and yielded 163 mg. of octahydro compound, m.p. 196–197° (IVa). The mother liquor contained about 100 mg. of hexahydrodibenz[*a,h*]anthracene (VII).

Filtrate 11 was evaporated to dryness and cooled. The crystalline residue weighed 560 mg. This was crystallized from benzene-hexane-ethanol. Yield, after three crystallizations, 320 mg., m.p. 95.5–96.5°, colorless long thin prisms.

Anal. Calcd. for $C_{22}H_{26}$: C, 90.97, H, 9.03. Found: C, 90.60, H, 9.16.

A further crop of the same compound was prepared from the mother liquor by decomposition of the purified trinitrofluorenone complex. The trinitrofluorenone complex was recrystallized from benzene-ethanol, red needles, m.p. 126.5–127.5°.

1,2,3,4,1a,4a,5,6,8a,11a,12,13,8,9,10,11-Hexadecahydrodibenz[a,h]-anthracene (IX). (a) Hexane filtrate 12 (above) was evaporated to dryness. The solid residue weighed 450 mg. Fractional crystallization from a variety of solvents failed to produce material with a sharp melting point, 247 mg. from benzene-ethanol melted at 114–120°, after recrystallization, m.p. 114–150°.

A trinitrofluorenone complex was prepared. A bright yellow precipitate appeared on cooling the benzene solution. A further crop of yellow crystals was obtained by adding ethanol to the mother liquor. The combined crystals were recrystallized from benzene-ethanol, m.p. 170.5–172°, yellow prisms.

The yellow complex was decomposed on a 24 × 4.5 cm. column of magnesia/Celite and the colorless filtrate evaporated to dryness. After crystallization from benzene-ethanol, yield, 180 mg.; m.p. 178.5–180.5°, long rectangular plates.

Anal. Calcd. for $C_{22}H_{30}$; C, 89.80, H, 10.20. Found: C, 89.92, H, 10.30. Infrared bands at 2875, 2940, 3002, 3123 cm.$^{-1}$.

(b) Dibenz[*a,h*]anthracene (337 mg.) was hydrogenated until no further hydrogen was taken up (the product of 5 days hydrogenation was rehydrogenated with a fresh batch of catalyst). The product (expected to be the perhydro compound) was crystalline and melted at 110–130°. After recrystallization from hexane the melting point was 115–150°. Trinitrofluorenone complex, yellow triangular prisms, m.p. 171–172°. The trinitrofluorenone complex was decomposed and the hydrocarbon crystallized from benzene-ethanol, yield, 80 mg., m p. 116–117°.

Anal. Calcd. for $C_{22}H_{30}$: C, 89.80, H, 10.20. Found: C, 89.64, H, 10.18. Infrared bands at 2866, 2935, 2997, 3118 cm.$^{-1}$

7,14-Dihydrodibenz[a,h]anthracene. About 0.5 g. of sodium was melted under xylene in a stoppered flask and vigorously shaken to pulverize the metal. After cooling, the xylene was decanted and 100 ml. of ether added, together with 107 mg. of dibenz[*a,h*]anthracene in 20 ml. benzene. The solution was stirred magnetically for 12 hr., by which time the color had changed from yellow to dark blue-green. Methanol, 50 ml., was added to the solution, the color becoming light green. Benzene was added, the water-soluble materials washed out and the benzene solution evaporated to a small volume. This was chromatographed on a 20 × 3.5 cm. column of magnesia/Celite, with hexane-benzene-acetone (2:1:1) as developer. A small blue fluorescent zone appeared below the major blue fluorescent zone (which was unchanged dibenz[*a,h*]anthracene) and passed into the filtrate. The residue after evaporation of the filtrate—35 mg.—was crystallized from benzene-hexane-ethanol; yield, 26 mg.; m.p. 222.5–223.5°, colorless rectangular flat plates.

Anal. Calcd. for $C_{22}H_{16}$; C, 94.22, H, 5.78. Found: C, 93.53, H, 6.19.

The trinitrofluorenone complex was recrystallized from benzene, m.p. 257–259°, clusters of hair-like orange needles.

Sodium-alcohol reduction of dibenz[a,h]anthracene. Dibenz[*a,h*]anthracene (200 mg.) was dissolved in 100 ml. of *n*-amyl alcohol, heated in an oil bath. Approximately 10 g. of clean sodium were added slowly in small pieces. The solution became yellow and eventually boiled. After dissolution of all the sodium, the solution was cooled, benzene added, followed by water and the water-soluble materials washed out. The benzene solution was diluted with hexane and chromatographed on a 24 × 4.5 cm. column of magnesia/Celite, the developer being acetone-benzene-hexane (2:1:7). No fluorescent zone could be seen. The filtrate was evaporated to dryness leaving a yellow solid. Fractional crystallization gave two products (a) 55 mg. prisms, m.p. 201–207°, after purification through the orange trinitrofluorenone complex, 13 mg., m.p. 208–214°, colorless needles, with a spectrum identical with that of 7,14-dihydrodibenz[*a,h*]anthracene. (b) 66 mg., forming a brown trinitrofluorenone complex, which, after recrystallization, gave green needles and prisms, m.p. 214.5–216.5°. The hydrocarbon was regenerated, 28 mg., m.p. (after recrystallization) 192–194°, colorless flat plates. The absorption spectrum was qualitatively very similar to that of 1,2,3,4,8,9,10,11-octahydrodibenz[*a,h*]anthracene (IV) a_M at 261 mμ = 28,600. Infrared bands at 2840, 2862, 2888, 2933, 3035 cm.$^{-1}$

CHICAGO, ILL.

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF G. D. SEARLE AND CO.]

The Use of Sodium Metal in the Birch Reduction of Aromatic Compounds[1]

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Contrary to the reports of previous investigators, Birch reductions of estradiol derivatives and other high molecular weight, relatively insoluble phenolic ethers can be effected in good yields with sodium. Suitable experimental conditions are described. Iron salts have been found to catalyze strongly the reaction between sodium and alcohols in liquid ammonia; the corresponding reaction between lithium and alcohols is much less strongly catalyzed by iron. In view of the common occurrence of colloidal iron compounds in commercial ammonia, these findings probably account for the failures of previous investigators to effect Birch reductions efficiently with sodium in contrast to the successful use of lithium.

In 1937 Wooster[2] reported that aromatic compounds are reduced by sodium and a proton donor in liquid ammonia solution. A. J. Birch greatly extended Wooster's observations and, as a result, the so-called Birch reduction has found considerable utility in synthetic organic chemistry.[3] Birch established that the reduction proceeds predominantly by the addition of hydrogen to afford

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(1) Presented at the 126th Meeting of the American Association for the Advancement of Science, Chicago, Ill., December 1959.

