Tetrahedron Letters,Vol.27,No.20,pp 2211-2214,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

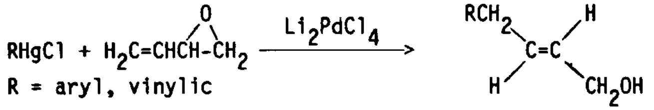
SYNTHESIS OF ALLYLIC ALCOHOLS VIA ORGANOPALLADIUM ADDITIONS TO UNSATURATED EPOXIDES

Richard C. Larock* and Steven J. Ilkka

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

Summary: The reaction of aryl- and vinylpalladium compounds with vinylic and allylic epoxides provides an excellent, high yielding, regio- and stereoselective route to functionally substituted allylic alcohols which can be made catalytic in palladium.

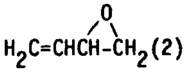
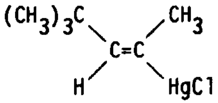
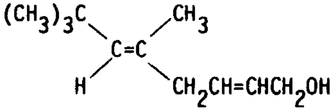
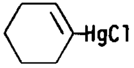
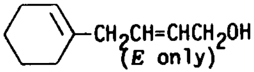
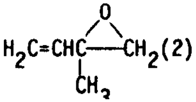
The reaction of vinylic epoxides and organolithium, -magnesium, -copper, and -boron compounds has been reported to afford allylic alcohols. Most of these reactions can accommodate little organic functionality and exhibit low regio- and/or stereoselectivity. Clean 1,4-addition is observed in the Pd(0)-catalyzed opening of vinylic epoxides by stabilized carbanions and the stereoselectivity is high, except with unhindered epoxides such as 3,4-epoxy-1-butene.[1-7] We wish to report procedures for the regio- and stereoselective formation of functionally substituted allylic alcohols via aryl- and vinylpalladation of unsaturated epoxides (eq. 1). Our results are summarized in Table I.

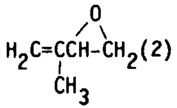
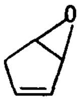
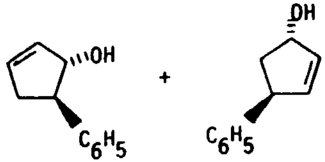
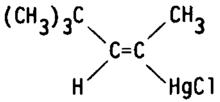
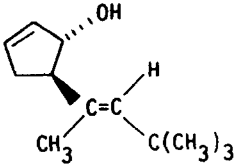
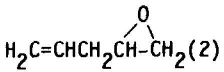


(1)

A thorough examination of a variety of reaction conditions for the reaction of phenylmercuric chloride and 3,4-epoxy-1-butene indicated that best results were obtained by employing 1 equiv of $PdCl_2$, 2 equiv of LiCl, 2 equiv of the epoxide, and running the reaction in 20:1 THF/H_2O at 0°C for a period of time and then warming briefly to room temperature. Under these conditions (Table I, entry 1), a 76% isolated yield of pure *E*-4-phenyl-2-buten-1-ol was obtained. By substituting saturated aqueous NH_4Cl for the water, higher yields could be obtained, but it was observed that the product was an 88:12 mixture of *E* and *Z* isomers (entry 2). If a stereoisomeric mixture of alcohols is acceptable, one can obtain nearly identical results using only 10% Li_2PdCl_4 in the presence of 1 equiv of $CuCl_2$ under an oxygen atmosphere (entry 3). Upon examining the yield and stereochemistry of the stereoselective process as a function of time, it was observed that the initial product consists of an ~ 8:1 mixture of *E* and *Z* isomers typically observed with most other organometallics such as organocopper or -boron reagents, but the product is gradually isomerized under the reaction conditions to the pure *E* isomer. The presence of NH_4Cl or $CuCl_2$ inhibits this isomerization. The reaction of 3,4-epoxy-1-butene and a variety of functionally substituted arylmercurials also gave good results (entries 4-6).

Table I. Synthesis of Allylic Alcohols

entry	organomercurial	unsaturated epoxide (equiv)	Li_2PdCl_4 equiv	reaction conditions[a]	product(s)[b] (*E*/*Z* ratio)[c]	yield, %[d]
	XC_6H_4HgCl				$XC_6H_4CH_2CH{=}CHCH_2OH$	
1	X=H	 $H_2C{=}CHCH\overset{O}{-}CH_2$(2)	1.0	0°C, 10-12h; then 25°C, 2-3h	(*E* only)	76
2			1.0	0°C, 10-12h; then 25°C, 2-3h 5% sat'd NH_4Cl	(88:12 *E*/*Z*)	85, 92
3			0.1	0°C, 10-12h; then 25°C, 2-3h 5% sat'd NH_4Cl	(86:14 *E*/*Z*)	89, 97
4	X = m-HCO		1.0	0°C, 5h	(*E* only)	50
5			0.1	25°C, 8h no H_2O or NH_4Cl	(89:11 *E*/*Z*)	69
6	X = m-NO_2		1.0	0°C, 6h	(*E* only)	61
7			1.0	0°C, 10-12h	 (91:9 *E*/*Z*)	81
8			1.0	0°C, 10-12h no H_2O	(*E* only)	52
9			0.1	0°C, 1-2h; then 25°C, 6-8h 5% sat'd NH_4Cl	(87:13 *E*/*Z*)	80
10			1.0	0°C, 10-12h no H_2O[e]	 (*E* only)	(55)
11	C_6H_5HgCl	 $H_2C{=}CH\underset{CH_3}{C}\overset{O}{-}CH_2$(2)	1.0	0°C, 10-12h; then 25°C, 2-3h	$C_6H_5CH_2CH{=}C(CH_3)CH_2OH$ (45:55 *E*/*Z*)	(74)

