DOI: 10.1002/adsc.201300439

Synthesis and Structures of Air-Stable Binuclear Hafnocene Perfluorobutanesulfonate and Perfluorobenzenesulfonate and their Catalytic Application in C−C Bond-Forming Reactions

Ningbo Li,[a] Xiaohong Zhang,[a] Xinhua Xu,[a,b,*] Yun Chen,[a] Renhua Qiu,[a,*] Jinyang Chen,[a] Xie Wang,[a] and Shuang-Feng Yin[a,*]

[a] State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University,
Fax: (+86)-731-8882-1546; e-mail: xhx1581@hnu.edu.cn or renhuaqiu@hnu.edu.cn or sf_yin@hnu.edu.cn
[b] State Key Laboratory of Elemento-Organic Chemistry, Nankai, University, Tianjing 300071, People's Republic of China

Received: May 20, 2013; Revised: June 13, 2013; Published online: August 13, 2013

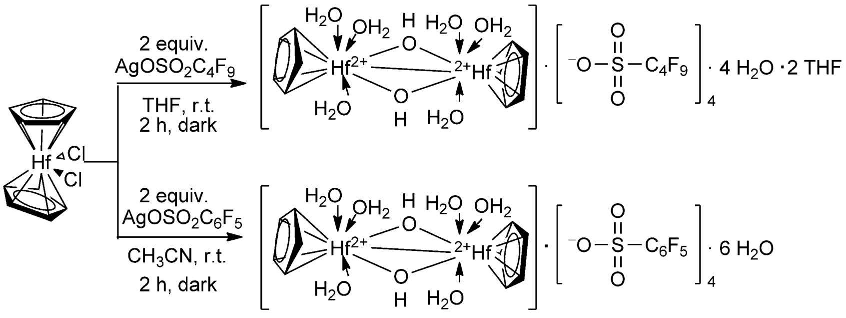
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201300439.

Abstract: The two air-stable μ^2-hydroxy-bridged binuclear hafnocene perfluorobutanesulfonate and perfluorobenzenesulfonate complexes were successfully synthesized. The high catalytic activity and recyclability of these complexes were exemplified for various carbon-carbon bond formation reactions. Compared with our previously reported hafnocene perfluorooctanesulfonate, these complexes show stronger Lewis acidity and better catalytic activity, and should find broad applications in organic synthesis.

Keywords: C−C bond formation; hafnocenes; homogeneous catalysis; Lewis acids; perfluorobutane(benzene)sulfonates

Organometallic Lewis acid catalysis has attracted much attention in organic synthesis, especially the bimetallic Lewis acid catalysis, which is commonly observed in metalloenzyme activities.[1] Recently, various scientific activities have been devoted to construct bimetallic Lewis acid catalysis systems to mimic such actions in the organic synthesis.[2] For example, we have prepared the binuclear organobismuth complexes bridged by sulfur atoms, and found that they showed higher cooperative catalytic effect in the chemical fixation of CO_2,[3] illustrating that by fixation of two metal centers in a suitable framework, the binuclear organometallic complexes show high catalytic efficiency compared with their monomer analogues.[4] Besides, we have synthesized anther two air-stable and water-tolerant binuclear zirconocene perfluorobenzenesulfonate $[\{CpZr(OH_2)_3\}_2(\mu^2\text{-}OH)_2][SO_3C_6F_5]_4\cdot 6H_2O$ (**1**$\cdot 6H_2O$), and binuclear hafonocene perfluorooctanesulfonate $[\{CpHf(OH_2)_3\}_2(\mu^2\text{-}OH)_2][SO_3C_8F_{17}]_4\cdot 4H_2O\cdot 2THF$ (**2**$\cdot 4H_2O\cdot 2THF$) Lewis acids catalysts, which showed moderate to high catalytic efficiency in C−C and C−O bond formation reactions.[5] However, it should be noted that their stabilities and Lewis acidity/catalytic activities are not only related to the special binuclear cations but also to the perfluoro anions, because the strong C−F bonds in the perfluoro anions can enhance the robustness and anti-oxidative role as well as the relative lipophobic ability.[6] Furthermore, the longer fluorocarbon chain will cause lower catalytic activity which, owing to the fact that the perfluoro anions well wrap the cationic metal center, make it hard for the lipophilic substrates to approach the center metal atom for activation. Besides, due to the strongly lipophobic property of the perfluorooctyl group, the complex usually exhibited low solubility in common organic solvents, such as hafnocene complex (**2**$\cdot 4H_2O\cdot 2THF$),[7] which may be another reason for the decline of catalytic efficiency. In addition, the features of the perfluorooctanesulfonate (PFOS) result in severe environmental pollution and potential toxicity to animals and human beings.[8]

According to the literature,[9] the toxicities of perfluorobutane(benzene)sulfonates were lower than that of PFOS, and their lipophobicities were weaker than that of the perfluorooctyl group.[7] Herein, by combining the binuclear hafnocene cation with the perfluorobutane(benzene)sulfonates anions, we successfully synthesized the hafnocene perfluorobutanesulfonate and perfluorobenzenesulfonate complexes, and assessed their catalytic activities in various carbon-carbon bond-forming reactions, such as the Mukaiyama–aldol reaction, Mukaiyama–Michael addition reaction, Michael addition reaction and Mannich reaction.



Scheme 1. Synthesis of **3**$\cdot$4 $H_2O$$\cdot$2 THF and **4**$\cdot$6 H_2O.

The hafnocene perfluorobutanesulfonate $[\{CpHf(OH_2)_3\}_2(\mu^2\text{-}OH)_2][OSO_2C_4F_9]_4\cdot 4H_2O\cdot 2THF$ (**3**$\cdot$4 $H_2O$$\cdot$2 THF) and perfluorobenzenesulfonate $[\{CpHf(OH_2)_3\}_2(\mu^2\text{-}OH)_2]$ $[OSO_2C_6F_5]_4\cdot 6H_2O$ (**4**$\cdot$6 H_2O) complexes were synthesized by treatment of Cp_2HfCl_2 with silver perfluorobutanesulfonate and perfluorobenzenesulfonate (AgX, for **3**, X = $OSO_2C_4F_9$; for **4**, X = $OSO_2C_6F_5$) (2 equiv.) in THF or CH_3CN (Scheme 1), respectively.

^{1}H NMR and elemental analyses show that the freshly prepared samples after recrystallization contain four H_2O molecules and two THF molecules for **3**, and six H_2O molecules for **4**. We found that **3**$\cdot$4 $H_2O$$\cdot$2 THF and **4**$\cdot$6 H_2O remained as dry crystals or powder and suffered no color change in a test period of one year in the open air. Therefore, the two complexes can be considered as air-stable complexes in the ambient environment and have great advantages over hafnocene triflates from the operational point of view.[10]

The cationic structures of these complexes in the solid state were confirmed by X-ray analysis. An ORTEP representation of **3**$\cdot$4 $H_2O$$\cdot$2 THF and **4**$\cdot$6 H_2O and selected bonds and angles are shown in Figure 1 and Figure 2. Accoding to the X-ray structure, it can be concluded that the hafnium atoms have distorted octahedral coordination geometry with the Cp group being *Ttrans* to OH consistent with $[CpHf^{2+}(OH_2)_3(\mu^2\text{-}OH)_2Hf^{2+}(OH_2)_3Cp]$ in **2**$\cdot$4 $H_2O$$\cdot$2 THF structure.[5b] The $C_4F_9SO_3^-/C_6F_5SO_3^-$ ions, the dissociated H_2O molecules, and solvating ligand THF are packed around the complex cation in such a way that their oxygen atoms point towards the H_2O ligands. The C_4F_9/C_6F_5 side chains of the anions, on the other hand, are clustered together to form the hydrophobic domains.

