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AN N.M.R. STUDY OF THE INTERACTIONS BETWEEN CADOXEN AND SACCHARIDES

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ABSTRACT

Cadoxen, an aqueous solution of cadmium oxide and ethylenediamine, is an effective solvent for cellulose and is known to form complexes with simpler saccharides. The ^{1}H-, ^{13}C-, and ^{113}Cd-n.m.r. spectra of D-glucose, cellobiose, methyl α-D-glucopyranoside, methyl β-D-glucopyranoside, and cellulose in cadoxen are reported. Cellulose gives a well resolved ^{13}C spectrum in this solvent, and it is assigned by comparison with the spectra of simpler sugars. The ^{113}Cd and ^{13}C results are *not* consistent with the formation of chelate alcoholate complexes involving the 2- and 3-hydroxyl groups. This form of interaction has been suggested in the literature. It seems rather that hydrogen-bonding interactions are dominant. It is suggested that the effectiveness of cadoxen and similar cellulose solvents is a result of enhanced hydrogen-bonding arising from a combination of steric and electronic factors. The metal ion serves the dual purpose of holding two amino groups in a favorable orientation for hydrogen bonding with a pair of equatorial hydroxyl groups on the carbohydrate, and of decreasing the pKa of the amino group by withdrawing electrons. Some analogies with the binding of sugars to concanavalin A are discussed.

INTRODUCTION

There exists a class of metal–amine complexes capable of dissolving cellulose. The original member of the class, cuprammonium hydroxide, was discovered by Schweizer[1] in 1857. More recently, Jayme[2] and his co-workers reported on the solubility of cellulose in aqueous solutions containing complexes of amines (usually ethylenediamine) and a variety of divalent metal ions (Cu^{2+}, Co^{2+}, Zn^{2+}, Ni^{2+}, and Cd^{2+}). The nature of the interactions between cellulose or simpler saccharides and these metal–amine compounds has been extensively discussed[3–9], but definitive information on the geometry and bonding-interactions of the resulting complexes is lacking. A number of investigators[3,6,8] have postulated the formation of a chelate alcoholate complex between the metal ion and the 2- and 3-hydroxyl groups of the glucose residues. These conclusions have been based on optical rotation[3], electronic

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spectra[5], and e.s.r. measurements[8]. Other authors[4] have concluded that bonding to the metal is minimal. In this case, presumably, hydrogen-bonding interactions are dominant. Chemical intuition would tend to favor the latter alternative, as all of the metal ions involved favor nitrogen- over oxygen-donors, and the amine must be present in large excess[10] to produce a good cellulose solvent. However, as the metal ion is an essential constituent of the solvent mixture, a proponent of the hydrogen-bonding model has the onus of finding a role for the metal ion if it is not directly bonded to the carbohydrate.

Our interest in this area originated from structural[11] and mechanistic[12] studies which showed that metal complexes could hold other molecules in the second coordination sphere by hydrogen bonding, and that such complexes could play an important role in both ligand exchange and catalytic mechanisms. To be effective reaction intermediates, such second-sphere complexes would have to have quite specific geometric structures. Carbohydrate systems are particularly amenable to n.m.r. studies, and therefore appeared to be suitable models for second-sphere interactions. It seemed reasonable to start with solvents where the interactions with the carbohydrates were known to be strong. If the mode of action of these cellulose solvents were understood, it might also be possible to develop more-versatile solvent systems. In the present paper, we report n.m.r. studies of the interactions of "cadoxen"[2,10] with D-glucose, cellobiose, methyl glucosides, and cellulose. "Cadoxen", a solution of cadmium oxide in ethylenediamine, is one of the better cellulose solvents, and has the added advantages of being relatively stable and diamagnetic. We report ^{113}Cd, ^{13}C, and ^{1}H spectra. The ^{113}Cd chemical shifts are very large[13] and are sensitive to the ligand environment. The ^{113}Cd spectra should, therefore, distinguish structures involving metal–oxygen bonding from those having only metal–nitrogen bonding. The ^{13}C spectra should establish the site or sites of complexation on the carbohydrate moiety. Proton spectra are structurally less useful, but provide a rapid assay for anomeric composition and have also been used to study the effects of changing the metal-ion concentration. The n.m.r. spectra also provide information on the lability of the metal amine–carbohydrate complexes.

