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Optimization study of the deoxydehydration reactions for the synthesis of muconamide from glucose

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Abstract

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In polymer industry, current supply of monomers has been met mostly by petroleum industry. However, due to gradually intensified problems on the depletion of petroleum, efforts are focused on the researches for a new method to produce petroleum-based chemicals. As a final product of this study, adipic acid, one of two monomers of nylon 6, 6, has predominantly been provided from petroleum industry, for that reason, potassium D-glucarate was introduced as starting material. It was synthesized by the oxidation of D-glucose, which is sustainable and inexpensive biomass resource, and was converted to D-glucaramide by simple reactions in high yield, furthermore, deoxydehydration reaction (DODH) facilitated the synthesis of muconamide, a significant intermediate. DODH reaction that effectively converts vicinal diol to alkene removed four successive diols on the carbon chain of D-glucaramide, resulting in two

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muconamides with its conjugated alkenes in two different stereochemistry, cis, trans and trans, trans. Catalyst, reductant and solvent are considered to be three key factors in the reaction and 3pentanol, a secondary alcohol, simultaneously played both roles of solvent and reductant and reduced esterification, regarded as a critical side reaction in the reaction, by the virtue of bulkiness on its alkyl chain. Of the rhenium catalysts used, ammonium perrhenate (APR) was the one that was intensely studied in this paper and gave over 90% yield of muconamides when using 0.1 equivalent of APR in 1 mmol scale. In addition, the use of 0.2 equivalent of pyridinium derivative catalysts, perrhenic acid or rhenium oxide (VII) was an alternative way to reduce the reaction time with over 90% yield even up to 10 mmol reaction scale.

Keyword : Biomass, petroleoum-based chemicals, deoxydehydration, Student Number : 2017-20626

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LIST OF ABBREVIATIONS

DODH	Deoxydehydration
МТО	Methyltrioxorhenium
APR	Ammonium perrhenate
n-BuOH	Normal butanol
MeOH	Methanol
DCM	Dichloromethane
NMR	Nuclear magnetic resonance
DMSO	Dimethyl sulfoxide $-d_6$
D_2O	Deuterium oxide
CDCl ₃	Chloroform-d
cat.	Catalyst
aq.	Aqueous
soln.	Solution
quant.	Quantitative yield

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1. Introduction

1-1. Methods for the synthesis of adipic acid

Adipic acid is a chemical compound, which is rarely found in the nature and has high demand in the polymer industry. Its use in the industry is often for a monomer of nylons. Nylon 6, 6 is the most significant polymer using adipic acid as a key component and its annual global market value is now growing faster. Since adipic acid is predominantly produced from the petroleum-based chemicals by oxidation with nitric acid, the process essentially accompanies toxic materials such as NO and NO₂ gases (**Figure 1**).

Several alternative methods have been introduced over a decade and the primary choice of starting material was the expensive biomass, galactaric acid in many articles.¹ Since galactaric acid has two pairs of *syn*-vicinal diols that are beneficial in the key reaction, deoxydehydration, it is frequently chosen for a starting material to synthesize adipic acid despite of its rarity in the nature. However, due to the lack of abundance of galactaric acid, glucose-derived aldaric acids such as glucaric acid and gluconic acid were second choices in order to reduce the cost of the process. Gluconic acid derivatives required more steps to synthesize adipic acid in the process so it was considered to be an inefficient choice of starting material. Starting from glucaric acid derivatives, one-pot processes were suggested, however, accompanied environmental concern and required highly pressurized reaction condition.



Figure 1. Adipic acid production from petroleum-based chemical



Nylon 6, 6

Figure 2. Synthesis of nylon 6, 6



Figure 3. Biomass-based synthesis of adipic acid and its precursors

1-2. D-Glucaric acid as starting material

D-Glucaric acid is a sugar-derived carboxylic acid and has high potential specially as a chemical compound constructing the frame of polymers. The acid has traditionally been synthesized by oxidizing D-glucose with nitric acid², moreover, recent studies included the use of heterogeneous metal catalyst³ or TEMPO derivatives⁴. Since D-glucaric acid can be converted to three possible lactone compounds due to spontaneous cyclization in its free acid form, its potassium salt is the only commercially available compound. For that reason, once retarding the cyclization of the acid with simple alteration on D-glucaric acid, it can be a reasonable starting material for deoxydehydration reaction in the process.



