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The halogen-mediated opening of epoxides in the presence of pyridine-containing macrocycles

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Abstract—The ring opening of epoxides with elemental iodine and bromine in the presence of three pyridine-containing macrocyclic diamides as new catalysts affords vicinal iodo alcohols and bromo alcohols in high yields. This new procedure occurs regioselectively under mild conditions in various aprotic solvents. The catalysts are easily recovered and can be reused several times.

1. Introduction

Vicinal halo alcohols have attained great significance in organic synthesis.[1–3] These compounds can be utilized for some useful synthetic transformations,[4,5] and are also key intermediates in the synthesis of halogenated marine natural products.[1] A variety of reagents such as hydrogen halides or hydrohalogenic acids,[6] are known to convert epoxides to halohydrins. However, these procedures suffer from certain limitations when protic acid-sensitive substrates are used. The ring opening of unsymmetrically substituted epoxides with $Li_2[NiBr_4]$,[7] pyridine·HCl,[8] haloboran reagents,[9–12] Br_2/PPh_3,[13] $Ti(O–iPr)_4$,[14] chlorosilanes,[15] $[n\text{-}Bu_4N]Br/Mg(NO_3)_2$,[16] Lewis acid metal halides,[2,3,17,18] and Me_3SiBr[19] have been reported. However, these methods are not always fully satisfactory, and suffer from disadvantages, such as acidity, handling and in situ preparation of the reagent, the noncatalytic nature of the reagents and relatively long reaction times.[11,15,20–22] Recently, it has been found that epoxides can be converted into iodohydrins and bromohydrins by means of elemental iodine and bromine,[23] but this method has some limitations such as low yield and regioselectivity with long reaction times and formation of acetonide byproducts in addition to the expected iodoadduct in acetone solution. Furthermore, iodination does not occur in CH_2Cl_2, $CHCl_3$, C_6H_6, CH_3CN, and THF solvents.

In conjunction with the ongoing work in our laboratory on the synthesis and complex formation of macrocyclic compounds with neutral molecules such as iodine and bromine,[24–26] we found that these compounds efficiently catalyzed the addition of elemental iodine and bromine to epoxides. Three pyridine-containing macrocyclic dilactams were selected as catalysts in these reactions.

2. Result and discussion

In recent years, there has been considerable interest in the use of macrocyclic ionophores incorporating heterocyclic subunits, because of their ability to form strong and selective interactions with various charged and neutral guest molecules. Pyridine and other nitrogen-containing heterocyclic groups incorporated in the macrocyclic ring provide rigidity and are able to participate in complexation through their soft nitrogen donor atoms. Pyridine-containing macrocycles are efficient complexing agents for metal cations.[27] They also displayed high log K values in complexation with ammonium salts.[27–29] Because of these interesting complexing properties, it is important to have a high yield for syntheses of these macrocyclic diamides.

In previous studies,[24] we reported a new efficient synthesis of macrocyclic diamides. No high-dilution technique was required in this method. We applied this approach to the synthesis of dilactams **1a–c** (Scheme 1).

o-Nitrophenol was reacted with dichlorides of olygoethylene glycols in the presence of potassium carbonate in dimethylformamide to yield the corresponding dinitro compounds **4a–c** in the range of 67–85% yields. The dinitro compounds **4a–c** were reduced by palladium on carbon with hydrazine into corresponding diamines **5a–c** in 94, 93 and 83% yields respectively.

The cyclization reaction between 2,6-pyridine dicarboxylic acid dichloride and the diamines **5a–c** was performed without the use of high-dilution techniques. In addition, the

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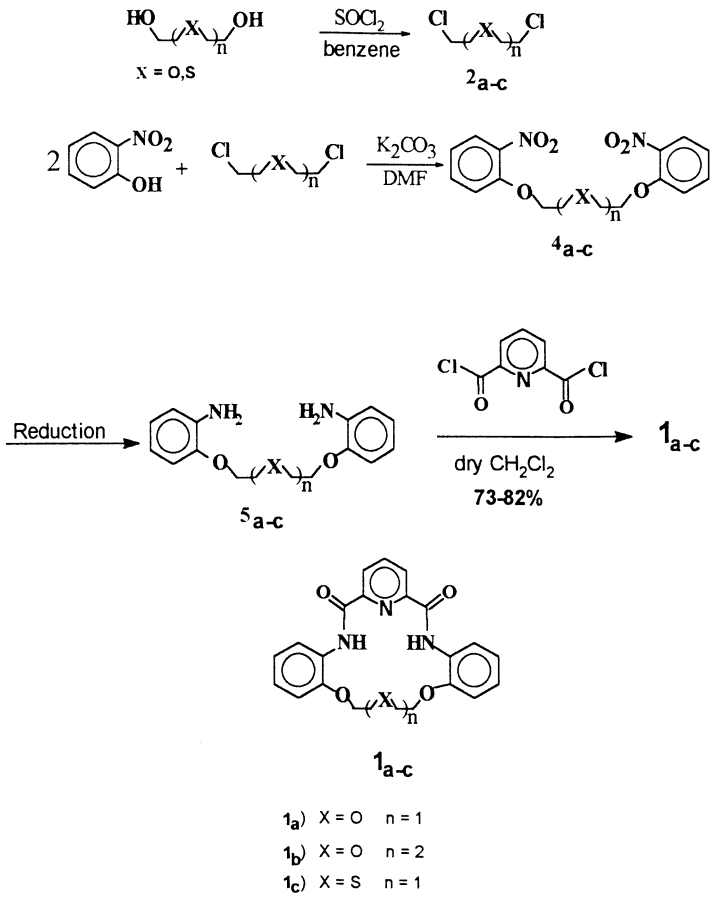


