

XXII.—*Researches on the Constitution and Reactions of Tyrosine.*

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PART I.

Oxidation of Tyrosine by means of Bichromate of Potash and dilute Sulphuric Acid.

The behaviour of tyrosine towards bichromate of potash and dilute sulphuric acid reminded us forcibly of oxalic acid, which, as is well known, is very readily attacked by chromates in acid solution. We were unable to find any trace of acetic, benzoic, or any volatile organic acid, except formic acid, among the products of this oxidation of tyrosine. Moreover the quantity of formic acid obtained even by the most cautious oxidation was exceedingly small, as will be appreciated on considering the bearing of the following experimental details.

Took, about 3 gramm. of tyrosine,
 (less than) 10 „ H_2OSO_3 ,
 100 c.c. of water,
 8 gramm. of bichromate of potash.

There was violent action with evolution of carbonic acid; a slight smell of formic acid was noticed. There was formation of 3 or 4 gramm. of an insoluble yellowish-green chromium-compound, of which more will be said directly. The whole product of the oxidation, including this powder, was introduced into a flask and distilled. The distillate was saturated with carbonate of baryta, and the baryta-salt resulting from this operation was weighed and found to be 0.0138 gramm., which, on examination, proved to be formate of baryta. It gave off no smell of acetic or higher fatty acid on being heated with sulphuric acid. It

had the property of very easily reducing silver salts. The total quantity of formic acid obtained in the experiment was, as will be found on calculation, about $\frac{1}{500}$ of the weight of tyrosine employed. The yellowish-green chromium-compound is formed only when the proportion of sulphuric acid is small. Our analyses point to the formula $C_9H_{11}NO_{12}Cr_2O_3 \cdot 2H_2O$ as the following comparison shows:—

- I. 0.6245 grm. (dried at 105° C.) gave on combustion with chromate of lead, a little copper turnings being used, 0.200 grm. H_2O and 0.4760 grm. CO_2 . H per cent. = 3.56; C per cent. = 20.79.
- II. 0.3590 grm. gave on combustion by Dumas' process 7.99 c.c. at 0° C., and 760 mm. pressure = 0.010 grm. of nitrogen; therefore N per cent. = 2.80.
- III. 0.3820 grm. gave on cautious ignition, and subsequent moistening with nitric acid and re-ignition 0.1078 grm. of Cr_2O_3 ; therefore Cr per cent. = 19.37.

The formula $C_9H_{11}NO_{12}Cr_2O_3 \cdot 3H_2O$ requires—

	Calculated.		Found.		
			I.	II.	III.
C_9	108	20.30	20.79	—	—
H_{17}	17	3.20	3.56	—	—
N.....	14	2.63	—	2.80	—
Cr_2	105	19.74	—	—	19.37
O_{18}	288	54.13	—	—	—
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	532	100.00			

This chromium-compound requires a good deal of drying, and the determination of the chromium presents some difficulties. It is necessary to heat very cautiously to avoid loss, and subsequently to moisten thoroughly with nitric acid and to ignite very strongly at last.

Properties of the compound $C_9H_{11}NO_{12}Cr_2O_3 \cdot 3H_2O$. It is a very light powder of a snuff colour, with a shade of yellowish-green. It is very nearly insoluble in water, insoluble in either cold or boiling acetic acid. It is slowly dissolved by hydrochloric acid. Boiling with strong hydrochloric acid occasions no evolution of chlorine, as was proved by leading the vapours into solution of iodide of potassium, from which there was no evolution of

iodine. This fact proves that the organic chromium-compound contains none of the chromium in the state of chromic acid.

Submitted to the action of heat it behaves in a very interesting manner. When a quantity of it is heated in a test-tube, long before the temperature of low redness is attained, a kind of dry effervescence sets in, the light dry powder being raised in little cones from which carbonic acid gas is very rapidly escaping. At the same time drops of water condense in the upper part of the test-tube. The residue is a pyrophorus, consisting of sesquioxide of chromium and finely divided carbon.

