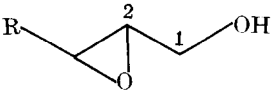
Tetrahedron Letters,Vol.27,No.36,pp 4343-4346,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

REGIOSELECTIVE TITANIUM MEDIATED REDUCTIVE OPENING OF 2,3-EPOXY ALCOHOLS

Li-xin Dai*, Bo-liang Lou, Ying-zhi Zhang, and Guang-zhong Guo
Shanghai Institute of Organic Chemistry, Academia Sinica
345 Lingling Road, Shanghai 200032, China

Summary: Lithium borohydride reduction of 2,3-epoxy alcohols was shown to yield 1,2-diols in high regioselectivity with the aid of titanium tetraisopropoxide in benzene solution.

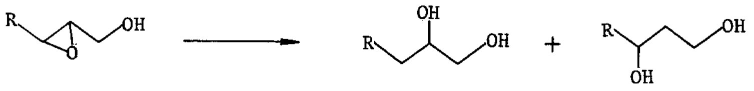
The simplicity and high enantioselectivity of the Sharpless epoxidation process renders the reaction to be an important tool in asymmetric synthesis.[1] As a consequence, many efforts have been devoted to the regioselective ring opening reaction of the resulting epoxy alcohols (1), in order to broaden the application of this reaction. Payne rearrangement followed by nucleophilic attack normally occurs at C_1 position.[2] The C_2 attack may be obtained by dialkylcuprate or Red-Al with high selectivity.[3] Oshima, Nozaki et al. reported a regioselective C_3 attack with organoaluminium reagents, such as Me_3Al, $PhC{=}CAlEt_2$ and Dibal.[4] Very recently, Sharpless and our group independently reported a $Ti(OPr\text{-}i)_4$ mediated ring opening process with a regioselective attack at C_3 postion by various nucleophiles (ROH, RCOOH, RNH_2--).[5] In the above three cases, when hydride is used as a nucleophile, C_1 attack will give a 2,3-diol, C_2 attack will give a 1,3-diol and C_3 attack, 1,2-diol. For 2,3-diol the selectivity ranges from 2.2:1 to 100:1, while that for 1,3-diol



(1)

(the best condition is Red-Al in THF) may amount to 150:1 (1,3 versus 1,2). For 1,2-diol, to the best of our knowledge, the highest selectivity (Dibal) is only 13:1 (1,2 versus 1,3).[3b] In this communication, we would like to report a more efficient method, which is a reductive ring opening of 2,3-epoxy alcohol by $LiBH_4$ (or $NaBH_4$) in benzene with the aid of titanium tetraisopropoxide to provide 1,2-diol. The results are listed in Table 1.

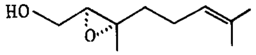
Typical procedure: Titanium tetraisopropoxide (0.9 mmol) was added to a solution of epoxy alcohol (0.6 mmol) in 6 ml THF under argon atmosphere with stirring at room temperature. After aging for 5 minutes, a THF solution of lithium borohydride (2.3 mmol) was then added, and the mixture stirred at temperature indicated till the completion of the reaction (monitored by TLC). The mixture was then diluted with ether and 5% sulfuric acid with vigorous stirring, till two clear layers separated. After working up as usual, the crude product was subjected to G.C. analysis or further purified by chromatography to give the isolated pure diols.



(2) R= C_6H_5
(3) R= C_7H_{15}
(4) R= C_4H_9

1,2-diol, C_3 attack

1,3-diol, C_2 attack



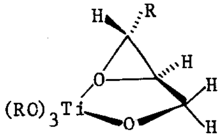
(5)

Table 1

Entry	Substrate[a]	$Ti(OR)_4$ equiv.	Condition temp.°c time	Ratio[b] 1,2:1,3	Yield[d] %
1	(2)	1.5	THF, 65, 1h	7.3:1[c]	83[e]
2	(2)	1.5	THF, 10, 2d	54:1[c]	75.8[e]
3	(3)	0	THF, 65, 1.5h	1.4:1	98.4
4	(3)	1.5	THF, 50, 30m	5.9:1	96.9
5	(3)	2	THF, 8, 1d	4.4:1	99
6	(3)	1.7	benzene, 50, 15m	31:1	96.8
7	(3)	1.9	benzene, 10, 20h	145:1	93.2
8	(4)	0	THF, 65, 1.5h	1.9:1	93.3
9	(4)	2	THF, 50, 35m	3:1	90.5
10	(4)	1.7	benzene, 50, 15m	46:1	99
11	(4)	1.7	benzene, 10, 18h	150:1	97
12	(4)	1.7	CH_2Cl_2, 50, 20m	26:1	95.5
13	(5)	1.5	THF, 65, 15m	1.7:1	84.3[e]
14	(5)	1.6	benzene, 50, 45m	6.8:1	96.3