Figure 4. X-ray structure of solid D-glucaric acid⁵



glucaro-1,4:3,6-dilactone

Figure 5. Equilibrium of glucaric acid and its three lactones forms.

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1-3. Deoxydehydration (DODH) reaction

DODH reaction was firstly reported by Cook and co-workers in 1996⁶ and has become a promising method for the conversion of biomass into the chemicals frequently produced from petroleum. DODH reaction effectively removes two adjacent diols by using rhenium catalyst such as MTO, ammonium perrhenate (APR) and rhenium oxide (VII) by means of solvent and reductant. The mechanism of the reaction involves three steps; condensation, reduction and extrusion, and has been studied mostly by density function theory (DFT). Three different mechanisms were suggested by Toste⁷, Abu-Omar⁸ and Wang⁹ as described in **Figure 6**. and it was revealed that condensation step in all cases are in equilibrium. Moreover, according to three researchers, the order of each step and the formation intermediates during the reaction were distinct in each research. Toste (pathway A) reasoned that the mechanism of DODH followed reduction, condensation and extrusion via methyl dioxide(V). In contrast, pathway suggested by Abu-Omar showed initial condensation step involving Re. (VII) complex. Most recently, Wang's group carried out more detailed computational study in order to reveal the ambiguity and proved a new mechanism with first reduction step followed by condensation via Re. (V) complex.

As specifically shown in **Figure 6.**, Deoxydehydration (DODH) reaction is composed of three major components; catalyst, reductant and solvent. Reductant in the reaction is oxygen acceptor, making itself oxidized and catalyst reduced to low-valent species. Reductants often used in DODH reactions are metals, PPh₃, sulfite, hydrogen gas, hydroaromatics and alcohols.¹⁰ Since required in

stoichiometric amount, expensive reductants are retarded.

Hydrogen gas-mediated DODH reactions are new methods introduced in recent researches due to its low cost and availability. Of the reductants employed in the reaction, secondary alcohols are regarded as the most effective and promising ones because side reactions, for example, esterification, are inhibited by means of bulkiness of secondary alcohols. In terms of solubility, reaction energy and the energy of transition state, the choice of solvent is also important in the reaction. For DODH reaction, substrates with diols cause solubility issue due to poorly soluble character in most organic solvents, in other words, only few solvents that solubilizes the substrates can be used. For that reason, alcohols have generally been employed. However, if the boiling point of the solvent was not high enough to overcome the reaction barrier for DODH reaction, the reaction rarely occur, therefore, solvent with the boiling point above 100 °C is necessary in almost all cases. Based on the DFT study, the use of secondary alcohol reduces energy levels compared to primary alcohol as accordingly described in **Figure 7**.⁹ Most of all, as shown in **Figure 6**. alcohol solvents can also be used as reductant simultaneously.

Firstly suggested by Andrew and Cook, rhenium catalyzed-DODH reaction has become the most favorable owing to its high reactivity. Including methyltrioxorhenium (MTO), perrhenic acid, rhenium oxide (VII), ammonium perrhenate (APR), potassium perrhenate and sodium perrhenate in general, new rhenium catalysts have been introduced such as pyridinium-derived and alkyl ammonium catalysts. However, due to expensive rhenium metal, new alternatives were proposed so as to reduce the cost of process.

Researchers initially focused on cheaper metals-mediated DODH, for instance, molybdenum and vanadium catalysts.¹¹ As of yet, through many studies concentrated on those metals, experimental data supported the high potential of inexpensive metals, but it is still challenging to overcome the less reactive character of the metals. Another emerging alternative was the development of reusable solid-supported heterogeneous rhenium catalysts.¹² It has recently been studied to combine two metals to conduct DODH and hydrogenation at the same time, for example, rhenium oxide and palladium metal was impregnated on various supporting solids under hydrogen gas.¹³ In addition, third option for DODH reaction was polymer supported catalysts, yet, leaching from the support was observed as well.



