82. *Further Complexes of Ferrous Dimethylglyoxime.*

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Further complexes of ferrous dimethylglyoxime, $Fe(DMG)_2$, have been studied. The stability and absorption spectra of these complexes are compared with the corresponding properties of complexes of ferrous porphyrins. Like the latter, $Fe(DMG)_2$ has a greater affinity for cyanide and carbon monoxide than for ligands such as ammonia and pyridine. The affinity for both aliphatic and aromatic bases is independent of the basic strength of the ligands.

In a search for models with similar physical properties, *e.g.*, absorption spectra and magnetic moments, to those of the iron porphyrin complexes we decided to study the properties of the further complexes of ferrous dimethylglyoxime. A series of such complexes will be briefly discussed here, leaving until later a detailed examination of the individual systems. The ferrous dimethylglyoxime complex itself, $Fe(DMG)_2$, is unstable even in the complete absence of oxygen unless a reducing agent and a base are also present. (The functions of both base and reducing agent can be fulfilled by hydrazine.) In the presence of this combination further complexes of the ferrous dimethylglyoxime with the bases are formed; their formulæ have been established [1,2,3] as $Fe(DMG)_2(Base)_2$. This stoicheiometry has been confirmed in the present work. The relative affinities of different bases for the ferrous dimethylglyoxine unit have been determined also.

The $Fe(DMG)_2$ *Complex with Hydrazine.*—Dimethylglyoxime is not very soluble in water. In order to work with its iron complex in the presence of excess of the reagent

[1] Griffing and Mellon, *Analyt. Chem.*, 1947, **19**, 1017.
[2] Banks and Byrd, *Analyt. Chim. Acta*, 1954, **10**, 129.
[3] Babko and Dubovenko, *J. Gen. Chem., U.S.S.R.*, 1954, **25**, 759.

25% aqueous dioxan was used as solvent. The ionic strength of all solutions in this solvent was kept at 0·3M by addition of appropriate amounts of sodium perchlorate. All measurements were made at 25°. Under these conditions the "practical" acid dissociation constant [4] of dimethylglyoxime is $pK = 12{\cdot}6 \pm 0{\cdot}1$, and that of hydrazine is $8{\cdot}15 \pm 0{\cdot}05$ as determined by pH titration against standardised sodium hydroxide. A comparison of the titration curve of 0·1M-hydrazine sulphate plus 5×10^{-3}M-dimethylglyoxime with the same titration in the presence of 10^{-3}M-ferrous ion showed that four protons are released by the ferrous ion on forming a complex. The reaction can be represented as

$$2N_2H_5^+ + 2DMGH_2 + Fe^{2+} \longrightarrow Fe(DMGH)_2(N_2H_4)_2 + 4H^+$$

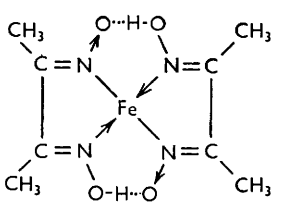
This agrees with the earlier work on the formula of the complex.[1,2,3] In the presence of a reducing agent which is not a base, *e.g.*, sodium formaldehydesulphoxylate, only a transient red colour was seen when the pH was raised rapidly to 7·0 before the brown ferric complex was formed. The transient species is very probably the unstable ferrous dimethylglyoxime complex $Fe(DMG)_2$, which begins to be formed at pH 7·0 and therefore has an overall stability constant, log K_2, of ~15. This value is of the expected order of magnitude relative to those of other transition-metal cations determined by us and by Freiser,[5] namely for Ni^{II}, 21·0; Cu^{II}, 22·5; Zn^{II}, 14·5; and Fe^{II}, 15·0.

The ferrous dimethylglyoxime complex with hydrazine has an intense absorption band, $\varepsilon_{max.} \sim 10^4$, in the visible region, $\lambda_{max.} = 525$ mμ (Table 1). This band is found in certain other ferrous complexes and does not belong to the ligand—it is absent in the other transition-metal cation complexes with dimethylglyoxime. The band has an intensity of $\varepsilon_{max.} = 10^4$ only in completely covalent diamagnetic ferrous complexes.[6] It will be assumed in what follows that the further complexes of ferrous dimethylglyoxime with bases (which have such strong absorption bands) are diamagnetic.

It is reasonable to suppose that the ferrous complex consists of a planar group of the cation and two dimethylglyoxime molecules, as is found in the nickel and cupric complexes.[7] This configuration is stabilised by hydrogen bonds (see inset). The second-step stability constant exceeds that of the first step in the formation of the cupric complex: this must be due to the hydrogen bonding.

