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The Regio-specific solvent controlled asymmetric Strecker reaction of trifluoromethyl α,β-unsaturated *N-tert*-butanesulfinyl ketimines with trimethylsilyl cyanide

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ABSTRACT

The stereoselectivity of the reaction of (*Rs*)-trifluoromethyl α,β-unsaturated *N-tert*-butanesulfinyl ketimines with TMSCN was studied. The diastereomers of α-trifluoromethyl unsaturated cyano amines were obtained, respectively, in good yields with excellent diastereoselectivities in terms of the different solvents used. In *c*-hexane, the (*S*, *Rs*)-isomer was obtained with up to 17:1 dr, whereas the (*R*, *Rs*)-isomer was generated as the main product with up to 145:1 dr in DMF at −60 °C.

1. Introduction

Fluorine-containing organic compounds are of great interest to both the academia and industrial community due to their unique biochemical and pharmacological properties [1]. Several synthetic approaches of α-trifluoromethyl-amino acids (α-Tfm AAs) have been reported, however they suffered from some drawbacks [2–5]. The use of *N-tert*-butylsulfinamide (TBSA) as a chiral auxiliary is thoroughly described in the diastereoselective synthesis of trifluoro-methylated derivatives [6–8]. Recently, Lu and co-workers have reported a facile TBSA-induced solvent-controlled stereoselective Strecker reaction for the preparation of α-trifluoromethylated α-amino acids with up to 99:1 dr [9]. We are interested in this solvent controlled high stereoselective reaction, and wish to further improve the stereoselectivity of the TBSA-induced and solvent-controlled Strecker reaction.

In the process of investigating the preparation and reaction property of trifluoromethyl α,β-unsaturated *N-tert*-butanesulfinyl ketimines, we found that they were more stable than their corresponding saturated counterparts, and able to isolate facilely by column chromatography [10,11]. We envisaged that enhancing the substrate's structural conjugation might improve the stereoselectivity of the Strecker reaction due to the increasing coplanarity of the molecular structure backbone. On the basis of our previous work [12–15] and some related novel published literature [16–26], we reported herein the study of the asymmetrical Strecker reaction of trifluoromethyl α,β-unsaturated *N-tert*-butanesulfinyl ketimines with trimethylsilyl cyanide under different conditions.

2. Results and discussion

Referrng to literature [9–11], our experiment started with the investigation of the Strecker reaction of (*Rs*)-trifluoromethyl *N*-tert-butanesulfinyl α,β-unsaturated ketimines **1a** with TMSCN at room temperature in DMF and *n*-hexane. Using DMF as a solvent, TLC showed that compound **1a** was converted completely within 4 h, and ^{19}F NMR spectroscopy of the crude reaction mixture indicated that the selectivity of the mixing adducts was achieved in 99% yield with an 8:1 dr (**2a**:**3a**) (entry 1 in Table 1). However, with *n*-hexane as a solvent, TLC showed that compound **1a** was converted incompletely even by lengthening reaction time to 48 h, and ^{19}F NMR spectroscopy of the crude reaction mixture showed that a reversed selectivity of the mixing adducts was obtained with a 1:12 dr (**2a**:**3a**) (entries 2 and 3 in Table 1). Considering that alkali

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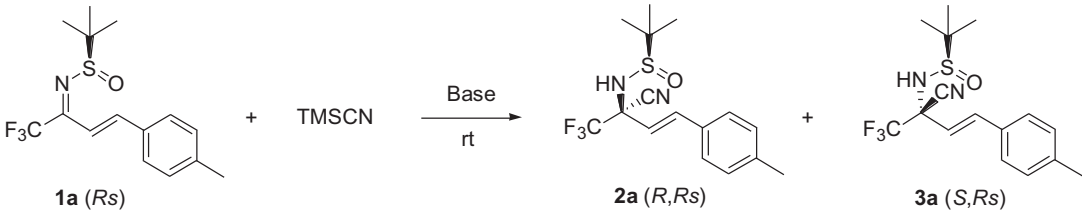
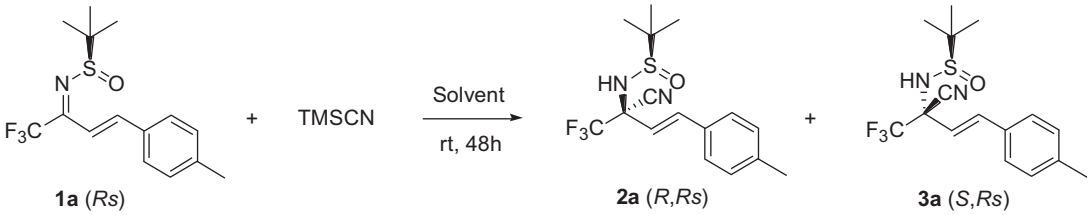
Table 1
Effect of bases on the asymmetric Strecker reaction.



