tone–methanol: m.p. 115–117°, α_D +6.5° Chf (*c* 1.07), λ^{Chf} 2.9 μ. A solution of the stenol in chloroform gives a bright yellow color with tetranitromethane; the Liebermann–Burchard test is deep brown.

Anal. Calcd. for $C_{27}H_{46}O$ (386.64): C, 83.87; H, 11.99. Found: C, 83.90; H, 11.81.

CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

A Superior Method for Reducing Phenol Ethers to Dihydro Derivatives and Unsaturated Ketones

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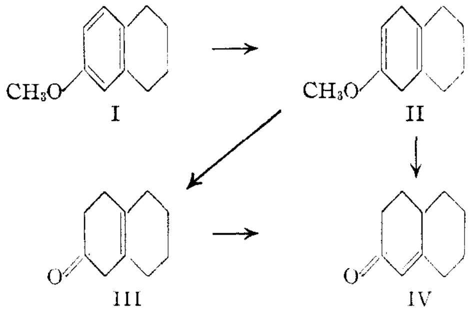
A new procedure has been developed for reduction of phenolic ethers to dihydro enol ethers, suitable for cleavage to β,γ- or α,β-unsaturated ketones. This method, using lithium in liquid ammonia and a cosolvent (ether or 1,2-dimethoxyethane) and adding alcohol last, is a more powerful reduction method than that of Birch; it has given markedly superior yields with 4-cyclohexylanisole, 4-cyclohexylphenoxyethanol, 1-methoxy-5,6,7,8-tetrahydronaphthalene, estradiol-3-methyl ether and hexahydrohexestrol monomethyl ether. It is at least as good as the Birch sodium procedure with the easily reducible compounds anisole and 2-methoxy-5,6,7,8-tetrahydronaphthalene. With the difficultly reducible 1-methoxytetrahydronaphthalene it is shown that the concentration of lithium metal and rate of addition of alcohol are critical factors. These and other observations are discussed in relation to the possible mechanism for the reduction.

The reduction of a phenolic ether to its dihydro derivative, by the action of sodium and alcohol in liquid ammonia, was first described by Wooster for anisole.[2] During the past nine years this reaction has been clarified, improved and utilized extensively by Birch and his associates.[3] In most favorable examples Birch's procedure gives excellent yields of the dihydro compound which, being an enol ether, can be hydrolyzed easily to a β,γ-unsaturated ketone. The latter frequently can be isomerized to the corresponding α,β-unsaturated ketone. Thus, 2-methoxytetrahydronaphthalene (I) was reduced to the enol ether II which was hydrolyzed to Δ^{9-10}-2-octalone (III) or Δ^{1-9}-2-octalone (IV), isolated as the 2,4-dinitrophenylhydrazones in yields as high as 82% based on I.[4] In certain other examples, however, the method has failed or given low yields.



We became interested in further perfecting and applying the method to certain rather insoluble and unreactive phenolic ethers, in order to convert them to unsaturated ketones, as intermediates for synthesis and as part of a program of preparing analogs of the non-aromatic steroidal hormones, under investigation in this Laboratory over the past twelve years.[5] 4-Cyclohexylanisole (V) has served as a useful example of a moderately difficult type suitable for studying this reduction, and its use has led to a simple but much more potent method than that of Birch.

The application of Birch's conditions to 4-cyclohexylanisole (V), *viz.*, addition of sodium metal to a mixture of liquid ammonia, alcohol and phenolic ether, gave little or no reduction, 95% of the starting ether being recovered. Moreover, the use of ether as a cosolvent, beneficial in other cases of compounds insoluble in ammonia at −33°,[6] and replacement of ethanol by methanol or the slower reacting isopropyl alcohol failed to give reduction. Indeed the latter modification applied to 4-methoxybiphenyl gave some reduction of the *non-oxygenated* ring affording 4-cyclohexylanisole in small yield.

Birch has found it necessary with hexestrol and estradiol to prepare derivatives more soluble in ammonia than the methyl ethers, such as the monoethers of ethylene glycol or glycerol, in order to obtain reduction in moderate yields.[7] In the present work the use of the β-hydroxyethyl ether of 4-hydroxybiphenyl resulted in a mixture which contained cyclohexylbenzene, the hydroxyethoxy group having been eliminated during reduction.[8] Evidently the remainder of the product did not contain the desired enol ether since no dinitrophenylhydrazone could be prepared from it. On the other hand, the hydroxyethyl ether of 4-cyclohexylphenol did give some reduction to the enol ether since a crude dinitrophenylhydrazone could be isolated in 19% yield. The limited extent of reduction, however, served to underline the inadequacy of the Birch method in this case.

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[1] Wisconsin Alumni Research Foundation Research Assistant, 1949–1950; Syntex Fellow, 1950–1951; Homer Adkins Fellow, 1951–1952.

[2] C. B. Wooster, U. S. Patent 2,182,242 (Dec. 5, 1939); see also C. B. Wooster and K. L. Godfrey, THIS JOURNAL, **59**, 596 (1937).

[3] (a) A recent reference: A. J. Birch, J. A. K. Quartey and H. Smith, *J. Chem. Soc.*, 1768 (1952); (b) reviewed by A. J. Birch, *Quart. Rev.*, **4**, 69 (1950), and (c) G. W. Watt, *Chem. Revs.*, **46**, 317 (1950).

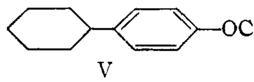
[4] A. J. Birch, *J. Chem. Soc.*, 430 (1944); 593 (1946); and Experimental of present paper.

[5] See, for example, A. L. Wilds and C. H. Shunk, THIS JOURNAL, **72**, 2388 (1950); also M. A. Spielman and P. G. Carpenter, unpublished work; see P. G. Carpenter, Ph.D. Thesis, University of Wisconsin, 1941.

