EXPERIMENTAL

α-Benzoyloxydimethyl sulfide (I). In 250 ml. dry benzene was placed 24.2 g. (0.2 mole) benzoic acid, 47.6 g. (0.4 mole) phenyl isocyanate, and 15.6 g. dimethyl sulfoxide. The mixture was refluxed overnight on a steam bath. After cooling, the solid was filtered and recrystallized from benzene-ether. It had a m.p. of 240–241° and was undepressed on admixture with authentic *sym*-diphenylurea. The melting point of the latter is given as 240° in the literature. The yield was 29.5 g. (70%).

The benzene filtrate was extracted once with 100 ml. of 10% sodium bicarbonate solution, and once with 100 ml. of water. Ten g. of benzoic acid was recovered by acidifying the extract. The benzene solution was dried over $MgSO_4$ and the benzene distilled off. The residue was distilled at reduced pressure to a slightly yellow liquid of b.p. 85–86°/0.1 mm. The weight was 10.5 g., or 50% yield based on unrecovered benzoic acid.

Anal. Calcd. for $C_9H_{10}O_2S$: C, 59.34; H, 5.48; S, 17.58; sapon. equiv., 182. Found: C, 59.4, 59.4; H, 5.2, 5.3; S, 17.6, 17.7; sapon. equiv., 176, 175.

The infrared spectrum of this compound had bonds at 3.3, 6.27, 6.34 and 6.74μ, indicative of an aromatic ring; at 5.83, 8.0, and 9.2μ for an aromatic ester; at 3.4–3.48μ for aliphatic C—H.

α-Benzoyloxydimethyl sulfone (III). Five g. of I was dissolved in 20 ml. *t*-butyl alcohol and heated to 85–90° in an oil bath. Ten ml. of 30% hydrogen peroxide was added and heating continued 1 hr. and 15 min. The *t*-butyl alcohol was distilled off at reduced pressure. The residue solidified on cooling. It was recrystallized three times from absolute ethanol to give 2.5 g. (43%) of the sulfone, melting at 105–106°.

Anal. Calcd. for $C_9H_{10}O_4S$: C, 50.46; H, 4.67; S, 14.95. Found: C, 50.4, 50.4; H, 4.5, 4.4; S, 14.7, 14.5.

Poly-bis(4-aminophenyl)methane carbonamide (II). In 20 ml. dry dimethyl sulfoxide was dissolved 2.42 g. (0.02 mole) benzoic acid. To it was added 5.0 g. (0.02 mole) methylene bis(4-phenylisocyanate). The reaction was allowed to proceed at room temperature with occasional shaking. The vessel was protected from moisture with a drying tube. In 3–4 hr., a clear, viscous yellow solution resulted. Clear, tough films were obtained by casting on glass plates and drying at 80° in a vacuum oven.

In another run, the polymer was precipitated into water, washed with water and methanol, then dried. The yield, 4.4 g., was quantitative. The inherent viscosity ($\eta inh = \frac{1}{c} \ln \frac{n}{n_0}$, where concentration is 0.5% in dimethyl sulfoxide at 25°) was 1.0.

The infrared spectrum obtained on a sample of the above film was identical to that of films of the polyurea obtained by mixing equimolar amounts of the diisocyanate and bis-(4-aminophenyl)methane in dimethylformamide and casting similarly.

If twice the amount of benzoic acid was used as given above, the reaction proceeded as above. The polymer was precipitated in methylene chloride, filtered, and washed thoroughly with more methylene chloride. The weight of polymer was again 4.4 g. The combined methylene chloride was extracted with 5% aqueous sodium bicarbonate solution, which was, in turn, extracted with ether. Acidification of the aqueous layer precipitated 2.2 g. of benzoic acid, virtually all that was in excess. When this procedure was carried out on a polymer solution made as described originally, with no excess benzoic acid present, no benzoic acid was recovered.

When benzoic acid was added portionwise to a solution of the diisocyanate in DMS, a maximum solution viscosity was achieved at 1:1 molar equivalence, beyond which no viscosity change occurred nor carbon dioxide evolved.

That carbon dioxide was evolved from the reaction was established by passing the evolved gas from a typical reaction through a calcium hydroxide solution. The familiar milky precipitate formed. No quantitative measure was made.

WILMINGTON, DEL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Synthesis of Urushenol, the Mono-olefinic Component of the Allergenic Principles of Poison Ivy and Japanese Lac

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The synthesis of urushenol has made available for clinical study for the first time one of the olefinic catechols that make up the allergenic principle of poison ivy and Japanese lac. The catechol hydroxyl groups are protected by benzylation during the construction of the olefinic side chain. The benzyl ethers are subsequently cleaved, and a double bond of the styrene type is simultaneously reduced, by means of sodium and butanol. The desired Δ8 olefinic bond is not altered during the reductive cleavage. It is believed that the method will be adaptable to the synthesis of the higher olefinic components of poison ivy urushiol.

It has been known for over twenty years that the toxic principle of poison ivy is chemically similar to Japanese lac urushiol.[2,3] Only recently, however, has the complete structure of each of these allergenic oils been elaborated.[4,5] Because of the extreme sensitivity of these compounds and for other

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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. Present address: Smith Kline and French Laboratories, Philadelphia, Pa.

(2) R. Majima and co-workers, *Ber.*, **55**, 172 (1922) and preceding papers.

(3) G. A. Hill, V. Mattacotti, and W. D. Graham, *J. Am. Chem. Soc.*, **56**, 2736 (1934).

(4) W. F. Symes and C. R. Dawson, *J. Am. Chem. Soc.*, **76**, 2959 (1954).

(5) S. V. Sunthankar and C. R. Dawson, *J. Am. Chem. Soc.*, **76**, 5070 (1954).

reasons pointed out previously,[6,7] none of the pure olefinic components of the poison ivy principle has been available heretofore, either from natural sources or by synthetic means, for clinical investigation. Consequently there has been interest in the development of a method of synthesis for such alkenyl phenols. The primary obstacle has been the extreme sensitivity of these compounds to polymerization by heat and acids. Recently a method of protecting phenolic groups by benzylation followed by removal of the benzyl groups by reductive cleavage using sodium and butanol has been described.[7] This development has made possible the synthesis of urushenol, described in this communication.

Urushenol,[8] the mono-olefinic component of both the lac and poison ivy urushiols has been shown to have the structure of 3-(8'-pentadecenyl)catechol[4,5] (V in Fig. 1). The olefinic bond in the side chain has the *cis* configuration, as do the higher olefinic components of the poison ivy "urushiol".[6]

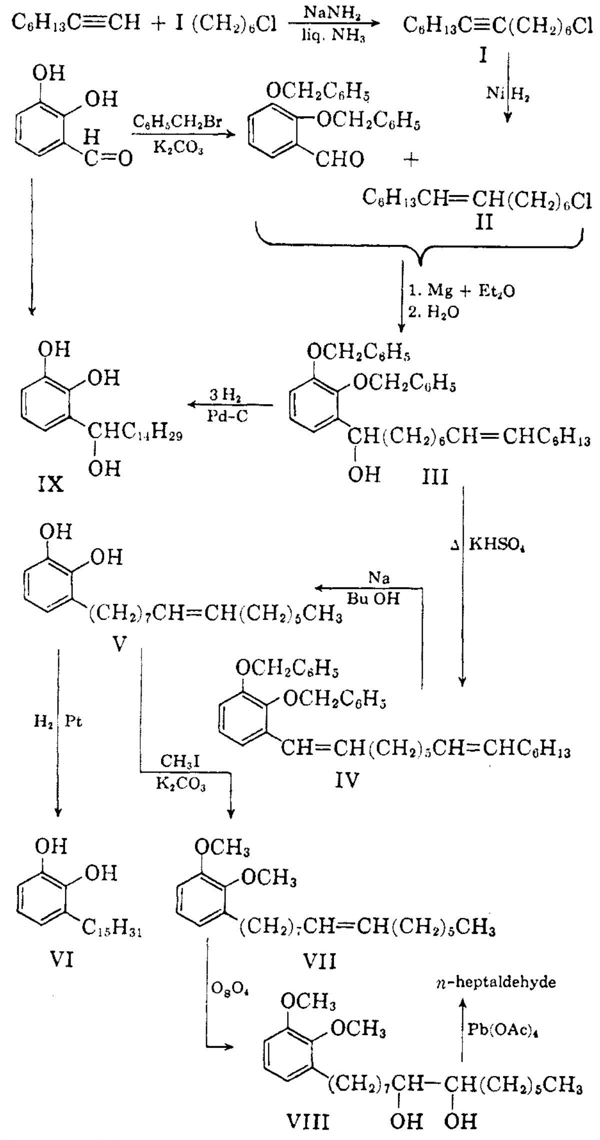

Fig. 1. Schematic diagram of the synthesis and confirmation of structure of urushenol (V)

The method of synthesis (Fig. 1), is partly based on a route developed earlier[6] in these laboratories for the synthesis of ethers of alkenyl phenols.[9] Most noteworthy in our synthesis is the use of benzyl rather than methyl ethers for protecting the phenolic hydroxyl groups during the Grignard reaction (see formation of III), and the subsequent removal of the benzyl groups by reaction with sodium and butanol with *simultaneous* reduction of the styrene type double bond[7] *without affecting the isolated olefinic bond* (IV → V). In the new synthesis, the olefinic side chain (II) is made up before utilizing the Grignard reaction, whereas in the earlier syntheses[9] of urushenol dimethyl ether the side chain was built up stepwise after introduction on the ring.

The acetylenic chloride (I), synthesized in a manner similar to that frequently used in the synthesis of unsaturated fatty acids,[10] exhibited some very interesting properties. Although it readily absorbed two moles of hydrogen on catalytic hydrogenation to give tetradecyl chloride, its infrared spectrum showed no absorption peak at 4.5 μ, the point where many acetylenes show absorption.[11] Furthermore it reacted only very slowly with bromine and was extremely resistant to permanganate oxidation and to ozonolysis. (Stearolic acid resisted bromination and ozonolysis under the same conditions.) The acetylenic chloride could not be induced to form the Grignard reagent even after careful purification nor when activated magnesium[12] and extensive refluxing were employed.

Similar peculiar properties of non-terminal acetylenes have previously been described.[13] Thus Wotiz and Miller[14] reported that the infrared ab-

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[6] B. Loev and C. R. Dawson, *J. Am. Chem. Soc.*, **78,** 1180 (1956).

[7] B. Loev and C. R. Dawson, *J. Am. Chem. Soc.*, **78,** 6095 (1956).

[8] See footnote 5 in ref. (6) for discussion of nomenclature.

[9] For another method of synthesis of alkenylveratroles and anisoles see D. Wasserman and C. R. Dawson, *J. Org. Chem.*, **8,** 73 (1943) and M. Sletzinger and C. R. Dawson, *J. Org. Chem.*, **14,** 849 (1949).

[10] K. Ahmad, F. M. Bumpus, and F. M. Strong, *J. Am. Chem. Soc.*, **70,** 3391 (1948); W. R. Taylor and F. M. Strong, *J. Am. Chem. Soc.*, **72,** 4263 (1950); W. F. Huber, *J. Am. Chem. Soc.*, **73,** 2730 (1951).

[11] These spectra are available in the dissertation of Bernard Loev, a microfilm copy of which may be obtained from the Columbia University Library.

[12] H. W. Underwood and J. C. Gale, *J. Am. Chem. Soc.*, **56,** 2117 (1934); H. Gilman and R. H. Kirby, *Rec. trav. chim.*, **54,** 577 (1935).

[13] A. W. Ralston, *Fatty Acids and their Derivatives*, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 163; R. Kuhn and K. Meyer, *Z. Physiol. Chem.*, **185,** 195 (1929); A. Steger and J. Van Loon, *Rec. trav. chim.*, **52,** 593 (1933).

[14] J. H. Wotiz and F. A. Miller, *J. Am. Chem. Soc.*, **71,** 3441 (1949).

sorption of the C≡C bond is most intense when the triple bond is near the end of the chain. When the triple bond is more than three positions from the end of the chain its infrared absorption becomes practically undetectable.

The olefinic chloride (II), prepared by the controlled reduction of I, behaved in a normal manner, *i.e.*, the olefinic bond was readily detected in the infrared, and II rapidly decolorized bromine. The olefinic chloride was readily oxidized by permanganate and ozone but formed the Grignard reagent rather slowly.

Partial reduction of the acetylene (I) using 10% palladium-on-charcoal, or 5% palladium-on-calcium carbonate as prepared by the method of Busch and Stove,[15] gave a mixture containing a large quantity of *trans* olefin, as indicated by the intense absorption at 10.4 μ in the infrared spectrum of the reduction product.

Partial reduction of I using either Raney nickel W-5 catalyst[16] or a palladium-on-calcium carbonate catalyst as described by Lindlar[17] gave predominantly the *cis* olefin. The presence of a small amount of *trans* olefin in the reduction product was revealed by a small 10.4 μ peak in the infrared spectrum.[11]

Preparation of the Grignard reagent of II required a twenty-four hour refluxing period under strictly anhydrous conditions. Addition of the 2,3-dibenzyloxybenzaldehyde to the refluxing Grignard reagent produced the expected olefinic alcohol (III) in better than 80% yield. A sample of III, purified by chromatography on alumina, was catalytically hydrogenated. The product (IX) proved to be identical to the alcohol obtained by direct reaction of tetradecylmagnesium bromide with 2,3-dihydroxybenzaldehyde.[18]

The crude olefinic alcohol (III) was dehydrated by heating with potassium bisulfate in a nitrogen atmosphere. We had previously shown that these dehydrating conditions have no effect on the position or configuration of the isolated double bond in the Δ8 position.[6] Treatment of a butanol solution of the crude diene (IV) with excess sodium caused simultaneous reduction of the olefinic bond conjugated with the ring and reductive cleavage of the benzyl ether groupings. The crude product (V), 3-(pentadecenyl-8′)-catechol or "urushenol," was obtained in excellent yield. However, on vacuum distillation a large portion polymerized to a black solid residue. Despite the large loss at this step the overall yield in the synthesis from II to purified V was 28%. The urushenol as distilled was practically colorless, but rapidly became a pale golden yellow in the receiver. On exposure to air it soon turned dark.

The structure of the synthetic urushenol (V) was confirmed in a number of ways. On catalytic reduction, V absorbed one mole of hydrogen to give hydrourushiol (3-pentadecylcatechol), VI, identified by mixed melting point with an authentic sample. Methylation of V gave dimethylurushenol (VII) having a refractive index in good agreement with that reported by Symes and Dawson[4] for the dimethyl ether of natural urushenol. The position of the double bond in the side chain of V was established by the method of synthesis, by the conversion of V to the known solid glycol VIII, and by oxidation of this glycol to give a quantitative yield of *n*-heptaldehyde.

The ultraviolet absorption spectra of the synthetic poison ivy urushenol (V) and of hydrourushiol (VI) were found to be identical, and characterized by an absorption band at 277 mμ. The dimethyl ethers of the natural and the synthetic urushenols also had identical ultraviolet absorption spectra, characterized by two bands, at 272 mμ and 278 mμ.[11]

The infrared absorption spectra of the synthetic urushenol and of hydrourushiol were very similar. Likewise the infrared absorption spectra of the dimethyl ethers of the natural and the synthetic urushenols were essentially identical except for the presence of a small absorption band at 10.4 μ in the synthetic material.[11] The intensity of this band was about the same as found in the spectra of the olefinic halide (II) used for the Grignard reaction. Consequently it may be inferred that no significant isomerization of the double bond occurred during steps in the synthesis subsequent to the Grignard reaction.

V gave a momentary green color, rapidly turning black, when treated with ferric chloride solution, and gave a dense white precipitate with methanolic lead acetate solution. On application to the skin (B.L.) it caused within a few hours the marked edema and blistering characteristic of poison ivy dermatitis. Each of these properties is the same as has been observed with the natural urushiol. Treatment of the synthetic urushenol (V) with dilute aqueous mineral acid caused extensive isomerization from the *cis* to *trans* configuration of the olefinic bond as evidenced by the appearance of a large absorption peak at 10.4 μ in the infrared spectra.[11] The isomerized (*trans*) material caused a typical poison ivy rash and the pale golden

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[15] M. Busch and H. Stove, *Ber.*, **49**, 1063 (1916).

[16] H. Adkins and H. R. Billica, *J. Am. Chem. Soc.*, **70**, 695 (1948).

[17] H. Lindlar, *Helv. Chim. Acta*, **35**, 446 (1952).

[18] We had originally hoped to be able to carry out the synthesis *without* the use of any protecting group. In order to test this route, we carried out the synthesis of IX by reaction of myristyl magnesium bromide with unprotected 2,3-dihydroxybenzaldehyde (see Exptl.). Although this first step proceeded in a surprisingly good yield, this route had to be abandoned when all attempts to dehydrate IX led only to polymeric materials,[7,19] even though dehydration of the corresponding monohydric phenols had been successfully carried out.[19]

[19] B. Loev and C. R. Dawson, *J. Am. Chem. Soc.*, **78**, 4083 (1956).

liquid solidified at about 10° (the *cis* isomer remains liquid when maintained at this temperature).

EXPERIMENTAL

1-Chlorotetradecyne-7 (I). Into a solution of 0.15 g. hydrated ferric nitrate in 1 l. of liquid ammonia was added portionwise a total of 8.6 g. (0.375 mole) of sodium. When all the sodium had been converted to sodamide[20] (90 min.) the color of the mixture was a gray-brown. After stirring the mixture for an additional hour, 41 g. (0.375 mole) of octyne-1[21] (b.p. 122–126°, n_D^{27} 1.440) was added over a period of 2 hr. The thick white precipitate which gradually formed during the addition was stirred for another hour before adding, dropwise, 92.3 g. (0.375 mole) of 1-chloro-6-iodohexane [b.p. 83–84° (2 mm.), n_D^{25} 1.5178] prepared as described by Gensler *et al.*[22] The mixture, which soon became transparent and colorless with a dark brown gum coating the sides of the flask, was stirred overnight (volume 300 cc.). On the slow addition of a cold dilute ammonium chloride solution a white precipitate formed which dissolved as more solution was added. The mixture then separated into a brown organic layer and a colorless aqueous layer. The organic material was taken up in ether, washed several times with water, once with dilute hydrochloric acid, and once with sodium thiosulphate. The ethereal solution was dried, and the ether and unreacted octyne-1 were removed by distillation, *in vacuo*, leaving 75.5 g. of an orange oil. Distillation of this oil gave 62.4 (73% yield) of I, b.p. 117–122° (2 mm.). This material was redistilled through a 23″ Widmer fractionating column, giving the 1-chlorotetradecyne-7 as a colorless liquid, b.p. 121–22° (1.5 mm.), n_D^{22} 1.4628.

Anal. Calcd. for $C_{14}H_{25}Cl$: C, 73.49; H, 11.01; Cl, 15.50. Found: C, 73.43; H, 11.01; Cl, 15.67.

A sample of I on prolonged reduction with W-5 nickel catalyst[16] or palladium-on-charcoal, absorbed two equivalents of hydrogen, giving tetradecyl chloride, n_D^{24} 1.4439 (lit.[23] n_D^{20} 1.4450).

A solution of I and potassium permanganate in acetone was refluxed for 1 hr. Upon working up the reaction mixture, I was recovered almost quantitatively. I was also recovered unchanged from refluxing aqueous alkaline permanganate solution.

A solution of I in carbon tetrachloride was treated with a drop of bromine. The color disappeared after standing about 30 min. in the dark. Although I absorbed a large quantity of bromine in this manner, the reaction was very slow.

When ozone (3%) was passed through a solution of I in ethyl acetate at 5°, no absorption of ozone occurred (as indicated by the immediate quantitative liberation of iodine from a potassium iodide solution in series with the solution of I).

When stearolic acid was used instead of I in the bromine and the ozone experiments, the results were the same as with I.

All attempts at the preparation of a Grignard reagent using I were unsuccessful.

A sample of I was converted to the iodide by refluxing with a solution of sodium iodide in acetone for 24 hr. When the iodide was used for the preparation of the Grignard reagent, apparently only coupling occurred for a large quantity of alcohol insoluble material was obtained.

1-Chlorotetradecene-7 (II). (*a*) *Reduction of I using various palladium catalysts.* Reduction of a 0.5 g. sample of I in ethyl acetate, using the palladium-on-calcium carbonate catalyst, as prepared by the method of Lindlar,[17] required 90 min., and practically ceased with the absorption of one equivalent of hydrogen. Removal of the catalyst and solvent left the *cis* olefin, II, n_D^{29} 1.4550. This reduction product showed a small infrared absorption at 10.4 μ, showing the presence of a small amount of *trans* olefin in the product.

When the reduction of I was carried out using either palladium-on-carbon or the palladium-on-calcium carbonate catalyst of Busch and Stove,[15] the reduction was stopped after one equivalent of hydrogen had been absorbed. The reduction products (n_D^{24} 1.4564 and n_D^{25} 1.4557, respectively) both showed an intense absorption at 10.4 μ, indicating the presence of a considerable amount of *trans* olefin in the reduction product.

(*b*) *Reduction of I using the Nickel W-5 catalyst.*[16] The reduction using this catalyst proceeded rapidly and the rate slowed down somewhat after one equivalent of hydrogen had been absorbed. A 40 g. sample of I in absolute alcohol was reduced in 45 min., the reduction being interrupted after one equivalent of hydrogen had been absorbed. The reduction product (II) was a colorless liquid, b.p. 113–114° (0.6 mm.), $n_D^{22\ 5}$ 1.4559. It showed a small absorption band in the infrared at 10.5 μ of about the same intensity as that of the product obtained using the palladium-on-calcium carbonate catalyst as prepared by Lindlar.[17]

A sample of II reacted rapidly with bromine and with permanganate. On ozonolysis, the theoretical quantity of ozone was absorbed, and the product smelled strongly of heptaldehyde, but the aldehyde was not isolated.

A sample of II was further hydrogenated using a palladium-on-charcoal catalyst. Exactly one equivalent of hydrogen was absorbed giving a quantitative yield of myristyl chloride.

3-(1′-Hydroxypentadecenyl-8′)-catechol dibenzyl ether (III). Approximately 50 cc. of anhydrous ether, prepared by refluxing with butyl Grignard reagent, was distilled into a well flamed vessel containing 3.35 g. (0.147 mole) magnesium. An equivalent amount (33.6 g.) of the halide (II) was added; one third at once and then the remainder dropwise over 2 hr. as the ether was maintained at reflux temperature. The volume of the solution was maintained at about 150 cc. by distilling in ether as necessary. After several hours a white suspension formed, and after 24 hr. most of the magnesium had disappeared. A 46.7 g. sample (0.147 mole) of 2,3-dihydroxybenzaldehyde dibenzyl ether, prepared as previously described,[7] was placed in the condenser supported by a plug of glass wool so that the refluxing ether slowly dissolved it. When all of the aldehyde had dissolved the solution was a dark yellow color with a greenish fluorescence. After another hour of heating, the Grignard complex was hydrolyzed by pouring the reaction solution into cold ammonium chloride solution (containing a small amount of acetic acid). The pale yellow organic layer was washed, dried, and the solvent removed leaving 76.5 g. of an oil having an odor of benzyl bromide. The oil was dissolved in 300 cc. of hot ethanol and a 3 g. precipitate of unreacted 2,3-dihydroxybenzaldehyde dibenzyl ether formed on cooling, m.p. 92–93.5°. After filtering and removing the solvent, *in vacuo*, 73.5 g. of III was obtained as a dark orange oil, n_D^{28} 1.5349. A small sample of III was chromatographed on alumina, using ligroin as the solvent, and a yellow oil of n_D^{28} 1.5517–1.5549 (λ_{max} 268 mμ) was collected. Also isolated from the column was a small amount of unreacted II. The chromatography experiment revealed that the 73.5 g. of product contained about 82% III corresponding to an 81% yield.

The identity of III was confirmed when a sample of the chromatographed III, on hydrogenation over palladium-on-carbon in ethyl acetate, absorbed three moles of hydrogen to give IX, m.p. 88–90°, identical to a sample of IX, m.p. 89.6–90.5°, prepared by the reaction of 2,3-dihydroxybenzaldehyde with myristyl magnesium bromide (see below).

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[20] T. H. Vaughn, G. F. Hennion, R. R. Vogt, and J. A. Nieuwland, *J. Org. Chem.*, **2**, 1 (1937).

