[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

# Synthesis of the Mono- and Dihydric Pentadecylphenols Related to Poison Ivy "Urushiol"

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In preparation for a clinical program on poison ivy dermatitis, the nine pentadecyl mono- and dihydric phenols have been synthesized. Three of these compounds are new and, in the case of five of the others, different and more convenient methods of synthesis have been developed, including a general method of synthesis for the 2-alkylresorcinols.

Little is known at present concerning the physiological mode of activity of the dermatitis-producing materials present in the poison ivy plant, the Japanese lac tree, the cashew nut tree and other members of the anacardiacea family, other than the fact that the 1,2- and 1,3-dihydric phenols are the most active in respect to their ability to produce a contact dermatitis.[2] In preparation for a clinical program to obtain more information about the relationship between chemical structure and activity in poison ivy-like dermatitis, the nine pentadecyl mono- and dihydric phenols have been synthesized. More information concerning the activity in relationship to the position of the alkyl side chain in such phenols may reveal their mode of action and provide a clue as to how the dermatitis condition can be combatted.

One of these alkyl phenols, 3-pentadecylcatechol (hydrourushiol) is known to be a component of the poison ivy principle.[3] It has been previously synthesized[4] and used clinically.[4,5] However, none of the olefinic phenols, which make up about 95% of poison ivy "urushiol,"[3] has been available in pure form for clinical evaluation. In view of our interest in the synthesis of the monoolefinic component,[6,7] the present study dealing with the preparation of phenols having saturated side chains has provided an opportunity for investigating a variety of routes that might serve also for the synthesis of phenols with unsaturated side chains. Such unsaturated phenols are characterized by extreme susceptibility to polymerization in acidic media. Hence, for several of the pentadecylphenols described here, more than one synthesis has been employed, and in some cases a route other than the most direct or obvious one has been used in order to avoid acidic conditions.

In connection with their work on establishing the structure of hydrocardanol (3-pentadecylphenol), Backer and Haack[8] synthesized 2-, 3- and 4-pentadecylphenol. They employed for this purpose the reaction of the appropriate methoxybenzaldehyde and the tetradecyl Grignard reagent, followed by dehydration of the resulting alcohol, reduction and then cleavage of the ether by heating with hydriodic acid in a sealed tube.

In the present investigation the 2- and 4-pentadecylphenols were prepared first by the more direct procedure of Friedel—Crafts acylation,[9] followed by Clemmensen reduction in a homogeneous solution.[10] This method, however, could not be used for the synthesis of 3-alkylphenols. Furthermore, neither this method nor the Backer and Haack synthesis is applicable to the synthesis of the corresponding olefinic phenols because of the strongly acidic conditions involved. For this reason the reaction of the Grignard reagent directly on the free phenolic aldehyde was investigated, for it did not involve strongly acidic conditions at any stage.

Pauly and co-workers,[11] in an extensive investigation of the reactions of phenolic aldehydes, found that they could obtain a 70% yield of the expected carbinol by the reaction of excess ethyl Grignard reagent on salicylaldehyde. From a similar reaction using the *p*-hydroxybenzaldehyde, they obtained a 25% yield of product. Backer and Haack[8] also considered this method of synthesis. However, when they carried out the reaction between tetradecylmagnesium bromide and salicylaldehyde, they obtained the desired carbinol in low yield and abandoned this scheme when dehydration of the carbinol resulted only in polymerization.

It has been found in the present investigation that even with the large alkyl Grignards, very satisfactory yields of the desired carbinol can be obtained. Using a one-mole excess of the tetradecylmagnesium bromide, the carbinol was obtained in 86% yield as compared with the 31% yield reported by Backer and Haack. Heating the carbinol to 150° caused resinification, and attempted dehydration by heating to 120° with oxalic acid[12] caused excessive polymerization. However, it was found that the carbinol could be simultaneously dehydrated and distilled in good yield by heating *in vacuo*.

Catalytic hydrogenation of the resulting olefin gave the desired 2-pentadecylphenol, identical to that obtained by the Friedel–Crafts reaction but of somewhat higher quality.

