CLXXI.—*The Action of Ammonia and Amines on 2-Phenyl-1:3-benzoxazine-4-one.*

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It has already been shown by one of the authors (Trans., 1910, **97**, 209) that 2-phenyl-1:3-benzoxazine-4-one (I) reacts with aniline readily with ring rupture, forming a yellow compound, salicylphenylbenzamidine. The addition of other amines and of ammonia has since been studied closely, and the observations are embodied in the present paper. It has been found that addition takes place with great readiness in all cases, and with ammonia, salicylbenzamidine (II) is formed, which crystallises in fine orange needles:

The constitution of the orange compound (II) has been confirmed by its independent synthesis from phenyl salicylate and benzamidine, thus:

In this synthesis a compound, $\text{C}_{21}\text{H}_{15}\text{ON}_3$, which crystallises in pale yellow needles, is also formed by a secondary reaction. The constitution of this compound, which has previously been obtained by Pinner (*Ber.*, 1890, **23**, 2934, 3824) from ethyl salicylate and benzamidine, is discussed on p. 1499. The authors show that it is formed by the further action of benzamidine on salicylbenzamidine, which was not isolated by Pinner.

2-Phenyl-1:3-benzoxazine-4-one reacts with primary amines in a similar way to ammonia, yielding amidines which are yellow, and have a similar constitution. These amidine derivatives show varying degrees of stability, and while the simple amidine (II) is perfectly stable at 100°, the substituted amidines, $\text{OH} \cdot \text{C}_6\text{H}_4 \cdot \text{CO} \cdot \text{N} \cdot \text{CPh} \cdot \text{NHR}$, at 90–100° lose the primary amine $\text{R} \cdot \text{NH}_2$ more or less readily, with production of the unsaturated cyclic compound (I). This has already been noted in the case of salicylphenylbenzamidine (*loc. cit.*), which readily dissociates at 100°. The methyl and ethyl derivatives (IV) obtained by the addition of methylamine or ethylamine to the cyclic compound (I) are much more thermostable than the phenyl derivative, but on long-continued heating in an open vessel at 100° they lose methylamine and ethylamine respectively, yielding 2-phenyl-1:3-benzoxazine-4-one (I). There can be little doubt that the unstable and hypothetical cyclic compound

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(III) is intermediate, both in the synthetic formation and reversible decomposition in each case:

and a similar mechanism holds in the case of the addition of ammonia, this view being supported by several considerations.

The open-chain amidine derivatives thus exhibit metoxazone tautomerism analogous to that observed among the acyl-salicylamides, in which the cyclic hydroxy-form, $\text{C}_6\text{H}_4 \begin{array}{l} \diagup \text{CO} \cdot \text{NH} \\ \diagdown \text{O} - \text{CPh} \cdot \text{OH} \end{array}$, is too unstable to exist in a free condition. They also exhibit ename-ketimine (amidine) tautomerism in the open-chain form, and in the case of salicylbenzamidine the tautomeric forms are:

Owing to the bright yellow colour of salicylbenzamidine and its derivatives, and the interest attaching to their true constitution, a close study of their relations has been made, the outcome of which is to make it probable that the ename type of formula (II and IV) is the correct one for the pure solid substances. Their properties, however, including their peculiar behaviour with acids and alkali referred to below, make it impossible to assign the yellow colour to any single type of structure, and these properties seem to be consistent only with the supposition that the open-chain forms are verging on ring-formation, and that the colour is due to some oscillatory play of residual affinities between the hydroxylic and the amidine groupings. Their behaviour with acids may be best illustrated by considering the case of salicylbenzamidine (II). The orange needles, which show both phenolic and basic properties, are insoluble in ammonia, but dissolve in sodium hydroxide to a nearly colourless solution, from which by neutralisation with acids a pale yellow, apparently amorphous precipitate is produced; if rapidly treated with ammonia, this dissolves to a pale yellow solution. From the latter, orange needles of the original substance rapidly separate on keeping. The unstable acid form, soluble in ammonia, may possibly be the imino-compound (V), but it is not possible to isolate it owing to the rapidity with which it is transformed into the orange needles (II).

