SYNTHESIS AND CALCIUM COMPLEXATION OF OXIDIZED CARBOHYDRATES AND MODEL POLYOXYGEN SYSTEMS

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Proefschrift

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Aan Rita

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CHAPTER I

GENERAL INTRODUCTION

Ca(II) complexation in biological and technical systems

The coordination of Ca(II) ions by organic and inorganic compounds is of interest because of the importance in both biological processes and also some technological applications.

The Ca(II) ion belongs to the four significant alkali and alkaline earth metal ions in living systems[1,2]. The regulation of many biological processes occurs by interactions of Ca(II) ions with proteins, e.g. muscle contraction, blood clotting, mineralization and growth. The proteins act as organic ligands with negatively charged and neutral oxygen donor atoms (carboxylate, carbonyl and hydroxyl) as well as nitrogen donor atoms.

A technological example in which Ca(II) coordination plays a role, is the formulation of detergents for washing processes[3,4,5]. When synthetic detergents were first introduced in the early 1940's for home laundry use, it was found that they could not equal the performance of soap without an effective so-called builder. A typical European detergent formulation of the 1960's and early 1970's is shown in Table I. It contains 30-40% (w/w) of such a builder, especially sodium triphosphate (STP). In the washing process STP plays a key role because of the following properties[6]: sequestering ability, deflocculating ability, alkalinity, buffering power, bleach compatability and additional safety and low cost. The most important of these properties is the sequestering ability, for it prevents the adverse effects of Ca(II) and Mg(II) ions present in hard water. These effects are:

- Precipitation of mineral salts on fabrics and washing machine parts.
- Precipitation of insoluble salts of surfactants, thereby reducing their concentration.
- Decrease of pigment soil removal from textiles.

Table I. Typical detergent formulation of the sixties and seventies[4].

Component type	% (w/w)	Example
Surfactant	10-15	anionic: alkyl benzene sulphonate, soap nonionic: ethoxylated linear alcohols
Complexing agent (builder)	30-40	sodium triphosphate
Bleaching agent	20-30	sodium perborate
Corrosian inhibitor	3-6	silicates
Foam inhibitor	2-3	special soaps
Anti redeposition agent	0.5-2	carboxymethylcellulose
Perfumes	0.1-0.2	--
Optical brightener	0.1-0.3	stilbene and pyrazolin derivatives
Stabilizing agent	0.2-2	EDTA, magnesium silicate
Filler	5-15	sodium sulphate, sodium chloride

- Increase of pigment soil redeposition.

During the last two decades, however, detergents containing phosphates have been under indictment as a significant cause of environmental problems: eutrophication in lakes and stagnant waters.

Phosphate and the environment

In the 1960's growing social awareness of and concern for the quality of the environment, especially the natural waters, began to focus on eutrophication phenomena. Of all of the 20 chemical elements essential to the growth of algae phosphorus is, in most cases, the limiting nutrient factor for the intensity of algal biological cycles. When phosphate is added to surface waters the nutrient situation becomes eutrophe: all elements are plenty available. In the summer, when light is not the limiting factor, algal growth becomes intensive. Oxygen- as well as lighttransport to deeper areas is hindered and detritus (biological and chemical degradation of the algae) starts. In the depth the water becomes anaerobe, causing H_2S development. Additionally blue-green algae produce toxines which cause fish mortality.

Internationally the discussion on eutrophication and its environmental effects was initiated by a report of Vollenweider[7], in the Netherlands by publications of Golterman[8]. A number of possible measures can be taken to decrease the phosphate supply to the surface water or to remove phosphates

from the surface water:

1. Removal of phosphates in a third stage of sewage plants. Upon addition of Fe(III) or Al(III) ions to the effluent of a two-stage sewage plant precipitation of Fe or Al phosphates occurs. In this case about 90% can be removed.
2. Substitution of phosphates (i.e. sodium triphosphate) in detergent formulations. In the Netherlands the contribution of detergent phosphates to the total phosphate supply in surface waters is 11-12% (1970: 8.8 10^6 kg P out of 80.3 10^6 kg P [9]; 1980: 12.3 10^6 kg P out of 108.0 10^6 kg P [10]). When the contribution of international rivers is excluded, this number becomes about 30%.
3. Removal of phosphates in the second stage of sewage plants. In some cases[11] 80-90% of the phosphate can be removed: 6-8% P is built in the cell of Acinetobacter when alternating anaerobic/aerobic circumstances are created. This method is already applied in the USA and South Africa. It may be noted that in a conventional biological sewage treatment 20% of phosphate is removed.
4. Removal of phosphate-containing mud by dredging.

Depending on local environmental situations and also political situations governments in Northern America and Western Europe have chosen for one or more of the above-mentioned measures. In the USA, Canada, Switzerland, Norway, Sweden, Finland, Italy and West Germany legal measures have been taken to decrease or even omit phosphates in detergent formulations. In addition many third stage sewage plants are now operable in the USA, Canada, Sweden and West Germany.

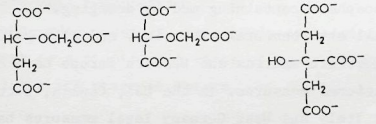
In 1979 the Dutch Government[12] has decided to choose two ways to decrease phosphates in surface waters: both introduction of third stage sewage plants and a 100% phosphate ban for detergents in 1985. As a consequence of the economical situation at this moment only a few third stages have been built, while a complete phosphate ban has been postponed until 1987. In the meantime detergent manufacturers have already decreased the phosphate content in phosphate-containing heavy-duty household detergents[13] (1977: 7-12% P[13]; 1984: 5% P[14]).

The contribution of phosphates from agriculture now has been recognized to be substantial too and measures are in progress[13].

Phosphate substitutes

Preceding the political decisions concerning the phosphate problem, extensive industrial research programs have been initiated to search for a suitable phosphate substitute. Phosphate substitutes must possess comparable builder properties as STP, they should be acceptable from an economical and technological point of view, and organic systems should owe an acceptable biodegradability. The outcome of these research efforts can be devided into four groups of phosphate substitutes:

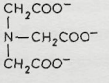
Low molecular weight organic systems. As there is at least some degree of environmental concern with the elements B, N, P and S the remaining elements to act in structural building units for organic builder systems are C, H and O together with Na and K as monovalent counterions. Among the numerous compounds mentioned in the (patent) literature one finds etherpolycarboxylates[15-22], especially carboxymethyloxysuccinate (CMOS)[23-25], carboxymethyloxymalonate (CMOM; "builder M") and citrate.



CMOS CMOM Citrate

CMOS, CMOM and citrate are only moderate builders, but are sufficiently biodegradible. The eventual success experienced by CMOS and CMOM will be affected by their ultimate builder performance and selling price. Citrate is used in some phosphate free detergent formulations in the USA. Its weaker sequestering properties are compensated by employing higher levels of surfactants.

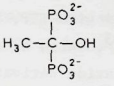
Despite their nitrogen content aminopolycarboxylates have also been investigated[15-17,20,26,27]. Studies of this type quickly led to ethylene-diamine tetraacetate (EDTA) and its structural analog nitrilotriacetate (NTA).



NTA

As EDTA is more expensive and less efficient in calcium sequestration on a weight basis and has also a worse biodegradability, NTA is the best known example of an aminopolycarboxylate builder[15,17]. It is the most developed candidate for the replacement of STP and the commercial production of NTA for detergent use in the USA has started in the late 1960's. On 18 December 1979 the Surgeon General of the US Department of Health, Education and Welfare demanded withdrawal of NTA from detergents, pending the resolution of questions concerning NTA's long term effects on human safety. After considerable research NTA has got the green light for use as a builder in the USA in 1980[28,29]. Canada, Sweden, Switzerland and the Netherlands have never forbidden NTA, whereas in West Germany NTA is allowed in limited amounts[30].

Polyphosphonates[15,17] have also been investigated. An increased calcium sequestering ability per gram P has been achieved, i.e. a partial reduction of the P-content of detergents. Especially 1-hydroxyethane 1,1-diphosphonate (HEDP)[17] may be mentioned. Widespread acceptance of phosphonates in detergents was prevented by their insufficient biodegradation.



HEDP

Sulphopolycarboxylates[20,31] have also been mentioned. Citrex-C5, a mixture of aliphatic sulphonated polycarboxylic acids, obtained starting from citric acid, act as a precipitation-inhibitor and not as a calcium complexing agent. During several years Citrex-C5 has been applied in a dutch detergent formulation, but in 1981 its manufacturer shifted to NTA as a builder.

Builder systems containing mixtures of D-glucarate and borate have been claimed by CCA in the Netherlands[32] and are being investigated in our laboratory by Van Duin[33].

Scientific contributions to the development of low-molecular weight organic builders have been made by Abe and Matsumura et al.[34-45], Ogino[46,47] and Chang[22].

In Table II the complex stability constants (K_{Ca}) of Ca(II) and Mg(II) complexes of some of the above-mentioned compounds are listed.

Table II. Ca(II) and Mg(II) complex stability constants of STP and potential STP substitutes

Complexing agent	Log K_{Ca}	Log K_{Mg}
STP	5.2	5.7
CMOS	4.0	2.7
CMOM	4.6	2.8
Citrate	3.5	2.8
EDTA	10.7	8.7
NTA	6.4	5.4
HEDP	6.0	6.6

High molecular weight organic systems. Among this group one finds all kinds of synthetic polymeric carboxylates[15,17,19-22,48-54], in particular polymers and/or copolymers of maleic acid, acrylic acid, methacrylic acid, methyl vinyl ether, and α-hydroxyacrylic acid. Some of these polymers give excellent builder performances when compared with STP, but biodegradation is often a problem. Acetal polycarboxylates[55], which have also been claimed as phosphate substitutes, as well as polysaccharide derivatives or oxidized polysaccharides[15,17,21,56-59] often possess better biodegradation properties, due to the presence of acetal moieties that tend to hydrolyse in acid (waste water) medium.

Low molecular weight inorganic systems[16,17,60]. Sodium carbonate is used in some non-phosphate detergent formulations, most often together with silicates. Silicates are long-established detergent components. In addition to providing alkalinity they act as deflocculants and anticorrosion agents, but are not able to sequester calcium ions. In such combined formulations sodium carbonate softens hard water by precipitation of insoluble calcium carbonate rather than by formation of soluble complexes. These precipitates build up deposits on textile. Moreover, these carbonate/silicate formulations exhibit a high alkalinity, which can cause skin or eye irritation. The above-mentioned formulations are mostly used in the USA as emergency formulations in 100% phosphate ban areas, awaiting better non-phosphate detergents. Due to the much harder water in Europe these systems have not been applied.

In the Netherlands AKZO[61] has introduced a so-called "washing-bag", which consists of a two-component paper bag. The bag is placed on the clothing inside the washing machine. During the washing process at first a mixture of

low-molecular organic acids is released from the first compartment in order to redissolve the calciumcarbonate deposits remaining from an earlier washing treatment. At higher temperature a carbonate/silicate detergent formulation starts to wash. This formulation is leaving behind a calciumcarbonate deposit which is removed the next time.

"High molecular weight" inorganic systems[62-73]. The major representatives of this group are the zeolites, especially zeolite NaA. This water insoluble inorganic ion exchanger takes over the phosphate role of decreasing calcium and magnesium ion concentration. Zeolite NaA cannot be used as phosphate substitute without a small amount of a water soluble builder. This so-called co-builder is removing calcium ions, that form bridges between textile and dirt via an adsorption/desorption process. In the washing water Ca(II) and to a lesser extent Mg(II) ions are being exchanged for Na(I) ions by the zeolite and the soluble builder can start its job again.

At the moment zeolite-containing detergents are used in both the USA and Europe. Table III is showing a typical zeolite detergent formulation as given by Diehl et al.[74]. In the USA Procter and Gamble changed from zeolites back to phosphates in 1983[75]. It has been stated that the performance of these zeolite-containing detergents at low temperature did not come up to expectations, although economical factors might be the true reasons[76].

Table III. Zeolite containing detergent formulation[74].

Component	% (w/w)
Alkyl benzene sulphonate	2.7
Ethoxylated fat alcohol	7.0
Soap	2.8
Zeolite NaA	21.0
Co-builder (NTA)	2.4
Sodium perborate	19.0
Sodium silicate	6.0
Sodium carbonate	3.0
Enzyme	0.2
EDTA	0.2
Optical brightener	0.2
Sodium sulphate	18.5
Water	7.0

Scope of this thesis

In attempting to mimic the various profitable properties of STP, its Ca(II) complexing properties are probably the most indispensable. In this laboratory calcium complexing properties of polyoxygen compounds have been studied[77,78] in order to deepen the insight into the stoichiometry of the complexes, the coordination behaviour and the conformation of the ligands.

In this thesis Ca(II) complexation phenomena have been studied from a more quantitative point of view by correlating structural and conformational influences on complex stability constants. In this way especially oxidized carbohydrates, of low, medium and high molecular weight, and a series of model compounds have been synthesized. Carbohydrates are often relatively inexpensive and attractive renewable base materials for the manufacture of oxygen-rich compounds. The required biodegradability of potential phosphate substitutes in the case of these oxidized carbohydrates is expected to be good. Because of the presence of acetal moieties, these substances are expected to undergo facile hydrolysis in acidic waste water, they are relatively stable under alkaline washing conditions.

The investigations as presented in this thesis have been performed from 1979 to 1984 and have been published or will be published soon. The thesis includes work on the syntheses (Ch. II[79], III[80], IV, V[81], VII[83]) and on the calcium complexing properties (Ch. V[81], VI[82], VII[83]) of a number of oxidized carbohydrates and model compounds.

A study on the combination of a low molecular weight organic system and a crystalline inorganic system (zeolite NaA) is described in Chapter VIII[84]. This study deals with equilibrium and kinetical measurements of Ca(II) and Mg(II) ion exchange by the zeolite.

Chapter IX deals with the complexation of lanthanide(III) ions with STP as studied with a number of NMR techniques[77,78] developed in this laboratory. Lanthanide(III) ions may serve as probes for Ca(II)[78]. The aim of this chapter is to elucidate the structure of the lanthanide(III)/$(STP)_2$ complex.

For the reader's convenience the matrix below shows the various aspects of this thesis as they appear in the chapters (they are given as keywords).

Chapter	Organic	Inorganic	Low molecular	High molecular	Synthesis	Complexation
II	●		●		●	
III	●		●		●	○
IV	●		●		●	
V	●		●		●	●
VI	●		●			●
VII	●			●	●	●
VIII	●	●	●	●		●
IX		●	●			●

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CHAPTER II

PERMANGANATE OXIDATION OF 4,7-DIHYDRO-1,3-DIOXEPINS: A NEW METHOD FOR THE PREPARATION OF BIS(CARBOXYMETHYL) ACETALS VIA ACETALISATION WITH (Z)-2-BUTENE-1,4-DIOL*

Several bis(carboxymethyl) acetals have been proposed as potential substitutes for phosphate in detergent formulations[1,2,3]. An important property of this type of compound is the low stability in acidic waste water, which facilitates degradation.

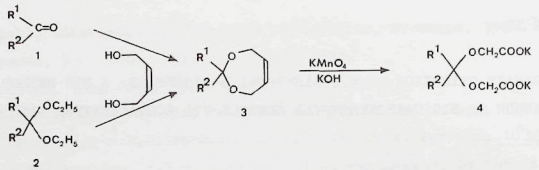
For the preparation of bis(carboxymethyl) acetals the reaction of carbonyl compounds with sodium ethyl glycolate and ethyl bromoacetate and the reaction of geminal dihalogen compounds with sodium ethyl glycolate have been reported in the patent literature[1,3]. When applying solid acids, such as amorphous silica-alumina, as catalysts[4] in the reaction of carbonyl compounds with an alkyl glycolate, yields proved to be poor. This is possibly due to preferential adsorption of the alkyl glycolate or the reaction product on the catalyst.

As an alternative we report here a convenient two step synthesis of bis(carboxymethyl) acetals (Scheme 1):

Firstly, the carbonyl compound (1) is converted to a 4,7-dihydro-1,3-dioxepin (3) by reaction with (Z)-2-butene-1,4-diol[5] or by trans-acetalisation via diethyl acetals (2)[6].

Secondly, 3 is oxidized by potassium permanganate in aqueous potassium hydroxide to the respective potassium bis(carboxymethyl) acetal 4.

* M.S. Nieuwenhuizen, A.P.G. Kieboom, and H. van Bekkum, Synthesis 1981, 612.



a: R^1 = H; R^2 = H
b: R^1 = CH_3; R^2 = H
c: R^1 = CH_3; R^2 = CH_3
d: R^1 = H; R^2 = $CH{=}CH_2$ (COOK in 4)
e: R^1 = CH_3; R^2 = COOK

Scheme I

In the preparation of 4e, pyruvic acid gave 3e as the (Z)-2-butene-1,4-diol ester, which was saponified before the permanganate oxidation. The overall yield for 4a-e was 45-90%. Permanganate oxidations of 3 occurred almost quantitatively *at 0 °C in aqueous potassium hydroxide. In the present* procedure potassium salts are obtained. Generally, preparation of the free acids with this method is not possible, due to low stability of the acetal bond at lower pH. Only the acetals 4d and 4e, which contain a stabilizing carboxylic group, could be obtained as the free acid by ion exchange at 0 °C.

4,7-Dihydro-1,3-dioxepins 3a-c from acetals 2a-c: A mixture of 2 (125 mmole), (Z)-2-butene-1,4-diol (23.3 g, 265 mmole) and p-toluenesulfonic acid hydrate (2 mg) was slowly distilled at atmospheric pressure. Redistillation yielded compounds 3: 3a (55%); b.p. 125-127 °C (Lit. 7: 127 °C), 3b (46%); b.p. 136-137.5 °C (Lit. 8: 137-138 °C), and 3c (65%); b.p. 144-146.5 °C (Lit. 6: 144.5-147 °C). The fractions were > 95% pure (GLC) and the ^{1}H NMR, ^{13}C NMR and MS spectra confirmed their structure.

2-Vinyl-4,7-dihydro-1,3-dioxepin (3d): A mixture of acrolein (14.0 g, 0.25 mmole), (Z)-2-butene-1,4-diol (22.0 g, 0.25 mole) and p-toluenesulfonic acid hydrate (5 mg) in benzene (150 ml) was boiled in a Dean and Stark equipment for 3 h to produce the theoretical amount of water (4.5 ml). Distillation yielded 18.8 g of 3d (60%); b.p. 155-159 °C (Lit. 9: 154-155 °C). ^{1}H NMR, ^{13}C NMR, and MS spectra confirmed its structure.

2-Carboxy-2-methyl-4,7-dihydro-1,3-dioxepin (3e): A mixture of pyruvic acid (17.6 g, 0.20 mole), (Z)-2-butene-1,4-diol (35.2 g, 0.4 mole) and p-toluenesulfonic acid hydrate (5 mg) in benzene (150 ml) was boiled in a Dean and Stark equipment for 12 h to produce the theoretical amount of water (7.2 ml). The reaction mixture was concentrated in vacuum and 150 ml 1.5 N potassium hydroxide was added. After 2 h the pH was brought to 9 with Dowex AG-50W-X8 (H^+) and water was evaporated at 45 °C. The residual syrup was extracted with 3 x 200 ml acetone to remove (Z)-2-butene-1,4-diol. The remaining solid was dried in vacuo above potassium hydroxide to yield 35.3 g of 3e (90%); m.p. 96-98 °C. $C_7H_9O_4K$: C: found 42.28% (calc. 42.84%), H: found 4.96% (calc. 4.62%). ^{1}H NMR (D_2O): δ = 1.47 (s, 3H, CH_3), δ = 4.25 (AA'BB', 4H, CH_2), δ = 5.73 ppm (m, 2H, CH). ^{13}C NMR (D_2O): δ = 19.8 (CH_3), δ = 61.7 (CH_2), δ = 128.1 (CH), δ = 102.2 (OCO), δ = 175.2 ppm (COO).

Permanganate oxidation of 3c: Compound 3c (1.3 g, 10 mmole) was added within 0.5 h to a solution of potassium permanganate (4.8 g, 30 mmole) and potassium hydroxide (0.5 g, 9 mmole) in H_2O (100 ml) at 0 °C. After 2 h the reaction mixture was filtered, brought to pH = 9 with Dowex AG-50W-X8 (H^+) and freeze dried from water (200 ml) to yield 4c as a solid (95%). M.p. 145 °C (decomp.). $C_7H_{10}K_2.2H_2O$: C: found 28.32% (calc. 27.63%), H: found 4.61% (calc. 4.60%) (Table 1).

Table 1. Bis(carboxymethyl) acetals 4 from dioxepins 3.

Comp.	δ (^{1}H NMR)[a]			δ (^{13}C NMR)[b]				
	CH_3	H	CH_2	CH_3	CH_2	OCO	COO	CO
4a	--	4.82 (s)	4.05 (s)	--	65.7	93.5	177.0	--
4b	1.38 (d)[c]	4.80 (q)[c]	4.00 (s)	17.7	63.7	99.0	176.8	--
4c	1.40 (s)	--	3.93 (s)	28.0	64.9	93.0	181.8	--
4d	--	4.87 (s)	4.00 (s)	--	64.3	97.8	176.3	172.4
4e	1.50 (s)	--	3.96 (s)	20.2	60.9	100.2	176.5	175.

[a] 37 °C, D_2O, sodium 2,2,3,3-tetradeutero-3-(trimethylsilyl)propionate as interna reference.

[b] 35 °C, D_2O, tetramethylammonium chloride as internal reference.

[c] J = 5 Hz.

Permanganate oxidation of 3a,b,e: Compound 3a, b, e were oxidized as above on a 4 mmole scale.

4a: M.p. 135 °C (decomp.). $C_5H_6O_6K_2.2H_2O$: C: found 21.82% (calc. 21.72%), H: found 3.37% (calc. 3.62%). Yield: 96%.

4b: M.p. 130 °C (decomp.). $C_6H_8O_6K_2.2H_2O$: C: found 24.32% (calc. 24.83%), H: found 4.02% (calc. 4.14%). Yield: 95%.

4e: M.p. 220 °C (decomp.). Yield: 94%.

The potassium salt 4e (0.67 g, 2 mmole) in water (50 ml) was treated with an excess of Dowex AG-50W-X8 (H^+) (8 meq) at 0 °C. After 1 h the reaction mixture was filtered and freeze dried from water (70 ml). Recrystallization from acetone yielded 0.36 g of the free carboxylic acid of 4e. M.p. 150 °C (decomp.). $C_7H_{10}O_8$: C: found 38.45% (calc. 37.85%), H: found 4.62% (calc. 4.54%). ^1H NMR (D_2O): δ = 1.78 (s, 3H, CH_3), δ = 4.43 ppm (s, 4H, CH_2).

Permanganate oxidation of 3d: Compound 3d (0.5 g, 4 mmole) was added within 0.5 h to a solution of potassium permanganate (3.8 g, 24 mmole) and potassium hydroxide (0.4 g, 7 mmole) in H_2O (50 ml) at 0 °C. After 4 h the reaction mixture was filtered and the filtrate treated with a slight excess of barium hydroxide octahydrate (0.66 g, 2.1 mmole) to remove formic acid. The solution was filtered again, brought to pH = 9 with Dowex AG-50W-X8 (H^+) and freeze dried from water (100 ml) to yield 4d as a solid (Table 1). M.p. 220 °C (decomp.). The potassium salt of 4d (0.32 g, 1 mmole) in water (50 ml) was treated with an excess of Dowex AG-50W-X8 (H^+) (8 meq) at 0 °C. After 1 h the reaction mixture was filtered and freeze dried from water (70 ml). Recrystallization from acetone yielded 0.15 g of the free carboxylic acid of 4d (98%). M.p. 135-137 °C (decomp.). $C_6H_8O_8$: C: found 34.58% (calc. 34.63%), H: found 3.87% (calc. 3.87%). ^1H NMR (D_2O): δ = 5.10 (s, 1H, H), $\delta \approx$ 4.27 ppm (s, 4H, CH_2).

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CHAPTER III

SYNTHESIS OF *MESO*- AND (±)-2,2'-BIS(CARBOXYMETHOXY)OXYDIACETIC ACID *VIA CIS*- AND *TRANS*-2,5-DIALLYLOXY-2,5-DIHYDROFURAN: MODEL COMPOUNDS FOR THE CALCIUM COMPLEXATION OF OXIDIZED SUCROSE*

Abstract

Cis- and *trans*-2,5-diallyloxy-2,5-dihydrofuran have been prepared by acid catalyzed transacetalization of 2,5-dimethoxy-2,5-dihydrofuran with allyl alcohol. As a by-product 1,1,3-triallyloxypropane was formed from 2-allyloxy-2,5-dihydrofuran intermediates. The *cis*/*trans* configuration has been determined by NMR (chiral lanthanide shift reagent) and MS (elimination of allyl alcohol). Oxidation of the *cis*- and *trans*-compounds by potassium permanganate yielded *meso*- and (±)-2,2'-bis(carboxymethoxy)oxydiacetic acid, respectively. The calcium sequestering properties of the latter compounds were better than for the acetal polycarboxylate obtained by sucrose oxidation. This is due to extra steric hindrance for the latter upon calcium complexation.

Introduction

In connection with our investigations[1] on the calcium sequestration of carbohydrate derivatives *meso* and *racemic* 2,2'-bis(carboxymethoxy)oxydiacetate (*meso* and (±)-6) were required as polycarboxylate model compounds, containing essential features of an oxidized carbohydrate. In *meso*- and (±)-6 three hydroxymethyl groups of oxidized sucrose (Fig. 1) are lacking. These groups are suspected to cause steric hindrance in the Ca(II) complex of oxidized sucrose. Furthermore, the specific (R,R,S,R) configuration of oxidized sucrose

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* M.S. Nieuwenhuizen, A.P.G. Kieboom, and H. van Bekkum, Recl. Trav. Chim. Pays-Bas 101, 339 (1982).

will also have its influence on Ca(II) complexation, so both meso and (±)-6 were required to establish stereochemical influences in Ca(II) complexation.

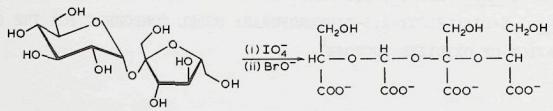


Fig. 1. Two-step oxidation of sucrose.

A laborious route to meso- and (±)-6 would be the synthesis of O-α-D-xylopyranosyl-α-D-xylopyranoside or O-β-D-xylopyranosyl-β-D-xylopyranoside, starting from triacetyl-α-D-xylopyranosyl bromide[2], followed by periodate and hypobromite oxidation[3].

A possible two-step synthesis would be the oxidation[4] of suitably substituted 2,5-dihydrofurans, which might be obtained by means of the Clauson-Kaas reaction[5], as shown in Fig. 2.

However, when using bifunctional alcohols as butyl glycolate or allyl alcohol[6], the desired product was formed only in small amounts accompanied by numerous other reaction products due to transesterification and/or transacetalization reactions.

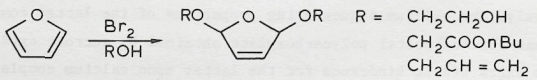


Fig. 2. Clauson-Kaas reaction to 2,5-dihydrofuran derivatives.

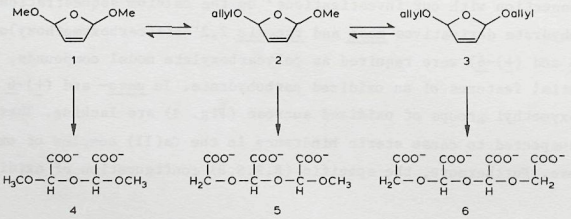


Fig. 3. Allyl alcohol transacetalization and permanganate oxidation of 2,5-dihydro-2,5-dialkoxyfurans

As an alternative we have studied the transacetalization of 2,5-dihydro-2,5-dimethoxyfuran with an excess of allyl alcohol and p-toluenesulfonic acid as the catalyst, followed by permanganate oxidation (Fig. 3). The Ca(II) complexation constants of meso- and (±)-6 thus synthesized are compared with that of oxidized sucrose.

Results and discussion

Reaction of 1 with a tenfold excess of allyl alcohol at room temperature gave 38% of the mixed acetals (2) and 42% of the diallyl acetals (3) at equilibrium. Selective adsorption of the methanol formed into zeolite KA and the addition of fresh acid and repeating this procedure gave the composition: 3% of 2 and 92% of 3. In another experiment methanol was removed by distillation. In this way 19% of 2 and 69% of 3 were obtained after 2 h. However, during this procedure and during distillation of a neutralized reaction mixture, considerable amounts of by-product 7 (Fig. 4) were formed. This by-product is also formed by reaction of acrolein and allyl alcohol under similar conditions (Fig. 4) by acetalization and addition.

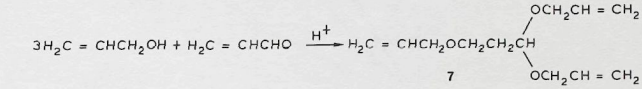


Fig. 4. Formation of by-product 7 from acrolein and allyl alcohol.

Probably, in situ formation of acrolein occurs by an acid catalyzed degradation of 2 or 3 (R: CH_3 or $CH_2CH{=}CH_2$, respectively) (Fig. 5).

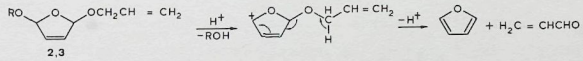


Fig. 5. Possible formation of acrolein from a 2-allyloxy-5-alkoxy-2,5-dihydrofuan.

As we required both 2 and 3 a reaction mixture consisting of 32% of 2 and 61% of 3 was separated by column chromtography into 2 and 3. Preparative gas

chromatography gave cis-3 (8.2%) and trans-3 (2.0%).

The structural assignment of cis-3 and trans-3 is based on the following spectroscopic data:

^{1}H NMR (200 MHz): All chemical shifts and coupling constants have been measured and checked by computer simulation. The main difference is noted for the acetal protons (trans-3: δ = 6.00 ppm; cis-3: δ = 5.74 ppm). A similar difference was observed by Barbier et al.[7] and Aito et al.[8] for 2,5-dihydro-2,5-dimethoxyfurans.

^{13}C NMR (20 MHz): All chemical shifts could be assigned on the basis of proton off-resonance spectra.

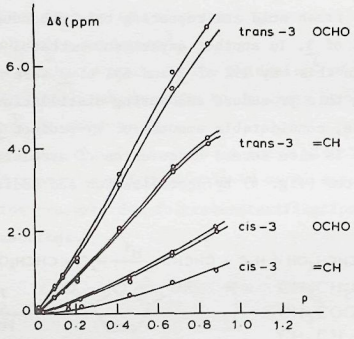


Fig. 6. Eu(hpc)$_3$ induced shifts ($\Delta\delta$) of acetal and vinylic ring protons of cis- and trans-3 versus the molar lanthanide-3 ratio (ρ) in $CDCl_3$.

