3. **Nitration of the Saturated Disalicylideneacetone (VII).**—The chromanol (VII, 1 g.) was dissolved in glacial acetic acid (20 cc.) and to it was added at 40° a solution of nitric acid (3 cc., d. 1.48) in glacial acetic acid (9 cc.). After standing for several hours at room temperature, the solution was poured into ice water (300 cc.). The resulting solid (1.7 g.) was crystallized from glacial acetic acid; m. p. 180–182°.

Anal. Calcd. for $C_{17}H_{12}O_{19}N_4$: N, 13.28. Found: N, 13.28.

4. **Nitration of Tetrahydrospiropyran (VI).**—Nitration of VI under the conditions at 40° set out above afforded a crystalline tetranitro compound, m. p. 180–182° alone or in admixture with a specimen of tetranitrotetrahydrospiropyran prepared as described above.

D. Condensation with Analogous Aldehydes

Condensations and conversions to chromenol derivatives from acetone and 3-methoxysalicylaldehyde, 5-methoxysalicylaldehyde, 3-nitrosalicylaldehyde, 5-nitrosalicylaldehyde were carried by the general methods described for salicylaldehyde and acetone. The properties of the derivatives are recorded in Table I.

E. Condensation of Salicylaldehyde with Various Ketones

1. Salicylaldehyde (3 mols) was condensed with acetylacetone (1 mol) in the presence of alkali in the same way as described for the formation of disodium disalicylideneacetone. The product in this case was also disodium disalicylideneacetone.

2. Equimolar proportions of salicylaldehyde (12.2 g.) and acetylacetone (10 g.) dissolved in ethanol (50 cc.) with sodium hydroxide (8 g. in 12 cc. water) were condensed by being shaken for thirty minutes and standing at room temperature for one day. The product was filtered rapidly and the solid recrystallized from aqueous ethanol. The red crystalline product (VIII, R = Na) was dissolved in water and treated with excess carbon dioxide until decolorization was complete. The resulting yellow precipitate was recrystallized from benzene; m. p. 85.5° (alone or mixed with an authentic specimen of salicylidene acetylacetone (VIII, R = H) prepared by the method of Knoevenagel).[14]

3. Acetonylacetone condensed with salicylaldehyde under alkaline conditions in every proportion yielded only disodium disalicylideneacetone. The method of preparation was described in A.1(a). The amount of salicylaldehyde varied from 1 mole to 3 moles. The resulting salt after conversion to the free compound by the method A.2 gave a crystalline compound, m. p. 160°. The mixed m. p. with disalicylideneacetone was unchanged.

Acknowledgment.—The authors are indebted to Dr. P. W. Kent for his advice and help in the preparation of the manuscript of this work.

Summary

1. Some evidence is given for a possible 2-chromenol structure in a model compound disalicylideneacetone.

2. Compounds, differently substituted on the phenolic hydroxyls of the model were prepared.

3. Diphenospiropyran and saturated derivatives were investigated.

4. Corresponding compounds were obtained from acetone condensed with 3-nitro- and 5-nitrosalicylaldehyde and 3-methoxy- and 5-methoxysalicylaldehyde. The condensation of acetylacetone or acetonylacetone with excess salicylaldehyde resulted in the formation of the same disodium salicylideneacetone.

PRINCETON, NEW JERSEY RECEIVED JULY 8, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Chemistry of Diazo Compounds. II. Evidence for a Free Radical Chain Mechanism in the Reduction of Diazonium Salts by Hypophosphorous Acid[1,2]

BY NATHAN KORNBLUM, GLENN D. COOPER[3] AND JAY E. TAYLOR

When a diazonium salt is reduced with hypophosphorous acid the diazonium group is replaced by hydrogen. Inasmuch as diazonium salts are readily obtained from aromatic primary amines, this provides a simple and effective means for replacing an aromatic primary amino group by hydrogen[4]

$$\text{Aryl-NH}_2 \xrightarrow[\text{HX}]{\text{HNO}_2} \text{Aryl-N}_2{}^+\text{X}^- \xrightarrow{\text{H}_3\text{PO}_2} \text{Aryl-H} + \text{N}_2 \quad (1)$$

Despite the widespread use of this deamination process, nothing was known about the mechanism of the second step of the above sequence when this investigation was begun.[5] As will become evident from the sequel, there now can be little doubt that the hypophosphorous acid reduction of diazonium salts is a free radical chain reaction.

After preliminary studies had shown that the hypophosphorus acid reduction of *p*-tolyldiazonium hydrogen sulfate is profoundly catalyzed[5a] by small amounts of certain oxidizing agents, among them potassium permanganate, cupric sulfate, and sodium nitrite, attention was directed to the kinetics of the uncatalyzed reaction. Although analytically pure, crystalline, *p*-tolyldiazonium hydrogen sulfate, *p*-anisyldiazonium

---

(1) Paper I in this series: Kornblum and Iffland, THIS JOURNAL, 71, 2137 (1949).

(2) A portion of this paper was presented at the New York meeting of the American Chemical Society, September, 1947.

(3) X-R Fellow of the Purdue Research Foundation 1947-1949.

(4) Kornblum in Adams, "Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1944, Vol. II, pp. 277-282.

(5) Recently Alexander and Burge [THIS JOURNAL, 72, 3100 (1950)] have found biphenyl and *p*-terphenyl among the products of the hypophosphorous acid reduction of benzenediazonium chloride and have suggested that the formation of these by-products involves free radicals.

(5a) Actually, this is an induced reaction. The distinction between catalyzed and induced reactions is not commonly made, however, and it is not invoked here.

hydrogen sulfate, *p*-nitrobenzenediazonium hydrogen sulfate and pentabromobenzenediazonium hydrogen sulfate were employed, in no instance could reproducible results be obtained even though very considerable efforts were made to insure identity of conditions. Figure 1 illustrates the variation observed when samples of a single freshly prepared batch of *p*-tolyldiazonium hydrogen sulfate were treated with hypophosphorous acid under "identical conditions."

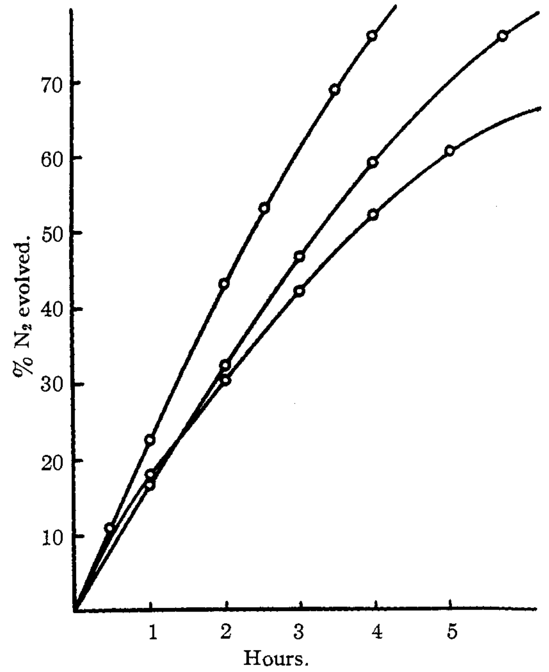


Fig. 1.—Variability of the rate of reduction of *p*-tolyldiazonium hypophosphite at 13.8°. The reaction mixture in each case contains $^1/_{200}$ mole of *p*-tolyldiazonium hypophosphite, $^1/_{20}$ mole of hypophosphorous acid, and $^1/_{200}$ mole of precipitated barium sulfate in 20 ml. of solution, *i. e.*, $^1/_{200}$ mole of barium hydroxide was added to a hypophosphorous acid solution of *p*-tolyldiazonium hydrogen sulfate. Oxygen was excluded. All three samples of the diazonium salt came from a single, freshly-prepared batch.

