crystalline solids. In particular, the experimental results justify the following conclusions:

1. The covalence of sodium, potassium, chlorine in chlorides, is zero.
2. The covalence of the central atom is 4 in nitrates, carbonates, sulfates, perchlorates, phosphates, permanganates, chromates, selenates, arsenates, borofluorides, etc.
3. Carbonates and sulfites are not isomorphous, the covalence of the central atom being 4 and 3, respectively.
4. Nitrates and chlorates are not isomorphous, the covalency of the chlorine being 3 in chlorates.
5. The applicability of the octet theory to complex inorganic compounds receives further confirmation by its ability to explain such cases of isomorphism as between Na_2BeF_4 and $MnCl_2.4H_2O$; K_2SO_4 and $ZnI_2.4NH_3$, $K_2SnCl_4.2H_2O$ and $K_2FeCl_5.H_2O$, $NaAlSi_3O_8$ and $CaAl_2Si_2O_8$, etc.

SCHENECTADY, N. Y.

[CONTRIBUTION FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

A STUDY OF SIDE CHAIN OXIDATIONS WITH POTASSIUM PERMANGANATE.[1]

BY LUCIUS A. BIGELOW.

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I. Introduction. II. Discussion of the Oxidation of *o*-, *m*-, and *p*-nitrotoluene. III. Experimental and Summary.

I. Introduction.

A careful review of the chemical literature upon potassium permanganate and its reactions reveals certain fundamental facts which are important both as a summary of our knowledge of the subject to date, and as a necessary introduction to an investigation in this particular field. These facts, which have been established, may briefly be expressed as follows:

1. Potassium permanganate, in concentrated aqueous solution, when treated with caustic alkali of sufficient strength and heated, spontaneously decomposes into potassium manganate and free oxygen.[2]

2. During most permanganate oxidations more or less free oxygen is evolved, and this evolution is caused by the presence of the lower oxides of manganese, or their compounds. Spontaneous decomposition of aqueous potassium permanganate solutions, with the production of free oxygen, is always brought about by the presence of these lower oxides, but does not

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[1] This paper has been constructed from a dissertation presented by the author in 1919 to the Faculty of the Graduate School of Yale University in partial fulfilment of the requirements for the Degree of Doctor of Philosophy.—T. B. JOHNSON.

[2] Åschoff, *J. prakt. Chem.*, [1] 81, 29 (1860); Wanklyn and Cooper, *Phil. Mag.*, [5] 7, 138 (1879); Sackur and Taegner, *Z. Elektrochem.*, 18, 718 (1912).

occur in their absence. The researches of Morse and his students,[1] supported by the work of many other investigators, have established these facts, although some contrary evidence has been presented.[2] The mechanism of the reactions to which the oxygen evolution is due has not been satisfactorily explained. One suggestion offered is to the effect that manganese dioxide, if precipitated, polymerizes at the expense of permanganic acid, liberating the oxygen from the latter.[3]

3. The decomposition of potassium permanganate, in aqueous solution, is stimulated by an increase in concentration, or a rise in temperature.[4]

4. Benzene derivatives of various structures, even those with the same substituents, but in different positions, show wide differences in susceptibility to oxidation by potassium permanganate and other oxidizing agents; yet these phenomena show little regularity. Remsen's law,[5] which does not by any means hold in all cases, seems to be the only important generalization which has been made in this field.

5. When organic compounds are oxidized by potassium permanganate in alkaline solution, an increase in the concentration of the alkali present may produce distinctly different effects in different cases.[6]

6. Catalyzers may greatly affect permanganate reactions.[7]

Insofar as I have been able to determine from the literature, no systematic attempt has been made to determine the manner in which the progressive variation of the conditions influencing the oxidation of any given series of aromatic compounds affects the products of such reactions. This applies both to the yields obtained and to the amounts of unchanged material recovered in the process. Moreover, most of the work described in the literature which in any way bears upon the subject, has been carried out with relatively very small quantities of material. It has been my object, in this investigation, to select a definite series of aromatic compounds, with an aliphatic side chain, and to submit this side chain to oxidation by potassium permanganate, in alkaline solution, in such a manner as to make possible a study of the influence of conditions upon the reactions. There have been taken into consideration not only the

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[1] Morse, Hopkins and Walker, *Am. Chem. J.*, 18, 401 (1896); Morse and Reese, *Ibid.*, 20, 521 (1898); Morse and Byers, *Ibid.*, 23, 313 (1900); Brand and Ramsbottom, *J. prakt. Chem.*, [2] 82, 382 (1910); Gooch and Danner, *Am. J. Sci.*, [3] 44, 301 (1892).

[2] Meyer and von Recklinghauser, *Ber.*, 29, 2549 (1896); Hirtz and Meyer, *Ibid.*, 29, 2828 (1896).

[3] Morse and Byers, *Am. Chem. J.*, 23, 313 (1900).

[4] Brand and Ramsbottom, *J. prakt. Chem.*, [2] 82, 382 (1910); Morse and Reese, *Am. Chem. J.*, 20, 521 (1898).

[5] Remsen, *Am. Chem. J.*, 1, 36 (1879); Remsen and Palmer, *Ibid.*, 4, 142 (1882); Richard Meyer, *Ann.*, 220, 16 (1883).

[6] Behrend, *Ann.*, 333, 159 (1904); Witzemann, THIS JOURNAL, 38, 150 (1916); Evans and Day, *Ibid.*, 38, 375 (1916).

[7] Doroschevski and Pavlov, *J. Chem. Soc.*, [2] 110, 24 (1916).

quantity and rate of addition of the oxidizing agent, but also the alkalinity of the oxidizing mixtures, the concentration and temperature of the solutions, and the influence of certain catalyzers. The work has been carried out on a moderately large laboratory scale, and it is hoped that the results may be of some value in the practical application of potassium permanganate as an oxidizing agent.

II. Discussion of the Oxidation of *o*-, *m*- and *p*-Nitrotoluenes.

For this work the 3 nitrotoluenes were selected as representative examples of aromatic side chain compounds to be submitted to oxidation by potassium permanganate. They were chosen for 3 reasons: (1) They are available in quantity, and each of them undergoes oxidation readily to the corresponding acid. (2) They constitute a typical series of disubstituted benzene derivatives, hence a study of their relative properties might throw some further light upon the benzene problem. (3) Two of the products of oxidation, *o*-, and *p*-nitrobenzoic acids, are of possible technical value; the former in the synthesis of dyes, and the latter in the manufacture of pharmaceuticals.

While the *o*- and *p*-nitrotoluenes can readily be purchased upon the market, the *m*-compound was not available in this way, and had to be synthesized in the laboratory. The only synthesis already described which seemed suitable for this purpose was that starting from *m*-nitro-*p*-toluidine, $C_6H_3(CH_3)(NO_2)(NH_2)$, which is converted into *m*-nitrotoluene by diazotization and reduction, substituting the amino group by hydrogen. The nitrotoluidine is best prepared from commercial *p*-toluidine, by acetylation, nitration, and subsequent saponification. All these reactions have been carefully studied, with the idea of establishing the best conditions under which they may be carried out, in order to obtain good yields with a minimum quantity of reagents and the smallest expenditure of time and effort. It has been found possible to effect the nitration by means of a small quantity of a "mixed acid" consisting of ordinary conc. nitric and sulfuric acids; while the diazotization and reduction take place much more smoothly in the presence of a small amount of copper powder, which acts as a catalytic agent. A practical laboratory method for carrying out the synthesis is described in the Experimental Part.

