J|A|C|S
COMMUNICATIONS

Bulky Diarylammonium Arenesulfonates as Selective Esterification Catalysts

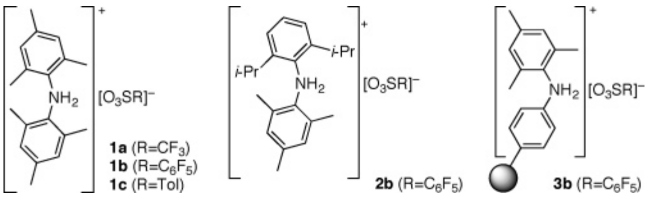
Kazuaki Ishihara,* Shoko Nakagawa, and Akira Sakakura

Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa, Nagoya 464-8603, Japan

Received January 13, 2005; E-mail: ishihara@cc.nagoya-u.ac.jp

A great deal of research focuses on more environmentally benign alternatives to ester condensation processes, which are in great demand by the chemical industry.[1−4] In 2000, Tanabe et al. reported that diphenylammonium triflate ($[Ph_2NH_2]^+[OTf]^-$, 1−10 mol %) efficiently catalyzed the ester condensation reaction of carboxylic acids with equimolar amounts of alcohols.[5] Although $[Ph_2NH_2]^+[OTf]^-$ can be used without removing water, its acidity is still strong. Therefore, it is difficult to adapt Tanabe's method to sterically demanding and acid-sensitive alcohols. Herein, we describe bulky diarylammonium pentafluorobenzenesulfonates **1b**−**3b** and tosylate **1c**, which are much milder acids than the corresponding ammonium triflates, that can be adapted to a variety of sterically demanding alcohols and acid-sensitive alcohols (Chart 1). In particular, bulky catalysts, such as **1b** and **2b**, are extremely active catalysts that form the corresponding esters from an equimolar mixture of carboxylic acids and primary alcohols even at room temperature without removing water.

Chart 1. Bulky Diarylammonium Arenesulfonates



The ester condensation of 4-phenylbutyric acid (**4**) with an equimolar amount of cyclododecanol (**5**) was examined in the presence of 5 mol % of bulky arylammonium perfluoroalkanesulfonates in heptane under reflux conditions (bath temp of 115 °C) (Figure 1). Cyclododecyl 4-phenylbutyrate (**6**) and the undesired cyclododecene (**7**) were produced in the presence of $[Ph_2NH_2]^+[OTf]^-$ (graph A). When a more bulky dimesitylammonium triflate (**1a**) was used, the esterification rates increased, but the dehydration rates from **5** to **7** decreased (graph B). Next, when dimesitylammonium pentafluorobenzenesulfonate (**1b**) was used instead of **1a**, the yield of the ester increased to more than 90% and the yield of **7** was suppressed to less than 10% (graph C). Finally, when the ester condensation was conducted at 80 °C in the presence of **1b**, the conversion to the ester after 23 h was 97% yield without producing a detectable amount of **7** (graph D).

The ester condensation reaction of **4** with 6-undecanol (**8**) was compared between the reflux conditions without removing water and the azeotropic reflux conditions while removing water (Figure 2). The reaction catalyzed by $[Ph_2NH_2]^+[OTf]^-$ was slightly decelerated under reflux conditions without removing the water produced (graph E). In contrast, the reaction catalyzed by more bulky catalyst **2b** proceeded very well without the influence of water (graph F).

