Tetrahedron 66 (2010) 8933–8937

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

One-pot asymmetric synthesis of α-trifluoromethylated amines from α-trifluoromethyl ketones

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ARTICLE INFO

Article history:
Received 3 July 2010
Received in revised form 11 September 2010
Accepted 14 September 2010
Available online 18 September 2010

Keywords:
α-Trifluoromethylated amine
Trifluoromethyl ketone
N-*tert*-Butanesulfinamide
Asymmetric synthesis

ABSTRACT

Diastereoselective reduction of (*Rs*)-*N*-*tert*-butanesulfinyl α-trifluoromethyl ketimines formed in situ from the corresponding α-trifluoromethyl ketones and *N*-*tert*-butanesulfinamide has been achieved, and either diastereomer of *N*-*tert*-butanesulfinyl α-trifluoromethyl amines was obtained in good yields with excellent diastereoselectivities (up to 99:1 dr) using $NaBH_4$ and L-Selectride as the reductants, respectively.

1. Introduction

Trifluoromethyl-containing compounds have gained growing interest in the field of agrochemistry, pharmaceutical industry, and materials science during the past decades[1] because the introduction of a trifluoromethyl group with strong electron-withdrawing ability can lead to significant changes in the physical, chemical, and biological properties of the molecules. Among such compounds enantiomerically pure α-trifluoromethyl amines have attracted considerable attention since these chiral synthons are important and common subunits in the synthesis of chiral fluorinated pharmaceuticals and agrochemicals.[1a,b,d] Based on its prime importance in the drug industry, a variety of methodologies have been developed for their asymmetric synthesis,[2–6] such as nucleophilic trifluoromethylation of *N*-(*tert*-butylsulfinyl)-imines,[3] addition of organometallic reagents to chiral trifluoromethyl imines or analogues,[4] reduction of enantiopure trifluoromethyl imines[5a,b] or catalytic asymmetric reduction of prochiral trifluoromethyl ketimines[5c] and so on.[6] However, most of them have suffered from some drawbacks, like for instance, only one enantiomer obtained, or restricted by the availability of organometallic derivatives, or having a narrow substrate scope. Therefore, there is still desirable to develop a more practical and general method suitable for the rapid synthesis of chiral α-trifluoromethyl amines.

Recently, much attention has been paid to the synthesis of chiral CF_3-substituted *N*-sulfinyl imines and their applications in the diastereoselective synthesis of trifluoromethyl amine derivatives.[7] During our studies on the reactions of CF_3-containing ketones,[8] we have synthesized a new class of chiral CF_3-substituted α,β-unsaturated *N*-*tert*-butanesulfinyl ketimines and explored their preliminary applications in the asymmetric synthesis of either diastereomer of trifluoromethyl allylic amines.[9] As part of our ongoing research in the development of practical methods for the synthesis of chiral α-CF_3 amines, we herein wish to report a facile one-pot approach for the asymmetric synthesis of either (*Rs*, *R*) or (*Rs*, *S*) isomer of *N*-*tert*-butanesulfinyl α-trifluoromethyl amines by the diastereoselective reduction of (*Rs*)-*N*-*tert*-butanesulfinyl α-trifluoromethyl ketimines, which are generated in situ from the condensation of α-trifluoromethyl ketones and (*Rs*)-*N*-*tert*-butanesulfinamide.

2. Results and discussion

We began our investigation with the $NaBH_4$-mediated one-pot reductive amination of 2,2,2-trifluoroacetophenone (**1a**) according to the conditions previously reported by Ellman and co-workers for the one-pot reductive amination of ketones with *N*-*tert*-butanesulfinamide.[10] Condensation of **1a** with **2** in dry THF in the presence of 2.5 equiv of $Ti(Oi\text{-}Pr)_4$ under reflux for 24 h,[11] followed by in situ reduction with 3.0 equiv of $NaBH_4$ at −78 °C for 3 h afforded the

