

XX.—*The Oximes of Benzaldehyde and their Derivatives.**

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It is well known that stereochemical explanations of the isomerism amongst compounds where the carbon is doubly linked to nitrogen, have received less unequivocal support from the behaviour of the aldoximes than from that of other oximido-derivatives. Of the latter, the benzenoid ketoximes may be mentioned as exhibiting in their general deportment a very fair accordance with what stereochemical hypotheses would lead us to expect.

On the other hand, the fact that the isomeric oximes of the benzenoid aldehydes, on methylation, &c., in the usual manner, yield structurally isomeric derivatives as the principal products, offers a difficulty in the way of regarding them as stereoisomers merely. The remarkable results obtained by Dunstan and Dymond (*Trans.*, 1894, **65**, 206) by treating paraffinoid aldoximes with phosphorus pentachloride, may be named as another illustration of the abnormal behaviour of oximido-derivatives containing aldehydic hydrogen.

At Professor Dunstan's suggestion I have carried out a series of experiments on the oximes of benzaldehyde, with a view of throwing further light on the nature of their isomerism, and I now communicate the principal results that have been obtained.

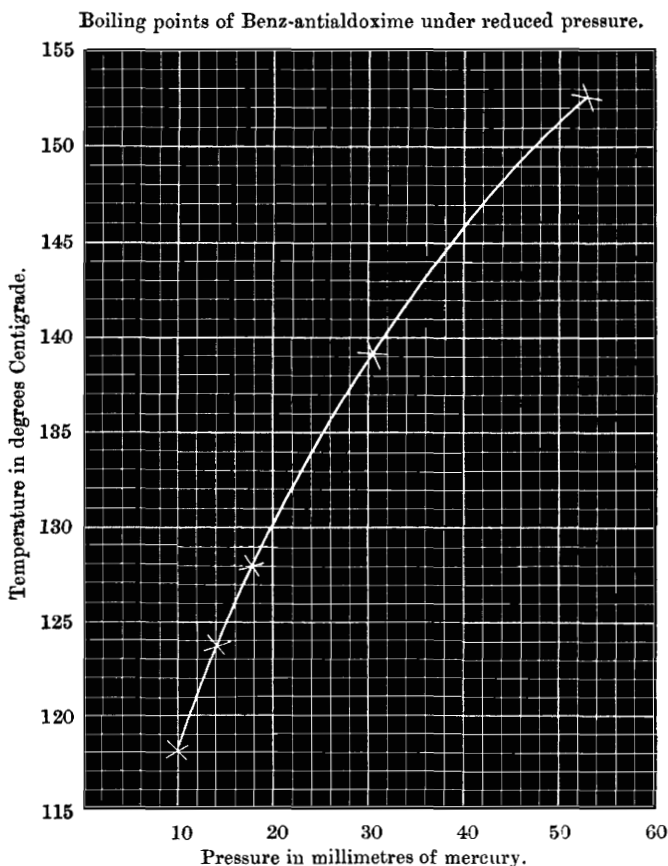
Benz-antialdoxime.

This is most conveniently prepared in the manner described by Beckmann (*Ber.*, 1890, **23**, 1684). After being distilled under reduced pressure, the strongly refractive liquid quickly solidifies on

* Part of a thesis accepted for the degree of Doctor of Science of the University of London.

touching it with a crystalline fragment. The melting point of the pure substance recrystallised from light petroleum is 34° ; this is readily depressed several degrees by minute traces of impurities (Dunstan and Luxmoore, *Proc.*, 1894, 253).

The boiling point of benz-antialdoxime is as follows (thermometer in vapour)—10 mm., $118-119^{\circ}$; 14 mm., $123-124^{\circ}$; 19 mm., $128-129^{\circ}$; 31 mm., $138-139^{\circ}$; 53 mm., $152-153^{\circ}$; these results are plotted out on the annexed curve.



Whether benzaldoxime is formed in the presence of an excess of sodium hydroxide, according to Beckmann's method, or by shaking an aqueous solution of hydroxylamine (made by mixing concentrated solutions of hydroxylamine hydrochloride and sodium carbonate in equivalent proportions) with an ethereal solution of benzaldehyde,

only the anti-modification appears to be formed; no benz-synaldoxime has been obtained in any case.

Benz-antialdoxime Hydrochloride.—This is instantly thrown down as a white pulverulent precipitate when dry hydrogen chloride is passed into an ethereal solution of benz-antialdoxime cooled to 0° . It melts gradually between 103° and 105° . When treated with dilute aqueous ammonia in the presence of broken ice, the oxime collects in oily drops, which are extracted with ether, and the ether allowed to evaporate; on touching the residue with a crystal of benz-antialdoxime it solidifies. The crystals obtained in this manner from the hydrochloride, prepared at zero or below, invariably consisted of benz-antialdoxime, mixed with, at the most, only a minute trace of benz-synaldoxime.

