the solution was tested by paper chromatography, which revealed two spots, one for 4-desoxypyridoxine (I) and the other for 2,4,5-trimethyl-3-pyridinol (VII). The solvent was then removed, and the residue was separated into two fractions: one was soluble in isopropyl alcohol and the other was insoluble. The former fraction was precipitated by adding ether. Yield: 25 mg. M.p. 215.0–216.0°. This was identified as 2,4,5-trimethyl-3-pyridinol hydrochloride (VII) by mixed melting point and by paper chromatography. The insoluble fraction was recrystallized from methanol-ether as fine needles (30 mg.). M.p. 267.0–268.0°. A mixed melting point with authentic 4-desoxypyridoxine hydrochloride (I) was also 267.0–268.0°. Paper chromatography showed that this fraction was 4-desoxypyridoxine hydrochloride (I).

Reduction of 4-desoxypyridoxine 3-monopalmitate (V). Five hundred milligrams of 4-desoxypyridoxine 3-monopalmitate (V) was hydrogenated in 30 ml. of isopropyl alcohol. The hydrogenated mixture was negative to the *N*,2,6-trichloro-*p*-quinoneimine test. After removal of the catalysts and the solvent, the residue was extracted with approximately 50 ml. of absolute ether. To this extract, ethanolic dry hydrogen chloride was added. The precipitate (75 mg.) melted at 153–159°. This product appeared to be a mixture of the hydrochlorides of 4-desoxypyridoxine 3-monopalmitate (V) and 2,4,5-trimethyl-3-pyridinol palmitate (VIII). This product after being refluxed in 2*N* ethanolic potassium hydroxide solution for 30 min. followed by acidification with alcoholic hydrogen chloride to Congo red gave two spots for 4-desoxypyridoxine hydrochloride (I) (intense) and 2,4,5-trimethyl-3-pyridinol hydrochloride (VII) (weak) upon paper chromatography.

Reduction of 2,4,5-trimethyl-3-pyridinol palmitate (VIII). Five hundred milligrams of 2,4,5-trimethyl-3-pyridinol palmitate (VIII) in 35 ml. of ethanol was hydrogenated. After removing the catalysts, the solvent was removed until dryness. The residue was extracted with ether, and the solution added to dry ether which contained hydrogen chloride. The precipitate (400 mg.) melted at 140.0–141.0°; a mixed melting point with the hydrochloride of 2,4,5-trimethyl-3-pyridinol palmitate (VIII) was 139.0–140.0°. No palmitic acid was isolated from the remaining ether extract.

Reduction of pyridoxine. One gram of pyridoxine hydrochloride was hydrogenated in 80 ml. of methanol. The catalysts were removed by filtration and the solution was evaporated until dryness. The residue had a melting point (241°) which was higher than any of the possible products, pyridoxine hydrochloride (206–208°), 5-desoxypyridoxine hydrochloride (VI) (143–143.5°),[2] and 2,4,5-trimethyl-3-pyridinol hydrochloride (VII) (216°). This suggested that the residue might contain 4-desoxypyridoxine hydrochloride (I) (267–268°). Upon paper chromatography, the residue revealed two spots corresponding to 4-desoxypyridoxine hydrochloride (I) and 2,4,5-trimethyl-3-pyridinol hydrochloride (VII).

The residue was dissolved in 5 ml. of water. Excess of potassium carbonate was added to make the solution alkaline, and the solution extracted with chloroform. The chloroform extract was thoroughly washed with water and after drying over anhydrous sodium sulfate, the solvent was removed. The residue was taken up in ethanol and upon addition of ether containing dry hydrogen chloride, a precipitate was obtained. Recrystallization was effected from approximately 3 ml. of absolute ethanol at −5°. Yield: 150 mg. M.p. 216.0–217.0°. A mixed melting point with authentic 2,4,5-trimethyl-3-pyridinol hydrochloride (VII) was 215.0–216.0°. This product was paper chromatographically homogeneous and showed an inhibition potency equivalent to that of authentic 2,4,5-trimethyl-3-pyridinol (VII) for the growth of *Saccharomyces carlsbergensis* (ATCC 4228).[5]

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Reduction of Polycyclic Phenols to Hydrocarbons

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In the course of studies on the Veratrum alkaloids, we recently had occasion[1] to reduce to the parent aromatic hydrocarbon a small amount of a phenolic degradation product,[2,3] $C_{18}H_{16}O$, derived from rubijervine[4,5] by selenium dehydrogenation. Experiments with zinc dust distillation showed that at temperatures high enough to effect reduction the only hydrocarbon isolated was chrysene, and this was subsequently shown to be a rearrangement product.[1] These circumstances, and the experience of other workers who have encountered unidentified phenols[6–10] during dehydrogenations, called to our attention the fact that few methods[9,11,12] are available to the natural product chemist for the reduction of small quantities (50–200 mg.) of phenols by procedures mild enough to preclude rearrangement.

