

370. *Ion-exchange Study of the Magnesium Citrate Complex.
Effect of Ionic Strength, Temperature, and pH.*

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The effect of ionic strength, temperature, and pH on the stability of the magnesium citrate complex has been determined by the ion-exchange method without using radio-tracers. Measurements were made in the presence of sodium ions and were corrected for NaCit^{2-} . The value of $\log K$ obtained by extrapolation to infinite dilution is 3.96 at 25° and pH 7.1. The resulting $\Delta F^\circ_{298} = -5380$ cal. Between 15 and 50° the stability was practically unchanged, but it increased slightly between pH 7 and 9

THE interaction between magnesium and citrate has been studied by biological assay,¹ pH measurement,² spectrophotometry,³ and ion-exchange without the use of radio-tracers.⁴ Previous measurements were made only of the apparent stability constant, k_c , usually at 25°, $\mu = 0.1-0.16$, and pH 7.1-7.2, in the presence of sodium or ammonium ions. In terms of the equilibrium ion-exchange formulation, the value of k_c is given by the equation:

$$k_c = [(K^\circ_d/K_d) - 1]/[\text{Cit}^{3-}]^x,$$

where K°_d and K_d are the distribution coefficients of magnesium in the absence and presence, respectively, of citrate, and x is the number of these ions bound per atom of magnesium. Reported values of $\log k_c$ varied between 2.90 and 3.70, but, after being corrected by Walser³ for NaCit^{2-} , the variations became smaller.

¹ Hastings, McLean, Eichelberger, Hall, and DaCosta, *J. Biol. Chem.*, 1934, **107**, 351.

² Nordbo, *Skand. Arch. Physiol.*, 1938, **80**, 341.

³ Walser, *J. Phys. Chem.*, 1961, **65**, 159.

⁴ Tobia and Milad, *J.*, 1963, 734.

In this Paper, the ion-exchange method has been used to investigate the effect of ionic strength, temperature, and pH on the MgCit^- complex. Measurements were made in the presence of sodium ions instead of ammonium ions so that the ionic strength could be controlled more accurately. Allowance was made for NaCit^{2-} in calculating the stability constant. The value of the thermodynamic stability constant was also determined by extrapolation to infinite dilution. A similar study was made by Schubert⁵ for the SrCit^- complex.

EXPERIMENTAL

Solutions.—Magnesium solution, 10^{-3}M in magnesium, was prepared from $\text{Mg}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$. 0.1M -Citrate solution was prepared from $\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$. Sodium chloride solution was 0.3M .

Resin.—The air-dried resin, Dowex-50 \times 12 (100—200 mesh) (Na^+ form) was used. Since measurements were made in unbuffered media, the resin was carefully conditioned to the required pH before use.

Procedure.—(a) *Determination of the stability constant.* Three series of equilibrium mixtures were prepared, at ionic concentrations 0.0451, 0.0601, and 0.0751, by adding to the resin (100 mg.) calculated volumes of the above solutions. After adjustment of the pH to 7.1—7.2 by addition of dilute hydrochloric acid, the volume was brought to 100 ml. with water. In each series, the concentration of magnesium in the final solution was 10^{-4}M and that of citrate ranged from 4×10^{-3} to 10^{-2}M . The citrate ion concentration referred to as $[\text{Cit}^{3-}]$ is in fact equal to $([\text{HCit}^{2-}] + [\text{Cit}^{3-}])$. For each value of K_a° and K_d , a blank was run containing all the required solutions except that of magnesium. The mixtures were shaken mechanically for 4 hr. at 25° , and magnesium was determined in the supernatant liquids. The same general procedure was followed in the following experiments, the $[\text{Mg}^{2+}]$ was kept constant at 10^{-4}M while the other variables were changed as stated below.

(b) *Effect of ionic strength.* This was studied at pH 7.1—7.2, using 6 different ionic strengths ranging from 0.01 to 0.09M , while the citrate concentration was kept at 10^{-2}M .

