[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

Reactions of Vanillin and its Derived Compounds. XVI.[1] The Synthesis of Vanillil[2]

BY IRWIN A. PEARL

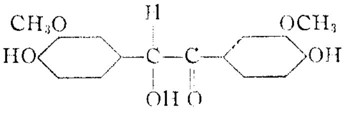
RECEIVED FEBRUARY 7, 1952

Failure to obtain a benzoin condensation with vanillin led to the use of hydrovanilloin as an intermediate for the preparation of vanillil. Hydrovanilloin was prepared in good yield by the electrolytic reduction of vanillin in alkaline solution at a lead cathode. Hydrobenzoins were also prepared from orthovanillin and ethylvanillin in the same manner. Alkaline copper oxidation of hydrovanilloin yielded only vanillin or its oxidation product, dehydrodivanillin. Oxidation of hydrovanilloin with cupric hydroxide in glacial acetic acid yielded the desired vanillil in good yield.

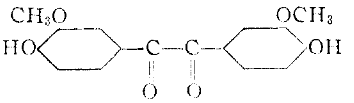
The recent isolation of vanillil from the products of an oxidation of spent sulfite liquor by Johnson and Marshall[3] and the isolation of vanillil in our laboratory from the cupric oxide oxidation of spent sulfite liquor[4] led to an investigation of the synthesis of vanillil for identification purposes and for degradation studies.

Several years ago, in connection with studies on the oxidation of vanillin with mercuric oxide, an experiment was performed on the oxidation of vanillin in a boiling alkaline solution at a mercury anode. A small yield of vanillil was obtained along with vanillic acid. The low yield together with difficulties encountered in the construction of a suitable apparatus for the oxidation in boiling strong sodium hydroxide solution prompted the search for a better synthesis.

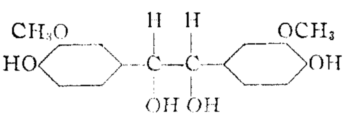
The obvious route for the preparation of vanillil (II) is that starting with vanillin *via* vanilloin (I). However, all attempts to prepare vanilloin by condensation of vanillin in the presence of alkali cyanide failed. Even attempts to prepare vanilloin through the benzyl ether of vanillin did not produce results. Therefore, hydrovanilloin (III) was employed as a starting material for the preparation of vanillil because hydrovanilloin has been produced in the past by electrolytic reduction of vanillin at metallic cathodes.[5] In fact, hydrovanilloin and 4,4'-dihydroxy-3,3'-dimethoxystilbene (IV) were the only previously known members of the bivanillyl series. Law[5] obtained hydrovanilloin in 40% yield by the reduction of vanillin at either polished nickel or platinum cathodes in dilute alkaline solution with a current of one ampere. We have found that electrolysis with a current of 3 amperes with lead electrodes yields 70–80% of pure hydrovanilloin and a little 4,4'-dihydroxy-3,3'-dimethoxystilbene as a by-product. Raising the current to 3.6 amperes resulted in the same yield of hydrovanilloin but the by-product in this case was isohydrovanilloin. Similarly, orthovanillin and ethylvanillin were reduced in alkaline solution at a lead cathode to yield 2,2'-dihydroxy-3,3'-dimethoxyhydrobenzoin and 3,3'-diethoxy-4,4'-dihydroxyhydrobenzoin, respectively.



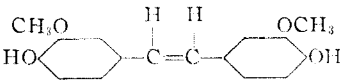
I



II



III



IV

For the oxidation of hydrovanilloin to vanillil, reactions were tried which were known to oxidize benzoins to benzils, but quantities were adjusted to take care of the difference in oxidation level of the benzoins and hydrobenzoins. Fehling solution gave a quantitative yield of vanillin. Copper hydrate in alkaline solution gave a high yield of vanillin and a small amount of the desired vanillil. Oxidation of hydrovanilloin with the cupric sulfate–pyridine reagent of Clarke and Dreger[6] yielded only dehydrodivanillin. Thus it is evident that, for the most part, cupric oxide under alkaline conditions oxidizes hydrovanilloin to the benzoin or isomeric "enediol," 3,3'-dimethoxy-α,α',4,4'-tetrahydroxystilbene, which then splits in accordance with known mechanisms to two molecules of the parent aldehyde, vanillin. It is interesting to note that the cupric sulfate–pyridine reagent further oxidizes the first formed vanillin to produce dehydrodivanillin, instead of oxidizing the "enediol" to the vanillil stage. To prove that vanillin was first formed in the reaction mixture, pure vanillin was treated in the same manner with cupric sulfate and pyridine. Only dehydrodivanillin was isolated from the reaction mixture.

