METAL-GLUCONATE COMPLEXES

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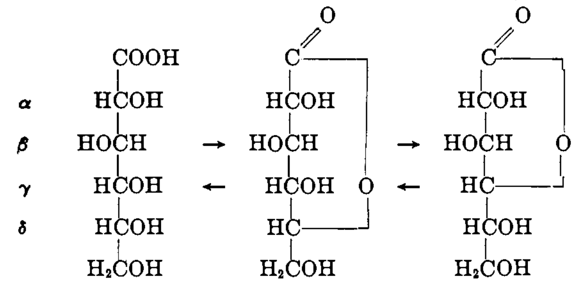
I. INTRODUCTION

Gluconic acid and its salts are used extensively as sequestering agents for metal ions in alkaline systems. The interest in this complexing agent has increased significantly during the past decade, and numerous new industrial applications have been reported. Because a complete review of the metal complexes formed by gluconic acid has not been made, the relevant literature on this sugar acid and its applications for metal ion complexing is obscure and in many cases literally not available. The obscure nature of the literature on the applications of gluconic acid has caused many to overlook potential advantages of this material. For this reason the present review has been undertaken. The intent has been to cover the literature from the time of the first reports through Dec. 31, 1963. The scope of this review covers the physical properties and chemistry of gluconic acid, its salts, its metal complexes, and the proposed structures for some of these complexes. In addition, the practical and industrial applications of metal–gluconate complexes are reviewed.

Within this review gluconic acid refers to the material derived from D-glucose, D-gluconic acid. This material undergoes equilibration in solution to give an equilibration mixture of the acid, the δ-lactone, and the γ-lactone of the acid.



These structures indicate this equilibration and also indicate how the positions of the secondary alcohol groups are systematized. These designations will be used throughout the review. Because the oxygens of these secondary hydroxyls are believed to participate in coordinate bonding, the custom has evolved of designating gluconic acid by HGH_4 (56, 94) where the first H refers to the carboxylic acid hydrogen and H_4 refers to the four hydrogens on the secondary alcohols. This symbolism will be used consistently in the review and coordination by the secondary alcohols will be reflected by a reduction in the number of hydrogens in the symbolism for the ligand. The two lactones that are normally in equilibrium with gluconic acid will be symbolized as L_δ and L_γ to represent the δ- and γ-lactone species. The anion of gluconic acid will be represented as GH_4^-.

II. PROPERTIES OF GLUCONIC ACID

Gluconic acid was first isolated by Boutroux in 1880 during the course of a study of lactic acid fermentation (7). Nef (89) carried out extensive research on the preparation and isolation of gluconic acid and its lactones and was the first to report physical properties for this sugar acid. A melting point of 152° was given for a lactone of the acid, which was referred to as the "β"-lactone, with a specific rotation of $[\alpha]^{20}_D +61.7°$. Nef also isolated a γ-lactone with a melting point of 134–136° and a specific rotation, $[\alpha]^{20}_D +67.8°$. The acid itself was obtained only as a viscous sirup and had a reported optical activity of $[\alpha]^{20}_D -1.7°$. The "β"-lactone of Nef was undoubtedly the δ-lactone, which is the most common form that gluconic acid is supplied in today (the melting point corresponds exactly with the known melting point for the δ-lactone). Although the specific rotations reported by Nef have been extensively used, reference to the original article indicates that these were frequently measured at times considerably after solution of the respective materials. For example, the γ-lactone rotation was measured after the material had been in solution for 12 min. Because it is now known that there is an over-all equilibration between the acid and its two lactones, these specific rotations are clearly inaccurate with respect to those for the pure substances.

Hedenberg (48) extended the work of Nef and reported specific rotations for the acid and its lactones; HGH_4, $[\alpha]^{20}D$ +2.19° (after 45 min. in solution); L_β (really L_δ), $[\alpha]^{20}D$ +63.40° (after 5 min.); and L_γ, $[\alpha]^{20}D$ +67.52° (after 9 min. in solution). The same melting points as reported by Nef (89) were obtained in this work. Another study (53) also has reported specific rotations for the acid and its lactones: HGH_4, $[\alpha]^{20}D$ −6.9°; L_δ, $[\alpha]^{20}D$ +66.2°; L_γ, $[\alpha]^{20}D$ +68.0° (all after 2 min. in solution). Recent measurements (116) have been made of the δ-lactone, the acid, and its sodium salt; the rotations have been measured as a function of time and extrapolated back to zero time to give the rotation for these three materials. The specific rotations reported are L_δ, $[\alpha]^{25}D$ +66.0°; HGH_4, $[\alpha]^{25}D$ +5.40°; and $NaGH_4$, $[\alpha]^{25}D$ +12.0°. Although this approach appears sound for determining the true optical rotations for the lactone and the salt of gluconic acid, it undoubtedly is an oversimplification in the case of the free acid. Because of the strong tendency for gluconic acid to form intermolecular esters (89), acidification of the gluconate salt probably leads to the formation, in part, of such esters. A sounder approach (106), based on the isolation of crystalline gluconic acid and measurement of its initial rotation, gives what is probably the most reliable specific rotation for the free acid, HGH_4, $[\alpha]^{20}D$ −6.7°.

A detailed investigation of the polarographic reduction of the γ- and δ-lactones has been made (79) which has helped to establish that the δ-lactone hydrolyses more rapidly than the γ-lactone. In 0.05 *M* lithium chloride the half-wave potentials *vs.* the saturated calomel electrode (s.c.e.) are −1.95 v. for L_γ and −1.97 v. for L_δ.

