

XLV.—CONTRIBUTIONS FROM THE RESEARCH LABORATORY OF THE PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.

*The Action of Alkalis on the Nitro-compounds of the Paraffin Series.
Formation of Isoxazoles.*

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IN 1888 we communicated to the Society (Proc., 1888, 117) a preliminary account of a remarkable reaction which we had observed to occur when nitroethane is warmed with aqueous solutions of alkali carbonates or hydroxides. The reaction was first observed in the autumn of 1887, when we had occasion to prepare some quantity of ethyl nitrite and nitroethane by acting on silver nitrite with ethyl iodide. The nitroethane was dried by digestion with, and distillation from, potassium carbonate, and after nearly all the nitroethane had been obtained, an aromatic oily substance (C_6H_5NO) passed over into the distillate. The brownish residue contained potassium nitrite. We could find no record of this reaction having been previously observed, and it soon became evident that the aromatic body belonged to a new class of organic compounds. We learned subsequently that the Russian chemist Sokoloff was also engaged in examining the action of alkalis on the paraffinic nitro-compounds, and that he had communicated an account of his experiments to the Russian Chemical Society (*J. Russ.*

Chem. Soc., 1887, 374; 1888, 498). Sokoloff had isolated and partly examined the new compound which he had produced by heating nitroethane with alcoholic ammonia in closed tubes. On comparing Sokoloff's results with those we had obtained, it became evident that he had not completely examined the nature of the reaction, and had, as we shall proceed to show, overlooked one of the most important products, namely, acetonitrile. Moreover, he does not appear to have investigated the constitution of the new compound. We therefore decided to continue the enquiry, and we now have the honour to lay before the Society a full account of the work we have done up to the present time. We have fully examined the products of the action of alkalis on nitroethane, and have investigated the properties and modes of decomposition of the new compound which results from this action. We have also succeeded in ascertaining the constitution of this substance, and in effecting its synthesis by an entirely independent reaction. In addition, preliminary experiments have been made with nitromethane, nitropropane, and other nitro-derivatives belonging to the same series.

I.—ACTION OF ALKALIS ON NITROETHANE.

Action of Alkali Carbonates and Hydroxides.

Dry potassium carbonate is without action on dry nitroethane. When, however, nitroethane is allowed to stand with a strong aqueous solution of potassium carbonate, the mixture becomes yellow, and potassium hydrogen carbonate separates in crystals. On warming the mixture, it darkens, and carbon dioxide is evolved. A brownish-yellow oil, corresponding with about one-third of the nitroethane taken, remains on the surface of the solution, which now contains abundance of nitrite and a little ammonia, but no nitrate. If the mixture has been warmed for some hours, the whole of the nitroethane is decomposed, and no further change occurs on boiling. The oily layer, after having been dried with potassium carbonate, may be separated by fractional distillation into two parts. A fraction is obtained, boiling between 75° and 80° , and a second large fraction between 160° and 170° ; a brown, resinous substance remains undistilled. By repeated distillation, the first fraction is resolved into a liquid boiling between 77° and 81° , which possesses all the properties of *acetonitrile*. It burns with a crimson flame, and is decomposed by ebullition with acids and alkalis, in the latter case with the evolution of ammonia. The acetonitrile was evidently contaminated with a trace of some substance which lowered its boiling point. To remove this impurity, it was distilled from a

crystal of potassium dichromate and a few drops of dilute sulphuric acid. The purified liquid now boiled at 81° , which is the boiling point of acetonitrile. Since the quantity obtained was too small for ultimate analysis, proof of its identity with acetonitrile was obtained by heating it with aqueous alkali and isolating the product of hydrolysis. As soon as the evolution of ammonia had ceased, the alkaline liquid was neutralised with dilute nitric acid, evaporated, and decomposed with silver nitrate. The resulting silver salt was crystallised from water and analysed. It contained 63.4 per cent. of silver; calculated for $\text{AgC}_2\text{H}_3\text{O}_2$, 64.6 per cent. The acetonitrile appears to constitute about 20 per cent. (by volume) of the liquid resulting from the action of potassium carbonate on nitroethane. A little is decomposed by the alkali during the reaction, and this probably accounts for the small quantity of ammonia which is invariably formed.

The higher fraction of the original liquid consists of the new compound. Its properties will be fully described in a later section of this paper.

The amount of potassium nitrite formed in this reaction has been carefully estimated. It constitutes 16.2 per cent. of the resulting products, that is to say, one-half of the nitrogen of the nitroethane appears in this form.

Sodium carbonate, like potassium carbonate, is decomposed by nitroethane even in the cold, with the production of sodium nitroethane and carbon dioxide, which forms sodium hydrogen carbonate with the excess of the carbonate. On warming, action proceeds further, with formation of *sodium nitrite*, *acetonitrile*, and the *new compound*.

The ability of nitroethane to decompose alkali carbonates even in the cold does not appear to have been previously noticed.

Warm aqueous soda and potash rapidly convert nitroethane into potassium nitrite, the new compound, ammonia, acetic acid, and a quantity of brown resin; the ammonia and acetic acid resulting from the hydrolysis of the acetonitrile which is first formed. Alcoholic potash and soda also produce the new compound from nitroethane. Aldehyde is simultaneously formed, together with nitrite and the brown resin. Calcium hydroxide does not act on nitroethane.

Action of Ammonia.

Formation of Ammonium Nitroethane.

No ammonium analogue of sodium nitroethane has hitherto been obtained. While examining the action of ammonia on nitroethane, it was found that at 0° dry ammonia readily united with nitroethane to form a crystalline compound. Some difficulty was experienced in determining the exact composition of this substance, since, although it

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does not quickly melt at ordinary temperatures, loss of ammonia occurs even when it is being dried in the cold. The following method of preparing the compound for analysis proved successful. Nitroethane was mixed with about four times its volume of dry ether; the mixture was cooled to about -20° , and dry ammonia gas passed through it until crystals ceased to form. The crystals were then rapidly collected with the aid of a pump, and quickly washed with ice-cold dry ether. They were then thrown out on a piece of paper, and when the ether had completely evaporated, were transferred to a weighed stoppered bottle.

The snow-like mass of tabular crystals is almost neutral to litmus, but on standing at the ordinary temperature it slowly loses ammonia.

