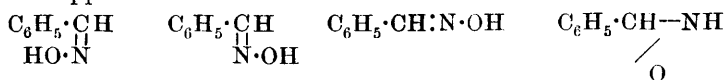


CXCV.—*The Isomerism of the Oximes. Part IV.*
The Constitution of the N-Methyl Ethers of the
Aldoximes and the Absorption Spectra of Oximes,
their Sodium Salts, and Methyl Ethers.

By OSCAR LISLE BRADY.

WHILST the Hantzsch-Werner stereochemical hypothesis is generally accepted as providing the most satisfactory explanation of the isomerism of the oximes, the earlier theory of Beckmann still finds some supporters. Thus for the two benzaldoximes we have:

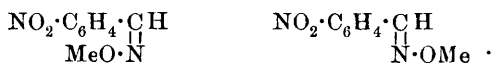


Hantzsch and Werner.

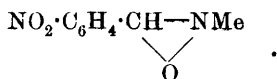
Beckmann.

* I desire to thank the Research Fund Committee of the Chemical Society for a grant which enabled me to contribute a share towards the expense of a former investigation on the synthesis of narcotine (Perkin and Robinson, T., 1911, 99, 775).
 —R. R.

The existence of two isomeric methyl ethers of, for example, *p*-nitrobenzaldoxime, both of which have the methyl group attached to oxygen, cannot be explained by Beckmann's formula but is readily accounted for by that of Hantzsch:

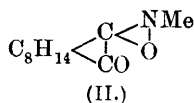
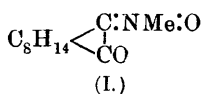


On the other hand, a third methyl ether is known, in which the methyl group is attached directly to nitrogen. Here the stereochemical theory is at fault, and the *iso*-oxime structure of Beckmann



has been generally assigned to this substance.

Forster and Holmes (T., 1908, **93**, 244), from a study of the properties of *isonitrosocamphor* methyl ether, arrived at the conclusion that this substance should be represented by formula I rather than by the more usual structure (II):



Angeli, Alessandri, and Aiazzi-Mancini (*Atti R. Accad. Lincei*, 1911, [v], **20**, i, 546) have extended this idea to the *N*-phenyl ethers of the oximes and they regard these compounds as containing a quinquivalent nitrogen atom, thus: $\text{R} \cdot \text{CH} \cdot \text{NPh} \cdot \text{O}$. Their conclusions are based on the fact that the *N*-ethers are unstable towards permanganate, differing in this respect from the oxides $\text{R} \cdot \text{CH} \cdot \text{CH} \cdot \text{R}$; further, the action of magnesium phenyl bromide on



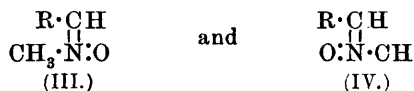
N-phenylbenzaldoxime, giving β -phenyl- β -diphenylmethylhydroxylamine, $\text{CHPh}_2 \cdot \text{NPh} \cdot \text{OH}$, is analogous to the action of that compound on benzyldineaniline, giving diphenylanilinomethane, $\text{CHPh}_2 \cdot \text{NHPH}$; in addition, Scheiber (*Ber.*, 1911, **44**, 761) has failed to obtain optically active modifications of *N*-alkylated ald-oximes such as are called for by the *iso*-oxime structure. It would appear that the formula containing quinquivalent nitrogen more easily explains the behaviour of these compounds, especially as they exhibit many unusual properties. The *N*-alkyl ethers of the aromatic ald-oximes are hydrolysed with extraordinary ease; indeed, the *N*-methyl ether of *m*-nitrobenzaldoxime is at once hydrolysed by cold concentrated hydrochloric acid; moreover, these compounds readily form additive products with sodium iodide (Goldschmidt

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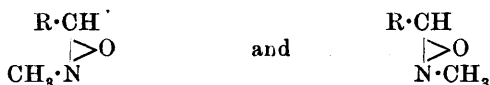
and Kjellin, *Ber.*, 1891, **24**, 2812), calcium chloride, phenyl-carbimide, and hydrogen haloids.

Before accepting the new structure, however, there are several facts to be noted which do not seem to have been fully considered by previous investigators.

