202. *The Effect of Co-ordination on Ionization. Part III.*[1] *Pyridine-2,6-dialdoxime and its Iron*(II) *Complex.*

By G. I. H. HANANIA, D. H. IRVINE, and F. SHURAYH.

The two oxime (N·OH) groups in pyridine-2,6-dialdoxime have strongly overlapping titration curves. For the first acid ionization, involving charges $0 \longrightarrow -1$, $\mathrm{p}K_1{}^\circ$ (25°) = 10·08 ± 0·025; $\Delta H_1{}^\circ = 5\cdot3 \pm 0\cdot9$ kcal./mole; and $\Delta S_1{}^\circ = -28 \pm 3$ e.u.; for the second ionization, involving charges $-1 \longrightarrow -2$, $\mathrm{p}K_2{}^\circ$ (25°) = 10·88 ± 0·025; $\Delta H_2{}^\circ = 6\cdot7 \pm 1\cdot0$ kcal./mole; and $\Delta S_2{}^\circ = -27 \pm 3$ e.u. In the bis(pyridine-2,6-dialdoxime)–iron(II) complex, the fourth oxime acid ionization, involving charges $-1 \longrightarrow -2$, has $\mathrm{p}K_4{}^\circ$ (25°) = 7·40 ± 0·025, with $\Delta H_4{}^\circ = 0 \pm 0\cdot9$ kcal./mole and $\Delta S_4{}^\circ = -34 \pm 3$ e.u.; and for the third oxime ionization, involving charges $0 \longrightarrow -1$, $\mathrm{p}K_3$ is about 5, but no thermodynamic datum was obtained.

The effect of co-ordination to iron(II) on the acid strength of the oxime group is discussed and compared with the corresponding effect in the pyridine-2-aldoxime system.

THE acid strength of a group on a ligand is increased when the ligand is co-ordinated to a metal, the magnitude of the effect depending on the bonding involved.[1,2] Thus, for the oxime (N·OH) group in the bidentate ligand pyridine-2-aldoxime and its iron(II) complex, pK° (25°) drops from 10·22 in the ligand to 7·13 in the complex, the charge types in both ionizations being $0 \longrightarrow -1$. On the other hand the effect is smaller in the case of the ligand 2-(2-pyridyl)imidazoline. Here, pK° (25°) for the imidazolinium ($\mathrm{NH^+}$) group drops from 9·2 in the free ligand to 6·6 in its iron(II) complex, even though the latter carries an extra positive charge which would be expected to increase further the acid strength of the $\mathrm{NH^+}$ group. The different magnitude of the effect in the two cases was attributed to the greater degree of conjugation in the iron complex of pyridine-2-aldoxime, an effect which favours increased acid strength through resonance stabilization of the oxime conjugate base ($=\mathrm{N{\cdot}O^-}$).

We now report similar measurements on the analogous, but terdentate, ligand pyridine-2,6-dialdoxime, and on its iron(II) complex. This system is structurally similar to that of pyridine-2-aldoxime, but the complex ion has one more oxime side group and carries an extra negative charge on its conjugate base. It is of interest to examine the effect of this extra charge on the thermodynamics of ionization of the oxime (N·OH) in the complex ion.

Ionizations in Pyridine-2,6-*dialdoxime*.—The ultraviolet absorption spectrum of pyridine-2,6-dialdoxime is shown in Fig. 1. Its two bands, with maxima at 227 and 296 mμ, are similar to those of pyridine-2-aldoxime[3] which has bands at 238 and 277 mμ. Both spectra undergo two reversible changes. In strongly acidic solutions, the 227 mμ band of pyridine-2,6-dialdoxime drops slightly, and the 296 mμ band shifts to 301 mμ, corresponding to the pyridinium ($\mathrm{NH^+}$) acid ionization with pK ~2. No spectral change is observed within the range of pH 4 to 8. In more strongly alkaline solutions, a band develops at 275 mμ with a shoulder at 310 mμ, but the spectral change between pH 8 and 12 does not correspond to a single equilibrium as can be seen from their intermediate spectrum at pH 10 which does not cross the other two spectra at their isosbestic point 250 mμ. This behaviour is consistent with the assumption that the two oxime (N·OH) ionizations occur in the pH range 10—11 and that they are strongly coupled making it impossible to obtain

