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A sustainable water-tolerant catalyst with enhanced Lewis acidity: Dual activation of Cp_2TiCl_2 via ligand and solvent

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ABSTRACT

A new strategy was developed to enhance the activity of titanocene dichloride for the synthesis of 2,4-disubstituted-3H-benzo[b]-[1,4]diazepine derivatives by using Cp_2TiCl_2 as a pre-catalyst. The titanocene was activated *in situ* in the catalytic system *via* the coordination with *m*-phthalic acid and alcohol solvent accompanied with the secession of a cyclopentadienyl ring, leading to the formation of an activated species, $[CpTi(OEt)_2(\eta^1\text{-}C_8H_5O_4)]$. In particular, the novel developed half-titanocene catalyst exhibited more superior stability than representative half-titanocene complex, indicated by not only water compatibility for the employment of 30 % aqueous ethanol solution but also the recyclability that the products could be generated without apparent yield decrease after 5 runs. In general, we present a paradigm for sustainable molecular catalysis of titanocene.

1. Introduction

Lewis acid catalysts have attracted widespread attention in organic synthesis and have been widely used in the industrial production of many products, such as fine chemicals and pharmaceuticals [1–6]. Meanwhile, with increasing environmental awareness, more concerns have been paid to the sustainability of catalysts as well as the use of environment-friendly systems [7–11]. However, one of the largest obstacles in the application of Lewis acid catalysts is their instability, especially towards moisture [12]. Therefore, tremendous efforts have been made to design air-stable and water-tolerant Lewis acids catalyst especially in the transitional meatal complex form [13–15]. Extensive studies have demonstrated that the incorporation of a polydentate ligand to the centre metal atom can make a Lewis acid more stable [16, 17]. A more popular strategy is based on the introduction of carbon ligands, especially sterically hindered ligands represented by Cp ligands, which can improve their stability from the perspective of electronic and steric hindrance [18–20]. Such a less electron-deficient steric-hindrance ligand could provide a hydrophobic domain to protect the Lewis acid centre from water [21–25].

Inspired by adoption as a co-catalyst of a Ziegler-Natta catalyst for alkene polymerization, Ti has aroused significant attention and has been applied to many important organic transformations [26–32]. However, there is still a general need for anhydrous conditions. Cyclopentadienyl (Cp) ligands have been introduced and successfully used to show that strictly anhydrous conditions are unnecessary [33–37]. However, the usual introduction of two Cp ligands increases the stability of a Lewis acid catalyst at the sacrifice of catalytic activity. For decades, chemists have made many efforts to reconcile the contradiction between the stability and activity of titanocene [38–42]. Due to the configuration variability of titanocene dichloride, a series of titanocene compounds have been developed by introducing various ligands apart from cyclopentadienyl. Specifically, O- [43–47], N- [48–51], and P-donor ligands [52–56] have been proven to enhance the activity and acidity of titanocenes. To further improve their catalytic activity, it is a prudent option to produce half-titanocene (IV) Lewis acid catalysts with one Cp [57–61]. However, half-titanocene (IV) Lewis acid catalysts are generally labile, even for bulkier Cp* ligands; for instance, the frequently used Cp^*TiCl_3, a high reactive catalyst, is strongly recommended to be used in a glove box. Therefore, to develop half-titanocene (IV) catalyst with good stability is still challenging and promising.

To test our hypothesis that retaining only one Cp ring towards

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Cp_2TiCl_2 may increase the catalytic power of a Lewis acid metal centre while maintaining relative stability, we took the synthesis of benzo[b]-[1,4]diazepines as a touchstone. Benzodiazepines are a kind of nitrogen heterocyclic compound with high pharmacological activity [62–67]. Many acid catalysts have been developed for the synthesis of such compounds, involving Brønsted acid or Lewis acid catalysts, such as Zn [(L)Proline]$_2$ [68], Ga(OTf)$_3$ [69], $CeCl_3$ [70], $SbCl_3$–Al_2O_3 [71], Au(I) [72], Yb(OTf)$_3$ [73], and so on. In our previous work, we found that amide ligand urea facilitates the removal of both Cp rings from titanocene [74]. Herein, we disclose the establishment of half-titanocene complexes with just one Cp ligand, which show excellent catalytic activity, water-insensibility and sustainability for the synthesis of benzo [b]-[1,4]diazepines (Scheme 1). The novel prepared half-titanocene complex is featured by the removal of one Cp ligand from the titanocene dichloride under the dual activation on of a N-donor ligand and alcohol solvent, the structure of which is elucidated by ^{1}H NMR and ES (+)-MS analysis. Cyclic experiments demonstrate the sustainability of the titanocene complex and the employment of an alcohol-water mixed solvent proves its tolerance towards water.

