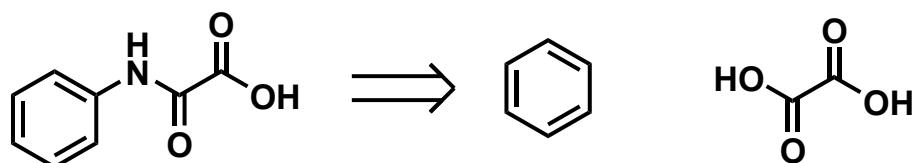
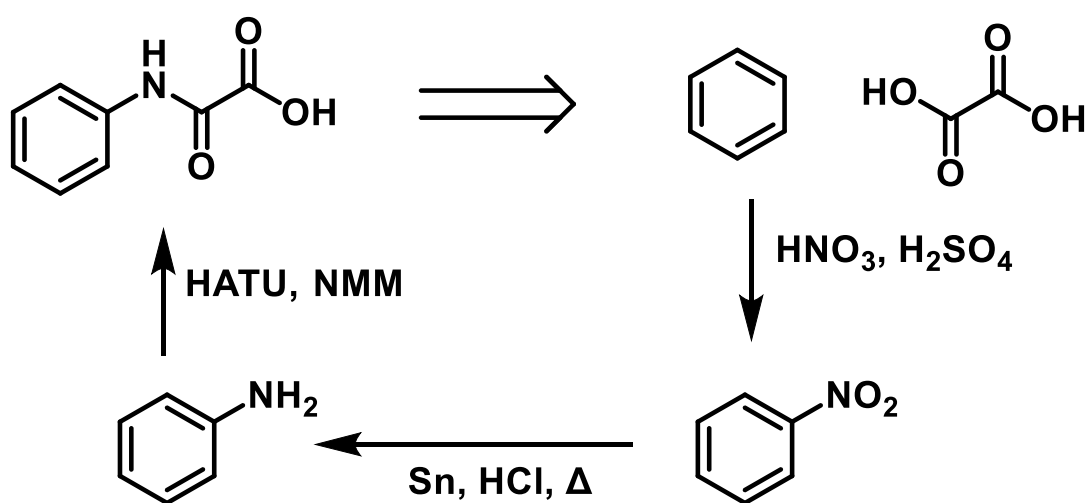


Retrosynthetic Problems FS2023

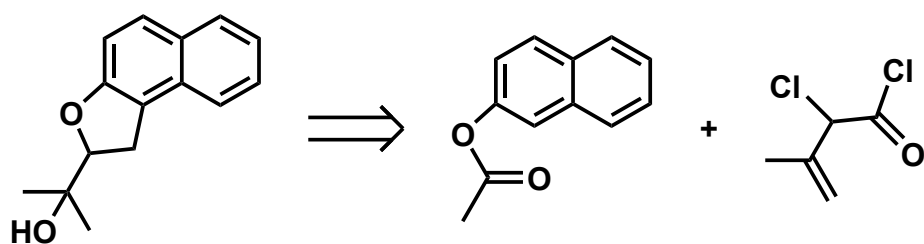
1)



Solution: Formation of aniline via nitration and reduction. Activation of carboxylic acid will facilitate formation of the amide.