When the solution of the orange needles in alkali is treated with

excess of dilute hydrochloric acid, the yellow precipitate dissolves to a colourless solution, which in a short time deposits a mass of fine colourless needles, consisting of a hydrochloride sparingly soluble in hydrochloric acid. On careful treatment with alkali, the orange-coloured base may be recovered unchanged. The same colourless hydrochloride is obtained by the action of concentrated hydrochloric acid on a solution of the orange compound in acetone. The colour immediately disappears, and a mass of colourless, transparent crystals is deposited. The hydrochloride, freed from acid, on treatment with water, undergoes partial dissociation, giving the solid orange-yellow compound and a pale yellow solution, which on keeping soon becomes turbid, and deposits eventually a pale yellow jelly consisting of *N*-benzoylsalicylamide (white) in a nearly pure form. If water containing a trace of hydrochloric acid instead of pure water is used, the hydrochloride dissolves to a colourless solution, which soon deposits a perfectly white precipitate (microscopic needles) of *N*-benzoylsalicylamide, and the same substance is similarly obtained by the direct treatment of the free base, salicylbenzamidine in aqueous alcohol, with dilute hydrochloric acid. The decomposition is, under ordinary conditions, nearly complete in an hour. The colourless, unstable hydrochloride, for reasons advanced below, is believed to be the cyclic compound (VI), a salt of the cyclic amino-compound (VII), which, however, cannot exist in the free state, but immediately undergoes rearrangement into the orange compound (II). On this view the cyclic hydrochloride in faintly acid aqueous solution suffers gradual loss of ammonia as ammonium chloride, yielding 2-phenyl-1:3-benzoxazine-4-one (I), which, being extremely sensitive to hydrogen ions, immediately suffers hydrolytic fission, as previously shown by one of the authors (Trans., 1910, **97**, 209), yielding *N*-benzoylsalicylamide (VIII):

The alternative view that the colourless hydrochloride is a salt of the open-chain base (II) is discountenanced by a consideration of the properties of *o*-methoxybenzoylbenzamidine (X), in which the mobile phenolic hydrogen atom is replaced. This compound was

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synthesised from phenyl *o*-methoxybenzoate (IX) by condensation with benzamidine, thus:

The compound (X) is a quite colourless base, and its hydrochloride is practically unaffected in presence of aqueous hydrochloric acid in the cold. On heating, however, it is slowly converted into *N*-benzoyl-*o*-methoxybenzamide, identical with the compound obtained by McConnan and Titherley (Trans., 1906, **89**, 1332). This relatively difficult hydrolysis by hot acids is the normal decomposition of amidines, and is precisely similar to that which can be effected under similar conditions with benzoylbenzamidine, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{N}:\text{CPh}\cdot\text{NH}_2$, which yields dibenzamide. The easy hydrolysis of salicylbenzamidine in the cold, and the still more rapid acid hydrolysis of its derivatives of the type

which is complete in the cold in the course of a few minutes, stands out as a different type of reaction from ordinary amidine hydrolysis.

In order to throw further light on the constitution of salicylbenzamidine and its derivatives, the behaviour of 2-phenyl-1:3-benzoxazine-4-one with secondary amines was studied, and for this purpose dimethylamine, diethylamine, and diphenylamine were chosen. Considerable difficulty was experienced, inasmuch as although addition takes place at once in the cold in presence of solvents, mixtures of labile isomeric forms result, which on evaporating give yellow, difficultly crystallisable syrups. In the addition of dimethylamine, separation could not be effected, but with diethylamine a definite crystalline solid was obtained in colourless crystals. This compound from its properties must be 2-diethylamino-2-phenyl-dihydro-1:3-benzoxazine-4-one (XI), and represents the simple additive compound of the unsaturated cycloid (I). It is, however, extremely labile, and slowly turns yellow, even in the solid condition. In solvents, it gives a pale yellow solution, which shows the properties of an equilibrium mixture of the cyclic form (XI) and open-chain, yellow form, salicyldiethylbenzamidine (XII), which, however, could not be isolated in a pure condition:

(XII.) Yellow (not isolated).

The colourless compound and yellow mixture dissolve at once in

dilute hydrochloric acid, forming a clear, colourless solution of the cyclic hydrochloride, which decomposes with great rapidity, in a similar manner to salicylbenzamidine. Diethylamine is eliminated, and a white precipitate of *N*-benzoylsalicylamide is produced. The extreme ease of this change, which is complete in the course of 5—6 seconds in the cold, confirms the supposition already expressed that in salicylbenzamidine (II) and all these derivatives the decomposition by acids is not simple amidine hydrolysis, and that acids produce salts of the (colourless) cyclic isomeric forms, which then more or less readily lose ammonia or amines, yielding the unsaturated cycloid (I); the latter, under the influence of acids, combines with water as it is formed, and by ring fission yields *N*-benzoylsalicylamide.

From these considerations it follows that in the majority of cases the stable existent form of these compounds in the free condition is the open-chain amidine form (as in II), which is yellow, whilst the hydrochlorides, which are colourless and more or less rapidly decomposed by water, possess the cyclic constitution, and are derivatives of dihydro-1:3-benzoxazine-4-one (as in VI). The only case observed where the stable form in the free condition possesses this cyclic structure is the diethylamino-derivative, which, however, rapidly comes into equilibrium with the yellow, open-chain amidine form in solution.

The addition of diphenylamine to 2-phenyl-1:3-benzoxazine-4-one (1) gave interesting results. In benzene solution the two combine, giving a deep yellow solution, which yields a syrupy mixture on evaporation. Difficulty was experienced owing to easy reversible dissociability of the additive compound into its constituents. When a hot solution of the unsaturated cyclic compound (I) in light petroleum was treated with an equivalent amount of diphenylamine, a colourless solution resulted, which became pale yellow on cooling. By keeping warm and adding an excess of diphenylamine (which is very soluble in light petroleum), the colour intensified as the increased mass of the diphenylamine increased the amount of the additive compound, until finally it separated out on cooling slightly as a mass of beautiful yellow needles. The constitution of this diphenylamine derivative presents some difficulty. Although its yellow colour, having regard to the above considerations, suggests the open-chain amidine structure (XIII), its insolubility in sodium

hydroxide and the fact that it gives no coloration with ferric chloride suggests the cyclic formula (XIV), which is also consistent with its very easy dissociability.

