THE BECKMANN REARRANGEMENT

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The past ten years have witnessed a considerable revival of interest on the part of organic chemists in the problems presented by the Beckmann rearrangement. Chiefly this has been due to a group of researches, initiated by Meisenheimer, which have made it necessary for organic chemists to consider seriously the advisability of reversing the configurations previously assigned by means of the Beckmann rearrangement to almost all ketoximes. These same investigations cannot but have an effect on our views of the mechanism of the Beckmann rearrangement and they should in the near future give rise to a renewed study of that mechanism. With this in mind, and particularly since the chemical literature dealing with the rearrangement is already so extensive as to make it difficult for persons not actively working on the problem to familarize themselves with it, the present survey of that literature has been prepared. For purposes of orientation we shall begin with brief descriptions of the discovery of the rearrangement, the methods employed for effecting the rearrangement, and the generality of rearrangement.

In its most general form the Beckmann rearrangement consists in the transformation of a ketoxime into an acid amide.

$$\underset{\underset{NOH}{\|}}{RCR} \rightarrow \underset{\underset{O}{\|}}{RCNHR}$$
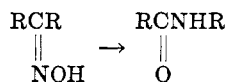
Its discovery in 1886 was quite accidental. Ernst Beckmann (1) was interested in developing a method for distinguishing between aldehydes and ketones and, in order to do so, proposed to make use of their respective oximes. It was known that aldoximes on treatment with phosphorus pentachloride furnished nitriles.

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Since a similar reaction seemed unlikely with ketoximes, Beckmann set out to determine the behavior of a typical ketoxime toward this reagent, choosing benzophenone oxime for this purpose. He found that the product of the reaction, after hydrolysis, was benzanilide and thus established the first example of the rearrangement which still carries his name. It is of sufficient historical interest to justify noting that three years prior to Beckmann's discovery, Janny (2) had found that acetoxime reacted vigorously with phosphorus pentachloride, but he was unable to identify the products of the reaction.

The rearrangement of a ketoxime to an acid amide can be effected by a surprisingly large number of reagents. Beckmann (1) early showed that phosphorus pentachloride and phosphorus oxychloride were suitable. He also employed acetyl chloride, sulfuric acid, and especially the so-called "Beckmann's mixture," consisting of acetic acid and acetic anhydride saturated with hydrogen chloride (3, 4). V. Meyer (5) shortly before this had used acetyl chloride in special cases. More recent work by Beckmann (6) has shown that antimony tri- and penta-chlorides are particularly effective, while a large number of metallic chlorides are capable of causing rearrangement. Metallic sulfates, oxides, and hydroxides, however, do not bring about the rearrangement. Other workers (7, 8) have shown that hydrogen chloride and oxime hydrochlorides will cause rearrangement, as will benzenesulfonyl chloride in an alkaline aqueous medium or in pyridine (9, 10, 11). Even chloral has been found capable of rearranging benzophenone oxime (12). Of this large list of reagents, however, only three merit more than passing mention. Sulfuric acid is the most satisfactory reagent for cyclic oximes of the type of cyclohexanone oxime (13). Benzenesulfonyl chloride, which is ordinarily thought of only in connection with the Beckmann rearrangement of the second order (see later), is of quite general applicability and permits the carrying out of a rearrangement in an alkaline medium. Phosphorus pentachloride, however, remains the most generally applicable and the most valuable reagent. Used in ether solution and at low temperatures it involves the minimum of complications and is quite deservedly the reagent

which first comes to mind at mention of the Beckmann rearrangement.

The rearrangement of a ketoxime to an acid amide is a reaction of considerable generality. Not only is it undergone by most ketoximes, but it has also been observed to take place with the nitrogen alkyl ethers of aldoximes (14, 15, 16). Two cases, even, have been reported of the rearrangement of aldoximes to acid amides (17). We shall confine our attention, however, to the ketoximes. Considering the general formula of this type of substance,

$$RCR$$
$$\parallel$$
$$NOH$$

one may say that rearrangement will take place if the R groups are aliphatic, aromatic (18), or heterocyclic (19, 20). If aliphatic they may be of large or small molecular weight, saturated or unsaturated (21, 22). If aromatic, the presence of substituents in the R group does not in general prevent rearrangement (23). There are, of course, isolated instances of oximes which either do not rearrange or from which no definite rearrangement products have been obtained (24, 25, 26). In contrast to these individual instances there are several well-defined classes of oximes which undergo rearrangement to yield products other than acid amides. We may review these special types of rearrangements briefly.

The oximes of some cyclic ketones on rearrangement undergo ring enlargement and furnish lactams. Examples are cyclohexanone oxime (27) and fluorenone oxime (28).
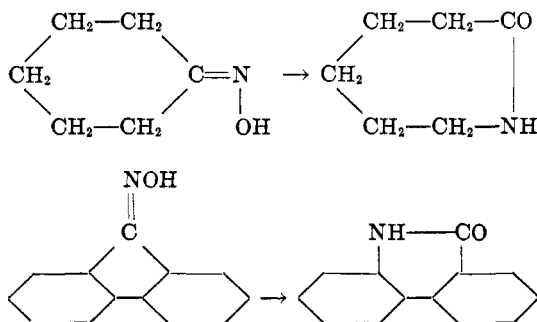
In different fashion the oximes of certain bicyclic ketones, such as camphor, yield unsaturated nitriles (29, 30),
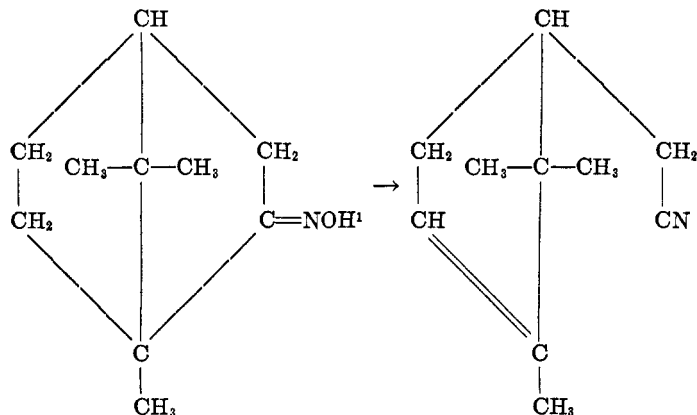

while the oximes of many unsaturated cyclic ketones furnish aromatic amines (31, 32, 33).

The oximes of α-hydroxyketones, such as benzoin, undergo cleavage on rearrangement and furnish an aldehyde and a nitrile or isonitrile (11).

$$C_6H_5CHOH$$
$$\mid \qquad\qquad \rightarrow C_6H_5CHO + C_6H_5CN \ (C_6H_5NC)$$
$$C_6H_5C{=}NOH$$
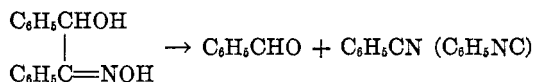
The monoximes of α-diketones, which rearrange normally on treatment with phosphorus pentachloride, undergo cleavage when treated with benzenesulfonyl chloride and alkali or pyridine (10, 34).

$$C_6H_5CCOC_6H_5$$
$$\| \qquad\qquad \rightarrow C_6H_5CN + C_6H_5CO_2H$$
$$HON$$
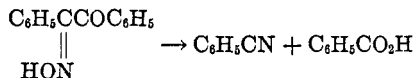
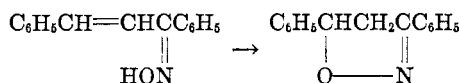These cleavage reactions of the α-diketone monoximes and the α-hydroxyketone oximes are generally referred to as Beckmann rearrangements of the second order (10, 11).

The oximes of certain α,β-unsaturated ketones, which rearrange

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[1] Certain oximes will be formulated in this fashion for the reason that there is, at present, no satisfactory evidence for assigning a configuration to them.

normally on treatment with phosphorus pentachloride, undergo an intramolecular ring closure when treated with sulfuric acid and yield isoxazolines (35, 36, 37, 38, 39).

$$\underset{\underset{\text{HON}}{\|}}{C_6H_5CH\!=\!CHCC_6H_5} \longrightarrow \underset{\underset{\text{O————N}}{|\quad\quad\|}}{C_6H_5CHCH_2CC_6H_5}$$

The oximes of ketones containing a benzyl group attached to the carbonyl carbon atom can be made to undergo normal rearrangement. Under certain conditions, however, they rearrange to furnish α-aminoketones or their cyclic condensation products. The mechanism of the process has been largely determined by its discoverer (40).

$$\underset{\underset{\text{HON}}{\|}}{C_6H_5CH_2CCH_3} \longrightarrow \underset{\underset{\text{NH}_2}{|}}{C_6H_5CHCOCH_3}$$
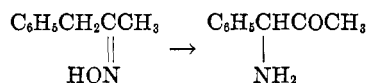
Finally attention should be called to the work of Scholl (41) on the dehydration undergone by the monoximes of certain 1-aroyl-anthraquinones.
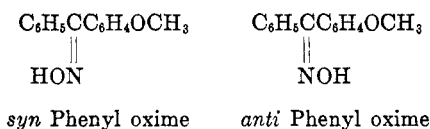
It is perhaps advisable at this place, after having devoted one general paragraph to the normal Beckmann rearrangement and six detailed paragraphs to the consideration of special cases of abnormal rearrangements, to correct the overemphasis given of necessity to these abnormal rearrangements by this method of presentation. Accordingly attention is called to the fact that the normal rearrangement of ketoximes to acid amides far outranks all the abnormal rearrangements both in frequency of occurrence and in importance. It is with the Beckmann rearrangement in its most general form—the transformation of a ketoxime to an acid amide —that we shall deal almost exclusively in the succeeding pages. Having outlined the methods of bringing about the rearrangement and the generality of the rearrangement, we are now in a position to consider the problems which it presents. Of these there are two major ones, distinct yet interrelated. The first deals with the configuration of ketoximes and the nature of the shift involved in their rearrangement, while the second deals with the mechanism of that shift. We shall take up these two problems in the order named, giving in each case a historical development sufficient to

make apparent the significance of the problem.   From the nature
of the material to be treated, our presentation falls into what will
be found to be essentially two separate essays.

I. THE CONFIGURATION OF KETOXIMES AND THE NATURE OF THE
SHIFT IN THE BECKMANN REARRANGEMENT

The configurations of isomeric ketoximes

With the discovery in the late eighteen-eighties that unsym-
metrical ketones (reference to aldehydes is intentionally omitted)
furnished in many cases two isomeric oximes, several theories were
advanced to account for this isomerism.   Of these theories the one
which has received general acceptance is that of Hantzsch and
Werner (42).   According to their view, the isomerism of oximes is
conditioned by three factors: the presence of two different substit-
uents on the carbonyl carbon atom, the absence of free rotation
about the carbon-nitrogen double linkage, and the distribution of
the three valences of the nitrogen atom in such wise that the single
valence is not in the same plane as the other two.   On this view
the isomerism of doubly linked trivalent nitrogen compounds is
analogous to that of ethylenic compounds of the maleic–fumaric
type and the isomerism of ketoximes can be represented, in a uni-
planar figure, by the following formulas.

$$C_6H_5CC_6H_4OCH_3 \qquad C_6H_5CC_6H_4OCH_3$$
$$\| \qquad\qquad\qquad \|$$
$$HON \qquad\qquad\qquad NOH$$

syn Phenyl oxime   *anti* Phenyl oxime

Such an explanation accounted admirably for the observed num-
ber of isomers but this, though necessary, was not sufficient.   In
general and in the particular case just illustrated by the formulas,
that of the phenyl anisyl ketoximes, it is essential to have some
method of assigning a definite formula (configuration) to each of
the isomers.   In 1891, a year after the general explanation of
oxime isomerism had been advanced, Hantzsch (43, 44) proposed
a method for determining the configurations of individual ketox-
imes.   The method was based upon the use of the Beckmann
rearrangement.

