ChemPubSoc Europe

DOI: 10.1002/ejoc.201801505

EurJOC European Journal of Organic Chemistry

Full Paper

Heterocyclic Synthesis*

Tandem Thioacylation-Intramolecular Hydrosulfenylation of Propargyl Amines – Rapid Access to 2-Aminothiazolidines

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Abstract: An investigation directed towards the preparation of α-substituted propargyl thioureas from the corresponding propargylamine resulted in a tandem thioacylation/*anti*-hydrosulfenylation and the formation of the corresponding thiazolidine in excellent (46–98 %) yields rather than the anticipated thiourea. Initial interpretation of this outcome was formulated in terms of the highly substituted nature of the α-carbon of these amines resulting in steric acceleration, however, even simple propargylamines engage in this chemistry. In light of these observations, it was determined subsequently that the formation of the thiourea is quite rapid, but cyclization occurred during chromatographic purification and is in fact facilitated by silica gel. Control reactions and monitoring the progress of the reaction by NMR spectroscopy clearly indicate that the cyclization is relatively slow until either purification or the introduction of silica gel results in cyclization. Subsequently, it was found that even the parent system afforded the thiazolidine when the reaction was conducted on silica gel. Overall, the reaction is tolerant of a variety of substitution patterns, internal and terminal alkynes and isothiocyanates providing rapid access to 2-aminothiazolidines.

Introduction

Alkynes have proven to be pivotal functional groups in the context of complex molecule synthesis, in particular, the stereo- and regiocontrolled addition of E^+/Nu^- across the triple bond have been particularly enabling. When this is rendered intramolecular, the construction of cyclic, including heterocyclic systems can be accomplished readily. We have been interested for several years in the utility of such chemistries for the construction of alkaloids belonging to the oroidin[1] and *Leucetta* family of marine sponge metabolites.[2] In the context of an investigation towards the total synthesis of two members of the *Leucetta* alkaloids[2–3] spirocalcaridine A (**3**) and B (**4**),[4] we have reported recently a tandem oxidative amination dearomatizing spirocyclization (TOADS) of propargyl guanidines **1** (X = NCO_2R) for construction of the ABC rings,[5] rapidly providing the complete natural product framework **2** in one synthetic operation which takes advantage of this feature of alkyne reactivity (Figure 1).[6] As part of this initial investigation, we extended this tandem cyclization process to the participation of ureas **1** (X = O) which led to the formation of the corresponding spiro iminooxazole **2** in good yields.[5] Our intent was to extend further this general process to thioureas **1** (X = S) as a means to access the related spiro iminothiazole, however, as will be detailed in this paper, accessing the requisite propargyl-substituted thioureas via the standard methods we had already employed for guanidine and urea synthesis were complicated by unanticipated events.[7]

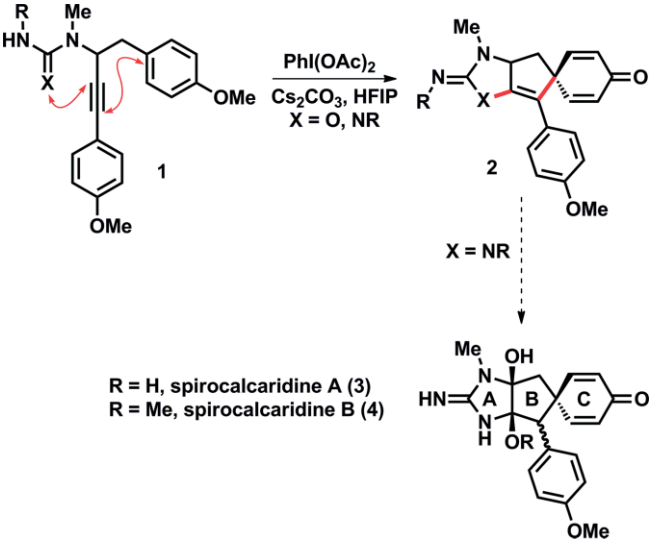

Figure 1. Dearomatizing spirocyclization approach to the complete framework of spirocalcaridine A and B.

Specifically, instead of isolating the thiourea **1** (X = S), we obtained thiazolidines in excellent yields instead. The conversion of propargylamines and isothiocyanates to the thiazolidine or thiazole has been known for a number of years (see Scheme 1),[8] however, generally relatively forcing conditions (heating neat,[8] refluxing in toluene[9] or microwave irradiation)[10] were employed. While these reactions are experimen-

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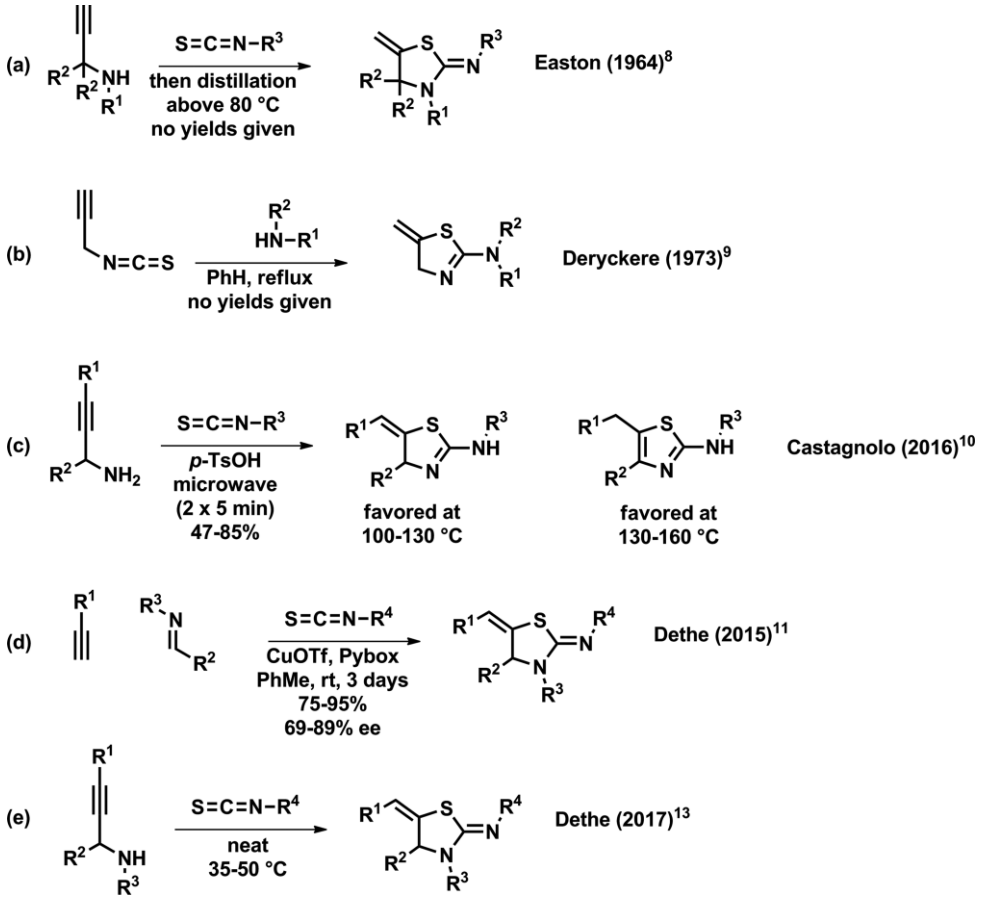
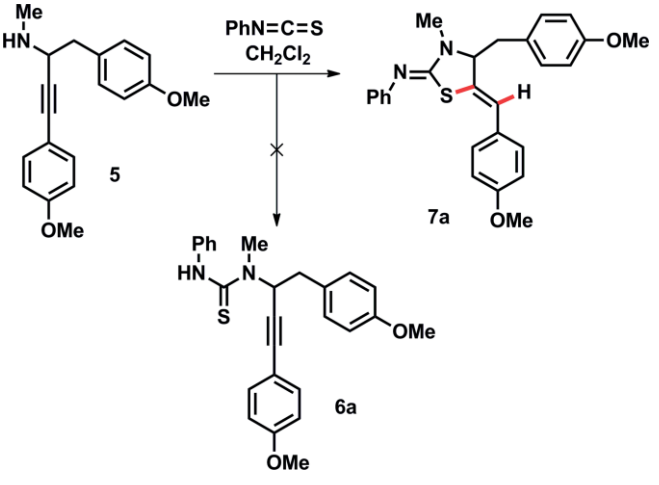


Scheme 1. Overview of prior thiazolidine synthesis from propargylamines.

tally convenient, depending upon the structures of the precursors, there can be issues with aromatization and formation of other by-products.[10] Two recent reports from the Dethe group have shown that thiazolidines can be obtained in good yields via a three component coupling under copper(I) catalysis,[11,12] including asymmetric variants, and through heating (35–50 °C) neat mixtures of the amine and isothiocyanate.[13] In these latter reports, no examples of either terminal alkynes, N-unsubstituted propargylamines, or systems lacking substituents at the propargylic carbon were described. Herein, we describe the discovery and development of a synthetic method that delivers the vinylidene substituted thiazoline from a propargylamine and an isothiocyanate as the exclusive product mediated by silica gel. The method has broad substrate scope and provides access to heterocycles primed for further elaboration.

Results and Discussion

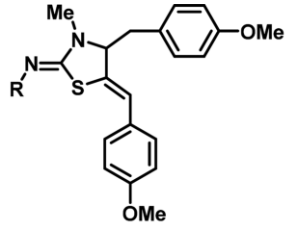
In the previously reported dearomatization chemistry from our group, the requisite cyclization substrates **1** were prepared from the corresponding *N*-methyl propargylamine **5** (obtained via a three-component coupling) by treatment with isothioureas and HgO (guanidines) or isocyanates (ureas) without event, but the reaction with isothiocyanates took a different course (Scheme 2).[7] Specifically, upon treatment of propargylamine **5** with phenyl isothiocyanate in dichloromethane at room temperature for 2 h, a single product was obtained in 93 % yield after chromatographic purification on silica gel. It was initially assigned as the expected thiourea **6a** but upon its subjection to the oxidative conditions with iodosobenzene diacetate (IBDA) to effect dearomatization only unreacted starting mate-

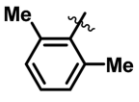
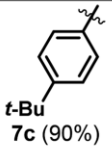
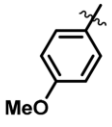
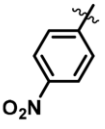
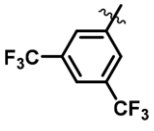
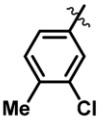
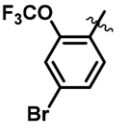


Scheme 2. Synthesis of thiazolidine during attempt to prepare thiourea **6a**.

rial was recovered. Upon closer analysis of the ^{1}H and ^{13}C NMR data for the molecule we had assigned as **6a** it became clear that the product was, in fact, the thiazolidine **7a** resulting from the tandem thio acylation and subsequent *anti*-hydrosulfenylation of the alkyne. Propargylamine **5** was reacted with several different isothiocyanates possessing varying electronic characteristics and in each case, cyclization occurred to afford the corresponding heterocycle **7b–k** in good yield (entries 1–10, Table 1).[14] Each thiazolidine derivative was obtained as the *Z*-isomer; this was established either through X-ray crystallography (**7b**, Figure 2) or a ROESY experiment (**7a**), the others were assigned by analogy (see also Table 2, Table 3, Table 4, and Table 5).

Table 1. Thiazolidines **7b–k**[a] from propargylamine **5**.



 **7b** (91%)	 **7c** (90%)
 **7d** (83%)	 **7e** (77%)
 **7f** (80%)	 **7g** (79%)
 **7h** (91%)	 **7i** (86%)
 **7j** (68%)	 **7k** (76%)

[a] Propargylamine **5** (1 equiv.), isothiocyanate (1 equiv.), CH_2Cl_2, r.t., 2 h then slurry on silica gel for column chromatography.

Initially, we were surprised by the observation of cyclization products as these reaction conditions are exceptionally mild, occurring at room temperature over a few hours. It was hypoth-

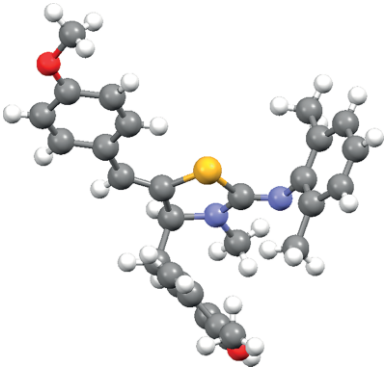
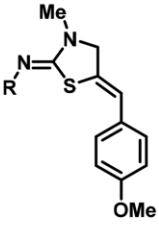
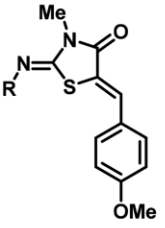
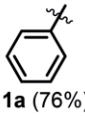
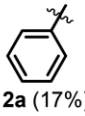
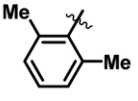
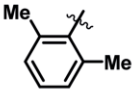
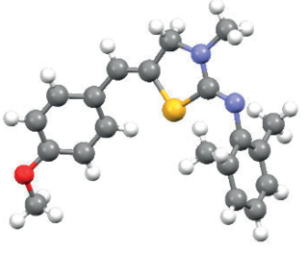
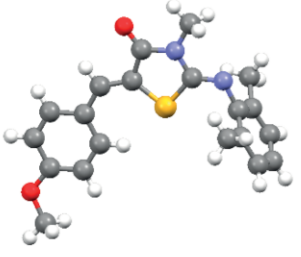
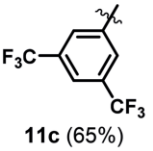
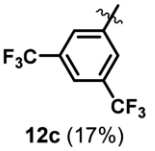


Figure 2. X-ray crystal structure of thiazolidine **7b**.