Because of the apparent instability of vanilloin or its tautomeric "enediol" in alkaline solution in the presence of oxidizing agents, hydrovanilloin was oxidized with two moles of cupric hydroxide in acetic acid solution. Under these conditions vanillil was obtained in 60–70% yield. The product was identical with that isolated from the cupric

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[1] For paper XV of this series, see THIS JOURNAL, **74**, 3188 (1952).

[2] This paper represents a portion of the results obtained in the research program sponsored by the Sulphite Pulp Manufacturers' Research League and conducted for the League by The Institute of Paper Chemistry. Acknowledgment is made by the Institute for permission on the part of the League to publish these results.

[3] A. M. Johnson and H. B. Marshall, paper presented before the Division of Cellulose Chemistry at the 118th Meeting of the American Chemical Society, Chicago, Illinois, Sept. 3–8, 1950.

[4] I. A. Pearl and E. E. Dickey, THIS JOURNAL, **74**, 614 (1952).

[5] H. D. Law, *J. Chem. Soc.*, **89**, 1512 (1906).

[6] H. T. Clarke and E. E. Dreger, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 87.

oxide oxidation of fermented spent sulfite liquor.[4] Isohydrovanilloin gave substantially identical results.

Ultraviolet absorption spectra of the hydrobenzoins prepared in this study were determined in 95% ethanol with a Beckman spectrophotometer at minimum slit width and are shown in Fig. 1.

Experimental

All melting points are uncorrected.

Electrolytic Reduction of Vanillin.—A solution of 100 g. of vanillin and 100 g. of sodium hydroxide in 1500 cc. of water at 60° was placed in an electrolysis apparatus comprising a 3-liter beaker and a 75 × 180-mm. porous cup. Forty-mm. and 140-mm. lead cylinders served as electrodes. Approximately 400 cc. of the alkaline vanillin solution was placed in the porous cup, and 1100 cc. was placed in the beaker. The catholyte thus contained 73 g. of vanillin. A current of 3 amperes was maintained across the cell for 5 hours, at which time the temperature had dropped to 25°. The catholyte was filtered and acidified with sulfur dioxide. White granular crystals precipitated. After a short while the solution became deep yellow in color. At this point the crystalline precipitate was filtered and washed with water to yield 51 g. (70%) of hydrovanilloin melting at 222–223°. Recrystallization from glacial acetic acid raised the melting point to 225–226°. Repeated recrystallization from ethanol raised the melting point to 233–234°. Law[5] recorded a melting point of 222°.

Anal. Calcd. for $C_{16}H_{18}O_6$: C, 62.73; H, 5.92. Found: C, 62.64; H, 6.04.

The tetraacetate was prepared with acetic anhydride in pyridine and was obtained as white crystals from ethanol melting at 195–196°.

Anal. Calcd. for $C_{24}H_{26}O_{10}$: C, 60.75; H, 5.52; CH_3O, 13.1. Found: C, 60.60; H, 5.59; CH_3O, 13.1.

The deep yellow filtrate was extracted with ether; the ether was dried and distilled to yield 1.8 g. of solid which, upon recrystallization from dilute ethanol, yielded light tan needles of 4,4′-dihydroxy-3,3′-dimethoxystilbene melting at 210–211°. This product was identical with a sample prepared from trithiovanillin by distillation in the presence of copper as reported by Richtzenhain and von Hofe.[7]

A similar electrolysis, employing a catholyte comprising 80 g. of sodium hydroxide and 110 g. of vanillin in 1600 cc. of water and an anolyte of 20 g. of sodium hydroxide in 400 cc. of water and maintaining a current of 3.6 amperes for 8.5 hours yielded 86 g. (78%) of hydrovanilloin as the main product after sulfur dioxide acidification. Upon standing for several days, the filtrate deposited 10 g. of silky needles of isohydrovanilloin which, upon recrystallization from benzene–ethanol, melted at 119–120°.

