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SELECTIVE LITHIUM-AMMONIA REDUCTION OF AROMATIC KETONES AND BENZYL ALCOHOLS. MECHANISTIC IMPLICATIONS.

Stan S. Hall, Sharon D. Lipsky, and Gary H. Small

Department of Chemistry, Rutgers University, Newark, New Jersey 07102.

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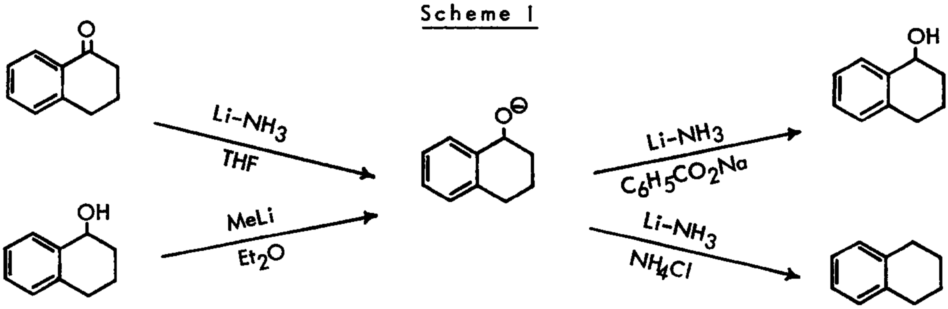
We wish to report conditions for the reduction of aromatic ketones and benzyl alcohols in lithium-ammonia solutions which are selective and simply involve the proper choice of quenching agent. By these methods aromatic ketones can be reduced to benzyl alcohols or aromatic hydrocarbons, and benzyl alcohols are reduced to aromatic hydrocarbons or can be protected during lithium-ammonia reductions.

When an aromatic ketone is refluxed in a lithium-ammonia (THF) solution it is reduced to the corresponding benzyl alkoxide which in turn is reduced rapidly to the aromatic hydrocarbon when the reaction mixture is quenched with ammonium chloride.[1] This quenching agent evidently protonates the benzyl alkoxide intermediate and the resulting benzyl alcohol is reduced to the aromatic hydrocarbon before all the excess lithium is destroyed.

In contrast, when the above reaction mixture containing the benzyl alkoxide is quenched with sodium benzoate, a procedure which destroys the excess reducing agent in the absence of an external proton source,[2] the benzyl alcohol is formed. Scheme I illustrates an example with 1-tetralone.

Scheme I



Benzyl alcohols, as the preformed benzyl alkoxides, behave similarly when subjected to these conditions. The general procedure is as follows. Ammonia is distilled into a metal-ammonia reaction vessel which contains the benzyl alkoxide in ether, generated by the addition of the benzyl alcohol to an ethereal solution of methyllithium, followed by the addition of excess lithium wire, and then the dark blue solution is quenched. The product isolated in excellent yield is the aromatic hydrocarbon when the reaction mixture is quenched with ammonium chloride, and recovered benzyl alcohol when sodium benzoate is used to destroy the excess lithium (Scheme I).

The alkoxide generation step can be omitted when it is desirable to reduce a benzyl alcohol to the aromatic hydrocarbon. For example, addition of a benzyl alcohol such as 1-tetralol in THF to a refluxing lithium-ammonia (THF) solution followed by an ammonium chloride quench resulted in an almost quantitative yield of tetralin. However, if a benzyl alcohol is to be protected, prior generation of the alkoxide is imperative.[3]

The above observations support the intermediacy of a benzyl alkoxide in the reduction of aromatic ketones which resists further reduction in the absence of an added proton source.

These procedures represent the first method of selectively reducing aromatic ketones and the best reported method for the selective protection or reduction of benzyl alcohols in dissolving metal-ammonia solutions.[4]

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REFERENCES

1. For a complete discussion and experimental details which are also applicable to the sodium benzoate quench, see Stan S. Hall, Sharon D. Lipsky, Frank J. McEnroe, Anne P. Bartels, *J. Org. Chem.*, **36**, 0000 (1971).
2. A.P. Krapcho and A.A. Bothner-By, *J. Amer. Chem. Soc.*, **81**, 3658 (1959).
3. Addition of 1-tetralol in THF to a lithium-ammonia (THF) solution followed by a sodium benzoate quench resulted in a mixture of tetralin (80%) and 1-tetralol (20%).
4. (a) R.L. Augustine, Ed., "Reduction", Dekker, New York, 1968, pp 107-108, 116-117; (b) H. Smith, "Organic Reactions in Liquid Ammonia. Chemistry in Anhydrous Liquid Ammonia.", Vol. 1, Part 2, Wiley, New York, 1963, pp 157-161, 216-219; and the references cited therein.