The authors thank Prof. A. K. N. Reddy, Indian Institute of Science, Banga'ore 560 012, for the IR spectra and Prof. G. K. N. Reddy for helpful discussions. One of the authors (D.S.M.) gratefully acknowledges the special research grant given by the University of Mysore.

1. Gaffre, A., In *Volumetric Analysis*, Vol. III, Ed. I. M. Kolthoff and R. Belcher, p. 386, Interscience, New York, 1957.
2. Pijck, J., Campe, A and Claeys, A., *Bull. Soc. Chim. Belges*, 1964, **73**, 898.
3. Suchomelova, L. and Zyka, J., *J. Electroanal. Chem.*, 1963, **5**, 57.
4. Mahadevappa, D. S. and Murthy, A. S. A., *Talanta*, 1970, **17**, 431.
5. — and —, *Curr. Sci.*, 1972, **41**, 100.
6. —, and Gowda, B. T., *Ibid.*, 1975, **44**, 306.
7. Morris, J. C., Salazar, J. R. and Wineman, M. A., *J. Amer. Chem. Soc.*, 1948, **70**, 2036.
8. Jacob, T. J. and Nair, C. G. R., *Talanta*, 1972, **19**, 347.
9. Jones, M. M., *Elementary Co-ordination Chemistry*, Prentice Hall, N.J., 1964, p. 254.
10. Chandrasekharan, M., Udupa, M. R. and Aravamudan, G., *Inorg. Chimica Acta*, 1973, **7**, 88.
11. Mahadevappa, D. S. and Murthy, A. S. A., *Australian J. Chem.*, 1972, **25**, 1565.
12. Suzuki, I., *Bull. Chem. Soc.*, Japan, 1962, **35**, 1286.
13. Higuchi, T., Ikeda, K. and Hussain, A., *J. Chem. Soc.*, B, 1967, p. 546.
14. Mahadevappa, D. S. and Gowda, B. T., *Talanta* (accepted for Publication).
15. Rao, V. R. S. and Murthy, A. R. V., *Curr. Sci.*, 1961, **30**, 176.

STUDY ON EQUILIBRIUM CONSTANTS OF UO_2^{2+} WITH MALONIC ACID AT DIFFERENT IONIC STRENGTHS

D. N. SHELKE AND D. V. JAHAGIRDAR

Department of Chemistry, Marathwada University, Aurangabad (Maharashtra)

ABSTRACT

The dissociation constants of the ligand and log K values of its complexes with uranyl ion have been investigated by Calvin-Bjerrum potentiometric titration technique at 30 ± 0·1° C and at various ionic strengths in aqueous medium. Uranyl forms both 1 : 1 and 1 : 2 complexes with malonic acid in the pH range 3–5. The plots of pK/log K *vs.* $\sqrt{\mu}$ were drawn to understand the exact complexation equlibria of 1 : 1 complex. The formation of 1 : 1 complex by the reaction $UO_2^{2+} + HL^- \rightleftharpoons UO_2L + H^+$ is confirmed. The thermodynamic constants at $\mu \rightarrow 0$ are reported.

INTRODUCTION

URANYL complexes of malonic acid were investigated by some workers[1,2]. Ramamoorthy and Santappa[3] have reported the uranyl complexes of malonic acid at 0·1 M $NaClO_4$. The present paper reports the study of the stability constants of UO_2^{2+} malonic acid system in aqueous medium at various ionic strengths.

EXPERIMENTAL

The details regarding the chemicals, apparatus are given in our earlier paper[4].

Calvin-Bjerrum Titration

The experimental procedure involved the potentiometric titration of carbonate free solution of (i) free $HClO_4$ ($4·40 \times 10^{-3}$ M), (ii) free $HClO_4$ ($4·40 \times 10^{-3}$ M) + malonic acid ($3·02 \times 10^{-3}$ M), (iii) free $HClO_4$ ($4·40 \times 10^{-3}$ M) + malonic acid ($3·02 \times 10^{-3}$ M) + uranyl ion ($4·32 \times 10^{-4}$ M) against sodium hydroxide (0·18 N) added from a microburette.

