44. *Degradation of α-Amino-acids to Aldehydes and Ketones by Interaction with Carbonyl Compounds.*

By Alexander Schönberg, Radwan Moubasher, and Akila Mostafa (Mrs. Said).

α-Amino-acids are degraded to the corresponding aldehydes or ketones containing one less carbon atom (*e.g.*, phenylaminoacetic acid ⟶ benzaldehyde) by the action of certain carbonyl compounds. Tables I and II respectively contain a list of the active and the inactive carbonyl compounds; they show that active agents must contain the grouping ·CO·[CH:CH]$_n$·CO·, where $n = 0$ or an integer, and that at least one carbonyl group must be aldehydic or ketonic. A proposed reaction mechanism is illustrated in the scheme on p. 178.

The antibacterial effect of 2-hydroxy-2′-methoxybenzil seems to be connected with its power of bringing about the above degradation.

Priority claims in respect of the synthesis of this substance are made.

Since Strecker's observation (*Annalen*, 1862, **123**, 363) that alloxan reacts with alanine to give carbon dioxide and acetaldehyde, a number of carbonyl compounds have been found which degrade α-amino-monocarboxylic acids, leaving the corresponding aldehyde or ketone with one less carbon atom, the latter being eliminated in the form of carbon dioxide. The reaction is carried out by treating the amino-acid with the carbonyl compound in aqueous solution or in suspension; only reactions of this type are described as Strecker degradations in this paper; the term does not refer to the degradation of α-amino-acids to aldehydes by the action of peroxides, catalysts, or enzymes.

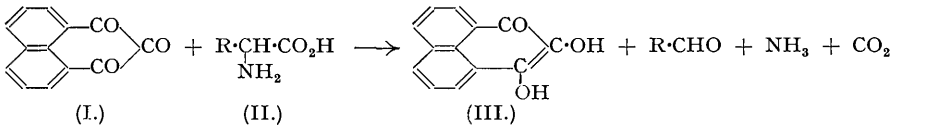
A detailed investigation of this degradation seemed justified because, *inter alia*, substances of much pharmacological interest are capable of effecting it, *e.g.*, dehydroascorbic acid, alloxan, and 2-methyl-1 : 4-naphthaquinone. Our results may be grouped as follows: (*a*) the relationship between the constitution of α-amino-acids and their power to undergo the Strecker degradation, (*b*) the final fate of the amino-group originally present in the α-amino-acids, (*c*) the relationship between the constitution of the carbonyl compounds and their power to effect this degradation, and its mechanism.

Nature of α-Amino-acids with which the Strecker Degradation may be carried out.—It has been established that the two hydrogen atoms attached to the nitrogen atom must be unsubstituted. We found that sarcosine (*N*-methylglycine) does not produce any aldehyde or ketone when boiled with " ninhydrin " (hydrate of V) or *peri*naphthindanetrione (I), which are strong agents in the Strecker degradation; further, proline, which is an *N*-substituted cyclic α-amino-acid, does not undergo the degradation when treated with ninhydrin (Grassmann and Arnim, *Annalen*, 1934, **509**, 288). On the other hand, the hydrogen atom attached to the α-carbon atom in (II) may be substituted; thus amino*iso*butyric acid yields acetone when treated with *p*-benzoquinone (Langenbeck, *Ber.*, 1928, **61**, 942), with methylglyoxal (Neuberg and Kobel, *Biochem. Z.*, 1927, **188**, 197), with ninhydrin, or with *peri*naphthindanetrione.

It seems that the Strecker degradation is a general reaction with all α-amino-acids having the structure (II), though glycine was not supposed to give formaldehyde when treated with ninhydrin (Ruhemann, *J.*, 1911, **99**, 1492; Abderhalden, *Z. physiol. Chem.*, 1938, **252**, 81). However, we obtained a good yield of formaldehyde when a glycine solution was allowed to react dropwise with a boiling ninhydrin solution in such a way that the formaldehyde formed was directly driven off with steam [see also p. 179, ref. (23)].

