

STUDIES IN THE POLYOXYPHENOL SERIES

VI. THE OXIDATION OF PYROGALLOL AND VANILLIN BY ALKALINE HYPOIODITE AND HYPOCHLORITE¹

BY G. DENIS THORN² AND C. B. PURVES

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ABSTRACT

Approximately 0.003 *M* solutions of pyrogallol and of vanillin in boric acid-sodium hydroxide buffers were used at 25°C. to reduce hypiodite and hypochlorite solutions made from sixfold molar amounts of the halogens. In all four cases the reduction reached a maximum in a narrow range near pH 9, and with hypiodite the production of iodoform was restricted to this range. Slower secondary reductions were superimposed on very fast primary reactions. When oxidized with an equimolecular amount of halogen near pH 8.5, vanillin gave a 90% yield of 5-iodovanillin and 65% of the 5-chloro derivative. These yields decreased with increasing alkalinity as the halogenations became slower. A new, simple preparation of trichloropyrogallol in 72% yield consisted of carrying out the chlorination with 3 moles of hypochlorite at pH 12. An equilibrium between pyrogallol-hypiodite and 3-hydroxy-1,2-benzoquinone-iodide appeared to exist at the same pH.

INTRODUCTION

Numerous researches have shown that a proper control of the hydrogen ion concentration and similar variables is of great importance in the removal of residual lignin from wood pulps by bleaching with alkaline hypochlorite. The results are difficult to interpret in a chemical sense because little is known about the structure of lignin beyond the fact that it is in great part based upon phenolic units related to vanillin and syringaldehyde. Soper and Smith (26), however, showed that simple monohydric phenols reacted with hypochlorous acid at a rate directly proportional to the concentration of the hydroxyl ion in the region of pH 7, but that the rate became inversely proportional near pH 12. Hypochlorous acid, unlike free chlorine, had no action on phenolic ethers, and the oxidation of phenols by hypiodite was relatively slow. The last observation had its counterpart in the lignin field, because Hixon and his collaborators (5, 29) found that the consumption of alkaline hypiodite by various lignins ceased at a rather low limit, whereas the consumption of hypochlorite proceeded almost indefinitely. The present research had the object of gaining information about the conditions necessary for the "limited" action of excess hypiodite on simple phenols, and of discovering whether the action of hypochlorite could also be limited. Pyrogallol and vanillin were chosen for the study because the results might eventually prove relevant to lignin.

REACTIONS WITH ALKALINE HYPOIODITE

The initial experiments were carried out with dilute aqueous solutions of pyrogallol containing a sixfold molar amount of iodine, and buffered with

boric acid – sodium hydroxide (Table I). Since hypiodite rapidly decomposed to iodate and iodide in solutions containing excess alkali (23), the estimation of unused hypiodite at any time had to include the by-product iodate. This

TABLE I
REDUCTION OF HYPOIODITE BY PYROGALLOL DURING 24 HR. AT 25°C.^a

Run	NaOH <i>M</i>	pH	Moles HIO reduced ^b	Run	NaOH <i>M</i>	pH	Moles HIO reduced ^b
Boric acid, 0.2 <i>M</i> ; I ₂ , 0.0204 <i>M</i>				Unbuffered; I ₂ , 0.21 <i>M</i>			
1	0.04	8.0 ^c	4.8	19	0.54	12.5	2.8
2	0.10	8.6	4.9	20	0.61	13	2.7
3	0.16	9.4	5.3	21	0.63	> 13	2.65
4	0.21	9.7	4.1	Unbuffered; I ₂ , 0.0205 <i>M</i>			
5	0.26	12.0	1.25	22	0.05	11.7	2.4
6	0.31	12.5	1.7	Boric acid, 0.2 <i>M</i> ; I ₂ , 0.0205 <i>M</i>			
7	0.36	> 13	1.7	23	0.26	11.9	0.71
8	0.42	> 13	1.7	24 ^d	0.26	11.9	0.74
9	0.47	> 13	2.5	25 ^e	0.26	11.9	0.72

^aAll concentrations in moles per liter, the molar ratio of iodine to pyrogallol being 6 : 1.

^bPer mole of pyrogallol.

^cFinal pH was 6.7 after 17.5 hr.

^dMolar ratio of iodine to pyrogallol, 3 : 1.

^eMolar ratio of iodine to pyrogallol, 2 : 1.

objective was attained by titrating the iodine liberated when aliquots were strongly acidified, and control experiments showed that the iodine consumed after the acidification was probably not more than 0.15 mole per mole of pyrogallol.

Columns 4 and 8 of Table I record the molar amounts of iodine (or hypiodite) reduced by 1 mole of pyrogallol after 24 hr., when the reaction had certainly ceased. These amounts passed through a maximum of 5.3 moles near pH 9.4 (run 3), and through a minimum of 1.25 moles near pH 12 (runs 5 to 9). Omission of the borate buffer and a 10-fold increase in the concentration both of iodine and pyrogallol gave solutions whose pH decreased seriously during the reaction unless the molarity of sodium hydroxide was at least 0.54 (run 19), but a greater concentration of alkali had little effect (runs 20, 21). Although the minimum of 1.25 moles near pH 12 was not maintained in the absence of the buffer (run 22), buffered solutions retained the minimum even when the molar ratio of iodine to pyrogallol was reduced from 6 : 1 to 3 : 1 and 2 : 1 (runs 23 to 25). The titrations in these particular runs could not be closely reproduced, and consumptions of iodine as high as 0.87 moles were observed at intermediate times.

The initial portions of the rate-plots for runs 1 to 6, and also for runs 9 and 25, (Fig. 1) clearly showed that the first stage in the reaction was always very

