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One-Pot Synthesis of 2-Imino-4-(trifluoromethyl)thiazolidin-4-ol Derivatives in a Three-Component Reaction: Application to Structurally Diverse Scaffolds of Biological Interest Through Subsequent Reactions

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A highly efficient method for the synthesis of 2-imino-4-(trifluoromethyl)thiazolidin-4-ol derivatives has been achieved by the one-pot, three-component reactions of primary amines, aryl isothiocyanates, and 3-bromo-1,1,1-trifluoropropanone. The reactions go via symmetrical and unsymmetrical thiourea intermediates. Subsequent reactions of the products allow the synthesis of various scaffolds, including isoxazoles, triazoles, and propargylamine derivatives.

Introduction

There has been increasing interest in the introduction of fluorine or a fluorinated group into organic compounds, since this influences the pharmacodynamic and pharmacokinetic properties of a drug.[1] The introduction of a trifluoromethyl group into cyclic compounds, especially at strategic positions of drug molecules, has become an important aspect of pharmaceutical research, owing to the unique physical and biological properties of fluorine.[2,3] Therefore, the development of fluorinated potential drugs is a key issue and a challenge for medicinal chemistry and related disciplines.[4] 2-Imino-1,3-thiazolidines and 2-imino-1,3-thiazolines have emerged as important classes of heterocyclic compounds, due to their diverse applications in medicinal chemistry.[5,6] These heterocycles show a wide range of biological properties, including anti-inflammatory, anodyne, anti-Alzheimer, antimicrobial, antihistaminic, antihypertensive, anticonvulsant activities, and also as myeloperoxidase inhibitors etc.[7,8] For example, 4,5-dialkyl-substituted thiazolidines **I** (Figure 1) are reported to be nitric oxide synthase inhibitors.[9] A member of another class of thiazolidines, 3-methylthiazolidine **II** (Figure 1; R^1 = H, R^2 = Me), is a potent inhibitor of indole–ethylamine *N*-methyltransferase.[10] β-(Hydroxyethyl)thiazolidines **III** (Figure 1) are reported to be effective antihypertensive agents.[11] 2-(Tetrahydronaphthalen-1-yl)iminothiazolidine **IV** (Figure 1) acts as an antidepressant.[12] 3-Substituted 2-(cyanoimino)-thiazolidines **V** (Figure 1) can be used in agriculture, due to their neonicotinoid insecticidal activity, and thiacloprid (**V**: R = H) is a commercially available insecticide released by Bayer in 2001.[13]

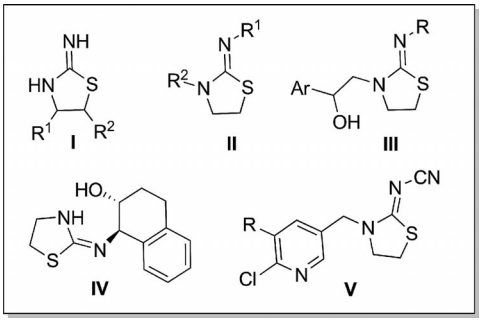

Figure 1. Biologically active 2-imino-1,3-thiazolidine motifs.

Furthermore, thiazoline derivatives have applications in agriculture as pesticides, acaricides, insecticides, and plant-growth regulators.[14] Consequently, in recent decades, there has been continuous interest in developing new synthetic strategies for the synthesis of such attractive target molecules.

A detailed literature survey revealed the various methods available for the synthesis of functionalized 2-iminothiazolidines and related compounds. These include acid-mediated intramolecular cyclization of *N*-(2-hydroxyethyl)thiourea, ring transformation of 2-(thiocyanomethyl)aziridines, treatment of aziridines with thiocyanuric acid, reaction of 2-vinylaziridine with phenyl isothiocyanate, condensation of α-halo ketones with thioureas, etc.[15,16] However, methods for the synthesis of 2-imino-1,3-thiazolidin-4-ol derivatives are

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rare in the literature.[17] The known methods use substituted thioureas as substrates, and have major drawbacks: they require the use of base and harsh reaction conditions, and the yields are low. To improve on these limitations, it is important to develop a simple and efficient method for the synthesis of 2-imino-thiazolidin-4-ols. Bearing in mind the biological importance of 2-imino-1,3-thiazolidine derivatives, we planned to insert a trifluoromethyl group into the thiazolidine ring to achieve a better biological profile. We envisioned that the reaction of 3-bromo-1,1,1-trifluoropropanone, a primary amine, and an aryl isothiocyanate would generate a 2-imino-thiazolidin-4-ol by the in situ generation of thiourea in one pot. To the best of our knowledge, there are no reports on the one-pot synthesis of 2-imino-4-(trifluoromethyl)thiazolidin-4-ols by such a three-component reaction.

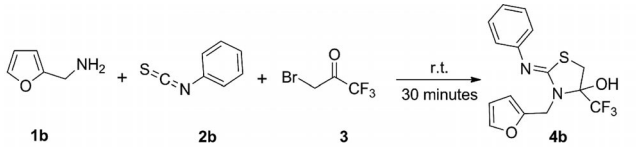
In a continuation of our research program into the synthesis of new heterocyclic compounds and their biological evaluation,[18] in this paper, we report a simple, efficient, catalyst-free, one-pot, three-component method for the synthesis of 2-imino-4-(trifluoromethyl)thiazolidin-4-ol derivatives. We also describe subsequent reactions of the products, using their free hydroxy group for the synthesis of structurally diverse scaffolds.

Results and Discussion

As a model reaction, we first attempted the reaction of furfurylamine (**1b**), phenyl isothiocyanate (**2b**), and 3-bromo-1,1,1-trifluoropropan-2-one (**3**) in *N*,*N*-dimethylformamide (DMF) at room temperature (Table 1, entry 1). The reaction proceeded smoothly to give corresponding 2-imino-4-(trifluoromethyl)thiazolidin-4-ol (i.e., **4b**) as the sole product in 98% yield. Later, we studied the same reaction in DMF/water (1:1), in water alone, and under solvent-free conditions to try to optimize the reaction outcome under green conditions (Table 1, entries 2–4). We found that when the water content increased, the yield of the product decreased. Of the solvents tested, DMF seemed to be the best choice.

We went on to investigate this process for various other primary amines and substituted phenyl isothiocyanates under the optimized reaction conditions, and the results are given in Table 2. Interestingly, several primary amines, including thiophen-2-ylmethylamine, tryptamine, 2-morpholinoethylamine, 2-(pyridin-2-yl)ethylamine, prop-1-ylamine, cyclopropylamine, and 2-methylprop-2-ylamine, and phenyl isothiocyanates, including 3- or 4-(trifluoromethyl)phenyl isothiocyanate, and 1-chloro-2-(trifluoromethyl)phenyl isothiocyanate, reacted with 3-bromo-1,1,1-trifluoropropanone to give the corresponding 2-imino-4-(trifluoromethyl)thiazolidin-4-ol derivatives (i.e., **4**) in good to excellent yields (Table 2, entries a, c–g, k–o). This method worked effectively not only for aliphatic and heteroaryl primary amines, but also for aromatic primary amines. For instance, aniline, 3-fluoroaniline, and 4-methoxyaniline reacted smoothly with various phenyl isothiocyanates and 3-bromo-1,1,1-trifluoropropanone to give the corresponding products (i.e., **4h**–**4j**) in good yields (Table 2, entries h–j). All the products were characterized by IR spectroscopy, ^{1}H and ^{13}C NMR spectroscopy, and mass spectrometry. The structure of **4d** (Table 2, entry d) was confirmed by X-ray crystallography. The X-ray structure of compound **4d** shows the *Z*-configuration of the imino group (Figure 2).[19]

Table 1. Solvent effects on the reaction of furfurylamine, phenyl isothiocyanate, and 3-bromo-1,1,1-trifluoropropan-2-one.



1b **2b** **3** **4b**

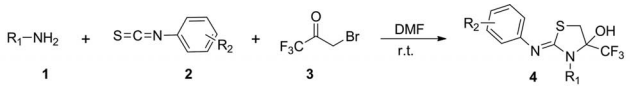
Entry	Solvent	Ratio of solvents	Yield (%)[a]
1	DMF	–	98
2	DMF:H_2O	2 : 1	92
3	DMF:H_2O	1 : 1	87
4	DMF:H_2O	1 : 2	78
5	H_2O	–	70
6	neat	–	60

Reaction conditions: amine (1 mmol), phenyl isothiocyanate (1 mmol), 3-bromo-1,1,1-trifluoropropan-2-one (1 mmol) at room temperature. [a] Isolated yield.

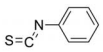
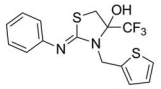
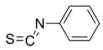
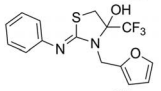
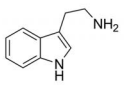
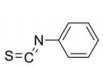
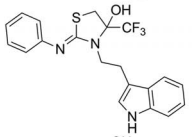
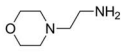
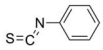
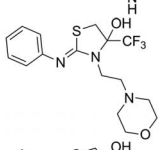
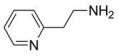
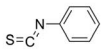
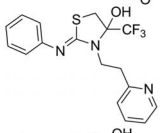
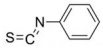
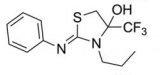
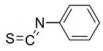
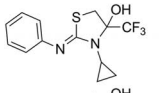
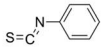
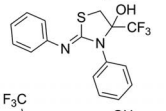
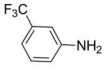
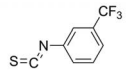
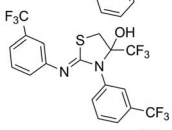
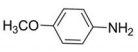
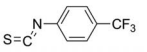
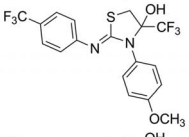
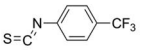
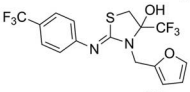
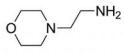
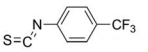
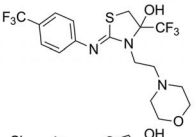
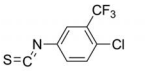
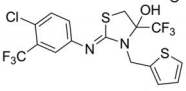
All the reactions were exothermic at room temperature, which suggests that the mechanism involved the in situ generation of thiourea from the primary amine and the phenyl isothiocyanate, followed by reaction with 3-bromo-1,1,1-trifluoropropanone to give product **4**. As may be seen in Table 2, the reactions provided a single regioisomer of **4** as the exclusive product in all those cases where reaction proceeded via an in-situ-generated unsymmetrical thiourea. The outcome is dependent on the pK_a value of the amines. It is reported that the amine with the lower pK_a of the two in the thiourea becomes part of the imine group, whereas the amine with the higher pK_a gives rise to the other heterocyclic nitrogen.[20]This protocol is simple, efficient, and base-free, and it provides the desired products in good to excellent yields.

