Synthetic Methods

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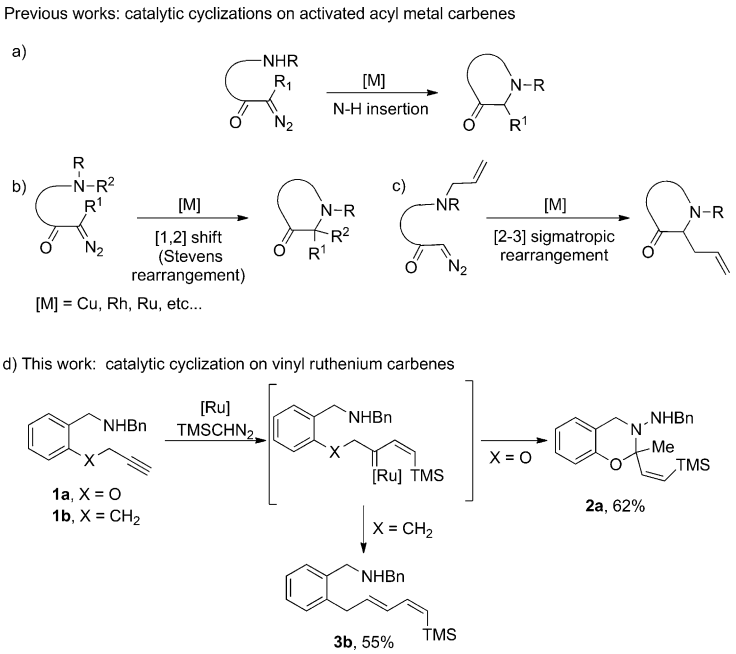
Nucleophilic Addition of Amines to Ruthenium Carbenes: *ortho*-(Alkynyloxy)benzylamine Cyclizations towards 1,3-Benzoxazines**

Carlos González-Rodríguez, José Ramón Suárez, Jesús A. Varela, and Carlos Saá**

Abstract: *A new ruthenium-catalyzed cyclization of ortho-(alkynyloxy)benzylamines to dihydro-1,3-benzoxazines is reported. The cyclization is thought to take place via the vinyl ruthenium carbene intermediates which are easily formed from [Cp*RuCl(cod)] and $N_2CHSiMe_3$. The mild reaction conditions and the efficiency of the procedure allow the easy preparation of a broad range of new 2-vinyl-2-substituted 1,3-benzoxazine derivatives. Rearrangement of an internal C(sp) in the starting material into a tetrasubstituted C(sp^3) atom in the final 1,3-benzoxazine is highly remarkable.*

The in situ generation of catalytically active metal carbenes from diazoalkanes (e.g., copper, rhodium, and ruthenium) has contributed to the recent development of synthetically useful transformations catalyzed by these intermediates.[1] Cyclopropa(e)nation reactions, which involve interaction of the generated metal carbenes with unsaturated units (alkenes, alkynes, enynes, etc.), and X–H bond insertions (X = C, O, S, N, Si, etc.) are characteristic transformations associated with these metal carbenes.[2] Recently, efficient syntheses of aza-heterocycles by direct rhodium-, copper-, and ruthenium-catalyzed intramolecular addition of amines to metal carbenes have been reported (Scheme 1). Metal carbenoid N–H insertion reactions (Scheme 1 a) and [1,2] rearrangements (Scheme 1 b) or [2,3] sigmatropic rearrangements of cyclic ammonium ylides (Scheme 1 c) afforded a broad range of azaheterocycles.[3] Nevertheless, the major drawback with these methods concerns the often troublesome installation of an activated diazoalkane (e.g., conjugated with a carbonyl group) within the starting material. A simple and mild generation of catalytic vinylcarbene ruthenium intermediates was recently introduced by Dixneuf and co-workers and employs a combination of a ruthenium precatalyst, a commercial diazo compound, and an alkyne.[4] We recently reported carbocyclizations involving the insertion of vinyl ruthenium carbenes into C(sp^3)–H bonds[5] and we have now envisioned a new entry into azaheterocycles by intramolecular nucleophilic addition of amines to these electrophilic ruthenium carbenes.[6] To test our hypothesis, we began the study with the cyclization of the alkynyloxyamine **1a** in the presence of the precatalyst [Cp*RuCl(cod)] and $TMSCHN_2$. To our surprise, the six-membered 2,2-disubstituted 1,3-benzoxazine **2a** was isolated in fairly good yield (Scheme 1 d).[7] The crucial role of the oxygenated tether in this unprecedented rearrangement[8] became evident when the alkynylamine **1b** smoothly evolved into the conjugated diene **3b**. To our knowledge, this is the first example of a nucleophilic addition of an amine to in situ generated vinyl ruthenium carbenes.