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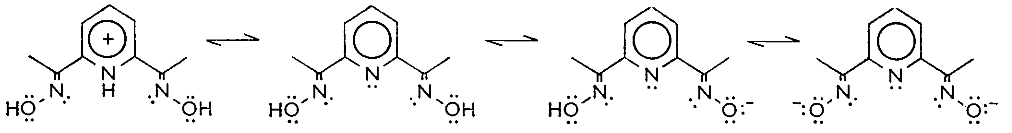
[1] Part II, Hanania and Irvine, *J.*, 1962, 2750.
[2] Hanania and Irvine, *J.*, 1962, 2745.
[3] Hanania and Irvine, *Nature*, 1959, **183**, 40.

the absorption spectrum for the intermediate (first) conjugate base. The three ionizations may be represented as follows:



($^+$HPH$_2$) (PH$_2$) (PH$^-$) (P$^=$)

corresponding to the acid–base equilibria (using the above notation):

$$^+HPH_2 \rightleftharpoons PH_2 + H^+ \ (K_N) \qquad (1)$$

$$PH_2 \rightleftharpoons PH^- + H^+ \ (K_1) \qquad (2)$$

$$PH^- \rightleftharpoons P^= + H^+ \ (K_2) \qquad (3)$$

in each case the acid dissociation constant K, at ionic strength I, is defined by the relation

$$K = a_{H^+} . [\text{base}]/[\text{acid}] \qquad (4)$$

where a_{H^+} is the activity of hydroxonium ions obtained from pH measurement and defined by the relation pH = $-\log a_{H^+}$, and [base]/[acid] is the ratio of concentrations of conjugate base to acid obtained spectrophotometrically.

K_N (eqn. 1), referring to the pyridinium (NH$^+$) group, could not be measured owing to the instability (presumably hydrolysis) of the oxime in strongly acidic solutions. The spectral change shown in Fig. 1 suggests that p$K_N \leqslant 1$, a value which is considerably lower than the corresponding one in pyridine-2-aldoxime [2] where pK_N = 3·4. The increased acid strength of the group in the former case is probably due more to steric hindrance than the extra stabilization of the conjugate base through resonance.

K_1 and K_2 (eqns. 2 and 3), referring to the two successive ionizations of the oxime groups, could be measured with fair precision even though the two titration curves overlap strongly. A method of successive approximations [4] was used in obtaining the K_1 and K_2 values reported in the Table:

Acid ionization constants for the two oxime groups in pyridine-2,6-dialdoxime.

Temp.	20·3°	25·0°	30·0°	35·0°
pK_1	10·04	10·00	9·92	9·85
pK_2	10·68	10·63	10·51	10·45

I = 0·050M. pK = $-\log$ (acid ionization constant) as defined in eqn. (4), referring to the ionizations in eqns. (2) and (3). Each value is the average of about 10 measurements, mean deviations being ±0·025.

The data were all obtained at constant ionic strength I = 0·050M. The ionic strength variation was not investigated, and it was assumed that a simple theoretical relation holds over the range of I up 0·050M, *viz.*,

$$pK_1 = pK_1^\circ - 0{\cdot}5I^{\frac{1}{2}}/(1 + 1{\cdot}6\, I^{\frac{1}{2}}) \qquad (5)$$

from which the thermodynamic value pK_1° (25°) = 10·08 ± 0·025. The four pK_1 values in the Table yield a mean enthalpy of ionization over the temperature range 20·3° to 35·0°, ΔH_1 = 5·3 ± 0·9 kcal. mole^{-1}, which may be assumed to be equal to the value at zero ionic strength ΔH_1°; and consequently ΔS_1° (25°) = -28 ± 3 e.u. For the second ionization constant the corresponding relation is

$$pK_2 = pK_2^\circ - 1{\cdot}5I^{\frac{1}{2}}/(1 + 1{\cdot}6\, I^{\frac{1}{2}}) \qquad (6)$$

from which we obtain pK_2° (25°) = 10·88 ± 0·03, and likewise $\Delta H_2 = \Delta H_2^\circ$ = 6·7 ± 1·0 kcal. mole^{-1} and ΔS_2° (25°) = -27 ± 3 e.u.