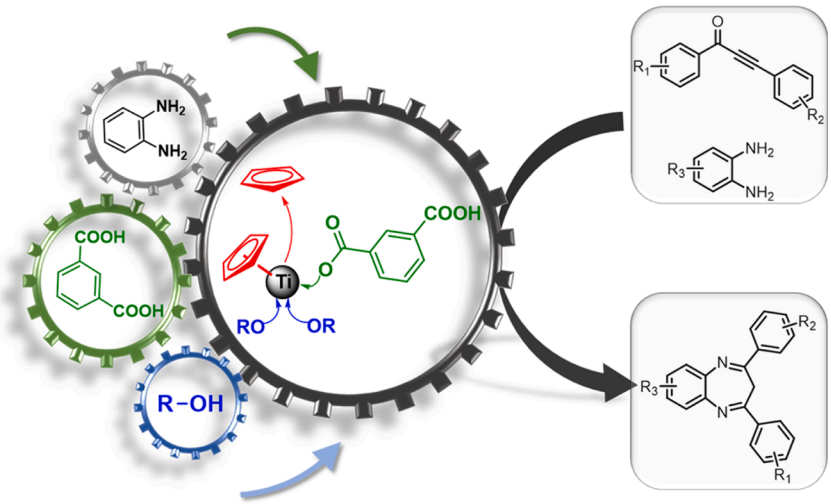
2. Results and discussion

Our investigation started with the evaluation of the ligand effect on the catalyst Cp_2TiCl_2 through synthesis towards benzo[b]-[1,4] diazepines from 1,3-ynone and *o*-phenylenediamine. Initially, we ran ligand-free conditions, and the target product was only generated with a low yield of 7% (Table 1, entry 1). Subsequently, a series of COOH ligands were examined (entries 2-7). As seen from the experimental results, the addition of COOH ligands improved the reaction efficiency, and *m*-phthalic acid proved to be the best choice, assuring a 40% yield for the products' generation. Next, the solvent effect was investigated systematically, with the results shown in entries 8-17. The worst situation was when the aprotic solvent toluene was adopted as a solvent because no product was detected (entry 8). Employment of regular polar solvents, such as DMF, DMSO, and CH_3CN (entries 9-11), assured that the product yield varied from 29% to 41%, commensurate to that of the case for 1,4-dioxane (entry 7). Generally, when alcoholic solvents were used as solvents, the yields were at a better level (entries 12-17), especially for monohydric alcohols (entries 14-17). In particular, when methanol and ethanol were employed, 96% yield products were afforded. From a green chemistry point of view, ethanol was chosen as the optimal solvent (entry 16). To confirm the ligand and solvent activation effect on the title reaction, attempts deviating from standard conditions were also performed. As shown in entries 18-20, Cp_2TiCl_2, ligand and ethanol are all indispensable for the smooth progression of the reaction because only 4%, 21% and 63% product could be obtained, respectively, for their absence.

To shed light on how the COOH ligand and alcoholic solvent activate Cp_2TiCl_2, a titration experiment was conducted by adding activator methanol and acid ligand to the deuterated chloroform solution of Cp_2TiCl_2, followed by the detection of the Cp signal in ^{1}H NMR spectra, which can be interpreted as the existence of titanocene species. As shown in Fig. 1, acid ligand (line 2) or methanol (line 3) alone does not cause any transformation of Cp_2TiCl_2, as verified by the unchanged signal for the Cp peak at δ 6.59 ppm (●). Combinative addition of ligand and methanol was also unable to activate Cp_2TiCl_2 (line 4). After adding *o*-phenylenediamine, two new signals immediately appeared at δ 6.37 ppm (▼) and δ 6.27 ppm (◆), accompanied by the disappearance of the signal at δ 6.59 ppm (in less than 1 min), suggesting that Cp_2TiCl_2 transformed into two new titanocene species. The chemical conversion of Cp_2TiCl_2 might be attributed to the induced effect of *o*-phenylenediamine, which was not only added as the reaction substrate, but also played as a crucial role in the removal of one Cp ligand. As the reaction time increased, the signal at δ 6.27 ppm gradually decreased and disappeared while the signal at δ 6.37 ppm increased, which indicated that the real catalytic species has experienced an intermediate state during the formation process.

