Pd(0)-Catalyzed Insertion−Cyclization Reaction of 2,3-Allenols with Aryl or Alkenyl Halides. Diastereoselective Synthesis of Highly Optically Active *trans*-2,3-Disubstituted Vinylic Oxiranes

Shengming Ma* and Shimin Zhao

Laboratory of Organometallic Chemistry
Shanghai Institute of Organic Chemistry
*Chinese Academy of Sciences, 354 Fenglin Lu*
Shanghai 200032, P. R. China

Allenes are a class of compounds with unique reactivities due to the existence of the two orthogonal π-bonds, and they have been found to be very useful intermediates in organic synthesis.[1−3] Among our efforts in the area of allene chemistry,[3] we developed an efficient one-step route to butenolides with potential biological activities via the Pd(0)-catalyzed cyclization reaction of 1,2-allenic carboxylic acids with aryl or 1-alkenyl halides.[3c] In this paper we give our results on the corresponding reaction of 2,3-allenols (Scheme 1).

The groups of Olsson[4] and Marshall[5] have shown that the Ag+-catalyzed cyclization reaction of 2,3-allenols affords 2,5-dihydrofuran derivatives, while Tsuji and co-workers[6] reported that the Pd(0)-catalyzed reaction of 2,3-dienols with aryl or alkenyl halides produced β-aryl- or alkenyl-β-methyl-α,β-unsaturated enones via an insertion−β-elimination mechanism (pathway a, Scheme 1). We are interested in the possibility of the Pd(0)-catalyzed reaction of organohalides and 2,3-allenols to form either 2,4-disubstituted-2,5-dihydrofurans (pathway b, Scheme 1) or 2,3-disubstituted vinylic oxiranes (pathway c, Scheme 1).

In our first attempt, we synthesized 1,2-octadien-4-ol[7] and studied its Pd(0)-catalyzed cyclization reaction with PhI under various reaction conditions (Scheme 2). Luckily and surprisingly, we observed in our first try the formation of the *three-membered ring,* i.e., 2-(1′-phenylethenyl)-3-(*n*-butyl)oxirane **3a**, under the conditions for the corresponding cyclization reaction of 1,2-allenyl carboxylic acids (Scheme 2).[3c] The formation of the 2,5-dihydrofuran derivative was not observed, and the Ag+ salt was not required (compare entries 1 with 2 and 3 with 4, Scheme 2). After we screened several different reaction conditions, the stereoselectivity of formation of the two diastereoisomers was increased to 30:1 by using DMF as the solvent (compare entries 1−4 with 5, Scheme 2). The relative configuration of the major isomer was established to be *trans*, as determined from the NOESY spectra of **3e** (entry 5, Table 1).

Using conditions A (entry 5, Scheme 2) as the standard reaction conditions, we studied the Pd(0)-catalyzed highly diastereoselec-

Scheme 1
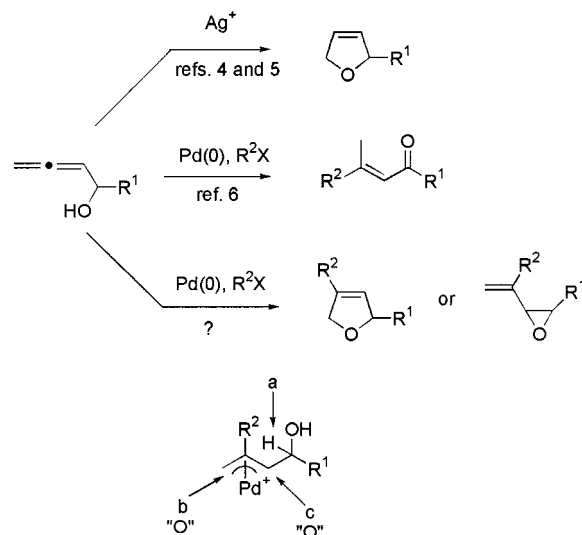
Scheme 2[a]
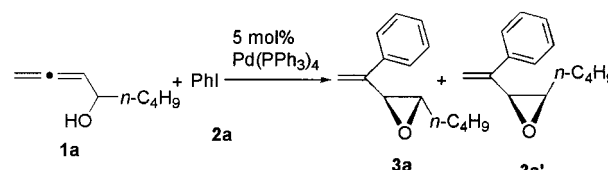
entry	conditions	Yield (%)[a] of **3a** +**3a'**	3a/3a'[a]
1	K$_2$CO$_3$, Ag$_2$CO$_3$, CH$_3$CN, reflux, 18 h	67[b]	18:1
2	K$_2$CO$_3$, CH$_3$CN, reflux, 18 h	62	14:1
3	K$_2$CO$_3$, Ag$_2$CO$_3$, CH$_3$CN, 65 °C, 18 h	33[c]	15:1
4	K$_2$CO$_3$, CH$_3$CN, 65°C, 18 h	32[d]	20:1
5[e]	K$_2$CO$_3$, DMF, 55 °C, 14 h	71[b]	30:1

