

THE REACTION OF 5-BROMOVANILLIN AND SODIUM METHOXIDE

By R. A. McIVOR AND J. M. PEPPER

Can. J. Chem. 31, 298-302 (1953)

Many methods of synthesis of syringaldehyde have been described, the more important of which have been given recently by Pearl (3), while a laboratory procedure has appeared in *Organic Synthesis* (1).

This report concerns preliminary studies of its preparation from vanillin by a two-stage introduction of a methoxyl group. It has recently been reported that universally unsuccessful results were obtained in similar experiments by other workers (4), although they do record a different method for the conversion of vanillin to syringaldehyde. Such a synthesis is of interest because of the ready availability of vanillin as an oxidation product of gymnosperm lignin residues. Of even greater value would be the possibility of thereby converting a mixture of vanillin and syringaldehyde, obtainable from a similar oxidation of hardwood lignin, into the latter chemical.

The reaction studied was the bromination of vanillin to yield 5-bromovanillin which was subsequently treated with methanolic sodium methoxide in the presence of a copper catalyst in an attempt to replace the halogen by the methoxyl grouping. Initial experiments in which the 5-bromovanillin, sodium methoxide, and anhydrous methanol were refluxed, either in the presence or absence of a copper catalyst, resulted only in the recovery of unchanged starting materials. The attempted replacement of the bromine by the fusion of 5-bromovanillin or its triacetate with anhydrous sodium methylate resulted in a very rapid reaction accompanied by a flash and dense white smoke, but a considerable amount of 5-bromovanillin only was recovered from the residue. The nature of this reaction was not further investigated, although qualitative tests showed that ionic bromide and considerable free carbon were formed.

TABLE I

REACTION OF 5-BROMOVANILLIN AND SODIUM METHOXIDE AT HIGH TEMPERATURES^a

Run number	Copper turnings, gm.	Average temp., °C.	Maximum temp., °C.	Time, hr.	Remarks
2	3	163	183	1.8	<i>b, c</i>
5	7	179	205	2.0	<i>c, d</i> (3.3 gm.)
6	7	173	186	3.0	<i>c, d</i> (2.9 gm.)
7	7	150	175	2.0	<i>c, b</i> (0.7 gm.)
8	7	169	189	1.0	<i>e</i>
9	5	158	178	1.5	<i>e</i>
10	5	162	172	4	<i>c, f</i> (5.0 gm.)
11	5	176	180	11.5	<i>f</i> (2.5 gm.)
12	5	186	197	9.3	<i>f</i> (1.0 gm.)

^aFor each run, 5-bromovanillin (15 gm.), methanol (250 ml.), and sodium methoxide (10.0 gm.) were used.

^bCrude 5-bromovanillyl alcohol.

^cFiltrate gave positive test for bromide ion.

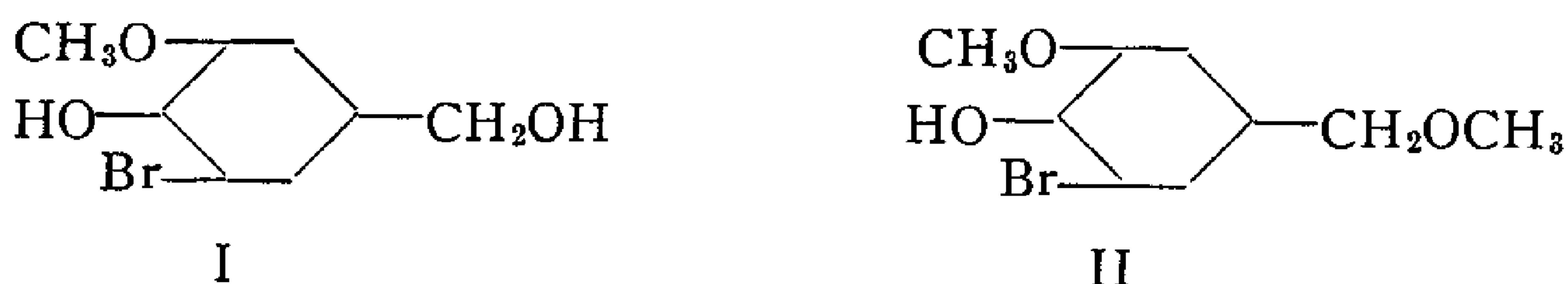
^dCrude 5-bromovanillyl methyl ether.

^e5-Bromovanillin all recovered.

^fCrude syringaldehyde.

