CCCXX.—*The Isomerism of the Oximes. Part XXVIII. The Beckmann Rearrangement of the* N-*Methyl Ethers of Aldoximes.*

By Oscar L. Brady and Frederick P. Dunn.

Beckmann (*Annalen*, 1909, **365**, 201) showed that *N*-methylbenzaldoxime on treatment with phosphorus pentachloride underwent rearrangement to benzomethylamide, PhCH:NMe:O ⟶ PhCO·NHMe, but this isolated observation in a paper not dealing specifically with the Beckmann rearrangement seems to have escaped notice. We have now found that this is a general reaction with *N*-methyl ethers of aldoximes and occurs with great ease on heating them with acetic anhydride to a temperature just below the b. p. of the reagent; indeed, with *N*-methylbenzaldoxime the reaction is extremely violent; the method is clean and no tarry by-products are formed. If the reaction mixture is cooled at once, in six out of the seven compounds investigated the amide itself is obtained and not the acetylated substance, and in the cases of *N*-methyl-*m*- and -*p*-nitrobenzaldoximes, it crystallises from the acetic anhydride on cooling. This is noteworthy since the methylamides are readily acetylated on boiling with acetic anhydride, and the reaction is of special interest since in these two cases the ultimate product of the Beckmann rearrangement is isolated without the final hydrolytic treatment which is required when phosphorus pentachloride is employed.

It is at once obvious that the numerous theories * of the mechanism of the Beckmann rearrangement involving the form-

---

* The relevant papers are too numerous to quote. The various theories are fairly fully discussed in Johnson and Hahn's translation of Henrich's "Theories of Organic Chemistry," 1922, pp. 131—134, and Chapter XIX.

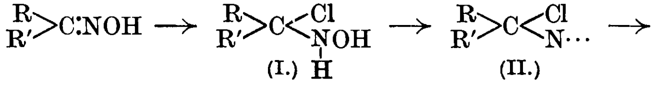
ation of an intermediate compound containing univalent nitrogen are here impossible; indeed, even Stieglitz has abandoned the notion on finding that β-triphenylmethyl-β-methylhydroxylamine suffers rearrangement to phenylmethylaminodiphenylcarbinol,

$$CPh_3{\cdot}NMe(OH) \longrightarrow CPh_2(OH){\cdot}NMePh$$

(Stieglitz and Leech, *J. Amer. Chem. Soc.*, 1914, **36**, 272). The fact that dehydrating agents are employed to bring about the Beckmann rearrangement has in the past strongly favoured the theory that the change is preceded by the elimination of water from a salt of the oxime, but Lachmann (*J. Amer. Chem. Soc.*, 1924, **46**, 1477; 1925, **47**, 260) has discredited this by bringing about the reaction in the presence of water. The behaviour of the *N*-methylbenzaldoximes supports the work of Lachmann, as it is difficult in this instance to devise a mechanism by which water can be eliminated. Lachmann has also shown that it is the hydrochloride and not the oxime which undergoes rearrangement when phosphorus pentachloride is used (see also Henrich, *Ber.*, 1911, **44**, 1533) and it is noteworthy that the *O*-methyl ethers of the aldoximes, which are devoid of basic properties, are not rearranged. The *N*-ethers may be regarded as containing " quinquevalent " nitrogen in themselves (compare Sugden, J., 1925, **127**, 1532), but in any case they readily form salts and it is becoming increasingly evident that the fundamental basis of isomeric change in the oximes is always dependent on the change in valency of the nitrogen atom.

We are of opinion that any explanation of the Beckmann rearrangement must have regard to the following considerations: (1) the rearranging compound must be a salt or a salt-like substance; (2) the elimination of water or the formation of a univalent nitrogen compound must not be essential postulates; and (3) the rupture of the carbon–nitrogen double bond must not be involved before the interchange of radicals takes place.

That condition (3) must be satisfied seems essential, since, in a mechanism such as was at one time suggested by Stieglitz (*Amer. Chem. J.*, 1896, **18**, 754; 1911, **46**, 327) and supported by Schroeter (*Ber.*, 1909, **42**, 2337, 3386; 1911, **44**, 1201), there is no adequate reason why the stereoisomeric ketoximes should give different amides, because (I) and (II) as prepared from either oxime must be racemic mixtures of two enantiomorphs and give the same products on changing.

