STUDIES ON AMINO-ACIDS AND RELATED COMPOUNDS. PART II. ELECTROLYTIC OXIDATION OF PYRROLIDONE-CARBOXYLIC ACID.

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In the previous communication,(1) it was stated that succinamic acid was obtained from the electrolysate of glutamic acid, and its formation was ascribed to the anodic oxidation of pyrrolidone-carboxylic acid, which could be formed, apart from electrolysis, by the dehydration of glutamic acid.

The formation of pyrrolidone-carboxylic acid from glutamic acid is well known. Menozzi and Appiani(2) first stated that glutamic acid is very easily converted by heating into its lactam, pyrrolidone-carboxylic acid. E. Abderhalden(3) reported that *l*- and *dl*-pyrrolidone-carboxylic acids were obtained from glutamic acid when it was heated to 150–160°C. and 180–190°C. respectively. F. W. Foreman(4) observed that glutamic acid was converted into its lactam when its aqueous solution was boiled for a certain length of time, and reversely, pyrrolidone-carboxylic acid was reconverted into glutamic acid by boiling with strong hydrochloric acid. C. Okinaka(5) found that above reversible reaction occurred even in the absence of acid or alkali, and studied the equilibrium points of above reversible reactions at 120°, 130° and 140°C. He also mentioned that the rate of transformation into the lactam was increased as the temperature was raised or by the presence of dilute alkali, and it was retarded in the presence of an excess of strong acids or alkalies.

The author intended to ascertain that such a reversible reaction would occur actually even in the solution in normal sulphuric acid and at a lower temperature, and has undertaken the following experiments.

d-Glutamic acid and *l*-pyrrolidone-carboxylic acid were dissolved in N.-sulphuric acid, and kept at 35° and 50°C., and amounts of amino-N in their solution were determined from time to time. The changes of amino-N

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(1) Y. Takayama, Studies on amino-acids and related compounds. Part I.

(2) Menozzi und Appiani, Abderhalden: „Biochem. Handlexikon" **4**, 615.

(3) E. Abderhalden und K. Kautzsch, *Z. physiol. Chem.*, **64** (1910) 447.

(4) F. W. Foreman, *Biochem. J.*, **8** (1914), 481.

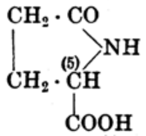
(5) C. Okinaka, "The Sexagint" (a collection of papers dedicated to Prof. Y. Osaka by his pupils in celebration of his 60th birthday) Kyoto, (1927), p. 27.

content thus obtained showed the degree of their conversions. The results obtained are tabulated in Fig. 1, Tables I and II.

From the above results it is clear that the reversible reaction proceeds even at such a low temperature as 35°C., and we can conclude that a solution of glutamic acid, kept under similar conditions as in the electrolytic oxidation, should contain a certain amount of pyrrolidone-carboxylic acid (i).

Next, in order to compare the rate of the electrolytic oxidation of glutamic acid with that of pyrrolidone-carboxylic acid, each of these acids was dissolved in N.-sulphuric acid and oxidised with a lead peroxide anode under the same conditions. The amounts of ammonia-N formed were determined at a certain interval of time. The results are given in Fig. 2, the curves representing ammonia-N/faradays per mol.

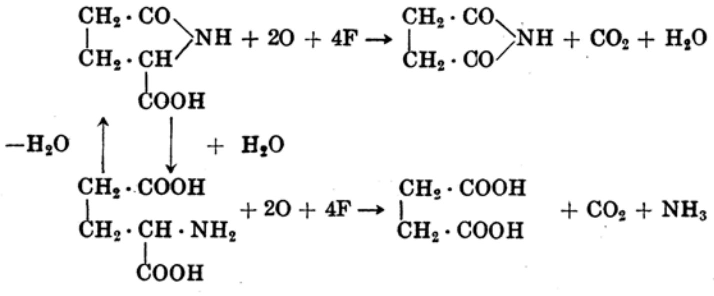
From these curves we see that the rate of oxidation of pyrrolidone-carboxylic acid is far greater than that of glutamic acid and the difference of the rates may be ascribed to the presence of the easily oxidisable carbon (5) in the former acid (ii).