[6] See J. C. Sheehan and G. D. Laubach, THIS JOURNAL, **72**, 2478 (1950).

[7] A. J. Birch and S. M. Mukherji, *J. Chem. Soc.*, 2531 (1949).

[8] Birch has also observed cases of elimination of the oxygen-containing group, *J. Chem. Soc.*, 102, 1642 (1947).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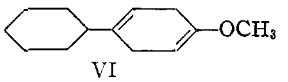
VI

On the assumption that the failures with sluggishly reduced compounds were due in part to an unfavorable competition between the reduction and simple liberation of hydrogen from the alcohol and metal, we were led to try addition of the alcohol *last* to the blue solution of sodium and cyclohexylanisole (V) in ammonia and ether.[9] Reduction now proceeded to an appreciable extent, and 35% of the dinitrophenylhydrazone could be isolated. In searching for a more potent metal, preliminary experiments with potassium (added last) showed little improvement over sodium.[10] We were pleased to discover, however, that lithium, with addition of the alcohol last, gave reduction of 4-cyclohexylanisole (V) to the crystalline dihydro derivative VI in 84–88% yields. This procedure has now been developed into an excellent and relatively general reduction method for a variety of difficultly reducible examples, as well as for types which reduce well under the previous conditions.

2-Methoxytetrahydronaphthalene (I) was reduced by the lithium procedure to the hexahydro derivative II in 90% yield, comparable to the 80–90% yields obtained with sodium in the present work. Anisole gave the 2,5-dihydro derivative in 84% yield with lithium, which probably is superior to the yield with sodium.

1-Methoxy-5,6,7,8-tetrahydronaphthalene (VII) provided a good test for the new procedure, since Birch reported that it gave only a trace of the reduction product by his method.[4] Using 1,2-dimethoxyethane as the cosolvent, the lithium method gave a mixture corresponding to 83–93% reduction, judging from the ultraviolet spectrum. The α,β-unsaturated ketone X was isolated in 55–58% yield as the dinitrophenylhydrazone. It was apparent that some of the conjugated enol ether isomeric with VIII also had been formed, for the further reduction products were present. These included some 10–16% of octalin, the result of elimination of the methoxyl group and shown by addition of nitrosyl chloride to be mainly the Δ^{9-10}-isomer (IX) with a trace of the Δ^{1-9}-isomer. In addition 7% of 1-decalone (XI) was isolated as the dinitrophenylhydrazone, evidently arising from further reduction of the $\Delta^{1-2,9-10}$ or $\Delta^{1-9,4-10}$-enol ether to the Δ^{1-9}-derivative. In spite of the difficult reduction in this example, only a trace (2%) of demethylation to 1-hydroxytetrahydronaphthalene occurred. Recently Birch, Murray and Smith[11] have reported obtaining some hydrocarbon and 1-decalone as well as 33% of the unsaturated ketone X from reduction with sodium of the hydroxyethyl ether corresponding to VII.

We have also found the new lithium procedure to give excellent results in the reduction of estradiol-3-methyl ether, affording a superior route to 19-nortestosterone as reported in the accompanying paper.[12] Our method has given good results in the hands of others,[13] and has been used in modified form by Miramontes, Rosenkranz and Djerassi to prepare 19-norprogesterone.[14]

Finally, it should be noted that we have found lithium to be advantageous for other reductions in liquid ammonia, particularly for controlling the stereochemistry of reduction of unsaturated ketones, such as that of 4-cholestene-3-one to the A:B *trans*-alcohol.[15] Further modifications of our method recently have been developed by the Merck[16] and Syntex[17] research groups for selective reduction of 11-keto-Δ^8-steroids to 11-ketosteroids with the natural configuration at C-8 and C-9.

We now turn to the interesting question of how these metal–ammonia reductions may proceed and the reasons for superior results using lithium and adding the alcohol last. It appeared *a priori* that these results were consistent with initial formation of a stable dilithium addition compound, convertible by alcohol to the dihydro derivative—a reasonable postulate in harmony with much work on alkali–metal reactions.[18] The additional time before destruction of the excess metal by alcohol provided by the new procedure, the greater tendency for lithium to form addition compounds (compared to sodium),[19] and the greater covalent character of the carbon–lithium bond[20] all would favor higher yields with lithium in terms of this mechanism. Attempts to obtain direct evidence for a stable lithium addition compound by treatment with carbon dioxide (after removal of ammonia, leaving the cosolvent, and before addition of methanol) were unsuccessful either with the easily reduced 2-methoxytetrahydronaphthalene or with 4-cyclohexylanisole. In each case the total amount of alkali-soluble material was only 1%, much of which was the corresponding phenol. On the other hand, some reduction took place, 18 and 31%, respectively; probably this occurred after the carbonation step when the finely divided lithium was destroyed with methanol.[21] The major material, however, was the starting ether.

It cannot be held that these results constitute conclusive evidence against the dilithium addition product hypothesis, since it is possible that the

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[9] Birch has implied that it is necessary for the alcohol to be present initially in excess, to avoid demethylation.

[10] Birch has reported potassium to be somewhat better than sodium in reducing estradiol 3-glyceryl ether, *J. Chem. Soc.*, 367 (1950).

[11] A. J. Birch, A. R. Murray and H. Smith, *J. Chem. Soc.*, 1945 (1951).

[12] A. L. Wilds and N. A. Nelson, This Journal, **75**, 5366 (1953).

[13] (a) W. S. Johnson and C. F. Allen, (b) A. S. Dreiding, private communications.

[14] L. Miramontes, G. Rosenkranz and C. Djerassi, This Journal, **73**, 3540 (1951).

[15] A. L. Wilds and R. Daniels; *cf.* Wilds, Abstracts, 120th Meeting A.C.S., New York, N. Y., Sept. 4–7, 1951, p. 20M. The details will be published in a future paper.

