is neither saturated at room temperature nor perfectly dry, the change in the degree of moistness of the air on becoming saturated is what the air originally lacked of being saturated. The appropriate correction to introduce is that fraction of the pressure of aqueous vapor for the room temperature which it lacked of saturation. Suppose the apparatus was originally filled with the air of the room, and that it was 40% saturated at room temperature, sixty one-hundredths of the pressure of aqueous vapor is the number to be subtracted from the observed barometer reading; the corrected reading is $B - \frac{100 - H}{100} w$, in which B is the barometer reading, H is the hygrometer reading in %, and w is the pressure of aqueous vapor for the room temperature.

Nearly all works accessible to the author give such directions for the manipulation as involve the use of the air of the room in the inner tube, yet give for the calculation the correction B–w. The error introduced in this way would be greatest if the air were saturated with moisture, and would then amount at a room temperature of 20° to 17 in approximately 760, or 1 in about 45, and this condition is closely approached in damp, warm weather. Omitting the correction altogether when the air used is nearly dry gives an equal error in the opposit direction, approximated in very cold weather.

A quite appreciable error, then, may be avoided and the calculation made more nearly correct, theoretically, by using the correction given above.

Of the works accessible to the author only H. Erdmann's Anorganische Chemie discusses the correction, directing that if the apparatus is filled with a dried gas the pressure of aqueous vapor should be deducted; if with ordinary air, no correction should be made. All other works fail to consider the point, some deducting the pressure, others not, without specifying the conditions.

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ON THE REACTIONS OF THE FORMAMIDINES. III. ON THE SYNTHESIS OF ISOXAZOLONE, ISOXAZOLE, CYANOACETIC AND BENZOYLACETIC ACID DERIVATIVES.

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In previous papers,[1] it has been shown that compounds containing a methylene group, CH_2, such as acetoacetic ester, benzoylacetic ester, cyanoacetic ester, methylphenylpyrazolone, etc., were capable of reacting with the aryl formamidines yielding derivatives of the type XYC : CHNHR, in which the two methylene hydrogens were replaced

[1] *Ber.*, **35**, 2496; THIS JOURNAL, **31**, 1148.

by the grouping : CHNHR. It seemed now probable that the isoxazolones of the general formula $RC(=N.O.CO)CH_2$, which contain methylene hydrogen, which are acidic in their nature and which, though more unstable, resemble in many particulars the pyrazolones, should react in the same way. Investigation has shown this to be true and the experimental work has proved that 3-phenyl-5-isoxazolone directly, and 3-methyl-5-isoxazolone indirectly, form derivatives in which the methylene hydrogen is replaced by the grouping : CHNHR.

Phenylisoxazolone[1] was prepared by heating, for a few minutes, benzoylacetic ethyl ester with hydroxylamine hydrochloride in alcohol solution. The best yield obtained was 90% of the theoretical. Prolonged heating on the water bath must be avoided, as this lessens to a marked degree the amount of isoxazolone obtained.

When molar quantities of phenylisoxazolone and diphenylformamidine were heated for an hour in an oil bath at 120°, the mixture melted and on cooling solidified. From this reaction product were isolated aniline and a new compound, *3-phenyl-4-anilidomethylene-5-isoxazolone*. The reaction is as follows:

$$PhC(=N.O.CO)CH_2 + PhN : CHNHPh = PhNH_2 + PhC(=N.O.CO)C : CHNHPh.$$

Analysis:

Calculated for $C_{16}H_{12}O_2N_2$: N, 10.61; found: N, 10.29, 10.29.

The compound is slightly soluble in hot water, soluble in most organic solvents and separates from ethyl acetate in yellow rhombic crystals, and melts at 145°. It dissolves in dilute sodium hydroxide and is precipitated unchanged by dilute acids. On standing or warming with alkalies it suffers decomposition, yielding a salt which is under investigation. This behavior with alkalies is characteristic for this class of derivatives.