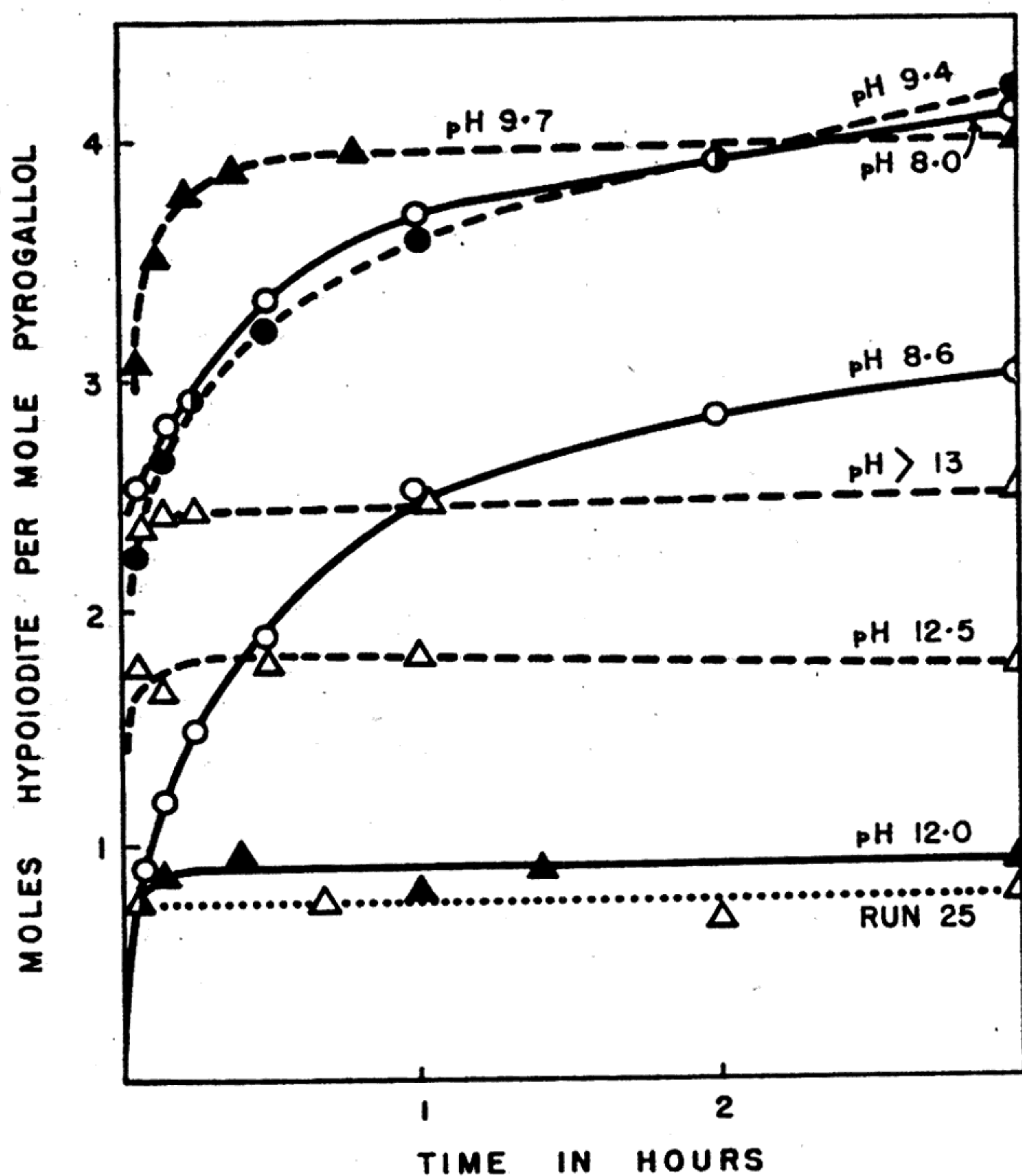
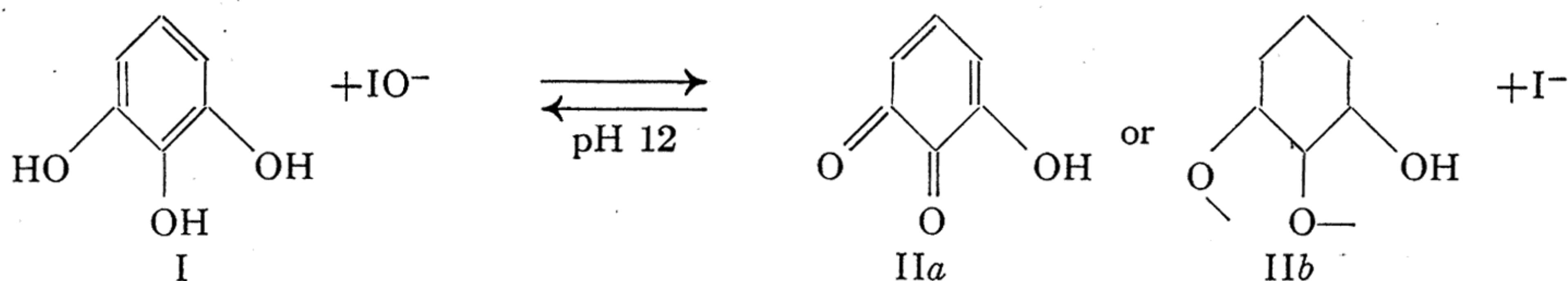


FIG. 1. Initial rate of reaction of 0.0033 *M* pyrogallol with 0.02 *M* iodine at 25°C. Moles of iodine reduced per mole of pyrogallol at the pH values shown. Run 25 with 0.01 *M* pyrogallol.

rapid, and that the ultimate consumption of iodine by the pyrogallol (Table I) depended on the progress of secondary reactions. These secondary reactions were most extensive at pH 9.4 and decreased to zero, both in speed and in amount, near pH 12. The minimum at the latter pH was not caused by the prior conversion of all excess hypoiodite to iodate, because the consumption was about 2.5 times greater in stronger alkali (pH > 13) where competition with the conversion to iodate would be still more serious (23). The first four oxidations (Table I) resulted in pale orange solutions, of which the first and fourth deposited only traces of iodoform, whereas the second and third yielded 0.14 and 0.16 moles respectively, per mole of pyrogallol. Iodoform was therefore produced only in the range pH 8.6 to 9.4, when the secondary reaction was unusually extensive and prolonged.

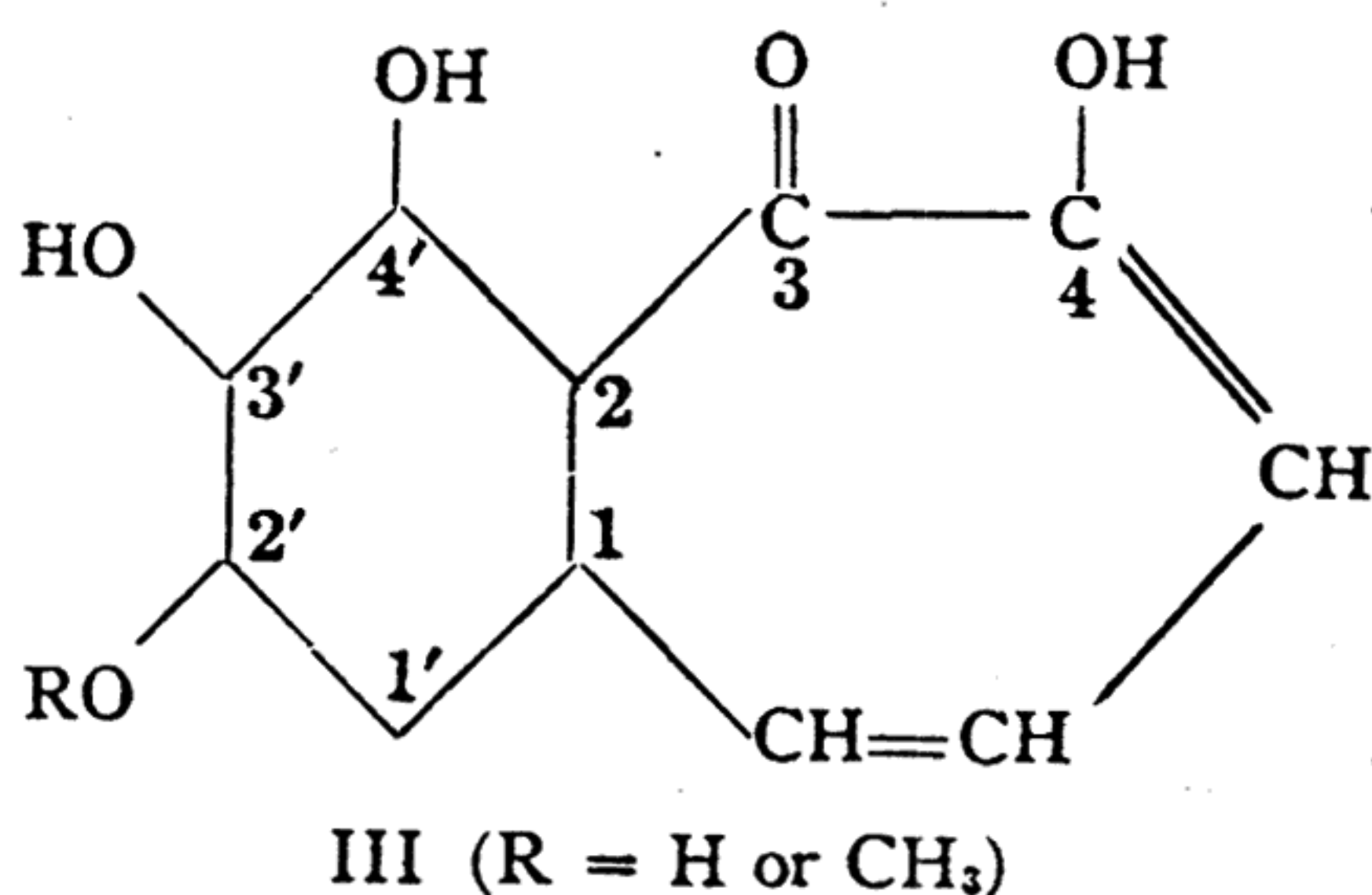
Since about one mole of iodine was reduced by pyrogallol (Structure I) at pH 12, the initial product could not be of a complicated nature, and the dark red color of the solution indicated the presence of a quinonoid rather than an aromatic structure. The most probable assumption (25, 33) for the initial product was the very labile 3-hydroxy-1,2-benzoquinone, (IIa), or the corresponding radical (IIb), (10) or other tautomer. Subsequent oxidations were carried out with equimolar amounts of iodine and pyrogallol in a borate

