# Stereoselective 1,3-Insertions of Rhodium(II) Azavinyl Carbenes

Stepan Chuprakov, Brady T. Worrell, Nicklas Selander, Rakesh K. Sit, and Valery V. Fokin*

Department of Chemistry, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, United States

S *Supporting Information*

ABSTRACT: Rhodium(II) azavinyl carbenes, conveniently generated from 1-sulfonyl-1,2,3-triazoles, undergo a facile, mild, and convergent formal 1,3-insertion into N−H and O−H bonds of primary and secondary amides, various alcohols, and carboxylic acids to afford a wide range of vicinally bisfunctionalized (Z)-olefins with perfect regio- and stereoselectivity. Utilizing the distinctive functionality installed through these reactions, a number of subsequent rearrangements and cyclizations expand the repertoire of valuable organic building blocks constructed by reactions of transition-metal carbene complexes, including α-allenyl ketones and amino-substituted heterocycles.
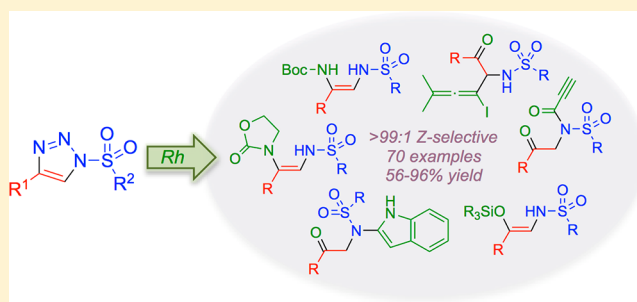
INTRODUCTION

Transition-metal-catalyzed reactions of diazo compounds are powerful methods for the formation of carbon−carbon and carbon−heteroatom bonds via additions and insertions of highly reactive metal carbene intermediates.[1] Thus, rhodium(II) and copper(I) carbenes derived from α-diazocarbonyl compounds readily undergo 1,1-insertion into N−H[2] and O−H[3] bonds to afford easy access to α-amino or α-oxy derivatives of ketones and esters (eq 1).
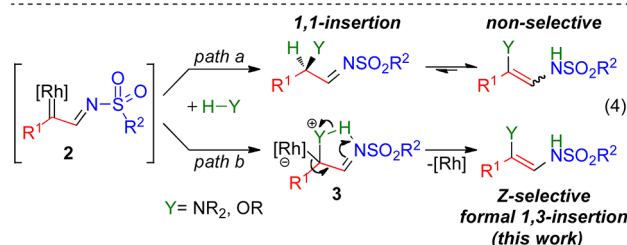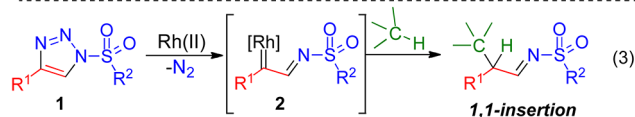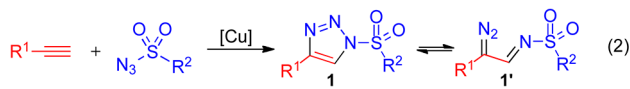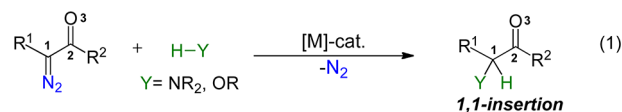
Certain electron-deficient 1,2,3-triazoles have recently emerged as convenient progenitors of diazo species.[4] Generally stable, crystalline compounds, they are easily prepared under mild copper(I)-catalyzed conditions from the corresponding sulfonyl azides and terminal alkynes (eq 2).[5] 1-Sulfonyltriazoles **1** exist in equilibrium with their diazoimine tautomers **1'**,[6] which can be efficiently intercepted by transition-metal catalysts to give rise to highly reactive rhodium(II) azavinyl carbenes **2** (eq 3). Although these intermediates share many features with the well-known donor−acceptor carbenes obtained from diazocarbonyl compounds (eq 1),[7] the aforementioned equilibrium and the presence of the aldimine group significantly alter their reactivity. The ring−chain tautomerism, which normally favors the ring structure **1**, slowly feeds the diazo imine species in the reaction, thus obviating controlled-addition requirements and simplifying the experimental setup. The pendant imine group allows fine-tuning of the steric and electronic properties of carbene **2**.[8] Its reactivity can be further exploited, for example, in subsequent cyclizations, expanding the repertoire of molecular architectures available from diazo compounds. Recent additions to the rapidly growing list of applications of 1-sulfonyl-1,2,3-triazoles under Rh(II) catalysis include transannulations and cyclopropanations,[9] C−H insertion,[10] ketone formation with water and O−H insertions/rearrangements,[11] ring expansions,[8,12] rearrangement reactions,[12a] and arylation with boronic acids.[13] In view of the efficiency of both the Cu(I)-catalyzed formation of triazole **1**[5] and its subsequent Rh(II)-catalyzed denitrogenative reactions,[8−13] this sequence of simple transformations can be viewed as a two-step regio- and stereoselective bisfunctionalization of the acetylenic backbone.

We recently reported a highly efficient insertion of Rh(II) azavinyl carbenes **2** into the C−H bonds of unactivated alkanes (eq 3).[10a] This 1,1-insertion likely proceeds via a direct hydride abstraction involving a three-membered transition state.[10b] In contrast, because of the polarized nature of N−H and O−H

bonds, we expected that they would react with azavinyl carbene **2** through a different insertion pathway.[1] For example, it has previously been proposed that insertion of rhodium carbenes derived from diazo ketones or esters into O−H bonds may proceed via the formation of an ylide intermediate followed by intra- or intermolecular proton abstraction, resulting in the overall 1,1-insertion (eq 1). As evidenced by previous work, products derived from azavinyl carbenes **2** are often isolated in the stable enamide tautomeric form as opposed to the sulfonyl imine derivative.[11−13] We envisioned that the related insertion of carbene **2** into O−H and N−H bonds could operate via two distinct mechanistic pathways (eq 4): (*i*) a direct 1,1-insertion followed by tautomerization, which could lead to an isomeric mixture of enamide products (path a); or (*ii*) the formation of ylide intermediate **3** followed by a stereospecific proton transfer (via a presumed hydrogen-bond-stabilized five-membered transition state), which could result in the syn-selective formation of enamide products (path b). Herein we report a modular and mild formal 1,3-insertion reaction of rhodium(II) azavinyl carbenes with various N−H- and O−H-containing reactants that yields highly functionalized enamide products as single geometrical isomers. We propose that this insertion reaction operates through the ylide-mediated mechanism (path b in eq 4), consistent with the high Z selectivity observed in this process.

■ RESULTS AND DISCUSSION

N−H Insertions with Primary Amides. The distinct reactivity of rhodium(II) azavinyl carbenes **2** toward N−H bonds was first observed when 1-mesyltriazole **1a** was allowed to react with 2 equiv of methyl carbamate (**4a**) in the presence of 1 mol % Rh(II) octanoate dimer at 65 °C (Table 1, entry 1).