It is noteworthy that in pyridine-2-aldoxime the single oxime group had pK° = 10·22,

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[4] Albert and Serjeant, " Ionization Constants of Acids and Bases," Methuen, London, 1962, ch. 4.

$\Delta H^\circ = 6{\cdot}8$ kcal. mole^{-1} and $\Delta S^\circ = -24$ e.u. at 25°. These values are close to the corresponding values obtained for both oxime groups in pyridine-2,6-dialdoxime. In the latter case, the conjugate base of each oxime group resonates with the pyridine ring but not with the other oxime group in the molecule; as a result, the two ionizations are nearly independent of each other with strongly overlapping titration curves as expected. Moreover, the second ionization is a little weaker, $K_1/K_2 = 6{\cdot}3$, with the difference in free energy appearing in the greater endothermicity of the second ionization but not in its entropy change.

*The Bis(pyridine-*2,6*-dialdoxime)-iron*(II) *Complex.*—Pyridine-2,6-dialdoxime reacts rapidly with dilute aqueous solutions of iron(II) salts forming a stable red complex ion within a minute. The composition of the complex is 2 moles of ligand to 1 mole of Fe in the pH range 5·5 to 10·5. This fact was ascertained by the Job's method of continuous variation and was confirmed by the constancy of the formation constant for the complex ion calculated on the basis of the above stoicheiometry. A stable structure could be constructed with Courtauld atomic models on a terdentate basis of the 3 N atoms in the ligand. The complex was stable throughout the pH range 5 to 11 and the visible absorption spectrum showed only one reversible change, shown in Fig. 2, corresponding to an ionization with pK ~7. At pH <5 a further spectral change was observed followed by an irreversible fading of the red colour in more acidic solutions.

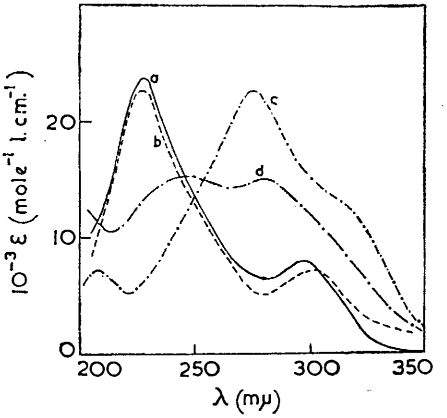

FIG. 1.

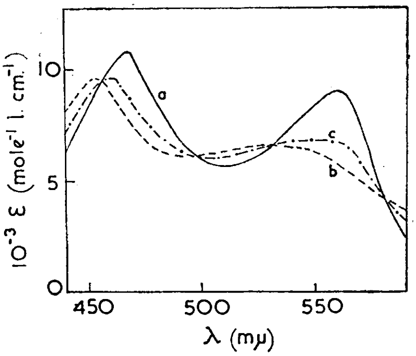

FIG. 2.

FIG. 1. Ultraviolet absorption spectrum of pyridine-2,6-dialdoxime giving extinction coefficient ε (M^{-1} cm.$^{-1}$) over the wavelengths range λ = 200—350 mμ. Values of ε at the band maxima are given below in parentheses following the wavelengths: (*a*) pH 4—8, dioxime diprotic acid with maxima at 227 mμ (23·7 × 10^3) and 296 mμ (8·0 × 10^3). (*b*) pH <1 (unstable), pyridinium acid with maxima at 227 mμ (22·6 × 10^3) and 301 mμ (7·2 × 10^3). (*c*) pH >12, di-anion conjugate base with maxima at 208 mμ (7·2 × 10^3) and 275 mμ (22·6 × 10^3); shoulder around 310 mμ (13·5 × 10^3). (*d*) pH 10, intermediate absorption spectrum; no isobestic points with other spectra but two proton ionizations over pH range 10 to 11.

