CCLIV.—*The Isomerism of the Oximes. Part XXV. The Dissociation Constants of some Isomeric Aldoximes.*

By Oscar L. Brady and Richard F. Goldstein.

Although no measurements of dissociation constants of aldoximes have been recorded in the literature, it has been shown qualitatively by two methods that the aromatic α-aldoximes are stronger acids than the corresponding β-aldoximes. From approximate cryoscopic measurements, Goldschmidt and Röder (*Ber.*, 1895, **28**, 2013) concluded that in aqueous solution the sodium salts of the α-aldoximes are mainly electrolytically dissociated, whilst the sodium salts of the β-aldoximes are mainly hydrolytically dissociated. Later, Swientoslawski and his co-workers (Swientoslawski, *Chem. Polski*, 1918, **15**, 1; Swientoslawski and Papow, *ibid.*, 1919, **16**, 1; Dorobialska, *Rocz. Chem.*, 1921, **1**, 424), by thermochemical measurements of the heats of neutralisation of the aldoximes with sodium hydroxide, found that the sodium salts of the β-aldoximes were hydrolysed to a somewhat greater extent than the corresponding α-compounds. His method, however, gave but approximate results, and as he worked on only two aldoximes (benzaldoxime and *m*-nitrobenzaldoxime), his results require confirmation.

An investigation of the dissociation constants of some isomeric aldoximes has been undertaken in the hope that it might throw some light upon the isomerism of the oximes. The aldoximes are weak acids, analogous to phenol, and hence their dissociation constants can be determined only hydrolytically. Of the methods available, that depending on the measurement of the degree of hydrolysis of the sodium salt by conductivity methods was finally chosen as the most suitable (Lundén, Ahrens' Sammlung, 1908, **14**, 42), and the dissociation constants of the aldoximes recorded in the table on p. 1923 have been determined.

It was unfortunately impossible to determine the dissociation constants of more than five β-aldoximes, on account of their very sparing solubility; even with those which were sufficiently soluble, conductivity measurements could be taken only at two dilutions, and were greatly hampered by decomposition caused by the platinum black on the electrodes.

From the values of the four pairs of isomeric aldoximes which were investigated, it will be seen that in all cases the α-aldoxime possesses a higher dissociation constant than the β-aldoxime, thereby confirming the conclusions of Goldschmidt and Röder and of Swientoslawski and his co-workers.

It was hoped that this research might give some clue to the reasons for the formation or non-formation of two forms of substituted benzaldoximes; it has been shown (Brady and Dunn, J., 1923, **123**, 1783) that the conversion of the α- into the β-isomeride through the hydrochloride depends upon an isomeric change in the hydrochloride itself and it was thought that the acidity of the oxime might have some bearing on the stability of the ammonium-type hydrochloride which, it was considered, was formed in the first instance; these expectations have not been realised. For example, although all attempts to obtain the β- form from α-*o*-methoxybenzaldoxime have been unsuccessful, whilst α-*p*-methoxybenzaldoxime is very easily converted into the β-compound, yet the two α-oximes have practically the same dissociation constants ($1{\cdot}3 \times 10^{-11}$ and $1{\cdot}2 \times 10^{-11}$, respectively). Again, the α-oxime-forming hydrochlorides of benzaldoxime and *p*-methoxybenzaldoxime change to the β-oxime-forming hydrochlorides at considerably lower temperatures than those of 3 : 4-dimethoxybenzaldoxime and 3 : 4-methylenedioxybenzaldoxime. There seems, however, to be a tendency for the α-oxime-forming hydrochlorides of the more strongly acidic oximes to be the least stable; roughly, the α-oxime-forming hydrochlorides can be arranged in order of their relative stabilities as follows, the values of their dissociation constants being shown in brackets: 3 : 4-methylenedioxybenzaldoxime ($1{\cdot}4 \times 10^{-11}$) > *p*-methoxybenzaldoxime ($1{\cdot}2 \times 10^{-11}$) > benzaldoxime ($2{\cdot}1 \times 10^{-11}$) > *m*-nitrobenzaldoxime ($7{\cdot}0 \times 10^{-11}$) > *p*-nitrobenzaldoxime ($10{\cdot}7 \times 10^{-11}$).

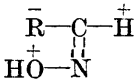
The isomeric change may therefore be the rearrangement of the molecule to the form which most favours hydrochloride formation, that is, the least acidic.

Doubt has recently been cast upon Hantzsch's original formulation of the configuration of the aldoximes (*Ber.*, 1891, **24**, 13), and it has been suggested that the α-isomeride has the so-called *syn*- and not the *anti*-configuration assigned to it by him.

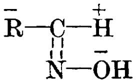
Apart from the chemical evidence in favour of this suggestion (Brady and Bishop, J., 1925, **127**, 1357; Auwers and Ottens, *Ber.*, 1925, **58**, 2060; Meisenheimer, Zimmermann, and Kummer, *Annalen*, 1926, **446**, 205), some evidence has been adduced from a consideration of the physical properties.

Beckmann, Liesche, and Correns (*Ber.*, 1923, **56**, 341) have suggested configurations for the aldoximes, based upon Abegg's electrochemical theory of the stability of the oximes (*Ber.*, 1899, **32**, 291); to quote from their paper "the higher-melting aldoximes, which readily form nitriles, are favoured by the action of acids, and must be represented as (I); the isomerides, which can be acylated and hydrolysed without decomposition, must then be represented as (II) :

(I.)



$$\begin{array}{ccc} \overset{-}{\mathrm{R}} - & \mathrm{C} & - \overset{+}{\mathrm{H}} \\ + & \| & \\ \mathrm{HO} - & \mathrm{N} & \end{array}$$



$$\begin{array}{ccc} \overset{-}{\mathrm{R}} - & \mathrm{C} & - \overset{+}{\mathrm{H}} \\ & \| & - \\ & \mathrm{N} & - \mathrm{OH} \end{array}$$

(II.) ”

Apart from the question of the validity of Abegg's electrochemical theory, the facts from which these deductions are drawn are incorrect. In accepting Abegg's theory, Beckmann, Liesche, and Correns acquiesced in his statement that the α-aldoximes are stable to alkali, and the β-aldoximes stable to acid; but this is not so, since the β-aldoximes of the aromatic series and their *O*-ethers are more or less rapidly converted into the corresponding α-compounds by the action of a small amount of acid (compare, *inter alia*, Luxmoore, J., 1896, **69**, 179; Brady and Dunn, J., 1923, **123**, 1788), whilst when dissolved in alkali, they are comparatively stable (compare Brady, J., 1914, **105**, 2114). The facts are that at low temperatures the α-oxime-forming hydrochloride, and at higher temperatures the β-oxime-forming hydrochloride, is stable, the temperature of transition varying with the individual oxime.

Auwers and Ottens (*Ber.*, 1924, **57**, 446) consider that their measurements of the optical properties of the aldoximes and the *O*-ethers favour the new formulation, but it is doubtful if these properties are a trustworthy guide when small differences of constitution are involved (compare Goss, Ingold, and Thorpe, J., 1924, **125**, 1927). On the other hand, if the principle, applied by Ostwald (*Z. physikal. Chem.*, 1892, **9**, 553) to the acids of the ethylene series, that in an acid the proximity of a so-called “ acidic ” group tends to increase the dissociation constant of the acid, can be applied to the aldoximes, the benzaldoxime of the *anti*-type, where the negative phenyl group is vicinal to the aldoximino-hydroxyl group, should have a higher dissociation constant than the *syn*-isomeride, in which the two groups are farther apart.

It has been possible to determine the dissociation constants of four pairs of isomeric aldoximes (see table on p. 1923) and in all these cases the α-aldoxime has a higher dissociation constant than the β-isomeride. A configuration of the *anti*-type should therefore be assigned to the α-aldoximes, and of the *syn*-type to the β-aldoximes, supporting Hantzsch's original view of the configuration of the aldoximes.

In all cases of isomerism in the ethylenic series, the *cis*-form has a greater solubility in water than the *trans*-form (Michael, *J. Amer. Chem. Soc.*, 1918, **40**, 1678). Since an *anti*-aldoxime corresponds to the *cis*-form, and a *syn*-aldoxime to the *trans*-form (Auwers and

Ottens, *Ber.*, 1924, **57**, 446),* one would expect the former to be more soluble in water than the latter. Although no quantitative data on the solubility of the aldoximes have been published, it is well known that the α-aldoxime is more soluble in water (and in most other solvents) than the β-aldoxime. The conclusions to be drawn from these considerations therefore agree with those drawn from measurements of dissociation constants.

The deductions from the physical properties of the aldoximes are thus at variance with those drawn from their chemical reactions, and it must be admitted that we are far from achieving finality.

It had been hoped, when this work was commenced, to follow the inversion of the β- to the α-aldoxime by measuring the change of conductivity with time of a solution of the sodium salt of a β-aldoxime, but unfortunately the β-aldoxime appears to suffer a profound decomposition in contact with the platinum-black used on the electrodes, and the curve obtained was inexplicable. Also attempts to detect any transient basic or acidic properties of an aldoxime on liberation from its sodium salt were unsuccessful. One other point deserves mention : it was found that on heating *o*-nitrobenzaldoxime with dilute sodium hydroxide, *o*-nitrobenzamide was produced in fair yield. It was at first thought that this was due to a Beckmann rearrangement, but Reissert (*Ber.*, 1908, **41**, 3815) has found that on heating α-*o*-nitrobenzaldoxime with a very weak alkali, such as potassium cyanide, an excellent yield of *o*-nitrobenzonitrile was produced, but that on increasing the strength of the alkali, *o*-nitrobenzamide, mixed with a little *o*-nitrobenzonitrile, was formed. The reaction appears to be an interesting case of dehydration followed by addition of water in a different direction, and is unique for *o*-nitrobenzaldoxime; with other oximes, either there is no change (α-3 : 4-methylenedioxybenzaldoxime, α-*p*-methoxybenzaldoxime), or complete decomposition takes place (α-6-nitro-3 : 4-methylenedioxybenzaldoxime).

EXPERIMENTAL.

The method used was that first devised by Walker (*Z. physikal. Chem.*, 1889, **4**, 319) and subsequently developed and improved by Bredig (*ibid.*, 1894, **13**, 289).

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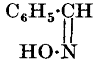
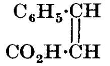
* The correspondence can be seen by comparing the cinnamic acids with the benzaldoximes :



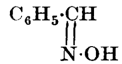
$$\begin{matrix} C_6H_5\cdot CH \\ \| \\ HO\cdot N \end{matrix}$$

anti-Oxime.



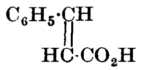
$$\begin{matrix} C_6H_5\cdot CH \\ \| \\ CO_2H\cdot CH \end{matrix}$$

cis-(*allo*-)Cinnamic acid.



$$\begin{matrix} C_6H_5\cdot CH \\ \| \\ N\cdot OH \end{matrix}$$

syn-Oxime.



$$\begin{matrix} C_6H_5\cdot CH \\ \| \\ HC\cdot CO_2H \end{matrix}$$

trans-Cinnamic acid.

If the observed conductivity of a solution of one mol. of the sodium salt of an oxime dissolved in v litres ofwater is $\Lambda_{\text{obs.}}$, the true conductivity of the unhydrolysed salt Λ_v, and the conductivity of the sodium hydroxide formed by hydrolysis Λ_{NaOH}, then the degree of hydrolysis, x, can be obtained from the equation :

$$\Lambda_{\text{obs.}} = (1 - x)\Lambda_v + x\Lambda_{\text{NaOH}}.$$

Furthermore, the hydrolysis constant, K_h, of the sodium salt is given by :

$$K_h = x^2/v(1 - x).$$

Finally,

$$K_a = K_w /K_h,$$

where K_a is the dissociation constant of the oxime, and K_w is the ionisation constant of water, assumed to be $1{\cdot}0 \times 10^{-14}$ as the mean of the most trustworthy determinations. By means of these three equations, K_a can be calculated from measurements of $\Lambda_{\text{obs.}}$, Λ_v and Λ_{NaOH}. Owing to experimental difficulties, Λ_v could not be directly measured, and had to be assumed from the empirical rules of Ostwald ("Lehrbuch der Allgemeine Chemie," II, i, p. 619) and Bredig (*loc. cit.*, p. 198).

The preparation of the oxime calls for no special remark. The crude oxime was recrystallised from suitable solvents, generally benzene and light petroleum, or dilute alcohol, until the m. p. recorded in the literature was obtained. A solution of the sodium salt was prepared by dissolving a weighed amount of the oxime in the calculated quantity of carbon dioxide-free sodium hydroxide and diluting the solution to the required volume. The sodium hydroxide was made by the action of water vapour on metallic sodium suspended on nickel gauze under a bell-jar through which was passed a slow current of carbon dioxide-free air to remove the hydrogen as it was formed; omission of this precaution led to several explosions. The strength of the sodium hydroxide was determined by titration against pure succinic acid. Solutions were preserved in silica vessels.

The conductivity measurements were made at 25° ± 0·02°, with a rotating double commutator, a Wheatstone bridge, and suspended-coil galvanometer. The bridge-wire was calibrated by the method recommended by Kohlrausch ("Leitvermögen der Elektrolyte," 1916, p. 48) and the resistances were checked against a standard resistance. An enclosed cell of hard glass was used for the alkaline solutions. The conductivity of the sodium hydroxide in the same dilutions as were used was frequently determined, and the values obtained were employed in the calculations. In all measurements, carbon dioxide-free water of conductivity $1{\cdot}5 - 2{\cdot}0 \times 10^{-6}$ mho was employed and the readings were corrected for this value. Determinations were made at as many as possible of the usual dilutions 32, 64, 128, 256, 512, and 1024 (see col. 3 in table).

Considerable difficulty was experienced with the β-oximes, as freshly deposited platinum black decomposed the sodium salts, bringing about a rapid fall of conductivity. This effect appears to be quite general for all β-aldoximes, *e.g.*, the sodium salt of β-heptaldoxime, which is only known in one form, is rapidly decomposed. It was ultimately found possible to destroy the activity of the electrodes, without impairing the accuracy of the conductivity measurements, by leaving them in contact with the sodium salt of a β-aldoxime for some time. By this means, the required conductivities could be determined satisfactorily.

TABLE.

			$K_h \times 10^5$.		
Oxime.	M. p.	*v* (litres).	Limits.	Mean	$K_a \times 10^{11}$.
α-Benzaldoxime	35°	32—1024	42—51	47	2·1
β- ,, ...	131—132	512—1024	210—220	215	0·47
α-*o*-Nitro-benzaldoxime ...	101—102	32—1024	10·6—12·2	11·5	8·7
β-*o*-Nitro- ,, ...	143—145	512—1024	54—56	55	1·8
α-*m*-Nitro- ,, ...	121	32—1024	13·7—14·8	14·3	7·0
β-*m*-Nitro- ,, ...	119—120	512—1024	55—58	56	1·8
α-*p*-Nitro- ,, ...	129	32—1024	8·9—10·3	9·3	10·7
α-2 : 4-Dinitro- ,, ...	127	128—1024	3·3—2·3	2·7	37 *
α-*o*-Methoxy- ,, ...	92	32—1024	71—78	75	1·3
α-*m*-Methoxy- ,, ...	38—39	128—1024	36—40	39	2·6
α-*p*-Methoxy- ,, ...	65	256—1024	80—84	82	1·2
α-3 : 4-Dimethoxy- ,, ...	94	128—1024	69—76	73	1·4
α-3 : 4-Methylenedioxy- ,,	111—112	64—1024	71—76	74	1·4
α-Cinnamaldoxime	75—76	128—1024	35—37	36	2·8
β- ,, ...	135	512—1024	71—82	77	1·3
α-*m*-Nitrocinnamaldoxime	157	1024	14·5	14·5	6·9 †
β-Heptaldoxime	55—56	512—1024	380—410	395	0·25

* With α-2 : 4-dinitrobenzaldoxime, the hydrolysis constant decreased regularly on dilution from 128 to 1024 litres. This change is probably due to partial conversion of the oxime into 4-nitrosalicylonitrile (Borsche, *Annalen*, 1912, **390**, 1).

† No consistent results could be obtained with this oxime at a dilution of 2048 litres. The value at 1024 litres has been confirmed by repetition.

Action of Alkali on o-*Nitrobenzaldoxime.*—A mixture of the α-oxime (1·32 g.) with an equivalent weight of *N*/5-sodium hydroxide was heated on the water-bath for 3 hours, left over-night, and heated for another 2 hours. The solution contained about 0·03 g. of sodium nitrite (estimated by Griess's colorimetric method) and the issuing vapours contained ammonia. On cooling and saturating the solution with carbon dioxide, a nearly white precipitate (0·22 g.) was obtained. Nothing could be isolated from the solution after filtration, and no salicylic acid was present. The precipitate (m. p. 172—175°) was shown to be *o*-nitrobenzamide by its reactions, and by a mixed m. p. with an authentic specimen.

About a 10% yield of *o*-nitrobenzamide can be obtained by boiling either the α- or the β-oxime for 15 minutes with double the equivalent quantity of *N*/5-sodium hydroxide. In this case, the amide separated on cooling, and treatment of the filtrate with carbon dioxide yielded an impure oxime.

Neutralisation Phenomenon with α-m-*Nitrobenzaldoxime.*—10 C.c. of *N*/128-hydrochloric acid were mixed with 10 c.c. of an *N*/128-solution of the sodium salt of α-*m*-nitrobenzaldoxime, and the conductivity was measured at frequent intervals, but no change was observed during 100 minutes, the equivalent conductivity being 126·4. The value given by Jones (Carnegie Inst. Pub., No. 170, 1912) for the equivalent conductivity of sodium chloride in *N*/256-solution is 124·1. It is therefore clear that no abnormal phenomenon takes place on neutralisation of the sodium salt of α-*m*-nitrobenzaldoxime.

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