Stabilized Alkali Metals for Safer, Scalable Birch Reductions

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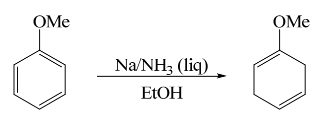
Abstract

The Birch reduction is the reduction of aromatic rings with alkali metals (Li, Na, K) dissolved in liquid ammonia. Birch reductions are generally avoided for scale-up due to the complexities of the large-scale process and the hazards associated with the use of the metal and liquid ammonia on scale. SiGNa Chemistry, Inc. has discovered and developed a proprietary method for encapsulating alkali metals in nano-scale porous oxides. The resulting sand-like powders are stable at room temperature and take a significant amount of the danger and associated costs out of using reactive metals. More importantly, the SiGNa materials retain the chemical utility associated with the parent metal. This presentation will highlight SiGNa's technology and how these novel materials can be applied to a range of chemical processes, specifically Birch reductions. A Birch reduction performed using SiGNa material removes the environmental and occupational hazards of alkali metals and does not require liquid ammonia or cryogenic temperatures.

The Birch Reduction



- The Birch reduction[1] is an alternative to hydrogenation that yields cyclohexadienes
- The reduction is carried out in liquid ammonia with dissolved sodium, lithium or potassium
- By dissolving the metal in liquid ammonia, a metal cation and a solvated electron are formed. This solvated electron is a powerful reducing agent
- The reaction mixture contains a stoichiometric amount of an alcohol which acts as a proton donor
- The first step of the mechanism is a one-electron transfer to form a radical anion which is then protonated to yield a cyclohexadienyl radical. This resonance-stabilized allyl radical is converted into a cyclohexadienyl anion by an additional one-electron transfer. Subsequently, the cyclohexadienyl anion is also protonated to yield the 1,4-cyclohexadiene

Issues with Birch Reductions

- Handling of alkali metals
- Handling of ammonia gas
- Cryogenic temperatures
- Choice and handling of materials
- Special design of the equipment
- Operational, waste treatment, and safety issues

Alkali metals[2]:

- React Immediately with the environment leading to onerous storage and handling requirements
- Increased risk of supply chain interruption and increased shipping expense

Ammonia[3]:

- Pungent odor detectable at 5 ppm
- Immediate danger to health at 500 ppm

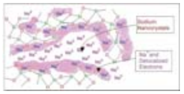
A need exists for alkali metals that can be easily handled without a loss in reactivity

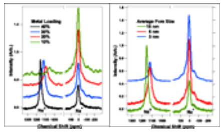
SiGNa's Technology

- Alkali metals encapsulted in nano-structured porous oxides[4]
- Alkali metal silica materials (M-SG); capacity up to 40 wt.%
- Stable in dry air / Safer to handle / easier to transport
- Free-flowing powders
- Reducing power of the parent metal/alloy retained
- Non-toxic by-products and waste streams – Sodium Silicate

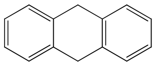
Material	Metals Used	Applications
Stage 0 M-SG	Liquid alloys (K_2Na, Na_2K, etc.)	Desulfurization, Polymer Initiation, etc.
Stage I M-SG	Liquid alloys and Na, K, Cs, Rb, etc.	Birch red., deprotections, Wurtz, etc.
Stage II M-SG	Liquid alloys and sodium	Hydrogenation, solvent drying, etc.
Sodium Silicide	Sodium metal	Hydrogen source, fuel cells, etc.

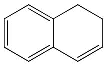
Theoretical Model of Stage I M-SG

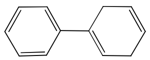


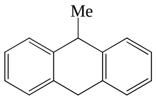


Birch Reduction Products

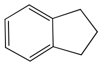

90%
(anthracene)

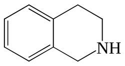

61%
(naphthalene)


60%
(biphenyl)

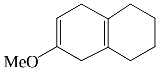


85%
(9-methylanthracene)

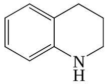

79%
(indene)



89%
(isoquinoline)

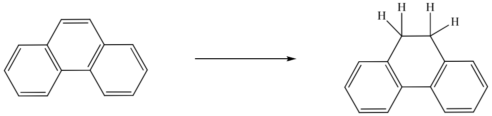


86%
(6-methoxy-1,2,3,4-tetrahydronaphthalene)



58%
(quinoline)

Birch Reduction Comparison



Classical Reaction Conditions[5]:

- Phenanthrene was dissolved in THF and charged to refluxing ammonia at -33 °C
- Lithium metal (3.5 equivalents) was added
- Reaction quenched with ethanol/water
- Desired product was isolated in 57% yield

SiGNa's Reaction Conditions:

- Phenanthrene and Na-SG(I) (3.5 equivalents) are charged to a round bottom flask
- THF added and the mixture is cooled to 0 °C
- *tert*-Butanol (1.75 equivalents) is added in one portion
- Desired product was isolated in 60% yield

NO CRYOGENIC TEMPERATURES!

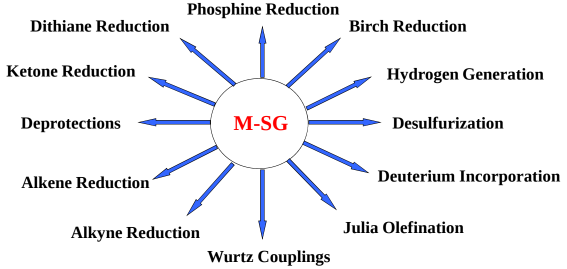
NO PYROPHORIC REAGENTS!

NO LIQUID AMMONIA!

Similar yields and purities were observed with:

- 2.0 to 7.5 equivalents of SG(I) with Na, Na_2K and K_2Na as parent metal
- *t*-butanol, *t*-amyl alcohol, NH_4Cl as proton source
- THF, Me-THF, MTBE, Toluene, Cyclohexane, Heptane, or DME as solvent
- Ethylenediamine as an additive

Synthetic Chemistry Applications



References

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Winner of the 2008 Presidential Green Chemistry Challenge Award