Study of the partial and exhaustive intramolecular dehydration of D-sorbitol

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Abstract

Sweetener, humectants, sequestrant, texturizer, stabilizer, bulking agent, D-sorbitol represents a leading product in the processing of the polysorbate class.

The scope of this work is to obtain details on the preparation and accession of D-sorbitol mono- and dianhydride as a method of chemical protection of primary and secondary hydroxyl functional groups (1:4) (3:6) as part of the strategy of controlled processing of polysorbates containing “homogeneous” polyoxyethylenic chains (n = 3, 6, 9, 18).

This work is investigating the dependence of yield of internal dehydration (partial and/or exhaustive, direct of D-sorbitol) on temperature (100-160°C and 120-200°C, respectively) and duration (5–35 minutes and 10–100 minutes, respectively) for the processing of 1,4-sorbitan and 2,5-isosorbide.

The evolution of the hydroxyl number (mg KOH/g D-sorbitol) (mg KOH/g 1,4-sorbitan) related to the theoretical (initial) value was followed and optimal values for the yield and dehydration parameters were established. Also in this work, the mathematical modeling of the dependence curves experimentally registered is realized.

Keywords: isosorbide, D-sorbitol, D-glucitol, D-sorbit, 1,4-sorbitan

1. Introduction

Linear hexahydroxy alcohols, hexitols [HOCH2(CH2OH)4CH2OH (Figure 1)], are related to monosaccharides, from which they are obtained via reduction sodium amalgam, catalytically with Raney nickel or electrolytically. They possess four asymmetric carbon atoms, forming two pairs with identical structure. Under the structure of each hexitol (Figure 1) there are shown the aldohexoses from which it is derived and the corresponding sugar acids, respectively [1].
Theory envisages the existence of ten stereoisomers, most of these being processed from hexoses via reduction. Some representatives [D-mannitol, D-sorbitol, D-iditol and galactitol (dulcitol; inactive)] are found in the free state in fruits or plant fluids.

By the reduction of the 16 aldohexoses, the 10 hexitols are obtained: four pairs of enantiomers (of which only the isomers in the D series are shown in Figure 1) and two meso forms.

Hexitols crystallize, are soluble in water and have sweet tastes. They do not reduce the Fehling solution, thus differing from hexoses.

Generally, polyols can form cyclic ethers by internal (intramolecular) elimination of one molecule of water between two hydroxyl groups.

The differences in the dehydration behavior of polyols are explained by the fact that in the rings of resulting ethers there exist tensions similar to those in rings composed exclusively of carbon atoms. The valence angle of oxygen in water is 104°, close to that of tetrahedral carbon, 109.5°.

This means that in pentamethylene oxide, tetrahydrofuran and dioxane there is no internal tension, while in ethylene oxide, 1,3-sorbitan, 1,6-sorbitan (Figure 2 d, e) the tension is high. Cyclic ethers with five-atom (furanose) (Figure 2 e, c, g, h, i) and six-atom (pyranose) rings (Figure 2 a) are stable, little reactive compounds, compatible with aliphatic acyclic ethers [1].

Legend: the arrow indicates free rotation around the C5-C6 bond for the proximity of the two hydroxyl groups and the occurrence of the 3,6 exhaustive dehydration process.
With formaldehyde, benzaldehyde and acetone, hexitols give cyclic acetals (kets) similar to those known in the saccharide class. Hexitols can be easily esterified with inorganic and organic acids.

By heating under vacuum, D-mannitol yields a mixture of internal ethers, from which D-\textit{mannitan} (1,4 anhydride) and isomannide (1,4-3,6 dianhydride) have been isolated.

D-sorbitol (CAS 50-70-4) is a leading polyol in food additivation, but also in the processing of polysorbates (Figure 3), a class of multifunctional food additives (E 432 – E 436) [emulsifiers, humectants, aerating agents, agents for monitoring the crystallization form of fats, coordinating (sequestering) agents, ameliorators of foaming capacity, volume and stability]. Having an admissible, limited toxicity, they are metabolized by the intestinal lipase, absorbed by the body and excreted through feces [2].

It is also known that the nucleophilic substitution of the hydroxyl functional group (and others) at ethylene oxide leads inevitably to a mixture of polyoxyethylene chain homologues. Their statistical distribution (Poisson, Weibull-Nycander) [3] is wider as the oligomerization degree increases.

