Article

아이소소바이드의 효과적 산화반응을 위한 루테늄/템포/나이트레이트 촉매 시스템 개발

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Development of Ruthenium/TEMPO/Nitrate Catalyst System for Efficient Oxidation of Isosorbide

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초 록

본 연구에서는 아이소소바이드(1,4:3,6-dianhydro-D-glucitol)로부터 그에 상응하는 아이소소바이드-디케톤[2,6-dioxabicyclo (3,3,0)octan-4,8-one]으로의 높은 선택적 전환을 통한 효율적인 루테늄/템포/나이트레이트 촉매 시스템 개발에 대해 보고한다. 미래의 제조 공정에서의 중요한 플랫폼 화합물 중 하나는 아이소소바이드이다. 오랜 시간 동안, TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl)는 알코올을 카보닐 화합물로 변환하는데 사용되어 왔다. 본 화학 반응에서는 산소 1atm 압력하에, Ru (10 mol%), TEMPO (5 mol%), 질산나트륨(0.03 mmol) 그리고 아이소소바이드(0.5 mmol)를 용매 아세트산(3 ml)을 사용하여 최적화되었다. 이러한 촉매 시스템은 이중 산화 촉매 반응 메커니즘에 대한 가능성뿐만 아니라, 생성물에 대한 원하는 반응물의 높은 선택성(> 97%)과 수율(87%)을 보여주었다.

Abstract

This research work reports the development of a Ruthenium/2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO)/nitrate catalyst system for the highly selective transformation of isosorbide (1,4:3,6-dianhydro-D-glucitol) to isosorbide-diketone (2,6-dioxabicyclo (3,3,0)octan-4,8-one). Isosorbide is a critical platform molecule for future manufacturing processes. TEMPO has been utilized to convert alcohols to carbonyl compounds for a long time. The optimal chemical reaction condition was found to be when using isosorbide (0.5 mmol) with supported Ru (10 mol%), TEMPO (5 mol%), and sodium nitrate (0.03 mmol) in the presence of acetic acid (3 ml) as a solvent at 50 °C and 1 atm oxygen pressure. This catalyst system demonstrated good selectivity (> 97%) and yield (87%) with respect to the desired product, in addition to a putative catalytic double oxidation mechanism.

Keywords: Ruthenium/TEMPO/nitrate, Isosorbide, Isosorbide-diketone, Double oxidation

1. Introduction

Due to environmental concerns, sustainability issues, and the high cost of crude-oil based goods, industrial and academic research on biomass-based energy production and utilization has been actively explored for past several decades[1,2]. The use of biomass-based feedstock, which is abundant and sustainable source of energy, is of a tremendous advantage in minimizing the exhaustion of petrol resources[3]. Sustainable carbon-containing compounds[4] can be made from lignocellulosic biomass which is a distinguishable source of carbohydrates, but they have a few shortcomings, including (a) incompatibility with high-temperature chemical processes in industries, (b) structural intricacy, and (c) attachment of a large number of functional groups[5]. If the number of functional groups on complicated carbohydrate moieties[6-9] can be controlled, stable and practical bio-based bifunctional building blocks can be produced; isohexides made from various carbohydrates like starch or cellulose are a well-known example. In this view, isosorbide (1,4:3,6-dianhydro-D-sorbitol, 1a, Figure 1) may be easily made from sorbitol (a sugar-based hexitol) us-
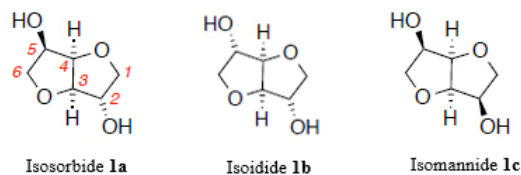
Figure 1. Platform chemicals produced from biomass; (1a) isosorbide, (1b) isoidide, (1c) isomannide.
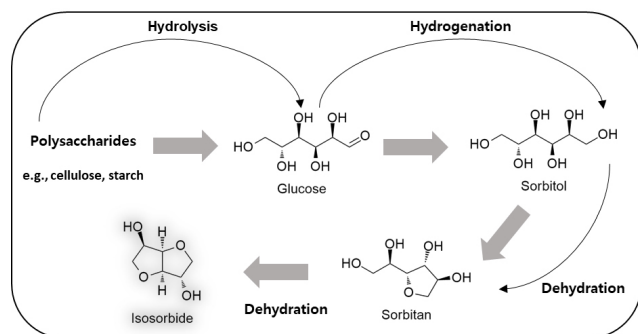

Figure 2. Simple flow chart for isosorbide production from biomass.

ing a double dehydration procedure (Figure 2), and its stereoisomers, isoidide (1b) and isomannide (1c) can also be interconverted via catalytic isomerization[10].