The thermal behavior of complexes **3**$\cdot$4 $H_2O$$\cdot$2 THF and **4**$\cdot$6 H_2O was investigated by TG-DSC in an O_2 atmosphere (Figure S1 in the Supporting Information). The curves showed that they were thermally stable up

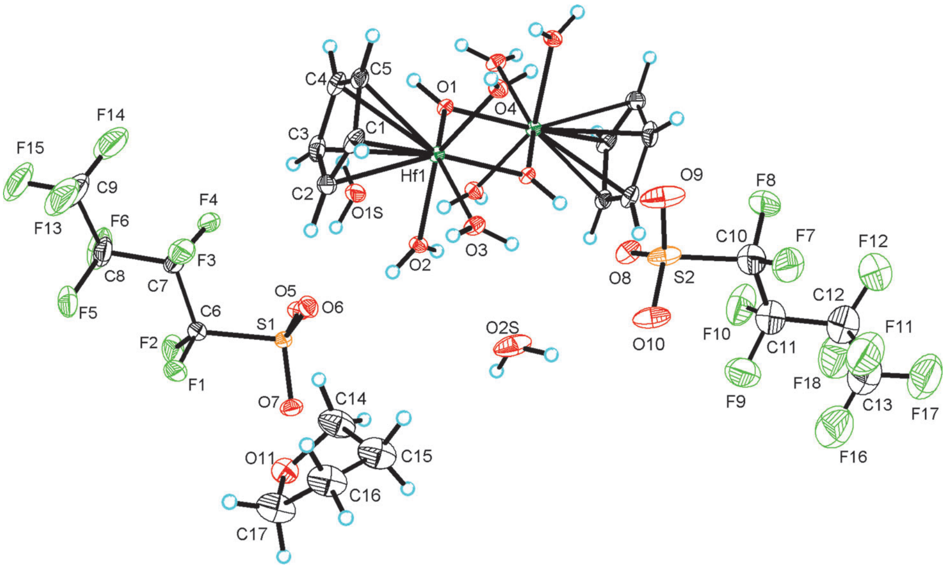


Figure 1. ORTEP view of crystal structure of **3**$\cdot$4 $H_2O$$\cdot$2 THF. Selected bond lengths (Å) and angles (deg): Hf1−O1, 2.091 (4); Hf1−O1A, 2.156 (4); Hf1−O2, 2.177(4); Hf1−O3, 2.187(4); Hf1−O4, 2.116(4); Hf1−C1, 2.501(6); Hf1−C2, 2.482(6); Hf1−C3, 2.482(6); Hf1−C4, 2.513(6); Hf1−C5, 2.521(5); Hf1−Hf1A, 3.4979(4); Hf1−O1−Hf1A, 110.88(16); O1−Hf1−O1A, 69.12(16); the two Cp ring planes are parallel.

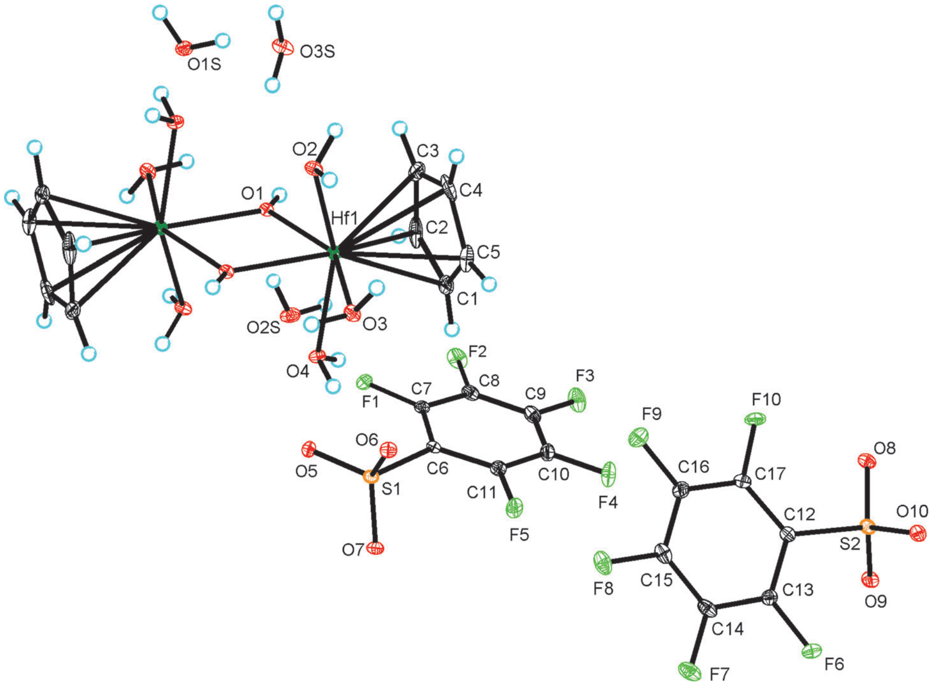


Figure 2. ORTEP view of crystal structure of **4**$\cdot 6H_2O$. Selected bond lengths (Å) and angles (deg): Hf1−O1, 2.082 (2); Hf1−O1A, 2.138 (2); Hf1−O2, 2.146(2); Hf1−O3, 2.171(2); Hf1−O4, 2.160(2); Hf1−C1, 2.510(3); Hf1−C2, 2.485(3); Hf1−C3, 2.481(3); Hf1−C4, 2.504(3); Hf1−C5, 2.523(3); Hf1−Hf1A, 3.4972(2); Hf1−O1−Hf1A, 111.05(9); O1−Hf1−O1A, 68.95(8); the two Cp ring planes are parallel.

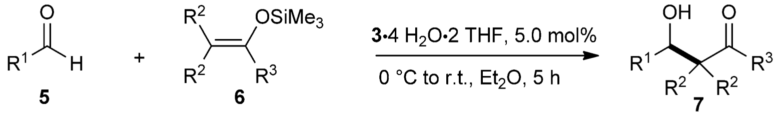
to about 300 °C, illustrating the antioxidative role of the perfluoro anions. The large molar conductivity value ($\Lambda = 398\ \mu S\cdot cm^{-1} mol^{-1}$; 295 $\mu S\ cm^{-1} mol^{-1}$, Table S1 in the Supporting Information) were consistent with the complete ionization of **3**$\cdot 4H_2O\cdot 2THF$ and **4**$\cdot 6H_2O$ into a 1:4 electrolyte.[11] In addition, **3**$\cdot 4H_2O\cdot 2THF$ and **4**$\cdot 6H_2O$ are highly soluble in methanol and in common polar organic solvents in sharp contrast to **2**$\cdot 4H_2O\cdot 2THF$ (Table S2 in the Supporting Information).

A significant red shift was observed in UV-Vis spectra due to the strong complex formation between 10-methylacridone and **3**$\cdot 4H_2O\cdot 2THF$, illustrating a large Lewis acidity of **3**$\cdot 4H_2O\cdot 2THF$ (Figure S2 in the Supporting Information).[12] We also estimated the Lewis acidity of complexes **2–4** by the red shift (λ_{em}) of Lewis acid metal ions (Hf^{2+}) with 10-methylacridone on the basis of fluorescence spectra.[13] The fluorescence maxima (λ_{max}) of complexes **2–4** are 464 nm, 472 nm and 470 nm, respectively (Figure S3 in the Supporting Information). Obviously, the Lewis acidity of **2**$\cdot 4H_2O\cdot 2THF$ is lower than those of **3**$\cdot 4H_2O\cdot 2THF$ and **4**$\cdot 6H_2O$. Besides, they have a relatively strong acidity with acid strength of $0.8 < Ho \leq 3.3$ (*Ho* being the Hammett acidity function),[14] larger than that of **2**$\cdot 4H_2O\cdot 2THF$ ($3.3 < Ho \leq 4.8$) detemined by the Hammett indicator method.[5] These characteristic features encouraged us to evaluate their performance as Lewis acid catalysts for carbon-carbon bond-forming reactions, such as the Mukaiyama–aldol reaction, Mukaiyama–Michael addition reaction, Michael addition reaction and Mannich reaction.

