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Organic Synthesis Inside Particles in Water: Lewis Acid−Surfactant-Combined Catalysts for Organic Reactions in Water Using Colloidal Dispersions as Reaction Media

Kei Manabe, Yuichiro Mori, Takeshi Wakabayashi, Satoshi Nagayama, and Shū Kobayashi*

Contribution from the Graduate School of Pharmaceutical Sciences, The University of Tokyo, CREST, Japan Science and Technology Corporation (JST), Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

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Abstract: A Lewis acid−surfactant-combined catalyst (LASC) has been developed and applied to Lewis acid-catalyzed organic reactions in water. LASCs are composed of water-stable Lewis acidic cations such as scandium and anionic surfactants such as dodecyl sulfate and dodecanesulfonate and are easily prepared. These catalysts have been successfully used for various typical carbon−carbon bond-forming reactions such as aldol, allylation, and Mannich-type reactions in water. Furthermore, the results of aldol reactions in various solvents show that water is the best solvent for the LASC-catalyzed reactions. A preliminary kinetic study of the aldol reaction showed that the initial rate in water was 1.3×10^2 times higher than that in dichloromethane. In the workup procedure, it was demonstrated that centrifugation of the reaction mixture led to phase separation without addition of any organic solvents. The LASCs was found to form stable colloidal dispersions rapidly in the presence of reaction substrates in water, even when the substrates are solid. The characterization of the colloidal particles has been carried out by means of dynamic light scattering, light microscopy, transmission electron microscopy, and atomic force microscopy. These observations revealed the size of ~1 μm and the spherical shape of the particles. It was suggested that most of the substrates and catalyst molecules were concentrated in the spherical particles, which acted as a hydrophobic reaction environment and enabled the rapid organic reactions in water. In light of the increased demand for reduction of organic solvents in industry, the surfactant-aided Lewis acid catalysis described here may have practical consequences in organic synthesis.

Most chemical reactions of organic substances conducted in the laboratory as well as in industry need organic solvents as reaction media, although water is safe, benign, environmentally friendly, and cheap compared with organic solvents. Although today's environmental consciousness imposes the use of water as a solvent on both industrial and academic chemists, organic solvents are still used instead of water for mainly two reasons. First, most organic substances are insoluble in water, and as a result, water does not function as a reaction medium. Second, many reactive substrates, reagents, and catalysts are decomposed or deactivated by water. Our goal is to develop a novel catalytic system which enables the use of water as a solvent for a wide range of reactions of organic materials.[1]

The first drawback in the use of water (the solubility problem) may be overcome by using surfactants, which solubilize organic materials or form colloidal dispersions with them in water. Indeed, surfactants have been occasionally used in organic synthesis.[2] One very successful example is emulsion polymerization.[3] Some late transition metal-catalyzed reactions in water have been also conducted in the presence of surfactants or surfactant-like ligands.[4] In many other cases, however, large quantities of surfactant molecules compared with the reaction substrates are needed for the desired reactions to proceed efficiently, and thus, the systems are impractical even if water can be used as a solvent.[5] From the viewpoints of practicability and applicability, the surfactant-aided organic synthesis is still at the preliminary stage.

In the course of our investigations to circumvent the second drawback in the use of water (the decomposition problem), we have found that some metal salts such as rare earth metal triflates (triflate = trifluoromethanesulfonate) can be used as water-stable Lewis acids.[6] Although Lewis acid catalysis is one of the most powerful tools in modern organic synthesis,[7] it had to be

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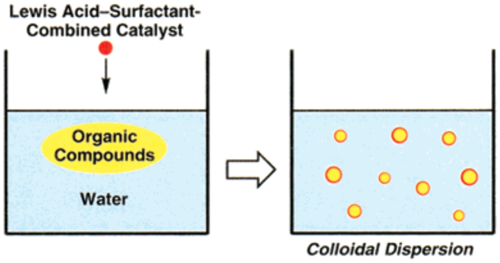


Figure 1. Illustration of the formation of the colloidal particles created by a LASC in the presence of organic substrates in water.

