Pd/C(en)-catalyzed regioselective hydrogenolysis of terminal epoxides to secondary alcohols

Hironao Sajiki, Kazuyuki Hattori and Kosaku Hirota*

Laboratory of Medicinal Chemistry, Gifu Pharmaceutical University, Mitahora-higashi, Gifu 502-8585, Japan. E-mail: hirota@gifu-pu.ac.jp

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Various terminal epoxides, such as 1,2-epoxyalkanes, glycidyl ethers and glycidol, were hydrogenolyzed to give secondary alcohols with high regioselectivity using a 10% Pd/C–ethylenediamine complex as a catalyst under entirely neutral conditions.

The reductive ring-opening reaction of epoxides, in particular terminal epoxides, to the corresponding alcohols is a transformation of considerable importance in organic synthesis¹ in connection with the recent progress in the development of practical and efficient methods for epoxidation of terminal olefins.² This important transformation has mainly been accomplished by stoichiometric metal hydride or dissolving metal reagents,³ and such reductive cleavage with most reducing agents generally produces a large quantity of metal sludge. Industry in particular requires high yield, high selectivity, sufficient productivity, low cost, safety, operational simplicity, and environmental consciousness among other technical factors.^{2a} In this context, the general advantages associated with heterogeneous catalysts for hydrogenolysis are convenient use and easy separation, production of no sludge and low cost. From investigation of the hydrogenolyses of 1,2-epoxyalkanes, it was found that while the primary alcohol is formed in greater quantity with a Ni catalyst, the secondary alcohol is predominant with a Pd catalyst.^{4,5} However, the Pd catalysts have not been practically applicable since a substantial ratio of the reverse opening primary alcohol is obtained (ca. 35-15%) in most cases.^{4,6} Some improvements were demonstrated by the combination of Pd/C with NaOH4,7 or ammonium formate.6 Although these few reports provide successful results, the basic

or nucleophilic conditions (NaOH or ammonia provided from ammonium formate) often restrict their use.⁷ Thus, there is a need for the development of novel hydrogenation catalysts that can provide high yields and selectivity as entirely heterogeneous catalysts under neutral conditions without any nucleophilic additives. We now disclose a very practical method that overcomes these serious problems.

Recently, we introduced a carbon-supported Pd–ethylenediamine complex [Pd/C(en)] as a catalyst of choice for general chemoselective hydrogenation of reducible functionalities such as olefin, acetylene, nitro, azide, aromatic bromine or benzyl ester moieties, in the presence of *O*-Bn or *N*-*Z* protective groups.⁸ During the course of our studies aimed at developing the Pd/C(en) complexes⁹ as catalysts for selective hydrogenation,^{8,10} we found that 10% Pd/C(en), without any nucleophilic additives, promotes the regioselective reductive ring-opening of terminal epoxides to afford the corresponding secondary alcohols with high yields and selectivity.

Hydrogenolysis of a variety of terminal epoxides in the presence of 10% Pd/C(en) (10% of the weight of the substrate, ca. 2 mol% as Pd metal) as catalyst in MeOH at room temperature was carried out and the results are summarized in Table 1. For example, 1,2-epoxydecane was hydrogenolyzed using 10% Pd/C(en) under 5 atm of hydrogen pressure to afford decan-2-ol as the sole product in 81% yield, whereas employment of 10% Pd/C (Aldrich) under 1 or 5 atm hydrogen pressure resulted in the formation of a mixture of decan-2-ol and decan-1-ol (82:18 or 84:16, Table 1, entries 1–3). The 10% Pd/C(en)-catalyzed hydrogenolysis proceeded with complete regiose-lectivity, although the completion of the reaction required

Table 1 Regioselective hydrogenolysis of terminal epoxides using 10% Pd/C(en) catalysta

