

Complexation between Molybdenum(VI) and Histidine. Least Squares Treatment of Potentiometric Titration Data

ERIK SYLVEST JOHANSEN and OLE JØNS

Danmarks farmaceutiske Højskole, Kemisk Institut AD, Universitetsparken 2, DK-2100 København Ø, Danmark

The molybdenum(VI)–histidine system has been investigated in the pH-range 4 to 7 using potentiometric titrations at constant ionic strength (0.15 M KNO_3) and 25 °C. Using a least squares method and taking into account the polymerization of molybdate the formation of a 1:1 complex is demonstrated and the corresponding stability constant is evaluated.

Complexation between the molybdate ion and chelating ligands has been the subject of many investigations. Several techniques^{1–8,10} have been applied to detect complex formation in aqueous solution. Often data from optical methods such as optical rotation, optical rotatory dispersion, IR- and UV-vis-spectroscopy have been treated by the method of continuous variations in order to determine the stoichiometry of the complexes formed.

Acid-base titration has also been attempted as a method for detecting complex formation and for calculating numerical values of the stability constants. Molybdenum acid represents, however, a system of great complexity since several polymer species are formed in slightly acid solution. Since the formation of a complex between molybdate and histidine takes place in the same pH region it is convenient to use an electronic computer to handle the involved equilibria. The feasibility of doing so has been demonstrated by Pettersson⁸ on the complicated reactions taking place in the molybdate–phosphate system.

Applying a least squares method to a series of titration curves makes a crucial test of the examined equilibria models possible. It allows one to test a

model without making simplifying assumptions, but, admittedly, it cannot discriminate between different models that give satisfactory fit to experiments.

EXPERIMENTAL

Chemicals and analysis. Stock solutions of potassium nitrate (Merck *p.a.*) were prepared using glass-redistilled water. Potassium nitrate (0.150 M) was used as the solvent salt for potassium molybdate and histidine solutions.

Potassium molybdate, AnalaR *a.r.* was analyzed gravimetrically by precipitation of molybdate as oxinate; the result was in agreement with the standardization of stock solution of K_2MoO_4 using a titration with $\text{Pb}(\text{NO}_3)_2$.¹⁴

L-Histidine, FLUKA puriss was used without further purification after drying in a desiccator with silica gel.

The dilute nitric acid was standardized against tris(hydroxymethyl)aminomethane.

Apparatus and procedure. The emf's were measured with a pH-meter (Radiometer pH 64) used as an electrometer. The free hydrogen ion concentration was measured with a glass electrode (Metrohm EA 109) and a calomel reference electrode (Metrohm EA 404). The liquid junction potential of the reference electrode has been tested against an Ag/AgCl electrode, and it proved to be negligible (<0.1 mV) in the pH interval from 11.9 to 2.0. The cell temperature was maintained at 25.00 ± 0.05 °C by means of a water thermostat and the whole experimental set-up was air thermostated at 25 ± 1 °C.

Titrations were performed in a semiautomatic set-up. Motorburettes and digital printout were controlled by electronic timers. Several printouts were produced at every titration point so that the

state of equilibrium could be documented.

A stream of nitrogen was constantly driven through the solutions during measurement. Nitrogen from a cylinder was purified by means of Fieser's solution and finally washed in 0.150 M KNO_3 .

The free hydrogen ion concentration, h , was calculated from the measured emf using eqn. (1), where

$$E = E_0 - 59.157 \log h \quad (1)$$

E_0 is a constant determined from separate titrations of 0.150 M KNO_3 with 0.1500 M HNO_3 . In fitting data from histidine, molybdate or molybdate-histidine mixtures mean values of E_0 recently obtained were applied.

The concentrations of molybdate and histidine were in the range 0.0025–0.0090 mol l^{-1} for solutions in which the metal-to-ligand ion ratios varied between 2:1 and 1:3.3. The pH-range covered in the titrations of molybdate and molybdate-histidine mixtures was ca 4.0–7.0. In titration of histidine the pH-range was extended to 2.4–7.0.

Method. The emf titrations. The present investigation has been carried out as a series of titrations of histidine, molybdate and mixtures of histidine and molybdate. Each such titration was combined with a pair of titrations of KNO_3 solutions with acid in order to determine E_0 . Activity factors were kept as constant as possible by a fixed salt medium background of 0.150 M KNO_3 . The ionic strength of 0.15 was chosen to simulate the conditions in biological fluids. No chloride ions were included in order to avoid possible complicating formation of molybdenum-chloride complexes.

