JOC The Journal of Organic Chemistry
Article
pubs.acs.org/joc

Synthesis of Trifluoromethyl-Containing Vicinal Diamines by Asymmetric Decarboxylative Mannich Addition Reactions

Lingmin Wu,[†] Chen Xie,[†] Haibo Mei,[†] Yanling Dai,[†] Jianlin Han,*[,†] Vadim A. Soloshonok,*[,‡,§] and Yi Pan[†]

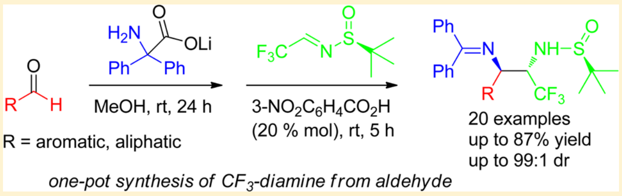
[†]School of Chemistry and Chemical Engineering, State Key Laboratory of Coordination Chemistry, Nanjing University, Nanjing, 210093, China

[‡]Department of Organic Chemistry I, Faculty of Chemistry, University of the Basque Country UPV/EHU, 20018 San Sebastian, Spain

[§]IKERBASQUE, Basque Foundation for Science, 48011 Bilbao, Spain

Ⓢ *Supporting Information*

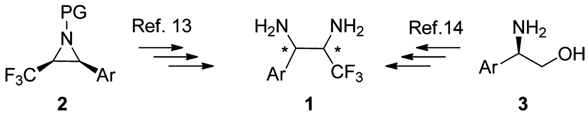
ABSTRACT: Herein is reported a study of asymmetric decarboxylative Mannich addition reactions between (S_s)-*N*-*t*-butylsulfinyl-3,3,3-trifluoroacetaldimine and Schiff bases derived from various aldehydes and lithium 2,2-diphenylglycinate. These reactions proceed with excellent diastereoselectivities and good chemical yields, providing a practical method for preparation of trifluoromethyl-containing vicinal diamines. The procedures can be conducted under convenient conditions, rendering this approach of high synthetic value.



INTRODUCTION

Numerous natural and synthetic biologically active compounds contain a 1,2-diamino functionality (vicinal diamines) as a key pharmacophoric moiety.[1] In particular, such types of therapeutic activities as anti-cancer,[2] -depressant,[3] and -hypertensive[4] are commonly associated with the 1,2-diamino group.[5] This proven biological importance of vicinal diamines has stimulated considerable research activity;[6] however, the development of new methods for more generalized and practical preparation of 1,2-diamines remains a significant challenge.[7] Considering the exciting biological profile of vicinal diamines, the fluorinated derivatives of this class of compounds might be of great pharmaceutical potential.[8,9] In fact, it is quite established that introduction of fluorine into the molecules of biologically active compounds usually leads to improved efficacy, enhanced membrane permeability, and significantly higher stability toward oxidative degradation.[10,11] Furthermore, the current pharmaceutical industry critically depends on the new methodological developments in fluorine chemistry, aiming at preparation of novel fluorinated structural types.[12] In this regard, 1-trifluoromethyl-1,2-diamines **1** (Scheme 1) represent a quite formidable and virtually unexplored chemical entity. Indeed, only in 2014, the De Kimpe[13] and Fustero[14] groups described preparation of compounds **1** in enantiomerically pure form. One method is based on selective trifluoromethyl-containing aziridine ring-opening,[13] while the other involves trifluoromethylation of the intermediate imine with CF_3-$SiMe_3$.[14] Both approaches reported significant breakthroughs, albeit the multistep procedure limits their synthetic value.

Scheme 1. Literature Approaches for Synthesis of Trifluoromethyl-Containing Vicinal Diamines 1



Consistent with our longstanding interests in the preparation of fluorine-containing biologically active compounds,[15] we were intrigued by the structure of trifluoromethyl-containing vicinal diamines **1** and consequently developed an asymmetric synthetic method for these compounds. Herein, we would like to disclose experimental details, a mechanistic rationale for the observed stereochemical outcome as well as some interesting chemical properties of 1-trifluoromethyl-1,2-diamines **1**.

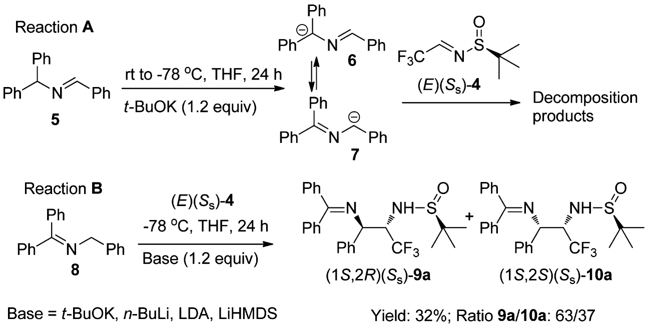
RESULTS AND DISCUSSION

In recent years, we were developing the chemistry of (R_s)- and (S_s)-*N*-*t*-butylsulfinyl-3,3,3-trifluoroacetaldimine **4**[16,17] (Scheme 2) as a general reagent for installation of a 2,2,2-trifluoro-1-(amino)ethyl [CF_3−$CH(NH_2)$−] pharmacophoric group[18] into various organic compounds.[19−22] On the basis of our knowledge of sulfinyl-imine **4** reactivity, we envisioned that the target vicinal diamines **1** can be obtained by the addition reactions between **4** and aldimine **5**.[23] It was expected that

Received: January 18, 2015
Published: February 25, 2015

DOI: 10.1021/acs.joc.5b00124
J. Org. Chem. 2015, 80, 3187−3194

Scheme 2. Reactions of Sulfinyl-Imine (*E*)(S_s)-4 with Aldimine 5 and Ketimine 8

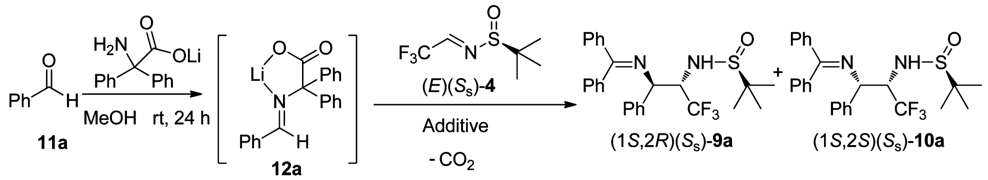


compound **5** (Reaction **A**, Scheme 2) under the basic conditions will afford carbanion **6**, which might undergo 1,3-proton shift,[24] generating in situ carbanion **7**. The latter ought to react with sulfinyl-imine **4**, giving the target Mannich-type addition products. Unfortunately, our attempts to execute this series of reactions failed, resulting in either no reaction or a mixture of unidentified decomposition products.

Next, we prepared imine **8**[25] (Reaction **B**) and conducted series of the reactions with sulfinyl-imine **4**. Application of sterically bulky *t*-BuOLi, LDA, and LiHMDS gave no expected products, while the use of *n*-BuLi gave us a breakthrough; addition products **9a** and **10a** were isolated in 32% yield and 63/37 ratio. To further improve the reaction conditions, we took a note of the recent discovery by the Zhao group[26] on the in situ decarboxylative generation of α-amino anion equivalents. Also, we have reported several examples of various types of decarboxylative generation of enolates and their reactions with imines.[27] Therefore, we decided to apply this method for reactions with sulfinyl-imine **4** (Table 1). The whole procedure (Table 1) includes the reaction of aldehyde **11** with lithium 2,2-diphenylglycinate, to form the intermediate Schiff bases **12**, followed by the decarboxylative Mannich addition with sulfinyl-imine **4**. It should be noted that the first step of this process is a quite rare example of a Schiff base preparation under basic conditions, requiring relatively strong bases and a prolonged reaction time.[28] The consequent reaction of Schiff base **12a** with imines is rather novel and still mechanistically obscure.[26] Our initial goals were to estimate the synthetic plausibility of this approach, gauge the reactivity of imine **4**, and optimize the reaction conditions.

Very surprisingly, we found that the addition reaction between Schiff base **12a** and imine **4**, conducted in THF without any additives, afforded almost no product (entry 1). Addition of organic bases, such as triethylamine (entry 2), also provide almost no products. On the other hand, the addition of 20 mol % of benzoic acid (entry 3) to the reaction mixture gave us a first breakthrough in this study. The target products **9a** and **10a** were isolated in 35% yield but, most importantly, with quite encouraging diastereoselectivity. Thus, considering that, in the reactions under study, simultaneous formation of two new stereogenic centers may give four stereoisomeric products, we were very pleased to detect only two with a rather good ratio of 96 to 4 (entry 3). Furthermore, the application of *para*-nitrobenzoic acid as the additive, (entry 4) allowed us to increase the yield (45%) and the diastereoselectivity (98/2). Running the same reaction at ambient temperature (entry 5) resulted in a bit lower yield (39%) but excellent stereoselectivity (99/1), underscoring the synthetic potential of this method. The use of less acidic *para*-methoxybenzoic acid (entry