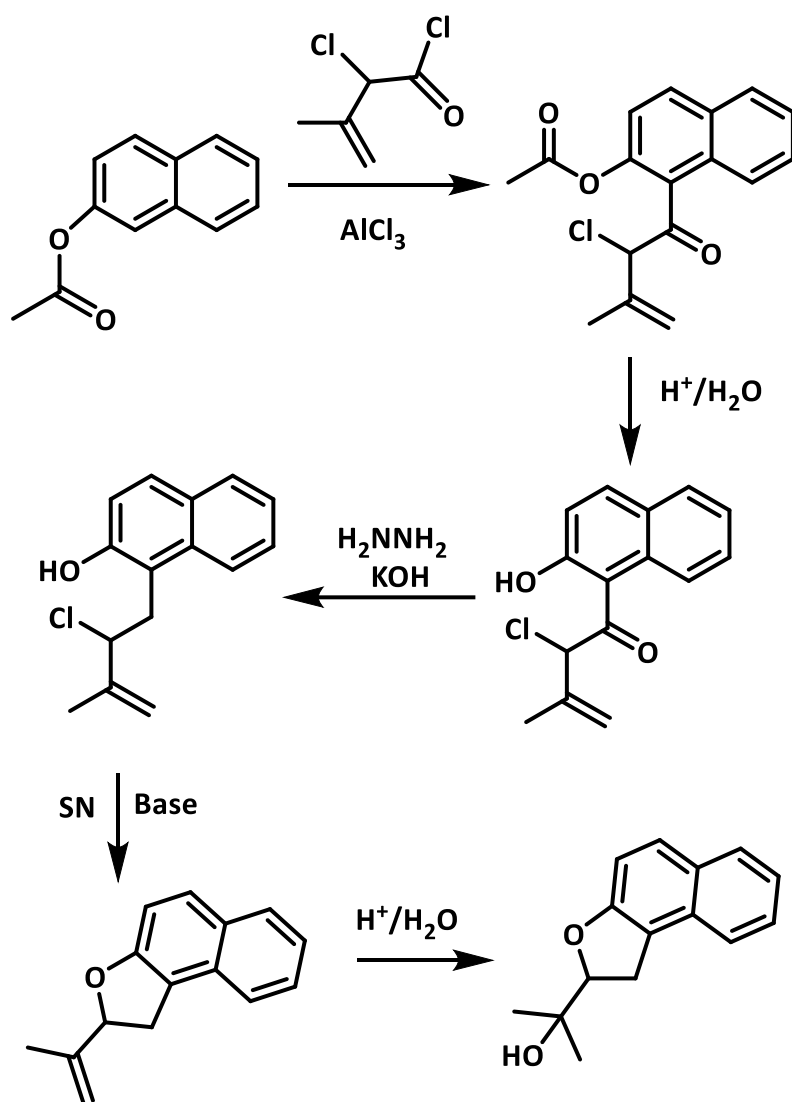


2)

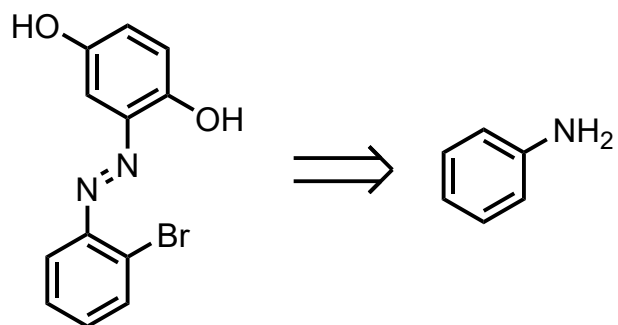


Solution: Friedel-Crafts will form the key C-C bond. Wolff-Kishner reduction of ketone and subsequent 5-exo tet cyclization via Sn2 mechanism forms the ring.