Anal. Calcd. for $C_{16}H_{18}O_6$: C, 62.73; H, 5.92. Found: C, 62.68; H, 6.03.

2,2′-Dihydroxy-3,3′-dimethoxyhydrobenzoin.—This compound was made in an identical manner by reduction of orthovanillin at 3.0 amperes and was obtained as a white powder which, upon recrystallization from ethanol, melted at 175–176°. The yield was 75%.

Anal. Calcd. for $C_{16}H_{18}O_6$: C, 62.73; H, 5.92. Found: C, 62.61; H, 6.02.

Acetylation by means of pyridine and acetic anhydride yielded the diacetate which melted at 176–177° when recrystallized from dilute ethanol.

Anal. Calcd. for $C_{20}H_{22}O_8$: C, 61.53; H, 5.68; CH_3O, 15.9. Found: C, 61.56; H, 5.72; CH_3O, 15.9.

3,3′-Diethoxy-4,4′-dihydroxyhydrobenzoin.—Ethylvanillin was reduced at a lead cathode in the same manner at 3.0 amperes to yield 93% 3,3′-diethoxy-4,4′-dihydroxyhydrobenzoin. The crude product melted at 193–198° and, when recrystallized from propanol, the compound was obtained as a white crystalline powder melting at 219–220°.

Anal. Calcd. for $C_{18}H_{22}O_6$: C, 64.65; H, 6.63. Found: C, 64.56; H, 6.69.

Oxidation of Hydrovanilloin with Cupric Hydroxide and Alkali.—A mixture of 15.3 g. (0.05 mole) of hydrovanilloin, 9.8 g. (0.10 mole) of cupric hydroxide, 4.0 g. (0.10 mole) of sodium hydroxide and 150 cc. of water was boiled under reflux with occasional stirring for 90 minutes and allowed to cool. The red cuprous oxide was filtered and washed with water. The combined filtrate and washings were acidified with sulfur dioxide, and the precipitate was filtered and recrystallized from glacial acetic acid to yield 2.6 g. of vanillil as pale yellow needles melting at 230–231° and not lowering a mixed melting point with authentic vanillil. The sulfur dioxide-saturated filtrate was further acidified with sulfuric acid and boiled a few minutes to remove dissolved sulfur dioxide. An oil separated which on cooling solidified to vanillin crystals melting at 80°. The yield was 12.6 g. (83%).

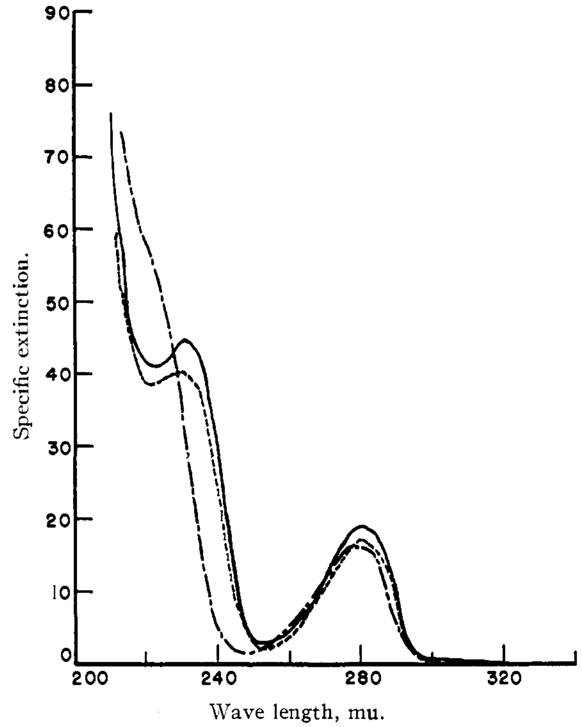

Fig. 1.—Ultraviolet absorption curves for hydrobenzoins: hydrovanilloin and isohydrovanilloin, —; 3,3′-diethoxy-4,4′-dihydroxyhydrobenzoin, ---; 2,2′-dihydroxy-3,3′-dimethoxyhydrobenzoin, -·-·-.