Table 1. N−H Insertion with Primary Amides: Optimization of the Reaction Conditions[a]
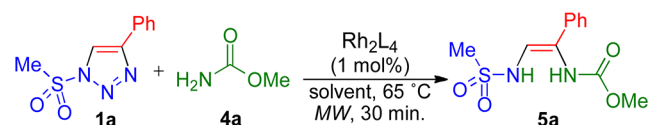
entry	catalyst	equiv of **4a**	solvent	yield (%)[b]
1	Rh$_2$(Oct)$_4$	2	CHCl$_3$	90
2	Rh$_2$(Oct)$_4$	1.1	CHCl$_3$	95
3	Rh$_2$(Oct)$_4$	1.1	1,2-DCE	79
4	Rh$_2$(Oct)$_4$	1.1	PhMe	0
5	Rh$_2$(OAc)$_4$	1.1	CHCl$_3$	95
6	Rh$_2$(OAc)$_4$	1.1	CHCl$_3$	89[c]
7	**Rh$_2$(Oct)$_4$**	**1.1**	**CHCl$_3$**	**95[c]**

[a]Conditions: triazole **1a** (0.20 mmol), methyl carbamate **4a**, and Rh$_2$L$_4$ (1.0 mol %) in 1 mL of dry CHCl$_3$ at 65 °C for 30 min in a microwave reactor. [b]NMR yields, unless otherwise noted. [c]Isolated yield (1.0 mmol scale).

Direct α-amination (1,1-insertion), similar to that previously reported for diazoesters reacting with carbamates,[2] was not observed in the N−H insertion with azavinyl carbenes **2**. Instead, diamine **5a** was rapidly formed in high yield as a single regio- and stereoisomer. The identity of this product was established by single-crystal X-ray analysis, confirming the Z geometry of the double bond (Figure 1).[14]

Optimization of the reaction conditions revealed that the amount of carbamate **4a** could be reduced to only 1.1 equiv (Table 1, entry 2), and the use of different organic solvents (toluene or 1,2-DCE) was not beneficial (Table 1, entries 3 and 4).
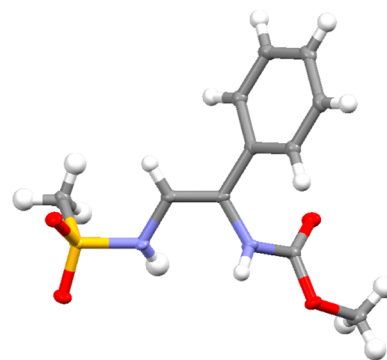

**Figure 1.** Crystal structure of enamide product **5a**.

Additionally, it was observed that rhodium(II) acetate gave comparable results to the more soluble rhodium(II) octanoate catalyst (Table 1, entry 5), but the latter proved to be a superior catalyst when used in larger-scale reactions (Table 1, entries 6 and 7).

With the optimized conditions (Table 1, entry 7) in hand, we examined the scope of this N−H insertion reaction.[15] Variously substituted 1-sulfonyl-1,2,3-triazoles **1** reacted smoothly with an array of primary amides **4**, leading to the substituted (Z)-enamides **5** with complete stereoselectivity (Table 2). Varying the electronic or steric nature of the sulfonyl group at N-1 of triazole **1** did not greatly affect the efficiency of this reaction. Accordingly, aliphatic and aromatic sulfonyl groups as well as sulfamoyl derivatives were tolerated in this reaction, giving excellent yields of products **5a−d** (84−95%; Table 2).

As Table 2 illustrates, a number of carbamates were effective in the formal 1,3-insertion with triazole **1**, including halo-substituted and bulky *tert*-butyl variants of **4**, which gave superb yields of the corresponding products **5e** and **5f** (96% and 93%, respectively). Additionally, alkyl, alkenyl, and aryl amides **4** readily afforded the desired products **5g−I** in good yields, while a number of functional groups (e.g., nitrile and nitro groups) were tolerated in this reaction. The efficiency of this transformation was not significantly affected by the nature of the C-4 aryl group in triazole **1**. Thus, substrates with electron-rich, electron-deficient, or heterocyclic groups gave comparable yields of the corresponding diamine products (**5j−m**; Table 2). Moreover, sulfonamides were also found to undergo facile N−H insertion to afford the expected 1,2-bis-sulfonamide products **5n−r** in good yields. Remarkably, the structurally complex Celecoxib analogue was shown to furnish the desired N−H insertion product **5p** in excellent yield (91%) despite bearing a pendent basic nitrogen atom.

The lack of information on these diamine products in the literature[16] prompted further investigation of their reactivity. In the course of our studies, we noted that these compounds were extremely configurationally stable: no isomerization of the double bond was noted even under forcing conditions. Furthermore, the configuration of the double bond remained intact even upon liberation of one of the amino groups: the Boc group in diamine **5f** could be efficiently removed using standard deprotection treatment with TFA (eq 5). The deprotected amine could be isolated as a single isomer in excellent yield as the trifluoroacetate salt **6**, which could further undergo hydrogenation, yielding the saturated diamine salt **7** in similarly good yield (eq 5).

In addition, we found that the catalytic hydrogenation of the enamide products **5** could be coupled with N−H insertion in an efficient and operationally simple one-pot procedure to deliver the saturated diamine **8** in excellent yield (eq 6). This