Calculations. All calculations were performed on the UNIVAC 1100/82 at the Regional Computing Center at Copenhagen University. A general mathematical model of an equilibrium system (without condensed phases) based on linear programming¹³ is used for calculations of equilibrium concentrations. A chemical species is characterized by a vector of stoichiometric coefficients and the corresponding logarithmic formation constant. When the mathematical model is supplied with a chosen set of such vectors and the total mass balance for the system, it calculates, besides all concentrations, the difference between the actual and the computed total concentration of hydrogen ions.

In order to supply the algorithm for non-linear least squares minimization with exact differential coefficients, the mathematical equilibrium model is expanded to compute these values by taking into account the implicit nature of equilibrium formulation.

The non-linear least squares minimization algorithm is a modified Gauss-Newton method with

good convergence properties. Modifications also ensure that the formation constants always are positive numbers.

In the case of very poor initial guesses concerning the unknown formation constants an alternative minimization method can be switched into the algorithm. This method, which has a much greater capture area, is implemented from the proposal of Davidon.¹² The algorithm cannot find sharp values of formation constants, so after a predetermined number of iterations control is transferred to the Gauss-Newton method. This facility has been of great value in actual model testing. Standard deviations reported in Table 1 are computed from diagonal elements of the covariance matrix.

RESULTS AND DISCUSSIONS

In order to test the formation of ternary complexes as carefully as possible, the binary complex species were determined in separate titrations. The formation constants so obtained were included as fixed parameters in the combined titrations.

For histidine and for molybdate the logarithmic formation constants found are shown in Table 1 together with the estimated standard deviations and the number of titrations pooled.

The first protonation step for histidine cannot be estimated with any accuracy from titrations in the pH-range 2.4–7.0. Chackravorty and Cotton¹⁵ found $\log \beta_1 = 9.17$ in 0.2 M KNO_3 and when this value is used the next two protonation steps can easily be determined. However, it turns out that $\log \beta_1 = 8.87$ gives a slightly better description of the titrations so this acidity constant was used throughout. The discrepancy is of no concern since ternary complexes exist in acidic solution only. The standard deviation for the second stability constant is extraordinary low, but the same value is found when using 9.17 for the first step.

For molybdate the same set of complex species as reported by Sillén and Sasaki¹¹ were used and it was found that a model comprising the species HMoO_4^- , $\text{Mo}_7\text{O}_{24}^{6-}$, $\text{HMo}_7\text{O}_{24}^{5-}$ and $\text{H}_2\text{Mo}_7\text{O}_{24}^{4-}$ was adequate in describing the molybdate titrations at the investigated concentrations, Fig. 1.

When mixtures of molybdate and histidine are titrated, one cannot account for the titration curves merely by superposition of the two protolytic systems. Some examples of the differences obtained are shown in Fig. 2.

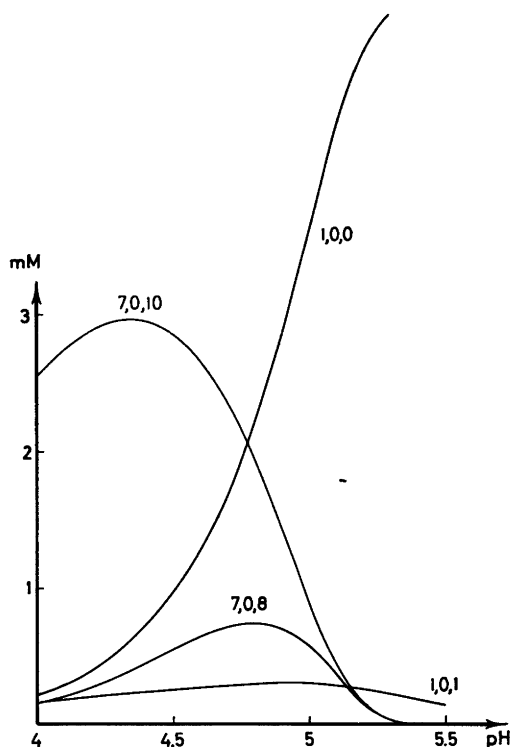


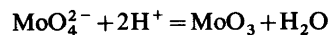
Fig. 1. Concentrations of the various molybdate species for one of the molybdate titrations. Stability constants used are given in Table 1. Total molybdate = 5.5 mM.