buffer at pH 12, and, as the solutions were reproducible and stable for hours, they were designated "oxidized pyrogallol solutions." In accord with the above assumption, the red color of the "oxidized pyrogallol solution" lightened



considerably when zinc dust was added as a reducing agent, and subsequent acetylation of the alkaline solution with acetic anhydride (3) recovered at least 52% of the pyrogallol as the crystalline triacetate. Sodium hydrosulphite also discharged the color of the solution to a light yellow, but pyrogallol triacetate could not be recovered, perhaps because sulphonation occurred (11). Although the addition of sodium thiosulphate failed to reduce the color of the solution noticeably, and presumably failed to reduce the supposed quinone, the subsequent acetylation gave an 89% yield of pyrogallol triacetate. The "oxidized pyrogallol solution" was then acetylated without prior reduction, and a control acetylation was made with a solution from which the iodine had been omitted. Pyrogallol triacetate was isolated in yields of 89% and 87%, respectively, from the two experiments. These observations suggested that the "oxidized pyrogallol solution" contained pyrogallol and hypoiodite in equilibrium with the hydroxyquinone and iodide, and that acetylation of the pyrogallol drove the equilibrium far to the left with the regeneration of hypoiodite. Aliquots of the solution, when acidified and titrated with standard sodium thiosulphate immediately before and after the acetylation, were found to contain 41% and 92%, respectively, of the original hypoiodite. An application of the law of mass action showed that the former figure corresponded to consumptions of 0.83 and 0.97 moles of iodine per mole of pyrogallol when the iodine was in twofold and sixfold molar amounts. The values found were of the same order (Fig. 1, run 25 and plot pH 12).

An attempt was then made to isolate the supposed 3-hydroxy-1,2-benzoquinone by acidifying the "oxidized pyrogallol solution" and extracting it with ether. Acidification with sulphuric acid, however, caused the prompt deposition of crystalline purpurogallin in 25% of the theoretical yield. Haworth and his collaborators (18) recently showed that purpurogallin had the structure (III, R = H). The ether extract from solutions acidified with acetic acid



contained dark red substances from which 17% to 46% yields of orange-red crystals were obtained after acetylation with an acidic catalyst. These crystals, melting at 162° to 163°C. were later identified (28) as a new triacetate of purpurogallin. In an endeavor to avoid the use of acid, the "oxidized pyrogallol solution" was methylated with dimethyl sulphate on the alkaline side of pH 10, and extraction of the methylated liquors with ethyl acetate recovered about 35% of the pyrogallol as an orange residue. The residue yielded the dark red needles of 2'-monomethyl purpurogallin (III; R=CH₃), which had been obtained by oxidizing a mixture of pyrogallol and its 1-methyl ether with hydrogen peroxide and peroxidase (33), or with potassium iodate (7). Since the production of purpurogallin from pyrogallol almost certainly required 3-hydroxy-1,2-benzoquinone (II) as an intermediate (6, 7, 33), the results supported the view that the quinone (or a tautomer) was present as such in the "oxidized pyrogallol solution". The experiments, however, failed to circumvent the great tendency of *o*-quinones to condense when in acid solution (12, 24, 27), and even the temporary local acidity accompanying the methylation apparently promoted condensation.

The oxidation of vanillin by a sixfold molar amount of iodine in sodium borate buffers, when continued to completion (Table II) revealed a maximum consumption of about 3.65 moles per mole near pH 10 (run 4). This maximum corresponded to a particularly rapid secondary oxidation during the first three hours, as shown in Fig. 2, in which the plots for the intermediate runs 2, 5, and 10 were not reproduced. Small, red, flocculent precipitates were

