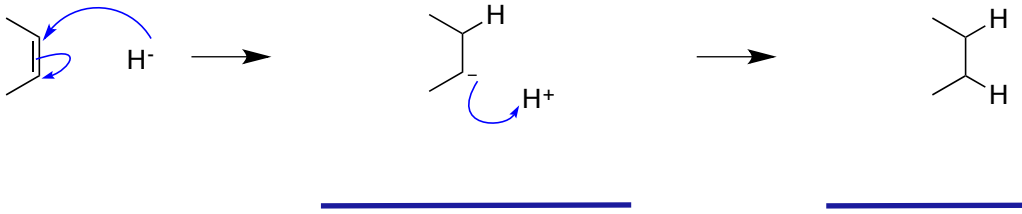
Hydridic Reductions

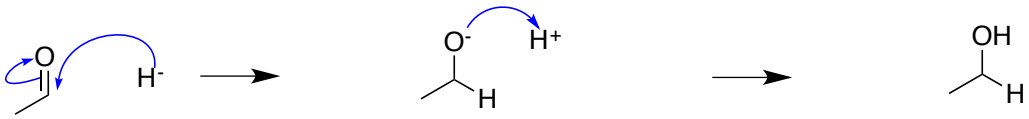
from chapter(s) _____ in the recommended text

A. Introduction

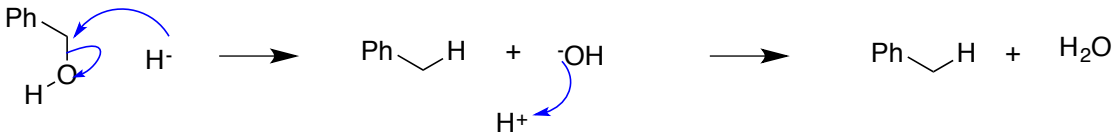
B. Mechanism



hard



easy



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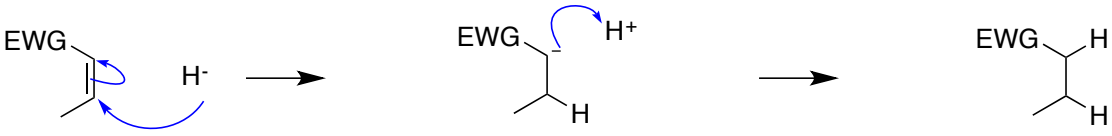
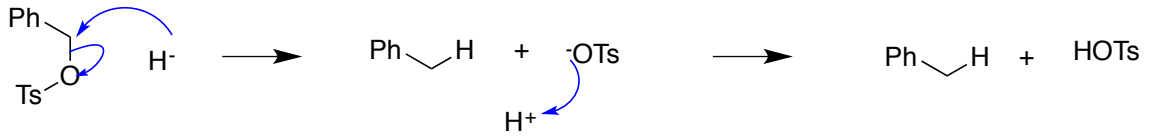
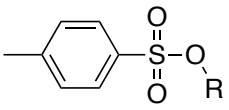


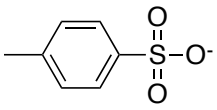
easy



easy



Ts



TsO⁻

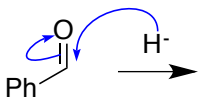
easy to reduce
hard to reduce them

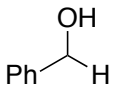
tosylates are
tosyl groups are
ionic
chemoselective reductions