The cold, aqueous solution is at first only very faintly, if at all, alkaline, but by degrees ammonia is set free. The composition of the substance was ascertained by titrating an aqueous solution with dilute sulphuric acid (1100 c.c. = H_2SO_4), which slowly combines with the ammonia and liberates nitroethane.

Weight of substance taken	1.751 grams.
Standard sulphuric acid required	10 c.c.
Ammonia in compound	17.6 per cent.
Calculated for $\text{C}_2\text{H}_4(\text{NH}_4)\text{NO}_2$	18.4 ,,

When the crystals are heated, they decompose into ammonia and nitroethane, but in the absence of water no condensation occurs, even when the experiment is made at 100° in a closed tube.

Aqueous ammonia and aqueous ethylamine act on nitroethane much less energetically than potassium and sodium carbonates. When strong aqueous ammonia is used, change occurs very slowly; indeed, it is necessary to heat the mixture in closed tubes at $110-120^{\circ}$ in order to complete the reaction. The products are ammonium nitrite, acetonitrile, and the new compound. Alcoholic ammonia has a similar effect, producing aldehyde in addition to these substances.

PHYSICAL AND CHEMICAL PROPERTIES OF THE NEW COMPOUND.

The new compound obtained in the manner above described is a colourless liquid, having a relative density of 0.986 at $15^{\circ}/15^{\circ}$. It boils at 171° (corr.) with slight decomposition, forming a resinous substance, and slowly darkens when exposed to light.

Distilled under reduced pressure (250 mm.), about one-half came over between 134° and 135° ; this fraction had a relative density of 0.9956 at $4^{\circ}/4^{\circ}$, 0.9859 at $15^{\circ}/15^{\circ}$, 0.9788 at $25^{\circ}/25^{\circ}$. The remainder of the liquid distilled between 135° and 136.5° , and its relative density was 0.9956 at $4^{\circ}/4^{\circ}$, 0.986 at $15^{\circ}/15^{\circ}$, 0.9788 at $25^{\circ}/25^{\circ}$. The corre-

spondence in the densities of the two fractions proves that the liquid is a single substance. When super-cooled, it freezes to a mass of crystals which melt at $3\cdot5^{\circ}$.

On combustion, the substance afforded the following data, the carbon and hydrogen being determined in a current of oxygen, and the nitrogen by burning with copper and copper oxide in a Sprengel vacuum.

- I. Substance taken, 0.1978 gram; H_2O found, 0.1504 gram; CO_2 found, 0.4633 gram.
 II. Substance taken, 0.3840 gram; N_2 found, 40 c.c. at 17° and 764 mm.

		Calculated for C_6H_9NO .
C	63.9 per cent.	64.8 per cent.
H	8.4 „	8.1 „
N	12.15 „	12.6 „

The molecular weight was determined by Raoult's method with acetic acid and benzene as the solvents. The following results were obtained:—

Benzene as the Solvent.

Wt. of substance	0.1322 gram.
Wt. of solvent	10.1446 „
Freezing point of solvent.....	$5\cdot833^{\circ}$
Freezing point of solution	$5\cdot25^{\circ}$
Depression for 1 gram of substance to 100 grams of solvent.....	$0\cdot447^{\circ}$

Molecular depression of benzene, 49; hence molecular weight of substance, $\frac{49}{0\cdot447} = 109\cdot5$. Calculated for C_6H_9NO , 111.

Acetic Acid as the Solvent.

Wt. of substance	0.134 gram.
Wt. of solvent.....	12.9416 „
Freezing point of solvent	$14\cdot65^{\circ}$
Freezing point of solution	$14\cdot3^{\circ}$
Depression for 1 gram of substance to 100 grams of solvent.....	$0\cdot338^{\circ}$

Molecular depression of acetic acid, 39; hence molecular weight of substance, $\frac{39}{0\cdot338} = 115$. Calculated for C_6H_9NO , 111.

We are indebted to Dr. Perkin and to Dr. Gladstone for having determined the magnetic rotation and the refractive indices of this compound.

Magnetic Rotation.

Relative densities, 0.9953 at 4°/4°; 0.9856 at 15°/15°; 0.9784 at 25°/25°.

<i>t.</i>	Rotations.		
	Sp. rot.	Mol. rot.	
15.5°	1.0879	6.809	
15.5	1.0824	6.775	
14.7	1.0824	6.786	
14.7	1.0864	6.796	
20.0	1.0837	6.806	
19.5	1.0823	6.794	
19.5	1.0823	6.794	
Average ..	17.0	1.0837	6.792

Dr. Perkin remarks that the calculated value for the formula C_6H_9NO is about 6.278, which is 0.514 lower than that actually found; this might indicate that the compound is unsaturated to the extent of four equivalents of hydrogen (H_4).

Specific Refraction.

Temp.	Rel. dens.	μ_A	μ_F	μ_G	μ_H	Found.		Calculated.	
						R_A	$R_H - A$	R_A	$R_H - A$
20.5	0.9802	1.4473	1.4608	1.4673	1.4733	50.65	2.95	50.8	2.92

The refractive indices, μ , have been determined for the lines A, F, G, and H. The molecular refraction, R , is given for the line A, and also the difference (molecular dispersion) between this number and that indicating the molecular refraction for the line H. The calculated values have been obtained on the supposition that the compound is unsaturated, the lower value for oxygen being taken, and the nitrogen reckoned as having the same value as in nitriles. The usual addition has been made of 2.2 for doubly-linked carbon for the line A, and of 3 for the line H. The correspondence between the observed and calculated molecular refraction and dispersion is remarkable.

The liquid has no action on a ray of polarised light. It dissolves sparingly in water, and distils with it. Alcohol, ether, chloroform, benzene, and light petroleum dissolve it freely. It has feebly basic properties, but is without action on litmus. Acids, if not too dilute, dissolve it and the resulting solutions have not the characteristic aromatic smell of the original liquid. These salt-solutions are decomposed by the addition of water, and on heating the solutions the original substance distils with the water. When dry

hydrochloric acid gas is led into the well-cooled substance, a crystalline hydrochloride, C_6H_9NO, HCl , is formed. When auric chloride is added to a solution of the hydrochloride, a crystalline precipitate is obtained, if the solution does not contain a large excess of hydrochloric acid. These crystals are best prepared by mixing aqueous solutions of gold chloride and the original substance. They contain 45.4 per cent. of gold, and are therefore a compound of the original substance with gold chloride. The formula $C_6H_9NO, AuCl_3$ requires 45.1 per cent. of gold, which agrees well with the number found. An unstable platinumochloride can also be obtained.