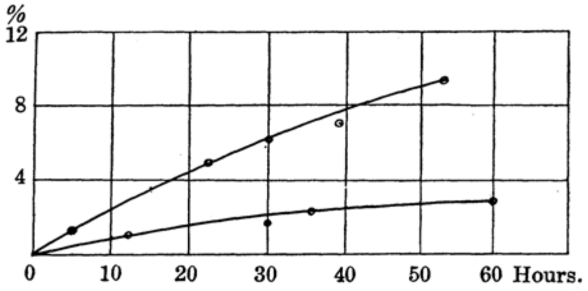


Pyrrolidone-carboxylic acid was dissolved in N.-sulphuric acid and oxidised at a lead peroxide anode. The oxidised solution contained a little of ammonia-N (MgO) and much of ammonia-N (NaOH), hence the presence of imino or amino compound is easily presumable (iii).

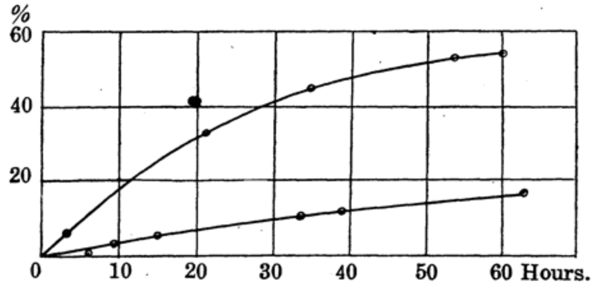
In fact, succinimide was isolated abundantly together with a small amount of succinic acid (iv).

From these facts, (i), (ii), (iii) and (iv), it is quite probable that the oxidation of pyrrolidone-carboxylic acid proceeds in the following scheme and that succinamic acid formed from glutamic acid is produced by the hydrolysis of sccinimide.



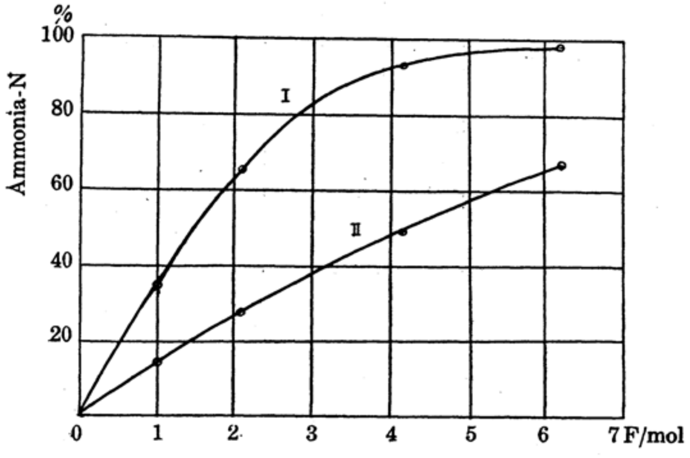


Glutamic Acid Changed.



Pyrrolidone-Carboxylic Acid Changed.

Fig. 1.



I = Pyrrolidone-Carboxylic acid.
II = Glutamic acid.

Fig. 2.

Experimental Part.

Conversion of Glutamic Acid into Pyrrolidone-Carboxylic Acid and vice versa.

d-Glutamic acid (N = 9.25% ; calc. N = 9.50%)
$[\alpha]^{20}_{D} = +30.5°$ (as hydrochloride).
l-Pyrrolidone-carboxylic acid (N = 10.67% ; calc. N = 10.85%)
$[\alpha]^{20}_{D} = -11.55°$ (aqueous solution).

The solutions used: 5 gr. of glutamic acid in 50 c.c. of N.-sulphuric acid, and 5 gr. of pyrrolidone-carboxylic acid in 50 c.c. of N.-sulphuric acid.

