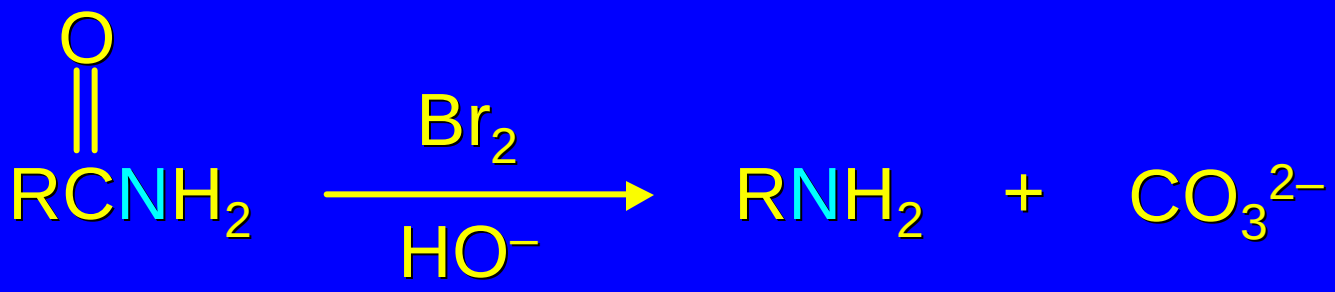
20.17

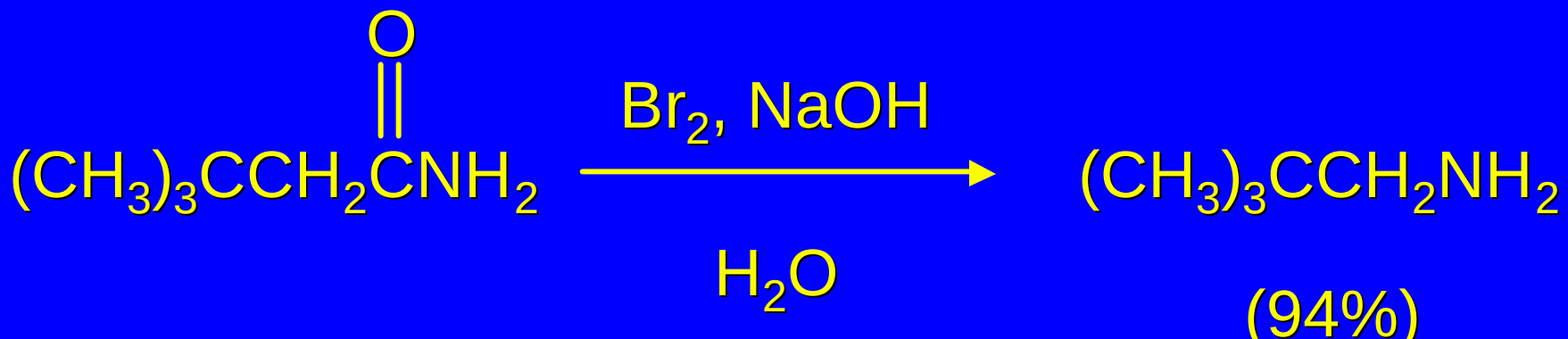
The Hofmann Rearrangement

The Hofmann Rearrangement

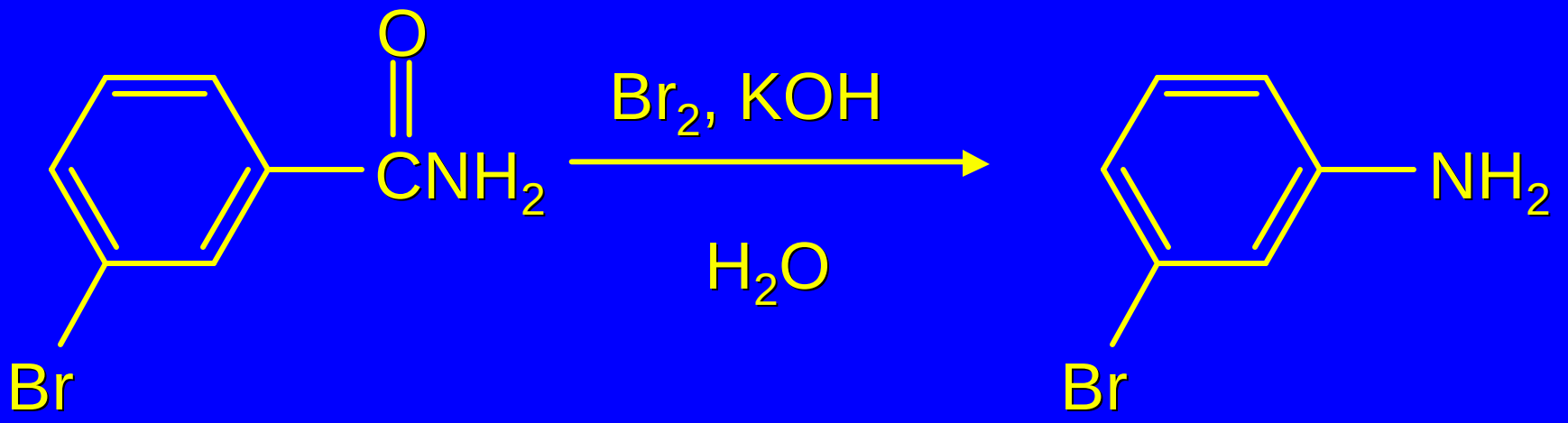
