Kinetic effects induced by cellulose on water-catalyzed reactions. Hydrolysis of 2,4-dinitrophenyl cellulose xanthate and some sugar xanthate ester analogues

Eduardo Humeres, Luiz Fernando Sequinel, Mauricéa Nunes, Célia M.S. Oliveira, and Patrick J. Barrie

Abstract: The hydrolysis of 2,4-dinitrophenyl cellulose xanthate (CelXDNP) was studied in 10% v/v aqueous ethanol at 25°C and $\mu = 0.1$ (KCl). The water-catalyzed hydrolysis showed that, as for *p*-nitrobenzyl cellulose xanthate, it occurs through two parallel reactions with rate constants $k'_{H2O} = 4.40 \times 10^{-3}$ s^{-1} for the fast hydrolysis, and $k''_{H2O} = 6.90 \times 10^{-5}$ s^{-1} for the slow hydrolysis. The entropy of activation of the fast hydrolysis was 0.7 ± 1.8 cal K^{-1} mol^{-1}. External nucleophiles such as hydroxide and simple amines show simple first-order kinetics. The spontaneous hydrolysis of CelXDNP in acetone–water mixtures indicates that the fast reaction does not occur through water polymers and that for water molarity higher than 30 M there are no acetone molecules (or very few) in the highly ordered cybotactic region of cellulose. The spontaneous hydrolysis of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 3-(*S*-*p*-nitrobenzyl-xanthate) although is faster than the 6-isomer, it is slower than the fast hydrolysis of *p*-nitrobenzyl cellulose xanthate (CelXNB). Also $\Delta S^{\neq}$ is highly negative (–41.0 cal K^{-1} mol^{-1}), as it is for alkyl and sugar analogues. Only for the fast hydrolyses of CelXDNP and CelXNB is the entropy of activation almost zero. It is concluded that there is no neighbouring OH effect on the fast hydrolysis of cellulose xanthate esters.

Key words: hydrolysis, water catalysis, cellulose xanthate esters, methyl glucose, xanthate esters, neighbouring OH effect.

Résumé : On a étudié l'hydrolyse du xanthate de 2,4-dinitrophénylcellulose (CelXDNP) en opérant à 25°C, en solutions aqueuses d'éthanol à 10% v/v et à $\mu = 0,1$ (KCl). L'hydrolyse catalysée par l'eau montre que, comme dans le cas du xanthate de *p*-nitrobenzylcellulose, celle-ci se produit par le biais de deux réactions parallèles avec des constantes de vitesse de $k'_{H2O} = 4,40 \times 10^{-3}$ s^{-1} pour l'hydrolyse rapide et de $k''_{H2O} = 6,90 \times 10^{-5}$ s^{-1} pour l'hydrolyse lente. L'entropie d'activation de l'hydrolyse rapide est égale à $0,7 \pm 1,8$ cal K^{-1} M^{-1}. Les nucléophiles externes, tels l'hydroxyde et les amines simples, réagissent avec une cinétique du premier ordre simple. L'hydrolyse spontanée du CelXDNP dans des mélanges eau–acétone indique que la réaction rapide ne se produit pas avec des polymères-eau et que, à des molarités d'eau supérieures à 30 M, il n'y a pas (ou très peu) de molécules d'acétone dans la région cybotactique bien organisée de la cellulose. L'hydrolyse spontanée du 3-(*S*-*p*-nitrobenzylxanthate) de 4,6-*O*-benzylidène-α-D-glucopyranoside de méthyle, même si elle est plus rapide que celle de son isomère en position 6, est plus lente que l'hydrolyse rapide du xanthate de la *p*-nitrobenzylcellulose (CelXNB). Les $\Delta S^{\neq}$ est très négatif (–41,0 cal K^{-1} mol^{-1}), comme c'est le cas avec les analogues alkylés ou avec les sucres. Ce n'est que dans le cas des hydrolyses rapides des CelXDNP et CelXNB que l'entropie d'activation est pratiquement égale à zéro. On en conclut qu'il n'y a pas d'effet avoisinant de OH sur l'hydrolyse rapide des esters xanthiques de la cellulose.

Mots clés : hydrolyse, catalyse par l'eau, esters xanthiques de la cellulose, esters xanthiques de glucosides de méthyle, effet avoisinant de OH.