Table 2. Thiazolidines **11a–d**[a] and thiazolidinones **12a–d**[b] obtained from propargylamine **10**.

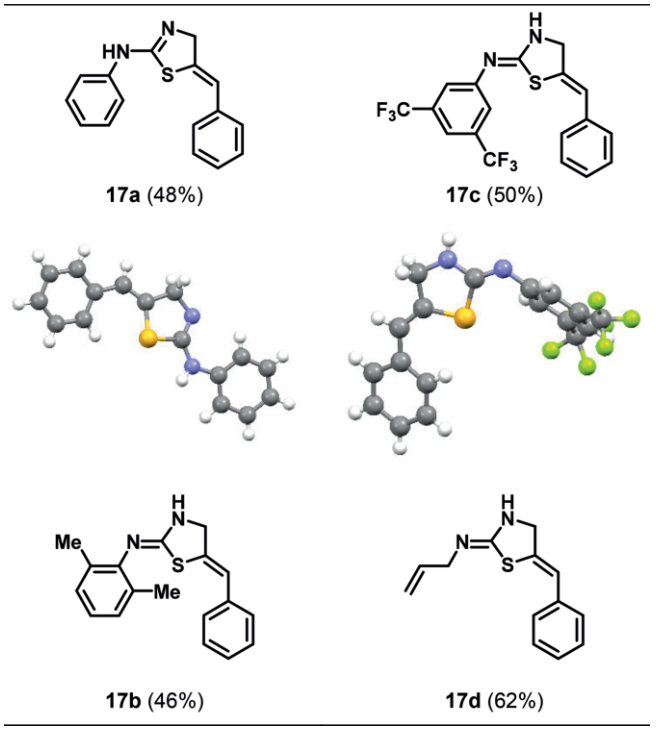




11	**12**
 **11a** (76%)	 **12a** (17%)
 **11b** (70%)	 **12b** (20%)
	
 **11c** (65%)	 **12c** (17%)
 **11d** (55%)	 **12d** (14%)

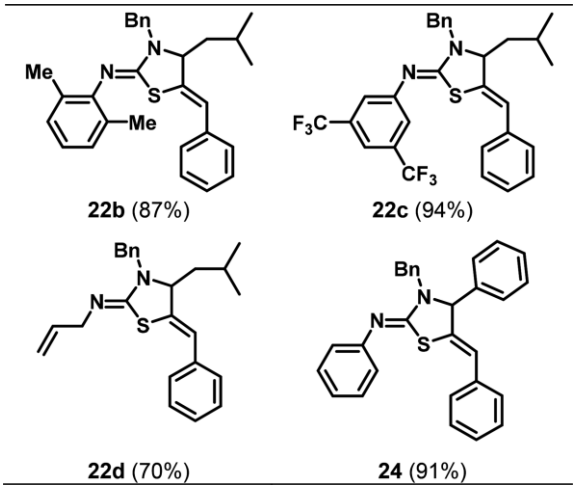
[a] Isothiocyanate (1 equiv.) was added to amine **10** (1 equiv.) in CH_2Cl_2 was stirred at r.t. for 2 h then slurried on silica gel for column chromatography. [b] **11a–d** were dissolved in $CDCl_3$ and allowed to stand open to the air at r.t. for 1–3 days.

Table 3. Thiazolidines **17a–d** derived from 3-phenylpropargylamine (**16**) and isothiocyanates.[a]



[a] Isothiocyanate (1 equiv.) was added to amine **16** (1 equiv.) in CH_2Cl_2 was stirred at r.t. for 2 h then slurried on silica gel for column chromatography.

Table 4. Synthesis of thiazolidines **22b–d** and **24** from Dethe's substrates **19** and **23**.[a]



[a] Isothiocyanate (1 equiv.) was added to amine **19** or **23** (1 equiv.) in CH_2Cl_2 was stirred at r.t. for 2 h then slurried on silica gel for column chromatography.

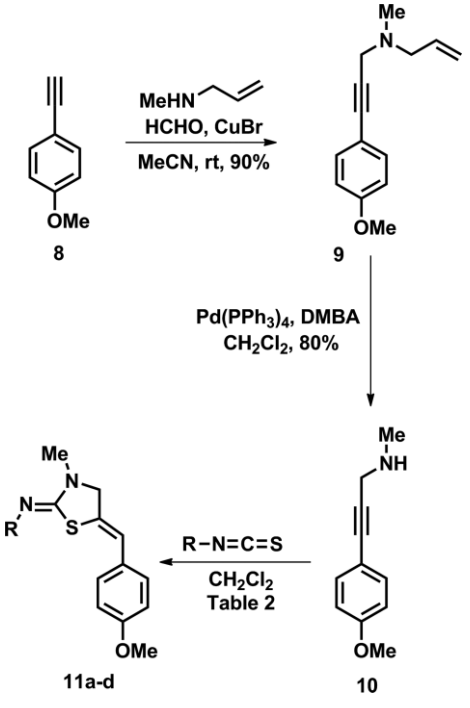
esized, initially, that it was conceivable that cyclization was facilitated by reactive rotamer effects due to the aryl substitution on the propargylic carbon and the enhanced nucleophilicity of sulfur compared to oxygen and nitrogen in the corresponding urea and guanidine. To address the issue of steric effects enhancing the rate, the less-substituted propargylamine **10** was

Table 5. Evaluation of solids to promote the cyclization reaction.[a]

Entry	Conditions	29a:31a:33a[b]
1	CH_2Cl_2	1:2:2
2	Silica gel	1:0:0
3	Alumina (Neutral)	1:0:0
4	Alumina (Acidic)	1:0:0
5	Alumina (Basic)	1:0:0
6	Celite	3:1:0.5
7	Molecular Sieves	1:1:0.5
8	Sand	4:1:0
9	Silica gel in CH_2Cl_2	1:1:1
10	Amberlyst	na
11	Dowex	2:1:1
12	Neat	1:1:0.1
13	Neat	1:1:0[c] 30a:32a:34a
14	CH_2Cl_2	0:1:0
15	Neat	0:1:0
16	Silca gel	4:1:0.5

[a] Reactions were performed on 25 mg scale on solid (1.75 g/mmol) for 2 h. [b] Product ratios obtained from ^1H NMR spectroscopy of crude reaction mixtures. [c] This reaction was conducted at 40 °C.

prepared according to the method of Looper and coworkers (Scheme 3) and evaluated in this chemistry.[15] Specifically, the terminal acetylene **8** was subjected to a copper-mediated three-component coupling with formaldehyde and the N-allyl methylamine derivative to produce the propargylamine **9**. Pd-Catalyzed deallylation then provided the requisite amine **10** in good yield. This substrate upon exposure to isothiocyanates delivered the corresponding thiazolidine **11a–d** (Table 2) in modest to good yield as single stereoisomers as established by X-ray crystallography of thiazolidine **11b**. Interestingly, these compounds underwent slow air oxidation to the corresponding 4-thiazolone **12a–d** (Table 2) upon standing for a few days in

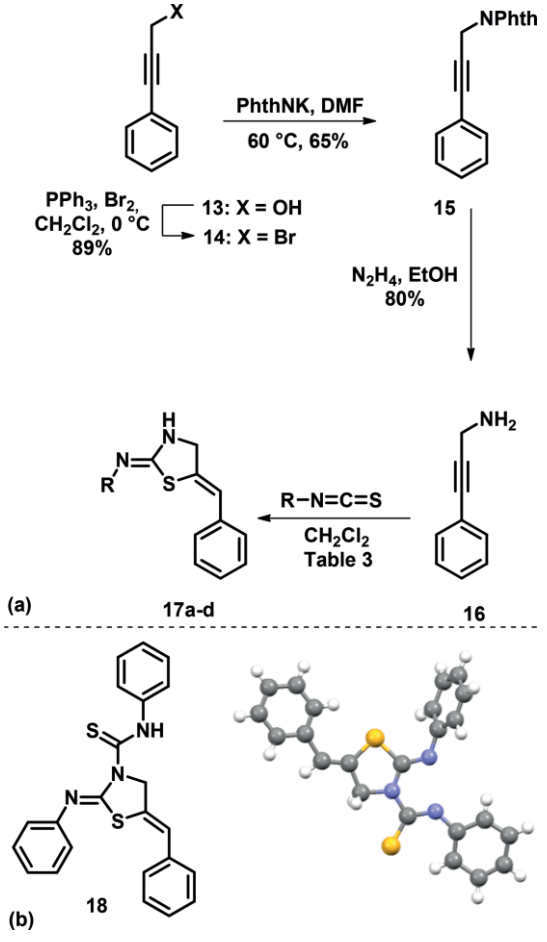


Scheme 3. Preparation and reaction of *p*-anisylpropargylamine **10**.

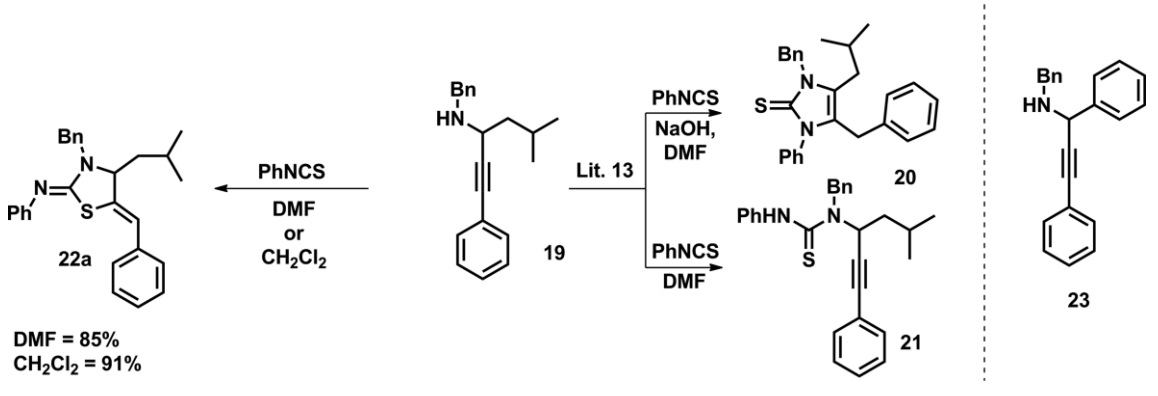
solution. This was evident from the disappearance of the methylene group in the ^{1}H NMR spectra, the appearance of a carbonyl absorption in the IR spectrum and finally confirmation through X-ray crystallography of compound **12b**. No attempt was made to optimize this transformation, but presumably, these thiazolones form via an autoxidation pathway.

There was still suspicion in our minds that even the *N*-methyl propargylic amine was undergoing this cyclization reaction because of reactive rotamer effects, specifically due to the *N*-methyl group and thus we decided to subject primary propargylamines to this chemistry. We prepared the phenyl propargylamine **16** from the corresponding bromide **14** via Gabriel chemistry (**14**→**15**→**16**, Scheme 4a) and subjected this substrate to reaction with the same group of isothiocyanates used with **10**.[16] Amine **16** upon exposure to isothiocyanates also delivered the corresponding thiazolidine **17a**–**d** (Table 3) in moderate yield as single stereoisomers as established by X-ray crystallography of thiazolidines **17a** and **17c**. Interestingly, Castagnolo has reported similar reactions of propargylamine **16** with isothiocyanates under microwave conditions with *p*TsOH as a catalyst, but these reactions delivered imidazo-2-thione derivatives in modest yields rather than the 2-aminothiazole derivatives.[10] In addition to the thiazolidines, with phenyl isothiocyanate, we observed the formation of a small amount of a 2:1 adduct **18** where the thiazolidine ring nitrogen underwent addition to provide **18**,[17] which was confirmed through X-ray crystallography (Scheme 4b). The yields of this series of thiazolidines were lower than those reported in Table 1 and Table 2 as propargylamine **16** was somewhat unstable.