Figure 6. Secondary alcohol-based mechanism of three different catalytic cycles in DODH reaction proposed by Toste (pathway A), Abu-Omar (pathway B) and Wang (pathway C).



Figure 7. Comparison of energy levels between primary and secondary alcohol in the reduction step of deoxydehydration reaction

2. Results and Discussion

2-1. Preparation of D-Glucaramide

As introduced above, D-glucaric acid has bent structure that causes spontaneous intramolecular cyclization resulting in 1,4lactone and 6,3-lactone. For this reason, it was required to prevent the cyclization by employing a new functional group. Based on basic organic chemistry, amide functional group was proper option to synthesize D-glucaric acid. In order to introduce amide functional group on it, esterification step was essential since it is not possible to synthesize amide directly from carboxylic acids by typical method. Potassium glucarate was the only commercially available form of Dglucaric acid thus, the first step of synthesizing D-glucaramide was protonation of potassium glucarate. After that, for the synthesis of alkyl glucarate and its lactones, esterification reaction was carried out in acidic condition by various options of strong acids. Crude products produced after acid-catalyzed esterification were used without purification in the next step, aminolysis. Since monolactones and bis-lactone are categorized generally in esters, it was possible for all of those compounds to be converted to Dglucaramide. As a result, D-glucaramide had poorer leaving group than carboxylic acid and ester functional groups did, preventing it from cyclization. In esterification and aminolysis, methanol and ammonia were used respectively because those are smallest molecules of alcohols and amine, in other words, the best nucleophile to accomplish both reactions in terms of steric hindrance.



Figure 8. Synthesis of D-glucaramide



It was initially needed for strong acids of interest to produce salts that are insoluble in the solvent. As entry 1 in Table 1 shows, using sulfuric acid produced potassium sulfate salt that caused additional purification step. The problem also occurred in case of entry 2. After protonated, D-glucaric acid and lactones were soluble in methanol and the salt was filtered off by washing with methanol. While having the advantage of easier removal of the acid, the use of methanolic HCl was not effect as well. All problems derived from acid-catalyzed esterification with HCl and H₂SO₄ were simply solved by using strongly acidic resin. Using the fact that intermediates after esterification were all soluble in methanol, 7 N methanolic ammonia was used for the aminolysis of crude products. Since aqueous ammonia can lead to difficulty in solvent removal. 5 mmol-scale synthesis of D-glucaramide gave only 81% probably due to lower reaction scale leading to loss of product in precipitation step of aminolysis. Eventually, the highest yield so far was obtained in 20 mmol scale reaction with Amberlite[®] 120 B as an acid source.

Entry	Acid	Scale	Salt formation	Yield of D-glucaramide
1^{a}	H ₂ SO ₄ (aq. soln.)		K_2SO_4	45 %
2 ^a	HCl (aq. soln.)	5	KCl	51 %
3 ^a	HCl (MeOH soln.)	mmol	KCl	62 %
4				81 %
5	Amberlite®	10 mmol	b	84 %
6	120 B	20 mmol	_	90 %
7		40 mmol		86 %

Table 1. Synthesis of D-glucaramide with various strong acids.

