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2,2,6,6-Tetramethylpiperidinium triflate (TMPT): a highly selective and self-separated catalyst for esterification

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ABSTRACT

An eco-friendly and readily accessible 2,2,6,6-tetramethylpiperidinium triflate was found as highly-selective and self-separated catalyst for esterification under solvent-free condition. The X-ray crystallography revealed that it formed a 'hydrophobic wall' which could effectively eliminate the generated water from the reactive sites. Moreover, it could precipitate from the reaction system with excellent recovery ratio (>99%) and be reused for ten times without any significant loss of activity.

Introduction

Esters are important products and intermediates in material science and chemical industries, they play a main role in organic synthesis.[1–4] Generally, esters are produced by acid-catalyzed dehydration reaction of carboxylic acids and alcohols in the presence of stoichiometric dehydrating reagents.[5] Traditional acidic catalysts such as H_2SO_4, HCl, etc. are usually adopted, but they are quite contaminative and corrosive, which always result in poor selectivity, high energy-consuming, and seriously environmental pollution.[6–9] Besides, separation of the dehydrating agents and catalysts from crude products requires considerable time and energy. Therefore, 'green' synthetic approaches for esters have attracted much attention, nevertheless wide varieties of achievements have been exploited in recent years, the development of environmentally benign and cost-effective method is still highly requested.[5,10–19]

Non-metallic organocatalysts with simple structure and low molecular weight are promising alternatives in organic synthesis, because they possess non-toxic, high-efficiency, and eco-friendly features.[20,21] In 2000, Tanabe et al.[22] developed the *N*,*N*-diphenylammonium triflate (DPAT) as an esterification catalyst. This metal-free organocatalyst displayed superior catalytic capability without the use of any dehydration system, but the selectivity of acid-sensitive alcohols is still poor because it is a strongly acidic salt.[23] Afterward, Ishihara et al.[23–26] reported the bulky *N*,*N*-diarylammonium pentafluorobenzenesulfonates ($[Ar_2NH_2]^+[O_3SC_6F_5]^-$) which have a weaker acidity and show higher selectivity and activity in esterification. However, the costly raw materials and complicated synthetic procedures limited their application.

Based on these researches, we discovered the readily accessible 2,2,6,6-tetramethylpiperidinium triflate (TMPT), which showed excellent selectivity and induced a spontaneous self-separation process in esterification (Scheme 1). In our research, we designed a series of piperidinium sulfonates to investigate the effects of acidity and steric group on catalytic activity. Furthermore, we examined the selectivity and catalyst reusability. Herein, we report the results catalyzed by alkyl piperidinium sulfonates under solvent-free condition.

Results and discussion

The alkyl piperidinium sulfonates (**1a–c** and **2a–c**) were prepared from a strongly basic alkyl piperidine and a strongly acidic sulfoacid, the combination made them have a weaker acidity (Scheme 2). Firstly, to investigate their catalytic activities, the esterification of phenylacetic acid with an equimolar amount of *n*-hexanol was performed in the presence of 5 mol % catalysts

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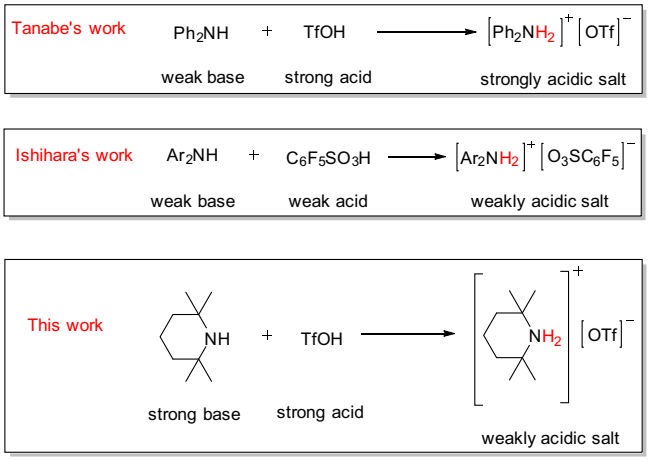


Scheme 1. Strategy to prepare a practical and selective catalyst based on Tanabe's and Ishihara's catalysts.

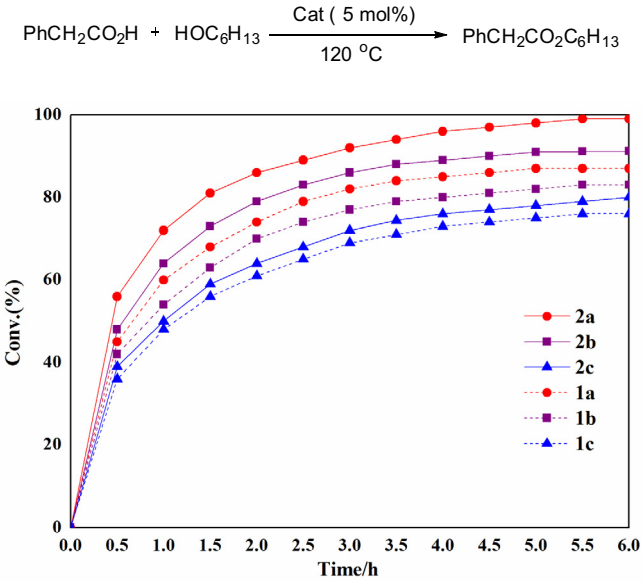
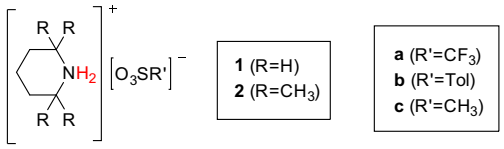


