Pergamon

Tetrahedron Letters 41 (2000) 1619–1622

TETRAHEDRON LETTERS

Palladium(II)-catalyzed intramolecular 1,2-oxidation of allenes involving nitrogen nucleophiles

Catrin Jonasson,[a] Willem F. J. Karstens,[b] Henk Hiemstra [b] and Jan-E. Bäckvall [a,*]

[a]*Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-106 91 Stockholm, Sweden*
[b]*Laboratory of Organic Chemistry, Institute of Molecular Chemistry, University of Amsterdam, Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands*

Received 12 November 1999; accepted 16 December 1999

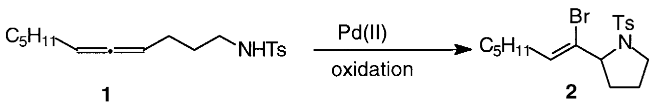
Abstract

A series of allenic tosylamides have been prepared and shown to undergo palladium(II)-catalyzed cyclization in the presence of lithium bromide and a copper(II) salt to give pyrrolidines. Palladium-catalyzed 1,2-oxidation of allenic lactams in the presence of LiBr and *p*-benzoquinone was also studied. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: allenes; cyclization; nitrogen heterocycles; palladium catalysis.

Palladium–catalyzed reactions of unsaturated hydrocarbons have been extensively studied and a large number of selective organic transformations have been reported.[1] In addition to dienes, acetylenes and olefins, allenes have in particular attracted considerable interest in recent years.[2–7] We have recently developed mild procedures for palladium-catalyzed 1,2-oxidation of allenes.[7] These reactions are carried out in acetic acid with palladium acetate as the catalyst and *p*-benzoquinone as the oxidant in the presence of two nucleophiles, which are added across the double bond. Nucleophiles that have been used so far include halides,[7a] carboxylates,[7b] and alcohols.[7c] It would be of great synthetic interest to extend these 1,2-oxidations to other nucleophiles such as carbon and nitrogen nucleophiles. In this communication we report on the use of nitrogen nucleophiles in the palladium-catalyzed 1,2-oxidation of allenes.

Palladium-catalyzed oxidation of allenic tosylamide **1**[8] in acetic acid employing *p*-benzoquinone as the oxidant and LiBr as the external nucleophile afforded only recovered starting material and no pyrrolidine **2** could be detected (Eq. (1)). Apparently, the amide nitrogen cannot act as a nucleophile under the slightly acidic conditions employed here.



(1)

Since *p*-benzoquinone requires acidic reaction conditions to work as an oxidant, alternative oxidants were examined. Thus, allenic tosylamide **1** was reacted with LiBr and $Pd(OAc)_2$ in THF using $CuCl_2$

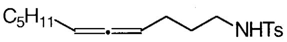
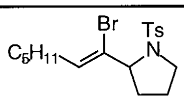
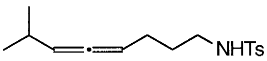
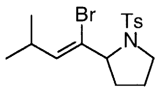
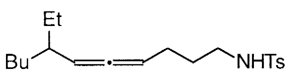
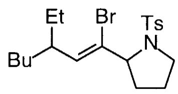
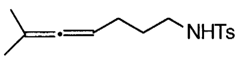
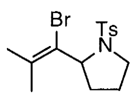
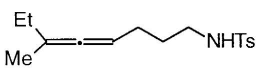
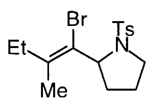
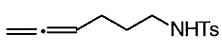
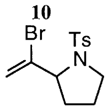
* Corresponding author. Tel: +46 8 6747178; fax: +46 8 154908; e-mail: jeb@organ.su.se (J.-E. Bäckvall)