The facility of these cyclization reactions, irrespective of the substitution patterns, was somewhat surprising based on existing precedent. As noted in the introduction (Scheme 1), there are prior reports of reactions of simple propargylamines[18] reacting with isothiocyanates giving 2-aminothiazolidines but these earlier methods either rely on Thorpe-Ingold type acceleration,[8] much more forcing conditions (e.g., heat or microwave irradiation)[19] or require lengthier reaction times in comparison to our observations where a thiazolidine is obtained under exceptionally mild conditions (r.t. for 2 h).[9–11] In contrast, Dethe and coworkers have shown that when various propargylamines and isothiocyanates are reacted in DMF with NaOH as base the corresponding imidazothione (cf. **19**→**20**, Scheme 5) is obtained and thus the reaction pathway observed by us is complementary.[20] Interestingly, according to this same report, when the reaction of **19** is conducted in DMF in the absence of NaOH the corresponding thiourea was obtained (cf. **19**→**21**, Scheme 5). However, in our hands, subjection of propargylamine **5** to these conditions described by Dethe (PhNCS, DMF) also resulted in the formation of the cyclization product **7a** after purification, although it is not necessary to run the reaction for



Scheme 4. (a) Synthesis and cyclization of phenylpropargylamine. (b) Structure and X-ray structure of bis addition product **18**.



Scheme 5. Divergent reaction pathways of propargylamine **19** with phenyl isothiocyanate.

12 h, similar results are obtained after 2 h. For comparative purposes and to convince ourselves that our observation with **5** was not simply an anomaly, we prepared propargylamine **19** reported by Dethe and co-workers and subjected it to reaction with phenyl isothiocyanate in DMF, surprisingly this also led to a thiazolidine, **22a** in our hands. We found also that treatment of **19** with phenyl isothiocyanate in dichloromethane for 2 h at room temperature resulted in the formation of the thiazolidine **22a** in good yield. This cyclization pathway appears to be general with amine **19** for the same types of isothiocyanates we have investigated previously delivering thiazolidines **22b–d** (Table 4).[13] While our own investigation was continuing, the Dethe lab reported that heating neat mixtures of propargylamines, including **19**, and an isothiocyanate does afford the corresponding thiazolidine, and we were able to reproduce this.[13] However, the divergence in product formation between the two labs on reaction of propargylamine **19** and phenylisothiocyanate when conducted in solution was troubling and we wished to elucidate the source of the discrepancy.

We closely examined the corresponding ^{1}H NMR spectrum from our synthesis of **22a** and that accompanying the published synthesis of **21**;[20] it was clear immediately that the two products were different, however, on closer inspection of the spectra reported by Dethe, at least one additional compound was present which resembled the spectroscopic data for **22a**. The presence of impurities suggested that this discrepancy between the data was attributable to the fact that Dethe and coworkers did not purify the product, but rather report both the yield and spectroscopic data for the crude product; this is not explicitly stated in the provided supporting information but assumed based on our own experience (vide infra and Figure 3). When we repeated the reaction of **19** with phenyl isothiocyanate in either dichloromethane or DMF and examined the ^{1}H and ^{13}C NMR spectrum of the crude reaction mixture, our data were a much closer match for that reported in the literature.[20] Interestingly, in Dethe's recent report they describe the reaction of **23** under nominally similar conditions to ours but requiring 12 h and affording **24** in 85 % yield after purification.[13] Repetition of this reaction in our hands, but with only 2 h reaction time, delivered **24** (Table 4) in essentially the same yield.

To begin to get a better understanding of what exactly is going on in these reactions, we chose to monitor the progress of the reaction by NMR spectroscopy. Indeed, when the reactions of propargylamine **19** with phenyl isothiocyanate were conducted in CD_2Cl_2, [D_7]DMF (shown) or [D_6]benzene and monitored by ^{1}H NMR spectroscopy showed relatively rapid and complete formation of the thiourea after 2 h and subsequently

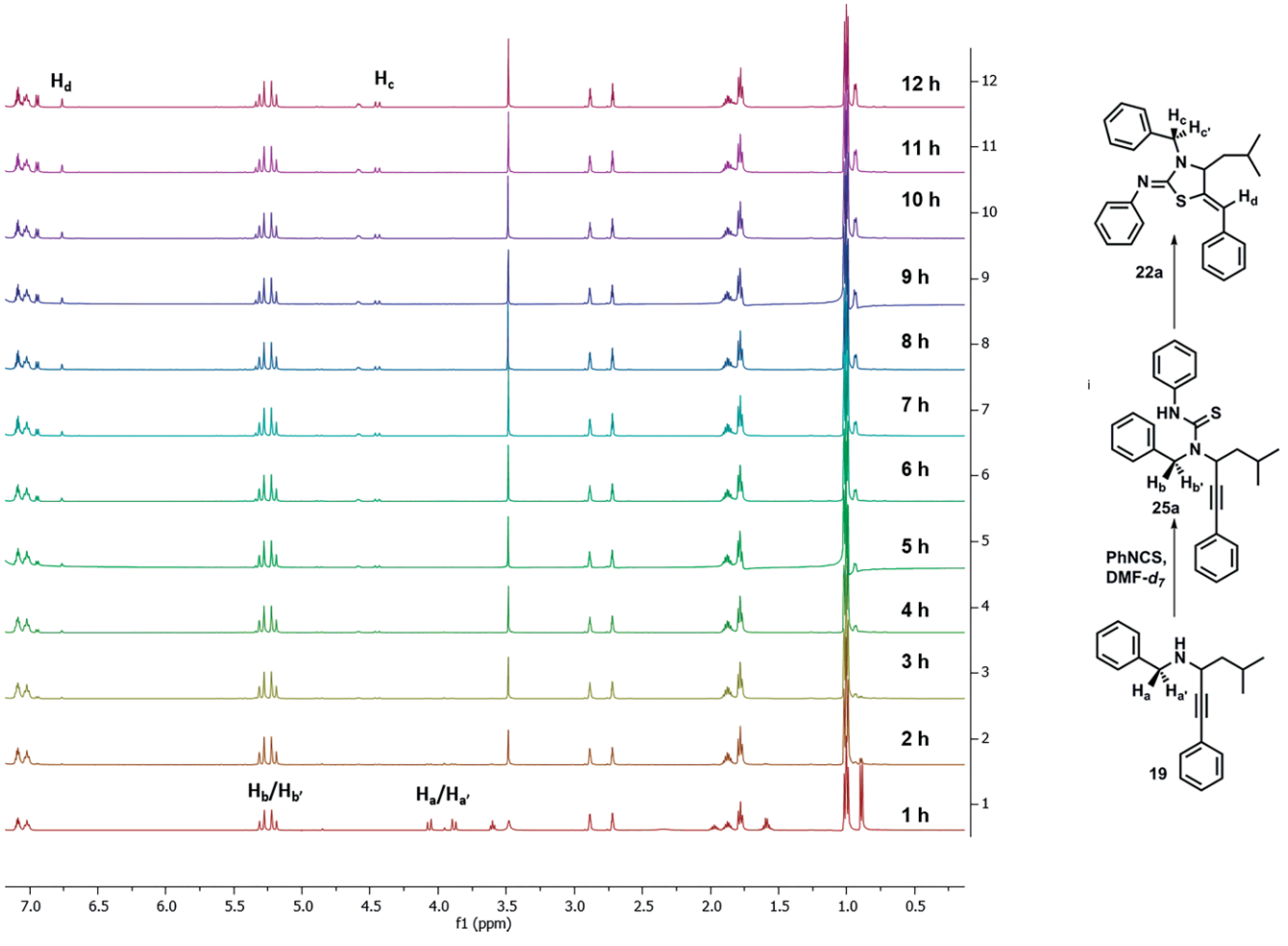


Figure 3. Time course of reaction between propargylamine **19** and phenyl isothiocyanate in [D_7]DMF analyzed by ^{1}H NMR spectroscopy.

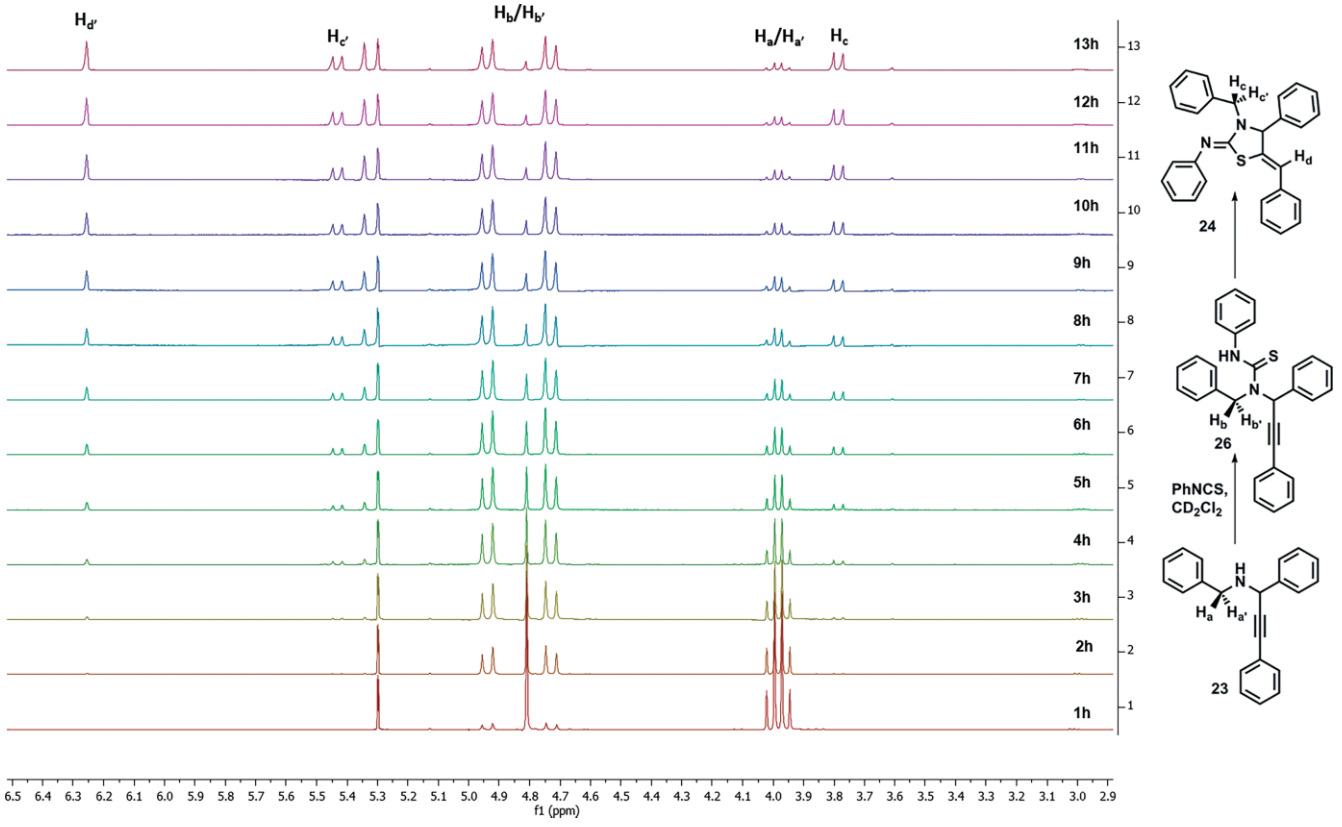


Figure 4. Time course of reaction between propargylamine **23** and phenyl isothiocyanate in CD_2Cl_2 analyzed by ^1H NMR spectroscopy.

slower cyclization. For example, propargylamine **19** with phenyl isothiocyanate in [D_7]DMF (Figure 3), shows the formation of the thiourea **25a** is fairly rapid and appears to be complete after 2 h. The characteristic vinylidine signal δ_{Hd} = 6.75 grows in much more slowly and is present to the extent of *ca.* 20 % after 12 h. These data show clearly that under these reaction conditions the thiourea is the major but not the only product formed and that prior to work-up the thiazolidine **22a** is only a minor component of the reaction mixture. As noted above, Dethe and coworkers reported the high yield formation of thiazolidine **24** after 12 h reaction time in CH_2Cl_2 from propargylamine **23** and phenyl isothiocyanate. Examination of this reaction in CD_2Cl_2 by ^1H NMR spectroscopy (Figure 4) exhibited similar characteristics to the reaction of **19**, the formation of the thiazolidine was incomplete after 12 h, although it starts to appear in the spectra after 3 h (Figure 4). It also appears that the formation of the thiourea is slower in dichloromethane than in DMF as there is still unreacted propargylamine **19**. In the case of substrate **5**, the thiourea **6a** formation was complete in less than one hour followed by slower cyclization (ca. 90 % after 12 h). This latter observation suggests that there is some acceleration of the cyclization due to substituent effects.[8]

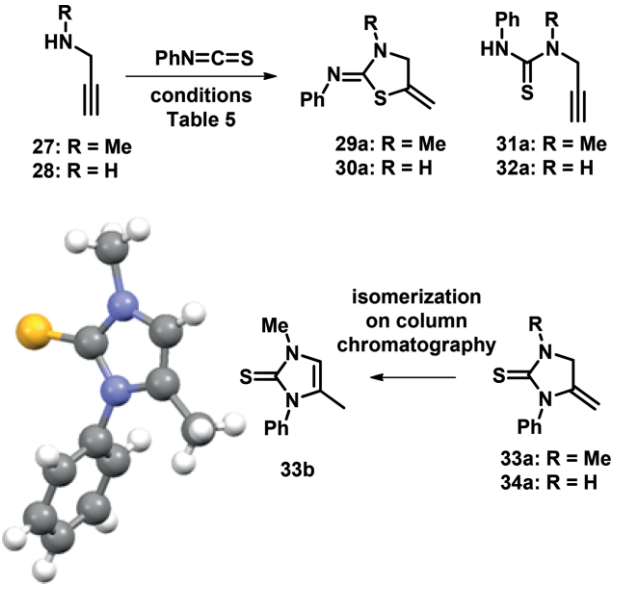
Taken in concert, these results are interesting because they suggest that the cyclization occurs predominantly after work-up and most likely during purification by chromatography on silica gel and, in order for the generally good isolated yields, must be occurring quite rapidly. A further observation with propargylamine **5** was confounding and surprising to us at this time, when known mixtures of thiourea and thiazolidine (established by NMR spectroscopy) were analyzed by TLC only one product was observed (other than a small amounts of unreacted isothiocyanate); in other words the TLC mobility of the thiourea appeared to be identical to the TLC mobility of the thiazolidine. In retrospect, this was deemed to be unlikely as the hydrogen-bond donor properties of the thiourea were expected to result in a relatively polar molecule and thus we concluded that all of these observations were pointing to the possibility that these cyclizations were facilitated by silica gel during the purification.