The technique used appears not to be at fault since reproducible first order rate constants were readily obtained when the decomposition of diazonium salts in the absence of hypophosphorous acid was studied, *i. e.*

$$\text{Aryl-N}_2^+ + H_2O \longrightarrow \text{Aryl-OH} + N_2 + H^+ \quad (2)$$

Furthermore, the rate of this reaction is not affected by the addition of potassium permanganate[6] (*cf.* Table I).

TABLE I

RATE OF DECOMPOSITION OF *p*-TOLYLDIAZONIUM HYDROGEN SULFATE IN WATER AT 40°

Diazonium salt	Other components	$k_{40°}$ (sec.$^{-1}$) $\times 10^5$
1/200 mole *p*-tolyl-diazonium hydrogen sulfate	20 ml. H_2O	3.39
1/200 mole *p*-tolyl-diazonium hydrogen sulfate	1/20 mole H_3PO_4 diluted to 20 ml.	3.38
1/200 mole *p*-tolyl-diazonium hydrogen sulfate	1/20 mole H_3PO_4, 1/200 mole $Ba(OH)_2$, 1/4000 mole $KMnO_4$, diluted to 20 ml.	3.34
1/200 mole *p*-tolyl-diazonium hydrogen sulfate	1/20 mole H_3PO_4, 1/4000 mole *p*-benzoquinone, diluted to 20 ml.	3.48

Despite the difficulty of obtaining genuinely quantitative data, in the absence of catalysts the various diazonium salts react with hypophosphorous acid at rates which are sufficiently diverse to permit them to be arranged in the following order of reactivity: $p\text{-OCH}_3 < p\text{-CH}_3 < p\text{-NO}_2 < \text{Br}_5$. Figure 2 contains representative curves for each of these salts. The results of a large number of measurements show that the average rate of reduction of *p*-tolyldiazonium hydrogen sulfate is approximately one and one-half times that of *p*-anisyldiazonium hydrogen sulfate; these two compounds are the only ones whose rates of reduction are even remotely comparable.

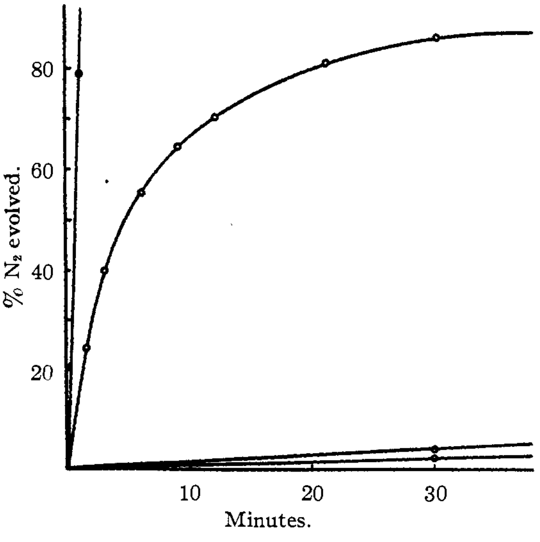


Fig. 2.—Comparison of rates of reduction of diazonium salts at 13.8°. The reaction mixture in each case contained $^1/_{200}$ mole of diazonium salt and $^1/_{20}$ mole of hypophosphorous acid in 20 ml. of solution: ●, pentabromobenzenediazonium hydrogen sulfate; O, *p*-nitrobenzenediazonium hydrogen sulfate; ◓, *p*-tolyldiazonium hydrogen sulfate; ◒, *p*-anisyldiazonium hydrogen sulfate.

The reaction between hypophosphorous acid and *p*-tolyldiazonium salts is not unique in its sensitivity to catalysis by small amounts of potassium permanganate, cupric sulfate and sodium

---

[6] It has also been shown by Mr. Alec E. Kelley in this Laboratory that copper sulfate does not alter the rate of decomposition of *p*-tolyldiazonium hydrogen sulfate in water.

nitrite. The hypophosphorous acid reductions of *p*-anisyldiazonium hydrogen sulfate and *p*-nitro benzenediazonium hydrogen sulfate are also catalyzed by these reagents. Catalysis was most extensively investigated using *p*-tolyldiazonium hydrogen sulfate and in Table II the results obtained with this compound are summarized.

TABLE II

EFFECT OF ADDED SUBSTANCES ON THE RATE OF REDUCTION OF *p*-TOLYLDIAZONIUM HYDROGEN SULFATE[a]

Strong catalysts: $KMnO_4$, $K_2Cr_2O_7$, $CuSO_4$, $FeSO_4$, Cu[b]
Moderate catalysts: MnO_2, $NaNO_2$, KIO_3[b]
Weak catalysts: $HgSO_4$, $KBrO_3$[b]
Little or no effect: $Fe_2(SO_4)_3$, $CoCl_2$, Na_2O_2, $CrCl_3$, $NiCl_2$, $K_2S_2O_8$, $KClO_3$[b]

[a] This classification is rather arbitrary; among other things, it takes no account of differences in the rate of solution. [b] We are indebted to Mr. Alec E. Kelley for carrying out these experiments.

The influence of various catalysts on the reduction of a number of diazonium salts is shown in Figs. 3, 4 and 5 (also *cf.* Table III). The most striking effect is that observed with *p*-anisyldiazonium hydrogen sulfate; here the addition of five mole per cent.[7] of copper sulfate increases the rate more than 700 times. In the case of pentabromobenzenediazonium hydrogen sulfate the uncatalyzed reaction is so very rapid, being complete in less than thirty seconds at 0°, that the effect of catalysts would not be easily observed. The isolation of pure toluene, anisole and nitrobenzene in 70–85% yields from reductions conducted in the presence of catalysts demonstrates that the reaction being catalyzed is actually the second stage of equation (1) and not some other process which also produces nitrogen.[8]

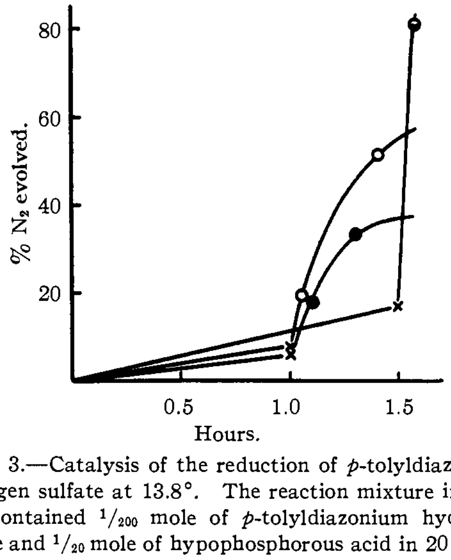


Fig. 3.—Catalysis of the reduction of *p*-tolyldiazonium hydrogen sulfate at 13.8°. The reaction mixture in each case contained $^1/_{200}$ mole of *p*-tolyldiazonium hydrogen sulfate and $^1/_{20}$ mole of hypophosphorous acid in 20 ml. of solution. At the point marked by a cross $^1/_{4000}$ mole of catalyst (solid, powdered) was added: O, potassium permanganate; ●, sodium nitrite; ⊖, copper sulfate.