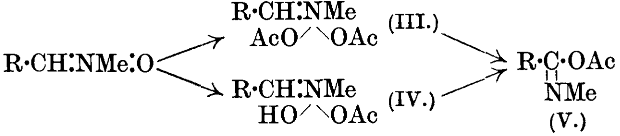


$$\begin{matrix}R\\R'\end{matrix}\!>C{:}NOH \longrightarrow \begin{matrix}R\\R'\end{matrix}\!>C<\!\begin{matrix}Cl\\NOH\\|\\H\end{matrix} \longrightarrow \begin{matrix}R\\R'\end{matrix}\!>C<\!\begin{matrix}Cl\\N\cdots\end{matrix} \longrightarrow$$

(I.) (II.)

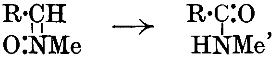
$$RCCl{:}NR' + R'CCl{:}NR \longrightarrow R{\cdot}CO{\cdot}NHR' + R'{\cdot}CO{\cdot}NHR.$$

That elimination of water is not essential seems obvious if one considers the possible intermediate compounds in the rearrangement of the *N*-ethers; addition of acetic anhydride (III) or acetic acid (IV) may occur :



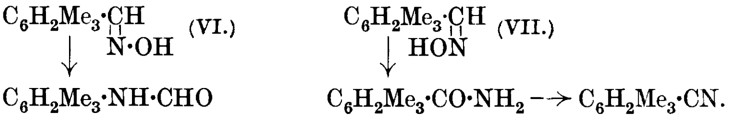
The elimination of acetic acid or water can take place only if the hydrogen attached to the carbon atom is involved, otherwise the *N*-ether would be re-formed; rearrangement would then involve the migration of the OAc group and it seems inconceivable, if compound (V) was formed, that the unacetylated methylamide R·CO·NHMe would crystallise from the excess of acetic anhydride.

The rearrangement of the *N*-ethers supplies the first indication of the configuration of these compounds. Unless the hydrogen atom is so mobile in comparison with the phenyl group that it migrates preferentially, we must assume that there is a definite orientation of the oxygen atom with respect to the groups attached to carbon. Accepting Meisenheimer's view that the Beckmann rearrangement takes place in the *trans*-direction, the change may be represented as



$$\begin{matrix}\mathrm{R{\cdot}CH}\\ \mathrm{O{:}NMe}\end{matrix} \longrightarrow \begin{matrix}\mathrm{R{\cdot}C{:}O}\\ \mathrm{HNMe}\end{matrix},$$

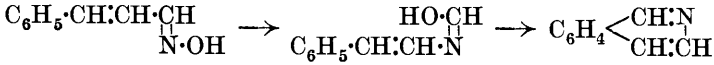
that is, the *N*-ethers have constitutions analogous to the β-oximes. Little work has been done on the Beckmann rearrangement of the aldoximes, but Comstock (*Amer. Chem. J.*, 1897, **19**, 485) has shown that the β-oximes give amides on treatment with cuprous chloride, and Hantzsch and Lucas (*Ber.*, 1895, **28**, 744) found that with phosphorus pentachloride α-mesitylaldoxime (VI) gave form-mesidide, and the β-oxime (VII) trimethylbenzonitrile, probably through the amide :



$$\begin{matrix}\mathrm{C_6H_2Me_3{\cdot}CH}\\ \mathrm{N{\cdot}OH}\end{matrix} \;\text{(VI.)} \quad\longrightarrow\quad \mathrm{C_6H_2Me_3{\cdot}NH{\cdot}CHO}$$

$$\begin{matrix}\mathrm{C_6H_2Me_3{\cdot}CH}\\ \mathrm{HON}\end{matrix} \;\text{(VII.)} \quad\longrightarrow\quad \mathrm{C_6H_2Me_3{\cdot}CO{\cdot}NH_2} \longrightarrow \mathrm{C_6H_2Me_3{\cdot}CN}.$$

Moreover, the formation of *iso*quinoline, and not quinoline, by the action of phosphorus pentoxide on cinnamaldoxime (Bamberger and Goldschmidt, *Ber.*, 1894, **27**, 1954) may, perhaps, be regarded as the result of a Beckmann rearrangement :



$$\begin{matrix}\mathrm{C_6H_5{\cdot}CH{:}CH{\cdot}CH}\\ \mathrm{N{\cdot}OH}\end{matrix} \longrightarrow \begin{matrix}\mathrm{HO{\cdot}CH}\\ \mathrm{C_6H_5{\cdot}CH{:}CH{\cdot}N}\end{matrix} \longrightarrow \mathrm{C_6H_4}\!\begin{matrix}\mathrm{<CH{:}N}\\ \mathrm{<CH{:}CH}\end{matrix}.$$

These two reactions indicate that one cannot assume that the hydrogen atom in the *N*-ether will migrate exclusively.