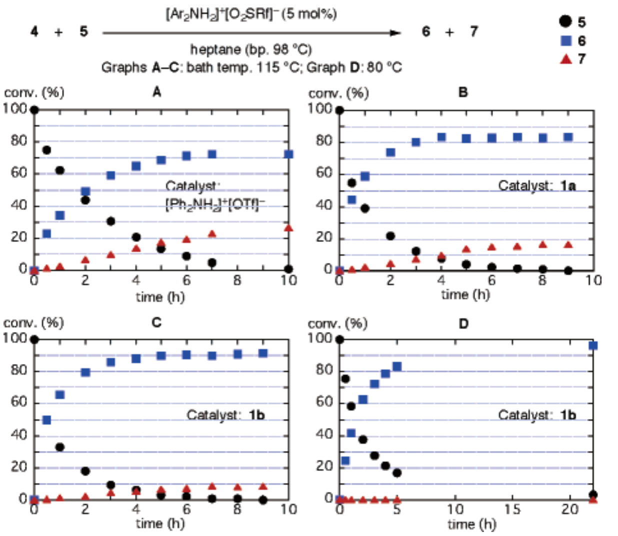


Figure 1. Ratio of **5**, **6**, and **7** in the reaction mixture of **4** (2 mmol) and **5** (2 mmol) in heptane (4 mL) over time was evaluated by ^1H NMR analysis.

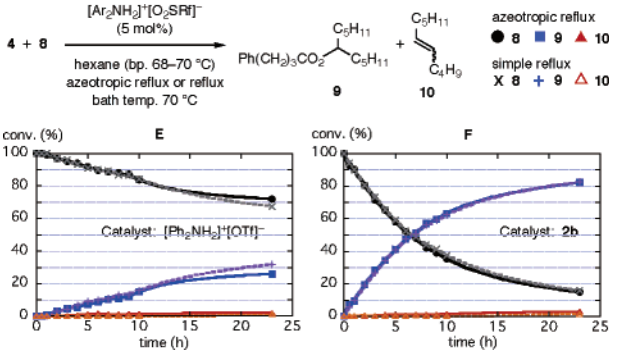
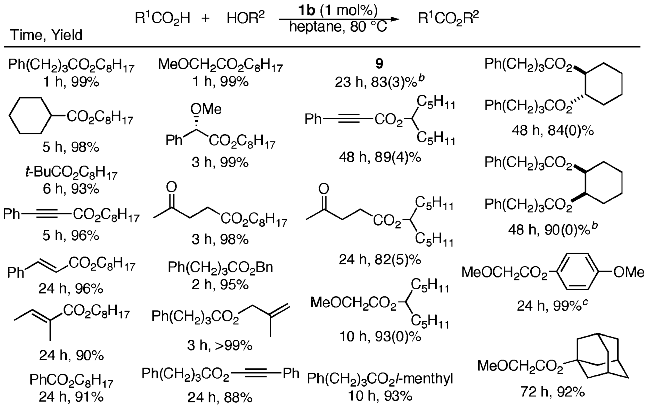


Figure 2. Catalytic activities of $[Ph_2NH_2]^+[OTf]^-$ and **2b** under reflux conditions without removing water (solid lines) and azeotropic reflux conditions (broken lines) were compared. Ratio of **8**, **9**, and **10** in the reaction mixture of **4** (2 mmol) and **8** (2 mmol) in hexane (4 mL) over time was evaluated by ^1H NMR analysis.

TfOH is a superacid (pK_a (CD_3CO_2D) = −0.74, $H_0 = -14.00$) that is stronger than concentrated H_2SO_4 (pK_a (CD_3CO_2D) = 7.5, $H_0 = -11.93$).[6,7] In contrast, $C_6F_5SO_3H$ (pK_a (CD_3CO_2D) = 11.1, $H_0 = -3.98$) is a weaker acid than TsOH (pK_a (CD_3CO_2D) = 8.5).[6,7] On the basis of this result,[6] the catalytic activities of dimesitylammonium tosylate (**1c**) and $[Ph_2NH_2]^+[OTs]^-$ for the ester condensation of **4** with **8** were compared with those of **1b** and Ph_2NH_2OTf, respectively, under the same conditions. Surprisingly, **1c** and **1b** exhibited similar catalytic activities, and $[Ph_2NH_2]^+[OTs]^-$ was better than $[Ph_2NH_2]^+[OTf]^-$. These experimental results suggested that the hydrophobic effect of bulky *N*-aryl and *S*-aryl groups, which surrounded NH_2^+ of diarylammonium arenesulfonates, might be more important than the strong acidity of NH_2^+ in promoting the dehydrative condensation reaction.[8] Bulky diarylammonium arenesulfonates were effective for the selective esterification of secondary alcohols because they