A quantitative determination of the products of this destructive distillation was made as follows :

0.1275 grm. was put into a narrow tube, which was subsequently drawn out so as to deliver gas, and then placed in the combustion furnace, and slowly heated to redness, the gas being collected over mercury.

The gas which was thus evolved measured 26.57 c.c. at 0° C., and 760 mm. pressure. Caustic potash was then introduced which occasioned an absorption, so as to leave a residue of 12.28 c.c. at 0° C and 760 mm. pressure.

Therefore 14.29 c.c. of CO_2 had been evolved = 0.0279 grm. of CO_2 .

The loss on heating was likewise ascertained by weighing before and after the ignition. The loss was 0.064 grm.

The total capacity of the tube was likewise measured, and found to be 5.62 c.c., and the quantity of air left in the tube at the end of the operation was measured and found to be 0.80 c.c.

Reduced to percentage we have :—

100 grm. of substance lose 50.2 grm. containing 21.9 grm. of CO_2 .

(In another experiment in which the measurements were made more roughly, 0.4905 grm. of substance experienced a total loss of 0.2445 grm. and gave off 45 c.c. of CO_2 .)

If the difference between the total loss and the CO_2 be taken as water, we have :—

100 grm. of substance lose

28.3 grm. water,

21.9 grm. CO_2 .

As no oxidising agent was used in this experiment, it follows that the oxygen evolved in the form of carbonic acid

and water was oxygen originally contained in the substance.

28.3 grms. of water contain 25.2 grms. of oxygen.

21.9 grms. of CO_2 contain. . 15.9 grms. of oxygen.

41.1

The experiment has therefore shown that, exclusive of the oxygen remaining in combination with the chromium, there is 41.1 per cent. of oxygen in the original compound. The theoretical percentage of oxygen uncombined with the chromium in the original compound is 45.1, as may be found on reference to the analysis. For a direct determination of oxygen the approximation is sufficiently close.

Another interesting consequence deducible from the experiment is that one-third of the total carbon of the substance escapes as carbonic acid, and two-thirds of the total carbon remain along with the sesquioxide of chromium, constituting the pyrophorus.

A considerable quantity of $\text{C}_9\text{H}_{11}\text{NO}_{12}\text{Cr}_2\text{O}_3\cdot 3\text{H}_2\text{O}$ has been prepared on different occasions. An attempt was made to get a base from it by reduction with hydriodic acid. The following are the details:—

3.50 grm. of $\text{C}_9\text{H}_{11}\text{NO}_{12}\text{Cr}_2\text{O}_3\cdot 3\text{H}_2\text{O}$ and 35 c.c. of hydriodic acid of sp. gr. 1.67 at $20^\circ \text{C}.$, and a little phosphorus, was boiled until half of the acid had distilled over. There was some reduction evidenced by liberation of iodine. The residue was diluted with water, supersaturated with potash, and distilled. In the distillate no base except ammonia was found, and there was only a trace of ammonia, as was shown by the following:—The distillate, after being rendered acid by hydrochloric acid was subsequently concentrated by evaporation in the water-bath, and then precipitated by chloride of platinum. The total quantity of chloroplatinate weighed 0.0786 grm., which on further drying weighed 0.0782 grm., and contained 0.0342 grm. of platinum or 43.74 per cent. (Chloroplatinate of ammonium yields 44.3 per cent. of platinum.)

Most probably this trace of ammonia is purely accidental, and at any rate it is not a main product. Hydriodic acid, therefore, does not reduce the chromium-compound so as to form a base.

Finally, the *yield* of the compound and the conditions under

which it is formed, were studied, and also the quantity of oxygen consumed in its production.