A characteristic reaction of the substance is the formation of a crystalline compound with mercuric chloride. When an aqueous solution of this salt is added to an aqueous solution of the substance, a white, crystalline, sparingly soluble precipitate is produced. This compound is difficult to dry without losing a little of the base. A specimen dried on a porous tile over calcium chloride contained 51 per cent. of mercury; calculated for $C_6H_9NO, HgCl_2$, 52 per cent. The base slowly volatilises from the compound when it is exposed to air, and the aqueous solution is completely decomposed when heated, the base distilling over with the water. The preparation of this compound constitutes an excellent method of identifying and purifying the base, the washed precipitate being distilled with water; when nearly the whole of the base condenses with the first portions of the steam, and floats as an oil on the surface of the liquid, from which it may readily be separated, and the small quantity which remains dissolved can be extracted with ether. By carefully distilling an ethereal solution, the whole of the ether may be removed, and a residue of the pure base obtained. The base has no action on a hot solution of silver nitrate even in the presence of ammonia, nor does it form a derivative with either hydroxylamine or phenylhydrazine. Nitrous acid does not attack it, and it does not give the Liebermann reaction with phenol and sulphuric acid. No compound with picric acid could be obtained, and the pine-splinter reaction gives no coloration. Acetyl and benzoyl chlorides are without action on the base even when heated with it.

From these reactions, it may be inferred that the nitrogen in the compound is not present in the form of a nitro- or nitroso-group, nor as amidogen. The substance does not appear to be a pyrrol derivative, an aldehyde, a ketone, or a hydroxyl derivative. It is isomeric with acetopropyl cyanide and also with "acrolein-ammonia," to which, however, it bears no resemblance. In order to obtain further knowledge of its constitution, its behaviour when heated with acids and alkalis was studied, and its oxidation and reduction products were examined.

ACTION OF ALKALIS AND ACIDS.

The alkali carbonates are without action on the compound, even at its boiling point. Concentrated solutions of ammonia and potash fail to dissolve it. Heated with strong potash for some hours in a closed tube at 100—120°, some darkening occurs, but nearly the whole of the compound may be recovered unchanged. With alcoholic soda, in a closed tube at 180°, there is a little action, and a small quantity of ammonia and acetic acid are produced.

In order to ascertain whether the compound is hydrolysed or otherwise attacked by strong acids it was dissolved, in concentrated hydrochloric acid, and the liquid heated for one hour in a closed tube at 100°. No effect having been produced, the temperature was raised to 130°, and the heating continued for 48 hours. Slight darkening occurred, but on distilling the liquid with water the greater part of the substance was recovered unchanged, together with a little acetic acid. Evaporation of the remaining acid solution left a small residue, consisting chiefly of ammonium chloride, together with a minute amount of a hydrochloride soluble in absolute alcohol. This was evidently the salt of a feeble base, since, on boiling it with water, some of the base was volatilised. We have not yet succeeded in obtaining sufficient of this compound, which has a characteristic odour, for examination. It is formed in small quantity by the action of dehydrating agents on the original substance.

Ordinary nitric acid dissolves the compound with formation of an unstable nitrate which is decomposed on dilution with water. When the solution in nitric acid is heated, oxidation occurs, but without the previous formation of a nitro-compound. All attempts to prepare a nitro-compound failed. Cold fuming nitric acid dissolves the substance, but on adding water the base is regenerated.

OXIDATION PRODUCTS.

Oxidation by Potassium Permanganate.

A solution of potassium permanganate at once attacks the substance. 5 grams of the liquid were oxidised by warming with a slight excess of permanganate, and the filtered liquid was acidified with dilute sulphuric acid and distilled. An acid smelling like acetic acid passed over, and towards the end of the operation, when the liquid became concentrated, *nitric acid* distilled. The distillate was neutralised and evaporated, when potassium nitrate crystallised. The remaining liquid, mixed with silver nitrate, yielded a crystalline silver salt, which was proved by analysis to be *silver acetate*. It contained

64.5 per cent. of silver; silver acetate contains 64.6 per cent. By evaporating the liquid which had yielded these crystals, a further quantity was obtained, which was also proved to be silver acetate. No other acid could be detected either in this solution or in the liquid which remained after distillation.

Oxidation by Nitric Acid.

Warm nitric acid oxidised the compound, nitrous fumes being evolved, together with traces of hydrogen cyanide. As soon as action had ceased, the liquid was cooled, when crystals of *oxalic acid* separated. On distillation, *acetic acid* was obtained, and recognised by conversion into the silver salt, which contained 64.8 per cent. of silver, the calculated quantity being 64.6 per cent. No silver salt other than the acetate was formed, the last fraction of crystals containing 64.5 per cent. of silver. No formic acid could be detected.

Unsuccessful attempts were made to obtain intermediate oxidation products by the limited action of permanganate and nitric acid, and also by the action of silver oxide.

REDUCTION PRODUCTS.

Reduction by Heated Zinc.

Six grams of the liquid were reduced by distillation over zinc-dust heated to low redness in a combustion tube, provided first with a bulb for collecting liquid products, and secondly with a gas burette filled with mercury to receive the considerable quantity of gaseous product. There condensed in the bulb about 3 c.c. of an almost colourless liquid having an alkaline reaction. The alkalinity was proved to be due for the most part to *ammonia*. The greater part of the liquid distilled rather below 100°, and this was repeatedly fractionated, the portions boiling between 75° and 85° being finally distilled from phosphoric oxide. The liquid now boiled constantly at 80–81°, and possessed all the properties of *acetonitrile*. Proof that it was this substance was obtained by hydrolysis with potash; ammonia was evolved, whilst the remaining liquid afforded a silver salt, which was shown by analysis to be silver acetate, with which it exactly corresponded in its chemical properties. The amount of silver found by analysis was 65.3 per cent., the calculated quantity for silver acetate being 64.6 per cent.

Besides acetonitrile, a small quantity of a weak base resulted from the reduction. The gas which had been collected was a mixture of methane, ethane, and hydrogen.