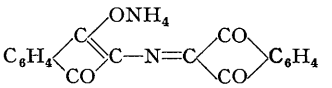
Final Fate of the Amino-group of the α-Amino-acid subjected to the Strecker Degradation.—This depends on the nature of the carbonyl compound employed: (*a*) The amino-group may be eliminated in the form of ammonia; this is, *e.g.*, the case when α-amino-acids are degraded by the action of *peri*naphthindanetrione (I), in which case dihydroxy*peri*naphthindenone (III) is precipitated and thus removed from the sphere of the reaction. (*b*) The amino-group may become linked to the carbonyl compound which effects the degradation, converting it into an

amino-compound of similar structure; thus, alanine is formed when α-aminophenylacetic acid is subjected to degradation by the action of pyruvic acid (Herbst and Engel, *J. Biol. Chem.*,



(I.) (II.) (III.) (*A*)

1934, **107**, 505; Herbst, " The Transamination Reaction ", in " Advances in Enzymology ", Vol. 4, p. 77, New York, 1946). (*c*) The amino-group may enter into combination with the carbonyl compound used as the degrading agent, producing a nitrogenous compound of rather complicated character, not closely related to the original compound. Thus when triketoindane (V) is used in the Strecker degradation it becomes transformed into a violet-blue imino-compound (IV) * (Grassmann and Arnim, *loc. cit.*; compare also Gilman, " Organic Chemistry ", 2nd edtn., Vol. II, 1099, and Virtanen *et al.*, *Z. physiol. Chem.*, 1940, **266**, 193).



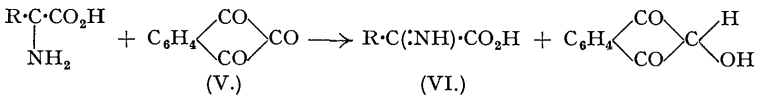
(IV.)

Nature of Carbonyl Compounds which bring about the Strecker Degradation.—Table I lists 36 substances which are active agents in this degradation, 21 being recorded by us for the first time. Table II gives the names of carbonyl compounds which cannot be used as agents in this reaction; for almost all of them this had not hitherto been reported.

Tables I and II reveal that the degradation cannot be effected by monocarbonyl compounds, but only by those containing the group ·CO·[CH:CH]$_n$·CO·; the double bond in which may be of an aromatic character. Nevertheless, not all substances containing this group effect the degradation; *e.g.*, parabanic acid (Traube, *loc. cit.*), *s*-dibenzoylethylene, and dibenzoylstilbene. The reason for this is that, when treated with primary amines in aqueous media, these and related substances do not form Schiff's compounds, the formation of which is the first and essential step in the degradation (see *B*). *cis*- and *trans-s*-Dibenzoylethylene, for example, react with primary amines by addition at the double bond; thus with aniline they form Ph·CO·CH$_2$·CH(NHPh)·COPh (Paal and Schulze, *Ber.*, 1900, **33**, 3799). So far all substances found to be active in the Strecker degradation are either aldehydic or ketonic.

Since the degradation can only be brought about by substances containing the group ·CO·[CH:CH]$_n$·CO·, this reaction can be used to ascertain the occurrence of such a grouping, but, as not all substances containing this grouping effect this degradation, this test is of diagnostic value only when positive.

Reaction Mechanism of the Strecker Degradation.—Obviously, all reaction schemes ignoring the above grouping have to be abandoned. Among those is that of Grassmann and Arnim (*loc. cit.*), which shows the α-imino-acid (VI) as an intermediate and triketoindane functioning only as a dehydrogenating agent :

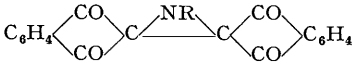


(V.) (VI.)

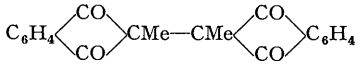
$$R\cdot C(:NH)\cdot CO_2H \xrightarrow{H_2O} R\cdot CHO + NH_3 + CO_2$$

Again if the degradation be due to direct dehydrogenation, it would be difficult to explain why it is brought about by such weak dehydrogenating agents as anthraquinone and not by the stronger dehydrogenating agents azobenzene and methylene-blue.

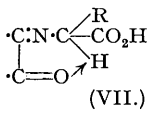
* For this compound the formulæ (IV*a*) and (IV*b*) have been advanced by Woker and Antener (*Helv. Chim. Acta*, 1937, **20**, 1260) without experimental proof. These formulæ are highly improbable, because substances of such structure should not be violet or blue [compare (IV*c*), which is colourless; Gabriel and Leupold, *Ber.*, 1898, **31**, 1159].