1,4-cyclohexadienes or 1,4-dihydro compounds as they are often called. If an aromatic ether is reduced the resultant product is an enol ether which, upon mild hydrolysis with acid, affords a Δ-3-cyclohexenone and, under more strenuous conditions, normally affords a Δ-2-cyclohexenone. The synthetic applications of the Birch reduction have been greatest in making compounds of these types. Our own interest in the Birch reduction stems from its utility in making 3-keto-Δ-4- or 3-keto-Δ-5(10)-19-norsteroids by the reduction of estradiol derivatives. We have developed a useful experimental procedure for the Birch reduction of estradiol derivatives with sodium and have discovered the probable reason for the failures of earlier workers to reduce these and other compounds in good yields with sodium.

Most of Birch's work was carried out using sodium as the reducing agent, although he occasionally used potassium. Methanol or ethanol was used as the proton source. The experimental procedure favored by Birch involved the addition of the alkali metal to a mixture of the alcohol and aromatic compound in liquid ammonia. Although this procedure gave fair to good yields of dihydro compounds when applied to many simple aromatic compounds, Birch found that it was less successful when applied to less-soluble, higher molecular weight compounds. Thus the reduction of hexestrol methyl ether failed,[4] even when cosolvents were added to the ammonia to aid in dissolving the compound, although the more soluble β-hydroxyethyl ether could be reduced in unstated yield. Likewise Birch found that reduction of the glyceryl ether of estradiol with potassium and ethanol in ammonia afforded only a 17% yield of 19-nortestosterone (VII) after hydrolysis of the intermediate 1,4-dihydro compound.[5] Reduction with sodium did afford a 33% yield of Δ-5(10)-19-nortestosterone (V) following mild hydrolysis of the dihydro intermediate.[4] Birch was unable to reduce estradiol methyl ether (I). Other workers[6] found that 4-cyclohexylanisole was not reduced appreciably under Birch's conditions.

In 1953 Wilds and Nelson[6] reported that the use of lithium instead of sodium afforded considerably better yields of dihydro compounds, particularly from compounds which they and Birch had found difficult to reduce with sodium. Thus they were able to convert estradiol methyl ether to 19-nortestosterone in an overall yield of 70–77%.[7] Ether was used as a cosolvent to assist in dissolving the steroid and it was deemed advantageous to add the proton source (ethanol) to a mixture of the aromatic compound, lithium, ammonia, and ether, rather than adding the alkali metal last as had been done by Birch. The apparent superiority of lithium over sodium was attributed in large part to its greater reduction potential (−2.99 v.) in liquid ammonia compared to those of sodium (−2.59 v.) and potassium (−2.73 v.). Since their report appeared, the procedure of Wilds and Nelson has become the standard one for effecting Birch reductions.

With the discovery of the clinical usefulness of 19-norsteroids such as 17α-ethyl-19-nortestosterone (norethandrolone) (VIII)[8] and 17α-ethynyl-17β-hydroxy-5(10)-estren-3-one (norethynodrel) (VI),[9] we became interested in carrying out Birch reductions on steroidal aromatic ethers on a large scale. Numerous workers in our laboratories had confirmed the superiority of the Wilds-Nelson procedure over the original one of Birch for the reduction of compounds such as estradiol 3-methyl ether and 17-ethylestradiol 3-methyl ether (II) but it was observed that the Wilds-Nelson procedure did not give reproducible results. The extent of the reduction varied from run to run without apparent cause, and this did not seem to be affected greatly by minor changes in the procedure, such as varying the rate of addition of the ethanol. For several reasons it became necessary for us to devise a Birch reduction procedure that gave complete reduction of the starting material as well as being reproducible and giving good overall yields.

RESULTS AND DISCUSSION

In our study of the Birch reduction the influence of the following factors was evaluated: (a) the alkali metal; (b) the proton source; (c) the cosolvent used; and (d) the structure of the particular compound being reduced. On the basis of the work of Wilds and Nelson as well as our own experience, it appeared that lithium was the only one of the alkali metals which was a useful reducing agent. This was puzzling since we did not feel that the small difference between the reduction potentials of sodium and lithium would make sodium so inferior to lithium. However in the absence of any other explanation of the facts, we confined our initial studies to the use of lithium. In the experiments to be discussed, the ammonia was distilled prior to use, the steroid was suitably purified, and the reactions were conducted under a Dry Ice reflux condenser in

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(2) C. B. Wooster and K. L. Godfrey, *J. Am. Chem. Soc.*, **59**, 596 (1937); C. B. Wooster, U. S. Pat. **2,182,242** (1938).

(3) For a recent review see A. J. Birch and H. Smith, *Quart. Rev.*, **12**, 17 (1958).

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

(5) A. J. Birch, *J. Chem. Soc.*, 367 (1950).

(6) A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5360 (1953).

(7) A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5366 (1953).

(8) F. B. Colton, U. S. Pat. **2,721,871** (1955); F. B. Colton, L. N. Nysted, B. Riegel, and A. L. Raymond, *J. Am. Chem. Soc.*, **79**, 1123 (1957); Anon., *Chem. Eng. News*, **34**, 2134 (1956).

(9) F. B. Colton, U. S. Pat. **2,725,389** (1955); Anon., *Chem. Eng. News*, **35**, No. 23, p. 30 (1957).

order to avoid loss of ammonia during the reductions.

The acidity of the proton source was expected to be of significance since the reaction between the proton donor and alkali metal undoubtedly was competing with the desired reduction. For a preliminary evaluation of several proton donors the Wilds-Nelson procedure was followed using 17-ethylestradiol 3-methyl ether as the substrate. Water, methanol, ethanol, and isopropyl alcohol all gave yields of 1,4-dihydro compound in the range of 67–72%. Thus varying the acidity of the proton source over a range of pK_a 14–18 effected no improvement in yield. Even acetic acid (pK_a *ca.* 5) gave a 28% yield of dihydro compound IV.

