5/9/12

Synthesis of amines

1) S_N2 from alkyl halides [8.3]
2) reduction of alkyl azides (S_N2) [8.3]
3) hydrogenation of nitriles [17.19]
4) reduction of amides [18.6]
5) reduction of imines [20.7]
6) reductive amination [18.8]
7) Gabriel synthesis [17.8]
8) reduction of nitro compounds [16.1]
9) Curtius + Hoffman ~~elimination~~ rearrangements

Hoffman elimination

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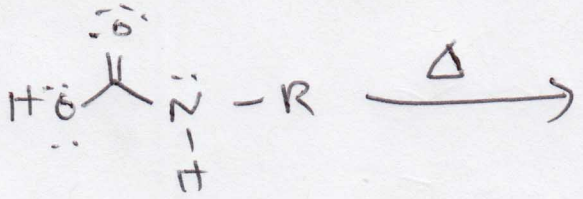
unstable carboxylic acids

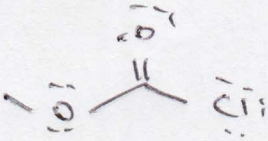
$\longrightarrow H_2O + CO_2$ (spontaneously)



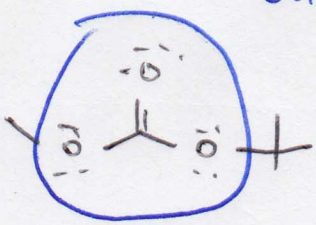
$\xrightarrow{\Delta} CO_2 + H_2\ddot{N}-R$

dialkyl carbonates

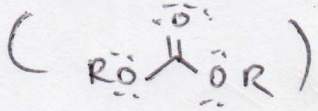
Carbamic acid

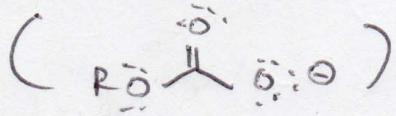


$+ \ddot{O}H \longrightarrow$

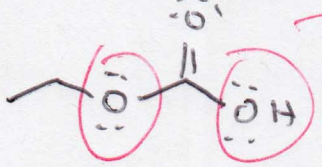


Dialkyl carbonates or monoalkyl carbonate salts

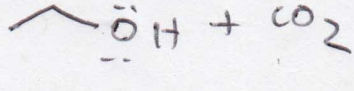




are isolatable and thermodynamically stable.



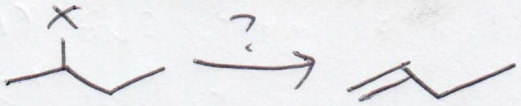
$\xrightarrow{\Delta}$



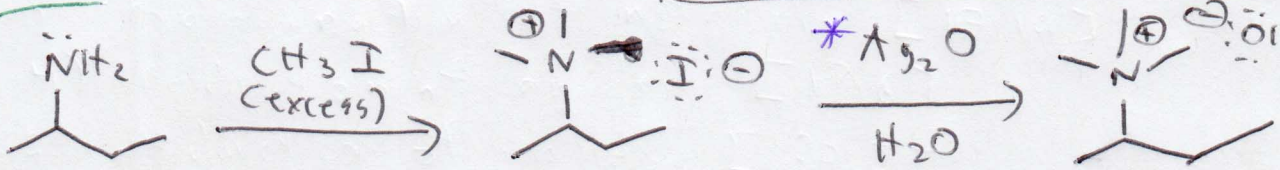
$+ CO_2$

If a carbonyl has two heteroatoms connected and if it has an -OH group, it will decarboxylate

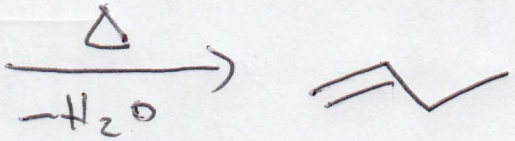
1) S_N2 of alkyl halides – Normally not successful due to multiple alkylation,



Zaitsev elimination



* Silver halides are very insoluble and rapidly form precipitates, which allows the ammonium halide to be converted to an ammonium hydroxide



Hoffmann elimination – To form the thermodynamically less favorable product during elimination

