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Air-stable Bis(pentamethylcyclopentadienyl) Zirconium Perfluorooctanesulfonate as an Efficient and Recyclable Catalyst for the Synthesis of N-substituted Amides

Ningbo Li,*[a] Lingxiao Wang,[a] Liting Zhang,[a] Wenjie Zhao,[a] Jie Qiao,*[a] Xinhua Xu,*[b] and Zhiwu Liang[b]

Abstract: Bis(pentamethylcyclopentadienyl) zirconium perfluorooctanesulfonate is an air-stable and water-tolerant Lewis acid. This complex exhibited good thermal stability and high solubility in polar organic solvents. The compound showed relatively strong acidity, with an acid strength of 0.8 < *Ho* ≤ 3.3, and high catalytic efficiency for the synthesis of N-substituted amides via the reaction of carboxylic acids with amines, the Ritter reaction of nitriles with alcohols, and the amination of alcohols with amides. Moreover, the complex had good reusability. This catalytic system affords a simple and efficient way to synthesize N-substituted amides.

Introduction

N-substituted amides are important building blocks for peptides, many natural products, synthetic materials and the pharmaceutical industry.[1] Various important marketed drugs such as itopride, moclobemide and atorvastatin contain an amide bond in their backbone (Figure 1).[2]

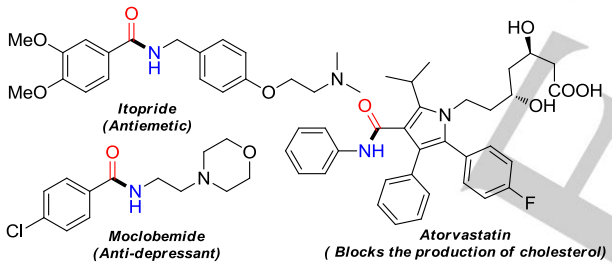
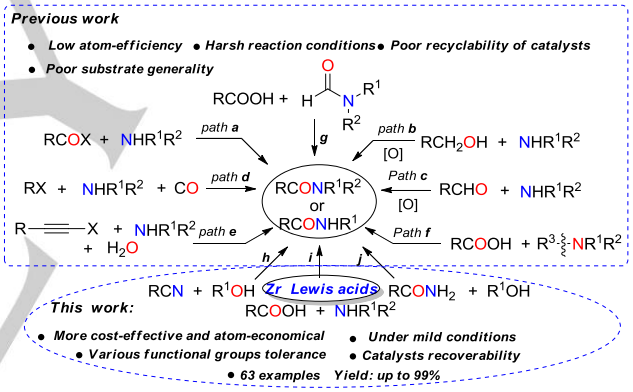


Figure 1. Drugs containing the amide moiety

Traditionally, N-substituted amides have been synthesized by acid chlorides or carboxylic acids with amines using coupling reagents (Scheme 1, paths a, i).[3] More recently, transition metal catalyzed oxidative amidation of alcohols or aldehydes with amines has been developed for amides synthesis (path b, c).[4] Alternative approaches including the carbonylation of alkyl or benzyl halides with amines (path d),[5a,5b] the reaction of substituted alkynyl bromides with amines (path e),[5c] the amidation of carboxylic acids with *tert*-amines through C-N bond cleavage (path f),[5d] and the oxidative coupling of carboxylic acids with formamides (path g)[5e] have been introduced. However, many of these approaches are problematic regarding cost and atom-efficiency, as well as functional group tolerance and recyclability. Presently, the more popular and highly attractive methods for N-substituted amide synthesis tend to be direct condensation by carboxylic acids and amines, the Ritter reaction of nitriles with alcohols, and the amination of alcohols with amides (paths h, i, j).[5f,5g] The popularity of these methods is because they are more cost-effective and greener processes than the other approaches, and they have extremely high atom economy.



Scheme 1. Different strategies for N-substituted amide synthesis.

Efforts have been made in recent years to develop the aforementioned protocols (paths h, i, j) for amide synthesis with improved efficiency under mild conditions.[6] For instance, Williams *et al.* and Adolfsson *et al.* demonstrated a method based on group IV metal compound catalysis ($ZrCl_4$, Cp_2ZrCl_2, $Ti(O\textit{i}\text{-}Pr)_4$ or Cp_2HfCl_2) for direct amide formation from unactivated carboxylic acids and amines.[7] Cook *et al.* and Cossy *et al.* described an iron-catalyzed system ($FeCl_3/AgSbF_6$ or $FeCl_2{\cdot}6H_2O$) for amide synthesis using the Ritter reaction of alcohols and nitriles.[8] Zhan *et al.* reported an efficient method for amide synthesis based on a $BiCl_3$-catalyzed substitution reaction of primary amides and propargylic alcohols.[9] Nonetheless, there are disadvantages with these methods, e.g., air or moisture sensitivity of catalysts, the need for strictly anhydrous reactions, poor substrate generality, low tolerance towards functional groups, high catalyst loadings and poor recyclability of catalysts. Thus, developing an air-stable, highly efficient and recyclable catalyst for N-substituted amide synthesis remains highly

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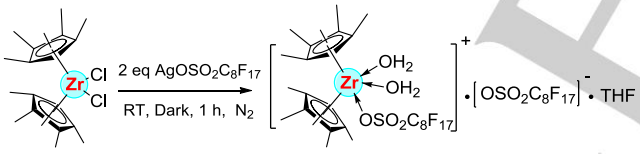
desirable.