In the light of this work, the symmetrical formula for the *N*-ethers suggested by one of us (J., 1914, **105**, 2104) cannot be maintained, neither can the argument, there put forward, that a stable α-*N*-ether may be formed during the methylation. It may also be pointed out that the suggested constitution of the sodium salt of the oxime used in connexion with the above argument is not in accord with modern views on the structure of the nitrogen atom. We have, therefore, no explanation of the fact that, whereas some unsymmetrical ketoximes give two *N*-ethers, aldoximes give but one (compare Brady, Dunn, and Goldstein, this vol., p. 2388).

Finally, we have been able to obtain a small yield of the methylamide by heating the hydrochloride of *N*-methyl-*m*-nitrobenzaldoxime; in other cases investigated, so much tar was formed that isolation of crystalline compounds was impossible.

EXPERIMENTAL.

The *N*-methyl ether was dissolved or suspended in five times its weight of pure, cold acetic anhydride and the mixture warmed cautiously on the sand-bath; in most cases, just before the b. p. of the anhydride was reached, there was a vigorous reaction and the solution boiled—in the case of *N*-methylbenzaldoxime, the reaction occurs at a lower temperature with almost explosive violence; the mixture was then cooled rapidly.

With *N*-methyl-*p*-nitrobenzaldoxime, the large quantity of solid which separated was collected, pressed on a porous tile, and crystallised from alcohol, giving *p*-nitrobenzomethylamide, m. p. 217°. With *N*-methyl-*o*-nitrobenzaldoxime, the excess of anhydride was decomposed with 2*N*-sodium carbonate and the precipitated *o*-nitrobenzomethylamide was collected, dried on a porous tile, and crystallised from benzene; m. p. 107°. With *N*-methyl-*m*-nitrobenzaldoxime, when the reaction mixture was cooled in ice, nearly pure *m*-nitrobenzomethylamide separated; a further quantity was obtained by treating the mother-liquor with sodium carbonate solution; one crystallisation from benzene gave the pure compound. With *N*-methylbenzaldoxime, after being treated with sodium carbonate, the mixture was extracted with chloroform; on removal of the solvent, the residual oil solidified on scratching, and after pressing on a porous tile and crystallising from benzene–light petroleum gave benzomethylamide (m. p. 78°). With 3 : 4-methylenedioxybenzaldoxime, the solid obtained after sodium carbonate treatment was crystallised from benzene–light petroleum and 3 : 4-methylenedioxybenzomethylamide (m. p. 136°) was obtained.

N-Methylcinnamaldoxime, after sodium carbonate treatment, gave an oil which solidified on keeping. The solid was collected, pressed on a porous tile and a small amount reserved; the rest was dissolved in benzene, light petroleum was added cautiously, and the solution seeded with a fragment of the reserved material, whereupon cinnamomethylamide (m. p. 111°) crystallised. With *N*-methyl-*o*-methoxybenzaldoxime, after sodium carbonate treatment and extraction with chloroform, an uncrystallisable oil was obtained; this was boiled under reflux with concentrated alcoholic potassium hydroxide for 8 hours, methylamine being evolved and identified by Valton's method (J., 1925, **127**, 40). The solution was diluted and extracted with chloroform to remove unchanged material, and the aqueous layer acidified with hydrochloric acid and again extracted with chloroform; on evaporation of the solvent and crystallisation of the residue from dilute alcohol, *o*-methoxybenzoic acid (m. p. 101°) was obtained and identified by comparison.

In every case except the last, the methylamide was identified by the method of mixed m. p.'s with a sample prepared in another way.

