

Fluoroalkyldistannoxane Catalysts for Transesterification in Fluorous Biphase Technology

Jiannan Xiang, Akihiro Orita, Junzo Otera*

Department of Applied Chemistry, Okayama University of Science, Ridai-cho, Okayama 700-0005, Japan
Fax: (+81)-86-256-4292, e-mail: otera@high.ous.ac.jp

Received October 10, 2001; Accepted November 26, 2001

Abstract: Novel, practical protocols of transesterification have been advanced with recourse to fluorous biphase technology. The fluoroalkyldistannoxane catalysts enable transesterification in FC-72 solvent to furnish 100% yields of the desired esters by use of reactants ester and alcohol in a 1:1 ratio. The catalysts also work in FC-72/organic solvent system as well as in toluene alone. A number of esters and alcohols bearing various functional groups are employable.

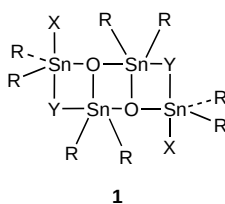
The catalysts can be totally recovered and reused. More conveniently, the catalyst solution in FC-72 which is separated from the reaction mixture is directly used for the next reaction.

Keywords: esters; fluorous biphase technology; Lewis acids; perfluorinated solvents; tin; transesterification.

Introduction

The fluorous biphase technology has paved the way for a new green chemical process.^[1] In particular, facile recovery of catalysts from reaction mixtures affords promise of overcoming serious drawbacks in homogeneous catalysis. For achieving high efficiency in the fluorous biphase system, it is crucial to render catalysts fluorophilic through incorporation of fluorous groups. A number of catalysts has been produced along this line. Organotin compounds are well suited to this end on account of facile formation as well as stability of alkyl-tin bonds. In fact, several fluorophilic organotin reagents have been successfully developed.^[2]

We have been involved in exploitation of organotin Lewis acid catalysts for a long time.^[3] 1,3-Disubstituted tetraalkyldistannoxanes **1** are amongst the most useful and versatile catalysts. One of their characteristic properties is the unique solubility in organic solvents. This was ascribed to the dimeric formulation where the central stannoxane core is surrounded by eight alkyl groups.^[4] This structural feature led us to synthesize fluoroalkyldistannoxanes which possessed high solubility in fluorocarbon solvents and high partition coefficients for fluorocarbons over common organic solvents.^[5] It is reasonable to postulate that such large partition coefficients can be utilized for fluorous biphase catalysis. The purpose of this paper is to apply these new compounds to fluorous biphase transesterification.



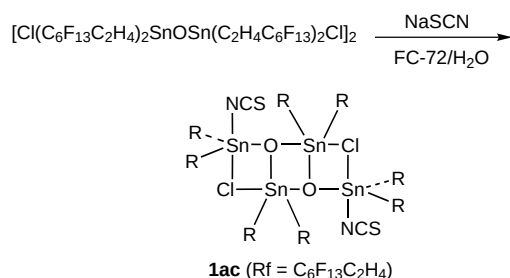
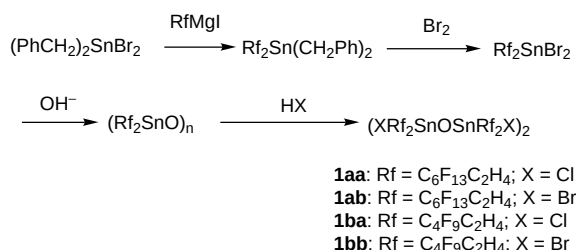
Transesterification has a long history but still occupies a central position in both laboratory work and industry.^[6] This reaction is simple in terms of chemical equation but difficult to achieve 100 % conversion because of equilibration. In order to shift the equilibrium completely into the products side, either of the reactants must be employed in excess or the produced alcohol must be constantly removed from the reaction mixture. Another problem to be solved is compatibility with functional groups. Since the reaction usually requires acid or base catalysts, many of functional groups cannot be tolerated under these conditions. As a whole, the ideal transesterification should satisfy the following requirements: (1) the use of reactants ester and alcohol in a 1:1 ratio, (2) no need for special reagents or technique of removing the alcohol liberated, (3) catalyst compatible with various functional groups as well as stable enough to be readily recovered and reused repeatedly without decrease of activity, and (4) 100% yield as well as conversion. Notably, the use of equimolar reactants is highly desirable in view of atom economy but meaningful only if the 100% conversion is realized. Otherwise, four components consisting of two reactants and two products, respectively, remain in the final reaction mixture. This situation is more complex and thus more disadvantageous to separation of the product than that arising from the use of one reactant in excess because, in this case, only three components remain after 100% conversion. Despite such practical importance, no precedents are available that succeeded in the 100% conversion by use of equimolar reactants.^[7]

We disclose herein that the fluorous biphase system, if properly designed, not only enables effective catalyst recovery but also changes the equilibration due to different solubility parameters of fluorocarbon solvents leading to the 100% yield even by use of reactants in a 1:1 ratio. In this study, the fluorous biphase technology is invoked in three ways. First, transesterification is conducted simply in perfluorohexanes (FC-72, 3M) to realize the ideal performance (single fluorous phase system).^[8] Moreover, two variations are put forth. Namely, an

FC-72/toluene or methanol biphasic solvent mixture is employed (binary solvent system) and finally, the reaction is run in toluene accompanied by catalyst recovery through extraction with FC-72 (single organic solvent system).