Scheme 1.

cyclization reaction was carried out with fast addition of a solution of diamine (2 mmol) in dry CH_2Cl_2 (10 ml) into a solution of 2,6-pyridine dicarboxylic acid dichloride (2 mmol) in dry CH_2Cl_2 (10 ml) over 5 s with vigorously stirring at room temperature. The reaction mixture was stirred for further 20 min to give pyridine-containing macrocyclic diamides **1a–c** in the range of 78–82% yields (Scheme 1).

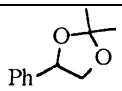
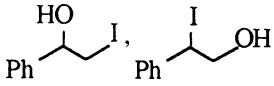
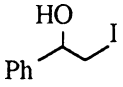
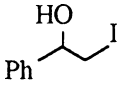
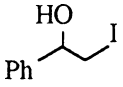
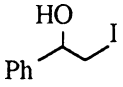
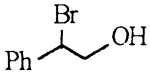
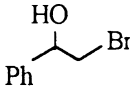
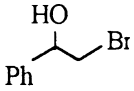
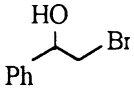
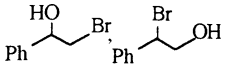
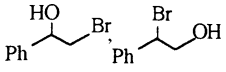
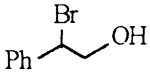
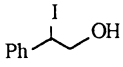
Epoxides of convenient volatility to allow GC analysis were chosen for study. As catalysts, three pyridine-containing macrocyclic diamides that were synthesized according to Scheme 1 were used. The result of the reactions of styrene oxide with elemental iodine and bromine in the presence of the above catalysts are summarized in Table 1. In each case, cleavage of epoxide ring occurs and upon thiosulfate workup, the corresponding iodohydrin and bromohydrin were obtained. The catalysts were easily recovered and could be reused several times. In comparison, the cleavage behavior of styrene oxide with elemental iodine and bromine in the absence of catalyst is given in entries 1,2 and 7.

As shown in Table 1, yields for both iodination and bromination with this methodology are quite good. Catalyst **1c** is the most effective, and reactions occur instantaneously in the presence of this catalyst (Table 1, entries 6 and 11). However, iodination of styrene oxide with an excess of elemental iodine in the absence of catalyst did not occur even under reflux and extension of reaction time to several days, and unreacted styrene oxide was completely recovered. In addition, the yield of the bromination reactions is very low in the absence of catalyst.

The results obtained with some representative epoxides in the presence of macrocycle **1c** as catalyst are summarized in Table 2 and are compared with the corresponding results obtained in the reaction of the same epoxides in the absence of catalyst (Table 2, entries 2, 4, 6, 9 and 12). When epoxides were allowed to react in the presence of a catalyst, an increase in the yields and regioselectivies were observed in all of the reactions studied. Generally, the optimum amounts of the catalyst were found to be 0.1 mol for 1 mol of epoxide and halogen.

However, the following factors can influence the yield and regioselectivity of the reactions: (1) the steric hindrance of epoxides, (2) the rate of admixing the reagents, (3) the order in which the reagents are combined, and (4) the nature of solvent. In cases of the rate and order in which the reagents are combined, for example, if bromine before the catalyst is added to epoxide, two isomeric bromo alcohols are produced. However, if the epoxide is added to the catalyst, and then bromine is added dropwise over a period of time, only one isomer is formed. Furthermore, the rapid addition of bromine reduced the regioselectivity.