Entry	Solvent	Base	Time (h)	Yield (%)[a]	d.r. (**2a**:**3a**)[a]
1	DMF	–	4	99	8:1
2	*n*-Hexane	–	4	50	1:12
3	*n*-Hexane	–	48	81	1:12
4	*n*-Hexane	CsF (0.1 equiv.)	4	90	3:1
5	*n*-Hexane	CsF (1 equiv.)	4	100	1.2:1
6	*n*-Hexane	K_2CO_3 (1 equiv.)	4	100	1:1.2

[a] Yield and diastereomeric ratios were determined by ^{19}F NMR spectroscopy of crude reaction mixture.

Table 2
Effect of solvent on the asymmetric Strecker reaction for 48 h at room temperature.



Entry	Solvent[a]	Yield (%)[b]	dr (**2a**:**3a**)[b]
1	*n*-Hexane	81	1:12
2	PE	81	1:15
3	*c*-Hexane	75	1:17
4	Et_2O	93	1:10
5	DCM	89	1:8
6	THF	93	4:1
7	CH_3CN	86	1:1.7
8	DMF	99	8:1

[a] Reaction was carried out at room temperature for 48 h.
[b] Yield and diasteromeric ratios were determined by monitored ^{19}F NMR spectroscopy on the crude reaction mixture.

circumstance would enhance the nucleophilicity of TMSCN, several bases were tried. As shown in Table 1, the addition of 0.1 equiv. of CsF resulted in 90% yield of compound 1a in 4 h, and in the presence of 1 equiv. of CsF or K_2CO_3, it was even converted completely into the corresponding adducts during the same time, whereas the dr (**2a**:**3a**) was decreased dramatically (entries 4–6 in Table 1), meaning that the presence of alkali is actually helpful to the accomplishment but detrimental to the stereoselectivity of this Strecker reaction.

A variety of solvents were sequentially attempted in the absence of base with prolonged reaction time from 4 h to 48 h. As listed in Table 2, despite the reaction was incomplete in most cases,

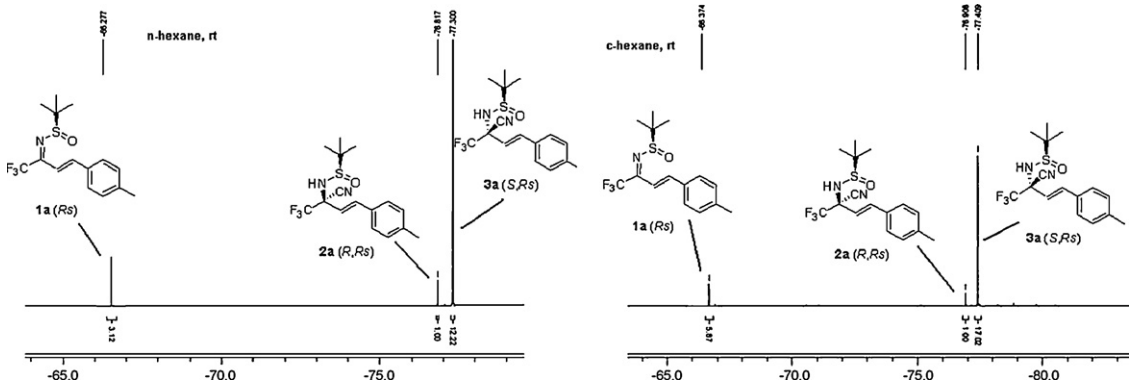
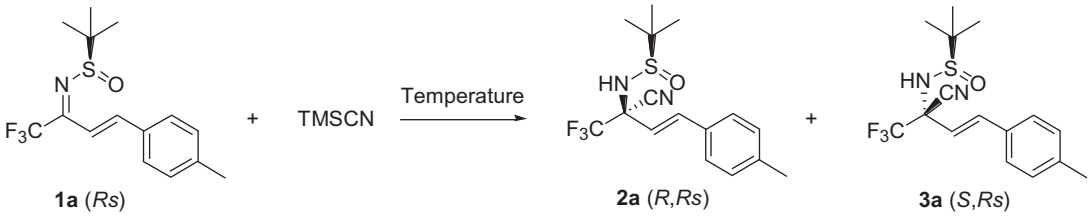


Fig. 1. ^{19}F NMR spectra of the crude reaction mixture to the reaction of **1a** with TMSCN in *n*-hexane or *c*-hexane at room temperature.

