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Synthesis of Biobased Succinimide from Glutamic Acid via Silver-Catalyzed Decarboxylation

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Glutamic acid was transformed into succinimide in a two step procedure involving a dehydration in water to pyroglutamic acid followed by an oxidative decarboxylation using a silver catalyst.

10 With the accelerated depletion of oil resources, the chemical industry is in the transition from a petrochemical based industry toward a biobased one. Large-scale production of biobased chemicals is becoming a reality due to that biomass is the most abundant renewable carbon resource, including agricultural and
15 forest residues, municipal solid and liquid wastes.[1-3] Amino acids, which are on account of a high content of low-value products from biofuels production such as sugar beet vinasse, soybean mean meal, corn starch etc., become interesting starting materials for the synthesis of bio-based chemicals.
20 For example, the production of glutamic acid in 2020 is expected to reach 20 million tons in the world.[4] With amino, carboxyl functional groups and small backbone, amino acids are good industrial
25 intermediates. In particular, it does not require re-introducing the nitrogen atom compared with traditional petrochemical methods in the production of nitrogenous organic compounds.[3]
30 On one hand, glutamic acid, with an amino and two carboxyl groups, is an economically viable platform molecular that can be utilized to produce numerous nitrogen containing chemicals, such as acrylonitrile,[4]
35 aminobutyricacid (GABA),[5] N-methylpyrrolidone (NMP),[6] N-vinylpyrrolidone (NVP),[6] succinonitrile,[7] 3-cyanopropanoic acid[8] and Adiponitrile[9]. On the other hand, because of its versatile functions and benign properties, succinimide is considered as one of the most promising reproducible molecules that can be
40 converted into organic intermediates for the production of pesticides and pharmaceuticals such as N-chlorosuccinimide (NCS), N-bromosuccinimide (NBS) and N-iodosuccinimide (NIS). Furthermore, succinimide has notable commercial applications in silver plating processes and assay techniques.
45 Conventionally, succinic acid and nitrogen sources, including ammonia and urea, are needed for succinimide synthesis (Scheme 1).[10] Therefore, the development of a highly efficient catalytic system, which can be applied in mild condition for the production of succinimide from glutamic acid without additional nitrogen
50 sources is imminent.

Herein we report the synthesis of succinimide, without the use of additional nitrogen, by using glutamic acid as feedstock in a two-step procedure (Scheme 1). The procedure involves the heating dehydration cyclization of glutamic acid to pyroglutamic
55 acid,[11] followed by oxidative decarboxylation using silver as catalyst and persulfate as oxidant. Using a catalytic amount of silver, this reaction achieves a sustainable industrial route to produce succinimide from biomass feedstock in mild condition and much higher yield by simple steps compared with some
60 previous methods.

In our experimental program, the second step is critical. The
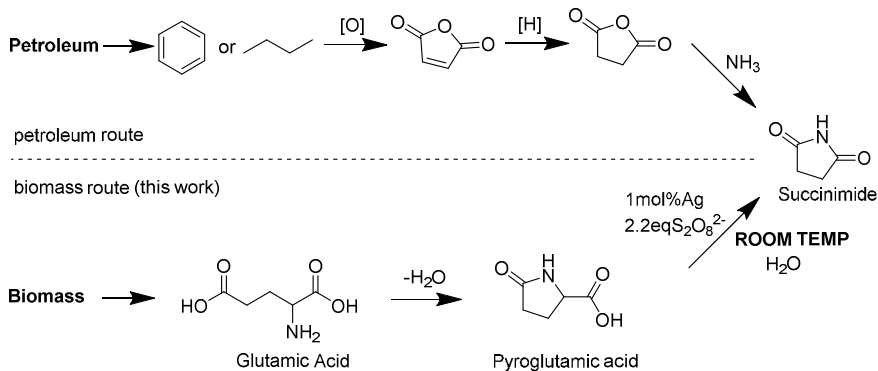
Scheme 1 Comparison chart of succinimide synthesis from petroleum and biomass

method using iodosobenzene to oxidative decarboxylation has been reported, but the yield was low and the reaction time was too long to be applied in industry.[12] Recently, Chaozhong Li et al.
65 reported the use of silver salts as catalyst for decarboxylative fluorination[13] and chlorination[14] of various aliphatic carboxylic acids in high yields under mild condition. Moreover, under the above condition, Chaozhong Li et al. realized the decarboxylation alkynylation with $K_2S_2O_8$ as the oxidant in aqueous solution
70 using $AgNO_3$ as catalyst.[15] In addition, Lu Lin et al. reported oxidative decarboxylation of levulinic acid to 2-butanone by $AgNO_3$ with persulfate.[16] These approaches are considered to be commercially viable, high efficient and chemselective methods under mild condition for decarboxylation.