Table 1. Reaction of styrene oxide with elemental iodine and bromine in the presence of representative catalysts

Entry	Catalyst	Conditions	Time (h)	Yield[a] (%)	Product(s)	Ref.
1	–	I_2, rt, acetone	2	83		23
2	–	I_2 (excess)/CH_2Cl_2	–	–	N.R.	23
3	–	LiI, AcOH, THF, rt	1.3	87 (1:2)		22
4	**1a**	I_2, rt/CH_2Cl_2	0.33	80		
5	**1b**	I_2, rt/CH_2Cl_2	0.33	50		
6	**1c**	I_2, rt/CH_2Cl_2	immed.	>95		
7	18-Crown-6	KI_3, rt H_2O/CH_2Cl_2	1	60		
8	–	Br_2, rt/CH_2Cl_2	1	31		23
9	**1a**	Br_2, rt/CH_2Cl_2	0.16	93		
10	**1b**	Br_2, rt/CH_2Cl_2	0.16	92		
11	**1c**	Br_2, rt/CH_2Cl_2	immed.	>95		
12	–	*n*-$Bu_4N^+Br^-$/ $Mg(NO_3)_2$, $CHCl_3$	5	78 (5:1)		7
13	–	$(Me_2N)_2BBr$/CH_2Cl_2, N_2 atm.	12	75 (1:4.5)		11
14	–	HBr, $CHCl_3$	0.25	>99		20
15	–	HI, $CHCl_3$	0.25	>99		20

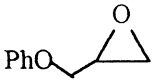
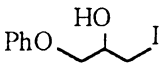
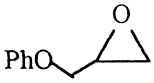
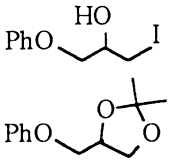
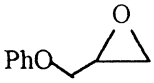
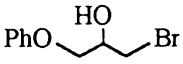
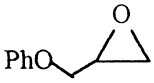
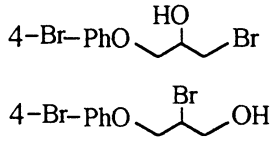
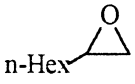
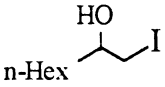
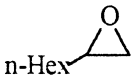
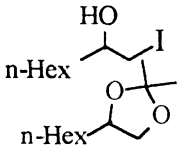
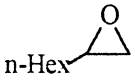
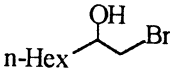
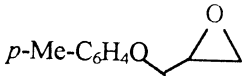
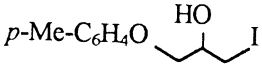
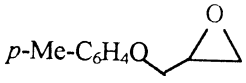
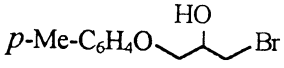
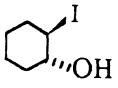
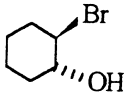
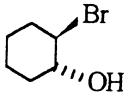
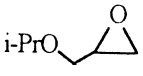
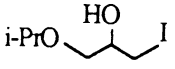
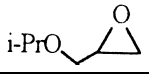
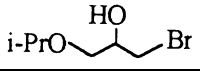
[a] GC yield.

The results of a halogenative cleavage of styrene oxide with iodine and bromine by catalyst **1c** in various aprotic solvents are reported in Table 3. The iodination and bromination reactions proceed most cleanly in CH_2Cl_2, $CHCl_3$, CH_3CN, and benzene solution, while those done in THF and acetone lead to a lower yield of halohydrins.

As shown in Table 2 (entries 10 and 11), in which only the trans isomer is obtained, the reactions are completely anti-stereoselective. As for the regioselectivity, an attack of the nucleophile preferentially occurs at the less-substituted oxirane carbon. An anti-Markovnikov-type[30] regioselectivity is generally observed in these reactions. In many cases, this type of regioselectivity appears to be the opposite of that observed in ring opening of the same epoxides with aqueous hydrogen halides under classic acidic conditions (entries 14 and 15, Table 1).

The regiochemical mode of epoxide cleavage by elemental iodine or bromine in the presence of macrocycle catalyst can be viewed as occurring via nucleophilic attack by the halide ion on the less sterically hindered epoxide carbon. This mechanism closely resembles the S_N2 model for aliphatic nucleophilic displacement. On the basis of our previous

Table 2. Reaction of epoxides with elemental iodin and bromine in the presence of representative catalysts

Entry	Epoxide	Catalyst	Conditions	Time (h)	Yield[a] (%)	Product(s)	Ref.
1		**1c**	I_2, rt, CH_2Cl_2	5	>95		
2		–	I_2, rt, acetone	–	94 (1:1)		23
3		**1c**	Br_2, rt CH_2Cl_2	0.3	>95		
4		–	Br_2, rt CH_2Cl_2	–	88 (5:1)		23
5		1c	I_2, rt, CH_2Cl_2	16	89		
6		–	I_2, acetone	–	79 (1:4)		23
7		**1c**	Br_2, rt CH_2Cl_2	0.33	88		
8		**1c**	I_2, rt, CH_2Cl_2	4	80		
9		**1c**	Br_2, rt CH_2Cl_2	0.75	87		
10		**1c**	I_2, rt, CH_2Cl_2	6	86		
11		**1c**	Br_2, rt, CH_2Cl_2	0.33	88		
12		–	LiBr, AcOH, THF, rt	5	90		22
13		**1c**	I_2, rt, CH_2Cl_2	18	78		
14		**1c**	Br_2, rt, CH_2Cl_2	0.33	85		