Chiral lanthanide shift reagent: Tris[3-(heptafluoropropylhydroxymethylene)-d-campharato]europium(III) (Eu(hpc)$_3$)[9] was used to distinguish between cis-3 (one 1:1 complex expected with the chiral shift reagent) and trans-3 (two diastereomeric 1:1 complexes expected). Fig. 6 shows the results.

Both signals of trans-3 are separated in accordance with the trans configuration. At $\rho > 0.2$ the signals of cis-3 are also separated i.e. the protons become diastereotopic upon complexation. That this is the case is shown by the observed AB-pattern for the vinylic ring protons (Fig. 7). Simulation points to $\delta_3 - \delta_4$ = 2.7 Hz; $J_{3,4}$ = 6.0 Hz.

^{13}C satellites: From the ^{13}C satellites in the ^{1}H NMR spectra (200 MHz) the coupling constants of the ring protons were obtained with the aid of computer simulation. These data are in agreement with the coupling constants obtained

from the experiments with the chiral lanthanide shift reagent. The main difference between cis-3 and trans-3 is shown by $J_{2,5}$. The results of Barbier et al.[7] for 2,5-dimethoxy- and 2,5-diacetoxy-2,5-dihydrofuran showed $J_{2,5}$ to be larger for the trans form, which is in accordance with our results.

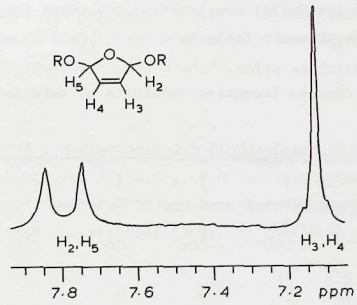


Fig. 7. ^{1}H NMR (200 MHz) spectrum of cis-3 in the presence of Eu(hpc)$_3$ (ρ = 0.67, see Fig. 6) in $CDCl_3$.

Mass spectrometry: The mass spectra of cis- and trans-3 show great resemblance except for m/e = 124, which is much larger for the cis-compound (see Fig. 8).

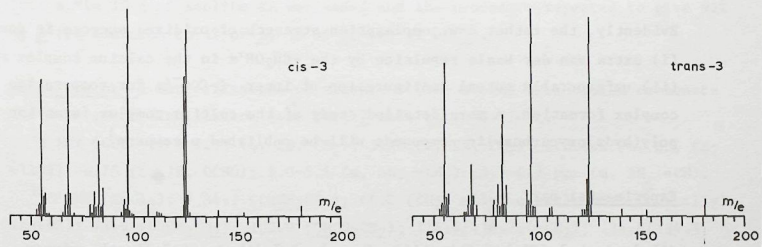


Fig. 8. Mass spectra of cis- and trans-3.

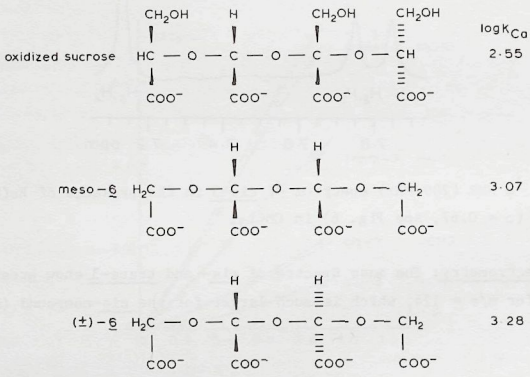
This fragment ion is formed by the loss of allyl alcohol. For the cis-compound this will easily occur by the abstraction of a methylene proton from the

opposite allyl group. In trans-3 the distances are too large for intramolecular H-abstraction.

The dihydrofurans 1, 2, cis-3 and trans-3 were easily oxidized by aqueous alkaline potassium permanganate at 0 °C to yield the corresponding oxydiacetic acid derivatives 4-6 (Fig. 3).

A comparison of the Ca(II) complexation constants for oxidized sucrose, meso- and (±)-6 is given in Table I.

Table I. Calcium complex formation constants of oxidized sucrose, (±)-6 and meso-6.



Evidently, the rather low complexation strength of oxidized sucrose is due to (i) extra van der Waals repulsion by the $-CH_2OH$'s in the calcium complex and (ii) unfavourable mutual configuration of inner $-C-COO^-$'s for cooperative complex formation. A more detailed study of the calcium complex formation of poly(hydr)oxycarboxylic compounds will be published elsewhere[1].

Experimental part

Allyl alcohol (Fisher Scientific Corp.), 2,5-dihydro-2,5-dimethoxyfuran (Aldrich), Eu(hpc)$_3$ (Aldrich) and silica (BDH) were reagent-grade and were used without further purification. Zeolite KA was activated at 400 °C.

^{1}H NMR spectra were recorded with a Varian T-60 and a Nicolet NT 200 spectrometer using TMS or sodium 3-trimethylsilyl-2,2,3,3-tetradeutero-propionate (TNP) as the internal standard. ^{13}C NMR spectra were recorded with a Varian CFT-20 spectrometer, using TMS or methanol as the internal standard.

GC-MS spectra were measured with a Varian Model 3700 gas chromatograph using a CP Sil 5 column connected to a Varian Mat 44 S mass spectrometer.

Preparative GLC was carried out with a Perkin-Elmer F21 Gas Chromatograph using a 3 m x 6 mm 10% SP-2230 column at 180 °C. Analytical GLC was carried out on a Varian Model 3700 apparatus using a 25 m CP Sil 5 capillary column (70 °C to 200 °C in 45 min). Complex stability constants (log KCa) were determined according to Craggs and Moody[10] using an Orion Model 93-20 Divalent Cation Electrode.

Transacetalization of 2,5-dimethoxy-2,5-dihydrofuran (1) with allyl alcohol: Compound 1 (13.0 g; 0.1 mole), 58.0 g (1.0 mole) of allyl alcohol and p-toluenesulfonic acid hydrate (15 mg) were stirred at room temperature during 24 h until equilibrium was attained (Mixt. A: 19% of 1, 38% of 2, 42% of 3, and 1% of 7).

Removal of methanol by distillation: The equilibrium mixture A was heated at 65 °C while N_2 was bubbled through. After 2 h mixture B was obtained: 1% of 1, 19% of 2, 68% of 3, and 12% of 7.

Treatment with zeolite KA: To the equilibrium mixture A (containing 0.1 mole of 2,5-dihydrofurans) was added 10 g of zeolite KA. After stirring for 1 h and filtration, 15 mg of p-toluene sulfonic acid hydrate was added and the mixture was stirred for another 3 h yielding 4% of 1, 30% of 2, 64% of 3, and 2% of 7. Then again 10 g of zeolite KA was added and the procedure repeated to give 92% of 3 (in addition to 1% of 1, 3% of 2, and 4% of 7).

Isolation of 7: Neutralization of mixture B (see above) with sodium carbonate and subsequent distillation gave pure 7 with b.p. 73-77 °C.

^{1}H NMR ($CDCl_3$): δ 1.92 (q, 2H, CH_2); 3.48 (t, 2H, CH_2); 3.8-4.2 (m, 6H, CH_2 allyl); 4.75 (t, 1H, OCHO); 5.0-5.4 (m, 6H, $=CH_2$); 5.7-6.1 ppm (m, 3H, =CH).

^{13}C NMR ($CDCl_3$): δ 34.1 ($\underline{CH}CH_2CH_2$); 66.2 (CH_2, allyl ether); 66.8 (CH_2 allyl acetal); 71.9 ($CHCH_2\underline{CH_2}$); 100.0 ($\underline{CH}CH_2CH_2$); 116.6/116.7 ($=CH_2$); 134.8/134.9 ppm (=CH).

MS (M = 212): m/e = 41, 57, 28, 71, 99, 113, 127, 155, 171.

Isolation of 2 and 3: A reaction mixture (19 g, containing 5% of 1, 32% of 2, 61% of 3, and 2% of 7) was treated with sodium carbonate during 1 h and filtered. Excess allyl alcohol was evaporated at 40 °C (20 torr). 2 (Rf =

0.36) and 3 (Rf = 0.46) were obtained after eluting the mixture over a silica column with hexane/ether (70:30). Yield of 2: 3.4 g.

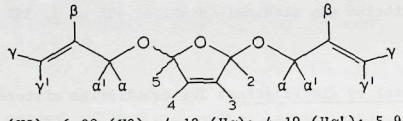
^{13}C NMR ($CDCl_3$): δ 134.7/134.5 (CH allyl); 132.0/131.7/131.6/131.2 (=CH ring); 117.2/117.0 (=CH_2); 108.7/107.4/107.2/105.8 (OCO); 68.3/68.1 (CH_2); 54.1/53.9 ppm (CH_3).

GC-MS: (M = 156); cis-2: m/e 99, 71, 68, 45, 125, 83, 155; trans-2: m/e 99, 71, 55, 83, 68, 97, 155.

Yield of 3: 6.2 g. Separation by preparative GLC gave 1.46 g of cis-3 and 0.37 g of trans-3.

^{13}C NMR (20 MHz) of cis-3 ($CDCl_3$): δ 131.4 (=CH ring); 105.8 (OCO); 67.8 (CH_2); 134.7 (=CH allyl); 116.9 ppm (=CH_2); trans-3 ($CDCl_3$): 131.9 (=CH ring); 107.5 (OCO); 68.2 (CH_2); 134.4 (=CH allyl); 117.1 ppm (=CH_2).

^1H NMR spectral data (200 MHz) are given below ($CDCl_3$).



cis-3: δ 5.74 (H2); 6.08 (H3); 4.12 (Hα); 4.19 (Hα'); 5.94 (Hβ); 5.18 (Hγ); 5.30 ppm (Hγ'); $J_{2,3}$ = 1.2, $J_{2,4}$ = 1,2, $J_{2,5}$ = 0.2, $J_{3,4}$ = 6.0, $J_{\alpha,\alpha'}$ = -12.9, $J_{\alpha,\beta}$ = 5.2, $J_{\alpha,\gamma}$ = 1.4, $J_{\alpha,\gamma'}$ = 1.4, $J_{\alpha',\beta}$ = 6.0, $J_{\alpha',\gamma}$ = 1.4, $J_{\alpha'\gamma'}$ = 1.4, $J_{\beta,\gamma}$ = 10.4, $J_{\beta,\gamma'}$ = 17.2, $J_{\gamma,\gamma'}$ = 1.6 Hz; $J_{C-2,H-2}$ = 166.5, $J_{C-3,H-3}$ = 160.6 Hz.

trans-3: δ 6.00 (H2); 6.10 (H3); 4.06 (Hα); 4.22 (Hα'); 5.94 (Hβ); 5.19 (Hγ); 5.30 ppm (Hγ'); $J_{2,3}$ < 0.5, $J_{2,4}$ < 0.5, $J_{2,5}$ = 4.0, $J_{3,4}$ = 6.0, $J_{\alpha,\alpha'}$ = -12.5, $J_{\alpha,\beta}$ = 6.2, $J_{\alpha,\gamma}$ = 1.4, $J_{\alpha,\gamma'}$ = 1.4, $J_{\alpha',\beta}$ = 5.1, $J_{\alpha',\gamma}$ = 1.4, $J_{\alpha',\gamma'}$ = 1.4, $J_{\beta,\gamma}$ = 10.3, $J_{\beta,\gamma'}$ = 16.4, $J_{\gamma,\gamma'}$ = 1.6 Hz; $J_{C-2,H-2}$ = 169.3, $J_{C-3,H-3}$ = 171.3 Hz.

Permanganate oxidation of 1: Compound 1 (2.6 g; 0.020 mole) was added within 0.5 h to a solution of potassium permanganate (9.5 g, 0.060 mole) and potassium hydroxide (1.0 g, 0.018 mole) in water (200 ml) at 0 °C. After 2 h the reaction mixture was filtered, brought to pH = 9 with Dowex AG-50W X8 (H^+) and freeze dried from water (250 ml) to yield 4.9 g (95%) of 4.

^1H NMR (D_2O): δ 4.90/4.95 (s, 2H, OCHO); δ 3.35/3.38 ppm (s, 6H, OCH_3).

^{13}C NMR (D_2O): δ 52.6/53.3 (OCH_3); 97.8/98.0 (OCO); 172.6/172.9 ppm (COO).

Permanganate oxidation of 2: Compound 2 (3.4 g; 0.020 mole) was added within 0.5 h to a solution of potassium permanganate (19.2 g; 0.120 mole) and potassium hydroxide (2.0 g; 0.036 mole) in water (300 ml) at 0 °C. After 2 h

the reaction mixture was filtered and the filtrate treated with a slight excess of barium hydroxide (3.5 g; 0.011 mole) to remove formic acid. The solution was filtered again, treated with 30 g of zeolite NaA, filtered and concentrated at 40 °C (20 torr) to 5 ml. Upon addition of methanol the trisodium salt of 5 precipitated as a white solid, which was dried in vacuum over P_2O_5. Yield: 2.9 g (48%).

^1H NMR (D_2O): δ 5.02/4.98/4.93 (s, 2H, OCHO); 4.07/4.02 (s, 2H, CH_2) 3.37/3.35 ppm (s, 3H, CH_3).

^{13}C NMR (D_2O): δ 172.2 (COO); 97.7/97.1 (OCO); 65.0/61.5 (CH_2); 53.4/52.4 ppm (CH_3).

Permanganate oxidation of cis-3 and trans-3: Compound cis-3 (0.45 g; 2.5 mmole) and 0.10 g (0.55 mmole) of trans-3 were oxidized similarly as 2 to yield the tetra sodium salts of meso-6 (0.931 g; 95%) and (±)-6 (0.183 g; 94%), respectively.

meso-6: ^1H NMR (D_2O): δ 5.10 (s, 2H, OCHO); 4.13 ppm (s, 4H, CH_2).
^{13}C NMR (D_2O): δ 172.5/164.6 (COO); 96.9 (OCO); 65.4 ppm (CH_2).

(±)-6: ^1H NMR (D_2O): δ 5.13 (s, 2H, OCHO); 4.05 ppm (s, 4H, CH_2).
^{13}C NMR (D_2O): δ 170.2/163.3 (COO); 96.8 (OCO); 64.4 ppm (CH_2).

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CHAPTER IV

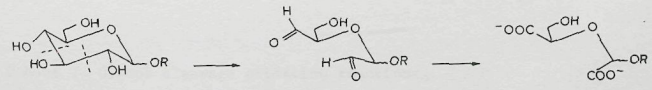
SYNTHESIS AND CHARACTERIZATION OF GLYCOL CLEAVAGE PRODUCTS OF SOME MONOSACCHARIDE DERIVATIVES AND OLIGOSACCHARIDES

Abstract

A series of acetal polycarboxylates has been synthesized by periodate oxidation and subsequent hypobromite oxidation of vicinol diol moieties of a number of glucosides, sucrose and raffinose. The products have been characterized by ^{1}H NMR and ^{13}C NMR spectroscopy.

Introduction

In connection with our investigations[1,2] on the calcium complexation of compounds containing only C, H and O, we have performed the glycol cleavage oxidation of a number of carbohydrate derivatives. Such calcium complexing compounds have our interest since they are potential phosphate substitutes in detergent formulations. In order to improve calcium complexing properties of carbohydrates, introduction of carboxylic groups by way of oxidation and/or derivatization is required. Glycol cleavage oxidation of carbohydrates with a derivatized anomeric hydroxyl group yields systems with carboxyl groups which contain the oxydiacetate (ODA) moiety[2] ($^{-}$OOC-C-O-C-COO^{-}). The ODA-moiety is known to have a good complexing ability for Ca(II) ions.



Malaprade[3,4] discovered the glycol cleavage of polyols by periodate ion and Criegee[5] subsequently found that lead tetraacetate also cleaves diols. Since then numerous papers have been published dealing with glycol cleavage oxidation, and have been reviewed by Perlin[6]. Also reviews especially on periodate oxidation[7-10] and on lead tetraacetate oxidation[11] have been published. The oxidations to dialdehyde carbohydrates are generally followed by oxidation with bromine in a $SrCO_3$-slurry (hypobromite oxidation)[12]. Direct oxidation of glycols to carboxylates by hypohalites[13,14] or by silver(I) oxide[15-18] has also been reported.

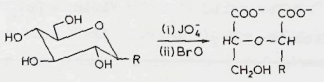
This chapter deals with the synthesis and characterization of a number of oxidized carbohydrates starting from some monosaccharide derivatives and from oligosaccharides. Two-step oxidation and to a minor extent one-step oxidation was applied and the two methods have been compared.

Results

The carbohydrates and carbohydrate derivatives 1 which were subjected to a two-step oxidation[12] have been summarized in Scheme 1 together with their oxidation products 2.

The two-step glycol cleavage oxidation was carried out either with periodate (method A) or with periodic acid (method B) followed by oxidation with hypobromite. The final reaction mixture was treated with zeolite NaA in order to obtain directly the sodium salts of the oxidation products. The results of the oxidation products are summarized in Table I.

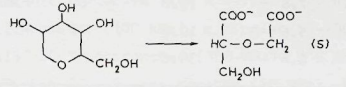
The products were characterized by ^1H NMR and ^{13}C NMR (see Experimental Part). The purity of the products was > 95%. It may be noted that $[\alpha]_D^{25}$-values of the Sr- or Ba-salts of 2 as reported in the literature differ substantially from those for the Na-salts as obtained by us. It was established that complexation of 2 with divalent cations influences $[\alpha]_D^{20}$ which is ascribed[22] to conformational changes of 2. The effect of addition of such ions on the optical rotation of 2a is illustrated in Fig. 1.



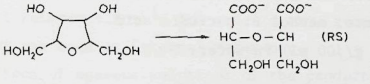
1 2

1a R = OCH_3 (α)
1b R = OCH_3 (β)
1c R = OCH_2COO^- (α)
1d R = OPO_3^{2-} (α)

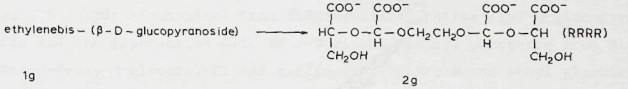
2a R = OCH_3 (RS)
2b R = OCH_3 (RR)
2c R = OCH_2COO^- (RR)
2d R = OPO_3^{2-} (RS)



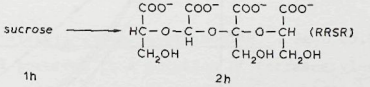
1e 2e



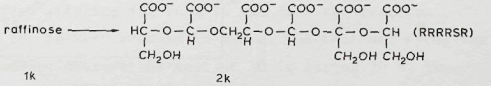
1f 2f



1g 2g



1h 2h



1k 2k

Scheme I. Glycol cleavage oxidation reactions.

Table I. Results of two-step glycol cleavage oxidation[a]

Comp.	Method[b]	Molar ratio IO_4^-/substr.	Molar ratio Br_2/substr.	Yield (%)	$[\alpha]_D^{25}$	(c)[c]	$[\alpha]_D^{25}$ (ref)
2a	B	9.8	5.0	87	-11.8°	(1.8)	-52.9°(24)[d]
2b	B	9.8	5.5	90	+44.9°	(1.5)	+35.9°(24)[e]
2c	A	10.0	7.5	83	+14.4°	(2.0)	
2d	A	5.6	4.8	63	+2.1°	(5.8)	
2e	B	9.4	4.0	62	-15.5°	(1.8)	-14.1°(25)[d]
2f	B	10.8	6.8	80			
2g	B	7.8	15.8	80	+38.9°	(1.0)	
2h	B	5.6	10.8	77	+33.6°	(1.0)	+23° (12)[d]
2k	B	8.4	30.6	57	+1.1°	(1.1)	

[a] For exp. conditions see Experimental Part.

[b] Method A: periodate; method B: periodic acid.

[c] Sodium salts (c; g/100 ml) in water.

[d] Sr-salt.

[e] Ba-salt.

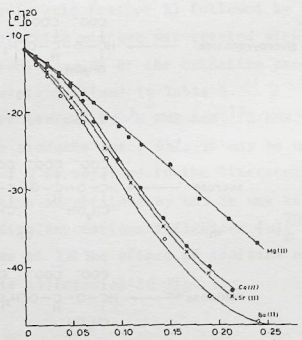


Fig. 1. $[\alpha]_D^{20}$ of sodium salt 2a as a function of M(II)/substrate molar ratio ρ (c = 4.0 g/100 ml).

The direct method of oxidizing vicinal diol units in carbohydrates into dicarboxylates by sodium hypochlorite[13,14] has also been applied. Optimalization of this method was not attempted, however. The carboxyl content appeared to be much lower than that obtained by the periodate/hypobromite procedure, as was observed for the oxidation of methyl α-D-glucoside (4.6 vs 8.4 mmole/g) and sucrose (5.3 vs 8.8 mmole/g). Direct oxidation using silver(I) oxide[15-18] also results into a lower degree of the carboxyl content in the case of sucrose (6.7 vs 8.8 mmole/g).

Experimental Part

^1H NMR spectra has been recorded with a Varian T-60 spectrometer (60 MHz), a Varian XL-100 spectrometer (100 MHz), a Nicolet NT-200 WB spectrometer (200 MHz) or a Varian SC-300 spectrometer (300 MHz). ^{13}C NMR spectra has been recorded with a Varian CFT-20 spectrometer (20 MHz). With D_2O as the solvent TNP (sodium 3-trimethylsilyl-2,2,3,3-tetradeuteropropionate) and methanol were used as internal reference for ^1H NMR and ^{13}C NMR, respectively. With $CHCl_3$ as the solvent, TMS was used as internal reference.

Optical rotations of aqueous solutions of the products were measured with a Perkin-Elmer P-141 polarimeter at 589 nm.

Methyl α-D-glucopyranoside and methyl β-D-glucopyranoside were obtained from Sigma, 1,5-anhydro-D-mannitol from Rhône-Poulenc, tetraacetyl-α-glucopyranosyl bromide and the dipotassium salt of α-D-glucopyranosyl phosphate from Aldrich, 2-amino-2-deoxy-D-glucose.HCl and raffinose from Merck and ethyl glycolate from Fluka. All other chemicals were reagent grade and were used without further purification.

Ethoxycarbonylmethyl tetraacetyl-β-D-glycopyranoside[19]. Ag_2O (5.0 g; 21.6 mmole) was added in small portions to a solution of tetraacetyl-α-D-glucopyranosyl bromide (10.0 g; 24.0 mmole) and ethyl glycolate (16.0 g; 154.0 mmole) in 35 ml $CHCl_3$. After stirring for 24 h in the dark the reaction mixture was filtered and the solvent removed in vacuo. The residual syrup was diluted with 75 ml H_2O and the mixture was kept at 10 °C during 20 h. The precipitate was collected and crystallized from ethanol to yield 6.0 g (60%) of ethoxycarbonylmethyl tetraacetyl-β-D-glucopyranoside, m.p. 81-83 °C (lit. 19: 83-84 °C).

^1H NMR ($CDCl_3$): δ = 1.28 (t, 3H, $CH_2\underline{CH_3}$); 2.0-2.1 (s, 12, H, CH_3); 4.27 (q, J = 7 Hz, 2H, $\underline{CH_2}CH_3$); 4.27 (s, 2H, CH_2); 5.10 (d, J = 8 Hz, 1H, OCHO); 3.5-4.7 (5H).

^{13}C NMR ($CDCl_3$): δ = 100.2 (C1); 71.1 (C2); 72.7 (C3); 68.5 (C4); 72.0 (C5); 61.1 (C6); 65.1 (OCH_2); 61.9 ($\underline{CH_2}CH_3$); 14.2 ($CH_2\underline{CH_3}$); 20.6 ($OO\underline{C}CH_3$); 170.7/170.2/169.7/169.5/169.2 (COO).

Sodium β-D-glucopyranosyloxy acetate (1c)[19]. Ethoxycarbonylmethyl tetraacetyl-β-D-glucopyranoside (6.0 g; 14.0 mmole) was treated with 250 ml 0.125 M $Ba(OH)_2$ for 24 h at room temperature. The mixture was brought at pH = 5 with CO_2 and subsequently towards pH = 2 with H_2SO_4 at 5 °C. The precipitate was filtered off and the filtrate was concentrated in vacuo at 50 °C. The residue was treated four times with 30 ml methanol followed by removal of methanol in vacuo. Then water (50 ml) was added and the pH adjusted to 8 with NaOH. The resulting mixture was freeze dried to yield 2.5 g (67%) of 1c.

^1H NMR (D_2O): δ = 4.53 (s, 2H, CH_2); 4.02 (m, 2H, CH_2OH); 5.05 (d, J = 8 Hz, 1H, OCHO); 4.1-4.8 (5H).

^{13}C NMR (D_2O): δ= 101.3 (C1); 72.2 (C2); 75.2 (C3); 68.6 (C4); 74.6 (C5); 59.6 (C6); 67.7 (CH_2); 176.5 (COO).

2,5-anhydro-D-mannitol (1f)[20]. 2-Amino-2-deoxy-D-glucose.HCl (10.8 g; 50.0 mmole) in 150 ml H_2O was stirred for 5 h at -2 °C to obtain mutarotational equilibrium. Then $NaNO_2$ (13.8 g; 0.2 mole) and acetic acid (9 ml) were added and the mixture was stirred at 0 °C for 4 h. After bubbling through nitrogen for 0.5 h the mixture was freeze dried. The remaining solid was dissolved in 150 ml H_2O at 0 °C and the pH brought at 8 with CO_2. $NaBH_4$ (2.9 g; 76.1 mmole) was added and the mixture stirred for 2 h. After standing overnight the pH was brought at 7 with acetic acid. The mixture was treated with MeOH (40 ml) which was removed in vacuo together with $B(OMe)_3$. This procedure was repeated three times. Ethanol (20 ml) was added, the mixture was filtered and again ethanol (50 ml) was added to the residue. After filtration the latter ethanol solution was concentrated in vacuo to yield 6.2 g (75%) of 1f.

^1H NMR (D_2O): δ = 3.9 (m, 4H, CH_2OH); 4.0-4.3 (m, 4H).

^{13}C NMR (D_2O): δ = 82.7 (C2, C5); 76.8 (C3, C4); 61.5 (CH_2OH).

2-hydroxyethyl tetraacetyl-β-D-glucopyranoside[21]. Ag_2CO_3 (12.0 g; 43.5 mmole) was added to a solution of tetraacetyl-α-D-glucopyranosyl bromide (10.0 g; 24 mmole) and glycol (35 g; 0.564 mole) in 65 ml benzene and the resulting suspension was stirred for 20 h in the dark. The organic layer was separated and the residue extracted thrice with 70 ml benzene. The combined benzene extracts were concentrated in vacuo to yield 8.7 g (92%) 2-hydroxyethyl tetraacetyl-β-D-glucopyranoside as an oil.

$[\alpha]_D^{25}$ = -28.7° (c = 2.8; $CHCl_3$) (lit. 21: -26.3°).

^1H NMR ($CDCl_3$): δ = 1.9-2.1 (4s, 12H, CH_3); 3.68 (s, 2H, $CH_2\underline{CH_2}OH$); 3.78 (s, 2H, $\underline{CH_2}CH_2OH$); 3.5-4.7 ppm (5H); 5.1 (d, 1H, OCHO).

^{13}C NMR ($CDCl_3$): δ = 101.5 (C1); 71.5 (C2); 73.0 (C3); 68.7 (C4); 72.8 (C5); 62.1 (C6); 72.1 (OCH_2); 62.0 (CH_2OH); 20.6 ($OOCCH_3$); 170.7/170.2/169.6/169.4 (COO).

Ethylene bis(tetraacetyl-β-D-glucopyranoside)[21]. Ag_2CO_3 (5.0 g; 18.1 mmole) was added to a solution of 2-hydroxyethyl tetraacetyl-β-D-glucopyranoside (7.1 g; 18.0 mmole) and tetraacetyl-α-D-glucopyranosyl bromide (5.0 g; 12.0 mmole) in 100 ml benzene and the solution was stirred for 20 h in the dark. After filtration and concentration in vacuo, the remaining syrup was poured into water and kept at 10 °C during 24 h. The precipitate was recrystallized from ethanol to yield 3.5 g (40%) ethylene bis(tetraacetyl-β-D-glucopyranoside).

$[\alpha]_D^{25}$ = -29.3° (c = 1.2; $CHCl_3$) (lit. 21: -31.8°).

^1H NMR ($CDCl_3$): δ = 2.0-2.2 (4s, 24H, CH_3); 3.82 (s, 4H, OCH_2CH_2O); 4.1-5.3 (12H, other H).

^{13}C NMR ($CDCl_3$): δ = 100.6 (C1); 71.5 (C2); 72.9 (C3); 68.6 (C4 and OCH_2); 71.9 (C5); 61.9 (C6); 20.7 ($OO\underline{C}CH_3$); 170.6/170.2/169.4/169.3 (COO).

Ethylene bis(β-D-glucopyranoside) (1g)[21]. A solution of ethylene bis(tetra-acetyl-β-D-glucopyranoside) (1.0 g; 1.4 mmole) and $Ba(OH)_2.8H_2O$ (2.8 g; 8.9 mmole) in 45 ml H_2O was stirred for 20 h at room temperature. Then the pH was brought at 6 with CO_2. After removal of the precipitate the remaining liquid was freeze dried to yield 0.33 g (93%) of 1g with m.p. = 109-113 °C and $[\alpha]_D^{25}$ = -9.2° (c = 0.7 g/100 ml).

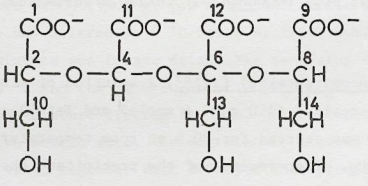
^1H NMR (D_2O): δ = 3.63 (s, 4H, OCH_2CH_2O); 4.75 (d, J = 7 Hz, 2H, OCHO); 3.5-4.4 (10H).

^{13}C NMR (D_2O): δ = 99.4 (C1); 70.7 (C2); 73.4 (C3, C5); 68.6 (C4); 58.3 (C6); 65.3 (OCH_2CH_2O).

Two-step glycol cleavage oxidation of 2a-k. In a typical synthesis a solution of methyl α-D-glucopyranoside (1.0 g; 0.0055 mole) and H_5IO_6 (12.3 g; 0.054 mole) in 75 ml H_2O was stirred during 20 h in the dark. Subsequently, the mixture was neutralized by stirring with the proper amount of $Ba(OH)_2.8H_2O$. $Ba(IO_3)_2$, $Ba(IO_4)_2$ and $Ba(OOCH)_2$ were removed by filtration. To the filtrate $SrCO_3$ (11 g) and Br_2 (1.5 ml) were added and the resulting suspension stirred for 20 h in the dark. Excess of Br_2 was removed by bubbling through a stream of air during 2 h. The $SrCO_3$ was filtered off and the remaining solution stirred with Ag_2CO_3 (5 g) during 2 h in the dark. The mixture was filtered and the filtrate stirred with zeolite NaA (10 g) for 2 h. After filtration the solution was concentrated in vacuo (T < 50 °C) to about 3 ml. Upon addition of 25 ml ethanol the syrup started to solidify. The solid material was filtered and dried in vacuo over P_2O_5 to yield 1.03 g (87%) of 2a.

