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Rhodium

Enantioselective Rhodium(I) Donor Carbenoid-Mediated Cascade Triggered by a Base-Free Decomposition of Arylsulfonyl Hydrazones

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Abstract: The reaction of diyne arylsulfonyl hydrazone substrates under rhodium(I)/BINAP catalysis gives access to sulfonated azacyclic frameworks in a highly enantioselective manner. This new cascade process considerably increases the molecular complexity by generating two C–C bonds, one C–S bond, and one C–H bond. Theoretical calculations, competitive experiments, and deuterium labeling have jointly been used to propose a mechanism that accounts for the reaction. The mechanism involves the formation of vinyl rhodium carbenoids, hydride migratory insertion, and intermolecular stereoselective nucleophilic attack. The last two steps are the key to the stereoselectivity of the process.

Introduction

Metal carbenoids are important reaction intermediates that are capable of mediating numerous different reactions, such as cyclopropanation, cyclopropenation, C–H insertion, C–C coupling, ylide formation, metathesis, and migratory insertion.[1] Owing to their versatility and high reactivity, they have great potential as participants in step-economic and waste-reducing cascade processes, which are particularly desirable for the construction of complex molecules.

The reactivity and stability of the metal carbenoids is highly dependent on their substitution pattern. Following Davies' classification, acceptor and acceptor/acceptor metal carbenoids are extremely reactive and behave as highly electrophilic species. On the other hand, donor/acceptor-substituted carbenoids facilitate highly chemoselective and stereoselective reactions due to the ability of the donor group to moderate their reactivity. Although the reactivity of these carbenoids is well established, a major challenge is to develop reactions of metal carbenoids without electron-withdrawing substituents, also known as donor carbenoids.

Among the different metals, rhodium(II) carbenoids, which can be formed by the decomposition of diazo compounds with rhodium(II) dimers, have shown great potential in stereoselective transformations.[2] Alternatively, *N*-tosylhydrazones[3] and *N*-sulfonyl-1,2,3-triazoles,[4] among other sources,[5] can be used to generate metal carbenoids in situ, which both circumvents the use of hazardous and potentially explosive diazo carbonyl compounds and broadens the range of possible synthetic transformations.

Rhodium(I) has also been reported to catalyze a few interesting reactions that involve carbenoid intermediates. The corresponding carbenoids have been formed by transmetallation from a chromium alkenyl Fischer carbene,[6] by oxidation of an ynamide,[7] by decomposition of diazo compounds,[8] and by decomposition of tosylhydrazones.[9] However, rhodium(I) complexes of donor carbenoids have only been achieved when chromium alkenyl Fischer carbenes[6] and tosylhydrazones[9] were used as carbenoid sources.

Although rhodium(I) complexes are known to mediate various asymmetric reactions,[10] the development of stereoselective processes that make use of rhodium(I)-carbene chemistry has been little explored (Scheme 1).

In 2010, Hayashi et al. reported the use of a cationic chiral diene–Rh^{I} complex for the asymmetric cyclopropanation of alkenes with dimethyl diazomalonate.[8b] Hu et al. also used a rhodium(I) complex with a chiral diene ligand to promote an enantioselective three-component reaction, in which an intermediate ylide was formed that was subsequently involved in a Michael addition-type reaction.[8c] In 2014, Murakami et al. reported the enantioselective insertion of cyclopentanols that was promoted by a Rh^{I}–carbene complex, which was formed upon decomposition of tosylhydrazones and was stabilized with diphosphine ligands.[9] Finally, Xu et al. very recently reported the asymmetric carbene insertion into B–H bonds to give access to functionalized organoboranes, again by using a chiral diene rhodium(I) complex.[8f] It should be noted that only in the case of tosylhydrazones[9] was an enantioselective process achieved with carbenes that do not have an electron-withdrawing group.

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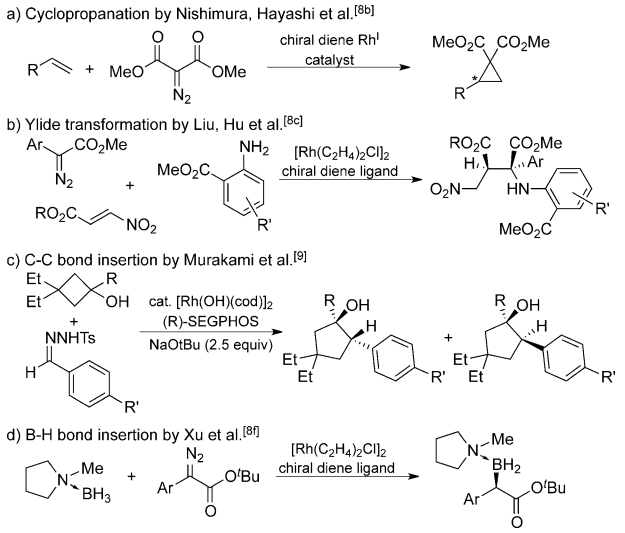


Scheme 1. Rhodium(I)–carbene-mediated asymmetric transformations.

