjects in organic synthesis.[1] In the past decades, transition metal-catalyzed cross-coupling reactions of alkyl halides or triflates with alkenyl nucleophiles (e.g., Still, Negishi, Hiyama and Heck coupling) have became fundamental and powerful tools for the construction of sp^3-sp^2 C–C bonds (Scheme 1, Path A).[2,3] Nevertheless, such well developed coupling reactions are inevitably accompanied with problems such as the need of extra preparation steps for the active precursors and the generation of stoichiometric amounts of wastes. Therefore, there is still a great demand for more technically feasible and, especially, environmentally friendly methods to conveniently form sp^3-sp^2 C–C bonds. Herein, we report a novel and efficient Brønsted acid TfOH-catalyzed sp^3-sp^2 C–C bond formation *via* the direct coupling of alcohols[4] with simple alkenes, in which water is the only side product (Scheme 1, Path B).



Scheme 1. Cross-coupling methods for sp^3-sp^2 C–C bond formation.

Although alcohols and alkenes as commercially available and versatile building blocks have been extensively used in organic synthesis, up to date, only few strategies for the direct coupling of alcohols with simple alkenes to construct sp^3-sp^2 C–C bonds were developed.[5–9] Almost all of these methods were limited to specific alcohols or alkenes and suffered from low yields and/or the relatively complicated reaction conditions. Muzart et al. reported that $H_6P_2W_{18}O_{62}$ catalyzed the direct coupling of 1-indanol with styrene to form 2,3-dihydro-1-styryl-1*H*-indene in very low yield and selectivity.[6] Yamamoto et al. reported the palladium-catalyzed coupling of benzylic alcohols with *p*-methylstyrene in the presence of a stoichiometric amount of $(CF_3CO)_2O$ (3 equiv.) leading to the the desired products in moderate yields.[7] Jamison et al. described a nickel-catalyzed coupling reaction of (*E*)-3-phenylprop-2-en-1-ol with ethylene by employing P(*o*-anisyl)$_3$ as ligand and excess amounts of Et_3N and Me_3SiOTf to give (*E*)-penta-1,4-dienylbenzene in only 56% yield.[8] Very recently, Liu et al. reported that $FeCl_3{\cdot}6H_2O$ catalyzed the direct coupling of aromatic olefins with benzylic alcohols to give substituted alkenes in the presence of a stoichiometric amount of TsOH.[9] The present method for the direct coupling of benzylic, allylic, and propargylic alcohols with un-

Table 1. Optimization of the reaction conditions.[a]



Entry	Catalyst	Solvent	Yield [%][b]
1	TfOH (5 mol%)	DCE	36
2	TfOH (5 mol%)	toluene	44
3	TfOH (5 mol%)	$CHCl_3$	72
4	TfOH (5 mol%)	DBE	80
5	$HNTf_2$ (5 mol%)	DBE	71
6	$HClO_4$ (5 mol%)	DBE	74
7	MSA (5 mol%)	DBE	9
8	PTSA (5 mol%)	DBE	<5
9	H_2SO_4 (5 mol%)	DBE	<5
10	HBF_4 (5 mol%)	DBE	<5
11	$HSbF_6$ (5 mol%)	DBE	7
12	TFA (5 mol%)	DBE	0
13	HNO_3 (5 mol%)	DBE	0
14	HCl (5 mol%)	DBE	0
15	$Zn(OTf)_2$ (5 mol%)	DBE	0
16	$Cu(OTf)_2$ (5 mol%)	DBE	0
17	$Al(OTf)_3$ (5 mol%)	DBE	0
18	$In(OTf)_3$ (5 mol%)	DBE	37
19	AgOTf (5 mol%)	DBE	34
20	**TfOH (7.5 mol%)**	**DBE**	**93**

[a] *Reaction conditions:* benzhydrol **1a** (0.5 mmol), styrene **2a** (0.6 mmol), solvent (1 mL), 60 °C, 4 h, under air.

