2. The reaction mixtures were examined quantitatively for pyruvic aldelyde, lactic, acetic and formic acids. Changes in temperature and alkali concentration produced changes in the yields of these compounds which were of the same general character as those obtained under exactly the same conditions from fructose and glucose.

3. The interdependence of the reactions producing pyruvic aldehyde, lactic, acetic and formic acids in alkaline solutions of glyceric aldehyde and dihydroxy-acetone is also found to exist between the reactions producing these same products when they are obtained from alkaline solutions of mannose, glucose and fructose under the same experimental conditions. This fact is regarded as evidence for the assumption that the formation of glyceric aldehyde, a fission product of 3,4-hexose enediols, is an intermediate step in the production of these compounds from the hexose sugars. It is predicted that this interdependence will be found to exist in the products of the interaction of aqueous solutions of potassium hydroxide and of all those hexose sugars which are not available for laboratory experimentation at the present time.

4. At the lower temperatures and the lower alkali normalities, the amounts of reaction products obtained from mannose, glucose and fructose are not the same. This is understood on the ground that the equilibria formed in each individual case with the hexose and the alkali are not quantitatively identical.

5. At 75° the amounts of lactic, acetic and formic acids obtained from mannose, glucose and fructose are practically the same in each case. These facts seem to support the view that the equilibrated systems in the alkaline solutions of these hexose sugars are identical at this temperature.

Columbus, Ohio

[Contribution from the Laboratory of Organic Chemistry of the State University of Iowa]

NEW BROMINE SUBSTITUTION PRODUCTS OF VANILLIN AND SOME OF THEIR DERIVATIVES[1]

By L. Chas. Raiford and W. C. Stoesser

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One purpose of this work was to complete the list of possible bromine substitution products of vanillin and to use these compounds in studying the effect of the ortho substituents of an aldehyde in its reaction with an amino compound. Kauffmann and Franck[2] were unable to convert 2-aminoresorcinoldimethyl ether into either a thiocarbanilide or a benzyli-

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[1] Condensed from a portion of the thesis submitted by W. C. Stoesser to the faculty of the Graduate College of the State University of Iowa in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] Kauffmann and Franck, *Ber.*, **40**, 3999 (1907).

dene derivative. Sachs and Appenzeller[3] failed to prepare both the oxime and the hydrazone from tetramethyl-2,4-diaminobenzaldehyde. In apparent opposition to this Blanksma[4] condensed 2,4,6-trinitrobenzaldehyde with aniline, but reported no yield, while Lowy and collaborators[5] obtained good yields of benzal derivatives from 2,4-dinitro- and 2,4,6-trinitrobenzaldehydes with various aromatic amines, though they studied no aldehyde containing a substituent other than the nitro radical.[6] These differences suggested further study of the question.

In previous reports[7] from this Laboratory one dibromo and two new monobromo compounds of vanillin were described. Each of these products was characterized by the preparation of several derivatives, especially those obtainable by reaction with amino compounds, but it was recognized that their activities as aldehydes should be studied further. In our previous work retardation due to the presence of ortho substituents was noted in a few cases only, though the work included no instance in which both ortho positions were substituted. It seemed necessary to test that point further because the work on record included too few radicals. Tabular summaries of the present work (see experimental part) will show that when only one ortho position is substituted the hindrance is not noticeable in the cases studied, and that when both are involved the retardation is less pronounced than might have been expected.

A second purpose in this study was to test further the extent to which substituents in the benzene nucleus may determine the positions taken by new groups. When Pschorr and Sumuleanu[8] nitrated acetylvanillin they obtained a 2-nitro derivative; later Raiford and Stoesser[7] found that bromination of the same starting material gives a 6-bromo compound exclusively, which shows that the acetoxy radical directs to the meta position, but to a different one in the instances cited, which suggests that the directive influence of this radical may depend on the specific character of the entering substituent. But in an unsymmetrical structure[9] like vanillin, it is not to be expected that positions 2 and 6 will be equally favored in substitution even by the same entering group. In fact, in a repetition of Pschorr and Sumuleanu's nitration, using a larger amount

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[3] Sachs and Appenzeller, *Ber.*, **41**, 98 (1908).

[4] Blanksma, *Chem. Weekblad*, **9**, 865 (1912).