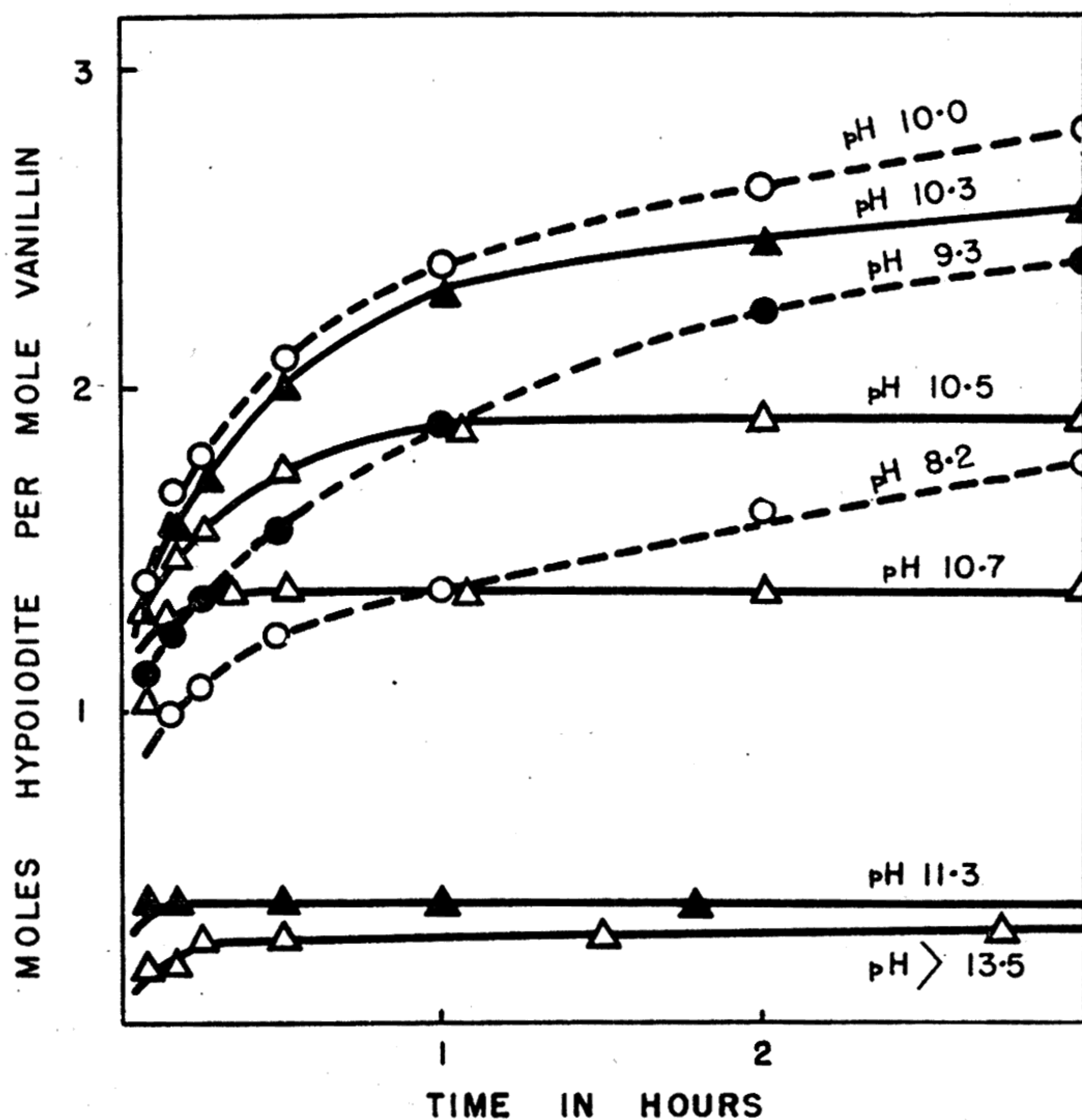


FIG. 2. Initial rate of reaction of 0.0033 *M* vanillin with 0.02 *M* iodine at 25°C. Moles of iodine reduced per mole of vanillin at the pH values shown.

formed in runs 1 to 5 (pH 8.2 to 10.2), and the mother liquors from these runs yielded 0.15, 0.16, 0.12, 0.06, and 0.0 moles of iodoform per mole of vanillin. As in the case of pyrogallol, therefore, the production of iodoform was at a maximum near pH 9, or when the secondary oxidation was approaching its greatest extent. Since vanillin very rapidly consumed about one mole of iodine in the pH range 8.2 to 10.7, equimolar amounts of vanillin and iodine were used in order to isolate the product of the initial reaction. Crystalline 5-iodovanillin was recovered in 90% yield from the reaction at pH 8.2, whereas the yield at pH 10 was only 62%, and 31% of hypoiodite remained at the end of the arbitrary period of 15 min. Although the oxidations at pH 11 or greater were not examined in detail, the lack of color in the solutions suggested the absence of quinones, and the small consumption of iodine put an upper limit of 35% on the production of 5-iodovanillin. The halogenating action of iodine on vanillin thus decreased abruptly on the alkaline side of pH 10. Erdtman's (9) similar preparation gave 73% of recrystallized 5-iodovanillin, and must therefore have been made in, or close to, the optimum pH range.

TABLE II
REDUCTION OF HYPOIODITE BY VANILLIN DURING 24 HR. AT 25°C.^a

Run	NaOH <i>M</i>	pH	Moles HIO reduced ^b	Run	NaOH <i>M</i>	pH	Moles HIO reduced ^b
1	0.04	8.2	2.7	7	0.22	10.5	1.9
2	0.06	8.9	2.75	8	0.23	10.7	1.35
3	0.10	9.3	3.3	9	0.24	11.3	0.35 ^c
4	0.16	10.0	3.65	10	0.28	12.6	0.3
5	0.20	10.2	3.2	11	0.32	13.5	0.3
6	0.21	10.3	2.6				

^aIn 0.2 *M* boric acid, 0.02 molar in iodine and 0.0033 molar in vanillin (mole ratio 6 : 1).

^bPer mole of vanillin.

^cConstant from 1 hr. to 9 hr.

REACTIONS WITH ALKALINE HYPOCHLORITE

The oxidation of pyrogallol with six times the molar amount of sodium hypochlorite in adequate borate buffers proceeded at all the pH values studied until the oxidant was almost entirely exhausted. Table III records the consumptions of oxidant after nine hours, when the oxidation at pH 8.8 (run 2) was practically complete; thereafter the necessary time increased to more than 24 hr. at pH 12.4 (run 8). The initial portions of the rate plots for runs 1, 3, 4, 5, 7, and 8 (Fig. 3) revealed a very rapid consumption of about three moles of hypochlorite per mole of pyrogallol, and a secondary consumption whose rate and extent went through a maximum near pH 11. These observations were supported by the plots at intermediate pH values (runs 2 and 6, not reproduced). The solutions remained colorless in the first three experiments (pH 8 to 9) but in the others initially ranged from light yellow to orange, becoming colorless only after 15 to 30 min. No precipitate was observed in any of the runs.

Pyrogallol, when mixed with a 3-molar proportion of chlorine dissolved in 10% sodium carbonate solution, within 10 min. gave a 72% yield of crystalline