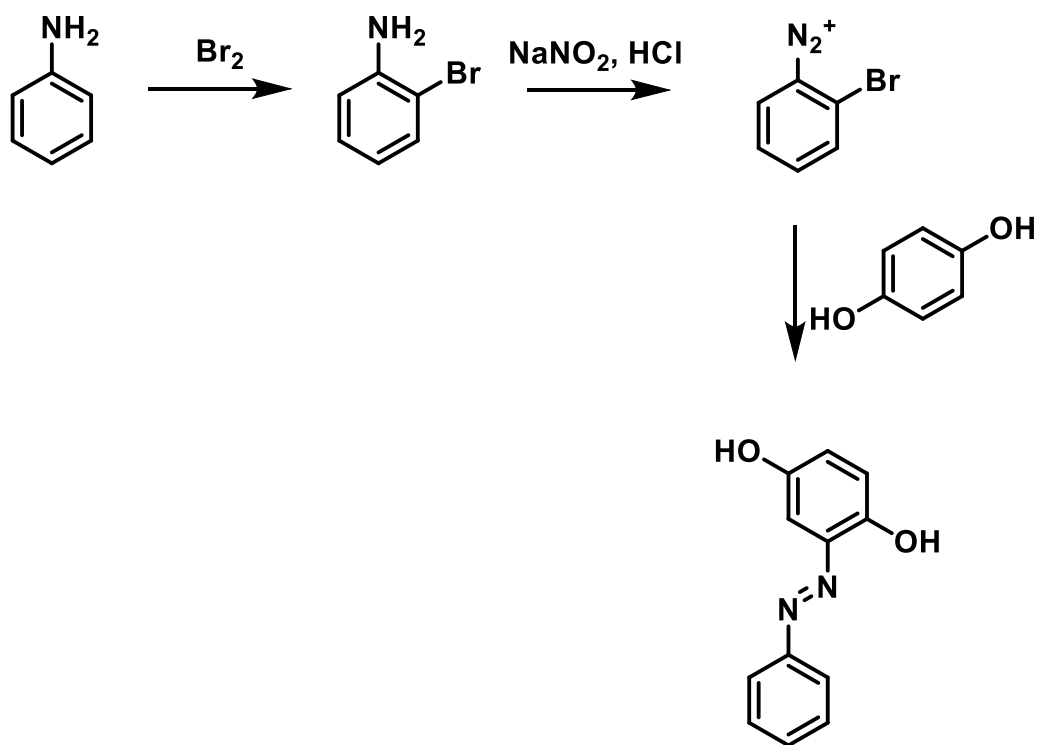
Note: Problem was simplified such that it is accessible to first years. The C-C bond to the aryl ring would ideally be formed [3,3] sigmatropic rearrangement.



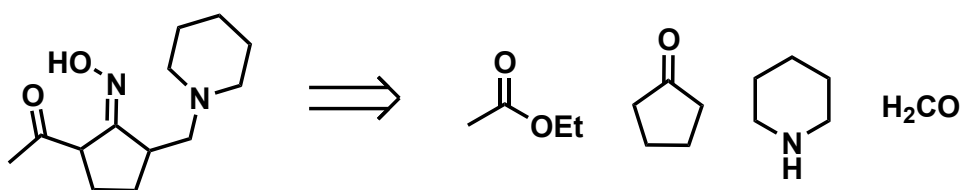
3)



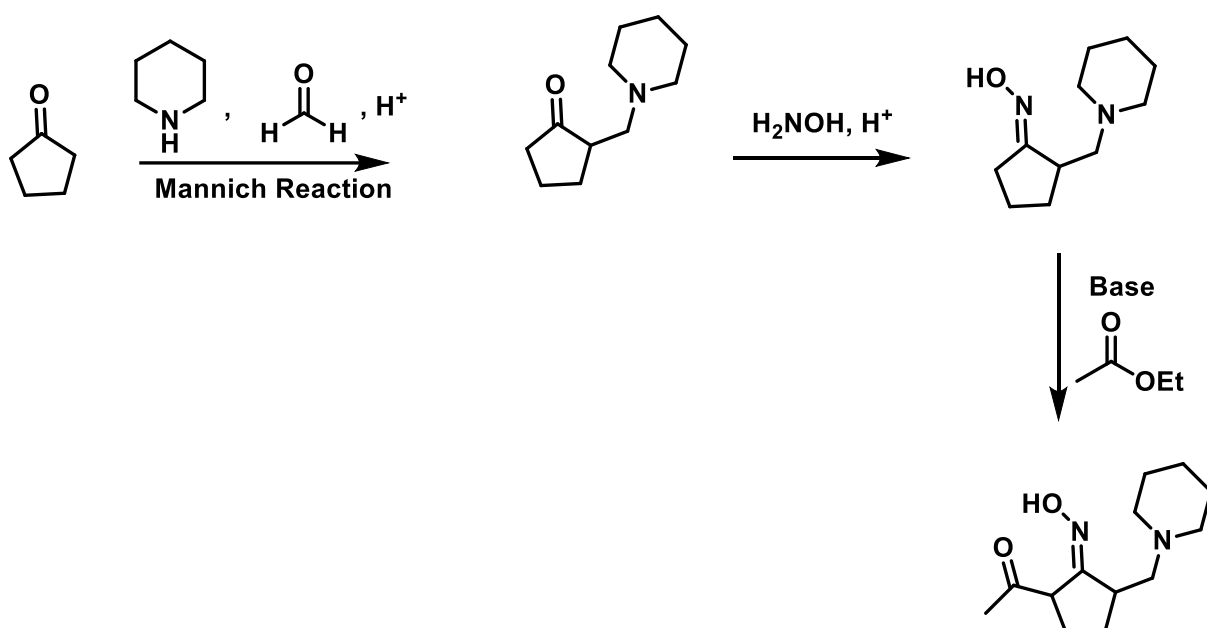
Solution: Bromination of aniline and subsequent formation of the diazonium salt yield the key intermediate that can be coupled via azo coupling.



