XCIII.—*The Interaction of Cyanodihydrocarvone, Amyl Nitrite, and Sodium Ethoxide. Part I.*

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IN extending the investigation of cyclic β -cyanoketones (Trans., 1906, 89, 955, 1819, and 1869) a method of degrading these to open-chain compounds was sought for and cyanodihydrocarvone was the first compound experimented on, as it is comparatively easy to obtain in considerable quantity. The method of breaking open the ring by the Beckmann process applied to the oxime, or Baeyer's method in which Caro's reagent is used to oxidise the ketone, failed to give satisfactory results. The use of alkyl nitrites in presence of mineral acids, which with saturated ketones containing the group $\text{:CH}\cdot\text{CO}\cdot$ often causes ring scission, was in this instance avoided because of the probability of attack at the propenyl group. Conversion of the compound into an α -monocarboxylic ester or the α -cyano-derivative was attempted, but again without success.

The effect of amyl nitrite in presence of sodium ethoxide instead of mineral acids was next investigated, it being anticipated that the isonitroso-compound,

would be found; but although the product has the empirical formula $\text{C}_{11}\text{H}_{14}\text{O}_2\text{N}_2$ it gave a colourless solution in alkalis, was apparently not affected by boiling with sodium bisulphite solution, and was not decomposed like isonitrosocamphor when heated in glacial acetic acid with sodium nitrite. After treatment with boiling acetyl chloride it

was nearly all recovered unchanged and, although it reacted with phosphorus pentachloride in the cold, the product when poured into water once more yielded the original substance.

It did not respond to any of the usual tests for ketonic compounds, and when heated with alkalis in presence of ferrous hydroxide did not yield a trace of ferrocyanide, the absence of the group $\text{C}(\text{CN})\cdot\text{CH}\cdot\text{CO}\cdot$ thus being indicated.

When the compound was warmed for some days with hydrochloric acid on the water-bath, ammonium chloride and a crystalline acid were formed, carbon dioxide being eliminated. The new acid had the formula $\text{C}_9\text{H}_{11}\cdot\text{CO}_2\text{H}$, was optically inactive, and when distilled with soda-lime gave a large proportion of a benzenoid hydrocarbon which was identified as ψ -cumene, of which, therefore, the inactive acid was evidently a nucleal monocarboxylic acid; as it was not identical with the two known nucleal acids it follows that it was probably the third, namely, that having the structure

The mechanism of the curious change whereby this compound was produced from cyanodihydrocarvone appeared worthy of careful investigation, and experiments have been in progress during the last two years with the object of ascertaining, if possible, what are the intermediate stages in this conversion, involving also the attempt to establish the constitution of the compounds dealt with. This paper contains an account of some of the more important results hitherto obtained.

The action of cold acids on the supposed *isonitroso*-compound was first investigated. This leads to the formation of (*a*) an isomeric compound (*L'*),* $\text{C}_{11}\text{H}_{14}\text{O}_2\text{N}_2$, with properties very like those of the original material, and probably stereoisomeric with it, (*b*) of two isomeric basic substances B and B', $\text{C}_{11}\text{H}_{16}\text{O}_3\text{N}_2$, formed by union with one molecular proportion of water. The relative amounts of these three products depends on the concentration of the mineral acid and the duration of its action.

When the original compound or the base formed in largest quantity is warmed with excess of sodium hydroxide for some time, traces of ammonia are evolved, and on subsequent titration of the solutions with acids it is found that one molecular proportion of alkali has been neutralised. On adding excess of acid to the solution in the latter

* For convenience in referring to some of the compounds dealt with, they are designated by suitable letters or symbols. The supposed *isonitroso*-compound having proved to be a lactam is referred to as the lactam (L).

instance the base is recovered unchanged, so that lactone formation occurs almost instantaneously.

In the case where the original compound (L) has been treated with excess of alkali, addition of mineral acid causes the precipitation of a new carboxylic acid (A) having the formula $C_{10}H_{15}ON_2 \cdot CO_2H$. This is amphoteric in character, dissolves readily in sodium carbonate solution and also in concentrated hydrochloric acid, and in the latter instance a crystalline hydrochloride is sometimes obtained. It is reconverted into the compound (L) by heat or by treatment with certain dehydrating agents, which suggests that the acid (A) contains an amino-group as well as a carboxyl group and may be represented as

and that the compound (L) is its lactam, $C_{10}H_{13}ON \begin{smallmatrix} \text{NH} \\ \diagup \\ \text{CO} \end{smallmatrix}$, a view supported by the bitter taste associated with the latter substance.

Satisfactory confirmation of this supposition has been obtained by converting the sodium derivative of the lactam into its methyl derivative (LMe) by the action of methyl iodide. This has no longer any acidic character, a fact explained by the conversion of the group $\cdot NH \cdot CO \cdot$ into $\cdot N(CH_3) \cdot CO \cdot$, but it is converted on heating with alkalis into the methylated amino-acid (AMe), $C_{10}H_{13}ON \begin{smallmatrix} \text{NH} \cdot CH_3 \\ \diagup \\ \text{CO}_2H \end{smallmatrix}$.

Both the methylated lactam and the acid are converted by cold strong hydrochloric acid into a basic compound closely resembling the lactonic base (B) of which it represents the methyl derivative and may be referred to as (BMe).

When the methylated base (BMe) is warmed with dilute acids and the solution is subsequently rendered alkaline and distilled, methylamine is evolved in nearly quantitative amount, an observation which supplies the last link in the chain of evidence that the supposed *isonitrosocyanodihydrocarvone* (L) is a lactam which owes its acidic character to the presence of the $\cdot NH \cdot CO \cdot$ group.