Table 3
Effect of temperature on the asymmetric Strecker reaction in *n*-hexane and DMF.



Entry	Solvent	Temperature (°C)	Reaction time	Yield (%)[a]	dr (**2a**:**3a**)[a]
1	*n*-Hexane	−78	48	48	1:17
2	*n*-Hexane	−60	48	62	1:17
3	*n*-Hexane	−40	48	69	1:17
4	*n*-Hexane	0	48	69	1:17
5	*n*-Hexane	25	48	81	1:12
6	DMF	−60	24	95	143:1
7	DMF	−40	24	98	24:1
8	DMF	−20	24	99	24:1
9	DMF	0	24	99	10:1
10	DMF	25	24	99	8:1

[a] Yields and diastereomeric ratios were determined by ^{19}F NMR spectroscopy of crude reaction mixture.

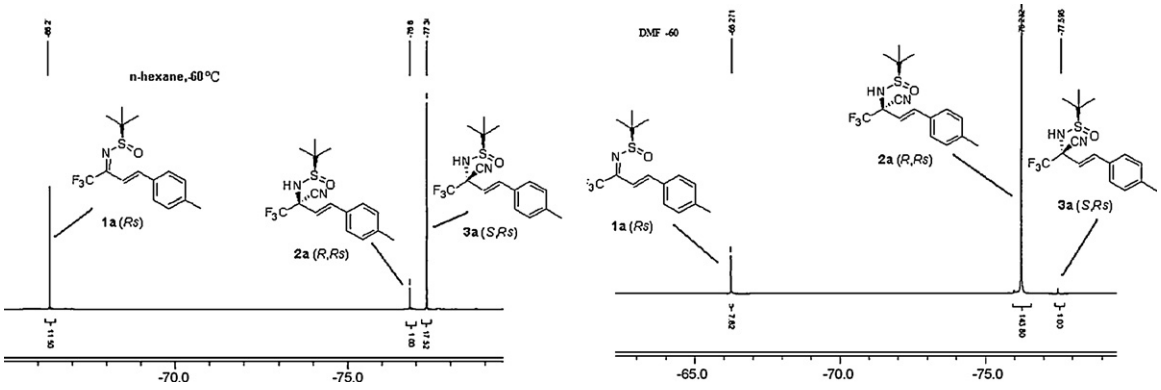


Fig. 2. ^{19}F NMR spectra of the crude reaction mixture to the reaction of **1a** with TMSCN in DMF or *n*-hexane at −60 °C.

the diastereoselectivity was improved. In *c*-hexane, PE and *n*-hexane, the resulting dr (**2a**:**3a**) was 1:17, 1:15 and 1:12 (entries 1–3 in Table 2, Fig. 1), respectively, whereas in DMF and THF, a reversed selectivity was observed with 8:1 and 4:1 dr (**2a**:**3a**), respectively (entries 6 and 8 in Table 2).

Encouraged by these results, the same reaction was performed at different temperature to investigate the effect of temperature. Though *c*-hexane has a slight good dr than *n*-hexane, but it will be solidified below 6.5 °C, therefore *n*-hexane instead of *c*-hexane was chosen as one of the typical solvents to investigate the effect of temperature on the reaction selectivity. As shown in Table 2, in *n*-hexane, the selectivity reached 1:17 dr (**2a**:**3a**) at 0 °C, whereas the decrease in temperature resulted in no apparent change in dr (entries 1–5 in Table 3). Therefore, comparing with *n*-hexane, *c*-hexane has a more convenient temperature (25 °C) to obtain the same reaction stereoselectivity. In contrast, the corresponding dr (**2a**:**3a**) in DMF was significantly varied with a similar decrease in temperature (entries 6–10 in Table 3), where a satisfactory 143:1 dr (**2a**:**3a**) was achieved at −60 °C (Fig. 2).

