Transformation of Glucose to 5-Hydroxymethyl-2-furfural by SiO_2–$MgCl_2$ Composite

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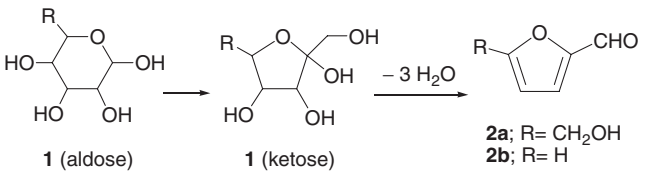
5-Hydroxymethyl-2-furfural (**2a**) was formed in a 70% yield by dehydration of glucose in MeCN at 140 °C in an autoclave using a composite of $MgCl_2$ with silica gel which served as an acid catalyst under dry conditions. 10% and 32% yields of **2a** were obtained from mannose and galactose, respectively.

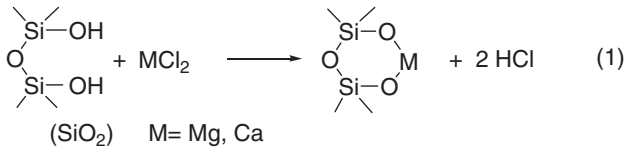
Chemical transformation of biomass to organic chemicals has been receiving much attention from the standpoint of organic synthesis using a renewable carbon source.[1] Saccharides **1** are C5 and C6 carbon sources available from biomass. Especially glucose (**1a**) is an abundant monosaccharide obtained by the saccharification of cellulose and starch. A typical transformation of **1** is the transformation from hexose and pentose to 5-hydroxymethyl-2-furfural (**2a**) and 2-furfural (**2b**) which are versatile compounds for the transformation to a variety of chemicals (Scheme 1). The formation of **2** from aldose proceeded via aldose–ketose (A–K) isomerization of **1** and the successive dehydration in the presence of acid catalysts.[2] Instead of mineral acid such as the H_2SO_4, H_3PO_4, or HI used in earlier studies,[3–5] a variety of heterogeneous catalysts involving solid acid (H-form zeolite,[6] ion-exchange resins,[7] and metal oxide[8]) and protic ionic liquids[9] have been used in the transformation of **1** to **2** for convenience of separation and recycling.

Recently we have studied the application of a composite (**3**; SiO_2–MCl_2) of MCl_2 (M = Mg and Ca) with silica gel which can generate protons under dry conditions (eq 1 in Scheme 2).[10] In the presence of H_2O, **3a** (M = Mg) readily turned neutral without the addition of other alkali (eq 2). We

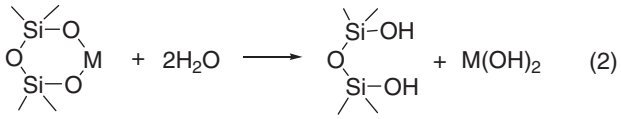


Scheme 1.

Under dry conditions



In the presence of H_2O



Scheme 2.

have applied the water-dependant pH-change to develop an SiO_2–$MgCl_2$–porphyrin composite acting as humidity indicators of desiccants.[11] Under dry conditions the protonated porphyrin was formed and turned to free base porphyrins under wet conditions, resulting in the color change from green to pink-orange. The acidity (pK_a) of **3a** was estimated to be 1.7 under dry conditions.[12] Thus, it was found that the pH of **3** can be controlled by the presence of water. If **3** can catalyze the dehydration of **1**, it will provide an environmentally conscious process without requiring strong acid and alkali.

SiO_2 (1.0 g; 40 μmϕ; Fuji Silysia BW 300) was added to a MeOH solution (40 cm^3) of $MgCl_2 \cdot 6H_2O$ (68–806 mg). After standing for 3 h at room temperature, the solvent was evaporated and dried under reduced pressure at 50 °C for 24 h to give **3a** where the content of $MgCl_2$ was 3–38 wt %/SiO_2. Also the SiO_2–$CaCl_2$ composite **3b** with 12–31 wt %/SiO_2 content of $CaCl_2$ was prepared.