Benz-synaldoxime Hydrochloride.—If hydrogen chloride is passed into an ethereal solution of benz-antialdoxime at the ordinary temperature heat is evolved, and the well-known pearly leaflets of benz-synaldoxime hydrochloride are gradually precipitated. In one experiment, a thermometer, immersed in the solution, rose from 10° to 28° . The same salt is obtained by the action of hydrogen chloride on benz-synaldoxime; purified by recrystallisation from chloroform and light petroleum it melts at $66\text{--}67^{\circ}$, if heated quickly.

The difference between the isomeric hydrochlorides is at once apparent on moistening them with water (or better with aqueous ammonia); both are dissociated, but whilst the one at once gives rise to oily drops of benz-antialdoxime, the other undergoes no change in appearance, as the liberated benz-synaldoxime is a white crystalline powder. If the acid is not neutralised, this, at the ordinary temperature, is soon converted into oily drops of benz-antialdoxime; in the presence of broken ice, however, even if it is not neutralised, the synaldoxime can be isolated, only slightly contaminated with its isomer, by quickly extracting with ether, washing the ethereal solution, and allowing it to evaporate spontaneously.

Isomeric Transformation of the Hydrochlorides.—On attempting to purify benz-antialdoxime hydrochloride by recrystallisation, it was found that by the mere act of dissolution it was converted into the isomeric syn-hydrochloride. A confirmation of this result was found in the observation that an ethereal filtrate from the preparation of benz-antialdoxime hydrochloride at -10° , when allowed to evaporate spontaneously, deposited a few crystals of the syn-hydrochloride.

Doubtless, therefore, the formation of benz-synaldoxime hydrochloride by the action of hydrogen chloride on benz-antialdoxime is always preceded by the formation of the hydrochloride of the latter, and if kept at or below zero only a trace of this can be dissolved by ether, and the remainder is therefore protected from isomeric change;

at higher temperatures it is more readily dissolved, and thus undergoes rapid transformation into the more stable benz-synaldoxime hydrochloride.

Benz-synaldoxime hydrobromide is obtained when dry hydrogen bromide is passed into an ethereal solution of benz-antialdoxime cooled below 0° . When recrystallised from chloroform and light petroleum, or from acetone and light petroleum, it melts at $77-78^{\circ}$, if rapidly heated. It is a white powder, becoming yellow on exposure to light. 0.157 gram required for neutralisation 7.1 c.c. decinormal ammonia. Calculated for C_7H_6NOH, HBr 7.8 c.c.

Benz-synaldoxime hydriodide is prepared in the same manner, the liquid soon becomes brown from liberated iodine. The hydriodide is unstable, rapidly becoming yellow on exposure to the air. 0.224 gram required 8.6 c.c. decinormal ammonia. Calculated for C_7H_6NOH, HI 9 c.c.

Benz-synaldoxime Dihydrofluoride.—When hydrogen fluoride is passed into an ethereal or chloroformic solution of benz-antialdoxime, this salt is precipitated. Its melting point lies between 50° and 60° , but it is difficult to determine as it decomposes on heating, and melts gradually. 0.193 gram required 22.9 c.c. decinormal ammonia. Calculated for C_7H_6NOH, H_2F_2 23.9 c.c.; for C_7H_6NOH, HF 13.7 c.c.

These three new haloid salts all yielded benz-synaldoxime on regeneration, neither a hydrofluoride, hydrobromide, nor hydriodide of benz-antialdoxime could be isolated; doubtless these derivatives were first formed, but were instantly transformed into salts of benz-synaldoxime, although the temperature was below 0° .

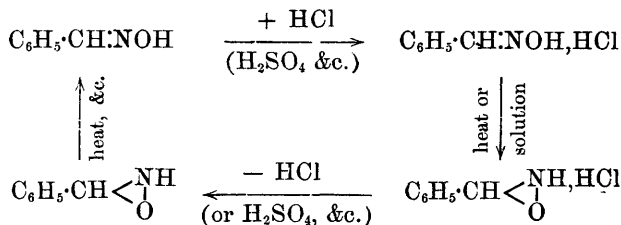
Benzaldoxime Sulphates.—When benz-antialdoxime is gradually added to strong sulphuric acid, the first portions completely dissolve; as soon as a molecular proportion ($C_7H_6NOH=121$ to $H_2SO_4=98$) has been added, the temperature rises, and the whole solidifies to a hard, white, deliquescent mass of benz-synaldoxime sulphate. If, however, sulphuric acid and benz-antialdoxime, both in ethereal solution, are gradually mixed whilst kept in a freezing mixture of ice and salt, an oil separates which is the sulphate of benz-antialdoxime, since it yields the latter by regeneration, when treated with aqueous ammonia at 0° . This oil quickly solidifies, especially on stirring, while the temperature still remains below zero; the solid thus obtained is benz-synaldoxime sulphate.

