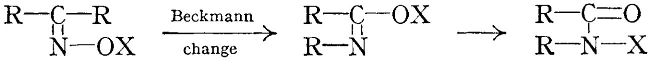
290. *Studies of the Beckmann Change. Part III. The Rearrangement of Ketoxime Hydrochlorides.*

By Arthur W. Chapman.

In Parts I and II of this series (J., 1933, 806; 1934, 1550), observations on the spontaneous Beckmann rearrangement of ketoxime esters and ethers (I) were discussed, and reasons were adduced (compare also *Chem. and Ind.*, 1935, **54**, 463) for regarding the exchange of positions by the hydrocarbon radical and the group —OX of the oxime ether in these cases as truly intramolecular.



$$\begin{matrix}\mathrm{R{-}C{-}R}\\ \Vert\\ \mathrm{N{-}OX}\end{matrix} \xrightarrow[\text{change}]{\text{Beckmann}} \begin{matrix}\mathrm{R{-}C{-}OX}\\ \Vert\\ \mathrm{R{-}N}\end{matrix} \longrightarrow \begin{matrix}\mathrm{R{-}C{=}O}\\ |\\ \mathrm{R{-}N{-}X}\end{matrix}$$

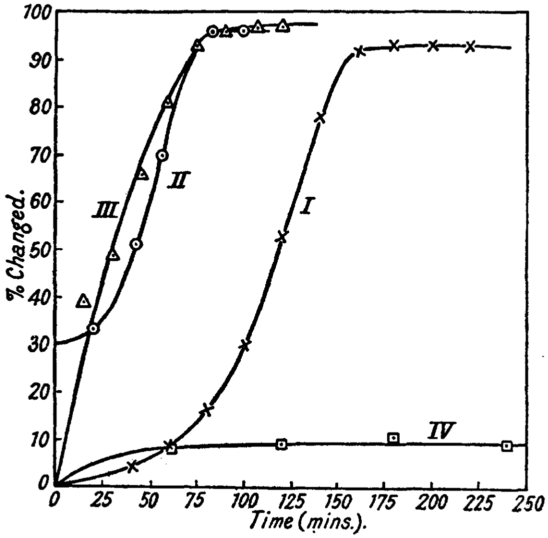
(I.) (II.) (III.)

(X = picryl and certain acyl radicals.)

The action of many of the reagents employed to bring about the Beckmann change of oximes may be explained as the initial production of such an ester (I) from the oxime and reagent, and its subsequent transformation whenever the group —OX has a sufficient attraction for electrons. The immediate product of rearrangement (II or III) is generally decomposed into the simple amide during the working up of the material. Reagents in this class are the chlorides and oxychlorides of phosphorus and sulphur, the arylsulphonyl chlorides, and probably sulphuric acid.

Hydrogen chloride, on the other hand, although a potent agent for effecting the Beckmann change, cannot be fitted into this simple system. An almost quantitative conversion of a ketoxime into the corresponding amide can be obtained by heating the oxime and hydrogen chloride together in a suitable solvent, or even by fusion of the dry oxime hydrochloride, whilst the efficacy of the chlorides of the weaker organic acids as reagents for the Beckmann change doubtless also depends on the formation of this compound. Stieglitz and Peterson (*Ber.*, 1910, **43**, 782) and Peterson (*Amer. Chem. J.*, 1911, **46**, 325) have shown, however, that the *N*-chloro-compounds $\begin{matrix}\mathrm{R{-}C{-}R}\\ \Vert\\ \mathrm{NCl}\end{matrix}$ (IV) which correspond with (I) do not undergo rearrangement. Numerous hypothetical mechanisms have been suggested but none has proved satisfactory. It was therefore decided to reinvestigate the whole question of the Beckmann change of a ketoxime in the presence of hydrogen chloride, by employing a homogeneous system and conditions which permitted a quantitative study of the rearrangement. Benzophenoneoxime was chosen as the oxime and ethylene dichloride as the solvent.