Admitting as working premises:

- the capacity of hexitols (D-sorbitol) of intramolecular (internal) dehydration as a mean of protection of the hydroxyl function in directed processings;
- low differences in reactivity between the primary and secondary hydroxyl functional groups;
- difficulty (impossibility, in practice) of isolating (separating) through classical physico-chemical means (molecular distillation, elution on open chromatographic columns etc.) the heterogeneous polyoxyethylene chains strictly on their nominal oligomerization degrees, the knowledge of the optimal parameters for the partial (1:4) and exhaustive (1:4; 3:6), respectively, intramolecular dehydration and rehydration acquires an increasing constant interest in the structuring of polysorbates containing „homogeneous” polyoxyethylene chains (n = 3, 6, 9, 18) (Figure 4).

Anhydrazation of polyols also occurs during transesterification. Interaction of mannitol with triglycerides at temperatures up to 270°C, with distillation of the glycerol formed, results in a mixture of the diesters of mannitol and isomannide (figure 4) [4].

If such transesterification reactions do not go to completion, the resulting products will contain glycerides in addition to esters of mono- and dianhydrohexitol [5].
Alcoholysis of 1 mole of linseed oil with 2 mole of sorbitol at 230 to 240°C with a sodium methylate catalyst forms a mixed linseed monoglyceride – monolinseed sorbitan esters [6].

The reports in the literature [7,8] have been mostly on the preparation of polysorbates with heterogeneous polyoxyethylenic chains (Figure 3), without specifying the length of each individual chain, only the overall one (x + y + z + w = 20).

This fact justifies the interest for the diversification of structured lipids („tailor-made lipids”) as potential new sources of novel triglycerides in the processing of polysorbates [caprocapryl behenin (C₆O∆, C₈O∆, C₂₂O∆) (Procter & Gamble)] (Figure 6 a) or conjugated PEGₙ[R;2R(LM;CS)] and PEGₙ[R;2R(LM;CS)] (Figure 6 b), respectively.

Pegylation in our concept [9-13] supposes the derivatization of certain „homogeneous” polyoxyethylenic chains with degrees of oligomerization n = 3, 9, 18 [processed by the method of Williamson adapted purified and characterized chemically and physico-chemically (colloidal)] with hydrocarbonate chains R[C₁₂H₂₅/C₁₄H₂₉ (7/3) -lauryl/miristyl (7/3) (L/M) or C₁₄H₃₃C₁₈H₃₇ (7/3) – cetyl/stearyl (7/3) (CS)] respectively, hydrocarbonate chains R' from fatty polyunsaturated acids, which were isolated purified and characterized gas-chromatographically from saponifiable fractions of grapes seeds (fruits) (Vitis vinifera) (R's) [C₁₆(0∆) 10,10 %; C₁₈(1∆) 24,80 %; C₁₈(2∆) 64,90 %], wild chestnut (Aesculus hippocastanum) (R'ca) [C₁₆ (0∆) 10,90 %; C₁₈ (1∆) 57,00 %; C₁₈ (2∆) 28,80 %; C₁₈ (3∆) 3,72 %], wild rose (Rosa canina) (R'm) [C₁₆ (0∆) 3,19 %; C₁₈ (1∆) 15,92 %; C₁₈ (2∆) 67,50 %; C₁₈ (3∆) 13,30 %], coriander (Coriandri fructus) (R'co) [C₁₆ (0∆) 2,7%; C₁₈ (1∆) 83,00 %; C₁₈ (2∆) 13,40 %].

The esterification of the mono- or diprotected glycerine by selective acylation in molar ratio R'/R = 1/2 respectively R'/R = 2/1, has enable the series of 48 conjugates PEGₙ-L (2R';R) (R';2R) which purified, were afterwards characterized physico-chemical (colloidal) [12].

Formation of internal ether linkages is a characteristic of the sugar alcohols and occurs under the influence of heat or acidic reagents or both [14]. Thus treatment of D-sorbitol with a small quantity of sulfuric acid at 140°C results in the formation of either 1,4-sorbitan [15] or isosorbide depending on the duration of heating [16]. Isosorbide is formed from D-sorbitol by refluxing with xylene at 130°C in the presence of p-toluenesulfonic acid [17].

