

Definitions

- **Disconnection:** An analytical operation, which breaks a bond and converts a molecule into a possible starting material. The reverse of a chemical reaction. Symbol \Rightarrow and a curved line drawn through the bond being broken.
- **FGI:** Functional Group Interconversion: The operation of writing one functional group for another so that disconnection becomes possible. The reverse of a chemical reaction. Symbol \Rightarrow with FGI written over it.
- **Reagent:** A compound which reacts to give an intermediate in the planned synthesis or to give the target molecule itself. The synthetic equivalent of a synthon.
- **Synthetic equivalent:** A reagent carrying out the function of a synthon which cannot itself be used, often because it is too unstable.
- **Synthon:** A generalized fragment, usually an ion, produced by a disconnection. (some people also use synthon for a synthetic equivalent).
- **Target Molecule:** The molecule whose synthesis is being planned.

Retrosynthesis

Retrosynthesis is the process of "deconstructing" a target molecule into readily available starting materials by means of

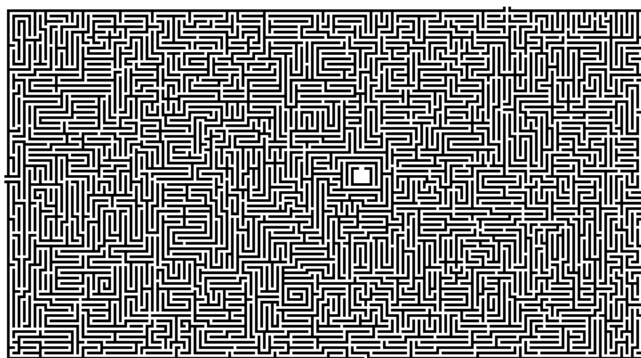
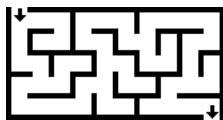
- imaginary breaking of bonds (*disconnections*) and by the conversion of one functional group into another (*functional group interconversions*).

The following factors need be taken into consideration:

Efficiency, e.g. the "arithmetic demon":

"The arithmetic demon dictates one of the major axioms of synthesis: Get the most done in the fewest steps and in the highest yield." (R. E. Ireland)

The Synthetic Route to a Target Molecule



Sierra, M. A.; De La Torre, M. C., "Dead ends and detours en route to total syntheses of the 1990s." *Angew. Chem. Int. Engl.* **2000**, 39, 1538-1550.
Zaragoza, D. F. "Side reactions in organic synthesis: A guide to successful synthesis design; Wiley 2004.

The Synthetic Route to a Target Molecule

The Planning

Starting
Materials

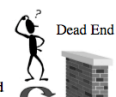


Target
Molecule

The Reality

Starting
Materials

Advanced
Intermediate



Dead End

Target
Molecule

Starting
Materials

Advanced
Intermediate

A failed key step



Needful
Knowledge

More and More Steps



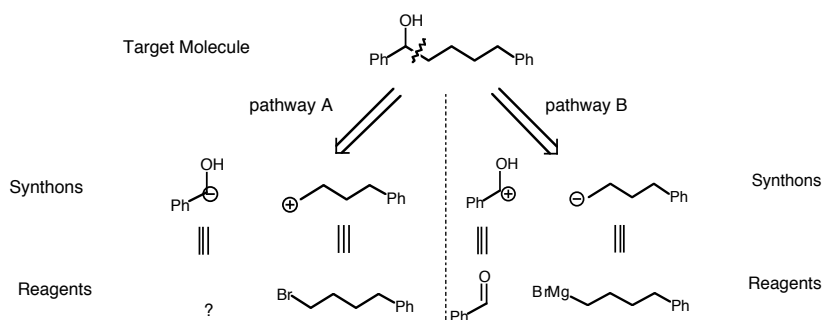
Bulls-Eye!
(Finally...)

ANGEWANDTE
CHEMIE

- Apply one- and two-group disconnections ("1,n-relationships), pericyclic reactions, etc.

Example:

Retrosynthesis 1:



Summary of retrosynthetic approaches:

