

Stereodivergent Intramolecular C(sp³)–H Functionalization of Azavinyl Carbenes: Synthesis of Saturated Heterocycles and Fused N-Heterotricycles

Vincent N. G. Lindsay, Hélène M.-F. Viart, and Richmond Sarpong*

Department of Chemistry, University of California, Berkeley, California 94720, United States

S Supporting Information

ABSTRACT: A general approach for the formation of five-membered saturated heterocycles by intramolecular C(sp³)–H functionalization is reported. Using *N*-sulfonyl-triazoles as Rh(II) azavinyl carbene equivalents, a wide variety of stereodefined *cis*-2,3-disubstituted tetrahydrofurans were obtained with good to excellent diastereoselectivity from readily available acyclic precursors. The reaction is shown to be amenable to gram scale, and judicious choice of reaction conditions allowed for stereodivergence, providing selective access to the *trans* diastereomer in good yield. The resulting products were shown to be valuable intermediates for the direct preparation of fused *N*-heterotricycles in one step by intramolecular C–H amination or Pictet–Spengler cyclization.

Saturated five-membered heterocycles such as tetrahydrofurans are ubiquitous structural motifs found in an array of natural products and other biologically relevant molecules.¹ For the synthesis of polysubstituted and ring-fused analogues of these compounds, efficient access to stereodefined products remains a formidable challenge.² The preparation of substituted tetrahydrofurans often proceeds by C–O bond formation via cyclization of linear substrates with predefined stereochemistry. A strategically powerful alternative to this approach involves intramolecular C–C bond formation from an acyclic aliphatic ether, where both the cyclization and the generation of stereocenters occur in the same step, ideally from an unactivated substrate. In recent years, metal-catalyzed carbenoid C–H insertion reactions have been shown to be robust processes for stereoselective C–C bond formation from ethereal C–H bonds.³ While such a strategy has been widely utilized for the intramolecular formation of stereodefined dihydrobenzofurans from aryl ethers,⁴ only scarce and specific examples have been reported for the analogous formation of polysubstituted tetrahydrofurans.^{4b,5} A common challenge in these reactions, typically using Rh(II) carbenoids derived from α -diazocarbonyl compounds, lies in the diastereocontrol of the intramolecular C–H insertion step when flexible aliphatic ethers are employed as substrates. Very recently, Che and co-workers demonstrated that Ru–porphyrin catalysts are particularly efficient in such a process with dialkyldiazomethanes formed in situ from *N*-sulfonylhydrazones, leading to a variety of stereodefined saturated heterocycles via a Ru dialkylcarbene (Scheme 1a).^{5g}

Scheme 1. Synthesis of Tetrahydrofurans and *N*-Heterocycles via Metal-Catalyzed C–H Insertion

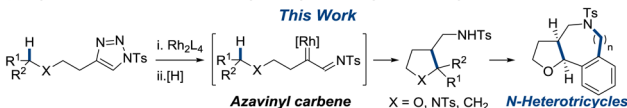
(a) Che's synthesis of tetrahydrofurans by Ru-catalyzed dialkylcarbene C–H insertion



(b) Synthesis of *N*-heterocycles from *N*-sulfonyltriazaoles via azavinyl carbene transfer



(c) Synthesis of fused *N*-heterotricycles by Rh-catalyzed azavinyl carbene C–H insertion