Reaction conditions and analytical results of the synthesis of 2a-k are summarized in Table I. All products were characterized with ^1H NMR and ^{13}C NMR. These results are listed in Table II for 2a-g and given below for 2h and 2k.

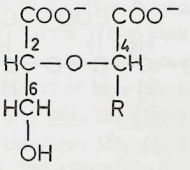
Oxidation product of sucrose (2h).



^1H NMR (300 MHz; D_2O): δ = 5.20 (H4); 4.42 (H2); 4.37 (H8); 3.90 (H10 and H10'); 3.87 (H14 and H14'); 3.78 (H13 and H13'); $J_{2,10} = J_{2,10'} = 2.0$ Hz; $J_{10,10'} = -12.0$ Hz; $J_{13,13'} = -12.2$ Hz; $J_{8,14} = J_{8,14'} = 3.3$ Hz; $J_{14,14'} = -12.0$ Hz.

^{13}C NMR (D_2O): δ = 177.5/175.9/172.8/171.4 (C1, C9, C11, C12); 102.1 (C4); 94.7 (C6); 78.8 (C2); 73.6 (C8); 62.2/61.6/61.3 (C10, C13, C14).

Table II. ^1H NMR and ^{13}C NMR chemical shifts and coupling constants of 2a-g.

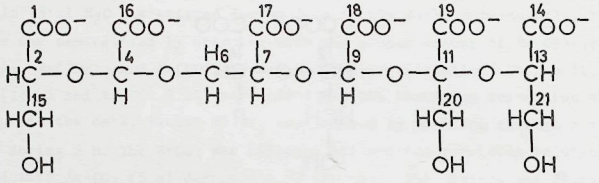


Compound	2a	2b	2c	2d	2e	2f	2g
R	$-OCH_3$	$-OCH_3$	$-OCH_2COO^-$	$-OPO_3^{2-}$	-H	$-CH_2OH$	$-CH_2-$
H_2	3.94	3.99	4.00	4.29	4.0	4.04	4.00
H_4	4.68	4.68	4.70	5.40[a]	3.8	4.04	4.76
H_6	3.71	3.69	3.80	3.84	3.7	3.91	3.71
$H_{6'}$	3.63	3.67	3.70	3.76	3.7	3.91	3.65
H in R	3.20	3.17	3.50	--	3.85	3.91	3.58
$J_{2,6}$	2.0	2.1	2	2	5	4.8	2.0
$J_{2,6'}$	7.1	6.5	6	7	6	6.1	6.7
$J_{6,6'}$	-13.0	-13.0	-11	-10	-11	-10	-13.3
C_2	80.9	77.0	75.5	77.3	82.2	80.6	77.0
C_4	101.0	98.1	95.6	93.8[b]	68.8	80.6	97.6
C_6	63.0	62.3	58.6	62.1	62.5	61.8	63.9
C in R	53.6	52.0	62.3	--	--	61.8	62.3
COO^-	177.3	176.0	174.5	190.8	178.1	176.8	176.2
	174.4	175.2	174.3	176.9	177.5		173.0
			171.1				

[a] $J_{H,P} = 7.3$ Hz.

[b] $J_{C,P} = 4.7$ Hz.

Oxidation product of raffinose (2k).



^{1}H NMR (200 MHZ; D_2O): δ = 5.12 (H9); 4.87 (H4); 4.38 (H2); 4.23 (H13); 4.06 (H7); 3.74 (H6); 3.70 (H6'); 3.78 (H15 and H15'); 3.73 (H21 and H21'); 3.70 (H20 and H20'); $J_{2,15} = J_{2,15'} = 3.5$ Hz; $J_{15,15'} = -10$ Hz; $J_{13,21} = J_{13,21'} = 3.5$ Hz; $J_{21,21'} = -10$ Hz; $J_{20,20'} = -12$ Hz; $J_{6,7} = 2.5$ Hz; $J_{6',7} = 6.5$ Hz; $J_{6,6'} = -10$ Hz.

^{13}C NMR (D_2O) (COO^- signals too small): δ = 100.7 (C9); 95.7 (C4); 80.2/-77.2/76.5/74.7 (C2, C7, C11, C13); 64.4/63.6/62.5/61.5 (C6, C15, C20, C21).

Periodate/hypobromite oxidation of glucuronic acid 1-phosphate. The same procedure as described for 2a-k (see Table I) using method A; molar ratio IO_4^-/substr. = 27.6, Br_2/substr. = 5.5. Yield: 86%.

^{1}H NMR (D_2O): δ = 5.14 (d, 1H, OCHO); 4.24 (s, 2H, CH_2); $J_{H,P} = 8$ Hz.

Sodium hypochlorite oxidations of 1a and 1h. The carbohydrate (2 g) was dissolved in water (20 ml). Within 2 h 80 ml NaOCl solution (containing 12 g Cl_2 and 13.5 g NaOH) was added (T < 20 °C). After additional stirring for 4 h the mixture was poured into a mixture of 250 ml methanol and 150 ml acetone. The precipitate was filtered off and dried in vacuo.

From 1a: $[\alpha]_D^{20}$ = +2.6° (c = 2.1). From 1h: $[\alpha]_D^{20}$ = +22.3° (c = 2.5). The carboxyl content was established according to the literature[23]. Product from 1a: 4.6 mmole/g. Product from 1h: 5.3 mmole/g.

Silver(I) oxide oxidation of 1h[17]. Ag_2O (6.0 g; 51.8 mmole) and finely devided Ag-powder (1.4 g) were added to a solution of sucrose (1.7 g; 7.3 mmole) and NaOH (1.6g) in water (40 ml). After stirring at 40 °C for 2 h the pH was brought to 8.5 with HCl. After filtration and evaporation of the solvent in vacuo, the addition of ethanol yielded a solid product. The carboxylic content was 6.7 mmole/g.

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CHAPTER V

SYNTHESIS AND CALCIUM COMPLEXATION OF A SERIES OF LOW MOLECULAR WEIGHT POLYCARBOXYLIC ACIDS: *DERIVATIVES OF OXYDIACETATE AND ETHYLENE GLYCOL DIACETATE*[*]

Abstract

A series of 25 polycarboxylic acids containing either the oxydiacetate (1; ODA) or the ethylene glycol diacetate (20; EGDA) moiety have been synthesized and their calcium complexation ability determined. Differences in log K_{Ca} values, which vary from 2.0 to 5.4 are discussed in terms of steric, electronic and entropy effects.

Introduction

Many compounds have been examined in the last decade in the search for substitutes for sodium triphosphate (STP), the main builder in detergent formulations. At the moment only a few systems are of commercial interest and ecologically acceptable. Among them are complexing agents (nitrilotriacetic acid and citric acid), a calcium precipitating agent (sodium carbonate) and an inorganic ion exchanger (zeolite NaA). In the case of zeolite NaA a water soluble complexing agent is required as so-called co-builder to complete the builder action of zeolite NaA[1]. Such a complexing agent should have a calcium complex stability constant (K_{Ca}) between 10^4 and 10^5 M^{-1}.

Up to now no low molecular organic polyoxygen compounds have been developed

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[*] M.S. Nieuwenhuizen, A.P.G. Kieboom, and H. van Bekkum, Tenside Detergents, submitted for publication.

which show both sufficient calcium complexation ability and good biodegradability and which are acceptable from an economic point of view.

In our study of calcium complexation phenomena of organic polyoxygen compounds[2], carbohydrates and derivatives thereof have our special interest. When glucosides are oxidized by vicinal diol cleaving agents a so-called ODA-moiety ($^-$OOC-C-O-C-COO$^-$) is obtained. When monosaccharides are hydrogenated alditols are obtained, which upon carboxymethylation afford products containing a so-called EGDA-moiety ($^-$OOC-C-O-C-C-O-C-COO$^-$). Both the ODA- and the EGDA-moiety are complexing sites for Ca(II) ions as appears from the log K_{Ca} values of ODA and EGDA itself (3.51 and 3.26, respectively).

In the crystalline state the ODA-Ca(II) complex (ODA) shows a planar conformation[3], whereas EGDA in the EGDA-Ca(II) complex[4] has a somewhat distorted zig-zag conformation (see Fig. 1).

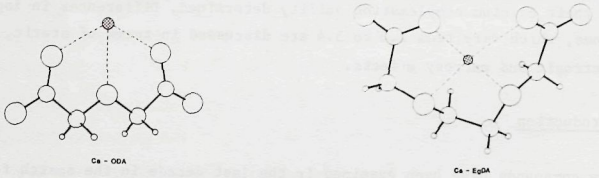


Fig. 1. Crystal structure of Ca-ODA[3] and Ca-EGDA[4] complexes.

From the literature it is known that ODA in the ODA-Ca(II) complex in solution also adopts a planar conformation[3], whereas the conformation of the EGDA-Ca(II) complex in solution is not fully elucidated[5].

In the present paper synthesis and calcium complexing properties of a series of substituted oxydiacetates (ODA compounds) and ethylene glycol diacetates (EGDA compounds) are described. The effect of introducing substituents in ODA and EGDA on the calcium complexing ability is discussed in terms of steric, electronic and entropy effects.

Results and Discussion

Calcium sequestering properties

The apparent stability constant as defined by

$$K_{Ca} = \frac{[\text{Ca-complex}]}{[\text{Ca(II)}][\text{ligand}]}$$

was determined according to Craggs *et al.*[6] at pH = 9 using a calcium ionselective electrode at a total ligand concentration of $0.7\text{-}1.3.10^{-3}$ M and a total calcium concentration of 10^{-3} M.

The calcium sequestering capacity (SC) was determined by turbidimetry at pH = 10 using sodium oxalate as the indicator according to Wilham and Mehltretter[7]. SC gives the weight amount of Ca(II) in mg which is sequestered by one gram of the sodium salt of the ligand at $[Ca(II)] = 10^{-5}$ M. The relation between the apparent stability constants K_{Ca} and stability constants calculated from SC (K_{Ca}^{SC}) is shown in Fig. 2 using the present data (Tables I and II) and those from previous work[8].

Log K_{Ca}^{SC} proves to be systematically higher than log K_{Ca}, in particular in the lower range of log K_{Ca} = 2-4. It has to be taken into account that in this region the amount of free ligand present during the SC determination is substantial. Adsorption of free ligands at the growing calcium oxalate crystals may inhibit crystal growth[9] and, up to certain Ca(II) levels, may thus keep the crystal diameter below the visible detection limit ($\emptyset \simeq 1$ µm). It may be noted that complexation in solution requires the coordination of the different oxygen atoms of the ligand to one and the same Ca(II) ion, whereas the adsorption may take place with several Ca(II) ions at the crystal surface. This means that compounds with a relatively low calcium complexing ability may still possess a good adsorption ability, *i.e.* a crystal-growth inhibiting effect.

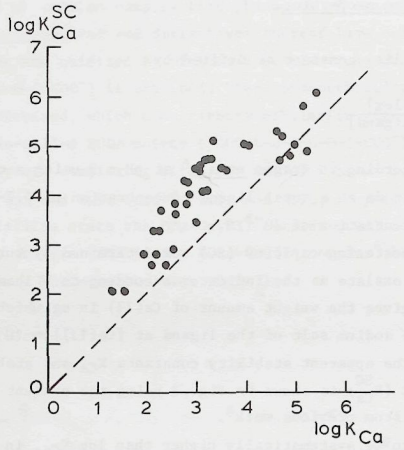


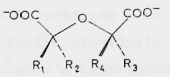
Fig. 2. Relation between log K_{Ca} (from ion selective electrode measurements) and log K_{Ca}^{SC} (from SC-measurements).

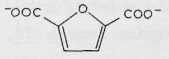
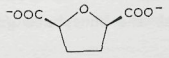
The effect of substitution at the ODA moiety

The ODA-derivatives investigated are listed in Table I, together with their log K_{Ca} and SC values.

Introduction of one substituent at the ODA-moiety gives rise to an increase of log K_{Ca} from 3.16 to 4.06 in the order: CH_2OH (2) < $CH_2OCH_2COO^-$ (15) < H (1) < OCH_2COO^- (12) < CH_2COO^- (7). At least three effects will play a role. First, the substituents disturb the zig-zag conformation of the ODA-moiety (Fig. 1) due to 1,3-syn repulsions. Secondly, a carboxylate-containing substituent may also coordinate with Ca(II) as is the case for 7, 12 and 15. A higher coordination number generally causes a complex to be more stable particularly through a more positive ΔS of the complex formation reaction.

Table I. Apparent stability constants (log K_{Ca}) and calcium sequestering capacities (SC) for ODA-derivatives.



	R_1	R_2	R_3	R_4	log K_{Ca} [a]	SC [b]
1	H	H	H	H	3.51	60
2	CH_2OH	H	H	H	3.16	65
3	CH_2OH	H	CH_2OH	H	3.06	40
4	CH_2OH	H	OCH_3	H	2.25	27
5[d]	CH_2OH	OCH_3	CH_2OH	OCH_3	2.29	7
6[d]	OCH_3	H	OCH_3	H	1.96	10
7[d]	CH_2COO^-	H	H	H	4.06	78
8[c]	$CH(OH)COO^-$	H	H	H	5.00[e]	--
9	CH_2COO^-	H	CH_2COO^-	H	5.26	50
10	CH_2COO^-	H	H	CH_2COO^-	4.69	41
11	CH_2COO^-	CH_2COO^-	H	H	4.20[f]	--
12	OCH_2COO^-	H	H	H	3.58	60
13	OCH_2COO^-	H	OCH_2COO^-	H	3.28	38
14	OCH_2COO^-	H	H	OCH_2COO^-	3.07	52
15	$CH_2OCH_2COO^-$	H	H	H	3.36	56
16	$CH_2OCH_2COO^-$	H	$CH_2OCH_2COO^-$	H	4.06	58
17	CH_2OH	H	H	OPO_3^{2-}	2.95	23
18					1.34	2
19					3.06	49

[a] μ = 0.1 (KCl); 25 °C; pH = 9. [b] mg Ca/g; 20 °C; pH = 10. [c] From diethyl D-tartrate and ethyldiazoacetate[10]. [d] Racemic mixture. [e] From reference 10. [f] From reference 11.

From inspection of molecular models one would expect log K_{Ca} to increase in the order CH_2COO^- (7) < OCH_2COO^- (12) < $CH_2OCH_2COO^-$ (15). That this is not the observed order may be ascribed to a third effect: increase of molecular motion of the ligand in the complex leading to a negative ΔS increment for the complex formation reaction. Also, an electronic effect on complex stability going from ether to acetal compounds will play a role[8]. Of the mono-substituted ODA-compounds only compound 8, containing the favourable α-hydroxycarboxylate moiety as the substituent, shows sufficiently high Ca(II) complexation. Unfortunately compound 8 has rather poor biodegradation properties[10].

Introduction of two substituents (R_1 and R_3 in Table I) in a threo configuration at the ODA moiety shows an increase of log K_{Ca} from 1.96 to 5.2 in the order di-OCH_3 (6) < OCH_3/CH_2OH (4) < di-CH_2OH (3) < di-OCH_2COO^- (13) < di-H (1) < di-$CH_2OCH_2COO^-$ (16) < di-CH_2COO^- (9). This order is consistent with that derived above for the mono-substituted ODA compounds. In previous work[8] we showed that the lower log K_{Ca} value for an erythro- with respect to a threo-disubstituted ODA (i.e. 14 < 13 and 10 < 9) is due to the 1,3-syn-repulsions in the former compounds. The presence of two CH_2COO^- groups at the same carbon atom of ODA (11) results in a lower log K_{Ca} value than the presence of two substituents at different carbon atoms (9 and 10). This is possibly due to a less optimal Ca(II) complexing site in which not all four carboxylic groups can participate simultaneously.

The relatively low stability constants of the methoxy-substituted ODA compounds 4, 5 and 6 in comparison with compound 3 result from electronic effects rather than steric effects. The lower electron density of an acetal oxygen compared to that of an ether is the main reason for the weaker Ca(II) coordination by acetal compounds. The importance of a relatively high electron density of the bridge-oxygen of the ODA moiety further appears from the decrease by 1.6-2.0 log K_{Ca}-units on going from 9, 10, and 19 to 13, 14 and 18, respectively.

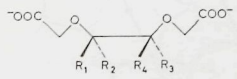
The fact that the log K_{Ca} value of the acetal phosphate ester 17 is higher than that of compound 4 indicates that the phosphate group is possibly involved in complexation.

Of the disubstituted ODA compounds threo-2,2'-di(carboxymethyl)oxydiacetate (10) is by far the best. Its biodegradability, however, proved to be insufficient[10].

The effect of substituents at the EGDA moiety

The derivatives of EGDA investigated are listed in Table II, together with their log K_{Ca} and SC values.

Table II. Apparent stability constants (log K_{Ca}) and calcium sequestering capacities (SC) for EGDA-derivatives.



	R_1	R_2	R_3	R_4	log K_{Ca} [a]	SC [b]
20	H	H	H	H	3.26	19
21	$CH_2OCH_2COO^-$	H	H	H	4.71	72
22[c]	$CH(OH)CH_2OCH_2COO^-$	H	H	H	4.69	70
23[d]	$CH(OH)CH_2OCH_2COO^-$	H	H	H	4.96	58
24	$CH_2OCH_2COO^-$	H	H	$CH_2OCH_2COO^-$	5.25	78
25	$CH_2OCH_2COO^-$	H	$CH_2OCH_2COO^-$	H	5.40	83

[a] μ = 0.1 (KCl); 25 °C; pH = 9. [b] mg Ca/g; 20 °C; pH = 10. [c] (RS)/(SR) mixture. [d] (RR)-configuration.

In contrast to ODA, the introduction of a $CH_2OCH_2COO^-$ group at the EGDA moiety (21) increases the log K_{Ca} value substantially (Δ log K_{Ca} = 1.45). In order to obtain structural information about the calcium complex of 21 we applied ^{17}O NMR[12,13] using Dy(III) as probe for Ca(II). Comparison of the Dy(III) induced shift (DyIS) of the ^{17}O signal of D_2O of a solution of 21 with that of pure D_2O points to 5 coordinating water molecules in the first coordination sphere of the 1:1 complex (Fig. 3). Taking into account a coordination number of 9 for Dy(III), it follows that the number of coordinating oxygens of the ligand is 4.

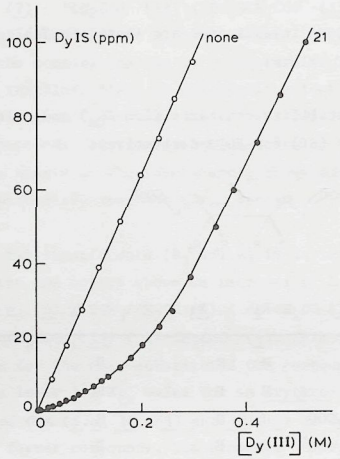


Fig. 3. Dy(III) induced shifts (DyIS) of the ^{17}O water resonance without and in the presence of compound 21 (0.35 M) at 73 °C.

This number is equal to that of EGDA (20) itself. The much stronger complex formation of 21 with respect to EGDA, however, cannot be explained by statistical factors alone. It, therefore, must find its origin in a fast interconversion of the two enantiomeric complexes without complete dissociation, as depicted in Fig. 4. This phenomenon has also been observed in the case of lanthanide(III)-citrate complexes[14].

Such a dynamic cooperation of carboxymethyloxy moieties, in addition to pure statistical factors, will also take place in the stereoisomeric mono- (22, 23) and di-substituted (24, 25) EGDA-compounds. That in such systems log K_{Ca} generally increases with the number of carboxymethyloxy moieties is demonstrated in Fig. 5 for a series of fully carboxymethylated alditols in which 21 and 24, 25 are the three- and tetracarboxymethylated derivatives, respectively, and in which also the literature[11] log K_{Ca}-value (5.8) for hexakis(O-carboxymethyl)-D-glucitol is included (see Fig. 5).

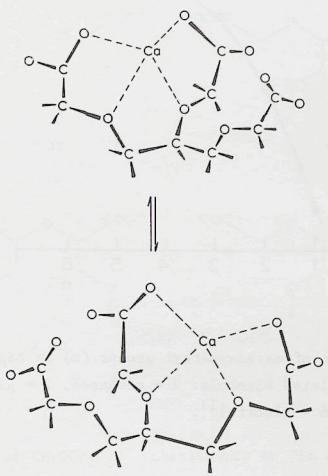


Fig. 4. Proposed Ca(II) complexation of 21.

Of the carboxymethylated alditols compound 21 combines acceptable calcium complexation properties with a relatively inexpensive starting material. Although this compound has been claimed[15] as potential phosphate substitute, no data on its biodegradability are available.

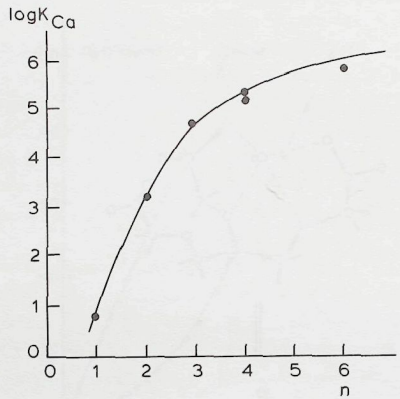


Fig. 5. Effect of number of carboxymethyl groups (n) on log K_{Ca} of *percarboxymethylated alcohols*: 1 = methanol, 2 = glycol, 3 = glycerol, 4 = tetritols, 6 = glucitol[11].

Final remarks

Two requirements for a potential builder or co-builder are (i) a log K_{Ca} value of 4-5 and (ii) good biodegradability. Introduction of two CH_2COO^-'s at the ODA-moiety is necessary to increase log K_{Ca} to an acceptable value, but biodegradability is mentioned to be poor[10]. When one or two OCH_2COO^- groups are introduced at the ODA moiety, (bio)degradation will be no problem as the acetal moieties easily hydrolyze in the acidic waste water, but the log K_{Ca} values are too low. As reported elsewhere[17] higher molecular weight acetal carboxylates, especially oxidized maltodextrins (α-1,4-D-glucans with a degree of polymerization of 10-15) have acceptable calcium complexation.

The effect of the introduction of $CH_2OCH_2COO^-$ substituents at both the ODA and the EGDA moiety on log K_{Ca} is summarized in Fig. 6.

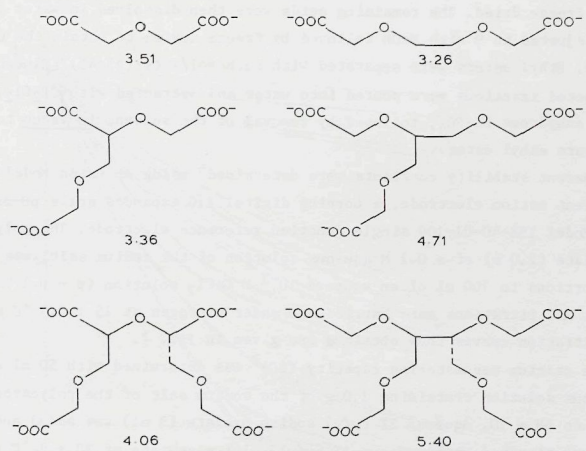


Fig. 6. Effect of $CH_2OCH_2COO^-$ substituents at ODA and EGDA on log K_{Ca}.

In the case of ODA the improvement of log K_{Ca} is too small to meet the calcium complexation requirement. In the case of the EGDA derivatives 21, 24 and 25 log K_{Ca} values are increased to an acceptable level. Biodegradability tests are required to settle their potential use as phosphate substitute.

Experimental Part

^1H NMR spectra were recorded with a Varian T-60 spectrometer (60 MHz) using D_2O as solvent and TNP (sodium 3-trimethylsilyl-2,2,3,3-tetradeutero-propionate) as internal standard, ^{13}C NMR spectra were recorded with a Varian CFT-20 spectrometer (20 MHz) using D_2O as solvent and methanol as internal standard.

Mass spectroscopy was performed with a Varian Mat 44S mass spectrometer.

Preparative HPLC was carried out with a Waters Prep LC/System 500 using C18 reverse phase columns and refractive index detection. Acids were chromatographed with water + 0.2% trifluoroacetic acid (Eluent A). Samples

were brought to pH = 2 with trifluoroacetic acid and the collected fractions were freeze dried. The remaining acids were then dissolved in water and the pH was adjusted to 9 with NaOH followed by freeze drying to obtain the sodium salts. Ethyl esters were separated with methanol/water(55:45) (Eluent B). Collected fractions were poured into water and extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4, followed by removal of the solvent in vacuo to obtain the pure ethyl esters.

Apparent stability constants were determined[6] using an Orion Model 93-20 divalent cation electrode, a Corning digital 110 expanded scale pH-meter and a HNU Model ISE-40-01-100 single junction reference electrode. The polycarboxylate (2.0 ml of a 0.1 M aqueous solution of the sodium salt) was added in 20 portions to 100 mL of an aqueous 10^{-3} M $CaCl_2$ solution (μ = 0.1 M with KCl). All titrations were carried out under nitrogen at 25 $\pm$ 0.5 °C and pH = 9. Titration curves thus obtained are given in Fig. 7.

The calcium sequestering capacity (SC)[7] was determined with 50 ml of an aqueous solution containing 1.0 g of the sodium salt of the polycarboxylic acid at pH = 10. Aqueous 2% (w/w) sodium oxalate (3 ml) was added and the mixture titrated with aqueous 1% (w/w) calcium acetate at 20 $\pm$ 2 °C until slight permanent turbidity. Each ml of the 1% calcium acetate solution counts for 2.54 mg Ca(II) sequestered.

Oxydiacetate and erythritol were obtained from Merck, 2,5-dihydroxymethylfuran and calcium glycerate from Aldrich. Compound 7 was a gift of the Unilever Research Laboratory (Vlaardingen, The Netherlands). The syntheses of compounds 6, 13, 14[18] and 12[19] have been described elsewhere.

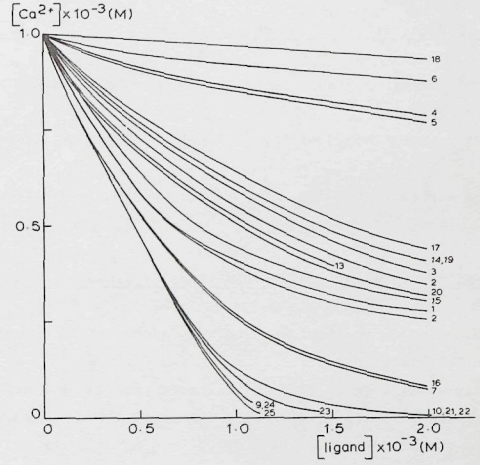


Fig. 7. Ion selective electrode titration curves: free [Ca(II)] in aqueous 10^{-3} M $CaCl_2$ at 25 °C and pH = 9 as a function of the ligand concentration. Numbers refer to the compounds listed in Tables I and II.

Disodium 2-(hydroxymethyl)oxydiacetate (2)

Using the procedure described by Hockett and Zief[20], consecutive oxidation of 1,5-anhydromannitol (2.3 g; 13.9 mmole) with periodic acid and strontium hypobromite followed by treatment with zeolite NaA yielded 1.8 g 2 (62%). $[\alpha]_D^{25}$: -15.5° (c = 1.8; H_2O).

^1H NMR (D_2O): δ = 4.0 (m, 1H, CH); 3.7 (m, 2H, CH_2); 3.8 (s, 2H, CH_2).

^{13}C NMR (D_2O): δ = 82.2 (HCO); 68.8 (CH_2); 62.5 (CH_2OH); 178.1/177.5 (COO).

Disodium (RS)-2,2'-di(hydroxymethyl)oxydiacetate (3)

Oxidation of 2,5-anhydromannitol (1.1 g; 6.7 mmole) as described for 2 yielded 1.3 g 3 (80%).

^{1}H NMR (D_2O): δ = 4.04 (m, 2H, CH); 3.91 (m, 4H, CH_2).
^{13}C NMR (D_2O): δ = 80.6 (CH); 61.8 (CH_2OH); 176.8 (COO).

Disodium (R,R)-2-(hydroxymethyl)-2'-(methoxy)oxydiacetate (4)

Oxidation of methyl α-D-glucopyranoside (1.0 g; 5.5 mmole) as described for 2 yielded 1.0 g of 4 (87%).

^{1}H NMR: δ = 3.94 (m, 1H, CH); 3.67 (m, 2H, CH_2); 4.68 (s, 1H, OCHO); 3.20 (s, 3H, OCH_3).

^{13}C NMR (D_2O): δ = 80.9 (HCO); 101.0 (OCO); 63.0 (CH_2OH); 53.6 (OCH_3); 177.3/174.4 (COO).

Dipotassium 2,2'-di(hydroxymethyl)-2,2'-di(methoxy)oxydiacetate (5)

Bromine (8.0 g; 0.050 mole) in 25 ml methanol was added within 1 h to 2,5-dihydroxymethylfuran (6.4 g; 0.049 mole) and sodium carbonate (15 g) in 60 ml methanol. The mixture was stirred for 2 h, filtered and the filtrate poured into 100 ml water. The resulting mixture was extracted three times with 50 ml diethyl ether. The combined extracts were dried (Na_2SO_4) and the solvent evaporated to yield 2,5-dihydroxymethyl-2,5-dimethoxyfuran as an oil. This oil (10.8 g) was added within 0.5 h to a solution of potassium permanganate (21.8 g; 0.138 mole) and potassium hydroxide (2.25 g; 0.040 mole) in water (200 ml) at 0 °C. After 2 h the reaction mixture was filtered, brought to pH = 9 with Dowex AG-50W-X8 (H^+) and extracted three times with 50 ml diethyl ether to remove 2,5-dihydroxymethylfuran. Freeze drying of the water layer yielded 12.6 g of 5 (79%).

^{1}H NMR (D_2O): δ = 3.27 (s, 6H, CH_3); 3.73 (s, 4H, CH_2OH).

^{13}C NMR (D_2O): δ = 52.3/53.1 (CH_3); 65.7 (CH_2OH); 97.5/97.8 (OCO); 172.7/178.5 (COO).