Other formamidines react with like ease with phenylisoxazolone, giving corresponding compounds. Thus molar quantities of di-*o*-tolylformamidine and phenylisoxazolone at 120° give *o*-toluidine and *3-phenyl-4-o-toluidomethylene-5-isoxazolone*. It was purified by crystallization from alcohol and ethyl acetate and then formed yellow crystals melting at 170°. Analysis:

Calculated for $C_{17}H_{14}O_2N_2$: N, 10.07; found: N, 10.02.

3-Phenyl-4-m-toluidomethylene-5-isoxazolone from di-*m*-tolylformamidine and phenylisoxazolone, yellow crystals which melt at 158°. Analysis:

Calculated for $C_{17}H_{14}O_2N_2$: N, 10.07; found: N, 10.13, 10.22.

[1] *Ber.*, **24**, 140.

3-Phenyl-4-p-toluidomethylene-5-isoxazolone was obtained in the form of slightly reddish crystals difficultly soluble in alcohol and glacial acetic acid. It melts at 190°. Analysis:

Calculated for $C_{17}H_{14}O_2N_2$: N, 10.07; found: N, 10.32.

3-Phenyl-4-o-anisidomethylene-5-isoxazolone, yellow needles from alcohol, melting at 138°. Analysis:

Calculated for $C_{17}H_{14}O_3N_2$: N, 9.53; found: N, 9.51, 9.59.

3-Phenyl-4-p-anisidomethylene-5-isoxazolone is difficultly soluble in benzene and melts at 168°. Analysis:

Calculated for $C_{17}H_{14}O_3N_2$: N, 9.53; found: N, 9.52, 9.54.

3-Phenyl-4-p-phenetidomethylene-5-isoxazolone has a melting point, when crystallized from alcohol, of 174°. Analysis:

Calculated for $C_{18}H_{16}O_3N_2$: N, 9.09; found: 8.91.

3-Phenyl-4-pseudocumidomethylene-5-isoxazolone crystallizes from glacial acetic acid, in which it is difficultly soluble, in yellow needles which melt at 180°. Analysis:

Calculated for $C_{19}H_{18}O_2N_2$: N, 9.15; found: N, 9.33, 9.16.

The corresponding derivative from di-*m*-nitrodiphenylformamidine, *3-phenyl-4-m-nitroanilidomethylene-5-isoxazolone*, forms yellow needles, slightly soluble in boiling alcohol and melts at 206°. Analysis:

Calculated for $C_{16}H_{11}O_4N_3$: N, 13.60; found: N, 13.90, 13.85.

Di-*p*-bromdiphenylformamidine and phenyl isoxazolone react readily on heating giving the light yellow *3-phenyl-4-p-bromanilidomethylene-5-isoxazolone*, which melts at 198°. Analysis:

Calculated for $C_{16}H_{11}O_2N_2Br$: N, 8.16; found: N, 8.36, 8.44.

This same product was obtained in another way. Anilidomethylene-phenylisoxazolone was dissolved in glacial acetic acid and bromine (one mol) added. On standing the oily product that was first formed became granular. It was then filtered off, washed thoroughly with glacial acetic acid and dried in a desiccator on a porous plate. The acetic acid filtrate contained large amounts of hydrobromic acid. The red solid melted at 148° and gave results which indicated the formation of a monobrom compound. Analysis:

Calculated for $C_{16}H_{11}O_2N_2Br$: N, 8.16; found: N, 8.03, 8.17.

When this monobrom derivative is dissolved in alcohol or pyridine, it suffers rearrangement and there is obtained *p*-bromoanilidomethylene-phenylisoxazolone, identical with that produced by the action of di-*p*-bromodiphenylformamidine on the phenylisoxazolone. The reactions involved will be discussed later under the corresponding methylisoxazolone derivatives.

Derivatives of 3-Methyl Isoxazolone.—Various methods were tried for the

preparation of methyl isoxazolone[1] but all were far from satisfactory. That of Uhlenhuth[2], however, gave the best results.

Here, for instance, 14 grams of the oxime of acetoacetic ester with 35 cc. of concentrated ammonium hydroxide gave 1.2 grams methyl isoxazolone. In the preparation it was found advisable to distil off the ammonium hydroxide under reduced pressure. No isoxazolone derivatives were obtained by the direct heating of methyl isoxazolone with the formamidines. Either no combination occurred or else the products suffered decomposition at the temperature necessary to effect reaction.

