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Palladium(II)-Catalyzed Oxidative Cyclization of Allylic Tosylcarbamates: Scope, Derivatization, and Mechanistic Aspects

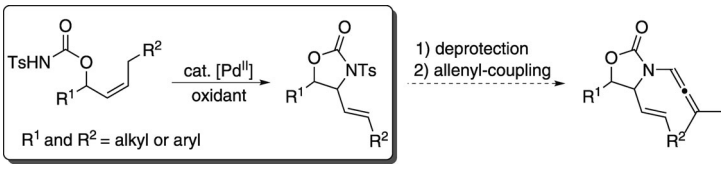
Antoine Joosten,[a] Andreas K. Å. Persson,[a] Renaud Millet,[a] Magnus T. Johnson,[b] and Jan-E. Bäckvall*[a]

Abstract: A highly selective oxidative palladium(II)-catalyzed (Wacker-type) cyclization of readily available allylic tosylcarbamates is reported. This operationally simple catalytic reaction furnishes tosyl-protected vinyl-oxazolidinones, common precursors to *syn*-1,2-amino alcohols, in high yield and excellent diasteroselectivity (>20:1). It is demonstrated that both stoichiometric amounts of benzoquinone (BQ) as well as aerobic reoxidation (molecular oxygen) is suitable for this transformation. The title reaction is shown to proceed through overall *trans*-amidopalladation of the olefin followed by β-hydride elimination. This process is scalable and the products are suitable for a range of subsequent transformations such as: kinetic resolution (KR) and oxidative Heck-, Wacker-, and metathesis reactions.

Keywords: amidopalladation · cyclization · oxazolidinones · oxidation · palladium

Introduction

Oxidation reactions are of fundamental importance in Nature and play a central role in organic synthesis.[1] Among them, Wacker-type oxidative cyclizations provide efficient access to oxygen and nitrogen heterocycles, and have been extensively studied.[2] Following our interest in the carbon–carbon bond-forming palladium(II)-catalyzed oxidative cyclization of dienallenes,[3] enallenes,[4] and aza-enallenes,[5] we were particularly interested in developing a new methodology leading to the construction of unsaturated (vinyl) oxazolidinones (Scheme 1). Oxazolidinones are common precursors for 1,2-aminoalcohols, a key structural component in many pharmaceutical compounds[6] and asymmetric ligands.[7,8]



Scheme 1. Outline and further perspectives of this study.

The palladium(II)-catalyzed intramolecular amination of homoallylic carbamates, rendering oxazolidinones, has recently attracted considerable attention.[9,10] This approach has also been extended to an intermolecular variant furnishing allylic *N*-carbamates.[11] In addition to these contributions, several efficient palladium-catalyzed cyclizations of allylic tosylcarbamates involving for example amino-halogenation,[12] amino-acetoxylation,[13] amino-alkynylation[14] and amino-carbonylation[15] have also been reported. In general, allylic and homoallylic substrates dominate this particular catalytic approach, however, oxidative examples involving carbamates with pending allenes[16] and alkynes[17] have also proven successful in previous studies. Although many intramolecular amidopalladation reactions were known at the outset of this work, there were, to the best of our knowledge, no palladium(II)-catalyzed oxidative procedures in which allylic carbamates are cyclized to form the unsaturated (vinyl) oxazolidinones by β-hydride elimination.[18] Related reactions in which allylic alcohols and amines are used to tether the nucleophiles for a Wacker-type cyclization reactions have been reported for the synthesis of imidazolidines,[19] oxazolidines,[20] thiadiazolidines,[21] or isoxazolidine.[22] Ideally, this synthetic approach would be effective starting from cheap starting materials (allylic alcohols) and readily available palladium catalysts. In this study we report on an intramolecular palladium-catalyzed oxidative cyclization of allylic tosylcarbamates leading to unsaturated oxazolidinones (Scheme 1). Different features of this transformation are presented, such as scalability, further derivatization, and mechanistic aspects.

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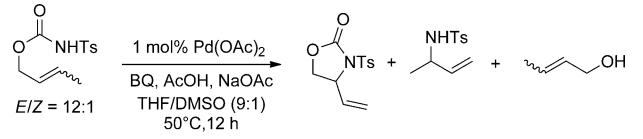
Results and Discussion

Model reaction and optimization: The model tosylcarbamate **1** was prepared in one step by the treatment of crotyl alcohol (*E*/*Z* 12:1) **4** with tosylisocyanate (TsNCO) in THF at room temperature. After considerable experimentation and screening for conditions furnishing acceptable amounts of the desired oxazolidinone, we found that $Pd(OAc)_2$ (1 mol%) in THF/DMSO (9:1) and in presence of benzoquinone (BQ, 1.5 equiv) provided the oxazolidinone in acceptable yield. In addition, we investigated the influence of sodium acetate and acetic acid on the outcome of the reaction (Table 1). Introduction of 0.5 equivalents of AcOH to the reaction mixture provided the expected oxazolidinone together with substantial amounts of allylic alcohol **4** (Table 1, entry 1). In this case, a small amount of a tosylamine **3** derived from a decarboxylative Overman-type isomerization was also observed. Using 0.5 equivalents of NaOAc provided more of the Overman-product **3** without substantially affecting the formation of the oxazolidinone (Table 1, entry 2).[23] The best reaction conditions were found to be those in which both acetic acid and sodium acetate were added in 7 and 0.5 equivalents, respectively (Table 1, entry 6). Although the same product ratio was obtained with a smaller amount of acetic acid (3.5 and 0.5 equiv, respectively, Table 1, entry 7), it appeared that yields were systematically better with the conditions of entry 6 (7 and 0.5 equiv, respectively). Under these conditions, oxazolidinone **2** was isolated in 83% yield (Table 1, entry 6). Evidently, buffered reaction conditions were crucial for the selectivity between the desired 5-*exo-trig* and the undesired 6-*endo-trig* reaction.

