ORGANIC LETTERS

2007
Vol. 9, No. 18
3527−3529

Highly Regioselective Synthesis of Indene Derivatives Including an Allene Functional Group via Pd/C-Catalyzed Cyclization Reaction in Air

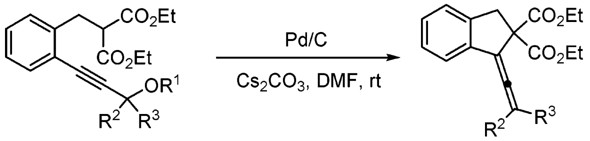
Hai-Peng Bi,[†] Xue-Yuan Liu,[†] Fa-Rong Gou,[†] Li-Na Guo,[†] Xin-Hua Duan,[†] and Yong-Min Liang*,[†,‡]

State Key Laboratory of Applied Organic Chemistry, Lanzhou University, and State Key Laboratory of Solid Lubrication, Lanzhou Institute of Chemical Physics, Chinese Academy of Science, Lanzhou 730000, People's Republic of China

liangym@lzu.edu.cn

Received June 12, 2007

ABSTRACT



Indene derivatives including an allene functional group are readily prepared in moderate to excellent yields with high regioselectivity under very mild reaction conditions by the Pd/C-catalyzed reaction of propargylic compounds. The resulting products can be further elaborated using Pd-catalyzed annulation reactions.

Allenes have received considerable attention in recent years.[1−3] The interesting reactivity of allenes originates mainly from their unique strained structure, and thus continuous efforts have been made to construct the 1,2-dienic moieties. Allenes are usually prepared by one of the following methods: (1) elimination of substituted alkenyl triflates/halides or allylic halides;[4] (2) reductive elimination of two vicinal halogen atoms from 2,3-dibromoalkenes;[5] (3) addition of organometallic reagents or metal hydrides to propargylic halides and analogues;[6] (4) rearrangement of acetylenic systems;[7] (5) reaction of 1,1-dihalocyclopropanes with MeLi;[8,9] (6) addition of organolithiums to vinylacetylenes;[10] and (7) coupling reaction of allenic metallic reagents with organohalides.[11]

To the best of our knowledge, there is no report about the synthesis of allenyl indene derivatives.

[†] Lanzhou University.

[‡] Lanzhou Institute of Chemical Physics.

(1) (a) *The Chemistry of the Allenes*; Landor, S. R., Ed.; Academic: London, 1982; Vol. 1. (b) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; Vols. 1 and 2. (c) Tsuji, J. *Topics in Organometallic Chemistry*; Springer-Verlag: Berlin, Heidelberg, 2005.

(2) (a) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (b) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12. (c) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (d) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196. (e) Reissig, H.-U.; Schade, W.; Amombo, M. O.; Pulz, R.; Hausherr, A. *Pure Appl. Chem.* **2002**, *74*, 175. (f) Ma, S. *Chem. Rev.* **2005**, *105*, 2829.

(3) For some of the most recent typical reactions of allenes, see: (a) Ng, S.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2005**, *127*, 7320. (b) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 74. (c) Lee, P. H.; Lee, K.; Kang, Y. *J. Am. Chem. Soc.* **2006**, *128*, 1139. (d) Lalonde, P. L.; Sherry, B. D.; Kang, E. J.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 2452. (e) Chang, H.-T.; Jayanth, T. T.; Cheng, C.-H. *J. Am. Chem. Soc.* **2007**, *129*, 4166. (f) Banaag, A. R.; Tius, M. A. *J. Am. Chem. Soc.* **2007**, *129*, 5328.

(4) Naso, F.; Ronzini, L. *J. Chem. Soc., Perkin Trans. 1* **1974**, 340.

(5) Bouis, M. *Ann. Chim. Paris* **1928**, *9*, 402.

(6) Brandsma, L.; Arens, J. F. *Rec. Trav. Chim.* **1967**, *86*, 734.

(7) Bowes, C. M.; Montecalvo, D. F.; Sondheimer, F. *Tetrahedron Lett.* **1973**, *34*, 3181.

(8) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; John Wiley & Sons: New York, 1988; p 20.

(9) Jones, W. M.; Grasley, M. H.; Brey, W. S., Jr. *J. Am. Chem Soc.* **1963**, *85*, 2754.

