

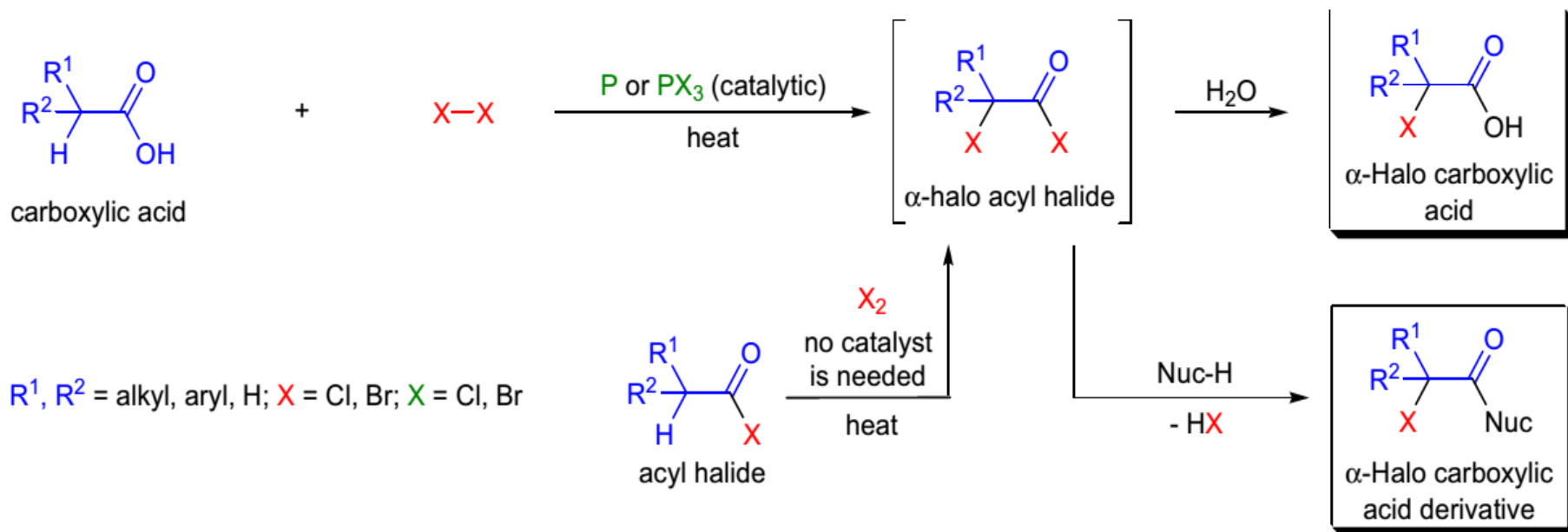
HELL-VOLHARD-ZELINSKY (HVZ) REACTION

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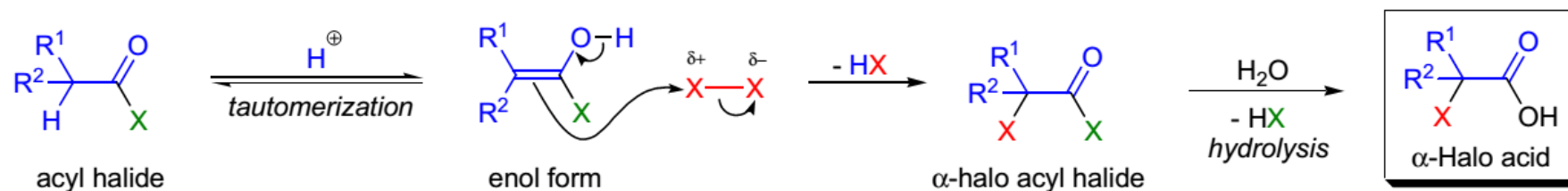
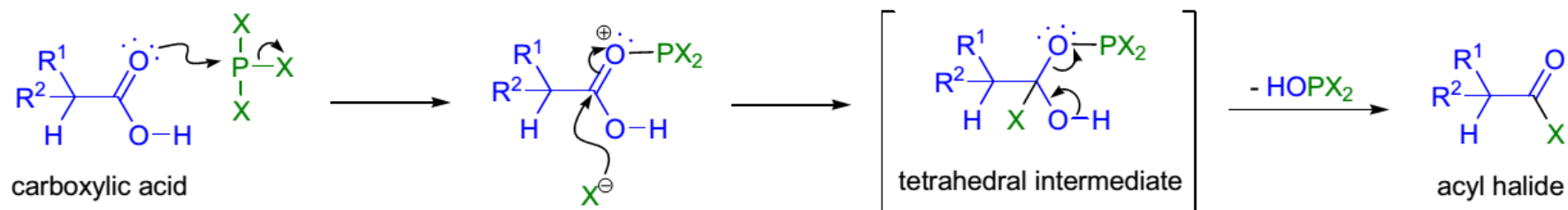
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一、What is HVZ reaction

