KINETICS AND MECHANISM OF THE BECKMANN REARRANGEMENT

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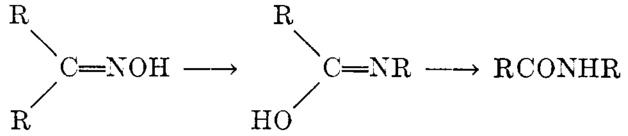
Progress in the field of reaction mechanism is slow and uncertain. Rarely have the mechanisms of chemical reactions been elucidated at their first investigation, and, looked at in retrospect, many of the early attempts to unravel their complexities reflect the gradual development of chemical thought and the increasing precision of physicochemical conceptions. The Beckmann rearrangement is here no exception. First observed in 1886, it was represented by Beckmann (1, 2) as a direct interchange of the hydroxyl group of the oxime and one of the hydrocarbon groups, followed by the spontaneous migration of the hydrogen to give the true amide.



Because the rearrangement could be readily effected by a wide variety of reagents, Beckmann considered it was highly unlikely that any single intermediate compound or any single type of intermediate compound was involved, and regarded the function of the reagent as simply that of a catalyst.

Attempts to formulate a detailed mechanism soon led to controversy. Theories based on the formation of intermediate compounds put forward independently by Hantzsch (11), Wallach (28), and others had but little success, for almost invariably the compounds formulated as intermediates were found by later workers to be incapable of undergoing rearrangement (*cf.* Montagne (22) and Stieglitz and Peterson (27)). Theories based on the formation of free radicals were no more successful. For example, although recent research has emphasized the close similarity and intramolecular character of several classes of carbon–nitrogen rearrangements, such as the Beckmann rearrangement, the Hofmann degradation of amides, and the Curtius and Lossen rearrangements, Stieglitz's early attempt to coördinate them by a single mechanism achieved such coördination only by overemphasizing formal similarities at the expense of real differences (*cf.* Watson (29)).

It is not necessary here to review in detail the early theories of the mechanism of the Beckmann change. A full account of them, and of Meisenheimer's elucidation of the migration as one involving *trans* groups, have been given by Blatt[1] (3). In recent years support for Meisenheimer's view has been given by Mills (21), who has shown that a *trans* migration is probable on stereo-

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[1] A complete bibliography of the early work on the Beckmann change is given by Blatt.

chemical grounds. The simultaneous wandering of the hydroxyl and hydrocarbon groups, and the greater ease with which this can occur in *trans* rather than in *cis* migration, is shown by the model in figure 1, which is due to Mills (21).

The present article reviews the advances made in the field of the kinetics and mechanism of the rearrangement, chiefly as a result of the researches of Kuhara and Chapman. These researches have greatly enlarged our knowledge of the factors which influence the change and have contributed much towards a final solution of the problem.

The most important of the earlier investigations of the mechanism of the rearrangement are those of Kuhara (14). Carrying out an extensive investigation of the effect of acid chlorides, he concluded that it is the esters (acyl derivatives) of the oximes and not the oximes themselves which undergo rearrangement—a view which had been adumbrated by Sluiter (25) for the rearrangement of acetophenone oxime in concentrated sulfuric acid. Kuhara (15) found that certain esters, such as the benzenesulfonyl ester of benzophenone oxime, rearranged spontaneously, while others, such as the acetate, required the presence of hydrogen chloride to bring about rearrangement. The conversion of benzophenone oxime under the influence of acetyl chloride was formulated by Kuhara as follows:

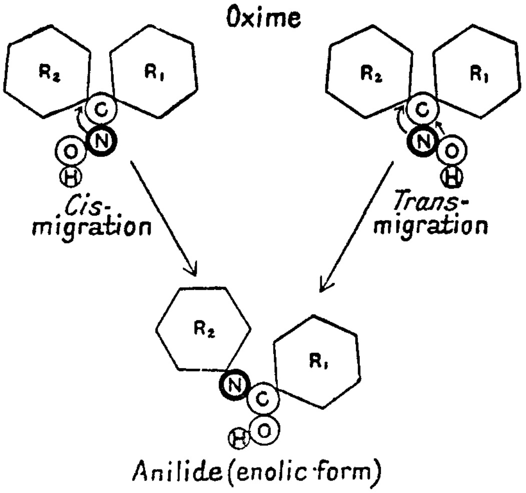
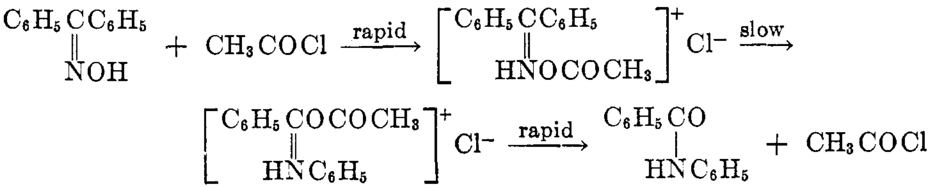


FIG. 1



$$\begin{array}{c} C_6H_5CC_6H_5 \\ \| \\ NOH \end{array} + CH_3COCl \xrightarrow{\text{rapid}} \left[\begin{array}{c} C_6H_5CC_6H_5 \\ \| \\ HNOCOCH_3 \end{array}\right]^+ Cl^- \xrightarrow{\text{slow}}$$

$$\left[\begin{array}{c} C_6H_5COCOCH_3 \\ \| \\ HNC_6H_5 \end{array}\right]^+ Cl^- \xrightarrow{\text{rapid}} \begin{array}{c} C_6H_5CO \\ | \\ HNC_6H_5 \end{array} + CH_3COCl$$

Here, the amount of oxime converted into benzanilide was independent of the quantity of acetyl chloride used, provided this was in excess.