[16] E. Schoenewaldt, L. Turnbull, E. M. Chamberlin, D. Reinhold, A. E. Erickson, W. V. Ruyle, J. M. Chemerda and M. Tishler, This Journal, **74**, 2696 (1952).

[17] F. Sondheimer, R. Yashin, G. Rosenkranz and C. Djerassi, *ibid.*, **74**, 2696 (1952).

[18] (a) See R. Willstätter, F. Seitz and E. Bumm, *Ber.*, **61**, 871 (1928); (b) W. Schlenk and E. Bergmann, *Ann.*, **463**, 1 (1928), etc.

[19] Reference 18b, p. 84ff.

[20] M. T. Rogers and A. Young, This Journal, **68**, 2748 (1946).

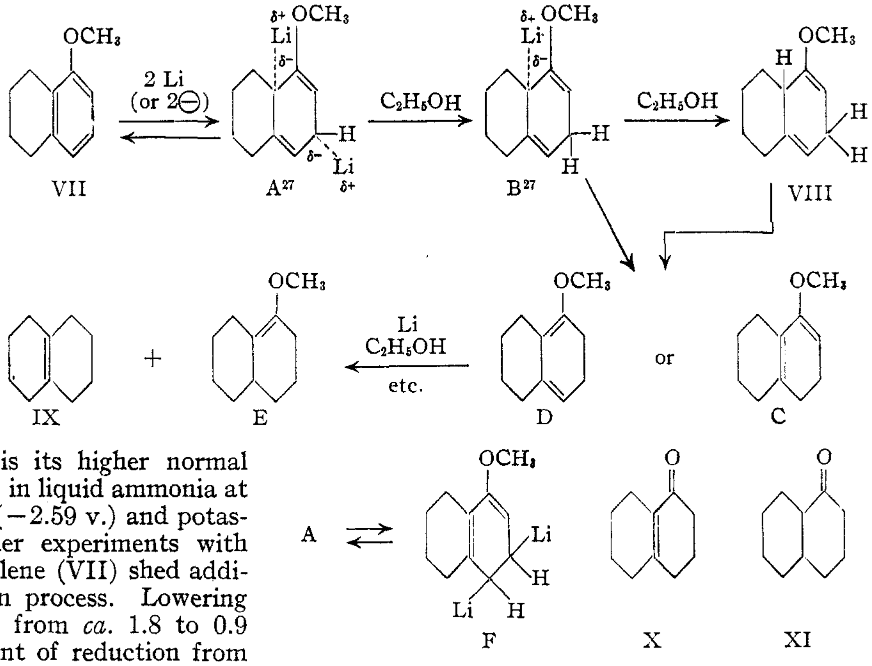
[21] The possibility of this reduction occurring because of reaction of a lithium addition compound with water, present with the crushed Dry Ice used for carbonation, is not a likely interpretation in our opinion. Hydrolysis would have to predominate overwhelmingly over carbonation, whereas it is known that Grignard reagents and organolithium and sodium compounds give reasonably good yields of acids under similar conditions.

equilibrium shifted to regenerate metal and aromatic ether upon removal of the ammonia before carbonation. Nevertheless, the failure to obtain any acid with the easily reduced 2-methoxytetrahydronaphthalene in the favorable solvent 1,2-dimethoxyethane,[22] demonstrates a highly unfavorable equilibrium in this solvent, and suggests that such an addition of lithium in ammonia is not the critical factor accounting for the superiority of lithium over sodium in these reductions.

Probably the most important reason for the greater potency of lithium is its higher normal reduction potential (−2.99 v. in liquid ammonia at −50°) compared to sodium (−2.59 v.) and potassium (−2.73 v.).[23,24] Further experiments with 1-methoxytetrahydronaphthalene (VII) shed additional light on the reduction process. Lowering the concentration of lithium from *ca.* 1.8 to 0.9 *M* decreased the total amount of reduction from 80–92% to 35%. Increasing the metal concentration to 2.5 *M*, on the other hand, effected no improvement. Doubtless this critical importance of having a high effective reduction potential, by maintaining a high metal concentration with a difficultly reducible compound, accounts for the fact that addition of the lithium last, as in the conventional Birch process, gave only 15% reduction.[25]

Similarly, when the concentration of alcohol was kept low, by slow addition over 100 minutes, rather than 20 minutes as in the normal procedure, the extent of reduction was negligible (*ca.* 5%). On the other hand, shortening the addition time to 10 minutes, or using the less reactive isopropyl alcohol to increase the actual alcohol concentration, gave no improvement over the normal procedure. These results point out the necessity of having a certain critical alcohol as well as metal concentration.[26] This may be interpreted to mean that the reduction either is a two-electron process, or if two one-electron steps are involved conditions must be favorable for the second to follow rapidly in order for a fruitful reduction to occur.

The following scheme seems to us to be in best agreement with the facts now known for these reductions; in this formulation we do not intend to imply preference for an ionic rather than a covalent character for the lithium derivatives (see below)



The equilibrium for the addition to form A[27] may lie mainly to the left, but provides the means for reduction to occur by stepwise reaction with an adequate hydrogen donor, forming VIII.[28] This direction of initial addition is that predicted according to the views of Birch,[3b] in which we concur in the main. The conjugated diene (C or D), which provides the further reduction products E and IX, can arise by reaction of B with alcohol or by isomerization of VIII. Or, in this example where addition of the second lithium atom (or solvated electron plus lithium ion) to the angular position may not be as favorable sterically as for easily reduced compounds such as I, the diene C or D conceivably could arise from a transient covalent intermediate such as F. The latter possibility cannot be ruled out, when one considers the covalent *vs.* ionic character of organolithium compounds. Rogers and Young[20] concluded, from dipole moment measurements, solubility in nonpolar solvents and low conductivity of solutions, that alkyl- and aryllithium compounds are largely covalent in character, in benzene solution.[29] Letsinger's[30] observation of retention of optical activity, in the conversion of 2-iodoöctane *via* the lithium derivative and carbonation to 2-methyloctanoic

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(22) N. D. Scott, J. F. Walker and V. L. Hansley, THIS JOURNAL, **58**, 2442 (1936), found this and other glycol ethers, as well as dimethyl ether, to be favorable solvents for rapid addition of sodium to naphthalene or biphenyl. Adding diethyl ether to the solution of addition product shifted the equilibrium back to the starting materials.

(23) V. A. Pleskov, *J. Phys. Chem.* (*U.S.S.R.*), **9**, 12 (1937); *C. A.*, **31**, 4214 (1937).

(24) We are indebted to Leonard Stalmann for bringing this fact to our attention.

(25) Presumably the concentration factor would be even more important with the less powerful reducing metals sodium and potassium.

(26) *Cf.* C. F. Pope, cited by A. J. Birch, ref. 3b, p. 91.

(27) The dotted line for the C–Li bond is intended to be non-committal as to whether this bond is covalent, corresponds to an ion-pair bond in a common solvent cage, or to a fully ionic bond. Such a distinction must await further study of liquid ammonia solutions of organolithium compounds.

(28) There seems at present to be no way of distinguishing experimentally between addition of solvated electrons (with or without associated lithium ions) or of lithium atoms. Until evidence can be found it is pointless, in our opinion, to be concerned with this aspect in writing a mechanistic scheme.

(29) The dipole moment for the Li–C bond in *n*-butyllithium of 1.37 *D* (benzene solution) was considered by them to indicate an ionic character about equal to that of the C–F bond in alkyl fluorides. In liquid ammonia, however, some ionization of the lithium derivatives would be expected.

(30) R. P. Letsinger, THIS JOURNAL, **72**, 4842 (1950).

acid, seems to require considerable covalent character for the lithium–carbon bond under the conditions of his experiment.

The superiority of lithium as a reducing metal lies in a nearly ideal combination of properties: (a) high normal reduction potential, (b) high solubility and low atomic weight, making possible high concentrations and high actual reduction potentials, and (c) slow rate of reaction with alcohols.[31] On the other hand, for selective reductions of conjugated double bonds in the presence of an easily reduced phenolic ether, sodium may offer some advantages.

Experimental[32]

General Procedure for Reduction with Lithium.—The apparatus used for all of the reductions in liquid ammonia was a three-necked flask equipped with stirrer, dropping funnel and soda lime drying tube. The flask was placed in a box stuffed with insulating wool or cotton. At the front of the box was a sealed double window with a cork spacer ring and rubber gasket against which the flask was placed. This arrangement prevented condensation of moisture on the flask or window, and with illumination from the top permitted observation of the reaction mixture at all times. The flask was filled from one-third to no more than one-half its capacity, to aid in control of foaming which occurred in some instances toward the end of alcohol addition.

To a solution of the compound to be reduced in dry diethyl ether or 1,2-dimethoxyethane was added liquid ammonia with stirring, and to the homogeneous solution was then added lithium wire[33] in small pieces over a period of 1 to 10 minutes, depending on the quantity of metal. After stirring for 10 minutes absolute alcohol was added dropwise over a period of about 20 minutes. In some cases there was a tendency for foaming to occur near the end of this addition. This was easily controlled by stopping the stirrer momentarily. When the blue color had disappeared the ammonia was evaporated, ether and water were added, separated and the aqueous layer was re-extracted. After washing the combined extract with saturated salt solution and drying over potassium carbonate, the ether was removed and the product isolated by crystallization or distillation as appropriate.

The reduction described below for anisole and 2-methoxy-5,6,7,8-tetrahydronaphthalene are considered typical for easily reduced liquids, that of estradiol-3-methyl ether[12] for a fairly readily reduced solid, of 4-cyclohexylanisole and 4-cyclohexylphenoxyethanol for compounds moderately difficult to reduce, of 1-methoxy-5,6,7,8-tetrahydronaphthalene for a difficultly reducible liquid and that of *dl*-*m*-3-(*p*-methoxyphenyl)-4-(4′-hydroxycyclohexyl)-hexane[12] as an example of a compound unusually difficult to reduce.

With less soluble ethers the cosolvent was used in sufficient amount to give a homogeneous solution of compound, cosolvent, ammonia and lithium. This required a larger volume of ammonia than cosolvent in order to prevent separation of a bronze lithium-ammonia layer. 1,2-Dimethoxyethane was used instead of ether for insoluble examples, although other inert cosolvents may be used, including tetrahydrofuran (Henry C. Dehm) and amines.

In small scale runs and with less soluble ethers the ratio of lithium to compound should be increased, the major consideration being to use a high concentration of lithium in the solvents (see below under variations in reducing 1-methoxytetrahydronaphthalene).

Procedure for 2,4-Dinitrophenylhydrazones of the α,β-Unsaturated Ketones.—To a hot solution of 0.54 g. of 2,4-dinitrophenylhydrazine in 20 ml. of absolute alcohol and 2.5 ml. of concentrated hydrochloric acid was added a solution of the dihydro derivative (using a 1:1 mole ratio of the latter and reagent) in 5 ml. of absolute alcohol. The solution was heated at reflux for 5 minutes and cooled to allow complete crystallization of the derivative.