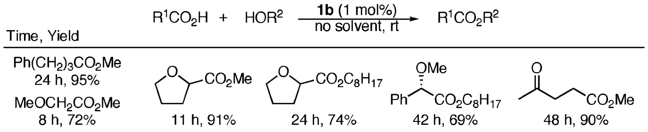
10.1021/ja050223v CCC: $30.25

Table 1. Esterification Reaction between an Equimolar Mixture of Carboxylic Acids and Alcohols Catalyzed by **1b**[a]



[a] Unless otherwise noted, a solution of carboxylic acids (2 mmol) and alcohols (2 mmol) in heptane (4 mL) was heated at 80 °C in the presence of **1b** (1 mol %). Yield of alkenes is shown in parentheses. [b] **1b** (5 mol %) was used. [c] **1b** (10 mol %) was used at 115 °C.

Table 2. Esterification Reaction without Solvents and Heating[a]



[a] A mixture of carboxylic acids (2 mmol) and alcohols (2.2 mmol) was stirred at room temperature in the presence of **1b** (1 mol %).

preferentially activated less-hindered carboxylic acids rather than secondary alcohols.

To explore the generality and scope of the selective esterification catalyzed by **1b** (1 mol %) at 80 °C, the condensation was examined with an equimolar mixture of various structurally diverse carboxylic acids and alcohols (Table 1). 2-Unsubstituted carboxylic acids, 2-monosubstituted carboxylic acids, and sterically demanding 2,2-disubstituted carboxylic acids were smoothly condensed to produce the corresponding esters. α,β-Unsaturated carboxylic acids and benzoic acids were also transformed into the corresponding esters. 2-Alkoxycarboxylic acids and 2-unsubstituted carboxylic acids were very reactive substrates, probably due to the favorable chelation between the substrates and **1b**. 4-Oxopentanoic acid was selectively esterified without a protecting ketone moiety. **1b** was adaptable for acid-sensitive alcohols, such as benzyl alcohol, allylic alcohols, propargylic alcohols, and secondary alcohols. In particular, it is noteworthy that the esterification with sterically demanding alcohol **8** proceeded to give the desired esters in good yield with less than 5% of alkenes. Although Lewis acidic metal salts such as Hf(IV) and Zr(IV) were not adapted to 1,2-diols due to tight chelation with metal ions,[4c] these diols were also esterified in high yield by **1b**. Relatively less reactive aryl alcohols and 1-adamantanol were also esterified in high yields.

Ester condensation reactions with relatively more reactive primary alcohols proceeded even at room temperature (22 °C) without solvents (Table 2). Most carboxylic acids were esterified with 1.1 equiv of methanol in good yield in the presence of 1 mol % of **1b**. 1-Octanol was also reactive. As far as we know, this is the first example of an ultimate green esterification process.

One major problem associated with using soluble catalysts lies in the recovery of the catalyst from the reaction medium. A simple solution is to immobilize the catalyst on a polymeric matrix.[9] Figure 3 describes the preparation of immobilized catalyst **3b**. 4-(*N*-Mesitylamino)polystyrene resin (**12**) was prepared by palladium-catalyzed cross-coupling of 4-bromopolystyrene resin cross-linked with 2% divinyl benzene (**11**, 2.71 mmol Br/g, 200−400 mesh)[10] with 2,4,6-trimethylaniline in 75% yield.[11] **3b** was then readily prepared in 97% yield by treating **12** with $C_6F_5SO_3H$. On the contrary, an immobilized catalyst could not be prepared from **12** and TfOH since **3b** decomposed with superacidic TfOH. **3b** was recovered by filtration and reused as the catalyst more than 10 times for the direct ester condensation reaction of **4** with octanol, and activity loss was not observed for the recovered catalyst.