The Hoffmann elimination

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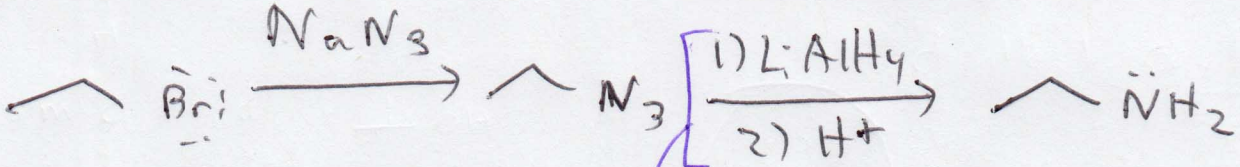
2) Alkyl azides



Mechanism not covered

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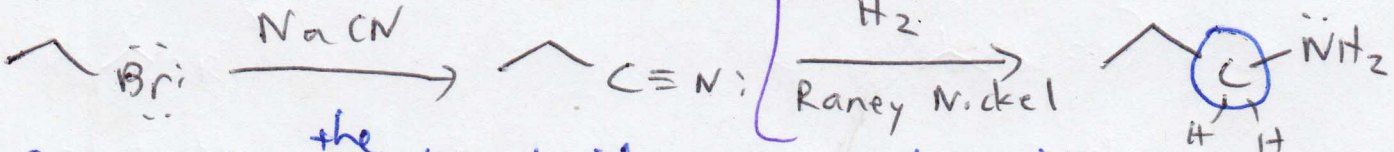
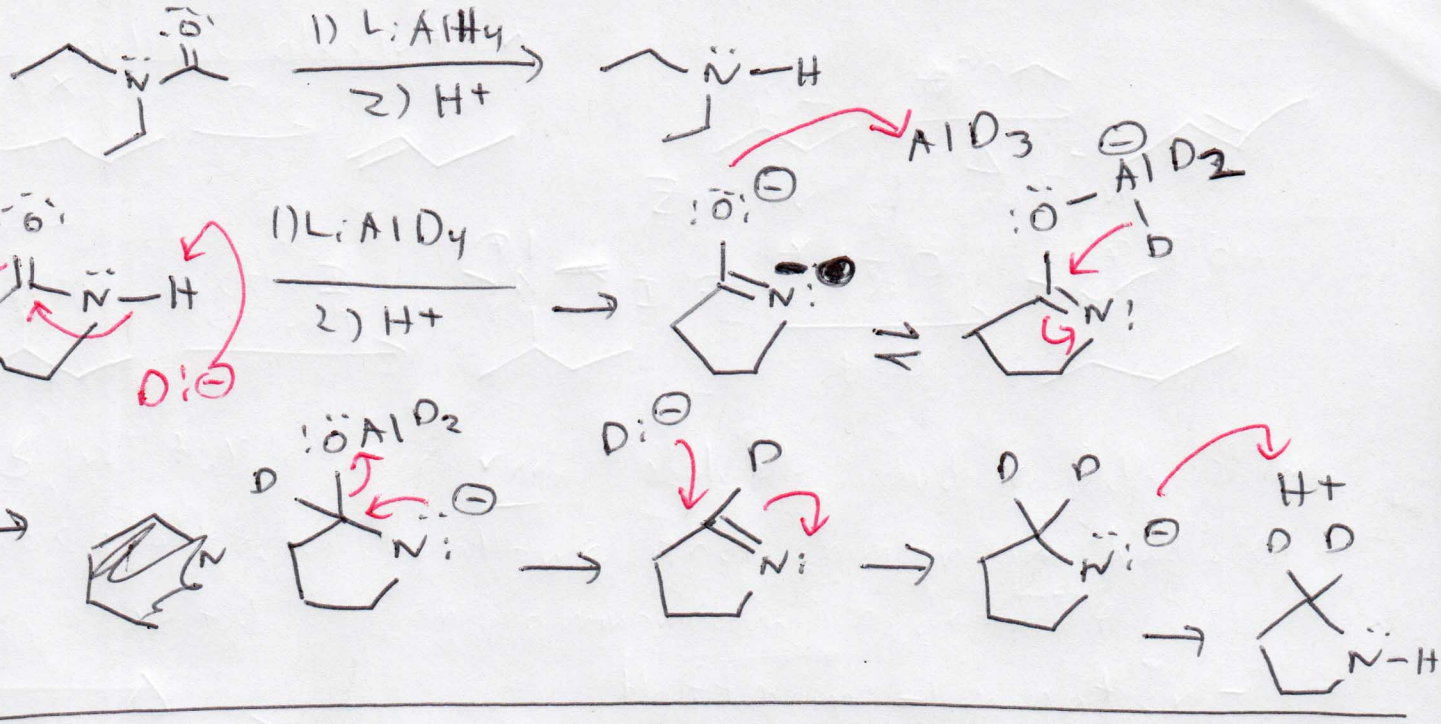
3) hydrogenation of nitriles