Previous mechanistic studies of the formation of the 2-imino thiazolines suggested that after cyclization, the tertiary hydroxy group in the intermediate undergoes dehydration to give the thiazole-2-imine.[15] However, our investigations revealed that the dehydration process was not taking place during the course of our reaction. Even when the reaction was carried out at 70–80 °C in DMF for 30 min, we still obtained the desired product (i.e., **4**) with a tertiary hydroxy group. This might be due to the electron-withdrawing effect of the trifluoromethyl group on same carbon. The proposed mechanism for the model reaction is outlined in Scheme 1. The reaction may proceed via thiourea **5**, which is generated in situ from the primary amine and the phenyl isothiocyanate. This is followed by attack of the thiocarbonyl group of thiourea **5** on the bromomethyl group of **3** to produce **6**. This compound may then undergo

Table 2. Synthesis of 2-imino-4-(trifluoromethyl)thiazolidin-4-ol derivatives.



1 2 3 4

Entry	Amines **1**	Isothiocyanate **2**	Product **4**[a]	Time (min)	Yield (%)[b]
a				20	96
b				20	98
c				20	89
d				20	93
e				20	90
f				20	92
g				20	95
h				20	92
i				30	78
j				25	85
k				25	87
l				30	90
m				30	91
n				30	87
o				30	86

Reaction was performed with 1 mmol of amine, 1 mmol of phenylisothiocyanate and 1 mmol of 3-bromo-1,1,1-trifluoropropan-2-one in DMF at room temperature. [a] All products were characterized by ^{1}H and ^{13}C NMR, IR and mass spectroscopy. [b] Yield refers to pure product after column chromatography.

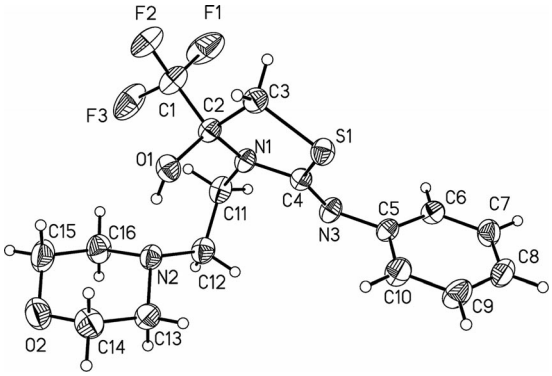
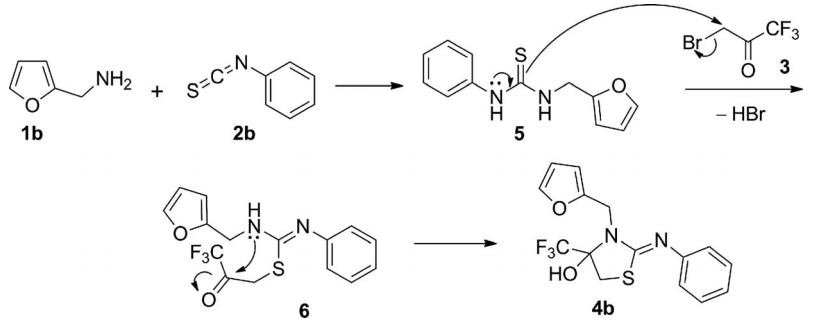


Figure 2. ORTEP structure of **4d**.

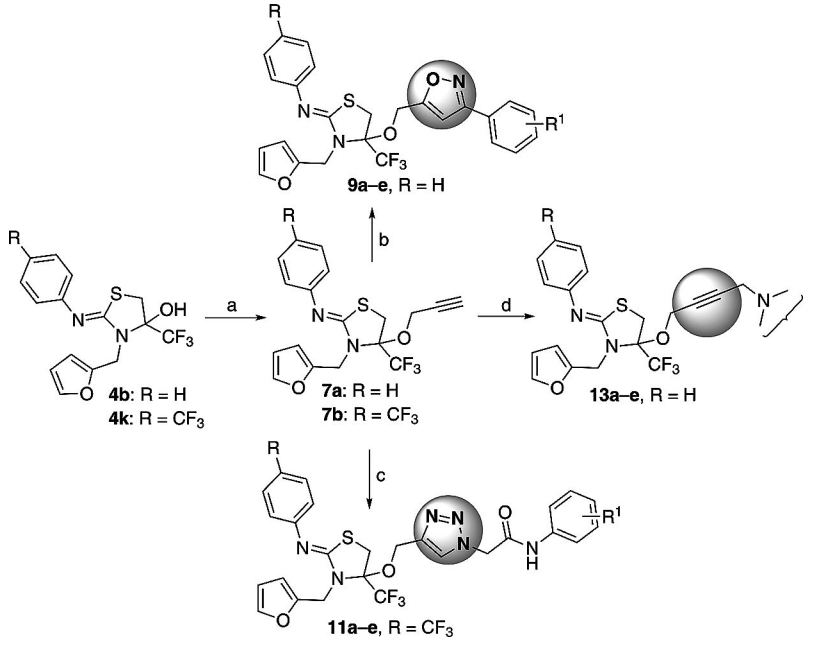
rapid cyclization to give the desired product (i.e., **4b**). The reaction proceeds in regioselective manner because of the higher acidity of NH proton flanked by a phenyl group.

Next, we turned our attention to structural diversification of the 2-imino-4-(trifluoromethyl)thiazolidin-4-ols (i.e., **4**; Table 2). Further reactions of the tertiary hydroxy group allow the synthesis of more attractive molecules with potentially improved biological properties. Isoxazoles and triazoles are important heterocyclic pharmacophores in the development of antiviral, anticancer, anti-HIV, anti-inflammatory, anticonvulsant, anticestoidal, antileprosy, antidiabetes, and antibiotic agents.[21,22] The Mannich reaction is also one of the most important multicomponent coupling reactions of aldehydes, alkynes, and amines in organic chemistry.[23] Propargylamines are of considerable interest; they have found applications in the chemical/pharmaceutical industry, and they also have various biological activities.[24]

We have used the tertiary hydroxy group in **4** to synthesize 2-imino-4-(trifluoromethyl)thiazolidine-tethered isoxazole and triazole derivatives using 1,3-dipolar cycloaddition reactions of propargylated 2-imino-4-(trifluoromethyl)thiazolidin-4-ols. Compounds **4b** and **4k** were chosen as model compounds for this study. Base-mediated propargylation of **4b** and **4k** gave terminal alkynes **7a** and **7b**, respectively (Scheme 2). 1,3-Dipolar cycloaddition of alkyne **7a** with (*E*)-4-methoxybenzaldehyde oxime (**8a**) in



Scheme 1. Plausible reaction mechanism.



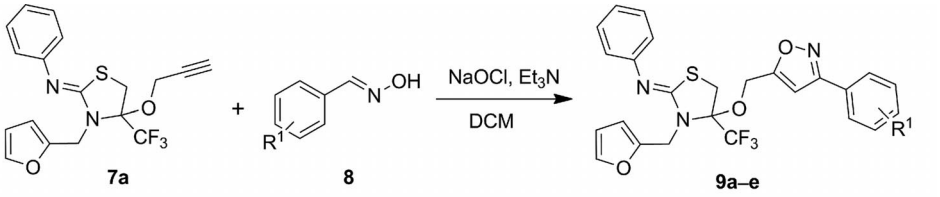
Scheme 2. Synthesis of isoxazole, triazole, and propargylamine derivatives of 2-imino-4-(trifluoromethyl)thiazolidinol. Reagents and conditions: (a) propargyl bromide, K_2CO_3, DMF, room temp.; (b) oxime **8**, NaOCl, Et_3N, CH_2Cl_2, 0 °C to room temp.; (c) azide **10**, CuI, dry THF, room temp.; (d) HCHO, *sec*. amine **12**, CuI, THF, room temperature.

the presence of sodium hypochlorite and triethylamine in dichloromethane gave the corresponding isoxazole derivative (i.e., **9a**) as a single product in 87% yield (Table 3, entry a). Interestingly, various other aromatic aldoximes **8b**–**8e** underwent smooth cycloadditions with alkyne **7a** to give the corresponding isoxazole derivatives **9b**–**9e** (Table 3, entries b–e) in good yields.

