

TECHNICAL NOTE

Roger A. Ely,¹ B.A. and Diane C. McGrath,¹ B.S.

Lithium-Ammonia Reduction of Ephedrine to Methamphetamine: An Unusual Clandestine Synthesis

REFERENCE: Ely, R. A. and McGrath, D. C., "Lithium-Ammonia Reduction of Ephedrine to Methamphetamine: An Unusual Clandestine Synthesis," *Journal of Forensic Sciences*, JFSCA, Vol. 35, No. 3, May 1990, pp. 720-723.

ABSTRACT: A suspected clandestine methamphetamine laboratory was seized in Vacaville, California. Ephedrine, a precursor for the manufacture of methamphetamine, was discovered at the site. However, the chemicals normally expected to be found at an ephedrine conversion laboratory were not recovered. Other chemicals found at the scene included tetrahydrofuran, ammonium chloride, lithium metal, and ammonia gas. Examination of the suspect's notes showed several different common synthesis routes to methamphetamine and a novel route utilizing a lithium/ammonia/ammonium chloride reduction. The reduction of ephedrine to methamphetamine using this dissolving metal procedure has not been reported in the literature. The authors reproduced the suspect's reaction scheme and found the lithium/ammonia/ammonium chloride reduction of ephedrine to be a viable synthesis for methamphetamine.

KEYWORDS: toxicology, methamphetamine, ephedrine

Case Report

The U.S. Drug Enforcement Administration's Western Regional Laboratory in San Francisco, California, assisted the San Francisco Clandestine Laboratory Task Force in the seizure of a suspected methamphetamine laboratory near Vacaville, California. The laboratory was located in and around a 14-ft (4-m) travel trailer sitting in a trailer park north of town. Small amounts of chemical glassware, solvents, and reagent chemicals were found at the location, including one 2-kg container of *l*-ephedrine hydrochloride. However, other chemicals and reagents commonly associated with an ephedrine conversion laboratory were not found. Two of the chemical items recovered from the scene, a 150 ft³ (4.2 m³) bottle of anhydrous ammonia gas and 25 lb (11 kg) of lithium metal wire, seemed oddly out of place for a clandestine methamphetamine laboratory.

During an examination of documents found in the trailer, numerous handwritten and typed "recipes" for the manufacture of methamphetamine and other controlled sub-

Received for publication 17 April 1989; accepted for publication 19 June 1989.

¹Forensic chemists, U.S. Drug Enforcement Administration, Western Laboratory, San Francisco, CA.

stances were discovered. One of the procedures detailed the use of lithium metal, ammonia gas, and ephedrine to manufacture methamphetamine. This methodology for the reduction of ephedrine has not been previously reported in the literature nor has it been observed in any prior clandestine laboratory seizure. Using the suspect's notes, the reaction was successfully duplicated.

This method is a departure from the methods of reducing ephedrine that are commonly found at clandestine laboratories. It is, therefore, important for enforcement personnel to be aware of the three major reagents in this method (anhydrous ammonia gas, lithium metal, and ammonium chloride) for intelligence-gathering purposes and for their safety in assessing and seizing such a laboratory.

Procedure

All the chemicals were reagent grade, with no special treatment of the tetrahydrofuran (THF), and the atmosphere above the condensed ammonia was not flushed with nitrogen gas.²

A three-neck flask was cooled in a dry ice/acetone bath. A condenser was fitted in the center neck, an additional funnel containing *l*-ephedrine base in THF was fitted into one side neck, and a rubber stopper fitted with a glass tube extending to the bottom of the flask was fitted in the third neck. Anhydrous ammonia gas was condensed and collected in the flask. Small pieces of lithium metal were rinsed in petroleum ether, patted dry, and added to the condensed ammonia. A deep royal blue color was noted as the lithium metal dissolved in the condensed ammonia.

The *l*-ephedrine was added dropwise to the lithium-ammonia solution over a period of approximately 10 min with stirring. When all of the *l*-ephedrine had been added, ammonium chloride was added slowly to the solution. The flask was removed from the cooling bath, and the condensed ammonia was allowed to warm to room temperature and evaporate from the flask through the side necks.

When most of the ammonia had evaporated, water was added to the remaining solution until it cleared and any remaining lithium metal was decomposed. The remaining solution was removed from the flask to a separatory funnel, where the aqueous layer was discarded. The THF layer was dried with magnesium sulfate, and the hydrochloride salt of the methamphetamine was made by bubbling hydrogen chloride through the THF.

The same procedure was used, substituting phenylpropanolamine and methylephedrine as the starting materials. A second synthesis was conducted with *l*-ephedrine, using the same procedure except that the reaction was not quenched with ammonium chloride.

The identification of the methamphetamine, amphetamine, and dimethylamphetamine was done by capillary gas chromatography connected serially to a Fourier transform infrared detector and a mass spectrometer. The optical rotation of the methamphetamine was determined by polarimetry.

Results

The reaction was found to reduce *l*-ephedrine to *d*-methamphetamine quickly and easily. Furthermore, it was found that the reaction converted phenylpropanolamine to amphetamine and methylephedrine to dimethylamphetamine. The time required for the

²The purpose of the experiment was to determine whether an individual in a makeshift laboratory could convert ephedrine to methamphetamine by using this method, taking into consideration the very limited capabilities of most clandestine chemists. Since most clandestine chemists are looking for the easiest and quickest route to a final product, it is doubtful that they would take the time to distill their THF from lithium aluminum hydride (LiAlH₄) or flush the atmosphere above the condensed ammonia gas as the literature [1] suggests, unless they absolutely had to.

