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Brønsted Acid Catalyzed Cyclization of Propargylic Alcohols with Thioamides. Facile Synthesis of Di- and Trisubstituted Thiazoles

Xiaoxiang Zhang, Wan Teng Teo, Sally, and Philip Wai Hong Chan*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637616, Singapore

waihong@ntu.edu.sg

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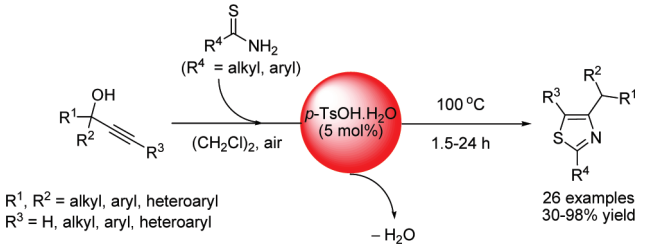

A general and efficient method to prepare 2,4-di- and trisubstituted thiazoles via *p*-TsOH·H_2O-catalyzed cyclization of trisubstituted propargylic alcohols with thioamides is described. The reaction was accomplished in moderate to excellent product yields under mild conditions that did not require the exclusion of air and moisture and offers an operationally simplistic and convenient route to this synthetically useful aromatic heterocycle.

Thiazoles are important structural moieties found in many natural products and compounds of current biological and material interest as well as versatile building blocks in organic synthesis.[1−4] Among the myriad reactions devoted to the construction of this aromatic heterocycle,[1−4] the most often relied upon synthetic method is the Hantzsch thiazole synthesis,[3] which makes use of α-halo ketones and thioamides as the substrates. While recent efforts have led to a number of advances made in the development of this reaction,[1,4] the establishment of more versatile and flexible methodologies to functionalized thiazoles with selective control of substitution patterns are still needed. This is all the more so if it can be accomplished with low cost and readily available starting materials and catalysts that follow the principles of atom economy.[5] One such synthetic strategy has been to replace the electrophile in these reactions with a propargylic alcohol in the presence of a Lewis acid catalyst.[4,6] According to the seminal reports by the groups of Zhan[4a] and Yoshimatsu,[4b] these catalytic systems are thought to proceed via either an allenic or propargylic cationic species that underwent the [3 + 2] cycloaddition process. Although shown to be efficient, producing H_2O as potentially the only byproduct, this was countered by the likelihood of forming metal impurities that lessened the potential of this approach for scale-up applications. Added to this is a substrate scope that is limited to ones containing functional groups that cannot take part in strong metal coordination. In this regard, we reasoned that these drawbacks could be readdressed by developing a Brønsted acid-catalyzed version of this regioselective thiazole forming reaction. An inexpensive and commercially available reagent class that has a high tolerance to air and moisture, Brønsted acids have been shown to mediate a wide variety of organic transformations in an efficient and selective manner.[7−9] Recently, this has included stereoselective C−X (X = C, N, O, S) bond formation strategies that combine the use of Brønsted acid catalysis with alcohol pro-electrophiles such as allylic, benzylic, and propargylic alcohols.[8,9] For example, we recently reported TfOH to be a highly efficient catalyst

(1) For selected reviews, see: (a) Jin, Z. *Nat. Prod. Rep.* **2009**, *26*, 382. (b) Chen, B.; Heal, W. Five-Membered Rings with Two Heteroatoms, Each with Their Fused Carbocyclic Derivatives. In *Comprehensive Heterocyclic Chemistry III*; Katrizky, R., Rees, C. W., Scriven, E. F. V., Taylor, R. J. K., Eds.; Pergamon: New York, 2008; Vol. 4, p 635. (c) Wu, Y.-J.; Yang, B. V. Five-Membered Ring Systems: With N and S (Se, Te) Atoms. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Elsevier: Oxford, 2007; Vol. 18, p 247. (d) Mustafa, S. M.; Nair, V. A.; Chittoor, J. P.; Krishnapillai, S. *Mini-Rev. Org. Chem.* **2004**, *1*, 375. (e) Jagodziński, T. S. *Chem. Rev.* **2003**, *103*, 197. (f) Eicher, T.; Hauptmann, S. *The Chemistry of Heterocycles: Structures, Reactions, Synthesis, and Applications*, 2nd ed.; Wiley-VCH: Weinheim, 2003. (g) Wipf, P. *Chem. Rev.* **1995**, *95*, 2115.