A structure involving a quinquevalent nitrogen atom allows for the existence of two isomeric nitrogen ethers, namely:



as does also the *iso*-oxime structure:

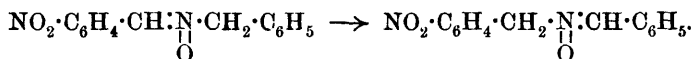


although here the isomerism depends only on the relative position of the hydrogen atom and the methyl group.

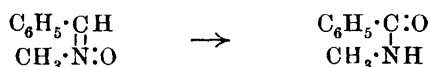
Luxmoore (T., 1896, **69**, 183) describes a second *N*-methyl ether of benzaldoxime, but Scheiber (*Annalen*, 1909, **356**, 215) has shown that the second ether obtained by Luxmoore is probably a hydrated form of the first, the same reason being assigned for the discrepancy in the melting point, etc., of *N*-methylanisalaldoxime as prepared by Goldschmidt (*Ber.*, 1890, **23**, 2186) and by Beckmann and Netscher. The existence of these hydrates is in accordance with the behaviour of the similarly constituted trimethylamine oxide, which readily forms hydrates and appears to act as $\text{NMe}_3(\text{OH})_2$, forming a salt, $\text{NMe}_3\text{Cl} \cdot \text{OH}$, with hydrochloric acid (Dunstan and Goulding, T., 1899, **75**, 795). It is noteworthy that the *N*-methyl ether of benzaldoxime is soluble in water and can be extracted from its aqueous solutions only with difficulty. These compounds, however, differ in many respects from the amine oxides; they do not give alkaline solution, indeed, the *N*-ethers of the nitrobenzaloximes are but very sparingly soluble in water; they are not hygroscopic, and do not form salts with the same ease; thus the *N*-methyl ether of *p*-nitrobenzalaldoxime is soluble in 50 per cent. hydrochloric acid in the cold, but the solution soon deposits crystals of *p*-nitrobenzaldehyde owing to hydrolysis; this offers a serious objection to the formula suggested by Angeli and his co-workers.

The only other recorded cases of isomerism among compounds of this class are those of the *N*-benzyl ether of *p*-nitrobenzalaldoxime (Behrend and Konig, *Ber.*, 1890, **23**, 2571) and the *N-p*-chlorobenzyl ether of benzaldoxime (Neubauer, *Annalen*, 1897, **298**, 187), both of which exist in two forms, the second being obtained from the first by the action of sodium ethoxide. These are apparently

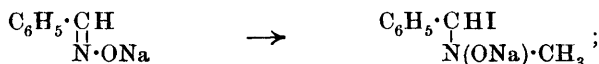
not stereoisomerides, their existence being explained by a change in the position of the double bond, thus:



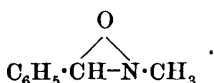
There is little direct evidence of the spacial structure of the *N*-ethers but formula III seems at first sight to be the more probable as these compounds are obtained more easily from the *syn*-oximes, and Beckmann (*Annalen*, 1909, **365**, 208) has shown that *N*-methylbenzaloxime on treatment with phosphorus pentachloride in ether yields *N*-methylbenzamide, a reaction which may be regarded as a case of the Beckmann change:



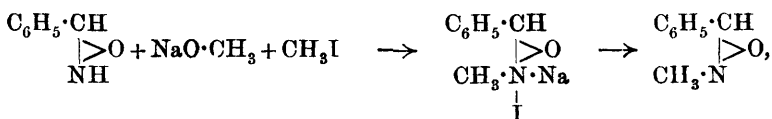
On the other hand, since Beckmann has described the preparation of the *N*-methyl ethers of such compounds as the hydroxybenzaloximes from the hydroxybenzaldehydes and β -methylhydroxylamine, it seems more reasonable, as the hydroxybenzaloximes are known only in the *anti*-form (compare Brady and Dunn, this vol., p. 824), to assign an *anti*- rather than a *syn*-structure to these compounds. The mechanism of the formation of the *N*-methyl ethers has received several interpretations; Goldschmidt (*loc. cit.*) explains the formation of the sodium iodide additive product as follows:



this compound then loses sodium iodide to give the *N*-ether,



Luxmoore (*loc. cit.*) assumes that the addition takes place at the nitrogen atom, which becomes quinquivalent:



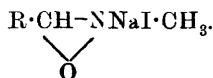
In this way a *N*-methyl ether is obtained from the *syn*-sodium salt, in which the hydrogen atom and the methyl group are in the *anti*-position to one another. Luxmoore, however, has had to assume that the sodium salt of the *syn*-aldoxime has the Beckmann *iso*-oxime structure, and also that the two hydrogen atoms are in a *syn*-position to one another, in fact, he combines the stereochemical and

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iso-oxime structures. This interpretation does not seem feasible,

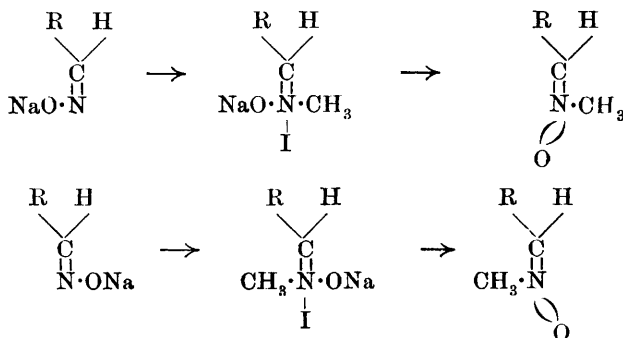
and in addition a compound of the structure
$$\begin{array}{c} \text{R} \cdot \text{CH} - \text{N} \cdot \text{CH}_3 \\ \diagdown \quad \diagup \\ \text{O} \end{array}$$
 would

not be likely to form additive compounds with sodium iodide and calcium chloride so readily if it is supposed that in the formation of these compounds the nitrogen atom becomes quinquivalent, thus:

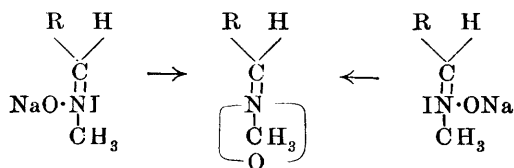


There remains to be considered the possibility that the *N*-ethers themselves contain quinquivalent nitrogen.

If the addition of the elements of methyl iodide takes place at the nitrogen atom, the structure of the products will depend on the relative positions taken by the methyl group and the iodine atom; if the latter is attached at the valency direction in the same plane as the double bonds, an *anti*- and a *syn-N*-ether will be obtained according as to which isomeride is employed:

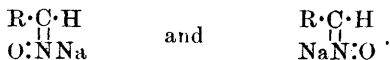


If, on the other hand, the methyl group takes up this position, there will be no chance of *anti-syn*-isomerism in the product:

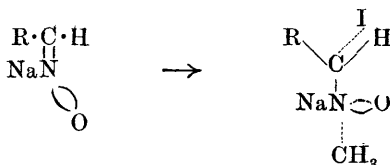


On this supposition the fact that the sodium salt of the *syn*-oxime yields a much larger quantity of the *N*-ether than that of the *anti*-oxime can perhaps be explained by the iodine taking up a position near the aromatic nucleus in the case of the *syn*-derivative, whilst in the case of the *anti*-compound, this position being occupied, the stable *O*-methyl ether is formed. A tempting explanation of the

action of methyl iodide on the sodium salts of the oximes is afforded if it be considered that the sodium salts of the oximes are capable of reacting in the forms:

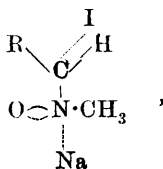


Methyl iodide might act on this compound in two ways, addition taking place either at the carbon-nitrogen or at the oxygen-nitrogen double bond. In the former case the reaction may be represented thus:

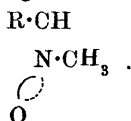


The dotted valency directions indicate that these are at right angles to the plane of the paper.

If rotation takes place through one right angle to bring the sodium and iodine atoms together, the compound becomes



which loses sodium iodide to give:



In this way the *anti*-form of the *N*-methyl ether is obtained from the sodium salt of the *syn*-oxime; conversely, the *anti*-sodium salt would yield the *syn-N*-methyl ether.