The Mukaiyama–aldol reaction mediated by a Lewis acid is one of the most convenient processes for the construction of carbon-carbon bonds in organic synthesis. This route provides a rapid access to synthesize β-hydroxy carbonyl compounds, and has induced many synthetic efforts due to these motifs often being seen in natural products and bioactive molecules.[15] Several efficient Lewis acid catalysts based on titanium, zirconium, copper and Brønsted acids have been reported. But in most cases, temperatures of −20 °C to −80 °C and strictly anhydrous conditions are required.[16] We hence assessed the catalytic efficiency with **3**$\cdot 4H_2O\cdot 2THF$ in the Mukaiyama–aldol reaction, and a high catalytic activity was observed (Table 1).

As shown in Table 1, the complex **3** showed high catalytic efficency in the Mukaiyama–aldol reaction, good-to-excellent yields were obtained (Table 1, **7a–7r**, 81–96%). Compared with our reported catalyst **2**$\cdot 4H_2O\cdot 2THF$, the yield was apparently improved but the reaction time was relatively reduced, and such special features were observed in cases of aromatic aldehydes with different electron-donating and electron-withdrawing groups (Table 1, entries 2–13). For example, as shown in Table 1, entry 5, the yield of **7e**

Table 1. Product yields for reaction of aldehydes and enol silyl ethers catalyzed by $\mathbf{3}\cdot 4H_2O\cdot 2THF$.[a]



Entry	R^1	R^2	R^3	Product	Yield [%][b]
1	Ph (**5a**)	CH_3 (**6a**)	OMe (**6a**)	**7a**	95
2	p-$CH_3C_6H_4$ (**5b**)	CH_3 (**6a**)	OMe (**6a**)	**7b**	92
3	p-$CF_3C_6H_4$ (**5g**)	CH_3 (**6a**)	OMe (**6a**)	**7c**	96
4	p-ClC_6H_4 (**5f**)	CH_3 (**6a**)	OMe (**6a**)	**7d**	94
5	Ph (**5a**)	H (**6b**)	Ph (**6b**)	**7e**	93
6	p-$CH_3C_6H_4$ (**5b**)	H (**6b**)	Ph (**6b**)	**7f**	90
7	p-$CH_3OC_6H_4$ (**5c**)	H (**6b**)	Ph (**6b**)	**7g**	89
8	o-FC_6H_4 (**5d**)	H (**6b**)	Ph (**6b**)	**7h**	92
9	p-ClC_6H_4 (**5e**)	H (**6b**)	Ph (**6b**)	**7i**	93
10	p-BrC_6H_4 (**5f**)	H (**6b**)	Ph (**6b**)	**7j**	91
11	p-$CF_3C_6H_4$ (**5g**)	H (**6b**)	Ph (**6b**)	**7k**	95
12	o-$CF_3C_6H_4$ (**5h**)	H (**6b**)	Ph (**6b**)	**7l**	94
13	o-$NO_2C_6H_4$ (**5i**)	H (**6b**)	Ph (**6b**)	**7m**	94
14	PhCH=CH (**5j**)	CH_3 (**6a**)	OMe (**6a**)	**7n**	92
15	m-$ClC_6H_4CH{=}CH$ (**5k**)	CH_3 (**6a**)	OMe (**6a**)	**7o**	93
16	o-$CH_3CH{=}CH$(**5l**)	CH_3 (**6a**)	OMe (**6a**)	**7p**	90
17	PhCH=CH (**5j**)	H (**6b**)	Ph (**6b**)	**7q**	87
18	$CH_3CH_2CH_2$ (**5m**)	H (**6b**)	Ph (**6b**)	**7r**	81

[a] $\mathbf{3}\cdot 4H_2O\cdot 2THF$: 0.05 mmol; **5**: 1.0 mmol; **6**: 1.2 mmol; solvent: Et_2O; 0 °C to room temperature.

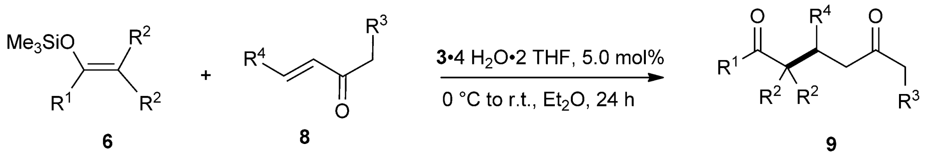
[b] Isolated yield.

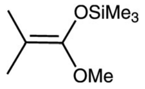
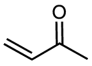
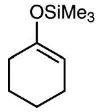
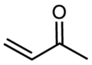
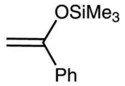
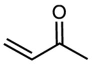
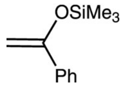
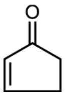
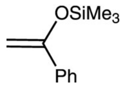
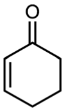
was up to 93% at 5 h with $\mathbf{3}\cdot 4H_2O\cdot 2THF$, while that with $\mathbf{2}\cdot 4H_2O\cdot 2THF$ with only 78% at 24 h.[5b] And the aldehydes with electron-withdrawing groups (such as chloride and trifluoromethyl) in the phenyl plane exhibited higher reaction activity than the aldehydes with electron-donating groups (for example, methyl and methoxy) (Table 1, entries 2–13). The parent cinnamaldehyde and substituted cinnamaldehydes with a double bond were also tolertaed in this catalytic system, and successfully reacted with different silyl enol ethers to form 1,2-addition adducts in high yields (Table 1, entries 14–17). The alkyl aldehyde also showed good reactivity with 81% yield with $\mathbf{3}\cdot 4H_2O\cdot 2THF$, while the yield of **7r** with catalyst of $\mathbf{2}\cdot 4H_2O\cdot 2THF$ under the same conditions was only 46%, illustrating a remarkable improvement of the catalytic efficiency.

The Mukaiyama–Michael addition is a powerful tool for the preparation of synthetically useful 1,5-dicarbonyl compounds, which are important building blocks for the synthesis of various biologically active molecules.[17] Presently, several catalysts are known for the direct Michael reaction, but for the Mukaiyama–Michael reaction of silyl enol ethers with enones, only few catalysts have been reported.[18] Therefore, the development of an efficient catalytic system for the Mukaiyama–Michael reaction still remains a challenge. We applied the complex $\mathbf{3}\cdot 4H_2O\cdot 2THF$ in the reaction of enol silyl ethers with enones in Et_2O for 24 h, and the desired Michael adducts were obtained in high yields (Table 2, **9a–9e**, 78–88%). Also the silyl enol ethers (**6a–6c**) with different substituents were found to react with methyl vinyl ketone in good to excellent yields with $\mathbf{3}\cdot 4H_2O\cdot 2THF$ as catalyst (Table 2, entries 1–3, **9a–9c**, 83–88%). The reaction of trimethyl(1-phenyl-vinyloxy)silane also showed good reactivity with cyclopentenone and cyclohexenone giving yields of 80% and 78%, respectively (**9d**, **9e**). It is interesting to note that the reaction of the enol silyl ethers with α,β-unsaturated ketones (Table 2, entries 3–5) is a 1,4-addition reaction, while the reaction of the enol silyl ethers with α,β-unsaturated aldehydes is a 1,2-addition reaction (Table 1, entries 14–17). To the best of our knowledge, such a difference may be owing to the steric hindrance and electron effect between the aldehydes and ketones.[19]