In general, the higher the temperature, the greater is the extent of inner ether formation during esterification of the hexitols. Esterification temperatures disclosed for reaction at atmospheric pressure range from 180°C (22) to 285°C [18], but preferred temperatures generally are from 225°C to 250°C (138-140). Acidic catalysts reported for hexitol esterification include concentrated sulfuric acid and phosphoric acid [5]. Esterification of hexitols, leading to anhydrohexitol surfactants, may be carried out with no added acidic material other than starting fatty acid. Alkaline catalysts such as sodium hydroxide may be use small proportions (e.g., 0.05 per cent) [19]; the actual catalyst in this case is the sodium salt of the fatty acid. Sodium acetate and lead oxide also are catalysts for hexitol esterification [18].
Figure 5. Anhydrazinization of D-sorbitol by transesterification (a) and internal eterification (b)

Figure 6. General structures of new tailor-made lipids

2. Materials and methods

**Materials. Reagents (selective list) (Sigma Aldrich, Merck):**

D-sorbitol (CAS 50-70-4); 1,4-sorbitan (CAS 27299-12-3); izosorbide (CAS 652-67-5)

**Equipments**

*Buchi TO-51 drying oven (complete).* Oven consists of two glass tubes mounted to a control base. Inner tube is coated with a transparent, electrically conductive heating layer that provides rapid, even heating without liquid heat transfer media. Provides direct viewing of material being dried. Thermocouple mounted on heating layer assures effective stabilization of preset working temperature. Temperature range 30 to 300°C±10°C (middle of oven). 260 x 140 x 220mm (without drying tube). Drying tube, 43mm i.d. x 210mm L, attaches to end cap with a vacuum tight flange. Ball joint on vacuum hose permits easy removal from drying tube.

*“CHEM-DRY” Integrated chemical dryers*

Dries samples using heat, vacuum and desiccant. Set drying temperature with calibrated dial thermometer
from ambient to 175°C. Built-in thermocouple automatically maintains selected temperature. Oven features a borosilicate glass sample viewing port and an integrated safety guard to prevent touching hot parts. Modular design permits the removal and storage of dried samples in sealed drying tubes. Process samples in rapid succession or service multiple users.


3. Results and discussion

Hygroscopic D-sorbitol absorbs neighboring humidity, which it retains (between 0.5-1 mole crystallization water per mole of polyol), changing its melting point to the 95-113°C range.

The six hydroxyl functional groups [two primary (positions 1 and 6) and 4 secondary (positions 2-5), respectively] display the reactivity specific to the function, but the mutual selectivity is limited, low. The directed attachment of higher acids and/or polyoxyethylenic chains with various degrees of oligomerization fails, in most cases resulting strictly directed a random, statistical distribution, a fact also confirmed by the general formulation preferred in the literature, $x + y + z + w = 20$ (Figure 3) [2].

The main scope of this work is represented by the knowledge of the operating parameters in the processing of 1,4 sorbitan (monoanhydride of D-sorbitol) and isosorbide (dianhydride of D-sorbitol) as potential alternatives of successive and/or simultaneous temporary blocking (protection) of the hydroxyl functional groups in D-sorbitol [19].

At the establishment of the working plan for the process of dehydration of D-sorbitol, its and its anhydrides’ (mono- and di-) main physico-chemical characteristics (Tables 1-3) were considered. From their comparative evaluation it results:

1. D-sorbitol in pure state being hygroscopic, it can crystallize with 0.5-1 mole water;
2. one of the major consequences of its hygroscopicity is the modification under improper storage conditions of its melting point towards the melting range (92°C →110-112°C);
3. the evolution of melting points in the series D-sorbitol → 1,4-sorbitan → isosorbide with a maximum at 112-113°C (1,4-sorbitan), suggests the interdependence among these values and the presence of hydrogen bonds in variable amount depending on the structure;
4. miscibility with water indicates their highly polar character

Azeotropic distillation which accesses one of the following solvents as entrainers: toluene (b.p. = 110°C), o-xylene (b.p. = 144,18°C), m-xylene (b.p. = 139,08°C) or p-xylene (b.p. = 138,35°C), is an experimental technique limited by these physical constants if the investigation of the dehydration efficiency at temperatures above these values is required.

Under the process conditions adopted, partial dehydration occurs energetically in solid phase (melt) at a constant rate within a short time period.

There are differences in the behavior at dehydration of (poly)glycols (polyols) which can be explain by the fact that in the ether ring tensions similar to those in cycloalkanes arise. The valence angle of oxygen in water (104°) is close to that of sp$^3$-hybridized carbon (109°28´). For this reason in furan (furanose) and pyran (pyranose) rings tensions should not be encountered. Consequently, cyclic ethers (including those of D-sorbitol) with five- (1,4;2,5-sorbitans) and six-membered rings (1,5;2,6-sorbitans or polygalitols) are lowly stable compounds which were not found in the processing mixture.

In this work, the continually increasing theoretical and applicative interest in the preparation of cyclic and/or acyclic ether (polyethers) of D-sorbitol is also due to the fact that it allows the classical directed successive (1;4), (3;6) or simultaneous protection, respectively, of the primary (positions 1 and 6) and secondary(positions 2-5), respectively, hydroxyl functional groups. In this context, monitoring the synthesis of polysorbates containing “homogeneous” polyoxyethylene chains ($n = 3, 6, 9, 18$) also becomes possible.