Kuhara's formulations of the transformations are by no means consistent, but the implication in the case of the acetate is that salt formation is a necessary prerequisite to rearrangement and that the ester of a weak acid rearranges only in the form of its salt. When the pure oxime acetate was treated with less than the equivalent of hydrogen chloride, the quantity of ester rearranged was proportional to the amount of acid used, while with an excess of hydrogen chloride it was proportional to the quantity of ester. Precisely what does occur during the rearrangement of the acetate in the presence of hydrogen chloride is not clear. The ion itself may rearrange; on the other hand, the salt of the ester may break down to give the oxime hydrochloride, which then rearranges in accordance with Chapman's mechanism (7) for ketoxime hydrochlorides. In this connection it is significant that the only product isolated and characterized by Kuhara from the rearrangement of benzophenone oxime acetate in the presence of hydrogen chloride was benzanilide.

TABLE 1

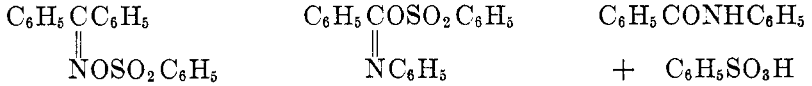
Rearrangement of benzophenone oxime to benzanilide by acid chlorides

$T = 60°C.$

TIME	PERCENTAGE BENZANILIDE		
REAGENT	$C_6H_5SO_2Cl$	$CH_2ClCOCl$	CH_3COCl
minutes			
10	93.2	61.0	0.0
30		66.1	9.4
60		70.7	26.9
90		74.9	37.2
120		76.9	43.9

At the time Kuhara was carrying out his investigations of the rearrangement, Meisenheimer's elucidation (20) of the change as one involving a *trans* interchange of groups had not been made, and, regarding the transformation as one involving a *cis* interchange, Kuhara suggested that the initiating factor in the change was the tendency of the acid residue to separate from the nitrogen atom. The rearrangement was found to be facilitated by an increase in temperature, by an increase in the hydrogen-ion concentration of the medium, and also by an increase in the electron-attracting nature of the acyl group, i.e., the greater the strength of the acid corresponding to the acyl group the more facile the rearrangement. This is shown by the data in table 1, where the relative effectiveness of acetyl, chloroacetyl, and benzenesulfonyl chlorides as reagents for the conversion of benzophenone oxime to benzanilide are compared, and also by the fact that the benzenesulfonyl ester will not only rearrange spontaneously but will do so in alkaline solution, whereas the acetate requires the presence of hydrogen chloride to induce it to undergo rearrangement. Kuhara (17) demonstrated that these rearrangements followed a unimolecular course (*cf.* Sluiter (25)).

A further important contribution was made by Kuhara and his school (16). From the reaction of benzenesulfonyl chloride and the sodium salt of benzophenone oxime at low temperature, the benzenesulfonate (I) of the oxime was isolated as a colorless crystalline solid; this gradually changed on standing at room temperature, or in chloroform solution, or on exposure to ultraviolet light to a viscous yellow ester (II). The same change occurred on melting, but now it occurred instantaneously and with explosive violence. The ester was unstable, and gradually changed in moist air, and instantly on treatment with water, to benzanilide and benzenesulfonic acid.



$$\begin{array}{ccc} \begin{array}{l} \mathrm{C_6H_5CC_6H_5} \\ \quad \| \\ \quad \mathrm{NOSO_2C_6H_5} \end{array} & \begin{array}{l} \mathrm{C_6H_5COSO_2C_6H_5} \\ \quad \| \\ \quad \mathrm{NC_6H_5} \end{array} & \begin{array}{l} \mathrm{C_6H_5CONHC_6H_5} \\ \\ + \quad \mathrm{C_6H_5SO_3H} \end{array} \end{array}$$

I (colorless) II (yellow)

It was shown, moreover, that the product obtained from benzanilideiminochloride[2] and silver benzenesulfonate had properties similar to those of the yellow ester (15), e.g., both exhibited the same absorption spectra.

Summarizing, it is clear that the special significance of Kuhara's work lies in the demonstration that esters of ketoximes may undergo the Beckmann change spontaneously and without the formation of obvious by-products. But since the yellow intermediate products obtained from the benzenesulfonyl derivatives were oils which could not be purified readily, and since, moreover, it was not certain whether the original esters were entirely free from sulfonic acid, the validity of Kuhara's view of the rearrangement could not be accepted without reserve. The conclusion to be drawn provisionally is that the esters of ketoximes rearrange spontaneously when the acid group is sufficiently electron-attractive in character but, when this is not so, then salt formation as in the case of the acetate is an essential prerequisite to rearrangement.