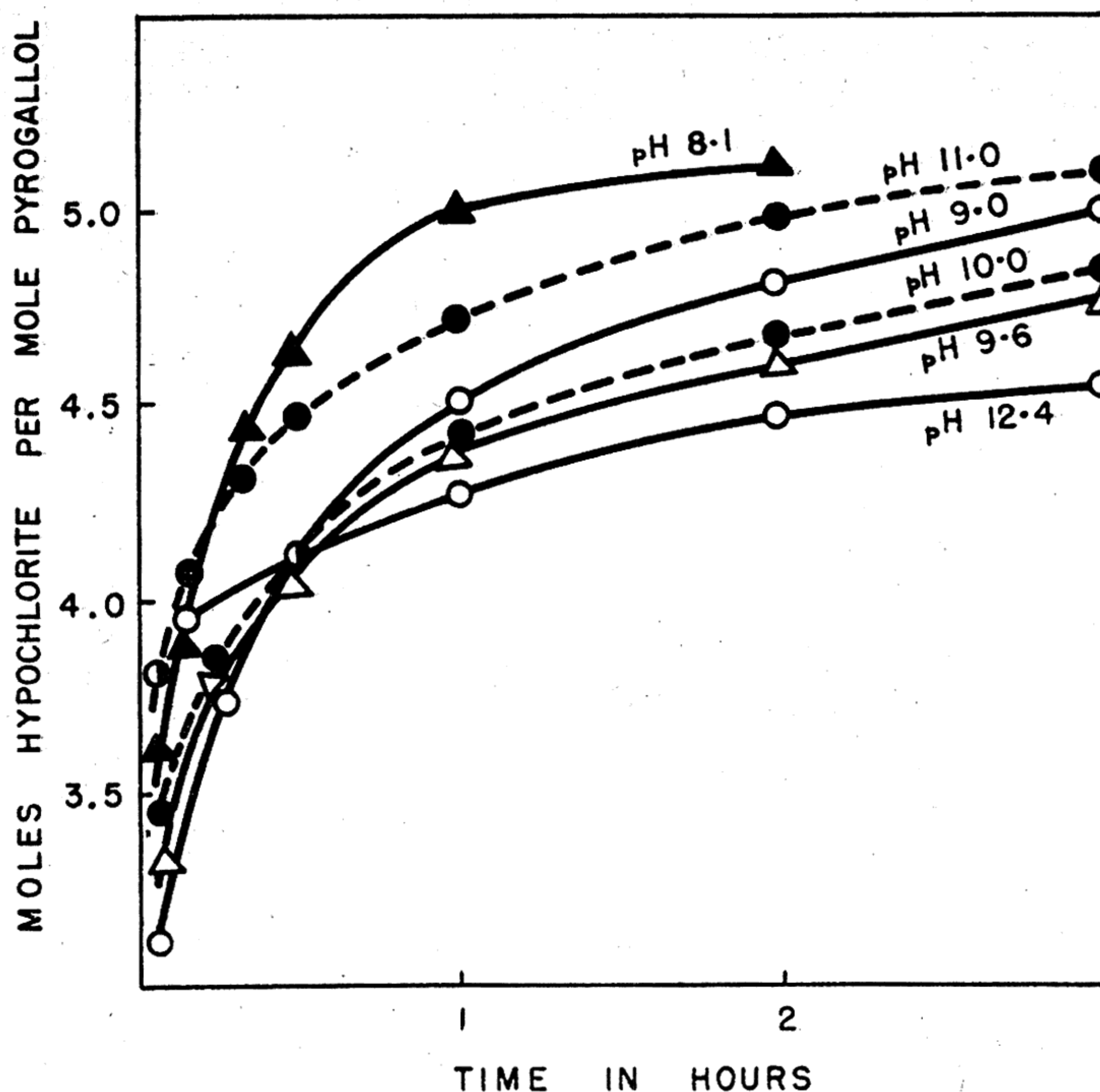


FIG. 3. Initial rate of reaction of 0.003 *M* to 0.004 *M* pyrogallol with a sixfold molar concentration of chlorine at 25°C. Moles of chlorine reduced per mole of pyrogallol at the pH values shown. Plot at pH 8.1 with 5.13 molar equivalents of chlorine.

trichloropyrogallol monohydrate. Even near pH 12, therefore, the initial action of hypochlorite was one of halogenation, and constituted a new and convenient method of preparing the trichloro derivative in good yield. The product was always contaminated with boric acid when a borate buffer was used in the preparation, and attempts to isolate the triacetate by adding acetic anhydride to the alkaline solution (3) failed. Webster (30) obtained

TABLE III
REDUCTION OF HYPOCHLORITE BY PYROGALLOL DURING NINE HOURS AT 25°C.^a

Run	NaOH <i>M</i>	Cl ₂ <i>M</i> × 10 ²	Pyrogallol <i>M</i> × 10 ²	pH	Moles HClO reduced ^b
1	0.03	1.54	0.299	8.1	5.1 ^c
2	0.10	1.96	0.327	8.8	5.9
3	0.12	1.96	0.327	9.0	5.6
4	0.16	1.96	0.327	9.6	5.3
5	0.20	1.96	0.327	10.0	5.3
6	0.22	1.96	0.327	10.5	5.4
7	0.24	2.4	0.40	11.0	5.5 ^d
8	0.28	2.4	0.40	12.4	5.0 ^e

^aIn 0.2 *M* boric acid with chlorine to pyrogallol in molar ratio 6 : 1.

^bPer mole of pyrogallol.

^cChlorine to pyrogallol molar ratio 5.13 to 1. Oxidant exhausted after two hours.

^dAfter nine hours pH was 10.6; after 24 hr. consumption was 5.94 moles.

^eConsumption 5.4 moles after 24 hr.

trichloropyrogallol in unstated yield by chlorinating pyrogallol in acetic acid, and Biétrix (1) in poor yield by chlorinating gallic acid suspended in chloroform. Biétrix also prepared the crystalline trichloro-triacetate.

The reduction of hypochlorite by vanillin was examined as in the case of pyrogallol and the details were therefore omitted from the experimental portion of this article. Vanillin consumed all of the oxidant much more rapidly than pyrogallol, but the minimum time required for complete reaction was at a pH near 10 (Table IV, run 5). The initial portions of the rate plots for runs 1, 3, 5, 7, and 8, together with the plots of the intermediate runs not shown in Fig. 4, showed, as expected, that the extent of the secondary reduction was