Efforts were now made to find some derivative of methyl isoxazolone, which would react with the formamidines by replacement of the substituting group. For this purpose 4-benzalmethylisoxazolone was tried, since here we have the loosely bound PhCH : group replacing the methylene hydrogen. Experiment soon showed that this compound gave the desired results. Benzalmethylisoxazolone has been investigated by Schiff and others and can be obtained easily and smoothly in quantity, by the following modification of Schiff's method. A mixture was made of 15 grams of hydroxylamine hydrochloride, 40 cc. of water and 20 cc. of pyridine. To this was added 25 cc. of acetoacetic ester dissolved in 50 cc. of alcohol. After standing a few minutes, there was a further addition of 22 cc. of benzaldehyde followed by 150 cc. 17% hydrochloric acid. The precipitation of the benzalmethylisoxazolone soon begins and is complete after several days. The product is now filtered with the aid of a suction pump and washed thoroughly with water. It can be purified by crystallization from alcohol but it was found that simply washing the crude material with alcohol gave a product pure enough for all purposes. The best yield was 88%. All heating of the reaction mixture must be avoided, since this diminished in a marked degree both the purity and the quantity of the isoxazolone.[3] An equimolecular mixture of diphenylformamidine and benzalmethylisoxazolone was heated in an oil bath to its melting point, about 140°, then the temperature was lowered to 115–120° and kept there for from 20 minutes to one hour. (In the preparation of these compounds as well as the corresponding phenyl derivatives, overheating must be avoided since in that case the isoxazolone ring is destroyed with the formation of tarry products.) On cooling, the contents of the flask solidify to a dark red mass, from which was isolated benzalaniline and a new compound 3-methyl-4-anilidomethylene-5-isoxazolone:

[1] *Ber.*, **24**, 497.

[2] *Ann.*, **296**, 46.

[3] Methyl benzal isoxazolone reacts with great ease with phenylhydrazine giving benzylidene phenylhydrazone and at least two other products. The study of the action of amines on benzal isoxazolone and pyrazolone is being continued in this laboratory.

MeC——C:CHPh + PhN : CHNHPh = PhCH : NPh + MeC——C:CHNHPh.
‖ | ‖ |
N.O.CO   N.O.CO

In many cases the separation is best effected by means of benzene, in which the isoxazolone derivatives are usually difficultly soluble.

The anilidomethylenemethylisoxazolone was purified by crystallization from benzene or glacial acetic acid. It then forms slightly yellow crystals melting at 158°. Analysis:

Calculated for $C_{11}H_{10}O_2N_2$: N, 13.86; found: N, 13.52.

The compound is soluble in dilute alkalies and if not heated or allowed to stand for any length of time is reprecipitated by acids unchanged. When, however, 20 grams of the anilidomethylenemethylisoxazolone was treated with a warm solution of 25 grams of potassium hydroxide in 75 cc. of water, everything went into solution. In a few minutes an oil, aniline, began to separate and the contents of the flask became semi-solid from the crystallization of a white potassium salt. This recrystallizes in fine needles from hot alcohol. This salt blackens and decomposes at 265–70°. The compound was found on analysis to contain; potassium, 23.91, 23.84. Nitrogen, 8.47, 8.17. These results agree well with the figures demanded for the potassium salt of 4-carboxylmethylisoxazole (K, 23.68, N, 8.48) but whether this is the salt or not, later investigation must decide. When bromine (1 mol) is added to a solution of anilidomethylenemethylisoxazolone in glacial acetic acid, a heavy yellow precipitate is formed. This very easily loses hydrobromic acid on drying. When it is dissolved in alcohol, it suffers change and there is formed *p-bromoanilidomethylenemethylisoxazolone*, with a melting point of 204°, which is identical with the compound formed from benzalmethylisoxazolone and di-*p*-bromodiphenylformamidine. It crystallizes from alcohol in difficultly soluble yellow needles. Analysis:

Calculated for $C_{11}H_9O_2N_2Br$: N, 9.97; found: N, 10.02, 10.15.

