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Hydrogenation and transfer hydrogenation of D-fructose catalyzed by dichlorotris(triphenylphosphine)ruthenium(II)

S. Rajagopal*

Department of Chemistry, University of Louisville, Louisville, KY 40292 (USA); tel. (+1-502)5886798, fax. (+1-502)5888149.

S. Vancheesan, J. Rajaram and J.C. Kuriacose

Department of Chemistry, Indian Institute of Technology, Madras 600036 (India)

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Abstract

D-Fructose is hydrogenated to D-glucitol and D-mannitol using $RuCl_2(PPh_3)_3$ as catalyst at 100°C and atmospheric pressure. Besides hydrogenation, fructose undergoes transfer hydrogenation when propan-2-ol and butan-2-ol are used as solvents. Under an inert atmosphere (nitrogen), only transfer hydrogenation of fructose is observed in these alcohols. The rate of hydrogenation is comparable with transfer hydrogenation under similar reaction conditions. Cyclohexanol, benzyl alcohol, 1-phenylethanol and benzhydrol are also found to be good hydrogen donors for fructose reduction. Both hydrogenation and transfer hydrogenation yield glucitol and mannitol whose ratio is always 1:1. The catalyst is deactivated when hydrogen donors such as 2-methoxyethanol and tetrahydrofurfuryl alcohol are employed. The deactivation is attributed to the formation of an inactive ruthenium carbonyl complex, *viz.*, $RuHCl(CO)(PPh_3)_3$. The hydrogen donating ability of these alcohols and their oxidation potentials are compared and the relative degrees of correlation are rationalized.

Key words: fructose; hydrogenation; phosphine ligands; ruthenium; transfer hydrogenation

Introduction

Only a few reports on the homogeneous hydrogenation of monosaccharides catalyzed by transition metal complexes have been published [1–4], although literature on heterogeneously catalyzed hydrogenation of monosaccharides is exhaustive [5,6]. The first example of homogeneous hydrogenation of monosaccharides was patented by Kruse [1] who made use of $RuCl_2(PPh_3)_3$ as catalyst at 110°C and 1750 psi of hydrogen. Using $RuCl_2(PPh_3)_3$, we had reported [2,7,8] hydrogenation and transfer hydrogenation of glucose under mild conditions such as 100°C and atmospheric pressure. Kruse and Wright

*Corresponding author.

[3] have disclosed their findings related to hydrogenation of glucose and fructose in amide solvents at 50 psig and 80°C using $RuHCl(PPh_3)_3$ as catalyst. Recently, Bayer *et al.* [4] have used a Ru CM-cellulose complex for the hydrogenation of glucose and fructose. In this system, glucitol was produced at the expense of mannitol.

Transfer hydrogenation of fructose catalyzed by transition metal complexes has not been reported in the literature. Nevertheless, some investigators have published results on transfer hydrogenation of fructose influenced by heterogeneous catalysts. The hydrogen donors and heterogeneous catalysts employed were: (i) cyclohexanol/Raney nickel [9], (ii) ethanol/Raney nickel [10], (iii) ethanol/zinc–nickel couple [11], and (iv) glucose/platinum or rhodium [12,13]. The products of the reaction were invariably a mixture of glucitol and mannitol except for the ethanol/zinc–nickel couple where only mannitol was observed. In the presence of glucose as hydrogen donor [12] fructose showed modest stereoselectivity, *i.e.*, the reduction products (mannitol and glucitol) were formed in 1.5–1.9:1 ratio.

In this article, the results of the hydrogenation of fructose under mild conditions, and hitherto unreported transfer hydrogenation of fructose by various hydrogen donors mediated by $RuCl_2(PPh_3)_3$ are presented.

