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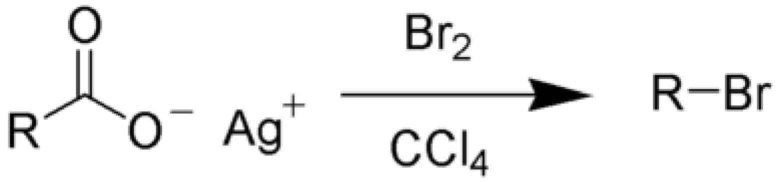
Hunsdiecker reaction

Hunsdiecker reaction	
Named after	Heinz Hunsdiecker Cläre Hunsdiecker Alexander Borodin
Reaction type	Substitution reaction
Identifiers	
Organic Chemistry Portal	hunsdiecker-reaction
RSC ontology ID	RXNO:0000106

The **Hunsdiecker reaction** (also called the **Borodin reaction** or the **Hunsdiecker–Borodin reaction**) is a name reaction in organic chemistry whereby silver salts of carboxylic acids react with a halogen to produce an organic halide.[1] It is an example of both a decarboxylation and a halogenation reaction as the product has one fewer carbon atoms than the starting material (lost as carbon dioxide) and a halogen atom is introduced its place. The reaction was first demonstrated by Alexander Borodin in his 1861 reports of the preparation of methyl bromide (CH3Br) from silver acetate (CH3CO2Ag).[2][3] Shortly after, the approach was applied to the degradation of fatty acids in the laboratory of Adolf Lieben.[4][5] However, it is named for Cläre Hunsdiecker and her husband Heinz Hunsdiecker, whose work in the 1930s[6][7] developed it into a general method.[1] Several reviews have been published,[8][9] and a catalytic approach has been developed.[10]



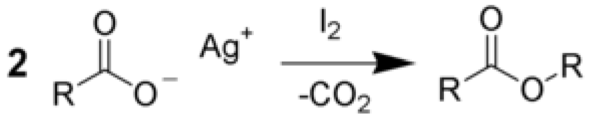
Contents

History

Alexander Borodin first observed the reaction in 1861 when he prepared methyl bromide from silver acetate.[2][3] The reaction is a decarboxylation in that alkyl halide product has one fewer carbon atoms than its parent carboxylate, lost as carbon dioxide.[1][8]

$$CH_3CO_2Ag + Br_2 \rightarrow CH_3Br + CO_2 + AgBr$$

Around the same time, Angelo Simonini was working as a student of Adolf Lieben at the University of Vienna, investigating the reactions of silver carboxylates with iodine.[8] They found that the products formed are determined by the stoichiometry within the reaction mixture. Using a carboxylate-to-iodine ratio of 1:1 leads to an alkyl iodide product, in line with Borodin's findings and the modern understanding of the Hunsdiecker reaction. However, a 2:1 ratio favours the formation of an ester product that arises from decarboxylation of one carboxylate and coupling the resulting alkyl chain with the other.[4][5]



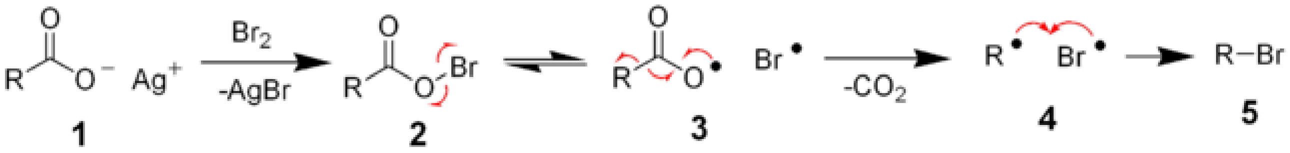
Using a 3:2 ratio of reactants leads to the formation of a 1:1 mixture of both products.[4][5] These processes are sometimes known as the **Simonini reaction** rather than as modifications of the Hunsdiecker reaction.[8][9]

$$3\,RCO_2Ag \;+\; 2\,I_2 \;\rightarrow\; RI \;+\; RCO_2R \;+\; 2\,CO_2 \;+\; 3\,AgI$$

