482 *J. Org. Chem.* **1995**, *60*, 482−483

Enantioselective, Palladium-Catalyzed Hetero- and Carboannulation of Allenes Using Functionally-Substituted Aryl and Vinylic Iodides

Richard C. Larock* and John M. Zenner

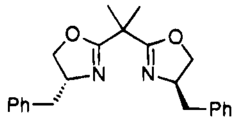
Department of Chemistry, Iowa State University, Ames, Iowa 50011

Received October 27, 1994

Enantioselective, palladium-catalyzed allylic substitutions have recently been shown to be a useful means of forming new chiral carbon−carbon and carbon−nitrogen bonds.[1] Most work in this area has focused on the development of improved chiral ligands for intermolecular, nucleophilic substitution of the symmetrical 1,3-diphenyl-π-allylpalladium system.[2] Relatively little work has been done on more complicated, unsymmetrical systems, and there appear to be only two examples of asymmetric induction in intramolecular π-allylpalladium displacements.[3]

Our recent success in the regioselective, palladium-catalyzed hetero- and carboannulation of allenes using functionally-substituted aryl[4] and vinylic[5] halides encouraged us to examine asymmetric versions of these annulation processes. We wish now to report the highest enantioselectivities yet observed for any palladium-catalyzed, intramolecular allylic substitution reactions.

A variety of reaction conditions have been examined for the model reaction of *N*-tosyl-2-iodoaniline and 1,2-undecadiene (see entry 1, Table 1). Asymmetric induction can best be effected in the presence of 1.2 ion equiv of the silver salt Ag_3PO_4 using DMF as the solvent. After optimization of the silver salt and the solvent, a variety of chiral ligands were employed in this reaction,[1a,c−e,2e−k] including several which have not previously been used in palladium-catalyzed, asymmetric displacement.[6] Best results were obtained using the bisoxazoline ligands developed by Pfaltz and others,[2b−d] particularly compound **1**. The following observations have been made with regard to ligand structure. Those ligands which when coordinated to palladium form a 6-membered ring lead to products of higher ee than those which form a 5-membered ring, and more electron-rich ligands tend to give higher asymmetric induction. The highest enantiomeric excesses were obtained using 1 equiv of the aryl or vinylic iodide, 2 equiv of the allene, 1.2 silver ion equiv of Ag_3PO_4, 5 or 10% $Pd(OAc)_2$ or $Pd(dba)_2$, and 5 or 10% of ligand **1** as catalyst, in DMF at a temperature low enough to achieve asymmetric induction, while still allowing the reaction to go to completion in a reasonable amount of time (Table 1).

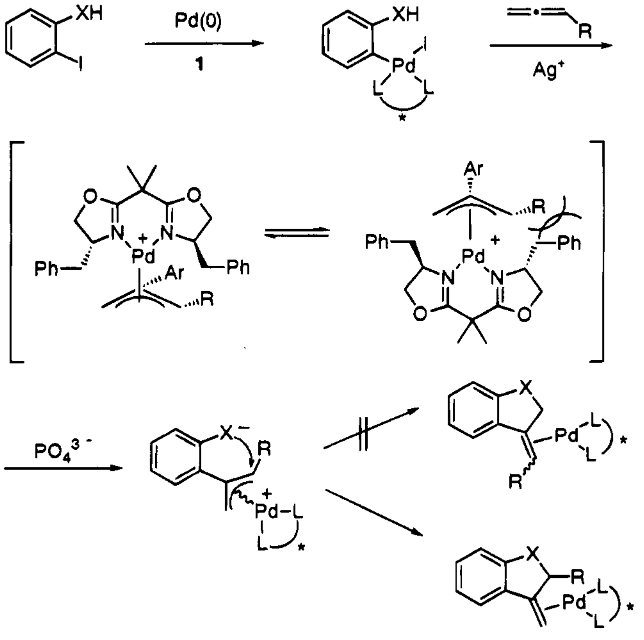


1

The regioselectivity of this annulation process is generally quite high, often better than that observed under our previously reported conditions using PPh_3 as the ligand.[4,5] The reaction of aryl or vinylic iodides and 1,2-undecadiene forms five- or six-membered ring products by nucleophilic attack exclusively at the more substituted end of the π-allylpalladium intermediate (entries 1, 4, 5 and 7). The regioselectivity of attack at the more sterically congested π-allyl terminus may be explained on the basis of two electronic factors: (1) the net positive charge on the π-allylpalladium species being more localized at the alkyl-substituted terminus, and (2) the observation that electron-rich palladium(0)-ligand complexes favor coordination to the more electron-deficient, less substituted, double bond of the observed product.[7] For these reasons, the transition state leading to the observed product may be favored.

