

CONCEPT: REVIEW OF NITRILES

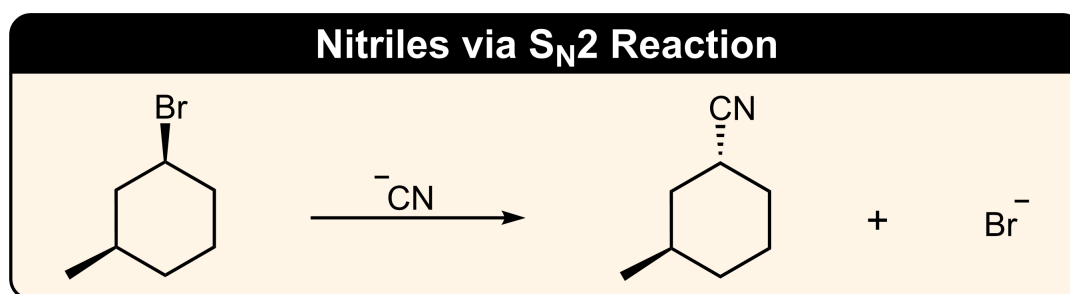
Synthesis of Nitriles

- Nitriles can be synthesized by:

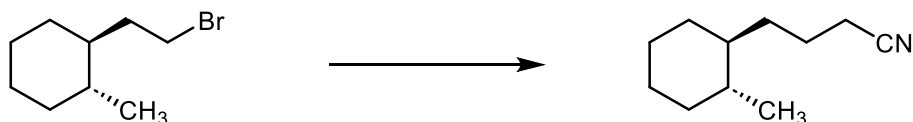
- 1 S_N2 Reactions:** reaction of _____ with _____.
- 2 Cyanohydrin Formation:** nucleophilic addition of CN⁻ to an aldehyde or a ketone.
- 3 Amide Dehydration:** reaction of an amide with a dehydrating agent (_____ or _____).

1 S_N2 Reactions

- Cyanide anion can displace halides to yield nitriles.



EXAMPLE: Select the best synthetic route to achieve the following transformation.



a) NaCN/DMSO

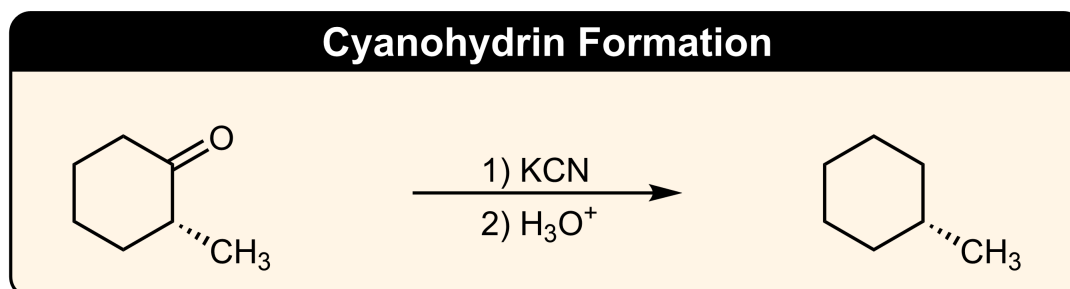
b) 1) Mg, ether; 2) H₂CO; 3) H₃O⁺; 4) SOCl₂; 5) KCN

c) 1. NaNH₂; 2. BH₃/H₂O₂; 3. SOCl₂; 4. KCN

d) 1) Mg, ether; 2) H₂CO; 3) H₃O⁺; 4) HCl; 5) KCN

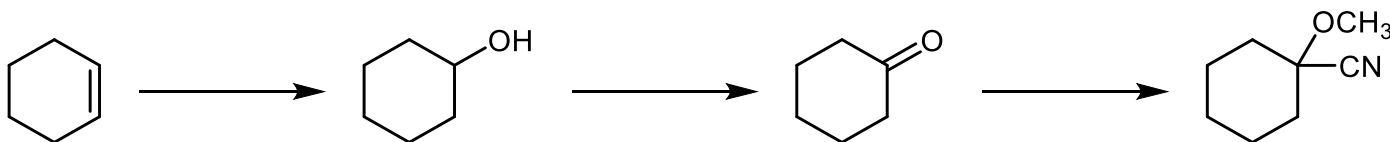
2 Cyanohydrin Formation

- Cyanohydrins are formed when an aldehyde or a ketone undergoes nucleophilic _____ with CN⁻.