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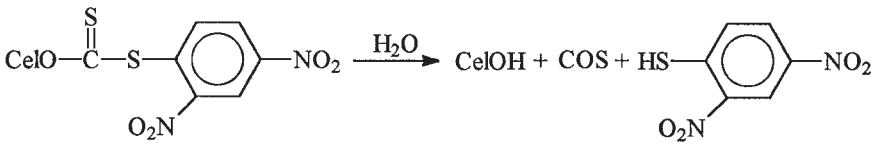
Introduction

The nonbonding interactions of carbohydrates with water depend on their stereochemistry and have been the subject of numerous studies (1). Kinetic medium effects induced by carbohydrates give some insight into the specificity of the stereochemical interaction with water (2) and are important to the understanding of their role in the sugar–protein recognition involved in carbohydrate transport (3).

The study of the reactivity of a moiety covalently bound to a polysaccharide system showed that the reaction of water was much faster compared to small analogue molecules (4). The water-catalyzed hydrolysis of *p*-nitrobenzyl cellulose xanthate

(CelXNB) occurred through a fast reaction and a slower parallel reaction. The faster hydrolysis was ascribed to the reaction of the C-2 + C-3 isomers and the slower hydrolysis to the C-6 isomer. The acceleration observed in the fast hydrolysis was attributed to an entropic effect due to a well-oriented water molecule, catalyzed by a second water molecule that acts as a general base as shown by proton inventory. However, it was also recognized that instead of a second water molecule, a neighbouring OH was able to act as a general base. External nucleophiles such as hydroxide ions and amines do not discriminate between the isomers and react like small analogue molecules (5).

This paper deals with the hydrolysis of 2,4-dinitrophenyl cellulose xanthate (CelXDNP), a cellulose ester with a good leaving group, in order to characterize the spontaneous reaction in comparison to CelXNB (eq. [1]).

[1] 

The hydrolysis of the 3- and 2,3-*p*-nitrobenzyl methyl glucose xanthate esters was studied to determine if there was a neighbouring OH group involved in the rate acceleration observed in the spontaneous hydrolysis of CelXNB.

Experimental

All chemicals and solvents were of analytical grade and were used as received, except the amines, which were previously distilled.

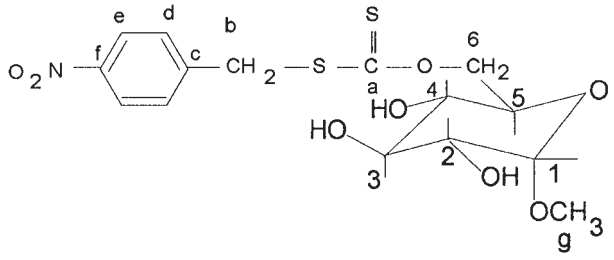
The solid-state ^{13}C NMR measurements were obtained using cross polarization (CP), magic angle spinning (MAS), and total sideband suppression (TOSS), and were performed using a Bruker MSL-300 spectrometer. The NMR spectra in solution were obtained with Bruker AC-200, WM-250, and AMX-400 equipment.

2,4-Dinitrophenyl cellulose xanthate (CelXDNP)

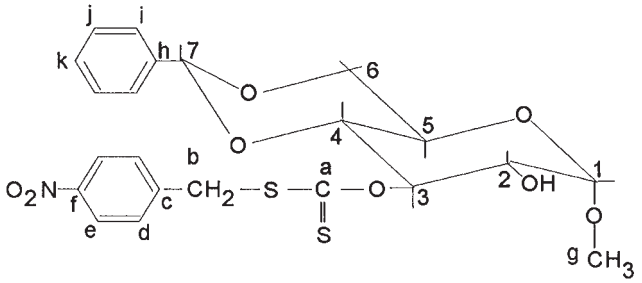
Commercial cotton tissue (2.2 g) was washed with 1 M HCl for 1 h and then several times with water. The sample was mechanically shaken in 100 mL of 2 M NaOH for 1 h. Half of the basic solution was taken away, a solution of 30 mL of CS_2 in 20 mL of *p*-dioxane was added, and the suspension was shaken for 2 h. The cellulose xanthate was filtered and treated with 0.1 M phosphate buffered solution at pH 8.0, then washed with dried acetone, and allowed to react with a solution of 3 g of 2,4-dinitro-1-fluorobenzene dissolved in 100 mL of dried acetone for 72 h with mechanical shaking. The cellulose xanthate ester was filtered, washed rapidly with 0.1 M HCl, then with acetone and finally with diethyl ether, and dried under vacuum for 10 h at room temperature over P_2O_5. The degree of substitution (DS, number of xanthate ester groups per 100 glucoanhydropyranose units) was 4.6 determined as described previously (4), measuring the number of moles of 2,4-dinitrothiophenol liberated in the ethylaminolysis, observed at 410 nm, using the extinction coefficient of 1.38×10^4 (6).

