ORGANIC LETTERS

1999
Vol. 1, No. 1
165−167

Palladium-Catalyzed Highly Diastereoselective Cyclic Carbopalladation–Carbonylative Esterification Tandem Reaction of Iododienes and Iodoarylalkenes†

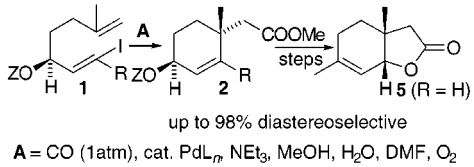
Christophe Copéret and Ei-ichi Negishi*

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907

negishi@purdue.edu

Received May 3, 1999

ABSTRACT



up to 98% diastereoselective

A = CO (1atm), cat. PdL_n, NEt_3, MeOH, H_2O, DMF, O_2

Pd-catalyzed reaction of iododienes and iodoarylalkenes represented by 1, 8, and 10 under 1 atm of CO and a small amount of O_2 in the presence of a base, e.g., NEt_3, as well as MeOH and H_2O in DMF can undergo a highly diastereoselective cyclic carbopalladation–carbonylative esterification tandem process (Type II C–Pd process) to give in high yields the corresponding ester-containing cyclization products, e.g., 2, 9, and 11, in as high as 98% diastereoselectivity.

Herein reported is a diastereoselective cyclic carbopalladation−esterification tandem process[1] displaying 1,4-chirality transfer in as high as 98% diastereoselectivity, as demonstrated by the transformations (**1** → **2**) shown in Scheme 1. Coupled with various known asymmetric syntheses of allylic alcohols,[2] this reaction promises to provide a stereocontrolled route to various cyclic natural products, as exemplified by the conversion of **2a** into the Colvin−Raphael lactone[3] (**5**), which has served as an intermediate for trichodermin[3] (**6**) and trichodiene[4] (**7**) (Scheme 2).

The cyclic carbopalladation−carbonylative esterification was discovered by us[5] as an unwanted side reaction of cyclic acylpalladation of alkynes. This process, termed Type II C−Pd process[1a] hereafter to distinguish it from the more conventional cyclic carbopalladation terminated by the Heck alkene substitution (Type I C−Pd process), has since been shown to be a useful method for terminating cascade cyclic carbopalladation.[6] The Type II C−Pd process has also been applied to the cyclization of iododienes and iodooligoenes.[7] With iodoalkenes, at least one asymmetric carbon center is generated. Although chirality transfer in the Type I C−Pd

† This paper is dedicated to Professor R. Keese of the University of Bern on the occasion of his 65th birthday.

(1) (a) For background information on cyclic carbopalladation, see: Negishi, E.; Copéret, C.; Ma, S.; Liou, S. Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365 and references therein. (b) For some examples of diastereoselective cyclic carbopalladation reactions of 1,1-disubstituted alkenes without the involvement of CO, see: Overman, L. E. *Pure Appl. Chem.* **1994**, *66*, 1423.

(2) See, for example: (a) Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867. (b) Brown, H. C.; Ramachandran, P. V. *Pure Appl. Chem.* **1991**, *63*, 307. (c) Brown, H. C.; Ramachandran, P. V. *Acc. Chem. Res.* **1992**, *25*, 16. (d) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738.

(3) (a) Colvin, E. W.; Raphael, R. A.; Roberts, J. S. *Chem. Commun.* **1971**, 858. (b) Colvin, E. W.; Malchenko, S.; Raphael, R. A.; Roberts, J. S. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1989.

(4) (a) Welch, S. C.; Rao, A. S. C. P.; Wong, R. Y. *Synth. Commun.* **1976**, *6*, 443. (b) Welch, S. C.; Gibbs, W. R. *Synth. Commun.* **1976**, *6*, 485.

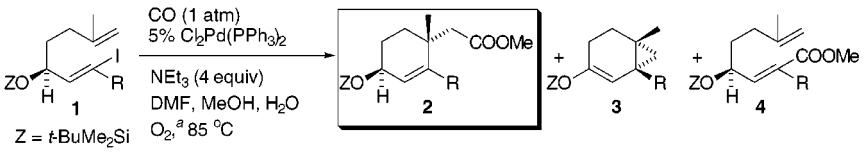
(5) Zhang, Y.; Negishi, E. *J. Am. Chem. Soc.* **1989**, *111*, 3454.