Tetraethyl (RR)/(SS)- and (RS)-oxydisuccinate[21]

Maleic anhydride (19.6 g; 0.2 mole) was dissolved in 100 ml H_2O and stirred for 15 min. (R)/(S)-Malic acid (32.2g; 0.24 mole) was added and the pH adjusted to 11.4 by $Ca(OH)_2$. After refluxing for 2 h Na_2CO_3 was added, the precipitate filtered off and the filtrate concentrated in vacuo. The residue was refluxed for 16 h in a mixture of 500 ml ethanol and 40 ml conc. H_2SO_4. The reaction mixture was poured into water, extracted three times with diethyl ether and the combined extracts concentrated in vacuo. After removal of

diethyl fumarate, diethyl maleate and diethyl malate by vacuum distillation, the residue was separated by preparative HPLC using eluent B to yield the tetraethyl esters of (RR)/(SS)- and (RS)-oxydisuccinic acid.

Addition of the chiral shift reagent tris[3-(heptafluoro-1-hydroxybutyl)-d-camphorato]europium(III) to the (RR)/(SS)-mixture in $CDCl_3$ resulted in double ^{1}H NMR signals, whereas this was not the case for the (RS)-compound.

Tetraethyl (RR)/(SS)-oxydisuccinate. Overall yield: 3.8%.

^{1}H NMR (D_2O): δ = 1.25 (t, 6H, $CH_2\underline{CH_3}$ inner COO); 1.28 (t, 6H, $CH_2\underline{CH_3}$ outer COO); 4.17 (q, 4H, $\underline{CH_2}CH_3$ inner COO); 4.23 (q, 4H, $\underline{CH_2}CH_3$ outer COO); 2.83 (d, 4H, CH_2); 4.53 (t, 2H, CH).

MS (M = 362): m/e = 145, 99, 71, 73, 174, 243, 289, 128, 117, 127.

Tetraethyl (RS)-oxydisuccinate. Overall yield: 3.7%.

^{1}H NMR (D_2O): δ = 1.30 (t, 12H, $CH_2\underline{CH_3}$); 4.17 (q, 4H, $\underline{CH_2}CH_3$ inner COO); 4.20 (q, 4H, $\underline{CH_2}CH_3$ outer COO); 2.80 (d, 4H, CH_2); 4.55 (t, 2H, CH).

MS (M = 362): m/e = 145, 99, 71, 73, 243, 289, 117, 127, 174, 128, 173.

Tetrasodium (RR)/(SS)- and (RS)-oxydisuccinate (9 and 10)

To a slurry of 4 ml Dowex AG 50W-X8 (H^+) in 30 ml H_2O 0.5 g of the ethyl ester of 9 or 10 was added. After 68 h at 60 °C the hydrolysis was complete according to ^{1}H NMR. Freeze drying yielded 9 and 10 in 95% yield.

Compound 9:

^{1}H NMR (D_2O): δ = 2.55 (d, 4H, CH_2); 4.07 (t, 2H, CH); J = 13 Hz.

^{13}C NMR (D_2O): δ = 40.6 (CH_2); 77.2 (CH); 178.3/178.9 (COO).

Compound 10:

^{1}H NMR (D_2O): δ = 2.58 (d, 4H, CH_2); 4.13 (t, 2H, CH); J = 12 Hz.

^{13}C NMR (D_2O): δ = 40.1 (CH_2); 77.5 (CH); 177.9/178.6 (COO).

Triethyl (S)-2-(carboxymethoxymethyl)oxydiacetate

Oxalic acid dihydrate (4.6 g; 0.037 mole) was added to a slurry of calcium (S)-glycerate dihydrate (10.5 g; 0.037 mole) in 100 ml water, the mixture stirred for 1 h and then filtered. The filtrate was concentrated in vacuo and the resulting syrup (7.3 g) heated in ethanol (60 ml) at 190 °C in an autoclave during 5 h. Distillation yielded 6.7 g of ethyl (S)-glycerate (79%) with b.p. 122 °C (14 Torr).

Ethyl diazoacetate (5.0 g; 0.044 mole) was added in small portions at 120 °C to ethyl (S)-glycerate (5.0 g; 0.045 mole) and Cu powder (0.5 g). The reaction mixture was filtered and diethyl (S)-maleate and diethyl fumarate were removed

in vacuo to yield 2.5 g triethyl (S)-2(carboxymethoxymethyl)oxydiacetate (76%).

^{13}C NMR (acetone-d_6): δ = 14.4 (CH_3); 61.0/61.3/61.7 (CH_2 ester); 67.8/69.2/72.4 (CH_2); 79.6 (CH); 170.0/170.2/170.5 (COO).

MS (M = 306): m/e = 59, 117, 89, 73, 101, 129, 175, 233, 260, 306.

Trisodium (S)-2-(carboxymethoxymethyl)oxydiacetate (15)

Triethyl (S)-2(carboxymethoxymethyl)oxydiacetate (2.5 g; 0.012 mole) was treated with sodium hydroxide (2.5 g) in 50 ml H_2O at 100 °C during 3 h. The mixture was brought at pH = 8 with Dowex AG 50W-X8 (H^+). Removal of water in vacuo yielded 2.4 g of 15 (99%).

^{1}H NMR (D_2O): δ = 3.98 (s, 2H, CH_2); 3.92 (s, 2H, CH_2). CH_2CH: ABC-system: δ_A = 3.81; δ_B = 3.90; δ_C = 4.03; J_{AC} = 3.6; J_{BC} = 3.7; J_{AB} = -12 Hz.

^{13}C NMR (D_2O): δ = 68.1 ($\underline{CH_2}CH$); 69.4 (OCH_2:2x); 78.8 ($CH_2\underline{CH}$); 175.9/176.6 (COO).

Tetrasodium (R,R)-2,2'-di(carboxymethoxymethyl)oxydiacetate (16)

Sodium hydroxide (6.0 g; 0.150 mole) and sodium chloroacetate (15.9 g; 0.150 mole) were added in six portions at intervals of 1 h to compound 3 (1.0 g; 0.0042 mole) in 50 ml H_2O at 50 °C. Purification by preparative HPLC (eluent A) yielded 0.6 g of 16 (42%).

^{1}H NMR (D_2O): δ = 3.82 (d, 4H, $\underline{CH_2}CH$); 4.28 (t, 2H, $CH_2\underline{CH}$); 4.18 (s, 4H, OCH_2); J = 4 Hz.

^{13}C NMR (D_2O): δ = 60.6 ($\underline{CH_2}CH$); 72.8 ($CH_2\underline{CH}$); 63.5 (OCH_2); 178.9/179.3 (COO).

Tetrasodium (R,R)-2-hydroxy-2'-(hydroxymethyl)oxydiacetate 2-phosphate (17)

Oxidation of α-D-glucopyranosyl phosphate (1.6 g; 5.5 mmole) as described for 2 yielded 1.1 g (63%) of 17.

$[\alpha]_D^{25}$ = +2.1° (c = 5.8; H_2O).

^{1}H NMR (D_2O): δ = 4.29 (m, 1H, CH); 3.80 (m, 2H, CH_2); 5.40 (d, 1H, OCHO).

^{13}C NMR (D_2O): δ = 77.3 (CH); 62.1 (CH_2); 93.8 (OCO).

Disodium 2,5-furandicarboxylate (18)

This compound has been synthesized according to Ackman et al.[22].

^{1}H NMR (D_2O): δ = 6.97 (s).

^{13}C NMR (D_2O, acid): δ = 114.8 (CH); 149.3 (C ring); 165.2 (COOH).

Disodium (R,S)-2,5-tetrahydrofurandicarboxylate (19)[23]

Compound 18 (2.21 g; 10.7 mmole) was hydrogenated with 0.25 g 5% Rh/carbon in 150 ml H_2O at room temperature and 1 atm for 3.5 h. The reaction mixture was filtered and concentrated. Upon addition of ethanol compound 19 precipitated and was dried in vacuo. Yield: 1.62 g (74%).

^{1}H NMR (D_2O): δ = 4.19 (m, 2H, $H_{2,5}$); 2.30 (m, 2H, $H_{3,4}$); 1.91 (m, 2H, $H_{3',4'}$); $J_{2,3} = J_{4,5}$ = 5.7 Hz; $J_{2,3'} = J_{4',5}$ = 1.5 Hz.

^{13}C NMR (D_2O): δ = 28.8 (C_3,C_4); 78.7 (C2,C5); 179.3 (COO).

Disodium salt of ethyleneglycoldiacetic acid (20)

Ethyl diazoacetate (7.4 ml; 0.070 mole) was added dropwise to a mixture of ethylene glycol (2.0 g; 0.032 mole) and Cu powder (1.0 g) at 90 °C. The reaction mixture was filtered and the filtrate chromatographed over silica with chloroform/ethyl acetate (10:1). The combined fractions of the diethyl ester of 20 were concentrated and refluxed for 1 h with a mixture of NaOH (3.2 g; 0.080 mmole), 8 ml ethanol and 32 ml H_2O. After cooling the solution was brought at pH = 8 (Dowex AG 50W-X8 (H^+)) and freeze dried to yield 3.5 g (38%) of 20.

^{1}H NMR (D_2O): δ = 3.80 (s, 4H, CH_2CH_2); 4.25 (s, 4H, OCH_2).

^{13}C NMR (D_2O): δ = 68.2 (CH_2CH_2); 68.6 (OCH_2); 176.8 (COO).

Trisodium tris(O-carboxymethyl)glycerol (21)

Reaction of glycerol (3.1 g; 0.034 mole) and ethyl diazoacetate (12.0 ml; 0.114 mole) followed by the work-up as given for 20 yielded 2.3 g (21%) of 21.

^{1}H NMR: δ = 3.97 (m, 5H, CH_2CHCH_2); 4.20 (s, 4H, outer OCH_2); 4.32 ppm (s, 2H, inner OCH_2).

^{13}C NMR: δ = 67.6 ($\underline{CH_2}CH\underline{CH_2}$); 68.8 ($CH_2\underline{CH}CH_2$); 69.3 (outer OCH_2); 76.0 (inner OCH_2); 176.8 (COO).

Trisodium 1,2,4-tris(O-carboxymethyl)erythritol (22) and tetrasodium 1,2,3,4-tetrakis(O-carboxymethyl)erythritol (24)

As described for 20 reaction of erythritol (4.9 g; 0.040 mole) and ethyl diazoacetate (21.0 ml; 0.200 mole) yielded 22 and 24 after separation of the acids by HPLC (eluent A).

Compound 22 (1.1 g; 17%).

^{1}H NMR: δ = 3.63 (m, 6H, $CH_2CHCHCH_2$); 4.00 (s, 4H, outer OCH_2); 4.12 (s, 2H, inner OCH_2).

^{13}C NMR: δ = 68.0 ($\underline{CH_2}CHCH\underline{CH_2}$); 68.3/68.9 ($CH_2\underline{CHCH}CH_2$); 69.2/70.7 (outer OCH_2); 78.2 (inner OCH_2); COO signals too small to analyse.

Compound 24 (0.8 g; 9%).

^{1}H NMR: δ = 3.80 (m, 6H, $CH_2CHCHCH_2$); 4.00 (s, 4H, outer OCH_2); 4.10 ppm (s, 4H, inner OCH_2);

^{13}C NMR (D_2O): δ = 68.4 ($\underline{CH_2}CHCH\underline{CH_2}$); 68.6 ($CH_2\underline{CHCH}CH_2$); 69.3 (outer OCH_2); 76.8 (inner OCH_2); 176.6/176.8 (COO).

Trisodium 1,2,4-tris(O-carboxymethyl)-D-threitol (23) and tetrasodium 1,2,3,4-tetrakis(O-carboxymethyl)-D-threitol (25)

As described for 22 and 24 reaction of D-threitol[24] (2.44 g; 0.020 mole) and ethyl diazoacetate (10.5 ml; 0.100 mole) yielded 23 and 25.

Compound 23 (0.6 g; 9%).

^{1}H NMR (D_2O): δ = 3.60 (m, 6H, $CH_2CHCHCH_2$); 3.87 (s, 4H, outer OCH_2); 4.00 (s, 2H, inner OCH_2).

^{13}C NMR (D_2O): δ = 68.5 ($\underline{CH_2}CHCH\underline{CH_2}$); 68.9/69.1 ($CH_2\underline{CHCH}CH_2$); 69.3 (outer OCH_2); 78.5 (inner OCH_2); COO^- signals too small to analyse.

Compound 25 (0.8 g; 9%).

^{1}H NMR (D_2O): δ = 3.67 (m, 6H, $CH_2CHCHCH_2$); 3.85 (s, 4H, outer OCH_2); 3.98 (s, 4H, inner OCH_2).

^{13}C NMR (D_2O): δ = 68.5 ($\underline{CH_2}CHCH\underline{CH_2}$); 69.0 ($CH_2\underline{CHCH}CH_2$); 69.2 (outer OCH_2); 76.7 (inner OCH_2); 176.7/176.8 (COO).

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CHAPTER VI

POLYCARBOXYLIC ACIDS CONTAINING ACETAL FUNCTIONS: CALCIUM SEQUESTERING COMPOUNDS BASED ON OXIDIZED CARBOHYDRATES*

Abstract

A number of polycarboxylic acids containing acetal functions have been prepared by a two-step oxidation of carbohydrates. Their calcium sequestering behaviour is compared with that of a series of model polycarboxylic acids. It is found that calcium sequestration by oxidized carbohydrates is less than that by corresponding ether polycarboxylates, since (i) acetal oxygens have a lower coordinating power than ether oxygens, and (ii) there is extra steric repulsion upon calcium complexation by both the additional CH_2OH groups and the unfavourable natural configuration of the oxidized carbohydrates investigated. Some of the oxidized carbohydrates show greater calcium sequestering capacities than corresponds to the stability constant. This is probably caused by crystal growth inhibition or precipitation-inhibition phenomena.

Two model compounds illustrate that the acetal moiety is sufficiently stable under washing conditions, whilst it hydrolyses under acidic waste water conditions into small (hydr)oxycarboxylates.

Introduction

Sodium tripolyphosphate (STP), the main builder in detergent formulations at the moment, is considered to stimulate eutrophication in lakes and stagnant

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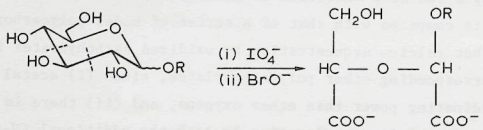
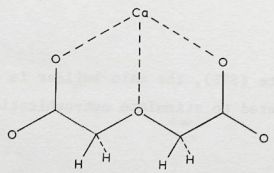
waters. In the last decade an intensive search for STP substitutes has been undertaken. Numerous organic and some inorganic substances have been examined. Up to now of commercial interest are two complexing agents (nitrilotriacetic acid and citric acid), a calcium precipitating agent (sodium carbonate) and an inorganic ion exchanger (zeolite NaA). These compounds and mixtures of them show good washing results, when they are fully or partially substituting STP in washing powders[1-4]. In addition, a phosphate-free two-step washing procedure has been developed and commercialized[5].

We are studying calcium complexation in aqueous medium by different NMR techniques and the synthesis of calcium sequestering compounds. In particular oxidized carbohydrates or carbohydrate derivatives, available from renewable raw material, have our interest as possible phosphate substitutes.

When glucosides are oxidized by a vicinal diol cleaving agent the following interesting structure is obtained.



In general an α-hydroxy- or α-oxycarboxylic moiety is a favourable structural unit for complexation with Ca(II)[6], as also has been found earlier in our laboratory[7,8]. Of particular importance is the $^-OOCCHOCHCOO^-$ moiety, which closely resembles oxydiacetic acid (ODA, 1). The main difference is that the central oxygen atom is a part of an acetal instead of a true ether function. This as well as extra internal steric repulsion in $^-OOCCHOCHCOO^-$-Ca complexes may disturb the ideal flat conformation as found for the ODA-Ca complex[9].



On the other hand, higher-dentate ligands may be obtained, which will favour the strength of calcium complexation.

Two important features are inherited from the parent carbohydrate: a given, natural chirality and the acetal moiety. Acetals are relatively stable in alkaline medium, but decompose in acid medium into the carbonyl and the hydroxylic part. This means, that 1-like acetal compounds are stable during the washing process and are hydrolized under the rather acidic waste-water conditions. Decomposition prior to biological degradation will accelerate full degradation to CO_2 and H_2O, which is an important requirement for acceptable phosphate substitutes.

This paper deals with the synthesis and the calcium sequestering properties of a number of oxidized carbohydrates together with a series of model compounds, some of which have already been disclosed in the patent literature[10,11,12,13]. Furthermore, the effect of an α-carboxylic group on acetal stability at different pH is illustrated with two model compounds.

Procedure

Calcium complex formation constants were determined using an ionselective electrode. A Corning digital 110 expanded scale pH-meter, an Orion Model 93-20 Divalent Cation Electrode and a HNU Model ISE-40-01-100 Single Junction Reference Electrode were used to follow changes in Ca(II) activity of an aqueous $CaCl_2$ solution by titration with a sequestering compound. The polycarboxylate compound (2.0 ml of a 0.1 M aqueous solution of its sodium salt) was added in 20 portions to 100 ml of an aqueous $CaCl_2$ solution (μ = 0.1 M with KCl). All titrations were carried out under nitrogen at 25 ± 0.5 °C and at pH = 9. Titration curves thus obtained are shown in Figure 1.

Calcium sequestering capacities (SC) were determined as follows. A solution of 1.0 g of the sodium salt of the polycarboxylic acid in 50 ml H_2O was adjusted to pH = 10 with NaOH. An aqueous 2% (w/w) sodium oxalate solution (3 ml) was added and the mixture titrated with 1% (w/w) calcium acetate in water at 20 ± 2 °C to slight permanent turbidity. Each ml of the 1% calcium acetate solution counts for 2.54 mg Ca(II) ion sequestered.

Preparative HPLC was carried out with a Waters Prep LC/System 500 using C18 reverse phase columns. Eluent: MeOH:H_2O (55:45).

All compounds have been characterized by ^1H NMR (60, 100, 200 or 300 MHz) and ^{13}C NMR (20 MHz).

Compound 1 was obtained from Merck, 2 from Fluka and 26 from Ventron. Compound 3 was synthesized from sodium sulfide and chloroacetic acid[26]. Compounds 4-6 were prepared by the reaction of ethyl 2-bromopropionate with ethyl (S)-lactate[27], followed by separation of the (±) and meso by preparative

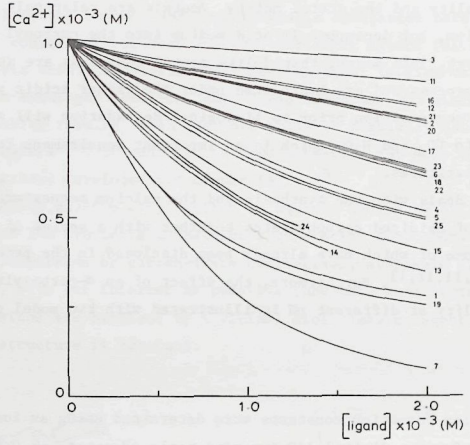


Fig. 1. Experimental ionselective electrode titration curves of an aqueous 10^{-3} M $CaCl_2$ solution with ligand solution.

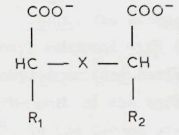
HPLC and saponification. Compounds 7-10 were synthesized from maleic anhydride and an α-hydroxycarboxylic acid according to the procedure of Lamberti et al.[11]. The (±) and meso compounds 9 and 10 were separated as their ethyl esters by preparative HPLC followed by saponification. Compounds 11-15 were obtained by permanganate oxidation in aqueous alkaline medium of the corresponding 2,5-dihydrofurans[11]. Syntheses of compounds 16-19 have been described previously[15]. α- and β-methyl glucopyranoside (Sigma), β-D-carboxymethyl glucopyranoside[28], sucrose (Merck), raffinose (Merck) and ethylenebis-(β-D-glucopyranoside)[29] were oxidized with periodate and hypobromite[17] to yield compounds 20-25, respectively. The strontium salts thus obtained were converted into the sodium salts with zeolite NaA in water.

Rates of hydrolysis of compounds 16 and 18 were determined by ^1H NMR (60 MHz) using the chemical shift difference of the CH_3 group between reactant and reaction product (16: 1.40 ppm and 2.23 ppm; 18: 1.50 ppm and 1.85 ppm, respectively).

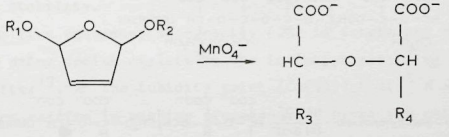
Results and Discussion

Synthesis of polycarboxylic acids

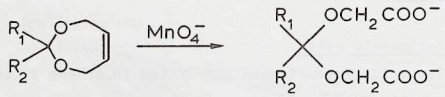
The polycarboxylic acids investigated are listed in scheme 1 (together with their mode of preparation).



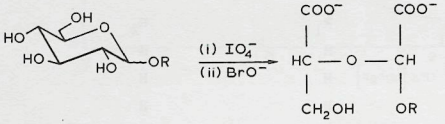
	X	R_1	R_2
1	O	H	H
2	NH	H	H
3	S	H	H
4	O	CH_3	CH_3
5	O	CH_3	CH_3 (RR + SS)
6	O	CH_3	CH_3 (RS)
7	O	H	CH_2COO^-
8	O	CH_2COO^-	CH_2COO^-
9	O	CH_2COO^-	CH_2COO^- (RR + SS)
10	O	CH_2COO^-	CH_2COO^- (RS)



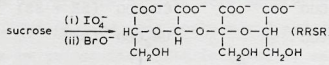
R_1	R_2		R_3	R_4
methyl	methyl	11	OCH_3	OCH_3
methyl	allyl	12	OCH_3	OCH_2COO^-
allyl	allyl	13	OCH_2COO^-	OCH_2COO^-
allyl	allyl	14	OCH_2COO^-	OCH_2COO^- (RR + SS)
allyl	allyl	15	OCH_2COO^-	OCH_2COO^- (RS)



	R_1	R_2
16	CH_3	CH_3
17	H	H
18	COO^-	CH_3
19	COO^-	H



	R
20	CH_3 (RR)
21	CH_3 (RS)
22	CH_2COO^- (RR)



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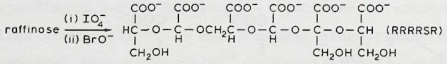

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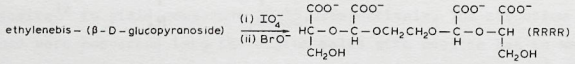


25

26	$Na_5P_3O_{10}$

Scheme I. Calcium sequestering compounds and their mode of preparation.

The ODA-derivatives 2-6 were obtained by reaction of a hydroxy-, amino- or thiocompound with an α-halocarboxylic acid or its ethyl ester in alkaline medium. Compounds 7-10 were synthesized by addition of glycolic acid and malic acid, respectively, to maleic acid in aqueous alkaline medium in the presence of a divalent cation, preferably Ca^{2+} [12]. The oxidation of 2,5-dialkoxy-2,5-dihydrofurans by $KMnO_4$ in aqueous alkaline medium yielded 11-15. Allyloxy groups were introduced by transacetalization of 2,5-dimethoxy-2,5-dihydrofuran with allylic alcohol[14]. $KMnO_4$ oxidation of 4,7-dihydro-1,3-dioxepins gave the acetalic model compounds 16-19. The dioxepins were obtained by acetalization of the respective carbonyl compound with (Z)-2-butene-1,4-diol[15]. A two-step oxidation of some carbohydrates (and derivatives) gave 20-25. In the first step the -CHOH-CHOH-CHOH- unit of the carbohydrate was oxidized to -CHO + HCOOH + OHC- by IO_4^- [16]. In the second step the aldehyde groups were further oxidized with BrO^- to yield the acids[17]. The oxidation products were fully characterized by ^1H and ^{13}C NMR.

Calcium sequestering properties

Two parameters have been chosen to establish quantitative differences in calcium sequestering abilities. The apparent stability constants

$$K_{Ca} = \frac{[\text{Ca-complex}]}{[\text{Ca}][\text{ligand}]}$$

have been determined according to Craggs et al.[18] at pH = 9 with a calcium ionselective electrode. For the region of ligand concentration ranging from 0.7-1.3 10^{-3} M, the K_{Ca} is calculated from the experimental Ca(II) concentration and the initial Ca(II) and ligand concentrations. This mole to mole basis quantity is used for the discussion on structural effects on the complex stability.

The calcium sequestering capacity (SC) is determined by turbidimetry at pH = 10 using sodium oxalate as the indicator according to Wilham and Mehltretter[19]. At the tubidity point [Ca(II)] = 10^{-5} M which is the upper limit for calcium in washing processes. SC gives the weight amount of calcium (in mg) which is sequestered by one gram of the sodium polycarboxylate. This weight to weight quantity is of importance from an economical point of view. In Table I log K_{Ca} and SC for the polycarboxylate compounds 1-25 have been summarized. For comparison, the data for STP (26) have been included.

Table I. Apparent stability constants (as log K_{Ca})[a] and calcium sequestering capacities (SC)[b].

Compound	log K_{Ca}	SC	Compound	log K_{Ca}	SC
1	3.51	60	14	3.28	38
2	2.21	14	15	3.07	32
3	1.54	2	16	2.09	7
4	2.81	12	17	2.42	8
5	2.86	16	18	2.57	10
6	2.57	9	19	3.58	36
7	4.06	78	20	2.25	26
8	4.92	46	21	2.20	27
9	5.26	50	22	2.58	39
10	4.69	41	23	2.55	33
11	1.96	10	24	3.14	32
12	2.12	25	25	2.86	55
13	3.20	36	26	5.05	122

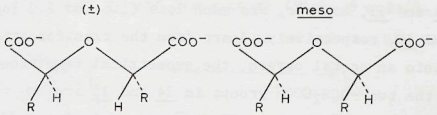
[a] μ = 0.1 (KCl); 25 °C; pH = 9; ionselective electrode titrations[22].
[b] mg Ca/g; 20 °C; pH = 10; calcium oxalate turbidity method[23].

Structural effects

As shown above, ODA acts as a planar tridentate ligand; Ca(II)-binding takes place by two carboxylic oxygens and the ether oxygen. The important contribution of the latter is shown by substituting this atom by S (3) or NH (2). The complex stability then decreases due to a different electronic and geometric nature of the central coordinating atom. When substituting the ether oxygen by CH_2 (glutaric acid) a log K_{Ca} value of 0.55 is mentioned[20].

In general inductive effects of substituents are less important than steric effects at the ODA-Ca moiety. This was shown by both CNDO-2 calculations (electronic effects) and valence force field calculations (steric effects). In the planar ODA-Ca complex there is a 1,3-syn interaction between the hydrogens of the CH_2 groups (H-H distance 0.25 nm). Upon introduction of a $-CH_3$ group at both $-CH_2$ units of ODA (5 and 6) the 1,3-syn repulsions in the calcium-complex increase in the order 1 (2 x H-H) < 5 (2 x H-CH_3) < 6 (H-H and CH_3-CH_3) as shown in Fig. 2. In order to avoid part of this steric interaction some twisting of the ODA-plane in the complex will occur, leading to a less optimal tridentate ligand with different Ca-O distances. The repulsion order is

directly reflected by a decrease in log K_{Ca} of 0.65 and 0.94 units, respectively, apart from minor inductive effects exerted by CH_3 groups.



	R		Δ log K_{Ca}
1	H	1	--
5	CH_3	6	0.29
9	CH_2COO^-	10	0.57
14	OCH_2COO^-	15	0.21
20	OCH_3, CH_2OH	21	0.05

Fig. 2. 1,3-Syn repulsions (H-H, H-R and R-R) in the planar conformations of di-R-substituted ODA compounds; differences in calcium complexation between (±) and meso compounds.

In 7 ("CMOS") one H of ODA is substituted by a $-CH_2COO^-$ group. A detailed NMR conformational study at this laboratory by Vijverberg et al.[21] shows that the ODA-plane is disturbed due to H-CH_2COO^- repulsion. This effect, however, is overruled by the additional coordinating COO^--group as shown by the increased complexation power (0.55 log K_{Ca}-units) of 7 with respect to 1.

In 9 and 10 two H's of ODA are replaced by a $-CH_2COO^-$ group. Due to coordination by four carboxylic groups complex stability is better than that of 1 and 4-7. As depicted in Fig. 2, 1,3-syn repulsions cause a difference in complexation strength between the meso-compound (10) and the racemic mixture (9). Further examples of this phenomenon are shown for 14 and 15 and for 20 and 21.

In 11 two H's of ODA are replaced by $-OCH_3$ groups, i.e. the ether oxygen has become an (double) acetal oxygen. Here two effects are of importance. First, H-OCH_3 and OCH_3-OCH_3 steric interactions occur, which are smaller than the H-CH_3 and CH_3-CH_3 interactions in 5 and 6. As log K_{Ca} of 11 is 0.6-0.9 units smaller than that of 5 and 6, also an electronic effect plays a role, viz. a lower coordinating power of an acetal oxygen relative to an ether oxygen, caused by some mutual electron-withdrawal.

When two $-OCH_2COO^-$'s are introduced at the ODA-moiety (14 and 15) the calcium complexation is 1.1-1.3 units better than for 11 due to the possible contribution of the extra carboxylic groups in the complexation. The calcium complexation abilities of 14 and 15, however, are much less (1.6 and 2.0 log K_{Ca} units) than that of 9 and 10, respectively. Apart from the transformation of the central oxygen atom into an acetal oxygen, the geometrical requirements for calcium-coordination of the two $-OCH_2COO^-$ groups in 14 and 15 are apparently less favourable than that of the two $-CH_2COO^-$ groups in 9 and 10.

The important role of an ODA back-bone is further shown by the better complexation of 18 and 19 in comparison to 16 and 17, respectively (Δ log K_{Ca} = 1.16 and 0.53). The log K_{Ca} difference of 1.0 unit between 18 and 19 is mainly caused by the extra 1,3-syn repulsion in the former.

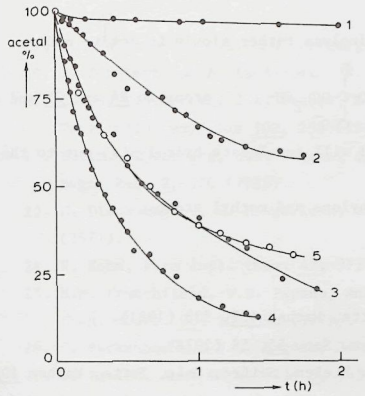
As shown in Table I, the oxidized carbohydrates 20-25 show a rather poor calcium complexation power. From the foregoing considerations we can give a number of reasons for that behaviour. Compounds 20, 21 and 22 contain 1,3-syn repulsions at the ODA moiety between the $-CH_2OH$ group and an $-OCH_3$ or $-OCH_2COO^-$ group. In addition, acetal oxygen atoms are involved in the complexation. The contribution of the β-hydroxy group in these compounds is poor, as was already stated as a general rule by Vijverberg et al.[22]. Oxidized sucrose (23) shows a lower log K_{Ca} value than 14 and 15 in which the three $-CH_2OH$ groups are lacking. Both the absence of these groups in 14 and 15 and the unfavourable (R,R,S,R) configuration of 23 causes this difference. Here the effect of a natural configuration inherited from the parent carbohydrate is clearly reflected.