The oxidation of the nitrotoluenes, the study of which constitutes the main problem under investigation, was entirely carried out in alkaline or nearly neutral solutions. The plan has been not so much to attain the highest possible purity of product upon a very small scale, as to make a product of high commercial quality in relatively large quantities. The reactions have been studied from the point of view of the investigator who desires to synthesize considerable amounts of material, or to acquire data of value in a commercial application of the reactions involved.

It has been found that every influence that has been studied, which can be brought to bear upon the oxidation of the nitrotoluenes with alkaline potassium permanganate, has a marked effect upon the results obtained. While it might naturally be expected that entirely different kinds of changes in the conditions of oxidation would produce widely different types of changes in the results, this is not the case. Whatever change of conditions was made, it was found, in general, that the result was merely to cause a *different proportion* of the nitrotoluene present to be attacked by the oxidizing agent. The yield in grams of nitrobenzoic acid is altered, but the weight of unchanged nitrotoluene recovered is also altered, in the inverse direction, and in such a manner that the sum of the two remains not far from a *constant quantity*. This holds true to a striking extent, notwithstanding the fact that certain changes of procedure do cause the "constant," as well as the quality of the product, to vary somewhat.

These facts plainly enable us to draw two important conclusions with regard to the oxidations, as follows: First, the quantity of nitrotoluene, or of nitrobenzoic acid, entirely destroyed by the oxidizing agent, is essentially constant for each nitrotoluene, and is not greatly affected by changes in the oxidation procedure. Second, inasmuch as the permanganater, usually present in excess, is in all cases entirely reduced, at least *two entirely independent changes* take place at the same time in the reacting mixture, namely, the oxidation of the organic compound, and the decomposition of the permanganate into manganese oxides and free oxygen. The effect of altering the conditions or procedure is thus either to *accelerate* or to *retard one* or the *other* of these changes, which will cause a greater or less proportion of the nitrotoluene to be converted into the corresponding acid *before* the whole of the permanganate present has been reduced. It has been well established that permanganate is nearly always decomposed with the evolution of oxygen when in the presence of any of the oxides of manganese, and these must of necessity be present in the alkaline reacting mixture as soon as any of the permanganate has been reduced by the organic matter present. It has been shown, however, that if a solution containing alkali and permanganate, in the proportions most frequently employed in this work, is boiled for a prolonged period, no decrease in its oxidizing power can be detected provided it contains no organic matter, and no suspended oxides of manganese.

Turning now to a consideration of the influence upon the reaction of the specific changes of conditions which have been studied, it is found that increasing the concentration of alkali in the oxidizing mixture up to a certain point *favors* the oxidation of *o*-nitrotoluene, beyond which point a further increase produces essentially no effect, all other conditions being kept constant. By this increase in alkaline concentration the oxidation of the *meta* compound is *hindered*, such oxidation being most effective in an essentially neutral medium; while that of the *para* isomer is *favored* up to a certain point, beyond which the quality of the product becomes very poor. In all probability, then, the presence of alkali on the one hand accelerates considerably the oxidation of the *o*- and *p*-nitrotoluene, and does not so much affect that of the *m*-nitrotoluene; while on the other hand it accelerates to a certain extent the decomposition of the permanganate. It is plain that if the alkali accelerates the oxidation of the *o*- and the *p*-nitrotoluenes more than it does the decomposition of the permanganate, the oxidation of these compounds will be favored by increasing concentrations of alkali; while if the oxidation of the *meta* isomer is not accelerated as much as the decomposition of the oxidizing agent, the oxidation of this derivative will be hindered by the presence of alkali.

The fact that the oxidation of the *o*- and *p*-compounds is so much more accelerated by the alkali than that of the *m*-compound, suggests to the writer that this difference in behavior is due to the difference in molecular construction of the 3 isomers. It is well known that aromatic combinations which can assume a quinoid structure are more susceptible to chemical attack than those which must retain the benzenoid form. Theoretically, especially in the presence of alkali, both *o*- and *p*-nitrotoluene can assume a quinoid structure, while no such configuration can be assigned to the *m*-compound. Consequently it seems logical to assume that the difference in chemical behavior may be due to these tautomeric changes.

Again, there is some evidence in the literature[1] to the effect that the presence of alkali in a solution in which potassium permanganate is reduced affects the physical state of the oxides of manganese precipitated. It is known that these oxides are very active in inducing the decomposition of permanganate, so that it seems reasonable to assume that the concentration of alkali, in our oxidations, might affect the rate of decomposition of the oxidizing agent. In all cases it has been found that alkali increases the rate of reaction. This is in accord with the assumptions which have been made regarding the quinoid structure in the cases of the *o*- and *p*-nitrotoluenes, and the increased rate of decomposition of the permanganate in the case of the *m*-isomer.

An increasing dilution of the reaction mixture favors the oxidation of all the nitrotoluenes, which is quite what would be expected from the statement in the literature that an increasing concentration of a permanganate solution stimulates the decomposition of the permanganate into manganese oxides and free oxygen. Highly concentrated, alkaline oxidation mixtures very rapidly become deep green, indicating the decompostition of the permanganate directly into manganate and free oxygen. It was found in the oxidation of the *p*-nitrotoluene that an in-

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[1] Jones, *J. Chem. Soc.*, 33, 95 (1878).

creasing quantity of permanganate in excess of the theoretical quantity favors the reaction up to a 10% excess, but not beyond this. A greater quantity of permanganate merely oxidizes nitrotoluene without increasing the yield of nitrobenzoic acid. The 10% excess also seems to give a better quality of product, and was arbitrarily adopted in the oxidation of the other nitrotoluenes. While most of the oxidations described in this investigation were carried out at the boiling temperature of the reacting mixture, the influence of lowering the temperature was studied in the case of the *p*-nitrotoluene. The yield obtained was considerably decreased, and the time of oxidation greatly increased by this procedure. This shows that while lowering the temperature decreases the rate of decomposition of the permanganate into manganese oxides and free oxygen, it decreases the rate of oxidation of the *p*-nitrotoluene to an even greater extent.

Catalytic influences upon the reaction have been studied in the oxidation of *o*- and *p*-nitrotoluenes, by carrying these out in 3 different types of container, one of iron, one of copper, and one lined with enamel, which is the equivalent of one of glass. It was found that in both cases nearly the same results were obtained in the copper and the enamel lined containers; but distinctly lower yields, and products of poorer quality, in the iron container, both with and without alkali. Evidently the metallic iron catalyzes the decomposition of permanganate. The addition of salts of calcium and magnesium to the reaction mixture in the oxidation of *p*-nitrotoluene in neutral solution produced no noticeable effect; nor did the addition of pyridine to a similar oxidation in alkaline solution, although it acts as a strong negative catalyst in certain permanganate reactions.[1]

Considering the results from the point of view of position in the benzene ring, it has been shown that *p*-nitrotoluene under all conditions is oxidized most readily, the *o*-compound next, and the *m*-isomer least. There seem to be no valid generalizations in the literature upon the relative rates of oxidation of *o*-, *m*-, and *p*-compounds to which these results may be compared intelligently. It appears, however, to be in accord with general experience, that the *o*-compound should oxidize somewhat more slowly than the *p*-isomer, on account of the protective influence of the strongly negative nitro group in the *o*-position to the methyl group (Remsen's law). Why the *m*-isomer should be so resistant to oxidation is quite obscure as yet, although there are some recorded cases[2] in which *m*-disubstituted benzene derivatives show this property. As far as my work has extended, all changes of the conditions of oxidation except one, affect the 3 isomers in the same general way. The exception is the influence of

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[1] Michael and Garner, *Am. Chem. J.*, **35**, 267 (1906).

[2] Bruckner, *Ber.*, **9**, 406 (1876); Renter, *Ibid.*, **17**, 2028 (1894).

alkali, which, as has already been described, stimulates the oxidation of the *o*- and *p*-nitrotoluenes, but retards that of the *m*-derivative.

