

3-Iodo-4-hydroxybenzoic acid, after one hour, showed little sign of reaction. After 5 hours, the solution contained considerable iodide, but the reaction was very incomplete.

Iodobenzene, treated as above and boiled for 5 hours, showed no evidence whatever of reaction. The same result was obtained when alcohol was added to render the substance more soluble. In both cases the test for iodides was negative.

Summary.

1. It has been shown that certain compounds containing iodine or bromine *ortho* or *para* to an amino or anhydroxyl group, when boiled with hydrochloric acid in part replace their halogen by hydrogen and in part give di- (or tri-) substitution products. Together, these reactions are considered to characterize these derivatives as containing positive halogen.

2. In similar compounds, iodine is more positive than bromine, and *ortho* than *para* compounds.

3. Compounds which, by the above standards, contain positive halogen, are abnormally readily dehalogenated by stannous chloride, in acid solution.

CHICAGO, ILL.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA.]

NITROMALIC ACID.

BY ARTHUR LACHMAN.

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The abnormal action of alkalis upon organic nitrates, whereby varying and at times considerable amounts of nitrous acid are produced, has been accounted for in two quite different manners. Nef¹ assumed what he called "methylene dissociation" to take place, and definitely ascribed this dissociation to the alkali. Klason and Carlson,² holding the view that nitric acid is a peroxide, looked upon the formation of nitrous acid as a direct hydrolysis of the nitric ester into nitrous acid and an organic peroxide. They also regarded the alkaline reagent as an essential factor.

The recently noted behavior of nitrotartaric acid,³ hydrolyzing normally and almost quantitatively as a true nitric ester in strongly acid media, and equally quantitatively as a nitrous ester in weaker acid, did not accord with either of the above interpretations. The suggestion was made that nitrotartaric acid goes over into a pseudo form, $\text{COOH.CH(ONO}_2\text{).-CH(ONO}_2\text{).COOH} \rightarrow \text{COOH.C(OH)(ONO).C(OH)(ONO).COOH}$. Nitrotartaric acid, being soluble both in water and organic solvents, seemed to offer a better opportunity for the investigation of what really happens in these intramolecular oxidations, than the esters studied by Nef and by Klason and Carlson. At the same time, Michael's view that

¹ Nef, *Ann.*, **309**, 176 (1899).

² Klason and Carlson, *Ber.*, **40**, 4183 (1907).

³ Lachman, *THIS JOURNAL*, **43**, 577 (1921).

the *solvent* frequently determines the course of a reaction, could be considered.

It proved difficult, however, to keep nitrotartaric acid under sufficient control for purposes of measurement. The search for a more suitable compound was fortunately of brief duration. Nitromalic acid, the nitrate of ordinary malic acid, soon gave promising results. This acid, which has not yet been described, is easily prepared.

Preparation and Properties of Nitromalic Acid.

Dissolve 10 g. of malic acid in 20 cc. of nitric acid (1.42), warming slightly if necessary. Add this solution, with careful cooling and stirring, to 40 cc. of fuming sulfuric acid (10-15%). Pack this material in ice, and allow it to stand for 2 hours. Pour the product upon cracked ice, extract the liquid twice with ether, wash the ether and extract it thrice with small quantities of ice water to remove the excess of nitric acid. Dry this solution thoroughly with calcium chloride. Careful evaporation of the ether gives a thick white oil, which soon solidifies to form a stellated mass of long, soft, white needles. Yield, 6 to 7 g.⁴

Nitromalic acid as thus obtained is sufficiently pure for analysis; a portion, however, was recrystallized from dry ether by addition of ligroin. It melts, with decomposition, at 110-112°. It is very soluble in water, alcohol, ether, and acetone, and is insoluble in ligroin and benzene. The composition is $C_4H_5NO_7$ corresponding to the structure $COOH.CH_2-CH(ONO_2).COOH$; mol. wt., 179.1.

Subs., 1.0054: 22.45 cc. of 0.5 *N* NaOH.⁵ Calc.: 22.47 cc.