Table 2. Substrate Scope of the Rh(II)-Catalyzed N−H Insertion of Primary Amides^{a,b}
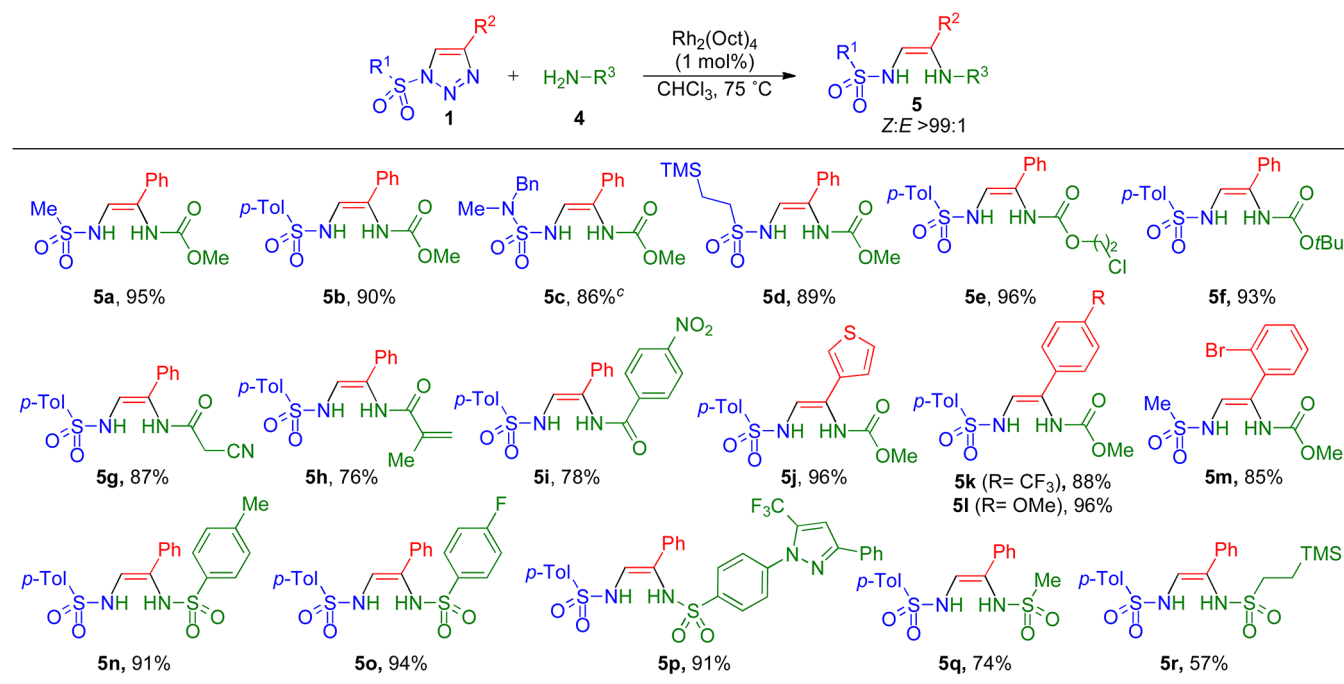
^{a}Conditions: 1-sulfonyl-1,2,3-triazole **1** (1.0 mmol), amide **4** (1.1 mmol), and Rh$_2$(Oct)$_4$ (0.01 mmol) in 3 mL of dry CHCl$_3$ at 75 °C for 1−3 h. ^{b}Isolated yields are shown. ^{c}100 °C.
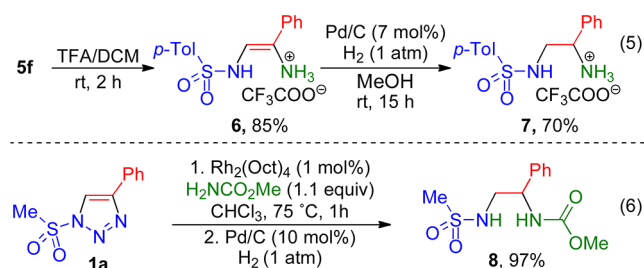

sequential procedure constitutes a simple route to vicinal diamines, which are valuable organic building blocks and common structural motifs found in many biologically active natural products, pharmaceuticals, and chiral ligands.[17]

N−H Insertions with Secondary Amides. Having identified an efficient route to diamine products **5** from primary amides **4** and triazoles **1**, we were naturally interested in exploring the reactivity of azavinyl carbenes with secondary amides. Compared with the unsubstituted congeners, secondary amides are more challenging substrates for N−H insertion reactions because of the presence of only one active N−H bond and the increased steric demands. In the conventional carbene reactions using diazocarbonyl compounds, the low activity of secondary amides or carbamates is usually circumvented by the use of a large excess of amide, by slow addition of the diazo compound, or, most commonly, by taking advantage of facile intramolecular insertion into a proximal N−H bond.[1] Given the intrinsically low concentration of the active diazoimine form of triazole **1**, in effect mimicking the high-dilution and large-excess techniques used for traditional diazocarbonyl compounds, we envisioned that a practical rhodium(II)-catalyzed intermolecular 1,3-insertion between a secondary N−H bond and triazole **1** could be achievable.

To test this possibility, we subjected triazole **1a** to reaction with oxazolidinone **9a** in the presence of rhodium(II) octanoate **13a** in CHCl$_3$ at 100 °C. To our surprise, along with a 53%

yield of the expected diamine **10a**, ketone derivative **11a** was formed in significant quantities (25%; Table 3). We propose that the formation of ketone **11a** arises from an initial O−H insertion of the azavinyl carbene into the hydroxy tautomer of **9a** followed by rearrangement of the putative intermediate **12** (Table 3). Similarly, reaction of tosyl-substituted triazole **1b**

Table 3. Effect of the Rh(II) Catalyst (13a−h) on the Regioselectivity of the Insertion with 2-Oxazolidone^a
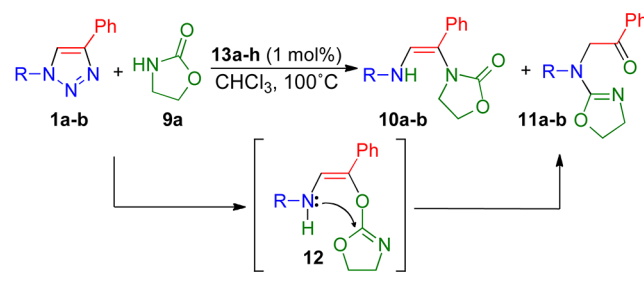
R=	%^{b} of	Rh(II) carboxylate catalysts (Figure 2)							
		13a	13b	13c	13d	13e	13f	13g	13h
Ms **1a**	10a	53^c	42	73	79	48	-	83	95
	11a	25^c	25	13	7	24	-	8	<5
Ts **1b**	10b	30	42	40	77	45	58	60	-
	11b	29	40	13	13	40	23	30	-

^{a}Conditions: triazole **1** (0.20 mmol), **9a** (0.22 mmol), and Rh$_2$L$_4$ (0.002 mmol) in 1 mL of dry CHCl$_3$ at 100 °C for 1 h. ^{b}NMR yields, unless otherwise noted. ^{c}Isolated yield (1.0 mmol scale).

with oxazolidinone **9a** under identical reaction conditions [1 mol % Rh(II) octanoate] provided nearly a 1:1 mixture of the corresponding N−H and O−H insertion products in moderate overall yield (Table 3).

The observed mixture of products (**10** and **11**) likely originates from the amide/imidic acid tautomerization equilibrium of substrate **9a** and subsequent competing formation of O- or N-ylides by the addition of Rh(II) azavinyl carbenes **2**. Therefore, the outcome of the 1,3-insertion reaction is expected to be determined primarily by the substrate, namely, the energy barrier of the aforementioned tautomerization. It has previously been shown that the electronic character of the carboxylate ligands on the rhodium complex can greatly bias the reactivity of the Rh carbene, which often allows for high levels of chemoselectivity (e.g., O−H vs C−H).[18] Taking into account the implicit difference in the electronic properties of the tautomeric forms of **9a**, we hypothesized that the use of electronically different ligands on rhodium could improve the selectivity of this reaction.

To this end, we screened a panel of catalysts **13a**−**h** (Figure 2) in conjunction with both triazoles **1a** and **1b** to ascertain the
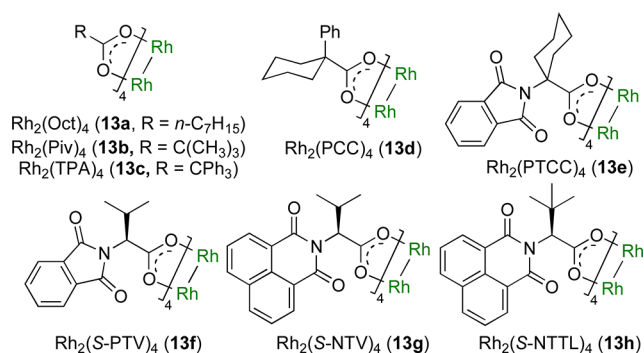

Figure 2. Rhodium(II) carboxylate catalysts employed in this study.

Rh₂(Oct)₄ (**13a**, R = *n*-C₇H₁₅)
Rh₂(Piv)₄ (**13b**, R = C(CH₃)₃)
Rh₂(TPA)₄ (**13c**, R = CPh₃)
Rh₂(PCC)₄ (**13d**)
Rh₂(PTCC)₄ (**13e**)
Rh₂(*S*-PTV)₄ (**13f**)
Rh₂(*S*-NTV)₄ (**13g**)
Rh₂(*S*-NTTL)₄ (**13h**)

parameters affecting the product distribution (Table 3). When phenylacetic acid-derived catalysts Rh₂(TPA)₄ (**13c**)[19] and Rh₂(PCC)₄ (**13d**)[20] (Figure 2) were employed with 1-mesyltriazole **1a**, higher selectivity toward the N−H insertion product **10a** was noted (73% and 79%, respectively; Table 3), while formation of ketone **11a** was suppressed (13% and 7%, respectively; Table 3).

Next, the performance of Rh(II) carboxylate complexes containing amino acid-derived ligands **13e**−**h** (Figure 2) was tested. The catalyst Rh₂(*S*-NTTL)₄ (**13h**)[21] in combination with 1-mesyltriazole **1a** was found to afford N−H insertion product **10a** in excellent yield and virtually as the exclusive product of the reaction (>95:5 selectivity). The structurally related catalyst **13g** was only slightly less efficient in the reaction with **1a**, while the electronically similar achiral complex Rh₂(PTCC)₄ (**13e**)[22] gave low selectivity and only moderate yields of the insertion products (Table 3). The regioselectivity of the insertion reaction with 1-tosyltriazole **1b** was found to be less responsive to the nature of the Rh(II) catalyst. The most effective catalyst, Rh₂(PCC)₄ **13d**, afforded only moderate selectivity toward N−H insertion (∼6:1) but gave a good overall yield (Table 3).

The scope of the N−H insertion reaction with secondary amides under these optimized conditions was examined next. As expected (vide supra), the selectivity and efficiency of the reaction were highly dependent on the nature of the amide partner (Table 4). Thus, the reaction of 1-mesyltriazole **1a** with *N*-methylbenzamide in the presence of Rh₂(*S*-NTTL)₄ produced intractable mixtures of products at elevated temperatures (75 °C). However, we found that this substrate reacted

Table 4. Substrate Scope of the Rh(II)-Catalyzed N−H Insertion of Secondary Amides[a,b]
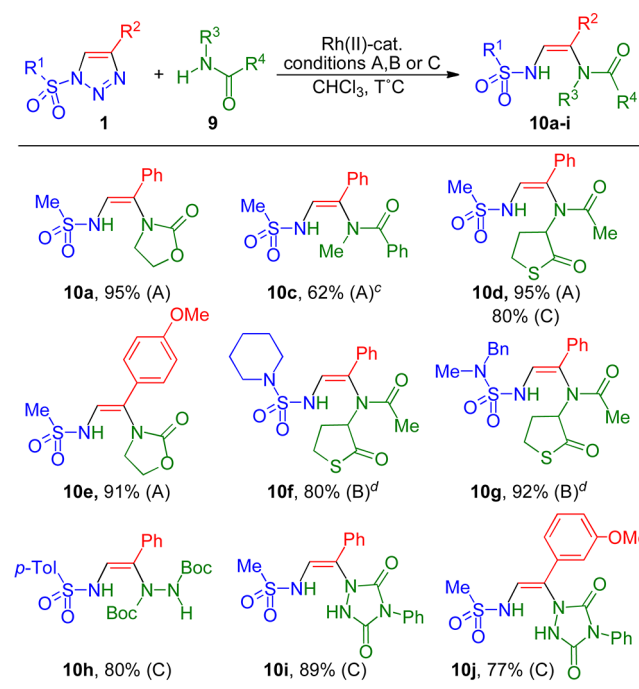
[a]General conditions: triazole **1** (1.0 mmol), **9** (1.1 mmol), and Rh₂L₄ (0.005−0.010 mmol) in 4 mL of dry CHCl₃ at 75 °C; (A) Rh₂-(*S*-NTTL)₄ (**13h**) 0.5 mol %, (B) Rh₂(PCC)₄ (**13d**) 1 mol %, (C) Rh₂(Oct)₄ (**13a**) 1 mol %. [b]Isolated yields are shown. [c]rt, 36 h. [d]120 °C, 5 h.

at room temperature and after a prolonged reaction time (36 h) afforded a good yield of the corresponding N−H insertion product **10c** (Table 4). This product was subjected to single-crystal X-ray analysis, which confirmed the predicted *Z* geometry of the double bond (Figure 3).[23]
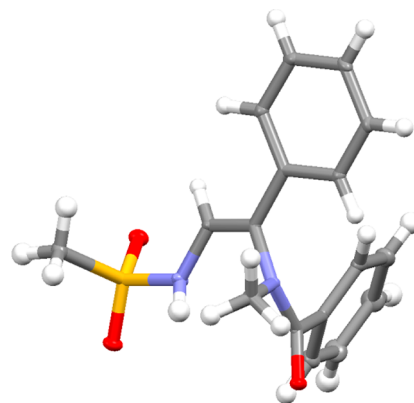

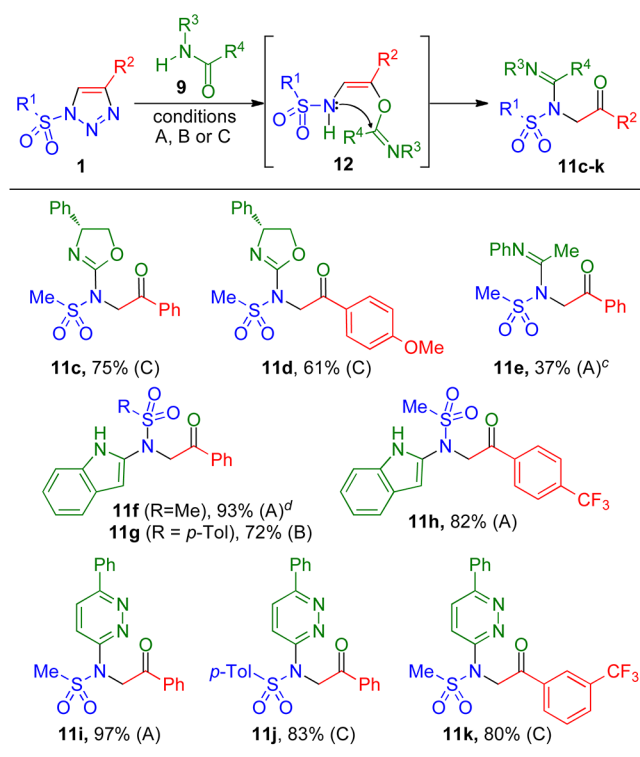**Figure 3.** Crystal structure of secondary diamine **10c**.