do not tend

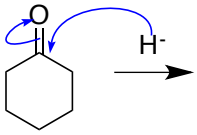
C. Substrate Scope

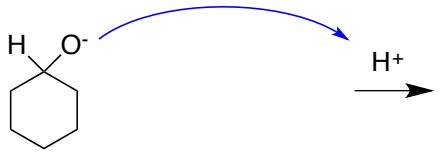
One Reduction

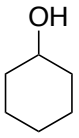




alkoxide

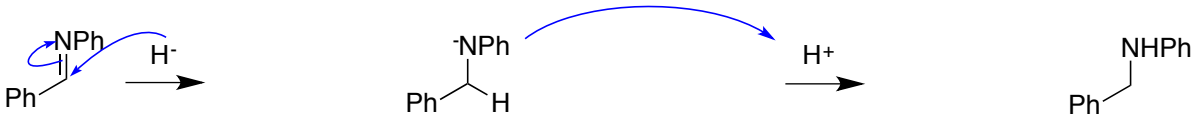




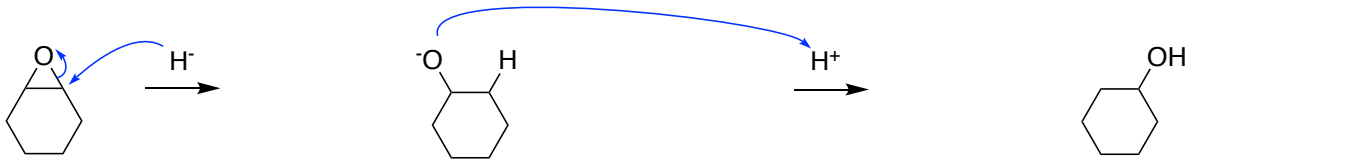


alkoxide

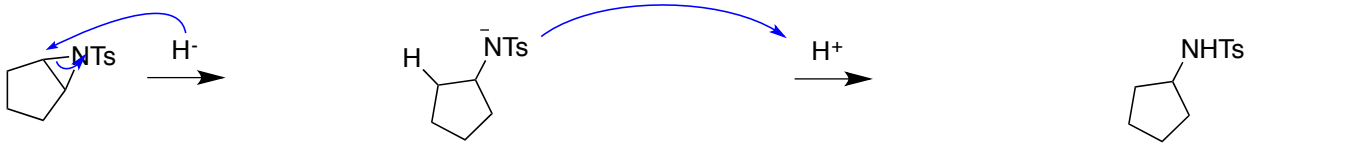
NaBH₄ because

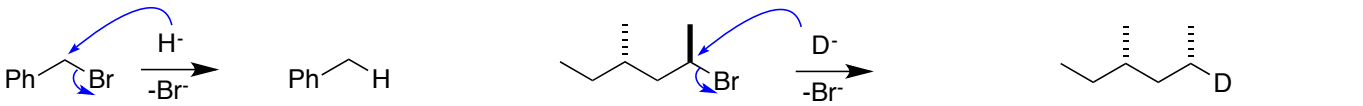


amide anion



alkoxide

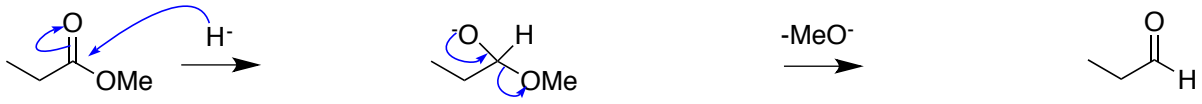


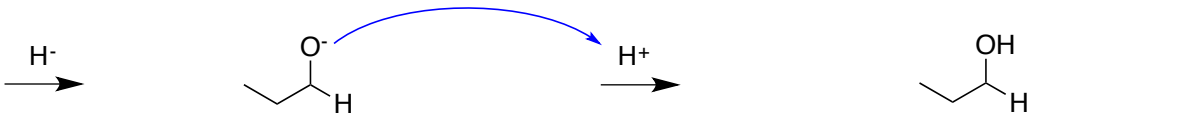