With the optimized reaction conditions in hand, a variety of trifluoromethyl α,β-unsaturated *N*-*tert*-butanesufinyl ketimines were employed as the starting material to explore the substrate scope of the Strecker reaction. Meanwhile, as totally reversed diastereoselectivity could be achieved while using *c*-hexane as the solvent instead of DMF, the same reactions were simultaneously performed in *c*-hexane and DMF for comparison. The reaction results listed in Table 4 showed that, for most substrates, **3** were the major products in *c*-hexane at room temperature with the highest 1:17 dr (**2**:**3**) for **1a** (entry 1 in Table 4), and the reverse isomers **2** were the major products in DMF at −60 °C with the highest 145:1 dr (**2**:**3**) for **1e** (entry 5 in Table 4).

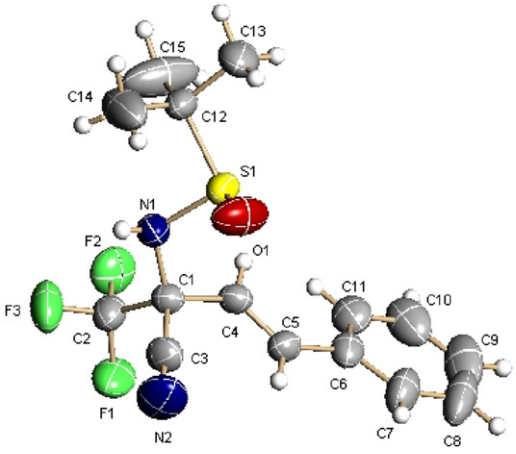
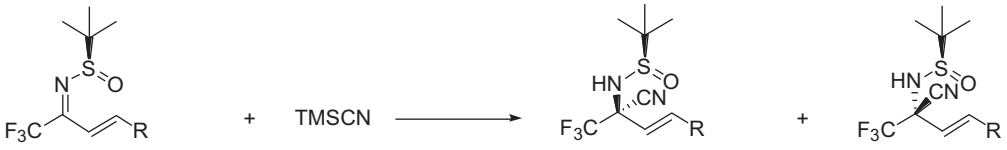


Fig. 3. X-ray crystal structure of **3b** (CCDC 845805).

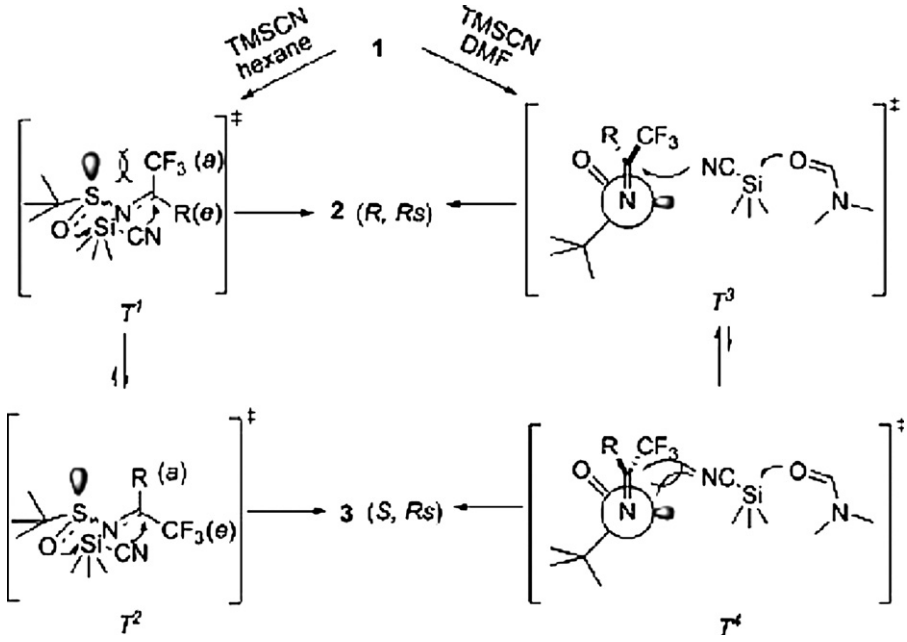
Table 4
Asymmetric Strecker reaction of **1** and TMSCN in *c*-hexane at room temperature and in DMF at −60 °C.



