CXXVIII.—*The Beckmann Transformation. Part I. The Production of Amidines during the Beckmann Transformation of Ketoximes and the Mechanism of their Formation.*

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CONTRARY to the statement of Pawlewski (*Bull. Acad. Sci. Cracow*, 1903, 8) that ketoximes are as a rule not attacked by thionyl chloride, we have found that they react vigorously with it. In all the cases examined, substituted amidines have been obtained

together with the amides resulting from the usual course of the Beckmann transformation of ketoximes.

Other reagents for effecting the transformation, namely, phosphorus pentachloride, acetyl chloride, and hydrogen chloride, also cause amidine formation : no statement to this effect has hitherto appeared in the literature.

A feature common to all the reagents employed is the presence of hydrogen chloride during the transformation, a fact which has an important bearing on the mechanism of amidine formation discussed on p. 888.

The course of the reaction is similar in the case of all the reagents mentioned above, but the use of thionyl chloride in anhydrous ether has two advantages : the reaction is easily controlled and the by-products are gaseous. The reaction proceeds in two stages. The first portions of thionyl chloride added to an ethereal solution of the oxime, cooled in ice and salt, cause the precipitation of a white solid—the hydrochloride of the ketoxime. On further addition of the reagent, the precipitate changes to a yellow oil, and the ether acquires the same colour. The yellow oil is hygroscopic and unstable, decomposing spontaneously at the ordinary temperature with evolution of hydrogen chloride, leaving a darker coloured oil. (The yellow oil is also formed when a suspension of the hydrochloride of the ketoxime in anhydrous ether is treated with thionyl chloride.) Treatment of either oil with water gives amide and amidine corresponding to the configuration of the ketoxime. The fact that the unstable yellow oil gives amide and amidine indicates that it is a post phase of the Beckmann transformation, and its decomposition with evolution of hydrogen chloride probably represents the dissociation of the amidodichloride hydrochloride discussed on p. 892.

The results of the investigation are tabulated below :

Oxime.	Amide.	Amidine.
Acetophenone	Acetanilide	Diphenylacetamidine
p-Methylacetophenone	Aceto-*p*-toluidide	Di-*p*-tolylacetamidine
Propiophenone	Propionanilide	Diphenylpropionamidine
n-Butyrophenone *	Butyranilide	Diphenyl-*n*-butyramidine
Phenyl benzyl ketone	Phenylacetanilide	Diphenylphenacetamidine
Benzophenone	Benzanilide	Diphenylbenzamidine
p-Ethoxybenzophenone *	Mixture of *p*-ethoxybenzanilide and benz-*p*-phenetidide	Mixture of amidines

In the examples marked * traces only of the amidine were formed. In the others the yield of amidine varied from 15 to 20% of the weight of oxime taken, the amide predominating in all cases.

A mechanism is now put forward which offers a satisfactory

explanation, supported by experimental evidence, of the formation of amidines from ketoximes during the Beckmann transformation. Since an amidine contains two nitrogen atoms, it is evident that combination of two molecules of oxime (or transformation product of the oxime) must have been involved in its formation. The simplest representation of this combination consistent with experimental data is the following :

$$CR_2{:}NOH \longrightarrow R{\cdot}CCl{:}NR \xrightarrow{HCl} R{\cdot}CCl_2{\cdot}NHR$$

(I.) Imidochloride (II.) Amidodichloride

$$(I) + (II) \longrightarrow \underset{(III.)}{\begin{matrix} R{\cdot}C{:}NR \\ | \\ R{\cdot}N{\cdot}CRCl_2 \end{matrix}} \xrightarrow{2H_2O} \underset{(IV.)\ \text{Amidine}}{\begin{matrix} R{\cdot}C{:}NR \\ | \\ NHR \end{matrix}} + R{\cdot}CO_2H + 2HCl$$

The formation of imidochlorides from ketoximes * is now a generally accepted fact (Beckmann, *Ber.*, 1886, **19**, 989) and an essential part of the various theories of the Beckmann transformation, although their mode of formation is a problem which still awaits solution.