RESULTS

(i) ^{13}*C- and* ^{1}*H-n.m.r. spectra.* — Table I records ^{13}C chemical-shift data for D-glucose, β-cellobiose, methyl α-D-glucopyranoside, methyl β-D-glucopyranoside, and cellulose in the solvents (where solubility permits) D_2O, D_2O–ethylenediamine, and cadoxen. Fig. 1 shows a ^{13}C spectrum of cellulose in cadoxen obtained at 100.62 MHz. In all instances, only a single ^{13}C-peak for ethylenediamine was observed.

The assignments for the spectra of glucose, cellobiose, and the methyl α- and β-D-glucosides in aqueous solution are available in the literature[14]. A recent paper[15] summarized these assignments and suggested some minor revisions for cellobiose. The spectra in ethylenediamine and in cadoxen require some comment, however.

With solutions of glucose, only the β anomer is observed in both ethylene-

TABLE I

^{13}C CHEMICAL SHIFTS[a] IN DIFFERENT SOLVENTS

Compound	*Solvent*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*CH_3*
α-D-Glucose	D_2O	93.5	72.9	74.2	71.1	72.7	62.0	
β-D-Glucose	D_2O	97.3	75.6	77.2	71.1	77.2	62.2	
	D_2O–en[b]	98.0	76.0	77.5	71.3	77.5	62.2	
	Cadoxen	102.9	77.2	79.0	72.5	78.7	62.9	
Methyl α-D-glucoside	D_2O	100.6	72.9	74.5	71.0	72.6	62.0	56.3
	D_2O–en[b]	100.5	73.0	74.2	70.8	72.4	61.6	56.0
	Cadoxen	101.6	74.1	75.7	72.5	73.7	62.7	56.4
Methyl β-D-glucoside	D_2O	104.5	74.5	77.2	71.1	77.2	62.2	58.5
	D_2O–en[b]	104.5	74.2	77.3	70.8	77.1	61.8	58.0
	Cadoxen	105.6	75.7	79.3	72.8	78.7	63.1	58.4
β-Cellobiose	D_2O	103.8	74.5	77.0	70.8	77.2	62.0	
		97.1	75.3	75.7	80.0	76.0	61.5	
Cellulose	Cadoxen	105.2	76.4	77.3	80.0	77.3	62.9	
Δβ-D-Glucose	Cadoxen–D_2O	5.6	1.6	1.8	1.4	1.5	0.7	
ΔMethyl α-D-glucoside	Cadoxen–D_2O	1.1	1.1	1.5	1.7	1.3	1.1	
ΔMethyl β-D-glucoside	Cadoxen–D_2O	1.1	1.5	2.0	2.0	1.6	1.3	

[a]Chemical shifts to low field relative to Me_4Si. [b]Ethylenediamine.

