ON THE SYNTHESIS OF LIVING ALBUMIN

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Having under the conditions given in the preceding papers determined the products which result from the complete hydrolysis of albumin, I will now proceed to consider what is the constitution of albumin itself, or in other words, what are the respective constituents of the albuminous molecule from which these products are derived.

In dealing with the origin of lactic acid I have already indicated the way in which, in the earlier stages of the genesis of organic matter in plants, the following substances may be formed, hydrocyanic acid; its condensed product amino-malonic nitrile, with its derivative tartronic nitrile; acetic anhydride; pyruvic nitrile; and methyl-tartronic nitrile. The series of changes by which we can proceed to the formation of the various fatty aldehydes, commencing with the lowest, namely, formic aldehyde, have also been referred to.¹ It remains now to consider what are the antecedents of tyrosine and in what form they exist in protein. Secondly, in what form do the antecedents of the amino-fatty acids exist therein, and lastly what are the antecedents of aspartic and glutamic acids.

The answer to these questions will be obtained by considering the synthesis of the respective bodies.

ON THE ANTECEDENTS OF TYROSINE IN LIVING PROTEIN

On page 199 I have already indicated the method by which the synthesis of tyrosine may be effected from *p.* oxybenzaldehyde, amino-malonic nitrile, and 2 HCN. Practically the result is—

1. See pages 195-8.

By similar reactions we may from *p.* amino-benzaldehyde obtain *p.* amino-phenyl alanine $p. \text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$ the hydrochloride of which treated with a single molecular equivalent of NaNO_2 at 0°C . and then boiled yields tyrosine; but if an excess of NaNO_2 is used the compound is decomposed into tyrosine and oxyphenyl lactic acid,¹ $\text{OH} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2 \cdot \text{CH}(\text{OH}) \cdot \text{COOH}$. Now when tyrosine is taken into the animal system it is converted into hydro-para-coumaric acid and *p.* oxy-phenyl-acetic acid². With this exception, however, all other para derivatives of benzene when taken into the animal system are immediately excreted, with very little change, in the urine³, so that it is improbable that either *p.* oxybenzoic aldehyde or *p.* amino-benzaldehyde exist in living protein. On the other hand *o.* amino-benzaldehyde under certain conditions combines with aldehydes and ketones to form chinoline derivatives⁴

and this suggests that *o.* amino benzaldehyde may be a constituent of living protein, since chinoline and its derivatives are obtained by the distillation of certain vegetable alkaloids which are derivatives of vegetable albumin. Some of the ortho-derivatives of benzene, moreover, under certain conditions, can be transformed into the para-compounds; *o.* oxybenzoic acid for instance when heated with potash to 220° is converted in some degree into *p.* oxybenzoic acid.⁵

I shall therefore assume that in the living protein amino-benzaldehyde exists in the *ortho*-form, and that in some way it is converted into the *para*-form before entering into the formation of tyrosine. In living protein then we have as the antecedents of tyrosine, amino-oxy-benzaldehyde, amino-malonic nitrile and hydrocyanic acid—

which with $8 \text{H}_2\text{O}$ form

1. Friedländer, *Annal.*, Bd. CCXIX, s. 223, u. Bd. CCXXIX, s. 227.

2. Blendermann, *Zeitsch. f. phys. Chemie*, Bd. VI, s. 234.

3. Schrotten, *ibid.*, Bd. VII, s. 23.

4. Friedländer, *Berichte*, Bd. XV, s. 2574, Bd. XVI, s. 1833, Bd. XXV, s. 1752.

5. Kolbe, *Journ. f. praktische Chemie* (2), Bd. XI, s. 24.

ON THE SYNTHESIS OF THE AMINO-FATTY ACIDS

Amino - Caproic Acid $(\text{CH}_3 \cdot (\text{CH}_2)_3 \cdot \text{CH}(\text{NH}_2)\text{COOH})$.— If valerianic aldehyde is mixed with aqueous ammonia the aldehyde is converted into valeral ammonia and this digested with hydrocyanic acid and hydrochloric acid, is converted into leucine.

