Metal-Ammonia Reduction of Aromatic Molecules

Ronald G. HARVEY
Ben May Laboratory, University of Chicago, Chicago, Illinois 60637

Metal-ammonia reduction is a highly efficient and convenient method of reduction of polycyclic as well as monocyclic aromatic hydrocarbons and their derivatives. With proper control over experimental conditions, reduction can generally be limited to a single stage: the structures of the primary products accord with theoretical predictions based on simple HMO calculations. Reduction in liquid ammonia and the related reductive alkylation reaction are reviewed from a preparative viewpoint with emphasis on the effects of structure, stereochemistry, and the selection of experimental techniques.


The solvated electrons present in solutions of alkali metals in liquid ammonia represent the simplest, and in a sense, the ultimate reducing agent. They permit efficient reduction of diverse organic functional groups.

Several excellent reviews1 - 5 concerned with theoretical aspects and synthetic applications exist. However, several years of experience have convinced the author that metal-ammonia reactions, despite their enormous potential synthetic utility, are frequently avoided by the practising chemist in favor of more familiar, often less satisfactory, techniques. Reluctance to deal with unconventional solvents is partially a consequence of the fairly common omission of such experience from academic programs6. A more serious obstacle to general acceptance is the likelihood of unsuccessful trial reactions due to failure to realize the importance of experimental variables (e.g., order of addition, presence

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of trace impurities, etc.) for transformations in liquid ammonia. This review is directed, therefore, towards counteracting these difficulties, at least with respect to reduction and related reactions of monocyclic and polycyclic aromatic hydrocarbons and their derivatives. The latter are surveyed from a preparative viewpoint with emphasis on limitations, interfering influences, effects of structure, stereochemistry, and the selection of experimental techniques.

1. General Reaction

In general, the reaction involves addition of electrons, either individually or in pairs, to an aromatic ring system with protonation taking place either alternately after the addition of each electron or finally after both have added to form the dianion (Scheme A):

\[
\begin{align*}
\text{ArH} & \rightarrow \text{ArH}^2^- \\
\text{ArH}^2^- & \rightarrow \text{ArH}^2^- \\
\text{ArH}^2^- & \rightarrow \text{ArH}_2^2 \\
\text{ArH}_2^2 & \rightarrow \text{ArH}_3
\end{align*}
\]

Scheme A

Monocyclic benzene derivatives do not readily form anions, even in liquid ammonia, and require the presence of alcohol or other proton source to displace to the right the initial unfavorable equilibrium (Birch conditions). Polycyclic aromatic systems, on the other hand, generally undergo facile transformation to the corresponding radical-anion and/or dianion in the absence of an added proton source. In these instances, ammonia itself (pK\text{a} ~ ~ ~ ~ 34) frequently serves the role of protonating agent.

Product structure can be predicted to a remarkable degree from theoretical considerations. According to HMO theory,\textsuperscript{7,8} the incoming protons occupy the positions of highest electron density in the intermediate ion, as determined by the coefficients of the lowest vacant molecular orbital; for alternant hydrocarbons, it is thought not to matter whether the orbital is singly or doubly occupied\textsuperscript{9,10}. Where calculations are impractical, qualitative predictions may be based on the relative stabilities of the possible intermediate anions\textsuperscript{11}:

- secondary > tertiary
- benzyl > allyl > aliphatic.

Correlation with experimental findings is generally high\textsuperscript{12}, despite neglect of steric, solvation, and other effects in the theory, and despite the complications sometimes introduced by secondary processes (e.g., isomerization, disproportionation, dimerization). Thus, product formation is generally under kinetic rather than thermodynamic control so that the less stable isomer frequently results (e.g., benzene provides 1,4-dihydro-benzene rather than the conjugated 1,2-dihydro derivative).

2. Conditions

Since impurities may drastically alter the course of reactions, precautions for their exclusion, though seldom mentioned in earlier literature, are highly recommended. Distillation of ammonia into the reaction vessel through a column of barium oxide\textsuperscript{13} effectively removes moisture and salts of ferrous metals. The colloidal metals formed upon reduction of the latter catalyze the consumption of alkali metals with both ammonia\textsuperscript{14,15} and alcohol\textsuperscript{16}. Since peroxides act similarly, cosolvents such as tetrahydrofuran should be freshly distilled from lithium aluminium hydride, and polycyclic aromatic hydrocarbons\textsuperscript{17} should be recrystallized or purified by passage through a column of alumina.

Operation under an inert atmosphere is generally desirable since oxygen vigorously catalyzes both the reduction process and interaction of the metal with ammonia\textsuperscript{18}; nitrogen may be employed with sodium, but it is less satisfactory with lithium due to the facile formation of lithium nitride (helium is recommended).

