CXXVI.—*The Isomerism of the Oximes. Part XXXIV. The Dissociation Constants of Isomeric Oximes and their Influence on the Production of the Isomerides in Alkaline Solution.*

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The results of the determination of the dissociation constants of a number of aldoximes (Brady and Goldstein, J., 1926, 1923) showed that in the case of substituted benzaldoximes, where only the α-aldoxime was produced when oximation was carried out in alkaline solution, the α- was about four times as strong an acid as the β-isomeride, but that α-cinnamaldoxime was only about twice as strong an acid as β-cinnamaldoxime. In the latter case oximation in alkaline solution yields both the α- and the β-oxime.

This suggested that when an aldehyde or unsymmetrical ketone was treated with an alkaline solution of hydroxylamine the configuration of the resulting oxime bore some relation to the dissociation constants of the two possible isomerides. That is, if the dissociation constants were widely different, only the oxime with the higher constant would be obtained, but if they were nearly the same both isomeric oximes would be formed. Further work bears out this hypothesis : the results are shown in Table I, where the dissociation constants of eight pairs of isomeric oximes are given.

TABLE I.

	$K_a \times 10^{11}$.	$K_a\alpha/K_a\beta$.
α-Benzaldoxime	2·1	4·5 : 1
β- ,,	0·47	
α-*o*-Nitrobenzaldoxime	8·7	4·8 : 1
β- ,,	1·8	
α-*m*-Nitrobenzaldoxime	7·0	3·9 : 1
β- ,,	1·8	
α-Cinnamaldoxime	2·8	2·1 : 1
β- ,,	1·3	
α-*o*-Methoxycinnamaldoxime	1·6	3·5 : 1
β- ,,	0·45	
α-Furfuraldoxime	1·5	1·1 : 1
β- ,,	1·4	
α-*p*-Nitrobenzophenoneoxime	1·4	1 : 2·4
β- ,,	3·4	
α-Phenyl-*p*-tolylketoxime	—	1·4 : 1 *
β- ,,	—	

* Deduced from quantitative methylation experiments.

o-Methoxycinnamaldehyde, unlike cinnamaldehyde, gives little if any of the β-oxime with hydroxylamine in alkaline solution, behaving more like the substituted benzaldoximes (Brady and Grayson, J., 1924, **125**, 1418), and it is found that the ratio $K_a\alpha/K_a\beta$ approaches that of the *m*-nitrobenzaldoximes. Furfuraldehyde, on the other hand, on oximation under these conditions readily gives an inseparable mixture of the α- and β-isomerides (Brady and Goldstein, J., 1927, 1959). Although we have no quantitative figures, qualitative experience shows that more of the β-isomeride is produced in this case than in that of cinnamaldehyde, as would be expected from the lower $K_a\alpha/K_a\beta$ ratio.

The α- and β-*p*-nitrobenzophenoneoximes do not differ greatly in their dissociation constants. Here the oxime to which the label β has been attached happens to be the stronger acid, but this has no real significance, since the α- and β-titles have not, in the ketoximes, the special connotation they bear in the aldoximes (Brady and Bishop, J., 1925, **127**, 1361). Similarly, the α- and β-phenyl-

p-tolylketoximes are both acids of about the same strength; direct measurement of the dissociation constants in this case has been found impracticable for reasons given in the experimental part, but some idea of the relative strengths of the two acids can be gained from a quantitative study of their methylation : this will be the subject of a later paper (compare Brady and Goldstein, J., 1926, 2403). *p*-Nitrobenzophenone and phenyl *p*-tolyl ketone on oximation in alkaline solution both give a mixture of the α- and the β-ketoxime (Brady and Mehta, J., 1924, **125**, 2298; Hantzsch, *Ber.*, 1890, **23**, 2325).

Brady and Goldstein (J., 1926, 1918) showed that if the new configurations for the benzaldoximes are accepted the relation between configuration and dissociation constant in these compounds is not analogous to that in the cinnamic acids, since the stronger acid is that in which the phenyl group is remote from the hydroxyl group. The dissociation constants of the two forms of *p*-nitrobenzophenoneoxime and phenyl-*p*-tolylketoxime bear this out, since, if the new configurations are adopted, the stronger acid has in the first case the *p*-nitrophenyl and in the second the phenyl group remote from the hydroxyl. The new configurations of the ketoximes rest on more experimental evidence than those of the aldoximes and either this evidence is also unsound or the analogy with *cis*- and *trans*-acids in the ethylene series will not hold. Since there is between the two acidic groups a chain of two atoms in the oximes and of three in ethylene compounds ($C_6H_5{\cdot}C{=}N{-}OH$, $C_6H_5{\cdot}C{=}C{-}C{-}OH$), the comparison may not be a fair one.

On the above lines it is possible to suggest an explanation of the apparent exclusive formation of β-aldoximes when aliphatic aldehydes are oximated. For example, in benzaldoxime the phenyl group has a greater electron affinity than the methine hydrogen atom; the effect of this is so transmitted that the hydrogen of the hydroxyl group is more easily expelled as an ion when the hydroxyl group is remote from the phenyl group, that is, the α-oxime is the stronger acid and is formed on oximation in alkaline solution. Now in the aliphatic aldoximes the methine hydrogen atom has a greater electron affinity than the alkyl group and consequently the stronger acid will be that in which the hydroxyl is remote from the methine hydrogen, namely, the β-oxime, which will consequently be formed on oximation. The lack of a suitable method of converting a stable β-aldoxime into the α-isomeride would explain the failure to obtain satisfactory evidence of the existence of the latter form among aliphatic aldoximes. Attempts to bring this change about through the benzoyl derivative, successful in the case of β-cinnamaldoxime (Brady and Grayson, *loc. cit.*), have so far yielded negative results.

Our conclusions have been drawn from a more limited number of examples than we could have desired, but owing to the very sparing solubility in water of most of the β-oximes and the ready hydrolysis of their sodium salts the determination of their dissociation constants presents unusual difficulties, and we have failed to obtain figures in other cases we have tried. Measurements of hydrogen-ion concentration with the glass electrode were unsuccessful owing to progressive hydrolysis of the oxime to aldehyde and hydroxylamine in the very dilute aqueous solutions that had of necessity to be employed. We are indebted to Mr. B. Prasad for investigating this method.

The dissociation constants of α-*p*-dimethylaminobenzaldoxime ($K_a = 0{\cdot}56 \times 10^{-11}$), acetophenoneoxime ($K_a = 0{\cdot}33 \times 10^{-11}$), and benzophenoneoxime ($K_a = 0{\cdot}50 \times 10^{-11}$) have also been measured.

EXPERIMENTAL.

The conductivity method previously employed (Brady and Goldstein, *loc. cit.*) for the measurement of the dissociation constants of some aldoximes cannot be used for those oximes which are very weak acids and sparingly soluble in water owing to the separation of the solid oxime when the sodium salt dissociates hydrolytically. For this reason the method of Farmer (J., 1901, **79**, 863), depending upon the measurement of the degree of hydrolysis of the sodium salt as determined by the distribution coefficient of the oxime between aqueous sodium hydroxide and an organic solvent, has been employed Even this method is not applicable to such weak acids as phenyl-*p*-tolylketoxime, as, owing to the very large proportion of the oxime that passes into the organic solvent, concordant results cannot be obtained.

In the following experiments, water and sodium hydroxide free from carbon dioxide were employed, the solutions were preserved in waxed bottles, and the usual precautions observed to prevent access of carbon dioxide during manipulation. The temperature throughout was 25° ± 0·04°. The mutual solubilities of water and benzene were taken as 100 c.c. of water dissolve 0·082 c.c. of benzene and 100 c.c. of benzene dissolve 0·211 c.c. of water.

In order to determine the distribution coefficient of the oxime between water and benzene, a weighed amount of oxime, insufficient to saturate the solvents, was shaken with a mixture of known amounts of benzene and water for 6 hours at constant temperature and the solutions were left in the thermostat to separate. Three portions of 10 c.c. were pipetted from the benzene layer and the oxime therein was determined either by evaporation on the water-bath and drying at 100° to constant weight or, with the more volatile oximes, by evaporation in a current of dry air at room temperature and drying in a vacuum to constant weight. The aqueous layer was examined in either of two ways. A quantity (100—400 c.c. depending on the solubility of the oxime) was extracted several times with chloroform, and the oxime determined by evaporation as before. Alternatively,. 100—500 c.c. were acidified with hydrochloric acid (25 c.c. of concentrated acid for each 100 c.c. of solution), a solution of 2 : 4-dinitrophenylhydrazine hydrochloride was added, and the mixture warmed and kept over-night. The very sparingly soluble dinitrophenylhydrazone was collected, dried at 100°, and weighed (compare Brady and Elsmie, *Analyst*, 1926, 77). In the case of oximes which did not give concordant results by this method owing to their very small solubility in water, the solubilities in water saturated with benzene and in benzene saturated with water were determined separately (compare Farmer, *loc. cit.*) and their ratio was taken as the distribution coefficient.

The degree of hydrolysis of the sodium salt was measured by shaking a weighed quantity of oxime with known amounts of benzene, water, and sodium hydroxide solution for 6 hours in a thermostat and then allowing the two layers to separate. The oxime in the benzene layer was determined as before. The results were calculated from the equations (Farmer, *loc. cit.*)

$$K = \frac{c[c_1 - c_2 + c(1 + qF)]}{c_2 - c(1 + qF)}, \quad m_1 = \frac{\sqrt{K^2 + 4Kc_2} - K}{2}$$

$$x = m_1/c_2, \quad K_h = x^2/(1 - x)v, \quad K_a = K_w/K_h,$$

where c = concentration of free oxime in the aqueous layer after

TABLE II.

		Vol. of water.	Vol. of benzene.	F.	$c_1 \times 10^3$.	$c_2 \times 10^3$.	G. of oxime in 20 c.c. of benzene layer.	$K_a \times 10^{11}$.
α-*o*-Methoxybenzaldoxime	(1)	500	50	60·30	14·32	14·12	0·2225	1·45
	(2)	500	50	60·30	17·05	13·59	0·1689	1·60
α-*m*-Nitrobenzaldoxime	(1)	270	50	24·00	10·20	9·20	0·0604	7·10
	(2)	500	100	24·00	17·05	14·62	0·0424	6·69
α-*p*-Nitrobenzaldoxime		500	50	18·05	18·84	17·88	0·0478	10·93
α-*p*-Dimethylaminobenzaldoxime	(1)	517	75	46·72	12·41	12·37	0·2472	0·55
	(2)	275	50	46·72	18·30	13·23	0·2466	0·57
α-Furfuraldoxime	(1)	276	50	1·01	18·92	18·92	0·0136	1·46
	(2)	125	50	1·01	18·30	17·34	0·0140	1·33
β-Furfuraldoxime	(1)	113	50	2·51	9·26	9·26	0·0284	1·57
	(2)	114	100	2·51	13·83	13·83	0·0262	1·43
α-*o*-Methoxycinnamaldoxime	(1)	250	50	162·0	7·19	6·16	0·2284	1·61
	(2)	500	50	162·0	10·79	7·25	0·2195	1·56
β-*o*-Methoxycinnamaldoxime	(1)	500	50	147·0	7·19	5·02	0·2520	0·45
	(2)	500	50	147·0	10·14	6·50	0·2972	0·44
α-*p*-Nitrobenzophenoneoxime	(1)	257	50	1072·0	5·27	5·02	0·4370	1·21
	(2)	520	50	1072·0	14·78	5·72	0·3972	1·59
β-*p*-Nitrobenzophenoneoxime		500	50	1943·0	7·19	6·35	0·2529	3·37
Benzophenoneoxime	(1)	500	50	1133·0	40·62	5·52	0·3291	0·48
	(2)	500	75	1133·0	13·58	4·88	0·2318	0·53
Acetophenoneoxime	(1)	500	50*	7·62	14·93	14·86	0·1288	0·33
	(2)	116	50*	7·62	11·71	11·35	0·1398	0·33

* Light petroleum (b. p. 60—80°) was used in place of benzene.

shaking with benzene, c_1 = concentration of sodium hydroxide in mols., c_2 = concentration of oxime in mols., q = ratio of volume of benzene layer to sodium hydroxide layer, F = distribution coefficient of oxime between benzene and pure water, m_1 = concentration of free oxime in the aqueous layer, x = degree of hydrolysis of the sodium salt of the oxime, K_h = hydrolysis constant, v = number of litres of water containing a gram-molecule of oxime, K_w = ionic constant of water = $1{\cdot}00 \times 10^{-14}$, K_a = dissociation constant of oxime. The observed figures are given in Table II.

The dissociation constants of *m*- and *p*-nitrobenzaldoximes and of *o*-methoxybenzaldoxime were determined by this method to test its applicability. The mean results, 6·9, 10·9, $1{\cdot}5 \times 10^{-11}$, respectively, agree satisfactorily with those determined by conductivity methods, 7·0, 10·7, $1{\cdot}3 \times 10^{-11}$ (Brady and Goldstein, *loc. cit.*).

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[*Received, February 4th,* 1929.]