[b] Isolated yields based on the benzhydrol **1a**.

activated aromatic and aliphatic alkenes is realized under mild conditions by employing a simple Brønsted acid, TfOH,[10] (7.5 mol%) as catalyst, which provides a wide range of polysubstituted olefins in good to excellent yields and high selectivity. Interestingly, when some cyclic alkenes or 3,3-disubstituted branched chain olefins were used to react with benzhydrol, a different 1,2-hydride shift of the carbocation intermediate or a cyclization reaction of the carbocation intermediate with the aromatic ring occurred under our standard conditions, which offers attractive strategies for the construction of tetrasubstituted olefins or indane compounds.

In an initial experiment, TfOH (5 mol%) was added to a mixture of benzhydrol **1a** and styrene **2a** in 1,2-dichloroethane (DCE) at 60 °C under air, the desired product **3aa** was generated in 36% yield (Table 1, entry 1). The screening of a range of solvents showed that the reaction performed in 1,2-dibromoethane (DBE)[11,12] or $CHCl_3$ was significantly better than those in toluene and DCE (entries 1-4). Although the starting materials disappeared comparatively quickly in DCE compared with DBE, larger amounts of by-products were generated in DCE.[13] Subsequently, the catalytic activity of other catalysts was investigated in DBE. Besides TfOH, $HNTf_2$ and $HClO_4$ could also efficiently catalyze this coulping reaction (entries 5 and 6). Nevertheless, other Brønsted and Lewis acids such as methanesulfonic acid (MSA), *p*-toluenesulfonic acid (PTSA), H_2SO_4, HBF_4, $HSbF_6$, trifluoroacetic acid (TFA), HNO_3, HCl, $Zn(OTf)_2$, $Cu(OTf)_2$, $Al(OTf)_3$, $In(OTf)_3$ and AgOTf did not or only sluggishly catalyzed this reaction (entries 7–19). Further optimization suggested that the best yield (93%) was obtained when the TfOH loading was increased to 7.5 mol% (entry 20). No conversion was observed in the absence of catalyst.

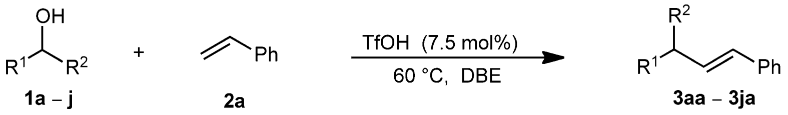
Under the optimized conditions, the scope and limitations of the reaction of various alcohols with styrene were investigated and the results are shown in Table 2. In general, benzhydrol and its derivatives which have electron-donating or electron-withdrawing groups on the aryl rings were suitable for this protocol, and the corresponding products were obtained in good to excellent yields (entries 1–6). 1-Phenylethanol could also be used in the reaction to give the expected product **3ga** in 83% yield (entry 7). In addition, propargylic alcohols such as 1-phenylprop-2-yn-1-ol and allylic alcohol such as (*E*)-1,3-diphenylprop-2-en-1-ol and cyclohex-2-enol were also compatible with this reaction, affording the desired products **3ha**–**3ja** in low to good yields (entries 8–10).

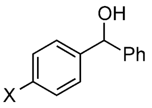
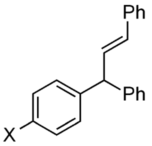
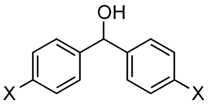
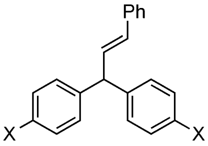
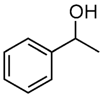
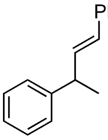
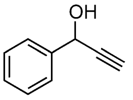
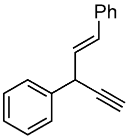
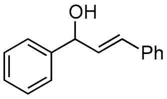
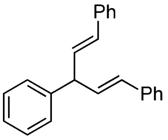
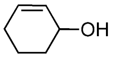
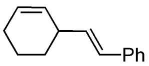
The scope of the TfOH-catalyzed coupling reaction was further expanded to a variety of alkenes (Table 3). In addition to styrene **2a**, a series of substituted styrenes containing either electron-rich or electron-deficient groups were all suitable substrates, and generated the corresponding products in excellent yields (entries 1–6). The sterically hindered disubstituted aromatic olefins such as ethene-1,1-diyldibenzene, prop-1-en-2-ylbenzene, and (*E*)-prop-1-enylbenzene were also tolerated in this process, leading to the desired products in good yields (entries 7–10).