At this stage the study of the Beckmann change was taken up by Chapman (10). To establish the correctness of Kuhara's view of the rearrangement it was necessary to replace the sulfonic esters by compounds which, if they underwent a similar change, would yield crystalline products which could be identified with certainty, tested for purity, and estimated quantitatively. Chapman showed that the oxime picryl ethers fulfilled these requirements and that their rearrangement was a true Beckmann change. Benzophenone oxime picryl ether (III) was transformed almost explosively at its melting point into benz-*N*-picrylanilide (V), and in a suitable solvent complete change took place without measurable by-products. In this rearrangement *N*-phenylbenziminopicryl ether (IV) is no doubt an intermediate product but is itself too unstable to be isolated, for reactions which should result in its formation yield benz-*N*-

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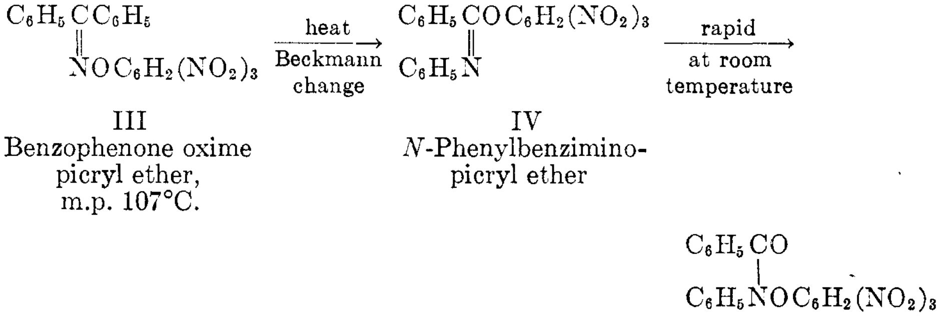
[2] Also called benzanilideimidochloride; the name "*N*-phenylbenzimidyl chloride" is preferred by *Chemical Abstracts*.

picrylanilide at room temperature (*cf.* Mumm, Hesse, and Volquartz (23); Chapman (5)).



$$\begin{array}{l}\text{C}_6\text{H}_5\text{CC}_6\text{H}_5\\ \quad\|\\ \quad\text{NOC}_6\text{H}_2(\text{NO}_2)_3\end{array}\xrightarrow[\text{Beckmann change}]{\text{heat}}\begin{array}{l}\text{C}_6\text{H}_5\text{COC}_6\text{H}_2(\text{NO}_2)_3\\ \qquad\|\\ \text{C}_6\text{H}_5\text{N}\end{array}\xrightarrow[\text{at room temperature}]{\text{rapid}}\begin{array}{l}\text{C}_6\text{H}_5\text{CO}\\ \qquad|\\ \text{C}_6\text{H}_5\text{NOC}_6\text{H}_2(\text{NO}_2)_3\end{array}$$

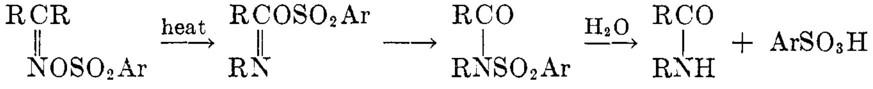
III
Benzophenone oxime picryl ether, m.p. 107°C.

IV
N-Phenylbenziminopicryl ether

V
Benz-*N*-picrylanilide, m.p. 199°C.

The picryl ether of actophenone oxime gave pure acet-*N*-picrylanilide, and the picryl and trinitro-*m*-tolyl ethers of other ketoximes underwent similar rearrangement.

In this connection it should be noted that Kuhara assigned formula VII to the rearrangement product of the sulfonyl ester (VI), but as this represents an imino ester derived from a strong acid, and as such would undergo intramolecular change to the *N*-acyl compound very readily, Chapman (10) suggested that formula VIII represents the more probable structure.



$$\begin{array}{l}\text{RCR}\\ \;\|\\ \text{NOSO}_2\text{Ar}\end{array}\xrightarrow{\text{heat}}\begin{array}{l}\text{RCOSO}_2\text{Ar}\\ \;\|\\ \text{RN}\end{array}\longrightarrow\begin{array}{l}\text{RCO}\\ \;|\\ \text{RNSO}_2\text{Ar}\end{array}\xrightarrow{\text{H}_2\text{O}}\begin{array}{l}\text{RCO}\\ \;|\\ \text{RNH}\end{array}+\text{ArSO}_3\text{H}$$

VI VII VIII

A kinetic study (see table 2) of the rearrangement (10) of the picryl ethers of acetophenone and benzophenone oximes in such solvents as carbon tetrachloride, benzene, chloroform, and ethylene dichloride at temperatures between 40° and 116° C. showed that the rearrangement followed a unimolecular course—the labile nature of the *N*-phenylbenziminopicryl ether ensuring that the values obtained represent the velocity of the Beckmann change. Plotted against $1/T$, the values of log k fell on a straight line, and gave for both oximes in the various solvents values of the activation energies varying from 25.5 to 28.5 kg. per gram-mole.

It should be noted that these and similar measurements represent the first occasion on which the velocity of the Beckmann change has been measured with certainty (*cf.* Sluiter (25) and Kuhara (17)). They provide also an elegant confirmation of Kuhara's view that the rearrangement of ketoximes involves, at least in certain instances, the formation of an ester of the type $R_2C{=}NOX$, which subsequently undergoes a spontaneous intramolecular change to give the anilide RCONHR when the group OX has, as in the picryl ethers, a sufficient attraction for electrons.

Further investigation (10) showed that the transformation of the oxime picryl ethers in solution did not require an external catalyst, except in so far as the solvent might be regarded as such, nor was it affected by the action of light. The effect of the solvent on the rate of change, however, was striking. The rate increased in the same order as the cohesions, the dipole moments, and the dielectric constants of the solvents, i.e., for ethylene dichloride, chloroform, and carbon tetrachloride as solvents, in the order $C_2H_4Cl_2 > CHCl_3 > CCl_4$. The transformation is clearly one which is facilitated by an environment of polar molecules.