1a-h (*Rs*) **2a-h** (*R*,*Rs*) **3a-h** (*S*,*Rs*)

Entry	Substrate (R)	Time (h)		Yield[d] (%)		dr (**2**:**3**)[c]	
		c-hexane	DMF	*c*-hexane [a]	DMF [b]	*c*-hexane	DMF
1	**1a** (*p*-Me-Ph-)	48	24	85	58	1:17	143:1
2	**1b** (Ph-)	48	24	70	65	1:16	71:1
3	**1c** (*p*-Cl-Ph-)	48	24	63	55	1:8	65:1
4	**1d** (Biphenyl-)	48	24	78	70	1:9	68:1
5	**1e** (2-MeO-Ph)	48	24	83	64	1:9	145:1
6	**1f** (*p*-MeO-Ph)	48	24	54	62	1:10	73:1
7	**1g** (*p*-Br-Ph-)	48	24	69	70	1:11	68:1
8	**1h** (Naphthyl-)	48	24	74	63	1:10	77:1

[a] Reactions were proceeded at room temperature in *c*-hexane.
[b] Reactions were proceeded at −60 °C in DMF.
[c] Diasteromeric ratios were determined by ^{19}F NMR spectroscopy on the crude reaction mixture.
[d] Total isolated yields of **2** and **3**.



Scheme 1. Proposed mechanism for asymmetric Strecker reaction of **1** with TMSCN.

To determine the absolute configuration of the product, isomer **3b** was separated by column chromatography, and its single crystal was cultured for X-ray diffraction analysis, which indicated the (*S*, *Rs*)-configuration (Fig. 3).

On the basis of the diastereoselectivity observed, a possible mechanism similar to the literature [9] was proposed for this reaction as depicted in Scheme 1. With *c*-hexane, PE, or *n*-hexane as a solvent, due to its weak interaction with reactants, **1** was preferred to form a chair-type cyclohexane-like transition state when reacting directly with TMSCN, where T^2 was favored for the stronger repulsion force between CF_3 and the lone electron pair on sulfur in T^1, thus generating **3** (*S*, *Rs*) in priority. However, as the reaction occurred in DMF medium, the stronger attraction between the silicon atom on TMS and the oxygen atom on DMF reduced its interaction to the oxygen atom on substrate **1**, thus transition state T_3 and T_4 were exhibited with T_3 favorable for the shorter distance from the sulfur atom to CF_3 in T^4, therefore **2** (*S*, *Rs*) was predominately afforded.

3. Conclusion

In summary, a solvent controlled high stereoselective asymmetric Strecker reaction of trifluoromethyl α,β-unsaturated *N*-*tert*-butanesulfinyl ketimines with TMSCN was realized. The diastereoselectivity of the Strecker reaction of unsaturated ketimine with TMSCN could be more facilely controlled by the solvents used. The reaction in *c*-hexane and *n*-hexane predominately afforded (*S*, *Rs*)-isomer **3**, whereas the (*R*, *Rs*)-isomer **2** was

furnished as the major product while using DMF as the solvent. In the case of **1a** and **1e** in DMF, the isomer (*R, Rs*)-**2a** and (*R, Rs*)-**2e** were obtained with 143:1 and 145:1 dr, respectively, which is better than the reported saturated ketimine [9]. This study would provide a new and efficient method for the preparation of novel α,β-unsaturated α-trifluoromethylated amine derivatives that are of biological interest.

4. Experimental

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 external standard. ^{13}C NMR spectra were recorded on Bruker 300 (75.5 MHz). 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 mode. Flash column chromatography was carried out on silica gel (300–400 mesh).

4.1. General procedure for preparing the mixture of *2* and *3*

To a solution of **1** (1 mmol) in DMF (2 mL) was added TMSCN (1.5 mmol) at −60 °C. After stirred for 24 h, the mixture was quenched with salt NH_4Cl. The mixture was extracted with EA for 3 times and the extraction was dried over Na_2SO_4. Removing solvent *in vacuo* and purifying by chromatography on silica gel (EA/PE = 1/6) gave the corresponding mixture **2** (major) and **3**. Direct analysis of the mixture gave the data of compounds **2** as following. The melting point was not measured because the separation of **2** and **3** was difficult and only the mixture of **2** and **3** were obtained.