The principal product besides methylamine, which results on hydrolysis of the base (BMe) with dilute acid, is identical with that which is obtained, together with ammonia, by the similar treatment of the non-methylated base (B). It is an acid which has the formula $C_{11}H_{17}O_5N$ and will be referred to as "the lactonic acid." It may be titrated with sodium hydroxide and behaves as a monobasic acid, but when warmed with excess of alkalis for some time it neutralises two equivalent proportions. Like the bases (B) and (BMe) therefore, it is lactonic in character, and the original acid is regenerated when liberated from the solution of the disodium salt.

Although the lactonic acid behaves in the cold as a monobasic acid

and decomposes carbonates, there is reason to doubt if it is a carboxylic acid, for if it is dissolved in ice-cold potassium carbonate and treated with potassium permanganate a compound separates from the alkaline solution which contains certainly either 10 or 11 carbon atoms, as shown by the ratio between the content of carbon and nitrogen, and yet no carbon dioxide, formic acid, or any other compound which could conceivably be produced by the elimination of one or two carbon atoms appears to be formed at the same time. We are forced to conclude therefore that the oxidation product contains all the carbon atoms present in the original compound, which therefore can hardly be a carboxylic acid. The lactone ring which it contains is thus probably the same as that present in the base (B) and arises from the carboxylic group of the amino-acid (A).

This acid gives a series of characteristic colour reactions and when it is heated with dilute mineral acids it is slowly transformed into trimethylbenzoic acid, with evolution of carbon dioxide and ammonia. It is extremely stable towards hot alkalis, apart from the rupture of the lactone ring, but it is reduced if ferrous hydroxide is present, ammonia being liberated. The products of this change are at present under examination.

The absence of a colour reaction with ferric chloride in the case of the base suggests that the change whereby it yields the lactonic acid involves the replacement of $\cdot\text{NH}_2$ by $\cdot\text{OH}$, the latter having a phenolic function. If so, then the grouping $>\text{C}:\dot{\text{C}}\cdot\text{NH}_2$ is present in the base (B) and in the acid (A) from which it is obtained. This is perhaps the cause of the peculiar behaviour of the last two compounds towards nitrous acid; both yield yellow precipitates with nitrous acid in extremely dilute solutions, but the methylated compounds do not behave in this way, nor does the lactonic acid from which the amino-group has been removed. It seems not unlikely that the formation of these products depends on the intermediate existence of diazo-compounds which the presence of the grouping $>\text{C}:\dot{\text{C}}\cdot\text{NH}_2$ would probably facilitate, since aromatic amines contain this otherwise unusual complex. The comparatively low basicity of these derivatives and the acid reaction of the amino-acids, a class of substances usually nearly neutral towards indicators, is perhaps also attributable to this structure.

The discussion of the precise constitution of the compounds described in this paper as well as of their relationship to the original cyanodihydrocarvone may be deferred until further experimental evidence has been adduced.

EXPERIMENTAL.

Dihydrocyanocarvone (59 grams) was mixed with an ice-cold solution of sodium (8 grams) in absolute alcohol (200 c.c.) and amyl nitrite (43 grams) gradually added, the temperature not being allowed to rise above 0° . The whole was allowed to remain for about twelve hours, when it was poured into about ten times its bulk of water. After filtering from a small quantity of resinous matter, carbon dioxide was passed into the clear brown solution, and the new compound separated as a white, voluminous, gelatinous precipitate; this was collected, dried, and crystallised from alcohol. The yield was about 45 grams:

0.2434 gave 0.5734 CO_2 and 0.1495 H_2O . $C = 64.2$; $H = 6.9$.

0.1282 „ 14.35 c.c. moist nitrogen at 11° and 773 mm. $N = 13.6$.

$C_{11}H_{14}O_2N_2$ requires $C = 64.0$. $H = 6.8$; $N = 13.4$ per cent.

The substance is very readily soluble in alcohol, chloroform, acetone, benzene, acetic acid, or ethyl acetate, less readily so in ether, carbon tetrachloride or carbon disulphide, sparingly soluble in cold carbon disulphide and nearly insoluble in light petroleum. It dissolves to some extent in hot water and the solution has a very bitter taste. It crystallises from alcohol or from hot water in slender needles melting at $138-139^{\circ}$.

The crystals are flat and show straight extinction in polarised light, their directions of greatest length and elasticity being coincident. When fused between glass slips the compound sets to translucent patches which crack radially from a number of centres, whilst at the edges of the mass are seen a few large, flat needles or oblique, six-sided plates.

One gram, dissolved and made up to 25 c.c. with absolute alcohol, was examined in a 2-dem. tube at 15° . The observed rotation was $+9.68^{\circ}$, whence $[\alpha]_D +121^{\circ}$.

The substance dissolves in a solution of sodium hydroxide, forming a colourless solution from which it is precipitated by carbon dioxide or sodium hydrogen carbonate as a mass of minute needles. It at once discharges the colour of ice-cold potassium permanganate or that of a solution of bromine in acetic acid, even when sodium acetate is present.

As this compound was at first believed to be an ordinary isonitroso-derivative of cyanodihydrocarvone, many attempts were made to cause it to undergo the Beckmann transformation. It was recovered unaltered, however, after prolonged treatment with boiling acetyl

chloride, cold phosphorus, pentachloride, or trichloride, or with toluene-sulphonic chloride and hot sodium hydroxide or pyridine. With hot phosphorus chlorides it was attacked, but the products contained much phosphorus. No trace of hydrogen cyanide was removed on boiling the substance with sodium hydroxide and ferrous hydroxide, but ammonia was liberated. It was not altered when heated with sulphurous acid in acetic acid solution or with boiling sodium bisulphite, and when shaken in sodium hydroxide solution and benzoyl chloride no benzoyl derivative was formed.