To test this further a detailed investigation of the kinetics of the rearrangement of benzophenone oxime picryl ether in the non-polar solvent carbon tetrachloride was made (6). It was found that the concentration of the solution had an important influence on the rate of change—an increase in concentration producing an increase in the speed of rearrangement. This suggests that the oxime ether, which contains strongly polar groups, is itself functioning as a catalyst, and since the unimolecular velocity coefficient remained constant throughout the course of any individual measurement, that the catalytic activities of the oxime ether and of its changed product must be approximately equal.

TABLE 2

Rearrangement of benzophenone oxime picryl ether into benz-N-picrylanilide in chloroform at 50°C.

Time (minutes)	30.5	60	90	120	180	240	
Per cent changed	25.5	41	56	66	82	90	
$k \times 10^3$	4.2	3.8	3.95	3.9	4.15	4.1	Mean 4.0

Since the velocity coefficients at any one temperature fell upon a straight line when plotted against the concentration, it follows that at any one concentration the observed velocity is the algebraic sum of (*1*) the velocity of the change at infinite dilution, and (*2*) an additional velocity, proportional to the concentration of the solution, which is to be attributed to the catalytic effect of solute molecules; that is, $k = k_0 + xc$, where k_0 is the velocity coefficient at infinite dilution, and x is the increase of velocity for a concentration of 1 gram-mole per liter.

The velocity coefficients, moreover, indicated that at infinite dilution the molecules of the oxime ether could be activated by collision with solvent molecules alone. Values of log (k_0/η) plotted against $1/T$ fell on a straight line and gave a value of 30,250 calories per gram-mole for the energy of activation. The observed rates of change, however, were approximately twenty times as great as those calculated from this value of E, showing that in practice the critical increment had a much lower value. Again plotting the values of log x against $1/T$ a straight line was obtained; its slope corresponded to a value of E of 22,600 calories per gram-mole. To account for this large difference in the critical increments, Chapman (6) suggested that a molecule of the oxime ether can be more easily activated and rearranged when it is in the neighborhood of another ether molecule (or of its change product) than when it is surrounded solely by molecules of an inert solvent.

Whilst, therefore, it is shown that the oxime ether can rearrange slowly when surrounded by non-polar molecules of a solvent, the rearrangement will occur with increasing facility as the collisions between polar molecules of the oxime ether and others of the same type (or molecules of the change product) become more and more frequent as the concentration increases.

If this view of the catalysis be correct, then the addition of foreign polar molecules of any kind should accelerate the rate of change, and in the same order as the strengths of their dipoles. Confirmation of this was obtained when various polar solvents were added to a standard solution of the oxime ether in carbon tetrachloride (6). The catalytic effects of the polar solvents which contain one principal dipole fell as shown in figure 2.

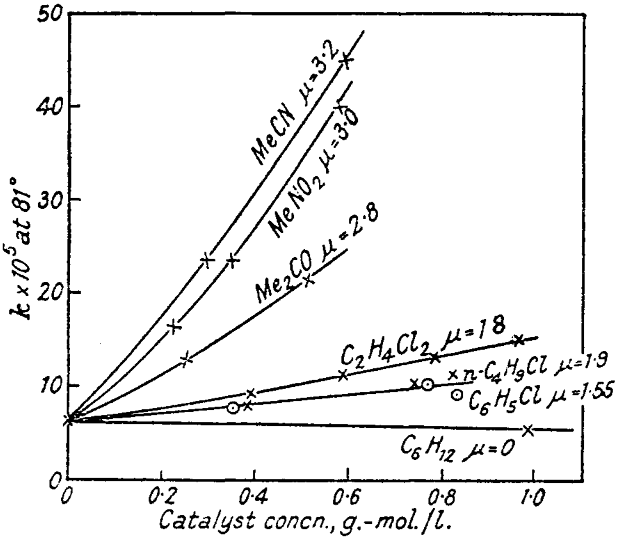


FIG. 2. Catalytic effects of polar solvents on the rearrangement of benzophenone oxime picryl ether in carbon tetrachloride (reference 6, p. 1552).

Apart from irregularities observed with large concentrations of the more highly polar catalysts, when their effects increased with rising concentration more rapidly than would be consistent with a linear relationship, the velocity of the transformation could be connected with the concentration (C) of the catalyzing solvent by the empirical equation

$$k = k_{\text{un.}} + xC + yC^2$$

where $k_{\text{un.}}$ is the velocity in the absence of catalyst.

This hypothesis of catalysis by the electrical field of polar solvents was subjected to yet another test. Compounds which contain two equal and opposite dipoles in the molecule, and are therefore non-polar, should function as catalysts provided the dipoles are sufficiently far apart for them to act independently. On the other hand, when the dipoles are close together they may be expected to neutralize each other as far as any external field is concerned. In agreement with this line of argument, *p*-dichlorobenzene and *cis*-1,4-dibromocyclohexane function as catalysts, while *trans*-dichloroethylene is ineffective (6).