Since we found that 17-ethylestradiol 3-methyl ether is only partially soluble in the ammonia-ether mixture used by Wilds and Nelson, we sought a more effective cosolvent than ether. Both tetrahydrofuran[10] and ethylene glycol dimethyl ether were found to be superior to ether and the former was examined in detail. Although it was possible to obtain a homogeneous solution of 17-ethylestradiol 3-methyl ether in liquid ammonia-tetrahydrofuran, application of the Wilds-Nelson reduction procedure to such a solution afforded only a 72% yield of the 1,4-dihydro compound. The typical Birch reduction mixture consists of a deep blue liquid phase covered by a layer of lithium-ammonia "bronze" and, in the hope of obtaining a more homogeneous mixture, an additional cosolvent was sought which might favor solution of the lithium as well as the steroid. Only alcohols seemed to offer promise in this regard. We found that not only did lithium react relatively slowly with an ammonia-tetrahydrofuran-*t*-butyl alcohol mixture (2:1:1), but that such a mixture readily dissolved 17-ethylestradiol 3-methyl ether. This mixture also appeared to retain more lithium in the lower phase than did ammonia-tetrahydrofuran alone. When this solvent mixture was employed in the Wilds-Nelson procedure, the yield of 1,4-dihydro compound was increased to 85%. Since it appeared probable that the *t*-butyl alcohol was functioning as a proton donor[11] as well as a solvent, the procedure was altered so as to add the lithium to a mixture of the other reactants without using ethanol as an additional proton source. The yield of 1,4-dihydro compound was then 87% with only 0.3% of the starting material remaining unreduced. Although both our new procedure and the Wilds-Nelson one gave yields of 80% on a several kilogram reaction scale, the amount of residual unreduced starting material was consistently in the range of 0.3–0.6% using the new procedure but varied from 0.5–4.0% with the Wilds-Nelson one. Application of our new procedure to estradiol 3-methyl ether afforded a 79% yield of 1,4-dihydro compound III containing only 0.3% of unreduced starting material. The yield on large scale reductions averaged 77% with residual aromatic contents consistently in the range of 0.3–0.6%. Wilds and Nelson[6] reported a 70–77% yield for this reduction by their method.

When we attempted to reduce estradiol 3-methyl ether using undistilled ammonia taken directly from a commercial cylinder, the lithium was consumed within thirty minutes as opposed to the usual three to five hours and at no time did the reaction mixture become deep blue. The crude product contained about 23% of unreduced starting material, and the aqueous mother liquors remaining after isolation of the product deposited a precipitate of ferric hydroxide. We presumed that iron compounds present in the ammonia were exercising a deleterious effect upon the reaction course, probably by catalyzing the reaction between the lithium and the *t*-butyl alcohol and effecting consumption of the metal before the aromatic compound had been completely reduced. The reaction was repeated with the same reagents but using distilled ammonia, whereupon the reduction proceeded normally and the product contained only 0.26% of unreduced starting material. Qualitative tests showed that iron salts did indeed strongly catalyze the reaction of lithium with *t*-butyl alcohol in liquid ammonia.

It now appeared probable that the previously reported failures of sodium to reduce steroidal aromatic ethers (and other high molecular weight aromatic compounds) in good yields were due not only to the insolubility of the steroid (which our solvent system circumvented) but also to the presence of iron [12] in the reaction system. When 17-ethylestradiol 3-methyl ether was reduced with sodium by our new procedure using distilled ammonia, an 88% yield[13] of the 1,4-dihydro compound (87% with

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[10] The use of tetrahydrofuran as a cosolvent was suggested by Wilds and Nelson (ref. 6) but it seems to have found little use except by A. J. Birch and H. Smith [*J. Chem. Soc.*, 4909 (1956)] and later papers.

[11] Shortly after the completion of this phase of our work G. Stork and W. N. White [*J. Am. Chem. Soc.*, **78**, 4604 (1956)] reported the use of *t*-butyl alcohol as a proton donor in the reduction of several aniline derivatives with lithium in ammonia.

[12] Essentially none of the papers in the literature describing Birch reductions indicates whether or not the ammonia used was distilled. Probably most workers used liquid ammonia taken directly from a commercial cylinder as did Birch (ref. 24). Under these circumstances the ammonia would have contained variable amounts of iron compounds and poor or erratic reductions would be anticipated, especially with sodium.

[13] Following the development of our ammonia-tetrahydrofuran-*t*-butyl alcohol solvent system but prior to the recognition of the catalytic effect of iron, we had tried to reduce 17-ethylestradiol 3-methyl ether with sodium instead of lithium. However the sodium reacted rapidly with the alcohol, and reduction occurred only to the extent of 60%. Apparently traces of iron had gotten into the system although, at the time, the failure was attributed to the use of sodium.

lithium) was obtained. The product contained 1% of residual aromatics.[14]

Similarly estradiol 3-methyl ether, when reduced with sodium under iron-free conditions, afforded an 88% yield of 1,4-dihydro compound containing 0.6% residual aromatics. This yield is definitely higher than that (79%) which we had obtained with lithium, and in this case sodium is actually superior to lithium as a reducing agent. Birch was unable to reduce estradiol 3-methyl ether with sodium, and Wilds and Nelson[7] reported that sodium left as much as 28% of the ether unreduced.

Potassium was also found to function well as a reducing agent in an iron-free system and afforded an 80% yield of 1,4-dihydro compound from 17-ethylestradiol 3-methyl ether. Further evidence that lithium is not unique as a reducing agent *per se* was obtained when we found that calcium metal (reduction potential in liquid ammonia is −2.39 v.[15]), in our solvent system converted estradiol 3-methyl ether to its 1,4-dihydro derivative in 86% yield. This yield is essentially the same as that obtained using sodium. This finding is of especial interest since calcium in liquid ammonia (or calcium hexammine) has been shown[16] to reduce aromatic hydrocarbons largely to cyclohexenes, although benzene affords a 30% yield of 1,4-cyclohexadiene under carefully controlled conditions.[17]

TABLE I

EFFECT OF IRON ON THE BIRCH REDUCTION OF ESTRADIOL 3-METHYL ETHER BY LITHIUM, SODIUM, AND POTASSIUM

Fe, ppm	% Unreduced Estradiol 3-Methyl Ether Li	Na	K
0	0.2	0.55	0.50
0.25	—	0.65	1.1
0.35	—	—	3.0
0.40	—	1.1	—
0.50	0.32	3.3	68
0.60	—	20	
0.75	—	26	
1.0	—	62	
1.5	0.28		
2.5	0.50		
6.0	0.60		
10.0	0.60		
25.0	0.95		
100.0	82		

TABLE II

EFFECT OF IRON ON THE RATE OF ALKALI METAL-ALCOHOL REACTIONS IN LIQUID AMMONIA[a]

Metal	Fe (ppm)	Reaction Time, Min. t-C_4H_9OH	C_2H_5OH	CH_3OH
Li	0	253	4	1
	0.5	144		
	1.0	72		
	10.0	16		
Na	0	255	9, 10	15, 17
	0.5	5	7	1.5
	1.0	4	5	
K	0	68		
	0.5	2.5		

[a] The reaction mixture contained 0.33 g.-atom of metal, 200 ml. of liquid ammonia, 0.85 mole of alcohol, and 80 ml. of tetrahydrofuran.