In recent years, zirconocene compounds have attracted much attention and have shown high catalytic activity in a variety of Lewis-acid-catalyzed reactions such as Friedel-Crafts acylation, the Mukaiyama-aldol reaction and the Mannich reaction.[10] Our group has reported a series of zirconocene perfluoroalkyl(aryl)sulfonate complexes that can be used as efficient catalysts for many organic reactions.[11] The remarkable air stability and strong Lewis acidity of these complexes primarily depend on the perfluoroalkyl(aryl)sulfonate groups. However, due to the strongly lipophobic property of the C_8F_{17} group, these complexes usually exhibit low solubility in common organic solvents, which may be another reason for the catalytic efficiency decrease. Thus, we envisioned that an alkyl group incorporated with a Cp ring may increase the solubility and the catalytic efficiency of these complexes. With this in mind, we successfully synthesized and characterized bis(pentamethylcyclopentadienyl) zirconium perfluorooctanesulfonate $[Cp^*_2Zr(H_2O)_2OSO_2C_8F_{17}]^+[OSO_2C_8F_{17}]^-\cdot$THF [**1**, Cp* = $(CH_3)_5Cp$)]. This compound exhibited high catalytic efficiency and good reusability, and can be used as a general catalyst for N-substituted amide synthesis.

Results and Discussion

Scheme 2 is the synthetic route for decamethyl zirconocene complex **1**. Treatment of $Cp^*_2ZrCl_2$ with $AgOSO_2C_8F_{17}$ in THF for one hour afforded complex **1** at a 71% yield.



Scheme 2. Synthesis of cationic complex **1**

Complex **1** was found to be air-stable, remaining as dry colorless crystals or a white powder for over three months in air. The crystal structure was confirmed using X-ray analysis. A crystal suitable for X-ray diffraction was obtained by diffusion of hexane into a saturated solution of **1** in THF. An ORTEP representation of **1** and selected bond lengths and angles are shown in Figure 2. The zirconium atom in the cationic ion is coordinated by two water molecules and a sulfonate group. However, the cationic ion $[Cp^*_2Zr(H_2O)_2OSO_2C_8F_{17}]^+$ differs from that of zirconocene perfluorooctanesulfonate $[Zr(Cp)_2(H_2O)_3]^{2+}$, even though their synthetic procedures are identical.[11a] The two H_2O molecules and the sulfonate group lie on the plane that bisects the angle between the Cp* ring planes. The other $C_8F_{17}SO_3^-$ ion and the THF molecule are packed around the zirconium cation so that their oxygen atoms point towards the H_2O ligands. The anionic C_8F_{17} chains are clustered together to produce hydrophobic domains in the crystal structure.

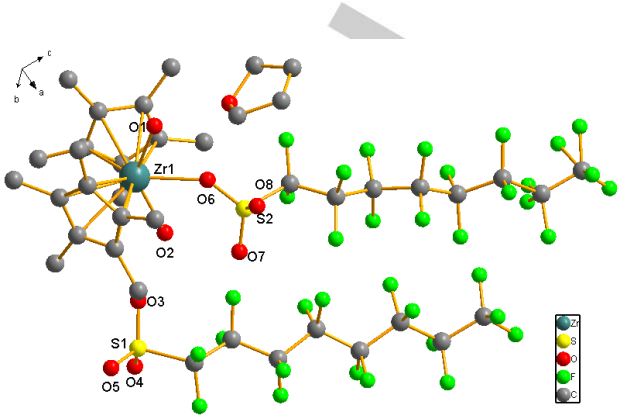


Figure 2. The crystal structure of complex **1** along with selected bond lengths (A˚) and angles (deg): Zr1-O7, 2.242(5); Zr1-N1, 2.303(6); Zr1-N2, 2.297(6); Zr1-C18, 2.570(7); Zr1-C19, 2.552(7); Zr1-C20, 2.546(6); Zr1-C21, 2.526(7); Zr1-C22, 2.515(7); O7-Zr-N1 70.87(18); O7-Zr-N2 71.30(18); N2-Zr-N1 142.2(2); and O7-Zr-C21 90.21(19).

The thermal behavior of **1** was investigated using thermogravimetry-differential scanning calorimetry (TG-DSC) under a nitrogen atmosphere (Figure 3). The thermal analysis curves show three stages of weight loss. The endothermic step below 100 °C can be assigned to the removal of water and THF. Complex **1** is stable up to approximately 260 °C. The exothermic weight loss at 300 °C is plausibly due to the oxidation of organic entities.

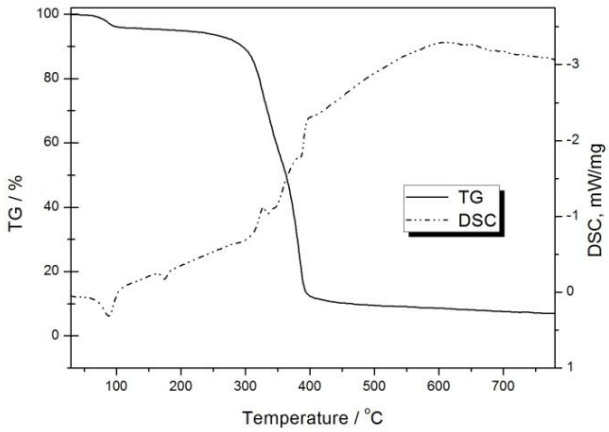


Figure 3. TG-DSC curves of complex **1**.