The order of addition of reagents often dramatically influences product distribution, and is the most important single variable to consider in selecting a reaction procedure. The three techniques commonly employed differ essentially in this respect:

A. The substance (S) to be reduced dissolved in alcohol and an ethereal cosolvent is added to a solution of the metal in ammonia: (M + NH\textsubscript{3}) + (S + H\textsuperscript{0}).

B. The alkali metal is added to a solution of the other reagents: (S + NH\textsubscript{3} + H\textsuperscript{0}) + (M).

C. The proton source is added after a suitable interval to a solution of the other reagents: (S + NH\textsubscript{3} + M) + (H\textsuperscript{0}).


\textsuperscript{9} This generalization does not extend to non-alternant systems. For example, indole and quinoline derivatives undergo reduction by lithium/ammonia in the heterocyclic ring in the absence of methanol and in the benzene ring in its presence (see reference 10). It is proposed that methanol intercepts radical-anion intermediates which have a different pattern of electron distribution than the related dianion intermediates.


The choice of method is dependent upon the structure and properties of the compound to be reduced, and variations of these procedures are often advantageous for particular reactions. For example, the Wilds and Nelson\textsuperscript{19} modification of method A involves addition of a solution of the substance to one of the alkali metal in ammonia followed by addition of alcohol over a short period: \((M + \text{NH}_3) + (\text{S} + \text{H}_2)\). This technique has seen extensive application in the steroid field. While it is also often successful with polycyclic hydrocarbons, the method found most generally applicable in the laboratory of the author is a variation of method C in which the metal is added over a short period to a solution of the hydrocarbon in ammonia; after a suitable interval, reaction is rapidly quenched with water, alcohol, or ammonium chloride: \((\text{S} + \text{NH}_3) + (M) + \text{H}_2\).\textsuperscript{19}

The influence of concentration has received less attention. Metal-ammonia solutions range from containing essentially free solvated electrons at very high dilution (0.003 M), through saltlike intermediate states (0.003 to 1.0 M), to solutions that behave as metals at very high concentrations\textsuperscript{21}. Solutions of the latter type are capable of reducing even relatively resistant molecules, such as phenols\textsuperscript{12}. Also, high concentration favors anionic over radical intermediates (e.g., the stereospecificity of reduction of cyclopropyl halides by sodium in ammonia is a function of the concentration of the metal\textsuperscript{23}).

The metals most frequently employed are sodium, lithium, and, to a lesser extent, potassium, calcium and magnesium. Lithium has both a higher molar solubility and a higher reduction potential in ammonia\textsuperscript{20} (\(-2.99\) v. at \(-50\)) than sodium (\(-2.59\) v.) or potassium (\(-2.73\) v.), and reactions with lithium are frequently “cleaner” than those with the heavier metals. The apparent superiority of lithium is a consequence of several factors, the predominant of which is reported to be the weaker tendency of lithium to undergo iron-catalyzed side reaction with alcohols\textsuperscript{16}. Also, lithium salts are generally less soluble than their sodium or potassium counterparts, and lithium amide is less efficient in catalyzing isomerization of double bonds into conjugation\textsuperscript{5} (leading to excessive reduction).

3. Apparatus

Laboratory scale reductions may be conducted satisfactorily in conventional glass multi-necked flasks equipped with a Dewar condenser. More elaborate apparatus required for special purposes is described in the literature\textsuperscript{6,18}.

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4. Synthesis of 1,4-Cyclohexadiene Derivatives

Benzenes is efficiently reduced to 1,4-cyclohexadiene by method C employing sodium and ethanol in liquid ammonia\textsuperscript{4,25}:

\[
\begin{array}{ccc}
\text{C}_6\text{H}_6 & \xrightarrow{\text{Na}/\text{ROH}} & \text{C}_6\text{H}_4
\end{array}
\]

1,4-Cyclohexadiene: The dry reaction vessel is purged with nitrogen before addition of solid carbon dioxide to the Dewar condenser or the cooling bath (\(-60\)). Liquid ammonia is then distilled into the round-bottomed flask and benzene (100 ml), dried over sodium, is added from a dropping funnel with vigorous stirring. Sodium (40 g) is added in small pieces under a stream of nitrogen at a rate to maintain the temperature of the liquid below \(-45\). When the metal is completely dissolved, the blue color of the solution is discharged by addition of ethanol (150 ml) from a dropping funnel. Sodium ethoxide separates from the solution, then redissolves upon addition of excess ethanol, necessitating efficient stirring. After the reaction, the ammonia is allowed to evaporate, then ice is added and the hydrocarbon layer is washed with water and dried. The crude 1,4-cyclohexadiene containing some unreacted benzene is purified through its tetrabromide, according to Wibaut and Haak\textsuperscript{24}: preparative gas chromatography, apparently never employed, may permit direct separation of the hydrocarbon product; yield from 25 g of tetrabromocyclohexane\textsuperscript{24}: \(4.5\) g (90\%); \(b, p. 88.3^\circ\) /741 mm, \(d^2\) : 0.8573; \(n_0^2\) : 1.4725.

