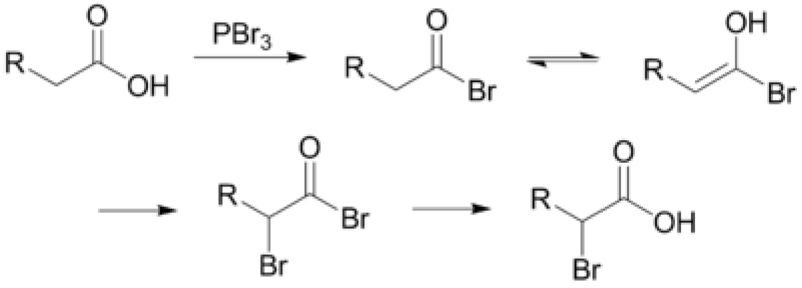
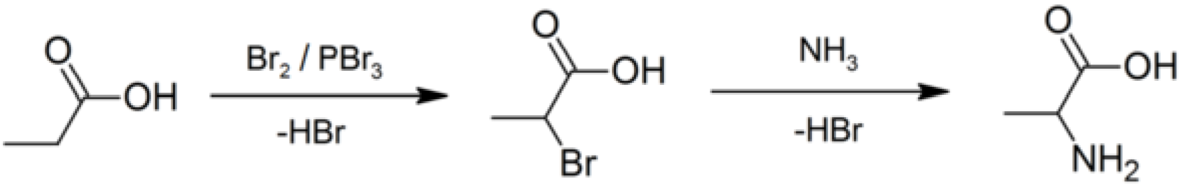
Hell–Volhard–Zelinsky halogenation

Hell–Volhard–Zelinsky halogenation	
Named after	Carl Magnus von Hell Jacob Volhard Nikolay Zelinsky
Reaction type	Substitution reaction
Identifiers	
Organic Chemistry Portal	hell-volhard-zelinsky-reaction

The **Hell–Volhard–Zelinsky halogenation** reaction halogenates carboxylic acids at the α carbon. The reaction is named after three chemists, the German chemists Carl Magnus von Hell (1849–1926) and Jacob Volhard (1834–1910) and the Russian chemist Nikolay Zelinsky (1861–1953).[1][2][3][4]

