Notes

Electronic Effects of Co-ordinated Methoxide on the Rates of Entry of Imidazole Derivatives into [Dimethyl-3,7,12,17-tetramethyl-8,13-divinylporphyrin-2,18-dipropanoato(2−)]-(methanol)methoxocobalt(III) in Methanol†

Smiljko Ašperger,* Gordana Vrban, Biserka Cetina-Čižmek and Mato Orhanović
Department of Chemistry, Faculty of Pharmacy and Biochemistry, University of Zagreb, and Rudjer Bošković Institute, Zagreb, Croatia, Yugoslavia

The rates of replacement of MeOH by imidazole derivatives in [Co^{III}L(MeO)(MeOH)] (L = dimethyl 3,7,12,17-tetramethyl-8,13-divinylporphyrin-2,18-dipropanoate) were measured. The most basic derivative enters most slowly, as was previously observed for pyridine derivatives. However the rates of entry of imidazoles are about 50 times smaller than those of pyridines. The energies and entropies of activation of the overall reactions with pyridine (py) and imidazole (Him) are E_a/kJ mol^{-1} = 40.0 ± 3.1 (py) and 76.4 ± 3.8 (Him), and $\Delta S^{\ddagger}$/J K^{-1} mol^{-1} = −105 ± 10 (py), and −13.2 ± 12.8 (Him). It is inferred that the transition state in the reaction with py is stabilised by σ and partial metal-to-ligand π bonding, while that in the reaction with imidazole involves σ bonding only.

In a previous paper[1] we reported that the best electron donors for promoting oxidation of the cobalt in cobalt(II) protoporphyrin IX dimethyl ester {[dimethyl 3,7,12,17-tetramethyl-8,13-divinylporphyrin-2,18-dipropanoato(2−)] cobalt(II)}, [Co^{II}L], in methanol are co-ordinated alkoxides (methoxide < isopropoxide < *sec*-butoxide). We noticed earlier[2,3] that the methoxide group in the [Co^{III}L(MeO)] intermediate strongly increases the electron density in the *trans* axial position which favoured the entry of the least basic amine ligand (not the most basic, as usually observed[4]). For example, in the replacement of MeOH in [Co^{III}L(MeO)(MeOH)] by 4CN-py, py and 4Me-py (py = pyridine) the competition ratio k_2/k_{-1} is 6800, 3700 and 2800, respectively, where k_{-1} is the rate of re-entry of MeOH and k_2 of the entry of the pyridine derivative.[2] We have now measured the rates of replacements of MeOH in the methoxomethanol complex by imidazole derivatives in methanol as solvent. The most basic derivative enters at the smallest rate, as was the case with pyridine derivatives, but the rates are much smaller than for pyridine derivatives. All the pyridine derivatives exhibited a limiting rate {D mechanism,[3] [S_N1 (lim)]}, while with imidazole derivatives, L′, no limiting rates could be observed up to [L′] = 10^{-1} mol dm^{-3}, at which concentration the solubility limit is attained. The observed rate constant ($k_{obs.}$) is equal to k_1k_2[L′]/(k_{-1}[MeOH] + k_2[L′]), where k_1 and k_{-1} are the rate constants of dissociation and association of ligand methanol, respectively, and k_2 is the rate constant of the reaction of the intermediate [Co^{III}L(MeO)] with L′.

Imidazole complexes of transition metals are of particular biological interest because the imidazole side chain of histidine often binds to metal centres in metalloproteins.

† Taken from the M.Sc. thesis by G. Vrban, to be submitted to the Faculty of Pharmacy and Biochemistry, University of Zagreb, and reported in part at the 28th International Conference on Co-ordination Chemistry, Gera, August 1990.

Results

The dark purple crystals of [Co^{III}L(Cl)] easily dissolve in methanol. Immediately on dissolution chloride is released and the complex equilibrates[2] as shown by equation (1). If no acid

$$\underset{\mathbf{1}}{[Co^{III}L(MeOH)_2]^+} \underset{H^+}{\rightleftharpoons} \underset{\mathbf{2}}{[Co^{III}L(MeO)(MeOH)]} \overset{MeO^-}{\rightleftharpoons} \underset{\mathbf{3}}{[Co^{III}L(MeO)_2]^-} \quad (1)$$

or alkali is added to the methanol the species **2** predominates.[2] The spectrum of this species is identical with that of the reaction product obtained from [Co^{II}L] in methanol in the presence of O_2; methanolic solutions of the methoxomethanol complex can be prepared in this way, too.

