Homologation reaction

A **homologation reaction**, also known as **homologization**, is any chemical reaction that converts the reactant into the next member of the homologous series. A homologous series is a group of compounds that differ by a constant unit, generally a (-CH_2-) group. The reactants undergo a **homologation** when the number of a repeated structural unit in the molecules is increased. The most common homologation reactions increase the number of methylene (-CH_2-) units in saturated chain within the molecule.[1] For example, the reaction of aldehydes or ketones with diazomethane or methoxymethylenetriphenylphosphine to give the next homologue in the series.

Examples of homologation reactions include:

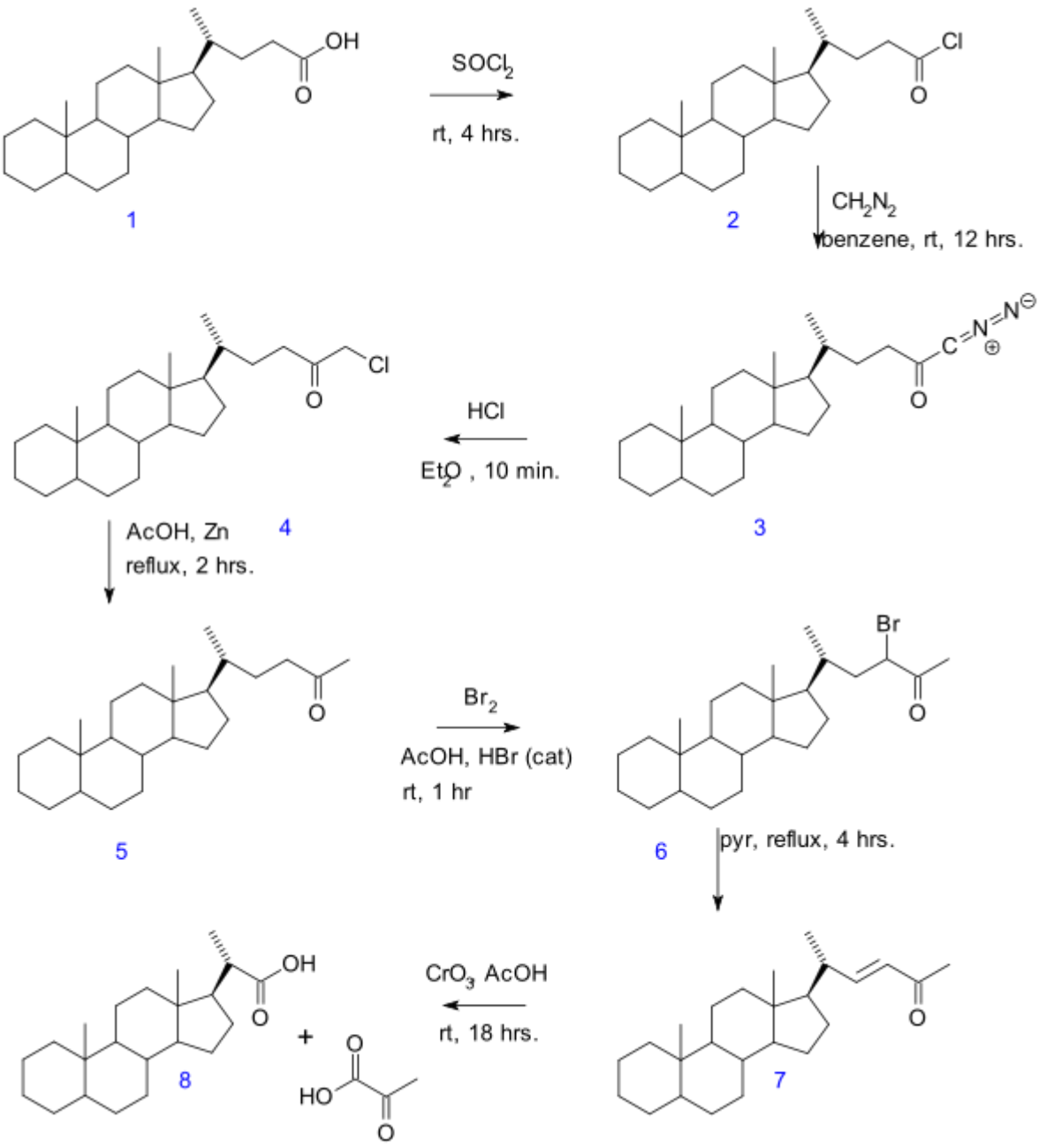
- Kiliani-Fischer synthesis, where an aldose molecule is elongated through a three-step process consisting of:
  1. Nucleophillic addition of cyanide to the carbonyl to form a cyanohydrin
  2. Hydrolysis to form a lactone
  3. Reduction to form the homologous aldose
- Wittig reaction of an aldehyde with methoxymethylenetriphenylphosphine, which produces a homologous aldehyde.
- Arndt–Eistert reaction is a series of chemical reactions designed to convert a carboxylic acid to a higher carboxylic acid homologue (i.e. contains one additional carbon atom)
- Kowalski ester homologation, an alternative to the Arndt-Eistert synthesis. Has been used to convert β-amino esters from α-amino esters through an ynolate intermediate.[2]
- Seyferth–Gilbert homologation in which an aldehyde is converted to a terminal alkyne and then hydrolyzed back to an aldehyde.