Boiling with water or solution in pyridine brings about the same change. A similar rearrangement has been noticed in a previous case. Thus when anilidomethylenecyanoacetic ester[1] was treated with bromine and the addition product recrystallized from alcohol, a monobrom derivative with a melting point of 148° was obtained. Recent experiments have shown that this product was ethyl *p*-bromoanilidomethylenecyanoacetate, *p*-$BrC_6H_4NHCH : C(CN)COOC_2H_5$, which was readily formed when di-*p*-bromodiphenylformamidine was heated with cyanoacetic ester. It separates from alcohol in white crystals with the above melting point.

It would seem that these results could be explained as follows: Bromine adds to the tautomeric form of the anilidomethylene derivative. This then very easily loses hydrobromic acid, while the resulting imidebromide

[1] *Ber.*, **35**, 2510.

under the influence of the solvent rearranges to the *p*-bromophenyl compound.[1]

$$R_2CHCH : NPh + Br_2 = R_2CHCHBrNBrPh =$$
$$R_2C : CHNBrPh + HBr = R_2C : CHNHC_6H_4Br.$$

Experiments have shown that diphenylformamidine, which also contains the grouping >C : NPh, adds bromine, yielding a yellow addition product which melts at 262°. This with dilute potassium hydroxide breaks down, giving *p*-bromoaniline, *p*-bromoformanilide and aniline.[2]

The following preparations show that the reaction between benzalmethylisoxazolone and the formamidines is one of general applicability.

3-Methyl-4-o-toluidomethylene-5-isoxazolone consists of slightly red crystals, which melt at 206°. Analysis:

Calculated for $C_{12}H_{12}O_2N_2$: N, 12.96; found: N, 12.85.

3-Methyl-4-m-toluidomethylene-5-isoxazolone crystallizes in brownish white needles from alcohol and melts at 168°. Analysis:

Calculated for $C_{12}H_{12}O_2N_2$: N, 12.96; found: N, 13.07.

3-Methyl-4-p-toluidomethylene-5-isoxazolone is difficultly soluble in alcohol, from which it separated in yellow needles melting at 204°. Analysis:

Calculated for $C_{12}H_{12}O_2N_2$: N, 12.96; found: N, 13.33.

When the isoxazolone is evaporated to dryness on the water bath with an alcoholic solution of hydrochloric acid, it suffers decomposition, the solid residue consisting of ammonium chloride and *p*-toluidine hydrochloride. Like the other isoxazolones investigated it readily adds bromine in acetic acid solution and a heavy yellow addition product melting at 161–3° is formed. From this bromide on treatment with alcohol or potassium hydroxide the original substance can be regained.

Boiling for a short time with acetic anhydride did not affect the isoxazolone. There was also no reaction with phenyl hydrazine in alcoholic solution, although the two substances, when heated without a solvent, react violently yielding a tarry mass.

Benzalmethylisoxazolone and di-*p*-anisylformamidine combine at 130° with the formation of benzal-*p*-anisidine and *3-methyl-4-p-anisidomethylene-5-isoxazolone*, yellow needles which melt at 190°. Analysis:

Calculated for $C_{12}H_{12}O_3N_2$: N, 12.07; found: N, 12.31.

In like manner, benzalmethylisoxazolone and di-*p*-phenetidylformamidine gave benzal-*p*-phenetidine and *3-methyl-4-p-phenetidomethylene-methylisoxazolone*, which crystallizes from alcohol in yellow needles melting at 169°. Analysis:

Calculated for $C_{13}H_{14}O_3N_2$: N, 11.38; found: N, 11.17, 11.61.

[1] Hantzsch, *Ber.*, **23**, 2774.

[2] The question of the addition of bromine to compounds containing the grouping >C : CHNHR, >CHCHN : R and RCH : NR is being investigated in this laboratory.

3-Methyl-4-m-xylidomethylene-5-isoxazolone consists of white crystals which melt at 166°. Analysis:

Calculated for $C_{13}H_{14}O_2N_2$: N, 12.18; found: N, 12.46.