Attention was first called to the fact that isomeric ketoximes furnished, as a result of the Beckmann rearrangement, isomeric acid amides. Again using the two isomeric phenyl anisyl ketoximes as illustrations, it was known that one isomer yielded the anilide of anisic acid while the second isomer furnished the anisyl amide of benzoic acid. Hantzsch next pointed out that, regardless of the actual mechanism of the process, the rearrangement of a ketoxime could be considered, formally at least, as being essentially a shift of places between the oximino hydroxyl group and one of the groups attached to the carbonyl carbon atom, followed by ketonization of the resulting imide.

$$
\begin{matrix} \text{RCR} \\ \| \\ \text{NOH} \end{matrix} \rightarrow \left[\begin{matrix} \text{RCOH} \\ \| \\ \text{NR} \end{matrix} \right] \rightarrow \begin{matrix} \text{RCO} \\ | \\ \text{NHR} \end{matrix}
$$

Hantzsch then assumed, again regardless of mechanism and purely on general stereochemical considerations, that the radical spatially nearer to the hydroxyl group would change places with the hydroxyl group—in simpler terms a *cis* shift would occur. Applied to the phenyl anisyl ketoximes we have chosen as illustrations we have:

$$
\begin{matrix} C_6H_5CC_6H_4OCH_3 \\ \| \\ \text{HON} \end{matrix} \rightarrow \left[\begin{matrix} \text{HOCC}_6H_4OCH_3 \\ \| \\ C_6H_5N \end{matrix} \right] \rightarrow \begin{matrix} \text{OCC}_6H_4OCH_3 \\ | \\ C_6H_5NH \end{matrix}
$$

$$
\begin{matrix} C_6H_5CC_6H_4OCH_3 \\ \| \\ \text{NOH} \end{matrix} \rightarrow \left[\begin{matrix} C_6H_5COH \\ \| \\ NC_6H_4OCH_3 \end{matrix} \right] \rightarrow \begin{matrix} C_6H_5CO \\ | \\ NHC_6H_4OCH_3 \end{matrix}
$$
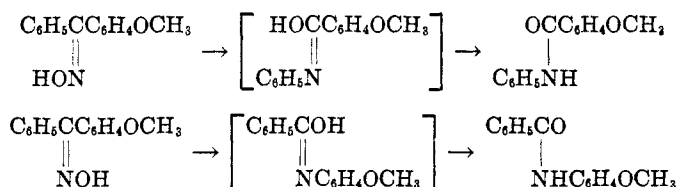
It is thus possible to assign a configuration to any ketoxime from a knowledge of its rearrangement product. For, making the assumption of a *cis* shift, the group spatially adjacent to the hydroxyl group in the oxime will appear attached to the nitrogen atom in the rearrangement product. On this basis, the *syn* phenyl configuration is assigned to the phenyl anisyl ketoxime which furnishes the anilide of anisic acid on rearrangement, while the *anti* phenyl configuration is assigned to the one which furnishes the anisyl amide of benzoic acid.
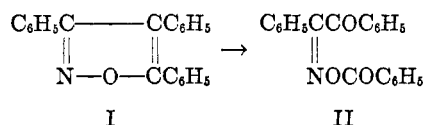
This method of assigning configurations is, it will be observed,

completely dependent upon an unverified assumption, namely, that the rearrangement involves a *cis* shift. This assumption, however, was in itself so inherently reasonable that for many years almost no objection to it was raised, while no effort was made either to verify or to disprove it. It was known that in several instances an individual ketoxime did furnish on rearrangement two isomeric amides. The difficulty in reconciling this behavior with a consistent *cis* shift was disposed of by Hantzsch (43) by showing that in general one oxime was less stable than its isomer and could easily be converted into that isomer. Doubtless, therefore, so the argument ran, the formation of both possible amides from a single oxime was due to the partial conversion of one ketoxime into its isomer before rearrangement took place. This explanation was supported by the fact that in the case of many aromatic ketoximes one isomer gave a homogeneous rearrangement product (a single acid amide) while the other isomer furnished some of that same amide but predominantly the isomeric amide. In the case of the oximes of aliphatic ketones, which so far as were examined were liquids and which quite generally gave mixtures of acid amides on rearrangement, there was not only the possibility of the interconversion of one isomer into the other, but also the further possibility that the liquid oximes were mixtures of isomers rather than chemical individuals (45).
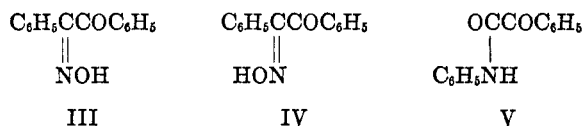
However, as we have said, there was little or no objection to the assignment to ketoximes of configurations which were based on an examination of their rearrangement products and the assumption of a *cis* shift in the rearrangement. Indeed on this basis Hantzsch in 1892 prepared a table showing the groups commonly present in ketoximes, arranged in the order of their attraction for the oximino hydroxyl group (19). It is true that Pfeiffer (46) in 1904 and Bucherer (47) in 1914 suggested the possibility of a *trans* shift in the rearrangement, but the scant acceptance with which their suggestion was received is best illustrated by pointing out that until 1921 the configurations of all ketoximes were assigned on the basis suggested and developed by Hantzsch thirty years earlier.

In 1921 there was presented for the first time a method of deter-

mining the configuration of ketoximes which was entirely independent of the Beckmann rearrangement. In a study of triphenylisoxazole (I) Meisenheimer found that this compound furnished on ozonization the benzoate of a benzil monoxime (48). An examination of the formulas will show that this benzoate should have, if no shift in configuration has taken place after ring opening, the configuration represented by formula II.

$$\begin{array}{cc}
C_6H_5C\text{———}CC_6H_5 & C_6H_5CCOC_6H_5 \\
\parallel \qquad \parallel \qquad \rightarrow & \parallel \\
N\text{—}O\text{—}CC_6H_5 & NOCOC_6H_5 \\
\text{I} & \text{II}
\end{array}$$

Now two benzil monoximes were known, a high melting or α-oxime and a low melting or β-oxime. Beckmann (49, 50), from an examination of the products which these two oximes furnished on rearrangement, and assuming a *cis* shift to have taken place on rearranging, had assigned to the α-oxime the configuration III and to the β-oxime the configuration IV.

$$\begin{array}{ccc}
C_6H_5CCOC_6H_5 & C_6H_5CCOC_6H_5 & OCCOC_6H_5 \\
\parallel & \parallel & | \\
NOH & HON & C_6H_5NH \\
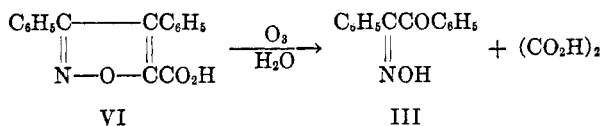\text{III} & \text{IV} & \text{V}
\end{array}$$

It is obvious from a comparison of formulas II and III that Meisenheimer's product from the ozonization of triphenylisoxazole should be the benzoate of the α-monoxime. Actually that product proved to be the benzoate of the β-monoxime! When it was further shown that the benzoylation of the β-oxime yielded the benzoate (II) and that the hydrolysis of this benzoate regenerated the β-oxime so that a shift of configuration was most improbable, then the full significance of Meisenheimer's work appeared. For, knowing the configuration of the β-monoxime from the ring opening to be that shown in formula III, and knowing the rearrangement product of that oxime to be the anilide of benzoylformic acid (V), it followed that the rearrangement of this oxime involved not a *cis* but a *trans* shift.

The question at once arose whether this *trans* shift in the Beck-

mann rearrangement was a general or an exceptional phenomenon. If it were general, then the Beckmann rearrangement could still be employed for assigning configurations, but almost all the configurations previously assigned would have to be reversed. While if it were not general, then all ketoxime configurations based on the Beckmann rearrangement would be uncertain. An answer, at least provisional, to the question of the nature and generality of the shift in the Beckmann rearrangement is possible as a result of the work done, chiefly by Meisenheimer, in the past eleven years. Three types of attack have been made on the problem,— chemical, physical, and stereochemical. The chemical attack, which is the one most used, has consisted in determining the configuration of an oxime by either ring opening or ring closure— assuming that rings open *cis* (51) and close *cis*. Then, knowing the configuration of the oxime and the structure of its rearrangement product, it is possible to tell whether the rearrangement proceeds through a *cis* or a *trans* shift. We shall review the available evidence before attempting to draw any general conclusions.
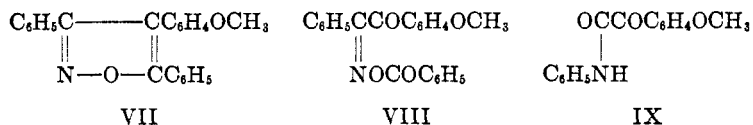
Chemical evidence of oxime configurations

The evidence of oxime configuration from ring opening is limited in amount. In addition to the case of triphenylisoxazole already cited there are but three other examples. The ozonization of 3,4-diphenylisoxazole-5-carboxylic acid (VI) by Kohler (20) is of particular importance, for the reaction does not furnish a derivative of a benzil monoxime, but yields directly the β-monoxime of benzil (III).

$$C_6H_5C \underline{\qquad\qquad} CC_6H_5 \qquad \xrightarrow[H_2O]{O_3} \qquad \begin{array}{c} C_6H_5CCOC_6H_5 \\ \| \\ NOH \end{array} \quad + \; (CO_2H)_2$$

$$\begin{array}{c} \| \qquad\qquad \| \\ N\!-\!O\!-\!CCO_2H \end{array}$$

VI   III

By thus confirming the configuration (III) assigned to the β-monoxime of benzil by Meisenheimer, this work strengthens the conclusion that the rearrangement of this β-monoxime involves a *trans* shift. A final confirmation of the configuration III for the β-monoxime of benzil was afforded by the ozonization of 3,4-diphenyl-5-*p*-bromophenylisoxazole which furnished the *p*-bromo-

benzoate of β-benzil monoxime (52). The ozonization of 3,5-diphenyl-4-anisylisoxazole (VII) has also been investigated (53). This reaction furnishes the benzoate of the β-monoxime of a p-methoxybenzil (VIII). Since the oxime corresponding to this benzoate yields on rearrangement the anilide (IX), it follows that in this rearrangement also a *trans* shift has taken place.

$$\underset{\text{VII}}{\overset{\displaystyle C_6H_5C\text{———}CC_6H_4OCH_3}{\underset{\displaystyle N\text{—}O\text{—}CC_6H_5}{||\qquad\qquad||}}}\qquad\underset{\text{VIII}}{\overset{\displaystyle C_6H_5CCOC_6H_4OCH_3}{\underset{\displaystyle NOCOC_6H_5}{||}}}\qquad\underset{\text{IX}}{\overset{\displaystyle OCCOC_6H_4OCH_3}{\underset{\displaystyle C_6H_5NH}{|}}}$$
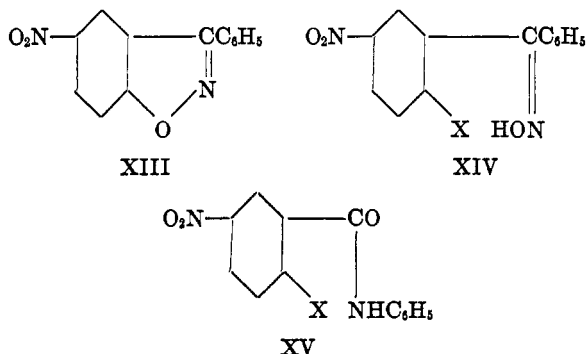
By far the greater part of our chemical evidence of oxime configurations has resulted from the study of ring closure of appropriately substituted ketoximes. As typical of this kind of evidence we may consider the results obtained with the oximes of certain ortho halogen substituted benzophenones. o-Chlorobenzophenone and o-bromobenzophenone yield each a single oxime. This single oxime in each case, as was shown in 1892 by Cathcart and V. Meyer (54), loses halogen acid on treatment with alkali to form the indoxazene (X). Strangely enough, the significance of this fact for the assignment of configurations to the oximes was not recognized at the time it was first observed. Meisenheimer (23), however, has pointed out that the loss of halogen acid by these oximes indicates the spatial proximity of the oximino hydroxyl group and the ortho substituent and is adequate evidence for assigning to the oximes the configuration XI (x = Cl, Br). Since both of the oximes in question yield on rearrangement the anilide of an ortho-halogenated benzoic acid (XII, x = Cl, Br), it follows that these rearrangements proceed through a *trans* shift.
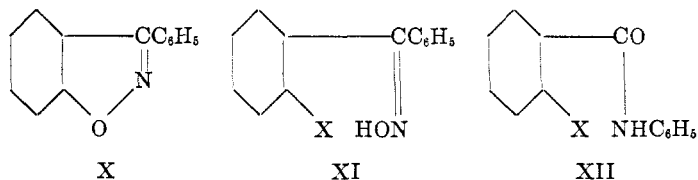

In the case of the ortho-halogenated benzophenone oximes, rather drastic treatment is necessary in order to bring about ring

closure to the indoxazene and there is the possibility of a shift in the configuration of the oximes during this treatment. To eliminate this possibility Meisenheimer took advantage of the well-known activating effect of para placed nitro groups and examined the oximes of 2-chloro-5-nitro-and 2-bromo-5-nitro-benzophenone (26). In each case but a single oxime could be obtained, and in each case the oxime lost halogen acid very readily to form the indoxazene (XIII). Consequently, to the oximes was assigned the configuration XIV (x = Cl, Br). And since on rearrangement each oxime yields an anilide of a substituted benzoic acid (XV, x = Cl, Br), we are furnished with two additional examples of *trans* shifts in the Beckmann rearrangement.

$$O_2N-\underset{\underset{\displaystyle XIII}{}}{\hexagon}-CC_6H_5 \qquad O_2N-\underset{\underset{\displaystyle XIV}{X}}{\hexagon}-CC_6H_5$$

$$O_2N-\underset{\underset{\underset{\displaystyle XV}{X\ \ NHC_6H_5}}{}}{\hexagon}-CO$$

Similar studies were attempted by Meisenheimer with dinitroketones of the general formula

$$O_2N-\underset{\underset{NO_2}{}}{\hexagon}\overset{}{\underset{X}{}}-COC_6H_5$$
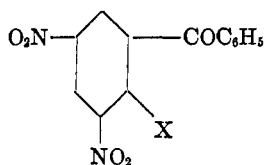
where x = Cl, Br, OCH₃, and with ketones having substituents in both phenyl groups, but, because of experimental difficulties quite unrelated to the question of oxime configuration, the results are of little significance (26, 55). Insofar as positive results were obtained they indicated *trans* shifts on rearrangement of the oximes studied.