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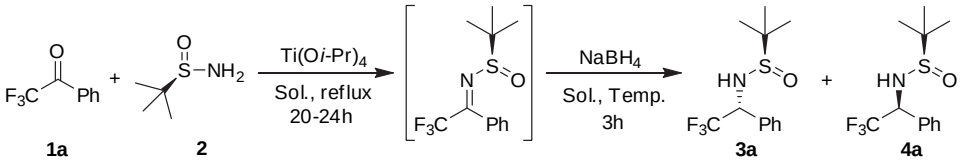
0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.09.047

α-trifluoromethyl sulfinamide **3a** in 52% yield and with a diastereomeric ratio of 98:2 (Table 1, entry 1). To achieve better results, the effect of the solvent was then surveyed. As shown in Table 1, using Et_2O instead of THF as the solvent, the yield of **3a** could be dramatically improved to 85% without any loss in the diastereomeric ratio (**3a**/**4a**=98:2, entry 2). When *n*-hexane was used as the solvent, the reaction gave similar yield and diastereoselectivity as using THF (entry 3). Other solvents, such as toluene, CH_2Cl_2, and CH_3CN furnished the α-trifluoromethyl sulfinamides **3a** and **4a** in moderate selectivity but gave lower yields (entries 4–6).

With the two optimized reaction conditions in hand (Table 2, entries 1 and 7), a variety of α-trifluoromethyl ketones were employed as the substrate to explore the scope of the one-pot reductive amination procedures and test the generality of the reversal in diastereofacial selectivity upon using $NaBH_4$ versus L-Selectride. As summarized in Table 3, all the one-pot reductive aminations of both α-trifluoromethyl aryl and α-trifluoromethyl alkyl ketones went smoothly and afforded the corresponding α-trifluoromethyl amines from **1** in good to excellent yields as well as high diastereoselectivities. α-Trifluoromethyl aryl ketones containing both

Table 1
Solvent screen for the $NaBH_4$-mediated one-pot reductive amination of **1a**



Entry[a]	Solvent	Temp (°C)	Yield[b] (%)	**3a**/**4a**[c]
1	THF	−78	52	98:2
2	Et_2O	−78	85	98:2
3	*n*-hexane	−78	54	98:2
4	Toluene	−78	34[d]	82:18
5	CH_2Cl_2	−78	31[d]	71:29
6	CH_3CN	−30 to −40	45[d]	60:40

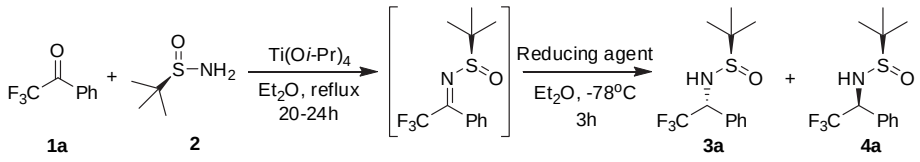
[a] All reductions were performed using 3.0 equiv of $NaBH_4$ in the appropriate solvent for 3 h.
[b] Isolated yield of **3a** in two steps unless otherwise noted.
[c] Diastereomeric ratios were determined by ^{19}F NMR of the crude reaction mixture.
[d] The overall yield of **3a** and **4a** in two steps. Determined by ^{19}F NMR of the crude reaction mixture.

Encouraged by the above results, we then examined a series of metal hydrides to test the possibility of stereoselectivity reversal using ether as the solvent.[9,10a,12] The results were promising, as revealed in Table 2. When DIBAL-H was used instead of $NaBH_4$ as the reductant, a slight improvement in diastereoselectivity (**3a**/**4a**=99:1) was observed but in a lower yield (entry 2). Catecholborane was less reactive and only 14% overall yield of **3a** and **4a** was obtained after 3 h (entry 3). $NaBH_3CN$ and $LiBH_4$ exhibited poor levels of diastereoselection in favor of isomer **3a** (entries 4–5). We were gratified to find the reversal of the diastereofacial selectivity when $LiBHEt_3$ was used as the reducing agent (entry 6). More excitingly, performing the reduction with L-Selectride resulted in the opposite stereoisomer **4a** in good yield with high diastereoselectivity (**4a**/**3a**=98:2, entry 7).[13]

