pyrolysis into carbon monoxide and ethylene. The concept of the "methane system" has been adapted to explain these results.

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TREMETOL, THE COMPOUND THAT PRODUCES "TREMBLES" (MILKSICKNESS)

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Tremetol is the active principle of two plants, richweed and rayless goldenrod, both of which cause the disease known as trembles. This disease is also known as milksickness, especially by the medical profession. Richweed or white snakeroot (*Eupatorium urticaefolium*) is responsible for the disease in the Central States; rayless goldenrod or jimmy weed (*Aplopappus heterophyllus*,) occurs in the Southwestern section of the United States, where it produces the same disease.

Extensive pharmacological study, the results of which have been published in other places[1] has demonstrated that the active constituent of these plants is a substance to which the name tremetol has been applied. This paper contains the results of the chemical study of tremetol.

To prepare tremetol the following procedure has been used successfully. The plant material should be fresh in the case of richweed; rayless goldenrod is still poisonous when dried but appears gradually to lose toxicity. Old dried richweed does not produce trembles. The plant is comminuted and extracted with alcohol. The solvent is distilled from the extract, best under diminished pressure, and the greenish fatty residue is extracted with boiling water as long as anything dissolves. The insoluble material is collected and thoroughly extracted with boiling 50% alcohol. The solvent is removed from this solution and the thick resinous mass that separates is allowed to cool and harden, when the watery portion of the residue may be poured off it. The resinous mass is now thoroughly extracted with boiling 30% alcohol and the solution is filtered hot from the insoluble matter. On cooling the filtrate crude tremetol ester separates. A further crop may be obtained by evaporating the alcohol from the mother liquors. The combined crops are now hydrolyzed by boiling with 5% alcoholic potash for four hours, the alcohol is distilled off and the residue is dissolved in water. The free tremetol is extracted from this solution with successive portions of ether. The ether solutions are united, concentrated to convenient volume and washed, first with dilute sodium hydroxide solution and then with water, to remove possible phenols and resin acids. The purified ether solution is now mixed with 4 volumes of petroleum ether, filtered from any precipitate and allowed to evaporate. The solution in ether and reprecipitation with petroleum ether should be repeated twice to insure purity. On removal of the solvent tremetol remains as a straw-yellow, thick oil of pleasant aromatic odor distantly reminiscent of clove and nutmeg. Should solid, waxy particles separate, the substance has not been thoroughly separated from a sterol that accompanies it in richweed

[1] *J. Agric. Res.*, **35**, 547–576 (1927); *J. Am. Med. Assocn.*, **91**, 234–6 (1928); *J. Am. Vet. Med. Assocn.*, (n. s.) **26**, 603–605 (1928). A report on rayless goldenrod is in course of publication.

and the 50 and 30% alcohol steps should be repeated. Criteria of purity are the optical rotation, index of refraction and molecular weight.

Properties of Tremetol.—Tremetol is a straw-yellow thick oil of aromatic odor. It has not been obtained in crystalline condition and decomposes when attempts to distil it are made, even when the pressure is reduced to 3 mm. It is slowly volatile in steam and appears to suffer some alteration during the process. Tremetol is insoluble in water, acids and alkalies. It is readily soluble in alcohol and the common organic solvents, less soluble in petroleum ether but readily in mixtures of that solvent with ether. It occurs in the plant in combination with a resin acid the chemical composition of which has not been determined. Tremetol readily oxidizes in the air, losing its characteristic odor and developing a rancid and acetous odor.

The analytical figures for tremetol indicate either of two formulas, $C_{16}H_{22}O_3$ or $C_{17}H_{24}O_3$, agreeing better with the latter. Molecular weight determinations, bromine absorption and molecular refractivity data agree closely with the requirements of the first formula and this has been chosen as the more likely. The high percentages of carbon and hydrogen found by analysis are considered to be due to small amounts of petroleum ether remaining in the tremetol, which cannot be driven off without decomposing the substance itself.

Tremetol absorbs four atoms of bromine per molecule at room temperature. Inasmuch as the formula indicates the presence of five double bonds, it may be concluded that the substance contains a phenyl nucleus and a side chain containing two double bonds. The function of the oxygen atoms has not been determined. Phenolic hydroxyls and alkoxyl groups are not detected by the appropriate tests. No crystalline oxime or hydrazone has been obtained. Aldehyde and carboxyl groups are absent. A study of the constitution of the substance is in progress.

Anal. Calcd. for $C_{16}H_{22}O_3$ (262.17): C, 73.24; H, 8.45. Calcd. for $C_{17}H_{24}O_3$ (274.18): C, 73.87; H, 8.75. Found: (substance from richweed) C, 73.89, 73.89, 73.33; H, 8.89, 8.58, 8.60; mol. wt., 257, 259; (substance from rayless goldenrod) C, 73.54, 73.72, 73.57; H, 8.66, 8.83, 8.94; mol. wt., 237, 262, 258. *Optical activity.* 2.9020 g. in enough alcohol to make 100 cc. rotated the plane of polarized light an average of 0.98° to the left when examined in a 10-cm. tube at 30°: whence $[\alpha]_D^{30}$ −33.82°.

Bromine Absorption.—In carbon tetrachloride solution 0.3882 and 0.4359 g. of the substance absorbed 0.4531 and 0.5466 g. of bromine at room temperature, or 1.167 and 1.254 g. of bromine per gram of substance (mol. wt. 262.17). One molecule of substance with two active double bonds reacting with four atoms of bromine requires 1.22 g. of halogen per gram; d_4^{25} 1.0787, n_D^{30} 1.5345, mol. refr. calcd. for $C_{16}H_{22}O_3$ (F_5), 76.12; for $C_{17}H_{24}O_3$ (F_5), 79.65. Found: 75.62.

Summary

Tremetol, the substance present in richweed and in rayless goldenrod, which produces the diseases known as milksickness and trembles is a straw

yellow oil, $C_{16}H_{22}O_3$, levorotatory, insoluble in water, acid and alkaline solutions, and soluble in the common organic solvents.

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[CONTRIBUTION FROM THE POLARIMETRY SECTION, BUREAU OF STANDARDS, U. S. DEPARTMENT OF COMMERCE]

RELATIONS BETWEEN ROTATORY POWER AND STRUCTURE IN THE SUGAR GROUP. XXI. BETA-THIOPHENOL GLYCOSIDES OF GLUCOSE, XYLOSE, LACTOSE AND CELLOBIOSE[1,2]

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Although the glycosides of the hydroxy alcohols form a numerous group which has been submitted to detailed study and whose optical properties have been classified through the work of Hudson,[3] too few of the thioglycosides have been prepared to render possible a similar mathematical examination of their molecular rotations. Apart from the α- and β-glucosides of methyl, ethyl, propyl and benzyl mercaptan described by Schneider and his co-workers,[4] the only other simple members of the series found recorded in the literature are β-thiophenol glucoside and β-thiophenol lactoside, which together form the subject of a paper by Fischer and Delbrück.[5] The thioglycosides, nevertheless, are of interest from an optical point of view, for they differ from their oxygen analogs in containing a bivalent and therefore unsaturated sulfur atom directly united to the first asymmetric center of the carbohydrate residue. It is impossible to predict the nature and the extent of the changes which this difference may bring about in their behavior toward plane-polarized light and, in consequence, the present investigation is one of several designed to gain information on this subject by experimental methods. This article is mainly concerned with four glycosides of thiophenol and with their acetylated derivatives.

At an early stage in the research it became apparent that an acetobromo sugar in ethereal or benzene solution reacted very slowly and sometimes incompletely with sodium thiophenate dissolved in water. This was the

[1] Publication approved by the Director of the Bureau of Standards, U. S. Department of Commerce.

[2] The author has arranged with Dr. C. S. Hudson, under whose direction the research was carried out, that it will be included as No. XXI in his series entitled "Relations between Rotatory Power and Structure in the Sugar Group." No. XX was published in THIS JOURNAL, **51**, 2788 (1929).

[3] Hudson, *ibid.*, **31**, 66 (1909).

[4] Schneider, Sepp and Stiehler, *Ber.*, **51**, 220 (1918).

[5] Fischer and Delbrück, *ibid.*, **42**, 1476 (1909).