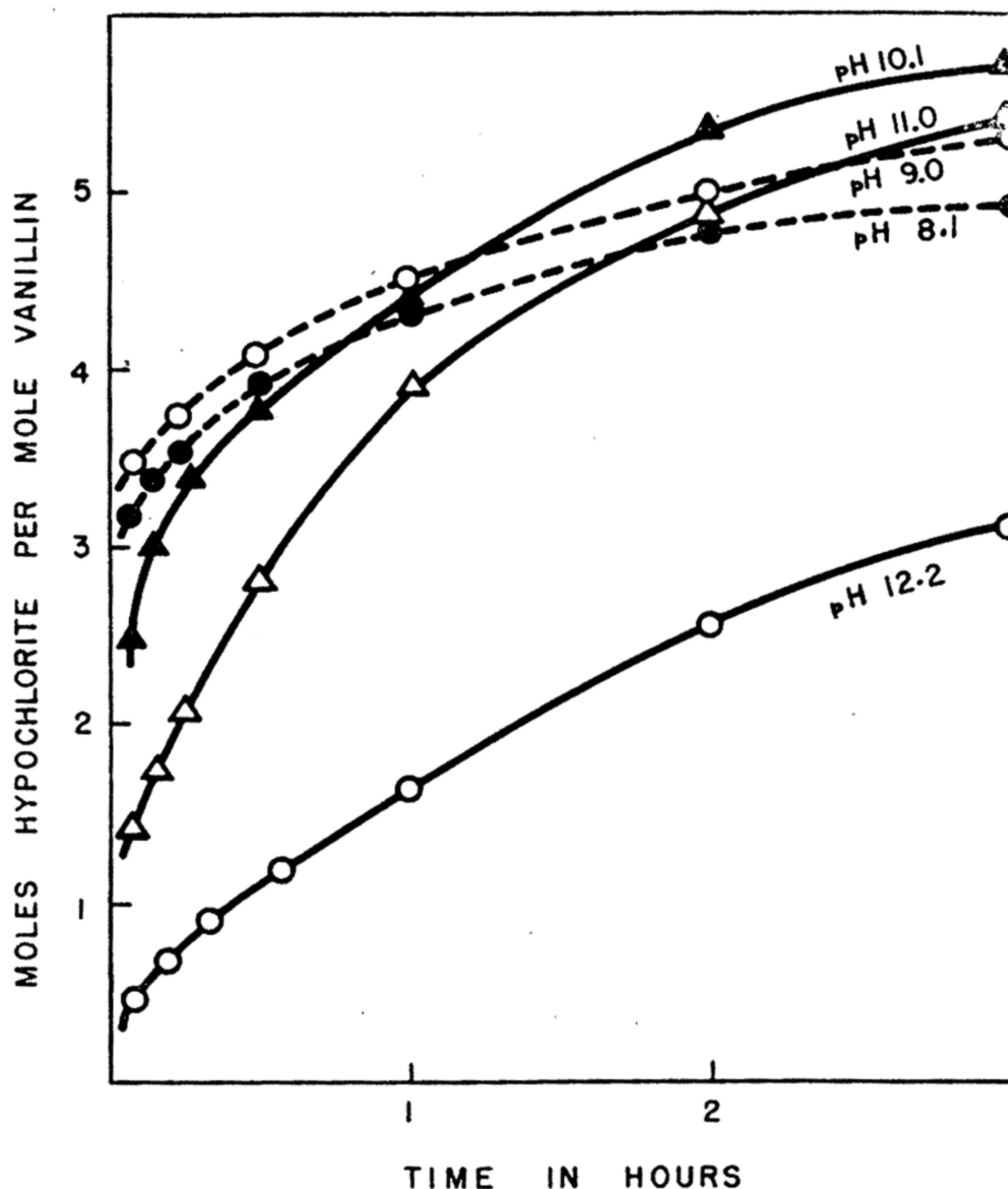


FIG. 4. Initial rate of reaction of 0.003 *M* to 0.004 *M* vanillin with a sixfold molar concentration of chlorine at 25°C. Moles of chlorine reduced per mole of vanillin at the pH values shown. Plot at pH 8.1 with 5.12 molar equivalents of chlorine.

greatest at pH 10. Run 1 at pH 8.1, however, was not closely comparable to the others because only 5 moles, instead of 6 moles, of hypochlorite per mole of vanillin was present. In all cases below pH 11 about three moles of chlorine was very rapidly consumed; all the solutions remained clear and colorless, but, when acidified after six to eight hours, deposited small amounts of a pink, flocculent substance.

Runs 2 and 8 (pH 8.7 and 12.2), when repeated with equimolecular amounts of vanillin and chlorine, required 10 min. and 60 min. respectively, for the oxidant to disappear. A 65% yield of 5-chlorovanillin resulted from the former experiment, but the latter gave only 43%, and 38% of the vanillin was recovered as the crystalline 2,4-dinitrophenylhydrazone. Since these figures

failed to account for about 19% of the vanillin and 57% of the chlorine, another reaction probably occurred involving the two components in the 1 : 3 molar ratio. These observations, together with a consideration of Fig. 4, showed that the initial reaction, consuming 3 moles of chlorine almost instantly at lower pH values, became quite slow at pH 12.2, although its nature probably did not change. Hopkins and Chisholm (20) obtained a 90% yield of 5-chlorovanillin by permitting 1.5 moles of sodium hypochlorite to act on 1 mole of vanillin for one hour, apparently in a sodium carbonate buffer.

TABLE IV
REDUCTION OF HYPOCHLORITE BY VANILLIN AT 25°C.^a

Run	NaOH M	Cl ₂ M × 10 ²	Vanillin M × 10 ²	pH	Hours ^b
1	0.08	1.54	0.30	8.1	2.6 ^c
2	0.10	2.4	0.40	8.7	5
3	0.12	2.4	0.40	9.0	5
4	0.16	2.4	0.40	9.5	5
5	0.20	2.3	0.38	10.1	3
6	0.22	2.3	0.38	10.5	4
7	0.24	2.3	0.38	11.0	5
8	0.28	2.3	0.38	12.2	9 ^d

^aIn 0.2 M boric acid with chlorine to vanillin in molar ratio 6 : 1.

^bApproximate time when 93% to 95% of the hydrochlorite was reduced.

^cChlorine-vanillin molar ratio 5.1 : 1.

^dOnly 4.7 moles (52%) of chlorine reduced in nine hours.

DISCUSSION

Since the reduction of hypiodite by pyrogallol ranged from about one mole to 5.3 moles, and of vanillin from 1.9 mole to 3.65 moles, according to the hydrogen ion concentration (Tables I and II), this factor required very close control when phenols were estimated by iodometric methods. Failure to observe this requirement in the same way or to the same extent explained why Messinger and Vortman (21) found that 1 mole of various phenols reduced integral even numbers of iodine atoms, and why Orloff (22) thought that the molar consumption in 24 hr. to 48 hr. was fractional. Orloff decided that pyrogallol required approximately five moles, but later workers (15, 25) varied the technique of the estimation and claimed that exactly 3 moles was reduced in a short time. This figure was again revised to approximately five moles (4). Wilkie (31, 32) carefully compared several of the older methods.

As already mentioned, iodoform was produced both from pyrogallol and from vanillin only in a narrow range about pH 9. Booth and Saunders (2) presumably operated in this range when they obtained iodoform by adding sodium hydroxide to a solution of pyrogallol and iodine, but none was observed by Slotta and Neisser (25), who added iodine to a solution of pyrogallol in aqueous sodium carbonate (pH ~ 12). Since iodoform could also be derived on occasion from various *o*- and *p*-hydroquinones (2, 25), from gallic acid, resorcinol, and phloroglucinol (2), the standard iodoform test for the

$\text{CH}_3\text{CO}-\text{C}\equiv$ and related groupings (13, 14) became ambiguous when phenols were present. The production of iodoform (or chloroform) from lignins oxidized by alkaline hypohalites (17, 29) was therefore no decisive proof that lignin contained either methyl ketone or $\text{CH}_3\text{CH}(\text{OH})-\text{C}\equiv$ units.

Green (16), who reviewed the inorganic chemistry of the hypohalites, quoted the dissociation constant of dilute aqueous hypochlorous acid as 6.5×10^{-8} , and of hypoiodous acid as of the order 5×10^{-13} . The former acid was therefore 79% dissociated to the hypochlorite ion at pH 8, and to practically 100% at pH 12; whereas the figures for the latter acid were about 0.005% and 49.5%, respectively. The species of oxidant present in alkaline solutions of iodine therefore varied greatly with pH, but change in the hypochlorite system was minor. With hypochlorite, the halogenating took precedence over the oxidizing action both for pyrogallol and for vanillin even at pH 12, when halogenation by hypoiodite was absent or slow.

If the standard potential of the redox system $\text{H}_2\text{O} + \text{Cl}^- = \text{HClO} + \text{H}^+ + 2e^-$ in acid solution was accepted as $E_0 = -1.49$ volts, and that of the corresponding iodide-hypoiodite couple as $E_0 = -0.99$ v. (16), calculation showed that these values corresponded to effective oxidation potentials of -1.14 v. and -0.64 v., respectively, at pH 12. When allowance was made for the approximate nature of the calculation, at pH 12 even hypochlorite might not oxidize vanillin, whose "critical oxidation potential" of $E_c = -1.08$ v. was among the highest found by Fieser (10) for the numerous phenols he examined. Since the "critical oxidation potential" of pyrogallol was $E_c = -0.609$ v., and the calculated normal potential of 3-hydroxy-1,2-benzoquinone was $E = 0.677$ v., the promotion of an equilibrium between these substances by hypoiodite at pH 12 might have been anticipated. These physical considerations supported the view that the action of the hypohalites on phenols became "limited", or less complex, on the alkaline side of pH 11 or 12.