Subs., 0.5044: (boiled with excess of diluted 0.5 *N* NaOH, cooled and titrated) 17.15 cc. Calc.: 17.05 cc. for 1.5 moles.

The *sodium* salt of nitromalic acid was prepared by carefully neutralizing the acid with sodium carbonate, and evaporating the solution at room temperature over sulfuric acid. It forms small hard white crystals, is very soluble, but not deliquescent. It holds two molecules of water. The dry sodium salt explodes when heated.

Analysis. Subs., 0.0897: Na_2SO_4 , 0.0500. Calc. for $Na_2C_4H_5NO_7 \cdot 2H_2O$: Na, 17.75. Found: 18.25.

The *silver* salt was prepared by addition of silver nitrate to a solution of the sodium salt. It forms small white crystals, and is moderately soluble in water. It is anhydrous. On heating, it explodes. For analysis, it was moistened with ammonium sulfide, and then ignited.

Analysis. Subs., 0.2321: Ag, 0.1271. Calc. for $Ag_2C_4H_5NO_7$: Ag, 54.9. Found: 54.8.

⁴ It is not desirable to prepare nitromalic acid in larger amounts. A lot made from 30 g. of malic acid, from which the ether was evaporating spontaneously, exploded during the night. A second preparation with similar quantities decomposed during the evaporation of the ether.

⁵ Nitromalic acid is not strong enough to be titrated with methyl orange as an indicator. The above titrations were made at 0°, with phenolphthalein as an indicator. Combustion gave high results for C, because of formation of nitric oxide. Calc.: H, 2.79. Found: 2.85.

Hydrolysis by Aqueous Alkali.

Nitromalic acid was treated with sodium hydroxide in water solution; both concentration of the acid and the excess of the alkali were varied within wide limits. The reaction was completed very rapidly; 5 minutes' heating on the water-bath sufficed. Temperature seems to have no effect on the production of nitrous acid; in two cases, the reaction mixture was allowed to stand in the cold for several days. The results obtained are given in the following table.

TABLE I.

HYDROLYSIS BY AQUEOUS ALKALI.				
Nitromalic Acid. Weight. G.	Millimols.	NaOH. Millimols.	Volume. Cc.	NaNO ₂ . %.
0.3056	1.7	10	70	21.0
0.5170	2.9	18	9	21.6
0.5009	2.8	55	9	21.0
0.1790	1.0	12	30	20.3
0.2720	1.5	30	10	20.6

The amount of nitrous acid formed is practically constant, regardless of temperature, concentration, or excess of alkali. This is in complete agreement with the data obtained by Klason and Carlson² who studied the hydrolysis of alkyl nitrates by alkalies in the presence of mercaptans.

The method of estimating the amount of nitrous acid produced in the above hydrolyses must be described briefly, as it subsequently led to interesting results. The small flasks containing the reaction mixture were connected to a carbon dioxide supply and when all the air had been swept out, to an azotometer. A solution of a slight excess of sulfanilic acid in dil. acetic acid was then added all at once through a dropping funnel. After allowing the diazo reaction about 5 minutes in which to complete itself, the material in the flask was slowly warmed to boiling; nitrogen is evolved so rapidly that the entire operation required about 20 minutes. Each mol. of nitrous acid gives one mol. of nitrogen.

Hydrolysis by Alkali in Methyl Alcohol.

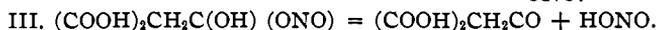
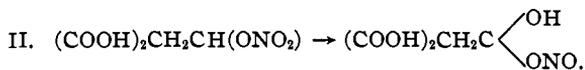
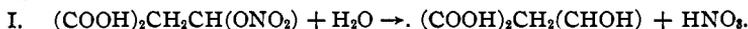
Upon the addition of sodium hydroxide, dissolved in methyl alcohol, to a solution of nitromalic acid in the same solvent, a portion of the sodium nitromalate first formed by neutralization, is precipitated. In spite of the lack of homogeneity in the system, the amount of nitrous acid formed is again practically independent of temperature, concentration, or excess of alkali; *but nearly twice as much is produced as when water is the solvent.*

TABLE II.
HYDROLYSIS BY ALKALI IN METHYL ALCOHOL.