Procedure for 2,4-Dinitrophenylhydrazones of the β,γ-Unsaturated Ketones.—A solution of 0.54 g. of the reagent in 40 ml. of absolute alcohol and 1.6 ml. of concentrated hydrochloric acid was filtered while hot and cooled to 0°. A solution of the dihydro derivative (using a 1:1 mole ratio) in 5 ml. of cold (0°) absolute alcohol was added, and the mixture was kept at 0° for 30–120 minutes to allow complete reaction before filtering. The derivative was washed with 10% sodium carbonate solution as well as with water to remove acid, and a small amount of pyridine was added during recrystallization. The above procedure gave more reproducible results than that of Birch.[4]

Preliminary Sodium Reduction of 4-Methoxybiphenyl and 4-Biphenyloxyethanol.—A solution of 7 g. of 4-methoxybiphenyl (m.p. 89–90°) in 150 ml. ether, 25 ml. of isopropyl alcohol and 200 ml. of ammonia was treated with 7 g. of sodium over a 15-minute period. No dinitrophenylhydrazone could be isolated from the product. A portion solidified and was recrystallized from dilute alcohol to give 0.3–1.05 g. (4–15%) of 4-cyclohexylanisole, m.p. 54–56°. After further recrystallizations the m.p. of the solid was 56.5–57.5° alone or when mixed with an authentic sample. The ultraviolet and infrared absorption spectra were also essentially the same as those of the authentic sample.

4-Biphenyloxyethanol was prepared in 71% yield from 4-hydroxybiphenyl and ethylene chlorohydrin essentially as described below for 4-cyclohexylphenoxyethanol, m.p. 122–123° (dilute alcohol); reported by Vernon, m.p. 122–123°.[34]

A number of reduction attempts, carried out in ammonia with ethanol and sodium, gave no reduction to an enol ether as evidenced by failure of dinitrophenylhydrazone formation.

The low-boiling fractions from several runs (4.5 g.) were refractionated to give 2.4–3.6 g. (10–20% over-all yield) of cyclohexylbenzene, b.p. 109° (14 mm.), $n^{25}D$ 1.5251 (reported $n^{20}D$ 1.5249).[35]

Anal. Calcd. for $C_{12}H_{16}$: C, 90.0; H, 10.07. Found: C, 89.3; H, 10.15.

2,5-Dihydroanisole.—A solution of 15 g. of anisole in 50 ml. of ether and 200 ml. of liquid ammonia was treated by the general reduction procedure outlined above with 4.5 g. (4.6 equivalents per mole) of lithium and finally with 35 g. of absolute alcohol (30 minute addition). After ether extractions, the concentrated aqueous layer (75 ml.) was acidified and treated with bromine, giving 0.90 g. of tribromophenol, m.p. 93–94.5°, which indicated only 2% demethylation. From the ether extracts was obtained 12.8 g. (84%) of product, b.p. 148–149° (*ca.* 745 mm.), $n^{25}D$ 1.4782. The ultraviolet absorption spectrum, λ_{max} 268–269 mμ (800) indicated the presence of about 20% of 2,3-dihydroanisole in the 2,5-dihydroanisole.[36] The distillate gave by the above general procedure a 97% yield of 2-cyclohexenone 2,4-dinitrophenylhydrazone, m.p. 162–163.5°, and an 88% yield of 3-cyclohexenone 2,4-dinitrophenylhydrazone, m.p. 132.5–133.5° (sint. 131°).[4]

4-Cyclohexylanisole (V).—A stirred suspension of 20 g. of powdered 4-cyclohexylphenol in a solution of 11.1 g. of potassium hydroxide in 120 ml. of water and 10 ml. of methanol at 30–40° was treated with 20 ml. of dimethyl sulfate over a 30-minute period, followed by a second equal portion of the alkaline solution and stirred 90 minutes longer. The recrystallized product, 20.8 g. (96%), melted at 57–58° (reported 57–58°)[37]; λ_{max} 277 mμ (1515), 283.5 mμ (1260).

4-Cyclohexylphenoxyethanol.—To a solution of 2.3 g. of sodium in 125 ml. of absolute alcohol was added 17.6 g. of 4-cyclohexylphenol and 8.8 g. of ethylene chlorohydrin.[38] After heating at 70° for 3 hours, 50 ml. of water was added, the mixture concentrated to 100 ml. and cooled. After

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[31] W. S. Johnson and B. Bannister have found that 1-methoxy-8-hydroxy-10a-methyldodecahydrochrysene, which failed to reduce dependably with the present conditions, underwent reduction with lithium and ammonia containing a large excess of alcohol.

[32] All melting points are corrected; those marked micro m.p. were determined with a calibrated microscope hot stage. Microanalyses were carried out by Bennett Buell, Edmund Eisenbraun, Edward Shiner and Gershen Winestock. Ultraviolet spectra were determined in 95% alcohol unless otherwise specified and molecular extinction coefficients ε are reported.

[33] From Metalloy Corp., Minneapolis, Minn.

[34] C. C. Vernon, U. S. Patent 2,140,824 (Dec. 20, 1938); *C. A.*, **33**, 2612 (1939).

[35] G. Egloff, "Physical Constants of Hydrocarbons," Vol. 3, Reinhold Publ. Corp., New York, N. Y., 1946, p. 265.

[36] A. J. Birch, *J. Chem. Soc.*, 1551 (1950), reported λ_{max} 268 mμ (4270) for 2,3-dihydroanisole.

[37] D. Bodroux, *Ann. chim.*, [10] **11**, 559 (1929).

[38] Purified by adding benzene and distilling, using the fraction b.p. 123.5–127° (*ca.* 745 mm.).

extraction with ether, washing the extracts repeatedly with 5% potassium hydroxide, water, saturated brine and drying, the product was crystallized from petroleum ether to afford 15.5 g. (71%) of white, silky needles, m.p. 60–63°. Further recrystallization gave material m.p. 64–65° (reported[39] m.p. 62–63°).

2,5-Dihydro-4-cyclohexylanisole (VI).—A solution of 4.0 g. of 4-cyclohexylanisole in 200 ml. of ether was reduced according to the general procedure using 250 ml. of liquid ammonia, 4.2 g. (29 equivalents per mole) of lithium wire and 37 g. of absolute alcohol. Crystallization of the product from dilute ethanol gave 3.38–3.55 g. (84–88%) of colorless dihydro derivative, m.p. 65–66°. From the ultraviolet absorption at 277 mμ this product contained less than 1% of unreduced material. Further recrystallization from 90% alcohol gave material of m.p. 65.4–66.2°; $\lambda_{max}^{CHCl_3}$ 5.90 and 6.02 μ[40]; no ultraviolet absorption maximum. The compound failed to give a significant m.p. depression when mixed with 4-cyclohexylanisole.