Substituent effects are in accord with the proposed mechanism. Electron-releasing groups deactivate the ring and direct protonation to unsubstituted 2,5-positions (Scheme B, path a) while electron-withdrawing groups have the opposite effect, promoting 1,4-reduction at the position bearing the substituent (path b):

\[
\begin{array}{c}
\text{Scheme B}
\end{array}
\]

\(a: R = \text{NR}_3, \text{OR}, \text{OH}, \text{alkyl}
\)

\(b: R = \text{COOH, CONH}_2, \text{Si(CH}_3)_3, \text{C}_6\text{H}_5
\)

Benzoic acid is smoothly reduced to 1,4-dihydrobenzoic acid (89–95\%\textsuperscript{a}) with sodium in liquid ammonia in the presence of ethanol\textsuperscript{26,27}.

Benzamide is reduced by sodium in liquid ammonia in the presence of \(t\)-butanol to 1,4-dihydrobenzamide\textsuperscript{27}. On the other hand, substitution of ethanol

\textsuperscript{13} Alternatively, one may employ distillation either from sodium metal or through a column of potassium hydroxide pellets.

\textsuperscript{14} R. G. Harvey, J. Org. Chem. 32, 238 (1967).


for 1-butanol leads to reduction primarily at the carbonyl, and N-alkylbenzamides are selectively transformed to the corresponding aldehydes when ammonium acetate is employed as the proton source. Reaction of 1,4-bis-[trimethylsilyl]-benzene with sodium and ammonium chloride in liquid ammonia furnishes the 1,4-dihydro derivative exclusively. Despite some earlier confusion, evidence is now clear that biphenyl is reduced selectively by sodium or lithium in liquid ammonia to 1,4-dihydrobiphenyl; thus, a phenyl substituent functions effectively as an electron-withdrawing group by stabilizing a negative charge at the benzylic position. Other electronegative groups (e.g., nitro, carbonyl) are themselves more susceptible to reduction than the aromatic ring system.

Monoalkylbenzenes are efficiently transformed to the corresponding 2,5-dihydrobenzene derivatives, and the rate of reduction decreases in the series methyl > ethyl > isopropyl > tert-butyl.

Reduction of anisole furnishes 2,5-dihydroanisole which upon mild hydrolysis is converted to 4-oxocyclohexene which in turn undergoes acid-catalyzed isomerization to 3-oxocyclohexene:

\[
\text{OCH}_3 \quad \rightarrow \quad \text{OCH}_3 \quad \rightarrow \quad \text{O} \quad \rightarrow \quad \text{O}
\]

This transformation, first observed by Birch, has had numerous applications in the steroid and related fields. The Wilds-Nelson modification of method C was developed for this purpose.

17β-Hydroxy-3-methoxy-estr-2,5-diene. Liquid ammonia (140 ml) is distilled into a solution of 17β-hydroxy-3-methoxy-estr-13,5-triene (1.38 g; m.p. 118-119°) in anhydrous ether (110 ml). To this is added lithium wire (1.4 g, 42 g-atoms) in small pieces, and 10 min later, absolute ethanol (16 ml) is added dropwise over a 10-20 min period. After evaporation of the ammonia, partition of the product between ether and water and conventional work-up, there is obtained the crude product which is recrystallized from ethanol/petroleum ether; yield: 1.0 g; m.p. 118-119.5°; [α]D: -112.7 ± 0.6° (chloroform).

Reduction of aromatic steroidal ethers with sodium has also been achieved (using iron-free ammonia, tert-butanol, and method B). Aromatic amines undergo analogous transformation to cyclohexenones; primary amines are more susceptible to reduction than the corresponding N-substituted anilines.

Although the related saturated ketones were obtained as major side products under the conditions employed, use of the Wilds-Nelson technique might substantially improve this situation. Phenols, long considered resistant, have been successfully reduced by means of concentrated solutions of lithium in ammonia:

\[
\text{HO} \quad \rightarrow \quad \text{HO}
\]

Competition between directive influences may result when two or more substituents are present. Many examples of the reduction of polysubstituted benzene derivatives may be found in Smith's excellent review (loc. cit., Table 18, p. 262). The usual empirical order of directive priority is carboxy > alkoxy > amino > alkyl.