[a] GC yield.

study on macrocycle diamides[23–26] and other works on the complexation of crown ethers with elemental halogens, halogenative cleavage of epoxides occurs according to the following four-step mechanism:

The first step involves the formation of a 1:2 or 1:1 molecular complex between macrocycle and elemental halogen, in which halogen ion (X_3^-) exists as a contact ion pair:

$$\text{Macrocycle} + 2X_2 \rightarrow (\text{macrocycle}\ldots X^+)X_3^-$$

or

$$2\ \text{Macrocycle} + 2X_2 \rightarrow (2\ \text{macrocycle}\ldots X^+)X^- \quad (1)$$

Table 3. Halogenation reaction of styrene oxide in the presence of 0.1 mol of catalyst **1c** in various solvents

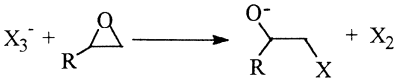
		Time (h)		Yield[a] (%)	
Entry	Solvent	Bromination	Iodination	Bromination	Iodination
1	CH_2Cl_2	0.3	0.03	>95	>95
2	$CHCl_3$	0.5	0.3	>95	>90
3	C_6H_6	0.6	0.5	>95	92
4	CH_3CN	0.6	1	90	90
5	CH_3COCH_3	2	10	85	75
6	THF	2	10	65	30

[a] GC yield.

In the second step this complex is further decomposed to release X_3^- ion into solution as

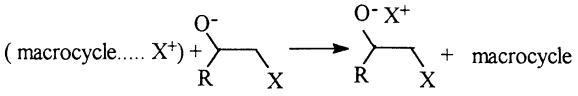
$$(\text{Macrocycle}\ldots X_3^+)X^- \rightarrow (\text{macrocycle}\ldots X^+) + X_3^- \quad (2)$$

Therefore, in this way, molecular iodine or bromine is converted to a nucleophilic halogen species in the presence of a suitable macrocycle and, in the third step, this ion participates in the ring opening reaction of epoxides



(3)

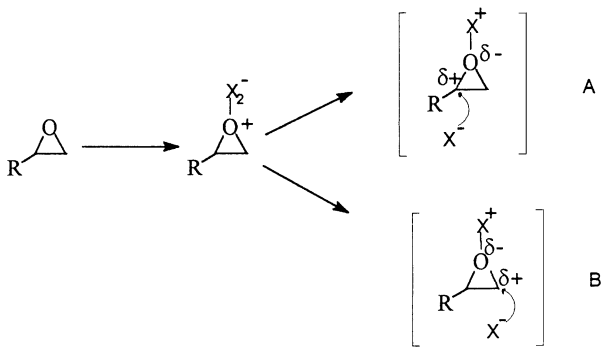
Finally, the catalyst is regenerated in step 4.



(4)

These steps occur continuously until all of the epoxides and halogen are consumed, and after workup, the catalyst can be recovered easily.

On the other hand, when catalyst is not present, cleavage of epoxides can occur via two limiting mechanistic pathways, either electrophilic attack by molecular halogen, behaving as Lewis acid, giving the more stable carbonium ion-like transition state (A), or via nucleophilic attack by halide ion on the epoxide or epoxide–halogen complex, giving the more stable transition state (B):



Most Lewis acidic compounds, such as titanium halides, foster electrophilic opening of the epoxide ring to yield transition state A. When weaker Lewis acids are employed, namely bromine or iodine, nucleophilic attack, by the halide ions generated should be fostered and transition state B may be expected to be lower in energy. In this case, the cleavage leads to a mixture of secondary alcohol and primary alcohol products.[3]

The variation in yield and rate of cleaving epoxides by elemental iodine or bromine in the presence of these catalysts (**1a**–**c**) can be satisfactorily rationalized in terms of the suggested mechanism. The macrocycle **1c** is the most active catalyst in these reactions.

In support of this mechanism, reaction of catalysts with iodine was followed by UV spectroscopy (Fig. 1). Fig. 1 shows a characteristic band in 364 nm is well known to be specific for the formation of triiodide ion, I_3^-.[31–34]

The decrease in regioselectivity that results by merely reversing the order of mixing of epoxide and halogen, namely the slow addition of bromine to epoxide, before catalyst was added, can readily be understood from the model. When