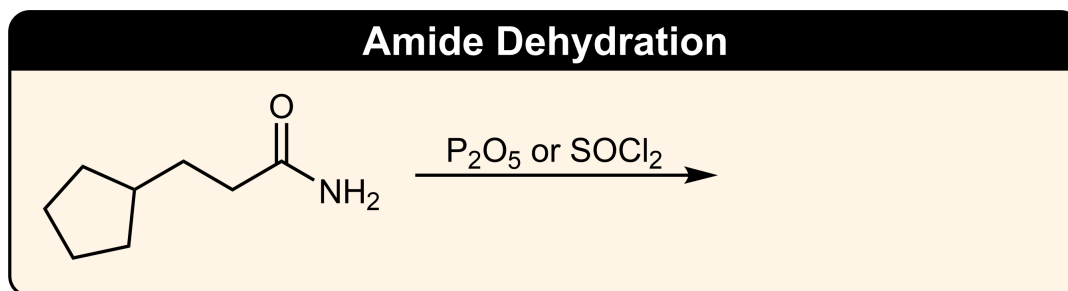
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EXAMPLE: Suggest reagents for each step of the following synthesis.

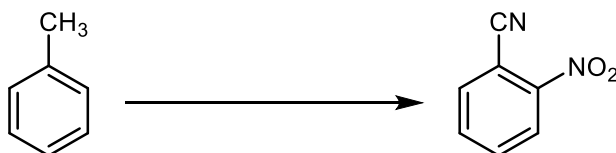


3 Amide Dehydration

- Primary amides can be dehydrated using P_2O_5 or $SOCl_2$ to produce nitriles.



EXAMPLE: Select the best set of reagents to achieve the following transformation.



- a) 1) $KMnO_4$; 2) HNO_3/H_2SO_4 ; 3) NH_3/DCC ; 4) P_2O_5
- b) 1) HNO_3/H_2SO_4 ; 2) $KMnO_4$; 3) NH_3/DCC ; 4) $SOCl_2$
- c) 1) SO_3/H_2SO_4 ; 2) HNO_3/H_2SO_4 ; 3) H_3O^+ ; 5) NBS; 6) $KCN/DMSO$
- d) 1) SO_3/H_2SO_4 ; 2) HNO_3/H_2SO_4 ; 3) H_3O^+ ; 5) $KMnO_4$; 6) NH_3/DCC ; 7) P_2O_5

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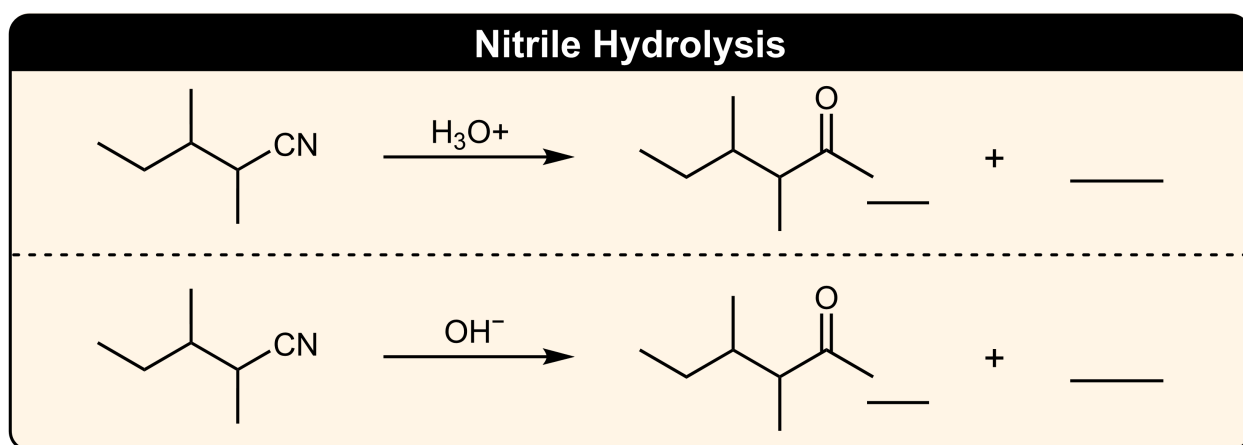
Reactions of Nitriles