The structures for the potassium and rubidium salts of gluconic acid have been determined by X-ray crystallography (73) and indicate that the alkali metal ions are each coordinated to six oxygen atoms, four of which are from the carboxylate groups and two from the hydroxyl groups. The structure is an α-linear zigzag molecule essentially analogous to the glucose molecule.

III. PHYSICAL PROPERTIES AND STRUCTURES OF METAL CHELATES

A value for the dissociation constant for gluconic acid first was reported in 1929 (80), $K \approx 1.65 \times 10^{-4}$. Subsequently, an additional study (11), based on pH measurements, gave another value for the constant, $K = 2.78 \times 10^{-4}$. Two additional studies (71, 116) have been made of the dissociation constant and are summarized at the top of Table I. The first (71) is concerned with activity effects and the second (116) with taking into account the equilibration between the lactones and the free acid. The reported equilibria are

$$\frac{[H^+][GH_4^-]}{[HGH_4] + [L]} = 1.76 \pm 0.05 \times 10^{-4}$$

$$\frac{[H^+][GH_4^-]}{[HGH_4]} = 1.99 \pm 0.07 \times 10^{-4}$$

$$\frac{[HGH_4]}{[L]} = 7.7$$

Gluconic acid is normally supplied in the solid form as the δ-lactone (19). When this material is introduced into solution it hydrolyzes to the acid, especially in the presence of base. The rate of this hydrolysis has been graphically presented (19) and more recently quantitatively measured (116). Over the pH range from 3 to 5, the rate of hydrolysis is independent of pH and follows a rate law

$$\frac{-d(L)}{dt} = k[L]$$

where the rate constant, k, at 25° has been evaluated to be 2.3×10^{-4} sec.$^{-1}$ as measured by optical rotation and 1.3×10^{-4} sec.$^{-1}$ as measured by coulometry. The activation energy has been estimated to be 15 kcal./mole for this hydrolysis reaction. Gluconic acid, its lactones, and its salts have been studied as a function of solution pH by nuclear magnetic resonance (n.m.r.) (9). The spectra indicate that there are approximately three different environments for the nonexchanging protons of the ligand.

Salts of gluconic acid were isolated first in 1929 (80), for the ions of Na(I), K(I), NH_4(I), Ba(II), Ca(II), Mg(II), Mn(II), Zn(II), and Pb(II). Two additional reports of gluconate salts appeared in 1936 (92, 133); for a number of the simple metal ion salts specific rotations were given (92): K(I), 13°; Na(I), 13.71°; Mn(II), 12.8°; Co(II), 12.31°; Cd(II), 11.47°; Cr(III), 11.93°; NH_4(I), 12.65°; Ba(II), 12.2°; Zn(II), 11.9°; Fe(III), 12.65°; Fe(II), 16.39°; and Ca(II), 11.03°. However, because of the difficulty in isolating pure solid gluconate compounds, these data may be of questionable value. The barium salts of the gluconate complexes of Al(III), Cr(III), Cu(II), Ni(II), Co(III), Co(II), Mn(II), Bi(III), and Sb(III) have been isolated. These can be made soluble by either conversion to the potassium salts or by adding an additional mole of gluconic acid for each mole of barium (133). Complexation of copper(II) and iron(III) by gluconic acid has been concluded to be the cause of the autoxidation of the ligand (134). The ions of cobalt(II), nickel(II), and manganese (II) also promote this autoxidation and are concluded to be complexed by the ligand. Additional evidence for complexation by the gluconate ion has been given by the observation that iron(II) ion is photooxidized in the presence of gluconic acid (90).

The first stability constants for gluconate complexes were reported in 1938 for the simple metal–acid monodentate systems. The data for these (11) constants, as well as other reported stability constants, are summarized in Table I. The constants reported for the alkaline earth ions and for zinc ion represent the stabilities for coordination by just the carboxylate group of the ligand. They are of relatively low stability and do not represent the most important systems for gluconate complexation. The remainder of the constants reported in Table I represent much more alkaline systems where coordination by the secondary alcohol groups can become important as the protons are displaced. With these conditions chelate rings can be formed and complexes of significantly greater stability are formed. The complexes summarized in Table I for these systems represent the most probable species in alkaline solution, or at least the most important, and provide a crude means of inner comparison.

In general, the alkaline earth complexes are assumed to be one-to-one complexes (11, 49, 122); however, a study based on solubility concluded that a complex involving two calcium ions per gluconate also is formed (58). Further evidence for coordination of calcium ion by gluconate ions is given by conductance measurements (54, 57) and by measurements of optical rotation (52). The gluconate complex of titanium and its preparation has been reported (91, 132); the complex is stated to be soluble in methanol.

A preparation of iron(III) gluconate was first reported in 1948 (4) and the isolated material was concluded to be $Fe(OH)_2OCH_2(CHOH)_4CO_2H$, with the iron bonded exclusively to the primary alcohol. This same work suggested that aluminum forms a similar complex with gluconic acid. Another complex has been prepared with two iron(III) ions per gluconate ion (127).