The CelXDNP was characterized from the ^{13}C NMR spectra with 12 h acquisition time, 2 ms contact time, 4 s recycle delay between scans, using CP/MAS TOSS (Table 1).

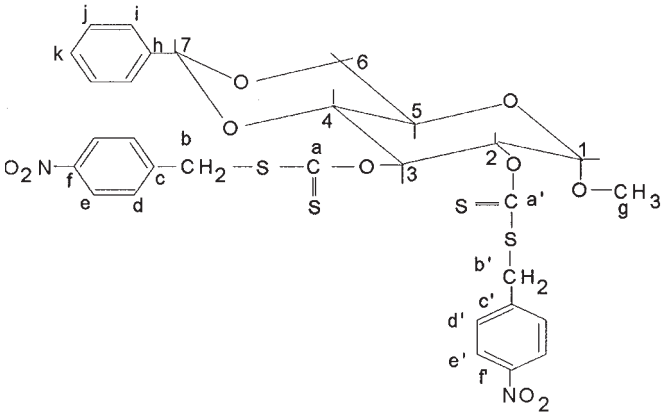
The thiocarbonyl signal of CelXDNP appears at 195 ppm, about 19 ppm at higher field than for the *p*-nitrobenzyl cellulose xanthate (CelXNB) where there is a methylene bridge between the xanthate group and the phenyl ring. All the signals



MGX - 6

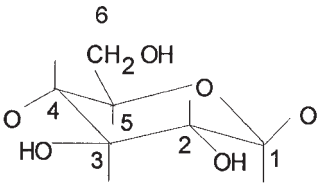
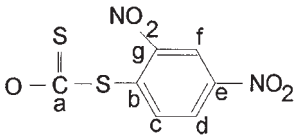


MGX - 3



MGX - 2,3

Table 1. ^{13}C chemical shifts of CelXDNP.[a]

Carbon	Chemical shift (ppm)		
			
C-1	104.5[b]	98.1[b]	
C-4	89.2[b]	83.4[c]	
C-2,-3,-5	75.2[b]	73.0[b]	71.8[c]
C-6	65.4[b]	62.7[c]	
			
C-*a*	195.0		
C-*b*	140.6 (140)		
C-*c*	129.0 (128)		
C-*d*	129.0 (130)		
C-*e*	155.7 (146)		
C-*f*	122.4 (119)		
C-*g*	155.7 (147)		

[a] CP/MAS TOSS.

[b] From crystalline components.

[c] From noncrystalline components (refs. 7 and 8). Values in parentheses are calculated (ref. 9).

for the 2,4-dinitrophenyl ring in the 120–150 ppm region agreed with the calculated values (9). Considering the area of the signals due to the 2,4-dinitrophenyl ring with respect to that of C-1, the DS was 5.1, reasonably close to that calculated by ethylaminolysis.

After *n*-butylaminolysis of CelXDNP, the NMR spectrum of *n*-butyl cellulose thioncarbamate showed that the signal at 195 ppm disappeared, producing a signal at 189.6 ppm assigned to the thioncarbamate group [O-C(S)-N] and the calculated signals for the *n*-butyl group at 45.1, 30.6, 20.6, and 14.5 ppm. This spectrum was identical to that obtained from CelXNB after *n*-butylaminolysis.

Methyl-D-glucopyranoside 6-(*S*-*p*-nitrobenzyl xanthate) (MGX-6)

In a solution of 20 g of methyl-α-D-glucopyranoside in 20 mL of water, 4.5 g of sodium hydroxide was slowly added, and when it was completely dissolved, 3.1 mL of carbon disulfide was mixed dropwise with constant stirring for 3 h at room temperature. The mixture was then neutralized with cooled acetic acid. A solution of 11.02 g of *p*-nitrobenzyl bromide in methylene chloride (20 mL) was added slowly while stirring, and the mixture was allowed to react for 2 h. The solution was concentrated under vacuum. The solid product was dissolved in 90% v/v aqueous ethanol and allowed to crystallize. Upon recrystallization in the same solvent, the white crystals were dried under vacuum over phosphorus pentoxide. The product gave positive test of carbohydrate, showing only one spot of TLC on alumina with ethyl acetate (R_f 0.75); mp 70–71°C; λ_{max} 283 nm; $[\alpha]_D^{25}$ +72.3 (*c* 0.41, chloroform). Anal. calcd. for $C_{15}H_{19}NO_8S_2$: C 44.4, N 3.4, H 4.7, S 15.8; found: C 43.1, N 3.4, H 4.8, S 15.5.

