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Rhodium(II)-Catalyzed Asymmetric Sulfur(VI) Reduction of Diazo Sulfonylamidines

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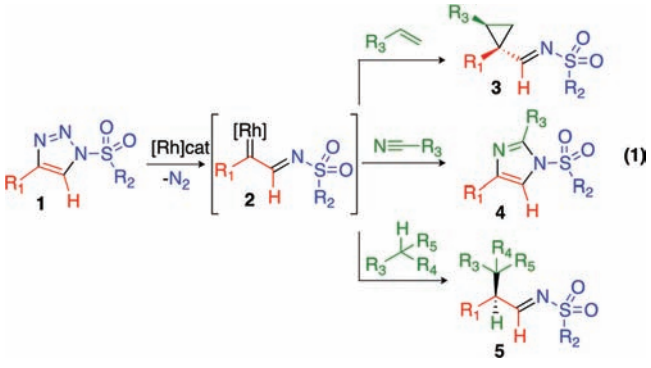
Supporting Information

ABSTRACT: Diazo sulfonylamidines readily undergo enantioselective oxygen transfer from sulfur to carbon atom in the presence of chiral rhodium(II) carboxylates resulting in chiral sulfinylamidines. This unusual asymmetric atom transfer "reduction" occurs rapidly under mild conditions, and sulfinylamidines are obtained in excellent yield.

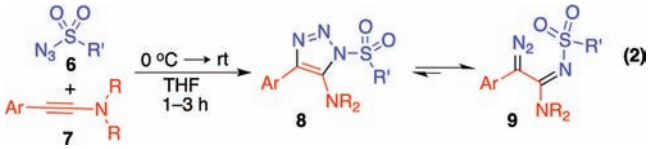
Chiral sulfinyl imines and sulfinamides are versatile intermediates and ligands in asymmetric synthesis.[1] As is the case for most chiral sulfur(IV) compounds, their preparation involves asymmetric oxidation of sulfur(II) starting materials. In this communication, we wish to report an unprecedented asymmetric formal reduction of sulfur(VI) in sulfonylamidines to sulfur(IV), leading to enantioenriched sulfinylamidines.

We have recently demonstrated the synthetic utility of 1-sulfonyl 1,2,3-triazoles (**1**) as stable and versatile progenitors of azavinyl carbenes. A clear advantage of this chemistry is the ability to access novel carbene intermediates without the need to prepare and isolate diazo compounds. The rhodium carbene intermediates (**2**) generated in situ from the sulfonyl triazoles, have been applied in highly enantioselective cyclopropanation of olefins (**3**),[2] transannulation with nitriles (**4**),[3] and in the alkane C−H insertion reactions (**5**),[4] thus expanding the repertoire of transformations of diazo compounds (eq 1).



(1)

Since the stability of the triazole ring is affected by the substituents at the N1, C4, and C5 atoms of the heterocycle, we turned our attention to 1-sulfonyl-5-dialkylamino 1,2,3-triazoles (**8**). We envisioned that the amino substituent at C5 would stabilize the open chain diazo amidine form, giving rise to novel azavinyl carbene species (**10**). To this end, we prepared a variety of amino-substituted adducts from the corresponding sulfonyl azides (**6**) and ynamines (**7**).[5] Although tautomers **8** and **9** may exist in equilibrium,[5c] we found that the diazo amidine chain form **9** was the dominant tautomer (eq 2; see Supporting Information for details).



(2)

Our initial studies employing the diazo sulfonylamidines **9** in the rhodium-catalyzed cyclopropanation of styrene gave no traces of the cyclopropane products. Instead, we observed rapid evolution of dinitrogen and selective formation of sulfinylamidines **11** (eq 3).

(3)

Only a few examples of uncatalyzed intramolecular reactions of the sulfonyl functionality with diazo compounds have been described in the literature.[6] However, the known reactions were slow (up to 3 days) and did not involve any transition metal catalysts. We found that in the presence of rhodium carboxylate catalysts, this reaction proceeded to completion within minutes at 0 °C. As the transfer of the oxygen atom from the sulfonyl group to the diazo carbon creates a chiral sulfur center, we envisioned that chiral rhodium carboxylates might render this reaction asymmetric.

