

This high halogen content probably shows substitution in the amorphous oxide, by the chlorine set free from the ring in the reaction.

Alcohol Filtrate.—The filtrate from the precipitation of the amorphous oxide by alcohol was evaporated to dryness on the water-bath. The residue consisted of a brown tar and a water-soluble residue of inorganic salts, presumably due to deferred action of the iodine on the sodium salt, and to adsorption. Undoubtedly the adsorbed part represents part of the "iodine unaccounted for."

This water-soluble part was acidified with nitric acid and treated with silver nitrate. The precipitate of silver chloride and iodide was separated by 2% ammonia as before. The silver iodide weighed 0.0436 g., corresponding to 0.087 g. for the whole sample. This is equivalent to 0.047 g. of iodine, or 5.43% of that added to the reaction mixture. The silver chloride was pure white and weighed 0.3007 g., corresponding to 27.6% of the available chlorine, calculated from the yield of amorphous oxide.

The tar was separated and weighed. It weighed only 0.040 g. when dry, and if calculated as a polymerized residue, it corresponds to 0.054 g. of sodium salt, or 1.6% yield.

Summary.

The action of iodine on the sodium salt of trichlorophenol can be explained most easily as occurring in the following stages.

1. The iodine removes the sodium atom forming sodium iodide and an unsaturated residue, $C_6H_2Cl_3O$.
2. The unsaturated residue loses an atom of chlorine, which expels the iodine from the sodium iodide forming sodium chloride.
3. The new unsaturated residue polymerizes forming poly-dichloro phenylene oxide.

MINNEAPOLIS, MINN.

LOBINOL—A DERMATITANT FROM RHUS DIVERSILOBA (POISON OAK).

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The specific cause of skin poisoning from *Rhus toxicodendron* L., and its 2 sub-species, *R. diversiloba* T. and G., and *R. radicans* L., has thus far been attributed successively to an emanation of vapor,¹ a non-volatile substance,² a hydrocarbon gas,³ a gum resin, mixed with a "subtil" acid

¹ S. Thompson, *J. Proc. Ham. Assoc.*, **8**, 126 (1892); J. J. Bennett, "Plantae Javanical Rariores," **1838**, p. 60.

² de V. Du Fresnoy, "Des caracteres, du traitement et de la cure des dartres et de la paralysie, etc.; par l'usage du rhus radicans," **1**, Paris an VII. F. Fontana, "Trattato del veleno della vipera de velem Americani," **1**, 148; **3**, 114-117; *Napoli*, **1787**. Translated by Joseph Skinner, 2nd Ed., **2**, 181-184, London, **1795**.

³ J. B. Van Mons, *Actes soc. med. chir. pharm.*, [2] **1**, 136-167. Bruxelles, **1797**.

principle, qualified to combine with a hydrocarbon gas which emanates from the plant after sunset;¹ a volatile alkaloid,² a non-volatile gum resin;³ a volatile organic acid (toxicodendric acid);⁴ and infection by bacteria (*Micrococcus toxicatus*, Burrill);⁵ a non-volatile oil (toxicodendrol);⁶ a glucoside of fisetin, rhamnose and gallic acid;⁷ toxicodendrin; a toxalbumin;⁸ and finally not a glucoside of fisetin, rhamnose and gallic acid.⁹

The following attempt at the separation of the principal irritant poison (lobinol) of *Rhus diversiloba* represents the culmination of a number of attempts at the separation of a pure substance. It is presented herewith in the hope that someone will continue further the work and determine the structural formula of the poison. The analysis of the crystalline compounds obtained may be of assistance in this direction.

Extraction and Purification of Lobinol.

Bark from old branches of *Rhus diversiloba* (T. and G.) was shaved off with a 2-handled draw knife. The pieces of bark thus obtained were immediately placed in 95% alcohol, this mixture was heated on a sand-bath under a reflux condenser for several days. The alcoholic solution was drawn off, concentrated to $\frac{1}{10}$ its original volume by distillation from a Kjeldahl flask and placed in a separatory funnel which had previously been filled to $\frac{1}{4}$ of its capacity with petroleum ether. Water was now added until it represented 3 times the amount of alcoholic solution. The mixture was shaken in the separatory funnel, and the watery layer drawn off and discarded. The petroleum ether layer was then shaken with several portions of 95% alcohol. The alcoholic layer was saved and the petroleum ether discarded.

Saturated sodium chloride solution was added. The substance thus obtained as a supernatant layer is a clear, amber-red, oily, non-volatile, viscous, poisonous liquid.

It was further purified from alcohol and sodium chloride by washing with distilled water.

It cannot be positively stated that the above method of isolation yields a definite chemical individual, but it is apparently at least a mixture of

¹ M. Lavini, *J. chim. med.*, 1, 249-251 (1825), Paris.

² J. Khittel, *Witt. Vierteilj. L. Prakt. Pharm.*, 7, 348 (1858).

³ de R. Milon, *Bull. Acad. de Med.*, 26, 501-505, 1860-61, Paris; *J. med. chirurg. pharm. Toulouse.*, Nov., 1892.

⁴ J. M. Maisch, *Am. Pharm. Assoc.*, 13, 166 (1865).

