practical optimum was reached with a proportion of Na to S corresponding to Na_2S_3.

Curve B shows the results obtained when the ratio of Na_2S_3 to *o*-nitrochlorobenzene was varied. The yield of 2-mercaptobenzothiazole increased very rapidly up to a ratio of 2 moles of Na_2S_3 to one of *o*-nitrochlorobenzene.

The effect of time of refluxing is shown by Curve C. It will be seen that the yield was only very slightly increased after three hours of refluxing. At a temperature of 70 to 80° the yield gradually increased with the time of refluxing up to seven hours. At higher temperatures, between 85 and 90°, the maximum yield was obtained in three hours.

Curve D shows the effect of temperature. Below 70° the yields of 2-mercaptobenzothiazole were very low. The maximum yield was obtained at a temperature of 85 to 90°, using a ratio of three moles of Na_2S_3 to one mole of *o*-nitrochlorobenzene.

Acknowledgment.—The authors wish to acknowledge the helpful assistance given by Dr. N. A. Shepard during this investigation.

Summary

A new method for the direct preparation of 2-mercaptobenzothiazole in one step from *o*-nitrochlorobenzene is described.

The optimum yields are obtained when *o*-nitrochlorobenzene is heated with an aqueous solution of sodium polysulfide (Na_2S_3) and carbon disulfide at 85–90° for three hours using three moles of Na_2S_3 to one mole of *o*-nitrochlorobenzene.

Akron, Ohio Received September 28, 1934

[Contribution from the Hall Laboratory of Chemistry, Wesleyan University]

The Toxic Principle of the Poison Ivy

By G. Albert Hill, Vincent Mattacotti and W. D. Graham

Within the past forty years, three notable attempts have been made to isolate and to identify the toxic principle of that member of the Rhus group known as poison ivy. In 1897, Pfaff[1] prepared an alcoholic extract of leaves and branches of Rhus Toxicodendron from which he ultimately obtained a nearly white precipitate by means of lead acetate. This precipitate yielded a very toxic, non-volatile oil, toxicodendrol. Pfaff went no further with the chemical study of his product.

In 1906, Acree and Syme[2,3] used material obtained from the leaves and flowers of poison ivy by extraction with ether. They decided that the toxic material, designated by them, toxicodendrin, was a complex glycoside, presumably containing fisetin, rhamnose and gallic acid.

Somewhat later, in 1916, McNair[4] experimented with a gasoline extract of the bark of Rhus Diversiloba, a plant almost indistinguishable from Rhus Toxicodendron. He came to the conclusion that the poison, lobinol, was an unsaturated *o*-dihydroxybenzene derivative. He did not, however, prove its structure, or identify it.

From 1907–22, Majima[5] and his co-workers published a series of papers dealing with the poisonous principle of Japan lac, obtainable from Rhus Vernicifera. From an alcoholic extract of the sap of this tree, Majima obtained a toxic oil of low volatility, which he called urushiol. By a study of the oxidation products of the oil and those of certain of its derivatives, Majima proved urushiol to be a mixture of *o*-dihydroxybenzenes with a normal fifteen carbon atom side chain in position three. Majima was not able to isolate chemical individuals from urushiol by distillation. A small quantity of saturated material is present, dissolved in at least two unsaturated substances with two double bonds in the chain, and possibly accompanied by a more highly unsaturated substance. When urushiol is reduced, all of the components are converted into a single substance, 1-*n*-pentadecyl-2,3-dihydroxybenzene, hydrourushiol. The structure of this substance was established by the synthesis of its dimethyl ether. Majima prepared a number of derivatives of it, and of urushiol.

In the light of these researches, the isolation and identification of the toxic principle of the poi-

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[1] Pfaff, *J. Exp. Med.*, **2**, 181 (1897).

[2] Acree and Syme, *Am. Chem. J.*, **36**, 301 (1906).

[3] Acree and Syme, *J. Biol. Chem.*, **2**, 547 (1906–1907).

[4] McNair, This Journal, **38**, 1417 (1916); **43**, 159 (1921).