Scheme 1. Azacyclizations catalyzed by metal carbenes. TMS = trimethylsilyl.

1,3-Benzoxazine derivatives often display a wide range of biological activities,[9] undergo useful synthetic transformations,[10] and also polymerize by cationic ring-opening polymerization to form polybenzoxazines, which are thermosetting polymers exhibiting versatility in a wide range of applications.[11] The remarkable and useful properties of these compounds means that their preparation is always of great interest,[12] even though procedures based on transition-

[*] Dr. C. González-Rodríguez, Dr. J. R. Suárez, Dr. J. A. Varela, Prof. C. Saá
Departamento de Química Orgánica y Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CIQUS), Universidad de Santiago de Compostela
15782 Santiago de Compostela (Spain)
E-mail: carlos.saa@usc.es
Homepage: http://www.usc.es/gi1603/saa

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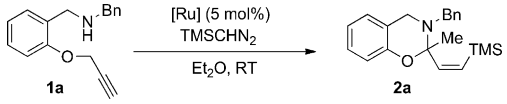
metal-catalyzed cyclizations remain scarce. Rhodium-catalyzed allylic rearrangement of 2-(allyloxy)benzylamines,[13] copper-catalyzed C–H bond oxidative activation[14] and photooxidation of aminoalcohols with photoredox catalysts of iridium[15] and ruthenium[16] are the most remarkable contributions. Herein we report a new and efficient ruthenium-catalyzed cyclization of *ortho*-(alkynyloxy)benzylamines towards 1,3-benzoxazines under very mild reaction conditions (Scheme 1 d).

The reaction was optimized using *N*-benzyl-1-[2-(prop-2-yn-1-yloxy)phenyl]methanamine (**1a**) as the test substrate (Table 1). The reaction of **1a** with $TMSCHN_2$ in the presence

Table 1: Optimization of the ruthenium-catalyzed cyclization of *N*-benzyl-1-[2-(prop-2-yn-1-yloxy)phenyl]methanamine **1a**.[a]



1a **2a**

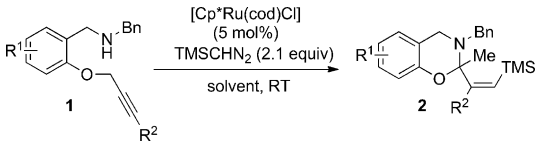
Entry	[Ru] catalyst	$TMSCHN_2$ (equiv)	Yield [%][b]
1	[Cp*Ru(cod)Cl]	2.1	62
2	[CpRu(cod)Cl]	2.1	–
3	$[Cp^*Ru(CH_3CN)_3]PF_6$	2.1	–[c]
4	$[Cp^*Ru(CH_3CN)_3]PF_6$/ NEt_4Cl	2.1	10
5	[Cp*Ru(cod)Cl]	2.1	46[d]
6	[Cp*Ru(cod)Cl]	3.0	50
7	[Cp*Ru(cod)Cl]	–[e]	–[f]

[a] Typical reaction conditions: [Ru] (5 mol%), **1a** (0.3 mmol), [**1a**] = 0.25 M, RT. [b] Yields of isolated products. [c] *N*-benzyl-*N*-methyl-1-[2-(prop-2-yn-1-yloxy)phenyl]methanamine (**1a′**) was obtained (9%). [d] Cp*Ru(cod)Cl, (10 mol%). [e] $N_2CHCOOEt$ (2.1 equiv) was used. [f] Ethyl 2-(benzyl(2-(prop-2-yn-1-yloxy)benzyl)amino)acetate **1a″** was obtained in 51% yield. cod = 1,5-cyclooctadiene, Cp* = C_5Me_5.

