Complex formation and lactonization reactions in aqueous solutions containing Ca$^{2+}$ or Nd$^{3+}$ ions and sugar-type ligands

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Ph.D. Theses

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1. Introduction

Polyhydroxy carboxylic acids can be synthetized by the oxidation of carbohydrates. D-gluconic acid, being a member of this family, is used in general as an additive for food industry, while its sodium salt (NaGluc) is applied in chelation therapy, metallurgy as well as in paper industry.

NaGluc, applied as an additive for the formulation of cementitious materials, is likely to be present in the pore water of low- and intermediate-level radioactive waste repositories established in underground salt mines. Based on literature results, highly stable binary and ternary complexes are formed between Gluc\(^-\), trivalent actinide ions (An\(^{3+}\)) as well as Ca\(^{2+}\) ions arising from Portland cement. The ligand therefore can facilitate the mobilization of radionuclides, originally deposited in the form of hydroxides of low solubilities. Hence, the complexation equilibria taking place between these species are pivotal to be quantitatively described from the point of view of environmental protection.

In our previous works, multinuclear complexes were found to be formed between Ca\(^{2+}\) and Gluc\(^-\) ions in strongly alkaline medium. For Nd\(^{3+}\), being frequently used as a model for An\(^{3+}\) ions, the formation of mononuclear complexes was only detected to date. Moreover, the impact of the configuration of the ligand on various association processes is still not fully understood. The stereochemistry can affect both the stability and the structure of coordination compounds being important in fundamental research.

2. Aims of the work

During this research, we aimed at determining the composition, stability constant and the metal ion-binding sties of complexes forming between Nd\(^{3+}\) and Gluc\(^-\) ions in the pH range of 2–8. Furthermore, our goal was to assess how the incident multinuclear complexes would affect the equilibria occurring in radioactive waste repositories.

In order to reveal the role of configuration, the diastereomer of D-gluconate, L-gulonate (Gul\(^-\)) that is, was chosen as a model compound. For a comprehensive description, we studied the lactonization processes taking
place in acidic medium as well as the Ca(II) complexation reactions occurring in neutral and alkaline solutions. We compared our results with those reported in the literature for D-gluconate and D-heptagluconate (Hpgl–). The effect of different functional groups for the stability was investigated via the complexes forming between Ca\(^{2+}\) ions and the derivatives of D-glucose.

3. Experimental

The protonation constant of Gul– was determined by potentiometric titrations, polarimetric, \(^1\)H and \(^{13}\)C spectroscopic measurements, while the \(\gamma\)- and \(\delta\)-lactonization constants for gulonic acid were estimated with the aid of \(^{13}\)C NMR spectra. In order to validate the results, the lactoniziton experiments were carried out with gluconate as well, and the results were compared with literature data. The relative stability of gulonolactones was assessed via quantum chemical computations as well. The time dependence of lactonization was followed by \(^{12}\)C NMR spectroscopy and polarimetry.

Concerning Ca\(^{2+}\) ions and D-glucose or its derivatives (D-sorbitol, D-mannitol, D-gluconate, D-heptagluconate, D-glucuronate and D-glucarate), the complex formation equilibria taking place in neutral medium were studied by potentiometric titrations applying Ca\(^{2+}\) ionselective electrode (Ca-ISE).

In the presence of Ca\(^{2+}\) and Gul– ions, the association and deprotonation processes occurring in neutral and alkaline media were followed potentiometrically employing Ca-ISE and hydrogen electrode. The conformational changes of the ligand upon complexation was studied by polarimetry, while the structure of the CaGul\(^{+}\) species was modelled by quantum chemical calculations. The possible coordination sites of Gul–, Gluc– and Hpgl– were deduced on the basis of \(^1\)H and \(^{13}\)C NMR spectra.

The complex formation processes between Nd\(^{3+}\) and Gluc– ions were studied by means of potentiometry and spectrophotometry. The binding sites were assigned on the basis of \(^1\)H NMR spectra, whilst the structure of the NdGlucH\(_2\)\(^0\) species was optimized by quantum chemical methods.
4. New scientific results

T1. Of the five- and six-membered cyclic esters of L-gulonic and D-gluconic acids, the L-gulonic aid γ-lactone (γ-HGul) was proven to be by far the most stable species.

The lactonization constant was estimated on the basis of the $^{13}$C NMR peak areas belonging to the lactone or the acid form. Our calculations were validated by comparing the determined and the literature values for the gluconolactones. As a result, the lactonization constant of γ-HGul is higher nearly by one order of magnitude than that of the other three isomers (δ-HGul, γ-HGluc, δ-HGluc). According to the time dependence of the lactonization reactions, the formation of the δ-lactone is much faster; however, the hydrolysis of the γ-lactone is much slower yielding larger equilibrium constant.