electron-donating and electron-withdrawing substituents at the *para* position proved to be excellent substrates in both systems, giving 90–96% de (entries 1–8). It is worth to be mentioned that both systems gave even better diastereoselectivities (dr up to 99:1) for α-trifluoromethyl alkyl ketones (entries 9–12). Thus, with two different reduction systems, the opposite stereocontrol could be easily achieved. The absolute configuration of product **3a** and **3d**, **4a** and **4d** was unequivocally assigned as (*Rs*, *R*) and (*Rs*, *S*) by cleaving the sulfinamide with HCl and examining the optical rotation of the known salts. By analogy, the absolute configuration of products **3b**–**c**, **e**–**f**, and **4b**–**c**, **e**–**f** is tentatively assigned as (*Rs*, *R*) and (*Rs*, *S*).

On the basis of the diastereoselectivity observed (Table 3), the rationale of the reversal in diastereofacial selectivity upon changing reductant from $NaBH_4$ to L-Selectride may be explained via a cyclic

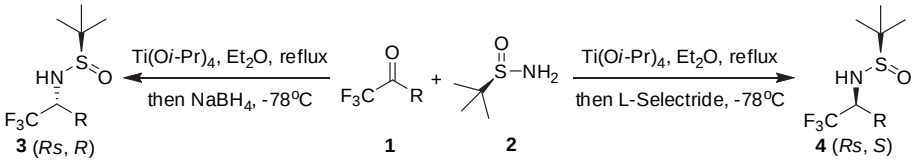
Table 2
The one-pot reductive amination of **1a** with various reducing agents



Entry[a]	Reducing agent	Yield[b] (%)	**3a**:**4a**[c]
1	$NaBH_4$	85 (**3a**)	98:2
2	DIBAL-H	46[d]	99:1
3	Catecholborane	14[d]	98:2
4	$NaBH_3CN$	40 (**3a**)	72:28
5	$LiBH_4$	58 (**3a**)	80:20
6	$LiBHEt_3$	43[d]	18:82
7	L-Selectride	78 (**4a**)	2:98

[a] All reductions were performed using 3.0 equiv of reducing agent in Et_2O at −78 °C for 3 h.
[b] Isolated yield of **3a** or **4a** in two steps unless otherwise noted.
[c] Diastereomeric ratios were determined by ^{19}F NMR of crude reaction mixture.
[d] The overall yield of **3a** and **4a** in two steps. Determined by ^{19}F NMR of crude reaction mixture.

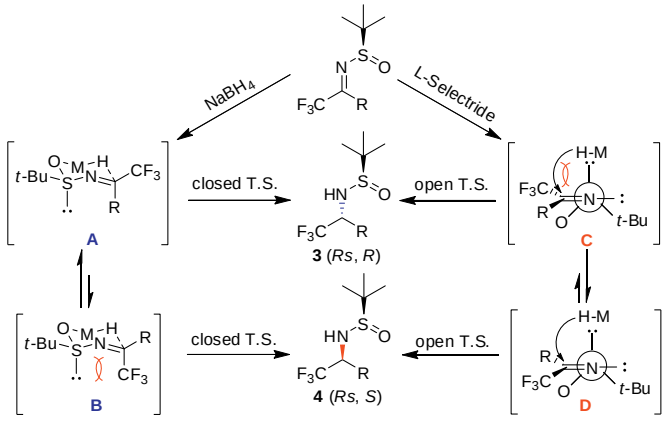
Table 3
The one-pot reductive amination of **1** with $NaBH_4$ and L-Selectride