Results and Discussion

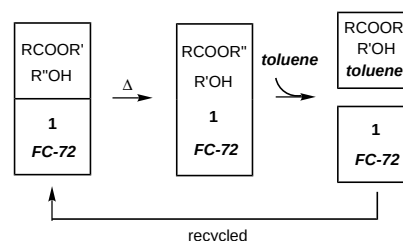
We have already reported elsewhere the procedure to prepare the catalysts **1** employed in this study (Scheme 1).^[5] They are air-stable crystalline compounds and highly soluble in fluorocarbon solvents. For example, the partition coefficients of tridecafluorooctyl ($C_6F_{13}C_2H_4$) derivative **1aa** for FC-72/organic solvents were found to be >100 for toluene and benzene, 99 for CH_2Cl_2 , 49 for methanol, and 32 for acetone although those of nonafluorohexyl ($C_4F_9C_2H_4$) derivatives **1ba** and **1bb** are slightly lower (24–99). With these results in hand, we began with general assessment of the catalytic activity in the single fluoruous phase system.



Scheme 1. Synthesis of fluoroalkyldistannoxanes.

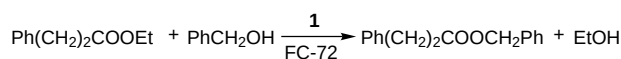
Single Fluorous Phase System

The general procedure is illustrated in Scheme 2: the reactants in a 1:1 ratio were heated at $150^\circ C$ in FC-72^[9] for 16 h and the reaction mixture was washed with toluene (Scheme 2). The catalytic activity was examined for the reaction between ethyl 3-phenylpropionate and benzyl alcohol. As given in Table 1, GLC analysis of the toluene layer exhibited a single peak assignable to the benzyl ester, the yield of which was found to be >99% with 5 mol % loading of the dichloro- and dibromodistannoxane catalysts (entries 1, 4, 6). The ethyl ester and benzyl alcohol were totally consumed. No virtual difference was observed between tridecafluorooctyl (**1aa** and **1ab**) and nonafluorohexyl (**1ba**) catalysts, and, hence, the chain length of fluoroalkyl groups proved to exert no influence on the catalytic activity. However, the distinction was apparent between these two types of fluoroalkyldistannoxanes with respect to recovery



Scheme 2. Transesterification in single fluoruous phase system.

Table 1. Evaluation of fluoroalkyltin catalysts for transesterification in single fluoruous phase system.^[a]



entry	1 (mol %)	GLC	yield (%)	catalyst recovery (%)
1	1aa (5.0)	>99	100	100
2	1aa (2.0)	>99	100	100
3	1aa (1.0)	96	100	100
4	1ab (5.0)	>99	100	100
5	1ac (1.0)	>99	100	100
6	1ba (5.0)	>99	98	98
7	none ^[b]	65		

^[a] Reaction conditions: ester (1.0 mmol); alcohol (1.0 mmol); FC-72 (5 mL); $150^\circ C$; 16 h; washing with toluene (5 mL, 1 mL $\times$ 2).

^[b] Control experiment.

from the reaction mixture. From the FC-72 layer, **1aa** and **1ab** returned in 100% recovery. This is rather surprising in such a small reaction scale (1 mmol) where only 20–90 mg of the catalyst are employed. On the other hand, a fraction of **1ba** leaked into the organic layer resulting in 98% recovery of the catalyst from the fluoruous layer. This decrease in the recovery ratio seems to be trivial so long as every single run is concerned but becomes serious upon recycled use of the catalyst because the deviation from the 100% recovery is multiplied (vide infra). Consequently, tridecafluorooctyldistannoxanes are the catalysts of our choice. Even with 2 mol % of **1aa**, a quantitative yield was obtained (entry 2), yet 1 mol % loading failed to furnish quantitative yield (entry 3). Notably, however, chloroisothiocyanate **1ac** is active enough to afford a quantitative yield with 1 mol % loading (entry 5). The somewhat enhanced activity of isothiocyanate derivatives was also found with tetrabutyltin distannoxane catalysts for urethane formation.^[10] Of course, the effectiveness of the catalysts is apparent from comparison with a control experiment which gave a lower yield (entry 7).

With these results in hand, we performed transesterification with various reactants under catalysis of **1aa**, **1ab**, and **1ac** (Table 2). Although the 2 mol % catalyst loading is enough for the completion of the reaction with **1aa** and **1ab** as described above, it is not practically necessary to decrease the amount of the catalyst to such a level because of its facile recovery or recycling (vide infra). Thus, the 5 mol % catalyst was loaded; this is easier for exact weighing of the catalyst than the 2 mol %

Table 2. Transesterification in single fluoros phase system.^[a]