The ionic strength of the solution was maintained by the addition of appropriate amount of 1 M sodium perchlorate solution. The exact ionic strength of the solution was calculated by taking $\mu = \frac{1}{2} \Sigma c_i z_i^2$ where c_i and z_i are the concentration and valency respectively of i-th ion,

RESULTS AND DISCUSSION

The probability of complex formation between UO_2^{2+} and the ligand anion was assumed and the factors like hydrolysis of uranyl ion and the formation of polynuclear species were neglected on the following points.

(i) The pH of hydrolysis of uranyl ion, obtained from the deviation of uranyl ion curve from the acid curve, was around pH 3·8. The departure of metal

titration curve from the ligand curve was observed around pH 2·6. This indicated that the complexation occurs before the commencement of hydrolysis of ion. (ii) The solution being very dilute, the probability of existence of polynuclear species was negligible.

The proton-ligand formation number $\bar{n}_A$ and metal ligand formation number $\bar{n}$ were calculated by Irving and Rossotti's expressions[5]. The approximate values of pK and log K were obtained by half integral method and accurate values were calculated by point-wise calculations[5]. The final values were also calculated by the method of least-squares.

The maximum value of $\bar{n}$ at each ionic strength was around 1·9. The metal-ligand ratio was taken as 1:5. No precipitation was observed in the metal complex titration upto pH 9. This showed that 1:1 and 1:2 complexes were formed before the commencement of hydrolysis. The thermodynamic values of pK_1, pK_2, $\log K_1$ and $\log K_2$ are given in Table I.

TABLE I

pK and log K thermodynamic values of UO_2^{2+}-malonic acid at various ionic strengths $t = 30°$ C

μ	pK_1	pK_2	$\log K_1$	$\log K_2$	$\log \beta$
0·032	2·83	5·59	5·87	3·54	9·41
0·052	2·80	5·50	5·75	3·66	9·41
0·072	2·73	·46	5·71	3·70	9·41
0·092	2·70	5·40	5·62	3·76	9·38
0·112	2·68	5·30	·56	3·80	9·36

TABLE II

Slope values and thermodynamic constants

Equilibrium constants		ΔZ^2	Thermodynamic contents at $\mu \to 0$
pK_1	..	2·17	3·00
pK_2	..	3·37	5·86
$\log K_1$	..	−3·87	6·20
$\log K_2$	..	+3·10	3·26

The stability constant data at different ionic strengths could be utilized to know the exact mechanism by which the complexation occurs at different pH. The data were analysed by Bronsted equation[6] as given

$$\log K = \log K^\circ + A \Delta Z^2$$

where A is Debye-Huckel constant ($A = 0{\cdot}5161$)[7], ΔZ^2 is the difference in the square of the charges of product and reactant ion and K° is the formation constant at zero ionic strength.

The values of pK_1, pK_2, $\log K_1$ and $\log K_2$ when plotted against $\sqrt{\mu}$ gave the following results:

(i) All the points fell on a straight line in all the plots.

(ii) The observed slope values (ΔZ^2), along with expected, for various reactions are given as follows:

Reaction equilibrium	Constants	Slope values	
		Expected	Observed
$H_2L \rightleftharpoons HL^- + H^+$	pK_1	2	2·17
$HL^- \rightleftharpoons L^{2-} + H^+$	pK_2	4	3·37

The agreement between the observed and expected values of slope is fairly satisfactory.

