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Trihaloisocyanuric Acid/Triphenylphosphine: An Efficient System for Regioselective Conversion of Epoxides into Vicinal Halohydrins and Vicinal Dihalides under Mild Conditions

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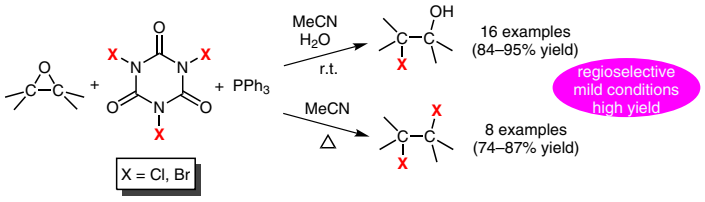

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Abstract A new synthetic method has been developed for the regioselective conversion of epoxides to vicinal chloro-/bromohydrins and vicinal dihalides by reaction with the system trihaloisocyanuric acid/triphenylphosphine in acetonitrile under mild and neutral conditions. The reactions proceed smoothly in high yield at room temperature and at reflux, respectively, over a short time.

Key words dihalide, epoxide, halohydrin, halogenation, N-halo reagent

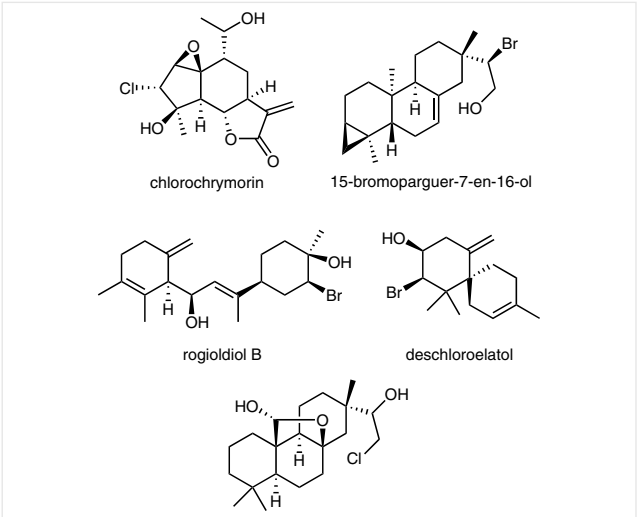

Figure 1 Examples of naturally occurring halohydrins

Epoxides occupy a privileged position in organic synthesis as important synthetic intermediates.[1] Their strained three-membered ring facilitates the attack of various species (e.g., nucleophiles, acids, bases, etc.); consequently the ring-opening reaction is a versatile transformation for the preparation of diverse moieties.[2] The most representative class of epoxide derivatives are vicinal halohydrins. In addition to being useful synthetic building blocks,[3] these compounds have been used for the preparation of a wide range of other functionalities.[4] Furthermore, vicinal haloalcohols are constituents of a variety of naturally occurring organohalogens in marine organisms[5] and, therefore, a potential source of medicinal drugs. A few examples of naturally occurring halohydrins are shown in Figure 1.

The ring-opening of epoxides to produce vicinal halohydrins is a well-known reaction and it is generally achieved by using hydrogen halides, molecular halogens, or metal halides.[6] However, these approaches face some disadvantages due to the use of expensive and toxic reagents. In addition, acid-sensitive substrates may not tolerate such harsh conditions. Therefore, a large number of alternative methods to accomplish these transformations are reported in the literature and a few examples include the use of haloboranes,[7] LiX,[8] LiCl/$TiCl_4$,[9] and pyridine hydrochloride.[10] Another interesting approach involves the use of triphenylphosphine combined with an electrophilic source of halogen (PPh_3/X_2,[11] PPh_3/*N*-halosuccinimides,[12] and PPh_3/*N*-halosaccharins[12]).

On the other hand, there are only a few methodologies to achieve the direct conversion of epoxides to vicinal dihalides. These include the reactions of epoxides with chlorobenzoxazolium salts,[13] triphenylphosphine dihalides,[14] or with in situ formed organophosphonium halides from phosphines in combination with carbon tetrahalides,[15] DDQ,[16] and *N*-halo compounds.[12,17] Recently, Denton et al. reported a convenient conversion of epoxides into corresponding vicinal dihalides promoted by the triphenylphosphine oxide (catalytic)/oxalyl chloride system.[18]

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Trihaloisocyanuric acids [1,3,5-trihalo-1,3,5-triazine-2,4,6-(1*H*,3*H*,5*H*)-triones, Figure 2], which are safe and stable electrophilic halogenating reagents, belong to the large group of *N*-haloimides. Trichloroisocyanuric acid (TCCA) is an inexpensive commercially available solid mainly used for cleaning and disinfection purposes.[19] Tribromoisocyanuric acid (TBCA)[20] is an analogue that can be easily prepared from inexpensive materials[21] (i.e., cyanuric acid, KBr, and Oxone™). From the green chemistry point of view, these reagents can transfer three electrophilic halogens atoms to a substrate, corresponding to up to 46% (TCCA) and 66% (TBCA) of their mass.[22] In addition, at the end of the halogenations process, cyanuric acid, which is obtained as a by-product, precipitates and can be recovered to produce more of the corresponding trihaloisocyanuric acid.[23]