Interestingly, competing formation of the O−H insertion product was never observed with a thiolactone-containing acetamide substrate regardless of the catalyst used (**10d**, **10f**, **10g**; Table 4). *N*-Sulfamoyltriazoles **1**,[9n] however, required higher temperatures (100 °C) and the more stable catalyst Rh₂(PCC)₄ **13d** to ensure a high yield of the 1,3-insertion product with this amide substrate (**10f**, **10g**), while *N*-mesyltriazole **1a** reacted smoothly in the presence of Rh(II)

198

dx.doi.org/10.1021/ja408185c | *J. Am. Chem. Soc.* 2014, 136, 195−202

octanoate dimer to provide enamide product **10d** in good yield (Table 4).

Likewise, it was found that bis-*N*-Boc-hydrazine and 4-phenylurazol reacted with different triazoles **1** regioselectively in the presence of Rh₂(Oct)₄, giving exclusively the N−H insertion products **10h−j** (77−89%; Table 4). Overall, the electronic character of the C-4 substituent of 1-mesyltriazoles **1** had little to no effect on the reactivity or selectivity in the reaction with oxazolidinone (cf. **10a** and **10e** in Table 4).

Another factor contributing to the selectivity of the 1,3-insertion reaction with secondary amides is the relative steric hindrance of the −OH and −NH groups. Thus, the 5-phenyl-substituted analogue of oxazolidinone **9a** smoothly underwent exclusive O−H insertion/rearrangement with 1-mesyltriazole **1a** in the presence of catalyst **13a** to give ketone **11c** in 75% yield (Table 5). The insertion reaction of 4-(*p*-methoxyphenyl)-

compared with the insertion reaction with isomeric *N*-methylbenzamide (**10b**; Table 3). Likewise, when oxindole, the cyclic analogue of *N*-phenylacetamide, was employed, selective O−H insertion/rearrangement products **11f−h** were formed in high yields (72−93%). Similarly, reactions of 1-mesyl- and 1-tosyltriazoles **1** with 4-phenylpyridazinone afforded analogous aminated heterocyclic products **11i−k** in excellent yields (80−97%). In the latter cases, the formation of a stable heteroaromatic system could be an additional factor contributing to a higher population of the hydroxy tautomer, giving rise to the observed selectivity noted with these substrates.

With the ketone-containing compounds **11i** and **11k** in hand, we were intrigued by the possibility of an intramolecular dehydrative condensation that would lead to unique fused heterocycles. To this end, **11i** and **11k** were submitted to acidic conditions (3:2 H₂SO₄/AcOH) at elevated temperature. The hitherto-unknown desulfonylated pyridazoimidazoles **14a** and **14b** were formed in excellent yields (86% and 80%, respectively; eq 7).

Table 5. Substrate Scope of the Rh(II)-Catalyzed O−H Insertion of Secondary Amides[a,b]

11c, 75% (C)   **11d**, 61% (C)   **11e**, 37% (A)[c]

11f (R=Me), 93% (A)[d]   **11h**, 82% (A)
11g (R = *p*-Tol), 72% (B)
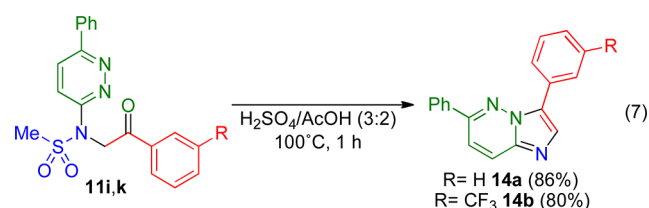
11i, 97% (A)   **11j**, 83% (C)   **11k**, 80% (C)

[a]General conditions: triazole **1** (1.0 mmol), **9** (1.1 mmol), and Rh₂L₄ (0.005−0.010 mmol) in 4 mL of dry CHCl₃ at 75 °C; (A) Rh₂(*S*-NTTL)₄ (**13h**) 0.5 mol %, (B) Rh₂(PCC)₄ (**13d**) 1 mol %, (C) Rh₂(Oct)₄ (**13a**) 1 mol %. [b]Isolated yields are shown. [c]rt, 36 h. [d]rt, 5 h.

substituted triazole with the same amide was similarly selective, furnishing the corresponding rearranged product **11d** in good isolated yield. Naturally, the O−H insertion discrimination observed in these cases, as opposed to the ambiguous selectivity of the parent carbamate **9a** (Table 3), can be attributed to the increased steric congestion of the N−H bond in the amide tautomer.

Similar reactivity was noted with *N*-phenylacetamide; although the corresponding product **11e** was obtained in poor yield (37% due to instability on silica gel; Table 5), steric arguments can likely be used to explain the observed exclusive formation of the O−H insertion product, particularly when

(7)

R= H **14a** (86%)
R= CF₃ **14b** (80%)

O−H Insertions with Carboxylic Acids. We recognized that the insertion of azavinyl carbenes into O−H bonds of carboxylic acids could yield intermediates akin to **12** (Table 5); a subsequent rearrangement would furnish synthetically appealing *N*-acyl α-amino ketones. To explore this transformation, we subjected 1-tosyl-1,2,3-triazole **1b** to the reaction with a slight excess of benzoic acid in the presence of 1 mol % rhodium(II) octanoate dimer **13a** in CHCl₃ at 75 °C. To our delight, 2-acyloxyenamine **16a** was rapidly formed as a sole, isolable product in 91% yield (Table 6). Surprisingly, the

**Table 6. Rh₂(Oct)₄-Catalyzed O−H Insertion with Carboxylic Acids[a,b]**
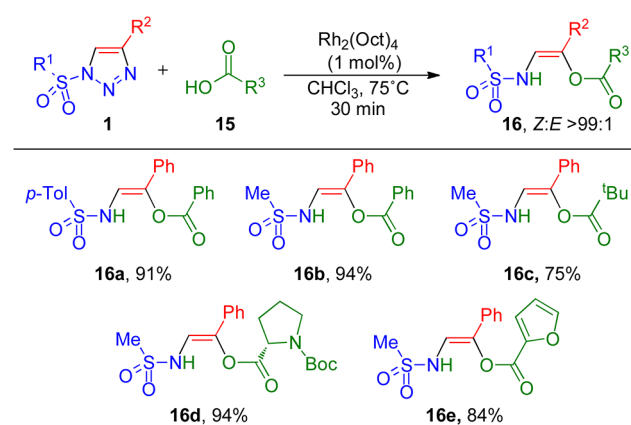
16a, 91%   **16b**, 94%   **16c**, 75%

16d, 94%   **16e**, 84%

[a]General reaction conditions: triazole **1** (1.0 mmol), acid **15** (1.1 mmol), and Rh₂(Oct)₄ (0.01 mmol) in 3 mL of dry CHCl₃ at 75 °C for 30 min. [b]Isolated yields are shown.

anticipated spontaneous rearrangement of product **16a** into the *N*-acyl α-amino ketone did not occur; further heating or

treatment with base, acid, or various amine catalysts yielded only decomposition products. Similar results were obtained with a number of different carboxylic acids **15** (Table 6). Thus, pivalic acid, *N*-Boc-protected proline, and 2-furoic acid were effective in the O−H insertion with 1-mesyltriazole **1a**, giving excellent yields of the 2-acyloxyenamine products **16c−e**, respectively (75−94%; Table 6).