As expected, cyclic alkenes such as 1-methylcyclopent-1-ene **2k** and 1-methylcyclohex-1-ene **2l** were suitable for this reaction, and the desired tetrasubstituted olefins **3ak**, **3ik** and **3al** were obtained in good to excellent yields (entries 11–13). Interestingly and unexpectedly, the product **3al** was generated in high yield when methylenecyclohexane **2m** was used as substrate (entry 14). This reaction might be carried out by the isomerization of **2m** to form the more stable 1-methylcyclohex-1-ene **2l**,[14] which then reacted with benzhydrol to give the product **3al**. Notably, owing to the high steric hindrance, reaction of cyclohexenylbenzene **2n** with benzhydrol **1a** offered the more stable trisubstituted olefin **3an** in 93% yield *via* the selective β-H elimination (entry 15).

Three different cyclic alkene products were isolated when unsubstituted cyclopentene **2o** or cyclohexene **2p** was allowed to react with benzhydrol **1a** under our standard conditions (Scheme 2). The following steps are considered to be involved in this transformation.

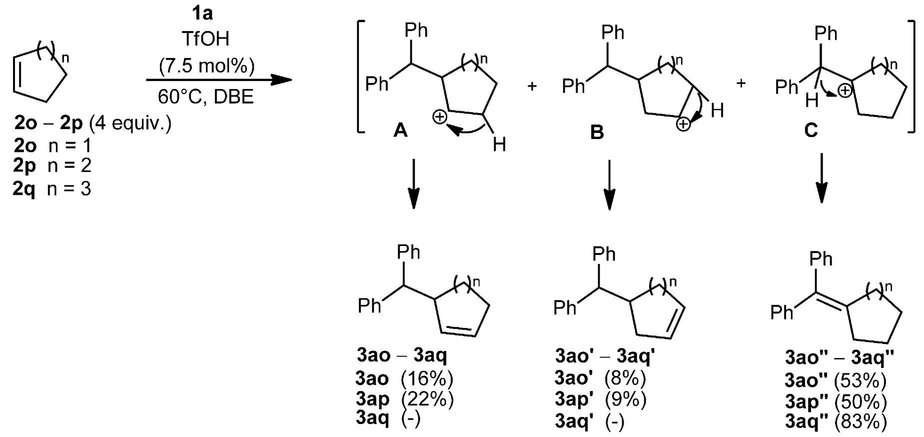
Table 2. TfOH-catalyzed direct coupling reaction of various alcohols **1** with styrene **2a**.[a]



Entry	Alcohols	X	Products		Yield [%][b]
1		H		**3aa**	93
2		Me		**3ba**	96
3		OMe		**3ca**	76
4		Cl		**3da**	92
5		Me		**3ea**	94
6		Cl		**3fa**	85
7				**3ga**	83
8				**3ha**	46
9				**3ia**	87
10				**3ja**	33

[a] *Reaction conditions:* alcohols **1** (0.5 mmol), styrene **2a** (0.6 mmol), TfOH (7.5 mol%), DBE (1 mL), 60 °C, 4–24 h, under air.

[b] Isolated yields based on alcohols **1**.