From 100 parts of tyrosine it is easy to obtain quite 100 parts of the chromium-compound. As before mentioned, excess of sulphuric acid must be avoided in the preparation of the substance. The following experiments illustrate the necessity of attending to this particular:—

Took 1.195 grm. of tyrosine, and dissolved it in hot water. Then added 10 grm. of bichromate of potash, which, along with 11 grm. of H_2OSO_3 , had been previously dissolved in 100 c.c. of water. There was reaction, but *no* formation of the insoluble chromium-compound.

Took 1.00 grm. of tyrosine,
3.00 grm. $\text{K}_2\text{O}_2\text{CrO}_3$,
1.00 c.c. H_2OSO_3 .

The bichromate of potash was dissolved in 50 c.c. of water, to which the sulphuric acid was added, and finally the tyrosine was added. It dissolved completely, and, on boiling, a precipitate of the chromium-compound was obtained, which, when washed and dried, weighed 1.108 grm.

On making a calculation of the amount of chromium-compound which a given weight of tyrosine could give, supposing total conversion into the chromium-compound, it will be seen that not so much as half the tyrosine is converted in the actual case.

The liquid which deposits the chromium-compound no doubt contains the remainder of the tyrosine, either as such, or in combination with sulphuric acid.

We have, moreover, observed that after the deposit of so much chromium-compound as is readily formed, a further crop of it may be obtained by long-continued boiling of the filtrate.

An estimation of the quantity of oxygen consumed in forming a given quantity of chromium-compound was effected as follows:—

A standard solution of bichromate of potash was made, containing 49.2 milligrammes of bichromate in every cubic centimetre. Each c.c. therefore contained 8 milligrm. of active oxygen.

A solution of protochloride of tin in hydrochloric acid was made of such a strength that *one measure* (5 c.c.) took 4.6 c.c. of

the standard bichromic solution to oxidize it completely. (Iodide of potassium and starch employed.)

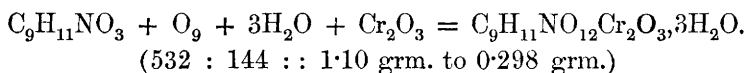
Took 1.00 grm. of tyrosine,

0.5 c.c. of H_2OSO_3 ,

50 c.c. of standard bichromate solution. Boiled: a precipitate formed. Filtered, and made up the filtrate to 100 c.c. Then titrated the filtrate. Found that one measure (5 c.c.) of the protochloride of tin took 21.5 c.c. of this filtrate. The whole filtrate, therefore, contained $21.4 \times 8 = 171.2$ milligram. of active oxygen.

There were employed $50 \times 8 = 400$ milligram. of active oxygen.

Therefore, $400 - 171.2 = 228.8$ milligram. of oxygen had been consumed by one grm. of tyrosine in giving the insoluble chromium-compound. From the 1.00 grm. of tyrosine the yield is, as determined by other experiments, 1.10 grm. of chromium-compound. If a calculation be made, it will be found that 0.298 grm. of oxygen is required to oxidize tyrosine according to the equation,



The quantity of oxygen consumed in making 1.10 grm. of $\text{C}_9\text{H}_{11}\text{NO}_{12}\text{Cr}_2\text{O}_3 \cdot 3\text{H}_2\text{O}$ is calculated to be 0.298 grm., and found to be 0.229 grm. The difference is probably due to our having rated the yield a little too high. A yield of 1.0 grm. of chromium-compound would require 0.270 grm. of oxygen. In either case it is quite plain that no other oxidation had taken place, and that the tyrosine which had not become $\text{C}_9\text{H}_{11}\text{NO}_{12}\text{Cr}_2\text{O}_3 \cdot 3\text{H}_2\text{O}$ remained unoxidized in the solution.

When tyrosine, therefore, is boiled with a solution of bichromate of potash, and not more than twice as much sulphuric acid as tyrosine, it is partially resolved into a singular chromium-compound, and the rest of it remains unoxidized.

When excess of acid is taken, so as to avoid formation of the insoluble chromium-compound, there is oxidation down to carbonic acid and water; a little formic, but no other volatile acid being produced.