The Isomeric Lactam (L'), C₁₁H₁₄O₂N₂.

The lactam (L) dissolves in a cold saturated aqueous solution of hydrogen bromide with evolution of heat. Ten grams were dissolved in 30 c.c. of the acid, any considerable rise of temperature being avoided. The solution was allowed to stand for thirty minutes and was then poured into water. A very voluminous, white precipitate separated, which was collected, washed with water, and crystallised first from alcohol and then from benzene. Yield, 3.5 grams:

0.2935 gave 0.6942 CO₂ and 0.1738 H₂O. C = 64.50; H = 6.58.

0.1576 „ 13.74 c.c. moist nitrogen at 10° and 763.4 mm. N = 13.74.

C₁₁H₁₄O₂N₂ requires C = 64.08; H = 6.79; N = 13.59 per cent.

The substance resembles the isomeric compound in general behaviour towards solvents, and separates from alcohol or benzene as a colourless, crystalline powder. On heating, it begins to turn yellow at about 160°, and melts completely to a red liquid at 180°.

It dissolves in cold sodium hydroxide solution, forming a colourless liquid from which it is reprecipitated unaltered by carbon dioxide, and generally resembles the isomeric lactam in chemical character.

The Amino acid (A), C₁₀H₁₃ON < $\begin{matrix} \text{NH}_2 \\ \text{CO}_2\text{H} \end{matrix}$

A solution of 20 grams of the lactam (L) in a 10 per cent. aqueous solution of sodium hydroxide (160 c.c.) was heated on the water-bath for five hours. The cooled solution was acidified with dilute hydrochloric acid and the precipitate collected, washed, and crystallised from boiling water or dilute alcohol. The yield of purified acid was 20 grams:

0.3152 gave 0.7582 CO₂ and 0.2280 H₂O. C = 58.9; H = 7.2.

0.2342 „ 25.6 c.c. moist nitrogen at 21° and 760.5 mm. N = 12.5.

C₁₁H₁₆O₃N₂ requires C = 58.9; H = 7.1; N = 12.5 per cent.

0.8085 required 3.6 c.c. *N*-sodium hydroxide for neutralisation,

whence the equivalent 225; the number calculated for a monobasic acid, $C_{11}H_{16}O_3N_2$, being 224.

The substance is sparingly soluble in boiling water, but dissolves freely in alcohol, glacial acetic acid, or acetone, and is nearly insoluble in ether, chloroform, benzene, or light petroleum. It separates from alcohol in short, colourless prisms, and from hot water in feathery aggregates of colourless needles melting at 155° .

The crystals, when small, are truncated, deeply striated needles having straight extinction in polarised light. In other cases, short, transparent prisms or rectangular prisms may be obtained. Crushed fragments of the larger crystals occasionally show in convergent polarised light one axis of a wide-angled, interference figure. The double refraction is moderate.

After fusion between glass slips, the compound solidifies slowly, and only when hot, to masses of long, curved, fibrous, parallel needles, the whole being much cracked in directions parallel to the needles.

0.8892 Gram dissolved and made up to 25.1 c.c. with absolute alcohol was examined in a 2-dm. tube at 13° . The observed rotation was -2.92° , whence $[\alpha]_D -41.2^\circ$.

The substance reacts strongly acid to litmus and expels carbon dioxide from solutions of carbonates. A neutral solution of the sodium salt gives with silver nitrate a white precipitate which is soluble in ammonia or in boiling water, being slowly decomposed in the latter instance, with deposition of metallic silver. With ferric chloride a pale red, and with mercuric chloride a white, precipitate is formed; no precipitates are obtained with soluble calcium, barium, or lead salts.

The acid is amphoteric in character, and dissolves appreciably more freely in dilute mineral acids than in water. When covered with concentrated hydrochloric acid, colourless crystals, probably of a hydrochloride, are formed, but these are decomposed on addition of water. No sparingly soluble platinichloride or aurichloride could be obtained, but an oily periodide is precipitated even from very dilute solutions of the acid on addition of hydriodic acid containing iodine in solution. The salts do not reduce boiling Fehling's solution, nor is the latter affected by the product obtained on heating the acid for some time with dilute mineral acids, so that hydroxylamine is not formed in the latter instance although ammonia may be detected. A solution of the acid in ten times its weight of 10 per cent. aqueous sodium hydroxide was heated on the water-bath for seven hours, but on acidification yielded the original acid almost entirely unchanged, and no appreciable quantity of ammonia was evolved.

Neutral solutions of the salts instantly decolorise dilute ice-cold permanganate solution and the free acid at once discharges the colour

of a solution of bromine in acetic acid, alone or with excess of sodium acetate. It is also attacked by alkaline hypobromite, but no bromo-form is produced.

The acid is very easily oxidised or reduced. When warmed with lead peroxide in dilute acetic acid solution, it is rapidly attacked and carbon dioxide is evolved, but profound decomposition occurs. It is not easily reduced by zinc with ammonia, acetic acid, or sodium hydroxide, or by sodium amalgam, but with sodium and alcohol it yields oily amino-acids. It is rapidly reduced in the cold by tin and hydrochloric acid, or by ferrous hydroxide and alkali, ammonia being formed. When it was heated with sodium bisulphite solution, a yellow coloration was developed, ammonia was found in the solution, and a stable organic sulphonic acid appeared to have been formed. The products obtained in some of these reactions have not yet been isolated in a pure form and are at present under examination.