Table 1. Optimization of Reaction Conditions[a]



entry	ratio (12a/4)	*T* (°C)	solvent	additive (mol %)	time (h)	yield (%)[b]	isomer ratio (9a:10a)[c]
1	1.1:1	0	THF		15	trace	
2	1.1:1	0	THF	Et_3N (20)	15	trace	
3	1.1:1	0	THF	$PhCO_2H$ (20)	15	35	96:4:0:0
4	1.1:1	0	THF	$4\text{-}NO_2C_6H_4CO_2H$ (20)	15	45	98:2:0:0
5	1.1:1	rt	THF	$4\text{-}NO_2C_6H_4CO_2H$ (20)	5	39	99:1:0:0
6	1.1:1	0	THF	$4\text{-}MeOC_6H_4CO_2H$ (20)	15	36	98:2:0:0
7	1.6:1	0	THF	$4\text{-}NO_2C_6H_4CO_2H$ (20)	15	50	97:3:0:0
8	1.6:1	rt	THF	$4\text{-}NO_2C_6H_4CO_2H$ (20)	5	70	97:3:0:0
9	1.6:1	rt	THF	$3\text{-}NO_2C_6H_4CO_2H$ (20)	5	74	99:1:0:0
10	1.6:1	rt	toluene	$3\text{-}NO_2C_6H_4CO_2H$ (20)	5	54	92:8:0:0
11	1.6:1	rt	DCM	$3\text{-}NO_2C_6H_4CO_2H$ (20)	5	60	98:2:0:0
12	1.6:1	rt	DMF	$3\text{-}NO_2C_6H_4CO_2H$ (20)	5	36[d]	66:34:0:0
13	1.6:1	rt	DMSO	$3\text{-}NO_2C_6H_4CO_2H$ (20)	5	43[d]	60:40:0:0
14	1.6:1	rt	THF	$3\text{-}NO_2C_6H_4CO_2H$ (50)	5	73	97:3:0:0
15	1.6:1	rt	THF	$3\text{-}NO_2C_6H_4CO_2H$ (10)	5	50	99:1:0:0
16	1.6:1	rt	THF	$3\text{-}NO_2C_6H_4CO_2H$ (20)	5	36[e]	97:3:0:0
17	2.0:1	rt	THF	$3\text{-}NO_2C_6H_4CO_2H$ (20)	5	59	99:1:0:0

[a] Reaction was performed with lithium salt **12a**, sulfinyl-imine **4** (0.2 mmol), and the additive in 2 mL of dry solvent under N_2. [b] Isolated yields of the major product. [c] Isomer ratio determined by ^{19}F NMR analysis of the crude reaction mixture. [d] Isolated yields of both major and minor products. [e] The starting material **12a** was used as a potassium salt, prepared with *t*-BuOK.

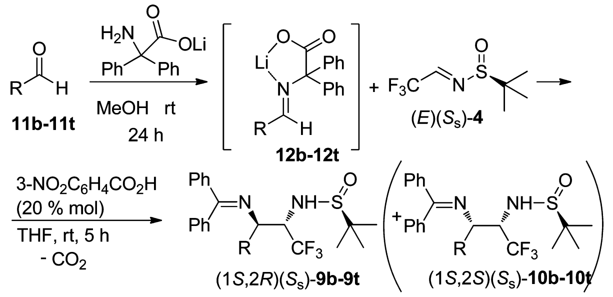
6), in THF at 0 °C, did not cause any dramatic effects, providing the formation of products **9a** and **10a** in yield (36%) and with diastereoselectivity (98/2) well in line with previous results. The higher yields were obtained when a greater excess of the starting and Schiff base **12a** were used. For example, the reaction conducted at 0 °C in THF using 1.6 equiv of **12a** (entry 7) gave rise to products **9a** and **10a** with noticeably improved yield (50%) and the intact, good stereoselectivity. Interestingly, carrying out the same reaction at ambient temperature (entry 8) resulted in synthetically acceptable 70% isolated yield of major diastereomer **9a**. Further improvement of the stereochemical outcome was made with application of *meta*-nitrobenzoic acid as the additive. In this case (entry 9), product **9a** was isolated as a diastereomerically pure compound in 74% yield.

Next, we decided to screen some solvents to further improve the chemical yields in these addition reactions. Unfortunately, this idea was rather futile as the results presented in entries 10–13 clearly suggest that THF is the solvent of choice. However, the stereochemical outcome obtained in the reactions conducted in DMF (entry 12) and DMSO (entry 13), albeit very unsatisfactory, might have very important bearing on the deduction of a plausible mechanism of these addition reactions. Finally, we would like to mention here also the attempts to use greater (entry 14) and lesser (entry 15) amounts of the additive, metal nature (Li vs K; entry 16), and a greater excess of Schiff base **12a** (entry 17). All of these experiments did not lead to improved chemical yields.

Then, we used the optimized reaction conditions to examine the structural generality of these addition reactions. The data obtained are summarized in Table 2. As the results presented in Table 2 show, in a series of monosubstituted benzaldehyde derivatives **11b–m** (entries 1–12), neither the nature of the substituent, such as Me (entries 1, 4, 7), MeO (entries 2, 5, 8) groups, or halogen atoms (Br: entries 3, 6, 11; Cl: entry 10; F: entry 9; I: entry 12), nor the position on the aromatic ring (*ortho*: entries 1–3; *meta*: entries 4–6; *para*: entries 7–12) has an apparent effect on the stereochemical outcome of these Mannich additions. In the case of disubstituted substrates **11n–p**, the reactions took place also quite smoothly, affording products **9n–p** in good chemical yields (entries 13–15). Among other structurally interesting substrates, we investigated the reactions of substrates containing ester (**11q**, entry 16), diphenyl (**11r**, entry 17), and (*E*)-styryl (**11s**, entry 18) moieties. These additions proceeded without any complications, giving rise to the expected products **9q–s** in diastereomerically pure form. Here, we would like also to mention the reaction of *tert*-butyl-containing substrate **11t**, which failed to react with imine **4** (entry 19), most likely, due to the vast steric bulk of a *tert*-butyl group. Albeit unsuccessful, this result was important to draw the structural limitations of this approach as well as provide valuable mechanistic clues.

Since four different diastereomeric products [(1*S*,2*S*)(S_s), (1*R*,2*S*)(S_s), (1*S*,2*R*)(S_s), (1*R*,2*R*)(S_s)] could be formed in this reaction, we felt it was necessary to carry out crystallographic analysis of both major and minor products. Taking advantage of the high crystallinity of compounds **10a** (minor diastereomer), containing an unsubstituted phenyl ring, and **9j** (major diastereomer), possessing a *para*-fluoro-phenyl group, we performed their single-crystal X-ray analysis (see the Supporting Information). According to the data obtained, the stereochemistry of major product **9j** is (1*S*,2*R*)(S_s), while the minor diastereomer **10a** is of (1*S*,2*S*)(S_s) absolute configuration. These results clearly demonstrate that the stereocontrol of imine **4** facial selectivity, provided by the (S_s)-*t*-butylsulfinyl group, is rather complete as no (1*R*)-configured products were detected in the reaction mixtures. This very strong preference for the observed (1*S*)-configuration is quite consistent with the previously reported data.[16,17,19−22] On the other hand, the absolute configuration of the second stereogenic carbon is rather unpredictable and has to be experimentally determined.

Table 2. Substrate Generality of the Decarboxylative Mannich Addition Reactions[a]



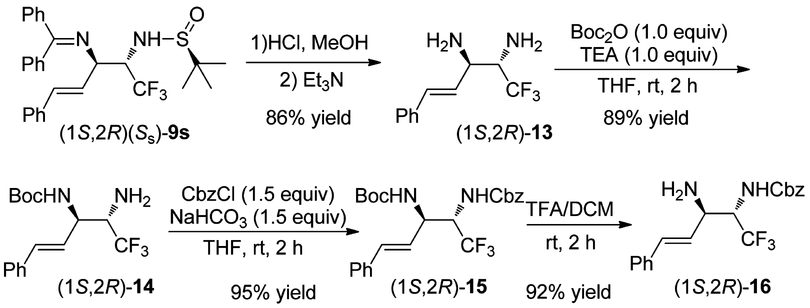
entry	R	product	yield (%)[b]	isomer ratio[c]
1	2-MeC_6H_4	**9b**	70	98:2:0:0
2	2-MeOC_6H_4	**9c**	78	99:1:0:0
3	2-BrC_6H_4	**9d**	54	97:3:0:0
4	3-MeC_6H_4	**9e**	83	96:4:0:0
5	3-MeOC_6H_4	**9f**	87	96:4:0:0
6	3-BrC_6H_4	**9g**	66	93:7:0:0
7	4-MeC_6H_4	**9h**	73	96:4:0:0
8	4-MeOC_6H_4	**9i**	68	96:4:0:0
9	4-FC_6H_4	**9j**	65	96:4:0:0
10	4-ClC_6H_4	**9k**	63	96:4:0:0
11	4-BrC_6H_4	**9l**	75	95:5:0:0
12	4-IC_6H_4	**9m**	55	95:5:0:0
13	3,4-$(CH_3)_2C_6H_3$	**9n**	68	97:3:0:0
14	3,4-$(MeO)_2C_6H_3$	**9o**	66	97:3:0:0
15	3,5-$(CH_3)_2C_6H_3$	**9p**	76	95:5:0:0
16	4-$CH_3COOC_6H_4$	**9q**	49	94:6:0:0
17	4-PhC_6H_4	**9r**	72	96:4:0:0
18	(*E*)-PhCH=CH	**9s**	79	92:8:0:0
19	*t*-Bu	**9t**	trace	

[a] Reactions were performed with lithium salt **12** (1.32 mmol), sulfinylimine **4** (0.83 mmol), and 3-$NO_2C_6H_4CO_2H$ (0.17 mmol) in 5 mL of dry THF at room temperature for 5 h under N_2. [b] Isolated yields of the major product. [c] Isomer ratio was determined by ^{19}F NMR analysis of the crude reaction mixtures.