The following experiment illustrates this fact:—

Took 1.00 grm. tyrosine,
3.25 grm. $\text{K}_2\text{O}_2\text{CrO}_3$,
3.00 c.c. H_2OSO_3 ,

and water up to 20 c.c. Great evolution of carbonic acid took place. After having kept the product at ordinary temperatures for some weeks, we distilled it, and converted the distillate into a baryta-salt. Weight of baryta-salt, 0.080 grm., which consisted *only* of *formate* (a little of it reduced nitrate of silver very readily and abundantly and no smell of acetic or other acid could be observed on warming with H_2OSO_3).

In this experiment, therefore, about 3 per cent. of formic acid had been given by the tyrosine. Neither much nor little sulphuric acid enables bichromate of potash to convert tyrosine into any other volatile acids except carbonic and formic.

This result is in contradiction to Fröhde, according to whom acetic and other acids are produced, and negatives the theories brought forward respecting the rational formula of tyrosine, which represent it as containing the radical ethyl.

PART II.

Tyrosine with Mercuric and Mercurous Nitrates and Mercurous Nitrite.

It is known that a deep red precipitate is obtained when tyrosine is boiled with these mercurial compounds. We have made a study of the tyrosine-compound produced by this means.

One gramme of tyrosine was dissolved in about 300 c.c. of boiling water, and mercuric and mercurous nitrates added, when a pale pinkish precipitate formed. This precipitate rapidly became crimson. The mercurous nitrate which was used contained some nitrite.

The precipitate was collected on a filter, washed and dried, first at 100°C ., and ultimately at 110°C . After being detached from the filter, it weighed 2.85 grammes. It was still further dried and analysed, with the following results:—

- I. 0.6870 grm., burnt with chromate of lead and a little copper turnings, gave 0.087 grm. H_2O , and 0.405 grm. of CO_2 . Therefore, H per cent. = 1.41, and C per cent. = 16.08.
- II. 0.7125 grm., burnt with oxide of copper and copper turnings, gave 33.33 c.c. of nitrogen gas at 0°C ., and 760 mm. = 0.04186 grm. Therefore, N per cent. = 5.87.
- III. 0.460 grm., ignited with chromate of lead and copper

turnings, gave 0.276 grm. of mercury. Therefore, Hg per cent. = 60.00.

These results accord with the formula $C_9H_9(NO_2)_2NO_3Hg_2$.

	Calculated.		Found.		
			I.	II.	III.
C_9	108	16.00	16.08	—	—
H_9	9	1.34	1.41	—	—
N_3	42	6.26	—	5.87	—
Hg_2	400	59.61	—	—	60.00
O_7	112	16.69	—	—	—
	<hr/>	<hr/>			
	671	100.00			

The following particulars relative to the production of the compound were ascertained. In two experiments the yields were respectively 318 and 320 from 100 parts of tyrosine. The theoretical yield for the total conversion of tyrosine into the mercury-compound $C_9H_9(NO_2)_2NO_3Hg_2$, is 370.7 parts of mercury-compound from 100 parts of tyrosine. From this it would seem that there is some slight destruction of the tyrosine during the process. Still, as the loss is only about 14 per cent., the destruction cannot be great.

The following details of an experiment may be cited:—Took 0.50 grm. of tyrosine and dissolved it in 300 c.c. of boiling water. Then added 15 c.c. of mercuric nitrate (strength: Liebig's standard for the determination of urea). There was no precipitation, only a red coloration. Added 10.5 c.c. of mercurous nitrate and nitrite (strength: 2.60 grm. of mercury in the 10.5 c.c.). Immediately on the addition of the mercurous salt the red precipitate fell down. This precipitate was put on a filter, washed and dried, and detached from the filter.

Ultimately it was dried at 110° C.

Weight of red precipitate (detached from filter) = 1.50 grm.