Attempts to prepare a benzoyl derivative of the acid by treating it with benzoyl chloride in warm pyridine or by the Schotten-Baumann reaction were unsuccessful, the acid being recovered unaltered, although in both instances the benzoyl chloride is decomposed very rapidly, the acid apparently acting as a catalyst. With toluene-sulphonic chloride and alkali, a gummy acid containing sulphur was obtained in small quantity.

When the acid is shaken with benzaldehyde and dilute aqueous sodium hydroxide the aldehyde dissolves rapidly, but is apparently only oxidised catalytically. On heating it with aqueous phenylhydrazine acetate on the water-bath, ammonia is evolved and a red neutral oil separates; at the ordinary temperature no change occurs. With hydroxylamine the acid is converted into an oil which is sparingly soluble in water and contains combined hydroxylamine, as it does not reduce Fehling's solution at once, but does so after being heated with dilute acids.

This substance may be obtained either by shaking the cooled alkaline solution of the acid in a considerable excess of 10 per cent. sodium hydroxide with a slight excess of dimethyl sulphate or by heating the silver salt of the acid with methyl iodide dissolved in absolute methyl alcohol. In the former case the product separated as an oil which crystallised when immersed in a freezing mixture; in the latter instance the crude product was purified by shaking it with dilute, aqueous sodium carbonate.

The compound is readily soluble in most of the usual media with the exception of cold water and light petroleum, and crystallises

from dilute alcohol in thin, fragile, rectangular plates which have straight extinction in polarised light and melt at 99–100°.

This ester is very distinctly basic in character, dissolves readily in dilute acids, forming colourless solutions from which it is reprecipitated by alkalis. It is insoluble in cold sodium hydroxide, but when heated with that reagent it dissolves slowly and the solution, on acidification, yields the derived amino-acid (A).

Conversion of the Amino-acid (A) into the Lactam (L).

When the amino-acid (A) was heated under reduced pressure it decomposed and water and some ammonia were evolved. The residue was extracted with aqueous sodium hydroxide and the filtered solution saturated with carbon dioxide, when a white mass was precipitated, which crystallised from alcohol in white needles melting at 139°, and was identical with the lactam (L).

The lactam may also be obtained from the amino-acid by boiling it for about nine hours with glacial acetic acid, or by treating it with excess of acetic anhydride or phosphorus trichloride. In these cases secondary reactions occur; the yield of the lactam is nearly quantitative, however, when acetyl chloride is used as a dehydrating agent.

The lactam (L) dissolves in cold concentrated hydrochloric acid without evolution of heat. If the solution is immediately diluted, the lactam is precipitated unchanged. If, however, the solution is allowed to stand for several days a few colourless needles, the hydrochloride of a base, separate. The main product of the reaction remains in the solution, and is precipitated on neutralising it with alkali. It is basic in character, but differs from the base obtained from the crystals.

Ten grams of the lactam (L) were dissolved in 50 c.c. of concentrated hydrochloric acid, and allowed to stand for two days. The solution was then neutralised with sodium hydroxide and the precipitated base collected and purified by crystallisation from hot water. The yield of crystallised product was 9.2 grams:

0.2151 gave 0.4634 CO_2 and 0.1397 H_2O . $\text{C} = 58.75$; $\text{H} = 7.22$.

0.1756 „ 18.3 c.c. moist nitrogen at 10° and 765 mm. $\text{N} = 12.6$.

$\text{C}_{11}\text{H}_{16}\text{O}_3\text{N}_2$ requires $\text{C} = 58.88$; $\text{H} = 7.14$; $\text{N} = 12.5$ per cent.

The compound dissolves in hot water, from which it separates almost completely on cooling in stellar aggregates of long, colourless needles. It is readily soluble in alcohol, chloroform, glacial acetic acid, or

acetone, but only slightly so in benzene or ether. It melts at 122—123°.

The large crystals of the compound are transparent prisms, faintly, but thickly, striated with longitudinal lines. The smaller ones are needles in which the directions of greatest elasticity and length are at right angles. Crushed fragments examined in convergent, polarised light show a uniaxial figure. The double refraction is strong and negative in sign. When fused it solidifies very slowly and incompletely, even at a temperature a few degrees below its melting point.

For the determination of the optical activity, 0.9985 was dissolved and made up to 24.9 c.c. with absolute alcohol, and examined in a 2-dm. tube at 13°. The rotation observed was +0.525°, whence $[\alpha]_D + 6.55^\circ$.

It is distinctly basic in character, dissolving readily in dilute acids, and forming crystalline salts. It decolorises bromine instantly, even in the presence of sodium acetate, and is also immediately oxidised by an ice-cold solution of potassium permanganate. It is very stable towards alkalis; after heating a solution in ten times its weight of 10 per cent. sodium hydroxide for thirty hours on the water-bath, the greater part was recovered unchanged on acidification, but when warmed with a measured quantity of *N*/10 sodium hydroxide for a few minutes and the alkali titrated with *N*/10 acid, it was found that salt formation had occurred.

0.2036 after boiling with 24.5 c.c. *N*/10 NaOH required 15.4 c.c. *N*/10 H₂SO₄, whence the equivalent = 224; the number calculated for a monobasic acid, C₁₁H₁₆O₃N₂, is 224.

The base is evidently the anhydro-derivative of a monocarboxylic acid, and is probably a lactone.

It is rapidly decomposed on heating with sodium hydroxide and ferrous hydroxide, ammonia being evolved in considerable quantity. A very dilute solution of the base in acids instantly gives a lemon-yellow precipitate on addition of sodium nitrite.

With acetyl chloride a vigorous reaction occurred, and an oily substance was formed, which was decomposed by warm dilute sodium carbonate solution, the original base being regenerated. Probably an unstable, acetyl derivative had been produced. It did not yield a semicarbazone, an oxime, or a phenylhydrazone.