A study of the progress of the rearrangement at 100° showed that the change was complex. The time required for a given amount of change to take place depended on the concentration of hydrogen chloride, but the general shape of the time–rearrangement curve was the same over a wide range of concentration. A typical example is shown in the figure (Curve I). At first the rearrangement was very slow but the rate steadily increased until, after about 30% of the material had been changed, it reached a nearly constant and relatively high value which was maintained until the conversion was complete, the product being almost pure benzanilide. An identical period of slow but increasing velocity of change was observed when the hydrogen chloride was introduced as oxime hydrochloride, so that delay in the formation of this compound was not the reason for the slow beginning. When, however, a mixture containing 30% of benzanilide and 70% of oxime was employed as starting material the initial slow period was much shorter, and was followed immediately by a rapid change identical with the rapid phase of the rearrangement starting from the pure oxime (Curve II). It was also found that replacement of part of the solvent ethylene dichloride by alcohol completely inhibited the change.



I. 0·42 *Mol.* HCl : *starting from pure oxime.*
II. 0·42 *Mol.* HCl : *starting from* 30% *anilide,* 70% *oxime.*
III. 0·41 *Mol.* HCl + 0·002 *mol. benzanilideimidochloride.*
IV. 0·002 *Mol. benzanilideimidochloride.*

These observations suggested that the main part of the rearrangement was brought about through the agency of some substance formed from the benzanilide first produced, and destroyed, or prevented from being formed, in the presence of alcohol. A possible substance of this kind was benzanilideimidochloride (V), for the production of which from benzanilide and hydrogen chloride there is already some evidence (Stephen and Bleloch, J., 1931, 886) :

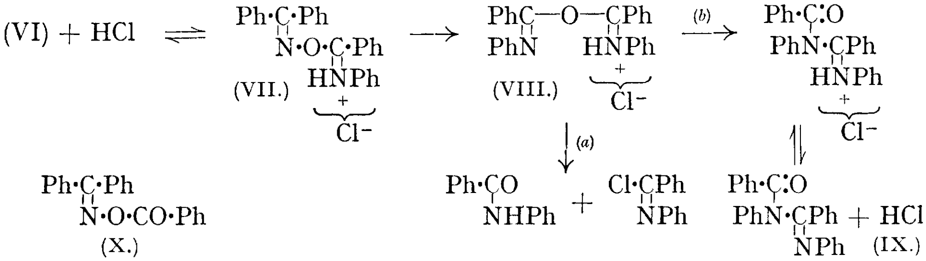
$$\mathrm{Ph{\cdot}CO{\cdot}NHPh + HCl \rightleftharpoons Ph{\cdot}CCl{:}NPh\ (V) + H_2O}$$

A test of the influence of this substance on the rearrangement was therefore carried out. In similar solutions and under conditions identical with those previously employed, the addition of 0·002 mol. of benzanilideimidochloride (reckoned on the oxime) completely abolished the initial slow period. Rearrangement took place throughout at approximately the rate of the rapid phase of the previous transformations (Curve III). Larger quantities of imidochloride caused the change to be too rapid for measurement. In ethereal solution at room temperature, when a large excess of hydrogen chloride failed to cause any appreciable change in 3 days, the addition of sufficient imidochloride brought about the transformation within 30 mins. In the absence of hydrogen chloride, however, the presence of traces of imidochloride was not sufficient to cause complete change. Under conditions similar to those used in the other quantitative experiments, 0·002 mol. of benzanilideimidochloride sufficed to convert only 10% of oxime into anilide, the process stopping at this stage (Curve IV). Both reagents, therefore, appear necessary for complete and rapid transformation unless considerable amounts of imidochloride are employed.

When these facts were compared with those obtained in the study of the oxime picryl ethers, a simple explanation became apparent. Condensation of benzanilideimidochloride and benzophenoneoxime should yield the oxime *ether* (VI) and hydrogen chloride :

$$\mathrm{Ph_2C{=}NOH + Ph{\cdot}C({:}NPh)Cl \longrightarrow Ph_2C{=}N{-}O{-}CPh{:}NPh\ (VI) + HCl}$$

Compound (VI) would not be expected to undergo spontaneous Beckmann transformation in the free state, since it is derived from the very feebly acidic benzanilide, but the opposite is true of the cation of its salts (VII). The positively charged nitrogen atom in the ether group would confer a strong attraction for electrons on the whole radical, which should then behave like the picryloxy-group in the oxime picryl ethers and readily undergo rearrangement to (VIII). The latter compound is of the imido-ether type and may undergo either



or both of two further reactions. It may, especially in the presence of an excess of hydrogen chloride, break down to benzanilide and benzanilideimidochloride (process *a*), which thus becomes available for reaction with further quantities of oxime ; or it may undergo further rearrangement, analogous to that of *N*-phenylbenzimidopicryl ether (compare Part I, *loc. cit.*, p. 807), yielding benzoyl-*s*.-diphenylbenzenylamidine (IX) (process *b*).