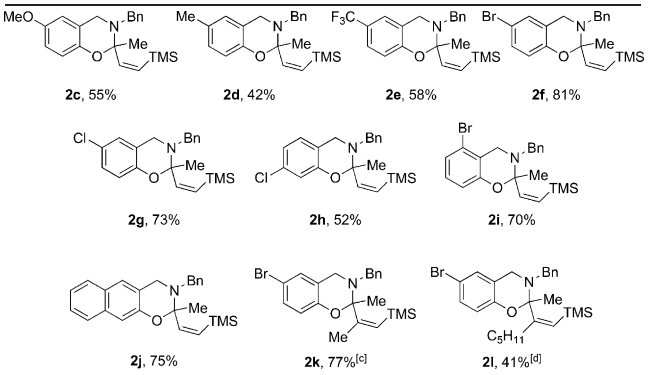
of [Cp*RuCl(cod)] (5% mol) in Et_2O at room temperature gave **2a** in 62% yield (entry 1). The reaction was extremely sensitive to the electronic and steric nature of the ruthenium catalyst since the starting material was totally recovered upon using [CpRuCl(cod)] (entry 2). Besides, cationic $[Cp^*Ru(CH_3CN)_3PF_6]$ or in situ formation of a neutral ruthenium catalyst, by treatment with Et_4NCl,[17] dramatically affected either the course of the reaction or the catalytic activity, thus giving very low yields of the methylated starting material **1a′** (9%)[3,18] or **2a** (10%), respectively (entries 3 and 4). Curiously, an increase in the catalyst loading or the amount of $TMSCHN_2$ was not beneficial for the cyclization reaction, with **2a** isolated in slightly lower yields (entries 5 and 6). The nature of the solvent was crucial as other cyclic ethers such as 1,4-dioxane or THF were tolerated but gave lower yields, but bulkier ethers and more polar protic or halogenated solvents were detrimental to the cyclization.[18] Electronic variation on the diazoalcane dramatically affected the course of the reaction since the α-aminoester **1a″**, derived from the carbenoid N–H insertion reaction,[3] was obtained when $N_2CHCOOEt$ was used (entry 7).[18]

Once the optimized reaction conditions were established, the scope and limitations of the cyclization reaction were explored by starting with electronically distinct benzylamine

Table 2: Ruthenium-catalyzed cyclization of the *ortho*-(alkynyloxy)-benzylamines **1c–l** to the 1,3-benzoxazines **2c–l**.[a,b]



1 **2**



2c, 55% **2d**, 42% **2e**, 58% **2f**, 81%

2g, 73% **2h**, 52% **2i**, 70%

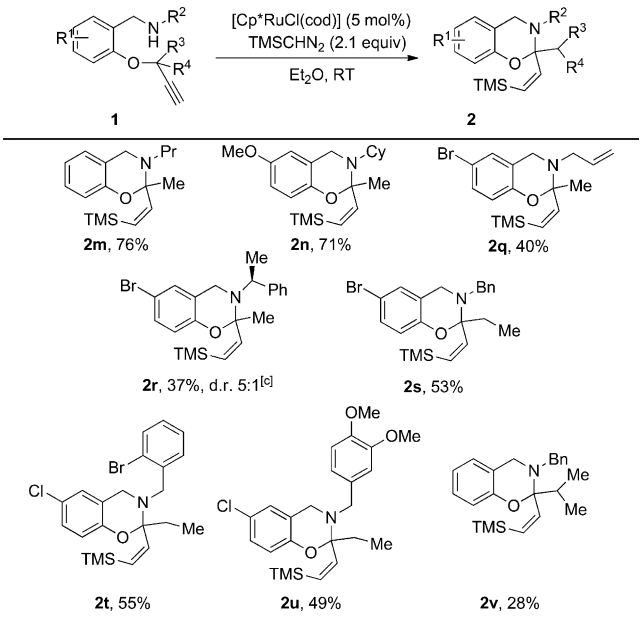
2j, 75% **2k**, 77%[c] **2l**, 41%[d]