The mechanism of this reaction has been outlined in our earlier publication.[4] The addition of aryl or vinylic palladium compounds to allenes is known to produce π-allylpalladium compounds which readily undergo intramolecular nucleophilic substitution.[4,5] In the presence

Scheme 1



---

(1) (a) Trost, B. M.; Strege, P. E. *J. Am. Chem. Soc.* **1977**, *99*, 1649−1651. (b) Fiaud, J. C.; Legros, J. Y. *J. Org. Chem.* **1990**, *55*, 4840−4846. (c) Yamaguchi, M.; Shima, T.; Yamagishi, T.; Hida, M. *Tetrahedron: Asymmetry* **1991**, *2*, 663−666. (d) von Matt, P.; Loiseleur, O.; Koch, G.; Pfaltz, A.; Lefeber, C.; Feucht, T.; Helmchen, G. *Tetrahedron: Asymmetry* **1994**, *5*, 573−584. (e) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1994**, *116*, 4089−4090.

(2) (a) Brunner, H. In *Topics in Stereochemistry*; Eliel, E., Wilen, S. H., Eds; John Wiley and Sons: New York, 1988; Vol. 18, pp 129−248. (b) Muller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232−240. (c) Helmchen, G.; Krotz, A.; Ganz, K. T.; Hansen, D. *Synlett* **1991**, 257−258. (d) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005−6008. (e) Leutenegger, U.; Umbricht, G.; Fahrni, C.; von Matt, P.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143−2156. (f) von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566−568. (g) Dawson, G. J.; Frost, C. G.; Williams J. M. J.; Coote, S. J. *Tetrahedron Lett.* **1993**, *34*, 3149−3150. (h) Togni, A. *Tetrahedron: Asymmetry* **1991**, *2*, 683−690. (i) Bovens, M.; Togni, A.; Venanzi, L. M. *J. Organomet. Chem.* **1993**, *451*, C28-C31. (j) Brenchley, G.; Merifield, E.; Wills, M.; Fedouloff, M. *Tetrahedron Lett.* **1994**, *35*, 2791−2794. (k) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062−4066.

(3) (a) Yamamoto, K.; Tsuji, J. *Tetrahedron Lett.* **1982**, *23*, 3089−3092. (b) Genet, J. P.; Grisoni, S. *Tetrahedron Lett.* **1988**, 29, 4543−4546.

(4) Larock, R. C.; Berrios-Pena, N. G.; Fried, C. A. *J. Org. Chem.* **1991**, *56*, 2615−2617.

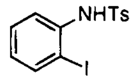
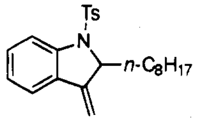
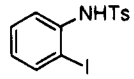
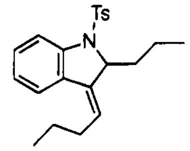
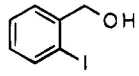
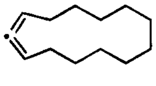
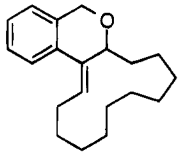
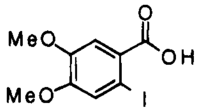
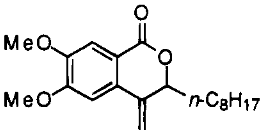
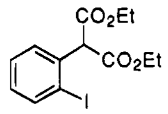
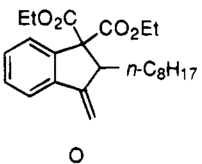
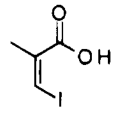
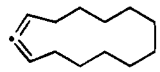
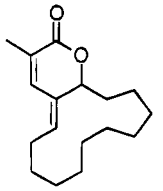
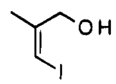
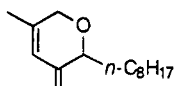
(5) Larock, R. C.; He, Y.; Leong, W. W. Manuscript in preparation.