We believed the preparation of deprotected, free trifluoromethyl-containing vicinal diamines should be demonstrated. For this goal, we selected (*E*)-styryl-containing compound **9s** and performed deprotection of the *t*-butylsulfinyl group under the standard acidic conditions.[29] The reaction proceeded without any complications, affording free diamine **13** in good (86%) isolated yield (Scheme 3).

Having thus prepared free vicinal diamine **13**, we were eager to study its novel chemistry, in particular the difference in reactivity of the amino functions. On the basis of our previous experience with the chemistry of CF_3-containing α-amino acids,[30] we expected that the amino group adjacent to the trifluoromethyl might be severely less basic, allowing for regioselective transformations. Fulfilling our expectations, the reaction of diamine **13** with 1 equiv of Boc_2O proceeded with

Scheme 3. Preparation of Free Vicinal Diamines and Their Chemical Properties



virtually complete selectivity, furnishing *β*-*N*-protected compound **14**. The remaining *α*-amino group can also be engaged in the reaction with acylating reagents but under forcing reaction conditions. Thus, using a strong base ($NaHCO_3$) and a 1.5 equiv excess of CbzCl, the diprotected derivative **15** was obtained in a good chemical yield of 95%. Taking advantage of the orthogonal protection of amino groups in **15**, we performed chemo-selective deprotection of the *N*-Boc group, affording monoprotected compound **16** with 92% yield.

As mentioned above, the mechanism of these decarboxylative Mannich addition reactions is obscure.[26] For example, the mode and order of the decarboxylation step and the role of the acidic additives are particularly puzzling. This work has clearly confirmed the significant effect of the additives. Furthermore, our new data have pointed to the critical role of the reaction solvent influencing dramatically the stereochemical outcome (Table 1, entries 12 and 13). Taking into account these factors as well as principles of geometric homogeneity[31] and minimum charge separation,[32] we were in the position to propose a plausible mechanistic rationale to account for the observed experimental results. One of the most important findings of this work is a low diastereoselectivity obtained from the reactions of lithiated derivatives of imine **8** (Scheme 2, Reaction **B**). To rationalize this stereochemical outcome, we can build transition states (TSs) **A**−**C** (Figure 1) leading to the products of (1*S*,2*R*) absolute configuration and TSs **D**−**F** responsible for the (1*S*,2*S*) stereochemistry of the minor diastereomers.

Considering the mode of stereochemical interactions in TSs **A**−**C**, we can suggest that TS **C** is the most favorable, placing the stereocontrolling trifluoromethyl group[33] in the least sterically congested position (CF_3/H/N vs CF_3/N/Ph and CF_3/H/Ph). Interestingly, the same type of stereochemical contacts can be found in a series of TSs **D**−**F** affording diastereomers with the opposite configuration at C2. On the basis of the same reasoning, TS **F** might be preferred over TSs **D** and **E**. Overall, among the TSs **A**−**F**, there are no apparent structural features to expect a great degree of stereochemical preferences and high diastereoselectivity. Therefore, the observed low stereoselectivity, about 1/2 ratio of diastereomers **9a** and **10a** (Scheme 2), is rather adequate.

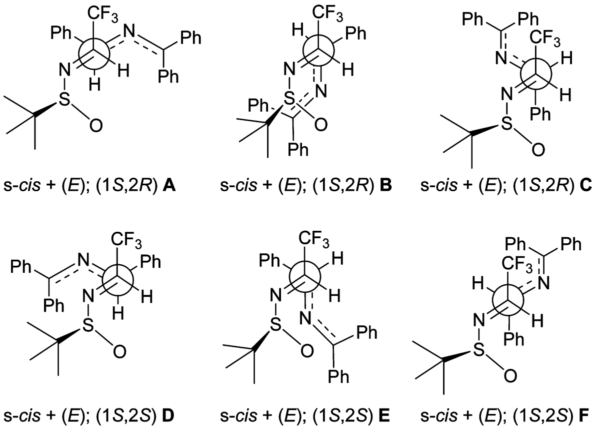


Figure 1. Possible TSs **A**−**F** in the reactions of lithiated **8** with imine **4**.

These considerations lead us to a conclusion that the very high level of diastereoselectivity obtained in the reactions of Schiff bases **12a** with imine **4** (Tables 1 and 2) might involve very different reaction species. Bearing this in mind, we would like to propose that the decarboxylative step occurs after or simultaneously with the asymmetric C−C bond formation via TSs **G**−**I** (Figure 2).

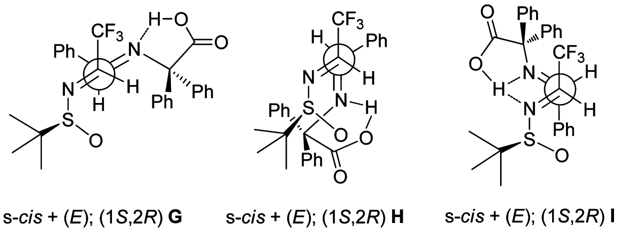


Figure 2. Possible TSs **G**−**I** in the reactions of Schiff bases **12a** with imine **4**.

In the design of TSs **G**−**I**, we incorporated the following assumptions: first, Schiff base **12a** reacts in protonated form to explain the crucial role of the acidic additives. Second, imine **4** reacts in the s-*cis* conformation,[29] consistent with the *α*-(*S*) absolute configuration of the major products.[19−22] Third, Schiff bases **12a** react in (*E*) conformation with the glycine moiety being hydrogen-bonded to form the five-membered ring.[34] The latter assumption can explain the critical role of the reaction solvent as application of strongly polar DMF and DMSO (Table 1, entries 12 and 13) might interfere with the intramolecular hydrogen bond.

Careful examination of TSs **G**−**I** allows us to note that TS **I** has the most sterically favorable position of the CF_3 group (CF_3/H/N vs CF_3/N/Ph and CF_3/H/Ph). However, most importantly, in TS **I**, the transfer of hydrogen can take place with a minimum charge separation from the glycine moiety to the imine **4** nitrogen. This structural feature renders TS **I** most plausible and explains all experimental facts encountered in this study.

■ CONCLUSION

To conclude, the results reported in this work evidently demonstrate that the decarboxylative Mannich addition reactions between (S_s)-*N*-*t*-butylsulfinyl-3,3,3-trifluoro-acetaldimine and Schiff bases derived from various aldehydes and lithium 2,2-diphenylglycinate represent a practical method for preparation of trifluoromethyl-containing vicinal diamines of high pharmaceutical potential. The reactions can be conducted under operationally convenient conditions[35] in good yields and diastereoselectivities. The method is clearly synthetically superior over the literature approaches and can be of immediate use for reliable preparation of the trifluoromethyl-containing vicinal diamines for synthetic and biological studies.

■ EXPERIMENTAL SECTION

Typical Procedure for the Asymmetric Decarboxylative Mannich Addition Reactions. Schiff base lithium salts were synthesized according to the literature.[26b] To a 25 mL vial equipped with a magnetic stirrer bar were added 2,2-diphenylglycine (0.3000 g, 1.32 mmol), *t*-BuOLi (0.1057 g, 1.32 mmol), and 3 Å molecular sieves (0.30 g). The sealed vial was evacuated and refilled with N_2 three times, followed by addition of anhydrous methanol (1.5 mL). After the mixture was stirred at room temperature for 30 min, benzaldehyde (0.1400 g, 1.32 mmol) was added. After stirring at room temperature for 24 h, the reaction mixture was submitted to filtration. The solid was washed with anhydrous methanol (3 mL × 3). The combined filtrate was concentrated via rotary evaporation at 50 °C under reduced pressure to give a white solid. The solid was further vacuumed by an oil pump for 2 h. To the solid were added *m*-nitrobenzoic acid (0.0277 g, 0.166 mmol), CF_3-sulfinylimine (0.1670 g, 0.83 mmol), and anhydrous THF (5.0 mL). The mixture was stirred under a N_2 atmosphere at room temperature for 5 h and quenched with H_2O (5 mL). The organic layer was taken, and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with water (2 × 30 mL) and brine solution (1 × 30 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated, and the crude mixture was charged onto silica gel and purified through flash chromatography (elute: PE/EtOAc = 4:1) to furnish the corresponding products **9**, **10**.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-phenylpropan-2-yl)-2-methylpropane-2-sulfinamide ***(9a)***. White solid, mp 122−123 °C. Yield: 290 mg (74%). $[\alpha]^{20}_{D}$ = +15.73 (*c* = 0.89, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68−7.63 (m, 2H), 7.48−7.42 (m, 1H), 7.41−7.35 (m, 3H), 7.35−7.19 (m, 7H), 6.93−6.89 (m, 2H), 4.99 (d, *J* = 10.5 Hz, 1H), 4.91 (s, 1H), 3.97−3.87 (m, 1H), 0.98 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.1, 141.0, 139.1, 135.8, 130.9, 129.0, 128.8, 128.6, 128.4, 128.3, 127.7, 127.1, 126.9, 125.0 (q, J_{FC} = 287.8 Hz), 63.8 (q, $^{3}J_{FC}$ = 27.3 Hz), 63.3, 57.1, 22.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.69. IR (cm^{-1}): 3360, 2979, 1610, 1600, 1573, 1446, 1406, 1318, 1264, 1163, 1153, 1137, 1075, 762, 705, 687. HRMS (TOF MS ESI): calcd for $C_{26}H_{28}F_3N_2OS$ [M + H]$^+$ 473.1874, found 473.1872.