this reaction proceeds with inversion

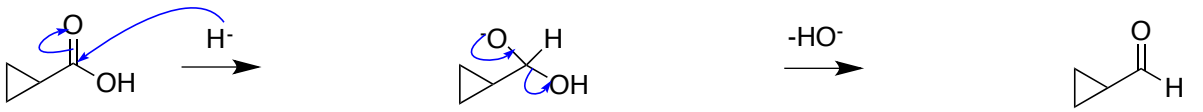
It takes *2*

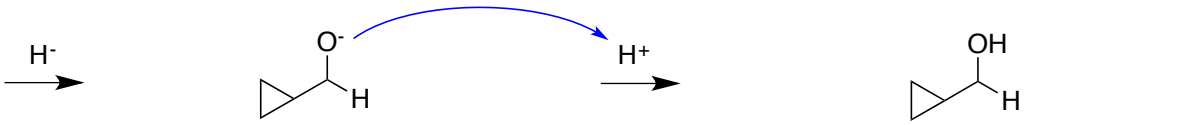
Two Step Reductions



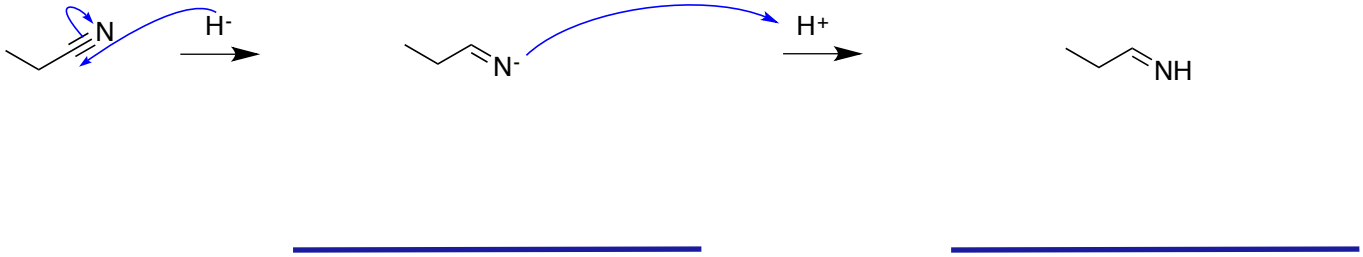


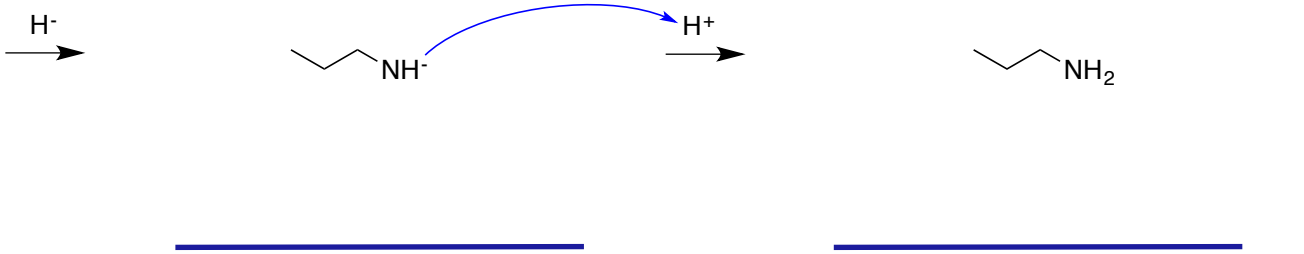
alkoxide

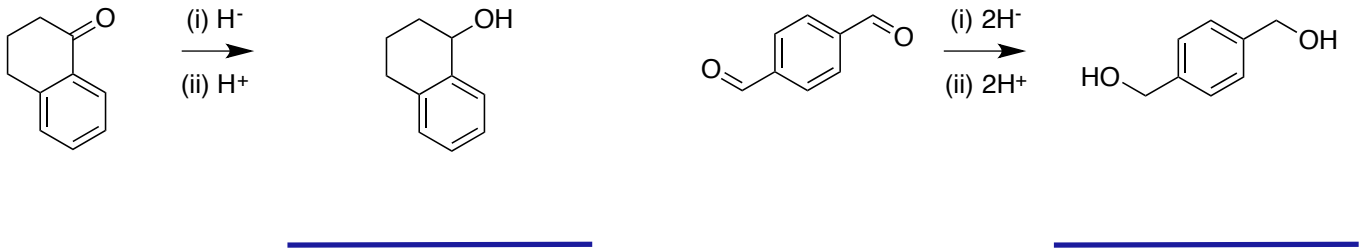


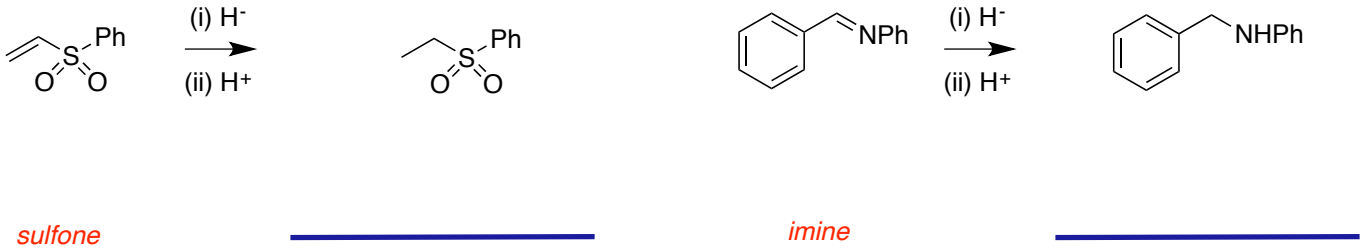


alkoxide



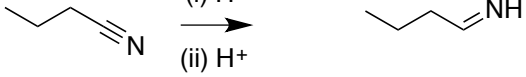


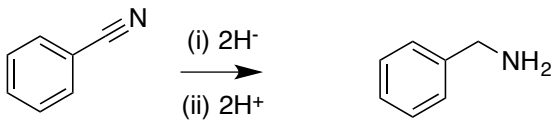


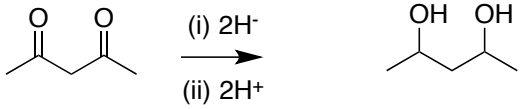