In none of the cases so far described was it possible to isolate

both isomeric oximes. The same difficulty was experienced by Meisenheimer in studying o-hydroxybenzophenone oxime (23). The one isomer available, which yielded on rearrangement salicylanilide (XVI), could not be dehydrated to furnish the indoxazene (X). In the face of this latter fact Meisenheimer, who was by this time convinced of the generality of the *trans* shift in the Beckmann rearrangement, assigned to the oxime the configuration XVII, and attempted to account for the failure to effect a ring closure to the indoxazene by the dubious assumption that such a ring closure would, by an exercise of residual valence forces, only take place between the ortho hydroxyl group and a spatially distant (*trans*) oximino hydroxyl group. Such a spatially distant hydroxyl group would be found in the then unknown isomeric oxime (XVIII). This assumption which, as we shall see, Meisenheimer also used in other cases was shown to be unjustified when Auwers and Jordan (56) found that o, o'-dihydroxybenzophenone oxime (XIX) could not be dehydrated to yield an indoxazene, and was completely discredited when Kohler and Bruce (57) succeeded in obtaining the hitherto missing o-hydroxybenzophenone oxime and found that it, like its isomer, could not be dehydrated to furnish the indoxazene (X).
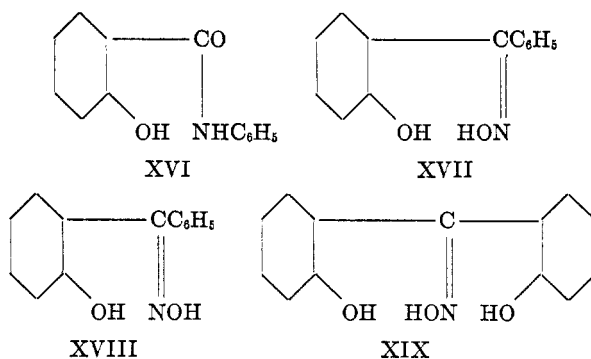

It is clear, therefore, that at present there is no method independent of the Beckmann rearrangement for establishing the configurations of the o-hydroxybenzophenone oximes and that, consequently, it is not possible to decide whether the rearrangement of these oximes proceeds through a *cis* or a *trans* shift. The same

statement applies to the various nuclear substituted *o*-hydroxy-benzophenone oximes (55, 56).

In contrast to these *o*-hydroxybenzophenone oximes it is possible with the oximes of *o*-aminobenzophenone (23, 58, 59) to assign configurations quite independently of the Beckmann rearrangement. Both isomers of *o*-aminobenzophenone oxime are known, both can be rearranged, and both can be converted into cyclic compounds. The high-melting (*h*) isomer on treatment with nitrous acid yields a soluble diazonium salt whose solutions on heating evolve nitrogen while the indoxazene (X) is formed. Consequently the configuration XX is assigned to the oxime. On rearrangement this oxime furnishes the anilide of anthranilic acid (XXI), obviously the result of a *trans* shift.

      X   XX   XXI
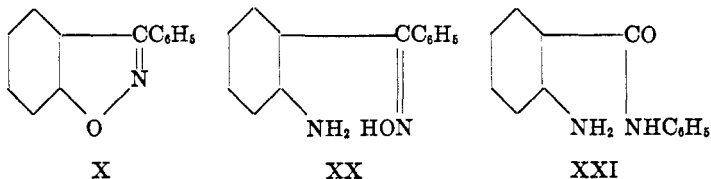
The isomeric low-melting (*n*) oxime on treatment with nitrous acid yields a diazo anhydride (XXIII), which in turn furnishes phenylanthranil (XXIV). (The mechanism of this process is considered later under the discussion of the oxime of *o*-aminoacetophenone.) On the basis of these facts the configuration XXII is assigned to the oxime. Since on rearrangement this oxime yields benzenyl phenylene amidine (XXV) we have another example of the *trans* Beckmann rearrangement.

      XXIV   XXIII   XXII

                            XXV
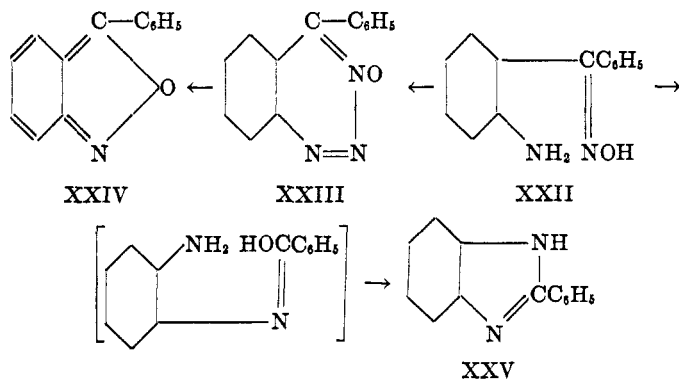
From the aminobenzophenone oximes we turn to the dioximes of benzil (48, 60). Here the facts are as definite as their interpretation is perplexing. The three benzil dioximes are known respectively as α, β, and γ. On rearrangement the α-dioxime furnishes the azoxime (XXVI), the β-dioxime furnishes oxanilide (XXVII), and the γ-dioxime furnishes benzoylphenylurea (XXVIII). For the α- and β-dioximes there is no adequate evidence independent of the Beckmann rearrangement for assigning configurations and, therefore, it is not possible to state whether their rearrangement involves a *cis* or a *trans* shift. On the older assumption of a *cis* shift the α-dioxime would be assigned the *syn* configuration and the β-dioxime the *anti* configuration. On the newer assumption of a *trans* shift these configurations would be reversed. It is true that the formation of the α-dioxime from the α-monoxime of benzil (IV) indicates the *anti* configuration for the α-dioxime and therefore a *trans* shift in the rearrangement of that dioxime. However, if the α-dioxime does have the *anti* configuration, then the formation of the azoxime (XXVI) on rearrangement involves a *trans* dehydration and ring closure. (Compare formula XXVIa. Diagram 1 gives a schematic survey of the rearrangements and ring closures observed with the benzil dioximes.)

In the case of the γ-dioxime the difficulties are even more pronounced. For to this γ-dioxime would be assigned the same, *amphi*, configuration on the basis of either a *cis* or a *trans* shift on rearrangement. Further, the formation of the γ-dioxime from the β-monoxime of benzil (III) would also indicate the *amphi* configuration. But the γ-dioxime, alone of the three benzil dioximes, can be converted into a cyclic compound—on dehydration it yields the furazane (XXIX). And the *syn* configuration which one would be tempted to assign to the γ-dioxime on the basis of this ring closure is incompatible not only with a *cis* shift on rearrangement but also, and equally so, with a *trans* shift. Meisenheimer has suggested, in order to reconcile the ring closure of the γ-dioxime with its behavior on rearrangement, that this ring closure involves a *trans* elimination of water and would be expected to take place only with an oxime having the *amphi* con-

DIAGRAM 1

The dioximes of benzil

Configurations on the basis of a *cis* shift

Configuration on the basis of a *trans* shift.

XXVIa

XXVI

XXVII

XXVIII

XXIX

α

β

γ
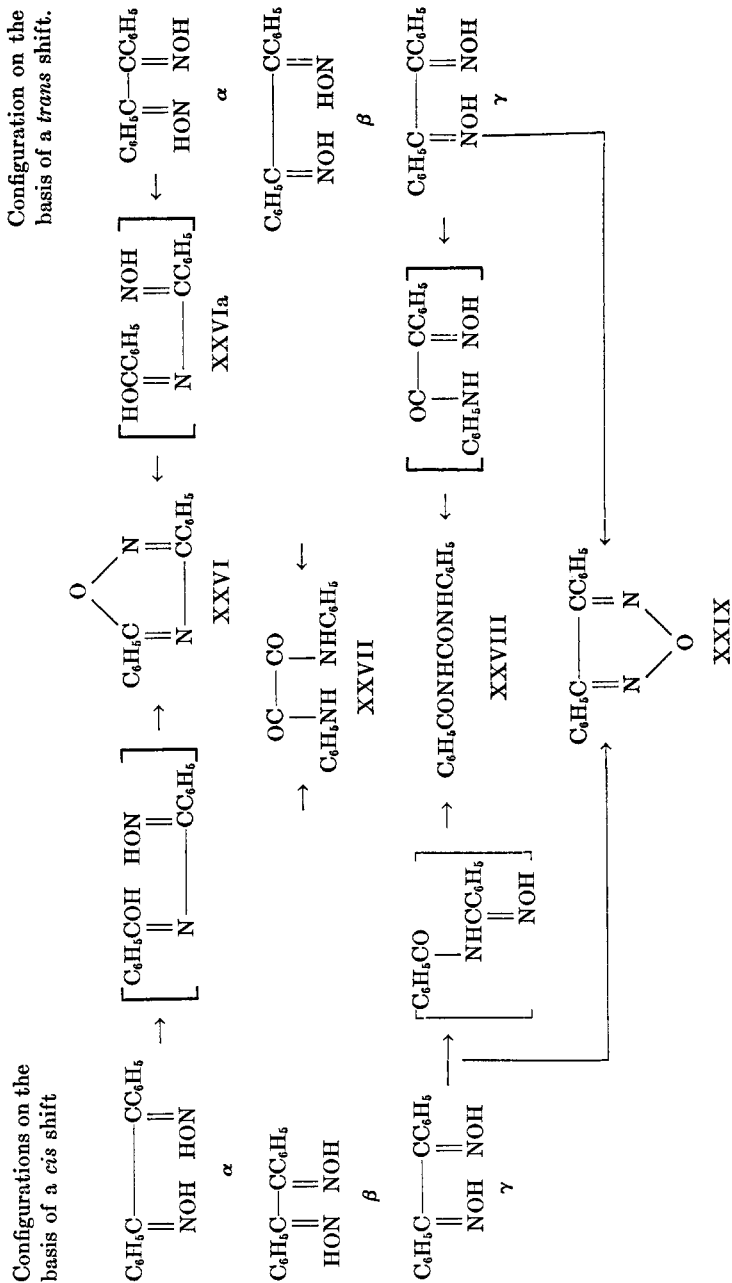
figuration. We have already seen that a similar assumption in the case of the *o*-hydroxybenzophenone oximes was unjustified. From what we have seen of the behavior of various *o*-hydroxy oximes there is good reason to suspect that the dehydration of these oximes to yield cyclic compounds is by no means the simple and direct process it appears in our ordinary formulation. It is probably better and certainly safer, since the configuration of the γ-dioxime of benzil as deduced from ring closure is consistent with neither a *cis* nor a *trans* shift on rearrangement, to admit that for the present the benzil dioximes, like the *o*-hydroxybenzophenone oximes, furnish no evidence one way or the other as to the nature of the shift in the Beckmann rearrangement.