1a was soluble in highly polar solvents such as dimethyl sulfoxide (DMSO) and *N*,*N*-dimethylformamide but the separation of **2a** from these solvents was troublesome in the follow-up procedure.[13] Also toluene where **1a** was insoluble was poor solvent for the formation of **2a**. Therefore, **1a** (0.5 g) and SiO_2 (1.0 g)–MCl_2 **3** were suspended in MeCN (40 cm^3) where **1a** was slightly soluble and then heated under stirring in an autoclave at various temperatures. After the reaction, **3** was separated from the reactants by filtration and then the solvent was evaporated to give crude **2a**. The **2a** was purified by column chromatography. The yields are summarized in Table 1. The yield of **2a** was plotted against the content of MCl_2 in **3** (Figure 1). The optimized content of $MgCl_2$ was 32 wt %/SiO_2. The reaction of **1a** using SiO_2 without the MCl_2 did not provide **2a** at all (Run 5). Moreover, the SiO_2–$CaCl_2$ composite **3b** was ineffective for the formation of **2a** (Run 6). Here, the formed H_2O was removed from the solvent by adsorption with SiO_2 to maintain the acidic condition of **3**. The maximum yield of **2a** from **1a** was 70% which was obtained from the reaction at 140 °C for 24 h using **3a** with 32 wt %/SiO_2 of the content of $MgCl_2$ (Run 2 in Table 1). This exceeded the maximum yields (53%[2] and 58%[14]) reported for the heterogeneous catalytic formation of **2a** from **1a** so far. In homogeneous catalytic reaction, 90% yield was reported for formation of **2a** from **1a** using $CrCl_3$ in ionic liquid under microwave irradiation.[15]

Time-conversion plots for the transformation from **1a** to **2a** are shown in Figure 2. The yield of **2a** reached its maximum at

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Table 1. Formation of Furfural Derivatives **2** from Saccharides **1** Using SiO_2–MCl_2 Composite **3**[a)]

Run	**1**	**3** (MCl_2/wt %)[b)]	Temp/°C[c)]	**2** (Yield/%)
1	**1a**	SiO_2–$MgCl_2$ (32)	160	**2a** (72)
2	**1a**	SiO_2–$MgCl_2$ (32)	140	**2a** (70)
3	**1a**	SiO_2–$MgCl_2$ (32)	120	**2a** (1)
4	**1a**	SiO_2–$MgCl_2$ (32)	100	**2a** (0)
5	**1a**	SiO_2	140	**2a** (0)
6	**1a**	SiO_2–$CaCl_2$ (25)	140	**2a** (19)
7	**1b**	SiO_2–$MgCl_2$ (32)	140	**2a** (10) [9][d)]
8	**1c**	SiO_2–$MgCl_2$ (32)	140	**2a** (32) [11][d)]
9	**1d**	SiO_2–$MgCl_2$ (32)	140	**2a** (82)
10	**1e**	SiO_2–$MgCl_2$ (32)	140	**2a** (32)
11	**1f**	SiO_2–$MgCl_2$ (32)	140	**2a** (10)
12	**1g**	SiO_2–$MgCl_2$ (32)	140	**2a** (31)
13	**1h**	SiO_2–$MgCl_2$ (23)	180	**2b** (17)[e)]

a) Reaction was performed for MeCN (40 cm^3) containing **1** (0.5 g) and SiO_2 (1.0 g)–MCl_2 **3** at a given temperature for 24 h in autoclave. b) The values in parenthesis were the content of MCl_2 (wt %) in SiO_2. c) Reaction temperature. d) In MeCN–DMSO (9:1, 40 cm^3) at 140 °C for 24 h. e) Reaction was performed for MeCN (40 cm^3) containing **1** (2.5 g) and SiO_2 (1.0 g)–$MgCl_2$ (0.23 g) at 180 °C for 1.5 h.