In order to attempt the replacement at much higher temperatures, a series of runs was made in which the 5-bromovanillin, mixed with anhydrous methanol, sodium methoxide, and copper turnings, was heated in a rocking autoclave. The conditions and results of these experiments are given in Table I. It is believed that the somewhat erratic results obtained under essentially similar conditions were due to the irreproducibility of the copper catalyst. In a forthcoming publication further evidence to support this belief will be presented.

The syringaldehyde was identified by the recrystallization of the crude product from water to yield needles with a melting point of 113°C ., undepressed by admixture with an authentic sample (2). The 2,4-dinitrophenylhydrazone melted at $234\text{--}235^{\circ}\text{C}$., reported m.p. $235.5\text{--}236.5$ (5). Both the previously unreported compounds, 5-bromovanillyl alcohol (I) (m.p. $129\text{--}130^{\circ}\text{C}$.) and 5-bromovanillyl methyl ether (II) (m.p. 66°C .), were characterized by an examination of their infrared spectra and the comparison of their



ultraviolet absorption spectra and their carbon, hydrogen, and methoxyl analyses with those of the synthetic products. Mixed melting point determinations with these authentic samples showed no depressions. No attempt is being made at this time to explain the mechanism of the formation of these derivatives. Fig. 1 includes, for purposes of comparison, the ultraviolet

