

**$\beta$ -3-(5-Phenylisoxazolyl)-propionic Acid.**—A solution of 2 g. of the above 6-phenyl-4-oxo-5-hexynoic acid, 1 g. of hydroxylamine hydrochloride and 1.5 g. of sodium acetate in 15 cc. of alcohol was refluxed for eight hours and allowed to stand overnight. The white solid was crystallized from benzene, m. p. 163–163.5°.

*Anal.* Calcd. for  $C_{12}H_{11}NO_3$ : C, 66.36; H, 5.07. Found: C, 66.20; H, 5.19.

Phthalic anhydride and sodium phenylacetylene yielded a small amount of a solid soluble in carbonate but of indefinite composition. Most of the phenylacetylene was recovered.

Ethyl phenylpropionate did not react appreciably with sodium phenylacetylene by Worrall's procedure for ethyl cinnamate. Only a small amount of resin was formed and most of the phenylacetylene was recovered.

**Acetylphenylacetylene and Butadiene.**—The ketone (21 g.) and butadiene (16 g.) were sealed in a Carius tube and heated at 170° for six hours. The reaction product was distilled at 4 mm. The fraction (8.7 g.) which distilled at 140° (4 mm.) was the only one for which analytical data approximated the theoretical.

*Anal.* Calcd. for  $C_{14}H_{14}O$ : C, 84.84; H, 7.07. Found: C, 85.68, 85.80; H, 7.04, 7.08.

This fraction reacted with semicarbazide hydrochloride in pyridine solution to form a solid which melted at 187°.

*Anal.* Calcd. for  $C_{13}H_{13}N_3O$ : C, 70.60; H, 6.6. Found: C, 71.55; H, 6.55.

These data correspond approximately to an adduct with one mole of butadiene and one mole of acetylphenylacetylene. The condensation was repeated under a variety of conditions but only in this one case was a constant boiling fraction obtained. Cyclopentadiene and 2,3-dimethylbutadiene gave no better results. The products boiled over a wide range and none of the fractions would form a semicarbazone.

**Preparation of Benzalacetophenone from Cinnamoyl Chloride and Diphenyl Cadmium.**—Cadmium chloride (30 g., 0.16 mole) was added to 0.16 mole of phenylmagnesium bromide in 160 cc. of ether. The solution was stirred for

three hours. Cinnamoyl chloride (27.7 g., 0.16 mole) in 100 cc. of ether was added slowly to the stirred suspension of diphenyl cadmium. After the vigorous reaction was over, the mixture was refluxed for one hour and decomposed with cold dilute sulfuric acid. The product was worked up in the usual manner. The benzalacetophenone melted at 50° and did not depress the melting point of an authentic sample; yield, 15.6 g. (44%).

**Reaction of Bis-phenylethynylcadmium with Acetic Anhydride and Acetyl Chloride.**—Phenylethynylmagnesium bromide was prepared from 0.16 mole of ethylmagnesium bromide in 100 cc. of ether and 0.18 mole of phenylacetylene in 50 cc. of ether. The solution was refluxed for two hours. Cadmium chloride (0.08 mole) was added to the Grignard solution and the mixture stirred for one hour. The acetic anhydride (15.8 g., 0.15 mole) in 15 cc. of ether was added slowly to the cadmium compound.

The product was decomposed with cold dilute acid, the ether layer separated, washed and dried. The dark oil which remained after the removal of the ether crystallized on standing. Extraction with hot alcohol and repeated crystallization from alcohol yielded nearly colorless needles, m. p. 110–111°; yield, 4.5 g. (13.8%). The recorded melting point of *bis*-phenylethynylmethylcarbinol is 111.5–112°. The same compound resulted when acetyl chloride was substituted for acetic anhydride, whether the acid chloride was added to the cadmium compound or *vice versa*. The viscous oils could not be distilled even at 1 mm. without extensive decomposition.

### Summary

Sodium phenylacetylene reacts smoothly with various types of acid anhydrides to form acetylenic ketones.

Viscous oils or resins were the principal products from the reaction of cadmium alkyls and unsaturated acid chlorides.

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## The Toxic Principles of Poison Ivy. III. The Structure of Bhilawanol<sup>1</sup>

BY HOWARD S. MASON

This investigation was undertaken to test degradative methods upon an accessible substance closely related to the toxic principles of poison ivy<sup>2,3,4,5</sup> preliminary to application of the methods to the poison ivy problem itself.

Bhilawanol is the allergenic oil which has been isolated from the shell of the Indian marking nut tree; it has been shown that hydrobhilawanol

(1) For the second article in this series, see Mason, *THIS JOURNAL*, **66**, 1156 (1944).