There is no recorded instance of the formation of amidodichlorides by addition of hydrogen chloride to imidochlorides as required by the above scheme, but Lander and Laws (J., 1904, **85**, 1695) obtained benzanilideamidochloroiodide by addition of hydrogen iodide to benzanilideimidochloride. In spite of a statement to the contrary by Lander and Laws (*loc. cit.*, p. 1696), benzanilideimidochloride readily combines with hydrogen chloride in ethereal solution, depositing large citron-yellow prisms of the *hydrochloride* of the *amidodichloride*, $Ph{\cdot}CCl_2{\cdot}NHPh,HCl$. This compound is sufficiently stable if handled rapidly. It tends to lose hydrogen chloride in two stages if heated fairly quickly to the melting point (68—69°), giving first the amidodichloride and finally the imidochloride. Complete dissociation is also effected by dissolving the amidodichloride in ether and removing the solvent under diminished pressure; the residue is pure benzanilideimidochloride. The hydrochloride behaves differently if dissociation is brought about gradually by heating at 40°, and diphenylbenzamidine, benzanilide, and benzoic acid are obtained. Condensation of imidochloride and amidodichloride formed during dissociation would explain the formation of the amidine † according to the scheme on p. 888 (R = Ph).

* Aldoximes may also give rise to the simpler imidochlorides, $R{\cdot}CCl{:}NH$, although such compounds cannot be isolated in a pure condition. Their formation when an ethereal solution of a nitrile is saturated with hydrogen chloride has been demonstrated beyond doubt (Pinner, " Die Imidoaether "; Hoesch, *Ber.*, 1915, **48**, 1122; Stephen, J., 1925, **127**, 1874).

† The yield of diphenylbenzamidine is increased if benzanilideimidochloride hydrochloride is added to the amidodichloride hydrochloride before dissoci-

The intermediate condensation product (III; R = Ph) was not isolated, and benzoyldiphenylbenzamidine, Ph·C(:NPh)·NPh·COPh, the first product of its hydrolysis, was not identified. This at first sight appeared to weaken the scheme of the original mechanism, since (III) may be regarded as analogous to the amidodichloride type (:N·CCl_2) and hence the group CCl_2 should readily hydrolyse to CO, giving benzoyldiphenylbenzamidine, a compound which has previously been described (Lander, J., 1902, **81**, 594). An attempt to prepare (III; R = Ph) by treating benzoyldiphenylbenzamidine with phosphorus pentachloride was unsuccessful. The bright yellow liquid remaining after removal of phosphorus oxychloride solidified, but owing to its extreme sensitiveness to moisture it could not be obtained in a pure condition. On treatment with water hydrolysis took place rapidly in the cold with the formation of diphenylbenzamidine hydrochloride and benzoic acid. Not a trace of the original benzoyl derivative was obtained.

All the evidence for the mechanism of amidine formation rests on the behaviour of benzanilideimidochloride described in the foregoing paragraphs. No other suitable case for treatment has been found, but there appears no reason to doubt that the general scheme would hold good for other individual cases.

The following experiments carried out during the course of this investigation are also of interest in connexion with what has been stated above, since they have a distinct bearing on the problem under discussion.

(1) The reaction between phosphorus pentachloride and benzanilide used by Wallach (*Annalen*, 1877, **184**, 79) to prepare benzanilideimidochloride always produces diphenylbenzamidine hydrochloride, which can be isolated from the residue after distillation of the imidochloride.

(2) Benzanilideimidochloride, heated in a stream of hydrogen chloride at 180—190°, gives a small amount of diphenylbenzamidine.