FIG. 2. Visible absorption spectrum of bis-(pyridine-2,6-dialdoxime)–iron(II) complex giving extinction coefficient ε (M^{-1} cm.$^{-1}$) over the wavelength range λ = 440—590 mμ. Values of ε at the band maxima are given below in parentheses following the wavelengths; (*a*) pH 10, fourth conjugate base (eqn. 10) with maxima at 467 mμ (10·8 × 10^3) and 560 mμ (9·0 × 10^3). (*b*) pH 5·8, 97% formed conjugate acid (eqn. 10), with maxima at 453 mμ (9·6 × 10^3) and 580 mμ (6·7 × 10^3). At pH <5 another spectral change occurs (eqn. 9). (*c*) pH 7, intermediate mixture showing isosbestics at 456, 480, 497, and 580 mμ.

*Ionizations in the bis-(pyridine-*2,6*-dialdoxime)-iron*(II) *complex.* Four successive acid ionizations of the oxime N·OH groups in the bis(pyridine-2,6-dialdoxime)–iron(II) complex are expected. Using the above notation (PH_2 for a molecule of the ligand where the 2 H atoms are the acidic hydrogens on the two oxime groups), the ionizations may be represented as follows:

$$Fe(P_2H_4)^{2+} \rightleftharpoons Fe(P_2H_3)^{+} + H^{+}\ (K_1) \qquad (7)$$

$$Fe(P_2H_3)^{+} \rightleftharpoons Fe(P_2H_2)^{0} + H^{+}\ (K_2) \qquad (8)$$

$$Fe(P_2H_2)^{0} \rightleftharpoons Fe(P_2H)^{-} + H^{+}\ (K_3) \qquad (9)$$

$$Fe(P_2H)^{-} \rightleftharpoons Fe(P_2)^{2-} + H^{+}\ (K_4) \qquad (10)$$

Since, as stated above, no reversible spectral change was observed in alkaline solution beyond the one around pH 7, it may be concluded that eqn. (10), referring to the fourth oxime ionization in the complex, has $pK_4 \sim 7$. Consequently, the other spectral change occurring at pH <5 may be attributed to the third oxime ionization in eqn. (9), with $pK_3 \sim 5$ (it was not possible to measure this equilibrium on account of the interference of irreversible changes, possibly dissociation of the complex). The second and first ionizations (eqns. 8 and 7) are evidently too strong to measure. This is comparable to the behaviour of the analogous pyridine-2-aldoxime complex.[2]

The fourth oxime ionization in the complex was measured spectrophotometrically over a range of ionic strength and temperature. At 25°, the following pK_4 values (eqn. 10) were obtained; 7·13 ($I = 0{\cdot}050$M); 7·22 ($I = 0{\cdot}018$M); 7·26 ($I = 0{\cdot}009$M); 7·34 ($I = 0{\cdot}004$M), the mean deviation in each case being 0·03 pK unit. As expected from the charges on the ions, these data were found to be consistent with a relation of the type given in eqn. (6), with the limiting slope $-1{\cdot}5$. Linear extrapolation to zero ionic strength gives $pK_4{}^{\circ} = 7{\cdot}40 \pm 0{\cdot}03$ at 25°. A similar set of runs at varying temperature and constant $I = 0{\cdot}050$M gave the following pK_4 values: 7·11 (14·6°); 7·12 (19·8°); 7·13 (25·0°); 7·09 (31·4°); 7·10 (36·1°) with a mean deviation of 0·03 pK unit in each case. ΔH_4 is thus $0 \pm 0{\cdot}9$ kcal. mole^{-1} which may also be assumed to be the value of $\Delta H_4{}^{\circ}$, and hence $\Delta S_4{}^{\circ} = -34 \pm 3$ e.u.