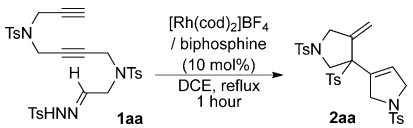
Considering that the formation of vinyl carbenes through the reaction of alkynes and rhodium(II) carbenoids (carbene–alkyne metathesis) constitutes an attractive entry to a cascade processes,[11] we envisioned that the use of rhodium(I) could afford a new enantioselective cascade process. Therefore, herein, we aimed to develop a cascade process that was triggered by the decomposition of arylsulfonyl hydrazones, which are a much safer and more versatile source of donor carbenoids, in the presence of a rhodium(I) complex to form a rhodium(I) carbenoid that could react in an intramolecular fashion with an alkyne. Accordingly, we report a cascade process that is mediated by rhodium(I) vinyl carbenoid intermediates.

Results and Discussion

As a first step, we designed and synthesized a diyne tosylhydrazone model substrate **1aa** with *N*-tosyl (NTs) groups as linkers (see the Supporting Information for details of the synthesis). We then evaluated the substrate reactivity with a series of rhodium catalysts (Table 1).

Abstract in Catalan: *La reacció catalitzada per rodi(I)/BINAP de substrats contenint dos alquins i una sulfonilhidrazona permet sintetitzar compostos nitrogenats amb un grup sulfona de forma altament enantioselectiva. Aquest nou procés en cascada augmenta considerablement la complexitat molecular ja que genera dos enllaços C–C, un enllaç C–S i un enllaç C–H. S'ha proposat un mecanisme per al procés desenvolupat en base als resultats obtinguts mitjançant càlculs DFT, experiments de competició i marcatge amb deuteri. El mecanisme involucra la formació d'un vinilcarbenoid de rodi, una inserció migratòria d'hidrur i un atac nucleofílic intermolecular estereoselectiu. Els dos darrers passos són claus per a l'enantioselectivitat del procés.*

Table 1. Optimization of the rhodium(I)-catalyzed cyclization of diyne tosylhydrazone **1aa**.[a]



Entry	[Rh]	Biphosphine	Base	Yield [%][b]	*ee* [%]
1	$[Rh(cod)_2]BF_4$	*rac*-BINAP	KO*t*Bu	–	–
2[c]	$[Rh(cod)_2]BF_4$	*rac*-BINAP	K_2CO_3	47	–
3	$[Rh(cod)_2]BF_4$	*rac*-BINAP		46	–
4	$[Rh(cod)_2]BF_4$	(*R*)-BINAP		58	>99
5	$[Rh(cod)_2]BF_4$	(*S*)-BINAP		45	>99[d]
6	$[Rh(cod)_2]BF_4$	(*R*)-DTBM-Segphos		–	–
7	$[Rh(cod)_2]BF_4$	BIPHEP		–	–
8	$[Rh(cod)_2]BF_4$	(*R*)-TolBINAP		55	>99
9[e]	$[Rh(cod)_2]BF_4$	(*R*)-TolBINAP		43	n.d.
10[f]	$[Rh(cod)_2]BF_4$	(*R*)-TolBINAP		48	n.d.
11[g]	$[Rh(cod)_2]BF_4$	(*R*)-TolBINAP		51	n.d.
12	$[RhCl(cod)_2]$	(*R*)-BINAP		–	–
13[h]	$[Rh_2(OAc)_2]$	–		–	–

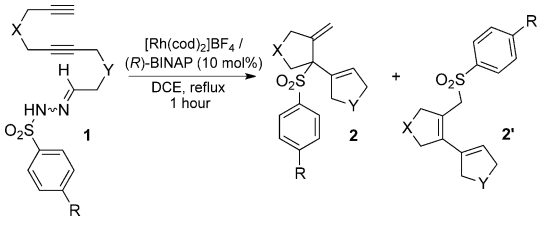
[a] Reaction conditions: $[Rh(cod)_2]BF_4$ (10 mol%), (*R*)-BINAP (10 mol%), **1aa** (0.10 mmol, 0.03 M), dichloroethane, heat at reflux, 1 h. [b] Yield of isolated product after column chromatography. [c] Reaction time: 1.5 h. [d] The reaction forms the opposite enantiomer to the one obtained with (*R*)-BINAP. [e] Reaction in chlorobenzene at 110 °C. [f] Reaction in chlorobenzene at 110 °C under microwave heating for 10 min. [g] Reaction concentration: 0.01 M. [h] Starting material was recovered.