If this leads to addition at a position bearing an alkoxy or an amino group, fission of that group follows, for example in the reduction of gallic acid trimethyl ether:

![Diagram of reaction]

The monoalkylbenzoic acids present an interesting case which illustrates some of the difficulties which may be encountered. Reduction of 2-methylbenzoic acid with sodium/liquid ammonia/ethanol afforded, in agreement with expectation, 2-methyl-1,4-dihydrobenzoic acid (1); under the same conditions (method B), 4-methylbenzoic acid gave the unconjugated tetrahydro acids 2 and/or 3. On the other hand, treatment of the ethyl ester and amide of 4-methylbenzoic acid with magnesium/liquid ammonia/ethanol afforded the conjugated tetrahydro ester 4 and the normal, 1,4-dihydroamide 5:

![Diagram of reaction]

Modified theories of the Birch reduction have been proposed to account for these results; however, recent studies demonstrate that under conditions chosen to minimize isomerization and over-reduction [namely, lithium metal (4 equivalents only),

short reaction time, and rapid quenching with ammonium chloride| 4-isopropylbenzoic acid is efficiently transformed (Scheme C) to the cis- and trans-1,4-dihydro acids 6 and 7 (1:2). Partial isomerization into the conjugated acid 8 was observed when addition was delayed. Further reduction of the latter provided either a mixture of the tetrahydro acids 9 and 10 or phellandric acid (11), depending on whether or not ammonium chloride was added to the reaction. It appears likely, therefore, that protonation of 4-alkylbenzoic acids is kinetically controlled providing the corresponding 1,4-dihydro derivatives as the primary products:

\[ \text{COOH} \rightarrow \text{COOH} + \text{COOH} \rightarrow \]

\[ \text{COOH} \rightarrow \text{COOH} \rightarrow \text{COOH} \]

\[ \text{COOH} \rightarrow \text{COOH} \rightarrow \text{COOH} \]

\[ \text{COOH} + \text{COOH} \]

\[ \text{COOH} \]

Scheme C

5. Linear Polycyclic Aromatic Derivatives

Although interaction of biphenyl with alkali metals was first described over forty years ago\(^{22}\), accurate structural assignment of the products has only recently been achieved. By using modern techniques of separation (GLC) and analysis (NMR) it has been established\(^{20}\) that the calculated dihydro derivative, 1,4-dihydrobiphenyl, is the initial product, and that rapid protonation is necessary to prevent its isomerization and further reduction. Biphenyl is reduced virtually quantitatively to 1,4-dihydrobiphenyl by lithium/liquid ammonia/ammonium chloride (method C)\(^{22}\).

\[ \text{H}_2\text{CO} \rightarrow \text{OH} \]

\[ \text{1,4-Dihydrobiphenyl}\] Liquid ammonia is distilled under a helium atmosphere into a dry 3-neck round-bottom flask equipped with a Dewar condenser. To this is added with magnetic stirring a solution of biphenyl (770 mg, 5 mmol) in tetrahydrofuran (75 ml), followed by lithium wire (76 mg, 12 g-atom), and 10 min later the color is discharged by addition of excess solid ammonium chloride. Conventional work-up procedures provide essentially pure 1,4-dihydrobiphenyl free of unreacted biphenyl and the 2,5-, 2,3-, and 3,4-dihydro isomers according to NMR data\(^{20}\). Similar reaction (with 2.5 g-atom lithium) quenched after 1 hr with ethanol affords equal proportion of 1,4- and 3,4-dihydrobiphenyl.

\[ \text{p-Terphenyl} \] upon treatment with sodium or calcium in liquid ammonia is transformed, according to Hückel and Bretschneider\(^{24}\), to a 2:1 mixture of a dihydroterphenyl and an unidentified hydrocarbon (m. p. 150-153\(^{3}\)). Catalytic hydrogenation of the dihydro compound afforded 4-cyclohexylbiphenyl, indicating reduction in an outer ring. On the other hand, calculation predicts the 7,10-dihydro structure, so that reinvestigation would appear desirable\(^{45}\).

Reduction of fluorene can be effected with sodium in liquid ammonia. An unstable dihydrofluorene assigned the 3,9a-dihydro structure on the basis of chemical evidence was isolated and further reduced to tetrahydro and hexahydro derivatives\(^{46}\). However, these products have not been adequately characterized, and the 2,4a-dihydro structure would appear more probable by analogy with biphenyl. Substituent effects may, of course, alter this pattern; Birch reduction of 2-hydroxy-7-methoxyfluorene with lithium/liquid ammonia/t-butanol gives the 5,8-dihydro derivative \[ \text{12}\]\(^{47}\):