$\text{RCOOR}' + \text{R}''\text{OH} \xrightarrow[\text{FC-72}]{\mathbf{1}} \text{RCOOR}'' + \text{R}'\text{OH}$					
entry	RCOOR'	R''OH	1	yield (%)	
				GLC	isolated
1	Ph(CH ₂) ₂ COOEt	C ₈ H ₁₇ OH	1aa	>99	100
2		C ₈ H ₁₇ OH	1ac	>99	
3		PhCH=CHCH ₂ OH	1aa	>99	100
4	Ph(CH ₂) ₂ COOMe	PhCH=CHCH ₂ OH	1aa	>99	100
5	Ph(CH ₂) ₂ COOEt	PhCH=CHCH ₂ OH	1ab	>99	100
6		PhCH=CHCH ₂ OH	1ac	>99	
7		geraniol	1aa	>99	98
8		geraniol	1ab	>99	
9		PhC≡CCH ₂ OH	1aa	>99	100
10		THPO(CH ₂) ₈ OH	1aa	>99	99
11		THPO(CH ₂) ₈ OH	1ab	>99	
12		TBSO(CH ₂) ₈ OH	1aa	>99	100
13		TBSO(CH ₂) ₈ OH	1ab	>99	
14		2-octanol	1aa	>99	100
15		2-octanol	1ab	>99	
16		2-octanol	1ac	>99	
17		cyclohexanol	1aa	>99	99
18		cyclohexanol	1ac	>99	
19		menthol	1aa	>99 ^[b]	
20		menthol	1ac	>99	
21		borneol	1aa	>99 ^[b]	
22		borneol	1ac	>99	
23		cholesterol	1ac	>99	
24	PhCH=CHCOOEt	PhCH=CHCH ₂ OH	1aa	>99	99
25	PhCOOEt	PhCH=CHCH ₂ OH	1aa	>99	100
26	PhCOOMe	PhCH=CHCH ₂ OH	1aa	>99	100

^[a] Reaction conditions: RCOOR' (1.0 mmol); R''OH (1.0 mmol); **1aa** or **1ab** (0.05 mmol) or **1ac** (0.01 mmol); FC-72 (5 mL); 150 °C, 16 h; washing with toluene (5 mL, 1 mL × 2).

^[b] At 160 °C.

loading. On the other hand, 1 mol % of **1ac** was loaded to highlight its higher catalytic activity. The reaction proceeded perfectly even by use of the reactants in the 1:1 ratio. No starting materials were detected after 16 h on the basis of GLC analysis. Aliphatic, α,β-unsaturated, and aromatic derivatives can be used as ester components. A variety of alcohols is also employable such as primary, secondary, allylic and propargylic alcohols. Geraniol suffered neither isomerization nor cyclization that easily occurs under acidic conditions (entries 7 and 8). Other acid-sensitive functions like propargylic, tetrahydropyranyl (THP) and *tert*-butyldimethylsilyl (TBS) groups survived (entries 9–13). Apparently, the neutral reaction conditions are responsible for the tolerance of these functional groups. In the reaction with sterically bulky menthol and borneol with **1aa**, small amounts of the reactants (1–3%) remained but the perfect outcomes were accessible by raising the reaction

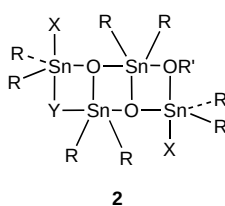
temperature to 160 °C (entries 19 and 21). Notably, more active **1ac** provided satisfactory results even under standard conditions with 1 mol % catalyst (entries 20 and 22).

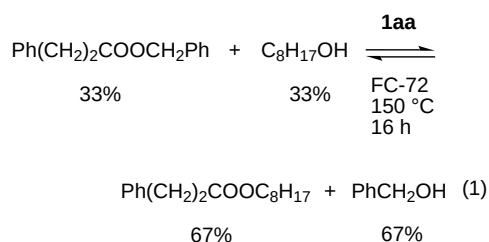
Evaporation of the FC-72 layer led to the complete recovery of the catalyst. A ¹¹⁹Sn NMR spectrum of the recovered catalyst exhibited entirely the same signals as original ones, implying a catalytic mechanism different from that proposed with tetraalkyldistannoxanes. In the latter case, the initial step is substitution of the bridging Y group to give an alkoxydistannoxane intermediate (structure 2) which works as an alkoxy donor.^[3] On the other hand, the recovery of the fluoroalkyldistannoxane catalyst in the original form suggests that no substitution took place at the bridging position by an alkoxy group. We found previously that the bridging chlorine in **1aa** was never substituted by isothiocyanate ion (Scheme 1)^[5] in contrast to the conventional distannoxanes which undergo facile replacement by the isothiocyanato group at both bridging and terminal positions. The present findings imply that the fluoroalkyldistannoxanes experience stronger association than the conventional alkyldistannoxanes. It may be suggested for the present reaction that both alcohol and ester coordinate on the terminal tin atom where the interchange of the alkoxy groups takes place.

Instead of recovering the catalyst from the FC-72 solution, the separated catalyst solution could be more conveniently used directly for the next reaction. Washing of the FC-72 solution with toluene twice is sufficient to remove the product remaining on the surface of FC-72 layer. The separated FC-72 solution could be forwarded to other reactions. Thus, many of the reactions shown in Table 2 were conducted with the same catalyst solution. On the other hand, the washing is not necessary if the same reaction is repeated. For instance, the reaction of entry 1 in Table 1 was repeated ten times with a single catalyst solution. The yield of the first run was found to be 95% without washing. However, the >99% yield was constantly obtained on the basis of GLC analysis during the second and tenth runs, indicating that nearly the same amount of the product remained on the FC-72 surface in each run. After tenth run, 97% of the catalyst was recovered.