The use of a combination of BINAP with a cationic rhodium source, such as $[Rh(cod)_2]BF_4$, in the presence of potassium *tert*-butoxide only led to the decomposition of the starting material (Table 1, entry 1). Nevertheless, changing the base to potassium carbonate[12] effectively furnished a new cyclization product **2aa** after 1.5 h (entry 2). Careful structural analysis by NMR spectroscopy (see the Supporting Information) showed that two new C–C bonds had formed by a carbocyclization reaction, hydride migration had constructed a new C–H bond, and a tosyl migration led to the generation of a C–S bond, with the corresponding loss of N_2. To our delight, carrying the reaction out in the absence of a base furnished the product **2aa** in the same yield over a decreased reaction time (entry 3). We then tested the process under enantioselective conditions; accordingly, the use of either (*R*)- or (*S*)-BINAP in combination with $[Rh(cod)_2]BF_4$ enabled the isolation of the two enantiomers of the cycloadduct **2aa**, respectively, with very high enantiomeric excesses (entries 4 and 5). No reaction took place when the temperature was lowered to 65 °C, and the use of biphosphines of different steric bulk resulted in a complete loss of reactivity (entries 6 and 7). (*R*)-TolBINAP gave analogous results to those that were obtained with (*R*)-BINAP (entry 8). The yield was not improved by increasing the reaction temperature to 110 °C, by either conventional or microwave heating (entries 9 and 10), or by changing the concentration of the reaction mixture (entry 11). Degradation of the substrate **1aa** was observed when the cationic rhodium source was replaced by a neutral one, such as $[RhCl(cod)_2]$ (entry 12). The use of $[Rh(OH)(cod)_2]$, either alone or in combination with bases, such

as KO*t*Bu, also led to decomposition of the substrate **1aa**. Interestingly, no reaction took place when the rhodium(II) dimer $[Rh_2(OAc)_4]$, which was previously used in the cyclization of diazo alkynyl ketones,[11b] was used as the catalyst, even when the reaction time was prolonged to 24 h. A control reaction without a transition-metal catalyst showed no reaction and only recovery of the starting material.

Having developed an extremely interesting new process for the formation of a C–S bond in an enantioselective manner,[13] we wished to examine how broadly this transformation could be applied (Table 2).

Table 2. Scope of the Rh^I-catalysed cyclization of diyne aryl hydrazones **1**.

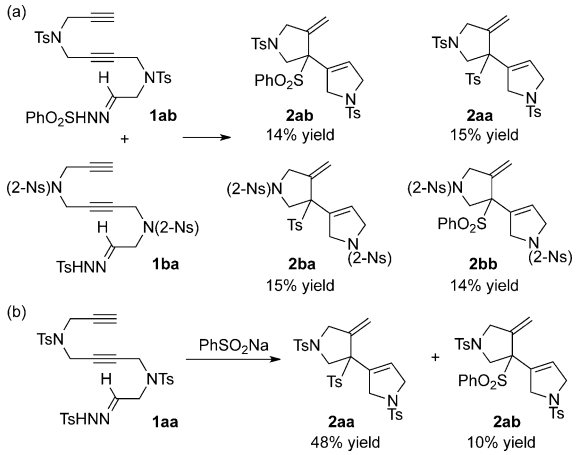


Entry	1	X	Y	R	2/2′[a]	Yield [%][b]	*ee* of 2 [%]
1	**1aa**	NTs	NTs	CH_3	>20:1	58	>99
2	**1ab**	NTs	NTs	H	3.2:1	55	>99
3	**1ac**	NTs	NTs	OMe	>20:1	33	>99
4	**1ad**	NTs	NTs	NO_2	1.4:1	34	>99
5	**1ba**	N(2-Ns)	N(2-Ns)	CH_3	>20:1	43	69
6	**1ca**	NTs	$C(CO_2Et)_2$	CH_3	>20:1	45	96
7	**1da**	O	NTs	CH_3	>20:1	44	93

[a] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture. [b] Yield of isolated product after column chromatography.

Changing the *p*-toluenesulfonyl ring of the hydrazone moiety to a phenylsulfonyl group promoted the formation of the two isomers **2** and **2′** in a 3.2:1 ratio, respectively, which was due to a variation in the positions that the phenylsulfonyl group migrated to (Table 2, entry 2). Switching to an electron-donating substituent on the phenyl ring, such as OMe, ensured that the reaction proceeded with high levels of regioselectivity (entry 3). On the other hand, an electron-withdrawing substituent on the phenyl ring, such as NO_2, promoted the reaction at the less hindered position and afforded a 1.4:1 ratio of regioisomers **2** and **2′** (entry 4). Therefore, we can assume that the regioselectivity would be high with electron-rich sulfonyl substituents on the phenyl ring. The influence of the tether group was then studied: changing the tosyl group to a 2-nitrophenylsulfonyl ring (N(2-Ns)) in the tether gave bicycle **2ba** with a slightly lower level of enantioselectivity (entry 5). The cycloaddition of substrates **1ca** and **da**, in which one of the nitrogenated tethers was substituted by either a malonate or oxygen, respectively, also furnished the corresponding cycloadducts in a highly regioselective and enantioselective way (entries 6 and 7).