Inspection of the above results shows that co-ordination has a profound effect on the acid strength of the oxime groups in pyridine-2,6-dialdoxime, and that the effect cannot be ascribed to electrostatic interaction of ferrous iron and ligand in the complex. Thus, comparing the data for the second oxime in pyridine-2,6-dialdoxime with the data for the fourth oxime in the complex (in both cases the ionization involving charges $-1 \longrightarrow -2$) we see that pK° (25°) drops from 10·88 in the free ligand to 7·40 in the complex, representing a 3000-fold increase in acid strength. A similar effect was observed in the analogous pyridine-2-aldoxime system[2] where the corresponding ionization involved charges $0 \longrightarrow -1$. In both cases, the effect may be attributed to resonance stabilization of the anionic conjugate base in the complex. It is noteworthy that the extra negative charge in the case of pyridine-2,6-dialdoxime does not alter the magnitude of this predominantly electronic effect.

The above thermodynamic data also show that co-ordination is accompanied by a favourable change in the enthalpy of ionization which decreases from 6·7 kcal. mole^{-1} in the free ligand to zero in the complex. On the other hand, the entropy of ionization is substantially unaltered, and in fact shows a slight tendency towards a more unfavourable value in the complex (-27 e.u. change to -34 e.u. with an uncertainty of ± 3 e.u. in each case). The pattern in the pyridine-2-aldoxime case is again very similar, ΔH° decreasing from 6·8 to 0·8 kcal. mole^{-1} and ΔS° changing from -24 to -30 e.u. This trend towards more unfavourable ΔS° values might possibly suggest some electrostatic contribution to the change in free energy, since in cases where electrostatic effects operate ΔH and ΔS values tend to change in opposite directions.

EXPERIMENTAL

Reagents and Materials.—Pyridine-2,6-dialdoxime, obtained from Aldrich Chemical Co., Milwaukee, Wisconsin, U.S.A., and K & K Laboratories Inc., Jamaica, N.Y., U.S.A., was recrystallized from water to constant m. p. 215—216°. All other chemicals were of analytical reagent grade. Conductivity water was used for making solutions, and ionic strengths were adjusted with sodium chloride.

Determination of pK_1 *and* pK_2 *in Pyridine*-2,6-*dialdoxime*.—Preliminary measurements indicated that the two oxime ionizations in pyridine-2,6-dialdoxime (eqn. 2 and 3) occur in the pH range 10 to 11 and are strongly overlapping. A spectrophotometric method involving a series of successive approximations was followed; it is similar to the method described in detail by Albert and Serjeant [4] except that data at one wavelength only were used throughout.

About twenty solutions were made for every run. These were $2{\cdot}2 \times 10^{-5}$M in pyridine-2,6-dialdoxime and were made up in buffer and salt to a pH between 8 and 12 at constant total $I = 0{\cdot}050$M. Borate buffers were used for the pH range 8—10·2, glycine buffers for 9·5—11·0, and phosphate buffers for 10·5—11·7. Every solution was divided into two parts. On one part, optical densities were read against a blank at 275 mμ in one set of experiments and at 227 mμ in another set (however, since the measurements at 275 mμ appeared consistently to be more precise, all results reported here were based on the former set of measurements). On the other part, simultaneous measurement of pH was made with the precautions described below. The runs were repeated at four temperatures (see Table). Ionization constants are as defined in eqn. (4). The calculations in every case involved the successive computation of progressively more precise values of pK_1 and pK_2 until the mean deviation of all pK_1 and pK_2 values approached $\pm 0{\cdot}025$ pK unit or less. A typical titration is shown in Fig. 3.