Compounds 23, 24 and 25 show some favourable effect of the increase of the size of the molecule and of the number of carboxylic groups, as is reflected in larger values of log K_{Ca}. Such an improvement of sequestering abilities can be extrapolated to oxidized oligosaccharides and will therefore be the subject for further investigations. Literature reports show that for oxidized polysaccharides[2,23,24] and polymeric acetal carboxylates[25] the sequestering ability per monomer unit increases with increasing chain length.

From Table I it is also noticed that the SC values of 23, 24 and 25 do not correlate with log K_{Ca} values: they are considerably too high. This will be caused by crystal growth inhibiton or precipiation-inhibition of calcium oxalate.

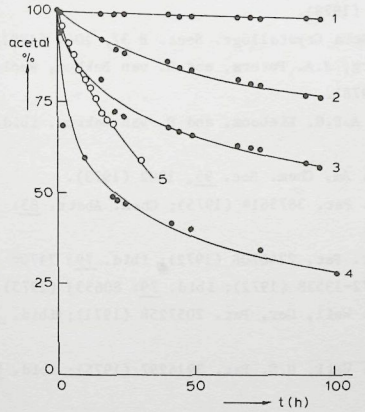
Stability of acetal compounds

In order to get an impression of the stability of the acetal moiety the hydrolytic decomposition of model compounds 16 and 18 has been studied at different pH and temperature (Figs. 3 and 4).



curve	pH_{start}	pH_{end}	T (°C)
1	9.6	9.5	35
2	8.0	7.9	35
3	7.3	7.2	35
4	7.0	6.8	35
5	9.6	9.4	79

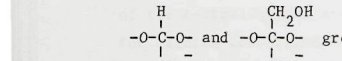
Fig. 3. Hydrolysis of 16 (0.45 M) in water.



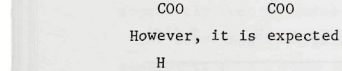
curve	pH_{start}	pH_{end}	T (°C)
1	7.2	7.1	35
2	3.5	3.1	35
3	2.8	2.5	35
4	1.7	1.4	35
5	7.3	7.1	80

Fig. 4. Hydrolysis of 18 (0.08 M) in water.

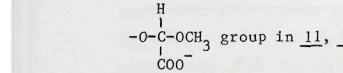
Although concentration and pH are not the same it can be concluded that 18 is much more stable than 16. Clearly, the electronegative carboxylate group in 18 largely prevents hydrolysis under mild conditions. In fact 16 and 18 present lower and upper limits in stability in relation to acceptability as phosphate substitutes. These data teach, that oxidized carbohydrates containing



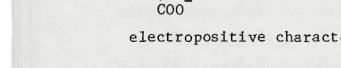
-O-C-O- and -O-C-O- groups will hydrolyse rather slowly in acidic medium.



However, it is expected, that the -O-C-OCH$_2$CH- group in 24 and 25 and the



-O-C-OCH$_3$ group in 11, 12, 20 and 21 will accelerate hydrolysis, due to the



electropositive character of the ethylene and methyl groups.

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CHAPTER VII

PREPARATION AND CALCIUM COMPLEXATION PROPERTIES OF A SERIES OF OXIDIZED POLYSACCHARIDES: STRUCTURAL AND CONFORMATIONAL EFFECTS*

Abstract

A number of polysaccharides of the starch type, including maltodextrins and cyclodextrins and some other well-known polysaccharides have been oxidized by periodate/chlorite (two-step method) or hypochlorite (one-step method), yielding ring-opened polycarboxylates. The oxidation products from the starch type show by far the best calcium complexing properties and have potential application as phosphate substitutes in detergent formulations.

A relatively sharp increase in calcium complexing ability is observed at a degree of polymerization of about ten, whereas just a slight further improvement occurs at higher degrees of polymerization. This phenomenon is explained by the formation of helix structures which contain efficient Ca(II) complexing sites. This idea is supported by ^{17}O NMR measurements showing that oxidized starch type compounds with $\bar{m} > 10$ behave as heptadentate ligands.

Introduction

Sodium triphosphate (STP), the main builder in detergent formulations at the moment, is considered to stimulate eutrophication in lakes and stagnant waters. Up to now the intensive search for substitutes for STP resulted in only a few systems that could meet the technical, commercial and environmental requirements. These substitutes include complexing agents (nitrilo triacetate

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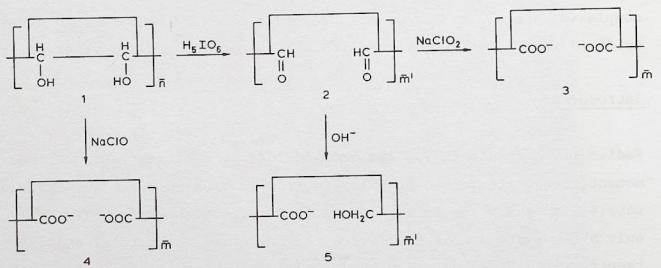
* M.S. Nieuwenhuizen, A.P.G. Kieboom, and H. van Bekkum, Starch, accepted for publication.

(NTA) and citrate), a precipitating agent (sodium carbonate) and an inorganic ion exchanger (zeolite NaA). The latter system is not able to substitute STP completely; in order to realize 100% STP substitution a so-called co-builder is needed, which possesses an intermediate calcium sequestering strength and is soluble in water. In this field we have studied the system NaA/complexing agent using NTA, oxydiacetate (ODA) and borate/glucarate as co-builders[1].

Research in our laboratory is devoted to both the elucidation of calcium complexation phenomena and the synthesis of organic calcium complexing compounds. A sufficiently high calcium complexing strength is a prerequisite for a detergent builder. In previous papers[2,3] we showed that the ODA-moiety ($^{-}$OOC-C-O-C-COO^{-}) is a structural feature which favours calcium complexation. We also recognized the less favourable effects of both the attachment of large groups to this moiety (steric hindrance) and the replacement of the ether oxygen of the ODA-moiety by an acetal oxygen (electronic effects).

Oxidized carbohydrates, which are available from renewable raw materials, often contain the above mentioned ODA-moiety.

Many papers have been published on the oxidation of starch, which have been excellently reviewed by Radley[4]. For our purpose the oxidation procedures for the conversion of vicinal diols into dicarboxylates are of importance. A two-step procedure[5] starts with periodate oxidation of a vicinal diol into a dialdehyde[6,7] as depicted in Scheme I.



Scheme I. Glycol cleavage oxidations and Cannizzaro reaction.

Regeneration of the iodate formed is possible by either electrochemical means[8,9] or by the use of hypochlorite[10]. Usually the periodate oxidation is followed by chlorite oxidation[4,11-14] converting dialdehydes into dicarboxylic acids (3). As an alternative the dialdehyde system may undergo oxidation-reduction (5) by means of an intramolecular Cannizzaro reaction in alkaline medium[15-18]. A one step oxidation procedure of vicinal diols uses hypochlorite as the oxidation reagent[4,14,19,20] yielding directly dicarboxylic polysaccharides 4. The occurrence of degradation reactions and the formation of coloured by-products are, however, a disadvantage of this procedure. Catalytic oxidation procedures involving oxygen or peroxides are hardly applied for polysaccharide oxidation[21-24].

In a previous paper we have described the calcium complexing properties of a number of oxidized mono- and disaccharides and derivatives thereof[2]. The acetal moieties in these compounds are relatively stable in alkaline medium (during the washing process) but are hydrolyzed under acidic conditions (in the waste water), which will enhance the rate of biodegradation.

It was observed[2] that an increasing number of carboxyl groups has a favourable effect on the calcium sequestering strengths. From the literature it is known that an increasing degree of polymerization of ligands gives rise to improved complexation in the case of alginates[25,26], polymeric acetal carboxylates[27] and other organic polymers[28-30], and some oxidized polysaccharides[19,20,31]. The rate of biodegradation, however, will decrease with increased degree of polymerization[19,20,26,27,31]. Obviously, the requirements of both good calcium complexation and rapid biodegradation asks for a compromise.

The present paper deals with a study on the preparation and the calcium complexation of oxidized polysaccharides containing α-1,4-glycosidic bonds with different degrees of polymerization, denoted as "the starch family": starch, amylopectin, amylose, maltodextrins, cyclodextrins, maltose and α-methylglucoside. For comparison, the oxidation products of some other well-known polysaccharides have been included: cellulose, carboxymethylcellulose, dextran, sodium alginate and inulin.

Experimental

Materials and reagents

Amylopectin, amylose, α-cyclodextrin, γ-cyclodextrin and the maltodextrins Paselli MD 10 and Passelli MD 20 were gifts from AVEBE (Veendam, The Netherlands). Potato starch was obtained from Lamens & Indemans ('s-Hertogenbosch, The Netherlands), β-cyclodextrin was obtained from Aldrich, sodium alginate from Fluka, while cellulose, inulin, maltose and α-methyl-glucoside were obtained from Merck. All other materials and reagents were reagent grade and used without further purification. Sodium chlorite and sodium hypochlorite were technical grade.

Apparatus

^{13}C NMR (20 MHz) spectra were recorded with a Varian CFT-20 spectrometer using D_2O as the solvent and methanol as an internal standard. ^{17}O NMR (27 MHz) spectra were recorded with a Nicolet NT-200 WB spectrometer using D_2O as solvent and as external standard.

Gas chromatography was performed using a Varian Model 3700 apparatus equipped with a capillary CP Sil 5 column (25 m) at 75-225 °C with 6 °C/min and a flame ionization detector.

Optical rotations were measured in water with a Perkin-Elmer P141 polarimeter using a 10 mm cell.

The water content of about 300 mg of the reaction products was determined by a Karl-Fisher titration using a Metrohm amperostatic titrator.

Chain length determinations ($\bar{n}$): A solution of 3 or 4 (0.5 g in 25 ml 0.5 M HCl) was refluxed for 7 h. After cooling to room temperature the pH was adjusted to 3-4 with Dowex AG1-X8 (OH^-) and the solution was freeze dried. A mixture of the solid obtained, 0.2 ml N,O-bis(trimethylsilyl)trifluoro-acetamide, 0.1 ml trimethylchlorosilane and 10 mg of myo-inositol (as internal standard) was shaken in a sealed tube during 4 h and analyzed by gas chromatography.

Fractionation of 3dII and 3e: Fractionation was performed over Sephadex G-25 medium (50-150 μm) in a 90 cm * (Ø = 2.5 cm) column with water as the eluens (70 ml/h) using refractive index detection. The fractions collected were freeze dried.

Determination of calcium sequestering capacity (SC)[32]: A solution of 1.0 g of the sodium salt of the oxidized carbohydrate in 50 ml H_2O was adjusted to pH = 10 with NaOH. Then 3 ml of a 2% aqueous sodium oxalate solution was added and the solution titrated with 1% aqueous calcium acetate until a slight permanent turbidity remained. Each titration was performed with the same addition rate (1 ml/min). One ml of 1% calcium acetate solution added corresponds with a sequestering capacity of 2.54 mg Ca(II)/g oxidized carbohydrate.

Calcium ion selective electrode measurements: A Corning digital 110 expended scale millivolt meter, a Radiometer calcium ion selective electrode and a HNU ISE-40-01-100 single junction reference electrode were used to follow Ca(II) ion activities upon addition of small amounts of oxidized polysaccharides (25 mg) to 100 ml 0.001 M $CaCl_2$ and 0.1 M KCl at pH = 9. The time between each addition was kept constant (2 min). The titrations were carried out under nitrogen.

Dialdehyde polysaccharides 2 [6,7,33]: Paraperiodic acid (H_5IO_6) (30 g) was added to a solution of 20 g of 1 in 400 ml H_2O at 0 °C. The mixture was stirred for 24 h in the dark. Three procedures have been applied to isolate 2, depending on the molecular weight and the nature of the reactant.

A. The reaction mixture was filtered. The collected solid was washed with water and dried in vacuum.
B. To the reaction mixture $Ba(OH)_2.8H_2O$ was added until pH = 7 in order to remove iodate, periodate and formate anions. The slurry was filtered. Freeze drying of the filtrate yielded 2.
C. The reaction mixture was poured into 800 ml acetone and the resulting precipitate was washed with acetone/water (1:1) and dried in vacuum.

The dialdehyde content of the product was determined according to Hofreiter et al.[15] by oxidation-reduction of the dialdehyde. To 0.5 g of 2 in 20 ml H_2O 10 ml 0.25 M NaOH solution was added. The mixture was treated in a 50 ml Erlenmeyer flask on a water bath for 2 min at 80 °C. After rapid cooling in ice water 65 ml 28.8 mM H_2SO_4 and 1 ml 0.2% phenolphthalein solution were added. Subsequently, the mixture was titrated with 0.25 M NaOH in order to determine the carboxyl content which was taken to be equal to the dialdehyde content. The results have been summarized in Table I.

Cannizzaro reaction products 5 [15-17]: A solution of 2 in 80 ml 0.25 M NaOH was stirred for 3.5 min at room temperature. Subsequently, the mixture was heated in a water bath at 85 °C for 1.5 min. the cooled mixture was neutralized with Dowex AG-50W-X8 (H^+). After filtration the solution was freeze dried to yield 5.

Dicarboxy polysaccharides 3 [11-14]: A mixture of 10 g 2, 40 mg Na_2CO_3 and 400 ml H_2O was heated for 45 min at 70 °C. At 10 °C a solution of 44 g $NaClO_2$ and 14 ml acetic acid in 60 ml H_2O was added during 1 h. The greenish yellow solution obtained was stirred at room temperature for 24 h. Nitrogen was passed through the now reddish brown solution for 3 h and the colourless solution obtained was poured into 800 ml ethanol. The precipitate was collected, washed with ethanol/water (2:1) and dried in vacuum.

The dicarboxyl content was measured according to Neale et al.[34]. A solution of 3 was treated twice with an excess of Dowex AG-50W-X8 (H^+) at 10 °C. 10 ml 5% NaCl solution and 20 ml 0.25 M NaOH were added and the mixture was titrated with 0.125 M H_2SO_4 using bromocresol purple as the indicator. From the amounts of NaOH and H_2SO_4 used the dicarboxyl content was calculated. In addition, the dicarboxyl content of the oxidized cyclodextrins was obtained from the CH_2OH signals in the ^{13}C NMR spectra, showing different signals for the dicarboxyl, dialdehyde and non-oxidized glucose-units (Fig. 1). The ^{13}C NMR spectra of 3a-3r are given in Fig. 1.

Sodium hypochlorite oxidations [4,14,19,20]: To a solution of 10 g 1 in 100 ml H_2O (pH = 9), 200 ml NaOCl solution (containing 30 g Cl_2 and 34 g NaOH) was added within 4 h at room temperature. After additional stirring for 24 h, 650 ml methanol was added. After 1 h the precipitate was collected by filtration, washed with methanol/water (1:1) and dried in vacuum.

(2R,2'S)-2-hydroxymethyl-2'-methoxy oxydiacetate (3m)[35]: Compound 3m was prepared by periodate oxidation followed by hypobromite oxidation of methyl α-D-glucopyranoside. The reaction product has been fully characterized by ^{13}C NMR (Fig. 1) and ^1H NMR: δ = 3.94 (m, 1H, CH),; 4.68 (s, 1H, CH); 3.67 (m, 2H, CH_2); 3.20 ppm (s, 3H, CH_3).

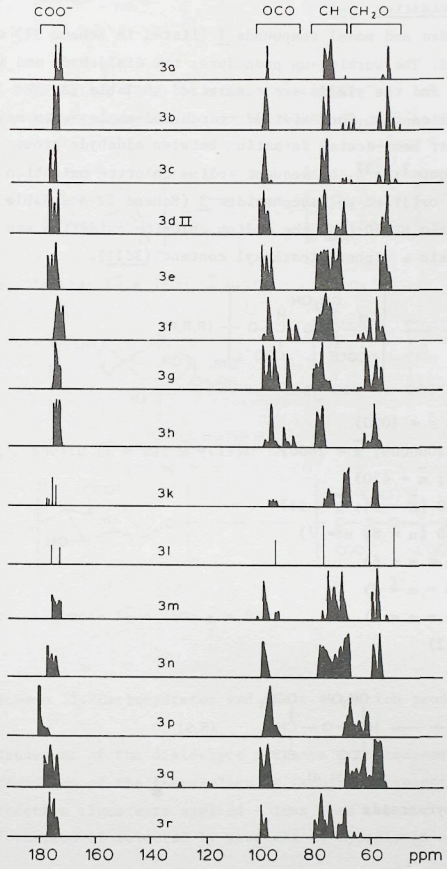
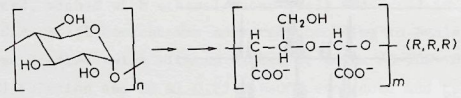


Fig. 1. ^{13}C NMR spectra of the polysaccharides 3.

Results and discussion

Preparation and characterization

A series of polysaccharides and model compounds 1 (listed in Scheme II) were oxidized by periodic acid. The working-up procedure, the dialdehyde and water content of the products, and the yields are summarized in Table IA. The somewhat lower dialdehyde content for oxidized starch and amylopectin may result from intramolecular hemi-acetal formation between aldehyde groups and non-oxidized hydroxyl groups[3,6,37]. Subsequent sodium chlorite oxidation yielded conveniently the oxidized polysaccharides 3 (Scheme II and Table IB). In the case of maltodextrin MD 10 (3d) the sodium chlorite oxidation was repeated in order to attain a higher dicarboxyl content (3dII).



1 3

a starch ($\bar{n}$ = 3850; $\bar{m}$ = 1000)

b amylopectin ($\bar{n}$ = 2000000; $\bar{m}$ = 2600)

c amylose ($\bar{n}$ = 3000; $\bar{m}$ = 420)

d/dII maltodextrin MD 10 ($\bar{n}$ = 14; $\bar{n}$ = 11)

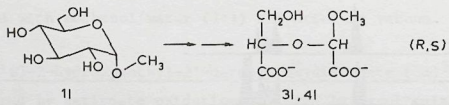
e maltodextrin MD 20 ($\bar{n}$ = 8; $\bar{n}$ = 7)

f α-cyclodextrin (n ≈ m = 6)

g ß-cyclodextrin (n ≈ m ≈ 7)

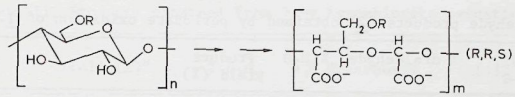
h γ-cyclodextrin (n ≈ m ≈ 8)

k *maltose* (n = m = 2)



11 31,41

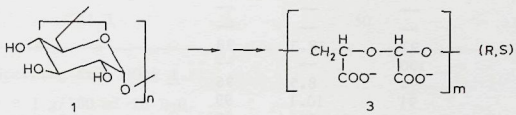
l methyl α-D-glucopyranoside



1 3

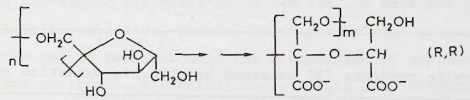
m cellulose (R=H) ($\bar{n}$ = 2800; $\bar{m}$ ≈ 660)

n carboxymethyl cellulose (R = 82% CH_2COO^- + 18% H) ($\bar{n}$ = 2500; $\bar{m}$ = 1100)



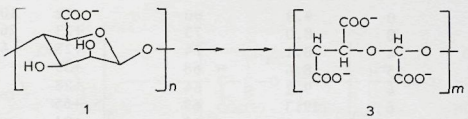
1 3

p dextran ($\bar{n}$ = 1500; $\bar{m}$ = 20)



1 3

q inulin ($\bar{n}$ = 22; $\bar{m}$ = 19)



1 3

r alginate ($\bar{n}$ = 660; $\bar{m}$ = 95)

Scheme II. Carbohydrates and their oxidation products.

Treatment of the dialdehyde polymers 2 in aqueous NaOH at 85 °C results in the formation of the intramolecular Cannizzaro reaction products 5. Here short reaction times were applied – less than two min – in order to prevent the formation of coloured by-products by hydrolysis and fragmentation reactions[38].

Table IA. Dialdehyde products (2) obtained by periodate oxidation of 1.

Nr	Method[a]	% dialdehyde	% H_2O	Product yield (%)
2a	A	73	5.2	90
2b	A	77	10.6	82
2c	A	88	11.2	85
2d	B	93	14.6	89
2e	B	86	8.9	93
2f	B	--	--	--
2g	B	--	--	--
2h	B	--	--	--
2k	B	97	18.3	98
2l	-	100	--	--
2m	A	94	8.5	96
2n	C	91	10.1	99
2p	C	66	8.1	63
2q	B	79	9.7	91
2r	C	90	8.8	97

Table IB. Dicarboxylic products (3) obtained by chlorite oxidation of 2.

Nr	% dicarboxyl	% dialdehyde	% H_2O	Overall product yield (%)	$[\alpha]_D^{20}$[b]	$\bar{m}$
3a	73	0	9.9	60	+22	1000
3b	77	0	8.0	73	+23	2600
3c	84	4	8.1	74	+25	420
3d	68	25	8.6	68	+35	12
3dII	89	4	9.2	64	+28	11
3e	80	6	19.3	69	+65	7
3f	69	16	--	89	+21	7
3g	43	42	--	75	+27	8
3h	78	12	--	95	+24	9
3k	96	1	--	64	+62	2
3l	100	0	--	87	-12	1
3m	64	30	3.7	56	-227	660
3n	72	19	7.2	87	-10	1100
3p	61	5	9.3	57	+15	20
3q	73	6	12.2	62	+15	19
3r	68	24	9.5	95	-18	96

[a] *See Experimental.*
[b] c ≈ 1 g/100 ml in H_2O.

Some results of the one-step oxidation procedure with sodium hypochlorite are summarized in Table II. The carboxyl content is comparable with or lower than that of products from the two-step oxidation procedure.

Table II. Products obtained from 1 by hypochlorite oxidation.

Nr	Yield (g)[a]	% H_2O	% dicarboxyl	$[\alpha]_D^{20}$[b]	$\bar{m}$
4a	9.1	5.1	77	+172	620
4d	9.4	7.1	76	+117	11
4e	10.0	3.1	74	+92	5
4k	12.5	~	90	+3	2
4l	11.3	~	50	+1	1

[a] *Starting from 10 g 1.*
[b] c ≈ 1 g/100 ml in H_2O.

During the acidic periodate oxidation and the alkaline chlorite or hypochlorite oxidation, partial hydrolysis of the polymers will occur. In order to get an impression of the mean degree of polymerization ($\bar{m}$) of the oxidized materials, a chemical chain length determination[39,40] has been developed, using their hydrolysis products in acid medium (Fig. 2).

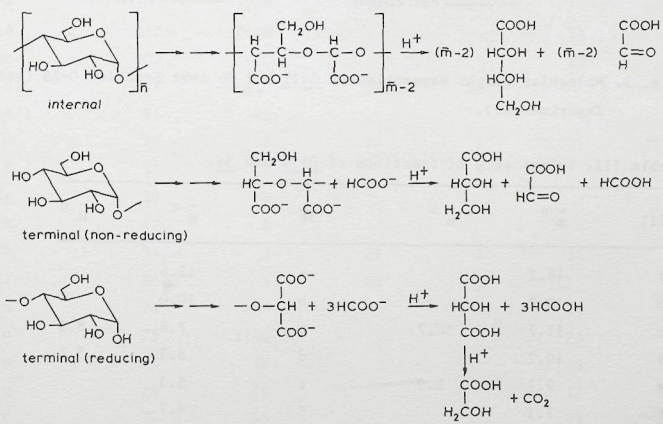


Fig. 2. Hydrolysis of internal and terminal oxidized glucose units.

An oxidized internal glucose unit of the 'starch family' yields erythronic and glyoxylic acid. The oxidized non-reducing terminal glucose unit yields glyceric acid, glyoxylic acid and formic acid, whereas the oxidized reducing terminal glucose unit yields tartronic acid and formic acid. Tartronic acid partially decarboxylates to glycolic acid.

The ratio $\alpha = \frac{\text{glyoxylic acid}}{\text{tartronic acid + glycolic acid}}$, as determined by gas chromatography after trimethylsilylation, equals $\frac{\bar{m} - 2 + 1}{1}$ and gives a measure of the degree of polymerization. The $\bar{m}$ values are given in Scheme II and Tables I-V. It should be realized that the $\bar{m}$ values have been corrected for the dicarboxylic content by multiplication by $\frac{100}{\% \text{ dicarboxylic}}$.

A molecular weight separation of 3dII and 3e was performed on Sephadex (Fig. 3). The $\bar{m}$ values thus obtained were in accordance with those determined by the hydrolysis method described above (Table III).

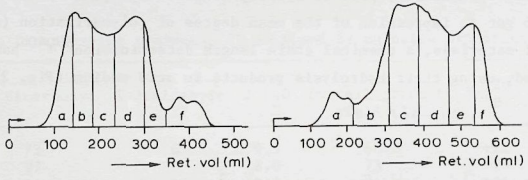


Fig. 3. Molecular weight separation of 3dII and 3e over Sephadex G-25 (see Experimental).

Table III. Values of $\bar{m}$ of fractions of 3dII and 3e.

3dII	$\bar{m}$ a	$\bar{m}$ b	3e	$\bar{m}$ a	$\bar{m}$ b
a	18.2		a	12.6	
b	13.2		b	10.0	
c	11.7	10.7	c	7.8	8.5
d	10.2		d	6.3	5.6
e	9.1	8.9	e	5.1	
f	7.1		f	4.7	

[a] Calculated from retention indexes.

[b] Determined by GC-method (Section 2.3).

Calcium sequestering capacities (SC)

Calcium sequestering capacities (SC) were determined by turbidimetry using sodium oxalate as the indicator according to Wilham and Mehltretter[32]. At the turbidity point $[Ca(II)] = 10^{-5}$ M, which is considered as the upper limit for Ca(II) in the washing process. The SC is defined as mg Ca(II) sequestered per gram of the sodium salt of an oxidized polysaccharide. This weight to weight quantity is of particular importance from a practical point of view. In some cases the SC values do not correlate well with other quantities that describe calcium complexing properties[2]. This may be caused by inhibitory effects of the complexing agents on both crystal growth and precipitation of calcium oxalate[41]. It may be noted that these effects will also explain the time-dependence of SC as observed by Mehltretter et al.[42] for a number of sugar acids. SC values of the oxidized polysaccharides 3, 4 and 5 are summarized in Table IV.

Table IV. Values of SC[a] and $\bar{m}$ of materials 3, 4, and 5.

No	3		4		5
	SC	$\bar{m}$	SC	$\bar{m}$	SC
a	106	1000	100	620	34
b	117	2600			31
c	109	420			19
dI	58	12	59	11	
dII	91	11			29
e	36	7	34	5	22
f	31	7			
g	38	8			
h	42	9			
k	34	2	25	2	12
l	26	1	18	1	
m	74	660			21
n	75	1100			26
p	57	20			18
q	24	19			17
r	77	96			39

[a] STP: SC = 122; NTA: SC = 155.

The oxidized polysaccharides 3a-3d with $\bar{m}$ > 10 show SC values, which are comparable with that of STP (SC = 122) or NTA (SC = 156). Oxidized cellulose, carboxymethylcellulose and alginate possess lower SC values irrespective if periodate/chlorite or hypochlorite oxidation has been applied. The SC values of compounds 5 clearly show that the presence of only one carboxyl group per unit results in weak calcium complexation ability, which is comparable with that for alginate, carboxymethylcellulose, and their dialdehyde oxidation products (SC = 13, 8, 21, and 25, respectively).

Calcium ion selective titrations

In order to study structural and conformational effects on calcium complexation we have determined the decrease in Ca(II) ion activity upon addition of oxidized polysaccharides to aqueous 0.001 M $CaCl_2$ (0.1 M KCl; pH = 9; T = 20 °C) (Fig. 4).

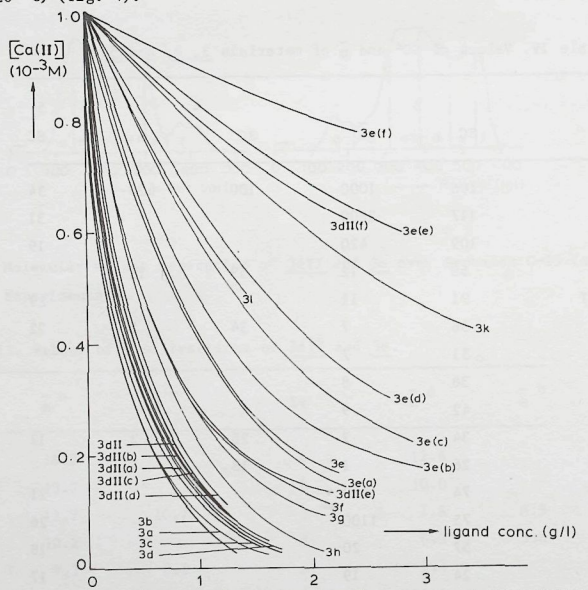


Fig. 4. Calcium ion selective electrode titration curves of oxidation products from the 'starch family' (see Table V).

Table V. Carboxylic contents, values of $\bar{m}$, $W_{50\%}$ and log K.

Compound	$\bar{m}$	Carbox. cont. (mmole/g)	$W_{50\%}$ (g/l)	log K
3a	1000	5.78	0.35	3.98
3b	2600	6.53	0.31	4.16
3c	420	7.14	0.30	3.96
3d	12	5.08	0.50	3.85
3dII	11	7.61	0.36	3.98
3dII(a)	18.2	7.61	0.32	4.00
3dII(b)	13.2	7.61	0.34	4.02
3dII(c)	11.7	7.61	0.35	3.84
3dII(d)	10.2	7.61	0.40	3.76
3dII(e)	9.1	7.61	0.55	3.34
3dII(f)	7.1	7.61	1.20[a]	2.18
3e	7	6.71	0.90	3.07
3e(a)	12.6	6.71	0.63	3.24
3e(b)	10.0	6.71	0.86	3.02
3e(c)	7.8	6.71	1.16	2.86
3e(d)	6.3	6.71	1.43	2.71
3e(e)	5.1	6.71	> 5	2.18
3e(f)	4.7	6.71	> 5	1.89
3f	7	6.43	0.66	3.39
3g	8	4.55	0.70	3.66
3h	9	7.06	0.45	3.53
3k	2	10.42	2.20	2.39
3l	1	8.40	1.30	2.52
3m	660	5.22	1.70	2.66
1n	2500	3.62	> 5	2.42
2n		3.31	3.00	2.81
3n	1100	5.68	1.60	2.69
3p	20	5.94	1.40	2.74
3q	19	7.01	2.90	2.21
1r	660	5.02	4.40	2.23
2r		4.55	0.89	2.47
3r	96	6.59	0.52	3.52
4a	620	6.51	0.37[b]	3.60
4d	11	6.44	0.87	3.04
4e	5	6.28	1.45	2.75
4k	2	7.65	3.60	2.30
4l	1	4.62	4.50	2.32
STP		13.66[c]	0.20	5.09
NTA		11.67	0.14	6.02
CMOS		11.63	0.14	4.86
Citrate		11.63	0.17	4.65

[a] Extrapolated value.
[b] Lit. 10: 0.38 g/l.
[c] Anionic charge in mmole/g.