(2) For selected recent examples, see: (a) Shi, B.; Blake, A. J.; Lewis, W.; Campbell, I. B.; Judkins, B. D.; Moody, C. J. *J. Org. Chem.* **2010**, *75*, 152. (b) Thomae, D.; Perspicace, E.; Xu, Z.; Henryon, D.; Schneider, S.; Hesse, S.; Kirsch, G.; Seck, P. *Tetrahedron* **2009**, *65*, 2982. (c) Kaleta, Z.; Makowski, B. T.; Soós, T.; Dembinski, R. *Org. Lett.* **2006**, *8*, 1625. (d) Kazmaier, U.; Ackermann, S. *Org. Biomol. Chem.* **2005**, *3*, 3184. (e) Shao, J.; Panek, J. S. *Org. Lett.* **2004**, *6*, 3083. (f) Rivkin, A.; Cho, S. S.; Gabarda, A. E.; Yoshimura, F.; Danishefsky, S. J. *J. Nat. Prod.* **2004**, *67*, 139. (g) Ganesh, T.; Schilling, J. K.; Palakodety, R. K.; Ravindra, R.; Shanker, N.; Bane, S.; Kingston, D. G. I. *Tetrahedron* **2003**, *59*, 9979. (h) DeRoy, P. L.; Charette, A. B. *Org. Lett.* **2003**, *5*, 4163. (i) Williams, D. R.; Patnaik, S.; Clark, M. P. *J. Org. Chem.* **2001**, *66*, 8463. (j) Bach, T.; Heuser, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 3184. (k) Cutignano, A.; Bruno, I.; Bifulco, G.; Casapullo, A.; Debitus, C.; Gomez-Paloma, L.; Riccio, R. *Eur. J. Org. Chem.* **2001**, 775.

(3) Hantzsch, A.; Weber, J. H. *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 3118.

(4) (a) Gao, X.; Pan, Y.; Lin, M.; Chen, L.; Zhan, Z.-P. *Org. Biomol. Chem.* **2010**, *8*, 3259. (b) Yoshimatsu, M.; Yamamoto, T.; Sawa, A.; Kato, T.; Tanabe, G.; Muraoka, O. *Org. Lett.* **2009**, *11*, 2952.

(5) (a) Trost, B. M. *Acc. Chem. Res.* **2002**, *35*, 695. (b) Trost, B. M. *Science* **1991**, *254*, 1471.

(6) For reviews on the use of alcohols as pro-electrophiles, see: (a) Bandini, M.; Tragni, M. *Org. Biomol. Chem.* **2009**, *7*, 1501. (b) Ljungdahl, N.; Kann, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 642. (c) Muzart, J. *Tetrahedron* **2008**, *64*, 5815. (d) Muzart, J. *Eur. J. Org. Chem.* **2007**, 3077. (e) Muzart, J. *Tetrahedron* **2005**, *61*, 4179. (f) Tamaru, Y. *Eur. J. Org. Chem.* **2005**, 2647.

(7) For recent reviews, see: (a) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744. (b) Busca, G. *Chem. Rev.* **2007**, *107*, 5366. (c) Shao, L.-X.; Shi, M. *Curr. Org. Chem.* **2007**, *11*, 1135. (d) Yamamoto, H. *Tetrahedron* **2007**, *63*, 8377. (e) Yamamoto, H.; Boxer, M. B. *Chimia* **2007**, *61*, 279. (f) Ishihara, K.; Yamamoto, H. In *New Frontiers in Asymmetric Catalysis*; Mikami, K., Lautens, M., Eds.; John Wiley & Sons: New York, 2007; p 359. (g) Enders, D.; Grondal, C.; Huettl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (h) Yamamoto, H. In *Asymmetric Synthesis*; Christmann, M., Braese, S., Eds.; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, 2007; p 153. (i) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520. (j) Connon, S. J. *Chem.—Eur. J.* **2006**, *12*, 5418. (k) Akiyama, T.; Itoh, J.; Fuchibe, K. *Adv. Synth. Catal.* **2006**, *348*, 999.