PII: S0040-4039(99)02343-6

tetl 16271

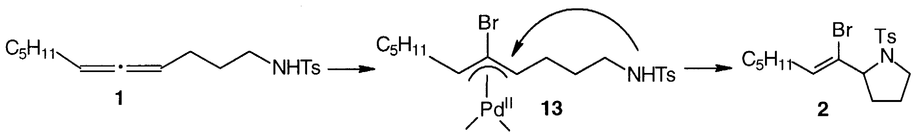
as the reoxidant, which afforded the corresponding pyrrolidine **2** in 30% yield. In order to optimize the reaction conditions other solvents (CH_2Cl_2, CH_3CN, acetone, ethanol, DMF) were tried, of which acetonitrile gave the best results. The yield was further improved by using one equivalent of base. However, the use of $CuCl_2$ as an oxidant gave rise to ca. 4% of a side product, resulting from attack of a chloride on the middle allene carbon instead of a bromide. To eliminate this side product, other oxidants ($CuBr_2$, $Cu(OTf)_2$, $Cu(OAc)_2$) were screened. The use of $Cu(OAc)_2$ gave the best result. Thus, reaction of allenic tosylamide **1** with LiBr, K_2CO_3 and $Cu(OAc)_2$ in the presence of a catalytic amount of $Pd(OAc)_2$ in acetonitrile under an O_2 atmosphere afforded the desired pyrrolidine **2** in 72% yield, with mainly *Z* stereochemistry (*Z*:*E*=93:7). The stereochemical assignment was made by NOE measurements. A few other *N*-tosylamides **3**, **5**, **7**, **9** and **11**[8] were also shown to cyclize under the palladium-catalyzed conditions (Table 1) affording the corresponding pyrrolidines **4**, **6**, **8**, **10** and **12**, respectively, in good isolated yields.[11] The non-substituted allenic amide **11** did, however, work better with $Cu(OTf)_2$ as an oxidant and the disubstituted allenic amides **7** and **9** worked best in the presence of $CuCl_2$. The disubstituted allenes did not show the side product resulting from chloride attack.

Table 1
Palladium-catalyzed 1,2-oxidation of substituted allenic tosylamides[a]

Entry	Allene	Product	*Z*/*E* [b]	Yield (%)[c]
1	 **1**	 **2**	93:7	72
2	 **3**	 **4**	89:11	76
3	 **5**	 **6**	89:11	80
4	 **7**	 **8**	-	68[d]
5	 **9**	 **10**	65:35	71[d]
6	 **11**	 **12**	-	69[e]

(a) Unless otherwise noted, the reactions were carried out at room temperature in acetonitrile (0.15M) employing 10 mol % of $Pd(OAc)_2$, 5 equiv. of LiBr, 2.1 equiv. of $Cu(OAc)_2$ and 1.2 eq of K_2CO_3 under an atmospheric pressure of O_2. Reaction times varied from 2-5 h. (b) Determined by NOE measurements. (c) Isolated yield after flash chromatography. (d) $CuCl_2$ was used instead of $Cu(OAc)_2$. (e) $Cu(OTf)_2$ was used instead of $Cu(OAc)_2$ and no K_2CO_3 was added.

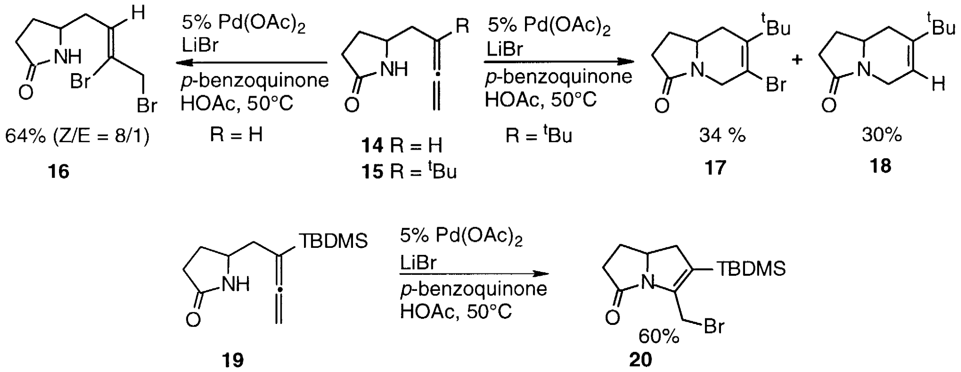
A likely mechanism for the palladium-catalyzed intramolecular oxidation is given in Eq. (2). Coordination of the allene **1** to palladium and subsequent bromide attack at the central allenic carbon produces a π-allyl palladium intermediate **13**, which undergoes an intramolecular nucleophilic attack to give the pyrrolidine product **2** and Pd(0). The copper(II) salt reoxidizes the Pd(0) back to Pd(II).