EXPERIMENTAL

Rate of Oxidation of Pyrogallol with Hypoiodite (Table I, Fig. 1)

In a typical experiment, 150 cc. of 0.667 *M* aqueous boric acid and the desired volume of 1.0 *N* sodium hydroxide were mixed in a 500 cc. volumetric flask; the mixture was diluted to about 250 cc. with distilled water, and 200 cc. of 0.1 *N* iodine (0.02 equivalents) in aqueous potassium iodide was added. The pH of the solution was measured with a Coleman Model 3 pH Electrometer, with correction as described by Dole (8) for the salt error of the glass electrode. Control experiments with a high alkalinity glass electrode showed that this correction was valid. At zero time, a solution of about 0.21 gm. of pyrogallol (about 0.0017 mole or one-sixth the molar amount of iodine) in 25 cc. of water was added; the total volume was made up to 500 cc. with distilled water, and was promptly and thoroughly mixed. The iodine and pyrogallol solutions had been brought to 25°C. prior to mixing, and were subsequently maintained at $25^\circ \pm 0.05^\circ\text{C}$. in a constant temperature bath. The

pH of the solution was measured at intervals, and runs in which the value decreased by more than 0.3 units in 24 hr. were rejected.

After various times, 10 cc. aliquots were discharged into a large excess, 100 cc., of 1% sulphuric acid, and the iodine liberated was promptly titrated with 0.025 *N* sodium thiosulphate. The starch indicator used was added before the titration was begun, since approach to the end point was masked by the color of the solution. It was necessary to accept the first end point reached, since traces of iodine continued to be liberated for some time in the acid solution.

To assess the error caused by acidifying the solution for titration, 0.047 millimoles of pyrogallol (5.78 mgm.) was added to 50 cc. of 2% sulphuric acid mixed with 50 cc. of 0.006 *N* iodine in potassium iodide. A prompt back-titration with 0.023 *N* sodium thiosulphate required 11.83 cc., when the first end point was accepted, whereas the value for a blank containing no pyrogallol was 12.30 cc. These data corresponded to a consumption of 0.12 mole of iodine per mole of pyrogallol; similar estimations with a 4 : 1 instead of a 6 : 1 molar ratio of iodine to pyrogallol were 0.11 and 0.14 moles.

Oxidations carried out at pH 8.6 and 9.4 (runs 2 and 3) deposited 0.095 gm. and 0.105 gm. of iodoform, or 0.14 and 0.16 moles, respectively, per mole of pyrogallol. The identification depended upon the characteristic odor of iodoform, and the proper melting point of 118° to 119°C. The only other precipitates observed were from oxidations carried out with 10-fold concentrations of iodine and pyrogallol at pH values drifting from 12 or 13 to 8 or less. These precipitates were jet black in color, did not melt below 300°C., and were not examined further.

"Oxidized Pyrogallol Solution"

Pyrogallol, 1.29 gm., or 0.01 mole, was added with stirring to 500 cc. of an aqueous solution containing 6.2 gm. of boric acid, 5.1 gm. of sodium hydroxide, and 2.59 gm. (0.01 mole) of iodine (added in potassium iodide solution). The mixture, whose pH was 12.0, immediately became red. This "oxidized pyrogallol solution" was kept at room temperature and under nitrogen for 30 min. to 2.5 hr. before use, and apparently did not change within the latter time.

Recovery of Pyrogallol Triacetate

An "oxidized solution" made 30 min. previously from 1.29 gm. of pyrogallol, was rapidly stirred with 5 cc. of acetic anhydride (3). A light cream-colored precipitate was obtained with a melting point of 163° to 164°C., undepressed by admixture with an authentic sample of pyrogallol triacetate, m.p. 164 to 165°C.; yield 2.29 gm. or 88.7%. A control experiment containing no iodine resulted in an 87% yield of the triacetate.

Aliquots, 10 cc., of a similar solution were removed before and after the addition of the acetic anhydride, and were discharged into 100 cc. of 1% sulphuric acid. The iodine in the mixtures was equivalent to 5.16 cc. and 11.6 cc., respectively, of 0.0324 *N* sodium thiosulphate. Since the blank containing neither acetic anhydride nor pyrogallol required 12.3 cc. of the thiosulphate, the recovery of iodine was 42% and 94%, respectively.

Recovery of Purpurogallin and Derivatives

(a) Pyrogallol, 1.89 gm. (0.015 mole) was dissolved in 400 cc. of water containing 1 gm. of sodium hydroxide, at room temperature and under nitrogen, and 150 cc. of 0.2 *N* iodine (0.015 mole) was added with stirring. The solution, pH 12.0, immediately became red-black in color, and after 10 min. gave a negative test for free iodine. Upon acidification with 10% sulphuric acid the color of the solution decreased considerably in intensity, and an orange, flocculent precipitate separated. After being washed and then dried *in vacuo*, the substance melted with decomposition at 264° to 268°C. Yield, 0.41 gm. or 25%. Recrystallization from toluene gave orange needles melting at 269° to 271°C., the value recorded for purpurogallin being 272° to 274°C. with decomposition (33).

A portion, 0.15 gm., was dissolved in 25 cc. of ethanol, and ether containing the diazomethane from 4 gm. of nitrosomethylurea was added. Next day the light yellow solution when evaporated to 50 cc. deposited 0.13 gm. (72%) of fine yellow needles, which when recrystallized from ether melted at 179° to 180°C. This melting point was 3°C. higher than the latest recorded value (18) and was not depressed by admixture with an authentic sample of 2',3', 4-trimethyl purpurogallin.

(b) An "oxidized solution", made 2.5 hr. previously from 1.3 gm. of pyrogallol, was acidified with acetic acid, and extracted continuously with ether for about five hours. After being concentrated, the dark-red extract was evaporated to dryness at room temperature and *in vacuo* over sodium hydroxide. Acetic anhydride, 15 ml., and five drops of concentrated sulphuric acid were added to the red-black mass. After 30 min. without external heating, the mixture was poured into 300 cc. of ice and water, and 0.3 to 0.8 gm. of a yellow precipitate formed. Repeated crystallization from ether yielded orange prisms with the composition of a purpurogallin triacetate and melting at 162° to 163°C. This melting point agreed with that of the isomer considered by Thorn and Barclay (28) to be the 4,2',3'-triacetate, although Haworth, Moore, and Pauson (19) recorded a melting point of 138° to 140°C. for this compound.

(c) An "oxidized solution", made 30 min. previously from 1.3 gm. of pyrogallol, was continuously stirred under nitrogen while 5 cc. of dimethyl sulphate was slowly added during a 30 min. period. This addition caused the color of the solution to increase and after four hours the pH had decreased from 12 to about 10. After acidification with acetic acid, the mixture was extracted continuously with ethyl acetate and the extract was distilled in steam. The hot aqueous residue in the still was filtered to remove a small amount of dark amorphous material, and the filtrate on cooling deposited 0.3 to 0.4 gm. of an orange-red substance. About one-fifth of this substance was high-melting, red in color, and insoluble in ether. The remaining four-fifths when recrystallized from ether gave shining, dark-red rosettes of monoclinic needles in a yield of 25 to 32% based on the pyrogallol, and melting at 194.5° to 195°C. Their composition was that of a monomethyl ether of purpurogallin, and their melting point was close to the value of 193°C. reported by Critchlow, Haworth, and Pauson for the 2' isomer (7).

