

Scandium Trisdodecylsulfate (STDS). A New Type of Lewis Acid That Forms Stable Dispersion Systems with Organic Substrates in Water and Accelerates Aldol Reactions Much Faster in Water Than in Organic Solvents

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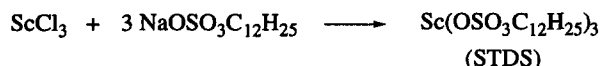
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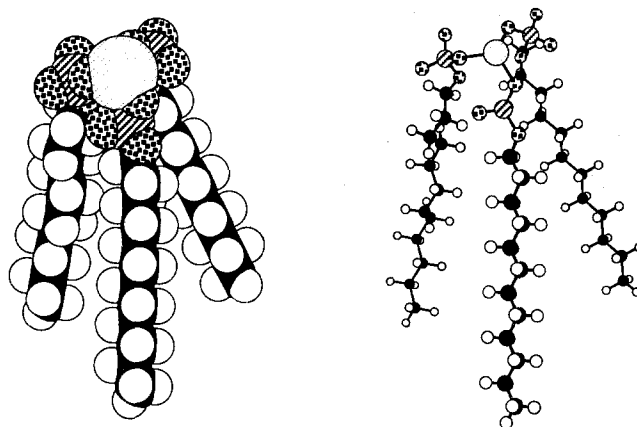
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Abstract: A new type of Lewis acid, scandium trisdodecylsulfate (STDS), was prepared. In the presence of a catalytic amount of STDS, aldol reactions of silyl enol ethers with aldehydes proceeded smoothly in water without using any organic solvents. It was proven that stable dispersion systems including the catalyst and organic substrates were formed in water and that catalytic activity in water was much higher than that in organic solvents. As far as we know, this is the first example of Lewis acid catalysis in stable dispersion system in water. © 1998 Elsevier Science Ltd. All rights reserved.

Organic reactions in water without using harmful organic solvents are now of great current interest especially in relation to today's environmental concerns.¹ However, the use of water in organic reaction processes is rather limited because many organic materials do not dissolve in water and many reactive intermediates and catalysts are decomposed in water.¹ Although Lewis acid-catalyzed reactions are of great current interest because of their unique reactivities, selectivities, and mild conditions used,² Lewis acids have been believed to be unstable in water and therefore not to be used in aqueous media. On the other hand, we have quite recently found that water-stable Lewis acids, lanthanide triflates, can be used in several carbon-carbon bond-forming reactions in aqueous solution.³ While several reactions proceeded smoothly in the presence of a catalytic amount of a lanthanide triflate in aqueous media, a certain amount of organic solvents such as THF, toluene, acetonitrile, ethanol, etc. had to be combined with water to promote the reactions efficiently. We have now designed and synthesized a new type of Lewis acid on the basis of our own findings. The new Lewis acid has been demonstrated to form stable dispersion systems with organic substrates and to work efficiently in water without using any organic solvents in aldol reactions of silyl enol ethers with aldehydes,^{4–6} one of the most representative Lewis acid-mediated reactions.

Quite recently we found that scandium triflate ($\text{Sc}(\text{OTf})_3$)-catalyzed aldol reactions of silyl enol ethers with aldehydes proceeded smoothly in water (without organic solvents) in the presence of a small amount of a surfactant.⁷ It was suggested that an excellent hydrophobic reaction field including micelles was created under these conditions in water. On the other hand, $\text{Sc}(\text{OTf})_3$ ⁸ is water-soluble and it was assumed that the concentration of $\text{Sc}(\text{OTf})_3$ in the hydrophobic reaction field would be low. To increase the scandium content in the hydrophobic field, we designed a Lewis acid-surfactant combined compound, scandium trisdodecylsulfate (STDS, $\text{Sc}(\text{OSO}_3\text{C}_{12}\text{H}_{25})_3$). It was expected that the ligands of STDS would create hydrophobic reaction fields while the scandium, an active Lewis acidic site, would be close to the hydrophobic fields. The synthesis was carried out by combining scandium chloride and sodium dodecylsulfate in water. STDS thus prepared was fully characterized by ¹H, ¹³C, and ⁴⁵Sc NMR and elementary analysis.^{9–11}





Scheme 1. Schematic representation of STDS. Space filling (left) and ball & stick models.