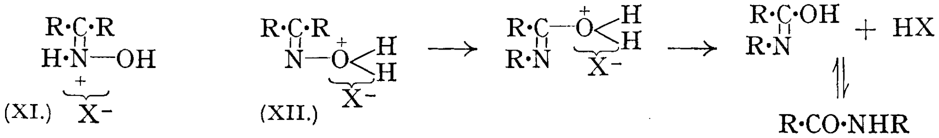
Provided that the major part of (VIII) be decomposed in the sense of reaction (*a*), the scheme provides an explanation of the catalytic effect of the imidochloride and, through the alternative process (*b*), furnishes a further reason for the presence, already recorded by Stephen and Bleloch (*loc. cit.*), of a small amount of *s*.-diphenylbenzenylamidine in the product obtained when benzophenoneoxime hydrochloride is heated.

A direct test of these views was, however, sought in the examination of the essential intermediate compound (VI). This substance was obtained, together with a small amount of the corresponding *N*-ether, by interaction of the sodium compound of benzophenoneoxime with benzanilideimidochloride in ethereal-alcoholic solution, and its constitution was confirmed by its oxidation under mild conditions to benzophenoneoxime benzoate (X). When heated alone, it decomposed without yielding any benzanilide, but with acid reagents it reacted immediately at room temperature precisely as required by the scheme of rearrangement. With concentrated aqueous hydrochloric acid it was converted quantitatively into benzanilide, and with excess of dry ethereal hydrogen chloride gave a mixture of benzanilide and benzanilideimidochloride ; whilst in ethereal solution with a trace of sulphuric acid, which would not be expected to bring about the rupture of (VIII), it yielded the alternative product benzoyl-*s*.-diphenylbenzenylamidine (IX). It also exerted a catalytic effect on the rearrangement of benzophenoneoxime by hydrogen chloride, identical with that of an equivalent amount of benzanilideimidochloride.

The conclusion cannot, therefore, be resisted that the main progress of the Beckmann rearrangement of ketoxime hydrochlorides of this type occurs through the intermediate steps described, and hence that the transformation proper takes place in a manner identical with that of the spontaneous change of the oxime ethers and esters.

To provide a complete explanation of the rearrangement a further mechanism is nevertheless necessary. The one already described will account for the change after the first trace of anilide has been formed, but this first trace must be produced by a different process which, no doubt, continues side by side with the other throughout the whole course of the conversion. As regards the nature of this second process, inspection of the time–rearrangement curve (Curve I) shows that its speed is of an altogether lower order than that of the change when catalysed by the imidochloride. In the second place, by substituting a different acid catalyst for hydrogen chloride, it has been shown that there is no reason to regard the anilideimidochloride as an intermediate product of the rearrangement (compare Stephen and Bleloch, *loc. cit.*, p. 888). Benzophenoneoxime was rearranged by heating in solution with picric acid. The process was very slow, like the initial stage of the rearrangement by hydrogen chloride, and the transformation product was benzanilide. Had the change occurred through *N*-phenylbenzimidopicryl ether (II; X = picryl), which for picric acid as catalyst corresponds with benzanilideimidochloride, the product would have been benz-*N*-picrylanilide (III; X = picryl), which is stable and could readily have been isolated under the conditions employed.

Although the course of this slow transformation cannot yet be formulated with certainty, there is one mechanism, suggested to the author by Professor G. M. Bennett, which does not conflict with any of the known facts. The salt of an oxime should contain both ammonium (XI) and oxonium (XII) forms in equilibrium, although the proportion of the latter may be exceedingly small. The group $\overset{+}{O}H_2$ in the oxonium salt will have an attraction for electrons greater even than, say, that of the picryloxy-group, and the oxonium ion will therefore readily undergo the Beckmann change. Any sufficiently



strong acid should thus be capable of bringing about the rearrangement of a ketoxime into the corresponding amide, but the transformation may be very slow on account of the minute amount of oxonium salt present. This suggestion would account for the rearrangement of benzophenoneoxime in aqueous acid solution (Lachmann, *J. Amer. Chem. Soc.*, **1925**, **47**, 260), and has the advantage of bringing the outstanding apparent exceptions into that general scheme of the Beckmann change which includes the spontaneous transformations of oxime ethers and esters.