Spence and Lee⁴ reported a 1:1 complex inferred from a continuous variations treatment of optical rotation data at pH = 6.00. At lower pH-values the maximum was found to be shifted to a lower value suggesting a complex with a higher ratio of histidine to molybdenum but, because of the limitations of the method, they drew no conclusions concerning the structure of the complex at this lower pH.

Since polymerization of molybdate takes place in the pH region between 4 and 5 there can be doubt that a new complex is formed. Butcher *et al.*⁹ synthesized $\text{Na}[\text{MoO}_3(\text{His})] \cdot \text{H}_2\text{O}$ among other molybdenum chelate complexes. IR-spectrum of this compound that was crystallized at pH = 6 shows the histidinate ion as a tridentate ligand coordinated to a *cis*-trioxo molybdenum core. A *cis*-dioxo molybdenum core was found with tetradentate ligands and in the case of glycine with two bidentate ligands.

If histidine at lower pH values has one of its ligating sites occupied by a hydrogen ion, it might be expected that a complex with two histidine molecules per molybdate could be formed.

The formation of a *cis*-trioxo molybdenum(VI) core requires two hydrogen ions:



whereas a *cis*-dioxo molybdenum(VI) species requires four:

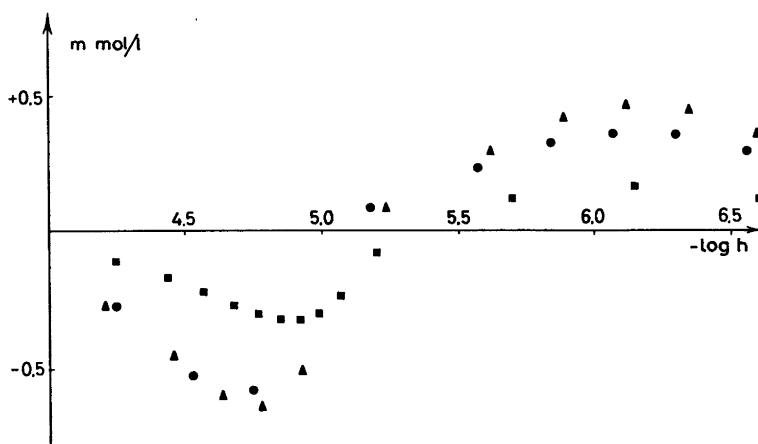
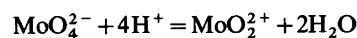


Fig. 2. Differences between calculated (assuming no complex formation) and actual curves for three different molybdenum/histidine ratios. Molybdate, mM/histidine, mM: ■, 4.9/2.4; ●, 2.8/9.1; ▲, 3.8/7.5.

Table 1. Stability constants ($\log \beta_{p,q,r}$) of complex species $M_pA_qH_r$ ($M = MoO_4^{2-}$, $A = \text{histidinate}$, $H = \text{proton}$) in 0.150 KNO_3 at 25 °C. V_{\min} = weighted error squares sum.

	Species			Number of titrations points/ Number of titrations	$\log \beta_{p,q,r}$ $\pm 3\sigma$	V_{\min}
	p	q	r			
1-Histidine	0	1	1	81/5	8.87	35
	0	1	2		14.90 ± 0.002	
	0	1	3		16.61 ± 0.02	
Molybdate	1	0	1	82/7	3.90 ± 0.05	122
	7	0	8		53.04 ± 0.07	
	7	0	9		58.25 ± 0.04	
	7	0	10		62.22 ± 0.11	
No ternary complex						15459
Molybdate-histidine with fixed primary parameters	1	1	2	107/9	16.76 ± 0.02	259
Same titrations with free parameters for molybdate. (i.e. fitting including all molybdate species)	1	1	2		16.79 ± 0.02	104
	1	0	1		3.96 ± 0.07	
	7	0	8		53.15 ± 0.23	
	7	0	9		58.34 ± 0.08	
	7	0	10		62.30 ± 0.14	