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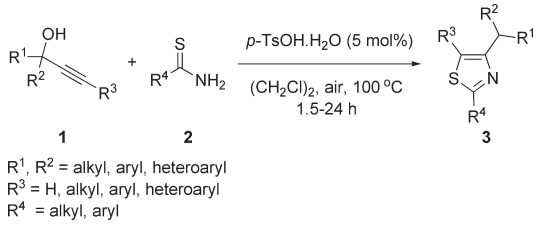
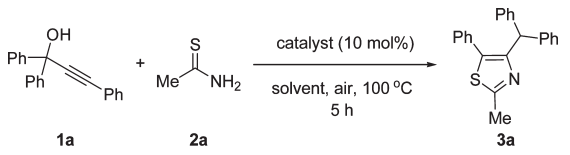
SCHEME 1. *p*-TsOH·H_2O-Catalyzed Formation of 2,4-Di- and Trisubstituted Thiazoles from Propargylic Alcohols and Thioamides



for the regioselective formation of conjugated enynes based on nucleophilic ring-opening of 1-cyclopropyl-2-propyn-1-ols with alcohols.[8b] As part of an ongoing program exploring the utility of alcohol pro-electrophiles in organic synthesis,[8b,9] we report herein *p*-TsOH·H_2O-catalyzed cyclization of trisubstituted propargylic alcohols with thioamides that did not require air- and moisture-free conditions (Scheme 1). The 2,4-di- and trisubstituted thiazole products were obtained as a single regioisomer in moderate to excellent yields comparable to those noted for the closely related metal-promoted approaches to this aromatic heterocycle.[4] To our knowledge, a synthetic approach to thiazoles from trisubstituted propargylic alcohols catalyzed by a Brønsted acid is not known.

We began by choosing 1,1,3-triphenylprop-2-yn-1-ol **1a** and thioacetamide **2a** as the model substrates to establish the reaction conditions (Table 1). This initially revealed that subjecting 1 equiv of **1a** and 2 equiv of **2a** to 10 mol % of *p*-TsOH·H_2O in 1,2-dichloroethane at 100 °C for 5 h gave the best result (entry 1). Under these conditions, 4-benzhydryl-2-methyl-5-phenylthiazole **3a** was afforded in 90% yield, comparable to those obtained for the closely related Sc- and Ag-catalyzed reactions.[4] The structure and regiochemistry of the thiazole product were determined on the basis of ^{1}H NMR measurements and X-ray crystallographic analysis (see Figure S33 in the Supporting Information).[10] A slightly lower product yield of 86% was obtained on decreasing the catalyst loading from 10 to 5 mol % (entry 2). In contrast, lower product yields were found when the reaction was repeated with 10 mol % of *p*-TsOH·H_2O at room temperature or on changing the solvent from 1,2-dichloroethane to $MeNO_2$, MeCN, 1,4-dioxane, or toluene (entries 3−7). A similar outcome was found when stronger Brønsted acid catalysts in place of *p*-TsOH·H_2O were examined (entries 8−10). In these latter reactions, the use of 10 mol % of TfOH, TFA, and H_3PO_4 in $MeNO_2$ gave **3a** in lower yields of 59−73%. On the basis of these studies, reaction of **1a** with **2a** in the presence of 5 mol % of *p*-TsOH·H_2O in 1,2-dichloroethane at 100 °C for 5 h was deemed to provide the optimal conditions. By applying these conditions, we were pleased to find that a product yield of 927 mg (77%) could be afforded when the reaction was repeated on a large scale with 1 g (3.52 mmol) of **1a** and 0.53 g (7.04 mmol) of **2a**.

TABLE 1. Optimization of the Reaction Conditions[a]



entry	catalyst	solvent	yield (%)
1	*p*-TsOH·H_2O	$(CH_2Cl)_2$	90
2	*p*-TsOH·H_2O[b]	$(CH_2Cl)_2$	86
3[c]	*p*-TsOH·H_2O	$(CH_2Cl)_2$	39
4	*p*-TsOH·H_2O	$MeNO_2$	81
5	*p*-TsOH·H_2O	MeCN	87
6	*p*-TsOH·H_2O	1,4-dioxane	25
7	*p*-TsOH·H_2O	PhMe	86
8	TfOH	$MeNO_2$	73
9	TFA	$MeNO_2$	70
10	H_3PO_4[d]	$MeNO_2$	59

[a]Unless stated otherwise, all reactions were performed at 100 °C for 5 h with a catalyst/**1a**/**2a** ratio of 1:10:20. [b]Reaction conducted with 5 mol % of *p*-TsOH·H_2O. [c]Reaction conducted at room temperature. [d]Used as a 80% solution in H_2O.