We were eager to gain a better understanding of the reaction mechanism to obtain a greater appreciation for the potential of this transformation. Initially, we focused our attention on establishing whether the migration of the sulfonyl group occurred by an intramolecular or intermolecular pathway. A crossover experiment between equimolar amounts of reactants **1ab** and **1ba**, which differ in both the tethers and the aryl group of the hydrazone, was conducted. The reaction yielded equal amounts of all four possible products, which clearly indicates that the migration proceeds in an intermolecular manner (Scheme 2a). To verify the form in which the sulfonyl group

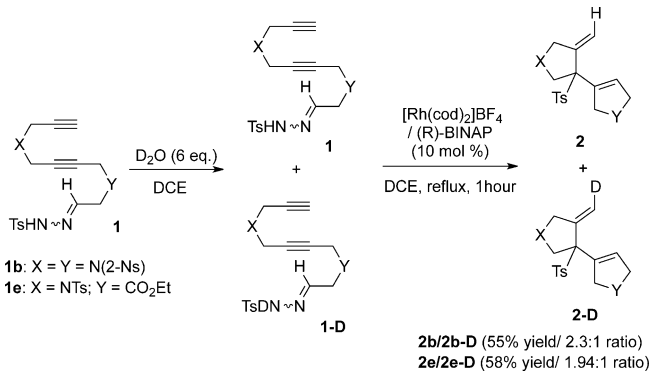


Scheme 2. Competitive experiments.[14]

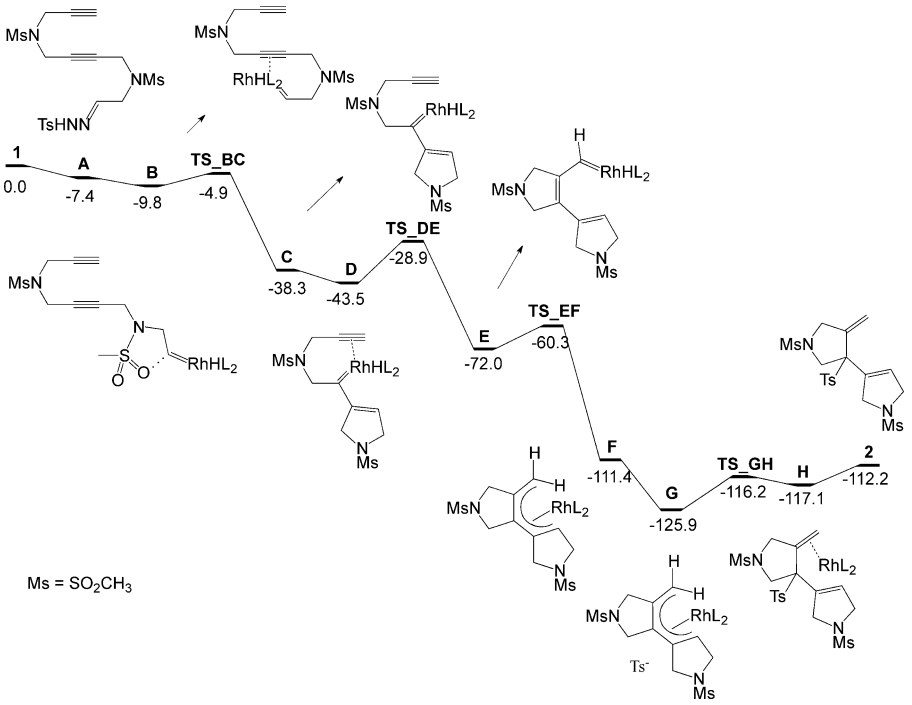
was transferred, we performed another competitive experiment by adding sodium phenylsulfinate to the cyclization reaction of **1aa**, which has a tosylhydrazone group (Scheme 2b). Analysis by mass spectrometry and NMR spectroscopy revealed that the reaction afforded a mixture of the expected product **2aa** and the competitive product **2ab**. The competition of the external sulfinate anion indicates that the decomposition of the hydrazone generates a sulfinate anion in situ.

