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A chiral triaminosulfonium salt: design and application to catalytic asymmetric synthesis

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Abstract

The first chiral triaminosulfonium salt, tris((*S*,*S*)-3,4-diphenylpyrrolidino)sulfonium difluorotriphenylstannate, catalyzes trifluoromethylation of benzaldehyde with (trifluoromethyl)trimethylsilane to give the corresponding optically active alcohol with 52% ee. © 1999 Elsevier Science Ltd. All rights reserved.

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Tris(dialkylamino)sulfonium difluorotrimethylsilicate (TASF)[1] has been proven as an effective Lewis base that mediates some important reactions such as aldol condensation of silyl enol ethers,[2] Michael addition of ketene silyl acetals,[3] stereoselective reduction of β-keto amides,[4] and γ-selective coupling of allyltrifluorosilanes with electrophiles.[5] However, asymmetric catalysis using chiral TASF analogs is not known. We became very interested in the development of chiral triaminosulfonium salts as asymmetric catalysts for enantioselective synthesis. The present paper discloses herein the design of chiral TASF analogs and their first application to catalytic asymmetric synthesis.

TASF is highly hygroscopic and easy to decompose to the corresponding bifluoride **1**. This instability due to the difluorotrimethylsilicate moiety is considered to disadvantage chiral TASF analogs in asymmetric synthesis. Thus, we began by preparing an achiral triaminosulfonium difluorotriphenylstannate and evaluating its stability and ability as a Lewis base catalyst.[6] Conversion of tripiperidinosulfonium chloride[7] to the corresponding fluoride using the anion-exchange resin, Amberlyst® A-26, prepared as the F^- form, followed by treatment with triphenyltin fluoride, gave the difluorotriphenylstannate salt **2** (Fig. 1). As expected, **2** was non-hygroscopic and stable to moisture and acts as an efficient catalyst for aldol reaction of ketene silyl acetals.

We next synthesized several chiral triaminosulfonium difluorotriphenylstannates including the tris((*S*,*S*)-3,4-diphenylpyrrolidino)sulfonium salt **3** which was prepared using almost the same procedure as **2** as shown in Scheme 1. (*S*,*S*)-3,4-Diphenylpyrrolidine (**4**), prepared according to the method reported by Nakajima et al.,[8] was converted to the diaminosulfide **5** in 49% yield by successive treatment

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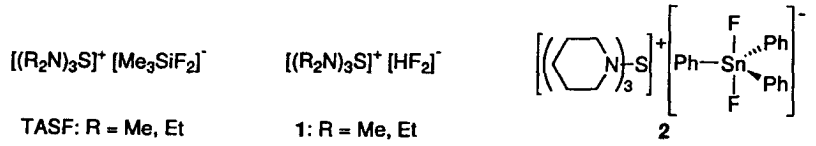
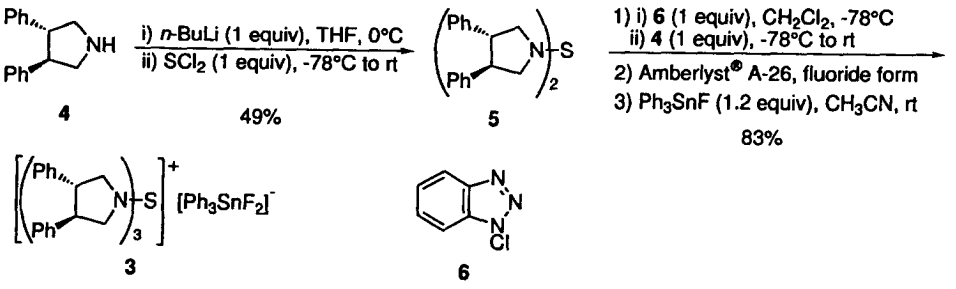


Figure 1.

with *n*-BuLi and sulfur dichloride. The diaminosulfide **5** was oxidized with 1-chlorobenzotriazole (**6**) and treated with the pyrrolidine **4** to afford the corresponding triaminosulfonium chloride which was converted to the desired product **3** in 83% overall yield by treatment with the anion-exchange resin and triphenyltin fluoride.[9] The other chiral triaminosulfonium salts were prepared in the same manner.



Scheme 1. Preparation of tris((*S*,*S*)-3,4-diphenylpyrrolidino)sulfonium difluorotriphenylstannate (**3**)

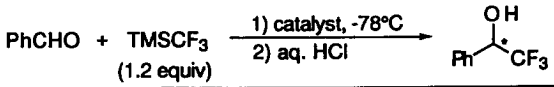
We have previously reported the first asymmetric trifluoromethylation of carbonyl compounds with (trifluoromethyl)trimethylsilane ($TMSCF_3$) catalyzed by chiral quaternary ammonium fluorides prepared from cinchonine.[10] The desired products, optically active 1-substituted-2,2,2-trifluoroethanols, are promising synthetic intermediates for medicinal agents and electronic materials such as liquid crystals. However, this transformation is not satisfactory for enantioselectivity. Thus, we decided to evaluate the ability of the newly prepared chiral triaminosulfonium salts to promote the trifluoromethylation of aldehydes.