3-Methyl-4-o-anisidomethylene-5-isoxazolone, yellow crystals melting at 169°. Analysis:

Calculated for $C_{12}H_{12}O_3N_2$: N, 12.07; found: N, 11.82.

p-Methoxybenzalmethylisoxazolone.—As the first step in the extension of the investigation, so as to show whether the derivatives of methylisoxazolone with aldehydes other than benzoic would react with the formamidines, anisalmethylisoxazolone was prepared. The same procedure was followed as in the preparation of the benzal derivative, only using anisic aldehyde, in place of the benzaldehyde. The yield is practically quantitative. 4-Anisal-3-methyl-5-isoxazolone forms bright intensely yellow crystals, which melt at 178°. It is soluble in chloroform, difficultly soluble in boiling alcohol and benzene and in glacial acetic acid with seeming slight decomposition. It dissolves in potassium hydroxide and can be reprecipitated with acids, but decomposition soon sets in on standing or warming with the alkali. Analysis:

Calculated for $C_{12}H_{11}O_3N$: N, 6.45; found: N, 6.58.

With the formamidines, it reacts like the benzal compound. Thus when molecular mixtures of anisalmethylisoxazolone and di-*p*-anisylformamidine were heated at 140°, two products are found in the reaction mixture, the difficultly soluble *p*-anisidomethylenemethylisoxazolone and anisal-*p*-anisidine.[1] Anisalmethylisoxazolone and diphenylformamidine gave in like manner anisalaniline and anilidomethylenemethylisoxazolone. Molar quantities of the isoxazolone and dipseudocumylformamidine were heated at 170° until both components were melted, then at 120–40° for a few minutes to complete the reaction, which gave 4-pseudocumidomethylene-3-methyl-5-isoxazolone.. This is a yellow crystallin substance, difficultly soluble in alcohol and melting at 192°. Analysis:

Calculated for $C_{14}H_{17}O_2N_2$: N, 11.43; found: N, 11.44.

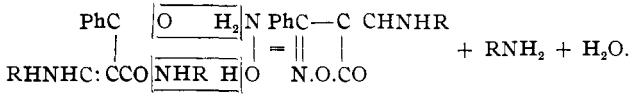
In addition there was isolated anisalpseudocumidine, $MeOC_6H_4CH : NC_6H_2Me_3$, white crystals, easily soluble in the ordinary solvents with a melting point of 71°. This was identical with the same substance prepared by warming a mixture of pseudocumidine and anisic aldehyde and crystallizing the product from alcohol. Analysis:

Calculated for $C_{17}H_{19}ON$: N, 5.53; found: N, 5.74.

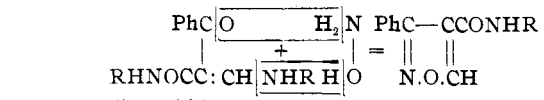
Isoxazole Syntheses.—The action of hydroxylamine on the substituted aminomethylene derivatives of benzoylacetic and acetoacetic esters was tried in the expectation of obtaining thereby isoxazole or isoxazolone compounds, there being a possibility of the formation of both classes of derivatives. For instance the phenylamide of anilidomethylenebenzoyl-

[1] *Ber.*, **34**, 832.

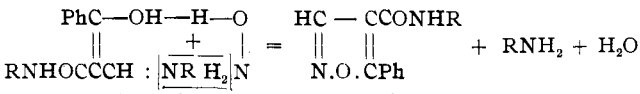
acetic acid is capable of reacting in three ways with hydroxylamine, as indicated in the following equations:

I. 

3-Phenyl-4-anilidomethylene-isoxazolone.

II. 

The anilid of 4-carboxyl-3-phenyl-isoxazole.

III. 

The anilid of 4-carboxyl-5-phenyl-isoxazole.