III. Experimental Part.

The Preparation of Meta-nitrotoluene.

All the nitrotoluene employed in this research was prepared in the laboratory from *p*-toluidine. This base was first converted into its acetyl derivative by digestion with glacial acetic acid and the acetate then subjected to nitration[1] with a mixture of sulfuric and nitric acids. It was found that it was unnecessary to use fuming nitric acid for this operation, and the results of several preliminary experiments showed that the best yields are obtained by nitrating at a temperature of 30 to 40°. The results of a series of nitrations with different proportions of acids are recorded in the table below.

TABLE I.

Nitrations with Different Proportions of Acids.

20 g. of acetotoluide used in each experiment.

Expt.	Sulfuric acid (S. G. 1.84). Cc.	Nitric acid. Cc.	Nitric acid. Mols.	Yield of nitrotoluide. %.	M. P. Degrees.	Character of the product.
1	20	68	8	85	93–4	Good
2	20	59.5	7	85	92–4	Good
3	20	51	6	85	91–2	Not so pure
4	40	42.5	5	77	80–	Impure
5	20	42.5	5	88	88–92	Not very pure
6	10	42.5	5	77	88–93	Fairly good
7	7.5	34	4	78	94–6	Good
8	7.5	25.5	3	78	93–4	Good
9	7.5	22.5	2.6	79	94–5	Good
10	0	22.5	2.6	67	75–90	Very impure
11	7.5	17	2	73	90–4	Good
12	5.0	17	2	62	92–4	Good

It will be observed that the proportions represented in Expts. 8 and 9 are productive of the maximum yield of *m*-nitro-*p*-acetotoluide, $C_6H_3(CH_3)(NO_2)^3(NH.COCH_3)^4$ for a low molecular concentration of nitric acid. The proportions represented in Expt. 8 were finally adopted as most advantageous on the whole, and were used in all nitrations upon a large scale. The product so obtained is of good quality, and the yield of the toluide, 78% of the theoretical, is quite satisfactory. A "mixed acid" made up in the following proportions gives good results: Nitric, 50%; sulfuric, 25%; and water, 25%. Twenty g. of *p*-acetotoluide requires 50.5 g. of this mixture. It has been my experience that this nitration proceeds very quickly and that it is not necessary to let the mixture

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[1] Beilstein and Kuhlberg, *Ann.*, **155**, 24 (1870); Gattermann, *Ber.*, **18**, 1482 (1885); Nolting and Collin, *Ibid.*, **17**, 264 (1884); Noyes, *Am. Chem. J.*, 10, 475 (1888); Reverdin and Le Duc, *Ber.*, **43**, 3460 (1910).

stand longer than 15 minutes after final addition of the acetotoluide to the mixed acids.

The acetyl derivative was hydrolyzed in the usual manner by digestion in alcohol with sodium hydroxide[1] and the nitrotoluidine then subjected to diazotization and reduction with alcohol in order to replace the amino group with hydrogen. A greater or less excess of sodium nitrite had but little effect upon the yield of nitrotoluene produced, and an excess of 20% was adopted as most convenient. I introduced one modification in Buchka's method, namely: the incorporation of copper powder to catalyze the reduction reaction. Although this metal has been used by several investigators, among whom may be mentioned Tobias,[3] St. Von Niementowski,[4] Ullmann and Bieleck[5] to catalyze the evolution of nitrogen from diazo compounds and to effect condensations, there does not seem to appear in the literature any description of its use in a process where reduction of a diazo group with alcohol is applied. I found that the yields of nitrotoluene could be greatly increased by use of the metal, and in the following table are recorded the results of a series of experiments showing its effect.

TABLE II.

Effect of Copper Powder on the Diazotization.

Weight of *m*-Nitro-*p*-toluidine in Each Case, 25 g. Time of Standing after Diazotization; 3 Hours.

Expt.	95% alcohol. Cc.	Sulfuric acid (conc.). Cc.	Nitrite solution, 100 g. $NaNO_2$ in 165 cc. H_2O. Cc.	Copper powder. G.	Yield of *m*-nitrotoluene. %.	Remarks.
1	95	14	22.5	2	73	......
2	95	14	22.5	2	72	Catalyzer added before diazotization
3	95	14	22.5	0	59	Much tar
4	95	14	22.5	12.5	73	Little tar
5	63	14	22.5	2	63	......
6	143	14	22.5	2	53	......
7	95	14	22.5	2	67	......
8	95	55 {HCl sp. gr. 1.20}	33.8	2	82	Product contained chlorine

It has been my experience that the alcohol recovered from a reduction process cannot be used again successfully as the aldehyde impurity interferes with the reaction. Attempts to reduce the diazo compound with stannous chloride in hydrochloric acid solution, or with sodium

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[1] Gatterman, *Loc. cit.;* Noyes, *Ibid.*

[2] Buchka, *Ber.*, **22**, 829 (1889).

[3] *Ber.*, **23**, 1628 (1890).

[4] *Ibid.*, **34**, 3325 (1901).

[5] *Ibid.*, **34**, 2174 (1901).

stannite in alkaline solution were unsuccessful. The exact procedure for carrying out the preparation of nitrotoluene from *m*-nitro-*p*-toluidine may now be summarized as follows:

100 g. of *m*-nitro-*p*-toluidine is added to a mixture of 375 cc. of 95% alcohol and 56 cc. of sulfuric acid, sp. gr. 1.84. The mixture is heated until solution is complete, cooled in ice water, and vigorously stirred. 90 cc. of a solution of sodium nitrite, containing 100 g. of sodium nitrate in 165 cc. of solution, is allowed to flow in, drop by drop, during a period of about 20 minutes. The reaction mixture is allowed to stand in the cold for 3 hours. 8 g. of copper powder is next added, in portions, and the flask placed in cold water. The mixture gradually warms to about 40°, and the nitrogen is promptly and rapidly evolved. The alcohol is then distilled off, the residue steam distilled and extracted with ether. After the removal of the ether the crude *m*-nitrotoluene is heated to its boiling point to expel the last traces of ether and is obtained as a red oil weighing about 66 g., equivalent to 73% of the theoretical yield. The crude product is purified by distillation. With the apparatus at my disposal, its boiling point was found to be 110° at 15 mm.; 113–14° at 18 mm.; 128° at 32 mm.; and 223° at ordinary pressure, "uncorrected." According to the literature, *m*-nitrotoluene boils at 228–231° ("uncorrected?") and melts at 16°.

The Oxidation of the Nitrotoluenes with Potassium Permanganate.

The oxidation of the 3 nitrotoluenes to the corresponding nitrobenzoic acids has long been known, and has been carried-out by numerous investigators. The oxidizing agents used by them for this purpose, notably potassium dichromate in sulfuric acid solution, and potassium permanganate in alkaline solution, have been very frequently applied, both in these and many other similar oxidations. A careful search of the literature, however, has failed to reveal any comparative series of oxidations similar to that described in the following pages. A summary of the numerous isolated examples which are recorded is not necessary at this point.