Table 2. ^{13}C chemical shifts (ppm) for some sugar xanthate esters.

Carbon	MGX-6[a]		MGX-3[b]	MGX-2,3[b,c]	
1	99.9	(100.0)	100.2	99.9	(99.9)
2	72.4	(72.2)	72.0	77.5	(72.4)
3	74.7	(74.1)	78.9	78.6	(70.5)
4	70.6	(70.6)	81.2	79.2	(80.8)
5	73.5	(72.5)	62.7	62.4	(62.0)
6	69.6	(61.6)	68.9	68.7	(68.5)
7			101.5	101.6	(101.5)
a	213.6		214.3	211.7; 212.7	(200)[d]
b	40.0		39.6	39.2; 39.4	
c	147.7		143.6	143.5; 143.2	(144.4)[e]
d	130.4		129.8	129.6; 129.9	(129.8)[e]
e	124.1		123.8	123.7; 123.8	(125.5)[e]
f	147.7		143.6	147.27; 147.29	(146.8)[e]
g	55.7	(55.9)	55.8	55.4	(54.9)
h			136.8	136.5	(137.7)[e]
i			129.2	129.3	(129.2)[e]
j			128.3	128.3	(128.4)[e]
k			126.1	126.0	(125.5)[e]

[a] In CD_2Cl_2. Values in parentheses for methyl α-D-glucopyranoside (ref. 11).

[b] In $CDCl_3$.

[c] Values in parentheses for methyl 4,6-*O*-benzylidene-α-D-glucopyranoside unless indicated (ref. 10).

[d] For CS_2 in solution.

[e] Calculated values (ref. 9).

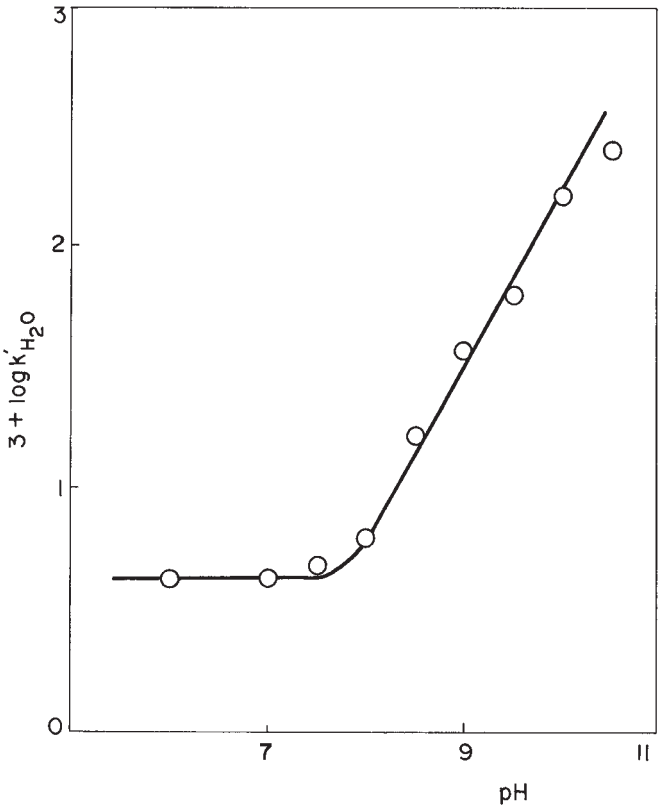
^{13}C NMR (Table 2); ^1H NMR (400 MHz, CD_2Cl_2), δ: 8.13 (d, *J* = 6.7 Hz, 2H, C_e-H), 7.54 (d, *J* = 6.7 Hz, 2H, C_d-H), 5.08 (s, 1H, OH), 4.85 (dd, *J* = 11.7, 2.0 Hz, 1H, C_6-H), 4.73 (d, *J* = 3.6 Hz, 1H, C_1-H, dd, *J* = 11.7, 6.0, 1H, C_6-H′), 4.46 (s, 3H, C_b-H2, H_2O?), 4.1 (d, *J* = 7.2, 1H, OH), 3.89 (ddd, *J* = 9.7, 5.8, 1.9, 1H, C_5-H), 3.73 (t, *J* = 9.2, 1H, C_3-H), 3.52 (m, 1H, C_2-H), 3.43 (ddd, *J* = 9.5, 9.5, 7.0, 1H, C_4-H), 3.37 (s, 3H, OMe). Couplings between C_6-H and C_5-H are not equal (2.0 and 6.0 Hz), showing that the side chain is in a preferred conformation.

Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 3- and 2,3-(*S*-*p*-nitrobenzyl-xanthate) (MGX-3 and MGX-2,3)

Twenty five milliliters of CS_2 and 10 mL of 5 N NaOH were added to a solution of 10 g of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside in 25 mL of *p*-dioxane, and the reaction mixture was stirred for 30 min at room temperature. Then it was neutralized with acetic acid at 5°C. *p*-Nitrobenzyl bromide (7.6 g) was slowly added, and the mixture was stirred for 5 h. The layers were separated, and the organic layer was concentrated under vacuum to a solid that was extracted with diethyl ether. After evaporation, the solid was recrystallized several times with dried 2-propanol, giving white crystals of MGX-3: TLC, alumina, 2-propanol, R_f 0.74; mp 176°C; λ_{max} 283; $[\alpha]_D^{22}$ + 51.9 (*c* 0.03, chloroform). Anal. calcd. for $C_{22}H_{23}NO_2S_2$: C 53.6, H 4.6, N 2.8, S 12.9; found: C 53.3, H 4.6, N 2.9, S 13.0.

IR (KBr): 3448 cm^{-1} (sharp, C_2-OH); ^{13}C NMR (Table 2); ^1H NMR (250 MHz, $CDCl_3$), δ: 8.10 (d, *J* = 7.7 Hz, 2H, C_e-H),

Fig. 1. pH–rate profile of the hydrolysis of CelXDNP at 25°C, in 10% v/v aqueous ethanol, μ = 0.1 (KCl).



7.48 (d, *J* = 7.7 Hz, 2H, C_d-H), 7.35 (m, 5H, Ar-H), 6.31 (dd, *J* = 9.7, 9.7 Hz, 1H, C_3-H), 5.46 (s, 1H, C_7-H), 4.86 (d, *J* = 3.9, 1H, C_1-H), 4.47 (ab, *J* = 14.6 Hz, 2H, C_b-H), 4.32 (dd, *J* = 10.1, 4.5 Hz, 1H, C_6-H), 3.91 (ddd, *J* = 9.9, 9.9, 4.3 Hz, 1H, C_5-H), 3.85 (ddd, *J* = 11.6, 9.5, 3.7 Hz, 1H, C_2-H), 3.76 (dd, *J* = 10.0, 10.0 Hz, 1H, C_6-H′), 3.70 (dd, *J* = 9.5, 9.5 Hz, 1H, C_4-H), 3.50 (s, 3H, OMe), 2.21 (d, *J* = 11.5 Hz, 1H, C_2-OH).

The solid left after the extraction with diethyl ether was then extracted with chloroform, concentrated, and crystallized in chloroform–hexane, giving white crystals of MGX-2,3: TLC on alumina producing one spot in chloroform:acetone (19:1), R_f 0.76; mp 72°C; λ_{max} 283 nm; $[\alpha]_D^{25}$ +64.1 (*c* 0.07, $CHCl_3$). Anal. calcd. for $C_{30}H_{28}N_2O_{10}S_4$: C 51.1, H 3.9, N 3.9, S 18.2; found: C 51.0, H 3.9, N 3.7, S 18.5.