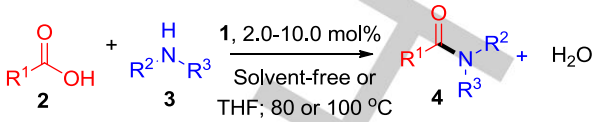
Conductivity measurement was used to investigate the ionic dissociation behavior of complex **1** in CH_3CN (1.0 mmol Ł$^{-1}$). The molar conductivity (Λ) of **1** was 124 μS cm^{-1} at 20 °C. This large value is consistent with complete ionization into a 1:1 electrolyte, implying that the complex is cationic in the solid state and solution. Another notable feature is the unusual solubility of **1** in

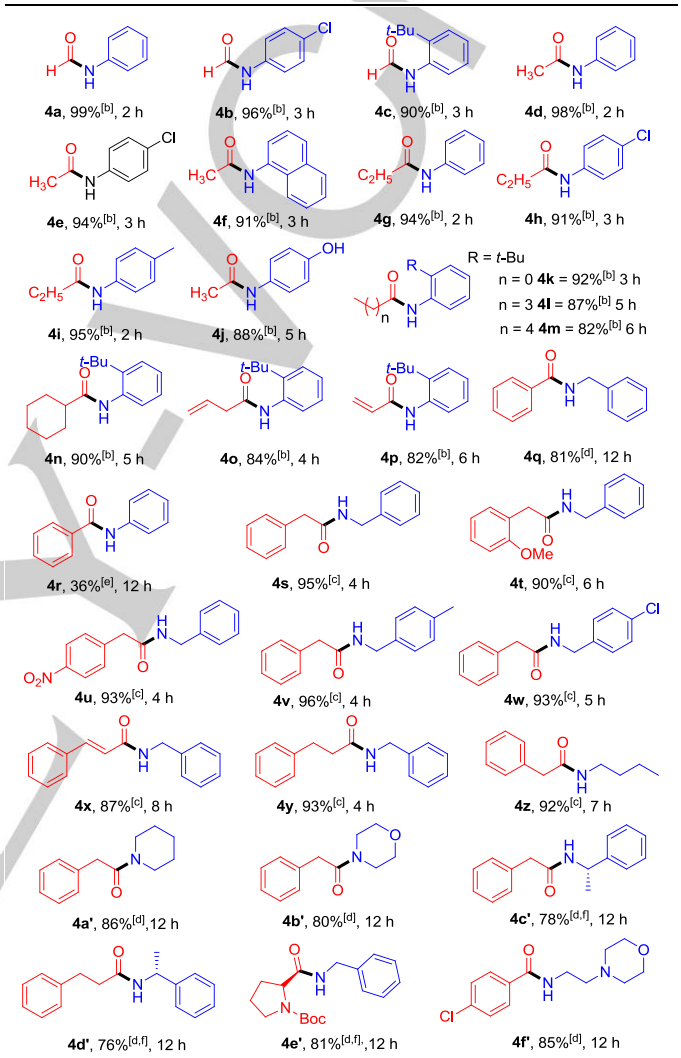
acetone, CH_3CN, THF, EtOAc and MeOH (Table S1, see SI). Due to the presence of decamethyl, complex **1** shows greater solubility than $[Zr(Cp)_2(H_2O)_3][OSO_2C_8F_{17}]_2$·THF in common polar organic solvents. Consistently, complex **1** was not soluble in CH_2Cl_2, much less polar toluene and apolar *n*-hexane, which reflects the amphiphilic nature of the long fluoroalkyl chain.[11a] In addition, we used the Hammett indicator method to determine the acidity of complex **1**,[12] and found that it showed strong acidity with an acid strength of $0.8 < H_0 < 3.3$ (where H_0 is the Hammett acidity function). These characteristic features encouraged us to evaluate the performance of complex **1** as a Lewis acid catalyst for N-substituted amide synthesis.

The direct condensation reaction of carboxylic acids with amines to form amides is highly desirable because it is atom-economical, inexpensive and environmentally friendly. To overcome problems such as poor atom efficiency and by-product formation using the coupling reagents,[13] several metal-catalyzed protocols have been established in recent years[14] such as $Zr(Ot\text{-}Bu)_4$,[15a] ZnO[15b] or $ZnCl_2$[15c], as well as procedures employing boronic acid and esters,[15d] and enzymes[15e] for amide synthesis. However, these procedures suffer from drawbacks, e.g., anhydrous solvents, a narrow substrate scope and a large excess of a particular substrate. In addition, these catalysts cannot be reused. Thus, we applied complex **1** for the direct amide formation from carboxylic acids and amines under solvent-free conditions or in THF for 2-12 h and obtained the desired amides in good to excellent yields (screening optimal conditions in the SI).

