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Note

Preparation of polymorphic crystalline phases of D-mannitol: influence of keggin heteropolyanions

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Abstract

Two crystalline forms of D-mannitol precipitated at room temperature from acetone/water mixtures in the presence of the Keggin heteropolyanions $[PW_{12}O_{40}]^{3-}$ or $[SiW_{12}O_{40}]^{4-}$ were identified by X-ray powder diffraction and solid state ^{13}C NMR spectroscopy. In the presence of $[SiW_{12}O_{40}]^{4-}$ (acid or K^+ salt) the α polymorph was the only form obtained. The κ form was the predominant component of a mixture of κ and α forms obtained in the presence of $H_3[PW_{12}O_{40}]$. In the absence of the polyanions, the β form was precipitated. © 1998 Elsevier Science Ltd. All rights reserved

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Mannitol is by far the most abundant polyol in nature, with important applications in the food and pharmaceutical industries. D-mannitol exists in several polymorphic crystalline forms denoted by Greek letters [1]. The form obtained depends on conditions of crystallisation such as the solvent used, temperature, concentration and rate of crystallisation [2–6]. Mixtures of different forms are frequently obtained. Crystallisation from the melt has also been reported to provide different polymorphs [3,7,8].

Grindley et al. [9] have reported that only three polymorphs, α, β and κ, could be obtained when D-mannitol was crystallised from water, ethanol–water and ethanol, and have shown that they can be distinguished by CP/MAS ^{13}C NMR. The correspondence with previously reported forms was made on the basis on X-ray diffraction data [9] (see Table 1). In this note we report the facile preparation of D-mannitol in different forms from aqueous solutions of some heteropolyanions. The polymorphs α, and κ were obtained. This work was undertaken as part of a study on the interaction of $[XW_{12}O_{40}]^{n-}$ anions (referred as Keggin anions) with polyols.

1. Experimental

$H_3PW_{12}O_{40}.nH_2O$ (Merck), $H_4SiW_{12}O_{40}.nH_2O$ (Fluka) were recrystallised from water before use. D-mannitol (BDH, Biochemicals) was used without further purification. $K_4SiW_{12}O_{40}.7H_2O$ was

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Table 1
Comparison of polymorphic forms of D-mannitol reported by different authors (adapted from [9])

Grindley et al. [9]	Jeffreys et al. [4,5]	Levy et al. [3,6]	Rye et al. [2]	Medium of crystallisation
α	α'	δ	α	100% ethanol; cold dilute aqueous solution.
β	β	β	β	Aqueous ethanol; aqueous solutions at room temp.
κ	κ	α	γ	1:1 water ethanol; rapid cooling aqueous solutions at 100 °C; methanol/boric acid; melt.

prepared by published methods [10]. Only the α-isomers of the heteropolyanions were considered.

Solid D-mannitol was precipitated by the addition of acetone to an aqueous solution of D-mannitol and heteropolyanion at room temperature, filtered, washed with acetone and dried in vacuum. Solutions of D-mannitol at 0.5 mol dm^{-3} were used throughout. Concentrations of heteropolyanions were approximately 0.05 mol dm^{-3}. The solids obtained were characterised by FTIR and ^{13}C NMR spectroscopy, X-ray powder diffraction and chemical analysis.

Infrared spectra were recorded on a Mattson 7000 FTIR spectrometer using KBr pellets. CP/MAS ^{13}C NMR spectra were recorded on a Bruker MSL-400P spectrometer, at 100.6 MHz, using a contact time of 8 ms, a ^{1}H 90° pulse of 4 μs, a recycle delay of 10 or 30 s and spinning rates of 5 kHz. TMS was used as reference. X-ray powder diffraction patterns were measured on a Philips PW 1710 diffractometer, using Cu K$_\alpha$ radiation, in the range $2\theta = 3 - 50°$. Analysis of phosphorus and silicon were performed by ICP spectrometry (University of Aveiro Central Laboratory of Analysis).

2. Results and discussion

Addition of acetone to an aqueous solution (0.5 mol dm^{-3}) of D-mannitol precipitated a microcrystalline white solid. Similar precipitation occurred in the presence of the heteropolyanions $[PW_{12}O_{40}]^{3-}$ or $[SiW_{12}O_{40}]^{4-}$, in the acid forms or the K$^+$ salt of the latter. FTIR spectra of the obtained compounds showed, by comparison with published spectra [3], that different polymorphs of D-mannitol had precipitated (Fig. 1). In the absence of the polymetallates, the β-form of D-mannitol is obtained. This is also the form of the commercial reagent used. The presence of $H_3PW_{12}O_{40}.nH_2O$ or $H_4SiW_{12}O_{40}.nH_2O$ gives rise to different polymorphs (κ and α, respectively, using the nomenclature of reference [9]). $K_4SiW_{12}O_{40}.nH_2O$ had the same effect as the corresponding acid.

