

A Comparison of Methods Using Lithium/Amine and Birch Reduction Systems

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Treatment of unsaturated organic compounds with sodium and alcohols in ammonia (the Birch reduction) or with lithium in low molecular weight amines (the Benkeser reduction) generally affords partially or fully reduced products, respectively, though reductive cleavages sometimes also occur. This review discusses the similarities and differences between the Birch and Benkeser methods as illustrated by their application to aromatics, heteroaromatics, alkynes, alkenes, ethers, alcohols, amines, carboxylic acids, ketones, heterocycles, and other compounds. In general, the Benkeser reduction is more powerful but less selective than the Birch reduction; however, the selectivity of the former method is increased by a judicious choice of solvents.

1. Reduction of Aromatic Hydrocarbons
2. Reduction of Alkynes
3. Reduction of Alkenes
4. Reduction of Unsaturated Ethers
5. Reduction of Acetals, Ketals and Related Compounds
6. Reduction of Unsaturated Alcohols
7. Reduction of Unsaturated Amines

8. Reduction of Aromatic Nitro Compounds
9. Reduction of Carboxylic Acids and their Derivatives
10. Reduction of Ketones and their Derivatives
11. Reduction of Epoxides
12. Reduction of Five- and Six-Membered Heterocycles
13. Reduction of Miscellaneous Sulfur Compounds

Die Umsetzung ungesättigter organischer Verbindungen mit Natrium und Alkoholen in Ammoniak (Birch-Reduktion) oder mit Lithium in niedermolekularen Aminen (Benkeser-Reduktion) liefert im allgemeinen gesättigte bzw. teilweise gesättigte Verbindungen neben reduktiver Spaltung. Dieser Übersichtsartikel beschreibt anhand der Reduktionen von Aromaten, Heteroaromaten, Alkynen, Alkenen und ungesättigten Äther-Alkoholen, Aminen, Carbonsäuren, Ketonen und anderen Verbindungen Ähnlichkeiten und Unterschiede zwischen der Birch- und Benkeser-Methode. Die Benkeser-Reduktion ist im allgemeinen wirksamer, jedoch unselektiver als die Birch-Reduktion; die Selektivität der erstgenannten Methode ist lösungsmittelabhängig.

Solutions of alkali and alkaline earth metals in anhydrous ammonia and in low molecular weight amines have long been known to constitute powerful reducing systems capable of converting unsaturated systems to more saturated ones. Such reductions are extremely useful synthetically and are usually effected by the following most common combination of reagents:

- Sodium/ammonia/alcohol: the Birch reduction.
- Lithium/methyl-, ethyl-, or *n*-propylamines or ethylenediamine: the Benkeser reduction.
- Sodium or lithium/ammonia.
- Calcium/ammonia.

This review will include a comparison of the products obtained on treatment of various unsaturated systems with sodium/alcohol/ammonia (the Birch reduction) with those realized with lithium-alkyl-

amines. By definition, a Birch reduction is one in which the metal, substrate, alcohol, and ammonia are present at the onset of the reaction. Thus, reductions effected by alkali metals in ammonia wherein the addition of alcohol is delayed will usually not be considered. Reductions effected by such metals in ammonia alone in the absence of alcoholic co-reagents will generally not be included since these reducing media fail to hydrogenate most aromatic systems and since several excellent reviews on these reagents are already available¹⁻⁵. The calcium/ammonia system will also be omitted since this reducing agent has not been as extensively studied as the others and since the resultant reaction products are usually similar to those obtained with lithium/amines.

¹ A. J. BIRCH, *Quart. Rev. (London)* **4**, 69 (1950).

² A. J. BIRCH, H. SMITH, *Quart. Rev. (London)* **12**, 17 (1958).

³ G. W. WATT, *Chem. Rev.* **46**, 317 (1950).

⁴ H. SMITH, *Organic Reactions in Liquid Ammonia. Chemistry in Non-aqueous Ionizing Solvents*, Vol. 1, Part 2, Wiley, New York, 1963.

⁵ M. SMITH, *Reductions*, edited by R. L. Augustine, Marcel Dekker, 1968, p. 95.

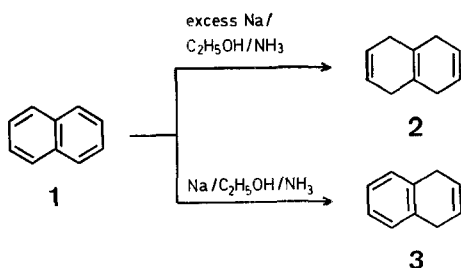
1. Reduction of Aromatic Hydrocarbons

Although dissolving metal reductions are among the oldest reactions known, it was not recognized until 1937 that monobenzenoid systems like alkylbenzenes could be so reduced. At that time, Wooster and Godfrey reported⁶ that toluene was converted to olefins by sodium or potassium and water in ammonia. That no reaction occurred in the absence of water supported the hypothesis that the reduction was effected by the combination of reagents rather than by the metal alone. This type of reduction was not systematically investigated until Birch began his studies in 1942.

Similarly, Ziegler and co-workers⁷ reported in 1934 that naphthalene was converted to 1,4-dihydronaphthalene, and certain diolefins and styrene were reduced to dihydro derivatives, by means of sodium in diethylamine, aniline, *N*-ethylaniline, and dicyclohexylamine. Since naphthalene could be reduced more conveniently by sodium in ammonia to give the same dihydronaphthalene⁸ or even reduced further to tetralin by excess sodium³, Ziegler's method offered no synthetic advantages over previous ones. Thus, the metal/amine system lay dormant until Benkeser reopened the investigation in 1952.

1.1. Reduction of Naphthalene and Tetralin

Naphthalene (**1**) has been extensively studied with regard to its reduction using the Birch and Benkeser methods. For example, treatment of **1** with an excess of sodium in ethanol, ether, and ammonia affords 1,4,5,8-tetrahydronaphthalene (**2**) in good yield^{10,11}. When the reaction is carried out with a deficiency of metal, though, less reduction occurs affording 1,4-dihydronaphthalene (**3**)¹¹. Incidentally, ether is used in these systems to increase the solubility of the hydrocarbon in the ammonia media.



⁶ C. B. WOOSTER, K. L. GODFREY, *J. Amer. Chem. Soc.* **59**, 596 (1937).

⁷ K. ZIEGLER, L. JAKOB, H. WOLLTHAN, A. WENZ, *Liebigs Ann. Chem.* **511**, 64 (1934).

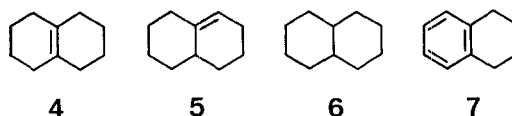
⁸ W. HÜCKEL, H. BRETSCHNEIDER, *Liebigs Ann. Chem.* **540**, 157 (1939).

⁹ C. B. WOOSTER, F. B. SMITH, *J. Amer. Chem. Soc.* **53**, 179 (1931).

¹⁰ A. J. BIRCH, A. R. MURRAY, H. SMITH, *J. Chem. Soc.* **1951**, 1945.

Reduction of Naphthalene to 1,4,5,8-Tetrahydronaphthalene (2)¹⁰: Naphthalene (10 g) in ethanol (40 ml) and diethyl ether (50 ml) is given rapidly to liquid ammonia (250 ml) with rapid stirring to give a fine precipitate. Sodium (15 g) is added in small pieces, the reaction being at first very vigorous. Water (200 ml) is then added, the solid is collected by filtration, well washed with water, dried and crystallized from methanol. The 1,4,5,8-tetrahydronaphthalene so obtained forms large plates (6.2 g); m. p. 42°.

As will be noted throughout this review, reductions effected by lithium/amines invariably give more extensively reduced products than the Birch method. Thus, treatment of **1** with lithium in ethylamine gives a 50:50 mixture of $\Delta^9(10)$ -(**4**) and $\Delta^1(9)$ -octalin (**5**)¹². Thus, the Benkeser reduction is more powerful, but less selective than the Birch reduction. The selectivity of the former method can, however, be dramatically increased by employing solvents consisting of primary and secondary amines. When naphthalene is so reduced by lithium in ethylamine/dimethylamine, octalins **4** and **5** are again obtained, but the isomer distribution consists of 80% of **4** and only 20% of **5**¹³. In a mixture of such amines, the amount of the more thermodynamically stable olefin always increases at the expense of the less stable ones.



Naphthalene has also been reduced by the even more powerful lithium/ethylenediamine system to afford the completely saturated decahydronaphthalene (**6**) in high yield¹⁴. A similar result is obtained with lithium in the lower molecular weight primary amines by employing a considerably higher concentration of this metal¹⁵.

One particularly interesting recent report concerns the reductive-amination of naphthalene effected by the interaction of this hydrocarbon with sodium in various primary and secondary amines¹⁶. These reactions give a mixture of products including tetralin (**7**), 1,4-dihydronaphthalene (**3**) and its 1,2-dihydro isomer **8**, 2-aminotetralins (**9**), and dimers **10** and **11**. Although **3** and **8** are generally formed in low yield, compounds **9**, **10**, and **11** are obtained in fair to good yields. Some of the amines investigated which give rise to **9** are cyclohexylamine, *n*-hexylamine, ethylamine, pyrrolidine, hexamethyleneimine, and morpholine. The aminotetralins (**9**) appear to arise via a conjugate addition of the sodium salts of the amines to 1,2-dihydro derivative **8**; the reactions have been extended to various alkylnaphthalenes.

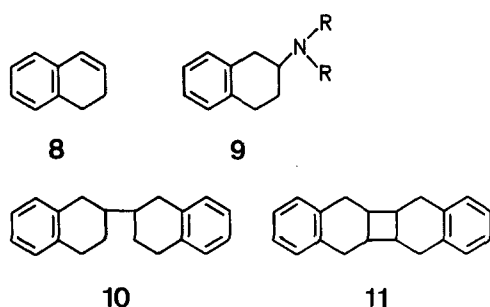
¹¹ W. HÜCKEL, H. SCHLEE, *Chem. Ber.* **88**, 346 (1955).

¹² R. A. BENKESER, R. E. ROBINSON, D. M. SAUVE, O. H. THOMAS, *J. Amer. Chem. Soc.* **77**, 3230 (1955).

¹³ R. A. BENKESER, E. M. KAISER, *J. Org. Chem.* **29**, 955 (1964).

¹⁴ J. D. BROOKS, R. A. DURIE, H. SILBERMAN, *Aust. J. Chem.* **17**, 55 (1964).

Parenthetically, a dimer like **10** is also observed on treatment of **1** with excess sodium in ethylamine but no 2-ethylaminotetralin has been reported¹⁷.



Reductive Amination of Naphthalene with Sodium and Hexamethylenimine¹⁶:

To naphthalene (6.4 g; 0.05 mol) and dispersed sodium (4.6 g; 0.02 g atom) is added hexamethylenimine (100 ml); a red color usually develops within 20 min. The mixture is stirred at 25° for 12 hr, and unreacted sodium which has agglomerated is removed. The reaction mixture is poured cautiously onto ice water whereupon the red color disappears. The product mixture is acidified with 10% aqueous hydrochloric acid. After the hydrocarbons have been removed by extraction with ether, the aqueous layer is made alkaline with dilute sodium hydroxide and excess hexamethylenimine is removed by steam distillation. The residue from the steam distillation is extracted with ether. Drying (Na₂SO₄) gives 6.2 g (55%) of crude N(1,2,3,4-tetrahydro-2-naphthyl)perhydroazepine (**9**); distillation yields a colorless oil (28% yield); b. p. 134–136°/0.8 mm.

Reduction of tetralin (**7**) by the Birch and Benkeser methods is similar to that of naphthalene. Thus, treatment of **7** with sodium/methanol/ammonia gives 1,2,3,4,5,8-hexahydronaphthalene (**12**)¹⁸, while the use of lithium/ethylamine gives a mixture of $\Delta^{9(10)}$ -(**4**) and $\Delta^{1(9)}$ -octalin (**5**)¹².

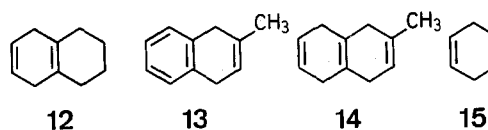
Reduction of Tetralin (**7**) to Afford $\Delta^{9(10)}$ - and $\Delta^{1(9)}$ -Octalins^{22b}:

To tetralin (0.1 mol) in ethylamine (300 ml) and dimethylamine (200 ml) is added in portions 0.45 g atom of lithium wire cut into small pieces. After 13.5 hr, the amines are allowed to evaporate. The flask is placed in an ice-bath and the residue is decomposed by the dropwise addition of water. The organic products are extracted by several portions of ether, the combined extracts are dried (CaSO₄), and the solution is concentrated. Distillation at 72–78°/14 mm gives a mixture of products in 66% yield which consist of $\Delta^{9(10)}$ -octalin (**4**), $\Delta^{1(9)}$ -octalin (**5**), and decalin in yields of 73%, 24%, and 3%, respectively.

Tetralin has also been reduced by electrocatalytic methods in ethylenediamine¹⁹ and in hexamethylphosphortriamide (HMPT)–ethanol²⁰ using lithium chloride as the electrolyte. In such electrolyses, it appears that the alkali metal cation is converted to alkali metal which is the actual reducing agent^{19, 21, 22a}. Such electrolyses in the former solvent give mixtures of hexahydro- and octahydronaphthalenes while those in the latter solvent afford very low conversions to decahydronaphthalene.

Incidentally, 2-methylnaphthalene has been reduced by sodium/methanol/ammonia to give 1,4-dihydro derivative **13** by using two equivalents of the metal; similar use of excess sodium, however, affords 1,4,5,8-

tetrahydro derivative **14**²³. 2-Methylnaphthalene appears not to have been reduced by the lithium/amine method.



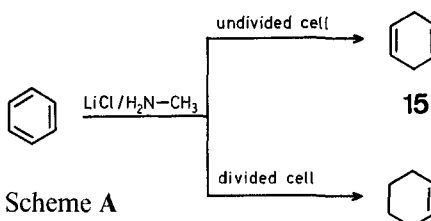
1.2. Reduction of Benzene

Benzene has been reduced to cyclohexadienes, cyclohexene and cyclohexane depending upon the reduction conditions. Thus, treatment of this hydrocarbon with even an excess of sodium in methanol and ammonia affords 1,4-cyclohexadiene (**15**) in good yield²⁴; use of ammonium chloride²⁴ or water²⁵ instead of methanol or other alcohols gives poorer yields of **15**.

In contrast, reduction of benzene by lithium/ethylamine affords cyclohexene in good yield together with some cyclohexane¹². This result illustrates the importance of carefully controlling the amount of lithium employed in the Benkeser reductions since complete hydrogenation of aromatic systems occurs if too much metal is used. This is particularly the case with the even more potent lithium/ethylene-diamine system where, for example, the reduction of benzene gives a mixture of cyclohexene and cyclohexane²⁶.

One confusing reduction of benzene has been reported²⁷ in which the hydrocarbon is reduced by a large excess of sodium and water in ammonia at 0° under pressure to give cyclohexene in good yield.

Benzene has also been reduced electrocatalytically in methylamine using lithium chloride as the electrolyte²². Two different cell designs have been employed: 1) an undivided cell consisting of a three-necked flask holding the two electrodes without a divider between them, and 2) a divided cell in which the electrodes are separated, usually by asbestos. Interestingly, electrolyses of identical solutions with the same amount of current in the two different cells gives quite different products. Thus, the undivided cell reduction of benzene affords **15** while the divided cell reaction of this compound gives cyclohexene (Scheme A). Such results have been ascribed to the fact that in the divided cell, a by-product in the catholyte, lithium dimethylamide, causes isomeriza-



Scheme A

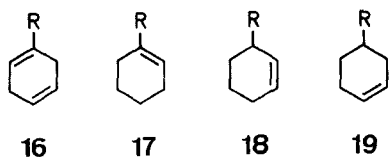
tion of unconjugated dienes like **15** to conjugated dienes which then readily undergo further reduction

to monoolefins. An anolyte product, methylamine hydrochloride, is prevented by the divider from neutralizing the lithium methylamide. On the other hand, in the undivided cell, the amine hydrochloride and the alkylamide are free to interact in a neutralization reaction. Thus, unconjugated dienes like **15** are not isomerized and the reductions stop cleanly at the Birch-type product.

More recently²⁸, benzene has been electrocatalytically reduced in ethanol/HMPT using lithium chloride as the electrolyte. This method is, however, not synthetically useful since the electrolysis was discontinued after only 15% of the benzene had been reduced, and the products consisted of a mixture of **15**, cyclohexene, and cyclohexane.

1.3. Reduction of Monoalkylbenzenes

Reduction of monoalkylbenzenes by the Birch procedure gives 2,5-dihydro-1-alkylbenzenes (**16**) while the Benkeser method gives various amounts of monoolefins **17**, **18** and **19** often accompanied by alkylcyclohexanes. When Benkeser reductions of such aromatic compounds are performed in mixed primary/secondary amine solvents, the amount of **17** always increases at the expense of **18** and **19**.



1.3.1. Toluene

Toluene is reduced by lithium in ammonia in the presence of various proton donors to give **16** ($R = \text{CH}_3$)²⁵. The yield of **16** ranges from only 2% when ammonium chloride is the acid to 88% with ethanol as the proton donor. Earlier mention was made of the sodium or potassium/water/ammonia reduction of this compound⁶.

The results obtained when toluene is reduced by lithium in amines are presented in Table 1. This table shows that the amount of 1-methylcyclohexene (**17**, $R = \text{CH}_3$) increases not only as the solvent is changed from methyl- to ethyl- to *n*-propylamine, but also as the amounts of secondary amine co-solvents are increased.