[a] Determined from 300 MHz ^{1}H NMR spectra of the crude product before separation using CH$_2$Br$_2$ as the internal standard. [b] Isolated yield. [c] 23% of **1a** was recovered. [d] 18% of **1a** was recovered. [e] This set of reaction conditions is defined as conditions A.

tive epoxide formation reaction carefully, and some of our typical examples were listed in Table 1. The following points should be mentioned:

(1) In most cases, the diastereoselectivities of this reaction are fairly high.

(2) Both aryl and 1-alkenyl halides could afford the corresponding products in moderate to good yields (for the reaction with 1-alkenyl iodides, see entries 4 and 11, Table 1).

(3) For the reaction of *p*-bromoiodobenzene, only the carbon−iodine bond reacted, while the carbon−bromine bond remained intact (entries 10 and 15, Table 1).

Optically active epoxides are considered as important synthetic intermediates.[8] Jung et al. studied the rearrangement of vinylic

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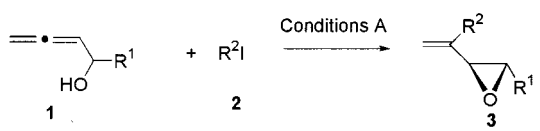
(3) For some of our recent results in allenes, see: (a) Ma, S.; Shi, Z.; Li, L. *J. Org. Chem.* **1998**, *63*, 4522. (b) Ma, S.; Wei, Q. *J. Org. Chem.* **1999**, *64*, 1026. (c) Ma, S.; Shi, Z. *J. Org. Chem.* **1998**, *63*, 6387.

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Table 1. Pd(0)-Catalyzed Insertion−Cyclization Reaction of 2,3-Allenol and Aryl or Alkenyl Halides

entry	**1,** R^1	**2,** R^2	temp (°C)	time (h)	product	yield (%)	dr^a
1	n-C$_4$H$_9$	Ph	55	14	**3a**	71	96/4
2	n-C$_4$H$_9$	p-MeO-C$_6$H$_4$	52	16	**3b**	71	97/3
3	n-C$_4$H$_9$	p-Me-C$_6$H$_4$	53	16	**3c**	70	97/3
4	n-C$_4$H$_9$	E-2-Ph-ethenyl	54	24	**3d**	65	92/8^b
5	n-C$_4$H$_9$	naphthyl	64	48	**3e**	76	96/4
6	Ph	p-Me-C$_6$H$_4$	52	16	**3f**	55	95/5
7	Ph	p-MeO-C$_6$H$_4$	53	16	**3g**	66	92/8^b
8	n-C$_7$H$_{15}$	p-Me-C$_6$H$_4$	54	16	**3h**	88	97/3
9	n-C$_7$H$_{15}$	p-MeO-C$_6$H$_4$	52	14	**3i**	81	99/1
10	n-C$_7$H$_{15}$	p-Br-C$_6$H$_4$	56	48	**3j**	80	98/2
11	n-C$_8$H$_{17}$	E-1-hexenyl	54	20	**3k**	59	c
12	n-C$_8$H$_{17}$	p-Me-C$_6$H$_4$	54	16	**3l**	95	97/3^d
13	n-C$_8$H$_{17}$	p-MeO-C$_6$H$_4$	54	16	**3m**	83	98/2^d
14	n-C$_8$H$_{17}$	Ph	58	18	**3n**	78	98/2
15	n-C$_8$H$_{17}$	p-Br-C$_6$H$_4$	56	18	**3o**	46	99/1^e