While these kinetic studies throw a great deal of light on the general character of the rearrangement and the function of the reagent, they leave unanswered the question of the precise manner in which the picryloxy and the hydrocarbon groups migrate between the nitrogen and the carbon atoms in the rearrangement. Some degree of dissociation of the original linkages must occur, and the amount of energy necessary to bring about this dissociation will largely determine the ease with which migration takes place. But the migrating group is never kinetically free. If it were, then an optically active ketoxime $CHRR'C(CH_3)=NOH$, in which the migrating group is linked to the rest of the molecule by an asymmetric carbon atom, would undergo racemization during its transformation to the substituted acetamide, $CHRR'NHCOCH_3$. That this does not occur is shown by the demonstration by Kenyon and Young (13) that the oxime of (−) methyl γ-heptyl ketone retained its optical activity in the course of its conversion into (+) aceto-γ-heptylamine. Electron sharing between the asymmetric migrating group and the remainder of the molecule must therefore be continuous throughout the rearrangement. This important new evidence, which incidentally illustrates the part studies of optical activity can play in the elucidation of reaction mechanism, strengthens the view previously held that the Beckmann transformation of ketoximes is best regarded as intramolecular in character.

TABLE 3

PICRYL ETHER OF		BENZOPHENONE OXIME	*p*-CHLOROBENZOPHENONE		DI-*p*-CHLOROBENZOPHENONE OXIME
			α-Oxime	β-Oxime	
Hydrocarbon group	migrating	C_6H_5	C_6H_5	p-C_6H_4Cl	p-C_6H_4Cl
	stationary	C_6H_5	p-C_6H_4Cl	C_6H_5	p-C_6H_4Cl
t		100.5°C.	99.8°C.	100.8°C.	100°C.
$k_0 \times 10^5$		36.4	15.4	7.74	3.24
E (calories per gram-mole)		29,200	30,800	30,200	31,500

PICRYL ETHER OF		PHENYL *p*-TOLYL KETONE		DI-*p*-TOLYL KETOXIME
		α-Oxime	β-Oxime	
Hydrocarbon group	migrating	C_6H_5	p-$C_6H_4CH_3$	p-$C_6H_4CH_3$
	stationary	p-$C_6H_4CH_3$	C_6H_5	p-$C_6H_4CH_3$
t		75.6°C.	75.3°C.	70.3°C.
$k_0 \times 10^5$		7.47	19.5	55.1
E (calories per gram-mole)		26,500	28,300	25,800

In an attempt to define more clearly the internal mechanism of the transformation, an investigation of the effects of substitution upon the rate of rearrangement of oxime picryl ethers and upon the energy of activation was made by Chapman and Fidler (9). The velocity was found to be very susceptible to the polar nature of the substituents: introduction of an electron-attracting chlorine atom into the phenyl group of the original oxime retarded the rearrangement, whereas the electron-repelling methyl group accelerated it. Furthermore, a substituent in the migrating nucleus had a much greater effect on the rate of change than it had in the stationary nucleus. The energies of activation also showed a considerable variation from the slowest to the fastest reaction, and, apart from minor anomalies in the oximes of isomeric monosubstituted ketones, the variations in E were of the order to be expected if the differences in the rates of transformation arise essentially from differences in the energy of activation. Table 3 summarizes the salient data. Here, only one value of the velocity coefficient is recorded for each picryl ether. In practice values were obtained at four temperatures over a range of about 30°C., so that the energies of activation could be calculated with a reasonably high degree of accuracy.

An interesting feature of the effects of chloro substitution in the phenyl nucleus on the velocity of rearrangement is that these are strictly additive. This is the only case investigated in which the measurements were sufficiently accurate to justify a fully quantitative analysis. With methyl as substituent experimental difficulties made it impossible to obtain accurate data, and it is not surprising therefore that the additivity is less apparent.

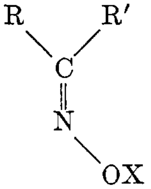
CHLORO COMPOUNDS				METHYL COMPOUNDS			
$10^4/T$	26	27	28	$10^4/T$	28	29	30
$A = \frac{k_0\text{ (unsubstituted)}}{k_0\text{ (}\alpha\text{-chloro)}}$	1.90	2.04	2.45	$A = \frac{k_0\text{(unsubstituted)}}{k_0\text{ (}\alpha\text{-methyl)}}$	0.41	0.36	0.32
$B = \frac{k_0\text{ (unsubstituted)}}{k_0\text{ (}\beta\text{-chloro)}}$	4.57	4.68	5.00	$B = \frac{k_0\text{(unsubstituted)}}{k_0\text{ (}\beta\text{-methyl)}}$	0.13	0.12	0.12
$A \times B$	8.71	9.55	11.7	$A \times B$	0.051	0.045	0.038
$C = \frac{k_0\text{ (unsubstituted)}}{k_0\text{ (dichloro)}}$	8.51	9.55	11.5	$C = \frac{k_0\text{(unsubstituted)}}{k_0\text{(dimethyl)}}$	0.036	0.031	0.026

The demonstration of an additive relationship in this rearrangement is of particular interest in view of the earlier discovery of similar relationships in the nuclear chlorination of a wide range of aromatic ethers (Bradfield and Jones (4); Jones (12)).

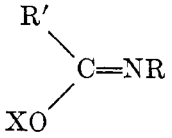
The scope for substitution in the picryl group was limited by the over-riding necessity to preserve its powerful electron-attracting character sufficiently for rearrangement to occur at a conveniently measurable rate. Only one case was fully investigated: the introduction of methyl to give the 2,4,6-trinitro-

m-tolyl group lowered the rate of rearrangement and raised the energy of activation by an approximately equivalent amount. The values of E in calories per gram-mole were 29,200 and 32,100, respectively.

