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Fluorous distannoxane-catalyzed acetylation of alcohols in heterogeneous single fluorous solvent system

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Abstract—Acetylation of alcohols with an equivalent amount of acetic anhydride is feasible in the presence of fluorous distannoxane catalyst in heterogeneous single fluorous system. The fluorous layer containing catalyst can be recycled and reused at least 10 times. © 2005 Elsevier Ltd. All rights reserved.

The last decade has witnessed great advance in fluorous biphase technology, which has now been modified into several variations.¹ The original protocol has its foundation on the thermomorphic nature of fluorous solvents.² That is, innately immiscible fluorous and organic solvents become homogeneous upon elevation of reaction temperature so that the desired reaction could readily proceed. Cooling the reaction mixture restores the two phases, and the fluorous phase containing a fluorous catalyst can be easily separated from the organic phase. Thus, the key to smooth reaction is attainment of homogeneous conditions. However, it turned out recently that heterogeneous conditions are also employable. For instance, fluorous rhodium-catalyzed hydroboration can be best performed in CF₃C₆F₁₁ without the second organic solvent.³ The mixture of substrate and borane was not soluble in the fluorous phase during the reaction at 40 °C. We report herein that highly efficient and convenient acetylation of alcohols is feasible with fluorous distannoxane catalyst 1 in a *heterogeneous* single fluorous solvent system, which offers a novel means to immobilize catalysts.⁴

We earlier disclosed that fluorous distannoxane 1 efficiently catalyzed (*trans*)esterification in a single fluorous solvent.⁵ The perfect conversion was achieved using reactants in a strict 1:1 ratio without recourse to any

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techniques for removing the alcohol or water co-product.



In this protocol, reaction at 150 °C under homogeneous conditions is crucial for biasing the equilibrium in favor of the products.⁶ Then, we were intrigued by applying this technology to synthetically important acetylation of alcohols. We expected that the reaction would smoothly occur with an equivalent amount of acetic anhydride even in a biphase system without elevation of the reaction temperature because this reaction is a non-equilibrium process. Thus, acetylation of 2-phenylethanol was attempted in the presence of 1 (5 mol %) in FC-72/toluene or FC-72/CH₂Cl₂ (Table 1). The reaction mixture was stirred at room temperature for 6 h while a biphasic system was maintained. Unfortunately, however, yields of the desired acetate were only 72% and 56%, respectively. With these unsatisfactory results in hand, we turned our attention to the single fluorous solvent system without the second organic solvent. An equimolar mixture of 2-phenylethanol and acetic anhydride was added to an FC-72 solution of 1 (5 mol%). The resulting heterogeneous mixture was stirred for

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6 h at room temperature, and the acetate was obtained in 99% yield (Table 2, entry 1). The product was formed atop the fluorous layer and extracted with octane which is immiscible with FC-72. This operation is necessary simply because of the small reaction scale and otherwise a portion of the product remains on the surface of the fluorous layer. In larger-scale reactions, however, the product could be directly separated by means of syringe (vide infra). From the fluorous layer, the catalyst was recovered almost quantitatively,7 but partially in modified structures. Such modification is reminiscent of the actual active species and thus caused no practical problem. In fact, the catalyst could be successfully recycled as described later. Primary alcohols provided excellent yields (entries 2 and 3). The mild conditions allowed substrates involving various acid-sensitive moieties like furfuryl alcohol, geraniol, and alcohols with THP, TBS, acetonide, or carbomethoxy groups to undergo smooth acetylation (entries 4-9). In all cases, excellent yields were obtained even by use of just one equivalent of acetic anhydride concomitant with quantitative recovery of the catalyst. On the other hand, secondary alcohols and phenol reacted sluggishly (entries 10–12).

Finally, the recycled use of the catalyst was performed for acetylation of 2-phenylethanol in a larger scale (Table 3). First, the ester (20 mmol) was exposed to one equivalent of acetic anhydride in the presence of

Table 1.

Ph	+ Ac_2O 1 (5 mc (1.0 eq) rt, 6 h	Ph OAc
Solvents	Yield (%)	Recovered catalyst ^a (%)
FC-72/toluene	72	90
FC-72/CH ₂ Cl ₂	56	91

^a Determined by weight of the recovered catalyst.