(6) (a) Sugihara, T.; Copéret, C.; Owczarczyk, Z.; Harring, L. S.; Negishi, E. *J. Am. Chem. Soc.* **1994**, *116*, 7923. (b) Copéret, C.; Sugihara, T.; Negishi, E. *Tetrahedron Lett.* **1995**, *36*, 1771. (c) Copéret, C.; Ma, S.; Sugihara, T.; Negishi, E. *Tetrahedron* **1996**, *52*, 11529.

(7) (a) Grigg, R.; Kennewell, P.; Teasdale, A. J. *Tetrahedron Lett.* **1992**, *33*, 7789. (b) Grigg, R.; Sridharan, V. *Tetrahedron Lett.* **1993**, *34*, 7471. (c) Brown, A.; Grigg, R.; Ravishankar, T.; Thornton-Pett, M. *Tetrahedron Lett.* **1994**, *35*, 2753. (d) Grigg, R.; Redpath, J.; Sridharan, V.; Wilson, D. *Tetrahedron Lett.* **1994**, *35*, 4429. (e) Negishi, E.; Ma, S.; Amanfu, J.; Copéret, C.; Miller, J. A.; Tour, J. M. *J. Am. Chem. Soc.* **1996**, *118*, 5919.

10.1021/ol9900663 CCC: $18.00
Published on Web 05/25/1999

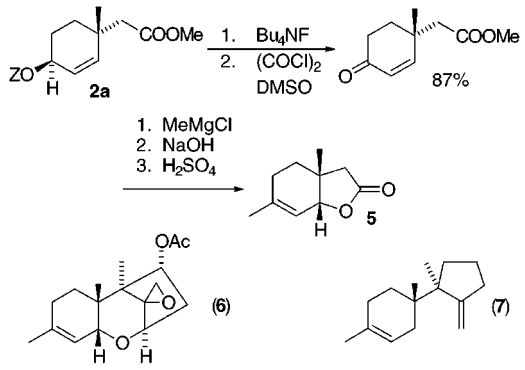
Scheme 1



Entry	R	Product yield (diastereoselectivity), % 2[b]	3	4
a	H	91 (94)	<2	<3
b	*n*-Bu	84 (95)	<2	5
c	$-(CH_2)_2CH{=}CH_2$	65 (85)	<2	<2
d	$-(CH_2)_2CH{=}CMe_2$	80 (93)	<2	<2

[a] After mixing all compounds, the reaction mixture was exposed to air for 20-30 seconds, flushed again with CO, and stirred until the mixture turned black over 0.5-1 h. [b] The number in parentheses indicates diastereoselectivity.

Scheme 2



process mainly in conjunction with the formation of spirocycles has been investigated,[1b,8] little or nothing has been investigated regarding chirality transfer in the Type II C−Pd process.

