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An Effective Method for Alcohol Preparation by Hydrolysis of Organohalides in the Presence of Copper and its Salts in Aqueous DMSO

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Hydrolysis of alkyl halides in the presence of copper and its salts in aqueous DMSO (molar ratio organohalide:$CuSO_4{\cdot}5H_2O$:DMSO:H_2O = 1:1:10–20:12–25) at 100–117 °C gives alcohols in high yields. Aryl halides containing no activating substituents are inert under the reaction conditions.

The hydrolysis of organohalides usually proceeds under the action of alkali or carbonates of alkaline-earth metals, less often with silver compounds. Good results were obtained in the case of compounds with active halogen, *e.g.* benzyl halides.[1,2] However, in a strongly basic medium, the reaction can also involve other functional groups, which limits the utility of this method in alcohol synthesis.

We previously found[3,4] that the solvolysis of halocyclopropanes in the presence of copper and its salts in aqueous DMSO leads not only to cyclopropane ring scission but also to hydrolysis of halides with the formation of the corresponding allylic alcohols. In the present work we have found that under these conditions, hydrolysis of various organyl halides occurs smoothly, producing the corresponding alcohols in high yields.

Comparative experiments of BuBr hydrolysis (Table 1) in the presence of neutral salts or under the action of alkali, including the usual conditions without DMSO,[1,2] as well as in the presence of a copper salt show some advantages of the latter method in comparison with the usual conditions of alkaline hydrolysis.

As an example of BuBr hydrolysis in the presence of copper and its salts (molar ratio organohalide:copper-containing compound:DMSO:H_2O = 1:1:10–20:12–25, 100–117 °C, 2–3.5 h),[†] we studied the influence of the counterion in the copper compound. In all cases, the hydrolysis product – butanol – is formed smoothly in nearly quantitative yields (Table 1). In particular, this makes it possible to successfully use the most usual copper compound, $CuSO_4$, under these conditions. Good activity under these conditions is also displayed by metallic copper, which is dissolved during reaction (1). When the quantity of copper or its salts becomes less than equimolar, the yields of alcohols are proportionally reduced and the yields of the final products become non-reproducible.

$$\mathrm{BuBr} + \mathrm{H_2O} \xrightarrow[\text{DMSO}]{\text{Cu salt or Cu}} \mathrm{BuOH} + \mathrm{HBr} \qquad (1)$$

It was found that under the conditions chosen, *i.e.* in the presence of $CuSO_4$, various organohalides give the corre-

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[†] *Experimental details.* Preparation of alcohols by hydrolysis in the presence of copper-containing compounds in aqueous DMSO (general method). Organohalide (0.01 mol) was added to a solution of 0.01 mol copper-containing compound in 3.5 ml (0.2 mol) water and 8 ml (0.1 mol) DMSO, and the mixture was heated with stirring to 100–117 °C. After 10–15 min, the mixture became homogeneous and turned intense blue. On futher heating, the colour changed to dark green. The reaction mixture was further heated until the reaction was complete (monitored by GLC); it was then cooled, diluted with water and extracted with ether. The ethereal layer was dried with $CaCl_2$, the solvent was distilled off and the residue was distilled.

The final products were identified by ^1H NMR (Bruker WM-250, 250 MHz) and chromato mass spectra (Finnigan MAT INCOS 50) as well as by comparison with standards (GLC analysis, 0.25×50 m glass capillary column with OV-1701 silicone).

Table 1 Yields of BuOH (GLC analysis) from the hydrolysis of BuBr in the presence of various compounds.[a]

Compound	Reaction time/h	Yield (%)
Comparative experiments[b]		
Without salt	0.5	~5
LiCl	0.5	~5
$Mn(NO_3)_2$	0.5	~5
NaOH	0.5	10
NaOH[c]	0.5	~5
$CuSO_4$	0.5	20
Copper compound		
$CuSO_4$	3	99
Copper(II) maleate	3.5	98
Copper(II) stearate	2	98
Copper(II) carbonate	2	98
CuCl	3	90
Metallic copper	2.5	80

[a] Reaction conditions: 1.5 g (0.01 mol) BuBr, 0.01 mol salt, 3.5 ml H_2O, 8.5 ml DMSO, 100–117 °C. [b] T = 100 °C. [c] Without DMSO, 15 ml H_2O.

sponding alcohols in up to 100% yields (only aryl halides do not react), reaction (2), and the addition of an equimolar quantity of pyridine or preliminary acidification by HCl does not influence the reaction (Table 2).

$$RX + H_2O \xrightarrow[\text{DMSO}]{CuSO_4} ROH + HX \qquad (2)$$

Thus, hydrolysis can proceed both in acid and neutral media.

Partial hydrolysis of 1-bromo-3-chloropropane in the presence of only 1 equiv. of $CuSO_4$ (100–105 °C, 1 h, conversion 50%) predominantly involves the more mobile bromine, so that the main product of the reaction (yield 66%) is 3-chloropropan-1-ol, while 3-bromopropan-1-ol is formed in only 13% yield, reaction (3).

$$Br(CH_2)_3Cl \xrightarrow[\text{DMSO, } H_2O]{CuSO_4} \underset{66\%}{Cl(CH_2)_3OH} + \underset{13\%}{Cl(CH_2)_3OH} \qquad (3)$$

Complete hydrolysis of 1-bromo-3-chloropropane occurs when reaction duration and the quantity of $CuSO_4$ are increased (2 equiv. $CuSO_4$, 100–105 °C, 3 h, conversion 100%), the yield of propane-1,3-diol is 80%, reaction (4).

$$Br(CH_2)_3Cl \xrightarrow[\text{DMSO, } H_2O]{2CuSO_4} \underset{80\%}{HO(CH_2)_3OH} \qquad (4)$$

Table 2 The yield of alcohols ROH (GLC analysis) from the hydrolysis of halides RX in the presence of $CuSO_4$.[a]

R	X	Reaction time/h	Yield of ROH (%)
Bu	Cl	3	98
Bu	Cl[b]	3	98
Bu	Cl	1	10
Bu	Br	3	99
Bu	Br	1	25
Bu	I	3	97
Bu	I	1	30
$PhCH_2$	Cl	0.5	~100
$PhCH_2$	Cl[c]	0.5	~100
$CH_2{=}CHCH_2$	Br	0.3	~100
cyclo-C_6H_{11}	Cl	1	~100
Bu^t	Br	0.2	~100
p-$NO_2C_6H_4$	Br	5	60[d]
Ph	Br	6	0[e]
Ph	I	6	0[e]

[a] Reaction conditions: 0.01 mol RX, 2.5 g (0.01 mol) $CuSO_4$, 3.5 ml H_2O, 8.5 ml DMSO, 100–117 °C. [b] With an equimolar quantity of pyridine. [c] Preliminary acidification by HCl. [d] Preparative yield. [e] No reaction.

The above examples show that the hydrolysis rate depends on the halide nature (I > Br > Cl) and on the organyl radical: allyl ≈ benzyl > tertiary > secondary > primary > p-$NO_2C_6H_4$- $\gg$ Ph (does not react), and the latter factor is the determining one.

Thus, hydrolysis of organohalides in the presence of copper and its salts in aqueous DMSO is a convenient preparative method for synthesizing the corresponding alcohols.

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