Reduction by Metal and Acid.

The compound is remarkable for the manner in which it withstands the attack of the usual reducing agents.

To a mixture of tin and hydrochloric acid, from which hydrogen was being briskly evolved, 5 grams of the substance was gradually added. After action had continued for some hours, the liquid was diluted with water and distilled. Nearly the whole of the substance was recovered. In other experiments the compound was dissolved in concentrated hydrochloric acid, and small pieces of tin added from time to time. Under these conditions also there was but little change; a small quantity of ammonium chloride was produced, but the greater part of the substance was unattacked.

A mixture of the substance with somewhat diluted sulphuric acid and granulated zinc, allowed to stand for some days, led to no better result, a little ammonia and acetic acid being formed.

When zinc-dust was added in small quantities at a time to a mixture of the compound with diluted sulphuric acid, rather more action occurred; ammonia and acetic acid were produced, together with a substance, probably an alcohol, of which sufficient could not be obtained to enable it to be identified. Amalgamated aluminium foil (prepared by immersing the foil in solution of mercuric chloride) was next tried as a reducing agent. In the absence of acid, it acted extremely slowly, but after some days' contact with a warm aqueous solution of the compound, some reduction had occurred. *Ammonia* and *acetic acid* had been formed, together with what appeared to be *secondary butyl alcohol*, but the amount of substance produced was insufficient for analysis. Amalgamated aluminium acted more rapidly in presence of dilute sulphuric acid, and here again ammonia, acetic acid, and a liquid having the properties of secondary butyl alcohol were produced, but, as in the previous experiment, enough of the alcohol could not be obtained to render analysis possible.

Reduction by Hydriodic Acid.

The substance was dissolved in an excess of concentrated hydriodic acid, a little amorphous phosphorus added, and the mixture heated at 50° in a closed tube for 17 hours; no change occurred. The temperature was then raised to 100°, and the heating continued for one hour. No change being produced, the mixture was heated at 180°, but without effect. After having been exposed to the higher temperature of 200° for some hours, the contents of the tube were diluted with water and distilled. A considerable quantity of the original compound was recovered unchanged. Some action had,

however, occurred, since ammonium iodide was detected in the aqueous liquid, but the other decomposition products were not formed in sufficient quantity to enable them to be separated and identified. Among them was the feeble base which we have already referred to as originating in the action of strong acids and dehydrating agents on the compound.

Reduction by Sodium.

Sodium-amalgam has very little action either on an aqueous or on an alcoholic solution of the substance; the nitrogen appears to be extremely slowly split off as ammonia.

By adding small pieces of sodium to an ethereal solution of the compound, standing over a small quantity of water kept below 15° , we have succeeded in effecting its reduction, and have obtained a crystalline *dihydride*. When the reduction is effected in this manner, no hydrogen is evolved, but the thin fragments of sodium acting at the juncture of the two layers become surrounded with a white, crystalline crust. If the temperature rises during the action, or if the action is too energetic, hydrogen is evolved, and the crystalline solid is decomposed with the liberation of ammonia.

The crystalline compound may be extracted from the liquid by means of chloroform, in which it is very soluble. An ethereal solution deposits well-defined, prismatic crystals melting at 110° (corr.), or they may be obtained by adding light petroleum to a solution in chloroform. The following results were afforded by the combustion of a number of different specimens of this substance:—

- I. 0.1487 gram substance (crystallised from ether) gave 0.3399 gram CO_2 and 0.1340 gram H_2O .
- II. 0.1262 gram substance (crystallised from ether) gave 0.2897 gram CO_2 and 0.1168 gram H_2O .
- III. 0.2185 gram substance (crystallised from ether) gave 0.505 gram CO_2 and 0.2012 gram H_2O .
- IV. 0.2212 gram substance (crystallised from ether) gave 0.5072 gram CO_2 and 0.2026 gram H_2O .
- V. 0.1667 gram substance (crystallised from ether) gave 18 c.c. N_2 at 12° and 757 mm.
- VI. 0.1526 gram substance (precipitated by light petroleum from a solution in chloroform) gave 0.3551 gram CO_2 and 0.1488 gram H_2O .
- VII. 0.1542 gram substance (precipitated by light petroleum from a solution in chloroform) gave 0.3594 gram CO_2 and 0.1510 gram H_2O .

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	Found.							Calculated for $C_6H_{11}NO$.
	I.	II.	III.	IV.	V.	VI.	VII.	
C ..	62·34	62·60	63·03	62·53	—	63·46	63·56	63·71 per cent.
H..	10·01	10·28	10·23	10·17	—	10·83	10·88	9·73 „
N..	—	—	—	—	12·75	—	—	12·39 „

The molecular weight of this dihydride was determined by Raoult's method, using benzene as the solvent.

	I.	II.	III.
Wt. of substance	0·0476	0·0405	0·0899 gram.
Wt. of solvent	5·3795	5·670	5·670 „
Freezing point of solvent....	5·59°	5·59°	5·59°
Freezing point of solution....	5·20°	5·275°	4·90°
Depression for 1 gram of substance to 100 grams of solvent	0·440°	0·441°	0·435°
Mol. depression of benzene ..	49	49	49
Mol. wt. of substance.....	111·3	111	112·6
Mean of the three determinations			111·6
Calculated for $C_6H_{11}NO$			113·0

The crystals dissolve readily in alcohol and chloroform, less readily in light petroleum. Cold water dissolves them slowly, hot water more quickly, but with some decomposition and evolution of ammonia. The aqueous solution is faintly alkaline to litmus, and produces with mercuric chloride an abundant white precipitate. Picric acid does not precipitate the solution, which also fails to give the pine splinter reaction for pyrrol. Alkalis and acids at once decompose the aqueous solution, in the former case with abundant production of ammonia.

On heating with water in a closed tube at 100°, the dihydride is decomposed into *ammonium acetate* and *methyl ethyl ketone* in accordance with the equation $C_6H_{11}NO + 2H_2O = CH_3 \cdot CO \cdot ONH_4 + CH_3 \cdot CO \cdot C_2H_5$. The ketone was identified by its boiling point (76—78°) and its single oxidation product, acetic acid; on oxidation with chromic acid, the distillate, after saturation with silver oxide, afforded pure silver acetate, the solution being fractionally crystallised, and the first and last fractions analysed with the following results:—

Percentage of silver in first fraction of salt, 64·1; percentage of silver in last fraction, 64·7; percentage of silver in silver acetate, 64·7.

