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SELECTIVE HYDROBROMINATION OF BRANCHED ALCOHOLS USING PHASE TRANSFER CATALYSIS

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In the presence of quaternary ammonium phase transfer catalysts hydrobromination of branched alcohols proceed via selective SN2 mechanism practically without rearrangements.

Hydrogen halides are known to be extracted from aqueous solutions by lipophilic quaternary ammonium salts in organic solvents[1]. This phenomenon is very pronounced with hydrogen chloride and particularly with hydrogen fluoride[2], but exists also, to a certain degree, with hydrogen bromide. Thus tetra-n-butylammonium bromide (TBAB), 0.1M in methylene chloride, upon contacting with concentrated hydrobromic acid extracted little less than one equivalent of HBr into the organic phase[3]. The extraction mechanism was explained by the formation of hydrogen bonded adducts of the general structure: $R_4NX(HX)_n$[3].

This phenomenon was applied synthetically for the cleavage of ethers[4] and lactons[5] by aqueous HBr and for the catalytic transformation of n-alkanols to the corresponding chlorides by concentrated hydrochloric acid[6]. Interestingly, when alcohols were reacted with concentrated hydrobromic acid the addition of phase transfer catalysts barely accelerated the formation of the bromides. When, for example, we have mixed 0.2 mole of n-decanol with 0.4 mole of 48% aqueous HBr at 120°C a reaction took place with 70% conversion after one hour and 90% conversion after 16 hours to n-decyl bromide. Upon addition of 10 mole% of TBAB we measured 75% after one hour and complete conversion after 16 hours. Aliquat 336® was found to have similar catalytic effect on the system. Although the effect of phase transfer catalysts on the rate of the hydrobromination process is minor; we have observed a unique effect on the selectivity of the process when applied on secondary alcohols or on alcohols with branching at a β-carbon. In presence of quaternary ammonium salts these alcohols do not suffer from skeletal rearrangements which are very common under conventional conditions.

It is known, for example, that 2-pentanol upon reaction with 48% HBr at 70°C for 24 hours gives 59% conversion to 2-bromopentane (70%) and to the rearranged product 3-bromopentane (30%)[7]. Replacement of the aqueous acid with anhydrous hydrogen bromide improved the selectivity yielding 13% of 3-bromopentane and 87% of 2-bromopentane[7]. Selective hydrobromination almost free from rearrangements can be obtained only by using more sophisticated non acidic reagents. Typical examples are phosphorus tribromide[8] and particularly, triphenylphosphine dibromide[9]. These reagents are obviously more expensive and more difficult to handle than aqueous HBr.

We have now observed that in the presence of an organic solvent and a quaternary ammonium phase transfer catalyst, even aqueous hydrobromic acid function selectively to yield practically pure 2-bromopentane.

In a typical example we have mixed 0.1 mole of 2-pentanol in 56 ml of chlorobenzene with 0.5 mole of 48% aqueous HBr in the presence of 1.8g (4 mole%) of aliquat 336® at 85° for 20 hours. Gas chromatographic analysis of the organic phase (with comparison to authentic samples) showed complete conversion of the alcohol with over 99% selectivity to 2-bromopentane. After phase separation the

product could be simply distilled from the solvent-catalyst mixture.

In a series of experiments it was found that high selectivity to the unrearranged product is obtained in systems where the substrate and the hydrobromic acid are kept apart, each in a different phase. Under conditions where free hydrobromic acid can dissolve in a the organic phase or the alcohol can distribute into the aqueous phase, rearrangement starts to take place. Thus, applying a smaller volume of solvent, a lower amount of catalyst, higher concentration of HBr or higher temperature, all rersulted in lower selectivity with formation of the isomer - 3-bromopentane. Using other solvents e.g. toluene, chlorobenzene or dichloromethane did not alter the composition of the product mixture.

The presence of an organic solvent is not critical when the substrate is less hydrophlic. When we reacted 0.2 mole of 2-ethylhexanol with 0.6 mole of 48% HBr at 100°, 72 hours were required for complete conversion. The product distribution, based on GC analysis, was: 1-bromo-2-ethylhexane (82%), 2-bromo-2-ethylhexane (16%) and 2-bromo-2-methylheptane (2%). When the same initial mixture was reacted in the presence of 3.6g of aliquat 336® (4 mole%) we obtained complete conversion after 14 hours with 98.8% yield of 1-bromo-2-ethylehxane. Similar behaviour was observed in the reaction of 2-phenyl ethanol under the same conditions. In the absence of the catalyst we obtained 93% of 2-phenylethylbromide and 7% of 1-phenylethylbromide. In the presence of 4 mole% aliquat 336® the selectivity to 2-phenylethylbromide was 98.7%.

Highly branched alcohols are very sensitive to rearrangements under hydrobromination conditions. Both 2,2-dimethyl-1-propanol and 3-methyl-2-butanol upon reaction with aqueous HBr yielded the same rearranged product 2-bromo-2-methylbutane only. With these substrates the addition of aliquat 336 gave only partial selectivity yielding up to 30% of 1-bromo-2,2-dimethylpropane and 2-bromo-3-methylbutane respectively.

We believe that upon the addition of the phase transfer catalyst the mechanism of the hydrobromination reaction shifts from partial Sn1 to pure Sn2 mechanism which is free from rearrangements. The adduct $R_4NX(HBr)_n$, which is the active intermediate in the catalyzed reaction, is a stronger nucleophile and, by far, a weaker acid than the free hydrobromic acid. In the catalytic reaction free protons are not available for protonation followed by dehydration of the alcohols and thus carbonium ions are not formed.

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