Massachusetts Institute of Technology

5.13: Organic Chemistry II *April 24, 2002*

Test 3

Question 1 _____/30 points

Question 2 _____/09 points

Question 3 _____/18 points

Question 4 _____/10 points

Question 5 _____/11 points

Question 6 _____/22 points

TOTAL _____/100 points

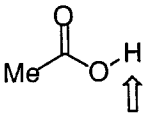
Name KEY

T.A. _____

There are seven pages (2-8) of questions in this exam.

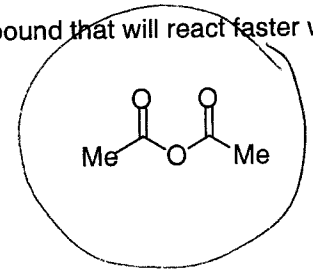
(1) (2 points each, 30 points total) Please provide the requested answer/data/reagents. If no reaction is expected, write "NR". Note: *n*-Bu = *n*-Butyl = $-CH_2CH_2CH_2CH_3$.

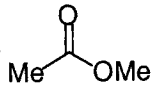
(a) pK_a of: $MeH_2\overset{\oplus}{N}H$ $\overset{\ominus}{Br}$ ⇧ | 9-11

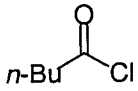
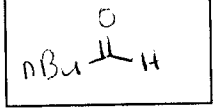
(b) pK_a of:  ⇧ | 4-6

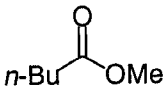
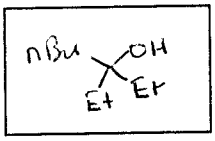
(c) pK_a of: MeO—H ⇧ | 16

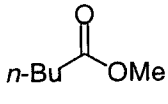
(d) Circle the compound that will react faster with Me_2NH:

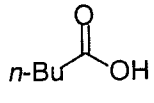
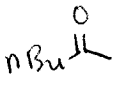


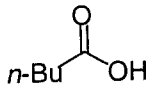


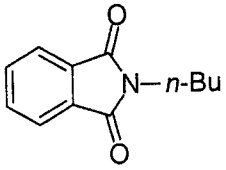
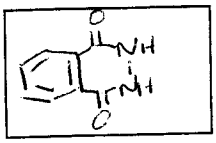
(e)  Li(*t*-BuO)$_3$AlH → workup → 

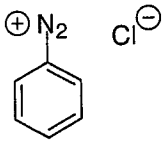
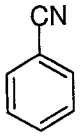
(f)  excess EtMgBr → workup → 

(g)  excess $NaBH_4$ → workup → NR

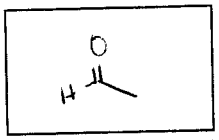
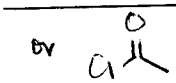
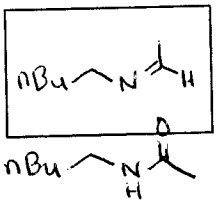
(h)  excess MeLi → workup → 

(i)  EtOH, base catalyst → NR

(j)  H_2NNH_2 → $nBu-NH_2$ + 

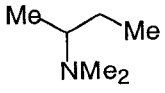
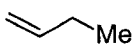
(k)  CuCN → 

(l) n-Bu–CN → 1. NaOH, H_2O; 2. H_3O^+, Δ or H_3O^+, Δ → n-Bu–OH

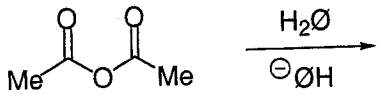
(m) n-Bu–NH_2 →  or  →  → $NaBH_3CN$ or any reducing agent or $LiAlH_4$ → n-Bu–NHEt

Your method should cleanly generate the secondary amine.

(n) n-Bu–OH → CrO_3, H_2SO_4 or $Na_2Cr_2O_7$, H^+ or $KMnO_4$, H_2SO_4 → n-Bu–OH

(o)  → 1. xs MeI, 2. Ag_2O or mCPBA, Δ → 

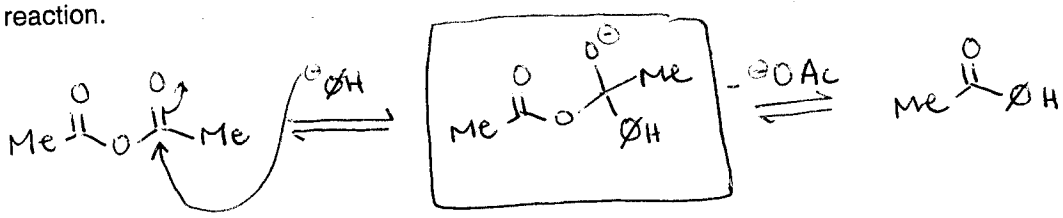
(2) (9 points) Consider the experiment outlined below:



stop the reaction at 50% conversion and examine the recovered anhydride for incorporation of Ø