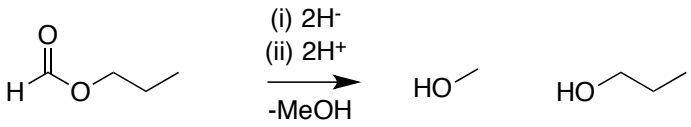
sulfone

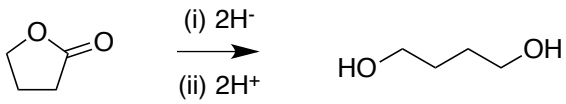
imine

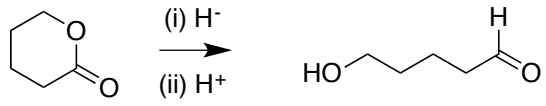

(i) H-
(ii) H+
N
NH

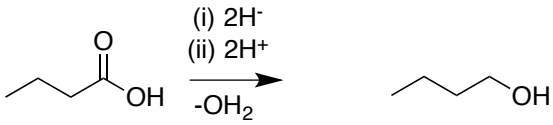

(i) 2H-
(ii) 2H+
N
NH2

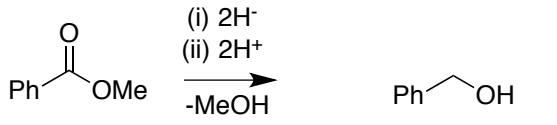

(i) 2H-
(ii) 2H+
O
O
OH
OH

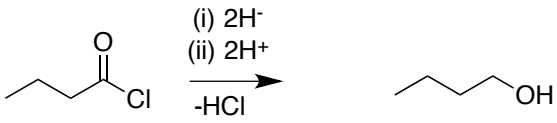

(i) 2H-
(ii) 2H+
-MeOH
O
H
O
HO
HO

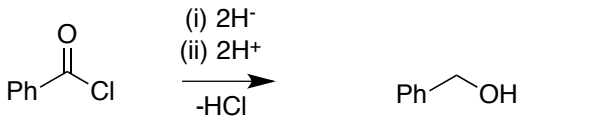

(i) 2H-
(ii) 2H+
O
O
HO
OH

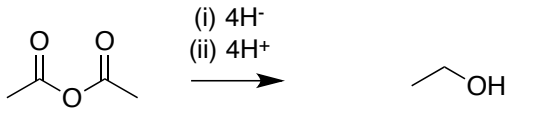