Isosorbide has a V-shaped geometry owing to the *cis*-bonding of two flattened tetrahydrofuranic ring. These two five-membered rings form a nearly 120° angle. Isosorbide was first reported in 1927[11], and its structure was conformed in 1946[12] when its crystalline form was synthesized in 1940[13]. The position of −OH groups in isosorbide and two of its structural isomers differs, with isoidide showing *exo* conformation and isomannide revealing *endo* conformation. Isosorbide structure has both *exo* and *endo* conformations, making it a one-of-a-kind molecule. *Exo* configuration is shown by the −OH group at position-2 in isosorbide, whereas *endo* is seen by the one at position-5. The difference in the physical properties of these three compounds, such as solubility, reactivity, and melting temperatures, is related to the different positions of the −OH functional group[14].

Isosorbide has been used as a platform material in a variety of applications during the last few decades, including catalysis[15], polymers[9], liquid crystalline composites[16], cosmetics and pharmaceutical additives[17], and ionic liquids[18]. This diverse use of isosorbide is attributed to its non-toxic nature, structural rigidity, relative stability, and chirality[10]. In comparison to isoidide and isomannide, the participation of the *endo* position -O atom of isosorbide in hydrogen bonding generates an increased nucleophilic ability, which sequentially amplifies the chemical reactivity of isosorbide. The steric hindrance[14] is the key factor which makes the −OH group at *exo* position less reactive towards nucleophilic attack. Alcohol oxidation reactions are a major focus of organic chemistry research since the resulting compounds have a wide scope of applications in chemical syntheses. Isosorbide is classified as a cyclic secondary alcohol, however there is
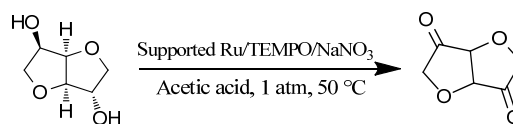

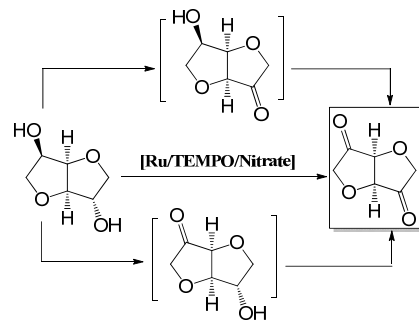Figure 3. Oxidation of isosorbide to isosorbide-diketone.

Figure 4. The possible reaction mechanism for double oxidation of isosorbide involving two hydroxyl groups.

relatively little literature on its oxidation processes. Various oxidizing agents and systems, such as chromic acid[1], TEMPO/laccase[19], Pt on carbon[20], sodium borohydride[21], and the TEMPO/NaNO$_2$/NaNO$_3$ system[22], have been employed in previous papers to depict the oxidation process. Isosorbide is oxidized to an isosorbide-diketone (2,6-dioxabicyclo(3,3,0)octan-4,8-one), which is a crucial precursor for the further derivatization of isosorbide into various efficient products such as isosorbide-diimine, isosorbide-diamine, or isosorbide-dialcohol. Use of isosorbide mono-nitrates and di-nitrates in medicine[23] and isosorbide dimethyl ether in pharmaceutical[24] solvent are worth mentioning. The previously reported procedures contain deficiencies in several reaction steps or the stoichiometric usage of expensive and hazardous reagents like bromine sources and organic solvents, which are a hurdle to the industrial scale preparation of isosorbide-diketone[22]. The use of catalysis under benign conditions is an economically promising and advantageous technique to solve most of the aforementioned challenges.

Therefore, we report the fabrication of a Ruthenium/TEMPO/nitrate catalytic system for efficient oxidation of bicyclic dialcohol, and it is successfully used for the oxidation of the hydroxyl group for the isosorbide in a halogen-free procedure under mild reaction conditions. At 50 °C, the procedure is carried out in the presence of a natural oxidant, O$_2$, as well as a nitroxyl radical such as TEMPO and NO source from nitrate or nitrite. Remarkably, the as-synthesized catalyst is capable of oxidizing both of hydroxyl groups at 2 and 5 position of isosorbide alcohol to give a isosorbide-diketone under benign conditions in Figure 3. In addition, as shown in Figure 4, we have suggested a plausible catalytic reaction mechanism for the two hydroxyl groups with different reactivity.

