DOI: 10.1002/chem.201402258

Palladium Catalysis

Influence of Catalyst Structure and Reaction Conditions on *anti*- versus *syn*-Aminopalladation Pathways in Pd-Catalyzed Alkene Carboamination Reactions of *N*-Allylsulfamides

Ryan M. Fornwald,[a] Jonathan A. Fritz,[b] and John P. Wolfe*[a]

Abstract: The Pd-catalyzed coupling of *N*-allylsulfamides with aryl and alkenyl triflates to afford cyclic sulfamide products is described. In contrast to other known Pd-catalyzed alkene carboamination reactions, these transformations may be selectively induced to occur by way of either *anti*- or *syn*-aminopalladation mechanistic pathways by modifying the catalyst structure and reaction conditions.

Introduction

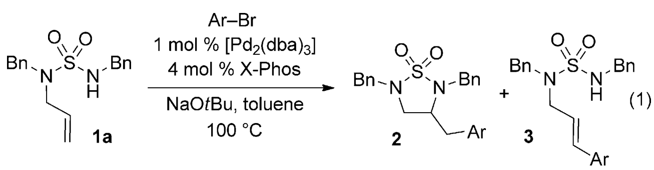
Cyclic sulfamides are an important class of heterocycle that have attracted attention in medicinal-chemistry applications as these functional groups can serve as isosteres for cyclic ureas and are also known to form attractive electrostatic interactions with proteins and enzymes.[1] Biologically active compounds that bear these units have been examined as protease inhibitors,[2] human leukocyte elastase (HLE) inhibitors,[3] renin inhibitors,[4] and norovirus inhibitors.[5] In addition, the SO_2 unit can be cleaved from these compounds to afford synthetically useful 1,2-diamines.[6,7] Cyclic sulfamides have also been employed as chiral auxiliaries for asymmetric aldol and alkylation reactions.[8]

Classical approaches to the synthesis of cyclic sulfamides frequently involve treatment of 1,2-diamines with sulfamide or related electrophiles and generally require relatively complex starting materials.[9] In recent years, a number of metal-catalyzed alkene diamination or oxidative cyclization reactions have been described that effect the conversion of readily available substrates into cyclic sulfamide derivatives.[7]

We have previously reported a method for the construction of cyclic ureas through Pd-catalyzed alkene carboamination reactions between acyclic *N*-allylureas and aryl or alkenyl halides.[10] We felt that related transformations of *N*-allylsulfamides could provide an attractive and simple approach to the generation of substituted cyclic sulfamides.[11] In addition, this strategy would complement existing methods as it would allow for the conversion of an acyclic *N*-allylsulfamide into a cyclic sulfamide with the generation of both a C–N and a C–C bond. Herein, we describe our studies in this area and our findings that the stereochemistry of the addition to the alkene can be controlled by the appropriate choice of catalyst and conditions, which influence the *syn*- versus *anti*-aminopalladation mechanistic pathways in the catalytic cycle.

Results and Discussion

Initially, we examined the Pd-catalyzed carboamination between **1a** and 4-bromobenzonitrile. After some exploration, the use of a catalyst composed of $[Pd_2(dba)_3]$ and the Buchwald X-Phos[12] ligand afforded the desired product **2a** in 79% yield of the isolated product [Eq. (1); dba = dibenzylideneacetone]. However, the scope of this reaction was limited to electron-deficient aryl bromides as a competing Heck arylation occurred in the reactions of the more electron-rich electrophiles.



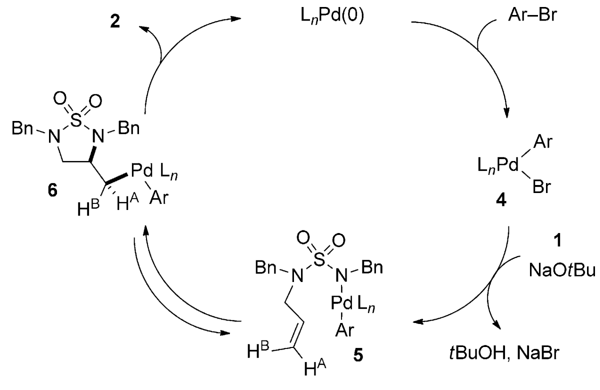
Ar = *p*-CN-C_6H_4: **2a**, 25:1 selectivity, 79% yield
Ar = Ph: **2b**, 2:1 selectivity, yield not determined

We initially postulated that the mechanism of the carboamination reactions of *N*-allylsulfamides was similar to that of other nucleophiles, such as ureas or amines.[13] Namely, the oxidative addition of the aryl bromide to a Pd^0 center to generate **4**, which reacts with substrate **1** and base to afford **5**.[14] The *syn*-aminopalladation reaction of **5** gives **6**, which can undergo reductive elimination to afford the observed product **2** (Scheme 1).

[a] R. M. Fornwald, Prof. Dr. J. P. Wolfe
Department of Chemistry
University of Michigan, 930 N. University Ave
Ann Arbor, MI 48109-1055 (USA)
E-mail: jpwolfe@umich.edu

[b] Prof. Dr. J. A. Fritz
Department of Chemistry
Aquinas College, 202 Albertus Hall
1607 Robinson Road SE, Grand Rapids MI 49506-1799 (USA)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201402258.



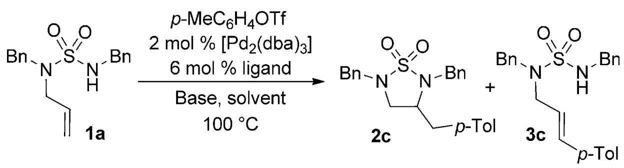
Scheme 1. The *syn*-aminopalladation mechanism.

We felt that two factors could potentially be the cause of the Heck arylation side reactions observed with relatively electron-rich aryl bromides: 1) the formation of a Pd–N bond (**4**→**5**) may be relatively slow for palladium complexes that are less electrophilic as a result of the electron-rich aryl groups bound to the metal center or 2) the aminopalladation step (**5**→**6**) may be reversible,[15] and competing migratory insertion of the alkene unit into the Pd–C bond of **4** (which leads to side-product **3**) may be faster with relatively electron-rich aryl groups.[16] These factors suggested that the use of aryl triflate substrates could potentially lead to improved results in Pd-catalyzed carboamination reactions of *N*-allylsulfamides. The oxidative addition of aryl triflates to the Pd^0 center leads to the formation of cationic palladium complexes,[17] which should undergo more facile Pd–N-bond formation due to the increased electrophilicity of these intermediates. In addition, the non-nucleophilic triflate anion is less likely to promote the formation of anionic complexes that are known to accelerate Heck reactions.[18]

We studied the coupling of **1** with *para*-tolyl triflate (Table 1) to test this idea, and our first results when using X-Phos as ligand were disappointing; namely, a 1:1 mixture of the desired product and the side product of the Heck reaction (**2c**/**3c**) was obtained. However, after further exploration, we discovered that the RuPhos ligand provided significantly better results, and a screen of bases revealed that the use of LiOtBu provided further improvement. Finally, switching to the more polar solvent benzotrifluoride resulted in the formation of the desired product, with only a trace amount of the side product from the Heck arylation reaction.

We proceeded to examine the scope of Pd-catalyzed carboamination reactions of *N*-allylsulfamides with a variety of different aryl triflates (Table 2). Both electron-withdrawing groups (Table 2, entries 2, 7, 9, and 13) and electron-donating groups (Table 2, entries 3, 10, and 12) were tolerated on the aryl triflate substrate. In addition, the reaction of an *ortho*-substituted aryl triflate also proceeded in good yield (Table 2, entry 4). Alkenyl triflates were also viable substrates (Table 2, entries 5 and 6), and the reactions proceeded with retention of the alkene geometry. The RuPhos ligand provided satisfactory results with most electrophiles that were examined. However, in a few cases, superior results were obtained with Brettphos, 2-di-tert-butylphosphino-2′-(N,N-dimethylamino)biphenyl (*t*Bu-Davephos), or 2-di-tert-butylphosphino-2′-(N,N-dimethylamino)biphenyl (*t*BuXPhos; Table 2, entries 5, 6 and 11, respectively). In most cases, the Pd-catalyzed carboamination reactions did not generate significant amounts of undesired side products. However, in a few instances, side products that result from a competing 6-endocyclization reaction were observed. In addition, in some cases, reactions of substrates that contained two different groups on the nitrogen atoms ($R \neq R^1$) generated side

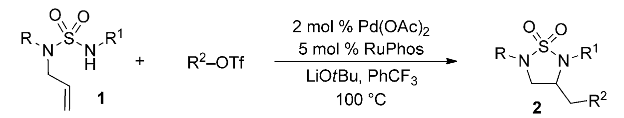
Table 1. Optimization of carboamination of aryl triflates.[a]

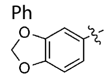


Entry	Ligand	Base	Solvent	**2c**/**3c**	Conversion [%][b]
1	X-Phos	NaO*t*Bu	toluene	1:1	81
2	RuPhos	NaO*t*Bu	toluene	9:1	90
3	RuPhos	LiO*t*Bu	toluene	19:1	100
4	RuPhos	LiO*t*Bu	$PhCF_3$	>25:1	100[c]

[a] Reaction conditions: **1a** (1.0 equiv), p-MeC_6H_4OTf (1.2 equiv), base (1.4 equiv), $[Pd_2(dba)_3]$ (2 mol %), ligand (6 mol %), solvent (0.25 M), 100 °C; [b] Conversion = percentage of starting material consumed. [c] The reaction was conducted using $Pd(OAc)_2$ (2 mol %) and ligand (5 mol %).