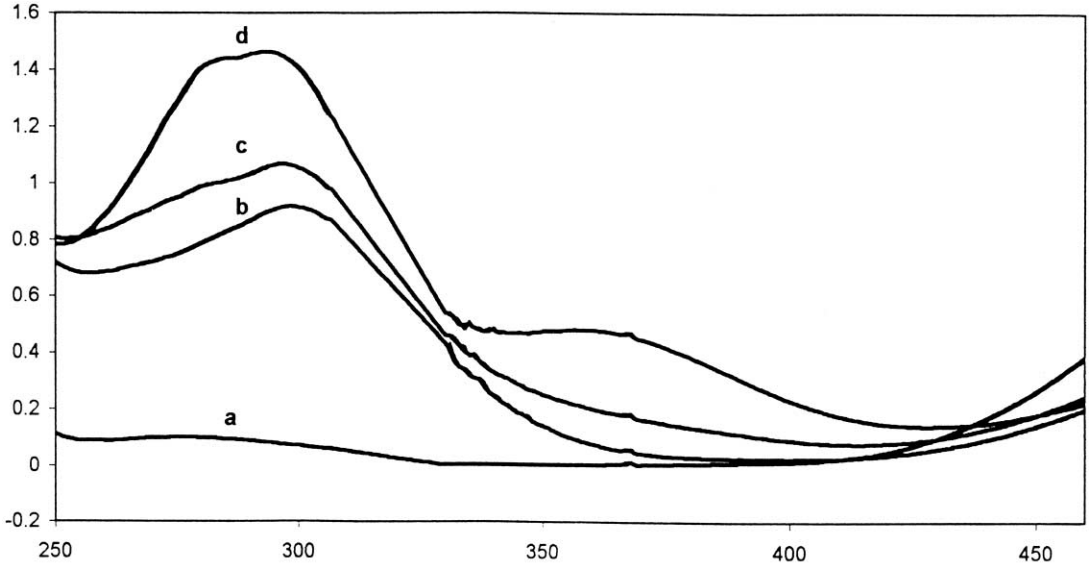


Figure 1. Absorption spectra of used macrocycle–iodine complexes. Spectra from bottom to top refer to iodine and macrocycles **1a**, **1b** and **1c**: iodine complexes.

the initial epoxide was introduced (in the absence or presence of catalyst), it would encounter an excess amount of bromine; electrophilic attack by bromine can then occur, giving the transition state A, and bromine anions will attack the more substituted carbon. On the other hand, slow addition of bromine to the mixture of catalyst and epoxide fosters the four-step mechanism presented above in which all of the elemental bromine is converted to Br_3^- by the catalyst and it then attacks the less substituted carbon selectivity.

In conclusion, we have found that suitable pyridine-containing macrocyclic compounds can catalyze the regioselective ring opening of epoxides by elemental iodine and bromine under neutral conditions with a variety of sensitive functional groups, as well as the convenience of this procedure, which make this synthetic technique highly useful.

3. Experimental

IR spectra were obtained on an Impact 400 D Nickolet FTIR spectrophotometer. NMR spectra were recorded on a Brucker Avance DPX-250 (90 MHz) in pure deuterated solvents. UV–vis spectra were obtained with a Philips PU8750 spectrometer. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instrument at 70 ev. The purity determination of the substrates and reactions monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates or GLC on a Shimadzu GC-10A instrument with a flame ionization detector using a column of 15% carbowax 20 M chromosorb W acid washed 60–80 mesh. Elemental analyses were performed at the National Oil Co. of Iran at Tehran Research Center. Column chromatography was carried out on short columns of silica gel 60 (230–400 mesh) in glass columns (2–3 cm diameter) using 15–30 g of silica gel per 1 g of crude mixture. Melting points were determined in open capillary tubes in a buchi-510 circulating oil melting point apparatus. Epoxides, and other chemical materials were purchased from Fluka and Merck in high purity and were used without further purification.

3.1. General procedure for the preparation of diamino compounds 5a–c

In a two necked round-bottomed flask (250 ml) equipped with a reflux condenser and a dropping funnel, a suspension of dinitro compounds **4a–c** (0.012 mol), palladium on carbon 5% (0.4 g) and absolute ethanol (200 ml) was prepared. The mixture was warmed and while being stirred magnetically, hydrazine hydrate 80% (10 ml) in ethanol (20 ml) was added dropwise over a 1.5 h period through the dropping funnel, while maintaining the temperature at about 50°C. The reaction mixture was refluxed for 2 h and filtered while hot. On cooling the filtrate gave the corresponding diamino compound after vacuum dried.

3.1.1. 1,5-Bis (*o*-aminophenoxy)-3-oxapentane (5a). White crystals, yield 94%, mp=65–66°C (lit.[24]: 63–65°C); IR (KBr): 735 (s), 950 (m), 1050 (m), 1138 (m), 1212 (s), 1273 (m), 1460 (m), 1508 (s), 1595 (m), 1605 (m), 2880 (w), 2932 (m), 3321 (s), 3388 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 3.58 (s, 4H), 3.88 (t, 4H, J=4.65 Hz), 4.12 (t, 4H, J=4.65 Hz), 6.59–6.78 (m, 8H).