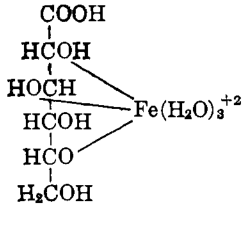
A detailed study of the iron(III) gluconate complexes has been made using polarography, spectrophotometry, pH titrations, and compound isolations (96). A one-to-one complex is reported which has a number of acidic dissociations. These are proposed to follow the steps

$$HFe(GH_3)^{+2} \rightarrow HFe(GH) + 2H^+ \quad pK = 4.6$$

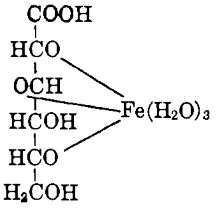
$$HFe(GH) \rightarrow Fe(GH)^- + H^+ \quad pK = 4.0$$

$$Fe(GH)^- + OH^- \rightarrow Fe(GH)(OH)^{-2} \quad pK = 13.3$$

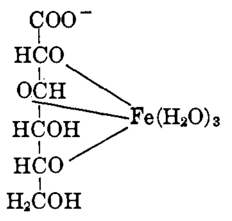
and have the indicated dissociation constants. Structures for these complexes were proposed



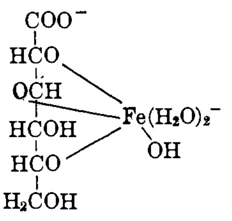
$HFe(GH_3)^{+2}$



HFe(GH)



$Fe(GH)^-$



$Fe(GH)(OH)^{-2}$

Thus iron(III) is concluded to bond to gluconate ion through the α, β, and δ oxygen atoms of the ligand. However, more recent work (45) has suggested that the bonding is by the α-, γ-, and δ-oxygens of the ligands. This conclusion is based on the similarity of the optical rotation for the sodium salt of the complex, $[\alpha]^{20}_D$ +64°, to that for the γ- and δ-lactones. The acid dissociation of the complex has been measured (45) and found to be equal to 2×10^{-5}.

The structures presented in this review represent deductions made by investigators that are based primarily on studies of the solutions of the complexes. They are not to be regarded as absolutely established but probably will have to be modified as more data are obtained. Also, the iron(III) complexes as well as those for many of the other metal ions are actually octahedral with the central metal ion attached to water molecules in addition to its coordination with the gluconate ligand.

The iron(III) complex has been studied also by pH titrations (136), spectrophotometry (129), compound isolation (43, 128), polarography (128), and by ion exchange (74). All of these studies indicate that a one-to-one complex is formed but in addition as many as four iron ions per gluconate ion have been isolated in complex systems.

The relative stability of nickel(II) gluconate to that for cobalt(II) gluconate has been measured and found to have a ratio of 25.2 at pH 5 (140).

The complexes of aluminum(III) and chromium(III) with gluconic acid have been studied and found to be similar to the iron(III) gluconate complex (43, 46). The bonding is concluded to be the same as for the iron(III) complex, *i.e.*, with the α-, γ-, and δ-oxygens of the ligand (43, 45). The solid complexes have been isolated and have the formulas (43, 46) $Cr_2(GH_3)(GH_4)_2(OH)_2$, $Al_2(GH_3)(GH_4)_2(OH)_2$, $H[Cr(GH)]\cdot 2H_2O$, $Na[Cr(GH)]$, and $Na[Al(GH)]$. An acidic solution of the chromium(III) gluconate complex is concluded to have two chromiums for three gluconate ligands and to have the structure