Chart 1

1a: $Sc(O_3SOC_{12}H_{25})_3$

1b: $Sc(O_3SC_{10}H_{21})_3$
1c: $Sc(O_3SC_{11}H_{23})_3$
1d: $Sc(O_3SC_{12}H_{25})_3$
1e: $Sc(O_3SC_{13}H_{27})_3$
1f: $Sc(O_3SC_{14}H_{29})_3$

generally carried out under strictly anhydrous conditions because of the water-labile nature of most Lewis acids. Although the water-stable Lewis acids mentioned above were found to catalyze several reactions efficiently in water-containing solvents, certain amounts of organic solvents such as tetrahydrofuran, ethanol, and acetonitrile still had to be combined with water to solubilize the substrates. To address this solubility issue, therefore, we planned to use surfactants for the Lewis acid-catalyzed reactions in water. Indeed, we found that scandium triflate ($Sc(OTf)_3$)-catalyzed reactions such as Mukaiyama aldol reactions of aldehydes with silyl enolates were greatly accelerated in the presence of an anionic surfactant, sodium dodecyl sulfate (SDS), in water ($Sc(OTf)_3$/SDS system).[8] This results prompted us to synthesize a more simplified catalyst, scandium tris(dodecyl sulfate) (**1a**, Chart 1). This new type of catalyst, "Lewis acid-surfactant-combined catalyst (LASC)", would act both as a catalyst to activate the substrate molecules and as a surfactant to form colloidal particles. That is, these colloidal particles would function as effective reaction media in water (Figure 1). In fact, we have quite recently demonstrated that LASCs also catalyze aldol reactions in water.[9] Independently, Engberts et al. reported their studies of Diels−Alder reactions in water using more than stoichiometric amounts of combined Lewis acid and micellar catalysts, in which a great rate enhancement was observed.[10] In this contribution, we describe detailed studies on LASC-catalyzed aldol reactions in water, application of LASCs to other types of Lewis acid-catalyzed reactions, and observation of the colloidal particles created by LASCs in the presence of reaction substrates in water.

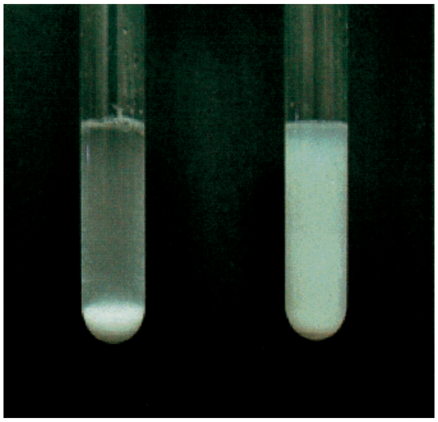


Figure 2. Mixtures of LASC **1d** in water (left) and LASC **1d** and benzaldehyde (1:10) in water (right).

Table 1. Effect of Alkyl Chain Length of LASCs on Aldol Reactions in Water

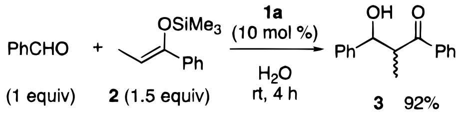
$$\underset{(1\ \text{equiv})}{\text{PhCHO}} + \underset{(1.5\ \text{equiv})}{\mathbf{2}} \xrightarrow[\text{H}_2\text{O, rt, 4 h}]{\text{LASC (10 mol \%)}} \mathbf{3}$$

LASC	yield (%)
$Sc(O_3SC_{10}H_{21})_3$ (**1b**)	60
$Sc(O_3SC_{11}H_{23})_3$ (**1c**)	68
$Sc(O_3SC_{12}H_{25})_3$ (**1d**)	83
$Sc(O_3SC_{13}H_{27})_3$ (**1e**)	76
$Sc(O_3SC_{14}H_{29})_3$ (**1f**)	19

Results and Discussion

Preparation of LASCs. LASC **1a** was easily prepared from scandium chloride ($ScCl_3$) and SDS. When these were mixed in water, **1a** precipitated because of its low solubility in water. LASC **1a** thus prepared was fully characterized by ^1H, ^{13}C, and ^{45}Sc NMR and elementary analysis. Other Sc(III)-based LASCs (**1b**−**f**, Chart 1) were also prepared from $ScCl_3$ and the corresponding sodium alkanesulfonates in similar ways.

Organic Reactions Catalyzed by LASCs in Water. 1. Aldol reaction. LASCs **1a,d** were first used for the aldol reaction of benzaldehyde with silyl enol ether **2** in water. While **1a** and **1d** only slightly dissolved in water, stable dispersions were formed upon addition of the aldehyde with stirring or vigorous mixing (Figure 2). Addition of **2**, followed by stirring at room temperature for 4 h, gave the desired aldol adduct **3** in high yields as shown in eq 1. It should be noted that hydrolysis of the silyl enol ether is not a severe problem under the reaction conditions despite the water-labile nature of silyl enol ethers under acidic conditions.