Keggin type polyanions give rise to characteristic, well defined, strong infrared absorption bands in the 1100–800 cm^{-1} range [11], observed at 1080, 992, 890, 810 nm and at 981, 928, 880, 785 nm in the spectra of $H_3PW_{12}O_{40}.nH_2O$ or $H_4SiW_{12}O_{40}.nH_2O$, respectively. The absence of these bands in the spectra suggested that D-mannitol was not

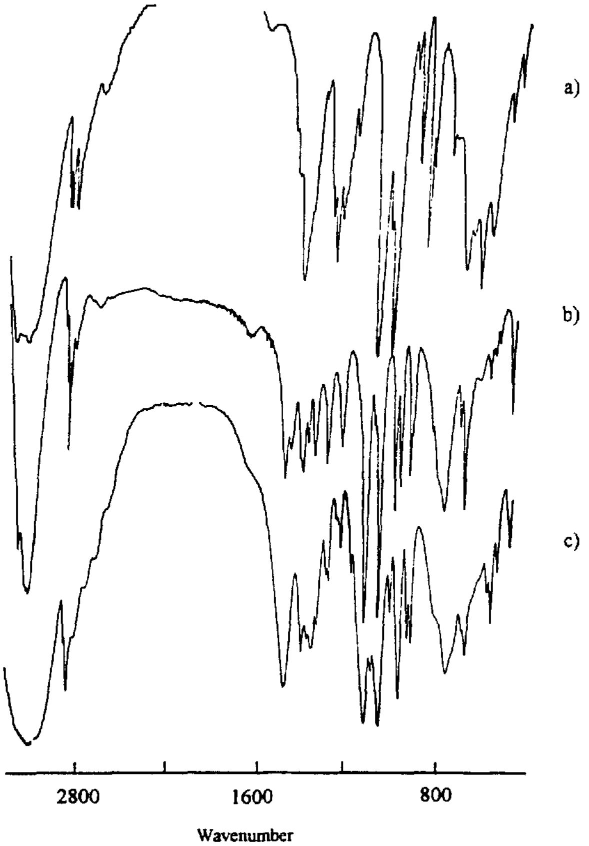

Fig. 1. Infrared spectra of D-mannitol obtained under different precipitation conditions: (a) in the absence of heteropolyanions (β form); (b) in the presence of $H_3PW_{12}O_{40}\cdot nH_2O$ (predominantly κ form); (c) in the presence of $H_4SiW_{12}O_{40}.nH_2O$ or $K_4SiW_{12}O_{40}.7H_2O$ (α form).

contaminated by the heteropolyanions. Elemental analysis yielded no P or Si in the solids obtained, confirming these results. X-ray diffraction powder patterns showed no evidence of the presence of the heteropoly compounds. The heteropolyacids are soluble in water or acetone [12]. This is not the case for the potassium salts, for which a small amount of contamination was detected.

X-ray powder diffraction and solid state ^{13}C NMR spectroscopy were used, together with FTIR spectroscopy, to identify the D-mannitol forms obtained. The ^{13}C NMR spectrum of Fig. 2(a) shows that the β form is the only one precipitated by addition of acetone to water solutions of D-mannitol [9]. In the presence of $[SiW_{12}O_{40}]^{4-}$ (acid or K^+ salt) the α polymorph is obtained instead. The κ form is the predominant component of a mixture of κ and α forms obtained in the presence of $[PW_{12}O_{40}]^{3-}$. Comparison of the X-ray powder diffraction of the obtained forms with indexed files [13] confirmed this.

