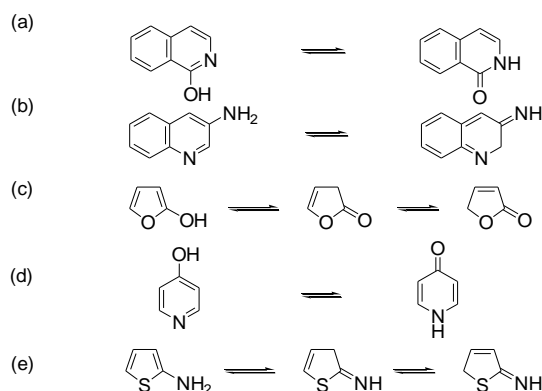


Chemistry II (Organic): Heterocyclic Chemistry

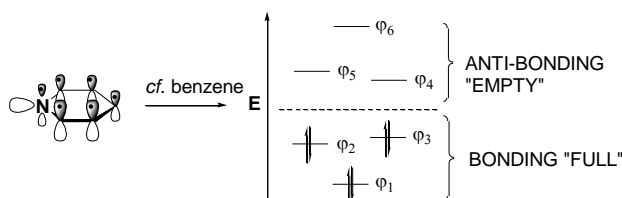
TUTORIAL PROBLEMS – OUTLINE ANSWERS

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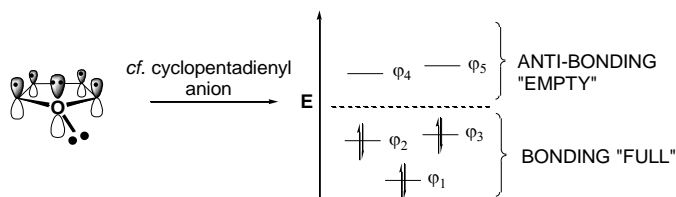


2 (a)



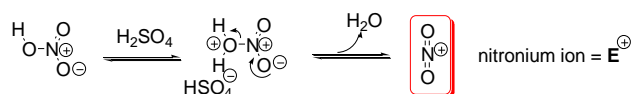
The MO diagram is very similar to that for benzene but now ϕ_2/ϕ_3 and ϕ_4/ϕ_5 are no longer strictly degenerate (*i.e.* they have slightly different energies). However they are close in energy and so the picture is very similar with one electron being 'donated' from each p-orbital to the π -system. Consequently, there are 6 electrons which fill the bonding orbitals (ϕ_1, ϕ_2 & ϕ_3) = $4n + 2$ electrons where $n=1$ (*i.e.* fulfilling Hückel's rule).

(b)

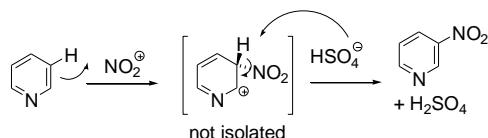


The MO diagram is very similar to that for the cyclopentadienyl anion but again ϕ_2/ϕ_3 and ϕ_4/ϕ_5 are no longer strictly degenerate (*i.e.* they have slightly different energies). In this case each p-orbital on carbon donates a single electron to the π -system and the oxygen lone pair p-orbital donates two electrons to give six electrons in total (*i.e.* $4n + 2$ where $n = 1$ for Hückel's rule).

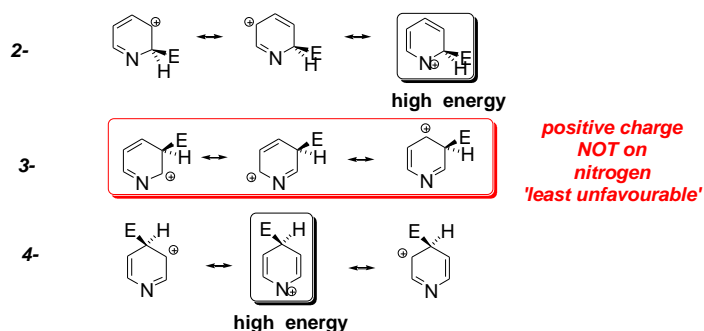
3 (a) (i) Sulfuric acid (H_2SO_4) is a stronger acid than nitric acid (HNO_3) and protonates the nitric acid resulting in the formation of the nitronium ion which is a potent electrophile.



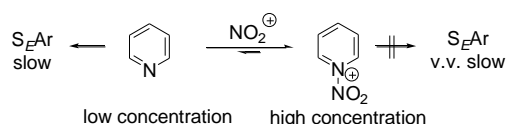
The nitronium ion reacts *via* an addition-elimination mechanism ($\text{S}_{\text{E}}\text{Ar}$) with the pyridine ring under kinetic control.