Entry[a]	R	Reductant	Product	Yield[b] (%)	dr[c]
1	Ph (**1a**)	$NaBH_4$	**3a**	85	98:2
2	Ph (**1a**)	L-Selectride	**4a**	78	98:2
3	4-$MeOC_6H_4$ (**1b**)	$NaBH_4$	**3b**	78	95:5
4	4-$MeOC_6H_4$ (**1b**)	L-Selectride	**4b**	68	96:4
5	4-MeC_6H_4 (**1c**)	$NaBH_4$	**3c**	72	97:3
6	4-MeC_6H_4 (**1c**)	L-Selectride	**4c**	70	96:4
7	4-BrC_6H_4 (**1d**)	$NaBH_4$	**3d**	66	98:2
8	4-BrC_6H_4 (**1d**)	L-Selectride	**4d**	60	96:4
9	$C_6H_5(CH_2)_3$ (**1e**)	$NaBH_4$	**3e**	69	99:1
10	$C_6H_5(CH_2)_3$ (**1e**)	L-Selectride	**4e**	68	99:1
11	*n*-C_8H_{17} (**1f**)	$NaBH_4$	**3f**	79	99:1
12	*n*-C_8H_{17} (**1f**)	L-Selectride	**4f**	84	99:1

[a] All reductions were performed using 3.0 equiv of $NaBH_4$ or L-Selectride in Et_2O at −78 °C for 3 h.
[b] Isolated yield of **3a**–**f** or **4a**–**f** in two steps.
[c] Diastereomeric ratios were determined by ^{19}F NMR of the crude reaction mixture.

transition state in the former reduction ($NaBH_4$) and an open transition state in the latter case (L-Selectride) as previously proposed by Andersen and co-workers[12c] (Scheme 1). Although the steric hindrance of CF_3 group is similar to phenyl and between those of ^{i}Pr and ^{t}Bu,[14] high diastereoselectivities were observed in all the cases examined (Table 3). These results indicated that the electronic effect of the C–F bond in the CF_3 group might play an important role in achieving high diastereoselectivities in both reduction systems. The electrostatic repulsion[15] of the lone pairs between the sulfur atom and the fluorine atom makes CF_3 group be far away from the sulfur atoms in both systems. Therefore TS-A is more stable than TS-B in the six-membered chairlike models under the $NaBH_4$ reduction and TS-D is more favored than TS-C in the open transition state under the L-Selectride reduction. Hence, the six-membered transition state in which the sulfinyl oxygen participates in the delivery of hydride in the $NaBH_4$ system gives (*Rs*, *R*)-3 as the major product, while an open transition state in the L-Selectride system affords the major product (*Rs*, *S*)-4.



Scheme 1. Proposed transition state for the one-pot reductive amination of **1**.

3. Conclusions

In summary, we have developed a facile protocol for the asymmetric synthesis of either stereoisomer of α-trifluoromethylated amines. The diastereoselective reduction of α-trifluoromethyl *N*-*tert*-butanesulfinyl ketoimines formed in situ from the corresponding α-trifluoromethyl ketones and *N*-*tert*-butanesulfinamide took place readily to give either diastereomer of the *tert*-butanesulfinyl-protected trifluoromethylated amines in good yields and with excellent diastereoselectivities by simply choosing the appropriate reducing agents. Further studies on the application of this method in the preparation of CF_3-containing natural product analogues are in progress in our laboratory.

4. Experimental section

4.1. General experimental methods

Unless otherwise mentioned, solvents, and reagents were purchased from commercial sources and used as received. Et_2O and THF were freshly distilled over Na/benzophenone. Melting points were measured on a Melt-Temp apparatus and uncorrected. ^1H NMR spectra were recorded on Bruker AM-300 or Mercury 300 (300 MHz) spectrometers with TMS as internal standard. ^{19}F NMR spectra were recorded on Bruker AM-300 or Mercury 300 (282 MHz) spectrometers with $CFCl_3$ as an external standard. ^{13}C NMR spectra were recorded on Bruker 300 (75.5 MHz) or DPX-400 (100.7 MHz) spectrometers. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Mass spectra were taken on a HP5989A spectrometer. High-resolution mass data were obtained on a high-resolution mass spectrometer in the EI or MALDI mode.