The dehydration was monitored through the evolution of the hydroxyl number, and the process yield by relating these values to the theoretical hydroxyl number of D-sorbitol and 1,4 sorbitan, respectively. From the comparative analysis of the experimental data (Figures 7, 8) it is observed that in the 100-160°C temperature range, for the same dehydration time, the number has a linear descending evolution (similar results were recorded in the absence of $\text{H}_2\text{SO}_4$ 2M).
A similar evolution was observed upon the modification of the dehydration time under isothermal conditions.

The experimental values recorded do not suggest the possibility of exhaustive evolution both through the hydroxyl number and the amount of water formed (dilution of the catalyst, sulfuric acid 2 molar). A practically identical slope for the linear regression equations is recorded over the entire temperature range tested, 100-160°C.

The processing yields calculated in relation to the theoretical hydroxyl number confirm reproducible values in the 92-97% range.

**Figure 7.** Time dependence of the hydroxyl number during the partial dehydration of D-sorbitol to 1,4-sorbitan at temperatures in the 100-160°C range, catalyst H₂SO₄ 2M.
Figure 8. Temperature dependence of the hydroxyl number during the partial dehydration of D-sorbitol to 1,4-sorbitan at time intervals of 5-35 minutes, catalyst H₂SO₄ 2M

Equation

<table>
<thead>
<tr>
<th>Linear</th>
<th>Polynomial</th>
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<tr>
<td>( y = -15.02x + 1823 )</td>
<td>( y = 2.35x^2 - 25.77x + 1835 )</td>
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<tr>
<td>( R^2 = 0.980 )</td>
<td>( R^2 = 0.999 )</td>
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<tr>
<td>( y = -15.48x + 1756 )</td>
<td>( y = 1.847x^2 - 24.66x + 1766 )</td>
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<tr>
<td>( R^2 = 0.988 )</td>
<td>( R^2 = 0.999 )</td>
</tr>
<tr>
<td>( y = -16.09x + 1689 )</td>
<td>( y = 2.182x^2 - 27.01x + 1700 )</td>
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<tr>
<td>( R^2 = 0.985 )</td>
<td>( R^2 = 1 )</td>
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<tr>
<td>( y = -14.28x + 1617 )</td>
<td>( y = 0.67x^2 - 17.38x + 1620 )</td>
</tr>
<tr>
<td>( R^2 = 0.953 )</td>
<td>( R^2 = 0.994 )</td>
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<tr>
<td>( y = -15.00x + 1551 )</td>
<td>( y = 2.14x^2 - 26.70x + 1562 )</td>
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<tr>
<td>( R^2 = 0.982 )</td>
<td>( R^2 = 0.997 )</td>
</tr>
<tr>
<td>( y = -17.3x + 1490 )</td>
<td>( y = 6.55x^2 - 50.16x + 1523 )</td>
</tr>
<tr>
<td>( R^2 = 0.886 )</td>
<td>( R^2 = 0.986 )</td>
</tr>
<tr>
<td>( y = -15.2x + 1411 )</td>
<td>( y = 1.56x^2 - 23.06x + 1419 )</td>
</tr>
<tr>
<td>( R^2 = 0.966 )</td>
<td>( R^2 = 0.975 )</td>
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<table>
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<th>Logarithmic</th>
<th>Exponential</th>
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<tr>
<td>( y = 32.5\ln(x) - 1811 )</td>
<td>( y = 1824e^{0.02x} )</td>
</tr>
<tr>
<td>( R^2 = 0.995 )</td>
<td>( R^2 = 0.981 )</td>
</tr>
<tr>
<td>( y = 33.1\ln(x) - 1744 )</td>
<td>( y = 1757e^{0.00a} )</td>
</tr>
<tr>
<td>( R^2 = 0.991 )</td>
<td>( R^2 = 0.999 )</td>
</tr>
<tr>
<td>( y = 24.7\ln(x) - 1677 )</td>
<td>( y = 1690e^{0.02x} )</td>
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<tr>
<td>( R^2 = 0.992 )</td>
<td>( R^2 = 0.986 )</td>
</tr>
<tr>
<td>( y = 30.4\ln(x) - 1606 )</td>
<td>( y = 1617e^{0.00a} )</td>
</tr>
<tr>
<td>( R^2 = 0.946 )</td>
<td>( R^2 = 0.953 )</td>
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<tr>
<td>( y = 24.3\ln(x) - 1538 )</td>
<td>( y = 1551e^{0.01a} )</td>
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<td>( R^2 = 0.985 )</td>
<td>( R^2 = 0.983 )</td>
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<td>( y = 39.2\ln(x) - 1477 )</td>
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<td>( R^2 = 0.977 )</td>
<td>( R^2 = 0.989 )</td>
</tr>
<tr>
<td>( y = 22.8\ln(x) - 1399 )</td>
<td>( y = 1412e^{0.01a} )</td>
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<tr>
<td>( R^2 = 0.974 )</td>
<td>( R^2 = 0.988 )</td>
</tr>
</tbody>
</table>