⁵ J. T. Burrill, *Am. Mo. Mic. J.*, 3, 192-196 (1882); *Am. Naturalist.*, 17, 319 (1883); *Garden and Forest*, 8, 368 (1895); L. C. Frost, *Med. Rec.*, 90, 1121-1123 (1916); J. B. McNair, *Med. Rec.*, 91, 1042-1043 (1917).

⁶ F. Pfaff, *J. Exp. Med.*, 2, 184 (1897).

⁷ S. F. Acree, and W. A. Syme, *Am. Chem. J.*, 36, 301 (1906).

⁸ B. Chyzer, *Vrtljschr. gerichtl. Med.*, Berlin, 3, F. 39, 2. *Suppl.*, 147-159 (1910).

⁹ J. B. McNair, *THIS JOURNAL*, 38, 1417-1421 (1916).

appreciably uniform composition, appreciably free from contamination.

The principal constituent gives positive tests for carbon, hydrogen and oxygen.

The Probable Position of Oxygen in Lobinol.—The substance reduces ammoniacal silver nitrate solution in the cold. As this action is common to aldehydes, polyhydric phenols, and a few carbohydrates, it was thought lobinol might give a positive test for the carbonyl group. When it was tested with the fuchsin aldehyde reagent as well as with sodium hydrogen sulfite the results were negative. A portion of the substance was also tested by heating with a mixture of phenylhydrazine and Fehling's with negative results.

These results indicate that the principal constituent is not an aldehyde or a ketone.

Probable Absence of the Carboxyl Group.—Approximately 0.5 g. of the viscous liquid was shaken with 50 cc. of distilled water. When the aqueous solution was titrated with 0.1 *N* potassium hydroxide solution only 2 drops of the alkali were required to make the solution alkaline.

When a solution of the substance was made in neutral alcohol it reacted similarly towards alkali.

In a further test for the presence of the carboxyl group some of the material was shaken with 10% aqueous sodium carbonate solution and filtered. When the filtrate was acidified with hydrochloric acid and shaken with ether no organic acid could be detected in the ethereal layer.

It is evident, therefore, that the presence of the carboxyl group cannot be positively proved.

The above tests do not exclude the possibility of the presence of a lactone structure.

Presence of the Hydroxyl Groups.—Lobinol forms an acetyl derivative when dissolved in benzene together with acetyl chloride and the solution boiled until the evolution of hydrochloric acid ceases.

Lobinol forms an acetyl derivative when mixed with an equal weight of dry sodium acetate and 3 or 4 parts of acetic anhydride, and boiled for 2 or 3 minutes in a reflux apparatus, according to the method of C. Liebermann and O. Hormann.¹

A benzoyl derivative of lobinol also was formed by means of benzoyl chloride. The Schotten-Baumann method was used as follows. Ten cc. of lobinol was placed in a 3-liter glass separatory funnel. On account of the instability of lobinol in the presence of caustic alkali the flask was filled with oil gas. In order that benzoylation should be as complete as possible, 500 cc. of 10% aqueous potassium hydroxide and 60 cc. of ben-

¹ *Ber.*, 11, 1619 (1878).

zoyl chloride were alternately added in small portions.¹ Shaking and gentle cooling were continued for about 20 minutes. In place of caustic alkali, sodium carbonate, sodium hydrogen carbonate, or sodium acetate may be used, as these make it unnecessary to fill the flask with illuminating gas.² The precipitated benzoyl derivative is white and semi-solid. It gradually hardens and crystallizes on prolonged contact with water. To make sure of the removal of all traces of benzoyl chloride or benzoic acid the derivative was dissolved in ether, the ether distilled off, and the residue treated with alcohol which decomposed the last portions of benzoyl chloride that had not been removed by prolonged shaking of the ethereal solution with concentrated alkali. The alcoholic liquid was treated with soda in excess, precipitated with water, and the alcohol and ethylic benzoate removed by means of a current of steam. The residue was then repeatedly crystallized from alcohol.

A benzoyl derivative of lobinol may also be prepared from its ether or benzene solution, with the aid of dry alkali carbonate.³

From the preceding experiments it is evident that the oxygen contained in lobinol may be contained in an hydroxyl group or groups.

Probable Phenolic Nature of the Dermatitant.

Nitration.—Like many aromatic compounds, lobinol is easily nitrated. The nature of the substance varies with the conditions of the reaction. On continued boiling with strong nitric acid the derivative is first a solid of orange color, then a yellow liquid from which crystals of oxalic acid separate on standing.

Probable Phenolic Character.—When sodium or potassium hydroxide is added to an alcoholic solution of lobinol the liquid assumes a color varying from green to brown. A highly dilute alcoholic solution of lobinol gives a green color with ferric chloride, which turns red on the addition of sodium carbonate. This result might lead one to consider the dermatitant an *orthodihydric* phenol. Also, as in the case of polyhydric phenols, lobinol reduces metallic salts, *e. g.*, a solution of ammoniacal silver nitrate in the cold to form a silver mirror.