Compared to the alkyl halide, the product has an additional carbon

4) reduction of amides



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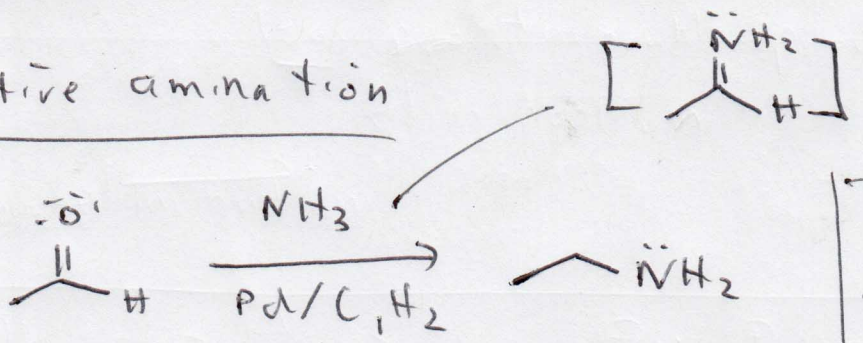
5) reduction of imines

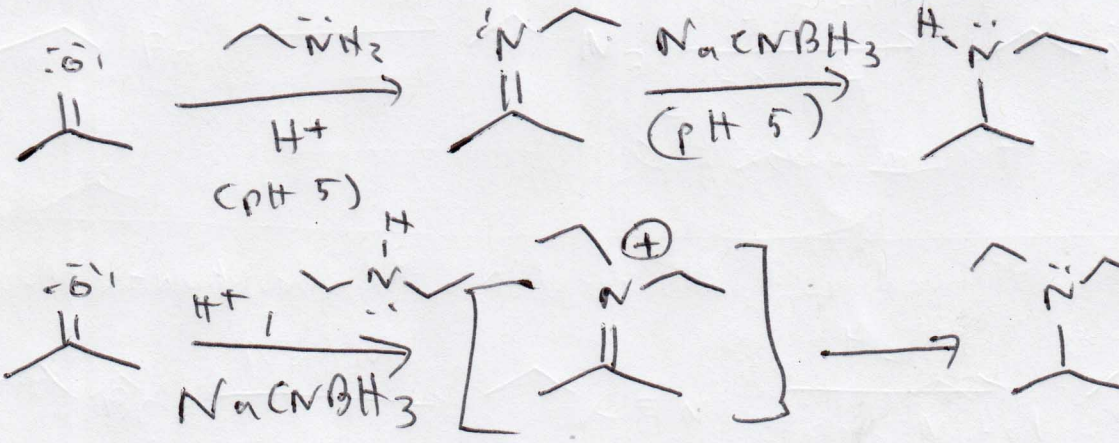
reductive amination

6) reductive amination

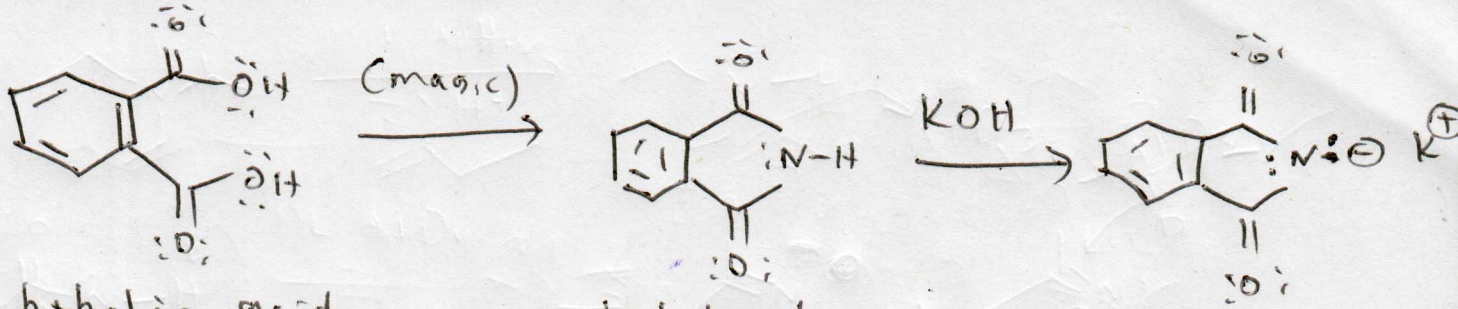


NaBH3CN
sodium cyanoborohydride
survives pH 3

imines

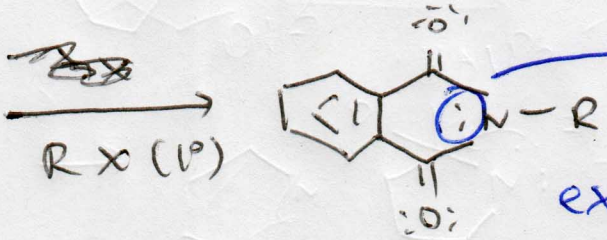


7) Gabriel Synthesis – phthalimide