0.124 gram required 11.7 c.c. decinormal ammonia, and yielded 0.627 gram benz-synaldoxime. Calculated for C_7H_6NOH, H_2SO_4 11.3 c.c. and 0.0681 gram.

The assumption of a structural isomerism between the two oximes of benzaldehyde does not lend itself to an explanation either of the

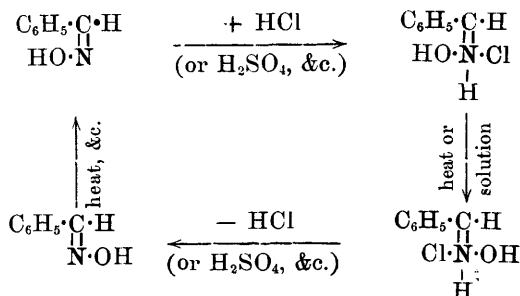
readiness with which the oxime of higher melting point is converted by heat or by dilute aqueous acids into its isomer, or of the reverse change of the hydrochloride, &c., which takes place even more readily, namely, by mere dissolution.

The only structural formulæ available for the oximes of benzaldehyde are $C_6H_5 \cdot CH : NOH$ and $C_6H_5 \cdot CH < \begin{smallmatrix} NH \\ O \end{smallmatrix}$. Adopting these formulæ for the oximes melting at 34° and 130° respectively, the changes in question would be expressed by the scheme



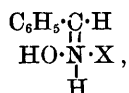
It is difficult to conceive of any reason why the transformation indicated in the left hand column by which the compound, having the isoxime formula, is very readily converted into the normal oxime should be exactly reversed in the hydrochlorides as indicated by the arrow in the right-hand column. If, on the other hand, the isoxime formula be attributed to α -benzaldehyde and β -benzaldehyde be regarded as the true oxime, a similar scheme, with the arrows reversed, would express the facts, and this would be equally difficult to understand.

On a stereochemical hypothesis, it is not difficult to suggest a partial explanation of the fact that the lability of the aldoximes is reversed in their salts with hydrogen haloids and sulphuric acid. These salts can be conveniently formulated in the plane of the paper consistently with Pickering's theory ('Trans.', 1893, **63**, 1069), and the transformation of the oximes clearly expressed as follows.



We may then suppose that, in the oximes themselves, the attraction of hydroxyl to phenyl is greater than to hydrogen, whilst the addition of the elements of hydrogen chloride, for instance, may disturb this equilibrium, because the directive attraction of hydrogen for hydroxyl added to that of phenyl for chlorine is greater than that of hydrogen for chlorine added to that of phenyl for hydrogen.

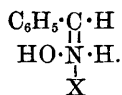
The fact that the hydrobromide and the hydriodide of benz-antialdoxime are less stable than the hydrochloride, suggested that this might be due to the greater mass of the bromine and iodine atoms, and for this reason the action of hydrogen fluoride was tried; but in this case also a syn-derivative only was obtained. As this was a dihydrofluoride, the question cannot be regarded as positively settled. The mass of the radicle X in the anti-alldoxime salt



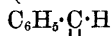
is approximately as follows:

HX	=	H ₂ F ₂	HCl	HBr	HI	H ₂ SO ₄
X	=	HF ₂	Cl	Br	I	HSO ₄
Mass of X	=	39	35.4	80	127	97

The mass of HF₂ would thus put it after Cl, but very close; while the mass of HSO₄ would put it between Br and I. In neither case is this in accordance with the facts. It is more likely that the greater solubility of the anti-salts that have not been obtained determined their very ready isomeric transformation. The fact, however, that different salts of benz-antialldoxime differ in their degree of stability, suggests that they should be formulated as above, and not with the chlorine, &c., in the median position,



Although Hantzsch (*Ber.*, 1893, **26**, 930) had obtained stereoisomeric hydrochlorides of anisalldoxime and cuminalldoxime, he represents the oximes of benzaldehyde (*Grundriss*, pp. 122, 123) as having



one hydrochloride of the formula $\begin{array}{c} \text{H}\cdot\text{N}\cdot\text{Cl} \\ \mid \\ \text{OH} \end{array}$, with the hydroxyl in the

median position. This perhaps is derived from van't Hoff's conception of pentad nitrogen as situated at the centre of a cube, the valencies being directed to five of its trihedral angles. Van't Hoff does no himself, however, seem to have used this cube for the representation

of oximido-compounds in which pentad nitrogen may be assumed. The fact that there are two hydrochlorides corresponding with parent oximes is best represented by formulæ in which the hydroxyl occupies the same position in the oximes themselves and in their salts, as used above; and, so far as it goes, this is in favour of Pickering's hypothesis rather than of van't Hoff's.

