this was prepared according to Smith and Brown[8] (also Bergmann, *et al.*[21]) a solid was obtained which recrystallized slowly from methanol–water as matted needles, m.p. 124–128°. This solid gave a neutralization equivalent of approximately 370 (calcd. for $C_{17}H_{17}NO_4$: 299) which was not lowered by prolonged drying *in vacuo*. If this solid was dissolved in ether, and the ethereal solution was washed with 1 *N* hydrochloric acid, and water, and dried over magnesium sulfate, evaporation of the ether gave an oil with a neutralization equivalent of approximately 310. **Carbobenzoxy-L-phenylalanine** was therefore prepared by acylation of L-phenylalanine in 2 *N* sodium hydroxide solution as described,[8,21] but after acidification the crude product was extracted into ether. This ethereal solution was washed with 1 *N* hydrochloric acid and water, and dried over anhydrous magnesium sulfate. Evaporation of the ether gave an oil. On the basis of the neutralization equivalent of the oil, the yield of carbobenzoxy-L-phenylalanine was 95%. This oil was then converted to the acid chloride as described,[8,21] and the remainder of the preparation of L-phenylalanyl-L-leucine was the same as the procedure described for D-phenylalanyl-D-leucine. The peptide was recrystallized from 50% ethanol (30 mg. per ml.) or absolute ethanol (10 mg. per ml.). Because of the above modification, the over-all yield from L-phenylalanine was 40% instead of 12%; m.p. 255–258°; $[\alpha]^{22}\mathrm{D}$ +7.5° (*c* 1, 0.10 *N* hydrochloric acid); $[\alpha]^{22}\mathrm{D}$ −21° (*c* 1, 1% sodium bicarbonate solution).

GENEVA, NEW YORK

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(21) M. Bergmann, L. Zervas, H. Rinke and H. Schleich, *ibid.*, **224**, 33 (1934).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Chemistry of Diazo Compounds. III. The Reduction of Diazonium Salts by Phosphorous Acid[1]

BY NATHAN KORNBLUM, ALEC E. KELLEY[2] AND GLENN D. COOPER[2]

Treatment of diazonium salts with phosphorous acid results in replacement of the diazonium group by hydrogen; this reaction is subject to catalysis by certain oxidizing agents. It is a much less efficient way of replacing the diazonium group by hydrogen than the procedure employing hypophosphorous acid. The synthesis of pentabromobenzenediazonium hydrogen sulfate is described.

The reduction of diazonium salts by hypophosphorus acid is an excellent way of replacing the

$$\text{Aryl-N}_2{}^+\ \text{X}^- \xrightarrow{H_3PO_2} \text{Aryl-H} + \text{N}_2$$

diazonium group by hydrogen.[1] Since phosphorous acid is also a strong reducing agent[3] its action upon four rather diverse diazonium salts was studied. Although phosphorous acid is able to replace the diazonium group by hydrogen, it turns out to be distinctly inferior to hypophosphorus acid for this purpose.

In every case studied the reduction with phosphorous acid is very much slower than with hypophosphorous acid. This provides an opportunity for competing processes to intervene, and notably in the case of the relatively unstable *p*-tolyldiazonium chloride[4] a large disparity in the yields of toluene results. With the more stable diazonium salts reduction by phosphorous acid is capable of giving good yields of reduced product, although it may be necessary to resort to catalysis (see below). In no instance, however, is there any advantage to the use of phosphorous acid in preference to hypophosphorous acid. Table I summarizes the best results obtained with phosphorous acid and compares them with those resulting from the use of hypophosphorous acid.

TABLE I

REDUCTION OF DIAZONIUM SALTS BY H_3PO_2 AND BY H_3PO_3

Salt	Product	Yield with H_3PO_2, %	Yield with H_3PO_3, %
Pentabromobenzenediazonium hydrogen sulfate	Pentabromobenzene	81[a]	63[b]
p-Methoxybenzenediazonium chloride	Anisole	80[c]	71[d]
p-Nitrobenzenediazonium chloride	Nitrobenzene	65[c]	56[d]
p-Tolyldiazonium chloride	Toluene	72[c]	11[d]

[a] Reaction time 10 minutes at 13.8°. [b] Reaction time 4 hours at 25°. [c] Reaction time 24 hours at 0°. [d] Catalysis by ether peroxide required; see Table II.