Anal. Calcd. for $C_{13}H_{20}O$: C, 81.2; H, 10.48. Found: C, 81.2; H, 10.56.

When the reduction was carried out in the same way except adding the alcohol to the ammonia–ether solution and adding the lithium last over a 10-minute period, 76% of the dihydro compound, m.p. 64–65.5°, was obtained. This contained 4% of starting material on the basis of ultraviolet absorption, and was converted in 91% yield to the conjugated dinitrophenylhydrazone. The oily filtrate gave additional derivative, m.p. 118–123°, to make the total yield of this derivative 76%, based on cyclohexylanisole, compared to 80–84% obtained above.

4-Cyclohexyl-3-cyclohexenone.—A cold (0°) mixture of 25 ml. of sulfuric acid and 75 ml. of water was added dropwise with mechanical stirring to a cold (5°) solution of 2.8 g. of dihydro-4-cyclohexylanisole in 75 ml. of benzene.[6] After 30 minutes at 5–10°, 30 minutes at 35°, 1 hour at 60° and 10 hours at room temperature the benzene layer and further benzene extracts were washed with sodium carbonate and dried. Distillation through a short Vigreux column gave 1.92 g. (74%) of ketone, b.p. 132–134° (10 mm.), n^{25}D 1.5030.

Anal. Calcd. for $C_{12}H_{18}O$: C, 80.9; H, 10.18. Found: C, 80.3; H, 10.47.

The 2,4-dinitrophenylhydrazone of 4-cyclohexyl-3-cyclohexenone, obtained in 77% yield, m.p. 101–103°, from ketone and in 87% yield, m.p. 103–104° (sint.), from dihydro-4-cyclohexylanisole was recrystallized from alcohol containing a few drops of pyridine and finally from alcohol alone as yellow plates, m.p. 103–104° (sint. 102°), $\lambda_{max}^{CHCl_3}$ 364 mμ (23,700).

Anal. Calcd. for $C_{18}H_{22}N_4O_4$: C, 60.3; H, 6.19. Found: C, 60.2; H, 6.30.

When this β,γ-unsaturated derivative was heated in alcohol containing about 5% of concentrated hydrochloric acid it was converted in 88% yield to the α,β-unsaturated derivative, m.p. 119.5–121°, not depressed on admixture with the derivative described below.

The semicarbazone of 4-cyclohexyl-3-cyclohexenone, prepared in 84% yield from the dihydro derivative in 95% alcohol–pyridine solution, was recrystallized from alcohol, m.p. 194–195° dec., λ_{max}^{EtOH} 228.5 mμ (17,400).

Anal. Calcd. for $C_{13}H_{21}N_3O$: C, 66.4; H, 9.00. Found: C, 65.9; H, 8.77.

The 2,4-dinitrophenylhydrazone of 4-cyclohexyl-2-cyclohexenone, prepared in 95% yield from dihydro-4-cyclohexylanisole, was recrystallized from 95% alcohol as orange-red plates, m.p. 124–125°, $\lambda_{max}^{CHCl_3}$ 382 mμ (28,100).

Anal. Calcd. for $C_{18}H_{22}N_4O_4$: C, 60.3; H, 6.19. Found: C, 60.6; H, 6.03.

The semicarbazone of 4-cyclohexyl-2-cyclohexenone resulted in 87% yield when the dihydro derivative was heated with semicarbazide hydrochloride and alcohol in the absence of pyridine. Recrystallization from alcohol gave material melting at 218.5–219° dec. when the sample was inserted in a bath preheated to 215°, λ_{max}^{EtOH} 263.5 mμ (22,000).

Anal. Calcd. for $C_{13}H_{21}N_3O$: C, 66.4; H, 9.00. Found: C, 66.5; H, 9.11.

Sodium Reductions of 4-Cyclohexylanisole.—The replacement of lithium by an equivalent amount of sodium in the above procedure gave incomplete reduction; conversion to the dinitrophenylhydrazone of the Δ^2-unsaturated ketone, m.p. 119–121°, indicated 35% reduction. In a variety of runs using ether, methylamine or no cosolvent with the liquid ammonia, employing ethanol or 2-propanol and adding the metal (sodium or potassium) last according to the general procedure of Birch, no reduction occurred, as evidenced by recovery of the starting material and failure to obtain any dinitrophenylhydrazone from the material after the reduction treatment.

Reduction of 4-Cyclohexylphenoxyethanol.—Treatment of 4.4 g. of this hydroxyethyl ether in 100 ml. of diethyl ether and 150 ml. of liquid ammonia with 2.1 g. (15 equivalents per mole) of lithium and 18.5 g. of alcohol resulted in 2.75 g. (62%) of crude product, m.p. 46–48°. The conversion of this to the impure dinitrophenylhydrazone of 4-cyclohexyl-2-cyclohexenone, m.p. 112–116°, in 68% yield, together with the crude derivative from the oily filtrate, indicated a maximum of 46% reduction with this derivative.

Using the general procedure of Birch,[4] except with 2-propanol and ether as cosolvent, adding the sodium last, the maximum extent of reduction was estimated to be 19%, based on the crude dinitrophenylhydrazone.