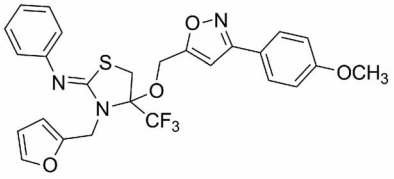
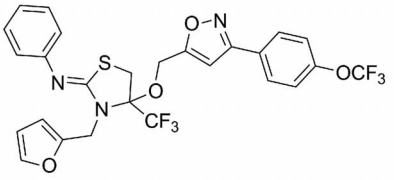
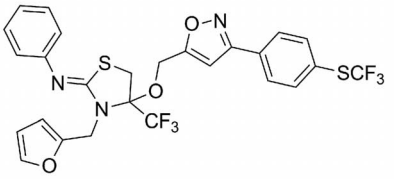
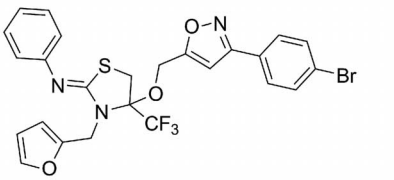
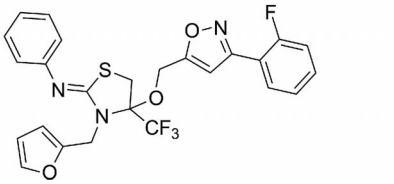
Next, the reaction of alkyne **7b** with azide **10a** in the presence of CuI (5 mol-%) in anhydrous tetrahydrofuran gave the corresponding triazole derivative (i.e., **11a**) in 88% yield in a Sharpless click chemistry reaction (Table 4, entry a). Similarly, other functionalized azides **10a**–**10e** also reacted well with alkyne **7b** to give the respective triazole derivatives (i.e., **11b**–**11e**) in good to excellent yields (Table 4, entries b–e).

In addition, a multicomponent coupling reaction of alkyne **7a**, formaldehyde, and morpholine (**12a**) in the presence of CuI (10 mol-%) in THF gave the respective propargylamine (i.e., **13a**) in 90% yield (Table 5, entry a). Several secondary amines were investigated in this reaction, and the results are summarized in Table 5. Other secondary amines **12b**–**12e** also reacted well under the same conditions to give the respective propargylamines (i.e., **13b**–**13e**) in satisfactory yields (entries b–e).

Table 3. Synthesis of isoxazole derivatives of 2-imino-4-(trifluoromethyl)thiazolidinol **9a**–**9e**.[a]

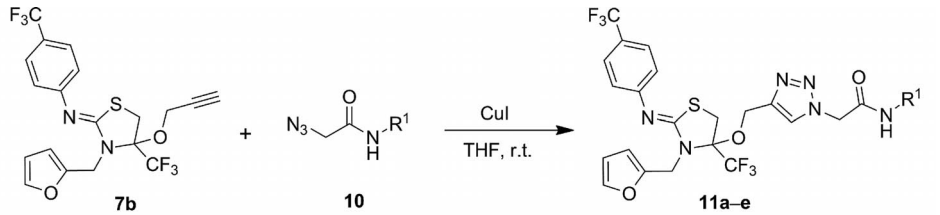


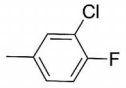
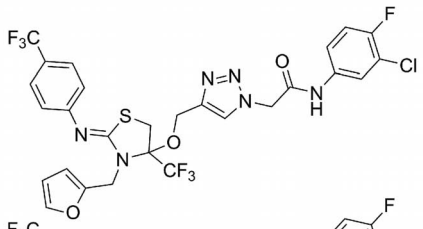
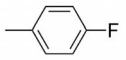
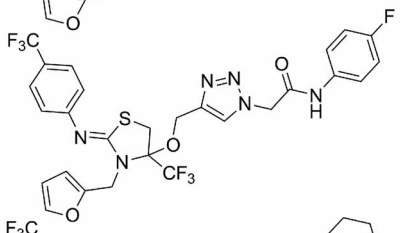
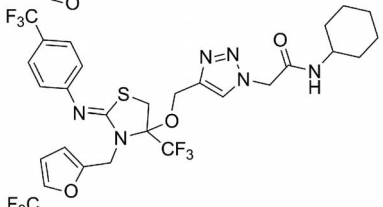
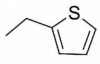
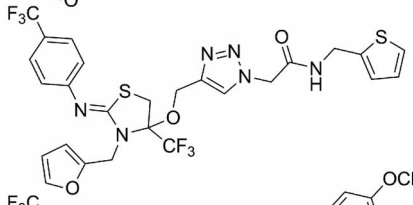
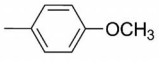
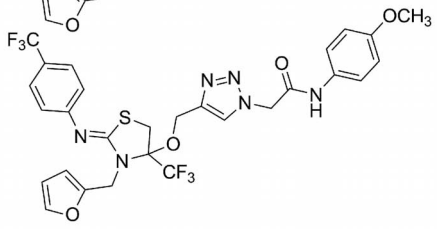
7a **8** **9a–e**

Entry	R^1	Product[a]	Time(h)	Yield(%)[b]
a	4-OCH_3		24	87
b	4-OCF_3		24	74
c	4-SCF_3		24	76
d	4-Br		24	82
e	2-F		24	80

Reaction was performed with 1 mmol of compound **5a**, 1 mmol of aldoxime, 1.6 mmol NaOCl and 1 mmol Et_3N in DCM at room temperature. [a] All products were characterized by ^1H and ^{13}C NMR, IR and mass spectroscopy. [b] Yield refers to pure product after column chromatography.

Table 4. Synthesis of triazole derivatives of 2-imino-4-(trifluoromethyl)thiazolidinol **11a**–**11e**.[a]



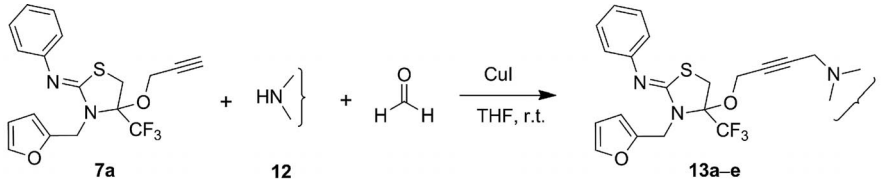
Entry	R^1	Product[a]	Time (h)	Yield(%)[b]
a			24	88
b			24	85
c			24	93
d			24	90
e			24	91

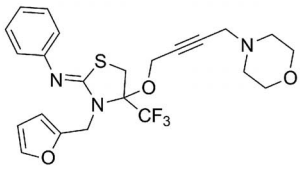
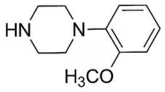
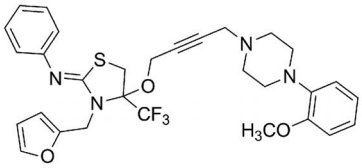
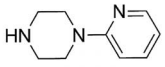
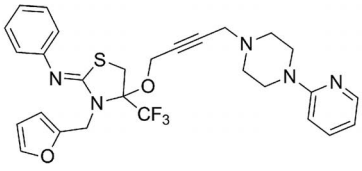
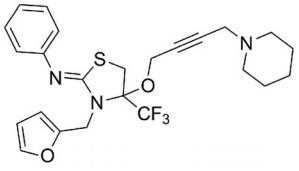
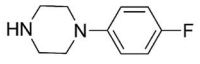
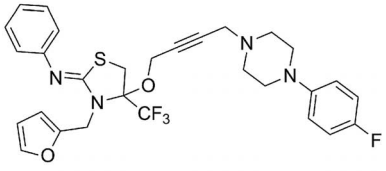
Reaction was performed with 1 mmol of compound **5b**, 1 mmol of azide and catalytic amount of CuI in THF at room temperature. [a] All products were characterized by ^1H and ^{13}C NMR, IR and mass spectroscopy. [b] Yield refers to pure product after column chromatography.

Conclusions

In conclusion, we have developed a simple one-pot protocol for the synthesis of 2-imino-4-(trifluoromethyl)thiazolidin-4-ol derivatives by the three-component reaction of a primary amine, an aryl isothiocyanate, and 3-bromo-1,1,1-trifluoropropan-2-one. The reaction uses easily available precursors and gives the desired products in excellent to good yields in single-step operation. The utility of the products for the synthesis of various scaffolds such as isoxazoles, triazoles, and propargylamine derivatives, which are found in many biological compounds, has been demonstrated. Since the thiazolidine ring itself has great biological importance, the newly synthesized products and their isoxazole, triazole, and propargylamine derivatives may find applications in medicinal chemistry. Biological screening of these new products is underway, and the results of these investigations will be reported in due course.

Table 5. Synthesis of propargylamine derivatives of of 2-imino-4-(trifluoromethyl)thiazolidinol **13a**–**13e**.[a]



Entry	HN	Product[a]	Time (h)	Yield(%)[b]
a			4	90
b			4	92
c			6	76
d			5	89
e			6	86

Reaction was performed with 1 mmol of compound **5a**, 1 mmol of secondary cyclic amine, 1 mmol HCHO and 10 mol-% CuI in THF at room temperature. [a] All products were characterized by IR, ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry. [b] Yield refers to pure product after column chromatography.

Experimental Section

General Remarks: All solvents were distilled before use. Dry reactions were conducted under a nitrogen atmosphere. Crude products were purified by column chromatography on silica gel (60–120 or 100–200 mesh). Thin-layer chromatography plates were visualized by exposure to ultraviolet light, exposure to iodine vapors, and/or exposure to a methanolic acidic solution of *p*-anisaldehyde followed by heating (<1 min) on a hot plate (ca. 250 °C). IR spectra were recorded with an FTIR spectrometer. ^{1}H, ^{19}F, and ^{13}C (proton decoupled) NMR spectra were recorded in $CDCl_3$ with 300 and 500 MHz NMR spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane, which was used as an internal standard. Coupling constants (J) are quoted in Hertz (Hz). High-resolution mass specta (HRMS) were obtained using electrospray ionization (ESI) and a orbitrap mass analyser.

Procedure for Synthesis of 2-Imino-4-(trifluoromethyl)thiazolidin-4-ol Derivatives 4a–4l: A solution of primary amine **1** (1 mmol) and aryl isothiocyanate **2** (1 mmol) in *N*,*N*-dimethylformamide (5 mL) was stirred for 5 min, and then 3-bromo-1,1,1-trifluoropropanone **3** (1 mmol) was added dropwise. The reaction mixture was stirred at room temperature for 20–30 min. After TLC indicated that the reaction was complete, the mixture was quenched with saturated $NaHCO_3$ solution (1 mL), diluted with water, and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine solution, dried (Na_2SO_4), filtered and concentrated. The resulting crude product was purified by column chromatography using EtOAc/*n*-hexane gradients to give pure product **4** (Table 2).