Since the hypophosphorous acid reduction of diazonium salts is strongly catalyzed by small amounts of potassium permanganate or copper sulfate,[1] the effect of these reagents on phosphorous acid reductions was briefly investigated. At 0° the reaction between pentabromobenzenediazonium hydrogen sulfate and phosphorous acid is unmistakably speeded up by the addition of as little as ten mole per cent.[5] of potassium permanganate; copper sulfate, however, has no effect at the ten mole per cent. level. Furthermore, when five mole per cent. of copper sulfate is added to a solution of *p*-tolyldiazonium hydrogen sulfate in phosphorous acid at 0° there is no catalysis.

Catalysis by a novel oxidizing agent was observed in the phosphorous acid reductions. Except for pentabromobenzene the various reduction products are liquids, and their isolation from the reaction mixtures entails extraction with diethyl ether. It was found that subsequent to this ether extraction further quantities of the various reduction products were formed.[6] Evidence in support of the hypothesis that ether peroxide is responsible for this catalysis is provided by the following experi-

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(1) Paper II in this series: N. Kornblum, G. D. Cooper and J. E. Taylor, THIS JOURNAL, **72**, 3013 (1950).

(2) X-R Fellows of the Purdue Research Foundation.

(3) Don M. Yost and H. Russell, "Systematic Inorganic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1946, p. 200.

(4) M. L. Crossley, R. H. Kienle and C. H. Benbrook, THIS JOURNAL, **62**, 1400 (1940).

(5) "Mole per cent." refers to the number of moles of catalyst per one hundred moles of diazonium salt.

(6) The H_3PO_2 reductions are so rapid that by the time the ether extractions were carried out the diazonium salts had been completely reduced. Hence there was no opportunity for catalysis.

ment. A solution of *p*-methoxybenzenediazonium chloride was divided into two equal portions, and one of these was allowed to react with phosphorous acid for 20 days at 25°. At the end of this time a 25% yield of pure anisole was obtained. When the phosphorous acid solution which remained after ether extraction was allowed to stand for ten days at 25°, an additional 42% yield of pure anisole was obtained. In contrast, treatment of the other half of the *p*-methoxybenzenediazonium solution with phosphorous acid in the presence of ether peroxide[7] for 20 days at 25° gave a 67% yield of pure anisole. On standing an additional ten days at 25° the phosphorous acid solution which remained after ether extraction produced a negligible amount of anisole. As shown in Table II, these are not isolated instances of catalysis by ether peroxide.

TABLE II

PHOSPHOROUS ACID REDUCTION OF DIAZONIUM SALTS CATALYZED BY ETHER PEROXIDE[a]

Salt, chloride	Product	Yield before extraction, %	Yield after extraction, %
p-Methoxybenzenediazonium	Anisole	9 after 7 days	62 after 23 days
		25 after 20 days	42 after 10 days
		67[b] after 20 days	<1 after 10 days
		35 after 30 days	....
p-Nitrobenzenediazonium	Nitrobenzene	4[c] after 13 days	52 after 1 day
p-Tolyldiazonium	Toluene	<2[d]	....
		....	11[e]

[a] Reaction temp. 25° unless otherwise specified. [b] Ether peroxide added; see footnote 7. [c] Reaction temp. 0°. [d] Reaction temp. 0° for 1 day followed by 5 days at 25°. [e] Following 1 day at 0° the reaction was ether extracted and then allowed to stand 4 days at 25°, at which time it was again extracted. From the combined extracts an 11% yield was obtained. We are indebted to Dr. D. C. Iffland for this experiment.

