

**Reactive Intermediates**

**Reading:** *Clayden (1st Edition): Chapters 37, 38, 40; (2nd Edition): Chapters 36, 38*  
*Moody and Whitham, 'Reactive Intermediates' (Oxford primer no. 8)*  
*Harwood, 'Polar Rearrangements' (Oxford primer no. 5)*

**Topics for notes:**

Make notes on the structure (including stabilising effects) and methods for the generation of carbocations, carbanions, carbenes, nitrenes, arynes (i.e. benzyne). The following reactions are typical of these reactive intermediates:

**Carbocations:** Rearrangements (1,2-shifts of alkyl groups and protons) such as the Pinacol, Wagner-Meerwein, and Tiffeneau-Demjanov reactions. Consider the driving force for rearrangement.

**Carbanions:** Rearrangements such as the Favorskii reaction and relatives. 2,3-Wittig rearrangement; Benzoin condensation.

**Carbenes:** Distinguish between singlet and triplet carbenes; electrophilic and nucleophilic carbenes. The main reactions: Rearrangement (e.g. Wolff), cyclopropanation, insertion into (C–H) bonds, attack on the carbene by nucleophiles; the acyloin reaction and equivalents in biology. Look briefly at metal carbenoids.

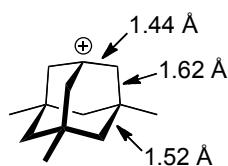
**Nitrenes:** Reactions which could formally be represented to proceed *via* nitrene intermediates such as the Curtius rearrangement; aziridination.

**Arynes:** Formation from arenes under a range of conditions; reactions with nucleophiles; substituent effects on the regioselectivity of nucleophilic attack.

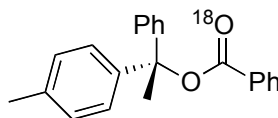
**Tutorial Problems**

1. Discuss the following observations:

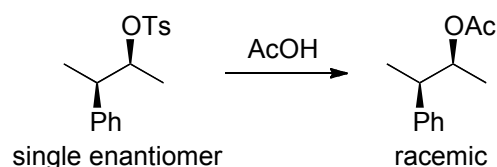
a) The bond lengths in this adamantyl cation are as follows:



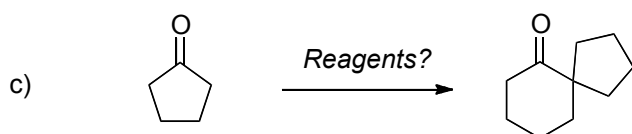
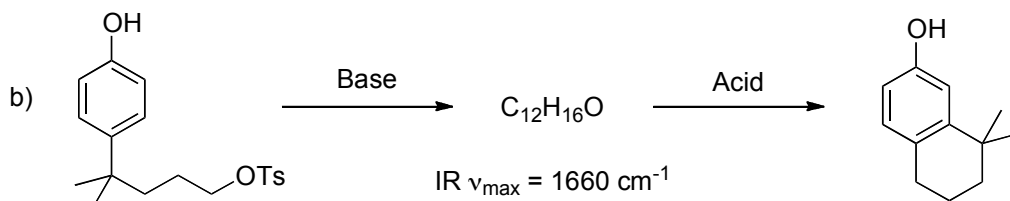
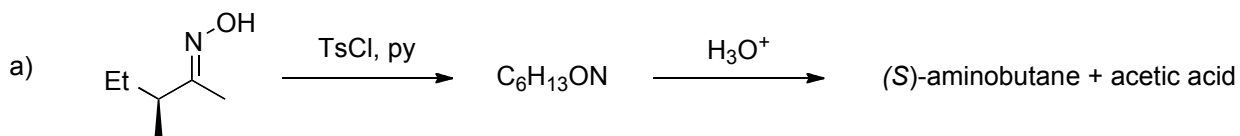
b) When dissolved in an ionising solvent, scrambling of the isotopically-labelled carbonyl oxygens occurs faster than racemisation