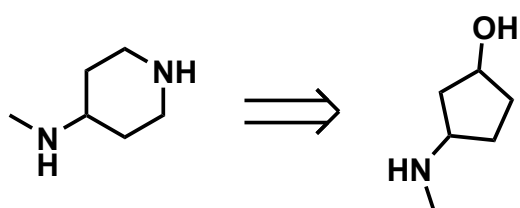
4)



Solution: Mannich reaction of cyclopentanone yields the 1,3 tertiary amine. Formation of oxime, deprotonation (strong, sterically hindered base) of the alpha position and subsequent addition of the ester yields the final product.

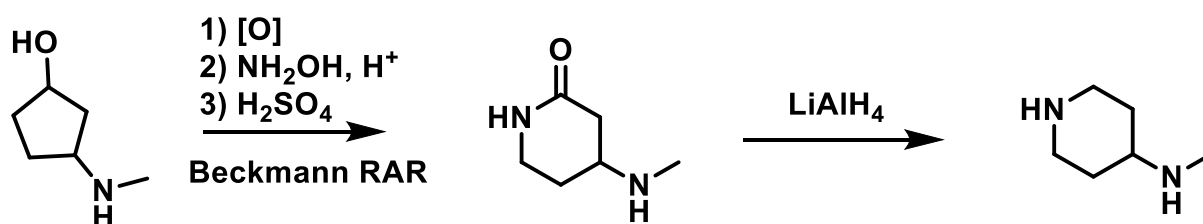


5)

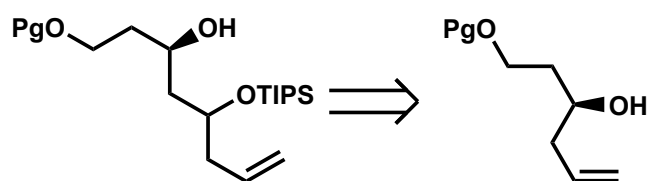


Solution: Oxidation of alcohol to ketone. Beckman rearrangement of the starting material and reduction with lithium aluminium hydride yield the final product.