6. Fused Polycyclic Aromatic Compounds

While comparison data are limited, method C (in which the proton source is withheld until late) appears superior to other techniques in limiting reduction of polycyclic hydrocarbons (naphthalene\(^{48}\), anthracene\(^{14}\), phenanthrene\(^{34,49,50}\), pyrene\(^{1,2,32,51,52}\) ) to a single stage. Naphthalene reacts with sodium in liquid ammonia to give a red complex


which is decomposed by methanol to 1,4-dihydronaphthalene\textsuperscript{44}; with sodium/liquid ammonia/alcohol (method B) at $-33^\circ$, both naphthalene and 1,4-dihydronaphthalene are converted to 1,4,5,8-tetrahydronaphthalene\textsuperscript{53,54}:

$$\text{Na/NH}_3 \rightarrow \begin{array}{c} \text{\textsuperscript{1,4}-dihydronaphthalene} \\ \text{Na/NH}_3/\text{ROH} \end{array}$$

Substituents in the 1-position direct reduction to the adjacent ring if electron-releasing (Scheme D, path a), and to the same ring if electron-withdrawing (path b). Thus, 1-methyl-, 1,2-dimethyl-, and 1,4-dimethyl-naphthalene\textsuperscript{55-57} are reduced to the corresponding 5,8-dihydro derivatives, while 1-naphthoic acid\textsuperscript{60} furnishes 1,4-dihydro-1-naphthoic acid (Table 1). On the other hand, 2-methylnaphthalene\textsuperscript{38}, 2-naphthol\textsuperscript{60}, and 2-naphthoic acid\textsuperscript{68} all undergo metal-ammonia reduction in the substituted ring:

Scheme D
\[ \begin{array}{c} \text{R} \\ \text{b: R = COOH, Si(CH}_3)_2 \end{array} \]

Acenaphthene, which may be regarded as a substituted naphthalene, undergoes reduction by sodium in liquid ammonia to a tetrahydro derivative, presumably the corresponding tetralin\textsuperscript{70}.

Anthracene is transformed to 9,10-dihydroanthracene (13) upon treatment with sodium in liquid ammonia (method C) in the presence of colloidal iron [formed \textit{in situ} from iron(III)-chloride):

$$\text{Anthracene} \rightarrow \begin{array}{c} \text{9,10-dihydroanthracene} \\ \text{Birch reduction} \end{array}$$

\[ \begin{array}{c} \text{13} \\ \text{stable} \\ \text{ROH} \end{array} \]

9.10-Dihydroanthracene\textsuperscript{14}: Lithium wire (87 mg) is added to a solution of anthracene (900 mg) and anhydrous ferric chloride (80 mg) in tetrahydrofuran (75 ml) and ammonia (150 ml). The resulting solution is maintained at reflux for 2 hr, then decomposed by addition of ethanol, then water. The product consists of essentially pure 13; m.p. 108°. It is free of both anthracene and further reduction products according to GLC and NMR analysis.

The 9,10-dianion of anthracene is formed rapidly, and is stable in liquid ammonia. The iron catalyzes consumption of excess alkali metal by reaction with ammonia\textsuperscript{71}, effectively preventing reduction of the hydrocarbon beyond the dihydro stage. A similar inhibition of overreduction may be achieved in the absence of added iron salts by the use of ammonia taken directly from a commercial cylinder. The presence of ferrous metal salts in impure ammonia\textsuperscript{16} may account for the reports of early workers\textsuperscript{70,72} that in the absence of a proton source anthracene is reduced only as far as 13. Further reduction of 13 with lithium in liquid ammonia (method C) is efficiently directed to 1,4,9,10-tetrahydro- or 1,4,5,8,9,10-hexahydroanthracene by suitable adjustment of the lithium ratio\textsuperscript{14}. The hexahydro derivative is also the major product from reduction of anthracene with either sodium/liquid ammonia/alcohol (method B)\textsuperscript{73}, or lithium in methylamine\textsuperscript{74}:

$$\text{13} \rightarrow \begin{array}{c} \text{1,4,9,10-tetrahydroanthracene} \\ \text{1,4,5,8,9,10-hexahydroanthracene} \end{array}$$

Birch reduction of 1,2,3,4-tetrahydroanthracene affords 1,2,3,4,5,8-hexahydroanthracene and 1,2,3,4,5,8,9,10-octahydroanthracene\textsuperscript{75}:

\[ \begin{array}{c} \text{13} \\ \text{stable} \end{array} \]

\[ \begin{array}{c} \text{1,4,9,10-tetrahydroanthracene} \\ \text{1,4,5,8,9,10-hexahydroanthracene} \end{array} \]