In concluding the discussion of diketone oximes, attention should be called to two recent articles on this subject. Taylor (61) has discussed the configurations of the monoximes of a considerable series of α-diketones. He accepted at the outset the configurations for these oximes as deduced from their Beckmann rearrangement products with the assumption of a *trans* shift in the rearrangement, and then showed that the collateral evidence for configuration agreed with the configurations thus assigned. This collateral evidence is of four types: the reactivity of the carbonyl group in the oximes, the behavior of the oximes in coordinate compound formation, the solubility of the oximes, and the coupling reactions of the oximes with aromatic diazonium compounds. Meisenheimer, in a very recent investigation (62), has presented evidence for a reversal of the configurations previously assigned to certain of the oximes of camphor quinone. The configurations assigned by Meisenheimer, taken in conjunction with the behavior on rearrangement, indicate for the camphor quinone oximes studied a *trans* shift on rearrangement.

In addition to the oximes of purely aromatic ketones, such as benzophenone, and of α-diketones, such as benzil, considerable attention has been given to the determination of the configuration of the oximes of mixed aliphatic-aromatic ketones. This has centered largely around the *o*-substituted acetophenones. Many years ago Claus (63) found that the simple *o*-halogenated acetophenones furnished each but a single oxime and that these single

oximes did not form indoxazenes on treatment with alkali. Meisenheimer (26) verified these observations and pointed out that the failure to form an indoxazene was indicative of the configuration XXX (x = Cl, Br), for the oximes in question. Since, furthermore, the members of this class of oximes yield on rearrangement halogenated acetanilides (XXXI, x = Cl, Br), it follows that their rearrangement involves a *trans* shift.
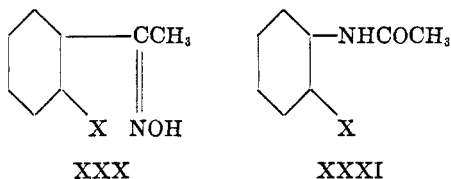
Again making use of a para nitro group to increase the reactivity of the aromatic halogen, Meisenheimer investigated 2-bromo-5-nitroacetophenone. From this ketone he was able to obtain both isomeric oximes. The stable oxime is not attacked by cold alkali and is only slightly attacked by hot alkali. Consequently the *anti* phenyl configuration (XXXII) is assigned to it. On rearrangement this oxime furnishes the 2-bromo-5-nitroanilide of acetic acid (XXXIII)—clearly the result of a *trans* shift.
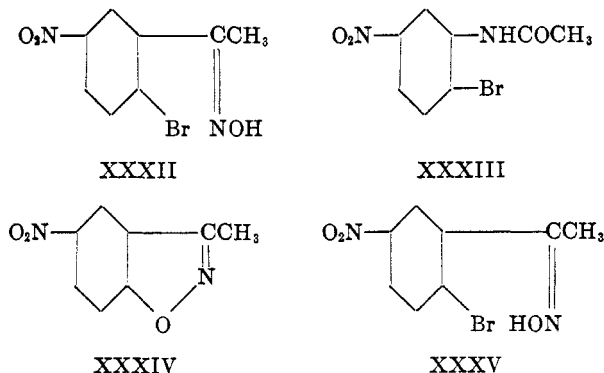
The labile oxime of this same ketone is very easily converted even by cold alkali into the indoxazene (XXXIV). Hence to the labile oxime is assigned the *syn* phenyl configuration (XXXV). Unfortunately for the completeness of the evidence, the labile

oxime is one of the few oximes which it has not been possible to rearrange.

The one known oxime of o-aminoacetophenone (59) is of interest in that its behavior on diazotization has shed light on the mechanism of the formation of phenylanthranil from the low-melting oxime of o-aminobenzophenone. To the oxime of o-amino-acetophenone, on the basis of the following sequence of reactions to form methylanthranil (XXXVII), is assigned the configuration XXXVI.

XXXVI

XXXVII
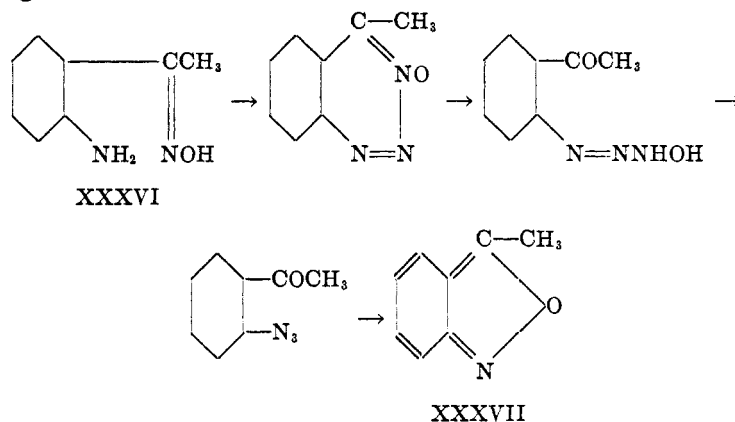
The acetophenones so far studied yield, with few exceptions, a single oxime. When it has been possible to determine the configuration of that single oxime it has been found to be the *anti* phenyl isomer. Since this isomer undergoes rearrangement in such manner that the aromatic group shifts, the rearrangement necessarily involves a *trans* shift. In the few instances where isomeric acetophenone oximes have been isolated, the statements just made apply to the stable isomer.

Only one other group of oximes, the oximes of α,β-unsaturated ketones, have had their configurations determined independently of the Beckmann rearrangement and need to be considered in discussing the nature of the shift in that rearrangement. It has long been known that α,β-unsaturated ketones, such as benzalaceto-phenone (XXXVIII), yield on treatment with hydroxylamine hydrochloride a single oxime, and on treatment with hydroxyl-

amine and alkali several products, among them an isoxazoline. Auwers (64, 35) has assigned a configuration to the oxime of benzalacetophenone on the following grounds. First, because the formation of the isoxazoline (XL) proceeds, according to Auwers' views, through the oxime (XXXIX) as an intermediary, there remains only the configuration XLI for the one oxime actually isolated. Second, because benzalacetophenone oxime is not converted into a cyclic compound by alkali, while α-bromobenzalacetophenone oxime, to which Auwers assigns the configuration XLII, is cyclized by this reagent, the configuration XLI is again assigned to benzalacetophenone oxime. With this configuration assigned to the oxime it follows, since on rearrangement the oxime yields cinnamanilide (XLIII), that the rearrangement proceeds through a *cis* shift.

$$C_6H_5CH{=}CHCOC_6H_5 \qquad C_6H_5CH{=}CHCC_6H_5 \qquad C_6H_5CHCH_2CC_6H_5$$

$$\underset{\text{HON}}{\overset{\|}{}} \qquad \underset{\text{O}\text{——}\text{N}}{\overset{|\qquad\|}{}}$$

$$\text{XXXVIII} \qquad\qquad\qquad \text{XXXIX} \qquad\qquad\qquad \text{XL}$$

$$C_6H_5CH{=}CHCC_6H_5 \qquad C_6H_5CH{=}CBrCC_6H_5 \qquad C_6H_5CH{=}CHCONHC_6H_5$$

$$\underset{\text{NOH}}{\overset{\|}{}} \qquad\qquad \underset{\text{HON}}{\overset{\|}{}}$$

$$\text{XLI} \qquad\qquad\qquad \text{XLII} \qquad\qquad\qquad \text{XLIII}$$
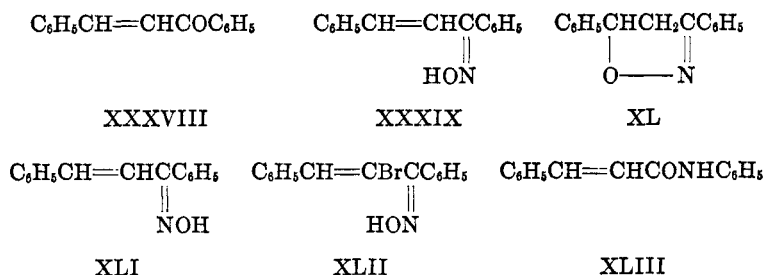
The conclusions of Auwers have not gone unchallenged by other workers (38, 39). In the case of benzal-*p*-bromoacetophenone (XLIV) it has been possible to isolate not only the isoxazoline (XLV) but also both of the isomeric oximes and to show that neither oxime yields the isoxazoline on treatment with alkali. The configuration of the predominant oxime, which corresponds to the one oxime obtained from benzalacetophenone, was established as shown in formula XLVI, by bromination to yield the dibromo oxime (XLVII) and by the conversion of this dibromo oxime into the isoxazole (XLVIII). It was also possible to show, by going back from the dibromo oxime to the unsaturated oxime, that no shift in configuration had taken place on bromination. With the configuration XLVI established for the oxime which on rearrangement furnishes the *p*-bromoanilide of cinnamic acid

(XLIX), this rearrangement must involve a *trans* shift. The configuration of the second oxime of benzal-*p*-bromoacetophenone could not be established by ring closure but had to be assigned by exclusion, for it was found that this oxime (L) on bromination underwent a shift of configuration and furnished the dibromo oxime (XLVII). From this work it would follow that the rearrangement of these α,β-unsaturated oximes proceeds through a *trans* shift. In two recent publications Auwers (36, 37) has shown from a study of the oximes of dibenzalacetone that his previous argument that an oxime with its hydroxyl group spatially adjacent to an ethylenic double bond would be unstable and would isomerize to an isoxazoline is not valid. Further, from an as yet incomplete comparison of the oximes of benzalacetophenone and benzalacetone and their derivatives, he has concluded that while the configuration he formerly advanced for benzalacetophenone oxime can no longer be considered as proved, still the alternative configuration derived from the work with benzal-*p*-bromoacetophenone oxime likewise cannot be considered to be conclusively established. Although there is not as yet complete agreement between the various workers on the question of the configurations of the oximes of α,β-unsaturated ketones, it would seem that the configurations established in the case where both isomeric oximes were isolated are the more reliable and that, therefore, it is legitimate to conclude that the rearrangement of α,β-unsaturated ketoximes involves a *trans* shift.

$$C_6H_5CH{=}CHCOC_6H_4Br \qquad \begin{array}{c} C_6H_5CHCH_2CC_6H_4Br \\ | \quad\quad || \\ O{-}{-}{-}N \end{array}$$

$$\text{XLIV} \qquad\qquad \text{XLV}$$

$$\begin{array}{c} C_6H_5CH{=}CHCC_6H_4Br \\ || \\ HON \end{array} \qquad \begin{array}{c} C_6H_5CHBrCHBrCC_6H_4Br \\ || \\ HON \end{array}$$

$$\text{XLVI} \qquad\qquad \text{XLVII}$$

$$\begin{array}{c} C_6H_5C{=}CHCC_6H_4Br \\ | \quad\quad || \\ O{-}{-}{-}N \end{array} \qquad C_6H_5CH{=}CHCONHC_6H_4Br \qquad \begin{array}{c} C_6H_5CH{=}CHCC_6H_4Br \\ || \\ NOH \end{array}$$

$$\text{XVIII} \qquad\qquad\qquad \text{XLIX} \qquad\qquad\qquad \text{L}$$
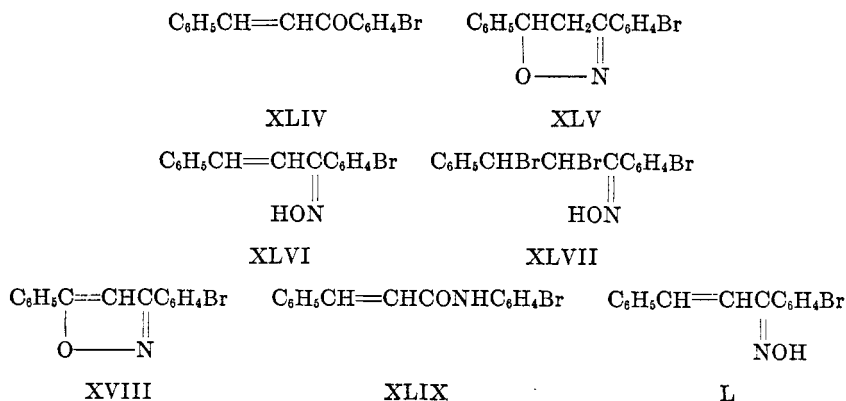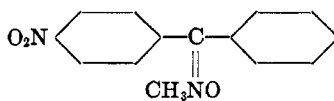
Physical evidence of oxime configurations