The *o*-nitrotoluene submitted to oxidation was purchased in the market. It was quite pure, boiling mostly from 213 to 218°, the true boiling point being 218°,[1] and was not further purified. The *m*-nitrotuluene was synthesized as already described, and the purified product employed in the oxidation experiments. The *p*-nitrotoluene was purchased upon the market. It melted at 54–6°, the true melting point being 54°,[2] and it was used directly in the subsequent work. The potassium permanganate employed as the oxidizing agent was the usual commercial product. Two large lots which were received at the laboratory were analyzed to determine their oxidizing power with the following results:

Lot A. 1 g. $KMnO_4 =\!\!\bigcirc\!\!= 1.974, 1.970$ g. $H_2C_2O_4.2H_2O$.
Calc., 1 g. $KMnO_4 =\!\!\bigcirc\!\!= 1.993$ g. $H_2C_2O_4.2H_2O$.
Lot B. 1 g. $KMnO_4 =\!\!\bigcirc\!\!= 2.207, 2.212$ g. $(NH_4)_2C_2O_4.H_2O$.
Calc., 1 g. $KMnO_4 =\!\!\bigcirc\!\!= 2.247$ g. $(NH_4)_2C_2O_4.H_2O$.

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[1] *Ber.*, 24, 1987 (1891).

[2] *Z. Chem.*, *N. F.*, 1, 220 (1865).

Therefore, the oxidizing power of the permanganate was 98.9, 98.4% of the theoretical value. As this potassium permanagnate was very nearly pure, at least with regard to its oxidizing power, it was used directly as the oxidizing agent. The sodium hydroxide used was the usual high grade commercial product, and the solvent employed was water.

The only part of the apparatus required in the process which merits any detailed description is the container in which the oxidation took place. In order to determine the catalytic effects of 3 different metals upon the reactions, 3 different types of container were used. They were a copper kettle, an enamel lined iron pot, and an iron drum. The copper kettle was made especially for this investigation. The enamel lined pot had been used for various purposes for some time, but although it was somewhat corroded, the enamel nevertheless covered almost all the surface of the iron. The iron drum was of the ordinary commercial variety, and was subjected to an extremely thorough cleaning before it was used in this work.

The general method employed in carrying out the oxidations was essentially the same in all cases, and was, in detail, as follows:

The water was first measured into the container, and the desired quantity, if any, of sodium-hydroxide weighed out and added to it. Next the nitrotoluene was carefully weighed out—in the majority of cases accurately to 0.1 g.—and poured into the sodium hydroxide solution. The container was then fitted with an inclined reflux condenser, and the contents heated nearly to boiling. In the meantime the potassium permanganate to be used was weighed and divided into a number of approximately equal parts, the first of which was added in the solid state to the hot alkaline solution containing the nitrotoluene in suspension. The mixture was finally heated to boiling. When the pink color imparted to the solution by the permanganate had disappeared, the next portion was added, and so on until all had been used up. The product was then distilled with steam, to recover the unchanged nitrotoluene. The steam distillate was extracted with ether, the ether solution dried, and the ether removed in the usual way. After the ether had distilled off the residue was heated for a time on the boiling water bath, to expel the last traces, and then cooled and weighed. The main solution was washed out of the container, evaporated over a free flame to a convenient volume, and filtered from the precipitated oxides of manganese. The filtrate was then further evaporated, and filtered again to remove the traces of manganese oxides which nearly always passed through the filter in the colloidal condition the first time. The filtrate, which was usually yellow in color and contained sodium nitrobenzoate, was finally further concentrated and acidified hot, with conc. hydrochloric acid. After cooling the solution, the nitrobenzoic acid which was deposited was filtered off, dried and weighed. It was not further purified.

In the oxidation of *o*-nitrotoluene, a 25 g. sample was used, but the results have all been calculated on the basis of a 50-g. sample for the sake of uniformity. The time in general required to decolorize one portion of the permanganate varied from half an hour to an hour, depending upon the proportion of alkali present. In all cases, the presence of alkali in the oxidation mixture increased the velocity of the reaction. The sodium *o*-nitrobenzoate solutions were light yellow in color, but of a progressively deeper shade as the alkalinity of the oxidation mixture increased. The *o*-nitrobenzoic acid always separated in the crystalline condition, the color of the product varying from almost pure white to distinctly yellow, following, in general, the color of the solution from which it separated. The solubility determinations of Oechsner de Coninck[1] show that a saturated solution of *o*-nitrobenzoic acid in dil. hydrochloric acid contains somewhat over 2 g. of the former in 500 cc., at 8.5°. The solutions were, therefore, evaporated to approximately that volume before precipitation, and cooled to 8 or 9° before filtration. Two g. was then added to the weight of acid obtained in order to get the true yield. The product was in every case nearly pure *o*-nitrobenzoic acid. It melted at 139–42°, but sintered at a slightly lower temperature. The melting points given in the literature are 141°,[2] 145°,[3] 147°.[4]

The *m*-nitrotoluene was also oxidized in 25 g. samples, but the results calculated on the basis of a 50-g. sample. The oxidation was at only a little slower rate than that shown by the *ortho* compound. It was accelerated by the presence of alkali. The color of the solutions and that of the product, which invariably separated in the crystalline condition, varied from white to yellow, depending upon the proportion of alkali present, as in the case of the *ortho* compound. Following the solubility determinations of de Coninck, the solutions were evaporated to 500 cc., cooled to 20° and 1.5 g. added to the weight of acid obtained in each oxidation, to allow for the quantity remaining in the mother liquors. The *m*-nitrobenzoic acid melted at 136–8° and was a satisfactory product. The melting point is given in the literature as 140–1°.[5]

The *p*-nitrotoluene was oxidized in 50-g. samples. Inasmuch as it is a solid at ordinary temperatures, the extraction of the steam distillate with ether was unnecessary. The unchanged material was filtered off, dried at a low temperature, and weighed. The speed of oxidation of the *para* compound was always essentially twice as great as that of the *ortho* isomer, and, furthermore, was twice as great in an alkaline as in a neutral

[1] *Compt. rend.*, **118**, 538 (1894).

[2] *Ann.*, **163**, 135 (1872).

[3] *Ibid.*, **166**, 133 (1873).

[4] *Ibid.*, **193**, 221 (1878).

[5] *Ibid.*, **193**, 213 (1878).

solution. Thus it required, in an alkaline medium, only about 15 minutes to decolorize one portion of the permanganate. The alkaline solutions of sodium *p*-nitrobenzoate varied in color all the way from very light yellow to dark red, and the precipitated product was either amorphous or crystalline, depending chiefly upon the quantity of alkali present during the oxidation. The amorphous variety varied in color from reddish brown through brown to light gray, while the crystalline modification varied from light brown through pink to almost pure white. As *p*-nitrobenzoic acid is exceedingly insoluble in water, the solutions were not evaporated to a volume much less than one liter, and no correction was applied for the acid remaining in the mother liquors. The solutions were filtered cold. The products in nearly all cases melted at 234–7°—a few at about 230°. The true melting point of *p*-nitrobenzoic acid is given as 238°.[1]

In all the oxidations, the products having the best appearance, which were crystalline, and white or nearly so, were obtained from neutral oxidation mixtures, but such products were no more pure than the rest, as shown by their melting points. In cases where the percentage concentration of the alkali in the solution was high, the pink color of the permanganate very rapidly gave place to a deep green. If the alkali concentration was low no green color whatever was produced. Lastly, the oxides of manganese precipitated in a neutral oxidation were darker and denser than those which were formed in the presence of alkali.

The Oxidation of *o*-Nitrotoluene, $C_6H_4(CH_3)^1(NO_2)^2$.—The first study made in the oxidation of *o*-nitrotoluene was that of the influence of a varying concentration of alkali upon the reaction. The quantity of permanganate used, 128 g., was 10% in excess of the calculated amount, which is 116 g. for a 50-g. sample. This excess had previously been found most advantageous in the oxidation of *p*-nitrotoluene. The results obtained are summarized in the following table:

TABLE III.

(Oxidations of *o*-Nitrotoluene in the Copper Containers.)

50 g. of *o*-Nitrotoluene, 128 g. of Potassium Permanganate and 3150 cc. of Water Used in Each Experiment.