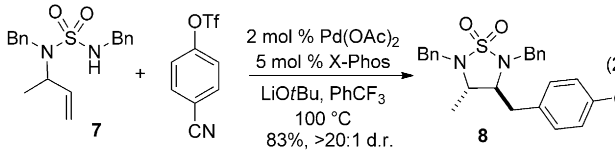
Table 2. Pd-catalyzed carboamination of *N*-allylsulfamides.[a]



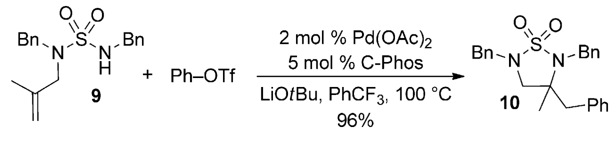
Entry	R	R^1	R^2	Product	Yield [%][b]
1	Bn	Bn	p-Me-C_6H_4	**2c**	85
2	Bn	Bn	p-NC-C_6H_4	**2a**	90
3	Bn	Bn	p-MeO-C_6H_4	**2d**	90
4	Bn	Bn	o-Me-C_6H_4	**2e**	85
5	Bn	Bn	1-cyclohexenyl	**2f**	87[c]
6	Bn	Bn	(*E*)-1-decenyl[e]	**2g**	80[d,e,f]
7	Me	Bn	p-Cl-C_6H_4	**2h**	79
8	Bn	PMB	p-Me-C_6H_4	**2i**	90
9	Bn	Me	m-F_3C-C_6H_4	**2j**	86
10	Bn	*t*Bu	p-MeO-C_6H_4	**2k**	92
11	Bn	PMP	Ph	**2l**	90[g]
12	Me	Bn		**2m**	84
13	*t*Bu	Bn	m-F_3C-C_6H_4	**2n**	88[h]
14	H	allyl	Ph	**2o**	51[i]

[a] Reaction conditions: **1** (1.0 equiv), R^2OTf (1.2 equiv), LiO*t*Bu (1.4 equiv), $Pd(OAc)_2$ (2 mol %), RuPhos (5 mol %), $PhCF_3$ (0.25 M), 100 °C. [b] Yield of the isolated product (average of two experiments). [c] The reaction was conducted with Brettphos as the ligand. [d] The reaction was conducted with *t*Bu-Davephos as the ligand. [e] The alkenyl triflate was used as a 5:1 mixture of *E*/*Z* isomers, and the product was obtained as a 5:1 *E*/*Z* mixture. [f] The reaction was conducted using R^2OTf (1.4 equiv) and LiO*t*Bu (1.6 equiv). [g] The reaction was conducted with *t*Bu-X-Phos as the ligand. [h] The reaction was conducted with 7.5 mol % ligand. [i] The reaction was conducted with R^2OTf (2.4 equiv) and LiO*t*Bu (2.4 equiv). PMB = *para*-methoxybenzyl ether, PMP = *para*-methoxyphenyl.

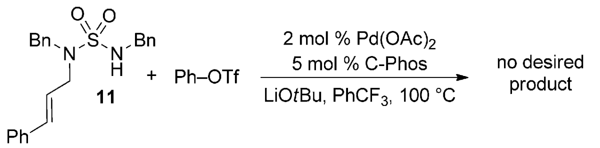
products from allylic transposition and cyclization. In a few instances, small amounts of a side product **3** from a Heck reaction were also generated. In cases in which this side product could not easily be separated by column chromatography, the side product from the Heck reaction was de-allylated (through Pd-catalyzed π-allyl formation/trapping) by the addition of 1,3-bis(diphenylphosphino)propane (DPPP) and morpholine to the reaction mixture.



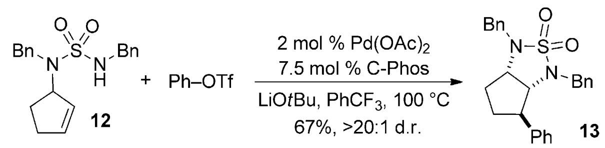
(2)



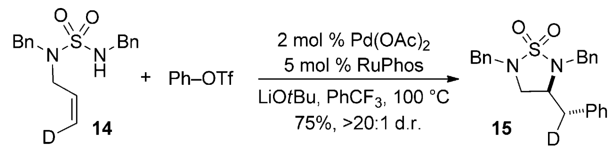
(3)



(4)



(5)

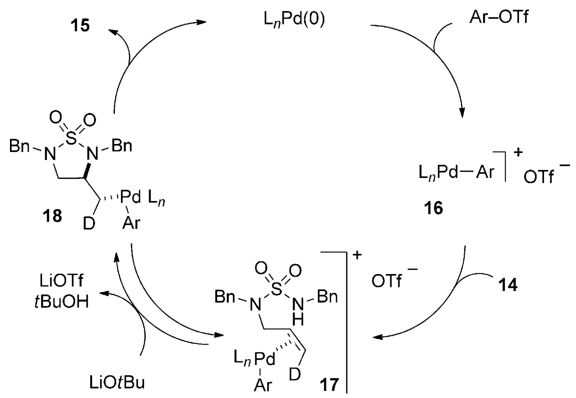


(6)

To further explore the scope of the sulfamide carboamination reactions, we examined transformations of more highly substituted substrates. After some exploration, we discovered that the C-Phos ligand provided higher yields and cleaner reactions than Ruphos in these transformations. Substrate **7**, with an allylic methyl group, was converted into **8** in good yield with >20:1 d.r. [Eq. (2)], and the presence of a methyl group on the internal alkene carbon atom was also tolerated in the conversion of **9** into **10** [Eq. (3)]. Efforts to cyclize substrate **11**, which bears an *E*-disubstituted alkene, were unsuccessful, with no reaction observed [Eq. (4)]. However, cyclopentene-derived substrate **12** was successfully coupled with phenyl triflate to afford bicyclic product **13** [Eq. (5)]. In contrast to the related carboamination reactions of other nucleophiles,[13] the carboamination of **12** proceeded with *anti* addition to the alkene. Similarly, the deuterated substrate **14** was converted into **15**, the product of *anti* addition to the alkene with high stereoselectivity [Eq. (6)].

The formation of products resulting from the *anti* addition to the alkene is in sharp contrast to previously reported alkene carboamination reactions, which afford *syn*-addition products.[11] As such, it appears that the mechanism of the Pd-catalyzed reactions of *N*-allylsulfamides with aryl triflates differs from other Pd-catalyzed carboamination reactions in which the Pd–N bond is generated through *syn*-aminopalladation of the alkene (i.e., migratory insertion of the alkene group into the Pd–N bond of an intermediate palladium–amido complex).[19]

The mechanism of the reactions between *N*-allylsulfamides and aryl triflates most likely proceeds as illustrated in Scheme 2. Oxidative addition of the aryl triflate to the Pd^0



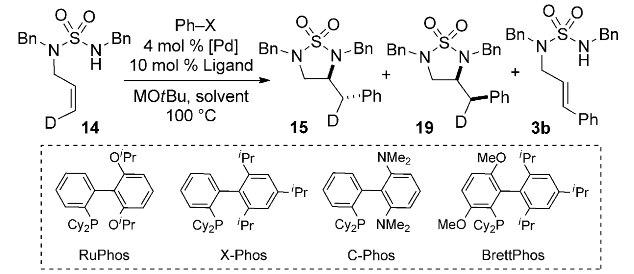
Scheme 2. The *anti*-aminopalladation mechanism.

center generates the cationic Pd^{II} complex **16**, which binds to the alkene moiety of substrate **14** to afford **17**. A sequence of deprotonation and *anti*-aminopalladation affords **18**, which can undergo C–C-bond-forming reductive elimination to provide the observed product and regenerate the Pd^0 catalyst.[20] Given the relatively low nucleophilicity of the sulfamide group, it is likely that the aminopalladation step (**17**→**18**) is reversible.[15] The favorability of the *anti*-aminopalladation pathway may also be due in part to the low nucleophilicity of the sulfamide group, which may lead to a relatively slow rate of Pd–N-bond formation (to generate the palladium–amido complex required for *syn*-aminopalladation; Scheme 1).

The formation of side products from 6-endocyclization most likely derives from a competing 6-endocyclization reaction of **17**; the formation of related side products that derive from 6-endocyclization pathways has previously been observed in other Pd-catalyzed alkene difunctionalization reactions that proceed through *anti*-heteropalladation reactions.[21] The side product from an allylic transposition appears to be generated through the oxidative addition of the *N*-allylsulfamide to the Pd^0 center to yield an intermediate allylpalladium complex and a deallylated sulfamide anion, which recombine to form the rearranged compound. Control experiments conducted in the absence of palladium did not lead to rearrangement.