The amidine formula (XIII) is believed by the authors to represent the true constitution of the compound, and the absence of phenolic properties is attributed to the powerful steric influence of the large amidine grouping carrying three phenyl radicles. It must, in fact, be supposed that although conventionally written as an open-chain system, it is one verging on ring-formation, and on this account, as well as on account of the magnitude of the groups in the critical position, the compound is virtually, so far as its properties are concerned, a cyclic compound, although there is a sufficient play of residual affinities in the open-chain form to produce colour. This disappearance of phenolic properties has been observed in another interesting case by the authors. When 2-phenyl-1:3-benzoxazine-4-one (I) in alcoholic solution is treated with benzamidine, a bright yellow solution results, evidently containing the complex amidine derivative (XVI). This, however, cannot be isolated owing to the remarkable tendency it has to undergo internal condensation, producing a compound $C_{21}H_{15}ON_3$, shown to be salicyldiphenylcyanidine (XVII), which rapidly separates out as a very pale yellow, crystalline powder, the yield being quantitative. The same compound (XVII) is produced, together with ammonia, by heating salicylbenzamidine and benzamidine together in alcoholic solution, and it is formed in this way as a by-product in the synthesis of salicylbenzamidine by the phenyl salicylate method (p. 1493):

The compound (XVII) is identical with that obtained by Pinner (*loc. cit.*), who, noting its insolubility in sodium hydroxide, gave it the formula:

Such a constitutional formula, is not inconsistent with its synthesis from 2-phenyl-1:3-benzoxazine-4-one, since it could be derived by internal condensation from the intermediate additive

compound (XV), but it is difficult to reconcile with its easy production from salicylphenylbenzamidine (II), which has no tendency to lose ammonia. Moreover, the compound is, like cyaphenine (triphenylcyanidine), devoid of basic properties such as should be associated with Pinner's formula. Taking all the facts into account, the compound must be regarded as *o*-hydroxycyaphenine, and the suppression of ordinary phenolic properties must be attributed to the steric influences already referred to. That the phenolic properties are not entirely suppressed has been shown by the authors in the fact that, although the compound gives no ferric chloride reaction and is not affected by aqueous sodium hydroxide, it yields with sodium ethoxide in alcohol a bright yellow sodium derivative, which is decomposed by excess of water with production of the unchanged compound.

A similar case of disappearance of phenolic properties has been lately observed by Torrey and Adams (*Ber.*, 1910, **43**, 3227) in certain hydrazone derivatives of pæonol like

which is not affected by alkali. The position of the hydroxyl group is similar in these derivatives to those of the authors.

EXPERIMENTAL.

Salicylbenzamidine, $\text{OH} \cdot \text{C}_6\text{H}_4 \cdot \text{CO} : \text{N} : \text{CPh} \cdot \text{NH}_2$.

(1) *Preparation from 2-Phenyl-1:3-benzoxazine-4-one*.—Twenty grams of 2-phenyl-1:3-benzoxazine-4-one dissolved in 200 c.c. alcohol were saturated with gaseous ammonia, and the bright yellow solution was allowed to evaporate. Salicylbenzamidine (20 grams) separated as a mass of practically pure, transparent, orange-yellow needles. By recrystallisation from a mixture of benzene and light petroleum (1:3), the compound was obtained in silky, orange needles, melting at 136°.

An alternative method of preparation consisted in treating the alcoholic solution of 2-phenyl-1:3-benzoxazine-4-one with concentrated aqueous ammonia, when, after half an hour, salicylbenzamidine separates as a mass of orange needles in nearly quantitative yield:

0.1669 gave 17.3 c.c. N_2 at 23° and 743 mm. $\text{N} = 11.42$.

$\text{C}_{14}\text{H}_{12}\text{O}_2\text{N}_2$ requires $\text{N} = 11.66$ per cent.

(2) *Preparation from Phenyl Salicylate*.—Two grams of phenyl salicylate were mixed with 1 gram of benzamidine, freshly prepared from its hydrochloride, when an immediate reaction took place with evolution of heat. A yellow colour developed, and a mass of nearly white crystals, probably the phenyl salicylate salt of benzamidine,

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were deposited. About 20 c.c. of alcohol were now added, and the mixture heated to the boiling point. A rapid reaction took place with formation of a clear, bright yellow solution, from which in a few moments a mass of nearly colourless, short, silky needles separated (0.15 gram). These melted at 248° , and consisted of *o*-hydroxytriphenylcyanidine (p. 1498). (Found, $N=12.69$. Calc., $N=12.90$ per cent.)