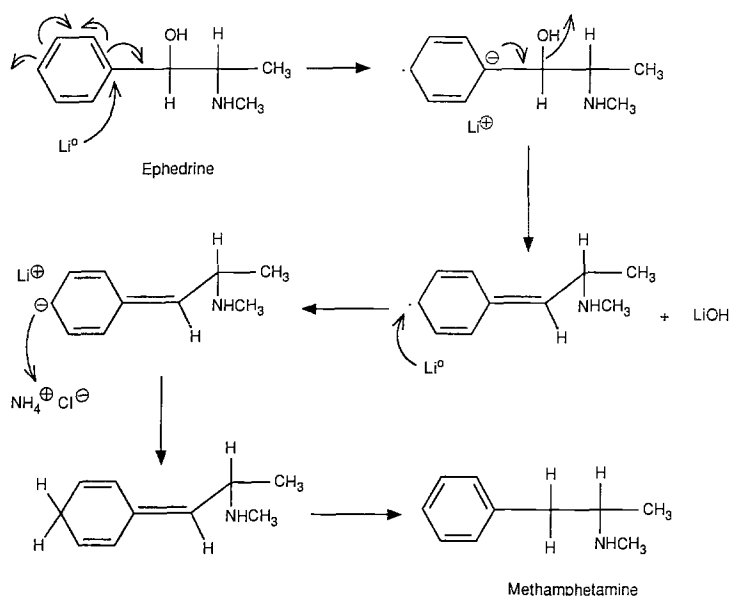


FIG. 1—The probable reaction mechanism for the lithium/ammonia/ammonium chloride reduction of ephedrine to methamphetamine.

reaction to proceed from the condensing of the ammonia gas in the reaction flask until the excess lithium was decomposed was approximately 1 h. The majority of this time was spent waiting for the condensed ammonia to evaporate from the reaction flask.

It was also found that the ephedrine would reduce to methamphetamine without the addition of ammonium chloride as a quenching agent.

Discussion

The use of dissolving metals in ammonia for reductions is well documented [1]. Birch [2] described the use of a sodium/ammonia/ethanol medium for reduction of benzyl alcohols to the corresponding aromatic hydrocarbons. Beginning around 1971, Hall et al. [3], Hall and Lipsky [4], and Small et al. [5] investigated the reductive properties of lithium/ammonia/ammonium chloride on aromatic ketones and benzyl alcohols. These studies also compared the reductive properties of the sodium/ammonia/ethanol medium with those of the lithium/ammonia/ammonium chloride medium. It was found that the former overreduced the benzyl alcohols, while the latter was much more selective in its reductions and produced higher yields. While ammonium chloride is the desired quenching agent for the reaction, water may also be used as an external proton source under some conditions [1].

The reduction of the ephedrine probably proceeds as shown in Fig. 1.³ The dissolved lithium metal gives up an electron to the ring and forms a radical anion. The hydroxyl group is eliminated, forming a double bond between the ring and the α carbon. A second atom of lithium gives up an electron to the radical, and the resulting carbanion is protonated by the ammonium chloride. Through keto-enol tautomerism, methamphetamine is formed as the more stable species.

³Klein, R. F. X., DEA Special Testing and Research Laboratory, McLean, VA, personal communication, 11 Oct. 1988.

Conclusion

The use of a lithium-ammonia dissolving metal reduction method, with or without an ammonium chloride quench, was found to convert phenylpropanolamine, ephedrine, and methylephedrine quickly and easily to their respective controlled substances amphetamine, methamphetamine, and dimethylamphetamine.⁴

Acknowledgments

The authors are grateful to Dr. R. F. X. Klein, DEA Special Testing and Research Laboratory, for his assistance and comments on this project.

References

- [1] Augustine, R. L., Ed., *Reduction: Techniques and Applications in Organic Synthesis*, Marcel Dekker, New York, 1968.
- [2] Birch, A. J., "Reduction by Dissolving Metals: Part II," *Journal of the Chemical Society*, 1945, pp. 809–813.
- [3] Hall, S. S., Lipsky, S. D., and Small, G. H., "Selective Lithium-Ammonia Reduction of Aromatic Ketones and Benzyl Alcohols: Mechanistic Implications," *Tetrahedron Letters*, No. 21, 1971, pp. 1853–1854.
- [4] Hall, S. S. and Lipsky, S. D., "Alkylation-Reduction of Aromatic Ketones and Aldehydes: A Convenient Synthesis of Aromatic Hydrocarbons," *Journal of the Chemical Society, Chemical Communications*, 1971, pp. 1242–1243.
- [5] Small, G. H., Minnella, A. E., and Hall, S. S., "Lithium-Ammonia Reduction of Benzyl Alcohols to Aromatic Hydrocarbons: An Improved Procedure," *Journal of Organic Chemistry*, Vol. 40, No. 21, 1975, pp. 3151–3152.

Address requests for reprints or additional information to
Roger A. Ely
Forensic Chemist
Drug Enforcement Administration
Western Field Laboratory
390 Main Street, Room 700
San Francisco, CA 94105

⁴*N,N*-Dimethylamphetamine was placed under temporary control as a Schedule I substance as of 3 Aug. 1988 pursuant to the Emergency Scheduling Provision (Federal Register Notice 53FR29232).