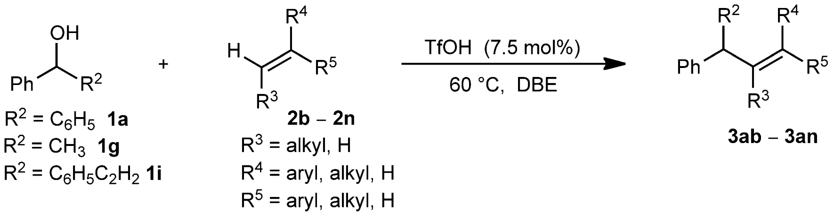


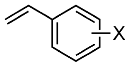
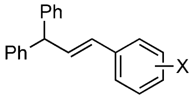
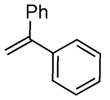
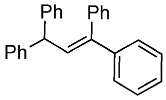
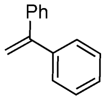
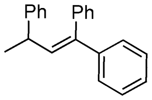
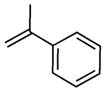
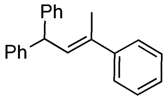
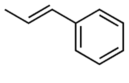
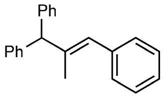
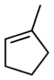
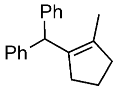
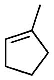
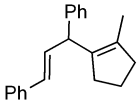
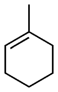
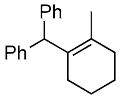
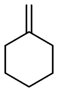
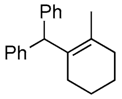
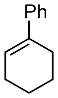
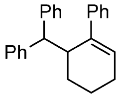
(**3ao**/**3ao'**) – (**3aq**/**3aq'**): Isolated yield and molar ratio was determined by ^{1}H NMR of crude mixture.

3ao" – **3aq"**: Isolated yield.

Scheme 2. TfOH-catalyzed direct coupling reactions of benzhydrol **1a** with cycloalkenes **2o**–**2q**.

Table 3. TfOH-catalyzed direct coupling reaction of alcohols **1** with various alkenes.[a]



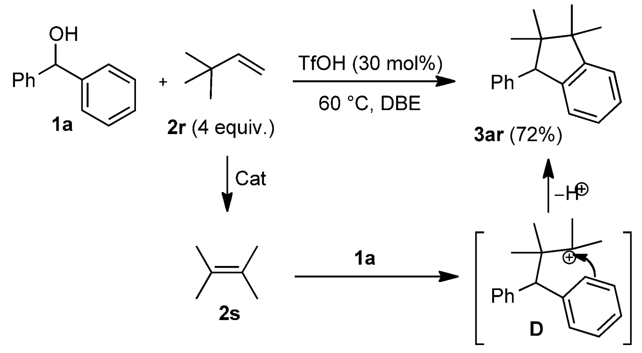
Entry	Alcohols	Alkenes	X		Products		Yield [%][b]
1	**1a**		*o*-Me	**2b**		**3ab**	90
2	**1a**		*m*-Me	**2c**		**3ac**	87
3	**1a**		*p*-Me	**2d**		**3ad**	80
4	**1a**		*p*-F	**2e**		**3ae**	98
5	**1a**		*p*-Cl	**2f**		**3af**	99
6	**1a**		*p*-Br	**2g**		**3ag**	96
7	**1a**			**3h**		**3ah**	98
8	**1g**			**3h**		**3gh**	62
9	**1a**			**2i**		**3ai**	77
10	**1a**			**2j**		**3aj**	89
11	**1a**			**2k**		**3ak**	96[c]
12	**1i**			**2k**		**3ik**	83[c]
13	**1a**			**2l**		**3al**	98[c]
14	**1a**			**2m**		**3al**	89[c]
15	**1a**			**2n**		**3an**	93[c]

[a] *Reaction conditions:* alcohols **1** (0.5 mmol), alkenes (0.6 mmol), TfOH (7.5 mol%), DBE (1 mL), 60 °C, 4-24 h, under air.

[b] Isolated yields based on alcohols **1**.

[c] Alkenes (2 mmol).