This completes our survey of the chemical evidence for oxime configurations and we may now consider the physical evidence on this point which has been accumulated in the last few years. This evidence in the main deals with the solubility of oximes (65), and their behavior in salt and coördinate compound formation (61, 66). In general, the evidence is favorable to oxime configurations which, taken in conjunction with the rearrangement products of the oximes in question, indicate *trans* shifts on rearrangement (67). Perhaps the most interesting single piece of physical evidence available at present is the measurement by Sutton and Taylor (68) of the dipole moments of the nitrogen methyl ethers of the oximes of *p*-nitrobenzophenone. The ether obtained from the α-oxime possesses a dipole moment slightly more than six times as large as the ether obtained from the β-oxime. Hence to the former ether is assigned the configuration LI and to the latter ether the configuration LII. On the assumption that no shifts have occurred on alkylation the α-oxime is assigned formula LIII and the β-oxime formula LIV. Since the α-oxime on rearrangement furnishes the anilide of *p*-nitrobenzoic acid (LV), while the β-oxime furnishes the *p*-nitroanilide of benzoic acid (LVI), the rearrangement of these oximes involves *trans* shifts.
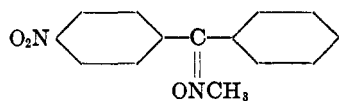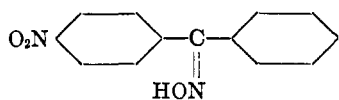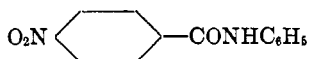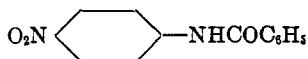
Stereochemical evidence of oxime configuration

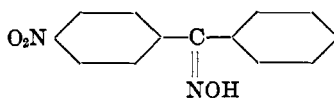Finally, there is the stereochemical evidence of oxime configuration to be considered. Meisenheimer, basing his attack on the recent work which has shown that hindrance to free rotation gives rise in many cases to isomerism (69), has studied the oximes of 1-aceto-2-hydroxy-3-naphthoic acid (70). This substance would be expected to furnish two oximes. One of these, the *syn* methyl (LVII), should not be resolvable, while the other, the *anti* methyl (LVIII) should, because of the hindrance to rotation about the nitrogen-oxygen linkage, be obtained as a racemic form capable of being resolved into its active components. These predictions were verified by experiment. The oxime which is not resolvable, the *syn* methyl isomer (LVII), was rearranged—to avoid complications the ethyl ester rather than the free acid was taken for rearrangement—and furnished the substituted naphthyl amide of acetic acid (LIX). The oxime which is resolvable, the *anti* methyl isomer (LVIII), on rearrangement, again *via* the ethyl ester, furnished the methyl amide of a substituted naphthoic acid (LX). In both cases, the first ones where oxime configurations have been determined on stereochemical rather than chemical grounds, the configurations so determined, taken in conjunction with the rearrangement products of the oximes, indicate unequivocally *trans* shifts on rearrangement.
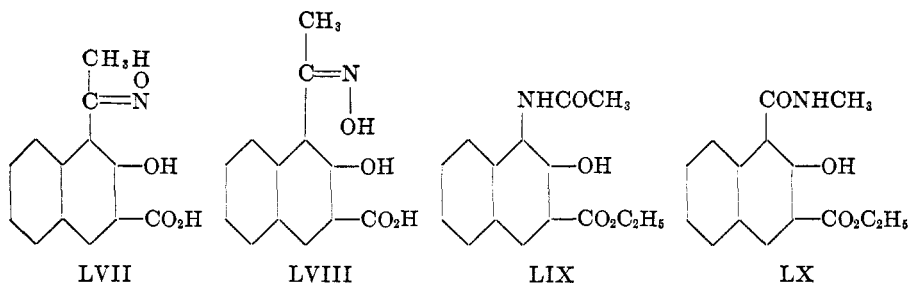
LVII   LVIII   LIX   LX

The generality of the trans shift in the Beckmann rearrangement

This concludes our survey of the evidence dealing with the nature and generality of the shift in the Beckmann rearrangement of ketoximes. What conclusions may be drawn from that evi-

dence?   At the outset it may be said that, with one exception, in every case where it has been possible to establish the configuration of a ketoxime by chemical, physical, or stereochemical means the configuration so established, taken in conjunction with the rearrangement product of the oxime, indicates that a *trans* shift has taken place on rearrangement.   The one exception is the γ-dioxime of benzil whose configuration as deduced from ring closure was, it will be remembered, incompatible not only with a *trans* shift b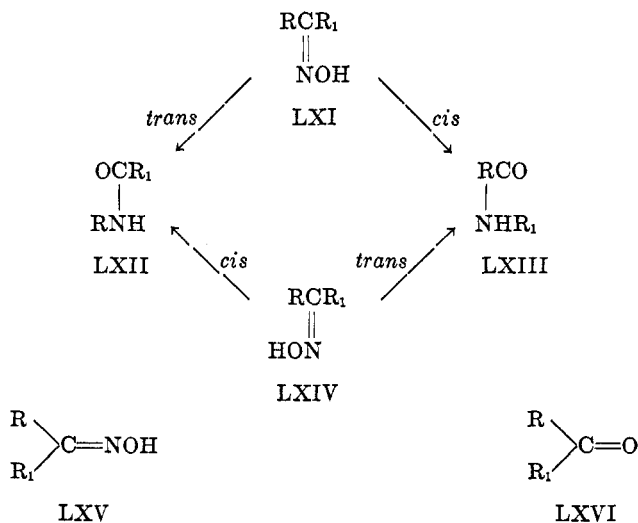ut also with a *cis* shift.   Once granted that in all established cases the rearrangement involves a *trans* shift, the question arises whether we are justified in assuming that the Beckmann rearrangement invariably proceeds through a *trans* shift. Such an assumption obviously involves a considerable amount of what may be termed logical extrapolation, but it has in its favor that it is the simplest explanation which fits the known facts. In view of the amount, the variety, and the consistency of the evidence favoring a *trans* shift, it is the writer's opinion that we are justified in assuming that the *trans* shift is general, and we may safely derive the configuration of ketoximes from a study of their rearrangement products and the assumption of a *trans* shift on rearrangement.[2,3]   It is only fair to point out, however, that any answer other than a statistical one to the question of the generality of the *trans* shift is not yet possible and will not become possible by the simple numerical process of collecting additional examples of *trans* shifts.   The collection of such additional examples will of course increase the probability that our assumption of a

[2] Raikowa (71) has questioned the validity of the use of the Beckmann rearrangement for determining the configuration of any ketoxime having a hydrogen atom on a carbon atom alpha to the $C{=}N$ group because of the possible existence of iso-oximes.   The none too substantial evidence adduced in favor of this view has been examined critically by Auwers (72), who was unable to verify the facts cited by Raikowa.   Compare also reference 104.

[3] We have avoided up to this point the consideration of the configuration of aldoximes.   However, attention should be called to the work of Brady and Bishop (73) which indicates that aldoxime configurations will probably require the same revision now being given to the configurations of ketoximes.   Also to the fact that the Beckmann rearrangement of the second order must, in view of the revised configurations assigned to the benzil monoximes, be considered as involving a *trans* cleavage.

general *trans* shift is correct, and these examples will be particu-
larly valuable when they deal with classes of oximes as yet un-
studied from this point of view, but a final answer to the question
of the nature and generality of the shift will be possible only when
the forces which bring about the Beckmann rearrangement and
the mechanism of the rearrangement are known.

At this point a digression is necessary in order to make clear that
the question whether the shift in the Beckmann rearrangement
is *cis* or *trans* does not enter into consideration when the rear-
rangement is used for the purpose of determining the structure of
ketoximes and thereby the structure of the ketones from which the
oximes are derived. This is of importance, since the Beckmann
rearrangement, followed by hydrolysis and identification of the
resulting acid and amine, is an extremely valuable method of
determining the structures of oximes and their parent ketones.
An example will make clear our point. From any given oxime
(LXI) one would obtain by a *trans* shift the amide (LXII), by a
cis shift the isomeric amide (LXIII). The isomeric oxime (LXIV)
by a *trans* shift would furnish the amide (LXIII), by a *cis* shift
the amide (LXII). But from both oximes only two amides can
result. And from either amide one can deduce the *structure* (not
the configuration) of the oxime as LXV and hence the *structure* of
the parent ketone as LXVI.

$$RCR_1$$
$$\|$$
$$NOH$$

trans   LXI   *cis*

$$OCR_1 \qquad\qquad RCO$$
$$| \qquad\qquad\qquad |$$
$$RNH \qquad\qquad NHR_1$$

LXII   *cis*   *trans*   LXIII

$$RCR_1$$
$$\|$$
$$HON$$

LXIV

$$\begin{array}{c} R \\ \diagdown \\ \diagup \\ R_1 \end{array} C{=}NOH \qquad\qquad \begin{array}{c} R \\ \diagdown \\ \diagup \\ R_1 \end{array} C{=}O$$

LXV   LXVI

The question whether the shift on rearrangement of a ketoxime is *cis* or *trans* is, we may repeat, of fundamental significance in connection with the configuration of ketoximes and the mechanism of the Beckmann rearrangement, but it has no bearing on the use of the rearrangement for the determination of structure.

We may now proceed to an examination of the various mechanisms proposed to elucidate the Beckmann rearrangement, keeping particularly in mind as a result of the discussion to this stage that any mechanism to be satisfactory must take into account the occurrence of the *trans* shift on rearrangement.

II. THE MECHANISM OF THE BECKMANN REARRANGEMENT

The views of Beckmann concerning the mechanism of the rearrangement

It is only appropriate that we begin our review of the work on the mechanism of the Beckmann rearrangement with a consideration of the views of Beckmann himself. Particularly is this true since, as we shall see, most of the chemists who have devoted their efforts to a study of this problem have come at the end of their work, whatever they may have thought at the beginning, to views essentially the same as those of Beckmann. Fairly early in his study of the rearrangement, Beckmann (74) came to the conclusion that because of the wide variety of reagents capable of effecting the rearrangement of ketoximes it was highly improbable that any single intermediate compound or even any single type of intermediate compound was involved. In his opinion the rearrangement was best represented in the following formal fashion

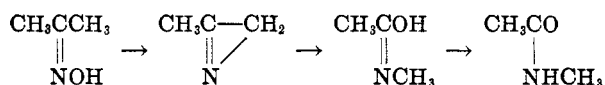$$\begin{array}{ccc} RCR & \left[RCOH \right] & RCO \\ \| & \to \| & \to \| \\ NOH & NR & NHR \end{array}$$

and it consisted of the migration of the hydroxyl group and one of the hydrocarbon residues of the oxime. The function of the reagent employed was purely and simply that of a catalyst. Beckmann (18), after the appearance of the work of Meisenheimer on

the *trans* shift, accepted the existence of such a shift and, while retaining his fundamental idea of a direct interchange of groups, employed the concept of partial valences to account for the fact that the groups spatially distant changed places. (The use of partial valences in explaining the *trans* shift will be considered in detail later.)

The mechanism suggested by Wallach

Beckmann's view of the direct interchange of groups was, of course, anathema to most organic chemists, as it still is in fact to many. Perhaps the reason for this unwillingness to accept the idea of a simple shift of groups, which is found not only in connection with the Beckmann rearrangement but also in connection with other rearrangements, lies in the thought that such an admission involves a weakening, if not an actual denial, of the validity of structural formulas. At any rate an attempt was not lacking to account for the Beckmann rearrangement on the basis of conventional intermediate compounds of such nature as to permit the establishment of the new linkages before the old ones were broken. The suggestion of Wallach may be considered in this connection. Wallach (75) assumed in the rearrangement of aliphatic and of mixed aliphatic-aromatic ketoximes the formation of a three-membered heterocyclic intermediate. According to this view the following steps were involved in the rearrangement.

$$
\begin{array}{ccccccc}
CH_3CCH_3 & & CH_3C\text{---}CH_2 & & CH_3COH & & CH_3CO \\
\| & \rightarrow & \|\diagup & \rightarrow & \| & \rightarrow & | \\
NOH & & N & & NCH_3 & & NHCH_3
\end{array}
$$

Montagne (76) almost immediately pointed out that this ingenious mechanism could be tested experimentally in the case of aromatic ketoximes and described the results of such a test. It will be observed from the reaction series A that the rearrangement of p, p'-dichlorobenzophenone oxime according to Wallach's view should yield the m-chloroanilide of p-chlorobenzoic acid—that is, after rearrangement the group which has migrated must be attached to the nitrogen atom by a different carbon atom than that

by which it was attached to the carbonyl carbon atom in the oxime.[4]

Cl—⟨ ⟩—C(=NOH)—⟨ ⟩—Cl → [Cl—⟨ ⟩—C—⟨ ⟩—Cl (with N bridging)] →

[Cl—⟨ ⟩—COH(=N—⟨ ⟩—Cl)] → Cl—⟨ ⟩—CO—NH—⟨ ⟩—Cl (A)
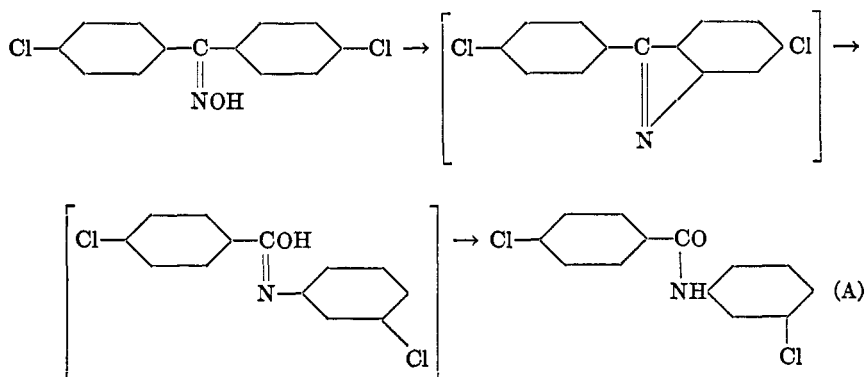
When Montagne rearranged the oxime of *p,p'*-dichlorobenzophenone he found that the product was not the *m*-chloroanilide of *p*-chlorobenzoic acid but was the *p*-chloranilide of that acid—that is, after rearrangement the group which has migrated is attached to nitrogen by the same carbon atom by which it was attached to the carbonyl carbon atom in the oxime. This, of course, disposed of Wallach's mechanism so effectively that it is almost superfluous to point out that it would be extremely difficult, if not impossible, to account for a *trans* shift on the basis of that mechanism.