The ability of potassium permanganate and of ether peroxide to catalyze the phosphorous acid reduction of a diazonium salt suggests that this reaction follows the same general pattern as the hypophosphorous acid reduction of diazonium salts.[1]

Experimental[8]

Preparation of Pentabromobenzenediazonium Hydrogen Sulfate.[9] (a) **2,6-Dibromo-4-nitroaniline.**—*p*-Nitroaniline was brominated according to Holleman[10a]; yield 97%; m.p. 202–204°; lit. values 204°,[11] 203°.[12]

(b) **3,5-Dibromonitrobenzene.**—Powdered sodium nitrite (105 g., 1.5 moles) was added in small portions to 200 ml. of 96% sulfuric acid with gentle stirring; the temperature was maintained at −5 to 0°. A solution of 139 g. (0.470 mole) of 2,6-dibromo-4-nitroaniline in 200 ml. of 96% sulfuric acid was added dropwise with stirring, the temperature being held below 5°. Stirring was continued for four to six hours in the ice-bath. The solution was then poured, with vigorous stirring, into a mixture of 660 g. (5 moles) of 50% hypophosphorous acid and 2000 g. of ice; considerable foaming occurred. The mixture was allowed to stand for several hours in an ice-bath with occasional stirring, and then overnight at room temperature. The brown solid was filtered off, washed with water and dried at around 50°. The dark brown amorphous solid was twice extracted with 200-ml. portions of boiling ethanol. Brown crystals separated on cooling the solution to 0°. A further small crop of crystals was obtained on evaporating off most of the solvent. Upon distilling the combined crops of crystals at 3 mm. a yellow-green solid was obtained; b.p. 112°. This, upon recrystallization from ethanol, gave 80 g. (61% yield) of pale yellow crystals; m.p. 105–106°, Meyer[13] reports m.p. 106°.

(c) **3,5-Dibromoaniline.**—3,5-Dibromonitrobenzene (193 g.), was reduced with 230 g. of precipitated iron, 6 liters of water and a total of 45 ml. of 96% sulfuric acid essentially according to Holleman.[10b] The product obtained on distillation at 3 mm. (b.p. 118°) was recrystallized from 35–37° petroleum ether. White needles (152 g., 90%) were obtained; m.p. 55–56°, lit. values 57°,[14] 56.5°.[15]

(d) **Pentabromoaniline.**—Bromination of 3,5-dibromoaniline in aqueous acetic acid gave an 80–85% yield of pentabromoaniline, m.p. 265–266° (from two volumes toluene and one volume ethanol); lit. value,[16] 261–262°.

(e) **Pentabromobenzenediazonium Hydrogen Sulfate.**—Four grams of pentabromoaniline was dissolved in 1400 ml. of hot absolute ethanol. The solution was cooled to room temperature and 40 ml. of 96% sulfuric acid was added. The solution was again cooled to room temperature and 40 ml. of freshly-prepared isoamyl nitrite was added in one portion. After one hour at room temperature a test portion of the yellow solution gave no immediate precipitate on dilution with water. The solution was allowed to stand at room temperature for another 30 minutes and then 1500 ml. of ether was added. The fine yellow precipitate thus produced was allowed to settle and most of the supernatant liquid was removed by decantation.

The precipitate was isolated by centrifugation and then washed several times with ether. The ether-wet material was kept overnight at 0° and a pressure of 2 mm. The yield of dry yellow powder was 2.9 g. (59%).

Anal. Calcd. for $C_6HBr_5N_2O_4S$: $SO_4^{=}$, 16.08; N, 4.69. Found: $SO_4^{=}$, 15.93, 16.10; N,[17] 4.68, 4.65.

Reduction of Pentabromobenzenediazonium Hydrogen Sulfate. (a) Uncatalyzed.—At room temperature 0.75 g. (0.00125 mole) of pentabromobenzenediazonium hydrogen sulfate was dissolved in 50 ml. of water, and to this, 50 ml. of an aqueous solution containing 20.5 g. (0.25 mole) of phosphorous acid was added. Gas was evolved slowly and a tan precipitate formed. After four hours at 25° the precipitate was filtered off and dried. Recrystallization from ethanol yielded 0.37 g. (63%) of pentabromobenzene; m.p. 158–159°. A mixed m.p. with an authentic sample of pentabromobenzene, m.p. 158–159° was undepressed. Jacobson and Loeb[16] reported 159–160° as the m.p.

Repetition of this experiment using hypophosphorous acid at 13.8° resulted in an 81% yield of pure pentabromobenzene, m.p. 160–161°. A reaction time of ten minutes was employed although nitrogen evolution was complete in three minutes.

Anal.[17] Calcd. for C_6HBr_5: C, 15.2. Found: C, 14.9.