\textsuperscript{35} W. Hückel, R. Schwen, Chem. Ber. 89, 150 (1956).
\textsuperscript{36} G. Stork, W. N. White, J. Amer. Chem. Soc. 78, 4604 (1956).
\textsuperscript{39} A. J. Birch, L. Bergmann, Liebigs Ann. Chem. 463, 92 (1928).
\textsuperscript{40} R. G. Harvey, unpublished results.
\textsuperscript{41} G. Krczko, A. A. Rothnack, J. Amer. Chem. Soc. 81, 3658 (1959).
\textsuperscript{42} A. J. Birch, J. Chem. Soc. 1946, 593.
\textsuperscript{44} P. Marck, C. Ivanoff, Tetrahedron Letters 1962, 1139.
\textsuperscript{46} W. Schlenk, L. Bergmann, Liebigs Ann. Chem. 463, 92 (1928).
\textsuperscript{47} W. Hückel, H. Bretschneider, Liebigs Ann. Chem. 540, 157 (1939).
9-Alkyl- and 9,10-dialkylanthracenes, like the parent hydrocarbon, undergo facile reduction in the meso region\textsuperscript{12}. The benzylic positions of 9,10-dihydroanthracene contain two conformationally distinct types of bonds, designated as quasiaxial (a') and quasiequatorial (e')\textsuperscript{76}, which are interconvertible via "boat-to-boat" ring inversion. As a consequence, 9,10-dihydroanthracenes may exist as cis (a', e'e', e') or trans (a', e'e', a') diastereomers. Reduction of 9,10-diethyl-, 9,10-dibutyl-, and 9-ethyl-10-methylandanthracene with lithium/liquid ammonia has been demonstrated\textsuperscript{12} to proceed stereospecifically to provide the corresponding trans-9,10-dialkyl-9,10-dihydroanthracenes (14). On the other hand, reduction of 9,10-dimethylanthracene provides cis- and trans-9,10-dimethyl-9,10-dihydroanthracene in approximately equal proportion:

\[ \text{R'} = \text{R''} = \text{C}_2\text{H}_5, n-\text{C}_2\text{H}_5, \text{CH}_3-\text{C}_2\text{H}_5 \]

R' = CH\textsubscript{3}, R'' = C\textsubscript{2}H\textsubscript{5}

These observations are explicable by a mechanism in which product structure is determined during the final protonation step. In the intermediate monoanion 15a\textsuperscript{75}e, orbital overlap should favor equatorial orientation of R\textsuperscript{2}, and the tendency to minimize steric interaction would require axial orientation of R\textsuperscript{1} for groups larger than methyl:

Protonation of the preferred intermediate 15a from the axial direction results in net trans-reduction. Consistent with these concepts, recent NMR studies\textsuperscript{77} have established preferred axial orientation of alkyl substituents in 9-alkyl-9,10-dihydroanthracenes.

Analogous reductive alkylation of anthracene with lithium in liquid ammonia and alkyl bromides also proceeds with high stereoselectivity\textsuperscript{78}, but provides the corresponding cis-9,10-dialkyl-9,10-dihydroanthracene (16) as the major product (80\%\textsubscript{c} for R = CH\textsubscript{3}, C\textsubscript{2}H\textsubscript{5})\textsuperscript{79}:

\[ \text{Li}/\text{NH}_3/\text{RBr} \rightarrow \]

\[ \text{16} \]

Reductive Ethylation of Anthracene\textsuperscript{78}: To a stirred solution of lithium (1.74 g, 25 mmol) dissolved in liquid ammonia (250 ml) is added a solution of anthracene (1.78 g, 10 mmol) in tetrahydrofuran (75 ml). The resulting deep red solution is maintained at reflux for 1 hr before addition of a solution of ethyl bromide (27 mmol) in tetrahydrofuran (10 ml) from a dropping funnel. The product is isolated by conventional extraction procedures, triturated with ethanol and recrystallized from the same solvent to provide pure 16 (R = C\textsubscript{2}H\textsubscript{5}); m.p. 58–59°.

Minor products of reductive alkylation are the trans isomer, 14 (R\textsuperscript{1} = R\textsuperscript{2} = CH\textsubscript{3}) from reductive methylation, and 9,9,10-trialkyl-9,10-dihydroanthracene (17) from reductive ethylation and isopropylation\textsuperscript{78}. The latter are thought to arise via alkylation of the monoanion (15a\textsuperscript{75}e) from interaction of alkyl lithium reagent formed in situ with the trans isomer. Products of attempted reductive t-butylation are 9-t-butyl-9,10-dihydroanthracene (14\%\textsubscript{c}) and 9,10-dihydroanthracene (68\%\textsubscript{c}). Methyl substituents in or adjacent to the meso region do not noticeably affect either the rate or the course of reaction. Thus, reductive methylation of 9,10-dimethyl- and 1,4-dimethylanthracene furnishes 9,9,10,10-tetramethyl- and cis-1,4,9,10-tetramethyl-9,10-dihydroanthracene (18, 19) respectively:

\[ 17 \]
\[ 18 \]
\[ 19 \]