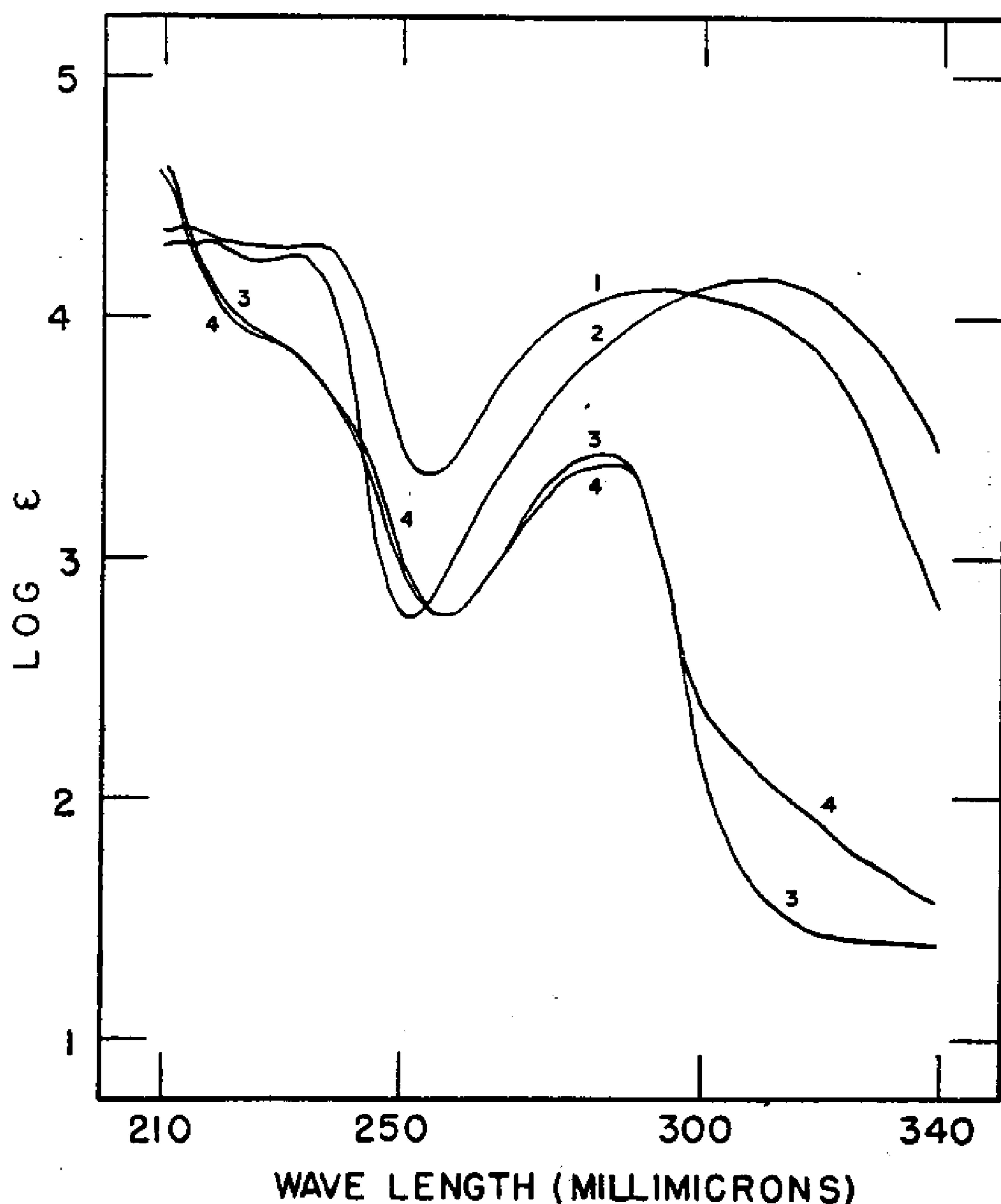


FIG. 1. Ultraviolet absorption spectra (95% ethanol).
 1. 5-Bromovanillin. 3. 5-Bromovanillyl alcohol.
 2. Syringaldehyde. 4. 5-Bromovanillyl methyl ether.

absorption spectra of 5-bromovanillin, syringaldehyde, 5-bromovanillyl alcohol, and 5-bromovanillyl methyl ether.

Although the preparation of syringaldehyde from 5-bromovanillin appeared quite promising, similar experiments using 5-iodovanillin gave excellent yields. The results of this later work will be presented in a separate article.

EXPERIMENTAL

All ultraviolet absorption spectra were observed on a Beckmann Model DU spectrophotometer in purified 95% ethanol solution. The infrared spectra were determined using a Perkin-Elmer single beam Model 12B spectrophotometer.

5-Bromovanillin

Vanillin (150 gm.) and sodium acetate (50 gm.) were dissolved in glacial acetic acid (350 ml.) and a solution of bromine (180 gm.) in acetic acid (300 ml.) was added slowly with shaking. On completion of the addition, sodium hydrosulphite (15 gm.) dissolved in water (75 ml.) was added, and after most of the excess bromine was reduced the mixture was poured into water (2 liters) containing further sodium hydrosulphite (15 gm.). The 5-bromovanillin readily precipitated; yield 221.8 gm. (97.5%). After recrystallization from ethanol the product melted at 164° C., reported by several workers, 164° C.

5-Bromovanillin-2,4-dinitrophenylhydrazone

The previously unreported 2,4-dinitrophenylhydrazone of 5-bromovanillin was prepared in the usual way; melting point, 295.5–296° C., with decomposition. Calc. for $C_{14}H_{11}N_4O_6Br$: C, 40.89; H, 2.70. Found: C, 40.68; H, 3.64.

5-Bromovanillin Triacetate

5-Bromovanillin (25 gm.) was suspended in acetic anhydride (80 ml.) to which a few drops of concentrated sulphuric acid were added. Solution took place immediately and, on cooling, a precipitate separated. This product was recrystallized from dilute ethanol and dilute acetic acid to give white plates melting at 109° C. Calc. for $C_{14}H_{15}O_7Br$: OCH_3 , 8.3; Ac, 34.4. Found: OCH_3 , 8.2; Ac, 34.4.

Interaction of 5-Bromovanillin and Sodium Methoxide

The experiments outlined in Table I were carried out in a stainless steel liner, capacity 1080 ml., of an Aminco high pressure hydrogenator, Model No. 406-01 DA. This rocking apparatus served as a high temperature autoclave. The reaction mixture, after cooling and separation of the copper catalyst, was diluted to twice its volume with water and acidified with sulphuric acid. Tarry products often separated at this point, but both the tar and the acidified mixture were exhaustively extracted with ether. This extract, after drying, was concentrated to give an alkali-soluble residue from which the reaction products reported in Table I were isolated. The major part of the syringaldehyde was obtained by re-extraction of the aqueous layers with ethyl acetate.

Identification of 5-Bromovanillyl Alcohol

The crude reaction product was purified to one melting at 129–130° C. by

two recrystallizations from methanol–water and finally by vacuum distillation. The infrared spectrum was determined in the carbonyl and hydroxyl regions in chloroform solution with a calcium fluoride prism. It showed two sharp bands in the OH stretching region at 3601 cm.^{-1} and 3525 cm.^{-1} with molar extinction coefficients of 63 and 138, respectively, the latter believed due to a phenolic hydroxyl group. The ultraviolet spectrum was identical with that of synthetic 5-bromovanillyl alcohol which is given in Fig. 1. A mixed melting point with an authentic specimen, m.p. 132° C. , prepared as given below, was undepressed, m.p. 131° C. Calc. for $\text{C}_8\text{H}_9\text{O}_3\text{Br}$: mol. wt. 233.1; OCH_3 , 13.30; C, 41.22; H, 3.89. Found: mol. wt. (Rast) 235; OCH_3 , 12.94; C, 40.71; H, 3.70.