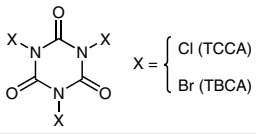
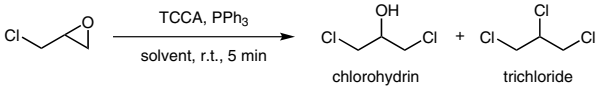


Figure 2 Trihaloisocyanuric acids (TXCA)

Recently, we reported an effective conversion of alcohols into alkyl bromides using the system PPh_3/TBCA[24] as an alternative to the Appel reaction.[25] Herein, we wish to report our results on the regioselective conversion of epoxides to vicinal halohydrins and dihalides using the system trihaloisocyanuric acid/PPh_3 under mild and neutral conditions.

Optimization studies were performed by using epichlorohydrin as a model substrate in a molar ratio 1.0:0.5:1.5 of epoxide/TCCA/PPh_3 at room temperature and the results are shown in Table 1. When dichloromethane and acetonitrile were used as solvents, a mixture of the trichloride and the chlorohydrin was obtained. However, when the reaction was performed in 2% aqueous acetonitrile, a highly chemoselective conversion of the epoxide to 1,3-dichloro-2-propanol was achieved.

Table 1 Optimization Studies for the Conversion of Epoxides to Vicinal Halohydrins



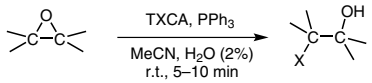
Solvent	Chlorohydrin/trichloride[a,b]
CH_2Cl_2	83:17
MeCN	26:74
MeCN/H_2O (2%)	100:0

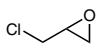
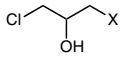
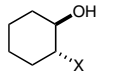
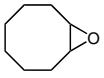
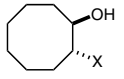
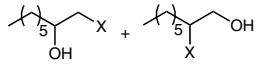
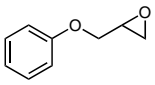
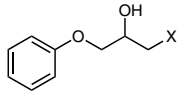
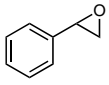
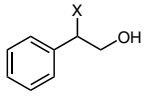
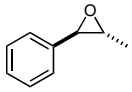
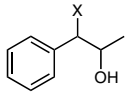
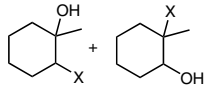
[a] Reactions were performed using a molar ratio 1.0:0.5:1.5 of epichlorohydrin/TCCA/PPh_3.
[b] Conversion determined by GC-MS.

Based on these results, the optimized conditions were extended to different epoxides **1** using TCCA and TBCA as electrophilic halogen sources to produce the corresponding vicinal halohydrins **2** in high yields (Table 2). Although trihaloisocyanuric acids are effective reagents for oxidation of alcohols[26] and halogenation of arenes,[27] none of these products were detected by the analytical techniques employed in the crude reaction.

Despite numerous reports on the chemistry of halophosphonium salts $[Ph_3PX]^+$ (i.e., the reactive species formed from triphenylphosphine and a halenium source[25a]), the mechanism of the conversion of epoxides to

Table 2 Conversion of Epoxides into Halohydrins with TXCA/PPh_3[a]



Entry[a]	Epoxide **1**	Halohydrin **2**	Yield (%)[b] X = Cl	Yield (%)[b] X = Br
a			89	91
b			88	93
c			88	85
d		 (3:1)[c]	87	84
e			90	92
f			93	95
g		 (3:1)[c,d]	89	93
h		 1:1 (X = Cl)[c] 2:1 (X = Br)[c]	87	90

[a] Reactions were performed using a molar ratio 1.0:0.5:1.5 of epoxide/TXCA/PPh_3.
[b] Isolated yield.
[c] Determined by GC-MS.
[d] Ratio of *anti*/*syn*.