Examination of a series of catalysts shown under Table 1 confirmed this hypothesis. Thus, sulfinylamidine **11a** was obtained in nearly quantitative yield with only 1 mol % of the rhodium catalyst. When chiral carboxylates were used, we found that the transfer of the oxygen atom was indeed stereoselective. Although only modest ee, 27%, was obtained using Müller's Rh_2(*S*-NTTL)$_4$[7] catalyst (Table 1, entry 1), rhodium carboxylates containing more sterically encumbered substituents led to improved enantioselectivity (entries 1−4). A racemic mixture of the product was obtained using the Rh_2(*S*-PTV)$_4$ catalyst, whereas the bulkier Rh_2(*S*-PTTL)$_4$[8] and Rh_2(*S*-

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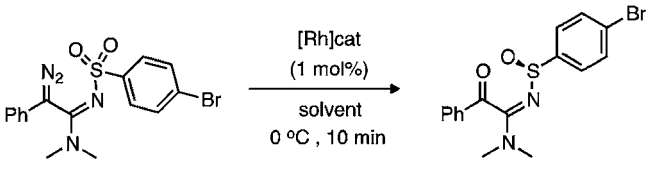
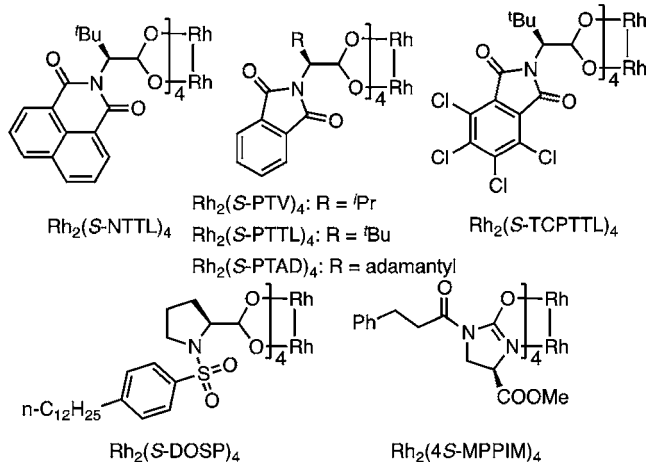
Table 1. Rh-Catalyzed Synthesis of Chiral Sulfinylamidines[a]



entry	catalyst	solvent	yield, %	ee, %
1	Rh_2(S-NTTL)$_4$	$CHCl_3$	90	27
2	Rh_2(S-PTV)$_4$	$CHCl_3$	96	-1
3	Rh_2(S-PTTL)$_4$	$CHCl_3$	96	42
4	Rh_2(S-PTAD)$_4$	$CHCl_3$	95	57
5	Rh_2(S-TCPTTL)$_4$	$CHCl_3$	96	62
6	Rh_2(S-DOSP)$_4$	$CHCl_3$	96	-3
7	Rh_2(4S-MPPIM)$_4$	$CHCl_3$	0	-
8	Rh_2(S-PTAD)$_4$	DCM	92	40
9	Rh_2(S-PTAD)$_4$	DCE	98	45
10	Rh_2(S-PTAD)$_4$	PhMe	96	49
11	Rh_2(S-PTAD)$_4$	MeOH (50 °C, 1h)	90	0



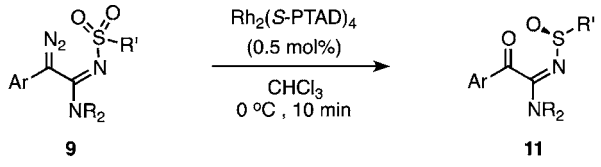
[a]One milliliter solution of **9a** (0.15 mmol) was added dropwise to a 1 mL solution of the catalyst (1 mol %).