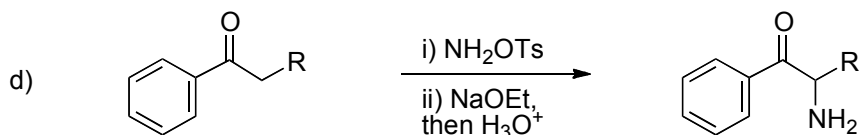
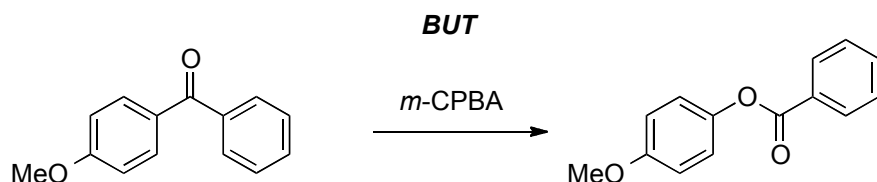
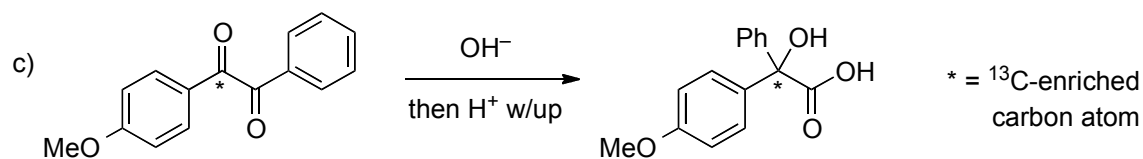
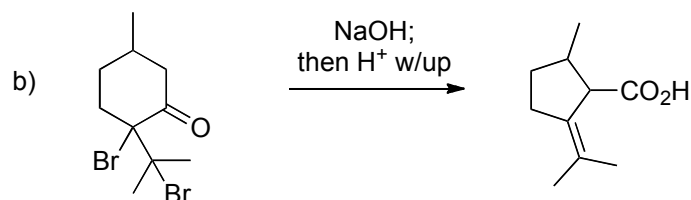
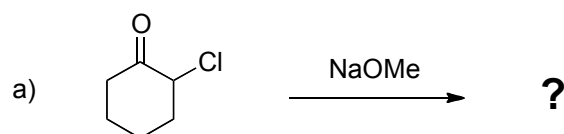
c) Acetolysis of this tosylate gives a racemic product from a single enantiomer