For the oxidized 'starch family' (3a-3l; 3dII(a)-3dII(e); 3e(a)-3e(e)) we have used $W_{50\%}$, defined as the required concentration of the polycarboxylic acid (in g/l) to complex 50% of Ca(II) in a 10^{-3} $CaCl_2$ solution, as a practical measure for the Ca(II) binding capacity.

In addition, a calcium complexation constant K has been defined by:

$$Ca^{2+} + (-COO)_4^{4-} \rightleftharpoons Ca(-COO)_4^{2-} \qquad K = \frac{[Ca(-COO)_4^{2-}]}{[Ca^{2+}][(-COO)_4^{4-}]}$$

Here it is assumed that each Ca(II) is coordinated by four carboxylate groups of the oxidized carbohydrate (vide infra). All concentrations are expressed as mmole/l, in which a $(-COO)_4^{4-}$ moiety of the ligand is considered as a monomeric unit. The $W_{50\%}$ and log K values thus obtained for a series of oxidized polysaccharides are summarized in Table V[50].

Consideration of the calcium complexation paramaters $W_{50\%}$ and K shows that: (i) a degree of polymerization of $\bar{m} > 10$ is required for acceptable calcium complexation (compare the 'starch family' 3a-3l with STP and NTA), (ii) an (R,R,R) configuration gives much better calcium complexation than the other configurations (compare the oxidized α-1,4-D-glucans ('starch family') with the other compounds), (iii) an increasing number of carboxyl groups per unit, i.e. an increasing number of ODA-moieties per unit, as such does not improve the calcium complexing properties (compare 3a-3d with 3r), and (iv) an increasing number of large groups attached to the ODA-moieties does effect calcium complexing properties (compare 3dII(a) with 3q).

The maltodextrin oxidation products, especially 3dII, show already a good calcium complexing ability at a rather low chain length ($\bar{m} \simeq 20$) and obey the before mentioned compromise between acceptable calcium complexation and acceptable rate of (bio)degradation.

The Ca(II) complexing site as studied with ^{17}O NMR

In order to obtain insight into the Ca(II) complexing sites of the oxidized polysaccharides we have applied ^{17}O NMR in the presence of Dy(III) cations. It is generally accepted that lanthanide(III) cations can be considered as model cations for Ca(II) as their complexes show great structural similarities with those of Ca(II)[47]. Upon coordination, paramagnetic lanthanide(III) cations induce large shifts of the NMR signals of the ligands. We have applied this technique for determining the number of waters in the first coordination sphere of the Ca(II)-oxidized polysaccharide complexes 3a and 3e. the results of the ^{17}O water NMR measurements are given in Fig. 8.

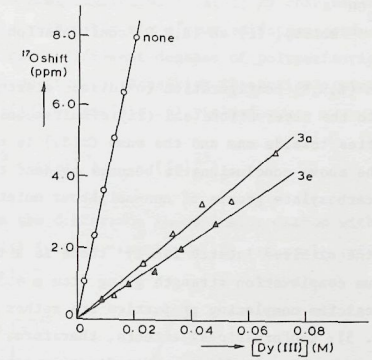


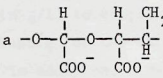
Fig. 8. Dy(III) induced shifts (DyIS) of the ^{17}O water resonance without and in the presence of oxidized starch (3g) or oxidized maltodextrin MD 20 (3e) at 73 °C. Ligand concentration 75.0 g/l.

When $DyCl_3$ is dissolved in D_2O, the ^{17}O NMR signal of D_2O is shifted proportionally to the amount of Dy(III) ions present in the system. The observed signal is an average of free D_2O and $Dy(D_2O)_9^{3+}$, i.e. the water exchange is fast on the ^{17}O NMR time scale.

In the presence of oxidized carbohydrates the DyIS (Dysprosium Induced Shift) of the water is substantially lower because of removal of water from Dy(III) upon complex formation. Using the concept of constant ^{17}O DyIS together with nine-coordination of Dy(III), which is dealt with in detail elsewhere[48], the DyIS data of the ^{17}O water resonance gives the number of waters in the Dy(III)-oxidized carbohydrate complexes and thus the number of coordinating oxygens of the ligand. In this way it is found that Dy(III)-3e contains 1.6 waters (7.4-coordination) and Dy(III)-3a contains 1.9 waters (7.1-coordination). This means that at least two ^-OOC-C-O-C-COO^- moieties of the oxidized carbohydrates are involved in the complexation of one Ca(II) ion.

Structural and conformational effects on calcium complexation

Inspection of molecular models shows that for complexation of Ca(II) by

a  moiety, (i) an (R,R,S) configuration (oxidized cellulose) is in favour of an (R,R,R) configuration (oxidized 'starch family'), which is in contradiction to the observations and (ii) simultaneous coordination of neighbouring moieties towards one and the same Ca(II) is not possible.

Together with the above conclusions it becomes evident that there must occur a cooperation of carboxylate groups of non-neighbour moieties in oxidized polysaccharides.

In the case of the oxidized 'starch family' there is a remarkably steap increase of calcium complexation strength going from $\bar{m}$ = 5 to $\bar{m}$ = 15, whereas above $\bar{m}$ = 15 the calcium complexing properties are rather independent of the chain length (Fig. 5). Conformational effects, therefore, seem of great importance for the creation of efficient coordination sites containing remote carboxylate groups. This will be discussed in more detail in section 3.6.

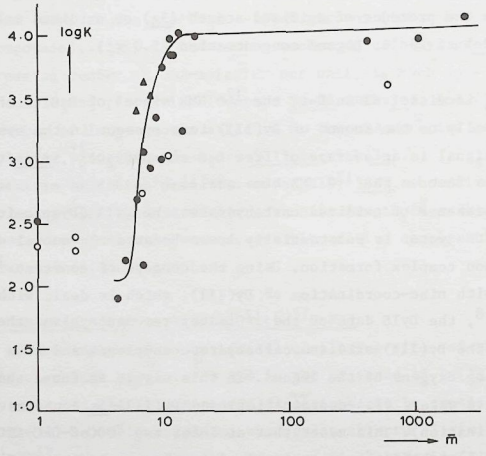


Fig. 5. Relation between log K and $\bar{m}$ for oxidized members of the 'starch family' (●), oxidized cyclodextrins (▲) and NaOCl oxidation products (○).

Rees et al.[43,44], Crescenzi[45], Smidsrod[46] and Kohn[25,26] have studied conformational changes of natural anionic polysaccharides (alginate, pectine, carrageenan) upon complexation with Ca(II) by changes in optical rotation. We have applied this method for six of our oxidation products (31, 3h, 3e, 3dII, 3c and 3a) with quite different degrees of polymerization (1, cyclo 9, 7, 11, 420 and 1000, respectively). Measuring the optical rotation as a function of the amount of Ca(II) added (Fig. 6) yielded

$$\Delta\,[\alpha]_D^{25} = ([\alpha]_D^{25})_{\rho=0} - ([\alpha]_D^{25})_\rho$$

which represents the difference in optical rotation without (ρ = 0) and in the presence of Ca(II) (with ρ = mmole Ca(II) per mmole $(-COO)_4^{4-}$ moieties present in the substrate).

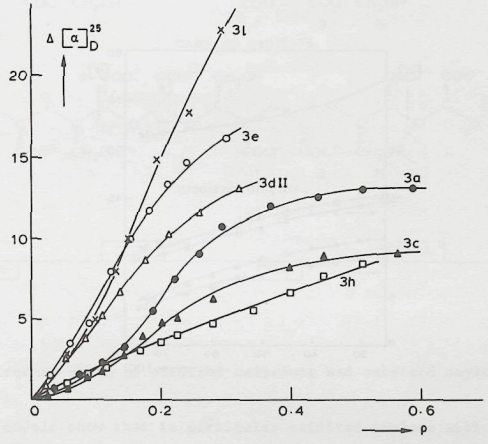


Fig. 6. Changes in optical rotation upon addition of $CaCl_2$ to oxidized members of the 'starch family'. ρ = Ca(II)/$(-COO)_4^{4-}$; ligand concentration is 40 g/l.

The monomer 31, oxidized methyl α-D-glucopyranoside, shows by far the greatest change in optical rotation, indicating that 31 undergoes a substantial conformational change upon complex formation with Ca(II). Molecular models show indeed that concomitant coordination of the two carboxylate groups, which is a prerequisite to explain log K = 2.52 for 31, requires a quite different

conformation in comparison with that in the uncomplexed state.

The less pronounced effect in optical rotation for 3e, 3dII, 3c and 3a, despite the fact that at a given ρ-value the amount of Ca(II) complexed is larger than in the case of 31, clearly parallels their value of $\bar{m}$. This implies that the conformational change upon complexation becomes less going from $\bar{m}$ = 7 to higher values. Probably, the conformation of the larger products already resembles that in the calcium complex. As expected, also relatively small conformational changes upon calcium complexation will occur in the macrocyclic system 3h.

Finally, the observed decrease in optical rotation at higher temperature is in accordance with an increasing disorder in conformational preference (Fig. 7).

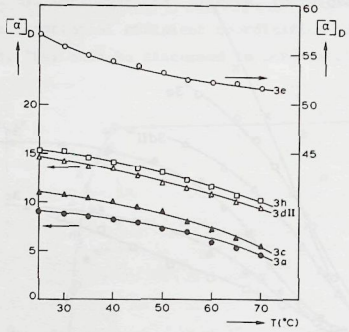


Fig. 7. Influence of the temperature on $[\alpha]_D$ of oxidized members of the 'starch family' in the presence of Ca(II); 3e: ρ = 0.30, 3h: ρ = 0.18; 3dII: ρ = 0.52; 3c: ρ = 0.56; 3a: ρ = 0.52.

Helix structure of Ca(II) complexes

Consideration of the stretched conformation for both oxidized cellulose and oxidized amylose (Fig. 9) reveals that (i) there is a greater tendency towards coiling for oxidized amylose because of the unfavourable 1,3-COO^-, COO^- and 3,5-COO^-, CH_2OH repulsions and (ii) the ^-OOC-C-O-C-COO^- moieties in the stretched conformations do not possess the right W-conformation for calcium complexation as earlier established for monomeric compounds as ODA (Fig. 10).

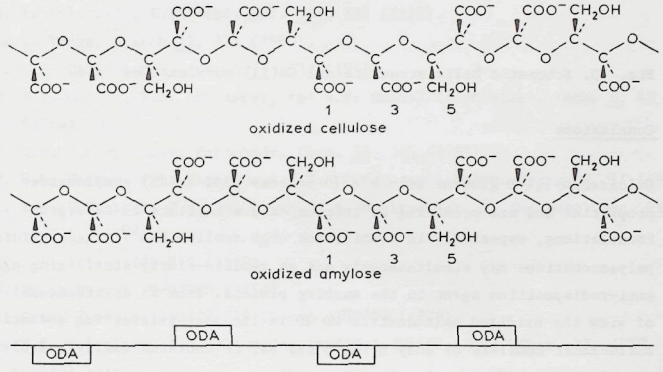


Fig. 9. Streched chain of oxidized cellulose and oxidized amylose.

Molecular models show that in particular oxidized amylose will easily coil towards a helix structure with a concomitant reorientation to favourable W-shaped ODA moieties, which are positioned in an alternating way above and below a coil. The picture thus derived is shown schematically in Fig. 10. A helix with 7 oxidized glucose units per coil creates good Ca(II) complexing sites containing four carboxylate groups and two acetal oxygens, which is in agreement with the observed changes in calcium complexation around $\bar{m}$ = 7 (section 3.5) and with the ^{17}O NMR measurement (section 3.4). The very efficient calcium complexation by four carboxylic groups is reflected in the initial Ca(II) complexation by 3dII of 1.68 mmol Ca(II)/g (theor. 1.91) which can be compared with only 0.56 mmol Ca(II)/g for 3e (theor. 1.68).

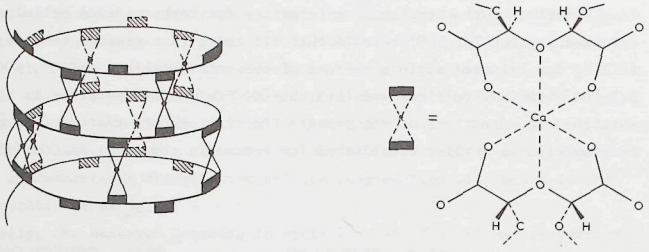
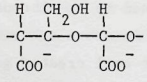


Fig. 10. Schematic helix structure and Ca(II) complexation site.

Conclusions

Oxidized α-1,4-D-glucans with $m \geq 10$ possess good Ca(II) complexation properties and are promising as triphosphate substitute in detergent formulations, especially in combination with zeolite NaA[49]. These oxidized polysaccharides may simultaneously act as zeolite-slurry stabilizing agents or anti-redisposition agent in the washing process. From an environmental point of view the oxidized maltodextrin MD 10 is the most interesting potential co-builder: it consists of only C, H, O and Na, it contains easily hydrolyzable acetal moieties (under the slightly acidic waste water conditions) and it possesses good calcium complexing properties at a relatively low degree of polymerization ($\bar{m} = 10$). These properties will ensure fast chemical and biological degradation into CO_2 and H_2O.

A degree of polymerization of the oxidized α-1,4-D-glucans of 10 or more is a prerequisite for good Ca(II)-complexing properties. In this respect, it is proposed that helix structure formation seems essential by which coordination of Ca(II) with two



moieties becomes possible. In this way complexation of each Ca(II) takes place by 6-7 oxygens of the oxidized carbohydrate.

Compounds derived by oxidation of other polysaccharides, e.g. cellulose, dextran, inulin, and alginate, possess much less calcium sequestration strengths than the above members of the "starch family". This might be connected with their less favourable configurations for helix formation.

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CHAPTER VIII

CATION EXCHANGE IN THE SYSTEM Ca(II) OR Mg(II)/COMPLEXING AGENT/ZEOLITE NaA: EQUILIBRIA AND KINETICS*

Abstract

Ion exchange was studied of Ca(II) and Mg(II) with the phosphate substitute zeolite NaA in the presence of the complexing agents: oxydiacetate, nitrilotriacetate, and borate/glucarate as potential co-builders. The ion exchange isotherms (32 °C and 60 °C) show that the total amount of the divalent ions in solution increased with increasing complexation strength of the co-builder. In the case of oxydiacetate adsorption of the complexing agent in the zeolite was observed.

Ion exchange kinetics were measured at 32 °C. Addition of complexing agents causes the ion exchange rate of Ca(II) with NaA to increase and the ion exchange rate of Mg(II) with NaA to decrease. These kinetic effects are largely due to diffusion phenomena in the zeolite, due to variations in cation composition of the zeolite during the exchange processes.

Introduction

The worldwide discussion concerning the eutrophication of surface water by phosphates has initiated a search towards new builders for detergent formulations. As only a few organic builders meet the technological, economical, ecological and toxicological requirements, also inorganic

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insoluble ion exchangers, particularly sodium aluminium silicates are of present interest.

The principal candidate is zeolite NaA[1,2] which is already being used in some detergent formulations replacing up to 50% of sodium tripolyphosphate (STP). Although zeolite NaA possesses a good ion exchange capacity for Ca(II) ions, together with a less pronounced ion exchange capacity for Mg(II), it cannot take over other builder properties of STP. For instance Ca(II) ions that form bridges between textile surfaces and dirt, are not removed by NaA, within the limitation in time of the washing process. Therefore a water soluble complexing agent is required in order to remove immobile Ca(II) ions from the dirt by desorption and complexation, and to transport Ca(II) towards the ion exchanger. This 'carrier' mechanism has been proposed by Smolka and Schwuger[3] who studied the 'Ca-carry-over' from a badly soluble calcium salt to NaA in the presence of STP, sodium nitrilotriacetate (NTA) or sodium citrate as the so-called co-builder. These zeolite/co-builder mixtures were also investigated by Berth[4,33] Schwuger and Smolka[5], and Borchert and Marino[6]. Also a number of patents have been disclosed in this field[7].

For the system zeolite NaA and Ca(II) and Mg(II) ions many literature data are available on ion exchange equilibria[8-12] and ion exchange kinetics[1,11,3-10]. Great differences between Ca(II) and Mg(II) have been observed. On the other hand, co-builder effects were often studied from a rather practical point of view. In some cases[2,3] it is not obvious whether equilibrium is attained or not, as samples were taken after a limited time. In other cases[1,4,6,17,18,33] the positive effects of the introduction of a co-builder were only established by washing tests.

In our laboratory we are studying the problem of STP substitution with particular attention for the complexation of Ca(II) ions with organic complexing agents[20]. Within this scope, we have investigated the influence of such agents on both the equilibria and kinetics of Ca(II) and Mg(II) ion exchange of zeolite NaA in aqueous medium. As the organic co-builders we chose oxydiacetate (ODA), NTA and a sodium glucarate (G)/borate (B) mixture (Fig. 1). In the latter system an ester is formed between one borate and two glucarate parts. The borate ester BG_2 has good Ca(II) complexation properties[21]. A more detailed study on the borate/glucarate system is in progress in this laboratory[23].

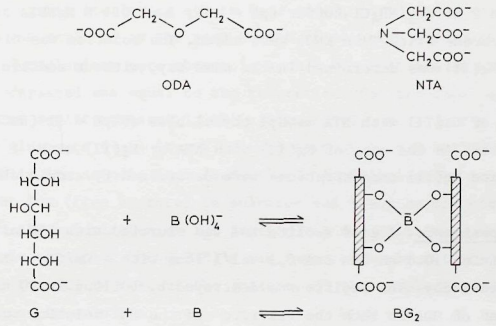


Fig. 1. Complexing agents.

Experimental

$CaCl_2.2H_2O$ (Merck), $MgCl_2.6H_2O$ (Merck), NaCl (Baker), EDTA (Baker), MgEDTA (Fisher), ODA (Merck), NTA (Merck), boric acid (Lamens & Indemans), glucaric acid mono potassium salt (Janssen Chimica), methyl thymol blue (Merck), eriochrome black T (Merck), were all reagent grade and used without further purification. Zeolite NaA (Degussa HAB A 40) was used air dried (see Table I).

Equilibrium measurements (at 32 ± 1 °C or 60 ± 0.5 °C). 1 g of zeolite NaA was slurried under N_2 in 250 ml containing 0.1 val/l (0.1 mole positive or negative charge/l) of $CaCl_2$ + NaCl or $MgCl_2$ + NaCl, at pH = 9. In the case of the addition of complexing agents 10.6 mM ODA, 7.1 mM NTA, or 4.7 mM boric acid + 9.4 mM glucaric acid were used. As boric acid is only half dissociated at pH = 9 the effective negative charge was chosen to be $-\frac{1}{2}$. It was established, that after 1 h (Ca(II)) and 5 h (Mg(II)) equilibrium was reached. At these times, samples were taken, filtrated and the filtrate analyzed (see below).

Kinetic measurements (at 32 ± 1 °C). Samples were taken from the above described solutions and filtrated within 10 sec. over a 0.22 µm BIORAD Uni pore cellulose ester filter using a BIORAD Uni pore disc prefilter. Starting time: addition of the divalent ion solution to the slurry. Sampling time: withdrawal of the sampling syringe from the solution.

Ca(II) concentrations were determined by adding 5 ml of the sample to 25 ml of water. Then 2 ml NH_3/NH_4Cl buffer (pH = 10), 1 ml 0.1 M MgEDTA solution and 30-40 mg eriochrome black T in KNO_3 were added. The solution was titrated with 0.01 M EDTA. Mg(II) was determined in the same way, without addition of MgEDTA.

In the case of Ca(II) with NTA methyl thymol blue at pH = 12 (NaCH) was used as the indicator. In the case of Mg(II) with NTA or Mg(II) with borate/glucarate Mg(II) concentrations were determined by atomic absorption spectrometry.

Adsorption experiments. 1 g of zeolite NaA was slurried with 250 ml of the solvent containing 10.6 mM ODA and 0.1 val/l ions with a Ca/(Ca + Na) ratio of 0 and 1, respectively. The zeolite was destroyed by boiling in 20 ml conc. HCl. The amount of ODA in both the filtrate and the HCl solution was measured by HPLC using a reverse phase column and H_2O + 0.1% trifluoroacetic acid as the eluent and UV detection at 210 nm.

Table I. Technical data of zeolite NaA (HAB A 40)[21]

bruto formula	$Na_{12}(AlO_2)_{12}(SiO_2)_{12}.27H_2O$
q_o = theoretical ion exchange capacity	5.62 mval/g air dried
average particle size	4 µm
ignition loss (20 h at 400 °C)	20.14% w/w

Results and Discussion

Equilibria

Ion exchange isotherms (IEI) were obtained by equilibrium measurements starting from different Ca/Na or Mg/Na ratios. 1 g of zeolite was slurried with 250 ml 0.1 val/l solution at pH = 9 (1 val/l = 1 mole/l positive or negative charge). The distribution of Ca(II) or Mg(II) between zeolite solution is defined by:

$$X_e = \frac{\text{val } M^{2+}}{\text{val } M^{2+} + \text{val } Na^{+}} = \frac{\text{val } M^{2+}}{25.0} \quad \text{(in solution)}$$

$$Y_e = \frac{\text{val } M^{2+}}{\text{val } M^{2+} + \text{val } Na^{+}} = \frac{\text{val } M^{2+}}{5.62} \quad \text{(in the zeolite)}$$

X_e and Y_e were calculated from the initial and final concentrations of the divalent ion in solution. In an IEI the relation between X_e and Y_e is expressed.

When organic complexing agents were added, part of the chloride counter ion charge was replaced by the same amount of negative charge of the complexing agent. Formulations were chosen in such a way that the amount of negative charge replaced was equal to the theoretical ion exchange capacity of the amount of zeolite present in the system (5.62 mval). In the case of borate/glucarate (1:2) it was assumed that at pH = 9 half of boric acid is present in its anionic form (borate). At equilibrium the total amount of divalent ion (free hydrated in solution and bound by the complexing agent) was used in the calculation of X_e. In this way a pseudo ion exchange isotherm (PIEI) is obtained. These PIEI's are expected to be situated on the right hand side of the IEI because of the presence of the complexing agent as a competitor in solution, causing relatively high values of X_e.

IEI's and PIEI's of the systems investigated are given in Fig. 2a (32 °C) and Fig. 2b (60 °C).

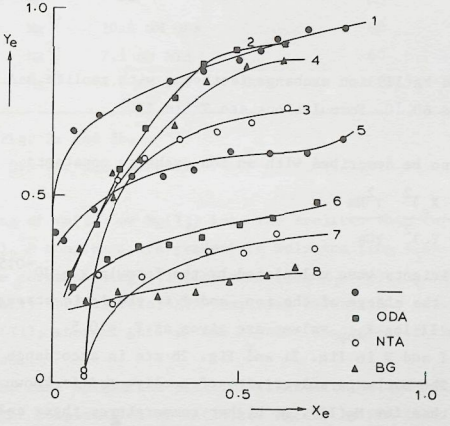


Fig. 2a. Ca(II) and Mg(II) ion exchange isotherms with zeolite NaA in water at pH = 9 and 32 °C. Formulations see Table II.

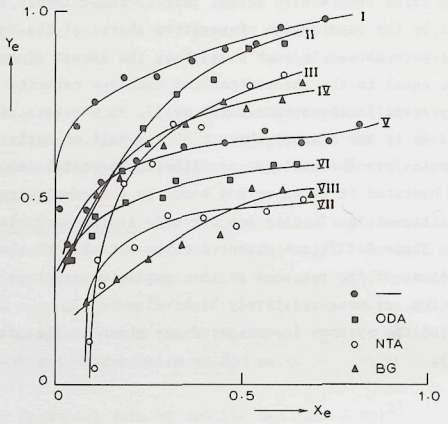


Fig. 2b. Ca(II) and Mg(II) ion exchange isotherms with zeolite NaA in water at pH = 9 and 60 °C. Formulations see Table II.

Equilibrium can also be described with an ion exchange constant:

$$K_{app} = \frac{Y_e\,(1 - X_e)^2}{X_e\,(1 - Y_e)^2} \cdot \frac{\gamma^2 Na}{\gamma Ca} .$$

The activity coefficients were calculated by the formula $\gamma = 10^{-0.505\, z_i^2 \sqrt{I}}$, where z_i expresses the charge of the ion, and I is the ionic strength of the solution. In Table II log K_{app} values are given at $Y_e = 0.5$.

The IEI's 1, 5, I and V in Fig. 2a and Fig. 2b are in accordance with literature data[9]. The exchange selectivity of zeolite NaA is known to be much better for Ca(II) than for Mg(II). At higher temperatures these selectivities are higher (positive $\Delta S°$)[9], i.e. IEI's at 60 °C are on the left hand side of the IEI's at 32 °C. When complexing agents are present this behaviour is more pronounced since complexation is weaker at elevated temperatures, i.e. also PIEI's at 60 °C are on the left hand side at the PIEI's at 32 °C. Furthermore, PIEI's lie on the right hand side of the IEI's in most cases as was expected. In the case of the strongest complexing agent NTA all curves (3, 7, III, VII) coincide at $X_e = 0.1$ and $Y_e = 0$. At this point there is hardly any measurable

Table II. Formulations and values of log K_{app} at $Y_e = 0.5$.

Curve[a]	Ion	Complexing agent	Temp. (°C)	log K'_{app} ($Y_e = 0.5$)
1	Ca^{2+}	--	32	1.3
2	Ca^{2+}	10.6 mM ODA	32	0.6
3	Ca^{2+}	7.1 mM NTA	32	0.3
4	Ca^{2+}	4.7 mM B + 9.4 mM G	32	0.5
5	Mg^{2+}	--	32	0.5
6	Mg^{2+}	10.6 mM ODA	32	--[b]
7	Mg^{2+}	7.1 mM NTA	32	--[b]
8	Mg^{2+}	4.7 mM B + 9.4 mM G	32	--[b]
I	Ca^{2+}	--	60	1.5
II	Ca^{2+}	10.6 mM ODA	60	0.6
III	Ca^{2+}	7.1 mM NTA	60	0.5
IV	Ca^{2+}	4.7 mM B + 9.4 mM G	60	0.7
V	Mg^{2+}	--	60	0.6
VI	Mg^{2+}	10.6 mM ODA	60	0.2
VII	Mg^{2+}	7.1 mM NTA	60	-0.8
VIII	Mg^{2+}	4.7 mM B + 9.4 mM G	60	-0.7

[a] See Fig. 2a and 2b.

[b] $Y_e = 0.5$ was not reached.

entering of Ca(II) or Mg(II) into the zeolite. When $Ca(NTA)_2^{4-}$ or $Mg(NTA)_2^{4-}$ complexes are present in solution (log $\beta_2 = 9$) X_e would be 0.071. For the corresponding 1:1 complexes (log $K_1 = 6$), X_e would be 0.142. Apparently the 1:2 metal-NTA complexes essentially prevent exchange of Ca(II) and Mg(II), whereas this is not anymore the case for the corresponding 1:1 complexes.

In the case of ODA the PIEI is situated relatively close to the IEI, because of weaker complexation of Ca(II) or Mg(II) by ODA than by NTA. In curve 2, however, the PIEI cuts the IEI, which is curious from a thermodynamic point of view. This discrepancy might be caused by some adsorption of ODA into the zeolite, which would enhance the ion exchange capacity of the zeolite. The molecular dimensions of ODA allow such an adsorption, especially at higher values of Y_e, because of the larger pore diameter of CaA compared with NaA (0.5 and 0.4 nm, respectively). NTA and BG_2 are too large to penetrate NaA, but when applying NaX, for instance, which is mentioned as detergent

builder[15,31], also with NTA or BG_2 such phenomena may occur.

The effect of possible adsorption of ODA into the zeolite is demonstrated in Fig. 3.

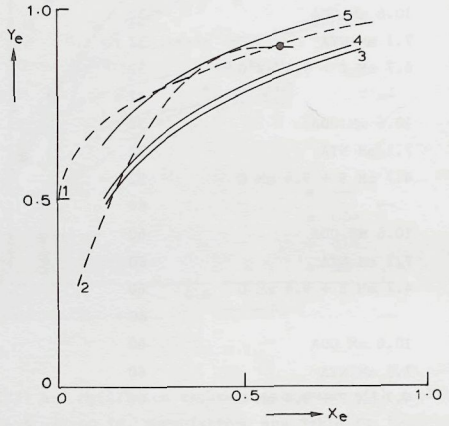


Fig. 3. Comparison of experimental and calculated Ca(II) ion exchange isotherms of the system (NaA/ODA/Ca(II)/32 °C).

curve 1: experimental IEI
curve 2: experimental PIEI
curve 3: calculated PIEI
curve 4: calculated PIEI assuming 10% adsorption of ODA
curve 5: calculated PIEI assuming 10% adsorption of CaODA
. : experimental point showing 4-7% adsorption of ODA

The PIEI was calculated from the IEI using a stability constant at the CaODA complex of $2.5 * 10^3$ (curve 3). It is seen that a 10% adsorption of ODA (curve 4) or CaODA (curve 5) explains the phenomenon of crossing PIEI and IEI curves.

Direct experimental evidence for ODA adsorption was obtained by measuring both the amount of ODA in solution and the amount of ODA released from the destroyed zeolite. In a typical equilibrium mixture (the point at $X_e = 0.59$; $Y_e = 0.89$ in Fig. 3) we found that 6.6% of ODA disappeared from the solution

and that 4.1% was released upon destruction of the zeolite, so about 18.5 µmole ODA per g zeolite was adsorbed. Monolayer adsorption outside the zeolite which was measured by Savitsky et al.[22] with cationic, nonionic and anionic surface active agents, would imply an adsorption of 2.5 µmole ODA per g zeolite. When no Ca(II) ions are present in the system no ODA could be detected in the destroyed zeolite, nor were found to be disappeared from the solution.