The results of the present study may therefore be summarised as follows. The Beckmann rearrangement of benzophenoneoxime by hydrogen chloride is complex, and two distinct processes are operative: (i) A relatively very slow change brought about by the acid alone, for which a provisional mechanism is outlined—the anilideimidochloride is not an intermediate product in this rearrangement. (ii) A much more rapid change, beginning as soon as a trace of benzanilide has been formed by process (i), and taking place through a series of recognisable intermediate products: this process accounts for the greater part of the transformation.

The course of the rearrangement in both cases is in agreement with the view, already applied to the spontaneous transformation of oxime ethers and esters, that the Beckmann change proper is an intramolecular exchange of positions by the hydrocarbon radical and the group attached to the nitrogen atom of the oxime derivative.

EXPERIMENTAL.

Ethylene dichloride was chosen as the solvent for most of the experiments as being chemically inert, a sufficiently good solvent for all the materials concerned, moderately polar, and easily evaporated. The commercially pure material was heated under reflux with phosphoric oxide to remove water and alcoholic impurities, and redistilled twice. It boiled over a range of 0·1°.

Rearrangement of Benzophenoneoxime in Ethylene Dichloride Solution.—2 G. of the oxime were placed in each of a number of glass tubes, and the appropriate quantities of ethylene dichloride, of solutions of dry hydrogen chloride, and, if necessary, of any other catalyst in the same solvent were added so as to give the amounts of reagents required and a total volume of 25 c.c. of solvent. The tubes were sealed, and heated in a water thermostat. On withdrawal, they were chilled in cold water, and the contents transferred to a separating funnel, diluted with chloroform, and washed, first with excess of *N*-sodium carbonate to remove hydrogen chloride and then with water, and finally evaporated to dryness on the steam-bath. The residues were powdered, dried first in a steam-oven and then in a vacuum desiccator, and analysed as described below.

If the heating had been sufficiently prolonged, the products obtained on evaporation of the ethylene dichloride–chloroform solutions consisted of almost pure benzanilide. M. p.'s up to 160° were obtained for the product of rearrangement with hydrogen chloride alone as catalyst, and of 162—164° when a small quantity of benzanilideimidochloride had also been added.

Analysis of the products of rearrangement. 1 G. of the dry powdered product was weighed into a beaker and stirred with 20% aqueous sodium hydroxide (20 c.c.), diluted with water (25 c.c.), heated with stirring to 90° to dissolve all unchanged oxime, cooled, warmed again to 40° to redissolve any oxime sodium compound that had crystallised out, and filtered through a weighed glass crucible. The residue of benzanilide was washed with 10% aqueous sodium hydroxide and then with water, dried at 110—120°, and weighed. Control experiments showed that the method gave results accurate to about 1%.

The results obtained in the quantitative experiments are given in the following tables, the values for Expts. 3, 4, and 5 showing the reproducibility attainable.

Rearrangement in presence of hydrogen chloride only as catalyst.

Temp. = 100° unless otherwise stated; *t* = time of heating (minutes); *x* = % benzanilide in product.

1.		2.		3.		4.		5.*		6.†		7.‡		8.		9.§		10.‖	
Mols. HCl per mol. of oxime.																			
1·17		0·75		0·41		0·41		0·42		0·39		0·42		0·16		0·40		1·1	
t.	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*
45	95	10	1	46	5	20	1	40	4	20	2	(0	30)	30	0	120	0	15	0
90	97	20	6	90	20	40	4	60	9	42	6	20	33	90	1			31	2
		40	22	135	60	60	9	80	16	71	12	43	51	186	6			45	5
		61	86	197	95	80	17	100	30	116	36	60	77	271	12			60	8
		80	95			100	34	120	53			83	96	357	19			75	13
								141	78			100	96					90	17
								160	92									106	27
								180	93									120	37
								200	93									135	65
								220	93									150	90

* The residues of benzanilide were collected from the crucibles and had m. p. 157—161°.
† Hydrogen chloride introduced in the form of oxime hydrochloride.
‡ Starting material: 0·6 g. benzanilide, 1·4 g. oxime per tube.
§ Solvent: 15 c.c. anhydrous EtOH, 10 c.c. ethylene dichloride per tube.
‖ At 80°.

Rearrangement in presence of hydrogen chloride and a further added catalyst.