As shown in Table 1, complex **1** functions well for the direct amide formation of different carboxylic acids and amines. Simple aliphatic acids such as formic acid, acetic acid, and propionic acid show high reactivity with aniline and substituted anilines (**4a-4i**, 90-99%). As expected, both the electron-donating groups and electron-withdrawing groups in aniline show outstanding reactivity. We also applied the reaction to the synthesis of a simple pharmaceutical drug, paracetamol (**4j**, 88%). Furthermore, we investigated the reactivity of the sterically hindered 2-*tert*-butylaniline with different acids under standard conditions. The results show that the catalytic system can be extended to acids with long alkyl chains or rings (**4k-4n**, 82-92%). The chain length of carboxylic acids has a slight effect on the reactivity. Moreover, the acids bearing a C=C double bond are also tolerated (**4o**, 84%; **4p**, 82%). We also investigated the reactivities of different aromatic carboxylic acids with benzylamine, substituted benzylamines and aliphatic *n*-butylamine in the present catalytic system. Benzoic acid, phenylacetic acid, 3-phenylpropionic acid and cinnamic acid all resulted in satisfactory yields (**4q**, **4s-4z**, 81-92%). However, upon applying the less nucleophilic aniline, product **4r** was obtained in only a 36% yield even after prolonged heating and increasing the amount of catalyst (10 mol%). Secondary amines such as piperidine and morpholine also show good reactivity (**4a'**, 86%; **4b'**, 80%). Moreover, chiral enantiomerically pure 1-phenylethylamine and Boc-L-proline were converted into their corresponding amides without racemization, illustrating the mildness of this procedure (**4c'**-**4e'**, see chromatograms in the SI).

Table 1. Direct amide formation from carboxylic acids and amines catalyzed by **1** [a]

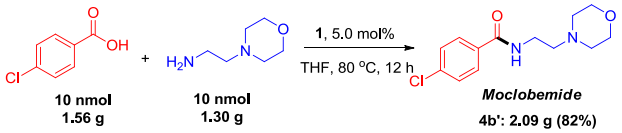




[a] Reaction conditions: Catalyst **1** (2-10 mol%); carboxylic acids (**2**; 1.0 mmol); amines (**3**; 1.0 mmol), Solvent: solvent-free or THF (1 mL); Temp.: 80 °C; Time: 2-12 h; isolated yield. [b] **1** (2 mol%), solvent-free, 80 °C. [c] **1** (2 mol%), THF, 80 °C. [d] **1** (5 mol%), THF, 100 °C. [e] **1** (10 mol%), THF; 100 °C. [f] No racemization was detected with chiral HPLC (AD-H column).

To illustrate the applicability of the catalytic system to pharmaceutical synthesis, we considered the generation of moclobemide (**4f'**) (Figure 1), which is used to treat depression, as an example. This compound can be synthesized from *p*-chlorobenzoic acid and 4-(2-aminoethyl) morpholine over complex **1** (5 mol%) at 100 °C for 12 h with an 85% yield, compared to that of $Cp^*_2ZrCl_2$ with only a 18% yield under the same conditions, illustrating a remarkable improvement in the

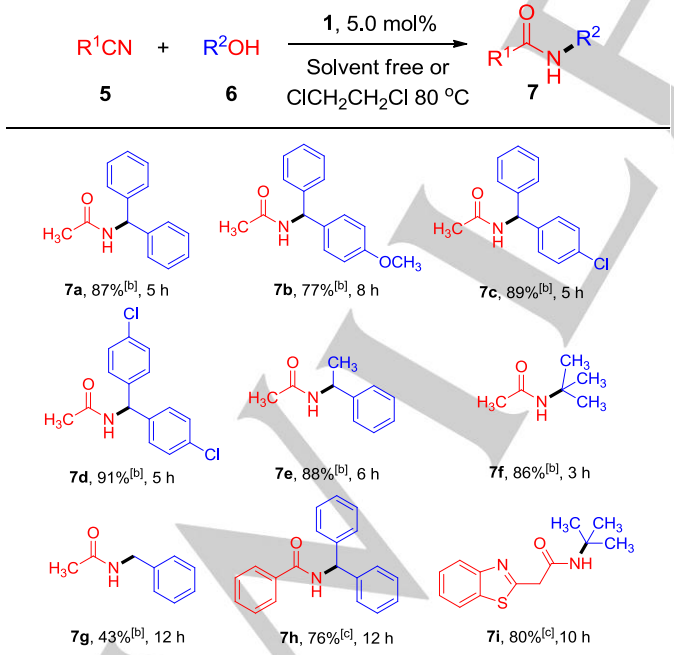
catalytic efficiency. Moreover, the reaction can be directly enlarged to a scale of 10 mmol, giving **4f'** in an 82% yield (2.09 g) (Scheme 3), which is a beneficial aspect of the catalyst system for industrial application.