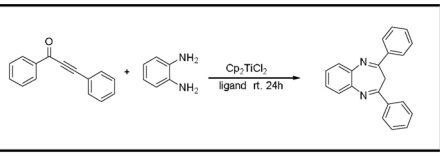
To further determine the structure of the real catalytic species, we analysed ^{1}H NMR spectra and ran an ESI-MS experiment. As can been seen from Fig. 2b, the proton number ratio for the benzene ring and Cp ring is 4:5, indicating that the ligand ratio for the acid and Cp is 1:1 in the titanocene catalytic species. The structure was further elucidated by ESI-MS analysis. As shown in Fig. 2c, the major signal with an *m/z* value of 175.0238 should correspond to Int-II′, where two OMe ligands and one Cp ligand are bound to the titanium metal centre. The other peak with an *m/z* value of 309.0246 (Fig. 2d) should correspond to the ion peak Int-II″, in which one Cp ligand, one OMe ligand and one acid ligand are coordinated to the titanium centre. Taking all the ^{1}H NMR spectra and ESI-MS spectra together, the catalytic species should be CpTi(OMe)$_2$(η^1-$C_8H_5O_4$), which is transformed from Cp_2TiCl_2 under dual activation of methanol and *m*-phthalic acid. To ensure that the titanocene species obtained by the ^{1}H NMR titration experiment was the real catalyst, the premade catalyst was used to catalyse the model reaction in Table 1, a commensurate yield of 97 % was obtained, verifying our proposal.

The complex of CpTi(OMe)$_2$(η^1-$C_8H_5O_4$) we disclosed were synthesized from Cp_2TiCl_2. This method for the synthesis of the half-titanocene complex was in low cost, because raw material Cp_2TiCl_2 was more stable and cheaper than most half-titanocene complexes. For comparison, the synthesis methods of reported half-titanocene complexes containing O-



Scheme 1. Titanocene complexes accelerated by a ligand strategy.

Table 1
Ligand effect and solvent effect in the reaction of 1,3-ynone with *o*-phenylenediamine. [a].



Entry	Catalyst	Ligand	Solvent	Yield(%)[b]
1	Cp_2TiCl_2	–	1,4-dioxane	7
2	Cp_2TiCl_2	benzoic acid	1,4-dioxane	14
3	Cp_2TiCl_2	p-cresol	1,4-dioxane	25
4	Cp_2TiCl_2	salicylic acid	1,4-dioxane	27
5	Cp_2TiCl_2	*o*-phthalic acid	1,4-dioxane	31
6	Cp_2TiCl_2	*p*-phthalic acid	1,4-dioxane	35
7	Cp_2TiCl_2	*m*-phthalic acid	1,4-dioxane	40
8	Cp_2TiCl_2	*m*-phthalic acid	toluene	ND
9	Cp_2TiCl_2	*m*-phthalic acid	DMF	29
10	Cp_2TiCl_2	*m*-phthalic acid	DMSO	37
11	Cp_2TiCl_2	*m*-phthalic acid	CH_3CN	41
12	Cp_2TiCl_2	*m*-phthalic acid	glycerol	23
13	Cp_2TiCl_2	*m*-phthalic acid	ethylene glycol	56
14	Cp_2TiCl_2	*m*-phthalic acid	*n*-propanol	88
15	Cp_2TiCl_2	*m*-phthalic acid	*n*-butanol	89
16	Cp_2TiCl_2	*m*-phthalic acid	ethanol	96
17	Cp_2TiCl_2	*m*-phthalic acid	methanol	96
18	–	–	ethanol	4
19	–	*m*-phthalic acid	ethanol	21
20	Cp_2TiCl_2	–	ethanol	63

[a] Reaction conditions: 0.5 mmol of 1,3-ynone, 0.6 mmol of *o*-phenylenediamine, 2 mol% of Cp_2TiCl_2 and 2 mol% of ligand in 0.5 mL solvent at room temperature for 12 h. [b] Yield of the Isolated product.

	Catalyst	Ligand	Solvent	Yield(%)[b]
1	Cp_2TiCl_2	–	1,4-dioxane	7
2	Cp_2TiCl_2	benzoic acid	1,4-dioxane	14
3	Cp_2TiCl_2	p-cresol	1,4-dioxane	25
4	Cp_2TiCl_2	salicylic acid	1,4-dioxane	27
5	Cp_2TiCl_2	*o*-phthalic acid	1,4-dioxane	31
6	Cp_2TiCl_2	*p*-phthalic acid	1,4-dioxane	35
7	Cp_2TiCl_2	*m*-phthalic acid	1,4-dioxane	40
8	Cp_2TiCl_2	*m*-phthalic acid	toluene	ND
9	Cp_2TiCl_2	*m*-phthalic acid	DMF	29
10	Cp_2TiCl_2	*m*-phthalic acid	DMSO	37
11	Cp_2TiCl_2	*m*-phthalic acid	CH_3CN	41
12	Cp_2TiCl_2	*m*-phthalic acid	glycerol	23
13	Cp_2TiCl_2	*m*-phthalic acid	ethylene glycol	56
14	Cp_2TiCl_2	*m*-phthalic acid	*n*-propanol	88
15	Cp_2TiCl_2	*m*-phthalic acid	*n*-butanol	89
16	Cp_2TiCl_2	*m*-phthalic acid	ethanol	96
17	Cp_2TiCl_2	*m*-phthalic acid	methanol	96
18	–	–	ethanol	4
19	–	*m*-phthalic acid	ethanol	21
20	Cp_2TiCl_2	–	ethanol	63