Anilidomethylenebenzoylacetanilide was suspended in alcohol, somewhat more than one molecule of hydroxylamine hydrochloride and a corresponding amount of pyridine added, and the whole warmed on a steam bath with a reflux condenser for several hours, until everything dissolved and remained so on cooling. This alcoholic solution contains both aniline and a white solid, which was precipitated by dilution with water. This was purified by recrystallization from dilute alcohol, from which it separated in fine, white needles, melting at 135°. Analysis:

Calculated for $C_{16}H_{12}O_2N_2$: N, 10.62; found: N, 10.91.

This result agrees with that demanded by any one of the three possible compounds before mentioned. The reaction cannot, however, proceed according to equation I, since in that case anilidomethylenephenylisoxazolone (m. p. 145°) should have been obtained, which was not the case. As a matter of fact, in no instance thus far investigated has the grouping —CONHR in this class of derivatives been attacked by either hydroxylamine or phenylhydrazine. The compound must be then the anilide of 4-carboxyl-3 or 5-phenylisoxazolone and its action with sodium hydroxide shows that it is the 5-phenyl derivative, $HC{=}CCONHC_6H_5$ (N.O.CC_6H_5).

The isoxazole melting at 135° is easily soluble in alkali. Acids, however, precipitate not the original compound but a substance melting at 203°, which proved to be benzoylcyanoacetanilide, PhCOCH(CN)CONHPh. This was proven by synthesizing the latter from benzoyl chloride and cyanoacetanilide dissolved in pyridine, and comparing the products. The two were identical. The formation of this cyan derivative is possible only in the case of the 5-phenylisoxazole, not with the 3-phenylisoxazole. This is in agreement with the work of Claisen,[1] who has shown that the

[1] *Ber.*, 36, 3672.

isoxazoles whose 3-position is unsubstituted easily go over into cyanoketones under the influence of alkali.

The isoxazole synthesis follows along exactly the same lines as does the action of phenylhydrazine on anilidomethyleneacetoacetanilide, whereby was obtained the phenyl amide of 1-phenyl-5-methylpyrazole-4-carboxylic acid.[1]

When *o*-toluidomethylenebenzoylacet-*o*-toluide was boiled in alcoholic solution with $1^1/_2$ molecules of hydroxylamine and the requisit amount of pyridine, there was obtained the *o-tolylamide of 5-phenylisoxazole-4-carboxylic acid*, which crystallized in white needles from alcohol and melts at 114°. Analysis:

Calculated for $C_{17}H_{14}O_2N_2$: N, 10.07; found: N, 10.24, 10.37.

When this isoxazole is dissolved in sodium hydroxide and reprecipitated with acid, the compound rearranges to *benzoylcyanoacet-o-toluide*, $PhCOCH(CN)CONHC_7H_7(o)$, white needles, less readily soluble than the isoxazole and melting at 132°. Analysis:

Calculated for $C_{17}H_{14}O_2N_2$: N, 10.07; found: N, 10.20.

Under like conditions, *p*-toluidomethylenebenzoylacet-*p*-toluide gave the *p-tolylamide of 5-phenylisoxazole-4-carboxylic acid.* This separated from alcohol, in which it is difficultly soluble, in white needles, which have a melting point of 158°. Analysis:

Calculated for $C_{17}H_{14}O_2N_2$: N, 10.07; found: N, 10.21, 9.86.

Solution of this in alkali and then neutralization with acid yielded benzoylcyanoacet-*p*-toluide, white needles which melt at 180°. The same cyan derivative, $PhCOCH(CN)CONHC_7H_7(p)$, was also prepared by treating a benzene solution of cyanoacet-*p*-toluide with sodium (one mol) and then allowing benzoyl chloride to act on the sodium salt. Analysis:

Calculated for $C_{17}H_{14}O_2N_2$: N, 10.07; found: N, 10.24.

In the early experiments, sodium carbonate instead of pyridine was used to neutralize the hydroxylamine hydrochloride. In these cases no isoxazoles but only the cyan derivatives were obtained, due doubtless to the presence of small amounts of free alkali. In the preparation of the *p*-tolylamide of *p*-toluidomethylenebenzoylacetic acid, which had been made previously by Ruggeberg,[2] there was obtained a product which crystallized from gasoline in yellow flakes melting at 98° and which was evidently the *ethyl p-toluidomethylenebenxoylacetate*, $PhCOC(COOC_2H_5):CHNHC_7H_7(p)$. Analysis:

Calculated for $C_{19}H_{19}O_3N$: N, 4.53; found: N, 4.91, 4.95.

