In a typical catalytic dihydroxylation, the **3b** material (100 mg) was added to a mixture of the olefin (1.6 mmol), NMO (1.6 mmol), and water (200 µL) in *t*BuOH:CH_2Cl_2 (3 mL; 2:1) solvent. The mixture was stirred at room temperature and regularly analyzed by GC.

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Stereoselective Nucleophilic Trifluoromethylation of *N*-(*tert*-Butylsulfinyl)-imines by Using Trimethyl(trifluoromethyl)-silane**

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Trifluoromethylated amines are important building blocks for pharmaceutical research.[1] The CF_3 group, because of its strongly electron withdrawing nature, lowers the basicity of the amide bond towards nonspecific proteolysis[2] when these amines are incorporated into peptides, as well as modify the solubility and desolvation properties.[3] In spite of its prime importance in the drugs industry, direct asymmetric synthesis of trifluoromethylated amines is a challenge. Pirkle et al.[4] and Mosher and Wang[5] prepared 2,2,2-trifluoro-1-phenylethylamine, and Soloshonok and Ono[6] recently reported an elegant method for the preparation of perfluorinated amines by a novel [1,3]-proton shift reaction. However, all of these methods require fluorinated ketones. Nucleophilic transfer of "CF_3" to nitrones and imines for direct preparation of trifluoromethylated amines was recently achieved by Nelson et al.[7] and Blazejewski et al.,[8] respectively. These methods suffer from low yield and lack generality. We now report the first stereoselective synthesis of trifluoromethylated amines by using $TMSCF_3$ **2** (TMS = $SiMe_3$).

Our systematic investigation began as an extension of our earlier work,[9] based on the fact that imines are less electrophilic than carbonyl compounds, and that O–Si bonds are stronger than N–Si bonds. We predicted that strongly electrophilic imines might be a solution to this problem under noncatalytic conditions. When *N*-sulfonylaldimines[10] were used as imine sources the reaction indeed proceeded smoothly in the presence of CsF and gave only the trifluoromethylated adducts in 45–95 % yield. Next we turned our attention to sulfinylimines **1** to make this reaction stereoselective. When chiral sulfinylimines[11] were subjected to similar reaction conditions little or no products were obtained. Sulfinylimines were recovered intact, but $TMSCF_3$ decomposed. We surmised that sulfinylimines are not reactive enough to add $TMSCF_3$. Use of different aprotic solvents and excess of reagents was not helpful. When an excess of $TMSCF_3$ was used, a number of unidentified fluorinated products with little or none of the expected adduct were obtained. TMS-Imidazole,[8] was recently reported to facilitate addition of $TMSCF_3$ to imines. In our case, however, it was ineffective. In all experiments the starting material was recovered.

The above results indicate that $TMSCF_3$ decomposes prior to reacting with the starting material. Hence, we thought that increasing the substrate concentration might be a solution to this problem. Indeed, when neat $TMSCF_3$ was added to a concentrated solution of the imines, the desired adduct was obtained. The mass balance corresponds to recovered starting material. Attempts to complete the reaction by using excess of reagent in different solvents was, however, unsuccessful. Imines were treated with $TMSCF_3$ in the presence of a stoichiometric amount of CsF to give the corresponding trifluoromethylated sulfinamides in 50–65 % yields of isolated products (Table 1, entries 1–7, values in parentheses). Imines with acidic α-hydrogen atoms gave lower yields because of competitive deprotonation. The diastereoselectivity was not very high.

During these investigations we thus encountered two problems: a) Conversion of imines was incomplete even in the presence of excess $TMSCF_3$ and CsF; b) imines with an α-hydrogen atom failed to react with $TMSCF_3$ because of the basic nature of CsF. However, we overcame these problems by employing a nonmetallic fluoride source. DeShong et al. reported that tetrabutylammonium difluorotriphenylsilicate (TBAT),[12] a soluble fluoride source, is very effective for nucleophilic displacement reactions. We found that TBAT is also effective in our system. Reaction of *N*-sulfonylaldimines

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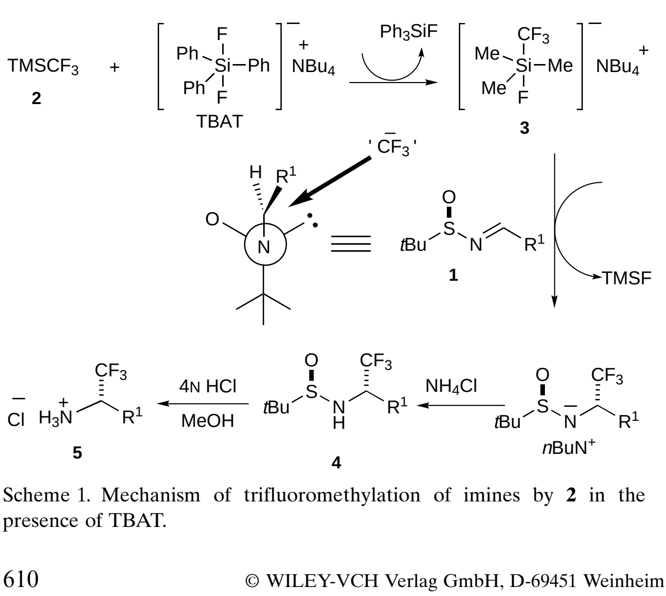
Table 1. Nucleophilic trifluoromethylation of sulfinylimines **1** with CsF or TBAT as fluoride source (see Scheme 1). Unless otherwise mentioned, yields and diastereomeric ratios are for TBAT as the fluoride source.