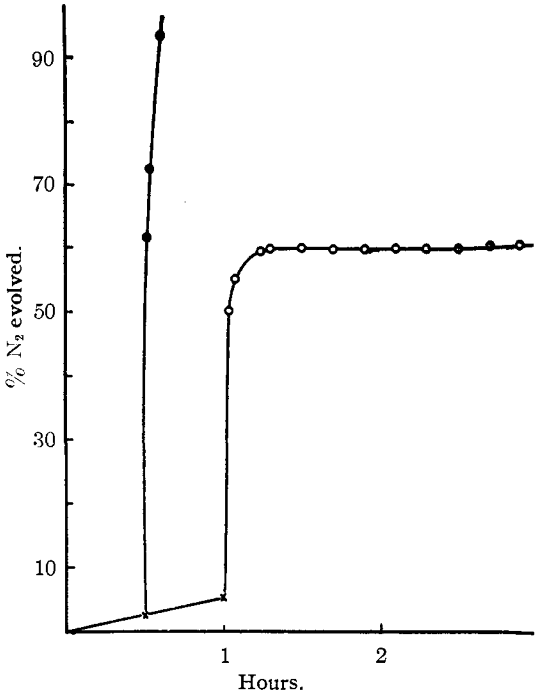


Fig. 4.—Effect of copper sulfate and potassium permanganate on the rate of reduction of *p*-anisyldiazonium hydrogen sulfate at 13.8°. The reaction mixture in each case contained $^1/_{200}$ mole of *p*-anisyldiazonium hydrogen sulfate and $^1/_{20}$ mole of hypophosphorous acid in 20 ml. of solution. At the point marked by a cross $^1/_{4000}$ mole of catalyst (solid, powdered) was added: ●, copper sulfate; O, potassium permanganate.

The effect of potassium dichromate and potassium permanganate on the reduction of *p*-anisyldiazonium salts (Figs. 4 and 5) calls for some comment, since the reaction is strongly catalyzed for a few minutes, following which it is completely inhibited for a considerable time. An explanation of this behavior is presented below.

Not only is the reduction greatly accelerated by oxidizing agents but, as would be anticipated for a free radical chain process, it is inhibited by small amounts of such substances as *p*-benzoquinone, tolu-*p*-quinone and quinhydrone. This is most clearly demonstrated in the case of *p*-anisyldiazonium hydrogen sulfate whose reduction is completely inhibited for 3.5 hours by five mole per cent. of benzoquinone at 13.8° (Fig. 6) and for an even longer period at 0°. Similarly the hypophosphorous acid reduction of *p*-tolyldiazonium hydrogen sulfate is completely stopped by benzoquinone, but for a shorter time (Fig. 7). In the case of the *p*-nitro- and pentabromobenzenediazonium salts, which react very rapidly with hypophosphorous acid, the addition of benzo-

---

[7] Throughout this paper "mole per cent." refers to the number of moles of catalyst (or inhibitor) per one hundred moles of diazonium salt.

[8] The usefulness of this catalysis from the synthetic point of view is now being studied.

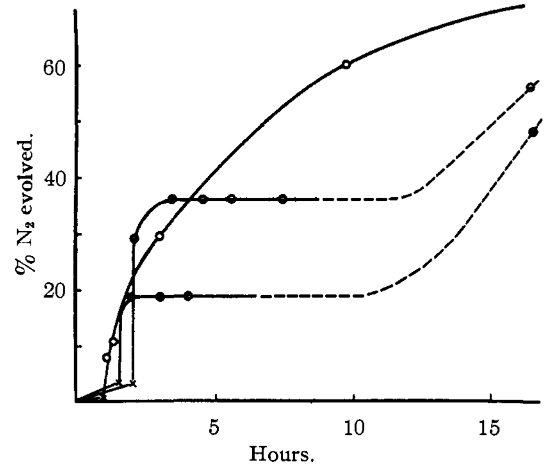


Fig. 5.—Effect of various substances on the rate of reduction of *p*-anisyldiazonium hypophosphite at 0°. The reaction mixture in each case contained one mole of hypophosphorous acid, $^1/_{10}$ mole of *p*-anisyldiazonium hypophosphite and $^1/_{10}$ mole of precipitated barium sulfate in 400 ml. of solution, *i. e.*, $^1/_{10}$ mole of barium hydroxide was added to a hypophosphorous acid solution of the diazonium hydrogen sulfate. At the point marked by a cross $^1/_{200}$ mole of the catalyst, dissolved in a few milliliters of water, was added dropwise: O, sodium nitrite; ●, potassium permanganate; ◒, potassium dichromate. Readings are not available for the dotted portions of two of these curves.

quinone does not stop the reduction but does retard it significantly (Table III).

TABLE III

CATALYSIS AND RETARDATION IN THE REDUCTION OF *p*-NITROBENZENEDIAZONIUM HYDROGEN SULFATE AND PENTABROMOBENZENEDIAZONIUM HYDROGEN SULFATE[a]

Diazonium salt	Added substance[7]	Time for 50% completion of reduction
p-Nitrobenzenediazonium hydrogen sulfate	None	17 min.
p-Nitrobenzenediazonium hydrogen sulfate	5 mole % potassium permanganate	3 min.
p-Nitrobenzenediazonium hydrogen sulfate	5 mole % copper sulfate	4 min.
p-Nitrobenzenediazonium hydrogen sulfate	5 mole % benzoquinone	30 min.
p-Nitrobenzenediazonium hydrogen sulfate	200 mole % benzoquinone	75 min.
Pentabromobenzenediazonium hydrogen sulfate	None	<15 sec.
Pentabromobenzenediazonium hydrogen sulfate	5 mole % benzoquinone	3 min.
Pentabromobenzenediazonium hydrogen sulfate	200 mole % benzoquinone	9 min.

[a] These experiments were carried out at 0° using $^1/_{400}$ mole of diazonium salt, $^1/_4$ mole of hypophosphorous acid and the added substance in a total volume of 100 ml.

