Advanced Synthesis & Catalysis

Accepted Article

Title: Rhodium(I)-Catalyzed Regioselective Azide-internal Alkynyl Trifluoromethyl Sulfide Cycloaddition and Azide-internal Thioalkyne Cycloaddition under Mild Conditions

Authors: Wangze Song, Nan Zheng, Ming Li, Junnan He, Junhao Li, Kun Dong, Karim Ullah, and Yubin Zheng

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201801216

Link to VoR: http://dx.doi.org/10.1002/adsc.201801216

10.1002/adsc.201801216

COMMUNICATION

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Rhodium(I)-Catalyzed Regioselective Azide-internal Alkynyl Trifluoromethyl Sulfide Cycloaddition and Azide-internal Thioalkyne Cycloaddition under Mild Conditions

Wangze Song,[a,*] Nan Zheng,[a,b] Ming Li,[a] Junnan He,[b] Junhao Li,[a] Kun Dong,[a] Karim Ullah,[a] and Yubin Zheng[b]

[a] State Key Laboratory of Fine Chemicals, School of Pharmaceutical Science and Technology, Dalian University of Technology, Dalian, 116024, P. R. China.
E-mail: wzsong@dlut.edu.cn

[b] State Key Laboratory of Fine Chemicals, School of Chemical Engineering, Dalian University of Technology, Dalian, 116024, P. R. China.

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. A regioselective method to access fully substituted 5-trifluoromethylthio-1,2,3-triazoles and 5-thio-1,2,3-triazoles from the internal alkynyl trifluoromethyl sulfides and internal thioalkynes by a rhodium(I)-catalyzed azide-alkyne cycloaddition (RhAAC) reaction under mild conditions has been developed. This approach features good compatibility with water and air, a broad substrate scope, good functional group tolerance, high yields and excellent regioselectivities. The high 1,5-regioselectivities were controlled by the strong coordination between the sulfur atom and the π-acidic rhodium. The advantages of this method further include its applicability to gram-scale preparation, the use of solid-phase synthesis technique, and the mutually orthogonal CuAAC-RhAAC reaction.

Keywords: 5-trifluoromethylthio-1,2,3-triazoles; 5-thio-1,2,3-triazoles; rhodium; regioselectivity; mild conditions

Recently, trifluoromethanesulfenyl groups (SCF_3) have attracted increasing interest due to their unique properties, such as their extremely high lipophilicity and strong electron-withdrawing effects.[1] The introduction of this functionality to the parent molecules is an important strategy in medicinal chemistry and agrochemistry for increasing bioavailability because the SCF_3 group can significantly enhance the transmembrane permeation and metabolic stability of the organic molecules.[2] For example, the anorectic effect of flutiorex is approximately twice as strong as that of fenfluramine.[3a-3c] Toltrazuril is a coccidiostatic drug in veterinary medicine.[3d,3e] Cefazaflur, a parenteral cephalosporin, is an important antibiotic drug.[3f,3g] Fipronil, a widely used phenylpyrazole insecticide, has many advantages over previous generations of insecticides such as organophosphates, carbamates and pyrethroids[3h, 3i] (Figure 1).

Fully substituted 1,2,3-triazoles are important heterocyclic scaffolds, and they have numerous applications in organic synthesis, materials science, and the pharmaceutical industry.[4] Trifluoromethylthio-1,2,3-triazole offers a unique combination of the well-known activity of the SCF_3 group and the 1,2,3-triazole core, allowing better bioactivities and bioavailabilities.[2] However, the methods for regioselectively accessing fully substituted trifluoromethylthio-1,2,3-triazoles are still very limited. The Huisgen 1,3-dipolar cycloaddition of azides and internal alkynes appears to be the most straightforward and atom-efficient approach.[5] However, low regioselectivities are usually obtained, and it often requires high temperatures and long reaction times. Since 2002, the Meldal group and the Sharpless group independently developed copper-catalyzed AAC (CuAAC) reactions.[6] Various transition metal catalysts were examined in the AAC reactions (MAAC) to solve the regioselective issues in the preparation of the fully substituted 1,2,3-triazoles.[7] Recently, it was reported that fully substituted 5-thio-1,2,3-triazoles could be obtained from azide-internal thioalkyne cycloadditions with high 1,5-regioselectivities by RuAAC[8] or IrAAC[9] reactions. An indirect two-step strategy with a strong Lewis acid catalyst to prepare 5-trifluoromethylthio-1,2,3-triazoles from bench-stable 5-stannyl triazoles *via* a Cu-catalyzed interrupted click reaction was disclosed by Xu's group (Scheme 1a).[10]