To test the hypothesis that silica gel was accelerating this cyclization,[21] we took the crude reaction mixture formed from a reaction between propargylamine **5** and phenyl isothiocyanate after 2 h and then analyzed it by ^1H NMR spectroscopy. This analysis revealed that the mixture contained ca. 40 % of desired product **7a** with ca. 60 % of the intermediate thiourea **6a** remaining unreacted. This same reaction mixture was then subjected to purification by column chromatography on silica gel which produced the thiazolidine in 89 % yield as the only product. Similarly, we evaluated the reactions of both **19** and **23** with phenyl isothiocyanate in solution for 2 h, quantified the compositions of the crude reaction mixture by ^1H NMR spectroscopy (*vide infra*) and then these mixtures were purified by silica gel chromatography affording the corresponding thiazolidines **22a** (from **19**) in 91 % yield and **24** (from **23**) also in 91 % yield as the only products. Specifically, in the case of the reaction of **19** with phenyl isothiocyanate, after 2 h in solution,

a mixture comprising thiazolidine **22a** (12 %), thiourea **25a** (80 %) and unreacted amine **19** (8 %) was obtained prior to purification. Similarly, amine **23** and phenyl isothiocyanate afforded a mixture of the thiazolidine **24** (15 %), the thiourea **26** (64 %) and unreacted starting amine **23** (21 %) prior to purification. Alternatively, conducting the reactions of all three amines with phenyl isothiocyanate directly on silica gel without using any solvent demonstrated that the reactions were essentially complete in 2 h (eluted with 10 % MeOH in CH_2Cl_2, concentrated by blowing dry nitrogen and analyzed) by ^1H NMR spectroscopy) and on purification by chromatography provided the expected thiazolidines in good yields, similar to those reported in Table 1 and Table 4. The NMR investigation and the latter control experiments where the composition of the crude products was established prior to purification show clearly that the cyclization reaction is quite slow and in some cases the formation of the thiourea is incomplete after 2 h, but these reactions are going to completion upon exposure to silica gel. It was obvious from these experiments that the rate of the reaction was increased by the presence of the silica gel, but it was not clear whether this was simply an acid-catalyzed process or perhaps a proximity-induced effect.

The fact that these reactions appeared to benefit from acceleration from silica gel was a potentially useful observation as two sets of substrates, specifically *N*-methyl propargylamine **27** and the unsubstituted congener **28**, afforded either mixtures of the thiazolidine **29a**, thiourea **31a** and the thioimidazoline **33a** (entry 1, Table 5) or gave the thiourea **32a** respectively (entry 14, Table 5) in the absence of SiO_2 (Scheme 6). In the case of **33a**, the initial product undergoes tautomerization to **33b** upon purification by chromatography, established by X-ray crystallography, presumably a reflection of the greater aromaticity of imidazoles versus thiazoles. Gratifyingly, when we evaluated *N*-methyl propargylamine with phenyl isothiocyanate on silica gel (entry 2, Table 5), the reaction produced the thiazolidine **29a** exclusively. Alumina (acidic, basic and neutral) gave similar results to silica gel (entries 3–5, Table 5). Celite, sand and molecular sieves, on the other hand, provided a mixture of products (entries 6–8, Table 5). Interestingly, when the reaction was conducted in solution with a suspension of silica gel (entry 9, Table 5), the reaction resulted in the formation of a mixture of the thiourea and thiazolidine. Use of solid acid supports did not afford any reaction, presumably, the amine is protonated and trapped. Attempts to perform the reaction using neat reagents resulted in mixtures of products (entries 12–13, Table 5) whether the reaction was performed at room temperature or 40 °C. While an exhaustive screen was not conducted, the parent propargylamine **29** showed similar trends as the *N*-methyl derivative. Neat reaction along with the reaction in CH_2Cl_2 produced the thiourea as a major product (entries 14 and 15). Whereas silica gel supported reaction produced the desired thiazolidine **30a**, along with smaller amounts of the thiourea **32a** and the 2-thioimidazoline **34a** (entry 16).

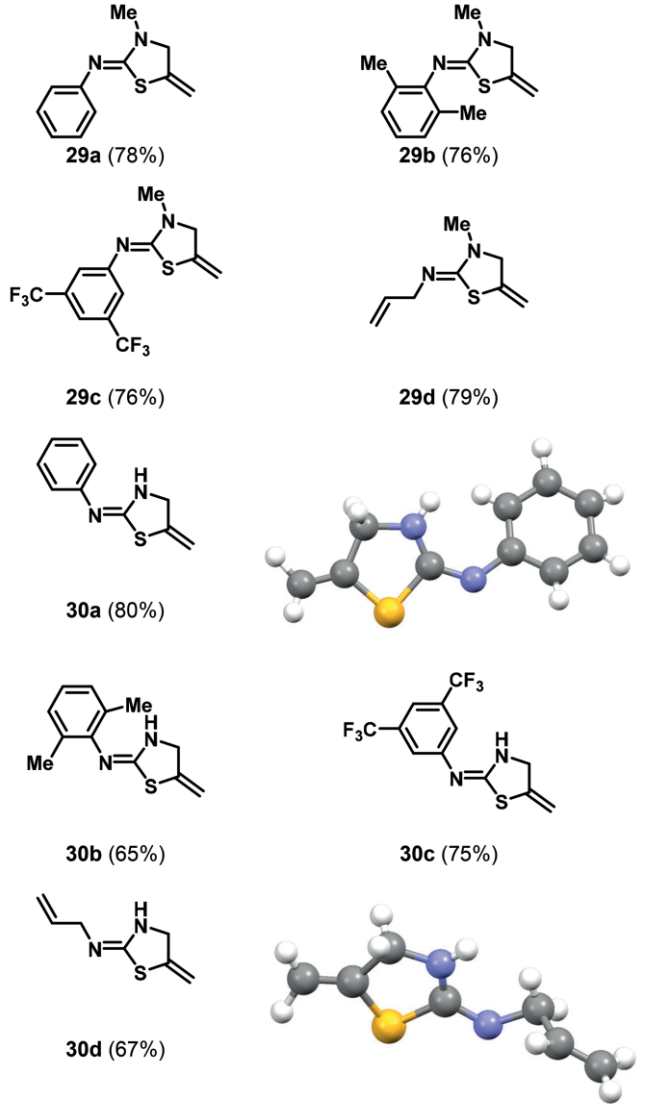
Based on these observations, we evaluated the direct application of reagents to silica gel followed by stirring the resulting mixture for 2 h. A series of N-methyl thiazolidines **29a–d** (Table 6) were prepared in good isolated yields using these conditions (Scheme 6). Likewise, a series of thiazolidines was prepared from propargylamine itself under identical conditions affording the corresponding thiazolidines **30a–d** in good yields (Table 6). Under the mild conditions employed the double bond does not migrate into the ring to generate the aromatic system which is in contrast to previous reports of the reaction of these reagents.[19] X-ray crystallography of adducts **30a** and **30d** clearly show the presence of the vinylidene moiety and the fact that the imino moiety exists as the *E*-isomer, presumably reflecting the reduced steric environment around the thiazolidine nitrogen. The isolated yield of **30a** appears to be higher than expected from the experiment described in Table 5 (entry 16), but we attribute this to the cyclization continuing during the purification process. The reactions with propargylamine **10** were repeated on silica gel and it was found that all four thiazolidines **11a–d** were obtained in >80 % yields, reflecting improved efficiency. In contrast, when the cyclizations involving amine **16** were repeated on silica gel, no improvements were obtained, perhaps due to increasing decomposition and there was a small increase in the formation of the 2:1 adduct, *cf.* compound **18** (Scheme 3b) The facile formation of the thiazolidine in the presence of silica gel suggests that the cyclization is mediated by solid support, whether this is a proximity effect caused by coordination of nitrogen to the surface or whether it is as a solid acid is not totally clear. The mildly acidic nature of silica gel is well appreciated and has been exploited in synthetic organic chemistry.[22] The NMR experiments discussed above indicate that thiourea **38** formation is relatively rapid but in the absence of any external catalyst, the cyclization is slow (Scheme 7). In the presence of silica gel, either added to the reaction mixture or exposure during purification[23] of the crude reaction mixture results in rate enhancement. With the exception of the terminal alkynes (R^3 = H) prior protonation of the alkyne would potentially lead to regioisomeric vinyl carbocations or in some cases (R^3 = Ar) the wrong isomer for forma-



Scheme 6. Selected optimization of reaction conditions for propargylamines **27** and **28** and X-ray structure of compound **33b**.

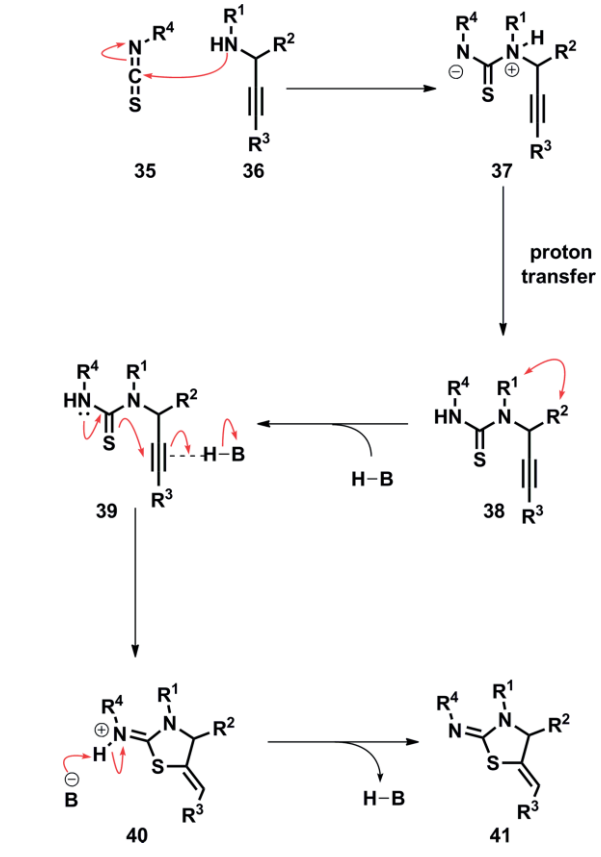
tion of the thiazolidine, therefore we propose that a π-complex **39** is formed which activates the triple bond to nucleophilic attack by sulfur affording **40**. Proton transfer then completes the process and provides the thiazolidine.[24] It is also feasible that the propargylamine nitrogen coordinates to the silica gel surface which in effect functions as a large substituent and increases the population of the reactive rotamer, further facilitating the reaction.

Table 6. Silica gel promoted hydrothiolation of terminal propargylamines.[a]

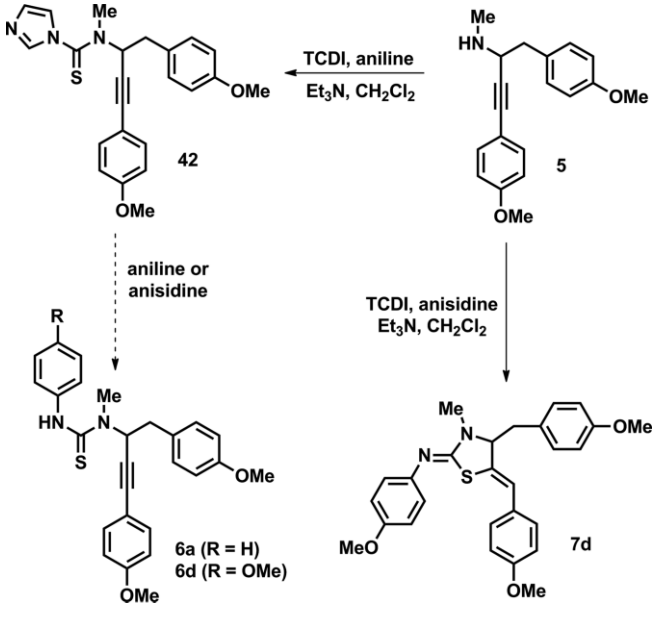


[a] To a vigorously stirred suspension of silica gel (1.75 g/mmol) was added the propargylamine (0.72 mmol) in CH_2Cl_2 (0.2 mL) and then the isothiocyanate (1 equiv.) was added dropwise. After 2 h of stirring at r.t., the residue was purified.