12			1.0	0°C, 10-12h; then 25°C, 2-3h 5% sat'd NH_4Cl	(43:57 *E*/*Z*)	95
13			0.1	0°C, 10-12h; then 25°C, 2-3h	(58:42 *E*/*Z*)	70
14		 $H_2C{=}C(CH_3)CH\text{-}CH_2$ (epoxide, O above) (2)	1.0	0°C, 10-12h; 5% sat'd NH_4Cl	$C_6H_5CH_2C(CH_3){=}CHCH_2OH$ (78:22 *E*/*Z*)	51
15		 (5)	1.0	0°C, 10-12h no H_2O	 2 : 1	79
16			1.0	0°C, 10-12h no H_2O		39
17	C_6H_5HgCl	 $H_2C{=}CHCH_2CH\text{-}CH_2$(2)	1.0	0°C, 10-12h 5% sat'd NH_4Cl	$C_6H_5CH_2CH_2CH{=}CHCH_2OH$ (82:18 *E*/*Z*)	68
18			0.1	0°C, 2h; then 25°C, 8h 5% sat'd NH_4Cl	(78:22 *E*/*Z*)	68

---

[a] All reactions were run using $PdCl_2$ (0.25 or 0.025 mmol), LiCl (0.5 or 0.05 mmol), organomercurial (0.25 mmol), 6 ml of tetrahydrofuran and 0.3 ml of water, except when the water was replaced by saturated aqueous NH_4Cl or the water or NH_4Cl were omitted as indicated. When 0.1 equiv of Li_2PdCl_4 was employed, 1 equiv of $CuCl_2$ was added and the reaction was run under 1 atmosphere of oxygen.

[b] All new compounds gave correct ^{13}C and ^1H NMR, IR, and exact mass or combustion analysis data.

[c] Ratio determined by integration of the 300 MHz NMR spectral peaks corresponding to the allylic hydrogens next to oxygen.

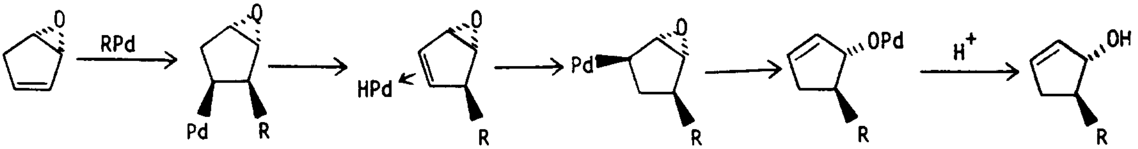
[d] Yield of isolated, purified product (yield determined by gas chromatographic analysis).

[e] The vinylmercurial was dissolved in 10 ml THF and added dropwise to the other reagents over a 2-3h period.

Vinylmercurials also react readily with 3,4-epoxy-1-butene to afford 2,5-dien-1-ols (entries 7-10). Using *E*-4,4-dimethyl-2-chloromercurio-2-pentene and the procedure which proved best for the synthesis of pure *E* aryl-substituted allylic alcohols, a high yield of the anticipated alcohol was observed (entry 7), but it was a 91:9 *E*/*Z* mixture about the newly generated double bond. The pure *E* isomer could be obtained by omitting the water, but the yield also decreased (entry 8). Using vinylmercurials and our previously developed procedure employing catalytic palladium, we are able to get good yields of dienols, but some loss of stereoselectivity is observed (entry 9).

The organopalladation of several unsaturated epoxides other than 3,4-epoxy-1-butene has also been examined. Phenylpalladation of the two monoepoxides of isoprene gave the anticipated trisubstituted olefinic alcohols in reasonable yields, but with low stereoselectivity (entries 11-14). Cyclopentadiene monoepoxide underwent phenylpalladation to afford two trans-substituted allylic alcohols (entry 15), while vinylpalladation of this system afforded exclusively one product (entry 16). Formation of these 1,2-substituted products is unique among the reactions of vinylic epoxides and organometallics. The major products in these reactions appear to arise via the following mechanism (Scheme 1), although we cannot rule out direct epoxide opening. The minor product of entry 15 presumably arises by addition of RPd to the olefin with the opposite regiochemistry and subsequent anti-elimination of palladium and oxygen.

Scheme 1



The remarkable ability of palladium to migrate can be taken advantage of in these reactions by employing allylic epoxides, such as 4,5-epoxy-1-pentene (entries 17, 18). Phenylpalladation, palladium migration, and ring-opening affords the expected product in 68% yield using either stoichiometric or catalytic amounts of palladium.

Acknowledgment. Financial support of this research by the National Institutes of Health (GM 24254) and generous loans of palladium chloride by Johnson Matthey, Inc. are gratefully acknowledged. We also thank Dr. Sudarsanan Varaprath for performing preliminary experiments.

References and Footnotes

(1) Tsuji, J.; Kataoka, H.; Kobayashi, Y. Tetrahedron Lett. 1981, 22, 2575.
(2) Trost, B. M.; Molander, G. A. J. Am. Chem. Soc. 1981, 103, 5969.
(3) Trost, B. M.; Warner, R. W. J. Am. Chem. Soc. 1982, 104, 6112.
(4) Takahashi, T.; Kataoka, H.; Tsuji, J. J. Am. Chem. Soc. 1983, 105, 147.
(5) Wicha, J.; Kabat, M. M. J. Chem. Soc., Chem. Commun. 1983, 985.
(6) Trost, B. M.; Warner, R. W. J. Am. Chem. Soc. 1983, 105, 5940.
(7) Takahashi, T.; Ootake, A.; Tsuji, J. Tetrahedron Lett. 1984, 25, 1921.

(Received in USA 7 February 1986)