Polycarboxylic Acids Containing Acetal Functions: Calcium Sequestering Compounds Based on Oxidized Carbohydrates

M.S. NIEUWENHUIZEN, A.P.G. KIEBOOM, and **H. VAN BEKKUM,** Laboratory of Organic Chemistry, Delft University of Technology, Julianalaan 136, 2628 BL Delft, The Netherlands

ABSTRACT

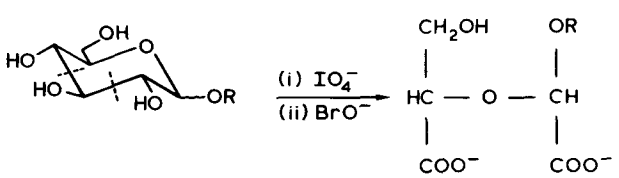
A number of polycarboxylic acids containing acetal functions have been prepared by a two-step oxidation of carbohydrates. Their calcium sequestering behavior is compared with that of a series of model polycarboxylic acids. It is found that calcium sequestration by oxidized carbohydrates is less than that by corresponding ether polycarboxylates, since (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 unfavorable 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

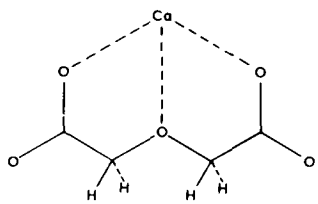
Sodium tripolyphosphate (STPP), the main builder in detergent formulations at the moment, is considered to stimulate eutrophication in lakes and stagnant waters. In the last decade, an intensive search for STPP substitutes has been undertaken. Numerous organic and some inorganic substances have been 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 STPP 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 nuclear magnetic resonance (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^{2+} (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 favor 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 hydrolyzed 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 seuestering 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 (10-13). 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^{2+} 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

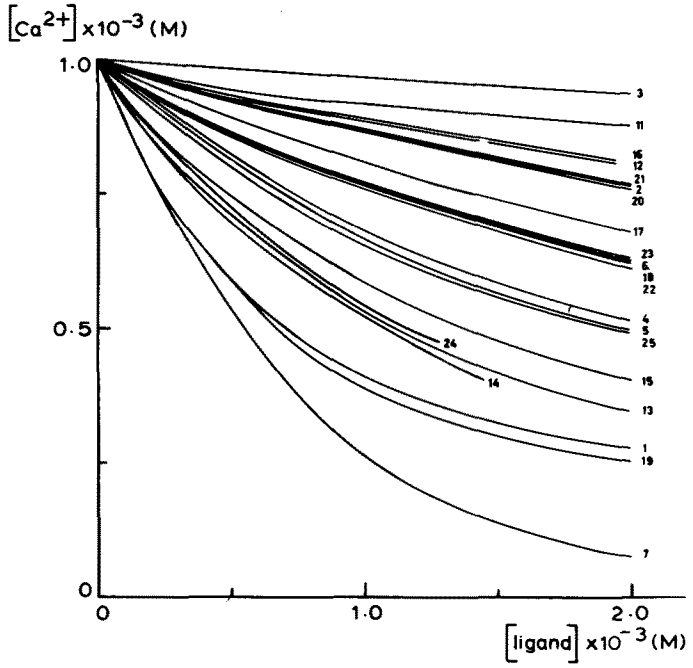


FIG. 1. Experimental ionselective electrode titration curves of an aqueous 10^{-3} M $CaCl_2$ solution with ligand solution.

(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^{2+} ion sequestered.

Preparative HPLC was carried out with a Waters Prep LC/System 500 using C18 reverse-phase columns. The eluent was MeOH:H_2O (55:45). All compounds were characterized by ^1H NMR (60, 100, 200 or 300 MHz) and ^{13}C NMR (20 MHz).

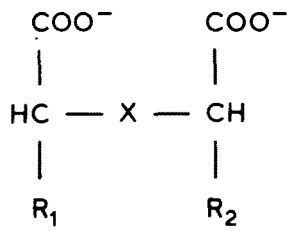
Compound 1 was obtained from Merck (Darmstadt, West Germany), 2 from Fluka (Buchs, Switzerland) and 26 from Ventron (Karlsruhe, West Germany). Compound 3 was synthesized from sodium sulfide and chloroacetic acid (14). Compounds 4-6 were prepared by the reaction of ethyl 2-bromopropionate with ethyl (±)-lactate (15), followed by separation of the (±) and *meso* by preparative 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 (20). Syntheses of compounds 16-19 have been described previously (16). α- and β-methyl glucopyranoside (Sigma), β-D-carboxymethyl glucopyranoside (17), sucrose (Merck), raffinose (Merck) and ethylene-*bis*-(β-D-glucopyranoside) (18) were oxidized with periodate and hypobromite (19) 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).

