Cleavage of 2,3-Epoxyalkylhalides by the Sonochemical Zinc–Copper Couple

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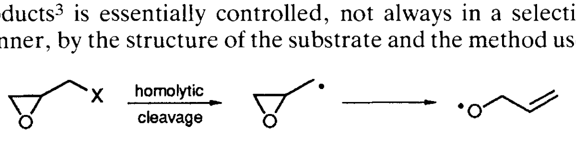
2,3-Epoxyalkylhalides are readily transformed into allylic alcohols when sonicated in the presence of a zinc–copper couple in aqueous ethanol.

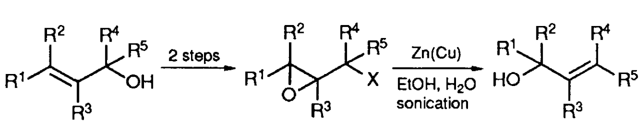
Generation of a radical in the position α to an epoxide function results in the cleavage of the C–O bond (Scheme 1) to give an allyloxy radical.[1]

The synthetic possibilities offered by this process have been investigated by several authors. The evolution of the reactive allyloxy radical either to the allylic alkoxide[2] or to cyclised products[3] is essentially controlled, not always in a selective manner, by the structure of the substrate and the method used to generate the radical. We wish to report a new procedure that allows the preparation of the allylic alcohol with a high selectivity, by the use of the zinc–copper couple under sonochemical conditions.

We recently described the possibilities of this reagent to promote the conjugate additions of alkyl halides to α,β-

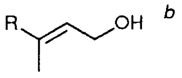
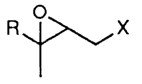
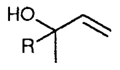
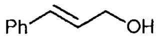
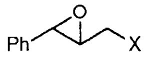
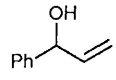
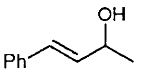
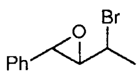
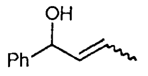
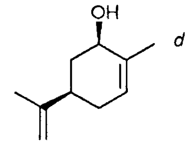
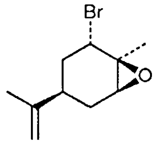
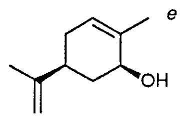
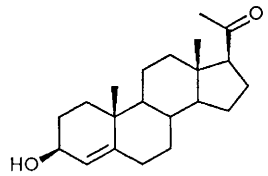
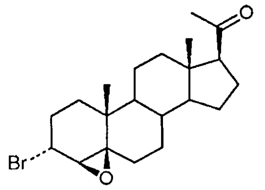
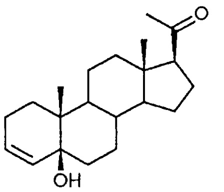


Scheme 1

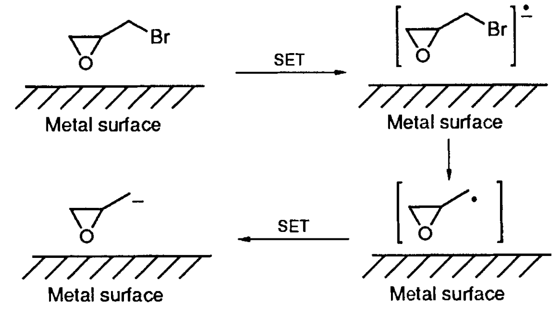


Scheme 2

Table 1

Run	Initial alcohol	Epoxyhalide[a] (yield %)	Final alcohol	Yields (%)[a]	
				From epoxyhalide	Overall
	 [b]				
1		X = Br (90)		94	84
2		X = I (60)		94	56
3		X = OTs, Cl		0	0
					
4		X = Br (97)		95	92
5		X = I (71)		92	65
6		 (74)	 [c]	93	68
7	 [d]	 (57)	 [e]	93	53
8		 (92)		89	82

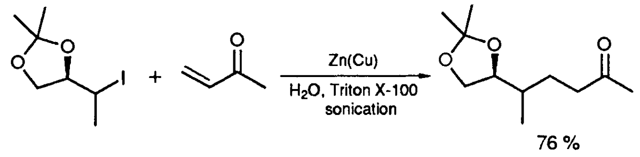
[a] Isolated yields of purified compounds, identified by the usual spectral and analytical methods. [b] Phytol. [c] $E:Z$ = 1.6:1. [d] From (−)-carvone by reduction ($NaBH_4$, $CeCl_3$, MeOH). $[\alpha]_D^{20}$ −39.1° (c 0.7 in acetone). [e] $[\alpha]_D^{20}$ +35.7° (c 0.7 in acetone).



Scheme 3

unsaturated carbonyl compounds.[4] Under the conditions specified, we reached the conclusion that the carbon–halogen bond is cleaved to a carbon centred radical. The same reaction effected from an alkyl halide bearing a vicinal epoxy group showed no trace of addition product but the exclusive formation of the epoxide cleavage product (Scheme 2). As epoxyhalides can be conveniently prepared by known methods from allylic alcohols,† our method provides an efficient procedure for the formal 1,3-transposition of the hydroxy group. Several examples are given in Table 1.

In comparison to previously reported methods, the zinc–copper mediated ring opening exhibits some interesting advantages.



Scheme 4

The reagent is extremely simple to prepare: sonication (Kerry Ultrasonics cleaning bath, Pulsatron 250, 38 kHz, 15 °C) of zinc powder and copper(I) iodide in aqueous ethanol (40% water) provides a black reagent in less than 5 min.[5] After injection of the substrate, a short sonication time (30–90 min) is sufficient to bring the reaction to completion.‡ In the absence of ultrasonic waves, the transformation occurs much more slowly. For instance, run 2 gives only 40% conversion after stirring for 48 h. Our new procedure uses readily prepared derivatives (bromides, iodides) under very simple conditions, in opposition to methods requiring more complicated starting materials (thionoimidazolide esters) or conditions (tin derivatives as reagents under reflux or photochemical irradiation).[2,3]

The stereoselectivity is governed as expected by that of the

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† Epoxyhalides were prepared from the corresponding allylic alcohols by epoxidation (m-chloroperbenzoic acid, satd. aq. $NaHCO_3$, $CHCl_3$) followed by reaction with CBr_4, PPh_3 (for bromides), or tosylation and exchange with NaI in acetone (for iodides).

‡ Zinc dust (585 mg, 9 mmol) and copper(I) iodide (570 mg, 3 mmol) are sonicated under argon in aqueous ethanol (10 ml, 40% water v/v). After the formation of the black suspension, a solution of the substrate (3 mmol) in ethanol (1 ml) was added and sonication is continued until disappearance of the starting material (TLC). Addition of satd. aq. NH_4Cl, filtration and extraction with diethyl ether gives the crude mixture, which can be purified by 'bulb-to-bulb' distillation or column chromatography.

epoxidation step. An example is provided by the transformation of (−)-*cis*-carveol to its enantiomer with a 91% selectivity (Table 1, run 7). Regarding the functional selectivity, a carbonyl group is not affected by the reductive conditions used in the reaction (Table 1, run 8). It can be noted that the method gives excellent results with primary and secondary bromides, while most of the recently reported transformations have been described for primary derivatives only.[6]

From a mechanistic point of view, it can be assumed that the first step of the reaction consists in a single electron transfer from the metal to the carbon–halogen bond, which breaks to give a radical. The next step is unknown. It is generally assumed that this radical opens to the allyloxy species, except when a radical is stabilised on the carbon. In this case the cleavage occurs on the C–C bond.[7] Under our conditions, this type of cleavage has never been observed, even with aromatic substrates. A possible interpretation would then consider a second, very rapid, electron transfer from the metal to the radical (Scheme 3) forming a carbanion which opens selectively to the alkoxide.

It is interesting to note the difference in behaviour between α-halogeno epoxides and α-halogeno dioxolannes. From the latter, the conjugate addition can be obtained, as we have shown with the example given in Scheme 4.

Further studies are under way for the synthetic exploitation of the particular reactivities of alkyl halides bearing carbon–oxygen bonds in various positions.

We thank Drs A. E. Greene and C. Dupuy for helpful discussions. One of us (L. A. S.) thanks NATO for a fellowship.

Received, 8th March 1991; Com. 1/01113H

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