(i) H-
(ii) H+
O
O
H
HO
O

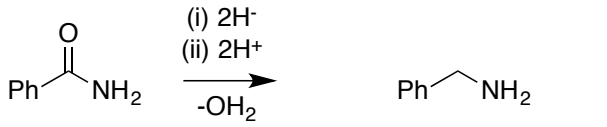

(i) 2H-
(ii) 2H+
-OH2
O
OH
OH

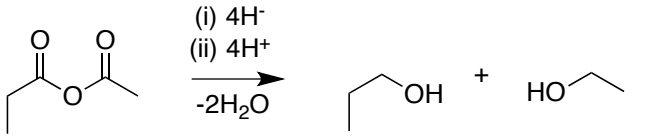

(i) 2H-
(ii) 2H+
-MeOH
O
Ph
OMe
Ph
OH

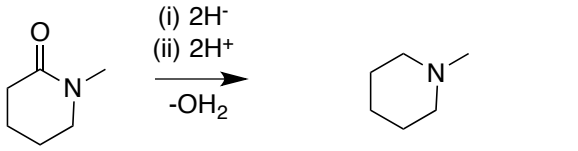

(i) 2H-
(ii) 2H+
-HCl
O
Cl
OH

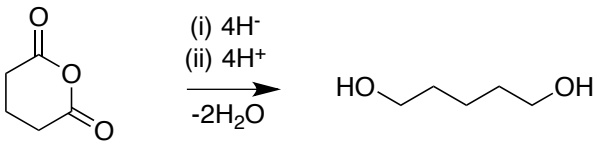

(i) 2H-
(ii) 2H+
-HCl
O
Ph
Cl
Ph
OH

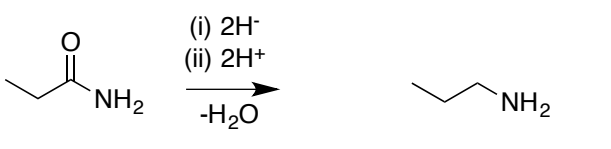

(i) 4H-
(ii) 4H+
O
O
O
OH


(i) 2H-
(ii) 2H+
-OH2
O
Ph
NH2
Ph
NH2


(i) 4H-
(ii) 4H+
-2H2O
O