N-Methylbenz-antialdoxime.

When equal quantities of benz-antialdoxime and methylic bromide dissolved in methylic alcohol, are heated at 80—90° for a couple of hours, a hydrobromide of a methyl derivative is obtained which, after recrystallisation from methylic alcohol and ether melts at 67—67·5°

0·4513 gave 0·3856 AgBr. Br = 36·4.

0·2482 „ 14·3 c.c. moist nitrogen at 12° and 766·2 mm. N = 6·87.

$C_7H_6NO \cdot CH_3, HBr$ requires Br = 37·0; N = 6·48 per cent.

The hydrobromide is readily hydrolysed, even by cold water, the odour of benzaldehyde becoming apparent at once on moistening; it is, therefore, impossible to obtain the base by regeneration in aqueous solution. It was, however, isolated by passing an excess of dry ammonia into an alcoholic solution, precipitating the ammonium bromide by ether, and evaporating to dryness in a vacuum without heat, the residue being redissolved in alcohol and ether added, repeating the process until the ammonium bromide was entirely removed; the methyl derivative was finally separated as a colourless oil by the addition of light petroleum. On stirring, this oil solidified to a waxy mass which could readily be broken up into an apparently amorphous, almost odourless, powder. The substance thus obtained in one experiment melted gradually between 45—49°. This specimen was used for a nitrogen determination.

0·3278 gave 29·4 c.c. moist nitrogen at 13° and 750 mm. N = 10·5.

Methylbenzaldoxime requires N = 10·37 per cent.

The methyl derivative was hydrolysed by distillation with dilute hydrochloric acid; from 2·95 grams, about 1·9 grams of benzaldehyde were obtained, besides a residue of 26 grams of benzoic acid formed by atmospheric oxidation. The hydrochloride obtained weighed 1·6 grams. The equation, $C_7H_6NO \cdot CH_3 + H_2O + HCl \rightarrow C_6H_5 \cdot COH + CH_3 \cdot NH_3OCl$, requires methylhydroxylamine hydrochloride 1·8 grams (found 1·6 grams), benzaldehyde 2·3 grams (found 2·1 grams). The methylhydroxylamine hydrochloride was purified by recrystallisation from methylic alcohol and ether, and was thus obtained in the form of silky needles which were very hygroscopic, and had a powerful reducing action on Fehling's solution. The melting point was found to be 80·5—81·0°, which is lower than that recorded for β

methylhydroxylamine (82—90°), doubtless through the difficulty of obtaining the crystals quite free from moisture. Since the melting point of the isomeric α -salt is 149°, and it has no reducing effect on Fehling's solution, there can be no doubt as to the identity of the product.

The substance was also reduced with hydriodic acid; the hydrochloride of the base formed was hygroscopic, and had otherwise the properties of methylamine hydrochloride. Converted into the platinochloride and ignited, 0.3120 gram gave 0.1320 gram platinum = 42.3 per cent. Calculated for methylamine platinochloride 41.3 per cent.

The new methyl derivative was found to be without constant melting point. A specimen melting, on one occasion, below 68° did not melt, a few days later, below 73°. This was found to be due to the gradual conversion of the substance into the isomeric derivative of benz-synaldoxime. Specimens, after keeping a few days and recrystallising from benzene and light petroleum, showed the correct melting point (81—82°), and had the other properties characteristic of the latter, some of which was prepared for comparison in the manner described by Goldschmidt (*Ber.*, 1891, **24**, 3808).

The isomeric change of the new methyl derivative into the N-methyl derivative of benz-synaldoxime takes place spontaneously in a short time, and without heating, so that the melting point of any specimen depends on the length of time since it was prepared from its hydrobromide, which is perfectly stable. The lowest melting point observed is that of 45—49°, recorded above; the melting point of the pure anti-derivative may, however, be lower than this.

This readiness of isomeric change confirms the conclusion drawn from the products of hydrolysis, that the new derivative is structurally identical with the "nitrogen methyl ether" of benz-synaldoxime, and has the formula $C_6H_5 \cdot CH < \begin{smallmatrix} N \cdot CH_3 \\ O \end{smallmatrix}$.

That the two substances are not identical is shown (1) by the difference in melting point, (2) by the tendency of the anti-derivative to superfusion, and (3) especially by the very different behaviour of the two derivatives towards water. As already mentioned, all attempts to regenerate the new methyl derivative from its hydrobromide in the presence of water failed on account of the great readiness with which it is hydrolysed even by cold water. The methyl derivative itself is also hydrolysed by water when freshly prepared, and gives an almost immediate reduction with Fehling's solution in the cold, although it loses this property if kept, in consequence of its conversion into the syn-derivative; the latter, on the contrary, is perfectly stable towards water and neutral saline solutions, being in fact

obtained by the dissociation of its sodium iodide compound by the action of water or of solution of sodium chloride.