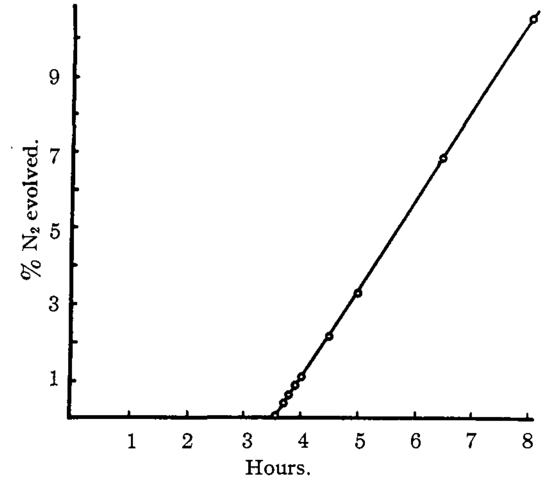


Fig. 6.—Inhibition of hypophosphorous acid reduction of *p*-anisyldiazonium hydrogen sulfate by benzoquinone at 13.8°. The reaction mixture contained $^1/_{200}$ mole of *p*-anisyldiazonium hydrogen sulfate, $^1/_{4000}$ mole of *p*-benzoquinone, and $^1/_{20}$ mole of hypophosphorous acid in 20 ml. of solution.

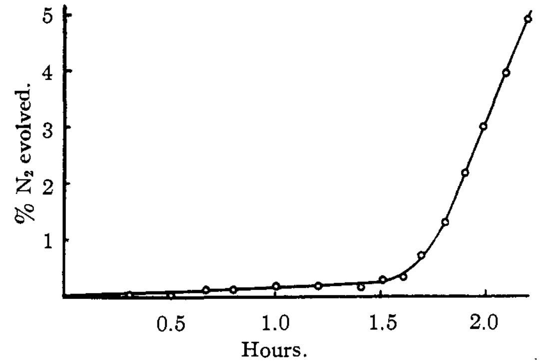


Fig. 7.—Inhibition of the hypophosphorous acid reduction of *p*-tolyldiazonium hydrogen sulfate by benzoquinone at 13.8°. The reaction mixture contained $^1/_{200}$ mole of *p*-tolyldiazonium hydrogen sulfate, $^1/_{4000}$ mole of *p*-benzoquinone, and $^1/_{20}$ mole of hypophosphorous acid in 20 ml. of solution.

The demonstration that quinones inhibit the hypophosphorous acid reduction of *p*-anisyldiazonium hydrogen sulfate serves to explain the fact, noted above, that the reduction of *p*-anisyldiazonium hydrogen sulfate is first promoted and then inhibited by potassium dichromate or potassium permanganate. If it is assumed that these powerful oxidizing agents are capable of converting the *p*-anisyldiazonium salt, or a reaction product, *e. g.*, anisole or *p*-hydroxyanisole, to a quinone or a semiquinone, the inhibition subsequent to catalysis, which is observed only with this diazonium salt, becomes understandable. This view is supported by the fact that those catalysts which are mild oxidizing agents, such as copper sulfate and sodium nitrite, simply catalyze the reduction of *p*-anisyldiazonium salts.

The foregoing data, as well as other results which follow, do not appear to be capable of explanation on any basis other than that of a free radical chain reaction. The following mechanism is suggested[9]:

Chain Initiation

$$\text{Aryl-N=N—Y} \longrightarrow \text{Aryl}^\cdot + N_2 + Y^\cdot \tag{3}$$

where Y = $OPOH_2$, Cl, OH, etc.

$$\text{or Aryl-}N_2^+ + Y^- \longrightarrow \text{Aryl}^\cdot + N_2 + Y^\cdot \tag{4}$$

Chain Propagation[10]

$$\text{Aryl}^\cdot + H_3PO_2 \longrightarrow \text{Aryl-H} + [H_2PO_2]^\cdot \tag{5}$$

$$\begin{array}{r} [H_2PO_2]^\cdot + \text{Aryl-}N_2^+ \longrightarrow \text{Aryl}^\cdot + N_2 + [H_2PO_2]^+ \\ \downarrow H_2O \\ H_3PO_3 + H^+ \end{array} \tag{6}$$

Initiation and Catalysis

The first of the two modes of initiation, (3), postulates a covalent diazo compound.[10a] This is in keeping with the order of reactivity observed for the uncatalyzed reductions, (p-$OCH_3 < p$-$CH_3 < p$-$NO_2 < Br_5$), since electron-attracting groups in the ring lower the electron density at the -N_2^+, thus increasing the tendency of the diazonium ion to go over to a covalent structure such as Aryl-N=N—O—POH_2, Aryl-N=N—OH, or, in the presence of chloride, Ar-N=N—Cl.[11] The second chain initiation process, (4), also seems to be in accord with the order of reactivity since depletion of the electron density of the ring would, presumably, serve to render the $-N_2^+$ more prone to accept an electron from $H_2PO_2^-$.

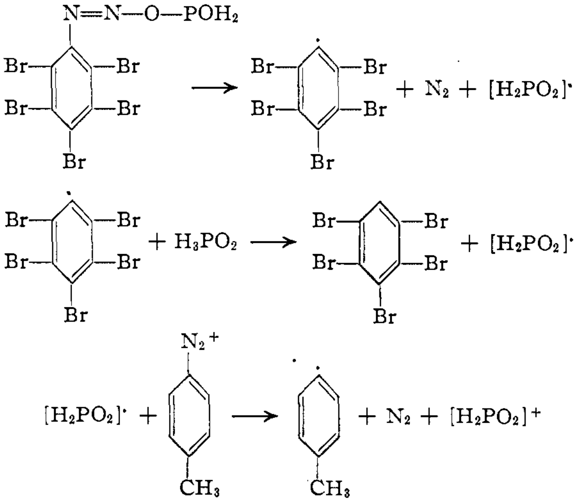
An attractive feature of the proposed mechanism is the simple explanation it provides for the catalytic effect of oxidizing agents upon the hypophosphorous acid reduction of diazonium salts. Those oxidizing agents are effective which are capable of bringing about a one-electron oxidation of hypophosphorous acid or the hypophosphite ion. The free radicals so produced react with the diazonium ion according to (6), thus starting the chain. For example, with copper sulfate the reaction would be

$$Cu^{++} + H_2PO_2^- \longrightarrow Cu^+ + [H_2PO_2]^\cdot$$

$$[H_2PO_2]^\cdot + \text{Aryl-}N_2^+ \longrightarrow \text{Aryl}^\cdot + N_2 + [H_2PO_2]^+$$

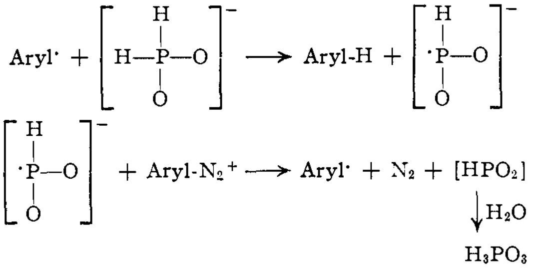
This catalysis of a reduction by oxidizing agents calls to mind the use of oxidation–reduction systems in catalyzing vinyl polymerizations, reactions which, it is generally agreed, proceed via a free radical chain mechanism.[12]