a. More than stoichiometric amount was used b. No salt formation

2-2. Optimization Study for DODH Reaction



Figure 9. Simple description of deoxydehydration

Deoxydehydration (DODH) reaction is the key step in the process of adipic acid synthesis from potassium glucarate. In this reaction, rhenium metal catalysts remove vicinal diols, resulting in the formation of (E, Z) – and (E, E) – muconamides. In the previous studies, the reaction was carried out in n-butanol, which caused esterification followed by lactonization. That was because of the Lewis acidity of rhenium catalyst and the absence of bulkiness on the primary alcohol, n-butanol. Therefore, the side reactions brought out a number of possibilities in the formation of by-products as listed in Figure 10. In consequence, the formation of partially deoxydehydrated products proved that esterification and lactonization may occur before DODH reaction. For this reason, something that reduces the acidity of rhenium catalyst or increases the steric effect of solvent was needed to decrease the number of side products. However, using amine or pyridine derivative ligands may reduce reactivity of rhenium catalyst thus, it was excluded from the options. Another option was the use of 3-pentanol, which is a secondary alcohol with bulkiness and other chemical advantages. 3-pentanolmediated DODH reaction was successful and esterification was retarded to a remarkable extent.



Figure 10. By-products produced in the DODH reaction with n-BuOH

It was also important to select a catalyst for DODH reaction. In standard DODH reaction, 0.2 equivalent of rhenium catalysts, from number 1 to number 11, were tested for screening the reaction. Catalysts 4 through 11 exist in perrhenate form and have differences only in cation. Rhenium oxide (VII) and perrhenic acid are known to be used interchangeably¹⁴, and methyltrioxorhenium (MTO) is the most general catalyst for DODH reaction. According to Table 2, purified yield of (E, Z) – and (E, E) – muconamide was the highest with ammonium perrhenate (4). Isolated yield over 90% was obtained also with catalysts 1,2,7,8 and 9.15 Of the catalysts used in the reaction, a few had poor reactivity in some reaction conditions. It was firstly assumed that solubility of the catalyst in 3-pentanol may lower the catalyst reactivity, however, it was not reasonable in cases of 10 and 11 because the solubility of those catalyst was much better than others. In addition, it was accidently found that combination of some catalysts were still effective in DODH reaction resulting in more than 90% except for entry 2 in Table 3.

As mentioned in the introduction, despite of the effectiveness of DODH reaction, expensive rhenium catalysts are always a concern of researchers. For that reason, ammonium perrhenate was chosen for further study because of its relatively cheaper cost. Table 4 showed optimization of DODH reaction with APR. Isolated yield was still very high with 0.1 equivalent of APR but decreased down to 80% even for longer reaction time. When reacted for 48 hours, 0.05 equivalent was enough to give more than 80%. Longer reaction time with 0.05 equivalent of APR rather reduced the yield probably due to the decomposition of muconamides.



Figure 11. Rhenium (VII) catalysts used in this article



Figure 12. 2 mmol-scale DODH reaction with 20 mol% of rhenium catalysts in 30 mL of 3-pentanol.

Table 2. DODH reaction with 0.2	2 equivalent of rhenium catalys
---------------------------------	---------------------------------

Catalyst	Amount (equiv.)	Time	Yield
1	0.1		93 %
2			93 %
3		12 h	82 %
4			99 %
5 6 7	0.2		88 %
			52 %
	0.1		97 %
8			90 %
9 10 11			91 %
			41 %
			45 %

Table 3. Combination of catalysts; pyridinium derivative

Entry	Catalyst	Amount (equiv.)	Time	Yield
1	1 + 7			94 %
2	1 + 8	0.05 + 0.1		86 %
3	1 + 9		12 h	94 %
4	2 + 7			96 %
5	2 + 8	0.1 + 0.1		93 %
6	2 + 9			92 %

perrhenates with rhenium oxide and perrhenic acid

 Table 4. Screening DODH reaction using ammonium perrhenate

Entry	Catalyst	Amount (equiv.)	Time	Yield
1		0.15	18 h	96 %.
2		0.1	24 h	quant.
3	4	0.075	48 h	80 %
4		0.05	10 11	81 %
5		0.05	72 h	73 %

2-3. Gram-scale DODH Reaction

It cannot be too enough to emphasize the importance of industrialization of a process by increasing the reaction scale. Therefore, it is very significant for a reaction scale to be grams so it has an industrial meaning. From potassium glucarate to adipic acid and hexamethylenediamine, the most challenging part of the process was the development of reaction conditions for large-scale deoxydehydration reaction. One or two millimole reactions, as discussed in 2-2, were mostly successful in 30 mL of 3-pentanol with 0.2 equivalent of catalyst. On the other hand, conversion in the reactions with 5 mmol of starting material was only around 50 % even in long reaction time. The problem of low conversion was solved by refreshing the solvent, 3-pentanol. In our conventional DODH reaction, *Dean-Stark* trap was used to remove 2 equivalent of water produced from 1 equivalent of starting material that possess two adjacent vicinal diol functional groups in the condensation step (based on the reaction mechanism most recently proposed by Wang⁹, Figure 13.).