It must also be observed that the hydrobromide of the new methyl derivative is formed from the anti-oxime under circumstances in which the syn-oxime cannot exist, whilst the methylimido-derivative of the syn-oxime is obtained in a manner which in no way renders it likely that the latter should be converted into the isomeric benz-anti-aldoxime.

Methylic iodide, when heated with benz-antialdoxime, also combines with it to form the corresponding hydriodide; this generally resembles the hydrobromide in its properties, but is very difficult to purify in consequence of the readiness with which it becomes coloured by the liberation of iodine. Methylic chloride, on the other hand, does not react with benz-antialdoxime; neither does ethylic iodide, so that it has been impossible to obtain an ethyl derivative in this manner.*

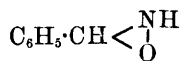
The hydrobromide of the so-called "nitrogen methyl ether" of benzsynaldoxime was prepared for the sake of comparison. It melts at 66—67°, that is to say, at almost the same temperature as the hydrobromide obtained from benz-antialdoxime and methylic bromide.

As it was possible this might be the same substance formed by hydrogen bromide having caused isomeric change in the reverse direction, the regeneration was conducted in the absence of water in the manner previously described; the quantity was small, and the whole of the operations were completed in a very short time, so that if the anti-methyl derivative had been the product of regeneration no time was allowed for its isomeric transformation back into the syn-derivative. The crystals of the base thus obtained, after merely draining for a few moments on a tile, and without being recrystallised, melted at 82—83°. Moreover, after boiling with water and cooling, they did not reduce Fehling's solution, showing that they were not hydrolysable by water. Evidently, therefore, they consisted of the nitrogen methyl derivative of benz-synaldoxime, and the two hydrobromides are distinct substances, though melting at about the same temperatures.

It is well known that in the usual method of methylating benz-antialdoxime by adding sodium methoxide and methylic iodide successively, the action being carried out on a water bath, the methoxy-

* There is no record of any previous experiments being made to bring about the addition of the elements of an alkylic haloid to an oxime by heating them together. An attempt was therefore made to extend this reaction so as to make it available for the preparation of the little known alkyl isoximido-derivatives of the ketoximes, but without success. Benzophenoxime heated with methylic iodide at 90° was not acted on; at a higher temperature, there was so much decomposition that the hydriodide of the methyl derivative could not be isolated. Methylamine, however, was obtained on reducing the product of the action, showing that an isoximido-derivative had been formed.

derivative of benz-antialdoxime, $C_6H_5 \cdot CH \cdot NO \cdot CH_3$, is almost the only product. As it seemed likely that the preformation of the sodium salt was in a great degree, at any rate, the cause of this, a few experiments were made to see whether the new methyl derivative would be obtained if the conditions of the experiment were slightly altered. To a mixture of methylic iodide with benz-antialdoxime, the calculated quantity of sodium methoxide dissolved in methylic alcohol was gradually added in the cold; the characteristic fruity odour of the oxygen methyl ether was at once apparent. A test portion of the product gave, after boiling with water and cooling, a notable reduction of Fehling's solution, due, doubtless, to the presence of the new nitrogen ether. It was, however, found impossible to isolate this; but the isomeric syn-derivative, into which it passed, was separated in the form of its sodium iodide compound. That this was not the first product of the action is proved firstly by the ease with which specimens of the product, tested shortly after its formation, were found to be hydrolysed by water; and, secondly, because, as was found in a separate experiment, benz-synaldoxime cannot exist in the presence of methylic iodide, so that a derivative of the latter oxime could only be formed from an anti-derivative first formed. Altogether, about 10 per cent. of the methyl derivative formed had the isoximido-structure, in other words, about 1 molecule in 10 was caught in the tautomeric form expressed by the formula



A review of the alkyl derivatives of the oximes furnishes conclusive evidence of the existence of isomerism which structural formulæ are insufficient to represent. The benzenoid aldoximes form two series of alkyl derivatives having the true oximido-structure, $:NOH$, and yielding identical products of hydrolysis and reduction; the chief distinctions between the corresponding alkyloxy-derivatives of anti- and syn-aldoximes lie in their melting and boiling points.