The trifluoromethylation of benzaldehyde, chosen as a model substrate, with $TMSCF_3$ was carried out using 10 or 20 mol% of triaminosulfonium salts (**3** and **7**–**12**) at −78°C. The results are summarized in Table 1. Sulfonium salt **3** having three (*S*,*S*)-3,4-diphenylpyrrolidine moieties showed a modest but significant enantioselection in toluene (entry 1), while replacement of the chiral moiety with the piperidino group resulted in complete loss of selectivity (entries 2 and 3). Use of Et_2O as a reaction medium remarkably improved the enantioselectivity. The reaction in the presence of 10 mol% **3** was carried out in Et_2O at −78°C for 24 h to provide (*S*)-α-(trifluoromethyl)benzyl alcohol in 96% yield and with 52% ee (entry 4).[11] The attachment of substituents, e.g., methyl, trifluoromethyl and methoxy groups, on the benzene rings in **3** dramatically suppressed the optical yields (entries 5–7). Although replacement of the anion moiety with fluoride in **3** accelerated the reaction, the obtained enantiomeric excess was rather low (entry 8).

Table 2 summarizes the results obtained from the reaction of a variety of aldehydes using 10 mol% of catalyst **3** in Et_2O at −78°C for 24 h. In all cases, the chemical yields were excellent-to-good. However, 2- or 4-substituted-benzaldehydes could not overcome benzaldehyde in the enantioselection (entries 2–5). The enantiomeric excesses obtained from 1-naphthaldehyde, (*E*)-cinnamaldehyde and cyclohexanecarboxaldehyde were also modest (entries 6–8).

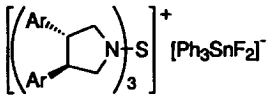
In conclusion, we have developed the first chiral TASF analog, tris((*S*,*S*)-3,4-diphenylpyrrolidino)-sulfonium difluorotriphenylstannate (**3**), which functions as a Lewis base catalyst for the trifluorome-

Table 1
Enantioselective trifluoromethylation of benzaldehyde with $TMSCF_3$ in the presence of triaminosulfonium salts

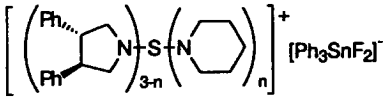


Entry	Catalyst (mol%)	Solvent	Reaction time (h)	Yield (%)[a]	ee (%)[b]
1	**3** (10)	toluene	24	88	16 (*S*)
2	**7** (20)	toluene	65	82	4 (*S*)
3	**8** (20)	toluene	65	75	2 (*S*)
4	**3** (10)	Et_2O	24	96	52 (*S*)
5	**9** (10)	Et_2O	24	92	26 (*S*)
6	**10** (10)	Et_2O	24	64	5 (*R*)
7	**11** (10)	Et_2O	24	23	4 (*S*)
8	**12** (10)	Et_2O	5	91	11 (*S*)

[a] Isolated yield.
[b] Determined by HPLC analysis using a chiral column (CHIRALCEL® OD-H, Daicel Chemical Industries, Ltd.).



3: Ar = Ph
9: Ar = 3,5-$Me_2C_6H_3$
10: Ar = 4-$CF_3C_6H_4$
11: Ar = 4-$MeOC_6H_4$



7: n = 1
8: n = 2

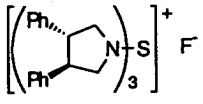


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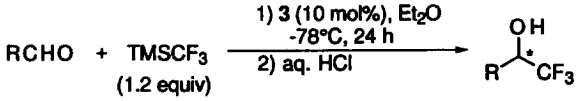
Table 2
Enantioselective trifluoromethylation of various aldehydes with $TMSCF_3$ catalyzed by triaminosulfonium salt **3**



Entry	RCHO	Yield (%)[a]	ee (%)[b]
1	PhCHO	96	52 (*S*)
2	4-$MeOC_6H_4CHO$	97	37
3	4-$CF_3C_6H_4CHO$	90	24
4	4-ClC_6H_4CHO	93	30
5	2-MeC_6H_4CHO	98	33
6	1-naphthaldehyde	71	12
7	(*E*)-PhCH=CHCHO	99	18
8	$C_6H_{11}CHO$	88	10[c]

[a] Isolated yield.
[b] Determined by HPLC analysis using a chiral column (CHIRALCEL® OD-H and CHIRALPAK® AD, Daicel Chemical Industries, Ltd.).
[c] Determined by HPLC analysis of the corresponding 3,5-dinitrobenzoate (CHIRALCEL® OD-H, Daicel Chemical Industries, Ltd.).

thylation and gives (*S*)-α-(trifluoromethyl)benzyl alcohol of 52% ee. Attempts to obtain optimal optical yields and further applications of catalyst **3** to other catalytic asymmetric reactions are now being carried out.