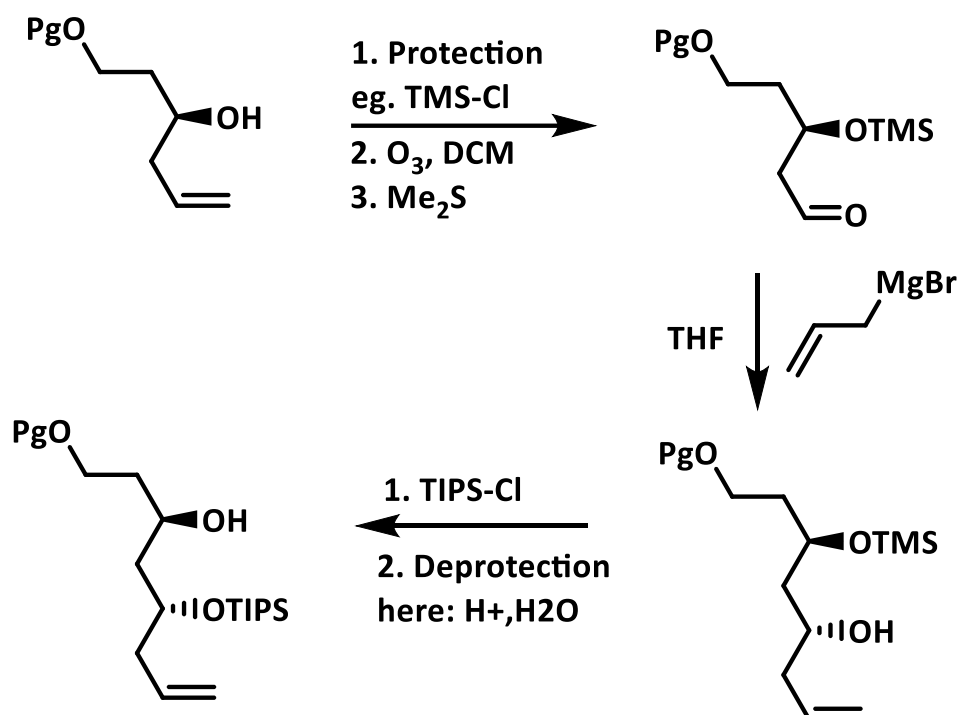
Note: Weaker reducing agents, or reduction via Wolff-Kishner or Clemmenson do NOT work.



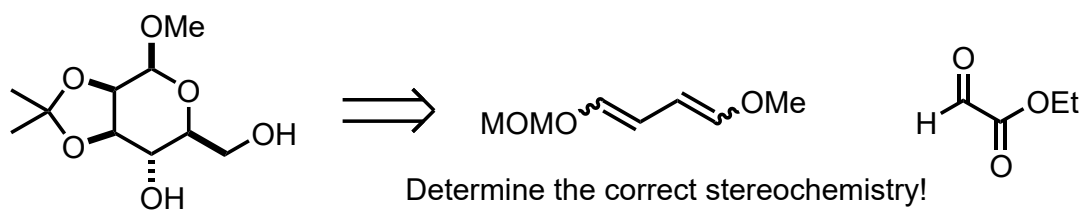
6)



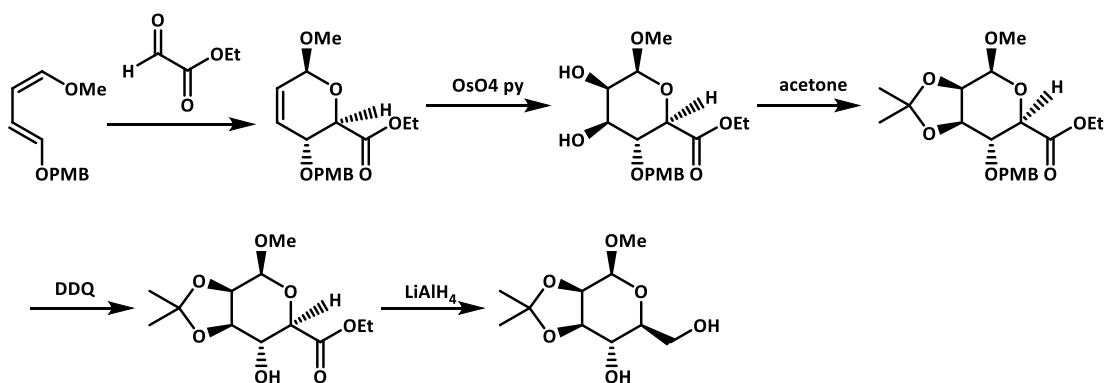
Solution: Ozonolysis of double bond yields the aldehyde. Addition of Grignard, and a protection/deprotection step yield the final product. Stereochemistry here is not important here.