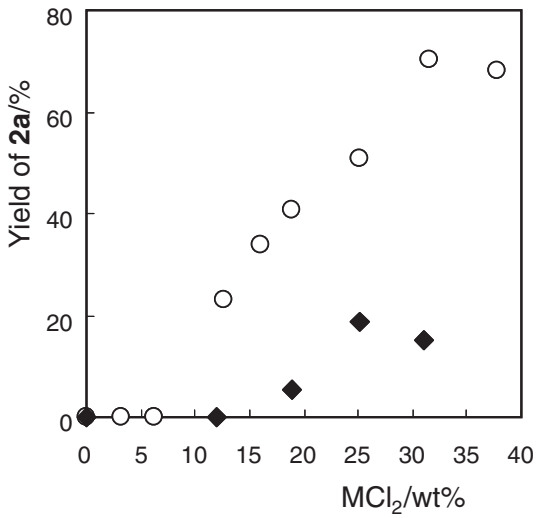


Figure 1. Plots of yield of 5-hydroxymethyl-2-furfural (**2a**) against the contents of $MgCl_2$ (○) and $CaCl_2$ (◆) in SiO_2–MCl_2 composites **3** in the reaction of **1a** at 140 °C for 24 h.

18 h. The dehydration reaction of **1a** was compared with that of other aldoses such as mannose (**1b**) and galactose (**1c**) and ketoses such as fructose (**1d**) and sorbose (**1e**) (Scheme 3). The conversions of **1b** and **1c** were slow. The conversion of **1d** was similar to the case of **1a**. Although A–K isomerization of both **1a** and **1b** gave the same **1d**, the conversion of **1b** was very slow compared with that of **1a**. Ketohexoses are known to produce **2a** more efficiently than aldohexoses.[16] Therefore, it was suggested that the A–K isomerization was the rate-determining step in the case of **1b**. Ebitani et al. have promoted A–K isomerization of **1** using a combination of basic hydrotalcite and acidic Amberlyst-15®.[14] Moreover, it was suggested that *cis*-elimination of H_2O from the C-4 and C-5 positions of

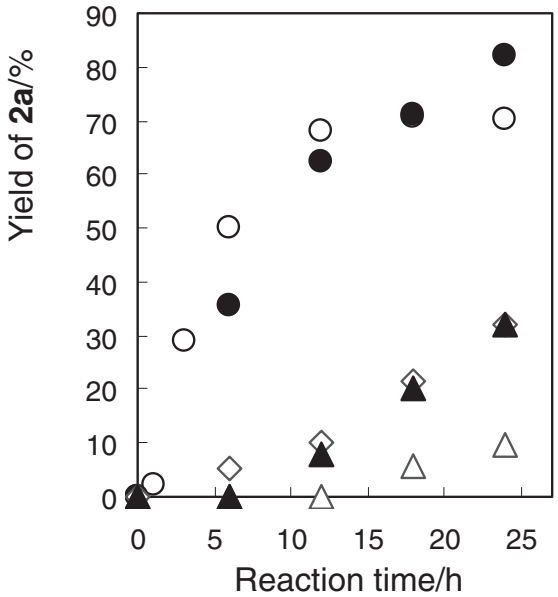
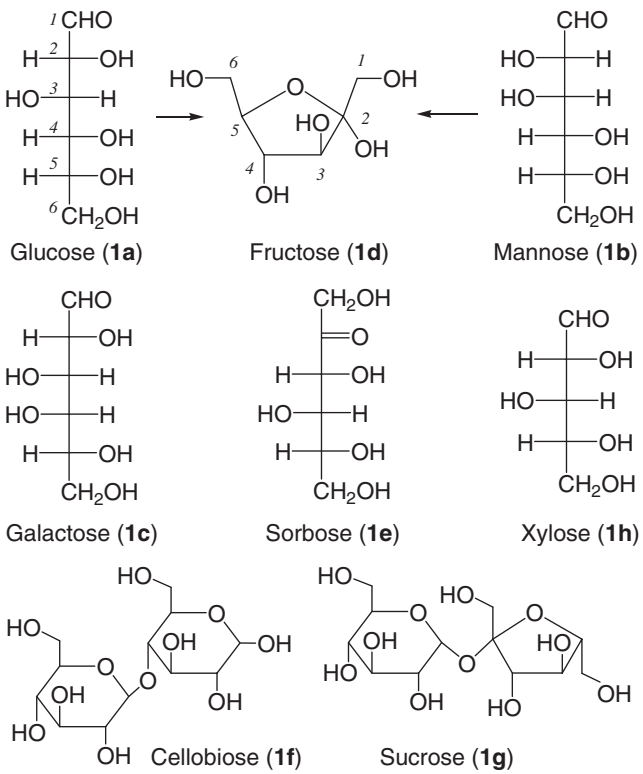