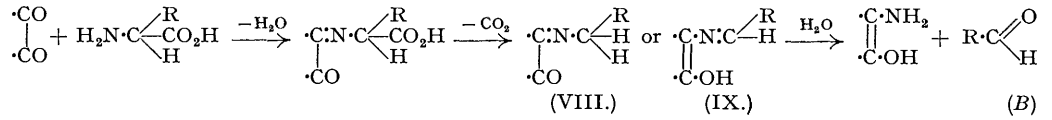
(IV*a*, R = H; IV*b*, R = NH$_4$.)



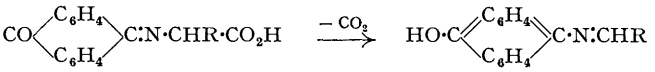
(IV*c*.)


(VII.)

The following scheme (*B*) is advanced for the mechanism: (VIII) and (IX) are isomers according to classical views, but they may be considered as extreme structures of a molecule having the nature of a resonance hybrid; the theory of hydrogen bonding (compare VII) should be applied. It is possible that the ease with which the degradation proceeds in a number of cases is due to the fact that the intermediate Schiff's bases, being hybrids, are ketonic as well as enolic.


(VIII.) (IX.) (*B*)

A similar scheme may be proposed for the vinylogues, *i.e.*, 1 : 4-dicarbonyl compounds. In the case of anthraquinone, the essential part of the reaction involved in the degradation is as follows:

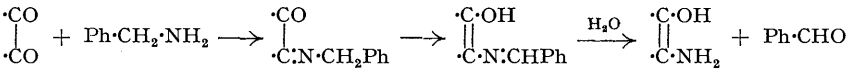


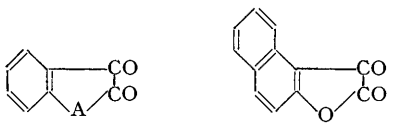
On the other hand, a similar mechanism cannot be put forward for the action of α-amino-acids on dibenzoylmethane, and this explains why this compound is incapable of bringing about the degradation.

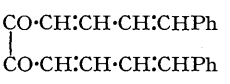
It is shown from scheme (*B*) that in accordance with the experimental results the two hydrogen atoms of the amino-group are essential for the Strecker degradation. The third hydrogen atom, attached to the α-carbon atom bearing the amino-group, which is also necessary, is either that already present in the amino-acid from the beginning, as in the case of alanine, or is formed during the reaction as the result of decarboxylation, as in the case of amino*iso*butyric acid. It is well known that α-imino-acids have a strong tendency to split off CO_2 (Wieland and Bergel, *Annalen*, 1929, **439**, 196):

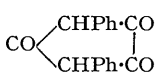

(*C*)

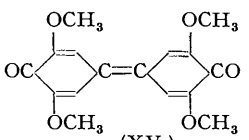
Scheme (*B*) connects the formation of aldehydes from α-amino-acids in the degradation with the formation of aldehydes from non-acidic substances, as in the formation of benzaldehyde from benzylamine by the action of alloxan or isatin (Traube, *loc. cit.*):

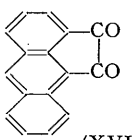


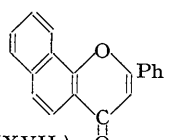

(X, A = O; XI, A = S.) (XII.)


(XIII.)


(XIV.)


(XV.)


(XVI.)


(XVII.)

2-Hydroxy-2′-methoxybenzil and the Strecker Degradation.—Kuhn, Birkofer, and Moller (*Ber.*, 1943, **76**, 900) describe the action of 2-hydroxy-2′-methoxybenzil on *Staphylococcus aureus*. (They overlook the fact that this benzil derivative had already been prepared by Schönberg and Kraemer, *Ber.*, 1922, **55**, 1185, by an almost identical method.) They found that cultures growing on a synthetic medium containing as nitrogenous supplement only organic nitrogenous compounds (apart from a small amount of arginine nitrate), amongst them being a number of α-amino-acids, such as *dl*-alanine, *dl*-leucine, and *dl*-phenylalanine, were greatly hindered in their growth when treated with 2-hydroxy-2′-methoxybenzil. No theory was proposed to explain this phenomenon, but the following is advanced: Kuhn's medium contained a number of α-amino-acids known to be important for the growth of *Staph. aureus* (Gladstone, *Brit. J. Exp. Path.*, 1937, **18**, 322), and we have found (see above) that, in experiments carried

TABLE I.