If the addition takes place at the oxygen-nitrogen double bond the *O*-methyl ethers will be obtained:



If both these actions can take place on treating the sodium salt of the *syn*-oxime with methyl iodide, it is to be expected that the addition will take place in such a way as to yield the most stable product, that is, the *anti-N*-methyl ether, although a little of the less stable *syn-O*-methyl ether will be obtained. On the other hand, the sodium salt of the *anti*-oxime will give mainly the stable *anti-O*-

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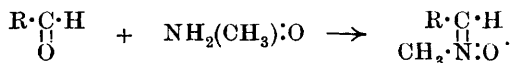
methyl ether and very little of the *syn-N*-methyl ether. This is what is found actually to be the case, with the exception that the *N*-ethers obtained are identical, but this may be explained by the extreme instability of the *syn*-ethers, the additive compound formed by the addition of the methyl group and iodine at the double bond between carbon and nitrogen undergoing intramolecular change leading to the formation of the *anti-N*-ether.

It is possible that the silver salts of the oximes which, with methyl iodide, give *O*-ethers unmixed with *N*-ether may have the normal structure, although a constitution similar to that of the sodium salts still affords an explanation of their action. Here the addition takes place solely at the nitrogen-oxygen double bond to ensure the more easy elimination of silver iodide.

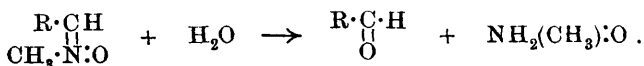
If this explanation is to be accepted, however, it must be noted that the sodium iodide additive compound of *N*-methylbenzaldoxime has a different structure from that assigned to it in the earlier portion of this paper; it is, however, possible that the sodium iodide additive compound isolated in the preparation of the *N*-ethers, or by evaporating a solution of the *N*-ether with sodium iodide, is not the primary product of the action of methyl iodide on the sodium salt of the *syn*-oxime, but a secondary product formed from the *N*-ether and the sodium iodide produced by the reaction.

The view that the sodium salts of the oximes can exist in a tautomeric form with the alkali metal attached directly to nitrogen in preference to oxygen is not without analogy, for there is little doubt that the alkali cyanates should be represented as *isocyanates*, $\text{NaN}:\text{C}:\text{O}$, rather than by the cyanate structure $\text{NaO}:\text{C}:\text{N}$.

The formation of the *N*-methyl ethers of the aromatic aldoximes from the aldehyde and β -methylhydroxylamine (Beckmann, *loc. cit.*) can be explained if that compound is regarded as acting in its tautomeric form, $\text{NH}_2(\text{CH}_3):\text{O}$, of which the amine oxides are derivatives:



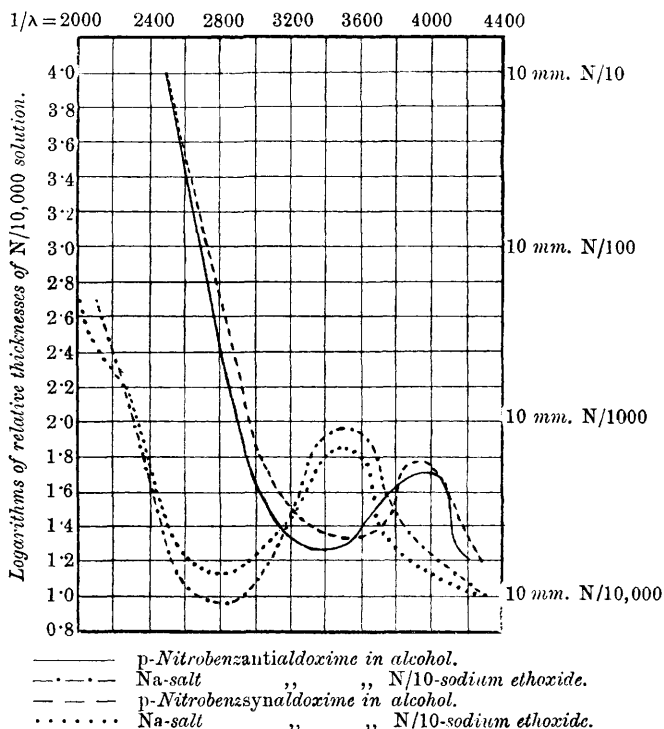
Similarly, the ready hydrolysis of the *N*-ethers may be interpreted thus:



It was thought possible that a study of the absorption spectra of these compounds would throw some light on the question, and the author has accordingly photographed the absorption spectra of benzanti- and benzsyn-aldoxime and the corresponding sodium salts, the *O*-methyl ether of benzantialdoxime and the *N*-methyl ether of benzaldoxime, the two *p*-nitrobenzaldoximes and their sodium salts

and *O*-methyl ethers, and the *N*-methyl ether of *p*-nitrobenzaldoxime. The chief reason for choosing *p*-nitrobenzaldoxime as a substituted benzaldoxime was that the author had a small quantity of the *syn-O*-methyl ether of this compound of undoubted purity (compare Brady and Dunn, T., 1913, **103**, 1625), whereas it is questionable whether most of the other *syn-O*-methyl ethers described in the literature are pure, owing to the difficulty of preparing these compounds in large quantities and freeing them from

FIG. 1.



the *anti*-isomeride. The *syn-O*-methyl ether of benzaldoxime has not been described, although the characteristic fruity odour observed on treating the sodium salt of benzsynaldoxime with methyl iodide is probably due to the formation of this compound in addition to the *N*-methyl ether (Goldschmidt and Kjellin, *loc. cit.*).

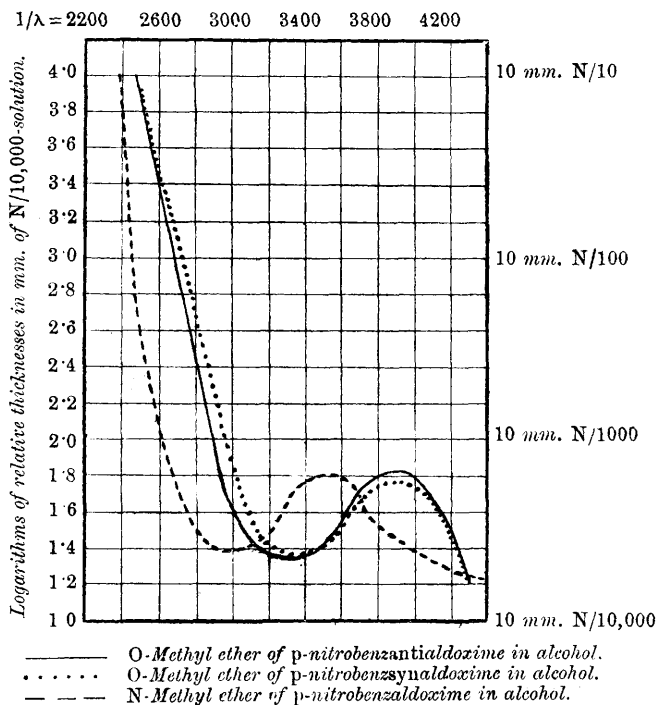
After taking the photographs it was found that Hantzsch (*Ber.*, 1910, **43**, 1661) had already published the absorption spectra of the two *p*-nitrobenzaldoximes and their sodium salts in a paper under the title of "Homochromoisomerism." He did not, however

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consider the ethers, and his conclusions were relative to his theory of homochromoisomerism and have no bearing on the question in hand.

The curves obtained by the present author independently are practically identical with those of Hantzsch, although the sodium salts show a rather deeper band. It was found necessary to take the sodium salts in a $N/10$ -solution of sodium ethoxide and to dilute the solution with $N/10$ -sodium ethoxide, as, if pure alcohol was used for dilution, the amount of the absorption was increased. Whilst

FIG. 2.



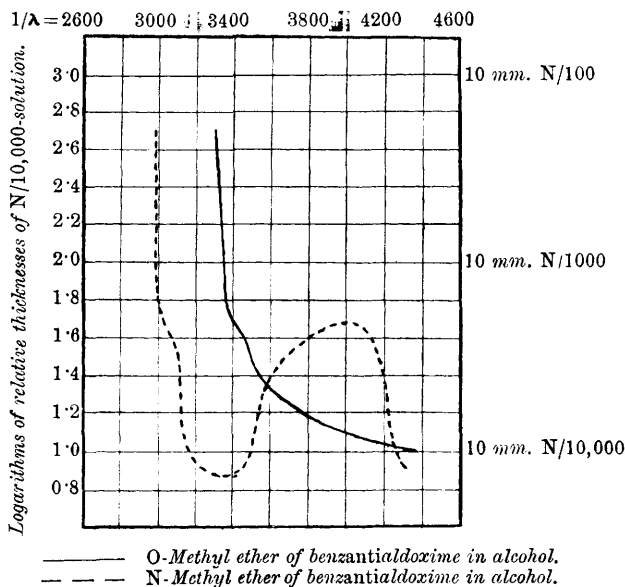
at greater concentrations the absorption of the oximes is identical, with more dilute solutions there is quite a marked difference, the usual rule being followed that the *anti* is more absorptive than the *syn*-isomeride, as is the case with the general absorption exhibited by maleic and fumaric acids.