Ø = isotopically labeled oxygen

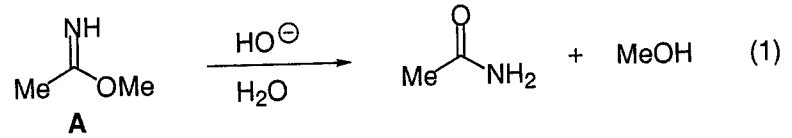
In analogy with the discussion in class regarding the labeling studies of acid chloride, amides, etc., carefully explain what level ("high" or "low") of Ø incorporation you expect to observe in the recovered anhydride. Your explanation should include the mechanism for this hydrolysis reaction.

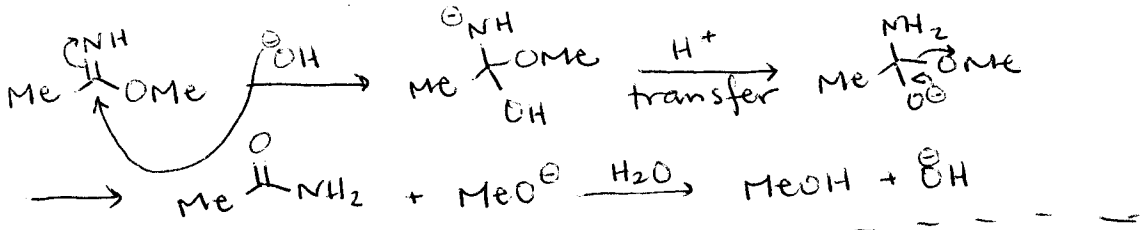


There should be a low incorporation of labelled Ø in the recovered anhydride because if the carbonyl were to reform by collapsing the electrons on the oxygen in boxed structure, it has a choice of eliminating $^{\ominus}ØH$ (to go to the structure on the left) or $^{\ominus}OAc$ (to go to the structure on the right). One should predict that the structure on the right is more accessible because $^{\ominus}OAc$ is a better LG than $^{\ominus}OH$. For this reason almost all the recovered anhydride will have no Ø incorporated.

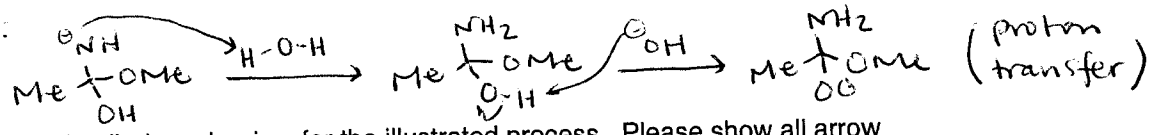
(3) (18 points total) Methyl acetimidate (**A**) is hydrolyzed in aqueous sodium hydroxide to (initially) give mainly acetamide and methanol (eq 1). In aqueous acid, **A** hydrolyzes to (initially) give primarily methyl acetate and the ammonium ion (eq 2).

(a) (7 points) Write a detailed mechanism for the illustrated process. Please show all arrow pushing.

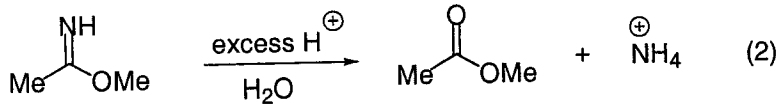


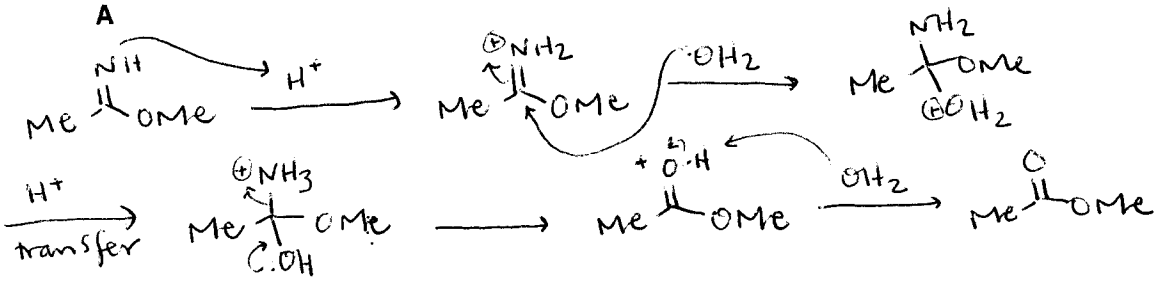


Also possible:



(b) (7 points) Write a detailed mechanism for the illustrated process. Please show all arrow pushing.