We then turned our attention to the C–H bond that is formed in the cyclization reaction. The working hypothesis for this step was that the H atom on the tosylhydrazone was transferred to the terminal alkyne. To confirm this theory, we conducted deuterium-labeling experiments. By stirring the corresponding substrate **1** in anhydrous dichloroethane in the presence of 6 equiv of D_2O, the NH was partially exchanged (1:6.1 ratio of products **1** and **1-D**, determined by ^{1}H NMR spectroscopy), which led to a deuterium-enriched sample. ^{1}H and ^{2}H NMR spectroscopy revealed the stereoselective incorporation of the deuterium at the olefinic *trans* position during the cyclization reaction under the optimized conditions (Scheme 3, see the Supporting Information).

To establish a mechanism that could account for the whole set of experimental results, DFT calculations were performed with the B3LYP functional.[15] The calculations were carried out on a model substrate, in which the *N*-tosyl tethers were replaced by *N*-mesyl tethers to reduce the computational cost. The results are summarized in the Gibbs energy profile in Scheme 4.



Scheme 3. Deuterium-labeling experiments.

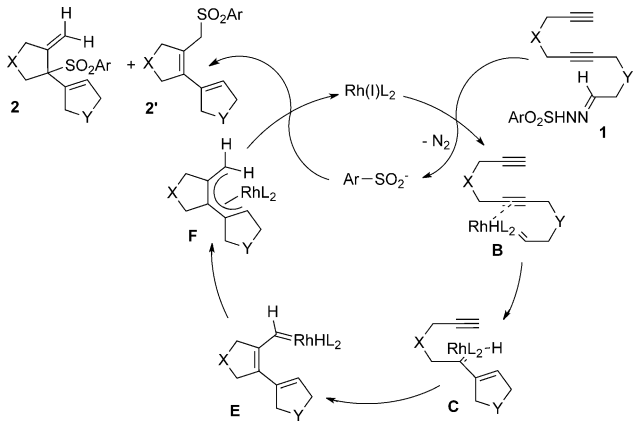


Scheme 4. Gibbs energy profile (in kcal mol^{-1}) for the cascade reaction of substrate **1** catalyzed by Rh^{I}/BINAP to form product **2**.

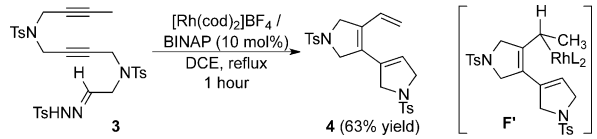
The first step involves the reaction of the arylsulfonyl hydrazone moiety in substrate **1** with the rhodium catalyst Rh^{I}L$_2$ (L$_2$ = biphosphine) to give the rhodium carbenoid complex **A**, which is stabilized by the coordination of one of the oxygen atoms of the sulfonamide moiety with the carbenic carbon.[16] This process, which releases N_2 and the arylsulfinate, is exergonic by 7.4 kcal mol^{-1}. Subsequent η^2-coordination of the Rh atom to the central alkyne group (Rh···C distances of 2.375 and 2.639 Å) leads to the rhodium carbenoid **B** through a process that is slightly exergonic by 2.4 kcal mol^{-1}. The next step involves a $[_{\pi}2_s + _{\pi}2_a]$ addition of the central alkyne to the rhodium carbenoid double bond and subsequent electrocyclic opening of the newly formed rhodacyclobutene to yield a new vinyl rhodium(I) carbene **C**. A similar ring opening of the rhodacyclobutene has already been described in a cobaltacyclobutene complex.[17] Transformation of intermediate **B** into **C** has a low Gibbs energy barrier of 4.9 kcal mol^{-1} and releases 28.5 kcal mol^{-1}. The 16-electron complex **C** rearranges to the 18-electron complex **D**, in which the terminal alkyne group is η^2-coordinated to the Rh atom. Intermediate **D** then reacts with the terminal alkyne to form vinyl rhodium(I) carbene **E**. The transformation of intermediate **D** into **E** follows the same reaction pathway as the process that converts intermediate **B** into **C**; it is exergonic by the same energy as in the conversion from **B** to **C** (28.5 kcal mol^{-1}), and it has to surmount a Gibbs energy barrier of 14.6 kcal mol^{-1}. The conversion from intermediate **D** to **E** is the rate-determining step (rds); accordingly, complex **D** and the transition state that arises in its conversion to complex **E** are the rate-determining intermediate and transition state, respectively.[18] Subsequent metal–carbene migratory insertion, in which the hydride migrates from the metal to the carbenic carbon, leads to a η^5-pentadienyl rhodium intermediate **F**. Transformation of complex **E** to **F** is thermodynamically very favorable (39.4 kcal mol^{-1}) and takes place through an energy barrier of 11.7 kcal mol^{-1}. In the final part of the reaction mechanism, the η^5-pentadienyl rhodium intermediate **G**, which constitutes complex **F** interacting with Ts$^-$, is attacked by the *p*-methylphenylsulfinate anion in a stereoselective way to furnish the final cyclized product **2** and to regenerate the catalytically active species. This last part of the reaction is slightly endergonic (13.2 kcal mol^{-1}).[19]

