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Communication

Ru(II)-catalyzed ring expansion of alkynylcyclopropanes in the presence of sulfonamides

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ABSTRACT

Ru(II)-catalyzed ring expansion of alkynylcyclopropanes to alkylidenecyclobutanamines using a variety of cyclopropane and sulfonamide substrates was developed and shown to give moderate to excellent yields.

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Transition metal-catalyzed reactions can be explored to construct new chemical bonds. This strategy has facilitated the development of new synthetic methods for constructing complex molecules [1–17]. Ru complexes are important transition metal catalysts [18–33]. Ring expansion reactions have been widely used in organic synthesis. Transition metal-based ring expansion has been used to build functional and complex molecules [34–41].

The four-membered carbocycles are the core of many natural products with biological activities [42,43] and are also very useful substrates that can be further transformed to various ring skeletons through organic synthesis [44,45]. In recent years, methods for synthesizing four-membered carbocycles have been limited to [2+2] cycloaddition, while ring expansion has not been well developed [46–48]. Alkynylcyclopropanes, alkynylcyclopropyl alkanols, and cyclopropenes were used as substrates for ring expansion catalyzed by Au, Ru, and Fe cata-

lysts (Scheme 1) [49–52]. In 2010, Ye and coworkers [52] reported that AuPPh₃Cl can catalyze ring expansion of unactivated alkynylcyclopropanes. However, Ru catalysts have not been reported for the ring expansion of alkynylcyclopropanes without the use of activating groups. Here, we studied Ru(II)-catalyzed ring expansion of non-activated alkynylcyclopropanes to alkylidenecyclobutanamines in the presence of sulfonamides. This strategy does not require the prior activation of alkynylcyclopropanes and is more ecologically friendly and economical.

We initiated our studies by optimizing the conditions for the reaction of alkynylcyclopropane (**1a**) and TsNH₂ (**2a**). It was quickly found that both simple [Ru(p-cymene)Cl₂]₂ and a combination of [Ru(p-cymene)Cl₂]₂ (5 mol) and AgSbF₆ (20%) failed to catalyze this reaction. Treatment of substrates **1a** and **2a** with [Ru(p-cymene)Cl₂]₂ (5 mol%), AgSbF₆ (20%), and acetic acid (4 equiv.) in 1,4-dioxane at 100 °C gave the desired product with 85% yield. NMR spectroscopic analysis identified

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Scheme 1. Transition metal-catalyzed ring expansion.

the product as an alkylidenecyclobutanamine **3aa**. We tried other aprotic solvents such as 1,2-dichloroethane (DCE) and acetone, but all these failed to improve the conversion or yield

to a synthetically useful level. We also increased the reaction temperature to 120 °C, but this did not produce a higher yield. Substituting the Ru catalyst with $[\text{RhCp}^*\text{Cl}_2]_2$ prevented the reaction from occurring. These data support a unique and specific role for Ru catalysts in this reaction.

Next, we explored the reactions with a variety of alkynylcyclopropanes with **2a** using the optimized conditions above (Table 1). This reaction gave good yield (85%) with the phenyl-substituted substrate. Alkynylcyclopropanes with halogen groups (**3ba** and **3ca**), an electron-withdrawing group (**3da**), and an electron-donating group (**3ea**) at the *para*-position could be used under these reaction conditions. The carbon-halogen bond should allow further functionalization, such as metal-catalyzed C–C cross-coupling. The substrates with an electron-rich aryl group (**3ea**) had a poorer yield (37%), while those with electron-withdrawing groups were highly compatible with this reaction. Moreover, the substrate with a *p*-OCH₃ group donated electrons to such an extent under these reaction

Table 1

Ring expansion of alkynylcyclopropanes.

Entry	R ¹	R ²	Product	Yield * (%)	Entry	R ¹	R ²	Product	Yield * (%)
1	Ph			85	8				89
	1a	2a	3aa			1b	2a	3ba	
2	Ph			90	9				84
	1a	2b	3ab			1c	2a	3ca	
3	Ph	Ph		61	10				91
	1a	2c	3ac			1d	2a	3da	
4	Ph			64	11				37
	1a	2d	3ad			1e	2a	3ea	
5	Ph			62	12				77
	1a	2e	3ae			1f	2a	3fa	
6	Ph			51	13				81
	1a	2f	3af			1g	2a	3ga	
7	Ph	—CH ₃		67	14				42
	1a	2g	3ag			1h	2a	3ha	

Reaction conditions: alkynylcyclopropanes 0.5 mmol, sulfonylhydrazides 0.75 mmol, $[\text{Ru}(\text{p-cymene})\text{Cl}_2]_2$ 5 mol%, AgSbF₆ 20 mol%, HOAc 4 equiv., 1,4-dioxane 2 mL, 100 °C, 12 h, sealed tube under N₂. * Isolated yield.