[a] Reaction conditions: 0.5 mmol of 1,3-ynone, 0.6 mmol of *o*-phenylenediamine, 2 mol% of Cp_2TiCl_2 and 2 mol% of ligand in 0.5 ml solvent at room temperature for 12 h.
[b] Yield of the Isolated product.

donor ligands were summarized in Table S1 (Supporting Information). For all of these half-titanocene complexes, amines or metal alkyl compounds were used as additive to induce ligand conversion, which was similar to the role of *o*-phenylenediamine in the synthesis of CpTi$(OMe)_2(\eta^1$-$C_8H_5O_4)$. However, almost all of them were synthesized from the unstable and expensive $CpTiCl_3$, which leads to a high cost,

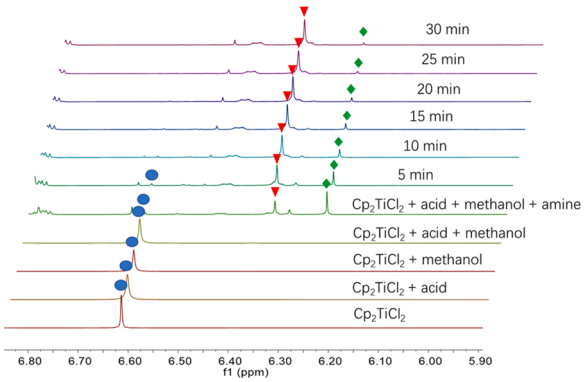


Fig. 1. 400 MHz ^{1}H NMR spectra for a Cp_2TiCl_2 solution with the addition of *m*-phthalic acid, methanol and *o*-phenylenediamine in $CDCl_3$. ●6.59 ppm [Cp_2TiCl_2]; ▼6.37 ppm [CpTi$(OMe)_2(\eta^1$-$C_8H_5O_4)$]; ◆6.27 ppm [$Cp_2Ti(OMe)_2$].

economically and experimentally. Therefore, the synthesis of half-titanocene complexes from Cp_2TiCl_2 is a strategy with potential development value.

For different half-titanocene complexes, ligands have a great effect on their stability and activity, and the interaction between Ti and ligands can be reflected by the Ti-ligand bond lengths. In order to further study the ligand effects on the catalytic activity of half-titanocene toward synthesis of 2,4-disubstituted-3H- benzo[*b*]-[1,4]diazepines, three frequently-used half-titanocene complexes, including $CpTiCl_3$, Cp^*TiCl_3 and $Cp^*Ti(OMe)_3$ were evaluated over our catalytic species. The employment of $CpTiCl_3$ and Cp^*TiCl_3 gave the yields of 65 % and 60 % (Fig. 3), respectively. Nevertheless, only trace product could be detected when $Cp^*Ti(OMe)_3$ was utilized as a catalyst. These results indicated that the half-titanocene catalyst with -Cl ligand has higher activity than that with alkoxy ligands, which was consistent with the difference in the binding force of Ti-ligand. From the published crystal data of half-titanocene complexes, the bond length between Ti and ligands follows the order of Ti-Cl (2.24–2.28 Å) > Ti−OOC (1.92–2.24 Å) > Ti-OAr (1.76–1.85 Å) > Ti-O (1.72–1.729 Å) (Table S1). However, $CpTiCl_3$ with the longest Ti-ligand bond just showed a moderate activity compared to CpTi$(OMe)_2(\eta^1$-$C_8H_5O_4)$ (97 %). This might be due to the high activity of Ti-Cl bond, so that a complex conversion occurred during the catalytic process. Therefore, we conducted a control experiment to study the catalytic effect of $CpTiCl_3$ after being placed in EtOH solvent for 24 h. The yield of 2,4-disubstituted-3H- benzo[*b*]-[1,4]diazepine had a dramatic decline, which verified that $CpTiCl_3$ with too active Ti-Cl bonds was unstable in EtOH, thereby reducing its catalytic activity. Therefore, there are two possible reasons why CpTi$(OMe)_2(\eta^1$-$C_8H_5O_4)$ showed high activity in this acid catalysis. Firstly, it contains two stable -OMe ligands, which ensure its stability during catalysis. In addition, it contains moderately active −COOH ligand, thus ensuring its high catalytic activity.