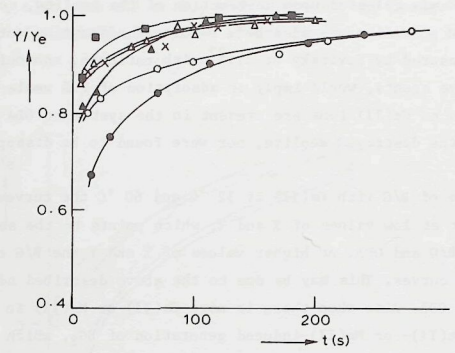
In the case of B/G with Ca(II) at 32 °C and 60 °C the curves (2, 4, II, IV) do not differ at low values of X and Y, which points to the same complexing strength of B/G and ODA. At higher values of X and Y the B/G curves are lower than the ODA curves. This may be due to the above described adsorption phenomena of ODA. Also when there is more Ca(II) or Mg(II) in the system, there is a Ca(II)- or Mg(II)-induced generation of BG_2, which is complexing these ions (cf. Fig. 1). At 60 °C the B/G curve is crossing the NTA curve. Although increasing temperature generally favours Ca(II) and Mg(II) ion exchange and causes decreasing complex formation, the B/G system shows temperature-independence. This was also measured with ^{11}B NMR[23].

Kinetics

The formulation of the divalent cation/organic ligand/zeolite system for the kinetic measurements has been chosen in such a way, that the amounts of these three species (expressed in mval) are the same, i.e. mval Ca(II) or Mg(II) = mval organic ligand = mval zeolite.

At time zero, the divalent cation is completely present in the bulk aqueous ligand phase of the mixture. The results of the kinetic measurements for Ca(II) and Mg(II) are summarized in Fig. 4a and 4b, respectively. In addition the average diffusion coefficient $\bar{D}$ for the transport of the appropriate divalent cation into the zeolite is included. The $\bar{D}$-values have been calculated according to the method of Ash et al.[24], and have been averaged over the Y_o-Y_e ranges passed through during the ion exchange process.

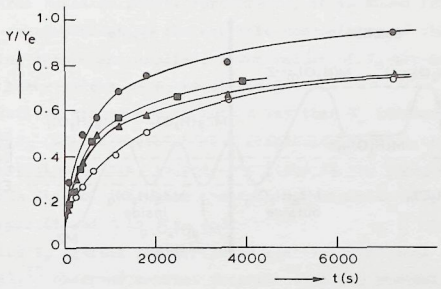
The results clearly show that Mg(II) ion exchange of zeolite NaA is much slower than Ca(II) ion exchange. The hydrated ions are too large to enter the zeolite (r_{hydr} (Ca(II)) = 4.5 Å; r_{hydr} (Mg(II)) = 5.9 Å; $r_{zeolite}$ = 2.4 Å)[25], so part of the hydration sphere of the cation has to be disrupted. Since the activation energy of dehydration of Ca(II) is lower than that of Mg(II) (7.4 and 10.8 kcal/mole, resp.)[26] Ca(II) ion exchange will be faster, because dehydration is the rate limiting step as the diffusing cations pass through the 8-membered O-rings of the zeolite. It may be noted that the leaving Na(I) ions with r_{hydr} = 3.4 Å will diffuse faster than the incoming divalent ions.



curve	X_o	X_e	Y_e	complexing agent	$\tilde{D}$ (10^{-12} cm^2/s)
●	0.226	0.086	0.623	--	40
*	0.068	0.001	0.297	--	240
▲	0.226	0.124	0.454	10.6 mM oDA	140
■	0.226	0.132	0.418	7.1 mM NTA	230
Δ	0.226	0.157	0.307	10.1 mM NTA	230
0	0.226	0.120	0.472	4.7 mM B + 9.4 mM G	72

Fig. 4a. Fractional attainment of equilibrium concentration vs time upon ion exchange of NaA with Ca(II) with water at pH = 9 and 32 °C.

In the case of organic cation exchangers approximate equations from the solution of Fick's second law by Reichenberg[27] show a linear relationship between a dimensionless time parameter Bt (calculated from Y/Y_e) and time. All our Bt vs t plots show non-linearity which has also been shown by Brown et al.[28,29]. This points to the fact that not only the mobility of cations in the zeolite (which is called particle diffusion or self-diffusion) is rate determining. A second rate determining process will be the final settlement of the divalent ions at the 6-membered O-rings (S_I sites) where they loose most of their hydration water and are more strongly bound than at the 8-membered O-rings. This process can be called the actual ion exchange. When there are several rate determining steps involved, only numerical solutions of the rate equation are possible as was shown by Drummond et al.[19] and Danes et al.[13,14] (see below).



curve	X_o	X_e	Y_e	complexing agent	$\tilde{D}$ (10^{-12} cm^2/s)
●	0.220	0.139	0.360	--	0.67
▲	0.220	0.150	0.310	10.6 mM ODA	0.37
■	0.220	0.162	0.258	7.1 mM NTA	0.36
0	0.220	0.69	0.227	4.7 mM B + 9.4 mM G	0.29

Fig. 4b. Fractional attainment of equilibrium concentration vs time upon ion exchange of NaA with Mg(II) in water at pH = 9 and 32 °C.

In the presence of organic complexing agents the exchange of Ca(II) becomes faster whereas the exchange of Mg(II) becomes slower (see Fig. 4a and 4b). In a system with complexing agents an additional rate determining step may occur: decomplexation upon arrival of the complex at the zeolite surface. In order to illustrate the different steps going from a complexed cation in solution towards the situation in which the cation is bound in a 6-membered ring, we have depicted an energy scheme (Fig. 5).

The energy scheme is constructed on the basis of two assumptions:

- there is, in principle, no difference between the coordination of an organic ligand with a cation in solution and that of a zeolite 6-membered O-ring with a cation, in so far the inner coordination sphere is involved,
- rates of association processes between a hydrated cation and a coordinating species (organic ligand or a zeolite 6-membered O-ring) are determined by inner sphere dehydration of the cation.

This means, for a certain hydrated cation that (i) the various activation energies of association are equal, i.e. $E_7-E_6 = E_5-E_2$ and (ii) the differences in complexation strengths are equal to differences in activation energies of

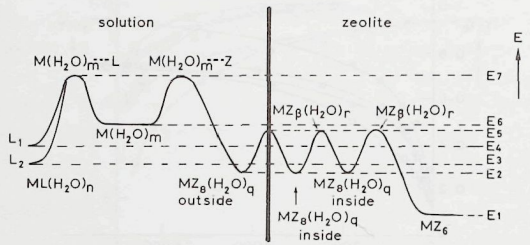


Fig. 5. Energy scheme of complexation and ion exchange.

the dissociation process, e.g. $(E_6-E_3)-(E_6-E_4) = (E_7-E_3)-(E_7-E_4)$. For these phenomena in heterogeneous solutions the reader is referred to the excellent review of Frey and Stuehr[30] and illustrations by Cram et al.[32] lately.

Going from left to right in Fig. 5 the following steps are involved in the transfer of a complexed cation from the solution into a location near a 6-membered O-ring inside an A-zeolite:

- dissociation of the cation/organic ligand complex,
- interaction of the hydrated cation with the outside of an outer 8-membered O-ring of the zeolite,
- passage through that ring and interaction with the inside of the 8-membered O-ring,
- dissociation of the cation/8-membered O-ring complex into a partially hydrated cation in a large zeolite cage,
- repetition of the three last mentioned steps with transfer of the cation to a neighbouring large cage,
- association of that cation with a 6-membered O-ring of the zeolite.

As the activation energy of dehydration is higher for Mg(II) than for Ca(II), the much lower exchange rate of Mg(II) can be easily understood by this energy scheme. The water exchange rates (10^{-5} s^{-1} for Mg(II) and 10^{-8} s^{-1} for Ca(II)[30]) thus explain their different behaviour.

In the presence of a ligand the Ca(II) and Mg(II) exchange rates with zeolite NaA would be expected to be lowered if the dissociation step of the complex is rate limiting. A rate lowering is observed for Mg(II). However, Ca(II) shows an increase in exchange rate. Consequently, other phenomena will also be of importance. An important feature is that during the cation exchange process, the composition and the character of the zeolite alters, i.e. goes

from NaA towards NaCaA or NaMgA. Furthermore, it is known that the diffusion coefficients are dependent on the cationic composition of the zeolite (Y). So, when complexing agents are applied, lower values of Y_e are attained and consequently other values of $\tilde{D}$ are obtained.

When formulations are chosen in such a way that Y_e (without complexing agent) equals Y_e (in the presence of a complexing agent), the same values of $\tilde{D}$ have to be obtained. This, indeed, was found in the case of Ca(II): the presence of NTA did not influence the exchange kinetics if the Y_e value remains the same (* and Δ in Fig. 4a).

When plotting Y_e against the diffusion coefficients Danes et al.[14] and Drummond et al.[19] observed maxima. Comparison of the present kinetic data (from the curves of Fig. 4a and 4b) with the plots extrapolated from the work of Danes et al.[14] shows a satisfactory agreement (Fig. 6a and 6b).

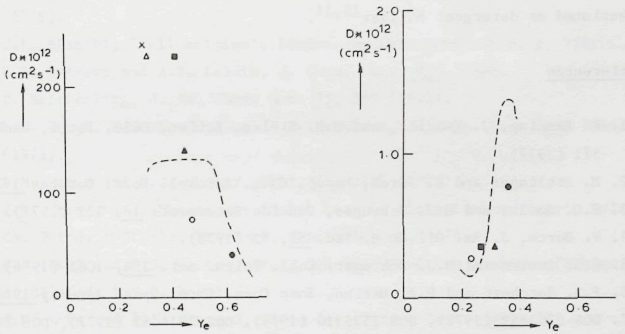


Fig. 6a. Experimental $\tilde{D}/Y_e$ relation, points from Fig. 4a and D_{eff}/Y_e curve (dotted line) from lit. 14, for Ca(II) ion exchange.

Fig. 6b. Experimental $\tilde{D}/Y_e$ relation, point from Fig. 4b and D_{eff}/Y_e curve (dotted line) from lit. 14 for Mg(II) ion exchange.

Ca(II) ion exchange becomes faster when complexing agents are applied, as Y_e is moving uphill on the $Y_e/\tilde{D}$ curve. With Mg(II) Y_e is moving downhill on the $Y_e/\tilde{D}$ curve, causing slower ion exchange.

Conclusions

With the formulations applied, addition of complexing agents increased Ca(II) ion exchange rates with zeolite NaA and decreased Mg(II) ion exchange rates. As ion exchange rates were found to be composition-dependent, complexing agents influence these rates in an indirect manner by causing lower values of the equilibrium composition of the zeolite (Y_e).

The borate/glucarate system seems to have advantages as co-builder above NTA, since the latter acts as a too strong competitor for cation exchange of the zeolite.

The combination of zeolite NaA and small complexing agents, like ODA, may lead to undesired adsorption of the complexing agents inside the zeolite. This effect might occur more readily with the large pore zeolite NaX, which also is mentioned as detergent builder[15,31].

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CHAPTER IX

MULTINUCLEAR NMR STUDY OF THE COMPLEXATION OF LANTHANIDE(III) CATIONS WITH SODIUM TRIPHOSPHATE: INDUCED SHIFTS AND RELAXATION RATE ENHANCEMENTS*

Abstract

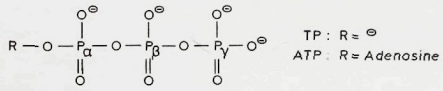
The complexation of lanthanide cations with ^{17}O labelled triphosphate was studied with the use of multinuclear NMR shift and relaxation rate measurements. Depending upon the choice of the lanthanide cation, separate signals for the 1:2 lanthanide-triphosphate complex and the free triphosphate ligand, or averaged spectra were obtained. The longitudinal relaxation was always in the fast exchange region. From the analyses of the shift and relaxation data it is concluded that the lanthanide ion is coordinated with two triphosphate ligands and one water in the first coordination sphere, while seven alkali counter ions are present in the second coordination sphere. Triphosphate is coordinated to the lanthanide ion via two oxygens of one PO_3 group, one oxygen of the other PO_3 group and one oxygen of the PO_2 moiety. In the exchange of triphosphate between the free and the complexed states both associative and dissociative mechanisms play a role.

Introduction

Sodium triphosphate (STP) is one of the most effective detergent builders[1]. Its main purpose is the sequestering of Ca(II) and Mg(II) cations. In addition, lanthanide(III) triphosphates have been demonstrated to be versatile aqueous NMR shift reagents for cations with application in, for example, the

* M.S. Nieuwenhuizen, J.A. Peters, A. Sinnema, A.P.G. Kieboom, and H. van Bekkum, J. Am. Chem. Soc. 107, 12 (1985).

study of the transport processes of alkali metal ions through biological membranes[2]. Complexes of Mg(II) and Ca(II) with esters of triphosphoric acid, such as adenosine triphosphate (ATP), play an important role in many biological processes and have been studied by several authors[3-9].



TP : R = ⊖
ATP : R = Adenosine

Up to now, however, the evidence as to the structure of ATP complexes with divalent cations is not conclusive: α,β,γ-tridentate[3,4], β,γ-bidentate[6,7], β-monodentate[8] as well as a mixture of α,β-, α,γ- and β,γ-bidentate coordination[5] have been proposed. Williams et al.[9] have studied the geometry of Ln(III) complexes of ATP in detail. It was concluded that the Ln(III) ion binds predominantly to the β- and γ-phosphate moiety. The complexes of TP and Ca(II), Mg(II) or Ln(III) ions, however, have been studied to a lesser extent. On the basis of the experiments published, no definitive conclusions about their structures could be derived[2,3,10-12].

The worldwide concern about the eutrophication of surface water by phosphates has initiated a search towards new builders for detergent formulations. In this field, we have studied with the use of multinuclear NMR several (hydr)oxycarboxylates in the presence of Ln(III) cations, as model cations for Ca(II). The use of Ln(III) cations as NMR probes for Ca(II) can be justified by the often observed structural similarity between the Ca(II) and the Ln(III) complexes of a particular ligand[9,13]. It has been shown that both the lanthanide induced shifts (LnIS) and the lanthanide induced relaxation rate enhancements (LnIRE) of the various nuclei can be translated into valuable structural information about the ligand[13].

We now report on a study of the complexation of Ln(III) by triphosphate (TP) with the use of ^{17}O and ^{31}P NMR. To get an impression about the position of monovalent counter ions near the negatively charged Ln(III)-triphosphate complex, also ^{23}Na and ^{6}Li NMR techniques were applied. The TP ligand has only a few different nuclei, which probably all will be at a relatively short distance from the lanthanide cation. Generally, for this situation Dy(III) induced ^{17}O shifts[14] and Gd(III) induced relaxation rate enhancements[15] are most suitable to obtain structural information. The close proximity of the

ligand nuclei to the Ln(III) ions in addition to the high association constants of the Ln(III)-triphosphate complexes[16], however, gave rise to slow ligand exchange phenomena in the NMR spectra. Therefore, some extensions of the previous developed techniques[13] were required. The problems encountered are expected to be characteristic for the study of the complexation of potential organic phosphate substitutes, which should have an association constant higher than the (hydr)oxycarboxylates studied so far by us.

Methods and materials

NMR measurements. All NMR spectra were recorded with a Nicolet NT-200 WB spectrometer. Measurements were performed with samples containing 0.35 M $Na_5P_3O_{10}.6H_2O$ in D_2O in the presence of various amounts of $LnCl_3.6H_2O$. The ^{17}O NMR spectra were recorded of 2.2% ^{17}O-enriched compounds using 1 K datapoints, 20 KHz spectral width and a repetition rate of 25 ms. Usually, about 10^4 transients were needed to obtain a good signal-to-noise ratio. The data were processed using zero filling to 4 K datapoints, followed by double exponential weighing. A baseline correction was applied to the transformed spectra. ^{17}O chemical shifts were measured with respect to D_2O as external standard, ^{31}P and ^{23}Na chemical shifts with respect to the $P_{\alpha,\gamma}$ and the ^{23}Na signal of $Na_5P_3O_{10}.6H_2O$ in D_2O as external standard, respectively, and ^{6}Li chemical shifts with respect to 5 M LiCl in D_2O as external standard. Downfield induced shifts are denoted as positive.

Relaxation rates were measured after bubbling nitrogen gas through the sample for 10 min. The longitudinal relaxation rates were determined using a $[(90^\circ_x\ 180^\circ_y\ 90^\circ_x)$-τ-(12°)-acq] inversion recovery pulse sequence. The $1/T_1$ values were calculated using a three parameter fit of the experimental data[17]. The $1/T_2$ values were calculated from the linewidths at half height by way of the relation $1/T_2 = \pi \Delta \nu_{\frac{1}{2}}$.

Materials. 20% ^{17}O-enriched water was obtained from Rohstoff-Einfuhr Düsseldorf and the $LnCl_3.6H_2O$ salts were from Alfa Products. STP (purity > 99%) was obtained by repetitive precipitation from 33% aqueous ethanol[18] of commercial STP (Alfa Products), which contained about 15% diphosphate.

^{17}O-enriched pentasodium triphosphate[18,19]. Water (5% ^{17}O-enriched, 13.9 ml, 0.772 mol) was added cautiously to PCl_5 (22.8 g, 0.110 mol) at 0 °C in the course of 30 min. The mixture was then kept under vacuo at 40 °C to remove HCl, yielding 16.4 g of a mixture of H_3PO_4 and H_2O. This mixture was brought at pH = 5.3 with a concentrated NaOH solution and heated at 550 °C for 5 h in a porcelain dish. After cooling an equal amount of pure non-labelled STP was

added to the reaction product and the resulting mixture was purified as described above to give 11.3 g 2.2% ^{17}O-enriched pentasodium triphosphate (as the hexahydrate) (23.7 mmol, yield 11%). ^{31}P NMR (80.99 MHz, D_2O, 25 °C) δ = 0.0 (d, $\underline{J}$ = 18.8 Hz), δ = -14.44 (t, $\underline{J}$ = 18.8 Hz). ^{17}O NMR (27.13 MHz, D_2O, 94 °C), δ = 124 (broad m), δ = 107.8 (d, $\underline{J}$ = 80 Hz), δ = 100.2 (partially overlapping with the signal at δ = 107.8).

Results and Discussion

Ln(III) induced ^{17}O shifts

Previously, we have observed that Dy(III) gives rise to an induced shift per bound oxygen, which is rather independent of the nature of the oxygen[14]. Therefore Dy(III) induced ^{17}O shifts are useful to determine the coordinating oxygens of a ligand. Unfortunately, upon addition of $DyCl_3$ to a solution of STP in D_2O at 73 °C no shift of the TP ^{17}O signals was observed. The intensities of the ^{17}O signals, however, were reduced proportionally to the amount of Dy(III) added. Apparently, the TP ligand exchange is slow on the NMR time scale. The signals of the Dy(III) complex could not be observed, probably as the result of extensive line broadening. The decrease of the intensity of the ^{17}O signals of the free ligand as a function of the molar ratio of added Dy(III)/total TP (ρ) confirmed the formation of a 1:2 Dy(III)-TP complex.[16] The behaviour of the water-^{17}O signal showed that the D_2O ligand exchange is fast with respect to the NMR time scale.

In order to obtain information on the coordination of TP we attempted to use an other Dy(III) shift reagent: NaDyEDTA. This should give rise to a mixed ligand complex: $[Dy(EDTA)(TP)]^{6-}$ with a lower stability constant than $Dy(TP)_2^{7-}$[20]. This might result in a shorter residence time of the TP ligand in the complex. Although a faster exchange of the TP ligand was indeed observed, line broadening still did not allow any conclusions on the TP coordination. Therefore, we screened some of the other Ln(III) cations as shift reagent for ^{17}O. It appeared that the lighter Ln(III) cations (La(III), Ce(III), Pr(III), Nd(III) and Sm(III)) gave rise to fast TP ligand exchange with respect to the NMR time scale. This may be ascribed to both the generally observed higher ligand exchange rate in complexes of the lighter Ln(III) cations[21,22], and the smaller shifts induced by these cations (vide infra). The bound shifts of the $Ln(TP)_2(D_2O)_x$ complexes, derived from the slopes of the straight lines in plots of the LnIS versus ρ, are summarized in Table I.

Table I. Observed ^{17}O bound shifts (ppm) in $Ln(TP)_2(D_2O)_x$ at 73 °C.

Ln	Δ $(PO_3)^a$	Δ $(PO_2)^b$	Δ $(D_2O)^c$
La	9	8 - 38	-110
Ce	69	67 - 100	95
Pr	160	159 - 219	205
Nd	201	193 - 264	490
Sm	-15	-16 - 5	20
Eu	d	d	-710
Dy	d	d	-2870
Yb	d	d	190

[a] PO_3: non-bridging oxygens at P_α and P_γ.

[b] PO_2: non-bridging oxygens at P_β. Upper and lower limits are given as the PO_2 signal is hidden under the larger PO_3 signal.

[c] Calculated as $\frac{55.3}{0.35}$ * slope of $LnIS(D_2O)$ vs ρ.

[d] Not observed due to slow exchange.

The experimental bound shifts can be corrected for any contributions caused by conformational changes, inductive effects and direct field effects by substracting the bound shifts of the corresponding diamagnetic La(III) or Lu(III) complexes. The resulting paramagnetic shift (Δ) is a combination of contact (through-bonds) shift and pseudocontact (through-space) shift, and can be expressed by equation (1):

$$\Delta = \Delta_c + \Delta_p = F < S_z > + GC^D \qquad (1)$$

Here the first term of the right-hand side represents the contact shift as the product of a ligand-dependent parameter F and a Ln(III) dependent parameter $< S_z >$, and the second term represents the pseudocontact shift as the product of a Ln(III) dependent parameter C^D and a term G dependent upon the geometry of the ligand:

$$G = K_1 \frac{(3\cos^2\theta - 1)}{r^3} + K_2 \frac{(\sin^2\theta \cos 2\phi)}{r^3} \qquad (2)$$

Here, r, θ and ϕ are the spherical coordinates of the observed nucleus with

respect to Ln(III) at the origin and with the principal magnetic axis of the system as z-axis. K_1 and K_2 are dependent upon crystal field parameters and temperature[23-26]. Rapid random reorientations of the ligand may cause vanishing of the pseudocontact shift.

Previously we observed that Dy(III) induced ^{17}O shifts of various relative weakly complexing ligands are predominantly of contact origin[14]. The induced shifts per bound oxygen were all in a rather small range. For TP - because of the required fast exchange - we had to rely on Ln(III) ions other than Dy(III). Since the assumptions made in the studies with Dy(III) might not be valid here, a separation of contact and pseudocontact shift was performed. The data of Table I were fitted to eqn (1) with Reilley's non-linear regression procedure[27], using literature values of $\langle S_z \rangle$[28] and C^D [29]. The resulting F and G values are given in Table II.

Table II. F and G values of $Ln(TP)_2(D_2O)_x$ calculated[a] from ^{17}O bound shifts at 73 °C.

signal	PO_3	PO_2	D_2O
F	-39.7 ± 0.3	-43 ± 12	-74 ± 7
G	-3.1 ± 0.1	-5 ± 4	+8 ± 2
Number of Ln(III)	4[b]	4[b]	8

[a] Using the data of Table I.

[b] La, Ce, Pr and Nd.

From the F-values in $Ln(H_2O)_9^{3+}$, given by Reilley[27], it can be calculated that the contribution to F per bound oxygen is -70 ± 11[30]. The F-value of the PO_3 group is an average of 6 oxygens, of which the contributions of the non-coordinating oxygens to the contact shift presumably can be neglected[31]. Therefore, the number of bound oxygens of the two PO_3 groups in TP is (6 * -39.7/-70 ≈) 3.4 ± 0.5.

Analogously, the number of coordinated PO_2-oxygens and D_2O-ligands can be calculated to be 1.2 ± 0.5 and 1.1 ± 0.2, respectively. Assuming a coordination number of 9 for the Ln(III) ion it can be concluded that the stoichiometry of the Ln(III)-TP complex is: $Ln(TP)_2(D_2O)$, with one of the PO_2-oxygens and three of the PO_3-oxygens of each TP ligand coordinated.

As the signal of the P-O-P-oxygens was very broad accurate LnIS values for these nuclei could not be determined. It was clear, however, that the LnIS did not exceed 10 ppm. This supports the assumption that the contact shift in non-coordinated oxygens can be neglected.

Ln(III) induced ^{31}P shifts

The shape of the observed ^{31}P NMR spectra of the Ln(III) doped samples appeared to be dependent upon the Ln(III) ion (as a consequence of the ionic radius and the induced shift), the concentration and the temperature: both fast and slow exchange with respect to the ^{31}P NMR time scale were observed (see Fig. 1).

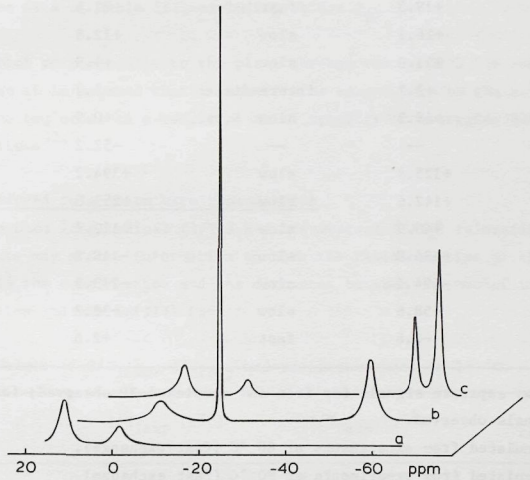


Fig. 1. Examples of ^{31}P NMR spectra of $Ln(TP)_2$ complexes, illustrating fast and slow exchange on the ^{31}P NMR time scale (25 °C; ρ = 0.25).
a: Ce(III) fast exchange δ = 9.7 ($P_{\alpha,\gamma}$), δ = -3.7 (P_β).
b: Eu(III) fast exchange for P_β: δ = -13.9, slow exchange for $P_{\alpha,\gamma}$: δ = 0.0 (free ligand), δ = -48.3 (complex).
c: Yb(III) slow exchange δ = 0.0 ($P_{\alpha,\gamma}$, free ligand), δ = -14.4 (P_β, free ligand), δ = -52.6 (P_β, complex), δ = -58.6 ($P_{\alpha,\gamma}$, complex).

In contrast to ^{17}O NMR, here in the cases with slow ligand exchange the signals for the complexed ligand could be observed. Once more, integrals in the slow exchange spectra confirmed the 1:2 stoichiometry of the Ln-TP

complex. The bound shifts were evaluated from plots of the LnIS versus ρ in the case of fast exchange or directly from the shift difference between free and complexed species in the case of slow exchange (Table III).

Table III. Observed ^{31}P bound shifts (ppm) in $Ln(TP)_2(D_2O)$ at 25 °C.

Ln	Δ P (α,γ)	exchange[a]	Δ P (β)	exchange[a]
La	-0.7	fast	+1.9	fast
Ce	+19.5	fast	+21.4	fast
Pr	+26.1	slow	+12.8	fast
Nd	+21.0	slow	+1.9	fast
Sm[b]	+3.2	intermediate	+9.1	intermediate
Eu	-48.3	slow	+0.9	fast
Gd[c]	--	--	-52.2	intermediate
Tb	+125.8	slow	+394.2	slow
Dy	+142.6	slow	+252.6	slow
Ho	+40.9	slow	+122.7	slow
Er	-134.8	slow	-118.2	slow
Tm	-194.1	slow	-213.2	slow
Yb	-58.6	slow	-38.2	slow
Lu	-0.6	fast	+2.6	slow

[a] Slow: separate signals for free and complexed TP observed; fast: averaged signals observed.

[b] Calculated from experiments at 80 °C (fast exchange).

[c] Calculated from experiments at 90 °C (fast exchange).

A separation between contact and pseudocontact shifts as described above afforded the F and G values given in Table IV. It may be noted that no break in F and G values was observed between the lighter (La-Gd) and heavier (Tb-Lu) lanthanides.

The contact shifts appear to be very small in comparison with those observed for ^{17}O (See Table II). Since the sign of these shifts is the same, a spin delocalization pathway, possibly in combination with a spin polarization pathway, is involved in the electron spin transmission through the TP ligand. The magnitudes of the G-values of the two different P-nuclei are about the same. The Ln(III) coordination derived from ^{17}O NMR implies equal Ln(III)-P distances. Inspection of molecular models shows that the (pseudo) magnetic

Table IV. F and G values of $Ln(TP)_2(D_2O)$ calculated[a] from ^{31}P bound shifts at 25 °C.

signal	$P_{\alpha,\gamma}$	P_β
F	-3.7 ± 0.3	-1.4 ± 0.5
G	-2.6 ± 0.1	-3.1 ± 0.2
Number of Ln(III)	13	13

[a] Using the data of Table III, excluding Tb for P_β.

axis is about perpendicular to the plane through the Ln(III) ion and the P-atoms, when it is assumed that in eqn (2) the second term on the right hand side can be neglected as a result of axial symmetry or averaging due to ligand reorientations[32,33].

Ln(III) induced relaxation rate enhancements

Ln(III) induced longitudinal ($1/T_1$) and transversal ($1/T_2$) relaxation rate enhancements may afford information on both the residence time of the entities involved in the complexation and the distances between the nuclei under consideration and the Ln(III) ion.

Table V. Values of $1/T_{1exp}$, $1/T_{2exp}$ and residence times at 25 °C.

Ln(III)	ρ	$1/T_{1exp}$ (s^{-1})		$1/T_{2exp}$ (s^{-1})		τ_{compl}[a] (10^{-3} s)
		$P_{\alpha,\gamma}$	P_β	$P_{\alpha,\gamma}$	P_β	
--	--	0.150	0.217	--	--	--
La	0.309	0.37	0.56	--	--	--
Nd	0.373	12.20	10.83	--	--	--
Eu	0.108	0.71	0.75	1525	--	0.66
Gd	0.0009	7.81	7.94	--	--	> 0.23
Tm	0.131	43.67	56.82	824	838	1.2
Yb	0.119	5.38	7.46	550	518	1.9

[a] Calculated from $1/T_{2exp} = 1/T_{2compl} + 1/\tau_{compl}$ with $1/T_{2compl} = 1/T_{1compl}$.

^{31}P LnIRE values were determined for a selection of Ln(III) ions (see Table V).

In those cases where separate signals were observed for free and complexed ligand (see Table III) the LnIRE values for both signals appeared to be identical. The magnetization recovery curve after the inverting non-selective 180° pulse was always single exponential within the experimental accuracy. Application of a selective (soft) 180° pulse[34-37] on either the signals for the free ligand or those for the complex gave analogous results: the magnetization transfer between free and complexed nuclei is fast on the experimental time scale. It can be concluded that the relaxation is in the fast exchange region as defined by McLaughlin and Leigh[38,39]. This phenomenon does not often occur when separate signals are observed for the exchanging entities. According to McLaughlin and Leigh, in the fast exchange region the following approximation is valid[39] for both the free ligand and the complex:

$$1/T_{1exp} = 2\ \rho/T_{1compl} + (1 - 2\ \rho)/T_{1f1} \qquad (3)$$

Here $1/T_{1exp}$ is the experimental longitudinal relaxation rate, $1/T_{1compl}$ is the relaxation rate of the $Ln(TP)_2$ complex and $1/T_{1f1}$ is the relaxation rate of the free ligand[40].