Weight adherent to filter = 0.10 „

Total = 1.60 „

The amount adherent to the filter was determined by combustion of the paper and estimation of the mercury, from which the quantity adherent to the paper admits of calculation.

Therefore, 100 parts of tyrosine yield 320 parts of the red compound.

The filtrate from the red precipitate was tested for mercuric salts by means of caustic alkali. There was no precipitation of mercuric oxide. In a second experiment, which differed from the first only in there being only 100 c.c. of boiling water instead of 300 c.c., absence of mercuric salts in the filtrate was likewise observed.

The mercurous salt, on the other hand, takes no direct part in the reaction. A quantitative determination has shown that as much is to be found after the reaction as was originally added.

The function of the mercurous salt is simply to convey nitrous acid or possibly simply to convey oxide of nitrogen (NO).

This is shown by the following facts :—

As a preliminary, it was proved that the mercurous salt contained some nitrite, by making an experiment in which all the mercurous compound was precipitated by chloride of sodium, filtering, and testing the filtrate (which would then contain any nitrite in the form of soda-salt) with permanganate solution. A great deal of permanganate was decolorised, showing the presence of nitrite in the original solution.

It was next shown that, although all the mercurous compound remains intact during the production of the red precipitate, nevertheless a large quantity of mercurous compound must be added in order to get the full yield of red compound. Thus 0.50 grm. of tyrosine and 15 c.c. of mercuric nitrate and only 2 c.c. of mercurous salt yielded only 1.08 grm. of red compound: whilst 0.50 grm. tyrosine, 15 c.c. mercuric nitrate, and 10.5 c.c. mercurous salt yielded 1.60 grm. of red compound.

When the mercurous salt is not added at all, and when double the quantity of mercuric salt is used, a pale pink precipitate is formed, which weighs still less.

Took 0.50 grm. tyrosine and
30 c.c. of mercuric nitrate.

The yield was 0.96 grm., and moreover the precipitate was quite different from the crimson compound. Finally, if tyrosine and mercuric nitrate, free from mercurous salt, be boiled, and oxide of nitrogen passed into the boiling liquid, immediately on the contact of the gas with the liquid, the dark red precipitate

will begin to form and a tolerable yield of the red compound may be obtained.

The formula for the red compound $C_9H_9(NO_2)_2NO_3Hg_2$ (more logically we should have written $C_9H_9N_3O_7Hg_2$) is to be taken quite empirically.

The red compound is attacked by alkalies with considerable energy, either potash or ammonia forming a deep-coloured red solution which deposits a sepia-like precipitate.

Nitric acid dissolves the red compound, forming a red solution, which evolves gas on being warmed.

PART III.

Action of Nitric Acid upon Tyrosine.

According to Strecker the first action of nitric acid on tyrosine consists in the formation of nitrate of nitrotyrosine, which crystallises very beautifully. According to Städeler,* when the treatment with the acid is pushed further a dinitro-compound is formed.

Städeler's investigation of this product does not, however, include a determination of the proportion of nitrogen in it, and, therefore, does not exclude the possibility of there being O_3 in place of NO_2 in the formula of his compound.

Thus, in his so-called dinitrotyrosine, Städeler found 39.30 per cent. of carbon and 3.46 per cent. of hydrogen; the nitrogen was not estimated.

This agrees with the formula $C_9H_{10}(NO_2)NO_6$ quite as well as with $C_9H_9(NO_2)_2NO_3$, as the following comparison shows:—

$C_9H_{10}(NO_2)NO_6$.				Calculated.	$C_9H_9(NO_2)_2O_3$.				Found.
C_9	108	39.42			C_9	108	39.85		39.30
H_{10}	10	3.65			H_9	9	3.32		3.46
N_2	28	—			N_3	42	—		
O_8	128	—			O_7	112	—		
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	274	100.00				271	100.00		

In like manner the analyses of the salts of so-called dinitrotyrosine accord with either formula; thus in dinitrotyrosine-lime

* *Ann. der Chem. u Pharm.* (1860) vol. cxvi, p. 82.