This is the usual way of obtaining leucine synthetically. Tiemann, however, has shown¹ that the amido-acids, both of the fatty and aromatic series, may be obtained by converting the aldehydes and ketones into cyan-alcohols, then into amino-nitriles or cyan-amides and thence into the amido acids. We may consequently have the following changes :—

1. Ber. XIV, s. 1985. 'The amido-acids of the fatty series are easily obtained by the familiar reactions which take place on treating aldehyde ammonia with hydrochloric and hydrocyanic acids, and which led Strecker to the discovery of alanine. . . The reactions indicated by Strecker take place unquestionably according to the following general formulae :—

The question arises, whether the cyanamide $\text{R} \cdot \text{CH} \begin{cases} \text{NH}_2 \\ \text{CN} \end{cases}$ could not be obtained more readily from the cyanhydrides of the aldehydes $\text{R} \cdot \text{CH} \begin{cases} \text{OH} \\ \text{CN} \end{cases}$ by digesting them with ammonia, expecting the ultimate change to be as follows :—

The truth of this supposition has been confirmed by experiment.—Ber. XIII, s. 382.

which by dehydration is converted into the anhydride $\text{C}_4\text{H}_9 \cdot \text{CH} \begin{Bmatrix} \text{NH} \\ \text{CO} \end{Bmatrix}$

This method is applicable generally to the production of the amino-acids and we have

Practically, however, we may regard the cyan-alcohols as the constituents in living albumin, which are the antecedents of, and by hydrolysis are converted into the amino-fatty acids, since omitting the intermediate formation of the nitrile of the amino acid we have

Tiemann has also shewn¹ that by treating the di-ethyl, ethyl-methyl, and di-methyl ketones in the same manner, other iso-amino acids are formed—

These amino-fatty acids can also be prepared² in the same way as tyrosine by combining the fatty aldehydes by means of Perkin's

1. *Berichte*, Bd. XIV, s. 1975.

2. E. Erlenmeyer, Jnr., *Annal. d. Chemie*, Bd. CCCVII, s. 74.

reaction with those derivatives of glycocoll which have one of the hydrogen atoms of the NH_2 replaced by an acid radicle such as

forming a lactimide which heated with dilute aqueous solution of soda is transformed into an acid. This on reduction becomes

On the Synthesis of Aspartic and Glutamic Acids.—

The lowest member of this series is amino-malonic acid $\text{CH}(\text{NH}_2) \cdot \text{COOH}$

the nitrile of which $\begin{matrix} \text{CH}(\text{NH}_2) \cdot \text{CN} \\ | \\ \text{CN} \end{matrix}$ is

formed as shewn on page 197, from the condensation of three molecules of HCN , and by desamination should be converted into tartronic nitrile. Theoretically it should be possible to convert these two bodies respectively into amino-malonic acid and tartrofic acid. Hitherto this has not been accomplished.

We have here, however, a demonstration of the existence of the nitrile of the lowest member of the aspartic series and this is a strong argument in favour of the existence of the nitriles of the two other members. The facts also that the antecedents of the amino-fatty acids are the fatty aldehydes combined with HCN, and that the antecedent of tyrosine is an aromatic aldehyde render it most probable that aspartic and glutamic acids have a similar origin. I shall now endeavour to shew how, in this way, their synthesis may possibly be accomplished.

Synthesis of Aspartic Acid.—Cyan-acet-aldehyde $\text{CH}_2(\text{CN}) \cdot \text{CHO}$ can be obtained from chloroacetal $\text{CH}_2\text{Cl} \cdot \text{CH}(\text{C}_2\text{H}_5\text{O})_2$ or, chloroacet-aldehyde $\text{CH}_2\text{Cl} \cdot \text{CHO}$ by converting the latter into iodoaldehyde, and thence into the cyanogen compound. Treating this compound with HCN and then with NH_3 we should obtain the corresponding cyanamide—

which acted upon by acids or alkalies would be converted into asparagine or aspartic acid—

consequently if oxysuccinic nitrile, which, I suggest, is the antecedent of aspartic acid in living protein, is heated in a sealed tube with BaH_2O_2 the following reaction would ensue :—

If, however, the cyan-acet-aldehyde is first combined with NH_3 we should have—

which reduced by nascent hydrogen (H_4) becomes

Combining this with HCN we obtain $\text{CH}_2(\text{NH}_2) \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2)\text{CN}$ which on saponification becomes $\text{CH}_2(\text{NH}_2) \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2)\text{COOH}$
diamino-butyric acid

Moreover, if by the Perkin's reaction we combine cyan-acetic-aldehyde with acetyl or benzoyl glyocoll (derived from amino-malonic nitrile) as in the synthesis of tyrosine, the following reactions should ensue :—

which on reduction with H_6 becomes

and is then resolved into

By bacterial action Ellinger¹ succeeded in converting this into

By combining cyanamide with ornithin, argenin is formed.