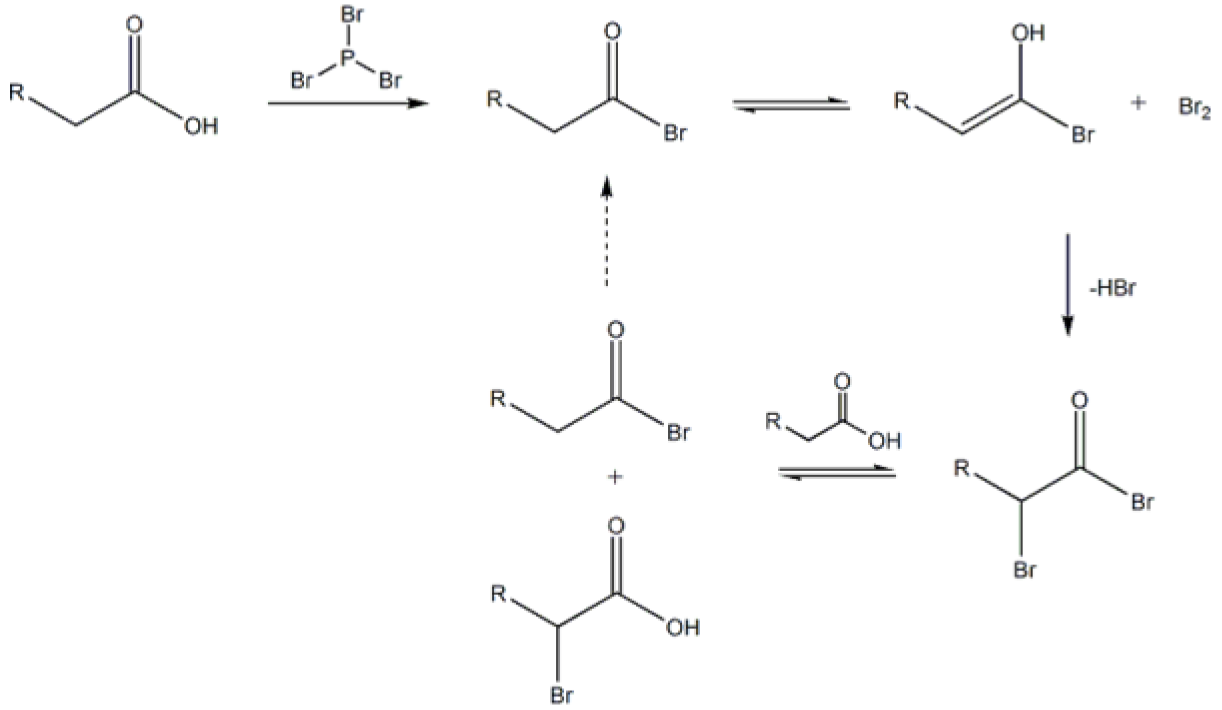


An example of the Hell–Volhard–Zelinsky reaction being used in practice can be seen in the preparation of alanine. An approach using a Strecker synthesis[5] was described as "excellent but tedious"[6] and so an alternative starting with propionic acid was developed. In its first step, a combination of bromine and phosphorus tribromide (catalyst) is used to prepare 2-bromopropanoic acid,[7] which is then converted to a racemic mixture of the amino acid product by ammonolysis.[6][8]



Mechanism

Unlike other halogenation reactions, this reaction takes place in the absence of a halogen carrier. The reaction is initiated by addition of a catalytic amount of PBr_3, after which one molar equivalent of Br_2 is added.

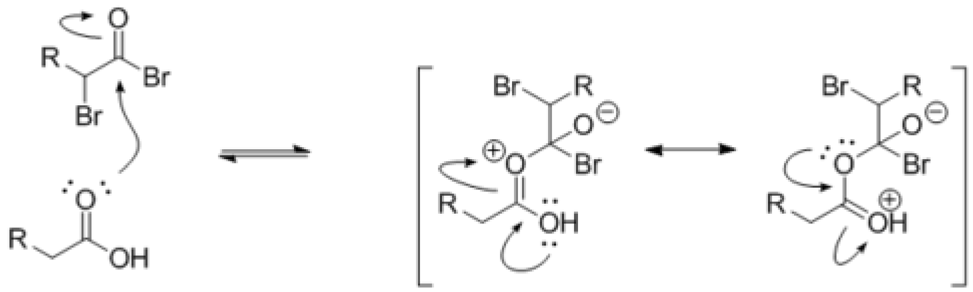


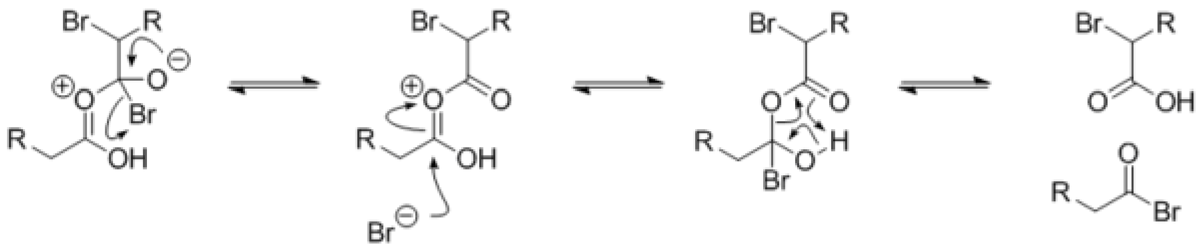
PBr_3 replaces the carboxylic OH with a bromide, resulting in a carboxylic acid bromide. The acyl bromide can then tautomerize to an enol, which will readily react with the Br_2 to brominate a second time at the α position.

In neutral to slightly acidic aqueous solution, hydrolysis of the α-bromo acyl bromide occurs spontaneously, yielding the α-bromo carboxylic acid in an example of a nucleophilic acyl substitution. If an aqueous solution is desirable, a full molar equivalent of PBr_3 must be used as the catalytic chain is disrupted.

If little nucleophilic solvent is present, reaction of the α-bromo acyl bromide with the carboxylic acid yields the α-bromo carboxylic acid product and regenerates the acyl bromide intermediate. In practice a molar equivalent of PBr_3 is often used anyway to overcome the slow reaction kinetics.

The mechanism for the exchange between an alkanoyl bromide and a carboxylic acid is below. The α-bromoalkanoyl bromide has a strongly electrophilic carbonyl carbon because of the electron-withdrawing effects of the two bromides.





See also

- Reformatsky reaction

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