Carbonyl compounds which are active agents in the Strecker degradation. The amino-acids mentioned in the footnotes indicate that each of them has been transformed into the corresponding aldehyde or ketone containing one less carbon atom, and that they have been separated as such or as derivatives.

Section I, ·CO·CO· type.

Glyoxal [1,17]
Methylglyoxal [2,17]
Pyruvic acid [3]
Diacetyl [4,17]
Alloxan [5]
(α-Ketoglutardialdehyde) [22]
(*o*-Benzoquinone and derivatives) [6]
Dehydroascorbic acid [7,17]
Dimethylalloxan [8]
Coumarandione (X) [17]
Thiacoumarandione (XI) [17]
Isatin [9]
Phenylglyoxal [10,16]
Phenylglyoxylic acid [16]
Triketoindane (V) [11,19,20,23]
Phenylpyruvic acid [12]
Camphorquinone [17]
Acenaphthenequinone [17]
β-Naphthacoumarandione (XII) [17]
*peri*Naphthindanetrione (I) [17,18,20]
Phenanthraquinone [17]
Benzil [16]
Diphenyl triketone [16]
2-Hydroxy-2′-methoxybenzil [17]
Aceanthraquinone (XVI) [17]
Oxalyl dibenzyl ketone (XIV) [16]
Retenequinone [17]
4 : 4′-Bisdimethylaminobenzil [16]
Di-(ω-phenylbutadienyl) diketone (XIII) [15,17]

Section II, ·CO·[CH:CH]·CO· type.

Benzoquinone [13]
Toluquinone [14]
2-Methyl-1 : 4-naphthaquinone [17]
Anthraquinone [17]
Thioindigo [17]
Indigo [17]

Section III, ·CO·$[CH{:}CH]_3$·CO· type.

Coerulignone (XV) [17]