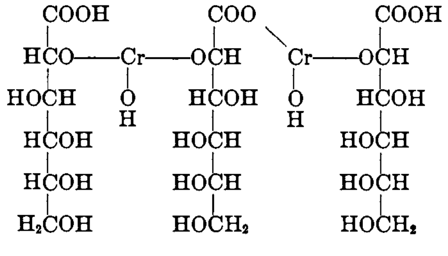


TABLE I
STABILITY CONSTANTS FOR METAL GLUCONATE COMPLEXES

Metal ion	Metal chelate	Formulation	log *K*	μ	*t*, °C.	Ref.
H(I)	HGH_4	$\frac{[HGH_4]}{[H^+][GH_4^-]}$	3.70	...	25.0	116
			3.76	...	17.0	71
			3.56	0.2	...	11
			3.78	...	...	80
Mg(II)	$Mg(GH_4)^+$	$\frac{[Mg(GH_4)^+]}{[Mg^{+2}][GH_4^-]}$	0.70	0.2	...	11
Ca(II)	$Ca(GH_4)^+$	$\frac{[Ca(GH_4)^+]}{[Ca^{+2}][GH_4^-]}$	1.21	0.2	...	11
			1.22	0.16	25.0	122
			2.16	...	...	49
Sr(II)	$Sr(GH_4)^+$	$\frac{[Sr(GH_4)^+]}{[Sr^{+2}][GH_4^-]}$	1.00	0.2	...	11
			1.01	0.16	25.0	122
Ba(II)	$Ba(GH_4)^+$	$\frac{[Ba(GH_4)^+]}{[Ba^{+2}][GH_4^-]}$	0.95	0.2	...	11
Zn(II)	$Zn(GH_4)^+$	$\frac{[Zn(GH_4)^+]}{[Zn^{+2}][GH_4^-]}$	1.70	0.2	...	11
Cu(II)	$Cu_2(GH_3)_2O(OH)^{-3}$	$\frac{[Cu_2(GH_3)_2O(OH)^{-3}]}{[Cu^{+2}]^2[GH_4^-]^2(OH^-)^5}$	36.6	...	25.0	94
Cu(II)	$Cu_2(GH_3)_4(OH)^{-5}$	$\frac{[Cu_2(GH_3)_4(OH)^{-5}]}{[Cu^{+2}]^2[GH_4^-]^4[OH^-]^5}$	38.9	0.45	25.0	94
Fe(III)	$Fe(G)^{-2}$	$\frac{[Fe(G)^{-2}]}{[Fe^{+3}][GH_4^-][OH^-]^4}$	37.2	...	25.0	96
Fe(II)	$Fe(GH_4)^+$	$\frac{[Fe(GH_4)^+]}{[Fe^{+2}](GH_4^-)}$	1.0	...	25.0	96
Pb(II)	$Pb(GH_4)^+$	$\frac{[Pb(GH_4)^+]}{[Pb^{+2}][GH_4^-]}$	2.6	0.1	25.0	95
Pb(II)	$Pb(GH_2)^-$	$\frac{[Pb(GH_2)^-]}{[Pb^{+2}](GH_4^-)[OH^-]^2}$	15.7	0.15	25.0	95
Cd(II)	$Cd(GH_4)_2$	$\frac{[Cd(GH_4)_2]}{[Cd^{+2}](GH_4^-)^2}$	2.1	...	25.0	97
Cd(II)	$Cd_2(GH_3)_3(OH)_2^{-4}$	$\frac{[Cd_2(GH_3)_3(OH)_2^{-4}]}{[Cd^{+2}]^2(GH_4^-)^3[OH^-]^5}$	10.2	1.0	25.0	97
Cd(II)	$Cd_2(G)(OH)^{-4}$	$\frac{[Cd_2(G)(OH)^{-4}]}{[Cd^{+2}]^2(GH_4^-)[OH^-]^5}$	8.7	1.0	25.0	97
Bi(III)	$Bi_2(GH_3)_2(OH)^+$	$\frac{[Bi_2(GH_3)_2(OH)^+]}{[Bi(OH)_4^-]^2[GH_4^-]^2}$	10.0	...	25.0	8
Ce(IV)	$Ce_2(GH)_3(OH)_2^{-6}$	$\frac{[Ce_2(GH)_3(OH)_2^{-6}]}{[Ce^{+4}]^2[GH_4^-]^3[OH^-]^{11}}$	63.0	...	25.0	115
Ce(III)	$Ce_2(G)(OH)_2^-$	$\frac{[Ce(G)(OH)_2^-]}{[Ce^{+3}]^2[GH_4^-][OH^-]^6}$	39.0	...	25.0	115
U(VI)	$UO_2(GH_2)^-$	$\frac{[UO_2(GH_2)^-]}{[UO_2(OH)^+][GH_4^-][OH^-]}$	6.3	...	25.0	118
La(III)	$La(GH_2)$	$\frac{[La(GH_2)]}{[La^{+3}][GH_4^-][OH^-]^2}$	16.7	...	25.0	64
Nd(III)	$Nd(GH_2)$	$\frac{[Nd(GH_2)]}{[Nd^{+3}][GH_4^-][OH^-]^2}$	18.0	...	25.0	64
Sm(III)	$Sm(GH_2)$	$\frac{[Sm(GH_2)]}{[Sm^{+3}][GH_4^-][OH^-]^2}$	18.3	...	25.0	64
Gd(III)	$Gd(GH_2)$	$\frac{[Gd(GH_2)]}{[Gd^{+3}][GH_4^-][OH^-]^2}$	18.6	...	25.0	64
Y(III)	$Y(GH_2)$	$\frac{[Y(GH_2)]}{[Y^{+3}][GH_4^-][OH^-]^2}$	18.8	...	25.0	64

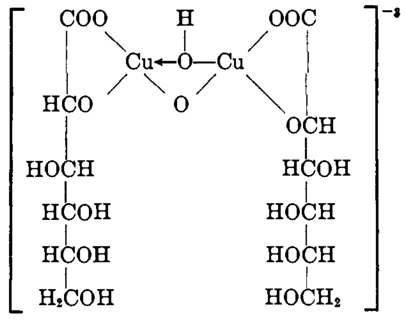
TABLE I (*Continued*)

Metal ion	Metal chelate	Formulation	log K		t, °C.	Ref.
Yb(III)	Yb(GH_2)	$\frac{[Yb(GH_2)]}{[Yb^{+3}][GH_4^-][OH^-]^2}$	20.0	...	25.0	64
Sb(III)	Sb(GH_2)	$\frac{[Sb(GH_2)]}{[SbO^+][GH_4^-]}$	6.0	...	25.0	93

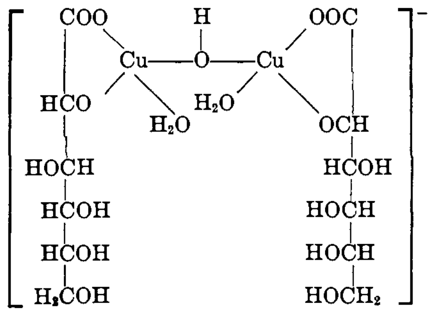
The pH values at which these various salts have been isolated are indicated; the acid dissociation constant for H[Cr(GH)] has a reported value of 2×10^{-6} (46).

Ion exchange also has been used to study the titanium(IV), zirconium(IV), and thorium(IV) complexes with gluconic acid (74). The extent of complexing was compared to that by saccharic acid which was found always to be superior to gluconic acid. A method was developed for separating iron(III) or titanium(IV) from zirconium(IV) or thorium(IV) by using these two sugar acids.

The complexes of copper(II) have been extensively studied by polarography, optical rotation, pH titrations, and spectrophotometry (56, 94). Evidence was obtained in basic media for metal-to-gluconate ratios of 2:4, 2:2, and 2:1 under various conditions; other 2:2 species were proposed for less alkaline solutions. Table I summarizes the stability constants for these systems. Two of the structures proposed are



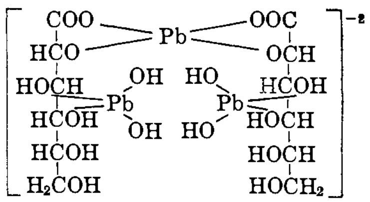
in strongly alkaline media and



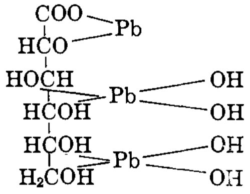
in solutions below pH 9.