We very much wanted to access thioureas derived from propargylamine **5** to evaluate our TOADS chemistry and thus sought an alternative approach. Accordingly, we decided to explore the preparation and reaction of the imidazolyl thiourea derivative **42** in Scheme 8 which would be accessed from the corresponding amine **5** and thiocarbonyl diimidazole (TCDI). Interestingly, an attempt to access the phenyl-substituted thiourea **6a** resulted in the isolation of the intermediate imidazolyl-substituted thiourea **42** but not the required thiourea **6a** (Scheme 8). However, upon treatment with the more nucleophilic *p*-anisidine, the same thiazolidine product **7d** as isolated previously (see Scheme 2 and Scheme 8) was obtained in good yield. Interestingly, attempts to convert the intermediate imid-



Scheme 7. Putative mechanism for the formation of the thiazole.



Scheme 8. Thiazolidine **7d** formation via the action of TCDI.

azolyl thiourea **42** into either the requisite thiourea **6** or thiazolidine **7** were not successful with either aniline or anisidine. Suggesting that anisidine was converted into the corresponding imidazolyl thiourea or isothiocyanate prior to reaction with propargylamine **5**. As noted above, access to mixtures of the thiourea and thiazolidines was possible if purification was avoided. Such a mixture was exposed to a mixture of IBDA, HFIP, Cs_2CO_3 (standard conditions for TOADS), but rather than obtaining the dearomatization product, the thiazolidine was the only isolable product.[25]

Conclusions

In summary, we have found that a wide variety of thiazolidines can be prepared in generally good to excellent yields via a tandem thioacylation-hydrosulfenylation of propargylamines and that these reactions are promoted by silica gel.[26] The reaction has a broad substrate scope with regard to both the propargylamine and the isothiocyanate. Initial uncertainty surrounding the preparation and lifetime of the thiourea intermediate was clarified when it was determined that the intramolecular hydrosulfenylation can be catalyzed by silica gel. The thiourea can be prepared by using short reaction times and avoiding purification. Initial attempts to engage crude samples of thiourea **6a** in TOADS chemistry were thwarted by the facile hydrosulfenylation reaction leading to a thiazolidine **7a**; indeed out of the systems investigated, propargylamine **5** upon conversion to the intermediate thiourea underwent cyclization to the corresponding thiazolidine most rapidly in the absence of silica gel. Our investigations to circumvent this are ongoing, as well as efforts to exploit the potentially useful thiazolidine derivatives and we will report these efforts in due course.

Experimental Section

All reagents were purchased from commercial suppliers and were used as received unless otherwise noted. Solvents were dried either by distillation over appropriate drying agents: tetrahydrofuran was distilled from sodium/benzophenone ketyl; acetonitrile, benzene, diethyl ether, and dichloromethane were dried using an alumina-based solvent purification system. ^{1}H and ^{13}C NMR (δ in ppm) spectra were recorded in $CDCl_3$ (unless otherwise noted) at 500 and 125.8 MHz, respectively (unless otherwise noted). Residual $CHCl_3$ (δ = 7.26) was utilized as reference for ^{1}H NMR spectra and carbon absorption of $CDCl_3$ (δ = 77.0) as internal reference for ^{13}C NMR were used. Infrared spectra were recorded neat using an ATR-FT-IR spectrometer. High-resolution mass spectra (HR-MS) were measured in the Shimadzu Center for Advanced Analytical Chemistry at UT Arlington. Analytical thin layer chromatography (TLC) was performed on silica gel $60F_{254}$ aluminum pre-coated plates (0.25 mm layer). All chromatographic purifications were performed using ICN silica gel (230–400 mesh).

General Procedure (A): To a stirred solution of propargylamine (125 mg, 0.42 mmol) in CH_2Cl_2 (2.0 mL) was added isothiocyanate (0.42 mmol). The resulting reaction mixture was stirred at r.t. for 2 h. A slurry was made by adding silica gel (2 g/mmol) to the reaction mixture and then the solvent was removed by rotary evaporation. The resulting mixture was applied to the top of the column of silica gel and then purified by flash chromatography to afford the thiazolidine.

General Procedure (B): To vigorously stirred silica gel (1.75 g/mmol), a solution of propargylamine (50 mg, 0.72 mmol) in CH_2Cl_2 (0.2 mL) and isothiocyanate (0.72 mmol) was added dropwise. The resulting slurry was stirred at r.t. for 2 h. After removal of the solvent by rotary evaporation, the crude product was then purified by flash chromatography to afford the thiazolidine.

General Procedure (C): Thiazolidines (50 mg) were dissolved in $CDCl_3$ (1 mL) and left open to the atmosphere for 1–3 days. After concentration, the crude product was purified by column chromatography to afford the oxidized product.

(*Z*)-*N*-Phenyl-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7a): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7a** (158 mg, 87 %) as a light-yellow gum. ^{1}H NMR: 7.28 – 7.24 (m, 2H), 7.09 (d, *J* = 8.5 Hz, 4H), 7.05 (tt, *J* = 8.5, 1.2 Hz, 1H), 6.89 (dd, *J* = 8.5, 1.2 Hz, 2H), 6.85 – 6.81 (m, 4H), 6.15 (s, 1H), 4.58 (td, *J* = 5.1, 1.2 Hz, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.23 (s, 3H), 3.06 – 3.05 (d, *J* = 5.1 Hz, 2H). ^{13}C NMR: 158.8, 158.7, 156.6, 150.9, 131.2, 130.0, 129.3, 129.0, 128.5, 127.8, 123.4, 122.6, 121.0, 114.1, 113.9, 71.2, 55.4, 40.0, 32.6. FT-IR (neat, cm^{-1}): 2951, 2931, 2834, 1610, 1584, 1508, 1461, 1300, 1244, 1175, 1028. HR-MS (*m*/*z*): calcd. for [M + H] $^+$ $C_{26}H_{26}N_2O_2S$, 431.1788, found 431.1792.

(*Z*)-*N*-(2,6-Dimethylphenyl)-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7b): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7b** (176 mg, 91 %) as a yellow solid. m.p. 74–78 °C. ^{1}H NMR: 7.09 (dd, *J* = 8.6, 1.6 Hz, 4H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.89 – 6.85 (m, 1H), 6.83–6.80 (m, 4H), 6.26 (s, 1H), 4.67 (t, *J* = 4.0 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.25 (s, 3H), 3.13 – 3.02 (m, 2H), 2.08 (s, 3H), 1.92 (s, 3H). ^{13}C NMR: 158.7, 158.6, 155.4, 148.9, 131.2, 130.6, 130.1, 129.8, 129.3, 128.6, 127.8, 127.6, 123.0, 120.4, 114.1, 114.0, 71.1, 55.4, 55.3, 40.3, 32.2, 18.3, 18.2. FT-IR (neat, cm^{-1}): 2918, 2832, 1656, 1609, 1508, 1462, 1380, 1249, 1175, 1031, 766. HR-MS (*m*/*z*): calcd. for [M + H] $^+$ $C_{28}H_{30}N_2O_2S$, 459.2101, found 459.2106.

(*Z*)-*N*-(4-*tert*-Butylphenyl)-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7c): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7c** (185 mg, 90 %) as a yellow solid. m.p. 60–65 °C. ^{1}H NMR: 7.27 – 7.24 (m, 2H), 7.12 – 7.06 (m, 4H), 6.85 – 6.81 (m, 4H), 6.81 – 6.77 (m, 2H), 6.14 (s, 1H), 4.56 (td, *J* = 5.1, 1.2 Hz, 1H), 3.80 (s, 3H), 3.77 (s, 3H), 3.19 (s, 3H), 3.04 (d, *J* = 5.1 Hz, 2H), 1.31 (s, 9H). ^{13}C NMR: 158.7, 158.6, 155.6, 148.6, 145.7, 131.2, 130.5, 129.3, 128.7, 127.9, 125.8, 121.7, 120.7, 114.0, 113.8, 70.8, 55.3, 40.0, 34.3, 32.4, 31.6. FT-IR (neat, cm^{-1}): 2957, 2836, 1594, 1508, 1460, 1246, 1174, 1028, 835. HR-MS (*m*/*z*): calcd. for [M + H] $^+$ $C_{30}H_{34}N_2O_2S$, 487.2414, found 487.2415.

(*Z*)-*N*-(4-Methoxyphenyl)-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7d): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7d** (162 mg, 83 %) as a light-yellow gum. ^{1}H NMR: 7.12 – 7.07 (m, 4H), 6.84 (d, *J* = 2.2 Hz, 2H), 6.81 (d, *J* = 2.2 Hz, 2H), 6.80 (d, *J* = 1 Hz, 4H), 6.13 (s, 1H), 4.54 (t, *J* = 5.7 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.76 (s, 3H), 3.18 (s, 3H), 3.03 (d, *J* = 5.7 Hz, 2H). ^{13}C NMR: 158.7, 158.6, 156.4, 155.7, 145.1, 131.2, 130.4, 129.3, 128.6, 127.9, 123.2, 120.7, 114.2, 114.0, 113.8, 71.0, 55.5, 55.4, 40.0, 32.4.

FT-IR (neat, cm^{-1}): 2954, 2933, 2836, 1609, 1509, 1463, 1243, 1158, 1030, 819. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{27}H_{28}N_2O_3S$, 461.1893, found 461.1897.

(*Z*)-*N*-(4-nitrophenyl)-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7e): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3: 7) to afford compound **7e** (155 mg, 77 %) as a yellow solid. m.p. 60–64 °C. ^{1}H NMR: 8.11 (d, *J* = 8.9 Hz, 2H), 7.07 (d, *J* = 8.9 Hz, 2H), 7.05 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 6.83 (d, *J* = 8.9 Hz, 2H), 6.24 (s, 1H), 4.65 (t, *J* = 4.9 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.25 (s, 3H), 3.11 – 3.05 (m, 2H). ^{13}C NMR: 159.0, 158.9, 143.4, 131.1, 129.3, 129.2, 128.5, 128.0, 127.1, 125.1, 122.9, 122.1, 114.2, 113.9, 113.9, 71.3, 55.4, 55.3, 40.1, 32.7. FT-IR (neat, cm^{-1}): 2914, 2834, 1610, 1561, 1508, 1459, 1325, 1245, 1172, 1027. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{26}H_{25}N_3O_4S$, 476.1639, found 476.1638.

(*Z*)-*N*-(3,4-Bis(trifluoromethyl)phenyl)-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7f): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7f** (191 mg, 80 %) as a light-yellow gum. ^{1}H NMR: 7.48 (s, 1H), 7.21 (s, 2H), 7.07 (dd, *J* = 8.7, 6.0 Hz, 4H), 6.84 (dd, *J* = 8.7, 6.0 Hz, 4H), 6.25 (s, 1H), 4.64 (t, *J* = 5.4 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.21 (s, 3H), 3.12 – 3.01 (m, 2H). ^{13}C NMR: 159.0, 158.9, 132.0 (q, *J* = 33.1 Hz), 131.2, 130.9, 129.3, 128.9, 128.1, 127.1, 123.5 (q, *J* = 271 Hz), 122.8, 121.8, 116.4, 114.2, 114.1, 113.8, 71.2, 55.4, 55.2, 40.2, 32.3. FT-IR (neat, cm^{-1}): 2933, 2839, 1596, 1510, 1463, 1369, 1274, 1248, 1167, 1122, 1030. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{28}H_{24}N_2O_2F_6S$, 567.1535, found 567.1533.

(*Z*)-*N*-(3-Chloro-4-methylphenyl)-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7g): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7g** (160 mg, 79 %) as a yellow solid. m.p. 58–60 °C. ^{1}H NMR: δ 7.10–7.06 (m, 5H), 6.85 (d, *J* = 2.2 Hz, 1H), 6.85 – 6.82 (m, 4H), 6.66 (dd, *J* = 8.0, 2.2 Hz, 1H), 6.16 (s, 1H), 4.56 (t, *J* = 4.5 Hz, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 3.17 (s, 3H), 3.05 – 2.99 (m, 2H), 2.32 (s, 3H). ^{13}C NMR δ 158.8, 158.7, 156.8, 150.3, 134.2, 131.2, 131.1, 130.3, 129.9, 129.3, 128.4, 127.6, 123.0, 121.1, 120.8, 114.1, 113.8, 71.1, 55.5, 55.4, 40.1, 32.4, 19.6. FT-IR (neat, cm^{-1}): 2998, 2834, 1618, 1592, 1508, 1438, 1388, 1245, 1175, 1030, 813. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{27}H_{27}N_2O_2SCl$, 479.1555, found 479.1562.