^{13}C NMR (Table 2); ^{1}H NMR (400 MHz, $CDCl_3$), δ: 8.18 (d, *J* = 8.8 Hz, 2H, C_e-H), 8.04 (d, *J* = 8.7 Hz, 2H, $C_{e'}$-H), 7.51 (d, *J* = 8.7 Hz, 2H, C_d-H), 7.46 (d, *J* = 8.7 Hz, 2H, $C_{d'}$-H), 7.38 (m, 5H, Ar-H), 6.70 (dd, *J* = 9.6, 9.6 Hz, 1H, C_3-H), 5.90 (dd, *J* = 9.8, 3.8 Hz, 1H, C_2-H), 5.46 (s, 1H, C_7-H), 5.10 (d, *J* = 3.7 Hz, 1H, C_1-H), 4.46 (d, *J* = 14.6 Hz, 1H, C_b-H), 4.45 (d, *J* = 15.0 Hz, 1H, $C_{b'}$-H), 4.37 (d, *J* = 15.0 Hz, 1H, $C_{b'}$-H″), 4.34 (dd, *J* = 10.5, 5.0 Hz, 1H, C_6-H), 4.17 (d, *J* = 14.6 Hz, 1H, C_b-H′), 4.01 (dt, *J* = 9.9, 4.9 Hz, 1H, C_5-H), 3.82 (dd, *J* = 10.4, 4.1 Hz, 1H, C_4-H), 3.80 (dd, *J* = 10.2, 4.9 Hz, 1H, C_6-H′), 3.38 (s, 3H, OMe).

For MGX-3 the C_2-OH proton couples to the C_2-H proton, which is also coupled to the anomeric proton. This coupling can only be due to a *trans*-CH-OH conformation. Thus, the hydroxyl is not hydrogen-bonding to either of the neighbouring methoxy or xanthate groups. The IR spectrum confirmed this, showing a sharp OH band. The other proton couplings are consistent with a rigid chair–chair conformation.

For the MGX-2,3, the assignment fits with the chair–chair conformation.

Table 3. Rate constant for the hydrolysis of some sugar xanthates in 10% v/v aqueous ethanol at 25°C.[a]

Ester		k_{H2O}, s^{-1}	k_{OH}, M^{-1} s^{-1}[b]
CelXDNP	k'_{H2O}	4.40×10^{-3}	9.25×10^{-2}
	k''_{H2O}	6.90×10^{-5}	
EtXDNP		3.85×10^{-6}[c]	5.22[c]
CelXNB[d]	k'_{H2O}	0.82×10^{-3}[e]	1.40×10^{-3}[b]
	k''_{H2O}	1.4×10^{-5}[e]	
EXNB		1.36×10^{-6}[c]	4.16×10^{-2}[c]
MGX-6		1.01×10^{-7}[c]	2.05[c]
MGX-3		1.87×10^{-5}[b]	43.10[b]
MGX-2,3	k_1	3.27×10^{-4}[b]	
	k_2	1.94×10^{-5}[b]	

[a] μ = 0.1 (KCl).
[b] μ = 1.0 (KCl).
[c] 20% v/v aqueous methanol (ref. 11).
[d] Reference 5.
[e] μ = 0.6 (KCl).

Kinetics

The hydrolysis of CelXDNP was studied in a continous-flow system, with mechanical stirring, under inert atmosphere, using deoxygenated water as described previously (5), following the appearance of 2,4-dinitrothiophenol at 410 nm. The basic hydrolysis was pseudo-first order. The spontaneous hydrolysis of CelXDNP showed a biphasic plot of ln Δ*A* vs. time similar to that observed for CelXNB, due to two parallel reactions with rate constants k'_{H2O} (fast) and k''_{H2O} (slow) (5).

In the range of pH 4–12 all the hydrolyses were carried out at three different buffer concentrations, and the rate constants were extrapolated to zero buffer concentration.

Hydrolyses of the methylglucose xanthates were followed by the disappearance of the xanthate at 283 nm. The spontaneous hydrolysis of MGX-2,3 showed also a biphasic plot as a consequence of the consecutive hydrolyses of the two xanthate groups with rate constants k_1 and k_2.

Activation parameters were calculated from the Eyring equations at four temperatures.