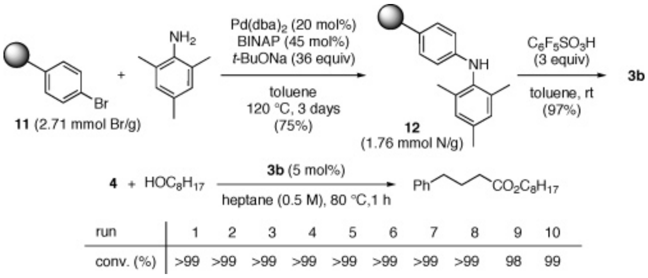


Figure 3. Preparation of **3b** and its recovery and reuse.

In conclusion, the hydrophobic effect of bulky diarylammonium sulfonates activated the esterification reaction, and steric hindrance suppressed the dehydrative elimination of secondary alcohols to produce alkenes. Thus, we achieved direct, catalytic ester condensation of carboxylic acids with an equimolar amount of primary alcohols without solvents at room temperature. In addition, the immobilization of bulky diarylammonium pentafluorobenzenesulfonate on a polymer support provided an efficient atom-economical esterification catalyst that could be easily recovered and reused.

Acknowledgment. Financial Support for this project has been provided by JSPS KAKENHI(15205021), the 21st Century COE Program "Nature-Guided Materials Processing" of MEXT, Shorai Foundation for Science and Technology, the Ogasawara Foundation for the Promotion of Science & Engineering, and the Noguchi Fluorous Project of the Noguchi Institute.

Supporting Information Available: Experimental procedures, full characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Otera, J. *Esterification*; Wiley-VCH: Weinheim, Germany, 2003.
(2) Manabe, K.; Sun, X.-M.; Kobayashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 10101.
(3) Xiang, J.; Orita, A.; Otera, J. *Adv. Synth. Catal.* **2002**, *344*, 84.
(4) (a) Ishihara, K.; Ohara, S.; Yamamoto, H. *Science* **2000**, *390*, 1140. (b) Ishihara, K.; Nakayama, M.; Ohara, S.; Yamamoto, H. *Synlett* **2001**, 1117. (c) Ishihara, K.; Nakayama, M.; Ohara, S.; Yamamoto, H. *Tetrahedron* **2002**, *58*, 8179. (d) Nakayama, M.; Sato, A.; Ishihara, K.; Yamamoto, H. *Adv. Synth. Catal.* **2004**, *346*, 1275.
(5) Wakatsugi, K.; Misaki, T.; Yamada, K.; Tanabe, Y. *Tetrahedron Lett.* **2000**, *41*, 5249.
(6) For the measurement of pK_a in CD_3CO_2D, see: Rode, B. M.; Engelbrecht, A.; Schantl, J. *Z. Physik. Chem. (Leipzig)* **1973**, *253* (1−2), 17. The pK_a values of diarylammonium sulfonates could not be estimated due to their low solubility.
(7) For the values of H_0, see: Habel, W.; Sartori, P. *J. Fluorine Chem.* **1982**, *20*, 559. The acidity of $C_6F_5SO_3H$ may be moderated by an intramolecular electrostatic interaction between H^+ and *o*-F.
(8) For the activation of $[Ph_2NH_2]^+[OTf]^-$ in fluorous media, see: Gacem, B.; Jenner, G. *Tetrahedron Lett.* **2003**, *44*, 1391. In contrast, **1b** and **2b** were not activated by fluorous media because of their sufficient hydrophobicity.
(9) Lei, M.; Ma, C.; Wang Y.-G. *Chinese J. Chem.* **2001**, *19*, 1309.
(10) Purchased from TCI, Co., Ltd., Japan.
(11) Vyskocil, S.; Jaracz, S.; Smrina, M.; Stícha, M.; Hanus, V.; Polásek, M.; Kocovsky, P. *J. Org. Chem.* **1998**, *63*, 7727.

JA050223V