Benzo-[a]-anthracene\textsuperscript{11}, tetracene\textsuperscript{12}, and dibenzo-[a;b]-anthracene\textsuperscript{11} undergo lithium-ammonia reduction in the manner of anthracene in the meso region. Reductive methylation of these acene hydrocarbons\textsuperscript{19} occurs with similar regiospecificity to furnish the related cis-dialkyldihydro derivatives\textsuperscript{78}. Carcinogenic benzo-[a]-anthracene derivatives (3-methylcholanthrene, 7-methylbenzo-[a]-anthracene, and 7,12-dimethylbenzo-[a]-anthracene) react with lithium in ammonia in the same region; in the case of the

\[ 57 \quad 58 \quad 59 \quad 60 \]
7,12-dimethyl derivative, reduction is trans stereospecific. Stepwise reduction of benzo-[α]-anthracene through the dodecahydro level has recently been described (Scheme E). Accurate structural assignment was complicated by the fact that the number of possible isomeric structures increases exponentially with the extent of reduction. However, the techniques of NMR and mass spectroscopy revealed a regular predictable pattern of reduction and the absence of isomerization or other complications. The positions of the incoming hydrogens were accurately predicted through consideration of the relative stabilities of the intermediate anionic species. The resistance of the B-ring to reduction with lithium-ammonia necessitated employment of the more powerful lithium/ammonia system. Isomerization and multiple-stage reduction by this reagent was avoided by the use of exceptionally brief reaction times (~1 min).

Scheme E

Phenanthrene and its 9-alkyl- and 9,10-dialkyl derivatives are efficiently reduced in the 9,10 position by lithium in ammonia in the presence of colloidal iron. 9,10-Dimethyl- and 9,10-diethylphenanthrene undergo stereospecific cis reduction under these conditions.

9,10-Dihydrophenanthrene is essentially a bridged biphenyl, reduction of which may be expected to afford the isomeric tetrahydrophenanthrene (20) related to 1,4-dihydrobiphenyl. Spectral data (UV, NMR) confirm this structural assignment. However, this second-stage reduction product spontaneously reverts to 9,10-dihydrophenanthrene on standing. The structure of 20 is further confirmed by analogous reductive methylation of 9,10-dihydrophenanthrene in liquid ammonia which provides the monomethyl derivative 21. The latter is also obtained via direct reductive angular methylation of phenanthrene itself. Phenanthrene on treatment with excess sodium under Birch conditions (method B) is converted to the octahydro compound (mainly trans); apparently, the intermediate 20 undergoes facile isomerization and further reduction under these conditions:

<table>
<thead>
<tr>
<th>Naphthalene</th>
<th>Reagent</th>
<th>Method</th>
<th>Yield(%)</th>
<th>Product</th>
<th>Physical Data</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–NH₄Cl</td>
<td>C(B)</td>
<td>71</td>
<td><img src="image2.png" alt="Product" /></td>
<td>bp₁: 110–111 °C; nD₂: 1.5637</td>
<td>55, 56(48)</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–NH₄Cl</td>
<td>C</td>
<td>74</td>
<td><img src="image2.png" alt="Product" /></td>
<td>bp₂: 104–105 °C; nD₂: 1.5568</td>
<td>48</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–NH₄Cl</td>
<td>C</td>
<td>74</td>
<td><img src="image2.png" alt="Product" /></td>
<td>mp: 82 °C</td>
<td>48</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–NH₄Cl</td>
<td>C</td>
<td>58</td>
<td><img src="image2.png" alt="Product" /></td>
<td>mp: 57–58 °C</td>
<td>57</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–NH₄Cl</td>
<td>C</td>
<td>59</td>
<td><img src="image2.png" alt="Product" /></td>
<td>mp: 142–143 °C; nD₂: 1.5640</td>
<td>57</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Li–C₆H₅OH</td>
<td>C</td>
<td>97</td>
<td><img src="image2.png" alt="Product" /></td>
<td>mp: 37–38 °C</td>
<td>59</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–C₅H₅NH₂OH</td>
<td>C</td>
<td>97–99</td>
<td><img src="image2.png" alt="Product" /></td>
<td>mp: 74 °C</td>
<td>59</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–C₅H₅NH₂OH</td>
<td>C</td>
<td>60</td>
<td><img src="image2.png" alt="Product" /></td>
<td>mp: 74 °C</td>
<td>60</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–C₅H₅H₂O</td>
<td>C</td>
<td>60</td>
<td><img src="image2.png" alt="Product" /></td>
<td>mp: 74 °C</td>
<td>60</td>
</tr>
<tr>
<td><img src="image1.png" alt="Naphthalene" /></td>
<td>Na–C₅H₅H₂O</td>
<td>C</td>
<td>5</td>
<td><img src="image2.png" alt="Product" /></td>
<td>mp: 140 °C</td>
<td>65</td>
</tr>
</tbody>
</table>