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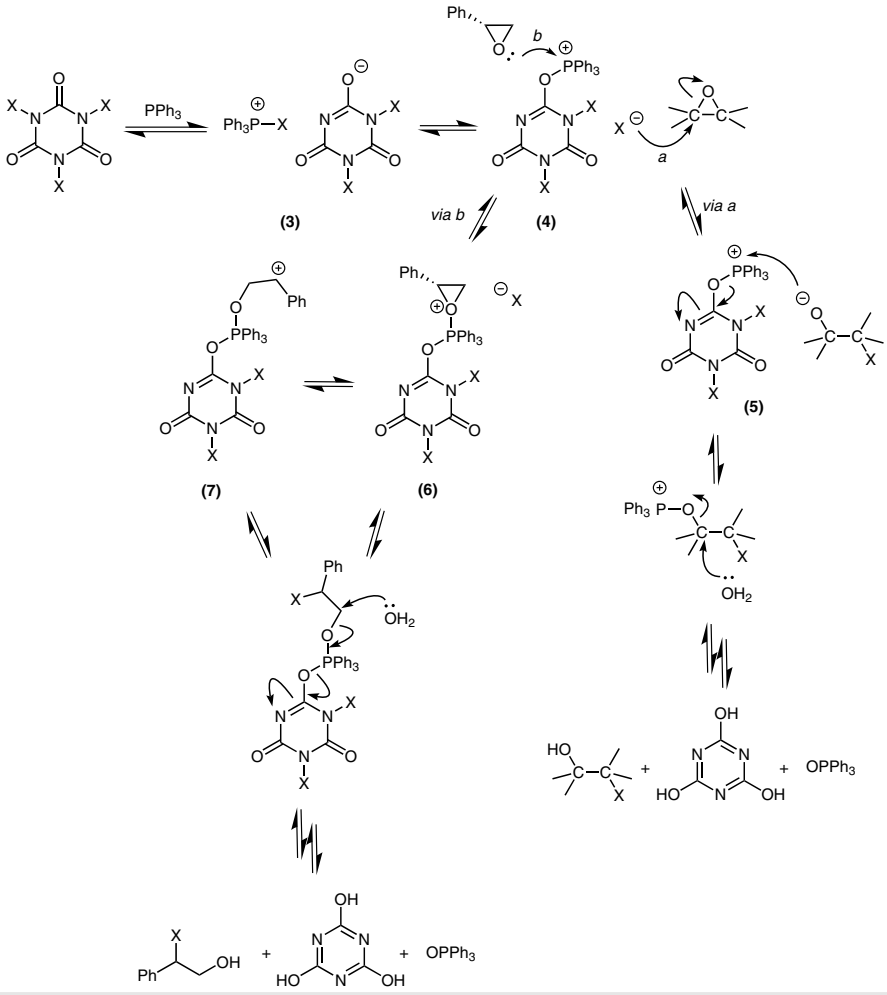
halohydrins is still complex and controversial as the conjunction of steric and electronic effects seems to be a key factor that controls the regioselectivity of the reaction.

Based on the results shown in Table 2, the regioselective formation of halohydrins **2a**–**e** suggested a nucleophilic opening of the epoxide on the less-substituted carbon. A plausible scheme for such a transformation (via *a* in Scheme 1) proceeds via the formation of a halophosphonium ion pair **3**, which is in equilibrium with the inverted species **4**.[25a] Further attack of the halide counterion opens the epoxide with subsequent formation of the alkoxyphosphonium **5**. Water reacts with **5** to produce the corresponding halohydrin along with triphenylphosphine oxide. After two repetitions of the whole process, cyanuric acid is formed and precipitates at the end of the reaction.

However, the regioselective formation of halohydrins **2f**,**g** demonstrates that the above mechanism is not always valid, especially when phenyloxiranes are the substrates. Using styrene oxide (**1f**), the reaction leads to a regioselective formation of 2-halo-2-phenylethanol **2f**, which suggests that a benzylic carbocation might be involved in these cases. In order to support this hypothesis, we performed the reaction using (*R*)-(+)-styrene oxide (97% ee) as substrate and obtained (*S*)-(+)-2-chlorophenylethanol in 43% ee by polarimetry[28] (44% ee by chiral-GC[29]), a considerable low ee value, implying a partial racemization during the reaction. On the other hand, *trans*-1-phenylpropene oxide (**1g**) gave a mixture of *syn*- and *anti*-1-halo-1-phenyl-2-propanols, the relative configurations of which were confirmed by chemical correlation. The diasteromeric mixture was converted into 1-phenylpropene oxide by alkaline treatment and the *cis*- and *trans*-epoxides were determined by co-injection in GC-MS with reference samples. The *syn*-halohydrin gives the *cis*-epoxide while the *anti*-halohydrin gives the *trans*-epoxide.[30]

Therefore, via *b* in Scheme 1 depicts a plausible way for these transformations via intermediacy of the pentavalent phosphorane **6**, formed from the attack of the epoxide to the inverted phosphonium species **4**. Epoxide ring-opening appears to occur mainly from a direct attack of the halide



Scheme 1 Mechanistic scheme for the formation of halohydrins from epoxides and TXCA/PPh_3