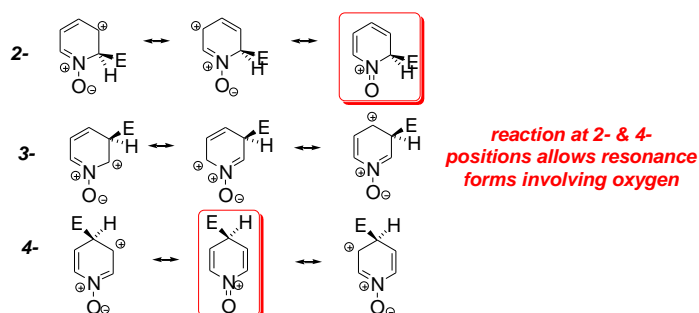
The regioselectivity for reaction at the 3- (β -) position arises because the Wheland intermediate *en-route* to this product is of lower energy than for reaction at either the 2- (α -) or 4- (γ -) positions:



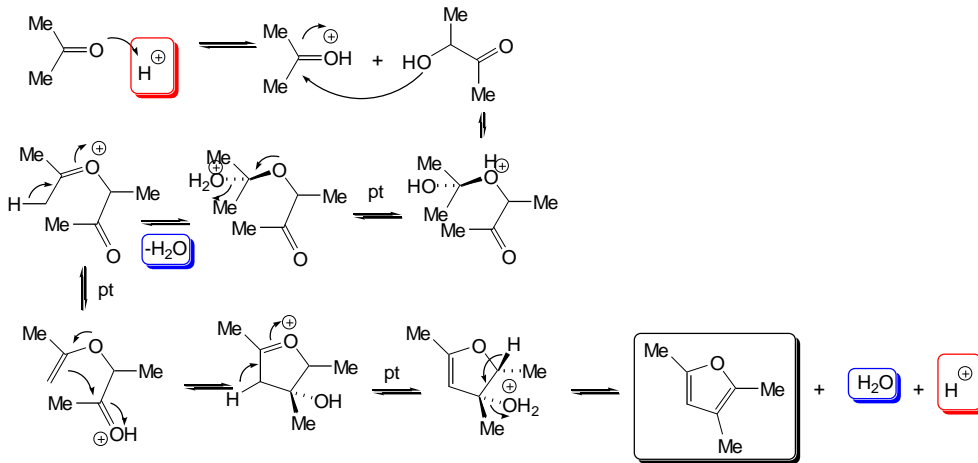
- (ii) The reactivity of pyridine is severely compromised by the fact that it contains a basic nitrogen lone pair that can add an electrophile, such as the nitronium ion, to give a positively charged pyridinium ion. The positively charged pyridinium ion is even less reactive towards electrophilic substitution than the π -deficient pyridine. An equilibrium is set up between the neutral pyridine and the pyridinium ion making the concentration of pyridine available for S_EAr reaction very low:



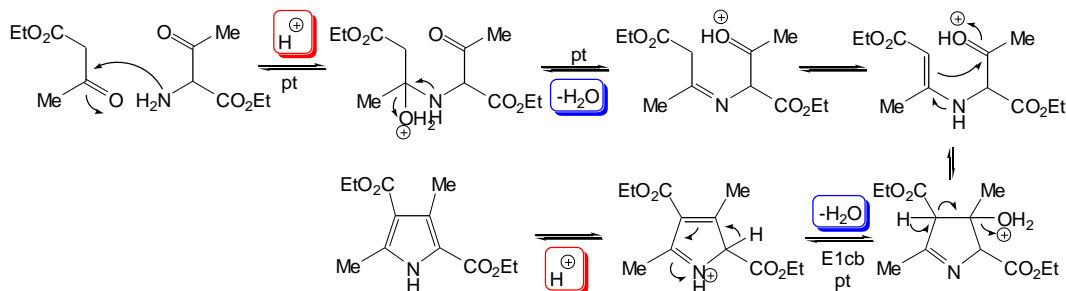
This cannot happen for pyridine-*N*-oxide. Examination of the delocalisation in Wheland intermediates for reaction of the nitronium ion with pyridine-*N*-oxide reveal that regioselective reaction at the 2- and 4-positions is expected because these have the lowest energy. That only reaction at the 4-position is observed is probably mainly for steric reasons:



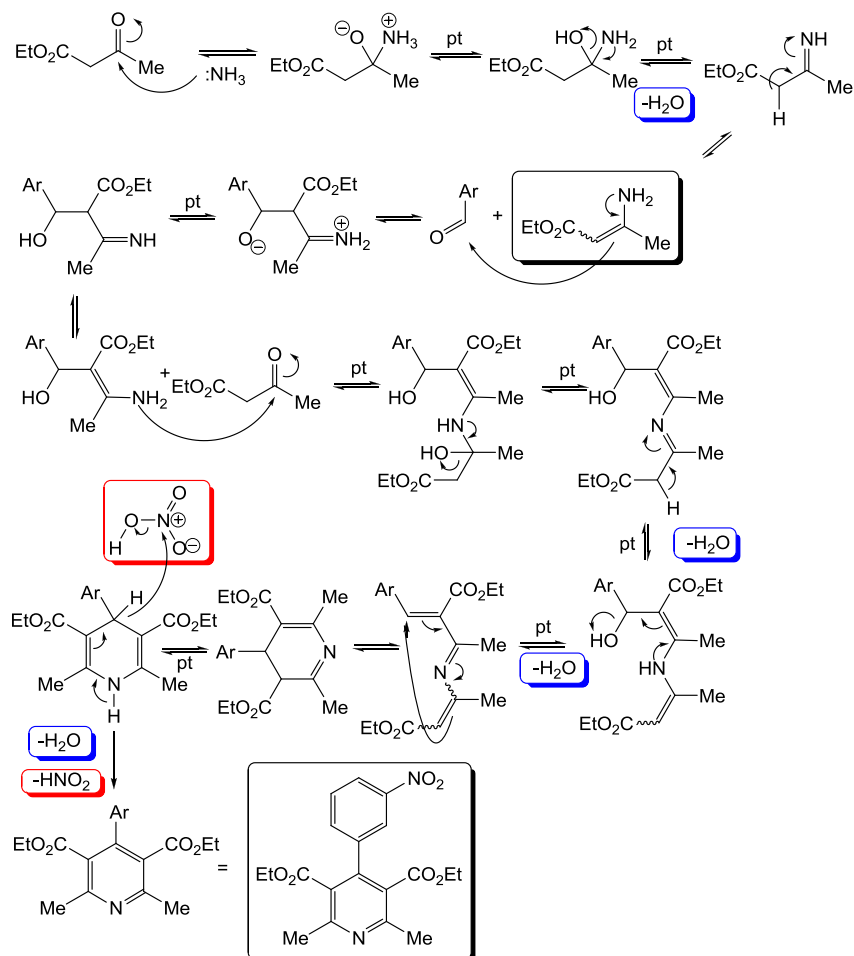
- 4 (a) Condensation reaction to form furan. Intermediates are not isolated and any reasonable mechanism is acceptable. Elimination of two equivalents of water overall.



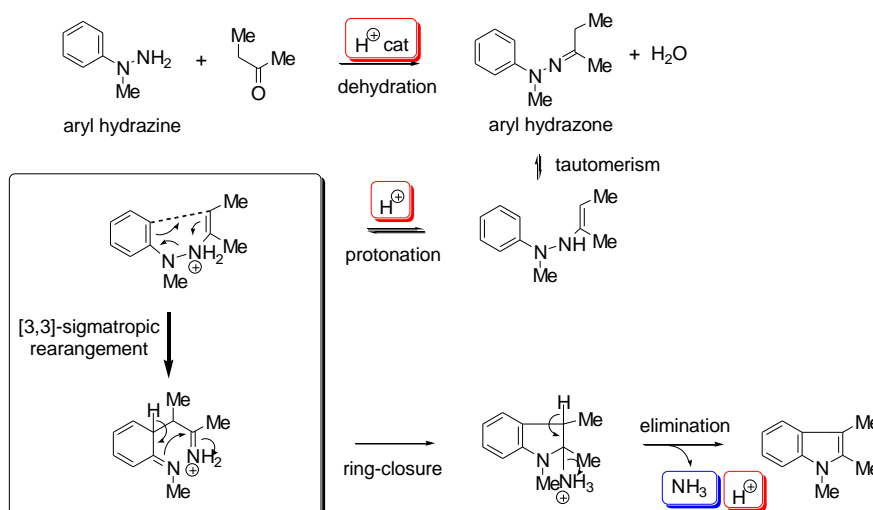
- (b) A Knorr pyrrole synthesis. Intermediates are not isolated and any reasonable mechanism is acceptable. Elimination of two equivalents of water overall.



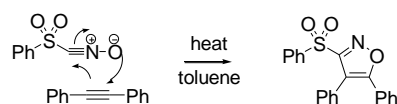
- (c) A Hantzsch pyridine synthesis. Intermediates are generally not isolated and any reasonable mechanism is acceptable. Elimination of four equivalents of water overall.



- 5 (a) This is a Fischer indole synthesis. Driving force: a) aromatic product, b) loss of ammonia and water, c) N-N (weak bond) broken; C-C (strong bond) formed. Regiochemistry of enamine formation favours more substituted enamine.



- (b) 1,3-Dipolar cycloaddition reaction of nitrile oxide with an alkyne. No regiochemical issues but key orbital interaction will be LUMO of 1,3-dipole with HOMO of dipolarophile.



Notes on writing mechanisms:

- *Full mechanisms should be drawn*, clearly indicating involvement of any catalyst (e.g. H^+ , which should not be consumed in the course of the mechanism) and the loss of any condensate molecule (e.g. H_2O).
- Most of the individual steps invoked will be reversible and should be indicated with equilibrium arrows. The driving force for the reactions to proceed in the directions shown is usually a combination of the physical removal of any condensate molecule rendering these steps essentially irreversible and the thermodynamic stability of the aromatic products.
- The exact mechanisms of almost all condensation reactions are not known with certainty and almost certainly vary according to the precise conditions, pH etc. and so there are a number of 'correct' mechanisms which can be drawn. Any reasonable mechanism is acceptable.