Reduction of 2-Methoxy-5,6,7,8-tetrahydronaphthalene (I).—Reduction of 15 g. of this methoxy compound in 50 ml. of ether and 200 ml. of ammonia with 3.2 g. (4.9 equivalents per mole) of lithium wire and 25 g. of ethanol gave 13.7 g. (90%) of product, b.p. 120–125° (16 mm.), n^{25}D 1.5120. The ultraviolet spectrum, λ_{max}^{EtOH} 270.5 mμ (645), indicated the presence of *ca.* 5% 3,4,5,6,7,8-hexahydroisomer in the major product, 1,4,5,6,7,8-hexahydro-2-methoxynaphthalene (II). The material was converted in as high as 91% yield to the conjugated dinitrophenylhydrazone, m.p. after recrystallization 180–181° dec.,[4] $\lambda_{max}^{CHCl_3}$ 389 mμ (29,100), and to the same derivative of $\Delta^{9,10}$-2-octalone in 70–90% yield, m.p. after recrystallization 173–173.5° dec. (inserted in bath at 165°),[4] $\lambda_{max}^{CHCl_3}$ 364 mμ (23,300).

Reduction with sodium by the general procedure of Birch[4] except using ether and 2-propanol gave the hexahydro-2-methoxynaphthalene in 80–90% yields, b.p. 115–124° (20 mm.), n^{25}D 1.5145–1.5154; this was converted in 90% yield to the conjugated dinitrophenylhydrazone, m.p. 174–176.5°.

1-Methoxy-5,6,7,8-tetrahydronaphthalene (VII).—1-Naphthol was reduced (by Stephen Kraychy) in absolute alcohol with W-7 Raney nickel[41] at 110° and 2500 p.s.i. From the neutral fraction was obtained 16% crude 1,2,3,4-tetrahydronaphthalene, b.p. 89–120° (14 mm.), n^{25}D 1.5390, and 36% 1,2,3,4-tetrahydro-1-naphthol, b.p. 120–130° (14 mm.), n^{25}D 1.5553. By recrystallization of the alkali-soluble fraction from petroleum ether, 39% of the desired phenol was obtained, most melting at 69–69.5°. The ultraviolet spectrum indicated the absence of 1-naphthol. The phenol was methylated in 92% yield using methyl sulfate, giving material of b.p. 118–118.5° (12 mm.), n^{25}D 1.5455, λ_{max}^{EtOH} 270.5 mμ (1120) and 278 mμ (1170).

Lithium Reduction of 1-Methoxy-5,6,7,8-tetrahydronaphthalene.—A solution of 20 g. of the methyl ether in 100 ml. of 1,2-dimethoxyethane[42] (from Arapahoe Chem., Inc., dried over potassium hydroxide and distilled from sodium) and 400 ml. of ammonia was reduced by the general procedure given before, using 6.4 g. (7.4 equivalents per mole) of lithium wire, stirring for 10 minutes and adding 25 g. of absolute alcohol or 60 g. of isopropyl alcohol over a 15 to 25 minute period. Distillation of the isolated product gave 16.8–17.5 g. (83–87%) of a mixture, b.p. 95–131° (20 mm.). From the absorption maximum at 278 mμ this may have contained as much as 8–21% of unreduced material in the various runs. Conversion to the dinitrophenylhydrazone of the conjugated ketone gave this derivative, m.p. 268° dec., in 55–58% over-all yields from 1-methoxytetrahydronaphthalene. The alkali-soluble fraction gave about 2% of 1-hydroxytetrahydronaphthalene.

Fractional distillation of the crude reduction product

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[39] G. H. Coleman and J. W. Zemba, U. S. Patent 2,130,525 (Sept. 20, 1937); *C. A.*, **32**, 9345 (1938).

[40] *Cf.* G. Stork, THIS JOURNAL, **73**, 504 (1951).

[41] H. Billica and H. Adkins, *Org. Syntheses*, **29**, 24 (1949); D. M. Musser and H. Adkins, THIS JOURNAL, **60**, 664 (1938).

[42] The extent of reduction was less using ethyl ether as cosolvent, resulting in 41% of dinitrophenylhydrazone, melting above 250° dec.

through a 21-cm. McMahon-packed column (stainless steel mesh Berl saddles) gave fractions varying in refractive index from n^{25}D 1.4978 to 1.5163; one fraction, b.p. 117.5° (20 mm.), n^{25}D 1.5061, probably contained *ca.* 5% of the conjugated hexahydro-1-methoxynaphthalene, since it had λ_{max} 270.5 mμ (219), but no maximum at 278 mμ, and gave the conjugated dinitrophenylhydrazone in 93% yield.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.5; H, 9.83. Found: C, 79.8, 79.9; H, 9.99, 10.09.

From the lower boiling fractions was obtained 10–16% of octahydronaphthalene, b.p. 86–88° (21 mm.). A fraction with n^{25}D 1.4980 was analyzed.

Anal. Calcd. for $C_{10}H_{16}$: C, 88.2; H, 11.84. Found: C, 88.3; H, 11.51.

This was proved to be mainly Δ^{9-10}-octahydronaphthalene (IX) containing some Δ^{1-9}-derivative by conversion to the nitrosyl chloride addition compound. To 1.5 g. of ethyl nitrite at −15° was added 1.0 g. of the liquid in 1.5 ml. of acetic acid, followed by 1.5 ml. of concentrated hydrochloric acid over 10 minutes. After 1 hour at −15°, 1.09 g. (74%) of blue **9-nitroso-10-chlorodecahydronaphthalene** was collected and washed with methanol, m.p. 89–91° (sint. 84°); reported m.p. 91°.[43] From the filtrate was obtained 0.01 g. (1%) of the crude **9-chloro-1-oximinodecahydronaphthalene**, m.p. 116–120° dec.; reported m.p. 127°.[44] Treatment of the latter product with dinitrophenylhydrazine in alcohol containing hydrochloric acid converted it into the expected derivative of Δ^{9-10}-1-ketoöctahydronaphthalene, m.p. 266.5–267° dec. alone or when mixed with an authentic sample.

