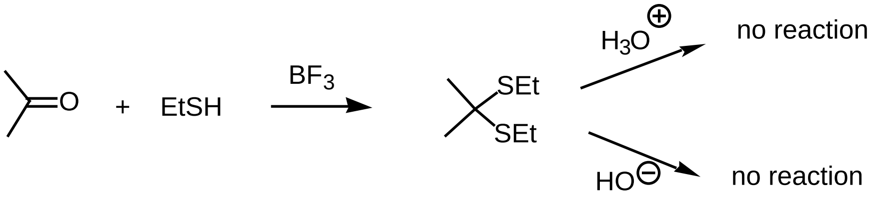
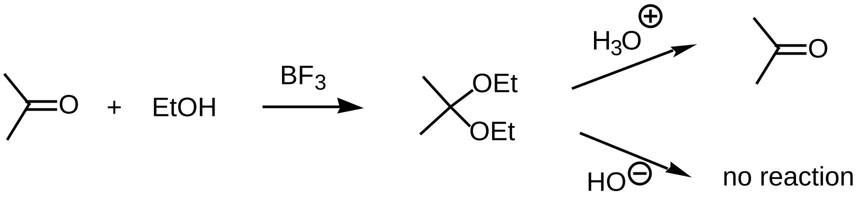
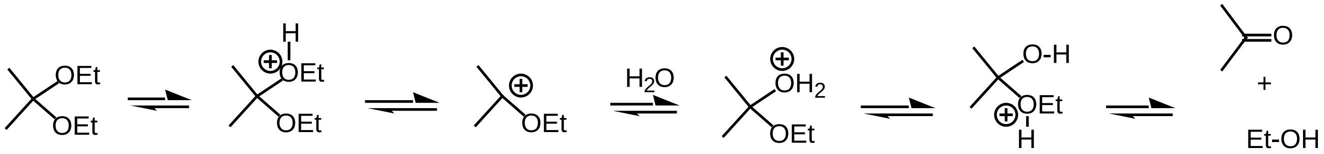
Chemistry 304B **KEY TO** Problem Set 11

1. Note the following reaction of a thiol with acetone, in the presence of a Lewis acid, BF_3. The product is a thioacetal, and has direct analogy with the simple oxygen analog, the acetal. One critical difference however: while the acetal is stable to base (in contrast to a hemiacetal, for example) and readily hydrolyzed back to the ketone in acidic water, the thioacetal is relatively stable to both acid and base

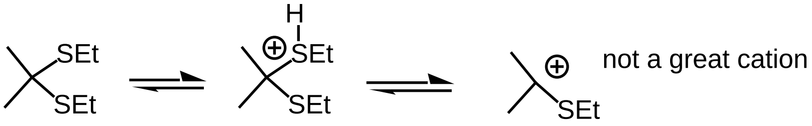
Explain with words and pictures (mechanism).







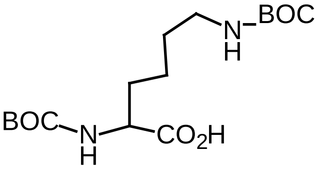
This acetal, when protonated, can ionize to give a well-stabilized carbocation, the oxonium ion. The addition of water and loss of EtOH (old story) leads back to the ketone, acetone.



This thioacetal can be protonated, but ionization is not favorable. The sulfur does not strongly stabilize the carbocation next door; the resonance donation of the lone pair is not particularly good because of a mismatch of orbitals (second row with first row element). Therefore, the whole process requires serious heating and strong acid to occur at all.

Both the acetals and the thioacetals are stable in base, because the only mechanism of hydrolysis back to the ketone would involve an S_N2 reaction which is strongly disfavored at a quarternary carbon (the acetal carbon).