Städeler found 15·07 per cent. of CaO , and wrote the formula $\text{C}_9\text{H}_7(\text{NO}_2)_2\text{NO}_3\text{CaO}, 3\text{H}_2\text{O}$, whilst the formula $\text{C}_9\text{H}_8(\text{NO}_2)\text{NC}_6\text{H}_5, 3\text{H}_2\text{O}$ will do equally well.

$\text{C}_9\text{H}_8(\text{NO}_2)\text{NO}_6\text{CaO}, 3\text{H}_2\text{O}$ requires CaO per cent. = 15·30.

$\text{C}_9\text{H}_7(\text{NO}_2)_2\text{NO}_3\text{CaO}, 3\text{H}_2\text{O}$ requires CaO per cent. = 15·43.

There was found CaO per cent. = 15·07.

We have hitherto failed in the attempt to make dinitrotyrosine, but have, on the other hand, succeeded in obtaining evidence of the existence of such a product as nitro-tyrosic acid, viz., $\text{C}_9\text{H}_{10}(\text{NO}_2)\text{NO}_6$, or at any rate the corresponding lime-salt.

4 grm. of tyrosine was converted into nitrate of nitrotyrosine thus:—It was made into a paste with 16 grm. of water, and to this paste 16 grm. of nitric acid, sp. gr. 1·3, was added by degrees. The tyrosine dissolved, the solution becoming hot and assuming a yellow and then an orange colour, but evolving only traces of gas. At this stage the vessel containing the materials was immersed in cold water, whereupon an abundant crop of crystals formed so as to make a magma, which was got on to a filter, and after having been drained from the mother-liquor, dried by pressure between folds of bibulous paper. The solid citron-yellow cake of nitrate of nitrotyrosine thus obtained was mixed with 16 grms. of water and 16 grms. of nitric acid (sp. gr. 1·3), according to Städeler's prescription, and subsequently evaporated at a very gentle heat (in a sand-bath gently heated by steam).

During this operation there was first frothing; later a perfect solution was given, which was dark green at first and afterwards became red. The yellow residue was resinous whilst hot, but became brittle on cooling. It dissolved in water without difficulty, and the solution so resulting was filtered from some resinous matter and boiled with excess of carbonate of lime. In this way a deep red solution of a lime-salt was obtained which, on standing over night, deposited a small crop of very beautiful orange-yellow crystals having a singular bronze lustre, and consisting of plates of irregular shape.

This crop of crystals was dried by standing over sulphuric acid, and weighed only 0·160 grm. A very careful determination of nitrogen was made in 0·0663 grm. of the crystals by

combustion with oxide of copper and copper turnings, the gas being collected and measured over mercury.

Vol. of N + NO = 4.9 c.c. at 18° C. (dry) and 704.4 mm. pressure, or 4.26 c.c. at 0° C. and 760 mm. pressure.

Vol. of N (after removal of the NO by means of excess of oxygen and pyrogallate of potash) = 2.6 c.c. at 18° C. and 704.4 mm. (dry), or 2.27 c.c. at 0° C. and 760 mm. pressure.

Therefore total nitrogen gas equals 3.27 c.c. at 0° C., and 760 mm. = 0.00408 grm. of nitrogen, or N per cent. = 6.08.

A determination of calcium was also made in 0.0943 grm. by ignition with H_2OSO_3 , whereby 0.0335 grm. of CaOSO_3 was obtained; therefore Ca per cent. = 10.45.