[1] THIS JOURNAL, 31, 1155.

[2] Diss., Freiburg, 1904.

p-Anisidomethylenebenzoylacet-p-anisidide, $PhCOC : CHNHC_6H_4OCH_3$ / $CONHC_6H_4OCH_3$ can be easily made by heating benzoylacetic ester with di-*p*-anisylformamidine at 140° for one hour. It is difficultly soluble in alcohol and benzene, from which it separates in yellow crystals melting at 196°. Analysis:

Calculated for $C_{24}H_{22}O_4N_2$: N, 6.97; found: N, 7.01, 7.11.

From this was obtained, in the usual manner with hydroxylamine, the *p-anisylamide of 5-phenylisoxazole-4-carboxylic acid.* This crystallized from alcohol in white needles with a melting point of 142°. Analysis:

Calculated for $C_{17}H_{14}O_3N_2$: N, 9.53; found: N, 9.87.

Like the preceding isoxazoles, this compound is readily rearranged by alkalies, hydrochloric acid precipitating from the solution in potassium hydroxide *benzoylcyanacet-p-anisidide.* This latter dissolves with difficulty in alcohol or glacial acetic acid and crystallizes from those solvents in white needles, which melt at 194°. Analysis:

Calculated for $C_{17}H_{14}O_3N_2$: N, 9.53; found: N, 9.47.

Derivatives of 5-Methylisoxazole-4-carboxylic Acid.—These can be obtained as were the preceding isoxazoles by heating the substituted amides of arylaminomethyleneacetoacetic acid with hydroxylamine hydrochloride and pyridine in alcohol solution; and with the same ease the isoxazole ring opens under the influence of alkali, the compounds going over into the corresponding amides of acetylcyanoacetic acid.

The *o-tolylamide of 5-methylisoxazole-4-carboxylic acid,* $HC{=}CCONHC_7H_7(o)$ / $N.O.CCH_3$ separates from dilute alcohol or benzene in white needles with a melting point of 112°. Analysis:

Calculated for $C_{12}H_{12}O_2N_2$: N, 12.97; found: N, 12.95.

Alkali changes this into the *o-tolylamide of acetylcyanoacetic acid,* $CH_3COCH(CN)CONHC_7H_7(p)$, white needles difficultly soluble in alcohol, which melt at 110°. The constitution was also proven by the synthesis of the same compound by the action of acetyl chloride on the sodium salt of cyanoaceto-*o*-toluide (from cyanoacettoluide and sodium in absolute ether). Analysis:

Calculated for $C_{12}H_{12}O_2N_2$: N, 12.97; found: N, 12.81, 12.78.

The *p*-toluidomethyleneacetoacet-*p*-toluide with hydroxylamine hydrochloride and pyridine after four hours' boiling in alcohol solution yields the *p-tolylamide of 5-methylisoxazole-4-carboxylic acid,* white needles from dilute alcohol, with a melting point of 140°. Analysis:

Calculated for $C_{12}H_{12}O_2N_2$: N, 12.97; found: N, 12.99, 13.02.

Alkali changes this into *acetylcyanaceto-p-toluide*, $CH_3COCH(CN)CONHC_7H_7(p)$, white needles sparingly soluble in alcohol. It melts at 176°. The same compound was also obtained from the sodium salt of cyanacet-*p*-toluide and acetyl chloride. Analysis:

Calculated for $C_{12}H_{12}O_2N_2$: N, 12.97; found: N, 12.79.