(3) Benzanilide, heated in a stream of hydrogen chloride at 180°, also gives small amounts of diphenylbenzamidine and benzoic acid. A slight modification of the original mechanism will explain this reaction:

(*a*) $Ph\cdot CO\cdot NHPh \longrightarrow Ph\cdot C(OH){:}NPh \xrightarrow{HCl} Ph\cdot CCl{:}NPh + H_2O$

(*b*) $Ph\cdot CO\cdot NHPh + Ph\cdot CCl{:}NPh \longrightarrow Ph\cdot CO\cdot NPh\cdot CPh{:}NPh \xrightarrow{H_2O} NHPh\cdot CPh{:}NPh + Ph\cdot CO_2$

Reaction (*b*) was confirmed by heating benzanilide with benz-

ation; this clearly indicates that the amidodichloride, the first dissociation product, combines with the added imidochloride, thus obviating to some extent the second phase of the dissociation.

anilideimidochloride at 160—170°, diphenylbenzamidine and benzoic acid being obtained. Hydrogen chloride was liberated during the reaction, the presence of which would cause reaction (*a*) to take place, thus providing the necessary molecule of water to bring about the subsequent hydrolysis of benzoyldiphenylbenzamidine formed in (*b*), which in consequence was not isolated.

Reactions (*a*) and (*b*) will also explain the formation of 2-phenyldihydroglyoxaline (ethylenebenzamidine) when ethylenedibenzamide is heated in presence of hydrogen chloride (Hofmann, *Ber.*, 1888, **21**, 2334) :

$$\begin{array}{l} CH_2\cdot NH\cdot COPh \\ | \\ CH_2\cdot NH\cdot COPh \end{array} \longrightarrow \begin{array}{l} CH_2\cdot N{:}C(OH)Ph \\ | \\ CH_2\cdot NH\cdot COPh \end{array} \longrightarrow \begin{array}{l} CH_2\cdot N{:}CClPh \\ | \\ CH_2\cdot NH\cdot COPh \end{array} \longrightarrow$$

$$\begin{array}{l} CH_2\cdot N \\ | \quad \diagdown\!\!> CPh \\ CH_2\cdot N\cdot COPh \end{array} \xrightarrow{H_2O} \begin{array}{l} CH_2\cdot N \\ | \quad \diagdown\!\!> CPh \\ CH_2\cdot NH \end{array} + Ph\cdot CO_2H$$

The observation of Nölting and Weingärtner (*Ber.*, 1885, **18**, 1340) that acetanilide hydrochloride when heated at 250° gives acetic acid and diphenylacetamidine hydrochloride is capable of a similar explanation.

(4) Chapman (J., 1923, **123**, 1676) found that when *N*-phenylbenzimidophenyl ether hydrochloride was heated, hydrogen chloride was evolved, and one of the products of the reaction was diphenylbenzamidine hydrochloride. He gave no completely satisfactory explanation of the formation of the amidine hydrochloride. This may now be readily accounted for on the basis of the mechanism discussed above, since according to Chapman the imidoether hydrochloride, when heated, first breaks down into benzanilideimidochloride and phenol. The former then reacts as in (2) with the hydrogen chloride subsequently evolved.

$$Ph\cdot C\begin{array}{l}\diagdown\!\!< NPh,HCl \\ \diagup\!\!< OPh\end{array} \longrightarrow Ph\cdot C\begin{array}{l}\diagdown\!\!< NPh \\ \diagup\!\!< Cl\end{array} + HOPh \longrightarrow Ph\cdot C\begin{array}{l}\diagdown\!\!< NPh \\ \diagup\!\!< OPh\end{array} + HCl$$

Phenylacetimidoethyl ether and *p*-tolylacetimidoethyl ether behave in a similar manner when heated in a stream of hydrogen chloride, giving diphenylacetamidine and di-*p*-tolylacetamidine, respectively, and the corresponding anilides.