Several other reductions of toluene deserve brief mention. Thus, electrocatalytic reduction of this compound in methylamine with lithium chloride electrolyte gives 2,5-dihydrotoluene (**16**, $R = \text{CH}_3$) in 95% yield in the undivided cell and methylcyclohexenes in 83% yield in the divided cell; the latter isomer distribution consisted of 53% of 1- and 47% of 3- and 4-methylcyclohexenes, respectively²². These same monoolefins have been obtained in the sodium/water/ammonia reduction of toluene at 0° under pressure²⁷.

Table 1. Lithium/Amine Reductions of Toluene

Solvent	Ratio of isomers (%)		Ref.
$\text{CH}_3-\text{NH}_2^a$	59	41	29
$\text{C}_2\text{H}_5-\text{NH}_2^a$	61	39	30
$n\text{-C}_3\text{H}_7-\text{NH}_2^a$	75	25	30
$\text{CH}_3-\text{NH}_2/(\text{CH}_3)_2\text{NH}(1/1)^b$	82	18	29
(1/2) ^b	69	30	30
(1/4) ^b	76	24	30

^a Reduction at -7° .

^b Volume to volume ratio.

1.3.2. Ethylbenzene

Ethylbenzene reductions by both the Birch and the Benkeser methods are similar to those realized with toluene. Thus, reduction of this compound by lithium/ethanol/ammonia²⁵ or by sodium/ethanol/ammonia³¹ gives the expected 2,5-dihydroethylbenzene (**16**, $R = \text{C}_2\text{H}_5$) in nearly quantitative yield. The potency of the lithium/amine reductions is reduced but their selectivity increased by the presence of alcohol. Using this method, ethylbenzene is likewise converted to (**16**, $R = \text{C}_2\text{H}_5$) in excellent yield.

Lithium in methylamine converts ethylbenzene to 1-ethylcyclohexene (60–62%), 3- and 4-ethylcyclohexene (30–38%), and ethylcyclohexane (0–10%) by using six or four equivalents of lithium, respectively³². Electrocatalytically, ethylbenzene is converted to its 2,5-dihydro derivative (**16**, $R = \text{C}_2\text{H}_5$) in 96% yield in the undivided cell, and to monoolefins in 89% yield in the divided cell²². Interestingly, reduction of ethylbenzene in the undivided cell in the presence of preformed lithium methylamide gives only monoolefins; dihydro products are absent.

1.3.3. Cumene

Cumene has been converted to 2,5-dihydro-*i*-propylbenzene (**16**, $R = i\text{-C}_3\text{H}_7$) in nearly quantitative yield by sodium/ethanol/ammonia and by lithium/*i*-propyl alcohol/methylamine³¹, and in fair yield by lithium/ethanol/ammonia²⁵.

Similar reductions effected by lithium in various amines in the absence of alcohols lead to isomeric *i*-propylcyclohexenes. The results, listed in Table 2, again indicate that the amount of the more thermodynamically stable 1-olefin increases with in-




¹⁵ L. D. MELIKADZE, T. A. ELIAVA, G. D. BABRATISHVILI, Soobscheniya Akad. Nauk Gruzin S.S.R. **23**, 657 (1959); C. A. **54**, 14659 (1960).

creasing bulk of the primary amine and with increasing amounts of secondary amine co-solvents. However, the extent of reduction is less in *n*-propylamine than in ethylamine. It should be noted in the table that Benkeser reductions fail in pure or nearly pure secondary amine solvents; furthermore, tertiary amine co-solvents do not affect the relative yields of monoolefins. The authors³⁰ suggest that the primary amine of choice is ethylamine since it results in more selectivity than methylamine but yet affords higher conversions to olefins than *n*-propylamine.

1.3.4. *t*-Butylbenzene

Birch-type reductions of *t*-butylbenzene have been achieved by several combinations of reagents. Thus, 2,5-dihydro-*t*-butylbenzene (**16**, R = *t*-C₄H₉) has been obtained in 86% yield with sodium/ethanol/ammonia, in 79% yield with lithium/*i*-propyl alcohol/methylamine³¹, in 37% yield with lithium/ethanol/ammonia, and in 61% yield with lithium/*t*-butyl alcohol/ammonia²⁵. Finally, an undivided-cell electrolysis of *t*-butylbenzene in methylamine with lithium chloride affords the same product in 75% yield²².

Table 2. Lithium/Amine Reduction of Cumene

Solvent	Ratio of isomers (%)		Ref.
		 + 	
CH ₃ -NH ₂ ^a	47	53	30
C ₂ H ₅ -NH ₂ ^a	58	42	30
<i>n</i> -C ₃ H ₇ -NH ₂ ^a	73	27	30
H ₂ N-CH ₂ -CH ₂ -NH ₂	76 ^b	19 ^b	29
CH ₃ -NH ₂ /(CH ₃) ₂ NH (3/2) ^c	55	45	30
(1/1) ^c	68	32	30
(1/4) ^c	77	23	30
(1/9.3) ^c	82	18	30
(1/9.6) ^c	0 ^d	0 ^d	30
(CH ₃) ₂ NH	0 ^c	0 ^c	30
CH ₃ -NH ₂ / <i>i</i> -C ₃ H ₇ -NH ₂ (1/1) ^c	65	19	29
CH ₃ -NH ₂ /morpholine (1/4) ^c	88	12	29
H ₂ N-CH ₂ -CH ₂ -NH ₂ /morpholine (1/4) ^c	87	13	29
C ₂ H ₅ -NH ₂ /(CH ₃) ₂ NH (~1/1) ^c	85	15	29

^a Reduction at -7°.

^b 5% Yield of *i*-propylcyclohexane as by-product.

^c Volume to volume ratio.

^d Only dihydroaromatics and cumene.

^e No reduction products.

Undivided and divided cell electrolyses of cumene with lithium chloride in methylamine give **16** (R = *i*-C₃H₇) and monoolefins in 81% yields, respectively²². Since it has been shown earlier that 2,5-dihydro-*i*-propylbenzene (**16**, R = *i*-C₃H₇) is isomerized to a mixture of conjugated isomers by lithium methylamide in methylamine³¹, an undivided cell electrolysis of this unconjugated isomer is interesting. Thus, its electrolysis with lithium chloride in methylamine in the presence of excess preformed lithium methylamide yields only divided cell products, i.e. monoolefins. This result constitutes further evidence that lithium methylamide is absent in normal undivided cell electrolyses.

Benkeser-type reductions of *t*-butylbenzene have been achieved by a variety of lithium-amine reagents; the results are listed in Table 3. Isomeric *t*-butylcyclohexenes are also obtained by divided cell electrolysis of the parent hydrocarbon in methylamine²².

²⁰ H. W. STERNBERG, R. E. MARKBY, I. WENDER, D. M. MOHILNER, *J. Amer. Chem. Soc.* **89**, 186 (1967).

²¹ A. J. BIRCH, *Nature* **158**, 60 (1946).

^{22a} R. A. BENKESER, E. M. KAISER, R. F. LAMBERT, *J. Amer. Chem. Soc.* **86**, 5272 (1964).

^{22b} E. M. KAISER, Ph. D. Thesis, 1964.

²³ W. HÜCKEL, R. CRAMER, S. LAUFEN, *Liebigs Ann. Chem.* **630**, 89 (1960).

²⁴ W. HÜCKEL, U. WÖRFFEL, *Chem. Ber.* **88**, 338 (1955).

²⁵ A. P. KRAPCHO, A. A. BOTHNER-BY, *J. Amer. Chem. Soc.* **81**, 3658 (1959).

²⁶ L. REGGEL, R. A. FRIEDEL, I. WENDER, *J. Org. Chem.* **22**, 891 (1957).

²⁷ Brit. Patent 1025426 (1964), Chiyoda Chemical Engineering and Construction Co., Ltd.; *C. A.* **64**, 19446 (1966).

²⁸ H. W. STERNBERG, R. E. MARKBY, I. WENDER, D. M. MOHILNER, *J. Amer. Chem. Soc.* **91**, 4191 (1969).

²⁹ R. A. BENKESER, R. K. AGNIHOTRI, M. L. BURROUS, *Tetrahedron Lett.* **1960**, 1.

³⁰ R. A. BENKESER, R. K. AGNIHOTRI, M. L. BURROUS, E. M. KAISER, J. M. MALLAN, P. W. RYAN, *J. Org. Chem.* **29**, 1313 (1964).

³¹ R. A. BENKESER, M. L. BURROUS, J. J. HAZDRA, E. M. KAISER, *J. Org. Chem.* **28**, 1094 (1963).






¹⁶ E. J. EISENBRAUN, R. C. BANSAL, D. V. HERTZLER, W. P. DUNCAN, P. W. K. FLANAGAN, M. C. HAMMING, *J. Org. Chem.* **35**, 1265 (1970).

¹⁷ L. REGGEL, H. W. STERNBERG, I. WENDER, *Nature* **190**, 81 (1961).

¹⁸ W. HÜCKEL, U. WÖRFFEL, *Chem. Ber.* **89**, 2098 (1956).

¹⁹ H. W. STERNBERG, R. MARKLEY, I. WENDER, *J. Electrochem. Soc.* **110**, 425 (1963).

Table 3. Lithium/Amine Reductions of *t*-Butylbenzene

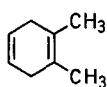
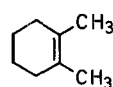
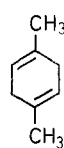
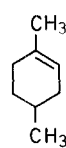
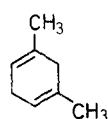
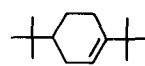
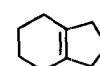
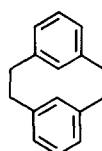
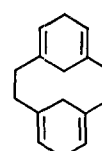
Solvent	Ratio of isomers (%)		Ref.
		 + 	
CH ₃ -NH ₂ ^a	42	58	30
C ₂ H ₅ -NH ₂ ^a	56	44	30
<i>n</i> -C ₃ H ₇ -NH ₂ ^a	77	23	30
H ₂ N-CH ₂ -CH ₂ -NH ₂	70	30	29
C ₂ H ₅ -NH ₂ /(CH ₃) ₂ NH ^b	86	14	29
H ₂ N-CH ₂ -CH ₂ -NH ₂ /  ^c	86	14	29
H ₂ N-CH ₂ -CH ₂ -NH ₂ /  ^d	86	14	30

^a Reduction at -7°.^c Volume to volume ratio 2:3.^b Volume to volume ratio ~1:1.^d Volume to volume ratio 1:2.**Electrocatalytic Reduction of *t*-Butylbenzene in an Undivided Cell^{22b}:**

A 1-liter three necked flask fitted with a dry-ice condenser in the middle neck and two 2 × 5 cm platinum electrodes in the outer necks, is charged with *t*-butylbenzene (13.4 g; 0.1 mol) lithium chloride (10.2 g; 0.24 mol) absolute ethanol (9.2 g; 0.2 mol) and methylamine (500 ml). Current is then passed through the mixture for 5.2 hr (1.75 A, 32 550 Cb). The solvent is allowed to evaporate and the product is extracted with ether; the extracts are washed with water, dried (CaSO₄), and concentrated. The residue is distilled to give 10.6 g of product; b.p. 167-172°. Analysis by glc (14 ft β,β'-oxydipropionitrile at 80°) indicates a mixture of 1-*t*-butylcyclohexene (12.1%), 3-*t*-butylcyclohexene (1.1%), 2,3-dihydro-*t*-butylbenzene (10.0%), 2,5-dihydro-*t*-butylbenzene (73.5%), and *t*-butylbenzene (3.3%).

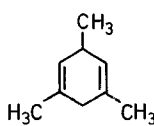
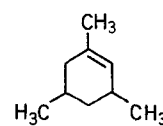
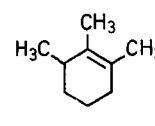
1.4. Reduction of Di- and Trialkylbenzenes

Two isomeric xylenes have been converted to dihydro and tetrahydro derivatives by Birch and Benkeser reductions, respectively. Thus, treatment of *o*-xylene with sodium/methanol/ammonia gives 1,2-dimethyl-1,4-cyclohexadiene (**20**) in good yield^{24,33}. On the other hand, reduction of this hydrocarbon with lithium in amines affords 1,2-dimethyl-1-cyclohexene (**21**)³⁴. Similarly, reduction of *p*-xylene with lithium/ethanol/ammonia gives 1,4-cyclohexadiene²⁵ **22** while lithium in low molecular weight amines yields 1,4-dimethyl-1-cyclohexene (**23**)³⁴. Although *m*-xylene appears not to have been reduced by lithium/amines, it has been converted to 1,5-dimethyl-1,4-cyclohexadiene (**24**) by lithium/ethanol/ammonia²⁵.

**20****21****22****23****24****25****26****27****28****29**

Certain other dialkylbenzenes have been likewise reduced. For example, *p*-di-*t*-butylbenzene has been converted to 1,4-di-*t*-butyl-1-cyclohexene (**25**) by lithium in ethylenediamine³⁵, but no reduction is realized with the less potent lithium/ethanol/ammonia system²⁵. Indane has been converted to 4,7-dihydroindane (**26**) by sodium/methanol/ammonia³⁶, and to 4,5,6,7-tetrahydroindane (**27**) by lithium in ethylamine³⁷. A particularly interesting Birch reduction has been carried out with paracyclophane **28** using sodium/ethanol/ammonia to give dihydro derivative **29**³⁸.

With regard to trialkylbenzenes, mesitylene has been converted in good yield to 1,3,5-trimethyl-1,4-cyclohexadiene (**30**) with lithium/ethanol/ammonia²⁵, and to 1,3,5-trimethyl-1-cyclohexene (**31**) using lithium in ethylenediamine¹⁴. The isomeric 1,2,3-trimethylbenzene has been reduced to 1,2,3-trimethyl-1-cyclohexene (**32**) by lithium/ethylenediamine¹⁴.

**30****31****32**

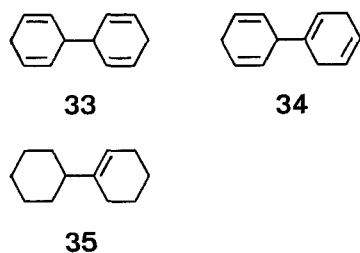
³² R. A. BENKESER, J. J. HAZDRA, R. F. LAMBERT, P. W. RYAN, *J. Org. Chem.* **24**, 854 (1959).

³³ W. HÜCKEL, S. GUPTA, M. WARTINI, *Chem. Ber.* **99**, 1388 (1966).

³⁴ R. K. AGNIHOTRI, *Diss. Abstr.* **24**, 4986 (1964).

1.5. Reduction of Miscellaneous Aromatic Hydrocarbons

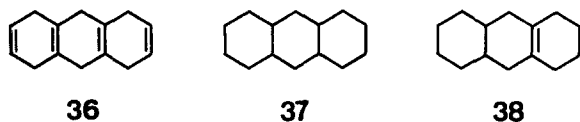
Biphenyl has been reduced to a tetrahydro derivative (**33** or **34**) by sodium and ethanol in liquid ammonia³⁹. More thorough reduction of this compound has been realized with lithium in methylamine³⁰, in methylamine/morpholine³⁰, and in ethylenediamine¹⁴ to give 1-cyclohexylcyclohexene (**35**) in yields of 49%, 92% and 90%, respectively.



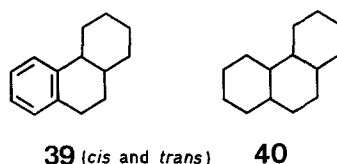
General Procedure for the Reduction of Aromatic Hydrocarbons by Lithium in Ethylenediamine¹⁴:

The hydrocarbon to be reduced is dissolved or suspended in 10–20 times its weight of ethylenediamine and the mixture is heated to 90–100° and stirred under nitrogen. Lithium (100% more than that theoretically required for complete reduction) is added in small pieces over 1.5–2.0 hr. A persistent blue color usually appears towards the end of the addition; afterwards the heating is continued for 1 hr. The reaction mixture is cooled somewhat, then poured onto ice and acidified with concentrated hydrochloric acid. In some cases, alcohol, then water and acid are added dropwise under nitrogen with external ice-cooling.

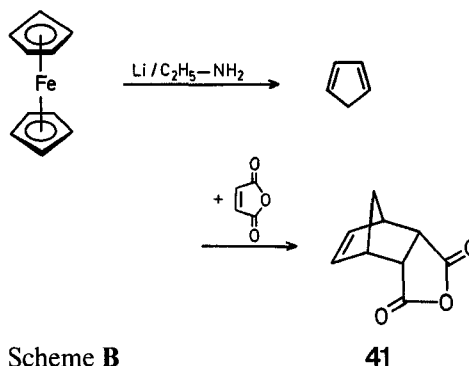
Reduction of anthracene by sodium/ethanol/ammonia affords 1,4,5,8,9,10-hexahydroanthracene (**36**)⁴⁰. Compound **36** is also obtained by the lithium/ethanol/ammonia reduction of 9,10-dihydroanthracene⁴¹. The parent anthracene has been reduced by excess lithium in low molecular weight amines to give the fully hydrogenated perhydroanthracene (**37**)¹⁵. With lithium in ethylenediamine an unspecified mixture of dodecahydro- and tetradeca-hydroanthracene is obtained²⁶. Dodecahydroanthracene is presumed to have structure **38** though the latter has not yet been completely elucidated.



Similarly, phenanthrene has been reduced to a mixture of *cis*- and *trans*-1,2,3,4,9,10,11,12-octahydrophenanthrene (**39**) by sodium/ethanol/ammonia in good yield⁴². More extensive reduction of the phenanthrene nucleus has been achieved by using lithium in low molecular weight amines to give perhydrophenanthrene¹⁵ (**40**), and with lithium in ethylenediamine to afford decahydro- and dodecahydrophenanthrenes^{14,26}.