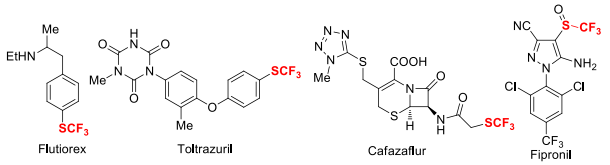
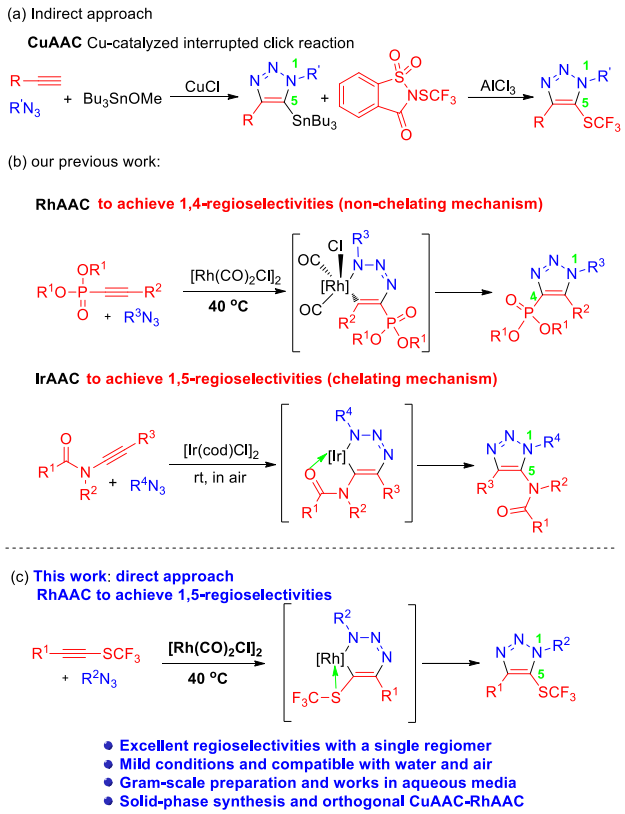


Figure 1. Selected Small Molecules with SCF_3 Group.

However, the direct synthesis of fully substituted 5-trifluoromethylthio-1,2,3-triazoles from azides and

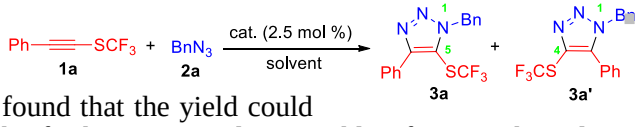
10.1002/adsc.201801216

internal alkynes in one step is still unsolved.[11] Previously, we developed a rhodium(I)-catalyzed AAC reaction (RhAAC) to access fully substituted 1,2,3-triazolyl-4-phosphonates with high 1,4-regioselectivity and the iridium(I)-catalyzed AAC reaction (IrAAC) to access fully substituted 5-amido-1,2,3-triazoles with high 1,5-regioselectivity.[12] The differences in the regioselectivities are derived from the chelating effect as well as the electronic character of the internal alkynes. Inspired by Xu, Jia, Sun, López, Mascareñas and others' endeavors[8-10] and as a continuation of our pursuit of highly regioselective AAC reactions, herein, we report the direct access to fully substituted 5-trifluoromethylthio-1,2,3-triazoles and 5-thio-1,2,3-triazoles with excellent 1,5-regioselectivity from internal alkynyl trifluoromethyl sulfides and internal thioalkynes by a rhodium(I)-catalyzed AAC (RhAAC) process under mild conditions (Scheme 1c). Remarkably, the gram-scale preparation, the application of solid-phase synthesis technique and the orthogonal CuAAC-RhAAC reactions underscore the advantages of this intermolecular RhAAC method.



Scheme 1. Synthesis of Fully-Substituted 5-Trifluoromethylthio-1,2,3-triazoles.