Later we moved to the Lewis acids-catalyzed Michael addition reaction of indole derivatives with α,β-unsaturated carbonyl compounds, which is another important carbon-carbon bond-forming reaction and has attracted much attention in organic synthesis in recent years.[20] Most of the recently developed catalytic systems are sensitive to air or moisture.[21] The highly efficient system of silica-Sc-IL/[DBIm]SbF_6 developed by Kobayashi also required ionic liquids as co-catalyst.[22] We hence applied the catalysts $\mathbf{3}\cdot 4H_2O\cdot 2THF$ and $\mathbf{4}\cdot 6H_2O$ in the Michael addition reaction of indole derivatives with enones in CH_3CN

Table 2. Product yields for reaction of enol silyl ethers with enones catalyzed by **3**·4H$_2$O·2THF.[a]



Entry	Enol silyl ethers		Enones		Product	Yield [%][b]
1		(**6a**)		(**8a**)	**9a**	88
2		(**6c**)		(**8a**)	**9b**	86
3		(**6b**)		(**8a**)	**9c**	83
4		(**6b**)		(**8b**)	**9d**	80
5		(**6b**)		(**8c**)	**9e**	78

[a] **3**·4H$_2$O·2THF: 0.05 mmol; **6**: 1.2 mmol; **8**: 1.0 mmol; solvent: Et$_2$O, 0 °C to room temperature.

[b] Isolated yield.

for 3 h and obtained the desired Michael adducts in high yields (Table 3).

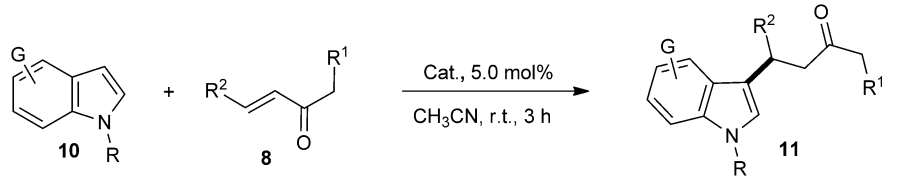
As shown in Table 3, the terminal but-3-en-2-one can be transformed to the corresponding 3-substituted indole with a monoindole group and the yield was up to 96% (**11a**). The internal α,β-unsaturated ketones non-3-en-2-one and 4-phenylbut-3-en-2-one can be also successfully reacted with indole derivatives to form the target products in yields of 94% and 85%, respectively (**11b**, **11e**). And we found that the large steric effect of the phenyl group did not have an effect on the catalytic activity. For example, the yields with the α,β-unsaturated cyclo ketones such as cyclopent-2-enone and cyclohex-2-enone were up to 90% and 88%, respectively (**11c**, **11d**). 5-Bromo-1*H*-indole and 2-methyl-1*H*-indole showed high reactivity in this catalytic system with cyclopent-2-enone, the yields were 87% and 90%, respectively (**11f**, **11g**). 2-Methyl-1*H*-indole and 1-methylindole also exhibited high reactivity with non-3-en-2-one and the yields were up to 91% and 92%, respectively (**11h**, **11i**). In addition, **4**·6H$_2$O also showed a relatively high catalytic efficiency towards the Michael addition reaction, giving yields of 76–85%.

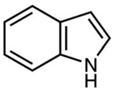
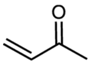
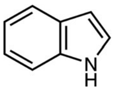
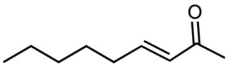
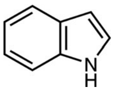
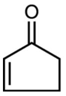
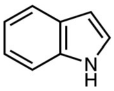
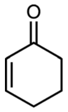
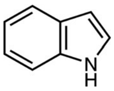
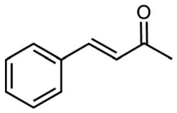
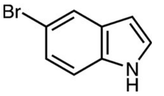
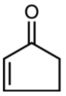
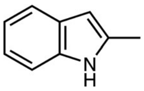
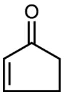
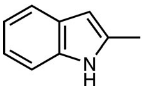
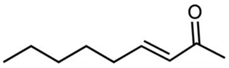
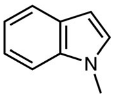
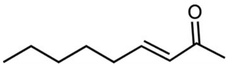
Nitroalkenes, similar to α,β-unsaturated carbonyl compounds, are very attractive Michael acceptors and have been widely used in organic synthesis.[23] Recently, many examples regarding the application of nitroalkenes as Michael acceptors in asymmetric catalytic reactions were reported.[24] The Friedel–Crafts alkylation reaction of indole derivatives with *trans*-β-nitrostyrenes has been reported.[24d] However, Zn(OTf)$_2$ as a catalyst is hygroscopic, and catalytic efficiency is low. Thus, we assessed **3**·4H$_2$O·2THF and **4**·6H$_2$O as a catalyst for this reaction. In the presence of 5.0 mol% of **3**·4H$_2$O·2THF or **4**·6H$_2$O, the Michael addition reaction of indole derivatives with *trans*-β-nitrostyrene occurred at room temperature in CH$_3$CN for 2.5–3 h, and good-to-excellent yields were obtained (Table 4).

As shown in Table 4, the complex **3** showed high catalytic efficiency in the Michael addition reaction of indole derivatives with *trans*-β-nitrostyrene, and the yield was up to 94%. The indole derivatives containing electron-withdrawing groups on the phenyl group (F, Cl, Br) showed slightly lower yields of 84%, 86% and 85%, respectively (**13b–13d**). When an electron-donating group was introduced into the indole ring (2-Me, 5-Me, 7-Me), the yield became relatively high from 91% to 94% (**13e–13g**). 1-Methylindole also had high reactivity in the current catalytic system and the yield was up to 89% (**13h**). And the complex **4** was also found to be an efficient catalyst in this Michael addition with the yields of 76–86%.

1-Amidoalkyl-2-naphthol derivatives are of importance as they can be easily converted to biologically

Table 3. Product yields for reaction of indole derivatives with enones catalyzed by **3**·4 H_2O·2 THF[a] and **4**·6 H_2O.[a]



Entry	Indoles (**10**)		Enones (**8**)		Product (**11**)	Yield [%][b]	
						3·4 H_2O·2 THF	**4**·6 H_2O
1		(**10a**)		(**8a**)	**11a**	96	85
2		(**10a**)		(**8d**)	**11b**	94	82
3		(**10a**)		(**8b**)	**11c**	90	81
4		(**10a**)		(**8c**)	**11d**	88	78
5		(**10a**)		(**8e**)	**11e**	85	76
6		(**10b**)		(**8b**)	**11f**	87	80
7		(**10c**)		(**8b**)	**11g**	90	81
8		(**10c**)		(**8d**)	**11h**	91	82
9		(**10d**)		(**8d**)	**11i**	92	83

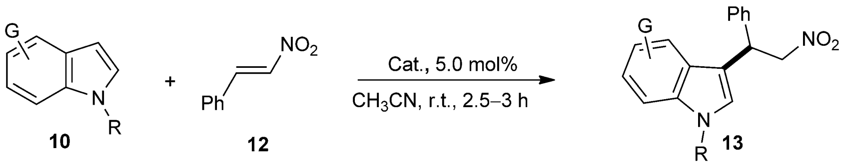
[a] **3**·4 H_2O·2 THF/**4**·6 H_2O: 0.05 mmol; **10**: 1.0 mmol; **8**: 1.0 mmol; solvent:CH_3CN; room temperature.
[b] Isolated yield.

active compounds.[25] A one-pot multi-component Mannich reaction of β-naphthol with aromatic aldehydes and amide derivatives has been used as a practical synthetic route toward 1-amidoalkyl-2-naphthols. Several Lewis and Brønsted acids have been applied to catalyze this reaction, such as *p*-toluenesulfonic acid, iodine, $HClO_4/SiO_2$, 4-(1-imidazolium)butanesulfonate.[26] However, these methods have disadvantage(s) such as low yield, long reaction time and disagreement with green chemistry protocols. We hence addressed these problems with **4**·6 H_2O as a catalyst (2.0 mol%) in a one-pot Mannich reaction in refluxing EtOH for 1–1.5 h, and good-to-excellent yields were obtained (Table 5).