(b) **Catalyzed by Potassium Permanganate.**—Using 1.49 g. (0.0025 mole) of pentabromobenzenediazonium hydrogen sulfate, 50 ml. of water and 50 ml. of a solution containing 20.5 g. (0.25 mole) of phosphorous acid the reaction was allowed to proceed at 0° with the addition of potassium permanganate as indicated in Table III. The rate of this reaction was followed by measuring the volume of nitrogen evolved.

After 18 hours the precipitate was isolated by filtration and dried. Vacuum sublimation followed by recrystallization from ethanol gave 0.58 g. (45% yield) of pentabromobenzene; m.p. and mixed m.p. 158–159°.

When ten mole per cent. of copper sulfate was substi-

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[7] Two liters of diethyl ether were evaporated under a jet of air to a volume of *ca.* 10 ml. (a test portion gave an immediate strong positive reaction for peroxide with neutral potassium iodide solution). The diazonium solution and phosphorous acid were immediately added to this peroxide residue.

[8] All m.ps. corrected.

[9] A. Hantzsch and J. S. Smythe [*Ber.*, **33**, 505 (1900)] reported that this diazonium salt could be isolated only in very poor yield; they did not report any analysis of their pentabromobenzenediazonium hydrogen sulfate.

[10] (a) A. F. Holleman, *Rec. trav. chim.*, **25**, 194 (1906); (b) *ibid.*, **25**, 186, 195 (1906).

[11] C. Wurster and E. Noelting, *Ber.*, **7**, 1564 (1874).

[12] A. E. Smith and K. J. P. Orton, *J. Chem. Soc.*, **91**, 149 (1907).

[13] R. Meyer, W. Meyer and K. Taeger, *Ber.*, **53**, 2042 (1920).

[14] D. Vorländer and E. Siebert, *ibid.*, **52**, 293 (1919).

[15] G. Körner, *Gazz. chim. ital.*, **4**, 368 (1874).

[16] P. Jacobson and A. Loeb, *Ber.*, **33**, 703 (1900).

[17] Microanalyses by Dr. H. Galbraith, of this Department.

TABLE III

REDUCTION OF PENTABROMOBENZENEDIAZONIUM HYDROGEN SULFATE BY PHOSPHOROUS ACID

Time (hours)	Theoretical amount N_2 evolved, %	Time (hours)	Theoretical amount N_2 evolved, %
0.5	0	15.0	57.7
3.0[a]	0	16.0[b]	58.9
3.5	7.0	17.0[b]	62.5
4.5	28.5	18.0	66.0
5.0	38.0		

[a] At this point 0.04 g. (0.00025 mole) of potassium permanganate in 2 ml. of water was added. [b] At this point 0.02 g. (0.000125 mole) of potassium permanganate in 1 ml. of water was added.

tuted for potassium permanganate in the above experiment it was completely ineffective as a catalyst.

Five mole per cent. of copper sulfate was also without effect in a similar experiment wherein crystalline *p*-tolyldiazonium hydrogen sulfate was treated with aqueous phosphorous acid at 0°.

Reduction of *p*-Nitrobenzenediazonium, *p*-Tolyldiazonium and *p*-Methoxybenzenediazonium Chlorides.—Here the diazonium salts were not isolated. In order to ensure that any differences observed between reductions employing hypophosphorous acid and phosphorous acid were not due to variations in the composition of the diazonium solution, the diazonium solutions were prepared at 0° from 0.4 mole of amine, 1.2 moles of hydrochloric acid, and 0.4 mole of sodium nitrite; the final volumes of these diazonium solutions were *ca.* 750 ml. Such a solution was divided in half, and one portion treated with hypophosphorous acid, the other with phosphorous acid. In the hypophosphorous acid reductions 320 ml. of the ice-cold 50% solution (3 moles H_3PO_2) was added. In the phosphorous acid reductions 3 moles of the acid in 330 ml. of solution were employed; after adding the phosphorous acid at 0° the reaction mixture was brought to the desired temperature.