For the preparation of fully substituted 5-trifluoromethylthio-1,2,3-triazole (**3a**), internal alkynyl trifluoromethyl sulfide (**1a**) and benzyl azide (**2a**) were initially chosen as the model substrates to optimize the cycloaddition conditions using dichloromethane (DCM) as the solvent without inert gas protection (Table 1). The CuAAC reaction failed to occur for substrate **1a** using CuI or $CuSO_4$ as the catalyst, which indicated that the CuAAC and RhAAC reactions may be mutually orthogonal (Table 1, entries 1 and 2). The RuAAC reaction proceeded with good yield but poor regioselectivity by the neutral Ru(II) catalyst instead of the cationic complex (Table 1, entries 3 and 4). To our delight, $[Rh(CO)_2Cl]_2$ was demonstrated to be the most efficient catalyst at room temperature and afforded desired **3a** in high yield with excellent regioselectivity (Table 1, entry 5). None of the desired cycloaddition products were observed with $[Rh(cod)_2]BF_4$ or $[Rh(cod)Cl]_2$ as catalysts (Table 1, entries 6 and 7). Rh(III) was ineffective in this transformation (Table 1, entry 8). Encouragingly, we



found that the yield could be further improved using chloroform as the solvent and the absolute 1,5-regioselectivity could be maintained (Table 1, entry 9). The yield could not be further increased by using DCE or toluene (Table 1, entries 10 and 11). The reaction failed to occur in hexane (Table 1, entry 12). When the reaction temperature was increased from room temperature to 40 °C, the yield remained similar (Table 1, entry 13).

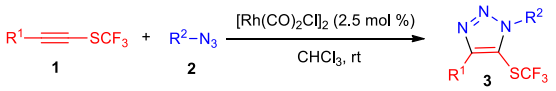
Table 1. Optimization of the Reaction Conditions[a]

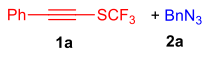
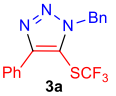
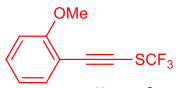
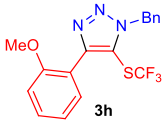
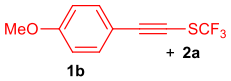
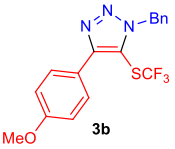
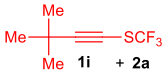
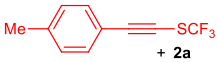
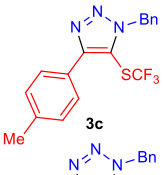
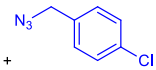
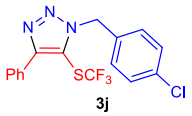
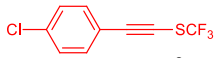
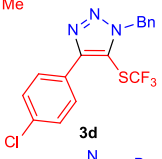
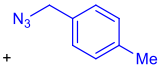
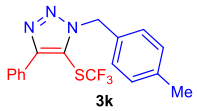
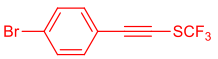
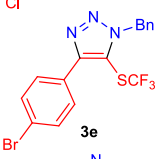
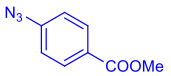
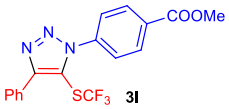
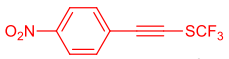
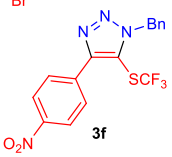
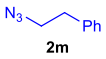
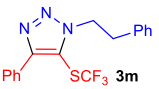
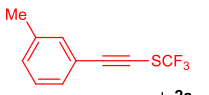
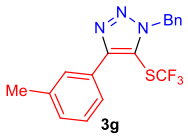
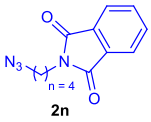
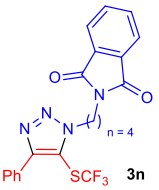
Entry	Catalyst	Solvent	Yield[b,c]	**3a**/**3a'**[b]
1	CuI	DCM	0	-
2	$CuSO_4$	DCM	0	-
3	$[Cp^*Ru(PPh_3)_2Cl]$	DCM	81	6:1
4	$[Cp^*Ru(MeCN)_3]PF_6$	DCM	trace	-
5	$[Rh(CO)_2Cl]_2$	DCM	84	>20:1
6	$[Rh(cod)_2]BF_4$	DCM	0	-
7	$[Rh(cod)Cl]_2$	DCM	0	-
8	$[Cp^*RhCl_2]_2$	DCM	0	-
9	$[Rh(CO)_2Cl]_2$	$CHCl_3$	92	>20:1
10	$[Rh(CO)_2Cl]_2$	DCE	83	>20:1
11	$[Rh(CO)_2Cl]_2$	toluene	65	>20:1
12	$[Rh(CO)_2Cl]_2$	Hexane	trace	-
13[d]	$[Rh(CO)_2Cl]_2$	$CHCl_3$	90	>20:1

[a] Conditions: **1a** (1.0 equiv), **2a** (1.5 equiv), solvent (0.1 M), catalyst (2.5 mol%), air atmosphere, rt for 12 h.
[b] Determined by ^1H NMR of the crude mixture with an internal standard.
[c] The combined yield of **3a** and **3a'** was reported.
[d] The reaction was set up at 40 °C.

