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High Pressure-Promoted Uncatalyzed Hydrolysis of Epoxides[1]

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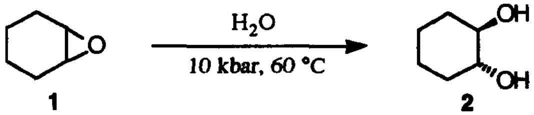
Abstract: A variety of epoxides are efficiently hydrolyzed to diols with water without using any catalysts under high pressure conditions.

Epoxides are versatile intermediates in synthetic organic chemistry mainly due to their susceptibility to several nucleophiles[2] and availability in optically pure forms.[3] Usually, epoxide ring opening reactions are catalyzed by acids or bases and in the absence of these catalysts the reaction is sluggish.[4] Consequently, these methods suffer from disadvantages of incompatibility with other functionality elsewhere in the substrate and of liability to cause other side-reactions such as isomerization and polymerization. In order to circumvent these problems, recent efforts have been directed toward the development of milder catalysts to accomplish the desired transformations.[5]

We have recently demonstrated that some reactive vinyl epoxides were efficiently reacted with relatively weak nucleophiles such as indoles and pyrroles at high pressure to provide tryptophol derivatives, wherein water acts as good catalyst.[6] These facts encouraged us to continue further investigations to perform hydrolysis of epoxides with water, since this type of reaction proceeds through ionic intermediates and, hence, high pressure technology works well.[7] In this communication we would like to describe our successful results that lead to a novel method for the transformation of epoxides into diols under essentially neutral conditions.[8, 9]

Our initial experiments revealed that cyclohexene oxide (**1**) was smoothly hydrolyzed to trans-1,2-cyclohexanediol (**2**) at 10 kbar pressure and the yields were slightly affected by the solvent used (Scheme 1).

Scheme 1



1 **2**

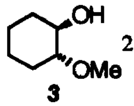
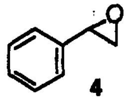
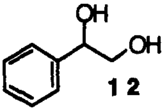
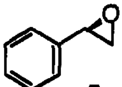
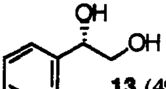
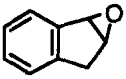
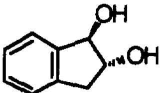
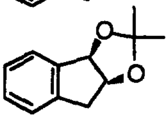
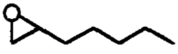
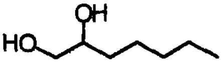
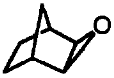
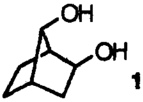
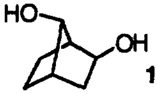
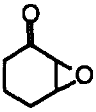
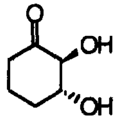
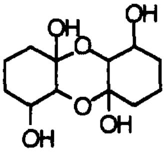
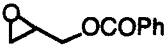
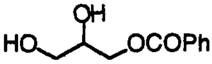
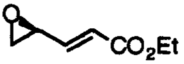
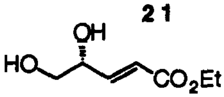
Solvent	H_2O (equiv)	Time, h	Yield, %	
acetone	10	48	95	
acetone	40	24	98	
THF	40	24	98	
MeOH	40	24	65	(+  28%) **3**
CH_3CN	40	24	45	

Table 1. High Pressure-Promoted Hydrolysis of Epoxides[a]

Run	Epoxide	Reaction Conditions	Product	Mp, °C (lit.[ref])	Yield, %[b]
1	 **4**	60 °C, 48 h[c]	 **12**	64 (69-70[11])	60 (35)
2		60 °C, 24 h			92
3	 **5**	60 °C, 24 h	 **13** (49% ee)[d]	63-64	93
4	 **6**	80 °C, 24 h	 **14**	160-161(158-160[12])	67
			 **15**	oil	25
5	 **7**	80 °C, 24 h	 **16**	Bp 103-105 / 10 mmHg (112-113 / 12 mmHg[13])	95
6	 **8**	80 °C, 24 h	 **17**	157-158 (178-179[14])	59
			 **18**	162-163 (204-206[14])	36
7	 **9**	50 °C, 24 h[e]	 **19**	86.5-87 (87[15])	47
			 **20**[f]	198-200	44
8	 **10**	80 °C, 40 h	 **21**	oil	76 (21)
9	 **11**	80 °C, 48 h	 **22** (54% ee)[g]	oil	89