To determine if other experimental variables also influence the *anti*- versus *syn*-aminopalladation pathway, we examined the coupling of deuterated substrate **14** with phenyl triflate under a number of different conditions (Table 3), moving from

Table 3. Influence of reaction conditions.[a]



Entry	X	Ligand	M	Solvent	15/19[b]	(15+19)/3b[c]
1	**OTf**	**RuPhos**	**Li**	**$PhCF_3$**	**>20:1**	**99:1**
2	OTf	RuPhos	Na	toluene	7:1	94:6[d]
3	OTf	X-Phos	Na	toluene	1:7	72:28[d]
4	**OTf**	**X-Phos**	**Li**	**dioxane**	**1:10**	**60:40**
5	OTf	X-Phos	Li	$PhCF_3$	10:1	93:7
6	**Br**	**X-Phos**	**Na**	**toluene**	**1:4**	**70:30**[d]
7	Br	RuPhos	Na	toluene	1:1	60:40[d]
8	Br	RuPhos	Na	toluene	1:1	60:40
9	Br	RuPhos	Na	$PhCF_3$	10:1	93:7
10	Br	X-Phos	Na	$PhCF_3$	1:1	60:40
11	Br	BrettPhos	Na	$PhCF_3$	10:1	98:2
12	**Br**	**C-Phos**	**Na**	**$PhCF_3$**	**>20:1**	**99:1**

[a] Reaction conditions: **14** (1.0 equiv), Ph-X (1.2 equiv), MO*t*Bu (1.4 equiv), $Pd(OAc)_2$ (4 mol %), ligand (10 mol %), solvent (0.0625 M), 100 °C. [b] The ratio of **15/19** as determined by NMR spectroscopic analysis. [c] The ratio of (**15**+**19**)/**3b** as determined by ^1H NMR spectroscopic analysis; in general, no significant amounts of other side products were generated in these reactions, and the yields estimated by ^1H NMR spectroscopic analysis were >90% for the combined total of **15**+**19**+**3b**. [d] $[Pd_2(dba)_3]$ (2 mol % complex, 4 mol % Pd) was used in place of $Pd(OAc)_2$.

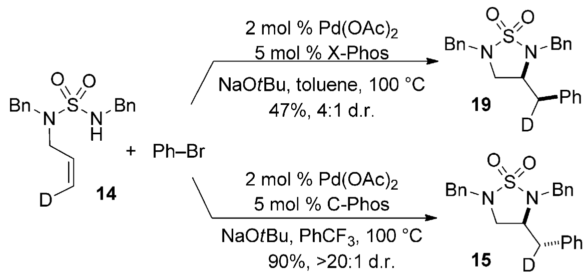
the "optimal" conditions for triflate coupling to those originally examined with aryl bromides (Table 3, entry 1 vs. 6, respectively). As shown below, most conditions examined for the reactions of aryl triflates favored the formation of the *anti*-addition product **15** (Table 3, entries 1, 2, and 5). However, both the ligand and the solvent polarity clearly have a significant impact on the reaction pathway as the use of X-Phos as a ligand in a nonpolar solvent, such as toluene or dioxane, favored the generation of the *syn*-addition product **19** (Table 3, entries 3 and 4), whereas the *anti*-addition product predominated in the $PhCF_3$ solvent (Table 3, entry 5). Reactions in which **19** was the major stereoisomer afforded comparatively large amounts of side product **3d** from a Heck arylation reaction.

In transformations involving bromobenzene as the electrophile, the X-Phos ligand also favored the formation of the *syn*-addition product in toluene (Table 3, entry 6). The use of the RuPhos ligand in toluene afforded a 1:1 mixture of *anti*/*syn* addition products (Table 3, entries 7 and 8). However, a survey of different, yet related, biaryl phosphanes in the polar solvent $PhCF_3$ revealed that the *anti*-addition product was favored for most ligands, with the exception of X-Phos (1:1 mixture; Table 3, entry 10), which lacks electron-donating alkoxy or amino groups on the biphenyl moiety.

Although the Pd-catalyzed carboamination of **14** is mechanistically complex, in general it appears that conditions that lead to a more electrophilic metal center and/or cationic intermediates (e.g., aryl triflate substrates, the relatively polar solvent $PhCF_3$[22] which may facilitate the generation of cationic intermediate palladium complexes) favor the *anti*-aminopalladation pathway. The observed influence of a phosphane-ligand structure also fits this general pattern as ligands that favor *anti*-addition pathways contain electron-donating groups on the biphenyl unit, which may stabilize cationic intermediates either due to an increased electron-donating ability of the phosphane (e.g., Brettphos) or through an electron-donating interaction between the biphenyl backbone and the metal center (e.g., RuPhos and C-Phos).

In contrast, the conditions that lead to a less electrophilic metal center and/or neutral intermediates (aryl bromide substrates, nonpolar solvents) appear to favor the *syn*-addition pathway. Importantly, these experiments also indicate that intermolecular[23] Pd-catalyzed carboamination reactions between aryl halides and alkenes that bear pendant nucleophiles can proceed through either *syn*- or *anti*-aminopalladation pathways under the appropriate reaction conditions.[24,25] The use of conditions that appear to be optimal for the *syn*-addition pathway in the coupling of **14** with bromobenzene afforded **19** in 47% yield and 4:1 d.r., whereas the conditions that are optimal for *anti*-addition afforded **15** in 90% yield and >20:1 d.r. [Eqs (7) and (8)].

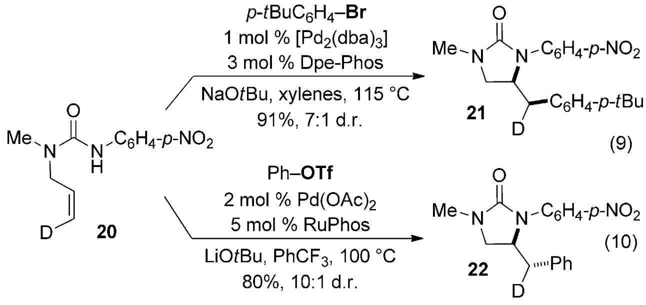
To determine whether this interesting influence of the reaction conditions on *syn*- versus *anti*-aminopalladation pathways



(7)

(8)

is limited solely to sulfamides or can be more broadly applicable to other nucleophiles, we examined *syn*- versus *anti*-addition reactions of the related *N*-allylurea **20** [Eqs (9) and (10)]. Our prior studies illustrated that the coupling of **20** with 4-bromo-*tert*-butylbenzene proceeds with *syn* addition in the presence of a Pd/bis[(2-diphenylphosphino)phenyl] ether (DpePhos) catalyst to generate **21**.[13d] In contrast, the Pd/RuPhos-catalyzed coupling of **20** with phenyl triflate proceeds with net *anti* addition to afford **22**. On the basis of this result, it appears that it will likely be possible to control the *syn*- versus *anti*-aminopalladation pathways in carboamination reactions of other nucleophilic species. However, further catalyst development will be necessary to broaden the scope to include internal alkene substrates, as efforts to apply optimized *syn*-addition conditions to cyclopentene-derived substrate **12** afforded a complex mixture of products (although the *anti*-addition product **13** was not formed).



Conclusion

We have developed a new approach to the construction of cyclic sulfamides through the Pd-catalyzed alkene carboamination of *N*-allylsulfamide derivatives. The mechanism of these reactions is dependent on the reaction conditions and can selectively proceed through either *syn*- or *anti*-aminopalladation pathways. These experiments suggest the use of different catalysts or reaction conditions to control the mechanistic pathways will extend beyond sulfamide substrates, which could have broadly significant implications in a number of different Pd-catalyzed alkene difunctionalization reactions. Further studies on the development of other alkene carboheterofunctionalization reactions that proceed through *anti*-heteropalladation processes are currently underway.

Experimental Section

General

All the reactions were carried out in a nitrogen atmosphere in flame-dried glassware, unless otherwise noted. Palladium precatalysts and phosphane ligands were purchased from commercial sources and used without purification. All other reagents were obtained from commercial sources and were used as obtained, unless otherwise noted. Bulk quantities of lithium *tert*-butoxide and sodium *tert*-butoxide were stored in a glove box and removed in small amounts (ca. 1–2 g) that were consumed within a few days. Toluene, THF, diethyl ether, and dichloromethane were purified by using a GlassContour solvent purification system. Anhydrous benzotrifluoride was obtained from commercial sources and was used without further purification. Yields refer to the yield of the isolated products of compounds estimated to be $\geq$95% pure as determined by ^{1}H NMR spectroscopic analysis, unless otherwise noted. The yields reported in the experimental section describe the result of a single experiment, whereas the yield of the isolated products reported in Tables 1–3 and Equations (1)–(10) are averages of the yields for two or more experiments. Thus, the yields reported in the experimental section may differ from those shown in Tables 1–3 and Equations (1)–(10).