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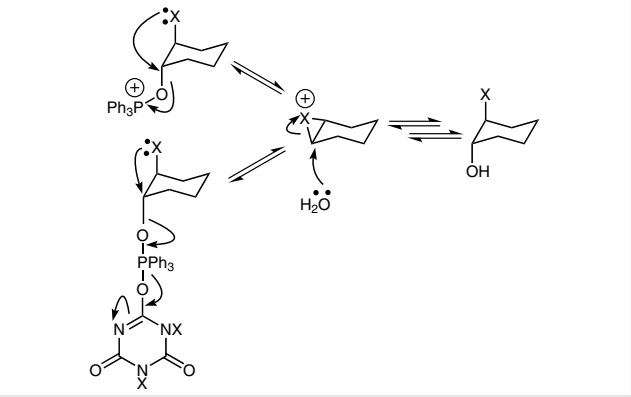
counterion to the pentavalent phosphorane adduct, which results in the inversion of stereochemistry at the benzylic position. Alternatively, equilibrium between species **6** and the benzylic cation **7**, followed by halide attack and further reaction with water yields the halohydrin along with triphenylphosphine oxide. Once more, after two repetitions of the whole process, cyanuric acid is formed.

As expected, regioselective formation of products **2f**–**h** is in agreement with the intermediacy of benzylic carbocations. Therefore, the reaction appears to proceed via two major competitive pathways (Scheme 1), depending on the nature of the substrate. The use of methylcyclohexene oxide (**1h**) as substrate evidenced the competitive nature of both mechanisms. Anyway, clearly the driving force of these reactions is the formation of a thermodynamically favored phosphine oxide by-product.

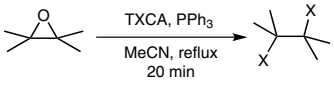
Another important consideration is based on the reaction of cycloalkene oxides **1b**,**c** with TXCA/PPh_3 system to form *trans*-halohydrins. In these cases, both mechanistic pathways lead to the desired product. However, displacement of triphenylphosphine oxide may occur via an anchimeric assistance of the halide. Further attack of water to the halonium ion results in the vicinal halohydrin with *anti*-stereochemistry (Scheme 2). The substrate scope of these reactions highlights how steric and electronic effects govern their reactivity pattern.

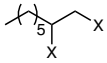
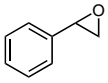
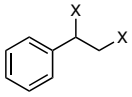
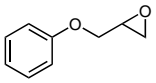
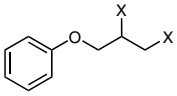


Scheme 2 Mechanistic scheme for the formation of *trans*-halohydrins

On the other hand, when the reaction was performed in acetonitrile under reflux using a molar ratio 1.0:0.85:2.5 of epoxide/TXCA/PPh_3, quantitative conversion of the epoxides to vicinal dihaloalkanes was achieved within 20 minutes (Table 3). These conditions avoid the use of strong acidic conditions and metal salts, traditionally employed in the synthesis of vicinal halohydrins and dihalides.[6,8–10,31] Based on the mechanistic proposals shown above, the transformation of the epoxide to its dihalide by the TXCA/PPh_3 system can be explained in an analogue form from Scheme 1.

Table 3 Conversion of Epoxides into Dihaloalkanes with TXCA/PPh3

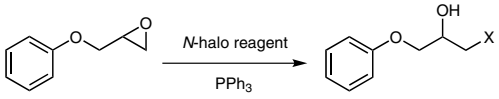


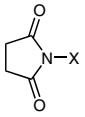
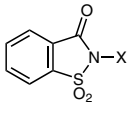
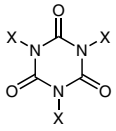
Epoxide	Dihalide	Yield (%)[a,b]	
		X = Cl	X = Br
		78	75
		85	80
		87	80
		74[c,d]	77[c,d]

[a] Reactions were performed using a molar ratio 1.0:0.85:2.5 of epoxide/TXCA/PPh_3.
[b] Isolated yield.
[c] Conversion (determined by GC-MS).
[d] Formed along with 3-halocyclohexene (ca. 23%).

Although TXCA gives similar yields compared to other *N*-halo reagents, they have advantages as being easily accessible (or prepared) and possess a higher percentage of mass

Table 4 Preparation of 1-Halo-3-phenoxy-2-propanol Using Diverse N-Halo Reagents



N-Halo reagent	Yield (%)		Mass transferred (%)[a]		Reference
	X = Cl	X = Br	X = Cl	X = Br	
	88	93	26.5	44.9	12
	92	95	16.3	30.4	12
	90	92	45.7	65.5	this work

[a] Mass of the reagent (%) transferred to PPh_3.

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transferred to triphenylphosphine to generate the halophosphonium salt (reactive species), which is consistent with the green chemistry approach[32] (Table 4).

In summary, we have developed an efficient route for the preparation of vicinal halohydrins from epoxides using TXCA/PPh_3 system under mild and neutral conditions. The chosen substrates allowed important mechanistic considerations. The reactions are easily reproducible and the products are obtained over a short period of time and high yield. We have also presented an alternative route to vicinal dihalides from epoxides and further examples are under investigation in our laboratory.

