Scandium triflate-catalyzed Strecker-type reactions of aldehydes, amines and tributyltin cyanide in both organic and aqueous solutions. Achievement of complete recovery of the tin compounds toward environmentally-friendly chemical processes

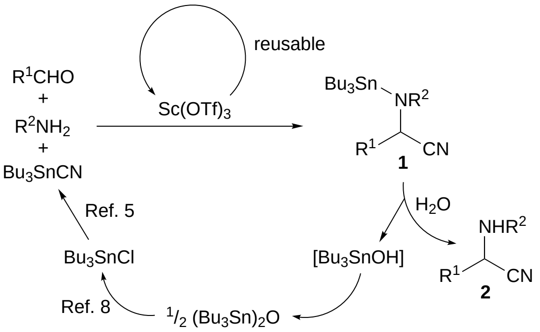
Shū Kobayashi,* Tsuyoshi Busujima and Satoshi Nagayama

Department of Applied Chemistry, Faculty of Science, Science University of Tokyo (SUT), and CREST, Japan Science and Technology Corporation (JST), Kagurazaka, Shinjuku-ku, Tokyo 162-0825, Japan

Scandium triflate ($CF_3SO_3^-$)-catalyzed Strecker-type reactions were successfully carried out by simply mixing aldehydes, amines and tributyltin cyanide at room temperature, to afford α-amino nitriles in high yields. The reactions proceeded smoothly in both organic and aqueous solutions, and complete recovery of the tin materials has been achieved.

The Strecker reaction provides one of the most efficient methods for the synthesis of α-amino nitriles, which are useful intermediates in the synthesis of amino acids[1] and nitrogen-containing heterocycles such as thiadiazoles, imidazoles, *etc.*[2] Although classical Strecker reactions have some limitations, use of trimethylsilylcyanide (TMSCN) as a cyano anion source provides promising and safer routes to these compounds.[1b,3] However, TMSCN is easily hydrolyzed in the presence of water, and it is necessary to perform the reactions under strict anhydrous conditions. In the course of our program to develop new synthetic reactions in aqueous media,[4] we have focused on tributyltin cyanide (Bu_3SnCN).[5] Bu_3SnCN is stable in water and a potential cyanate source, albeit there have been no reports of Strecker-type reactons using Bu_3SnCN to the best of our knowledge. Here we report scandium triflate ($CF_3SO_3^-$)-catalyzed Strecker-type reactions of aldehydes, amines and Bu_3SnCN in both organic and aqueous solutions. Complete recovery of the toxic tin compounds is also described.

We chose valeraldehyde, diphenylmethylamine and Bu_3SnCN as models, and the Strecker-type reaction was first performed in the presence of 10 mol% of $Sc(OTf)_3$ in organic solvents. The reactions proceeded smoothly at room temperature in acetonitrile, benzene, dichloromethane and toluene to afford the corresponding α-amino nitrile in high yields. Among these solvents tested, acetonitrile–toluene (1 : 1) gave the best yield (84%). It was found that no dehydration reagents such as molecular sieves, $MgSO_4$, drierite, *etc.* were needed in these reactions. We then performed the reaction in water. It was found that the model Strecker-type reaction also proceeded smoothly in the presence of a catalytic amount of $Sc(OTf)_3$‡ to give the corresponding α-amino nitrile in a 94% yield. No surfactant was needed in this reaction.[4a–c] The reaction is assumed to proceed *via* imine formation and successive cyanation,§ and it is noted that the dehydration process (imine formation) proceeded smoothly in water. Moreover, it was found that the reaction rate in water was almost the same as those in organic solvents.