1. Typical procedure for trifluoromethylation with $TMSCF_3$. (*S*)-α-(Trifluoromethyl)benzyl alcohol

To a suspension of catalyst **3** (54 mg, 0.05 mmol) in Et_2O (1.5 ml) was added benzaldehyde (51 μl, 0.5 mmol) and $TMSCF_3$ (89 μl, 0.6 mmol) at −78°C under argon. After stirring for 24 h, the reaction mixture was poured into saturated aqueous NH_4Cl and extracted with Et_2O. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The oily residue was dissolved in a mixture of THF (10 ml) and 2 M HCl (1 ml) and stirred at room temperature for 1 h, followed by extraction with Et_2O. The ethereal extracts were washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, EtOAc:*n*-hexane, 1:10) to afford (*S*)-α-(trifluoromethyl)benzyl alcohol (85 mg, 96% yield) as a colorless oil. $[\alpha]_D^{25}$ +19.9 (*c* 0.85, $CHCl_3$) (52% ee); IR (neat): 3405, 2911, 1708, 1267, 1170, 1128, 705 cm^{-1}; ^1H NMR ($CDCl_3$, TMS): δ 2.60 (d, *J*=4.6 Hz, 1H), 5.02 (dq, *J*=4.6, 6.7 Hz, 1H), 7.35–7.52 (m, 5H); ^{19}F NMR ($CDCl_3$, CCl_3F): δ −79.02 (d, J=6.7 Hz, 3F); MS: *m/z* 176 [M^+], 107, 789, 69.

References

1. (a) Middleton, W. J. U.S. Pat. 3940402, 1976; *Chem. Abs.* **1976**, *85*, P6388j. (b) Middleton, W. J. *Org. Synth.* **1985**, *64*, 221–225.
2. Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1981**, *103*, 2106–2108.
3. RajanBabu, T. V. *J. Org. Chem.* **1984**, *49*, 2083–2089.
4. Fujita, M.; Hiyama, T. *J. Am. Chem. Soc.* **1985**, *107*, 8294–8296.
5. Hatanaka, Y.; Ebina, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1991**, *113*, 7075–7076.
6. Tetrabutylammonium difluorotriphenylstannate is not hygroscopic or hydrated. See: Gingras, M. *Tetrahedron Lett.* **1991**, *32*, 7381–7384.
7. (a) Minato, H.; Okuma, K.; Kobayashi, M. *J. Chem. Soc., Chem. Commun.* **1975**, 868–869. (b) Minato, H.; Okuma, K.; Kobayashi, M. *J. Org. Chem.* **1978**, *43*, 652–658.
8. Nakajima, M.; Tomioka, K.; Koga, K. *Tetrahedron* **1993**, *49*, 9735–9750.
9. Tris((*S*,*S*)-3,4-diphenylpyrrolidino)sulfonium difluorotriphenylstannate (**3**): colorless needles; mp 160.5–160.9°C (Et_2O–toluene); $[\alpha]_D^{23}$ −71.5 (*c* 0.51, CH_3CN); IR (KBr): 3654, 1602, 1497, 1128, 1017, 700 cm^{-1}; ^1H NMR (CD_3CN, TMS): δ 3.53–3.88 (m, 12H), 4.10–4.22 (m, 6H), 7.12–7.40 (m, 39H), 7.85–8.24 (m, 6H); ^{19}F NMR (CD_3CN, CCl_3F): δ −159.5–161.5 (m, 2F); MS (FAB): *m/z* 699; HRMS calcd for $C_{48}H_{48}N_3S$ [sulfonium cation]: 698.3569. Found: 698.3578; Anal. calcd for $C_{66}H_{63}F_2N_3SSn$: C, 72.93; H, 5.84; N, 3.87; F, 3.50. Found: C, 72.70; H, 5.94; N, 4.14; F, 4.04.
10. Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1994**, *35*, 3137–3138.
11. The absolute configuration of the major enantiomer was determined to be *S* by comparison of the $[\alpha]_D$ value with the reported data. See: Pirkle, W. H.; Sikkenga, D. L.; Pavlin, M. S. *J. Org. Chem.* **1977**, *42*, 384–387.