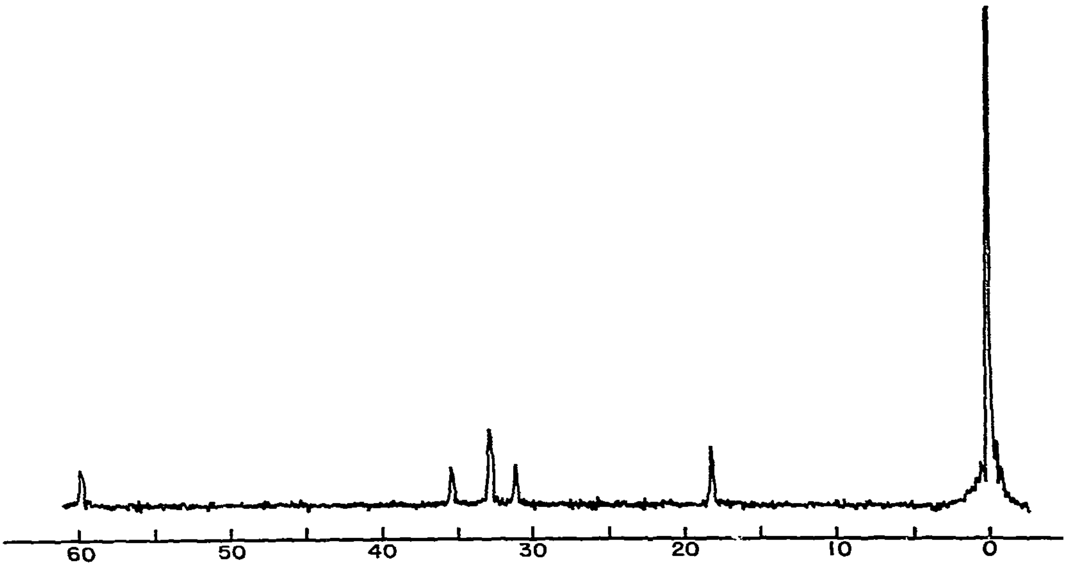

Fig. 1. The ^{13}C-N.m.r. spectrum of cellulose in cadoxen at 100.62 MHz. Shifts are in p.p.m. from ethylenediamine (δ ethylenediamine, 44.3 p.p.m.).

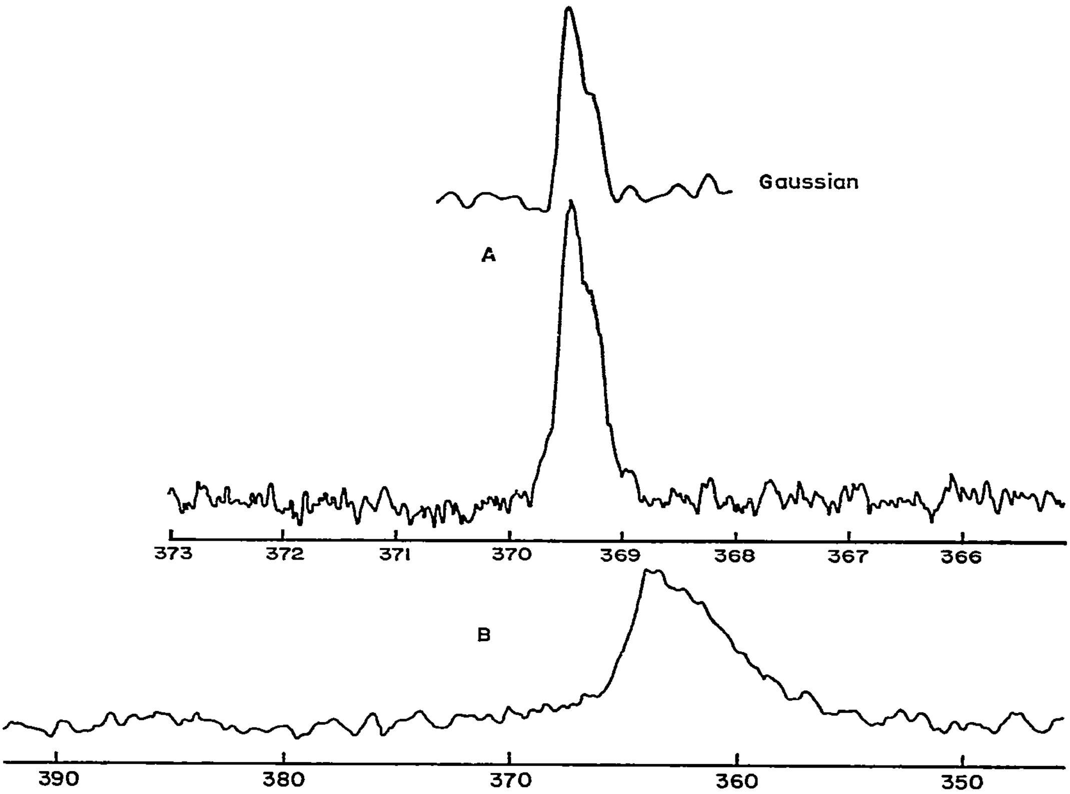

Fig. 2. ^{113}Cd-N.m.r. spectra. A: Cadoxen; B: cellulose in cadoxen, at 88.743 MHz. Shifts in p.p.m. from cadmium propionate. The upper spectrum in A confirms the shoulder by using a computer-smoothing routine.