4.2. General procedure for the one-pot reductive amination of 1 with $NaBH_4$

Trifluoromethyl ketones **1** (0.4 mmol) were added to a solution of (*R*)-**2** (0.5 mmol) and Ti(O*i*-Pr)$_4$ (1.0 mmol) in Et_2O (4 mL) at room temperature. The reaction mixture was stirred under reflux and the reaction was monitored by ^{19}F NMR. After the reaction was complete, the mixture was cooled to room temperature and then to −78 °C $NaBH_4$ (1.2 mmol) was added dropwise, and the resulted mixture was stirred at −78 °C for 3 h (monitored by TLC). After reaction, the mixture was quenched with saturated NaCl solution (5 mL) at −78 °C and then warmed to room temperature while being rapidly stirred. The resulting suspension was filtered through a plug of Celite, and the filter cake was washed with EtOAc. The filtrate was washed with saturated NaCl solution. The aqueous layer

was extracted with EtOAc (10 mL×3). The combined organic solution was dried over Na_2SO_4. After the removal of volatile solvents under vacuum, the crude product was further purified by column chromatography on silica gel to give product **3**.

*4.2.1. (Rs,R)-N-(2,2,2-Trifluoro-1-phenylethyl)-tert-butanesulfinamide (**3a**).* Colorless viscous oil, yield 85%; FT-IR (film, cm^{-1}): ν 3196, 2962, 2930, 2872, 1495, 1366, 1265, 1173, 1125, 1073, 693; ^1H NMR ($CDCl_3$): δ 7.46–7.40 (m, 5H), 4.94–4.81 (m, 1H), 3.90 (s, 1H), 1.24 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −74.33 (d, J=7.1 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 131.67, 129.70, 129.26, 128.73, 124.47 (q, J=281.8 Hz), 60.52 (q, J=30.4 Hz), 56.35, 22.31; EIMS (*m*/*z*, %): 280 (M^++1, 4.29), 223 ($M^+-{}^t$Bu+1, 9.94), 159 (17.29), 57 (100.00); HRMS (EI) calcd for $C_{12}H_{16}F_3NOS$ [M^+]: 279.0905; found: 279.0901.

*4.2.2. (Rs,R)-N-(2,2,2-Trifluoro-1-(4-methoxyphenyl)ethyl)-tert-butanesulfinamide (**3b**).* Colorless viscous oil, yield 78%; FT-IR (film, cm^{-1}): ν 3209, 2962, 2910, 2871, 1615, 1518, 1466, 1366, 1253, 1172, 1126, 1073, 829, 732, 585; ^1H NMR ($CDCl_3$): δ 7.29 (d, J=8.7 Hz, 2H), 6.86 (d, J=8.7 Hz, 2H), 4.83–4.68 (m, 1H), 3.84 (s, 1H), 3.75 (s, 3H), 1.24 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −74.70 (d, J=5.6 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 160.57, 130.58, 123.32, 114.13, 124.55 (q, J=281.5 Hz), 59.85 (q, J=30.4 Hz), 56.16, 55.17, 22.31; EIMS (*m*/*z*, %): 310 (M^++1, 5.26), 253 ($M^+-{}^t$Bu+1, 6.01), 189 (100.00), 57 (84.83); HRMS(EI) calcd for $C_{13}H_{18}F_3NO_2S$ [M^+]: 309.1010; found: 309.1012.

*4.2.3. (Rs,R)-N-(2,2,2-Trifluoro-1-p-tolylethyl)-tert-butanesulfinamide (**3c**).* Colorless viscous oil, yield 72%; FT-IR (film, cm^{-1}): ν 3198, 2960, 2929, 2870, 1458, 1365, 1266, 1172, 1126, 1075, 811, 728, 670; ^1H NMR ($CDCl_3$): δ 7.32 (d, J=7.2 Hz, 2H), 7.22 (d, J=7.2 Hz, 2H), 4.80–4.85 (m, 1H), 3.84 (s, 1H), 2.38 (s, 3H), 1.24 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −74.50 (d, J=7.1 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 139.55, 129.34, 129.05, 128.60, 124.48 (q, J=281.7 Hz), 60.19 (q, J=30.2 Hz), 56.16, 22.20, 21.05; EIMS (*m*/*z*, %): 294 (M^++1, 1.52), 237 ($M^+-{}^t$Bu+1, 12.76), 173 (36.95), 57 (100.00); HRMS (EI) calcd for $C_{13}H_{18}F_3NOS$ [M^+]: 293.1061; found: 293.1073.