4.1.1. (Rs)-N-((R,E)-2-cyano-1,1,1-trifluoro-4-p-tolylbut-3-en-2-yl)-2-methylpropane-2-sulfinamide (*2a*)

White solid, separated yield of the mixture of **2a** and **3a**: 58%; FT-IR (KBr, cm^{-1}): ν 3218, 2927, 1714, 1618, 1364, 1259, 1222, 1164, 1115, 1072, 970, 831, 692; ^1H NMR ($CDCl_3$): δ 7.17–7.34 (m, 5H, 4Ar-H and 1 = CH), 6.10 (d, *J* = 14.5 Hz, 1H, =CH), 3.89 (s, 1H, NH), 2.29 (s, 3H, CH_3), 1.21 (s, 9H, $C(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −76.6 (s, 3F) (for (S, Rs)-isomer 3a: −77.1); ^{13}C NMR ($CDCl_3$): δ 141.2, 139.9, 130.9, 129.7, 127.5, 122.0 (q, $^1J_{CF}$ = 286.3 Hz), 115.5, 113.0, 62.4 (q, $^2J_{CF}$ = 27.2 Hz), 58.0 22.2, 21.4; EIMS (*m/z*, %): 261 (30.60), 224 (7.72), 198 (19.97), 57 (100.00); HRMS (EI) calcd. for $C_{16}H_{19}F_3N_2OS$ [M^+]: 344.1170; found: 344.1170.

4.1.2. (Rs)-N-((R,E)-2-cyano-1,1,1-trifluoro-4-phenylbut-3-en-2-yl)-2-methylpropane-2-sulfinamide (*2b*)

Colorless viscous oil, separated yield of the mixture of **2b** and **3b**: 65%; FT-IR (film, cm^{-1}): ν 3168, 2968, 2868, 1450, 1364, 1267, 1165, 1123, 1053, 970, 751, 693; ^1H NMR ($CDCl_3$): δ 7.27–7.45 (m, 6H, 5Ar-H and 1 = CH)), 6.02 (d, *J* = 14.1 Hz, 1H, 1 = CH), 4.42 (s, 1H, NH), 1.27 (s, 9H, $C(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −76.7 (s, 3F); ^{13}C NMR ($CDCl_3$): δ 140.0, 133.7, 129.8, 128.9, 127.6, 122.0 (q, $^1J_{CF}$ = 281.4 Hz), 114.7, 112.9, 63.4 (q, $^2J_{CF}$ = 32.2 Hz), 58.1, 22.2; EIMS (*m/z*, %): 247 (26.96), 210 (3.15), 57 (100.00); HRMS (EI) calcd. for $C_{15}H_{17}F_3N_2OS$ [M^+]: 330.1014; found: 330.1019.

4.1.3. (Rs)-N-((R,E)-4-(4-chlorophenyl)-2-cyano-1,1,1-trifluorobut-3-en-2-yl)-2-methylpropane-2-sulfinamide (*2c*)

White solid, separated yield of the mixture of **2c** and **3c**: 55%; FT-IR (KBr, cm^{-1}): ν 3295, 2975, 1495, 1255, 1220, 1187, 1083, 979, 865, 596; ^1H NMR ($CDCl_3$): δ 7.16–7.41 (m, 5H, 4Ar-H and 1 = CH), 6.20 (d, *J* = 14.6 Hz, 1H, =CH), 3.83 (s, 1H, NH), 1.26 (s, 9H, $C(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −76.6 (s, 3F) (for (S, Rs)-isomer 3c: −77.2); ^{13}C NMR ($CDCl_3$): δ 140.1, 138.8, 132.1, 129.2, 128.8, 121.9 (q, $^1J_{CF}$ = 286.6 Hz), 117.5, 112.7, 63.4 (q, $^2J_{CF}$ = 32.4 Hz), 58.1, 22.2; EIMS (*m/z*, %): 281 (11.45), 244 (3.11), 57 (100.00); HRMS (EI) calcd. for $C_{15}H_{16}F_3N_2OS$ [M^+]: 364.0624; found: 364.0626.

4.1.4. (Rs)-N-((R,E)-4-(biphenyl-4-yl)-2-cyano-1,1,1-trifluorobut-3-en-2-yl)-2-methylpropane-2-sulfinamide (*2d*)

White solid, separated yield of the mixture of **2d** and **3d**: 70%; FT-IR (KBr, cm^{-1}): ν 3250, 2994, 2930, 1648, 1606, 1561, 1488, 1252, 1208, 1101, 967, 762, 696; ^1H NMR ($CDCl_3$): δ 7.21–7.52 (m, 10H, 9Ar-H and 1 = CH), 6.16 (d, *J* = 15.2 Hz, 1H, =CH), 4.37 (s, 1H, NH), 1.18 (s, 9H, $C(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −76.4 (s, 3F) (for (S, Rs)-isomer 3d: −77.4); ^{13}C NMR ($CDCl_3$): δ 142.9, 140.7, 140.1, 139.5, 132.7, 128.9, 128.1, 127.9, 127.6, 127.1, 122.1 (q, $^1J_{CF}$ = 285.9 Hz), 116.7, 113.1, 62.5 (q, $^2J_{CF}$ = 32.2 Hz), 58.2, 22.2; EIMS (*m/z*, %): 323 (50.13), 274 (45.25), 57 (100.00); HRMS (EI) calcd. for $C_{21}H_{21}F_3N_2OS$ [M^+]: 406.1327; found: 406.1331.