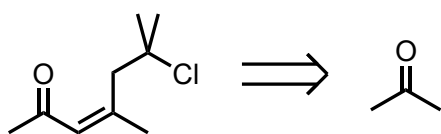
7)



Solution: Hetero Diels-Alder yields the cyclisation product. Dihydroxylation of the alkene and subsequent protection yields the acetal. Oxidation using DDQ deprotects the PMB group, and reduction of the ester yields the final product.



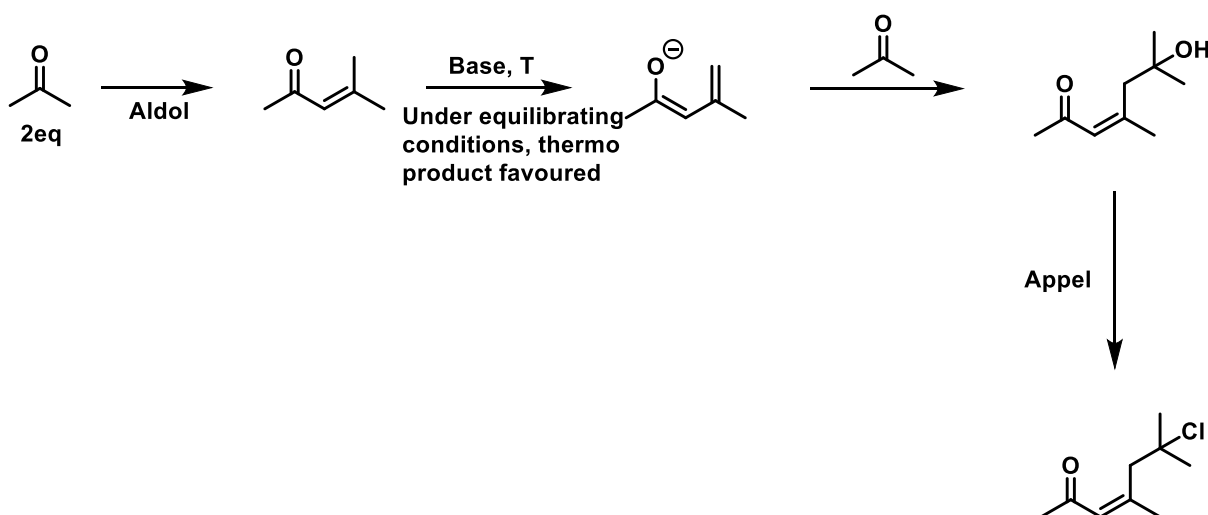
8)



Note: All carbons must come from Acetone!

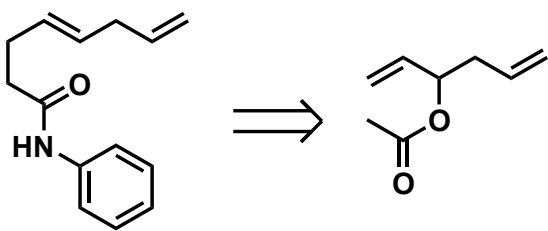
Solution: Aldol condensation, then deprotonation at the gamma-position under equilibrating conditions. Addition of a third equivalent of acetone forms the aldol addition product, Appel conditions form the alkyl halide.

Note: For deprotonation, using equilibrating conditions, deprotonation occurs at the gamma position as the thermodynamic product, due to delocalisation over more atoms than at the alpha position. In practice, deprotonation at the gamma position can also be achieved by double deprotonation at first the alpha position, then at the gamma position using a base such as tBuLi.