Treatment of amides with bromine in basic solution gives an amine with loss of the carbonyl carbon.



Examples

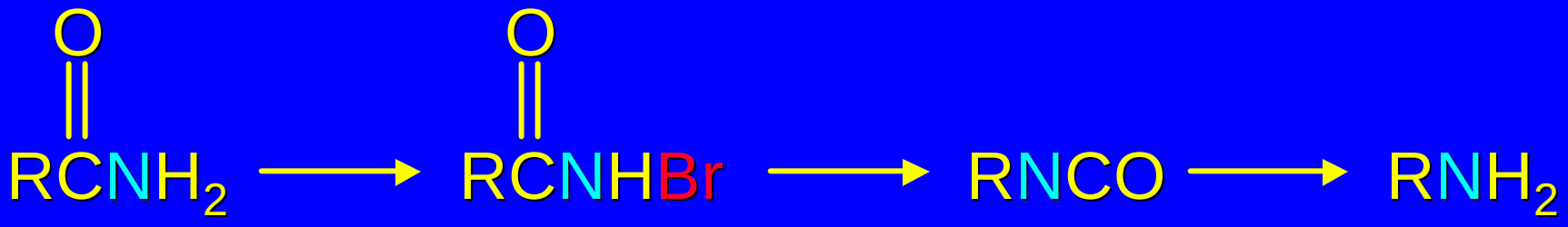


(94%)



(87%)