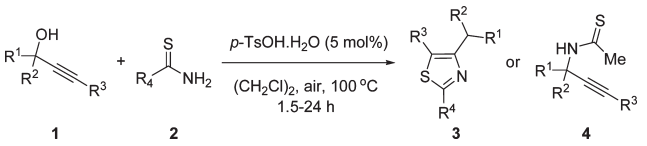
To define the generality of the present procedure, we next examined a series of propargylic alcohols **1b**−**w** and thioamides **2a**−**h** (Table 2). Reactions of propargylic alcohols bearing either an electron-withdrawing or electron-donating group on the carbinol or alkyne carbon with **2a** gave the corresponding thiazoles in good to excellent yields (entries 1−13). Similarly, the analogous cyclizations with starting alcohols containing either an alkyl functional group at R^1 or R^3 or a terminal alkyne moiety afforded **3o**−**q** in 54−79% yield, albeit requiring a catalyst loading of 30 mol % (entries 14, 15, and 17). In contrast, recovery of both the propargylic alcohol and thioamide was found when both substituents on the carbinol carbon of the alcohol substrate were an alkyl functional group as in **1q** (entry 16). A propargylic alcohol containing an acid-sensitive acetylenic ketone moiety was also examined under the standard conditions but was found to give a mixture of decomposition products that could not be identified by ^{1}H NMR analysis of the crude mixture (entry 22). On the other hand, propargylic alcohols bearing a nitrile, thiophene, or carboxamide moiety were found to proceed well under the present conditions and give the corresponding thiazoles **3e**, **3r**, and **3s** (at a catalyst loading of 30 mol %) in excellent yields (entries 4, 18, and 19). Additionally, reactions of starting alcohols **1a** and **1c** with other thioamide nucleophiles were found to give the corresponding thiazoles in moderate to excellent yields (entries 23−29). This included one example of a cyclic thioamide (**2b**) that gave **3t**

(8) For selected examples on Brønsted acid-catalyzed reactions with alcohol pro-electrophiles, see: (a) Jin, T.; Himuro, M.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 5893. (b) Mothe, S. R.; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 5887. (c) Bras, J. L.; Muzart, J. *Tetrahedron* **2007**, *63*, 7942. (d) Sanz, R.; Martínez, A.; Guilarte, V.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Eur. J. Org. Chem.* **2007**, 4642. (e) Sanz, R.; Miguel, D.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Org. Lett.* **2007**, *9*, 2027. (f) Sanz, R.; Martínez, A.; Miguel, D.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Org. Lett.* **2007**, *9*, 727. (g) Shirakawa, S.; Kobayashi, S. *Org. Lett.* **2007**, *9*, 311. (h) Sanz, R.; Martínez, A.; Miguel, D.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Adv. Synth. Catal.* **2006**, *348*, 1841. (i) Motokura, K.; Fujita, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2605. (j) Sanz, R.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Eur. J. Org. Chem.* **2006**, 1383. (k) Young, J.-J.; Jung, L.-J.; Cheng, K.-M. *Tetrahedron Lett.* **2000**, *41*, 3415.

(9) For selected recent works by us see: (a) Kothandaraman, P.; Rao, W.; Foo, S. J.; Chan, P. W. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 4619. (b) Kothandaraman, P.; Foo, S. J.; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 5947. (c) Zhang, X.; Teo, W. T.; Chan, P. W. H. *Org. Lett.* **2009**, *11*, 4990. (d) Rao, W.; Zhang, X.; Sze, E. M. L.; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 1740. (e) Rao, W.; Chan, P. W. H. *Chem.—Eur. J.* **2008**, *14*, 10486.

(10) CCDC 753779-753780 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

TABLE 2. Synthesis of Substituted Thiazoles 3b−z Catalyzed by *p*-TsOH·H_2O[a]