10.1002/adsc.201801216

Table 2. Substrate Scope of the RhAAC with Internal Alkynyl Trifluoromethyl Sulfides[a]



Entry	Substrates	Product (3)	Yield (%) [b]	Entry	Substrates	Product (3)	Yield (%) [b]
1			88	8			83
2			86	9		No reaction [c]	-
3			85	10			89
4			92	11			84
5			90	12			71
6			82	13			86
7			84	14			84

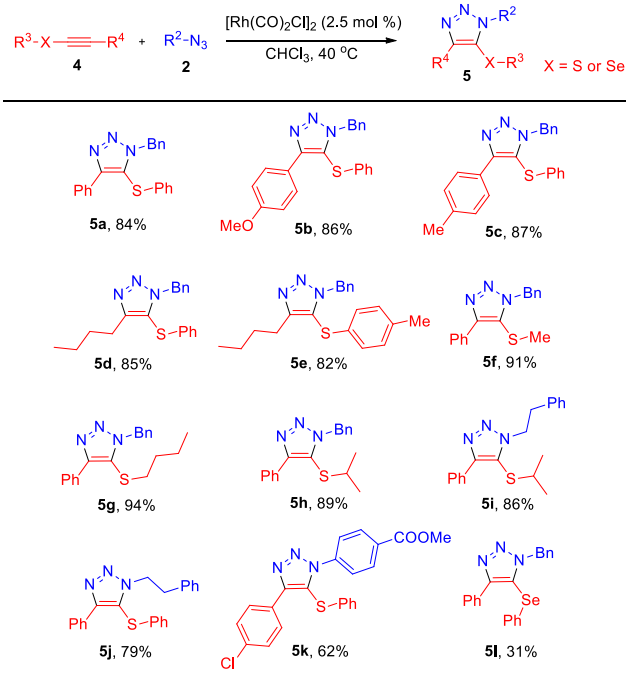
[a] Standard conditions: **1** (1.0 equiv), **2** (1.5 equiv), $CHCl_3$ (0.1 M), $[Rh(CO)_2Cl]_2$ (2.5 mol%), air atmosphere, for 12-24 h.
[b] Isolated yield. Regioselectivities (**3**/**3'**) were >20:1 (determined by ^1H NMR of the crude reaction mixture).
[c] The reaction was set up at 60 °C for 24 h.

With the optimized conditions in hand, we explored the substrate scope of the RhAAC reaction between internal alkynyl trifluoromethyl sulfides **1** and azides **2**. Various fully substituted 5-trifluoromethylthio-1,2,3-triazoles were synthesized at room temperature without inert gas protection in good yields (up to 92%) and excellent regioselectivities (Table 2). In addition to the (phenylethynyl)(trifluoromethyl)sulfane **1a**, other trifluoromethyl sulfides, such as *p*-methoxy, *p*-methyl, *p*-chloro and *p*-bromo phenylethynyl (trifluoromethyl)sulfanes could also smoothly participate in the RhAAC reaction (Table 2, entries 1-5). The yields for **3a**-**3e** were similar, and no obvious electronic effects were observed in these entries. However, when using *p*-nitrophenylethynyl (trifluoromethyl)sulfane (**1f**) as the substrate, the yield of the corresponding product (**3f**) was lower than other substrates, yet the regioselectivity was excellent (Table 2, entry 6). The *meta*-substituted and *ortho*-substituted phenylacetylenes **1g** and **1h** could also achieve the RhAAC reactions in good yields (Table 2, entries 7 and 8). Unfortunately, the reaction failed to occur for alkyl-substituted internal alkynyl trifluoromethyl sulfide **1i**, even with an extended reaction time and higher reaction temperature, and this may have been due to the combination of the unfavorable electronic and steric factors (Table 2, entry 9). When using alkyl or aryl azides as substrates, the desired products could be prepared in good yields and excellent regioselectivities. Various functional groups, including halogen, ester and carbonyl groups, were well tolerated in this transformation (**3j**, **3l** and **3n**). The yield (**3j**) for the electron-withdrawing alkyl azide was slightly higher (89%) than that of the electron-donating substrate (**3k**) (Table 2, entries 10 and 11). When aryl azides were used instead of alkyl azides, the yield decreased dramatically (**3l**) (Table 2, entry 12). Good yields and regioselectivities were obtained using ethyl or butyl azides (**2m** and **2n**) (Table 2, entries 13 and 14). The broad substrate

scope allows for the further modification of the fully substituted 5-trifluoromethylthio-1,2,3-triazoles.