Some of these compounds have not been previously described. *o*-Nitrobenzoyl chloride (5 g.) was added to methylamine (6 c.c. of 30% solution diluted with 25 c.c. of water) and the mixture shaken for some minutes; the solid formed, after being collected, washed, dried, and crystallised from benzene to which a little light petroleum had been added, gave o-*nitrobenzomethylamide* in short, colourless, prismatic needles, m. p. 107° (Found : N, 15·8. $C_8H_8O_3N_2$ requires N, 15·6%). Ethyl 3 : 4-methylenedioxybenzoate was added to excess of 33% methylamine and enough methyl alcohol added to give a clear solution. After 5 days at room temperature, water was added and the solid collected, dried on a porous tile, and crystallised from benzene–light petroleum; 3 : 4-*methylenedioxybenzomethylamide* was thus obtained in slightly brown needles, m. p. 136° (Found: N, 8·0. $C_9H_9O_3N$ requires N, 7·8%). Cinnamomethylamide may be easily prepared in a similar way from ethyl cinnamate, by seeding the mixture after dilution with a trace of the methylamide and recrystallising the product from benzene–light petroleum with seeding.

In carrying out the Beckmann change with the *N*-ethers, it is important not to boil with acetic anhydride for any length of time, otherwise the methylamide is acetylated; for example, *p*-nitrobenzomethylamide was boiled with excess of acetic anhydride for 2 hours under reflux; after cooling and treatment with 2*N*-sodium carbonate, the solid obtained was crystallised twice from alcohol and found to be *aceto*-p-*nitrobenzomethylamide*, colourless prisms, m. p. 125° (Found: N, 12·8. $C_{10}H_{10}O_4N_2$ requires N, 12·6%). On heating on the water-bath with concentrated hydrochloric acid, the compound dissolved and *p*-nitrobenzomethylamide slowly crystallised from the solution; warming with concentrated sulphuric acid and alcohol gave ethyl acetate. The same compound was obtained from *N*-methyl-*p*-nitrobenzaldoxime by boiling with acetic anhydride for 1 hour.

In spite of all precautions, such as rapid cooling immediately the violent reaction occurred, *p*-methoxybenzomethylamide could not be obtained from *N*-methyl-*p*-methoxybenzaldoxime, the product being invariably the acetylated compound. This was synthesised for comparison by boiling anisic acid (4 g.) under reflux with thionyl chloride (25 c.c.) for 1 hour, removing the excess of thionyl chloride on the water-bath under reduced pressure, and pouring the remaining anisoyl chloride into a mixture of methylamine (6 c.c. of 33% solution), water (18 c.c.), and 2*N*-sodium hydroxide (25 c.c.), shaking, and keeping for 30 minutes. The granular precipitate was collected, washed, and crystallised from benzene and then from hot water, giving p-*methoxybenzomethylamide* in brilliant, colourless needles, m. p. 116° (Found : N, 8·8. $C_9H_{11}O_2N$ requires N, 8·5%). This compound was boiled with acetic anhydride under reflux for 1 hour and the solution cooled and poured into excess of ice-cold 2*N*-sodium carbonate; after shaking until free from anhydride, the precipitate was crystallised from dilute alcohol and gave *aceto*-p-*methoxybenzomethylamide* as white plates, m. p. 50° (Found : N, 6·9. $C_{11}H_{13}O_3N$ requires N, 6·8%). Hydrolysis by boiling with concentrated hydrochloric acid for 30 minutes gave anisic acid.

The hydrochloride of *N*-methyl-*m*-nitrobenzaldoxime, on being heated at 100° for 2½ hours in a tube to which a calcium chloride guard-tube was attached, underwent no appreciable change; on being heated, however, at 168—170° in an oil-bath for 20 minutes, the hydrochloride slowly melted and then decomposed with evolution of hydrogen chloride; when this had ceased, the melt was cooled, the brown mass ground up and extracted with boiling acetone, the solvent removed and the tarry residue extracted with a little boiling benzene; on cooling the solution, *m*-nitrobenzomethylamide separated. When *O*-methyl-*m*-nitrobenzaldoxime was boiled for 2 hours with acetic anhydride and the solution treated with excess of sodium carbonate solution, the ether was recovered unchanged.

In conclusion, we wish to express our thanks to Dr. R. F. Goldstein for help with the experimental work.

THE RALPH FORSTER LABORATORIES OF ORGANIC CHEMISTRY,
UNIVERSITY COLLEGE, LONDON.
[*Received, July* 23*rd*, 1926.]