In addition to the simple carboxylic acid complex of zinc ion (11), a more stable complex appears to be formed under strongly alkaline conditions (45, 119). Three cadmium gluconate complexes (see Table I) have been reported at various pH values although no structures have been given (97).

A lead(II) gluconate complex first was noted and studied by using measurements of optical rotation (52). This study indicated that a one-to-one complex is formed with bonding to the lead ion by the carboxylate group and the α-hydroxyl group. More recently, an extensive study of the gluconate complexes of lead(II) has been made (45, 95) in which polarography and measurements of optical rotation have been important in elucidating the various species present. A one-to-one species is formed in acidic solution which involves the simple complex with a dissociation constant whose pK is 2.6. In neutral solutions a solid insoluble one-to-one species is formed. In more alkaline media a species containing three lead ions per two gluconate ligands and an insoluble species containing three lead ions to one gluconate ion are formed. In extremely strong base only a one-to-one species is observed. Structures, which are quite speculative, are proposed for two of the alkaline species (95)



and



Studies of the lead gluconate complex by n.m.r. have confirmed that the bonding for the one-to-one complex is primarily by the carboxylate and the α-oxygen of the ligand (9). However, in strongly alkaline solutions the β-oxygen also appears to bond to the lead ion. X-Ray data for solid $Pb(GH_4)_2$ have been reported (98).

A recent polarographic study of bismuth(III) gluconate has indicated that a stable one-to-one complex is formed in strongly alkaline solution and that the formation reaction involves one or two hydroxide ions per bismuth species (8). Again n.m.r. studies indicate that the bonding involves the carboxylate and the α-oxygen of the ligand and possibly the β-oxygen (9).

Complexes of molybdenum(VI) and (V) with gluconate ion were first reported as a result of a polarographic investigation which indicated that the complexes are weaker than the molybdenum EDTA complexes (114). However, the molybdenum gluconate complexes are of sufficient stability to interfere with the molybdenum blue method for determining silicic acid (111). Studies of this interference have led to the conclusion that the molybdenum(VI) complex contains two molybdenum ions per gluconate ion on the basis of conductometric, pH, and potentiometric studies. Conversely, another study concluded that the complex contained one molybdenum ion per two gluconate ions on the basis of similar studies (109). The tungsten(VI) complex has been reported to contain two tungsten ions per one gluconate (110). A more recent study has concluded that the most important species is the one-to-one complex with two acid dissociation constants, $pK_1 = 2.42$ and $pK_2 = 6.18$ (27). Another recent polarographic study of the molybdenum(VI)–gluconate system indicates that at low pH values two molybdenum ions per gluconate ion exist, while at higher pH values a simple one-to-one complex becomes important (125).

Extremely stable gluconate complexes of ruthenium(III) have been reported (117, 120) on the basis of polarographic, polarimetric, potentiometric, and spectrophotometric measurements. Although as many as six ruthenium ions combine initially with one gluconate ion, the species is unstable and slowly hydrolyzes to a stable one-to-one complex. Above pH 8 the complex, in the presence of a tenfold excess of gluconate ion and at a pH of 14, follows Beer's law and has an adsorption maximum of 337 mμ with a molar adsorbtivity of 4170. A specific analytical determination for ruthenium, using sodium gluconate as the supporting electrolyte, has been developed (120).

Similar studies have been made of the uranium(VI) and osmium(VI, IV, III) gluconate systems (118, 121). For uranium, both a one-to-one complex as well as one containing three uranium ions per gluconate are suggested. The osmium complexes have been studied primarily by polarography, spectrophotometry, and optical rotation. The osmium(VI) complex has two species, one in the range of pH 7 to 10, which has an absorption maximum at 290 mμ and another above pH 10 which has an absorption maximum of 270 mμ. The polarographic reduction wave for osmium(VI) is independent of gluconate concentration, which indicates that both the osmium(VI) and osmium(IV) species have the same number of ligands per osmium. Two gluconate ions per osmium(VI) are proposed for the complex and the polarographic reduction sequence is given as

$$\mathrm{Os(GH_4)_2(OH)_6^{-2} + 2e^- \rightarrow Os(GH_4)_2(OH)_3^- + 3OH^-}$$
$$\mathrm{Os(GH_4)_2(OH)_3^- + e^- \rightarrow Os(GH_4)_2(OH)_3^{-2}}$$

Because polarography has been used rather extensively in the study of metal gluconate complexes and because a number of essentially analytical methods have been developed from such studies, the polarographic constants for metal gluconate complexes are summarized in Table II. In addition, the supporting electrolyte, the oxidation state of the product, and the reversibility of the polarographic waves are indicated.