diamine and cadoxen. This is to be expected because of the high pH of these solutions (~13–14), which favors the β anomer[16]. It was demonstrated by ^{1}H-n.m.r. that sodium hydroxide added to a concentration corresponding to the basicity of the cadoxen solution showed only the β anomer of glucose to be present. On being kept, solutions of glucose and cellobiose show additional sets of ^{13}C peaks in either ethylenediamine or in cadoxen. The formation of compounds giving rise to these additional peaks may be monitored either by ^{1}H- or by ^{13}C-n.m.r. The intensities of the additional peaks increase with the concentration of *N*,*N*,*N'*,*N'*-tetradeuterioethylenediamine or deuterated cadoxen. There is slow exchange with unreacted glucose. The glucose peaks are unshifted and broadened only slightly in these solvents. The rate of appearance of these new peaks parallels changes in the optical rotation of the solutions. It appeared probable that glucosylamines[17,19] were being formed, and this hypothesis was confirmed by synthesis of samples of both the mono- and di-D-glucosylethylenediamine, and by demonstrating that they accounted for the additional lines in both the ^{13}C and ^{1}H spectra. It is not clear whether the hydrogen-bonded complexes between ethylenediamine and D-glucose reported by Moulik and Mitra[20] differ from the glucosylamines reported earlier. No additional resonances are observed in solutions of the methyl glucosides in ethylenediamine or cadoxen. The ^{13}C shifts caused by these solvents may therefore be readily measured. Those for D-glucose were obtained from freshly prepared solutions, but reaction between cellobiose and ethylenediamine occurred too rapidly to obtain reliable assignments in cadoxen.

(ii) ^{113}Cd-n.m.r. spectra. — The ^{113}Cd-n.m.r. spectra of both pure cadoxen and of solutions in cadoxen of D-glucose, cellulose, methyl α-D-glucoside, or methyl β-D-glucoside all show a single line. The ^{113}Cd chemical-shift of cadoxen [329 p.p.m. to low field of $Cd(ClO_4)_2$] is consistent with results for other *N*-bonded complexes[21,22]. On addition of cellulose, glucose, or either of the glucosides, the peak is shifted upfield to a maximum extent of 35 p.p.m., and is broadened. Fig. 2 shows spectra obtained at 88.743 MHz. We speculate that the shoulders visible on these lines, which are not observed at lower fields, may be due to incomplete averaging of the chemical-shift anisotropy in these viscous media.

Table II lists the chemical shifts of a number of cadmium(II) samples. Samples 1–3 show that the shift of the hydrated Cd^{2+} ion is relatively little affected by acids. Sample 4 shows a shift of ~14 p.p.m. to high field, caused by second coordination-sphere effects of a different solvent. Sample 5 shows that interaction of glucose with the Cd^{2+} ion is minimal. Samples 6 and 7 illustrate typical chemical-shifts for complexes with ligands containing both oxygen and nitrogen donors. Samples 8–11 show chemical shifts typical of complexes having nitrogen donor ligands. We note that the shifts of cadoxen and of cadoxen with excess alkali are not substantially different from that of the pure cadmium–ethylenediamine complex. The shift on adding cellulose is very minor on the scale of the 300-p.p.m. range of the shifts in these samples, as already noted. Table III presents some data for the shift of the ^{113}Cd

TABLE II

CADMIUM-N.M.R. CHEMICAL SHIFTS RELATIVE TO CADMIUM PERCHLORATE IN D_2O[a]

Sample	*Sample description*	*Chemical shift (p.p.m.)*
1	0.432M $Cd(ClO_4)_2$, aqueous	0.0
2	0.456M $Cd(ClO_4)_2$ in 0.455M $HClO_4$	0.0
3	0.3M $Cd(ClO_4)_2$ in 6M $HClO_4$	5.0
4	0.469M $Cd(ClO_4)_2 \cdot 6H_2O$ in acetonitrile	14.2
5	0.521M $Cd(ClO_4)_2$ in 1.72M aqueous D-glucose solution	−1.54
6	$Cd(ClO_4)_2$ saturated in 5.17M aqueous 2-dimethylaminoethanol	−77.5
7	$Cd(EDTA)^{2-}$, aqueous, pH = 5	−85
8	$Cd(ClO_4)_2$ saturated in 30% aqueous ethylenediamine solution	−350
9	Cadoxen	−329
10	Alkaline cadoxen containing 0.5M sodium hydroxide	−323
11	Cellulose solution in cadoxen, 1 g/20 g cadoxen	−319.4

[a]All negative shifts imply downfield resonance with respect to the reference signal.