Next, it was found that the use of less bulky or nonaromatic carboxylic acids **15** under identical reaction conditions led to the direct formation of *N*-acyl α-amino ketones **17** (Table 7).

**Table 7. Rh(II)-Catalyzed O−H Insertion/Rearrangement Cascade with Carboxylic Acids**[a,b]
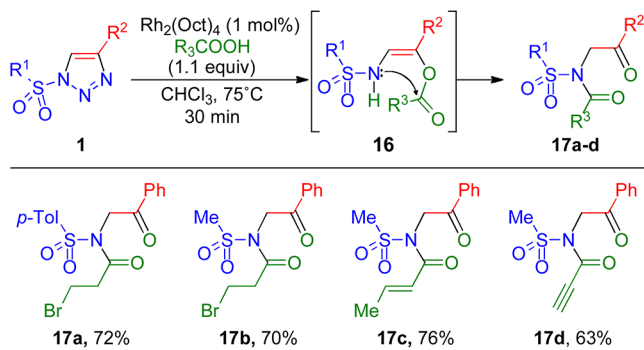
[a]General reaction conditions: triazole **1** (1.0 mmol), acid **15** (1.1 mmol), and Rh₂(Oct)₄ (0.01 mmol) in dry CHCl₃ (3 mL) at 75 °C for 30 min. [b]Isolated yields are shown.

Presumably, the easily accessible primary alkyl-, alkenyl-, or alkynyl-substituted carbonyl group in the initial O−H insertion product **16** could rapidly be attacked by the nitrogen atom of the enamide to furnish the rearranged products **17a−d** in good yields (63−76%; Table 7).

O−H Insertions with Alcohols. As a logical expansion of our study, we sought to explore simple alcohols as reactive substrates in 1,3-insertion reactions of rhodium(II) azavinyl carbenes.[24] First, 1-tosyltriazole **1b** was tested in the reaction with ethanol in the presence of the rhodium(II) octanoate dimer catalyst. While the expected alkoxy enamine was smoothly formed in high yield as judged by NMR analysis of the crude mixture, isolation by silica gel chromatography was problematic because of instability of the product. We hypothesized that the use of bulkier alcohol reactants could give more stable and isolable O−H insertion products. Indeed, treatment of triazole **1b** with isopropyl alcohol afforded the desired alkoxy enamine **19a** in good isolated yield (78%; Table 8). The use of isopropyl alcohol was equally effective with 1-mesyltriazole **1a**, affording product **19b** (69%; Table 8). Further exploration in regard to the scope of effective alcohol components **18** revealed that several secondary and tertiary alcohols were successful in this O−H insertion reaction, efficiently producing the corresponding alkoxy enamine products **19c−f** in good yields (69−83%; Table 8).

This O−H insertion was also efficient with triphenylsilanol as a reactant, giving rise to various silyl enol ethers in good yields (Table 7). This silanol substrate was found to be effective with multiple triazoles **1** possessing various aryl groups at the C-4 position (**19j−l**) as well as with different arylsulfonyl groups at N-1 (**19g−i**). Of note, the silyl enol ethers **19** generated by this 1,3-insertion reaction were formed as single geometrical isomers and are formal descendants of α-amino ketones.

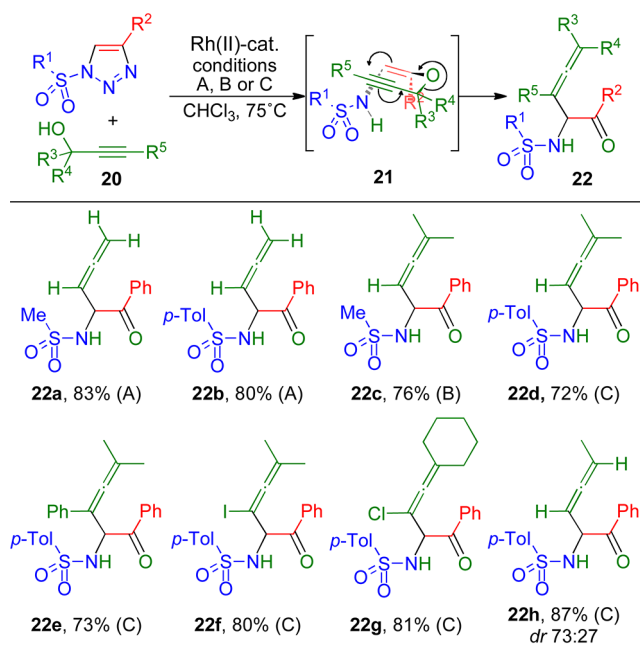**Table 8. Substrate Scope of the Rh(II)-Catalyzed O−H Insertion with Alcohols and Triphenylsilanol**[a,b]
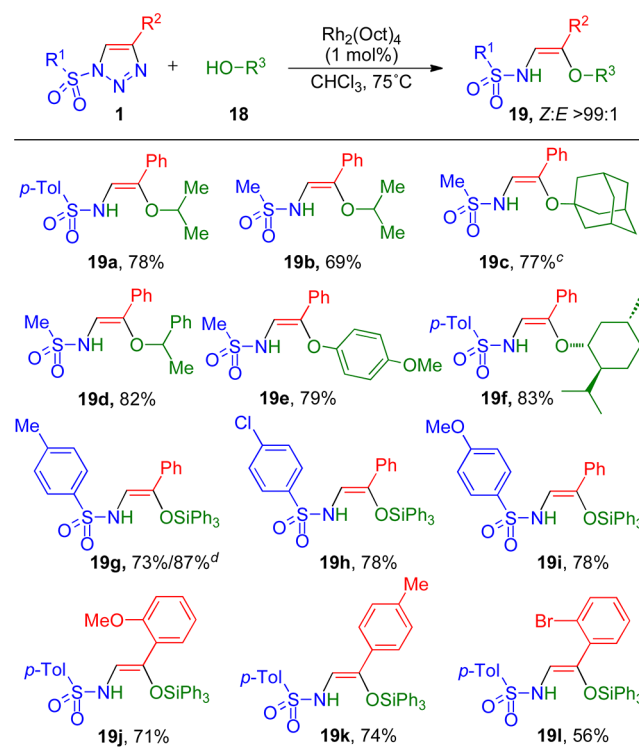
[a]General reaction conditions: triazole **1** (1.0 mmol), alcohol **18** (1.1 mmol), and Rh₂(Oct)₄ (0.01 mmol) in 3 mL of dry CHCl₃ at 75 °C for 1−5 h. [b]Isolated yields are shown. [c]Catalyst **13b** was used instead of Rh₂(Oct)₄. [d]10 mmol scale.