(2)

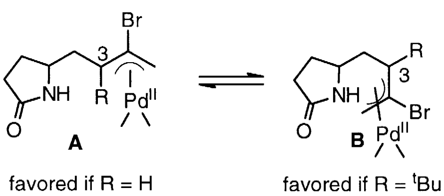
In most palladium-catalyzed reactions with allenes, nucleophiles (such as nitrogen and oxygen nucleophiles) attack one of the terminal sp^2–carbon atoms.[9] However, some unexpected regioselectivity was recently observed in an intramolecular palladium(0)-catalyzed reaction. Thus, a lactam nitrogen atom, with a two-carbon tether between the allene and the nitrogen atom, reacted at the middle *sp*-carbon of the allene to form five-membered ring enamides.[10] It was, therefore, of interest to study these compounds in the present palladium(II)-catalyzed 1,2-oxidations. The allenic lactams were prepared using a copper(I)-mediated displacement of propargylic tosylates with the zinc reagent of the corresponding lactam to afford different substituted allenes in moderate yields.[10b]

Allenic lactam **14** was subjected to the previously developed cyclization conditions with *p*-benzoquinone as the reoxidant,[7] which gave the 1,2-dibromo product **16** as an 8:1 mixture of double bond isomers (Scheme 1). No cyclic enamide product could be detected. To find out if there was any steric influence on the outcome of the reaction, the allenic lactam was substituted with a *t*-butyl group (**15**). This did not give rise to nitrogen atom attack at the middle *sp*-carbon but instead the two products **17** and **18**[12] were isolated. Here, a nitrogen attack had occurred at the terminal sp^2-carbon, probably via an intramolecular attack on the intermediate (π-allyl)palladium complex. Interestingly, subjecting the TBDMS (*t*-butyldimethylsilyl) substituted allene **19** to the same reaction conditions led to product **20** in which the nitrogen had indeed attacked the central *sp*-carbon (Scheme 1). The TBDMS group increases the electrophilicity of the *sp*-carbon making it easier for the nitrogen atom to attack.



Scheme 1.

The difference between **14** and **15** in the palladium-catalyzed oxidation can be explained from the equilibrium between the (π-allyl)palladium complexes **A** and **B** (Scheme 2). A large substituent in the C-3 position of the allene is expected to shift the equilibrium towards π-allyl complex **B**, whereas with a small substituent (R=H), **A** should predominate. Thus, after the first bromide attack at C-2, **14** would give mainly π-allyl complex **A**, whereas **15** would give π-allyl complex **B**. The latter complex is required for intramolecular attack by nitrogen at C-1.



Scheme 2.

Acknowledgements

Financial support from the Swedish Natural Science Research Council, the Swedish Foundation for Strategic Research, and the Council for Chemical Sciences of the Netherlands Organization for Scientific Research (CW-NWO) is gratefully acknowledged.