From the accumulated data relating to the transformation it is possible, following Kuhara and Chapman, to formulate in general outline a mechanism for the rearrangement of ketoximes. First in the sequence of reactions is the formation from the oxime and the reagent of a compound of the type



followed, when the group OX exerts a sufficiently powerful attraction for electrons, by a spontaneous isomeric change to give the compound



which yields the amide R′CONHR on subsequent hydrolysis. The initiating factor in this change is the tendency of the group OX to dissociate as anion. This withdrawal of electrons from the nitrogen creates in the $\overset{\delta+}{\mathrm{N}}$—$\overset{\delta-}{\mathrm{O}}$ bond a dipole with its positive end on the nitrogen atom. Because of the configuration of the oxime ester molecule, the field of this dipole is so oriented as to include the electrons of the bond R—C on the far side of the nitrogen atom within its influence, but hardly those of C—R′ on the near side. When the molecule, already in this state of stress, acquires enough energy, rearrangement takes place, the group R becoming anchored to the nitrogen atom and OX migrating in compensation at the same instant to the central carbon atom. Such an interpretation appears to be in agreement with all the data relating to the rearrangement. It provides for the fact that the structure of the change product is determined solely by the spatial configuration of the oxime, and for the retention of optical activity during the rearrangement of optically active ketoximes, since it visualizes the endowment of the migrating group with its full octet of electrons throughout the transference. It accounts also for the influence of polar substituents in the groups R and R′. For instance, an electron-repelling substituent situated in the group R should facilitate the rearrangement by increasing the electron density in the bond R—C. In R′ the same substituent should be less effective. This is borne out by the data relating to the methyl group as substituent.

This formulation resembles in essentials the earlier one due to Mills (21), but (*a*) it emphasizes the importance of the strong electron attraction of the group OX, and (*b*) it assigns to the union of the nitrogen atom and the group R a more important place among the factors which determine the ease of rearrangement. Were the rate of change determined entirely by the polarization of the N—O link, or by the attraction of OX for the central carbon atom, then the effects of substituents in the groups R and R′ would be more nearly equal instead of being markedly different.

Watson (30) gives a similar but more detailed analysis of the possible electronic processes concerned in the rearrangement. Electron sharing between the migrating hydrocarbon radical R and the rest of the molecule is again visualized as being continuous, with R carrying its full complement throughout the change.

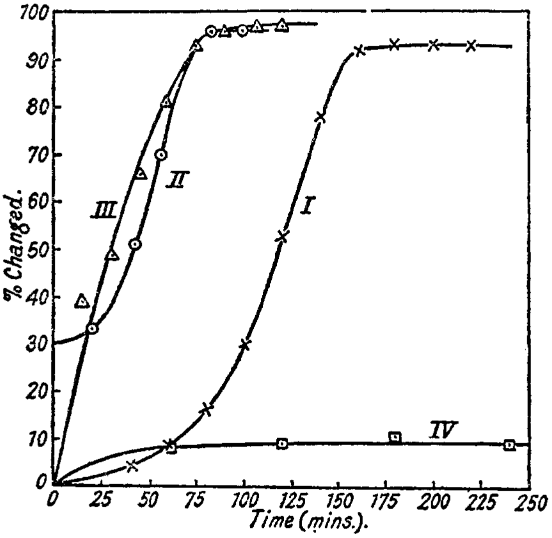


FIG. 3. Velocity of the Beckmann rearrangement of benzophenone oxime—effect of hydrogen chloride as catalyst (reference 7, p. 1224):

Curve I. 0.42 mole HCl: starting from pure oxime.
Curve II. 0.42 mole HCl: starting from 30 per cent anilide, 70 per cent oxime.
Curve III. 0.41 mole HCl + 0.002 mole benzanilideiminochloride.
Curve IV. 0.002 mole benzanilideiminochloride.

From these researches of Kuhara and Chapman it is clear that the action of most of the reagents which bring about the Beckmann transformation of ketoximes can be accounted for by the formation of an ester, $R_2C{=}NOX$, followed by its spontaneous rearrangement when the group OX exerts a sufficient attraction for electrons as in the benzenesulfonyl esters and the picryl ethers. On the other hand, hydrogen chloride, which is known to be an effective and energetic reagent for the transformation, cannot be reconciled with this view of the mechanism, since Stieglitz and Peterson (27) and Peterson (24) showed that the esters $R_2C{=}NCl$ do not undergo rearrangement. A reinvestigation, under conditions which allowed of a quantitative study of the rearrangement of benzophenone oxime in ethylene dichloride solutions of hydrogen chloride at 100°C., was therefore undertaken by Chapman (7). The transformation was shown to be complex: the rate was dependent on the concentration of the hydrogen chloride, but the general shape of the time–rearrangement curve was the same over a wide range of concentration. An initial period of low reactivity was followed by a steady rise until approximately 30 per cent of the oxime had been rearranged, when a rapid change at almost constant speed was maintained until the conversion was complete, the product being almost pure benzanilide. Such behavior suggests autocatalysis (curve I in figure 3).

An initial period of slow but gradualy increasing reactivity was also observed when the hydrogen chloride was introduced as oxime hydrochloride, proving that delay in the formation of this compound was not the cause of the initial low velocity. On the other hand, the presence at the outset of benzanilide (the change product) reduced the initial slow period. A mixture of 70 per cent oxime and 30 per cent benzanilide not only showed an initial slow period of short duration, but this was followed immediately by a rapid reaction identical in form with the rapid phase of the rearrangement of the pure oxime. Replacement of some of the solvent by ethyl alcohol completely inhibited the transformation.