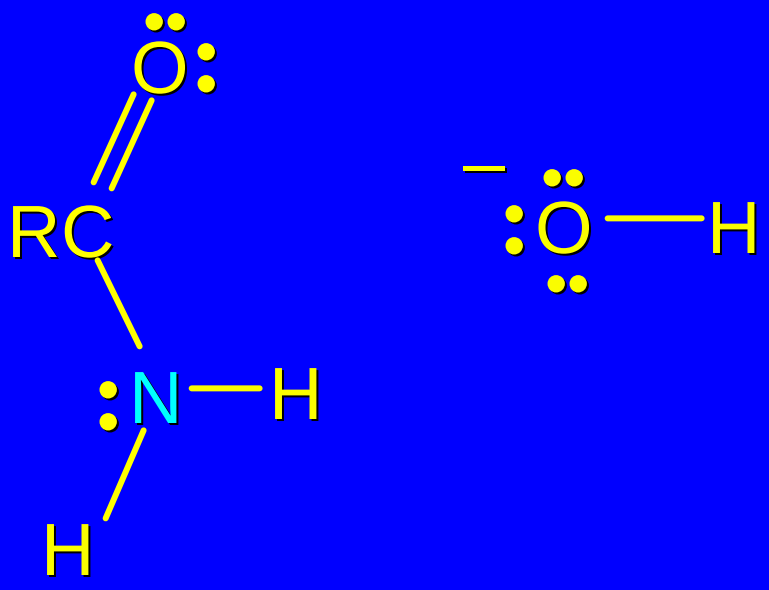
Mechanism of the Hofmann Rearrangement



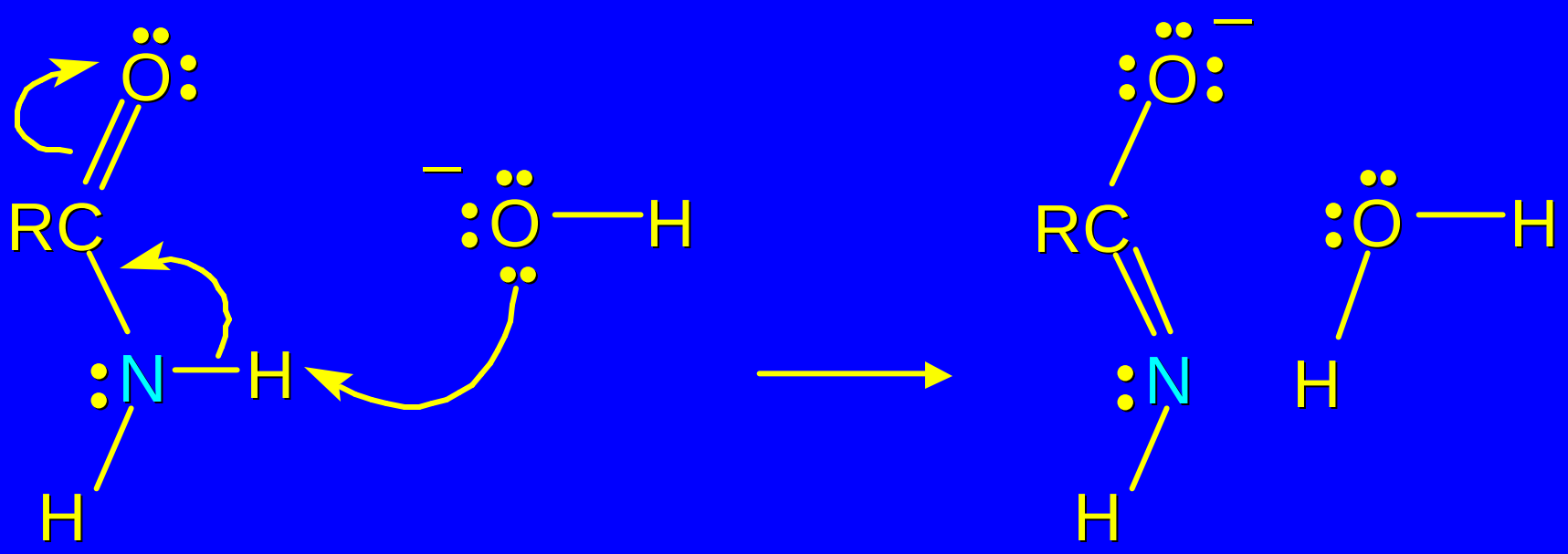
The Hofmann rearrangement involves 6 steps in 3 stages.

1. formation of an *N*-bromo amide (2 steps)
2. conversion of the *N*-bromo amide to an isocyanate (2 steps)
3. hydrolysis of the isocyanate (2 steps)