(*Z*)-2-(Phenylimino)-3-(thiophen-2-ylmethyl)-4-(trifluoromethyl)-thiazolidin-4-ol (4a): Solid (347 mg, 96%), m.p. 126–128 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.09 (br. s, 1 H), 3.16 (d, J =

12.1 Hz, 1 H), 3.53 (d, J = 12.1 Hz, 1 H), 4.72 (d, J = 15.9 Hz, 1 H), 5.38 (d, J = 15.9 Hz, 1 H), 6.93–6.98 (m, 1 H), 7.01–7.07 (m, 2 H), 7.08–7.17 (m, 2 H), 7.27–7.38 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 35.1, 41.7, 91.3 (q, J = 32.7 Hz), 121.5, 124.0, 126.2, 127.0, 127.3, 129.0, 140.0, 150.1, 156.4 ppm. IR (KBr): $\tilde{\nu}$ = 3063, 2363, 1607, 1584, 1437, 1338, 1303, 1176 cm^{-1}. MS (ESI): m/z = 359 [M + H]$^+$. HRMS (ESI): calcd. for $C_{15}H_{14}ON_2F_3S_2$ 359.0484 [M + H]$^+$; found 359.0494.

(*Z*)-3-(Furan-2-ylmethyl)-2-(phenylimino)-4-(trifluoromethyl)-thiazolidin-4-ol (4b): Solid (335 mg, 98%), m.p. 105–107 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.20 (d, J = 12.1 Hz, 1 H), 3.55 (d, J = 12.1 Hz, 1 H), 3.98 (br. s, 1 H), 4.46 (d, J = 16.2 Hz, 1 H), 5.22 (d, J = 16.2 Hz, 1 H), 6.34–6.39 (m, 1 H), 6.40–6.46 (m, 1 H), 6.85–6.94 (m, 2 H), 7.02–7.12 (m, 1 H), 7.23–7.34 (m, 2 H), 7.34–7.44 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 34.8, 39.6, 90.7 (q, J = 32.4 Hz), 109.8, 110.9, 121.4, 123.8, 125.1, 129.0, 142.0, 150.0, 150.2, 156.0 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –78.81 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3061, 2690, 1605, 1581, 1427, 1331, 1302, 1192, 1153 cm^{-1}. MS (ESI): m/z = 343 [M + H]$^+$. HRMS (ESI): calcd. for $C_{15}H_{14}O_2N_2F_3S$ 343.0713 [M + H]$^+$; found 343.0722.

(*Z*)-3-[2-(1*H*-Indol-3-yl)ethyl]-2-(phenylimino)-4-(trifluoromethyl)-thiazolidin-4-ol (4c): Solid (360 mg, 89%), m.p. 128–130 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.78–2.94 (m, 2 H), 2.95–3.07 (m, 1 H), 3.40–3.60 (m, 2 H), 3.62–3.76 (m, 1 H), 4.01–4.15 (m, 1 H), 6.98–7.28 (m, 6 H), 7.30–7.42 (m, 3 H), 7.68–7.78 (m, 1 H), 8.15 (br. s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 23.0, 34.8, 45.4, 111.4, 113.5, 118.9, 119.9, 121.8, 122.5, 123.8, 125.3, 127.0, 129.0, 136.0, 150.3 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –80.45 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3409, 3062, 2683, 1606, 1585, 1420, 1311, 1182, 1147 cm^{-1}. MS (ESI): m/z = 406 [M + H]$^+$. HRMS (ESI): calcd. for $C_{20}H_{19}ON_3F_3S$ 406.1182 [M + H]$^+$; found 406.1195.

(*Z*)-3-(2-Morpholinoethyl)-2-(phenylimino)-4-(trifluoromethyl)-thiazolidin-4-ol (4d): Solid (348 mg, 93%), m.p. 124–126 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.29–2.39 (m, 1 H), 2.41–2.95 (m, 4 H), 2.98–3.11 (m, 1 H), 3.22 (d, J = 12.0 Hz, 1 H), 3.42–3.55 (m, 2 H), 3.62–3.94 (m, 4 H), 4.19–4.29 (m, 1 H), 6.87–6.96 (m, 2 H), 7.03–7.12 (m, 1 H), 7.24–7.35 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 34.9, 41.1, 53.7, 55.0, 66.0, 89.9 (q, J = 31.2 Hz), 121.5, 123.7, 123.9 (q, J = 288.7 Hz), 129.0, 150.6, 157.3 ppm. IR (KBr): $\tilde{\nu}$ = 3065, 2669, 1619, 1594, 1456, 1356, 1303, 1163 cm^{-1}. MS (ESI): m/z = 376 [M + H]$^+$. HRMS (ESI): calcd. for $C_{16}H_{21}O_2N_3F_3S$ 376.1292 [M + H]$^+$; found 376.1301.

(*Z*)-2-(Phenylimino)-3-[2-(pyridin-2-yl)ethyl]-4-(trifluoromethyl)-thiazolidin-4-ol (4e): Solid (330 mg, 90%), m.p. 103–105 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.18 (d, J = 12.1 Hz, 1 H), 3.21–3.32 (m, 1 H), 3.42–3.48 (m, 1 H), 3.52 (d, J = 12.1 Hz, 1 H), 3.78–3.90 (m, 1 H), 4.38–4.51 (m, 1 H), 6.52–6.61 (m, 2 H), 6.95–7.04 (m, 1 H), 7.14–7.36 (m, 4 H), 7.68–7.76 (m, 1 H), 8.41–8.49 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 33.6, 36.0, 41.3, 91.1 (q, J = 31.3 Hz), 121.5, 121.9, 123.4, 125.1, 125.8, 128.7, 138.0, 146.4, 150.3, 156.7, 158.6 ppm. IR (KBr): $\tilde{\nu}$ = 2989, 2649, 1619, 1588, 1443, 1295, 1248, 1186 cm^{-1}. MS (ESI): m/z = 368 [M + H]$^+$. HRMS (ESI): calcd. for $C_{17}H_{17}ON_3F_3S$ 368.1029 [M + H]$^+$; found 368.1038.

(*Z*)-2-(Phenylimino)-3-propyl-4-(trifluoromethyl)thiazolidin-4-ol (4f): Solid (279 mg, 92%), m.p. 130–132 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.94 (t, J = 7.6 Hz, 3 H), 1.60–1.93 (m, 2 H), 3.16 (d, J = 12.1 Hz, 1 H), 3.23–3.61 (m, 4 H), 6.89–6.95 (m, 2 H), 7.04–7.12 (m, 1 H), 7.25–7.34 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 11.3, 21.4, 35.1, 45.8, 90.9 (q, J = 31.9 Hz), 121.6, 123.7, 129.0, 150.6, 156.1 ppm. IR (KBr): $\tilde{\nu}$ = 3062, 2658, 1606, 1584, 1494, 1361, 1319, 1183 cm^{-1}. MS (ESI): m/z = 305 [M + H]$^+$. HRMS (ESI): calcd. for $C_{13}H_{16}ON_2F_3S$ 305.0916 [M + H]$^+$; found 305.0929.

(*Z*)-3-Cyclopropyl-2-(phenylimino)-4-(trifluoromethyl)thiazolidin-4-ol (4g): Solid (286 mg, 95%), m.p. 159–161 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.79–1.01 (m, 3 H), 1.14–1.25 (m, 1 H), 2.52–2.61 (m, 1 H), 3.16 (d, J = 11.7 Hz, 1 H), 3.51 (d, J = 11.7 Hz, 1 H), 3.61 (s, 1 H), 6.86–6.95 (m, 2 H), 7.06–7.12 (m, 1 H), 7.27–7.34 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 5.0, 5.6, 24.8, 32.4, 89.7 (q, J = 31.3 Hz), 116.7, 120.1, 121.8, 124.3, 127.2, 127.4, 149.7, 156.0 ppm. IR (KBr): $\tilde{\nu}$ = 3103, 2115, 1609, 1586, 1486, 1342, 1163 cm^{-1}. MS (ESI): m/z = 303 [M + H]$^+$. HRMS (ESI): calcd. for $C_{13}H_{14}ON_2F_3S$ 303.0765 [M + H]$^+$; found 303.0773.

(*Z*)-3-Phenyl-2-(phenylimino)-4-(trifluoromethyl)thiazolidin-4-ol (4h): Solid (310 mg, 92%), m.p. 152–154 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.31 (d, J = 12.1 Hz, 1 H), 3.62 (br. s, 1 H), 3.71 (d, J = 12.1 Hz, 1 H), 6.84–6.91 (m, 2 H), 7.01–7.09 (m, 1 H), 7.22–7.30 (m, 2 H), 7.32–7.51 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 34.5, 91.0 (q, J = 31.9 Hz), 120.8, 121.6, 124.0, 124.6, 128.9, 129.3, 130.4, 136.7, 150.6, 159.0 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –78.24 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3025, 1619, 1585, 1490, 1324, 1183 cm^{-1}. MS (ESI): m/z = 339 [M + H]$^+$. HRMS (ESI): calcd. for $C_{16}H_{14}ON_2F_3S$ 339.0763 [M + H]$^+$; found 339.0773.