The Synthesis of Glutamic Acid.—We may assume that with β cyanpropionic aldehyde $\text{CH}_2(\text{CN}) \cdot \text{CH}_2 \cdot \text{CHO}$ similar reactions will take place to those with cyan-acet-aldehyde. Treating it with

* Which is excreted by birds after the ingestion of benzoic acid (Kossel).

1. *Zeitsch. f. phys. Chemie*, Bd. XXIX, s. 334.

HCN, and then with NH_3 , the cyan-alcohol would first be formed and then the cyan-amide or

which by saponification would be converted into

If, however, the cyan-propionic aldehyde is first combined with NH_3 and then undergoes reduction the following reactions will take place :—

which reduced by

combining this with HCN, and then saponifying, we again obtain ornithin or

On the other hand if we combine the cyan-propionical dehyde with acetyl or benzoyl-glycocoll by the Perkin's reaction and then reduce the resulting compound we should obtain

which combined with cyanamide forms Drechsel's lysatinine.

By bacterial action also lysin is converted into cadaverine

It follows from this that aspartic acid and ornithin have a common origin, which is also the case with glutamic acid and lysine. Furthermore, that oxy-succinic or malic nitrile and oxy-glutaric nitrile are the antecedents in living albumin of aspartic acid and glutamic acid respectively, since by heating them in a sealed tube with BaH_2O_2 these two acids would be produced.

Finally, we have to determine the antecedents in the protein molecule, of Schutzenberger's polynomial ;

The very simplicity of this polynomial makes it difficult to determine its antecedents, for the possible ways in which they may arise may truly be said to be innumerable. It is, however, unnecessary for me to discuss the possibilities. I shall content myself with stating the result at which I have arrived, briefly indicating the grounds which have led me to it.

In describing the synthesis of tyrosine I have shewn that its antecedents are—

which with eight molecules of H_2O give

thus furnishing $(\text{COOH})_2 + \text{CO}_2 + 5 \text{NH}_3$ towards the polynomial. Again in describing the synthesis of glutamic, aspartic and amino-malonic acids I have represented these as resulting from oxyglutaric, malic and tartronic nitriles. These under the action of baryta in a sealed tube become respectively—

furnishing three more molecules of NH_3 . The remaining portion of the polynomial—

is, therefore, all that remains to be considered.

It has been shewn that all the compounds hitherto dealt with may be derived from the cyanides or nitriles. It is not improbable, therefore, that the sulphur in albumin is present also as a cyanide, namely, as sulpho-cyanide, and this assumption is rendered more probable as this compound is found, though in small quantities, in the saliva, and is also excreted in the urine.¹

Sulphocyanic acid $\text{CN} \cdot \text{SH}$ is very unstable, and is quickly resolved into hydrocyanic acid and persulphocyanic acid² which under

certain conditions are resolved as follows :—³

and

This is the form, then, in which I suggest the sulphur exists in the albuminous molecule, and which furnishes these constituents of the polynomial.

We have now only to determine the origin of the remaining terms

In a previous paper (see page 200) I endeavoured to show that diacetyl-dicyanide was a constituent of protein, being the antecedent of methyl-tartronic nitrile. Now diacetyl-dicyanide acted upon by alkalies in the cold is resolved into NH_3 , HCN and $\text{CH}_3 \cdot \text{COOH}$, and when the temperature is raised we have

I have also shown that 3HCN and $(\text{CH}_3 \cdot \text{CO})_2\text{O}$ are among the

1. *Gschleiden, Jahresb. über die Fortsch. d. Chemie*, s. 1001, 1877.
2. *Watt's Dictionary of Chemistry*, Vol. V, p. 505.
3. *Ibid.*, Vol. IV, p. 379.

earliest products in the genesis of protein. These two substances acted upon by BaH_2O_2 are hydrolysed as follows :—