4.1.5. (Rs)-N-((R,E)-2-cyano-1,1,1-trifluoro-4-(2-methoxyphenyl)but-3-en-2-yl)-2-methylpropane-2-sulfinamide (*2e*)

White solid, separated yield of the mixture of **2e** and **3e**: 64%; FT-IR (KBr, cm^{-1}): ν 3188, 2930, 1602, 1491, 1463, 1250, 1213, 1176, 1078, 1031, 984, 761, 597; ^1H NMR ($CDCl_3$): δ 6.83–7.51 (m, 5H, 4Ar-H and 1 = CH), 6.28 (d, *J* = 15.2, 1H, =CH), 3.82 (s, 3H, NH), 3.70 (s, 1H, OCH_3), 1.22 (s, 9H, $C(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −76.7 (s, 3F), (for (*S, Rs*)-isomer 3e: −77.3); ^{13}C NMR ($CDCl_3$): δ 157.8, 136.7, 131.1, 128.4, 122.5, 121.1 (q, $^1J_{CF}$ = 272.6 Hz), 120.7, 117.2, 115.4, 111.2, 58.0, 57.7 (q, $^2J_{CF}$ = 28.4 Hz), 55.5, 22.3; EIMS (*m/z*, %): 277 (39.58), 240 (13.99), 198 (28.31), 57 (100.00); HRMS (EI) calcd. for $C_{16}H_{19}F_3N_2O_2S$ [M^+]: 360.1119; found: 360.1122.

4.1.6. (Rs)-N-((R,E)-2-cyano-1,1,1-trifluoro-4-(4-methoxyphenyl)but-3-en-2-yl)-2-methylpropane-2-sulfinamide (*2f*)

White solid, separated yield of the mixture of **2f** and **3f**: 62%; FT-IR (KBr, cm^{-1}): ν 3252, 2980, 2937, 1651, 1607, 1516, 1257, 1216, 1184, 1082, 983, 810, 596; ^1H NMR ($CDCl_3$): δ 7.37 (d, *J* = 9.0 Hz, 2H, 2Ar-H), 7.29 (d, J = 9.1 Hz, 2H, 2Ar-H) 7.18 (d, *J* = 15.5 Hz, 1H, =CH), 6.01 (d, *J* = 15.9 1H, =CH), 3.83 (s, 1H, NH), 3.79 (s, 3H, OCH_3), 1.21 (s, 9H, $C(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −76.5 (s, 3F) (for (*S, Rs*)-isomer **3f**: −76.9); ^{13}C NMR ($CDCl_3$): δ 160.0, 140.7, 129.1, 126.4, 122.1 (q, $^1J_{CF}$ = 283.4 Hz), 114.1, 113.1, 112.0, 63.4 (q, $^2J_{CF}$ = 30.4 Hz), 58.0, 55.4, 22.4; EIMS (*m/z*, %): 360 (M^+ + 1, 1.30), 277 (43.42), 240 (26.10), 228 (32.65), 57 (100.00); HRMS (EI) calcd. for $C_{16}H_{19}F_3N_2O_2S$ [M^+]: 360.1119; found: 360.1124.

4.1.7. (Rs)-N-((R,E)-4-(4-bromophenyl)-2-cyano-1,1,1-trifluorobut-3-en-2-yl)-2-methylpropane-2-sulfinamide (*2g*)

White solid, separated yield of the mixture of **2g** and **3g**: 70%; FT-IR (KBr, cm^{-1}): ν 3316, 3069, 2966, 1649, 1588, 1491, 1406, 1255, 1200, 1087, 1010, 983, 809, 722, 599; ^1H NMR ($CDCl_3$): δ 7.33–7.54 (m, 4H, Ar-H), 7.27 (d, *J* = 14.5 Hz, 1H, =CH), 6.23 (d, *J* = 14.7 Hz, 1H, =CH), 4.00 (s, 1H, NH), 1.29 (s, 9H, $C(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −76.5 (s, 3F) (for the (*S, Rs*)-isomer **3g**: −77.0); ^{13}C NMR ($CDCl_3$): δ 140.0, 138.7, 132.1, 129.0, 124.3, 121.9 (q, $^1J_{CF}$ = 332.3 Hz), 117.6, 112.7, 63.4 (q, $^2J_{CF}$ = 30.2 Hz), 58.2, 22.2; EIMS (*m/z*, %): 325 (8.81), 209 (6.79), 140 (10.20), 57 (100.00); HRMS (EI) calcd. for $C_{15}H_{16}F_3N_2OS$ [M^+−Br]: 329.0935; found: 329.0934.