Anilidomethyleneacetoacetanilide reacts readily with hydroxylamine, but the resulting product is so soluble that it is difficult to isolate. After evaporating off the alcohol, the oil was taken up with ether, which was dried and distilled at 20 mm. pressure. A small amount of a white product melting at 136° was obtained, which is doubtless the phenylamide of the methylisoxazole, since it rearranges with alkalies giving acetylcyanoacetanilide. This forms white needles from alcohol which melt at 145° and is identical with the same substance prepared by the action of acetyl chloride on the sodium salt of cyanoacetanilide. Analysis:

Calculated for $C_{11}H_{10}O_2N_2$: N, 13.86; found: N, 13.73.

In comparing the properties of the isoxazoles with the isomeric cyan derivatives, it will be noticed that with but one exception the melting points of the latter are higher and the solubilities decidedly less that those of the corresponding isoxazoles.

In the course of the investigation several other compounds were obtained which do not seem to be recorded in the literature, hence they will be briefly noted here.

When di-*m*-xylylformamidine and acetoacetic ethyl ester are heated at 140–50°, the main product is the *m*-xylylamide of *m*-xylidomethyleneacetoacetic acid (m. p. 188°). When the temperature is kept at 120°, the secondary reaction between the *m*-xylidine and the carbethoxy group does not seem to occur and there is obtained instead *ethyl m-xylidomethyleneacetoacetate*, white crystals which melt at 122°.[1] Analysis:

$$(CH_3COC : CHNHC_6H_3(CH_3))_2$$
$$|$$
$$COOC_2H_5$$

Calculated for $C_{15}H_{18}O_3N$: N, 5.39; found: N, 5.66.

Cyanoaceto-m-toluide.—*m*-Toluidine reacts after several hours' heating with cyanoacetic ester at 160° to give the cyanoacet-*m*-toluide. The white crystals from benzene melt at 138°. Analysis:

Calculated for $C_{10}H_{10}ON_2$: N, 16.09; found: N, 16.20.

Cyanoacet-p-anisidide.—This requires the heating of the two components at 160–70° and forms white crystals with a melting point of 138°. Analysis:

Calculated for $C_{10}H_{10}O_2N_2$: N, 14.74; found: N, 14.91.

[1] This Journal, **31**, 1148.

Summary of Results.

1. Phenylisoxazolone reacts with the formamidines, yielding substituted aminomethylene derivatives of the phenylisoxazolone.

2. Benzal and anisalmethylisoxazolone give with the formamidines substituted aminomethylenemethylisoxazolones and the benzal or anisal derivatives of the amines.

3. In some cases the substituted isoxazolones form bromine compounds, which, under the influence of solvents, rearrange to *p*-bromophenyl compounds.

4. When hydroxylamine acts on the amides of aminoethyleneaceto or benzoylacetic acids, there are formed derivatives of 5-methyl or phenylisoxazole-4-carboxylic acids.

5. These isoxazoles, under the influence of alkalies, rearrange to substituted amides of acetyl or benzoylcyanacetic acid.

6. A number of compounds have been made to illustrate the reactions involved.

ON THE REACTIONS OF THE FORMAMIDINES. IV.

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The following paper[1] constitutes a further study of the reactivity of the substituted formamidines with compounds containing methylene hydrogen,[2] the general purpose being to ascertain whether there is any special relation between the nature of the substituting group and the reactions of the formamidines.

The previous papers have shown that the general reaction between the formamidines and a compound containing methylene hydrogen can be formulated as follows:

$$XYCH_2 + RN : CHNHR = XYC : CHNHR + RNH_2.$$

If Y, for instance, is a carbethoxy group, —$COOC_2H_5$, the freed amine may react with it to give an amide CONHR and alcohol. Whether this secondary reaction occurs or not is largely a question of temperature, the lower the temperature, the less the amide formation, although in the case of malonic ester, this secondary reaction seems always to occur.

Derivatives of p-Benzyloxyaniline. — The free amine was readily prepared by the reduction of the nitro compound with iron and acetic acid, according to the method of Spiegel and Sabbath.[3] The free amine was dissolved in benzene and dry hydrochloric acid gas passed into the

[1] The work though incomplete is published at this time owing to the departure of one of the authors from the university.

[2] See previous paper. Also *Ber.*, **35**, 2496; THIS JOURNAL, **31**, 1148.

[3] *Ber.*, **34**, 1944.