The effect of iron on the reduction of estradiol 3-methyl ether by lithium, sodium, and potassium was studied further in a series of reductions in which known concentrations of iron (added as ferric chloride dissolved in tetrahydrofuran) were present. The crude reduction products were analyzed for unreduced aromatic compound giving the data shown in Table I. The reductions with lithium were unaffected by iron concentrations of up to 1.5 ppm and were only slightly affected by concentrations of up to 25 ppm. The adverse effect of iron on the sodium reductions was definite at 0.4 ppm of iron, whereas the potassium reductions were affected by as little as 0.25 ppm. Above an iron concentration of 1.0 ppm[18] neither sodium nor potassium are useful reducing agents. That this effect of iron is due to catalysis of the alkali metal-alcohol reaction is shown by the data in Table II. The times required for 0.33 g. atom of the three alkali metals to react with t-butyl alcohol in liquid ammonia-tetrahydrofuran were determined both in the presence and absence of iron. In the absence of iron, lithium and sodium react with t-butyl alcohol at about the same rate whereas potassium reacts about three times faster. However in the presence of 0.5 ppm of iron, the reaction rate of lithium is increased by a factor of 2, that of sodium by a factor of 50, and that of potassium by a factor of at least 27. We were less successful in estimating the catalytic effect of iron on the rates of the reactions of lithium and sodium with methyl and ethyl alcohols because of the much greater reaction rates involved, even in the absence of iron.[19] Catalytic effects were noted, however, with sodium and methyl and ethyl alcohols and probably occur with lithum as well. Metals other than iron

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[14] The crude steroidal 1,4-dihydro compounds undergo a rapid increase in aromatic content after isolation. Hence the ultraviolet spectra (see Experimental) of the crude reduction products should be taken at once. Some of the aromatic contents reported in this work are probably high because of delays in having the spectra run.

[15] V. A. Pleskov, *J. Phys. Chem.* (*U.S.S.R.*), 9, 12 (1937); *Chem. Abstr.*, **31**, 4214 (1937).

[16] M. Boer and P. M. Duinker, *Rec. Trav. Chim.*, **77**, 346 (1958).

[17] The formation of a 1,4-dihydro compound in good yield from estradiol-3-methyl ether under our conditions is undoubtedly due to the presence of the relatively acidic proton source, t-butyl alcohol, which prevents the formation of amide ion, as normally occurs in calcium hexammine reductions. Both Birch[3] and Boer and Duinker[16] have suggested that the cyclohexenes produced in calcium hexammine reductions arise from amide ion catalyzed isomerization of the kinetically formed 1,4-dihydro compounds to 1,3-dienes followed by further reduction. Our finding supports these suggestions. See also ref. 20.

[18] Iron concentrations of this magnitude are common in commercial undistilled liquid ammonia.

TABLE III

Compound	ROH	Metal	% Unreduced	% Yield
Estradiol 3-methyl ether (I)	t-C_4H_9OH	Li	0.3	79
	t-C_4H_9OH	Li	0.5	81^b
	CH_3OH	Li	0.6	84
	t-C_4H_9OH	Na	0.6	88
	t-$C_5H_{11}OH$	Na	1.4	85
	i-C_3H_7OH	Na	0.6	88
	t-C_4H_9OH	Ca	1.4	86
17-Ethylestradiol 3-methyl ether (II)	t-C_4H_9OH	Li	0.3	87
	t-$C_5H_{11}OH$	Li	0.8	82
	t-C_4H_9OH	Na	3.0	87
	t-$C_5H_{11}OH$	Na	0.4	91
6-Methoxytetralin	t-C_4H_9OH	Li	1.1	72
	t-C_4H_9OH	Na	0.2	74
4-Cyclohexylanisole	t-C_4H_9OH	Na	0.35	84
5-Methoxytetralin	t-C_4H_9OH	Li	<1	63
	t-C_4H_9OH	Na	51	47^a
Podocarpinol 12-methyl ether (IX)	t-C_4H_9OH	Li	0.2	54
	t-C_4H_9OH	Na	0.3	56
	t-C_4H_9OH	Ca	1.7	57
	CH_3OH	Li	0.7	59
trans-1β-Hydroxy-8-methyl-4,5-[4-methoxybenzo]hydrindane (X)	t-C_4H_9OH	Li	—	65
	t-C_4H_9OH	Li	0.7	71^b

[a] Yield based upon compound actually reduced. [b] Reaction conducted at −78°

(when added as salts or chelates) were found to catalyze the sodium *t*-butyl alcohol reaction in ammonia; such metals include copper (present in one cylinder of liquid ammonia which we examined), nickel, manganese, cobalt, and palladium.

After the completion of most of our work, Krapcho and Bothner-By[20] published data giving the relative rates of reduction of benzene by lithium, sodium, and potassium as 62.5:1:0.23.[21] Our work in conjunction with these data provides a rational explanation for the seeming superiority of lithium in Birch reductions as reported by earlier workers. If we assume that these relative rates hold approximately for any aromatic compound[22] and recognize that iron is a common contaminant in commercial liquid ammonia, then in a Birch reduction using sodium, when as little as 0.5 ppm of iron is present, the aromatic compound is being reduced at about 1/60th the rate as it would be by lithium, whereas the sodium is being consumed by reaction

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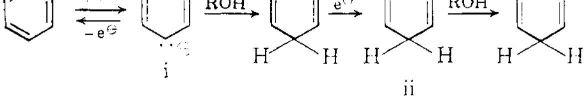
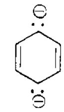
[19] E. J. Kelly, C. W. Keenan, H. V. Secor, and J. F. Eastham (abstracts of 136th Meeting, American Chemical Society, September 1959, p. 17N) have reported that lithium reacts with alcohol in liquid ammonia more rapidly than does sodium. Our rough data are in accord with their more precise data.

[20] A. P. Krapcho and A. A. Bothner-By, *J. Am. Chem. Soc.*, **81**, 3658 (1959). These authors discuss the mechanism of the Birch reduction and present kinetic data supporting it. For other recent papers on the mechanism of the Birch reduction see refs. 25 and 27 and A. J. Birch and D. Nasipuri, *Tetrahedron*, **6**, 148 (1959).

It appears established that the Birch reduction of most benzenoid compounds with alkali metals proceeds by the addition of one electron to give a radical-ion (i), which must then be protonated before addition of a second electron and proton can occur, as shown. Furthermore, ammonia is not acidic enough to effect this protonation; hence it is



necessary to use an alcohol. No one seems to have pointed out that reductions with calcium in ammonia (or calcium hexammine) which proceed with ammonia as the only proton source must, thereby, occur by a different mechanism, probably one involving a dicarbanion such as iii.