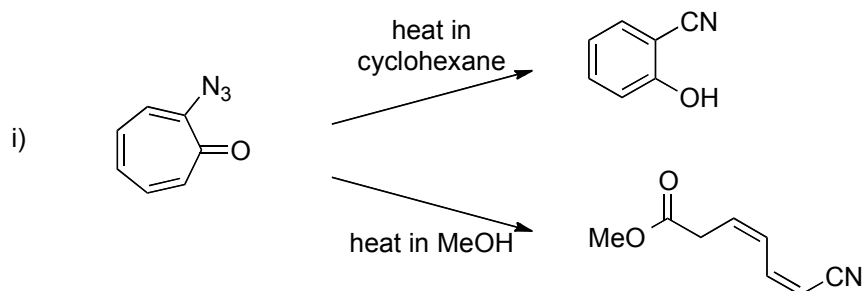
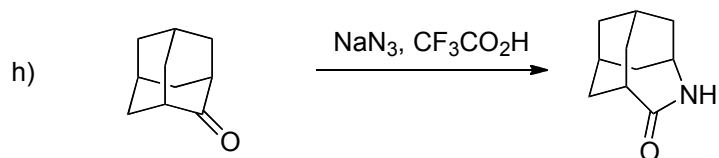
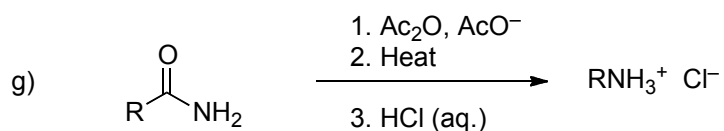
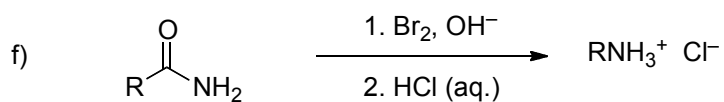
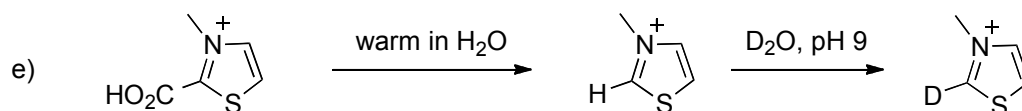
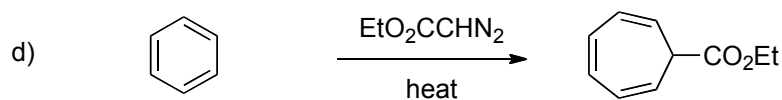
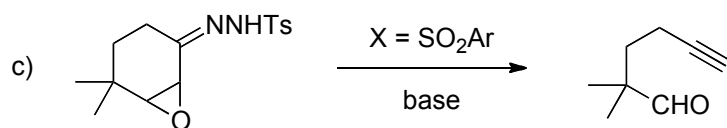
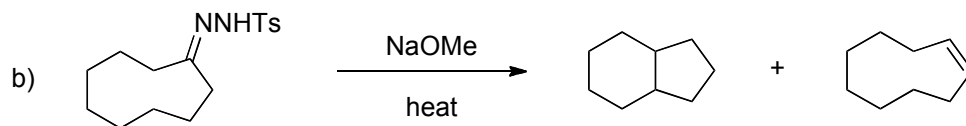
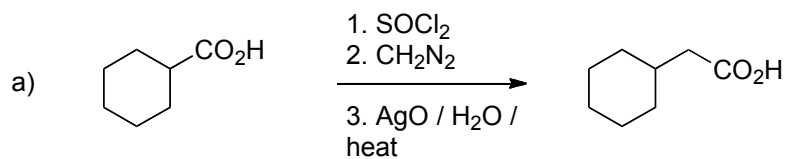
2. Give mechanisms to explain the following transformations, and identify intermediates where appropriate. Comment on any aspects of selectivity. For part c), you should also suggest reagents.



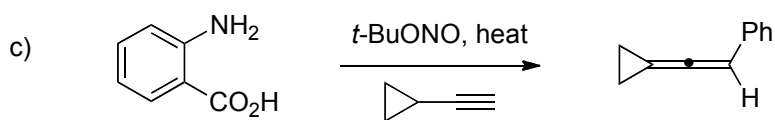
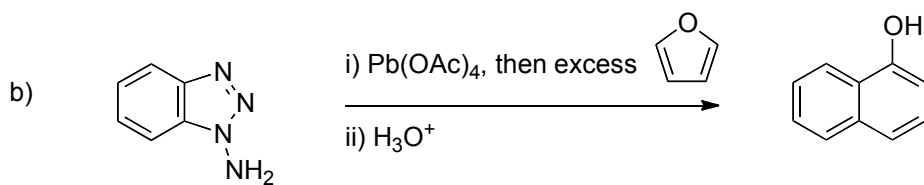
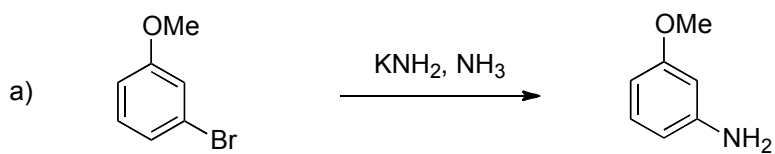
3. Suggest a product and mechanism for part a), and mechanisms for parts b-d). Explain the contrasting outcomes observed in part c).