Table 1. Optimization of the palladium(II)-catalyzed cyclization of allylic tosylcarbamate **1**.[a]

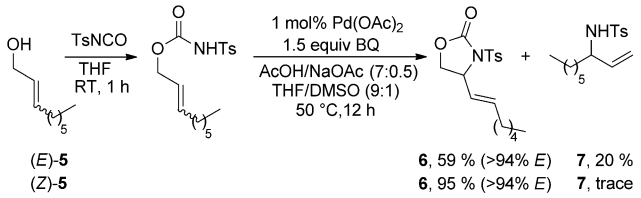


1 2 3 4

Entry	HOAc [equiv]	NaOAc [equiv]	Conversion [%][c]	Distribution **2/3/4**[c]
1	0.5	0	100	45:5:50
2	0	0.5	100	40:20:40
3	2	1	100	75:20:5
4	1	2	65	55:35:10
5	7	1	100	80:10:10
6	7	0.5	100 (83)[b]	85:10:5
7	3.5	0.5	100	85:10:5

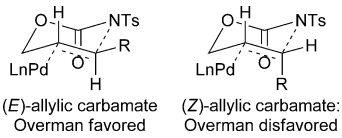
[a] 1 mol% $Pd(OAc)_2$, 1.5 equiv of BQ, HOAc/NaOAc, THF/DMSO (9:1), 50°C, 12 h. [b] Yield of the isolated product. [c] Determined by ^{1}H NMR spectroscopy of crude reaction mixtures.

Influence of *E*/*Z*-isomerism: Since our model reaction was run with an *E*/*Z*-mixture of allylic alcohol (12:1), we decided to investigate the effect of the stereochemistry around the double bond. When the allylic alcohol (*E*)-**5** was subjected to the reaction conditions described in Table 1, a mixture of the desired oxazolidinone **6** (59%) and tosylamine **7** (20%), originating from the decarboxylative Overman-type isomerization, was obtained (Scheme 2).



Scheme 2. Effects observed on oxazolidinone formation using *E*- or *Z* allylic carbamates.

On the contrary, when (*Z*)-**5** was subjected to the same reaction conditions, the desired isolated oxazolidinone was obtained in 95% yield (Scheme 2). The transition states for the Overman-rearrangement leading to **7** are different for the *E*- and *Z* isomers. The transition state for the (*E*)-allylic alcohol will be lower in energy compared with that of the (*Z*)-allylic alcohol because of the pseudoaxial methyl group in the latter (Scheme 3). This will favor formation of the Overman side product from the *E* isomer.



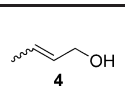
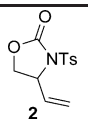
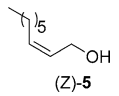
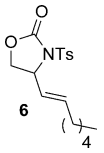
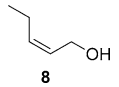
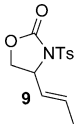
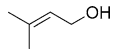
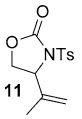
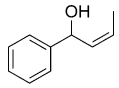
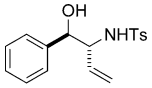
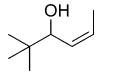
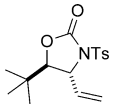
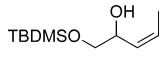
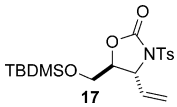
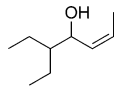
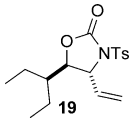
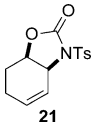
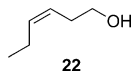
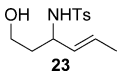
Scheme 3. Proposed transition states for the Overman rearrangement.

Reaction scope: Having established that (*Z*)-allylic alcohols provided better results than the corresponding (*E*)-isomer we went on to further explore the scope of this reaction. The readily available allylic alcohols were submitted to the reaction conditions described in Scheme 2. The allylic alcohols (*Z*)-**5** and **8** provided oxazolidinones as crystalline solids in excellent yields (Table 2, entries 2 and 3), accompanied by very small amounts of the corresponding Overman side product. The trisubstituted prenyl-alcohol **10** proved to be a much less effective substrate, and only 40% yield of the corresponding isolated oxazolidinone **11** was obtained after increasing the catalytic loading to 10 mol% and extending the reaction time to 48 h (Table 2, entry 4). Clearly, terminally disubstituted allylic alcohols were reluctant to undergo this palladium(II)-catalyzed amidation.

Starting from the secondary, phenyl-substituted allylic alcohol **12**, *syn*-1,2-amidoalcohol **13** was obtained in 61% yield after hydrolysis of the corresponding oxazolidinone under basic conditions (Table 2, entry 5). The additional hydrolysis step was required due to purification difficulties of the oxazolidinone.

We were pleased to find that secondary allylic alcohols (Table 2, entries 6–9) produced *trans*-oxazolidinones with

Table 2. Scope and limitations of the cyclization of allylic tosylcarbamates.[a]

Entry	Alcohol	Product	d.r.	Yield [%][b]
1	 **4**	 **2**	–	83
	$E/Z = 12/1$			
2	 (Z)-**5**	 **6**	–	95[c]
3	 **8**	 **9**	–	81[c]
4	 **10**	 **11**	–	40[d]
5	 **12**	 **13**	>20:1	61[e,f]
6	 **14**	 **15**	>20:1	79[f]
7	 **16**	 **17**	>20:1	78[f]
8	 **18**	 **19**	>20:1	83[f]
9	 **20**	 **21**	>25:1	81[d]
10	 **22**	 **23**	–	46[c,d,e]