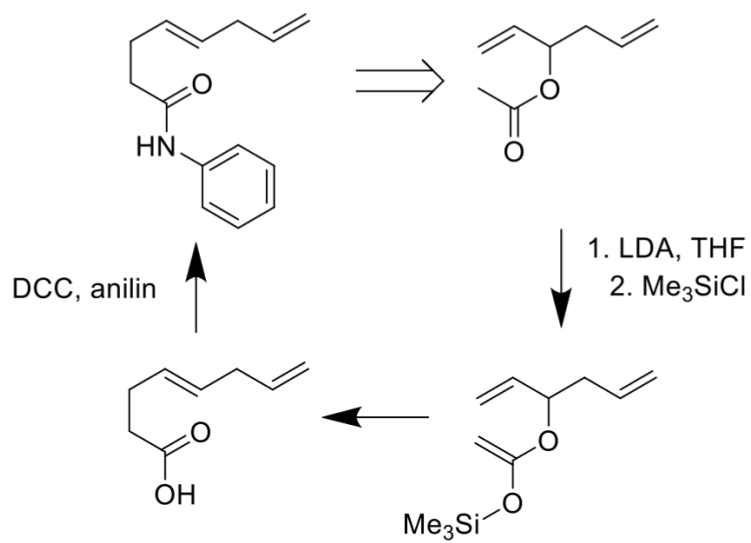




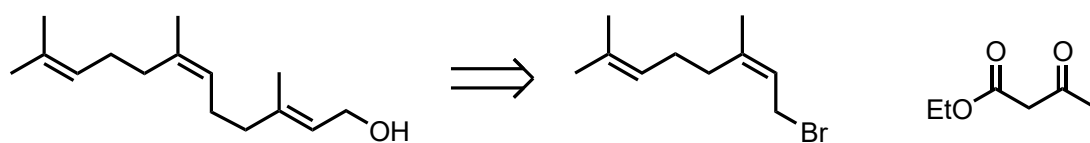
9)



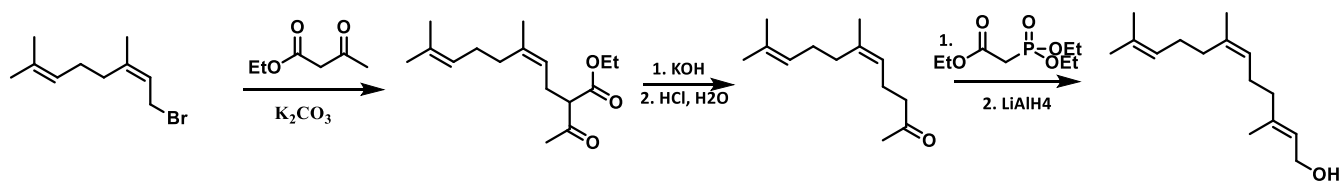
Solution: Ireland-Claisen rearrangement with subsequent hydrolysis of the TMS ester yields the gamma-delta unsaturated carboxylic acid. Activation and addition of aniline form the amide.



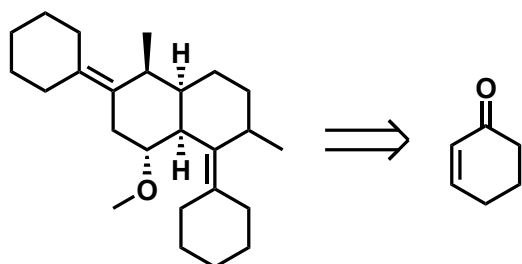
10)



Solution: Alkylation of the keto-ester and subsequent decarboxylation yields the ketone intermediate. HWE and subsequent reduction of the ester yield the product.