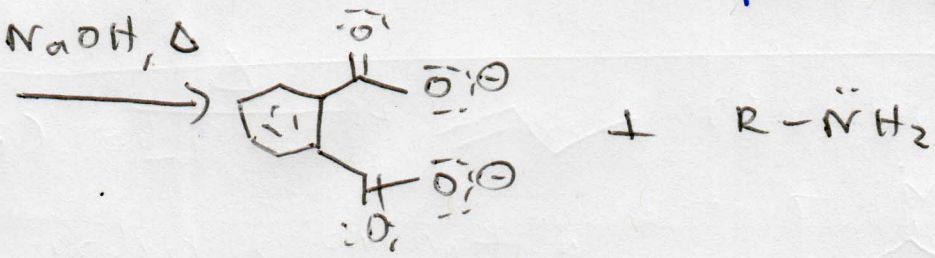


phthalic acid

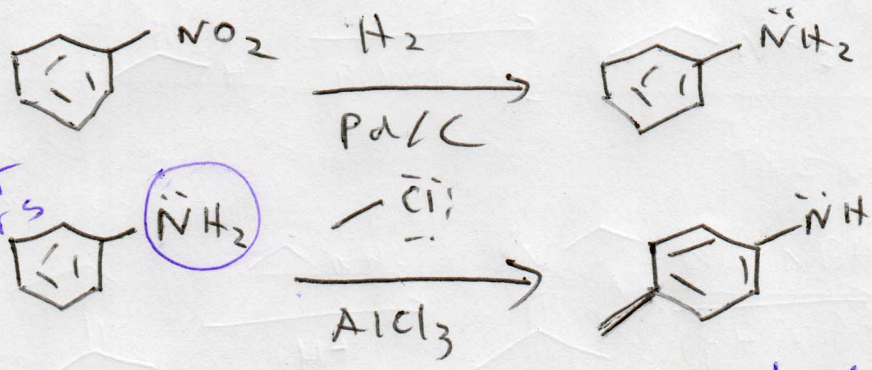
phthalimide



NOT basic or nucleophilic (when neutral) because of the extensive delocalization of the lone pair → only mono alkylation occurs



8) Reduction of nitro compounds



one of the strongest activators

Aniline is so reactive that electrophilic aromatic substitution often occurs @ multiple times

One solution

much less reactive