Sluiter's measurements of the rate of rearrangement

Measurements of the rate of rearrangement of acetophenone oxime were made by Sluiter (77), who used concentrated sulfuric acid as both solvent and reagent and who followed the progress of the reaction by hydrolysis of the resulting acetanilide and titration of the acetic acid thus liberated. Sluiter found that the reac-

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[4] The argument still holds even if one cares to make the very unlikely assumption that the intermediate anhydro compound is formed through the *meta* position in the phenyl group.

Cl—⟨ ⟩—C(=N)—⟨ ⟩—Cl
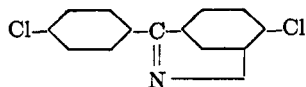
tion had a large temperature coefficient and that the reaction velocity was increased by an increase in the strength of the sulfuric acid used. He found, further, that with acid of a given strength and at a given temperature the reaction measured was of the first order, for the amount of acetanilide formed under these conditions was proportional only to the amount of oxime present. On the basis of this last fact Sluiter formulated the rearrangement in the manner shown in the reaction series B.

$$
\underset{\substack{\| \\ \text{NOH}}}{\text{RCR}'} + \text{HX} \xrightarrow{\text{rapid}} \underset{\substack{\| \\ \text{NX}}}{\text{RCR}'} \xrightarrow{\text{slow}} \underset{\substack{\| \\ \text{NR}'}}{\text{RCX}} + \text{H}_2\text{O} \xrightarrow{\text{rapid}} \underset{\substack{| \\ \text{NHR}'}}{\text{RCO}} \quad \text{(B)}
$$
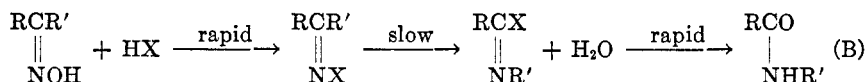
Sluiter's interpretation of his results offers an illustration of the caution which must be exercised in analyzing organic reactions solely on the basis of physical measurements. His results, as well as later experiments by Kuhara, do show definitely that the slowest reaction involved in the Beckmann rearrangement is a reaction of the first order; they give, however, no evidence of the nature of that first order reaction and certainly cannot be considered as proof that any particular first order reaction is the one actually measured. Indeed later, as we shall see shortly, Stieglitz showed that intermediates of the type postulated by Sluiter did not undergo the Beckmann rearrangement.

Stieglitz' study of the Beckmann rearrangement

Next to be considered are the efforts of Stieglitz and his collaborators to determine the mechanism of the Beckmann rearrangement. Stieglitz' work, covering the period from 1896 to 1916, is with that of Kuhara, which we shall consider later, the most important work on this problem. Stieglitz (78), like Hoogewerff and van Dorp (79) before him, called attention to the analogy between the Beckmann rearrangement of oximes and the Hofmann degradation of amides—in each case a group attached to carbon in the starting material is found attached to nitrogen in the end product of the rearrangement. He further suggested that in each case the rearrangement might proceed through a substance

containing a univalent nitrogen atom as an intermediary. Thus
in the case of the Hofmann reaction,

$$RCONH_2 \rightarrow RCONHBr \rightarrow R-\underset{\underset{O}{\|}}{C}-N \rightarrow R-N{=}C{=}O$$
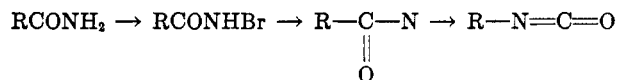
and in the case of the Beckmann rearrangement,

$$\underset{R'}{\overset{R}{\diagdown}}C{=}NOH \rightarrow \underset{R'}{\overset{R}{\diagdown}}C-N\underset{\diagdown H}{\overset{\overset{Cl}{|}}{\diagup OH}} \rightarrow \underset{R'}{\overset{R}{\diagdown}}\overset{\overset{Cl}{|}}{C}-N \rightarrow \overset{R}{\diagup}\underset{\diagup}{\overset{\overset{Cl}{|}}{C}}{=}NR \rightarrow RCONHR$$
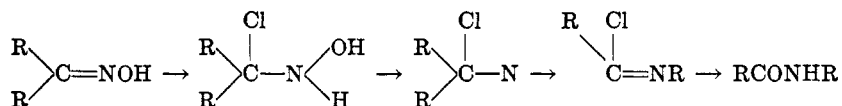
This hypothesis was in accord with the observed facts that to
bring about the Hofmann rearrangement alkali was used as the
reagent, while for the Beckmann rearrangement an acidic and
dehydrating reagent was used. It was not in accord with the
view held by many chemists (80) that the first step in the Beck-
mann rearrangement was the replacement of the oximino hydroxyl
group by a "negative" group to yield an intermediate product
such as I. Stieglitz was then able to show that a substance simi-
lar to I, namely the chloroimino ester II, did not undergo a rear-
rangement of the Beckmann type (78). In later work isomeric
chloroimino esters (81), corresponding to isomeric ketoximes,
were obtained and neither isomer could be rearranged while,
finally, it was possible to isolate isomeric chloroimino ketones
(III and IV) themselves and to show that even they underwent
no Beckmann rearrangement (82, 83).

$$\begin{array}{cccc} \underset{\|}{RCR} & \underset{\|}{C_6H_5COC_2H_5} & \underset{\|}{C_6H_5CC_6H_4Cl} & \underset{\|}{C_6H_5CC_6H_4Cl} \\ NCl & NCl & NCl & ClN \\ I & II & III & IV \end{array}$$
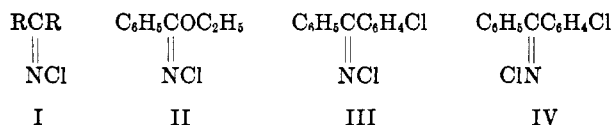
Meanwhile the Curtius rearrangement of acyl azides, like the
Hofmann degradation of amides, was shown to be capable of
assimilation by the univalent nitrogen hypothesis (84), while
Jones (85) pointed out that the Lossen rearrangement of hydrox-

amic acids could be similarly treated.   We have then a formal analogy for these four types of carbon-nitrogen rearrangements.

$$\text{Hofmann: } R-\underset{\underset{O}{\|}}{C}-NHBr \rightarrow R-\underset{\underset{O}{\|}}{C}-N \rightarrow R-N{=}C{=}O \qquad (C)$$

$$\text{Curtius: } R-\underset{\underset{O}{\|}}{C}-N{\overset{\diagup N}{\underset{\diagdown N}{\|}}} \rightarrow R-\underset{\underset{O}{\|}}{C}-N \rightarrow R-N{=}C{=}O \qquad (D)$$

$$\text{Lossen: } R-\underset{\underset{O}{\|}}{C}-NHOH \rightarrow R-\underset{\underset{O}{\|}}{C}-N \rightarrow R-N{=}C{=}O \qquad (E)$$

$$\text{Beckmann: } R-\underset{\underset{R}{|}}{C}{=}NOH \rightarrow R-\underset{\underset{R}{|}}{\overset{\overset{Cl}{|}}{C}}-NHOH \rightarrow R-\underset{\underset{R}{|}}{\overset{\overset{Cl}{|}}{C}}-N \rightarrow R-\overset{\overset{Cl}{|}}{C}{=}NR \quad (F)$$

$$\qquad\qquad\qquad\qquad\qquad V \qquad\qquad\qquad VI$$

In all of these reactions, according to Stieglitz, the reagent gives rise to the univalent nitrogen derivative and then the tendency of the univalent nitrogen atom to revert to a more normal valence state is the driving force which brings about the rearrangement.

From a comparison of the reaction series C, D, E, and F, it will be observed that the application of the univalent nitrogen theory to the Beckmann rearrangement involves, in contrast to its application to the other rearrangements, a preliminary addition reaction in order to furnish a product (V) which in turn is capable of forming the univalent nitrogen derivative (VI).   No such addition product as V has ever been isolated, but Stieglitz (86, 87) obtained evidence, by analogy, for the behavior of such a substance from a study of triphenylmethylhydroxylamine (VII).   This latter substance, like the intermediate V, is a methylhydroxylamine with three substituents on the methyl carbon atom.   When it is treated with certain of the reagents which bring about the Beckmann rearrangement, triphenylmethylhydroxylamine does

undergo a carbon-nitrogen rearrangement to furnish benzophenone anil (VIII).

$$(C_6H_5)_3CNHOH \rightarrow (C_6H_5)_2C\!\!=\!\!NC_6H_5$$

VII   VIII
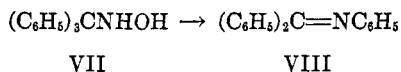
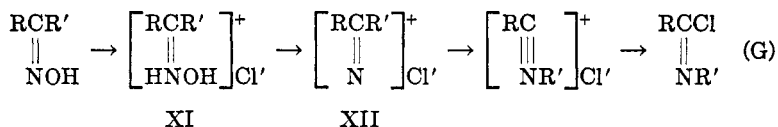While the development which we have just sketched was taking place, Montagne (88) brought forward a critical analysis of the univalent nitrogen theory which completely undermined the validity of that theory, as it was then stated, insofar as the Beckmann rearrangement was concerned. Montagne called attention to the fact that the addition products corresponding to V would be identical from stereoisomeric ketoximes. For, as will be seen from formulas IX and X, the addition of halogen acid to the carbon-nitrogen double bond results in the formation of a single linkage, and with free rotation possible about this carbon-nitrogen single linkage the differences between IX and X disappear. Consequently, since the addition products from stereoisomeric ketoximes are identical, it follows that the same univalent nitrogen intermediate would be formed from both isomeric oximes, and both oximes should yield the same amide as their rearrangement product. Of course, stereoisomeric oximes on rearrangement yield not the same but isomeric amides, so that the univalent nitrogen theory in the form in which it was first advanced is untenable.

$$
\begin{array}{cc}
\text{RCR}' & \text{RCR}' \\
\| & \| \\
\text{NOH} & \text{HON} \\
\downarrow & \downarrow \\
\text{Cl} & \text{Cl} \\
| & | \\
\text{R--C--R}' & \text{R--C--R}' \\
| & | \\
\text{HNOH} & \text{HONH} \\
\text{IX} & \text{X}
\end{array}
$$
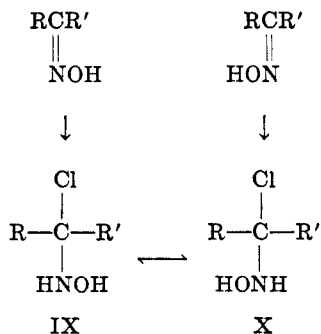
Stieglitz was quick to admit the validity and importance of Montagne's criticism and to modify the univalent nitrogen theory, insofar as ketoximes were concerned, accordingly. The modified

theory was formulated in electronic terms at a time when a non-polar linkage was assumed to be due to the complete transfer of an electron from one atom to another. The reader is therefore referred to the original article (87) for the details of this electronic formulation, as we shall present the modified theory in more modern terms as, indeed, has already been done elsewhere with Stieglitz' approval (89). In its essentials the new view involved the addition of hydrogen chloride to the nitrogen atom of the oxime to yield an ammonium salt (XI).