[5] Lowy and others, THIS JOURNAL, **43**, 1961 (1921).

[6] The results of Meyer [*Z. physik. Chem.*, **24**, 219 (1897)], Fischer and Giebe [*Ber.*, **31**, 546 (1898)] and Baly and Collie [*J. Chem. Soc.*, **87**, 1340 (1905)] tend to indicate that the effect of the nitro radical is not typical of the behavior of benzene substituents under the conditions of these experiments.

[7] (a) Raiford and Stoesser, THIS JOURNAL, **49**, 1077 (1927); (b) Raiford and Hilman, *ibid.*, **49**, 1571 (1927).

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

[9] The directive influence of the acetoxy radical in symmetrical structures is being studied by Mr. McCormack in this Laboratory.

of starting material, it was found that if the total mass of acetylnitro product is hydrolyzed before an attempt is made to purify it, two compounds may be isolated: 80% of the 2-nitro derivative, m. p. 136°, described by the authors named, and about 5% of another mononitro product, m. p. 212°, which should be the 6-derivative.[10]

A third purpose in this study was to test further the observations of Brady and Dunn[11] that "no evidence of the existence of a second isomeride has been obtained in the case of any of the hydroxybenzaldoximes," but that "certain negative substituents in the benzene ring seem to favor the existence of two isomeric oximes." In the work described below one oxime, probably the *anti* form, was readily obtained from every bromine derivative of vanillin. Attempts to obtain the isomeride by Goldschmidt's[12] method caused the loss of the methyl radical and the formation of the oxime of the corresponding bromoprotocatechuic aldehyde.[13] Treatment of the available forms with gaseous hydrogen chloride for the purpose of transmutation[14] failed also.

Experimental Part

Derivatives of 6-Bromovanillin

Acetate[15] of the Oxime of 6-Bromovanillin.—Ten g. of the oxime[7a] was mixed with 20 cc. of acetic anhydride, allowed to remain for one hour with occasional stirring and the solid filtered off; yield, 98%. Repeated crystallization from benzene gave nearly colorless needles, m. p. 149–151°.[16]

Anal. Subs., 0.2248: 7.79 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{10}H_{10}O_4NBr$: Br, 27.78. Found: 27.72.

The Oxime of Acetyl-6-bromovanillin.—A mixture of 5 g. of the acetyl derivative, 1.58 g. of hydroxylamine hydrochloride, an equal weight of sodium acetate and 15 cc. of alcohol was refluxed for half an hour. Addition of water precipitated a yield of 89%. Crystallization from alcohol gave colorless needles; m. p. 150–152°. A mixture of this and its isomer, just described, melted between 122 and 130°.

Anal. Subs., 0.2163: 7.43 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{10}H_{10}O_4NBr$: Br, 27.78. Found: 27.48.

Acetate of the Oxime of Acetyl-6-bromovanillin.—Four g. of the acetyl derivative just described and 8 cc. of acetic anhydride were heated to the boiling point and allowed

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[10] The other one demanded by theory melts at 176° [Bentley, *Am. Chem. J.*, **24**, 173 (1900)] and was proved by Vogel [*Monatsh.*, **20**, 383 (1899)] to have the nitro radical in position 5.

[11] Brady and Dunn, *J. Chem. Soc.*, **105**, 824 (1914); **107**, 1859 (1915).

[12] Goldschmidt, *Ber.*, **16**, 2176 (1883).

[13] *Anal.* Subs., 0.2111: 9.15 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_7H_6O_3NBr$: Br, 34.48. Found: 34.68.

[14] Luxmore, *J. Chem. Soc.*, **69**, 181 (1896).

[15] The acetyl group has here replaced the hydrogen of the oxime radical.

[16] In about six months this had dropped to 140–141°, which accords with the observations of Janny [*Ber.*, **15**, 2782 (1882)], Gabriel [*Ber.*, **16**, 520 (1883)] and Holleman, [*Rec. trav. chim.*, **13**, 429 (1894)].

to cool and crystallize. Removal of the solid and treatment of the filtrate with water gave additional product; total yield, 87%. Recrystallization from alcohol gave colorless diamond-shaped plates; m. p. 153–154°. This product was also obtained by warming a mixture of the acetate of the oxime, acetic anhydride and one drop of sulfuric acid until all was dissolved and allowing it to crystallize.