T2. It has been demonstrated that gulonic acid is able to catalyze its own lactonization as well as the reverse reaction, the hydrolysis of the lactone.

Assuming solely the well-known proton-catalyzed esterification, hydrolysis does not result in satisfactory fitting between the measured and calculated optical rotations. The deviations can be markedly decreased by considering that the formation and hydrolysis of the predominant γ-lactone can also be catalyzed by L-gulonic acid as a source of protons. The respective rate coefficients are smaller by an order of magnitude than those of the traditional acid catalysis. This finding can be explained considering that $\text{H}^+$ more readily dissociates from $\text{H}_2\text{O}^+$ than from HGul.

T3. In addition to the known 1:1 calcium(II) complexes, species with 1:2 stoichiometry were found to be formed with aliphatic polyhydroxy carboxylates in neutral medium.

By means of the potentiometric method, the formation of 1:2 complexes can be detected for L-gulonate, D-gluconate as well as D-heptagluconate on applying high ligand to metal ratios. Additionally, our findings are confirmed by the literature data corresponding to Gluc$^-$. Furthermore, the fact that such
species cannot be observed for the cyclic D-glucuronate points to the key role of ligand flexibility.

T4. It has been established that the stability of the 1:1 calcium(II) complexes ranges in the order of D-glucose < D-mannitol < D-sorbitol < D-glucuronate < L-gulonate < D-heptagluconate ≈ D-gluconate < D-glucarate.

This order reflects the role of (i) ligand flexibility (glucose < sorbitol and glucuronate < gluconate), (ii) spatial arrangement of the OH groups (mannitol < sorbitol), (iii) participation of the COO\(^-\) functional group (sorbitol < gluconate) and (iv) the number of COO\(^-\) moieties.

T5. Our results confirmed that the highly stable Ca\(_3\)Gul\(_2\)H\(_4\)\(_0\) species was readily formed in alkaline medium in agreement with previous findings found for Gluc\(^-\) and Hpgl\(^-\). It was shown that the conformation of the complexed Gul\(^-\) markedly differed from that of the free anion inferring the deprotonation of the OH group(s).

In agreement with our previous results, the interpretation of the potentiometric titration curves requires the assumption of the trinuclear, neutral complex. It can be stated that the complexation reactions of polyhydroxy carboxylates are very similar in a given pH-range, while the processes taking place in neutral or alkaline solutions are very different. When the Ca\(^{2+}\)/Gul\(^-\)-system is concerned, the metal-promoted deprotonation of the ligand leads to significant change in the conformation, hence, the specific rotation of Gul\(^-\).

T6. It was found that for the complexes forming in alkaline medium, the different configurations result in different coordination sites.

For Gluc\(^-\), the C2-OH and C3-OH, while for Gul\(^-\) and Hpgl\(^-\), the C2-OH and C4-OH functions (beyond COO\(^-\)) are the most probable metal ion binding sites. Consequently, if the configuration of the C2-OH and C3-OH groups is threo (Gluc\(^-\)), the C3-OH, if it is erythro (Gul\(^-\), Hpgl\(^-\)), the C4-OH group participates in the complexation. (The arrangement of the C3-OH and C4-OH functions is treo in each ligand.)
T7. Beside the already known mononuclear species, unexpected binuclear Nd(III) gluconate complexes were found to be formed on applying higher metal ion concentrations. By our calculations, however, these species do not affect the equilibria under the conditions prevailing in radioactive waste repositories.

Simultaneous fitting of the potentiometric and spectrophotometric data resulted in that the (previously unknown) Nd₂Gluc₃H₂⁺ and Nd₂Gluc₄H₂₀⁻ complexes were formed to a significant extent. Conversely, the solubility of Nd(OH)₃ and the estimated concentration of gluconate being present in waste deposits (< 0.01 M) indicates that these binuclear species do not have considerable impact on the equilibria occurring in pore waters. On the other hand, the mononuclear NdGlucH₂₀⁻ species becomes predominant upon increasing pH.

5. Practical applications

Although, our work was mostly of fundamental nature, we believe that the results presented here help to better understand and model the complicated equilibrium systems affecting the long-term stability of waste repositories. Moreover, our findings concerning the stability and structure of Ca(II) complexes forming in neutral and alkaline media may be useful for the characterization of certain industrial processes, when polyols, polyhydroxy carboxylates and/or other metal ions are applied.

