NEF REACTION

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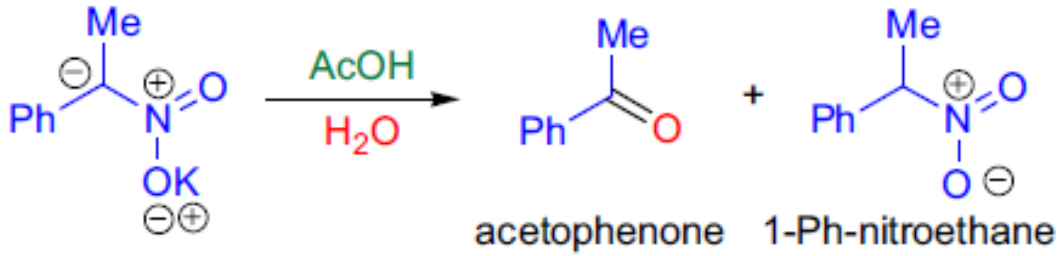
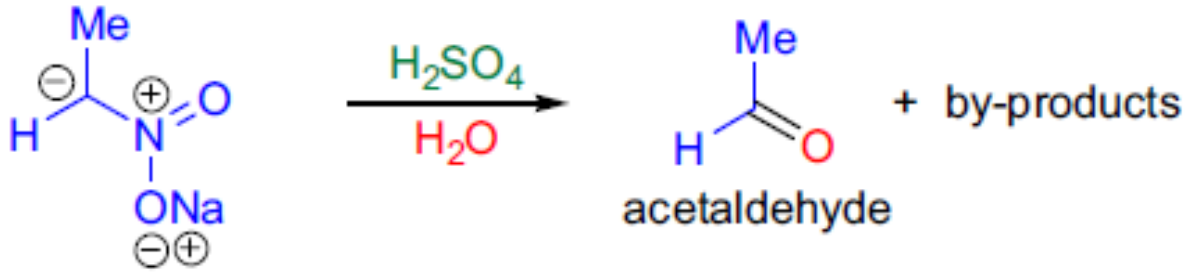
2016.8.23

Discovery

Konovalov (1893):



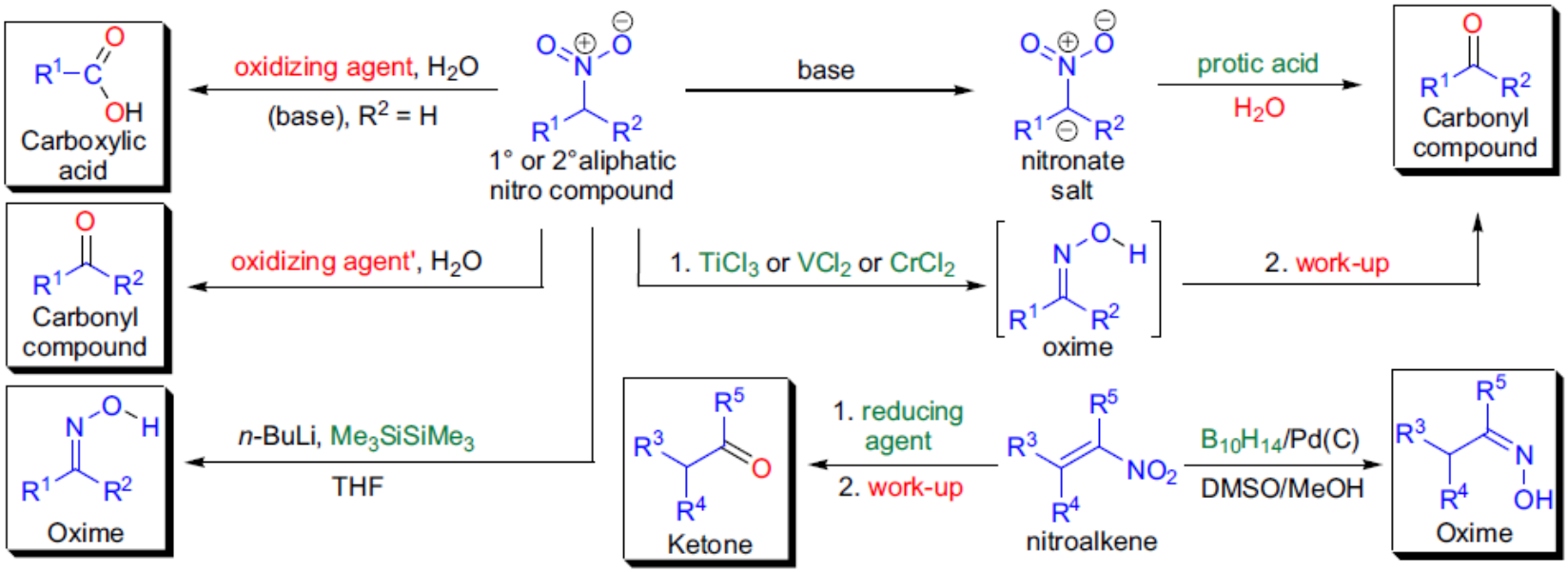
Nef (1894):