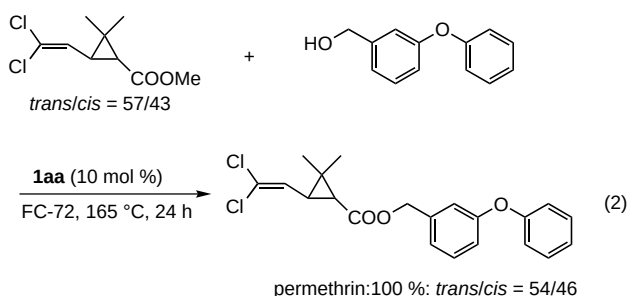
In the above experiments, the 100 % yield with equimolar amounts of the reactants has been realized when substrate esters with a lighter alcohol component (methoxy or ethoxy) were treated with a heavier alcohol. It turned out that the situation changed if an ester with a heavy alkoxy group had been subjected to the same reaction. A benzyl ester was treated with 1-octanol in the presence of 5 mol % of **1aa**. After 16 h, the equilibrium was reached where 67% of octyl ester formed while 33% of the benzyl ester remained (Eq. 1). Treatment of the octyl ester with benzyl alcohol in a 1:1 ratio under the same conditions induced the reaction in the reverse direction resulting in the same distribution of the esters and alcohols. It follows therefore that the complete bias in the reactions shown in Tables 1 and 2 can be ascribed to liberation of light alcohols which may be less soluble in FC-72 than the heavier alcohols at 150 °C.^[11]

In the hope of exemplifying the practical utility of the present protocol, synthesis of a pyrethroid, permethrin,^[12] was performed starting from the readily available methyl ester (Eq. 2). Treatment of this ester with *m*-phenoxybenzyl alcohol





under standard conditions as established above furnished only a 35% yield of the desired ester. The reduced reactivity may be attributable to the steric hindrance of α,α -dimethylcyclopropyl group. Accordingly, the reaction was conducted with 10 mol % of **1aa** at 165 °C for 24 h and then a 100 % yield was achieved. Needless to say, the catalyst was recovered completely.



Binary Solvent System

If the use of solvent is preferable, an FC-72/organic solvent binary system is employable (Scheme 3). The reaction was conducted in a 1:1 mixture of FC-72 and toluene (Table 3). However, a mixture of equimolar reactants failed to give complete conversion. The use of a slight excess amount of alcohol (1.2–1.3 equiv.) was required for satisfactory yields. The catalyst was recovered without loss (> 99%) from the FC-72 layer. The control experiment without the catalyst afforded only a 23% yield (entry 15).

The complete conversion was accessible when substrate alcohol was used as co-solvent (Table 4). When the reaction was performed in a mixture of FC-72 (4 mL) and alcohol (2 mL), the desired esters were obtained in 100% yields. It should be noted that this protocol enables the conversion of substrate esters bearing a heavier alcohol component to the lower analogues (entries 1, 4–6). Apparently, use of the alcohol component in large excess allows the equilibrium to shift in favor of the product side. This is a useful procedure to arrive at a variety of esters irrespective of the kind of substrate esters. Moreover, the operation is quite simple as evaporation

Table 3. Transesterification catalyzed by **1aa** in FC-72/toluene binary system.^[a]

$\text{RCOOR}' + \text{R}''\text{OH} \xrightarrow[\text{FC-72/toluene}]{\mathbf{1aa}} \text{RCOOR}'' + \text{R}'\text{OH}$				yield (%)	
entry	RCOOR'	R''OH	alcohol/ester	GLC	isolated
1	Ph(CH ₂) ₂ COOEt	PhCH ₂ OH	1.0	95	
2		PhCH ₂ OH	1.1	98	
3		PhCH ₂ OH	1.2	>99	96
4	PhCOOEt	PhCH ₂ OH	1.0	90	
5		PhCH ₂ OH	1.1	95	
6		PhCH ₂ OH	1.2	>99	93
7	Ph(CH ₂) ₂ COOEt	PhCH=CHCH ₂ OH	1.2	>99	94
8		geraniol	1.3	>99	100
9		TBSO(CH ₂) ₈ OH	1.3	>99	98
10	PhCH=CHCOOEt	PhCH ₂ OH	1.0	92	
11		PhCH ₂ OH	1.2	>99	100
12		PhCH=CHCH ₂ OH	1.0	95	
13		PhCH=CHCH ₂ OH	1.1	96	90
14		PhCH=CHCH ₂ OH	1.2	>99	100
15 ^[b]	Ph(CH ₂) ₂ COOMe	PhCH ₂ OH	1.2	23	

^[a] Reaction conditions: RCOOR' (1.0 mmol); R''OH (1.0 mmol); **1aa** (0.05 mmol); FC-72 (5 mL); toluene (5 mL); 150 °C, 16 h; washing with toluene (1 mL × 2).

^[b] Control experiment without catalyst.