- Nitrile reactions are similar to other carboxylic acid derivatives:

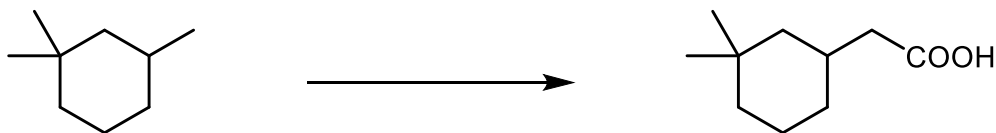
- Hydrolysis:** nitriles undergo hydrolysis to produce carboxylic acids.
- Reduction:** catalytic or hydride reduction produces ___ amines.
- Conversion to ketones:** nitriles react with _____ reagents to yield ketones.

1 Hydrolysis

- Nitriles produce carboxylic _____ in acidic hydrolysis and carboxylate _____ in basic hydrolysis.



EXAMPLE: Select the best set of reagents to achieve the following transformation.

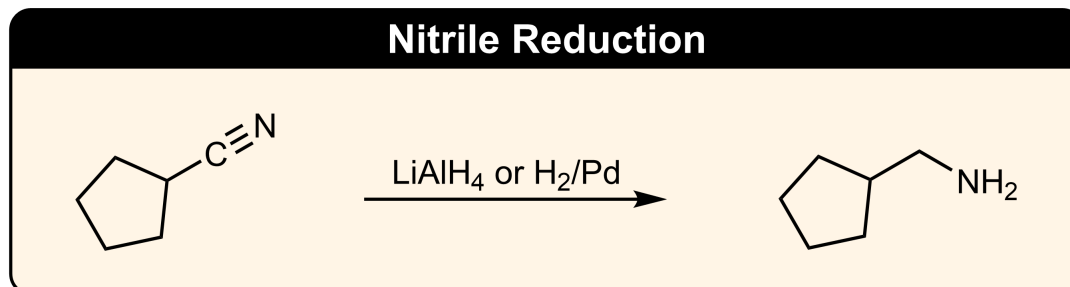


- 1) Br₂/hν; 2) NaOEt/EtOH; 3) HBr/H₂O₂; 4) KCN/DMSO, 5) H₂O/H⁺
- 1) Br₂/hν; 2) NaOEt/EtOH; 3) HBr/H₂O₂; 4) KCN/DMSO, 5) H₂O/H⁺
- 1) Br₂/hν; 2) KOtBu/tBuOH; 3) HBr/H₂O₂; 4) KCN/DMSO, 5) H₂O/H⁺
- 1) Cl₂/hν; 2) KOtBu/tBuOH; 3) HBr/H₂O₂; 4) KCN/DMSO, 5) H₂O/H⁺

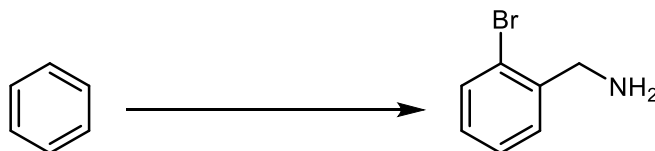
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2 Reduction

- Nitriles can be converted into 1° amines by reduction (e.g. _____ or _____).