The alcoholic filtrate on careful dilution with water gave salicylbenzamidine as a mass of orange-yellow needles (0.8 gram), melting, after recrystallisation from a mixture of benzene and light petroleum, at $136-137^{\circ}$:

0.2889 gave 28.3 c.c. N_2 at 17° and 764 mm. $N=11.43$.

$C_{14}H_{12}O_2N_2$ requires $N=11.66$ per cent.

Salicylbenzamidine is readily soluble in alcohol, acetone, or chloroform, moderately so in ether or benzene, and practically insoluble in light petroleum. Its solution in acetone gives an intense purple-red colour with alcoholic ferric chloride. It is immediately soluble in dilute sodium hydroxide to a very pale yellow solution, which with dilute hydrochloric acid gives a yellow precipitate, which at once dissolves in excess of acid. The resulting colourless solution, after one minute, deposits a thick mass of fine white needles, consisting of a hydrochloride insoluble in hydrochloric acid. The hydrochloride on keeping soon changes to *N*-benzoylsalicylamide. Even if it is rapidly collected this decomposition cannot be avoided, and on washing the precipitate it becomes pale yellow, owing to partial dissociation. The pure *hydrochloride* was obtained by treating a solution of 1 gram of salicylbenzamidine in 15 c.c. of acetone with 1 c.c. of concentrated hydrochloric acid. It separated after a short time as a mass of small, colourless needles (1.25 grams), which were washed with acetone and dried in a vacuum, in which, however, slight dissociation occurred, and a slightly yellow colour developed. It was analysed by decomposition with water containing a small quantity of nitric acid. The *N*-benzoylsalicylamide formed was weighed, and the hydrochloric acid determined by titration:

0.2078 gave 0.1650 *N*-benzoylsalicylamide (theory 0.1810) and required 7.1 c.c. *N*/10- $AgNO_3$. $Cl=12.13$.

$C_{14}H_{12}O_2N_2.HCl$ requires $Cl=12.8$ per cent.

The hydrochloride on heating to 120° partly melted, and lost ammonium chloride, giving 2-phenyl-1:3-benzoxazine-4-one, which was isolated by extraction with benzene, washing the benzene solution with alkali, and evaporating. After recrystallisation from light petroleum, it melted at 106° , and gave the characteristic reaction with hydrochloric acid (Trans., 1910, 97, 207).

The hydrochloride dissolves fairly readily in alcohol with slight dissociation and a faint yellow colour. This solution gives a port-wine tint with alcoholic ferric chloride, but if previously treated with very dilute alcoholic hydrogen chloride until just colourless the solution gives no ferric chloride coloration.

The hydrochloride is partly dissociated by water, forming a pale yellow solution, and generally leaving a little free base insoluble as a yellow solid, but a colourless solution results if a small quantity of free hydrochloric acid is added. The pale yellow aqueous solution on being kept for a few minutes deposits pale yellow needles (m. p. 132°) of salicylmethylbenzamidinium, and later a sulphur-yellow precipitate, consisting of a mixture of this and *N*-benzoylsalicylamide. The acidified colourless solution on keeping deposits continually a white precipitate of pure *N*-benzoylsalicylamide (m. p. 208°). The decomposition is nearly complete in an hour at the ordinary temperature, as shown in the curve on p. 1508; at higher temperatures it is practically instantaneous.

Salicylmethylbenzamidinium, $\text{OH}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{N}^+\text{CPh}\cdot\text{NHMe}$.

One gram of 2-phenyl-1:3-benzoxazine-4-one in saturated alcoholic solution was treated with 0.45 gram of a 33 per cent. aqueous solution of methylamine. A yellow colour was immediately produced, and after some time salicylmethylbenzamidinium separated in large, yellow, hexagonal plates, leaving a yellow syrup. After washing with dilute alcohol and recrystallising from light petroleum, it was obtained in bundles of yellow needles, melting at 95° :

0.6332, by Kjeldahl's method, required 50.0 c.c. *N*/10-HCl.
N = 11.06.

$\text{C}_{15}\text{H}_{14}\text{O}_2\text{N}_2$ requires N = 11.03 per cent.

Salicylmethylbenzamidinium is fairly soluble in the cold in alcohol or ether, and readily so in acetone or benzene. It is easily soluble in all hot solvents. It gives a strong red coloration with ferric chloride. On heating at 90 – 100° , it gradually loses methylamine, and leaves 2-phenyl-1:3-benzoxazine-4-one, the yield of which on small quantities is nearly theoretical in six days (0.1270 gave 0.1130; theory requires 0.1115). Salicylmethylbenzamidinium dissolves in sodium hydroxide to a very pale yellow solution, and in dilute hydrochloric acid to a colourless solution, from which *N*-benzoylsalicylamide is rapidly deposited, the decomposition being practically complete at 15° in about fifteen minutes.

Salicylethylbenzamidine, $\text{OH}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{N}:\text{CPh}\cdot\text{NH}\text{Et}$.