2,4-Dinitrophenylhydrazones of 1-Keto-Δ^{4-10}-octahydronaphthalene and 1-Ketodecahydronaphthalene.—The crude distillate from reduction of 1-methoxytetrahydronaphthalene (1 g. in 10 ml. of alcohol) was added at 0° to a clear solution of 0.61 g. of dinitrophenylhydrazine in 20 ml. of absolute alcohol and 2.2 ml. of concentrated hydrochloric acid. After 2 hours the precipitate was removed, washed with bicarbonate solution and dried, 0.91 g. (44%), m.p. 150–184° (sint. 125°). This mixture was recrystallized from 30% benzene in absolute alcohol containing some pyridine, then from 20% benzene in absolute alcohol, giving 0.086 g., m.p. 212–215° dec., and 0.09 g., m.p. 195–206° dec., of the crude derivative of 1-ketodecahydronaphthalene and 0.180 g., m.p. 125–135.5°. Further recrystallizations of the last from absolute alcohol gave the light orange 2,4-dinitrophenylhydrazone of 1-keto-Δ^{4-10}-octahydronaphthalene, m.p. 130–133.5° (sint. 128°), $\lambda_{max}^{CHCl_3}$ 364.5 mμ (23,000).

Anal. Calcd. for $C_{16}H_{18}N_4O_4$: C, 58.2; H, 5.49. Found: C, 57.9; H, 5.22.

Recrystallization of the higher melting material from 30% benzene in absolute alcohol gave the orange dinitrophenylhydrazone of 1-ketodecahydronaphthalene, m.p. 224–225° (dec., and sint. 221°), $\lambda_{max}^{CHCl_3}$ 366 mμ (22,700) (reported m.p. 222–222.5°).[45]

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.8; H, 6.07. Found: C, 58.1; H, 6.04.

A mixed m.p. with an authentic sample showed no depression. Recrystallization from alcohol containing some hydrochloric acid gave material melting as high as 234–235° dec. The over-all yield of the derivative of the decahydronaphthalene ketone from 1-methoxytetrahydronaphthalene amounted to as much as 7%. The Δ^{4-10}-derivative was isomerized in 96% yield to the red 2,4-dinitrophenylhydrazone of 1-keto-Δ^{9-10}-octahydronaphthalene by heating with alcohol containing hydrochloric acid, m.p. 268° dec., $\lambda_{max}^{CHCl_3}$ 259 mμ (16,700), 387.5 mμ (26,200) (reported m.p. 266.5–267° dec.).[45]

Effect of Variations on Reduction of 1-Methoxy-5,6,7,8-tetrahydronaphthalene.—When the lithium reduction was carried out as described above except that the alcohol was added over 1.76 hours, the material recovered (83%) contained 95% starting material (ultraviolet spectrum) and gave only 4% dinitrophenylhydrazone. When the alcohol was added immediately after the lithium and over a 10-minute period, 77% of distillate resulted, containing 23% starting material and giving 56% of the conjugated dinitrophenylhydrazone. Adding the lithium last, as in Birch's usual procedure for sodium, gave 90% of distillate, the ultraviolet spectrum of which indicated 88% starting material, and which formed 15% of dinitrophenylhydrazone. When the total amount of lithium was increased to 11 equivalents, except added in three equal portions each followed by the theoretical amount of ethanol before adding the next portion, no improvement resulted (81% containing 39% starting material by ultraviolet, giving 43% dinitrophenylhydrazone). Increasing the amount of lithium to 15 equivalents and doubling the amount of solvents to maintain the same metal concentration gave essentially the same results (85% containing 12% starting material by ultraviolet, giving 66% of crude and 50% of relatively pure conjugated dinitrophenylhydrazone).

When the proportion of reagents was unchanged but the concentration of lithium reduced to one-half, the distillate (84%) contained 65% starting material (ultraviolet) and gave only 26% of crude dinitrophenylhydrazone. Increasing the lithium concentration by using 11 equivalents of metal but keeping the solvents the same and using a Dry Ice condenser, gave essentially the same results as described (85% distillate, containing 23% unchanged material by the spectrum and giving 55–62% of the dinitrophenylhydrazone). Increasing the lithium to 15 equivalents under these conditions, however, gave poor results due to separation of a lithium–ammonia phase (88% of distillate, 94% unchanged material, giving 8% dinitrophenylhydrazone).

Attempts to Carbonate a Lithium Addition Compound.—A solution of 5 g. of 2-methoxytetrahydronaphthalene in 60 ml. of 1,2-dimethoxyethane and 100 ml. of ammonia was treated with 1 g. of lithium, and after 10 minutes the ammonia was removed at low temperature by distillation, finally under reduced pressure, and the remaining material was forced under nitrogen onto crushed solid carbon dioxide. After decomposition of the lithium with methanol, the alkali-soluble fraction amounted to only 1% of oil. The neutral fraction (92%, b.p. 118–119° at 10 mm.) contained 20% of the reduction product as indicated by the yield of dinitrophenylhydrazone, m.p. 167–171°, the remainder being unchanged starting material, λ_{max} 279 mμ (1640), 287.5 mμ (1520).

A similar experiment was carried out with 2 g. of 4-cyclohexylanisole in 90 ml. of ether and 125 ml. of ammonia, using 2 g. of lithium, except the ammonia solution was flash distilled by adding dropwise to an evacuated suction flask and the residue was treated with ether followed by crushed Dry Ice. The alkali-soluble fraction (1% yield) gave some impure 4-cyclohexylphenol, m.p. 117–126°, as the only solid material. The neutral fraction, 85% yield, m.p. 57–59°, gave 36% of dinitrophenylhydrazone, m.p. 118.5–121°, most of the remainder being unreduced material (58% from ultraviolet absorption).

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(43) W. Huckel, R. Danneel, A. Schwartz and A. Gercke, *Ann.*, **474**, 132 (1929).

(44) W. Huckel and H. Naab, *Ann.*, **502**, 148 (1933).

(45) J. W. Cook and C. A. Lawrence, *J. Chem. Soc.*, 817 (1937).