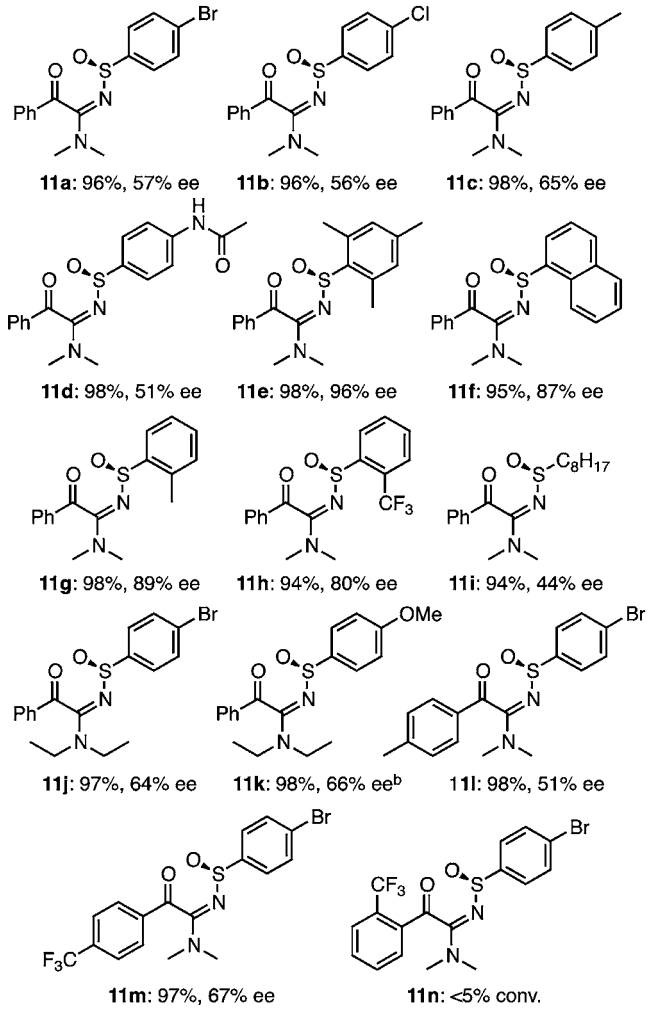
PTAD)$_4$[9] catalysts gave 42% and 57% ee, respectively. In addition, the tetrachloro-substituted Rh_2(S-TCPTTL)$_4$ catalyst led to a slight further improvement of the ee (62%). No induction of chirality was observed in the presence of Rh_2(S-DOSP)$_4$[10] and no reaction occurred when carboxamidate Rh_2(4S-MPPIM)$_4$[11] was used.

Reactions performed in other solvents (DCM, 1,2-DCE, and toluene; entries 8−10) resulted in a slightly lower enantioselectivity, although the yield of **11a** remained excellent. It is noteworthy that the reaction also proceeded in high yield in methanol at elevated temperature, but enantioselectivity was lost (entry 11). This experiment points to the facility of this intramolecular process.

Using chloroform and 0.5 mol % of the commercially available Rh_2(S-PTAD)$_4$ catalyst, we then investigated the scope of the reaction with respect to various sulfonylamidines (Table 2). The 4-halogenated benzene sulfonyl amidines resulted in similar enantioselectivities, **11a** (57%) and **11b** (56%). Tosyl amidine led to a slight improvement of enantioselectivity (65% ee, **11c**). Interestingly, the reaction also proceeded in high yield in the presence of amide substituents, albeit with a lower ee value (**11d**). No insertion of the rhodium carbene into the N−H bond or catalyst

Table 2. Reactivity of Various Diazo Sulfonylamidines[a]





[a]Two milliliter solution of **9** (0.50 mmol) was added dropwise to a 2 mL solution of the catalyst (0.5 mol %). [b]Reaction carried out for 90 min.

deactivation was observed in this case. Increasing the steric bulk at sulfur resulted in a significant improvement of the ee, 96% for **11e** and 87% for **11f**, with consistently high yields. High enantioselectivity was also observed for ortho-functionalized aromatic substituents on sulfur. Sulfinylamidine **11g** was isolated in 95% yield with 89% ee, whereas an electron-withdrawing group in the ortho position led to a drop in ee (80% for **11h**). Alkyl-substituted sulfonylamidine was equally reactive, although the product **11i** was obtained with a lower enantioselectivity (ee 44%).