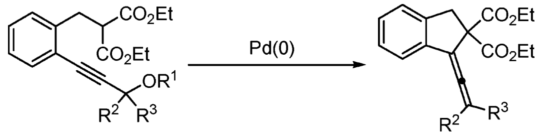
(10) Petrov, A. A.; Kormer, V. A.; Savich, I. G. *Zh. Obshch. Khim.* **1960**, *30*, 3845.

(11) (a) Ruitenberg, K.; Kleijn, H.; Meijer, J.; Oostveen, E. A.; Vermeer, P. *J. Organomet. Chem.* **1982**, *224*, 399. (b) de Graaf, W.; Boersma, J.; van Koten, G.; Elsevier, C. J. *J. Organomet. Chem.* **1989**, *378*, 115. (c) Aidhen, I. S.; Braslau, R. *Synth. Commun.* **1994**, *24*, 789. (d) Badone, D.; Cardamone, R.; Guzzi, U. *Tetrahedron Lett.* **1994**, *35*, 5477. (e) Gillmann, T.; Weeber, T. *Synlett* **1994**, 649.

10.1021/ol071385u CCC: $37.00

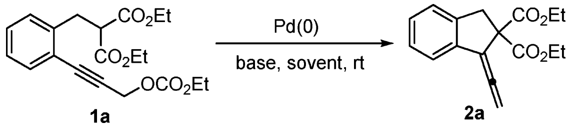
Pd-catalyzed reactions of propargylic compounds have been shown to be extremely effective for the construction of carbon−carbon and carbon−heteroatom bonds.[12] In this process, however, expensive and air-sensitive Pd catalysts, environmentally harmful phosphine ligands, and high temperature were usually used. In connection with our research on carboannulation reactions,[13] we herein report a novel cyclization reaction of propargylic compounds for the synthesis of indene derivatives with high regioselectivity in the presence of a phosphine-free catalyst Pd/C under ambient conditions of temperature and air. An allene functional group was also formed in the product that could be engaged in post-transformations (Scheme 1).

Scheme 1



Our initial study began with the reaction of 3-(2-(2,2-di-(ethoxycarbonyl)ethyl)phenyl)prop-2-ynyl ethyl carbonate (**1a**, 0.5 mmol) and 10% Pd/C (0.05 equiv) in the absence of base in DMF at room temperature in air. The desired product **2a** was isolated in a 69% yield with high regioselectivity (Table 1, entry 1). K_2CO_3 and Cs_2CO_3 were investigated as bases. Cs_2CO_3 provided an excellent yield and short reaction time (entries 2 and 3). Other solvents such as THF and toluene were less effective (entries 4 and 5). Next, the catalytic activity of palladium catalysts was examined (entries 6−9). $Pd(PPh_3)_4$ and $Pd_2(dba)_3$ also showed good results. Other palladium catalyst systems such as $Pd_2(dba)_3$/dppf and $Pd(OAc)_2/PPh_3$ gave poor yields. Finally, the amount of Pd/C was examined (entries 10−12). We found that 0.5 mol % of Pd/C also afforded product in an excellent yield. Although 0.2 mol % of Pd/C proved to be effective, the use of 0.5 mol % of Pd/C realized high yield with good reproducibility. The optimum reaction conditions thus far developed employ 1.0 equiv of **1a**, 2.0 equiv of Cs_2CO_3, and 0.5 mol % of Pd/C in DMF at room temperature in air.

Table 1. Optimization of the Pd-Catalyzed Cyclization of Propargylic Carbonate **1a**[a]

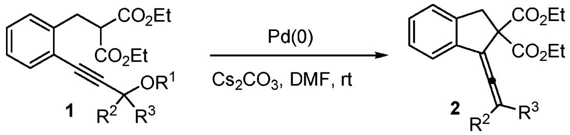


entry	catalyst	base	solvent	Pd (mol %)	time (h)	yield[b] (%)
1	Pd/C		DMF	5	14	69
2	Pd/C	K_2CO_3	DMF	5	3	88
3	Pd/C	Cs_2CO_3	DMF	5	2	96
4	Pd/C	Cs_2CO_3	THF	5	8	43
5	Pd/C	Cs_2CO_3	toluene	5	8	56
6	$Pd(PPh_3)_4$	Cs_2CO_3	DMF	5	2	96[c]
7	$Pd_2(dba)_3$	Cs_2CO_3	DMF	5	2	92[c]
8	$Pd_2(dba)_3$/dppf	Cs_2CO_3	DMF	5	14	24[c]
9	$Pd(OAc)_2/PPh_3$	Cs_2CO_3	DMF	5	14	9[c]
10	Pd/C	Cs_2CO_3	DMF	1	3	96
11	Pd/C	Cs_2CO_3	DMF	0.5	6	96
12	Pd/C	Cs_2CO_3	DMF	0.2	10	64