[a] Allylic alcohol (1 equiv) and TsNCO (1 equiv) were stirred in THF at RT for 1 h. DMSO was added to give THF/DMSO 9:1 and this carbamate solution was used for the cyclization. Unless noted otherwise the following reaction conditions were employed for the cyclization: $Pd(OAc)_2$, (1 mol%), BQ (1.5 equiv), AcOH (7 equiv), NaOAc (0.5 equiv), THF/DMSO (9:1), 50°C, 12 h. [b] Yield of the isolated product. [c] The E/Z ratio was >20:1). [d] 10 mol% of $Pd(OAc)_2$, 48 h. [e] Hydrolysis of the crude oxazolidinone was performed to facilitate purification of the product. [f] Same conditions as in [a] but with 5 mol% of $Pd(OAc)_2$ and 48 h reaction time.

excellent diastereoselectivity (see Figure 1 for X-ray structures) in yields in the range of 80%. For example, the TBDMS-protected allylic alcohol **16** provided the isolated *trans*-oxazolidinone **17** in 78% yield with excellent diastereoselectivity (>20:1). Following the same procedure, it was possible to obtain oxazolidinones bearing different alkyl chains in good yields and with excellent diastereoselectivities (Table 2, entries 6–8). The diastereoselectivity of the oxazolidines is higher than that previously obtained with related protocols.[9a,c]

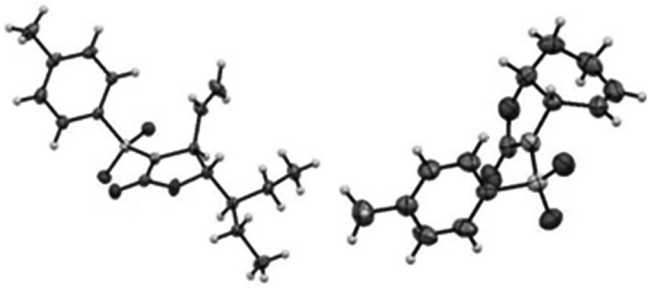
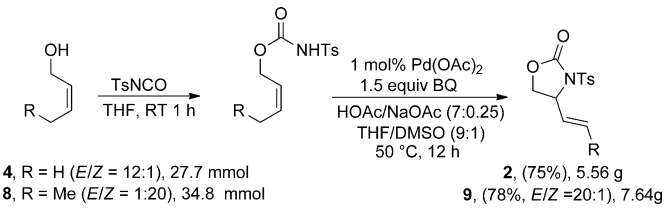


Figure 1. X-ray structure of oxazolidinones **19** (left) and **21** (right).

The developed catalytic process was also compatible with cyclic allylic alcohols. With some modifications, mainly increasing the catalytic loading and extending the reaction time, the isolated bicyclic *cis*-oxazolidinone **21** was obtained in 81% yield after 48 h (Table 2, entry 9). These bicyclic oxazolidinones have previously been prepared through palladium(0) catalysis.[24] Finally, 1,3-amidoalcohol **23** was obtained from homoallylic alcohol **22** by the same procedure and subsequent hydrolysis. In this particular case, a higher catalytic loading and a longer reaction time was required (Table 2, entry 10).

As we were interested in some further reactivity of the acquired oxazolidinones (see below) we decided to evaluate a scale up of this reaction. Starting with 2 g (27.7 mmol) of allylic alcohol **4**, the reaction with TsNCO at 0°C furnished the desired allylic tosyl carbamate **1** (not isolated). Treatment of the latter species under the reaction conditions described in Table 2 produced 5.56 g (75%) of the desired vinyloxazolidinone **2** as a colorless solid in a one-pot procedure. Similarily, 7.64 g (78%) of **9** was obtained starting from 3 g (34.8 mmol) of allylic alcohol **8** (Scheme 4). In the latter case, the pure product was isolated by precipitation of the oxazolidinone after extraction. Unfortunately, the same approach was not possible for **2**, as precipitation failed to separate the Overman product from the oxazolidinone.



Scheme 4. Scale up of the palladium-catalyzed oxidative cyclization of allylic tosylcarbamates.

Biomimetic reoxidation procedure: Among the Wacker type oxy- and azapalladation, a number of catalyst systems have

been reported for an aerobic version. The most widely used systems involve the use of $Pd(OAc)_2$[19,20,25] or $Pd(OOCCF_3)_2$[21] with DMSO or $Pd(OAc)_2$ with pyridine.[26] Unfortunately, with our allylic tosylcarbamates, these systems gave poor yields and selectivities and we observed large amounts of Overman and overoxidation products. To further enhance the synthetic utility, as well as evaluating a green(er) process for this transformation, an aerobic (biomimetic) reoxidation system was investigated. In this approach, catalytic amounts of BQ is used in combination with an oxygen-activating cobalt complex (**24**), which allows the use of molecular oxygen as terminal oxidant instead of BQ. We have previously reported such procedures for a variety of palladium-catalyzed reactions, in which O_2 is serving as a terminal oxidant.[4b,c,27]

To demonstrate the efficiency of this aerobic protocol, allylic alcohol **4** was, after derivatization with TsNCO, subjected to $Pd(OAc)_2$ (5 mol%), Cobalt(II)-salophen (5 mol%, Figure 2), BQ (10 mol%) and an ambient pressure of molecular oxygen, under otherwise similar reaction conditions as those employed in the stoichiometrically, BQ-mediated reaction (Scheme 5).

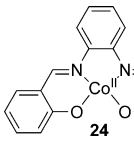
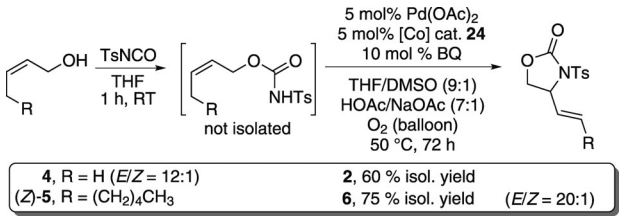


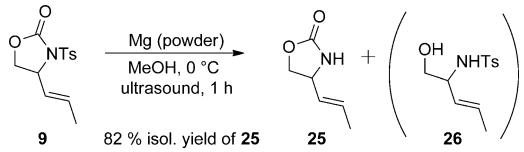
Figure 2. Structure of oxygen activating Co^{II}-salophen.