Scheme 3. Gram-scale reaction for the synthesis of **4f'**

The Ritter reaction is another important conversion from nitriles reacting with alkenes or alcohols for the preparation of N-substituted amides.[8b] The traditional method uses a stoichiometric amount of sulfuric acid as a catalyst.[16] In recent years, as an alternative to sulfuric acid, the Ritter reaction has been catalyzed by $H_3PW_{12}O_{40}$,[17a] $Bi(OTf)_3$,[17b] *t*-BuOAc/H_2SO_4,[17c] $Al(HSO_4)_3$,[17d] $Cu(OTf)_2$,[17e] etc. The main disadvantages of these procedures are an excess amount of corrosive acids, harsh reaction conditions, the use of air- or water-sensitive catalysts, and difficulties in the separation and recycling of catalysts. Hence, we applied complex **1** to catalyze the Ritter reaction of nitriles with alcohols under solvent-free conditions or in $ClCH_2CH_2Cl$ for 3-12 h to afford the desired N-substituted amides in moderate to high yields (screening optimal conditions in the SI).

Table 2. The Ritter reaction of nitriles with alcohols catalyzed by **1** [a]



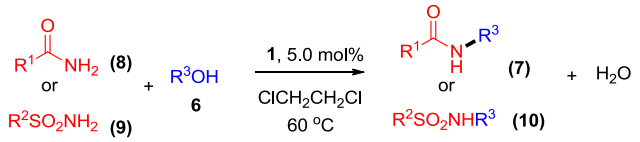
[a] Catalyst **1** (0.05 mmol); nitriles (**5**; 1.0 mmol); alcohols (**6**; 1.0 mmol); Temp: 80 °C; isolated yield. [b] Solvent-free; [c] $ClCH_2CH_2Cl$ (1 mL).

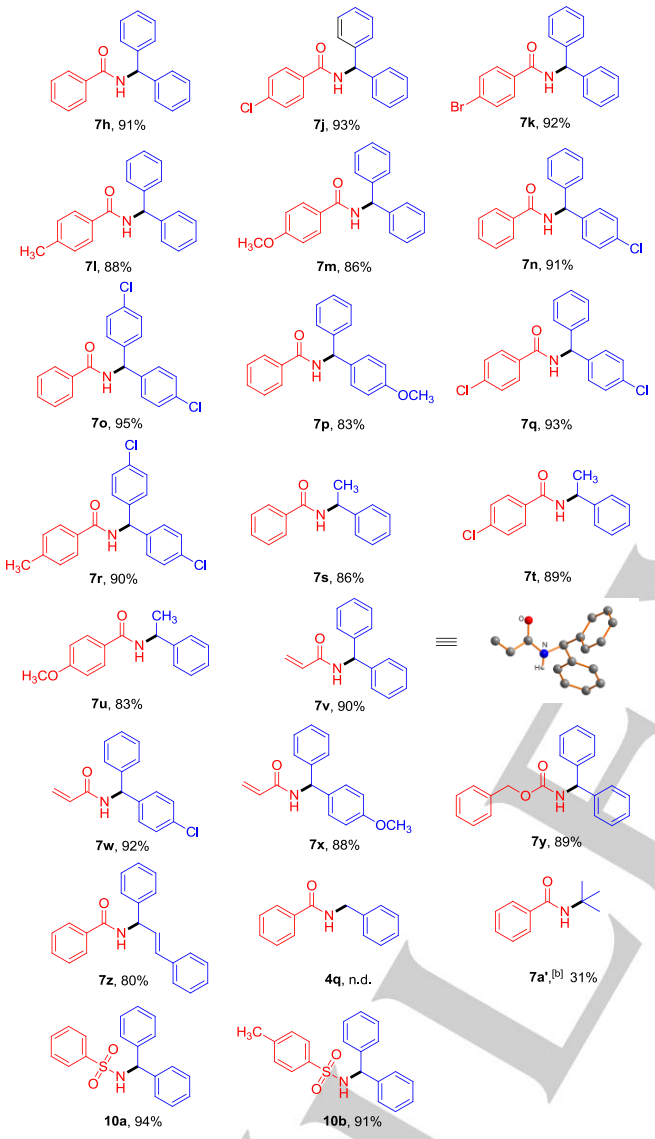
As shown in Table 2, the aliphatic acetonitriles with different secondary or tertiary alcohols were converted to the corresponding amides in high yields (**7a-7f**, 77-91%). In addition, acetonitrile with a low boiling point could be used as a solvent and a substrate. For substituted benzhydrol, the electron-donating and electron-withdrawing groups in the aromatic ring have a slight effect on the reactivity (**7b**-**7e**). Nonetheless, upon using benzyl alcohol in this reaction, product **7g** was obtained in only a 43% yield. Reactions of benzonitrile with a high boiling point or solid 2-benzothiazoleacetonitrile with benzhydrol or tertiary butanol proceed in 1,2-dichloroethane at 80 °C, giving yields of 76% and 80%, respectively (**7h**, **7i**). The above results prove that complex **1** can be used as an effective catalyst to synthesize N-substituted amides by the Ritter reaction.

Direct catalytic amination of alcohols, which generates only water as a coproduct, is a straightforward and desirable process for C-N bond formation.[18] Although a number of direct aminations of alcohols catalyzed by transition metals have been reported, the use of a primary amide with weak nitrogen nucleophiles is uncommon and requires harsh conditions.[19] Recently, a few Lewis acid and Brønsted acid catalyzed aminations of alcohols with primary amides have been described, including those of $FeCl_3$,[20a] $MoCl_5$,[20b] triflate salts,[20c] I_2,[20d] phosphotungstic acid,[20e] and $HClO_4/SiO_2$[20f]. However, these methods have disadvantage(s) such as a requirement for toxic or expensive metal reagents, drastic reaction conditions, unsatisfactory yields and poor recyclability of catalysts. Hence, we addressed these problems using complex **1** as a catalyst (5.0 mol%) for the direct amination of primary amides and alcohols in $ClCH_2CH_2Cl$ for 12 h, and gained moderate to excellent yields (screening optimal conditions in the SI).