[a] Reactions were carried out on a 0.5 mmol scale in 3.0 mL of solvent at room temperature in air for the specified period of time with 1.0 equiv of **1a**, 2.0 equiv of base, and [Pd]. [b] Isolated yields. [c] The reactions were run under argon.

Under the optimized reaction conditions above, the breadth and scope of the reaction of substituted secondary and tertiary propargyl substrates were investigated next. Substituted secondary carbonates, having methyl or phenyl substituents, produced high yields of the indene derivatives (Table 2 entries 2−6). Similarly, 2-furyl-substituted propargyl compound **1g** led to desired product **2g** in 80% yield (entry 7).

Table 2. Pd-Catalyzed Cyclization of Propargylic Compounds **1**



entry	1	C[a]	time (h)	2	yield[b] (%)
1	$R^1 = CO_2Et$, $R^2 = H$, $R^3 = H$ **1a**	A	6	**2a**	96
2	$R^1 = CO_2Et$, $R^2 = H$, $R^3 = Me$ **1b**	A	6	**2b**	92
3	$R^1 = CO_2Et$, $R^2 = H$, $R^3 = Ph$ **1c**	A	6	**2c**	89
4	$R^1 = CO_2Et, R^2 = H$, $R^3 = p$-Tol **1d**	A	6	**2d**	91
5	$R^1 = CO_2Et$, $R^2 = H$, $R^3 = p\text{-}ClC_6H_4$ **1e**	A	6	**2e**	95
6	$R^1 = CO_2Et$, $R^2 = H$, $R^3 = p\text{-}BrC_6H_4$ **1f**	A	6	**2f**	93
7	$R^1 = CO_2Et$, $R^2 = H$, $R^3 =$ 2-furyl **1g**	A	6	**2g**	80
8	$R^1 = COMe$, $R^2 = Me$, $R^3 = Me$ **1h**	B	8	**2h**	75
9	$R^1 = COMe$, $R^2 = R^3 = (CH_2)_4$ **1i**	B	10	**2i**	73
10	$R^1 = COMe$, $R^2 = R^3 = (CH_2)_5$ **1j**	B	10	**2j**	78
11	$R^1 = COMe$, $R^2 = Ph$, $R^3 = Ph$ **1k**	B	12	**2k**	66
12	$R^1 = CO_2Me$, $R^2 = R^3 = H$ **1l**	A	6	**2a**	93
13	$R^1 = COMe$, $R^2 = R^3 = H$ **1m**	A	6	**2a**	91
14	$R^1 = COPh$, $R^2 = R^3 = H$ **1n**	A	6	**2a**	86
15	$R^1 = PO(OEt)_2$, $R^2 = R^3 = H$ **1o**	A	4	**2a**	93

[a] Conditions A: **1** (0.5 mmol), Cs_2CO_3 (2.0 equiv), and Pd/C (0.5 mol %) in DMF (3 mL) at room temperature in air. Conditions B: **1** (0.5 mmol), Cs_2CO_3 (2.0 equiv), and $Pd_2(dba)_3$ (5 mol %) in DMF (3 mL) at 100 °C under argon. [b] Isolated yields.

---

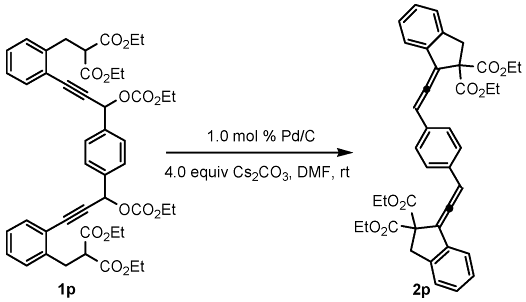
(12) For reviews on palladium-catalyzed reactions of propargylic compounds, see: (a) Tsuji, J. *Acc. Chem. Res.* **1969**, *2*, 144. (b) Tsuji, J.; Mandai. T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2589.

