Name (Print)_	
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PS #8 - Condensation Chemistry for the Synthesis of Heterocycles

Part A) In 1998 Pfizer was searching for a heart medication and discovered Viagra, a potent PDE 5 inhibitor. The core of the drug contains a pyrazole fused to a pyrimidine ring which gives rise to a bicyclic aromatic **heterocycle**. Condensation of an acid chloride with an amide/amine bis-functionalized pyrazole ring generates the desired pyrimidine ring. Working together, propose a reasonable mechanism for this ring formation. *Note that nucleophilic attack of the nitrogen atom of one amide on the carbonyl of another amide would be unlikely to occur unless the product were thermodynamically favorable, ie. an aromatic heterocycle!*

Viagra; Pfizer, 1998

$$C_1$$
 + H_2N N pyridine

Part B) In 2001, Bayer (in competition with Pfizer) began clinical trials with Levitra (Vardenafil-hydrochloride). It is structurally very similar to Viagra, however, Bayer was clever and moved one of the nitrogen atoms in the heterocyclic core to get around the Viagra patent owned by Pfizer. Condensation of an imido hydrazide and an α -ketoester will form part of the heterocyclic core. As a group, come up with a reasonable synthesis of the α -ketoester starting from **alanine** using any additional reagents you require.

Levitra; Bayer, 2001