(1)

We then evaluated several Sc(III) alkanesulfonates (**1b**−**f**) with various alkyl groups in the aldol reaction in water. The results are summarized in Table 1. The dodecanesulfonate (**1d**) was found to give the best results, and the LASCs with shorter or longer alkyl chains resulted in lower yields.

We also found that LASC **1a** worked well in water rather than in organic solvents. The effect of solvents on the aldol reaction of benzaldehyde with **2** is shown in Table 2. While the reaction in water afforded the product in high yield, low yields were observed in other organic solvents. These solvent

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Table 2. Effect of Solvents on LASC (**1a**)-Catalyzed Aldol Reactions[a]

$$\underset{(1\ \text{equiv})}{\text{PhCHO}} + \underset{(1.5\ \text{equiv})}{\mathbf{2}} \xrightarrow[\text{H}_2\text{O, rt, 4 h}]{\mathbf{1a}\ (10\ \text{mol}\ \%)} \mathbf{3}$$

solvent	yield (%)
H_2O	92
CH_3OH	4
DMF	14
DMSO	9
CH_3CN	3
CH_3Cl_2	3
THF	trace
Et_2O	trace
toluene	trace
hexane	4
- (neat)	31

[a] When solvents other than H_2O an CH_3OH were used, the initially formed trimethylsilyl ether was converted to **3** (1 N HCl/THF (1/20), 0 °C).

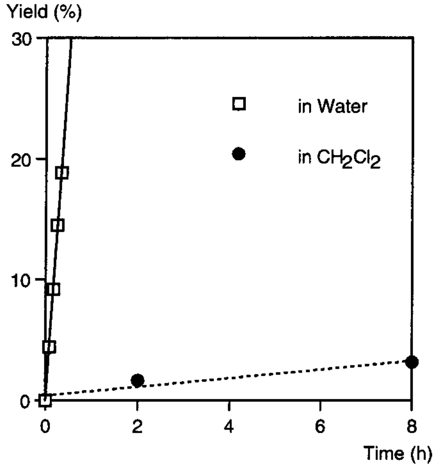
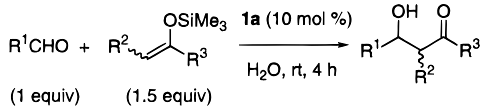


Figure 3. Initial rate kinetics for the aldol reaction in water and in CH_2Cl_2.

effects indicate that water plays an essential role in the LASC-catalyzed aldol reactions. The difference between water and organic solvents cannot be attributed to the solubility difference of **1a** in these solvents because, while **1a** is soluble in MeOH, DMF, DMSO, and THF, it is insoluble or only slightly soluble in the other solvents including water. To study the solvent effects in further detail, we carried out kinetic experiments of the aldol reaction in water and CH_2Cl_2 (Figure 3). The initial rate of the aldol reaction in water (2.61×10^{-5} M s^{-1}) was found to be 1.3×10^2 times higher than that in CH_2Cl_2 (1.95×10^{-7} M s^{-1}).[11]

Under neat conditions without using any solvents, the aldol reaction of benzaldehyde with **2** was also accelerated by LASC **1a** (Table 2). However, the yield (31%) was lower than that in water (92%) due to formation of many byproducts, showing the advantage of the use of water for the present reaction.[9b,c,12]

Table 3. LASC (**1a**)-Catalyzed Aldol Reactions in Water



R^1	R^2	R^3	product	yield (%)	*syn*/*anti*
Ph	Me	Ph	**3**	92	49/51
$Ph(CH_2)_2$	Me	Ph	**4**	88	44/56
PhCH=CH	Me	Ph	**5**	91	40/60
2-pyridyl	Me	Ph	**6**	84[a]	24/76
PhCO	Me	Ph	**7**	86	66/34
Ph	Me	Et	**8**	84	78/22
p-ClPh	Me	Et	**9**	91	79/21
$Ph(CH_2)_2$	Me	Et	**10**	82[a]	72/28
PhCH=CH	Me	Et	**11**	87	71/29
PhCH=CH	$-(CH_2)_4-$		**12**	85[a]	52/48
Ph	H	Ph	**13**	94[a,b]	
Ph	Me_2	SEt	**14**	98	
Ph	Me_2	OMe	**15**	80[a,b]	

[a] **1a** (20 mol %). [b] Silyl enolate (3 equiv).