The reactions were allowed to proceed at either 0 or 25° for varying lengths of time (*cf.* Table II), and then the organic phase was isolated by extraction with diethyl ether. The ether extracts were washed with aqueous sodium hydroxide, then dried and distilled. The yields reported in Tables I and II refer to carefully purified products whose physical constants agree with the literature values. In the phosphorous acid reductions the aqueous phase was then allowed to react further as indicated in Table II, and the additional reaction product was isolated as before.

In the various reductions of *p*-methoxybenzenediazonium chloride by phosphorous acid an appreciable amount of crystalline residue remained after distillation of the anisole. Recrystallization from petroleum ether and then from absolute ethanol gave *ca.* 0.3 g. of yellow crystals of 4,4'-dimethoxyazobenzene, m.p. 164–164.8°; lit. m.p.[18] 164°, 165°.

Anal. Calcd. for $C_{14}H_{14}O_2N_2$: N, 11.6. Found: N, 11.6.

In the reductions by hypophosphorous acid smaller amounts of a similar solid residue were obtained but were not investigated.

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(18) D. Vorländer, *Ber.*, **71**, 1692 (1938); C. Weygand and R. Gabler, *ibid.*, **71**, 2399 (1938).

LAFAYETTE, INDIANA RECEIVED DECEMBER 10, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Basis for the Report that Rearrangements Occur when Cyclopentyl Iodide and Cyclohexyl Iodide React with Silver Nitrite[1]

BY NATHAN KORNBLUM AND CHARLES TEITELBAUM[2]

RECEIVED DECEMBER 18, 1951

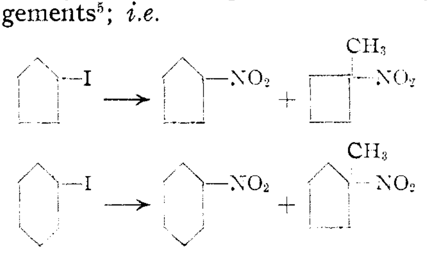
The report that cyclopentyl and cyclohexyl iodides on treatment with silver nitrite give rearranged tertiary nitro compounds, in addition to the expected secondary nitrocycloparaffins, has been investigated. No rearranged products were found. Instead, pure cyclopentyl and cyclohexyl nitrates were isolated.

For many years it was believed that the reaction of silver nitrite with alkyl halides yields only the nitroparaffin and the alkyl nitrite.[3]

$$RX + AgNO_2 \longrightarrow R{-}NO_2 + R{-}O{-}N{=}O + AgX \quad (1)$$

In 1947, however, it was found that when 2-bromooctane is treated with silver nitrite 2-nitroöctane, 2-octyl nitrite, 2-octyl nitrate, 2-octanol, 2-octanone and other, unidentified, products are formed.[4] Analogous results were obtained with 2-iodobutane. Of special interest in connection with the present study is the fact that in neither case could the nitrate ester be removed from the nitro compound by rectification.

In 1915 Rosanow reported the results of experiments in which cyclopentyl iodide and cyclohexyl iodide were treated with silver nitrite. In each instance he obtained an alkali-insoluble substance, isomeric with the expected nitrite ester and nitroparaffin, yet unmistakably different from these. He concluded that the alkali-insoluble substances were tertiary nitro compounds resulting from rearrangements[5]; *i.e.*



(2)

(3)

This claim that rearrangements occur is of considerable importance in evaluating the reaction of silver nitrite with organic halides as a means of ob-

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[1] (1) This is the fourth paper in the series. Paper III, N. Kornblum and G. Graham, THIS JOURNAL, **73**, 4041 (1951).

[2] (2) Atomic Energy Commission Fellow 1949–1950.

[3] (3) V. Meyer and O. Stuber, *Ber.*, **5**, 203 (1872); G. Schmidt, *J. Chem. Ed.*, **27**, 557 (1950).

[4] (4) N. Kornblum, N. N. Lichtin, J. T. Patton and D. C. Iffland, THIS JOURNAL, **69**, 307 (1947); N. Kornblum, J. T. Patton and J. B. Nordmann, *ibid.*, **70**, 746 (1948).

[5] (5) (a) N. A. Rosanow, *J. Russ. Phys. Chem. Soc.*, **47**, 591 (1915); (b) *ibid.*, **48**, 309 (1916) (*Chem. Zentr.*, **87**, I, 925 (1916); *ibid.*, **95**, I, 2425 (1924).