Lehmann (*Z. angew. Chem.*, 1923, **36**, 360) has observed that the Beckmann transformation can be brought about at 110—120° by heating the oxime in a current of hydrogen chloride or the hydrochloride of the oxime alone, and mentions the case of benzophenoneoxime. This case has been confirmed and the same holds for all the oximes examined in this investigation, amidines being formed simultaneously. Lachman (*J. Amer. Chem. Soc.*, 1924, **46**, 1477),

working on similar lines but using mixtures of small amounts of benzophenoneoxime hydrochloride and oxime, found that the Beckmann transformation took place at temperatures slightly higher than that stated by Lehmann. Lachman's experiments were repeated and the results obtained were substantially the same, but in all cases amidine formation had also taken place. In view of this fact the Beckmann transformation of benzophenoneoxime cannot be represented by the simple change, $CPh_2{:}NOH,HCl$ = $COPh{\cdot}NHPh + HCl$, as suggested by Lachman. It is also significant that the yields of benzanilide obtained by Lachman were not quantitative.

From evidence adduced above and in conformity with the proposed mechanism of amidine formation from oximes, it is exceedingly probable that imidochloride formation is the first stage in Lachman's experiments: $CPh_2{:}NOH,HCl \longrightarrow Ph{\cdot}CCl{:}NPh + H_2O \longrightarrow Ph{\cdot}CO{\cdot}NHPh + HCl$. After the first molecule of benzanilide has been produced, the conditions are favourable for amidine formation [see (3), above].

During a study of the action of phosphorus pentachloride on acetanilide Wallach (*Annalen*, 1882, **214**, 193) obtained a compound, formed by condensation of two molecules of acetanilideimidochloride, which has been identified as diphenylchlorovinylacetamidine (VI) by von Braun, Jostes, and Heymons (*Ber.*, 1927, **60**, 92), who have given a mechanism to account for its formation. It is suggested that an alternative mechanism based on the views of amidine formation developed in this communication would be more in keeping with the experimental results. The conditions of the reaction are favourable to the production of acetanilideamidodichloride and acetanilideimidochloride necessary for the formation of the amidine:

$$\begin{matrix} CH_3{\cdot}CCl{:}NPh \\ + \\ CH_3{\cdot}CCl_2{\cdot}NHPh \end{matrix} \longrightarrow \begin{matrix} CH_3{\cdot}C{:}NPh \\ | \\ CH_3{\cdot}CCl_2{\cdot}NPh \\ \text{(V.)} \end{matrix} \xrightarrow{-HCl} \begin{matrix} CH_3{\cdot}C{:}NPh \\ | \\ CH_2{:}CCl{\cdot}NPh \\ \text{(VI.)} \end{matrix}$$

The formation of (VI) by loss of hydrogen chloride from the intermediate condensation product (V), which contains the ethylidene dichloride structure in a basic molecule, may be compared with the formation of vinyl chloride from ethylidene dichloride.

Reference was made on p. 887 to a bright yellow oil formed by the action of phosphorus pentachloride or thionyl chloride on ketoximes. Henrich and Ruppenthal (*Ber.*, 1911, **44**, 1533) state that this yellow phase is the imidochloride, $R{\cdot}CCl{:}NR$. As, however, imidochlorides do not possess the same intense yellow colour,*

* Von Braun, Jostes, and Münch (*Annalen*, 1927, **453**, 113) have prepared a number of imidochlorides, the majority of which are colourless.

it is probable that the yellow phase is more correctly represented as an amidodichloride, R·CCl_2·NHR, or its hydrochloride, a representation which would account for the readiness with which the yellow oil decomposes, evolving hydrogen chloride with the formation of the imidochloride. The compounds Ph·CCl_2·NHPh, Ph·CClI·NHPh (Lander and Laws, *loc. cit.*), and Ph·CCl_2·NPh_2 are all yellow. Whether the amidodichloride is formed directly from the ketoxime during the Beckmann transformation is a problem which still awaits solution.

