

Questions "Strategies of Synthesis"

1. Why total synthesis? Give at least 5 reasons ...
2. How is the ideality of a total synthesis defined, at least according to Baran's definition?
3. The highly efficient BASF synthesis of citral starts from prenol and prenal. Outline the steps.
4. What is the atom economy of the Wittig reaction of cyclohexane carbaldehyde, methyl triphenylphosphonium bromide and *n*-BuLi?
5. What is a synthon? Precisely, what would be the a^3 synthon of a carbonyl compound? Please give a reaction possibility forming the a^3 - d^4 bond of carbonyl compound.
6. Give two synthetic equivalents of the following synthons formed by retrocut of a carbonyl compound: a^1 , d^2 , d^4 .
7. Cut 4-phenylbutan-2-one in three different ways and propose possible synthetic equivalents of the synthons.
8. What does the term "umpolung" mean? Give two synthetic equivalents of the following synthons formed by retrocut of a carbonyl compound: d^1 , a^2 , d^3 .
9. Ancient reactions: convert benzaldehyde to 1,3-diphenylpropan-1-one by employing the Corey-Seebach-Umpolung, including removal of the sulfur!
10. Convert benzaldehyde and methyl vinyl ketone to a 1,4-diketone!
11. Outline the mechanism of the Stetter reaction, indicating the Breslow intermediate. What happens, if you forget to add the α,β -unsaturated component? Do you remember the benzoin condensation? Catalyst?
12. What could be done towards an enantioselective Stetter reaction? Ethyl (*R*)-2-(4-oxochroman-3-yl)acetate was obtained in this way.
13. In the original 1975 Corey system, complex carbocyclic skeletons were analyzed for "primary" and "secondary" rings. From there, "strategically significant rings" were identified. What does that mean? Conduct this analysis for tricyclo[3.3.0.0^{2,7}]octane. Do even older routes follow these rules?
14. Questions from the older syntheses: pinacol rearrangement? Traceless removal of a 1,3-dithiolane? Alkyne + allyl cation? Eschenmoser's hydrazone? What is a non-classical carbocation?
15. Propose a pathway from cyclohexanone to β -hydroxycycloheptanone!
16. Synthesis of cyclopropanes: anything else but Simmons-Smith? How would you make an α -diazoester, and why?
17. Doubly acyl-substituted cyclobutanes can be made from acyclic enones via photoredox catalysis. Analyze the mechanism.
18. How would you synthesize a cyclobutene? Au?
19. It would be nice to obtain cyclopentenes by cycloaddition. Precursors? Au again, for instance.

20. Synthesis of cycloheptadiene by [4+3] cycloaddition: how does this work? Where does the Cope rearrangement take place?
21. Interesting is also Gevorgyan's procedure, which reduces a secondary alcohol to a migrated alkene. Look up the mechanism in the literature!
22. Outline the rule-of-thumb for the determination of the electrophilicity or nucleophilicity of a radical. Give examples of one electrophilic and one nucleophilic radical.
23. How would you convert a β -ketoester into a radical? And how could an alkyl radical be formed from a halide?
24. How could tetrachlorophthalimide be useful as precursor of alkyl radicals?
25. Treatment of acyl tellurides with $\text{Et}_3\text{B}/\text{O}_2$ affords alkyl radicals that undergo further reactions useful for synthesis. Please outline the mechanism.
26. What is characteristic for hydrogen atom transfer (HAT) reactions? Provide an example.
27. How could indole and cyclohexenone be cross-coupled in a radical reaction? Discuss also the electrophilicity and nucleophilicity of the radical synthons.
28. The first retrostep starting from citral (=geranial) is a retro-Cope rearrangement, followed by a retro-Claisen rearrangement. What is the precursor and how would you synthesize it starting from prenyl?
29. How would you synthesize the following target molecules?