O
O
OH
+
HO

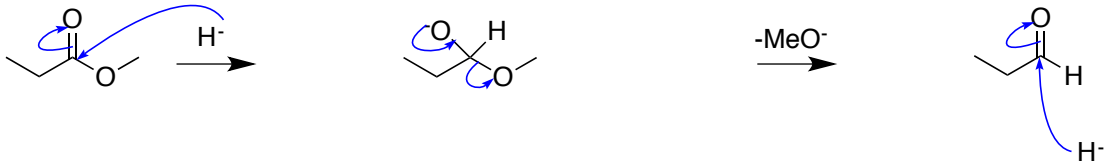

(i) 2H-
(ii) 2H+
-OH2
O
N
N


(i) 4H-
(ii) 4H+
-2H2O
O
O
O
HO
OH

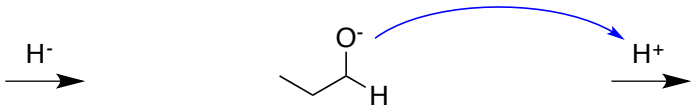

(i) 2H-
(ii) 2H+
-H2O
O
NH2
NH2

Difference Between Hydridic Reductions Of Amides And Esters

a

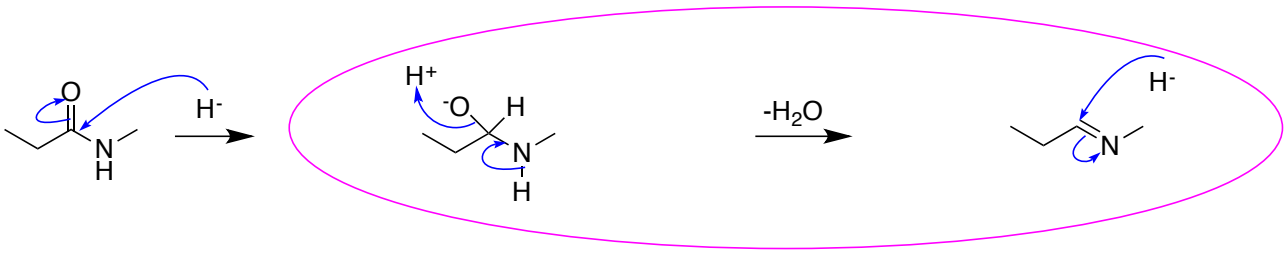


tetrahedral intermediate *aldehyde*

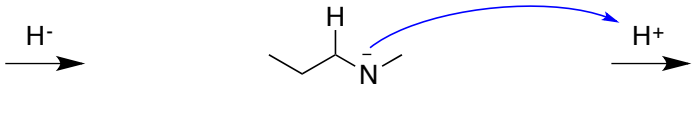


alkoxide

b

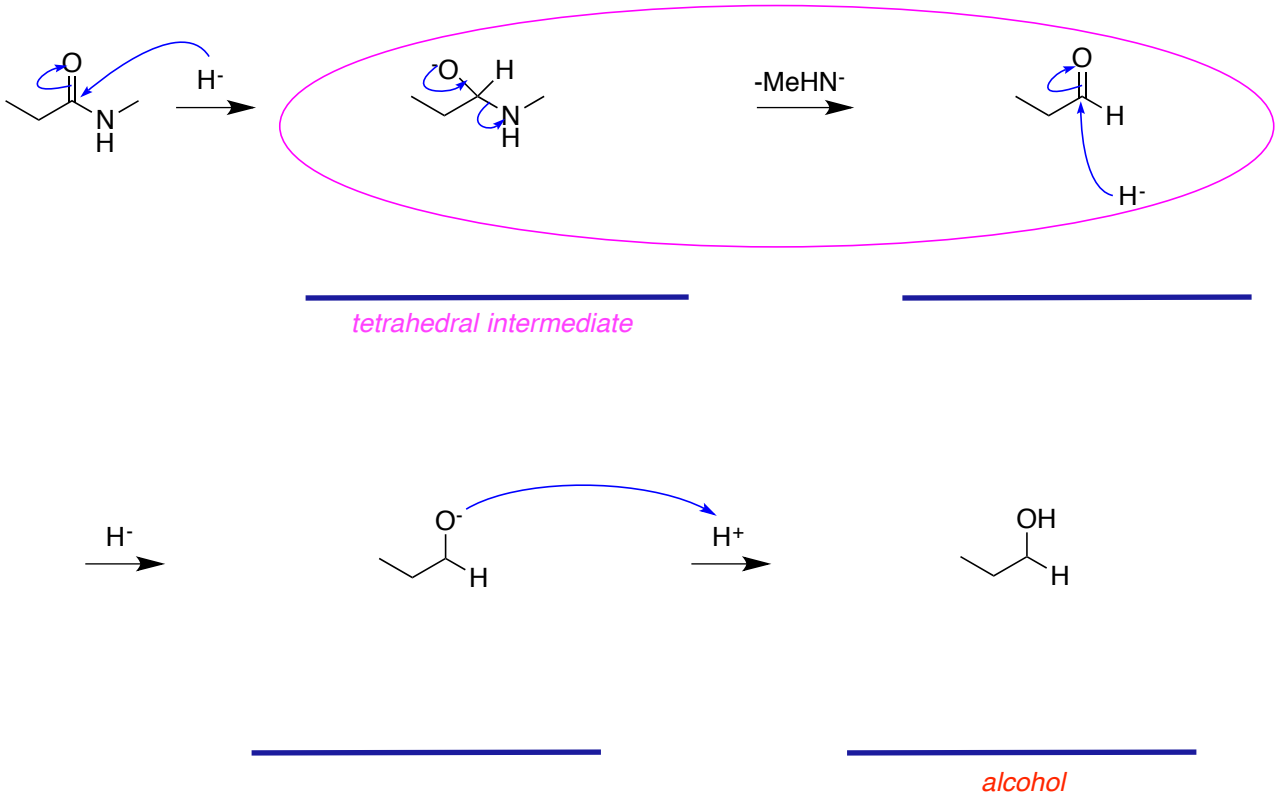


tetrahedral intermediate *imine*



amine