One additional lithium/amine reduction of an aromatic system, namely that of ferrocene, deserves mention. Thus, treatment of ferrocene with lithium in ethylamine rapidly gives cyclopentadiene and atomic iron (Scheme B)⁴³. The cyclopentadiene was either isolated in 53% yield or was added to maleic anhydride in a Diels-Alder reaction to afford bicyclic **41** in 71% yield. A more recent report⁴⁴ involved similar reductive cleavages of ferrocene and its 1,1'-dimethyl-, 1,1'-diethyl-, and 1,1'-dibenzyl derivatives using lithium in *n*-propylamine.



Scheme B

2. Reduction of Alkynes

In general, alkynes are rapidly reduced to *trans*-olefins by sodium/ammonia^{45,46} and lithium/amine⁴⁷ reagents without the use of "strongly acidic" co-reagents like alcohols or ammonium salts. On the other hand, while 1-alkynes can be reduced by lithium in amines, similar reductions using sodium in ammonia are best carried out in the presence of ammonium sulfate⁴⁸ to avoid formation of the sodio acetylides which are difficult to reduce by this system. In all cases employing the lithium/amine method, care must be taken to use only a stoichiometric amount of lithium metal since this procedure can reduce the olefinic products to alkanes⁴⁷.

³⁵ R. D. STOLOW, J. A. WARD, *J. Org. Chem.* **31**, 965 (1966).

³⁶ E. GIOVANNINI, H. WEGMÜLLER, *Helv. Chem. Acta.* **41**, 933 (1958).

³⁷ A. P. KRAPCHO, R. DONN, *J. Org. Chem.* **30**, 641 (1965).

³⁸ J. REINER, W. JENNY, *Helv. Chim. Acta* **52**, 1624 (1969).

³⁹ W. HÜCKEL, R. SCHWEN, *Chem. Ber.* **89**, 150 (1956).

⁴⁰ A. J. BIRCH, P. FITTON, D. C. C. SMITH, D. E. STEERE, A. R. STELFOX, *J. Chem. Soc.* **1963**, 2209.

⁴¹ R. G. HARVEY, *J. Org. Chem.* **32**, 238 (1967).

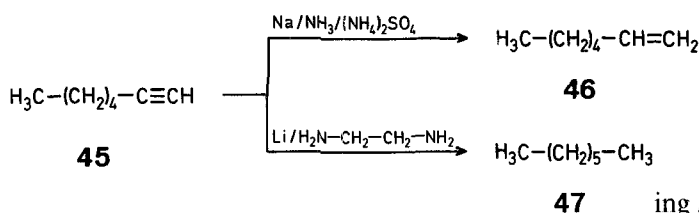
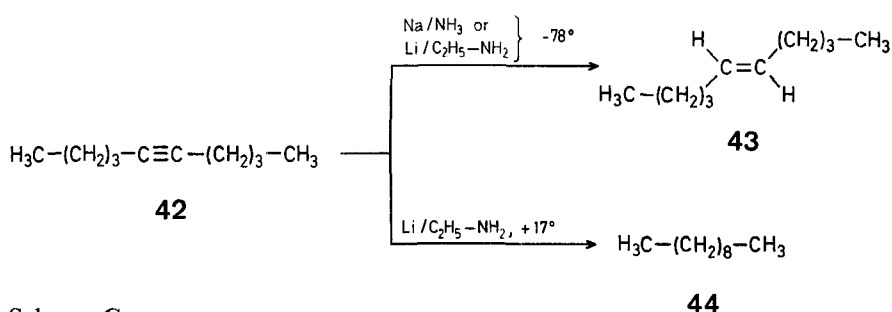
⁴² S. MEJER, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.* **9**, 773 (1961); *C. A.* **60**, 4073 (1963).

⁴³ D. S. TRIFAN, L. NICHOLS, *J. Amer. Chem. Soc.* **79**, 2746 (1957).

⁴⁴ A. D. BROWN, JR., H. REICH, *J. Org. Chem.* **35**, 1191 (1970).

⁴⁵ K. N. CAMPBELL, L. T. EBY, *J. Amer. Chem. Soc.* **63**, 216 (1941).

3-Octyne and 5-decyne (**42**) have been reduced in good yields to *trans*-3-octene and *trans*-5-decene (**43**), respectively by sodium in ammonia at -33° ⁴⁵ and by lithium in ethylamine at -78° (Scheme C)⁴⁷. When the lithium/ethylamine reduction of 5-decyne is carried out at 17° with excess lithium, substantial amounts of *n*-decane (**44**) are obtained⁴⁷; this reaction, which proceeds *via trans*-5-decene, represented the first chemical reduction of a non-terminal double bond (Scheme C). Similarly, 1-heptyne (**45**) is cleanly reduced by sodium/ammonium sulfate/ammonia to 1-heptene (**46**)⁴⁸; this technique represents the method of choice for chemically converting 1-alkynes to 1-alkenes⁴⁸. 1-Heptyne has also been reduced by lithium in ethylenediamine to give heptane in fair yield (Scheme D)²⁶.



Scheme D

Incidentally, sodium/*t*-butyl alcohol/HMPT has recently been utilized as a more powerful reducing system⁴⁹. Since it readily reduces olefins (see below), it is not suitable for the preparation of these compounds *via* reduction of alkynes. However, this system does reduce alkynes to alkanes in high yield as witnessed by the conversion of 3-hexyne to *n*-hexane and *trans*-3-hexene in yields of 79% and 14%, respectively.

⁴⁶ K. N. CAMPBELL, L. T. EBY, J. Amer. Chem. Soc. **63**, 2683 (1941).

⁴⁷ R. A. BENKESER, G. SCHROLL, D. M. SAUVE, J. Amer. Chem. Soc. **77**, 3378 (1955).

⁴⁸ A. L. HENNE, K. W. GREENLEE, J. Amer. Chem. Soc. **65**, 2020 (1943).

⁴⁹ G. M. WHITESIDES, W. J. EHMANN, J. Org. Chem. **35**, 3565 (1970).

⁵⁰ R. A. BENKESER, C. TINCHER, J. Org. Chem. **33**, 2727 (1968).

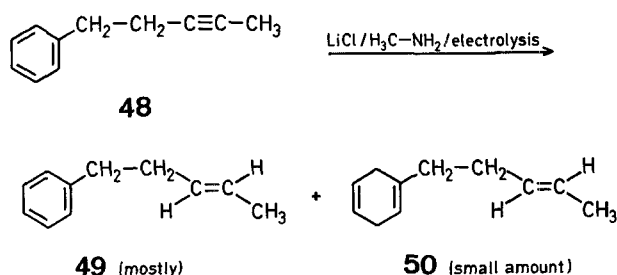
⁵¹ A. J. BIRCH, J. Chem. Soc. **1947**, 1642.

⁵² T. J. KING, J. Chem. Soc. **1951**, 898.

⁵³ H. GREENFIELD, R. A. FRIEDEL, M. ORCHIN, J. Amer. Chem. Soc. **76**, 1258 (1954).

Certain alkyl- and arylalkynes have been subjected to electrocatalytic reductions in methylamine using lithium chloride as the electrolyte⁵⁰. Thus, undivided cell electrolyses of 2-octyne, 3-octyne and 5-decyne give good to excellent yields of the corresponding *trans*-olefins accompanied by only minute amounts of the *cis*-olefins. Phenylacetylene and 1-phenyl-1-butyne, upon electrocatalytic reduction, afford 1-phenylethane and 1-phenylbutane, respectively, accompanied by nearly equal amounts of the starting alkynes. Thus, alkynes conjugated with aromatic systems can not be selectively reduced to aromatic olefins by this method. On the other hand, application of these electrocatalytic reductions to unconjugated arylalkynes like 4-phenyl-1-butyne and 5-phenyl-2-pentyne (**48**), give mostly the correspond-

ing *trans*-olefins (Scheme E) in good yield. While the latter two reductions also afford a small amount of the 2,5-dihydro derivatives (e.g., **50**, Scheme E), the conjugated arylalkynes described above give none of these products.



Scheme E

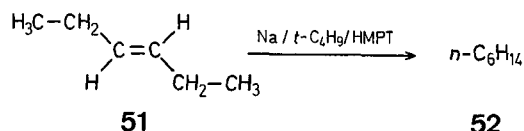
One similar electrocatalytic reduction in a divided cell is also interesting⁵⁰. In this case, 3-octyne is reduced using lithium chloride as the electrolyte to give *trans*-3-octene (37%), *trans*-2-octene (33%), *cis*-2-octene (4%), *trans*-4-octene, and other compounds. Obviously, substantial isomerizations occur and both allenes and alkynes are apparently reduced. These isomerizations are in marked contrast to monoolefins where such isomerizations are not realized^{30,51}.

3. Reduction of Alkenes

1-Alkenes are reduced both by sodium/alcohol/ammonia⁵² and by lithium/amines⁴⁷ to yield alkanes; non-terminal olefins, though, are hydrogenated only by the latter method.

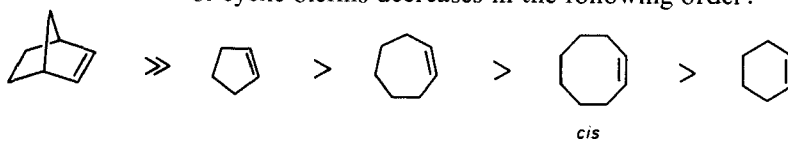
3.1. Reduction of Isomeric Hexenes

1-Hexene is converted to *n*-hexane in fair yield by sodium/methanol/ammonia⁵², by lithium/methanol/ammonia⁵³, by lithium/ethylamine⁵⁴, and by lithium/*t*-butyl alcohol/ethylamine⁵⁴. 1-Hexene is also converted to *n*-hexane by sodium/*t*-butyl alcohol/HMPT in quantitative yield⁴⁹. The latter method should be the one of choice since it has been found to nearly quantitatively reduce even non-terminal olefins; for example, *trans*-3-hexene (**51**) is reduced to *n*-hexane (**52**) in 97% yield⁴⁹. The related 2-hexene, in contrast, is not reduced by sodium/methanol/ammonia⁵³.



Reduction of 5,5-Dimethyl-1,3-hexadiene by Lithium in Methylamine^{22b}:

To the blue solution formed from lithium (0.64 g; 0.09 g atom) in methylamine (200 ml) is added 5,5-dimethyl-1,3-hexadiene (4.0 g; 0.036 mol) in ether (20 ml) at a rate sufficient to maintain the coloration. After 10 min., the excess metal is destroyed by the addition of ammonium chloride and the solvent is allowed to evaporate. The residue is decomposed by the slow addition of water. After extracting the aqueous solution four times with ether, drying (CaSO₄) and removing the solvent, the crude material is distilled at 93–94° to give a mixture of products. Gas chromatography shows the mixture to consist of *trans*-2,2-dimethyl-3-hexene (15%), *trans*-5,5-dimethyl-2-hexene (68%), and *cis*-5,5-dimethyl-2-hexene (7%).



The potency of this system in HMPT is also illustrated by its use to convert cyclohexene to cyclohexane in 99% yield⁴⁹. A similar reduction accomplished by lithium in ethylamine at 17° gives cyclohexane in only 51% yield, and the reaction fails at –78°⁴⁷.

3.2. Relative Ease of Reductions of Olefins

As mentioned, both the Birch or Benkeser systems reduce 1-alkenes, but the Birch system does not reduce non-terminal olefins. Moreover, the Benkeser system reduces disubstituted olefins more easily than trisubstituted ones³². This has been demonstrated by subjecting 1-methylcyclohexene (**17**, R = CH₃) and 3-methylcyclohexene (**18**, R = CH₃) to reduction by two equivalents of lithium in methylamine; the former compound gives methylcyclohexane in only 4% yield while the latter compound affords the same hydrocarbon in 59% yield. Similar results are realized with the isomeric *i*-propylcyclohexenes. Such differences in the extent of reduction have been ascribed to an electronic effect wherein the inductive effect of alkyl groups bonded directly to sp²-hybridized carbon atoms reduce the uptake of electrons³².

Of course, the more powerful reducing systems can overcome the relative slow reactivity of tri- and tetrasubstituted olefins. Thus, sodium-*t*-butylalcohol/HMPT reduction of 1-methylcyclohexene (**17**, R = CH₃) affords methylcyclohexane in 100% yield⁴⁹. Similarly reduction of Δ⁹⁽¹⁰⁾-octalin (**4**) with lithium/ethylenediamine²⁶ and with sodium/*t*-butyl alcohol/HMPT⁴⁹ gives decahydronaphthalenes in yields of 37% and 94%, respectively.

Several series of olefins have been studied with respect to their relative rate of reductions with lithium/ethylamine⁵⁴. For example, the relative rates of the following pairs have been reported: cyclopentene/1-methylcyclopentene, 25.0; 1-methylcyclopentene/1-ethylcyclopentene, 1.4; and cyclohexene/1-methylcyclohexene, 25.2; others are listed. In addition, it has been found that the ease of reduction of cyclic olefins decreases in the following order:

Except for cyclooctene, this trend has been ascribed mainly to the relative amounts of ground state strain being relieved on conversion to the corresponding hydrogenated hydrocarbons⁵⁴.

3.3. Reduction of Phenyl-substituted Alkenes

Olefins conjugated with aryl groups (or with other olefins) are readily reduced by alkali metals in ammonia without the use of alcohol co-reagents⁵⁵. Thus, this method is suggested for the conversion of compounds like styrene or stilbene affording ethylbenzene and 1,2-diphenylethane, respectively⁵⁵.

Two studies dealing with Benkeser-type reductions of styrene deserve brief mention. Thus, this compound is reduced by lithium in methylamine to a mixture of 1-ethylcyclohexene and ethylcyclohexane⁵⁶; no ethylbenzene is formed. Undivided-cell

⁵⁴ A. P. KRAPCHO, M. E. NADEL, J. Amer. Chem. Soc. **86**, 1096 (1964).

⁵⁵ H. SMITH, *Organic Reactions in Liquid Ammonia. Chemistry in Non-aqueous Ionizing Solvents*, Vol. 1, Part 2, p. 226, Wiley, New York, 1963.

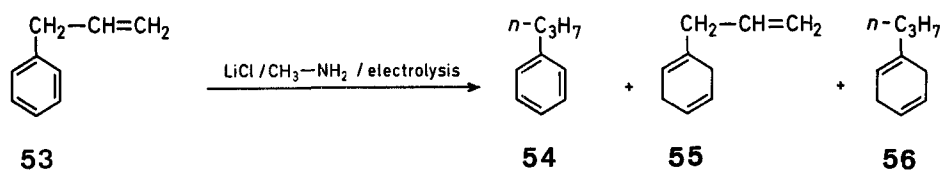
⁵⁶ R. A. BENKESER, C. ARNOLD, Jr., R. F. LAMBERT, O. H. THOMAS, J. Amer. Chem. Soc. **77**, 6042 (1955).

⁵⁷ R. A. BENKESER, S. MELS, J. Org. Chem. **34**, 3970 (1969).

⁵⁸ J. G. TRAYNHAM, J. Org. Chem. **25**, 833 (1960).

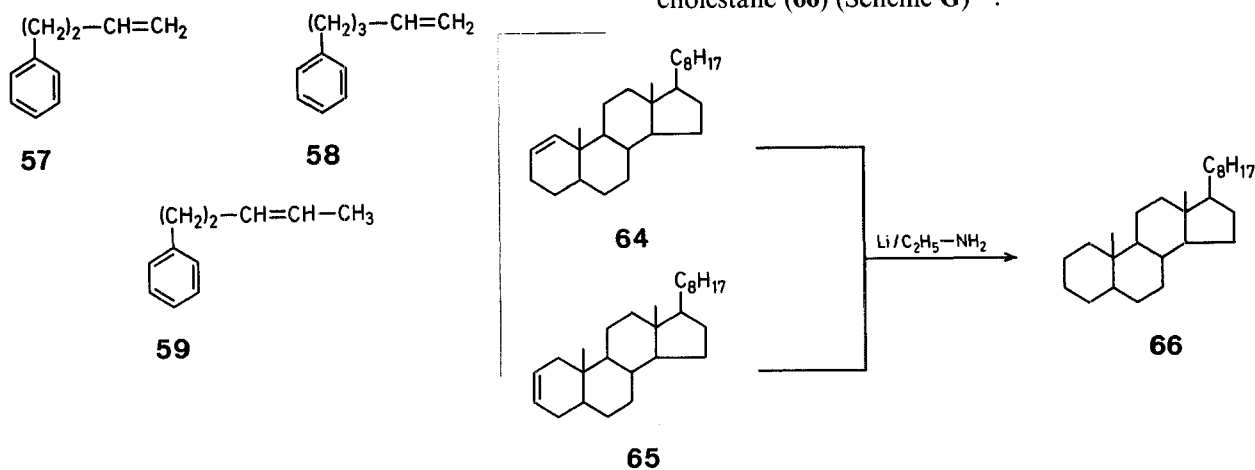
⁵⁹ B. P. ORTIZ DE MONTELLANO, B. A. LOVING, T. C. SHIELDS, P. D. GARDNER, J. Amer. Chem. Soc. **89**, 3365 (1967).

electrolyses of styrene in methylamine with lithium chloride do, however, give ethylbenzene in 69% yield⁵⁷. The related electrocatalytic reduction of allylbenzene (**53**) using enough current to reduce only the allylic double bond gives *n*-propylbenzene (**54**) in good yield accompanied by small amounts of triene **55** and diene **56** (Scheme F)⁵⁷. Interestingly, when the reduction is carried out in the presence of ethanol, **55** is formed as the major product and hydrocarbons **54** and **56** are generated only in low yield. When the electrolysis with ethanol is realized with enough current to reduce two double bonds, though, diene **56** becomes the major product. Since the unconjugated dienes do not undergo isomerization in undivided cell electrolyses²², it is not sur-



Scheme F

prising that such an electrolysis of **55** in the presence of ethanol leads to **56** in good yield⁵⁷. Unconjugated olefins **57**, **58** and **59** afford reduction products in the undivided cell which are similar to those realized with **53**⁵⁷.