Scheme 5. Biomimetic, $Pd(OAc)_2$-catalyzed oxidative cyclization of allylic tosylcarbamates.

Using these catalytic conditions, oxazolidinone **2** was obtained in 60% yield after 72 h. Similarily, oxazolidinone **6** was obtained in 75% yield starting from allylic alcohol (*Z*)-**5**. It is worth pointing out that these conditions are not yet optimized and further investigations on this and other alternative aerobic reoxidation protocols (ligand modulation) are currently being investigated in our laboratories.

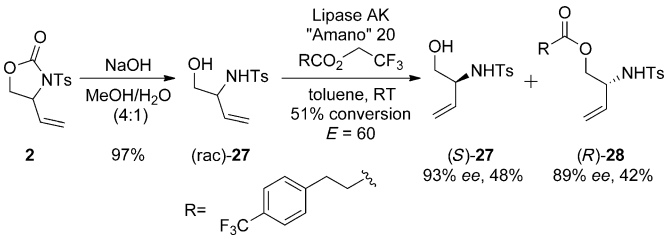
Further derivatization: Removal of the tosyl protecting group is generally a quite impractical and time-consuming process involving, for example, reductive cleavage using sodium/lithium and naphthalene.[28] On the basis of an earlier report by Ragnarsson and co-workers,[29] we set out to investigate the possibility of cleaving the N–Ts bond using magnesium under ultrasonic conditions. It turned out that the tosyl group was readily removed using this protocol. Treatment of **9** with magnesium in dry methanol at 0°C under ultrasonic irradiation provided oxazolidinone **25** in 82% isolated yield, accompanied by approximately 10% of



Scheme 6. Deprotection of oxazolidinone **9** using magnesium in methanol.

the tosyl-protected amidoalcohol **26** (Scheme 6). The development of an efficient and simple deprotection is the first step towards our final goal of attempting N-allenylation and subsequent oxidative carbocyclization of these interesting substrates (see Scheme 1).

Vinyl-substituted β-aminoalcohols and its protected analogues have been widely used as building blocks for the synthesis of unnatural amino acids,[30] pharmaceutically relevant compounds,[31] and natural products.[32] We thus decided to investigate an enzymatic kinetic resolution (KR) strategy to obtain enantioenriched derivatives. The tosyl-protected vinyloxazolidinone **2**, in racemic form, was hydrolyzed and subsequently subjected to an enzymatic KR in the presence of 2,2,2-trifluoroethyl 3-(4-(trifluoromethyl)phenyl)propanoate as acyldonor and lipase AK "Amano" 20 as biocatalyst[33] (Scheme 7). Fortunately, the lipase showed a decent selectivity for this substrate ($E=60$). At 51% conversion the alcohol (*S*)-**27** was isolated in 48% yield and with an enantiomeric excess (*ee*) of 93%, whereas the ester (*R*)-**28** was obtained in 42% yield and 89% *ee*.

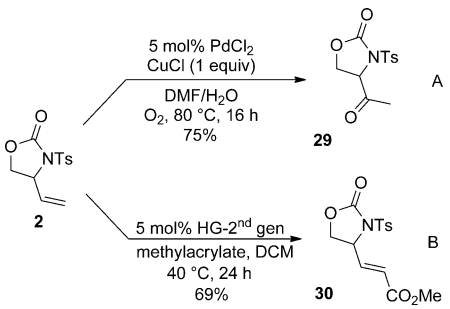


Scheme 7. Enzymatic kinetic resolution of (*rac*)-**27**.

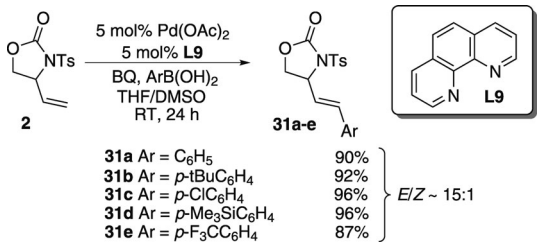
The vinyl moiety of the oxazolidinone **2** can also be functionalized leading to interesting precursors of 1,2-aminoalcohols. As an example, classical palladium-catalyzed oxidations were conducted. A Wacker type oxidation of the double bond in oxazolidinone **2** led to the selective formation of the ketone **29** in 75% yield (95:5 ketone to aldehyde selectivity), using conditions previously reported.[34]

Furthermore, a cross metathesis reaction between methyl acrylate and oxazolidinone **2** afforded product **30** in 69% isolated yield in the presence of 5 mol% of Hoveyda-Grubbs 2nd generation catalyst (HG 2nd-gen, Scheme 8).

Finally, inspired by the recent interest in oxidative-Heck reactions,[35] oxazolidinone **2** was allowed to react with $Pd(OAc)_2$ (5 mol%), 1,10-phenanthroline (5 mol%, **L9**), and 1.5 equivalents of an arylboronic acid in a 1:1 mixture of DMSO and THF at 50°C for 24 h to furnish the arylated oxazolidinones (**31**) (Scheme 9).



Scheme 8. Functionalization of the vinyl moiety of oxazolidinone **2**.



Scheme 9. Palladium(II)-catalyzed oxidative Heck reaction.

Indeed, these catalytic conditions rendered predominantly *trans*-arylated tosyl-oxazolidinones in excellent yield and with high *E*/*Z* selectivity (>15:1) (Scheme 9). Initially we intended to perform this reaction in a one-pot procedure coupled to the cyclization, but we were unable to obtain satisfactory conversions with this strategy.[36] Nevertheless, the two-step procedure tolerated electronically diverse aryl boronic acids.

Although we initially started this project with the purpose of gaining access to substrates suitable for a copper(I)-catalyzed allenylation, we are also currently looking into applying this cyclization startegy in natural product synthesis. Primarily, we are investigating a synthesis of Kainic acid (Figure 3, **34**) starting from oxazolidinone **2**. Other potential targets, are for example sphingosine or pachastrissamine (jaspine B) (Figure 3, **32** and **33**).