A slight increase in ee was observed when the dimethyl amine group was replaced with the diethyl amine (cf. 57% for **11a** and 64% for **11j**). A similar ee, 66%, was observed for **11k**, however, this reaction required 90 min to proceed to completion. Finally, the aromatic group attached to the diazo carbon was modified. We found that an electron withdrawing para-substituent gave 67% ee (**11m**), while an electron

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donating group led to a lower ee value, 51% for **11l** (cf. 57% for **11a**). Furthermore, the ortho-substituted **11n** reacted very slowly: after 10 h, less than 5% conversion was observed, indicating either an unfavorable electronic interaction and/or too bulky environment for the formation of the corresponding Rh-carbene.

The very short reaction times and high yields obtained under mild conditions clearly demonstrate the facility of the intramolecular reduction of sulfur compared to those obtained with other intra- and intermolecular processes, such as C−H, N−H, or O−H insertions, carbene dimerization, or cyclopropanation. The reaction also took place in the presence of a variety of substituents with different steric and electronic properties. A probable explanation for the observed reactivity was unveiled by examination of the data from single-crystal X-ray crystallographic analysis of compounds **9a** and **11a** (Figure 1).

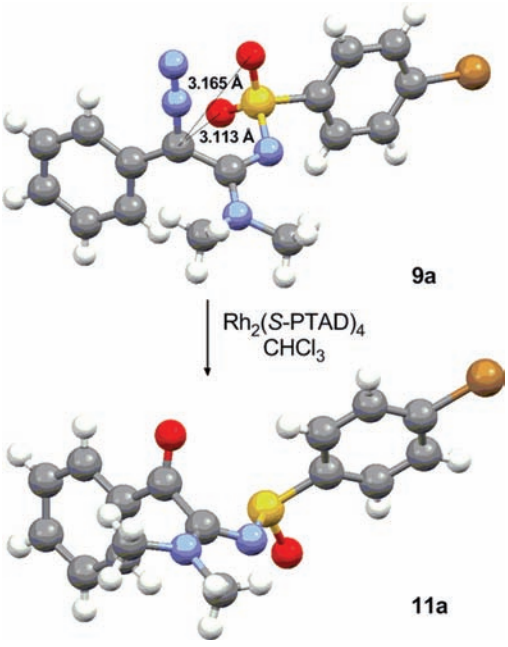
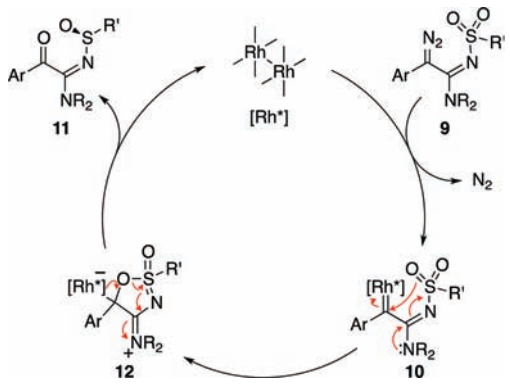


Figure 1. Crystal Structures of **9a** and **11a**.

The most intriguing feature of structure **9a** is the close proximity and the spatial alignment of the sulfonyl oxygen atoms (3.113 Å and 3.165 Å, respectively) with respect to the diazo carbon. The short distance between the oxygen atom and the latent carbene center, in addition to the electron-donating character of the dialkylamino substituent, provides a logical explanation of the unexpectedly fast intramolecular oxygen transfer. Furthermore, the exclusive *E*-geometry of the amidine bond in **9a** may influence the outcome of the reaction. It is important to point out that the intramolecular oxygen atom transfer was not observed at all in our previous studies of Rh-carbenes **2** generated from 1-sulfonyl 1,2,3-triazoles (**1**) lacking the 5-amino substituent.[2−4] In the latter system, the sulfonyl group in the azavinyl carbene is likely pointing away from the carbene center (cf. structures **2** in eq 1 and **9a** in Figure 1).