[21] Purchased from Farchan Research Laboratories, Cleveland, Ohio.

[22] W. J. Gensler and G. R. Thomas, *J. Am. Chem. Soc.*, **73**, 4601 (1951).

[23] L. R. Drake and C. S. Marvel, *J. Org. Chem.*, **2**, 387 (1937).

3-(1'-Hydroxypentadecyl)catechol (IX). To a chilled solution containing the Grignard reagent prepared from 147.7 g. (0.49 mole) tetradecylbromide, was slowly added a solution of 16.4 g. (0.122 mole) of 2,3-dihydroxybenzaldehyde in anhydrous ether containing sufficient anhydrous benzene to bring the aldehyde into solution. The mixture was refluxed for several hours and then hydrolyzed by pouring into dilute acetic acid containing a little sodium hydrosulfite. After washing several times with dilute hydrosulfite solution, the ether was distilled. The remaining brown liquid was dissolved in boiling ethanol and then chilled. The octacosane that precipitated on cooling was filtered and the liquid tetradecane which oiled out of the ethanol was separated. Removal of the ethanol left a pink oil that solidified on cooling. Recrystallization from ligroin gave 22.9 g. (56%) of the carbinol (IX), as feathery white crystals, m.p. 89.6–90.5°; λ_{max} 280 mμ; green color with ferric chloride. The use of three equivalents of the Grignard reagent per mole of aldehyde resulted in a lower (40.5%) yield of the carbinol.

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 74.98; H, 11.05.

IX, prepared as described above, proved to be identical to IX previously prepared by catalytic reduction of 2,3-dibenzyloxyphenyl tetradecyl carbinol.[7]

3-(1',8'-Pentadecadienyl)-catechol dibenzyl ether (IV). The crude III (70 g.) was heated to 175° in a nitrogen atmosphere with a small amount of potassium bisulfate until the vigorous bubbling ceased. The resulting oil was taken up in ether, washed with water, treated with a little charcoal and alumina, and filtered. The solvent was removed, leaving 61 g. IV as a dark oil, n_D^{23} 1.5481, λ_{max} 256 mμ. The crude IV was used for the next step without purification.

3-(Pentadecenyl-8')-catechol (*urushenol*) (V). Sodium, 61 g., was added as rapidly as refluxing would permit to a solution of 30.7 g. of IV in 600 cc. hot anhydrous butyl alcohol. The solution immediately turned dark blue-green. This color soon changed to a dark red-brown, and then proceeded to a pale yellow color, during the first 5 min. of the reaction. When all of the sodium had reacted (2 hr.), the solution was allowed to cool to room temperature under nitrogen. Cold water, containing a little hydrosulfite, was cautiously added causing vigorous boiling. As more water was added, a precipitate formed and then redissolved. A cold dilute solution of slightly more than the theoretical quantity of acetic acid required to neutralize the sodium hydroxide (and containing a little sodium hydrosulfite) was added. The solution was then saturated with sodium chloride and separated. The organic layer was washed with saturated salt solution containing some bicarbonate and hydrosulfite, and then with a small quantity of distilled water. Another 28 g. of IV was reductively cleaved in the same fashion and the solutions were combined. The solvent and any unreacted halide which had been carried through were removed by distillation under nitrogen, *in vacuo*, leaving 37.2 g. of V as a dark brown oil, a small sample of which gave a dense precipitate with methanolic lead acetate.

On vacuum distillation there was obtained, following a small forerun of low boiling material, 13.4 g. of a pale yellow oil (V) of b.p. 207–208° (0.8 mm., bath at 265–290°) corresponding to a 28.5% overall yield from II. The product, n_D^{25} 1.4970, darkened rapidly on standing in air but remained pale yellow for a long period when stored in an evacuated or nitrogen-filled sealed vial. The residue in the distilling flask polymerized to a viscous black mass.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.20; H, 10.76. Found: C, 79.30; H, 10.86.

A solid derivative of V, the di-naphthylurethan, was made by heating a mixture of 0.3 g. V, 0.3 cc. of α-naphthyl isocyanate, and 3 drops of pyridine for 5 min. on a steam bath. The resulting solid was triturated with hexane, filtered, and recrystallized from benzene-hexane, 0.34 g., m.p. 139–141°.