[a] Typical reaction conditions: [Ru] (5 mol%), **1** (1 equiv), $TMSCHN_2$ (2.1 equiv), [**1**] = 0.25 M, RT. [b] Yields of the isolated products. [c] [Cp*Ru(cod)Cl], (10 mol%). [d] [Cp*Ru(cod)Cl], (10 mol%), 1,4-dioxane as solvent, 65 °C.

derivatives (Table 2). Electron-withdrawing and electron-donating aryl substituents are tolerated since the 1,3-benzoxazines **2c–f** were obtained in reasonably good yields. Thus, *para*-methoxy-, *para*-methyl-, *para*-trifluoromethyl-, and even *para*-bromobenzylamine smoothly gave the substituted 1,3-benzoxazines **2c–f**, with slightly better yields obtained for substrates bearing electron-poor substituents in the position *para* to the propargylic ether. Interestingly, the functionalized 4-, 5-, and 6-halo-substituted benzylamines could be efficiently converted into their corresponding halo-substituted 1,3-benzoxazines **2f–i** in fairly good yields. Further manipulation of the above aryl bromides and chlorides using palladium-catalyzed cross-coupling reactions provide an easy entry to polysubstituted benzoxazines.[19] Notably, cyclization of the naphthylamine derivative **1j** smoothly gave the naphthoxazine **2j** in very good yield. Gratifyingly, the non-terminal benzylamine derivative **1k** also cyclized to give **2k** in very good yield,[20] albeit with a longer reaction time compared to that of **2f** (60 h versus 6 h) and the need for a higher catalyst loading (10 mol%). Even a benzylamine with a long-chain-substituted alkyne, that is, **1l**, was able to cyclize to the corresponding 1,3-benzoxazine **2l**, albeit in low yield. In all cases the benzoxazines **2** were isolated with complete *Z* stereoselectivity for the silylated double bond.

We proceeded to investigate the effect of the N- and propargylic substitutions on the course of the reaction (Table 3). Gratifyingly, the presence of primary and secondary alkyl substituents on the nitrogen atom of the benzylamines **1**, for example, cyclohexyl or propyl, allowed the corresponding 1,3-benzoxazines **2m** and **2n** to be obtained in very good yields.[21] The chemoselectivity of the reaction was analyzed in the cyclization of the N-allyl-substituted benzylamine **1q**, from which **2q**, with an intact allyl group, was isolated in moderate yield. Interestingly, this result indicates

Table 3: Ruthenium-catalyzed cyclization of N-substituted *ortho*-(alkynyloxy)benzylamines (**1m–n**, **1q–v**) to 1,3-benzoxazines (**2m–n**, **2q–v**).[a,b]



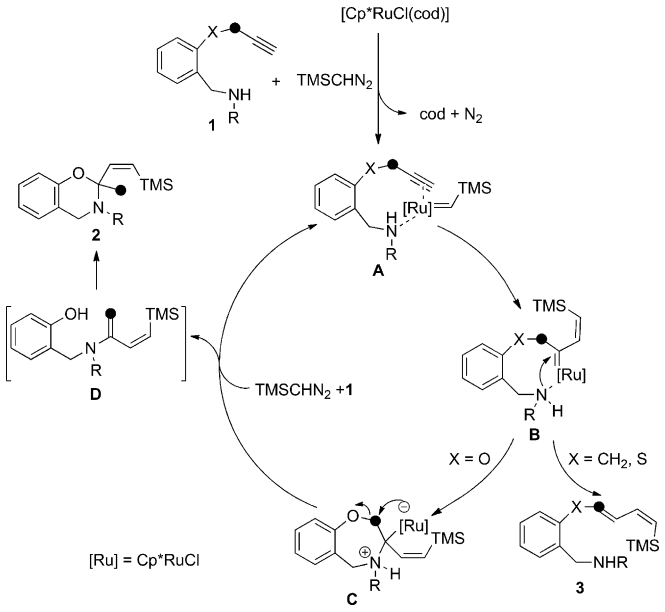
[a] Typical reaction conditions: [Ru] (5 mol%), **1** (1 equiv), $TMSCHN_2$ (2.1 equiv), [**1**] = 0.25 M, RT. [b] Yields of the isolated products. [c] [Cp*RuCl(cod)], (10 mol%).

that polar nucleophile/electrophile interactions dominate the reactivity of the putative carbene intermediate. Finally, the diastereoselectivity of the cyclization was explored with the chiral benzylamine **1r**, which gave **2r** (5.1 d.r. ratio) in low yield.

