Tetrahedron 74 (2018) 4211–4219

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Cationic-lanthanide-complex-catalyzed reaction of 2-hydroxychalcones with naphthols: Facile synthesis of 2,8-dioxabicyclo[3.3.1]nonanes

Yanan Zhu, Zhigang Yao, Fan Xu*

Key Laboratory of Organic Synthesis, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, PR China

ARTICLE INFO

Article history:
Received 30 April 2018
Received in revised form
11 June 2018
Accepted 15 June 2018
Available online 20 June 2018

Keywords:
Lanthanide
Cationic complex
2,8-Dioxabicyclo[3.3.1]nonane
Catalysis

ABSTRACT

Cationic lanthanide complexes $[Ln(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot CH_3CN$ served as efficient catalysts for the tandem Friedel–Crafts alkylation/ketalization reaction of 2-hydroxychalcones with naphthols/substituted phenols to produce diaryl-fused 2,8-dioxabicyclo[3.3.1]nonanes in moderate to high yields. The high catalytic efficiency of the cationic lanthanide complex $[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot CH_3CN$ compared with that of $YbCl_3$ can be attributed to the increased Lewis acidity of the Yb species as a result of cation formation.

1. Introduction

The 2,8-dioxabicyclo[3.3.1]nonane skeleton is an important structural unit in a series of molecules of pharmaceutical or biological interest [1]. Its derivatives are known to have a broad spectrum of biological activities such as antiviral, anti-inflammatory, anticancer, antioxidant, and antiplatelet aggregation activities. The development of efficient methods for the synthesis of 2,8-dioxabicyclo[3.3.1]nonane and its derivatives, e.g., the common diaryl-fused 2,8-dioxabicyclo[3.3.1]nonanes, has therefore received considerable attention in recent years. There are two routes that are generally used for the synthesis of diaryl-fused 2,8-dioxabicyclo[3.3.1]nonanes. One is condensation of a substituted phenol/naphthol with appropriate flavylium [2] or carbonyl reagents [3], e.g., β-ketoaldehydes and mixtures of β-ketoesters and salicylaldehyde. The other [4] involves treatment of 2-hydroxychalcones or 2-benzyloxychalcones with phenol derivatives such as (2-benzyloxyphenyl)magnesium bromide or 2-hydroxyphenylboronic acid. However, the most straightforward method for the synthesis of diaryl-fused 2,8-dioxabicyclo[3.3.1]nonanes, namely direct condensation of a 2-hydroxychalcone with a substituted phenol/naphthol, was not reported until 2013. Yin [5] used a catalytic amount of silver triflate in the reactions of 2-hydroxychalcones with naphthols/substituted phenols in refluxing toluene to generate diaryl-fused 2,8-dioxabicyclo[3.3.1]nonanes. Yao and Zhang [6] evaluated 10-camphorsulfonic acid as the catalyst for similar reactions. Ganguly [7] used $CeCl_3$/NaI-catalyzed regioselective coupling of 2-hydroxychalcones with resorcinols or phloroglucinols to synthesize dibenzo-2,8-dioxabicyclo[3.3.1]nonanes. Lee [8] developed a catalyst-controlled regio- and stereoselective method for synthesizing various dibenzo-2,8-dioxabicyclo[3.3.1]nonanes via ethylenediammonium diacetate- or *p*-toluenesulfonic acid-catalyzed reactions between a number of 2-hydroxychalcones and resorcinols with ester and ketone substituents. Despite these successes in research on the synthesis of 2,8-dioxabicyclo[3.3.1]nonanes, there is still a need to improve the synthetic efficiency. The development of novel catalysts and highly efficient methods for the synthesis of 2,8-dioxabicyclo[3.3.1]nonanes is still needed to meet the growing demand for this type of biologically active molecule.

Cationic metal complexes, which are more electropositive than their neutral precursors, generally have high Lewis acidity. The use of cationic metal complexes as catalysts can therefore increase the reaction activity. Lanthanide complexes are typical Lewis acids and cationic lanthanide complexes are well-known catalysts for olefin polymerization and copolymerization [9]. However, examples of

* Corresponding author.
E-mail address: xufan@suda.edu.cn (F. Xu).

https://doi.org/10.1016/j.tet.2018.06.038
0040-4020/

the catalysis of organic transformations with cationic lanthanide complexes are limited [10]. In our previous study [11], cationic lanthanide complexes $[Ln(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot CH_3CN$, which are readily prepared by reacting anhydrous lanthanide trichlorides ($LnCl_3$) with anhydrous $AlCl_3$ in CH_3CN [12], were found to be efficient catalysts for the intramolecular hydroalkoxylation of unactivated alkenols. As part of our study of the construction of C–O bonds catalyzed by cationic lanthanide complexes, the reactions of 2-hydroxychalcones with naphthols/substituted phenols were examined and a series of diaryl-fused 2,8-dioxabicyclo[3.3.1] nonanes were obtained. The results are presented in this paper.