Nitromalic Acid. Weights G.	Millimols.	NaOH. Millimols.	Volume. Cc.	NaNO ₂ . %.
0.5353	3.0	9.2	5	32.6
0.5001	2.8	18	9	39.9
0.5163	2.9	50	20	34.4
0.3775	2.1	17	15	35.5
0.3163	1.8	10	23	34.6
0.2383	1.3	30	30	35.6

Hydrolysis in Acid Solution.

The preceding data pointed to the conclusion that the solvent is the determining factor in the abnormal hydrolysis of nitrates; but on further consideration it became clear that what was measured above was not the formation of nitrous acid, *but the competition between two or three different reactions.*



Reaction I represents the normal hydrolysis of nitromalic acid into its components. Reaction II is the process of isomerization according to the present conception; it might represent equally well, with a slight change in formulation, what Nef called "methylene dissociation," or Klason's "peroxide formation." Reaction III is the simple hydrolysis of the nitrous ester.

Klason and Carlson have found that the normal saponification of a nitrate takes a measurable time, while the hydrolysis of nitrites is practically instantaneous. The data obtained above, then, represent the ratios of the velocities of Reactions I and II; and any influence that can be exerted upon Reaction I to slow it down, will inevitably increase the proportion in which Reaction II takes place.

This makes clear the influence of methyl alcohol upon the amount of nitrous acid produced; Reaction I requires water for its mechanism, and as the amount of water present is very small, it must be greatly retarded. Consequently, more time is available for the structural change, and more nitrous acid is found.

It is further clear that if Reaction I could be retarded still further, even more nitrous acid might be expected. With this purpose in mind, alkali was excluded altogether, and nitromalic acid warmed directly with aqueous sulfanilic acid.

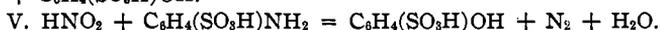
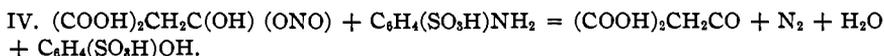
Nitrogen was found to be given off slowly, and at a rapidly diminishing rate. The first experiment was maintained for 2 hours at water-bath

temperature, and gave 65% nitrogen. A second test, lasting 5 hours, gave 78.3%.

These striking figures at once eliminate the hypotheses of Nef and of Klason.

Velocity of the Structural Change.

The very moderate rate at which nitrogen was evolved in the experiments just described, made it possible to measure the velocity of the process. Besides the reactions under (II) and (III), both of which are monomolecular, the following possibilities were to be considered.



Equation IV represents the possible direct interaction of nitromalic acid, either in the normal or the pseudo form, with sulfanilic acid. Equation V is the reaction upon which the method of measurement is based. Of these reactions, (II) and (III) are monomolecular; but (III) is very rapid in comparison to (II), and will therefore interfere to but a small extent. Reaction IV is bimolecular; (V) is also bimolecular, but very rapid.

The results obtained in two series of measurements are given in the following table. Nitromalic and sulfanilic acids were dissolved in cold water, and not placed in the boiling water-bath until all air had been expelled. Carbon dioxide was bubbled through the liquid at the rate of 3 bubbles per second. The gas was not entirely free from air; the amount of air accumulated per hour was determined, and the volume of nitrogen corrected accordingly. The temperature of the azotometer was constant within 1°. Time was recorded from the beginning of heating. This seemed better than making a perhaps dubious allowance for the initial lag. Towards the end of the reaction, the carbon dioxide was absorbed rather slowly making the volume readings uncertain; the later values are not included.

TABLE III.

REACTION BETWEEN NITROMALIC AND SULFANILIC ACIDS.

0.4172 G. of nitromalic acid + 0.7420 g. of sulfanilic acid; volume 45.0 cc. Bath at 100°. Gas measured at 21°—740 mm. (corr.). 1 cc. of N₂ equivalent to 0.000877 mols./liters transformed.