Temp. = 100°; V = benzanilideimidochloride; VI = benzophenoneoxime *O*-α-phenyliminobenzyl ether.

Experiment.	11.*		12.†		13.		14.		15.		16.		17.	
Mols. HCl per mol. of oxime	0·39		0·36		0·36		0·41		0·42		nil		nil	
	V.		V.		V.		V.		VI.		V.		V.	
Added catalyst, mols. per mol. of oxime ...	0·05		0·02		0·002		0·002		0·002		0·002		0·01	
	t.	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*	*t.*	*x.*
	20	98	20	97	20	37	15	39	15	36	62	8	30	25
	40	98	40	98	40	51	30	49	30	48	120	9	60	32
					60	70	45	66	45	65	180	10	90	36
					80	84	60	81	60	79	240	9	120	35
							75	93	75	93			150	36
							90	96	90	96			180	37
							105	97	105	97				
							120	97	121	96				

* Residue from evaporation of washed solutions before analysis, m. p. 162—164°.
† ,, ,, ,, ,, ,, ,, ,, 160—162°.

Preparation and Properties of Benzophenoneoxime O-α-*Phenyliminobenzyl Ether* (VI).—To benzophenoneoxime (92 g.), dissolved in dry ether (1 l.), was added a solution of sodium (10 g.) in absolute alcohol (600 c.c.) and then one of benzanilideimidochloride (82 g.) in dry ether (500 c.c.). Sodium chloride was rapidly precipitated, and the mixture was set aside over-night. The ethereal solution was then washed with water to remove sodium salts, alcohol (350 c.c.) was added to it to replace some of that washed out (in order to avoid decomposition on evaporation), and the bulk of the ether distilled off. To the resulting alcoholic solution, a further 150 c.c. of alcohol were added, and the material was allowed to crystallise. The resulting crude product (78 g.) melted at 71—74° to a turbid liquid still containing minute crystals, which cleared at about 113°.

Purification of the material from the higher-melting by-product was finally achieved by solution in light petroleum (b. p. 60—80°), which left the impurity almost entirely undissolved, crystallisation from this solvent, and recrystallisation from alcohol. *Benzophenoneoxime* O-*α-phenyliminobenzyl ether*, thus obtained, formed pale yellow crystals, m. p. 72—76°, moderately soluble in alcohol and light petroleum (Found * : C, 82·8; H, 5·3; N, 7·6. $C_{26}H_{20}ON_2$ requires C, 82·9; H, 5·35; N, 7·45%). When heated at or above 100°, it changed into a brown material from which no definite substance has been isolated.

In the following experiments the identities of all materials produced were confirmed by mixed m. p.'s with authentic samples.

3 G. of (VI), dissolved in glacial acetic acid (20 c.c.), were added to a mixture of finely powdered potassium permanganate (9 g.) and glacial acetic acid (25 c.c.); the solution turned brown at once and became warm. After standing for 2 hours, the mixture was filtered, and the filtrate diluted with water (700 c.c.) and reduced with sulphur dioxide. Benzophenoneoxime benzoate was left as a copious white precipitate, m. p. 94—98°, and 101—103° after crystallisation from alcohol.

To 1 G. of (VI), concentrated hydrochloric acid (5 c.c.) was added. The solid immediately became white, and the mixture became warm. After dilution with an equal bulk of water, and short standing, the mixture was made slightly alkaline with sodium hydroxide, and the residual benzanilide filtered off, and dried (1 g., m. p. 157—160°).

To 1 G. of (VI), dissolved in dry ether (5 c.c.), was added a solution of dry hydrogen chloride in ether (5 c.c., approx. 3·5*N*). A vigorous reaction took place at once, and a crystalline deposit was formed. After short standing, the solution was filtered. The residue (0·45 g.) consisted of benzanilide, m. p. 161—162°. The filtrate was poured into excess of a solution of sodium phenoxide in alcohol, from which was then isolated *N*-phenylbenzimidophenyl ether (0·5 g., m. p. after recrystallisation 105°), which could only have been produced from benzanilideimidochloride in the original filtrate.

To 1 G. of (VI) in dry ether was added sulphuric acid (0·01 g.) in ethereal solution. A trace of salt was deposited, the solution turned deeper yellow, the ether began to boil, and a copious deposit of crystals was formed. When obvious reaction was over, the mixture was filtered, and the residue was found to consist of benzoyl-*s*.-diphenylbenzenylamidine (m. p. 165—170°, and 172—173° after recrystallisation).