3.1.2. 1,8-Bis (*o*-aminophenoxy)-3,6-dioxaoctane (5b).[35] White crystals, yield 93%, mp=48–50°C; IR (KBr): 750 (m), 950 (m), 1060 (m), 1140 (m), 1225 (s), 1275 (s), 1510 (m), 1608 (m), 2885 (m), 2940 (m), 3060 (s), 3370 (s), 3470 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 3.67 (s, 4H), 3.77 (s, 4H), 3.85 (t, 4H, J=4.5 Hz), 4.2 (t, 4H, J=4.5 Hz), 6.54–6.77 (m, 8H); Mass m/z (%): 333(M^++1, 7.0), 332(M^+, 32.7), 224(17.7), 153(12), 136(49.2), 109(57.1), 92(38.3), 80(53.1), 65(30.9), 44(base peak).

3.1.3. 1,5-Bis (*o*-aminophenoxy)-3-thiopentane (5c). White crystals, yield 89%, mp=28–29°C; IR (KBr): 735 (m), 1017 (m), 1212 (s), 1273 (m), 1470 (m), 1508 (s), 1608 (m), 2871 (w), 2928 (w), 3070 (w), 3328 (m), 3408 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 3.03 (t, 4H, J=6.50 Hz), 3.73 (b, 4H), 4.20 (t, 4H, J=6.50 Hz), 6.66–6.84 (m, 8H); Mass m/z (%): 304(M^+, 2.5), 196(12.6), 168(23.4), 123(18.8), 105(base peak), 80(32.4), 61(53.8), 45(65.6).

3.1.4. 3,15,21-Triaza-4,5;13,14-dibenzo-6,9,12-trioxabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (1a). White crystals; yield 82%; mp 223–224°C; IR (KBr): 3395.52 (NH), 1682.84 cm^{-1} (CO); ^1H NMR ($CDCl_3$, 250 MHz), δ 3.86 (t, 4H, J=4.0 Hz), 4.20 (t, 4H, J=4.0 Hz), 6.80 (dd, 2H, J_1=7.85 Hz, J_2=1.75 Hz), 6.94 (dt, 2H, J_1=7.75 Hz, J_2=1.75 Hz), 7.08 (dt, 2H, J_1=7.75 Hz, J_2=1.8 Hz), 8.00 (t, 1H, J=6.35 Hz), 8.18 (dd, 2H, J_1=7.75 Hz, J_2=1.8 Hz), 8.47 (dd, 2H, J_1=7.8 Hz, J_2=1.65 Hz), 9.64 (s, 2H); UV (chloroform) λ (ε_{max}): 248 (10741), 300.3 nm (12489); MS m/z 421 (M^++2, 5.5), 420 (M^++1, 29.8), 419 (M^+, base peak), 375 (12.3), 331 (4.1), 214 (22.4), 134 (77.9), 107 (18.2); Anal. Calcd for $C_{23}H_{21}N_3O_5$: C, 65.86; H, 5.05; N, 10.02. Found: C, 65.73; H, 5.13; N, 9.92.

3.1.5. 3,18,24-Triaza-4,5;16,7-dibenzo-6,9,12,15-tetraoxabicyclo[18.3.1]tetra-eicosa-1(24),20,22-triene-2,19-dione (1b). White crystals; yield 78%; mp 139–141°C; IR (KBr):3314.93 (NH), 1682.84 cm^{-1} (CO); ^1H NMR ($CDCl_3$, 250 MHz), δ 3.51 (s, 4H), 3.74 (t, 4H, J=4.0 Hz), 4.20 (t, 4H, J=4.0 Hz), 7.00–7.16 (complex, 6H), 8.01 (t, 1H, J=8.3 Hz), 8.10 (d, 2H, J=7.8 Hz), 8.43 (d, 2H, J=6.3 Hz), 10.12 (b, 2H); UV (chloroform) λ (ε_{max}): 243.7 (9250), 302.7 nm (9991); MS m/z 465 (M^++2, 7.0), 464 (M^++1, 28.9), 463 (M^+, 24.1), 409 (16.2), 248 (12.9), 214 (29.1), 134 (99.3), 106 (41.6), 92 (16.0), 45 (base peak); Anal. Calcd for $C_{25}H_{25}N_3O_6$: C, 64.79; H, 5.44; N, 9.06. Found: C, 64.91; H, 5.59; N, 8.81.