Overall, our data suggests that the Rh-catalyzed cyclization proceeds by the mechanism that is depicted in Scheme 5. The rhodium(I) carbenoid is formed through a $[_{\pi}2_s + _{\pi}2_a]$ addition with the alkyne and subsequent electrocyclic opening of the rhodacyclobutene to release N_2 and arylsulfinate, which generates vinyl rhodium carbenes **C** and **E**. A metal-to-carbene migratory insertion step then leads to the η^5-pentadienyl rhodium intermediate **F**, which undergoes an intermolecular, stereoselective reaction with the arylsulfinate to furnish the final cyclization product **2** and to regenerate the catalytically active species.

To further confirm the mechanism, we evaluated the reactivity of substrate **3** that featured a methyl substituent at the terminal alkyne, in which β-hydride elimination could efficiently compete after the metal-to-carbene migratory insertion. Substrate **3** was reacted under the optimized conditions to afford product **4**, in which the sulfonyl group was not incorporated (Scheme 6). Trienic product **4** arises from a β-hydride elimina-



Scheme 5. Proposed mechanism for the rhodium-catalyzed cyclization reaction.



Scheme 6. Rhodium-catalyzed cyclization of a substrate that contains two internal alkynes.

tion of one of the H atoms of the methyl group of intermediate **F′**, which is formed upon metal-to-carbene hydride migratory insertion.

Conclusion

We have described a new stereoselective cascade reaction that affords a sulfonated azacyclic framework through a process in which two C–C bonds are formed and both a hydrogen atom and a sulfonyl group migrate in a stereoselective manner. We proposed, with the support of DFT calculations, that this mechanism, which has also been studied by competitive and isotope-labeling experiments, takes place through rhodium(I)–carbene intermediates and involves a metal-to-carbene migratory insertion step.

Experimental Section

General procedure for the cyclization reaction

$[Rh(cod)_2]BF_4$ (0.0040 g, 0.01 mmol) and (*R*)-BINAP (0.0068 g, 0.01 mmol) were dissolved in dichloromethane (3 mL) under nitrogen. Hydrogen gas was bubbled through the stirred catalyst solution for 30 min, and the resulting mixture was concentrated in vacuo. The residue was dissolved in 1,2-dichloroethane (1.5 mL), and a solution of the substrate **1** (0.10 mmol) in dichloroethane (1.5 mL) was added. The reaction mixture was heated at reflux for 1 h (monitoring by TLC). The solvent was evaporated in vacuo and the residue was purified by column chromatography on silica gel to afford the cyclization product **2**.

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Keywords: carbenoids · cascade · cyclization · density functional calculations · rhodium

[1] For monographs, see: a) 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**; b) *Metal Carbenes in Organic Synthesis* (Ed.: F. Zaragoza-Dörwald), Wiley-VCH, Weinhem, **1999**; c) *Metal Carbenes in Organic Synthesis* (Ed.: K. H. Dötz), Springer, New York, **2004**; d) *Contemporary Carbene Chemistry* (Eds.: R. A. Moss, M. P. Doyle), John Wiley & Sons, Hoboken, **2014**. For selected reviews, see: e) M. P. Doyle, *Chem. Rev.* **1986**, *86*, 919–939; f) A. Padwa, M. D. Weingarten, *Chem. Rev.* **1996**, *96*, 223–269; g) M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, *98*, 911–935; h) H. M. L. Davies, S. J. Hedley, *Chem. Soc. Rev.* **2007**, *36*, 1109–1119; i) H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417–424; j) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326–3350; k) H. M. L. Davies, J. R. Denton, *Chem. Soc. Rev.* **2009**, *38*, 3061–3071; l) A. Padwa, *Chem. Soc. Rev.* **2009**, *38*, 3072–3081; m) R. de Frémont, N. Marion, S. P. Nolan, *Coord. Chem. Rev.* **2009**, *253*, 862–892; n) G. C. Vougioukalakis, R. H. Grubbs, *Chem. Rev.* **2010**, *110*, 1746–1787; o) J. Barluenga, C. Valdés, *Angew. Chem. Int. Ed.* **2011**, *50*, 7486–7500; *Angew. Chem.* **2011**, *123*, 7626–7640; p) Y. Xia, Y. Zhang, J. Wang, *ACS Catal.* **2013**, *3*, 2586–2598; q) Q. Xiao, Y. Zhang, J. Wang, *Acc. Chem. Res.* **2013**, *46*, 236–247; r) L. Zhang, *Acc. Chem. Res.* **2014**, *47*, 877–888; s) L. Fensterbank, M. Malacria, *Acc. Chem. Res.* **2014**, *47*, 953–965.