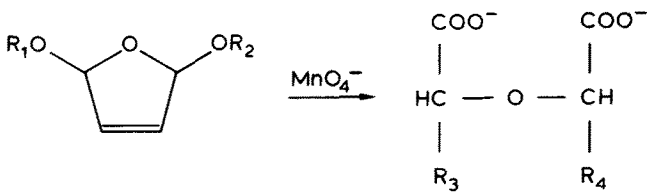
RESULTS AND DISCUSSION

Synthesis of Polycarboxylic Acids

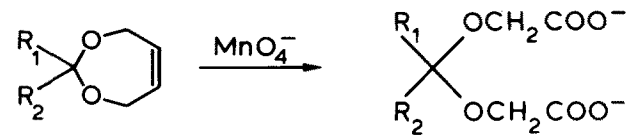
The polycarboxylic acids investigated are listed in Scheme 1 (together with their mode of preparation).



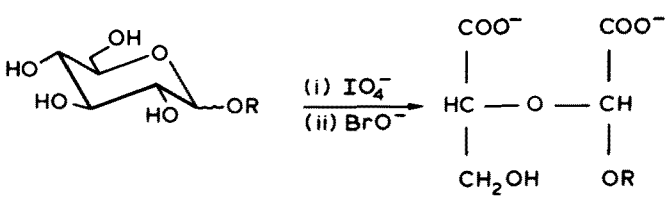
	X	R_1	R_2
1	O	H	H
2	NH	H	H
3	S	H	H
4	O	CH_3	CH_3
5	O	CH_3	CH_3 (RR + SS)
6	O	CH_3	CH_3 (RS)
7	O	H	CH_2COO^-
8	O	CH_2COO^-	CH_2COO^-
9	O	CH_2COO^-	CH_2COO^- (RR + SS)
10	O	CH_2COO^-	CH_2COO^- (RS)



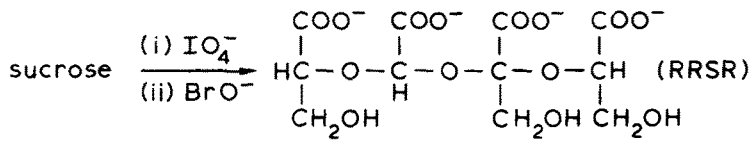
R_1	R_2		R_3	R_4
methyl	methyl	11	OCH_3	OCH_3
methyl	allyl	12	OCH_3	OCH_2COO^-
allyl	allyl	13	OCH_2COO^-	OCH_2COO^-
allyl	allyl	14	OCH_2COO^-	OCH_2COO^- (RR + SS)
allyl	allyl	15	OCH_2COO^-	OCH_2COO^- (RS)



	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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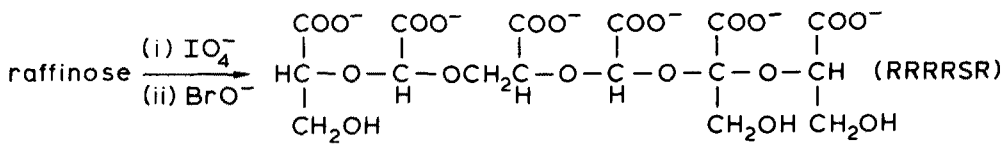

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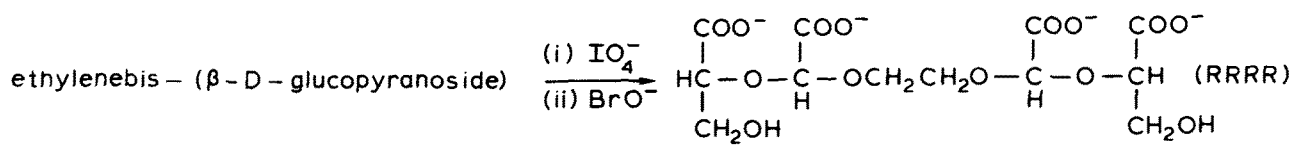


25

26 $Na_5P_3O_{10}$

SCHEME 1. 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 (20). $KMnO_4$ 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 (16). 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^- (21). In the second step, the aldehyde groups were further oxidized with BrO^- to yield the acids (19). The oxidation products were fully characterized by ^1H and ^{13}C NMR.

Calcium Sequestering Properties

Two parameters have been chosen to establish quantative 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. (22) 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^{2+} concentration and the initial Ca^{2+} 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 (23). At the tubidity point, $[Ca^{2+}] = 10^{-5}$ 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 STPP (26) have been included.

Structural Effects

As shown above, ODA acts as a planar tridentate ligand; Ca^{2+}-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 (24).

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)

TABLE I

Apparent Stability Constants (as log K_{Ca})[a] and Calcium Sequestering Capacities (SC)[b]

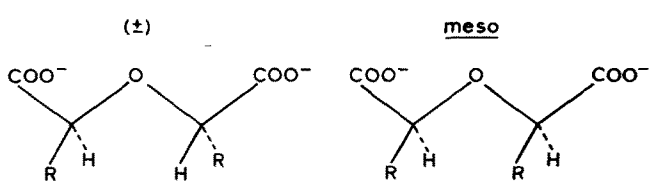
Compound	log K_{Ca}	SC	Compound	log K_{Ca}	SC
1	3.51	60	14	3.28	38
2	2.21	14	15	3.07	32
3	1.54	2	16	2.09	7
4	2.81	12	17	2.42	8
5	2.86	16	18	2.57	10
6	2.57	9	19	3.58	36
7	4.06	78	20	2.25	26
8	4.92	46	21	2.20	27
9	5.26	50	22	2.58	39
10	4.69	41	23	2.55	33
11	1.96	10	24	3.14	32
12	2.12	25	25	2.86	55
13	3.20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

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 × H-H) < 5 (2 × H-CH_3) < 6 (H-H and CH_3-CH_3) as shown in Figure 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.