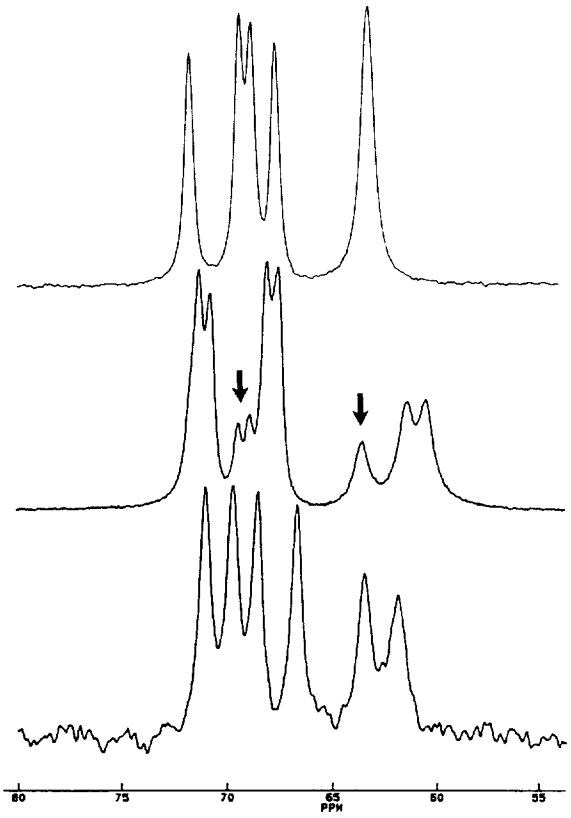

Fig. 2. CP/MAS ^{13}C NMR of D-mannitol obtained in different precipitation conditions: (a) in the absence of heteropolyanions (β form) (b); in the presence of $H_3PW_{12}O_{40}.nH_2O$ (κ and α form); (c) in the presence of $H_4SiW_{12}O_{40}.nH_2O$ or $K_4SiW_{12}O_{40}.7H_2O$ (α form). Arrows in (b) show peaks derived from contamination with α-form.

^{13}C NMR spectroscopy seems to be the most useful technique to identify the three polymorphs formed by D-mannitol, as pointed out by Grindley et al. [9]. Infrared spectra of our samples agree with those reported by Lévy [3], and correspond to the forms indicated in Table 1. The κ-form of D-mannitol prepared from solutions with $H_3[PW_{12}O_{40}]$ was always contaminated with the α-form, but the infrared spectrum was identical to that published for the main constituent. Possibly the positions of the peaks on the infrared spectra of the different polymorphs overlap in part thereby preventing the identification of small amounts of one form in the presence of an excess of another.

^1H NMR studies of D-mannitol in D_2O have provided evidence for the presence of two predominant conformers [14]. The addition of the polyanions to the solutions does not alter much the ^1H NMR spectra and so does not provoke any large change of the conformer population.

The different polymorphs of D-mannitol are due to several possible packing arrangements differing on the H-bonding network constructed, and so the polymorphism corresponds to different hydrogen bonded arrangements of nearly identical molecules [4,5]. X-ray crystal structures were determined for the β and κ polymorphs [4,5], and a study in two dimensions is available for the α form [4]. In all these three polymorphs the molecules of D-mannitol adopt the same conformation, with the carbon atoms approximately all in the same plane. All the hydroxy oxygen atoms of the molecule donate and accept an H-bond that link the molecules in sheets and provide the bonding between these sheets in the β and κ forms (structure of the α polymorph was not completely determined). In the solid state the molecules are arranged in a very regular pattern, which uses their full potential for intermolecular H-bonding.

Crystallisation from solution in systems with different polymorphs is far from being a simple process. At a particular temperature the solid phase with the lowest solubility at that temperature generally exists. The isolation of metastable phases depends on several factors, namely on the form of the solubility versus temperature curves and the corresponding metastable zone widths (that vary for the different polymorphs with the solvent or mixtures of solvents considered), and on the rate of crystal formation and growth [15]. Different temperatures and different mixtures of solvents were, generally, used to prepare the D-mannitol polymorphs (Table 1). In the presence of boric acid the κ form of D-mannitol crystallises [5]. The situation reported here is not comparable to the crystallisation from solutions of boric acid, as the heteropolyacids are strong acids, and formation of complexes similar to those of boric acid with polyols does not occur. A previous report states that the salinity of the aqueous solutions did not alter the crystalline form obtained by evaporation [3]. We assume that the different polymorphs obtained in this study are due to the presence of different ions in solution. The presence of ionic species will necessarily alter the solubility curves or the metastable zone width for each polymorph. No specific interaction could be found to justify the different influence of the tungstophosphate or tungstosilicate compounds on the crystallisation of D-mannitol.

3. Conclusions

The existence of different polymorphs is a common situation in organic chemistry, whose importance needs no emphasis. The difference in solubility of the polymorphs can, for instance, alter the possible end uses of a product. Methods relying generally on crystallisation by evaporation of aqueous or ethanol/water solutions of D-mannitol had been described for the preparation of the different known polymorphs of this substance. We have found that rapid precipitation of D-mannitol from aqueous solutions, in the presence of some polyoxotungstates, will also produce different polymorphic forms. The possible explanation for this interesting phenomenon seems to be the influence of the salinity on the solubility of the different metastable forms, but further study is needed to clarify how these influences originate.

Acknowledgements

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