As shown in Table 3, the reactions of benzamide or substituted benzamides with secondary benzylic alcohols proceeded smoothly, giving the corresponding products in high yields (**7h, 7j-7z**, 80-95%). In addition, we found that the electron-deficient benzamides and benzhydrylic alcohols showed better reactivity, giving higher product yields than the electron-rich ones. 1-Phenylethanol showed good reactivity in this catalytic system with benzamide, *p*-chlorobenzamid and *p*-methylbenzamide, and the yields were 86%, 89% and 83%, respectively (**7s-7u**). To our delight, acrylamide and benzyl carbamate were also tolerated, giving the corresponding products in high yields (**7v-7x**, 88-92%). The structure of compound **7v** was confirmed using X-ray crystallography. Gratifyingly, upon using benzyl carbamate and (*E*)-1,3-diphenylprop-2-en-1-ol in this reaction, products **7y** and **7z** were obtained in 89% and 80% yields, respectively, demonstrating the good tolerance of complex **1** towards ester groups and C=C bonds. Although this reaction was highly efficient for secondary benzylic alcohols, benzyl alcohol itself did not react under these conditions even after prolonged heating (**4q**). Moreover, we investigated the tertiary butanol, and found that product **7a'** was obtained in only a 31% yield. In addition, the reactions of sulfamides with benzhydrol gave good yields of 94% and 91% (**10a**, **10b**).

Table 3. The direct amination of amides with alcohols catalyzed by **1** [a]

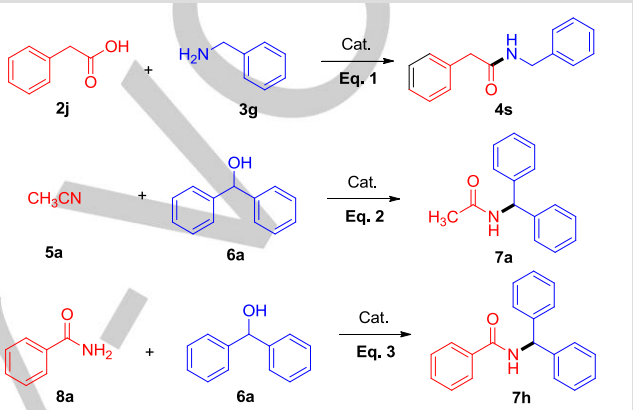




[a] Catalyst **1** (0.05 mmol); amides (**8**; 1.0 mmol); alcohols (**6**; 1.0 mmol); Solvent: $ClCH_2CH_2Cl$ (1 mL); Time: 12 h; Temp: 60 °C; isolated yield. [b] 80 °C. [c] n.d.: not detected.

To illustrate the advantage of using complex **1**, we compared its catalytic activities with those of $ZrCl_4$, Cp_2ZrCl_2, $Cp^*_2ZrCl_2$, $Cp_2Zr(OSO_2CF_3)_2$, $AgOSO_2C_8F_{17}$, $Sc(OSO_2C_8F_{17})_3$ and $[Cp_2Zr(H_2O)_3][OSO_2C_8F_{17}]_2$·THF. As shown in Table 4, high yields were consistently achieved with complex **1** as a catalyst, which may be because one of the micro-catalytic systems recently reported by us[11d] contributed to product auto-separation. Catalysts such as zirconium chlorides, zirconocene dichloride and triflates showed much lower yields, plausibly due to their weaker Lewis acidity or moisture-sensitive features. However, these water-tolerant catalysts such as $AgOSO_2C_8F_{17}$, $Sc(OSO_2C_8F_{17})_3$ and $[Cp_2Zr(H_2O)_3][OSO_2C_8F_{17}]_2$·THF showed low to moderate catalytic efficiency compared to complex **1**, which may be due to their low solubility in common organic solvents.

Table 4. Comparison with other Lewis acids catalysts[a]



Entry	Catalyst	Yield (%) [a]		
		Eq. 1	Eq. 2	Eq. 3
1	$ZrCl_4$	58	43	49
2	Cp_2ZrCl_2	32	17	23
3	$Cp^*_2ZrCl_2$	38	19	27
4	$Cp_2Zr(OSO_2CF_3)_2$	83	76	80
5	$AgOSO_2C_8F_{17}$	27	18	38
6	$Sc(OSO_2C_8F_{17})_3$	48	36	70
7	$[Cp_2Zr(H_2O)_3][OSO_2C_8F_{17}]_2$·THF	87	78	83
8	Complex **1**	95	87	91

[a] Under the same conditions as those shown in Tables 1, 2, and 3.

To test the reusability of the catalyst and the reproducibility of its catalytic performance, complex **1** was subjected to recycling experiments in the above reactions (**Eq 1: 2j+3g → 4s; Eq 2: 5a+6a → 7a; Eq 3: 6a+8a → 7h**). The change in product yield was negligible in a trial of five recycling experiments, demonstrating that catalyst **1** is stable and suitable for reuse (Table 5).