The ammonium acetate was characterised by conversion into the silver salt, which was found to contain 64·3 per cent. of silver.

ACTION OF PHOSPHOROUS AND PHOSPHORIC CHLORIDES.

Phosphorous chloride does not attack the compound, even when strongly heated with it.

Phosphoric chloride does not react in the cold, but when the mixture is heated at 100° a complicated reaction ensues, hydrogen chloride is evolved, and phosphorous chloride distils, together with a mixture of chloro-derivatives. A considerable quantity of resin and some ammonium chloride are also produced. One of the chloro-derivatives is an oily liquid, having a most irritating effect on the eyes and mucous membrane of the nose. It distilled with steam, but could not be distilled alone without decomposition, even under reduced pressure. This compound contained 25.1 per cent. of chlorine, and is therefore probably a monochloro-derivative of the parent substance; the formula C_6H_5ClNO requires 24.3 per cent. of chlorine.

All attempts to replace by chlorine the single atom of oxygen which the original compound contains were failures. Although the phosphoric chloride was caused to react under various conditions, the result was always the production of chloro-derivatives containing oxygen, whilst, owing to the simultaneous occurrence of a more profound change, resin and ammonium chloride were also formed.

ACTION OF THE HALOGENS.

Dry chlorine, free from hydrogen chloride, was passed into the cooled liquid. As soon as the chlorine was no longer absorbed, the current of gas was stopped, and any free halogen the liquid might contain removed by exposure in a vacuum. No hydrogen chloride was evolved. The oily liquid had a pungent, aromatic odour. When heated, it darkened with evolution of hydrogen chloride, and even when it was distilled under reduced pressure, some change occurred, resulting in the separation of hydrogen chloride and the formation of resin. The washed and dried liquid was therefore first analysed without distillation. It contained 47.5 per cent. of chlorine. The liquid was now distilled under reduced pressure, the greater part of it was obtained near 130° (127 mm.); a little hydrogen chloride escaped. Some resin was produced, and also a small quantity of the highly irritating chloro-derivative which had been found to result from the action of phosphoric chloride. The liquid which had distilled at 130° was purified by shaking with aqueous sodium hydrogen carbonate to remove acid, the chlorine compound dissolved from the solution with ether, the ether well washed with water and dried with calcium

chloride. The residue left on the distillation of the ether was then analysed. It contained 47.9 per cent. of chlorine.

The liquid resulting from the action of chlorine on the original compound therefore seems to be a mixture of two chlorides, a dichloride and a tetrachloride. The formula $C_6H_9NOCl_2$ requires 39.01 per cent. of chlorine; the formula $C_6H_9NOCl_4$, 56.1 per cent. These compounds are unstable, and are decomposed when heated, forming, among other substances, the pungent chloro-derivative already alluded to and ammonium chloride. The action of alkalis on these chlorides also leads to the separation of the nitrogen as ammonia.

The action of bromine on the original substance is similar to that of chlorine. The addition of bromine causes the evolution of heat, but no hydrogen bromide is produced. On distilling the liquid, to which about half its volume of bromine has been added, under reduced pressure (8 mm.), the liquid, which distils near 100° , solidifies to a mass of six-sided, tabular crystals. Simultaneously hydrogen bromide is slowly formed, and a pungent, tear-exciting oil passes into the distillate. It was not found possible to recrystallise the solid from any solvent; the crystals were, therefore, washed with ether and analysed. They contained 52 per cent. of bromine, and were, therefore, probably an impure dibromide of the original substance. The formula $C_6H_9NOBr_2$ requires 58.9 per cent. of bromine. On heating this bromide with water, it was converted into a highly irritating bromo-derivative ($C_6H_9BrNO?$), closely resembling the chloro-derivative which has already been described; resin and ammonium bromide were also formed.

The results obtained by acting on the compound with chlorine and bromine leave no doubt as to its ability to form additive compounds with the halogens, and prove it to be an unsaturated compound.

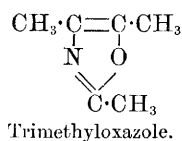
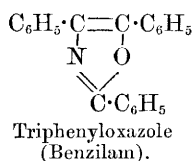
Owing to the very great difficulty of obtaining satisfactory evidence of the purity of these unstable halogen compounds, the formulæ we have suggested above require further confirmation. The complete investigation of the complicated reactions with chlorine, bromine, and phosphoric chloride, which in this case acts like the halogens, would need much larger quantities of material than we have had at our disposal.

CONSTITUTION OF THE COMPOUND.

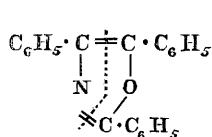
The reactions of the compound are opposed to the view that it is a pyridine or pyrrol derivative, and they do not correspond with those of a keto-cyanide, acetopropyl cyanide, or propionylethyl cyanide; these compounds dissolve in ammonia, and are readily and com-

pletely hydrolysed by fixed alkalis, the acetopropyl compound yielding ammonia together with acetic and butyric acids, and the propionylethyl compound, ammonia and propionic acid. The properties of the substance point to the conclusion that the nitrogen, as well as the oxygen, forms part of a closed ring of carbon atoms. When we first made this inference from our experimental results, no paraffinic representatives of this class of compounds, the oxazoles, $\begin{matrix} R' C - O \\ | \quad | \\ R' C N : C R' \end{matrix}$,

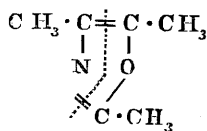
had been prepared, although benzene derivatives having this constitution had been obtained and investigated, among other workers, by Japp and his *collaborateurs*. The phenyl analogue of the nitro-ethane derivative, assuming it to be an oxazole, is the "benzilam" of Laurent, the true formula and constitution of which was established by Japp,



A remarkable resemblance may be traced in the characters of benzilam and those of our compound. On oxidation, benzilam yields benzoic acid, whilst the new compound yields acetic acid. Both substances are distinguished by their great stability, being almost unacted on by strong acids and alkalis. The reduction products of benzilam do not appear to have been investigated, but, like our compound, it seems to be very difficult to attack. From its constitution, it may be inferred that if it were reduced the nitrogen would appear as an amine, probably as benzylamine, whilst under similar conditions our compound might be expected to yield ethylamine. The line through the formulæ indicates the direction that the change would probably take.*



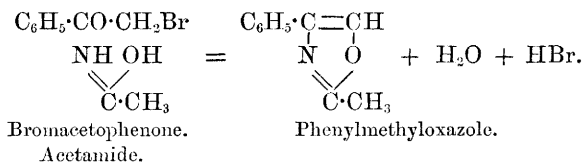
Reduction of triphenyloxazole.