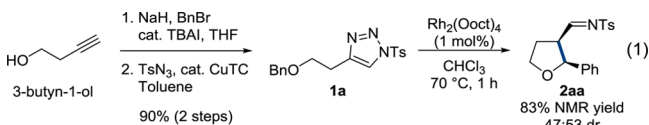
In the past few years, 1-sulfonyl-1,2,3-triazoles have proven to be extremely versatile Rh(II) azavinyl carbene equivalents in numerous carbene transfer processes.⁶ In contrast with α -diazocarbonyl compounds or dialkyldiazomethanes, the use of *N*-sulfonyltriazaoles as carbenoid precursors can lead to the rapid elaboration of substituted *N*-heterocycles by cyclization of the resulting imino group after the carbene transfer has occurred (Scheme 1b).^{6a} When these transformations are applied in an intramolecular sense, ring-fused *N*-heterocycles are directly obtained from acyclic precursors in a particularly efficient manner.⁷ In our continuing efforts to utilize such intramolecular azavinyl carbene transfer reactions for the expedient synthesis of fused *N*-heterocycles,^{7c,d} we envisioned that the corresponding intramolecular C–H insertion into an ethereal C–H bond would lead to a stereodefined 3-iminotetrahydrofuran, which could be elaborated into fused *N*-heterocycles by engaging the resulting *N*-sulfonylamino moiety of the product (Scheme 1c).⁸ In this work, we report a general approach to the synthesis of saturated heterocycles using a stereodivergent intramolecular Rh-catalyzed azavinyl carbenoid C(sp³)–H insertion reaction. Moreover, the resulting products were directly utilized for the synthesis of ring-fused *N*-heterotricycles such as a tetrahydroquinoline and a tetrahydrobenzazepine by means of an intramolecular C–H amination and Pictet–Spengler cyclization, respectively. In view of the ubiquity of polysubstituted and ring-fused tetrahydrofurans and the lack of a unified route for their stereoselective

Received: April 25, 2015

Published: June 20, 2015

formation, this work should find broad applicability in the elaboration of complex molecules.

In order to evaluate the viability of our approach, we first synthesized *N*-sulfonyltriazole **1a** in two simple steps from commercially available 3-butyne-1-ol and subjected it to standard conditions for Rh(II)-catalyzed azavinyl carbene transfer reactions (eq 1).^{6a} While the desired 3-iminotetrahydrofuran



2aa was cleanly formed in good NMR yield (83%), only very poor diastereoselectivity was obtained (47:53). Interestingly, no 1,2-hydride shift side product was observed, a common problem with alkyl-substituted carbenoid precursors.^{7e,9}

A survey of various Rh(II) catalysts revealed that the nature of the carboxylate ligands had an enormous impact on the diastereoselectivity of the reaction, with the most hindered complexes affording the highest *cis:trans* ratio of **2aa** (Table 1,

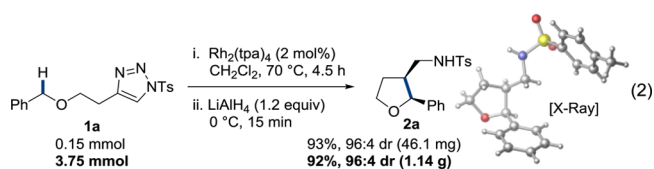
Table 1. Optimization of the Intramolecular Rh(II)-Catalyzed Azavinyl Carbene C–H Insertion

entry	Rh ₂ L ₄	R	time (h)	yield (%) ^{a,b}	dr (<i>c:t</i>) ^a
1	Rh ₂ (O ₂ CH) ₄	H	1	23 (77)	38:62
2	Rh ₂ (OAc) ₄	Me	1	72 (13)	33:67
3	Rh ₂ (Ooct) ₄	<i>n</i> -C ₇ H ₁₅	1	83 (<5)	47:53
4	Rh ₂ (tfa) ₄	CF ₃	1	<5 (83)	-
5	Rh ₂ (Adc) ₄	1-Ad	1	83 (<5)	69:31
6	Rh ₂ (OPiv) ₄	CMe ₃	1	80 (<5)	72:28
7	Rh ₂ (esp) ₂	^c	1	79 (<5)	82:18
8	Rh ₂ (tpa) ₄	CPh ₃	1	17 (71)	95:5
9	Rh ₂ (tpa) ₄	CPh ₃	4	72 (5)	93:7
10 ^d	Rh ₂ (tpa) ₄	CPh ₃	4	81 (18)	96:4
11 ^{d,e}	Rh ₂ (tpa) ₄	CPh ₃	4.5	96 (<5)	96:4

^aDetermined by NMR analysis of the crude mixture using 1,3,5-trimethoxybenzene as an internal standard. ^bYields of remaining **1a** are given in parentheses. ^cRh₂(esp)₂ = bis[rhodium($\alpha,\alpha,\alpha',\alpha'$ -tetramethyl-1,3-benzenedipropionic acid)]. ^dCH₂Cl₂ was used as the solvent. ^e2 mol % catalyst was used.