Figure 13. Reversible condensation step recently proposed by Wang

It was, however, found that separation of water from 3pentanol by the apparatus was not successful due to high temperature on the top part of *Dean-Stark* trap. Even though water is theoretically immiscible with 3-pentanol, high temperature made it possible for two liquids to be solubilized each other as describe in **Figure 14.** This problem was more serious for the water molecules generated relatively later during the reaction. Since D-glucaramide was poorly soluble in 3-pentanol, there must be time difference between early and late production of water. Accordingly, it was hypothesized for *Dean-Stark* trap to be drained several times over the reaction so it can be possible to drive the equilibrium to the product side.



Figure 14. Partial dissolution of water with 3-pentanol at the top of heated *Dean-Stark* trap.

Collidinium perrhenate, perrhenic acid and rhenium oxide were three representative catalysts chosen for 5 mmol-scale deoxydehydration reaction. Reactions were conducted by using the apparatus as depicted in **Figure 14**., overcoming the problem. For all three cases in **Table 6**, 10 mL of anhydrous 3-pentanol was added and that in the trap was removed 5 times each over the reaction time, as a result, any of three catalysts gave more than 93% isolated yield for the DODH reaction. In contrast, another three cases in **Table 5**. was not successful, providing at most 23% lower yield as in the reaction with perrhenic acid. Thus, it was proved that removing waste 3-pentanol in Dean-Stark trap and adding 3-pentanol, balancing the initial amount of solvent, was very effect in terms of optimizing the 5 mmol-scale DODH reaction.



Figure 15. Apparatus for gram-scale DODH reaction (1st generation)

Table 5. 5 mmol-scale DODH reaction without addition and removal

Scale	Catalyst (equiv.)	Reaction time	Isolated yield
	Collidinium perrhenate		77.0%
	(0.2)		11 %
5 mmol	Perhenic acid	24 h	71 %
(1.04 g)	(0.2)	24 11	11 /0
	Rhenium oxide		7100
	(0.1)		1 4 70

of 3-pentanol

Table 6. 5 mmol-scale DODH reaction by supplying fresh 3-pentanoland removing the 3-pentanol trapped in Dean-Stark

Scale	Catalyst (equiv.)	Reaction time	Isolated yield
	Collidinium perrhenate		03 %
	(0.2)		30 10
5 mmol	Perhenic acid	24 h	0.1 %
(1.04 g)	(0.2)	24 11	54 10
	Rhenium oxide		05 %
	(0.1)		30 70

2 gram-scale reaction was also tried with only 0.175 equivalent of collidinium perrhenate in 24 hours, giving 90 % yield.

Table 7. 10 mmol-scale DODH reaction by supplying fresh 3-pentanol and removing the 3-pentanol trapped in *Dean-Stark*

Scale	Catalyst (equiv.)	Reaction time	Isolated yield
10 mmol	Collidinium perrhenate	24 h	90 %
(2.08 g)	(0.175)		

Here, a new device was invented for more effective removal of water. **Figure 16** offers detailed descriptive explanation about the device equipped with dropping funnel filled with 3-5 angstrom molecular sieves. Whole part of the apparatus was flame-dried under nitrogen flushing before use to completely remove residual water inside of it. Evaporated 3-pentanol followed up the arm of dropping funnel and then, was refluxed down to a pile of activated molecular sieves. After dehydrated, 3-pentanol was anhydrous enough to drive the equilibrium more to product side in condensation step of DODH reaction.