General features

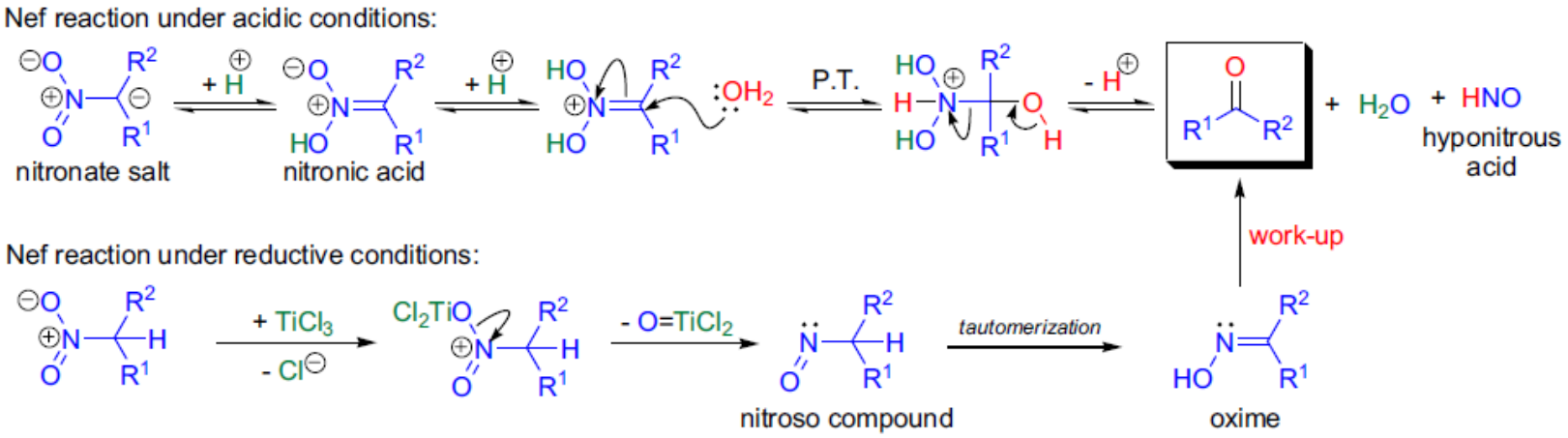
- pH related: A number of by-products such as oximes and hydroxynitroso compounds can be formed when pH > 1.
- Original reaction conditions required the addition of the nitronate salt to the solution of the acid to avoid the formation of undesired products.