(2) Among the numerous species of the family *Anacardiaceae* is a large group of plants, including poison ivy, which elaborate oils of a powerful allergenic nature. This has been reviewed by Wasserman and Dawson, *J. Chem. Ed.*, **20**, 448 (1943). It must be noted, however, that these authors imply bhilawanol to be a homogeneous substance containing "one double bond in the side chain," and refer to the paper of Pillay and Siddiqui for evidence. Pillay and Siddiqui (see ref. 3), on the other hand, indicated that bhilawanol was doubly unsaturated. Data are presented in this investigation which make it likely that bhilawanol is a *mixture*.

(3) Pillay and Siddiqui, *J. Indian Chem. Soc.*, **8**, 517 (1931).

(4) Hill, Mattacotti and Graham, *THIS JOURNAL*, **56**, 2736 (1934).

(5) Goldsmith, *J. Am. Med. Assoc.*, **123**, 27 (1943).

is identical with 3-*n*-pentadecylcatechol, and, by means of bromine titration, that there are two aliphatic double bonds in the parent compound.<sup>3</sup> In this study the latter was isolated by a method essentially the same as that previously used<sup>3</sup>; its physical properties were found to be similar to those already reported and its reactions with qualitative reagents for phenols and catechols were identical. The substance was readily reduced by hydrogen in the presence of Adams catalyst, and 3-*n*-pentadecylcatechol was isolated from the product in 70% yield. However, only 59% of the hydrogen required to saturate two double bonds was absorbed. This is equivalent to 118% of that required for one double bond. In the light of the rapidity with which phenols react with bromine, it seems reasonable to conclude that the degree of unsaturation observed by Pillay and Siddiqui may be explained in part by ring substitution. It was found in fact that 3-*n*-

pentadecylcatechol, dissolved in carbon tetrachloride, decolorized dilute solutions of bromine readily. Similarly, Majima has shown<sup>6</sup> that urushiol dimethyl ether produces hydrobromic acid upon reaction with bromine, although this takes place more slowly.

While 3-*n*-pentadecylcatechol and its derivatives are crystalline solids, the 3-*n*-pentadecenylcatechols and their derivatives are liquids. This fact has made it difficult to prove the homogeneity of unsaturated substances isolated from the natural oils. It is evident that the hydrogenation data presented above may be interpreted by assuming the oil to be any of numerous theoretical mixtures of 3-*n*-pentadecylcatechol with mono-, di- and polyolefinic 3-*n*-pentadecacatechols. Majima has shown by the ozonization of urushiol<sup>6</sup> that this material, which averages two double bonds, is actually a mixture of at least four substances of varying degrees of unsaturation; on the other hand, Backer and Haack have found that rhengol, which averages one double bond, was ozonized as though it were homogeneous.<sup>7</sup>

In the hope of finding a derivative of bhilawanol which would permit the separation of its possible components by chromatographic analysis, the diphenylmethane ether of this material was prepared by the pinene procedure already described.<sup>1</sup> This expectation however was realized only in part: by chromatographing bhilawanol diphenylmethane ether upon activated alumina an adsorptively homogeneous oil was obtained as the principal fraction. Upon repeated molecular distillation, this oil yielded fractions the analyses of which were not constant and which cannot be regarded as significant except in that they indicated a close relationship to bhilawanol diphenylmethane ether. From one fraction, however, a solid which melted at 37–38° was crystallized; the yield was very low. This substance had an empirical formula correct for the mono-olefinic compound.

In view of the small amounts of crystalline material available, and the failure to separate homogeneous fractions by the procedures described above, the various fractions were combined and collectively ozonized following the technique of Majima.<sup>6</sup> The method of ozonization closely followed that described by Henne and Perilstein,<sup>8</sup> who found that ethanol is an excellent solvent for the ozonolytic synthesis of aldehydes. Molar proportions of ozone were employed to avoid attacking the benzenoid portion of the molecule; the ozonide which formed absorbed upon catalytic reduction 80% of the hydrogen theoretically required, and from the products of the reductive cleavage, heptaldehyde 2,4-dinitrophenylhydrazone was obtained in 19% yield.

(6) Majima, *Ber.*, **55B**, 172 (1922).

(7) Backer and Haack, *Rec. trav. chim.*, **57**, 225 (1938). Nevertheless, the analytical data were equivocal, and the yield of valeraldehyde was low.

(8) Henne and Perilstein, *THIS JOURNAL*, **65**, 2183 (1943).

The melting points of the 2,4-dinitrophenylhydrazones of the five to ten carbon normal aldehydes are not distinguishing characteristics; final identification depended upon the nitrogen content of this derivative and upon its mixed melting point with an authentic sample. Small amounts of other 2,4-dinitrophenylhydrazones were obtained, but these were intractable.