Results

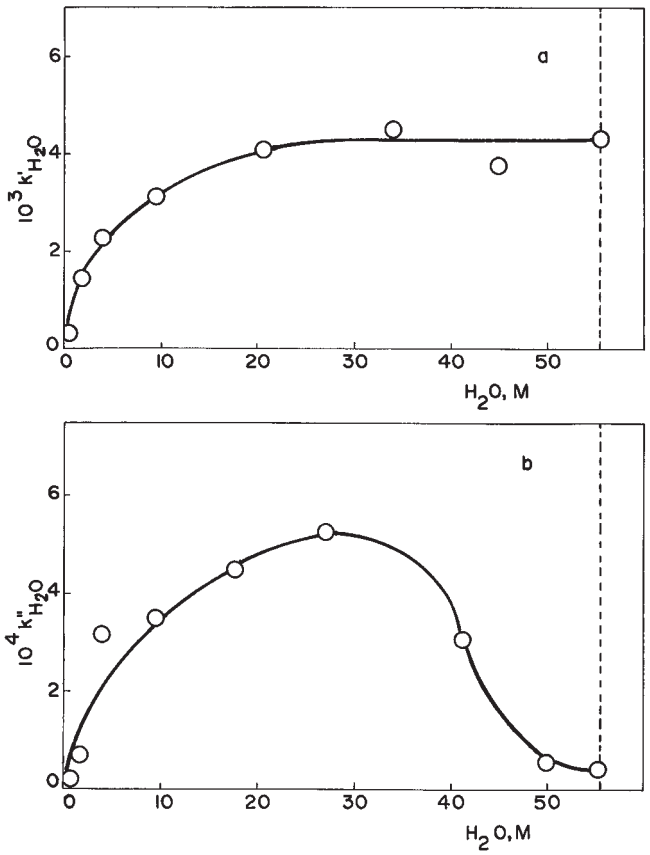
Hydrolysis of sugar xanthates

The spontaneous hydrolysis of CelXDNP occurs through two parallel reactions with rate constants k'_{H2O} for the fast hydrolysis and k''_{H2O} for the slow hydrolysis. At high pH where the hydroxide catalyzed reaction predominates, kinetics become simple first-order.

The pH–rate profile of the fast spontaneuos hydrolysis of CelXDNP is shown in Fig. 1. It is similar to other xanthate esters and can be represented by eq. [2], where k_{obs} is the rate constant extrapolated to zero buffer concentration; k'_{H2O} and k_{OH} are

$$[2] \quad k_{obs} = k'_{H2O} + k_{OH}[OH^-]$$

Fig. 2. Hydrolysis of CelXDNP in aqueous acetone at 25°C; (*a*) fast hydrolysis (k'_{H2O}); (*b*) slow hydrolysis (k''_{H2O}).



the rate constants for the water-catalyzed fast reaction and hydroxide-catalyzed reaction, respectively. In Table 3 are shown k'_{H2O}, k''_{H2O}, and k_{OH} for CelXDNP and some sugar xanthates. The rate constants for the ethylxanthate ester analogues are also included for comparison. All sugar xanthates, except the 6-substituted methylglucose xanthates (MGXB and MG-6), hydrolyze faster than the ethyl analogues. The rate constant k_2 for MG-2,3 is the same as that for MG-3.

Hydrolysis in aqueous acetone

To observe if the active species involved in the spontaneous hydrolysis were water polymers, the reaction of CelXDNP in acetone with increasing molarity of water was studied. The rate constants showed a downward curve for both the fast and slow spontaneous hydrolysis (Fig. 2), which is the reverse of the type of the curve expected when water polymers are involved in the transition state of the spontaneous hydrolysis (12). Both rate constants k'_{H2O} and k''_{H2O} increase with water molarity, following the change of dielectric constant of the medium, up to ca. 30 M water, whereas k'_{H2O} remains approximately constant with further increase while k''_{H2O} decreases rapidly in pure water.

Activation parameters

The activation parameters for the hydrolysis of sugar xanthates are shown in Table 4. The average value of $\Delta G^{\neq}$ was obtained from four temperatures, and $\Delta H^{\neq}$ was obtained from the least-squares fit of ln(k/T) vs. 1/T. It is important to note that only

Table 4. Activation parameters for the hydrolysis of sugar xanthates in 10% v/v aqueous ethanol, μ = 1.0 (KCl).

Ester	Nucleophile	$\Delta G^{\neq}$, kcal mol^{-1}	$\Delta H^{\neq}$, kcal mol^{-1}	$\Delta S^{\neq}$, cal K^{-1} mol^{-1}[a]
CelXDNP	H_2O (fast)[b]	20.68 ± 0.22	20.87 ± 0.43	0.7 ± 1.8
	OH-	18.56 ± 0.18	7.50 ± 0.23	–37.1 ± 0.8
CelXNB	H_2O (fast)[c]	21.67 ± 0.03	22.68 ± 0.20	3.3 ± 0.8
	OH-	21.17 ± 0.06	11.20 ± 0.30	–33.4 ± 0.8
MGX-3	H_2O	24.13 ± 0.12	11.90 ± 0.01	–41.0 ± 0.4
	OH-	18.15 ± 0.12	4.35 ± 0.15	–46.3 ± 0.6
MGX-2,3 (k_1)	H_2O	22.23 ± 0.12	14.65 ± 1.06	–25.4 ± 3.7
(k_2)	H_2O	23.52 ± 0.29	12.10 ± 0.97	–38.3 ± 1.0

[a] 1 M, 25°C.
[b] μ = 0.1 (KCl).
[c] μ = 0.6 (KCl), ref. 5.

for the spontaneous hydrolysis of the cellulose esters is the entropy of activation near zero. For the other sugar xanthates, MGX-3 and MGX-2,3 (k_1 and k_2), the values of $\Delta S^{\neq}$ are highly negative, as they also are for all the hydroxide ion-catalyzed reactions.