Benzhydrol **1a** reacts with cyclic alkene **2o** or **2p** to form a secondary carbocation intermediate **A**, which undergoes a selective β-H elimination to generate disubstituted olefin **3ao** or **3ap**. Meanwhile, the initially formed intermediate **A** suffers a different 1,2-hydride shift leading to the secondary carbocation intermediate **B** and tertiary carbocation intermediate **C**. Subsequently, a β-H elimination from intermediate **B** and

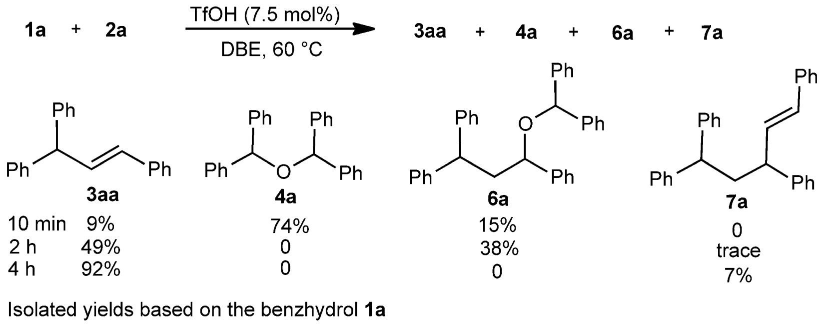


Scheme 3. TfOH-catalyzed direct coupling reaction of benzhydrol **1a** with 3,3-dimethylbut-1-ene **2r**.

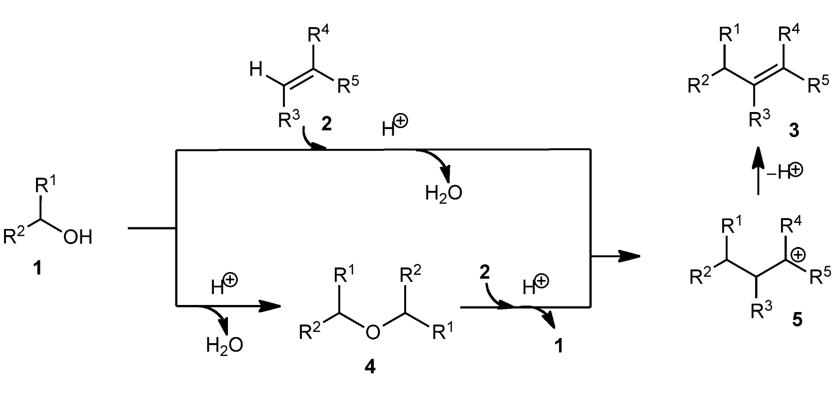
intermediate **C** would give the minor product **3ao′** or **3ap′** and major product **3ao″** or **3ap″**. When cycloheptene **2q** was allowed to react with **1a**, the major product **3aq″** was obtained in good yield, and products **3aq** and **3aq′** were not isolated in our reaction system. The tetrasubstituted olefins **3ao″**, **3ap″**, and **3aq″** were obtained as the major products, which might be caused by the easy formation of the more stable tertiary carbocation intermediates **C** and a subsequent regiospecific elimination of the tertiary β-hydrogen atom.

It was noteworthy that an indane compound **3ar** was obtained in 72% yield when an aliphalic terminal alkene was used in this protocol (Scheme 3).[15] This unique reaction may proceed through the methyl-rearrangement of 3,3-dimethylbut-1-ene **2r** to generate the more stable 2,3-dimethylbut-2-ene **2s**.[16] Then alkene **2s** reacts with benzhydrol **1a** giving rise to a carbocation intermediate **D**, which leads to the formation of indane **3ar** through intramolecular aromatic electrophilic substitution. This reaction system provides a useful synthetic method to indane structural motifs, which are extensively existed in nature products, biologically active compounds and pharmaceuticals.[17]