*4.2.4. (Rs,R)-N-(1-(4-Bromophenyl)-2,2,2-trifluoroethyl)-tert-butanesulfinamide (**3d**).* Colorless viscous oil, yield 66%; FT-IR (film, cm^{-1}): ν 3198, 2962, 2929, 2872, 1493, 1366, 1266, 1175, 1126, 1075, 728, 670; ^1H NMR ($CDCl_3$): δ 7.56 (d, J=7.5 Hz, 2H), 7.32 (d, J=7.5 Hz, 2H), 4.75–4.94 (m, 1H), 3.85 (s, 1H), 1.24 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −74.41 (d, J=6.5 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 135.78, 132.06, 130.53, 127.59, 124.16 (q, J=281.6 Hz), 59.98 (q, J=31.0 Hz), 56.55, 22.24; EIMS (*m*/*z*, %): 357 (M^+, 2.40), 301 ($M^+-{}^t$Bu+1, 1.82), 237 (10.46), 57 (100.00); HRMS (EI) calcd for $C_{12}H_{15}BrF_3NOS$ [M^+]: 357.0010; found: 357.0017.

*4.2.5. (Rs,R)-N-(1,1,1-Trifluoro-5-phenylpentan-2-yl)-tert-butanesulfinamide (**3e**).* White solid, yield 69%; mp 68–70 °C; FT-IR (KBr, cm^{-1}): ν 3207, 3029, 2959, 2933, 2870, 1604, 1541, 1498, 1465, 1365, 1275, 1180, 1163, 1126, 1067, 749, 700; ^1H NMR ($CDCl_3$): δ 7.37–7.14 (m, 5H), 3.77–3.56 (m, 1H), 3.44 (d, J=9.0 Hz, 1H), 2.66 (t, J=4.5 Hz, 2H), 2.05–1.80 (m, 2H), 1.78–1.65 (m, 2H), 1.18 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −75.13 (d, J=7.6 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 141.14, 128.36, 128.23, 125.97, 125.24 (q, J=282.8 Hz), 57.83 (q, J=29.0 Hz), 56.94, 35.15, 28.71, 26.85, 22.42; EIMS (*m*/*z*, %): 265 ($M^+-{}^t$Bu+1, 11.18), 217 (2.68), 57 (100.00); HRMS (EI) calcd for $C_{11}H_{14}F_3NOS$ [$M^+-{}^t$Bu+1]: 265.0748; found: 265.0755.

*4.2.6. (Rs,R)-N-(1,1,1-Trifluorodecan-2-yl)-tert-butanesulfinamide (**3f**).* Colorless viscous oil, yield 79%; FT-IR (film, cm^{-1}): ν 3297, 2958, 2928, 2859, 1468, 1366, 1276, 1168, 1133, 1112, 1066, 940, 885, 847, 795, 693, 580; ^1H NMR ($CDCl_3$): δ 3.72–3.55 (m, 1H), 3.43 (s, 1H), 1.90–1.47 (m, 4H), 1.37–1.26 (m, 10H), 1.25 (s, 9H), 0.88 (t, J=5.7 Hz, 3H); ^{19}F NMR ($CDCl_3$): δ −75.26 (d, J=6.5 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 125.30 (q, J=283.1 Hz), 57.99 (q, J=29.6 Hz), 56.90, 31.65, 29.12, 29.03, 28.94, 25.18, 22.49, 22.40, 13.90; EIMS (*m*/*z*, %): 316 (M^++1, 6.09) 259 ($M^+-{}^t$Bu+1, 2.70), 57 (100.00); HRMS (EI) calcd for $C_{14}H_{28}F_3NOS$ [M^+]: 315.1844; found: 315.1833.