(*Z*)-*N*-Benzyl-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7h): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7h** (171 mg, 91 %) as a light-yellow gum. ^{1}H NMR ([D$_4$]methanol) δ 7.20 (t, *J* = 7.0 Hz, 2H), 7.14–7.11 (m, 3H), 7.07 (d, *J* = 7.0 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 6.71 (d, *J* = 8.6 Hz, 2H), 6.23 (s, 1H), 4.50 (t, *J* = 4.1 Hz, 1H), 4.25 (ABq, J_{AB} = 14.9 Hz, V_{AB} = 39.1 Hz, 2H), 3.68 (s, 3H), 3.66 (s, 3H), 2.99 (s, 3H), 2.97 – 2.86 (m, 2H). ^{13}C NMR ([D$_4$]methanol): δ 159.2, 158.8, 158.7, 140.3, 131.0, 129.2, 128.6, 128.0, 127.7, 127.2, 126.4, 121.0, 113.8, 113.4, 70.8, 57.9, 54.6, 54.5, 39.6, 31.6. FT-IR (neat, cm^{-1}): 2931, 2834, 1602, 1508, 1451, 1358, 1244, 1174, 1026, 813. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{27}H_{28}N_2O_2S$, 445.1944, found 445.1950.

(*Z*)-*N*-Benzoyl-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7i): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetatehexanes = 3:7) to afford compound **7i** (166 mg, 86 %) as a light-yellow gum. ^{1}H NMR: 8.30 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.27 – 7.20 (m, 2H), 7.01 (d, *J* = 7.4 Hz, 2H), 6.85 (d, *J* = 8.2 Hz, 2H), 6.75 (d, *J* = 7.4 Hz, 2H), 6.03 (s, 1H), 4.48 (m, 1H), 3.76 (s, 3H), 3.71 (s, 3H), 3.29 (s, 3H), 3.09–3.06 (m, 1H), 2.94–2.90 (m, 1H). ^{13}C NMR: 175.4, 168.4, 158.9, 158.8, 136.7, 132.0, 131.2, 131.1, 131.0, 129.8, 128.2, 128.1, 127.0, 122.8, 114.1, 113.9, 69.4, 55.4, 55.2, 39.9, 33.8. FT-IR (neat, cm^{-1}): 3191, 2835, 1716, 1665, 1604, 1508, 1463, 1374, 1245, 1174, 1027, 702. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{27}H_{26}N_2O_3S$, 459.1737, found 459.1737.

(*Z*)-*N*-Allyl-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7j): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7j** (113 mg, 68 %) as a light-yellow gum. ^{1}H NMR: 7.17 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 6.05 (s, 1H), 5.91 (ddt, *J* = 17.1, 10.5, 5.3 Hz, 1H), 5.17 (dq, *J* = 17.1, 1.8 Hz, 1H), 5.04 (dq, *J* = 10.5, 1.8 Hz, 1H), 4.43 (ddd, *J* = 6.8, 4.1, 1.2 Hz, 1H), 3.82 (dt, *J* = 5.3, 1.8 Hz, 2H), 3.80 (s, 3H), 3.77 (s, 3H), 3.04 (s, 3H), 3.01 (dd, *J* = 13.5, 4.3 Hz, 1H), 2.89 (dd, *J* = 13.5, 4.3 Hz, 1H). ^{13}C NMR: 158.6, 158.5, 156.3, 136.8, 131.1, 130.1, 129.4, 128.8, 128.3, 120.8, 114.6, 114.0, 113.7, 70.9, 56.9, 55.4, 55.3, 39.8, 32.3. FT-IR (neat, cm^{-1}): 3025, 2917, 2834, 1610, 1508, 1459, 1242, 1177, 1025. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{23}H_{26}N_2O_2S$, 395.1788, found 395.1798.

(*Z*)-*N*-(4-Bromo-2-trifluoromethoxyphenyl)-4-(4-methoxybenzyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (7k): Synthesized following general procedure A, (125 mg, 0.42 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **7k** (190 mg, 76 %) as a light-yellow gum. ^{1}H NMR: 7.34 – 7.33 (m, 1H), 7.38 – 7.26 (m, 1H), 7.06 (dd, *J* = 8.9, 5.3 Hz, 4H), 6.83 (dd, *J* = 5.3, 8.9 Hz, 4H), 6.73 (d, *J* = 8.9 Hz, 1H), 6.19 (s, 1H), 4.61 (t, *J* = 6.0 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.19 (s, 3H), 3.04 (d, *J* = 6.0 Hz, 2H). ^{13}C NMR: 158.8, 158.7, 157.4, 143.8, 142.1, 142.0, 131.1, 130.5, 129.3, 129.2, 128.3, 127.5, 125.5, 125.1, 121.3, 120.7 (q, *J* = 256.6 Hz), 114.9, 114.1, 113.8, 71.2, 55.4, 55.3, 40.0, 32.3. FT-IR (neat, cm^{-1}): 2934, 2837, 1599, 1509, 1463, 1243, 1159, 1028. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{27}H_{24}N_2O_3F_3SBr$, 593.0716, found 593.0723.

(*Z*)-*N*-Phenyl-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (11a): Synthesized following general procedure A, (50 mg, 0.28 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **11a** (67 mg, 76 %) as a light-yellow gum. ^{1}H NMR: 7.30 (dd, *J* = 8.4, 7.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 7.07 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.97 (dd, *J* = 8.4, 1.1 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.47 (t, *J* = 2.0 Hz, 1H), 4.42 (d, *J* = 2.0 Hz, 2H), 3.78 (s, 3H), 3.12 (s, 3H). ^{13}C NMR: 158.6, 156.6, 151.5, 129.2, 129.1, 128.6, 126.4, 123.3, 122.4, 119.6, 114.1, 59.5, 55.4, 33.1. FT-IR (neat, cm^{-1}): 3001, 2929, 2834, 1622, 1584, 1508, 1460, 1247, 1175, 1027, 765. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{18}H_{18}N_2OS$, 311.1213, found 311.1202. Note: The yield was improved (98 %) when the reaction was done following general procedure B.

(*Z*)-*N*-(2,6-Dimethylphenyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (11b): Synthesized following general procedure A, (50 mg, 0.28 mmol), purified by column chromatography (ethyl acetate/hexanes = 2: 8) to afford compound **11b** (67 mg, 70 %) as a light-yellow gum. ^{1}H NMR: 7.15 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 7.8 Hz, 2H), 6.91 (t, *J* = 7.8 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.46 (bs, 1H), 4.46 (s, 2H), 3.77 (s, 3H), 3.16 (s, 3H), 2.15 (s, 6H). ^{13}C NMR: 158.6, 156.1, 148.9, 129.8, 129.3, 128.6, 127.9, 126.4, 123.1, 119.4, 114.1, 60.1, 55.3, 33.0, 18.3. FT-IR (neat, cm^{-1}): 2963, 2913, 2833, 1646, 1623, 1585, 1508, 1461, 1248, 1176, 1033, 773. HR-MS (*m/z*): calcd. for $[M + H]^+$ $C_{20}H_{22}N_2OS$, 339.1526, found 339.1517.

Note: The yield was improved (99 %) when the reaction was done following general procedure B.

(*Z*)-*N*-(3,5-Bis(trifluoromethyl)phenyl)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (11c): Synthesized following general procedure A, (50 mg, 0.28 mmol), purified by column chromatography (ethyl acetate/hexanes = 1:3) to afford compound **11c** (83 mg, 65 %) as a light-yellow gum. ^{1}H NMR ([D$_4$]methanol): 7.54 (s, 1H), 7.38 (s, 2H), 7.10 (d, *J* = 8.8 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.50 (s, 1H), 4.41 (s, 2H), 3.68 (s, 3H), 3.03 (s, 3H). ^{13}C NMR (125 MHz, [D$_4$]methanol): 158.9, 158.6, 153.3, 132.0 (q, *J* = 32.8 Hz), 128.9, 128.2, 124.2, 123.4 (q, *J* = 270.3 Hz), 122.7, 120.5, 115.7 (q, *J* = 4.1 Hz), 113.7, 59.1, 54.3, 37.6, 31.7. FT-IR (neat, cm^{-1}): 2921, 2837, 1621, 1593, 1509, 1370, 1165, 1120, 1026, 842. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{20}H_{16}N_2OF_6S$, 447.0960, found 447.0968. Note: The yield was improved (99 %) when the reaction was done following general procedure B.

(*Z*)-*N*-Allyl-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-2-imine (11d): Synthesized following general procedure A, (100 mg, 0.57 mmol), purified by column chromatography (ethyl acetate) to afford compound **11d** (86 mg, 55 %) as a light-yellow gum. ^{1}H NMR: 7.31 – 7.24 (m, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.50 (s, 1H), 5.96 (ddt, *J* = 16.8, 11.8, 5.4 Hz, 1H), 5.25 (dq, *J* = 16.8, 1.8 Hz, 1H), 5.09 (ddd, *J* = 11.8, 3.1, 1.8 Hz, 1H), 4.33 (d, *J* = 1.8 Hz, 2H), 3.91 (dt, *J* = 5.4, 1.8 Hz, 2H), 3.82 (s, 3H), 3.02 (s, 3H). ^{13}C NMR: 158.6, 157.2, 136.7, 129.3, 128.8, 126.4, 119.5, 114.9, 114.1, 59.5, 57.1, 55.4, 33.1. FT-IR (neat, cm^{-1}): 2952, 2835, 1649, 1602, 1509, 1416, 1298, 1250, 1176, 1029, 854. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{15}H_{18}N_2OS$, 275.1218, found 275.1210. Note: The yield was improved (80 %) when the reaction was done following general procedure B.

(*Z*)-2-(Phenylimino)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-4-one (12a): Synthesized following general procedure C, (60 mg, 0.19 mmol), purified by column chromatography (ethyl acetate/hexanes = 1:19) to afford compound **12a** (11 mg, 17 %, 60 % brsm) as a light-yellow solid. m.p. 146–148 °C (lit.[27] m.p. 146 °C). ^{1}H NMR: 7.71 (s, 1H), 7.39 (td, *J* = 7.1, 1.1 Hz, 4H), 7.21–7.18 (m, 1H), 7.02 (dd, *J* = 8.4, 1.1 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 3.82 (s, 3H), 3.45 (s, 3H). ^{13}C NMR: 167.2, 160.9, 151.4, 148.4, 131.9, 130.8, 129.4, 126.5, 124.9, 121.3, 118.9, 114.6, 55.5, 29.7. FT-IR (neat, cm^{-1}): 3054, 2948, 2836, 1703, 1637, 1593, 1509, 1412, 1364, 1253, 1182, 1023. HR-MS (*m*/*z*): calcd. for [M + Na]$^+$ $C_{18}H_{16}N_2O_2S$, 347.0825, found 347.0834.

(*Z*)-2-(Dimethylphenylimino)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-4-one (12b): Synthesized following general procedure C, (60 mg, 0.17 mmol), purified by column chromatography (ethyl acetate/hexanes = 1:19) to afford compound **12b** (13 mg, 20 %, 57 % brsm) as an off-white solid. m.p. 168–172 °C. ^{1}H NMR: 7.71 (s, 1H), 7.36 (d, *J* = 8.9 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 7.01 (dd, *J* = 8.2, 6.8 Hz, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 3.81 (s, 3H), 3.50 (s, 3H), 2.13 (s, 6H). ^{13}C NMR: 167.3, 160.9, 151.2, 145.9, 131.9, 130.7, 130.6, 128.5, 128.3, 126.4, 124.4, 119.1, 114.6, 55.5, 29.6, 18.0. FT-IR (neat, cm^{-1}): 3065, 2946, 2836, 1697, 1633, 1589, 1509, 1461, 1255, 1181, 1030, 764. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{20}H_{20}N_2O_2S$, 353.1318, found 353.1311.

(*Z*)-2-(Bistrifluoromethylphenylimino)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-4-one (12c): Synthesized following general procedure C, (50 mg, 0.11 mmol), purified by column chromatography (ethyl acetate/hexanes = 0.5:9.5) to afford compound **12c** (9 mg, 17 %, 67 % brsm) as off-white solid. m.p. 146–148 °C. ^{1}H NMR: 7.78 (s, 1H), 7.68 (s, 1H), 7.46 (s, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 3H), 3.44 (s, 3H). ^{13}C NMR: 166.8, 161.4, 153.9, 149.8, 132.8 (q, *J* = 33.3 Hz), 132.5, 132.1, 125.9, 123.3 (q, *J* = 210.4 Hz), 121.9, 118.2 (q *J* = 3.7 Hz), 117.4, 114.8, 55.5, 29.7. FT-IR (neat, cm^{-1}): 2840, 1711, 1626, 1593, 1510, 1366, 1277, 1181, 1122, 1021. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{20}H_{14}N_2O_2F_6S$, 461.0758, found 461.0772.