Table 5. Synthesis of N-substituted amides (**Eq 1**, **Eq 2**, **Eq 3**) catalyzed by recovered catalyst **1**[a]

Cycle	**Eq 1** Yield (%)[b]	**Eq 2** Yield (%)[b]	**Eq 3** Yield (%)[b]
1	95	86	92
2	94	85	91
3	94	83	91
4	92	81	90
5	90	80	88

[a] Under the same conditions as those shown in Tables 1, 2, and 3. [b] Isolated yield of the desired product.

Conclusions

In summary, an air-stable and strongly acidic decamethyl zirconocene complex **1** was synthesized and characterized. This complex can be used as a general catalyst for N-substituted amide synthesis using different approaches. The advantages of these protocols are (i) a high atom economy, (ii) a wide substrate scope, (iii) mild conditions, (iv) good functional group tolerance and (v) a recyclable catalyst.

Experimental Section

General

All chemicals were purchased from Aldrich. Co. Ltd and used as received unless otherwise indicated. The preparation of the catalyst was performed under a nitrogen atmosphere with freshly distilled solvents unless otherwise noted. $Sc(OSO_2C_8F_{17})_3$ was prepared according to the literature[21]. The NMR spectra were recorded at 25 °C over an INOVA-400M (Varian) instrument calibrated with tetramethylsilane (TMS) as an internal standard. Elemental analysis was performed using VARIO EL III. Conductivity was measured on a REX conductivity meter DDS-307. IR spectra were recorded on an 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 a SMART-APEX and a RASA-7A by the Shanghai Institute of Organic Chemistry, China Academy of Science. The acidity was measured using the Hammett indicator method as described previously. The acid strength was expressed in terms of the Hammett acidity function (H_0) as scaled by the *pK*a value of the indicators.

Preparation of complex 1: A solution of $AgOSO_2C_8F_{17}$ (1.21 g, 2 mmol) in 10 mL THF was added to a solution of $Cp^*_2ZrCl_2$ (0.432 g, 1 mmol) in 20 mL THF. After the mixture was stirred at room temperature for 1 h in the absence of light, it was filtered. Dry *n*-hexane (40 mL) was placed over the colorless filtrate, and after storage in a refrigerator for 24 h, the colorless crystal was collected (1.04 g, 71%). Recrystallization of this complex in THF/hexane produced good crystals suitable for X-ray analysis. Complex 1: Mp: 185-187 °C, ^{1}H NMR (400 MHz, [d_6] acetone) δ: 1.81-1.77 (m, 4H, THF), 2.95 (s, 12H, CH_3), 2.70 (s, 6H, CH_3), 2.50 (s, 12H, CH_3), 3.65-3.62 (m, 4H, THF); ^{13}C NMR (100 MHz, [d_6] acetone) δ: 123.6 (Cp*), 126.0 to 100.0 (C_8F_{17}), 10.3 (CH_3); ^{19}F NMR (376 MHz, [d_6] acetone): δ: -76.04 to -76.16 (m, 3F; CF_3-), -109.11 to -109.19 (m, 2F; -CF_2-), -115.37 to -115.54 (m, 2F; -CF_2-), -117.04 to -116.48 (m, 6F; -CF_2-), -117.60 to -117.88 (m, 2F; -CF_2-), -121.11 to -121.33 (m, 2F; -CF_2-); IR(KBr): v = 3428, 2983, 2922, 1612, 1537, 1450, 1365, 1240, 1208, 1150, 1065, 1031, 940, 854, 737, 651, 561 cm^{-1}. Anal. Calc'd for $C_{40}H_{42}F_{34}O_9S_2Zr$: C, 32.73; H, 2.88; found: C, 32.70; H, 2.90.

Crystal data for **1**: $C_{40}H_{42}F_{34}O_9S_2Zr$; *Mr* = 1468.08, Monoclinic, space group *P 21/c*, *a* = 14.6265(18) Å, *b* = 22.107 (3) Å, *c* = 17.328 (2) Å; *V* = 5484.0(12) Å ^{3}; *T* = 293(2) K; *Z* = 4; Reflections collected/unique, 33627/7145, R_{int} = 0.0910, R_1 = 0.0548, wR_2 = 0.1887; *GOF* = 0.991; CCDC-1565683 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 direct amide formation from carboxylic acids and amines catalyzed by complex 1: To a round-bottom flask was added acetic acid (60 mg, 1.0 mmol), aniline (93 mg, 1.0 mmol) and complex **1** (29.4 mg, 0.02 mmol). The mixture was stirred at 80°C for 2 h and monitored using TLC. After cooling the reaction mixture to room temperature, CH_2Cl_2 (10 mL × 3) was added and the catalyst was filtered for the next reaction cycle (the recovered catalyst should be dried in a vacuum oven at 60 ^{o}C for 2 hours). The solvent was removed under reduced pressure and the residue was purified using column chromatography with ethyl acetate/petroleum ether (50/50) to afford 132.2 mg of the white solid (**4d**) in a 98% yield. Carboxylic acids and amines are commercially available.