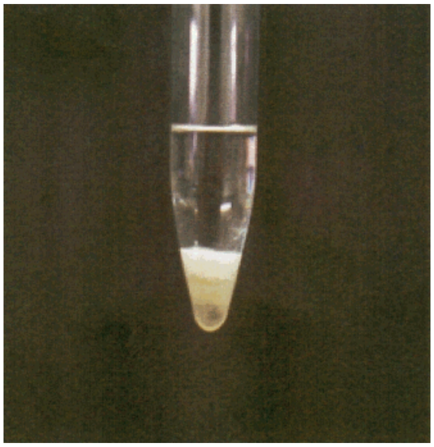


Figure 4. Separated phases after centrifugation of the reaction mixture of the aldol reaction of benzaldehyde with **2** in the presence of **1a**. Upper phase: water, middle phase: **1a**, lower phase: mixture of organic compounds.

Various substrates have been successfully used in the present LASC-catalyzed aldol reaction. Table 3 summarizes representative examples of the reactions. Aromatic as well as aliphatic, α,*β*-unsaturated, and heterocyclic aldehydes worked well. Even a solid aldehyde (*p*-chlorobenzaldehyde, mp 47−50 °C) also reacted smoothly. As for silyl enolates, silyl enol ethers derived from ketones, as well as ketene silyl acetals derived from a thioester, and an ester reacted well to give the corresponding adducts in high yields. It is noted that highly water-sensitive ketene silyl acetals reacted smoothly in water under these conditions. The very labile silyl enol ether derived from cyclohexanone could be also used in the present system to give adduct **12**, in contrast to the $Sc(OTf)_3$/SDS system,[8a] in which the silyl enol ether decomposed rapidly.

In the workup procedure for the aldol reactions stated above, the crude products were extracted with ethyl acetate after quenching the reactions. The addition of ethyl acetate in this procedure facilitates the phase separation between the organic and aqueous phase and makes the separation of organic products facile. It is more desirable, however, to develop a workup procedure without using any organic solvents such as ethyl acetate. In addition, the development of a protocol for recovery and reuse of the catalysts is indispensable to apply the LASC system to large-scale syntheses. Therefore, it is worthy to mention that centrifugation of the reaction mixture of a LASC-catalyzed aldol reaction led to phase separation without addition of organic solvents (Figure 4). After centrifugation at 3500 rpm for 20 min, the colloidal mixture became a tri-phasic system

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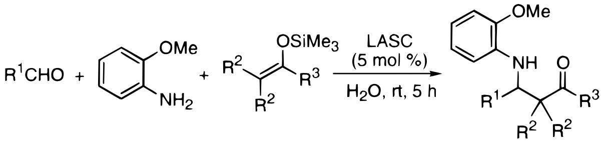
[11] Although we also attempted to determine second-order rate constants, their determination was not successful probably due to complicated kinetic behavior caused by hydrolysis of the silyl enol ether and effects of the product on the catalytic efficiency in this colloidal system.

[12] In addition, it was revealed that reactions under neat conditions had substrate limitation and sometimes lacked reproducibility of experiments. Kobayashi, S.; Busujima, T.; Nagayama, S. *Tetrahedron Lett.* **1998**, *39*, 1579.

Table 4. Three-Component Mannich-Type Reactions in Water



R^1	R^2	R^3	LASC	product	yield (%)
Ph	H	Ph	**16**	**17**	85
Ph	Me	OMe	**16**	**18**	90
Ph	Me	OMe	**1a**	**18**	72
2-furyl	Me	OMe	**16**	**19**	85
PhCH═CH	Me	OMe	**16**	**20**	73
$(CH_3)_2CHCH_2$	Me	OMe	**16**	**21**	93[a]

[a] The reaction was carried out at 0 °C.

where LASC **1a** was deposited between a transparent water phase and an organic product phase. The organic phase was checked by NMR (CD_3OD as a solvent), and **1a** was not detected in the NMR sample. It is noted that this procedure enables, in principle, the recovery and reuse of LASCs and the separation of the organic products without using organic solvents.

2. Mannich-Type Reaction. Mannich and related reactions provide a basic and useful method for the synthesis of β-amino carbonyl compounds, which constitute various pharmaceuticals, natural products, and versatile synthetic intermediates.[13] Recently, Lewis acid-mediated Mannich reactions using imines and silyl enolates as substrates have been developed.[14] Furthermore, three-component Mannich-type reactions, in which imines are generated from aldehydes and amines in situ, have also been reported.[8c,15]

LASC **1a** as well as copper bis(dodecyl sulfate) (**16**),[10,16] another type of LASC, were found to catalyze three-component Mannich-type reactions of aldehydes, amines, and silyl enolates in water. Copper-based LASC **16** gave better yields than **1a** did.[17] The results are shown in Table 4. Not only benzaldehyde but also heteroaromatic, α,β-unsaturated, and aliphatic aldehydes reacted smoothly to afford the desired adducts in high yields.