entries 1–8). Commercially available catalyst Rh₂(tpa)₄ gave optimal diastereoselectivity, though it proved to be significantly less reactive and the reaction time had to be increased to 4 h in order to achieve complete conversion (entries 8 and 9). Most noncoordinating solvents were tolerated, but the use of CH₂Cl₂ led to an increase in both the yield and diastereoselectivity (entry 10).¹⁰

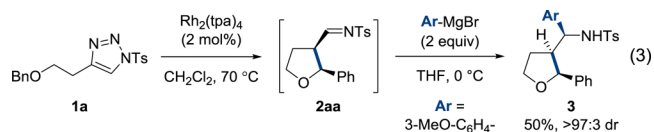
In view of developing a general method, the catalyst loading was increased to 2 mol %, ensuring complete conversion in a timely fashion for most substrates (entry 11). Prolonged reaction times (>5 h) or higher reaction temperatures led to partial decomposition of the product and were therefore avoided.¹¹ While the resulting imine product is somewhat unstable toward silica gel chromatography, isolation of the product was readily achieved after reduction with LiAlH₄, which was directly added to the crude mixture at 0 °C (eq 2).^{8a} Under the optimized



conditions, the resulting *N*-sulfonylamide **2a** was isolated in 93% yield with 96:4 dr, and the procedure could be conducted on a gram scale with similar efficiency.

With these conditions in hand, a variety of stereodefined saturated five-membered heterocycles were efficiently prepared (Table 2). Various substituted benzyl ethers were well-tolerated as substrates, as well as an electron-rich heterocyclic variant (entries 1–7). C(sp³)–H insertion into an allylic ethereal position is also possible, with a minimal amount of competitive cyclopropanation observed on the proximal double bond (entry 8). Gratifyingly, a substrate bearing an aliphatic R group, though less activated toward C–H insertion, afforded a high yield of the corresponding tetrahydrofuran (entry 9). Insertion into methine C–H bonds, leading to highly substituted analogues **2j** and **2k**, was also found to proceed in good yields (entries 10 and 11). In addition to tetrahydrofurans, the formation of products such as **2l** and **2m** demonstrate that pyrrolidines and cyclopentanes can be accessed by this method with excellent diastereoselectivity (entries 12 and 13). The use of a homologated substrate such as **1n** afforded tetrahydrofuran **2n** instead of the expected tetrahydropyran, presumably by a Rh(II)-catalyzed oxonium ylide formation/[1,2]-alkyl shift sequence (Scheme 2).¹²

The crude imine intermediate obtained following C–H insertion can be directly used as an electrophile in a 1,2-addition reaction, as exemplified by Grignard addition to imine **2aa** to afford tetrahydrofuran **3** possessing three contiguous stereocenters (eq 3).^{12b,13,14}



While sterically hindered Rh₂(tpa)₄ affords the *cis* product with high diastereoselectivity, our initial investigations had revealed that the use of other catalysts such as Rh₂(OAc)₄ can provide a *trans*-selective reaction, allowing the development of a stereo-divergent approach (see Table 1, entry 2). Such an effect on the diastereoselectivity might be due to a difference in the degrees of freedom of the substituents around the C–C bond being formed, where small carboxylates such as OAc allow these groups (here, Ph and C=NTs) to be placed in a more stable *trans* configuration in the transition state. After further optimization,¹⁰ performing the Rh₂(OAc)₄-catalyzed reaction with substrate **1a** in toluene in the presence of 2-picoline as an additive (5 mol %)¹⁵ allowed access to the *trans* diastereomer in good yield (Scheme 3).