Taking all the aforementioned mechanism results together, a plausible mechanism for the synthesis of 2,4-disubstituted-3H- benzo[*b*]-[1,4]diazepine derivatives is proposed (Scheme 2). Initially, the pre-catalyst Cp_2TiCl_2 is activated by *m*-phthalic acid and methanol under the assistance of *o*-phenylenediamine, forming the catalytic species CpTi$(OMe)_2(\eta^1$-$C_8H_5O_4)$. Then, the 1,3-ynone is activated by the newly formed titanocene species, facilitating the Michael addition with *o*-phenylenediamine. After that, the carbonyl group of the Michael adduct is attacked by another amino group to form N, O-acetal. Subsequent ligand dissociation releases the N, O-acetal(VI) and regenerates the catalytic species II. Finally, dehydration and isomerization of compound VI lead to the 2,4-disubstituted-3H- benzo[*b*]-[1,4]diazepine target.

The resistance of the catalyst to water was studied by investigating the catalytic activity in the presence of a small amount of water. A certain amount of water was artificially introduced into the reaction to

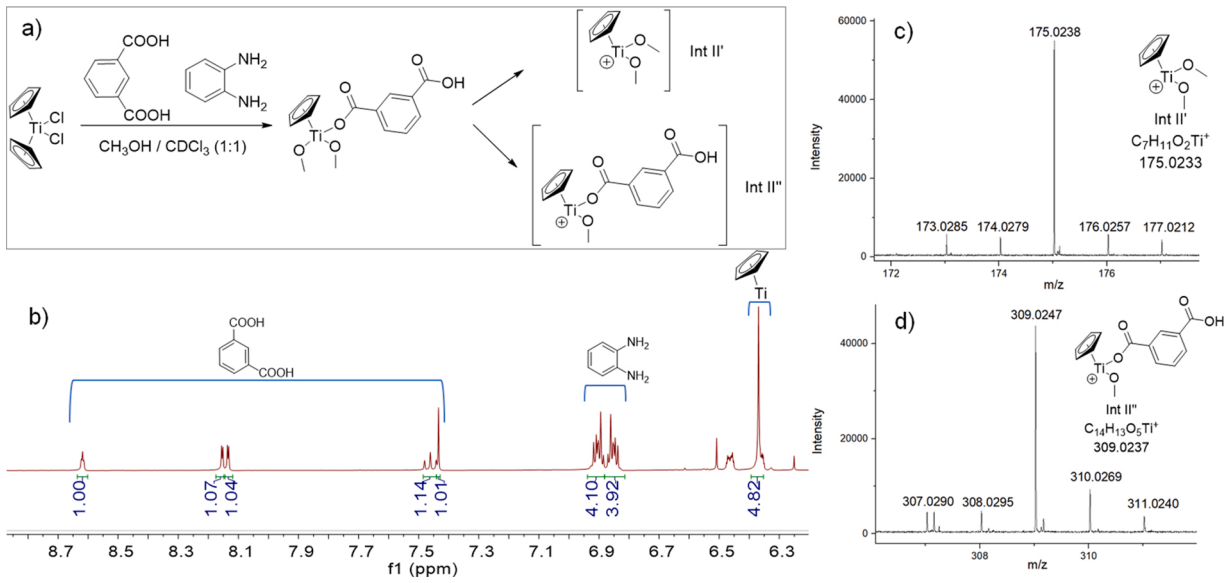


Fig. 2. 400 MHz ^{1}H NMR spectra and ESI-MS analysis for the new titanocene complex species.