2. Experimental

2.1. Catalyst preparation

The following is how the supported Ruthenium catalyst was produced: Powdered MnO_2 was pretreated at 300 °C for 5 h, then rapidly mixed with aqueous $RuCl_3$ (8.3 mM, 60 mL) at room temperature. While stirring, pH of the mixture was adjusted to 13 by adding 1 M of sodium hydroxide. The resulting slurry was left to agitate for 24 hours. It was then dried at room temperature to obtain a fully dried powder of supported Ruthenium catalyst. The Ruthenium content was 2.1-2.2 wt% by ICP-AES (inductively coupled plasma atomic emission spectroscopy) analysis.

2.2. Instruments and materials

The substrates and products were analyzed using a Younglin GC-6500 instrument with a flame ionization detector (FID) and an HP-INNOWAX capillary column (internal diameter = 0.25 mm, length = 30 m). Mass spectra (GC/MS) were recorded on Hewlett Packard 6850 gas chromatograph system with 5973 MSD (Hewlett Packard, USA) at an ionization voltage of 70 eV equipped with a DB-5 capillary column (internal diameter = 0.25 mm, length = 30 m). Elemental analysis for transition metals was carried out an ICP-AES (Shimadzu ICPS-7510). Sigma-Aldrich provided the isosorbide and Ruthenium precursors, while Tokyo Chemical Industry Inc. offered the TEMPO. $NaNO_3$ was obtained from ACROS Organics. All additional reagents and solvents were used as received, with no further purification.

2.3. Catalyst reaction procedures

All operations were carried into a Pyrex-glass vial in a tubular type reactor. A typical reaction procedure was conducted as follows. Ruthenium catalyst (10 mol%) was put into acetic acid (3 ml) in the vial. Isosorbide substrate (0.5 mmol), TEMPO (5 mol%), and $NaNO_3$ (0.03 mmol) in order was added with cross-shaped magnetic bar. The reaction mixture was stirred (500 rpm) at 50 °C under 1 atm of molecular oxygen. After several hours, the catalyst and the product(s) were separated by the filtration or centrifugation. The residue solid was washed with water. Then, diphenyl as an internal standard was added to the combined organic solution and the solution was analyzed by Gas Chromatography (GC) and GC/MS.

3. Results and discussion

3.1. Characterization of the supported Ruthenium catalyst (Ru/MnO₂)

The X-ray diffraction (XRD) and transmission electron microscopy (TEM) were used to characterize the prepared Ru/MnO_2 catalyst. The analysis results are demonstrated in Figure 5 and Figure 6. The XRD patterns of supported Ruthenium catalysts were identical to those of the parent supports, with no signs of Ru metal clusters or RuO_2 (Figure 5). These findings show that Ruthenium species are widely dispersed on the surface of supports. Figure 6 shows TEM images of Ru/MnO_2 at different resolutions, including 10, 20, and 50 nm. All of the elements of the Ru/MnO_2 catalyst, such as Ruthenium, manganese,
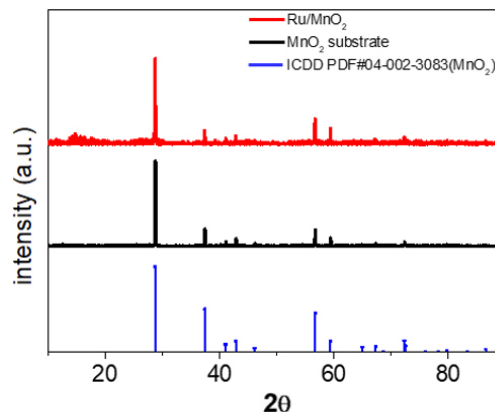

Figure 5. XRD spectra of Ru/MnO₂ and pristine MnO₂.

and oxygen, might be clearly shown in the images.

3.2. Double oxidation of isosobide with Ruthenium/TEMPO/nitrate

The isosorbide oxidation reaction was carried out by catalyst system of supported Ruthenium/TEMPO/Nitrate with isosorbide substrate and acetic acid as a solvent in a tubular type reactor with a teflon-coated magnetic stir bar at 50°C. The reaction was performed at 1 atm molecular oxygen pressure during 10 h. Reaction conditions were optimized using various catalyst systems and solvents. Table 1 shows the summary of the results. The supported Ru in the presence of TEMPO and $NaNO_3$ demonstrated a good catalytic activity with a conversion rate of 90% and excellent selectivity (>97%) of the desired product (isosorbide-diketone) in 10 h (Entry 1). In the presence of other solvents except acetic acid, the systems did not produce the corresponding diketones (Entry 2-4). The supported Ruthenium without TEMPO did not catalyze the transformation (Entry 5). Not having Ruthenium or TEMPO, the reactions were not proceeded regardless of calcination of support MnO_2 (Entry 6-7). There was no reaction in the absence of the Ru/TEMPO/Nitrate catalyst system for the conversion of isosorbide (Entry 8). All product samples were analyzed using GC and GC/MS[19].