These determinations accord sufficiently with the formula of an oxidized nitro-salt of calcium, viz., with $\text{C}_9\text{H}_5\text{Ca}(\text{NO}_2)\text{NO}_6 \cdot 3\text{H}_2\text{O}$ which requires:—

	Calculated.		Found.	
			I.	II.
C_9	108	29.51	—	—
H_{14}	14	3.82	—	—
N_2	28	7.65	6.08	—
Ca.....	40	10.93	—	10.45
O_{11}	176	48.09	—	—
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	366	100.00		

Städeler's formula for dinitrotyrosate of calcium requires 11.5 per cent. of nitrogen, which does not agree with our analysis.

The circumstance that, as just described, there is evolution of gas, and green coloration of the liquid (evidently from N_2O_3) even on very careful treatment of nitrotyrosine with dilute nitric acid, is in itself a strong indication that the action of the nitric acid on nitrotyrosine consists of an oxidation (a mere substitution of NO_2 for H gives rise to water as the complementary product).

There can be very little doubt that Städeler's dinitrotyrosine was an oxidized nitrotyrosine.

When the action of nitric acid is pushed further, there is, as others have observed before us, an abundant production of oxalic acid. From 4 gramm. of tyrosine we obtained 0.6435 gramm. of perfectly dry pure oxalate of ammonia, and we think it probable that about an equal quantity was lost in the washing, so that the yield of oxalic acid by oxidation of tyrosine with nitric acid is very considerable.

A combustion of 0.1550 gramm. of this ammonia-salt with oxide of copper and copper turnings, gave 0.0990 gramm. H_2O and 0.091 gramm. CO_2 .

$\text{C}_2\text{O}_2(\text{NH}_4\text{O})_2\text{H}_2\text{O}$ requires—			Found.
C_2	24	16.90	16.01
H_{10}	10	7.04	7.10
N_2	28	—	—
O_5	80	—	—
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	142	100.00	

From the ammonia-salt we made a silver-salt, which was analysed as follows:—

I. 0.3045 gramm., dried in vacuo over H_2OSO_3 , was burnt with oxide of copper, and gave 0.0080 gramm. H_2O , and 0.0862 gramm. CO_2 .

II. 0.6195 gramm. of silver-salt dried at 80°C ., gave on combustion with oxide of copper, 0.0085 gramm. H_2O , and 0.1760 gramm. CO_2 . These numbers accord with the formula of oxalate of silver.

Calculated.		Found.	
		I.	II.
C_2	24	7.89	7.74
H_0	0	0.00	0.29
Ag_2	216	71.05	—
O_4	64	21.06	—
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	304	100.00	

The explosive character of the silver-salt on being heated, also the insolubility of the lime-salt in acetic acid, and the production of carbonic oxide on strongly heating the lime-salt, were verified. The analysis of the silver-salt shows that no mes-oxalic acid is produced, a circumstance to which we attach some importance. There is moreover no production of picric acid.

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Action of Nitrous Acid.

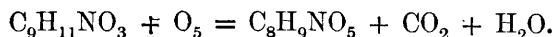
According to Städeler, nitrous acid also produces dinitro-tyrosine. We have not been able to verify this observation. When tyrosine is suspended in water through which N_2O_3 (evolved by the action of nitric acid on arsenious acid) is passed, gradual solution of the tyrosine takes place, the liquid assuming a yellow colour and evolving some gas. This solution was saturated with carbonate of lime, filtered, and the filtrate left to evaporate over sulphuric acid. A brown scum continually formed on the surface of the solution of lime-salt; this was removed by filtration, and acetate of lead was added to the filtrate, wherein it occasioned a chocolate-coloured precipitate of lead-salt. This precipitate was washed, dried at 110°C ., and analysed.

- I. 0.4660 grm. burnt with oxide of copper and a little copper turnings gave 0.0840 grm. of H_2O and 0.3880 grm. of CO_2 ; therefore C per cent. = 22.71 and H per cent. = 2.00.
 II. 0.1755 grm. gave 6.42 c.c. nitrogen at 0°C ., and 760 mm. = 0.00807 grm. N per cent. = 4.60.
 III. 0.2600 grm. ignited with H_2OSO_3 gave 0.1970 grm. of PbOSO_3 . Pb per cent. = 51.77.
 IV. 0.1425 grm. gave 0.105 grm. PbOSO_3 ; therefore Pb per cent. = 50.34.