Experimental

D-Fructose (Centron Research Laboratories), glucitol (Koch–Light), mannitol (BDH), $RuCl_3 \cdot xH_2O$ (Johnson Matthey Chemicals), triphenylphosphine (Ventron Corporation) and benzhydrol (Koch–Light) were used as received. All solvents and hydrogen donors except 1-phenylethanol (Fluka) and dimethylacetamide (Koch–Light) were obtained from BDH (AnalaR grade). All the liquid samples were purified by standard procedures [14] and stored under nitrogen. Ultra high pure hydrogen and nitrogen were used for hydrogenation and transfer hydrogenation reactions. The catalyst, $RuCl_2(PPh_3)_3$, was prepared by the method of Stephenson and Wilkinson [15]. $RuHCl(CO)(PPh_3)_3$ was synthesized by published procedures [16].

The experimental set-up consists of a specially designed double-walled glass vessel of 75 cm^3 capacity provided with a mechanical stirrer, a gas inlet, a double surface condenser, a thermometer-well and a manostat. Fructose, deaerated hydrogen donor and solvents were placed in the inner portion of the vessel and heated to 100°C by the vapors of butan-2-ol. The catalyst was then added to the solution under hydrogen or nitrogen atmosphere. A small positive pressure of hydrogen or nitrogen (flow rate = 5 cm^3/min) was always maintained above the reaction medium to avoid exposure to oxygen. The estimation of unreacted fructose was achieved using Fehling's solution [17]. Interference due to glucitol, mannitol, hydrogen donors, dehydrogenated products and catalysts were verified and found to be negligible. Fructose and its reduction prod-

ucts, namely, glucitol and mannitol were separated and detected on silica gel-G plates (TLC) using methyl acetate + pyridine + water (20:6:1) as eluent and ammoniacal $AgNO_3$ as detecting agent. A gas chromatograph (Varian model 1800) equipped with thermal conductivity detector (TCD) and a column (20% Carbowax 20M on Chromosorb P) was used to separate alcohols and their dehydrogenated products. Glucitol and mannitol were isolated from the reaction mixture, first removing the catalyst by heating several times with activated charcoal and water, followed by filtration; the filtrate was then evaporated and the syrup containing both glucitol and mannitol were separated by fractional crystallization in methanol. They were further characterized using IR spectroscopy (Perkin–Elmer IR spectrophotometer 257).

Results and discussion

Finding a suitable solvent for both fructose and transition metal complexes such as $RuCl_2(PPh_3)_3$ is difficult. Thus, mixed solvent systems have been used to solubilize both the substrate and the catalyst. Fructose dissolves freely in water whereas the catalyst requires an organic solvent with or without some coordinating character. Therefore, the chosen solvent system has a mixture of three solvents: one for the fructose, another for the catalyst and the third one to homogenize both. For example, a toluene + dioxane + water system is utilized for hydrogenation reactions. Compounds such as dimethylformamide (DMF) and dimethylacetamide (DMA) are also found to be good solvents for the catalyst. Among these two, DMA gave encouraging results in terms of fructose conversion, therefore it has been extensively used. Because a large concentration of a coordinating solvent such as DMF or DMA is detrimental to the rate of reaction, its concentration in the reaction medium is restricted. This is compensated by adding a non-coordinating and water soluble solvent such as dioxane or aliphatic alcohols to the reaction system. In the aliphatic alcohol category, 2-methoxyethanol and tetrahydrofurfuryl alcohol are included as they have an additional advantage of dissolving monosaccharides. The β-alkoxyalcohol group (ROCCOH) present in these two alcohols is responsible for the solubility of sugars.

Hydrogenation of D-*fructose*

The percent conversions of D-fructose to glucitol and mannitol at 100°C and atmospheric pressure in three solvent systems, *viz.*, toluene + dioxane + water, DMA + water, and DMA + dioxane + water are 60, 30 and 50 respectively (Table 1). It is beyond doubt that DMA is an excellent solvent for the catalyst, but its adverse effect on the activity is clearly visible from these conversion results, *i.e.*, on comparing entries 1 with 3, and 2 with 3. Mixed solvent systems of the type, DMA + alcohol + water where alcohol is propan-2-ol, bu-

