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REGIOSELECTIVE REDUCTIVE OPENING OF 2,3-EPOXY ALCOHOL DERIVATIVES WITH LITHIUM BOROHYDRIDE IN A SOLID STATE

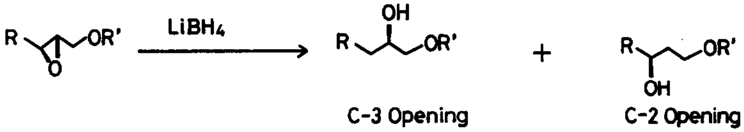
Keisuke Sugita, Makoto Onaka,* and Yusuke Izumi*
Department of Synthetic Chemistry, School of Engineering,
Nagoya University, Chikusa, Nagoya 464, Japan

Summary: 2,3-Epoxy alcohol derivatives were reduced regiospecifically with lithium borohydride in a solid state suspended in hexane to yield the corresponding C-3 opening products.

Regioselective ring opening of 2,3-epoxy alcohols with nucleophiles is an intriguing synthetic subject since optically pure 2,3-epoxy alcohols can be easily synthesized by Sharpless epoxidation process.[1] For ring opening with hydride, recently several groups have reported: Red-Al reduction of 2,3-epoxy alcohols yielded exclusively C-2 opening products,[2] while $LiBH_4$ reduction yielded exclusively C-3 opening products with the aid of titanium tetraisopropoxide.[3] In this $Ti(O^iPr)_4$-$LiBH_4$ system, $Ti(O^iPr)_4$ induces a regioselective attack of the hydride at C-3 by forming the chelate complex with 2,3-epoxy alcohol. In this communication, we would like to report regiospecific $LiBH_4$ reduction of 2,3-epoxy alcohol derivatives without the aid of $Ti(O^iPr)_4$. The results are listed in Table 1.

Typical procedure: $LiBH_4$ (1.5 mmol) was added to a solution of 2,3-epoxy alcohol derivative (0.5 mmol) in 5 ml hexane under argon atmosphere with stirring at room temperature. The reaction was quenched with aq. NH_4Cl, the organic products were extracted with ethyl acetate. The regioisomeric ratios of the products were determined by ^{1}H-NMR (200 MHz) and capillary GLC (PEG-HT, 25 m) after peracetylation of the product.

Interestingly, a suspended $LiBH_4$ in hexane reacted with 1a smoothly at room temperature to give C-3 opening product with higher regioselectivity than a perfectly dissolved $LiBH_4$ in THF (Runs 1, 2). We assumed that the $LiBH_4$ reduction of 2,3-epoxy alcohol might involve initial complexation of $LiBH_4$ with the hydroxyl group and followed by intramolecular hydride reduction,[2-a] so that high regioselectivity for C-3 opening could not be achieved. Converting 1a to epoxy silyl ether 1b, in order to prevent the above initial complexation of $LiBH_4$, improved the regioselectivity for C-3 opening (Run 3). Similarly, the other epoxy silyl ethers 2b and 3b reacted with $LiBH_4$ in hexane to give C-3 opening products with higher regioselectivity than $LiBH_4$-$Ti(O^iPr)_4$ system (compare 6 and 7; 9 and 10).



1a: R=^{n}Pr, R'=H; 1b: R=^{n}Pr, R'=Me_3Si; 1c[4]: R=^{n}Pr, R'=CH_3
2a: R=cyclohexyl, R'=H; 2b: R=cyclohexyl, R'=Me_3Si
3a: R=^{i}Pr, R'=H; 3b: R=^{i}Pr, R'=Me_3Si; 3c: R=^{i}Pr, R'=2-tetrahydropyranyl

Table 1. Reduction of 2,3-epoxy 1-ol derivatives[a)]

Run	Substrate	Reagent	Solvent	Time/h	Yield/%	C-3 : C-2
1	1a	$LiBH_4$	THF	2	70	67 : 33
2	1a	$LiBH_4$	hexane	2	74	87 : 13
3	1b	$LiBH_4$	hexane	2	90	96 : 4
4	1a	$LiBH_4$-$Ti(O^iPr)_4$[b)]	benzene	2	80	98 : 2
5	2a	$LiBH_4$	hexane	24	84	76 : 24
6	2b	$LiBH_4$	hexane	24	82	99 : 1
7	2a	$LiBH_4$-$Ti(O^iPr)_4$[b)]	benzene	7	70	89 : 11
8	3a	$LiBH_4$	hexane	6	62	79 : 21
9	3b	$LiBH_4$	hexane	6	89	85 : 15
10	3c	$LiBH_4$	hexane	96	85	88 : 12
11	3a	$LiBH_4$-$Ti(O^iPr)_4$[b)]	benzene	4	75	69 : 31

a) Reactions were carried out at room temperature.
b) Epoxide (0.5 mmol), $Ti(O^iPr)_4$ (0.75 mmol), $LiBH_4$ (1.5 mmol).

References and Notes

1. T. Katsuki and K. B. Sharpless, J. Am. Chem. Soc., **102**, 5974 (1980).
2. a) J. M. Finan and Y. Kishi, Tetrahedron Lett., **23**, 2719 (1982). b) S. M. Viti,. ibid., **23**, 4541 (1982).
3. L. -X. Dai, B. -L. Lou, Y. -Z. Zhang, and G. -Z. Guo, ibid., **27**, 4343 (1986).
4. Stirring 1c in hexane with $LiBH_4$ for 2h gave C-3 and C-2 opening products in 95 : 5 regioselectivity and 80 % yield. Analysis of the MTPA ester[5] derived from the above products indicated >90 %ee. Since optical purity of 1a was 92 %ee from analysis of the MTPA ester of 1a, the ring opening by $LiBH_4$ completely occurred in an S_N2 fashion.
5. J. A. Dale, D. L. Dull, and H. S. Mosher, J. Org. Chem., **34**, 2543 (1969).

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