Table 1 Optimisation of the oxidative decarboxylation of pyroglutamic acids using different kinds and amount of the oxidizing reagents [a]

Entry	Cat. (mol%)	Oxidant (eq)	Time/h	Conv./%[b]	Yield/%[b]
1	AgNO$_3$ (1%)	K$_2$S$_2$O$_8$ (1.0)	10	71	36
2	AgNO$_3$ (1%)	K$_2$S$_2$O$_8$ (2.2)	10	100	97
3	AgNO$_3$ (1%)	K$_2$S$_2$O$_8$ (2.2)	2	100	71
4	AgNO$_3$ (1%)	Na$_2$S$_2$O$_8$ (2.2)	2	100	98
5	**AgNO$_3$ (1%)**	**(NH$_4$)$_2$S$_2$O$_8$ (2.2)**	**2**	**100**	**>99 (96)**
6	AgNO$_3$ (1%)	0	10	27	0
7	0	K$_2$S$_2$O$_8$ (2.2)	10	19	7
8	0	(NH$_4$)$_2$S$_2$O$_8$ (2.2)	10	18	6

[a] Reaction conditions: pyroglutamic acid (130mg, 1mmol), AgNO$_3$(1.7mg, 0.01mmol), water (3mL), persulfate (2.2mmol), room temperature; [b] Determined by HPLC, yield of isolated product is in parenthesis.

Inspired by the above works, we initially investigated the influence of the amount and types of persulfate on the yields. The initial experiments were performed at room temperature in water in the presence of 1mol% of the AgNO$_3$ catalyst. After 10 h, for 1
5 equivalent of K$_2$S$_2$O$_8$, we observed that the succinimide yield was 36% (Table 1, entry 1). However, when the amount of K$_2$S$_2$O$_8$ increased to 2.2 eq, the yield increased to 97% (Table 1, entry 2). It was foreseeable that without the catalyst, the yield decreased to 7% (Table 1, entry 7).
10 Such experimental results suggested the catalytic mechanism of silver as shown in Scheme 2. Firstly, one mole of Ag(I) ions are oxidized to Ag(II) ions by 0.5 mole of the persulfate ions, the generated Ag(II) ions convert free carboxyl group in the pyroglutamic acid into a carboxyl radical, and Ag(II) ions return
15 to Ag(I) ions. Next, the unstable carboxyl radical decarboxylates into carbon radical, which is affected by the adjacent nitrogen atom's higher electronegativity and oxidized to enamine by 0.5 mole of the persulfate ions. Then, by an addition of water, the unsaturated enamine is converted into hydramine. Finally, by
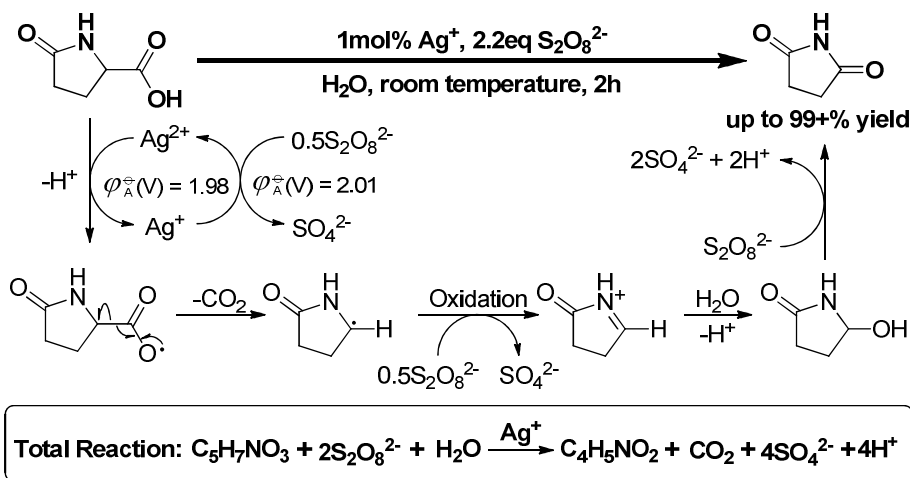
Table 2 The effect of different silver salts on the yield of succinimide [a]