In addition to the internal alkynyl trifluoromethyl sulfides **1**, internal thioalkynes and internal alkynyl selenides **4** could also undergo this RhAAC reaction with azides **2** under mild conditions (Table 3). Compared to the RhAAC reactions shown in Table 2, the reaction temperature was increased to 40 °C for the reactions shown in Table 3. Various aryl or alkyl internal thioalkynes could participate well in this transformation and give desired 5-thio-1,2,3-triazoles **5** in moderate to good yields. The yields (**5f-5i**) for the substrates with alkyl sulfanes were slightly higher than those of substrates with aryl sulfanes (**5a-5e**). However, using aryl azide instead of alkyl azides resulted in a moderate yield (62%) for **5k**. The RhAAC reaction could also occur for internal alkynyl selenides, albeit in notably lower yields (**5l**).

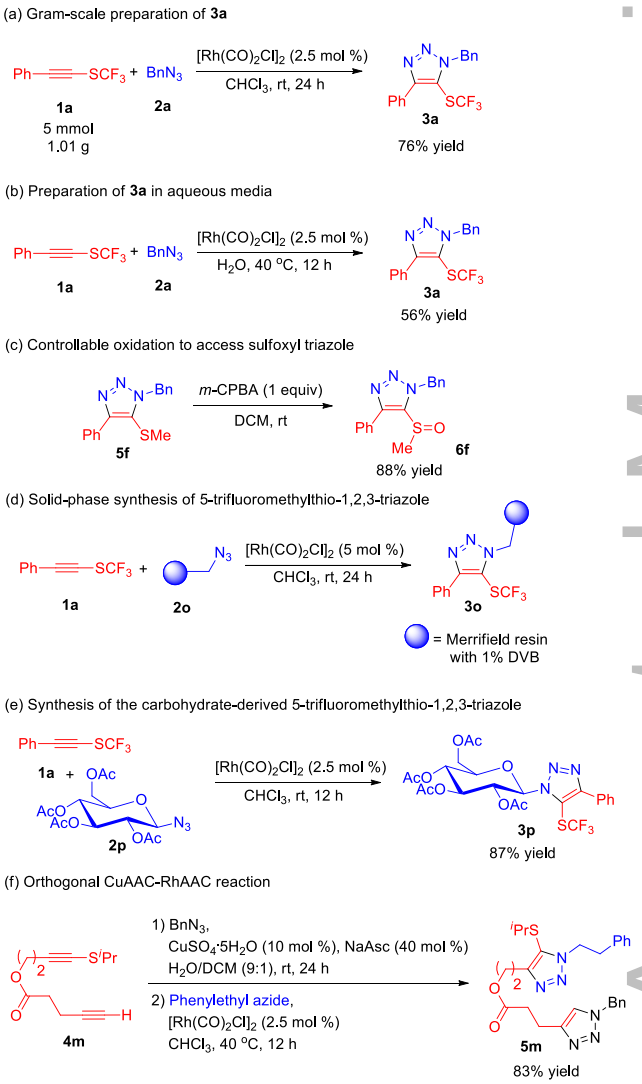
Table 3. Substrate Scope of the RhAAC with Internal Thioalkynes or Alkynyl Selenides[a][b]



[a] Standard conditions: **4** (1.0 equiv), **2** (1.5 equiv), $CHCl_3$ (0.1 M), $[Rh(CO)_2Cl]_2$ (2.5 mol%), air atmosphere, at 40 °C for 12-24 h.

[b] Isolated yield. Regioselectivities (**5**/**5'**) determined by ^1H NMR of the crude reaction mixture were >20:1.