Expt.	NaOH. G.	Unchanged *o*-nitrotoluene. G.	Yield of *o*-nitrobenzoic acid. G.	Yield + unchanged G.
1	0	12.0	38.0	50
2	4	9.8	37.0	47
3	8	8.6	38.8	47
4	16	7.2	40.8	48
5	32	6.2	41.0	47
6	64	6.2	44.6	51
7	84	4.6	45.2	50
8	104	5.2	44.6	50
9	128	4.8	45.4	50

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[1] *Ann.*, **193**, 226 (1878).

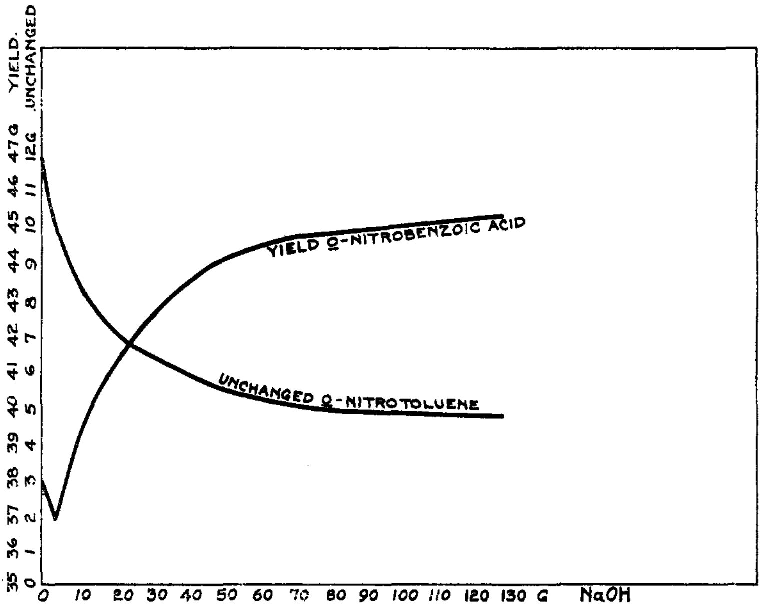

Fig. 1.—*o*-Nitrobenzoic acid produced and *o*-nitrotoluene recovered *vs.* alkali.

The results show that an increasing percentage concentration of the alkali in the solution favors the oxidation of *o*-nitrotoluene up to a certain point, but beyond that has but little effect. Expt. 6 represents the most favorable concentration.

Next a study of the influence of dilution upon the oxidation was made, both with and without the optimum concentration of alkali. The results are recorded below:

Table IV.

Effect of Dilution.

Oxidations in the Copper Container.

50 g. of *o*-Nitrotoluene and 128 g. of Potassium Permanganate Used in Each Experiment.

Expt.	Portions of $KMnO_4$.	Water. Cc.	NaOH. G.	Unchanged *o*-nitrotoluene. G.	Yield of *o*-nitrobenzoic acid. G.	Yield + unchanged. G.
1	8	500	64	29.4	9.4	39
2	8	1575	64	10.2	37.6	48
3	4	3150	64	6.2	44.6	51
4	2	6300	64	5.4	49.8	55
5	8	500	0	23.6	18.8	42
6	8	1575	0	13.4	31.4	45
7	4	3150	0	12.0	38.0	50

In the absence of alkali, the time required to decolorize $^1/_8$ of the permanganate was as high as 1.5 hours. The results show that both with and without alkali, increasing dilution very greatly favors the oxidation.

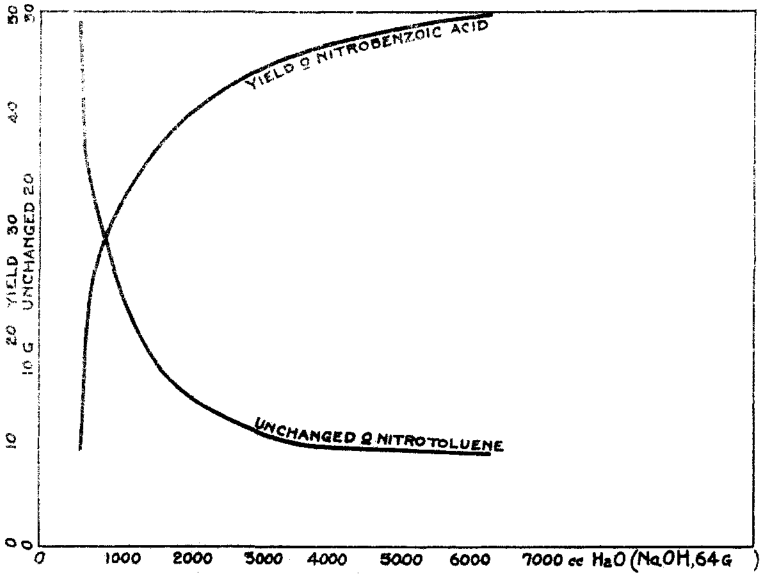

Fig. 2.—*o*-Nitrobenzoic acid produced and *o*-nitrotoluene recovered *vs.* dilution.

A study of the catalytic effect of the container upon the oxidation was now carried out with the following results:

Table V.

Catalytic Effect of the Container.

50 g. of *o*-Nitrotoluene, 128 g. of Potassium Permanganate in 4 Portions, and 3150 cc. of Water Used in Each Experiment.

Expt.	NaOH. G.	Unchanged *o*-nitrotoluene. G.	Yield of *o*-nitrobenzoic acid. G.	Unchanged + yield. G.	Container used.
1	64	14.0	36.0	50	Iron
2	64	6.2	44.6	51	Copper
3	64	7.0	44.0	51	Enamel
4	64	8.2	42.8	51	Enamel
5	0	14.0	32.0	46	Iron
6	0	12.0	38.0	50	Copper
7	0	14.0	36.0	50	Enamel

Here it is seen that both with and without alkali, the oxidations performed in the copper and enamel containers gave essentially the same results, while those carried out in the iron drum gave a lower yield. They also gave a more highly colored product.

The best conditions found for oxidizing *o*-nitrotoluene to *o*-nitrobenzoic acid are those represented in Expt. 2, Table V. The product obtained is satisfactory, and the yield is 73% of the theoretical amount. If the unchanged nitrotoluene recovered is allowed for, the yield becomes 84% of the calculated amount. The yield obtained in Expt. 4, Table IV, is considerably higher, but the dilution is so great that it is not practical to employ the proportions there used.

The Oxidation of *m*-Nitrotoluene, $C_6H_4(CH_3)^1(NO_2)^3$.—The reagents, apparatus, methods of operation and general considerations have already been described.

The influence of alkali upon the oxidation was first studied, and the results obtained, which were quite unexpected, are summarized below:

TABLE VI.

Influence of Alkali.

Oxidations in the Copper Container.

50 g. of *m*-Nitrotoluene, 128 g. of Potassium Permanganate in 4 Portions and 3150 cc. of Water Used in Each Experiment.