Entry	Cat. (mol%)	Oxidant (eq)	Time/h	Conv./%[b]	Yield/%[b]
1	AgOAc (1%)[c]	(NH$_4$)$_2$S$_2$O$_8$ (2.2)	2	100	>99 (96)
2	Ag$_2$SO$_4$ (0.5%)[d]	(NH$_4$)$_2$S$_2$O$_8$ (2.2)	2	100	96 (92)
3	Ag$_2$CO$_3$ (0.5%)[e]	(NH$_4$)$_2$S$_2$O$_8$ (2.2)	2	100	99 (93)
4	Ag$_3$PO$_4$ (0.3%)[f]	(NH$_4$)$_2$S$_2$O$_8$ (2.2)	2	100	>99 (94)
5	AgCl (1%)[g]	(NH$_4$)$_2$S$_2$O$_8$ (2.2)	2	48	34

[a] Reaction conditions: apyroglutamic acid (130mg, 1mmol), Ag(I) ion (0.01mmol), water (3ml), (NH$_4$)$_2$S$_2$O$_8$ (0.50g, 2.2mmol), room temperature; [c] Determined by HPLC, yield of isolated product is in parenthesis; [c] AgOAc (1.7mg, 0.01mmol); [d] Ag$_2$SO$_4$ (1.7mg, 0.05mmol); [e] Ag$_2$CO$_3$ (1.4mg, 0.05mmol); [f] Ag$_3$PO$_4$ (1.4mg, 0.003mmol); [g] AgCl (1.5mg, 0.01mmol).

20 another one mole of the persulfate ions, the hydramine is oxidized into an amide. Throughout the course of this reaction, the process to succinimide consumes a total of two mole of the persulfate ions.[17] Silver, as a catalyst, plays a crucial role in the reaction: The reduction potential of Ag(II) is about 1.98V and the
25 reduction potential of S$_2$O$_8^{2-}$ is about 2.01V, at this point, silver is selected as a bridge connecting pyroglutamic acid with oxidant S$_2$O$_8^{2-}$ and leads pyroglutamic acid to a radical decarboxylation way which requires only mild conditions based on the literatures where oxidation of carboxylate anions by Ag(II) complexes was
30 mentioned.

Next, we reduced the reaction time to 2h with all other conditions unchanged, the yield reduced to 71% (Table 1, entry 3). However, when the oxidant was changed to Na$_2$S$_2$O$_8$, the yield increased to 98% and with the oxidant of (NH$_4$)$_2$S$_2$O$_8$, it
35 showed the highest yield more than 99% (Table 1, entry 4 and 5). The results demonstrate the effect of different persulfates on yields and the difference may be due to their different solubility. Under the conditions described in the experimental section (water 3mL, persulfate 2.2mmol), the concentration of persulfate
40 theoretically was about 0.7mol/L. However, at room temperature, the concentration of persulfate was less than 0.2mol/L. As a result, K$_2$S$_2$O$_8$ can not be completely dissolved by calculation so that the ratio theoretically required of pyroglutamic acid and persulfate can
5 not be achieved. Whereas, the solubility of Na$_2$S$_2$O$_8$ or (NH$_4$)$_2$S$_2$O$_8$ can be far from meeting the ratio to obtain a high yield.[18]

With the optimized oxidant
0 (NH$_4$)$_2$S$_2$O$_8$, we then explored the effect of different silver salts on the yield and the results were summarized in Table 2. To investigate the catalytic efficiency of different silver salts, we
5 used AgOAc (1mol%), Ag$_2$SO$_4$ (0.5mol%), Ag$_2$CO$_3$ (0.5mol%), Ag$_3$PO$_4$ (0.3mol%) and AgCl (1mol%) instead of AgNO$_3$ (1mol%) with all other conditions unchanged.
0 When the Ag(I) ion was added with an amount of 1 mol%, most of the

Scheme 2 The proposed catalytic mechanism

Total Reaction: C$_5$H$_7$NO$_3$ + 2S$_2$O$_8^{2-}$ + H$_2$O $\xrightarrow{Ag^+}$ C$_4$H$_5$NO$_2$ + CO$_2$ + 4SO$_4^{2-}$ + 4H$^+$

silver catalyst efficiency remained at a high level (Table 2, entries 1 ~ 4) except AgCl. The yield of AgCl was markedly reduced to 34% (Table 2, entry 5). Based on these results, taking into account the major difference of these catalysts on solubility, we predicted that the solubility of the catalyst would largely affect the catalytic efficiency when the amount of dissolved catalyst was insufficient to achieve the required amount of catalytic theory. After calculation, based on the amount of catalyst added and their respective K_{sp},[19] the actual concentration of Ag(I) from AgCl dissolved in the aqueous solution was only 1.34×10^{-5}mmol/mL. For Ag_2CO_3 (0.5mol%) and Ag_3PO_4 (0.3mol%), whose yields remained at more than 99%, the actual amount of water-soluble salt was only about 2.96×10^{-4}mmol/mL and 1.43×10^{-4}mmol/mL. Seen in this light, the amount of catalyst required in the process of oxidative decarboxylation using silver as catalyst and persulfate as oxidant is minimal (high TON up to 10^4), which is crucial for practical applications.