Figure 2. Time-conversion plots of the yields of **2a** in the reaction of glucose (**1a**; ○), mannose (**1b**; △), galactose (**1c**; ◇), fructose (**1d**; ●), and sorbose (**1e**; ▲) under 140 °C using the SiO_2–$MgCl_2$ (32 wt %).



Scheme 3. Monosaccharides **1a**–**1c**, **1e**, and **1h** shown by Fisher projection form and fructose (**1d**) and disaccharides **1f** and **1g** written by furanose and pyranose forms.

ketoses is preferable since the conversion of **1c** and **1e** was slower than that of **1a** and **1d**. It has been reported that DMSO performs effectively as base for dehydration.[17] In the present cases, however, the reaction of **1c** in MeCN–DMSO (v/v 9:1) could not enhance the yield of **2a** (Runs 7 and 8).

The **2a** was obtained in 10% and 31% yields from disaccharides such as cellobiose (**1f**) and sucrose (**1g**), respectively (Table 1, Runs 11 and 12). The bond-fission of the β-1,4-bond in **1f** showed the possibility of the formation of **2a** from cellulose. However, 2-furfural (**2b**) was formed from xylose (**1h**) in only a 17% yield under the optimized reaction conditions at 180 °C for 1.5 h using **3a** where the content of $MgCl_2$ was 23 wt %/SiO_2 (Run 13). These show that **3a** is a poor catalyst for the A–K isomerization of **1h**.

Thus, the **3a** catalyzed specifically under the dehydration of mono- and disaccharides containing glucose unit which is an abundant biomass. Since **3a** was simple composite composed of only light elements such as Mg, Si, and Cl, a low environmental damage process will be constructed in transformation from biomass to commodities.

Experimental

Materials and Instruments. Saccharides **1** were purchased from Wako Chemicals as D-forms except for L-sorbose. ^{1}H and ^{13}C NMR spectra were taken on a Bruker AV 400M spectrometer for $CDCl_3$ solutions with tetramethylsilane used as an internal standard.

Dehydration of 1 in the Presence of 3. Typical procedure for the formation of **2a** from **1a** was as follows: **3a** was dried by heating at 50 °C for 3 h under reduced pressure before use. **1a** (0.5 g) and **3a** (1.0 g) were placed in an autoclave vessel. Water-free MeCN (40 cm^3) was introduced into the vessel and heated at 140 °C under stirring in the autoclave. The pressure reached 0.4 MPa. After reaction for 24 h, **3a** was separated from the reactants by filtration and then washed with $CHCl_3$. The solvent was evaporated to give an oily residue. **2a** was isolated from the residue by column chromatography on SiO_2 (Fuji Silysia BW 300) using $CHCl_3$ as an eluent. The structure of **2a** was identified by comparison of NMR spectra with an authentic sample.

5-Hydroxymethyl-2-furfural (2a): ^{1}H NMR: δ 4.72 (s, 2H), 6.52 (d, $J = 8.7$ Hz, 1H), 7.22 (d, $J = 8.7$ Hz, 1H), 9.59 (s, 1H); ^{13}C NMR: δ 57.02, 110.06, 124.11, 151.96, 161.44, 173.05.

2-Furfural (2b): Oil. ^{1}H NMR: δ 6.63 (dd, $J = 3.6$, 1.6 Hz, 1H), 7.29 (d, $J = 3.6$ Hz, 1H), 7.72 (brt, $J = 1.6$ Hz, 1H), 9.67 (s, 1H); ^{13}C NMR: δ 112.42, 121.63, 148.08, 152.64, 177.59.

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