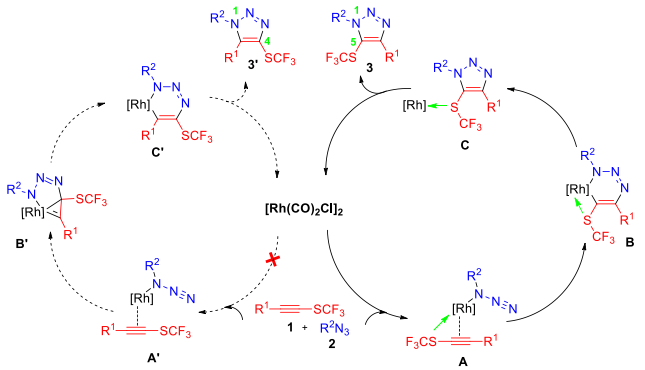
Subsequently, the applicability of this RhAAC reaction was investigated. The reaction could be performed on the gram scale. Subjecting **1a** (5.0 mmol, 1.01 g) to the conditions shown in Table 2 afforded **3a** in 76% yield (3.8 mmol, 1.27 g) after column purification (Scheme 2a). The ability to conduct the AAC transformation in aqueous media is very important for potential biological applications in the future.[13] Encouragingly, fully substituted 5-trifluoromethylthio-1,2,3-triazole could be prepared in water as the solvent in moderate yield (Scheme 2b). The sulfoxyl triazole (**6f**) could be generated by the subsequent controllable oxidation of the RhAAC products (Scheme 2c). (Azidomethyl) polystyrene resin **2o** could be employed for the solid-phase synthesis of fully substituted 5-trifluoromethylthio-1,2,3-triazole (**3o**) through the RhAAC process, providing a powerful tool for surface modification and heterogeneous catalysis (Scheme 2d). The carbohydrate-derived 5-trifluoromethylthio-1,2,3-triazole (**3p**) could be accessed efficiently from the cycloaddition reaction (Scheme 2e). The orthogonal CuAAC and RhAAC reactions were successfully performed using benzyl azide and phenylethyl azide, respectively.[8] Product **5m**, with two triazole moieties in one molecule, was obtained in good yield (Scheme 2f). All of the above applications suggest that the RhAAC reaction may be further applied in biochemistry, medicinal chemistry, material science and other areas.



Scheme 2. Applications of the RhAAC Reactions.

Based on the previous experiments and theoretical calculations for the MAAC reactions,[9, 12] a general mechanism for the RhAAC reaction is proposed in Scheme 3. Complex **A** or **A'** could be generated by the initial combination of π-acidic Rh(I) with internal alkynyl trifluoromethyl sulfide **1**. Azide **2** coordinates with Rh by the internal nitrogen atom in

intermediate**A** and **A'**. Oxidative cyclization yields metallacycles **B** and **B'**. For intermediate **B**, the SCF_3 group strongly coordinates to the Rh, stabilizing the system and providing high 1,5-regioselectivity, which makes intermediate **B** more stable than **B'**. Hence, the 1,4-regioisomers **3'** were not observed in this transformation. Reductive elimination of intermediate **B** affords intermediate **C**, which results in desired fully substituted 5-trifluoromethylthio-1,2,3-triazole **3** with high 1,5-regioselectivity.



Scheme 3. Proposed Mechanism of the RhAAC Reaction.

In summary, we have developed a regioselective method for accessing fully substituted 5-trifluoromethylthio-1,2,3-triazoles and 5-thio-1,2,3-triazoles from the internal alkynyl trifluoromethyl sulfides and internal thioalkynes by a rhodium(I)-catalyzed azide-alkyne cycloaddition (RhAAC) under mild conditions. The proposed approach exhibits a broad substrate scope, good functional group tolerance, good compatibility with water and air, high yields and excellent regioselectivities. The potential utilities of this RhAAC reaction were demonstrated by a gram-scale synthesis, conducting the reaction in the aqueous media, conducting the reaction on the solid-phase and the orthogonal CuAAC and RhAAC reactions. Further mechanistic studies and advanced theoretical calculations for the transition states and intermediates of this reaction are underway in our laboratory.

Experimental Section

General procedure for the synthesis of 3a: To a vial containing $[Rh(CO)_2Cl]_2$ (2.0 mg, 0.025 equiv, 0.005 mmol) in $CHCl_3$ (2 mL) under air was added (phenylethynyl)(trifluoromethyl)sulfane (40.4 mg, 1 equiv, 0.2 mmol) and benzyl azide (40.2 mg, 1.5 equiv, 0.3 mmol). It was necessary to add the azide at last. The vial was closed and the mixture was stirred at room temperature for 12 h. The mixture was purified with flash column chromatography (33% EtOAc in petroleum ether) to give the pure product (59 mg, 88%) as a yellow oil.

Acknowledgements

This work was supported by grants from the Doctoral Program Foundation of Liaoning Province (Nos. 20170520378, 20170520274), the Fundamental Research Funds for the Central Universities (Nos. DUT16RC(3)114, DUT18LK25) and the National Natural Science Foundation of China (Nos. 21702025, 51703018). We thank Prof. Baomin Wang (Dalian University of Technology) for his enthusiastic help.