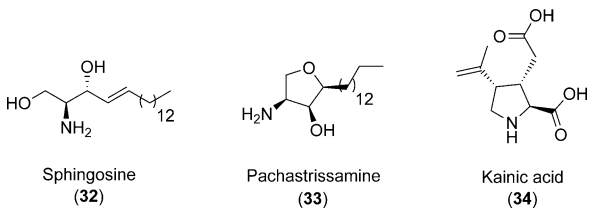
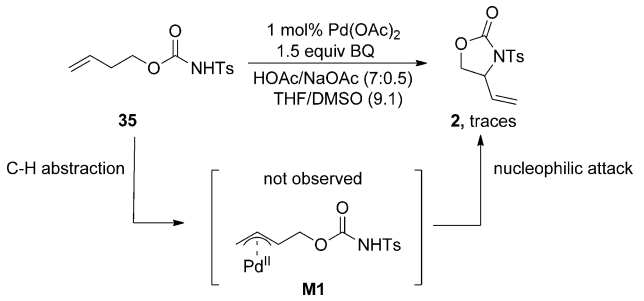


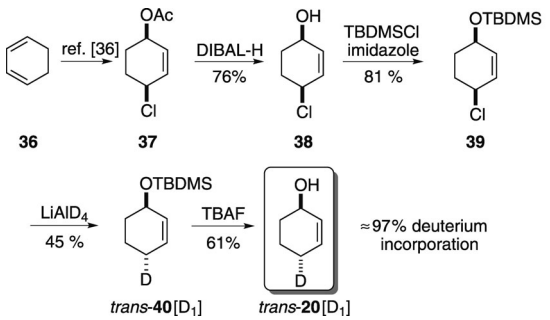
Figure 3. Possible target molecules.

Mechanistic investigation: Palladium(II)-catalyzed aminations of olefins can potentially occur through a variety of different mechanisms. Normally, the mechanism has to be studied for each individual reaction as the choice of solvent, additives and amine/amide-nucleophile can potentially affect the mechanistic outcome. For our oxidative cyclization, three mechanisms were considered for the formation of the oxazolidinone (Scheme 12).[2i] First, the reaction could proceed through a (π-allyl)palladium(II)-intermediate, much similar to procedures reported by White and Fraunhoffer.[9a] The other two possibilities are *cis*- or *trans*-amidopalladation of the olefin, followed by *syn*-β-hydride elimination. (Scheme 12). To probe the mechanistic process that was operating in our catalytic reaction, we first attempted to cyclize the homoallylic alcohol **35** under the conditions described in Scheme 2. Interpretation of the crude ^{1}H NMR spectrum from this reaction revealed that only trace amounts of the desired oxazolidinone **2** was formed (Scheme 10) Based on this observation we conclude that the cyclization most likely does not proceed through *syn* C–H abstraction to give a (π-allyl)palladium intermediate (**M1**). The small amount of product observed in this reaction was considered to originate from terminal/internal olefin isomerization, followed by amidopalladation.

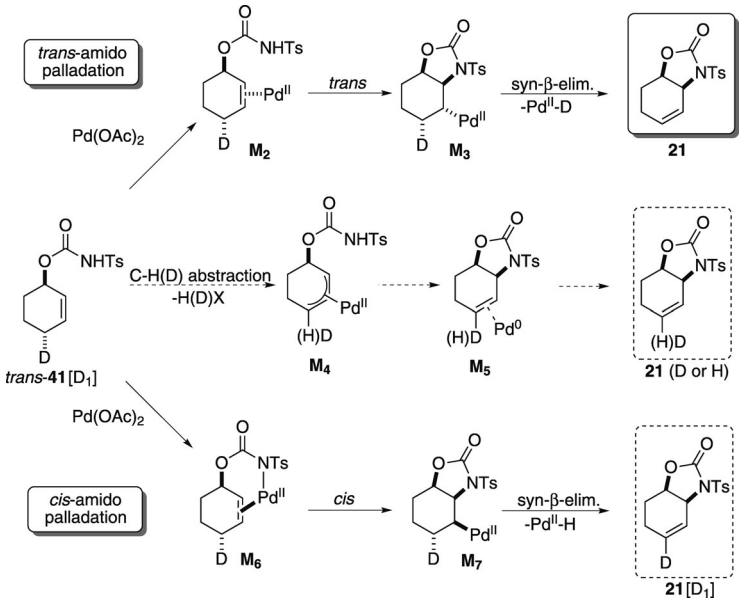


Scheme 10. Attempt to observe formation of a π-allyl complex in the cyclization of homoallylic tosylcarbamates.

Having excluded the above pathway we turned our focus to oxidative amidopalladation processes. It has been shown on previous occasions that the stereochemistry of true aminopalladations are *trans*.[37] On the contrary, in the case of amidopalladation, sulfonamidopalladation and sulfoacetamidopalladation, the addition across the double bond can occur with either *cis*[38] or *trans* stereochemistry.[2i,13,38a–c,39] Stahl and co-workers carried out an elegant and systematic study on the aza-Wacker addition of different sulfonamides to double bonds,[38c] which is similar to the work of Stoltz and co-workers for oxypalladation.[26b] This study revealed that both the substrate and the additives have a strong influence on the stereochemical outcome of the reaction. Using a similar strategy, we decided to analyze the stereochemistry of the amidopalldation step in our catalytic reaction. For this purpose we synthesized the deuterium-labeled allylic alcohol *trans*-**20**[D_1] (Scheme 11).[40] The synthesis started with a stereoselective *cis*-1,4-chloroacetoxylation of 1,3-cyclohexadiene **36**.[41] The acetyl group in the acetoxychlorinated product **37** was then carefully deprotected using DIBAL-H at 0 °C to give **38**, avoiding the formation of the epoxycyclohexene byproduct. Chloroalcohol **38** was then protected as a silyl ether with TBDMSCl to furnish **39** in 81 % yield. Incorporation of the deuterium was achieved by S_N2-type nucleophilic substitution of the chloride by a deuterium ($LiAlD_4$)



Scheme 11. Synthesis of the *trans*-deuterated cyclic alcohol **20**.