(c) *Effect of temperature.* Determinations were carried out using separate mixtures equilibrated at 15, 25, 35, and 50° . The pH, μ , and $[\text{Cit}^{3-}]$ were kept constant at 7.2, 0.0451M , and 10^{-2}M , respectively.

(d) *Effect of pH.* Measurements were made over the pH range 7.1—9.0. Where necessary, the pH was adjusted by the addition of dilute hydrochloric acid or sodium hydroxide. All the determinations were carried out at 25° , $[\text{Cit}^{3-}]$ 10^{-2}M , and μ 0.0451M . The addition of sodium hydroxide causes a slight increase in the ionic strength.

(e) *Determination of magnesium.* After the removal of citrate ion by anion exchange,⁴ magnesium was determined by titration against 10^{-3}M -disodium ethylenediaminetetra-acetate with Eriochrome Black as indicator. Concordant results could be obtained only when the same concentration of indicator was employed in every titration. For this reason, the Eriochrome-sodium chloride mixture (1:500) was dissolved in the ammonium chloride-ammonium hydroxide buffer (1 g. of the mixture per 100 ml. of buffer). The solution was prepared just before use, and 2 ml. was used per 25 ml. of the solution. By use of a microburette, the relative mean deviation did not exceed 2%.

RESULTS AND DISCUSSION

In the discussion that follows, K_c represents the apparent stability constant for MgCit^- after being corrected for NaCit^{2-} . The corrected value was obtained from the equation:³

$$K_c = k_c(1 + [\text{Na}]K_{c(\text{NaCit}^{2-})}),$$

where k_c is the uncorrected apparent stability constant, and $K_{c(\text{NaCit}^{2-})} = 5$. The plots of $\log(K_a^\circ/K_d - 1)$ against $\log[\text{Cit}^{3-}]$ are shown in Fig. 1. The slopes indicate a 1:1 complex, and an average value of $\log k_c = 2.98$. The results in Table 1 show that, after correction for NaCit^{2-} , the average value increased to 3.12. This value is closer to 3.16, which was obtained previously in the presence of ammonium ions.⁴

The data relating to the effect of ionic strength on the stability constant are presented

⁵ Schubert, *J. Phys. Chem.*, 1952, **56**, 113.

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in Table 2. The ionic strength is assumed to be due to the total sodium and magnesium ions, neglecting the slight change due to complex formation. The range of ionic strengths which could be studied was limited by the fact that errors become magnified at relatively

TABLE 1.
Results for K_c in the presence of sodium ions at 25° and pH 7.1—7.2.

μ	K_c				Average K_c	log K_c
	Citrate concentration (M)					
	4×10^{-3}	6×10^{-3}	8×10^{-3}	10^{-2}		
0.0451	1335	1367	1387	1421	1378 ± 26	3.14
0.0601	1300	1300	1333	1335	1317 ± 17	3.12
0.0751	1316	1306	1301	1317	1310 ± 7	3.11

TABLE 2.
Effect of ionic strength on the stability constant of MgCit^- , at 25°, pH 7.2,
 $[\text{Cit}^{3-}] 10^{-2}\text{M}$.

μ	K_a°	K_c	Ratio of activity coefficients	K	log K
0.0901	1.35	1305	13.5	17,618	4.25
0.0751	1.86	1317	11.3	14,870	4.17
0.0601	2.45	1335	9.6	12,605	4.10
0.0451	3.35	1421	7.1	10,098	4.00
0.0301	15.70	1622	5.1	8272	3.92
0.0101	59.0	2836	3.2	9075	3.95
0.0	—	—	1.0	9120	3.96*

* Obtained by extrapolation to infinite dilution (Fig. 2).

high values of K_a° , obtained below $\mu 0.01\text{M}$, when most of the magnesium will be in the resin phase. Above $\mu 0.09\text{M}$, the differences in K_a° were too small to be detected by titrations.