There has been extensive investigation of the gluconate complexes of the rare earths by a number of Russian workers, particularly by Kostromina (44, 60, 62, 63, 64, 65, 66, 67). This extensive research was initiated on the lanthanum(III) ion, which was studied by pH measurements, conductivity measurements, and optical rotation (44). In acid solutions, one to six ligands per metal ion combine while in alkaline solutions a maximum of two ligands per metal ion is ob-

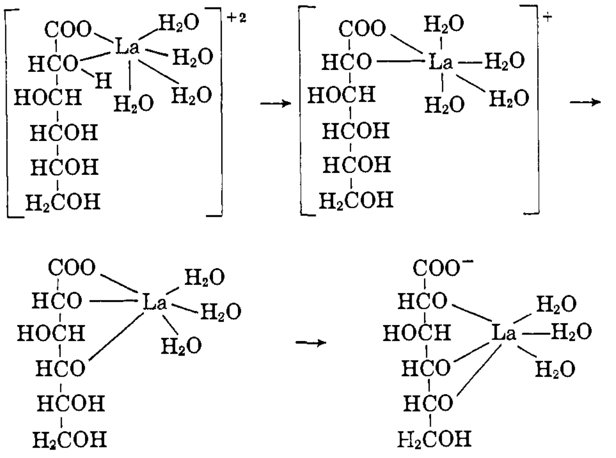
TABLE II

POLAROGRAPHIC DATA FOR METAL GLUCONATE SYSTEMS

Metal ion	Supporting electrolyte	$E_{1/2}$ s.c.e., v.	Oxid. state of product	I_{max}	Notes	Ref.
HGH_4, L_γ	0.05 *F* LiCl	−1.95	...	...	...	79
HGH_4, L_δ	0.05 *F* LiCl	−1.97	...	...	...	79
Fe(III)	0.2 *F* $NaGH_4$, 2 *F* NaOH	−1.68	0	...	Irrev.	96
Cu(II)	0.1 *F* $NaGH_4$, 1.0 *F* NaOH	−0.51	0	...	Rev.	94
Zn(II)	0.15 *F* $NaGH_4$, 0.01 *F* NaOH	−1.41	0	...	...	119
Cd(II)	0.20 *F* $NaGH_4$, pH 6.0	−0.599	0	...	Rev.	97
Cd(II)	0.20 *F* $NaGH_4$, 0.5 *F* NaOH	−0.827	0	...	Rev.	97
Pb(II)	0.10 *F* $NaGH_4$, 1.0 *F* NaOH	−0.815	0	...	Rev.	95
Bi(III)	0.10 *F* $NaGH_4$, 1.0 *F* KOH	−0.80	0	...	Irrev.	8
Mo(VI)	0.20 *F* $NaGH_4$, pH 6.0	−0.570	V	...	Irrev.	114
Mo(VI)	0.05 *F* $NaGH_4$, 0.1 *F* KCl, pH 6.0	−0.60	V	...	Rev.	125
Mo(V)	0.20 *F* $NaGH_4$, pH 6.0	(−0.068)	VI	...	Irrev.	114
Ru(III)	0.20 *F* $NaGH_4$, pH 14.0	−0.67	II	1.18	Rev.	117, 120
U(VI)	0.3 *F* $NaGH_4$, 0.1 *F* NH_4ClO_4, pH 11.0	−1.17	...	2.27	Irrev.	118
Os(VI)	0.1 *F* $NaGH_4$, 1 *F* NaOH	−0.495	IV	2.44	Rev.	121
Os(VI)	0.1 *F* $NaGH_4$, 1 *F* NaOH	−1.465	III	...	...	121

served. A number of compounds were isolated at various pH values and their formulas determined to be: $[La(GH_4)\cdot 2H_2O]Cl_2$, $[La(GH_4)_2\cdot 2H_2O]Cl$, $[La(GH_4)_3\cdot 3H_2O]$, $H_3[La(GH_4)_6]$, $[La(GH_3)\cdot 2H_2O]Cl$, $Na_3[La(GH_4)_6]$, $[La(GH_2)\cdot 3H_2O]$, $Na[LaGH\cdot 3H_2O]$, and $Na[La(GH_3)_2]$.

In solution the structure for the lanthanum(III) complex is concluded to change with increasing pH as



and ultimately to take on a structure similar to the iron(III) (45), aluminum(III), and chromium(III) complexes (46) with the lanthanum ion being coordinated to the α-, γ-, and δ-oxygens of the gluconate molecule in a one-to-one complex. In another study, the complexes of gadolinium(III), yttrium(III), and ytterbium(III) have been studied (63) and a number of compounds isolated at various pH values; $Y(GH_3)Cl$, $Y(GH_2)$, $Y(GH_4)_2Cl$, $Na[Y(GH_3)_2]$, $Y(GH_4)_3$, and $Na_3[Y(GH_4)_6]$. A detailed summary of the stability constants of the various rare earth complexes under a number of conditions has been made (64); the constants are summarized in Table III.

TABLE III

GLUCONATE COMPLEXES OF RARE EARTH IONS

Metal ion	$\frac{[M^{+3}][HGH_4]}{[M(GH_4)^{+2}]}$	$\frac{[M(GH_3)^+][H^+]}{[M^{+3}][GH_4^-]}$	$\frac{[M(GH_2)][H^+]^2}{[M^{+3}][GH_4^-]}$
La(III)	2.53×10^{-3}	0.92×10^{-4}	0.50×10^{-11}
Ce(III)	2.42×10^{-3}	—	—
Nd(III)	1.91×10^{-3}	1.87×10^{-4}	1.10×10^{-10}
Sm(III)	1.51×10^{-3}	3.33×10^{-4}	2.2×10^{-10}
Gd(III)	1.71×10^{-3}	2.32×10^{-4}	4.4×10^{-10}
Y(III)	2.51×10^{-3}	0.50×10^{-4}	6.8×10^{-10}
Yb(III)	2.65×10^{-3}	—	8.90×10^{-9}

The cerium(VI) and cerium(III) gluconate complexes have been studied in detail using spectrophotometric, pH, and optical rotation measurements (115). Although an initial complex containing six cerium(IV) ions per gluconate ion is formed, it hydrolyzes to give $Ce_2(GH_4)_3(OH)_9^{-4}$ at pH 7.5 and $Ce_2(GH_4)_3(OH)_{11}^{-6}$ at pH 11. The cerium(IV) gluconate complex obeys Beer's law in a solution containing 0.08 *M* sodium gluconate at pH 14 and has an absorption maximum of 288 mμ with a molar adsorptivity of 4200.