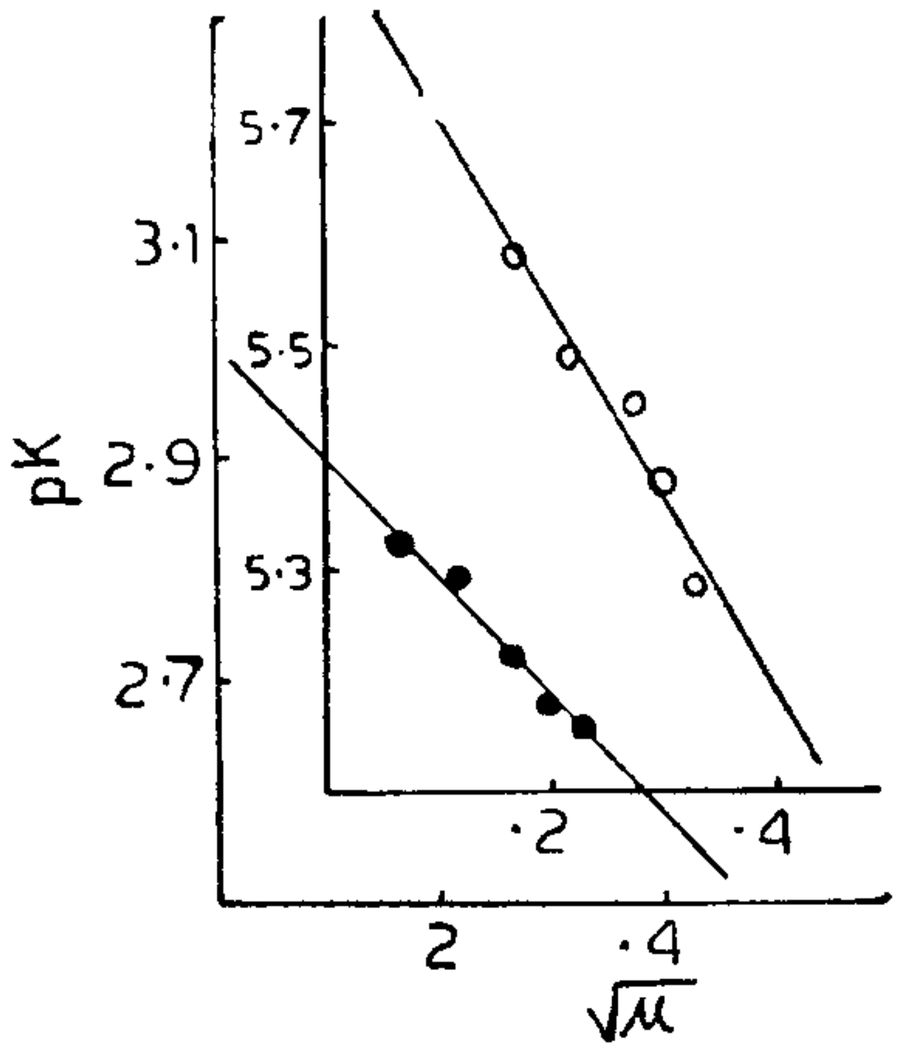


FIG. 1. Plots of pK_1 *vs.* $\sqrt{\mu}$ (●) and pK_2 *vs.* $\sqrt{\mu}$ (○) of the ligand malonic acid.

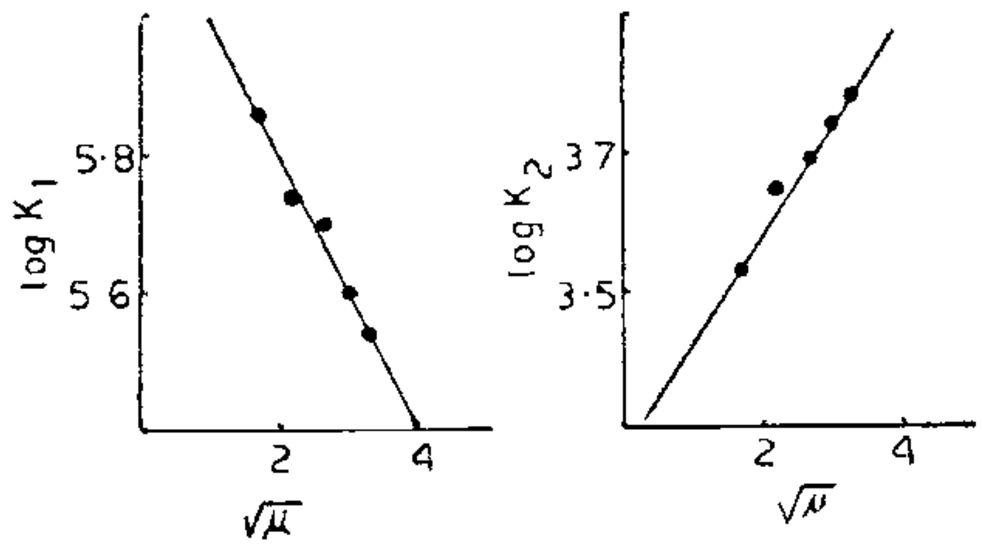


FIG. 2. Plots of $\log K_1$ *vs.* $\sqrt{\mu}$ and $\log K_2$ *vs* $\sqrt{\mu}$ for UO_2^{2+}-malonic acid complexes.