The 4-pentadecylphenol has also been prepared by this procedure. In this case, however, the yields were considerably lower, corresponding

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[1] This paper is based on a portion of the thesis submitted by Bernard Loev in 1952 to Columbia University in partial fulfillment of the requirements for the Ph.D. degree in chemistry.

[2] H. Keil, D. Wasserman and C. R. Dawson, *Ind. Med.*, **14**, 825 (1945); *Science*, **102**, 274 (1945).

[3] W. F. Symes and C. R. Dawson, THIS JOURNAL, **76**, 2959 (1954).

[4] C. R. Dawson, D. Wasserman and H. Keil, *ibid.*, **68**, 534 (1946); H. S. Mason, *ibid.*, **67**, 1538 (1945).

[5] H. Keil, D. Wasserman and C. R. Dawson, *J. Allergy*, **16**, 275 (1945).

[6] B. Loev and C. R. Dawson, THIS JOURNAL, **78**, 1180 (1956).

[7] The synthesis of this compound will be described in a later paper.

[8] H. J. Backer and N. H. Haack, *Rev. trav. chim.*, **60**, 661 (1941).

[9] A. W. Ralston and S. T. Bauer, *J. Org. Chem.*, **5**, 165 (1940).

[10] R. R. Reed and J. Wood, *Org. Syntheses*, **20**, 57 (1940).

[11] H. Pauly, *et al.*, *Ann.*, **383**, 230 (1911).

[12] M. A. Mounie, *Bull. Soc. Chim. France*, **29**, 350 (1903).

closely to those obtained by Pauly[11] using the ethyl Grignard reagent.

The synthesis employing the free phenolic aldehydes requires far less time than either of the other methods mentioned and gives a much purer product. It has the disadvantage, of course, that one equivalent of the Grignard reagent is destroyed by reaction with the free phenolic hydroxyl group. However, usually the alkyl halide is more expendable than the carbonyl compound, and such a loss is therefore not a serious drawback.

The third compound, 3-pentadecylphenol (hydrocardanol), was obtained by catalytic reduction of the naturally occurring cardanol.[13]

Two methods have been described for the synthesis of resorcinols carrying an alkyl group between the hydroxyl groups (2-alkylresorcinols), but neither has been found to be applicable to the synthesis of higher molecular weight alkylresorcinols. One of these methods, the "Nidhone" process,[14] is very long, involving steps of low yields, and is apparently restricted to substituents having five carbons or less.[15] The other method involves a Grignard reaction with 2,6-dimethoxybenzonitrile.[16] Although this method gives good yields when small alkyl groups are involved, Russel and Gulledge[17] found that it failed in the synthesis of high molecular weight compounds such as 2-tridecylresorcinol.

A synthesis of 2-pentadecylresorcinol was attempted using the reaction of pentadecanoylchloride with the 2-lithium derivative[18] of the ditetrahydropyranyl ether of resorcinol.[19] However, no recognizable products, other than pentadecanoic acid, could be isolated. Conversion of the lithium derivative to the cadmium compound did not prove fruitful.[20]

The desired 2-pentadecylresorcinol was synthesized in satisfactory yield by first treating myristylmagnesium bromide with 2,6-dimethoxybenzaldehyde in boiling benzene. The resulting carbinol was then dehydrated, etc., as previously described.[4] The Grignard reaction was unsuccessful when carried out in diethyl ether.

The 4-pentadecylresorcinol was readily prepared by acylation of resorcinol with pentadecanoic acid, using anhydrous zinc chloride as catalyst, according to the general procedure for the Nencki reaction.[21] The resulting 4-pentadecanoylresorcinol was then reduced by the Clemmensen method.

The 5-pentadecylresorcinol (hydrocardol) was obtained by reduction of the naturally occurring cardol.[13]

During his investigation of the structure of the Japanese lac urushiol, Majima synthesized 4-pentadecylcatechol.[22] In the present investigation superior yields were obtained by treating piperonal with myristylmagnesium bromide, followed by dehydration of the carbinol, catalytic reduction of the olefin and aluminum chloride cleavage of the methylene ether.

As pointed out earlier, 3-pentadecylcatechol (hydrourushiol) has been synthesized previously.[4] However, the method, based on the reaction of myristylmagnesium bromide with 2,3-dimethoxybenzaldehyde has been troublesome in the last stage, *i.e.*, the cleavage of the methyl ether groups. It has been found in this investigation that reducing the reaction time of the aluminum chloride cleavage from 3 hr. to 15 minutes gives a more easily purified product.

In a search for ways of avoiding the strongly acidic aluminum chloride cleavage, several other methods of synthesis of 3-pentadecylcatechol were investigated. These methods included an attempted alkaline cleavage of the methyl ethers and the use of other protecting groups, such as the acetate and the pyranyl ethers.[20] Of particular interest was the reaction involving the direct use of excess Grignard reagent on 2,3-dihydroxybenzaldehyde. Although the desired carbinol was obtained in fairly good yield, it could not be dehydrated. All attempts led only to dark polymeric materials.[20]

Pentadecylhydroquinone has been previously synthesized by diazotization of 4-amino-3-pentadecylphenol. However, the yields were quite low, and the product was difficult to purify.[23] For this reason, the conversion of the aminophenol to the hydroquinone by dichromate oxidation followed by sodium hydrosulfite reduction[24] was investigated. The pentadecylhydroquinone was obtained in good yield. Pentadecylhydroquinone was also prepared employing the Friedel–Crafts acylation of hydroquinone dimethyl ether, followed by Clemmensen reduction and ether cleavage.[25]

## Experimental[26,27]

**2- and 4-Pentadecanoylphenol.**—Pentadecanoyl chloride, 26 g. (0.1 mole), b.p. 160° (0.6 mm.), was added over a period of 40 minutes, with cooling, to a mixture of 26 g. (0.2 mole) aluminum chloride, 10 g. (0.106 mole) phenol and 20 cc. of dry nitrobenzene. The resulting brown solution was stirred at 60–70° for 6 hr., and then poured into cold dilute hydrochloric acid. The nitrobenzene was steam distilled, and the brown solid that formed on cooling was filtered.

The solid material, a mixture of the 2- and 4-isomers, was

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[13] Kindly supplied by the Irvington Varnish and Insulator Co., Irvington, N. J.

[14] D. B. Limaye, *Ber.*, **67**, 12 (1934); D. B. Limaye, *Rasayanam*, **1**, 64 (1936); *C. A.*, **31**, 2182 (1937); A. Russel and J. R. Frye, *Org. Syntheses*, **21**, 22 (1941).

[15] A. Russel, J. R. Frye and W. L. Mauldin, THIS JOURNAL, **62**, 1441 (1940).

[16] H. L. Haller, *ibid.*, **55**, 3032 (1933).

[17] A. Russel and H. C. Gulledge, *ibid.*, **64**, 1313 (1942).

[18] G. Wittig, *Angew. Chem.*, **53**, 241 (1940).

[19] W. E. Parham and E. L. Anderson, THIS JOURNAL, **70**, 4187 (1948).

[20] Details of these investigations are available in the dissertation of B. Loev, a microfilm of whch may be obtained from the Columbia University Library.

[21] A. R. L. Dohme, E. H. Cox and E. Miller, THIS JOURNAL, **48**, 1688 (1926); R. D. Desai and W. S. Waravdekar, *Proc. Indian Acad. Sci.*, **13A**, 177 (1941); *C. A.*, **36**, 90 (1942).

[22] R. Majima and I. Nakamura, *Ber.*, **48**, 1597 (1915).

[23] D. Wasserman and C. R. Dawson, THIS JOURNAL, **72**, 4994 (1950).

[24] L. F. Fieser, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 383.

[25] W. M. McLamore, THIS JOURNAL, **73**, 2221 (1951), has described a more convenient procedure for the acylation of hydroquinone using boron trifluoride. This paper appeared, however, after the work described herein had been completed. Many of the observations and reactions described by McLamore are similar to those reported here.

[26] All melting points are corrected. Ultraviolet spectra were taken on a Cary recording spectrophotometer, using 95% ethanol as solvent.

[27] Microanalysis was performed by Tiedcke Laboratory of Microchemistry, Teaneck, N. J., and Micro-Tech Laboratories, Skokie, Ill.

triturated with 20% ethanol containing 1.5% sodium hydroxide and then filtered. The insoluble material, m.p. 40–50°, was recrystallized from ethanol, giving 8 g. of 2-pentadecanoylphenol as a tan solid, m.p. 42.5–43.5° (25%). In ethanol it gave a red color with a drop of aqueous ferric chloride solution.

On acidification of the alkaline filtrate above, separation of the solid 4-pentadecanoylphenol occurred. Recrystallization from petroleum ether gave 26.5 g. of white crystals, m.p. 72.8–73.5° (68%), no coloration with ferric chloride.

**4-Pentadecylphenol. Clemmensen Reduction of 4-Pentadecanoylphenol.**—The 4-pentadecanoylphenol, 12 g., was dissolved in a solution of 70 cc. of water, 70 cc. of concd. hydrochloric acid and 50 cc. of ethanol[10] and boiled under reflux with vigorous stirring for three days with 35 g. of amalgamated zinc. The solution was extracted with benzene and the benzene then removed, leaving 12 g. of a brown oil which shortly solidified. The tan solid, insoluble in dilute base, could not be purified by recrystallization. On vacuum sublimation, the 4-pentadecylphenol was obtained in 80% yield as a white solid, m.p. 68.5–69.8°, reported[8] 72–73°. Repeated vacuum sublimations and recrystallizations did not raise the melting point.

*Anal.* Calcd. for $C_{21}H_{36}O$: C, 82.83; H, 11.92. Found: C, 82.51; H, 12.07.

**2-(1′-Hydroxypentadecyl)-phenol.**—The Grignard reagent was prepared in the customary manner from 150 g. (0.55 mole) of tetradecyl bromide and 13.4 g. (0.55 mole) of magnesium in 250 cc. of anhydrous ether. To the chilled solution was added, over a period of 2.5 hr., 30 g. (0.24 mole) of freshly distilled salicylaldehyde ($n^{26}$D 1.5079) in 100 cc. of anhydrous ether. The color of the solution turned bright yellow after about three-quarters of the aldehyde had been added. The mixture was stirred an additional hour, hydrolyzed in dilute sulfuric acid and washed with dilute base. The solvent was removed and the residual liquid was then dissolved in 400 cc. of boiling ethanol. On cooling, 11 g. of colorless waxy plates of octacosane precipitated and were filtered. Removal of the solvent left 66 g. of the white solid alcohol, m.p. 48–56° (86%). Recrystallization from petroleum ether gave a white granular precipitate, m.p. 57.5–58°, no color with ferric chloride.

*Anal.* Calcd. for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32. Found: C, 78.64; H, 11.40.

A small amount of the alcohol, on heating to 180° for 30 minutes, turned to an amber resin. The same result was obtained on heating at 180° for 15 minutes with a small amount of potassium bisulfate.

A small amount of the alcohol and anhydrous oxalic acid was heated at 118°. At first a considerable amount of water was evolved. After 4 hr., the resulting yellow oil was taken up in ether, washed with dilute sodium carbonate solution and dried. The solvent was removed and an attempt was made to distil the oil, but only a few drops of an alcohol-insoluble oil distilled. The residue solidified to a brown glass.

**2-(Pentadecenyl-1′)-phenol.**—Distillation of 10 g. of the above alcohol at 2.5 mm. (bath temp. 250°), resulted in simultaneous dehydration, as evidenced by the copious quantities of water vapor evolved. A pale yellow oil, b.p. 187–188° ($n^{25}$D 1.5061), distilled over having a strong phenolic odor. After standing for several days the oil solidified and was recrystallized from a small volume of petroleum ether, giving 7.6 g. of the olefinic phenol as a white solid, m.p. 39–40° (79.6%), $\lambda_{max}$ 248 m$\mu$, no color with ferric chloride.

*Anal.* Calcd. for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.10; H, 11.36.

**2-Pentadecylphenol.**—Hydrogenation of the above olefinic phenol over 5% palladium-on-charcoal, or platinum oxide, in ethyl acetate, gave a quantitative yield of the 2-pentadecylphenol, m.p. 47–50°. Vacuum sublimation gave a white solid, m.p. 53–53.4°, reported[8] 54.5–55°. Several recrystallizations from methanol and from petroleum ether did not alter the melting point, $\lambda_{max}$ 275 m$\mu$.

*Anal.* Calcd. for $C_{21}H_{36}O$: C, 82.83; H, 11.92. Found: C, 82.74; H, 12.07.

**4-(1′-Hydroxypentadecyl)-phenol.**—A solution of 30 g. (0.25 mole) of *p*-hydroxybenzaldehyde in 250 cc. of ether and 60 cc. of dry dioxane was slowly added to a solution of 0.55 mole of tetradecylmagnesium bromide in 200 cc. of ether. The color of the reaction mixture first became gray, then turned purple. The solution eventually became so viscous that it could no longer be stirred, and addition of the aldehyde was stopped (only 14 g. of the aldehyde had been added at this point). The mixture was hydrolyzed and the octacosane removed (as previously described). The residual orange liquid, on standing in the cold with petroleum ether, deposited a small amount (4.5 g.) of the crystalline alcohol, m.p. 83.5–90°. Recrystallization from petroleum ether raised the melting point to 94.6–96.8°, $\lambda_{max}$ 275 m$\mu$, no color with ferric chloride.

*Anal.* Calcd. for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.10; H, 11.36.

**4-(Pentadecenyl-1′)-phenol.**—The filtrates from the above petroleum ether crystallizations (containing most of the alcohol in crude form) were combined, the solvent removed and the residue distilled *in vacuo*. After a forerun of tetradecane, 9.5 g. of the olefin distilled, b.p. 198–203° (0.4 mm.), and solidified in the receiver. The total yield of alcohol and olefin was 19.5% based on the *p*-hydroxybenzaldehyde used. The olefin crystallized from benzene as a white solid, m.p. 86.2–86.5°, no color with ferric chloride.

*Anal.* Calcd. for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.18; H, 11.02.

The non-distillable residue, 9 g., solidified on cooling and crystallized from petroleum ether as a white solid, m.p. 78–81°. It did not absorb hydrogen and was not further investigated.

**4-Pentadecylphenol.**—The above olefin absorbed the theoretical quantity of hydrogen in a few minutes using 5% palladium-on-carbon in ethyl acetate. The 4-pentadecylphenol crystallized from petroleum ether as a white solid in 90% yield, m.p. 71–71.6°, reported[8] 72.5–73°. Vacuum sublimation did not raise the melting point. A mixed melting point with the 4-pentadecylphenol obtained by the Clemmensen reduction procedure, previously described, showed no depression.

*Anal.* Calcd. for $C_{21}H_{36}O$: C, 82.83; H, 11.92. Found: C, 83.17; H, 12.16.

**3-Pentadecylphenol (Hydrocardanol).**—Cardanol[13] was catalytically reduced using 5% palladium-on-charcoal in ethyl acetate to give a 90% yield of hydrocardanol, m.p. 51.6–52.4° (from petroleum ether), reported[8] 51.5–52.5°.

*Anal.* Calcd. for $C_{21}H_{36}O$: C, 82.83; H, 11.92. Found: C, 82.82; H, 11.74.

Hydrocardanol acetate was prepared in essentially quantitative yield by heating a benzene solution of hydrocardanol with acetic anhydride and several drops of concentrated sulfuric acid. The acetate was found to be quite soluble in petroleum ether. It was recrystallized from ethanol giving white plates, m.p. 38.2–38.8°.

*Anal.* Calcd. for $C_{23}H_{38}O_2$: C, 79.71; H, 11.05. Found: C, 79.77; H, 11.00.

Hydrocardanol benzyl ether was prepared by refluxing a mixture of hydrocardanol, benzyl bromide and potassium carbonate in acetone[28] for 24 hr. At the end of this time, the salts were filtered and the solvent removed. The residual solid was recrystallized from acetone–alcohol giving the benzyl ether in 86% yield, m.p. 39–48°.