The following compounds, therefore, may be regarded as the antecedents of the polynomial :—

that is to say—

which with the terms $\text{CO}_2 + 5 \text{ NH}_3 + (\text{COOH})_2$ furnished by the hydrolysis of the antecedents of tyrosine, and with 3 NH_3 resulting from the hydrolytic decomposition of tartronic, malic and oxyglutaric nitriles in a sealed tube make up—

which, as $2 \text{ H} \cdot \text{COOH}$ heated in a sealed tube with BaH_2O_2 is converted into $\text{H}_2 + (\text{COOH})_2$ becomes

From these data the composition of living albumin may be represented in the following tabular form :—

COMPOSITION OF LIVING ALBUMIN

(i)	(ii)	(iii)	(iv)	(v)	(vi)
3 HCN	$(\text{NH}_2)\text{C}_6\text{H}_4 \cdot \text{CHO}$ amino-benzaldehyde	$\text{CH}(\text{OH}) \cdot \text{CN}$	$3 \text{CH}_3 \cdot (\text{CH}_2)_2 \cdot \text{CH}$ butene cyan-alcohol	$2 \text{CH}_3 \cdot \text{CH}$ ethylidene cyan-alcohol	$3 \text{CH}_3 \cdot (\text{CH}_2)_3 \cdot \text{CH}$ pentene cyan-alcohol
3 CNHS thio-cyanic acid	$\text{CH}(\text{NH}_2)(\text{CN})_2$ amino malonic nitrile + 2 HCN	$\text{CH}(\text{OH}) \cdot \text{CN}$ $\text{CH}_3 \cdot \text{CN}$ malic or oxy-succinic nitrile	$3 \text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}$ propylidene cyan-alcohol	$2 \text{CH}_3 \cdot \text{CH}$ ethylidene cyan-alcohol	$3 \text{CH}_3 \cdot (\text{CH}_2)_2 \cdot \text{CH}$ butene cyan-alcohol
$(\text{CH}_3 \cdot \text{CO})_2\text{O}$ acetic anhydride		$\text{CH}(\text{OH}) \cdot \text{CN}$ CN tarttronic, or oxy-malonic nitrile			$9 \text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}$ propylidene cyan-alcohol
$(\text{CH}_3 \cdot \text{CO} \cdot \text{CN})_2$ diacetyl-dicyanide					$\text{CH}_3 \cdot \text{CH}$ ethylidene cyan-alcohol
		$\text{CH}_3 \cdot \text{C}(\text{NH}) \cdot \text{CH}(\text{C}_2\text{H}_5) \cdot \text{COOH}$ imino-ethyl-acetyl-acetic acid			$3 \text{CH}_3 \cdot (\text{NH}) \cdot \text{CH}(\text{C}_2\text{H}_5) \cdot \text{COOH}$ imino-ethyl-acetyl-acetic acid
		$\text{CH}_3 \cdot \text{C}(\text{NH}) \cdot \text{CH}(\text{CH}_3) \cdot \text{COOH}$ imino-methyl-acetyl-acetic acid			$3 \text{CH}_3 \cdot \text{C}(\text{NH}) \cdot \text{CH}(\text{CH}_3) \cdot \text{COOH}$ imino-methyl-acetyl-acetic acid
		$\text{CH}_3 \cdot \text{C}(\text{NH}) \cdot \text{CH}_2 \cdot \text{COOH}$ imino-acetyl-acetic acid		$2 \text{CH}_3 \cdot \text{C}(\text{NH}) \cdot \text{CH}_2 \cdot \text{COOH}$ imino-acetyl-acetic acid	$9 \text{CH}_3 \cdot \text{C}(\text{NH}) \cdot \text{CH}_2 \cdot \text{COOH}$ imino-acetyl-acetic acid
					$\text{CH}_3 \cdot \text{C}(\text{NH}) \cdot \text{COOH}$ imino-pyruvic acid
$\text{C}_{16}\text{H}_{18}\text{N}_6\text{O}_8\text{S}_3$ + $19 \text{H}_2\text{O}$ $\text{C}_{16}\text{H}_{168}\text{N}_6\text{O}_{24}\text{S}_3$	$\text{C}_{12}\text{H}_{12}\text{N}_6\text{O}$ + $8 \text{H}_2\text{O}$ $\text{C}_{12}\text{H}_{28}\text{N}_6\text{O}_9$	$\text{C}_{27}\text{H}_{39}\text{N}_9\text{O}_9$ + $9 \text{H}_2\text{O}$ $\text{C}_{27}\text{H}_{67}\text{N}_9\text{O}_{18}$	$\text{C}_{27}\text{H}_{45}\text{N}_6\text{O}_8$ + $6 \text{H}_2\text{O}$ $\text{C}_{27}\text{H}_{60}\text{N}_6\text{O}_{12}$	$\text{C}_{14}\text{H}_{24}\text{N}_6\text{O}_8$ + $2 \text{H}_2\text{O}$ $\text{C}_{14}\text{H}_{28}\text{N}_6\text{O}_9$	$\text{C}_{144}\text{H}_{255}\text{N}_{32}\text{O}_{48} = \text{C}_{240}\text{H}_{392}\text{N}_{68}\text{O}_{75}\text{S}_3$ + $16 \text{H}_2\text{O} = 60 \text{H}_2\text{O}$ $\text{C}_{144}\text{H}_{288}\text{N}_{32}\text{O}_{64} = \text{C}_{240}\text{H}_{512}\text{N}_{68}\text{O}_{75}\text{S}_3$

