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## COMMUNICATION

## HOTf mediated cascade reactions of 1-arenoylcyclopropanecarboxylic acids with arenes<sup>†</sup>

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The cascade reactions of 1-arenoylcyclopropanecarboxylic acids with arenes proceed smoothly in freshly distilled HOTf to give the corresponding tetrahydro-5*H*-benzo[*c*]fluorene derivatives in good yields along with high stereoselectivities under mild conditions.

It has been well known that transition metal or Lewis acid (or Brønsted acid) catalyzed/mediated ring-opening reaction of cyclopropane is a powerful synthetic approach for the rapid construction of molecular complexity in organic synthesis.<sup>1</sup> A number of pharmaceutically interesting substances and biologically active natural products have been synthesized by this synthetic approach.<sup>2</sup> In this communication, we wish to present an interesting trifluoromethanesulfonic acid CF<sub>3</sub>SO<sub>3</sub>H (HOTf) mediated cascade reaction of 1-arenoylcyclopropanecarboxylic acid with arenes in the rapid generation of tetrahydro-5*H*-benzo[*c*]fluorene derivatives in good yields along with high stereoselectivities under mild conditions.

We initiated our investigations by seeking the optimal conditions for the cascade reaction of 1-benzoylcyclopropanecarboxylic acid **1a** with benzene. After screening of Lewis acids such as BF<sub>3</sub>·OEt<sub>2</sub> and Sc(OTf)<sub>3</sub> as well as freshly distilled Brønsted acids such as HOTf and trifluoroacetic acid (TFA), we found that **1a** could react with benzene smoothly in HOTf at 60 °C to give a novel tetrahydro-5*H*-benzo[*c*]fluorene derivative, (*6aS*,11*bR*)-11*b*-phenyl-6,6*a*-dihydro-5*H*-benzo[*c*]fluoren-7(11*bH*)-one **2a**, as a single diastereoisomer in 84% yield within 0.5 h (Table 1, entry 4) and other catalysts are totally ineffective in this reaction (entries 1–3 and 5).<sup>3</sup> The structure of **2a** has been unambiguously determined by X-ray diffraction and its ORTEP drawing and the CIF data have been presented in the ESI.<sup>‡4</sup>

With these optimal reaction conditions in hand, we subsequently turned our attention to examine the substrate scope of this interesting cascade reaction with respect to a variety of 1-arenoylcyclopropanecarboxylic acids **1** with benzene. The results are summarized in Table 2. As can be seen from Table 2, all

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Table 1 Optimization of the reaction conditions

benzene, 60 °C Lewis acid or Bronsted acid  $Yield^{d}$  (%) Lewis acids or Brønsted acids Time/h Solvent 2a Entrv  $1^a$ 12 BF3·OEt2  $2^{b}$  $3^{b}$ Sc(OTf)<sub>3</sub> 12 DCE 12 DCE Complex HOTf  $4^c$ HOTf 0.5 84

The reaction was performed in a 25 mL flame and vacuum dried Schlenk tube. <sup>*a*</sup> 0.3 mmol of **1a**, 0.2 mL of benzene and 0.8 mL of BF<sub>3</sub>·OEt<sub>2</sub>. <sup>*b*</sup> 0.3 mmol of **1a**, 0.2 mL of benzene and 0.3 mmol of Sc(OTf)<sub>3</sub> or HOTf, 0.8 mL DCE. <sup>*c*</sup> 0.3 mmol of **1a**, 0.2 mL of benzene and 0.8 mL of HOTf (entry 4) or TFA (entry 5). <sup>*d*</sup> Isolated yields.

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 Table 2
 HOTf mediated cascade reactions of substrates 1 and benzene

$R \xrightarrow{0}_{I} OH \xrightarrow{benzene}_{HOTF, 60 °C} OH \xrightarrow{R}_{OH} OH \xrightarrow{Ph}_{OH} OH \xrightarrow$				
			Yield <sup><math>b</math></sup> (%)	
Entry <sup>a</sup>	R	$t/\mathbf{h}$	2	3
1	<i>p</i> -Br, <b>1b</b>	1.0	<b>2b</b> , 83	
2	<i>p</i> -CH <sub>3</sub> , 1c	0.5	<b>2c</b> , 72	
3	<i>p</i> -Cl, 1d	1.0	2d, 92	
4	<i>p</i> -F, 1e	2.0	<b>2e</b> , 88	
5	<i>m</i> -Cl, 1f	2.0	_	<b>3f</b> , 67
6	m Dr. 1a	2.0		20 72

<sup>*a*</sup> Reaction conditions: 0.3 mmol of **1**, 0.2 mL of benzene and 0.8 mL of HOTf. <sup>*b*</sup> Isolated yields.

the reactions proceeded smoothly to give the corresponding tetrahydro-5*H*-benzo[*c*]fluorene derivatives **2b–2e** and **3f** and **3g** as a single diastereoisomer in good to high yields for the substrates **1b–1g** bearing different substituents at the benzene ring (Table 2, entries 1–6).