Figure 16. Apparatus for gram-scale DODH reaction (2nd generation)

3. Conclusion

In accordance with the depletion and lack of petroleum, next generation resources have been on the table to replace existing industrial supply of monomers. Renewable and sustainable biomass is one of the most proper choices in terms of abundance and cost. Herein, D-glucose was the biomass of interest for this study since it can be oxidized by simple method using nitric acid, resulting in Dglucaric acid. Our process started with potassium D-glucarate, the salt form of D-glucaric acid with linear structure, and the salt was easily converted to D-glucaramide in 90% yield. Since there are four adjacent hydroxyl groups in the molecule, deoxydehydration (DODH) reaction was employed for highly effective removal of diols. The use of 3-pentanol added more effectiveness to the reaction by playing roles of both reductant and solvent simultaneously. The secondary alcohol also had contribution on the inhibition of side reactions. Most of all, reactivity of rhenium catalyst was the key factor for successful reaction. DODH reaction carried out with 0.2 equivalents of some catalysts such as rhenium oxide (VII), perrhenic acid, 2chloropyridinium perrhenate, collidinium perrhenate, lutidinium perrhenate and ammonium perrhenate (APR) gave over 90% yield of (E, Z) – and (E, E) – muconamide. Of the achievement in this work, gram-scale DODH reaction was very meaningful with regard to possibility of industrialization. 2 g scale (10 mmol) reaction was conducted not with Dean-Stark trap but with the apparatus newly built in this article, overcoming existing technical problems. In conclusion, DODH reaction provided 90% of muconamides up to 10 mmol scale in only 24 hours.

4. Experimental Details

4–1. General Information

All commercially available reagents were used without further purification unless any specification is stated. Potassium Dsaccharide (D-glucarate), NH₄ReO₄, Re₂O₇, KReO₄ and Pd/C (10 wt%), were purchased from Aldrich. NaReO₄ was purchased from Alfa-Aesar. NMR spectra were collected in DMSO-d6 and chloroform-d solvents with TMS as internal standard. 1 H, 13C and 15N NMR (¹H at 400 MHz and ¹³C at 100 MHz unless stated otherwise) were recorded on Bruker Ascend[™] 400 MHz NMR spectrometer. Chemical shifts are reported as follows in ppm from the internal standard (TMS, 0.0 ppm). The data are reported as (s: singlet, d : doublet, t : triplet, m : multiplet or unresolved, br : broad single, coupling constant(s) in Hz, integration). High resolution mass spectra were obtained with a JEOL JMS-AX505WA gas chromatography-mass spectrometer and performed using a magnetic sector instrument by chemical ionization (CI). Elementary analysis was performed on a LECO Corp, US/CHNS-932. Melting points were determined with an open capillary melting point (Electrothermal IA9100). Purification by column apparatus chromatography was conducted on Kiesel gel 60 (70-230 mesh).

4-2. Preparation of D-Glucaramide

Synthesis of D-glucaramide; esterification and aminolysis.

Potassium glucarate (Aldrich, $\geq 98\%$) (40 mmol, 10 g), Amberlite[®] IR120 (Aldrich, strongly acidic) (20 g) and 150 mL of MeOH were mixed in 250 mL flask for 20 min and refluxed for 4 h in air. Then, the resin was filtered and washed with 100 mL of MeOH. The filtrate, containing methyl ester 1,4-lactone, methyl ester 3,6lactone 1,4:3,6-glucarodilactone concentrated and was approximately to 10 mL homogeneous solution. To the flask in ice bath was added 7 N ammonia in methanol (Aldrich, 30 mL) dropwise and the solution turned heterogeneous after 10 min. Stirring was continued for two additional hours to complete the reaction. After filtration of the product followed by drying overnight in vacuum oven at 50 °C, the highest yield for two steps was 90%. Mp. 160.4-160.9 °C; ¹H NMR (DMSO- d_6 , 400 MHz): δ 7.28 (s, 2H), 7.16 (s, 1H), 5.43 (d, 1H, J=6 Hz), 5.26 (d, 1H, J=5.2 Hz), 4.75 (d, 1H, J=5.2 Hz), 4.62 (d, 1H, J=6.8 Hz), 3.94 (t, 1H, J=4 Hz), 3.87 (m, 2H, J=x Hz), 3.69 (quin, 1H, J=4 Hz). ¹³C NMR (DMSO- d_6 , 100 MHz): δ 175.73, 174.79, 73.19, 72.86, 71.45, 70.32. Anal. Calcd for C₆H₁₂N₂O₆: C 34.62, H 5.81, N 13.46, O 46.11; Found: C 34.8126, H 5.9166, N 13.3842, O 46.1930; HRMS (CI) calcd for $C_6H_{13}N_2O_6$, [M+H]⁺ 209.0773; found 209.0772