STDS was first used in the model reaction of (Z)-1-phenyl-1-trimethylsiloxypropene (**1**) with benzaldehyde in water. While STDS only slightly dissolved in water, a white dispersion was formed after adding the silyl enol ether and the aldehyde and stirring. After the mixture was stirred for 4 h at rt, the desired aldol adduct was obtained in a 92% yield. It is noted that oily particles including STDS and the organic substrates were dispersed stably in water, and that the desired aldol reaction proceeded smoothly in such a system. In addition, the catalytic activity of STDS was found to be much higher than $\text{Sc}(\text{OTf})_3$ in water. Namely, while the aldol adduct was produced in a 92% yield in the reaction of **1** with benzaldehyde using STDS (0.1 eq.) in 35 mM Triton X-100 solution at rt for 4 h, only a 21% yield of the adduct was obtained when $\text{Sc}(\text{OTf})_3$ (0.1 eq.) was used under the same reaction conditions.¹² We also prepared several similar scandium sulfates, sulfonates, and alkylbenzenesulfonates, and these scandium salts were evaluated in the above model aldol reaction (Table 1). As for the alkyl groups, the dodecyl groups gave the best results in all cases (sulfates, sulfonates, and alkylbenzenesulfonates). In the scandium sulfonate series, $\text{Sc}(\text{OSO}_2\text{C}_{12}\text{H}_{25})_3$ gave an 83% yield of the aldol adduct, while $\text{Sc}(\text{OSO}_2\text{C}_{10}\text{H}_{21})_3$ and $\text{Sc}(\text{OSO}_2\text{C}_{14}\text{H}_{29})_3$ afforded the products in 60% and 19% yields, respectively. The mixture of $\text{Sc}(\text{OSO}_2\text{C}_{12}\text{H}_{25})_3$ and the organic substrates or $\text{Sc}(\text{OSO}_2\text{C}_{10}\text{H}_{21})_3$ and the organic substrates formed stable dispersion systems, and their particle sizes were proved to be 1.1 μm and 0.7 μm , respectively.¹³ On the other hand, the mixture of $\text{Sc}(\text{OSO}_2\text{C}_{14}\text{H}_{29})_3$ and the organic substrates did not form a stable dispersion system.¹⁴ It was indicated from these results that an excellent large hydrophobic reaction field was formed when $\text{Sc}(\text{OSO}_2\text{C}_{12}\text{H}_{25})_3$ and the organic substrates were combined in water, and that the desired aldol reaction proceeded smoothly in the reaction field.¹⁵

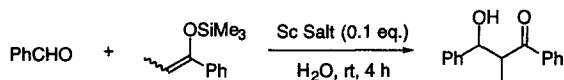


Table 1. Effects of Alkyl Chains of the Sc Salts^a

R	$\text{Sc}(\text{OSO}_3\text{R})_3$	$\text{Sc}(\text{OSO}_2p\text{-R-C}_6\text{H}_4)_3$	$\text{Sc}(\text{OSO}_2\text{R})_3$
$\text{C}_{10}\text{H}_{21}$	—	55	60 (0.7 μm) ^b
$\text{C}_{11}\text{H}_{23}$	—	—	68
$\text{C}_{12}\text{H}_{25}$	92	91	83 (1.1 μm) ^b
$\text{C}_{13}\text{H}_{27}$	—	—	76
$\text{C}_{14}\text{H}_{29}$	73	33	19 (0.4 μm) ^{b,c}
$\text{C}_{16}\text{H}_{33}$	—	14	12

^aNumbers shown in the columns are isolated yields (%). ^bParticle sizes of the dispersions. ^cSee Ref. 14.