A saturated alcoholic solution of 3 grams of 2-phenyl-1:3-benzoxazine-4-one was treated with 3 grams of 33 per cent. aqueous ethylamine. A yellow colour was produced immediately, and in a short time yellow needles of salicylethylbenzamidine formed, which were collected after three hours. The yield was 2 grams, and the compound, after recrystallising from light petroleum, melted at 118—119°:

0.4824, by Kjeldahl's method, required 35.5 c.c. *N*/10-HCl.
 $\text{N} = 10.30$.

$\text{C}_{16}\text{H}_{16}\text{O}_2\text{N}_2$ requires $\text{N} = 10.45$ per cent.

Salicylethylbenzamidine is very sparingly soluble in cold ether or light petroleum, readily so in cold acetone or benzene, and moderately so in cold alcohol. When heated at 90—100° it slowly loses ethylamine, leaving 2-phenyl-1:3-benzoxazine-4-one (m. p. 106°), the decomposition being complete in six days. (0.1340 gave 0.1120, theory requires 0.1115.) *Salicylethylbenzamidine* gives a deep red coloration with ferric chloride; it dissolves in sodium hydroxide to a very pale yellow solution, and in dilute hydrochloric acid to a colourless solution, from which *N*-benzoylsalicylamide is rapidly deposited, the decomposition being practically complete at 15° in five minutes.

Action of Dimethylamine on 2-Phenyl-1:3-benzoxazine-4-one.

The interaction between these substances was tried under a variety of conditions, using ether, alcohol, benzene, and light petroleum as solvents, and in each case yellow solutions were obtained, which on evaporation left viscid, yellow syrups. The latter evidently consisted of a mixture of salicyldimethylbenzamidine and 2-dimethylamino-2-phenyldihydro-1:3-benzoxazine-4-one, and on keeping in a vacuum for several weeks partly crystallised, but owing to the tendency which these two compounds have to suffer rearrangement, forming an equilibrium mixture, it was found impossible to effect a proper separation. The crystals, which were obtained only in very small quantity, melted at temperatures between 90° and 106°. A determination of nitrogen in the syrupy mixture was made:

0.2244, by Kjeldahl's method, required 16.8 c.c. *N*/10-HCl.
 $\text{N} = 10.48$.

$\text{C}_{16}\text{H}_{16}\text{O}_2\text{N}_2$ requires $\text{N} = 10.45$ per cent.

The mixture gave a deep reddish-violet colour with ferric chloride, and was rapidly decomposed by dilute hydrochloric acid, yielding dimethylamine and *N*-benzoylsalicylamide.

*Action of Diethylamine on 2-Phenyl-1:3-benzoxazine-4-one.**2-Diethylamino-2-phenyldihydro-1:3-benzoxazine-4-one,*

—Similar difficulties were encountered to those mentioned in the case of dimethylamine, but after several trials one of the two products formed (the cyclic diethyl derivative) was definitely isolated as follows: Five grams of 2-phenyl-1:3-benzoxazine-4-one in 50 c.c. of pure benzene were treated with a solution of 1.5 grams of diethylamine in benzene. A yellow colour rapidly developed, and on evaporation at 15° a yellow syrup was left, which in a few days set to a crystalline mass. The solid consisted essentially of the cyclic base, and after draining weighed 5.5 grams. By careful treatment with cold 5 per cent. aqueous sodium hydroxide, the isomeric yellow salicyldiethylbenzamidine present was removed, leaving a white solid (5 grams). Attempts to obtain salicyldiethylbenzamidine from the alkaline filtrate by cautious treatment with acetic acid or carbon dioxide gave only *N*-benzoylsalicylamide, diethylamine being eliminated. The solid remaining after treatment with alkali was recrystallised by dissolving in alcohol at 40°, and cautiously adding water; on keeping, pure 2-diethylamino-2-phenyldihydro-1:3-benzoxazine-4-one separated in colourless needles, melting at 81°, and weighing 3 grams:

0.4124, by Kjeldahl's method, required 27.0 c.c. *N*/10-HCl.
N = 9.17.

$\text{C}_{18}\text{H}_{20}\text{O}_2\text{N}_2$ requires N = 9.46 per cent.

The cyclic base undergoes partial rearrangement to the yellow open-chain isomeride, even in the solid condition, and the change can be traced in the yellow colour which the colourless crystals acquire on keeping a few hours. The tautomeric change appears to be practically instantaneous in solution. The compound dissolves easily in cold benzene, acetone, or chloroform to pale yellow solutions, which leave a syrupy mixture of the two isomerides on spontaneous evaporation. In carbon tetrachloride and ethyl acetate, in which the compound is readily soluble, and in alcohol, in which it is moderately soluble, the yellow colour is only very slight, and the equilibrium between the colourless ring and yellow open-chain isomerides is clearly dependent on the nature of the solvent. The solutions in alcohol and acetone give a reddish-violet colour with ferric chloride. The cyclic base, like salicylmethylbenzamidine and salicylethylbenzamidine, readily dissociates on heating to about 90°. Diethylamine is lost, and after heating for fifteen hours the liquid sets to a crystalline mass of 2-phenyl-1:3-benz-