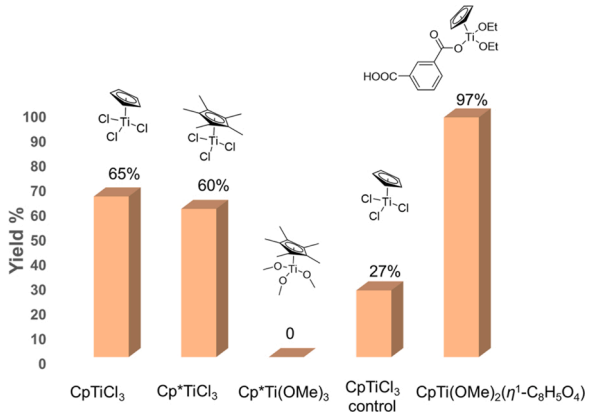


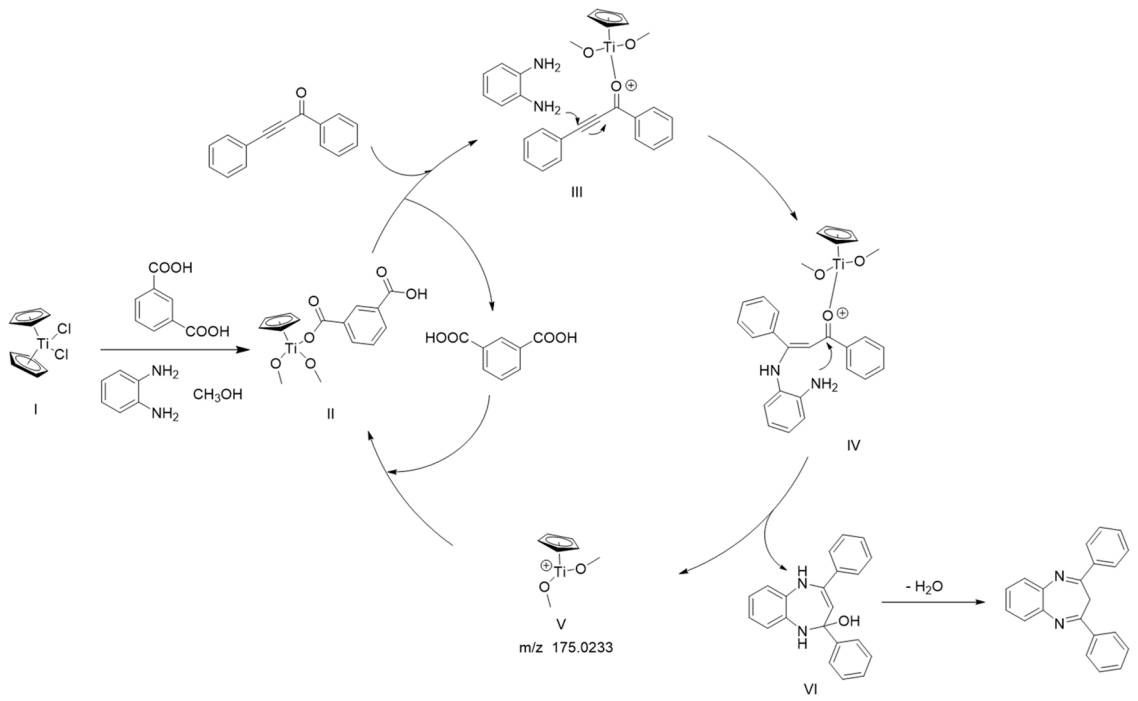
Fig. 3. Catalytic effect comparison of half-titanocene complexes.

generate a series of EtOH:H_2O mixtures as solvents at ratios of 9:1, 8:2 and 7:3 (Fig. 4a). These solvents containing water gave high yields of 93 %, 92 % and 92 %, respectively. When the proportion of water in the solvent was continuously increased and the ratio of EtOH:H_2O reached 1:1, the yield dropped sharply to 53 %, which could be due to the low solubility of the substrate in the 50 % ethanol solution. This result indicates that the organometallic titanocene complex catalyst is resistant to water. The Cp ligand, which has a larger spatial structure, stabilizes the Lewis acid metal centre, making it hard to bond with water, avoiding hydrolysis and improving the stability of the Lewis acid. In the presence of large amounts of water, the catalyst was not deactivated.

From an economic point of view, the sustainable catalytic effect of a catalyst is particularly important. The good stability of this Lewis acid catalyst was reflected in its recyclability, which is rare in other Lewis acid catalysts. The sustainability of this acidic catalytic system was studied in catalysing the cyclization reaction of 1,3-ynone and o-phenylenediamine. When the catalytic reaction was completed, the product was isolated by filtration and the filtrate was collected for the next catalytic cycle. A pure phase of the product was obtained by washing the filter cake with ethanol several times. The filtrate containing the catalytic species and solvent was directly reused in the next catalytic cycle by just adding the corresponding substrates without supplementing any pre-catalyst or ligand. For the recycled catalytic system, the synthesis towards benzo[*b*]-[1,4]diazepine from 1,3-ynone and *o*-phenylenediamine in the 2nd, 3rd, 4th and 5th cycles achieved high yields of 93 %, 86 %, 86 % and 87 %, respectively. As shown in Fig. 4b, the activity of the system containing catalyst was maintained very well during the recycling process. This result confirms that the CpTi $(OMe)_2(\eta^1\text{-}C_8H_5O_4)$ can remain stable in the catalytic system and is a sustainable catalyst.