As shown in Table 5, the reaction proceeded well for a variety of aromatic aldehydes (84–98%). The aromatic aldehydes with electron-withdrawing groups (e.g., Cl, Br, and NO_2) exhibited higher reactivity in this Mannich reaction than those with electron-donating groups in the *para*-position of the phenyl plane (e.g., methyl and methoxy) (Table 5, entries 2–6). Benzamide and urea also showed high reactivity in this catalytic system with benzaldehyde and β-naphthol and the yields were 89% and 84%, respectively (**16g**, **16h**).

To show the advantage of **3**·4 H_2O·2 THF and **4**·6 H_2O, we compared the catalytic activities of **3**·4 H_2O·2 THF and **4**·6 H_2O with those of Cp_2HfCl_2,

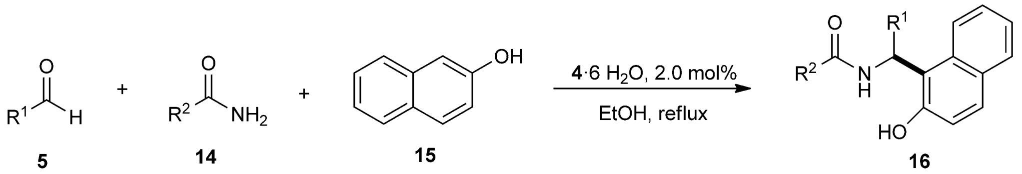
Table 4. Product yields for reaction of indole derivatives with *trans*-β-Nitrostyrene catalyzed by **3**·4 H_2O·2 THF[a] and **4**·6 H_2O.[a]



Entry	G	R	Time [h]	Product (**13**)	Yield [%][b]	
					3·4 H_2O·2 THF	**4**·6 H_2O
1	H (**10a**)	H	3	**13a**	94	83
2	5-F (**10e**)	H	3	**13b**	84	77
3	5-Cl (**10f**)	H	3	**13c**	86	79
4	5-Br (**10b**)	H	3	**13d**	85	76
5	2-Me (**10c**)	H	2.5	**13e**	91	82
6	5-Me (**10g**)	H	2.5	**13f**	94	85
7	7-Me (**10h**)	H	2.5	**13g**	92	86
8	H (**10d**)	CH_3	2.5	**13h**	89	84

[a] **3**·4 H_2O·2 THF/**4**·6 H_2O: 0.05 mmol; **10**: 1.0 mmol; **12**: 1.0 mmol; solvent: CH_3CN; room temperature.
[b] Isolated yield.

Table 5. Product yields for reaction of β-naphthol with aromatic aldehydes and amide derivatives catalyzed by **4**·6 H_2O.[a]



Entry	R^1	R^2	Time [h]	Product	Yield [%][b]
1	Ph (**5a**)	CH_3 (**14a**)	1.0	**16a**	97
2	*p*-$CH_3C_6H_4$ (**5b**)	CH_3 (**14a**)	1.0	**16b**	90
3	*p*-$CH_3OC_6H_4$ (**5c**)	CH_3 (**14a**)	1.0	**16c**	92
4	*p*-ClC_6H_4 (**5e**)	CH_3 (**14a**)	1.0	**16d**	97
5	*p*-BrC_6H_4 (**5f**)	CH_3 (**14a**)	1.0	**16e**	96
6	*m*-$NO_2C_6H_4$ (**5n**)	CH_3 (**14a**)	1.0	**16f**	98
7	Ph (**5a**)	Ph (**14b**)	1.5	**16g**	89
8	Ph (**5a**)	NH_2 (**14c**)	1.5	**16h**	84

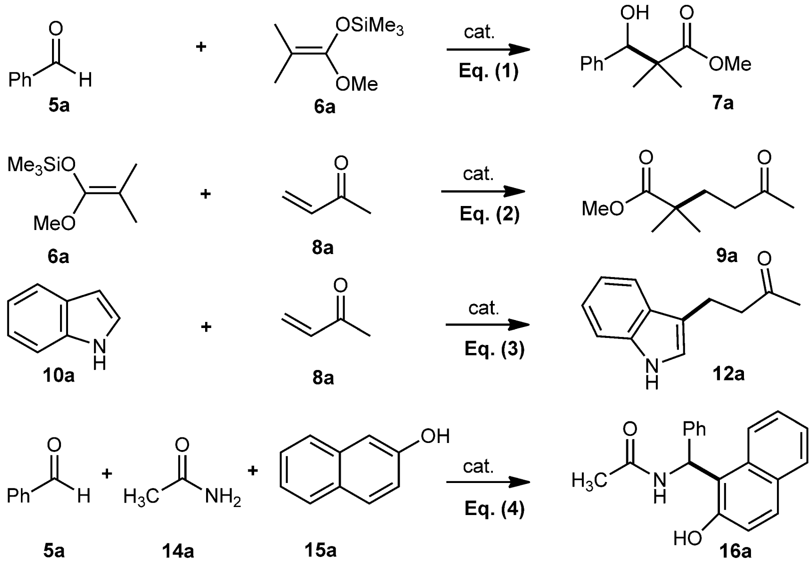
[a] **4**·6 H_2O: 0.02 mmol; **5**: 1.0 mmol; **14**: 1.2 mmol; **15**: 1.0 mmol; solvent: EtOH; 80 °C.
[b] Isolated yield

$Cp_2Hf(OSO_2CF_3)_2$ (**17**) and **2**·4 H_2O·2 THF. As shown in Table 6, high yields were constantly gained over complex **3**·4 H_2O·2 THF or **4**·6 H_2O as catalysts, while the other catalysts showed much lower yields, plausibly due to their lower Lewis acidity or moisture-sensitive features (Table 6).

To test the reusability of the catalyst and the reproducibility of its catalytic performance, **3**·4 H_2O·2 THF was subject to recycling experiments of above reactions [Eq. (1): **5a** + **6a** → **7a**; Eq. (2): **6a** + **8a** → **9a**; Eq. (3): **10a** + **8a** → **12a**; Eq. (4): **5a** + **14a** + **15a** → **16a**]. The change in product yield was negligible in a trial of five recycling experiments, demonstrating that the catalyst is stable and suitable for reuse (Table 7).

In conclusion, we have synthesized and characterized two air-stable μ^2-hydroxy-bridged binuclear hafnocene Lewis acid complexes with perfluorobutanesulfonate and perfluorobenzenesulfonate as counter anions with strong Lewis acidity. These complexes can be used as a general catalyst in Lewis acid-catalyzed carbon-carbon bond-forming reactions. Due to their highly catalytic efficiency, stability, storability, low toxicity and reusability, they should find board application in organic synthesis.

Table 6. Catalyst comparison in carbon-carbon bond-forming reactions.



Entry	Catalyst	Yield [%][a]			
		Eq. (1)	Eq. (2)	Eq. (3)	Eq. (4)
1	Cp_2HfCl_2	8	5	15	18
2	**2**$\cdot 4H_2O\cdot 2THF$	67	59	71	79
3	**3**$\cdot 4H_2O\cdot 2THF$	95	88	96	98
4	**4**$\cdot 6H_2O$	86	80	85	91
5	$Cp_2Hf(OSO_2CF_3)_2$(**17**)	40	39	46	59

[a] Same conditions as shown in the previous Tables 1, 2, 3, and 5.