[1] Neuberg and Kobel, *Biochem. Z.*, 1927, **185**, 477 (alanine).
[2] *Idem, ibid.*, **188**, 197 (alanine, amino*iso*butyric acid, leucine, phenylaminoacetic acid).
[3] Herbst and Engel, *loc. cit.* (glycine, phenylalanine, phenylaminoacetic acid); Herbst, *loc. cit.* (alanine, leucine, *p*-methoxyphenylalanine).
[4] Neuberg and Kobel, see (1). They stress the importance of their finding diacetyl as a metabolic product (*Biochem. Z.*, 1927, **188**, 198).
[5] Strecker, *loc. cit.* (alanine); Hurtley and Wootton, *J.*, 1911, **99**, 288 (glycine, alanine, leucine, α-aminobutyric acid); Traube, *loc. cit.* (phenylaminoacetic acid); Abderhalden, *loc. cit.* (valine, alanine, α-aminobutyric acid).
[6] Schaaf, *Biochem. Z.*, 1929, **205**, 449 (alanine in presence of catechol and oxygen yields acetaldehyde, *o*-benzoquinone is believed to be an intermediate). Berrenscheen and Danzer (*Z. physiol. Chem.*, 1933, **220**, 57) obtained formaldehyde when glycine was treated in presence of oxygen with *o*-$C_6H_4(OH)_2$, 3 : 4-$(OH)_2C_6H_3$·CO·CH_2·NH_2, 3 : 4-$(OH)_2C_6H_3$·CO·CH_2·NHMe, and 3 : 4-$(OH)_2C_6H_3$·CO·CH_2·NHEt. Formaldehyde was also produced with adrenaline in a similar experiment (Edlbacher and Kraus, *ibid.*, 1928, **178**, 239).
[7] Abderhalden, *Fermentforschung*, 1937, **15**, 360; he allowed ascorbic acid, in the presence of oxygen, to react with glycine and alanine and obtained the corresponding aldehyde with one less carbon atom. He discussed (p. 361) whether the Strecker degradation was brought about by ascorbic acid itself or by dehydroascorbic acid, but left the question open. *Idem, ibid.*, 1938, **15**, 522 (α-aminobutyric acid, norvaline, valine, norleucine, leucine, *iso*leucine, phenylalanine).
[8] Hurtley and Wootton, *loc. cit.* (names of amino-acids not given).
[9] Traube, *loc. cit.* (phenylaminoacetic acid); Abderhalden, *Z. physiol. Chem.*, 1938, **252**, 81 (alanine, α-aminobutyric acid, norvaline, valine, leucine, *iso*leucine, norleucine, phenylalanine).
[10] Neuberg and Kobel, *loc. cit.* (alanine). The formation of formaldehyde by the action of glycine on phenylglyoxal was proved by colour reaction and by titration (*Biochem. Z.*, 1927, **188**, 197).
[11] Ruhemann, *loc. cit.* (alanine); Virtanen *et al.*, *loc. cit.* (alanine, valine, leucine, *iso*leucine, phenylalanine, methionine); compare Abderhalden, *loc. cit.* (leucine, alanine, α-aminobutyric acid).
[12] Herbst and Engel, *loc. cit.* (phenylaminoacetic acid).
[13] Traube, *loc. cit.* (phenylaminoacetic acid; he failed to obtain benzaldehyde when he worked with chloranil); Wieland and Bergel, *loc. cit.* (alanine); Langenbeck, *loc. cit.* (amino*iso*butyric acid).
[14] Traube, *loc. cit.* (phenylaminoacetic acid).
[15] Karrer and Cochand, *Helv. Chim. Acta*, 1945, **28**, 1181 (method of preparation).
[16] This paper (alanine).
[17] This paper (phenylaminoacetic acid).
[18] This paper (valine, leucine, phenylalanine, amino*iso*butyric acid).
[19] This paper (amino*iso*butyric acid).
[20] This paper (glycine).
[21] Traube, *loc. cit.* (phenylaminoacetic acid).
[22] Akabori (*Ber.*, 1933, **66**, 143) believes that α-ketoglutardialdehyde is formed when a pentose or furfuraldehyde is allowed to react with an α-amino-acid; a corresponding substance is believed to be produced when glucose is used in place of a pentose. Akabori is of the opinion that the action of α-ketoglutardialdehyde and related substances may be explained by the formation of a peroxide form  , which has an oxidising action on the α-amino-acids.
[23] MacFadyen (*J. Biol. Chem.*, 1945, **158**, 132) has shown that ninhydrin at pH 1 evolves 0·81 mol. of formaldehyde from glycine, measurable by the chromotropic acid procedure.

TABLE II.

Carbonyl compounds which are not active in the Strecher degradation. (The footnotes indicate the the amino-acids which were tried without success.)

Urea [17]	Benzophenone [16]
Oxamide [17]	Benzoin [16]
Parabanic acid [17, 21]	Benzylideneacetophenone [16]
Piperonal [17]	Dibenzoylmethane [16]
Coumarin [17]	Dibenzoylethylene [16]
Phorone [17]	Dibenzylideneacetone [16]
Camphor [16]	α-Naphthaflavone (XVII) [16]
Fluorenone [16]	Dibenzoylstilbene [16]
Xanthone [17]	

out under physiological conditions of temperature and pH, 2-hydroxy-2′-methoxybenzil converts α-amino-acids into the corresponding aldehydes containing one less carbon atom; it is believed that the same reactions took place also in the synthetic medium used by Kuhn, and that growth was hindered because the essential α-amino-acids were destroyed by the action of 2-hydroxy-2′-methoxybenzil.

It is also possible that 2-hydroxy-2′-methoxybenzil shows " Strecker activity " towards essential enzyme systems (connected with *Staph. aureus*) which are thus degraded.

Kuhn *et al.* found that the growth of *Staph. aureus* was not hindered indefinitely by addition of 2-hydroxy-2′-methoxybenzil to the culture, for when it was used in a concentration of $3{\cdot}0 \times 10^{-5}$ and $5{\cdot}0 \times 10^{-5}$ g., per c.c. of culture, growth was completely inhibited only for 48 and for 96 hours respectively. This can be explained on the basis of the above theory that the inhibition of growth is due to elimination from the medium of α-amino-acids important for growth if Gladstone's results are taken into consideration. He found that *Staph. aureus* grew on a medium containing glycine, valine, leucine, proline, phenylalanine, tyrosine, methionine, aspartic acid, lysine, arginine, histidine, and cystine, but that no growth occurred for 24 hours or even longer if the phenylalanine was omitted. After 96 hours, however, good growth, in some cases maximum growth, was observed. Similar results were obtained when a medium was used containing the above mentioned amino-acids, including phenylalanine, but without glycine or valine or leucine.