[5] Majima, *Ber.*, **55B**, 172 (1922).

son ivy was undertaken in this Laboratory. About 900 pounds of poison ivy leaves were gathered in the vicinity of Middletown. Some were used fresh, other batches were dried and pulverized. The first experiments were along the lines of Pfaff's work. However, because of the difficulty of getting samples of lead derivatives with agreeing analyses, and because the yields of toxic oil were exceedingly small, this procedure was abandoned. For some time thereafter, the experiments were based on McNair's, using leaf material. Some of the poison was obtained, but it was always contaminated by waxy impurities, which rendered purification by low pressure distillation exceptionally difficult.

Work with ivy leaves was therefore given up and henceforth bark was employed exclusively. It was usually obtained as required, but that gathered in the winter was found to be nearly devoid of toxic material. The bark was refluxed with ethyl alcohol, and the alcoholic solution concentrated. The cooled concentrate deposited waxy and gummy materials, and was then filtered by suction. The filtrate was extracted with xylene. This solution was concentrated in a vacuum and the residue distilled at a pressure lower than 1 mm., yielding a very toxic, straw-colored oil. In dilute alcohol solution, this material gave a green color with ferric chloride. Upon the subsequent addition of sodium carbonate the color was changed from green to red, indicative of the presence of a 1,2-dihydroxybenzene structure. These facts, together with the observations that the boiling point, analyses, and the molecular weight of the yellow oil agreed with the corresponding values for urushiol, pointed to this material as that responsible for the irritant action of poison ivy.

To establish the identity of the poison ivy poison with urushiol, a group of derivatives was prepared. The dimethyl ether of the ivy oil closely resembled urushiol dimethyl ether. The unsaturated oil from poison ivy was reduced catalytically and yielded a solid apparently identical with hydrourushiol. All the saturated derivatives in these series are solids, whereas the unsaturated ones are liquids. The dimethyl ether, the diacetate and the dibenzoate of the solid just mentioned were produced by the methods employed by Majima, and in each instance seemed to be identical with the corresponding substance prepared from hydrourushiol.

A comparison of certain derivatives of urushiol with similarly constituted products obtained from poison ivy is given in Table I.

TABLE I

IVY PRODUCTS

	B. or m. p., °C.	Constants of urushiol series, B. or m. p., °C.	Color and state	Molecular weight[a]	Formula	Analyses,[a] % Carbon	Analyses,[a] % Hydrogen
1 Urushiol	B 210 (0.5 mm.)	B 210 0.4–0.6 mm.	Yellow oil	303	$C_{21}H_{32}O_2$	79.53	10.72
2 Urushiol dimethyl ether	B 208 (1.2 mm.)	B 190–195 0.3–0.6 mm.	Yellow oil	321	$C_{23}H_{36}O_2$	79.92	10.57
3 Hydrourushiol	M 58.5–59	M 59	White needles	324	$C_{21}H_{36}O_2$	78.42	11.37
4 Hydrourushiol dimethyl ether	M 36–37	M 36.2–37	White prisms	345	$C_{23}H_{40}O_2$	79.95	11.72
5 Hydrourushiol diacetate	M 50–51	M 50.2	White rhombs	397	$C_{25}H_{40}O_4$	74.12	10.35
6 Hydrourushiol dibenzoate	M 59.5–60.5	M 59–60.5	White needles	528[b]	$C_{35}H_{44}O_4$	79.43	8.42[b]

[a] Averages of series of values experimentally determined.
[b] These values were obtained by A. J. Cofrancesco.

Tests were made of the physiological activity of some of the ivy products. The unsaturated phenol was exceedingly toxic, and caused the characteristic dermatitis of poison ivy. The dimethyl ether made from this oil was non-toxic. The saturated phenol was only somewhat less toxic than its unsaturated analog, while the dimethyl ether of the saturated phenol was without toxic action. These observations are in accord with the experience of Toyama[6] with the analogous derivatives of urushiol.

On the basis of all of these results, it seems safe to say that the toxic principle of the poison ivy is urushiol.

The study of poison ivy will be continued in this Laboratory. It is a pleasure to acknowledge the assistance of Messrs. Pierczyk and Russell, who procured most of the experimental material. The Connecticut State Highway Department, and the Connecticut Parks Commission kindly granted us permission to gather poison ivy on state property. Without the financial aid from the Atwater Fund, this study could not have been undertaken.

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(6) Toyama, *J. Cut. Dis.*, **36**, 157 (1918); see also *Ber.*, **55B**, 208 (1922).