It is now well established that mercuric oxide can also be used to effect this transformation.[11][12] The reaction has been applied to the preparation of ω-bromo esters with chain lengths between five and seventeen carbon atoms, with the preparation of methyl 5-bromovalerate published in *Organic Syntheses* as an exemplar.[13]

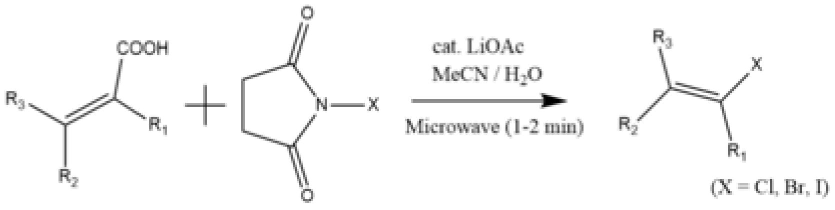
Reaction mechanism

The reaction mechanism of the Hunsdiecker reaction is believed to involve organic radical intermediates. The silver salt of the carboxylic acid **1** will quickly react with bromine to form acyl hypohalite intermediate **2**. Formation of the diradical pair **3** allows for radical decarboxylation to form the diradical pair **4**, which will quickly recombine to form the desired organic halide **5**. The trend in the yield of the resulting halide is primary > secondary > tertiary.[8][9]



Reaction with α, β-Unsaturated Carboxylic Acids

Chowdhury and Roy noted several drawbacks of using Hunsdiecker reaction, namely that some reagents, such as molecular bromine and salts of mercury, thallium, lead, and silver, are inherently toxic and that reactions with α, β-unsaturated carboxylic acids result in low yield.[14] Regarding reactions using α, β-unsaturated carboxylic acids, Kuang et al. modified the reaction with using a new halogenating agent, N-halosuccinimide, and lithium acetate as the catalyst, which resulted in higher yield of β-Halostyrenes.[15] They found that using the microwave irradiation could synthesize (*E*)-β-arylvinyl halide much quicker with higher yields.[15] This is useful because synthesizing (*E*)-vinyl bromide in general is not very practical due to the complexity of alternative reagents



Synthesis of β-arylvinyl halide by microwave-induced Hunsdiecker reaction.

(e.g. organometallic compounds), longer reaction times, and lower yields.[16] Using microwave irradiation also allows the synthesized arylvinyl halide to carry electron-donating groups (in addition to electron-withdrawing groups), which is not possible with alternative synthetic methods.[16] While tetrabutylammonium trifluoroacetate (TBATFA) could be used as an alternative catalyst for a metal-free reaction,[17] it was noted that lithium acetate resulted in higher yields compared to other relatively complex catalysts, including tetrabutylammonium trifluoroacetate.[15][18] An alternative method using micelles was found, with green characteristics.[19] Micelles generally facilitate reactions thanks to their solublization capability and here, it was found that a reaction with α, β-unsaturated aromatic carboxylic acids and N-halosuccinimide catalyzed by cetyl trimethyl ammonium bromide (CTAB), sodium dodecyl sulfate (SDS), and Triton-X-100 in dichloroethane (DCE) carried out under reflux conditions of 20–60 minutes formed β-Halostyrenes in excellent yields with high regioselectivity.

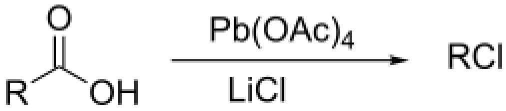
Variations

Mercuric oxide

Lampman and Aumiller used mercuric oxide and bromine to prepare 1-bromo-3-chlorocyclobutane from 3-chlorocyclobutanecarboxylic acid in a modification of the Hunsdiecker reaction.This is known as Cristol-Firth modification.[12] The product had previously been shown by Wiberg to react with molten sodium metal to form bicyclobutane via a Wurtz coupling in good yield.[20][21]

Kochi reaction

The Kochi reaction is a variation on the Hunsdiecker reaction developed by Jay Kochi that uses lead(IV) acetate and lithium chloride (lithium bromide can also be used) to effect the halogenation and decarboxylation.[22]



See also

- Barton Decarboxylation
- Barton–McCombie deoxygenation

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External links

- Animation of the reaction mechanism (https://commons.wikimedia.org/wiki/File:Hundsdiecker_startAnimGif.gif)