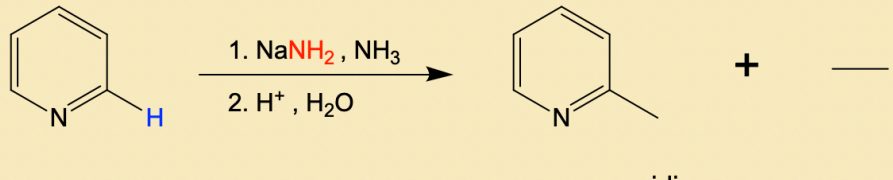
CONCEPT: SNAr REACTIONS OF PYRIDINE

- The electron _____ of pyridine makes it more susceptible to nucleophilic aromatic substitution than benzene.
  - □ Two major S_NAr reactions of pyridine involve substitution on the ___-position.
    1. **Chichibabin Reaction:** typical S_NAr of _____ onto the pyridine ring.
    2. **Organometallic Reactions:** S_NAr of an _____ _____ onto the pyridine ring.

1 Chichibabin Reaction

- A method to create _____pyridine by reacting pyridine with sodium amide.

Chichibabin Reaction



- **Recall:** Nucleophilic Aromatic Substitution occurs by an _____–_____ mechanism.

EXAMPLE: Provide the mechanism for the Chichibabin reaction of 4-methylpyridine.

Step 1	Step 2	Step 3a	Step 3b
Nucleophilic Attack	Leaving Group	Proton Transfer	Protonation

STEP 1: Amide ion attacks the *o*-position of pyridine, forming a _____ intermediate.

STEP 2: The N atom reforms the double bond, kicking out the H as a _____ ion to restore _____.

STEP 3a: _____ of the amino group by the hydride ion.

STEP 3b: _____ of the conjugate base anion by water forms 2-aminopyridine.

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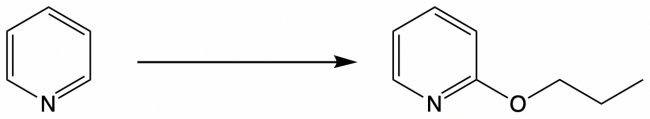
PRACTICE: Select the best set of reagents for the following synthesis.



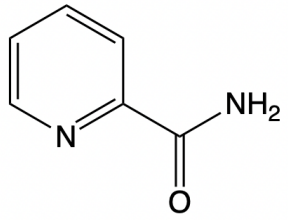
a) 1) $NaNH_2$, NH_3 2) H^+, H_2O 3) $NaNO_2$/HCl; 4) NaCN/DMSO; 5) CH_3I; 6) $Br_2/h\nu$

b) 1) $NaNH_2$, NH_3 2) H^+, H_2O 3) $NaNO_2$/HCl; 4) H_3O^+; 5) NaOH; 6) $CH_3CH_2CH_2Br$

c) 1) $NaNH_2$, NH_3 2) H^+, H_2O 3) $NaNO_2$/HCl; 4) HBF_4; 5) CH_3I; 6) $Br_2/h\nu$

d) 1) $NaNH_2$, NH_3 2) H^+, H_2O 3) $NaNO_2$/HCl; 4) H_3O^+; 5) H_3PO_3; 6) $CH_3CH_2CH_2Br$

PRACTICE: Starting from pyridine, use your knowledge of diazonium salts and the Chichibabin Reaction to synthesize the following product.



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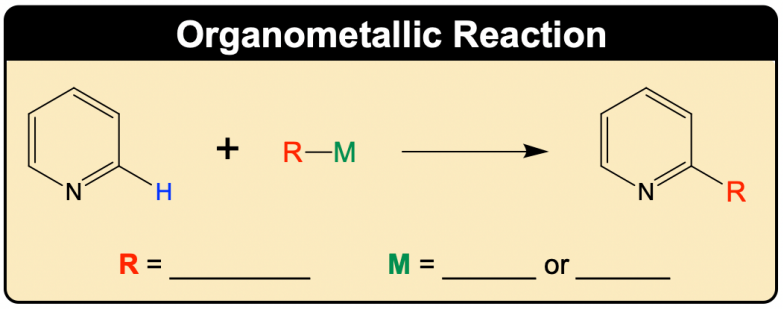
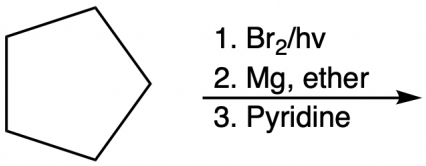
2 Organometallic Reactions

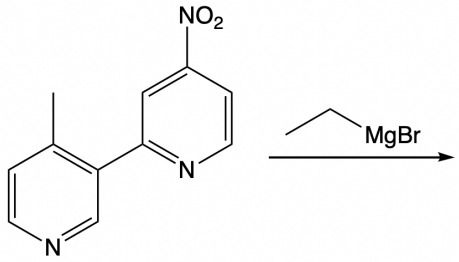
- Treatment of pyridine with either a Grignard or organolithium reagent to produce an ___-_____ pyridine ring.



EXAMPLE: Predict the final product based on the list of reagents given.



PRACTICE: Determine the final product for the following reaction.



CONCEPT: SNAr REACTIONS OF PYRIDINE

PRACTICE: Propose a synthetic route for the following transformation.