3.1.6. 3,15,21-Triaza-4,5;13,14-dibenzo-6,12-dioxa-9-thiabicyclo[15.3.1]heneicosa-1(21),17,19-triene-2,16-dione (1c). White cream crystals; yield 80%; mp 168–170°C; IR (KBr): 3382.22 (NH), 1682.84 cm^{-1} (CO); ^1H NMR ($CDCl_3$, 250 MHz), δ 3.02 (t, 4H, J=5.4 Hz), 4.38 (t, 4H, J=5.4 Hz), 7.00 (dd, 2H, J_1=7.45 Hz, J_2=1.8 Hz), 7.05–7.17 (m, 4H), 8.13 (t, 1H, J=7.8 Hz), 8.43 (dd, 2H, J_1=7.55 Hz, J_2=2.1 Hz), 8.45 (d, 2H, J=7.8 Hz), 10.00 (s, 2H); UV (chloroform) λ (ε_{max}): 244.5 (11294.5), 304 nm (12832.5); MS m/z 437 (M^++2, 5.8), 436 (M^++1, 20.6),

435 (M^+, 24.6), 375 (2.6), 331 (2.8), 214 (5.7), 187 (9.2), 134 (15.3), 120 (7.3), 105 (13.4), 93 (3.3), 87 (base peak); Anal. Calcd for $C_{23}H_{21}N_3O_4S$: C, 63.43; H, 4.86; N, 9.65; S, 7.36. Found: C, 63.69; H, 4.59; N, 9.91; S, 7.09.

3.2. General procedure for halogenative cleavage of epoxides

Epoxide (1 mmol) in CH_2Cl_2 (5 ml) was added to a stirred solution of catalyst (0.1 mmol) in CH_2Cl_2 (5 ml) at room temperature. Next, a solution of elemental halogen (1 mmol) in CH_2Cl_2 (5 ml) was added portionwise (15 min) to the above mixture. The progress of the reaction was monitored by GLC and TLC. After complete disappearance of the starting material, the reaction mixture was washed with 10% aqueous $Na_2S_2O_3$ (2×10 ml) and water (2×10 ml). The aqueous layer was extracted with CH_2Cl_2 (2×10 ml).The combined organic layer was dried over anhydrous $MgSO_4$ and evaporated to give crude alcohol–catalyst. The crude products were purified by crystallization in diethyl ether. After cooling, the catalyst was filtered off and washed with cold ether. The solvent was evaporated and pure halohydrin was obtained. The halohydrins obtained throughout this procedure were identified by comparison, where possible, with authentic samples prepared in accordance with literature procedures.[18,22,23,36,37]

3.2.1. 1-Bromo-2-octanol. ^{1}H NMR($CDCl_3$, 250 MHz) δ 0.89 (t, 3H, J=6.5 Hz), 1.25–1.63 (m, 8H), 1.86 (q, 2H, J=7.1 Hz), 2.22 (s, 1H), 3.42 (t, 2H, J=7.1 Hz), 3.75–3.84 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 14.0, 22.5, 25.6, 29.1, 31.7, 35.05, 40.7, 71.0; IR (neat) 720 (m), 830 (m), 1050 (s), 1075 (s), 1125 (m), 1225 (m), 1265 (m), 1385 (m), 1425 (m), 1470 (s), 2860 (vs), 2935 (vs), 2970 (vs), 3380 (br s) cm^{-1}.

3.2.2. 1-Iodo-2-octanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.89 (t, 3H, J=7.0 Hz), 1.26–1.58 (m, 10H), 2.24 (s, 1H), 3.24–3.55 (m, 3H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 14.1, 16.45, 22.6, 25.6, 29.1, 31.7, 36.9, 70.9; IR (neat) 725 (m), 1015 (br s), 1105 (m), 1130 (m), 1185 (s), 1385 (s), 1425 (m), 1470 (s), 2860 (vs), 2935 (vs), 2970 (vs), 3380 (br s) cm^{-1}.

3.2.3. 2-Bromocyclohexanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.26–1.42 (m, 3H), 1.78–1.98 (m, 3H), 2.18–2.32 (m, 1H), 2.32–2.38 (m, 1H), 2.68 (s, 1H), 3.58–3.64 (m, 1H), 3.82–3.92 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 24.5, 27.0, 33.95, 36.6, 62.1, 75.7; IR (neat) 690 (s), 793 (w), 865 (m), 960 (s), 1038 (m), 1075 (br s), 1123 (m), 1189 (s), 1372 (m), 1460 (s), 2882 (s), 2960 (br s), 3425 (br s) cm^{-1}.

3.2.4. 2-Iodocyclohexanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.26–1.44 (m, 3H), 1.75–1.95 (m, 3H), 2.15–2.30 (m, 1H), 2.30–2.35 (m, 1H), 2.72 (s, 1H), 3.58–3.62 (m, 1H), 3.90–4.00 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 24.5, 26.6, 32.75, 35.4, 59.8, 71.6; IR (neat) 690 (s), 790 (w), 870 (m), 948 (s), 1038 (w), 1082 (br s), 1123 (m), 1189 (s), 1372 (m), 1462 (s), 2882 (s), 2960 (br s), 3425 (br s) cm^{-1}.

3.2.5. 1-(Isopropyloxy)-3-bromo-2-propanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.16 (d, 6H, J=4.0 Hz), 2.78 (s, 1H), 3.42–3.65 (m, 5H), 3.92 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 22.3, 35.4, 69.6, 70.4, 72.7; IR (neat) 675 (m), 798 (w), 923 (m), 1051 (s), 1085 (s), 1125 (m), 1375 (m), 1467 (m), 2871 (m), 2925 (m), 2972 (s), 3435 (br s) cm^{-1}.