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This ion would be expected to be considerably more basic than the radical-ion (i) and hence would almost certainly be capable of removing a proton from an ammonia molecule. A simple consideration of the reduction potentials of the three alkali metals and of calcium would not have predicted that, of the four metals, calcium is actually the most potent reducing agent in liquid ammonia, in the sense that it can effect reductions with only a very weak proton donor present. In the presence of a relatively acidic proton donor, as in our experiments, reductions with calcium may, perhaps, proceed *via* radical-ion intermediates as in the case of the alkali metals.

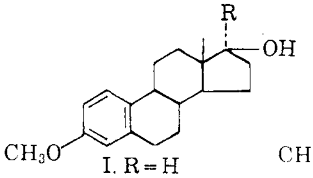
[21] The data on which these rates are based have been criticized by J. F. Eastham, C. W. Keenan, and H. V. Secor [*J. Am. Chem. Soc.*, **81**, 6523 (1959)]. In rebuttal Krapcho and Bothner-By [*J. Am. Chem. Soc.*, **82**, 751 (1960)] concede that the rate constant for the sodium reduction may be low by 20–30% and that of the potassium reduction by a factor of 2–3. These revisions do not sensibly alter our arguments.

[22] Attempts to estimate roughly the relative rates of reduction of estradiol 3-methyl ether by sodium and lithium were unsuccessful due to the very rapid rates of reduction. At −33° only 1.3% of the ether remained unreduced by sodium and *t*-butyl alcohol after five minutes. At −78° only 4.2% of the material remained unreduced by lithium after five minutes, although 56% remained unreduced with sodium.

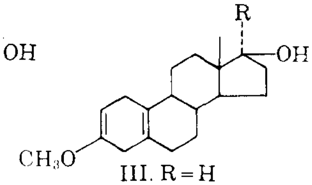
with the *t*-butyl alcohol about 30 times faster than lithium would be. At higher iron concentrations the sodium would be undergoing reaction with the alcohol at an even faster rate. Clearly then, lithium has an advantage over sodium when iron is present.[23] In an iron-free system, however, when the rate of loss of sodium by reaction with the alcohol is at a minimum, the longer reaction times which are possible offset the inherently slower rate of reduction by sodium, and this metal is found to be as or even more effective a reducing agent than is lithium.

Although we cannot rationalize this pronounced catalytic effect of iron on the alkali metal-alcohol reaction in liquid ammonia, it must be analogous to the well known catalytic effect of iron on amide formation from an alkali metal and ammonia. The alcohol reaction does not proceed via initial amide formation, however, since qualitative experiments showed that a small amount of an iron salt catalyzes the alcohol reaction to a much greater degree than it does amide formation. Birch, in his earliest paper,[24] observed that the reductions of 6-methoxytetralin and sodium β-naphthoxide failed to occur in the presence of ferric nitrate. However, the amount of iron involved was enormous (compared to 1 p.p.m.) being equal to about 1% of the weight of the aromatic compound used. In a paper published after the completion of our work, Hückel, Graf, and Münkner[25] reported a similar catalytic effect of various metals on the reaction of sodium with methanol in liquid ammonia. Again the amounts of metal involved were gross (*ca.* 0.5 g./200 ml. of ammonia). To the best of our knowelge, no one has observed previously the striking effect which a minute amount of iron can have on the course of Birch reductions with sodium. This pronounced catalytic effect is observed only when the iron is produced in a very finely divided state, as by reduction of the colloidal iron compounds present in most commercial ammonia. Large pieces of rust are less effective, and Birch reductions can be run in stainless steel equipment without difficulty.[26, 27]

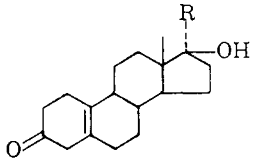
To compare further the effectiveness of lithium and sodium under our reaction conditions, we carried out Birch reductions of several other compounds including some which had been found to be difficult to reduce under the original Birch conditions. The data are included in Table III. In several cases alcohols other than *t*-butyl alcohol were used, and in two cases reductions were carried out at −78°. In general sodium is as effective as lithium in Birch reductions and is superior in some cases. The nature of the alcohol used as the proton donor has a relatively minor effect upon yields, although *t*-amyl alcohol is distinctly superior to *t*-butyl alcohol for the reduction of 17-ethylestradiol 3-methyl ether with sodium. The former alcohol in large scale reductions gives an average yield of 89% of dihydro compound with some runs giving as high as 94%, whereas the yields with *t*-butyl alcohol consistently run lower. In either case the residual aromatics are of the order of 0.3%. Lowering the reaction temperature to −78° does not favor the desired 1,4-reduction over hydrogenolysis reactions, although the overall reaction rate is decreased (see compounds I and X). The one reduction for which lithium is definitely superior to sodium is that of 5-methoxytetralin. Lithium gives far more complete reduction (99+%) than does sodium (*ca.* 50%) and a greater yield (63% *vs.* 42–48%) of ketonic material based upon starting material reduced. Since 5-methoxytetralin is a difficult compound to reduce[6] and reduces slowly, the 60-fold greater rate of reduction by lithium than by sodium becomes significant. Thus during the longest reaction period (six and



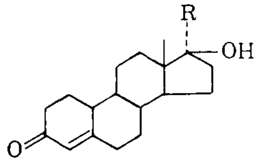
I. R = H
II. R = -C$_2$H$_5$



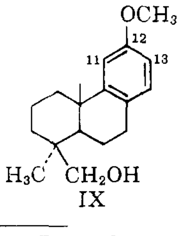
III. R = H
IV. R = -C$_2$H$_5$



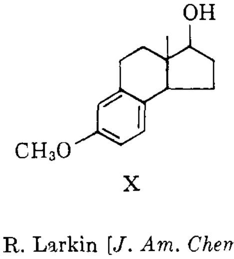
V. R = H
VI. R = -C≡CH



VII. R = H
VIII. R = -C$_2$H$_5$



IX



X

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[23] We have no evidence to indicate whether or not the rate of the Birch reduction itself is affected by the presence of iron.

[24] A. J. Birch, *J. Chem. Soc.*, 430 (1944).

[25] W. Hückel, B. Graf, and D. Münkner, *Ann.*, **614**, 47 (1958).

[26] Hückel, *et al.* (ref. 25) reported that the addition of 1.5 g. of finely divided iron, prepared by reduction of the oxide with hydrogen, did not affect the yield (90%) of 1,4-cyclohexadiene when it was added to a reaction mixture of 500 cc. liquid ammonia, 12.0 g. sodium, 15.6 g. benzene, and 24 g. of methanol.