TABLE III

EFFECT OF D-GLUCOSE ON CADMIUM-N.M.R. SHIFTS IN CADOXEN[a]

C_g[b]	$(C_{en}$[c] $- C_g)/C_g$	ν_{obs} (p.p.m.)	$1/(\nu_{obs} - \nu_{en}) \times 10^2$ (p.p.m.$^{-1}$)
0.000		−328.2	
0.322	14.53	−312.8	6.49
0.634	6.89	−304.4	4.20
0.923	4.42	−299.8	3.52
1.356	2.69	−295.4	3.05
1.662	2.01	−293.2	2.84

[a] Reference, $Cd(ClO_4)_2$ in D_2O. [b] C_g, concentration of glucose. [c] C_{en}, concentration of ethylenediamine.

resonance on adding D-glucose to cadoxen solutions. There is a smooth shift to higher field with increasing concentration of D-glucose. The cellulose solution, sample 11 of Table II, is approximately 0.22M in glucose residues and gives a shift that corresponds very closely to that expected from a solution of glucose of the same concentration. A number of these solutions were also examined by ^{111}Cd-n.m.r. at 19.08 MHz. In each instance the chemical shift in p.p.m. was identical, within experimental error, with that obtained from the ^{113}Cd spectrum.

DISCUSSION

The ^{113}Cd data are not consistent with Cd–O bonding. There is a 300-p.p.m. difference between the ^{113}Cd shift of the hexa-aquo complex and that of the hexa-amine complex[21]. The data of Table II allow us to compare this shift with that of the cadoxen–cellulose complex. The observation of a single ^{13}C-peak for ethylenediamine clearly shows that there is fast exchange between free and complexed ethylenediamine. The ^{113}Cd data show that there is fast exchange between Cd associated with glucose and that not associated with glucose. The data of Table III permit calculation of both the shift of ^{113}Cd in the glucose complex and the equilibrium constant for the formation of this complex. The details of this calculation vary slightly depending on the model assumed. In each case, fast exchange is assumed and the concentration dependence of the chemical shift is related to a specific chemical equilibrium. We have explored three models. If a molecule of D-glucose simply replaces a molecule of ethylenediamine coordinated to the complex, $\Delta\nu_0 = -276$ p.p.m. and $K = 6.5$. If a molecule of D-glucose forms a 1:1 addition complex with $Cd(en)_3^{2+}$, $\Delta\nu_0 = -276$ p.p.m. and $K = 1.3$. If there is rapid exchange between an ethylenediamine molecule coordinated to Cd^{2+} and an ethylenediamine molecule having an attached molecule of D-glucose, $\Delta\nu_0 = -284$ p.p.m. and $K = 7.7$. All of these models give

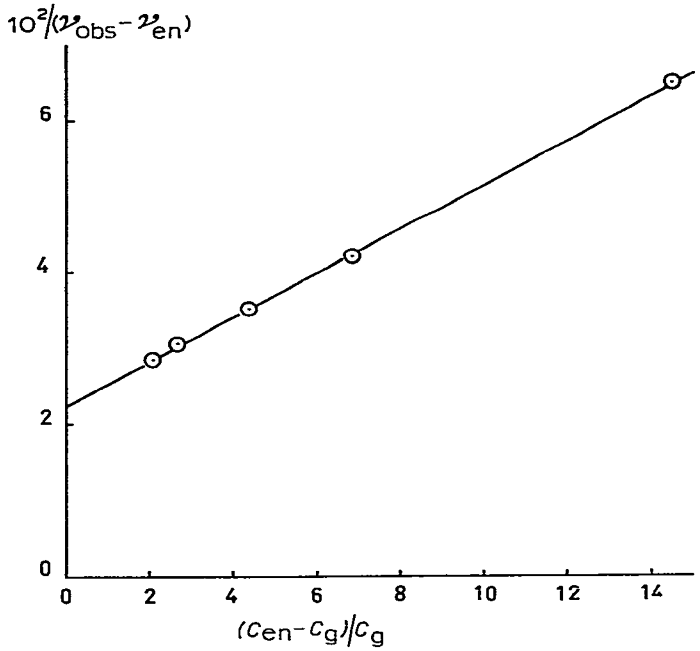

Fig. 3. Plot of chemical-shift data of ^{113}Cd of D-glucose in cadoxen to obtain shift of complex and equilibrium constant (see text).