TABLE 1

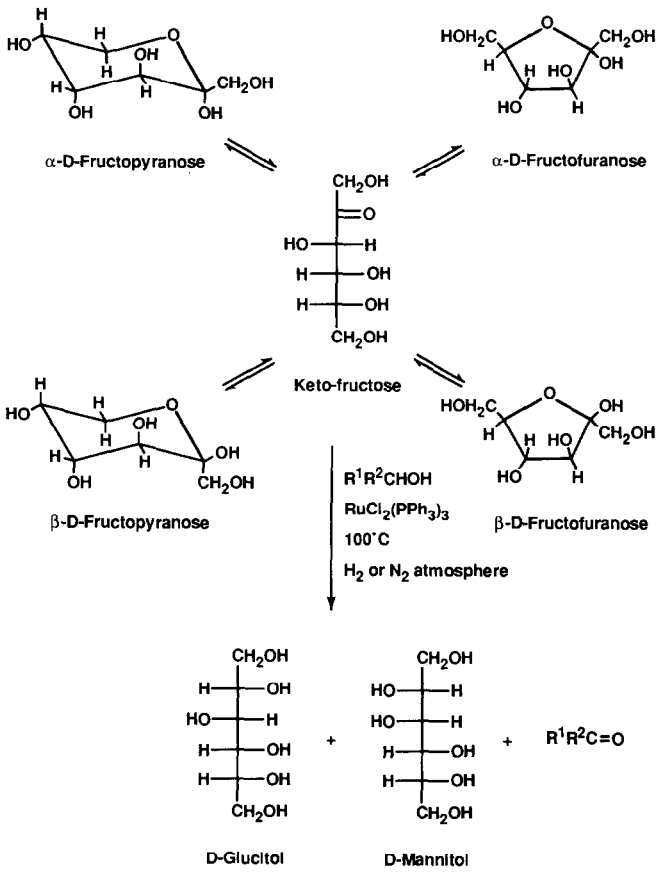
Homogeneous hydrogenation of fructose at atmospheric pressure[a]

Entry	Solvent system	Conversion, %[b]
1	toluene + dioxane + water (2:20:3)[c]	60
2	DMA + water (22:3)	30
3	DMA + dioxane + water (4:18:3)	50
4	DMA + propan-2-ol + water (4:18:3)	100[d]
5	DMA + butan-2-ol + water (4:18:3)	100[e]
6	DMA + 2methoxyethanol + water (4:18:3)	92
7	DMA + tetrahydrofurfuryl alcohol + water (4:18:3)	93

[a][Fructose]: 0.2 M; $[RuCl_2(PPh_3)_3]$: 3.34×10^{-3} M; [fructose]/$[RuCl_2(PPh_3)_3]$: 60; temp: 100 °C; H_2 pressure: ≈ 18 psia; time: 10 h.
[b]The conversions are reproducible within a 5% range. Glucitol and mannitol are the only products.
[c]Volume in ml in parentheses.
[d]Reaction complete in 7 h.
[e]Reaction complete in 6 h.

tan-2-ol, 2-methoxyethanol or tetrahydrofurfuryl alcohol were also tested for the hydrogenation reaction. These solvent systems are far superior to the above three non-alcoholic solvent mixtures (see Table 1 for conversions). In the case of propan-2-ol and butan-2-ol, fructose underwent transfer hydrogenation reaction in addition to the expected hydrogenation (Scheme 1). The evidence comes from the following observations: (i) the rate of transfer hydrogenation is comparable with that of hydrogenation, for example, in DMA + butan-2-ol + water system (4:18:3 by volume), fructose is completely converted to glucitol and mannitol in 6 and 9 h under hydrogen and nitrogen atmospheres respectively, and (ii) the dehydrogenated products of the hydrogen donors (acetone and butan-2-one) are also formed under hydrogenation conditions. These ketones were identified by gas chromatography but quantitative estimation was not attempted. In 2-methoxyethanol and tetrahydrofurfuryl alcohol, the formation of glucitol and mannitol is exclusively due to hydrogenation by molecular hydrogen. This was substantiated by carrying out separate experiments employing these alcohols under nitrogen atmosphere which yielded negligible amounts of the corresponding polyols and traces of side products. The total conversion of fructose in these alcohols is less than 5%.