The chief products, however, of the action of alkylic iodides and sodium alcoholates on syn-aldoximes are the so-called "nitrogen ethers," in which there is evidence of direct linking between alkyl and nitrogen. No evidence of the existence of such isoximido-derivatives of the antialdoximes has hitherto been forthcoming, the supposed isomeric benzylimido-derivative of furfuraldoxime which Werner (*Ber.*, 1890, **23**, 2336) assumed to be an anti-derivative having been shown by Goldschmidt (*Ber.*, 1892, **25**, 2573) to be a compound of the syn-derivative with water of crystallisation. The methyl derivative obtained from benz-antialdoxime by the action of methylic bromide being structurally identical with that obtained from

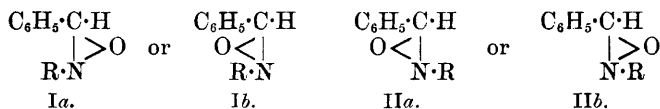
benz-synaldoxime by the action of methylic iodide and sodium methoxide, completes the set of four methyl derivatives obtainable from the oximes of benzaldehyde.

Thus there are four distinct series of derivatives, two of which have the oximido- and two the isoximido-structure, whilst one of each pair is an anti- and the other a syn-derivative. For these four methyl derivatives of the oximes of benzaldehyde, only two structural formulæ are available.

It seems, therefore, necessary to admit some other cause of isomerism amongst the alkyl derivatives of the benzenoid aldoximes than can be expressed by structural formulæ. Without attempting to draw any definite conclusions as to the exact disposition of the atoms in space, we may accept as a working hypothesis the assumption that the isomerism that cannot be satisfactorily accounted for by different modes of atomic linking is due to a condition of asymmetry in the molecule, the hydrogen or alkyl being nearer to the aldehydic hydrogen in the one isomer, and to the phenyl in the other. In true oximido-compounds this will be represented by the following configuration formulæ in the plane of the paper.



The same isomerism would obtain amongst the isoximido-compounds, which we may express by the formulæ

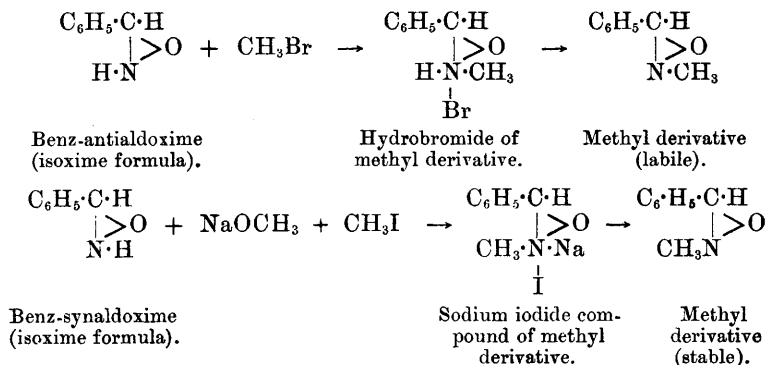


But the formulæ Ia and Ib must be taken to be identical, as must the formulæ IIa and IIb, as it is simplest to assume that the oxygen and its two valencies are in the same plane (at right angles to the plane of the paper) as that containing the nitrogen and carbon atoms and the four valencies by which they are linked to each other and to oxygen.

Whilst it seems clear that stereoisomerism exists amongst the alkyl derivatives of the benzenoid aldoximes, and it is therefore reasonable to admit that it also obtains amongst the oximes themselves, it cannot be denied that this is an incomplete explanation of the isomerism of the two oximes of benzaldehyde, since it fails to account for the fact that the principal products of their methylation in the usual manner have different structures. Hantzsch, indeed, maintains (*Grundriss der Stereochemie*, p. 113) that the :NOH formula represents the normal structure of both oximes, and that the formation of

isoximido-derivatives is due to the action of water; and Goldschmidt (*Ber.*, 1891, **24**, 2808), in his description of the sodium iodide compound formed when benz-synaldoxime, methylic iodide, and sodium methoxide react, gives a very ingenious explanation of the way in which he supposes the isoximido-methyl derivative to be formed from the parent substance supposed to have the normal structure :NOH. But the formula which he gives to the intermediate sodium iodide compound is very improbable, and his explanation cannot be regarded as valid. The fact that, when benz-antialdoxime and methylic bromide are heated together (in the absence of water), the hydrobromide of the isoximido-methyl derivative is formed, completely disproves this statement of Hantzsch's, for it shows that both oximes are very ready to react in the sense of the isoximido-formula, though the benzsynaldoxime does so more readily than its isomer.

It seems likely that Goldschmidt's sodium iodide compound is formed by the addition of the elements of methylic iodide to the sodium derivative of the syn-oxime with the isoxime structure, in a manner analogous to the formation of the hydrobromide of the methyl derivative from benz-antialdoxime. If we represent these changes according to positional formulæ we get the scheme



That is, the anti-aldoxime yields a methyl derivative having the syn-configuration, and the syn-aldoxime yields a derivative having the anti-configuration. Although this appears to be supported by the fact that the anti-derivatives generally (exclusive of those containing pentad nitrogen) are more stable than the corresponding syn-derivatives, nevertheless it is not sufficiently certain to justify any change of name, and it will be wise, therefore, to continue to designate these methyl derivatives after the parent aldoxime.

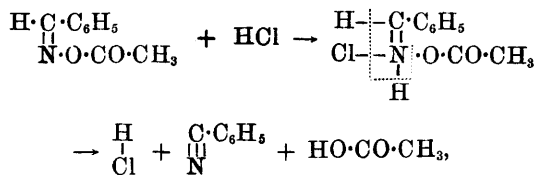
Acetylbenz-antialdoxime.

This substance, prepared by the action of acetyl oxide on crystal-

lised benz-antialdoxime, can be solidified by cooling to -10° and persistently stirring, although it has been described as an oil by previous observers; it melts between 14° and 16° . That this crystalline substance was a true derivative of the anti-oxime was established by regeneration.

When dry hydrogen chloride is passed into a cooled ethereal solution of acetylbenz-antialdoxime, benzonitrile is formed, as stated by Minunni (*Gazzetta*, 1892, **22**, ii, 174); in many cases benzamide is also obtained, and sometimes a hydrochloride of benzamide is precipitated, even when every trace of water is most carefully excluded. A number of experiments have been made to elucidate this action, and it has been ascertained that the latter are secondary products. In view of the difficulty of accounting for the formation of benzamide in the absence of moisture, a direct experiment was made to determine whether the elements of water could be abstracted from acetic acid by benzonitrile in the presence of hydrogen chloride with the concurrent formation of acetyl chloride or acetyl oxide. The acetic acid used was freed from water by mixing it with excess of acetyl oxide, and repeatedly redistilling till it boiled constantly at 119° . It was then mixed with benzonitrile and ether (distilled over sodium) and dry hydrogen chloride passed in, the whole being allowed to remain for a short time, and then fractionally distilled. Benzamide (m. p. 128°) was obtained equivalent to about half the benzonitrile taken. The early fractions of the distillate appeared to indicate that probably both acetyl chloride and acetyl oxide had been formed.

Whilst Minunni's experimental results are thus confirmed, the conclusions he draws from them, in opposition to Hantzsch's use of the acetyl derivative as a criterion of configuration, do not appear to be adequately supported. As the hydrogen chloride is evidently a potent factor in the action, it would seem reasonable to suppose that a compound is at first formed which is of a very unstable nature, and which, by immediate loss of the elements of hydrogen chloride and hydrogen acetate, yields benzonitrile. Assuming the hydrogen chloride to be added on somewhat in the same way as in the salts of the oximes, we get the following scheme.



in which the remaining affinities of pentad nitrogen are made use of according to Pickering's theory.

My attempts to isolate such an intermediate compound have been unsuccessful, and, therefore, it would not be proper to lay too much stress on the above explanation; however, such a compound would, of course, be very unstable, and the above considerations seem sufficient to show that Minunni's objection to the stereochemical representation of the aldoximes cannot be maintained by means of this decomposition.

Action of Phosphorus Pentachloride on Benzaldoximes.

An excess of phosphorus pentachloride was gradually added to an ethereal solution of benz-antialdoxime kept below -8° by a freezing mixture. A small quantity of a white powder was precipitated, probably benz-antialdoxime hydrochloride. The orange-coloured liquid was poured into ice-cold water and the mixture distilled; in the aqueous portion of the distillate, formic acid was identified, an aliquot portion yielding, with mercuric chloride, a precipitate corresponding to 0.03 gram on the whole quantity. An oil had also come over which was a mixture of benzaldehyde and benzonitrile; the latter, when hydrolysed with potassium hydroxide, gave a quantity of ammonium chloride corresponding to 2.1 grams of benzonitrile on the whole quantity. Hydroxylamine and aniline were identified in the residue from the original distillation. Benz-antialdoxime had thus yielded, under the influence of phosphorus pentachloride, the hydrolytic products of formanilide 0.08 gram, and benzonitrile 2.1 grams, and some oxime had been regenerated.

Benz-synaldoxime, treated in the same way, gave similar results. 0.06 gram of formanilide and 2.3 grams of benzonitrile were obtained besides regenerated oxime. The formation of formanilide as a product of the action of phosphorus pentachloride on the oximes of benzaldehyde does not appear to have been noticed by previous workers, but it was, of course, probable considering that the formation of formamide from acetaldoxime had been observed by Dunstan and Dymond (*loc. cit.*). It is, nevertheless, very difficult to explain this result. In the first place it is quite clear that benz-antialdoxime is not in this experiment converted into benz-synaldoxime by the action of hydrogen chloride, for it has been shown that at these low temperatures the anti-hydrochloride suspended in ether is stable; moreover, the quantity of hydrochloride precipitated is only very small. If, however, in the experiment with benz-antialdoxime, it be assumed that either the hydrogen chloride formed, or the phosphorus pentachloride favours the transformation into the synaldoxime, so that the benzonitrile is formed as the result of the action of the pentachloride on the latter, then it would be necessary to make a further assumption that in the experiments with benz-synaldoxime under identical con-

ditions, the same reagent favoured a transformation of part of the synaldoxime into anti-aldoxime which yielded the formanilide.