comparable fits to the data. The third model, for example, leads to the relationship:

$$\frac{1}{\Delta \nu_{obs}} = \frac{1}{\Delta \nu_0}\left(\frac{C_{en} - C_g}{KC_g} + 1\right),$$

where C_{en} is the concentration of ethylenediamine and C_g the concentration of D-glucose. The approximation is made that the concentrations of both ethylenediamine and D-glucose are large compared to that of Cd^{2+}. A plot of $1\text{—}\Delta \nu_{obs}$ versus $(C_{en} - C_g)/C_g$ should therefore be linear, with a slope of $1/\Delta \nu_0 K$ and an intercept of $1/\Delta \nu_0$. This plot is shown in Fig. 3. The significant feature of these results is that the calculated chemical shift is consistent with Cd–N bonding but not Cd–O bonding. The equilibrium constant found for the first model would imply that glucose is a better ligand than ethylenediamine, which is unrealistic and contrary to the direct observation (sample 5, Table II) that glucose has only a small interaction with Cd^{2+}. We conclude, therefore, that the ^{113}Cd-n.m.r. results strongly favor a hydrogen-bonding model.

Fig. 2 shows that there is considerable broadening of the ^{113}Cd resonance on adding cellulose (by a factor of ~10). It is possible that this broadening is at least partly caused by rapid chemical-exchange between the different environments for the Cd ion. It could, however, also reflect a much longer correlation-time resulting from association of Cd with the macromolecule (cellulose).

The ^{13}C results are consistent with the foregoing conclusion and also provide some information on the interacting hydroxyl groups. Consider first glucose and the methyl glucosides. The assignments of these spectra are well established. A recent paper provides a definitive resolution of soms ambiguities[15]. The shifts of the ^{13}C resonances on passing from water to water–ethylenediamine mixtures in the same proportions as in the cadoxen solutions are no more than 0.1–0.5 p.p.m. The only exception is the anomeric carbon atom of D-glucose, for which the shift of 0.7 p.p.m. reflects ionization of the hydroxyl group at the high pH of the ethylenediamine solutions (see later). The ethylenediamine apparently causes only modest changes in the hydrogen-bond environment, that is, it probably does not compete extensively with water.

The shifts from D_2O to cadoxen are summarized in Table I. They are all to low field, as expected for hydrogen-bonding effects[23], and are generally in the range 1–2 p.p.m., that is, considerably larger than with ethylenediamine alone. The shifts are significantly larger for methyl β-D-glucoside than for methyl α-D-glucoside. The anomalously large shift of the anomeric carbon atom for β-D-glucose can again be correlated with hydroxyl-group ionization[24]. The shifts of all carbon atoms are quite similar, and this is not consistent with the formation of a cadmium complex engaging the 2- and 3-hydroxyl groups, as has been suggested. It appears, rather, that there is an increase in hydrogen bonding involving all of the hydroxyl groups, with perhaps some preference for 3- and 4-OH.