Moreover, using *p*-xylene as the nucleophile instead of benzene, we found that the reactions also proceeded efficiently

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<sup>†</sup> Electronic supplementary information (ESI) available: Experimental procedures and characterization data of new compounds. CCDC 834559, 837266, 844935, 848746, 855051. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc17581a

Table 3 HOTf mediated cascade reactions of substrates 1 and p-xylene

p-xylene HOTf. r.t. Yield<sup>b</sup> (%) 4 5 Entry R t/h H, 1a 1 0.5 4a, 80 2 *p*-Br, 1b 1.5 4b, 68 3 p-CH<sub>3</sub>, 1c 1.0 4c, 94 4 p-Cl, 1d 1.0 4d. 69 5 p-F, 1e 2.04e, 74 5f. 67 6 *m*-Cl. 1f 2.07 *m*-Br, 1g 2.0 5g, 67

<sup>*a*</sup> Reaction conditions: 0.3 mmol of **1**, 0.2 mL of *p*-xylene and 0.8 mL of HOTf. <sup>*b*</sup> Isolated yields.

to produce the corresponding tetrahydro-5*H*-benzo[*c*]fluorene derivatives **4a–4e** and **5f** and **5g** in good to high yields as a single diastereoisomer at room temperature (25 °C) under the standard conditions (Table 3, entries 1–7). When the aromatic group in **1** was replaced by a heteroaromatic moiety, complex product mixtures were formed under the standard conditions (for some other unsuccessful examples, please see Table SI in the ESI†).

Their structures have been determined by spectroscopic data, Mass and HR-Mass. Furthermore, the structures of **2c**, **3g**, and **4a** have been further confirmed by X-ray diffraction. Their ORTEP drawings and CIF data are presented in the ESI.<sup>†5</sup>

A combined plausible reaction mechanism is shown in Scheme 1 using **1a** as a model. **1a** first produces compound **8** through an intramolecular Friedel–Crafts reaction mediated by HOTf *via* intermediate **A**. The reaction of **8** with an arene gives ring-opened intermediate **B**, which undergoes intramolecular cyclization in the presence of HOTf to afford intermediate **C**. Deprotonation of intermediate **C** produces intermediate **D** 



Scheme 1 A proposed reaction mechanism for the formation of 2a and 4a.

and dehydration of intermediate **D** affords intermediate **E** or **F**. The Friedel–Crafts reaction of intermediate **E** with benzene gives product **2a** and the hydride transfer between intermediate **F** and *p*-xylene produces product **4a**, respectively (Scheme 1). The different reaction pathways in the formation of **2a** and **4a** are presumably due to the different steric hindrance of benzene and *p*-xylene. On the other hand, using *o*-xylene to replace *p*-xylene in the above cascade reaction, the corresponding product **6** was obtained as a regioisomeric mixture in 65% yield, further suggesting that the steric effect of xylene is crucial in the reaction outcome (Scheme 2).

To verify the key reaction intermediate, two control experiments have been carried out under the standard conditions. We found that the authentically prepared compound  $7^6$  gave **2a** in 90% yield and another possible intermediate **8** afforded complex product mixtures, suggesting that 7 might be the key intermediate in the above cascade reaction (Scheme 3).

Another significant verification of the mechanism is that when the cascade reaction of **1b** was carried out in HOTf containing a trace of water, the reaction product was rather complex, but **9**, derived from intermediate **F**, can be obtained in 31% yield after recrystallization from DCM and PE (1:1). Its structure has been further determined by X-ray diffraction (Scheme 4).<sup>7</sup>

The hydride transfer between intermediate **F** and *p*-xylene<sup>8</sup> can be verified by the formation of the by-product **G** during the reaction of **1** with *p*-xylene under the standard conditions. Obviously, compound **G** was derived from the intermolecular Friedel–Crafts reaction of *p*-xylene with the generated cationic intermediate, which has been identified by <sup>1</sup>H NMR spectroscopic data and mass spectrum (Scheme 5, also see ESI†). On the other hand, it should be also noted that complex product mixtures derived from the further intermolecular Friedel–Crafts reaction of compound **G** with the generated cationic intermediate



Scheme 2 Reaction of 1a with o-xylene.



Scheme 3 Control experiments.





Scheme 5 Intermolecular Friedel–Crafts reaction of *p*-xylene.

could be formed in the above cascade reaction as well, giving rather complex product mixtures (Scheme 5).

In summary, we have developed a novel and highly stereoselective cascade reaction of 1-arenoylcyclopropanecarboxylic acids with arenes mediated by freshly distilled HOTf, affording the corresponding tetrahydro-5*H*-benzo[*c*]fluorene derivatives in good yields under mild conditions. A plausible reaction mechanism has been also proposed on the basis of control experiments.

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