If this structure is correct the two molecules of base must be added above and below the plane of the complex, as in the structure previously given.[8] Thus the complexes may well be very similar indeed to iron porphyrin proteins.

Evidence supporting the suggested structure has arisen through the study of the ferric dimethylglyoxime complexes. When alkali was added to ferric ions and dimethylglyoxime in acid solution a yellow complex was completely formed by pH 3·5 with the displacement of three protons. This complex was not formed when ferric dimethylglyoxime was prepared by the addition of alkali to ferrous ion and dimethylglyoxime in the presence of a reducing agent such as sodium formaldehydesulphoxylate at pH 6—7. The latter complex was fully formed, as measured by its absorption spectrum, when the ratio of ligand to iron was equal to or greater than 2 : 1 but the former complex was not. Moreover, the brown complex could not be obtained by starting from the ferric state. Both ferric complexes were formed with the displacement of three protons. The first is considered to be $Fe(DMG)_3$ and the second $Fe(DMG)_2(OH)(H_2O)$. It is difficult to reach any conclusion but that the second complex is formed directly from planar $Fe^{II}(DMG)_2$ which was seen as a transient red species at pH 6—7 in the preparation of the brown ferric compound.



[4] Irving and Rossotti, *J.*, 1954, 2910.
[5] Freiser, *Analyst*, 1952, **77**, 830.
[6] Williams, *J.*, 1955, 137.
[7] Godycki and Rundle, *Acta Cryst.*, 1953, **6**, 487.
[8] Welcher, "Organic Analytical Reagents," Vol. III, Van Nostrand Co. Inc., New York, 1947, p. 210.

Exchange of Bases.—The hydrazine molecules which are bound to the $Fe(DMG)_2$ complex can be replaced by other bases. By carrying out competition exeriments between hydrazine and these bases in the solvent system described, and using the changes in absorption spectrum to follow the reactions, equilibrium constants K (Table 1) were obtained, where

$$K = [Fe(DMG)_2(N_2H_4)(base)][N_2H_4]/\{[Fe(DMG)_2(N_2H_4)_2][base]\}$$

Typical experimental data are given in Table 2. The constants refer to the replacement of only one hydrazine molecule of the two present in $Fe(DMG)_2(N_2H_4)_2$. This was established by the constancy of K at different hydrazine and base concentrations (see experimental data). The replacement of the second hydrazine molecule will be described later.

The affinity of a base for $Fe^{II}(DMG)_2$ is not related to its pK value. Usually, some relationship between relative stability (equilibrium) constants and pK values is found.

TABLE 1. *The equilibrium constants,* K, *and absorption spectra of the ferrous dimethylglyoxime complexes.*

Ligand	K	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	Ligand	K	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
$(N_2H_4)_2$	—	525	9,200	(N_2H_4)–CO ...	~1000	390	>5,000
(N_2H_4)Py	1·40 ± 0·10	510	8,900	(N_2H_4)–NH_3	—	527·5	9,100
		385	5,600	(N_2H_4)–Pr·NH_2	1·0 ± 0·5	535	9,050
$(N_2H_4)_3$–BrPy	1·24 ± 0·05	510	9,000	$(Py)_2$	—	512	9,200
	—	385	5,700			385	6,300
$(N_2H_4)_4$–CNPy	1·36 ± 0·14	505	13,500	$(4\text{-CNPy})_2$ ...	—	495	9,500
		475 *	—			475 *	—
$(N_2H_4)_3$–CNPy	1·28 ± 0·05	508	7,200	$(Histidine)_2$ ...	—	525	4,500
		460	7,000	$(CN)_2$	—	375	6,000
(N_2H_4)–CN ...	820 ± 200	495	9,000	(Py)(CN)	—	490 †	9,000

Py = Pyridine, Pr = Propyl, CNPy = cyanopyridine, BrPy = bromopyridine.
* = Inflexion. † No second band.

In fact, here, pyridines have a slightly greater affinity than aliphatic bases despite pyridines' being weaker bases. Amongst pyridines there is surprisingly little selectivity. On the other hand, cyanide and carbon monoxide have a much higher affinity for the iron complex than any other ligand. Ferrous porphyrins also form very stable complexes with cyanide and carbon monoxide, which accounts for the very toxic properties of these molecules. In the treatment of the latter complexes it has been suggested that their stability arises from the donation of the d_ϵ electrons of the iron atom into the empty π states of the ligand. This type of double bond also stabilises ferrous dipyridyl and *o*-phenanthroline complexes or indeed any other complex between iron(II) and a conjugated base such as dimethylglyoxime. This interpretation being accepted, the equal stability of the pyridine and aliphatic base complexes can be explained as follows.