It is a further consequence of the mechanism outlined above that the very rapid reduction of p-nitro- and pentabromobenzenediazonium salts is due to the ease with which initiation takes place. On this basis it would be predicted that a small amount of a rapidly reducible salt, such as pentabromobenzenediazonium hydrogen sulfate, would catalyze the reduction of a salt which is but slowly reduced, *e. g.*, p-tolyldiazonium hydrogen sulfate. The pentabromo salt would initiate a large number of chains and these would be carried on by the relatively abundant p-tolyldiazonium ion



---

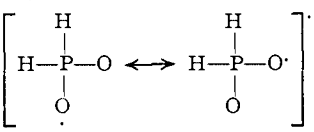
[9] Minor modifications of this scheme are easily envisioned. For example, in the chain propagating sequence.



$$\text{Aryl}^\cdot + \left[H-\overset{H}{\underset{O}{P}}-O\right]^- \longrightarrow \text{Aryl-H} + \left[\cdot\overset{H}{\underset{O}{P}}-O\right]^-$$

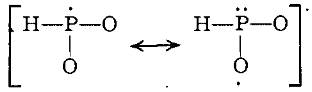
$$\begin{array}{r} \left[\cdot\overset{H}{\underset{O}{P}}-O\right]^- + \text{Aryl-}N_2^+ \longrightarrow \text{Aryl}^\cdot + N_2 + [HPO_2] \\ \downarrow H_2O \\ H_3PO_3 \end{array}$$

[10] The $[H_2PO_2]^\cdot$ radical produced in reactions (3) and (4) would not be the same as that of equation (5), if, as seems likely, a P-H bond rather than an O-H bond is broken in (5). The hypophosphite radical in (3) and (4) would have the structure



$$\left[H-\overset{H}{\underset{\underset{\cdot}{O}}{P}}-O \longleftrightarrow H-\overset{H}{\underset{O}{P}}-O^\cdot\right]^\cdot$$

whereas that formed by reaction (5) would be



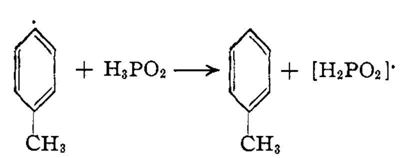
$$\left[H-\underset{O}{\dot{P}}-O \longleftrightarrow H-\underset{\underset{\cdot}{O}}{\ddot{P}}-O\right]^\cdot$$

The structural assignment for the $[H_2PO_2]^\cdot$ radical produced in (5) is based on the considerable difference in the strength of the P-H bond and O-H bond, the latter being 32 kcal. per mole stronger [Pitzer, THIS JOURNAL, **70**, 2140 (1948)]. It is entirely possible that these two radicals would be tautomeric, since hypophosphorous acid itself is known to exchange all three of its hydrogens with water.

[10a] ADDED IN PROOF.—Very recently Atkinson, Warren, Abell and Wing [THIS JOURNAL, **72**, 915 (1950)], in order to explain the results of their polarographic examination of diazonium salts, have suggested that, even in strongly acid solutions, there is some Aryl—N=N—OH present and that the equilibrium Aryl—$N_2^+ + H_2O \rightleftarrows$ Aryl—N=N—OH + H^+ is mobile.

[11] The rate of the hypophosphorous acid reduction of diazonium salts is considerably increased by large amounts of chloride ion. This is not a "salt effect" since an equivalent quantity of sulfate ion caused no such increase (J. E. Taylor, Ph.D. Thesis, Purdue University, 1947).

[12] Bacon, *Trans. Faraday Soc.*, **42**, 140 (1946); M. G. Evans and Baxendale, *ibid.*, **42**, 195 (1946).



This prediction has been completely confirmed experimentally. Thus, the rate of reduction of *p*-tolyldiazonium hydrogen sulfate is increased more than three hundred times by the addition of five mole per cent. of pentabromobenzenediazonium hydrogen sulfate (Fig. 8). *p*-Nitrobenzenediazonium hydrogen sulfate, the second of the two readily reducible salts, also catalyzes the reaction of hypophosphorous acid with the slowly reduced salts (Fig. 8).

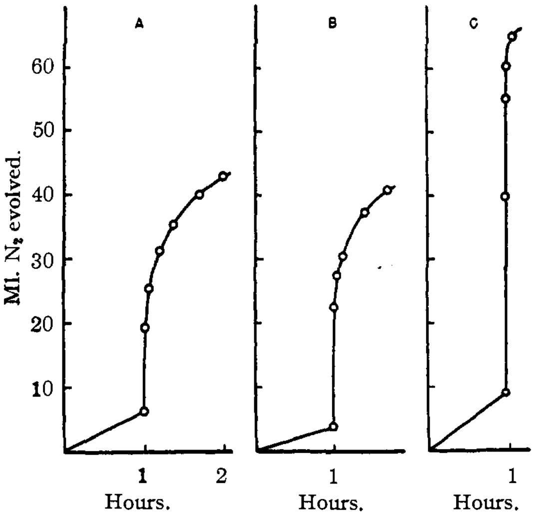


Fig. 8.—Diazonium salts as catalysts, temp. 13.8°: A. Reaction mixture contained $^1/_{200}$ mole *p*-tolyldiazonium hydrogen sulfate and $^1/_{20}$ mole hypophosphorous acid in 20 ml. of solution. After one hour $^1/_{4000}$ mole of *p*-nitrobenzenediazonium hydrogen sulfate was added. B. Identical with A except that *p*-anisyldiazonium hydrogen sulfate was substituted for *p*-tolyldiazonium hydrogen sulfate. C. $^1/_{200}$ mole *p*-tolyldiazonium hydrogen sulfate and $^1/_{20}$ mole hypophosphorous acid in 20 ml. of solution. After one hour $^1/_{4000}$ mole of pentabromobenzenediazonium hydrogen sulfate was added.

The observation that the reduction of unreactive diazonium salts is catalyzed by traces of the more reactive ones makes it unlikely that the thermal decomposition of hypophosphorous acid into neutral fragments

$$H_3PO_2 \longrightarrow H^\cdot + [H_2PO_2]^\cdot \qquad (7)$$

is responsible for chain initiation since it is difficult to see how an initiation step involving hypophosphorous acid alone could account for such catalysis. Nor does chain initiation depend upon reaction (7) photochemically induced—or for that matter any photochemical process. The reduction of *p*-tolyldiazonium hydrogen sulfate proceeds at the usual rate in complete darkness.