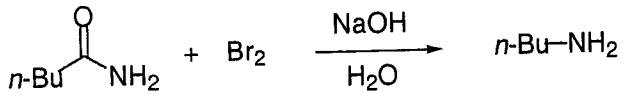


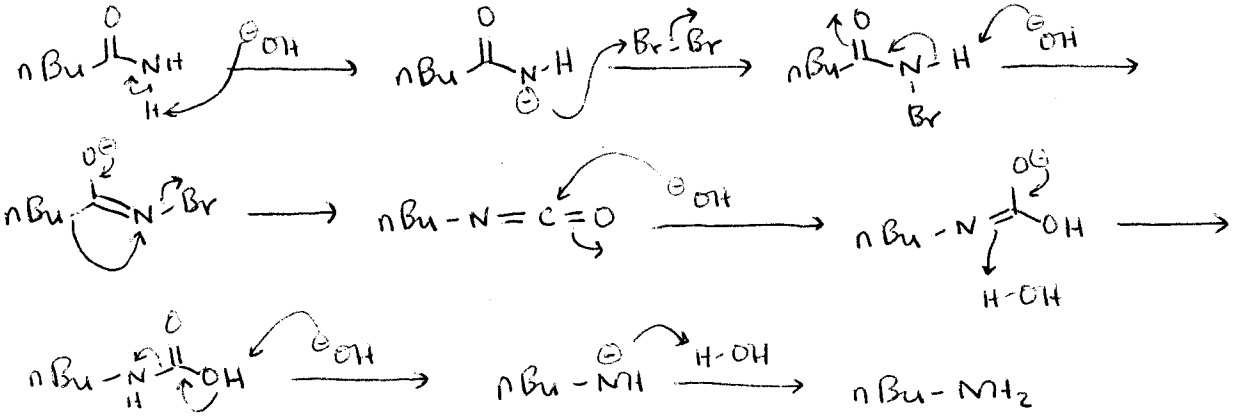


(c) (4 points) Briefly explain why the two reactions provide different products.

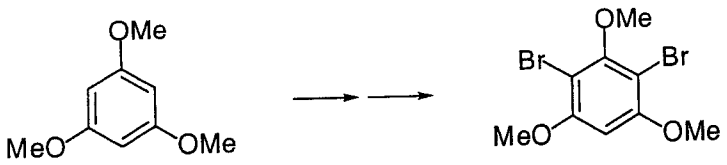
Basically, $^{\ominus}NH_2$ is a poor LG so the basic medium always gives the amide. However under acidic conditions, $^{\oplus}NH_4$ is a very weak nucleophile so the ester formation will be irreversible.

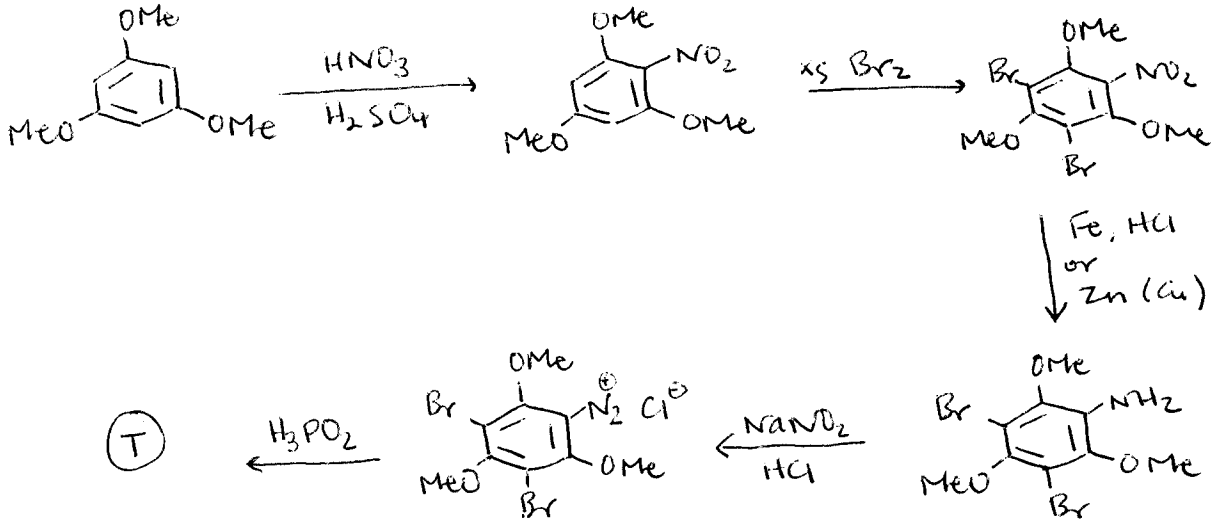
(4) (10 points) Provide a mechanism for the Hoffmann rearrangment. Please show all arrow pushing.