Since heptaldehyde was formed in relatively good yield, and since correspondingly good yields of other aldehydes were not found, it is probable that 3-*n*-pentadecen-8-ylcatechol is a major component of bhilawanol oil.

**Acknowledgment.**—Mr. Theodore D. Perrine constructed the ozonizer which was used in this study.

### Experimental

All melting points and boiling points were measured with totally immersed thermometers.

**Purification of Crude Bhilawanol.**—The oil studied in this investigation was obtained by agents of the U. S. Government in New Delhi, India. The sample was identified as "Indian Bhilawan Shell Liquid; *Semecarpus anacardium*." The black liquid (about 75 g.) was taken up in ethanol and treated until colorless with activated charcoal. The ethanol was then evaporated and the residual sirup distilled in vacuum. A fore-run which boiled up to 165° (0.01 mm.) probably corresponded to that obtained by Pillay and Siddiqui, boiling at 185–190° (2.5 mm.), and which they named *semecarpol*, a monohydric phenol. The principal fraction was obtained between 166 and 190° (0.01 mm.), a thick yellow oil which set to a glass at –15°. An alcoholic solution of this fraction turned deep green in the presence of ferric chloride and shortly afterward deposited a black precipitate. If the green solution were treated with aqueous sodium carbonate, a red orange color appeared. This behavior is characteristic of catechols. A total of 17 g. of this fraction was obtained.

**Catalytic Reduction of Bhilawanol.**—Exactly 1.00 g. (0.00314 mole, calculated as C<sub>21</sub>H<sub>34</sub>O<sub>2</sub>) was dissolved in 10 cc. of ethanol, and 0.19 g. of Adams catalyst added to the solution. The calibration for this weight of catalyst was 38 cc. In fifteen minutes the mixture absorbed 130 cc. of hydrogen, the rate of addition changing sharply at this point. The calculated volume of hydrogen absorbed by 0.00314 mole of a mono-olefinic substance at 28.5° (room temperature) is 78 cc. Therefore the actual absorption was 118% of this amount.

The solution was filtered and evaporated. The residue was dissolved in toluene and cooled. Needles appeared overnight; they were filtered off and sublimed in high vacuum. The sublimate weighed 0.7 g. and melted at 58–59°. Backer and Haack<sup>7</sup> report a melting point of 58–59° for hydrourushiol; furthermore, the compound did not depress the identical melting point of a sample of synthetic hydrourushiol.

**Bhilawanol Diphenylmethane Ether.**—Following the pinene procedure described in a previous paper,<sup>1</sup> 15.45 g. (0.0484 mole) of bhilawanol was dissolved in 53 g. (0.3872 mole) of freshly distilled pinene. To this mixture was added 11.52 g. (0.0486 mole) of diphenyldichloromethane. The mixture was warmed on a steam-bath for sixteen hours; only a slight darkening was observed. At the end of this period the solution was distilled. After a fraction had been obtained at 105–115° (0.15 mm.) the temperature at the head of the still began to decline, and the distillation was stopped. The residue was only slightly soluble in methanol; it was however soluble in a mixture of petroleum ether (boiling at 35–75°) and dry methanol. This solution was passed through a column 50 mm. by 50 mm. of alumina (Aluminum Ore Company, minus 80 mesh). A broad red band remained on the column after washing with

the original solvent, and this turned purple when brushed with alcoholic ferric chloride solution. Since it could not be eluted, it is likely that it was phenolic in nature. The eluate was further decolorized with activated charcoal and the solvent evaporated in vacuum. A residue of 20.0 g. remained, corresponding to a yield of 85%. All efforts to crystallize this pale yellow oil were unsuccessful.

**Fractionation of Bhilawanol Diphenylmethylene Ether.**—The diphenylmethylene ether was dissolved in petroleum ether (b. p. 35–75°, Mallinckrodt purified reagent) and adsorbed upon 25 × 150 mm. column of alumina in 2.5 g. batches. Four fractions were developed with petroleum ether as the eluent: from the top, (1) a fixed dark blue-brown band with no fluorescence in ultraviolet light; (2) a yellow band, migratory but not fluorescent; (3) a colorless band with bright yellow fluorescence, moving more rapidly; (4) a colorless band with a little fluorescence, which was washed from the column readily. The first band could not be eluted. Each chromatographic analysis yielded about 0.10 g. of the second band, a thick yellow oil which failed to crystallize. The brightly fluorescent band yielded about 0.3 g. of a yellow fluid oil with a sharp terpenoid odor. The fourth band was found to contain the principal fraction, about 2.1 g. of a colorless, odorless, oil. Attention was focussed principally on this material. It was found to have the following composition<sup>9</sup>: found, C, 84.47; H, 9.68. For the purposes of comparison, the calculated compositions of possible bhilawanol diphenylmethylene ethers are given in Table I.