The complexation between UO_2^{2+} and malonic acid commences around pH 3. The dissociation of the first-COOH group of the acid occurs around the same pH ($pK \sim 2{\cdot}83$). The ligand, therefore, may be present as a neutral malonic acid (H_2L) molecule or a malonate ion (HL^-). The alternate complexation equilibria for 1:1 complex are

$$UO_2^{2+} + H_2L \rightleftharpoons UO_2HL^+ + H^+$$

$$UO_2^{2+} + HL^- \rightleftharpoons UO_2L + H^+$$

The magnitude of ΔZ^2 would be −2 or −4 for the first and the second equilibria respectively. The observed ΔZ^2 (Table II) is in favour of second equilibrium.

The formation of 1:2 complex occurs around pH 5 at which the ligand is certainly present as HL^-. The 1:2 complexation therefore takes place by equilibrium

$$UO_2L + HL^- \rightleftharpoons UO_2L_2^{2-} + H^+$$

The observed ΔZ^2 confirm this speculation. The overall reaction is presented as

$$UO_2^{2}{}_+ + 2HL^- \rightleftharpoons UO_2L_2^{2-} + 2H^+$$

The changes in ionic strength could not affect this reaction. This has been concluded from the values ($\log \beta$) which remain constant.

ACKNOWLEDGEMENT

The authors wish to thank Prof. D. D. Khanolkar, Head of the Chemistry Department, Marathwada University, for his keen interest and encouragement in this work.

1. Athavale, V. T., Mahadevan, N., Mathur, P. K. and Sathe, R. M., *J. Inorg. Nucl. Chem.*, 1967, **29**, 1947.
2. Rajan, K. S. and Martell, A. E., *Ibid*, 1967, **29**, 523.
3. Ramamoorthy, S. and Santappa, M., *Bull. Chem. Soc. Japan*, 1969, **42**, 411.
4. Jahagirdar, D. V. and Khanolkar, D. D., *J. Inorg. Nucl. Chem.*, 1973, **35**, 921.
5. Irving, H. and Rossotti, H., *J. Chem. Soc.*, 1954, p. 2904.
6. Amis, A. S., *Solvent Effect on Reaction Rates and Mechanism*, Academic Press, N.Y., 1966, p. 24.
7. Robinson, R. A. and Stroke, R. H., *Electrolyte Solutiones*, 2nd Ed., Butterworths, 1959, p 468.

NEUROMUSCULAR EFFECTS OF PHENETHYLBIGUANIDE (DBI)*

M. BANSINATH, SUDHAKARA KARANTH, K. RAMABADRAN AND M. N. GURUSWAMI
Department of Pharmacology, Kasturba Medical College, Manipal 576 119

ABSTRACT

Activity of Phenethylbiguanide (DBI, Phenformin) has been studied on neuromuscular junction. It is shown that, DBI inhibits neuromuscular junction. Experiments to elucidate mechanism of this inhibition have shown that DBI has membrane stabilizing activity.

INTRODUCTION

IT is a long-known fact that the same structural features in different compounds are attended by similar pharmacological properties[1]. The structure of phenethylbiguanide (DBI, Phenformin), an oral hypoglycemic agent, consisting of a benzyl ring with two carbon atoms separating a biguanide radical, suggested the possibility of sympathetic action.