Having established the broad scope of the methodology, we investigated propargylic-substituted benzylamines (**1s–v**; Table 3). Interestingly, the ethyl-substituted 1,3-benzoxazines **2s–u** were the exclusive cyclized products in the ruthenium-catalyzed cyclization of the corresponding benzylamines **1s–u** bearing a methyl substituent in the propargylic position (R^3 = Me, R^4 = H). Furthermore, the isopropyl-substituted 1,3-benzoxazine **2v** was isolated from the reaction of the dimethylated substrate **1v** (R^3, R^4 = Me). These results clearly indicate that the propargylic carbon atom of the starting *ortho*-(alkynyloxy)benzylamines **1** becomes the alkyl substituent of the generated 2-vinyl-2-alkyl 1,3-benzoxazines **2**. This new rearrangement takes place starting from benzylamines bearing *ortho*-alkynyloxy substituents. However, when *ortho*-alkynylthio or *ortho*-alkynyltosylamide substituents were present in the starting benzylamine, the reaction did not give any cyclized products.[22]

In an effort to gain further insights into the mechanism of the reaction, a deuterium-labeling experiment was conducted. When the ruthenium-catalyzed cyclization of deuterated benzylamine [D]-**1f** (R^2 = D) was carried out under the optimized reaction conditions, deuterium scrambling was not observed and the deuterium atom was located at the vinylic position of the corresponding benzoxazine [D]-**2f**.[18]

The results obtained, including those of the labeling study and the cyclization of the propargylic-substituted benzylamines **2s–v**, strongly support the initial mechanistic hypothesis shown in Scheme 2.[23] The reaction begins with the starting complex, [Cp*RuCl(cod)], which easily loses its cod ligand in the presence of $TMSCHN_2$ and **1** to give the ruthenium carbene species **A**. Oxidative coupling to the ruthenacyclobutene followed by ring opening would lead to the ruthenium vinyl carbene species **B**, in which the coordination of the pendant amine could disfavor the coordination of a second diazoalkane unit.[24] The electrophilic ruthenium carbene could induce nucleophilic attack by the amine group to afford the zwitterionic intermediate **C**.[25] This intermediate is probably not formed when the nucleophilic character of the amine is diminished as in the tosylamide **1o**. Ring strain of the cyclic intermediate **C**, which has a good leaving group (phenoxide), would facilitate ring opening to afford the enamine intermediate **D**, with recovery of **A**. The reaction yields obtained for 1,3-benzoxazines (e.g., **2f** versus **2c**) seem to be consistent with the leaving capacity of the phenoxides **1**. In the absence of a phenoxide as a leaving group, the cyclization did not take place and **B** would evolve by β-elimination to afford the observed diene **3**. Finally, iminium formation from **D** is trapped with the phenoxide to give the final 1,3-benzoxazine **2** with concomitant release of the ruthenium complex which re-enters the catalytic cycle.[26]



Scheme 2. Mechanistic proposal for the ruthenium-catalyzed cyclization of *ortho*-(alkynyloxy)benzylamines.

In conclusion, we report a novel entry to 1,3-benzoxazines by ruthenium-catalyzed cyclization of *ortho*-(alkynyloxy)benzylamines. Our method relies on key features such as the use of readily available *ortho*-(alkynyloxy)benzylamines, commercially available $TMSCHN_2$, and [Cp*RuCl(cod)], the ability to introduce functionality at the different positions of the benzoxazine ring and the mild reaction conditions employed. This methodology is also the first example of the addition of an amine nucleophile to in situ generated vinyl ruthenium carbene intermediates for the direct formation of heterocyclic compounds. Rearrangement of an internal C(sp) of the starting material into a tetrasubstituted C(sp^3) in the final 1,3-benzoxazine is highly remarkable.