Finally, the 3-(sulfonamido)methyl moiety of the products obtained following imine reduction can be further utilized for the rapid construction of *N*-heterotricycles by intramolecular C–N bond formation events (Scheme 4). As exemplified with *N*-sulfonylamide **2a**, the use of commercially available 1,3-diiodo-5,5-dimethylhydantoin (DIH) allowed the direct formation of 5-6-6 fused tetrahydroquinoline **4** by a metal-free C–H amination process.¹⁶ Furthermore, modified Pictet–Spengler conditions using paraformaldehyde, TFAA, and MsOH in DCE provided

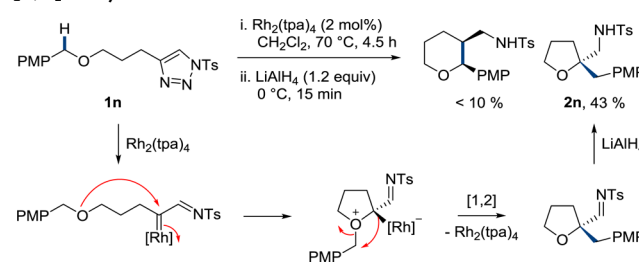
Table 2. Substrate Scope of the Intramolecular Rh(II)-Catalyzed Azavinyl Carbene C–H Insertion

entry	substrate	product	yield (%) ^a	dr (c:t) ^b
1			93	96:4
2			89	93:7
3			89	90:10
4			80	98:2
5			77	95:5
6			78	89:11
7			81	97:3
8 ^c			71	82:18
9			88	87:13
10			82	-
11 ^d			97	-
12 ^e			58	>98:2
13			67	>98:2

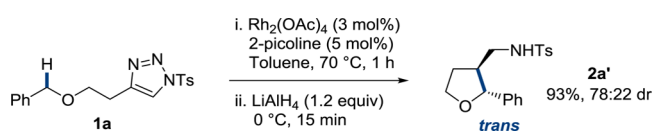
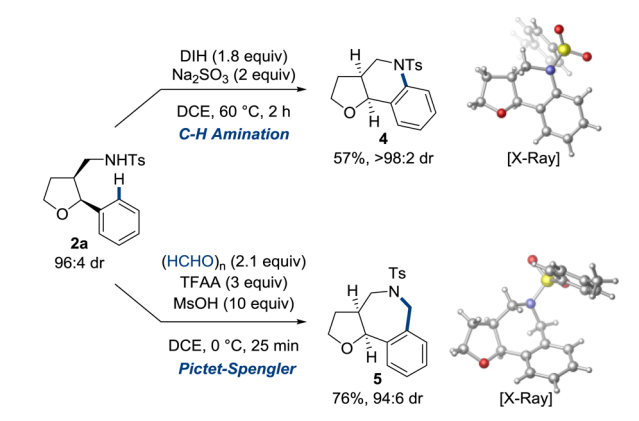
^aIsolated yields. ^bDetermined by NMR analysis of the crude mixtures. ^cRh₂(S-PTAD)₄ (2 mol %) was used as the catalyst. ^dRh₂(Adc)₄ (3 mol %) was used as the catalyst. ^e3 mol % Rh₂(tpa)₄ was used.

fused tetrahydrobenzazepine **5** in good yield without the need for an electron-donating aromatic ring.¹⁷ In both cases, X-ray analyses were performed to unambiguously confirm the structures of the *N*-heterocyclic products.

In summary, a general and stereodivergent intramolecular Rh(II)-catalyzed azavinyl carbene C(sp³)-H insertion reaction was developed, providing access to an array of stereodefined cis-

Scheme 2. Rh(II)-Catalyzed Oxonium Ylide Formation/[1,2]-Alkyl Shift with Extended Tethers^a

^aPMP = 4-MeO-C₆H₄.

Scheme 3. Stereodivergence of the C(sp³)-H Insertion: Access to the *trans* DiastereomerScheme 4. Synthesis of *N*-Heterotricycles via Intramolecular C–H Amination and Pictet–Spengler Reactions

2,3-disubstituted saturated heterocycles. The reaction proceeds on a gram scale with similar efficiency, and the use of an alternative set of conditions provides access to the *trans* diastereomer in good yield. The resulting products were utilized for the rapid formation of fused *N*-heterotricycles through different intramolecular C–N bond-forming processes. Cognizant of the ubiquity of polysubstituted and ring-fused tetrahydrofurans, this work should find broad applicability in the synthesis of biologically relevant molecules. Future studies in the field of intramolecular azavinyl carbene insertion reactions will seek to render these transformations enantioselective.¹¹

■ ASSOCIATED CONTENT

Supporting Information

Experimental details and spectroscopic data. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.Sb04295.