Inhibition and Retardation

As noted earlier, the hypophosphorous acid reduction of diazonium salts is subject to inhibition and retardation. When five mole per cent. of *p*-benzoquinone is added to a solution of *p*-tolyldiazonium hydrogen sulfate and hypophosphorous acid, reduction is completely stopped for 100 ± 5 minutes (Table IV, Fig. 7). Once the reaction starts up it proceeds at the normal rate, indicating that the inhibitor has been destroyed. If the quinone is consumed by reacting with free radicals formed in (3) or (4)—or in stopping chains initiated by these radicals—then a measurable amount of nitrogen should be evolved, even during the period of inhibition. However, during this time only about 1 ml. of nitrogen is evolved and most of this is derived from the competing reaction (2)—a process known to be unaffected by benzoquinone (Table I). Clearly, then, the major portion of the quinone is destroyed in some way other than capturing the free radicals formed in (3) or (4).

TABLE IV

EFFECT OF PRETREATMENT OF BENZOQUINONE WITH HYPOPHOSPHOROUS ACID ON THE LENGTH OF THE INHIBITION PERIOD (REDUCTION OF *p*-TOLYLDIAZONIUM HYDROGEN SULFATE)[a]

Moles benzoquinone per mole of diazonium salt	Minutes benzoquinone and hypophosphorous acid were kept at 13.8° before being added to the diazonium salt	Inhibition period, minutes
1/20	0	100
1/20	0	101
1/20	0	100
1/20	0	96
1/20	30	88
1/20	60	75
1/20	102	71
1/20	150	65
1/20	300	46
1/20	720 (at room temp.)	8
1/5	0	216
1/80	0	34

[a] These experiments were carried out at 13.8° using $^1/_{200}$ mole *p*-tolyldiazonium hydrogen sulfate, $^1/_{20}$ mole of hypophosphorous acid and the indicated amount of benzoquinone in a total volume of 20 ml.

Further investigation showed that benzoquinone is readily reduced by hypophosphorous acid, first to quinhydrone and then to hydroquinone.[13] Since hydroquinone does not inhibit the hypophosphorous acid reduction of diazonium salts this alternative mode of using up the quinone, at first glance, seems to explain the small amount of nitrogen evolved during inhibition. And, indeed, when a solution of benzoquinone in hypophosphorous acid was allowed to stand overnight prior to adding *p*-tolyldiazonium hydrogen sulfate, essentially no inhibition was noted (Table IV).

---

[13] G. D. Cooper, Ph.D. Thesis, Purdue University, 1949.

Quantitatively, this explanation is unsatisfactory. It will be recalled that in the presence of five mole per cent. of benzoquinone the reduction of *p*-tolyldiazonium hydrogen sulfate at 13.8° does not begin until 100 minutes have elapsed (Table IV). Consequently, if the hypophosphorous acid reduction of benzoquinone is the principal cause of its disappearance, it would be expected that upon treating benzoquinone with hypophosphorous acid at 13.8° for 100 minutes and then adding *p*-tolyldiazonium hydrogen sulfate no inhibition would be observed. Actually, even after five hours of such pretreatment reduction of the diazonium salt is inhibited for forty-five minutes. A reasonable interpretation is that the reaction between benzoquinone and hypophosphorous acid is facilitated by the diazonium salt; alternatively, still another reaction, not involving the loss of nitrogen from the diazonium salt, is of significance in the destruction of the quinone.

It appears very likely then that the hypophosphorous acid reduction of diazonium salts is a free radical chain reaction since on this basis a diversity of experimental facts fall into an orderly pattern. However, the fact that either metallic copper or ferrous sulfate catalyzes this reaction would not have been anticipated, since, except for these two, the substances which catalyze the reduction of diazonium salts are capable of acting as oxidizing agents with hypophosphorous acid.

The catalytic power of copper might be explained in several ways. It has been reported[14] that copper catalyzes the decomposition of hypophosphorous acid into hydrogen, phosphorous acid, and other products. This could be a source of free radicals which initiate the reduction. Or, alternatively, copper may react with diazonium ions in the manner proposed for the Gattermann reaction[15]

$$\mathrm{Cu} + \mathrm{Aryl\text{-}N_2}^+ \longrightarrow \mathrm{Cu}^+ + \mathrm{Aryl}^\cdot + \mathrm{N_2}$$

There seems to be no obvious explanation for the fact that ferrous ion, but not ferric ion, promotes the hypophosphorous acid reduction of diazonium salts.[16] It should be pointed out, however, that the chemistry of hypophosphorous acid is very imperfectly understood. Thus, in order to account for the kinetics obtained when various inorganic ions are reduced by hypophosphorous acid it is necessary to invoke the hypothesis that hypophosphorous acid exists in a "normal" and an "active" form; the nature of this "activated" hypophosphorous acid is not known.[17] Under such circumstances it is not surprising that one anomaly exists.

Acknowledgments.—We wish to express our sincere thanks to the Purdue Research Foundation for an X-R Fellowship and to Mr. Alec E. Kelley for carrying out some of the experiments recorded in this paper.

Experimental

The hypophosphorous acid used in these experiments was Mallinckrodt "purified 50%." The organic compounds employed, unless otherwise specified, were Eastman Kodak Co. White Label products, recrystallized to constant melting point. The inorganic salts were C. P. or Reagent grade, and were used without further purification. The "distilled water" employed was ordinary distilled water which had been redistilled in all glass equipment from potassium hydroxide. Glassware was routinely cleaned with hot, concentrated, sulfuric acid containing a small amount of nitric acid; at no time was chromic acid used.

Preparation of Diazonium Salts

p-**Tolyldiazonium Hydrogen Sulfate.**—Fifteen grams of *p*-toluidine was dissolved in 150 ml. of absolute ethanol and diazotized at 25–30° with sulfuric acid and freshly prepared isoamyl nitrite[18] according to the procedure of Knoevenagel.[19] After about thirty minutes the shiny white plates of *p*-tolyldiazonium hydrogen sulfate were isolated by filtration, thoroughly washed with absolute ethanol and then with ether. The ether-wet product was immediately transferred to a large, ice-cold, test-tube having a ground-glass stopper. The tube was then immersed in an ice-bath and connected to a vacuum pump (3 mm. pressure) for 12–16 hours. The yields of dry, white plates ranged from 35–53%. The salt was stored in Dry-Ice under nitrogen.

Anal. Calcd. for $C_7H_8N_2O_4S$: $SO_4^=$, 44.4. Found: $SO_4^=$, 44.4, 44.1.

p-**Anisyldiazonium Hydrogen Sulfate.**—Sixty-nine grams of *p*-anisidine was added to a solution of 40 ml. of 96% sulfuric acid in 130 ml. of water. The solution was cooled to 0° in an ice–salt-bath and ethyl nitrite was then passed into the thick slurry of *p*-anisidine hydrogen sulfate until nearly all the solid disappeared; the temperature was maintained at 0–5°. The mixture was filtered and ethyl nitrite was passed into the filtrate until a positive reaction was obtained with starch–iodide paper. A liter of acetone, cooled to −5°, was added with vigorous stirring. The white crystals which separated were filtered off and washed with a total of three liters of cold acetone. The product was dried and stored in the same way as the *p*-tolyl salt; yield 80 g. (64%).

Anal. Calcd. for $C_7H_8N_2O_5S$: $SO_4^=$ 41.4. Found: $SO_4^=$, 41.4, 41.5.