3.3. The proposed double oxidative catalytic mechanism

In the transformation of isosorbide, the *exo*-hydroxy ketone production from oxidative hydrogen transfer of isosorbed is requried higher energy than *endo*-hydroxy ketone production[19]. This can be explained by the unique V shape of isosorbide which has distinctive reactivities of hydroxyl groups in 2 and 5[14]. These two seconday alcohols should overcome remarkable energy barrier to be oxidized. The Ruthenium/TEMPO as catalyst sytem was reported by Sheldon research group for oxidation of considerably unreactive secondary alcohols[25]. The corresponding diketone was not obtained as the oxidation reaction of the secondary alcohols without Ruthenium/TEMPO/Nitrate and acetic acid as a solvent in Table 1. In addition, the profile of reaction for the double oxidation of isosorbide showed that *exo*-hydroxyl (or *endo*-) monoketone was initially formed followed by the formation of final product, diketone (Figure 7). Therefore, the transformation of isosorbide with Ruthenim/TEMPO/Nitrate system in acetic acid solvent
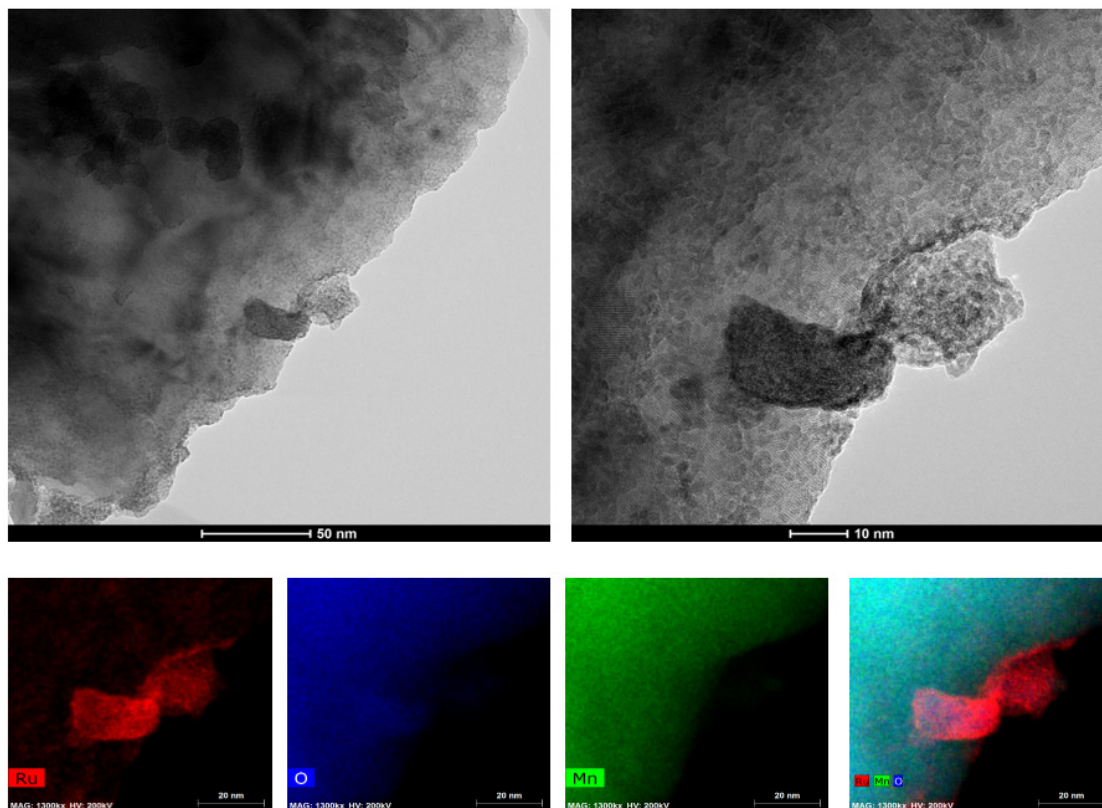
Figure 6. TEM images for Ru/MnO$_2$ catalyst at different magnifications.