References

1. (a) Tsuji, J. *Palladium Reagents and Catalysts*: *Innovations in Organic Synthesis*; John Wiley & Sons: Chichester, 1995. (b) Bäckvall, J. E. In *Metal-catalyzed Cross Coupling Reactions*; Stang, P.; Diederich, F., Eds.; VCH: Weinheim, 1998; pp. 339–382. (c) Henry, P. M. *Palladium-catalyzed Oxidation of Hydrocarbons*; D. Reidel: Dordrecht, Holland, 1980. (d) Harrington, P. J. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, G. A.; Wilkinson, G., Eds.; Pergamon: New York, 1995; Vol. 12 (vol. Ed. Hegedus, L. S.), pp. 797–904. (e) Müller, T. E.; Beller, M. *Chem. Rev*. **1998**, *98*, 675.
2. (a) Davies, I. W.; Scopes, D. I. C.; Gallagher, T. *Synlett* **1993**, 85. (c) Besson, L.; Goré, J.; Cazes, B. *Tetrahedron Lett*. **1995**, *36*, 3853.
3. (a) Walkup, R. D.; Guan, L.; Mosher, M. D.; Kim, S. W.; Kim, Y. S. *Synlett* **1993**, 88. (b) Walkup, R. D.; Guan, L.; Kim, Y. S.; Kim, W. K. *Tetrahedron Lett*. **1995**, *36*, 3805.
4. (a) Zenner, J. M.; Larock, R. C. *J. Org. Chem*. **1999**, *64*, 7312. (b) Larock, R. C.; Tu, C.; Pace, P. *J. Org. Chem*. **1998**, *63*, 6859. (c) Trost, B. M.; Gerusz, V. J. *J. Am. Chem. Soc.* **1995**, *117*, 5156. (d) Grigg, R.; Monteith, M.; Sridharan, V.; Terrier, C. *Tetrahedron* **1998**, *54*, 3885.
5. (a) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev*. **1999**, *28*, 199. (b) Meguro, M.; Yamamoto, Y. *J. Org. Chem*. **1999**, *64*, 694.
6. (a) Xiao, W. J.; Vasapollo, G.; Alper, H. *J. Org. Chem*. **1998**, *63*, 2609. (b) Kimura, M.; Tanaka, S.; Tamaru, Y. *J. Org. Chem*. **1995**, *60*, 3764. (c) Ma, S.; Shi, Z.; Yu, Z. *Tetrahedron Lett*. **1999**, *40*, 2393. (d) Hashmi, A. S. K.; Ruppert, T. L.; Knöfel, T.; Bats, J. W. *J. Org. Chem*. **1997**, *62*, 7295. (e) Ogawa, A.; Kawakami, J.; Sonoda, N.; Hirao, T. *J. Org. Chem*. **1996**, *61*, 4161.
7. (a) Bäckvall, J. E.; Jonasson, C. *Tetrahedron Lett*. **1997**, *38*, 291. (b) Jonasson, C.; Bäckvall, J. E. *Tetrahedron Lett*. **1998**, *39*, 3601. (c) Jonasson, C.; Bäckvall, J. E. unpublished results.
8. (a) The mono- and non-substituted allenic tosylamides were prepared from a copper(I)-mediated reaction of 2-cyanoethylzinc iodide and the corresponding propargylic tosylate. 2-Cyanoethylzinc iodide could be generated from 3-iodopropionitrile and activated zinc. The organozinc iodides were then transmetallated into copper compounds of the type RCu(CN)ZnI, using the soluble salt CuCN·2LiCl[8b,c] and subsequently treated with the appropriate tosylated propargylic alcohol[8d] to give the corresponding allenic nitriles. The disubstituted allenic nitriles were prepared according to literature procedures.[8e] The resulting allenic nitriles were then reduced with $LiAlH_4$ and tosylated[8f] to give the *N*-tosylamides **1**, **3**, **5**, **7**, **9** and **11**. (b) Yeh, M.-C. P.; Knochel, P. *Tetrahedron Lett*. **1988**, *29*, 2395. (c) Yeh, M.-C. P.; Sheu, B.-A.; Fu, H.-W.; Tau, S.-I.; Chuang, L.-W. *J. Am. Chem. Soc.* **1993**, *115*, 5941. (d) Dunn, M. J.; Jackson R. F. W.; Pietruszka, J.; Turner, D. *J. Org. Chem.* **1995**, *60*, 2210. (e) Mori, K.; Nukada, T.; Ebata, T. *Tetrahedron* **1981**, *37*, 1343. (f) Shaw, R. W.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1* **1994,** 3549.
9. Ref 1a, p. 166.
10. (a) Karstens, W. F. J.; Rutjes, F. P. J. T.; Hiemstra, H. *Tetrahedron Lett*. **1997**, *38*, 6275. (b) Karstens, W. F. J.; Stol, M.; Rutjes, F. P. J. T.; Hiemstra, H. *Synlett* **1998**, 1126.
11. Selected NMR data: 2-(1-Bromo-2-methyl-1-propenyl)-1-(toluene-4-sulfonyl)pyrrolidine (**8**) ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.69 (d, *J*=8.4 Hz, 2H), 7.27 (m, 2H), 4.87 (dd, *J*=7.9, 6.2 Hz, 1H), 3.64 (m, 1H), 3.39 (ddd, *J*=10.2, 8.7, 6.0 Hz, 1H), 2.42 (s, 3H), 1.93 (s, 3H), 1.87–2.10 (m, 3H), 1.80 (s, 3H), 1.64 (m, 1H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 142.9, 136.6, 133.4, 129.1, 127.2, 124.3, 60.4, 49.3, 32.4, 25.8, 25.2, 21.6, 21.1.
12. Compound **18** was probably formed via a palladium-catalyzed intramolecular hydroamination reaction; see: Meguro, M.; Yamamoto, Y. *Tetrahedron Lett*. **1998**, *39*, 5421.