It seems more reasonable to assume that the action of phosphorus pentachloride in some way removes the cause that makes the stereoisomerism possible. For instance, it may combine in a loose way with the oxime, so that the latter ceases to have a double link between carbon and nitrogen, and the action goes on mainly in the sense of the most favoured (syn) configuration, whilst a small proportion of the molecules are caught in the less favoured configuration, and undergo the Beckmann transposition, yielding formanilide.

Action of Phosphorus Trichloride on Benz-antialdoxime.

On adding phosphorus trichloride to a cooled ethereal solution of benz-antialdoxime a white precipitate of hydrochloride is thrown down, and the filtrate, having been poured into water and neutralised with sodium hydroxide, is found to contain much benzonitrile, but to regenerate a certain quantity of the oxime. By reversing the process, and adding the oxime to a large excess of phosphorus trichloride, less of the hydrochloride is precipitated, but still the elements of hydrogen chloride are eliminated from some of the chlorine compound, so that the product of the action consists of a mixture of the very unstable chlorine substitution compound, $C_6H_5\cdot CHNCl$, benzonitrile, and the excess of phosphorus trichloride. From this mixture it is impossible to isolate the new compound, as there is no means of separating it from the benzonitrile. Its presence was, however, proved by decomposing the phosphorus trichloride with the least possible quantity of water, and then, after distilling off the ether under diminished pressure and extracting the residue with light petroleum, in which hydrogen phosphite is insoluble, the solution thus obtained was freed from the last trace of phosphite compound by shaking with a drop of water; on now decomposing it by sodium hydroxide, it was found to contain a considerable quantity of chlorine, evidently from the presence of the chlorine substitution compound $C_6H_5\cdot CH\cdot HO\cdot N$.

This compound was ultimately obtained as follows. Benz-antialdoxime, dissolved in a very little ether, was gradually added to a large excess of phosphorus trichloride below 0° ; the precipitate formed, supposed to be the hydrochloride of the oxime, was filtered off, but after a few minutes it became liquid, and had the characteristic odour of benzonitrile. As it seemed likely that this was the compound which it was desired to isolate, and that had thus evolved its hydrogen chloride on exposure, the experiment was repeated using scarcely any ether at all. The precipitate which was formed was set to drain in a beaker well surrounded by a freezing mixture, but it

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presently began to evolve hydrogen chloride with almost explosive violence, and after standing in a desiccator for a short time the residual liquid gave, on hydrolysis, no trace of hydroxylamine, all the oxime having been converted into nitrile. In these experiments, no hydrogen chloride was evolved while the oxime was being added to the phosphorus trichloride, and no hydrochloride of the oxime was formed.

The chlorine substitution compound of benz-antialdoxime,

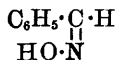


is therefore a white solid, nearly insoluble in phosphorus trichloride, moderately soluble in ether. In the pure state it decomposes into benzonitrile and hydrogen chloride below 0° , but can be kept for a short time in dilute solution.

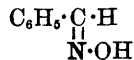
Action of Phosphorus Trichloride on Benz-synaldoxime.

When phosphorus trichloride is added to an ethereal solution of benz-synaldoxime at -10° , half of the oxime is instantly converted into benzonitrile, the other half being converted into the hydrochloride by the hydrogen chloride which is eliminated. If the filtered liquid is poured into water, no oxime is regenerated. Thus the compound formed by the substitution of chlorine for hydroxyl in benz-synaldoxime is so unstable as to be incapable of existence; it instantly decomposes into benzonitrile and hydrogen chloride, and although the latter combines with more oxime, if any is present, to form the hydrochloride, this has no share in effecting the decomposition. This was proved by adding benz-synaldoxime in small portions to a large excess of phosphorus trichloride; hydrogen chloride was freely evolved, and only a comparatively small quantity of hydrochloride was precipitated. This experiment was carried out so as to be strictly comparable with that in which the chlorine substitution compound was obtained from benz-antialdoxime, but no corresponding derivative could be obtained. It evidently breaks up at the moment of its formation.

Evidently this difference of behaviour between the two oximes when treated with phosphorus trichloride, confirms the configuration formulæ assigned to them.



Benz-antialdoxime, m. p. 34° .



Benz-synaldoxime, m. p. 130° .

This investigation was carried out at the Research Laboratory of the Pharmaceutical Society, and I desire to express my warmest thanks to Professor Dunstan, not only for many valuable suggestions, but also very especially for his kind and unflinching encouragement.