TABLE I

CALCULATED COMPOSITIONS OF POSSIBLE BHILOWANOL  
DIPHENYLMETHYLENE ETHERS

Compound	Carbon, %	Hydrogen, %
Hydrobhilawanol ether	84.25	9.15
Mono-olefinic ether	84.60	8.77
Di-olefinic ether	84.95	8.39
Tri-olefinic ether	85.31	8.00

The material was then subjected to molecular distillation at temperatures between 125–225° (0.05–0.10 mm.). A very fluid first fraction had the composition<sup>10</sup>: found, C, 87.2; H, 7.19. This material was discarded. The principal fraction obtained had the composition: found, C, 84.0; H, 9.20. A dark brown tarry residue remained after distillation.

The major fraction was dissolved in a mixture of methanol and benzene and cooled to about 10° for a week. A small crop of crystals was deposited, and since it did not increase on further standing, was filtered off and sublimed in high vacuum. In this manner, about 0.20 g. of colorless needles of a soft nature was obtained. This substance melted at 37–38° and possessed the composition: found, C, 84.77; H, 8.66. Further molecular distillation of residual oil in the mother liquor failed to yield fractions which crystallized.

(9) For this microchemical analysis we are indebted to Mr. Edward A. Garlock.

(10) For this and the subsequent microchemical analysis we are indebted to Dr. Arthur T. Ness.

**Ozonization of Bhilawanol Diphenylmethylene Ether.**—The fractions obtained by the last molecular distillation were combined, and together weighed 13.0 g. (0.027 mole). This oil was dissolved in 85 cc. of ethanol; since upon slight cooling the solution became clouded and oil droplets appeared, it was necessary to add 15 cc. of anhydrous ethyl acetate, which satisfactorily kept the ether in solution. The apparatus was arranged with a cut-off between the ozonization flask and generator so that the amount of ozone being produced could be conveniently checked. With the conditions employed in this experiment 0.0168 mole of ozone per hour was generated with a flow of 10 liters of oxygen per hour—a yield of 6.2%. Ozone was passed in fine bubbles (from a sintered glass plate) through the solution of compound at room temperature for one hour and thirty-six minutes. At the end of this period, the product was placed in a hydrogenation flask with 0.5 g. of palladized barium sulfate.<sup>11</sup> The mixture absorbed 80% of the hydrogen theoretically required; at this point, the solution failed to oxidize acidified potassium iodide solution, and the hydrogenation began to proceed at a sharply reduced rate. The solution was filtered and then distilled.

The first distillation was carried out at atmospheric pressure. No aldehydic fractions were obtained until the temperature of the still head vapors reached 165–200°, when 1.0 g. of a liquid smelling strongly of heptaldehyde was collected. The residual oil was distilled at 19 mm.; between 85–95°, 0.5 g. of a liquid similar to that above in odor was obtained. The residue was then distilled at 0.03 mm.; 0.3 g. was collected at 124–134°, and 3.1 g. of very thick oil was obtained at 180–210°. The first two fractions mentioned readily yielded crude 2,4-dinitrophenylhydrazones which melted at 92–94° and weighed 1.5 g., or 19% of the theoretical yield (based on heptaldehyde) from a mono-olefinic bhilawanol diphenylmethylene ether. After recrystallization from alcohol and from petroleum ether, the yellow compound melted at 104–105°. Its mixed melting point with authentic heptaldehyde 2,4-dinitrophenylhydrazone (m. p. 105–106°) was found to be 104–105°, that with authentic valeraldehyde 2,4-dinitrophenylhydrazone (m. p. 103–104°) to be 85–88°, and that with authentic octaldehyde 2,4-dinitrophenylhydrazone (m. p. 105–106°) to be 94–96°.

The 2,4-dinitrophenylhydrazone obtained had the composition: found, N, 19.02; calculated for heptaldehyde 2,4-dinitrophenylhydrazone, N, 19.04; for the hexaldehyde derivative, 20.00; and for the octaldehyde derivative, 18.18. The derivatives obtained from the higher boiling fractions tended to be oils, and could not be recrystallized to purity.

### Summary

The ozonization of bhilawanol diphenylmethylene ether yielded as a principal product, heptaldehyde. It is therefore concluded that a probable component of bhilawanol is 3-*n*-pentadecen-8-ylcatechol.

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(11) Schmidt, *Ber.*, **52**, 409 (1919).