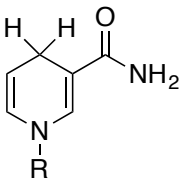
c



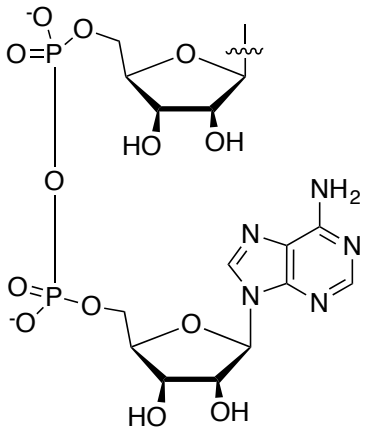
mechanism ***b***.

Because the amine anion is not a good leaving group.

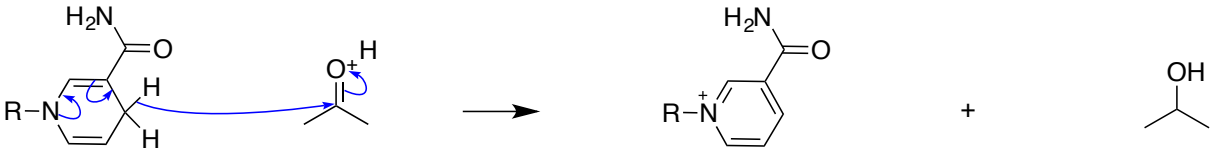
D. NADH: A Hydride Source *In Vivo*



R =

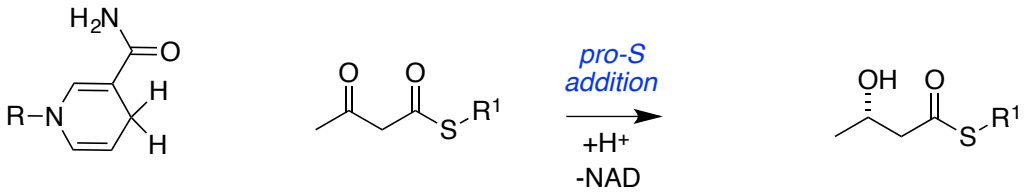


NADH full name: Reduced nicotinamide adenine dinucleotide



by-product full name: Nicotinamide adenine dinucleotide (NAD)

is *NAD*.


H2N
O
H
R–N
H
O
O
S
R1
pro-S
addition
+H+
-NAD
OH
O
S
R1