References

[1] For the recent examples and reviews: a) J. Zhang, J.-D. Yang, H. Zhang, X.-S. Xue, H. Mayr, J.-P. Cheng, *Angew. Chem. Int. Ed*. **2018**, *57*, 12690. b) P. Zhang, L. Lu, Q. Shen, *Acta Chim Sinica*. **2017**, *75*, 744. c) S. Barata-Vallejo, S. Bonesi, A. Postigo, *Org. Biomol. Chem*. **2016**, *14*, 7150. d) H.-Y. Xiong, X. Pannecoucke, T. Besset, *Chem. Eur. J*. **2016**, *22*, 16734. e) X.-H. Xu, K. Matsuzaki, N. Shibata, *Chem. Rev*. **2015**, *115*, 731. f) C. Ni, M. Hu, J. Hu, *Chem. Rev*. **2015**, *115*, 765. g) X. Shao, C. Xu, L. Lu, Q. Shen, *Acc. Chem. Res*. **2015**, *48*, 1227. h) K. Zhang, X.-H. Xu, F.-L. Qing, *Chin. J. Org. Chem*. **2015**, *35*, 556. i) A. Tlili, T. Billard, *Angew. Chem. Int. Ed*. **2013**, *52*, 6818. j) S. Alazet, L. Zimmer, T. Billard, *Angew. Chem. Int. Ed*. **2013**, *52*, 10814.

[2] a) F. Leroux, P. Jeschke, M. Schlosser, *Chem. Rev*. **2005**, *105*, 827. b) K. Muller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881. c) W. K. Hagmann, *J. Med. Chem*. **2008**, *51*, 4359. d) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev*. **2008**, *37*, 320. e) P. Jeschke, *Pest Manage. Sci*. **2010**, *66*, 10. f) N. A. Meanwell, *J. Med. Chem*. **2011**, *54*, 2529. g) B. Manteau, S. Pazenok, J.-P. Vors, F. R. Leroux, *J. Fluorine Chem*. **2010**, *131*, 140. h) V. N. Boiko, *Beilstein J Org. Chem*. **2010**, *6*, 880. i) T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem. Int. Ed*. **2013**, *52*, 8214. j) F. Toulgoat, S. Alazet, T. Billard, *Eur. J. Org Chem*. **2014**, 2415. and the references in above literatures.

[3] a) J. F. Giudicelli, C. Richer, A. Berdeaux, *Br. J. Pharmacol*. **1976**, *3*, 113. b) J. N. André, L. G. Dring, G. Gillet, C. Mas-Chamberlin, *Br. J. Pharmacol*. **1979**, *66*, 506P. c) T. Silverstone, J. Fincham, J. Plumley, *Br. J. Clin. Pharmacol*. **1979**, *7*, 353. d) P. Laczay, G. Vörös, G. Semjén, *Int. J. Parasitol*. **1995**, *25*, 753. e) P. Pommier, A. Keïta, S. Wessel-Robert, B. Dellac, H. C. Mundt, *Rev. Med. Vet*. **2003**, *154*, 41. f) G. W. Counts, D. Gregory, D. Zeleznik, M. Turck, *Antimicrob. Agents Chemother*. **1977**, *11*, 708. g) N. Aswapokee, H. C. Neu, *Antimicrob. Agents Chemother*. **1979**, *15*, 444. h) R. Islam, J. W. Lynch, *Br. J. Pharmacol*. **2012**, *165*, 2707. i) A. Aajoud, M. Raveton, D. Azrou-Isghi, M. Tissut, P. Ravanel, *J. Agric. Food Chem*. **2008**, *56* 3732.

[4] For recent examples and reviews: a) H. Amdouni, G. Robert, M. Driowya, N. Furstoss, C. Métier, A. Dubois, M. Dufies, M. Zerhouni, F. Orange, S. Lacas-Gervais, K. Bougrin, A. R. Martin, P. Auberger, R. Benhida, *J. Med. Chem*. **2017**, *60*, 1523. b) A. Lauria, R. Delisi, F. Mingoia, A. Terenzi, A. Martorana, G. Barone, A. M. Almerico, *Eur. J. Org. Chem*. **2014**, *2014*, 3289. c) B. T. Worrell, J. A. Malik, V. V. Fokin, *Science*, **2013**, *340*, 457. d) B. T. Worrell, S. P. Ellery, V. V. Forkin, *Angew. Chem. Int. Ed*. **2013**, *52*, 13037. e) P.