(*Z*)-4-(Trifluoromethyl)-3-[3-(trifluoromethyl)phenyl]-2-[3-(trifluoromethyl)phenylimino]thiazolidin-4-ol (4i): Solid (369 mg, 78%), m.p. 106–108 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.40 (d, J = 12.1 Hz, 1 H), 3.70 (br. s, 1 H), 3.81 (d, J = 12.1 Hz, 1 H), 7.0 –7.20 (m, 2 H), 7.29–7.46 (m, 2 H), 7.55–7.79 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 35.2, 91.1 (q, J = 32.4 Hz), 118.6, 120.7, 121.7, 124.4, 124.8, 125.3, 125.9, 127.3, 129.5, 129.9, 131.3 (q, J = 32.4 Hz), 131.4 (q, J = 32.4 Hz), 133.9, 137.2, 150.4, 159.0 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –62.60 (s, 3 F), –62.70 (s, 3 F), –78.22 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3160, 2660, 1583, 1451, 1334, 1158 cm^{-1}. MS (ESI): m/z = 475 [M + H]$^+$. HRMS (ESI): calcd. for $C_{18}H_{12}ON_2F_9S$ 475.0498 [M + H]$^+$; found 475.0497.

(*Z*)-3-(4-Methoxyphenyl)-4-(trifluoromethyl)-2-[4-(trifluoromethyl)phenylimino]thiazolidin-4-ol (4j): Solid (370 mg, 85%), m.p. 154–156 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.39 (d, J = 12.1 Hz, 1 H), 3.43 (br. s, 1 H), 3.75 (d, J = 12.1 Hz, 1 H), 3.81 (s, 3 H), 6.91–7.02 (m, 4 H), 7.24–7.32 (m, 2 H), 7.46–7.55 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 34.4, 55.3, 91.0 (q, J = 31.8 Hz), 114.8, 120.8, 121.9, 124.6, 126.1, 128.6, 131.4, 153.7, 159.8 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –61.82 (s, 3 F), –78.43 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3158, 2847, 1589, 1510, 1462, 1410, 1322, 1160 cm^{-1}. MS (ESI): m/z = 437 [M + H]$^+$. HRMS (ESI): calcd. for $C_{18}H_{15}O_2N_2F_6S$ 437.0728 [M + H]$^+$; found 437.0752.

(*Z*)-3-(Furan-2-ylmethyl)-4-(trifluoromethyl)-2-[4-(trifluoromethyl)phenylimino]thiazolidin-4-ol (4k): Solid (356 mg, 87%), m.p. 98–100 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.26 (d, J = 11.76 Hz, 1 H), 3.60 (d, J = 11.76 Hz, 1 H), 3.89 (br. s, 1 H), 4.47 (d, J = 16.3 Hz, 1 H), 5.23 (d, J = 16.3 Hz, 1 H), 6.35–6.45 (m, 2 H), 6.95–7.00 (m, 2 H), 7.39–7.43 (m, 1 H), 7.51–7.57 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 34.9, 39.7, 90.8 (q, J = 32.7 Hz), 110.0, 111.0, 121.7, 123.2 (q, J = 287.9 Hz), 125.8, 126.2, 126.3, 142.2, 149.7, 153.2, 156.4 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –61.84 (s, 3 F), –78.84 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3431, 2926, 1590, 1427, 1329, 1304, 1166, 1124 cm^{-1}. MS (ESI): m/z = 411 [M + H]$^+$. HRMS (ESI): calcd. for $C_{16}H_{13}O_2N_2F_6S$ 411.0582 [M + H]$^+$; found 411.0596.

(*Z*)-3-(2-Morpholinoethyl)-4-(trifluoromethyl)-2-[4-(trifluoromethyl)phenylimino]thiazolidin-4-ol (4l): Solid (398 mg, 90%), m.p. 92–

94 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.32–2.39 (m, 1 H), 2.41–2.94 (m, 4 H), 2.96–3.05 (m, 1 H), 3.25 (d, J = 11.9 Hz, 1 H), 3.45–3.58 (m, 2 H), 3.64–3.94 (m, 4 H), 4.20–4.28 (m, 1 H), 6.98–7.04 (m, 2 H), 7.52–7.57 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 34.9, 41.2, 53.3, 55.0, 66.0, 90.0 (q, J = 31.3 Hz), 121.8, 126.2, 126.3, 146.9, 153.6, 158.0 ppm. IR (KBr): $\tilde{\nu}$ = 3036, 2687, 1588, 1541, 1477, 1420, 1320, 1173, 1140 cm^{-1}. MS (ESI): m/z = 444 [M + H]$^+$. HRMS (ESI): calcd. for $C_{17}H_{20}O_2N_3F_6S$ 444.1158 [M + H]$^+$; found 444.1150.

(*Z*)-2-[4-Chloro-3-(trifluoromethyl)phenylimino]-3-(thiophen-2-ylmethyl)-4-(trifluoromethyl)thiazolidin-4-ol (4m): Solid (418 mg, 91%), m.p. 123–125 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.09 (br. s, 1 H), 3.23 (d, J = 12.3 Hz, 1 H), 3.59 (d, J = 12.3 Hz, 1 H), 4.73 (d, J = 15.8 Hz, 1 H), 5.36 (d, J = 15.8 Hz, 1 H), 6.94–7.02 (m, 1 H), 7.10–7.20 (m, 2 H), 7.28–7.33 (m, 1 H), 7.34–7.39 (m, 1 H), 7.41–7.51 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 35.3, 41.8, 121.1, 125.9, 126.4, 127.2, 127.5, 132.0, 139.5, 148.8, 157.8 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –62.65 (s, 3 F), –78.44 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3074, 2704, 1585, 1475, 1415, 1313, 1161 cm^{-1}. MS (ESI): m/z = 461 [M + H]$^+$. HRMS (ESI): calcd. for $C_{16}H_{12}ON_2ClF_6S_2$ 460.9967 [M + H]$^+$; found 460.9978.

(*Z*)-2-[4-Chloro-3-(trifluoromethyl)phenylimino]-3-[2-(pyridin-2-yl)-ethyl]-4-(trifluoromethyl)thiazolidin-4-ol (4n): Solid (408 mg, 87%), m.p. 118–120 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.22 (d, J = 11.5 Hz, 1 H), 3.25–3.33 (m, 1 H), 3.34–3.41 (m, 1 H), 3.56 (d, J = 11.5 Hz, 1 H), 3.76–3.88 (m, 1 H), 4.38–4.50 (m, 1 H), 6.66–6.78 (m, 2 H), 7.22–7.37 (m, 3 H), 7.69–7.78 (m, 1 H), 8.40–8.48 (m, 1 H), 11.29 (br. s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 33.8, 36.2, 41.6, 91.4 (q, J = 31.3 Hz), 121.3, 122.0, 125.2, 125.7, 131.7, 138.0, 146.6, 149.2, 158.2, 158.5 ppm. IR (KBr): $\tilde{\nu}$ = 3031, 2720, 1611, 1587, 1477, 1420, 1343, 1197, 1142 cm^{-1}. MS (ESI): m/z = 470 [M + H]$^+$. HRMS (ESI): calcd. for $C_{18}H_{15}ON_3ClF_6S$ 470.0505 [M + H]$^+$; found 470.0523.

(*Z*)-3-*tert*-Butyl-2-[4-chloro-3-(trifluoromethyl)phenylimino]-4-(trifluoromethyl)thiazolidin-4-ol (4o): Solid (361 mg, 86%), m.p. 80–82 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.95 (t, J = 7.0 Hz, 3 H), 1.18–1.44 (m, 3 H), 1.57–1.84 (m, 2 H), 3.23 (d, J = 13.0 Hz, 1 H), 3.45–3.68 (m, 3 H), 7.00–7.06 (m, 1 H), 7.22–7.29 (m, 1 H), 7.36–7.43 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 13.7, 20.2, 30.1, 35.1, 44.2, 91.0 (q, J = 32.4 Hz), 120.9, 121.2, 121.3, 123.0 (q, J = 287.6 Hz), 124.5, 126.0, 126.4, 131.9, 149.3, 157.6 ppm. IR (KBr): $\tilde{\nu}$ = 3078, 2667, 1607, 1582, 1496, 1350, 1182 cm^{-1}. MS (ESI): m/z = 421 [M + H]$^+$. HRMS (ESI): calcd. for $C_{15}H_{16}ON_2ClF_6S$ 421.0556 [M + H]$^+$; found 421.0570.

Procedure for Propargylation of 2-Imino-4-(trifluoromethyl)thiazolidin-4-ol (7a and 7b): Propargyl bromide (1 mmol) was slowly added to a stirred solution of 2-imino-4-(trifluoromethyl)thiazolidinol **4b** or **4j** (1 mmol) and K_2CO_3 (2 equiv.) in DMF (5 mL), and the reaction mixture was stirred at ambient temperature for 24 h. After the reaction was complete, it was quenched with saturated $NaHCO_3$ solution (3–4 mL), and the mixture was extracted with EtOAc (2× 15 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography using EtOAc/*n*-hexane gradients to give pure product **7a** or **7b**.

(*Z*)-*N*-[3-(Furan-2-ylmethyl)-4-(prop-2-ynyloxy)-4-(trifluoromethyl)thiazolidin-2-ylidene]aniline (7a): Viscous liquid (330 mg, 87%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.50 (t, J = 2.4 Hz, 1 H), 3.47–3.66 (m, 2 H), 4.09 (dd, J = 16.0, 2.4 Hz, 1 H), 4.24 (dd, J = 16.0, 2.4 Hz, 1 H), 4.72 (d, J = 16.0 Hz, 1 H), 4.85 (d, J = 16.0 Hz, 1 H), 6.28–6.36 (m, 1 H), 6.37–6.45 (m, 1 H), 6.91–7.00 (m, 2 H), 7.05–7.15 (m, 1 H), 7.23–7.40 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.3, 40.2, 51.7, 75.1, 78.4, 94.4 (q, J = 31.8 Hz), 109.2, 110.4, 121.4, 122.6 (q, J = 287.0 Hz), 123.9, 129.0, 141.6, 150.2, 150.3, 156.4 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –78.10 (s, 3 F) ppm. IR (Neat): $\tilde{\nu}$ = 2927, 1635, 1592, 1321, 1183, 1135 cm^{-1}. MS (ESI): m/z = 381 [M + H]$^+$. HRMS (ESI-orbitrap): calcd. for $C_{18}H_{16}O_2N_2F_3S$ 381.0866 [M + H]$^+$; found 381.0879.

(*Z*)-*N*-[3-(Furan-2-ylmethyl)-4-(prop-2-ynyloxy)-4-(trifluoromethyl)thiazolidin-2-ylidene]-4-(trifluoromethyl)aniline (7b): Viscous liquid (367 mg, 82%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.51 (t, J = 2.3 Hz, 1 H), 3.56–3.65 (m, 2 H), 4.11 (dd, J = 15.6, 2.3 Hz, 1 H), 4.24 (dd, J = 15.6, 2.3 Hz, 1 H), 4.72 (d, J = 16.4 Hz, 1 H), 4.84 (d, J = 16.4 Hz, 1 H), 6.31–6.35 (m, 1 H), 6.36–6.41 (m, 1 H), 6.99–7.08 (m, 2 H), 7.33–7.40 (m, 1 H), 7.51–7.60 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.2, 40.4, 51.8, 75.3, 78.2, 94.5 (q, J = 32.4 Hz), 109.3, 110.4, 118.6, 120.4, 122.5 (q, J = 287.6 Hz), 124.0 (q, J = 272.8 Hz), 124.9, 129.5, 131.3 (q, J = 31.8 Hz), 141.8, 150.0, 150.5, 157.4 ppm. IR (Neat): $\tilde{\nu}$ = 2934, 1634, 1442, 1320, 1183, 1129 cm^{-1}. MS (ESI): m/z = 449 [M + H]$^+$. HRMS (ESI-orbitrap): calcd. for $C_{19}H_{15}O_2N_2F_6S$ 449.0743 [M + H]$^+$; found 449.0752.

Typical Procedure for the Synthesis of Isoxazole Derivatives 9a–9e of 2-Imino-4-(trifluoromethyl)thiazolidinol: NaOCl (9–12% aqueous solution; 1.6 mmol) was slowly added over a period of 1 h to a stirred solution of alkyne **7a** (1 mmol) and triethylamine (1 mmol) in dichloromethane (5 mL) at 0 °C. Then a solution of oxime **8** (1 mmol) in dichloromethane (2 mL) was added. The reaction mixture was stirred at room temperature for 24 h, and after TLC indicated that the reaction was complete, the dichloromethane was removed under reduced pressure. Water (5 mL) was added, and the mixture was extracted with ethyl acetate (2× 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography using ethyl acetate/*n*-hexane gradients to give pure product **9** (Table 3).

(*Z*)-*N*-(3-(Furan-2-ylmethyl)-4-{[3-(4-methoxyphenyl)isoxazol-5-yl]methoxy}-4-(trifluoromethyl)thiazolidin-2-ylidene)aniline (9a): Solid (460 mg, 87%), m.p. 73–75 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.41 (d, J = 13.6 Hz, 1 H), 3.67 (d, J = 13.6 Hz, 1 H), 3.85 (s, 3 H), 4.45 (d, J = 12.8 Hz, 1 H), 4.69–4.79 (m, 2 H), 4.96 (d, J = 15.8 Hz, 1 H), 6.29–6.33 (m, 1 H), 6.41–6.45 (m, 1 H), 6.50 (s, 1 H), 6.92–7.02 (m, 4 H), 7.07–7.15 (m, 1 H), 7.28–7.38 (m, 3 H), 7.71–7.78 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.7, 40.2, 55.3, 56.8, 94.4 (q, J = 32.4 Hz), 101.1, 109.4, 110.5, 114.3, 121.0, 121.4, 124.0, 124.5, 128.1, 129.0, 130.2, 150.0, 150.1, 156.0, 161.0, 162.0, 167.3 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –78.19 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 2962, 1633, 1593, 1531, 1433, 1256, 1181 cm^{-1}. MS (ESI): m/z = 530 [M + H]$^+$. HRMS (ESI): calcd. for $C_{26}H_{23}O_4N_3F_3S$ 530.1343 [M + H]$^+$; found 530.1355.

(*Z*)-*N*-[3-(Furan-2-ylmethyl)-4-({3-[4-(trifluoromethoxy)phenyl]-isoxazol-5-yl}methoxy)-4-(trifluoromethyl)thiazolidin-2-ylidene]-aniline (9b): Viscous liquid (431 mg, 74%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.40 (d, J = 13.4 Hz, 1 H), 3.68 (d, J = 13.4 Hz, 1 H), 4.48 (d, J = 13.2 Hz, 1 H), 4.72 (d, J = 15.8 Hz, 1 H), 4.76 (d, J = 13.2 Hz, 1 H), 4.98 (d, J = 15.8 Hz, 1 H), 6.29–6.34 (m, 1 H), 6.41–6.46 (m, 1 H), 6.55 (s, 1 H), 6.94–7.02 (m, 2 H), 7.07–7.15 (m, 1 H), 7.27–7.37 (m, 4 H), 7.44–7.55 (m, 1 H), 7.64–7.77 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.7, 40.0, 56.8, 94.4 (q, J = 32.4 Hz), 101.2, 109.4, 110.5, 116.8, 118.6, 119.3, 120.6, 121.3, 122.0, 122.5, 124.0, 124.5, 125.1, 126.0, 128.3, 129.0, 130.0, 130.4, 141.7, 149.5, 149.9, 150.1, 156.0, 161.2, 168.2 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –57.80 (s, 3 F), –78.12 (s, 3 F) ppm. IR (Neat): $\tilde{\nu}$ = 2926, 1638, 1593, 1448, 1260, 1182 cm^{-1}. MS (ESI): m/z

= 584 $[M + H]^+$. HRMS (ESI): calcd. for $C_{26}H_{20}O_4N_3F_6S$ 584.1066 $[M + H]^+$; found 584.1073.

(*Z*)-*N*-[3-(Furan-2-ylmethyl)-4-(trifluoromethyl)-4-({3-[4-(trifluoromethylthio)phenyl]isoxazol-5-yl}methoxy)thiazolidin-2-ylidene]-aniline (9c): Viscous liquid (455 mg, 76%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.41 (d, J = 13.4 Hz, 1 H), 3.70 (d, J = 13.4 Hz, 1 H), 4.49 (d, J = 13.2 Hz, 1 H), 4.68–4.82 (m, 2 H), 4.99 (d, J = 15.8 Hz, 1 H), 6.29–6.34 (m, 1 H), 6.41–6.46 (m, 1 H), 6.58 (s, 1 H), 6.94–7.01 (m, 2 H), 7.07–7.15 (m, 1 H), 7.28–7.38 (m, 3 H), 7.72–7.80 (m, 2 H), 7.83–7.91 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.8, 40.0, 56.8, 101.3, 109.5, 110.5, 121.4, 124.0, 127.7, 128.7, 129.0, 131.0, 136.6, 141.7, 149.9, 150.1, 155.9, 161.3, 168.3 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –42.20 (s, 3 F), –78.01 (s, 3 F) ppm. IR (Neat): $\tilde{\nu}$ = 2923, 1634, 1592, 1429, 1261, 1183, 1117, 1085 cm^{-1}. MS (ESI): m/z = 600 $[M + H]^+$. HRMS (ESI): calcd. for $C_{26}H_{20}O_3N_3F_6S_2$ 600.0841 $[M + H]^+$; found 600.0844.

(*Z*)-*N*-(4-{[3-(4-Bromophenyl)isoxazol-5-yl]methoxy}-3-(furan-2-ylmethyl)-4-(trifluoromethyl)thiazolidin-2-ylidene)aniline (9d): Solid (473 mg, 82%), m.p. 96–98 °C;^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.40 (d, J = 13.6 Hz, 1 H), 3.69 (d, J = 13.6 Hz, 1 H), 4.46 (d, J = 13.6 Hz, 1 H), 4.72 (d, J = 15.8 Hz, 1 H), 4.75 (d, J = 13.6 Hz, 1 H), 4.98 (d, J = 15.8 Hz, 1 H), 6.29–6.34 (m, 1 H), 6.41–6.46 (m, 1 H), 6.53 (s, 1 H), 6.94–7.01 (m, 2 H), 7.07–7.16 (m, 1 H), 7.29–7.37 (m, 3 H), 7.57–7.72 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.8, 40.0, 56.8, 94.4 (q, J = 32.4 Hz), 101.1, 109.5, 110.5, 121.4, 124.0, 124.5, 127.5, 128.3, 129.0, 132.2, 141.7, 149.9, 150.1, 156.0, 161.5, 168.0 ppm. IR (KBr): $\tilde{\nu}$ = 3139, 3004, 1632, 1592, 1431, 1260, 1180, 696 cm^{-1}. MS (ESI): m/z = 578 $[M + H]^+$. HRMS (ESI): calcd. for $C_{25}H_{20}O_3N_3BrF_3S$ 578.0353 $[M + H]^+$; found 578.0355.