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oxazine-4-one, melting at 103° . The behaviour of the compound with hydrochloric acid was studied in order to throw light on the action of hydrochloric acid on salicylbenzamidine (p. 1500). The cyclic base dissolves readily in excess of cold dilute hydrochloric acid to a colourless solution, which, if the solution is not too dilute, in a few seconds deposits a white, microcrystalline precipitate of the hydrochloride. The latter on warming with aqueous ammonia dissolves to a bright yellow solution, which on cooling deposits a mass of needles of salicylbenzamidine, melting at 135° . 2-Phenyl-1:3-benzoxazine-4-one is undoubtedly first produced, and then combines with ammonia, and the same mechanism explains the ready decomposition of the hydrochloride with water. When the cyclic base in a finely divided state is suspended in sufficient water (to prevent the hydrochloride being precipitated), on adding dilute hydrochloric acid a clear solution is formed, but hydrolysis rapidly takes place, and an abundant precipitate of *N*-benzoylsalicylamide (m. p. 200°) begins to be deposited in about five seconds. By collecting at short intervals it was found that the decomposition (with formation of diethylamine) was practically complete in three minutes. The hydrochloride of the cyclic base is therefore very much more rapidly hydrolysed than that of 2-amino-2-phenyl-dihydro-1:3-benzoxazine-4-one (p. 1501).

The pure *hydrochloride* was obtained by treating a solution of 2 grams of the cyclic base in benzene solution with dry hydrogen chloride:

0.0740 required 2.15 c.c. *N*/10- AgNO_3 . $\text{Cl} = 10.31$.

$\text{C}_{18}\text{H}_{21}\text{O}_2\text{N}_2\text{Cl}$ requires $\text{Cl} = 10.38$ per cent.

The hydrochloride rapidly decomposes in moist air, and after twenty-four hours contained only 5.61 per cent. of chlorine. At the end of three weeks the remaining white solid consisted almost entirely of *N*-benzoylsalicylamide.

Action of Diphenylamine on 2-Phenyl-1:3-benzoxazine-4-one.

Salicyldiphenylbenzamidine, $\text{OH}\cdot\text{C}_6\text{H}_4\cdot\text{CO}\cdot\text{N}\cdot\text{CPh}\cdot\text{NPh}_2$. — A solution of 2.3 grams of 2-phenyl-1:3-benzoxazine-4-one in dry benzene was treated with a benzene solution of 1.7 grams of diphenylamine. A bright yellow colour was produced at once, and on allowing to evaporate, a syrup remained, which slowly crystallised. After draining and recrystallising from benzene, *salicyldiphenylbenzamidine* was obtained as a bright yellow, crystalline powder, melting at 92° :

0.6012, by Kjeldahl's method, required 30.1 c.c. *N*/10- HCl . $\text{N} = 7.01$.

$\text{C}_{26}\text{H}_{20}\text{O}_2\text{N}_2$ requires $\text{N} = 6.98$ per cent.

The compound gives no reaction with ferric chloride, and is insoluble in sodium hydroxide.

It is sparingly soluble in cold light petroleum, moderately so in cold alcohol or ether, and readily so in cold acetone or benzene, giving yellow solutions in each case. The yellow colour is not lost in hot alcohol, but it disappears in excess of hot benzene or light petroleum, and reappears on cooling, owing to the ready dissociation of the compound into 2-phenyl-1:3-benzoxazine-4-one and diphenylamine. The former can, in fact, be isolated from the hot light petroleum solution, if not too dilute, by cooling. An alternative method of preparation consisted in adding an excess of diphenylamine to a hot solution of 2-phenyl-1:3-benzoxazine-4-one in light petroleum, and allowing to cool, when the compound separated in bright yellow, silky needles melting at 92° .

Action of Piperidine on 2-Phenyl-1:3-benzoxazine-4-one.

A yellow syrup only could be obtained, consisting apparently of open-chain and cyclic isomerides, which could not be separated. The syrup was easily soluble in benzene and acetone, and was practically insoluble in alkali. With acids, it yielded *N*-benzoyl-salicylamide.

o-Methoxybenzoylbenzamidine, $\text{MeO} \cdot \text{C}_6\text{H}_4 \cdot \text{CO} \cdot \text{N} : \text{CPh} \cdot \text{NH}_2$.

The object in synthesising this compound was to compare its properties with those of salicylbenzamidine, and its synthesis was effected from benzamidine and phenyl *o*-methoxybenzoate, which was obtained from *o*-methoxybenzoic acid by a modification of the method described by Seifert (*J. pr. Chem.*, 1844, [ii], **31**, 474). *o*-Methoxybenzoic acid has been obtained by several methods (Cahour, *Annalen*, 1854, **92**, 315; Graebe, *Annalen*, 1866, **139**, 137; Graebe and Ullmann, *Ber.*, 1896, **29**, 825; Bromwell, *Amer. Chem. J.*, 1898, **19**, 577; Weida, *Amer. Chem. J.*, 1898, **19**, 552; Lander, *Trans.*, 1900, **77**, 745), but as on trial these methods gave unsatisfactory yields it was prepared by the authors from salicylamide by methylation and subsequent hydrolysis as follows:

o-Methoxybenzamide.—Thirty grams of salicylamide in 200 c.c. alcohol were treated with a solution of 4.6 grams of sodium in 50 grams of alcohol, and then with 40 grams of methyl iodide. After boiling for an hour and a-half and distilling off most of the alcohol, *o*-methoxybenzamide was precipitated with water. It was purified by digesting with sodium hydroxide and recrystallising from hot water (yield 25 grams, m. p. 128°).