Oxidation of Hydrovanilloin with Cupric Sulfate and Pyridine.—A mixture of 15.3 g. (0.05 mole) of hydrovanilloin, 50 g. (0.20 mole) of hydrated cupric sulfate, 50 g. of pyridine, and 20 g. of water was heated to boiling under a reflux for 2 hours and allowed to cool. The cooled solution was poured into a large excess of water and acidified with hydrochloric acid. The product was redissolved in sodium hydroxide solution and acidified with sulfur dioxide. The resulting almost clear solution was filtered and the filtrate was acidified with dilute sulfuric acid. The precipitate was recrystallized from glacial acetic acid to yield fine needles of dehydrodivanillin melting at 315–317° and not depressing a mixed melting point with authentic dehydrodivanillin[8] which had been recrystallized from glacial acetic acid.

Vanillil.—A mixture of 30.6 g. (0.10 mole) of hydrovanilloin, 39.0 g. (0.20 mole) of cupric hydroxide and 600 cc. of glacial acetic acid was boiled under reflux for one hour. The blue color of the hot solution turned to green after a few minutes of boiling and, after cooling, a bluish precipitate separated. The entire mixture was filtered, and the precipitate was washed thoroughly with a large volume of water. The bluish cuprous acetate dissolved, leaving a mixture of red cuprous oxide and light yellow crystals. The precipitate was leached with dilute sodium hydroxide solution and the alkaline solution acidified. The precipitate thus obtained was recrystallized from glacial acetic acid to give 1.7 g. of pale yellow crystals of vanillil melting at

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[7] H. Richtzenhain and C. von Hofe, *Ber.*, **72**, 1892 (1939).

[8] K. Elbs and H. Lerch, *J. prakt. Chem.*, **93**, 1 (1916).

233–234°. The original filtrate upon dilution with the wash water gave a crystalline precipitate. This was washed with cold glacial acetic acid and then recrystallized from glacial acetic acid to yield 18.7 g. of very light yellow needles of vanillil melting at 233–234°. The yield was 68%. The ultraviolet absorption spectrum in ethanol was identical with that of the vanillil isolated from the cupric oxide oxidation of fermented spent sulfite liquor,[4] and in alkaline ethanol it was identical with that found earlier[4] and that reported by Johnson and Marshall.[3]

Acknowledgment.—The author wishes to thank Mr. Donald McDonnell for the analyses and spectra reported in this paper.

APPLETON, WISCONSIN

[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

Reactions of Vanillin and its Derived Compounds. XVII.[1] A Synthesis of Syringaldehyde from Vanillin[2]

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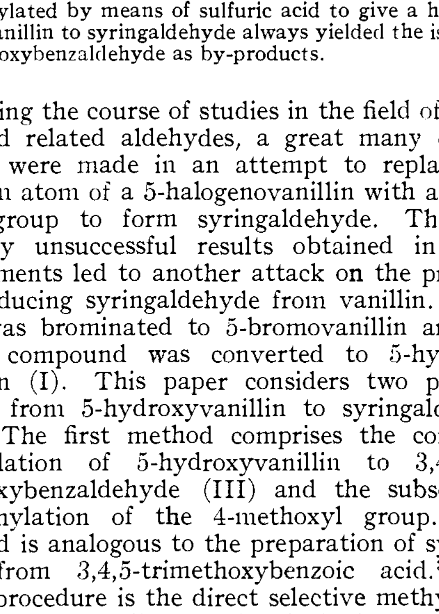
Vanillin was brominated to 5-bromovanillin which in turn was hydrolyzed to 5-hydroxyvanillin. 5-Hydroxyvanillin was completely methylated with dimethyl sulfate and alkali and the resulting 3,4,5-trimethoxybenzaldehyde was partially demethylated by means of sulfuric acid to give a high yield of syringaldehyde. Attempts to selectively methylate 5-hydroxyvanillin to syringaldehyde always yielded the isomeric 5-hydroxyveratraldehyde and the completely methylated 3,4,5-trimethoxybenzaldehyde as by-products.