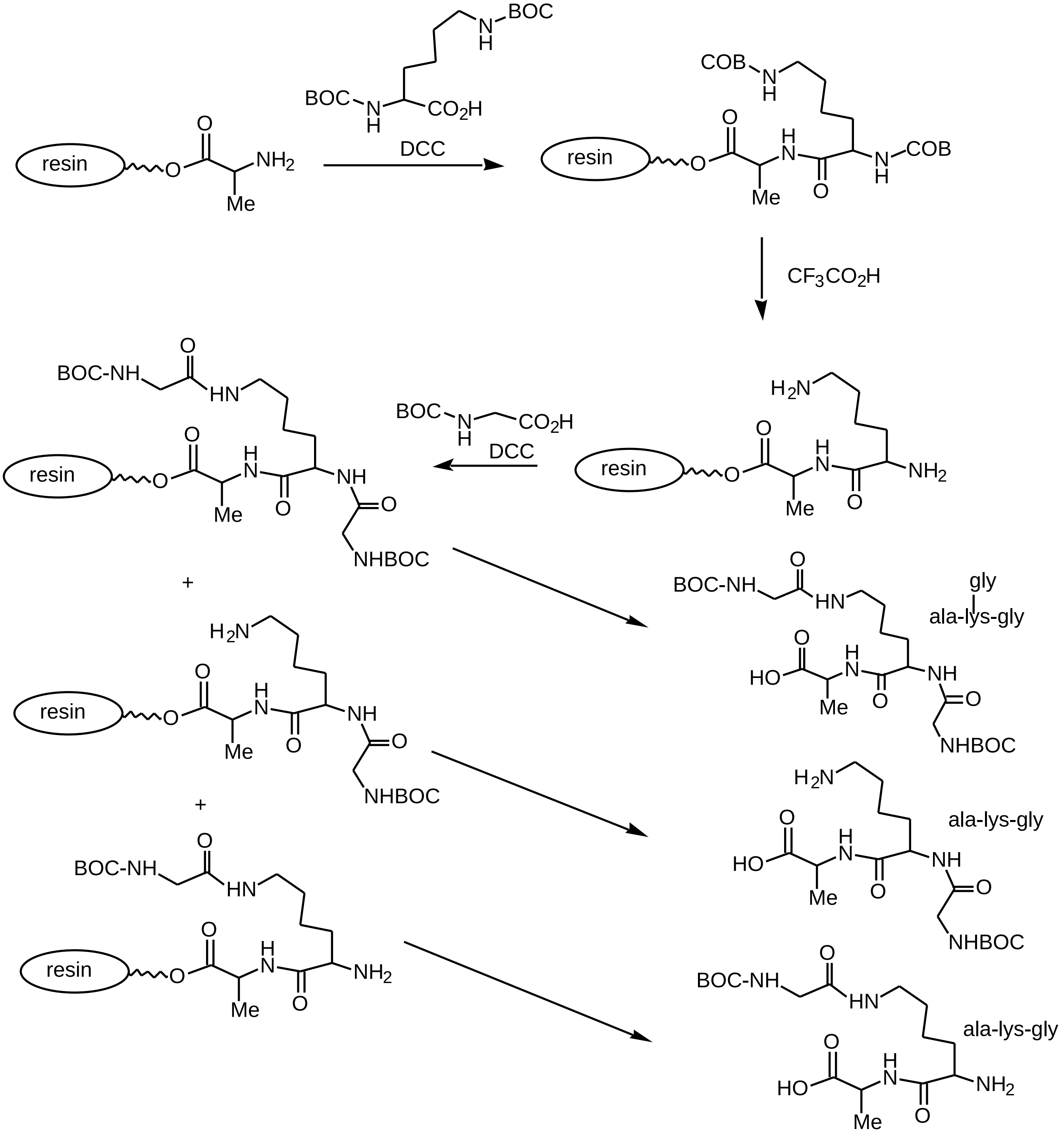
2. An aspiring peptide chemist decided to attempt the synthesis of the peptide gly-lys-ala using the solid-phase method. To the Ala resin, she couples the following derivative of lysine:



After the coupling this unit onto the resin-bound Ala, she then completes the synthesis in the usual way by coupling BOC-Gly, deprotecting the peptide, and removing it from the resin. She is shocked to find a mixture of several peptide products. Two of them give the amino acid analysis [ala, gly, lys; no sequence intended] and one gives the analysis [ala, 2 gly, lys].

What is the structure of the Ala-resin starting material?