Thirumurugan, D. Matosiuk, K. Jozwiak, *Chem. Rev*. **2013**, *113*, 4905. f) S. G. Agalave, S. R. Maujan, V. S. Pore, *Chem. Asian J*. **2011**, *6*, 2696. g) K. D. Hänni, D. A. Leigh, *Chem. Soc. Rev*. **2010**, *39*, 1240. h) S. K. Mamidyala, M. G. Finn, *Chem. Soc. Rev*. **2010**, *39*, 1252. i) J. C. Jewett, C. R. Bertozzi, *Chem. Soc. Rev*. **2010**, *39*, 1272. j) H. C. Kolb, K. B. Sharpless, *Drug Discovery Today* **2003**, *8*, 1128.

[5] a) R. Huisgen, *Angew. Chem. Int. Ed*. **1963**, *2*, 565. b) R. Huisgen, *Angew. Chem. Int. Ed*. **1963**, *2*, 633.

[6] a) C. W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem*. **2002**, *67*, 3057. b) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed*. **2002**, *41*, 2596. c) H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed*. **2001**, *40*, 2004. For CuAAC Reviews: d) J. E. Hein, V. V. Fokin, *Chem. Soc. Rev*. **2010**, *39*, 1302. e) M. Meldal, C. W. Tornøe, *Chem. Rev*. **2008**, *108*, 2952. f) P. Wu, V. V. Fokin, *Aldrichimica Acta*. **2007**, *40*, 7. g) J. E. Moses, A. D. Moorhouse, *Chem. Soc. Rev*. **2007**, *36*, 1249.

[7] For recent examples and reviews: a) W. G. Kim, M. E. Kang, J. B. Lee, M. H. Jeon, S. Lee, J. Lee, B. Choi, P. M. S. D. Cal, S. Kang, J, -M. Kee, G. J. L. Bernardes, J. -U. Rohde, W. Choe, S. Y. Hong, *J. Am. Soc. Chem*. **2017**, *139*, 12121. b) Y. Liao, Q. Lu, G. Chen, Y. Yu, C. Li, X. Huang, *ACS Catal*. **2017**, *7*, 7529. c) C. Wang, D. Ikhlef, S. Kahlal, J.-Y.Saillard, D. Astruc, *Cood. Chem. Rev*. **2016**, *316*, 1. d) F. Wei, W. Wang, Y. Ma, C.-H. Tung, Z. Xu, *Chem. Commun*. **2016**, *52*, 14188.

[8] P. Destito, J. R. Couceiro, H. Faustino, F. López, J. L. Mascareñas, *Angew. Chem. Int. Ed*. **2017**, *56*, 10766.

[9] a) S. Ding, G. Jia, J. Sun, *Angew. Chem. Int. Ed*. **2014**, *53*, 1877. b) Q. Luo, G. Jia, J. Sun, Z. Lin, *J. Org. Chem*. **2014**, *79*, 11970.

[10] a) F. Wei, T. Zhou, Y. Ma, C.-H. Tung, Z. Xu, *Org. Lett*. **2017**, *19*, 2098. b) W. Wang, Y. Lin, Y. Ma, C.-H. Tung, Z. Xu, *Org. Lett*. **2018**, *20*, 2956. c) W. Wang, X. Peng, F. Wei, C.-H. Tung, Z. Xu, *Angew. Chem. Int. Ed*. **2016**, *55*, 649.

[11] Two examples have been previously reported with moderate yields, see: S. Alazet, L. Zimmer, T. Billard, *Angew. Chem. Int. Ed*. **2013**, *52*, 10814.

[12] a) W. Song, N. Zheng, M. Li, K. Ullah, Y. Zheng, *Adv. Synth. Catal.* **2018**, *360*, 2429. b) W. Song, N. Zheng, *Org. Lett.* **2017**, *19*, 6200.

[13] a) J. Miguel-Ávila, M. Tomás-Gamasa, A. Olmos, P. J. Pérez, J. L. Mascareñas, *Chem. Sci*. **2018**, *9*, 1947. b) Y. Bai, X. Feng, H. Xing, Y. Xu, B. K. Kim, N. Baig, T. Zhou, A. A. Gewirth, Y. Lu, E. Oldfield, S. C. Zimmerman, *J. Am. Chem. Soc*. **2016**, *138*, 11077.

10.1002/adsc.201801216

COMMUNICATION

Rhodium(I)-Catalyzed Regioselective Azide-internal Alkynyl Trifluoromethyl Sulfide Cycloaddition and Azide-internal Thioalkyne Cycloaddition under Mild Conditions

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Wangze Song,* Nan Zheng, Ming Li, Karim Ullah, Junhao Li, Kun Dong and Yubin Zheng