During the course of studies in the field of vanillin and related aldehydes, a great many experiments were made in an attempt to replace the halogen atom of a 5-halogenovanillin with a methoxyl group to form syringaldehyde. The universally unsuccessful results obtained in these experiments led to another attack on the problem of producing syringaldehyde from vanillin. Vanillin was brominated to 5-bromovanillin and the latter compound was converted to 5-hydroxyvanillin (I). This paper considers two possible routes from 5-hydroxyvanillin to syringaldehyde (II). The first method comprises the complete methylation of 5-hydroxyvanillin to 3,4,5-trimethoxybenzaldehyde (III) and the subsequent demethylation of the 4-methoxyl group. This method is analogous to the preparation of syringic acid from 3,4,5-trimethoxybenzoic acid.[3] The other procedure is the direct selective methylation of 5-hydroxyvanillin to syringaldehyde.



5-Hydroxyvanillin was methylated in high yield to 3,4,5-trimethoxybenzaldehyde by means of dimethyl sulfate and alkali. The 3,4,5-trimethoxybenzaldehyde was treated with concentrated sulfuric acid at room temperature to give an almost quantitative yield of the desired syringaldehyde. Thus syringaldehyde becomes a derivative of vanillin and obtainable from the latter in four steps, all in good yield.

The selective methylation of 5-hydroxyvanillin was not so straight forward. Methylation with one mole of potassium hydroxide and one mole of dimethyl sulfate gave a mixture of the desired syringaldehyde with 3,4,5-trimethoxybenzaldehyde, 5-hydroxyveratraldehyde (3,4-dimethoxy-5-hydroxybenzaldehyde) and unchanged 5-hydroxyvanillin. These compounds were easily separated by adsorption chromatography. Methylation with one mole of methyl iodide and two moles of alkali in accordance with the procedure employed by Bertram[4] for the preparation of vanillin from protocatechualdehyde yielded the same products, but the yield of the desired syringaldehyde was much less. Several other experiments with a variety of methylating conditions indicated that chances for a selective methylation of 5-hydroxyvanillin to syringaldehyde alone are not very good.

For the preparation of 5-hydroxyvanillin in this study the process of Bradley, Robinson and Schwarzenbach,[5] who heated 5-bromovanillin with a solution of sodium hydroxide in the presence of copper bronze,[6] was employed. Attempted hydrolysis of the 5-bromovanillin without the bronze catalyst resulted in a small yield of 5-hydroxyvanillin and the recovery of the unchanged bromovanillin. Substitution of the bronze by an active copper catalyst gave interesting side reactions. In addition to the desired 5-hydroxyvanillin, guaiacol, vanillin, vanillic acid and 5-bromovanillic acid were obtained.

Experimental

All melting points are uncorrected.

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(1) For paper XVI of this series, see THIS JOURNAL, **74**, 4260 (1952).

(2) This paper represents a portion of the results obtained in the reearch program sponsored by the Sulphite Pulp Manufacturers' Research League and conducted for the League by The Institute of Paper Chemistry. Acknowledgment is made by the Institute for permission on the part of the League to publish these results.

(3) M. T. Bogert and B. B. Coyne, THIS JOURNAL, **51**, 569 (1929).

(4) J. Bertram, German Patent 63,007 (Aug. 19, 1890); *Ber.*, **25**, R823 (1892).

(5) W. Bradley, R. Robinson and G. Schwarzenbach, *J. Chem. Soc.*, 793 (1930).

(6) The bronze powder employed was a bronze pigment, Copper Brilliant 104, manufactured by the Crescent Bronze Powder Co., Chicago, Ill.