1 2 3 4

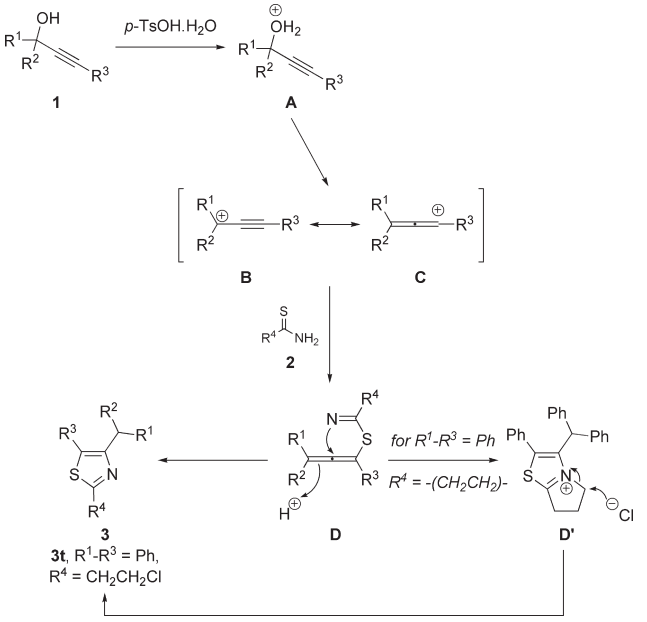
entry	1, $R^1/R^2/R^3$	2, R^4	3	yield (%)
1	**1b**, 4-FC_6H_4/Ph/Ph	**2a**, Me	**3b**	96
2	**1c**, 4-ClC_6H_4/Ph/Ph	**2a**	**3c**	98
3	**1d**, 4-BrC_6H_4/Ph/Ph	**2a**	**3d**	93
4	**1e**, 4-CNC_6H_4/Ph/Ph	**2a**	**3e**	98
5	**1f**, 4-MeC_6H_4/Ph/Ph	**2a**	**3f**	79
6	**1g**, 4-FC_6H_4/4-FC_6H_4/Ph	**2a**	**3g**	94
7	**1h**, 4-ClC_6H_4/4-ClC_6H_4/Ph	**2a**	**3h**	85
8	**1i**, 4-BrC_6H_4/4-BrC_6H_4/Ph	**2a**	**3i**	88
9	**1j**, 4-MeC_6H_4/4-MeC_6H_4/Ph	**2a**	**3j**	74
10	**1k**, Ph/Ph/4-FC_6H_4	**2a**	**3k**	86
11	**1l**, Ph/Ph/4-ClC_6H_4	**2a**	**3l**	87
12	**1m**, Ph/Ph/4-MeC_6H_4	**2a**	**3m**	89
13	**1n**, Ph/Ph/4-$MeOC_6H_4$	**2a**	**3n**	69
14[b]	**1o**, *i*-Pr/Ph/Ph	**2a**	**3o**	76
15[b]	**1p**, Ph/Ph/*n*-Bu	**2a**	**3p**	79
16	**1q**, Me/Me/Ph	**2a**		*c*
17[b]	**1r**, Ph/Ph/H	**2a**	**3q**	54
18	**1s**, 4-ClC_6H_4/4-ClC_6H_4/2-thienyl	**2a**	**3r**	96
19[b]	**1t**, Ph/Ph/$(CH_2)_2$CONHPh	**2a**	**3s**	78
20	**1u**, H/Ph/Ph	**2a**	**4a**	75
21	**1v**, H/4-FC_6H_4/4-BrC_6H_4	**2a**	**4b**	72
22	**1w**, Ph/Ph/COC≡CPh	**2a**		*d*
23	**1a**	**2b**, $-(CH_2CH_2)-$	**3t**	30
24	**1c**	**2c**, Ph	**3u**	91
25	**1c**	**2d**, 4-FC_6H_4	**3v**	92
26	**1c**	**2e**, 4-ClC_6H_4	**3w**	90
27	**1c**	**2f**, 2-ClC_6H_4	**3x**	93
28	**1c**	**2g**, 4-BrC_6H_4	**3y**	93
29	**1c**	**2h**, 4-$MeOC_6H_4$	**3z**	97

[a]All reactions were performed at 100 °C for 1.5−24 h with *p*-TsOH·H_2O/**1**/**2** ratio = 1:20:40.[11] [b]Reaction conducted at 30 mol % catalyst loading. [c]No reaction based on TLC and ^1H NMR analysis of the crude mixture after a reaction time of 24 h. [d]Mixture of side products obtained that could not be identified by ^1H NMR analysis of the crude mixture.

and the structure of which was confirmed by X-ray crystallography (entry 23 and Figure S34 in Supporting Information).[10] In our hands, reactions of secondary alcohols **1u** and **1v** were the only instances where the corresponding *N*-propargylation products **4a** and **4b** were preferentially obtained as the sole product in 75 and 72% yield, respectively (entries 20−21). This contrasts markedly to a recent work reporting *p*-TsOH·H_2O to catalyze the reaction of a closely related secondary propargylic alcohol and thioamide in chlorobenzene giving the corresponding thiazole in 12% yield.[4a]