Figure 1. Conversion of phenylacetic acid over the reaction time was evaluated by GC analysis.

under solvent-free condition. The conversion of phenylacetic acid over the reaction time was evaluated by GC analysis. It was shown that despite the esterifications were conducted without the removal of water, they proceeded smoothly within a short time (Fig. 1). **1a–c** gained conversions of 83%, 80%, and 76% in 6 h, while **2a–c** appeared more active, they obtained 99%, 91%, and 87% conversions, respectively. By comparison, we found that the sulfoacid acidity considerably affected the catalytic activity. Generally, CF_3SO_3H > TsOH > CH_3SO_3H in terms of acid strength, and the catalytic activities were in accordance with the sequence, i.e., triflates > tosylates > mesylates. Additionally, the experimental data also revealed that the bulky 2,2,6,6-tetramethylpiperidinium sulfonates (**2a–c**) were superior to piperidinium sulfonates (**1a–c**). Take piperidinium triflate (PPT, **1a**) and 2,2,6,6-tetramethylpiperidinium triflate (TMPT, **2a**) for comparison, the latter was 16% higher in conversion, however, the former was more acidic because 2,2,6,6-tetramethylpiperidine (pK_a (protonated 2,2,6,6-tetramethylpiperidine) = 11.25) is more basic than piperidine (pK_a (protonated piperidine) = 11.05).[27,28] It seemed that the bulky methyl groups around NH_2^+ in TMPT made greater contribution than the acidity to promote the reaction.

To verify our hypothesis, the X-ray crystallographic analysis of PPT and TMPT were carried out. It was illustrated that TMPT formed a dimeric compound consisted of two triflate anions and two 2,2,6,6-tetramethylpiperidinium cations.[29] The two ammonium cations were linked by four intermolecular N—H···O hydrogen bonds, which made the dimeric cyclic ion pairs a ring-shaped structure (Fig. 2a and b).[30,31] On account of the bulky groups around the reactive site, TMPT formed a hypothetical 'hydrophobic wall'[25] which could effectively prevent the generated water from approaching to the reactive sites and thus inhibiting the inactivation of the catalyst by water (Fig. 2c). While PPT could not form similar structure, and the catalytic activity was not as good as TMPT (Fig. 3).[32] Hence, we deduced that the hydrophobic effect deriving from the steric hindrance was of great importance



Scheme 2. Simple alkyl piperidinium sulfonates of **1a–c** and **2a–c**.

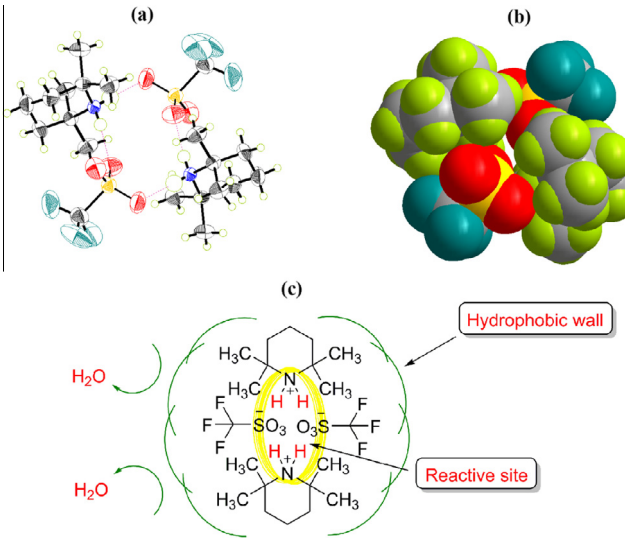


Figure 2. X-ray crystallography structure of TMPT (**2a**): N = blue, O = red, F = green, S = yellow; (a) ORTEP diagram (drawn at 50% probability); (b) space-filling diagram; (c) schematic diagram of the 'hydrophobic wall' (green) and reactive site (yellow).

for the high catalytic activity. Apparently, among all the catalysts, TMPT showed the best performance.

The difficulty of recycling is usually the main drawback in the use of homogeneous catalysts. To our surprise, an obvious phase transformation occurred in **1a–c** and **2a–c** after the esterifications (Fig. 4). Initially, they were completely dissolved in the reaction system, forming a homogeneous solution (Fig. 4b). However, they were spontaneously precipitated from the reaction medium to form a liquid–solid biphase at the end of the reaction (Fig. 4d). The unique phenomenon might attribute to their excellent solubility in polar alcohols and very poor dissolubility in apolar esters. We recovered **1a–c** and **2a–c** from the reaction system and found that **2a** (TMPT) had the highest recovery ratio (99%), the excellent result might owe to its high reaction conversion (99%) and hydrophobic environment. Different from the traditional soluble catalysts, such