Table 7. Yields of the Mukaiyama aldol reaction [Eq. (1)]; Mukaiyama–Michael addition reaction [Eq. (2)]; Michael addition reaction [Eq. (3)] and Mannich reaction [Eq. (4)] catalyzed by recovered catalyst.[a]

Cycle	Yield [%][b]	Cat [%][c]	Yield [%][b]	Cat [%][c]	Yield [%][b]	Cat [%][c]	Yield [%][b]	Cat [%][c]
	Eq. (1)		Eq. (2)		Eq. (3)		Eq. (4)	
1	95	97	88	91	96	97	98	99
2	94	95	87	89	95	98	96	98
3	93	98	86	90	96	99	97	98
4	95	96	87	91	92	95	98	99
5	94	97	85	90	95	96	97	98

[a] Same conditions as shown in the previous Tables 1, 2, 3 and 5 and the equivalents are expanded to ten times.
[b] Isolated yield of desired product.
[c] Isolated yield of recovered catalyst.

Experimental Section

General

All chemicals were purchased from Aldrich. Co. Ltd and used as received unless otherwise indicated. The preparation of catalyst was carried out under a nitrogen atmosphere with freshly distilled solvents unless otherwise noted. THF and hexane were distilled from sodium/benzophenone. Acetonitrile was distilled from CaH_2. The NMR spectra were recorded at 25 °C on an Inova-400M (USA) calibrated with tetramethylsilane (TMS) as an internal reference. Elemental analyses were performed with a Vario EL III. Conductivity was measured on a REX conductivity meter DDS-307. IR spectra were recorded on a Nicolet 5700 FTR spectrophotometer (Thermo Electron Corporation). TG-DSC analysis was performed on an HCT-1 (Henven, Beijing, China) instrument. X-ray single crystal diffraction analysis was performed with SMART-APEX and RASA-7A by Shanghai Institute Organic Chemistry, China Academy of Science. UV/Vis (Shimadzu UV-1601) and fluorescence spectroscopy (Hitachi F-4600) was measured in the State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University (China). The acidity was measured by the Hammett indicator method as described previously.[5] Acid strength was expressed in terms of Hammett acidity function (H_o) as scaled by pK_a value of the indicators.

Preparation of $3{\cdot}4\,H_2O{\cdot}2\,THF$

To a solution of Cp_2HfCl_2 (0.379 g, 1.0 mmol) in 20 mL THF was added a solution of $AgOSO_2C_4F_9$ (0.814 g, 2.0 mmol) in 10 mL THF. After the mixture had been stirred at 25 °C for 2 h in the absence of light, it was filtered. The filtrate was placed in a small jar and then put into a larger jar to which was added 40 mL dry hexane and then the larger jar was obdurated. After being kept in the refrigerator for 24 h, colorless crystals were obtained; yield: 837 mg (82%). Recrystallization of this complex in THF/hexane produced good crystals suitable for X-ray analysis. ^1H NMR (400 MHz, acetone-d_6, 25 °C, TMS) $\delta = 1.77$ to 1.80 (m, 2H, THF), 3.61 to 3.64 (m, 2H, THF), 4.86 (s, nH, H_2O), 6.59 (s, 2H, Cp), 6.62 (s, 2H, Cp), 6.81 (s, 6H, Cp); ^{19}F NMR (376 MHz, acetone-d_6, 25 °C): $\delta = -76.21$ to -76.26 (m, 3F, CF_3), -109.73 to -109.78 (m, 2F, CF_2), -116.52 to -116.57 (m, 2F, CF_2), -121.10 to -121.18 (m, 2F, CF_2); IR(KBr): $\nu = 3430$, 2965, 2925, 2359, 1670, 1515, 1430, 1260, 1117, 1023, 925, 828, 753, 666, 569 cm^{-1}; elemental analysis calculated (%) for $C_{34}H_{48}F_{36}Hf_2O_{26}S_4$: C 20.00, H 2.37; found: C 20.01; H 2.35.

Crystal data for $3{\cdot}4\,H_2O{\cdot}2\,THF$: $C_{17}\ H_{24}\ F_{18}\ Hf\ O_{13}S_2$; $Mr = 1020.97$, triclinic, space group P-1, $a = 10.4026(9)$ Å, $b = 10.8999(9)$ Å, $c = 15.5637(13)$ Å; $V = 1656.3(2)$ Å^3; $T = 173(2)$ K; $Z = 2$; reflections collected/unique, 12721/7145, $R_{int} = 0.0189$, final R indices $[I > 2\sigma(I)]$ $R_1 = 0.0379$, $wR_2 = 0.1041$; R indices (all data), $R_1 = 0.0410$, $wR_2 = 0.1073$. $GOF = 1.089$; CCDC 916236 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.

Preparation of $4{\cdot}6\,H_2O$

To a solution of Cp_2HfCl_2 (0.379 g, 1.0 mmol) in 20 mL CH_3CN was added a solution of $AgOSO_2C_6F_5$ (0.772 g, 2.0 mmol) in 10 mL CH_3CN. After the mixture had been stirred in the absence of light at room temperature for 2 h, it was filtered and evaporated under vacuum and the resulting residue was diluted with 10 mL THF followed by five drops of dry hexane and then was stood in the refrigerator for 24 h; colorless crystals were obtained; yield: 673 mg (78%). Recrystallization of this complex in THF/hexane produced good crystals suitable for X-ray analysis. ^1H NMR (400 MHz, acetone-d_6, 25 °C, TMS): $\delta = 4.32$ (s, nH, H_2O), 6.54 (s, 1H, Cp), 6.59 (s, 2H, Cp), 6.73 (s, 6H, Cp), 6.89(s, 1H, Cp); ^{19}F NMR (376 MHz, acetone-d_6, 25 °C): $\delta = -139.03$ (s, 2F, C_6F_5), -155.30 (s, 1F, C_6F_5), -163.98 (s, 2F, C_6F_5); IR(KBr): $\nu = 3121$, 2358, 1658, 1533, 1501, 1313, 1177, 1115, 1042, 979, 833, 634, 488 cm^{-1}; elemental analysis calculated (%) for $C_{34}H_{36}F_{20}O_{26}S_4Hf_2$ (as dodecahydrate): C 23.66, H 2.10; found: C 23.60, H 2.08.

Crystal data for $4{\cdot}6\,H_2O$: $C_{34}H_{36}F_{20}Hf_2O_{26}S_4$; $Mr = 1725.85$, orthorhombic, space group $Pbca$, $a = 15.2866(8)$ Å, $b = 12.0159(7)$ Å, $c = 28.7517(15)$ Å; $V = 5281.2(5)$ Å^3; $T = 296(2)$ K; $Z = 4$; reflections collected/unique, 21924/4894, $R_{int} = 0.0192$, final R indices $[I > 2\sigma(I)]$ $R_1 = 0.0246$, $wR_2 = 0.0567$; R indices (all data), $R_1 = 0.0258$, $wR_2 = 0.0572$. $GOF = 1.092$; CCDC 916237 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.