It was also found that STDS worked well in water rather than in organic solvents. The effect of solvents on the aldol reaction of **1** with benzaldehyde is shown in Table 2. While the reaction proceeded smoothly in water, very slow reactions were observed in other organic solvents. A preliminary kinetic study was performed by using ^1H NMR in the model reaction of benzaldehyde with the silyl enol ether derived from 3-pentanone. It was shown that the aldol reaction proceeded 5×10^3 times faster in water than in dichloromethane.¹⁶

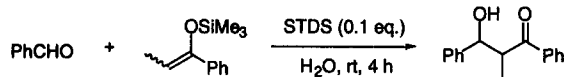


Table 2. Effects of Solvents^a

Solvent	Yield/%	Solvent	Yield/%
H ₂ O	92	CH ₂ Cl ₂	3
CH ₃ OH	4	THF	trace
DMF	14	Et ₂ O	trace
DMSO	9	toluene	trace
CH ₃ CN	3	hexane	4

^aWhile STDS is dissolved in CH₃OH, DMF, DMSO, and THF, it is not dissolved or slightly dissolved in other solvents.

Several examples of STDS-catalyzed aldol reactions were tested and the results are summarized in Table 3.^{17,18} In all cases, the reactions proceeded smoothly in the presence of a catalytic amount of STDS (0.1–0.2 eq.) at rt in water, to afford the corresponding aldol adducts in high yields, albeit moderate diastereoselectivities were observed. No organic solvents and surfactants were needed in the reactions. Not only aromatic, but also aliphatic and α,β -unsaturated aldehydes worked well under the standard conditions. As for silyl enolates, ketone-derived silyl enol ethers as well as ketene silyl acetals derived from thioesters and esters 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.

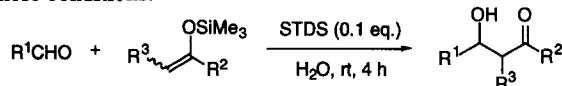


Table 3. STDS-Catalyzed Aldol Reactions in Water

R ¹	R ²	R ³	Yield/%	syn/anti	R ¹	R ²	R ³	Yield/%	syn/anti
Ph	Ph	Me	92	49/51	Ph	Ph	H	94 ^{a,b}	—
Ph(CH ₂) ₂	Ph	Me	88	44/56	Ph	EtS	Me ₂	98	—
PhCH=CH	Ph	Me	91	40/60	C ₅ H ₁₁	EtS	Me ₂	91	—
Ph	Et	Me	84	78/22	PhCH=CH	EtS	Me ₂	92	—
p-ClPh	Et	Me	91	79/21	Ph	MeO	Me ₂	80 ^{a,b}	—
Ph(CH ₂) ₂	Et	Me	82 ^a	72/28	2-pyridine	Ph	Me	84 ^a	24/76
PhCH=CH	Et	Me	87	71/29	PhCO	Ph	Me	86	66/34
PhCH=CH	-(CH ₂) ₄ -	Me	85 ^a	52/48					

^aSTDS (0.2 eq.). ^bSilyl enolate (3.0 eq.).

In summary, a Lewis acid-surfactant combined compound, STDS, was first prepared and has been shown to be an excellent catalyst in the aldol reactions of silyl enol ethers with aldehydes in water without using any organic solvents. The newly-designed Lewis acid has very different characteristics from conventional Lewis acids. In particular, it is noteworthy that stable dispersion systems were formed including the catalyst and organic substrates in water and that a much higher catalytic activity in water rather than in organic solvents has been achieved. Use of these types of Lewis acids will expand organic reactions in water and further investigations according to this line are now in progress in our laboratories.