General procedure for Pd-catalyzed carboamination reactions of *N*-allylsulfamide and *N*-allylurea derivatives with aryl trifluoromethanesulfonates

A test tube was charged with $Pd(OAc)_2$ (2 mol%), phosphane ligand (5 mol%), sulfamide substrate (1.0 equiv), and LiO*t*Bu (1.4 equiv). The test tube was purged with N_2 and benzotrifluoride was added (the reactions were conducted at 0.25 M substrate concentration, unless specified otherwise), followed by aryl trifluoromethanesulfonate (1.2 equiv). The resulting mixture was heated to 100 °C and ,stirred overnight. The reaction mixture was cooled to room temperature, quenched with saturated aqueous ammonium chloride, and extracted with dichloromethane. The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

4-[(2,5-Dibenzyl-1,1-dioxido-1,2,5-thiadiazolidin-3-yl)methyl]benzonitrile (2a): The general procedure was employed for the coupling of 1-allyl-1,3-bis-benzylsulfamide (**1a**; 79 mg, 0.25 mmol) and 4-cyanophenyl trifluoromethanesulfonate (75 mg, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 94 mg (90%) of the product as a white solid. M.p. 107–108 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 7.9 Hz, 2H), 7.43–7.28 (m, 10H), 6.99 (d, *J* = 7.9 Hz, 2H), 4.43 (d, *J* = 14.7 Hz, 1H), 4.28 (d, *J* = 13.6 Hz, 1H), 4.23 (d, *J* = 14.7 Hz, 1H), 4.07 (d, *J* = 13.7 Hz, 1H), 3.50 (td, *J* = 3.9, 7.7 Hz, 1H), 3.13 (dd, *J* = 7.2, 9.4 Hz, 1H), 2.91 (dd, *J* = 5.7, 13.6 Hz, 1H), 2.75 (dd, *J* = 5.7, 9.5 Hz, 1H), 2.70 ppm (dd, *J* = 8.4, 13.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.7, 135.1, 134.7, 132.4, 130.0, 128.9, 128.8, 128.6, 128.3, 118.6, 110.9, 57.0, 51.7, 50.4, 49.3, 39.7 ppm; IR (film): $\tilde{\nu}$ = 2228, 1321, 1158 cm^{-1}; MS (ESI): *m/z* calcd for $C_{24}H_{23}N_3O_2S$: 418.1584 $[M+H]^+$; found: 418.1581.

2,5-Dibenzyl-3-(4-methylbenzyl)-1,2,5-thiadiazolidine-1,1-dioxide (2c): The general procedure was employed for the coupling of **1a** (79 mg, 0.25 mmol) and *para*-tolyl trifluoromethanesulfonate (54 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 84 mg (83%) of the product as a yellow solid. M.p. 96–99 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49–7.44 (m, 2H), 7.44–7.30 (m, 8H), 7.03 (d, *J* = 7.8 Hz, 2H), 6.81 (d, *J* = 7.9 Hz, 2H), 4.46 (d, *J* = 14.9 Hz, 1H), 4.33 (dd, *J* = 5.8, 14.3 Hz, 2H), 4.06 (d, *J* = 13.9 Hz, 1H), 3.49 (dtd, *J* = 4.9, 6.6, 9.5 Hz, 1H), 3.08 (dd, *J* = 6.9, 9.4 Hz, 1H), 2.89 (dd, *J* = 4.9, 13.5 Hz, 1H), 2.84 (dd, *J* = 6.3, 9.5 Hz, 1H), 2.61 (dd, *J* = 9.6, 13.5 Hz, 1H), 2.29 ppm (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.6, 135.5, 135.0, 132.9, 129.4, 129.0, 128.7, 128.7, 128.6, 128.1, 57.6, 50.9, 50.7, 49.6, 39.0, 21.0 ppm; IR (film): $\tilde{\nu}$ = 1286, 1160 cm^{-1}; MS (ESI): *m/z* calcd for $C_{24}H_{26}N_2O_2S$: 407.1788 $[M+H]^+$; found: 407.1791.

2,5-Dibenzyl-3-(4-methoxybenzyl)-1,2,5-thiadiazolidine-1,1-dioxide (2d): The general procedure was employed for the coupling of **1a** (79 mg, 0.25 mmol) and 4-methoxyphenyl trifluoromethanesulfonate (54 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 93 mg (88%) of the product as a pale-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 (dd, *J* = 1.7, 7.8 Hz, 2H), 7.44–7.30 (m, 8H), 6.83 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 4.44 (d, *J* = 14.8 Hz, 1H), 4.32 (d, *J* = 14.5 Hz, 2H), 4.05 (d, *J* = 13.8 Hz, 1H), 3.76 (s, 3H), 3.46 (ddd, *J* = 5.0, 6.9, 9.7 Hz, 1H), 3.07 (ddd, *J* = 1.4, 7.0, 8.4 Hz, 1H), 2.86 (dd, *J* = 5.0, 13.6 Hz, 1H), 2.82 (dd, *J* = 6.4, 9.4 Hz, 1H), 2.58 ppm (dd, *J* = 9.4, 13.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 188.0, 158.6, 135.5, 135.0, 130.1, 129.0, 128.7, 128.7, 128.6, 128.1, 128.0, 114.1, 57.6, 55.2, 50.9, 50.7, 49.6, 38.6 ppm; IR (film): $\tilde{\nu}$ = 1246, 1160 cm^{-1}; MS (ESI): *m/z* calcd for $C_{24}H_{26}N_2O_3S$: 423.1737 $[M+H]^+$; found: 423.1739.

2,5-Dibenzyl-3-(2-methylbenzyl)-1,2,5-thiadiazolidine-1,1-dioxide (2e): The general procedure was employed for the coupling of **1a** (79 mg, 0.25 mmol) and *ortho*-tolyl trifluoromethanesulfonate (54 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 86 mg (85%) of the product as a white solid. M.p. 120–122 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.30 (m, 10H), 7.07

(ddd, $J=7.2$, 14.7, 25.7 Hz, 3H), 6.86 (dd, $J=1.4$, 7.5 Hz, 1H), 4.37 (s, 2H), 4.30 (d, $J=13.7$ Hz, 1H), 4.13 (d, $J=13.7$ Hz, 1H), 3.51 (ddt, $J=5.5$, 6.8, 9.4 Hz, 1H), 3.09 (dd, $J=6.9$, 9.4 Hz, 1H), 2.98 (dd, $J=5.2$, 13.6 Hz, 1H), 2.87 (dd, $J=5.8$, 9.4 Hz, 1H), 2.69 (dd, $J=9.6$, 13.6 Hz, 1H), 1.99 ppm (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=$ 136.3, 135.4, 135.0, 134.4, 130.6, 130.1, 128.9, 128.7, 128.7, 128.7, 128.2, 128.1, 127.1, 126.1, 55.7, 50.7, 50.6, 49.6, 36.8, 19.1 ppm; IR (film): $\tilde{\nu}=1283$, 1164 cm^{-1}; MS (ESI): *m/z* calcd for $C_{24}H_{26}N_2O_2S$: 407.1788 $[M+H]^+$; found: 407.1790.

2,5-Dibenzyl-3-(cyclohex-1-en-1-ylmethyl)-1,2,5-thiadiazolidine-1,1-dioxide (2 f): The general procedure was employed for the coupling of **1 a** (79 mg, 0.25 mmol) and 1-cyclohexenyl trifluoromethanesulfonate (52 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and BrettPhos (6.7 mg, 0.0125 mmol). This procedure afforded 89 mg (90%) of the product as a pale-yellow solid. M.p. 66–68 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=$ 7.45 (d, $J=7.0$ Hz, 2H), 7.42–7.29 (m, 8H), 5.33 (s, 1H), 4.49 (d, $J=15.0$ Hz, 1H), 4.36 (d, $J=13.8$ Hz, 1H), 4.26 (d, $J=15.0$ Hz, 1H), 4.05 (d, $J=13.8$ Hz, 1H), 3.47–3.36 (m, 1H), 3.21 (dd, $J=7.0$, 9.4 Hz, 1H), 2.81 (dd, $J=6.6$, 9.4 Hz, 1H), 2.23 (dd, $J=2.2$, 14.0 Hz, 1H), 2.04 (dd, $J=9.7$, 13.6 Hz, 1H), 1.94–1.80 (m, 2H), 1.73–1.59 (m, 1H), 1.59–1.33 ppm (m, 5H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=135.8$, 135.7, 135.1, 132.2, 128.7, 128.7, 128.6, 128.0, 127.9, 125.5, 54.8, 50.8, 50.6, 49.9, 41.9, 28.3, 25.1, 22.6, 22.0 ppm; IR (film): $\tilde{\nu}=1286$, 1154 cm^{-1}; MS (ESI): *m/z* calcd for $C_{23}H_{28}N_2O_2S$: 397.1944 $[M+H]^+$; found: 397.1949.

(*E*)-2,5-Dibenzyl-3-(undec-2-en-1-yl)-1,2,5-thiadiazolidine-1,1-dioxide (2 g): The general procedure was employed for the coupling of **1 a** (79 mg, 0.25 mmol) and (*E*)-dec-1-en-1-yl trifluoromethanesulfonate (101 μL, 0.35 mmol, 5:1 mixture of *E/Z* isomers) using LiO*t*Bu (32 mg, 0.40 mmol) and a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and *t*BuDavePhos (4.3 mg, 0.0125 mmol). This procedure afforded 90 mg (79%) of the product as a yellow oil. The compound was judged to be a 5:1 mixture of *E/Z* isomers by ^{1}H NMR spectroscopic analysis. Data are given for the major *E* isomer: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.51$–7.42 (m, 2H), 7.42–7.29 (m, 8H), 5.44 (dt, $J=7.4$, 11.0 Hz, 1H), 5.16–5.06 (m, 1H), 4.51 (d, $J=15.1$ Hz, 1H), 4.36 (d, $J=13.7$ Hz, 1H), 4.26 (d, $J=14.8$ Hz, 1H), 4.02 (d, $J=13.7$ Hz, 1H), 3.33 (ddd, $J=5.6$, 9.2, 11.1 Hz, 1H), 3.22 (dd, $J=7.0$, 9.3 Hz, 1H), 2.79 (dd, $J=7.1$, 9.3 Hz, 1H), 2.27 (dddd, $J=5.5$, 7.5, 13.5, 15.9 Hz, 1H), 2.16 (dt, $J=8.4$, 15.2 Hz, 1H), 1.81 (tt, $J=6.9$, 12.9 Hz, 2H), 1.35–1.18 (m, 12H), 0.91 ppm (q, $J=6.5$ Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=135.7$, 134.9, 134.4, 128.7, 128.7, 128.7, 128.6, 128.1, 128.0, 122.1, 56.3, 50.9, 50.6, 49.6, 31.9, 30.5, 29.5, 29.4, 29.3, 29.3, 27.4, 22.7 ppm, 14.1; IR (film): $\tilde{\nu}=$ 1304, 1164 cm^{-1}; MS (ESI): *m/z* calcd for $C_{27}H_{38}N_2O_2S$: 455.2727 $[M+H]^+$; found: 455.2735.