The *hydrochloride*, C₁₁H₁₆O₃N₂.HCl, was prepared by adding hydrochloric acid to an alcoholic solution of the base (B) and precipitating with ether. It was obtained as a white mass of small needles:

0.7765 gave 0.4313 AgCl. Cl = 13.7.

C₁₁H₁₆O₃N₂.HCl requires Cl = 13.6 per cent.

Direct Conversion of the Amino-acid (A) into the Lactonic Base (B).

On mixing the amino-acid with five times its weight of cold concentrated hydrochloric acid the mass at first set to a solid cake, probably of the hydrochloride as already suggested, but when this was stirred a clear liquid was finally obtained. At the end of twenty-four hours, on neutralising the solution with sodium hydroxide, a white compound was precipitated which crystallised from water in colourless needles melting at 122—123°, and was in all respects identical with the lactonic base (B). The yield was about 60 per cent. of the calculated amount.

The crystals which separated from the solution of the lactam (L) in hydrochloric acid yielded on decomposition with alkali a base which was crystallised from hot water :

0.3165 gave 0.6823 CO₂ and 0.2044 H₂O. C = 58.79 ; H = 7.17.

0.1736 „ 18.85 c.c. moist nitrogen at 18.5° and 764 mm. N = 12.57.

C₁₁H₁₆O₃N₂ requires C = 58.88 ; H = 7.14 ; N = 12.50 per cent.

This base is therefore isomeric with the one previously described. It is formed in small quantity by the action of hydrochloric acid on the lactam (L'), but can be obtained in an almost quantitative yield by treating the isomeric lactam (L') with hydrochloric acid. It is readily soluble in hot alcohol, glacial acetic acid, or acetone, very sparingly soluble in cold alcohol, chloroform, benzene, or ether, and insoluble in light petroleum. It is fairly soluble in hot water, from which it separates almost completely on cooling in colourless crystals melting at 157—158°.

The crystals are opaque, fern-like forms, and the compound after fusion sets slowly and incompletely to a mass of small, thin plates with strong, double refraction ; the optical characters of these forms could not be distinguished.

0.290 Gram dissolved and made up to 20 c.c. with absolute alcohol was examined in a 2-dcm. tube at 15°. The observed rotation was + 0.18, whence $[\alpha]_D + 6.21^\circ$.

Action of Nitrous Acid on the Lactonic Base (B).

On adding a solution of sodium nitrite to a dilute solution of the base in hydrochloric acid, a lemon-yellow, amorphous precipitate separated in light, flocculent masses practically insoluble in water. All attempts to purify the substance by crystallisation from organic

solvents were unsuccessful, and it was therefore merely washed with water and dried on porous porcelain in a vacuum :

0.1991 gave 0.4076 CO_2 and 0.1231 H_2O . $\text{C} = 55.83$; $\text{H} = 6.75$.

0.1009 „ 10.575 c.c. moist nitrogen at 14° and 757.5 mm. $\text{N} = 12.3$.

$\text{C}_{21}\text{H}_{32}\text{O}_7\text{N}_4$ requires $\text{C} = 55.75$; $\text{H} = 7.08$; $\text{N} = 12.38$ per cent.

The reaction takes place according to the equation :

That this equation does actually express the course of the reaction was confirmed by titrating a solution of the base in dilute sulphuric acid with sodium nitrite solution until the filtered liquid gave no further precipitate with the reagent. It was thus found that 2 molecules of the base required 1.03 molecules of sodium nitrite for complete precipitation ; the filtrate was free from nitrous acid, but contained ammonia.

The substance dissolves readily in alcohol, ether, benzene, glacial acetic acid, or chloroform to yellow solutions, from which it separates in the form of a resin ; it is not dissolved by light petroleum. On heating, it begins to soften at 75° , and decomposes with evolution of gas at about 98° . It dissolves in sodium hydroxide to a deep yellow solution, from which it is reprecipitated on addition of acids ; it also dissolves, but not so readily, in aqueous sodium carbonate. Its solution in alkali reduces ammoniacal silver solution instantly in the cold. It does not give Liebermann's nitroso-reaction, but gives an intense red coloration with concentrated sulphuric acid and phenol or concentrated hydrochloric acid and β -naphthol.

It dissolves in cold concentrated hydrochloric acid to a yellow solution ; on allowing this solution to stand for three days and then diluting with water, a yellow precipitate separated, which was crystallised from alcohol :

0.3310 gave 0.7262 CO_2 and 0.2086 H_2O . $\text{C} = 59.86$; $\text{H} = 7.00$.

0.1540 „ 10.35 c.c. moist nitrogen at 15.5° and 762 mm.
 $\text{N} = 10.15$.

$\text{C}_{21}\text{H}_{29}\text{O}_6\text{N}_3$ requires $\text{C} = 60.14$; $\text{H} = 6.92$; $\text{N} = 10.02$ per cent.

Hydroxylamine had therefore been eliminated in accordance with the equation :

An indication of the formation of hydroxylamine in this reaction was obtained in the reduction of Fehling's solution by the filtrate.

The substance dissolves in hot alcohol to a pale yellow solution, but is almost insoluble in cold alcohol. Its solution in boiling benzene is colourless. It dissolves readily in glacial acetic acid to a yellow solution and also to a slight extent in boiling water, forming a deep yellow solution ; the colour, however, disappears on addition of a drop of

acid; with aqueous alkalis it forms deep yellow solutions, from which it separates on the addition of acids as a colourless precipitate.

When the base is heated with dilute acids it is slowly hydrolysed with formation of ammonia and a new nitrogenous acid. This acid is also formed when the lactam (L) or the amino-acid (A) is heated with dilute sulphuric acid, and on leaving the base (B) with a cold saturated hydrobromic acid. The hydrolysis of the base with hot dilute sulphuric acid was examined quantitatively. 1.12 Grams (1 mol.) of the base was heated on the water-bath with 20 c.c. of *N*-sulphuric acid (4 mols.) during one hour. On distilling with alkali, 0.88 mol. of ammonia was liberated.

For the preparation of the acid, a solution of the base (40 grams) in *N*-sulphuric acid (800 c.c.) was heated on the water-bath during two hours. On cooling, crystals separated, which were collected, washed with water, and dried by exposure to air. For analysis, the substance was crystallised from a mixture of chloroform and benzene and dried by exposure to air:

0.4708 gave 0.9382 CO_2 and 0.2984 H_2O . $\text{C} = 54.35$; $\text{H} = 7.04$.

0.3180 „ 16.4 c.c. moist nitrogen at 16° and 750 mm. $\text{N} = 5.93$.

$\text{C}_{11}\text{H}_{17}\text{O}_5\text{N}$ requires $\text{C} = 54.32$; $\text{H} = 7.00$; $\text{N} = 5.76$ per cent.

0.7498 required 31.4 c.c. *N*/10 sodium hydroxide for neutralisation, whence the equivalent was 239; the number required for a monobasic acid, $\text{C}_{11}\text{H}_{17}\text{O}_5\text{N}$, is 243. It is readily soluble in hot water, alcohol, chloroform, acetic acid, ethyl acetate, or acetone, and sparingly so in cold water, carbon tetrachloride, benzene, or carbon disulphide. The acid when quite pure is colourless, but generally separates in the form of pale yellow crystals melting at $70-72^\circ$.

The crystals are thin, rectangular plates containing minute air bubbles, and having straight extinction in polarised light; occasionally, however, thick rhomboidal plates or rhombohedra are obtained, and in these the extinction directions approximately bisect the angles of the rhombs. Examined in convergent polarised light, some fragments show indistinctly one axis of a wide-angled interference figure. The double refraction is moderate, but its sign could not be determined.

0.6830 Gram dissolved and made up to 24.9 c.c. with absolute alcohol was examined in a 2-dcm. tube at 11° . The observed rotation was $+2.06^\circ$, whence $[\alpha]_D + 37.60^\circ$.

The acid is not altered by exposure to air, even during several months, but when placed in a vacuum desiccator over sulphuric acid

it changes into a pasty mass. It reacts strongly acid to litmus and decomposes carbonates. On addition of ferric chloride to an aqueous solution of the acid, a dark blue colour is produced, which gradually disappears, a white, flocculent precipitate being formed. A neutral solution of the sodium salt gives with copper sulphate a deep yellowish-brown colour. It reduces ammoniacal silver nitrate, but does not affect Fehling's solution. A solution of the acid in acetic acid reacts instantly with bromine, even when excess of sodium acetate is present. An alkaline solution of the sodium salt is instantly oxidised by an ice-cold solution of potassium permanganate. On adding potassium permanganate to a solution of the acid in dilute sulphuric acid, a white, amorphous precipitate separates. Potassium dichromate and dilute sulphuric acid gives with an aqueous solution of the acid a pale yellow precipitate. This precipitate separates even from very dilute solutions of the acid. A similar precipitate is also formed when potassium ferricyanide is added to a solution of the acid in excess of sodium carbonate.

The acid dissolves readily in cold concentrated hydrochloric acid; on diluting the solution with water the unchanged acid was precipitated even after the liquid had been allowed to stand for four days.

On boiling with concentrated hydrochloric acid it is decomposed with formation of ψ -cumenecarboxylic acid.

On boiling the acid with excess of sodium hydroxide and acidifying the cooled liquid, the unchanged acid separated, but on using a measured quantity of sodium hydroxide and estimating the excess of alkali it was found that a disodium salt had been formed.

1.215 after boiling with 25 c.c. *N*-sodium hydroxide required 15 c.c. *N*-sulphuric acid for neutralisation, whence the equivalent = 121.5; the number calculated for a dibasic acid, $C_{11}H_{17}O_5N$, is 121.5.

The acid is therefore an anhydro-derivative of a dibasic acid in which a carboxyl group is probably engaged in the formation of a lactone ring.

It reacts rapidly with sodium hydroxide and ferrous hydroxide, ammonia being evolved and ferric hydroxide produced.

A solution of equimolecular proportions of the lactam (L), methyl iodide, and sodium methoxide in absolute methyl alcohol was heated on the water-bath for three hours, after which water was added and the methyl alcohol expelled by a current of steam. The monomethyl derivative remained as a viscous, colourless oil which was insoluble in

water, alkalis, or dilute mineral acids, and withstood all attempts to cause it to solidify. It was therefore not analysed, but converted directly into :

This was obtained by heating the preceding compound with eight times its weight of 10 per cent. sodium hydroxide on the water-bath for about two hours, when solution was complete. The liquid was then cooled and acidified, and the resulting crystalline powder recrystallised from dilute alcohol :

0.1241 gave 12.5 c.c. moist nitrogen at 16° and 767 mm. $N = 11.9$.

$C_{12}H_{18}O_3N_2$ requires $N = 11.8$ per cent.

0.807 required 33.7 c.c. of $N/10$ sodium hydroxide for neutralisation, whence the equivalent = 239, whilst a monobasic acid, $C_{12}H_{18}O_3N_2$, requires 238.