■ AUTHOR INFORMATION

Corresponding Author

*rsarpong@berkeley.edu

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the NSF (CAREER 0643264 to R.S. and under the CCI Center for Selective C–H Functionalization, CHE-1205646). We are grateful to the FRQNT (B3) for a postdoctoral scholarship to V.N.G.L., to the Carlsberg Foundation for a postdoctoral scholarship to H.M.-F.V., and to Abbott, Eli Lilly, and Roche for financial support. We thank A. DiPasquale for solving the crystal structures of **2a**, **4**, and **5** (displayed with CYLView), supported by NIH Shared Instrumentation Grant (S10-RR027172).

REFERENCES

- (1) For reviews of THF-containing natural products, see: (a) Faul, M. M.; Huff, B. E. *Chem. Rev.* **2000**, *100*, 2407. (b) Alali, F. Q.; Liu, X.-X.; McLaughlin, J. L. *J. Nat. Prod.* **1999**, *62*, 504. (c) Ward, R. S. *Nat. Prod. Rep.* **1999**, *16*, 75. (d) Boto, A.; Alvarez, L. In *Heterocycles in Natural Product Synthesis*; Majumdar, K. C., Chattopadhyay, S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2011; pp 99–152. (e) Lorente, A.; Lamariano-Merketegi, J.; Albericio, F.; Álvarez, M. *Chem. Rev.* **2013**, *113*, 4567. (f) Bermejo, A.; Figadere, B.; Zafra-Polo, M.-C.; Barrachina, I.; Estornell, E.; Cortes, D. *Nat. Prod. Rep.* **2005**, *22*, 269. (g) Saleem, M.; Kim, H. J.; Ali, M. S.; Lee, Y. S. *Nat. Prod. Rep.* **2005**, *22*, 696. (h) Kang, E. J.; Lee, E. *Chem. Rev.* **2005**, *105*, 4348.
- (2) For reviews of the synthesis of tetrahydrofurans, see: (a) Wolfe, J. P.; Hay, M. B. *Tetrahedron* **2007**, *63*, 261. (b) Elliott, M. C. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2301. (c) Koert, U. *Synthesis* **1995**, 115. (d) Harmange, J.-C.; Figadere, B. *Tetrahedron: Asymmetry* **1993**, *4*, 1711. (e) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309. (f) Graening, T.; Thrun, F. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Ramsden, C. A., Scriven, E. F. V., Taylor, R., Eds.; Elsevier: Oxford, U.K., 2008; Vol. 3, pp 497–569.
- (3) For selected recent examples of intermolecular carbenoid insertion into ethereal C–H bonds, see: (a) Guptill, D. M.; Davies, H. M. L. *J. Am. Chem. Soc.* **2014**, *136*, 17718. (b) Wang, H.; Li, G.; Engle, K. M.; Yu, J.-Q.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 6774. (c) Qin, C.; Davies, H. M. L. *J. Am. Chem. Soc.* **2014**, *136*, 9792. (d) Davies, H. M. L.; Yang, J. *Adv. Synth. Catal.* **2003**, *345*, 1133. (e) Caballero, A.; Díaz-Requejo, M. M.; Belderrain, T. R.; Nicasio, M. C.; Trofimenko, S.; Pérez, P. *J. Organometallics* **2003**, *22*, 4145.