o-Methoxybenzoic Acid.—Twenty-five grams of *o*-methoxybenz-

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amide were boiled with 60 c.c. of 10 per cent. sodium hydroxide for forty-five minutes, when the hydrolysis was complete. On cooling, diluting with water, and acidifying, *o*-methoxybenzoic acid was precipitated, and recrystallised from hot water (yield 18 grams, m. p. 93°).

Phenyl o-Methoxybenzoate.—Fifteen grams of *o*-methoxybenzoic acid mixed with 15 grams of freshly distilled phosphoryl chloride were treated at 75° with 9 grams of phenol, and the whole kept at 75° for four hours. The resulting red liquid after cooling was treated with water and shaken with 10 per cent. sodium hydroxide, and the insoluble oil extracted with ether. On evaporation a red oil remained, which solidified on stirring with a little dilute sodium hydroxide. The solid phenyl *o*-methoxybenzoate was purified by recrystallising first from aqueous alcohol and finally from pure alcohol, from which it separated in colourless, six-sided prisms, weighing 17 grams, and melting at 59°.

Condensation of Phenyl o-Methoxybenzoate and Benamidine.—Five grams of phenyl *o*-methoxybenzoate in 10 c.c. of alcohol were treated with 6 grams of benamidine, and the mixture heated to 50° for ten minutes. On cooling and adding water, *o*-methoxybenzoyl benamidine (8 grams) was precipitated as a mass of colourless needles, which, after recrystallising from a little alcohol, melted at 128°:

0.2386, by Kjeldahl's method, required 18.7 c.c. *N*/10-HCl.
N = 10.97.

$C_{15}H_{14}O_3N_2$ requires N = 11.02 per cent.

o-Methoxybenzoylbenzamidine is moderately soluble in cold alcohol, ether, or benzene, and readily so in acetone. It dissolves at once in dilute hydrochloric acid, forming a clear solution, which is only very slowly decomposed at 15°, but at 50° begins after half an hour to deposit *N*-benzoyl-*o*-methoxybenzamide in long needles. (Found: N = 5.76. Calc., N = 5.50 per cent.) The stability of the hydrochloride in presence of dilute hydrochloric acid was compared with that of salicylbenzamidine and benzoylbenzamidine, $NBz \cdot CPh \cdot NH_2$.

The latter compound, which has been described by Pinner (*Ber.*, 1878, **11**, 764; 1889, **22**, 1606) and by Beckmann and Sandel (*Annalen*, 1897, **296**, 285), was prepared by the authors by the condensation of phenyl benzoate (10 grams) and benamidine (7.2 grams), which were heated at 50° for three hours. On cooling and adding water, an oil was precipitated, which was treated with dilute hydrochloric acid to separate the benzoylbenzamidine, which dissolved, from unchanged phenyl benzoate (1.5 grams). The acid filtrate on treatment with alkali gave the base as an oil, which

rapidly solidified (7 grams). After recrystallisation from light petroleum it was obtained in fine colourless needles, melting at 98°. In comparing the relative stability of the three amidines towards hydrochloric acid, attempts were made to carry out the measurements under strictly similar conditions, but whilst this is possible as between benzoylbenzamidine and *o*-methoxybenzoylbenzamidine, which are only very slowly decomposed, giving dibenzamide and *N*-benzoyl-*o*-methoxybenzamide respectively, in the case of salicylbenzamidine the hydrolysis is too rapid. Further, owing to the slight solubility in hydrochloric acid of the cyclic hydrochloride resulting from the latter, more water was necessary than can be used in the case of the first two amidines, since the basis of the measurements depended on weighing the resulting secondary amides, which are appreciably soluble in water; the secondary amide derived from salicylbenzamidine, however (*N*-benzoylsalicylamide), is extremely insoluble in water, excess of which does not therefore vitiate the results. The first experiments give a comparison between benzoylbenzamidine and *o*-methoxybenzoylbenzamidine. Two portions of 0.5 gram in each case were dissolved in 10 c.c. of 10 per cent. hydrochloric acid, and the resulting clear solutions allowed to remain (1) at 15°, and (2) at 40°. The crystalline secondary amide produced by hydrolysis was weighed after twenty-four hours in (1), and at intervals in (2), the readings being shown in Fig. 1.

Benzoylbenzamidine (0.5 gram).

(1).	Temp.	Time.	Weight of dibenzamide.	Percentage hydrolysed.
	15°	24 hours	0.13 gram	25.8

o-Methoxybenzoylbenzamidine (0.5 gram).