The *p*-ethoxybenzophenone required for the experiments on this substance was prepared from phenetole and benzoyl chloride in the usual way; it melted at 48° and distilled at 220°/15 mm., in agreement with Torres y Gonzale (*Bull. Soc. chim.*, 1925, **37**, 1591). The oxime was obtained by the action of hydroxylamine on the ketone in alkaline solution and melted, as reported by Torres y Gonzale (*loc. cit.*), at 135—136°. Repeated crystallisation from alcohol did not change the melting point of the oxime, which thus behaved as an individual substance. The Beckmann transformation, however, gave rise to a mixture of the two amides corresponding to the two forms of the oxime. When the oxime in ethereal solution was treated with hydrogen chloride, a hydrochloride was precipitated from which the oxime of m. p. 135—136° was recovered. The ethereal filtrate deposited a second hydrochloride, from which an *oxime* was obtained, m. p. 143—145°, and 159—160° after repetition of the hydrogen chloride treatment. A mixture (equal parts) of the two oximes melted at 140—150°. The higher-melting oxime gave *p*-ethoxybenzophenone on hydrolysis, and, when subjected to the Beckmann transformation by means of thionyl chloride, yielded *p*-ethoxybenzanilide (approx. 90%) and a trace of amidine. Possibly the lower-melting oxime (135°) is the *anti* *(phenyl)-form (β), and the higher melting one (159—160°) the *syn* *-form (α). Hantzsch (*Ber.*, 1891, **24**, 54) has shown that the two oximes obtained from *p*-methoxybenzophenone are separable by crystallisation and recoverable unchanged from their respective hydrochlorides.

Experimental.

The treatment of the ketoximes with thionyl chloride was the same in all cases, a solution of thionyl chloride (1 mol.) in anhydrous ether (10 vols. : a stronger solution caused the reaction to proceed too violently) being added gradually to an ethereal solution of the ketoxime (1 mol.) at − 5°. The subsequent treatment is outlined in the introduction.

The majority of the amidines and amides isolated are known and

* These terms have the usual significance.

need no description. Diphenylphenacetamidine obtained from phenyl benzyl ketoxime crystallised in needles, m. p. 91° (Luckenbach, *Ber.*, 1884, **17**, 1427, and Busch and Hobein, *Ber.*, 1907, **40**, 4297, give m. p. 107—108°) (Found: C, 83·9; H, 6·3. Calc. for $C_{20}H_{18}N_2$: C, 83·9; H, 6·3%). A specimen identical with it was prepared by treating phenylacetanilide (3·2 g.; 1 mol.) with phosphorus pentachloride (3·2 g.; 1 mol.), removing the phosphoryl chloride under diminished pressure, warming the residual brown oil with aniline (2·8 g.; 2 mols.) on the water-bath for 5 minutes, extracting the product with hot water, making the filtered solution alkaline with ammonia, and crystallising the precipitated amidine from dilute methyl alcohol.

Transformation Products of p-*Ethoxybenzophenoneoxime* (m. p. 135—136°).—The action of thionyl chloride on the oxime produced a mixture of *p*-ethoxybenzanilide and benz-*p*-phenetidide, m. p. 145—151° [a synthetic mixture of equal parts of *p*-ethoxybenzanilide (m. p. 172°) and benz-*p*-phenetidide (m. p. 173°) softens at 146° and melts at 152°]. The mixture was warmed with sulphuric acid (1 : 1), and the acids precipitated on addition of water were collected, dissolved in aqueous sodium carbonate, reprecipitated from the filtered solution by addition of sulphuric acid, and cooled to 0°. The precipitate produced was crystallised from dilute alcohol, *p*-ethoxybenzoic acid being obtained in needles, m. p. and mixed m. p. 195°. The filtrate from the precipitate was extracted with ether, from which benzoic acid was isolated.