In the fast exchange region (with separate signals for complex and free ligand) the transversal relaxation rates of TP in the free and the complexed state can be evaluated with eqn (4) and eqn (5), respectively[39]:

$$\text{free ligand: } 1/T_{2exp} = 1/T_{2f1} + 1/\tau_{f1} \qquad (4)$$

$$\text{complex : } 1/T_{2exp} = 1/T_{2compl} + 1/\tau_{compl} \qquad (5)$$

Here τ_{f1} and τ_{compl} are the residence times of the TP ligand in the free and the complexed state, respectively. From eqn (3) and (5), and assuming that $1/T_{2compl} = 1/T_{1compl}$ [42] the values of τ_{compl} for the Eu(III)-, Tm(III)- and Yb(III) complexes were calculated (see Table V). The magnitudes of τ_{compl} obtained were in good agreement with the rough estimate of τ_{compl} for $Lu(TP)_2$ from coalescence ($\tau_{compl} = 3.10^{-3}$ s). The magnitudes of τ_{compl} also agree with the generally observed trend of increasing life times upon decreasing Ln(III) ionic radius[21,22]. Therefore, the τ_{compl} values show that the condition for the use of the fast exchange approximation for $1/T_1$ (eqn (3)) is fulfilled[39].

Gd(III) is often the Ln(III) ion of choice in relaxation rate enhancement studies because of its isotropic g-tensor. Moreover, the enhancements induced by Gd(III) are much larger than those by the other Ln(III) ions, due to its much larger electron relaxation time[43]. Therefore, the measurements with Gd(III) were performed at low ρ-values ($\rho < 10^{-3}$). Under this condition eqn (6) can be used to obtain $1/T_{1compl}$[38].

$$1/T_{1exp} = 2\ \rho/(T_{1compl} + \tau_{compl}) + 1/T_{1f1} \qquad (6)$$

The values of $1/T_{1exp}$ for the Gd(III) system are of the same order of magnitude as the $1/\tau_{compl}$ values obtained so far. Although in this case an accurate value of T_{1compl} cannot be evaluated from these relaxation rates from $1/T_{1exp}$ and eqn (6) it can be concluded that $\tau_{compl} > 0.23*10^{-3}$ s.

The $1/T_{1compl}$ values for the other paramagnetic Ln(III) ions were corrected for any diamagnetic contributions by using the $1/T_{1compl}$ value of $La(TP)_2$ to give $1/T'_{1compl}$. The ratio of $1/T'_{1compl}$ for $P_{\alpha,\gamma}$ and P_β appears to be rather independent of the Ln(III) ion used, showing that the interaction with the Ln(III) ion gives rise to an isotropic relaxation behaviour[42]. Assuming that the contact contribution to the LnIRE is negligible,[42] $1/T'_{1compl}$ can be related to the distances between the Ln(III) ion and the P nucleus under consideration with the reduced Solomon-Bloembergen equation (7)[42,43].

$$1/T'_{1compl} = 4/3\ (\mu_o/4\pi)^2\ (\mu^2\gamma^2\beta^2 T_{1e}/r^6) \qquad (7)$$

Here $\mu_o/4\pi$ is the magnetic permeability in vacuum, μ is the magnetic moment, γ is the magnetogyric ratio, β is the Bohr magneton, and T_{1e} is the electron spin relaxation time. The latter parameter is shown to be rather independent of the ligation of the Ln(III) cation.[44] Using the T_{1e} values for the Ln(III)-aquo cations given by Alsaadi et al.[44], from $1/T'_{1compl}$ and eqn (7), the Ln(III)-P distances were calculated (Table VI).

Table VI. Ln(III)-P distances (Å) as calculated from $1/T'_{1compl}$

Ln	$Ln\text{-}P_{\alpha,\gamma}$	$Ln\text{-}P_\beta$
Nd	3.44 ± 0.05	3.52 ± 0.05
Eu	3.06 ± 0.08	3.13 ± 0.08
Tm	3.59 ± 0.08	3.43 ± 0.05
Yb	3.57 ± 0.05	3.38 ± 0.05

The distances obtained point to a structure of $Ln(TP)_2(D_2O)$ in which the two PO_3 groups and the PO_2 moiety are coordinated with the Ln(III) cation. Any

substantial contribution of structures in which only two of the phosphate moieties of TP are coordinated can be excluded. The structural picture thus obtained is analogous to that proposed for the Ln-ATP complex by Williams et al.[9].

The triphosphate ligand exchange mechanism

The TP exchange mechanism has been studied in some detail for the Yb(III)-TP system. Several equilibria (8-11) have to be considered. In these equilibria D_2O and the monovalent counter ions are not taken into account.

$$Yb^{3+} + TP^{5-} \underset{k_{1-}}{\overset{k_1}{\rightleftharpoons}} Yb(TP)^{2-} \qquad (8)$$

$$Yb(TP)^{2-} + TP^{5-} \underset{k_{2-}}{\overset{k_2}{\rightleftharpoons}} Yb(TP)_2^{7-} \qquad (9)$$

$$Yb(TP)_2^{7-} + TP^{5-} \underset{k_{3-}}{\overset{k_3}{\rightleftharpoons}} Yb(TP)_3^{12-} \qquad (10)$$

$$Yb(TP)_2^{7-} + Yb(TP)^{2-} \underset{k_{4-}}{\overset{k_4}{\rightleftharpoons}} (TP)\,Yb(TP)\,Yb(TP)^{9-} \qquad (11)$$

In eqn (10) a 1:3 Yb-TP complex is involved. Since the coordination number of Yb(III) usually does not exceed 9 or 10, the coordination of TP in this complex will differ from that in $Yb(TP)_2^{7-}$.

Equilibrium (11) is a self-association mechanism, in which a binuclear complex is involved. Self-association is a commonly observed phenomenon in Ln-complexation[13]. Eqns (12) and (13) for the residence times τ_{f1} and τ_{compl} can be derived from eqn (8) - (11).

$$1/\tau_{f1} = k_1[Yb^{3+}] + k_2[Yb(TP)^{2-}] + k_3[Yb(TP)_2^{7-}] \qquad (12)$$

$$1/\tau_{compl} = k_{2-} + k_3[TP^{5-}] + k_4[Yb(TP)^{2-}] \qquad (13)$$

From eqn (12) it follows that $1/\tau_{f1}$, and concurrently the linewidth of the free ligand signals, should increase upon increase of ρ. This was indeed observed. The linewidth of the complex signals, on the other hand, appeared to decrease upon increase of ρ (see Fig. 2).

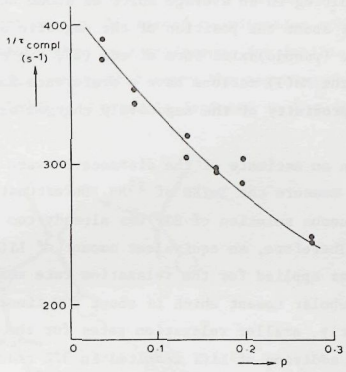


Fig. 2. Relation between $1/\tau_{compl}$ and ρ in the Yb(III)-TP system.

Since $k_3[TP^{5-}]$ is the only term in eqn (13) that decreases at higher ρ values, equilibrium (10) will play an important role in the exchange mechanism.

Fitting of the experimental $1/\tau_{compl}$ values to eqn (13) with neglect of $k_4[Yb(TP)^{2-}]$ gives $k_{2-} = 120\ s^{-1}$ and $k_3 = 780\ l.mol^{-1}.s^{-1}$. Inclusion of $k_4[Yb(TP)^{2-}]$ into the fitting procedure gives only a slight improvement of the fit, which was rather insensitive for the value of k_4. Anyhow, it is clear that both associative (eqn (10) and/or (11)) and dissociative (eqn (9)) mechanisms are operative in the TP-ligand exchange.

Monovalent counter ions

As stated before, the highly charged Ln-TP complexes have a strong affinity for cations. This has led to the application of these systems as shift reagents for monovalent cations[2]. Up to the maximum ρ values used in the present study ($\rho \leq 0.25$), a linear relation between the LnIS and ρ was observed for ^{23}Na. A bound ^{23}Na shift of 61.3 ppm in the $Na_7Tm(TP)_2$ (D_2O) complex, which is expected to be almost completely dipolar in origin was calculated from extrapolation of the TmIS to $\rho = 0.5$. This rather high value compared with the bound ^{31}P shifts (see Table III) suggests that the Na(I) counter ions in the $Na_7Tm(TP)_2(D_2O)$ complex prefer distinct positions. If this would not be the case, Na(I) would experience all possible pseudocontact

shifts equally, resulting in an average shift of about zero[47]. Using our previous assumptions about the position of the magnetic axis and the applicability of the (pseudo)axial form of eqn (2), the sign of the induced shift implies that the Na(I) cations have a preference for sites with $-54.7° < \theta < +54.7°$, in the proximity of the negatively charged oxygens coordinated to the Ln(III) ion.

In order to obtain an estimate of the distance between Na(I) and Tm(III), an attempt was made to measure the TmIRE of ^{23}Na. Unfortunately, the relaxation rate in a 0.35 M aqueous solution of STP was already too high to allow any TmIRE measurement. Therefore, an equivalent amount of LiCl (up to 1.75 M) was added and ^{6}Li NMR was applied for the relaxation rate measurements. The ^{6}Li nucleus has a quadrupolar moment which is about 100 times smaller than that for ^{23}Na. Consequently, smaller relaxation rates for the undoped samples are to be expected. The addition of LiCl resulted in 37% reduction of the TmIS for ^{23}Na. The TmIS for ^{6}Li was about equal to the reduction of the TmIS for ^{23}Na and, therefore, it may be concluded that 37% of Na(I) coordinated to $Tm(TP)_2^{7-}$ is replaced by Li(I). From the observed TmIRE for ^{6}Li at $\rho = 0.25$[48], the longitudinal relaxation rate in the complex $M_7Tm(TP)_2$ (M = Li and Na) was calculated to be 1.25 s^{-1}. From this, with the use of eqns (3) and (7), a mean Tm-Li distance of 5.8 Å was calculated. This suggests that the 7 monovalent cations are in the second coordination sphere of the Tm(III)(TP) system. When the number of monovalent cations in the second coordination sphere would be lower, the calculation would result in a smaller Tm-Li distance, which seems less likely.

It may be noted that a structure analogous to the binuclear complex $NaLn(TP)_2^{6-}$ suggested by Chu et al.[2], in which the monovalent cation is very close to Ln(III), would give rise to a much larger TmIRE than was observed.

Conclusions

The ^{31}P NMR data reveal that the 1:2 Ln-TP complexes are isostructural. Both ^{31}P and ^{17}O NMR show that the two PO_3 groups and the PO_2 moiety of TP are all coordinated to the Ln(III) cation. The Ln(III) induced ^{17}O shifts indicate that the PO_2 and one of the PO_3 groups are coordinated in a monodentate fashion, while the other PO_3 group is coordinated in a bidentate fashion. The *experiments show that the two* PO_3 *groups show a rapid interconversion as to* their coordination. One D_2O ligand is also present in the first coordination sphere leading to a coordination number of 9 for Ln(III). The ^{23}Na and ^{6}Li NMR data indicate that the negative charge of the $Ln(TP)_2^{7-}$ complex is neutralized

data indicate that the negative charge of the $Ln(TP)_2^{7-}$ complex is neutralized by 7 monovalent cations in the second coordination sphere of the Ln(III) cation. These cations show some preference for positions in the proximity of Ln-coordinated oxygen atoms that carry the negative charge. The resulting structure of the $Ln(TP)_2^{7-}$ system is depicted in Fig. 3.

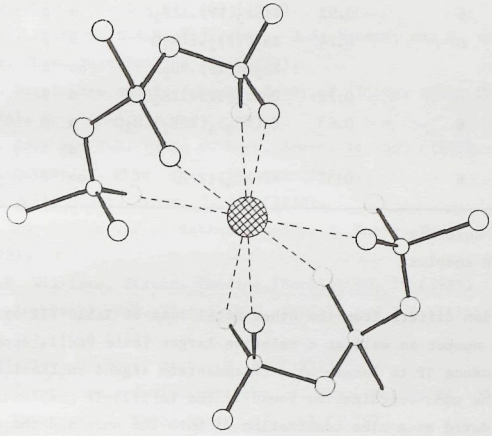


Fig. 3. Structure of the $Ln(TP)_2^{7-}$ system.

The present study demonstrates that slow exchange phenomena sometimes may hamper the use of LnIS measurements on ^{17}O and of LnIRE measurements. Since the exchange rate usually is dependent upon the Ln(III) cation, these problems can be overcome by a proper choice of the shift reagent and/or by the study of mixed ligand systems.

X-ray analyses[49-54] have been performed of several (transition) metal-TP complexes. In Table VII the mode of coordination is compared with the coordination in crystalline metal-TP structures.

Table VII. Coordination in TP-containing complexes

Metal ion	Coordination number	r_{ion} (Å)	Complex composition	Coordinating TP-oxygens			Ref.
Ln(III)[a])	9	0.85-1.05	$Ln(TP)_2.H_2O$	αα	β	γ	this work
Cd(II)[b]	6	0.92	$CdNa_3(TP).12H_2O$	α	β	γ	49
Zn(II)[b]	6	0.74	$Zn_5(TP)_2.17H_2O$	α	β		50
			$Zn_2Na(TP).9H_2O$	αα	β		51
Cu(II)[b]	6	0.72	$CuNa_3(TP).12H_2O$	α	β	γ	52
Co(III)[b]	6	0.63	$Co(NH_3)_4(TPH_2).H_2O$	α	β		53
				α		γ	
Al(III)[b]	6	0.51	$Al(NH_4)(TPH)$	αα	β		54

[a] Complex in solution.

[b] Crystalline complex.

The Ln(III) ion differs from the other metal ions of Table VII by a higher coordination number as well as a relative larger ionic radii. Apparently these properties induce TP to behave as a tetradentate ligand in the Ln(III)-TP complexes. The αaβγ-coordination found in the Ln(III)-TP complexes in solution may be considered as a nice combination of both the αaβ- and the αβγ-coordination for TP in the crystalline state.

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SUMMARY

This thesis describes the synthesis and calcium complexing properties of a series of oxidized monosaccharide derivatives, oligo- and polysaccharides and of some low molecular weight model systems.

In Chapter I a general introduction is presented on the subject of phosphate substitutes for detergent formulations and studies concerning calcium complexation by low and high molecular weight organic systems.

Chapter II describes the synthesis of bis(carboxymethyl) acetals by oxidation of 4,7-dihydro-1,3-dioxepins with potassium permanganate. The dioxepins have been obtained by acetalization of a carbonyl compound with (Z)-2-butene-1,4-diol or by transacetalization via diethyl acetals.

Chapter III describes the preparation of cis- and trans-2,5-diallyloxy-2,5-dihydrofuran by acid catalyzed transacetalization of 2,5-dimethoxy-2,5-dihydrofuran. As a by-product, 1,1,3-triallyloxypropane was formed from 2-allyloxy-2,5-dihydrofuran intermediates. The cis/trans configuration has been determined by NMR (chiral lanthanide shift reagent) and MS (elimination of allyl alcohol). Oxidation of the cis and trans compounds by potassium permanganate yielded meso- and (±)-2,2'-bis(carboxymethoxy)oxydiacetic acid, respectively. The calcium sequestering properties of the latter compounds were superior to those of the acetal polycarboxylate obtained by sucrose oxidation. This is due to the extra steric hindrance encountered for the latter polycarboxylate upon calcium complexation.

Chapter IV describes the synthesis of a number of polycarboxylates by periodate oxidation and subsequent hypobromite oxidation of vicinal diol moieties of sucrose, raffinose and a number of glucosides. This two-step oxidation procedure yields defined products, which have been characterized by ^1H NMR and ^{13}C NMR.

In Chapter V a series of 25 polycarboxylic acids containing either the

oxydiacetate (ODA) or the ethylene glycol diacetate (EGDA) moiety have been synthesized and their Ca(II) complexation ability determined. Differences in log K_{Ca} values, which vary from 2.0-5.4, are discussed in terms of steric, electronic and entropy effects.

Chapter VI describes the calcium complexation of a number of oxidized carbohydrates compared with that of a series of model polycarboxylic acids. It is found that calcium sequestration by oxidized carbohydrates is less than that by corresponding ether polycarboxylates, since (a) acetal oxygens have a lower coordinating power than ether oxygens, and (b) there is extra steric repulsion upon calcium complexation by both the additional CH_2OH groups and the unfavourable natural configuration of the oxidized carbohydrates investigated. Some of the oxidized carbohydrates show greater calcium sequestering capacities than corresponds to the stability constant. This is probably caused by crystal growth inhibition or precipitation-inhibition phenomena. Two model compounds illustrate that the acetal moiety is sufficiently stable under washing conditions, whilst it hydrolyses under acidic waste water conditions into small (hydr)oxycarboxylates.

In Chapter VII a number of polysaccharides of the starch type, including maltodextrins and cyclodextrins and some other well known polysaccharides, have been oxidized by periodate/chlorite (two-step method) or hypochlorite (one-step method), yielding ring-opened polymeric polycarboxylates. The oxidation products from the starch type show by far the best calcium complexing properties and have potential application as phosphate substitutes in detergent formulations. A relatively sharp increase in calcium complexation is observed at a degree of polymerization of about ten, whereas just a slight further improvement occurs at higher degrees of polymerization. This phenomenon is explained by the formation of helix structures which contain efficient Ca(II) complexing sites. This idea is supported by ^{17}O NMR measurements showing that oxidized starch type compounds with DP > 10 behave as heptadentate ligands.

Chapter VIII describes an ion exchange study of Ca(II) and Mg(II) with the inorganic phosphate substitute zeolite NaA in the presence of the complexing agents: oxydiacetate, nitrilotriacetate and borate/glucarate as potential co-builders. The ion exchange isotherms (32 °C and 60 °C) show that the total amount of the divalent ions in solution increased with increasing complexation strength of the co-builder. In the case of oxydiacetate, adsorption of the complexing agent in the zeolite was observed. Ion exchange kinetics were measured at 32 °C. Addition of complexing agents causes the ion exchange rate of Ca(II) with NaA to increase, the ion exchange rate of Mg(II) with NaA was

found to decrease. These kinetic effects are largely due to diffusion phenomena in the zeolite, due to variations in cation composition of the zeolite during the exchange processes.

Chapter IX deals with the complexation of lanthanide(III) cations with ^{17}O labelled triphosphate as studied by the use of multinuclear NMR shift and relaxation rate measurements. Depending upon the choice of the lanthanide cation, separate signals for the 1:2 lanthanide-triphosphate complex and the free triphosphate ligand, or averaged spectra were obtained. The longitudinal relaxation was always in the fast exchange region. From the analyses of the shift and relaxation data it is concluded that the lanthanide(III) cation is coordinated with two triphosphate ligands and one water in the first coordination sphere, while seven alkali counter ions are present in the second coordination sphere. Triphosphate is coordinated to the lanthanide(III) cation via two oxygens of one PO_3 group, one oxygen of the other PO_3 group and one oxygen of the inner PO_2 moiety. In the exchange of triphosphate between the free and the complexed state both associative and dissociative mechanisms play a role.

SAMENVATTING

Dit proefschrift beschrijft de synthese en calciumcomplexerende eigenschappen van een aantal geoxideerde monosaccharide derivaten, oligo- en polysacchariden alsmede van een aantal laagmoleculaire modelsystemen.

Hoofdstuk I geeft een algemene inleiding op het gebied van fosfaatvervangers ten behoeve van wasmiddelformuleringen en de bestudering van calciumcomplexering door laag- en hoogmoleculaire organische systemen.

Hoofdstuk II beschrijft de synthese van bis(carboxymethyl)acetalen door oxidatie van 4,7-dihydro-1,3-dioxepines met kaliumpermanganaat. De dioxepines werden bereid door acetalisering van carbonyl verbindingen met (Z)-2-buteen-1,4-diol of door transacetalisering via diethylacetalen.

Hoofdstuk III beschrijft de bereiding van cis- en trans-2,5-diallyloxy-2,5-dihydrofuranen door zuurgekatalyseerde transacetalisering van 2,5-dimethoxy-2,5-dihydrofuran met allylalcohol. De cis/trans configuratie werd bepaald met NMR (chiraal lanthanide shiftreagens) en massaspectrometrie (eliminatie van allylalcohol). Oxidatie van de cis- en trans-verbindingen gaf, respectievelijk, meso- en (±)-bis(carboxymethoxy)oxydiacetaat. De calciumcomplexerende eigenschappen van deze verbindingen waren beter dan die van het acetaalpolycarboxylaat uit de oxidatie van sucrose. Dit laatste wordt veroorzaakt door het optreden van extra sterische hindering bij complexering met calcium in het geval van het sucrose-oxidatieproduct.

Hoofdstuk IV beschrijft de bereiding van een aantal acetaalpolycarboxylaten door perjodaatoxidatie, gevolgd door hypobromietoxidatie van vicinale diol eenheden in sucrose, raffinose en een aantal glucosides. Deze tweetraps procedure geeft goed gedefinieerde producten die werden gekarakteriseerd met ^{1}H NMR en ^{13}C NMR.

Hoofdstuk V beschrijft de synthese van een 25-tal polycarboxylzuren die een oxydiacetaat (ODA) of een ethyleenglycoldiacetaat (EGDA) basiseenheid bevat-

ten. Hiervan werden tevens de complexerende eigenschappen bestudeerd. Verschillen in complexstabiliteitsconstanten (log K variërend van 2.0 tot 5.4) werden verklaard in termen van sterische, electronische of entropy effecten.

In hoofdstuk VI wordt de calciumcomplexering van een aantal geoxideerde koolhydraten vergeleken met die van een aantal modelverbindingen. Vastgesteld werd dat de calciumcomplexering van geoxideerde koolhydraten minder goed is dan die van overeenkomstige etherpolycarboxylaten. Dit vanwege het feit dat (a) acetaalzuurstofatomen minder sterk coördineren dan etherzuurstofatomen en (b) er sprake is van extra sterische hindering door zowel de aanwezigheid van een aantal hydroxymethylgroepen als de vaak ongunstige natuurlijke configuratie van de geoxideerde koolhydraten. Enkele geoxideerde koolhydraten bezitten een groter calciumcomplexerend vermogen dan uit de stabiliteitsconstante zou volgen. Dit wordt waarschijnlijk veroorzaakt door kristalgroei-inhibitie en/of kristallisatie-inhibitie verschijnselen. Twee modelverbindingen laten zien dat de acetaaleenheid voldoende stabiel is onder alkalische omstandigheden (wasproces), terwijl er onder zure omstandigheden (afvalwater) hydrolyse optreedt naar lagere (hydr)oxycarboxylaten.

Hoofdstuk VII beschrijft de oxidatie van polysacchariden van de zetmeelfamilie, waaronder maltodextrinen en cyclodextrinen en een aantal andere bekende polysacchariden. Zowel de tweestaps perjodaat/chloriet-oxidatie als de eenstaps hypochloriet-oxidatie leidt tot ringgeopende polymere polycarboxylaten. *Oxidatieproducten uit de zetmeelreeks vertoonden de beste calcium*complexerende eigenschappen en kunnen worden aangemerkt als potentiële fosfaatvervangers voor wasmiddelen. Een sterke toename van de calciumcomplexering per unit berekend, trad op omstreeks DP = 10, terwijl daarboven slechts een geringe verbetering optrad. Dit verschijnsel wordt verklaard door de vorming van helixstructuren aan te nemen, die zeer efficiënte calciumbindende sites bevatten. Dit idee wordt gesteund door ^{17}O NMR experimenten waarbij werd vastgesteld dat boven DP = 10 deze verbindingen zich als heptadentaatliganden gedragen.

Hoofdstuk VII beschrijft een studie van de ionwisseling van Ca(II) of Mg(II)-ionen met zeoliet NaA in de aanwezigheid van de complexvormers oxydiacetaat, nitrilotriacetaat en het boraat/glucaraat systeem als potentiële co-builders. Ionwisselingsisothermen (32 °C en 60 °C) toonden aan dat de totale hoeveelheid tweewaardige ionen in oplossing toenam bij toenemende complexsterkte van de co-builder. In het geval van oxydiacetaat werd tevens adsorptie van het ligand in de zeoliet waargenomen. Ionwisselingskinetiekmetingen bij 32 °C toonden aan dat toevoeging van complexvormers de Ca(II)-wisseling met NaA versnelde, terwijl de Mg(II)-wisseling met NaA werd

vertraagd. Deze effecten berusten voornamelijk op diffusieverschijnselen in de zeoliet ten gevolge van variaties in kationensamenstelling van de zeoliet gedurende het uitwisselingsproces.

In hoofdstuk IX is de complexering van lanthanide(III) kationen met ^{17}O verrijkt trifosfaat bestudeerd met behulp van multikern NMR metingen (chemische verschuivingen en relaxatiesnelheden). Afhankelijk van het lanthanide(III) kation werden wel of geen aparte signalen voor het 1:2 lanthanide-trifosfaat complex en het vrije trifosfaat ligand verkregen. De longitudinale relaxatie was altijd in het snelle uitwisselingsgebied. Uit de geïnduceerde verschuivingen en relaxatietijden volgt dat het lanthanide(III) kation wordt gecoördineerd door twee trifosfaatliganden en een watermolecuul in de eerste coördinatiesfeer, terwijl zeven eenwaardige kationen zich in de tweede coördinatiesfeer bevinden. De coördinatie van trifosfaat aan het lanthanide(III) kation vindt plaats door twee zuurstofatomen van de ene PO_3-groep, één zuurstofatoom van de andere PO_3-groep en één zuurstofatoom van de (binnenste) PO_2 eenheid. Bij de uitwisseling van trifosfaat tussen vrije en gecomplexeerde toestand speelt zowel een associatief als een dissociatief mechanisme een rol.

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CURRICULUM VITAE

Maarten Simon Nieuwenhuizen werd op 19 december 1954 geboren te 's-Gravenzande. Na aldaar de lagere school te hebben bezocht, werd in 1973 het diploma atheneum-B behaald aan de Chr. Scholengemeenschap "Groen van Prinsterer" te 's-Gravenhage. In 1973 werd begonnen met de studie voor scheikundig ingenieur aan de Technische Hogeschool Delft. Na een afstudeerperiode onder leiding van prof.dr.ir. H. van Bekkum werd in januari 1980 het doctoraal examen afgelegd. Van 1 februari 1980 tot 31 juli 1984 werkte hij aan de Technische Hogeschool te Delft als wetenschappelijk ambtenaar aan een promotieonderzoek onder leiding van prof.dr.ir. H. van Bekkum en dr.ir. A.P.G. Kieboom in het Laboratorium voor Organische Chemie. Sinds 15 januari 1985 is hij werkzaam bij TNO te Rijswijk.

S T E L L I N G E N

1. De weergave van Santhanagopalan c.s. van de structuur van calciumcomplexen van citraat en carboxymethyloxysuccinaat is in strijd met hetgeen bekend is over de stoichiometrie en de structuur van deze complexen.

   S. Santhanagopalan, H. Raman en S.K. Suri, J. Am. Oil Chem. Soc. 61, 1267 (1984).
   A.P.G. Kieboom, C.A.M. Vijverberg, J.A. Peters en H. van Bekkum, Recl. Trav. Chim. Pays-Bas 96, 315 (1977).
   C.A.M. Vijverberg, J.A. Peters, A.P.G. Kieboom en H. van Bekkum, Recl. Trav. Chim. Pays-Bas 102, 255 (1983).

2. Grote fouten in de structuurweergave van enkele van de gemeten verbindingen maken een deel van de beschouwingen van Chang twijfelachtig.

   D.M. Chang, J. Am. Oil Chem. Soc. 60, 618 (1983).

3. De door Jacobsen c.s. in tabelvorm gegeven dipoolmomenten leiden tot een andere cis/trans-toekenning van 2,5-diacetoxy-2,5-dihydrofuran dan is geschied.

   J.P. Jacobsen, J.T. Nielsen en K. Schaumburg, Acta Chem. Scand. 25, 2785 (1971).

4. De in de octrooiliteratuur geclaimde bereidingswijze voor 2,5-dichlooradipinezuur leidt tot 2,2-dichlooradipinezuur.

   CIBA A.G., Schweiz. Patentschrift 242837 (1946).

5. De mechanistische beschouwing van Lamberti c.s. over de vorming van carboxymethyloxysuccinaat uit maleaat en glycolaat onder invloed van calciumionen, is voor verbetering vatbaar.

   V. Lamberti, M.D. Konort en I. Weil, U.S. Patent 3954858 (1976).

6. In enkele studies over calcium-complexering, waar sprake is van liganden met meerdere chirale centra, wordt ten onrechte niet vermeld aan welk stereoisomeer of mengsel van stereoisomeren is gemeten.

M.M. Crutchfield, J. Am. Oil Chem. Soc. 55, 58 (1978).
H.C. Kemper, R.J. Martens, J.R. Nooi en C.E. Stubbs, Tenside Det. 12, 47 (1975).

7. De door Sharma en Tandon toegepaste formuleringen zijn niet in overeenstemming met de opgegeven constante ionensterkte van 0.1 M.

R.D. Sharma en J.P. Tandon, Monatsch. Chem. 105, 55 (1974).

8. Het gebruik door Martin c.s. van één-en-dezelfde Langmuir-adsorptie-isotherm voor de adsorptie van een serie uiteenlopende verbindingen aan ZnO is aanvechtbaar.

S.J. Martin, K.S. Schweizer, S.S. Schwartz en R.L. Gunshor, Proceedings of the IEEE Ultrasonics Symposium, Dallas, 1984.

9. De blindenstok functioneert thans niet naar behoren; een mentale heroriëntatie van de verkeersdeelnemers alsmede onderzoek naar alternatieve blindensignaleringssystemen is gewenst.

10. Het verdient aanbeveling een algemene, internationale gebarentaal voor verkeersdeelnemers te ontwikkelen voor het doen van zakelijke mededelingen (en het eventueel uitdrukken van gemoedsgesteldheden).

11. Ten onrechte wordt bij het jaarlijks samenstellen van een Europese topscorerslijst voor de hoogste nationale voetbalcompetities geen rekening gehouden met het totaal aantal te spelen wedstrijden in zo'n competitie.

12. De ver doorgevoerde kunstmatige inseminatie in de rundveeteelt heeft een dierlijke dimensie toegevoegd aan de uitdrukking "zich stierlijk vervelen".

M.S. Nieuwenhuizen, Delft, 9 mei 1985.