Temp.	Time.	Weight of <i>N</i> -benzoyl- <i>o</i> -methoxybenzamide	Percentage hydrolysed.
15°	24 hours	0.03 gram	5.9

In the second group of experiments salicylbenzamidine was treated with the same volume of dilute hydrochloric acid, containing one, two, and three molecular equivalents of hydrogen chloride respectively. 0.2 Gram of the substance was dissolved in (i) 8.4 c.c. of *N*/10-hydrochloric acid and 16.8 c.c. of water; (2) 16.8 c.c. of *N*/10-hydrochloric acid and 8.4 c.c. of water; and (3) in 25.2 c.c. of *N*/10-hydrochloric acid. At higher concentrations than these it is impossible to prevent the insoluble hydrochloride being precipitated. The temperature was kept at 15°, and the insoluble *N*-benzoylsalicylamide which continually separated out, was collected at intervals, dried, and weighed. The results are expressed in Fig. 2.

(2).

FIG. 1.

- I. Benzoyl benzamidine (0.5 gram) at 40°.
 II. o-Methoxybenzoylbenzamidine (0.5 gram) at 40°.

FIG. 2.

Salicylbenzamidine (0.2 gram) at 15°.

From a comparison of these curves, although the conditions are not the same, it is evident that the velocity of hydrolysis of salicylbenzamidine is vastly greater than that of the other two amidines, even at a higher temperature. It is noteworthy that of the two latter, *o*-methoxybenzoylbenzamidine is hydrolysed much more slowly than benzoylbenzamidine, and this is probably due to steric hindrance. The results in any case are only approximate, since molecular quantities were not taken, and owing to the error due to the slight solubility in water and supersaturation tendency of dibenzamide and *N*-benzoyl-*o*-methoxybenzamide. An unexpected feature in the case of salicylbenzamidine is the slightly inhibitory effect of excess of hydrochloric acid, which appears to increase the stability of the hydrochloride. This effect is probably connected with the fact, previously referred to, that in stronger solutions the hydrochloride is precipitated as a crystalline solid by excess of hydrochloric acid. The reverse effect would be expected if the decomposition were true hydrolysis, and increase in the concentration of the acid catalyst would cause corresponding increase in the velocity of hydrolysis. As it appeared therefore that the mechanism of decomposition was one in which ammonia was eliminated from the cyclic hydrochloride, yielding 2-phenyl-1:3-benzoxazine-4-one as the first product, it appeared to be desirable to examine the velocity of addition of water to this compound (producing *N*-benzoylsalicylamide) under the influence of varying quantities of hydrochloric acid. Alcoholic solutions of 2-phenyl-1:3-benzoxazine-4-one diluted with water to incipient turbidity were treated with the acid, and the resulting precipitate collected at intervals, but it was found that in all cases the velocity was so great that proper measurements could not be made. With one molecular equivalent of dilute alcoholic hydrochloric acid at *N*/40-concentration, the reaction is practically complete in sixty seconds. With 1/45 of the molecular equivalent of acid at *N*/3000-concentration the reaction is complete in eight minutes. As the velocity of decomposition is greater than that of salicylbenzamidine and its derivatives, it would appear that the rate of decomposition of the latter by hydrochloric acid is controlled by the rate at which ammonia or amines are eliminated from their cyclic hydrochlorides.

*Condensation of (1) 2-Phenyl-1:3-benzoxazine-4-one, and
(2) Salicylbenzamidine, with Benzamidine.*

o-Hydroxytriphenylcyanidine, $\text{HO}\cdot\text{C}_6\text{H}_4\cdot\text{C}\begin{smallmatrix} \nearrow\text{N}\cdot\text{CPh} \\ \nwarrow\text{N}\cdot\text{CPh} \end{smallmatrix}\text{N}$.—This compound, under another constitutional formula, has already been described by Pinner (*loc. cit.*).

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(1) A saturated alcoholic solution of 4.6 grams of 2-phenyl-1:3-benzoxazine-4-one was treated with an alcoholic solution of 2 grams of benzamidine freshly prepared from 2.8 grams of the hydrochloride. An immediate yellow colour was produced, which in the course of a few seconds gave place to a pale yellow, microcrystalline precipitate of pure *o*-hydroxytriphenylcyanidine. After washing with alcohol, it weighed 6.2 grams, and melted at 245°. A further small quantity was obtained from the filtrate on keeping. (Found: N=13.00. Calc., N=12.92 per cent.)

(2) A saturated alcoholic solution of 1 gram of salicylbenzamidine was heated with 0.35 gram of benzamidine for several hours. The cyanidine derivative slowly separated from the hot solution as a pale yellow solid in a practically pure form (0.3 gram). It was identical in all respects with that prepared by method (1) and with the by-product (p. 1500) obtained in the condensation between benzamidine and phenylsalicylate.

The compound does not show normal phenolic properties. Attempts to methylate it by diazomethane and to acetylate it by acetic anhydride and pyridine failed entirely. On treating with sodium ethoxide in alcohol, however, a bright yellow sodium salt was obtained, which was completely decomposed by water, forming the original compound.

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