Based on the foregoing results, we may now make a reasonable assignment of the cellulose–cadoxen spectra by using the β-cellobiose spectrum to infer the effects of polymerization. This assignment is shown in Table I. Carbon atoms 1 and 6 may be assigned immediately as the lowest- and highest-field resonances, respectively. Interestingly, C-6 clearly has the longest T_1 value (as shown by its greater apparent intensity in Fig. 1), consistent with more mobility for the CH_2OH side-chain than for the polymer backbone. This is in contrast to D-glucose in water, for which we find that T_1 for C-6 is 0.6 sec and the remaining T_1 values are ~1.1 sec, reflecting the two hydrogen atoms attached to C-6 and the single hydrogen atom on other carbon atoms. Polymerization leads to C-4 being the next-lowest-field carbon resonance, and it is assigned accordingly. The remaining carbon atoms are assigned by analogy with methyl β-D-glucoside in cadoxen. Comparison between β-cellobiose and methyl β-D-glucoside suggests that, in the absence of hydrogen-bonding effects, C-3 would resonate to high field in cellulose as compared with the glucoside, C-4, substantially to low field (as already noted), and C-2 and C-5 would be relatively unaffected. Allowing for these differences, the data in Table I indicate that the hydrogen-bonding interactions between cellulose and cadoxen are essentially the same as those between methyl β-D-glucoside and cadoxen, except that the slightly favored positions are now C-2 and C-3. These n.m.r. data thus lead to the conclusion that cadoxen dissolves cellulose not because of its ability to form alcoholate chelate complexes, but because of its hydrogen-bonding properties. This conclusion is in agreement with the findings of Vink[4], but contrary to the conclusions of Lindberg and Swan[3]. This conclusion does not necessarily apply to solvents containing other metal ions, but it seems most reasonable to suppose that the series of ethylenediamine solvent-systems containing Cd^{2+}, Cu^{2+}, Ni^{2+}, Co^{2+}, and Zn^{2+} all function similarly. Most of the evidence for metal–oxygen bonding has been obtained on the Cu^{2+} system. Small changes in the ligand-field spectra[5] and in the e.s.r. spin Hamiltonian parameters[8] have been interpreted in terms of Cu–O bonding. It seems quite possible that modest changes of this nature, and also the optical-rotation results of Lindberg and Swan[3], could be interpreted on a hydrogen-bonding model.

There remains the question as to the role that the Cd^{2+} ion plays in enhancing the hydrogen-bonding abilities of ethylenediamine. Steric factors must certainly play a part. We note in this context the greater interaction with methyl β-D-glucoside than with methyl α-D-glucoside, and the necessity for adjacent equatorial hydroxyl-groups for interaction with cadoxen as found by Lindberg and Swan[3]. A molecular model suggests that, in a octahedral tris(ethylenediamine) chelate, a pair of N-H groups from different ethylenediamine molecules has favorable geometry for forming a cyclic, hydrogen-bonded complex with two equatorial hydroxyl-groups on a sugar moiety. The NH_2 groups of a single ethylenediamine molecule are less favorably oriented for this type of interaction. It seems clear, though, that there must also be an electronic effect. Complexation of ethylenediamine removes electrons from the nitrogen atom to make the NH_2 group a stronger acid. This is demonstrated by the rapid exchange of such protons[25] with water and by the participation of the $-NH^-$ ligand in base-catalyzed, ligand-exchange processes[26]. The more acidic NH_2 will be more favorable for hydrogen bonding. The pKa value of coordinated ethylenediamine in the Cd(III) complex is thought[27] to be >14. It is likely to be somewhat higher for the Cd(II) compound because of the lower positive charge on the metal ion. The anomeric hydroxyl-group of glucose has[24] a pKa of 12.35 at 25°, but other hydroxyl groups have[28] significantly higher pKa values. Values of pKa for the hydroxyl groups of cellulose[29] have been estimated to be ~ 15. It is likely, therefore, that neither reaction *1* nor reaction *2* proceeds to a significant extent in solutions (pH 13+) of cellulose in cadoxen.

$$\text{cellulose -C-OH} + OH^- \rightleftarrows \text{-C-O}^- + H_2O \qquad (1)$$

$$\text{cadoxen Cd-NH}_2 + OH^- \rightleftarrows \text{Cd-NH}^- + H_2O \qquad (2)$$

The gain in enthalpy resulting from the formation of a hydrogen bond could, however, favor reaction *3*.

$$\text{Cd-NH}_2 + \text{-C-OH}^- + OH^- \rightleftarrows \text{Cd-NH}\cdots\text{H}\cdots{}^-\text{O-C-} + H_2O \qquad (3)$$

It has indeed been suggested that intramolecular hydrogen-bonding may increase the acidity of the hydroxyl groups of carbohydrates[24]. It has also been observed[7] that hydrogen ions are released in the reaction of cuprammonium hydroxide with sugars[7]. We note also that cobalt(III)–ethylenediamine complexes have been shown[27] to hydrogen-bond to hydroxyl ions with an "apparent pK" of 12.5. A similar process could account for the 6-p.p.m. high-field shift of sample 10, Table II, relative to cadoxen and rationalize the observed high-field shifts with carbohydrates.