Anal. Subs., 0.2399: 7.25 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{12}H_{12}O_5NBr$: Br, 24.24. Found: 24.18.

3-Methoxy-4-acetoxy-6-bromobenzonitrile.—This was obtained in nearly quantitative yield by boiling 5 g. of the acetate of the oxime with 10 cc. of acetic anhydride for an hour and then adding water. Repeated crystallization from alcohol gave nearly colorless masses that appeared like cotton; m. p. 148–149°.

Anal. Subs., 0.2044: AgBr, 0.1422. Calcd. for $C_{10}H_8O_3NBr$: Br, 29.63. Found: 29.60.

6-Bromovanillic Acid.—Ten g. of the above-described nitrile and 100 cc. of 6 *N* potassium hydroxide solution were refluxed for three and one-half hours and then acidified with hydrochloric acid: yield, 98%. Repeated crystallization from dilute alcohol gave irregular masses that, after drying at 110°, melted at 190–191°.

Anal. Subs., 0.2101: AgBr, 0.1595. Calcd. for $C_8H_7O_4Br$: Br, 32.39. Found: 32.31.

Dibromo and Tribromovanillin Derivatives

Nitration of Acetylvanillin.—One hundred g. of acetylvanillin was rapidly added to 400 g. of fuming nitric acid which was kept between 2 and 6°, and the clear red solution was poured into 1.5 liters of ice and water. The product separated as a green oil which solidified after a brief period. When this was hydrolyzed by boiling with potassium hydroxide solution, and the clear but very dark-colored liquid was poured into excess of concentrated hydrochloric acid, a mixture of two nitro compounds was precipitated. Extraction of the dry material with cold alcohol removed 2-nitrovanillin; m. p. 136°. Crystallization of the residue from acetic acid gave yellow plates of the isomeric 6-nitro derivative; m. p. 212°. The latter was analyzed.

Anal. Subs., 0.4834: 31.8 cc. of N_2 at 21° and 730 mm. Calcd. for $C_8H_7O_5N$: N, 7.11. Found: 7.3.

Acetyl-2-nitro-5-bromovanillin.—Ten g. of acetyl-5-bromovanillin[17] was added to 40 g. of fuming nitric acid, the mixture held between 25 and 30° and stirred until clear, and the solution then poured into ice and water. The oil which separated at first solidified after a short time; yield, 80%. It was repeatedly crystallized by treatment of its hot benzene solution with ligroin (b. p. 60–70°) and was obtained in nearly colorless granules that became yellow on exposure to light; m. p. 128°.

Anal. Subs., 0.4090, 0.2446: 17.5 cc. of N_2 at 25° and 729 mm.; AgBr, 0.1439. Calcd. for $C_{10}H_8O_5NBr$: N, 4.40; Br, 25.16. Found: N, 4.7, Br, 25.04.

2-Nitro-5-bromovanillin.—This was obtained by hydrolysis of the above-described acetyl derivative and also by bromination of 2-nitrovanillin. Sixty g. of the nitro compound and 1 g. of iodine were added to a solution of 16.5 cc. of bromine in 200 cc. of acetic acid, the mixture warmed until all was dissolved and allowed to stand overnight. When the solution was poured into water the bromine derivative was precipi-

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[17] This was obtained in 90% yield by slowly adding acetyl chloride to a cold 40% solution of 5-bromovanillin in pyridine, allowing the mixture to stand overnight and then pouring it into an excess of dilute sulfuric acid.

tated in 95% yield. Crystallization from benzene gave nearly colorless prisms, m. p. 150–151°.

Anal. Subs., 0.2326: 8.39 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_8H_6O_5NBr$: Br, 28.99. Found: 28.86.

2-Amino-5-bromovanillin.—Ferrous hydroxide was prepared by treatment of a solution of 300 g. of ferrous sulfate in 1 liter of water with 400 cc. of concentrated ammonia water, and to this hot mixture was slowly added 35 g. of the above-described nitro compound. This was boiled for fifteen minutes, 600 cc. of boiling water was added and the mixture filtered hot. The residue was extracted with hot water and the combined filtrates acidified with dilute sulfuric acid; yield, 96.8%. Crystallization from dilute acetone gave long tan-colored needles; m. p. 139–140°.