The three-component reactions proceed via the formation of imines, which are activated by a catalytic amount of the Lewis acidic metal cation in water. It should be noted that the dehydrative formation of the imines occurred smoothly in water, and that water-labile imines reacted efficiently to afford the desired Mannich-type adducts in high yields. It is also worthy to mention that the *o*-methoxyphenyl group on the nitrogen atom of the Mannich adducts can be readily removed by the action of cerium ammonium nitrate.[18]

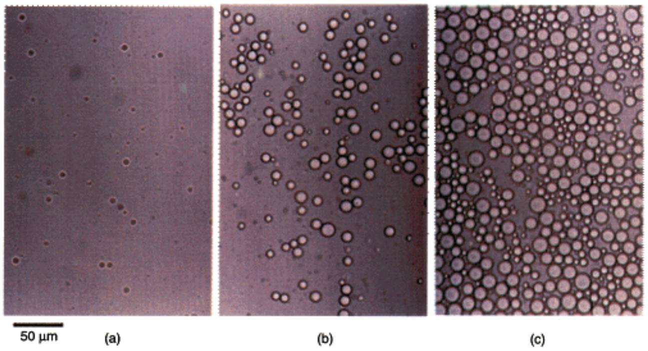
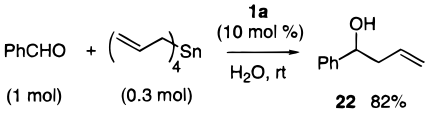


Figure 5. Mixtures of LASC **1d** and benzaldehyde as detected by light microscopy. (a) **1d**:benzaldehyde = 1:10; (b) **1d**:benzaldehyde = 1:20; (c) **1d**:benzaldehyde = 1:100. In all cases, the concentration of **1d** was 16.7 mM.

3. Allylation Reaction. The LASC-catalyzed reaction is also applicable to transformations using organometallics. The utility of organometallic reagents is now well recognized in organic synthesis, and recently, much attention has been focused on the reactions of allyl organometallics with carbonyl compounds in water-containing solvents.[19] By using the LASCs, we have attained Lewis acid-catalyzed allylation reactions in water (eq 2). Tetraallyltin was found to be the allylating reagent of choice, and the corresponding homoallylic alcohol **24** was obtained in 82% yield.



(2)

Characterization of the Colloidal Particles Created by LASCs. LASCs such as **1a** and **1d** do not dissolve in water to a significant extent due to their low solubility in water. On the other hand, when the LASC was mixed with organic substrates such as benzaldehyde in water, a white turbid mixture formed through colloid formation as shown in Figure 2. To characterize these stable colloidal particles, we undertook their observation by means of several tools.

The average sizes of the colloidal particles formed from **1d** and **1b** in the presence of benzaldehyde (LASC:PhCHO = 1:20) in water were measured by dynamic light scattering, and proved to be 1.1and 0.7 μm in diameter, respectively. These sizes are within a range of typical emulsion sizes created in water. In the case of LASC **1f**, which was an ineffective catalyst for the aldol reaction (Table 1), the dispersion system was stable only within a few minutes, and quick measurement of the particle size was indicated that its particle size was 0.4 μm in diameter. This low stability of the dispersion may be the reason for the low yield of the aldol adduct as shown in Table 1.

Light microscopic observations of the colloidal particles revealed their spherical shape (Figure 5). When LASC **1d** was mixed with benzaldehyde in a ratio of 1:10, both the spherical colloidal particles and the crystals of **1d** were observed (Figure 5a). As the amount of benzaldehyde increased (Figure 5b, c),

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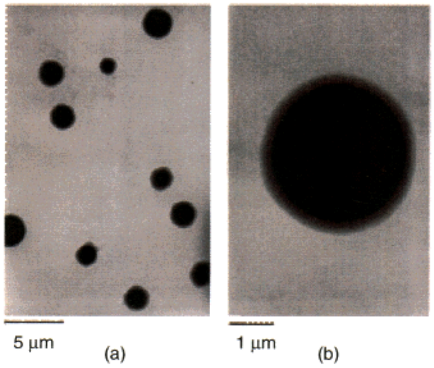

Figure 6. Mixture of LASC **1d** and benzaldehyde as detected by TEM. (a) ×2600; (b) ×10000.