- (4) From Rh(II) carbenoids: (a) Davies, H. M. L.; Grazini, M. V. A.; Aouad, E. *Org. Lett.* **2001**, *3*, 1475. (b) Saito, H.; Oishi, H.; Kitagaki, S.; Nakamura, S.; Anada, M.; Hashimoto, S. *Org. Lett.* **2002**, *4*, 3887. (c) Lou, Y.; Horikawa, M.; Kloster, R. A.; Hawryluk, N. A.; Corey, E. J. *J. Am. Chem. Soc.* **2004**, *126*, 8916. (d) Soldi, C.; Lamb, K. N.; Squitieri, R. A.; González-López, M.; Di Maso, M. J.; Shaw, J. T. *J. Am. Chem. Soc.* **2014**, *136*, 15142. (e) Ma, X.; Wu, F.; Yi, X.; Wang, H.; Chen, W. *Chem. Commun.* **2015**, *51*, 6862. From Ir(I) carbenoids: (f) López-Sánchez, C.; Álvarez-Corral, M.; Muñoz-Dorado, M.; Rodríguez-García, I. *Synlett* **2012**, *23*, 2469. From free carbenes: (g) von Itter, F.-A.; Vögtle, F. *Chem. Ber.* **1985**, *118*, 2300. (h) Tomioka, H.; Watanabe, M.; Kobayashi, N.; Hirai, K. *Tetrahedron Lett.* **1990**, *31*, 5061. (i) Tomioka, H.; Nakanishi, K.; Izawa, Y. *J. Chem. Soc., Perkin Trans. 1* **1991**, 465. (j) Tomioka, H.; Kimoto, K.; Murata, H.; Izawa, Y. *J. Chem. Soc., Perkin Trans. 1* **1991**, 471. (k) Kirmse, W.; Özkir, I. S. *J. Am. Chem. Soc.* **1992**, *114*, 7590. (l) Lombard, F. J.; Coster, M. J. *Org. Biomol. Chem.* **2015**, *13*, 6419.
- (5) (a) Adams, J.; Frenette, R. *Tetrahedron Lett.* **1987**, *28*, 4773. (b) Adams, J.; Poupart, M.-A.; Grenier, L.; Schaller, C.; Ouimet, N.; Frenette, R. *Tetrahedron Lett.* **1989**, *30*, 1749. (c) Ye, T.; McKervey, M. A.; Brandes, B. D.; Doyle, M. P. *Tetrahedron Lett.* **1994**, *35*, 7269. (d) Taber, D. F.; Song, Y. *Tetrahedron Lett.* **1995**, *36*, 2587. (e) Taber, D. F.; Song, Y. *J. Org. Chem.* **1996**, *61*, 6706. (f) Brown, R. C. D. *Chem. Commun.* **1998**, 1895. (g) Reddy, A. R.; Zhou, C.-Y.; Guo, Z.; Wei, J.; Che, C.-M. *Angew. Chem., Int. Ed.* **2014**, *53*, 14175.
- (6) For reviews and seminal examples of the use of *N*-sulfonyltriazoles as Rh azavinyl carbene equivalents, see: (a) Davies, H. M. L.; Alford, J. S. *Chem. Soc. Rev.* **2014**, *43*, 5151. (b) Anbarasan, P.; Yadagiri, D.; Rajasekar, S. *Synthesis* **2014**, *46*, 3004. (c) Chattopadhyay, B.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2012**, *51*, 862. (d) Gulevich, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2013**, *52*, 1371. (e) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 14972. (f) Chuprakov, S.; Kwok, S. W.; Zhang, L.; Lercher, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2009**, *131*, 18034.
- (7) For examples of the synthesis of fused *N*-heterocycles via intramolecular azavinyl carbene transfer, see: (a) Miura, T.; Funakoshi, Y.; Murakami, M. *J. Am. Chem. Soc.* **2014**, *136*, 2272. (b) Alford, J. S.; Spangler, J. E.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 11712. (c) Schultz, E. E.; Sarpong, R. *J. Am. Chem. Soc.* **2013**, *135*, 4696. (d) Schultz, E. E.; Lindsay, V. N. G.; Sarpong, R. *Angew. Chem., Int. Ed.* **2014**, *53*, 9904. (e) Yang, J.-M.; Zhu, C.-Z.; Tang, X.-Y.; Shi, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 5142. (f) Shi, Y.; Gevorgyan, V. *Org. Lett.* **2013**, *15*, 5394.
- (8) For other examples of Rh(II)-catalyzed azavinyl carbene C(sp³)-H insertion reactions, see ref 4e and: (a) Chuprakov, S.; Malik, J. A.; Zibinsky, M.; Fokin, V. V. *J. Am. Chem. Soc.* **2011**, *133*, 10352. (b) Shen, M.-H.; Pan, Y.-P.; Jia, Z.-H.; Ren, X.-T.; Zhang, P.; Xu, H.-D. *Org. Biomol. Chem.* **2015**, *13*, 4851.