Anal. Subs., 0.5598, 0.2498: 29 cc. of N_2 at 22° and 731 mm., 10.17 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_8H_8O_3NBr$: N, 5.69; Br, 32.52. Found: N, 5.8; Br, 32.57.

2,5-Dibromovanillin.—A smooth paste was made by mixing 33.1 g. of the above-described finely powdered amino compound, 60 cc. of constant boiling hydrobromic acid and 20 cc. of water. This was cooled below 0°, diazotized by adding 9.5 g. of sodium nitrite in small portions and then 15 g. of cuprous bromide in 60 cc. of hydrobromic acid was poured in. After heating on a water-bath for one and one-half hours, an equal volume of dilute hydrochloric acid (1:1) was added and the dibromo compound filtered out, yield, 79%. Crystallization from acetic acid gave colorless needles, m. p. 189°.

Anal. Subs., 0.2018: AgBr, 0.2454. Calcd. for $C_8H_6O_3Br_2$: Br, 51.61. Found: 51.75.

2,5-Dibromo-3-methoxy-4-acetoxybenzal Diacetate.—Ten g. of the dibromo compound just described was suspended in 20 cc. of acetic anhydride and one drop of concentrated sulfuric acid added. When all of the solid had dissolved, the liquid was warmed gently for about two minutes. Addition of water to decompose excess of anhydride precipitated the diacetate in 97% yield. Repeated crystallization from alcohol gave colorless plates; m. p. 157–158°. After drying at 120° it was analyzed for bromine.

Anal. Subs., 0.3046: 13.38 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{14}H_{14}O_7Br_2$: Br, 35.24. Found: 35.14.

Hydrolysis of the diacetate with potassium hydroxide solution gave a 98% yield of 2,5-dibromovanillin.

Acetyl-2,5-dibromovanillin.—Ten g. of the dibromo compound, an equal weight of sodium bisulfite[18] and 20 cc. of acetic anhydride were mixed and warmed until the dibromovanillin had dissolved. The bisulfite appeared thus far to be unchanged. Fifty cc. of water was added, the mixture stirred and warmed until nearly all was in solution and then filtered hot. The bisulfite addition product that crystallized on cooling was removed, decomposed by sodium carbonate solution and the acetyl derivative separated; yield 74%. Recrystallization from alcohol gave colorless prisms; m. p. 68–70°.

Anal. Subs., 0.3962: 22.46 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{10}H_8O_4Br_2$: Br, 45.46. Found: 45.35.

This dibromovanillin was further characterized by the study of the derivatives indicated in Table I.

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[18] Attempts to prepare the acetyl derivative by the usual methods failed to give a pure product. One of the impurities was the benzal diacetate described above. Its formation under the conditions was prevented by the bisulfite.

TABLE IA

DERIVATIVES OF 2,5-DIBROMOVANILLIN

No.	Compound	Solvent	Crystal form	Yield, %
1	*p*-Nitrophenylhydrazone	Dil. pyridine	Yellow needles	99
2	Semicarbazone[a]	Dil. acetic acid	Fine colorless needles	95
3	*bis*-Benzidine[b]	Pyridine	Bright orange granules	..
4	Oxime	Benzene	Nearly colorless needles	97
5	Acetate of oxime	...	Uncrystallizable	93
6	Acetate of acetyloxime	Ligroin (140–150)	Colorless needles	72
7	Acetoxynitrile	Dil. acetic acid	Colorless needles	90
8	Dibromovanillic acid	Acetic acid	Colorless needles	91

[a] Drying over potassium hydroxide under partial pressure at room temperature for several days caused loss of some acetic acid of crystallization. *Anal.* Subs., 0.2300: loss in wt. at 120°, 0.0376. Calcd. for 2 moles of $C_2H_4O_2$: 24.64. Found: 16.35.

[b] Product changed color and lost pyridine of crystallization when heated at 120°, but the amount was not determined.