2-Benzyl-3-(4-chlorobenzyl)-5-methyl-1,2,5-thiadiazolidine-1,1-dioxide (2 h): The general procedure was employed for the coupling of **1 b** (60 mg, 0.25 mmol) and 4-chlorophenyl trifluoromethanesulfonate (52 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 68 mg (78%) of the product as a white solid. M.p. 133–135 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.41$–7.36 (m, 4H), 7.36–7.31 (m, 1H), 7.23 (d, $J=8.3$ Hz, 2H), 6.92 (d, $J=8.3$ Hz, 2H), 4.43 (d, $J=14.9$ Hz, 1H), 4.25 (d, $J=14.9$ Hz, 1H), 3.51 (dtd, $J=5.2$, 6.9, 9.3 Hz, 1H), 3.17 (dd, $J=7.0$, 9.3 Hz, 1H), 2.89 (dd, $J=5.2$, 13.6 Hz, 1H), 2.86 (dd, $J=6.8$, 9.3 Hz, 1H), 2.73 (s, 3H), 2.61 ppm (dd, $J=9.3$, 13.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=135.3$, 134.5, 132.9, 130.4, 128.9, 128.8, 128.7, 128.1, 57.1, 52.5, 51.2, 39.0, 33.2 ppm; IR (film): $\tilde{\nu}=1297$, 1149 cm^{-1}; MS (ESI): *m/z* calcd for $C_{17}H_{19}ClN_2O_2S$: 351.0929 $[M+H]^+$; found: 351.0926.

5-Benzyl-2-(4-methoxybenzyl)-3-(4-methylbenzyl)-1,2,5-thiadiazolidine-1,1-dioxide (2 i): The general procedure was employed for the coupling of **1 c** (87 mg, 0.25 mmol) and *para*-tolyl trifluoromethanesulfonate (54 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 95 mg (87%) of the product as a pale-yellow solid. M.p. 109–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.42$–7.25 (m, 7H), 6.99 (d, $J=7.8$ Hz, 2H), 6.92–6.86 (m, 2H), 6.79 (d, $J=7.9$ Hz, 2H), 4.36–4.21 (m, 3H), 4.01 (d, $J=13.8$ Hz, 1H), 3.81 (s, 3H), 3.49–3.37 (m, 1H), 3.02 (dd, $J=7.0$, 9.4 Hz, 1H), 2.86 (dd, $J=5.0$, 13.5 Hz, 1H), 2.78 (dd, $J=6.2$, 9.4 Hz, 1H), 2.56 (dd, $J=9.5$, 13.5 Hz, 1H), 2.26 ppm (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=159.5$, 136.5, 135.0, 133.0, 130.4, 129.4, 129.0, 128.7, 128.6, 128.1, 127.3, 114.0, 57.1, 55.3, 50.6, 50.3, 49.5, 39.0, 21.0 ppm; IR (film): $\tilde{\nu}=1281$, 1158 cm^{-1}; MS (ESI): *m/z* calcd for $C_{25}H_{28}N_2O_3S$: 437.1893 $[M+H]^+$; found: 437.1885.

5-Benzyl-2-methyl-3-(3-(trifluoromethyl)benzyl)-1,2,5-thiadiazolidine-1,1-dioxide (2 j): The general procedure was employed for the coupling of **1 d** (60 mg, 0.25 mmol) and 3-trifluoromethylphenyl trifluoromethanesulfonate (60 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 78 mg (81%) of the product as a pale-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.52$ (d, $J=7.8$ Hz, 1H), 7.43 (t, $J=7.7$ Hz, 1H), 7.40 (d, $J=1.6$ Hz, 1H), 7.38–7.29 (m, 6H), 4.31 (d, $J=13.9$ Hz, 1H), 3.99 (d, $J=13.9$ Hz, 1H), 3.44 (m, 1H), 3.16 (dd, $J=6.9$, 9.4 Hz, 1H), 3.12 (dd, $J=5.7$, 13.6 Hz, 1H), 2.85–2.78 (m, 2H), 2.75 ppm (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=$ 136.9, 134.8, 132.7, 131.2 (q, $J=33.8$ Hz), 129.3, 128.7, 128.6, 128.2, 125.8, 124.1, 123.9 (q, $J=272.4$ Hz), 59.6, 50.8, 49.5, 38.8, 33.6 ppm; IR (film): $\tilde{\nu}=1242$, 1127 cm^{-1}; MS (ESI): *m/z* calcd for $C_{18}H_{19}F_3N_2O_2S$: 385.1192 $[M+H]^+$; found: 385.1193.

5-Benzyl-2-(tert-butyl)-3-(4-methoxybenzyl)-1,2,5-thiadiazolidine-1,1-dioxide (2 k): The general procedure was employed for the coupling of **1 e** (71 mg, 0.25 mmol) and 4-methoxyphenyl trifluoromethanesulfonate (54 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 90 mg (93%) of the product as a white solid. M.p. 104–106 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=$ 7.47–7.32 (m, 5H), 6.79 (d, $J=8.6$ Hz, 2H), 6.71 (d, $J=8.6$ Hz, 2H), 4.46 (d, $J=13.5$ Hz, 1H), 3.77 (d, $J=13.6$ Hz, 1H), 3.75 (s, 3H), 3.54 (dddd, $J=1.3$, 4.1, 5.8, 10.4 Hz, 1H), 2.98–2.78 (m, 4H), 1.53 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=158.4$, 135.4, 130.2, 129.3, 128.8, 128.7, 128.1, 114.0, 57.8, 55.4, 55.2, 49.0, 47.1, 40.8, 28.2 ppm; IR (film): $\tilde{\nu}=1279$, 1142 cm^{-1}; MS (ESI): *m/z* calcd for $C_{21}H_{28}N_2O_3S$: 389.1893 $[M+H]^+$; found: 389.1893.

3,5-Dibenzyl-2-(4-methoxyphenyl)-1,2,5-thiadiazolidine-1,1-dioxide (2 l): The general procedure was employed for the coupling of 1-allyl-1-benzyl-3-(4-methoxyphenyl)sulfamide (**1 f**; 83 mg, 0.25 mmol) and phenyl trifluoromethanesulfonate (49 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and *t*BuXPhos (5.3 mg, 0.0125 mmol). This procedure afforded 91 mg (89%) of the product as a yellow solid. M.p. 95–97 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.45$–7.30 (m, 7H), 7.29–7.19 (m, 3H), 7.07–6.97 (m, 4H), 4.41 (d, $J=14.0$ Hz, 1H), 4.21–4.12 (m, 1H), 4.06 (d, $J=14.0$ Hz, 1H), 3.85 (s, 3H), 3.24 (dd, $J=6.5$, 9.2 Hz, 1H), 3.03 (dd, $J=7.6$, 9.4 Hz, 1H), 3.00 (dd, $J=4.2$, 13.8 Hz, 1H), 2.71 ppm (dd, $J=9.5$, 13.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=$ 159.2, 135.5, 134.9, 129.2, 128.8, 128.7, 128.7, 128.6, 128.2, 128.1, 127.0, 115.0, 58.6, 55.5, 51.2, 49.7, 38.7 ppm; IR (film): $\tilde{\nu}=1289$, 1157 cm^{-1}; MS (ESI): *m/z* calcd for $C_{23}H_{24}N_2O_3S$: 409.1580 $[M+H]^+$; found: 409.1577.

3-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-2-benzyl-5-methyl-1,2,5-thiadiazolidine-1,1-dioxide (2 m): The general procedure was employed for the coupling of **1 b** (60 mg, 0.25 mmol) and 3,4-methylenedioxyphenyl trifluoromethanesulfonate (52 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 76 mg (84%) of the product as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.45$–7.29 (m, 5H), 6.69 (d, $J = 7.8$ Hz, 1H), 6.49–6.42 (m, 2H), 5.91 (m, 2H), 4.43 (d, $J = 15.0$ Hz, 1H), 4.25 (d, $J = 14.9$ Hz, 1H), 3.47 (dtd, $J = 4.9$, 6.9, 9.7 Hz, 1H), 3.17 (dd, $J = 6.9$, 9.4 Hz, 1H), 2.88 (dd, $J = 6.9$, 9.4 Hz, 1H), 2.83 (dd, $J = 5.0$, 13.5 Hz, 1H), 2.72 (s, 3H), 2.53 ppm (dd, $J = 9.7$, 13.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 147.8$, 146.6, 135.4, 129.6, 128.8, 128.7, 128.1, 122.1, 109.2, 108.4, 101.0, 57.4, 52.5, 51.0, 39.2, 33.2 ppm; IR (film): $\tilde{\nu} = 1246$, 1150 cm^{-1}; MS (ESI): m/z calcd for $C_{18}H_{20}N_2O_4S$: 361.1217 $[M+H]^+$; found: 361.1219.