The following mechanism has been proposed for the hydrogenation of D-fructose. It has been well established [18] that $RuCl_2(PPh_3)_3$, on dissolving in a solvent, dissociates into $RuCl_2(PPh_3)_2$ and PPh_3 (eqn. (1)). The resultant solvated ruthenium complex activates molecular hydrogen to yield a hydridochloro complex (eqn. (2)), which in turn transfers hydrogen to the coordinated fructose (eqn. (4); generally a rate-limiting step), leading to the formation of polyols. The active complex is then regenerated and the catalytic cycle continues. Since both glucitol and mannitol are formed in equal ratios,



Scheme 1. Hydrogenation and transfer hydrogenation of fructose.

the attack of hydride on the carbonyl carbon is considered nonstereospecific in the present case.

$$RuCl_2(PPh_3)_3 + xS \rightleftharpoons RuCl_2(PPh_3)_2(S)_x + PPh_3 \quad (1)$$

$$RuCl_2(PPh_3)_2(S)_x + H_2 \rightleftharpoons RuHCl(PPh_3)_2(S)_x + HCl \quad (2)$$

$$RuHCl(PPh_3)_2(S)_x + >C{=}O \rightleftharpoons RuHCl(PPh_3)_2(>CO)(S)_x \quad (3)$$

$$RuHCl(PPh_3)_2(>C{=}O)(S)_x \rightarrow RuCl(PPh_3)_2(>CHO)(S)_x \quad (4)$$

$$RuCl(PPh_3)_2(>CHO)(S)_x + HCl \rightarrow RuCl_2(PPh_3)_2(>CHOH)(S)_x \quad (5)$$

$$RuCl_2(PPh_3)_2(>CHOH)(S)_x \rightarrow RuCl_2(PPh_3)_2(S)_x + >CHOH \quad (6)$$

where S = solvent; $x = 1$ or 2 depending on the stage in the catalytic cycle; $>C{=}O$ = fructose; $>CHOH$ = glucitol and mannitol.

Transfer hydrogenation of D-*fructose*

Fructose is transfer hydrogenated by various carbinols under the catalytic influence of $RuCl_2(PPh_3)_3$ at 100°C and atmospheric pressure. The products are the same as in hydrogenation, *viz.*, glucitol and mannitol which are formed in equal proportions. Hydrogen donors such as propan-2-ol, butan-2-ol, cyclohexanol, benzyl alcohol, 1-phenylethanol and benzhydrol have shown promising results. The other hydrogen donors that were tested but proved ineffective under the same reaction conditions were dioxane, 2-methoxyethanol and tetrahydrofurfuryl alcohol. The poor donating ability of dioxane may be attributable to the absence of very active hydrogens in this compound; in other words, they (hydrogens) are not labile enough to be abstracted by the catalyst at the temperature used. The inability of the latter two alcohols to act as hydrogen donors is ascribed to catalyst deactivation through the abstraction of CO from the initially formed aldehydes yielding an inactive transfer hydrogenation catalyst, $RuHCl(CO)(PPh_3)_3$. After the reaction, the catalyst was isolated from the reaction mixture and identified using IR spectroscopy ($\nu_{RuH}=2040$ cm^{-1} and $\nu_{CO}=1940$ cm^{-1}; literature values [16] are 2010 and 1920 cm^{-1} respectively). Fig. 1 shows the IR spectra of the catalyst isolated from the reaction product and an authentic sample of $RuHCl(CO)(PPh_3)_3$. The observed shift in frequencies to higher values could be due to the electronic influence of the additional ligand (dehydrogenated product of the alcohols) in the isolated sample. In contrast to the above observation, 2-methoxyethanol and tetrahydrofurfuryl alcohol, when used as solvents for hydrogenation re-