- (9) (a) Taber, D. F.; You, K. K.; Rheingold, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 547. (b) Taber, D. F.; Hennessy, M. J.; Louey, J. P. *J. Org. Chem.* **1992**, *57*, 436. (c) Miura, T.; Biyajima, T.; Fujii, T.; Murakami, M. *J. Am. Chem. Soc.* **2012**, *134*, 194.
- (10) See the Supporting Information for details.
- (11) Attempts to develop an enantioselective version of this reaction using chiral Rh(II) catalysts were unsuccessful (<25% ee; see the Supporting Information). This is a common and recurrent problem in intramolecular azavinyl carbene transfer reactions (see refs 6 and 7).
- (12) For related Rh(II)-catalyzed rearrangements from *N*-sulfonyltriazoles, see: (a) Boyer, A. *Org. Lett.* **2014**, *16*, 5878. (b) Fu, J.; Shen, H.; Chang, Y.; Li, C.; Gong, J.; Yang, Z. *Chem.—Eur. J.* **2014**, *20*, 12881. (c) Xu, H.-D.; Jia, Z.-H.; Xu, K.; Zhou, H.; Shen, M.-H. *Org. Lett.* **2015**, *17*, 66.
- (13) Rh(I)-catalyzed addition of PhB(OH)₂ and Cu(I)-catalyzed addition of Et₂Zn led to only very low yields of the corresponding adducts in this case because of various side reactions.
- (14) For recent reviews of the addition of nonstabilized carbanions to imines, see: (a) Lindsay, V. N. G.; Charette, A. B. In *Comprehensive Organic Synthesis*, 2nd ed.; Molander, G. A., Knochel, P., Eds.; Elsevier: Oxford, U.K., 2014; Vol. 1, pp 365–394. (b) Kobayashi, S.; Mori, Y.; Fossey, J. S.; Salter, M. M. *Chem. Rev.* **2011**, *111*, 2626. (c) Yamada, K.-i.; Tomioka, K. *Chem. Rev.* **2008**, *108*, 2874. (d) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407.
- (15) For a review and recent examples of the use of Lewis basic additives to affect the stereoselectivity of Rh(II)-catalyzed reactions, see: (a) Trindade, A. F.; Coelho, J. A. S.; Afonso, C. A. M.; Veiros, L. F.; Gois, P. M. P. *ACS Catal.* **2012**, *2*, 370. (b) Lindsay, V. N. G.; Nicolas, C.; Charette, A. B. *J. Am. Chem. Soc.* **2011**, *133*, 8972. (c) Lebel, H.; Piras, H.; Bartholoméüs, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 7300.
- (16) (a) Moroda, A.; Furuyama, S.; Togo, H. *Synlett* **2009**, 1336. For a review and selected examples of intramolecular C(sp²)-H amination using *N*-sulfonylamides, see: (b) Wang, C.; Han, J.; Zhao, Y. *Synlett* **2015**, *26*, 997. (c) Togo, H.; Hoshina, Y.; Yokoyama, M. *Tetrahedron Lett.* **1996**, *37*, 6129. (d) Mei, T.-S.; Wang, X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 10806. (e) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996.
- (17) The Pictet–Spengler conditions were modified from: (a) Orazi, O. O.; Corral, R. A.; Giaccio, H. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1977. (b) Hoshino, O.; Ishizaki, M.; Saito, K.; Yumoto, K. *J. Chem. Soc., Chem. Commun.* **1990**, 420. (c) Ishizaki, M.; Hoshino, O.; Iitaka, Y. *Tetrahedron Lett.* **1991**, *32*, 7079.