	$R \xrightarrow{0} H$	0% Pd/C 0% Pd/C(en) H ₂ (1–5 atm) MeOH	R R 2	н \	+ R	OH 3		
					Viold	Relative yield (%) ^c		
Entry	Substrate	Catalyst	P _{H2} /atm	t/h	$(\%)^{b}$	2	3	
1	$1a R = C_8 H_{17}$	\mathbf{A}^d	1	6	70	82	18	
2	$1a R = C_8 H_{17}$	\mathbf{A}^d	5^e	3	72	84	16	
3	$1a R = C_8 H_{17}$	В	5^e	24	81	100	NDf	
4	$\mathbf{1b} \mathbf{R} = \mathbf{Bu}$	В	5^e	24	75	>95	g	
5	$1c R = HO(CH_2)_8$	В	5^e	32	94	>95	g	
6	$\mathbf{1d} \mathbf{R} = \mathbf{Ph}\mathbf{CH}_{2}\mathbf{CH}_{2}$	В	5^e	24	95	>95	g	
7	$1e R = PhOCH_2$	В	1	24	95	100	NDf	
8	$\mathbf{1f} \mathbf{R} = \mathbf{X} \mathbf{C} \mathbf{H}_2 \mathbf{O} \mathbf{C} \mathbf{H}_2^h$	В	1	24	99	100	ND^{f}	
9	$1g R = CyCH_2OCH_2$	В	1	66	79	100	ND ^f	
10	$1\mathbf{\tilde{h}} \mathbf{R} = \mathbf{HOCH}_2$	В	1	22	89	100	NDf	
11^{i}	$\mathbf{1g} \mathbf{R} = 4 - \mathrm{ClC}_6 \mathrm{H}_4 \mathrm{OCH}_2$	В	1	24	89	100 ^j	$ND^{f,j}$	

^{*a*} Unless otherwise specified, the reaction was carried out using 0.5 mmol of the substrate in methanol (1 ml) with 10% Pd/C(en) (10% of the weight of the substrate) under hydrogen atmosphere (1–5 atm) for the given reaction time. ^{*b*} Isolated yield. ^{*c*} Determined by ¹H NMR. ^{*d*} 10% Pd/C was purchased from Aldrich Co. ^{*e*} Reaction was performed using Ishii Medium Pressure Hydrogenator CHA-E. ^{*f*} Not detectable. ^{*s*} Trace (less than 5%). ^{*h*} X = 2,3-dihydro-1,4-benzodioxan-2-yl. ^{*i*} Reaction was performed in the presence of Et₃N (1.2 equiv. *vs.* substrate) to neutralize the resulting HCl. ^{*j*} Dechlorinated product.

higher hydrogen pressure (5 atm). 1,2-Epoxyhexane, 1,2-epoxydecan-10-ol and 1,2-epoxy-4-phenylbutane were similarly hydrogenolyzed (5 atm) with 10% Pd/C(en) to give the corresponding secondary alcohols in high yields (entries 4–6). The hydrogenolysis of glycidyl ethers and glycidol gave the corresponding secondary alcohols in high yields even under 1 atm hydrogen pressure without the formation of any detectable by-products, such as primary alcohols (entries 7–11). In the case of 4-chlorophenyl glycidyl ether, non-nucleophilic Et₃N (1.2 equiv.) was added to the reaction mixture as a base, which traps HCl generated during the reaction (entry 11). In this reaction the dechlorinated product, 1-phenoxypropan-2-ol, was obtained in 89% yield as the sole product.

The 10% Pd/C(en) catalyst is stable and retains high efficiency during consecutive catalytic cycles. The catalyst could be recovered almost quantitatively following simple filtration of the catalyst, washing with MeOH and Et₂O and drying, and it could be reused at least three times without any decrease in the yield and regioselectivity of the hydrogenolyzed product. One drawback of this method is the inapplicability encountered in the hydrogenolysis of styrene oxide (1 R = Ph). Styrene oxide was converted to a 14:86 mixture of phenethyl alcohol (3 R = Ph) and 1-phenylethylene glycol monomethyl ether **4**, which may be formed *via* Pd/C(en)-catalyzed regioselective solvolysis with MeOH.¹¹



The exact role of the ethylenediamine of the 10% Pd/C(en) complex catalyst in facilitating the regioselective hydrogenolysis of terminal epoxides remains unclear. The catalytic activity of 10% Pd/C(en) to the reductive ring-opening reaction of terminal epoxides was lower than that of 10% Pd/C. It should be noted that higher regioselectivity was observed with the less active catalyst.

As described, the present 10% Pd/C(en)-catalyzed hydrogenolysis of terminal epoxides would provide a new catalytic method for regioselective synthesis of secondary alcohols under entirely neutral and heterogeneous reaction conditions.

Notes and references

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- 11 By use of EtOH instead of MeOH as a solvent, styrene oxide could also be converted to an 87:13 mixture of phenethyl alcohol (**3** R = Ph) and 1-phenylethylene glycol monoethyl ether.

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