What are Organic Synthesis Strategies?

Worksheet

Retrosynthesis breaks a target molecule into smaller precursors by 'disconnecting' key bonds, then finding simple starting materials that can be recombined. Convergent synthesis assembles independent fragments in parallel; linear synthesis builds step by step.

Questions

1. In retrosynthetic analysis, the arrow points

A) Forward in the synthetic route
B) Backward from the target to precursors
C) From starting materials to the product
D) Bidirectionally

2. Which is a key advantage of convergent over linear synthesis?

A) Fewer starting materials needed
B) Fewer total steps to build complex molecules
C) Lower cost of reagents
D) Easier to perform experimentally

3. Friedel-Crafts alkylation (CH + RX CHR) is a common synthetic disconnection. What type of bond is formed?

A) C-O bond
B) C-C bond (benzene ring to alkyl group)
C) C-N bond
D) C-H bond

4. In retrosynthesis, what does 'umpolung' mean?

A) Using protecting groups
B) Reversing the polarity of a functional group
C) Choosing the shortest route
D) Using expensive reagents

5. Design a retrosynthetic route to acetophenone (CH-CO-CH) from benzene.

6. Retrosynthetically analyze ethyl acetate (CH-CO-O-CHCH). What starting materials?

7. For 2-methylbutanenitrile (CHCHCH(CH)CN), identify a convergent synthesis plan.

8. Define: What is retrosynthesis?

9. Define: What is a 'disconnection'?

10. Define: What is convergent synthesis?

Answer Key

1. B) Backward from the target to precursors - Retrosynthetic arrows (usually drawn with a barbed arrow) point backward from the target to precursors, showing how the target would have been made.

2. B) Fewer total steps to build complex molecules - Convergent synthesis assembles independent branches in parallel, reducing total steps. For a large target, this is often more efficient than building linearly step by step.

3. B) C-C bond (benzene ring to alkyl group) - Friedel-Crafts alkylation forms a C-C bond between the benzene ring and the alkyl group, breaking the R-X bond to generate R.

4. B) Reversing the polarity of a functional group - Umpolung (polarity reversal) is a strategy where a normally nucleophilic group is converted to electrophilic, or vice versa, to enable a key disconnection.

5. Target: acetophenone CH-CO-CH Disconnect: C-CO bond benzene (CH) + acetyl source (CHCO). Friedel-Crafts acylation of benzene with acetyl chloride (CHCOCl) or acetic anhydride gives acetophenone directly. Forward: CH + CHCOCl CH-CO-CH (1 step, one of many ways).

6. Disconnect: acyl-O bond acetic acid (CHCOH) + ethanol (CHOH). Esterification: CHCOH + CHOH CHCOCH (Fischer esterification, acid-catalyzed). Starting materials: acetic acid (cheap, available) and ethanol (common).

7. Target: branched nitrile. Convergent approach: synthesize (a) 2-methylbutyl bromide CHCHCH(CH)CHBr and (b) cyanide (CN). SN2 displacement: CHCHCH(CH)CHBr + KCN CHCHCH(CH)CN (in DMSO, 1 step). Two independent fragments (alkyl halide + nucleophile) combined in one step.

8. A problem-solving technique where you work backward from a target molecule, mentally disconnecting bonds to identify simple precursor molecules. The reverse steps form the synthetic route.

9. The mental breaking of a bond in a target molecule, proposed to suggest a synthetic reaction that forms that bond. It asks: 'What bond would I break if I were decomposing this molecule?'

10. A strategy where two or more complex fragments are synthesized separately (in parallel), then combined in one or few final steps to form the target. More efficient than linear synthesis for large molecules.