(*Z*)-*N*-(4-{[3-(2-Fluorophenyl)isoxazol-5-yl]methoxy}-3-(furan-2-ylmethyl)-4-(trifluoromethyl)thiazolidin-2-ylidene)aniline (9e): Solid (413 mg, 80%), m.p. 79–81 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.43 (d, J = 13.4 Hz, 1 H), 3.70 (d, J = 13.4 Hz, 1 H), 4.48 (d, J = 13.2 Hz, 1 H), 4.74 (d, J = 15.8 Hz, 1 H), 4.77 (d, J = 13.2 Hz, 1 H), 4.98 (d, J = 15.8 Hz, 1 H), 6.31–6.35 (m, 1 H), 6.42–6.46 (m, 1 H), 6.71 (d, J = 3.6 Hz, 1 H), 6.95–7.00 (m, 2 H), 7.07–7.38 (m, 6 H), 7.40–7.50 (m, 1 H), 7.95–8.03 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.8, 40.0, 56.7, 94.5 (q, J = 31.8 Hz), 104.0 (d, J = 9.3 Hz), 109.5, 110.5, 116.4 (d, J = 21.9 Hz), 121.4, 124.0, 124.6 (d, J = 3.8 Hz), 129.0, 131.8 (d, J = 8.8 Hz), 141.7, 150.0, 150.2, 156.1, 157.8, 161.9, 167.3 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –78.14 (s, 3 F), –114.31 (s, 1 F) ppm. IR (KBr): $\tilde{\nu}$ = 2926, 1633, 1591, 1470, 1258, 1178 cm^{-1}. MS (ESI): m/z = 518 $[M + H]^+$. HRMS (ESI): calcd. for $C_{25}H_{20}O_3N_3F_4S$ 518.1147 $[M + H]^+$; found 518.1156.

Typical Procedure for the Synthesis Triazole Derivatives 11a–11e of 2-Imino-4-(trifluoromethyl)thiazolidinol: CuI (10 mol-%) was added to a stirred solution of alkyne **7b** (1 mmol) in dry tetrahydrofuran (5 mL). The mixture was stirred for 5–10 min at room temperature under a nitrogen atmosphere, then a solution of azide **10** (1 mmol) in dry THF (2 mL) was added. Stirring was continued for 24 h at the same temperature. After TLC indicated that the reaction was complete, the reaction was quenched with saturated NH_4Cl solution (1–2 mL), then the mixture was diluted with water and extracted with ethyl acetate (3× 10 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography using ethyl acetate/*n*-hexane gradients to give triazole derivative **11** as a pure product (Table 4).

(*Z*)-*N*-(3-Chloro-4-fluorophenyl)-2-[4-({3-(furan-2-ylmethyl)-4-(trifluoromethyl)-2-[4-(trifluoromethyl)phenylimino]thiazolidin-4-yloxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide (11a): Solid (594 mg, 88%), m.p. 64–66 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.54 (d, J = 13.6 Hz, 1 H), 3.70 (d, J = 13.6 Hz, 1 H), 4.55 (d, J = 12.0 Hz, 1 H), 4.71 (d, J = 15.8 Hz, 1 H), 4.79–4.95 (m, 2 H), 5.15–5.29 (m, 2 H), 6.29–6.33 (m, 1 H), 6.36–6.41 (m, 1 H), 7.02–7.12 (m, 3 H), 7.24–7.33 (m, 2 H), 7.54–7.61 (m, 2 H), 7.65–7.71 (m, 1 H), 7.77 (s, 1 H), 8.37 (br. s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.6, 40.1, 53.1, 57.2, 94.4 (q, J = 31.8 Hz), 109.4, 110.6, 116.6 (d, J = 21.9 Hz), 119.8 (d, J = 7.1 Hz), 120.6, 121.7, 122.3, 125.0, 126.3 (d, J = 3.3 Hz), 133.5 (d, J = 2.7 Hz), 141.7, 143.7, 149.9, 153.0, 155.0 (d, J = 247.5 Hz), 157.1, 163.1 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –61.70 (s, 3 F), –78.27 (s, 3 F), –118.67 (s, 1 F) ppm. IR (KBr): $\tilde{\nu}$ = 3287, 2956, 1639, 1501, 1260, 1182, 1062 cm^{-1}. MS (ESI): m/z = 677 $[M + H]^+$. HRMS (ESI): calcd. for $C_{27}H_{21}O_3N_6ClF_7S$ 677.0968 $[M + H]^+$; found 677.0967.

(*Z*)-*N*-(4-Fluorophenyl)-2-[4-({3-(furan-2-ylmethyl)-4-(trifluoromethyl)-2-[4-(trifluoromethyl)phenylimino]thiazolidin-4-yloxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide (11b): Solid (545 mg, 85%), m.p. 86–88 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.55 (d, J = 13.3 Hz, 1 H), 3.69 (d, J = 13.3 Hz, 1 H), 4.55 (d, J = 12.3 Hz, 1 H), 4.72 (d, J = 16.1 Hz, 1 H), 4.83 (d, J = 12.3 Hz, 1 H), 4.91 (d, J = 16.1 Hz, 1 H), 5.15–5.24 (m, 2 H), 6.28–6.32 (m, 1 H), 6.37–6.40 (m, 1 H), 6.98–7.08 (m, 4 H), 7.28–7.31 (m, 1 H), 7.40–7.46 (m, 2 H), 7.52–7.58 (m, 2 H), 7.74 (s, 1 H), 8.02 (br. s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.6, 40.2, 53.3, 57.3, 94.4 (q, J = 31.3 Hz), 109.4, 110.5, 115.8 (d, J = 22.5 Hz), 121.7, 122.0 (d, J = 8.2 Hz), 124.8, 126.3, 132.7, 141.7, 143.8, 150.0, 153.0, 157.0, 159.8 (d, J = 245.3 Hz), 162.9 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –61.77 (s, 3 F), –78.34 (s, 3 F), –116.15 (s, 1 F) ppm. IR (KBr): $\tilde{\nu}$ = 3300, 2929, 1639, 1510, 1259, 1182, 1063 cm^{-1}. MS (ESI): m/z = 643 $[M + H]^+$. HRMS (ESI): calcd. for $C_{27}H_{22}O_3N_6F_7S$ 643.1345 $[M + H]^+$; found 643.1365.

(*Z*)-*N*-Cyclohexyl-2-[4-({3-(furan-2-ylmethyl)-4-(trifluoromethyl)-2-[4-(trifluoromethyl)phenylimino]thiazolidin-4-yloxy}methyl)-1*H*-1,2,3-triazol-1-yl]acetamide (11c): (585 mg, 93%). Solid, m.p. 68–70 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.05–1.22 (m, 2 H), 1.24–1.41 (m, 2 H), 1.48–1.98 (m, 6 H), 3.57 (d, J = 13.0 Hz, 1 H), 3.68 (d, J = 13.0 Hz, 1 H), 3.72–3.82 (m, 1 H), 4.53 (d, J = 12.0 Hz, 1 H), 4.74 (d, J = 16.0 Hz, 1 H), 4.82 (d, J = 12.0 Hz, 1 H), 4.89 (d, J = 16.0 Hz, 1 H), 4.96–5.07 (m, 2 H), 5.93 (s, 1 H), 6.30–6.35 (m, 1 H), 6.37–6.44 (m, 1 H), 7.01–7.12 (m, 2 H), 7.30–7.34 (m, 1 H), 7.52–7.63 (m, 2 H), 7.71 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.6, 25.2, 30.6, 32.6, 40.1, 48.9, 53.1, 57.5, 94.4 (q, J = 30.7 Hz), 109.3, 110.5, 121.7, 124.3, 126.2, 126.3, 141.7, 143.8, 150.0, 153.0, 157.0, 163.7 ppm. IR (KBr): $\tilde{\nu}$ = 3305, 2935, 1642, 1553, 1257, 1185, 1060 cm^{-1}. MS (ESI): m/z = 631 $[M + H]^+$. HRMS (ESI): calcd. for $C_{27}H_{28}O_3N_6F_6NaS$ 653.1721 $[M + Na]^+$; found 653.1740.

(*Z*)-2-[4-({3-(Furan-2-ylmethyl)-4-(trifluoromethyl)-2-[4-(trifluoromethyl)phenylimino]thiazolidin-4-yloxy}methyl)-1*H*-1,2,3-triazol-1-yl]-*N*-(thiophen-2-ylmethyl)acetamide (11d): Viscous liquid (579 mg, 90%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.54 (d, J = 13.6 Hz, 1 H), 3.67 (d, J = 13.6 Hz, 1 H), 4.51 (d, J = 12.0 Hz, 1 H), 4.62 (d, J = 5.3 Hz, 2 H), 4.67–4.95 (m, 3 H), 5.00–5.13 (m, 2 H), 6.28–6.34 (m, 1 H), 6.37–6.41 (m, 1 H), 6.46 (s, 1 H), 6.90–6.98 (m, 2 H), 7.01–7.11 (m, 2 H), 7.19–7.34 (m, 2 H), 7.52–7.62 (m, 2 H), 7.70 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.5, 38.3, 40.1, 52.6, 57.3, 109.2, 110.5, 121.7, 122.5, 124.6, 125.3, 126.3, 126.9, 139.6, 141.6, 143.6, 150.0, 153.0, 157.1, 164.7 ppm. IR (Neat): $\tilde{\nu}$ = 3301, 2932, 1645, 1551, 1250, 1182, 1060 cm^{-1}. MS

(ESI): m/z = 645 [M + H]$^+$. HRMS (ESI): calcd. for $C_{26}H_{23}O_3N_6F_6S_2$ 645.1155 [M + H]$^+$; found 645.1171.

(*Z*)-2-[4-({3-(Furan-2-ylmethyl)-4-(trifluoromethyl)-2-[4-(trifluoromethyl)phenylimino]thiazolidin-4-yloxy}methyl)-1*H*-1,2,3-triazol-1-yl]-*N*-(4-methoxyphenyl)acetamide (11e): Solid (595 mg, 91%), m.p. 76–78 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.54 (d, J = 13.6 Hz, 1 H), 3.68 (d, J = 13.6 Hz, 1 H), 3.77 (s, 3 H), 4.52 (d, J = 12.0 Hz, 1 H), 4.68–4.95 (m, 3 H), 5.12–5.26 (m, 2 H), 6.28–6.32 (m, 1 H), 6.36–6.40 (m, 1 H), 6.80–6.88 (m, 2 H), 7.01–7.10 (m, 2 H), 7.28–7.42 (m, 3 H), 7.52–7.60 (m, 2 H), 7.78 (s, 1 H), 8.12 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.5, 40.1, 53.2, 55.3, 57.3, 94.4 (q, J = 32.5 Hz), 109.3, 110.5, 114.1, 121.7, 122.0, 124.8, 126.3, 129.7, 141.7, 143.7, 150.0, 153.0, 157.0, 157.1, 162.9 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –61.81 (s, 3 F), –78.42 (s, 3 F) ppm. IR (KBr): $\tilde{\nu}$ = 3291, 2930, 1639, 1552, 1249, 1180, 1062 cm^{-1}. MS (ESI): m/z = 655 [M + H]$^+$. HRMS (ESI): calcd. for $C_{28}H_{25}O_4N_6F_6S$ 655.1544 [M + H]$^+$; found 655.1556.