Table 1. Transformation of Isosorbide with Various Catalyst Systems[a]

Entry	Catalyst	Co-catalyst/NO	Solvent	Yield(%)[b]
1	Ru/MnO$_2$	TEMPO/NaNO$_3$	Acetic acid	87 / >9[c]
2	Ru/MnO$_2$	TEMPO/NaNO$_3$	Toluene	>5
3	Ru/MnO$_2$	TEMPO/NaNO$_3$	Water	>3
4	Ru/MnO$_2$	TEMPO/NaNO$_3$	Dioxane	>3
5	Ru/MnO$_2$	NaNO$_3$	Acetic acid	>5
6	MnO$_2$[d]	NaNO$_3$	Acetic acid	>5
7	MnO$_2$[e]	NaNO$_3$	Acetic acid	>3
8	None	None	Acetic acid	>1

[a] Reaction conditions: Isosorbide (0.5 mmol), catalyst (Ru: 10 mol%), TEMPO (5 mol%), NaNO$_3$ (0.03 mmol), solvent (3 mL), 50 °C, and 10 h under 1 atm of O$_2$. [b] Yields were calculated by GC analyses (HP-INNOWAX column) using an internal standard technique. [c] Without NaNO$_3$. [d] Calcination at 300 °C. [e] No calcination
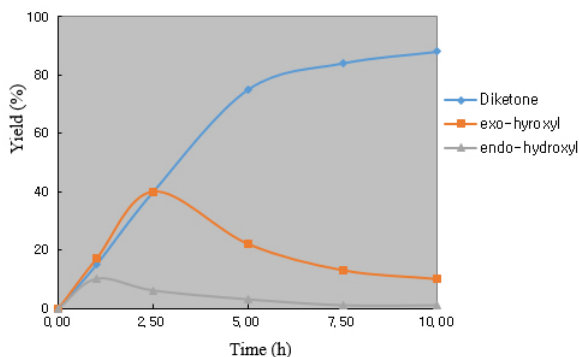

Figure 7. Reaction profiles for the Ruthenium/TEMPO/Nitrate-catalyzed transformation of isosorbide.

potentially proceeds through cascade sequence reactions to yield the isosorbide diketone.

The potential double oxidative reaction mechanism is proposed in Figure 8. Initially, This mechanism can be divided into four steps. In the first step, an oxoammonium salt is generated into based on the catalytic cycle of TEMPO oxidation[26] (Step I). In second step, this salt may react with the respective alcohol to produce endo- or exo-hydroxyl monoketones as intermediates and a hydroxylamine (Step II). In third step, the hydroxylamine can regenerate the oxoamonium salt to continue the catalytic cycle (Step III). Finally, the monoketones experience the same oxidation process to formation of the diketones, desirable products (Step IV).
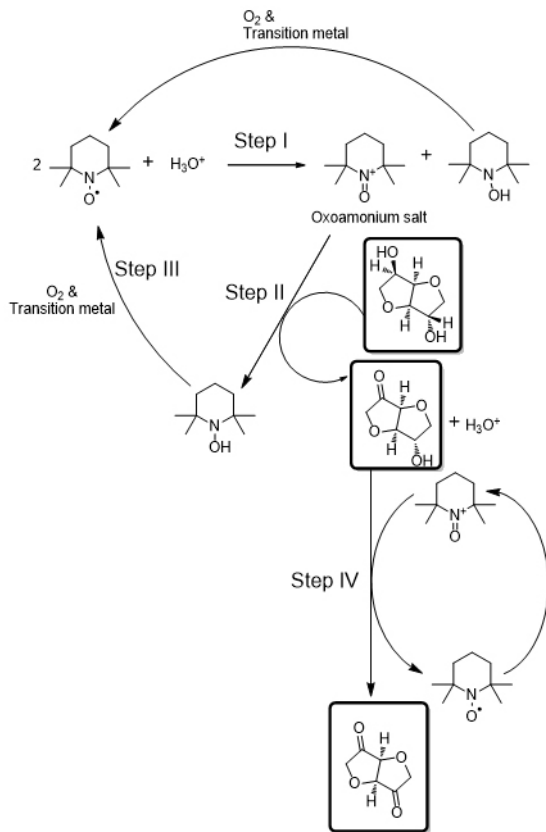
Figure 8. The proposed reaction mechanism for double oxidation of isosorbide with Ruthenium/TEMPO/Nitrate catalyst system.

4. Conclusion

In conclusion, the supported Ruthenium/TEMPO/nitrate catalytic system showed excellent selectivity (>97%) and high yield (87%) in presence of acetic acid solvent under environmentally benign reaction conditions. The possible reaction mechanism of isorsorbide transformation to isosorbide-diketone was proposed by intermediates, *endo*- or *exo*-hydroxyl monoketones during the reactions via reaction profiles and various catalyst systems. Based on these proposition, double oxidation and oxoamonium salt should play an important role in producing largely unreactive seconday alcohols such as isohexides.

Acknowledgement

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