(13) (a) Guo, L.-N.; Duan, X.-H.; Bi, H.-P.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2006**, *71*, 3325. (b) Duan, X.-H.; Guo, L.-N.; Bi, H.-P.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2006**, *8*, 3053. (c) Duan, X.-H.; Guo, L.-N.; Bi, H.-P.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2006**, *8*, 5777. (d) Guo, L.-N.; Duan, X.-H.; Bi, H.-P.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2007**, *72*, 1538−1540. (e) Bi, H.-P.; Guo, L.-N.; Duan, X.-H.; Gou, F. -R.; Huang, S.-H.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2007**, *9*, 397.

The reactions of tertiary propargyl acetates **1h**, **1i**, and **1j** have also been studied. Good yields of the expected products have been obtained in the presence of $Pd_2(dba)_3$ (entries 8−10). Fortunately, 1,1-diaryl-1,2-allene **2k** was also obtained in a moderate yield (entry 11).[14] Pd/C showed poor results in the reactions of tertiary propargyl compounds. Table 2 also shows results of propargyl substrates involving different leaving groups. The reactions of propargyl carbonate **1l**, propargyl acetate **1m**, propargyl benzoate **1n**, and propargyl phosphate **1o** gave the desired products **2a** in excellent yields (entries 12−15).

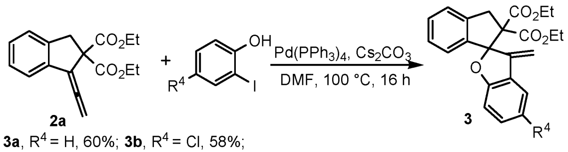
The facility with which this carboannulation process occurs encouraged us to attempt a double cyclization. When compound **1p** was reacted in the presence of 1.0 mol % of Pd/C and 4.0 equiv of Cs_2CO_3 in DMF at room temperature in air for 7 h, the double-annulation product **2p** was formed in 83% yield (Scheme 2).

Scheme 2



An interesting feature of this process is the fact that the indene derivatives produced by carboannulation can be further elaborated by using various Pd-catalyzed processes. For example, the reaction of **2a** with 2-iodophenols afforded the spirocyclic products **3** in moderate yields (Scheme 3).

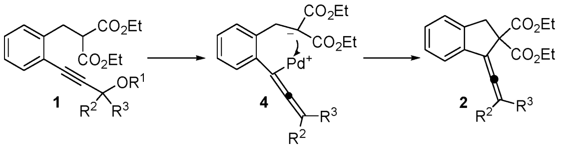
Scheme 3



3a, R^4 = H, 60%; **3b**, R^4 = Cl, 58%;
3c, R^4 = NO_2, 65%; **3d**, R^4 = Ac, 68%

The mechanism shown in Scheme 4 is proposed for this process. It consists of the following key steps: (a) palladium(0) initially promotes decarboxylation of propargylic compound **1** to generate an allenylpalladium complex **4**;[15,16] (b) regioselective intramolecular nucleophilic attack of the carbanion forms product **2**.

Scheme 4



In conclusion, we have developed a novel Pd/C-catalyzed reaction without phosphine ligands for the synthesis of indene derivatives from propargylic compounds with high regioselectivity under ambient conditions of temperature and air. It is noteworthy that lower catalyst loadings were used in this process. Further studies into the chirality of the carboannulation reaction are underway.

Acknowledgment. We thank the NSF (NSF-20621091, NSF-20672049) and the “Hundred Scientist Program” from the Chinese Academy of Sciences for financial support.

Supporting Information Available: Typical experimental procedure and characterization data for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

OL071385U

---

[14] The methods for the synthesis 1,1-diaryl-1,2-allenes seem limited probably due to the steric hindrance and instability; see ref 9.

[15] (a) Yoshida, M.; Morishita, Y.; Fujita, M.; Ihara, M. *Tetrahedron Lett.* **2004**, *45*, 1861. (b) Yoshida, M.; Morishita, Y.; Fujita, M.; Ihara, M. *Tetrahedron* **2005**, *61*, 4381.

[16] Kozawa, Y.; Mori, M. *J. Org. Chem.* **2003**, *68*, 8068.