ON THE COMPOSITION OF DEAD ALBUMIN

In my Croonian Lectures in 1886 delivered at the Royal College of Physicians,¹ and again in 1897² I suggested that in dead proteid, the antecedents of the amino-fatty acids are their anhydrides, a triple union of each taking place :—

or generally—

compounds which, when the ring is broken, are now known as polypeptides.³

Further in accordance with Pflüger's⁴ view that ammonium cyanate is the type of living and urea of dead nitrogen, and that the conversion of the former into the latter is an image of the essential change which takes place when a living proteid dies, I suggested that

when $\text{R} \cdot \text{CH} \begin{array}{c} \text{NH} \\ \diagup \quad \diagdown \\ | \\ \text{CO} \end{array}$ in the above triple molecule becomes part of

living tissue it is transformed into the cyan-alcohol $\text{R} \cdot \text{CH} \begin{array}{c} \text{OH} \\ \diagdown \quad \diagup \\ \text{CN} \end{array}$
and *vice versa*.

On this assumption the cyan-alcohols in columns (vi), (v), and (iv) of the table giving the composition of living albumin, are in dead albumin transformed into their respective anhydrides.

1. 'On some points in the Pathology of Rheumatism, Gout and Diabetes.' Deighton, Bell & Co., Cambridge, 1887.

2. 'On the Synthesis of Dead and Living Proteid.' Deighton, Bell & Co., Cambridge, 1897.

3. For the mode of preparation of these polypeptides see E. Fischer and others, *Ber.*, 1901, Bd. XXXIV, s. 2868; Bd. XXXV, 1095; Bd. XXXVI, sn. 2094, 2106, 2592, etc.

4. *Pflüger's Archiv.*, Bd. X, s. 337.

and the three nitriles in column (iii) are also transformed in a similar way, into their respective anhydrides—

the last being the antecedent of di-amino propionic acid (see page 204).

As the proteid passes from the living to the dead state the amido-benzaldehyde in column (ii) is converted into the para-form, and the amino-malonic nitrile + 2 HCN is by molecular transformation converted into adenine (see page 203) a substance which according to Kossel¹ exists in all animal and vegetable cells. The composition of adenine is isomeric with prussic acid, its formula being $\text{H}_5\text{C}_5\text{N}_5$ or 5 HCN, and since by the action of nitrous acid it can be transformed into hypoxanthine, it belongs to the uric acid series and may be represented by the formula—

its transformation into hypoxanthine being represented by the following equation—

1. *Zeitsch. f. physiol. Chemie*, Bd. X, s. 258.

Heated in a sealed tube with hydrochloric acid (sp. gr. 1.19) for from twelve to fourteen hours, adenine is resolved into glycoll, formic acid, carbonic acid gas and ammonia,¹

precisely what takes place when amino-malonic nitrile and two molecules of hydrocyanic acid are treated in the same way :—

and

The relationship, therefore, between amino-malonic nitrile and adenine may be represented as follows :—

The compounds 3 HCN, 3 CNHS, $(\text{CH}_3 \cdot \text{CO} \cdot \text{CN})_2$ in column (i) are transformed as the protein passes from the living to the dead state into 2 HCN, $(\text{HCN})_2\text{S}_3$ and $2 \text{CH}_3 \cdot \text{C}(\text{OH}) \cdot (\text{CN})_2$, the latter

being further transformed into $2 \text{CH}_3 \cdot \text{C} \begin{array}{l} \text{NH} \\ \diagup \quad \diagdown \\ \text{CO} \end{array}$ the antecedent