Discussion

The spontaneous hydrolysis of cellulose esters is faster than it is for ethyl xanthates. For CelXDNP, k'_{H2O} is more than 1000 times the rate constant of 2,4-dinitrophenyl ethylxanthate (EXDNP), and the ratio k'_{H2O}/ k''_{H2O} is about 60. Therefore the kinetic behaviour of the spontaneous hydrolysis CelXDNP is similar to that of CelXNB. For CelXNB it was found that the water molecule acting as a nucleophile is general-base catalyzed by a second water molecule (5). The fast hydrolysis has been attributed to the reaction of isomers C-2 + C-3. The reaction of CelXDNP in aqueous acetone showed that k'_{H2O} is insensitive to the increase of the molarity of water higher than 30 M (Fig. 2), suggesting that the cybotactic region is tight enough to expulse the cosolvent. The slow hydrolysis (k''_{H2O}) due to C-6 isomer is more sensitive to the composition of the medium because C-6 might be in a looser region.

We then addressed the question as to whether the observed acceleration of the fast hydrolysis of cellulose esters, such as CelXNB, could be a consequence of the

neighbouring effect of the OH in the C-2 or C-3 positions. The effect was expected to be the same for the 2- or 3-substituted ester. The spontaneous hydrolysis of the 3-isomer is indeed about 200 times faster than the 6-isomer (Table 3). However, it is still slower than the fast hydrolysis of CelXNB. The ratios of the rate constants for CelXNB (k'_{H2O}):MGX-3:EXNB are 603:14:1, and for CelXNB (k''_{H2O}):MGX-6:EXNB they are 10:0.1:1. The fast hydrolysis of CelXNB is much faster than expected from the 3-isomer. In addition, the acceleration of the spontaneous hydrolysis is due not only to the sugar moiety, because the 6-isomer is slower than EXNB. The ratio k'_{H2O}/k''_{H2O} for CelXNB is 64, also very different to the ratio MGX-3:MG-6 of 185.

The main argument against the anchimeric assistance of the hydroxyl group comes from the activation parameters. In Table 4 is shown that only for the fast hydrolyses of CelXDNP and CelXNB is the entropy of activation almost zero. For the other water- and hydroxide ion-catalyzed hydrolyses, $\Delta S^{\neq}$ is

highly negative, supporting the theory that the rate acceleration observed for the cellulose esters is due to the ordered water around the cellulose matrix.

The spontaneous hydrolysis of the first xanthate group of MG-2,3 might be faster than the second due to steric compression that is relieved in that step. The hydrolysis of MGX-2,3 raises the possibility that k'_{H2O} and k''_{H2O} correspond to the rate constants of the hydrolysis of dixanthated anhydroglucopyranose rings in CelXNB. The ratios k'_{H2O}/k_1 and k''_{H2O}/k_2 for the rate constants of CelXNB and the hydrolysis of MGX-2,3 are 2,5 and 0.7, respectively. However, there are two pieces of evidence against this alternative. In the first place, the C-6 isomer should predominate over the C-2 + C-3 isomers, because the xanthation of methylglucose in alkaline solution produces mainly the C-6 isomer (13, 14). Therefore, if k'_{H2O} and k''_{H2O} correspond to the hydrolysis of di- and monoxanthated rings, the reactivity of the C-6 isomer should be the same as the C-2 or C-3 isomer, when actually it is about 100 times slower than MGX-3 (Table 3). The second piece of evidence comes again from the negative entropies of activation of the water catalyzed hydrolysis of MG-2,3 (Table 4).

As for the CelXNB, the hydroxide ion-catalyzed hydrolysis of CelXDNP follows simple first-order kinetics, and this reaction is slower than that of the ethylxanthate analogue, as can be observed in Table 3. The slower rates might be due to a diffusion effect of the bulky hydrated OH- through the cybotactic region of cellulose.

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