**2-(1′-Hydroxypentadecyl)-resorcinol Dimethyl Ether.**—An ether solution of tetradecylmagnesium bromide was prepared in the usual manner using 65.8 g. (0.214 mole) of tetradecyl bromide and 5.1 g. (0.212 mole) of magnesium. The ether was then removed by distillation and to the dark brown residual oil was added a boiling solution of 24 g. (0.15 mole) of 2,6-dimethoxybenzaldehyde[18] in 100 cc. of anhydrous, thiophene-free benzene. The solution was then heated under reflux, with stirring, for 12 hr. After hydrolysis in dilute acid and removal of the octacosane, the solvent was distilled. The residual oil solidified giving 62.6 g. of a yellow solid, m.p. 54–58°. After several recrystallizations from petroleum ether, the white solid alcohol, m.p. 71–72°, was obtained in 62% yield. The alcohol was found to be soluble in cold ethanol and gave with concentrated sulfuric acid a red-violet color which gradually turned deep yellow.

*Anal.* Calcd. for $C_{23}H_{40}O_3$: C, 75.77; H, 11.06. Found: C, 75.89; H, 11.11.

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[28] L. Claisen and O. Eisleb, *Ann.*, **401**, 21 (1913).

**2-(Pentadecenyl-1′)-resorcinol Dimethyl Ether.**—The above alcohol, 18 g., was heated to 120°. Two grams of freshly fused potassium bisulfate was added, and the temperature was raised to 160° for 30 minutes and then finally to 175° for 10 minutes. Cessation of vigorous boiling indicated that dehydration was complete. The dark brown oil was distilled and the olefin was obtained in 66% yield as a pale, yellow liquid, b.p. 205–206° (0.5 mm.), 11 g. The olefin was insoluble in ethanol.

**2-Pentadecylresorcinol Dimethyl Ether.**—The above olefin slowly absorbed the theoretical amount of hydrogen when catalytically hydrogenated over 5% palladium-on-charcoal in ethyl acetate. Distillation of the product gave a colorless liquid, b.p. 206–207° (0.5 mm.), m.p. 42–43° (80.6%), insoluble in ethanol.

*Anal.* Calcd. for $C_{23}H_{40}O_2$: C, 79.25; H, 11.57. Found: C, 79.55; H, 11.59.

**2-Pentadecylresorcinol.**—A 9.1-g. sample of the above dimethyl ether was dissolved in 91 cc. of anhydrous chlorobenzene to which was added 9.1 g. of aluminum chloride. After heating under reflux for 0.5 hr., the solution was poured into ice-cold hydrochloric acid, extracted with ether, treated with Norit and dried. The solvent was removed, *in vacuo*, leaving a dark red oil that soon crystallized (pink solid). This material was distilled, b.p. 189–191° (0.5 mm.), m.p. 69–74.5°. The solidified distillate after being triturated with cold petroleum ether melted at 78–79°, 3 g. (39.3%). A small sample recrystallized from petroleum ether for analysis melted at 79–80.5°.

*Anal.* Calcd. for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32. Found: C, 78.30; H, 11.17.

**4-Pentadecanoylresorcinol.**—Anhydrous zinc chloride was prepared by pouring molten zinc chloride into anhydrous toluene contained in a mortar resting on a balance, until the desired amount had been weighed out. The zinc chloride solidified on contact with the toluene and was pulverized by grinding directly under the anhydrous medium. Other methods of obtaining anhydrous zinc chloride were unsuccessful. Unless the zinc chloride is completely anhydrous, the following reaction does not work.

Pentadecanoic acid, 0.098 mole, was heated to 150°. The toluene was decanted from the zinc chloride, and the powdered anhydrous zinc chloride (0.05 mole) was added, with stirring, to the molten acid. Resorcinol, 0.118 mole, was added portionwise during the course of 30 minutes. The deep red solution was maintained at 140–150° for 3 hr., while being stirred, and was then poured into 100 cc. of 1:1 hydrochloric acid. The orange precipitate which formed was recrystallized from toluene to give a 55% yield of pale yellow crystalline ketone, m.p. 91.2–91.8°. The ketone gave a red color with ferric chloride.

**4-Pentadecylresorcinol.**—The above ketone was reduced by the Clemmensen procedure, previously described, giving 4-pentadecylresorcinol in 56% yield as white crystals, m.p. 82.4–82.6° (from petroleum ether–toluene).

*Anal.* Calcd. for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32. Found: C, 78.99; H, 11.40.