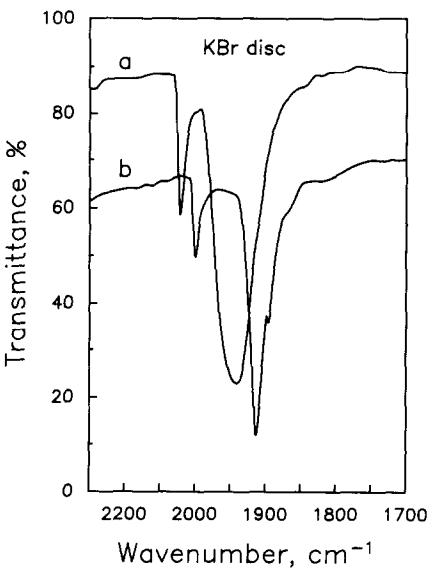


Fig. 1. IR spectra of (a) the catalyst isolated from the product mixture when 2-methoxyethanol was used as hydrogen donor, and (b) an authentic sample of $RuHCl(CO)(PPh_3)_3$.

action, did not deactivate the catalyst. The reason could be that under hydrogenation conditions, the rate of transfer hydrogenation by these alcohols is much lower than hydrogenation and therefore not high enough concentrations of dehydrogenated products of these alcohols (aldehydes) are formed to carbonylate the catalyst.

A mixed solvent system of the type, toluene + secondary alcohol + water (2:22:3) has also been tested for transfer hydrogenation but it has posed a problem of catalyst deposition, especially in the case of lower alcohols such as propan-2-ol and butan-2-ol. In DMF + secondary alcohol + water system, the transfer hydrogenation reaction is not facile. This is attributed to the inability of keto-fructose to displace coordinated DMF for the reaction to proceed. But fructose underwent a smooth reduction when DMA replaced DMF. The fructose conversions in DMA + propan-2-ol + dioxane + water and DMA + butan-2-ol + dioxane + water systems are 85 and 90% respectively (Table 2). With the other four hydrogen donors, *viz.*, cyclohexanol, benzyl alcohol, 1-phenylethanol and benzhydrol, the fructose conversions are in the range 62–81%. The dehydrogenated products of the hydrogen donors *viz.*, acetone, butan-2-one, benzaldehyde, cyclohexanone and acetophenone were identified by gas chromatography, and benzophenone by thin-layer chromatography. Deactivation of the catalyst is not a serious problem when the solvent system is composed of DMA + secondary alcohol + dioxane + water. This is indicated by the red color of the solution that remained throughout the reaction period. Even in benzyl alcohol, the catalyst was stable. Under the present experimental conditions, benzaldehyde seems to be a less effective carbonylating agent when compared to methoxyacetaldehyde or tetrahydrofurfural, which are aliphatic in nature. In other words, the reason for the stability of $RuCl_2(PPh_3)_3$ in the presence of benzaldehyde could be that CO is stabilized by the benzene ring. Also, deactivation of the catalyst by fructose *via* carbonylation is absent. In this context, it is reminded that stoichiometric carbonylation of $RhCl(PPh_3)_3$ to $RhCl(CO)(PPh_3)_2$ by fructose at 130°C in *N*-methyl-2-pyrrolidinone is

TABLE 2

Transfer hydrogenation of fructose by various alcohols[a]

Entry	Hydrogen donor[b]	Solvent system	Conversion, %[c]
1	propan-2-ol (10)	DMA + dioxane + water (4:8:3)	85
2	butan-2-ol (10)	DMA + dioxane + water (4:8:3)	90
3	cyclohexanol (10)	DMA + dioxane + water (4:8:3)	73
4	benzyl alcohol (10)	DMA + dioxane + water (4:8:3)	70
5	1-phenylethanol (10)	DMA + dioxane + water (4:8:3)	81
6	benzhydrol (10)	DMA + dioxane + water (4:18:3)	62

[a] [Fructose]: 0.2 M; $[RuCl_2(PPh_3)_3]$: 3.34×10^{-3} M; [fructose]/$[RuCl_2(PPh_3)_3]$: 60; temp: 100°C; N_2 pressure: ≈ 18 psia; time: 10 h.

[b] Volume in ml in parentheses except benzhydrol where it is the amount in g.

[c] The conversions are reproducible within a 5% range. Glucitol and mannitol are the only products.

possible [19,20]. In this example, fructose is transformed to furfuryl alcohol and a small amount of 1-deoxyerythritol.