Typical Procedure for the Synthesis of Propargylamine Derivatives 13a–13e of 2-Imino-4-(trifluoromethyl)thiazolidinol: CuI (10 mol-%) was added to a stirred solution of alkyne **7a** (1 mmol) in tetrahydrofuran (5 mL). The mixture was stirred for 15–20 min at room temperature, then formaldehyde (1.5 equiv.) and secondary cyclic amine **12** (1 mmol) were added. Stirring was continued for 4–6 h at the same temperature. After TLC indicated that the reaction was complete, the reaction was quenched with saturated NH_4Cl solution (1–2 mL). The mixture was diluted with water and extracted with ethyl acetate (2 × 15 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography using ethyl acetate/*n*-hexane gradients to give propargylamine **13** as a pure product (Table 5).

(*Z*)-*N*-[3-(Furan-2-ylmethyl)-4-(4-morpholinobut-2-ynyloxy)-4-(trifluoromethyl)thiazolidin-2-ylidene]aniline (13e): Viscous liquid (431 mg, 90%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.45–2.60 (m, 4 H), 3.29–3.36 (m, 2 H), 3.64–3.77 (m, 6 H), 4.13 (d, J = 15.7 Hz, 1 H), 4.28 (d, J = 15.7 Hz, 1 H), 4.74 (d, J = 15.8 Hz, 1 H), 4.82 (d, J = 15.8 Hz, 1 H), 6.30–6.35 (m, 1 H), 6.38–6.42 (m, 1 H), 6.90–6.98 (m, 2 H), 7.05–7.12 (m, 1 H), 7.26–7.38 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.4, 39.7, 47.3, 51.8, 52.2, 66.8, 79.9, 81.8, 94.3 (q, J = 31.8 Hz), 109.0, 110.3, 121.4, 122.5 (q, J = 287.0 Hz), 123.8, 128.9, 141.5, 150.0, 150.3, 156.3 ppm. IR (Neat): $\tilde{\nu}$ = 2931, 1630, 1596, 1512, 1451, 1321, 1183, 1130 cm^{-1}. MS (ESI): m/z = 480 [M + H]$^+$. HRMS (ESI): calcd. for $C_{23}H_{25}O_3N_3F_3S$ 480.1546 [M + H]$^+$; found 480.1563.

(*Z*)-*N*-(3-(Furan-2-ylmethyl)-4-{4-[4-(2-methoxyphenyl)piperazin-1-yl]but-2-ynyloxy}-4-(trifluoromethyl)thiazolidin-2-ylidene)aniline (13b): Viscous liquid (537 mg, 92%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.77 (t, J = 4.5 Hz, 4 H), 3.02–3.20 (m, 4 H), 3.38–3.43 (m, 2 H), 3.54–3.59 (m, 2 H), 3.85 (s, 3 H), 4.14 (d, J = 15.8 Hz, 1 H), 4.29 (d, J = 15.8 Hz, 1 H), 4.74 (d, J = 15.8 Hz, 1 H), 4.84 (d, J = 15.8 Hz, 1 H), 6.31–6.36 (m, 1 H), 6.38–6.43 (m, 1 H), 6.82–7.15 (m, 7 H), 7.24–7.41 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.2, 40.2, 47.2, 50.4, 52.1, 52.2, 55.3, 79.9, 82.3, 94.3 (q, J = 31.8 Hz), 109.0, 110.4, 111.0, 118.2, 120.9, 121.5, 123.0, 123.8, 128.9, 141.0, 141.6, 150.2, 150.4, 152.2, 156.4 ppm. IR (Neat): $\tilde{\nu}$ = 2927, 1636, 1590, 1498, 1449, 1239, 1179 cm^{-1}. MS (ESI): m/z = 585 [M + H]$^+$. HRMS (ESI): calcd. for $C_{30}H_{32}O_3N_4F_3S$ 585.2135 [M + H]$^+$; found 585.2141.

(*Z*)-*N*-(3-(Furan-2-ylmethyl)-4-{4-[4-(pyridin-2-yl)piperazin-1-yl]-but-2-ynyloxy}-4-(trifluoromethyl)thiazolidin-2-ylidene)aniline (13c): Viscous liquid (421 mg, 76%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.63–2.74 (m, 4 H), 3.37–3.45 (m, 2 H), 3.51–3.66 (m, 6 H), 4.12 (d, J = 15.6 Hz, 1 H), 4.27 (d, J = 15.6 Hz, 1 H), 4.72 (d, J = 16.0 Hz, 1 H), 4.84 (d, J = 16.0 Hz, 1 H), 6.30–6.34 (m, 1 H), 6.38–6.42 (m, 1 H), 6.59–6.71 (m, 2 H), 6.90–7.01 (m, 2 H), 7.05–7.15 (m, 1 H), 7.24–7.40 (m, 3 H), 7.43–7.54 (m, 1 H), 8.15–8.25 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.1, 40.0, 44.7, 46.8, 51.4, 51.9, 80.2, 81.5, 94.2 (q, J = 31.8 Hz), 107.0, 108.9, 110.3, 113.3, 121.3, 122.5 (q, J = 287.6 Hz), 123.2, 123.7, 128.8, 129.5, 137.4, 141.4, 144.4, 147.6, 150.0, 150.2, 156.3, 159.0, 169.0 ppm. IR (Neat): $\tilde{\nu}$ = 2924, 1632, 1590, 1508, 1457, 1325, 1178, 1136 cm^{-1}. MS (ESI): m/z = 556 [M + H]$^+$. HRMS (ESI): calcd. for $C_{28}H_{29}O_2N_5F_3S$ 556.1976 [M + H]$^+$; found 556.1966.

(*Z*)-*N*-{3-(Furan-2-ylmethyl)-4-[4-(piperidin-1-yl)but-2-ynyloxy]-4-(trifluoromethyl)thiazolidin-2-ylidene}aniline (13d): Viscous liquid (424 mg, 89%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.47–1.68 (m, 5 H), 2.32–2.55 (m, 5 H), 3.27 (s, 2 H), 3.56 (s, 2 H), 4.13 (d, J = 16.0 Hz, 1 H), 4.26 (d, J = 16.0 Hz, 1 H), 4.73 (d, J = 16.0 Hz, 1 H), 4.82 (d, J = 16.0 Hz, 1 H), 6.29–6.34 (m, 1 H), 6.37–6.42 (m, 1 H), 6.90–7.00 (m, 2 H), 7.04–7.12 (m, 1 H), 7.24–7.39 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 23.7, 25.7, 30.1, 40.1, 47.7, 52.0, 53.3, 79.3, 82.8, 94.3 (q, J = 31.8 Hz), 108.9, 110.3, 121.3, 122.5 (q, J = 287.0 Hz), 123.7, 128.8, 141.4, 150.1, 150.3, 156.3 ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –78.72 (s, 3 F) ppm. IR (Neat): $\tilde{\nu}$ = 2925, 1638, 1593, 1496, 1447, 1235, 1182 cm^{-1}. MS (ESI): m/z = 478 [M + H]$^+$. HRMS (ESI): calcd. for $C_{24}H_{27}O_2N_3F_3S$ 478.1755 [M + H]$^+$; found 478.1748.

(*Z*)-*N*-(4-{4-[4-(4-Fluorophenyl)piperazin-1-yl]but-2-ynyloxy}-3-(furan-2-ylmethyl)-4-(trifluoromethyl)thiazolidin-2-ylidene)aniline (13e): Viscous liquid (491 mg, 86%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.66–2.77 (m, 4 H), 3.07–3.20 (m, 4 H), 3.34–3.44 (m, 2 H), 3.49–3.63 (m, 2 H), 4.14 (d, J = 15.8 Hz, 1 H), 4.29 (d, J = 15.8 Hz, 1 H), 4.74 (d, J = 15.8 Hz, 1 H), 4.84 (d, J = 15.8 Hz, 1 H), 6.30–6.36 (m, 1 H), 6.38–6.44 (m, 1 H), 6.81–7.03 (m, 6 H), 7.05–7.16 (m, 1 H), 7.24–7.42 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 30.1, 40.2, 46.9, 49.8, 51.8, 51.9, 79.9, 81.9, 94.2 (q, J = 31.9 Hz), 108.9, 110.3, 115.3 (d, J = 22.0 Hz), 117.7 (d, J = 7.1 Hz), 121.3, 123.7, 128.8, 141.4, 147.6, 150.0, 150.3, 156.2, 157.0 (d, J = 238.8 Hz) ppm. ^{19}F NMR ($CDCl_3$, 500 MHz): δ = –78.60 (s, 3 F), –124.30 (s, 1 F) ppm. IR (Neat): $\tilde{\nu}$ = 2926, 1635, 1592, 1510, 1454, 1320, 1181 cm^{-1}. MS (ESI): m/z = 573 [M + H]$^+$. HRMS (ESI): calcd. for $C_{29}H_{29}O_2N_4F_4S$ 573.1933 [M + H]$^+$; found 573.1941.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C NMR spectra of products **4a**–**4o**, **7a**, **7b**, **9a**–**9e**, **11a**–**11e**, and **13a**–**13e**; X-ray data of compound **4d** are provided in the CIF file.

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