(6) (a) Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518−8519. (b) Uozum, V.; Hayashi, T. *Tetrahedron Lett.* **1993**, *34*, 2335−2338. (c) Nishiyama, H.; Sakaguchi, H.; Nakamura, T.; Horihata, M.; Kondo, M.; Itoh, K. *Organometallics* **1989**, *8*, 846−848.

(7) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033−2046.

0022-3263/95/1960-0482$09.00/0

Table 1. Palladium-Catalyzed, Asymmetric Annulation of Allenes Using Chiral Bisoxazoline Ligand 1[a]

entry	organic iodide	allene	catalyst[b]	temp. (°C)	time (d)	product	% isolated yield	% e.e.[c]	$[\alpha]_D$
1		$n\text{-}C_8H_{17}CH{=}C{=}CH_2$	A	90	1		94	82	-19.4°
2		$n\text{-}C_3H_7CH{=}C{=}CH\text{-}n\text{-}C_3H_7$	A	90	1		95	80	-32.5°
3			A	80	3		29	77	-148.9°
4		$n\text{-}C_8H_{17}CH{=}C{=}CH_2$	B	40	6		78	71	-52.6°
5		$n\text{-}C_8H_{17}CH{=}C{=}CH_2$	C	90	3		67	75	+48.8°
6			D	40	3		52	61	-202.6°
7		$n\text{-}C_8H_{17}CH{=}C{=}CH_2$	A	80	4		70	79	-11.5°

[a] All reactions were run in the presence of 1.2 silver ion equiv of Ag_3PO_4 in DMF (1.0 mL/0.50 mmol of organic iodide). [b] Catalyst A: 5 mol % $Pd(OAc)_2$, 10 mol % ligand 1. Catalyst B: 5 mol % $Pd(dba)_2$, 5 mol % ligand 1. Catalyst C: 10 mol % $Pd(dba)_2$, 10 mol % ligand 1. Catalyst D: 5 mol % $(Pd(dba)_2$, 10 mol % ligand 1. [c] The ee of all products was determined using the chiral NMR shift reagent $Eu(hfc)_3$.

of Ag^+, the iodide is removed as AgI, allowing the formation of a 16 electron Pd intermediate to which the bidentate chiral ligand is coordinated (Scheme 1).[8] This system then resembles those investigated by Bosnich in which interconversion between diastereomers is accomplished via a $\pi{-}\sigma{-}\pi$ process.[7,9] This interconversion is known to occur rapidly in terminal π-allylpalladium species, and this is no doubt of paramount importance to eventual enantiodiscrimination.[9] Bosnich's work has suggested that the major π-allylpalladium intermediate gives rise to the major enantiomer observed. In light of this, we speculate that steric interactions between the benzyl groups of the ligand and the terminal alkyl substituent of the π-allylpalladium intermediate lead to a preference for one diastereomer over the other, which then goes on to form the major observed enantiomer. Factors leading to enantioselectivity in the symmetrical π-allylpalladium system have been well described elsewhere.[10] We are presently attempting to establish the absolute configurations of the annulation products to elucidate the actual mechanism at work in these types of systems. Full details of this continuing study will be reported in due course.

Acknowledgment. We gratefully acknowledge the U.S. Department of Education for financial support in the form of a GAANN fellowship and Prof. Andreas Pfaltz for his generous contribution of chiral bisoxazoline ligands. In addition, we thank the following for contributing chiral ligands used in this study: Prof. T. Hayashi, Prof. H. Nishiyama, Prof. B. M. Trost, Prof. L. M. Vananzi, Prof. A. Togni, Prof. M. Wills, and Hoffman LaRoche.

Supplementary Material Available: General experimental procedure and spectral data for all products (11 pages).

JO941796L

---

(8) Sato, Y.; Sodeoka, M.; Shibasaki, M. *Chem. Lett.* **1990**, 1953–1954.

(9) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046–2053.

(10) (a) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339–345. (b) Reiser, O. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 547–549. (c) Sprinz, J.; Kiefer, M.; Helmchen, G.; Reggelin, M.; Huttner, G.; Walter, O.; Zsolnai, L. *Tetrahedron Lett.* **1994**, *35*, 1523–1526.