These valuable electronically rich olefinic building blocks are not accessible by direct deprotonation/silylation of the corresponding ketone products because of the presence of the pendant amide moiety.[25]

Interestingly, when propargyl alcohol and triazole **1a** were allowed to react under the standard 1,3-insertion conditions (vide supra), the usual O−H insertion product was not observed. Instead, the expected product **21** underwent a smooth Saucy−Marbet-type [3,3]-sigmatropic rearrangement to afford α-allenyl ketone **22a** in high isolated yield (83%; Table 9).[26] Naturally, we were interested in studying the scope of this novel cascade, involving formation of the previously unknown and apparently highly reactive electron-rich propargyloxy enamides **21** en route to versatile and valuable allenyl-containing building blocks.[27]

It was found that a series of variously substituted propargyl alcohols **20** underwent this O−H insertion/rearrangement cascade smoothly to afford the corresponding allene products **22b−h** in good yields (72−87%; Table 9). Increasing the steric bulk at the propargyl position of alcohol **20** did not affect the efficiency of this reaction (**22c** and **22d**; Table 9). Moreover, internal alkynes bearing either 1-aryl or 1-halo substituents furnished the corresponding tetrasubstituted allenes in good yields (**22e−g**; Table 9). The use of racemic monomethyl propargyl alcohol **14** afforded allene **22h** in high yield, albeit with moderate diastereoselectivity (dr 73:27). Although the structures of products **22** were evident from NMR data, additional confirmation was obtained through single-crystal X-ray analysis of α-allenyl ketone **22e** (Figure 4).[28]

Table 9. O−H Insertion/[3,3]-Sigmatropic Rearrangement Cascade with Propargyl Alcohols[a,b]

| 22a, 83% (A) | 22b, 80% (A) | 22c, 76% (B) | 22d, 72% (C) |
| 22e, 73% (C) | 22f, 80% (C) | 22g, 81% (C) | 22h, 87% (C) dr 73:27 |

[a] General reaction conditions: triazole **1** (1.0 mmol), propargyl alcohol **20** (1.1 mmol), and Rh(II) carboxylate (0.01 mmol) in dry CHCl$_3$ (3 mL) at 75 °C for 0.5−3 h; (A) Rh$_2$(Oct)$_4$, (B) Rh$_2$(Piv)$_4$, (C) Rh$_2$(PCC)$_4$. [b] Isolated yields are shown.
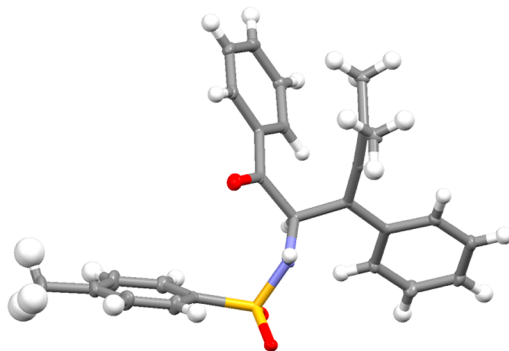
Figure 4. Crystal structure of α-allenyl ketone **22e**.

CONCLUSIONS

The new family of highly efficient O−H and N−H insertion reactions of rhodium(II) azavinyl carbenes reported here exploits the distinct reactivity of these reactive intermediates directly generated from 1-sulfonyl-1,2,3-triazoles. As opposed to 1,1-insertions typically observed with conventional donor–acceptor carbenes derived from diazocarbonyl precursors, these reactions proceed via an unusual formal 1,3-insertion pathway, stereoselectively yielding densely functionalized (Z)-enamide products. The regioselectivity of the 1,3-insertion (N−H vs O−H) is often determined by the nature of the substrate; however, it can also be controlled by the catalyst in a number of cases. The (Z)-enamide products undergo further transformations to furnish valuable heterocyclic products and building blocks amenable to further derivatization. These novel and highly modular methods for regio-, chemo-, and stereoselective bis-amination and oxyamination of the acetylenic triple bond via C−N and C−O bond-forming reactions underscore the

versatility of acetylenes and should find applications in the synthesis of complex molecular architectures.

EXPERIMENTAL SECTION

Typical Preparative Procedure. To a 2−5 mL microwave vial were added 1-mesyl-4-phenyl-1,2,3-triazole (**1a**) (0.223 g, 1.0 mmol) and methyl carbamate (**4a**) (0.083g, 1.1 mmol), followed by 7.8 mg (0.01 mmol) of rhodium(II) octanoate dimer **13a**. The vial was sealed with a Teflon microwave cap, and dry CHCl$_3$ (4.0 mL) was added to the reaction mixture. The vial was stirred at 75 °C in an oil bath for 30 min or until the reaction was complete by TLC and LC−MS analysis. Column chromatography on silica gel using 2:1 ethyl acetate/hexane as the eluent was directly performed on the reaction mixture to afford 0.257 g (0.95 mmol, 95% yield) of (Z)-methyl (2-methylsulfonamido-1-phenylvinyl)-carbamate (**5a**) as a colorless crystalline solid.

Data for **5a**: ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.53 (d, J = 10.0 Hz, 1H), 7.39−7.33 (m, 4H), 7.32−7.28 (m, 1H), 6.40 (bs, 1H), 6.10 (s, 1H), 3.80 (s, 3H), 3.10 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d$_6$): δ 154.8, 137.1, 128.3, 126.6, 124.2, 119.4, 117.2, 51.7, 41.1. LRMS (ESI): m/z 293.2 [M + Na]$^+$.

ASSOCIATED CONTENT

S **Supporting Information**

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

AUTHOR INFORMATION

Corresponding Author
fokin@scripps.edu

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

REFERENCES

(1) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998.

(2) For rhodium(II)-catalyzed intermolecular N−H insertions, see: (a) Paulissen, R.; Hayez, E.; Hubert, A. J.; Teyssie, P. *Tetrahedron Lett.* **1974**, *15*, 607. (b) Osipov, S. N.; Sewald, N.; Kolomiets, A. F.; Fokin, A. V.; Burger, K. *Tetrahedron Lett.* **1996**, *37*, 615. (c) Bagley, M. C.; Buck, R. T.; Hind, S. L.; Moody, C. J.; Slawin, A. M. Z. *Synlett* **1996**, 825. For copper(I)-catalyzed intermolecular N−H insertions, see: (d) Yates, P. *J. Am. Chem. Soc.* **1952**, *74*, 5376. (e) Lee, E. C.; Fu, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 12066.