 Table 2. Acetylation of alcohols in a heterogeneous single fluorous system

ROH + Ac_2O $\overrightarrow{FC-72 (2 mL), rt}$ ROAc								
Entry	ROH	Time (h)	Yield ^a (%)	Recovered catalyst ^b (%)				
1	PhCH ₂ CH ₂ OH	6	99	95				
2	PhCH ₂ OH	6	98	95				
3	$C_8H_{17}OH$	6	99	95				
4	Furfuryl alcohol	6	99	95				
5	Geraniol	6	99	96				
6	THPO(CH ₂) ₈ OH	6	94	96				
7	TBSO(CH ₂) ₈ OH	10	99	96				
8	НО	7	98	95				
9	MeOC(O)(CH ₂) ₈ OH	24	99	96				
10	PhCH(OH)CH ₃	6	25	93				
11	2-Octanol	6	43	94				
12	PhOH	24	63	92				

1 (5 mol%)

^a Isolated yield.

^b Determined by weight of the recovered catalyst.

Table 3.

$Ph \longrightarrow OH + Ac_2O \longrightarrow Ph \longrightarrow OAc$ 20 mmol $Pc-72 \rightarrow Ph \longrightarrow OAc$										
Entry	Run									
	1	2	3	4	5	6	7	8	9	10
1 ^{a,b}	96	96	94	93	91	88	84	82	78	73
$2^{c,d}$	98	98	97	95	94	94	92	91	88	86 ^e

^a 1 (3 mol %) Ac₂O (1.0 eq.), FC-72 (10 mL), rt, 12 h.

^b Isolated yield.

^c1 (5 mol %) Ac₂O (1.2 eq.), FC-72 (14 mL), rt, 9 h.

^d GLC yield.

^e After 10th run, 83% of catalyst was recovered.

3 mol% of 1 in FC-72 (10 mL). After reaction for 12 h, the upper organic layer was separated from the fluorous layer by means of syringe and the acetate was isolated through column chromatography after usual workup. The catalyst solution can be used directly for the next reaction without isolation of the catalyst. To the FC-72 solution was added the alcohol and acetic anhydride again, and the reaction was repeated as above. The yield decreased gradually down to a 73%isolated yield (75% by GLC) in the 10th run. Next, the reaction was conducted using 1.2 equiv of acetic anhydride in the presence of 5 mol % of 1 in FC-72 (14 mL). After 9 h, the yield was determined by GLC. Under these conditions the yield in the 10th run was increased to 86%. The catalyst was recovered in 83% by weight after the 10th run.8

In summary, a single fluorous system has proved to be more effective than that of the conventional biphasic system for fluorous distannoxane-catalyzed acetylation. Excellent yields of acetates of primary alcohols with various functions are obtained using just 1 equiv of acetic anhydride. The catalyst can be recycled at least 10 times without significant loss of catalytic activity. Neither use of the second organic solvent nor elevation of reaction temperature makes operations very convenient and, hence, the heterogeneous single fluorous system will find many applications as a useful means to immobilize catalysts.

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- 7. Usually, the catalyst was recovered more than 95% by weight. It is reasonable to assume that the recovery is virtually perfect because a slight loss might be attributed to the small-scale reaction.
- 8. Representative procedure (Table 3, entry 1, run 1): To an FC-72 solution (10 mL) of 1 (1.03 g, 0.6 mmol) was added 2-phenylethanol (2.44 g, 20.0 mmol) and acetic anhydride (2.04 g, 20.0 mmol), and the mixture was stirred at rt for 12 h. After the organic layer had been separated from the fluorous layer by a syringe and transferred to a separating funnel, the syringe was rinsed with AcOEt (1 mL \times 2). After the organic layer was washed with NaHCO₃aq (10 mL), the aqueous layer was extracted with AcOEt (10 mL \times 3), dried over MgSO₄, filtered, and evaporated. The combined organic layer was subjected to column chromatography on silica gel to afford 2-phenylethyl acetate (3.15 g, 96%). The recovered FC solution of catalyst 1 was reused for the next acetylation.