The use of the recyclable organometallic Lewis acid catalyst, CpTi $(OMe)_2(\eta^1\text{-}C_8H_5O_4)$, in alcohol solvent is a new method for the synthesis of 2,4-disubstituted-3H- benzo[*b*]-[1,4]diazepine. The reaction was performed in a combination containing 1.0 equiv of 1,3-ynone, 1.2 equiv of 1,2-diaminobenzene, 2 mol% of Cp_2TiCl_2, 2 mol% of *m*-phthalic acid and 0.5 ml EtOH at room temperature. The scope and limitation of this catalytic system was evaluated with a series of 1,3-ynone and 1,2-diaminobenzene derivatives under optimized conditions. As shown in Table 2, the reactivity of different 1,3-ynones was studied by introducing electron-donating and electron-withdrawing groups at the carboxyl group side, respectively. When we change the groups on the aromatic ring, *p*-methyl shows yields of 99 % (3b), *p*-methoxy provides a 52 % yield (3c), *m*-methoxy shows an excellent yield of 97 % (3d) and *o*-methoxy shows a good yield of 84 % (3e), respectively. Electron-withdrawing halogen groups like *p*-fluoro, *p*-chloro and *p*-bromo show yields of 98 %, 98 % and 96 %, respectively (3f-3 h). When the chlorine group is introduced, *p*-chloro, *m*-chloro, and *o*-chloro show yields of 98 % (3 h), 93 % (3i), and 0%, respectively. A 3,5- dichlorosubstituted substrate showed a fairly large decrease in yield (3 l). Heterocyclic substitution was also investigated: thienyl-, furyl-, and naphthyl- gave good yields of 84 %, 88 %, and 82 %, respectively (3n-3p). The introduction of a strong electron-absorbing nitro- group showed yields of 81 % and 52 % (3 j, 3k). Surprisingly, a single aliphatic alkyl group, methyl, showed an excellent yield of 92 % (3 m).

Alternatively, we investigated the reaction using 1,3-ynone with electron-donating and electron-withdrawing groups at the alkyne side and 1,2-diaminobenzene under optimized conditions (Table 3). There was no significant impact on the reaction, with excellent yields of 91 %–98 % (3q-3 s). The aliphatic derivative of 1,3-ynone gave a yield of 57 % (3 t). Then, the impact on the reaction due to changes in the 1,2-diaminobenzene derivatives was investigated. When methyl derivatives were used, no significant impact on the reaction was observed, with a yield of 96 %–98 % (3u-3 w); when 4,5-dibromobenzene-1,2-diamine was used, a yield of 96 % was obtained (3x), but no reaction occurred when 4-nitro-*o*-phenylenediamine was used as the diaminobenzene derivative.



Scheme 2. Proposed mechanism for the synthesis of diazepine derivatives by the mixed ligand catalytic system of titanocene.

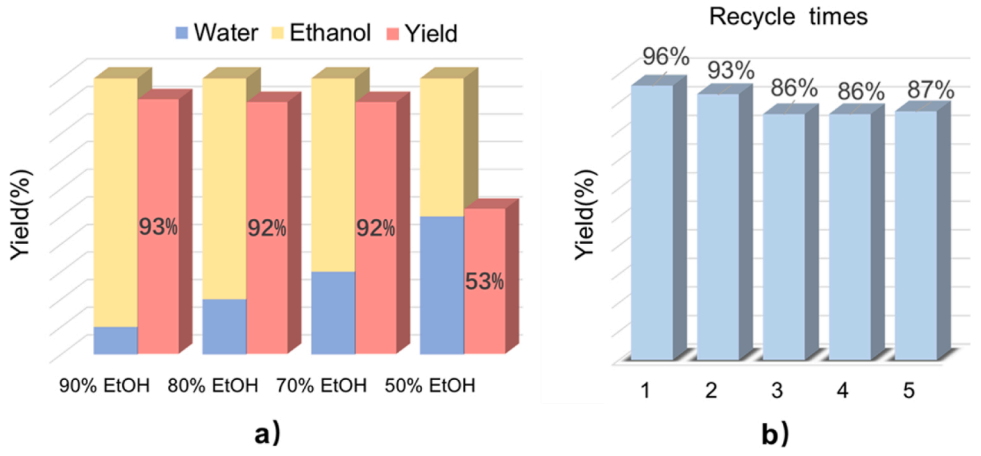


Fig. 4. Recycling efficiency and water tolerance study of the $CpTi(OMe)_2(\eta^1\text{-}C_8H_5O_4)$ catalyst.