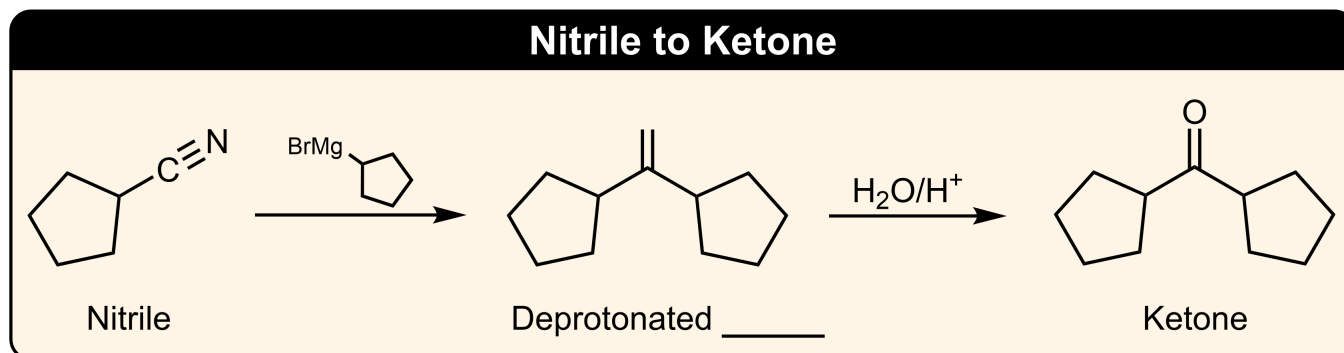
EXAMPLE: Identify the set of reagents that can be used for the following synthesis.



- a) 1) $\text{Br}_2/\text{FeBr}_3$; 2) $\text{HNO}_3/\text{H}_2\text{SO}_4$; 3) H_3O^+ ; 4) Sn/HCl ; 5) NaNO_2/HCl ; 6) CuCN ; 7) LiAlH_4
b) 1) $\text{Br}_2/\text{FeBr}_3$; 2) $\text{SO}_3/\text{H}_2\text{SO}_4$; 3) $\text{HNO}_3/\text{H}_2\text{SO}_4$; 4) H_3O^+ ; 5) Sn/HCl ; 6) NaNO_2/HCl ; 7) CuCN ; 8) LiAlH_4
c) 1) $\text{HNO}_3/\text{H}_2\text{SO}_4$; 2) $\text{Br}_2/\text{FeBr}_3$; 3) Sn/HCl ; 4) NaNO_2/HCl ; 5) CuCN ; 6) LiAlH_4
d) 1) $\text{Br}_2/\text{FeBr}_3$; 2) $\text{SO}_3/\text{H}_2\text{SO}_4$; 3) $\text{HNO}_3/\text{H}_2\text{SO}_4$; 4) H_3O^+ ; 5) NaNO_2/HCl ; 6) CuCN ; 7) LiAlH_4

3 Conversion to Ketones

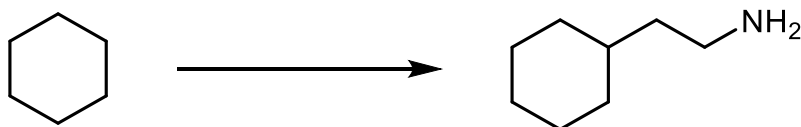
- Reaction of nitriles with Grignard reagent followed by _____, produces ketones.



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EXAMPLE: Propose a synthesis to convert benzene to benzophenone with at least one step being a nitrile reaction.

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



- a) 1) $\text{Br}_2/\text{h}\nu$; 2) Mg/ether ; 3) CH_3I ; 4) $\text{Br}_2/\text{h}\nu$; 5) $\text{KOtBu}/\text{tBuOH}$; 6) $\text{HBr}/\text{H}_2\text{O}_2$; 7) NaCN/DMSO ; 8) H_2/Pd
- b) 1) $\text{Br}_2/\text{h}\nu$; 2) CH_3MgBr ; 3) $\text{Br}_2/\text{h}\nu$; 4) $\text{KOtBu}/\text{tBuOH}$; 5) $\text{HBr}/\text{H}_2\text{O}_2$; 6) NaCN/DMSO ; 7) H_2/Pd
- c) 1) $\text{Br}_2/\text{h}\nu$; 2) Mg/ether ; 3) CH_3I ; 4) $\text{Br}_2/\text{h}\nu$; 5) NaOEt/EtOH ; 6) $\text{HBr}/\text{H}_2\text{O}_2$; 7) NaCN/DMSO ; 8) H_2/Pd
- d) 1) $\text{Br}_2/\text{h}\nu$; 2) $\text{CH}_3\text{CH}_2\text{MgBr}$; 3) $\text{Br}_2/\text{h}\nu$; 4) NaCN/DMSO ; 5) H_2/Pd

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PRACTICE: Propose a synthetic route for the following transformation.