Typical Procedure for the Mukaiyama–Aldol Reaction of Aldehydes with Enol Silyl Ethers Catalyzed by $3{\cdot}4\,H_2O{\cdot}2\,THF$

Complex **3**$\cdot 4\,H_2O\cdot 2\,THF$ (0.05 mmol), and enol silyl ether (**6**) (1.2 mmol) were added to a solution of aldehyde (**5**) (1.0 mmol) in diethyl ether (3.0 mL) at 0 °C. Then the temperature was raised to room temperature slowly. After the mixture had been stirred at room temperature for 5 h and monitored by TLC, it was subject to evaporation under vacuum at room temperature, the residue was dissolved in *n*-hexane (10 mL × 3) and the catalyst was collected by means of filtration for the next cycle of reaction. To the combined hexane solution, MeOH and HCl (aq.) were added and the mixture was stirred for 15 min. $NaHCO_3$ (aq.) was added for neutralization. The mixture was subject to evaporation, and the solids thus obtained were dissolved in AcOEt and water. After extraction with AcOEt (three times), the organic layer was washed with NaCl (aq.) and dried over $MgSO_4$. After evaporation, the residue was subject to silica gel column chromatography (petroleum ether : ethyl acetate = 8:1), colorless crystals (**7a**) were obtained; isolated yield: 95%. Aldehydes and enol silyl ethers are commercially available.

Typical Procedure for the Mukaiyama–Michael Addition Reaction Catalyzed by $3{\cdot}4\,H_2O{\cdot}2\,THF$

Complex **3**$\cdot 4\,H_2O\cdot 2\,THF$ (0.05 mmol), and enol silyl ether (**6**) (1.2 mmol) were added to a solution of enone (**8**) (1.0 mmol) in diethyl ether (3.0 mL) at 0 °C. Then the temperature was raised to room temperature slowly. After the mixture had been stirred at room temperature for 24 h and monitored by TLC, it was subject to evaporation under vacuum at room temperature. The residue was dissolved in *n*-hexane (10 mL × 3) and the catalyst was collected by means of filtration for the next cycle of reaction. To the combined hexane solution, MeOH and HCl (aq.) were added and the mixture was stirred for 15 min. $NaHCO_3$ (aq.) was added for neutralization. The mixture was subject to evaporation, and the solids thus obtained were dissolved in AcOEt and water. After extraction with AcOEt (three times), the organic layer was washed with NaCl (aq.) and dried over $MgSO_4$. After evaporation, the residue was subject to silica gel column chromatography (petroleum ether:-ethyl acetate = 5:1), a colorless oil (**9a**) was obtained; isolated yield: 88%. Enol silyl ethers and enones are commercially available.

General Procedure for the Michael Addition Reaction of Indoles with Enones or Nitroalkenes by $3{\cdot}4\,H_2O{\cdot}2\,THF/4{\cdot}6\,H_2O$

A mixture of enone (1.0 mmol) or nitroalkene (1.0 mmol), indole (1.0 mmol) and **3**$\cdot 4\,H_2O\cdot 2\,THF$/**4**$\cdot 6\,H_2O$ (0.05 mol) in acetonitrile (3 mL) was stirred at room temperature for 3 h and monitored by TLC. Then the solvents of the resulting mixture were removed by evaporation under vacuum, CH_2Cl_2 (10 mL) was added to the reaction mixture and the catalyst was filtered for the next cycle of reaction. From the filtrate, after evaporation of the solvent, a pinkish solid mixture was obtained. The residue was purified by short column chromatography eluted with ethyl acetate/petroleum ether (petroleum ether:ethyl acetate = 5:1) and a colorless oil (**11a**) was obtained; isolated yield: 96%. Indoles, enones and nitroalkene are commercially available.

Typical Procedure for the Mannich Reaction Catalyzed by 4·6 H_2O

A well-ground mixture of β-naphthol (1.0 mmol), aldehyde (1.0 mmol), amide derivative (1.2 mmol) and **4**·6 H_2O (0.02 mmol) was heated to reflux in ethanol until the reaction was completed as indicated by TLC. After that, the mixture was subject to silica gel column chromatography; the product (**16a**) was obtained; isolated yield: 97%. After the completion of column chromatography, the upper part of the silica gel in the chromatography column was taken out, THF (10 mL) was added to the catalyst and gel mixture. The catalyst was collected by means of evaporation of the solvent (THF) for the next cycle of reaction. Aldehydes, amide derivative and β-naphthol are commercially available.

Acknowledgements

This work was supported by the NSFC (21172061, 21273068, 21273067, 21003040), the NSF of Hunan Province (10JJ1003, 11JJ5009), and the Fundamental Research Funds for the Central Universities. All authors thank Profs. J. Otera and A. Orita of Okayama University of Science for helpful discussion. R. Qiu thanks the Prof. N. Kambe and Dr. T. Iwsakai of Osaka University for helpful discussion and JSPS for a fellowship.

References

[1] a) H. Yuan, W. J. Woo, H. Miyamura, S. Kobayashi, *J. Am. Chem. Soc.* **2012**, *134*, 13970–13973; b) C. Li, S. Cheng, M. Tjahjono, M. Schreyer, M. Garland, *J. Am. Chem. Soc.* **2010**, *132*, 4589–4599; c) M. North, R. Pasquale, *Angew. Chem.* **2009**, *121*, 2990–2992; *Angew. Chem. Int. Ed.* **2009**, *48*, 2946–2948; d) H. Yuan, W. J. Woo, H. Miyamura, S. Kobayashi, *Adv. Synth. Catal.* **2012**, *354*, 2899–2904; e) M. P. Weberski Jr, C. Chen, M. Delferro, T. J. Marks, *Chem. Eur. J.* **2012**, *18*, 10715–10732.

[2] a) M. R. Radlauer, A. K. Buckley, L. M. Henling, T. Agapie, *J. Am. Chem. Soc.* **2013**, *135*, 3784–3787; b) T. Yasukawa, H. Miyamura, S. Kobayashi, *J. Am. Chem. Soc.* **2012**, *134*, 16963–16966; c) M. H. Perez-Temprano, J. A. Casares, P. Espinet, *Chem. Eur. J.* **2012**, *18*, 1864–1884; d) Z. C. Wang, N. Dietl, R. Kretschmer, T. Weiske, M. Schlangen, H. Schwarz, *Angew. Chem.* **2011**, *123*, 12559–12562; *Angew. Chem. Int. Ed.* **2011**, *50*, 12351–12354.

[3] a) S. F. Yin, J. Maruyama, T. Yamashita, S. Shimada, *Angew. Chem.* **2008**, *120*, 6692–6695; *Angew. Chem. Int. Ed.* **2008**, *47*, 6590–6593; b) R. H. Qiu, Y. Chen, S. F. Yin, X. H. Xu, C. T. Au, *RSC Adv.* **2012**, *2*, 10744–10793; c) R. H. Qiu, Z. G. Meng, S. F. Yin, X. X. Song, N. Y. Tan, Y. B. Zhou, K. Yu, X. H. Xu, S. L. Luo, C. T. Au, W. Y. Wong, *ChemPlusChem* **2012**, *77*, 404–410; d) S. F. Yin, S. Shimada, *Chem. Commun.* **2009**, 1136–1138.

[4] a) B. Y. Lee, H. Y. Kwon, S. Y. Lee, S. J. Na, S. i. Han, H. Yun, H. Lee, Y. W. Park, *J. Am. Chem. Soc.* **2005**, *127*, 3031–3037; b) W. Clegg, R. W. Harrington, M. North, P. Villuendas, *J. Org. Chem.* **2010**, *75*, 6201–6207; c) J. Meléndez, M. North, P. Villuendas, C. Young, *Dalton Trans.* **2011**, *40*, 3885–3890.

[5] a) R. H. Qiu, X. H. Xu, Y. H. Li, G. P. Zhang, L. L. Shao, D. L. An, S. F. Yin, *Chem. Commun.* **2009**, 1679–1681; b) R. H. Qiu, G. P. Zhang, Y. Y. Zhu, X. H. Xu, L. L. Shao, Y. H. Li, D. L. An, S. F. Yin, *Chem. Eur. J.* **2009**, *15*, 6488–6494.