Scheme 2. Reaction mechanism.

Scheme 3. H/D exchange reaction.

conditions that the product was not formed. Furthermore, under the the standard conditions, *ortho*- and *meta*-substitution still allowed the transformation into the expected products (**3fa**, **3ga**, and **3ha**), suggesting that steric effects did not significantly affect reactivity.

The use of sulfonamides as substrates was explored next. Sulfonamides bearing a chloro group (**3ab**) and nitro group (**3ac**) at the *para*-position were suitable substrates. The phenyl-substituted sulfonamide (**3ad**) showed a reduction of the catalytic activity for ring expansion to 61%. Notably, the yields of **3aa** and **3ab** were not significantly different (85% and 90%, respectively). Based on these results, we believe that the electron-donating and electron-withdrawing groups of sulfonamides do not have important roles in this reaction. It was further demonstrated that this reaction was applicable with substrates bearing *ortho*-methyl (**3ae**) and *ortho*-chloro (**3af**) groups. The substrates with an *ortho*-group tended to react slowly but yielded similar amounts of product (64% and 62%). More important, a comparably high efficiency was also achieved with the alkyl-substituted sulfonamide, with ring expansion to product **3ag** with 67% yield. Thus, the aryl group does not appear to be necessary for this reaction.

From the results, the following mechanism is proposed. Cationic species were generated by the coordination of Ru(II) to the carbon-carbon triple bond of the alkynylcyclopropanes. Then, the cation triggered ring expansion to generate four-membered carbocyclic cations. Next, in the presence of nucleophile **2a**, the cations were trapped to produce the intermediate. Finally, the C–M bond was cleaved to yield the four-membered carbocyclic products (Scheme 2).

H/D exchange was performed to test this hypothesized mechanism. ¹H NMR analysis of the product revealed significant H/D (53% H) exchange at the *sp*² C coordinated to the phenyl (Scheme 3), indicating that our mechanism is correct.

In conclusion, we developed a novel Ru(II)-catalyzed ring expansion of alkynylcyclopropanes with the help of sulfonamides. This ring-expansion reaction usually results in high yields and tolerates a variety of functional groups on the al-

kynylcyclopropanes and sulfonamides. The strategy provides an efficient way for making synthetic medicinal alkynylcyclobutanamines.