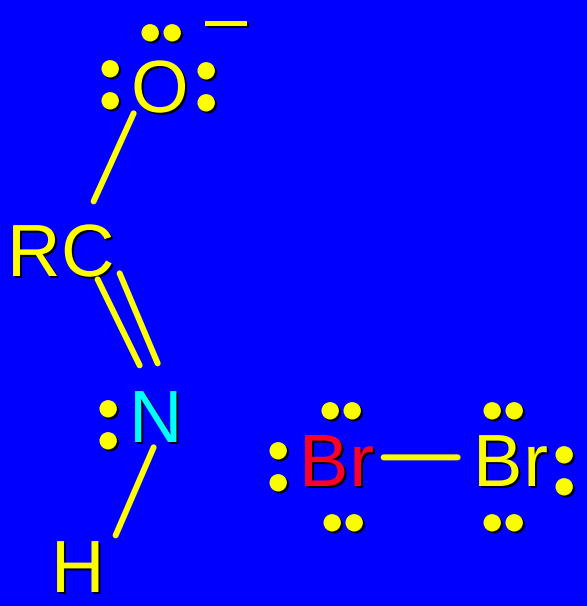
Step 1



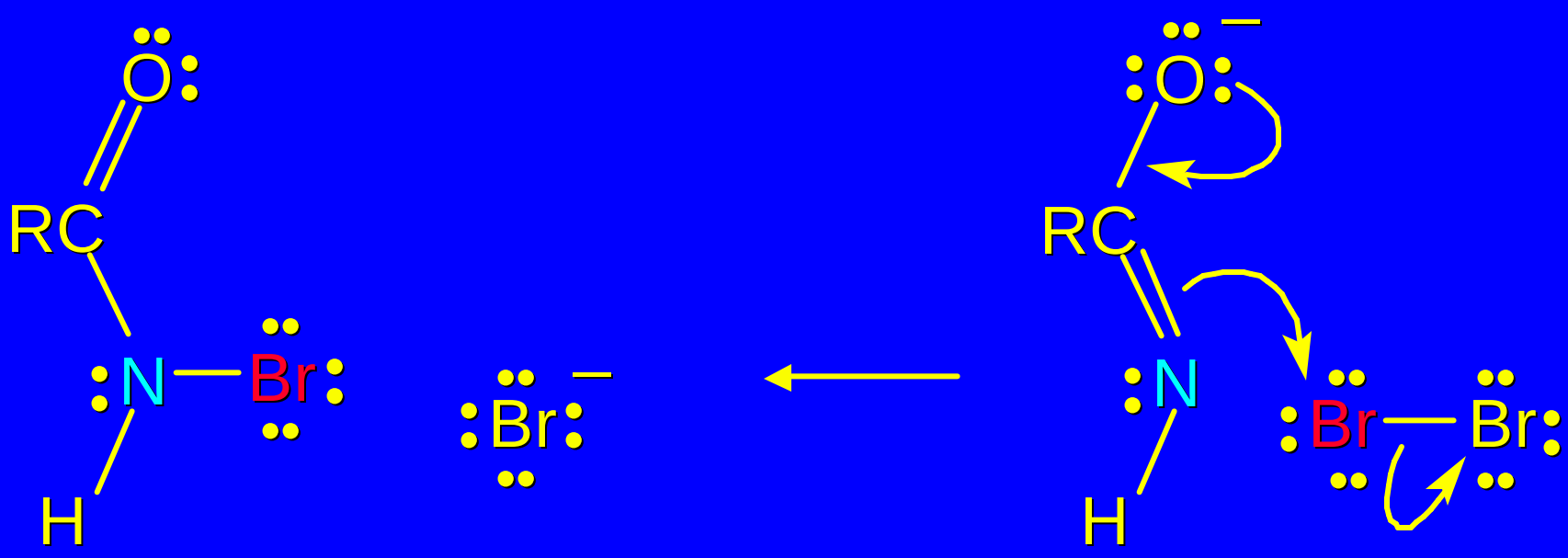
Step 1



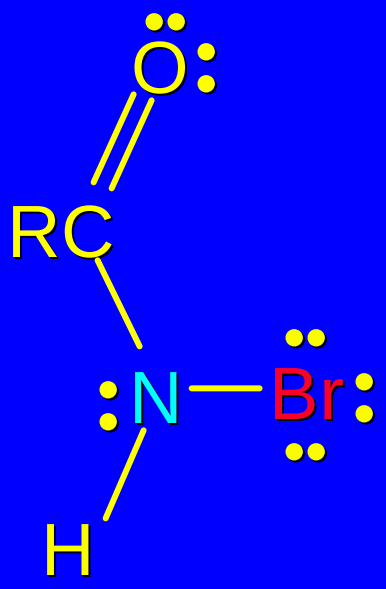
Step 2