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[1] For synthetic applications of metal carbenes, see: a) *Contemporary Carbene Chemistry* (Eds.: R. A. Moss, M. P. Doyle), Wiley, Hoboken, **2014**; b) F. Zaragoza, *Metal Carbenes in Organic Synthesis*, Wiley-VCH, Weinheim, **1999**; c) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*, Wiley, New York, **1998**.

[2] For reviews, see: a) S.-F. Zhu, Q.-L. Zhou, *Acc. Chem. Res.* **2012**, *45*, 1365 – 1377; b) X. Zhao, Y. Zhang, J. Wang, *Chem. Commun.* **2012**, *48*, 10162 – 10173; c) H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417 – 424; d) Z. Zhang, J. Wang, *Tetrahedron* **2008**, *64*, 6577 – 6605; e) M. P. Doyle, *Top. Organomet. Chem.* **2004**, *13*, 203 – 222; f) M. P. Doyle, *Chem. Rev.* **1986**, *86*, 919 – 939.

[3] For selected metal carbenoid N-H insertions, see: a) N. Ishida, Y. Shimamoto, T. Yano, M. Murakami, *J. Am. Chem. Soc.* **2013**, *135*, 19103 – 19106; b) A. C. B. Burtoloso, C. R. D. Correia, *Tetrahedron Lett.* **2004**, *45*, 3355 – 3358; c) F. A. Davis, J. Deng, *Tetrahedron* **2004**, *60*, 5111 – 5115; d) F. A. Davis, T. Fang, R. Goswami, *Org. Lett.* **2002**, *4*, 1599 – 1602; e) R. M. Williams, B. H. Lee, M. M. Miller, O. P. Anderson, *J. Am. Chem. Soc.* **1989**, *111*, 1073 – 1081; For a review on the formation of nitrogen ylides from metal carbene complexes, see: f) J. Wang in *Comprehensive Organometallic Chemistry III* (Eds.: D. M. P. Mingos, R. H. Crabtree), Elsevier, Oxford, **2007**, pp. 151 – 178; For selected examples of the [1,2] shift (Stevens rearrangement), see: g) J. A. Vanecko, F. G. West, *Org. Lett.* **2005**, *7*, 2949 – 2952; h) J. A. Vanecko, F. G. West, *Org. Lett.* **2002**, *4*, 2813 – 2816; i) A. Padwa, L. S. Beall, C. K. Eidell, K. J. Worsencroft, *J. Org. Chem.* **2001**, *66*, 2414 – 2421; For selected examples of the [2,3] sigmatropic rearrangement, see: j) C.-Y. Zhou, W.-Y. Yu, P. W. H. Chan, C.-M. Che, *J. Org. Chem.* **2004**, *69*, 7072 – 7082; k) J. S. Clark, M. D. Middleton, *Org. Lett.* **2002**, *4*, 765 – 768; l) J. S. Clark, P. B. Hodgson, M. D. Goldsmith, A. J. Blake, P. A. Cooke, L. J. Street, *J. Chem. Soc. Perkin Trans. 1* **2001**, 3325 – 3337; m) D. L. Wright, R. M. Weekly, R. Groff, M. C. McMills, *Tetrahedron Lett.* **1996**, *37*, 2165 – 2168.

[4] a) S. Moulin, H. Zhang, S. Raju, C. Bruneau, S. Dérien, *Chem. Eur. J.* **2013**, *19*, 3292 – 3296; b) C. Vovard-Le Bray, S. Dérien, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2009**, *48*, 1439 – 1442; *Angew. Chem.* **2009**, *121*, 1467 – 1470; c) F. Monnier, C. Vovard-Le Bray, D. Castillo, V. Aubert, S. Derien, P. H. Dixneuf, L. Toupet, A. Ienco, C. Mealli, *J. Am. Chem. Soc.* **2007**, *129*, 6037 – 6049; d) F. Monnier, D. Castillo, S. Dérien, L. Toupet, P. H. Dixneuf, *Angew. Chem. Int. Ed.* **2003**, *42*, 5474 – 5477; *Angew. Chem.* **2003**, *115*, 5632 – 5635; e) J. Le Paih, S. Dérien, I. Özdemir, P. H. Dixneuf, *J. Am. Chem. Soc.* **2000**, *122*, 7400 – 7401.