4.1.8. (Rs)-N-((R,E)-2-cyano-1,1,1-trifluoro-4-(naphthalen-1-yl)but-3-en-2-yl)-2-methylpropane-2-sulfinamide (*2h*)

White solid, separated yield of the mixture of **2h** and **3h**: 63%; FT-IR (KBr, cm^{-1}): ν 3151, 2962, 1686, 1593, 1513, 1253, 1211, 1196, 1137, 1098, 1079, 967, 830, 792; ^1H NMR ($CDCl_3$): δ 7.

40–8.12 (m, 8H, 7Ar-H and 1 = CH), 6.24 (d, J = 15.2 Hz, 1H, =CH), 4.42 (s, 1H, NH), 1.25 (s, 9H, $C(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −76.6 (s, 3F) (for the (*S*, *Rs*)-isomer **3h**: −77.4); ^{13}C NMR ($CDCl_3$): δ 137.6, 133.5, 130.3, 128.7, 127.1, 127.0, 126.5, 125.4, 125.4, 125.1, 123.3, 122.5 (q, $^1J_{CF}$ = 292.4 Hz), 118.0, 114.0, 62.3 (q, $^2J_{CF}$ 28.7 Hz), 58.2, 22.2; EIMS (*m*/*z*, %): 297 (24.68), 248 (29.64), 234 (20.33), 57 (100.00); HRMS (EI) calcd. for $C_{19}H_{19}F_3N_2OS$ [M^+]: 380.1170; found: 380.1173.

4.2. The procedure for preparing and purifying compounds **3b**

To a solution of 1 (1 mmol) in *c*-hexane (2 mL) was added TMSCN (1.5 mmol) at room temperature. After stirred for 48 h, the mixture was quenched with salt NH_4Cl. The mixture was extracted with EA for 3 times and the extraction was dried over Na_2SO_4. Removing solvent *in vacuo* and purifying by chromatography on silica gel (EA/PE = 1/6) gave the corresponding mixture **3b** (major) and **2b**. Compound **3b** was carefully isolated from the mixture by chromatography on silica gel and its single crystal was cultured in the mixing solvent of EA and *n*-hexane.

4.2.1. (Rs)-N-((S,E)-2-cyano-1,1,1-trifluoro-4-phenylbut-3-en-2-yl)-2-methylpropane-2-sulfinamide (**3b**)

White solid, yield 70%; mp 50–52 °C; $[\alpha]_D^{20}$ −204.43 (c = 0.67, $CHCl_3$); FT-IR (KBr, cm^{-1}): ν 3159, 2965, 2872, 1650, 1452, 1367, 1254, 1208, 1195, 1073, 969, 749, 693; ^1H NMR ($CDCl_3$): δ 7.42–7.51 (m, 5H, Ar-H), 7.39 (d, J = 15.2 Hz, 1H, =CH), 6.52 (d, J = 15.4 Hz, 1H, =CH), 4.20 (s, 1H, NH), 1.30 (s, 9H, $3CH_3$); ^{19}F NMR ($CDCl_3$): δ −77.2 (s, 3F); ^{13}C NMR ($CDCl_3$): δ 141.2, 133.7, 129.8, 129.0, 127.6, 122.0 (q, $^1J_{CF}$ = 286 Hz), 114.7, 113.8, 62.4 (q, $^2J_{CF}$ = 32.2 Hz), 57.5, 22.4; EIMS (*m*/*z*, %): 247 (26.96), 210 (3.15), 57 (100.00); HRMS (EI) calcd. for $C_{15}H_{17}F_3N_2OS$ [M^+]: 330.1014; found: 330.1019.

For the monitored reactions of compounds **1** with TMSCN in different solvents at different temperature, only ^{19}F NMR spectroscopy of the crude reaction mixture was analyzed to determine the conversion ratios of compounds **1**, the yields and dr values of their corresponding products **2** and **3**.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2012.07.017.

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