Expt.	NaOH. G.	Unchanged *m*-nitrotoluene. G.	Yield of *m*-nitrobenzoic acid. G.	Unchanged + yield. G.
1	0	20.2	27.1	47
2	4	19.6	27.3	47
3	8	20.6	25.9	47
4	16	20.8	24.9	46
5	32	22.4	22.7	45
6	64	25.2	18.9	44
7	84	26.8	17.7	45
8	104	28.0	16.5	45
9	128	28.4	16.1	45

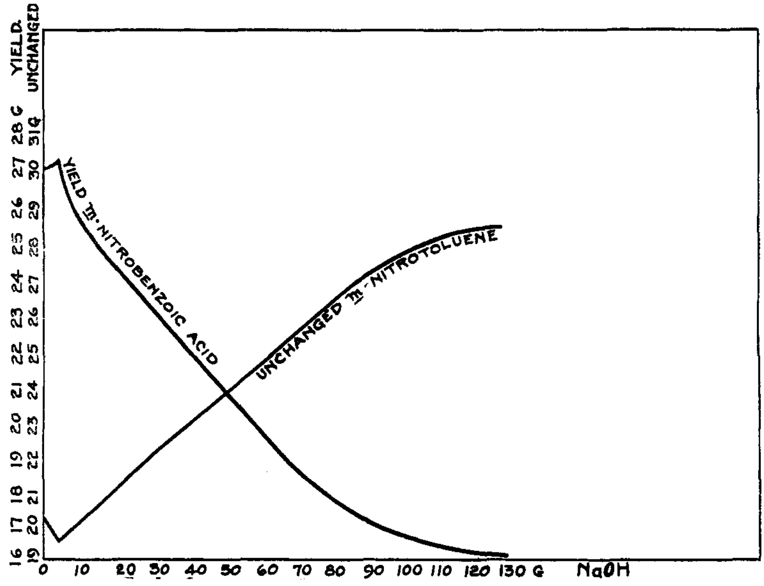

Fig. 3.—*m*-Nitrobenzoic acid produced and *m*-nitrotoluene recovered *vs.* alkali.

The results show that in this case the effect of the alkali is just the reverse of what it is in the oxidation of the *ortho* compound, as here an increase in the percentage concentration of the alkali in the oxidizing mixture *hinders* the oxidation, which is most efficient in an essentially *neutral* medium.

The influence of various degrees of dilution upon the reaction is shown by the following summary:

TABLE VII.

Influence of Various Degrees of Dilution.

Oxidations in the Copper Container.

50 g. of *m*-Nitrotoluene and 128 g. of Potassium Permanganate Used in Each Experiment.

Expt.	Portions of $KMnO_4$.	Water. Cc.	NaOH. G.	Unchanged *m*-nitrotoluene G.	Yield of *m*-nitrobenzoic acid. G.	Unchanged + yield. G.
1	8	500	0	32.0	8.7	41
2	..	1000	0	25.2	14.7	40
3	8	1575	0	23.4	19.1	43
4	4	3150	0	20.2	27.1	47
5	2	6300	0	17.2	32.3	50

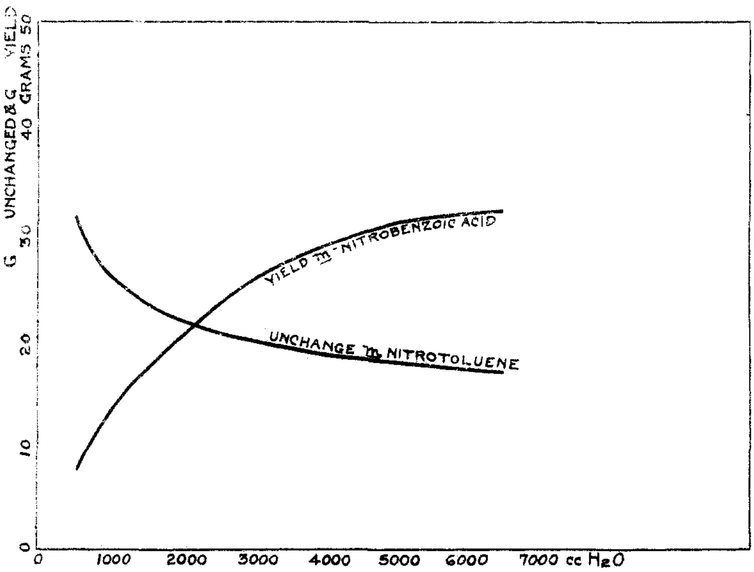

Fig. 4.—*m*-Nitrobenzoic acid produced and *m*-nitrotoluene recovered *vs.* dilution.

These results indicate that the oxidation of the *m*-nitrotoluene, in common with that of the *ortho* compound is greatly favored by increasing dilution of the solution.

The most advantageous conditions for the oxidation of *m*-nitrotoluene are on the whole represented in Expt. 1, Table VI. The product is of good quality, and the yield is 44% of the theoretical. If allowance is made for the unchanged nitrotoluene recovered, the yield is raised to 74% of the calculated amount. As in the case of the *ortho* compound, a higher dilution improves the yield (Expt. 5, Table VII), but is hardly practical for general use.

To determine whether or not the potassium permanganate was decomposing spontaneously in the boiling solutions, 16.0 g. of permanganate, 1575 cc. of water, and 32 g. of sodium hydroxide were placed in the copper kettle, and the mixture boiled for about 8 hours. Before boiling the solution, an aliquot part was taken out and titrated against a standard solution of ammonium oxalate, containing 0.0100 g. per cc. After boiling the solution, another aliquot part was taken out and titrated in a similar manner. It oxidized an amount of oxalate identical with the first. Therefore, the oxidizing power of the potassium permanganate solution was not decreased by boiling it for 8 hours in an alkaline solution of a strength equal to that employed in the oxidation experiments which gave the best results.

To this permanganate solution was next added 2.5 g. *m*-nitrotoluene, and the boiling resumed. A partial reduction of the permanganate took place immediately, but the last of the pink color of the solution disappeared very gradually, about 7 hours of boiling being required to decolorize the mixture entirely. The resulting solution was worked up in the usual manner. There was recovered 0.4 g. of unchanged nitrotoluene, and the yield of *m*-nitrobenzoic acid produced was 2.1 g. (= 0.6 + 1.5).

This indicates that a small amount of the *m*-nitrobenzoic acid had been burned up, and that the presence of the organic matter in the solution did not catalyze the decomposition of the permanganate to any very significant extent.

The Oxidation of *p*-Nitrotoluene, $C_6H_4(CH_3)^1(NO_2)^4$.—The oxidation of the *p*-nitrotoluene was investigated much more fully than that of either of the other two isomers; and some of the relative proportions of the reagents involved which were adopted in the oxidations of the other nitrotoluenes, were derived from the results of the work upon the *para* compound. The reagents, the apparatus, and the general method are described above. The oxidizing mixture first used was approximately that suggested by Noyes[1] the quantity of permanganate employed being the calculated amount.

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[1] "Organic Chemistry for the Laboratory," 1897, p. 26. Chem. Pub. Co., Easton, Pa.

The first study made was, as usual, upon the influence of alkali upon the oxidation, and the results obtained are expressed in the table below:

TABLE VIII.

Influence of Alkali.

Oxidations in the Enamel-lined Container.

50 g. of *p*-Nitrotoluene, 116 g. of Potassium Permanganate in 5 Portions and 1575 cc. of Water Used in Each Experiment.