[5] F. Cambeiro, S. López, J. A. Varela, C. Saá, *Angew. Chem. Int. Ed.* **2012**, *51*, 723 – 727; *Angew. Chem.* **2012**, *124*, 747 – 751.

[6] For a nucleophilic addition of carbonyl groups to electrophilic ruthenium carbenes, see: F. Cambeiro, S. López, J. A. Varela, C. Saá, *Angew. Chem. Int. Ed.* **2014**, *53*, 5959 – 5963; *Angew. Chem.* **2014**, *126*, 6069 – 6073.

[7] For synthesis of vinyl benzoxazines and benzoxazinones, see: a) S. Shaaban, B. Peng, N. Maulide, *Synlett* **2013**, 1722 – 1724; b) V. Scherrer, M. Jackson-Mülly, J. Zsindely, H. Schmid, *Helv. Chim. Acta* **1978**, *61*, 716 – 731; c) A. O. Fitton, M. P. Ward, *J. Chem. Soc. C* **1971**, 146 – 149.

[8] For a related rearrangement toward benzofuranones, see: M. Padmanaban, A. T. Biju, F. Glorius, *Org. Lett.* **2011**, *13*, 5624 – 5627.

[9] For recently described examples, see: a) B. P. Mathew, A. Kumar, S. Sharma, P. K. Shula, M. Nath, *Eur. J. Med. Chem.* **2010**, *45*, 1502 – 1507; b) E. Petrlíková, K. Waisser, H. Divišova, P. Husaková, P. Vrabcova, J. Kuneš, K. Kolár, J. Stolariková, *Bioorg. Med. Chem.* **2010**, *18*, 8178 – 8187; c) S. Wang, Y. Li, Y. Liu, A. Lu, Q. You, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 4095 – 4097; d) G. R. Madhavan, R. Chakrabarti, K. A. Reddy, B. M. Rajesh, V. Balraju, P. B. Rao, R. Rajagopalan, J. Iqbal, *Bioorg. Med. Chem.* **2006**, *14*, 584 – 591.

[10] a) G. Cheng, X. Wang, D. Su, H. Liu, F. Liu, Y. Hu, *J. Org. Chem.* **2010**, *75*, 1911 – 1916; b) Y. Dong, J. Sun, X. Wang, X. Xu, L. Cao, Y. Hu, *Tetrahedron: Asymmetry* **2004**, *15*, 1667 – 1672; c) J. Lu, X. Xu, S. Wang, C. Wang, Y. Hu, H. Hu, *J. Chem. Soc. Perkin Trans. 1* **2002**, 2900 – 2903.

[11] a) *Handbook of benzoxazine resins* (Eds.: H. Ishida, T. Agag), Elsevier, Amsterdam, **2011**; b) N. N. Ghosh, B. Kiskan, Y. Yagci, *Prog. Polym. Sci.* **2007**, *32*, 1344 – 1391; For recent examples, see: c) L. Jin, T. Agag, Y. Yagci, H. Ishida, *Macromolecules* **2011**, *44*, 767 – 772; d) T. Agag, C. R. Arza, F. H. J. Maurer, H. Ishida, *Macromolecules* **2010**, *43*, 2748 – 2758.