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. (25) 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 Hs 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 Figure 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.



	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-subsituted ODA compounds; differences in calcium complexation between (±) and *meso*-compounds.

In 11, two Hs 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, an electronic effect also 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 favorable than that of the two $-CH_2COO^-$ groups in 9 and 10.

The important role of an ODA backbone 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 behavior. 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. (26). 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 unfavorable (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.

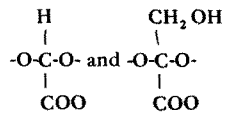
Compounds 23, 24 and 25 show some favorable effect of the increase of the size of the molecule and of the number of carboxylic groups, as is reflected in larger values of log K_{Ca}. Such an improvement of sequestering abilities can be extrapolated to oxidized oligosaccharides and will therefore be the subject for further investigations. Literature reports show that for oxidized polysaccharides (2,27,28) and polymeric acetal carboxylates (29) 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 inhibition or precipitation-inhibition of calcium oxalate.

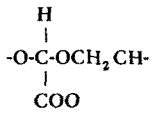
Stability of Acetal Compounds

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).

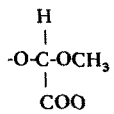
Although concentration and pH are not the same, it can be concluded that 18 is much more stable than 16. Clearly, the electronegative carboxylate group in 18 largely prevents hydrolysis under mild conditions. In fact, 16 and 18 present lower and upper limits in stability in relation to acceptability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



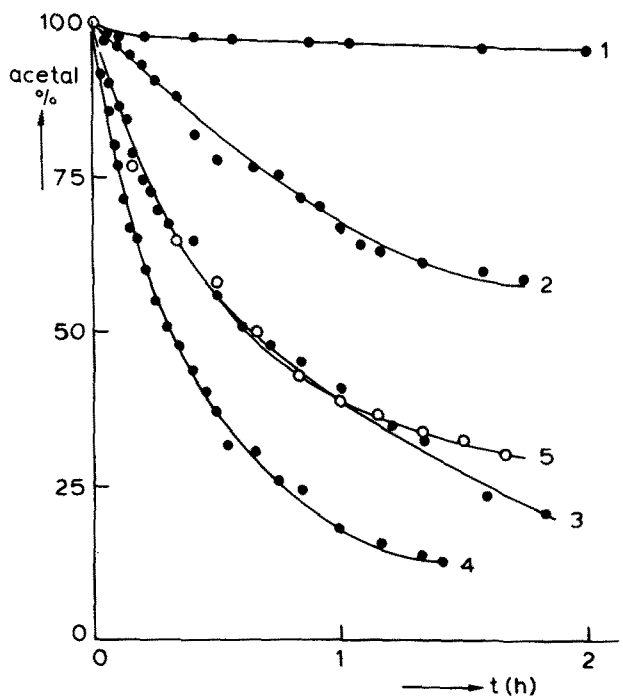
groups will hydrolyse rather slowly in acidic medium. However, it is expected, that the



group in 24 and 25 and the

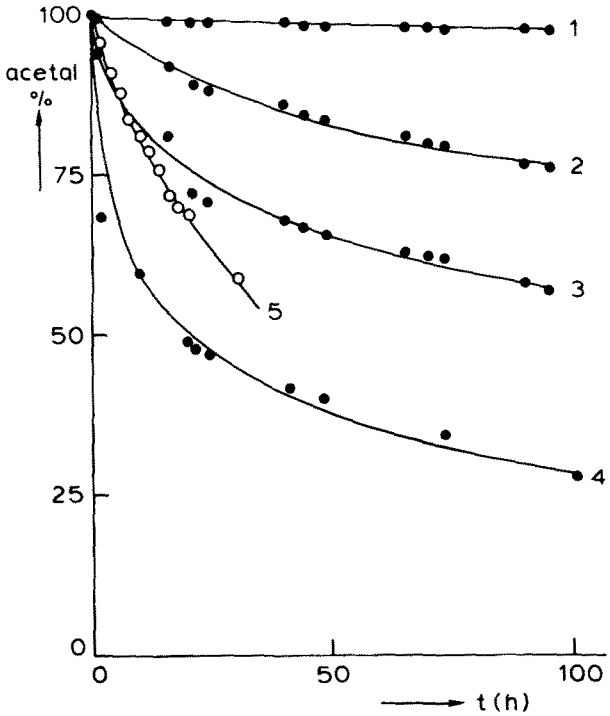


group in 11, 12, 20 and 21 will accelerate hydrolysis, due to the electropositive character of the ethylene and methyl groups.



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.

ACKNOWLEDGMENT

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