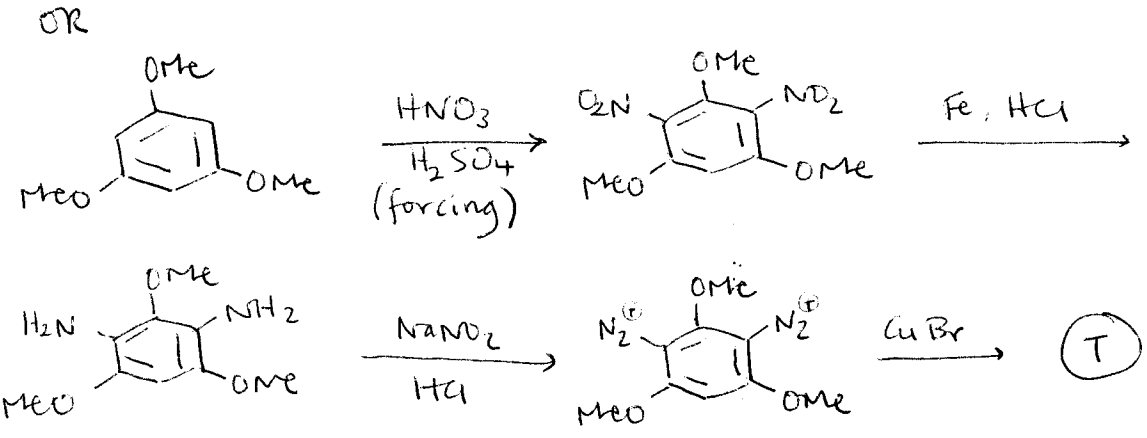




(5) (11 points) Provide a synthesis that will **selectively** convert A to B. Show all of the key intermediates and furnish all of the important reagents.

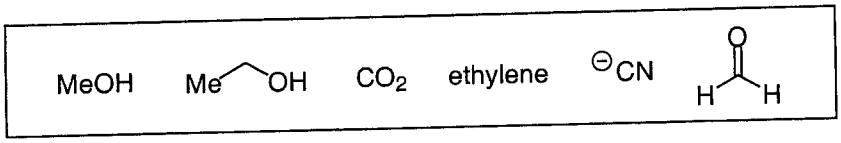


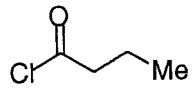




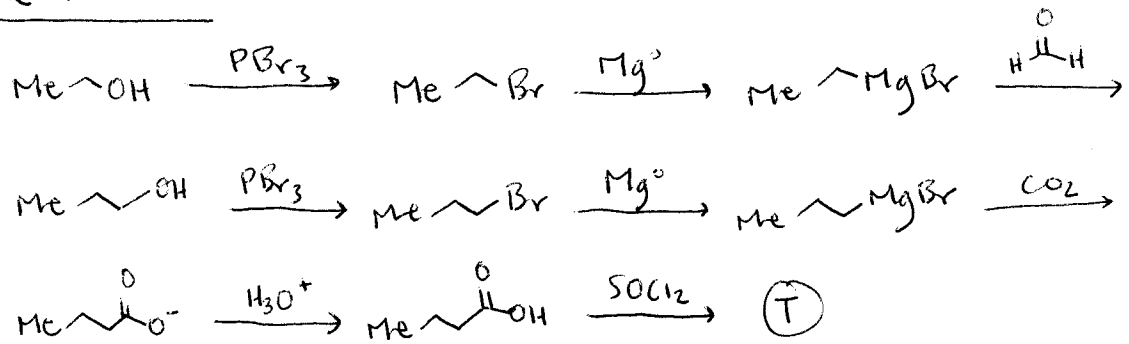
(6) (11 points each, 22 points total) Synthesize the indicated compounds from the allowed starting materials shown below. All of the carbons of the target compounds should be derived from the allowed starting materials.

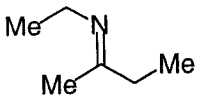
Allowed starting materials



(a) 

One solution



(b) 

One solution