Kinetics of Reaction of [Co^{III}L(MeO)(MeOH)] *with Imidazole Derivatives in Methanol.*—The imidazole derivatives (L′) used were benzimidazole (Hbzim) (pK_a = 5.53),[5] imidazole (Him) (pK_a = 6.95),[6] 1-methylimidazole (1-mim) (pK_a ≈ 7.0,[7] 7.06‡), 2-mim (pK_a = 7.85,[7] 7.54‡) and 2-ethylimidazole (2-eim) (pK_a = 8.00,[7] 7.87‡). All pK_a values are for aqueous solutions. The rates were measured by the stopped-flow technique. The solutions of the complex were always freshly prepared. The dimerisation of the complex did not interfere since its rate is *ca.* 1000 times smaller than the rates of replacement. The Soret peak of the methoxomethanol complex is at 415 nm. (ε *ca.* 6.5 × 10^4 dm^3 mol^{-1} cm^{-1} in methanol at 25 °C). The kinetics was measured at 417 nm where the differences in absorptions were the largest. The replacements of the MeOH and MeO^- ligands proceed consecutively in that order. The difference in rates of the two replacements is large enough to permit independent determination of the first step. On increasing the concentration of the entering ligand the basicity of the medium increases which might cause some conversion of the

‡ Determined by pH measurements in this Laboratory.

Table 1 Rates of replacement of MeOH (k_{obs}/s^{-1}) in [Co^{III}L(MeO)(MeOH)] with L′ in methanol[a]

10^4 [L′]/ mol dm^{-3}	Entering ligand (L′)				
	Hbzim	Him	1-mim	2-mim	2-eim
1	0.133[b]	0.133	0.082		0.0355
	0.006[c]	0.006	0.003		0.0007
	4[d]	5	4		4
10	0.478	0.21	0.151		0.066
	0.006	0.008	0.006		0.002
	4	4	3		4
20	0.835	0.29	0.23		0.10
	0.025	0.01	0.01		0.009
	4	3	4		3
40	1.58	0.46	0.39		0.179
	0.04	0.01	0.01		0.006
	5	4	5		4
50	2.21	0.55	0.46		0.216
	0.17	0.02	0.01		0.008
	3	4	4		5
100	3.65	0.99	0.85		0.42
	0.05	0.008	0.03		0.02
	4	4	3		4
500	17.3	7.27	6.36	5.75	3.0
	1.1	0.19	0.39	0.20	0.09
	5	5	4	3	4
600	21.7	9.7	8.2	7.6	4.3
	1.01	0.2	0.4	0.3	0.1
	5	5	3	4	5
800	29.3	12.4	11.8	10.6	6.5
	1.0	1.0	1.0	1.0	0.2
	4	4	4	5	3
1000	38.5	17.0	16.1	15.4	10.5
	1.0	1.0	1.0	1.0	1.0
	5	5	5	5	4

[a] Concentration of the complex = 5×10^{-6} mol dm^{-3} (the solvent contained about 5% v/v benzene); kinetics followed spectrophotometrically (417 nm) by the stopped-flow technique (25 ± 0.05 °C). [b] Mean first-order rate constant. [c] Standard error of the mean. [d] Number of kinetic runs.