Some reactions increase the chain length by more than one unit. For example, the following are considered **two-carbon homologation reactions.**

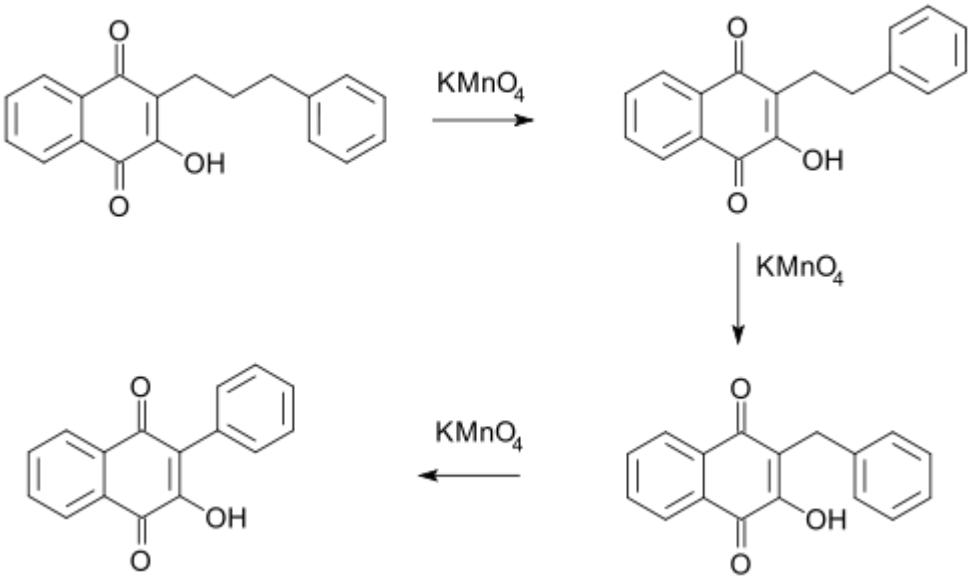
Chain reduction

Likewise the chain length can also be reduced:

- In the **Gallagher–Hollander degradation** (1946) pyruvic acid is removed from a linear aliphatic carboxylic acid yielding a new acid with 2 carbon atoms less.[3] The original publication concerns the conversion of bile acid in a series of reactions: acid chloride (**2**) formation with thionyl chloride, diazoketone formation (**3**) with diazomethane, chloromethyl ketone formation (**4**) with hydrochloric acid, organic reduction of chlorine to methylketone (**5**), ketone halogenation to **6**, elimination reaction with pyridine to enone **7** and finally oxidation with chromium trioxide to *bisnorcholanic acid* **8**.



- In the **Hooker reaction** (1936) an alkyl chain in a certain naphthoquinone (phenomenon first observed in the compound lapachol) is reduced by one methylene unit as carbon dioxide in each potassium permanganate oxidation.[4][5]



Mechanistically oxidation causes ring-cleavage at the alkene group, extrusion of carbon dioxide in decarboxylation with subsequent ring-closure.

See also

- Homologous series

References

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4. *On the Oxidation of 2-Hydroxy-1,4-naphthoquinone Derivatives with Alkaline Potassium Permanganate* Samuel C. Hooker J. Am. Chem. Soc. **1936**; 58(7); 1174-1179. doi:10.1021/ja01298a030 (https://doi.org/10.1021%2Fja01298a030)
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