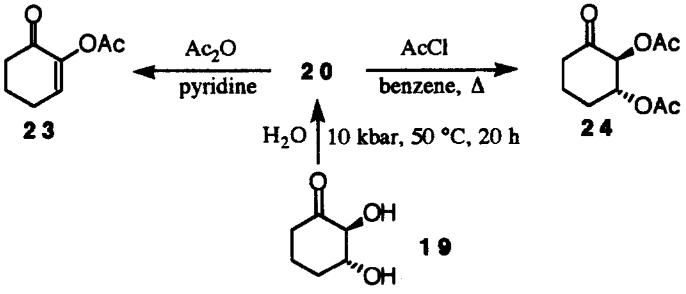
[a] All reactions were carried out using 40 equiv of water in acetone at 10 kbar pressure unless otherwise noted. [b] Isolated yields. Yields in parentheses are recovery. [c] 10 equiv of water was used. [d] Determined by chiral HPLC (Daicel, Chiralcel OB). [e] The reaction was conducted in water. The use of standard conditions was less effective. [f] Tentatively assigned structure. See Text. [g] Based on optical rotation measurements.

Thus, the use of smaller amounts of water was less effective to complete the conversion in shorter reaction period and the best result was obtained when the reaction was conducted in acetone (usually 0.4 M solution) in the presence of 40 equiv of water. Using methanol as a solvent resulted in a concomitant formation of **3**, indicating methanolysis is a competitive process at high pressure. Further examples to elucidate the general scope of this scheme are summarized in Table 1.[10]

From these results the following features become apparent. A variety of epoxides were converted nearly quantitatively into the corresponding diols. Particularly noteworthy is an excellent chemoselectivity as exemplified in Runs 8 and 9, in which ester group survives completely. With optically active epoxides such as **5** and **11**, the ring opening proceeded with low stereoselectivity, while the major process was an S_N2 like inversion (Runs 3 and 9). The reaction of indene oxide (**6**) gave acetonide **15** in addition to the desired trans-diol **14** in a ratio of approximately 1 : 3.[16] Although it might be conceivable that acetonide formation must be unfavorable in an aqueous media, the result means that **6** has a great tendency to attack acetone because of its steric demand.[17] In accordance with the previous reports,[18] norbornene oxide (**8**) gave the rearranged diol **17** and **18**. The structures of these compounds were easily confirmed by comparison with authentic samples except for their melting points.[19]

Interestingly, when 1,2-epoxy-3-cyclohexanone (**9**) was hydrolyzed with water, besides the expected diol **19**[15] a considerable amount of **20**[20] was isolated as a highly crystalline solid. The IR spectrum of **20** showed only an O-H stretch band at 3378 and 3177 cm^{-1} and no C=O band. Unfortunately, this compound was insoluble in most of organic solvents, e.g., $CHCl_3$, acetone, methanol and DMSO, and no further spectral data were obtained. The MS data ($M^+=130$) of **20** were consistent with those of **19** probably arising from its spontaneous fragmentation. Accordingly, derivatization of **20** with acetic anhydride in pyridine or with acetyl chloride in refluxing benzene gave only enolacetate **23** and diacetate **24**, respectively (Scheme II). In a separate work we could recognize that **19** is in equilibrium with **20**: compression of **19** in water (10 kbar, 50 °C, 20 h) gave a mixture of **19** (57%) and **20** (37%). Based on these evidences we tentatively assigned the structure of **20** having a dimeric hemiacetal structure as depicted in Table 1.[21]

Scheme II



In conclusion, a new powerful method has been shown to transform epoxides into diols. The procedure consists of simple operation in aqueous acetone, and can avoid the needless use of acid or base catalysts. In this work we could again clarify the utility of high pressure to promote the reactions involving ionic intermediates.

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References and Notes

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16. The corresponding cis-diol could not be detected.
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18. Meinwald, J.; Crandall, J. K.; Gassman, P. G. *Tetrahedron* **1962**, *18*, 815; Crandall, J. K. *J. Org. Chem.* **1964**, *29*, 2830; Grützmacher, H. F.; Fechner, K. H. *Tetrahedron* **1971**, *27*, 5011.
19. We wish to thank Prof. K. Naemura of Osaka University for sending us the spectral data of authentic samples. Satisfactory analytical results were obtained for **17** and **18** after several times of sublimation.
20. **20**: FTIR (KBr) 3378, 3177, 1148, 1103, 1086, 1049, 982, 870, 851 cm^{-1}; MS *m/z* (rel intensity) 130 (M$^+$, 19), 112 (25), 101 (12), 86 (100), 84 (45), 74 (57), 70 (42), 57 (65), 44 (22), 32 (15). Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.75. Found: C, 55.27; H, 7.74.
21. Unambiguous confirmation of this structure is now under investigation.

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