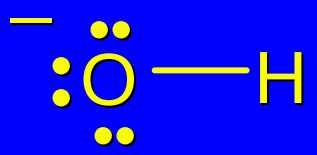


Step 2

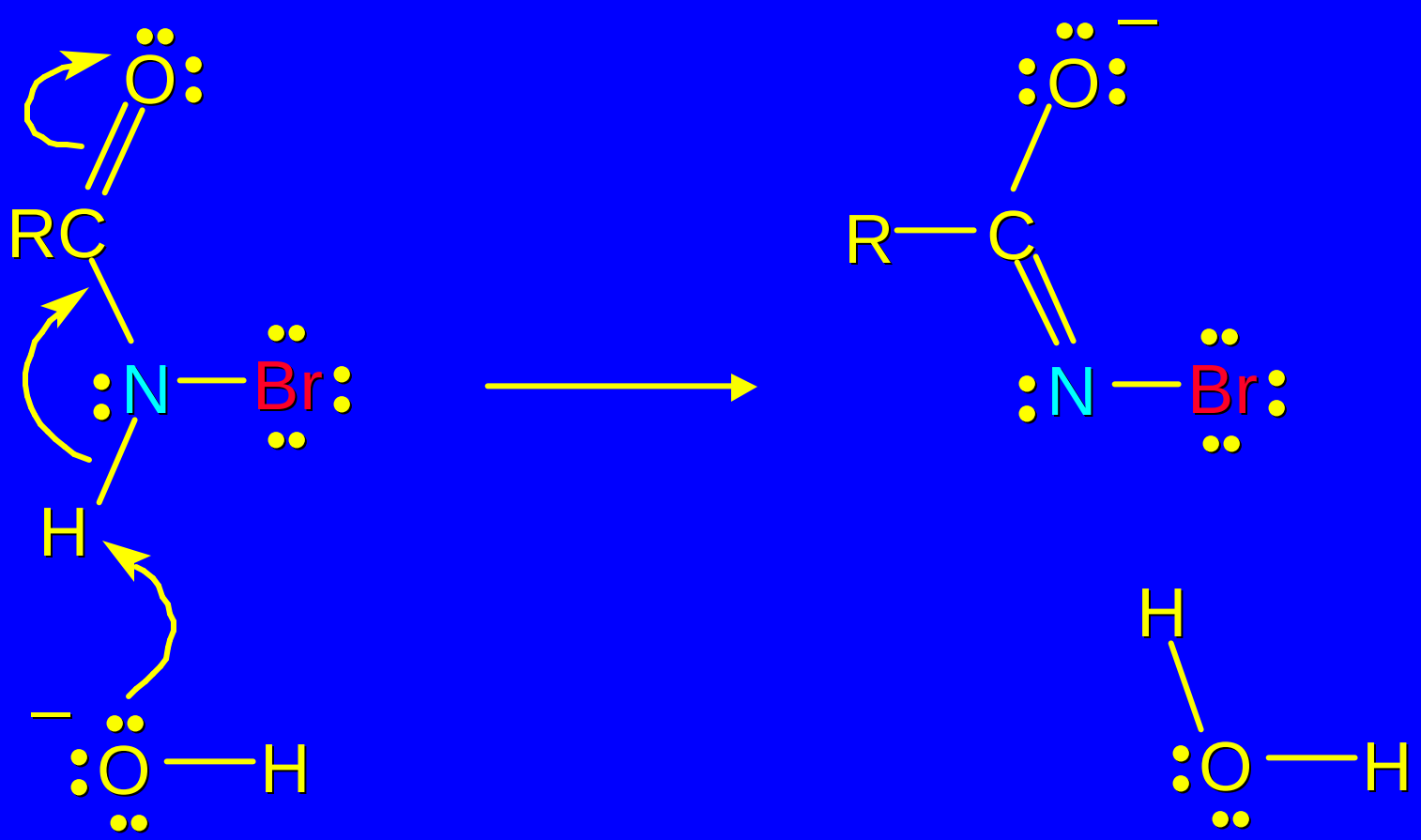


Step 3

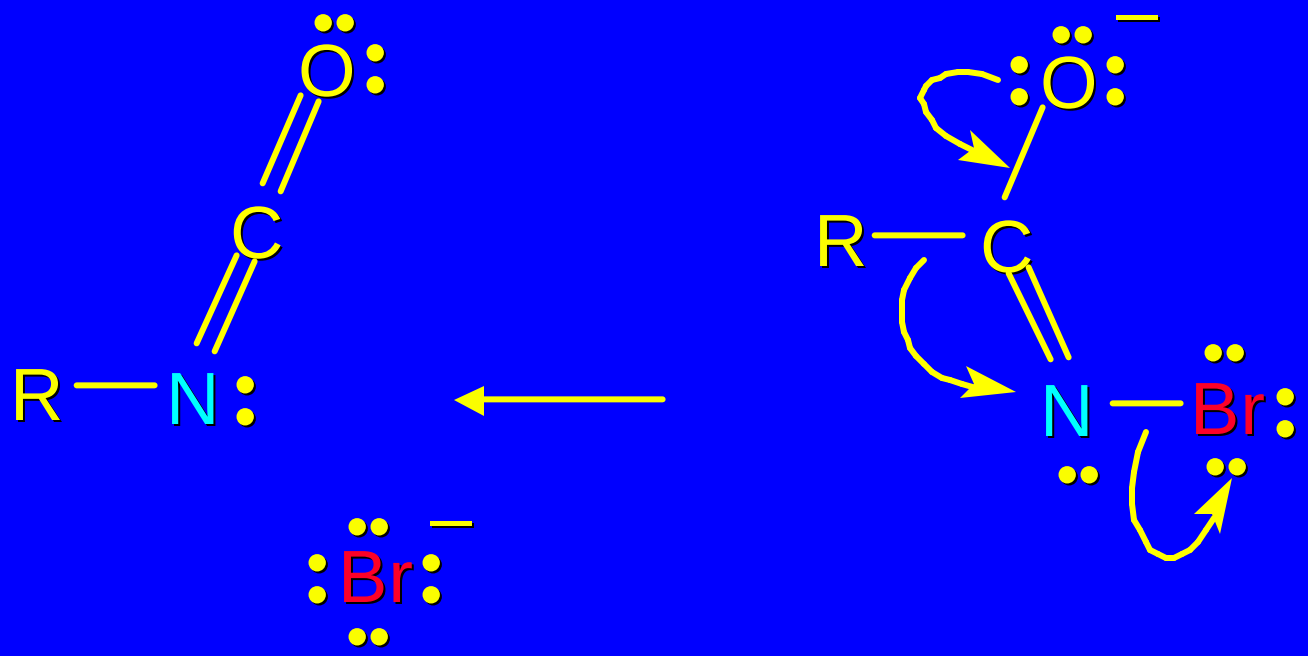