Epoxides were purchased from Aldrich or prepared by epoxidation of the corresponding alkenes with *m*CPBA. All products are known compounds and identified by their spectral data in comparison with the literature data. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 300 spectrometer at 300 MHz and 75 MHz, respectively. IR spectra were recorded on a Nicolet 6700FT-IR spectrophotometer as neat films on KBr plates. MS (electron impact) were recorded on a GCMS-QP2010S. Chiral-GC analysis were performed on a Shimadzu GC2010 (FID) using a Supelco β-Dex120 (30 m × 0.25 mm × 0.25 µm) column. Analysis conditions: H_2 pressure: 90 kPa, injector: 200 °C, detector: 200 °C, temperature program: 112–122 °C (0.4 °C/min)//122–170 °C (15 °C/min)//170 °C (15 min). Polarimetric analysis was done in a Perkin Elmer 341LC polarimeter.

Vicinal Halohydrins; General Procedure

TXCA (0.5 mmol) was added to a stirred solution of PPh_3 (393 mg, 1.5 mmol) in 2% aq MeCN (10 mL) at r.t. The appropriate epoxide (1 mmol) was added to the mixture and the reaction mixture was stirred for 5–10 min. After completion of the reaction (TLC or GC), the suspension was filtered and the solvent was removed under reduced pressure. The crude residue was purified by column chromatography on silica gel using pentane/Et_2O (1:1) to give the corresponding vicinal halohydrin (Table 2).

1,3-Dichloro-2-propanol[8]

Colorless oil (114 mg, 89% yield).

IR (neat): 3399, 2962, 2917, 1430, 1297, 1280, 1253, 1076, 1052, 964, 885, 829, 759, 701, 572 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.06 (quint, *J* = 5.3 Hz, 1 H), 3.69 (d, *J* = 5.3 Hz, 4 H), 2.57 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 70.9, 45.8.

MS (70 eV): *m*/*z* = 131 (M^+ + 4), 129 (M^+ + 2), 127 (M^+), 81, 79 (100%), 43.

1-Bromo-3-chloro-2-propanol[8]

Light yellow oil (157 mg, 91% yield).

IR (neat): 3399, 2962, 2908, 1429, 1382, 1294, 1261, 1193, 1089, 1068, 1041, 995, 865, 821, 761, 711, 669, 642, 551, 522, 497 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.04 (m, 1 H), 3.76–3.67 (m, 2 H), 3.57 (d, *J* = 5.3 Hz, 2 H), 2.66 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 70.6, 46.6, 34.9.

MS (70 eV): *m*/*z* = 175 (M^+ + 2), 173 (M^+), 125, 123, 81, 79, 43 (100%).

2-Chloro-2-phenylethanol[8]

Colorless oil (145 mg, 93% yield).

IR (neat): 3372, 3085, 3064, 3031, 3008, 2948, 2927, 2871, 1492, 1454, 1386, 1253, 1195, 1066, 1025, 966, 914, 842, 798, 761, 698, 615, 518 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.43–7.33 (m, 5 H), 5.00 (dd, *J* = 7.2, 5.9 Hz, 1 H), 3.99–3.89 (m, 2 H), 2.08 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.0, 129.1, 129.0, 127.6, 68.1, 65.0.

MS (70 eV): *m*/*z* = 158 (M^+ + 2), 156 (M^+), 127, 126, 125 (100%), 91, 77, 65, 51.

2-Bromo-2-phenylethanol[8]

Light yellow oil (191 mg, 95% yield).

IR (neat): 3263, 3095, 6064, 3031, 2950, 2935, 2888, 1492, 1454, 1390, 1209, 1195, 1078, 1056, 1022, 1002, 984, 840, 761, 698, 682, 617, 592, 559, 509 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.43–7.30 (m, 5 H), 5.06 (dd, *J* = 7.7, 5.8 Hz, 1 H), 2.15 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.4, 129.1, 129.0, 128.1, 67.7, 57.0.

MS (70 eV): *m*/*z* = 202 (M^+ + 2), 200 (M^+), 171, 169, 121 (100%), 103, 91, 77, 65, 51.

trans-2-Chlorocyclohexanol[33]

Colorless oil (118 mg, 88% yield).

IR (neat): 3399, 2940, 2861, 1450, 1363, 1261, 1214, 1126, 1074, 1037, 960, 865, 798, 734, 705, 559, 476 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.71 (ddd, *J* = 11.5, 9.3, 4.4 Hz, 1 H), 3.50 (td, *J* = 11.8, 4.6, Hz, 1 H), 2.51 (br s, 1 H), 2.25–2.06 (m, 2 H), 1.76–1.56 (m, 3 H), 1.41–1.21 (m, 3 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 75.5, 67.6, 35.3, 33.2, 25.8, 24.1.

MS (70 eV): *m*/*z* = 136 (M^+ + 2), 134 (M^+), 118, 116, 80, 57 (100%), 44, 41.

trans-2-Bromocyclohexanol[21]

Light yellow oil (166 mg, 93% yield).

IR (neat): 3394, 2939, 2859, 1448, 1361, 1186, 1072, 1035, 956, 862, 690, 555 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.91 (ddd, *J* = 12.0, 9.4, 4.3 Hz, 1 H), 3.61 (td, *J* = 9.4, 4.3 Hz, 1 H), 2.41–2.32 (m, 2 H), 2.17–2.15 (m, 1 H), 1.87–1.69 (m, 3 H), 1.46–1.21 (m, 3 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 75.5, 62.0, 36.4, 33.7, 26.8, 24.3.

MS (70 eV): *m*/*z* = 180 (M^+ + 2), 178 (M^+), 134, 132, 99, 81 (100%), 57, 41.

trans-2-Chlorocyclooctanol[34]

Colorless oil (143 mg, 88% yield).

IR (neat): 3423, 2928, 2857, 1464, 1446, 1239, 1078, 1050, 1002, 988, 825, 743, 707, 571 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.11 (ddd, *J* = 9.7, 7.5, 2.8 Hz, 1 H), 3.86 (m, 1 H), 2.43 (s, 1 H), 2.26–2.16 (m, 1 H), 2.06–1.43 (m, 11 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 76.4, 71.4, 32.5, 32.1, 25.9, 25.8, 24.9, 24.2.

MS (70 eV): *m*/*z* = 146, 144, 116, 109, 95, 82, 67, 57 (100%), 41.

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***trans*-2-Bromocyclooctanol**[35]

Colorless oil (176 mg, 85% yield).

IR (neat): 3425, 2927, 2858, 1463, 1444, 1047, 823, 665 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 4.29 (ddd, *J* = 9.8, 7.3, 2.8 Hz, 1 H), 3.98 (m, 1 H), 2.36–2.25 (m, 2 H), 2.14–1.39 (m, 11 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 76.8, 67.2, 33.1, 32.3, 25.9, 25.8, 25.2.

MS (70 eV): *m*/*z* = 190, 188, 109, 81, 67, 57 (100%), 41.

1-Chloro-1-phenyl-2-propanol[36]

Mixture of diastereomers 3:1 (*anti*/*syn*); colorless oil (151 mg, 89% yield).

***anti*-Isomer**

^1H NMR ($CDCl_3$, 300 MHz): δ = 7.43–7.28 (m, 5 H), 4.78 (d, *J* = 5.9 Hz, 1 H), 4.79–4.06 (m, 1 H), 2.10 (br s, 1 H), 1.26 (d, *J* = 6.2 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.0, 128.7, 128.2, 127.8, 71.9, 68.3, 19.2.

MS (70 eV): *m*/*z* = 172 (M^+ + 2), 170 (M^+), 126, 91 (100%), 77, 65, 45.

***syn*-Isomer**

^1H NMR ($CDCl_3$, 300 MHz): δ = 7.43–7.28 (m, 5 H), 4.70 (d, *J* = 7.8 Hz, 1 H), 4.79–4.06 (m, 1 H), 2.13 (br s, 1 H), 1.06 (d, *J* = 6.2 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.7, 128.9, 128.89, 128.81, 72.1, 71.1, 19.5.

MS (70 eV): *m*/*z* = 172 (M^+ + 2), 170 (M^+), 126, 91 (100%), 77, 65, 45.

1-Bromo-1-phenyl-2-propanol[37]

Mixture of diastereomers 3:1 (*anti*/*syn*); colorless oil (200 mg, 93% yield).

***anti*-Isomer**

^1H NMR ($CDCl_3$, 300 MHz): δ = 7.49–7.42 (m, 2 H), 7.38–7.31 (m, 3 H), 4.89 (d, *J* = 6.3 Hz, 1 H), 4.28–4.17 (m, 1 H), 2.15 (br s, 1 H), 1.36 (d, *J* = 6.3 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.2, 128.7, 128.7, 128.6, 71.5, 60.7, 20.0.

MS (70 eV): *m*/*z* = 172 (M^+ + 2), 170 (M^+), 126, 91 (100%), 77, 65, 45.

***syn*-Isomer**

^1H NMR ($CDCl_3$, 300 MHz): δ = 7.49–7.42 (m, 2 H), 7.38–7.31 (m, 3 H), 4.88 (d, *J* = 8.1 Hz, 1 H), 4.28–4.17 (m, 1 H), 2.15 (br s, 1 H), 1.12 (d, *J* = 6.2 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.1, 128.7, 128, 128,0, 71.5, 65.0, 19.6.

MS (70 eV): *m*/*z* = 172 (M^+ + 2), 170 (M^+), 126, 91 (100%), 77, 65, 45.

1-Chloro-3-phenoxy-2-propanol[8]

Colorless oil (167 mg, 90% yield).

IR (neat): 3399, 3095, 3062, 3041, 2950, 2931, 2879, 1598, 1588, 1496, 1243, 1045, 754, 692, 509 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 7.35–7.26 (m, 2 H), 7.04–6.85 (m, 3 H), 4.24 (quint, *J* = 5.2 Hz, 1 H), 4.15–4.06 (m, 2 H), 3.81 (dd, *J* = 11.3, 5.4 Hz, 1 H), 3.76 (dd, 11.3, 5.4 Hz, 1 H), 2.63 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.2, 129.5, 121.2, 114.5, 69.8, 68.4, 45.9.

MS (70 eV): *m*/*z* = 188 (M^+ + 2), 186 (M^+), 169, 107, 94 (100%), 77, 65, 51.

1-Bromo-3-phenoxy-2-propanol[8]

Colorless oil (212 mg, 92% yield).

IR (neat): 3409, 3093, 3062, 3039, 2931, 2877, 1598, 1588, 1496, 1243, 1045, 754, 692, 509 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.28 (m, 2 H), 7.04–6.93 (m, 3 H), 4.22 (quint, *J* = 5.2 Hz, 1 H), 4.16–4.05 (m, 2 H), 3.69 (dd, *J* = 10.4, 5.1 Hz, 1 H), 3.61 (dd, *J* = 10.5, 5.6 Hz, 1 H), 2.37 (br s, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 158.1, 129.5, 121.4, 114.5, 69.5, 69.1, 34.9.

MS (70 eV): *m*/*z* = 232 (M^+ + 2), 230 (M^+), 137, 133, 107, 94 (100%), 77, 51.

1-Chloro-2-octanol and 2-Chloro-1-octanol[33]

Mixture of regioisomers (3:1); colorless oil (143 mg, 87% yield).

1-Chloro-2-octanol

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 71.6, 50.7, 34.4, 31.8, 29.3, 25.6, 22.7, 14.2.

MS (70 eV): *m*/*z* = 147, 115, 97, 79, 69, 55 (100%), 43.

2-Chloro-1-octanol

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 67.2, 65.5, 34.4, 31.7, 28.9, 26.4, 22.7, 14.2.

MS (70 eV): *m*/*z* = 123, 121, 93, 91, 82, 81, 70, 57, 55 (100%), 43, 41.

1-Bromo-2-octanol and 2-Bromo-1-octanol[21]

Mixture of regioisomers (3:1); light yellow oil (175 mg, 84% yield).

1-Bromo-2-octanol

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 71.0, 40.4, 35.0, 31.6, 29.0, 25.4, 22.4, 13.9.

MS (70 eV): *m*/*z* = 193, 191, 125, 123, 115, 97, 69, 55 (100%), 43.

2-Bromo-1-octanol

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 67.1, 59.9, 34.8, 31.5, 28.5, 27.3, 22.4, 13.9.

MS (70 eV): *m*/*z* = 167, 165, 137, 135, 111, 69 (100%), 55, 43, 41.

2-Chloro-1-methylcyclohexanol and 2-Chloro-2-methylcyclohexanol[38]

Mixture of regioisomers (1:1); colorless oil (129 mg, 87% yield).

2-Chloro-1-methylcyclohexanol

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 72.8, 70.2, 38.0, 33.5, 24.9, 22.6, 21.9.

MS (70 eV): *m*/*z* = 150 (M^+ + 2), 148 (M^+), 114, 112, 71 (100%), 58, 43.

2-Chloro-2-methylcyclohexanol

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 77.2, 77.1, 40.7, 30.0, 23.3, 23.1, 22.6.

MS (70 eV): *m*/*z* = 150 (M^+ + 2), 148 (M^+), 132, 130, 104, 102, 95, 94, 68, 57 (100%), 41.

2-Bromo-1-methylcyclohexanol and 2-Bromo-2-methylcyclohexanol[39]

Mixture of regioisomers (2:1); colorless oil (173 mg, 90% yield).

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2-Bromo-1-methylcyclohexanol

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 72.5, 66.0, 38.2, 34.7, 26.2, 23.1, 22.8.

MS (70 eV): *m*/*z* = 194 (M^+ + 2), 192 (M^+), 113, 95, 71 (100%), 43.

2-Bromo-2-methylcyclohexanol

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 77.8, 75.9, 42.4, 34.7, 29.9, 23.8, 23.6.

MS (70 eV): *m*/*z* = 148, 146, 113, 95 (100%), 67, 57.