CN

of iso-malic acid (see page 201). The acetic anhydride remains unchanged. From the foregoing data the composition of dead albumin may therefore be represented in the following tabular form :—

1. Martin Krüger, *Zeitschrift für physiologische Chemie*, Bd. XVI, s. 160.

COMPOSITION OF DEAD ALBUMIN

(i)	(ii)	(iii)	(iv)	(v)	(vi)
2 HCN (H₂CN)₂S₃ persulphocyanic acid (CH₃ · CO)₂O acetic anhydride	(NH₂)₂C₆H₄ · CHO amino-benzaldehyde N = C(NH₂) or adenine	CH₂ · CH₂ · CN amino-butyric anhydride CH₂ · CH₂ · CN amino-butyric anhydride CH₂ · CH₂ · CN amino-butyric anhydride	3 CH₃ · (CH₂)₂ · CH₂ · NH amino-valerianic anhydride 3 CH₃ · (CH₂)₂ · CH₂ · NH amino-valerianic anhydride 3 CH₃ · (CH₂)₂ · CH₂ · NH amino-butyric anhydride	3 CH₃ · (CH₂)₃ · CH₂ · NH amino-caproic anhydride 3 CH₃ · (CH₂)₄ · CH₂ · NH amino-valerianic anhydride 9 CH₃ · (CH₂)₃ · CH₂ · NH amino-butyric anhydride CH₃ · (CH₂)₂ · CH₂ · NH amino-propionic anhydride	3 CH₃ · (CH₂)₅ · CH₂ · NH amino-caproic anhydride 3 CH₃ · (CH₂)₆ · CH₂ · NH amino-valerianic anhydride 9 CH₃ · (CH₂)₄ · CH₂ · NH amino-butyric anhydride CH₃ · (CH₂)₃ · CH₂ · NH amino-propionic anhydride
2 CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	2 CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	2 CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	2 CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid
CH₃ · C(NH) · CH₂ · COOH imino-ethyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-ethyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-ethyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-ethyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-ethyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-ethyl-acetyl-acetic acid
CH₃ · C(NH) · CH₂ · COOH imino-methyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-methyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-methyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-methyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-methyl-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-methyl-acetyl-acetic acid
CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid	CH₃ · C(NH) · CH₂ · COOH imino-acetyl-acetic acid
CH₃ · C(NH) · CH₂ · COOH imino-pyruvic acid	CH₃ · C(NH) · CH₂ · COOH imino-pyruvic acid	CH₃ · C(NH) · CH₂ · COOH imino-pyruvic acid	CH₃ · C(NH) · CH₂ · COOH imino-pyruvic acid	CH₃ · C(NH) · CH₂ · COOH imino-pyruvic acid	CH₃ · C(NH) · CH₂ · COOH imino-pyruvic acid
C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O
C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O	C₁₄₄H₁₅₆N₃₂O₄₈ + 16 H₂O

NOTE ADDED JUNE 5TH, 1908

The four imino-ketonic acids—imino-pyruvic, -acetyl-acetic, -methyl-acetyl-acetic, and -ethyl-acetyl-acetic—which in the preceding tables are indicated as being constituents of protein, represent, in my opinion, the simplest forms of those bodies. If, however, imino-methyl-acetyl-acetic, and imino-ethyl-acetyl-acetic acids in either columns (iii) or (vi), or in both, were replaced by imino-laevulinic acid $\text{CH}_3 \cdot \text{C}(\text{NH}) \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{COOH}$ and imino-acetyl-butyric acid $\text{CH}_3 \cdot \text{C}(\text{NH}) \cdot (\text{CH}_2)_3 \cdot \text{COOH}$ (the formation of which is described on page 224) a different protein compound would result, having, however, the same molecular weight and the same ultimate composition as that given in the previous tables. Again, if for the amino-fatty acids in the tables, the iso-amino acids (the preparation of which from the ketones is in some degree indicated on page 244) were substituted, other protein substances would result; having, likewise, the same molecular weight and ultimate composition. These facts appear to me to explain why so many protein substances have the same ultimate composition but vary considerably both as to their physical and chemical properties.