Thus one could argue that it is energetically favorable for cellulose to form hydrogen bonds with cadoxen rather than with the hydroxyl groups of another cellulose molecule if the pKa values are suitable to allow reaction *3* to occur preferentially. This results in the concurrent formation of a hydrogen bond and neutralization of a mole of base. This model, involving a combination of steric and electronic factors, is consistent with all of the n.m.r. data.

Finally, we note some interesting parallels between the interactions discussed here and the binding[30] of sugars to concanavalin A. In both instances, metal ions are necessary for binding, but the requirements are not specific. Thus Mn(II) and Ca(II) are the metal ions in naturally occurring conconavalin A, but both may be replaced by Cd(II) without loss of saccharide-binding ability[31]. On binding saccharide, one of the ^{113}Cd resonance shifts 8 p.p.m. to high field[32], a result that is very similar to that already discussed. The shifts of the ^{13}C resonances[33] of the sugar are apparently smaller than those reported in the present study. It has been shown by both X-ray[34] and n.m.r.[33] studies that the sugar is not directly bonded to the metal. Hydroxyl groups are necessary at C-3, C-4, and C-6 of the sugar, and the α anomer of D-glucopyranose binds preferentially[35]. These steric restrictions, although differing in detail, are reminiscent of the conditions for complex-formation with cadoxen. Thus we suggest that the mechanism for sugar binding to concanavalin A could be similar to that discussed here, with the metal ions having the dual role of controlling the stereochemistry to place hydrogen-bonding groups in the correct dispositions and of adjusting the pKa values of substituents on the protein for optimal hydrogen-bonding ability.

EXPERIMENTAL

Preparation of cadoxen solutions[10]. — Ethylenediamine was purified by stirring for 5 h with potassium hydroxide followed by distillation (118.5°) over molecular sieves. Purified ethylenediamine (22.5 mL) was added to a mixture of D_2O (15 mL for the n.m.r. lock) and distilled water (37.5 mL). The solution was cooled in ice, and 7.5 g of finely powdered cadmium oxide was added slowly with vigorous stirring. A white precipitate of cadmium hydroxide settled overnight, leaving a clear, colorless solution. This procedure gave a cadoxen solvent analysis of which gave 0.34M (Cd(II) and 5.09M ethylenediamine. The apparent pH was 13.7.

To obtain proton-n.m.r. spectra, *N*-deuteriocadoxen was needed. Purified ethylenediamine (15.0 mL) was 97% *N*-deuterated by repeated addition of D_2O (15.0 mL) and removed of water by distillation (4 cycles). The solution was dried over anhydrous sodium sulfate. *N*-Deuterated ethylenediamine (12.5 mL) was added to D_2O (29.5 mL) and the solution was cooled in ice. The flask was slowly flushed with argon to exclude moisture while 4.2 g of cadmium oxide was added with rapid stirring.

Cadoxen prepared in this manner readily dissolved α-cellulose (Sigma), as reported by Henley[10]. Other carbohydrates were obtained commercially and used without further purification.

N.m.r. spectroscopy. — Most of the ^{13}C and ^{113}Cd spectra were obtained with a Bruker WH-90 FT spectrometer using 20° pulses. The ^{13}C spectra were recorded at 22.62 MHz and the ^{113}Cd at 19.96 MHz. As it is possible to obtain spurious FT n.m.r. resonances when large chemical shifts are involved, a few samples were also examined by ^{111}Cd n.m.r. at 19.08 MHz, to confirm the chemical-shift assignments. Proton spectra were obtained at 90 MHz with a Varian EM390 spectrometer. A few ^{13}C and ^{113}Cd spectra were recorded, by courtesy of Bruker Spectrospin, on a 400-MHz superconducting FT instrument. No new features were observed at high field, although there was the expected improvement in dispersion and signal-to-noise ratio. The ^{13}C chemical-shifts were obtained relative to external tetramethylsilane and are reported as δ values. Susceptibility corrections were small. The ^{113}Cd spectra were referenced to a 0.5M solution of cadmium perchlorate.

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