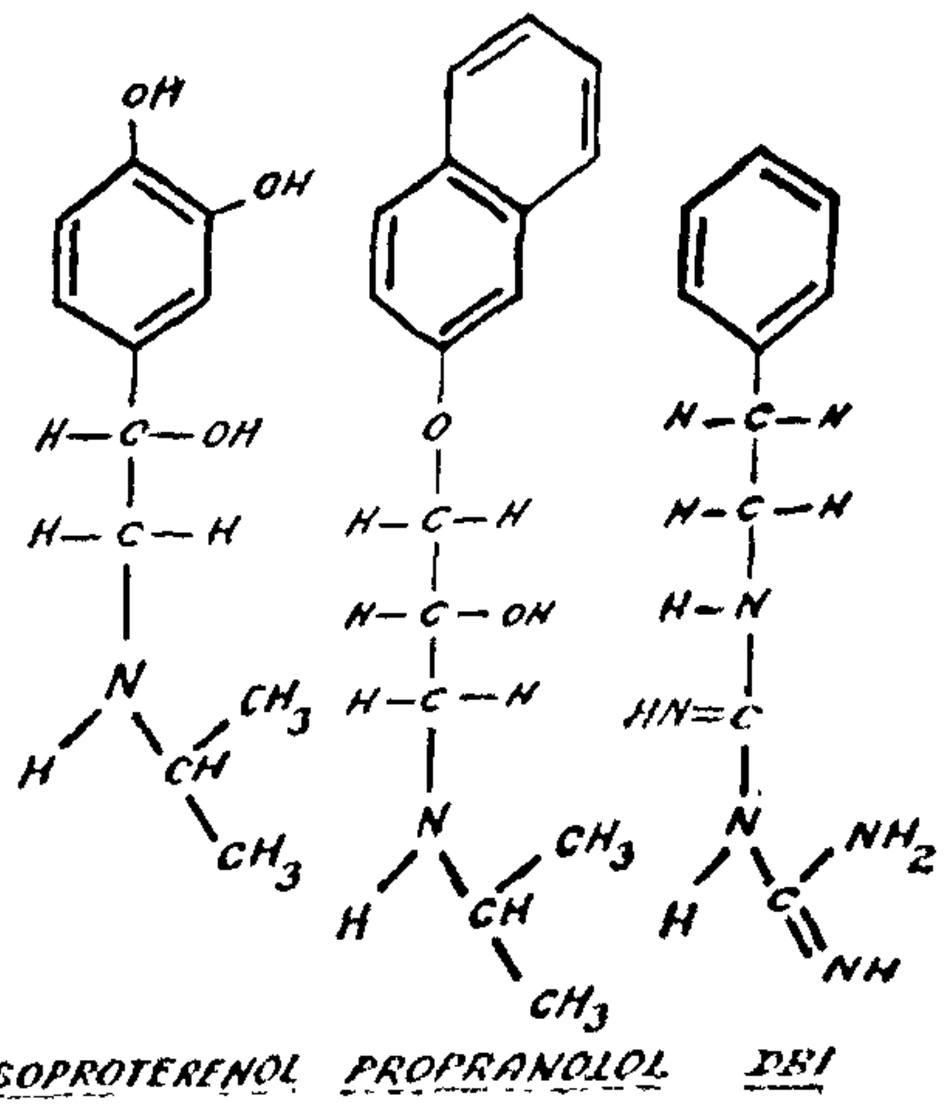
There are claims that DBI lacks a potentiating or blocking action, either to adrenaline or acetylcholine[2], and also that, only upon intravenous injection, in dogs, DBI produces an adrenergic block[3]. DBI is also reported to have negative chrontropic effect comparable to that of propranolol[4]. These contradictory reports, in spite of structural semblance of DBI with Beta-adrenergic drugs, suggested the need for critical reassessment.

There are reports that Beta-adrenergic drugs have both stimulatory[5] and inhibitory[6,7] activity at neuromuscular junction. Hence it was decided to study the activity of DBI on neuromuscular junction. Results obtained in such a study provide the basis for this report.

MATERIALS AND METHODS

(a) Frog's Rectus Abdominis Muscle

The procedure used is essentially as described by MacIntosh and Perry[8], with the following modifications. Magnification is ten fold, tension one gram; 20 to 30 min are allowed for relaxation in Frog Ringer solution (Composition, NaCl 0·65%, KCl 0·01%, $CaCl_2$ 0·012%, $NaHCO_3$ 0·01%, all W/V) before addition of physostigmine (Eserine) sulfate (2 mg/l) to sensitize the muscle. Another 20 to 30 min. are allowed for sensitization to be complete. Fifteen preparations were used for the study.



* Presented at the Second Southern Regional Conference of the Indian Pharmacological Society, Madras, October 30-31, 1974.