The by-product from the preparation of (VI), which was separated by its insolubility in light petroleum, formed 5—10% of the whole crude material. On recrystallisation from alcohol, it yielded intensely yellow crystals, m. p. 178—179° (Found * : C, 82·9; H, 5·4; N, 7·6. $C_{26}H_{20}ON_2$ requires C, 82·9; H, 5·35; N, 7·45%). It also yielded benzanilide with concentrated hydrochloric acid, and benzanilide and benzanilideimidochloride with ethereal hydrogen chloride, but it did not yield any benzoyl-*s*.-diphenylbenzenylamidine with ethereal sulphuric acid. It was accordingly regarded as *benzophenoneoxime* N-*α-phenyliminobenzyl ether*. The formation of benzanilide and benzanilideimidochloride from it may be explained as a decomposition into oxime and anilideimidochloride, followed by the immediate Beckmann change that has been found to occur under such conditions.

Beckmann Rearrangement of Benzophenoneoxime by Benzanilideimidochloride at Room Temperature.—To benzophenoneoxime (1 g.), dissolved in dry ether (10 c.c.), was added benzanilideimidochloride (1 g.) in the same solvent (5 c.c.). After some time, flaky crystals began slowly to deposit, and after standing over-night they filled the solution. They were collected, washed with ether, and identified as benzanilide (0·85 g., m. p. 161—162°).

To benzophenoneoxime (1 g.) in dry ether (5 c.c.) was added benzanilideimidochloride (1 g. in 5 c.c. ether), followed by a concentrated solution of hydrogen chloride in dry ether (5 c.c., approx. 6*N*). An immediate granular precipitate of oxime hydrochloride was produced, but this rapidly gave place to shining flakes of benzanilide (0·85 g., m. p. 159—161°), the whole process being complete within 30 minutes.

* Micro-determinations by Dr. A. Schoeller.

A similar addition of ethereal hydrogen chloride to benzophenoneoxime (1 g.) in ether (10 c.c.) in the absence of benzanilideimidochloride produced a stable precipitate of oxime hydrochloride. After the mixture had stood for 3 days, the precipitate was still completely soluble in aqueous sodium hydroxide.

Rearrangement of Dry Benzophenoneoxime Hydrochloride.—The hydrochloride (5 g.), contained in an open test-tube, was heated slowly in an oil-bath. Reaction began at about 130°, the temperature of the mass rose to over 200° in 15 seconds, and torrents of hydrogen chloride were evolved. After cooling, the product melted at 145—156°. It gave pure benzanilide on recrystallisation from alcohol, but on extraction with water and dilute hydrochloric acid yielded *s*.-diphenylbenzenylamidine (m. p. 138—142°; 145—146° after recrystallisation) in quantities ranging from 2 to 5% of the crude change product. These yields are distinctly lower than those recorded by Stephen and Bleloch. On the other hand, when the hydrochloride was heated in a sealed tube for 3 hours at 180—200°, a sticky product was obtained, consisting mainly of benzanilide, but yielding 20% by weight of the amidine.

Rearrangement of Benzophenoneoxime by Picric Acid.—Benzophenoneoxime (2 g.), picric acid (5 g.), and ethylene dichloride (25 c.c.) were heated in a sealed tube at 100° for 15 hours. The solvent was evaporated, and the residue repeatedly extracted with warm dilute aqueous sodium carbonate to remove picric acid. The residue (1·7 g.) consisted of unchanged oxime, m. p. 138—142°. Repetition of this procedure with nitromethane as solvent (12 hrs.' heating) gave a crude product, m. p. 112—125°, which on separation with aqueous sodium hydroxide yielded benzanilide (0·95 g., m. p. after recrystallisation 162—163°) and unchanged oxime (0·55 g., m. p. 138—142°). No benz-*N*-picrylanilide could be detected, and blank experiments showed that this material was quite stable under the conditions employed. The oxime was not rearranged by similar heating alone in nitromethane solution.

Unsuccessful attempts were made to prepare di-(α-phenyliminobenzyl) ether, the base corresponding with (VIII), by interaction of benzanilideimidochloride and dry silver oxide. They yielded benzoyl-*s*.-diphenylbenzenylamidine and a little benzanilide as the only isolable products.

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