4.3. General procedure for the one-pot reductive amination of 1 with L-Selectride

Trifluoromethyl ketones **1** (0.4 mmol) were added to a solution of (*R*)-**2** (0.5 mmol) and Ti(O*i*-Pr)$_4$ (1.0 mmol) in Et_2O (4 mL) at room temperature. The reaction mixture was stirred under reflux and the reaction was monitored by ^{19}F NMR. After the reaction was completed, the mixture was cooled to room temperature and then to −78 °C. A solution of L-Selectride (1.2 mL, 1.2 mmol, 1.0 M solution in THF) was added slowly, and the resulted mixture was stirred at −78 °C for 3 h (monitored by TLC). After reaction, the mixture was quenched with saturated NaCl solution (5 mL) at −78 °C and then warmed to room temperature while being rapidly stirred. The resulting suspension was filtered through a plug of Celite, and the filter cake was washed with EtOAc. The filtrate was washed with saturated NaCl solution. The aqueous layer was extracted with EtOAc (10 mL×3). The combined organic solution was dried over Na_2SO_4. After the removal of volatile solvents under vacuum, the crude product was further purified by column chromatography on silica gel to give product **4**.

*4.3.1. (Rs,S)-N-(2,2,2-Trifluoro-1-phenylethyl)-tert-butanesulfinamide (**4a**)[3a].* White solid, yield 78%; mp 139–141 °C; FT-IR (KBr, cm^{-1}): ν 2995, 2964, 1498, 1460, 1365, 1265, 1155, 1123, 1058, 1014, 930, 761, 702; ^1H NMR ($CDCl_3$): δ 7.47–7.36 (m, 5H), 4.90–4.76 (m, 1H), 3.70 (s, 1H), 1.24 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −73.29 (d, J=7.1 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 133.68, 129.70, 129.12, 127.90, 124.58 (q, J=281.1 Hz), 61.35 (q, J=30.9 Hz), 58.89, 22.28; EIMS (*m*/*z*, %): 223 ($M^+-{}^t$Bu+1, 7.80), 159 (13.71), 57 (100.00); HRMS (EI) calcd for $C_8H_7F_3NOS$ [$M^+-{}^t$Bu]: 222.02000; found: 222.0193.

*4.3.2. (Rs,S)-N-(2,2,2-Trifluoro-1-(4-methoxyphenyl)ethyl)-tert-butanesulfinamide (**4b**).* White solid, yield 68%; mp 164–167 °C; FT-IR (KBr, cm^{-1}): ν 3247, 3116, 2989, 2966, 2906, 1616, 1519, 1467, 1365, 1263, 1183, 1121, 1058, 812, 711, 528; ^1H NMR ($CDCl_3$): δ 7.28 (d, J=8.1 Hz, 2H), 6.85 (d, J=8.1 Hz, 2H), 4.88–4.64 (m, 1H), 3.54 (s, 1H), 3.76 (s, 3H), 1.18 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −73.52 (d, J=7.3 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 160.40, 129.20, 125.78, 114.54, 124.69 (q, J=281.4 Hz), 60.84 (q, J=30.9 Hz), 56.84, 55.29, 22.31; EIMS (*m*/*z*, %): 310 (M^++1, 0.78), 253 ($M^+-{}^t$Bu+1, 3.13), 189 (51.20), 57 (100.00); HRMS (EI) calcd for $C_{13}H_{18}F_3NO_2S$ [M^+]: 309.1010; found: 309.1013.

*4.3.3. (Rs,S)-N-(2,2,2-Trifluoro-1-p-tolylethyl)-tert-butanesulfinamide (**4c**).* White solid, yield 70%; mp 174–176 °C; FT-IR (KBr, cm^{-1}): ν 3198, 2971, 2927, 1517, 1458, 1365, 1268, 1156, 1124, 1064, 806, 724, 547; ^1H NMR ($CDCl_3$): δ 7.31 (d, J=8.1 Hz, 2H), 7.10 (d, J=8.1 Hz, 2H), 4.95–4.76 (m, 1H), 3.69 (s, 1H), 2.35 (s, 3H), 1.26 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −73.38 (d, J=6.8 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 139.56, 130.78, 129.83, 127.78, 124.67 (q, J=281.6 Hz), 61.16 (q, J=30.2 Hz), 56.88, 22.32, 21.13; EIMS (*m*/*z*, %): 237 ($M^+-{}^t$Bu+1, 7.44), 173 (26.30), 57 (100.00); HRMS (EI) calcd for $C_9H_9F_3NOS$ [$M^+-{}^t$Bu]: 236.0357; found: 236.0365.