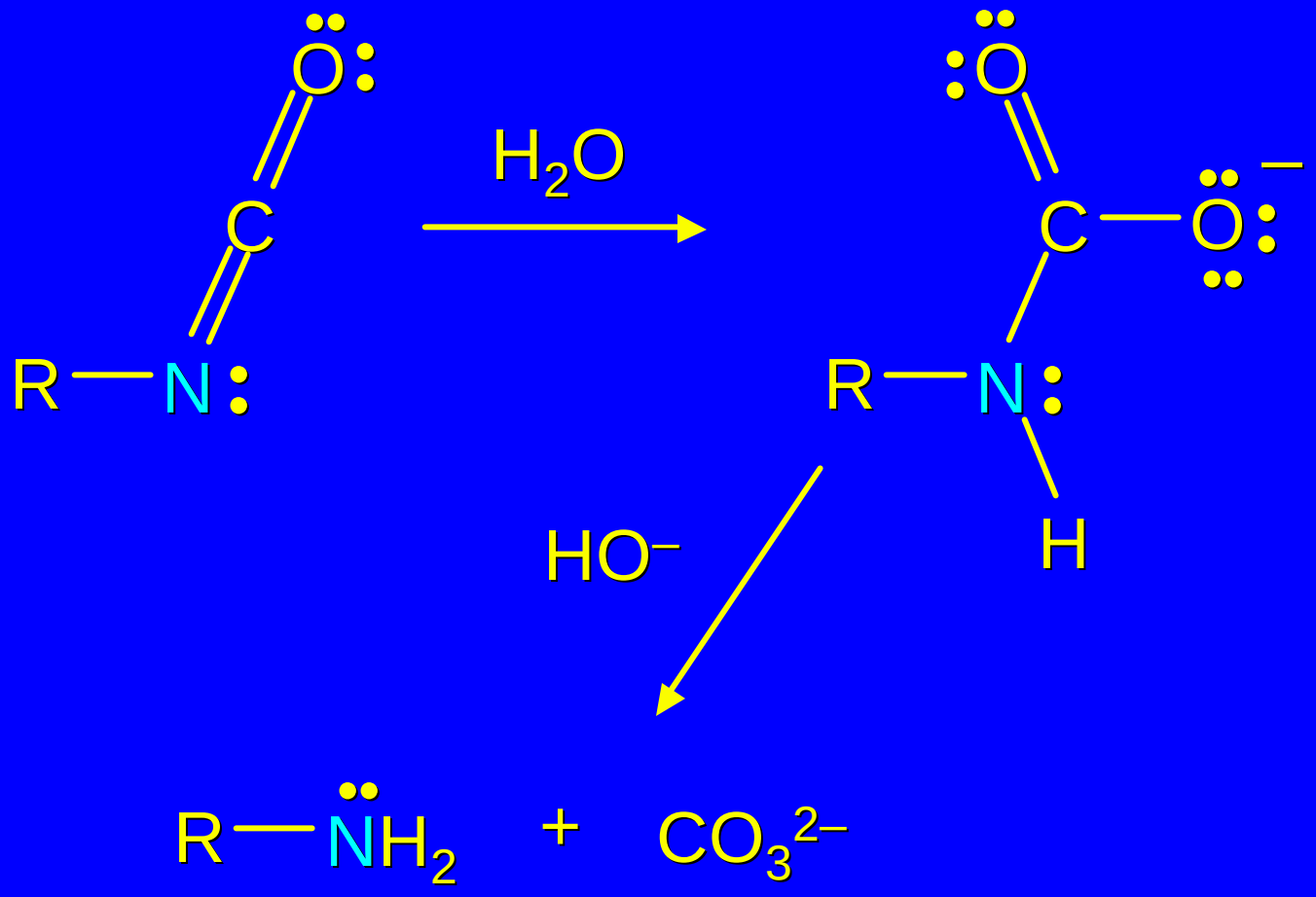
Step 3



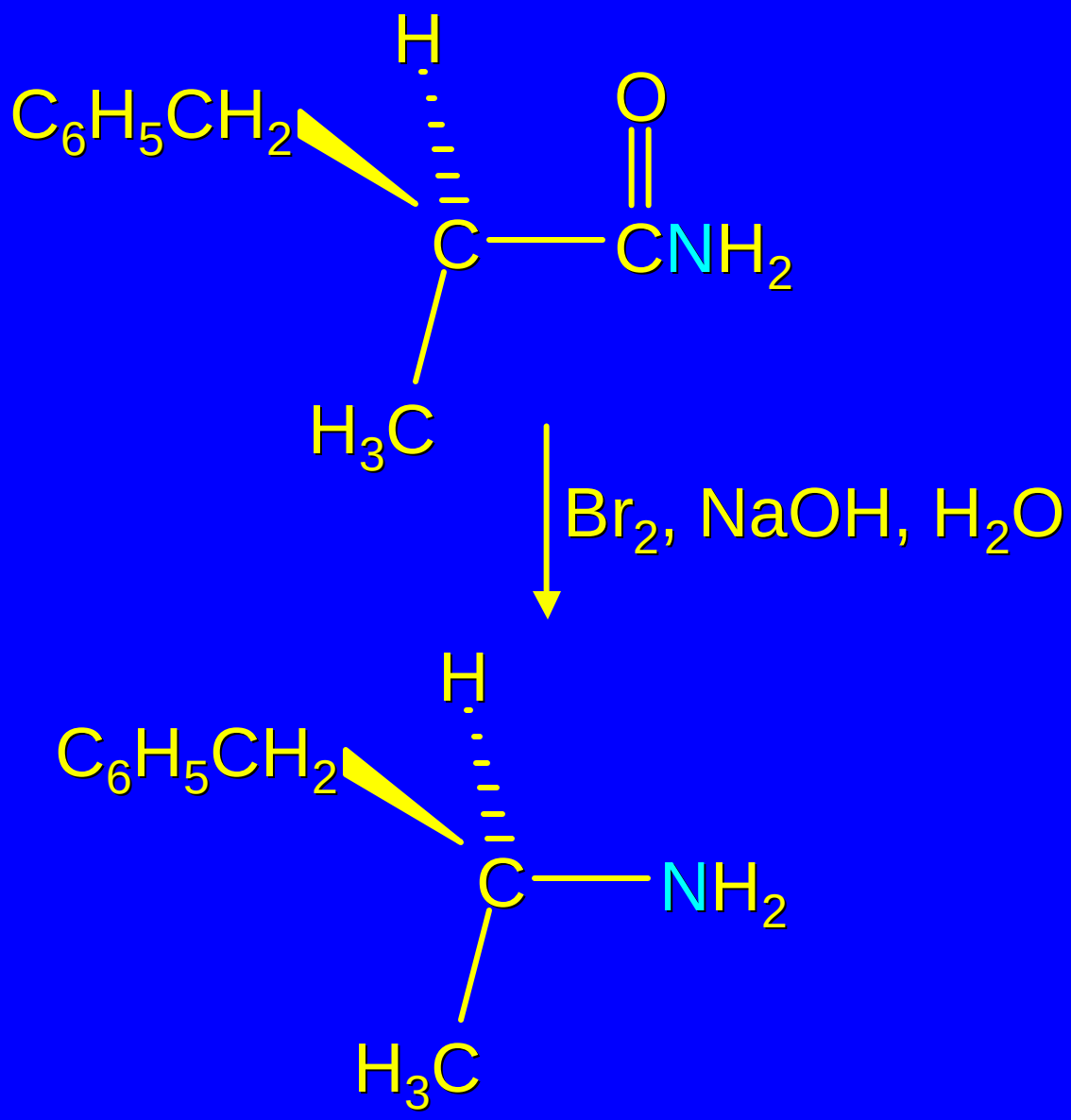
Step 4



Steps 5 and 6



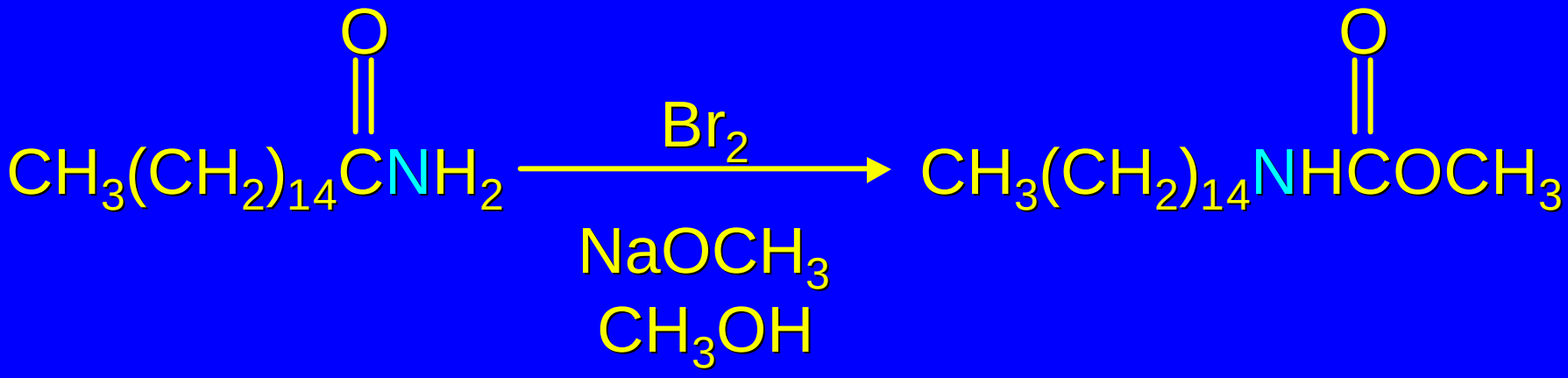
Stereochemistry