p-Ethoxybenzoic acid was conveniently prepared by dissolving *p*-hydroxybenzoic acid (13·8 g.; 1 mol.) in sodium hydroxide (9 g.; 2·25 mols.) in water (90 c.c.), slowly adding ethyl sulphate (19·3 g.; 1·3 mols.), and hydrolysing the oily ethyl *p*-ethoxybenzoate by heating with excess (6 g.) of sodium hydroxide. The solution was acidified and heated to boiling and the very sparingly soluble *p*-ethoxybenzoic acid was filtered off and crystallised from dilute alcohol; m. p. 195° (yield, 12 g.).

p-*Ethoxybenzophenoneoxime*, m. p. 159—160°, cystallised from methyl alcohol in rhombic prisms (Found: C, 74·9; H, 6·3. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·3%).

Experiments with Benzanilideimidochloride.—The imidochloride was prepared according to Wallach (*loc. cit.*) and purified by distillation and by crystallisation from benzene. The diphenylbenzamidine hydrochloride remaining in the distilling flask was dissolved in hot water, and the base precipitated by ammonia and identified by comparison with an authentic specimen.

Benzanilideamidodichloride Hydrochloride, $CPhCl_2{\cdot}NHPh,HCl$.—A solution of the imidochloride (5 g.) in 30 c.c. of anhydrous ether

was saturated with hydrogen chloride. After 2 hours, large yellow prisms were deposited, which were rapidly collected, washed with dry ether, and transferred immediately to a desiccator (Found : Cl, 37·3. $C_{13}H_{12}NCl_3$ requires Cl, 36·9%). The crystals melted indefinitely between 69° and 72° with effervescence, and the melt, after solidifying, remelted at 41° (benzanilideimidochloride). One gram of the crystals was heated in a weighed U-tube in a water-bath at 75°, a slow stream of dry air being passed through the tube. The hydrogen chloride evolved was absorbed in a known volume of *N*-sodium hydroxide [Found : loss in weight (i) 25·5, (ii) 24·54; HCl absorbed (i) 26·33, (ii) 24·55. Calculated loss in weight corresponding to 2HCl, 25·28%]. The contents of the U-tube were treated with water, and the residue of benzanilide removed. The filtrate gave diphenylbenzamidine (0·1 g.) on neutralisation with ammonia.

A weighed quantity of the yellow crystals was placed in a weighed tube in a desiccator, which was evacuated, and the loss in weight of the material observed from time to time. Loss : (i) 3% after 12 hours; (ii) 12·47% (36 hours); (iii) 19·76% (60 hours); (iv) 24·7% (4 days) (constant). The loss in (ii) corresponds to 1 mol. of hydrogen chloride (calc., 12·6%), and the condition at this stage would be amidodichloride, $CPhCl_2{\cdot}NHPh$. The final stage (iv) corresponds to a loss of 2 mols. of hydrogen chloride (calc., 25·28), and the residue was benzanilideimidochloride. A weighed quantity of the yellow crystals was dissolved in anhydrous ether, the solvent removed under diminished pressure, and the residue weighed (Found : loss, 24·5. Calc. for loss of 2HCl : 25·28%).

The quantity of benzanilide formed by treating the yellow crystals with water was determined (Found : 67·07. Calc. : 68·31%). The aqueous filtrate, treated with ammonia, gave a small amount of diphenylbenzamidine, the formation of which can only be explained on the assumption that some of the amidodichloride hydrochloride had already lost hydrogen chloride, the imidochloride formed then reacting as indicated in the introduction.

Effect of Heat on the Hydrochlorides of Ketoximes.—The hydrochlorides of acetophenoneoxime, *p*-methylacetophenoneoxime, propiophenoneoxime, *n*-butyrophenoneoxime, and benzophenoneoxime were separately heated until reaction began, indicated by a vigorous effervescence. After treatment of the product in each case with water, the anilides formed as a result of the Beckmann transformation were isolated by filtration, and the amidines precipitated from the filtrates by ammonia. The results were as given on p. 887. The yield of each amidine from 1 g. of ketoxime was 0·1 g.

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