2-Benzyl-5-(*tert*-butyl)-3-[3-(trifluoromethyl)benzyl]-1,2,5-thiadiazolidine-1,1-dioxide (2 n): The general procedure was employed for the coupling of **1 g** (71 mg, 0.25 mmol) and 3-trifluoromethylphenyl trifluoromethanesulfonate (60 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 91 mg (85%) of the product as a yellow solid. M.p. 104–106 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.49$ (d, $J = 7.8$ Hz, 1H), 7.42–7.29 (m, 6H), 7.26–7.19 (m, 2H), 4.38 (d, $J = 14.8$ Hz, 1H), 4.19 (d, $J = 14.8$ Hz, 1H), 3.53–3.43 (m, 1H), 3.25 (dd, $J = 6.6$, 8.9 Hz, 1H), 3.10–2.98 (m, 2H), 2.74 (dd, $J = 9.1$, 13.6 Hz, 1H), 1.42 ppm (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 137.6$, 135.5, 132.6, 131.0 (q, $J = 32.1$ Hz), 129.2, 128.8, 128.6, 128.0, 125.7 (q, $J = 3.7$ Hz), 123.9 (q, $J = 272.3$ Hz), 123.8 (q, $J = 3.8$ Hz), 56.2, 56.1, 50.6, 45.6, 38.5, 27.4 ppm; IR (film): $\tilde{\nu} = 1302$, 1120 cm^{-1}; MS (ESI): m/z calcd for $C_{21}H_{25}F_3N_2O_2S$: 427.1662 $[M+H]^+$; found: 427.1663.

2-Allyl-3-benzyl-1,2,5-thiadiazolidine-1,1-dioxide (2 o): The general procedure was employed for the coupling of **1 h** (44 mg, 0.25 mmol) and phenyl trifluoromethanesulfonate (98 μL, 0.60 mmol), using Li*Ot*Bu (48 mg, 0.60 mmol) and a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 30 mg (48%) of the product as a pale-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.37$–7.24 (m, 3H), 7.24–7.15 (m, 2H), 5.94 (dddd, $J = 5.6$, 7.7, 10.1, 17.5 Hz, 1H), 5.36–5.25 (m, 2H), 4.44 (t, $J = 7.5$ Hz, 1H), 3.78 (ddt, $J = 1.5$, 5.6, 15.1 Hz, 1H), 3.72 (ddt, $J = 5.1$, 6.8, 8.4 Hz, 1H), 3.67 (ddt, $J = 1.2$, 7.7, 15.1 Hz, 1H), 3.39 (dt, $J = 6.9$, 11.7 Hz, 1H), 3.22 (ddd, $J = 4.7$, 6.7, 11.6 Hz, 1H), 3.07 (dd, $J = 5.4$, 13.5 Hz, 1H), 2.77 ppm (dd, $J = 8.3$, 13.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 136.0$, 132.5, 129.3, 128.8, 127.2, 120.0, 61.1, 48.7, 44.9, 39.2 ppm; IR (film): $\tilde{\nu} = 3242$, 1296, 1159 cm^{-1}; MS (ESI): m/z calcd for $C_{12}H_{16}N_2O_2S$: 253.1005 $[M+H]^+$; found: 253.1005.

2-Benzyl-6-(4-methoxyphenyl)-4-phenyl-1,2,6-thiadiazinane-1,1-dioxide (S2): The general procedure was employed for the coupling of **1 f** (83 mg, 0.25 mmol) and phenyl trifluoromethanesulfonate (49 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). The major product generated in this reaction was **2 l** (described above), and a small amount of side-product **S2** was also formed. Compound **S2** was isolated by careful chromatographic purification (7 mg, 7%) as a pale-yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.47$–7.42 (m, 4H), 7.42–7.36 (m, 2H), 7.33 (tq, $J = 1.5$, 8.3 Hz, 3H), 7.30–7.25 (m, 1H), 7.25–7.21 (m, 2H), 6.96–6.92 (m, 2H), 4.69 (d, $J = 14.0$ Hz, 1H), 4.48 (d, $J = 14.0$ Hz, 1H), 4.24 (t, $J = 11.8$ Hz, 1H), 4.04–3.94 (m, 1H), 3.83 (s, 3H), 3.61–3.47 (m, 2H), 3.29 ppm (ddd, $J = 2.3$, 4.1, 14.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 158.9$, 137.8, 135.5, 134.4, 128.9, 128.8, 128.1, 128.0, 127.7, 127.5, 114.5, 59.1, 55.5, 53.2, 52.7, 36.9 ppm; IR (film): $\tilde{\nu} = 1344$, 1157 cm^{-1}; MS (ESI): m/z calcd for $C_{23}H_{24}N_2O_3S$: 409.1580 $[M+H]^+$; found: 409.1581.

(±)-(3*R*,4*R*)-4-[(2,5-Dibenzyl-4-methyl-1,1-dioxido-1,2,5-thiadiazolidin-3-yl)methyl]benzonitrile (8): The general procedure was employed for the coupling of **7** (83 mg, 0.25 mmol) and 4-cyanophenyl trifluoromethanesulfonate (75 mg, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and X-Phos (6.0 mg, 0.0125 mmol). This procedure afforded 86 mg (80%) of the product as a white solid. M.p. 102–108 °C; This compound was obtained as a >20:1 mixture of diastereomers as judged by ^{1}H NMR spectroscopic analysis. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.46$ (d, $J = 8.2$ Hz, 2H), 7.43–7.31 (m, 8H), 7.30–7.24 (m, 2H), 6.96 (d, $J = 8.2$ Hz, 2H), 4.36–4.16 (m, 4H), 3.12 (td, $J = 3.6$, 7.1 Hz, 1H), 3.03 (qd, $J = 3.6$, 6.3 Hz, 1H), 2.91 (dd, $J = 6.5$, 13.6 Hz, 1H), 2.73 (dd, $J = 7.4$, 13.6 Hz, 1H), 0.95 ppm (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 142.2$, 135.5, 134.9, 132.3, 130.1, 129.1, 128.8, 128.7, 128.7, 128.2, 128.1, 118.6, 110.8, 64.0, 56.7, 51.9, 48.6, 39.1, 18.6 ppm; IR (film): $\tilde{\nu} = 1294$, 1132 cm^{-1}; MS (ESI): m/z calcd for $C_{25}H_{25}N_3O_2S$: 432.1740 $[M+H]^+$; found: 432.1740.

2,3,5-Tribenzyl-3-methyl-1,2,5-thiadiazolidine-1,1-dioxide (10): The general procedure was employed for the coupling of **9** (83 mg, 0.25 mmol) and phenyl trifluoromethanesulfonate (49 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and C-Phos (5.5 mg, 0.0125 mmol). This procedure afforded 97 mg (95%) of the product as an off-white solid. M.p. 129–131 °C; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.54$ (d, $J = 7.2$ Hz, 2H), 7.45–7.35 (m, 7H), 7.32 (t, $J = 7.4$ Hz, 1H), 7.22–7.10 (m, 2H), 6.88 (d, $J = 6.6$ Hz, 1H), 4.42 (s, 2H), 4.38 (d, $J = 13.6$ Hz, 1H), 4.02 (d, $J = 13.6$ Hz, 1H), 3.17 (d, $J = 9.3$ Hz, 1H), 3.01 (d, $J = 13.1$ Hz, 1H), 2.78 (d, $J = 13.1$ Hz, 1H), 2.70 (d, $J = 9.2$ Hz, 1H), 1.21 ppm (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 137.0$, 135.7, 135.0, 130.3, 129.0, 128.7, 128.6, 128.4, 128.3, 128.2, 127.8, 126.9, 61.8, 54.4, 50.2, 44.9, 43.0, 22.3 ppm; IR (film): $\tilde{\nu} = 1299$, 1167 cm^{-1}; MS (ESI): m/z calcd for $C_{24}H_{26}N_2O_2S$: 407.1788 $[M+H]^+$; found: 407.1789.