(S)-N-((2S,3S)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-phenylpropan-2-yl)-2-methylpropane-2-sulfinamide ***(10a)***. White solid, mp 133−134 °C. Yield: 2.9 mg (0.75%). $[\alpha]^{20}_{D}$ = −19.55 (*c* = 0.27, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66−7.62 (m, 2H), 7.44−7.20 (m, 11H), 6.96−6.92 (m, 2H), 4.66 (d, *J* = 6.7 Hz, 1H), 4.32−4.21 (m, 1H), 3.27 (d, *J* = 10.6 Hz, 1H), 0.95 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 168.9, 139.5, 139.2, 136.2, 130.5, 128.7, 128.7, 128.6, 128.5, 128.4, 128.1, 128.0, 127.5, 125.0 (q, J_{FC} = 285.2 Hz), 66.5, 63.6 (q, $^{3}J_{FC}$ = 27.0 Hz), 57.1, 22.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ −70.68. IR (cm^{-1}): 3317, 2956, 2924, 1623, 1455, 1446, 1259, 1167, 1129, 1109, 1080, 703, 692. HRMS (TOF MS ESI): calcd for $C_{26}H_{27}F_3N_2OSNa$ [M + Na]$^+$ 495.1694, found 495.1692.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-(o-tolyl)propan-2-yl)-2-methylpropane-2-sulfinamide ***(9b)***. White solid, mp 65−66 °C. Yield: 283 mg (70%). $[\alpha]^{20}_{D}$ = +77.78 (*c* = 0.11, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69−7.65 (m, 2H), 7.51−7.47 (m, 1H), 7.46−7.40 (m, 1H), 7.41−7.34 (m, 3H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.17−7.10 (m, 2H), 7.10−7.05 (m, 1H), 6.82 (d, *J* = 7.1 Hz, 2H), 5.21 (d, *J* = 10.4 Hz, 1H), 5.03 (s, 1H), 3.79−3.69 (m, 1H), 1.89 (s, 3H), 1.11 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.7, 139.6, 139.0, 136.4, 133.7, 130.8, 130.5, 128.9, 128.8, 128.8, 128.4, 128.3, 127.5, 127.0, 125.9, 125.1 (q, J_{FC} = 286.8 Hz), 61.0 (q, $^{3}J_{FC}$ = 28.3 Hz), 59.8, 57.3, 22.3, 18.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ −73.03. IR (cm^{-1}): 3358, 2956, 1617, 1448, 1404, 1272, 1158, 1142, 1124, 1105, 1087, 1076, 761, 700. HRMS (TOF MS ESI): calcd for $C_{27}H_{30}F_3N_2OS$ [M + H]$^+$ 487.2031, found 487.2030.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-(2-methoxyphenyl)propan-2-yl)-2-methylpropane-2-sulfinamide ***(9c)***. White solid, mp 160−161 °C. Yield: 325 mg (78%). $[\alpha]^{20}_{D}$ = +46.75 (*c* = 0.95, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69−7.64 (m, 2H), 7.42−7.38 (m, 1H), 7.38−7.29 (m, 4H), 7.27−7.18 (m, 3H), 6.92−6.85 (m, 3H), 6.81 (d, *J* = 8.1 Hz, 1H), 5.16 (s, 1H), 5.02 (d, *J* = 10.7 Hz, 1H), 4.23−4.16 (m, 1H), 3.65 (s, 3H), 0.97 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 155.4, 139.4, 136.0, 130.7, 129.2, 129.1, 128.8, 128.6, 128.5, 128.2, 127.2, 127.1, 125.3 (q, J_{FC} = 287.8 Hz), 120.6, 110.6, 60.1 (q, $^{3}J_{FC}$ = 27.3 Hz), 58.6, 57.0, 55.4, 22.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.73. IR (cm^{-1}): 3345, 2958, 1628, 1492, 1291, 1268, 1245, 1238, 1164, 1155, 1142, 1124, 1109, 1081, 759, 755, 695. HRMS (TOF MS ESI): calcd for $C_{27}H_{30}F_3N_2O_2S$ [M + H]$^+$ 503.1980, found 503.1979.

(S)-N-((2S,3R)-3-(2-Bromophenyl)-3-((diphenylmethylene)-amino)-1,1,1-trifluoropropan-2-yl)-2-methylpropane-2-sulfinamide ***(9d)***. White solid, mp 113−114 °C. Yield: 247 mg (54%). $[\alpha]^{20}_{D}$ = +128.61 (*c* = 0.78, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70−7.65 (m, 2H), 7.55 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.50 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.48−7.42 (m, 1H), 7.40−7.24 (m, 6H), 7.13 (td, *J* = 7.7, 1.7 Hz, 1H), 6.85−6.80 (m, 2H), 5.21 (s, 1H), 4.98 (d, *J* = 10.9 Hz, 1H), 4.12−4.02 (m, 1H), 1.04 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.9, 139.8, 138.9, 135.9, 133.0, 131.2, 131.0, 129.3, 129.1, 128.9, 128.5, 128.3, 127.3, 127.0, 124.9 (q, J_{FC} = 287.8 Hz), 121.8, 62.9, 60.4 (q, $^{3}J_{FC}$ = 28.3 Hz), 57.2, 22.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.44. IR (cm^{-1}): 3356, 2923, 1613, 1467, 1442, 1407, 1266, 1178, 1160, 1142, 1125, 1118, 1086, 759, 699, 686. HRMS (TOF MS ESI): calcd for $C_{26}H_{27}BrF_3N_2OS$ [M + H]$^+$ 551.0980, found 551.0976.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-(m-tolyl)propan-2-yl)-2-methylpropane-2-sulfinamide ***(9e)***. White solid, mp 139−140 °C. Yield: 335 mg (83%). $[\alpha]^{20}_{D}$ = +10.83 (*c* = 0.72, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69−7.64 (m, 2H), 7.49−7.43 (m, 1H), 7.42−7.36 (m, 3H), 7.35−7.30 (m, 2H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 9.2 Hz, 2H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.95−6.91 (m, 2H), 5.01 (d, *J* = 10.5 Hz, 1H), 4.89 (s, 1H), 3.95−3.85 (m, 1H), 2.31 (s, 3H), 1.01 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.8, 141.0, 139.2, 138.1, 135.8, 130.8, 128.9, 128.8, 128.4, 128.3, 128.3, 128.2, 127.6, 127.3, 124.9 (q, J_{FC} = 286.8 Hz), 124.0, 63.8 (q, $^{3}J_{FC}$ = 28.3 Hz), 63.2, 57.1, 22.0, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.77. IR (cm^{-1}): 2964, 1627, 1607, 1448, 1405, 1317, 1292, 1262, 1177, 1168, 1133, 1090, 1080, 788, 709, 697, 631. HRMS (TOF MS ESI): calcd for $C_{27}H_{30}F_3N_2OS$ [M + H]$^+$ 487.2031, found 487.2031.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-(3-methoxyphenyl)propan-2-yl)-2-methylpropane-2-sulfinamide ***(9f)***. Pale yellow solid, mp 125−126 °C. Yield: 363 mg (87%). $[\alpha]^{20}_{D}$ = +17.38 (*c* = 0.66, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68−7.63 (m, 2H), 7.43−7.39 (m, 1H), 7.38−7.26 (m, 5H), 7.20 (t, *J* = 8.1 Hz, 1H), 6.95−6.91 (m, 2H), 6.82−6.75 (m, 3H), 5.01 (d, *J* = 10.5 Hz, 1H), 4.90 (s, 1H), 3.99−3.88 (m, 1H), 3.74 (s, 3H), 1.00 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.1, 159.8, 142.6, 139.1, 135.8, 130.9, 129.6, 129.0, 128.8, 128.4, 128.3, 127.2, 124.9 (q, J_{FC} = 286.8 Hz), 119.3, 113.4, 112.4, 63.7 (q, $^{3}J_{FC}$ = 28.3 Hz), 63.2, 57.1, 55.3, 22.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.65. IR (cm^{-1}): 3361, 2947, 2882, 1629, 1604, 1493, 1279, 1268, 1253, 1170, 1136, 1121, 1072, 1061, 1033, 794, 783, 706, 699. HRMS (TOF MS ESI): calcd for $C_{27}H_{30}F_3N_2O_2S$ [M + H]$^+$ 503.1980, found 503.1979.

(S)-N-((2S,3R)-3-(3-Bromophenyl)-3-((diphenylmethylene)-amino)-1,1,1-trifluoropropan-2-yl)-2-methylpropane-2-sulfinamide ***(9g)***. White solid, mp 56−57 °C. Yield: 302 mg (66%). $[\alpha]^{20}_{D}$ = +2.67 (*c* = 0.75, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67−7.63 (m,