	Calculated.		Found.			
			I.	II.	III.	IV.
C_8	96	23.71	22.71	—	—	—
H_7	7	1.73	2.00	—	—	—
N.....	14	3.46	—	4.60	—	—
Pb.....	207	51.23	—	—	51.77	50.34
O_5	80	19.87	—	—	—	—
	<hr/>	<hr/>				
	404	100.00				

It would, therefore, seem that nitrous acid disintegrates the tyrosine to a certain extent, at any rate under the influence of an alkali.

The acid corresponding to this lead-salt should have the formula $\text{C}_8\text{H}_9\text{NO}_5$, and be derived from tyrosine as follows:—



Inasmuch as the new compound is highly coloured, analogy would lead us to suspect that it is derived from tyrosine by condensation of the molecule ; probably, therefore, the formula is at least double.

PART IV.

Action of Iodide of Ethyl.

We sealed up together 1.00 grm. of tyrosine with about 4 grm. of iodide of ethyl and heated the mixture to 100° C. The tyrosine shrunk together in a wonderful manner, but on subsequently opening the tube and warming at 100°, all the iodide of ethyl evaporated, leaving the one gramme of tyrosine unaltered in weight, and apparently quite unchanged in properties. There is, therefore, no easy action between tyrosine and iodide of ethyl.

Action of Reducing Agents.

We failed to reduce tyrosine by means of hydriodic acid at 130° C.

PART V.

General Considerations.

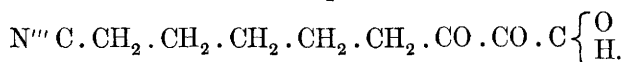
The chemical history of tyrosine is now sufficiently complete for the determination of its rational constitution.

The nitrogen contained in it cannot be in the nitro-state, because Will and Varrentrappe's process is available for the estimation of the nitrogen. Neither can the nitrogen exist as amidogen or as imidogen. Iodide of ethyl effects no substitution. Therefore, the nitrogen must be altogether in direct combination with the carbon.

There is no hydroxyl, otherwise hydriodic acid would effect a reduction. Therefore, all the oxygen must be in direct and complete union with the carbon. There is certainly no sign of highly condensed oxygen in tyrosine.

Tyrosine appears to be derived from C_9H_{20} , being the fully expanded hydride of nonyl, which has undergone substitution to a considerable extent, three atoms of hydrogen having been replaced by N''' and six atoms of hydrogen by three atoms of oxygen.

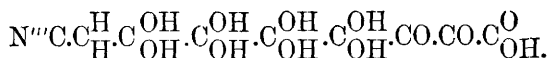
Tyrosine ought to be volatile, without decomposition, at diminished barometric pressure. At one pole of the molecule there will exist N''' , at the other pole $CO.H$, thus:—



The great stability of tyrosine is a sign that the grouping of its carbon is regular. Everything in its chemical history converges towards this rational formula.

The fact that with dilute chromic acid it gives no acetic acid negatives the assumption of there being ethyl in union with part of the nitrogen, or in union with oxygen. The easy formation of carbonic acid is in harmony with the existence of the three atoms of carbonic oxide. The non-production of picric acid by oxidation with nitric acid is significant of the non-existence of the aromatic group.

The remarkable chromium-compound is most probably a compound highly charged with hydroxyl, thus:—



The hydrated oxide of chromium being possibly tacked on to the nitrogen, which has the faculty of being pent-atomic; and the salts of tyrosine in general are probably held together by the pent-atomic power of the nitrogen.

(The researches described in this paper have been made in the pathological laboratory at St. Thomas's Hospital).

Pathological Laboratory, St. Thomas's Hospital,
July, 1869.