[27] J. F. Eastham and D. R. Larkin [*J. Am. Chem. Soc.*, 81, 3652 (1959)] recently reported that oxygen strongly catalyzes both the Birch reduction and the alkali metal-alcohol reaction. We have not looked specifically for oxygen catalysis, but we have observed in large scale reductions that the reaction time was longer if the solution of the steroid in the organic solvents had been stored under nitrogen overnight. This may be the result of the removal of dissolved oxygen from the solution. The air in the apparatus used in our experiments probably was displaced by ammonia gas before the start of the reductions.

one half hours) which we employed, the sodium reduction did not have time to go to completion. In addition it appears that with sodium there is a greater loss of starting material in side reactions which are of lesser consequence with lithium because the desired reduction goes more rapidly. These findings are probably general for compounds of the 5-methoxytetralin type in which one hydrogen atom must enter an alkyl substituted position if 1,4-reduction is to occur.

Podocarpinol 12-methyl ether (IX) and *trans*-1β-hydroxy-8-methyl-4,5-[4-methoxybenzo]-hydrindane (X) bear a close structural similarity to the aromatic A-ring steroids as regards the degree of substitution of the aromatic ring and the location of the substituents with respect to the ether function; however these compounds afford considerably lower yields of 1,4-dihydro products than do the steroids when reduced with either sodium or lithium. It is noteworthy that the former compound gives the same yield of 1,4-dihydro compound when reduced with calcium as it does with lithium and sodium. In each case the only other product isolated is a cyclohexene-type compound in which the ether oxygen has been lost.[28] Evidently subtle structural features in the two compounds favor hydrogenolysis reactions at the expense of 1,4-reduction. Krapcho and Bothner-by[20] have pointed out that hydrogenolysis products probably arise from protonation of the final carbanion intermediate (ii, footnote 20) so as to give a 1,3-diene system, capable of further reduction, rather than a 1,4-diene system, which is resistant to further reduction. The same authors point out that steric effects both in the aromatic compound and the proton donor can affect the rate, and hence, point, of proton transfer to the aromatic substrate. In particular they found that the reduction of benzene with lithium and *t*-butyl alcohol proceeds at only $^1/_{14}$th the rate of a reduction using ethanol, thus indicating the greater difficulty of protonating the radical-ion and presumably carbanion intermediates (i and ii, footnote 20) by the bulkier alcohol. In the hope that the use of an alcohol less bulky than *t*-butyl alcohol would lead to a greater preponderance of 1,4-reduction, the reduction of podocarpinol 12-methyl ether was carried out with lithium using methanol as the proton source. The increase in yield of the 1,4-reduction product was negligible however. An examination of a Catalin molecular model of podocarpinol 12-methyl ether does suggest that approach of a proton donor to C-11 from the front side of the molecule would be hindered by the angular methyl group at C-10. Protonation of C-13 with resultant 1,2-reduction might then occur at a rate competitive with that at C-11 and thus account for the high yield of hydrogenolysis product. Models of X are less enlightening as to why 1,2-reduction might be encouraged because of steric factors.

In summation the success of the experimental conditions, which we have devised for carrying out Birch reductions, is due to the maintenance in solution of high concentrations of aromatic compound, alkali metal, and proton donor for a sufficient period of time to allow the reduction to go to completion. Under these conditions most aromatic ethers are reduced as successfully by sodium as by lithium; the only exception seems to be compounds of the 5-methoxytetralin type for which lithium is the superior reducing agent. For any given aromatic compound the yield of 1,4-dihydro compound is limited ultimately by structural features which determine the rate of 1,4-reduction relative to the rate of 1,2-reduction.

EXPERIMENTAL[29]

General procedure for Birch reductions. A 1-l. three-neck flask is fitted with a stainless steel stirrer, a wide bore adapter inlet tube for ammonia gas, and a three-way parallel side arm connector carrying a large Dry Ice reflux condenser and a ground glass stopper. Ammonia (300 ml.) is distilled into the flask. This is best done, especially on a larger scale, by distilling the impure liquid from a three-neck flask equipped with a magnetic stirrer using an electric mantle for heating. The gas is led through a Kjeldahl trap containing a wad of cotton to trap solid particles and through suitable wide-bore adapters into the reaction flask. After the required volume of ammonia has been collected, the inlet tube is replaced with a dropping funnel, and a solution of 0.035 mole of the aromatic steroidal ether in a mixture of 150 ml. of tetrahydrofuran (preferably material stabilized with butylated hydroxy-anisole) and 150 ml. of *t*-butyl alcohol is added with stirring. To the resulting solution is added 0.6 g.-atom of the alkali metal during a 15-min. period. Alternatively about $^1/_4$ of the metal may be added initially with additional portions added as the metal is consumed. After 4-5 hr. the metal normally will have been consumed (as shown by the disappearance of the blue color) and the mixture is treated cautiously with 40 ml. of methanol.[30] If metal is still present, additional methanol may be added to speed up its consumption. The ammonia is allowed to boil off through a mercury bubbler trap so as to prevent access of air to the mixture. After the mixture has come to room temperature, the reaction flask is fitted with a condenser set for downward distillation into an ice-cooled receiver. The apparatus is evacuated with a water aspirator, the mixture stirred, and 250 ml. of water is added cautiously. The flask is warmed with a heating mantle (40° max.) to distil the tetrahydrofuran; an additional 250 ml. of water is added as the distillation proceeds. When the tetrahydrofuran has distilled, the precipitated steroid is collected on a filter and washed well with cold water. The material is best air-dried although samples for spectral analysis should be

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[28] For the structure of the by-product from IX see R. M. Bible, Jr., and R. R. Burtner, *J. Org. Chem.* **26**, 1174 (1961). We have learned from Dr. Bible (private communication) that the NMR spectrum has shown that this deoxy compound is the Δ-8,9 isomer. The deoxy compound from X has been shown to contain a tri-substituted double bond. (L. J. Chinn and H. L. Dryden, Jr., to be published.)

[29] All spectral analyses were performed by Dr. R. T. Dillon and his associates of our Analytical Division.

[30] If the addition of methanol is omitted, deterioration of the product occurs after the mixture has warmed to room temperature. This may be due to *t*-butoxide ion catalyzed conjugation of the double bonds in the 1,4-dihydro compound (*cf.* A. C. Cope and F. A. Hochstein, *J. Am. Chem. Soc.,* **72**, 2515 (1950)).

dried at 56°, 0.1 mm., to remove the water of hydration which is present in some cases.