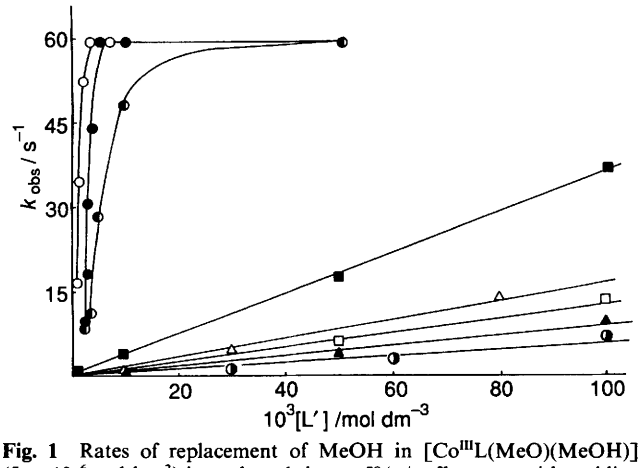

Fig. 1 Rates of replacement of MeOH in [Co^{III}L(MeO)(MeOH)] (5×10^{-6} mol dm^{-3}), in methanol plus ≈ 5% v/v of benzene, with pyridine and imidazole derivatives at 25 ± 0.05 °C. Symbols: (○), 4CN-py (pK_a = 2.0); (●), py (pK_a = 5.2); (◐), 4Me-py (pK_a = 6.0); (■), Hbzim; (△), Him; (□), 1-mim; (▲), 2-mim; (◑), 2-eim (pK_a values are for aqueous solutions)

methoxomethanol into the dimethoxo complex. However, it appears that the small variations in the concentration of the methoxomethanol complex involved are of minor kinetic importance: when we carried out the replacements of MeOH by pyridine in [Co^{III}L(MeO)(MeOH)] in buffered solutions the kinetic results were practically the same as in unbuffered ones.[2] With imidazole as entering ligand L′ ([L′] = 10^{-3}, [complex] = 5×10^{-6} mol dm^{-3}) k_{obs} = 0.20 s^{-1}; in buffered solution, when the ratio [Him]/[H_2im$^+$] was 2:1 (pH 7.25), k_{obs} was 0.21 s^{-1}. The difference in rate is too small to affect the arguments put forward in this paper. The kinetic results are given in Table 1 and in Fig. 1. The previous results[2] obtained with pyridine derivatives, also varying in basicity, are also shown in Fig. 1. We can see that pyridines and imidazoles give rise to two groups of curves which differ considerably in rates. Within a group the rates depend on the basicity of L′: the higher the basicity the smaller is the rate. In addition, while the pyridines exhibit limiting rates (57.8 s^{-1}, 25 °C) at relatively low entering ligand concentration (0.01 mol dm^{-3}), the imidazoles don't, even at 10-fold larger concentration.

Table 2 Rates of replacement of MeOH (k_{obs}/s^{-1}) in [Co^{III}L(MeO)(MeOH)] with L′ in methanol,[a] and the values of the observed (composite) energies and entropies of activation

	Entering ligand (L′)	
T/°C	py	Him
14.00	2.36[b]	0.032
	0.19[c]	0.002
	3[d]	4
20.00	5.0	0.104
	0.5	0.0035
	2	3
25.00	6.41	0.163
	0.49	0.007
	6	3
30.00	7.92	0.247
	0.41	0.016
	5	3
35.00	8.97	0.398
	0.44	0.034
	3	3
41.00	11.2	0.56
	0.7	0.06
	3	3
$E_{a(obs)}$/kJ mol^{-1}	40.0 ± 3.1	76.4 ± 3.8
$\Delta S^{\ddagger}_{obs}$/J K^{-1} mol^{-1}	−105 ± 10	−13.2 ± 12.8

[a] Concentration of the complex is 5×10^{-6} mol dm^{-3} (the solvent contained about 5% v/v benzene); concentrations of entering ligands are 2×10^{-3} mol dm^{-3}. [b] Mean first-order rate constant = k_1k_2[L′]/k_{-1}[MeOH]. [c] Standard error of the mean. [d] Number of kinetic runs.