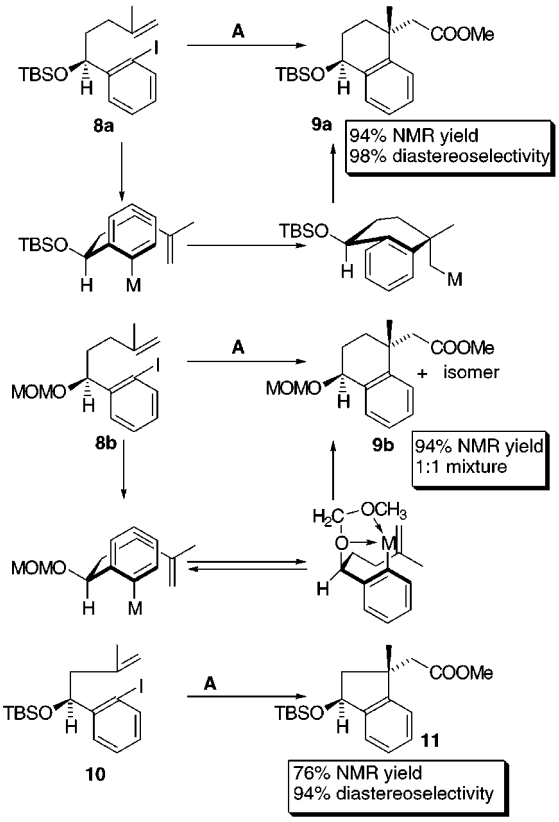
The following findings pertinent to observing high-yielding and highly diastereoselective Type II C−Pd processes are noteworthy. (1) As reported earlier,[7e] favorable Type II C−Pd processes have been observed in a medium consisting of 1:2:0.1 MeOH−DMF−H_2O, and it is essential to heat the reaction mixture at reflux to minimize premature esterification, i.e., the formation of **4** in Scheme 1. (2) Although Pd-induced cyclopropanation[5,9] can be a significant side reaction,[7e] none of the substrates shown in Scheme 1 gave cyclopropanation products in detectable yields under the indicated conditions. (3) Selection of the hydroxy protecting group is also critically important. Thus, for example, the reaction of **8a** protected with a bulky *t*-BuMe_2Si (TBS hereafter) group leads to the formation of **9a** in 94% NMR yield in 98% diastereoselectivity. The same sense of chirality transfer has also been observed in the formation of a five-membered ring (**10** → **11**). On the other hand, the corresponding reaction of **8b** protected with a CH_3OCH_2 (MOM) group gives a 1:1 diastereomeric mixture in 94% NMR yield. These results can be rationalized on the basis of the following assumptions. (i) The reaction must proceed via a boat or boatlike transition state.[1b] (ii) For carbopalladation, which may be thought to proceed by a concerted process, the C−Pd bond and the interacting C−C π-bond must become essentially coplanar. Even simple molecular models readily indicate that the proposed boatlike conformation would be by far the most favorable one for satisfying the second assumption. (iii) Whereas the bulky TBSO group strongly favors the pseudoequatorial orientation, this tendency is counterbalanced by the chelation effect favoring the axial orientation of the MOM group in the latter case (Scheme 3). Although the stereochemistry assigned to **2**, **9**, and **11** was consistent with both their NMR spectral data and the interpretation presented above, an unequivocal establishment of the stereochemistry depended on the X-ray crystallographic analysis of the *p*-nitrobenzoyl derivative of **2b** (R = *n*-Bu).

It is noteworthy that the diastereoselectivity also significantly depends on the method of termination of carbopalladation. Thus, the Pd-catalyzed bicyclization reaction of **1c** in the absence of CO and MeOH gave a 2:1 mixture of *cis*- and *trans*-**12** along with a minor amount (<3−5%) of **13** (Scheme 4). The observed low diastereoselectivity may also be due, in part, to the presence of a homoallyl group that can exert a chelation effect. Clearly, further studies are necessary to clarify these intricate stereochemical details. Nonetheless, it does appear that the carbonylative trapping of organopalladium intermediates (Type II C−Pd process) offers favorable features which may not be shared by the more usual Type I C−Pd process. It should also be pointed out that, in sharp contrast with the previously developed cyclic acylpalladation reactions,[7e,10] the Type II C−Pd reaction requires alkynes and 1,1-disubstituted alkenes. Thus, for example, the reaction of **14** under the conditions that are satisfactory for the Type II C−Pd reaction of **1**, **8**, and **10**,

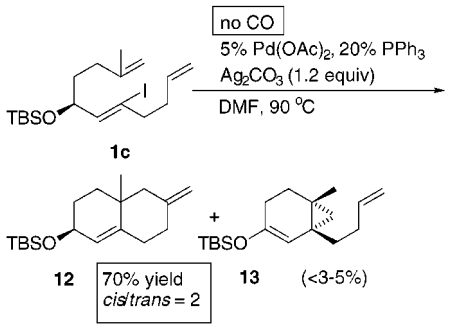
(8) (a) Abelman, M. M.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 2328. (b) Abelman, M. M.; Overman, L. E.; Tran, V. D. *J. Am. Chem. Soc.* **1990**, *112*, 6959. (c) Overman, L. E.; Ricca, D. J.; Tran, V. D. *J. Am. Chem. Soc.* **1993**, *115*, 2042.