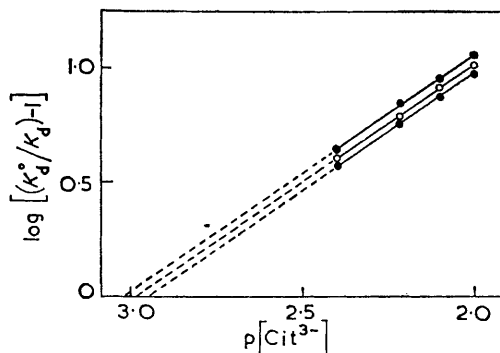


FIG. 1. Variation of $\log [(K_a^\circ/K_a) - 1]$ with $\log [\text{Cit}^{3-}]$.
Top line, $\mu = 0.0451$; middle line $\mu = 0.0601$;
bottom line, $\mu = 0.0751$.

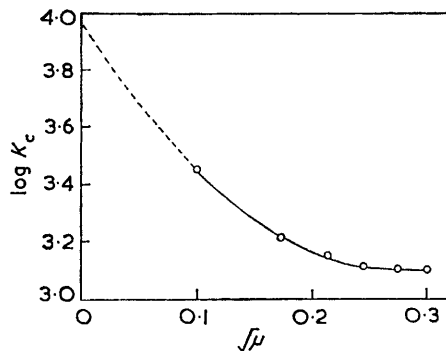


FIG. 2. Variation of the stability constant with ionic strength.

The thermodynamic stability constant, K , was calculated by multiplication, at a given ionic strength, of the K_c value by the activity coefficient ratio which was calculated from individual ion activity coefficients as tabulated by Kielland.⁶ No data were available for the activity coefficient of the MgCit^- ion, and it was assumed to be equal to that of the H_2Cit^- ion. Schubert made the same assumption with the SrCit^- ion.⁵ The value of K obtained by extrapolation to infinite dilution (Fig. 2) is in good agreement with that

⁶ Kielland, *J. Amer. Chem. Soc.*, 1937, 59, 1675.

calculated from the individual ion activity coefficients. The slope of the extrapolated region below $\sqrt{\mu}$ 0.05 is -6.4 . The resulting value of ΔF_{298}° for MgCit^- is -5380 cal., compared with -5700 and -6300 cal. for SrCit^- and CaCit^- , respectively, as was found by Schubert.⁵

The results in Table 3 indicate that between $15-50^\circ$ the stability constant is almost unchanged. This is to be expected since the temperature coefficient of the third ionisation constant of citric acid ($pK_3 \sim 4.6$) is negligibly small at this temperature range, as was found by Bates and Pinching.⁷ On the other hand, the increase in stability constant with increase of pH may be explained as being due to the superposition of two factors, *viz.*, the gradual increase in $[\text{Cit}^{3-}]$ (being ~ 80 and $\sim 97.5\%$ at pH 7 and 8, respectively⁸), and the decrease in pK_3 due to the slight increase in ionic strength. However, at the range of ionic strengths used, the influence exerted by the second factor is smaller.⁷

TABLE 3.

Effect of temperature on the stability constant of MgCit^- , at μ 0.0451M, pH 7.2, $[\text{Cit}^{3-}]$ 10^{-2}M .

Temp.	K_d°	K_c	$\log K_c$
15	3.30	1400 ± 20	3.15
25	3.35	1421 ± 25	3.15
35	3.50	1450 ± 30	3.16
50	3.60	1380 ± 35	3.14

TABLE 4.

Effect of pH on the stability constant of MgCit^- at 25° ; $[\text{Cit}^{3-}]$ 10^{-2}M .

Temp.	K_d°	μ	K_c	$\log K_c$
7.1	3.35	0.0450	1421 ± 25	3.15
7.8	3.81	0.0450	2240 ± 40	3.35
8.4	4.20	0.0454	3653 ± 20	3.56
9.0	4.68	0.0457	4615 ± 30	3.66

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⁷ Bates and Pinching, *J. Amer. Chem. Soc.*, 1949, **71**, 1274.

⁸ Bjerrum and Unmack, *Kgl. danske Videnskab. Selskab, Math-fys. Medd.*, 1929, **9**, 1.