6. Publications and conference participations

6.1. Full papers directly related to the Theses published in peer-reviewed journals

1. B. Kutus, Cs. Dudás, G. Peintler, I. Pálinkó, P. Sipos: Configuration-dependent complex formation between Ca(II) and sugar carboxylate ligands in alkaline medium: comparison of L-gulonate with D-gluconate and D-heptagluconate
impact factor (2016): 2.096

    impact factor (2016): 4.029

3. B. Kutus, D. Ozsvár, N. Varga, I. Pálinkó, P. Sipos: ML and ML₂ complex formation between Ca(II) and D-glucose derivatives in aqueous solutions
    impact factor (2016): 4.029

4. B. Kutus, Á. Buckó, G. Peintler, I. Pálinkó, P. Sipos: Calcium-complexation and acid-base properties of L-gulonate, a diastereomer of D-gluconate
    impact factor (2016): 4.029

6.2. Full papers directly related to the Theses published in conference proceedings

1. Á. Buckó, B. Kutus, G. Peintler, I. Pálinkó, P. Sipos: Az L-gulonátió protonálódásának és laktonizációjának vizsgálata (Studying the protonation and lactonization of the L-gulonate ion)

6.3. Full papers not directly related to the Theses published in peer-reviewed journals

    impact factor (2016): 4.029
2. A. Gácsi, B. Kutus, Z. Csendes, T. Faragó, G. Peintler, I. Pálinkó, P. Sipos: Calcium L-tartrate complex formation in neutral and in hyperalkaline aqueous solutions


impact factor (2016): 4.029

3. A. Gácsi, B. Kutus, Z. Kónya, Á. Kukovecz, I. Pálinkó, P. Sipos: Estimation of the solubility product hydrocalumite-hydroxide, a layered double hydroxide with the formula of \([\text{Ca}_2\text{Al(OH)}_6]\text{OH}\cdot\text{nH}_2\text{O}\)


impact factor (2016): 2.059

4. B. Kutus, A. Gácsi, A. Pallagi, I. Pálinkó, G. Peintler, P. Sipos: A comprehensive study on the dominant formation of the dissolved \(\text{Ca(OH)}\text{2(aq)}\) in strongly alkaline solutions saturated by \(\text{Ca(II)}\)

*RSC Advances*, 2016, 6, pp. 45231–45240.


5. Gácsi A., B. Kutus, Á. Buckó, Z. Csendes, G. Peintler, I. Pálinkó, P. Sipos: Some aspects of the aqueous chemistry of the \(\text{Na}^+\)/\(\text{Ca}^{2+}\)/\(\text{OH}^-\)/\(\text{Cit}^{3-}\) system: The structure of a new calcium citrate complex forming under hyperalkaline conditions


impact factor (2016): 1.753

6. A. Pallagi, É. G. Bajnóczi, S. E. Canton, T. Bolin, G. Peintler, B. Kutus, Z. Kele, I. Pálinkó, P. Sipos: Multinuclear complex formation between \(\text{Ca(II)}\) and gluconate ions in hyperalkaline solutions


impact factor (2014): 5.330

7. A. Pallagi, Z. Csendes, B. Kutus, E. Czeglédi, G. Peintler, P. Forgo, I. Pálinkó, P. Sipos: Multinuclear complex formation in aqueous solutions of \(\text{Ca(II)}\) and heptagluconate ions


impact factor (2013): 4.097
8. Z. Csendes, J. T. Kiss, B. Kutus, P. Sipos, I. Pálinkó: Ni-S(uper)o(xide)-D(ismutase) inspired Ni(II)-amino acid complexes covalently grafted onto Merrifield’s resin – synthesis, structure and catalytic activity  
   impact factor (2013): 0

6.4. Other full papers not directly related to the Theses published in conference proceedings

1. Á. Buckó, B. Kutus, G. Peintler, I. Pálinkó, P. Sipos: Temperature dependence of proton dissociation and complexation processes in the Ca\(^{2+}\)/gluconate system under hyperalkaline conditions  

2. C. Dudás, B. Kutus, R. Bélteki, A. Gácsi, I. Pálinkó, P. Sipos: Acid-base properties and calcium complexation of α-ketoglutarate in strongly alkaline aqueous solutions  

3. É. Böszörményi, Cs. Dudás, B. Kutus, I. Pálinkó, P. Sipos: Az izoszacharinát- és a glükonát-ion sav-bázis és kalcium-komplexképző tulajdonságainak összehasonlítása (Comparison of the acid-base properties and the calcium complexing ability of the isosaccharinate and the the L-gulonate ions)  

5. **B. Kutus**, G. Peintler, A. Pallagi, I. Pálinkó, P. Sipos: Kalcium-cukorkarboxilát komplexek vizsgálata egyszerű fizikai-kémiai módszerekkel (Studying calcium(II) sugar carboxylate complexes by simple physico-chemical methods)


6.5. **Other conference participations**

Co-author of 15 lectures presented in international conferences
Co-author of 16 lectures presented in Hungarian conferences
Co-author of 12 posters presented in international conferences

**Full papers published in peer-reviewed journals:**

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10