Scheme G

3.4. Reductions of Miscellaneous Olefins

Norbornene (**60**) has been reduced by lithium in ethylamine^{54,58} and by sodium/*t*-butyl alcohol/HMPT⁴⁹ to afford norbornane (**61**) in yields of 42% and 73%, respectively. This reduction has even been accomplished in about 5% yield with lithium/methanol/ammonia⁵⁴, a reagent which normally does not reduce non-terminal olefins. Norbornadiene (**62**) has been reduced by lithium in ethylamine to afford **60**, **61**, and nortricyclene (**63**). Diene **62** has also been reduced by sodium/ammonia in the absence of alcohols to give **60**; this result is discussed in relation to the reduction of certain non-conjugated systems with their long wavelength UV absorption⁵⁹.

Both cholest-1-ene (**64**) and cholest-2-ene (**65**) have been reduced by lithium in ethylamine to give cholestane (**66**) (Scheme G)⁶⁰.

⁶⁰ A. S. HALLSWORTH, H. B. HENBEST, T. I. WRIGLEY, *J. Chem. Soc.* **1957**, 1969.

⁶¹ H. M. WALBORSKY, M. S. ARONOFF, M. F. SCHULMAN, *J. Org. Chem.* **36**, 1036 (1971).

⁶² H. SMITH, *Organic Reactions in Liquid Ammonia. Chemistry in Non-aqueous Ionizing Solvents*, Vol. 1, Part 2, p. 161, 245, Wiley, New York, 1963.

⁶³ A. L. WILDS, N. A. NELSON, *J. Amer. Chem. Soc.* **75**, 5360 (1953).

⁶⁴ G. STORK, W. N. WHITE, *J. Amer. Chem. Soc.* **78**, 4604 (1956).

⁶⁵ A. J. BIRCH, *J. Chem. Soc.* **1947**, 102.

⁶⁶ C. D. HURD, G. L. OLIVER, *J. Amer. Chem. Soc.* **81**, 2795 (1959).

⁶⁷ H. L. DRYDEN, Jr., G. M. WEBBER, R. R. BURTNER, J. H. CELLA, *J. Org. Chem.* **26**, 3237 (1961).

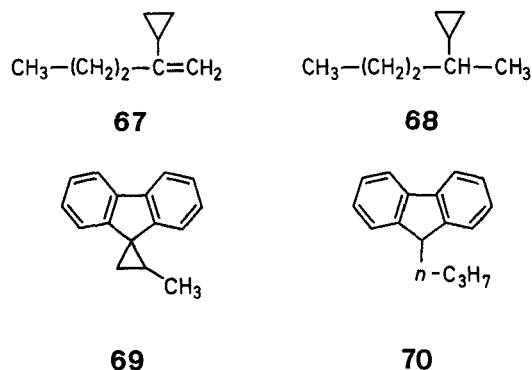
⁶⁸ R. A. BENKESER, R. F. LAMBERT, P. W. RYAN, D. G. STOFFEY, *J. Amer. Chem. Soc.* **80**, 6573 (1958).

⁶⁹ A. J. BIRCH, S. M. MUKHERJI, *J. Chem. Soc.* **1949**, 2531.

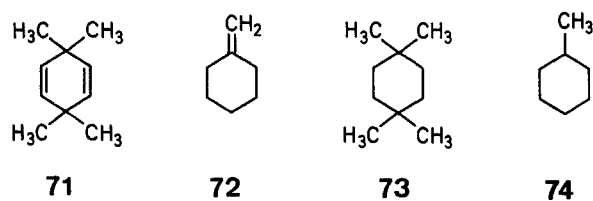
⁷⁰ A. J. BIRCH, *J. Chem. Soc.* **1950**, 367.

⁷¹ A. L. WILDS, N. A. NELSON, *J. Amer. Chem. Soc.* **75**, 5366 (1953).

rene derivative **69**, the cyclopropyl ring is cleaved in preference to reduction of the aromatic system to give *n*-propylfluorene (**70**) in excellent yield⁶¹.



Two more examples of the sodium/*t*-butyl alcohol/HMPT method will further demonstrate its potency. Thus, reduction of 3,3,6,6-tetramethyl-1,4-cyclohexadiene (**71**) and of methylenecyclohexane (**72**) with this system give the saturated hydrocarbons **73** and **74** in yields of about 40% and 100%, respectively⁴⁹. By using *t*-butyl alcohol-*O-d* in these reductions, deuterium may be incorporated into hydrogenated hydrocarbons.

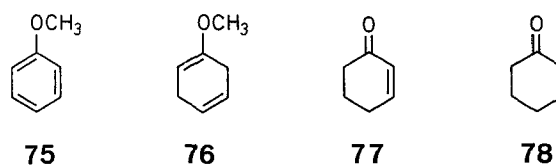


4. Reduction of Unsaturated Ethers

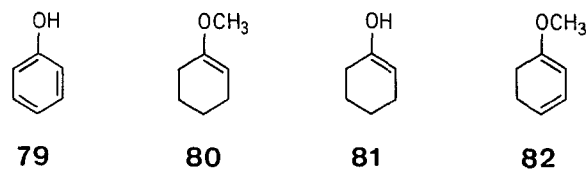
Unsaturated ethers have been extensively studied with respect to their interactions with alkali metals in ammonia⁶² and related solvents. Both the nature of the ether and of the reducing media can have a marked effect on the course of the reactions which can range from cleavages to reductions of aromatic rings to no reactions at all.

4.1. Reduction of Anisole

At first glance, interactions of anisole (**75**) with Birch or Benkeser reagents lead to a variety of products which are, at best, confusing. For example, treatment of **75** with sodium or lithium/ethanol/ammonia or lithium/ethanol/methylamine affords 2,5-dihydroanisole (**76**) in 81–85% yield^{25,31,63}. Similar use of lithium/*t*-butyl alcohol/ammonia leads however to unsaturated ketone **77** in 49% yield along with cyclohexanone in 10% yield⁶⁴. The formation of **77** is, however, easily explained since acid-catalyzed hydrolysis of **76** leads to **77**. In addition, the saturated cyclohexanone is thought to arise from reduction of conjugated dienes formed in the basic reaction medium⁶³, probably to afford **80**, which is then hydrolyzed to **78**.



Anisole can be converted to phenol (**79**) by sodium in ammonia in the absence of an alcohol^{65,66}. This reductive cleavage presumably proceeds via the intermediacy of the resonance stabilized phenoxide ion. The use of the more powerful lithium/ethylamine system using excess lithium not only gives phenol (**79**) in 48% yield, but also affords cyclohexanone (**78**) in 40% yield⁵⁶. The latter compound can apparently arise either from the reduction of anisole (**75**) followed by hydrolysis of enol ether **80** or by the reduction of lithium phenoxide. Both routes should give rise to enol **81** which tautomerizes to **78**.



Surprisingly, when the lithium/ethylamine reduction of anisole is effected by only two equivalents of lithium metal, diene **76** is formed in 53% yield accompanied by conjugated diene **82** formed in 47% yield⁵⁶. This result represents one of the few examples where lithium/amine reductions in the absence of alcohol lead to a conjugated diene instead of a monoolefin. Anisole is also converted by lithium in ethylenediamine to cyclohexanone and cyclohexanol in yields of 50% and 6%, respectively²⁶.

4.2. Reduction of Methyl Naphthyl Ethers and Related Compounds

By far, most reductions in this area have been effected by Birch-type systems. For example, 2-methoxynaphthalene (**83**) has been reduced by sodium/ethanol/ammonia to give tetrahydro derivative **84** which is converted by aqueous sulfuric acid to dienone **85**¹⁰. Similar reduction of 6-methoxytetralin (**86**) followed by hydrolysis gives enone **87**¹⁰, while reduction of **86** with lithium/ethanol/ammonia affords diene **88**⁶³. Similarly, **86** has been reduced

⁷² W. S. JOHNSON, R. PAPPO, W. F. JOHNS, *J. Amer. Chem. Soc.* **78**, 6339 (1956).

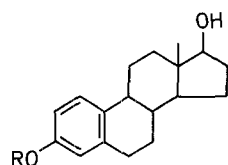
⁷³ K. B. WIBERG, J. G. PFEIFFER, *J. Amer. Chem. Soc.* **92**, 553 (1970).

⁷⁴ A. R. PINDER, H. SMITH, *J. Chem. Soc.* **1954**, 113.

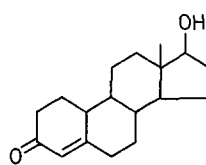
⁷⁵ T. H. VAUGHN, J. A. NIEUWLAND, *Ind. Eng. Chem. Anal. Ed.* **3**, 274 (1931).

⁷⁶ W. GRIMME, J. REISDORFF, W. JUNEMANN, E. VOGEL, *J. Amer. Chem. Soc.* **92**, 6335 (1970).

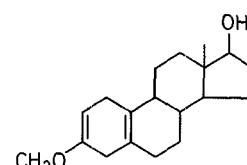
⁷⁷ E. M. KAISER, C. G. EDMONDS, S. D. GRUBB, J. W. SMITH, D. TRAMP, *J. Org. Chem.* **36**, 330 (1971).



92

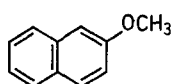


93

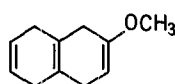


94

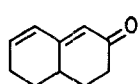
by lithium or sodium/*t*-butyl alcohol/ammonia to give **88** in very good yield⁶⁷.



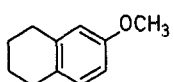
83



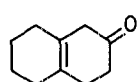
84



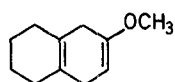
85



86

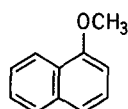


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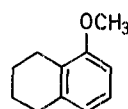


88

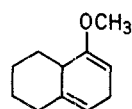
On the other hand, 1-methoxynaphthalene (**89**) has been reduced by lithium/methylamine to give 5-methoxytetralin (**90**) and $\Delta^{1(9)}$ -octalin (**5**) in low yields⁶⁸. Reduction of **89** by lithium or sodium/*t*-butyl alcohol/ammonia⁶⁷, or by lithium/ethanol/ammonia⁶³ gives diene **91**.



89



90

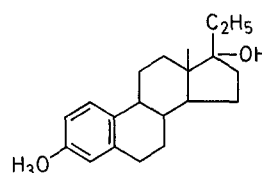


91

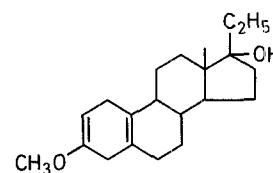
4.3. Unsaturated Steroidal Ethers

It has been reported that the 3-glyceryl ether of estradiol (**92**, R = CH₂—CHOH—CH₂OH) can be reduced by sodium or potassium/ethanol/ammonia to ultimately afford 19-nortestosterone (**93**) in low yield^{69,70}. Two more recent reports, however, have disclosed that such Birch reductions can be effected in much better yields. Thus, one group⁶³ of authors have suggested to add the alcohol to the reaction mixture after the other reagents have already been mixed together. Thus, **92** (R = CH₃) is converted, apparently via diene **94**, to **93** in 70–77% yield⁷¹. The other group⁶⁷, however, has suggested that the above modified procedure does not give reproducible results and that Birch's low yields in the conversion of **92** (R = CH₂—CHOH—CH₂OH) to **93** may be ascribed to iron contaminants in the ammonia. This was demonstrated by reducing **92** (R = CH₃) to **94** in yields of 79–88% with lithium, sodium, or calcium in pure ammonia containing alcohols such as methanol or *t*-butyl alcohol⁶⁷.

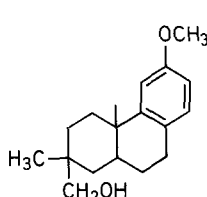
Three other similar methyl ethers have been reduced by the Birch method to give dihydro products⁶⁷. Thus, 17-ethylestradiol methyl ether (**95**) is converted to diene **96** by lithium or sodium/*t*-amyl or *t*-butyl alcohol/ammonia in 82–91% yield. Similarly, podocarpinol methyl ether (**97**) is converted by various metals in *t*-butyl alcohol or methanol/ammonia to diene **98** in 54–59% yield. Finally, hydrindane derivative **99** is reduced to **100** by lithium/*t*-butyl alcohol/ammonia in 65–71% yield.



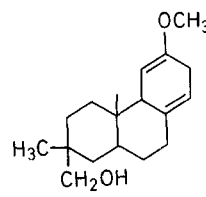
95



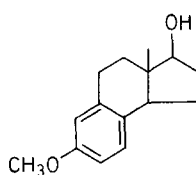
96



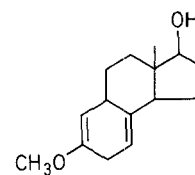
97



98



99



100

Also, decahydrochrysenes derivative **101** has been reduced by lithium/ethanol/ammonia to give, after hydrolysis, enones **102** and **103**; compound **102** predominates⁷². 3β -Methoxycholest-4-ene (**104**) has been subjected to an unrelated Benkeser reduction using lithium in ethylamine to give the demethoxylated product, cholest-4-ene (**105**)⁶⁰.

⁷⁹ B. C. NEWMAN, E. L. ELIEL, *J. Org. Chem.* **35**, 3641 (1970).

⁸⁰ N. S. CROSSLEY, H. B. HENBEST, *J. Chem. Soc.* **1960**, 4413.

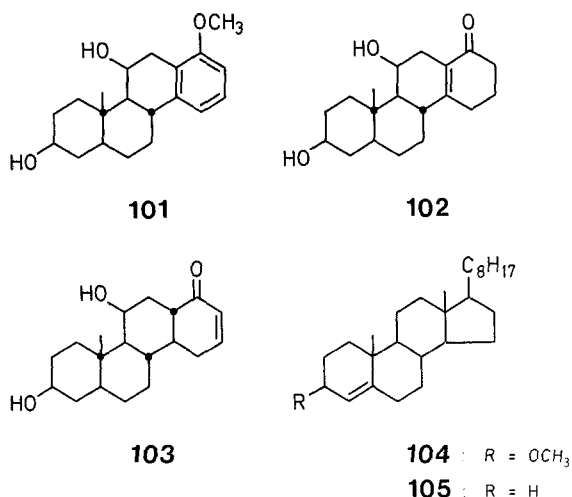
⁸¹ A. J. BIRCH, *J. Chem. Soc.* **1945**, 811.

⁸² J. M. VAN DER ZANDEN, A. P. TER BORG, *Rec. Trav. Chim.* **75**, 1115 (1956).

⁸³ A. J. BIRCH, *J. Chem. Soc.* **1944**, 430.

⁸⁴ J. F. EASTHAM, D. R. LARKIN, *J. Amer. Chem. Soc.* **80**, 2887 (1958).

⁷⁸ E. L. ELIEL, T. W. DOYLE, *J. Org. Chem.* **35**, 2716 (1970).



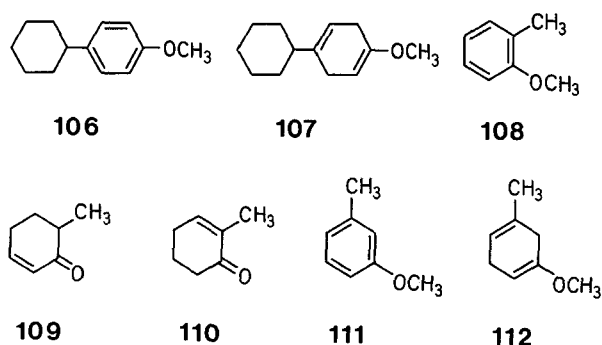
4.4. Reduction of Miscellaneous Unsaturated Ethers

p-Cyclohexylanisole (**106**) has been reduced by sodium/*t*-butyl alcohol/ammonia⁶⁷ and by lithium/ethanol/ammonia⁶³ to give **107** in excellent yield. *o*-Methylanisole (**108**) has been converted by lithium/*t*-butyl alcohol/ammonia primarily to enones **109** and **110** in good yield⁶⁴.

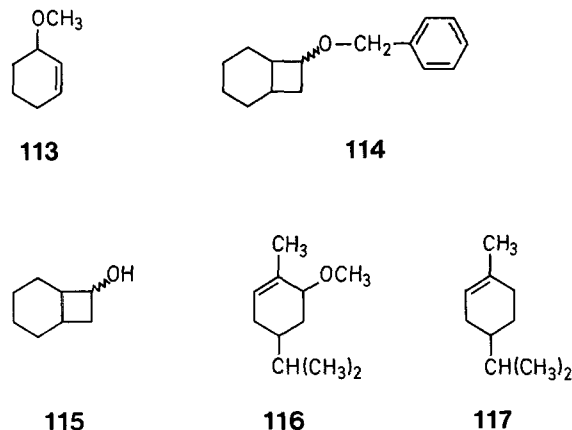
Reduction of 4-Cyclohexylanisole (**106**)⁶⁷:

4-Cyclohexylanisole (10.0 g; 0.52 mol) is reduced with sodium (12.0 g; 0.52 mol) in a mixture of distilled liquid ammonia (600 ml), tetrahydrofuran (300 ml), and *t*-butyl alcohol (300 ml). After 5 hr, the mixture is still blue, and the excess sodium is destroyed by the cautious addition of methanol (70 ml). The product is isolated by evaporation of the tetrahydrofuran and extraction into pentane; weight of crude solid: 8.62 g. The crude yield corresponds to an 84% yield of the 1,4-dihydro compound **107**.

In the first electrocatalytic reduction effected in ammonia or amines²¹, *m*-methylanisole (**111**) is apparently converted to 2,5-dihydro derivative **112** by electrolyzing the ether in ammonia containing sodium ethoxide.