Table 4. Transesterification catalyzed by **1aa** in FC-72/alcohol binary system.^[a]

$\text{RCOOR}' + \text{R}''\text{OH} \xrightarrow[\text{FC-72}]{\mathbf{1aa}} \text{RCOOR}'' + \text{R}'\text{OH}$				yield (%)	
entry	RCOOR'	R''OH		GLC	isolated
1	Ph(CH ₂) ₂ COOEt	CH ₃ OH		>99	100
2		2-butanol		>99	100
3	Ph(CH ₂) ₂ COOMe	C ₂ H ₅ OH		>99	100
4	Ph(CH ₂) ₂ COOBn	CH ₃ OH		>99	100 ^[b]
5		C ₂ H ₅ OH		>99	100 ^[b]
6		CH ₂ =CHCH ₂ OH		>99	100 ^[b]

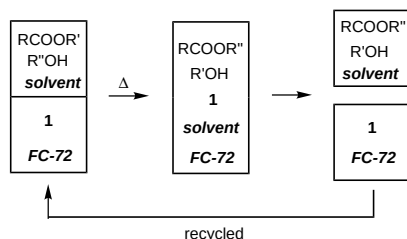
^[a] Reaction conditions: RCOOR' (2.0 mmol); R''OH (2.0 mmol); **1aa** (0.10 mmol); FC-72 (4 mL); 150 °C, 16 h; washing with toluene (5 mL, 1 mL × 2).

^[b] Isolated by column chromatography.

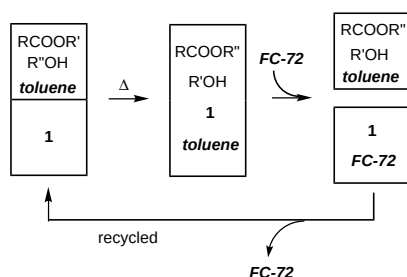
of the organic layer to remove the low-boiling point alcohol leaves pure esters. It should be noted that the reaction of entry 1 in Table 4 was repeated 20 times. The GLC yield was constantly over 99% each time, the 91% of the catalyst was recovered after 20th run indicative of virtually no loss and no deactivation of the catalyst during the repeated operations.

Single Organic Solvent System

The fluorous biphase technology is also invoked to recover catalysts in normal transesterification (Scheme 4). Transesterification was effected by fluoroalkyldistannoxane catalysts (5 mol %) in refluxing toluene. However, the use of equimolar amounts of the reactants failed to achieve the perfect conversion (91% yield) and, hence, the alcohol component was employed in excess (1.2 equiv.) to give quantitative yields. Such a smooth reaction was rather unexpected since the catalysts are insoluble



Scheme 3. Transesterification in binary solvent system.



Scheme 4. Transesterification in single organic solvent system.

in toluene at room temperature, yet the reaction mixture looked to be homogeneous at reflux temperature. This finds strong support from the following fact: the catalysts that had been powdery before use turned crystalline in toluene after the reaction mixture had been cooled. The catalysts were as active as in the previous protocols and, thus, there is no difference in activity between FC-72 and toluene solvents. Quantitative yields of the desired esters were obtained in various combinations of reactants esters and alcohols (Table 5). The same chemoselectivity as found formerly holds in the present case as well, and of more synthetic significance is the successful use of ethyl acetoacetate (entries 23 and 24). This substrate was not employable in the reaction using FC-72 because the reaction at 150 °C induced thermal decomposition of the ester. No decomposition occurred in refluxing toluene. Again, a big decrease in yield was confirmed in control experiment (entry 28). After 16 h, the reaction mixture was washed with FC-72. Evaporation of the FC-72 solution returned the catalyst, recovery yields of which are 100% for **1aa** and 99% for **1ba**, respectively. This difference was increased upon recycled use of the catalysts. Apparently, the catalyst with higher fluorine content is more efficiently recovered.

Conclusion

Three protocols have been advanced for fluorous biphasic transesterification under catalysis of fluoroalkyldistannoxanes. The single fluorous phase system almost realized the ideal transesterification as defined in the Introduction. The binary solvent system allows us to use organic solvent. In particular, the employment of solvent alcohol offers an extremely convenient procedure. The usual transesterification technology benefits a great deal from the single organic solvent system through facile recovery and recycling of the catalysts. The practical transesterification is available by choosing an appropriate one from these three protocols.

Experimental Section

General Remarks

NMR spectra were recorded on JEOL Lambda 300 and 500 instruments at 25 °C and calibrated with tetramethylsilane (TMS) as an internal standard. GC analysis was performed on Shimadzu GC17A attached with CBP1 capillary column. FC-72 (fluorohexanes, 3M) was used without purification.