We tentatively propose the mechanism of the present reaction to proceed in a manner similar to that described for the analogous metal-catalyzed cyclizations of di- and trisubstituted propargylic alcohols with thioamides.[4] As depicted in Scheme 2, this could involve Brønsted acid-mediated dehydration of **1** to deliver alkynyl cation species **B** and its allenic resonance form **C**. Subsequent attack by the thioamide at the sterically less hindered acetylenic carbon center of **B** or allenic carbcation center **C** when followed by 5-*exo*-*trig* cyclization of the newly formed intermediate **D** would then provide the thiazole product. It might be anticipated that trapping at the sterically less hindered carbon center of **B** or **C** when R^1 and/or R^2 = aryl would limit any

SCHEME 2. Tentative Mechanism for *p*-TsOH·H_2O-Catalyzed Cyclization of 1 with 2



1 A B C 2 3 D D'

unfavorable steric interactions between the incoming nucleophile and these substituents of the cationic species.[12] Indeed, our earlier findings showing the exclusive formation of the *N*-propargylation adduct in cases where less sterically demanding secondary alcohols were examined would be consistent with the influence of such steric interactions on the regioselectivities found (entries 20 and 21 in Table 2). We surmise the origin of the chloro-substituted thiazole **3t** could be due to ring-opening of the iminium cation **D′** by a chloride anion generated in situ from the 1,2-dichloroethane solvent under the acidic conditions.

In summary, we have developed a Brønsted acid-catalyzed method for the cyclization of tertiary propargylic alcohols with thioamides as an efficient approach to 2,4-di- and trisubstituted thiazoles under conditions that did not require the exclusion of air and moisture. The reaction was shown to be applicable to a broad substrate scope that compliments the metal-mediated versions of this transformation.[4] Moreover, the possibility of the present operationally simplistic method as a potential regioselective scale-up strategy for thiazole synthesis was exemplified by the large-scale preparation of one example in excellent yield. This is notable given the recent demand for more rapid and direct atom economical chemical processes that can make use of low cost and readily available reagents and catalysts.

Experimental Section

Representative Procedure for *p*-TsOH·H_2O-Catalyzed Synthesis of 2,4-Di- and Trisubstituted Thiazoles 3. To a 5 mL round-bottom flask containing 1,2-dichloroethane (3 mL) were successively added **1a** (0.25 mmol), **2a** (0.5 mmol) and *p*-TsOH·H_2O (12.5 μmol). The resultant reaction mixture was heated to 100 °C and stirred for

(11) See the Supporting Information for the reaction times.

(12) For similar regioselectivties observed in other reactions with propargylic cations, see refs 8f, 9c, and: (a) Huang, W.; Shen, Q. S.; Wang, J. L.; Zhou, X. G. *J. Org. Chem.* **2008**, *73*, 1586. (b) Ishikawa, T.; Aikawa, T.; Mori, Y.; Saito, S. *Org. Lett.* **2003**, *5*, 51. (c) Ishikawa, T.; Okano, M.; Aikawa, T.; Saito, S. *J. Org. Chem.* **2001**, *66*, 4635. (d) Edens, M.; Boerner, D.; Chase, C. R.; Nass, D.; Schiavelli, M. D. *J. Org. Chem.* **1977**, *42*, 3403.

5 h. On cooling to room temperature, the reaction mixture was concentrated under reduced pressure, and the residue obtained was directly purified by flash column chromatography on silica gel (eluent: *n*-hexane/EtOAc = 8:1) to give the title compound.

4-Benzhydryl-2-methyl-5-phenylthiazole (3a): white solid; mp 163−164 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 2.65 (s, 3H), 5.51 (s, 1H), 7.17−7.19 (m, 2H), 7.20−7.27 (m, 8H), 7.36−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 19.5, 50.0, 126.4, 128.1, 128.3, 128.7, 129.2, 129.9, 132.0, 133.3, 143.4, 151.6, 163.9; IR (neat) 3019, 1599, 1533, 1493, 1215, 1074, 1030, 669, 634, 617, 584, 507 cm^{-1}; MS (ESI) *m*/*z* 342 $[M + H]^+$; HRMS (ESI) calcd for $C_{23}H_{20}NS$ 342.1316, found 342.1316.

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Supporting Information Available: Characterization data and ^{1}H and ^{13}C NMR spectra for the starting alcohols **1**, thiazole products **3**, and *N*-propargylation adducts **4** and X-ray data for compounds **3a** and **3t** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.