In searching for a method which might be applicable to the small-scale reduction of phenols, we noted the recent paper of Kenner and Williams[13] which describes the conversion of phenols to aryl diethyl phosphates and their subsequent reduction to aromatic hydrocarbons with sodium or lithium in liquid ammonia.

$$\mathrm{ArOH} + \mathrm{HO{-}P(O)(OC_2H_5)_2} + \mathrm{CCl_4} + (\mathrm{C_2H_5})_3\mathrm{N} \longrightarrow \mathrm{ArOP(O)(OC_2H_5)_2} + \mathrm{CHCl_3} + (\mathrm{C_2H_5})_3\mathrm{N{\cdot}HCl}$$

(1) S. W. Pelletier and D. M. Locke, *J. Am. Chem. Soc.*, **79**, 4531 (1957).

(2) W. A. Jacobs and L. C. Craig, *J. Biol. Chem.*, **148**, 41 (1943).

(3) Y. Sato and W. A. Jacobs, *J. Biol. Chem.*, **179**, 623 (1949).

(4) V. Prelog and O. Jeger, "Solanum and Veratrum Alkaloids," in *The Alkaloids, Chemistry and Physiology*, edited by R. H. F. Manske and H. L. Holmes, Academic Press, Inc., New York, 1953, Vol. III, pp. 277–280.

(5) J. McKenna, *Quart. Rev.*, **7**, 231 (1953).

(6) G. A. R. Kon and F. C. J. Ruzicka, *J. Chem. Soc.*, 187 (1936).

(7) L. Ruzicka, M. W. Goldberg, and K. Hofmann, *Helv. Chim. Acta*, **20**, 325 (1937).

(8) L. Ruzicka, H. Schellenberg, and M. W. Goldberg, *Helv. Chim. Acta*, **20**, 791 (1937).

(9) L. Ruzicka, K. Hofmann, and J. Frei, *Helv. Chim. Acta*, **19**, 386 (1936).

(10) L. Ruzicka, K. Hofmann, and H. Schellenberg, *Helv. Chim. Acta*, **19**, 1391 (1936).

(11) A. v. Baeyer, *Ann.*, **140**, 295 (1866).

(12) G. W. Kenner and M. A. Murray, *J. Chem. Soc.*, S 178 (1949).

(13) G. W. Kenner and N. R. Williams, *J. Chem. Soc.*, 522 (1955).

$$ArO\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2 + 2M + NH_3 \longrightarrow ArH + MNH_2 + MO—\overset{O}{\overset{\uparrow}{P}}—(OC_2H_5)_2$$

Mono- and dihydric phenols derived from benzene together with α- and β-naphthol were reduced in this way. Since both steps of the reaction sequence proceeded at or below room temperature, its mildness seemed assured. It remained to be determined whether the method could be adapted to small-scale operation and whether it was applicable to the polycyclic phenols which were our principal concern.

Our initial success in reducing 45 mg. of the phenol from rubijervine to 1′-methyl-1,2-cyclopentenophenanthrene in 35% yield[1] has led us to investigate the generality of the method. In this paper we wish to report the small scale reduction of a number of polycyclic phenols, both mono- and dihydric, and to record typical experimental procedures.

Twelve phenols (Table I) were included in this study. In each case the procedure proved useful for the purpose envisioned, *i.e.*, 50–200 mg. of the phenol furnished sufficient hydrocarbon to permit careful purification and identification. The yields varied from 18–52% and are reported on the basis of purified material suitable for purposes of identification. The higher yields reported by Kenner and Williams[13] are based on the crude reduction product, and this is paralleled by our experience. For example, in our hands, β-naphthol consistently gave 85–95% yields of crude material (Kenner and Williams' data give 92%). However, purification by chromatography and sublimation indicated that only about one-half of this material was naphthalene.

In this study, the yields of hydrocarbon from dihydric phenols were not greatly different from the monohydric compounds, and indeed, in the case of 2,2′-dihydroxybiphenyl, rather good yields were obtained. In contrast to these results, Kenner and Williams[13] indicated that the reduction of dihydric phenols was comparatively unsuccessful. It may be significant that in our examples of dihydric phenols no two hydroxyls are located on the same ring.