In the 3*d* states of diamagnetic ferrous ion there are six paired electrons which go into the three d_ϵ states. The remaining two d_γ states are empty and can be used as σ-electron acceptors. The strength of a bond from a base to the ferrous ion depends upon (1) its σ-donor strength, ammonia > pyridine, and (2) its π-acceptor strength, pyridine > ammonia. The two orders are opposed and explain the equal binding of aliphatic and aromatic bases. This series of stabilities illustrates, too, the increasing importance of d_ϵ-donor bonding as the charge on a cation is reduced, for ammonia binds singly and, to a greater degree, doubly charged cations much more strongly than pyridine. Amongst pyridines there is little difference in affinity for the ferrous complex. On the other hand, there are very great differences in absorption spectra between the different pyridine complexes which will now be described.

The Absorption Spectra of the $Fe(DMG)_2$ *Complexes.*—Table 1 lists the position of the absorption maxima in the different complexes of ferrous dimethylglyoxime. Amongst aliphatic bases the maximum moves to longer wavelengths as the strength of the base

increases. This order is the same as that observed by Griffing and Mellon [1] and by Sone [9] in similar series of complexes. These authors also observed that pyridine moves the absorption band to shorter wavelengths (Table 1). In the several pyridines used in the present study, the greater the π-electron-withdrawing character of the substituent the greater the shift of $\lambda_{max.}$ to shorter wavelengths. As further examples of this effect of π-electron-withdrawing groups the pyridine complexes can be compared with carbon monoxide and cyanide complexes. The latter move the absorption band to very short wavelengths. The following interpretation of the spectra is offered. In the absence of π-acceptor groups other than dimethylglyoxime, the d_ϵ electrons of ferrous ion form strong π-donor bonds from the cation to the dimethylglyoxime. The transition to the excited state involves the transfer of one of the d_ϵ electrons to a higher electron state of the ferrous ion, possibly $4p$, which interacts more strongly with the ligand. The electron is partially transferred to the ligand. This kind of electron transition is common to a large number of ferrous complexes.[6] When the $Fe(DMG)_2$ group is combined with unsaturated bases they stabilise the ground rather than the excited state, for such compounds also act as acceptors of the d_ϵ electrons which are responsible for the absorption. Thereby they reduce the ease of electron transfer to the dimethylglyoxime and the band moves to shorter wavelengths. On the other hand, π-electron-donor bases such as substituted amines shift the band to long wavelengths as they lower the relative stability of the ground state, repelling the d_ϵ electrons and facilitating charge transfer.

In the pyridine complexes, apart from the band at ~500 mμ, there is a band between 360 and 500 mμ, whose exact position depends upon the substituent in the pyridine. This band is at longer wavelengths for 4-cyanopyridine than in pyridine, 3-bromopyridine, or 3-cyanopyridine complexes. The explanation we offer for its appearance is that it is a charge-transfer band of a d_ϵ electron to the empty π-states of the pyridines. It moves to longer wavelengths in the 4-cyano-compound than in the other ligand complexes because of the greater electron-acceptor properties of this ligand.

Returning to the stability of the different pyridine complexes of ferrous dimethylglyoxime, we can interpret their almost equal stabilities consistently with our earlier remarks. The stability of the complex depends on the donor and acceptor character of the pyridines. The 4-cyanopyridine is the strongest π-electron acceptor but the weakest σ donor. Pyridine is a stronger σ-electron donor but a weaker π acceptor than the cyano-compounds. Similar stability of the different pyridine complexes arises through a balancing of the two parts of the bonding. It is surprising, however, that the two parts should so exactly compensate one another. The bonding through the d_ϵ-donor character of the ferrous ion has an important consequence in biological systems. If two kinds of ligand compete for the fifth and sixth positions of the co-ordination sphere of a cation in a complex, such as that of ferrous dimethylglyoxime, at a fixed pH then, because of the equal ability of the ligands to co-ordinate the ferrous ion, the weaker base, *i.e.*, the unsaturated compound, will be preferred. Thus in a biological system it is not surprising that ferrous porphyrins are further co-ordinated to glyoxalines and not to aliphatic amino-groups, for the glyoxalines have dissociation constants close to 7·0 whereas the amino-group constant is close to 9·0. The pH in a biological system is approximately 7·3.