The mechanism of the action of the antibiotic effect of some *p*-quinones is now under discussion (Hoffman-Ostenhof and Blach, *Experientia*, 1946, **2**, 405; Hoffman-Ostenhof, *Science*, 1947, **105**, 549; cf. also Oxford, *J. Soc. Chem. Ind.*, 1942, **61**, 48, 189). The hypothesis is advanced that the action may be explained as above in the case of 2-hydroxy-2′-methoxybenzil. The antibiotic action of certain quinones has hitherto been connected with their activity in interfering with sulphhydryl groups of enzymes concerned in bacterial metabolism; another possible mechanism has been derived from the relatively high oxidation–reduction potential of these quinones, which are believed to act as antibiotics by interfering with bacterial respiratory enzymes.

EXPERIMENTAL.

The Strecker degradation was principally carried out by allowing the amino-acid to react with the carbonyl compound dissolved or suspended in boiling water for 15 minutes in an atmosphere of carbon dioxide. The detailed procedure varied according to the nature of the carbonyl compound used, *e.g.*, its solubility and volatility and also the nature of the amino-acid; the main variations were as follows: (*a*) When the carbonyl reagent was soluble in water and not volatile in steam, the procedure was similar to that described in the case of *peri*naphthindanetrione and phenylaminoacetic acid. (*b*) When the degrading reagent was volatile in steam, an excess of the amino-acid was refluxed with the carbonyl compound for 15 minutes; on distillation of the reaction mixture, the aldehyde or ketone formed, and not the degrading reagent, passed over with steam. (*c*) When the carbonyl compound was sparingly soluble in water, the procedure was usually similar to that described in the case of anthraquinone and phenylaminoacetic acid or of diphenyl triketone and alanine. The addition of glycerol served to facilitate the wetting of the carbonyl compound, or to increase its solubility. Glycerol was chosen because it is soluble in water, has no chemical action on the α-amino-acids or the carbonyl compounds used, and is not steam-volatile. The degradation reactions are grouped below according to the method used.

The aldehyde or ketone formed was converted into its phenyl- or 2 : 4-dintrophenyl-hydrazone, and identified by m. p. and mixed m. p. Benzaldehyde was also identified by the red colour of the phenylhydrazone when exposed to the sun.

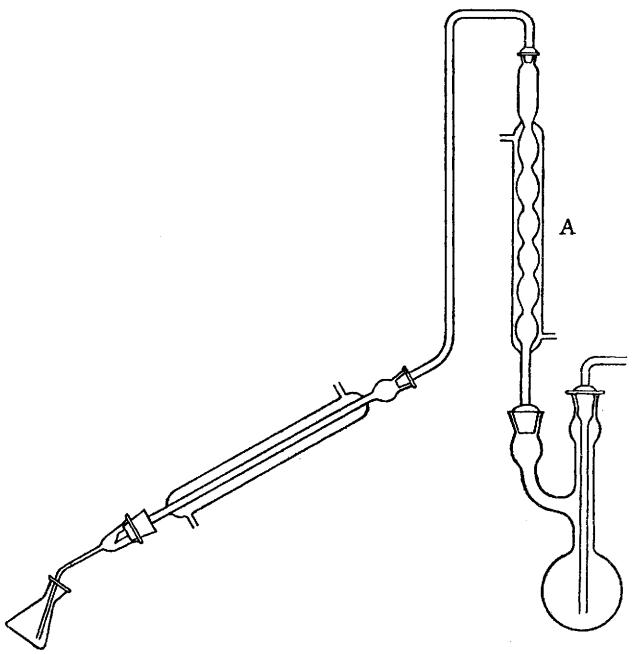
In all experiments, provided that the degradation took place at all, the yield was over 25% of the theoretical; no conclusion can be drawn from the yield as to the velocity of the various degradations owing to the differences in the conditions of reaction.