The gluconate complexes of cerium(III), neodymium(III), and samarium(III) (65) are proposed to have structures which are similar to those for lanthanum(III) (44). Ion exchange also has been used to study the neodymium(III) and ytterbium(III) complexes (62). One to six gluconate ligands per metal ion are proposed for the complex under various conditions; some stability constants are given.

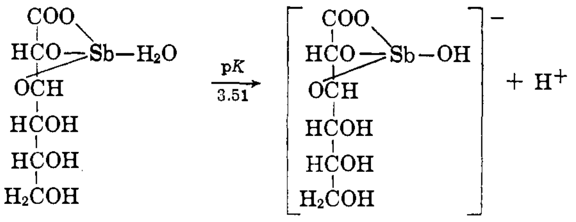
A review on rare earth complexes and methods of determining their stability constants has been given (61). Recent work using ion exchange and potentiometric titrations has been reported for the gluconate complexes of lanthanum(III), neodymium(III), samarium(III), gadolinium(III), yttrium(III), and ytterbium(III) (60). Another recent study of the lanthanum(III)–gluconate system at pH 3 has been made using ion exchange (66). The constants for the simple equilibria involving from one to three gluconates per lanthanum are

$$\frac{[La^{+3}][GH_4^-]}{[La(GH_4)^{+2}]} = 4.4 \times 10^{-3}; \quad \frac{[La(GH_4)^{+2}][GH_4^-]}{[La(GH_4)_2^+]} = 1.3 \times 10^{-2};$$

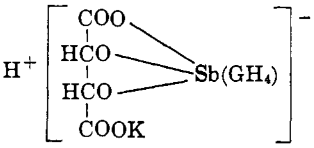
$$\frac{[La(GH_4)_2^+][GH_4^-]}{[La(GH_4)_3]} = 3.8 \times 10^{-2}$$

A general study has been made of the cation complexes formed between the rare earth ions and gluconic acid (67).

A gluconate complex with germanium(IV) has been reported which consists of two metal ions per three gluconate ions (28). No such complex was observed for silicon(IV). The solubility of antimony oxide has been used as a means of studying a complex formed by gluconate with this metal ion (93). The structures proposed for this complex and its anion are



A mixed gluconate–tartrate complex also has been reported (26) with the simplified formula



Polarimetric measurements have shown that calcium gluconate forms a mixed complex with boric acid (12, 135). This has been used as a means of analyzing gluconate by optical rotation (12). pH titrations also have been used for studying the calcium gluconate–boric acid system (13); the complexes are proposed to be of the diol–boric acid type. Gluconate ion is concluded to be as effective as mannitol for determining boric acid and borates. In another study the conclusion is made that one boric acid molecule combines with two calcium gluconate groups to form the mixed complex; acid–base titrations and conductivity measurements are the basis of the conclusion (72).

IV. USES FOR METAL GLUCONATE COMPLEXES

A. ANALYTICAL APPLICATIONS

A procedure based on optical rotation has been outlined for the determination of gluconic acid and its lactones in solution (19). This procedure is only applicable when gluconic acid and its hydrolysis products are the sole materials in solution; the numbers given in the particular equation may well be erroneous because of the specific rotations used in developing the formula (48). Another procedure has been developed for determining gluconate ion which is based on the copper gluconate complex and a subsequent iodometric titration of the copper (69, 70).

A quantitative procedure for the determination of calcium phosphate has been developed using gluconic acid as a means of bringing the material into solution for subsequent determination (55). Also, in the gravimetric determination of nickel with dimethylglyoxime, gluconic acid prevents interference by ferric ion (103). Another procedure has been reported for titrating aluminum ion by first making it soluble with sodium gluconate in order that the ion may be titrated by potassium fluoride (137). A procedure has been reported for the use of calcium gluconate in the volumetric determination of boric acid (15).

The barium salt of the cobalt(III) gluconate complex has been used to resolve racemic mixtures of various ligands including propylenediamine, alanine, and tartaric acid (32).

B. INDUSTRIAL APPLICATIONS

There have been a number of summaries of the commercial methods for producing gluconic acid and its salts together with reviews of applications for this material and its metal complexes (5, 18, 101, 138). A specific review has been presented of the use of this acid in pharmacology and the textile industry (138). A review of synthetic methods, including various chemical, electrochemical, and fermentation processes, and the patents covering these processes also has been presented (18). This same article indicates some of the commercial applications, *e.g.*, aluminum etching, cleaning of milk cans and of beerstone, bottle washing, aluminum cleaning, leather tanning, and general sequestration of metal ions.

The sequestration of iron and calcium ions by gluconic acid has been noted (101); the complexing of these two ions as well as copper ion by gluconic acid has been compared to that by other sugar acids (85). This comparison indicates that saccharic acid is the most effective agent in alkaline solution, but that gluconic acid is a close second. Sodium galactonate also is extremely effective for sequestering copper and ferric ions. An optimum solution for dissolving iron(III) hydroxide is reported to contain 3% sodium hydroxide and 0.5% gluconic acid (42). Another report indicates that at pH 4 citric acid is completely effective in sequestering iron(III) while gluconic acid is only partially effective (81). Another report has indicated the general utility of gluconate solutions for the sequestration of metal ions (99); however, the ligand is concluded not to be useful as a color reagent or for titrimetric purposes but that it is especially good for solubilizing ions in alkaline solutions for paper chromatography and electrophoresis.