Table 5. Transesterification in single organic solvent system.^[a]

$\text{RCOOR}' + \text{R}''\text{OH} \xrightarrow[\text{toluene}]{\text{1}} \text{RCOOR}'' + \text{R}'\text{OH}$				
entry	RCOOR'	R''OH	1	GLC yield (%)
1	Ph(CH ₂) ₂ COOMe	PhCH ₂ OH	1aa	>99 ^[b]
2		PhCH ₂ OH	1ab	>99 ^[c]
3		PhCH ₂ OH	1ba	>99
4		PhCH ₂ OH	1bb	>99
5	Ph(CH ₂) ₂ COOEt	THPO(CH ₂) ₈ OH	1aa	>99
6		THPO(CH ₂) ₈ OH	1ba	>99
7		TBSO(CH ₂) ₈ OH	1aa	>99
8		TBSO(CH ₂) ₈ OH	1ba	99
9		TBSO(CH ₂) ₈ OH	1bb	>99
10		PhCH=CHCH ₂ OH	1aa	>99
11		PhCH=CHCH ₂ OH	1ba	98
12		PhCH=CHCH ₂ OH	1bb	97
13		geraniol	1aa	99
14		menthol	1aa	>99
15		menthol	1ab	98
16		menthol	1ba	>99
17		menthol	1bb	88
18		borneol	1aa	99
19		PhCH(CH ₃)OH	1aa	>99
20		PhCH(CH ₃)OH	1ba	94
21		PhCH(CH ₃)OH	1bb	88
22	<i>n</i> -C ₈ H ₁₇ COOMe	PhCH ₂ OH	1aa	>99
23	CH ₃ COCH ₂ COOEt	PhCH ₂ OH	1aa	>99
24		menthol	1aa	96
25	PhCOOEt	PhCH ₂ OH	1aa	>99
26		PhCH ₂ OH	1ba	>99
27		PhCH ₂ OH	1bb	>99
28	Ph(CH ₂) ₂ COOMe	PhCH ₂ OH	none ^[d]	3

^[a] Reaction conditions: RCOOR' (1.0 mmol); R''OH (1.2 mmol); **1** (0.05 mmol); toluene (5 mL); reflux, 6 h; washing with FC-72 (5 mL × 2).

^[b] Catalyst recovery: 100%.

^[c] Catalyst recovery: 99%.

^[d] Control experiment without catalyst for 12 h.

All the products except 2-(2-tetrahydropyranloxy)ethyl 3-phenylpropanoate and 2-*t*-butyldimethylsilyloxyethyl 3-phenylpropanoate have been reported: benzyl 3-phenylpropanoate,^[13] octyl 3-phenylpropanoate,^[14] cinnamyl 3-phenylpropanoate,^[15] geranyl 3-phenylpropanoate,^[16] 1-phenylpropynyl 3-phenylpropanoate,^[17] 2-octyl 3-phenylpropanoate,^[18] cyclohexyl 3-phenylpropanoate,^[19] menthyl 3-phenylpropanoate,^[14] bornyl 3-phenylpropanoate,^[20] cholesteryl 3-phenylpropanoate,^[21] cinnamyl cinnamate,^[22] cinnamyl benzoate,^[23] benzyl cinnamate,^[24] benzyl benzoate,^[25] methyl 3-phenylpropanoate,^[26] 2-butyl 3-phenylpropanoate,^[27] ethyl 3-phenylpropanoate,^[28] 3-propenyl 3-phenylpropanoate,^[29] 1-phenethyl 3-phenylpropanoate,^[30] benzyl nonanoate,^[31] benzyl acetoacetate,^[32] and menthyl acetoacetate.^[33]

Transesterification in Single Fluorous Phase System (Table 1, Entry 1)

A test tube (50 mL) charged with ethyl 3-phenylpropionate (178 mg, 1.0 mmol), benzyl alcohol (108 mg, 1.0 mmol), **1aa** (86 mg, 0.05 mmol, 5 mol %) and FC-72 (5.0 mL) was placed in a stainless pressure bottle and heated at 150 °C for 16 h. After having been cooled, toluene (5.0 mL) was added to the reaction mixture. The toluene and FC-72 layers were separated and the latter layer was washed with toluene (1.0 mL × 2). The combined organic layer was analyzed with GC to prove a quantitative yield of benzyl 3-phenylpropionate. Evaporation of the FC-72 phase afforded quantitative recovery of **1aa** (86 mg).

Transesterification in Single Fluorous Phase System (Table 2, Entry 1)

A test tube (50 mL) charged with ethyl 3-phenylpropionate (178 mg, 1.0 mmol), 1-octanol (130 mg, 1.0 mmol), **1aa** (86 mg, 0.05 mmol, 5 mol %) and FC-72 (5.0 mL) was placed in a stainless pressure bottle and heated at 150 °C for 16 h. After having been cooled, toluene (5.0 mL) was added to the reaction mixture. The toluene and FC-72 layers were separated and the latter layer was washed with toluene (1.0 mL $\times$ 2). The combined organic layer was analyzed with GC to prove a quantitative yield of 1-octyl 3-phenylpropionate. Evaporation of the organic layer followed by column chromatography (hexane/AcOEt = 10/1) furnished 1-octyl 3-phenylpropionate as a colorless oil; yield: 262 mg (100%).

Other reactions were conducted analogously.