Typical procedure for the Ritter reaction from nitriles and alcohols catalyzed by complex 1: To a round-bottom flask was added diphenylmethanol (184 mg, 1.0 mmol), CH_3CN (1.0 mmol) and complex **1** (73.5 mg, 0.05 mmol). The mixture was stirred at 80°C for 5 h and monitored using TLC. Then, the solvent was removed from the mixture to leave behind the residue; CH_2Cl_2 (10 mL × 3) was added to the reaction mixture and the catalyst was filtered for the next reaction cycle (the recovered catalyst should be dried in a vacuum oven at 60 ^{o}C for 2 h). For the filtrate, after evaporation of the solvent a crude amide mixture was obtained. The residue was separated using short column chromatography eluted with ethyl acetate/petroleum ether (80/20) to afford 195.8 mg of the white solid (**7a**) in an 87% yield. Nitriles and alcohols are commercially available.

Typical procedure for the amidation reaction of alcohols with carboxamides or sulfonamides catalyzed by complex 1: A well-ground mixture of diphenylmethanol (1.0 mmol), acrylamide (1.0 mmol), and complex **1** (0.05 mmol) was heated at 60 °C in $ClCH_2CH_2Cl$ (1 mL) for 12 h and monitored using TLC. Then, the solvent was removed from the mixture to leave behind the residue, CH_2Cl_2 (10 mL × 3) was added to the reaction mixture and the catalyst was filtered for the next reaction cycle (the recovered catalyst should be dried in a vacuum oven at 60 ^{o}C for 2 hours). For the filtrate, after evaporation of the solvent a white solid mixture was obtained. The residue was separated using short column chromatography eluted with ethyl acetate/petroleum ether (80/20) to afford 213.3 mg of the white solid (**7v**) at a 90% yield. Alcohols and amides are commercially available.

N-benzhydrylacrylamide (**7v**):[20d] White solid; M.p. 179-180 °C; ^{1}H NMR (400 MHz, d_6-Acetone): δ: 8.27 (d, *J* = 6.4 Hz, 1H), 7.33-7.24 (m, 10H), 6.45 (q, *J* = 6.8 Hz, 1H), 6.35 (d, *J* = 8.8 Hz, 1H), 6.25 (dd, *J* = 2.4 Hz, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, d_6-Acetone) δ: 169.35, 147.66, 147.65, 147.64, 136.64, 133.58, 132.66, 132.24, 130.64, 61.77; Ms (m/z): 237.1 (M^+).

Crystal data for **7v**: $C_{16}H_{15}NO$; *Mr* = 237.29, Monoclinic, space group *P 21/c*, *a* = 9.3631(5) Å, *b* = 15.6423 (8) Å, *c* = 9.6090 (5) Å; *V* = 1310.01(12) Å ^{3}; *T* = 293(2) K; *Z* = 4; Reflections collected/unique, 16973/2667, R_{int} = 0.0800, R_1 = 0.0571, wR_2 = 0.1301; *GOF* = 1.025; CCDC-1565689 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 catalyst recovery and reuse: To a round-bottom flask was added phenylacetic acid (272 mg, 2.0 mmol), benzylamine (214 mg, 2.0 mmol), complex 1 (58.8 mg, 0.04 mmol) and and THF (2 mL). The mixture was stirred at 80°C for 4 h and monitored by TLC. THF was removed from the mixture to leave behind the residue. Then the residue was diluted with CH_2Cl_2, and subject to filtration for the recovery of catalyst (the recovered catalyst should be dried in a vacuum oven at 60 ^{o}C for 2 hours). For the filtrate, after evaporation of the solvent a crude amide mixture was obtained. Finally, the product was purified by column chromatograph on silica gel (petroleum ether/ethyl acetate=1:1). The same procedure was used for the synthesis of other N-substituted amides catalyzed by recovered catalyst 1.

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Keywords: Lewis acids • N-substituted amides • decamethyl zirconocene • perfluorooctanesulfonates • homogeneous catalysis

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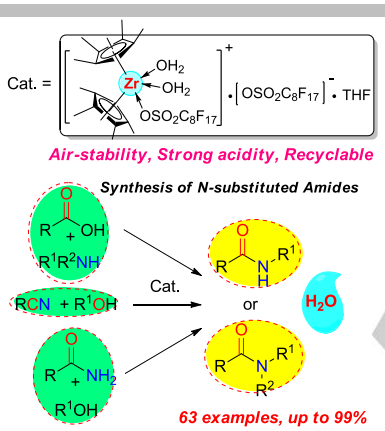
Entry for the Table of Contents

FULL PAPER

An air-stable Lewis acidic complex bis(pentamethylcyclopentadienyl) zirconium perfluorooctanesulfonate was successfully synthesized, and found to show relatively strong acidity, and high catalytic efficiency for the synthesis of N-substituted amides. Moreover, the complex had good reusability.



Ningbo Li, Lingxiao Wang, Liting Zhang, Wenjie Zhao, Jie Qiao,* Xinhua Xu,* and Zhiwu Liang*

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Air-stable Bis(pentamethylcyclopentadienyl) Zirconium Perfluorooctanesulfonate as an Efficient and Recyclable Catalyst for the Synthesis of N-substituted Amides