Modifications

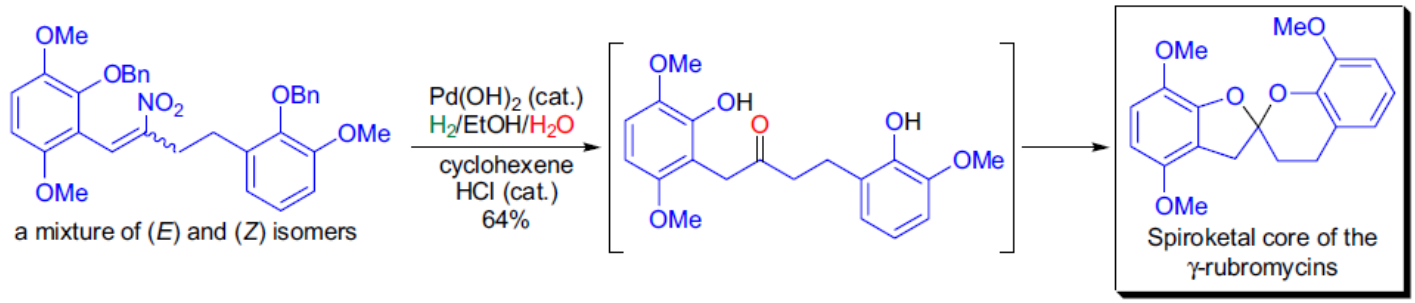


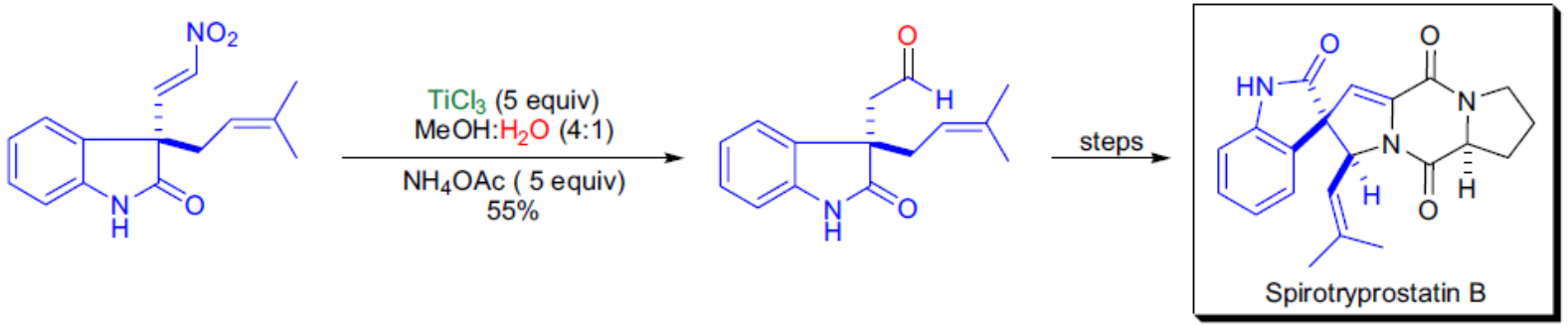
$R^{1\text{-}2}$ = H, alkyl, aryl; $R^{3\text{-}5}$ = H, aryl, alkyl; oxidizing agent: $KMnO_4$ (at pH~11), Oxone, $(OTMS)_2$, TPAP/NMO, $Cu(OAc)_2/O_2$, $NaNO_2$/AcOH/DMSO; oxidizing agent': to get aldehydes (R^2 = H) use DMDO, $Na_2CO_3 \cdot 1.5\ H_2O_2$. $KMnO_4$ while for ketones use any of the above oxidants; reducing agent: Al powder/$NiCl_2 \cdot 6H_2O$, Zn dust/TFA, Mg powder/$CdCl_2$; protic acid: HCl, H_2SO_4, AcOH

Mechanism


Nef reaction under acidic conditions:
nitronate salt
nitronic acid
P.T.
+ H2O
+ HNO
hyponitrous acid
work-up
Nef reaction under reductive conditions:
+ TiCl3
- Cl⊖
- O=TiCl2
nitroso compound
tautomerization
oxime

Synthetic applications





Synthetic applications