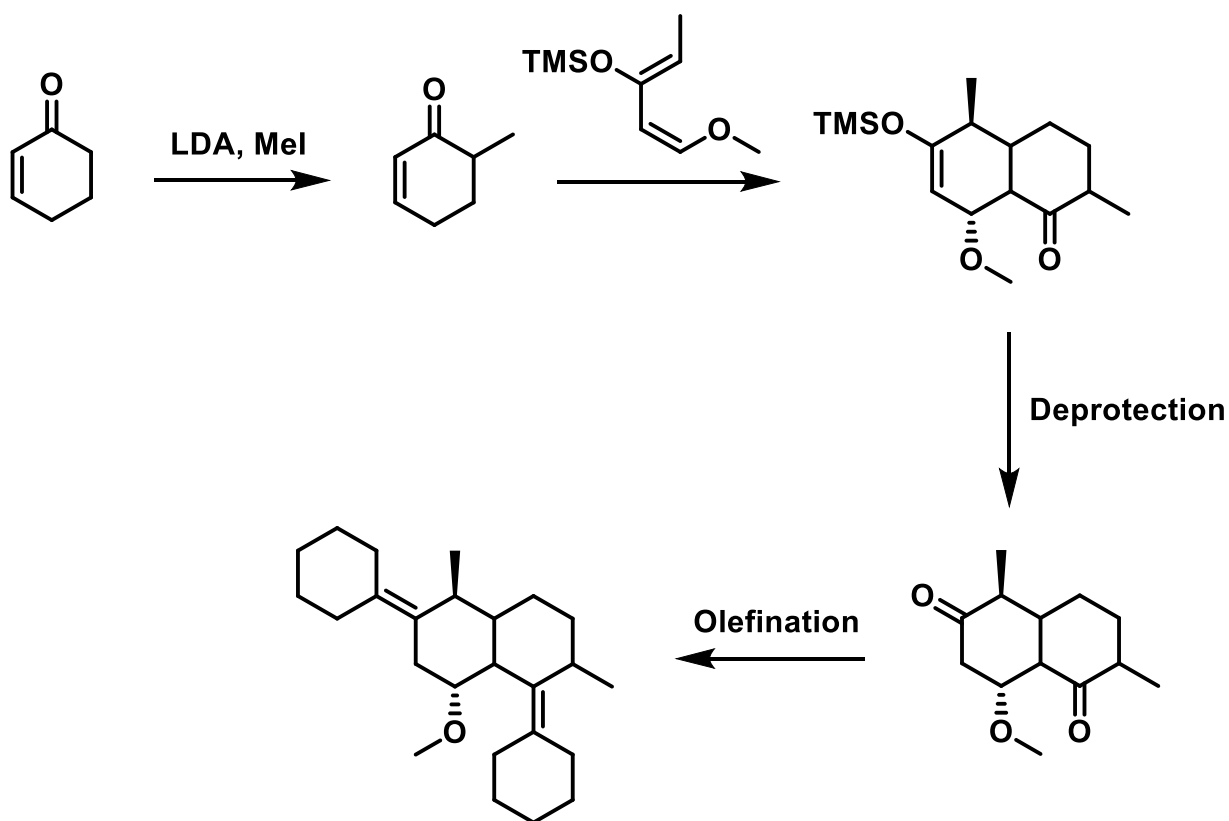


11)

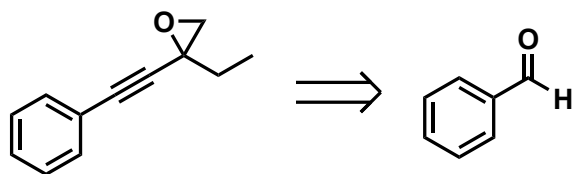


Solution: Alkylation of cyclohexanone in the alpha position, with subsequent Diels-Alder using Danishevsky's diene yield the bicycle product. Deprotection of TMS and equilibration to the ketone, with subsequent olefination, yield the final product.

Note: Olefination can be done (in theory) with a Wittig, however in practice tetrasubstituted alkenes cannot be formed like this. In industry, the reaction would be accomplished via a McMurry coupling with an excess of cyclohexanone.



12)



Solution: Corey-Fuchs alkylation of the aldehyde yields the lithium alkyne. Addition of aldehyde forms the alcohol, which can be oxidized to a ketone using numerous conditions (mild ones are best, in order to prevent oxidation of the alkyne). Corey-Chaykovsky epoxidation yields the final product.