3. Conclusions

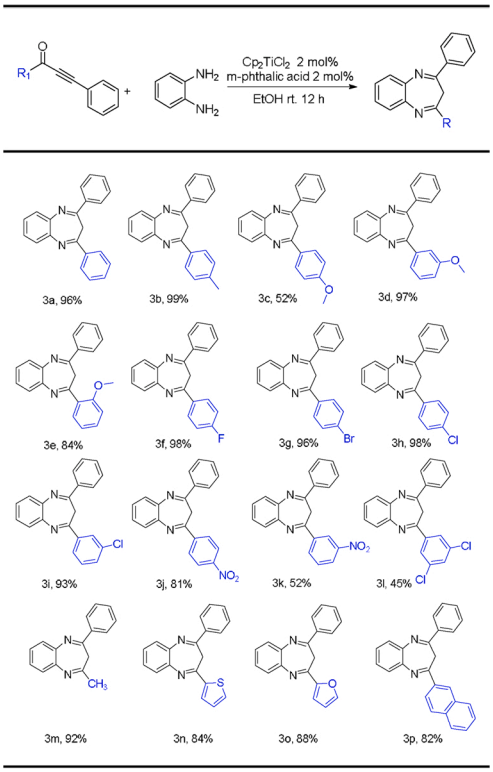
In summary, a novel ligand activation strategy for titanocene species was developed through the activation of inert Cp_2TiCl_2 by ethanol and *m*-phthalic acid at the same time for the efficient synthesis of 2,4-disubstituted-3H- benzo[*b*]-[1,4]diazepine derivatives. The catalytic ability of Cp_2TiCl_2 was more intensively improved, especially towards many two Cp ligand containing titanocene catalysts, as only 2 mol% of Cp_2TiCl_2 was needed for catalysis. Mechanistic studies including ^1H NMR and MS analysis indicate the novel formation of catalytic titanocene species $[CpTi(OEt)_2(\eta^1\text{-}C_8H_5O_4)]$. These results illuminate a new catalytic system, which allows for an efficient, mild, water-insensitive, sustainable and environmentally friendly protocol for the synthesis of 2,4-disubstituted-3H- benzo[*b*]-[1,4]diazepine derivatives.

4. Experimental section

4.1. General procedure for recycling tests

A reactor equipped with a magnetic stirring bar was charged with 1,3-ynone (103 mg, 0.5 mmol), *o*-phenylenediamine (64.8 mg, 0.6 mmol), Cp_2TiCl_2 (2.48 mg, 0.01 mmol), *m*-phthalic acid (1.66 mg, 0.01 mmol) and EtOH (0.5 mL). Then, the reaction system reacts with magnetic stirring at room temperature. After 12 h, the reaction was transferred to ice water to cool down; the precipitate, which is the expected product, was then filtered and washed twice with ice EtOH (2 mL). The filtrate was then concentrated to 0.5 ml under vacuum and used for a new catalytic run: 1,3-ynone (0.5 mmol), *o*-phenylenediamine (0.6 mmol) were introduced. The tube was stirred for the required time period.

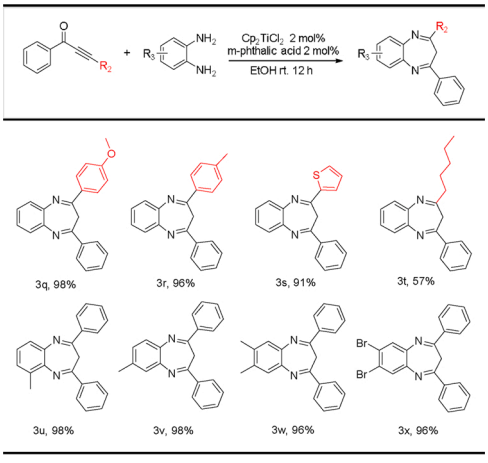
Table 2
New titanocene complex accelerated cyclization of 1,3-ynone and *o*-phenylenediamine.



[a] reaction conditions: 0.5 mmol of 1,3-ynone, 0.6 mmol of *o*-phenylenediamine in the presence of 2 mol% titanocene dichloride, 2 mol% of *m*-phthalic acid and 0.5 mL EtOH at room temperature for 12 h. [b] Isolated yields were obtained after purification by column chromatography.

[a] reaction conditions: 0.5 mmol of 1,3-ynone, 0.6 mmol of *o*-phenylenediamine in the presence of 2 mol% titanocene dichloride, 2 mol% of *m*-phthalic acid and 0.5 ml EtOH at room temperature for 12 h. [b] Isolated yields were obtained after purification by column chromatography.

Table 3
New titanocene complex accelerated cyclization of 1,3-ynone and *o*-phenylenediamine.



[a] reaction conditions: 0.5 mmol of 1,3-ynone, 0.6 mmol of *o*-phenylenediamine in the presence of 2 mol% titanocene dichloride, 2 mol% of *m*-phthalic acid and 0.5 mL EtOH at room temperature for 12 h. [b] Isolated yields were obtained after purification by column chromatography.

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CRediT authorship contribution statement

Mingming Yang: Data curation, Investigation, Writing - original draft. **Yanyan Wang:** Conceptualization, Visualization. **Yajun Jian:** Conceptualization, Writing - review & editing. **Deying Leng:** Investigation, Validation. **Weiqiang Zhang:** Visualization. **Guofang Zhang:** Supervision. **Huaming Sun:** Software. **Ziwei Gao:** Funding acquisition, Project administration, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.mcat.2020.111247.

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