Finally, unsaturated ether **113** has been quantitatively converted to cyclohexene by means of lithium/ethanol/ammonia²⁵, *cis*- and *trans*-benzyl ether **114** to *cis*- and *trans*-alcohol **115** by lithium in ethylamine⁷³, and ether **116** to *p*-menth-1-ene (**117**) by lithium in ethylamine⁶⁰.



5. Reduction of Acetals, Ketals and Related Compounds

In general, acetals and ketals which are derived from strictly aliphatic aldehydes or ketones are stable to reduction by both the Birch and the Benkeser procedures. Similarly, those derived from carbonyl compounds which also possess an aromatic nucleus are stable provided the original carbonyl carbon is at least two carbon atoms removed from the aromatic nucleus. However, in the latter compounds, the aromatic nucleus can undergo reduction. Ketals derived from phenone-type ketones, mono- and di-thioketals, and monothioacetals and ketals can be cleaved easily not only by Birch and Benkeser-type reagents, but even by sodium or other metals in ammonia in the absence of alcohols. Methylene-dioxyaromatics seem to represent a special case: they can be easily reduced under Birch conditions usually without reduction of the aromatic ring.

5.1. Attempted Reduction of Non-benzylic Ketals

The diethylketal of acetone is not reduced even by the potent lithium/methylamine system⁵⁶. Similarly, the ketal linkage of 1,3-dioxolane **118** is not reduced by alkali metals in ammonia in the presence of alcohols⁷⁴. In fact, dimethylacetal is sufficiently stable to alkali metals in ammonia that it is often used as a cosolvent in Birch reductions⁷⁵. The lithium/methylamine reduction of the diethylketal of 4-

⁸⁵ C. D. GUTSCHE, H. H. PETER, *Organic Syntheses*, Coll. Vol. 4, edited by N. RABJOHN, Wiley, New York, 1963, p. 887.

⁸⁶ J. F. EASTHAM, D. R. LARKIN, *J. Amer. Chem. Soc.* **81**, 3652 (1959).

⁸⁷ J. E. STARR, R. H. EASTMAN, *J. Org. Chem.* **31**, 1393 (1966).

⁸⁸ A. J. BIRCH, *Nature* **160**, 754 (1947).

⁸⁹ B. B. MILLWARD, *J. Chem. Soc.* **1960**, 26.

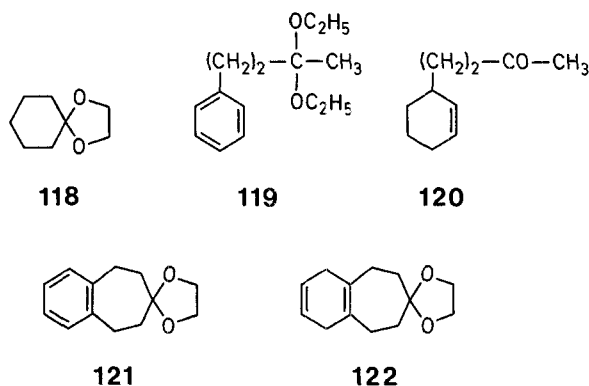
⁹⁰ A. J. BIRCH, *J. Chem. Soc.* **1946**, 593.

⁹¹ A. J. BIRCH, R. W. RICKARDS, K. J. S. STAPLEFORD, *Aust. J. Chem.* **22**, 1321 (1969).

⁹² G. W. WATT, C. M. KNOWLES, L. O. MORGAN, *J. Amer. Chem. Soc.* **69**, 1657 (1947).

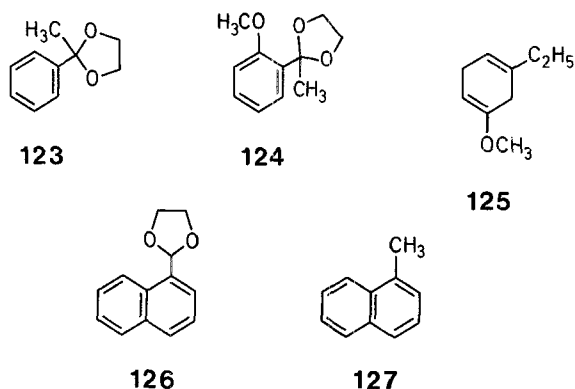
⁹³ H. PLENIKER, G. EGE, *Angew. Chem.* **70**, 505 (1958).

phenyl-2-butanone (**119**) is interesting since the aromatic ring, but not the ketal, is reduced to afford enone **120**⁵⁶. Also, only the aromatic ring of 1,3-dioxolane **121** is reduced by lithium/ethanol/ammonia to afford 2,5-dihydro derivative **122**⁷⁶.

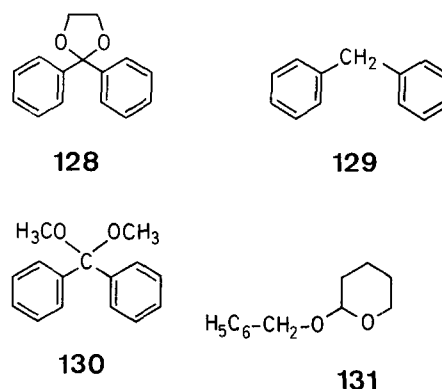


5.2. Reduction of Benzylic Ketals

2-Methyl-2-phenyl-1,3-dioxolane (**123**) and its *o*-methoxy derivative **124** have been reduced by sodium/methanol/ammonia to ethylbenzene and *o*-methoxyethylbenzene, respectively⁷⁴. Similar reduction of the corresponding *m*-methoxy derivative, though, gives dihydro derivative **125**⁷⁴. These reactions may also be accomplished by means of sodium in ammonia without alcohol since 1,3-dioxolane **126** has been converted to 1-methylnaphthalene (**127**) using only sodium in ammonia⁷⁷.



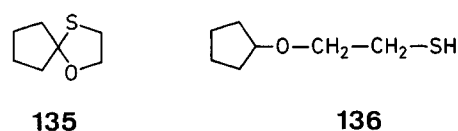
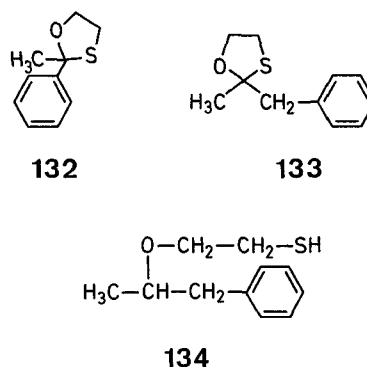
Even more facile reductions are realized with ketals derived from benzophenone. Thus, 2,2-diphenyl-1,3-dioxolane (**128**) can be reduced to diphenylmethane (**129**) in good yield by either sodium/ethanol/ammonia or by sodium/ammonia⁷⁷. The related reaction effected by lithium in ethylamine, gives however diphenylmethane in which the aromatic rings have also been reduced⁷⁷. Similar results are obtained with dimethoxydiphenylmethane (**130**)⁷⁷.



One related reduction deserves brief mention. Thus, reduction of tetrahydropyran derivative **131** with lithium in ethylamine gives 1-methylcyclohexene (**17**, R = CH₃) and methylcyclohexane⁵⁶.

5.3. Reduction of Sulfur Derivatives of Acetals and Ketals

The oxathiolane derivative of acetophenone (**132**) has been converted to ethylbenzene along with a little 2,5-dihydroethylbenzene (**16**, R = C₂H₅) using sodium/methanol/ammonia⁷⁴. Certain monothioacetals and ketals have been reduced by metals in ammonia without alcohol co-reagents to give alkoxymercaptans⁷⁸; in fact, the yields of products are lowered by the presence of alcohols. For example, ethylenemonothioacetal **133** is converted by calcium in ammonia to **134** in 88% yield⁷⁸. Similarly, 1,3-oxathiolane **135** is reduced to **136** by sodium in ammonia in low yield⁷⁸; other examples are included. These reductions are said to be less powerful when effected by lithium in methyl- or ethylamine⁷⁸.



Several 1,3-dithiolanes have been reduced to either thiomercaptans or to hydrocarbons. For example,

⁵⁴ M. E. KUEHE, B. F. LAMBERT, J. Amer. Chem. Soc. **81**, 4278 (1959).

⁵⁵ A. O. BEDENBAUGH, J. H. BEDENBAUGH, W. A. BERGIN, J. D. ADKINS, J. Amer. Chem. Soc. **92**, 5775 (1970).

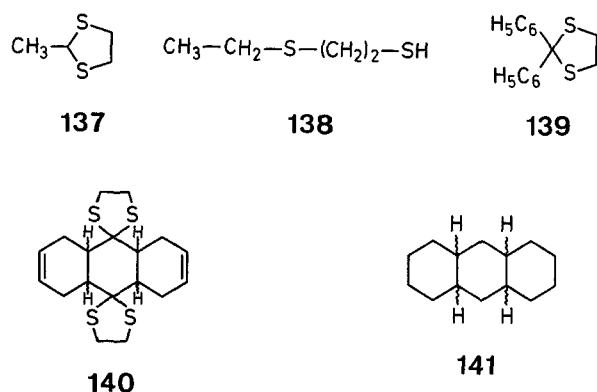
⁵⁶ A. J. BIRCH, P. HEXTRALL, S. STERNHILL, Aust. J. Chem. **7**, 256 (1954).

⁵⁷ A. W. BURGSTALLER, L. R. WORDEN, J. Amer. Chem. Soc. **83**, 2587 (1961).

137 has been converted by calcium in ammonia to **138** in excellent yield⁷⁹. Benzophenone derivative **139** is similarly converted by sodium in ammonia to diphenylmethane in 98% yield⁷⁷. Finally, the isomeric *cis*- or *trans*- bis-dithioketals (**140**) are converted to their respective perhydrogenated hydrocarbons **141** by lithium in ethylamine in 86 to 90% yields⁸⁰.

Preparation of 4 α , 8 α β , 9 α β , 10 α -Perhydroanthracene⁸⁰:

Bis-dithioketal **140** (1.1 g) is suspended in ethylamine (100 ml). Small pieces of lithium (870 mg) are added; the flask is then stoppered, cooled to -20° , and shaken for 45 min with periodic release of the pressure. Water is then added to discharge the blue color and the ethylamine is allowed to evaporate overnight. The product is extracted with light petroleum ether (b. p. $40-60^\circ$), and the extracts are filtered through 10 g of alumina to give 480 mg (86%) of the above perhydroanthracene; m. p. $120-121^\circ$ (from acetone).



6. Reduction of Alcohols

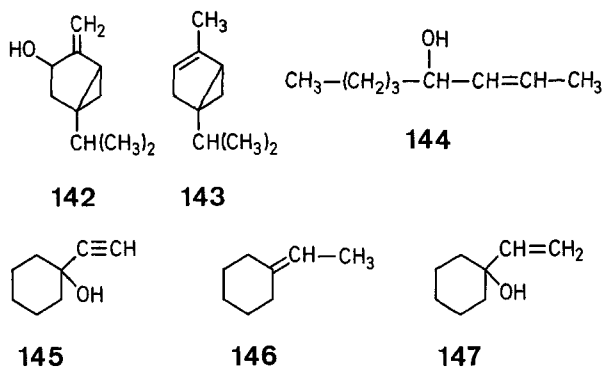
The nature of the products derived from Birch or Benkeser reductions of unsaturated alcohols is dependent on the type of alcohol used. Thus, benzylic and allylic alcohols are reductively cleaved by either procedure; however, a proton donor must be present in the Birch method to prevent alkoxide formation. Aromatic alcohols like naphthols or alcohols which contain an aromatic nucleus at least two carbon atoms removed from the alcoholic function undergo normal ring reduction.

6.1. Reduction of Allylic and Benzylic Alcohols

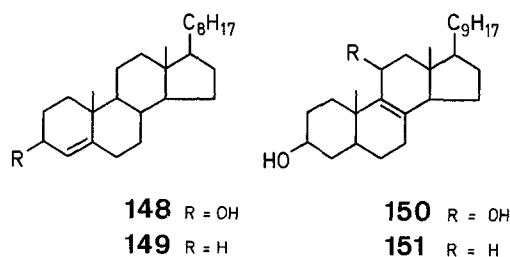
In one of his early papers⁸¹, Birch reported that a wide variety of allylic alcohols underwent reductive cleavage with sodium/ethanol/ammonia. For example, this reagent converts *d*-sabinol (**142**) to α -thujene (**143**), 4-hydroxy-2-octene (**144**) to 2- and 3-octene, and 1-ethynylcyclohexanol (**145**) to ethylenecyclohexane (**146**). The latter reduction apparently proceeds via 1-vinylcyclohexanol (**147**) which can be isolated. Other examples are reported⁸¹.

The Conversion of *d*-Sabinol (**142**) to α -Thujene (**143**)⁸¹:

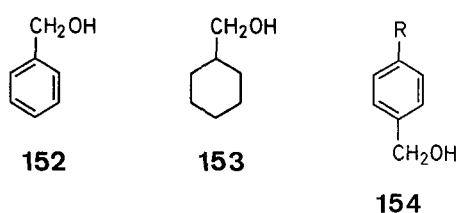
A mixture of *d*-sabinol (14 g) ($\alpha_D +5.6^\circ$) and ethanol (10 g) is added dropwise to a stirred solution of sodium (10 g) in liquid ammonia (200 ml). Further ethanol (8 g) is then added and, after the blue color has disappeared, the solution is cautiously decomposed with water (200 ml). The oil is taken up into ether and fractionated through a column to give 9.8 g of crude α -thujene; b. p. $154-156^\circ$; redistillation over sodium gives 8.2 g of an oil (**143**); b. p. $155-156^\circ$; n_D^{19} 1.4555, d_4^{19} 0.8332, $[\alpha]_D -29.7^\circ$.



Allyl alcohols are also usually reductively cleaved by lithium in amines even in the absence of alcohols. These facts may suggest that alkoxides are cleaved as lithium oxide rather than as the metal hydroxide observed in the Birch systems. Thus, cholest-4-en-3 β -ol (**148**) is cleaved by lithium in ethylamine to give cholest-4-ene (**149**)⁶⁰. The same reagent similarly reduces ergosta-8,22-diene-3 β ,11 β -diol (**150**) to ergosta-8,22-diene-3 β -ol (**151**). It should be noted that the unactivated alcohol in **150** is not reduced.



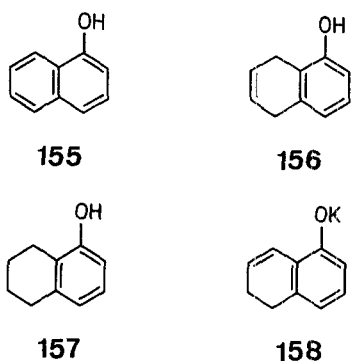
Benzylic alcohols behave nearly analogously to allylic ones. For example, benzyl alcohol (**152**) has been converted to toluene by sodium/ethanol/ammonia⁸¹. Surprisingly reduction of this alcohol by lithium in ethylenediamine gives cyclohexylmethyl alcohol (**153**)²⁶. Even stranger results have been realized in the sodium-ammonia reduction of 4-*i*-propyl- and 4-*t*-butylbenzyl alcohols (R = *i*-C₃H₇, *t*-C₄H₉, **154**) to give cumene and *t*-butylbenzene, respectively; in these cases, addition of ethanol was delayed⁸².



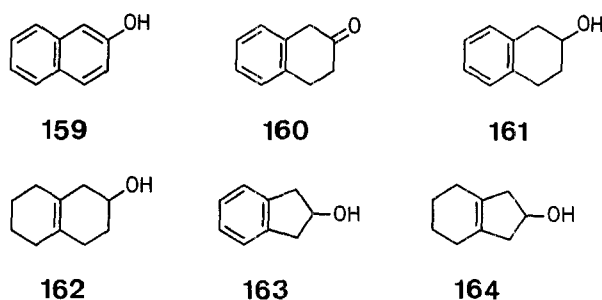
⁹⁸ A. W. BURGSTALLER, L. R. WORDEN, J. Amer. Chem. Soc. **86**, 96 (1964).

6.2. Reduction of Aromatic Alcohols, and Aliphatic Alcohols Containing Non-benzylic Aromatic Rings

The Birch and Benkeser reductions of α -naphthol (**155**) have been rather extensively studied. Thus, **155** has been converted to dihydro derivative **156** by sodium/*t*-amyl alcohol/ammonia⁸³, by potassium/ethanol/ammonia⁸⁴, and by lithium/ethanol/ammonia⁸⁵. The potassium salt of α -naphthol has been similarly reduced to **156** by potassium/*t*-amyl alcohol/ammonia⁸⁶. In contrast, **155** is converted to 5-tetralol **157** by lithium in methylamine⁶⁸; the same product (**157**) is obtained by the potassium/*t*-amyl alcohol/ammonia reduction of dihydro derivative **158**⁸⁶.

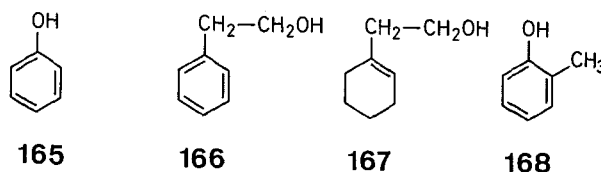


β -Naphthol (**159**) has also been reduced by sodium/*t*-amyl alcohol/ammonia to give β -tetralone (**160**)⁸³. The related β -tetralol (**161**) is converted to monoolefin **162** by lithium in a mixture of ethyl- and *n*-propylamines⁸⁷. Similarly, 2-indanol (**163**) is converted by lithium in *n*-propylamine to olefin **164**⁸⁷.