(±)-(3a*R*,4*R*,6a*S*)-1,3-Dibenzyl-4-phenylhexahydro-1*H*-cyclopenta[*c*][1,2,5]thiadiazole-2,2-dioxide (13): The general procedure was employed for the coupling of 1,3-bis-benzyl-1-cyclopent-2-enylsulfamide (**12**; 86 mg, 0.25 mmol) and phenyl trifluoromethanesulfonate (81 μL, 0.50 mmol) using Li*Ot*Bu (44 mg, 0.55 mmol) and a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and C-Phos (8.2 mg, 0.01875 mmol). This procedure afforded 70 mg (67%) of the product as an off-white solid. M.p. 118–120 °C; This compound was obtained as a >20:1 mixture of diastereomers as judged by ^{1}H NMR spectroscopic analysis. ^{1}H NMR (500 MHz, C_6D_6): $\delta = 7.28$–7.21 (m, 2H), 7.16–7.02 (m, 4H), 6.99–6.89 (m, 7H), 6.65–6.57 (m, 2H), 4.24 (d, $J = 14.2$, 1H), 4.15 (d, $J = 14.8$, 1H), 4.08 (d, $J = 14.2$, 1H), 4.04 (d, $J = 14.8$, 1H), 3.38 (dd, $J = 6.9$, 9.2, 1H), 3.27 (dt, $J = 6.9$, 9.2, 1H), 3.11 (dt, $J = 6.7$, 10.8, 1H), 1.74–1.51 (m, 2H), 1.32 (dtd, $J = 2.8$, 6.7, 13.2, 1H), 0.93 ppm (dtd, $J = 6.4$, 10.7, 12.3, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 142.0$, 135.2, 134.9, 129.0, 128.8, 128.7, 128.7, 128.3, 128.1, 127.7, 127.2, 126.7, 66.1, 60.2, 51.0, 49.8, 49.6, 33.0, 30.9 ppm; IR (film): $\tilde{\nu} = 1310$, 1156 cm^{-1}; MS (ESI): m/z calcd for $C_{25}H_{26}N_2O_2S$: 419.1788 $[M+H]^+$; found: 419.1784.

(±)-(1′*S*,3*S*)-2,5-Dibenzyl-1′-deuterio-3-(4-methylbenzyl)-1,2,5-thiadiazolidine-1,1-dioxide (15): The general procedure was employed for the coupling of **14** (79 mg, 0.25 mmol) and phenyl trifluoromethanesulfonate (49 μL, 0.30 mmol) using a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and RuPhos (5.8 mg, 0.0125 mmol). This procedure afforded 75 mg (76%) of the product as a yellow solid. M.p. 74–76 °C. This compound was obtained as a >20:1 mixture of diastereomers as judged by ^{1}H NMR spectroscopic analysis. Data are given for the major isomer: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.48$–7.43 (m, 2H), 7.43–7.29 (m, 8H), 7.26–7.15 (m, 3H), 6.92 (dd, $J = 1.9$, 7.6 Hz, 2H), 4.44 (d, $J = 14.9$ Hz, 1H), 4.34 (d, $J=14.8$ Hz, 1H), 4.32 (d, $J=13.8$ Hz, 1H), 4.07 (d, $J=13.8$ Hz, 1H), 3.51 (td, $J=5.0$, 6.6 Hz, 1H), 3.08 (dd, $J=7.0$, 9.4 Hz, 1H), 2.90 (d, $J=5.0$ Hz, 1H), 2.84 ppm (dd, $J=6.2$, 9.5 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=136.0$, 135.4, 134.9, 129.0, 128.9, 128.7, 128.6, 128.1, 128.1, 127.0, 57.3, 50.9, 50.6, 49.5, 39.1 ppm (t, $J=19.4$ Hz); IR (film): $\tilde{\nu}=1324$, 1154 cm^{-1}; MS (ESI): m/z calcd for $C_{23}H_{23}DN_2O_2S$: 394.1694 $[M+H]^+$; found: 394.1698.

(±)-(1′*S*,3*S*)-2,5-Dibenzyl-1′-deuterio-3-(4-methylbenzyl)-1,2,5-thiadiazolidine-1,1-dioxide (15): The general procedure was employed for the coupling of **14** (79 mg, 0.25 mmol) and bromobenzene (32 μL, 0.30 mmol) using NaO*t*Bu (34 mg, 0.35 mmol; in place of LiO*t*Bu) and a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and C-Phos (5.5 mg, 0.0125 mmol). This procedure afforded 91 mg (92%) of the product as a yellow solid. This compound was obtained as a >20:1 mixture of diastereomers as judged by ^1H NMR spectroscopic analysis. The physical properties and spectroscopic data were identical to those provided above.

2,5-Dibenzyl-(1′*R*,3*S*)-1′-deuterio-3-(4-methylbenzyl)-1,2,5-thiadiazolidine-1,1-dioxide (19): The general procedure was employed for the coupling of **14** (79 mg, 0.25 mmol) and bromobenzene (32 μL, 0.30 mmol) using NaO*t*Bu (34 mg, 0.35 mmol; in place of LiO*t*Bu) and toluene (in place of $PhCF_3$) and a catalyst composed of $Pd(OAc)_2$ (1.1 mg, 0.005 mmol) and X-Phos (6.0 mg, 0.0125 mmol). After the starting material had been completely consumed, DPPP (2.1 mg, 0.0125 mmol) and morpholine (65 μL, 0.75 mmol) in xylene (1 mL) were added, and the reaction mixture was heated to 120 °C for 2 h (this step was employed to facilitate purification by de-allylating small amounts of a side product from a competing Heck arylation reaction). The reaction mixture was worked up according to the general procedure. This procedure afforded 46 mg (47%) of the product as a yellow solid. M.p. 74–76 °C. This compound was obtained as a 4:1 mixture of diastereomers as judged by ^1H NMR spectroscopic analysis. Data are given for the major isomer: ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.49$–7.43 (m, 2H), 7.43–7.30 (m, 8H), 7.25–7.17 (m, 3H), 6.96–6.89 (m, 2H), 4.44 (d, $J=14.8$ Hz, 1H), 4.34 (d, $J=14.8$ Hz, 1H), 4.32 (d, $J=13.8$ Hz, 1H), 4.07 (d, $J=13.8$ Hz, 1H), 3.51 (dt, $J=6.5$, 9.3 Hz, 1H), 3.09 (dd, $J=7.0$, 9.4 Hz, 1H), 2.85 (dd, $J=6.2$, 9.4 Hz, 1H), 2.63 ppm (d, $J=9.5$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=136.0$, 135.4, 134.9, 129.1, 128.9, 128.7, 128.6, 128.1, 128.1, 127.0, 57.3, 50.9, 50.6, 49.5, 39.2 ppm (t, $J=19.6$ Hz); IR (film): $\tilde{\nu}=1323$, 1155 cm^{-1}; MS (ESI): m/z calcd for $C_{23}H_{23}DN_2O_2S$: 394.1694 $[M+H]^+$; found: 394.1699.

(1′*S*,4*S*)-1′-Deuterio-4-benzyl-1-methyl-3-(4-nitrophenyl)imidazolidin-2-one (22): The general procedure was employed for the coupling of (*Z*)-1-(3-*d*-allyl)-1-methyl-3-(4-nitrophenyl)urea (30 mg, 0.125 mmol) and phenyl trifluoromethanesulfonate (25 μL, 0.15 mmol) using a catalyst composed of $Pd(OAc)_2$ (0.6 mg, 0.0025 mmol) and RuPhos (2.9 mg, 0.00625 mmol). This procedure afforded 33 mg (85%) of the product as a bright-yellow solid (m.p. 167–168 °C). This compound was obtained as a 10:1 mixture of diastereomers as judged by ^1H NMR spectroscopic analysis. Data are given for the major isomer: ^1H NMR (500 MHz, C_6D_6): $\delta=7.99$ (d, $J=9.3$, 2H), 7.55 (d, $J=9.3$, 2H), 7.10–7.00 (m, 3H), 6.72 (d, $J=7.4$, 2H), 3.58 (dt, $J=3.3$, 8.6, 1H), 2.49 (dt, $J=1.7$, 3.2, 1H), 2.40 (dd, $J=3.1$, 8.9, 1H), 2.30 ppm (s, 4H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=156.7$, 145.1, 141.9, 135.5, 129.1, 128.9, 127.3, 125.0, 117.7, 53.6, 48.4, 37.4 (t, $J=19.2$ Hz), 30.8 ppm; IR (film): $\tilde{\nu}=1702$ cm^{-1}; MS (ESI): m/z calcd for $C_{17}H_{16}DN_3O_3$: 313.1405 $[M+H]^+$; found: 313.1407.

Acknowledgements

The authors acknowledge the NIH-NIGMS (GM 098314) for financial support of this work.

Keywords: addition reactions · alkenes · heterocycles · palladium · stereoselectivity