3.2.6. 1-(Isopropyloxy)-3-iodo-2-propanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.15 (d, 6H, J=4.0 Hz), 2.92 (s, 1H), 3.38–3.59 (m, 5H), 3.79 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 22.8, 36.2, 67.3, 69.8, 72.5; IR (neat) 743 (w), 923 (m), 1050 (s), 1085 (s), 1128 (s), 1375 (m), 1467 (m), 2870 (m), 2926 (m), 2975 (s), 3472 (br s) cm^{-1}.

3.2.7. 1-Phenoxy-3-bromo-2-propanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.75 (s, 1H), 3.61 (d, 2H, J=5.0 Hz), 4.03 (m, 1H), 4.11 (d, 2H, J=7.0 Hz), 6.78 (d, 1H, J=5.0 Hz), 6.94 (d, 2H, J=8.0 Hz), 7.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 69.6, 69.8, 69.9, 115.0, 116.8, 121.9, 130.0, 132.8; IR (neat) 641 (w), 688 (m), 756 (m), 823 (m), 1038 (s), 1112 (w), 1239 (s), 1375 (m), 1494 (s), 1588 (s), 2878 (m), 2925 (s), 3059 (m), 3415 (br s) cm^{-1}.

3.2.8. 1-Phenoxy-3-iodo-2-propanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.10 (s, 1H), 3.48 (d, 2H, J=5.0 Hz), 4.06 (m, 1H), 4.13 (d, 2H, J=5.6 Hz), 6.78–6.90 (m, 3H), 7.36 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 67.2, 69.7, 70.0, 115.0, 116.9, 121.8, 129.9, 132.9; IR (neat) 650 (w), 678 (w), 760 (m), 823 (m), 1038 (s), 1113 (w), 1240 (s), 1375 (m), 1494 (s), 1588 (s), 2877 (m), 2927 (s), 3050 (m), 3418 (br s) cm^{-1}.

3.2.9. 1-(*p*-Tolyloxy)-3-bromo-2-propanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.12 (s, 1H), 2.53 (s, 3H), 3.16 (d, 2H, J=5.0 Hz), 3.47 (m, 1H), 4.11 (d, 2H, J=7.0 Hz), 6.93 (d, 2H, J=8.8 Hz), 7.19 (d, 2H, J=7.5 Hz); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 26.2, 59.8, 69.4, 70.65, 95.9, 115.3, 130.4, 157.2; IR (neat) 659 (s), 819 (m), 1016 (s), 1075 (w), 1123 (s), 1242 (s), 1285 (m), 1381 (w), 1458 (m), 1512 (s), 1585 (m), 1613 (m), 2875 (m), 2927 (s), 2962 (m), 3035 (m), 3425 (br, s) cm^{-1}.

3.2.10. 1-(*p*-Tolyloxy)-3-iodo-2-propanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.15 (s, 1H), 2.49 (s, 3H), 3.02 (d, 2H, J=4.1 Hz), 3.46 (m, 1H), 4.16 (d, 2H, J=5.6 Hz), 6.95 (d, 2H, J=8.5 Hz), 7.23 (d, 2H, J=8.2 Hz); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 24.1, 58.3, 66.2, 69.4, 95.8, 114.45, 130.1, 156.8; IR (neat) 665 (s), 743 (w), 814 (m), 1015 (s), 1072 (w), 1123 (s), 1240 (s), 1286 (m), 1378 (w), 1462 (m), 1512 (s), 1586 (m), 1611 (m), 2875 (m), 2928 (s), 2962 (m), 3038 (m), 3422 (br, s) cm^{-1}.

3.2.11. 2-Bromo-1-phenylethanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.98 (s, 1H), 4.01 (m, 2H), 4.98 (t, 1H, J=5.0 Hz), 7.19–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 57.4, 68.0, 128.3, 129.3, 129.4, 139.0; IR (neat) 689 (m), 766 (m), 823 (m), 1036 (s), 1115 (w), 1233 (s), 1375 (m), 1494 (m), 1600 (s), 2875 (m), 2935 (s), 3064 (m), 3405 (br, s) cm^{-1}.

3.2.12. 2-Iodo-1-phenylethanol. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.02 (s, 1H), 3.76 (d, 2H), 4.78 (t, 1H, J=5.0 Hz), 7.17–7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 62.89 MHz) δ 54.7, 66.9, 128.2, 129.1, 129.2, 138.2; IR (neat) 748 (m), 915 (m), 1032 (s), 1121 (w), 1243 (s),

1365 (m), 1492 (m), 1602 (s), 2885 (m), 2930 (s), 3061 (m), 3398 (br, s) cm^{-1}.

Acknowledgements

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