Table 2 contains the rates of replacements of MeOH in [Co^{III}L(MeO)(MeOH)] with pyridine and imidazole entering ligands, carried out under exactly the same reaction conditions. The energies and enthalpies of activation ($E_{a(obs)}$ and $\Delta H^{\ddagger}_{obs}$) and entropies of activation ($\Delta S^{\ddagger}_{obs}$) for the overall reactions were determined in two ways: from plots of ln k vs. $1/T$ and ln (k/T) *vs.* $1/T$, by the least-squares method, using a computer program. Both plots gave almost exactly the same results. The values for E_a^{obs} and $\Delta S^{\ddagger}_{obs}$ are given in Table 2. Since the concentrations of py and Him are small and equal (2×10^{-3} mol dm^{-3} and $k_{obs} = k_1k_2$[L′]/k_{-1}[MeOH] the equation $k^{py}_{obs}/k^{Him}_{obs} = k^{py}_2/k^{Him}_2$ must hold. Consequently $E^{Him}_{a(obs)} - E^{py}_{a(obs)} = E^{Him}_{a(k_2)} - E^{py}_{a(k_2)} = 36.4 \pm 3.8$ kJ mol^{-1} and $\Delta S^{\ddagger}_{obs(Him)} - \Delta S^{\ddagger}_{obs(py)} = \Delta S^{\ddagger}_{k_2(py)} - \Delta S^{\ddagger}_{k_2(Him)} = 91.8$ J K^{-1} mol^{-1}.

Discussion

As already pointed out, one might expect that the most basic amine ligand will react with the largest rate with the [Co^{III}L(MeO)] intermediate, but just the opposite is the case. It appears that the methoxide in the [Co^{III}L(MeO)] strongly increases the electron density at the *trans*-axial position, which favours the entry of the less basic amine ligand. (*trans*-OH^- is

listed as the best electron donor among 21 ligands;[8] methoxide should be an even better electron-donor than hydroxide, due to the electron-donating effect of the methyl group.) The metal–ligand π bonding is considered to be small in the metal(III) complexes. The 'soft' character of the cobalt porphyrin complex may make π-back bonding a more important effect than might otherwise be the case with a metal(III)–ligand bond.[9] This back bonding should stabilise the transition state, which additionally explains why, among pyridine derivatives, the rate of ligand entry is largest with 4 CN-py. This ligand is the best π-back bonding acceptor of all L′ we investigated. Wright *et al.*[10] have identified an iron-to-pyridine charge-transfer transition in a bis(pyridine)iron(II) haem by resonance-Raman spectroscopy. They observed enhancement of an iron-pyridine stretching mode with excitation within a band at about 490 nm which they assigned to a $d_\pi \longrightarrow \pi^*_{py}$ charge-transfer transition. A similar charge-transfer transition for an imidazoleiron(II) haem would be expected to occur in the UV,[11] since imidazole is a considerably poorer acceptor than pyridine.[12] It should be mentioned that imidazole-to-iron charge-transfer transitions have not been identified for oxyhaemoglobin and oxymyoglobin.[11] Consequently, one should expect that the transition states of [Co^{III}L(MeO)] and imidazole-type reagents are higher in energy than those with pyridine-type reagents. Therefore, relatively slower reactions should be expected with the imidazole-type reagents, as is indeed observed. From the data in Table 2 it can be seen that the reaction with pyridine proceeds with a lower energy activation, and more negative entropy of activation, than the reaction with imidazole. This is in agreement with our assumption that the transition state in the former reaction is stabilised by σ and partial metal-to-ligand π bonding, while in the latter reaction the stabilisation involves σ bonding only.

Experimental

Materials.—Protoporphyrin IX dimethyl ester (H_2L)(Fluka, purum) and cobalt(III) acetate (Merck, AR grade) were used. Chlorocobalt(III) protoporphyrin IX dimethyl ester, [Co^{III}L(Cl)], was prepared as previously described.[2] A very pure product was obtained, as judged from its NMR spectrum and the α/β peak ratio of 1.2:1. It releases its chloride immediately on dissolution in methanol, and equilibrates as in equation (1). The species [Co^{III}L(MeO)MeOH] predominates and the rates of replacements of methanol by amine ligands can be studied. The complex [Co^{II}L] was prepared from cobalt(II) acetate and H_2L according to the literature.[13] It was recrystallised from chloroform–methanol and then from benzene. In methanol (5–10% v/v benzene) it undergoes oxidation (absence of amine ligand), yielding mainly [Co^{III}L(MeO)(MeOH)], at a rate 10^2–10^3 times smaller than that with amine ligands.[2,3] In this case co-ordinated methanol acts as a weak electron donor, promoting electron transfer from cobalt to molecular oxygen. The spectra of [Co^{III}L(MeO)(MeOH)] obtained in this way or from [Co^{III}L(Cl)] are identical.