With *p*-anisidine the method of Knoevenagel[19] yielded a salt which gave a satisfactory analysis for sulfate, but from which only about two-thirds of the calculated amount of nitrogen was liberated on treatment with hypophosphorous acid. Knoevenagel, himself, stated that he could obtain only one-third of the theoretical amount of nitrogen from the diazonium salt prepared in this way, even after boiling an aqueous solution for 24 hours. Presumably the diazonium salt was contaminated with *p*-anisidine hydrogen sulfate which has a sulfate content not far from that of the diazonium salt.

p-**Nitrobenzenediazonium Hydrogen Sulfate.**—Six grams of *p*-nitroaniline was dissolved in 150 ml. of absolute ethanol. Fifteen grams of 96% sulfuric acid was added and the solution cooled to 10° under nitrogen following which 9 g. of freshly prepared isoamyl nitrite was added in

---

[14] Sieverts and Loessner, *Z. anorg. Chem.*, **76**, 10 (1912).

[15] Waters, *J. Chem. Soc.*, 266 (1942).

[16] The oxidation of hypophosphorous acid by air is catalyzed by ferrous ion [Wieland and Franke, *Ann.*, **464**, 101 (1928)]. That this reaction is not the source of initiating radicals is shown by the observation that ferrous sulfate catalyzes the reduction of *p*-tolyldiazonium hydrogen sulfate equally well in the presence or absence of air. Possibly, upon still more rigorous exclusion of air, ferrous sulfate will fail to catalyze the reduction of diazonium salts.

[17] Mitchell, *J. Chem. Soc.*, **117**, 1322 (1920); Hayward and Yost, THIS JOURNAL, **71**, 915 (1949).

[18] Noyes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 108.

[19] Knoevenagel, *Ber.*, **28**, 2049 (1895).

one portion. After five minutes the faintly yellow crystals were isolated by filtration and washed, first with ethanol and then with ether. The salt was dried and stored in the same way as *p*-tolyldiazonium hydrogen sulfate; yield 6.1 g. (57%).

Anal. Calcd. for $C_6H_5N_3O_6S$: $SO_4^{=}$, 38.9. Found: $SO_4^{=}$, 38.5, 38.7.

Reduction of Diazonium Salts by Hypophosphorous Acid

The examples given below illustrate the technique which was used, with but minor variations, in carrying out the various reduction studies. For further details the doctoral dissertation of G. D. Cooper, Purdue University, 1949, should be consulted.

Reduction of *p*-Tolyldiazonium Hypophosphite.—In order to determine whether the presence of oxygen was responsible for the inability to obtain reproducible rates the apparatus shown in Fig. 9 was employed. To the reaction flask A was added 1.08 g. (0.005 mole) of *p*-tolyldiazonium hydrogen sulfate. Barium hydroxide octahydrate (1.58 g., 0.005 mole) was dissolved in 6.6 g. (0.05 mole) of 50% hypophosphorous acid, the solution was diluted to 20 ml. with distilled water which had been freshly boiled and cooled under nitrogen,[20] and then nitrogen was bubbled through the solution for one-half hour. The solution was transferred to bulb B, the apparatus was assembled, and reaction vessel A was cooled in Dry-Ice. With stopcock E open the apparatus was evacuated through stopcock C to a pressure of about 3 mm. Stopcock C was then closed and pure nitrogen was admitted through D to a pressure somewhat greater than one atmosphere. Stopcock D was closed and the system evacuated again. This process was repeated several times. Then with stopcock C closed and the apparatus filled with nitrogen, stopcock G was opened to the atmosphere and a rapid current of nitrogen was passed through the apparatus for four hours. The apparatus was then placed (completely submerged, except for the buret and three-way stopcock) in a constant-temperature bath at 13.8°. The current of nitrogen was reduced to a very slow rate. After fifteen minutes stopcock F was opened, allowing the hypophosphorous acid solution to flow into vessel A. Stopcocks D, E and F were then closed and stopcock G opened to the gas measuring buret. The solution was stirred from below by means of a magnetic stirrer.

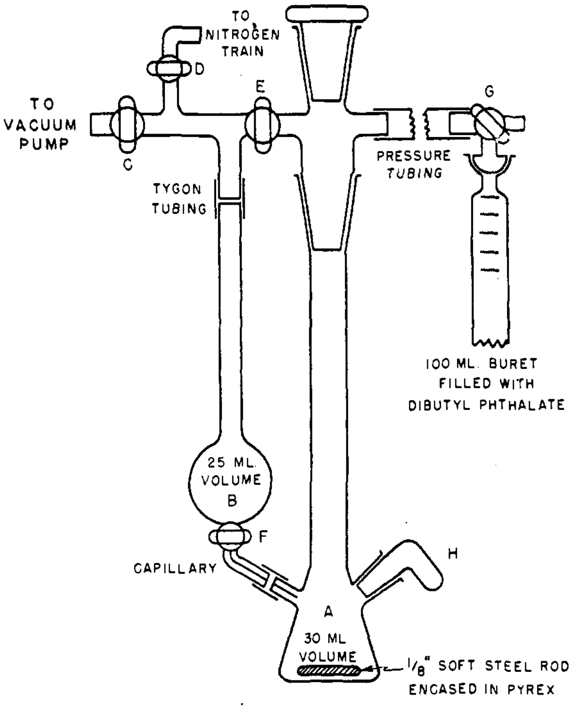


Fig. 9.

Time, hours	N_2 evolved, %[21]	Time, hours	N_2 evolved, %[21]
0.5	10.4	4.5	77.8
1.0	21.1	5.0	81.2
2.0	41.6	6.0	85.0
2.5	50.6	7.0	86.5
3.5	65.3	8.0	87.2
4.0	73.1	10.0	88.6

Despite the considerable pains taken, strict reproducibility could not be attained. Nor were reproducible results obtained when the barium hydroxide was omitted. Since the absence of oxygen did not improve matters most succeeding runs were made in the presence of air.

Catalysis by Copper Sulfate.—The apparatus of Fig. 9 was used without excluding air. Twenty milliliters of an aqueous solution containing 0.05 mole of hypophosphorous acid was placed in B and 1.16 g. (0.005 mole) of *p*-anisyldiazonium hydrogen sulfate in A. Side tube H was loaded with 0.064 g. (0.00025 mole) of finely powdered copper sulfate pentahydrate. The assembled apparatus was immersed in a constant temperature bath (13.8°) and after fifteen minutes stopcock F was opened allowing the hypophosphorous acid to flow into A. Stopcocks E and F were then closed and G opened to the gas buret. Constant stirring was provided. After one-half hour the copper sulfate was introduced into A by rotating H 180° and tapping it gently.

Time, hours	N_2 evolved, %[21]
0.5	2.5
0.516	61.4
0.533	73.6
0.6	95.0
3.4	99.7

Catalysis by Pentabromobenzenediazonium Hydrogen Sulfate.—This was done in the manner described above, except that 1.08 g. (0.005 mole) of *p*-tolyldiazonium hydrogen sulfate was substituted for the *p*-anisyl salt, and 0.149 g. (0.00025 mole) of pentabromobenzenediazonium hydrogen sulfate[22] was used instead of copper sulfate.