Min.	N ₂ Cc.	<i>x</i> .	<i>a</i> - <i>x</i> .	<i>K</i> .	<i>b</i> - <i>x</i> .	<i>K'</i> .
0	0.0518	0.0788
5	2.5	0.0022	0.0496	0.0038	0.0766	0.0044
10	5.6	0.0049	0.0469	0.0043	0.0739	0.0055
15	8.0	0.0070	0.0448	0.0042	0.0718	0.0054
20	10.7	0.0094	0.0424	0.0043	0.0694	0.0057
25	13.4	0.0118	0.0400	0.0045	0.0670	0.0061
40	19.6	0.0172	0.0346	0.0044	0.0616	0.0063
55	24.5	0.0215	0.0303	0.0042	0.0573	0.0063
70	28.6	0.0251	0.0267	0.0041	0.0537	0.0064
85	32.0	0.0281	0.0237	0.0040	0.0507	0.0063

0.4031 G. of nitromalic acid + 0.4838 g. of sulfanilic acid. Volume, 35.0 cc. Bath at 100°. Gas measured at 21°. 740 mm. 1 cc. of N₂ = 0.001132 mol./liters transformed.

TABLE III (continued).

Min.	Ns. Cc.	x .	$a-x$.	K .	$b-x$.	K' .
0	0.0643	0.0661
6	2.2	0.0025	0.0618	0.0028	0.0636	0.0093
12	5.4	0.0061	0.0582	0.0036	0.0600	0.0600
20	9.9	0.0112	0.0531	0.0042	0.0549	0.0611
32	16.1	0.0182	0.0461	0.0045	0.0479	0.0764
40	19.1	0.0216	0.0427	0.0045	0.0445	0.0847
70	28.2	0.0319	0.0324	0.0043	0.0342	0.0945
90	33.9	0.0384	0.0259	0.0041	0.0277	0.1003
120	37.9	0.0429	0.0214	0.0040	0.0232	0.1095

In the table K is the value of the constant calculated for monomolecular reaction, K' for bimolecular. Considering the rather imperfect technique, there is good agreement for K in the two series, in spite of the considerable difference in concentration. The values of K' do not agree among themselves and in the second series they become absurd.

The conclusion is therefore justified that the reaction in question is monomolecular, and that Equation IV may be excluded from further consideration. Inasmuch as Reaction III is known to be a very rapid process, the value of K obtained above may be regarded as substantially indicating *the velocity of the structural change*.

The formation of oxalo-acetic acid, according to Equation III, was definitely established. From 1.0 g. of nitromalic acid, heated for several hours with a solution of sulfanilic acid, there was obtained by ether extraction 0.15 g. of crude product, melting at about 120°; on recrystallizing from ether and ligroin, the melting point rose to 180°.

Hydrolysis in Neutral Solution.

In order to ascertain the action of nitromalic acid in a solution as nearly neutral as possible, 1.0 g. of sodium nitromalate was dissolved in 100 cc. of water. To this solution, about 1.0 g. of calcium carbonate was added, and the mixture was boiled vigorously, with mechanical stirring, for 2 hours. The volume was maintained approximately constant.

The amount of nitrous acid formed was 8%. The residual solution, free from nitrous acid, gave a copious precipitate with nitron, showing the presence of nitric acid; and the filtrate from this, on evaporation, left a residue which was identified as calcium malate.

Discussion of Results.

The very considerable variation in the amount of nitrous acid formed from nitromalic acid (from 8% to 80%) under varying experimental conditions, is a convincing illustration of the need of closely defining the working conditions, if a clear picture of the course of an organic reaction is to result. In far too many cases it has been the custom to seize upon the

product that happens to be formed more readily under one set of circumstances, and to regard that product as the main, or even the exclusive, result of the reaction.

In the present case, it would have been quite possible, merely by discontinuing the work, to reach two fallacious conclusions; (1) that the production of nitrous acid is due chiefly to the action of alkali; (2) that alcoholic alkali exerts a greater influence than aqueous.