This compound is soluble in boiling water and separates almost entirely on cooling. It dissolves readily in alcohol, acetone, ethyl acetate, chloroform, or glacial acetic acid, sparingly in ether or benzene and is nearly insoluble in carbon disulphide or light petroleum. It melts at 155° and slowly decomposes at this temperature, evolving methylamine.

The crystals from dilute alcohol are transparent, truncated needles having straight extinction in polarised light, their direction of greatest elasticity and length being coincident. Crushed fragments examined in convergent polarised light show in some the acute bisectrix of an interference figure of moderate angle. The axial dispersion is moderately large, the angle for blue being greater than red light. The double refraction is strong and positive in sign.

This compound dissolves in cold dilute hydrochloric acid and the resulting solution does not give a precipitate on the addition of sodium nitrite, in which respect it differs from the non-methylated acid. It reduces warm ammoniacal silver solutions, and in faintly alkaline solution instantly discharges the colour of ice-cold potassium permanganate. It is apparently not changed when warmed with strong, aqueous sodium hydroxide on the water-bath, but if ferrous hydroxide is present a mixture of ammonia and methylamine is evolved, the iron compound being converted into ferric hydroxide; in a quantitative experiment which was not quite completed, one and one-third equivalents of base (ammonia and methylamine) were expelled; cyanide is not formed even in traces during this reaction. When the acid was treated with sodium hydroxide and ferrous hydroxide in the cold, ammonia with no trace of methylamine was evolved.

Action of Dimethyl sulphate and Alkali on the Amino-acid (A).

Both the original acid and its ester are further methylated when warmed with dimethyl sulphate and alkali in methyl-alcoholic solution, and prolonged heating causes the elimination of trimethylamine from the product. In an experiment where the mixture was heated for ten minutes only, the liquid was diluted, acidified, and mixed with a solution of iodine in potassium iodide, when an oily periodide was precipitated.

Some quantity of the periodide prepared in this way was decomposed by suspending it in water and passing sulphur dioxide into the warm liquid; the colour disappeared and a clear solution was obtained from which nothing could be isolated by extracting with any of the usual solvents. Finally, however, it was found that on adding concentrated aqueous potassium iodide and hydrochloric acid to the solution, an oily substance which slowly crystallised could be salted out, and this was collected and crystallised from chloroform:

0.4710 dissolved in water required 12.00 c.c. AgNO_3 . $\text{I} = 32.4$.

0.2995 gave 0.3354 CO_2 and 0.1155 H_2O . $\text{C} = 39.8$; $\text{H} = 5.6$.

0.2100 „ 12.2 c.c. moist nitrogen at 15° and 753 mm. $\text{N} = 6.8$.

$\text{C}_{13}\text{H}_{21}\text{O}_3\text{N}_2\text{I}, \text{H}_2\text{O}$ requires $\text{I} = 32.7$; $\text{C} = 39.4$; $\text{H} = 5.3$; $\text{N} = 7.1$ per cent.

The substance was boiled for some time with strong potassium hydroxide and the distillate collected in dilute hydrochloric acid; the contained base was proved, by analysis of its platinichloride ($\text{Pt} = 39.4$, $\text{C}_4\text{H}_{16}\text{N}_2\text{Cl}_6\text{Pt}$ requires $\text{Pt} = 39.2$ per cent.), to be dimethylamine, and the iodide from which it was obtained must therefore have been derived from a dimethylated acid. The product in the residual alkaline solution could not be obtained in a pure form.

These results indicate that the compound here dealt with was the hydriodide, $\text{C}_{10}\text{H}_{13}\text{ON} \begin{smallmatrix} \text{N}(\text{CH}_3)_2 \cdot \text{HI} \\ \text{CO}_2\text{H} \end{smallmatrix}$, of the dimethylated acid.

The methylated amino-acid (AMe) (30 grams) was dissolved in cold concentrated hydrochloric acid (150 c.c.), a process which was accompanied by an appreciable rise in temperature. At the end of twenty-four hours the whole was exactly neutralised with sodium hydroxide. The oil which separated soon solidified to a crystalline mass, which was collected, washed, and crystallised from boiling water. The amount of base obtained was 28 grams:

0.1527 gave 15.5 c.c. moist nitrogen at 16° and 758 mm. $N = 11.8$.

$C_{12}H_{18}O_3N_2$ requires $N = 11.8$ per cent.

The compound resembles the non-methylated base (A) in solubility in various media and separates from boiling water in long crystals which melt at 129—130°.

The crystals are well formed, elongated, transparent plates through the larger faces of which the bisectrix of an interference figure of moderate axial angle passes perpendicularly. The double refraction is moderate and negative in sign.

For the determination of its optical activity, 0.6505 gram was dissolved and made up to 25.1 c.c. with absolute alcohol at 11° and the rotation examined in a 2-dcm. tube. The rotation observed was +0.37°, whence $[\alpha]_D + 7.1^\circ$.

When a strong solution of the methylated base in hydrochloric acid is treated with sodium nitrite, a nearly colourless oil is precipitated, and no yellow precipitate is formed as is the case with the non-methylated base.

Action of Warm Dilute Acids on the Methylated Lactonic Base (BMe).

This base is not decomposed by 10 per cent. aqueous sodium hydroxide, but on warming with dilute acid for some time and subsequently with alkali, methylamine is liberated.