The procedure: The solution to be examined was introduced into a stoppered flask and kept at 35° or 50°C. in a thermostat. After a certain interval of time, 2–5 c.c. of the solution were taken, and total-N as well as amino-N (van Slyke) in it were determined. The results of the experiment are shown in Tables I and II.

Table I.

<table>
<tr><th colspan="5">Glutamic acid at 50°C.</th></tr>
<tr><th>Time.</th><th>Total-N. in 100 c.c.</th><th>NH_2-N. in 100 c.c.</th><th>Glutamic acid.</th><th>Glutamic acid changed.</th></tr>
<tr><td>0 hrs.</td><td>0.8762 gr.</td><td>0.8694 gr.</td><td>99.2%</td><td>0 %</td></tr>
<tr><td>5</td><td>,,</td><td>0.8578</td><td>97.9</td><td>1.3</td></tr>
<tr><td>23</td><td>,,</td><td>0.8256</td><td>94.2</td><td>5.0</td></tr>
<tr><td>30</td><td>,,</td><td>0.8175</td><td>93.3</td><td>5.9</td></tr>
<tr><td>39</td><td>,,</td><td>0.8100</td><td>92.5</td><td>6.7</td></tr>
<tr><td>54</td><td>0.8798</td><td>0.7912</td><td>89.9</td><td>9.3</td></tr>
<tr><th colspan="5">Glutamic acid at 35°C.</th></tr>
<tr><td>6 hrs.</td><td>0.8896 gr.</td><td>0.8768 gr.</td><td>98.6%</td><td>1.4%</td></tr>
<tr><td>12</td><td>0.8932</td><td>0.8806</td><td>98.6</td><td>1.4</td></tr>
<tr><td>30</td><td>0.8861</td><td>0.8710</td><td>98.3</td><td>1.7</td></tr>
<tr><td>36</td><td>0.8896</td><td>0.8680</td><td>97.6</td><td>2.4</td></tr>
<tr><td>60</td><td>0.8896</td><td>0.8616</td><td>96.9</td><td>3.2</td></tr>
</table>

Table II.

Time	Total-N. in 100c.c.	NH_2-N (increased) in 100 c.c.	Pyrrolidone-carboxylic acid changed.
Pyrrolidone-carboxylic acid at 50°C.			
3 hrs.	1.052 gr.	0.0558 gr.	5.3%.
21	,,	0.3486	33.1
27	,,	0.3828	36.4
35	1.045	0.4632	44.3
54	,,	0.5645	54.4
60	1.055	0.5814	55.1
Pyrrolidone-carboxylic acid at 35°C.			
6 hrs.	1.029 gr.	0.0114 gr.	1.1%
9	1.030	0.0378	3.7
15	,,	0.0597	5.8
33	,,	0.1105	10.8
39	,,	0.1323	12.8
63	,,	0.1860	18.1

Rates of Oxidation of Glutamic Acid and Pyrrolidone-Carboxylic Acid. A solution containing 14.714 gr. of glutamic acid in 280 c.c. of N.-sulphuric acid and a solution containing 12.921 gr. in 280 c.c. of N.-sulphuric acid were electrolysed in undivided cells which were connected in series under the following conditions: The electrodes are of equal size (4×5 cm.), anode: lead peroxide sheet, cathode: lead sheet, C.D.: 2 amp./dm^2., temperature: 19–20°C.

The process of investigation: In the course of electrolysis at every definite consumption of electricity, 10 c.c. of the solution were drawn out and the total ammonia-N (NaOH) in it was determined and its percentage to total-N was calculated, which denotes the percentage of amino-acid oxidised. The results of this experiment are shown in Table III.

Table III.