In order to obtain clear mechanistic insights into this reaction, an NMR spectroscopy study was performed on a mixed solution of benzhydrol **1a**, styrene **2a**, and TfOH (7.5 mol%) in $CDCl_3$ at 60 °C (see Supporting Information, Scheme S1). Signals for the dimeric ether **4a**, **6a**, and a small amount of alkene **7a** were observed and the corresponding compounds were also isolated together with the desired product **3aa** (Scheme 4). The product **3aa** was almost quantitatively obtained when a separate experiment was performed between ether **4a** and styrene under our standard conditions, suggesting that dimeric ether **4** (Scheme 5) might be an intermediate in this reaction. Nevertheless, the direct alkylation of an alkene with



Scheme 4. Reaction of benzhydrol **1a** and styrene **2a**.



Scheme 5. Plausible mechanism.

an alcohol could not be excluded at the present stage.[18] Furthermore, the formation of compounds **6a** and **7a** indicated that alkyl cation **5** (Scheme 5) might be involved in this reaction system.

Based on the above results and previous studies,[18] we propose possible mechanisms for this coupling reaction as shown in Scheme 5. One pathway could be a direct alkylation of alkene **2** with alcohol **1** to generate alkyl cation **5**. Then, the deprotonation of **5** leads to the formation of the desired product **3**. Another probable pathway is that the starting alcohol **1** is rapidly converted to corresponding dimeric ether **4** in the presence of TfOH. Then, the alkylation of alkene **2** by dimeric ether **4** occurs, affording the desired product **3** and releasing the starting alcohol.

In summary, we have successfully developed a convenient and efficient method for sp^3-sp^2 C–C bond formation through the direct coupling of various benzylic alcohols with alkenes by employing a simple Brønsted acid, TfOH, as catalyst under mild conditions. The present protocol provides an attractive approach to a diverse range of polysubstituted olefins in good to excellent yields with high stereo- and regioselectivities. Studies on the detailed mechanism and its application are ongoing.

Experimental Section

General Remarks

All commercially available reagent grade chemicals were purchased from Aldrich, Acros and Alfa Aesar Chemical Company. All reagents and solvents were used as received without further purification unless otherwise stated. NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 600 spectrometer with TMS as internal standard (600 MHz ^{1}H, 150 MHz ^{13}C) at room temperature, and the chemical shifts (δ) are expressed in ppm and J values are given in Hz. The following abbreviations are used to indicate the multiplicity: s (singlet), d (doublet), t (triplet), m (multiplet), br (broad). Mass analyses and HR-MS were obtained on an Agilent 5973N MSD mass spectrometer and a Waters Micromass GCT Premier mass spectrometer by the EI method, respectively.

General Procedure for the Direct Coupling of an Alcohol with an Alkene

To a stirred mixture of alcohol (0.5 mmol) and alkene (0.6 mmol) in DBE (1 mL) under air, was added the TfOH (7.5 mol%). The mixture was heated at 60 °C and stirred for 4–24 h. Upon completion of the reaction, the mixture was filtered through silica gel and washed with ethyl acetate (10 mL) to give a brown solution. After filtration, the solvent was removed by vacuum evaporation. The residue was purified by silica-gel flash column chromatography by using hexane/ethyl acetate as the eluent. The desired product was isolated as a white solid, which was suitable for analytical purposes.

Acknowledgements

We are grateful for the financial support from the National Natural Science Foundation of China (20802072).

References

[1] For reviews, see: a) *Metal-Catalyzed Cross-Coupling Reactions*, (Eds.: A. D. Meijere, F. Diederich), Wiley-VCH, New York, **2004**; b) *Acid Catalysis in Modern Organic Synthesis*, (Eds.: H. Yamamoto, K. Ishihara), Wiley-VCH, New York, **2008**.

