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Sonochemistry of Epoxyalkylhalides in the Presence of a Zinc-Copper Couple

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Under sonication in aqueous ethanol, a zinc-copper couple induces the conjugated addition of epoxyalkyl groups to electron deficient alkenes in synthetically useful yields, provided that the two reducible functionalities are sufficiently far apart; 3,4-epoxyalkylhalides have been found to form cyclopropane adducts.

The epoxide functionality, an important building block in organic synthesis that is present in many natural products, cannot normally be introduced into a molecule by carbanion chemistry.¹ It has recently become possible to prepare epoxyalkylcopper reagents,² but they cyclise intramolecularly.³ In view of our results on the sonochemical addition of alkyl halides to α,β -unsaturated carbonyl compounds and nitriles in the presence of a zinc-copper couple in aqueous media (Scheme 1),⁴ we envisaged the possibility of extending the procedure to epoxyalkylhalides. We first found⁵ that owing to ring opening, 2,3-epoxyalkylhalides do not serve for introduction of the epoxide group by this means. We have now studied 3,4-epoxyalkylhalides (1, Scheme 2).[†]

These compounds were prepared by zinc promoted allylation of aldehydes,⁶ followed by epoxidation⁷ and conversion of the epoxyalcohol to the bromide.⁸ However, sonication of epoxyhalides **1** in the presence of a zinc–copper couple and an α , β -unsaturated carbonyl compound, did not give rise to the conjugated addition product but to cyclopropyl alcohols **2**. Although this route to cyclopropyl alcohols has not yet been optimised, the yields listed in Table 1 are encouraging. The ring opening–ring formation process involved is to some extent analogous to the recently reported Lewis acid catalysed

$$R^1 - X + Z \xrightarrow{Zn(Cu)} R^1 Z$$

$$R^1 = Br, I = Z = CHO, COR, CO_2R, CONR_2, CN$$

[†] All new compounds exhibited satisfactory spectral (¹H NMR, IR, MS) and analytical data.

Table 1

Starting material 1 R ¹	R ²	Cyclopropylmethanol 2 yield (%) ^{<i>a</i>}
c-C ₆ H ₁₁	Н	36
$n-C_6H_{13}$	Н	42
PhCH(Me)–CH ₂	Н	30
Pr	Me	60
PhCH(Me)-CH ₂	Me	58

^{*a*} Among the other detected reaction products, secondary alcohols from the reduction of both the C–Br and CH₂–O epoxide bonds in some cases composed up to 40% of the converted material.



1,3-elimination-cyclisation of 3,4-epoxyalkylstannanes,⁹ for which the conformation and configuration are important for the chemical fate of the initially formed radical.

In contrast to the above results, epoxyalkylhalides 4 and 7 (Scheme 3) in which the reducible groups are separated by at least two carbons, did not undergo intramolecular reactions, but the desired conjugated additions. Compound 4 was prepared from 6-methyl-5-hepten-2-ol 3 in 51% overall yield [p-MeC₆H₄SO₂Cl (p-TsCl), pyridine (py); m-chloroperbenzoic acid (MCBA), CHCl₃; NaI, acetone], and 7 was obtained by the same sequence (71%) from β -citronellol 6. The zinc-copper couple was prepared as usual by sonication‡ of a mixture of zinc dust (3 equiv.) and copper(1) iodide (1 equiv.) suspended in a minimal amount of water. After addition of the reaction solvent (30% aq. ethanol) and the unsaturated substrate (4 equiv.), the epoxyalkylhalide was slowly introduced as a solution in a minimum of ethanol. Then more zinc (1.5 equiv.) and copper(1) iodide (0.5 equiv.) were added, and ultrasonic irradition was continued for 30-90 min until the starting material had disappeared (TLC). Work-up⁴ and purification gave the adduct (5 or 8) in satisfactory yields (Scheme 3).

In most of the cases, the purification of the adduct was very easy, the only impurity being small amounts, usually less than 15%, of the dehalogenated epoxide. The use of an excess of alkene stems from the necessity to intercept efficiently the first reactive species generated, the radical derived from the alkylhalide component. Reductive opening of the epoxide ring does not seem to take place to a significant extent, as the corresponding products are not detected in the mixture. Nor was cyclisation of the initial epoxyhalide by intramolecular attack observed.

We hypothesize that in the presence of a strong reducing agent such as a zinc-copper couple, epoxyalkylhalides first undergo a single electron transfer to give a radical ion,¹⁰ which is more or less readily cleaved to a radical. It should be borne in mind that these processes take place at the surface of the reducing metal, and that electron transfers are strongly





Scheme 3 Reagents and conditions: i, p-TsCl, py, 0 °C; ii, MCPBA, CHCl₃ satd. aq. NaHCO₃, room temp.; iii, NaI, acetone, reflux; iv, Zn, CuI, EtOH: H_2O (7:3), sonication, room temp.

influenced by ultrasonic waves.¹¹ If the reducible groups are too close to each other, their mutual interactions prevent the conjugated addition that, in keeping with normal radical behaviour, does occur if the reducible groups are farther apart.

Though only a limited number of cases have been investigated (Scheme 3), we believe that this method should be useful for synthetic purposes owing to its simplicity. It is worth mentioning that Rieke's method, using active copper solutions has only been used for the coupling of epoxyalkylhalides with acyl chlorides, there have been no reports of conjugated additions.³

The reactions described here for 3,4-epoxyalkylhalides with closely adjacent reducible groups may be useful, in many cases, for simple, rapid, inexpensive synthesis, in satisfactory yields, of cyclopropylmethanols, which are present in many natural products.

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References

- 1 J. Gorzynski-Smith, *Synthesis*, 1984, 629; A. S. Rao, S. K. Paknikar and J. G. Kirtane, *Tetrahedron*, 1983, **39**, 2323.
- 2 R. M. Wehmeyer and R. D. Rieke, *Tetrahedron Lett.*, 1988, **29**, 4513.
- 3 T. C. Wu and R. D. Rieke, Tetrahedron Lett., 1988, 29, 6753.
- 4 C. Dupuy, C. Petrier, L. A. Sarandeses and J. L. Luche, Synth. Commun., 1991, 21, 643.
- 5 L. A. Sarandeses, A. Mouriño and J. L. Luche, J. Chem. Soc., Chem. Commun., 1991, 818.
- 6 C. Petrier and J. L. Luche, J. Org. Chem., 1985, 50, 910; C. Einhorn and J. L. Luche, J. Organomet. Chem., 1985, 322, 177.
- 7 R. Bloch, J. Abecassis and D. Hassan, J. Org. Chem., 1985, 50, 1544.
- 8 P. J. Kocienski, G. Cernigliaro and G. Feldstein, J. Org. Chem., 1977, 42, 353.
- 9 L. Plamadon and J. D. Wuest, J. Org. Chem., 1991, 56, 2066.
- 10 A. Samat, B. Vacher and M. Chanon, J. Org. Chem., 1991, 56, 3524.
- 11 J. L. Luche, C. Einhorn, J. Einhorn and J. V. Sinisterra-Gago, *Tetrahedron Lett.*, 1990, **31**, 4125.