TABLE IB

DERIVATIVES OF 2,5-DIBROMOVANILLIN

No.	Formula	M. p., °C.	Subs., g.	Cc. of 0.1 *N* $AgNO_3$ or wt. of AgBr	Halogen, % Calcd.	Halogen, % Found
1	$C_{14}H_{11}O_4N_3Br_2$	249[a]	0.2034	0.1717 g.	35.96	35.92
2	$C_9H_9O_3N_3Br_2$	233–234	.3085	16.91 cc.	43.60	43.85
3	$(C_{14}H_{10}O_2NBr_2)_2$	<350	.3089	16.16 cc.	41.67	41.85
4	$C_8H_7O_3NBr_2$	154–155	.1784	0.2071 g.	49.23	49.40
5	$C_{10}H_9O_4NBr_2$	184–185	.3299	18.05 cc.	43.60	43.77
6	$C_{12}H_{11}O_5NBr_2$	137–139	.4034	19.85 cc.	39.12	39.36
7	$C_{10}H_7O_3NBr_2$	89– 90	.2996	17.20 cc.	45.85	45.93
8	$C_8H_6O_4Br_2$	179–180	.3376[b]	20.60 cc.	49.08	48.82

[a] After removal of pyridine of crystallization. *Anal.* Subs., 0.2099: loss in wt. at 120°, 0.0319. Calcd. for 1 mole of C_5H_5N: 15.08. Found: 15.20.

[b] After removal of acetic acid of crystallization. *Anal.* Subs., 1.0023: loss in wt. at 120°, 0.1447. Calcd. for 1 mole of $C_2H_4O_2$: 15.54. Found: 14.44.

2-Nitro-6-bromovanillin.—Fifty g. of acetyl-6-bromovanillin[19] was gradually added with stirring to 200 g. of fuming nitric acid which was kept between 0 and 6°. When the clear red solution so obtained was poured into ice and water, the oil that separated became solid on standing. The product was heated with potassium hydroxide solution to remove the acetyl group and the free nitro compound was precipitated in 78% yield by the addition of hydrochloric acid. Repeated crystallization from dilute acetic acid gave cream-colored needles that melted at 168–170°, which seemed to be constant.

Anal. Subs., 0.5231: 18.81 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_8H_6O_5NBr$: Br, 28.99. Found: 28.77.

2-Amino-6-bromovanillin.—The above-described nitro compound was reduced by ferrous hydroxide as previously explained, except that an additional 50 cc. of concentrated ammonia water was added just before filtration. The amino compound was obtained in 94% yield. Recrystallization from alcohol gave yellow needles that shrink at 210° and melt at 217–218°.

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[19] Ref. 7a, p. 1079.

Anal. Subs., 0.5205: 21.16 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_8H_8O_3NBr$: Br, 32.52. Found: 32.52.

2,6-Dibromovanillin.—To a solution containing 30 cc. of sulfuric acid and 10 cc. of water, 9.8 g. of the above-described amino compound was added and the mixture stirred into a smooth paste. Four g. of solid sodium nitrite was slowly added with continual stirring, while the temperature was kept between 10 and 15° by standing the container in a cooling bath. Five g. of ice was slowly added to the reaction mixture every fifteen minutes during one and one-fourth hours. This was then poured into a solution containing 9 g. of cuprous bromide in 50 cc. of constant boiling hydrobromic acid, the whole heated for some time on a water-bath, 100 cc. of hydrochloric acid (1:1) added and the mixture filtered. The yield was 85%. After purification by extraction with benzene, which left a small portion of insoluble material, repeated crystallization from dilute alcohol gave nearly colorless needles; m. p. 155–156°. The substance was further identified by study of the derivatives indicated in Table II.

Anal. Subs., 0.3378: 21.86 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_8H_6O_3Br_2$: Br, 51.61. Found: 51.77.

TABLE IIA

DERIVATIVES OF 2,6-DIBROMOVANILLIN

No.	Compound	Solvent	Crystal form	Yield,
1	Oxime	Benzene	Colorless needles	73
2	*p*-Bromophenylhydrazone	Dil. acetic acid	Flesh-colored needles	56
3	Semicarbazone[a]	Acetic acid	Colorless needles	73
4	*bis*-Benzidine[b]	Pyridine	Yellowish-brown plates	74

[a] Drying under partial vacuum over potassium hydroxide for several hours probably caused loss of some acetic acid of crystallization. *Anal.* Subs., 0.3671: loss in wt. at 120°, 0.0865. Calcd. for 2 moles of $C_2H_4O_2$: 24.64. Found: 23.56.