Gluconic acid has been used as a solubilizing agent for metal ions used as carriers for the concentration and separation of plutonium from fission products (130).

Sodium gluconate has extensive commercial applications in bottle washing solutions to prevent scale and filming (14, 20, 38, 39). The effectiveness of this material in such solutions appears to be due to the caustic nature of the solution and the ability of gluconate to solubilize calcium and iron salts. Gluconate solutions reportedly attack both the boron and the silicon dioxide in the glass (14). The general use of gluconic acid in detergent compounds also has been discussed (108).

The general use of sequesterants and the sequestering of metal ions in hard water has been reviewed (20). Saccharate, gulonate, and glucuronate ions appear to be superior to gluconate ion in general (29), but gluconate is four times as effective as EDTA under these conditions. The use of a mixture of gluconic acid and boric acid has been reported for sequestering various metal ions in hard water (30). A general discussion of gluconic acid and its applications in bottle washing, paint stripping, and aluminum cleansing formulations has been presented (35).

Gluconic acid salts have found use in zinc plating baths to give a semibright and smooth deposit of zinc (22, 23, 25) and in acid pickling baths for steel (24). Chromium gluconate has been used for etching iron in sulfuric acid solutions (100) and sodium gluconate has found application as a pretreating agent of iron prior to electroplating (86). Apparently in the latter application the gluconic acid dissolves iron(III) oxide and rusts to give a clean iron surface for subsequent electroplating. Sodium gluconate has been found to be extremely useful in producing a rinsable scale on aluminum in caustic baths (36, 40, 102); by its use a bright and mirrorlike finish has been obtained. Gluconate salts also are effective for stripping paint from aluminum (84) and for cleaning aluminum surfaces of oxide prior to plating (104). Gluconic acid has been used for cleaning aluminum surfaces (83) and magnesium surfaces (82) prior to spot welding. Addition of gluconic acid to plating solutions helps to provide a dense, fine grained, and adherent plate of antimony (37). Use of chromium salts together with gluconic acid improves surfaces for bonding and adhesion to organic polymers (47).

The dye industry has reported several uses for gluconic acid and its salts; one of the earliest has been its use to increase the solubility of borate in diazo reproduction processes (21). The complexing agent also has been used as a reducing agent in vat dyes containing polyvalent metal ions (3) and also for the stabilization of other dye systems at high pH values (88). Peroxide bleaching solutions are reported to be stabilized by the addition of magnesium gluconate under alkaline conditions (139).

In the tanning industry sodium gluconate has been used to complex iron(III) solutions in order to increase the iron uptake and provide higher shrinkage temperatures (16, 34, 131). The acid has been used also in tanning solutions containing chromium ions (17) and zirconium ions (105). Gluconate complexes of stannous ion have been reported to be effective curing agents for organopolysiloxanes (124).

C. MEDICAL APPLICATIONS

The properties and physiological importance of the gluconates of calcium(II), magnesium(II), sodium(I), potassium(I), and iron(II) have been reviewed (126). These gluconate salts plus those of copper(II), ammonium(I), cobalt(II), and manganese(II) have been reviewed in terms of their properties and biochemical applications (41). Gluconate salts are important in biological applications because the gluconate radical is not metabolized by animal tissues but is excreted.

Gluconate ion has been used to provide a dialyzable iron(III) compound (68) and as a means of freeing calcium bound by protein and thereby increasing the amount of free calcium ion in the blood (78). Distribution of radioactive hafnium(IV) between various organs has been studied using gluconate ion as a complexing agent (75). Also, a mixture of sodium citrate and calcium gluconate has been used to eliminate radioactive cerium ions from rats (113).

There have been reports that copper(II) gluconate is useful as a central nerve stimulant (31) and that sodium antimony gluconate is useful for treating Indian cala-azar (33). The calcium and ammonium salts of antimony gluconate have been reported as new antibilharzial compounds (77). The mixed complex formed by calcium ion, boric acid, and gluconic acid has been found useful for treating milk fever (2, 76).

A number of applications of gluconic acid have been reported for stabilizing tetracycline (1, 50, 87, 107, 112). These have involved complexation of zirconyl halides (87) as well as a number of complexes formed by the aluminum–gluconate–tetracycline system with the ions of calcium, antimony, cadmium, chromium, cobalt, copper, gold, iron, manganese, nickel, selenium, silver, strontium, tin, and zinc (112). Aluminum and copper ions have been used together with gluconic acid to stabilize tetracycline-type antibiotics (107). The addition of aluminum ion and gluconic acid is reported to permit a higher level of the antibiotic in the blood (1). The addition of gluconic acid apparently permits the inclusion of a number of metal ions that leads to a stabilization of the antibiotic, an increase in its solubility, and a decrease in its toxicity. Gluconate salts also have been used to sequester iron(III) out of alkaline solutions which are to be used for precipitating the potassium salt of penicillin (10).

Addition of gluconate ion to a dentifrice containing stannous ion and fluoride ion has been recommended as a means of decreasing the solubility of dental enamel (51). The use of gluconic acid to produce a water-soluble aluminum complex has been suggested for antiperspirant preparations (59).

D. AGRICULTURAL APPLICATIONS

Ferric gluconate has been reported to be an ineffective agent as a foliar spray for chlorosis in pear trees (6). On the other hand, ammonium gluconate has been found useful as a foliage spray to help prevent after-cooking darkening of potatoes (123). This is believed to be due to complexing of iron(III) in the tubers and thereby masking it from subsequent reaction.

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