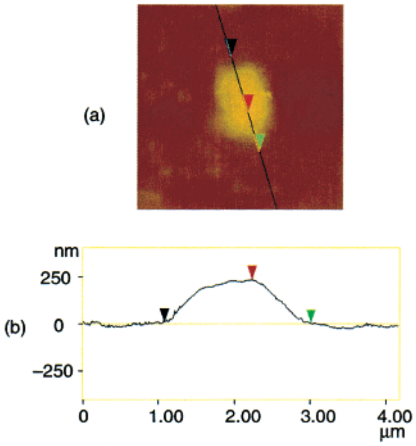

Figure 7. Mixture of LASC **1d** and benzaldehyde as detected by AFM. (a) Microscopic photograph of the colloidal particle; (b) vertical sectional view taken on the line of (a). The diameter of the particle (the distance between the two triangles at the bottom of the particle) is 1.93 μm. The height of the particle (the height of the position shown by the triangle at the top of the particle) is 0.226 μm.

the amount of the crystals of **1d** decreased, and finally, all of **1d** formed the spherical colloidal particles with the aldehyde in a **1d**:benzaldehyde ratio of 1:100 (Figure 5c). LASC **1a** also showed similar behavior.

We assumed at first that LASCs **1a** and **1d** form monolayers around the organic substrates in the colloidal dispersions, taking into account the low solubilities of these LASCs both in water and in benzaldehyde. Supposing that all of the particles formed in the mixture of **1d** and benzaldehyde in water have the diameter of 1 μm and that the molecular area of **1d** is 132 $Å^2$,[20] we found, however, only about 0.08 mol % **1d** compared with benzaldehyde is sufficient to form monolayers around the aldehyde. Therefore, we conclude that, when more than 0.08 mol % **1d** is used, an excess LASC should be stacked at the interface between water phase and benzaldehyde phase.

The shape and the size of the colloidal particles were also confirmed by transmission electron microscopy (TEM) (Figure 6) and atomic force microscopy (AFM) (Figure 7). The TEM pictures also reveal that scandium ions, which act as a stain in the pictures, are mainly located on the surface of the colloidal particles and inside the particles.

Mechanism of the Catalytic Reactions. From the observations stated above, we speculate the mechanism of the LASC-catalyzed reactions in water as follows. In the presence of organic substrates, LASC molecules form stable colloidal particles in which the surfactant moiety of the LASCs surrounds the organic substrates and the countercations are attracted to the surface of the particles through electrostatic interactions between the anionic surfactant molecules and the cations. Although each Sc(III) cation is hydrated by several water molecules, they can be readily replaced by a substrate because of the high exchange rate of Sc(III) for substitution of inner-sphere water ligands.[21] The substrates to be activated move to the interface from the organic phase, coordinate to the cations, and then react with nucleophilic substances there.

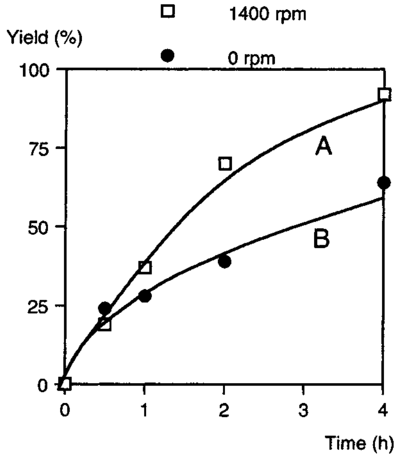

Figure 8. Plot of yield versus time for the aldol reaction of benzaldehyde with **2** in the presence of **1a** at stirring rates of 1400 (curve A) and 0 rpm (curve B).