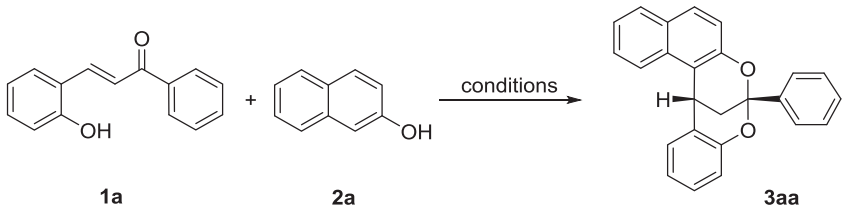
2. Results and discussion

First, as a model reaction, 2-hydroxychalcone (**1a**) and β-naphthol (**2a**) were stirred in refluxing chlorobenzene for 24 h in the presence of 7 mol% of $[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot CH_3CN$. The expected product, 1-phenyl-diaryl-fused 2,8-dioxabicyclo[3.3.1]nonane (**3aa**), was obtained in 84% yield. The reaction conditions, namely the solvent, catalyst loading, ratio of substrates, and time, were then investigated. The results are summarized in Table 1. Halogen-containing solvents gave relatively good results (Table 1, entries 1 and 2), as can be seen by taking the results for chlorobenzene and toluene (Table 1, entry 4) as examples. Chlorobenzene was the best solvent among those screened. Decreasing the catalyst loading from 7 mol% to 1 mol% led to a decrease in yield from 84% to 44% (Table 1, entries 1 and 8–10). However, increasing the amount of β-naphthol and prolonging the reaction time both resulted in increased yields (Table 1, entries 9 and 11–14). A 90% yield was obtained under the optimum reaction conditions, namely **1a**:**2a** = 1:1.2 in the presence of 3 mol% of $[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot CH_3CN$ in chlorobenzene under reflux for 72 h.

Bronsted acids including HCl and TsOH were tried as catalysts under the optimum conditions and the desired product was obtained in rather low yields (Table 1, entries 15 and 16). Several cationic lanthanide complexes were tested to investigate the effect of the central metal on the catalytic activity. The results show that the decrease in the Ln(III) ionic radius from the light rare-earth La to the heavy rare-earth Yb affected the reaction, and the yield of **3aa** showed an upward trend (Table 1, entries 14 and 17–20). The cationic complex of Yb, the smallest metal among those tested, was chosen for subsequent studies.

Control experiments were performed to identify the true catalytic species in this process. The results are listed in Table 2. The cationic lanthanide complex $[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot CH_3CN$ was synthesized by reacting $YbCl_3$ and $AlCl_3$ in CH_3CN, therefore $YbCl_3$ and $AlCl_3$ were used alone to determine whether they can act independently as catalysts under the same reaction conditions as were used with the cationic Yb/Al complex. Yields of 43% and 34% were obtained with $YbCl_3$ and $AlCl_3$, respectively (Table 2, entries 1 and 2). The model reaction with 3 mol% $YbCl_3$ and meanwhile 9 mol % $AlCl_3$ as catalyst in the same batch was conducted and a yield of 67% was observed (Table 2, entry 3). These results indicate that the catalytic activity of the cationic Yb/Al complex does not arise from a combination of the activities of the individual $YbCl_3$ and $AlCl_3$

Table 1
Condition screening for reaction of **1a** with **2a**.[a]



1a **2a** **3aa**

Entry	Catalyst (Loading/mol%)	Solvent	Yield[b]/%
1	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (7)	PhCl	84
2	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (7)	DCE	74
3	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (7)	CH_3CN	71
4	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (7)	toluene	63
5	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (7)	CH_3NO_2	37
6	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (7)	EtOH	33
7	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (7)	THF	12
8	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (5)	PhCl	82
9	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	65
10	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (1)	PhCl	44
11[c]	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	72
12[d]	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	80
13[d,e]	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	88
14[d,f]	$[Yb(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	90
15[d,f]	HCl (3)	PhCl	19
16[d,f]	TsOH (3)	PhCl	28
17[d,f]	$[La(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	71
18[d,f]	$[Nd(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	75
19[d,f]	$[Sm(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	67
20[d,f]	$[Gd(CH_3CN)_9]^{3+}[(AlCl_4)_3]^{3-}\cdot(CH_3CN)$ (3)	PhCl	84

[a] Reactions were performed by reacting 2-hydroxychalcone (0.5 mmol) with β-naphthol (0.5 mmol) in solvent (4 mL) under reflux for 24 h. Catalyst loading is relative to 2-hydroxychalcone.
[b] Determined through LC analysis using acetophenone as internal standard.
[c] 0.55 mmol β-naphthol was used.
[d] 0.6 mmol β-naphthol was used.
[e] 48 h.
[f] 72 h.