2H), 7.46–7.42 (m, 2H), 7.41–7.30 (m, 6H), 7.17 (t, J = 7.8 Hz, 1H), 7.12 (d, J = 7.9 Hz, 1H), 6.92–6.88 (m, 2H), 4.94 (d, J = 10.7 Hz, 1H), 4.90 (s, 1H), 3.92–3.82 (m, 1H), 1.03 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 171.9, 143.4, 138.9, 135.6, 131.1, 130.9, 130.4, 130.2, 129.2, 128.9, 128.5, 128.4, 127.1, 125.6, 124.7 (q, J_{FC} = 287.8 Hz), 122.8, 63.7 (q, $^3J_{FC}$ = 27.3 Hz), 63.0, 57.3, 22.1. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.43. IR (cm^{-1}): 3342, 3060, 2958, 1627, 1595, 1571, 1474, 1446, 1290, 1266, 1192, 1163, 1137, 1074, 783, 730, 668. HRMS (TOF MS ESI): calcd for $C_{26}H_{27}BrF_3N_2OS$ $[M + H]^+$ 551.0980, found 551.0979.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-(p-tolyl)propan-2-yl)-2-methylpropane-2-sulfinamide ***(9h)***. White solid, mp 117–118 °C. Yield: 295 mg (73%). $[\alpha]_D^{20}$ = −8.80 (*c* = 0.86, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.69–7.64 (m, 2H), 7.46–7.40 (m, 1H), 7.39–7.33 (m, 3H), 7.30 (t, J = 7.2 Hz, 2H), 7.10 (s, 4H), 6.95–6.90 (m, 2H), 5.05 (d, J = 10.4 Hz, 1H), 4.90 (s, 1H), 3.97–3.86 (m, 1H), 2.31 (s, 3H), 1.00 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 170.9, 139.2, 138.0, 137.2, 135.8, 130.8, 129.2, 129.0, 128.8, 128.3, 128.3, 127.2, 126.8, 125.0 (q, J_{FC} = 286.8 Hz), 63.8 (q, $^3J_{FC}$ = 27.3 Hz), 63.0, 57.2, 22.1, 21.1. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.68. IR (cm^{-1}): 3354, 3064, 2979, 2968, 2923, 2899, 1611, 1405, 1334, 1317, 1291, 1271, 1187, 1163, 1152, 1138, 1125, 1086, 811, 701, 679, 687. HRMS (TOF MS ESI): calcd for $C_{27}H_{30}F_3N_2OS$ $[M + H]^+$ 487.2031, found 487.2029.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-(4-methoxyphenyl)propan-2-yl)-2-methylpropane-2-sulfinamide ***(9i)***. Pale yellow solid, mp 62–63 °C. Yield: 284 mg (68%). $[\alpha]_D^{20}$ = −2.47 (*c* = 0.57, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.66–7.62 (m, 2H), 7.47–7.42 (m, 1H), 7.41–7.31 (m, 5H), 7.14–7.10 (m, 2H), 6.93–6.89 (m, 2H), 6.85–6.80 (m, 2H), 4.98 (d, J = 10.4 Hz, 1H), 4.85 (s, 1H), 3.91–3.81 (m, 1H), 3.78 (s, 3H), 1.01 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 170.8, 158.9, 139.2, 135.8, 133.1, 130.8, 128.9, 128.8, 128.3, 128.3, 128.0, 127.2, 127.1, 124.9 (q, J_{FC} = 286.8 Hz), 113.9, 63.8 (q, $^3J_{FC}$ = 28.3 Hz), 62.7, 57.1, 55.3, 22.2. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.71. IR (cm^{-1}): 3351, 3061, 2934, 1628, 1512, 1265, 1251, 1176, 1136, 1113, 1076, 1031, 824, 699. HRMS (TOF MS ESI): calcd for $C_{27}H_{30}F_3N_2O_2S$ $[M + H]^+$ 503.1980, found 503.1982.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-(4-fluorophenyl)propan-2-yl)-2-methylpropane-2-sulfinamide ***(9j)***. White solid, mp 159–160 °C. Yield: 265 mg (65%). $[\alpha]_D^{20}$ = +23.17 (*c* = 0.49, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.67–7.63 (m, 2H), 7.48–7.44 (m, 1H), 7.42–7.30 (m, 5H), 7.20 (dd, J = 8.6, 5.4 Hz, 2H), 7.00 (t, J = 8.6 Hz, 2H), 6.89 (d, J = 6.9 Hz, 2H), 4.94 (d, J = 10.6 Hz, 1H), 4.90 (s, 1H), 3.93–3.83 (m, 1H), 1.02 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 171.4, 162.1 (d, J_{FC} = 247.5 Hz), 139.0, 136.8 (d, $^5J_{FC}$ = 3.0 Hz), 135.7, 131.0, 129.1, 128.8, 128.7, 128.6, 128.4 (d, $^4J_{FC}$ = 9.9 Hz), 127.1, 124.8 (q, J_{FC} = 286.8 Hz), 115.5 (d, $^3J_{FC}$ = 21.4 Hz), 63.7 (q, $^3J_{FC}$ = 27.9 Hz), 62.7, 57.2, 22.1. ^{19}F NMR (376 MHz, CDCl$_3$): δ −114.41, −72.52. IR (cm^{-1}): 3366, 3056, 2960, 1627, 1508, 1315, 1265, 1219, 1164, 1139, 1124, 1084, 827, 706, 693, 685. HRMS (TOF MS ESI): calcd for $C_{26}H_{27}F_4N_2OS$ $[M + H]^+$ 491.1780, found 491.1780.

(S)-N-((2S,3R)-3-(4-Chlorophenyl)-3-((diphenylmethylene)-amino)-1,1,1-trifluoropropan-2-yl)-2-methylpropane-2-sulfinamide ***(9k)***. White solid, mp 142–143 °C. Yield: 265 mg (63%). $[\alpha]_D^{20}$ = −22.28 (*c* = 0.84, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.64 (d, J = 7.1 Hz, 2H), 7.49–7.43 (m, 1H), 7.41–7.26 (m, 7H), 7.17 (d, J = 8.3 Hz, 2H), 6.89 (t, J = 6.8 Hz, 2H), 4.94 (d, J = 10.6 Hz, 1H), 4.88 (s, 1H), 3.93–3.82 (m, 1H), 1.02 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 171.7, 139.6, 138.9, 135.7, 133.4, 131.1, 129.1, 128.9, 128.7, 128.5, 128.4, 128.3, 127.1, 124.7 (q, J_{FC} = 286.8 Hz), 63.6 (q, $^3J_{FC}$ = 28.3 Hz), 62.8, 57.3, 22.1. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.51. IR (cm^{-1}): 3354, 2954, 2942, 1611, 1490, 1266, 1257, 1164, 1156, 1134, 1109, 1074, 815, 701, 685. HRMS (TOF MS ESI): calcd for $C_{26}H_{26}ClF_3N_2OSNa$ $[M + Na]^+$ 529.1304, found 529.1302.

(S)-N-((2S,3R)-3-(4-Bromophenyl)-3-((diphenylmethylene)-amino)-1,1,1-trifluoropropan-2-yl)-2-methylpropane-2-sulfinamide ***(9l)***. Pale yellow solid, mp 147–148 °C. Yield: 343 mg (75%). $[\alpha]_D^{20}$ = −29.00 (*c* = 0.80, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.67–7.62 (m, 2H), 7.47–7.43 (m, 3H), 7.41–7.31 (m, 5H), 7.11 (d, J = 8.4 Hz, 2H), 6.91–6.87 (m, 2H), 4.93 (d, J = 10.6 Hz, 1H), 4.87 (s, 1H), 3.93–3.82 (m, 1H), 1.01 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 171.7, 140.1, 138.9 135.6, 131.7, 131.1, 129.1, 128.9, 128.8, 128.5, 128.3, 127.1, 124.7 (q, J_{FC} = 286.8 Hz), 121.5, 63.5 (q, $^3J_{FC}$ = 28.3 Hz), 62.9, 57.3, 22.1. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.48. IR (cm^{-1}): 3353, 2953, 2940, 1611, 1487, 1257, 1164, 1134, 1108, 1053, 1012, 812, 700, 683. HRMS (TOF MS ESI): calcd for $C_{26}H_{27}BrF_3N_2OS$ $[M + H]^+$ 551.0980, found 551.0978.

(S)-N-((2S,3R)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-3-(4-iodophenyl)propan-2-yl)-2-methylpropane-2-sulfinamide ***(9m)***. White solid, mp 51–52 °C. Yield: 273 mg (55%). $[\alpha]_D^{20}$ = −38.68 (*c* = 0.70, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.66–7.61 (m, 4H), 7.48–7.43 (m, 1H), 7.42–7.30 (m, 5H), 6.98 (d, J = 8.3 Hz, 2H), 6.90 (d, J = 6.8 Hz, 2H), 4.95 (d, J = 10.6 Hz, 1H), 4.86 (s, 1H), 3.92–3.82 (m, 1H), 1.00 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 171.7, 140.8, 138.9, 137.6, 137.4, 135.6, 131.1, 129.1, 129.0, 128.9, 128.5, 128.3, 127.1, 124.7 (q, J_{FC} = 286.8 Hz), 63.6 (q, $^3J_{FC}$ = 28.3 Hz), 63.0, 57.3, 22.1. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.47. IR (cm^{-1}): 3347, 2925, 1627, 1484, 1446, 1399, 1316, 1284, 1266, 1182, 1109, 1079, 1060, 1006, 811, 784, 695. HRMS (TOF MS ESI): calcd for $C_{26}H_{27}F_3IN_2OS$ $[M + H]^+$ 599.0841, found 599.0844.

(S)-N-((2S,3R)-3-(3,4-Dimethylphenyl)-3-((diphenylmethylene)-amino)-1,1,1-trifluoropropan-2-yl)-2-methylpropane-2-sulfinamide ***(9n)***. White solid, mp 85–86 °C. Yield: 283 mg (68%). $[\alpha]_D^{20}$ = −7.77 (*c* = 0.85, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.69–7.65 (m, 2H), 7.47–7.41 (m, 1H), 7.40–7.35 (m, 3H), 7.32 (t, J = 7.2 Hz, 2H), 7.05 (d, J = 7.8 Hz, 1H), 6.99 (s, 1H), 6.96–6.91 (m, 3H), 5.06 (d, J = 10.4 Hz, 1H), 4.88 (s, 1H), 3.95–3.84 (m, 1H), 2.23 (s, 3H), 2.22 (s, 3H), 1.02 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 170.7, 139.3, 138.4, 136.6, 135.9, 135.8, 130.7, 129.7, 128.9, 128.9, 128.3, 128.3, 128.1, 127.3, 125.0 (q, J_{FC} = 287.8 Hz), 124.4, 63.9 (q, $^3J_{FC}$ = 28.3 Hz), 63.1, 57.2, 22.1, 19.8, 19.4. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.76. IR (cm^{-1}): 3346, 2957, 2922, 1630, 1448, 1406, 1292, 1266, 1165, 1136, 1121, 1077, 819, 700. HRMS (TOF MS ESI): calcd for $C_{28}H_{32}F_3N_2OS$ $[M + H]^+$ 501.2187, found 501.2186.