Pyridine was kept over KOH and freshly distilled before use. All imidazoles were from Sigma. Imidazole, 2-methyl- and 2-ethyl-imidazole were purified by sublimation, dried *in vacuo* and sealed. 1-Methylimidazole was vacuum distilled over potassium hydroxide. Benzimidazole was recrystallised from hot water[14] dried *in vacuo*, and sealed under vacuum.

Spectrophotometry.—Absorption spectra were recorded on a Cary 16 K spectrophotometer.

Kinetics.—A Durum D-110 stopped-flow spectrophotometer was used for kinetic measurements. A Haake cryostat assured the desired temperature. Thermal equilibrium was reached in about half an hour, as shown by temperature measurements of the water in the stopped-flow thermostat. Several kinetic runs were done at each desired temperature. The stock solution of [Co^{II}L] was 10^{-4} mol dm^{-3} in benzene. Reaction solutions were prepared by mixing the stock solution with methanol and a methanolic solutions of the imidazoles. The final complex concentration was 5×10^{-6} mol dm^{-3} (solutions contained 2–5% benzene; variations of the benzene concentration in this range did not affect absorption spectra or kinetics).

Acknowledgements

This work was supported in part by the Joint Yugoslav–American Commission for research (Board of Research of the Republic of Croatia and National Institutes of Health). We are grateful to Professor D. A. Sweigart, Brown University, Providence, Rhode Island, for most useful suggestions and donation of some imidazole ligands. Thanks are also due to Professor A. Bezjak, University of Zagreb, who did the computer calculations.

References

1 D. Pavlović, S. Ašperger, Xh. Ahmeti, B. Cetina-Čižmek, B. Jurišić and Z. Veksli, *Inorg. Chem.*, 1988, **27**, 1515.
2 D. Pavlović, S. Ašperger, Z. Dokuzović, B. Jurišić, Xh. Ahmeti, M. Sertić and I. Murati, *J. Chem. Soc., Dalton Trans.*, 1985, 1095.
3 Z. Dokuzović, D. Pavlović, S. Ašperger and I. Murati, *J. Chem. Soc., Chem. Commun.*, 1984, 1060.
4 Z. Dokuzović, Xh. Ahmeti, D. Pavlović, I. Murati and S. Ašperger, *Inorg. Chem.*, 1982, **21**, 1576.
5 K. Nagai and T. Kitagawa, *Proc. Natl. Acad. Sci. USA*, 1980, **77**, 2033; D. D. Perrin, *J. Chem. Soc.*, 1965, 5590.
6 *Handbook of Chemistry and Physics*, 53rd edn., The Chemical Rubber Co., Cleveland, OH, 1972, pp. D117–118; A. H. M. Kirby and A. Neuberger, *Biochem. J.*, 1938, **32**, 1146.
7 D. D. Perrin, *Dissociation Constants of Organic Bases in Aqueous Solution*, Butterworths, London, 1965.
8 F. Basolo and R. G. Pearson, *Mechanism of Inorganic Reactions*, Wiley, New York, 1967, p. 171.
9 R. F. Pasternack, M. A. Cobb and N. Sutin, *Inorg. Chem.*, 1975, **14**, 866.
10 P. G. Wright, P. Stein, J. M. Burke and T. G. Spiro, *J. Am. Chem. Soc.*, 1979, **101**, 3531.
11 C. M. Jones, C. R. Johnson, S. A. Asher and R. E. Shepherd, *J. Am. Chem. Soc.*, 1985, **107**, 3772.
12 C. R. Johnson and R. E. Shepherd, *Inorg. Chem.*, 1983, **22**, 3506.
13 J. E. Falk, *Porphyrins and Metalloporphyrins*, Elsevier, Amsterdam, 1964, vol. 2, p. 139.
14 A. I. Vogel, *A. Textbook of Practical Organic Chemistry*, Longman, London, 1951, p. 791.

Received 16*th January* 1991; *Paper* 1/00235J