Reducive and Transition-Metal-Free: Oxidation of Secondary Alcohols by Sodium Hydride

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Normal Behavior of NaH


Brou&n, F-E.; Colobert, F. *Org. Lett.* **2005**, *7*, 3737-3740
NaH-Promoted Oxidation

\[
\text{NaH (2 eq)} \rightarrow \text{THF, rt, 10 h}
\]

NaH-Promoted Oxidation: Proposed Mechanism

With electron withdrawing group
- Retardation of the reaction rate

Increase in the Concentration of the reaction
- No Noticeable effect on the reaction rate

Enhancement of the reaction rate
- Substantial effect on the reaction rate

# NaH-Promoted Oxidation: Reaction Conditions

![Reaction Scheme]

- **Reagents**
  - Na: Inactive
  - NaOMe: Less efficient
  - NaH: Most efficient
  - NaH = 2 equiv due to low solubility in THF

- **Solvents**
  - THF = Optimal Solvent
  - DMF
  - Toluene
  - Ether
  - (preliminary computational study suggest the coordination of THF to Na atom)

- **Concentration**
  - 0.2 M with respect to alcohol

- **Temperature**
  - 0 °C - rt

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NaH-Promoted Oxidation: Substrate Scope

- Low yields for 11, 15
- 5 g scale of 5, 6, 7, 8, 13, 14
- 13, 14 in 83% and 88% using recovered NaH (2 eq.)

Reversible hydride conjugate reduction event following the alcohol oxidation

NaH-Promoted Tandem Alcohol Oxidation-Hydride Conjugative Reduction of Heterocyclic Allylic Alcohols

NaH-Promoted Oxidative Amidations of Some Heterocyclic Aldehydes

Conclusion

• Unprecedented reactivities of NaH uncovered on:
  1. Alcohol oxidation
  2. Tandem allylic alcohol oxidation-hydride conjugate reduction
  3. Aldehyde oxidative amidation

• A significant level of material accessibility

• Operational simplicity

• Environmental compatibility (no metal residue or decomposition waste)

• NaH can be recovered and has the same reactivity

• Large scale reactions up to 5 g

• Could be used for economic preparation of pharmaceutically meaningful heterocyclic compounds