This ammonium salt, under the influence of the dehydrating agent used to bring about the rearrangement, loses a molecule of water to form the salt (XII) which is considered to be essentially a univalent nitrogen derivative. By this scheme the necessity for breaking the carbon-nitrogen double linkage on the oxime is avoided, but it is difficult to see any significance or reality in the hypothetical salts such as XII.

$$
\underset{\text{XI}}{\begin{array}{c}RCR' \\ \parallel \\ NOH\end{array}} \rightarrow \underset{\text{XI}}{\left[\begin{array}{c}RCR' \\ \parallel \\ HNOH\end{array}\right]^{+}_{Cl'}} \rightarrow \underset{\text{XII}}{\left[\begin{array}{c}RCR' \\ \parallel \\ N\end{array}\right]^{+}_{Cl'}} \rightarrow \left[\begin{array}{c}RC \\ \parallel\parallel\parallel \\ NR'\end{array}\right]^{+}_{Cl'} \rightarrow \begin{array}{c}RCCl \\ \parallel \\ NR'\end{array} \quad \text{(G)}
$$

In the meantime Stieglitz (87, 90) had been continuing the study of the triphenylmethylhydroxylamines and had found that methyl triphenylmethylhydroxylamine (XIII), which would not be expected to furnish a univalent nitrogen derivative, does undergo a rearrangement involving the shift of a phenyl group from carbon to nitrogen.

$$
(C_6H_5)_3CN{\Large\langle}^{CH_3}_{OH} \rightarrow (C_6H_5)_2CO + C_6H_5NHCH_3
$$

XIII
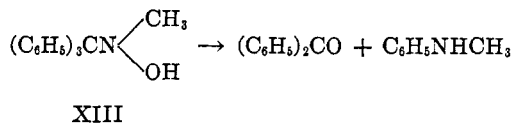
As a result of this work and of the work of Kuhara, Stieglitz concluded that the Beckmann rearrangement might take place in more than one way. One process, the reaction series G, would involve the formation of an ammonium salt, its dehydration to yield a univalent nitrogen salt, and then rearrangement of the
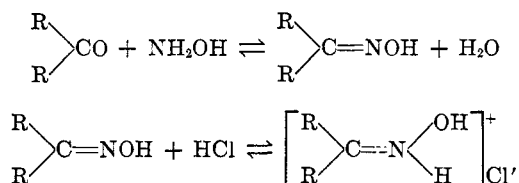
positive ion of this salt. Another process would be the direct interchange of groups as suggested by Beckmann.

The univalent nitrogen mechanism as advanced originally by Stieglitz found many adherents, notable among them Schroeter, who offered a considerable amount of experimental work to verify this mechanism (91). Despite the stereochemical criticism of Montagne, the theory was reaffirmed by Schroeter (92) and re-advanced in essentially its original form by Houben (93) in 1921. Stieglitz' theory does offer the advantage of coördinating by a single hypothesis several different classes of carbon-nitrogen re-arrangements. It is, however, a debatable point whether this unified view is not arrived at by emphasizing formal similarities and neglecting essential differences. Certainly this feature of the theory in the hands of others than Stieglitz has led to some embarrassing difficulties. For in order to emphasize the similarities between the various types of carbon-nitrogen rearrangements, several chemists have adopted the questionable expedient of referring to them all as Beckmann rearrangements. They have as a result found themselves in the awkward predicament of writing about four types of Beckmann rearrangements, advancing a single theory (univalent nitrogen) to explain these four types of rearrangements, and then being forced to admit that the general explanation of the Beckmann rearrangement (in the wider sense) did not apply to the Beckmann rearrangement itself.

In concluding this discussion of the univalent nitrogen mechanism it should be pointed out that this mechanism offers no explanation for the *trans* shift. Furthermore, it is only fair to note that the difficulties to which we have called attention in the application of this mechanism to the rearrangement of ketoximes are not encountered when the mechanism is applied to other types of carbon-nitrogen rearrangements. The merits of the univalent nitrogen mechanism when dealing with the Hofmann, Curtius, and Lossen rearrangements should be considered quite apart from its merits when dealing with the Beckmann rearrangement.

At this place it will be advisable to depart from such chronological sequence as we have followed, in order to consider the work of Lachmann, who emphasized the view that salt formation is an

essential step in the Beckmann rearrangement (8). Lachmann, like Henrich (94) and Lehmann (7), showed that oxime salts rearranged. He then called attention to the equilibria existing in acid solutions of oximes, from which he concluded that even in an aqueous solution of an oxime it should be possible to bring about rearrangement if the hydrogen-ion concentration is sufficient to ensure the presence of the oxime as a salt.

$$\begin{array}{c} R \\ \diagdown \\ R \diagup \end{array} CO + NH_2OH \rightleftharpoons \begin{array}{c} R \\ \diagdown \\ R \diagup \end{array} C{=}NOH + H_2O$$

$$\begin{array}{c} R \\ \diagdown \\ R \diagup \end{array} C{=}NOH + HCl \rightleftharpoons \left[\begin{array}{c} R \\ \diagdown \\ R \diagup \end{array} C{=}N \begin{array}{c} \diagup OH \\ \diagdown H \end{array} \right]^{+} Cl'$$
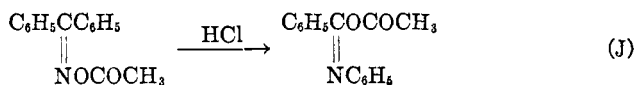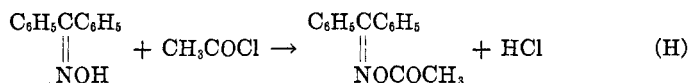
In conformity with this view Lachmann was able to effect the rearrangement of benzophenone oxime in aqueous solution (95). This fact led him to adopt essentially Beckmann's view of the rearrangement as a direct interchange of groups—this interchange, however, occurring according to Lachmann in the positive ion of the oxime salt rather than in the oxime itself, and no dehydration of the oxime salt being necessary to bring about rearrangement. No explanation was advanced to account for the fact that the interchange involves groups spatially distant from one another.
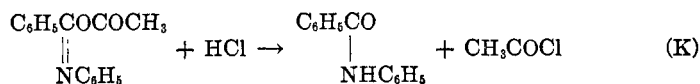
Review of the work of Kuhara

It is our next task to undertake a review of the work of Kuhara. This work, carried on during the fourteen years between 1906 and 1920, we shall consider in considerable detail both on account of its interest and because of its comparative inaccessibility (96). Kuhara's thesis, to state it at the outset in its simplest form, is that the acyl derivatives of oximes undergo rearrangement and that this rearrangement involves a direct interchange of spatially adjacent groups. This is, it will be noted, essentially Beckmann's idea of the direct interchange of groups with the reagent acting as a catalyst. However, according to Kuhara, the acyl derivatives of the oximes and not the oximes themselves rearrange, while the reagent which in one stage of the rearrangement functions as a

true catalyst actually takes part in a subsequent stage of the process. For example, Kuhara formulated the rearrangement of benzophenone oxime on treatment with acetyl chloride in the following fashion (97).

$$
\begin{array}{c}
C_6H_5CC_6H_5 \\
\parallel \\
.NOH
\end{array}
+ CH_3COCl \rightarrow
\begin{array}{c}
C_6H_5CC_6H_5 \\
\parallel \\
NOCOCH_3
\end{array}
+ HCl \qquad (H)
$$

$$
\begin{array}{c}
C_6H_5CC_6H_5 \\
\parallel \\
NOCOCH_3
\end{array}
\xrightarrow{\ HCl\ }
\begin{array}{c}
C_6H_5COCOCH_3 \\
\parallel \\
NC_6H_5
\end{array}
\qquad (J)
$$

$$
XIV
$$

$$
\begin{array}{c}
C_6H_5COCOCH_3 \\
\parallel \\
NC_6H_5
\end{array}
+ HCl \rightarrow
\begin{array}{c}
C_6H_5CO \\
\mid \\
NHC_6H_5
\end{array}
+ CH_3COCl \qquad (K)
$$

According to this view an oxime acetate (XIV) should rearrange if hydrogen chloride is present (reaction J), but since the hydrogen chloride takes part in and is used up by the subsequent reaction (K), it follows that a given quantity of hydrogen chloride should be capable of rearranging only an equivalent amount of an oxime acetate. In other words, considering the reaction in its entirety, the effect of the hydrogen chloride is not catalytic in the usual sense of the term. This, by experiment, was found to be the case. Using the acetate (XIV), the amount rearranged was found to be proportional to the amount of hydrogen chloride present.
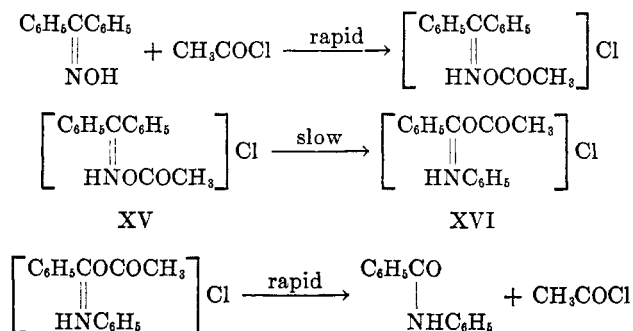
By a continuation of his reasoning that the acyl derivatives of oximes rather than the oximes themselves rearranged, Kuhara came to the conclusion that the rates of rearrangement of a given oxime by a series of acid chlorides should be in the same order as the "negativity" of the acyl groups; in more precise terms, the rates of rearrangement of a given oxime by a series of acid chlorides should be in the same order as the strengths of the acids derived from these acid chlorides. This also was verified experimentally using benzophenone oxime (98) and acetophenone oxime (99) with acetyl chloride, chloroacetyl chloride, and benzenesulfonyl chloride. Some typical results obtained with benzophenone oxime are given in table 1.

Calculations made from data of the type presented in table 1 showed that the reaction being measured was of the first order.
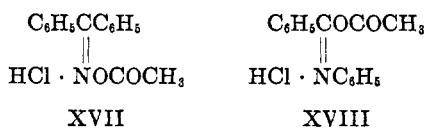
TABLE 1

Rearrangement of benzophenone oxime by acid chlorides

TIME	BENZANILIDE FROM BENZOPHENONE OXIME		
	With CH$_3$COCl	With ClCH$_2$COCl	With C$_6$H$_5$SO$_2$Cl
minutes	*per cent*	*per cent*	*per cent*
10	0.0	61.0	93.2
60	26.9	70.7	—
120	43.9	76.9	—

Similar calculations from the rate of rearrangement of the acetate of benzophenone oxime by hydrogen chloride showed that here also the reaction measured was of the first order. At this point Kuhara revised slightly his method of formulating the rearrangement in favor of the following presentation.

$$C_6H_5CC_6H_5 \quad \underset{NOH}{\overset{\|}{}} + CH_3COCl \xrightarrow{\text{rapid}} \left[\underset{HNOCOCH_3}{\overset{C_6H_5CC_6H_5}{\overset{\|}{}}} \right] Cl$$

$$\left[\underset{HNOCOCH_3}{\overset{C_6H_5CC_6H_5}{\overset{\|}{}}} \right] Cl \xrightarrow{\text{slow}} \left[\underset{HNC_6H_5}{\overset{C_6H_5COCOCH_3}{\overset{\|}{}}} \right] Cl$$

$$\text{XV} \qquad\qquad \text{XVI}$$

$$\left[\underset{HNC_6H_5}{\overset{C_6H_5COCOCH_3}{\overset{\|}{}}} \right] Cl \xrightarrow{\text{rapid}} \underset{NHC_6H_5}{\overset{C_6H_5CO}{\overset{|}{}}} + CH_3COCl$$

In his original publication Kuhara wrote the salts XV and XVI as XVII and XVIII, respectively.

$$\underset{HCl \cdot NOCOCH_3}{\overset{C_6H_5CC_6H_5}{\overset{\|}{}}} \qquad \underset{HCl \cdot NC_6H_5}{\overset{C_6H_5COCOCH_3}{\overset{\|}{}}}$$

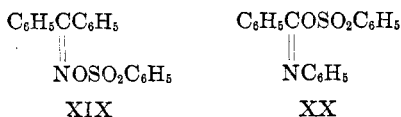$$\text{XVII} \qquad\qquad \text{XVIII}$$

This method of formulating the rearrangement as involving an ammonium salt is not used consistently in Kuhara's articles and is not adhered to even in the discussion which accompanies its origi-

nal presentation (98), for in that discussion Kuhara states that the rearrangement is essentially a shift of the following type.

$$\begin{array}{ccc} \text{RCR}' & & \text{RCOCOR}'' \\ \| \updownarrow & \rightarrow & \| \\ \text{NOCOR}'' & & \text{NR}' \end{array}$$
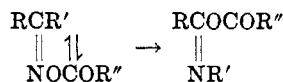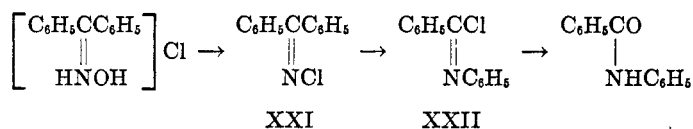
This change is accelerated by an increase in the temperature and an increase in the hydrogen-ion concentration of the rearranging medium. Further, the tendency of the acyl group to migrate is conditioned by its "negativity," as measured by the dissociation constant of the acid derived from the acyl group. This, according to Kuhara, is shown by the fact that whereas the acetate of benzophenone oxime (XIV) requires the presence of hydrogen chloride to undergo rearrangement, the benzenesulfonate of benzophenone oxime (XIX) rearranges even in alkaline solution—that is, rearrangement occurs on treatment of benzophenone oxime in sodium hydroxide with benzenesulfonyl chloride. Apparently a fair résumé of Kuhara's views at this time would be given by the statement that the acyl derivatives of oximes rearrange as such if the acyl group is sufficiently "negative," but if the acyl group does not have sufficient "negativity" to bring about spontaneous rearrangement, then salt formation is a necessary prerequisite to the process. Kuhara would not, as we shall see later, admit that oxime salts, as opposed to the salts of acyl derivatives of oximes, rearranged.