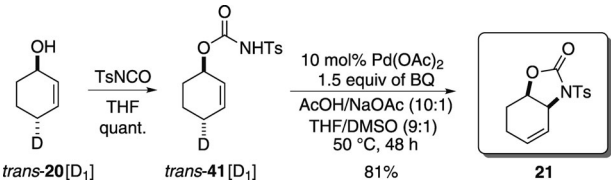


Scheme 12. Three possible mechanistic scenarios.

to give *trans*-**40**[D_1]. Finally, deprotection of the silyl group using TBAF afforded the desired deuterium-labeled cyclohexenol *trans*-**20**[D_1] in 61% yield (≈97% deuterium incorporation).

Using *trans*-**20**[D_1] as starting material, we argued that it would be possible to determine whether the reaction occurs through *trans*- or *cis*-amidopalladation (Scheme 12). The first mechanism involves initial binding of a palladium(II) species to the double bond on the opposite side (*trans*) of the carbamate, followed by attack of the nitrogen and β-deuteride elimination leading to exclusive formation of **21** (Scheme 12, upper pathway). The second pathway (Scheme 12, lower pathway), *cis*-amidopalladation, occurs if the tosyl carbamate coordinates to palladium(II) followed by *cis*-migratory insertion of the olefin and subsequent β-hydride elimination.[2i] This process would lead to formation of the deuterated bicyclic oxazolidinone **21**[D_1].

Reaction of the allylic alcohol *trans*-**20**[D_1] with tosyl isocyanate produced the corresponding carbamate, *trans*-**41**[D_1]. Subjecting this carbamate to the catalytic conditions described in Scheme 13 afforded **21**, with complete removal



Scheme 13. Cyclization of deuterium-labeled carbamate *trans*-**41**[D_1].

of the deuterium atom. This result clearly demonstrates that the reaction proceeds through a *trans*-amidopalladation. In our case, the large excess of acetic acid may favor coordination of the alkene to palladium, which would lead to *trans*-amidopalladation.

Conclusion

In conclusion, we have developed a new and highly diastereoselective cyclization of allylic carbamates. This reaction involves inexpensive starting materials, in the form of allylic alcohols, together with a readily available catalyst (Pd(OAc)$_2$) and oxidant (BQ). The method also proved scalable, highly diastereoselective, and quite general. In this study, we have also shown that the stereochemistry of this sulfonylcarbamatopalladation is *trans*. This stereochemical pathway opens up routes for asymmetric versions of this reaction catalyzed by chiral Pd^{II} complexes.

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[1] J. E. Bäckvall, *Modern Oxidation Methods*, 2nd Edition, Wiley-VCH, Weinheim, Germany, **2010**.

[2] For reviews see: a) L. S. Hegedus, in *Comprehensive Organic Synthesis* Vol. 4 (Eds: M. F. Semmelhack), Pergamon Press, Inc.: Elmsford, **1991**, pp. 551–569; b) T. Hosokawa, S.-I. Murahashi, in *Handbook of Organopalladium Chemistry for Organic Synthesis* Vol. 2 (Eds: E. Negishi, A. de Meijere), John Wiley and Sons, Inc.: New York, **2002**, pp. 2169–2192; c) T. Hosokawa in *Handbook of Organopalladium Chemistry for Organic Synthesis* Vol. 2 (Eds: E. Negishi, A. de Meijere), John Wiley and Sons, Inc.: New York, **2002**, pp. 2211–2225; d) G. Zeni, R. C. Larock, *Chem. Rev.* **2004**, *104*, 2285; e) S. S. Stahl, *Angew. Chem.* **2004**, *116*, 3480; *Angew. Chem. Int. Ed.* **2004**, *43*, 3400; f) E. M. Beccalli, G. Broggini, M. Martinelli, S. Sottocornola, *Chem. Rev.* **2007**, *107*, 5318; g) A. Minatti, K. Muñiz, *Chem. Soc. Rev.* **2007**, *36*, 1142; h) V. Kotov, C. C. Scarborough, S. S. Stahl, *Inorg. Chem.* **2007**, *46*, 1910; i) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981.

[3] a) J. Löfstedt, J. Franzén, J. E. Bäckvall, *J. Org. Chem.* **2001**, *66*, 8015; b) J. Piera, A. Persson, X. Caldentey, J. E. Bäckvall, *J. Am. Chem. Soc.* **2007**, *129*, 14120; c) E. A. Karlsson, J. E. Bäckvall, *Chem. Eur. J.* **2008**, *14*, 9175.

[4] a) J. Franzén, J. E. Bäckvall, *J. Am. Chem. Soc.* **2003**, *125*, 6056; b) J. Piera, K. Närhi, J. E. Bäckvall, *Angew. Chem.* **2006**, *118*, 7068;

Angew. Chem. Int. Ed. **2006**, *45*, 6914; c) E. V. Johnston, E. A. Karlsson, S. A. Lindberg, B. Åkermark, J. E. Bäckvall, *Chem. Eur. J.* **2009**, *15*, 6799; d) A. K. Å. Persson, T. Jiang, M. T. Johnson, J. E. Bäckvall, *Angew. Chem.* **2011**, *123*, 6279; *Angew. Chem. Int. Ed.* **2011**, *50*, 6155; e) T. Jiang, A. K. Å. Persson, J. E. Bäckvall, *Org. Lett.* **2011**, *13*, 5838.

[5] A. K. Å. Persson, J. E. Bäckvall, *Angew. Chem.* **2010**, *122*, 4728; *Angew. Chem. Int. Ed.* **2010**, *49*, 4624.