(S)-N-((2S,3R)-3-(3,4-Dimethoxyphenyl)-3-((diphenylmethylene)-amino)-1,1,1-trifluoropropan-2-yl)-2-methylpropane-2-sulfinamide ***(9o)***. White solid, mp 57–58 °C. Yield: 292 mg (66%). $[\alpha]_D^{20}$= +8.63 (*c* = 0.83, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.63–7.59 (m, 2H), 7.39–7.34 (m, 1H), 7.34–7.25 (m, 5H), 6.88 (d, J = 7.0 Hz, 2H), 6.76 (s, 2H), 6.69 (s, 1H), 5.01(d, J = 10.4 Hz, 1H), 4.82 (s, 1H), 3.93–3.83 (m, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 1.00 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 171.0, 149.0, 148.4, 139.1, 135.8, 133.5, 130.8, 128.9, 128.8, 128.3, 128.2, 127.2, 124.9 (q, J_{FC} = 286.8 Hz), 119.5, 111.1, 110.1, 63.7 (q, $^3J_{FC}$ = 27.3 Hz), 63.0, 57.1, 56.0, 55.9, 22.1. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.57. IR (cm^{-1}): 3346, 3237, 3061, 2958, 2907, 1628, 1516, 1465, 1414, 1265, 1239, 1170, 1082, 1027, 784, 701. HRMS (TOF MS ESI): calcd for $C_{28}H_{31}F_3N_2O_3SNa$ $[M + Na]^+$ 555.1905, found 555.1905.

(S)-N-((2S,3R)-3-(3,5-Dimethylphenyl)-3-((diphenylmethylene)-amino)-1,1,1-trifluoropropan-2-yl)-2-methylpropane-2-sulfinamide ***(9p)***. White solid, mp 131–132 °C. Yield: 316 mg (76%). $[\alpha]_D^{20}$= +9.95 (*c* = 0.82, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.71–7.66 (m, 2H), 7.47–7.41 (m, 1H), 7.41–7.35 (m, 3H), 7.35–7.29 (m, 2H), 6.96–6.92 (m, 2H), 6.88 (s, 1H), 6.84 (s, 2H), 5.06 (d, J = 10.4 Hz, 1H), 4.88 (s, 1H), 3.95–3.84 (m, 1H), 2.27 (s, 6H), 1.04 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 170.8, 141.0, 139.3, 138.0, 135.9, 130.8, 129.2, 129.0, 128.9, 128.3, 128.3, 127.4, 125.0 (q, J_{FC} = 286.8 Hz), 124.8, 64.0 (q, $^3J_{FC}$ = 27.3 Hz), 63.4, 57.2, 22.0, 21.3. ^{19}F NMR (376 MHz, CDCl$_3$): δ −72.75. IR (cm^{-1}): 2980, 2963, 2952, 2922, 1627, 1446, 1403, 1289, 1267, 1248, 1168, 1138, 1125, 1087, 839, 710, 701, 694. HRMS (TOF MS ESI): calcd for $C_{28}H_{32}F_3N_2OS$ $[M + H]^+$ 501.2187, found 501.2186.

Methyl 4-((1R,2S)-2-((S)-1,1-Dimethylethylsulfinamido)-1-((diphenylmethylene)amino)-3,3,3-trifluoropropyl)benzoate ***(9q)***. White solid, mp 61–62 °C. Yield: 216 mg (49%). $[\alpha]_D^{20}$ = −17.91 (*c* = 0.54, CH$_2$Cl$_2$). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.97 (d, J = 8.4 Hz, 2H), 7.66–7.61 (m, 2H), 7.46–7.40 (m, 1H), 7.39–7.33 (m, 3H), 7.32–7.26 (m, 4H), 6.85 (d, J = 7.1 Hz, 2H), 4.98–4.93 (m, 2H), 3.99–3.89 (m, 1H), 3.87 (s, 3H), 0.95 (s, 9H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 171.9, 166.7, 146.2, 138.8, 135.6, 131.1, 129.8, 129.5, 129.1, 128.9, 128.4, 128.3, 127.1, 127.0, 124.7 (q, J_{FC} = 286.8 Hz), 63. Five (q, $^3J_{FC}$ = 28.3 Hz), 63.3, 57.2, 52.2, 22.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.49. IR (cm^{-1}): 3342, 2955, 1724, 1627, 1612, 1446, 1411, 1316, 1275, 1181, 1136, 1109, 1019, 768, 697. HRMS (TOF MS ESI): calcd for $C_{28}H_{29}F_3N_2O_3SNa$ $[M + Na]^+$ 553.1749, found 553.1746.

*(S)-N-((2S,3R)-3-([1,1′-Biphenyl]-4-yl)-3-((diphenylmethylene)-amino)-1,1,1-trifluoropropan-2-yl)-2-methylpropane-2-sulfinamide (**9r**).* White solid, mp 72–73 °C. Yield: 328 mg (72%). $[\alpha]_D^{20}$ = −63.72 (c = 0.66, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 7.9 Hz, 2H), 7.64–7.58 (m, 4H), 7.49–7.34 (m, 11H), 7.04–6.99 (m, 2H), 5.09 (d, J = 10.5 Hz, 1H), 5.05 (s, 1H), 4.08–3.98 (m, 1H), 1.04 (s, 9H). ^{13}C NMR (101 MHz, CDCl3): δ 171.3, 140.6, 140.5, 140.1, 139.2, 135.8, 131.0, 129.1, 129.0, 128.8, 128.5, 128.4, 127.6, 127.5, 127.3, 127.1, 127.0, 125.0 (q, J_{FC} = 287.8 Hz), 63.9 (q, $^3J_{FC}$ = 28.3 Hz), 63.2, 57.2, 22.1 ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.43. IR (cm^{-1}): 2957, 1627, 1488, 1405, 1290, 1266, 1163, 1137, 1125, 1085, 764, 698. HRMS (TOF MS ESI): calcd for $C_{32}H_{32}F_3N_2OS$ $[M + H]^+$ 549.2187, found 549.2186.

*(S)-N-((2S,3R,E)-3-((Diphenylmethylene)amino)-1,1,1-trifluoro-5-phenylpent-4-en-2-yl)-2-methylpropane-2-sulfinamide (**9s**).* Yellow oil. Yield: 327 mg (79%). $[\alpha]_D^{20}$ = −88.56 (c = 0.61, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70–7.65 (m, 2H), 7.49–7.43 (m, 4H), 7.42–7.30 (m, 6H), 7.29–7.24 (m, 1H), 7.20–7.16 (m, 2H), 6.32 (s, 2H), 5.24–5.18 (m, 1H), 4.57 (s, 1H), 3.98–3.87 (m, 1H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.0, 139.1, 126.4, 136.0, 132.3, 130.9, 129.1, 128.8, 128.7, 128.5, 128.3, 128.1, 128.0, 127.3, 126.4, 124.9 (q, J_{FC} = 286.8 Hz), 62.4, 61.5 (q, $^3J_{FC}$ = 28.3 Hz), 57.5, 22.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.46. IR (cm^{-1}): 3350, 3059, 2958, 2929, 1626, 1447, 1283, 1265, 1170, 1123, 1084, 970, 696. HRMS (TOF MS ESI): calcd for $C_{28}H_{30}F_3N_2OS$ $[M + H]^+$ 499.2031, found 499.2029.

Procedure for Deprotection of 9s. Cleavage of the protecting groups of diphenylketimine and chiral *tert*-butylsulfinyl was carried out in a 25 mL round-bottom flask where **9s** (0.2493 g, 0.5 mmol) and MeOH (5 mL) were added. Then, aqueous HCl (36%, 1.0 mL) was added dropwise with stirring at room temperature. After 3 h, when the reaction was completed by monitoring of the TLC, volatiles were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL), and Et_3N (15.0 mmol) was added. The mixture was stirred at rt for 1 h, and then H_2O (10 mL) was added. The organic layer was taken, washed with water and brine, and dried with anhydrous Na_2SO_4. The mixture was filtered and concentrated. The crude product was purified by flash chromatography on silica gel (elute: PE/EA/TEA = 50:50:1) to give the product free vicinal diamine **13** in 86% yield.

*(2S,3R,E)-1,1,1-Trifluoro-5-phenylpent-4-ene-2,3-diamine (**13**).* Yellow oil. Yield: 87.8 mg (86%). $[\alpha]_D^{20}$ = −17.84 (c = 0.43, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.28 (m, 2H), 7.27–7.21 (m, 2H), 7.20–7.16 (m, 1H), 6.55 (d, J = 15.9 Hz, 1H), 6.18 (dd, J = 15.8, 7.2 Hz, 1H), 3.82 (ddd, J = 7.3, 3.6, 1.2 Hz, 1H), 3.14 (qd, J = 8.1, 3.6 Hz, 1H), 1.54 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 135.4, 130.4, 128.9, 127.6, 126.8, 125.5, 125.4 (q, J_{FC} = 283.8 Hz), 56.5 (q, $^3J_{FC}$ = 27.3 Hz), 51.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −74.61. IR (cm^{-1}): 3389, 3318, 3028, 1600, 1495, 1450, 1376, 1267, 1155, 1125, 1075, 968, 751, 695. HRMS (TOF MS ESI): calcd for $C_{11}H_{13}F_3N_2Na$ $[M + Na]^+$ 253.0929, found 253.0894.