In a very important paper Kuhara (100) investigated in detail the action of benzenesulfonyl chloride on benzophenone oxime. By operating carefully he was able to isolate the benzenesulfonate (XIX) of that oxime and to establish its structure as such by hydrolysis to the oxime and benzenesulfonic acid. The benzenesulfonate, a crystalline solid melting at 62°C., rearranged to yield the ester (XX), instantaneously on melting, more slowly on standing as a solid or by exposure, again as a solid, to ultra-violet radiation. The ester, an oil, could be hydrolyzed by water to furnish benzanilide and benzenesulfonic acid.

$$\begin{array}{ccc} \text{C}_6\text{H}_5\text{CC}_6\text{H}_5 & \qquad & \text{C}_6\text{H}_5\text{COSO}_2\text{C}_6\text{H}_5 \\ \| & & \| \\ \text{NOSO}_2\text{C}_6\text{H}_5 & & \text{NC}_6\text{H}_5 \\ \text{XIX} & & \text{XX} \end{array}$$

Kuhara also worked with oxime salts, the hydrochlorides of acetophenone oxime and of benzophenone oxime. These he found to undergo rearrangement on heating (12). In his attempt to interpret this behavior in the light of his view that rearrangement took place spontaneously when a sufficiently negative group was attached to the oximino nitrogen atom, Kuhara was forced to adopt Procrustean tactics in handling the facts. In his opinion the rearrangement of an oxime hydrochloride involved the following steps. (Kuhara, of course, wrote the hydrochloride in a fashion analogous to formula XVII.)

$$\left[\begin{array}{c} C_6H_5CC_6H_5 \\ \| \\ HNOH \end{array} \right] Cl \rightarrow \begin{array}{c} C_6H_5CC_6H_5 \\ \| \\ NCl \end{array} \rightarrow \begin{array}{c} C_6H_5CCl \\ \| \\ NC_6H_5 \end{array} \rightarrow \begin{array}{c} C_6H_5CO \\ | \\ NHC_6H_5 \end{array}$$

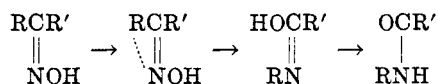$$\qquad\qquad\qquad XXI \qquad\qquad XXII$$

Kuhara was aware that Stieglitz and Peterson (82, 83) had already prepared the imino chlorides of ketones and had showed that they do not undergo a Beckmann rearrangement. To reconcile these facts with his theory, Kuhara was forced to make the experimentally unverifiable assumption that the intermediate (XXI) which he postulated contained a negative chlorine atom instead of the positive chlorine atom found in chloroimino ketones. A ketone chloroimide containing negative chlorine will, according to Kuhara, be incapable of isolation, since its one and immediate reaction will be rearrangement to furnish an imide chloride (XXII).
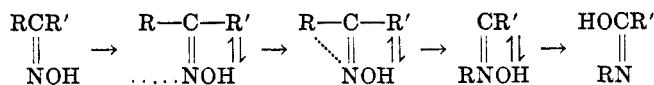
Mechanisms which account for a trans shift on rearrangement

Kuhara's mechanism, like all the other mechanisms which we have examined up to this time, makes no provision for the occurrence of a *trans* shift on rearrangement. There are a number of mechanisms, however, which either do attempt to take into account the *trans* shift or are capable of being extended so as to take it into account. These mechanisms have in common the feature of pictorializing the Beckmann rearrangement as a continuous process by the use of partial or residual valences. The earliest is that of Bucherer (47), who considered that in an oxime par-

tial valence forces are set up between the nitrogen atom and the hydrocarbon residue spatially distant from the oximino hydroxyl group. As the strength of these partial valences increases so as to approximate an ordinary linkage the hydroxyl group shifts.

$$
\begin{array}{ccccccc}
\text{RCR}' & & \text{RCR}' & & \text{HOCR}' & & \text{OCR}' \\
\| & \rightarrow & \backslash\| & \rightarrow & \| & \rightarrow & | \\
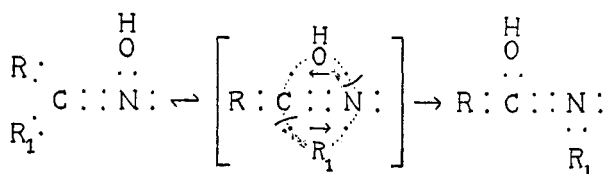\text{NOH} & & \text{NOH} & & \text{RN} & & \text{RNH}
\end{array}
$$

Similar views can be found in the papers of Biltz (101) dealing generally with the problem of organic rearrangements. Meisenheimer (48), also, has suggested a pictorial view of the rearrangement in order to account for the *trans* shift. In his view the attraction between the oximino hydroxyl group and the hydrocarbon residue spatially near it is sufficient to release partial valences on the nitrogen atom so that it eventually captures the hydrocarbon residue spatially distant from the hydroxyl group. This leaves a gap molecule with free valences which then shifts to yield the final product.

$$
\begin{array}{ccccccccc}
\text{RCR}' & & \text{R—C—R}' & & \text{R—C—R}' & & \text{CR}' & & \text{HOCR}' \\
\| & \rightarrow & \| \;\; \| & \rightarrow & \backslash\| \;\; \| & \rightarrow & \| \;\; \| & \rightarrow & \| \\
\text{NOH} & & \text{....NOH} & & \text{NOH} & & \text{RNOH} & & \text{RN}
\end{array}
$$

Perhaps the most definite of these pictorial mechanisms is that of Ramart-Lucas (102), who postulated the existence of single electron linkages or semi-valences. Applied to the Beckmann rearrangement and in somewhat greater detail than is given in the original article we have:
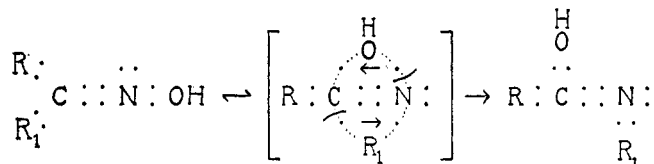
It is odd that at the time this view was put forward (1927) it was not presented as involving a *trans* shift for, superficially at least, as will be seen from the formulas to follow, it is far more easily represented in this fashion than in the way in which it was originally advanced.

$$R : \overset{\overset{\displaystyle H}{\overset{\displaystyle O}{\ldots}}}{\underset{R_1 :}{C :: N :}} \rightleftharpoons \left[R : \overset{\overset{\displaystyle H}{\overset{\displaystyle O}{\ldots}}}{\underset{\overset{\displaystyle \rightarrow}{R_1}}{C :: N :}} \right] \rightarrow R : \overset{\overset{\displaystyle H}{\overset{\displaystyle O}{\ldots}}}{C :: N :} \underset{R_1}{}$$

Classification of the mechanisms suggested for the Beckmann rearrangement

This concludes our survey of the mechanisms advanced for the Beckmann rearrangement. A summary of these mechanisms is now in order and for the purpose of this summary we shall divide the mechanisms into four general classes. This division into classes and the remarks to be made about the various classes will, it is believed, apply not only to the particular mechanisms which we are considering but also to a certain extent to the general problem of the mechanism of organic rearrangements. For in many, if not most, types of organic rearrangements the same four classes of mechanisms will be found to be advanced and, while in certain rearrangements one class of mechanism may be preferred, in general the merits and difficulties found in connection with the four classes as applied to the Beckmann rearrangement will also be found in connection with other rearrangements.

First to be considered is that type of mechanism, exemplified by Wallach's heterocyclic intermediate hypothesis, which seeks to avoid the necessity of admitting a direct interchange of groups or the direct migration of a single group. This end is to be accomplished by the use of intermediate compounds of such nature that the new linkage is established before the old linkage is destroyed. The intermediate compounds postulated by this theory employ only the normal valences of the atoms involved and are such as to be capable of isolation in appropriately chosen cases. We have seen that the one mechanism of this type advanced to account for the Beckmann rearrangement is experimentally untenable. After forty-five years of study of the Beckmann rearrangement with no success, it seems unlikely that this type of mechanism is capable of furnishing an adequate accounting for the processes involved in the rearrangement.

The second group of mechanisms to be considered is that group which attempts a formulation of the rearrangement on the basis of hypothetical intermediate compounds containing free valences —"Lückenmolekülen." The mechanisms of this group treat the rearrangement as a discontinuous process involving first the formation of a gap molecule and next the shift of one or more atoms or groups in that gap molecule to furnish the structural skeleton of the rearrangement product. The best example of this type of mechanism is furnished by the univalent nitrogen hypothesis of Stieglitz. This type of mechanism, in the opinion of the writer, offers little advantage. It is incapable of direct experimental test and it is so flexible that it is hardly possible to test the deductions which can be made from it. There is, it is true, a correspondence between theory and reality in that the correct end-products are predicted by the theory. Since, however, the prediction is made after the fact, it is of little significance. The advantage of this type of mechanism lies chiefly in providing a memory-aiding correlation of various types of rearrangements. It is an open question, however, whether this advantage is not too dearly purchased, for the gap molecule mechanism, by giving an apparent explanation of a set of phenomena, tends to discourage experimentation.[5]

The third group of mechanisms to be considered is exemplified by the views of Bucherer, Biltz, and Ramart-Lucas. (The mechanism advanced by Meisenheimer shares the characteristics of both the second and third groups.) The type of mechanism advanced by these chemists attempts, by the use of partial valences or single electron linkages, to represent the rearrangement as a continuous process. The comments made about the second group of mechanisms apply also to the present group, for the mechanisms of this latter group are also incapable of experimental verification and are of value chiefly as aids in visualizing rearrangements. One member of this group of mechanisms, that of Ramart-Lucas, offers a stimulating possibility. For, formulated in

[5] As an example of the extent to which the idea of intermediates with free valences has been carried, attention may be called to a recent article by Schroeter (33). For a further general discussion of the usefulness of this type of mechanism see Hückel (103).

electronic terms instead of qualitatively by the use of partial valences, one may hope that it will become capable of experimental test with the increase in knowledge of atomic and molecular structure.

Finally there is the group of mechanisms, if mechanisms they may be called, which simply admit an interchange of groups and attempt to determine the point at which the interchange takes place. This was the original view of Beckmann, who held that the oximes themselves rearranged. It was also the view of Kuhara, who showed that the acyl derivatives of oximes rearranged, and the view of Lachmann who held that oxime salts rearranged. Common to all these is the admission of an interchange of groups with no statements about the way in which the interchange takes place. And in the present state of our knowledge of the Beckmann rearrangement we are justified only in such a restatement of the facts. We know that oxime salts rearrange. We know that the acyl derivatives of oximes rearrange. We know that the slowest reaction involved in the rearrangement is a reaction of the first order. And we know that rearrangement takes place between groups spatially distant in the oxime. Other than this we cannot speak with certainty about the Beckmann rearrangement.

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