1.190 grams (1 mol.) of the methylated base were heated on the water-bath with 20 c.c. of $N/2$ sulphuric acid (2 mols.) during one and a half hours. On rendering the solution alkaline and distilling, methylamine (0.74 mol.) was liberated as determined by titration with $N/5$ hydrochloric acid. In a second experiment in which the heating lasted three hours, a larger amount of methylamine (0.95 mol.) was obtained. That methylamine and no ammonia was formed was proved by evaporating the neutralised distillate to dryness, when a crystalline, hygroscopic mass was obtained. This, under the polarising microscope, was found to be entirely composed of doubly refracting crystals; it was entirely soluble in absolute alcohol and after conversion into platinichloride gave the following analytical result:

0.3920 gave 0.0775 CO_2 and 0.0925 H_2O . $C = 5.4$; $H = 2.6$.

$C_2H_{12}N_2Cl_6Pt$ requires $C = 5.1$. $H = 2.6$ per cent.

The liquid from which the methylamine had been removed by distillation was acidified with sulphuric acid, and after remaining for twenty-four hours it deposited crystals which were collected and recrystallised from hot water. The substance obtained melted at 66—67°, and reacted with ferric chloride, copper sulphate, and potassium dichromate in exactly the same way as did the lactonic acid

prepared from the unmethylated base (B). When mixed with the latter compound the melting point was 67—68°, so that the identity of the two compounds is beyond question.

Methylation of the Lactonic Base (B).

Dimethyl sulphate acts rapidly on this base at the ordinary temperature, heat being generated and an oily salt being produced. This is very readily soluble in water, but on treatment with alkali yields only an oily base which is apparently not identical with the methylated base (BMe). Solutions of the salt, even when highly dilute, yield a liquid periodide. Methyl iodide slowly forms a crystalline methiodide when heated with the base in a closed tube at 100°. This substance rapidly dissolves in water and the product appears to correspond with the methylated compound just described. Both substances, when heated with acids, furnish methylamine in considerable quantity.

Attempts were made to methylate the original base exhaustively by heating it with excess of dimethyl sulphate and alkali. Whilst considerable quantities of trimethylamine were formed, the other products were extremely soluble in water and were impossible to purify. They yielded ammonia when warmed with ferrous hydroxide and alkali.

Formation of 2:3:6-Trimethylbenzoic Acid.

The lactam (L) was heated during two days with four times its weight of concentrated hydrochloric acid on the water-bath; the originally colourless liquid gradually darkened and deposited a small quantity of a black oil, carbon dioxide being very slowly evolved. On cooling, the whole set to a mass of crystals consisting of ammonium chloride mixed with fine needles. This was collected, washed with water to remove inorganic matter, and finally extracted with dilute sodium carbonate solution. The filtered extract was acidified and the solid acid collected, washed, dried, and crystallised from petroleum; it contained no nitrogen:

0.2535 gave 0.6794 CO_2 and 0.1632 HO_2 . $\text{C} = 73.1$; $\text{H} = 7.2$

$\text{C}_{10}\text{H}_{12}\text{O}_2$ requires $\text{C} = 73.2$; $\text{H} = 7.3$ per cent.

0.2079 required 12.1 c.c. $N/10$ NaOH for neutralisation, whence the equivalent = 166; the number calculated for a monobasic acid, $\text{C}_{10}\text{H}_{12}\text{O}_2$, being 164.

The acid, which can be obtained by similar treatment of any of the compounds convertible by acids into the lactonic acid (p. 989), dissolves freely in all the usual media with the exception of light petroleum and water, which dissolve it only when hot. It separates from hot light petroleum in small needles, and from hot water in long, silky,

glistening needles. It is dimorphous, and when heated in a melting point tube fuses at 84° unless the temperature is raised too slowly, setting, almost at once, to a solid mass which melts at $105\text{--}106^{\circ}$.

The compound was found to be optically inactive in alcohol or ethyl acetate, and as it behaved as a saturated compound was evidently a benzene derivative.

Some quantity of the acid was therefore converted into its calcium salt and distilled with soda-lime under reduced pressure. An excellent yield of an hydrocarbon was obtained which was collected, dried over sodium, and distilled. The whole passed over between $166\text{--}168^{\circ}$, and on analysis :

0.1823 gave 0.6006 CO_2 and 0.1991 H_2O . $\text{C} = 89.8$; $\text{H} = 12.1$.

C_9H_{12} requires $\text{C} = 90.0$; $\text{H} = 12.0$ per cent.

The hydrocarbon agreed closely in properties with ψ -cumene, and in order fully to identify it the bromo- and nitro-derivative were prepared.

On analysis of the bromo-derivative :

0.1436 gave 0.2286 AgBr . $\text{Br} = 66.5$.

$\text{C}_9\text{H}_9\text{Br}_3$ requires $\text{Br} = 66.9$ per cent.

The substance crystallised in slender, white needles melting at $224\text{--}226^{\circ}$ and agreed in all particulars with the tribromo- ψ -cumene obtained by Fittig and Laubinger (*Annalen*, 1869, 151, 264).

Portions of the hydrocarbon were also nitrated and two nitro-derivatives obtained. One of these formed transparent, yellow needles melting at $70\text{--}71^{\circ}$, the other having a more slender habit and melting at $183\text{--}184^{\circ}$. These were evidently identical with the mono- and tri-nitro- ψ -cumenes obtained by Schäfer (*Zeitsch. für Chem.*, 1867, 12) and by Fittig and Laubinger respectively (*Annalen*, 1869, 151, 261). There is thus no doubt that the hydrocarbon was ψ -cumene, and the acid from which it was prepared was therefore a nucleal ψ cumenecarboxylic acid. Two of the three possible acids of this type are known, namely, those with the structures $\text{Me}_3\cdot\text{CO}_2\text{H} = 3:4:6:1$ and $2:3:5:1$. These melt at $149\text{--}150^{\circ}$ and 127° respectively, so that the acid dealt with in the present instance is probably the hitherto unknown $2:3:6$ -trimethylbenzoic acid.

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