Brief Exploration of Chemistry of Deprotected Product 13. *14 was Prepared As Follows.* Free vicinal diamine **13** (0.0817 g, 0.4 mmol) in THF (5 mL) was added to triethylamine (56 μL, 0.4 mmol) and di-*tert*-butyl dicarbonate (0.0873 g, 0.4 mmol) at room temperature. The solution was stirred for 2 h at room temperature, and then volatiles were removed under reduced pressure. The crude product was purified by flash chromatography on silica gel (elute: PE/EA = 3:1) to give product **14** as a white solid in 89% yield.

*tert-Butyl ((3R,4S,E)-4-Amino-5,5,5-trifluoro-1-phenylpent-1-en-3-yl)carbamate (**14**).* White solid, mp 95–96 °C. Yield: 118 mg (89%). $[\alpha]_D^{20}$ = −66.37 (c = 0.23, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.34 (m, 2H), 7.33–7.27 (m, 2H), 7.27–7.21 (m, 1H), 6.63 (dd, J = 15.8, 1.3 Hz, 1H), 6.12 (dd, J = 15.9, 6.5 Hz, 1H), 5.21 (s, 1H), 4.70 (s, 1H), 3.42 (s, 1H), 1.51 (s, 2H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 155.1, 136.1, 132.5, 128.6, 128.0, 126.6, 126.1, 125.9 (q, J_{FC} = 282.8 Hz), 80.1, 56.2 (q, $^3J_{FC}$ = 27.2 Hz), 52.3, 28.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ −74.51. IR (cm^{-1}): 3394, 2976, 1685, 1518, 1309, 1190, 1163, 1146, 1131, 964, 750, 693. HRMS (TOF MS ESI): calcd for $C_{16}H_{21}F_3N_2O_2Na$ $[M + Na]^+$ 353.1453, found 353.1450.

15 Was Prepared by the Procedure As Follows. To a solution of amine **14** (0.0994 g, 0.3 mmol) in THF/H_2O (50:50, 0.25 M) cooled to 0 °C were added sodium bicarbonate (0.0378 g, 0.45 mmol) and benzyl carbonochloridate (64 μL, 0.45 mmol). The reaction mixture was stirred for 2 h at rt, then diluted with EtOAc and sat. NH_4Cl. The organic layer was washed with sat. $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. The resulting product was purified by column chromatography (elute: PE/EA = 4:1) to give product **15** as a white solid in 95% yield.

*Benzyl tert-Butyl ((2S,3R,E)-1,1,1-Trifluoro-5-phenylpent-4-ene-2,3-diyl)dicarbamate (**15**).* White solid, mp 153–154 °C. Yield: 132 mg (95%). $[\alpha]_D^{20}$ = −34.75 (c = 0.24, CH_2Cl_2). ^{1}H NMR (400 MHz, DMSO): δ 7.87 (d, J = 10.0 Hz, 1H), 7.36–7.14 (m, 11H), 6.50 (d, J = 16.0 Hz, 1H), 6.19 (dd, J = 16.0, 5.2 Hz, 1H), 5.14 (d, J = 12.7 Hz, 1H), 5.00 (d, J = 12.7 Hz, 1H), 4.86–4.79 (m, 1H), 4.72–4.65 (m, 1H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, DMSO): δ 156.3, 154.8, 136.6, 136.1, 130.5, 128.7, 128.3, 127.8, 127.8, 127.3, 126.9, 126.3, 124.8 (q, J_{FC} = 283.8 Hz), 78.5, 65.9, 54.8 (q, $^3J_{FC}$ = 28.3 Hz), 50.6, 28.1. ^{19}F NMR (376 MHz, DMSO): δ −71.55. IR (cm^{-1}): 3339, 1712, 1682, 1540, 1291, 1254, 1291, 1254, 1189, 1163, 1130, 747, 697. HRMS (TOF MS ESI): calcd for $C_{24}H_{27}F_3N_2O_4Na$ $[M + Na]^+$ 487.1821, found 487.1819.

16 Was Prepared by the Procedure As Follows. A solution of **15** (0.0928 g, 0.2 mmol) in CH_2C1_2 (4 mL) was stirred with CF_3CO_2H (1 mL) at room temperature for 2 h. Then, triethylamine (0.85 mL, 6.0 mmol) was added and the mixture was stirred for 1 h. To the mixture was added H_2O (10 mL), and the mixture was extracted with CH_2Cl_2 (10 mL × 3), washed with brine, dried (Na_2SO_4), and concentrated to give **16** in 92% yield as a white solid after purification by column chromatography (elute: PE/EA = 1:1).

*Benzyl ((2S,3R,E)-3-Amino-1,1,1-trifluoro-5-phenylpent-4-en-2-yl)carbamate (**16**).* White solid, mp 72–73 °C. Yield: 67 mg (92%). $[\alpha]_D^{20}$ = −57.97 (c = 0.28, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.19 (m, 10H), 6.60 (dd, J = 15.9, 1.2 Hz, 1H), 6.16 (d, J = 9.3 Hz, 1H), 6.08 (dd, J = 15.9, 6.8 Hz, 1H), 5.16–5.06 (m, 2H), 4.37–4.25 (m, 1H), 4.13 (d, J = 6.7 Hz, 1H), 1.34 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 156.4, 136.1, 132.1, 128.7, 128.6, 128.2, 128.1, 128.0, 128.0, 126.6,126.6, 125.3 (q, J_{FC} = 284.8 Hz), 67.3, 55.7 (q, $^3J_{FC}$ = 28.3 Hz), 50.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −73.40. IR (cm^{-1}): 3391, 3340, 3032, 1724, 1499, 1288, 1268, 1227, 1171, 1101, 739, 725, 692. HRMS (TOF MS ESI): calcd for $C_{19}H_{20}F_3N_2O_2$ $[M + H]^+$ 365.1477, found 365.1476.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Full spectroscopic data for compounds **9**, **10**, and **13–16**; copies of ^{1}H and ^{13}C NMR spectra; and the X-ray crystallographic data of **10a** and **9j**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: hanjl@nju.edu.cn (J.H.).
*E-mail: vadym.soloshonok@ehu.es (V.A.S.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the financial support from the National Natural Science Foundation of China (Nos. 21102071 and 21472082); the Jiangsu 333 program (for Y.P.) and the Changzhou Jin-Feng-Huang program (for J.H.) are also acknowledged.

■ REFERENCES

(1) (a) Kotti, S. R. S. S.; Timmons, C.; Li, G. *Chem. Biol. Drug Des.* **2006**, *67*, 101−114. (b) Michalson, E. T.; Szmuszkovicz, J. *Prog. Drug Res.* **1989**, *33*, 135−149. (c) Viso, A.; Fernández de la Pradilla, R.; García, A.; Flores, A. *Chem. Rev.* **2005**, *105*, 3167−3196. (d) Merino, P.; Lanaspa, A.; Merchán, F. L.; Tejero, T. *Tetrahedron: Asymmetry* **1998**, *9*, 629−646.

(2) Mibu, N.; Yokomizo, K.; Miyata, T.; Sumoto, K. *Chem. Pharm. Bull.* **2007**, *55*, 1406−1411.

(3) Szmuszkovicz, J.; Von Voigtlander, P. F.; Kane, M. P. *J. Med. Chem.* **1981**, *24*, 1230−1236.

(4) Szilagyi, G.; Kasztreiner, E.; Matyus, P.; Kosary, J.; Czako, K.; Cseh, G.; Huszti, Z.; Tardos, L.; Kosa, E.; Jaszlits, L. *Eur. J. Med. Chem.* **1984**, *19*, 111−117.

(5) (a) Bennani, Y. L.; Hanessian, S. *Chem. Rev.* **1997**, *97*, 3161−3195. (b) González-Sabín, J.; Rebolledo, F.; Gotor, V. *Chem. Soc. Rev.* **2009**, *38*, 1916−1925. (c) Lucet, D.; Le Gall, T.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580−2627. (d) Viso, A.; Fernández de la Pradilla, R. *Recent Res. Dev. Org. Chem.* **2000**, *4*, 327−334. (e) Michalson, E. T.; Szmuszkovicz, J. *Prog. Drug Res.* **1989**, *33*, 135−149.