Furthermore, phenol and β -phenylethyl alcohol have been reduced under Benkeser conditions. Thus, phenol is converted to cyclohexanone in 96% yield by lithium in methyl- or ethylamine provided the hydrolysis of the reaction mixture is carried out rapidly with little lithium remaining⁵⁶. The cyclohexanone presumably arises from tautomerization of vinyl alcohol **81**. A similar reduction of phenol is also realized with lithium in ethylenediamine²⁶. As expected, the aromatic ring of β -phenylethyl alcohol (**166**) is reduced to monoolefin **167** by lithium in

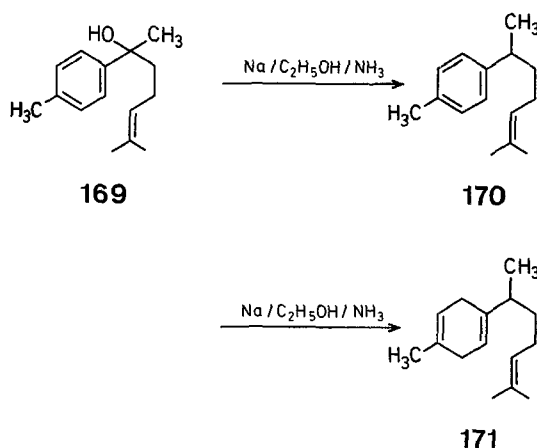
methyl- and ethylamine⁵⁶ and in ethylamine/morpholine³⁰; the yield of **167** is higher with the latter solvent mixture than with others.



Surprisingly, *o*-cresol (**168**) is reported not to undergo reduction by lithium/*t*-butyl alcohol/ammonia⁶⁴.

6.3. Reduction of 2-*p*-Tolyl-6-methylhept-5-ene-2-ol (**169**)

Reduction of this aromatic-olefinic alcohol (**169**) has been separated from the other examples cited because it nicely illustrates the selective reductions that can be realized with the Birch reduction⁶⁹. Thus, reduction of **169** with sodium/ethanol/ammonia leads first to α -curcumene (**170**) as a result of reductive cleavage of the benzylic alcohol. Treatment of **170** with additional sodium and ethanol in ammonia then results in reduction of the aromatic system to give β -curcumene (**171**); the olefinic double bond in the side chain is not reduced. Although none of these compounds has been reduced by Benkeser-type reagents, certain selective reactions on compounds **169**, **170**, and **171** should likewise be realizable.



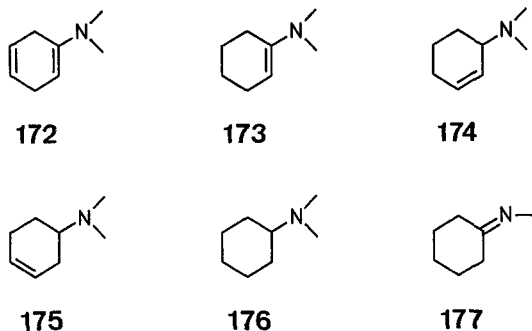
7. Reduction of Unsaturated Amines

In the area of Birch and Benkeser reductions of unsaturated amines, aromatic ones, chiefly aniline and its derivatives, have been studied particularly extensively. Birch reductions of such systems primarily seem to stop at the stage of the dihydro derivative (for example: **172**) regardless of whether the amine is primary, secondary, or tertiary; subsequent hydrolysis of **172** gives unsaturated ketones. Benkeser reductions of such systems proceed to the tetrahydro

⁹⁹ A. W. BURGSTALLER, L. R. WORDEN, T. B. LEWIS, *J. Org. Chem.* **28**, 2918 (1963).

¹⁰⁰ E. CHABLAY, *Comp. Rend.* **156**, 1020 (1913).

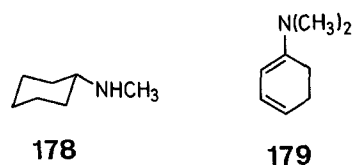
stage (for example: **173**, **174** and **175**) where reductions of **174** and **175** afford completely hydrogenated amines **176**. The final disposition of **173**, however, depends on whether the amine is primary, secondary or tertiary; primary and secondary amines of this type are thought to isomerize to **177** which readily undergoes reduction to hydrogenated amine. When



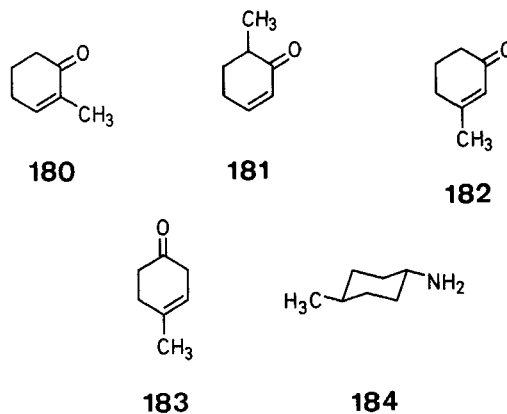
173 is, however, a tertiary amine, isomerization and subsequent reduction are resisted; hydrolysis thus gives cyclohexanone derivatives.

7.1. Reduction of Aniline and its Derivatives

Aniline itself is reduced primarily to enone **77** by sodium/methanol/ammonia⁸⁸ and by lithium/*t*-butyl alcohol/ammonia⁶⁴. Reduction of *N*-methylaniline with lithium in ethylamine, though, leads to fully hydrogenated cyclohexylamine **178**⁶⁸. *N,N*-Dimethylaniline is converted to enone **77** by lithium/*t*-butyl alcohol/ammonia⁶⁴. Another worker has carried out the latter reduction with sodium/ethanol/ammonia and has isolated, by avoiding hydrolysis, the conjugated diene **179** in good yield⁸⁹. In methylamine, *N,N*-dimethylaniline is converted to cyclohexanone and to 3- and 4-olefins **174** and **175** by employing only four equivalents of lithium metal³². When the reduction is, however, conducted with an excess of metal, cyclohexanone and *N,N*-dimethylcyclohexylamine are obtained, without any **174** and **175**³².

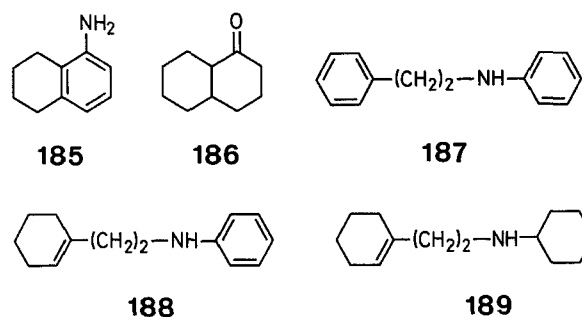


Treatment of *o*-toluidine with lithium/*t*-butyl alcohol/ammonia affords unsaturated ketones, probably **180** and **181**⁶⁴. These ketones are also obtained by reduction of *N,N*-dimethyl-*o*-toluidine using sodium/ethanol/ammonia⁹⁰. Similar reduction of *N,N*-dimethyl-*m*- and *p*-toluidines gives enones **182** and **183**, respectively⁹⁰. Reductions of *o*-, *m*- and *p*-toluidines with lithium in ethylamine, though, lead to the isomeric methylcyclohexylamines in which all groups are equatorial^{32,68}; thus, *p*-toluidine affords amine **184**.

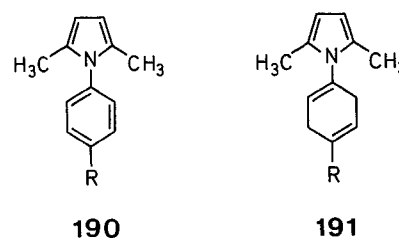


7.2. Reduction of Miscellaneous Amines

1-Aminonaphthalene and its *N,N*-dimethyl derivative are reduced by lithium in low molecular weight amines to give tetrahydro derivative **185**, $\Delta^9(10)$ -octalin (**4**) and α -decalone (**186**), respectively⁶⁸. That the 1-aminonaphthalene gives less extensive reduction is ascribed to the fact that the *N*-lithio salt is probably formed first; the negatively charged nitrogen atom then precludes reduction of the ring bound to it. Emphasis is laid on this point by similarly reducing amine **187** to obtain **188** and **189** in yields of 46% and 10%, respectively⁶⁸.



Finally, certain pyrrole derivatives (**190**, R = H, CH₃) have been reduced by sodium/ethanol/ammonia to give dihydro derivatives **191** (R = H, CH₃)⁹¹.



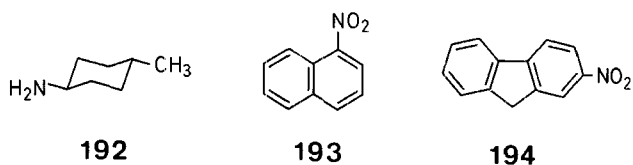
Reduction of 2,5-Dimethyl-1-phenylpyrrole (**190**)⁹¹:

2,5-Dimethyl-1-phenylpyrrole (**190**, R = H) (3.42 g) in hot methanol (8 ml) is added to liquid ammonia (150 ml). After the addition of sodium (2.6 g) in small pieces, the reaction mixture is diluted with water (50 ml) and the product (3.14 g) is collected by filtration. Crystallization from methanol gives 1-(cyclohexa-1,4-dienyl)-2,5-dimethylpyrrole (**191**, R = H); m. p. 60–62°.

¹⁰¹ E. WENKERT, B. G. JACKSON, J. Amer. Chem. Soc. **80**, 217 (1958).

8. Reduction of Aromatic Nitro Compounds

Only a small number of aromatic nitro compounds appear to have been subjected to Birch or Benkeser reductions. Thus, nitrobenzene and *p*-nitrotoluene have been converted to the corresponding anilines by sodium/methanol/ammonia⁹² and lithium/methylamine⁶⁸, respectively. When *p*-nitrotoluene is reduced by lithium/ethylamine, *p*-toluidine and 1-amino-4-methylcyclohexane (**192**) are formed⁶⁸.



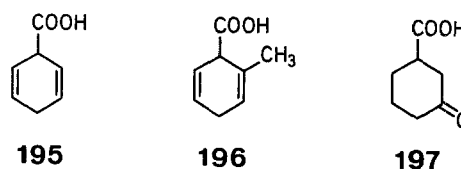
1-Nitronaphthalene (**193**) has been found to be only partially converted to 1-aminonaphthalene using sodium/ammonium bromide/ammonia⁹²; however, the use of sodium/methanol/ammonia gives di- and tetrahydro-1-aminonaphthalenes of undetermined structure⁹²; Under the latter conditions, 2-nitrofluorene (**194**) is similarly converted to tetra- and hexahydro-2-aminofluorenes⁹².

9. Reduction of Carboxylic Acids and their Derivatives

Birch reductions of aromatic carboxylic acids and certain of their derivatives seem unique because 1,4- rather than 2,5-dihydro products are obtained, apparently because the carboxyl group is the only electron-withdrawing functional group that is not reduced before the aromatic ring. Application of the Benkeser procedure to such acids also leads to reduction of the aromatic ring, but the structure of the products has not yet been elucidated. Certain reductions of aliphatic acids afford aldehydes involving reduction of the carboxyl group.

9.1. Reduction of Aromatic Acids

Benzoic acid has been reduced by sodium in methanol⁹³ or ethanol^{25,94} and ammonia to give 1,4-dihydrobenzoic acid (**195**). Similar reduction of this acid with lithium/methylamine is reported to give reduction of both the aromatic ring and the carboxyl group⁹⁵; however, the use of ammonium nitrate as a co-reagent unexpectedly gives benzaldehyde in low yield. Benzoic acid derivatives like *o*-methylbenzoic acid and *m*-methoxybenzoic acid are also reduced by sodium/ethanol/ammonia to dihydro derivative **196** and ketoacid **197**, respectively⁹⁶. Other similar reductions are known^{4,5}.

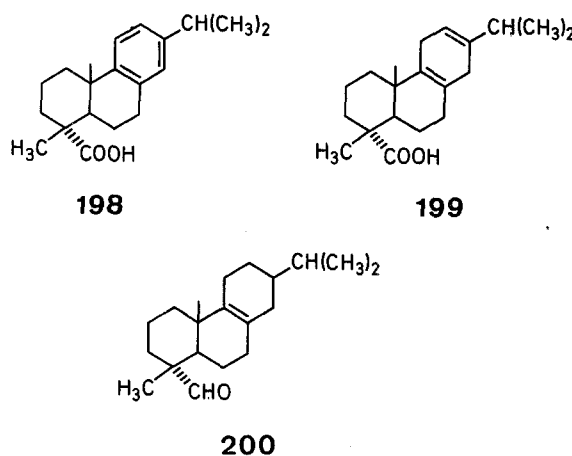


Birch Reduction of Benzoic Acid⁹³:

To a solution of benzoic acid (10.0 g) and methanol (30 g) in anhydrous liquid ammonia (300 ml) at -75° (cold bath) is added under a stream of nitrogen 6.0 g of sodium in pea-sized particles; 70 min are sometimes required. Toward the end of the reaction, the blue color of the solution disappears rather quickly. To the resulting white suspension is added solid ammonium chloride (50 g) followed by cold water (70 ml). After removing the ammonia in vacuum and the addition of water (30–50 ml), the salt suspension is treated with peroxide-free ether (100 ml). On cooling to -20° , the ethereal solution is treated with 20% hydrochloric acid. The product is extracted into ether; the extracts are then washed with water, dried (MgSO_4), and concentrated to give 8.5–9.0 g of **195**; m. p. $10\text{--}15^{\circ}$ (from butyric acid at -20°).

9.2. Reduction of Aliphatic Carboxylic Acids

Dehydroabietic acid (**198**), a compound containing an aromatic ring and a carboxyl group, is reduced by lithium/*t*-amyl alcohol/ethylamine to give dihydro derivative **199** in excellent yield⁹⁷. A similar reduction of **198** with lithium in ethylamine in the absence of alcohol affords chiefly aldehyde **200**⁹⁷ which is apparently formed via a base-stable intermediate^{97,98}.



The above reduction of a carboxylic acid to an aldehyde has been extended to other aliphatic acids; however, an early report suggests the method to be of little synthetic value⁹⁹. Thus, except for lauric and stearic acids, lithium/ethylamine reductions of compounds like cyclohexanecarboxylic acid (**201**) and *n*-octanoic acid give the corresponding aldehydes

¹⁰⁴ A. J. BIRCH, J. CYMERMAN-CRAIG, M. SLAYTON, *Aust. J. Chem.* **8**, 512 (1955).

¹⁰⁵ R. A. BENKESER, H. WATANABE, S. J. MELS, M. A. SABOL, *J. Org. Chem.* **35**, 1210 (1970).

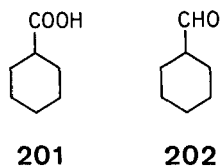
¹⁰⁶ H. L. LOCHTE, J. HORECZY, P. L. PICKARD, A. D. BARTON, *J. Amer. Chem. Soc.* **70**, 2012 (1948).

¹⁰⁷ D. H. R. BARTON, C. H. ROBINSON, *J. Chem. Soc.* **1954**, 3045.

¹⁰² P. MARKOV, K. IVANOV, *Tetrahedron Lett.* **1962**, 1139.

¹⁰³ G. R. CLEMO, T. J. KING, *J. Chem. Soc.* **1948**, 1661.

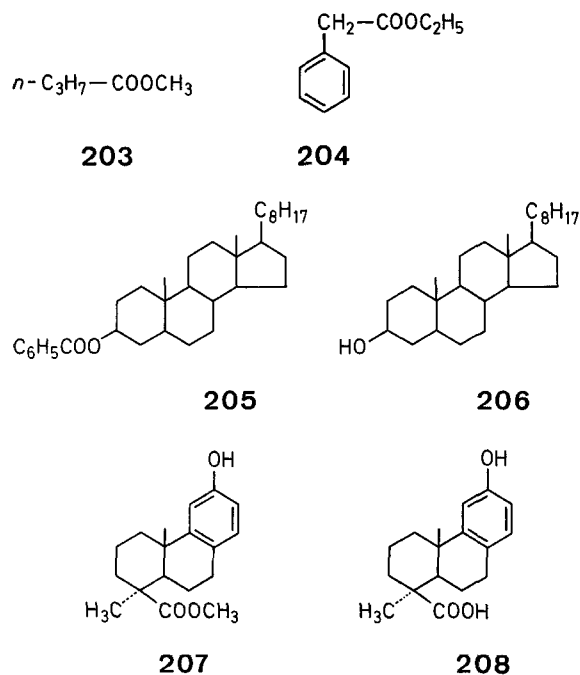
(for example, **202**) in only low yields⁹⁹. It is important to note that the above reactions have been neutralized with ammonium chloride, a strong acid in ethylamine, and no attempt has been made to extract nitrogen containing products.



More recently, it has been found that such conversions of acids to aldehydes by lithium in ethylamine proceed via imines which probably form upon mild hydrolysis of α -hydroxyamines⁹⁵. Because of this realization, the yields of the reductions have been considerably enhanced, ranging from 59 to 84%; for example, pentanoic acid is converted to pentanal in 66% yield⁹⁵.

9.3. Reduction of Esters

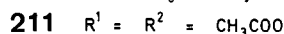
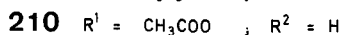
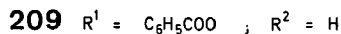
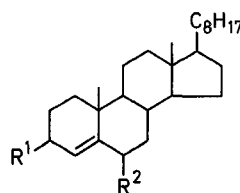
Simple, aliphatic esters are reduced by either sodium/alcohol/ammonia or by lithium in amines to alcohols in a Bouveault-Blanc-reaction. Thus, methyl *n*-butyrate (**203**) and ethyl phenylacetate (**204**) are converted by sodium/ethanol/ammonia to *n*-butyl alcohol and β -phenylethyl alcohol (**166**), respectively¹⁰⁰. Many other examples are known¹⁰⁰. Similarly, lithium/ethylamine reduction of cholestanyl benzoate (**205**) gives rise to cholestan-3-ol (**206**)⁶⁰. Certain esters have been found to undergo hydrolysis on reaction with lithium in ammonia in the absence of alcohol; ester **207** is thus converted to podocarpic acid (**208**) by means of this reagent¹⁰¹. It should be noted that the aromatic ring is not reduced in this reaction.