[2] For selected recent examples, see: a) H. Qiu, M. Li, L.-Q. Jiang, F.-P. Lv, L. Zan, C.-W. Zhai, M. P. Doyle, W.-H. Hu, *Nat. Chem.* **2012**, *4*, 733–738; b) H. Wang, D. M. Guptill, A. Varela-Alvarez, D. G. Musaev, H. M. L. Davies, *Chem. Sci.* **2013**, *4*, 2844–2850; c) B. T. Parr, H. M. L. Davies, *Angew. Chem. Int. Ed.* **2013**, *52*, 10044–10047; *Angew. Chem.* **2013**, *125*, 10228–10231; d) X. Xu, P. Y. Zavalij, M. P. Doyle, *J. Am. Chem. Soc.* **2013**, *135*, 12439–12447; e) S. W. Kwok, L. Zhang, N. P. Grimster, V. V. Fokin, *Angew. Chem. Int. Ed.* **2014**, *53*, 3452–3456; *Angew. Chem.* **2014**, *126*, 3520–3524; f) C. Qin, H. M. L. Davies, *J. Am. Chem. Soc.* **2014**, *136*, 9792–9796.

[3] For reviews, see: a) J. R. Fulton, V. K. Aggarwal, J. de Vicente, *Eur. J. Org. Chem.* **2005**, 1479–1492; b) Z. Shao, H. Zhang, *Chem. Soc. Rev.* **2012**, *41*, 560–572.

[4] For a review, see: H. M. L. Davies, J. S. Alford, *Chem. Soc. Rev.* **2014**, *43*, 5151–5162.

[5] a) F. Miege, C. Meyer, J. Cossy, *Angew. Chem. Int. Ed.* **2011**, *50*, 5932–5937; *Angew. Chem.* **2011**, *123*, 6054–6059; b) A. Archambeau, F. Miege, C. Meyer, J. Cossy, *Angew. Chem. Int. Ed.* **2012**, *51*, 11540–11544; *Angew. Chem.* **2012**, *124*, 11708–11712; c) H. Zhang, K. Wang, B. Wang, H. Yi, F. Hu, C. Li, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2014**, *53*, 13234–13238; *Angew. Chem.* **2014**, *126*, 13450–13454; d) C. Soldi, K. N. Lamb, R. A. Squitieri, M. González-López, M. J. Di Maso, J. T. Shaw, *J. Am. Chem. Soc.* **2014**, *136*, 15142–15145.

[6] a) J. Barluenga, R. Vicente, L. A. López, E. Rubio, M. Tomás, C. Álvarez-Rúa, *J. Am. Chem. Soc.* **2004**, *126*, 470–471; b) J. Barluenga, R. Vicente, P. Barrio, L. A. López, M. Tomás, *J. Am. Chem. Soc.* **2004**, *126*, 5974–5975; c) J. Barluenga, R. Vicente, P. Barrio, L. A. López, M. Tomás, J. Borge, *J. Am. Chem. Soc.* **2004**, *126*, 14354–14355; d) J. Barluenga, R. Vicente, L. A. López, M. Tomás, *J. Am. Chem. Soc.* **2006**, *128*, 7050–7054.

[7] R. Liu, G. N. Winston-McPherson, Z.-Y. Yang, X. Zhou, W. Song, I. A. Guzei, X. Xu, W. Tang, *J. Am. Chem. Soc.* **2013**, *135*, 8201–8204.

[8] a) A. Demonceau, F. Simal, A. F. Noels, C. Viñas, R. Nuñez, F. Teixidor, *Tetrahedron Lett.* **1997**, *38*, 7879–7882; b) T. Nishimura, Y. Maeda, T. Hayashi, *Angew. Chem. Int. Ed.* **2010**, *49*, 7324–7327; *Angew. Chem.* **2010**,

122, 7482 – 7485; c) X. Ma, J. Jiang, S. Lv, W. Yao, Y. Yang, S. Liu, F. Xia, W. Hu, *Angew. Chem. Int. Ed.* **2014**, *53*, 13136 – 13139; *Angew. Chem.* **2014**, *126*, 13352 – 13355; d) Y.-T. Tsoi, Z. Zhou, W.-Y. Yu, *Org. Lett.* **2011**, *13*, 5370 – 5373; e) Y. Xia, Z. Liu, Z. Liu, R. Ge, F. Ye, M. Hossain, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2014**, *136*, 3013 – 3015; f) D. Chen, X. Zhang, W.-Y. Qi, B. Xu, M.-H. Xu, *J. Am. Chem. Soc.* **2015**, *137*, 5268 – 5271.