References

- [1] Arockiam P B, Bruneau C, Dixneuf P H. *Chem Rev*, 2012, 112: 5879
- [2] Ritleng V, Sirlin C, Preffer M. *Chem Rev*, 2002, 102: 1731
- [3] Kakiuchi F, Chatani N. *Adv Synth Catal*, 2003, 345: 1077
- [4] Song G Y, Wang F, Li X W. *Chem Soc Rev*, 2012, 41: 3651
- [5] Lyons T W, Sanford M S. *Chem Rev*, 2010, 110: 1147
- [6] Giri R, Shi B F, Engle K M, Mauge N, Yu J Q. *Chem Soc Rev*, 2009, 38: 3242
- [7] Beletskaya I P, Cheprakov A V. *Chem Rev*, 2000, 100: 3009
- [8] Chen X, Engle K M, Wang D H, Yu J Q. *Angew Chem Int Ed*, 2009, 48: 5094
- [9] Daugulis O, Do H Q, Shabashov D. *Acc Chem Res*, 2009, 42: 1074
- [10] Alberico D, Scott M E, Lautens M. *Chem Rev*, 2007, 107: 174
- [11] Engle K M, Mei T S, Wasa M, Yu J Q. *Acc Chem Res*, 2012, 45: 788
- [12] Sun C L, Li B J, Shi Z J. *Chem Rev*, 2011, 111: 1293
- [13] Colby D A, Bergman R G, Ellman J A. *Chem Rev*, 2010, 110: 624
- [14] Ackermann L, Vicente R, Kapdi A R. *Angew Chem Int Ed*, 2009, 48, 9792
- [15] Wencel-Delord J, Dröge T, Liu F, Glorius F. *Chem Soc Rev*, 2011, 40: 4740
- [16] Cho S H, Kim J Y, Kwak J, Chang S. *Chem Soc Rev*, 2011, 40: 5068
- [17] Yeung C S, Dong V M. *Chem Rev*, 2011, 111: 1215
- [18] Ackermann L, Fenner S. *Org Lett*, 2011, 13: 6548
- [19] Li B, Feng H L, Xu S S, Wang B Q. *Chem Eur J*, 2011, 17: 12573
- [20] Li B, Ma J F, Wang N C, Feng H L, Xu S S, Wang B Q. *Org Lett*, 2012, 14: 736
- [21] Chinnagolla R K, Jeganmohan M. *Chem Commun*, 2012, 48: 2030
- [22] Ackermann L, Wang L H, Lygin A V. *Chem Sci*, 2012, 3: 177
- [23] Chinnagolla R K, Jeganmohan M. *Eur J Org Chem*, 2012, 77: 417
- [24] Ackermann L, Pospech J, Graczyk K, Rauch K. *Org Lett*, 2012, 14: 930
- [25] Ackermann L, Pospech J. *Org Lett*, 2011, 13: 4153
- [26] Chinnagolla R K, Pimparkar S, Jeganmohan M. *Org Lett*, 2012, 14: 3032
- [27] Parthasarathy K, Senthilkumar N, Jayakumar J, Cheng C H. *Org Lett*, 2012, 14: 3478
- [28] Thirunavukkarasu V S, Donati M, Ackermann L. *Org Lett*, 2012, 14: 3416
- [29] Ackermann L, Lygin A V. *Org Lett*, 2012, 14: 764
- [30] Ackermann L, Lygin A V, Hofmann N. *Org Lett*, 2011, 13: 3278
- [31] Padala K, Jeganmohan M. *Org Lett*, 2012, 14: 1134
- [32] Padala K, Jeganmohan M. *Org Lett*, 2011, 13: 6144
- [33] Padala K, Pimparkar S, Madasamy P, Jeganmohan M. *Chem Commun*, 2012, 48: 7140
- [34] Wang Y, Chi Y, Zhang W X, Xi Z F. *J Am Chem Soc*, 2012, 134: 2926
- [35] Zhu L L, Li X X, Zhou W, Li X, Chen Z L. *Org Chem*, 2011, 76: 8814
- [36] Zhu L Y, Song L Y, Tong R B. *Org Lett*, 2012, 14: 5892
- [37] Kleinbeck F, Toste F D. *J Am Chem Soc*, 2009, 131: 9178
- [38] Fesenko A A, Trafimova L A, Shutalev A D. *Org Biomol Chem*, 2012, 10: 447
- [39] Ye S Y, Yu Z X. *Chem Commun*, 2011, 47: 794
- [40] Li C W, Pati K, Lin G Y, Sohel S M A, Hung H H, Liu R S. *Angew Chem Int Ed*, 2010, 49: 9891
- [41] Barluenga J, Siqueiro R, Vicente R, Ballesteros A, Tomas M, Rodriguez M A. *Angew Chem Int Ed*, 2012, 51: 10377

Graphical Abstract

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Ru(II)-catalyzed ring expansion of alkynylcyclopropanes to alkylidenecyclobutanamines has been developed, where sulfonamides are needed.

- [42] Liao Y H, Houghton P J, Hoult J R S. *J Nat Prod*, 1999, 62: 1241
 [43] Fattorusso C, Stendardo E, Appendino G, Fattorusso E, Luciano P, Romano A, Tagliatela-Scafati O. *Org Lett*, 2007, 9: 2377
 [44] Yoshida M, Maeyama Y, Al-Amin M, Shishido K. *J Org Chem*, 2011, 76: 5813
 [45] Dabrowski J A, Moebius D C, Wommack A J, Kornahrens A F, Kingsbury T S. *Org Lett*, 2010, 12: 3598
 [46] Shibata T, Takami K, Kawachi A. *Org Lett*, 2006, 8: 1343

- [47] Canales E, Corey E J. *J Am Chem Soc*, 2007, 129: 12686
 [48] Ogasawara M, Okada A, Nakajima K, Takahashi T. *Org Lett*, 2009, 11: 177
 [49] Li C W, Pati K, Lin G Y, Sobel S M A, Hung H H, Liu R S. *Angew Chem Int Ed*, 2010, 49: 9891
 [50] Trost B M, Xie J, Maulide N. *J Am Chem Soc*, 2008, 130: 17258
 [51] Chen A J, Lin R Y, Lin Q J, Jiao N. *Chem Commun*, 2009: 6842
 [52] Ye S Y, Yu Z X. *Org Lett*, 2010, 12: 804

苯磺酰胺参与下二价钌催化环丙乙炔扩环反应

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摘要: 将二价钌配合物用于催化环丙乙炔扩环生成四元环结构的反应, 扩展了一系列环丙乙炔底物和磺酰胺底物, 并得到了较高的产率。

关键词: 过渡金属; 钌催化; 扩环反应; 苯磺酰胺

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