Table 1: Metal-Ammonia Reduction of Naphthalene Derivatives
Table 1, continued

<table>
<thead>
<tr>
<th>Naphthalene</th>
<th>Reagent</th>
<th>Method</th>
<th>Product</th>
<th>Yield %</th>
<th>Physical Data</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Na—H₂O</td>
<td>C</td>
<td></td>
<td>8</td>
<td>bp₁₂: 140°</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>Na—NH₄Cl</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>Na—NH₄Cl</td>
<td>C</td>
<td></td>
<td>57 + 7</td>
<td></td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>Na—C₂H₅OH</td>
<td>A</td>
<td></td>
<td>81</td>
<td></td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>Na—CH₃OH</td>
<td>B</td>
<td></td>
<td></td>
<td></td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>Na—CH₃OH</td>
<td>A</td>
<td></td>
<td>62</td>
<td></td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>Na—C₂H₅OH</td>
<td>B</td>
<td></td>
<td>63</td>
<td></td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Na—C₂H₅OH</td>
<td>B</td>
<td></td>
<td>74</td>
<td></td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Na—C₂H₅OH</td>
<td>B</td>
<td></td>
<td>75</td>
<td>m.p. 91°</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Li (K)—C₂H₅OH</td>
<td>B</td>
<td></td>
<td>96</td>
<td>m.p. 67–68°</td>
<td>62, 63</td>
</tr>
<tr>
<td></td>
<td>Na—ROH</td>
<td>B (°)</td>
<td></td>
<td>76 (82)</td>
<td>m.p. 66.5–69°</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>Na—C₂H₅OH</td>
<td>B</td>
<td></td>
<td>61</td>
<td></td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>Li—C₂H₅OH</td>
<td>C</td>
<td></td>
<td>61</td>
<td>m.p. 144–145°</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td>Na</td>
<td>C</td>
<td></td>
<td>61</td>
<td>m.p. 75°</td>
<td>60</td>
</tr>
</tbody>
</table>
Reduction of 1,2,3,4-tetrahydrophenanthrene with sodium/liquid ammonia/ethanol takes place in the outer ring to give 1,2,3,4,5,8-hexahydrophenanthrene\(^8\) (23):

\[
\begin{array}{c}
\text{23}
\end{array}
\]

Preferential reduction of the central ring of 1,2,3,4-tetrahydrophenanthrene is possible after its activation by suitable substituents. Thus, 4-oxo-1,2,3,4-tetrahydrophenanthrene (24) is transformed by sodium/liquid ammonia/ethanol to its dihydro derivative 25 in which the double bond has isomerized into conjugation\(^8\):

\[
\begin{array}{c}
\text{24} \rightarrow \text{25}
\end{array}
\]

The substituted 17-oxo-15,16-dihydro-17H-cyclopenta[a]-phenanthrene 26 undergoes reduction contrary to phenanthrene to give the novel ring C-aromatic bisnorsteroid 27 upon treatment with excess lithium and t-butanol in liquid ammonia\(^8\):

\[
\begin{array}{c}
\text{26} \rightarrow \text{27}
\end{array}
\]

Pyrène interacts with alkali metals readily; however, the structure of the dihydropyrene formed on protonation is the subject of conflicting claims, unresolved at present.

An early report\(^8\) suggested the 1,8- or the 2,7-dihydro structure for the diacid obtained on carboxylation of the lithium pyrene adduct in ether.

\[
\begin{array}{c}
\text{28}
\end{array}
\]

However, 4,5-dihydropyrene (12\%) was recovered\(^11\) from the reaction of pyrene with sodium/liquid ammonia/ammonium

---


\(^10\) P. Lebeau, M. Picot, Compt. Rend. 159, 70 (1914).

\(^11\) Reaction of alkali metals with ammonia proceeds only to the extent of \(\sim 0.1\%\) in 24 hr in the absence of a catalyst; J. F. Denis, G. Le Poutre, J. Amer. Chem. Soc. 76, 3369 (1954).

\(^12\) H. F. Miller, G. B. Bachman, J. Amer. Chem. Soc. 57, 768 (1935).


Fluoranthene, the only non-alternant hydrocarbon to be investigated, is transformed by sodium/liquid ammonia/methanol (method C) to dimeric and polymeric products. The dimeric product, assigned the structure 1,2,2',3,3',10b-hexahydro-1,2'-bifluoranthyl,

![Chemical structure diagram]

is presumed to arise via isomerization of the first product of reduction, namely, 3,10b-dihydrofluoranthene (predicted by MO theory), to the conjugated 2,3-dihydro isomer, followed by Michael addition to this of its conjugate anion.

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