		Sulfinamide **4**		Amine **5**	
Entry	R^1 in **1**	Yield [%][a, g]	$(R_S,S)/(R_S,R)$[b, c]	Config.[e]	$[\alpha]_D^{25}$[f]
1	pClC$_6$H$_4$	95 (53)	> 99 (85:15)	*S*	+ 25.9 (c = 0.72)
2	pBrC$_6$H$_4$	90 (50)	> 99 (80:20)	*S*	+ 11.2 (c = 1.5)
3	pCF$_3$C$_6$H$_4$	84 (57)	95:05 (85:15)	*S*	+ 8.4 (c = 1.5)
4	2-pyridyl	95 (60)	99:01 (90:10)	*S*	+ 11.7 (c = 2.0)
5	3-pyridyl	92 (60)	99:01 (85:15)	*S*	+ 14.9 (c = 1.0)
6	2-furyl	85 (55)	97:03 (80:20)	*S*	+ 6.6 (c = 2.0)
7	Ph	80 (65)	97:03 (75:25)	*S*[d]	+ 28.6 (c = 0.65)
8	2-Naphthyl	83	96:04	*S*	+ 26.0 (c = 0.75)
9	9-Anthryl	90	99:01	*S*	+ 28.8 (c = 3.0)
10	Cyclohexyl	88	99:01	*S*	− 2.2 (c = 3.0)
11	tBu	75	99:01	*S*	+ 11.3 (c = 0.65)
12	PhCH$_2$CH$_2$	84	90:10	*S*	− 15.7 (c = 1.5)

[a] In parentheses yields with CsF as fluoride source. [b] In parentheses d.r. values with CsF as fluoride source. [c] Diastereomeric ratios were determined by ^{19}F NMR spectroscopy on the crude reaction mixture. [d] Configuration was determined by comparison with the known compound. [e] Configurations were assigned from transition state model. [f] Optical rotations were measured in methanol. [g] Yields of isolated analytically pure material.

with TMSCF$_3$ in the presence of TBAT afforded the trifluoromethylated product in good to excellent yields.[10] When chiral sulfinylimines were subjected to similar reaction conditions, high diastereoselectivities and high yields were obtained.

The above method provides a straightforward and powerful tool for the preparation of trifluoromethylated amines in enantiomerically pure form. A remarkable feature of this reaction is that it can be applied to nonenolizable, enolizable, aromatic, and heterocyclic imines alike. The optimized reaction conditions for the *p*-chlorophenyl derivative (entry 1) in the presence of a stoichiometric amount of TBAT in THF gave the corresponding trifluoromethylated sulfinamide in good yield (95%) and diastereoselectivity (d.r. > 99%): TMSCF$_3$ (1.2 equiv, 0.6 mmol) in THF (2 mL) was added to a mixture of the imine (0.5 mmol) and TBAT (1.1 equiv, 0.55 mmol) in THF (8 mL) at −55°C. Reaction mixtures were usually stirred over 0.5 to 1 h. Disappearance of the white slurry of TBAT indicates completion of the reaction. Saturated NH$_4$Cl solution (2 mL) was added at lower temperature, and the reaction mixture was warmed to room temperature. The quenched reaction mixture was extracted three times with ethyl acetate, and the combined organic layers were dried over anhydrous Na$_2$SO$_4$. Evaporation of the solvent under vacuum, Flash chromatography (silica gel, hexanes:ethyl acetate 8:2) gave the sulfinamides as white solids. The above conditions were applied to a wide array of structurally diverse imines (Table 1, entries 2–12). All adducts were hydrolyzed to amine salts by using a reported procedure.[11]



Scheme 1. Mechanism of trifluoromethylation of imines by **2** in the presence of TBAT.

The rationale for high stereoselectivity is depicted in Scheme 1. In the presence of a stoichiometric amount of fluoride source, pentavalent intermediate[13] **3** is formed. This pentavalent intermediate, with its large Bu$_4$N$^+$ counterion, preferably adds to the imines from the less hindered *Re* face to give the selective Cram products **4**, which can be transformed to the amines **5**. The preferred conformation of imines[14] and the addition of organometallic reagents to them under nonchelating conditions[15] are well documented.

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