The modifications we have incorporated into the experimental conditions were necessitated by the small scale of operation and by the decreasing solubility of the phenols and their aryl esters with their increasing molecular weight. Thus, 2,7-naphthalenediol was not sufficiently soluble in carbon tetrachloride to permit esterification. The use of a small amount of tetrahydrofuran gave a homogeneous reaction mixture from which the ester could be obtained in good yield. Optimum yields of most of the aryl esters were obtained by allowing the phenol to react with a 5% excess of diethyl phosphite[14] and triethylamine in carbon tetrachloride for twenty-four hours. With 2,7-naphthalenediol, however, a reaction time of three days was necessary.

With the exception of those of the bicyclic phenols, all the aryl esters were relatively insoluble in liquid ammonia. The use of 25–30% of ether, or preferably tetrahydrofuran, in liquid ammonia gave a medium in which all the reductions could be conveniently conducted. Sodium was used in preference to lithium since its larger molecular weight facilitated weighing the exact amount of metal required. The use of excess metal leads to products which are difficult to purify.

(14) H. McCombie, B. C. Saunders, and G. J. Stacey, *J. Chem. Soc.*, 380 (1945).

EXPERIMENTAL

General remarks. Sources of the various phenols are indicated in Table I. Purity of these materials was judged by comparison of the physical constants with those recorded in the literature. The esterifications and reductions were carried out by the procedures illustrated below. In the reduction step, the addition of two moles of sodium was occasionally accompanied by a deep blue color. In some cases this was obscured by the deep brown color of the reaction mixture, and occasionally no color whatever developed. In a few cases yields varied between experiments under apparently identical conditions.

TABLE I

POLYCYCLIC HYDROCARBONS FROM PHENOLS

Phenol	Reaction Product	Yield,[a]
2-Naphthol	Naphthalene	43,[h] 47,[i] 40[j]
o-Phenylphenol[b]	Biphenyl	48,[h] 47[i]
p-Phenylphenol[b]	Biphenyl	39,[h] 50[i]
2-Hydroxyfluorene[c]	Fluorene	18,[h] 27[i]
1-Phenanthrol[c,d]	Phenanthrene	30[h]
2-Phenanthrol[e]	Phenanthrene	33[h]
3-Phenanthrol[c]	Phenanthrene	30,[h] 39[i]
9-Phenanthrol[c,f]	Phenanthrene	25[h]
Phenol, $C_{18}H_{16}O$, from rubijervine[g]	1′-Methyl-1,2-cyclopenteno-phenanthrene	36[h]
2,2′-Dihydroxybiphenyl[c]	Biphenyl	42,[h] 52[i]
2,7-Naphthalenediol[b]	Naphthalene	22,[h] 17[i]
1,1′-Bi-2-Naphthol[b]	1,1′-Binaphthyl	18,[h] 18[i]

[a] The overall yields from phenol to hydrocarbon are reported on the basis of material purified by chromatography and sublimation. [b] Eastman Organic Chemicals. [c] Supplied by Professor L. F. Fieser. [d] Supplied by Dr. Erich Mosettig. [e] Synthesized as by L. F. Fieser, *J. Am. Chem. Soc.*, **51**, 2460 (1929), m.p. 168–169°. [f] Chromatographed in benzene over neutral alumina. Crystallized as tan needles, m.p. 151–154°. [g] Reference 1–3. [h] In liquid ammonia-ether. [i] In liquid ammonia-tetrahydrofuran. [j] In liquid ammonia.

Reduction of o-phenylphenol. A solution of 170 mg. (1.0 mmole) of *o*-phenylphenol in 2.0 ml. of a solution of diethyl phosphite[14] in carbon tetrachloride (75 mg./ml.) was treated with 0.18 ml. of triethyl amine and allowed to stand for 24 hr. The amine hydrochloride separated slowly as needles and eventually a solid mass was formed. The mixture was diluted with 10 ml. of chloroform and washed once with 5% hydrochloric acid, four times with 3% sodium hydroxide, and once with water. Evaporation of the solution *in vacuo* gave 288 mg. of the ester. The latter was dissolved in 1 ml. of dry tetrahydrofuran, cooled in a Dry Ice–Cellosolve bath,

and anhydrous ammonia was introduced until about 4 ml. had condensed. Clean sodium (43 mg.) was added in small pieces with shaking, while the solution was maintained just below the boiling point. After completion of the reduction, ethanol (*ca.* 1 ml.) was added, and the ammonia was boiled off. The mixture was taken up in chloroform and water, washed with sodium bicarbonate, sodium hydroxide, and water, and evaporated to dryness *in vacuo*. The 154 mg. of bright yellow crystals were chromatographed in benzene over alumina to give 76 mg. of white crystals. Sublimation at 100° at 14 mm. gave 73 mg. (47.7% yield) of biphenyl, m.p. 68–70° (corr.).