4-3. Preparation of Catalysts

2-chloropyridinium perrhenate, 7

75% aqueous solution of perrhenic acid (1 g, 3.0 mmol) was added to a DCM solution (6 mL) of 2-chloropyridine (340 mg, 3.0 mmol) and the mixture was stirred at room temperature for 12 hours with formation of a white precipitate. After removal of DCM under reduced pressure, the solid was passed through MgSO4 pad and the solvent removed under reduced pressure to obtain 7 as a white solid (1.02 g, 98%).

Lutidinium perrhenate, 8

75% aqueous solution of perrhenic acid (1 g, 3.0 mmol) was added to a solution 2,6-lutidine (321 mg, 3 mmol) in toluene (3.0 mL) and the mixture was stirred at roomtemperature for 12 hours. After diluted with additional toluene and washed with water, the aqueous phase was extracted with CH_2Cl_2 , dried over MgSO₄, and concentrated under reduced pressure to obtain **8**, (1.09 g, >99 %)

Collidinium perrhenate, 9

75% aqueous solution of perrhenic acid (1 g, 3.0 mmol) was added to a solution 2, 4, 6-collidine (363 mg, 3 mmol) in toluene (3.0 mL) and the mixture was stirred at roomtemperature for 12 hours. After diluted with additional toluene and washed with water, the aqueous phase was extracted with CH_2Cl_2 , dried over MgSO4, and concentrated under reduced pressure to obtain **9**, (1.11 g, >99 %)

Tetra-n-hexyl ammonium perrhenate, 10

An aqueous solution of ammonium perrhenate (268 mg, 1.0 mmol) was added to a solution of tetra-*n*-hexylammonium bromide (430 mg, 1.0 mmol) in chloroform (4 mL) and water (2 mL), and stirred for 6 h at room temperature after which the two layers were separated and the aqueous layer extracted with chloroform (2 x 10 mL). The combined chloroform extracts were dried over MgSO₄ and the solvent was evaporated under reduced pressure to give **10** as a colorless solid (587 mg, 97 %).

3-methyl-1-pentyl imidazolium perrhenate, 11

3-methyl-1-pentyl imidazolium bromide (1.17 g, 5 mmol) was added to the flask filled with 20 mL of acetone. APR (1.61g, 6 mmol) was then added to the mixture and stirred for 48 hours for ion exchange. The resulted slurry was dried under reduced pressure and extracted DCM (3 x 30 mL). After drying over MgSO₄ and removal of solvent, 1.79 g (89 %) of **11** was obtained.

4-4. Deoxydehydration

In 50 mL flask were added D-glucaramide (2 mmol, 416 mg), ammonium perrhenate (0.20 mmol, 53.6 mg) and 3-pentanol (30 mL). The suspension was refluxed with *Dean-Stark* trap for 24 hours under argon. After completion of the reaction, the solution was evaporated under reduced pressure, giving brown syrup. The crude product was purified by column chromatography (DCM : MeOH = 10 : 1), resulting in the quantitative yield of (*E*, *Z*)-muconamide. ¹H NMR (DMSO- d_6 , 400 MHz): δ 8.23 (dd, 1H, J = 15.5 Hz, 11.5 Hz), 7.57 (s, 1H), 7.55 (s, 1H), 7.13 (s, 1H), 7.10 (s, 1H), 6.50 (t, 1H, J=11.5 Hz), 6.14 (d, 1H, J=15.5 Hz), 5.97 (d, 1H, J=11.5 Hz). ¹³C NMR (DMSO- d_6 , 100 MHz): δ 166.73, 166.39, 137.02, 135.11, 130.87, 126.95.