These observations suggest that the rearrangement is accomplished through the agency of some compound which is formed from the benzanilide produced in the slow first stage, and which can be destroyed or inhibited by ethyl alcohol. Such a compound is benzanilideiminochloride, for the formation of which from hydrogen chloride and benzanilide there is some evidence (Stephen and Bleloch (26)).

$$C_6H_5CONHC_6H_5 + HCl \rightleftarrows C_6H_5C(Cl){=}NC_6H_5 + H_2O$$

Under standard conditions it was found that the addition of 0.002 mole of benzanilideiminochloride had a powerful effect on the reaction (curve III); it completely abolished the slow period and the rearrangement progressed throughout at approximately the same speed as the rapid phase of curve I. In the presence of hydrogen chloride larger amounts of the iminochloride accelerated the rate until it became too rapid for measurement. On the other hand, in the absence of hydrogen chloride 0.002 mole of the iminochloride converted only 10 per cent of the oxime to the anilide (curve IV). It appears, therefore, that for the rapid and complete transformation of the oxime into benzanilide both reagents are necessary.

From these results Chapman (7) concluded that the Beckmann rearrangement of benzophenone oxime in the presence of hydrogen chloride proceeds by the following series of reactions:

(1) The slow production of a small quantity of benzanilide.

(2) The conversion of a trace of the benzanilide into benzanilideiminochloride by hydrogen chloride:

$$C_6H_5CONHC_6H_5 + HCl \rightarrow C_6H_5C(Cl){=}NC_6H_5 + H_2O$$

(3) The condensation of the oxime and the iminochloride to form the oxime ether:

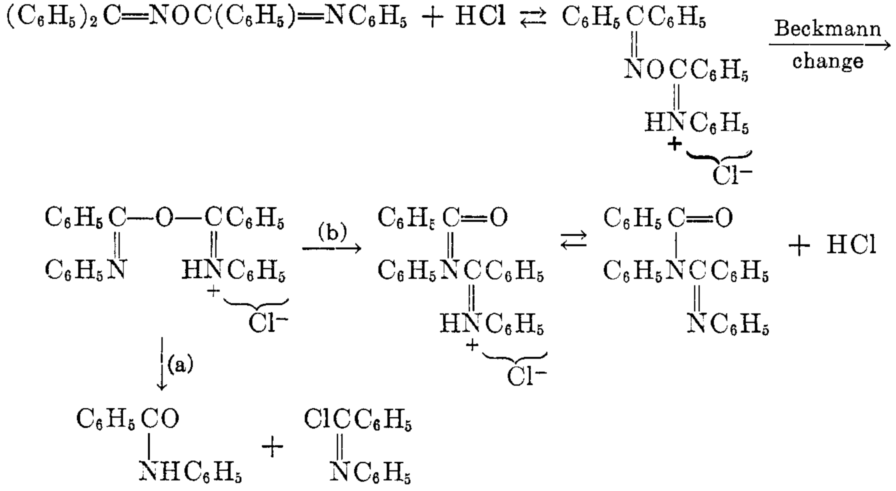
$$(C_6H_5)_2C{=}NOH + C_6H_5C(Cl){=}NC_6H_5 \rightarrow (C_6H_5)_2C{=}NOC(C_6H_5){=}NC_6H_5 + HCl$$

(4) The conversion of this oxime ether into the cation:

$$(C_6H_5)_2C{=}NOC(C_6H_5){=}NC_6H_5 + H^+ \rightarrow (C_6H_5)_2C{=}NOC(C_6H_5){=}\overset{+}{N}HC_6H_5$$

The positively charged nitrogen atom in this cation, like the picryloxy group in the oxime picryl ethers, endows the radical $—OCC_6H_5{=}\overset{+}{N}HC_6H_5$ with strong electron-attracting properties and thereby enables it to initiate the rearrangement to an imido ether type of compound which, in the presence of an excess of hydrogen chloride, may undergo two alternative reactions (a or b). The series of reactions can be formulated as follows:

$$(C_6H_5)_2C{=}NOH + C_6H_5C({=}NC_6H_5)Cl \rightarrow$$



$$(C_6H_5)_2C{=}NOC(C_6H_5){=}NC_6H_5 + HCl \rightleftarrows \begin{array}{l} C_6H_5CC_6H_5 \\ \;\| \\ NOCC_6H_5 \\ \quad\;\| \\ \quad H\overset{+}{N}C_6H_5\;Cl^- \end{array} \xrightarrow[\text{change}]{\text{Beckmann}}$$

$$\begin{array}{l} C_6H_5C—O—CC_6H_5 \\ \;\;\|\qquad\quad\;\| \\ C_6H_5N\quad H\overset{+}{N}C_6H_5\;Cl^- \end{array} \xrightarrow{(b)} \begin{array}{l} C_6H_5C{=}O \\ \qquad\| \\ C_6H_5NCC_6H_5 \\ \qquad\;\| \\ \quad H\overset{+}{N}C_6H_5\;Cl^- \end{array} \rightleftarrows \begin{array}{l} C_6H_5C{=}O \\ \qquad| \\ C_6H_5NCC_6H_5 \\ \qquad\;\| \\ \qquad NC_6H_5 \end{array} + HCl$$

$$\downarrow (a)$$

$$\begin{array}{l} C_6H_5CO \\ \;\;| \\ NHC_6H_5 \end{array} + \begin{array}{l} ClCC_6H_5 \\ \;\;\| \\ NC_6H_5 \end{array}$$