For the reduction of relatively soluble compounds such as 5-methoxytetralin or *trans*-1β-hydroxy-8-methyl-4,5-[4-methoxybenzo]hydrindane the tetrahydrofuran may be replaced by an equal volume of ether. In these cases the product may be isolated by adding water to the residue remaining after evaporation of the ammonia and extracting the product with pentane or pentane-ether. The combined extracts are washed several times with water to remove *t*-butyl alcohol, dried over potassium carbonate, and the solvent is removed.

For large scale laboratory reductions (*ca.* 100 g. of an aromatic steroid) the Dry Ice reflux condenser may be omitted, but the reaction flask should be insulated (a heating mantle is convenient), and the amount of liquid ammonia used should be increased by about 25%. If too much ammonia is lost the reaction mixture loses its blue color, even though a layer of metal-ammonia "bronze" is present; in this event more ammonia should be added.

Reductions with alcohols other than *t*-butyl alcohol were carried out using the general procedure given above and replacing the *t*-butyl alcohol by an equivalent amount of the other alcohol.

Spectral analysis of products. Residual aromatic ether contents were determined from the absorbance at 278 mμ of the crude reduction products in methanol solution. For the steroidal ethers concentrations of 1 mg./ml. were employed. The content of 1,4-dihydro compound was determined, if possible, by hydrolysis to the α,β-unsaturated ketone followed by ultraviolet analysis. A solution of the crude reaction product (usually 0.01 mg./ml. concentration) in methanol containing about $^1/_{15}$ its volume of water and concentrated hydrochloric acid respectively was kept at room temperature for 2–4 hr. The absorbance at *ca.* 240 mμ was measured and, from this, the 1,4-dihydro compound content could be calculated. Longer hydrolysis times did not increase the absorbance at 240 mμ.

Reduction of podocarpinol 12-methyl ether with calcium. The calcium metal (14.4 g.; 0.36 g.-atom) was dissolved in 300 ml. of distilled ammonia. About one-half of a mixture of 150 ml. each of tetrahydrofuran and *t*-butyl alcohol was added followed by a solution of the podocarpinol 12-methyl ether[31] (10.0 g.; 0.0364 mole) in the remainder of the solvent mixture. Within 30 min. after the addition had been completed, the calcium was consumed. Methanol (50 ml.) was added cautiously, and the ammonia was allowed to evaporate. The residual sludge was treated with 250 ml. of water containing 50 g. of potassium carbonate and the mixture was filtered. The gelatinous precipitate was washed repeatedly on the filter with methanol, stirred with methanol in a beaker, and again collected on a filter and washed with methanol. The precipitate was air-dried and then washed further with methanol. The combined filtrates were distilled under an aspirator vacuum to remove the methanol, and the water insoluble product was collected. It was taken up in ether, the solution stirred with charcoal and then filtered, and the product recovered by removal of the solvent; yield, 9.3 g. Spectral analysis showed the presence of 1.7% starting material and 57% 1,4-dihydro compound. The structure of the dihydro compound has been discussed by Bible and Burtner.[28]

The reduction of estradiol 3-methyl ether with calcium was carried out in a similar fashion.

Reduction of 5-methoxytetralin. (*a*) *with lithium.* The 5-methoxytetralin (10.0 g.; 0.0618 mole) was reduced with lithium (7.0 g.; 1.01 g.-atom) in a mixture of 300 ml. of distilled ammonia, 150 ml. of ether, and 150 ml. of *t*-butyl alcohol. After a reaction period of 6.5 hr. the excess lithium was destroyed by the cautious addition of 60 ml. of methanol, and the ammonia was allowed to evaporate. The residue was diluted with 400 ml. of water, and the product isolated by extraction with pentane as described above. The crude oil was dissolved in 60 ml. of methanol containing 5 ml. of water and 1 ml. of concd. hydrochloric acid. After 2 hr. a solution of 7 g. of semicarbazide hydrochloride and 10 g. anhydrous sodium acetate in 15 ml. of water was added, and the mixture was warmed on a steam bath for 1 hr. After being cooled, the mixture was diluted with 30 ml. of water, the methanol was removed under vacuum and the semisolid precipitate was collected. It was washed with water, ether and pentane and then air-dried: wt., 8.1 g. (*ca.* 63%); m.p. 180–195°. Wilds and Nelson[6] obtained a 55–58% yield of Δ-9,10-octalone-1-(3,4,5,6,7,8-hexahydro-1(2)-naphthalenone),[32] a 7% yield of 1-decalone (3,4,4a,5,6,7,8,8a-octahydro-1(2)-naphthalenone),[33] and a 10–16% yield of octalins by reduction of 5-methoxytetralin with lithium.

The nonketonic material (2.0 g.; 24% assuming material to be largely octalins[6] recovered from the steam distillate and ether and pentane washings had no carbonyl absorption in the infrared, and the ultraviolet absorption at 278 mμ showed the presence of less than 3% of starting material. This is equivalent to less than 1% of the original starting material.

(b) *With sodium.* A similar reduction of 5-methoxytetralin with sodium (23 g.) afforded 2.75 g. (21%) of semicarbazone and 6.60 g. of nonketonic material. This latter assayed 75% starting material which corresponds to 50% of the original starting material. A duplicate reduction gave a 24% yield of semicarbazone and a 51% recovery of starting material.

Reduction of 4-cyclohexylanisole with sodium. 4-Cyclohexylanisole (10.0 g.; 0.052 mole) was reduced with sodium (12.0 g.; 0.052 mole) in a mixture of 600 ml. of distilled liquid ammonia, 300 ml. of tetrahydrofuran and 300 ml. of *t*-butyl alcohol. After 5 hr. the mixture was still blue, and the excess sodium was destroyed by the cautious addition of 70 ml. of methanol. The product was isolated by removal of the tetrahydrofuran and extraction into pentane as described above; wt. crude product, 8.62 g. The ultraviolet spectrum showed the presence of 0.35% unreduced starting material. Five grams of the crude solid was converted to the semicarbazone of 4-cyclohexyl-3-cyclohexenone by refluxing in 30 ml. of methanol and 5 ml. of water with 3.9 g. of semicarbazide hydrochloride and 2.9 g. anhydrous sodium acetate for 2.5 hr. The mixture was cooled, the product collected on a filter, washed with water and ether, and air-dried; wt. 5.90 g. m.p. 182–192°, lit.[6] m.p. 194–195°. The crude yield corresponds to an 84% over-all yield of 1,4-dihydro compound. Wilds and Nelson[6] reported an 84–88% yield in this reduction using lithium.

A duplicate reduction using only one-half the volumes of solvents gave similar results except that the crude product contained 7.4% of residual starting material. The starting material and its 1,4-dihydro derivative were not completely soluble in the smaller volume of solvent. Incomplete reduction (6.3% unreduced) was also observed when the tetrahydrofuran was replaced by the less effective solvent ether.