8-(2-Tetrahydropyranyloxy)octyl 3-phenylpropanoate: ^1H NMR (500 MHz, CDCl_3): δ = 1.20–1.83 (m, 18H), 2.62 (t, J = 7.7 Hz, 2H), 2.95 (t, J = 7.7 Hz, 2H), 3.31–3.52 (m, 2H), 3.68–3.88 (m, 2H), 4.05 (t, J = 6.7 Hz, 2H), 4.57 (s, 1H), 7.18–7.32 (m, 5H); ^{13}C NMR (125 MHz, CDCl_3): δ = 19.7, 25.5, 25.8, 26.1, 28.6, 29.2, 29.3, 29.7, 30.8, 31.0, 35.9, 62.4, 64.6, 67.6, 98.9, 126.2, 128.3, 128.5, 140.6, 173.0. Anal. calcd. for $\text{C}_{22}\text{H}_{34}\text{O}_4$: C 72.89, H 9.45; found: C 72.91, H 9.63.

8-tert-Butyldimethylsilyloxyoctyl 3-phenylpropanoate: ^1H NMR (500 MHz, CDCl_3): δ = 0.05 (s, 6H), 0.89 (s, 9H), 1.28–1.60 (m, 12H), 2.62 (t, J = 7.8 Hz, 2H), 2.95 (t, J = 7.8 Hz, 2H), 3.60 (t, J = 6.6 Hz, 2H), 4.05 (t, J = 6.6 Hz, 2H), 7.18–7.31 (m, 5H); ^{13}C NMR (125 MHz, CDCl_3): δ = –5.3, 18.4, 25.7, 25.8, 26.0, 28.6, 29.2, 29.3, 31.0, 32.8, 35.9, 63.2, 64.6, 126.2, 128.3, 128.5, 140.6, 173.0; HRMS (EI): calcd. for $\text{C}_{23}\text{H}_{40}\text{O}_3\text{Si}$: 392.2747; found: 392.2767.

Transesterification Catalyzed in FC-72/Toluene Binary System (Table 3, Entry 8)

A test tube (50 mL) charged with ethyl 3-phenylpropionate (178 mg, 1.0 mmol), geraniol (201 mg, 1.3 mmol), **1aa** (86 mg, 0.05 mmol, 5 mol %), FC-72 (5.0 mL) and toluene (5.0 mL) was placed in a stainless pressure bottle and heated at 150 °C for 16 h. After having been cooled, the reaction mixture was separated and the FC-72 layer was washed with toluene (1.0 mL $\times$ 2). The combined organic layer was analyzed with GC to prove a quantitative yield of geranyl 3-phenylpropionate. Evaporation of the organic layer followed by column chromatography (hexane/AcOEt = 10/1) furnished geranyl 3-phenylpropionate as a colorless oil; yield: 286 mg (100%).

Fluorous Biphasic Transesterification in FC-72/Alcohol Binary System (Table 4, Entry 1)

A test tube (50 mL) charged with ethyl 3-phenylpropionate (356 mg, 2.0 mmol), methanol (2 mL), **1aa** (172 mg, 0.1 mmol, 5 mol %) and FC-72 (4.0 mL) was placed in a stainless pressure bottle and heated at 150 °C for 16 h. After having been cooled, toluene (5.0 mL) was added to the reaction mixture. After separation of the organic layers from FC-72, the FC-72 layer was washed with toluene (1.0 mL $\times$ 2). The combined organic layer was analyzed with GC to prove a quantitative yield of methyl 3-phenylpropionate. Evaporation of the organic layer followed by column chromatography (hexane/AcOEt = 10/1) furnished methyl 3-phenylpropionate as a colorless oil; yield: 328 mg (100%).

Transesterification in Single Organic Solvent System (Table 5, Entry 1)

Methyl 3-phenylpropionate (164 mg, 1.0 mmol), benzyl alcohol (130 mg, 1.2 mmol), **1aa** (86 mg, 0.05 mmol, 5 mol %) and toluene (5.0 mL) were added into a 50-mL, two-necked flask equipped with a condenser. The reaction mixture was heated at reflux for 6 h. After having been cooled, the reaction mixture was extracted with FC-72 (5 mL $\times$ 2). The combined

organic layer was analyzed with GC to prove a quantitative yield of benzyl 3-phenylpropionate. Evaporation of the FC-72 phase afforded quantitative recovery of **1aa** (86 mg).

Synthesis of *m*-Phenoxybenzyl Dichlorochrysanthemate (Eq. 2)

A test tube (50 mL) charged with methyl dichlorochrysanthemate (223 mg, 1.0 mmol, E/Z = 57/43), *m*-phenoxybenzyl alcohol (200 mg, 1.0 mmol), **1aa** (172 mg, 0.1 mmol, 10 mol %) and FC-72 (5.0 mL) was placed in a stainless pressure bottle and heated at 165 °C for 24 h. After having been cooled, toluene (5.0 mL) was added to the reaction mixture. After separation of the toluene and FC-72, the latter layer was washed with toluene (1.0 mL $\times$ 2). The combined organic layer was analyzed with GC to prove a quantitative yield of *m*-phenoxybenzyl dichlorochrysanthemate (E/Z = 54/46).

Acknowledgements

The authors are very grateful to Sumitomo Chemical for supplying samples of chrysanthemates.