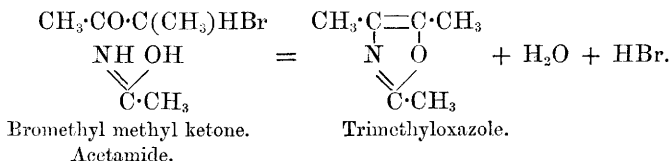
Reduction of trimethyloxazole.

* The results which Schatzmann (*Annalen*, 261, 7) has just published on the reduction of the thiazoles, confirm the correctness of this inference.

We have carefully searched for an amine among the reduction products of our compound, but have not been able to detect a trace of such a substance. The nitrogen is separated exclusively as ammonia. We must, therefore, conclude that although the compound is closely allied to, it is nevertheless distinct from the oxazoles. The recent work of Hantzsch and the Zurich School on these compounds has since made it possible for us to devise a method of preparing trimethyloxazole, and to show that it is not identical with our compound. Lewy (*Ber.*, **21**, 925) has shown that methylphenyloxazole may be obtained by heating bromacetophenone with acetamide:—



It follows from this that bromethyl methyl ketone should react with acetamide, forming trimethyloxazole:—



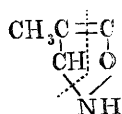
Brom-ethyl methyl ketone was prepared by oxidising secondary butyl alcohol with chromic acid. The resulting ketone was purified by means of its hydrogen sodium sulphite compound. The calculated amount of bromine was added in small portions to a weighed quantity of the ketone. Action rapidly occurred, the bromine being decolorised and hydrogen bromide evolved. The bromo-derivative was dissolved out with ether, and the solvent removed by distillation. The bromo-derivative, which cannot be distilled under ordinary pressure without decomposition, was heated with excess of acetamide in a closed tube at 120—130° for one hour. The contents of the tube were distilled with water, when a liquid was obtained having feebly basic properties, and in many other respects resembling the nitroethane derivative, but differing entirely from it in its odour and physical properties. Crystalline compounds with mercuric chloride and auric chloride were obtained. Since the base was not identical with our compound, its properties were not further examined.

The behaviour of the nitroethane derivative on reduction suggests that its molecular constitution differs from that of an oxazole in con-

taining oxygen in union with nitrogen. The formula

$$\begin{array}{c} \text{CH}_3 \cdot \text{C} = \text{C} \cdot \text{CH}_3 \\ | \quad | \\ \text{CH}_3 \cdot \text{C} \quad \text{O} \\ \diagdown \quad / \\ \text{N} \end{array}$$

correctly summarises all the reactions of the substance, its feebly basic properties, its ability to combine directly with hydrogen and with the halogens, its oxidation to acetic acid by permanganate, and to acetic and oxalic acids by nitric acid, and also the formation of ammonia and secondary butyl alcohol on reduction, as well as the remarkable hydrolysis of the dihydride into ammonium acetate and methyl ethyl ketone, when the "ring" is split in the direction indicated by the line which has been drawn through the formula:—



The production of secondary butyl alcohol on reduction is, of course, due to the hydrogenation of this ketone. The molecular refraction and magnetic rotation of the original substance do not help us to adopt this formula, chiefly because these properties have not been examined in other bodies of similar constitution: so that no data exist for comparison. They are, however, not inconsistent with this view of the structure of the compound, and they do distinctly confirm the existence of unsaturated carbon which this formula assumes.

SYNTHESIS OF THE COMPOUND FROM METHYLACETYLACETONE.

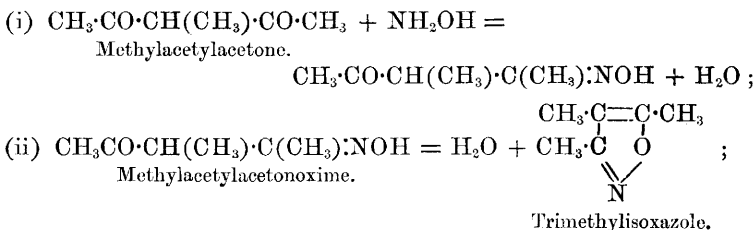
When we commenced this inquiry, no compound having this constitution had been obtained, either in the paraffin or benzene series, but, more recently, Claisen (*Ber.*, **21**, 18) has described a substance produced by the dehydration of the hydroxime of benzoylacetone, to

which he has assigned the formula $\begin{array}{c} \text{HC} = \text{C} \cdot \text{CH}_3 \\ | \quad | \\ \text{C}_6\text{H}_5 \cdot \text{C} \quad \text{O} \\ \diagdown \quad / \\ \text{N} \end{array}$, and classified

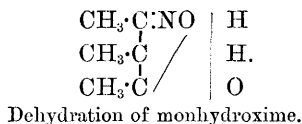
as a monazole.

But neither in this communication nor in later papers by Claisen's pupils (Zedel, *Ber.*, **21**, 2178), is any information given about the reactions of these compounds. Their oxidation and reduction products do not appear to have been studied, and the constitution assigned to them is supported almost entirely by evidence derived from synthetical experiments. We were, therefore, unable to ascertain how far the

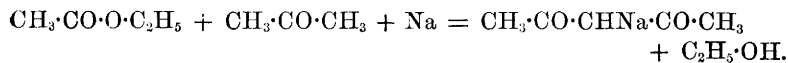
reactions of our compound corresponded with those of the substance obtained by Claisen. Accepting as correct Claisen's inferences as to the mode of production of the monazoles from the symmetrical β -diketones, we attempted to prepare the derivative of nitroethane by a reaction analogous to that by means of which he obtained phenylmethylmonazole* or phenylmethyloxazole, namely, by the action of hydroxylamine on methylacetylacetone (diacetylene), which should, *ex hypothesi*, lead to the formation of our compound, if it were trimethylisoxazole. The reaction may be represented as occurring in two stages: the first, in which the monhydroxime of the diketone is produced, and the second, in which this hydroxime undergoes dehydration.



or more graphically



Acetylacetone was prepared by Claisen's method (*Ber.*, **22**, 1014), a mixture of ethyl acetate and acetone being decomposed with sodium,



The sodium acetylacetone thus obtained was converted into the insoluble, purple copper salt, which was collected, washed, and the diketone liberated from it by the addition of diluted sulphuric acid. The compound was extracted with ether, and then distilled from the solution after it had been dried with calcium chloride. The acetylacetone boils, apparently with slight decomposition, at 136° .