(*Z*)-2-(Allylimino)-5-((*Z*)-4-methoxybenzylidene)-3-methylthiazolidin-4-one (12d): Synthesized following general procedure C, (50 mg, 0.18 mmol), purified by column chromatography (ethyl acetate/hexanes = 1:9) to afford compound **12d** (7 mg, 14 %, 54 % brsm) as an off white solid. m.p. 80–82 °C. ^{1}H NMR: 7.69 (s, 1H), 7.49 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 2H), 6.01 (ddt, *J* = 17.1, 10.4, 5.4 Hz, 1H), 5.30 (dq, *J* = 10.3, 1.6 Hz, 1H), 5.18 (dq, *J* = 10.3, 1.6 Hz, 1H), 4.07 (dt, *J* = 5.4, 1.6 Hz, 2H), 3.86 (s, 3H), 3.34 (s, 3H). ^{13}C NMR: 167.1, 160.8, 134.7, 131.9, 130.1, 126.7, 116.2, 114.6, 55.5, 55.0, 29.6. FT-IR (neat, cm^{-1}): 3079, 2923, 2848, 1702, 1647, 1631, 1597, 1508, 1412, 1359, 1293, 1253, 1173, 1102. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{15}H_{16}N_2O_2S$, 289.1010, found 289.1002.

(*Z*)-*N*-Phenyl-5-((*Z*)-benzylidene)thiazolidin-2-imine (17a): Synthesized following general procedure A, (50 mg, 0.38 mmol), purified by column chromatography (ethyl acetate/hexanes = 1:4) to afford compound **17a** (48 mg, 48 %) as a light-yellow solid. m.p. 128–130 °C. ^{1}H NMR: 7.38 – 7.25 (m, 8H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.09 (tt, *J* = 7.6, 1.2 Hz, 1H), 6.57 (t, *J* = 2.1 Hz, 1H), 4.87 (s, 2H). ^{13}C NMR: 158.0, 136.4, 129.3, 128.9, 128.7, 128.5, 127.7, 126.9, 125.4, 123.7, 121.0, 118.9, 63.1. FT-IR (neat, cm^{-1}): 3372, 3247, 3021, 2923, 2853, 1607, 1590, 1531, 1494, 1444, 1315, 1263, 1176, 1032, 828, 749. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{16}H_{14}N_2S$, 267.0955, found 267.0932.

(*Z*)-*N*-(2,6-Dimethylphenyl)-5-((*Z*)-benzylidene)thiazolidin-2-imine (17b): Synthesized following general procedure A, (50 mg, 0.38 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **17b** (52 mg, 46 %) as an off-white solid. m.p. 85–90 °C. ^{1}H NMR: 7.30 (d, *J* = 7.6 Hz, 2H), 7.25 – 7.14 (m, 3H), 7.09 – 7.02 (m, 3H), 6.51 (s, 1H), 4.71 (s, 2H), 2.24 (s, 6H). ^{13}C NMR: 149.9, 136.1, 133.3, 129.2, 128.6, 128.2, 127.8, 126.9, 126.2, 125.3, 119.4, 60.5, 18.4. FT-IR (neat, cm^{-1}): 3024, 2913, 2849, 1655, 1620, 1466, 1444, 1319, 1273, 1175, 1091, 766, 690. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{18}H_{18}N_2S$, 295.1263, found 295.1266.

(*Z*)-*N*-(3,5-Di(trifluoromethyl)phenyl)-5-((*Z*)-benzylidene)thiazolidin-2-imine (17c): Synthesized following general procedure A, (50 mg, 0.38 mmol), purified by column chromatography (ethyl acetate/hexanes = 3: 7) to afford compound **17c** (78 mg, 50 %) as an off-white solid. m.p. 178–180 °C. ^{1}H NMR: 7.59 (s, 2H), 7.57 (s, 1H), 7.50 – 7.32 (m, 2H), 7.31 – 7.20 (m, 3H), 6.62 (t, *J* = 2.5 Hz, 1H), 4.74 (d, *J* = 2.5 Hz, 2H). ^{13}C NMR: 159.9, 148.2, 135.7, 132.5 (q, *J* = 33.2 Hz), 128.8, 127.8, 127.5, 123.3 (q, *J* = 271 Hz), 121.4, 120.8, 116.8 (q, *J* = 4.1 Hz), 57.9. FT-IR (neat, cm^{-1}): 3031, 2918, 2867, 2833, 1651, 1598, 1475, 1367, 1273, 1177, 1116, 948. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{18}H_{12}N_2F_6S$, 403.0698, found 403.0701.

(*Z*)-*N*-Allyl-5-((*Z*)-benzylidene)thiazolidin-2-imine (17d): Synthesized following general procedure A, (50 mg, 0.38 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **17d** (54 mg, 62 %) as a light-yellow gum. ^{1}H NMR: 7.38 – 7.33 (m, 2H), 7.28 (d, *J* = 7.2 Hz, 2H), 7.20 (tt, *J* = 7.2, 1.2 Hz, 1H), 6.55 (t, *J* = 1.9 Hz, 1H), 5.93 (ddt, *J* = 17.1, 10.3, 5.5 Hz, 1H), 5.26 (dq, *J* = 17.1, 1.9 Hz, 1H), 5.17 (dq, *J* = 10.3, 1.6 Hz, 1H), 4.95 (d, *J* = 1.9 Hz, 2H), 3.98 (dt, *J* = 5.5, 1.6 Hz, 2H). ^{13}C NMR: 158.8, 139.6, 136.7, 134.2, 128.6, 127.6, 126.6, 117.9, 116.7, 69.2, 46.7. FT-IR (neat, cm^{-1}): 3206, 2922, 2853, 1615, 1543, 1493, 1239, 1073, 912, 717. HR-MS (*m*/*z*): calcd. for [M + H]$^+$ $C_{13}H_{14}N_2S$, 231.0955, found 231.0935.

(*Z*)-5-((*Z*)-benzylidene)-*N*-phenyl-2-(phenylimino)thiazolidine-3-carbothioamide (18): Synthesized following general procedure A,

(50 mg, 0.38 mmol), purified by column chromatography (ethyl acetate/hexanes = 1: 9) to afford compound **18** (13 mg, 9 %) as an off-white solid. m.p. 146–150 °C. ^{1}H NMR: 7.59 (d, *J* = 9.1 Hz, 2H), 7.40 (td, *J* = 8.3, 3.1 Hz, 4H), 7.34 (t, *J* = 7.9 Hz, 2H), 7.27–7.23 (m, 4H), 7.20 (d, *J* = 7.9 Hz, 2H), 7.10 – 7.01 (m, 2H), 6.67 (d, *J* = 2.4 Hz, 1H), 5.59 (d, *J* = 2.4 Hz, 2H). ^{13}C NMR: 178.2, 156.8, 147.7, 138.7, 135.3, 129.6, 128.9, 128.8, 127.9, 127.7, 126.6, 125.7, 125.2, 123.2, 121.7, 121.5, 61.6. FT-IR (neat, cm^{-1}): 3080, 2918, 2849, 1603, 1565, 1488, 1450, 1396, 1317, 1188, 1063, 881, 744. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{23}H_{19}N_3S_2$, 402.1093, found 402.1090.

(*Z*)-*N*-Phenyl-3-benzyl-5-((*Z*)-benzylidene)-4-isobutylthiazolidin-2-imine (22a):[13] Synthesized following general procedure A, (100 mg, 0.36 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **22a** (135 mg, 91 %) as a light-yellow gum. ^{1}H NMR: 7.40 (m, 4H), 7.37 – 7.32 (m, 5H), 7.27 (dd, *J* = 8.4, 1.5 Hz, 2H), 7.24 – 7.20 (m, 1H), 7.11 (tt, *J* = 7.6, 1.5 Hz, 1H), 7.05 (dd, *J* = 8.4, 1.5 Hz, 2H), 6.45 (s, 1H), 5.53 (d, *J* = 15.3 Hz, 1H), 4.42 (ddd, *J* = 7.5, 3.2, 0.9 Hz, 1H). 4.22 (d, *J* = 15.3 Hz, 1H), 1.92 – 1.80 (m, 2H), 1.68 (ddd, *J* = 13.9, 8.5, 3.2 Hz, 1H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR: 155.9, 151.3, 137.0, 133.7, 129.1, 128.9, 128.7, 128.2, 128.1, 127.7, 127.5, 123.3, 122.4, 121.2, 65.2, 47.5, 42.5, 24.0, 23.9, 22.7. FT-IR (neat, cm^{-1}): 3026, 2954, 2925, 2867, 1634, 1614, 1585, 1489, 1446, 1216, 1071, 750. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{27}H_{28}N_2S$, 413.2046 , found 413.2056.

(*Z*)-N-(2,6-Dimethylphenyl)-3-benzyl-5-((E)-benzylidene)-4-isobutylthiazolidin-2-imine (22b): Synthesized following general procedure A, (100 mg, 0.36 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **22b** (138 mg, 87 %) as a light-yellow gum. ^{1}H NMR: 7.41 (m, 4H), 7.36 – 7.29 (m, 3H), 7.25 – 7.18 (m, 3H), 7.09 (d, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 7.3 Hz, 1H), 6.95 (t, *J* = 7.3 Hz, 1H), 6.43 (s, 1H), 5.56 (d, *J* = 15.4 Hz, 1H), 4.51 (ddd, *J* = 6.8, 3.0, 1.1 Hz, 1H), 4.27 (d, *J* = 15.4 Hz, 1H), 2.27 (s, 3H), 2.13 (s, 3H), 1.87 (ddd, *J* = 14.9, 7.3, 1 Hz, 2H), 1.73 – 1.66 (m, 1H), 1.03 (d, *J* = 6.4 Hz, 3H), 0.97 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR: 155.2, 137.2, 135.8, 133.8, 128.8, 128.7, 128.2, 128.1, 128.0, 127.6, 127.1, 123.1, 120.7, 65.9, 47.3, 42.7, 24.0, 23.9, 23.0, 18.5, 18.4. FT-IR (neat, cm^{-1}): 3025, 2952, 2918, 2867, 1641, 1617, 1586, 1492, 1397, 1281, 1212, 1154, 752, 692. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{29}H_{32}N_2S$, 441.2359, found 441.2357.

(*Z*)-*N*-(3,5-Di(trifluoromethylphenyl)-3-benzyl-5-((*Z*)-benzylidene)-4-isobutylthiazolidin-2-imine (22c): Synthesized following general procedure A, (100 mg, 0.36 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **22c** (186 mg, 94 %) as a light-yellow gum. ^{1}H NMR (500 MHz, [D$_4$]methanol): 7.57 (s, 1H), 7.41 (s, 2H), 7.38–7.37 (m, 4H), 7.29 (t, *J* = 7.7 Hz, 3H), 7.20 (d, *J* = 7.7 Hz, 3H), 6.60 (s, 1H), 5.30 (d, *J* = 15.3 Hz, 1H), 4.53 (ddd, *J* = 7.8, 3.4, 1.4 Hz, 1H), 4.37 (d, *J* = 15.3 Hz, 1H), 1.89 – 1.74 (m, 2H), 1.71 (m, 1H), 0.94 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (125 MHz, [D$_4$]methanol): 158.0, 153.2, 136.6, 135.5, 132.2, 131.9, 131.5, 128.6, 128.3, 127.9 (q, *J* = 326 Hz), 127.8, 127.7, 127.5, 127.3, 122.5, 122.4, 115.7 (q, *J* = 4.0 Hz), 65.9, 41.9, 23.7, 22.7, 21.5. FT-IR (neat, cm^{-1}): 2957, 2927, 2870, 1636, 1597, 1494, 1369, 1276, 1172, 1132. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{29}H_{26}F_6N_2S$, 549.1800, found 549.1830.

(*Z*)-*N*-Allyl-3-benzyl-5-((*Z*)-benzylidene)-4-isobutylthiazolidin-2-imine (22d): Synthesized following general procedure A, (100 mg, 0.36 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound **22d** (95 mg, 70 %) as a light-yellow gum. ^{1}H NMR: 7.41 – 7.31 (m, 6H), 7.30 – 7.24 (m, 4H), 6.42 (s, 1H), 5.99 (ddt, *J* = 17.1, 10.2, 5.2 Hz, 1H), 5.36 (d, *J* = 15.4 Hz, 1H), 5.24 (dq, *J* = 17.1, 1.9 Hz, 1H), 5.08 (dq, *J* = 10.2, 1.9 Hz, 1H), 4.28 (ddd, *J* = 8.7, 3.3, 1.0 Hz, 1H), 4.07 (d, *J* = 15.4 Hz, 1H), 3.98 (ddt, *J* = 8.7, 4.6, 1.7 Hz, 2H), 1.79 (dtt, *J* = 8.7, 4.6, 1.7 Hz, 1H), 1.70 (ddd, *J* = 13.6, 8.1, 3.5 Hz, 1H), 1.58 (ddd, *J* = 13.6, 8.1, 3.5 Hz, 1H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR: 137.3, 136.8, 136.0, 133.8, 128.7, 128.6, 128.2, 128.1, 127.4, 127.2, 120.9, 114.7, 64.8, 56.7, 47.4, 42.2, 23.9, 23.8, 22.5. FT-IR (neat, cm^{-1}): 3026, 2954, 2925, 2867, 1648, 1617, 1543, 1493, 1399, 1280, 993, 909, 730, 693. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{24}H_{28}N_2S$, 377.2046, found 377.2045.