[1] A. B. Reitz, G. R. Smith, M. H. Parker, *Expert Opin. Ther. Pat.* **2009**, *19*, 1449–1453.
[2] A. Spaltenstein, M. R. Almond, W. J. Bock, D. G. Cleary, E. S. Furfine, R. J. Hazen, W. M. Kazmierski, F. G. Salituro, R. D. Tung, L. L. Wright, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1159–1162.
[3] J. Zhong, X. Gan, K. R. Alliston, W. C. Groutas, *Bioorg. Med. Chem.* **2004**, *12*, 589–593.
[4] S. H. Rosenberg, J. F. Dellaria, D. J. Kempf, C. W. Hutchins, K. W. Woods, R. G. Maki, E. de Lara, K. P. Spina, H. H. Stein, J. Cohen, W. R. Baker, J. J. Plattner, H. D. Kleinert, T. J. Perun, *J. Med. Chem.* **1990**, *33*, 1582–1590.
[5] D. Dou, S. R. Mandadapu, K. R. Alliston, Y. Kim, K. O. Chang, W. C. Groutas, *Eur. J. Med. Chem.* **2012**, *47*, 59–64.
[6] S. V. Pansare, A. N. Rai, S. N. Kate, *Synlett* **1998**, 623–624.
[7] a) R. I. McDonald, S. S. Stahl, *Angew. Chem.* **2010**, *122*, 5661–5664; *Angew. Chem. Int. Ed.* **2010**, *49*, 5529–5532; b) K. Muñiz, J. Streuff, C. H. Hövelmann, A. Núñez, *Angew. Chem.* **2007**, *119*, 7255–7258; *Angew. Chem. Int. Ed.* **2007**, *46*, 7125–7127; c) K. Muñiz, C. H. Hövelmann, E. Campos-Gómez, J. Barluenga, J. M. González, J. Streuff, M. Nieger, *Chem. Asian J.* **2008**, *3*, 776–788; d) H. Hamaguchi, S. Kosaka, H. Ohno, N. Fujii, T. Tanaka, *Chem. Eur. J.* **2007**, *13*, 1692–1708; e) B. Zhao, W. Yuan, H. Du, Y. Shi, *Org. Lett.* **2007**, *9*, 4943–4945; f) B. Wang, H. Du, Y. Shi, *Angew. Chem.* **2008**, *120*, 8348–8351; *Angew. Chem. Int. Ed.* **2008**, *47*, 8224–8227; g) R. G. Cornwall, B. Zhao, Y. Shi, *Org. Lett.* **2013**, *15*, 796–799; h) T. P. Zabawa, D. Kasi, S. R. Chemler, *J. Am. Chem. Soc.* **2005**, *127*, 11250–11251.
[8] F. Fécourt, G. López, A. Van Der Lee, J. Martinez, G. Dewynter, *Tetrahedron: Asymmetry* **2010**, *21*, 2361–2366.
[9] For representative examples, see: a) D. Dou, K. C. Tiew, G. He, S. R. Mandadapu, S. Aravapalli, K. R. Alliston, Y. Kim, K. O. Chang, W. C. Groutas, *Bioorg. Med. Chem.* **2011**, *19*, 5975–5983; b) S. J. Kim, M. H. Jung, K. H. Yoo, J. H. Cho, C.-H. Oh, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5815–5818.
[10] a) J. A. Fritz, J. S. Nakhla, J. P. Wolfe, *Org. Lett.* **2006**, *8*, 2531–2534; b) J. A. Fritz, J. P. Wolfe, *Tetrahedron* **2008**, *64*, 6838–6852.
[11] For recent reviews, see: a) J. P. Wolfe, *Top. Heterocycl. Chem.* **2013**, *32*, 1–38; b) D. M. Schultz, J. P. Wolfe, *Synthesis* **2012**, *44*, 351–361.
[12] a) D. S. Surry, S. L. Buchwald, *Chem. Sci.* **2011**, *2*, 27–50; b) D. S. Surry, S. L. Buchwald, *Angew. Chem.* **2008**, *120*, 6438–6461; *Angew. Chem. Int. Ed.* **2008**, *47*, 6338–6361.
[13] Our prior studies have illustrated that Pd-catalyzed carboamination reactions between aryl bromides and alkenes bearing pendant nucleophiles, such as anilines, carbamates, ureas, and hydroxylamines proceed through *syn*-addition pathways, see: a) J. E. Ney, J. P. Wolfe, *Angew. Chem.* **2004**, *116*, 3689–3692; *Angew. Chem. Int. Ed.* **2004**, *43*, 3605–3608; b) M. B. Bertrand, J. D. Neukom, J. P. Wolfe, *J. Org. Chem.* **2008**, *73*, 8851–8860; c) G. S. Lemen, N. C. Giampietro, M. B. Hay, J. P. Wolfe, *J. Org. Chem.* **2009**, *74*, 2533–2540; d) B. A. Hopkins, J. P. Wolfe, *Angew. Chem.* **2012**, *124*, 10024–10028; *Angew. Chem. Int. Ed.* **2012**, *51*, 9886–9890.
[14] Pd-catalyzed *N*-arylation reactions of sulfamides are believed to proceed through intermediates similar to **5**, see: L. Alcaraz, C. Bennion, J. Morris, P. Meghani, S. M. Thom, *Org. Lett.* **2004**, *6*, 2705–2708.
[15] It has been illustrated that aminopalladation reactions of relatively electron-poor nucleophiles are reversible, see: P. B. White, S. S. Stahl, *J. Am. Chem. Soc.* **2011**, *133*, 18594–18597.
[16] a) W. Rauf, J. M. Brown, *Chem. Commun.* **2013**, *49*, 8430–8440; b) D. L. Dodds, M. D. K. Boele, G. P. F. van Strijdonck, J. G. de Vries, P. W. N. M. van Leeuwen, P. C. J. Kamer, *Eur. J. Inorg. Chem.* **2012**, 1660–1671.
[17] In nonpolar solvents, $[L_nPd(Ar)(OTf)]$ (OTf = triflate) complexes exist as tight ion pairs, and these complexes are fully dissociated into solvent-

separated ions in polar solvents, see: A. Jutand, A. Mosleh, *Organometallics* **1995**, *14*, 1810 – 1817.

[18] B. P. Carrow, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 79 – 81.

[19] For studies on the mechanism of *syn*-migratory insertion of alkenes into Pd–N bonds, see: a) J. D. Neukom, N. S. Perch, J. P. Wolfe, *J. Am. Chem. Soc.* **2010**, *132*, 6276 – 6277; b) P. S. Hanley, D. Marković, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 6302 – 6303; c) J. D. Neukom, N. S. Perch, J. P. Wolfe, *Organometallics* **2011**, *30*, 1269 – 1277; d) P. S. Hanley, J. F. Hartwig, *J. Am. Chem. Soc.* **2011**, *133*, 15661 – 15673; e) Reference [15].

[20] It has previously been illustrated that Pd-catalyzed arene C–H functionalization/alkene carboamination reactions of *N*-pentenyl amides proceed through *anti*-aminopalladation pathways; these transformations involve a Pd^{II}/Pd^{IV} catalytic cycle as opposed to the Pd^{0}/Pd^{II} cycle for the sulfamides described herein, see: P. A. Sibbald, C. F. Rosewall, R. D. Swartz, F. E. Michael, *J. Am. Chem. Soc.* **2009**, *131*, 15945 – 15951.

[21] M. F. Semmelhack, C. Bodurow, *J. Am. Chem. Soc.* **1984**, *106*, 1496 – 1498.

[22] $PhCF_3$ is more polar than toluene and dioxane as measured by dielectric-constant values (toluene: 2.38; dioxane: 2.21; $PhCF_3$: 9.4) or E^N values (toluene: 0.099, dioxane: 0.164, $PhCF_3$: 0.241), see: a) C; Reichardt, *Chem. Rev.* **1994**, *94*, 2319 – 2358; b) A. Ogawa, K. Tsuchii, "α,α,α-Trifluorotoluene" in *The Electronic Encyclopedia of Reagents for Organic Synthesis*. http://mrw.interscience.wiley.com/eros/.

[23] Although there is an intramolecular component to the reactions described herein, the aryl/alkenyl halide and urea substrate are separate components coupled in an intermolecular process.

[24] We have previously demonstrated that ligand effects can influence alkene *syn*- vs. *anti*-heteropalladation pathways in intramolecular Pd-catalyzed carboalkoxylation and carboamination reactions, see: J. S. Nakhla, J. W. Kampf, J. P. Wolfe, *J. Am. Chem. Soc.* **2006**, *128*, 2893 – 2901.

[25] Ligands, bases, and oxidants influence *syn*- versus *anti*-aminopalladation pathways in Wacker-type oxidative cyclizations of aminoalkenes, see: a) G. Liu, S. S. Stahl, *J. Am. Chem. Soc.* **2007**, *129*, 6328 – 6335; b) A. B. Weinstein, S. S. Stahl, *Angew. Chem.* **2012**, *124*, 11673 – 11677; *Angew. Chem. Int. Ed.* **2012**, *51*, 11505 – 11509; c) X. Ye, P. B. White, S. S. Stahl, *J. Org. Chem.* **2013**, *78*, 2083 – 2090; d) C; Martínez, Y. Wu, A. B. Weinstein, S. S. Stahl, G. Liu, K. Muniz, *J. Org. Chem.* **2013**, *78*, 6309 – 6315.

Received: February 19, 2014
Published online on ■■ ■■, 0000

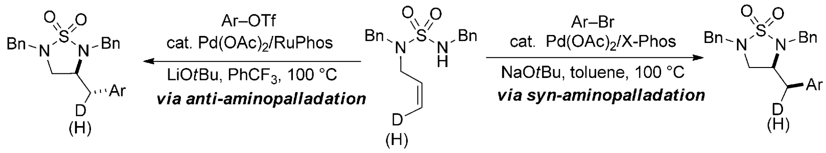
FULL PAPER

Palladium Catalysis

*R. M. Fornwald, J. A. Fritz, J. P. Wolfe**

■■ – ■■

Influence of Catalyst Structure and Reaction Conditions on *anti*- versus *syn*-Aminopalladation Pathways in Pd-Catalyzed Alkene Carboamination Reactions of *N*-Allylsulfamides



A constructive approach: A concise, efficient approach has led to the synthesis of cyclic sulfamides by using Pd-catalyzed alkene carboamination reactions of *N*-allylsulfamides (see picture; OTf = triflate, RuPhos = 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl, X-phos = 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl). The mechanism of these transformations is highly dependent on the catalyst structure and reaction conditions. The reactions can be induced to proceed selectively through either *syn*- or *anti*-aminopalladation pathways under appropriate conditions.