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9. Preparation of scandium trisdodecylsulfate (STDS): To sodium dodecylsulfate (SDS, 3.4 g, 11.56 mmol) in H₂O (100 ml) was added ScCl₃·6H₂O (1.0 g, 3.85 mmol) in H₂O (20 ml) at room temperature. White precipitates appeared immediately, and the mixture was stirred for 10 min. The white solid was filtrated, washed with water (50 ml x 5), and dried (0.1 mmHg/20 °C, 20 h) to afford STDS (2.30 g, 71%). Mp 240 °C (dec.). IR (KBr) 1165, 1300 cm⁻¹; ¹H NMR (CD₃OD) δ 0.89 (t, 9H, J = 6.7 Hz), 1.20-1.44 (m, 54H), 1.63-1.71 (m, 6H), 4.11 (t, 6H, J = 6.6 Hz); ¹³C NMR (CD₃OD) δ 14.4, 23.7, 26.8, 30.3, 30.4, 30.5, 30.68, 30.71, 30.76, 30.83, 33.1, 70.6; ⁴⁵Sc NMR (CD₃OD) δ -109.3. Anal. Calcd for C₃₆H₈₁O₁₅S₃Sc (Sc(OSO₃C₁₂H₂₅)₃·3H₂O): C, 48.30; H, 9.12; S, 10.74. Found: C, 48.15; H, 9.02; S, 10.53.
10. We have recently reported a new micellar system, Sc(OTf)₃-sodiumdodecylsulfate (SDS).⁷ This system is very different from STDS. This means that Sc(OTf)₃ does not react with SDS to form STDS or related compounds. While the Sc(OTf)₃-SDS system makes a kind of micelle (not dispersion), the STDS system makes stable dispersion (probably not micelle but dispersion colloid). See also Ref. 17.
11. Recently, rate enhancement in the presence of Cu(II) dodecylsulfate in Diels-Alder reaction in water was reported. Otto, S.; Bertoncin, F.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* 1996, 118, 7702.
12. While a 92% yield of the aldol adduct was isolated from 1 and benzaldehyde using STDS in water, only less than 3 % yield of the adduct was obtained by using Sc(OTf)₃ under the same reaction conditions. In the case using Sc(OTf)₃ as a catalyst, decomposition of 1 was very fast.
13. Measurement was performed by using Coulter® Sub-micron Particle Analyzer, Model N4MD (Coulter Electronics, Inc.). We are grateful to Dr. Kazuhisa Takahashi, Department of Applied Chemistry, Faculty of Science, Science University of Tokyo (SUT), for measurement of the particle sizes. We also thank Prof. Minoru Ueno, SUT, for his helpful discussion on the dispersion systems.
14. The dispersion system was stable within a few minutes. Quick measurement of this system was indicated that its particle size was 0.4 μm.
15. Cf. (a) Rideout, D.; Breslow, R. *J. Am. Chem. Soc.* 1980, 102, 7816. (b) Breslow, R. in *Structure and Reactivity in Aqueous Solution*, Craner, C. J.; Truhlar, D. G. Eds., ACS Symposium Series 568; American Chemical Society: Washington, DC, 1994, p. 291. (c) Blokzijl, W.; Engberts, J. B. F. N. in *Structure and Reactivity in Aqueous Solution*, Craner, C. J.; Truhlar, D. G. Eds., ACS Symposium Series 568; American Chemical Society: Washington, DC, 1994, p. 303.
16. H₂O: k = 1.1 (l/mol·sec); CH₂Cl₂: k = 2.2 × 10⁻⁴ (l/mol·sec).
17. While a very labile silyl enol ether (such as the silyl enol ether derived from cyclohexanone) decomposed rapidly in the Sc(OTf)₃-SDS system, it could be successfully used in the STDS system (Table 3, run 8).
18. A typical experimental procedure for the STDS-catalyzed aldol reactions of silyl enol ethers with aldehydes: To STDS (0.05 mmol, 0.1 eq.) in water (3 ml) was added an aldehyde (0.50 mmol) and a silyl enol ether (0.75 mmol). The mixture was stirred for 4 h at rt. Brine was added and the aqueous layer was extracted with ethyl acetate. The combined 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.