**5-Pentadecylresorcinol (Hydrocardol).**—Cardol[13] was catalytically hydrogenated as previously described giving hydrocardol as white crystals from toluene–ligroin, m.p. 94–94.5, reported[8] 95.5–96°.

*Anal.* Calcd. for $C_{21}H_{38}O_2$: C, 78.69; H, 11.32. Found: C, 78.80; H, 11.23.

**1-(3,4-Methylenedioxyphenyl)-1-pentadecanol.**—Tetradecylmagnesium bromide, prepared from 46 g. (0.166 mole) tetradecyl bromide in the usual manner, was treated with an ethereal solution containing 25 g. (0.167 mole) of piperonal. A dense white precipitate formed. After refluxing for 30 minutes, the mixture was poured into cold dilute ammonium chloride solution. The ether layer was washed and dried, and the octacosane removed in the manner already described. The residual oil, on cooling, formed a brown solid melting at about 55°. This crude alcohol, obtained in 95% yield, was used in the next step without further purification.

**1,2-Methylenedioxy-4-(1-pentadecenyl)-benzene.**—The above alcohol was dissolved in 100 cc. of xylene to which 5 g. of fused potassium bisulfate had been added, and the mixture was refluxed for 30 minutes. The xylene was then distilled, removing the water as an azeotrope. The process was repeated until no more water was evident in the distillate. The residual oil was dissolved in hot alcohol. Addition of a small amount of petroleum ether caused precipitation of the olefin in 75% yield as white crystals, m.p. 47–48°.

**1,2-Methylenedioxy-4-pentadecylbenzene.**—The above olefin absorbed the theoretical quantity of hydrogen on catalytic reduction, giving a white solid, which was used in the next step without further purification.

**4-Pentadecylcatechol.**—A 15.3-g. sample of the above methylene ether was treated with 15 g. of aluminum chloride in 150 cc. of anhydrous chlorobenzene, following the procedure previously described. The resulting dark brown solid, after several recrystallizations from benzene–petroleum ether, gave the catechol in 34% yield as white crystals, m.p. 92.2–93°, reported[22] 91°.

*Anal.* Calcd. for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32. Found: C, 78.58; H, 11.21.

**3-Pentadecylcatechol (Hydrourushiol).**—This compound was prepared starting with 2,3-dimethoxybenzaldehyde and tetradecylmagnesium bromide according to the procedure of Dawson, Wasserman and Keil,[4] except that the reaction time of the aluminum chloride demethylation was reduced to 15 minutes. The hydrourushiol so obtained melted at 58–59°, reported[4] 59–60°.

Hydrourushiol dibenzyl ether was prepared in 58% yield in the same manner as previously described for the benzyl ether of hydrocardanol. The product was recrystallized from acetone–alcohol, m.p. 52.4–53.0°.

**Pentadecylbenzoquinone.**—A 6-g. sample of 4-amino-3-pentadecylphenol[23] was dissolved in 100 cc. of a 50:50 acetone–water mixture. The boiling solution, containing 2 cc. of concd. sulfuric acid, was poured rapidly into a solution of 4 g. of sodium dichromate in 100 cc. of water.[24] The resulting purple granular precipitate was filtered, washed thoroughly with cold water, then dissolved in 100 cc. of hot ethanol. A small amount of tar, insoluble in the alcohol, was removed. On chilling, a 51% yield of golden colored pentadecylbenzoquinone was obtained, m.p. 72–74°.

**Pentadecylhydroquinone.**—The addition of a solution of 3 g. of sodium hydrosulfite in 5 cc. of water to a solution of the above quinone in 20 cc. of ethanol caused the color of the solution to disappear. The solution was heated on the steam-bath for 30 minutes and then poured into a large volume of water (saturated with sulfur dioxide). The ivory colored precipitate that formed was extracted with ether (saturated with sulfur dioxide). Removal of the ether left 3.1 g. (82%) of the hydroquinone as a light tan solid, m.p. 102–104°. Vacuum sublimation gave voluminous, white feathery crystals, m.p. 107.6–108°, reported[23] m.p. 105.5–106.5°. The product gave a positive Tollens test.

*Anal.* Calcd. for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32. Found: C, 78.44; H, 11.05.

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