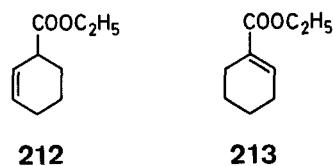
Reduction of Cholestanyl Benzoate⁶⁰:

Cholestanyl benzoate (0.2 g) dissolved in dry ethylamine (10 ml) in a glass-stoppered bottle is reduced by lithium (50 mg) cut into small pieces. After the initial effervescence has ceased, the stopper is fitted firmly and the mixture shaken vigorously until a blue color persists. The bottle is cooled to 0° before opening and the steroid is then isolated with ether in the usual way. Chromatography of the product on 10 g of alumina using benzene/ether (9:1) as eluent affords cholestan-3-ol **206** (0.11 g); m. p. 140–141°.

Allylic esters are also susceptible to deacylation using lithium in either ammonia or in ethylamine⁶⁰. Thus, reduction of 3 β -benzoyloxycholest-4-ene (**209**, R¹ = C₆H₅COO, R² = H) with this metal in ammonia gives cholest-4-ene (**149**); poor solubility of **209** in ammonia, though, results in only a low yield of **149**⁶⁰. The same conversion, however, can be effected in good yield with lithium in ethylamine, a solvent in which **209** is much more soluble. Olefin **149** is also obtained by lithium/ethylamine reductions of 3 β -acetoxycholest-4-ene (**210**, R¹ = CH₃COO, R² = H) and 3 β ,6 β -diacetoxycholest-4-ene (**211**, R¹ = R² = CH₃COO)⁶⁰.



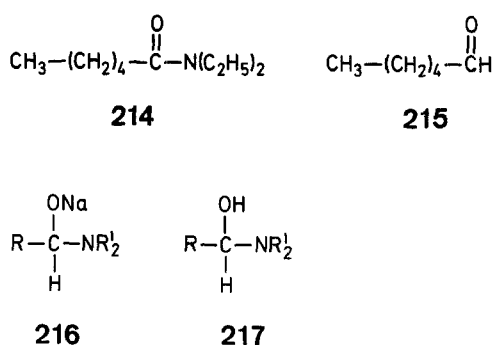
Two reductions of ethyl esters of benzoic acid deserve special mention since they seem to give rise to unexpected products. Thus, reduction of ethyl benzoate and of ethyl *p*-methylbenzoate by magnesium/ethanol/ammonia strangely give rise to monoolefins **212** and **213**, respectively¹⁰². It seems surprising that monoolefins are formed instead of dienes and that the ester groups seem not to be reduced.



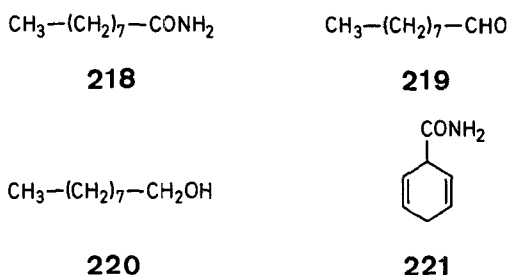
9.4. Reductions of Carboxamides

Aliphatic amides have been known to undergo reduction by sodium/alcohols/ammonia for some time to afford aldehydes. Thus, reduction of strychnine to an aldehyde by means of sodium/ethanol/ammonia apparently proceeds via an intermediate α -hydroxyamine¹⁰³. Later, it has been demonstrated that the amount of aldehyde formed in such reductions is a function of the acid strength of the proton donor, more aldehyde being isolated with acetic acid (am-

monium acetate) than with ethanol¹⁰⁴. Thus, reduction of N,N-diethylhexanamide (**214**) with sodium/acetic acid/ammonia gives hexanal (**215**) in 53% yield; the use of ethanol, though, gives **215** in only 23% yield. It has been suggested that such reductions proceed via intermediates like **216** which can be protonated by stronger proton donors to give α -hydroxyamines like **217**; **217** then resists further reduction, and its hydrolysis leads to aldehydes. It has further been suggested that if **216** is not protonated, it loses NaNR'_2 to give an aldehyde in the presence of sodium which is then reduced to the alcohol¹⁰⁴; no alcohols have however been isolated by these workers¹⁰⁴.



Lithium/amine reductions of aliphatic amides have been accomplished electrocatalytically using lithium chloride and methylamine in an undivided electrolysis cell¹⁰⁵. These reductions are profoundly affected by the presence or absence of ethanol, aldehydes or alcohols being obtained, respectively¹⁰⁵. For example, such electrolyses of nonanamide (**218**) with and without ethanol give nonanal (**219**) and nonanol (**220**), respectively. N-Methyl- and N,N-dimethylamides behave similarly¹⁰⁵.



Finally, benzamide has been converted to its 1,4-dihydro derivative (**221**) by sodium/*t*-butyl alcohol/ammonia⁹⁴ and by magnesium/ethanol/ammonia¹⁰². Other aromatic amides react analogously¹⁰².

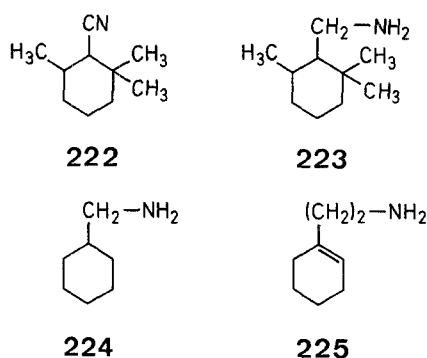
Reduction of Benzoylpiperidine:

The benzoylpiperidine (18.9 g) is dissolved in the proton source (e.g., acetic acid, slightly more than theoretically required) and added to 70 ml of liquid ammonia. Sodium (0.021 mol) is added in small pieces. When the sodium has reacted, ammonia is evaporated and the mixture acidified to congo paper with dilute hydrochloric acid. The resulting solution is extracted with ether and distilled to give 8.2 g (68%) of benzaldehyde: b. p. 70°/15 mm; 2,4-dinitrophenylhydrazone: m. p. 235°.

9.5. Reduction of Nitriles

Reduction of nitriles by either Birch or the Benkeser methods leads to "hydrogenation" of the nitrile to give amines. Although aromatic rings present in the latter reactions are also reduced, no aromatic nitriles appear to have been subjected to the Birch reduction; however, dihydro products would be expected from such reactions.

Three nitriles have been reduced. Thus, reduction of nitrile **222** with sodium/methanol/ammonia¹⁰⁶ and of benzonitrile with lithium in ethylamine⁵⁶ gives amines **223** and **224**, respectively. Similar reduction of phenylacetone nitrile with lithium in ethylamine gives mostly **225**⁵⁶.



10. Reduction of Ketones and their Derivatives

Although enolizable ketones seem not to be reduced by alkali metals in ammonia without added proton donors, such reactions can be realized to give alcohols in the presence of "acids" and by lithium/amine reagents. When "acids" are not present in the former system, enolates are formed which resist reduction by the less potent ammonia system. When aromatic rings are also present, they are reduced by the Benkeser but not by the Birch method. When cyclic ketones are converted to alcohols, the hydroxy group usually assumes the more stable equatorial position¹⁰⁷.

10.1. Reduction of Aliphatic Ketones and Imines

Several 11-keto steroids have been converted to 11- α -hydroxy compounds in high yield by lithium/methanol/ammonia in which the hydroxy groups are

¹⁰⁸ F. SONDEIMER, O. MANCERA, G. ROSENKRAZ, C. DJERASSI, *J. Amer. Chem. Soc.* **75**, 1282 (1953).

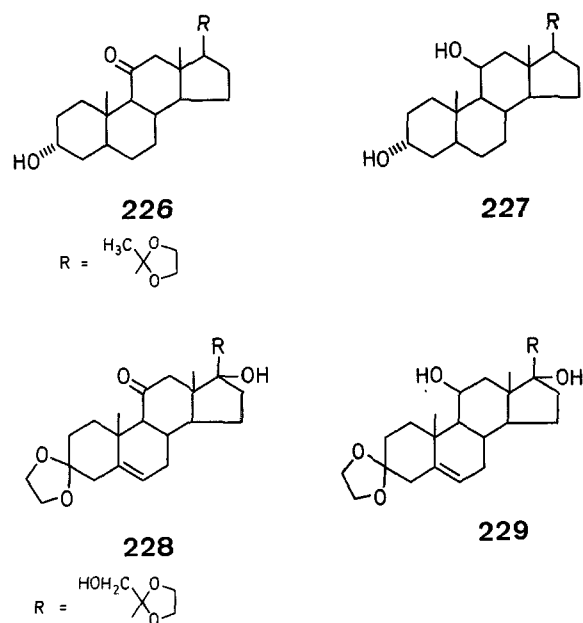
¹⁰⁹ S. BERNSTEIN, R. LITTELL, J. H. WILLIAMS, *J. Amer. Chem. Soc.* **75**, 1481 (1953).

¹¹⁰ J. W. HUFFMAN, J. T. CHARLES, *J. Amer. Chem. Soc.* **90**, 6486 (1968).

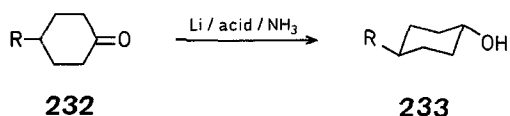
¹¹¹ G. OURISSON, A. RASSAT, *Tetrahedron Lett.* **1960**, 16.

¹¹² R. A. BENKESER, S. J. MELS, *J. Org. Chem.* **35**, 261 (1970).

equatorial^{108,109}. For example, pregnane derivative **226** has been converted to **227**, cortisone derivative **228** to **229**, and spirostenone **230** to **231** by lithium/methanol/ammonia¹⁰⁸. The latter example is interesting because in the absence of methanol, the olefinic double bond and ester group are reduced, but the keto group is not¹⁰⁸.

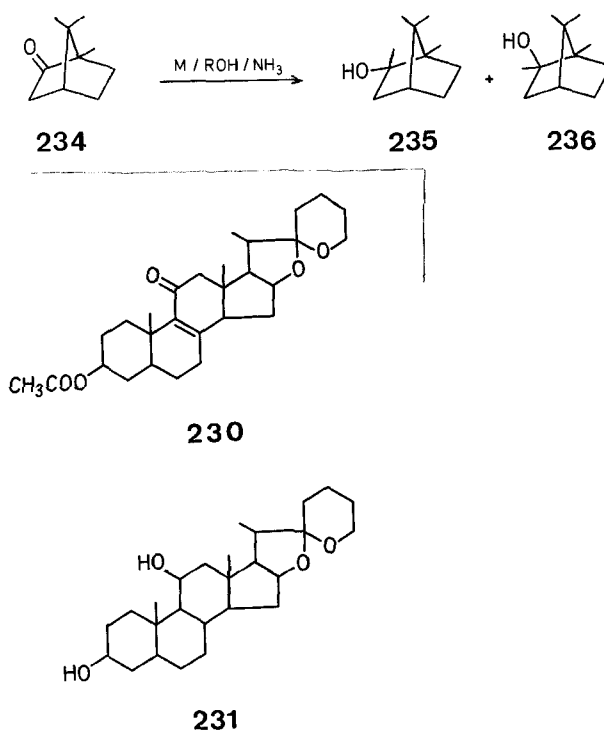


Another study further illustrates that Birch-type reductions of cyclic ketones usually lead to the more stable equatorial alcohol¹¹⁰. Thus, three 4-substituted cyclohexanes (**232**) have been converted to the corresponding alcohols (**233**) by lithium in ammonia in the presence of a variety of proton donors including ethanol, *n*-propyl alcohol, *t*-butyl alcohol, and ammonium chloride. Regardless of whether the 4-substituent is methyl, isopropyl, or *t*-butyl, and regardless of the acid, the percentage of the more stable equatorial alcohol ranges from 94 to 99%.



It has been suggested¹⁰⁷ that such reductions proceed via carbanions which can undergo inversion similar to the nitrogen atom in amines. The preferred configuration of such carbanions seems to be that which, on protonation, gives the most thermodynamically stable product, for example, equatorial rather than axial alcohols. However, the above rule may not be applied to strongly sterically hindered molecules; in this case the less stable product may be formed which has been demonstrated in reductions of camphor (**234**) to afford the more stable borneol (**235**) and the less stable isoborneol (**236**)¹¹¹. The amount of **236** is not only a function of steric hindrance in the ketone and its carbanion intermediate, but also of the proton donor. Thus, the percentage of **236** increases from 8% with ammonium chloride

to 42% with a large excess of ethanol¹¹¹. Similar results have been obtained with norcamphor¹¹⁰.



To illustrate lithium/amine reductions of ketones, 4-heptanone has been converted to the expected alcohol by lithium/ethylenediamine in fair yield²⁶. From a synthetic standpoint, a more recent report dealing with electrocatalytic reductions of aliphatic ketones in methylamine in an undivided cell is more useful. Thus, 2-heptanone, cyclohexanone, cyclopentanone, and others are converted to the corresponding alcohols in good to excellent yields by adding the ketone to lithium chloride/methylamine and electrolyzing immediately (Scheme H)¹¹². On the other hand, if the reagents are mixed and allowed to stand for six hours prior to electrolysis, the ketones are converted to *N*-methyl alkylamines in good yield¹¹². The results are rationalized simply since

¹¹³ A. D. BEDENBAUGH, J. H. BEDENBAUGH, J. D. ADKINS, W. A. BERGIN, *J. Org. Chem.* **35**, 543 (1970).

¹¹⁴ S. MEJER, L. JABLONSKI, B. BORATYNASKA, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.* **12**, 743 (1964); *C. A.* **62**, 10477 (1965).

¹¹⁵ A. S. HALLSWORTH, H. B. HENBEST, *J. Chem. Soc.* **1957**, 4604.

¹¹⁶ A. S. HALLSWORTH, H. B. HENBEST, *J. Chem. Soc.* **1960**, 3571.

¹¹⁷ H. C. BROWN, S. IKEGAMI, J. H. KAWAKAMI, *J. Org. Chem.* **35**, 3243 (1970).

¹¹⁸ S. D. DARLING, K. D. WILLS, *J. Org. Chem.* **32**, 2794 (1967).

¹¹⁹ D. P. BRUST, D. S. TARBELL, *J. Org. Chem.* **31**, 1251 (1966).

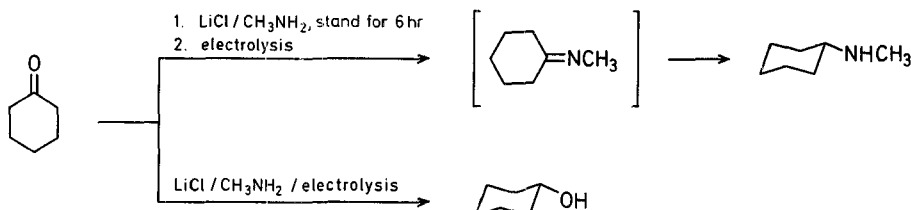
¹²⁰ L. H. BRANNIGAN, D. S. TARBELL, *J. Org. Chem.* **35**, 2339 (1970).

¹²¹ S. F. BIRCH, D. T. MCALLAN, *Nature* **165**, 899 (1950).

¹²² W. HÜCKEL, I. NABIH, *Chem. Ber.* **89**, 2115 (1956).

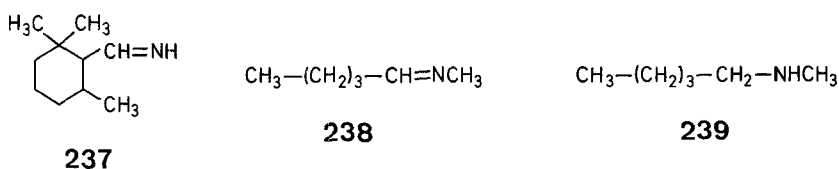
¹²³ W. A. REMERS, G. J. GIBS, C. PIDACKS, M. J. WEISS, *J. Org. Chem.* **36**, 279 (1971).

during the six hour waiting period, the ketones are converted to their N-methylimines which then undergo reduction to the amines¹¹².



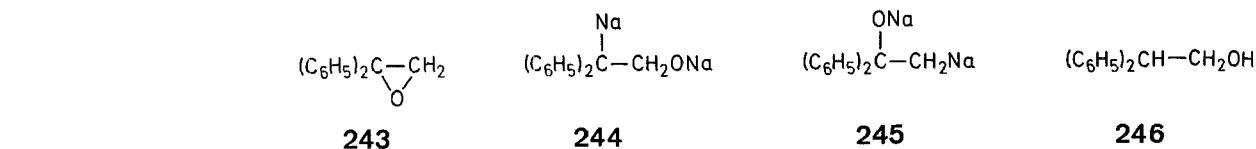
Scheme H

Incidentally, a few other imines have been reduced by Birch or Benkeser procedures to afford amines. Thus, imine **237** is converted to amine **223** by sodium/methanol/ammonia¹⁰⁶, and imine **238** is reduced to amine **239** by lithium/methylamine^{95, 113}.

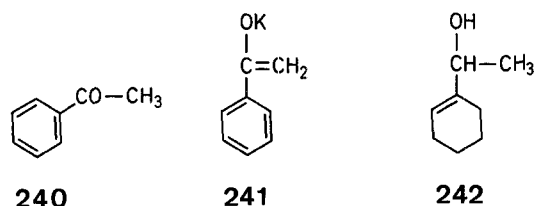


10.2. Reduction of Acetophenone

Acetophenone (**240**) has been subjected to reduction by excess potassium in ammonia in the presence of *t*-butyl alcohol and potassium *t*-butoxide⁷⁴. When the metal is added immediately to the mixture of the other reagents, ethylbenzene is obtained in good yield. On the other hand, when the addition of the metal is delayed for three hours, no reduction is observed and acetophenone is recovered. Presumably, the latter reaction mixture contains the enolate anion **241** which resists reduction⁷⁴. Lithium/methylamine reduction of acetophenone gives alcohol **242** generated by reduction of both the carbonyl group and the aromatic ring^{30, 56}. This result is in marked



contrast to the above Birch reduction which results in cleavage of the alcohol.