- The preparation of α -halo carboxylic acids by treating the corresponding carboxylic acid with elemental halogen (Cl_2 or Br_2) at elevated temperatures in the presence of catalytic amounts of red phosphorous (P) or phosphorous trihalide (PCl_3 or PBr_3)



二、Mechanism of HVZ reaction

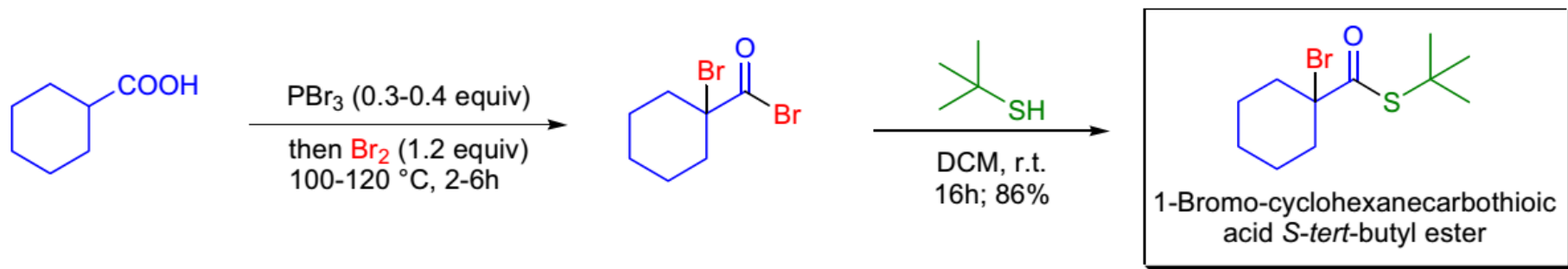


三、 Features of HVZ reaction

- 1) reaction conditions are relatively harsh, involving high temperatures (usually above 100 °C) and extended reaction times;
- 2) usually less than one equivalent of P or PX₃ catalyst is needed;
- 3) certain activated carboxylic acids and acid derivatives (e.g. anhydrides, acyl halides, 1,3-diester) that are readily enolized can be halogenated in the absence of a catalyst;
- 4) α -bromination of substrates with long alkyl chains is completely selective; however, α -chlorination competes with random free radical chlorination processes so a mixture of mono- and polychlorinated products are obtained;
- 5) attempts to bring about the fluorination or iodination of carboxylic acids under HVZ conditions have not been successful;
- 6) conducting the reaction at too high a temperature may result in the elimination of hydrogen halide from the product resulting in the formation of α,β -unsaturated carboxylic acids.

四、Applications of HVZ reaction

A convenient one-pot procedure for the preparation of α -bromo thioesters from carboxylic acids based on the HVZ reaction was developed by H.-J. Liu and co-workers.²⁰ The neat carboxylic acid was mixed with 0.4 equivalents of PBr_3 , the resulting mixture was heated to 100-120 °C in an oil bath and 1.2 equivalents of liquid bromine was added in 1.5h. In the same flask, now containing the α -bromo acyl bromide, the solution of the thiol in dichloromethane was added to give the desired α -bromo thioesters in high yield.



The preparation of C_2 -symmetric 2,5-disubstituted pyrrolidines (utilized as chiral auxiliaries) often calls for *meso*-2,5-dibromoadipic esters as starting materials. An improvement in the synthesis of the *meso* stereoisomer was published by T. O'Neill and co-workers.²¹ The authors began with the α -bromination of adipoyl chloride followed by esterification with ethanol to obtain a complex mixture of dibromo adipates (racemic + *meso*) in quantitative yield. The racemic and *meso*-dibromoadipates have very different crystalline properties, and these stereoisomers were found to be in equilibrium in an alcohol solution. Crystallizing the higher melting *meso* isomer and removing it from the equilibrium caused the remaining racemic mixture to convert to the *meso* isomer by shifting the equilibrium to the right, according to *Le Chatelier's principle*.

