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Metalloporphyrins as New Catalysts in the Highly Regioselective Conversion of Epoxides to Halohydrins with Molecular Halogen

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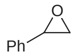
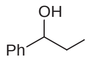
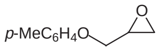
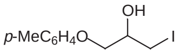
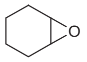
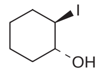
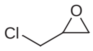
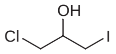
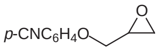
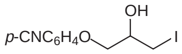
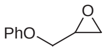
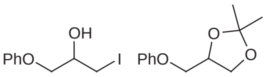
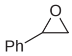
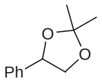
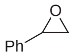
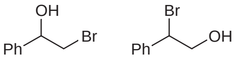
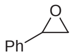
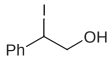
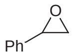
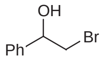
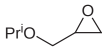
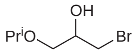
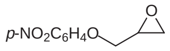
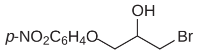
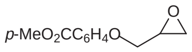
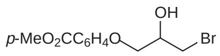
The highly regioselective cleavage of epoxides by means of molecular iodine and bromine in the presence of metalloporphyrins affords vicinal iodohydrins and bromohydrins in high yields.

Epoxides are among the most versatile intermediates in organic synthesis.[1] A variety of reagents such as hydrogen halides or hydrohalogenic acids,[3] are known to convert epoxides to halohydrins. However, these procedures suffer from certain limitations when protic acid-sensitive substrates are used. A great effort has been made in recent years to find new mild procedures for converting epoxides into halohydrins.[4] Recently, it has been found[5] that epoxides can be converted into iodohydrins and bromohydrins by means of molecular iodine and bromine, but this method has a number of limitations such as low regioselectivity and yield, formation of acetonide byproducts in addition to the expected iodo adduct in acetone solution (entries 12 and 14, Table 2), and long reaction times. Biomimetic compounds, metalloporphyrins, have found important applications, as catalysts, in organic synthesis.[6–9] In conjunction with ongoing work in our laboratory on the complex formation of metalloporphyrins with neutral molecules such as iodine and bromine, we found that these complexes effectively catalyzed the ring opening reactions of epoxides with molecular iodine and bromine under neutral and mild conditions in aprotic solvents to produce the corresponding vicinal halohydrins in high yields and with high regioselectivity. In this study, in order to examine the catalytic

Table 2 Reaction of various epoxides with iodine and bromine in the presence of 0.05 mol% Mn(TPP) catalyst (see corresponding table in full text for complete set of entries 1–31)

Entry	Substrate **1a–h**	Conditions[a]	Time/h	Yield[b](%)	Products(s) **3a–p**
1		I_2, **2b**, r.t. CH_2Cl_2	0.5	>95	
3		I_2, **2b**, r.t. CH_2Cl_2	6	80	
6		I_2, **2b**, r.t. CH_2Cl_2	10	67	
9		I_2, **2b**, r.t. CH_2Cl_2	1.5	90	
10		I_2, **2b**, r.t. CH_2Cl_2	6.5	83	
12		I_2, r.t., acetone	—	94(53:47)	
14		I_2, r.t., acetone	—	83	
17		$Bu^n{}_4N^+Br^-$/ $Mg(NO_3)_2$, $CHCl_3$	5	78(5:1)	
19		HI, $CHCl_3$	0.25	>99	
21		Br_2, **2b**, r.t., CH_2Cl_2	—[c]	>95	
24		Br_2, **2b**, r.t., CH_2Cl_2	2.5	80	
27		Br_2, **2b**, r.t., CH_2Cl_2	1.25	94	
31		Br_2, **2b**, r.t., CH_2Cl_2	2	90	

[a]Reactions were carried out at 25 °C. [b]GC yield based on epoxide. [c]Immediate reaction.

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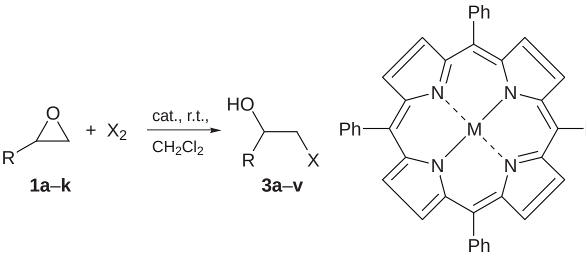
* To receive any correspondence.



Cat. **2a–g**

R	Epoxide **1a–k**	Halohydrin, **3a–v** X: I	Br
Ph	**a**	**a**	**l**
$PhOCH_2$	**b**	**b**	**m**
p-$ClC_6H_4OCH_2$	**c**	**c**	**n**
p-$MeC_6H_4OCH_2$	**d**	**d**	**o**
p-$NO_2C_6H_4OCH_2$	**e**	**e**	**p**
p-$CNC_6H_4OCH_2$	**f**	**f**	**q**
p-$MeO_2CC_6H_4OCH_2$	**g**	**g**	**r**
Cyclohexene oxide	**h**	**h**	**s**
$ClCH_2$	**i**	**i**	**t**
Pr^iOCH_2	**j**	**j**	**u**
n-Hexyl	**k**	**k**	**v**

M^{2+}	
—	**a**
Mn^{2+}	**b**
Fe^{2+}	**c**
Co^{2+}	**d**
Ni^{2+}	**e**
Cu^{2+}	**f**
Zn^{2+}	**g**

Scheme 1

effects of metals in the reaction, a number of tetraphenylporphyrin complexes of first-row transition metal(II) complexes were employed (Scheme 1).

The yields of reactions with this new method are quite good with the Mn(TPP) complex being the most effective catalyst. For comparison, some other methods[4,10–12] are given for conversion of epoxides to halohydrins (entries 17 and 19, Table 2). The reactions are completely anti-stereoselective (entry 6, Table 2) and chemoselective (entries 9, 10, and 31, Table 2). As for the regioselectivity, attack of the nucleophile occurs only at the less substituted epoxide carbon. This mechanism closely resembles the S_N2 model for aliphatic nucleophilic displacement. In conjunction with our study on metalloporphyrins and other work reported on the different ligands[13–17] with molecular halogens, it seems that in these reactions trihalide ion, X_3^-, is formed and acts as nucleophile.

In conclusion, the ring opening by these catalysts can eliminate some of the disadvantages usually encountered in other methods, such as, high acidity,[24] unsatisfactory regioselectivity,[25] inconvenient handling requirements[26] and long reaction time.[25]

Techniques used: ^1H NMR, ^{13}C NMR, IR, UV, GLC

References: 32

Figure: 1

Schemes: 2

Table 1: Ring opening of styrene oxide with molecular iodine and bromine in the presence of various catalysts

Table 3: Halogenative cleavage of styrene oxide in the presence of catalyst **2b** in various solvents at 25 °C

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