Phenolic Ether Formed.—In common with other benzyl ethers of phenols, lobinol benzyl ether is produced by heating with benzyl chloride and sodium ethylate for 3 or 4 hours. The ether is a neutral yellow liquid soluble in hot alcohol and ether and gives no apparent reaction with ferric chloride or sodium hydroxide.

According to the results of the foregoing experiments the principal dermatitant of *Rhus diversiloba* may contain a phenol group.

¹ *Ber.*, 25, 1045 (1892).

² *Ann.*, 265, 148 (1891); and Meyer and Jacobson, "Lehrbuch der organischen chemie," II, p. 546.

³ *Ber.*, 27, 3183 (1894).

Unsaturation.

To about 0.1 g. of substance in 2 cc. of carbon tetrachloride 2 or 3 drops of bromine solution were added. The bromine solution was prepared by dissolving 2 cc. of bromine in 50 cc. of carbon tetrachloride. Decolorization took place without evolution of hydrogen bromide, either immediately or within 3 minutes, or even when warmed gently for 2 minutes. The substance therefore may be unsaturated.¹

Lobinol is easily brominated when bromine is added to its ethereal solution.

Conclusion.

The principal dermatitant of *Rhus diversiloba*, if pure and not a mixture, has an unsaturated compound of the aromatic series containing carbon, hydrogen, and oxygen. The oxygen may exist combined as hydroxyl.

Its behavior is phenolic and it may contain 2 hydroxyl groups in the *ortho* position. This chemical finding is in agreement with the action of *Rhus* oxidase.² This oxidase accelerates the oxidation of readily oxidizable bodies, particularly those of the benzene series, which possesses at least 2 hydroxyl or amine groups when these groups occupy the *para* or *ortho* positions.

In accordance with reactions to halogens lobinol is unsaturated.

From the evidence at hand the principal dermatitant appears to be a poly-hydricphenol and I propose for it the name of lobinol. The terminal syllable *ol* of this word refers to its phenolic nature in accordance with the rules of the Chemical Society of London. The first two syllables of the word, *lobi*, are derived from the species name of the plant *diversiloba*.

Provisional Reactions of Lobinol.

1. It absorbs bromine readily.
2. Its alcoholic solution upon the addition of ferric chloride turns temporarily green, then black, and forms a black precipitate.
3. When its alcoholic solution is highly dilute the addition of ferric chloride produces a green color which turns red when sodium carbonate is added.
4. It forms a gummy mass with hydriodic acid, whose alcoholic solution turns green when ferric chloride is added.
5. Metallic carbonates are not decomposed by it.
6. Acetyl chloride or acetic anhydride produces an acetyl derivative. Benzoyl chloride yields a benzoyl derivative.
7. It forms an α -naphthyl-urethane with α -naphthyl-isocyanate. Phenyl-isocyanate forms a phenyl carbonate.

¹ H. C. Biddle, "Organic Chemistry," 1911, p. 76.

² J. B. McNair, *J. Infect. Dis.*, 20, 485-498 (1917).

8. A phenolic benzyl ether is formed with benzyl chloride and sodium alcoholate.

9. Millon's reagent gives a red color with it, a property of the hydroxyphenyl group.

10. A salt is formed when picric acid is added to its alcoholic solution.

11. It is easily darkened, dried, and hardened by means of manganese peroxide, barium peroxide, magnesium peroxide, litharge, manganese hydroxide and potassium dichromate.

12. It hardens at a temperature above 96° in the absence of its enzyme or any oxidizing agent.

13. It is slightly soluble in aqueous potassium hydroxide, but entirely soluble in alcoholic potassium hydroxide.

14. It reduced metallic salts especially silver nitrate on heating and ammoniacal silver nitrate in the cold.

15. It is precipitated by lead acetate, and forms a green precipitate with barium hydroxide.

16. On gradually adding alkali to its alcoholic solution a temporary green color is first produced which, on successive additions of alkali, turns red and brownish-red.

17. It forms a nitric compound with a violent reaction when concentrated nitric acid is added to it.

18. It is soluble in ether, chloroform, alcohol, methyl alcohol, benzin (b. p. below 60°), benzene, toluene, xylol, acetone, toluidine, pyridine, quinoline, carbon tetrachloride, amyl acetate, acetic ether, nitrobenzol, turpentine oil, glacial acetic acid, 80% solution of chloral hydrate and concentrated sodium and potassium hydroxide solutions.

19. It is precipitated from alcoholic solution by lead acetate, silver nitrate, mercurous nitrate, cupric acetate, ferric chloride, barium hydroxide, bromine, iodine, platinum chloride, gold chloride, uranium acetate, and copper nitrate.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MCGILL UNIVERSITY.]

THE PROPERTIES OF OXYNITRILASE.

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Rosenthaler, in 1908,¹ discovered that emulsin, when allowed to act on benzaldehyde and hydrocyanic acid, produced an optically active nitrile. That this reaction is catalyzed by an independent enzyme present in emulsin is very likely and the name oxynitrilase has usually been given to it. Rosenthaler in later papers showed that it is rather widely distributed, and one of us has shown that a particularly active form can

¹ Rosenthaler, *Arch. Pharm.*, **246**, 365 (1908).