[b] *Anal.* Subs., 0.4141: loss in wt., 0.0718. Calcd. for 2 moles of C_5H_5N: 17.06. Found: 17.34.

TABLE IIB

DERIVATIVES OF 2,6-DIBROMOVANILLIN

No.	Formula	M. p., °C.	Subs., g.	0.1 *N* $AgNO_3$, cc.	Halogen, % Calcd.	Halogen, % Found
1	$C_8H_7O_3NBr_2$	144–145	0.3618	22.26	49.23	49.22
2	$C_{14}H_{11}O_2N_2Br_3$	168–170	.3061	19.26	50.10	50.34
3	$C_9H_9O_3N_3Br_2$	216–217[a]	.2806	15.32	43.60	43.68
4	$(C_{14}H_{10}O_2NBr_2)_2$	238–239[b]	.3423	17.87	41.67	41.76

[a] After heating at 120° to remove acetic acid.

[b] After removal of pyridine of crystallization.

2,5,6-Tribromovanillin.—A mixture of 12 g. of 2,6-dibromovanillin, 4 g. of sodium acetate and 40 cc. of acetic acid was warmed until all was in solution, after which 2.4 cc. of bromine was added and the liquid allowed to stand for a short time. The red color disappeared almost immediately. When water was added a 95% yield of the tribromo compound was precipitated. Crystallization from acetic acid gave fine, colorless needles; m. p. 177–178°. The product was further characterized by the preparation of the derivatives indicated in Table III.

Anal. Subs., 0.3150: 24.25 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_8H_5O_3Br_3$: Br, 61.70. Found: 61.59.

TABLE IIIA

DERIVATIVES OF 2,5,6-TRIBROMOVANILLIN

No.	Compound	Solvent	Crystal form	Yield, %
1	Oxime	*Iso*butyl alcohol	Small, nearly colorless needles	98
2	*p*-Bromophenylhydrazone	Acetic acid	Almost colorless needles	Quant.
3	Semicarbazone[a]	Dilute pyridine	Almost colorless needles	96
4	*bis*-Benzidine[b]	Pyridine	Brown granules	84

[a] *Anal.* Subs., 0.3274: loss in wt., 0.0489. Calcd. for 1 mole of C_5H_5N: 15.05. Found: 14.94.

[b] *Anal.* Subs., 0.3382: loss in wt., 0.0535. Calcd. for 2 moles of C_5H_5N: 14.58. Found: 15.82.

TABLE IIIB

DERIVATIVES OF 2,5,6-TRIBROMOVANILLIN

No.	Formula	M. p., °C.	Subs., g.	0.1 *N* AgNO$_3$, cc.	Halogen, % Calcd.	Halogen, % Found
1	$C_8H_6O_3NBr_3$	192	0.3164	23.45	59.41	59.29
2	$C_{14}H_{10}O_2N_2Br_4$	169–170	.2953	21.20	57.35	57.43
3	$C_9H_8O_3N_3Br_3$	222–223[a]	.2785	18.83	53.81	54.09
4	$(C_{14}H_9O_2NBr_3)_2$	<330	.2847	18.36	51.84	51.59

[a] After heating at 120° to remove pyridine.

Summary and Conclusions

1. Nitration of acetylvanillin as directed by Pschorr and Sumuleanu gives mainly the 2-nitro derivative described by them and a small portion of another nitro compound not hitherto recorded, which probably has the nitro group in Position 6.

2. The list of possible bromine substitution products of vanillin has been completed. Each new one has been characterized by the study of several derivatives.

3. In the reactions which involved the aldehyde radical, the presence of one ortho substituent caused no noticeable hindrance; when both these positions were substituted the yields of products were lower but the effect was less pronounced than expected.

4. The hydroxyl and acetoxyl radicals, respectively, as substituents in a benzene derivative may direct entering groups to different positions. This result may depend, in part, on the chemical character of the entering substituent.

5. In no case was there obtained more than one of the oximes demanded by theory. The one obtained, probably the *anti* form, could not be transmuted by hydrogen chloride, and an attempt to prepare the isomeride from the 6-bromo compound by the Goldschmidt method caused the loss of the methyl radical and the formation of the oxime of the corresponding protocatechuic aldehyde. Thus far the results agree with Brady and Dunn's observations.

6. Further work is in progress in this Laboratory.

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