Identification of 5-Bromovanillyl Methyl Ether

The crude reaction product was purified to one melting at 66° C. by two vacuum sublimations. The infrared spectrum was determined in the 3800 cm.^{-1} to 650 cm.^{-1} region in carbon disulphide solution with a sodium chloride prism. It showed only one peak in the hydroxyl region at 3500 cm.^{-1} with a molar extinction coefficient of 94, doubtless due to the phenolic hydroxyl group. The ultraviolet spectrum was identical with that of synthetic 5-bromovanillyl methyl ether which is given in Fig. 1. A mixed melting point with an authentic specimen, m.p. $64\text{--}67^\circ\text{ C.}$, prepared as given below was undepressed. Calc. for $\text{C}_9\text{H}_{11}\text{O}_3\text{Br}$: C, 43.74; H, 4.49. Found: C, 43.83; H, 4.57.

Syntheses of Reference Compounds

5-Bromovanillyl Alcohol

5-Bromovanillin (1.884 gm.) was added to an excess of alkali in water (40 ml.). The sodium salt, which formed immediately, did not dissolve. A solution of sodium borohydride (170 mgm.) in water was added. The faint yellow color of the solution gradually disappeared and the precipitated salt dissolved in 10 min. The solution, after standing at room temperature over night, was acidified with concentrated hydrochloric acid. 5-Bromovanillyl alcohol separated as micro needles. Yield, 1.67 gm. (88%), m.p. 132° C. More of the product could be obtained by extraction of the mother liquors.

5-Bromovanillyl Methyl Ether

5-Bromovanillyl alcohol (133 mgm.) was dissolved in methanol (5 ml.) and concentrated sulphuric acid (1 ml.) added. After the solution had been allowed to stand at room temperature for 36 hr. it was refluxed for five minutes, made alkaline with sodium hydroxide, and extracted with chloroform. The residual aqueous solution was acidified with hydrochloric acid and again extracted with chloroform. This extract was dried and the excess solvent removed to yield a gum (203 mgm.) which readily crystallized in long needles. Vacuum sublimation gave white crystals (110 mgm., 88%), m.p. $64\text{--}67^\circ\text{ C.}$ Calc. for $\text{C}_9\text{H}_{11}\text{O}_3\text{Br}$: OCH_3 , 25.12. Found: OCH_3 , 24.7.

Absorption Spectra Data

The following ultraviolet and infrared absorption data were recorded,

TABLE II

ULTRAVIOLET ABSORPTION DATA FOR 5-BROMOVANILLIN AND DERIVED COMPOUNDS

Compound	Absorption maxima ^a , m μ	Absorption minima ^a , m μ
5-Bromovanillin	213.5 (4.36) 234 (4.29) 291 (4.10)	226 (4.28) 255 (3.34)
Syringaldehyde	215 (4.31) 231 (4.25) 308.5 (4.16)	225 (4.23) 251 (2.75)
5-Bromovanillyl alcohol	221 (3.95) 286 (3.42)	257 (2.76)
5-Bromovanillyl methyl ether	221 (3.93) 286 (3.39)	257 (2.75)

^aLog molar extinction coefficients given in brackets.

TABLE III

INFRARED ABSORPTION DATA FOR 5-BROMOVANILLYL METHYL ETHER^a
ABSORPTION BANDS^b, CM.⁻¹

3500 (94)	1237 (139)	914 (34)
2911 (81)	1186 (248)	838 (105)
2824 (70)	1140 (161)	827 (158)
1345 (115)	1100 (185)	788 (41)
1275 (378)	1052 (360)	726 (30)
1250 (112)	961 (39)	

^aDetermination in carbon disulphide with a sodium chloride prism.^bMolar extinction coefficients given in brackets.

1. ALLEN, C. F. H. and LEUBNER, G. W. *Org. Syntheses*, 31: 92. 1951.
2. HAWKINS, W. L., WRIGHT, G. F., and HIBBERT, H. *J. Am. Chem. Soc.* 59: 2447. 1937.
3. PEARL, I. A. *J. Am. Chem. Soc.* 70: 1746. 1948.
4. PEARL, I. A. and BEYER, D. L. *J. Am. Chem. Soc.* 74: 4262. 1952.
5. PYLE, J. J., BRICKMAN, L., and HIBBERT, H. *J. Am. Chem. Soc.* 61: 2198. 1939.