[6] a) M. Hudlický, A. E. Pavlath, (Eds.), *Chemistry of organic fluorine compounds*, ACS Monograph 187, ACS, Washington DC, **1995**, pp 979–1010; b) J. A. Gladysz, M. Jurisch, *Top. Curr. Chem.* **2012**, *308*, 1–24.

[7] a) J. A. Gladysz, (Ed.), *Handbook of Fluorous Chemistry*, Wiley-VCH, Weinheim **2004**, pp 13–15; b) N. K. Terrett, *Combinatorial Chemistry*, Oxford University Press, London, **1998**, pp 68–69.

[8] a) M. Llorca, M. Farré, M. S. Tavano, B. Alonso, G. Koremblit, D. Barceló, *Environ. Pollut.* **2012**, *163*, 158–166; b) S. Fuentes, M. T. Colomina, P. Vicens, J. L. Domingo, *Toxicol. Lett.* **2007**, *171*, 162–170.

[9] a) E. D. Oldham, W. Xie, A. M. Farnoud, J. Fiegel, H. J. Lehmler, *J. J. Phy. Chem. B:* **2012**, *116*, 9999–10007; b) C. Lau, J. L. Butenhoff, J. M. Rogers, *Toxicol. Appl. Pharm.* **2004**, *198*, 231–241.

[10] T. K. Hollis, B. Bosnich, *J. Am. Chem. Soc.* **1995**, *117*, 4570–4581.

[11] G. J. Janz, R. P. T. Tomkins, in: *Nonaqueous Electrolytes Handbook*, Academic Press, New York, **1972**, pp 419–443.

[12] S. Fukuzumi, N. Satoh, T. Okamoto, K. Yasui, T. Suenobu, Y. Seko, M. Fujitsuka, O. Ito, *J. Am. Chem. Soc.* **2001**, *123*, 7756–7766.

[13] a) S. Fukuzumi, K. Ohkubo, *J. Am. Chem. Soc.* **2002**, *124*, 10270–10271; b) K. Ohkubo, S. C. Menon, A. Orita, J. Otera, S. Fukuzumi, *J. Org. Chem.* **2003**, *68*, 4720–4726.

[14] D. T. Yazıcı, C. Bilgic, *Surf. Interface Anal.* **2010**, *42*, 959–962.

[15] a) D. E. Frantz, R. Fassler, C. S. Tomooka, E. M. Carreira, *Acc. Chem. Res.* **2000**, *33*, 373–381; b) Y. J. Mei, P. Dissanayake, M. J. Allen, *J. Am. Chem. Soc.* **2010**, *132*, 12871–12873; c) P. Goodrich, C. Hardacre, C. Paun, A. Ribeiro, S. Kennedy, M. J. V. Lourenco, H. Manyar, C. A. Nieto de Castro, M. Besnea, V. I. Pârvulescu, *Adv. Synth. Catal.* **2011**, *353*, 995–1004; d) T. Ollevier, B. Plancq, *Chem. Commun.* **2012**, *48*, 2289–2291.

[16] a) H. Ishitani, Y. Yamashita, H. Shimizu, S. Kobayashi, *J. Am. Chem. Soc.* **2000**, *122*, 5403–5404; b) G. Hou, J. P. Yu, C. B. Yu, G. P. Wu, Z. W. Miao, *Adv. Synth. Catal.* **2013**, *355*, 589–593; c) M. Rueping, B. J. Nachtsheim, W. Ieawsuwan, I. Atodiresei, *Angew. Chem.* **2011**, *123*, 6838–6853; *Angew. Chem. Int. Ed.* **2011**, *50*, 6706–6720.

[17] a) P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis* Pergamon, Oxford, **1992**, pp 93–98; b) D. Enders, C. Grondal, M. Httl, *Angew. Chem.* **2007**, *119*, 1590–1601; *Angew. Chem. Int. Ed.* **2007**, *46*, 1570–1581.

[18] a) X. Xu, W. H. Hu, M. P. Doyle, *Angew. Chem.* **2011**, *123*, 6516–6519; *Angew. Chem. Int. Ed.* **2011**, *50*, 6392–6395; b) D. A. Evans, K. A. Scheidt, J. N. Johnston, M. C. Willis, *J. Am. Chem. Soc.* **2001**, *123*, 4480–4491; c) J. George, B. V. S. Reddy, *Adv. Synth. Catal.* **2013**, *355*, 383–385.

[19] a) E. M. Carreira, in: *Modern Carbonyl Chemistry*, (Ed.: J. Otera), Wiley-VCH, Weinheim, Germany, **2000**, Chapter 8; b) X. F. Xu, W. H. Hu, M. P. Doyle, *Angew. Chem.* **2011**, *123*, 6516–6519; *Angew. Chem. Int. Ed.* **2011**, *50*, 6392–6395.

[20] a) Q. Cai, C. Liu, X. W. Liang, S. L. You, *Org. Lett.* **2012**, *14*, 4588–4590; b) F. Rajabi, S. Razavi, R. Luque, *Green Chem.* **2010**, *12*, 786–789; c) M. Bandini, M. Fagioli, A. Umani-Ronchi, *Adv. Synth. Catal.* **2004**, *346*, 545–548; d) D. Das, S. Pratihar, S. Roy, *J. Org. Chem.* **2013**, *78*, 2430–2442.

[21] a) M. L. Kantam, J. Yadav, B. M. Choudary, B. Sreedhar, *Adv. Synth. Catal.* **2006**, *348*, 867–972; b) D. A. Evans, K. R. Fandrick, H. J. Song, K. A. Scheidt, R. S. Xu, *J. Am. Chem. Soc.* **2007**, *129*, 10029–10041.

[22] Y. L. Gu, C. Ogawa, J. Kobayashi, Y. Mori, S. Kobayashi, *Angew. Chem.* **2006**, *118*, 7375–7378; *Angew. Chem. Int. Ed.* **2006**, *45*, 7217–7220.

[23] O. M. Berner, L. Tedeschi, D. Enders, *Eur. J. Org. Chem.* **2002**, 1877–1894.

[24] a) M. Ganesh, D. Seidel, *J. Am. Chem. Soc.* **2008**, *130*, 16464–16465; b) W. G. Huang, H. S. Wang, G. B. Huang, Y. M. Wu, Y. M. Pan, *Chem. Eur. J.* **2012**, *18*, 2012, 5839–5843; c) J. Itoh, K. Fuchibe, T. Akiyama, *Angew. Chem.* **2008**, *120*, 4080–4082; *Angew. Chem. Int. Ed.* **2008**, *47*, 4016–4018; d) Y. X. Jia, S. F. Zhu, Y. Yang, Q. L. Zhou, *J. Org. Chem.* **2006**, *71*–75.

[25] a) T. Dingermann, D. Steinhilber, G. Folkers, *Molecular Biology in Medicinal Chemistry*, Wiley-VCH, Weinheim, **2004**, pp 363–380; b) A. Y. Shen, C. T. Tsai, C. L. Chen, *Eur. J. Med. Chem.* **1999**, *34*, 877–882.

[26] a) M. M. Khodaei, A. R. Khosropour, H. Moghanian, *Synlett* **2006**, 916–920; b) B. Das, K. Laxminarayana, B. Ravikanth, B. R. Rao, *J. Mol. Catal. A: Chem.* **2007**, *261*, 180–183; c) H. R. Shaterian, H. Yarahmadi, M. Ghashang, *Tetrahedron* **2008**, *64*, 1263–1269; d) D. Kundu, A. Majee, A. Hajra, *Catal. Commun.* **2010**, *11*, 1157–1159.