* The nomenclature which has since been suggested by Hantzsch (*Annalen*, **249**, 1) for compounds containing this nucleus seems to us more expressive and convenient. We shall, therefore, adopt it in this paper. Compounds containing the group



are termed oxazoles, and those containing the nucleus



In order to convert this substance into its methyl derivative, the sodium compound was heated with methyl iodide in closed tubes at 140°. The resulting methylacetylacetone was purified by fractional distillation. It is a colourless liquid, having a slightly aromatic odour, boiling at 169°. To its alcoholic solution was added an alcoholic solution of hydroxylamine hydrochloride. Reaction immediately occurred with rise of temperature. The mixture was heated for a short time at 100°, then largely diluted with water, and distilled. There passed over with the steam a liquid which was at once recognised as the derivative we had obtained from nitroethane by the action of alkalis. After purification by conversion into its compound with mercuric chloride, it boiled at 171° (corr.), and was identical in all its properties with the nitroethane derivative. On analysis, it yielded data corresponding with those deduced from the formula C_6H_9NO .

- I. Substance taken, 0.0444 gram; H_2O obtained, 0.0348 gram;
 CO_2 obtained, 0.1054 gram.
 II. Substance taken, 0.2986 gram; N obtained, 31.6 c.c. at 10° and
 762.3 mm.

	Found.	Calculated for C_6H_9NO .
C	64.7 per cent.	64.8 per cent.
H	8.7 ,,	8.1 ,,
N	12.69 ,,	12.7 ,,

This synthesis confirms the view of the constitution of the substance which we had inferred from its reactions, and satisfactorily establishes its identity with trimethylisoxazole. By the action of hydroxylamine on methylacetylacetone, besides trimethylisoxazole, *acetone nitrile* was formed. It was separated from the oxazole by fractional distillation and hydrolysed by alcoholic potash in the usual manner. Ammonia was produced, together with a volatile acid, which was proved by the analysis of its silver salt to be acetic acid, the percentage of silver found being 64.28.

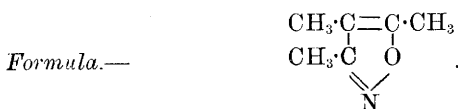
The formation of the nitrile in this reaction may be accounted for by supposing that an acetyl group is eliminated as aldehyde, which would be converted into acetalhydroxime by the hydroxylamine. The hydroxime on dehydration would yield acetonitrile, $CH_3 \cdot CH \cdot NOH = H_2O + CH_3 \cdot CN$.

For the purposes of the foregoing discussion we have accepted as correct the constitution usually assigned to the β -diketones, which satisfactorily accounts for the usual reactions of these compounds. In the course of our work, however, we have obtained evidence which suggests the possibility that they are ring-compounds,

the ring containing oxygen as well as carbon, or at all events that these compounds on some occasions act as if they were thus constituted. Further experiments are being made on this important question.

Since trimethylisoxazole is now prepared for the first time, and as the reactions of the known isoxazoles have not been fully examined, it is desirable to recapitulate here the principal properties and reactions which we have already described as belonging to the derivatives of nitroethane, which is now proved to be trimethylisoxazole.

Principal Properties and Reactions of Trimethylisoxazole.



Modes of Formation.—By the action of alkalis on nitroethane, and of hydroxylamine on methylacetylacetone.

Boiling point	171° (corr.)	Magnetic rotation	6·792
Freezing point	3·5° (corr.)	Molecular refraction	50·8
Relative density	0·986 at 15°/15°	Molecular dispersion	2·92
Rotatory power	None		

Mercurochloride	C ₆ H ₉ NO, HgCl ₂
Gold chloride compound	C ₆ H ₅ NO, AuCl ₃
Chlorides	C ₆ H ₉ NOCl ₂ ; C ₆ H ₉ NOCl ₁ (?).
Bromides	C ₆ H ₉ NOBr ₂ .
Chloro- and bromo-derivatives	C ₆ H ₈ ClNO; C ₆ H ₈ BrNO (?).
Oxidation products	Acetic (and oxalic) acid.
Reduction products	Ammonia, acetic acid, secondary butyl alcohol.
Products of reduction by heated zinc	Acetonitrile, &c.
Product of hydrogenation by sodium and water	Dihydride of trimethylisoxazole,
	$\begin{array}{c} \text{CH}_3 \cdot \text{C} = \text{C} \cdot \text{CH}_3 \\ \quad \\ \text{CH}_3 \cdot \text{CH} \quad \text{O} \\ \quad \quad \quad \diagdown \\ \quad \quad \quad \text{NH} \end{array}$
Hydrolytic products of the dihydride	Ammonium acetate, methylethylketone.

MECHANISM OF THE REACTION BETWEEN ALKALIS AND NITROETHANE.

We have ascertained that when alkalis react with nitroethane, the products of the change are formed approximately in accordance with the proportions indicated by the equation



The occurrence of such a reaction as this between an alkali and a nitro-compound is most remarkable, and cannot be satisfactorily explained, if the usual formula for nitroethane be rigidly adhered to. By modifying the formula, in accordance with the doctrine of tautomerism, and supposing the compound to contain one or two hydroxyl groups, more than one mode of interaction becomes possible. We do not, however, now propose to discuss this question, on which much might be written by way of suggestion, until we have ascertained whether any intermediate compounds can be isolated which would throw light on the mechanism of the change. Experiments we have already made would lead us to conclude that alcohol is not one of these transition compounds, and that the acetonitrile is not produced at the expense of the isoxazole by the action either of alkali or of hydroxylamine. On the other hand, it seems possible that a derivative of a β -diketone is concerned in the transformation, this substance originating from the nitro-compound. It is a fact of much significance that, whilst alkalis act on nitroethane, forming trimethylisoxazole and acetonitrile, these same compounds result from the action of hydroxylamine on methylacetylacetone.