Reduction of 9-phenanthrol. A 100-mg. sample of 9-phenanthrol was dissolved in 1.0 ml. of a solution of diethyl phosphite[14] in carbon tetrachloride (75 mg./ml.). To this solution was added 0.09 ml. of triethylamine, and after standing overnight, the solution was worked up as above to give 165 mg. of crude ester. This material was dissolved in 2 ml. of ether. Sufficient ammonia was introduced into the solution, cooled as above, to raise the total volume to 7 ml. A 23-mg. sample of sodium cut in small pieces was slowly added to the reaction mixture. At the end of the addition a deep black color persisted. The reaction mixture was then worked up as described to give, after chromatography and sublimation at 150° and 14 mm., 23.1 mg. (25% yield) of phenanthrene, m.p. 96–98° (corr.).

Reduction of 2,7-naphthalenediol. To a solution of 161 mg. of 2,7-naphthalenediol in 0.3 ml. of tetrahydrofuran was added 4.05 ml. of a solution of diethyl phosphite[14] in carbon tetrachloride (75 mg./ml.) and 0.35 ml. of triethylamine. After standing over the week end, the reaction was worked up as above to give 460 mg. of crude ester. The ester was dissolved in 3 ml. of tetrahydrofuran, and 8 ml. of liquid ammonia was added. Clean sodium (85 mg.) was then added. The yellow-brown solution was worked up in the usual fashion to give 22.5 mg. (17.5%) of naphthalene.

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1-Keto-3-methyl-2-tetralylacetic Acid from Cyclization of β-Carboxy-γ-methyl-δ-phenylvaleric Acid

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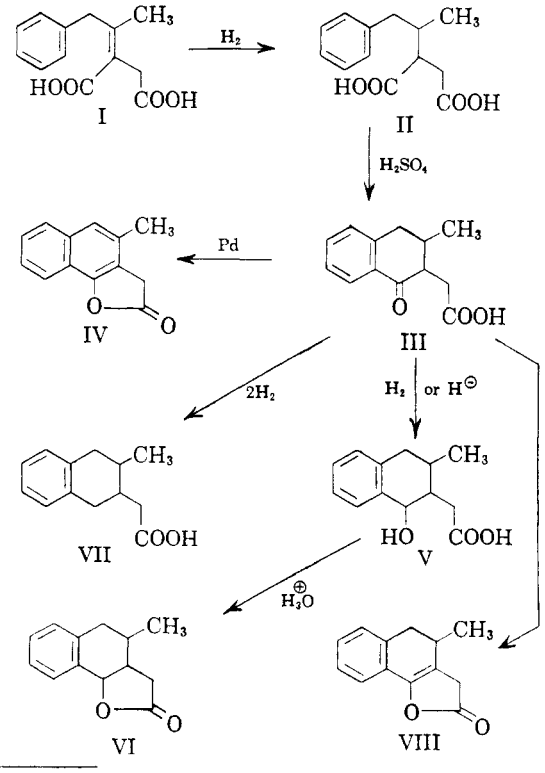
It has been reported[1] that acid-esters derived by Stobbe condensation of succinates with phenylacetone are cyclized to benzosuberenones. Different results have now been observed with corresponding *saturated* di-acids obtained from the same reaction.

The di-acid I described earlier[1] was prepared in 40% yield by Stobbe condensation of phenylacetone and ethyl succinate in the presence of sodium methoxide, and subsequent alkaline hydrolysis. The location of the double bond as shown in I was established previously[1] through ozonolysis, and further evidence for this assignment is now found in the fact that the infrared spectrum of I clearly shows the presence of both unconjugated (5.84 μ) and conjugated (5.93 μ) carboxyl groups. Hydrogenation of I in the presence of palladium-charcoal gave a mixture of two stereoisomers of II, an outcome which might be anticipated in analogy with Newman's finding,[2] that two isomers of β-carboxy-γ,δ-diphenylvaleric acid are formed in hydrogenation of a phenyl-(in place of methyl) substituted di-acid similar to I. Likewise in a sense similar to that of cyclizations reported by Newman,[2] it was found that cyclization of the mixture of acids II with sulfuric acid at room temperature gave the tetralone derivative III in 56% yield.

Structure III was established by the following facts, which exclude the alternative cyclization product, 3-carboxy-4-methylbenzosuberene-1-one. Keto acid III was esterified very readily. In fact it was not possible to prepare a 2,4-dinitrophenylhydrazone of III itself, for in the presence of alcohol and dilute sulfuric acid at room temperature, esterification took place during the preparation of the derivative, giving the 2,4-dinitrophenylhydrazone



(1) J. R. Dice and G. R. Allen, *J. Am. Chem. Soc.*, **74**, 1231 (1952).

(2) M. S. Newman and R. T. Hart, *J. Am. Chem. Soc.*, **69**, 298 (1947).