[2] a) H. Tang, K. Menzel, G. C. Fu, *Angew. Chem.* **2003**, *115*, 5233–5236; *Angew. Chem. Int. Ed.* **2003**, *42*, 5079–5082; b) J. Zhou, G. C. Fu, *J. Am. Chem. Soc.* **2003**, *125*, 12527–12530; c) S. R. Dubbaka, P. Vogel, *J. Am. Chem. Soc.* **2003**, *125*, 15292–15293; d) S. L. Wiskur, A. Korte, G. C. Fu, *J. Am. Chem. Soc.* **2004**, *126*, 82–83; e) D. A. Powell, T. Maki, G. C. Fu, *J. Am. Chem. Soc.* **2005**, *127*, 510–511; f) X. Dai, N. A. Strotman, G. C. Fu, *J. Am. Chem. Soc.* **2008**, *130*, 3302–3303; g) Y. Kobayashi, Y. Tokoro, K. Watatani, *Eur. J. Org. Chem.* **2000**, 3825–3834; h) N. Tsukada, T. Sato, Y. Inoue, *Chem. Commun.* **2001**, 237–238; i) L. Firmansjah, G. C. Fu, *J. Am. Chem. Soc.* **2007**, *129*, 11340–11341.

[3] Some reports for the coupling of alcohols with metallic alkenyl nucleophiles, see: a) Y. Nishimoto, M. Kajioka, T. Saito, M. Yasuda, A. Baba, *Chem. Commun.* **2008**, 6396–6398; b) G. W. Kabalka, M. L. Yao, S. Borella, Z. Z. Wu, *Org. Lett.* **2005**, *7*, 2865–2867.

[4] For some examples of the Lewis and Brønsted acid-catalyzed direct substitution reaction of alcohols, see: a) M. Noji, T. Ohno, K. Fuji, N. Futaba, H. Tajima, K. Ishii, *J. Org. Chem.* **2003**, *68*, 9340–9347; b) K. Mertins, I. Iovel, J. Kischel, A. Zapf, M. Beller, *Angew. Chem.* **2005**, *117*, 242–246; *Angew. Chem. Int. Ed.* **2005**, *44*, 238–242; c) I. Iovel, K. Mertins, J. Kischel, A. Zapf, M. Beller, *Angew. Chem.* **2005**, *117*, 3981–3985; *Angew. Chem. Int. Ed.* **2005**, *44*, 3913–3917; d) K. Mertins, I. Iovel, J. Kischel, A. Zapf, M. Beller, *Adv. Synth. Catal.* **2006**, *348*, 691–695; e) M. Rueping, B. J. Nachtsheim, W. Ieawsuwan, *Adv. Synth. Catal.* **2006**, *348*, 1033–1037; f) J. Liu, E. Muth, U. Flörke, G. Henkel, K. Merz, J. Sauvageau, E. Schwake, G. Dyker, *Adv. Synth. Catal.* **2006**, *348*, 456–462; g) M. Rueping, B. J. Nachtsheim, A. Kuenkel, *Org. Lett.* **2007**, *9*, 825–828; h) R. Sanz, D. Miguel, A. Martínez, J. M. Álvarez-Gutiérrez, F. Rodríguez, *Org. Lett.* **2007**, *9*, 727–730; i) S. Shirakawa, S. Kobayashi, *Org. Lett.* **2007**, *9*, 311–314; j) U. Jana, S. Biswas, S. Maiti, *Tetrahedron Lett.* **2007**, *48*, 4065–4069; k) W. Huang, J. Wang, Q. Shen, X. Zhou, *Tetrahedron Lett.* **2007**, *48*, 3969–3973; l) S. Y. Zhang, Y. Q. Tu, C. A. Fan, F. M. Zhang, L. Shi, *Angew. Chem.* **2009**, *121*, 8917–8921; *Angew. Chem. Int. Ed.* **2009**, *48*, 8761–8765; m) E. Emer, R. Sinisi, M. G. Capdevila, D. Petruzziello, F. De Vincentiis, P. G. Cozzi, *Eur. J. Org. Chem.* **2011**, 647–666.