(6) (a) Gasc, M. B.; Lattes, A.; Perie, J. J. *Tetrahedron* **1983**, *39*, 703−731. (b) Pini, D.; Iuliano, A.; Rosini, C.; Salvadori, P. *Synthesis* **1990**, 1023−1024. (c) Swift, G.; Swern, D. *J. Org. Chem.* **1967**, *32*, 511−517. (d) Kalyanam, N.; Venkateswara Rao, G. *Tetrahedron Lett.* **1993**, *34*, 1647−1648. (e) Baruah, B.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **1995**, *36*, 6747−6750. (f) Tanaka, H.; Dhimane, H.; Fujita, H.; Ikemoto, Y.; Torii, S. *Tetrahedron Lett.* **1988**, *29*, 3811−3814. (g) Aurrecoechea, J. M.; Fernández-Acebes, A. *Tetrahedron Lett.* **1992**, *33*, 4763−4766. (h) Pansare, S. V.; Malusare, M. G. *Tetrahedron Lett.* **1996**, *37*, 2859−2862. (i) Reetz, M. T.; Jaeger, R.; Drewlies, R.; Hübel, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 103−106. (j) Reetz, M. T.; Röhrig, D.; Harms, K.; Frenkling, G. *Tetrahedron Lett.* **1994**, *35*, 8765−8768. (k) Dondoni, A.; Merchán, F. L.; Merino, P.; Tejero, T.; Bertolasi, V. *J. Chem. Soc., Chem. Commun.* **1994**, 1731−1733. (l) Morris, M. L.; Sturgess, M. A. *Tetrahedron Lett.* **1993**, *34*, 43−46. (m) Merino, P.; Lanaspa, A.; Merchán, F. L.; Tejero, T. *Tetrahedron: Asymmetry* **1997**, *8*, 2381−2401. (n) Wu, H.; Ji, X. Y.; Sun, H.; An, G. H.; Han, J. L.; Li, G. G.; Pan, Y. *Tetrahedron* **2010**, *66*, 4555−4559. (o) Han, J. L.; Li, T. F.; Pan, Y.; Kattuboina, A.; Li, G. G. *Chem. Biol. Drug Des.* **2007**, *71*, 71−77. (p) Xiong, Y. W.; Qian, P.; Cao, C. H.; Mei, H. B.; Han, J. L.; Li, G. G.; Pan, Y. *Beilstein J. Org. Chem.* **2014**, *10*, 1802−1807.

(7) (a) Shang, D.; Liu, Y.; Zhou, X.; Liu, X.; Feng, X. *Chem.—Eur. J.* **2009**, *15*, 3678−3681. (b) Handa, S.; Gnanadesikan, V.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 4925−4934. (c) Hernández-Toribio, J.; Gómez Arrayás, R.; Carretero, J. C. *Chem.—Eur. J.* **2010**, *16*, 1153−1157. (d) Lu, G.; Yoshino, T.; Morimoto, H.; Matsunaga, S.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 4382−4385. (e) Jiang, J.; Xu, H. D.; Xi, J. B.; Ren, B. Y.; Lv, F. P.; Guo, X.; Jiang, L. Q.; Zhang, Z. Y.; Hu, W. H. *J. Am. Chem. Soc.* **2011**, *133*, 8428−8431. (f) Rueping, M.; Antonchick, A. P. *Org. Lett.* **2008**, *10*, 1731−1734. (g) Singh, A.; Johnston, J. N. *J. Am. Chem. Soc.* **2008**, *130*, 5866−5867. (h) Kobayashi, S.; Yazaki, R.; Seki, K.; Yamashita, Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 5613−5615. (i) Uraguchi, D.; Koshimoto, K.; Ooi, T. *J. Am. Chem. Soc.* **2008**, *130*, 10878−10879. (j) Uraguchi, D.; Koshimoto, K.; Ooi, T. *J. Am. Chem. Soc.* **2008**, *130*, 14088−14089. (k) Zhang, H.; Syed, S.; Barbas, C. F., III *Org. Lett.* **2010**, *12*, 708−711. (l) Davis, T. A.; Wilt, J. C.; Johnston, J. N. *J. Am. Chem. Soc.* **2010**, *132*, 2880−2882. (m) Davis, T. A.; Johnston, J. N. *Chem. Sci.* **2011**, *2*, 1076−1079.

(8) (a) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308−319. (b) Zhang, W.; Cai, C. *Chem. Commun.* **2008**, 5686−5694. (c) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359−4369. (d) Dolbier, W. R. *J. Fluorine Chem.* **2005**, *126*, 157−163. (e) Smart, B. E. *J. Fluorine Chem.* **2001**, *109*, 3−11. (f) O'Hagan, D.; Rzepa, H. S. *Chem. Commun.* **1997**, 645−652. (g) Schlosser, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1496−1513.

(9) Xie, C.; Mei, H. B.; Wu, L. M.; Han, J. L.; Soloshonok, V. A.; Pan, Y. *Eur. J. Org. Chem.* **2014**, 1445−1451.

(10) (a) Isanbor, C.; O'Hagan, D. *J. Fluorine Chem.* **2006**, *127*, 303−319. (b) Begue, J. P.; Bonnet-Delpon, D. *J. Fluorine Chem.* **2006**, *127*, 992−1012.

(11) (a) Ojima, I. *J. Org. Chem.* **2013**, *78*, 6358−6383. (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320−330. (c) Böhm, H. J.; Banner, D.; Bendels, S.; Kansy, M.; Kuhn, B.; Müller, K.; Obst-Sander, U.; Stahl, M. *ChemBioChem* **2004**, *5*, 637−643.

(12) Zhu, W.; Wang, J.; Wang, S.; Gu, Z.; Aceña, J. L.; Izawa, K.; Liu, H.; Soloshonok, V. A. *J. Fluorine Chem.* **2014**, *167*, 37−54.

(13) Moens, M.; De Kimpe, N.; D'hooghe, M. *J. Org. Chem.* **2014**, *79*, 5558−5568.

(14) Sanchez-Rosello, M.; Delgado, O.; Mateu, N.; Trabanco, A. A.; Van Gool, M.; Fustero, S. *J. Org. Chem.* **2014**, *79*, 5887−5894.

(15) Soloshonok, V. A.; Hayashi, T.; Ishikawa, K.; Nagashima, N. *Tetrahedron Lett.* **1994**, *35*, 1055−1058.

(16) For review and large-scale synthesis, see: Liu, J.; Hu, J. B. *Future Med. Chem.* **2009**, *1*, 875−888.

(17) Liu, Y. L.; Yang, Y.; Huang, Y.; Xu, X. H.; Qing, F. L. *Synlett* **2015**, 67−72.

(18) (a) Ishida, Y.; Iwahashi, N.; Nishizono, N.; Saigo, K. *Tetrahedron Lett.* **2009**, *50*, 1889−1892. (b) Cho, J.; Nishizono, N.; Iwahashi, N.; Saigo, K.; Ishida, Y. *Tetrahedron* **2013**, *69*, 9261−9269.

(19) For the reactions with ketone-derived enolates, see: (a) Xie, C.; Mei, H. B.; Wu, L. M.; Soloshonok, V. A.; Han, J. L.; Pan, Y. *RSC Adv.* **2014**, *4*, 4763−4768. (b) Mei, H.; Xiong, Y.; Han, J.; Pan, Y. *Org. Biomol. Chem.* **2011**, *9*, 1402−1406.

(20) For the reactions with ester-derived enolates, see: Xie, C.; Mei, H.; Wu, L.; Soloshonok, V. A.; Han, J.; Pan, Y. *Eur. J. Org. Chem.* **2014**, 1445−1451.

(21) For the reactions with lithiated aromatic/heterocyclic compounds, see: Mei, H.; Xie, C.; Wu, L.; Soloshonok, V. A.; Han, J.; Pan, Y. *Org. Biomol. Chem.* **2013**, *11*, 8018−8021.

(22) For other types of nucleophiles, see: Röschenthaler, G. V.; Kukhar, V. P.; Kulik, I. B.; Belik, M. Y.; Sorochinsky, A. E.; Rusanov, E. B.; Soloshonok, V. A. *Tetrahedron Lett.* **2012**, *53*, 539−542.

(23) Antilla, J. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 5099−5100.

(24) Cainelli, G.; Giacomini, D.; Trerè, A.; Boyl, P. P. *J. Org. Chem.* **1996**, *61*, 5134−5139.

(25) O'Donnell, M. J.; Bennett, W. D.; Bruder, W. A.; Jacobsen, W. N.; Knuth, K.; LeClef, B.; Pelt, R. L.; Bordwell, F. G.; Mrozack, S. R.; Cripe, T. A. *J. Am. Chem. Soc.* **1988**, *110*, 8520−8525.

(26) (a) Ding, L.; Chen, J.; Hu, Y.; Xu, J.; Gong, X.; Xu, D.; Zhao, B.; Li, H. *Org. Lett.* **2014**, *16*, 720−723. (b) Liu, X.; Gao, A.; Ding, L.; Xu, J.; Zhao, B. *Org. Lett.* **2014**, *16*, 2118−2121.

(27) Xie, C.; Wu, L. M.; Mei, H. B.; Soloshonok, V. A.; Han, J. L.; Pan, Y. *Org. Biomol. Chem.* **2014**, *12*, 7836−7843.

(28) Ueki, H.; Ellis, T. K.; Martin, C. H.; Soloshonok, V. A. *Eur. J. Org. Chem.* **2003**, 1954−1957.

(29) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600−3740.

(30) Kobzev, S. V.; Soloshonok, V. A.; Galushko, S. V.; Yagupolskii, Y. L.; Kukhar, V. P. *Zh. Obshch. Khim.* **1989**, *59*, 909−912.

(31) Soloshonok, V. A.; Cai, C.; Hruby, V. J.; Meervelt, L. V.; Yamazaki, T. *J. Org. Chem.* **2000**, *65*, 6688−6696.

(32) Soloshonok, V. A.; Ueki, H.; Tiwari, R.; Cai, C.; Hruby, V. J. *J. Org. Chem.* **2004**, *69*, 4984−4990.

(33) Soloshonok, V. A.; Kirilenko, A. G.; Kukhar, V. P.; Resnati, G. *Tetrahedron Lett.* **1993**, *34*, 3621−3624.

(34) O'Donnell, M. J.; Polt, R. L. *J. Org. Chem.* **1982**, *47*, 2663−2666.

(35) For examples of OCC: Boyall, D.; Frantz, D.; Carreira, E. M. *Org. Lett.* **2002**, *4*, 2605−2606.