Anal. Calcd. for $C_{43}H_{48}O_4N_2$: C, 78.49; H, 7.51. Found: C, 78.10; H, 7.62.

Mixed melting point with the di-naphthylurethan of hydrourushiol, m.p. 149–150° (from $CHCl_3$), showed a marked depression.

On treatment with ferric chloride solution, V gave a momentary green color changing rapidly to black. A small sample of V on catalytic hydrogenation absorbed slightly more than the theoretical quantity of hydrogen for a mono-olefin and gave, after one recrystallization from petroleum ether, hydrourushiol (VI) as a pale yellow solid of m.p. 57.5–58.5°. A mixed melting point with an authentic sample of hydrourushiol showed no depression.

Chromatographic purification of urushenol (V).[24] As the result of subsequent investigations in this laboratory involving the mono-olefinic component of poison ivy "urushiol" as isolated from natural sources, it became apparent from refractive index values that the synthetic urushenol (V) was contaminated with material which did not significantly affect the analysis data, the double bond value, or the ultraviolet or infrared spectra. The refractive index of V (n_D^{25} 1.4970) was considerably lower than that of the natural product (n_D^{25} 1.5083). Considering the method of synthesis of V it seemed possible that the contaminating material was a side product of the Grignard reaction, *i.e.* the R-R coupling product octacosadiene-7,21.

It had recently been found in these laboratories[25] that alkenylphenols in ligroin can be adsorbed on acid washed Alumina, Grade III (Merck), and then quantitatively eluted with anhydrous diethyl ether. Consequently a small sample of V was placed on an acid washed alumina column and washed repeatedly with ligroin. The eluate contained a colorless oil (n_D^{25} 1.4584). This oil gave negative tests for the catechol nucleus, had no ultraviolet spectrum above 220 mμ and its infrared spectrum showed only those peaks expected of an unsaturated hydrocarbon,[26] and also present in the natural and synthetic mono-olefin, 3-pentadecenyl-8'-catechol. Extraction of the column with anhydrous diethyl ether gave a 72% recovery of a brown wax, n_D^{25} 1.5108. This material was molecularly distilled to give a light yellow oil of n_D^{25} 1.5081, which crystallized on standing at 0°. On warming it starts to soften at 22° and melts at 33°. Its ultraviolet and infrared spectra, as well as its refractive index, were identical with those of the mono-olefinic component isolated from poison ivy urushiol.[27]

Dimethyl urushenol (VII). A 3 g. sample of V was refluxed for 24 hr. with excess methyl iodide and potassium carbonate in acetone.[28] The precipitated salts were filtered and the solvent distilled. The product was a pale yellow oil, 1.5 g., n_D^{25} 1.4870. It was insoluble in alcohol and gave a negative ferric chloride test. A sample of this material was chromatographed on alumina (grade I) using ligroin as solvent. The resulting product was made up of fractions having refractive index n_D^{25} 1.4940–1.4950 in satisfactory agreement with the product derived from poison ivy (n_D^{25} 1.4930–1.4945).[4]

Hydroxylation of VII *with osmium tetraoxide.* A 0.5 g. sample of VII was treated with osmium tetraoxide as previously described.[6] The resulting 0.43 g. of glycol, VIII, melted at 95–96°, and the melting point of a mixture of VIII and the glycol obtained in a similar manner from the natural dimethyl urushenol (m.p. 94–95°)[6] also melted at 95–96°. Cleavage of VIII by means of lead tetra-acetate[28] gave heptaldehyde which was steam distilled from the reaction

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(24) Experimental work by K. H. Markiewitz.

(25) V. J. Paul, unpublished observations, Columbia University (1956).

(26) The presence of significant quantities of this hydrocarbon would not materially change the analysis.

(27) A method for isolating the various olefinic components of Poison Ivy "Urushiol" in their free phenolic and allergenically active form has recently been developed by K. H. Markiewitz in these laboratories.

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

mixture and identified as the 2,4-dinitrophenylhydrazone, melting sharply at 106.5–107°, and showing no depression when mixed with an authentic sample of the 2,4-dinitrophenylhydrazone of *n*-heptaldehyde.

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