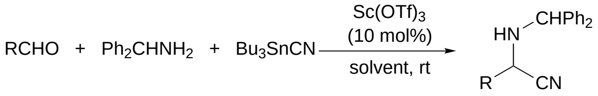
Scheme 1 Recycle system of the novel Strecker-type reactions

While the desired reaction proceeded smoothly, it was thought that use of the toxic tin reagent might restrict the application of the reaction.[6] We then tried to recover the tin materials after the reaction (Scheme 1). The Strecker-type reaction was performed using an equimolar amount of an aldehyde and an amine, and a slight excess of Bu_3SnCN. After the reaction was completed, excess Bu_3SnCN was treated with a weak acid to form bis(tributyltin) oxide.[7] On the other hand, the adduct, α-(tributylstannylamino) amino nitrile (**1**), was hydrolyzed by adding water to produce α-amino nitrile **2** and tributyltin hydroxide, which was readily converted to bis(tributyltin) oxide.[7] Thus, all tin sources were converted to bis(tributyltin) oxide, which could be recovered quantitatively (*vide infra*). It has already been reported that bis(tributyltin) oxide can be converted to tributyltin chloride[8] and then to Bu_3SnCN.[5] Since the catalyst, $Sc(OTf)_3$, is also recoverable and reusable,[9] the present Strecker-type reactions represent a completely recyclable system.

Several examples of the Strecker-type reaction are shown in Table 1. In all cases, including aromatic, aliphatic, heterocyclic, as well as α,β-unsaturated aldehydes, the reactions proceeded smoothly to afford the corresponding α-amino nitriles in high yields. While the adducts, α-(*N*-benzhydryl)amino nitriles, were readily converted to α-amino acids,[10] the present Strecker-type reactions using other amines such as aniline and benzylamine also proceeded smoothly to afford the corresponding adducts in high yields.

A typical experimental procedure is as follows. To a solution (3 ml) of aq. $Sc(OTf)_3$ (0.05 mmol, 10 mol%) were added an amine (0.5 mmol), Bu_3SnCN (0.75 mmol) and an aldehyde (0.5

Table 1 $Sc(OTf)_3$-catalyzed Strecker-type reactions



R	Yield (%) [in MeCN–toluene (1 : 1)]	Yield (%) (in H_2O)
Ph	88	88
PhCH=CH	83	84
2-Furyl	88	89
$Ph(CH_2)_2$	94	79
Bu	84	94
c-C_6H_{11}	86	94

mmol) successively, and the mixture was stirred at room temperature. After 20 h, the mixture was diluted with water, and the aqueous layer was extracted with ethyl acetate. Sc(OTf)$_3$ was recovered from the aqueous layer quantitatively and reused.[9] The combined organic layers were dried, filtered, and concentrated. The crude materials were treated with THF–1 M HCl (4 : 1, 3 ml) at room temperature for 1 h. Hexane and aq. saturated NaHCO$_3$ were added and the aqueous layers were extracted with ethyl acetate. The combined organic layers were dried, filtered and concentrated. The adduct was purified by column chromatography on alumina to afford the pure desired α-amino nitrile. Bis(tributyltin) oxide was recovered quantitatively (> 98%) by eluting with MeOH.

In summary, we have developed Strecker-type reactions of aldehydes, amines and Bu$_3$SnCN using Sc(OTf)$_3$ as a catalyst. The reactions proceeded smoothly in both organic and aqueous solutions to afford α-amino nitriles in high yields. Note that the experimental procedure is very simple; just mixing the three components and Sc(OTf)$_3$ in an appropriate solvent at room temperature. Moreover, complete recovery of the tin materials in these reactions has been achieved. While many useful tin reagents have been developed, their toxicity has sometimes limited their use in organic synthesis. This report provides a solution to this problem, and moves us further toward environmentally-friendly chemical processes.

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Notes and References

† E-mail: skobayas@ch.kagu.sut.ac.jp

‡ We found that rare earth triflates are stable Lewis acids in water.[9] Other rare earth triflates are also available in the present Strecker-type reactions.

§ It was confirmed that imine formation was much faster than cyanohydrin ether formation under these reaction conditions.

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