(9) Owczarczyk, Z.; Lamaty, F.; Vawter, E. J.; Negishi, E. *J. Am. Chem. Soc.* **1992**, *114*. 10091.

Scheme 3

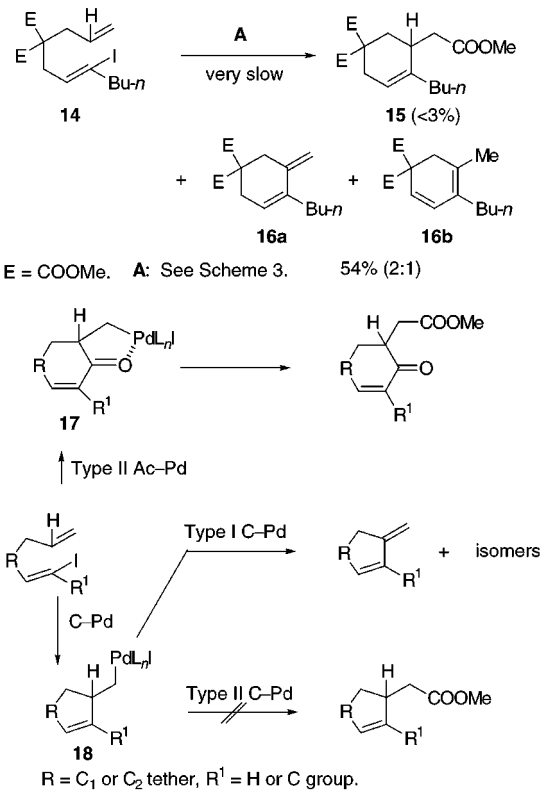


Scheme 4



i.e., condition **A** in Scheme 3, little or none of the desired product **15** was obtained, the only products obtained in 54% combined yield being a roughly 2:1 mixture of the cyclic Heck reaction products (Type I C−Pd) **16a** and **16b**[1] (Scheme 5). It appears reasonable to propose that, in the previously developed cyclic acylpalladation−carbonylative esterification tandem process (Type II Ac−Pd), cyclized organopalladium intermediates **17** are stabilized against dehydropalladation through chelation with the carbonyl

Scheme 5



group. This effect is absent in **18** formed via cyclic carbopalladation (Scheme 5).

With **2a** (R = H) in hand, we converted it into the Colvin−Raphael lactone **5**[3,4] in 44% overall yield by (i) treatment with Bu_4NF followed by oxidation with $(COCl)_2$ and DMSO and (ii) addition of MeMgCl to the ketone followed by lactonization and elimination according to the literature procedure[3,4] (Scheme 2).

The required iodoallyl alcohols **1** are readily preparable via reduction of the corresponding propargylic alcohols with $LiAlH_4$ and NaOMe[11] followed by iodinolysis. Since propargyl alcohols are enantioselectively preparable by known methods,[2] the overall process can, in principle, be enantioselective.

Acknowledgment. We thank the National Institutes of Health (GM 36792) for support of this research, Johnson-Matthey for palladium compounds, and Purdue University for providing a Graduate Fellowship to C.C. We also thank Dr. P. Fanwick of our department for X-ray analytical service.

Supporting Information Available: Experimental procedures and spectroscopic data for compounds **1a**−**d**, **8a**,**b**, and **10** and crystallographic data for the *p*-nitrobenzoyl derivative of **18e**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL9900663

(10) (a) Tour, J. M.; Negishi, E. *J. Am. Chem. Soc.* **1985**, *107*, 8289. (b) Negishi, E.; Wu, G.; Tour, J. M. *Tetrahedron Lett.* **1988**, *29*, 6745. (c) Negishi, E.; Copéret, C.; Ma, S.; Mita, T.; Sugihara, T.; Tour, J. M. *J. Am. Chem. Soc.* **1996**, *118*, 5904.

(11) Corey, E. J.; Katzenellenbogen, J. A.; Posner, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 4245.