*4.3.4. (Rs,S)-N-(1-(4-Bromophenyl)-2,2,2-trifluoroethyl)-tert-butanesulfinamide (**4d**)[3a].* White solid, yield 60%; mp 164–167 °C; FT-IR (KBr, cm^{-1}): ν 2968, 2928, 1493, 1365, 1265, 1161, 1123, 1058, 1014, 917, 811, 728; ^1H NMR ($CDCl_3$): δ 7.56 (d, J=7.5 Hz, 2H), 7.32 (d, J=7.5 Hz, 2H), 4.88–4.72 (m, 1H), 3.56 (s, 1H), 1.24 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −73.95 (d, J=7.1 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 135.63, 132.35, 131.54, 127.54, 123.96 (q, J=281.1 Hz), 61.35 (q, J=30.9 Hz), 57.25, 22.17; EIMS (*m*/*z*, %): 301 ($M^+-{}^t$Bu+1, 0.66), 237 (4.07), 57

(100.00); HRMS (EI) calcd for $C_8H_6BrF_3NOS$ [$M^+-{}^tBu$]: 299.9306; found: 299.9304.

*4.3.5. (Rs,S)-N-(1,1,1-Trifluoro-5-phenylpentan-2-yl)-tert-butanesulfinamide (**4e**).* White solid, yield 68%; mp 74–76 °C; FT-IR (KBr, cm^{-1}): ν 3219, 3031, 2962, 2871, 1605, 1498, 1456, 1365, 1275, 1180, 1163, 1126, 1058, 750, 696; ^1H NMR ($CDCl_3$): δ 7.37–7.14 (m, 5H), 3.77–3.56 (m, 1H), 3.07 (s, 1H), 2.80–2.55 (m, 2H), 2.10–1.72 (m, 2H), 1.69–1.44 (m, 2H), 1.23 (s, 9H); ^{19}F NMR ($CDCl_3$): δ −75.83 (d, J=7.2 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 141.03, 128.36, 128.33, 125.89, 125.26 (q, J=288.8 Hz), 58.56 (q, J=29.6 Hz), 56.65, 34.93, 28.77, 26.30, 22.28; EIMS (m/z, %): 322 (M^++1, 0.75), 265 ($M^+-{}^tBu$+1, 14.95), 217 (3.25), 57 (100); HRMS (EI) calcd for $C_{11}H_{14}F_3NOS$ [$M^+-{}^tBu$+1]: 265.0748; found: 265.0760.

*4.3.6. (Rs,S)-N-(1,1,1-Trifluorodecan-2-yl)-tert-butanesulfinamide (**4f**).* Colorless viscous oil, yield 84%; FT-IR (film, cm^{-1}): ν 3209, 2958, 2929, 2860, 1495, 1366, 1276, 1168, 1133, 1111, 1046, 887, 723, 697; ^1H NMR ($CDCl_3$): δ 3.72–3.59 (m, 1H), 3.08 (d, J=7.2 Hz, 1H), 1.67–1.40 (m, 4H), 1.36–1.26 (m, 10H), 1.24 (s, 9H), 0.88 (t, J=5.7 Hz, 3H); ^{19}F NMR ($CDCl_3$): δ −75.94 (d, J=7.1 Hz, 3F); ^{13}C NMR ($CDCl_3$): δ 124.36 (q, J=281.1 Hz), 58.75 (q, J=30.2 Hz), 56.70, 31.74, 29.56, 29.14, 28.05, 24.87, 22.55, 22.33, 13.98; EIMS (m/z, %): 316 (M^++1, 1.22), 259 ($M^+-{}^tBu$+1, 4.02), 57 (100.00); HRMS (EI) calcd for $C_{14}H_{28}F_3NOS$ [M^+]: 315.1844; found: 315.1857.

Acknowledgements

Financial support from the National Natural Science Foundation of China (No. 20872166), Doctoral Fund of Ministry of Education of China, and Postdoctoral Fund of China is gratefully acknowledged.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.09.047. These data include MOL files and InChiKeys of the most important compounds described in this article.

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