4-(Benzylamino)formoyldiphenylammonium Triflate (BDPAT):An Efficient, Recoverable Biphasic Catalyst For Esterification of Carboxylic Acids with Equimolar Amounts of Alcohols

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Abstract: Esterification of carboxylic acid with equimolar amounts alcohol can be efficiently catalyzed by biphasic 4-(benzylamino)formoyldiphenylammonium triflate (BDPAT, **3**) in good yield. The catalyst can be easily recovered without loss of activity.

 $Keywords: \ 4-(Benzylamino) for moyl diphenylammonium \ triflate\ ,\ biphasic\ catalyst,\ esterification.$

Esterification of carboxylic acid with alcohol is one of the most fundamental and important reactions in organic synthesis and a great number of methods have been developed ¹. From a recent atom-economical standpoint, the uses of equimolar amounts of carboxylic acids and alcohols are strongly required. Mukaiyama and Shiina reported such direct esterification mediated by $TiCl_2(CIO)_2$ and $TiCl(OTf)_3$ reagents², which, however, necessitated more than equimolar amounts of anhydride and silyl dehydrating additives, respectively. More recently, Wakasugi found that diphenylammonium triflate (DPAT) could efficiently catalyze the esterification between equimolar amounts of carboxylic acids and alcohols in good yields under mild conditions³.

Facile catalyst separation and reuse are of prime importance in both industrial and academic settings. Although immobilization of the catalyst on a polymeric matrix can provide a simple solution to the recovery of the catalyst from the reaction medium, it needs more reaction steps for the synthesis of catalysts. Here, we report an efficient biphasic catalyst, 4-(benzylamino)formoyldiphenylammonium triflate (BDPAT, 3), which could be recovered by simple liquid separation method, for the esterification between carboxylic acids with equimolar amounts of alcohols.

The preparation of the biphasic catalyst **3** is described in **Scheme 1**. Condensation of 4-iodobenzoic acid with benzylamine afforded the 4-iodobenzamide (**1**). Using Pd-catalyzed amination⁴, **1** coupled with 1.1 equiv. phenyl amine under 0.1 equiv. Pd(OAc)₂ and 0.1 equiv. 1,1'-bis(diphenylphosphino)ferrocene (DPPF) in the presences of 2 equiv. Cs_2CO_3 to give biphenyl amine (**2**)⁵. Catalyst **3** was then readily prepared from **2** by treating with CF_3SO_3H .

Biphasic catalyst 3 was then used as catalyst for esterification between equimolar

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amounts of carboxylic acids and alcohols⁶. The results are shown in **Table 1**. Only 1-5 mol% catalyst was sufficient for primary alcohols with various acids to give corresponding esters in high yields. By comparison, **3** is more efficient than DPAT.

Scheme 1

$$HOOC - \underbrace{ \begin{array}{c} & & \\ &$$

a. PhCH₂NH₂, dicyclohexylcarbodiimide (DCC), 0.1 equiv. 4-dimethylaminopyridine (DMAP), RT., 8 h. 98% b. PhNH₂, 0.1 equiv. Pd(OAc)₂, 0.1 equiv. DPPF, 2 equiv. Cs_2CO_3 , toluene, 100°C, 24 h. 99%. c. 1.05 equiv. CF_3SO_3H , CH_2CI_2 , RT., 1 h. 100%.

Several functionalities such as a double bond and a halogen are tolerated (entries 2 and 4). This method did not necessitate special use of the dehydrating reagent and/or the technique of azeotropic removal of water. The biphasic catalyst could be easily recovered and reused for three times without loss of activity.

Entry	Carboxyl acid	Alcohol	3 (mol%)	Time (h)	Yield (%)
1	PhCH ₂ CH ₂ COOH	n-octanol	1	4	94
2	PhCH ₂ CH ₂ COOH	BrCH ₂ (CH ₂) ₇ CH ₂ OH	1	8	95
3	PhCH ₂ CH ₂ COOH	PhCH ₂ CH ₂ OH	1	8	90
4	PhCH=CHCOOH	n-octanol	2	24	94
5	(CH ₃) ₂ CHCOOH	PhCH ₂ CH ₂ OH	2	24	92
6	(CH ₃) ₃ CCOOH	n-octanol	1	6	93
7	CH ₃ (CH ₂) ₆ COOH	PhCH ₂ CH ₂ OH	3	24	90
8	PhCOOH	n-octanol	5	24	94

 Table 1
 Esterification conditions and results ^a

a. In toluene at 80°C Molar ratio/ R^1CO_2H : $R^2OH = 1:1$.

References and Notes

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- 5. Spectral data of compound. **2**:¹H-NMR(CDCl₃,500MHz, δ ppm) 7.72-6.97(m, 14H, ArH), 6.34 (t, 1H, -NHCO-), 6.08(br, 1H, -NH-), 4.63(d, 2H, ArCH₂-); IR (KBr, cm⁻¹) 3409, 3322, 3224, 3053, 3035, 1634, 1593, 1518, 1329; MS (*m/z*) 302 (M⁺),196(100),167; mp.108~110°C; Anal. Calcd for C₂₀H₁₈N₂O: C:79.49; H:5.96; N:9.27, Found: C:79.02; H:5.79; N:9.11.
- 6. **Typical procedure for esterification:** 3-Phenylpropionic acid (150 mg, 1.0 mmol), 9-bromo 1-nonanol (223 mg, 1.0 mmol), and **3** (4.5 mg, 0.01mmol) were heated (80°C) in toluene with stirring for 8 h. The toluene layer was separated then evaporated under reduced pressure gave the crude material, which was purified by column chromatography (hexane: ethyl acetate = 10:1) to give carboxylic ester (337 mg, 95%).

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