Figure 9. Time dependence of the yield of partial dehydration of D-sorbitol to 1,4-sorbitan at temperatures in the 100-160°C range, catalyst H₂SO₄ 2M

Equation

<table>
<thead>
<tr>
<th>Linear</th>
<th>Polynomial</th>
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<tbody>
<tr>
<td>( y = 3.674x + 72.37 )</td>
<td>( y = 0.005x^2 + 3.718x + 72.31 )</td>
</tr>
<tr>
<td>( R^2 = 0.999 )</td>
<td>( R^2 = 0.999 )</td>
</tr>
<tr>
<td>( y = 3.75x + 70.85 )</td>
<td>( y = -0.013x^2 - 3.854x - 70.69 )</td>
</tr>
<tr>
<td>( R^2 = 0.999 )</td>
<td>( R^2 = 0.999 )</td>
</tr>
<tr>
<td>( y = 3.69x + 70.37 )</td>
<td>( y = 0.006x^2 - 3.746x - 70.29 )</td>
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<tr>
<td>( R^2 = 0.999 )</td>
<td>( R^2 = 0.999 )</td>
</tr>
<tr>
<td>( y = 3.72x + 69.6 )</td>
<td>( y = 0.003x^2 + 3.749x + 69.55 )</td>
</tr>
<tr>
<td>( R^2 = 0.999 )</td>
<td>( R^2 = 0.999 )</td>
</tr>
</tbody>
</table>
Figure 9. Time dependence of the yield of partial dehydration of D-sorbitol to 1,4-sorbitan at temperatures in the 100-160°C range, catalyst H$_2$SO$_4$ 2M

Mathematical modeling of the partial dehydration leads to dependences with very good correlation coefficients (Figures 7, 8).

Mathematical modeling of the process confirms an evolution similar to the variant of partial dehydration, with optimal regression coefficients for the linear and parabolic equations.

From the comparative evaluation of the time and temperature dependences of partial dehydration yields (Figures 9, 10), in the first case a continuously increasing ascendant evolution up to quantitative values is observed, while in the second case the values are slightly descendant.
This fact would be unexplainable were it not for the fact that in the ratio, the practical (experimental) hydroxyl number decreases and the theoretical remains constant (the value of the fraction decreases).
In the variant of exhaustive dehydration of D-sorbitol to isosorbide, unfolding in the time range 10-100 minute and temperature range 120-200°C, the evolution of the process is similar and the yields computed by relating to the theoretical hydroxyl number were dependent on the operating parameters (Figures 11, 12).

During the course of the intramolecular dehydration process, the B value decreases continuously and C increases, therefore the C/A ratio follows the same ascendant evolution (Figures 13, 14).

If we use A to indicate the theoretical hydroxyl number of the initial structure, B for the experimental hydroxyl number, and C for the difference (A-B), then the ratio C/Ax100 has the meaning of an intramolecular dehydration yield.

Figure 13. Time dependence of the yield of exhaustive dehydration of D-sorbitol to isosorbide at temperatures in the 120-200°C range, catalyst H₂SO₄ 2M

Figure 14. Temperature dependence of the yield of exhaustive dehydration of D-sorbitol to isosorbide at time intervals of 10-100 minutes, catalyst H₂SO₄ 2M
4. Conclusion

Partial and/or exhaustive dehydration of D-sorbitol allows the formation of 1,4-sorbitan and isosorbide, respectively, under mild, controlled conditions. The cyclic intramolecular ethers formed are thermally stable and can later accessed as technological alternatives for chemical protection in the selective, directed attachment of “homogeneous” hydrocarbon and polyoxyethylenic chains in the structuring of “homogeneous” polysorbates.

Acknowledgement

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Compliance with Ethics Requirements

Authors declare that they respect the journal’s ethics requirements. Authors declare that they have no conflict of interest and all procedures involving human and/or animal subjects (if exists) respect the specific regulations and standards.

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