II. THE ACTION OF ALKALIS ON NITROMETHANE.

The action of alkalis on nitromethane is much more rapid and intense than on nitroethane, and it proceeds further. The character of the change appears to be similar. When nitromethane is mixed with aqueous ammonia or potassium carbonate, reaction is immediate, the mixture darkens, and finally becomes almost black. Nitrite is formed, together with *hydrogen cyanide* and a large quantity of a resinous substance. From our study of the action of alkalis on nitroethane, we

should infer that nitromethane would yield isoxazole, $\begin{array}{c} \text{HC}=\text{CH} \\ | \quad | \\ \text{HC} \quad \text{O} \\ \diagdown \quad / \\ \text{N} \end{array}$,

the parent base of which the compound resulting from the action of alkalis on nitroethane is the trimethyl derivative. So far, however, we have not been able to isolate this interesting compound, which seems to be instantly decomposed, but our investigation of the reaction is not yet completed.

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The results of the recent work of Claisen and Stock (*Ber.*, **24**, 130) on the action of hydroxylamine on benzoylacetalddehyde, renders it probable that this isoxazole, in presence of alkali, would pass into the alkali salt of the isomeric cyanacetic aldehyde, $\begin{matrix} \text{H}\cdot\text{CO} \\ | \\ \text{CH}(\text{M})\text{CN} \end{matrix}$.

III. ACTION OF ALKALIS ON PRIMARY NITROPROPANE.

The action of alkalis on nitropropane is much weaker than on its two lower homologues. Aqueous ammonia hardly attacks this nitro-compound, even at a temperature of 100–120°, in a closed tube. Potassium carbonate solution acts slowly, and in order to completely decompose the nitropropane it is necessary to heat the mixture for some hours at 100°. On distillation, an oily liquid condenses with the steam, whilst *potassium nitrite* and *resin* remain in the residue. The oily liquid, after having been separated and dried in the usual manner, was resolved, by fractional distillation, into two substances; one of these, which was difficult to purify, finally distilled between 98° and 100°, and had all the characteristic properties of *propionitrile*. Since only a small quantity was available, its identity was established by hydrolysing it with aqueous potash, when ammonia was abundantly evolved. The resulting potassium propionate was converted into the silver salt, which was analysed in the ordinary way. It contained 59·12 per cent. of silver; silver propionate contains 59·6 per cent.

The liquid which remained after the propionitrile had distilled consisted of a body which, after fractionation, boiled at 214° (corr.). Its relative density was 0·9382 at 15°/15°.

On combustion it afforded the following data:—

	I.	II.	III.	IV.
Substance taken	0·1738 grm.	0·1656 grm.	0·2282 grm.	0·1614 grm.
CO ₂ obtained ..	0·4442 „	0·4212 „	0·5836 „	—
H ₂ O „ ..	0·1577 „	0·1438 „	0·2022 „	—
N ₂ „ at 12·5°, 764 mm.	—	—	—	12 c.c.

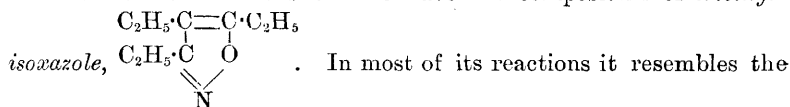
	Found.				Calculated for C ₉ H ₁₆ NO.
	I.	II.	III.	IV.	
C	70·2 per cent.	69·3 per cent.	69·7 per cent.	—	70·5 per cent.
H	10·08 „	9·64 „	9·84 „	—	9·8 „
N ₂	— „	— „	— „	9·1	9·14 „

The molecular weight of the liquid was ascertained by Raoult's method, using acetic acid as the solvent.

	I.	II.
Wt. of substance.....	0·0778 gram.	0·1556 gram.
Wt. of solvent.....	6·5378 „	6·5378 „
Freezing point of solvent....	15°	15·02°
Freezing point of solution....	14·7°	14·42
Depression for 1 gram of substance to 100 of solvent....	0·258°	0·258°
Mol. depression of solvent....	39	39
Mol. weight of substance.....	151	151

The molecular weight corresponding with the formula $C_9H_{15}NO$ is 153.

The substance is thus shown to have the composition of *triethyl-*



trimethylisoxazole obtained under similar conditions from nitroethane.

We have, however, not succeeded in solidifying it, and it does not appear to form a compound with either mercuric chloride or gold chloride. In these particulars it differs from trimethylisoxazole. When oxidised with nitric acid, a volatile acid was obtained, which, by the analysis of its silver salt, was proved to be *propionic acid*. The percentage of silver in the silver salt was 59·8, the percentage of silver in silver propionate being 59·6.

The compound is somewhat more difficult to oxidise than the trimethylisoxazole, and since it was thought that it might be the dihydride of triethylisoxazole, the hydrogen being united to the two doubly-linked carbon atoms, attempts were made, by the action of silver oxide, and by the limited action of nitric acid, to oxidise these two hydrogen atoms and so to obtain triethylisoxazole. No such effect could, however, be observed. Under no circumstances was a compound produced which combined with mercuric chloride, although an intermediate oxidation product was obtained, which is being further examined.

We are indebted to Mr. A. J. Simons, one of the workers in this laboratory, for the assistance he has given us in examining the properties of this compound.

The reaction between alkalis and primary nitropropane seems to be represented by the equation



IV. ACTION OF ALKALIS ON SECONDARY NITROPROPANE.

The results recorded in the foregoing pages relate to the action of alkalis on primary nitro-compounds. It became of interest to determine whether a similar reaction occurs with secondary and tertiary nitro-compounds. Our observations on the behaviour of these bodies are not yet completed, but we have already noticed that secondary nitropropane undergoes a change which is, in all probability, similar in kind to that sustained by primary nitropropane, although the products of the reaction are different. Alkali *nitrite* is produced, but no triethylisoxazole. Another substance, responding to the reactions of a pseudo-nitrol, has been isolated, and is being examined.

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