Finally, we comment upon the rate at which the different complexes are formed. The reaction

$$Fe(DMG)_2(N_2H_4)_2 + \text{pyridine (py)} \longrightarrow Fe(DMG)_2(N_2H_4)(py) + N_2H_4 \quad . \; . \; . \quad (1)$$

is not instantaneous, implying once again that the ferrous complexes are inner orbital, *i.e.*, covalent and diamagnetic. The time for 50% conversion of one form into another is some 5 min. Now $Fe(DMG)_2(pyridine)_2$ has also been prepared and its properties examined. All its replacement reactions are exceedingly slow, so that oxidation occurs before exchange. The rate of reaction has been reduced by the d_ϵ–π double bonding. This is shown, too, in reaction (2) which is also very slow. If other bases are studied in place of

[9] Sone, *Bull. Chem. Soc. Japan*, 1952, **25**, 1.

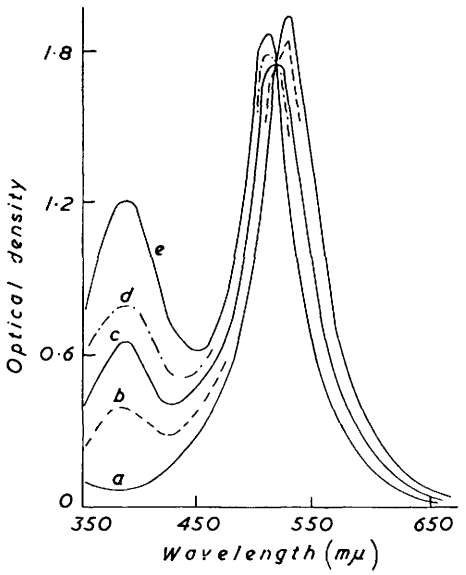
pyridine in reaction (1), the exchange of bases occurs at about the same rate, but if the base is unsaturated then the complex formed, *e.g.*, $Fe(DMG)_2(N_2H_4)CO$, reacts only slowly

$$Fe(DMG)_2(N_2H_4)\,(py) + py \longrightarrow Fe(DMG)_2(py)_2 + N_2H_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

with further base, *e.g.*, CO, and the reaction is only slowly reversible. These systems are being studied further as the parallel reactions of iron porphyrins are of great importance in biological systems.

Experimental

Materials.—Dioxan was purified by Weissberger and Proskauer's method.[10] " AnalaR " hydrated ferrous sulphate, potassium cyanide, and hydrazine hydrogen sulphate were used without further purification. Dimethylglyoxime was twice recrystallised from aqueous alcohol



Absorption spectra of ferrous dimethylglyoxime in the presence of 0·1M-*hydrazine sulphate at* pH 8·09 *together with different molarities of* 3-*bromopyridine*: (*a*) 0·00M, (*b*) 0·015M, (*c*) 0·036M, (*d*) 0·067M, (*e*) 0·95M; (*e*) *is taken to be the spectrum of the pure pyridine form.*

and then had the accepted m. p. 234°. It is often contaminated with small quantities of hydroxylamine. " AnalaR " pyridine was redistilled before use. Pure samples of substituted pyridines were given by Dr. A. R. Katritsky, whom we thank. Cylinder carbon monoxide was used without further purification.

Titrations.—All titrations were made at 25° in a thermostat, a Cambridge pH meter [4] being used. The calculation of the number of protons displaced in a given reaction was made from the difference in amounts of alkali required to reach a given pH in the presence and the absence of the cation. Suitable simple corrections were made for the dissociation of the ligand groups. Stability constants were obtained by the Bjerrum–Calvin method.[4] Acid dissociation constants are " practical " constants.[4]

Spectra.—All measurements were made in matched cells on a Unicam spectrophotometer S.P. 600. A typical set of observations is given in the Figure. Table 2 illustrates the accuracy of the calculation of equilibrium constants.

Table 2. *Equilibrium constant for the formation of the* 3-*bromopyridine complex.*

Concn. of 3-bromopyridine (mole/l.)	0·015	0·026	0·036	0·046	0·067
Optical density at 385 mμ	0·396	0·516	0·615	0·658	0·751
% of complex in pyridine form	29·9	40·9	50·1	53·9	62·4
Equilibrium constant	1·30	1·24	1·31	1·19	1·17

In this series of experiments the pH was buffered by the hydrazine (0·100M) at pH 8·09. The free hydrazine calculated from the dissociation constant given earlier was therefore

[10] Weissberger and Proskauer, " Organic Solvents," Oxford Univ. Press, 1935, p. 139.

0·0453M. All measurements were made in the solvent and salt background given on p. 463 and at 25°. Total ferrous ion (added as sulphate) was 10^{-3}M. Calculation of an equilibrium constant on the basis of the replacement of two hydrazine molecules by pyridine gives values ranging from 10·0 to 0·5. Similar results, not quoted, were obtained in all the other experiments. Saturated solutions of carbon monoxide were used to estimate the affinity of CO for the complex.

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