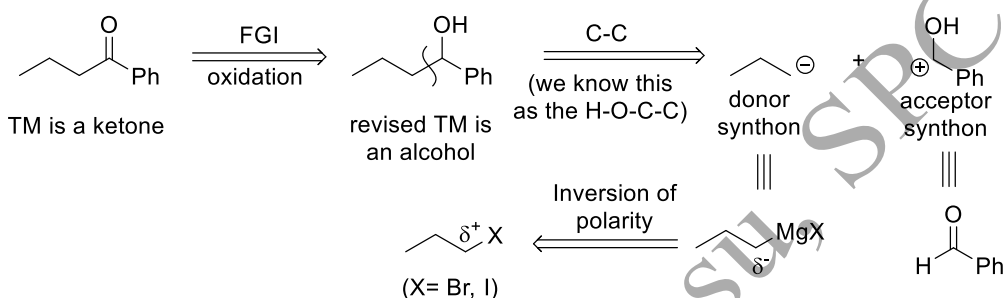


## A few key terms used in retrosynthetic analysis of organic molecules.

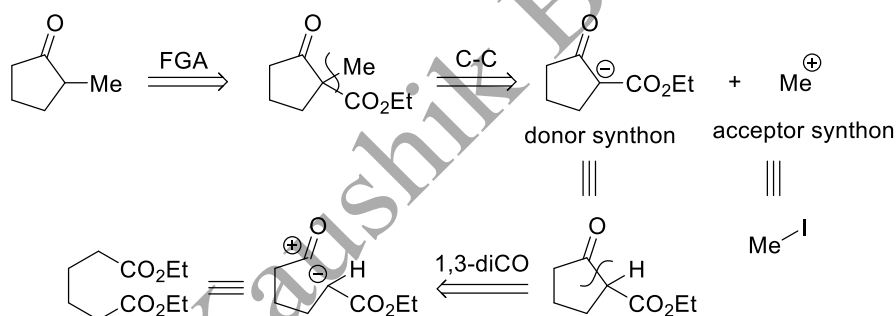
**Synthons:** The idealized fragment, usually positively or negatively charged, that results from a disconnection. This may or may not be an intermediate in the corresponding forward reaction.

**Donor (nucleophilic) and acceptor (electrophilic) synthons:** Heterolytic retrosynthetic disconnection of a carbon-carbon bond in a target molecule breaks the TM into a positively-charged synthon, a carbocation, and a negatively-charged synthon, a carbanion. The former is an electrophilic, acceptor synthon and the latter is a nucleophilic, donor synthon. In a formal sense, the synthetic step - the formation of a C-C bond - then involves the union of an electrophilic acceptor synthon and a nucleophilic donor synthon.

**Functional group interconversion (FGI):** The process of converting one functional group of a target molecule in another to revise the target by substitution, addition, elimination, oxidation or reduction so that the disconnection is facilitated.

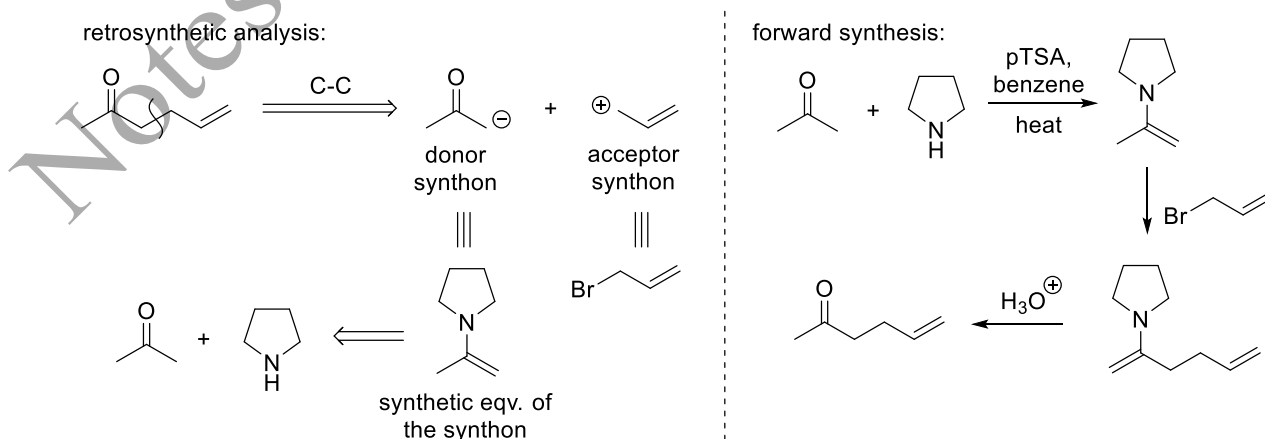


**Functional group addition (FGA):** The process of adding one functional group in a target molecule to facilitate the disconnection of the revised TM.