a, One equiv. of epoxy alcohol and 3-4 equiv. of lithium borohydride were employed. Epoxy alcohols used in these experiments were prepared by Sharpless asymmetric epoxidation process. b, Determined by capillary G.C. (SE-52, 50mx0.2mm, 100°-230°). c, Determined by ^1H NMR, 200 MHz. d, Determined by capillary G.C. (SE-52, 50mx0.2mm). e, Isolated yield.

$LiAlH_4$ is not compatible with the titanium tetraisopropoxide. $NaBH_4$ is good in regioselectivity but the reaction is rather slow due to its low solubility. Therefore, the results of lithium borohydride are disclosed preliminarily. The effect of $Ti(OR)_4$ is obvious, by comparison of entries 3 and 8 with others. Furthermore, the reaction time is also shortened by $Ti(OR)_4$. Interestingly, the selectivity seems to be very sensitive to the solvent used, compare 4 and 6; 9 and 10; 13 and 14 respectively. That means benzene is a much better solvent than THF in the titanium mediated hydridic attack on C_3. This is in contrast with the Red-Al hydridic C_2 attack reported by Kishi et al, where THF is much better than benzene. This result may be rationalized by using the putative intermediate (6) of Sharpless in the nucleophilic C_3 attack. The complexation of epoxide oxygen to Ti is a decisive condition for weakening of the C_3-O bond.[5a] Using THF as solvent is detrimental to this complexation by the competitive complexation of the THF solvent molecules. Therefore benzene is better than THF in this Ti mediated reductive C_3 attack, while in the case of Red-Al ($NaAlH_2(OCH_2CH_2OCH_3)_2$) reductive C2-attack, the process seems to involve an initial reaction of Red-Al with the OH group followed by proximate intramolecular hydridic reduction[3]. By using THF as solvent, THF may reduce any further complexation of Al atom with the epoxide oxygen and enhance the C_2 selectivity. In benzene solution, Al atom may to some extent complexe with the epoxide oxygen. Although the intermediate is still a tentative one, much evidence supports this type of complexation.[6] This phenomenon is also in accordance with that observed by Oshima et al. in the C_3 attack by organoaluminium reagents (including Dibal), which can only be carried out in non-polar solvents such as hexane, and will not take place in ether or THF[4], a similar complexation has been invoked.



(6)

As we mentioned above, Dibal is the best reducing agent for preparing 1,2-diol from 2,3-epoxy alcohol in the literature, therefore we compare the results of the Dibal reduction with that of the $LiBH_4$-$Ti(OR)_4$ system in Table 2. It is evident that the lithium borohydride system is a better one than Dibal for reduction of 2,3-epoxy alcohol to 1,2-diol.

Table 2

Entry	Substrate	Ratio 1,2:1,3	
		Dibal	$LiBH_4$-$Ti(OR)_4$
1	(2)	20:1	54:1
2	(3)	5:1	150:1
3	(4)	13.5:1	145:1
4	(5)	1.2:1	6.8:1

References

1 T. Katsuki and K. B. Sharpless, J. Am. Chem. Soc., 1980, 102, 5974.

2 K. B. Sharpless, C. H. Behrens, T. Katsuki, A. W. M. Lee, V. S. Martin, M. Takatani, S. M. Viti, F. J. Walker and S. S. Woodard, Pure & Applied Chem., 1983, 55, 589.

3 a, M. R. Johnson, T. Nakata, and Y. Kishi, Tetrahedron Lett. 1979, 20, 4343. b, J. M. Finan and Y. Kishi, Tetrahedron Lett. 1982, 23 2719.

4 T. Suzuki, H. Saimoto, H. Tomioka, K. Oshima and H. Nozaki, Tetrahedron Lett., 1982, 23, 3597.

5 a, M. Caron and K. B. Sharpless, J. Org. Chem., 1985, 50, 1557. b, L. X. Dai, Y. Z. Zhang, B. L. Lou, paper submitted to the Symposium of Organometallic Chemistry, Chendu, China at Nov. 1985.

6 S. M. Viti, Tetrahedron Lett., 1982, 23, 4541.

(Received in Japan 31 May 1986)