(3) For rhodium(II)-catalyzed intermolecular O−H insertions, see: (a) Paulissen, R.; Reimlinger, H.; Hayez, E.; Hubert, A. J.; Teyssie, P. *Tetrahedron Lett.* **1973**, *14*, 2233. (b) Noels, A. F.; Demonceau, A.; Petiniot, N.; Hubert, A. J.; Teyssie, P. *Tetrahedron* **1973**, *38*, 2733. (c) Cox, G. G.; Haigh, D.; Hindley, R. M.; Miller, D. J.; Moody, C. J. *Tetrahedron Lett.* **1994**, *35*, 3139. For copper(I)-catalyzed intermolecular O−H insertions, see: (d) Saegusa, T.; Ito, Y.; Kobayashi, S.; Hirota, K.; Shimizu, T. *J. Org. Chem.* **1968**, *33*, 544. (e) Maier, T. C.; Fu, G. C. *J. Am. Chem. Soc.* **2006**, *128*, 4594.

(4) For recent reviews, see: (a) Chattopadhyay, B.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2012**, *51*, 862. (b) Gulevich, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2013**, *52*, 1371.

(5) (a) Yoo, E. J.; Ahlquist, M.; Kim, S. H.; Bae, I.; Fokin, V. V.; Sharpless, K. B.; Chang, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 1730. (b) Raushel, J.; Fokin, V. V. *Org. Lett.* **2010**, *12*, 4952. (c) Liu, Y.; Wang, X.; Xu, J.; Zhang, Q.; Zhao, Y.; Hu, Y. *Tetrahedron* **2011**, *67*, 6294.

(6) (a) Dimroth, O. *Ann. Chem.* **1909**, *364*, 183. (b) Gilchrist, T. L.; Gymer, G. E. *Adv. Heterocycl. Chem.* **1974**, *16*, 33. Also see ref 5a.

(7) For recent reviews of donor−acceptor carbenes, see: (a) Davies, H. M. L.; Morton, D. *Chem. Soc. Rev.* **2011**, *40*, 1857. (b) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417.

(8) For example, see: Liu, R.; Zhang, M.; Winston-McPherson, G.; Tang, W. *Chem. Commun.* **2013**, *49*, 4376.

(9) For transannulations, see: (a) Chuprakov, S.; Hwang, F. W.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2007**, *46*, 4757. (b) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 14972. (c) Miura, T.; Yamauchi, M.; Murakami, M. *Chem. Commun.* **2009**, 1470. (d) Chattopadhyay, B.; Gevorgyan, V. *Org. Lett.* **2011**, *13*, 3746. (e) Zibinsky, M.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2013**, *52*, 1507. (f) Chuprakov, S.; Kwok, S. W.; Fokin, V. V. *J. Am. Chem. Soc.* **2013**, *135*, 4652. (g) Schultz, E. E.; Sarpong, R. *J. Am. Chem. Soc.* **2013**, *135*, 4696. (h) Parr, B. T.; Green, S. A.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 4716. (i) Spangler, J. E.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 6802. (j) Alford, J. S.; Spangler, J. E.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 11712. For cyclopropanations, see: (k) Chuprakov, S.; Kwok, S. W.; Zhang, L.; Lercher, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2009**, *131*, 18034. (l) Grimster, N.; Zhang, L.; Fokin, V. V. *J. Am. Chem. Soc.* **2010**, *132*, 2510. (m) Alford, J. S.; Davies, H. M. L. *Org. Lett.* **2012**, *14*, 6020. (n) Culhane, J. C.; Fokin, V. V. *Org. Lett.* **2011**, *13*, 4578.

(10) (a) Chuprakov, S.; Malik, J. A.; Zibinsky, M.; Fokin, V. V. *J. Am. Chem. Soc.* **2011**, *133*, 10352. For a discussion of mechanism, see: (b) Doyle, M. P. Catalytic Carbene Complexes in Organic Synthesis: Diazodecomposition—Insertion and Ylide Chemistry. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon Press: New York, 1995; Vol. 12, Chapter 5.2.

(11) (a) Miura, T.; Biyajima, T.; Fujii, T.; Murakami, M. *J. Am. Chem. Soc.* **2012**, *134*, 194. (b) Miura, T.; Tanaka, T.; Biyajima, T.; Yada, A.; Murakami, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 3883.

(12) (a) Selander, N.; Worrell, B. T.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2012**, *51*, 13054. (b) Miura, T.; Funakoshi, Y.; Morimoto, M.; Biyajima, T.; Murakami, M. *J. Am. Chem. Soc.* **2012**, *134*, 17440.

(13) Selander, N.; Worrell, B. T.; Chuprakov, S.; Velaparthi, S.; Fokin, V. V. *J. Am. Chem. Soc.* **2012**, *134*, 14670.

(14) The structure has been deposited with the Cambridge Crystallographic Data Centre (CCDC 934421). See the Supporting Information for details.

(15) Simple and weakly basic amines (e.g., aniline) were studied as substrates in this reaction but in all cases failed to afford the desired N−H insertion products.

(16) No reports of vicinal diamine compounds akin to products **5** or **10** could be found using SciFinder Scholar.

(17) For a recent review, see: Jong, S. D.; Nosal, D. G.; Wardrop, D. J. *Tetrahedron* **2012**, *68*, 4067.

(18) (a) Padwa, A.; Austin, D. J.; Hornbuckle, S. F.; Semones, M. A. *J. Am. Chem. Soc.* **1992**, *114*, 1874. (b) Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. *J. Am. Chem. Soc.* **1993**, *115*, 8669.

(19) (a) Hashimoto, S.; Watanabe, N.; Ikegami, S. *Tetrahedron Lett.* **1992**, *33*, 2709. (b) Hashimoto, S.; Watanabe, N.; Sato, M.; Ikegami, S. *Tetrahedron Lett.* **1993**, *34*, 5109.

(20) The previously unreported catalyst 1-phenylcyclohexanecarboxylate (PCC) rhodium(II) dimer was prepared in a manner similar to that given in ref 18a. See the Supporting Information for experimental details.

(21) Müller, P.; Allenbach, Y.; Robert, E. *Tetrahedron: Asymmetry* **2003**, *14*, 779.

(22) The previously unreported catalyst 1-phthalamidocyclohexane-carboxylate (PTCC) rhodium(II) dimer was prepared in a manner similar to that given in ref 18b. See the Supporting Information for experimental details.

(23) The structure has been deposited with the Cambridge Crystallographic Data Centre (CCDC 934423). See the Supporting Information for details.

(24) A singular example of an O−H insertion with *tert*-butyl alcohol under rhodium(II) catalysis was recently shown to give the 1,3-insertion product in a moderate yield in a syn-selective manner. See ref 11.

(25) Aggarwal, V. K.; Sheldon, C. G.; Macdonald, G. J.; Martin, W. P. *J. Am. Chem. Soc.* **2002**, *124*, 10300.

(26) While this manuscript was in preparation, a singular example of this transformation was reported. However, the product was not isolated (the NMR yield was reported). See ref 11b.

(27) Norbert, K.; Hashmi, A. S. K. *Modern Allene Chemistry*; Wiley: New York, 2004.

(28) The structure has been deposited with the Cambridge Crystallographic Data Centre (CCDC 934422). See the Supporting Information for details.