Expt.	NaOH. G.	Unchanged *p*-nitrotoluene. G.	Yield of *p*-nitrobenzoic acid. G.	Unchanged + yield. G.	Character of product.
1........	4	15	32	47	Amorphous
2........	8	12	34	46	Amorphous
3........	16	12	36	48	Amorphous
4........	32	8	39	47	Amorphous
5........	64	9	39[1]	48	Amorphous
6........	128	5	42	47	Reddish and amorphous

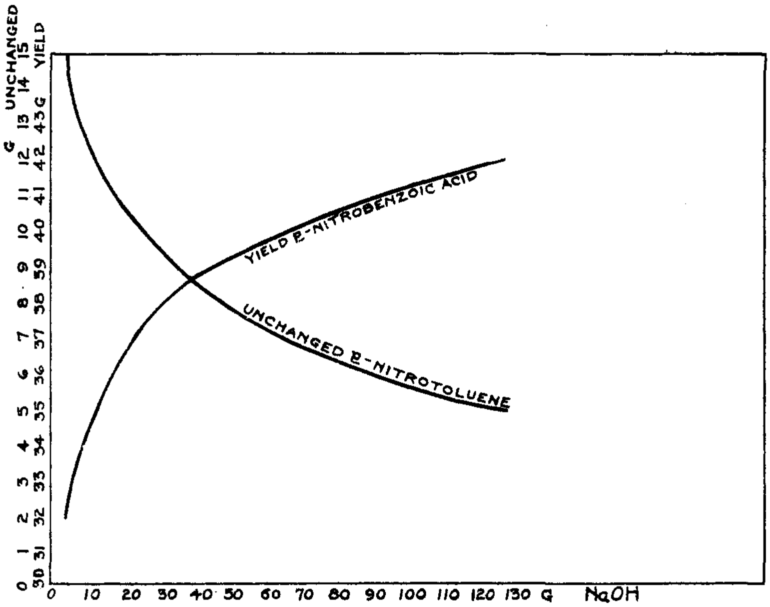

Fig. 5.—*p*-Nitrobenzoic acid produced and *p*-nitrotoluene recovered *vs.* alkali.

These results indicated that an increasing percentage concentration of alkali in the solution favors the *p*-nitrotoluene oxidation up to a certain point only, and that the best concentration was that used in Expt. 5. It was employed in most subsequent oxidations.

The influence of dilution was next studied, with the following results:

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[1] Precipitated acid, after filtration, washed by decantation.

TABLE IX.

Influence of Dilution.

Oxidations in the Enamel-Lined Container.

50 g. of *p*-Nitrotoluene and 116 g. of Potassium Permanganate Used in Each Experiment.

Expt.	Portions KMnO$_4$.	Water. Cc.	NaOH. G.	Unchanged *p*-nitrotoluene. G.	Yield of *p*-nitrobenzoic acid. G.	Unchanged + yield. G.	Character of product.
1.....	15	500	64	14	32	46	Amorphous
2.....	5	1575	64	9	39[1]	48	Amorphous
3.....	3	3150	64	5	43[2]	48	Amorphous
4.....	1	6300	64	6	43[3]	49	Amorphous

Oxidations in the Copper Container.

50 g. of *p*-Nitrotoluene and 128 g. of Potassium Permanganate Used in Each Experiment.

Expt.	Portions KMnO$_4$.	Water. Cc.	NaOH. G.	Unchanged *p*-nitrotoluene. G.	Yield of *p*-nitrobenzoic acid. G.	Unchanged + yield. G.	Character of product.
5.....	8	500	0	21.8	22.0	44	....
6.....	8	1575	0	12.4	34.8	47	....
7.....	4	3150	0	9.0	45.0	54	Crystalline (nearly white)

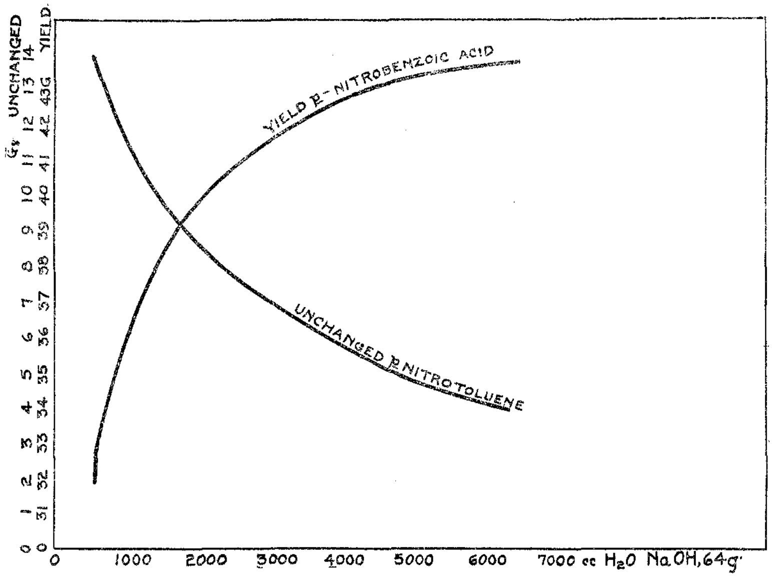

Fig. 6.—*p*-Nitrobenzoic acid produced and *p*-nitrotoluene recovered *vs.* dilution.

These results show that increasing dilution favors the oxidation both with and without alkali, and that, on the whole, the proportion of water used in Expt. 3 is the best. This was used in subsequent oxidations.

The influence upon the oxidation of employing different amounts of

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[1] Precipitated acid washed by decantation.

[2] Precipitated acid dissolved in alkali, filtered and reprecipitated.

[3] The same amount allowed for inorganic material in the precipitate as was allowed in Expt. 3, *i. e.*, 3 g.

permanganate in excess of the calculated quantity was next investigated. The results are given in the following scheme:

Table X.

Influence of Excess of Permanganate.

Oxidations in the Enamel-Lined Container.

50 g. of *p*-Nitrotoluene, 3150 cc. of Water and 64 g. of Sodium Hydroxide Used in Each Experiment.

Expt.	$KMnO_4$. G.	Portions $KNnO_4$.	Unchanged *p*-nitrotoluene. G.	Yield of *p*-nitrobenzoic acid. G.	Unchanged + yield. G.	Character of product.
1.......	116	3	5	43[1]	48	Amorphous
2.......	122	3	4	40	54	Amorphous
3.......	128	4	3	52	55	Crystalline
4.......	141	4	2	52	54	Crystalline
5.......	155	4	0.4	52	52	Crystalline

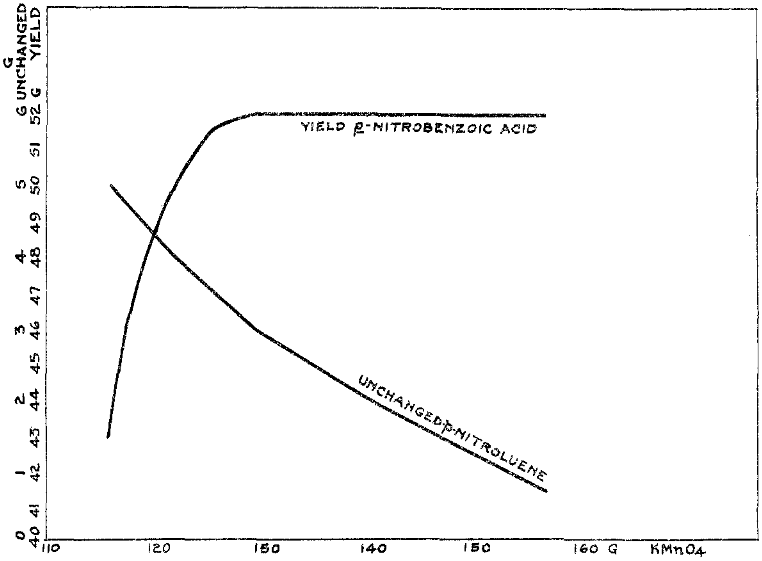

Fig. 7.—*p*-Nitrobenzoic acid produced and *p*-nitrotoluene recovered *vs*. permanganate in excess of the calculated quantity.

The best results were obtained in Expt. 3, in which permanganate 10% in excess of the theoretical amount was used. This excess was subsequently employed, not only in this series of oxidations, but also in the other two series.

A study of the influence of temperature upon the reaction necessitated a slight change in the apparatus, namely, the introduction of a vigorous mechanical stirrer which was used in the oxidations taking place below the boiling temperature of the solution. The results follow:

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[1] Precipitated acid dissolved in alkali and reprecipitated.