Action of Phenylaminoacetic acid on Dehydroascorbic Acid, Acenaphthenequinone, peri*Naphthindanetrione* (I), *and Aceanthraquinone* (XVI).—*peri*Naphthindanetrione (0·78 g.) (Errera, *Gazzetta*, 1913, **43**, I, 584; **44**, II, 18), phenylaminoacetic acid (1 g.), and water (100 c.c.) were boiled for 15 mins. in a stream

of carbon dioxide in a distilling flask provided with a condenser dipping into 50 c.c. of alcohol containing 0·5 g. of 2 : 4-dinitrophenylhydrazine. At the end of the experiment the contents of the receiver were warmed for some time, treated with 15 c.c. of concentrated hydrochloric acid, and left to cool. Benzaldehyde 2 : 4-dinitrophenylhydrazone was precipitated, crystallised from alcohol, and identified by m. p. and mixed m. p. (Found : C, 54·3; H, 3·7; N, 20·1. Calc. for $C_{13}H_{10}O_4N_4$: C, 54·5; H, 3·5; N, 19·6%).

The experiments with the other three compounds were carried out essentially as above, but the condenser dipped into ice-cold water to trap any benzaldehyde developed in the reaction, and the distillate was finally treated with an aqueous-alcoholic solution of phenylhydrazine hydrochloride; in all cases benzaldehyde phenylhydrazone was formed.

Action of peri*Naphthindanetrione* (I) *on Valine, Leucine, Phenylalanine, and Sarcosine.*—The trione was treated with these four amino-acids severally under the above conditions for its reaction with phenylaminoacetic acid. *iso*Butaldehyde, *iso*valeraldehyde, and phenylacetaldehyde were obtained from the first three amino-acids and identified as 2 : 4-dinitrophenylhydrazones (Found : C, 47·6; H, 4·8; N, 21·8. Calc. for *iso*butaldehyde dinitrophenylhydrazone, $C_{10}H_{12}O_4N_4$: C, 47·6; H, 4·8; N, 22·2%. Found : C, 49·8; H, 5·1; N, 20·9. Calc. for *iso*valeraldehyde dinitrophenylhydrazone, $C_{11}H_{14}O_4N_4$: C, 49·6; H, 5·3; N, 21·0%), but sarcosine did not give an aldehyde or ketone.



Action of Phenylaminoacetic Acid on Glyoxal, Methylglyoxal, Pyruvic Acid, and Diacetyl.—Phenylaminoacetic acid (1½—2 mols.) was treated with each of the four carbonyl compounds (1 mol.), and the mixture refluxed for 15 minutes using a very efficient refluxing condenser and then distilled. The distillate was treated with phenylhydrazine hydrochloride and in all cases benzaldehyde phenylhydrazone was precipitated.

Action of Phenylaminoacetic Acid on Coumarandione (X), *Thiocoumarandione* (XI), *Camphorquinone, β-Naphthacoumarandione* (XII), *Phenanthraquinone, Retenequinone, Di-(ω-phenylbutadienyl) Diketone* (XIII), *2-Methyl-1 : 4-naphthaquinone, Anthraquinone, Indigo, Thioindigo, and Coerulignone* (XV).—The amino-acid was refluxed with the carbonyl compound in aqueous glycerol (100 c.c. glycerol; 25—100 c.c. water) in a stream of carbon dioxide for 30 mins. An efficient condenser was used for refluxing, its upper end being connected with a tube dipping into an aqueous-alcoholic solution of phenylhydrazine hydrochloride to trap any benzaldehyde. When the reaction mixture was distilled, benzaldehyde was obtained in all cases.

Phenylaminoacetic Acid and Urea, Oxamide, Parabanic Acid, Piperonal, Coumarin, Phorone, Fluorenone, Xanthone, and Benzoin.—In similar experiments to those just described, except that glycerol was omitted in that with urea, benzaldehyde could not be detected.

Action of Alanine on Phenylglyoxal, Phenylglyoxylic Acid, Benzil, Diphenyl Triketone, Oxalyl Dibenzyl Ketone (XIV) *and 4 : 4′-Bisdimethylaminobenzil.*—Alanine and the carbonyl compound were refluxed with 100 c.c. of *ca.* 50% aqueous glycerol in the apparatus shown in the figure. For the first 15 minutes water was passed through the condenser *A*, then *A* was emptied and heating was continued for another 10 minutes. The above procedure was followed to ensure that the acetaldehyde formed in the process would pass over with steam. It was detected in each case in the receiver by means of its 2 : 4-dinitrophenylhydrazone.