Effect of iron on the rate of reaction of alcohols with alkali metals in liquid ammonia and on the Birch reduction of estradiol 3-methyl ether. The alkali metal (0.33 g.-atom; 2.31 g. of lithium, 7.67 g. of sodium, 13.0 g. of potassium) was added to a mixture of 200 ml. of distilled ammonia, 80 ml. of tetrahydrofuran, and 0.85 mole of the alcohol (80 ml. of *t*-butyl alcohol, 50 ml. of ethanol, 34 ml. of methanol). The resulting two phase mixture was stirred vigorously under a Dry Ice reflux condenser, and the time required for the disappearance

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(31) Kindly donated by Dr. R. H. Bible, Jr.

(32) The semicarbazone of Δ-9,10-octalone-1 has been reported [J. W. Cook and C. A. Lawrence, *J. Chem. Soc.*, 1637 (1935)] to melt at 242–243°.

(33) The melting point of *trans*-1-decalone semicarbazone has been reported as 229–230° [W. Hückel, *Ann.*, **441**, 1 (1925)] and as 270° [D. Biquard, *Bull. soc. chim.*, **8**, 725 (1941)].

of the blue color was noted. For the introduction of iron, aliquots of a stock solution of 0.1 g. of anhydrous ferric chloride in 100 ml. of tetrahydrofuran were added. Thus for example, in one experiment using *t*-butyl alcohol, 1 ml. of this solution was added; assuming that the liquid volumes are additive, this is equivalent to 0.001 mg. of iron per ml. of reaction mixture which we regard, for convenience, as equivalent to 1 p.p.m. Corresponding aliquots were taken for other iron concentrations and experiments using the other alcohols. In cases where the reaction times were very short (<10 min.), the alcohol and/or ferric chloride were added last to the other reagents so as to avoid the time normally required for the metal to "melt" in the reaction mixture.

The effect of iron on the Birch reduction of estradiol 3-methyl ether was studied using 6.5 g. of the steroid and the quantities of other reagents (*t*-butyl alcohol as proton donor) given directly above. Likewise the addition of definite amounts of iron was done in a fashion similar to that described. The products were isolated and analyzed for unreduced starting material as described earlier.

CHICAGO 80, ILL.

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORIES, UNIVERSITY OF NORTH CAROLINA]

Preparation of Substituted Ferrocenes from Fulvenoid Compounds[1]

WILLIAM F. LITTLE AND ROBERT C. KOESTLER[2]

Received January 18, 1961

1,2-Diaroylcyclopentadienes readily form substituted cyclopentadienide ions with bases, but these anions do not react with ferrous chloride to yield substituted ferrocenes. However, prior reduction of the carbonyl groups with lithium aluminum hydride followed by treatment with ferrous chloride yields 1,1′,2,2′-tetrabenzylferrocenes. Unsubstituted tetrabenzylferrocene and a series of substituted tetrabenzylferrocenes were prepared. The substituents, on all four benzyl groups in each case, included *p*-methyl, *p*-fluoro, *o*-chloro *p*-chloro, *m*-bromo, and *p*-bromo.

Fulvenes have proved to be useful starting materials for preparation of unusual heteroannular disubstituted ferrocenes[3-6] by addition of reagents such as phenyllithium, lithium aluminum hydride, and sodium to the *exo* double bonds of alkyl and aryl fulvenes to generate substituted cyclopentadienide ions that will "sandwich" with ferrous chloride. Knox[7] has added phenyllithium to the fulvenoid compound, diazocyclopentadiene, and has prepared phenylazoferrocenes similarly.

Acylcyclopentadienes may be considered as fulvenoid compounds in that enolization of these systems produces α-hydroxyfulvenes; in fact, some acylcyclopentadienes have been demonstrated to exist principally as enols.[8] This consideration has suggested a likely approach to the preparation of additional ferrocenes of novel structure.

Linn and Sharkey[8] reported that aroyl halides react with cyclopentadiene to yield exclusively 1,2-diaroylcyclopentadienes. These substances were demonstrated to exist to an extent greater than 90% in the hydrogen bonded enol form, II.

Diaroylcyclopentadienes readily form salts with strong bases; this suggested a possible route to tetraaroylferrocenes, III, by reaction with ferrous ions. No difficulty was encountered in preparing salts of dibenzoylcyclopentadiene; however, the resulting anion failed in all attempts to "sandwich" with iron. The attempts employed as bases phenyllithium in ether, sodium ethoxide in ethanol, and diethylamine as both base and solvent. Only recovery of dibenzoylcyclopentadiene resulted with the phenyllithium and with sodium ethoxide, while diethylamine produced only tars. Apparently the *pi* electrons in the dibenzoylcyclopentadienide ion are too delocalized for effective sandwiching.

The failures of the above reactions were ascribed to excessive delocalization of the *pi* electrons for the sandwiching reaction with ferrous chloride. Accordingly, in order to circumvent this difficulty and to increase the availability of the ring electrons, the carbonyl groups of dibenzoylcyclopentadiene were reduced with lithium aluminum hydride prior to sandwiching. The reduction mixture in ether was directly introduced to anhydrous ferrous chloride in tetrahydrofuran, and from the resulting reaction was isolated 1,1′,2,2′-tetrabenzylferrocene, IVa, in 13% yield.

The generality of this procedure as a method for preparing tetrabenzylferrocenes of known substitution patterns was established by preparing similar derivatives starting with substituted benzoyl chlorides. Starting with *p*-methyl-, *p*-fluoro-, *o*-chloro-, *p*-chloro-, *m*-bromo-, and *p*-bromobenzoyl

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(1) Presented at the Southeastern Regional Meeting of the American Chemical Society, Birmingham, Ala., Nov. 3-5, 1960.

(2) R. J. Reynolds Fellow, Feb.--June, 1960.

(3) R. C. Koestler and W. F. Little, *Chem. & Ind. (London)*, 1589 (1958).

(4) P. L. Pauson and G. R. Knox, *Proc. Chem. Soc.*, 289 (1958).

(5) R. L. Pruett, personal communication; K. L. Rinehart, A. K. Frericks, P. A. Kittle, L. E. Westman, D. H. Gustafson, R. L. Pruett, and J. E. McMahon, *J. Am. Chem. Soc.*, **82**, 4111 (1960).

(6) W. F. Little and R. C. Koestler, in press.

(7) G. R. Knox, *Proc. Chem. Soc.*, 56 (1959).

(8) W. J. Linn and W. H. Sharkey, *J. Am. Chem. Soc.*, **79**, 4970 (1957).