^{a} Diastereomer ratio; determined from 300 MHz ^{1}H NMR spectra of the crude products before separation. In all cases, except entries 4 and 7, the two isomers could not be separated via chromatography on silica gel using the conditions described in this paper. ^{b} The minor isomer could be isolated by chromatography on silica gel. ^{c} *Cis* isomer not observed. ^{d} The data were also confirmed by HPLC. ^{e} Determined from 400 MHz ^{1}H NMR spectrum.

epoxides for the synthesis of α-alkyl amino aldehydes and acids.[9] With our protocol for the highly diastereoselective synthesis of *trans*-2,3-disubstituted vinylic epoxides in hand, we utilized the highly enantioselective reduction of 1-undecyn-3-one to make optically active (*R*)-1-undecyn-3-ol,[10] which can be easily converted to the optically active (*R*)-1,2-dodecadien-4-ol (**1b**) (Scheme 3).[7] Its cyclization reaction with (1*E*)-hexenyl iodide, *p*-methylphenyl iodide, and *p*-methoxyphenyl iodide afforded (*R*,*R*)-**3k**, (*R*,*R*)-**3l**, and (*R*,*R*)-**3m**, respectively (Scheme 3).[11]

In conclusion, we have developed a mild, good-yielding, and highly diastereoselective methodology for the synthesis of *trans*-2,3-disubstituted vinylic oxiranes. Using the readily available chiral 2,3-allenols,[12] the corresponding vinylic oxiranes with high ee value can be synthesized.[13−15] Due to the wide synthetic importance of vinylic oxiranes, this methodology will show its utility in organic synthesis.

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(11) %ee was determined by HPLC with a CHIRALPAK AD column (φ 0.46 cm × 25 cm from Daicel Chemical Ind., Ltd.).
(12) According to Corey's method, chiral 2,3-dienols can be synthesized in one step via the reaction of aldehydes with chiral borane reagents. This makes our methodology highly attractive. Corey, E. J.; Yu, C.-M.; Lee, D.-H. *J. Am. Chem. Soc.* **1990**, *112*, 878.

Scheme 3
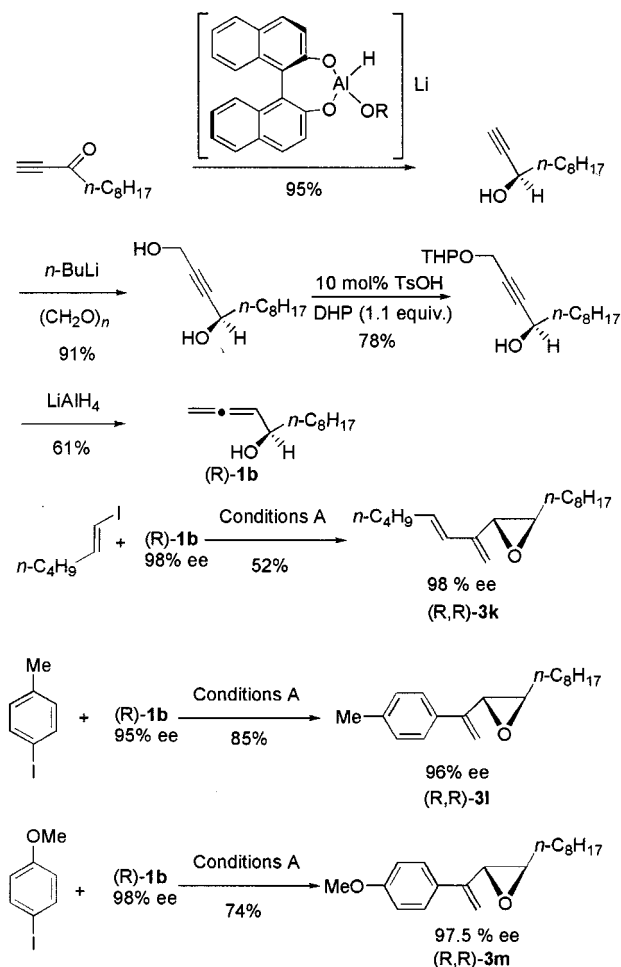
Supporting Information Available: Experimental details and ^{1}H NMR spectra of **3a−o** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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