

Thème "Synthèse des organobromés"

Synthesis of alkyl bromides via halogen exchange processes

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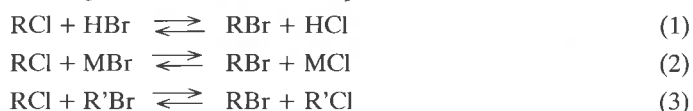
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Introduction

Alkyl and benzyl chlorides are usually more readily available than the corresponding bromides and since the latter are more reactive, e.g. in organometallic reactions, it is highly desirable, under certain circumstances, to convert alkyl or aralkyl chlorides to their bromide counterparts. To this end three types of halogen exchange reactions were developed :



Where R, R' is a linear or branched alkyl or arylalkyl group and M is an alkali or earth alkali metal as well as boron, aluminium, or phosphor. The author is unaware of exchange reactions where R or R' is an aryl group. Excluded from this presentation are processes where the brominating agent is elementary bromine.

All the three reactions are reversible in nature and certain conditions should be applied in order to shift the equilibrium composition to the desired direction. Using large excess of a brominating agent is an obvious solution. An alternative is an instant removal of a product as it is formed, for instance by distillation. Another technique takes advantage of solubility differences of halide salts in an aqueous phase.

Activation energies for reactions (1), (3) are high and the presence of a catalyst is essential for practical reaction rates. Typical catalysts are Lewis acids or nucleophilic catalysts like quaternary onium salts or crown ethers which function also, mainly in reaction (2), as phase transfer catalysts.

Halogen exchange reactions are chemoselective and no side products are usually obtained. In numerous synthetic examples the utilization of an exchange process is favoured over direct bromination of the parent hydrocarbon, due to higher specificity.

While the main application of these three reactions is the preparation of alkyl bromides they can also be employed for the synthesis of hydrobromic acid and metal bromide salts by reversing reactions (1) and (2) respectively. Reactions (1) and (2) can, in principle, be used also as separation method e.g. for the isolation of HBr from a mixture of acids or, applying process (2) as a bromide "pump" to separate bromide anion from a mixture of salts. Considering a combined two-stage process one can think of "pumping" bromide from a brine at a first stage and converting it to a desired metal bromide salt at a second stage (both using reaction (2)).

Exchange reactions with hydrogen bromide

This is the procedure for the transformation of branched alkyl chlorides to the corresponding bromides [1]. The recommended catalyst is ferric bromide. In the presence of 7 : 1 molar excess of gaseous hydrogen bromide substrates like cyclohexyl chloride or tertbutyl chloride are quantitatively converted to bromides

within 10-20 minutes at room temperature. The method is also suitable for the substitution of vicinal dichlorides which are substituted with stereochemical retention. Thus d,1,2,3-dichlorobutane afforded the d,1-2,3-dibromobutane and the meso-dichloride gave the meso-3,4-dibromobutane. n-Alkyl chlorides react very slowly under these conditions.

This catalytic system is very sensitive to the presence of moisture and it also suffers from side reactions namely skeletal rearrangements and disproportionations.

Quaternary ammonium salts, on the other hand, are water resistant catalysts which are also active in reaction (1) though in higher temperatures [2]. This allows the utilization of aqueous hydrobromic acid as the brominating agent. We were able to prepare benzyl bromide by reacting 35-65 % aqueous HBr with benzyl chloride in presence of tetra-n-hexylammonium bromide at 80 °C. The equilibrium conversion obtained was found to depend on the concentration of the aqueous HBr.

Exchange with metal bromide salts

These reactions are heterogeneous in nature and are practiced in liquid-liquid or solid-liquid systems. Phase transfer catalysts like lipophilic onium salts or crown ethers are required in these processes. Almost complete conversion of e.g. n-octyl chloride to bromide is observed when it is reacted with lithium or calcium bromide containing traces of water in the presence of a lipophilic onium catalyst [3]. Dilution of these salts with water or applying other bromides reduced the conversion. The yield is particularly low with potassium or sodium bromide in aqueous solutions and with these salts the reverse action is dominant. This method is suitable only for the synthesis of normal alkyl bromide. Secondary and tertiary alkyl chlorides did not react. Vicinal dichlorides like 1,2-dichloroethane, 1,3-dichloropropane and 1,4-dichlorobutane were easily transformed to the dibromides. 1,2-dichloro-

propane, on the other hand, did not react at all. Dichloromethane yielded both dibromomethane and bromochloromethane. Detailed kinetic and mechanistic study of this reaction has been published [4].

Exchange between alkyl halides

Reactions of type (3) are catalyzed by bromide or chloride anion. If sodium bromide is the catalyst then a highly polar solvent is required. N-methyl-2-pyrrolidinone combined with large excess of ethyl bromide was applied for the transformation of many alkyl chlorides to bromides under mild conditions [5].

Simpler catalytic system is obtained when the halide anion is introduced as a lipophilic ion pair. No solvent is necessary for this catalyst which can also be prepared in situ [6]. When volatile alkyl bromides are applied as the brominating agents the system can be driven to the desired direction simply by distilling out the resulting alkyl chloride. This concept was found to be useful in the synthesis of alkyl heterodihalides e.g. bromochlorides [7]. Secondary and tertiary halides did not react, however, under these conditions.

A process for the synthesis of benzyl bromide via reaction of ethylene dibromide with benzyl chloride have been presented in the lecture.

Reactions of type 3 are feasible also in the gas phase. The catalysts of choice are phosphonium salts supported on silica, alumina or glass beads which can be utilized in a continuous plug-flow reactor [8]. At temperature of 140 °C residence time of a few seconds is sufficient for n-butyl bromide and n-propyl chloride to equilibrate. The reaction was found to obey a reversible second order rate equation. Gas-liquid diffusion affected the rate particularly when high catalyst/support ratios were used. Catalytic systems of this type did not lose activity even after several weeks of continuous operation [9].

References

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