In this mechanism, the roles of water in the reactions are assumed as follows:[22] (1) hydrophobic interactions in water lead to increase of the activity coefficient of the catalyst and the substrates, resulting in the higher reaction rate in water; (2) aggregation of the substrates through the hydrophobic interactions in water results in protection of water-labile substrates such as silyl enol ethers from their hydrolysis and in making formation of imines thermodynamically favorable; (3) in addition, hydration of Sc(III) ion and the counteranion by water molecules leads to dissociation of the LASC salt to form highly Lewis acidic species such as $[Sc(H_2O)_n]^{3+}$. The third assumption was made on the basis of the fact that the aldol reactions proceeded slowly under neat conditions (without any solvents). This role of water to generate highly Lewis acidic, cationic species may be also responsible for the acceleration of $Yb(OTf)_3$-catalyzed aldol reactions in THF by addition of certain amounts of water.[6d,e,23]

To support the mechanism in which the catalytic reactions take place at the interface of the colloidal particles, we studied the effect of stirring on LASC-catalyzed aldol reactions. If the rate-determining step of the aldol reaction, which has been suggested to be the step of the addition of the silyl enolate to the aldehyde, occurs at the interface, the rate of the reaction should depend on total area of the interface. Stirring of the reaction mixture would increase the total area of the interface and, as a consequence, lead to higher reaction rate.

Figure 8 shows the results of aldol reactions with or without stirring. With stirring throughout the reaction at 1400 rpm, the

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(20) This value is estimated as three times the minimum area (44 $Å^2$) of the sulfonate group in dodecanesulfonate. See: Rosen, M. J.; Gao, T.; Nakatsuji, Y.; Masuyama, A. *Colloids Surf., A* **1994**, *88*, 1.

(21) (a) Martell, A. E., Ed.; *Coordination Chemistry*; ACS Monograph 168; American Chemical Society: Washington, DC, 1978; Vol. 2. (b) Kobayashi, S.; Nagayama, S.; Busujima, T. *J. Am. Chem. Soc.* **1998**, *120*, 8287.

(22) Effects of water on organic reactions have been discussed. For example: (a) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159. (b) Otto, S.; Bertoncin, F.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1996**, *118*, 7702.

(23) Kobayashi, S.; Hachiya, I. *Tetrahedron Lett.* **1992,** *33*, 1625.

1a-catalyzed aldol reaction of benzaldehyde with silyl enol ether **2** completed in 4 h at 30 °C (Figure 8, curve A). On the other hand, when stirring was stopped after the initial 10 min, the reaction was gradually slowed (Figure 8, curve B). During the reactions without stirring, the reaction mixture, which was a white dispersion at the beginning, gradually underwent phase separation. These results suggest that the Sc-catalyzed reactions take place at the colloid interface, the total area of which is kept larger with stirring.

Conclusions

We have developed several useful carbon−carbon bond-forming reactions in water. The key is the use of newly developed Lewis acid-surfactant-combined catalysts. While most organic substrates are not soluble in water, stable colloidal dispersions are formed immediately by combining the catalyst and organic materials in water, and Lewis acid-catalyzed organic reactions proceed smoothly. In addition, the surfactant-type catalysts can be, in principle, removed from the reaction mixture without using organic solvents. Although several Lewis acid-catalyzed reactions have been demonstrated in this paper, this method will be applied to a great number of other Lewis acid-catalyzed reactions. Furthermore, the idea of the surfactant-type catalysts is not limited to Lewis acid catalysis, and may be applied to various types of catalytic reactions in water. In light of the increased demand for reduction of organic solvents in industry, new methods of catalysis in water should be urgently developed. The surfactant-type catalysts described in this article will contribute to progress in chemical processes by reducing the use of organic solvents.

Experimental Section

Preparation of 1a. To a solution of SDS (3.4 g, 11.6 mmol) in water (100 mL) was added a solution of $ScCl_3 \cdot 6H_2O$ (1.0 g, 3.85 mmol) in water (20 mL) at room temperature. White precipitates appeared immediately, and the mixture was stirred for 10 min. The white solid was filtered, washed with water (50 mL × 5), and dried (0.1 mmHg, 20 h) to afford **1a** (2.3 g, 71%); mp 240 °C; IR (KBr) 1165, 1300 cm^{-1}; ^1H NMR (CD_3OD) δ 0.89 (9H, t, $J = 6.7$ Hz), 1.20−1.44 (54H, m), 1.63−1.71 (6H, m), 4.11 (6H, t, $J = 6.6$ Hz); ^{13}C NMR (CD_3OD) δ 14.4, 23.7, 26.8, 30.3, 30.4, 30.5, 30.7, 30.7, 30.8, 30.8, 33.1, 70.6; ^{45}Sc NMR (CD_3OD) δ −109.3; Anal. Calcd for $C_{36}H_{75}O_{12}S_3Sc \cdot 3H_2O$: C, 48.30; H, 9.12; S, 10.74. Found: C, 48.15; H, 9.02; S, 10.53.