We hypothesize that the intramolecular reaction described here proceeds via the intermediates shown in Scheme 1. It begins with a rapid formation of rhodium carbene **10** from the diazo amidine **9**. Attack at the electrophilic carbene center by a sulfonyl oxygen atom is facilitated by the electron-rich dialkylamine substituent and the dirhodium moiety, which acts as an "electron sink", yielding intermediate **12**. The enantioselectivity of the process is determined by the geometry of intermediate **10**, favoring attack by one of the oxygen atoms in favor of the other. Decomposition of intermediate **12** regenerates the rhodium catalyst and delivers chiral product **11**.

Scheme 1. Proposed Catalytic Cycle



In addition to providing a practical synthesis of enantioenriched sulfinylamidines, this work demonstrates that rhodium azavinyl carbenes are sufficiently electrophilic to effect an unexpected oxygen transfer from the thermodynamically stable and generally considered inert sulfonamide sulfur(VI) atom. The role of dirhodium carboxylates in this transformation is two-fold: in addition to catalyzing decomposition of the diazo amidine, the dirhodium center acts as an electron buffer which orchestrates a complex sequence of bond-forming events. The facility, experimental simplicity, and high yields and good to excellent enantioselectivity make this newly discovered transformation a convenient method for the synthesis of densely functionalized sulfinylamidine derivatives and a useful reactivity probe for studying other heteroatom transfer reactions involving metal-stabilized carbenes.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, characterization data, NMR spectra, and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) (a) Carreno, M. C. *Chem. Rev.* **1995**, *95*, 1717. (b) Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35*, 984. (c) Fernández, I.; Khiar, N. *Chem. Rev.* **2003**, *103*, 3651. (d) Pellissier, H. *Tetrahedron* **2006**, *62*, 5559. Collins, S. G.; Maguire, A. R. In *Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*; Ramsden, C. A., Ed.; Georg Thieme Verlag KG: Stuttgart, 2007; Vol. *31a*, p 907. (e) García Ruano, J. L.; Cid, M. B.; Martín-Castro, A. M.; Alemán, J. In *Science of Synthesis: Houben-Weyl Methods of*

Molecular Transformations; Kambe, N., Ed.; Georg Thieme Verlag KG: Stuttgart, 2008; Vol. *39*, p 245.
(2) (a) Chuprakov, S.; Kwok, S. W.; Zhang, L.; Lercher, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2009**, *131*, 18034. (b) Grimster, N. P.; Zhang, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2010**, *132*, 2510.
(3) (a) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 14972. (b) Zibinsky, M.; Fokin, V. V. *Org. Lett.* **2011**, *13*, 4870.
(4) Chuprakov, S.; Malik, J. A.; Zibinsky, M.; Fokin, V. V. *J. Am. Chem. Soc.* **2011**, *133*, 10352.
(5) (a) Harmon, R. E.; Stanley, F. Jr.; Gupta, S. K.; Johnson, J. *J. Org. Chem.* **1970**, *35*, 3444. (b) Regitz, M.; Himbert, G. *Tetrahedron Lett.* **1970**, 2823. (c) Studies of the equilibria between the triazole and diazo form are reported in refs 5a. and 5b; the position of the equilibrium was found to be dependent on the triazole ring substituents and solvents but not on temperature.
(6) (a) Frank, D.; Himbert, G.; Regitz, M. *Chem. Ber.* **1978**, *111*, 183. (b) He, P.; Zhu, S. *Tetrahedron* **2006**, *62*, 549.
(7) (a) Müller, P.; Allenbach, Y.; Robert, E. *Tetrahedron: Asymmetry* **2003**, *14*, 779. (b) Müller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri, M.; Flack, H. D. *Org. Lett.* **2004**, *6*, 1725.
(8) Anada, M.; Watanabe, N.; Hashimoto, S. *Chem. Commun.* **1998**, 1517.
(9) Reddy, R. P.; Lee, G. H.; Davies, H. M. L. *Org. Lett.* **2006**, *8*, 3437.
(10) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6897.
(11) Doyle, M. P.; Zhou, Q.-L.; Raab, C. E.; Roos, G. H. P.; Simonsen, S. H.; Lynch, V. *Inorg. Chem.* **1996**, *35*, 6064.