[6] T. A. Mukhtar, G. D. Wright, *Chem. Rev.* **2005**, *105*, 529.

[7] S. C. Bergmeier, *Tetrahedron* **2000**, *56*, 2561.

[8] a) D. A. Evans, J. M. Takacs, L. R. McGee, M. D. Ennis, D. J. Mathre, J. Bartroli, *Pure Appl. Chem.* **1981**, *53*, 1109; b) D. A. Evans, *Aldrichimica Acta* **1982**, *15*, 23; c) D. J. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.* **1996**, *96*, 835.

[9] a) K. J. Fraunhoffer, M. C. White, *J. Am. Chem. Soc.* **2007**, *129*, 7274; b) G. T. Rice, M. C. White, *J. Am. Chem. Soc.* **2009**, *131*, 11707; c) X. Qi, G. T. Rice, M. S. Lall, M. S. Plummer, M. C. White, *Tetrahedron* **2010**, *66*, 4816.

[10] a) F. Nahra, F. Liron, G. Prestat, C. Mealli, A. Messaoudi, G. Poli, *Chem. Eur. J.* **2009**, *15*, 11078; b) S. D. R. Christie, A. D. Warrington, C. J. Luniniss, *Synthesis* **2009**, 148.

[11] a) S. A. Reed, M. C. White, *J. Am. Chem. Soc.* **2008**, *130*, 3316; b) G. Yin, Y. Wu, G. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 11978.

[12] M. R. Manzoni, T. P. Zabawa, D. Kasi, S. R. Chemler, *Organometallics* **2004**, *23*, 5618.

[13] E. J. Alexanian, C. Lee, E. J. Sorensen, *J. Am. Chem. Soc.* **2005**, *127*, 7690.

[14] S. Nicolai, S. Piemontesi, J. Waser, *Angew. Chem. Int. Ed.* **2011**, *50*, 4680.

[15] H. Harayama, A. Abe, T. Sakado, M. Kimura, K. Fugami, S. Tanaka, Y. Tamaru, *J. Org. Chem.* **1997**, *62*, 2113.

[16] a) G. Liu, X. Lu, *Org. Lett.* **2001**, *3*, 3879; b) C. Jonasson, W. F. J. Karstens, H. Hiemstra, J. E. Bäckvall, *Tetrahedron Lett.* **2000**, *41*, 1619.

[17] A. Lei, X. Lu, *Org. Lett.* **2000**, *2*, 2699.

[18] The use of allylic tosylcarbamates as starting materials have, to the best of our knowledge, only been attempted by White et al. (ref. [11]). However, using their approach, only between 9–20% of the desired oxazolidinone could be observed.

[19] R. A. T. M. Van Benthem, H. Hiemstra, G. R. Longarela, W. N. Speckamp, *Tetrahedron Lett.* **1994**, *35*, 9281.

[20] R. A. T. M. Van Benthem, H. Hiemstra, J. J. Michels, W. N. Speckamp, *J. Chem. Soc. Chem. Commun.* **1994**, 357.

[21] R. I. McDonalds, S. Stahl, *Angew. Chem.* **2010**, *122*, 5661; *Angew. Chem. Int. Ed.* **2010**, *49*, 5529.

[22] A. V. Malkov, M. Barłóg, L. Miller-Potucká, M. A. Kabeshov, L. J. Farrugia, P. Kočovský, *Chem. Eur. J.* **2012**, *18*, 6873.

[23] a) L. E. Overman, *J. Am. Chem. Soc.* **1976**, *98*, 2901; b) L. E. Overman, *Acc. Chem. Res.* **1980**, *13*, 218; c) L. E. Overman, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 579.

[24] a) B. M. Trost, D. L. Van Vranken, C. Bingel, *J. Am. Chem. Soc.* **1992**, *114*, 9327; b) B. M. Trost, D. L. Van Vranken, *J. Am. Chem. Soc.* **1993**, *115*, 444; c) B. M. Trost, D. L. Van Vranken, *Chem. Rev.* **1996**, *96*, 395.

[25] a) R. C. Larock, T. R. Hightower, L. A. Hasvold, K. P. Peterson, *J. Org. Chem.* **1996**, *61*, 3584; b) M. Rönn, J.-E. Bäckvall, P. G. Andersson, *Tetrahedron Lett.* **1995**, *36*, 7749.

[26] a) S. R. Fix, J. L. Brice, S. S. Stahl, *Angew. Chem.* **2002**, *114*, 172; b) R. M. Trend, Y. K. Ramtohul, B. M. Stoltz, *J. Am. Chem. Soc.* **2005**, *127*, 17778.

[27] a) J. Piera, J. E. Bäckvall, *Angew. Chem.* **2008**, *120*, 3558; *Angew. Chem. Int. Ed.* **2008**, *47*, 3506; b) B. W. Purse, L. H. Tran, J. Piera, B. Åkermark, J. E. Bäckvall, *Chem. Eur. J.* **2008**, *14*, 7500; c) E. V. Johnston, E. A. Karlsson, H. L. Tran, B. Åkermark, J. E. Bäckvall, *Eur. J. Org. Chem.* **2009**, 3973; d) J. E. Bäckvall, R. B. Hopkins, H. Grennberg, M. Mader, A. K. Awasthi, *J. Am. Chem. Soc.* **1990**, *112*, 5160.

[28] T. W. Green, P. G. M. Wuts in *Protective Groups in Organic Synthesis* Wiley-Interscience, 3rd ed., Wiley, New York, **1999**, pp. 603–607.

[29] B. Nyasse, L. Grehn, U. Ragnarsson, *Chem. Commun.* **1997**, 1017.

[30] a) F. Brackmann, N. Colombo, C. Cabrele, A. de Meijere, *Eur. J. Org. Chem.* **2006**, 4440; b) A. Krebs, V. Ludwig, J. Pfizer, G. Dürner, M. W. Göbel, *Chem. Eur. J.* **2004**, *10*, 544; c) M. Suhartono, M. Weidlich, T. Stein, M. Karas, G. Dürner, M. W. Göbel, *Eur. J. Org. Chem.* **2008**, 1608.