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APPENDICES

List of ¹H NMR Spectra of Selected Compounds

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1. 400 MHz ¹H NMR Spectrum (DMSO) of D-glucaramide



-0.0002





2. 400 MHz ¹H NMR Spectrum (DMSO) of (*E, Z*)-muconamide





00.00



3. 400 MHz ¹H NMR Spectrum (DMSO) of 2-chloropyridinium perrhenate



4. 400 MHz $^1\mathrm{H}$ NMR Spectrum (CDCl_3) of lutidinium perrhenate



5. 400 MHz ¹H NMR Spectrum (DMSO) of collidinium perrhenate



6. 400 MHz $^1\mathrm{H}$ NMR Spectrum (CDCl_3) of tetrahexylammonium perrhenate



7. 400 MHz ¹H NMR Spectrum (CDCl₃) of 3-methyl-1-pentyl-imidazolium perrhenate

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1. 100 MHz ¹³C NMR Spectrum (DMSO) of D-glucaramide





Abstract in Korean

현시대의 고분자 산업에서 단량체 공급은 대부분 석유 산업에서 충족되 어 왔다. 하지만 점차 심화되는 석유 고갈 문제로 인해, 새로운 공급원 을 찾는 데에 많은 노력이 집중되고 있다. 이 논문의 최종 목표 물질로 서 나일론 6, 6의 단량체 중 하나인 아디프산의 경우는 특히 그 공급이 석유산업에 집중되어있기 때문에, 이를 대체하기 위해서 시작 물질로 글 루카릭산 칼륨염이 사용되었다. 이것은 매우 저렴하고 지속적으로 공급 가능한 바이오매스인 글루코스로부터 산화시켜 만들어 지며, 간단한 반 응을 통해 높은 수율의 글루카라마이드로 전환이 가능하고, 이후 효율적 인 탈산소탈수화반응(DODH)을 통해 중요한 중간체인 뮤코나마이드를 합성 할 수 있다. 탈산소탈수화반응은 비시널 다이올을 이용해 알킨을 합성할 수 있는 효율적인 방법으로써, 반응물인 글루카라마이드의 네 개 의 연속된 하이드록실 작용기들을 두개의 알킨으로 전화하여 최종적으로 시스, 트랜스 그리고 트랜스, 트랜스 두 형태의 뮤코나마이드를 합성 하 였다. 이 반응에서 중요한 것은 촉매, 환원제, 용매 세가지 인데, 3-펜탄 올은 2가 알코올로써 반응 내에서 용매와 환원제 두가지 역할을 모두 수행할 수 있었고, 벌키함 때문에 중요한 부반응으로 간주되는 에스터리 피케이션 반응을 막는 역할을 하였다. 다양한 레늄촉매가 시도되었고 그 중 암모늄퍼리네이트가 가장 집중적으로 연구되었으며, 0.1 당량 암모늄 퍼리네이트를 사용하여 1미리몰 스케일에서 90% 이상의 뮤코나마이드 를 합성할 수 있었다. 추가적으로, 0.2 당량의 피리디늄 계열 촉매 혹은 퍼레닉 애시드와 레늄옥사이드(VII)를 사용했을 때 상대적으로 단시간에 90% 이상의 수율의 결과를 얻을 수 있었고, 10미리몰 스케일까지 증가 시켰을 때도 90% 이상의 뮤코나마이드를 얻을 수 있었다.

주요어 : 바이오매스, 석유 기반 화학물질, 탈산소 탈수화 반응 학번 : 2017-20626