[12] For reviews, see: a) ref. [11a] and [11b]; b) K. Bujnowski, A. Adamczyk, L. Synoradzki, *Org. Prep. Proced. Int.* **2007**, *39*, 417 – 446; For recent examples, see: c) M. T. Richers, M. Breugst, A. Y. Platonova, A. Ullrich, A. Dieckmann, K. N. Houk, D. Seidel, *J. Am. Chem. Soc.* **2014**, *136*, 6123 – 6135; d) S. Mahato, S. Haldar, C. K. Jana, *Chem. Commun.* **2014**, *50*, 332 – 334; e) D. Xu, Y. Lin, Y. Chen, J. Zhang, W. Cao, J. Chen, M. S. Wong, *Tetrahedron* **2013**, *69*, 6144 – 6149; f) I. Szatmári, M. Heydenreich, A. Koch, F. Fulop, E. Kleinpeter, *Tetrahedron* **2013**, *69*, 7455 – 7465; g) V. A. Osyanin, E. A. Ivleva, D. V. Osipov, Y. N. Klimochkin, *Chem. Heterocycl. Compd.* **2011**, *47*, 845 – 850; h) S. Vellalath, I. Coric, B. List, *Angew. Chem. Int. Ed.* **2010**, *49*, 9749 – 9752; *Angew. Chem.* **2010**, *122*, 9943 – 9946; i) B. P. Mathew, M. Nath, *J. Heterocycl. Chem.* **2009**, *46*, 1003 – 1006.

[13] E. M. Campl, W. R. Jackson, Q. J. McCubbin, A. E. Trnacek, *J. Chem. Soc. Chem. Commun.* **1994**, 2763 – 2763.

[14] M. L. Deb, S. S. Dey, I. Bento, M. T. Barros, C. D. Maycock, *Angew. Chem. Int. Ed.* **2013**, *52*, 9791 – 9795; *Angew. Chem.* **2013**, *125*, 9973 – 9977.

[15] J. Xuan, Z.-J. Feng, S.-W. Duan, W.-J. Xiao, *RSC Adv.* **2012**, *2*, 4065 – 4068.

[16] C. L. Mathis, B. M. Gist, C. K. Frederickson, K. M. Midkiff, C. C. Marvin, *Tetrahedron Lett.* **2013**, *54*, 2101 – 2104.

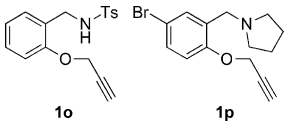
[17] For the in situ generation of neutral $Cp^*RuCl(CH_3CN)_2$, see: J. A. Varela, L. Castedo, C. Saá, *Org. Lett.* **2003**, *5*, 2841 – 2844.

[18] See the Supporting Information for details.

[19] M. Å. Petersen, E. Deniz, M. B. Nielsen, S. Sortino, F. M. Raymo, *Eur. J. Org. Chem.* **2009**, 4333 – 4339.

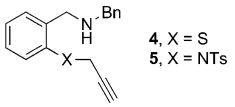
[20] The structure of compound **2k** was unequivocally assigned by X-ray diffraction analysis. CCDC 1027739 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[21] With a poorly coordinating and less nucleophilic nitrogen atom in tosylamide **1o** the reaction resulted in a complex mixture. On the other hand, tertiary pyrrolidine derivative **1p** was recovered unaltered after 24 h.



1o **1p**

[22] The reaction of thioether **4** under optimized reaction conditions afforded the corresponding dienyl sulfide **3** in 56% yield and the reaction of tosylamide **5** gave a complex reaction mixture. See Supporting Information for details.



4, X = S
5, X = NTs

[23] Alternatively, direct attack of the amine to the triple bond followed by ring opening without formation of the initial ruthenium carbene cannot be ruled out (O,N- "extended" Rautenstrauch rearrangement).[4b] However, when **1b** (X = CH_2) was subjected to the reaction conditions, smooth formation of the diene **3b** was observed and suggests the formation of a vinyl ruthenium carbene intermediate.

[24] J. Le Paih, C. Vovard-Le Bray, S. Dérien, P. H. Dixneuf, *J. Am. Chem. Soc.* **2010**, *132*, 7391 – 7397.

[25] The mechanistic alternative based on1,2-propargylic shift to give an enolether intermediate followed by the amine nucleophilic attack was discarded since the parent (prop-2-yn-1-yloxy)benzene gave the expected disylilated *Z*,*Z*-diene (84%, via a vinyl Ru carbene, Ref. [24]) instead the rearranged enolether derivative (Rautenstrauch product). See the Supporting Information for details.

[26] For a Brønsted acid catalyzed cyclization through benzoylimine intermediates, see Ref. [12h].