Faradays per mol.	Oxidised solution.	Glutamic acid oxidised N. in 10 c.c.	Pyrrolidone-carboxylic acid N. in 10 c.c.
1.00 F	0.100 mol 280 c.c.	Total-N, 47.80 mg. NH_3-N 6.68 14.0%	47.80 mg. 16.72 35.0%
2.07 F	0.093 mol 260 c.c.	Total-N, 47.40 mg. NH_3-N 12.90 27.4%	48.50 mg. 31.90 65.8%
4.07 F	0.0858 mol 240 c.c.	Total-N, 46.45 mg. NH_3-N 22.60 48.6%	48.80 mg. 45.40 93.0%
6.24 F	0.0786 mol 220 c.c.	Total-N, 45.70 mg. NH_3-N 31.10 68.1%	48.80 mg. 48.00 98.4%

Electrolytic Oxidation of Pyrrolidone-Carboxylic Acid. Separation of Oxidation Products. 6.45 Gr. of pyrrolidone-carboxylic acid was dissolved in 120 c.c. of N.-sulphuric acid and electrolysed with a lead peroxide anode and a lead cathode with an anodal current density of 2 amp./dm^2. The amount of electricity was 7.97 amp. hours, and the temperature was 23–28°C.

The nitrogen distribution of the oxidised solution was as follows:

Total-N	100.0%
Ammonia-N (MgO)	15.7
Ammonia-N (NaOH)	80.6

The solution was neutralised with barium hydroxide, and the precipitated barium sulphate was filtered off. The filtrate was evaporated to dryness under reduced pressure, and extracted with alcohol (A). The mass insoluble in alcohol was treated with acetone (B), after acidifying with hydrochloric acid. From (B) a small quantity of succinic acid, m.p. 181°C., was obtained.

On distilling off alcohol from (A), crystals were obtained which were found to be almost pure succinimide (3.2 gr.).

Similarly 6.45 gr. of pyrrolidone-carboxylic acid was oxidised with a current quantity of 8.0 amp. hours (at 24°C.). The oxidised solution was neutralised with potassium hydroxide, evaporated to dryness under reduced pressure, and extracted with absolute alcohol. The crystals formed after removal of alcohol, were recrystallised from acetone in colourless crystals (3.4 gr.), m.p. 126°C., alone or when mixed with a pure sample of succinimide (Kahlbaum).

Anal.: Subst. = 0.1114, 0.0919; CO_2 = 0.1980, 0.1641; H_2O = 0.0489, 0.0406 gr.
Subst. = 0.2626; NH_3 = 26.56 c.c. of N./10–H_2SO_4.
Found: C = 48.49, 48.68; H = 4.89, 4.94; N = 14.17%.
Calc. for $C_4H_5O_2N$ (succinimide): C = 48.48; H = 5.02; N = 14.15%.

From the residue, after separating succinimide, succinic acid, m.p. 183°C., was obtained.

Oxidation of Glutamic Acid. A solution consisting of 530 c.c. of N.-sulphuric acid and 50 gr. of glutamic acid was electrolysed with a lead peroxide anode, the amount of electricity applied being 32.8 amp. hours. The ammonia-N (NaOH) of the oxidised solution amounts to 12.3% of total nitrogen.

The solution was neutralised with barium carbonate, and filtered. The filtrate was evaporated to dryness, and extracted with acetone containing a little hydrochloric acid. The residue, after removal of acetone, was recrystallised from acetone and alcohol, succinamic acid being obtained (0.5 gr.) in colourless crystals, m.p. 154–155°C.

Anal.: Subst. = 0.1155; NH_3 = 10.10 c.c. of N./10–H_2SO_4.
Found: N = 12.26%.
Calc. for $C_4H_7O_3N$ (succinamic acid): N = 11.94%.

The above attempt to obtain succinimide from the electrolysate of glutamic acid by the similar treatments as in the case of pyrrolidonecarboxylic acid was a failure, while a small amount of succinamic acid was obtained. This fact is explained as follows. A small amount of succinimide, perhaps once formed in the solution, may have been completely hydrolysed to succinamic acid during electrolysis and various treatments for its isolation.

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