[31] a) R. F. Keyes, J. J. Carter, X. Zhang, Z. Ma, *Org. Lett.* **2005**, *7*, 847; b) K. Hashimoto, M. Horikawa, H. Shirahama, *Tetrahedron Lett.* **1990**, *31*, 7047; c) M. Horikawa, K. Hashimoto, H. Shirahama, *Tetrahedron Lett.* **1993**, *34*, 331; d) K. Shimamoto, M. Ishida, H. Shinozaki, Y. Ohfune, *J. Org. Chem.* **1991**, *56*, 4167; e) J. R. Del Valle, M. Goodman, *J. Org. Chem.* **2004**, *69*, 8946.

[32] a) B. M. Trost, D. B. Horne, M. J. Woltering, *Angew. Chem.* **2003**, *115*, 6169; *Angew. Chem. Int. Ed.* **2003**, *42*, 5987; b) P. Dewi-Wülfing, S. Blechert, *Eur. J. Org. Chem.* **2006**, 1852; c) F. Yokokawa, T. Asano, T. Okino, W. H. Gerwick, T. Shioiri, *Tetrahedron* **2004**, *60*, 6859; d) M. Tang, S. G. Pyne, *J. Org. Chem.* **2003**, *68*, 7818; e) H. Takahata, Y. Banba, H. Ouchi, H. Nemoto, A. Kato, I. Adachi, *J. Org. Chem.* **2003**, *68*, 3603.

[33] Lipase AK "Amano" 20 appeared to be more selective in this case than the previously described PPL. For a previously reported kinetic resolution of such an amino alcohol, see: a) F. Francalanci, P. Cesti, W. Cabri, D. Bianchi, T. Martinengo, M. Foa, *J. Org. Chem.* **1987**, *52*, 5079; b) V. Gotor, R. Brieva, F. Rebolledo, *J. Chem. Soc. Chem. Commun.* **1988**, 957; c) S. Fernández, R. Brieva, F. Rebolledo, V. Gotor, *J. Chem. Soc. Perkin Trans. 1* **1992**, 2885.

[34] a) B. Weiner, A. Baeza, T. Jerphagnon, B. L. Feringa, *J. Am. Chem. Soc.* **2009**, *131*, 9473; b) J. Muzart, *Tetrahedron* **2007**, *63*, 7505; c) C. N. Cornell, M. S. Sigman, *Inorg. Chem.* **2007**, *46*, 1903.

[35] a) E. W. Werner, M. S. Sigman, *J. Am. Chem. Soc.* **2011**, *133*, 9692; b) P. A. Enquist, J. Lindh, P. Nilsson, M. Larhed, *Green Chem.* **2006**, *8*, 338; c) K. S. Yoo, C. P. Park, C. H. Yoon, S. Sakaguchi, J. O'Neill, K. W. Jung, *Org. Lett.* **2007**, *9*, 3933; d) J. Ruan, X. Li, O. Saidi, J. Xiao, *J. Am. Chem. Soc.* **2008**, *130*, 2424; e) J. Lindh, P. A. Enquist, Å. Pilotti, P. Nilsson, M. Larhed, *J. Org. Chem.* **2007**, *72*, 7957; f) J. H. Delcamp, A. P. Brucks, M. C. White, *J. Am. Chem. Soc.* **2008**, *130*, 11270.

[36] During the preparation of this manuscript, the group of White published a sequential one-pot procedure that achieves the same overall reaction using homoallylic carbamates, see: C. Jiang, D. J. Covell, A. F. Stepan, M. S. Plummer, C. M. White, *Org. Lett.* **2012**, *14*, 1386.

[37] a) B. Åkermark, J. E. Bäckvall, K. Siirala-Hansén, K. J. Sjöberg, K. Zetterberg, *Tetrahedron Lett.* **1974**, *15*, 1363; b) B. Åkermark, J. E. Bäckvall, L. S. Hegedus, K. Zetterberg, K. Siirala-Hansén, K. J. Sjöberg, *Organomet. Chem.* **1974**, *72*, 127; c) L. S. Hegedus, G. F. Allen, E. L. Waterman, *J. Am. Chem. Soc.* **1976**, *98*, 2674; d) J. E. Bäckvall, *Acc. Chem. Res.* **1983**, *16*, 335; e) J. E. Bäckvall, E. E. Björkman, *Acta Chem. Scand. B.* **1984**, *38*, 91.

[38] a) G. Liu, S. S. Stahl, *J. Am. Chem. Soc.* **2006**, *128*, 7179; b) K. Isomura, N. Okada, M. Saruwatari, H. Yamasaki, H. Taniguchi, *Chem. Lett.* **1985**, 385; c) G. Liu, S. S. Stahl, *J. Am. Chem. Soc.* **2007**, *129*, 6328; d) X. Ye, G. Liu, B. Popp, S. S. Stahl, *J. Org. Chem.* **2011**, *76*, 1031; e) K. Muñiz, C. H. Hövelmann, J. Streuff, *J. Am. Chem. Soc.* **2008**, *130*, 763.

[39] P. A. Sibbald, C. F. Rosewall, R. D. Swartz, F. E. Michaels, *J. Am. Chem. Soc.* **2009**, *131*, 15945.

[40] a) H. E. Schink, H. Petterson, J. E. Bäckvall, *J. Org. Chem.* **1991**, *56*, 2769; b) P. G. Andersson, *J. Org. Chem.* **1996**, *61*, 6968.

[41] a) J. E. Bäckvall, J. E. Nyström, R. E. Nordberg, *J. Am. Chem. Soc.* **1985**, *107*, 3676; b) J. E. Bäckvall, K. L. Granberg, R. B. Hopkins, *Acta Chem. Scand.* **1990**, *44*, 492.

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