4. Give mechanisms to explain the following transformations.

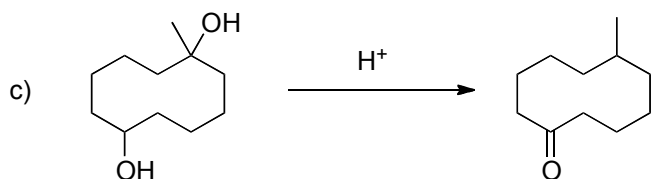
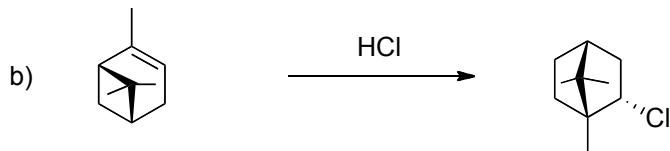
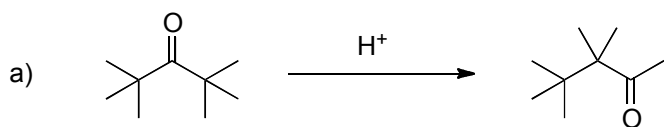


5. Provide mechanisms, and explanations for selectivity where appropriate, for the following reactions:

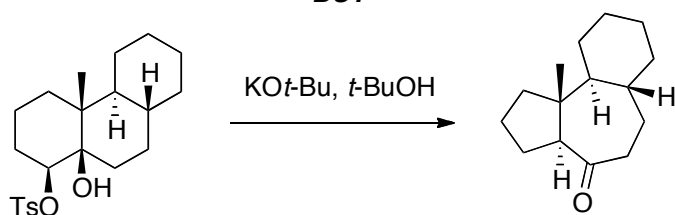
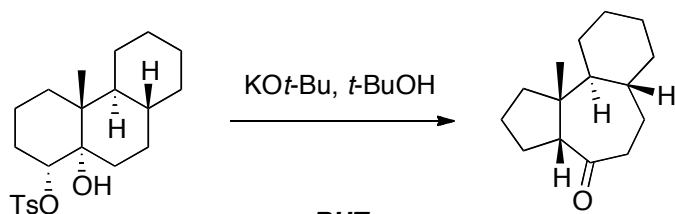


**Optional problems**

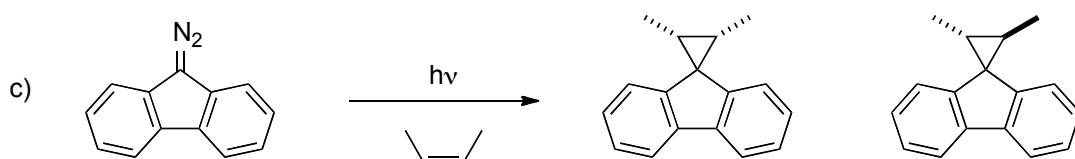
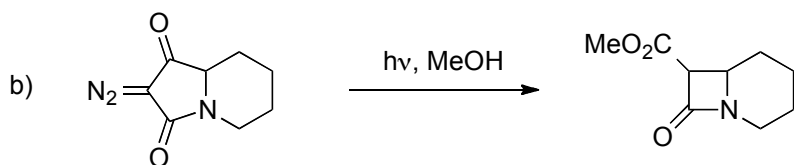
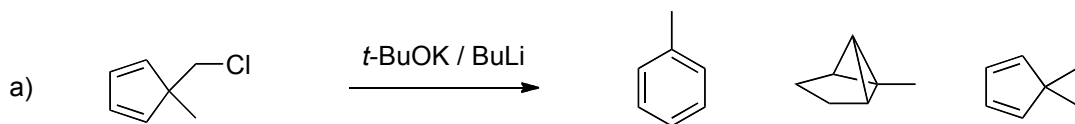
6. Give mechanisms for the following acid-mediated transformations:



7. Explain the contrasting selectivities of the following pair of reactions:



8. Give mechanisms to explain the outcome of the following reactions. Comment on aspects of selectivity as appropriate.



2 : 1