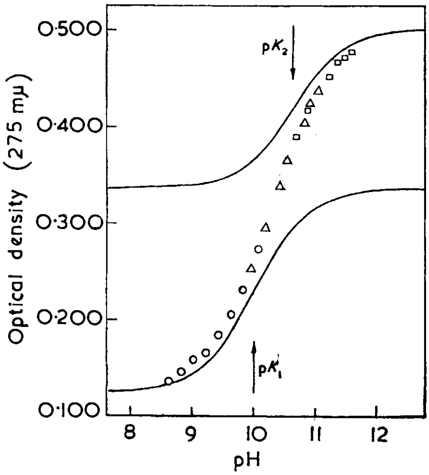

FIG. 3. Titration curve of $2{\cdot}2 \times 10^{-5}$M-pyridine-2,6-dialdoxime at 25° and $I = 0{\cdot}050$M. Experimental data: ○ with borate buffers. △ with glycine buffers. □ with phosphate buffers. Optical densities at 275 mμ: dioxime PH_2 at pH 8, $d_0 = 0{\cdot}125$; di-anion P^{2-} at pH >12, $d_2 = 0{\cdot}500$; hypothetical mono-anion PH^-, $d_- = 0{\cdot}335$ obtained by numerical analysis of data. Series of successive approximations yield best fit of data in terms of two single ionizations: p$K_1 = 10{\cdot}00 \pm 0{\cdot}025$ ($d_0 = 0{\cdot}125 \longrightarrow d_- = 0{\cdot}335$); p$K_2 = 10{\cdot}63 \pm 0{\cdot}025$ ($d_- = 0{\cdot}335 \longrightarrow d_{2-} = 0{\cdot}500$). The two theoretical single titration curves are shown.

Determination of pK_4 *in Bis*-(*pyridine*-2,6-*dialdoxime*)-*iron*(II) *Complex*.—The iron(II) complex of pyridine-2,6-dialdoxime was formed as follows: a stock ferrous solution between 1·0 and $2{\cdot}5 \times 10^{-3}$M was made from $Fe(NH_4)_2(SO_4)_2,6H_2O$ with twice the equivalent amount of $HClO_4$; an aliquot part of 0·01M-pyridine-2,6-dialdoxime (near the limit of its solubility in water at room temperature) was then added, and the mixture allowed to stand for a few minutes before diluting with buffer to the required pH. The final concentration of iron was $2{\cdot}2 \times 10^{-5}$M and total ligand about $2{\cdot}5 \times 10^{-4}$M. Molar ionic strengths were reckoned on the basis of buffer and salt, contributions from the other ions being neglected.

The fourth oxime ionization constant in the complex was determined spectrophotometrically. About fifteen solutions were made for every run, covering the pH range 5—9. Every solution was divided into two parts. On one part, optical densities were read at 560 mμ against a blank. On the other part, simultaneous measurement of pH was made with the precautions described below. The optical density corresponding to 100% conjugate base, $Fe(P_2)^{2-}$ of eqn. (10), was measured directly at pH 10, but that of the 100% acid $Fe(P_2H)^-$ could not be obtained directly at pH <5 because of the overlap with the third oxime ionization (p$K_3 \sim 5$, eqn. 9). However, the acid end of the titration, could easily be corrected by use of results at pH >6 to obtain an approximate value for pK_4 and consequently for the optical density of the hypothetical conjugate acid $Fe(P_2H)^-$, and then repeating the calculation to get a more precise result. The ionization constant was computed on the basis of eqn. (4), in every case the value representing the average of about ten individual measurements, with mean deviations of ±0·025. Similar runs were made at ionic strengths I = 0·050, 0·018, 0·009, and 0·004M (all at 25°), and at 14·6, 29·8, 25·0, 31·4, and 36·1° (all at I = 0·050M).

Measurement of Optical Density and of pH. Optical density measurements were made, against the appropriate blank on a Unicam S.P. 500 quartz spectrophotometer with a thermostated cell compartment. Measurements of pH were made on a Radiometer PHM4 pH meter with a thermostated cell assembly. Primary standards of pH were used, following the recommendations of the U.S. National Bureau of Standards,[5] and a precision of ±0·005 was achieved. In all experiments temperature was controlled to ±0·05° or better by circulating water from a refrigerated thermostat.

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[5] Bates, " Electrometric pH determinations," Wiley, 1954, ch. 5.