alkyl group migrates with retention of configuration

Isocyanates are intermediates

When the reaction is carried out in methanol instead of water, the product shown is isolated.



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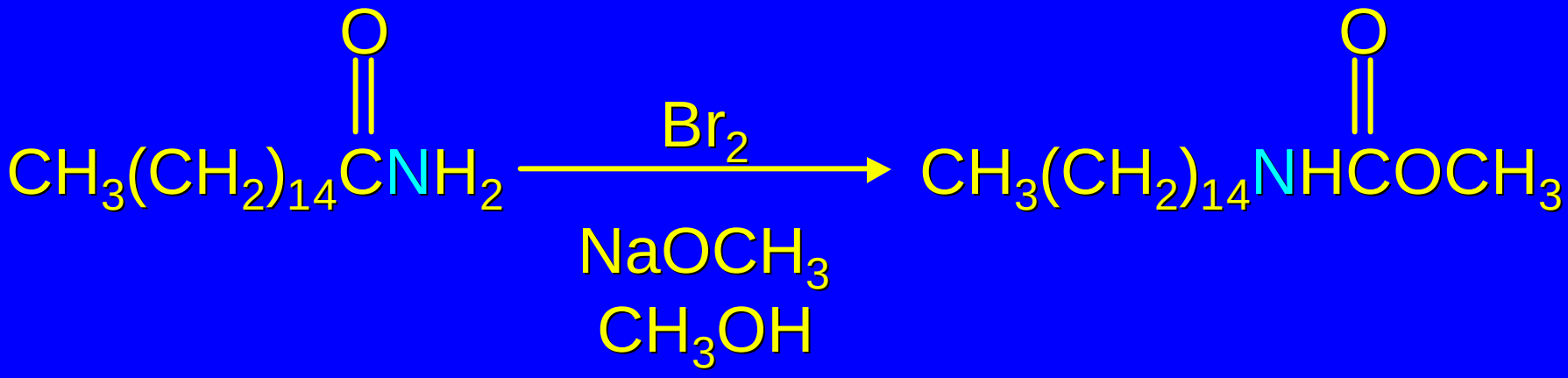

via: $CH_3(CH_2)_{14}N{=}C{=}O$