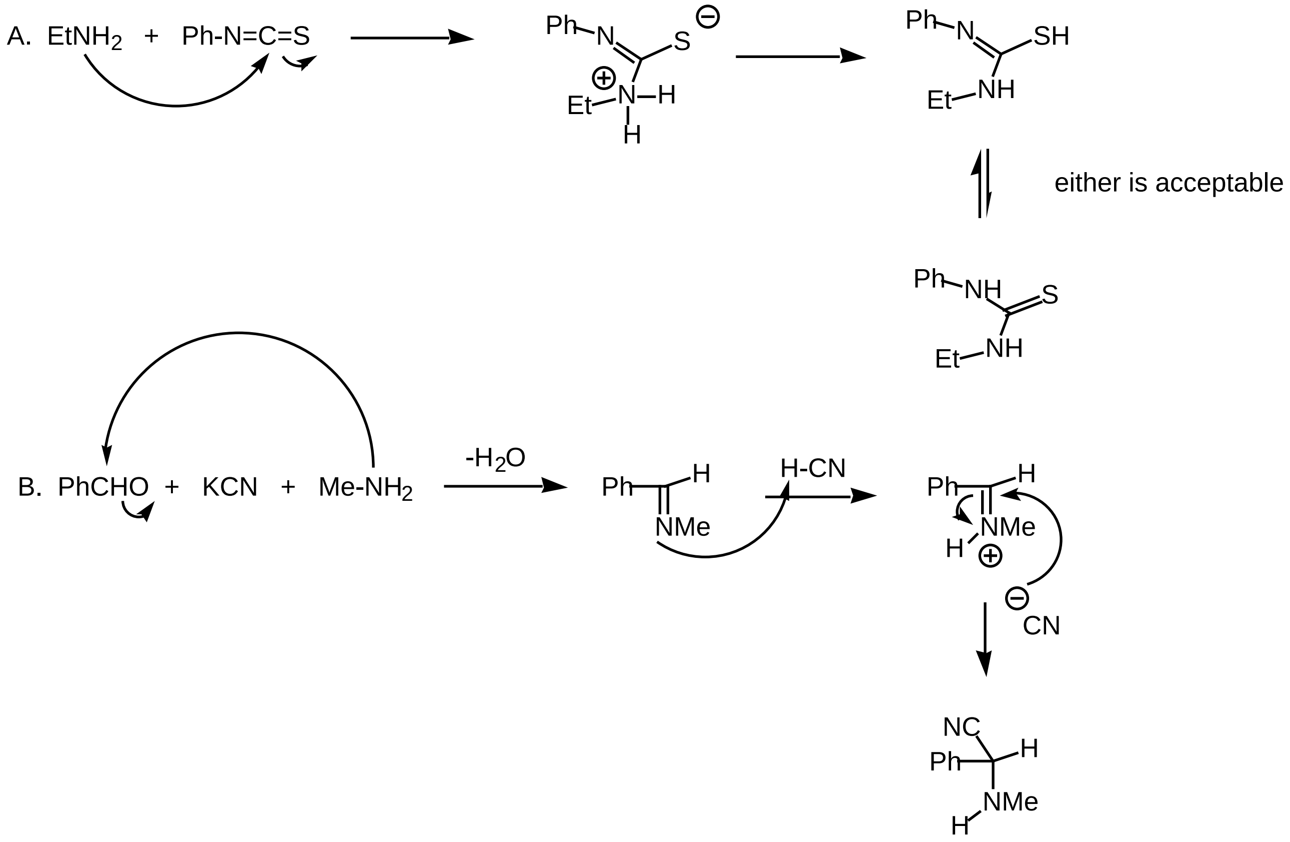
Suggest a structure for each product and explain what happened with structures.



Being well up on her protecting group chemistry, she repeated the sequence with a different lysine derivative and successfully produced the desired tripeptide. *What derivative do you suppose she chose?*

The key point is to differentially protect the two amino groups on lys. The a-amino group should be -BOC for standard deprotection, but the side chain amino should be protected with something stable to the conditions for removal of BOC, such as the benzyloxycarbonyl group, CBZ.

3. Complete the following reactions by giving the structure of the major organic product:



4. The following intermediate has been used in amino acid synthesis. Write a mechanism for the conversion shown: