perature, this melted at 69°. Mixtures of approximately equal amounts of the natural and the synthetic acids melted at 68.5°. Repeated simultaneous determinations showed that such mixtures melted possibly a trifle higher, certainly no lower, than the unmixed synthetic acid. The absence of a marked melting-point depression, characteristic of conglomerates, shows that the *dextro* and *levo* substances form mixed crystals.

dl-Chaulmoogric acid has the same peculiar odor as the natural substance. This is more readily perceptible when the substances are stored in closed containers.

Five g. of *dl*-chaulmoogric acid was oxidized with potassium permanganate in acetic acid as described in an earlier paper.[9] A product sparingly soluble in ether was obtained, the melting point (125°) of which was not depressed by admixture with γ-keto-n-pentadecane-α,α'-dicarboxylic acid (m p., 126°) from natural chaulmoogric acid.

Summary

In studies aiming to produce anti-leprosy drugs superior to those obtainable from chaulmoogra-group oils, various lower homologs of chaulmoogric acid were required. A method of synthesis was developed for the preparation of these. Aceto-acetic ester was condensed with ω-cyano-undecanoyl chloride and then with Δ^2-chlorocyclopentene. The resulting diketo ester gave, on hydrolysis, *dl*-λ-ketochaulmoogric acid.

The keto acid, on reduction with hydrazine and sodium ethylate, yielded *dl*-chaulmoogric acid.

The synthetic chaulmoogric acid is very similar to the natural dextrorotatory substance and, judging from melting-point determinations, isomorphous with it. The structural identity of the two was confirmed by oxidation of the new product to γ-keto-n-pentadecane-α,α'-dicarboxylic acid.

CULION, PHILIPPINE ISLANDS

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE UNIVERSITY OF IOWA]

NEW MONOBROMO DERIVATIVES OF VANILLIN

BY L. CHAS. RAIFORD AND W. C. STOESSER

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Hitherto, the only known bromine derivative of vanillin is that melting at 164°[1] and having the halogen in Position 5 (CHO = 1). In the work reported here two other derivatives have been obtained, melting at 154–155° and 178°, respectively.

The first of these was prepared from an aminovanillin,[2] m. p. 127°, by the Sandmeyer reaction. The structure of the amine has been fixed in the following way: Pschorr and Sumuleanu[3] obtained a nitrovanillin

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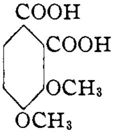
[9] Perkins, THIS JOURNAL, **48**, 1723 (1926).

[1] Tiemann and Haarmann [*Ber.*, **7**, 615 (1874)], who first prepared it, recorded 160–161°.

[2] Sumuleanu [*Ann. Sci. Univ. Jassy*, **2**, 131 (1902–1903)] found 128–129°.

[3] Pschorr and Sumuleanu, *Ber.*, **32**, 3408 (1899).

which they converted into a methoxy derivative in the usual way. This was oxidized by alkaline permanganate into 2-nitroveratric acid which was then reduced to the corresponding amino compound. When the amine was diazotized and the resulting solution treated with cuprous cyanide, a nitrile was obtained. Hydrolysis of the latter gave hemipinic acid, I.



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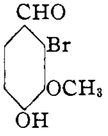

II

This new bromine derivative is, therefore, 2-bromovanillin, II.

When an acetic acid solution of vanillin is treated with bromine at room temperature, the 5-bromo compound[1] appears to be the only product,[4] regardless of the amount of bromine employed. If acetylvanillin is used, and the bromination is carried out with one molecular proportion of bromine; under the conditions just stated, three products are formed: 5-bromovanillin, a second monobromo derivative, m. p. 178°, which was shown by mixed-melting-point determinations to be different from the other two, and in which bromine must occupy Position 6, along with a dibromo derivative; m. p., 218°.[5] Bromination of the acetylated compound in the presence of sodium acetate[6] gives the 6 derivative only; however, this product is very readily converted into the dibromo compound specified above, while the 5 derivative undergoes further bromination with difficulty.[5] Nevertheless, both give the same dibromo product from which it follows that the latter is 5,6-dibromovanillin. It seems probable, therefore, that the presence of the three products in the mixture obtained by brominating acetylvanillin in the absence of sodium acetate may be explained as follows. The liberation of hydrogen bromide in the formation of 6-bromovanillin, which is easily obtained from the acetyl derivative, hydrolyzes some of the acetyl compound to free vanillin. The latter gives only the 5 derivative under the conditions of this experiment while, as stated above, the 6 derivative readily gives the dibromo compound.

To test the hydrolysis of acetylvanillin by hydrogen bromide, 0.5 cc. of constant-boiling acid was added to 5 cc. of an acetic acid solution of the acetyl derivative of approximately 20%, and the mixture allowed

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[4] Report by Raiford and Hilman soon to be published from this Laboratory.

[5] The preparation by other methods and the properties of this compound are described in a succeeding paper by Raiford and Hilman.

[6] This interacts with the hydrogen bromide which is formed during the substitution, and thus prevents hydrolysis of the acetyl derivative. This difference in directive influence between the hydroxyl and the acetoxyl radicals will be further studied in this Laboratory.

to stand for five hours at about 45°. The precipitate formed when this liquid was poured into water was extracted with dil. ammonium hydroxide solution,[7] and from this extract vanillin was recovered. When the original mixture is allowed to stand for two days at room temperature, hydrolysis is practically complete. In a subsequent test it was shown that hydrolysis occurred at the lowest temperature at which acetic acid remains liquid.

Experimental Part

4-Bromophenylhydrazone of 2-Aminovanillin.—This was prepared in order to identify further the starting material used in the derivatives described below. The product crystallized in needles from dilute alcohol; m. p., 168°.

Anal. Subs., 0.2081: AgBr, 0.1161. Calcd. for $C_{14}H_{14}O_2N_3Br$: Br, 23.81. Found: 23.74.

2-Bromovanillin.—The corresponding amino compound was dissolved in an excess of dil. hydrobromic acid and diazotized with the calculated quantity of sodium nitrite. The resulting liquid was added gradually with stirring to cuprous bromide solution, and the mixture heated on a water-bath until no more nitrogen was evolved. After 24 hours, half a volume of concd. hydrochloric acid was added and the solid filtered off; yield, 83%. Boiling its dilute alcoholic solution with animal charcoal, filtering and cooling the filtrate gave nearly colorless needles: m. p., 154–155°.

Anal. Subs., 0.2145: AgBr, 0.1749. Calcd. for $C_8H_7O_3Br$: Br, 34.63. Found: 34.70.

6-Bromovanillin.—A mixture of 7.5 g. each of acetylvanillin and dried sodium acetate, 0.1 g. of iodine and slightly more than one molecular proportion of bromine in 35 cc. of acetic acid was warmed to 45°, then allowed to cool and stand overnight. When the mixture was poured into water, an oil separated. Shaking caused it to solidify;

TABLE I

MONOBROMOVANILLIN DERIVATIVES

Compound	Solvent	Crystal form	M. p., °C.	Anal.			
				Subs., g.	AgBr, g.	Halogen, % Calcd.	Found
2-Bromovanillin *p*-bromophenylhydrazone, $C_{14}H_{12}O_2N_2Br_2$	Dil. alcohol	Light tan needles	157	0.1508	0.1423	40.00	40.16
2-Bromovanillin semicarbazone. $C_9H_{10}O_3N_3Br$	Dil. pyridine	Almost colorless needles	216–217	.2032	.1340	27.78	28.06
bis-2-Bromovanillidenebenzidine. $(C_{14}H_{11}O_2NBr)_2$	Pyridine	Irreg. orange granules	221–222	.2073	.1271	26.23	26.09
6-Bromovanillin *p*-bromophenylhydrazone, $C_{14}H_{12}O_2N_2Br_2$	Acetic acid	Cream-colored needles	176	.1682	.1579	40.00	39.95
6-Bromovanillin semicarbazone. $C_9H_{10}O_3N_3Br$	Dil. pyridine	Needles with slightly greenish tinge	231–232	.2315	.1516	27.78	27.87
bis-6-Bromovanillidenebenzidine. $(C_{14}H_{11}O_2NBr)_2$	Pyridine	Irreg. orange granules	268–269	.2053	.1245	26.23	25.81
6-Bromovanillin oxime. $C_8H_8O_3NBr$	Dil. alcohol	Colorless needles	158–159	.1946	.1496	32.52	32.72

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[7] It was previously shown that acetylvanillin is not hydrolyzed by ammonium hydroxide under these conditions.

yield, 87.6%. Hydrolysis with potassium hydroxide gave a 92.6% yield of the bromovanillin. Repeated crystallization from alcohol gave colorless needles; m. p., 178°.

Anal. Subs., 0.1987: AgBr, 0.1621. Calcd. for $C_8H_7O_3Br$: Br, 34.63. Found: 34.72.

Each of these products was further identified by the study of several of its derivatives, as shown in Table I.

Summary

1. Two new monobromovanillin substitution products have been prepared and their structures established.
2. A dibromovanillin has been obtained and the halogen atoms oriented.
3. The study of these compounds will be continued in this Laboratory.

IOWA CITY, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE OF INDUSTRIAL RESEARCH, UNIVERSITY OF PITTSBURGH]

RECIPROCAL SOLUBILITY OF THE NORMAL PROPYL ETHERS OF 1,2-PROPYLENE GLYCOL AND WATER. CLOSED SOLUBILITY CURVES. II

BY HENRY L. COX, WILLIAM L. NELSON AND LEONARD H. CRETCHER

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In a discussion of concentration-temperature curves for partially miscible liquids, Findlay[1] has stated that the general form of solubility curve for all pairs of liquids may be ellipsoidal. While there are as yet insufficient data to prove the correctness of this view, considerable evidence in its favor has been presented by various investigators, notably Rothmund,[2] who found a tendency toward the formation of closed solubility curves in the systems β-collidine–water, methylethyl ketone–water at low pressure and diethylketone–water. The system ether–water investigated by Klobbie,[3] Hill,[4] and others may be classified among the systems exhibiting a similar tendency. In this case it is true that the upper consolute temperature lies above the critical point of one of the components and that the lower consolute temperature lies below the point at which a solid phase appears. The fact that the portions of these curves experimentally determinable are concave with respect to a common center is strongly indicative, however, of a closed solubility curve.[5]

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[1] Findlay, "The Phase Rule," Longmans, Green and Co., London, **1923**, 5th ed., p. 82.

[2] Rothmund, *Z. physik. Chem.*, **26**, 433, 492 (1898).

[3] Klobbie, *ibid.*, **24**, 615 (1897).

[4] Hill, THIS JOURNAL, **45**, 1143 (1923).

[5] It is true that Hill's data for the solubility of water in ether show that this part of the curve is substantially a straight line. It may be pointed out, however, that only a very small portion of the complete curve was determined.