On one occasion orange yellow crystals of m.p. 194° to 195°C . were obtained in place of the dark red needles, but there was no depression of melting point when the two forms were mixed.

Oxidations of Vanillin with Hypoiodite (Table II, Fig. 2)

Solutions of 3.09 gm. of boric acid in 75 cc. volumes of water were mixed with the proper volume of *N* sodium hydroxide (10 cc. to 80 cc.) to obtain the desired pH. After dilution to about 150 cc. with distilled water, 50 cc. of 0.2 *N* iodine in potassium iodide (0.005 mole) was added. Vanillin, 0.127 gm. or 0.00083 mole, was introduced at zero time as an aqueous suspension; the total volume was diluted to 250 cc. and the vanillin dissolved almost immediately. Solutions between pH 10 and 11 (runs 6 to 9) were orange to light yellow in color and remained clear, while those between pH 12 and 13.5 (runs 10 and 11) were both clear and colorless. The consumption of iodine at various times was followed as in the oxidations of pyrogallol, but the end point was definite and easy to observe. Iodoform was isolated after 24 hr. by making the solutions strongly alkaline and extracting with two 50 cc. volumes of ether. After being dried and evaporated, the extracts from runs 1, 2, 3, and 4 yielded 0.05, 0.052, 0.041, and 0.019 gm., respectively, of iodoform, which was identified by its melting point and odor.

5-Iodovanillin

The borate buffer - iodine solution was made up exactly as described, 10 cc. of the sodium hydroxide solution being included to give pH 8.2, and the amount of vanillin was increased to 0.76 gm. or 0.005 mole. Titration of an aliquot acidified after 15 min. indicated 2.9% of unused hypoiodite, and the equivalent amount of sodium thiosulphate was added to the remainder. The solution was then acidified with 10% sulphuric acid; the resulting cream colored precipitate was washed well with water and dried. Yield, 1.25 gm. (90%), and melting point 177° to 179°C . Two recrystallizations from glacial acetic acid yielded pale yellow needles with the analytical composition of an iodovanillin, and with a melting point, 181° to 182°C ., in agreement with the recorded value of 180°C . (9) for 5-iodovanillin.

The above experiment, when repeated with a borate buffer including 50 cc. of *N* sodium hydroxide to keep the pH at 10, yielded a solution with the deep red color of iodine. This color required 15 min. to fade to a pale orange. An aliquot, when acidified at this time and titrated, contained 31% of "free" iodine, which presumably originated from by-product iodate. The remainder of the solution yielded 0.87 gm. (62.7%) of 5-iodovanillin, melting at 171° to 175°C ., raised to the correct value of 181°C . by recrystallization.

Rate of Oxidation of Pyrogallol with Hypochlorite (Table III, Fig. 3)

The chlorine obtained from the action of excess hydrochloric acid on 4 gm. of potassium permanganate was swept with nitrogen into 250 cc. of *N* sodium hydroxide to yield a stock solution approximately 0.2 *M* in chlorine. Some of this stock solution, 25 cc. (0.005 mole) was transferred to a dark brown, glass bottle containing 75 cc. of 0.67 *M* boric acid and the amount of *N* sodium

hydroxide to give the desired alkalinity. After the mixture had been diluted with distilled water to 225 cc. and had been brought to $25^{\circ} \pm 0.05^{\circ}\text{C}$., 0.11 gm. (0.00083 mole) of pyrogallol dissolved in 25 cc. of water at 25°C . was added.

The consumption of hypochlorite was followed by transferring 10 cc. aliquots into 100 cc. of water containing 0.1 to 0.2 gm. of potassium iodide; 10 cc. of 10% sulphuric acid and the starch indicator were added, and the liberated iodine was rapidly titrated with 0.025 *N* sodium thiosulphate solution. The end point was transitory.

Recovery of Trichloropyrogallol

A solution consisting of 200 cc. of 10% sodium carbonate and 25 cc. of 0.227 *M* chlorine (0.0058 mole) in *N* sodium hydroxide was added to 0.24 gm. (0.0019 mole) of pyrogallol dissolved in 25 cc. of water. Ten minutes later, when the hypochlorite was completely reduced, 1 gm. of zinc dust was added, the mixture (pH about 12) was acidified with 10% sulphuric acid, and was continuously extracted for 12 hr. with ether. Evaporation of the dried extract to 10 cc., followed by dilution with petroleum ether, caused the separation of 0.34 gm., (73%) of a white crystalline substance. When dried *in vacuo* over phosphorus pentoxide, this substance sintered markedly at 110°C . and melted at 179° to 180°C . with decomposition, as described for trichloropyrogallol monohydrate (1, 30). A sample was therefore dehydrated at 110°C . for 30 min. for analyses. Found: C, 30.9, 31.1; H, 1.51, 1.55; Cl, 45.7, 45.9%. Calc. for $\text{C}_6\text{H}_3\text{O}_3\text{Cl}_3$: C, 31.4; H, 1.3; Cl, 46.4%.

Recovery of 5-Chlorovanillin

(a) A suspension of 0.88 gm. of vanillin (0.0058 mole) in 100 cc. of water was mixed at room temperature with a solution composed of 75 cc. of 0.67 *M* boric acid, 25 cc. of *N* sodium hydroxide made 0.23 *M* (0.0058 mole) in chlorine, and 50 cc. of water. This mixture, pH 8.8, after 10 min. gave a negative test for hypochlorite. Acidification with 10% sulphuric acid then caused the deposition of 0.71 gm. of slightly yellow crystals, which sintered and darkened near 150°C . before melting to a red-black liquid at 158° to 162°C ; yield, 65%. Solution in hot ethanol removed 70 mgm. of insoluble material, and the filtrate on cooling deposited pale yellow plates with the methoxyl and chlorine content of a chlorovanillin. The melting point of 163° to 164°C . was correct for the 5-chloro isomer (20), and admixture with an authentic sample of 5-chlorovanillin did not depress this value.

(b) The preparation in (a) was repeated with the exception that 45 cc. of *N* sodium hydroxide was substituted for the 50 cc. of water included in the mixture. This change altered the pH to 12.0, and one hour elapsed before the solution gave a negative test for hypochlorite. Acidification caused the precipitation of 0.46 gm. (41%) of 5-chlorovanillin melting at 158° to 162°C ., undepressed by admixture with an authentic sample.

A red, flocculant precipitate immediately formed when the acidified mother liquor was mixed with 100 cc. of a saturated solution of 2,4-dinitrophenylhydrazine. After recovery, this precipitate weighed 0.92 gm. (39%), melted at 256° to 258°C ., and contained no chlorine. Recrystallization from ethanol gave

dark red crystals of vanillin 2,4-dinitrophenylhydrazone with the correct methoxyl content and the correct melting point of 264° to 265°C., not depressed by admixture with an authentic sample.

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