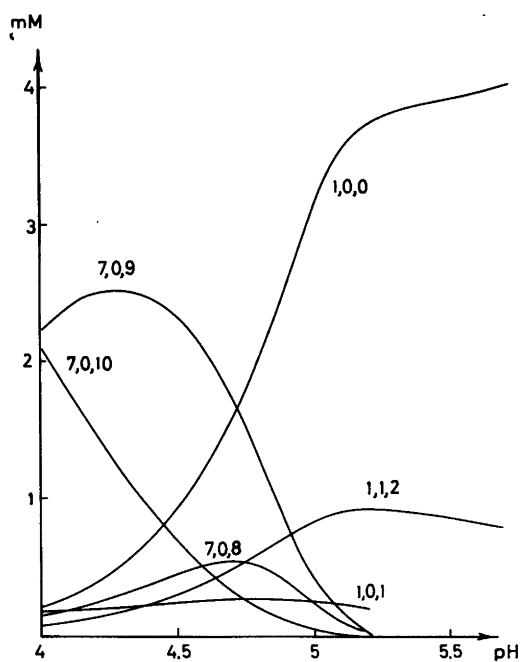
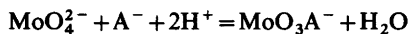


Fig. 3. Concentrations of molybdate species and the ternary complex $[MoO_3His]^-$. Stability constants used are given in Table 1. Total molybdate = 4.9 mM and total histidinate = 4.8 mM.

The 1:1 complex with tridentate histidine thus has Mo:His:Proton equal to 1:1:2



The 1:2 complex with bidentate histidine with totally two ligating sites masked by protons has 1:2:6 stoichiometry. In our calculations on the titrations of mixtures of histidine and molybdate using fixed parameters of molybdate and histidine, a series of complexes, singly or combined, have been tested by the least squares method. Only the 1:1:2 species discussed above gives a satisfactory fit to the experiments ($\log \beta_{1,1,2} = 16.76$).

The fit is slightly more satisfying when a model combining the 1:1:2 and the 1:2:6 species is tested, but, since the first complex gives an adequate description of experiments well within the estimated error, there seems to be no justification for including the latter species in the model. The computed distribution of the ternary complex and the other molybdate species is shown in Fig. 3.

The model 1:2:6 alone cannot describe the experimental data. This result with only complex species of molybdate and histidine 1:1:2 was verified using calculations of the same titrations, but now allowing the least squares program to fit the data in

a five parameter adjustment. Table 1 shows the agreement with separately determined stability constants and corresponding standard deviations.

REFERENCES

1. Brown, D. H. and MacPherson, J. J. *Inorg. Nucl. Chem.* 34 (1972) 1705.
2. Kula, R. J. *Anal. Chem.* 39 (1967) 1171.
3. Kula, R. J. *Anal. Chem.* 38 (1966) 1382.
4. Spence, J. T. and Lee, J. Y. *Inorg. Chem.* 4 (1965) 385.
5. Spence, J. T. and Chang, H. H. Y. *Inorg. Chem.* 2 (1963) 319.
6. Spence, J. T. and Tocatlian, J. J. *Am. Chem. Soc.* 84 (1961) 816.
7. Rabenstein, D. L., Greenberg, M. S. and Saetre, R. *Inorg. Chem.* 16 (1977) 1241.
8. Pettersson, L. *Acta Chem. Scand.* 25 (1971) 1959.
9. Butcher, R. J., Powell, H. K. J., Wilkins, C. J. and Young, S. H. *J. Chem. Soc. Dalton Trans.* (1976) 356.
10. Zare, K., Lagrange, P. and Lagrange, J. J. *Chem. Soc. Dalton Trans.* (1979) 1372.
11. Sillén, L. G. and Sasaki, Y. *Acta Chem. Scand.* 18 (1964) 1014.
12. Chesick, J. P. and Davidon, W. C. *Acta Crystallogr. A* 32 (1976) 120.
13. Johansen, E. S. *Acta Chem. Scand.* 21 (1967) 2273.
14. Püschel, R., Lassner, E. and Scharf, R. Z. *Anal. Chem.* 163 (1957) 104.
15. Chakravorty, A. and Cotton, F. A. *J. Phys. Chem.* 67 (1963) 2878.

Received October 6, 1980.