The sodium salts in dilute solution behave similarly, although in more concentrated solution a reversal takes place, and the *syn*-isomeride is more absorptive than the *anti*. The curves for the sodium salts show a very marked shift in the position of the band

towards the red end of the spectrum, and, whilst the solutions of the oximes are colourless, those of the sodium salts are bright yellow. The curves obtained from the three methyl ethers are shown in Fig. 2.

Those of the two *O*-methyl ethers are practically coincident with those of the corresponding oximes; on the other hand, the curve for the *N*-methyl ether shows a shift towards the red end of the spectrum, although not so great as in the case of the sodium salts. A similar result is to be observed in the case of the *O*-methyl ether and *N*-methyl ether of benzaldoxime. Here, however, the effect is

FIG. 3.



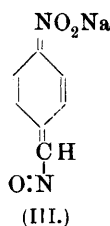
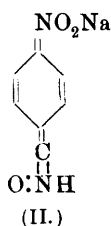
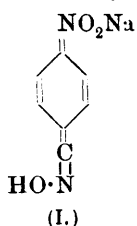
much more marked, and, whilst the *O*-methyl ether exhibits only general absorption, the *N*-ether shows a deep band. The effect of conjugated double bonds in producing colour or increased absorption has long been known, and, whilst it is necessary to observe caution in interpreting spectroscopic results when applied to organic compounds, it seems reasonable to suppose that the spectroscopic evidence is in favour of the structure $R \cdot CH:N(CH_3):O$ for the *N*-methyl ethers of the aromatic aldoximes rather than against it (compare Crymble, Stewart, Wright, and Glendinning, T., 1911, **99**, 451).

The evidence is also in favour of a structure for the two oximes similar to that of the *O*-methyl ethers, that is, the structure assigned

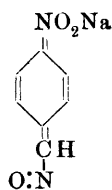
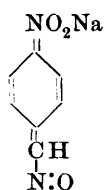
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to these compounds by Hantzsch; moreover, the absorption spectra of the oximes resemble those of *cis-trans*-isomerides.

The character of the absorption spectra of the nitrobenzaldoximes and their sodium salts raises the vexed question of the relation between constitution and colour. Baly, Tuck, and Marsden (T., 1910, **97**, 571) have discarded the quinonoid structure proposed by Hantzsch for the sodium salts of the nitrophenols, etc., but this theory still finds many supporters. Now both the *syn*- and *anti*-forms of *p*-nitrobenzaldoxime are practically colourless, whilst their sodium salts are bright yellow. If, as Hantzsch supposes, in the case of the nitrophenols the sodium salt exists in the *aci*-form, the sodium salt of *p*-nitrobenzaldoxime can be written structurally only in the following ways:



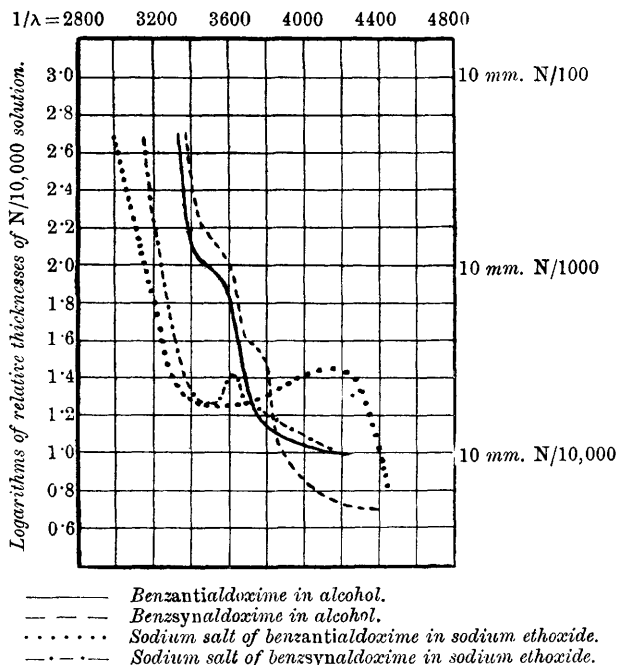
Formula I is very improbable as it is impossible to obtain a disodium salt such as this demands; moreover, the sodium salt of *m*-nitroacetophenoneoxime, $\text{NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{CMe}:\text{NOH}$, is also yellow, whilst the parent substance is, when pure, colourless. It is to be supposed that the change in this compound on salt-formation would resemble that of the nitrobenzaldoximes, and here there is no opportunity for such a structure as I above. The same reason disposes of formula II. There remains formula III, to which there are also very serious objections: first, the formation of a coloured *N*-methyl ether from the sodium salt of the *syn*-oxime, in which the methyl group is undoubtedly attached to the oximino-nitrogen atom, and secondly, if such a structure is assigned to both *syn*- and *anti*-oxime sodium salts:



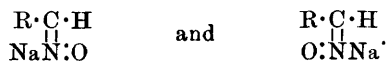
there is free rotation of the nitrogen atom, and these two compounds would be identical. It would, therefore, be expected that, on acidifying a solution of the sodium salts of either oxime, either the

stable *anti*-oxime would be obtained or an equilibrium mixture of the *syn*- and *anti*-oximes. It is well known that on acidifying a solution of the sodium salt of *p*-nitrobenz*anti*-aldoxime the *anti*-oxime is obtained in a pure state, and the author has found that on acidifying a solution of the sodium salt of *p*-nitrobenz*syn*-aldoxime practically pure *syn*-oxime is recovered, even if the alkaline solution has remained for an hour. In addition, the preparation of the isomeric *O*-methyl ethers of *p*-nitrobenz*syn*- and *anti*-aldoxime from the silver salts obtained from the corresponding sodium salts

FIG. 4.



shows that the isomerism persists even in the sodium salts. It is, therefore, evident that the sodium salts of the nitro-oximes do not exist in the *aci*-form. On the other hand, it is not possible to show that there is no change in structure on salt-formation, and it is quite possible that the sodium salts exist in the forms:



Hartley and Dobbie (T., 1900, 77, 509) have stated that the absorption spectra of the two benzaldoximes are identical, and, as

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this was not in agreement with the results for the *p*-nitrobenzaloximes, this work has been repeated. It has been found that the *anti*- is slightly more absorptive than the *syn*-isomeride, the benzaloximes thus forming no exception to the general rule.

In a private communication to the author Dr. Dobbie states that this was observed by himself and the late Prof. Hartley, but, as the difference did not amount to more than a few units, it was not considered at the time of sufficient importance for special attention to be called to it.

There is some difficulty in deciding whether a band exists in the absorption spectra of the benzaloximes, as Drs. Dobbie and Fox (private communication) by taking a large number of thicknesses between 30 and 15 mm. of *N*/10,000-solution have confirmed the presence of a shallow but decided band in the position originally found by Hartley and Dobbie. The author, however, has taken several photographs of this substance without detecting this band. The benzantialdoxime used by the author was prepared in the usual way, and after pressing on several porous plates to remove oily matter it was recrystallised from benzene and light petroleum.* The *syn*-oxime was recrystallised from warm benzene, was without odour and melted sharply at 132°. The sodium salts of these compounds exhibit a decided shift towards the red end of the spectrum and show a shallow band. The oximes and their sodium salts show in this respect an analogy to the *O*- and *N*-methyl ethers of benzaloxime.

In conclusion, the author wishes to express his indebtedness to Dr. Crymble for taking the photographs of the *p*-nitrobenzaloximes and their ethers, and to Miss R. M. Johnson for assistance in taking the other photographs.

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THE IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
SOUTH KENSINGTON.

* The failure of the present author to obtain a band does not seem to be due to a defect in the instrument or to impurity in the oxime. The same solution as was used to photograph the absorption spectrum of the oxime was employed, with the addition of a few drops of sodium ethoxide solution, to photograph that of the sodium salt; in the latter case the band is plainly marked, whereas, if the increased absorption was due to the spectroscopie being at fault, or to an impurity being present, it would hardly be expected that light previously cut off by either of these causes would now be transmitted.