[5] a) N. Tsukada, T. Sato, Y. Inoue, *Chem. Commun.* **2003**, 2404–2405; b) K. Komeyama, Y. Kouya, Y. Ohama, K. Takaki, *Chem. Commun.* **2011**, 5031–5033.

[6] A. Tarlani, A. Riahi, M. Abedini, M. M. Amini, J. Muzart, *J. Mol. Catal. A: Chem.* **2006**, *260*, 187–189.

[7] H. Narahashi, T. Shimizu, A. Yamamoto, *J. Organomet. Chem.* **2008**, *693*, 283–296.

[8] R. Matsubara, T. F. Jamison, *J. Am. Chem. Soc.* **2010**, *132*, 6880–6881.

[9] Z.-Q. Liu, Y. Zhang, L. Zhao, Z. Li, J. Wang, H. Li, L.-M. Wu, *Org. Lett.* **2011**, *13*, 2208–2211.

[10] For some TfOH-catalyzed reactions, see: a) R. M. Roberts, A. M. El-Khawaga, K. M. Sweeney, M. F. El-Zohry, *J. Org. Chem.* **1987**, *52*, 1591–1599; b) H. Kotsuki, K. Arimura, T. Araki, T. Shinohara, *Synlett* **1999**, 462–464; c) T. Mukaiyama, H. Jona, K. Takeuchi, *Chem. Lett.* **2000**, 696–697; d) T. Ohishi, T. Kojima, T. Matsuoka, M. Shiro, H. Kotsuki, *Tetrahedron Lett.* **2001**, *42*, 2493–2496; e) T. Jin, F. Yang, C. Liu, Y. Yamamoto, *Chem. Commun.* **2009**, 3533–3535; f) S. Hwang, Y. Lee, P. H. Lee, S. Shin, *Tetrahedron Lett.* **2009**, *50*, 2305–2308; g) Á. Pintér, A. Sud, D. Sureshkumar, M. Klussmann, *Angew. Chem.* **2010**, *122*, 5124–5128; *Angew. Chem. Int. Ed.* **2010**, *49*, 5004–5007.

[11] Properties of 1,2-dibromoethane: colourless liquid, density: 2.17 $g cm^{-1}$, melting point: 9–10 °C, boiling point: 131–132 °C.

[12] For an example using DBE as solvent, see: K. Ren, M. Wang, L. Wang, *Eur. J. Org. Chem.* **2010**, 565–571.

[13] Besides the by-product **7a** (isolated yield: 23%), other by-products that were difficult to separate on silica gel column chromatography were finally analyzed by GC-MS. GC-MS analysis see the Supporting Information.

[14] B. T. Khai, A. Arcelli, *Chem. Ber.* **1993**, *126*, 2265–2268.

[15] a) B. Charleux, A. Rives, J. P. Vairon, *Macromolecules* **1996**, *29*, 5777–5783; b) P. Vázquez, L. Pizzio, C. Cáceres, M. Blanco, H. Thomas, E. Alesso, L. Finkielsztein, B. Lantaño, G. Moltrasio, J. Aguirre, *J. Mol. Catal. A: Chem.* **2000**, *161*, 223–232; c) see ref.[4a]

[16] G. M. Brooke, J. R. Cooperwaite, A. G. Morpeth, *J. Chem. Soc. Perkin Trans. 1* **1985**, 2637–2642.

[17] M. Zhang, L. Zhu, X. Ma, *Tetrahedron: Asymmetry* **2003**, *14*, 3447–3453.

[18] a) M. Yasuda, T. Somyo, A. Baba, *Angew. Chem.* **2006**, *118*, 807–810; *Angew. Chem. Int. Ed.* **2006**, *45*, 793–796; b) R. Sanz, D. Miguel, A. Martínez, J. M. Álvarez-Gutiérrez, F. Rodríguez, *Org. Lett.* **2007**, *9*, 2027–2030.