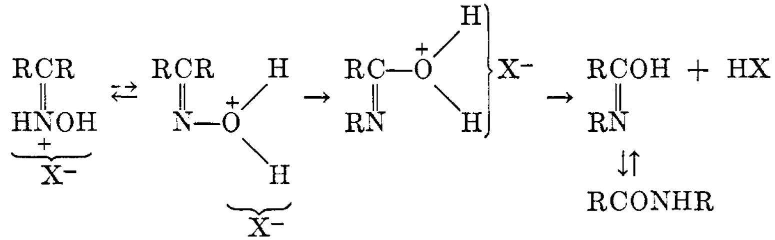
Process (a) would lead to the formation of benzanilide and benzanilide-iminochloride, which may enter into further reaction with the oxime, while process (b) yields benzoyl-*s*-diphenylbenzenylamidine by a process analogous to the transformation of *N*-phenylbenziminopicryl ether into benzylpicrylaniline.

If the decomposition process (a) predominates over (b), then the above scheme accounts satisfactorily for the catalytic effect of the iminochloride, while the alternative process (b) furnishes reason for the presence of a small quantity of *s*-diphenylbenzenylamidine in the benzanilide obtained when benzophenone oxime hydrochloride undergoes rearrangement on heating.

This mechanism of the rearrangement of benzophenone oxime in the presence of hydrogen chloride was tested and confirmed by the examination of the essential intermediate compound $(C_6H_5)_2C{=}NOC(C_6H_5){=}NC_6H_5$, formed from benzophenone oxime and benzanilideiminochloride. Treated with aqueous hydrogen chloride it was converted rapidly and quantitatively into benzanilide; with an excess of dry hydrogen chloride in ether it gave a mixture of benzanilide and benzanilideiminochloride; while in ether containing a trace of sulfuric acid it yielded the alternative product benzoyl-*s*-diphenylbenzenylamidine by process (b). Finally, its catalytic effect on the transformation of benzophenone oxime by hydrogen chloride was precisely the same as that of an equivalent amount of benzanilideiminochloride.

The rapid Beckmann rearrangement of ketoximes under the influence of hydrogen chloride as a reagent is thus seen to fall into line with the spontaneous change of the oxime ethers and esters, since it is due to the spontaneous rearrangement of an oxime derivative which is similar in nature to the ester of a strong acid.

This mechanism provides a satisfactory picture of the rearrangement once the first trace of benzanilide has been formed, but it offers no explanation of the slow consecutive reaction (curve I, figure 3) during which the requisite trace of benzanilide is actually formed. A mechanism for the slow production of benzanilide has been suggested by Bennett (see reference 8, p. 1226). This takes into account the fact that the salt of an oxime should contain both ammonium and oxonium forms in equilibrium. Now, although the proportion of the oxonium form may be exceedingly small, the group $\overset{+}{O}H_2$ would attract electrons powerfully—more so even than the picryloxy or benzenesulfonyl groups. As a result, the oxonium ion would readily undergo the Beckmann change:



If this be so, it follows that any sufficiently strong acid should be capable of inducing the rearrangement of a ketoxime, but on account of the minute amount of oxonium salt that would be present the rate of change would of course be slow. Direct experimental confirmation of this has been provided, using picric acid as the agent for producing the transformation. In nitromethane solution benzophenone oxime gave benzanilide; no benz-*N*-picrylanilide could be detected (6). The above suggestion accounts satisfactorily also for the rearrangement of benzophenone oxime in aqueous acid solution (Lachmann (19)), and has the merit that it brings the outstanding apparent exceptions into that general scheme of the Beckmann rearrangement which includes the spontaneous transformation of esters and oxime ethers.

It is clear, therefore, that the Beckmann rearrangement of benzophenone oxime by hydrogen chloride is complex, with two distinct processes operating consecutively: (*1*) a very slow change to benzanilide brought about by the acid reagent—in this the anilideiminochloride type of compound is not an intermediate—and (*2*) a much more rapid transformation starting immediately a trace of benzanilide has been formed by the first process, and occurring through a series of recognizable intermediate products. This second process accounts for the greater part of the rearrangement.

These studies of the kinetics and mechanism of the transformation of ketoximes reveal for the first time certain definite general characteristics of the change, which may be summarized as follows:

(*1*) The essential unity of the rearrangement. The transformation of ketoximes under the influence of various reagents depends on the intermediate formation of an ester-like compound which is capable of undergoing spontaneous rearrangement. The ease with which these esters, ethers, and salts undergo rearrangement is determined by the capacity of the radical attached to the nitrogen atom to attract electrons; the more powerful this attraction, the more facile the change.

(*2*) There is no evidence that the spontaneous transformation of such compounds involves any actual dissociation into free ions, although the effect of polar molecules on the velocity of rearrangement suggests that some partial dissociation occurs as a preliminary to rearrangement. The retention of optical activity during the conversion of optically active ketoximes shows, however, that the migrating hydrocarbon group is never kinetically free. The change is best regarded as intramolecular in nature.

(*3*) A picture of the mechanism of the rearrangement can be drawn along the lines developed by Kuhara and Mills as elaborated by Chapman and Watson.

It is clear from this brief review that although much has been achieved in recent years, more needs to be discovered before the mechanism of this Mona Lisa of molecular rearrangements is fully understood. Further investigation of other 'exchange' rearrangements would probably disclose resemblances and perhaps contribute materially to the elucidation of their characters.

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