Alanine and Camphor, Benzophenone, Benzoin, Benzylideneacetophenone, Dibenzoylmethane, Dibenzoylethylene (m. p. 111°), *Dibenzylideneacetone, α-Naphthaflavone* (XVII), *and Dibenzoylstilbene.*—Under similar conditions to the last experiments, acetaldehyde could not be detected.

Action of α-Aminoisobutyric Acid on Ninhydrin and peri*Naphthindanetrione* (I).—The experiments were carried out as in the two preceding cases but without glycerol. Acetone was formed in both cases and identified as dinitrophenylhydrazone.

Action of Glycine on Ninhydrin and peri*Naphthindanetrione.*—1 G. of ninhydrin (or 1·3 g. of *peri*naphthindanetrione) in 100 c.c. was placed in a Claisen flask attached to a condenser. Through one opening of the flask, a current of carbon dioxide was bubbled through the solution, and the other opening was provided with a separating funnel containing a solution of 0·4 g. of glycine in 15 c.c. of water. The ninhydrin solution was boiled, and the glycine solution added dropwise. The distillate was collected during 15 minutes, and the formaldehyde formed identified as 2 : 4-dinitrophenylhydrazone (Found, from *peri*naphthindanetrione: C, 40·3; H, 3·9; N, 26·8. Calc. for $C_7H_6O_4N_4$: C, 40·0; H, 2·9; N, 26·7%).

Phenylaminoacetic Acid and 2-Hydroxy-2′-methoxybenzil.—The reaction was carried out in a flask provided with a delivery tube dipping into a solution of phenylhydrazine hydrochloride in aqueous alcohol. The flask, containing the benzil derivative (0·3 g.), phenylaminoacetic acid (0·3 g.), and water (100 c.c.), was put in a thermostat at 37° for 48 hours; the contents of the reaction vessel were then distilled under reduced pressure, the temperature being kept below 37°. The distillate (50 c.c.), which was cooled in ice, was treated with alcoholic phenylhydrazine solution, and benzaldehyde phenylhydrazone (0·2 g.) was formed.

*Dihydroxy*peri*naphthindenone* (III).—*peri*Naphthindanetrione (I) (0·5 g.) and alanine (0·5 g.) were boiled with 200 c.c. of water for 10 minutes in a stream of carbon dioxide; red crystals gradually separated, and the reaction mixture was cooled, and the red compound crystallised from alcohol; it formed red needles, m. p. 255°, proved to be (III) (Errera, *loc. cit.*, p. 583) by m. p., mixed m. p., and comparison of properties; yield almost theoretical (Found: C, 73·5; H, 3·7. Calc. for $C_{13}H_8O_3$: C, 73·6; H, 3·8%).

*Oxidation of Dihydroxy*peri*naphthindenone.*—(a) *By bromine* (cf. Errera, *Gazzetta*, 1913, **43**, I, 353). Bromine-water was added gradually and with shaking to a suspension of 0·5 g. of the red substance in 25 c.c. of warm water till the colour persisted. The reaction mixture was then concentrated and cooled in ice. Yellow crystals were obtained, which proved to be *peri*naphthindanetrione hydrate, by m. p., mixed m. p., and colour reaction with sodium hydroxide.

(b) *By nitric acid.* Nitric acid (5 c.c., *d* 1·1) and water (5 c.c.) were added to a suspension of 0·5 g. of the red substance in 25 c.c. of water. After being heated in a water-bath for 20 minutes the reaction mixture was concentrated. On cooling, yellow crystals of *peri*naphthindanetrione hydrate were obtained and identified as above.

Action of Methylene-blue and Azobenzene on Phenylaminoacetic Acid.—The procedure was the same as in the reaction of *peri*naphthindanetrione and phenylaminoacetic acid, but the triketone was replaced by methylene-blue (1·5 mols.) or azobenzene (1·5 mols.). In neither case was any benzaldehyde obtained. When, however, at the end of either experiment 0·5 g. of ninhydrin in 50 c.c. of water was added to the reaction mixture, a good yield of benzaldehyde was obtained. This proves that the methylene-blue and azobenzene do not react with phenylaminoacetic acid in such a way as to hinder its undergoing the Strecker degradation.

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