Reduction of Acetophenone⁷⁴:

a) A solution of potassium (2.6 g) in *t*-butyl alcohol (100 ml) is added to liquid ammonia (400 ml) with stirring followed by

addition of acetophenone (8.0 g). Reduction with 16.0 g of potassium gives 5.5 g of ethylbenzene; b. p. 136–137°, n_D^{20} 1.487, and 1.0 g of unchanged acetophenone; b. p. 202°.

b) A solution of potassium (3.25 g) in *t*-butyl alcohol (175 ml) is added to liquid ammonia (500 ml) followed by acetophenone (10.0 g) and the solution is left for 3 hr. Further treatment with 20.0 g of potassium has no observable effect, 5.5 g of acetophenone being recovered.

11. Reduction of Epoxides

Epoxides have been reductively cleaved not only by Birch and Benkeser systems, but also by alkali metals in ammonia to afford alcohols. In fact, the first cleavages of epoxides were realized with the latter system⁴, and more recently, they have been shown to proceed via the most stable of the two possible carbanion intermediates⁷⁷. Thus, for example, 1,1-diphenylethylene oxide (**243**) is cleaved by sodium in ammonia via **244**, rather than via **245** to give alcohol **246**; dianion **244** has been trapped with benzyl chloride⁷⁷. Lower yields of alcohols are obtained in the above reductions with either Birch or Benkeser types of reagents, however⁷⁷.

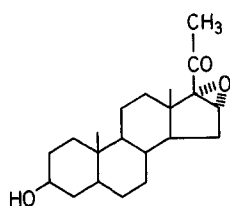
On the other hand, sodium/ethanol/ammonia reduction of 16 α ,17 α -epoxy-5 α -pregnan-3 β -ol-20-one (**247**) gives rise to 5 α -pregnane-3 β ,16 α ,20 α -triol (**248**)¹¹⁴; a related pregnene triol is also obtained by a similar reduction of an oxidopregnenone acetate (**249**)¹¹⁴. As above, these cleavages proceed via the most stable carbanion.

¹²⁵ N. J. LEONARD, C. K. STEINHARDT, C. LEE, *J. Org. Chem.* **27**, 4027 (1962).

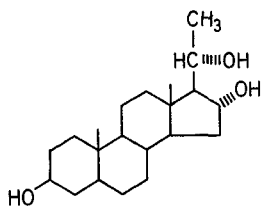
¹²⁶ A. J. BIRCH, D. NASIPURI, *Tetrahedron* **6**, 148 (1959).

¹²⁷ S. O'BRIEN, D. C. C. SMITH, *J. Chem. Soc.* **1960**, 4609.

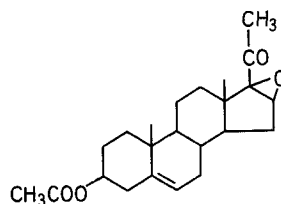
¹²⁴ A. P. GRAY, P. E. HEITMEIER, *J. Amer. Chem. Soc.* **80**, 6274 (1958).



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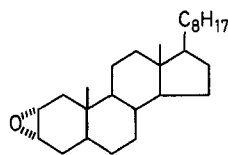


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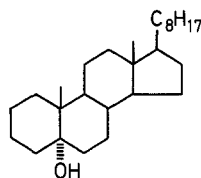


249

A variety of epoxysteroids have been similarly reduced by lithium in ethylamine^{115,116}. For example, 2 α ,3 α -epoxycholestane (**250**) and the corresponding 5 α ,6 α -derivative are converted to cholestan-3 α -ol (**206**) and cholestan-5 α -ol (**251**), respectively¹¹⁵. This method of reducing the related 7 α ,8 α -, and 9 α ,11 α -epoxysteroids is clearly superior to lithium aluminum hydride since the latter reagent fails to effect cleavage of these hindered epoxides¹¹⁵.



250



251

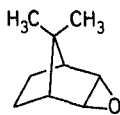
Reduction of 2 α ,3 α -Epoxycholestane¹¹⁶:

Reduction of 2 α ,3 α -epoxycholestane (0.15 g) with lithium (75 mg) in ethylamine (10 ml) gives a product which is chromatographed on deactivated alumina (10 g). Elution with 40–60° petroleum ether/benzene (1:1) gives 0.105 g of material from which cholestan-3 α -ol, m. p. 182°, [α] +27°, is obtained on one crystallization from ethanol.

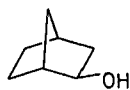
Certain non-steroidal epoxides have recently been reductively cleaved by lithium in ethylenediamine¹¹⁷. For example, norbornene oxide (**252**) and 7,7-dimethylnorbornene oxide (**253**) are reduced to norbornanol (**254**) and 7,7-dimethylnorbornanol (**255**) in excellent yields, respectively¹¹⁷. Several other reductions are listed. In these examples, at least, lithium in ethylenediamine is superior to lithium in ethylamine or to lithium aluminum hydride¹¹⁷.



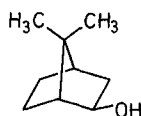
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253



254



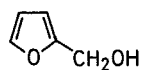
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Incidentally, certain aziridines similar to epoxides are converted to amines by sodium in ammonia⁷⁷.

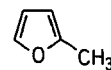
12. Reduction of Five- and Six-membered Heterocycles

12.1. Reduction of Furans

2-Furfuryl alcohol (**256**) has been reduced by sodium/ethanol/ammonia to 2-methylfuran (**257**) in 20% yield along with recovered **256**⁸¹. In contrast, **256** is reduced by the more potent lithium in methylamine, but the nature of the products is strongly dependent on the amount of lithium employed¹¹³. Thus, two equivalents of metal afford **257** in 52% yield. With increasing amount of metal, however, the yield of **257** decreases while the amount of products derived from ring-opening augments; such products are diverse and include alcohols, ketones, imines, and amines, and are too numerous to mention here¹¹³. Furan itself and 2-methylfuran (**257**) are reduced by lithium in methylamine to give a mixture of products¹¹³.

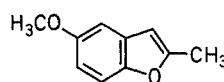


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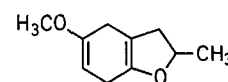


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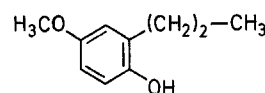
On the other hand, the reduction of other furan derivatives under Birch conditions usually does not result in cleavages of the heterocyclic ring provided that a sufficient quantity of alcohol is present. For example, furan **258** is converted to **259** in 70–80% yield using lithium in excess ethanol/ammonia but to **260** in good yield under similar conditions employing only two equivalents of ethanol¹¹⁸. Furan **261** is similarly converted to **262** in the presence of excess ethanol. Tetrahydrobenzofurans **259** and **262** are also obtained by reduction of **263** and **264**, respectively, using lithium in excess ethanol/ammonia¹¹⁸.



258

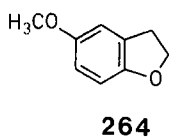
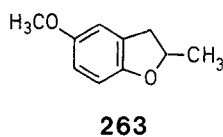
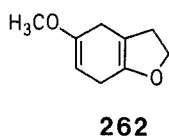
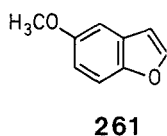


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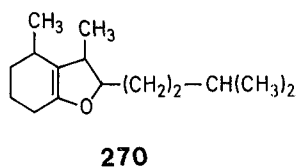
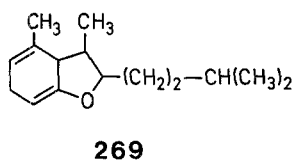
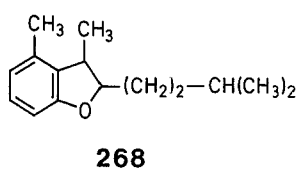
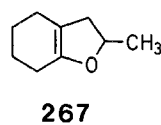
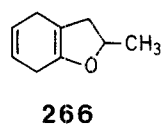
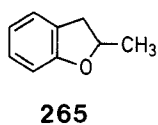


260

¹²⁸ H. DRESSLER, M. E. BAUM, J. Org. Chem. 26, 102 (1961).

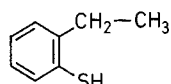
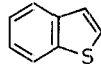


Birch reductions of two other benzofurans proceed similarly. Thus, lithium/*t*-butyl alcohol/ammonia reduction of **265** gives **266** and **267**¹¹⁹, while that of **268** affords **269** and **270**¹²⁰.



12.2. Reduction of Thiophenes

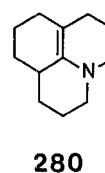
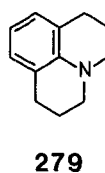
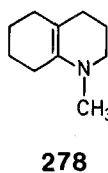
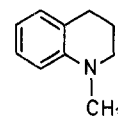
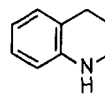
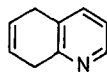
Thiophenes appear not to have been reduced by lithium/amine reagents though cleavage of the ring would be expected since sodium/methanol/ammonia reduction of thiophene itself gives dihydro derivatives **271** and **272** along with 1-mercapto-2-butene, isomeric *n*-butenes, and hydrogen sulfide¹²¹. In addition, sodium/ethanol/ammonia reduction of thianaphthene (**273**) gives ring-opened product **274** in good yield¹²².



12.3. Reduction of Quinolines and Indoles

Reduction of quinoline with lithium/methanol/ammonia gives **275** in low yield; interestingly, if the addition of methanol is delayed for 1 hr, the predominant reduction occurs in the other ring giving **276** in 36% yield¹²³. Similar results are obtained with 6-methoxyquinoline¹²³. More extensive reduction is realized with lithium in *n*-propylamine as

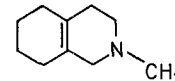
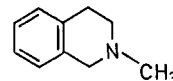
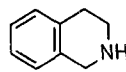
evidenced by the conversion of 1-methyl-1,2,3,4-tetrahydroquinoline (**277**) into octahydro derivative **278** and certain of its isomers^{124, 125}. Julolidine (**279**) has been similarly reduced by lithium in *n*-propylamine to **280** in good yield¹²⁵.



Reduction of Julolidine (**279**)¹²⁵:

A mixture of julolidine (25.1 g; 0.145 mol) dissolved in *n*-propylamine and 10.15 g (1.45 g atom) of ether-washed chopped lithium wire is diluted with *n*-propylamine (400 ml) and stirred under nitrogen (Dry ice condenser) for 12.5 hr. Unchanged lithium is removed and excess *n*-propylamine is distilled from the flask. The semi-solid residue is cooled in an ice-bath, overlaid with ether, and neutralized slowly with solid ammonium chloride. The mixture is diluted cautiously with water, the ether layer is separated, and the aqueous layer is extracted four times with ether. The residue obtained after evaporation of the ether extracts is distilled through a Vigreux column, yielding 23.7 g (92%) of impure 8,9,10,10a-tetrahydrojulolidine (**280**). This crude material is gas-chromatographed (6', 1/4 in o.d. column of 20% carbowax 20-M which has been washed with methanolic potassium hydroxide). Enamine **280** is present to the extent of 72%.

Birch and Benkeser reductions of isoquinolines are similar to those of quinoline. Thus, reduction of isoquinoline with sodium/ethanol/ammonia gives 1,2,3,4-tetrahydro derivative **281** while reduction with lithium in *n*-propylamine gives a mixture of tetrahydroisoquinolines¹²⁶. Reduction of 1,2,3,4-tetrahydro derivative **282** with the latter reagent gives octahydro derivative **283** in 61% yield¹²⁴.



Reduction of Isoquinoline¹²⁶:

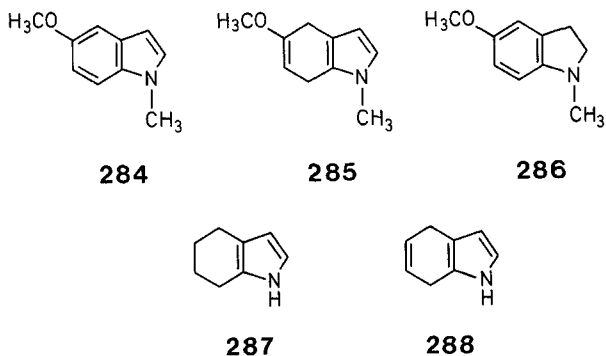
To a solution of 12.5 g of isoquinoline in 450 ml of liquid ammonia and 70 ml of ethanol is added 10.0 g of sodium in small pieces over 5 min. After evaporation of the ammonia, water is added and the product is worked-up in the usual way to give 1,2,3,4-tetrahydroisoquinoline (**281**) as an almost colorless oil; yield: 11.5 g; b.p. 118–120°/10 mm.

Finally, 1-methyl-5-methoxyindole **284** is reduced by lithium/methanol/ammonia to **285** in good yield; in the absence of methanol, however, the aromatic ring is not reduced and **286** is obtained¹²³. Indole itself is also reduced by lithium/methanol/ammonia

¹²⁹ R. C. KRUG, S. TOCKER, *J. Org. Chem.* **20**, 1 (1955).

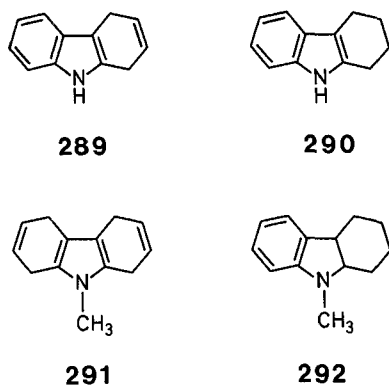
¹³⁰ S. CHANDRA, U.S. At. Energy Comm., TID-21381 (1961); *C. A.* **62**, 14455 (1965).

to give **287** and **288**¹²³. Similar products are formed in the reduction of 1-methylindole with sodium/ethanol/ammonia¹²⁷.



12.4. Reduction of Carbazoles

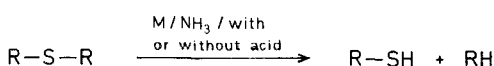
Carbazole is reduced by sodium/ethanol/ammonia to 1,4-dihydrocarbazole (**289**)¹²⁷, and by lithium in *n*-propylamine or in ethylenediamine to 1,2,3,4-tetrahydrocarbazole (**290**)¹²⁸. 9-Methylcarbazole is reduced by the above Birch reagent to 1,4,5,8-tetrahydro derivative **291**¹²⁷ and by the above Benkeser reagents to **292**¹²⁸.



13. Reduction of Miscellaneous Sulfur Compounds

Thioethers are reduced by metals with or without proton donors in ammonia^{82,129,130} and by lithium in methylamine^{131,132,133} to give a hydrocarbon and a mercaptan. Similar reductions of sulfones with the latter reagent afford a hydrocarbon and a sulfinate salt. Benkeser reagents appear to give rise to higher yields than the Birch systems.

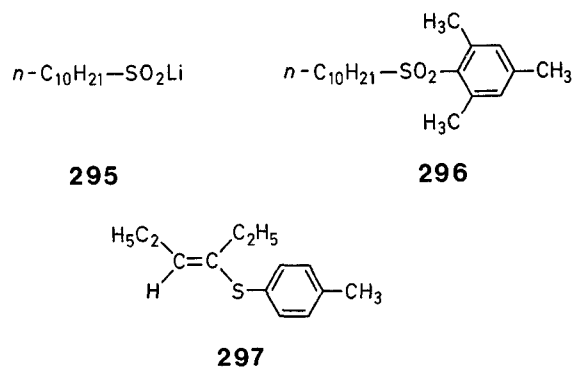
A few specific examples follow. Thus, treatment of di-*n*-propyl-, di-*n*-butyl-, or di-*n*-hexyl sulfides with sodium, lithium, or beryllium in ammonia with or without ammonium chloride, ammonium bromide, or ammonium sulfate gives one equivalent each of the corresponding mercaptan and hydrocarbon in yields up to 35%¹²⁹.



Similarly, di-*n*-decyl sulfide is cleaved by lithium in methylamine to give *n*-decylmercaptan (**293**) and *n*-decane in yields of 86% and 85%, respectively¹³¹. Aryl alkyl sulfides seem to be always cleaved by the Benkeser method to give the aromatic mercaptan and the aliphatic hydrocarbon¹³². Thus, *p*-tolyl *n*-butyl sulfide is cleaved to *p*-tolylmercaptan (**294**) in quantitative yield¹³².



Sulfones behave similarly towards lithium in amines, but are not effectively cleaved in ammonia. Thus, di-*n*-decyl sulfone is cleaved by lithium in methylamine to lithium *n*-decylsulfinate (**295**) in 90% yield¹³¹. In the case of aryl alkyl sulfones, reduction usually gives the aliphatic sulfinate salt and the aromatic hydrocarbon. For example, mesityl *n*-decyl sulfone (**296**) is cleaved to mesitylene and **295**¹³¹.



Finally, *cis*-vinyl sulfide **297** is reduced by lithium in methylamine and by lithium or sodium in ammonia¹³³. With the former reducing medium, **297** gives *cis*- and *trans*-3-hexene in 33% and 67% yield, respectively. Interestingly, reduction of **297** with lithium in ammonia gives *cis*- and *trans*-3-hexene in 82% and 18% yield, respectively¹³³. Thus, the latter system is more stereospecific than the former.

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¹³¹ W. E. TRUCE, D. P. TATE, D. N. BURDGE, J. Amer. Chem. Soc. **82**, 2872 (1960).

¹³² W. E. TRUCE, J. J. BREITER, J. Amer. Chem. Soc. **84**, 1621 (1962).

¹³³ W. E. TRUCE, J. J. BREITER, J. Amer. Chem. Soc. **84**, 1623 (1962).