TABLE XI.
Influence of Temperature.
Oxidations in the Enamel-Lined Container.
50 g. of *p*-Nitrotoluene, 128 g. of Potassium Permanganate in 4 Portions, 3150 cc. of Water, and 64 g. of Sodium Hydroxide Used in Each Experiment.

Expt.	Unchanged *p*-nitrotoluene. G.	Yield of *p*-nitrobenzoic acid. G.	Unchanged + yield. G.	Temperature. Degrees.	Character of product.
1	8	46	54	60–65	Very crystalline
2	8	45	53	85	Very crystalline
3	3	52	55	Boiling point	Crystalline

The boiling temperature is thus found to be most favorable to the oxidation. The time of oxidation was greatly increased by a decrease in the temperature. In Expt. 1, it required 2 hours of heating to decolorize $^1/_4$ of the permanganate as compared with approximately 15 minutes in Expt. 3.

The influence of the container upon the oxidation was now studied, both in the neutral and alkaline solutions. The results are given in Table XII.

TABLE XII.
Influence of the Container.
50 g. of *p*-Nitrotoluene, 128 g. of Potassium Permanganate in 4 Portions, 3150 cc. of Water, and 54 g. of Sodium Hydroxide Used in Each Experiment.

Expt.	Unchanged *p*-nitrotoluene. G.	Yield of *p*-nitrobenzoic acid. G.	Unchanged + yield. G.	Container.	Character of product.
1	4	47	51	Iron	Amorphous
2	6	46	52	Iron	Amorphous
3	4	50	53	Copper	Amorphous but lighter colored
4	3	48	51	Copper	Amorphous but lighter colored
5	3	52	55	Enamel	Crystalline
6	3.8	30	54	Enamel	Crystalline but tinged brown
No sodium hydroxide used in the following experiments.					
7	11	39	50	Iron	Crystalline but tinged brown
8	13	38	50	Iron	Crystalline but tinged pink
9	9	45	54	Copper	Crystalline nearly white
10	10	44	54	Enamel	Crystalline nearly white

These results indicate that oxidations conducted in the iron drum give in all cases both the poorest yield and the poorest quality of product. Those carried out in the copper and enamel containers give approximately the same yields, but the quality of the resulting product is better when the enamel-lined pot is used. In all cases the absence of alkali in the oxidation mixture greatly decreases the yield, but improves the quality of the product. The best appearing product was obtained in Expts. 9 and 10, but it failed to melt any more sharply than the rest.

The best conditions which were attained for the oxidation of *p*-nitrotoluene are those represented in Expt. 5. The amount of material recovered unchanged was at a minimum, and the yield of acid at a maximum.

The product was entirely crystalline, and of a light grayish color. It was obtained in an 85% yield. If the unchanged material is allowed for the yield is raised to 91% of the calculated quantity.

A number of experiments were made studying various isolated influences which may be brought to bear upon the oxidations of *p*-nitrotoluene, which did not fit especially well in any of the above series. The results of these are collected in the following table:

Table XIII.

Other Experiments.

Oxidations in the Enamel-Lined Container.

Expt.	Portions KMnO.	NaOH. G.	Unchanged *p*-nitrotoluene. G.	Yield of *p*-nitrobenzoic acid. G.	Unchanged + yield. G.	Character of product.
Using 50 g. of *p*-Nitrotoluene, 128 g. of Potassium Permanganate and 3150 cc. of Water.						
1	8	64	2	51	53	Crystalline
2	4	64	3	52	55	Crystalline
3	4	102[1]	11	39	50	Crystalline tinged pink
4	4	45[2]	10	38	48	Crystalline tinged pink
5(*a*)	5	64	6	48	52	Amorphous
Using 50 g. of *p*-Nitrotoluene, 116 g. of Potassium Permanganate and 500 cc. of Water.						
6(*b*)	5	20	25	20	45	Amorphous
7(*b*)	15	20	19	25	44	Amorphous
Using 50 g. of *p*-Nitrotoluene, 116 g. of Potassium Permanganate and 3150 cc. of Water.						
8	3	128	4	44[3]	48	Amorphous
9(*c*)	..	64	4	47[4]	51	Amorphous
Using 100 g. of *p*-Nitrotoluene[4], 256 g. of Potassium Permanganate and 3150 cc. of Water.						
10	8	64	14	85	99	.....

Expts. 1 and 2 indicate the effect upon the oxidation of varying only the number of portions in which the permanganate is added. The smaller number of portions is as advantageous, if not more so, than the larger.

Expts. 3 and 4 show the results of limiting the alkaline strength of the solution to that of $Mg(OH)_2$ and $Ca(OH)_2$, respectively. They also illustrate the influence of the metals, if any. The product obtained under these conditions was of very good quality, but the yield was poor.

Expt. 5 was carried out to show any catalytic effect of pyridine upon the oxidation. The presence of the pyridine only decreased the yield slightly.

In Expt. 9 the permanganate was added gradually, in hot solution, 116 g. of permanganate to 400 cc. of water, to note the effect of increasing

[1] $MgSO_4.7H_2O$. Alkaline strength of $Mg(OH)_2$.

[2] $CaCl_2$, anhydrous. Alkaline strength of $Ca(OH)_2$.

[3] Allowed 4.8% for SiO_2 in the product, according to analysis.

[4] In two 50 g. portions.

(*a*) 25 g. pyridine added.

(*b*) NaOH and water reduced proportionately from Expt. 5, Table VIII.

(*c*) $KMnO_4$ added in solution.

to infinity the number of portions in which the oxidizing agent was added. This procedure is troublesome and of no advantage.

Expt. 10 shows that increasing the concentration of the organic matter in the mixture, while the concentration of alkali in the solution remains constant, decreases the yield obtained.

To determine whether or not *p*-nitrobenzoic acid was oxidized itself by alkaline permanganate, the following experiment was tried. Nine g. of *p*-nitrobenzoic acid, 985 cc. of water, 3 g. of sodium hydroxide, and 21 g. of permanganate (added in 5 separate portions) were boiled together under a reflux condenser. Each portion required about $^3/_4$ hour to become decolorized. When the solution had become colorless, the mixture was filtered and acidified, and there was recovered 6 g. of the acid. Three g. had, therefore, been burned up, which would theoretically reduce 24 g. of permanganate if converted entirely into carbon dioxide and water.

Summary.

A comparative study of experimental conditions, which have an influence on the oxidation of the isomeric nitrotoluenes by means of potassium permanganate in alkaline solution, have led to the following results:

(1) A gradually increasing concentration of alkali in the oxidizing mixture favors the oxidation of *o*- and *p*-nitrotoluene, up to a certain point, while the oxidation of the *m*-compound takes place best in an essentially neutral medium.

(2) An increasing dilution of the solution favors the oxidation of all the nitrotoluenes.

(3) *p*-Nitrotoluene is oxidized most readily, the *o*-compound next, and the *m*-derivative least.

In conclusion the writer desires to express his thanks for the constant and friendly interest of Professor Treat B. Johnson, under whose direction this work has been carried out.

NEW HAVEN, CONN.

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH.]

AROMATIC ARSENIC COMPOUNDS. I.

A PLAN OF PROCEDURE FOR THE SYNTHESIS OF ARSENICALS FOR CHEMOTHERAPEUTIC RESEARCH.

BY WALTER A. JACOBS AND MICHAEL HEIDELBERGER.

Received July 2, 1919.

In the following communications and in those which will appear later, we shall describe certain groups of aromatic arsenic compounds which have been the subject of our studies for several years. In collaboration with Drs. Wade H. Brown and Louise Pearce, who have had charge of the biological phases of the work, we have prepared these substances for the treatment of experimental trypanosome and spirochaete infections.