Typical Experimental Procedure for LASC-Catalyzed Aldol Reactions. To a LASC (0.05 mmol) in water (3 mL) was added an aldehyde (0.50 mmol) and, after 10 min, a silyl enolate (0.75 mmol). The mixture was stirred (∼1400 rpm) for 4 h at room temperature. Brine and a saturated aqueous $NaHCO_3$ solution were added, and the aqueous layer was extracted with ethyl acetate. The organic layer was dried and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the desired aldol adduct.

Typical Experimental Procedure for the LASC-Catalyzed Mannich-Type Reactions. To a LASC (0.025 mmol) in water (3 mL) was added an amine (0.50 mmol), a silyl enolate (0.75 mmol), and an aldehyde (0.50 mmol). The mixture was stirred (∼1400 rpm) for 5 h at room temperature. Brine and a saturated aqueous $NaHCO_3$ solution were added, and the aqueous layer was extracted with ethyl acetate. The organic layer was dried and concentrated under reduced pressure. The residue was purified by silica gel chromatography to afford the desired product.

Experimental Procedure for the 1a-Catalyzed Allylation Reaction. To a suspension of **1a** (0.025 mmol) in water (1.5 mL) was added benzaldehyde (0.25 mmol) and tetraallyltin (0.075 mmol). After stirring (∼1400 rpm) at room temperature for 10 h, the reaction was quenched with a saturated aqueous $NaHCO_3$ solution (5 mL). The product was extracted with ethyl acetate, washed with brine, dried over Na_2SO_4, concentrated, and purified by silica gel chromatography to give the desired product (82%).

Experimental Procedure for Kinetic Studies of the Aldol Reaction of Benzaldehyde with 2 (for Initial Rate Determination, Figure 3). The aldol reaction in water was carried out at 30 °C with a stirring of 1400 rpm as described in the typical procedure for aldol reactions in the presence of acetophenone (10−20 mol %) as an internal standard. At the times as given in Figure 3, a small portion of the reaction mixture was taken in a mixture of hexane and a saturated aqueous $NaHCO_3$ solution. Yields of the products in the hexane layer were measured by the comparison of the peak areas of the products and acetophenone by HPLC analysis (R-SIL-5A-06, YMC; hexane/ethyl acetate = 9/1; flow rate, 1 mL/min; retention time, acetophenone: 8.5 min, aldol product (*syn*): 18.0 min, aldol product (*anti*): 21.8 min). The yields were calculated as an average value of three experiments. For the reaction in CH_2Cl_2, the reaction was quenched with a saturated aqueous $NaHCO_3$ solution, and the products were extracted with CH_2Cl_2. After evaporation of the solvent, a mixture of 1 N HCl and THF (1:20) was added, and the whole was stirred at 0 °C for 1 h. After evaporation of the solvents, the mixture was dissolved in CH_2Cl_2, washed with a saturated aqueous $NaHCO_3$ solution and then brine, dried over Na_2SO_4, and concentrated. Acetophenone and hexane were added, and HPLC analysis was carried out as described above.

Light Scattering Measurement. A dispersion of a LASC and benzaldehyde (1:20) in water were diluted with water until the dispersion became transparent, and then light scattering measurement was performed by using Coulter Sub•micron Particle Analyzer, model N4MD (Coulter Electronics, Inc.).

TEM Analysis. One drop of the colloidal solution containing **1d** and benzaldehyde in water was placed onto a carbon-coated copper grid, and then the excess solution was immediately removed with the help of filter paper. The grid was kept in a desiccator for 3 days and was then observed by TEM (JEM-100CX, JEOL Co.).

AFM Analysis. One drop of the colloidal solution was placed onto a mica surface, and then the excess solution was immediately removed with help of filter paper. The surface of the mica was imaged with a Digital Instruments Nano Scope IIIa Scanning Probe Microscope Controller and software.

Experimental Procedure for a Study on the Effect of Stirring Rates (Figure 8). For the reaction at 1400 rpm, the procedure same as that for the initial rate study was used. For the reaction at 0 rpm, the reaction mixture was stirred at 1400 rpm for the initial 10 min after addition of **2** to a mixture of **1a**, benzaldehyde, and water at 30 °C. Then, the stirring was stopped, and the mixture was placed in a bath (30 °C) without stirring. At the time as given in Figure 8, the reaction was quenched, and the product was isolated. The yields of the product were isolated yields.

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Supporting Information Available: Experimental procedures, data for characterization of LASCs (**1a**−**f**) and compounds **17**−**21**, and ^1H and ^{13}C NMR spectra of **17**−**21** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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