References and Notes

- [1] T. Horváth, *Acc. Chem. Res.* **1998**, *31*, 641; D. P. Curran, *Angew. Chem. Int. Ed.* **1998**, *37*, 1174; E. G. Hope, A. M. Stuart, *J. Fluorine Chem.* **1999**, *100*, 75.
- [2] D. P. Curran, S. Hadida, S.-Y. Kim, Z. Luo, *J. Am. Chem. Soc.* **1999**, *121*, 6607; M. Larhed, M. Hoshino, S. Hadida, D. P. Curran, A. Hallberg, *J. Org. Chem.* **1997**, *62*, 5583; D. P. Curran, S. Hadida, M. He, *J. Org. Chem.* **1997**, *62*, 6714; B. Bucher, D. P. Curran, *Tetrahedron Lett.* **2000**, *41*, 9617.
- [3] J. Otera in *Advances in Detailed Reaction Mechanism*, Vol. 3, (Ed.: J. M. Coxon), JAI Press Inc., Greenwich, Conn., **1994**, pp. 167.
- [4] J. Otera, S. Ioka, H. Nozaki, *J. Org. Chem.* **1989**, *54*, 4013.
- [5] J. Xiang, A. Orita, J. Otera, *J. Organomet. Chem.* submitted.
- [6] J. Otera, *Chem. Rev.* **1993**, *93*, 1449.
- [7] Transesterification of β -keto esters was carried out using reactants in a 1:1 ratio, yet yields were not perfect (50–97%): S. P. Chavan, P. K. Zubaidha, S. W. Dantale, A. Keshavaraja, A. V. Ramaswamy, T. Ravindranathan, *Tetrahedron Lett.* **1996**, *37*, 233; B. S. Balaji, M. Sasidharan, R. Kumar, B. Chanda, *Chem. Commun.* **1996**, 707; D. E. Ponde, V. H. Deshpande, V. J. Bulbule, A. Sudalai, A. S. Gajare, *J. Org. Chem.* **1998**, *63*, 1058; B. P. Bandgar, V. S. Sadavarte, L. S. Uppalla, *Chem. Lett.* **2001**, 894.
- [8] For a preliminary report on this protocol, see: J. Xiang, S. Toyoshima, A. Orita, J. Otera, *Angew. Chem. Int. Ed.* **2001**, *40*, 3670.
- [9] Although any fluorocarbon solvents are employable, FC-72 is the solvent of our choice in this study because it is cheapest among them.
- [10] J. Otera, T. Yano, R. Okawara, *Organometallics* **1986**, *5*, 1167.
- [11] We have no data about the solubility of alcohols in FC-72 at elevated temperatures due to difficulties of measurement.
- [12] M. Elliott, A. W. Farnham, N. F. Janes, P. H. Needham, D. A. Pullman, J. H. Stevenson, *Nature* **1973**, *246*, 169.
- [13] J. Izumi, I. Shiina, T. Mukaiyama, *Chem. Lett.* **1995**, 141.
- [14] K. Wakasugi, T. Misaki, K. Yamada, Y. Tanabe, *Tetrahedron Lett.* **2001**, *41*, 5249.
- [15] G. V. Subbaraju, D. Rajasekhar, *Indian J. Chem. Sect. B* **1996**, *35*, 615.
- [16] G. Vernin, *J. Essent. Oil Res.* **1993**, *5*, 563.
- [17] S. Takahashi, L. A. Cohen, H. K. Miller, E. G. Peake, *J. Org. Chem.* **1971**, *36*, 1205.
- [18] R. C. Lloyd, M. Dickman, J. B. Jones, *Tetrahedron: Asymmetry* **1998**, *9*, 551.
- [19] K. Saitoh, I. Shiina, T. Mukaiyama, *Chem. Lett.* **1998**, 679.
- [20] G. Appendino, G. Cravotto, P. Gariboldi, B. Gabetta, E. Bombardelli, *Gazz. Chim. Ital.* **1994**, *124*, 1.
- [21] M. Tavares, R. Ramasseul, J. C. Marchon, *Catal. Lett.* **1990**, *4*, 163.

- [22] G. Trapani, A. Reho, A. Latrofa, G. Liso, *Synthesis* **1990**, 853.
[23] M. Al-Masum, Y. Yamamoto, *J. Am. Chem. Soc.* **1998**, *120*, 3809.
[24] H. J. Breunig, J. Probst, *J. Organomet. Chem.* **1998**, *571*, 297.
[25] A. Ahmed, H. Fukuda, K. Inomata, H. Kotake, *Chem. Lett.* **1980**, 1161.
[26] C. Kashima, S. Tsuruoka, S. Mizuhara, *Tetrahedron* **1998**, *54*, 14679.
[27] T. Ooi, H. Sugimoto, K. Maruoka, *Heterocycles* **2001**, *54*, 593.
[28] G. M. Poliskie, M. M. Mader, R. Van Well, *Tetrahedron Lett.* **1999**, *40*, 589.
[29] I. Shiina, S. Miyoshi, M. Miyashita, T. Mukaiyama, *Chem. Lett.* **1994**, 515.
[30] K. Manju, S. Trehan, *Chem. Commun.* **1999**, 1929.
[31] X-L. Fu, S-H. Wu, *Chin. J. Chem.* **1997**, *15*, 90.
[32] P. Langer, E. Holtz, I. Karime, N. N. R. Saleh, *J. Org. Chem.* **2001**, *66*, 6057.
[33] B. P. Bandgar, L. S. Uppalla, V. S. Sadavarte, *Green Chem.* **2001**, *3*, 39.
-