[9] A. Yada, S. Fujita, M. Murakami, *J. Am. Chem. Soc.* **2014**, *136*, 7217 – 7220.

[10] *Modern Rhodium-Catalyzed Organic Reactions* (Ed.: P. A. Evans), Wiley-VCH, Weinheim, **2005**.

[11] a) T. R. Hoye, C. J. Dinsmore, *J. Am. Chem. Soc.* **1991**, *113*, 4343 – 4345; b) A. Padwa, *J. Organomet. Chem.* **2000**, *610*, 88 – 101; c) S. Jansone-Popova, J. A. May, *J. Am. Chem. Soc.* **2012**, *134*, 17877 – 17880; d) Y. Shi, V. Gevorgyan, *Org. Lett.* **2013**, *15*, 5394 – 5396.

[12] Treatment of **1aa** in dioxane at 110 °C in the presence of K_2CO_3 and without a rhodium catalyst afforded a bicyclic pyrazole as similarly observed by: a) V. K. Aggarwal, J. de Vicente, R. V. Bonnert, *J. Org. Chem.* **2003**, *68*, 5381 – 5383; b) M. C. Pérez-Aguilar, C. Valdés, *Angew. Chem. Int. Ed.* **2013**, *52*, 7219 – 7223; *Angew. Chem.* **2013**, *125*, 7360 – 7364.

[13] For a review on C–S bond formation reactions, see: a) H. Liu, X. Jiang, *Chem. Asian J.* **2013**, *8*, 2546 – 2563. For selected recent examples on the synthesis of optically enriched sulfones, see: b) H.-J. Gais, T. Jagusch, N. Spalthoff, F. Gerhards, M. Frank, G. Raabe, *Chem. Eur. J.* **2003**, *9*, 4202 – 4221; c) M. Ueda, J. F. Hartwig, *Org. Lett.* **2010**, *12*, 92 – 94; d) X.-S. Wu, Y. Chen, M.-B. Li, M.-G. Zhou, S.-K. Tian, *J. Am. Chem. Soc.* **2012**, *134*, 14694 – 14697; e) Z. Jin, J. Xu, S. Yang, B.-A. Song, Y. R. Chi, *Angew. Chem. Int. Ed.* **2013**, *52*, 12354 – 12358; *Angew. Chem.* **2013**, *125*, 12580 – 12584; f) Q.-G. Wang, Q.-Q. Zhou, J.-G. Deng, Y.-C. Chen, *Org. Lett.* **2013**, *15*, 4786 – 4789; g) J. Choi, P. Martín-Gago, G. C. Fu, *J. Am. Chem. Soc.* **2014**, *136*, 12161 – 12165.

[14] Reactions ran under optimized conditions: $[Rh(cod)_2]BF_4$ (10 mol%), (*R*)-BINAP (10 mol%), DCE, heated at reflux, 1 h.

[15] Reported Gibbs energies are B3LYP/cc-pVDZ-PP electronic energies corrected with ZPEs, thermal energies, entropy effects, and solvent effects (dichloroethane solution). Further computational details are given in the Supporting Information.

[16] The hydride transfer from the amino group to the Rh atom can occur at any step of the reaction mechanism prior to the formation of complex **E**. In the Gibbs profile that is depicted in Scheme 4, the hydride is already coordinated to the Rh atom in complex **A**. We have analyzed alternative pathways in which the incorporation takes place later in the reaction path (see the Supporting Information); all these alternatives lead to profiles with higher energy barriers than those that are involved in the profile shown in Scheme 4. Consequently, we have concluded that the hydride transfer occurs at the beginning of the reaction mechanism, although a later transfer cannot be totally ruled out.

[17] J. M. O'Connor, K. K. Baldridge, C. L. Vélez, A. L. Rheingold, C. E. Moore, *J. Am. Chem. Soc.* **2013**, *135*, 8826 – 8829.

[18] S. Kozuch, S. Shaik, *Acc. Chem. Res.* **2011**, *44*, 101 – 110.

[19] As we found in deuterium-labeling experiments, the final product **2** incorporates the migrated H atom in the olefinic *trans* position. We have calculated an alternative reaction pathway that leads to the same final product **2**, but with the transferred H atom in the olefinic *cis* position (see the Supporting Information). The latter pathway has a higher energy barrier (25.6 kcal mol^{-1}), and its rate-determining step is the transformation from intermediate **E** to **F**. Moreover, complex **E**, with the H atom in the *cis* position, can be easily transformed into the isomeric complex **E** with the H atom in the *trans* position. The latter, which is more stable than the *cis* conformer by 2.3 kcal mol^{-1}, evolves rapidly to the final product.

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