The proposed mechanism of transfer hydrogenation is not far different from the hydrogenation process. The only major difference appears to be the way the metal hydride is formed. In hydrogenation, hydride formation is a straightforward step, while in transfer hydrogenation, the hydride is formed *via* abstraction of α-hydrogen from the alkoxide by the central metal atom. (eqn. (8)). This process is usually a slow step in the overall mechanism.

$$RuCl_2(PPh_3)_2(S)_x + R^1R^2CHOH \rightarrow RuCl(PPh_3)_2(R^1R^2CHO)(S)_x + HCl \quad (7)$$

$$RuCl(PPh_3)_2(R^1R^2CHO)(S)_x \rightarrow RuHCl(PPh_3)_2(R^1R^2CO)(S)_x \quad (8)$$

where R^1R^2CHOH = hydrogen donor

From the conversion results, an attempt was made to compare the hydrogen donating ability of these alcohols with their oxidation potentials. It is known that the lower the oxidation potential of the corresponding dehydrogenated product, the better the hydrogen donating power of the parent alcohol. According to the literature [21], the oxidation potentials of the corresponding carbonyl compounds follow the order: benzaldehyde > cyclohexanone > benzophenone = acetone > butanone > acetophenone (E_0 = 197, 162, 129, 129, 123, and 118 mV). As seen from Fig. 2, the fructose conversion and oxidation po-

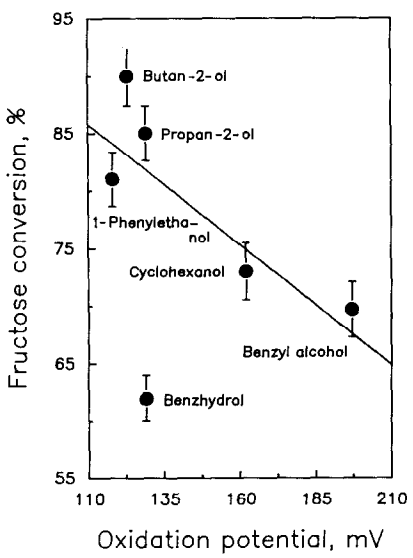


Fig. 2. Correlation of oxidation potentials of the dehydrogenated products of hydrogen donors with fructose conversion.

tentials of the donors follow a trend with one notable exception, namely benzhydrol. Steric hindrance seems to be an overriding factor in deciding the hydrogen donating efficiency of this alcohol. This reasoning is justified since the approach of benzhydrol towards the central metal atom having bulky ligands such as triphenylphosphine may be restricted. In the lower alcohols (propan-2-ol and butan-2-ol), a slight deviation in conversion towards the higher side can also be noticed. Here, partial evaporation of the corresponding dehydrogenated products (acetone and butanone) has contributed to the shift in equilibrium to the right causing more fructose conversion than expected.

In both hydrogenation and transfer hydrogenation experiments, the selectivity towards hexitols is almost 100%, unlike in the case of glucose where disproportionation is the side reaction leading to the formation of glucitol and glucono-1,5-lactone. Such a redox reaction is favored in glucose because α- and β-*D*-glucopyranoses serve as good hydrogen donors [2]. In fructose, there are no such anomeric secondary hydroxyl groups in any of the four cyclic forms, namely, α- and β-D-fructopyranoses and α- and β-D-fructofuranoses (Scheme 1). This may be the principal reason for the absence of redox reaction in the case of fructose.

Conclusions

Fructose was hydrogenated at ambient conditions in the presence of a homogeneous catalyst, $RuCl_2(PPh_3)_3$. When hydrogen donors were present as one of the solvents, transfer hydrogenation of fructose was observed in addition to hydrogenation. Without molecular hydrogen, only transfer hydrogenation by various carbinols was noted. Propan-2-ol, butan-2-ol, cyclohexanol, benzyl alcohol, 1-phenylethanol, and benzhydrol have proven to be good hydrogen donors for fructose. The efficiency of these hydrogen donors and the oxidation potentials of their corresponding dehydrogenated products have been correlated.

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