(*Z*)-*N*-Phenyl-5-methylidene-3-methylthiazolidin-2-imine (29a): Synthesized following general procedure B, (50 mg, 0.72 mmol), purified by column chromatography (ethyl acetate/hexanes = 1.5:8.5) to afford compound 29a (115 mg, 78 %) as a colorless gum. ^{1}H NMR: 7.31 – 7.25 (m, 2H), 7.07 – 7.02 (m, 1H), 6.94 (dd, *J* = 8.4, 1.2 Hz, 2H), 5.18 (q, *J* = 2.1 Hz, 1H), 5.06 (td, 2.3, 1.5 Hz, 1H), 4.23 (t, *J* = 2.3 Hz, 2H), 3.06 (s, 3H). ^{13}C NMR: 156.9, 151.9, 137.6, 129.0, 123.3, 122.2, 105.4, 58.0, 33.1. FT-IR (neat, cm^{-1}): 3055, 2914, 2848, 1647, 1617, 1572, 1466, 1419, 1376, 1272, 1190, 1066, 946, 847, 774. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{11}H_{12}N_2S$, 205.0794, found 205.0793.

(*Z*)-*N*-(2,6-Dimethylphenyl)-5-methylidene-3-methylthiazolidin-2-imine (29b): Synthesized following general procedure B, (50 mg, 0.72 mmol), purified by column chromatography (ethyl acetate/hexanes = 1:9) to afford compound 29b (127 mg, 76 %) as a colorless gum. ^{1}H NMR: 7.02 (d, *J* = 7.4 Hz, 2H), 6.92 – 6.89 (m, 1H), 5.17 (q, *J* = 2.1 Hz, 1H), 5.01 (q, *J* = 2.4 Hz, 1H), 4.26 (t, *J* = 2.1 Hz, 2H), 3.11 (s, 3H), 2.16 (s, 6H). ^{13}C NMR: 156.7, 149.5, 137.7, 129.7, 127.9, 123.2, 105.2, 58.7, 33.1, 18.2. FT-IR (neat, cm^{-1}): 3058, 2914, 2848, 1648, 1617, 1578, 1466, 1238, 1162, 1066, 950, 848, 766. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{13}H_{16}N_2S$, 233.1107, found 233.1109.

(*Z*)-*N*-(3,5-Bis(trifluoromethyl)phenyl-5-methylidene-3-methylthiazolidin-2-imine (29c): Synthesized following general procedure B, (50 mg, 0.72 mmol), purified by column chromatography (ethyl acetate/hexanes = 1:9) to afford compound 29c (220 mg, 90 %) as a colorless gum. ^{1}H NMR: 7.51 (s, 1H), 7.37 (s, 2H), 5.26 (q, *J* = 2.1 Hz, 1H), 5.13 (q, *J* = 2.4 Hz, 1H), 4.32 (t, *J* = 2.1 Hz, 2H), 3.08 (s, 3H). ^{13}C NMR: 158.2, 153.0, 136.2, 132.1 (q, *J* = 32.8 Hz), 123.4 (q, *J* = 271 Hz), 122.6, 116.3 (q, *J* = 4.0 Hz), 106.4, 58.0, 33.0. FT-IR (neat, cm^{-1}): 2923, 2872, 1642, 1618, 1595, 1425, 1366, 1272, 1119, 966, 845, 702. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{13}H_{10}F_6N_2S$, 341.0542, found 341.0539.

(*Z*)-*N*-Allyl-5-methylidene-3-methylthiazolidin-2-imine (29d): Synthesized following general procedure B, (50 mg, 0.72 mmol), purified by column chromatography (ethyl acetate/hexanes = 1:3) to afford compound 29d (96 mg, 79 %) as a light-yellow gum. ^{1}H NMR: 5.93 – 5.83 (m, 1H), 5.19 – 5.13 (m, 2H), 5.09 – 5.06 (m, 1H), 5.01 (dq, *J* = 10.2, 1.6 Hz, 1H), 4.07 (t, *J* = 2.2 Hz, 2H), 3.75 (dt, *J* = 5.4, 1.6 Hz, 2H), 2.87 (s, 3H). ^{13}C NMR: 157.2, 137.7, 136.7, 114.7, 105.3, 57.9, 57.5, 33.1. FT-IR (neat, cm-1): 3077, 2921, 2866, 2807, 1649, 1616, 1580, 1416, 1236, 1106, 913, 857, 654. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_8H_{12}N_2S$, 169.0794, found 169.0799.

(*E*)-*N*-Phenyl-5-methylidenethiazolidin-2-imine (30a):[9–10, 28] Synthesized following general procedure B, (50 mg, 0.9 mmol), purified by column chromatography (ethyl acetate/hexanes = 1.5:8.5) to afford compound 30a (138 mg, 80 %) as a light-brown solid. m.p. 104–108 °C (Lit.[9] m.p. 113 °C). ^{1}H NMR: 7.32 – 7.25 (m, 2H), 7.22 – 7.16 (m, 2H), 7.06 (m, 1H), 5.21 (q, *J* = 2.2 Hz, 1H), 5.15 – 5.10 (m, 1H), 4.61 (t, *J* = 2.2 Hz, 2H). ^{13}C NMR: 159.6, 145.6, 143.9, 129.2, 123.7, 121.4, 104.3, 58.3. FT-IR (neat, cm^{-1}): 3242, 3191, 3027, 2856, 1590, 1550, 1492, 1444, 1314, 1077, 1037, 747. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{10}H_{10}N_2S$, 191.0637, found 191.0630.

(*E*)-*N*-(2,6-Dimethylphenyl)-5-methylidenethiazolidin-2-imine (30b): Synthesized following general procedure B, (25 mg,

0.45 mmol), purified by column chromatography (ethyl acetate/hexanes = 1.5:8.5) to afford compound 30b (64 mg, 65 %) as a white solid. m.p. 94–98 °C. ^{1}H NMR: ^{1}H NMR: 7.02 (d, J = 7.6 Hz, 2H), 6.96 (dd, J = 7.6, 6.6 Hz, 1H), 6.43 (bs, 1H), 5.14 (q, J = 2.1 Hz, 1H), 5.02 (bs, 1H), 4.42 (bs, 2H), 2.21 (s, 6H). ^{13}C NMR: 145.4, 143.0, 132.2, 128.1, 124.8, 104.6, 60.5, 55.8, 18.3. FT-IR (neat, cm^{-1}): 3171, 3095, 2900, 2836, 1652, 1619, 1586, 1463, 1277, 1172, 1075, 774. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{12}H_{14}N_2S$, 219.0950, found 219.0943.

(*E*)-*N*-(3,5-Bis(trifluoromethyl)phenyl)-5-methylidenethiazolidin-2-imine (30c): Synthesized following general procedure B, (25 mg, 0.45 mmol), purified by column chromatography (ethyl acetate/hexanes = 1.5:8.5) to afford compound 30c (115 mg, 78 %) as a white solid. m.p. 80–82 °C. ^{1}H NMR: 7.54 (s, 1H), 7.49 (s, 2H), 6.90 (bs, 1H), 5.27 (q, J = 2.2 Hz, 1H), 5.17 (q, J = 2.5 Hz, 1H), 4.45 (t, J = 2.5 Hz, 2H). ^{13}C NMR: 161.8, 149.7, 140.3, 132.4 (q, J = 32.9 Hz), 123.2 (q, J = 271.1 Hz), 121.9, 116.9 (q, J = 3.8 Hz), 106.4, 54.0. FT-IR (neat, cm^{-1}): 3092, 2851, 2828, 1648, 1610, 1483, 1378, 1352, 1175, 1117. HR-MS (*m/z*): calcd. for [M + H] $^+$ $C_{12}H_8F_6N_2S$, 327.0385, found 327.0383.

(*E*)-*N*-Allyl-5-methylidenethiazolidin-2-imine (30d):[9–10] Synthesized following general procedure B, (25 mg, 0.45 mmol), purified by column chromatography (ethyl acetate/hexanes = 3:7) to afford compound 30d (47 mg, 67 %) as a white solid. m.p. 96–98 °C (lit.[9] m.p. 92–94 °C). ^{1}H NMR: 5.87 (ddt, J = 17.1, 10.3, 5.5 Hz, 1H), 5.21 (dq, J = 17.1, 1.4 Hz, 1H), 5.12 (dq, J = 10.3, 1.4 Hz, 2H), 5.08 (td, J = 2.8, 1.4 Hz, 1H), 4.67 (t, J = 2.8 Hz, 2H), 4.55 (bs, 1H), 3.88 (dt, J = 5.5, 1.4 Hz, 2H). ^{13}C NMR: 158.5, 148.8, 134.4, 116.5, 102.5, 67.0, 46.6. FT-IR (neat, cm-1): 3186, 3003, 2891, 2838, 1623, 1551, 1415, 1294, 1237, 1069, 1025, 841, 643, 593. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_7H_{10}N_2S$, 155.0637, found 155.0629.

Synthesis of 1,4-dimethyl-3-phenyl-1,3-dihydro-2H-imidazole-2-thione (33b): Synthesized following general procedure B, ^{1}H NMR: 7.51 – 7.47 (m, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.27 (dd, J = 8.2, 1.2 Hz, 2H), 6.53 (d, J = 1.2 Hz, 1H), 3.61 (s, 3H), 1.90 (s, 3H). ^{13}C NMR: 163.5, 136.7, 129.5, 129.1, 128.4, 126.1, 115.3, 34.9, 10.9. FT-IR (neat, cm^{-1}): 3058, 2914, 2848, 1648, 1617, 1578, 1466, 1238, 1162, 1066, 950, 848, 766. HR-MS (*m/z*): calcd. for [M + H]$^+$ $C_{11}H_{12}N_2S$, 204.0721, found 204.0692.

Synthesis of thiocarbonyl intermediate: To a stirred solution of propargylamine **5** (120 mg, 0.40 mmol) in CH_2Cl_2 (2.0 mL) at r.t. was added Et_3N (124 mg, 1.21 mmol) followed by the addition of thiocarbonyldiimidazole (73 mg, 0.40 mmol). After 12 h, the reaction mixture was diluted with water (5 mL) and CH_2Cl_2 (5 mL), two layers were separated. The aqueous part was back extracted with CH_2Cl_2 (2x10 mL). Combined organic extracts were washed with brine (20 mL), dried with sodium sulfate and concentrated under reduced pressure. The thus obtained crude material was purified by column chromatography (MeOH/CH_2Cl_2 = 1:9) to afford the thiourea 35 (112 mg, 68 %) as an off-white solid. m.p. 118–120 °C. ^{1}H NMR: 7.62 (bs, 1H), 7.37 (d, J = 9.1 Hz, 4H), 7.03 (bs, 2H), 6.84 (d, J = 9.1 Hz, 4H), 3.79 (s, 3H), 3.77 (s, 3H), 3.34–3.12 (m, 5H). ^{13}C NMR: 179.2, 160.2, 159.1, 133.4, 130.2, 129.8, 127.5, 119.5, 114.3, 114.2, 113.7, 87.4, 82.8, 58.2, 55.4, 55.4, 37.4. FT-IR (neat, cm^{-1}): 3168, 3115, 2922, 2839, 2222, 1604, 1523, 1454, 1368, 1290, 1240, 1168, 1069, 1024, 835, 744. HR-MS (*m/z*): calcd. for [M + Na]$^+$ $C_{23}H_{23}N_3O_2S$, 428.1403, found 428.1414.

Acknowledgments

This work has been supported by the Robert A. Welch Foundation (Y-1362). NMR spectra were obtained on instruments purchased with grants from the NSF (CHE-0234811 and CHE-0840509). We thank Maciej Kukula in the Shimadzu Center for Advanced Analytical Chemistry for obtaining the HRMS data reported in this manuscript. We are grateful to Taru Bharadwaj (Welch Summer Scholar 2016) for some preliminary experiments.

Keywords: Cyclization · Alkynes · Heterocycles · Isothiocyanates · Synthetic methods

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[25] In unpublished work, we have discovered that simple thioureas engage in oxidative dearomatization reactions and so failure of these systems reflects the nucleophilicity of sulfur. For comparative purposes, thiocarbamates related to **5** do participate in the dearomatization pathway and this presumably reflects the attenuated nucleophilicity of the sulfur in this functional group.

[26] We subjected propargylamines **10** and **16** to cyclization with phenylisothiocyanate under Dethe's recently reported conditions (neat, 40 °C) and found that the thiazolidine is formed efficiently. Thus, while internal alkynes appear to cyclize under both the Dethe conditions and the conditions reported herein, terminal alkynes do not cyclize under neat reaction conditions.

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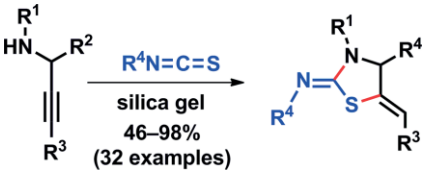
Received: October 3, 2018

Heterocyclic Synthesis*



A metal-free coupling reaction between propargylamines and isothiocyanates affords good yields of vinylidene substituted thiazolidines. Control reactions suggest that these reactions are in fact mediated by silica gel. A broad substrate scope and a variety of substitution patterns are accessible.

DOI: 10.1002/ejoc.201801505