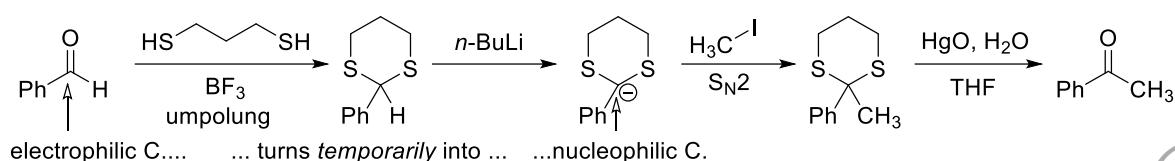


**Synthetic equivalent:** A synthetic equivalent is a compound with the following properties. i) It reacts in a way that the actual substrate or reagent cannot; ii) after reacting, it can be modified in such a way that the same product is obtained indirectly whose direct generation from the actual substrate or reagent was not possible.

For example, enamines are synthetic equivalents of ketonic or aldehydic enols, used for the electrophilic functionalization at the  $\alpha$ -position of the carbonyl.

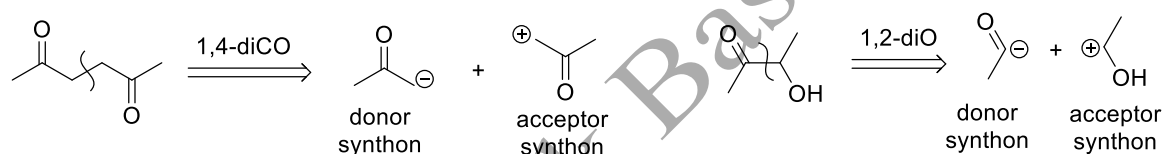


**Umpolung (inversion/reversal of polarity):** A general class of reactions in which the characteristic reactivity of a functional group or atom is temporarily reversed. For example, the carbonyl carbon's electrophilic nature is temporarily reversed into nucleophilic character of the same carbon in the *S,S*-acetal.



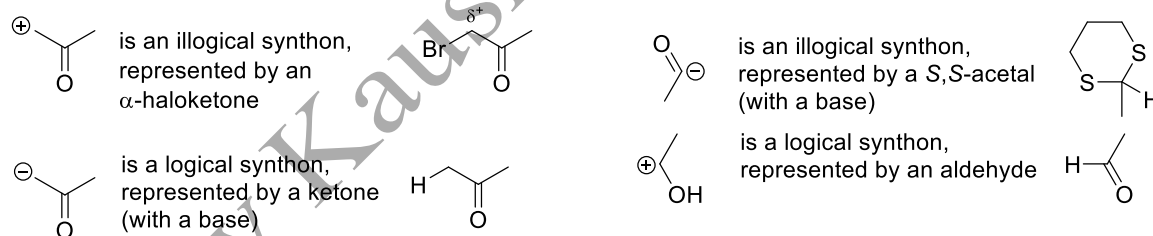
**Logical and illogical synthons; 'logical' and 'illogical' electrophiles and nucleophiles:** The heterolytic disconnection of a target molecule generates an electrophilic (positively-charged) and a nucleophilic (negatively-charged) synthon. For logical synthons, the charge on the synthon matches with the latent polarity imparted by the functional group present at the appropriate position of the synthon. For illogical synthons, there is a mismatch between the charge on the synthon and the latent polarity imparted by the functional group present. In other words, for logical synthons, the charge on the synthon coincides with the natural polarity imparted by the functional group present, while for illogical synthons, the charge on the synthon is opposite to the same. Thus, logical synthons are often also called natural synthons and illogical synthons are known as unnatural synthons. The synthetic equivalent representing a logical electrophilic synthon is called a 'logical' electrophile while an illogical electrophilic synthon is represented by an 'illogical' electrophile. The same pattern is followed for nucleophilic synthons.

retrosynthetic analysis:

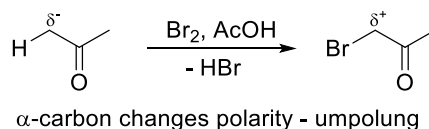


a =O group imparts the following latent polarity on a carbon chain to which it is attached to:

Thus,

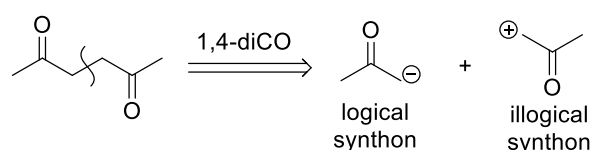


Illogical synthetic equivalents involve umpolung in their preparation.

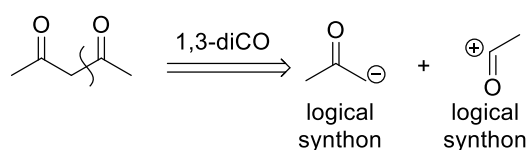


**Logical and illogical disconnections:** Retrosynthetic disconnections that generate at least one illogical synthon are known as illogical disconnections while those leading to only logical synthons are termed logical disconnections.

illogical disconnection



logical disconnection



**References:**

1. Designing organic synthesis: A programmed introduction to the synthon approach, by Stuart Warren, ISBN: 9788126520862,
2. Modern organic synthesis: An introduction, by George S. Zweifel *et al*, Second Ed., ISBN: 9781119086536,
3. Study guide to organic chemistry: A problem-solving approach, Volume 5, by Chandan Saha *et al*, ISBN: 9788193853085

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