Vicinal Dihalides; General Procedure

TXCA (0.85 mmol) was added to a stirred solution of PPh_3 (655 mg, 2.5 mmol) in MeCN (15 mL). The appropriate epoxide (1 mmol) was added to the mixture and the system was refluxed for 20 min. After the completion of the reaction (GC), the suspension was filtered and H_2O (5 mL) was added to the solution. The mixture was extracted with pentane (3 × 7 mL). The combined organic phase were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography on silica gel using pentane/Et_2O (8:2) to give the corresponding vicinal dihalide (Table 3).

1,2-Dichlorooctane[40]

Colorless oil (142 mg, 78% yield).

IR (neat): 2956, 2927, 2858, 1465, 1444, 1432, 1378, 727, 663 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.08–4.00 (m, 1 H), 3.76 (dd, *J* = 11.2, 5.0 Hz, 1 H), 3.65 (dd, *J* = 11.3, 7.4 Hz, 1 H), 2.04 (m, 1 H), 1.76–1.65 (m, 1 H), 1.56–1.30 (m, 8 H), 0.90 (t, *J* = 6.7 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 61.4, 48.4, 35.2, 31.7, 28.8, 25.9, 22.7, 14.2.

MS (70 eV): *m*/*z* = 155, 153, 141, 139, 104, 97, 81, 70, 55, 43 (100%).

1,2-Dibromooctane[41]

Colorless oil (204 mg, 75% yield).

IR (neat): 2956, 2929, 2858, 1465, 1432, 1145, 725, 646, 570 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.23–4.10 (m, 1 H), 3.87 (dd, *J* = 10.2, 4.4 Hz, 1 H), 3.65 (t, *J* = 10.0 Hz, 1 H), 2.21–2.10 (m, 1 H), 1.90–1.74 (m, 1 H), 1.63–1.32 (m, 8 H), 0.91 (t, *J* = 6.4 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 53.3, 36.5, 36.2, 31.7, 28.6, 26.9, 22.7, 14.2.

MS (70 eV): *m*/*z* = 193, 191, 151, 149, 137, 135, 111, 69 (100%), 41.

1,2-Dichloro-3-phenoxypropane[42]

Colorless oil (178 mg, 87%).

IR (neat): 3063, 3041, 2932, 2876, 1600, 1589, 1497, 1458, 1302, 1292, 1244, 1173, 1079, 1057, 1039, 932, 817, 755, 691 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.34–7.26 (m, 2 H), 7.03–6.92 (m, 3 H), 4.38 (quint, *J* = 5.3 Hz, 1 H), 4.30–4.25 (m, 2 H), 3.98 (dd, *J* = 11.5, 6.1 Hz, 1 H), 3.91 (dd, *J* = 11.5, 5.1 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 157.9, 129.8, 121.9, 115.0, 68.4, 57.5, 45.2.

MS (70 eV): *m*/*z* = 208 (M^+ + 4), 206 (M^+ + 2), 204 (M^+), 107, 94 (100%), 77, 65, 51.

1,2-Dibromo-3-phenoxypropane[43]

Light yellow oil (235 mg, 80%).

IR (neat): 3064, 3039, 2923, 2868, 2849, 1598, 1588, 1496, 1455, 1243, 753, 690, 577 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.36–7.28 (m, 2 H), 7.05–6.95 (m, 3 H), 4.50–4.35 (m, 3 H), 4.00–3.86 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 157.9, 129.5, 121.6, 114.8, 69.1, 47.7, 32.7.

MS (70 eV): *m*/*z* = 296 (M^+ + 4), 294 (M^+ + 2), 292 (M^+), 94 (100%), 77, 65, 51.

1,2-Dichloro-1-phenylethane[18]

Colorless oil (148 mg, 85%).

IR (neat): 3065, 3033, 2952, 1493, 1455, 1426, 771, 733, 697, 592 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.38–7.32 (m, 5 H), 4.97 (dd, *J* = 7.9, 6.6 Hz, 1 H), 3.97 (dd, *J* = 11.3, 6.6 Hz, 1 H), 3.89 (dd, *J* = 11.3, 7.8 Hz, 1 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 137.9, 129.1, 128.7, 127.3, 61.7, 48.3.

MS (70 eV): *m*/*z* = 178 (M^+ + 4), 176 (M^+ + 2), 174 (M^+), 141, 139, 127, 125 (100%), 103, 77, 51.

1,2-Dibromo-1-phenylethane[44]

White solid (211 mg, 80%); mp 72–73 °C (Lit.[45] mp 73–74 °C).

IR (neat): 3064, 3029, 2980, 2922, 1496, 1455, 1431, 769, 691, 589, 553 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.45–7.35 (m, 5 H), 5.17 (dd, *J* = 10.4, 5.5 Hz, 1 H), 4.14–4.01 (m, 2 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.6, 129.1, 128.8, 127.6, 50.8, 34.9.

MS (70 eV): *m*/*z* = 266 (M^+ + 4), 264 (M^+ + 2), 262 (M^+), 185, 183, 104 (100%), 77, 51.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560408.

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