Combined Action of Enzyme and Metal Catalyst, applied to the Preparation of D-Mannitol

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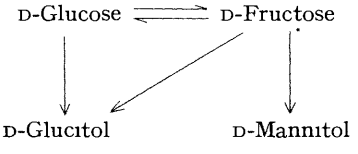
Summary A novel catalytic approach involving co-operation of a bio- and a chemo-catalyst has been applied in the simultaneous enzymatic interconversion and platinum metal-catalysed hydrogenation of D-fructose–D-glucose mixtures (water, pH 7—8, 60 °C, 20 atm hydrogen), this gives an enhanced yield of D-mannitol

SIMULTANEOUS action of a bio- and a chemo-catalyst is an attractive possibility for several catalytic processes in solution For example, one might think of a specific enzymatic conversion of the starting material into some intermediate compound that is concomitantly transformed by the chemo-catalyst into the final product Some problems to be faced with such a combined catalytic system are the narrow condition range of the enzyme, the preferential conversion of the intermediate compound by the chemo-catalyst, and the possible mutual poisoning of the two different catalysts

As the first example of this approach we report here the combined use of glucose isomerase and platinum in the preparation of the sugar substitute D-mannitol from D-glucose–D-fructose mixtures (*e g* invert sugar or iso-glucose) At present, D-mannitol is commercially obtained in yields of less than 25% by the catalytic hydrogenation of invert sugar (1 : 1 D-glucose–D-fructose) The combination of either base[1]- or molybdic acid[2]-catalysed isomerization of D-glucose and invert sugar with catalytic hydrogenation and isomerization of D-glucitol[3] have been proposed as possible alternative procedures

The present approach uses a dual heterogeneous catalytic system consisting of immobilized glucose isomerase and supported platinum This combined one-pot approach is based on the enzymatic interconversion of the starting components D-glucose and D-fructose with concomitant and preferential hydrogenation of the latter (Scheme)



SCHEME

Optimal D-mannitol formation in such a procedure requires (i) preferential hydrogenation of D-fructose with respect to D-glucose, (ii) selectivity towards D-mannitol for the D-fructose hydrogenation, (iii) relatively fast D-glucose ⇌ D-fructose interconversion in order to maintain the D-fructose concentration at a maximum, (iv) minimum interference of the two catalytic species, including their different demands for sufficient activity Preliminary experiments have shown that these requirements may indeed be fulfilled to a large extent by an appropriate choice of the metal catalyst and the reaction conditions Firstly, it was found that platinum is a suitable catalyst metal for the required selective hydrogenation of D-fructose in the presence of D-glucose The D-mannitol/D-glucitol ratio obtained upon hydrogenation of D-fructose was slightly higher than 1 Secondly, glucose isomerase proved to be sufficiently active under applicable hydrogenation conditions if small amounts of both $MgSO_4$ and $CaCO_3$ were present to stabilize the enzyme and to maintain

the correct pH, respectively. The Table shows an example with 5% Pt/C and glucose isomerase (immobilized in gelatin cross-linked by glutaraldehyde[4]) as the catalysts. The observed simultaneous 1:1 production of D-mannitol and D-glucitol clearly shows that the major part of D-glucose has been converted *via* D-fructose by the enzymatic isomerization reaction.

TABLE. Composition (mol %) of the reaction mixture as a function of time for the simultaneous isomerization and hydrogenation of a 1:1 D-glucose/D-fructose mixture.[a]

Reaction time/h	0	22	70	146	264	335
D-Glucose	50	42	33	17	9	5
D-Fructose	50	41	26	12	6	3
D-Glucitol	0	9	21	36	43	46
D-Mannitol	0	8	20	35	42	46

[a] 60 g in water (250 ml) in the presence of 5% Pt/C (5 g), immobilized glucose isomerase (from Gist-Brocades, Delft; 10 g, containing 70% water), $MgSO_4$ (0·4 g), $CaCO_3$ (0·5 g) at 60 °C and 20 atm hydrogen.

So far, platinum and ruthenium have proved to be the best metal catalysts, the latter being more deactivated by the enzyme. On the other hand, Raney nickel strongly deactivated the enzyme, whereas supported nickel, rhodium, palladium, osmium, and iridium catalysts were of insufficient activity.

It may be noted that the possible non-enzymatic isomerization and, in particular, degradation reactions were found to be negligible under the reaction conditions used. This is a great improvement over other approaches reported in the literature.[1–3] Obviously, the present method is also applicable to D-glucose as a starting material for which partial pre-isomerization by glucose isomerase followed by the dual catalytic procedure outlined above seems preferable for an optimal D-mannitol yield.

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