Time, hours	Volume N_2 (ml.) at S. T. P.
0.5	4.5
1.0[a]	9.7
1.0083	40
1.0167	58.4
1.033	62.3
1.05	63.1
1.10	64.8

[a] After one hour the 0.149 g. of pentabromo salt was added. The maximum amount of nitrogen to which this quantity of pentabromobenzenediazonium hydrogen sulfate can give rise is 5.6 ml. The maximum amount of nitrogen which 1.08 g. of *p*-tolyldiazonium hydrogen sulfate can yield is 112 ml.

---

[20] The nitrogen used in these experiments was freed of oxygen and water according to Fieser ["Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 2nd ed., 1941, pp. 395-396].

[21] "Per cent. nitrogen evolved" refers to that fraction of the diazonium nitrogen which is released as gaseous nitrogen. Because of competing reactions some of the diazonium nitrogen is not liberated as gas. Consequently, the per cent. nitrogen evolved rarely reached the 100 mark although it often ran well over 90%, especially with readily reduced salts or under the influence of catalysts.

[22] Kornblum, Cooper, Kelley and Iffland, THIS JOURNAL, to be published.

Inhibition by *p*-Benzoquinone.—Without excluding air, 20 ml. of a solution containing 0.05 mole of hypophosphorous acid was cooled to 13.8° and 0.0275 g. (0.00025 mole) of *p*-benzoquinone was dissolved in it by vigorous shaking. The solution was placed in B and 1.08 g. (0.005 mole) of *p*-tolyldiazonium hydrogen sulfate was put in A. The apparatus was assembled and placed in the constant temperature bath held at 13.8°. After five minutes the reactants were mixed and the gas produced measured as described previously.

Time, minutes	N_2 evolved,[21] %	Time, minutes	N_2 evolved,[21] %
30	0.0	108	1.5
60	.3	114	2.5
90	.4	120	3.5
96	.5	180	9.5
102	.8		

Summary

The hypophosphorous acid reduction of diazonium salts is catalyzed by traces of oxidizing agents and inhibited by small amounts of quinones. This, in conjunction with other facts, leads to the conclusion that the reduction of diazonium salts by hypophosphorous acid is a free radical chain reaction. A detailed mechanism is presented.

WEST LAFAYETTE, INDIANA RECEIVED SEPTEMBER 6, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Cleavage of the Carbon–Sulfur Bond. Rates of Hydrolysis of Some Alkyl Acetates and the Corresponding Thiolacetates in Aqueous Acetone

BY PAUL N. RYLANDER AND D. STANLEY TARBELL

This paper describes the results of a kinetic study of the hydrolysis of a series of thiolacetates and the corresponding oxygen esters in aqueous acetone, and is a continuation of work on the cleavage of the carbon–sulfur bond being carried out in this Laboratory.[1]

The only previous quantitative work on the hydrolysis of thiolesters is the recent research of Schaefgen[2] on the hydrolysis of ethyl thiolacetate in aqueous acetone. This medium was also used in the present study, because its solvent properties were satisfactory over the range of composition studied, and the measurements were not complicated by back-reactions or exchange reactions. The compounds investigated were the methyl, ethyl, isopropyl, isobutyl and *t*-butyl acetates, and the corresponding thiolacetates. The rates of hydrolysis were measured under basic conditions with sodium hydroxide, and under acidic conditions with hydrochloric acid as catalyst.

Experimental

Preparation of Materials.—Methyl, ethyl, isopropyl and isobutyl thiolacetate were prepared by dropping the appropriate mercaptan slowly into excess acetyl chloride. The resulting solution was diluted with ice, the layers separated, and the ester layer was washed with saturated sodium bicarbonate solution and with water. The thiolester was dried over Drierite, and fractionally distilled twice from anhydrous potassium carbonate through an efficient column. The center fraction which was collected each time boiled over a range of less than 1°. The observed properties are tabulated below.

ALKYL THIOLACETATES, CH_3COSR

R	B. p., °C., 760 mm.	$n^{22.5}$D	d^{30}_4
CH_3[a]	95–96	1.4661	1.0111
$(CH_3)_2CH$[b]	126–127	1.4502	0.9322
$(CH_3)_2CHCH_2$[c]	151–152	1.4555	.9291
$(CH_3)_3C$[d]	38 (14 mm.)	1.4490	.9290

[a] Wenzel and Reid, THIS JOURNAL, **59**, 1089 (1937), report b. p. 98° (760 mm.); n^{25}D 1.4600; d^{25}_4 1.0170. [b] Ralston and Wilkinson, *ibid.*, **50**, 2160 (1928), report the b. p. as 122–123°. [c] The same b. p. is given by Ipatieff and Friedman, *ibid.*, **61**, 71 (1939). [d] Rheinboldt, Mott and Motzkus, *J. prakt. Chem.*, **134**, 274 (1932), report the b. p. as 31–32° (11 mm.).

***t*-Butyl Thiolacetate.**—This compound was prepared in about 20% yield by the method described for *t*-butyl acetate.[3] The low yield was probably due to mechanical difficulties. The thiolester prepared by this method was used in the kinetic study.

The following modification of the above method gave quite satisfactory yields. Eighty-seven grams (1.10 moles) of dry pyridine was dissolved in 400 cc. of dry chloroform and the solution cooled in an ice-bath. To this was added 86 g. (1.10 moles) of acetyl chloride drop by drop with cooling and constant stirring. When done in this manner the resulting solution was nearly colorless. *t*-Butyl mercaptan (90.2 g., 1.00 mole) was added dropwise over several hours, and the solution allowed to warm spontaneously by standing overnight. Water was added, the layers separated and the chloroform layer washed with water, 10% sulfuric acid, saturated sodium bicarbonate, and again with water. It was dried over Drierite and anhydrous potassium carbonate, and fractionally distilled. The yield was 81% of material with a b. p. of 38° (14 mm.).[4]

The oxygen esters were dried over calcium chloride, then over Drierite, and were twice fractionally distilled through an efficient column from potassium carbonate, the center fraction being collected each time. The physical properties agreed well with those in the literature.

The acetone-water mixtures were made up by mixing the correct quantity of boiled distilled water and purified acetone. The acetone was purified by distillation from potassium permanganate, followed by drying the distillate over anhydrous potassium carbonate, and fractionation through an efficient column from potassium carbonate.

---

(1) Harnish and Tarbell, THIS JOURNAL, **70**, 4123 (1948).

(2) Schaefgen, *ibid.*, **70**, 1308 (1948).

(3) Hauser, *et al.*, "Organic Syntheses," Vol. 24, p. 19.

(4) The preparation of this compound, in unspecified yield, by the action of acetyl chloride on mercury *t*-butyl mercaptide, has been reported by Rheinboldt, Mott and Motzkus, *J. prakt. Chem.*, **134**, 274 (1932).