Experimental Part

Isolation of the Toxic Material.—About 30 pounds of bark was stripped from freshly cut branches of Rhus Toxicodendron, placed in a 12-liter round-bottomed flask, equipped with a reflux condenser, and boiled with 95% ethyl alcohol for four days. The alcoholic solution was poured off, and concentrated on a steam-bath to about one-tenth of its volume under somewhat reduced pressure (water pump). The concentrate was cooled slowly, finally in ice, to precipitate waxy impurities. Under these conditions the solids formed a compact mass, filterable by the use of a suction pump. The deep red filtrate was saturated with solid sodium chloride and extracted with about three liters of xylene. This solution was dried with calcium chloride or with sodium sulfate and concentrated on the steam-bath under reduced pressure to from 50–100 cc. No air was bubbled through any of the solutions during the concentrations. The xylene concentrate was also cooled in a refrigerator to eliminate more of the waxy material. The liquid portion was decanted from the solids and subjected to vacuum distillation in an atmosphere of nitrogen. A toxic, yellow oil was obtained: b. p. 210° (0.5 mm.). A single run yielded from 5–12 cc. of the oil.

Conclusions

1. The toxic principle of the poison ivy, Rhus Toxicodendron, has been isolated and identified as urushiol, a material previously obtained by another investigator from Rhus Vernicifera.

2. Personal experiments have verified Toyama's conclusion that the hydroxyl groups in urushiol are the chief cause of its well-known violently vesicant action.

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[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA, No. 148]

An Improved Method for the Preparation of Morphenol (3-Hydroxy-4,5-phenanthrylene Oxide) from Morphine[1]

BY ERICH MOSETTIG AND ERICH MEITZNER

In a systematic comparative chemical and pharmacological study of hydroxyphenanthrenes, the preparation of 4,5-phenanthrylene oxide, the inner ether of 4,5-dihydroxyphenanthrene, and its derivatives became desirable. Since at the present time no method of synthesizing this compound is available, we turned our attention toward a satisfactory method for the preparation of morphenol (3-hydroxy-4,5-phenanthrylene oxide) from morphine or codeine,[2] through the methylmorphimethines.

Our attempts to improve the method of Vongerichten[3] led us to a new and surprising observation. β-Methylmorphimethine methohydroxide is stable in aqueous solution even when boiled with alkali. When the aqueous solution is evaporated to dryness in a desiccator, an almost colorless lacquer remains, which on contact with water decomposes spontaneously into amine and methylmorphenol. The mere process of drying must have converted the β-methylmorphimethine methohydroxide into a new compound of yet unknown nature. This intermediate apparently has the side chain still attached, but so loosely that hydrolysis under extremely mild conditions results in complete aromatization.[4,5] It is possible that this intermediate plays a part in the mechanism of the many degradations of opium alkaloids[2] to phenanthrene derivatives.

To avoid the use of expensive methyl iodide and silver oxide in large-scale operations, we converted morphine by treatment with dimethyl sulfate and alkali into codeine methomethyl sulfate, which could be degraded smoothly to α-methylmorphimethine. The rearrangement to β-methylmorphimethine was carried out in the usual fashion. A solution of β-methylmorphimethine methohydroxide was prepared from the corresponding methomethyl sulfate by saponification with 20% sulfuric acid and subsequent removal of the sulfate ion with barium hydroxide.[6] The dried β-methylmorphimethine methohydrox-

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(1) The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia and the University of Michigan.

(2) A recent review of the known reactions may be found in the "Chemistry of the Opium Alkaloids," by Small and Lutz, U. S. Government Printing Office, 1932, pp. 268–289.

(3) Vongerichten, *Ber.*, **30**, 2439 (1897); **33**, 358 (1900); **34**, 2722 (1901); **38**, 1853 (1905).

(4) Whether α-methylmorphimethine methohydroxide undergoes an analogous change could not be ascertained because of the instability of its aqueous solution. The tendency to form colloidal solutions containing silver is a further complication.

(5) Vongerichten seems to have noticed the effect of water on the decomposition. He evaporated the solution of β-methylmorphimethine methohydroxide in open dishes on the steam-bath and recommends "gelegentliches Anfeuchten" of the residue during the decomposition. He failed, however, to detect the above intermediate.

(6) This method is described by von Braun and Anton, *Ber.*, **64**, 2865 (1931).