The truth is that alkali merely catalyzes the formation of nitrous acid, *i. e.*, increases the rate at which it is produced. But at the same time, the alkali catalyzes the normal hydrolysis into *nitric* acid to a still greater extent; and the net result of employing alkali is to diminish the *amount* of nitrous acid, as compared with that formed in acid solution.

It is clear, then, that in the hydrolysis of nitric esters two processes are occurring side by side. Any factor which will hasten one, will make the other lag in comparison. What appears to be an equilibrium, as for instance in the case of hydrolysis by aqueous alkali, is merely a ratio of two rates of reaction. The real action of alcohol, which appears to increase the proportion of nitrous acid, is to slow down the normal hydrolysis into nitric acid.

There can be little doubt that many such false equilibria have served to cloud our understanding of organic reactions. This is conspicuously the case in the so-called molecular rearrangements. Molecular rearrangements resemble the behavior of nitrotartaric and nitromalic acids in that they also involve intramolecular oxidations and reductions. We are not justified in drawing conclusions in this complex field on the basis of a single product which may represent less than half the material originally taken, or even when the product is quantitatively defined but its mode of preparation not varied between sufficiently wide limits.

By the aid of this point of view, it has been possible to secure some interesting and unexpected results along well-worn trails. These will be reported in the near future.

The present studies were begun and completed in the laboratory of the University of California, which with unexampled and unlimited generosity has placed all its facilities at my disposal. It is difficult to express my indebtedness to and gratitude for the courtesies and encouragement extended by Professors G. N. Lewis and E. O'Neill and the entire staff.

Summary.

1. The preparation and properties of nitromalic acid are described.
2. Nitromalic acid yields a mixture of nitric and nitrous acids when hydrolyzed with aqueous alkali. The percentage of nitrous acid is independent of temperature, concentration or excess of alkali.

3. Hydrolysis in alcoholic solution gives similar results; the percentage of nitrous acid is independent of experimental conditions, but nearly twice as much is formed as in the previous case.

4. The reason for this difference is discussed.

5. It was found that when alkali is excluded altogether, and a substance like sulfanilic acid added, which can take up nitrous acid as fast as formed, the production of nitrous acid is greatly increased.

6. The rate of formation of nitrous acid under the latter conditions was found to be monomolecular.

7. In the hydrolysis of nitric esters two processes occur independently of each other. One is the normal saponification into alcohol (or oxyacid) and nitric acid; the other is isomerization to a nitrous ester, which subsequently hydrolyzes into a carbonyl compound (aldehyde or ketone) and nitrous acid. Each of these reactions proceeds at its own rate under the given conditions.

8. The constant yield of nitrous acid obtained when, for example, aqueous alkali is employed is a false equilibrium. The real constant is the ratio of the rates of the two reactions.

BERKELEY, CALIFORNIA.

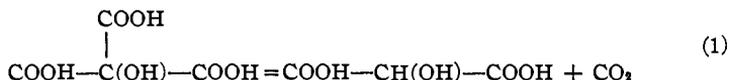
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DIHYDROXY-TARTARIC ACID.

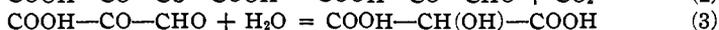
By ARTHUR LACHMAN.

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Dihydroxy-tartaric acid was first obtained by Gruber,¹ by the action of nitrous acid on protocatechuic acid. He found that it readily lost carbon dioxide, with formation of tartronic acid; he therefore named the compound carboxy-tartronic acid, and ascribed to it the following structure.



As the formation of an acid of this structure from the oxidation of a benzene ring appeared to support the prism rather than the hexagon formula, the subject was promptly investigated by Kekulé.² The latter obtained Gruber's acid from nitrotartaric acid, and was able to reconvert it into tartaric acid by reduction. He explained the formation of tartronic thus: first, loss of carbon dioxide and production of an aldehydo-acid, and second, rearrangement of the aldehydo-acid.



¹ Gruber, *Ber.*, **12**, 514 (1879).

² Kekulé, *Ann.*, **221**, 245 (1883).