The above silver-catalyzed oxidative decarboxylation was then extended to other transition metal such as copper and nickel. Nevertheless, these compounds, such as $Cu(NO_3)_2$ (1mol%), $CuSO_4$ (1mol%), $Cu(OAc)_2$ (1mol%), $Ni(NO_3)_2$ (1mol%) and $Ni(OAc)_2$ (1mol%), did not exhibit good catalytic effect (Table 3, entries 1 ~ 5), even though they have a good solubility in water without considering the factor that the dissolved amount is too small to exert its effect. In addition, we selected $Al(NO_3)_3$ as a typical example of short-period mental elements as a catalyst, but an unsatisfactory result was also presented with the yield of 3% (Table 3, entry 6). These results all support the involvement redox cycling reaction of silver mechanism in the oxidation by $S_2O_8^{2-}$. We know that the reduction potential of $S_2O_8^{2-}$ is about 2.01V. At this point, silver was selected as a bridge connecting pyroglutamic acid and oxidant $S_2O_8^{2-}$ thanks to the reduction potential of 1.98V to promote the oxidative decarboxylation based on the literatures where oxidation of carboxylate anions by Ag(II) complexes was mentioned.[20] Until now, we have chosen silver as the best catalyst for the oxidative pyroglutamic of pyroglutamic acid.

Table 3 The effect of different metals on the yield of succinimide[a]

Entry	Cat. (mol%)	Oxidant (eq)	Time/h	Conv./%[b]	Yield/%[b]
1	$Cu(NO_3)_2$ (1%)[c]	$(NH_4)_2S_2O_8$ (2.2)	2	39	6
2	$CuSO_4$ (1%)[d]	$(NH_4)_2S_2O_8$ (2.2)	2	40	7
3	$Cu(OAc)_2$ (1%)[e]	$(NH_4)_2S_2O_8$ (2.2)	2	36	6
4	$Ni(NO_3)_2$ (1%)[f]	$(NH_4)_2S_2O_8$ (2.2)	2	38	5
5	$Ni(OAc)_2$ (1%)[g]	$(NH_4)_2S_2O_8$ (2.2)	2	36	3
6	$Al(NO_3)_3$ (1%)[h]	$(NH_4)_2S_2O_8$ (2.2)	2	38	3

[a] Reaction conditions: apyroglutamic acid (130mg, 1mmol), Ag(I) ion (0.01mmol), water (3ml), $(NH_4)_2S_2O_8$ (0.50g, 2.2mmol), room temperature; [b] Determined by HPLC; [c] $Cu(NO_3)_2$ (1.9mg, 0.01mmol), [d] $CuSO_4\cdot5H_2O$ (2.5mg, 0.01mmol), [e] $Cu(OAc)_2$ (1.8mg, 0.01mmol), [f] $Ni(NO_3)_2\cdot6H_2O$ (2.9mg, 0.01mmol), [g] $Ni(OAc)_2\cdot4H_2O$ (2.5mg, 0.01mmol) and [h] $Al(NO_3)_3\cdot9H_2O$ (3.7mg, 0.01mmol).

Conclusions

In summary, we reported a sustainable succinimide preparation method without the use of additional nitrogen. Using silver as the catalyst, we achieved the conversion from a biobased chemical (glumatic acid) to target product (succinimide) in excellent yields under mild conditions. We observed the yield up to 96% in aqueous solution at room temperature after only 2h with the minimal amount of catalyst. At the same time, this process was simple and green with only two steps and water as the solvent instead of some organic solvents which were toxic or expensive. In this way, it opened a green way for succinimide production from biomass and pushed the skylight to see the broad application prospects of biomass resources.

Experimental Section

Preparation of pyroglutamic acid from glutamic acid:
In a typical experiment, a beaker was filled with glutamic acid (100g) and placed in an oil bath (145~150℃). The dehydration reaction incubated for 45 minutes and the solution gradually turned brown. After the dehydration reaction, the solution was poured into boiling water (350ml) and dissolved in the water. When the temperature droped to 40~50℃, the solution was bleached by activated carbon twice and became colorless. The colorless solution was concentrated by directly heating until the volume was reduced to about half, then the solution was placed in a water both. When the volume of solution continued to decline to 1/3, the heat source was removed. The solution cooled and crystallized slowly. After 10~ 20h, a kind of colorless prismatic crystal (pyroglutamic acid) was prepared.

Preparation of succinimide
In a typical experiment, a reaction tube was filled with pyroglutamic acid (0.13g, 1mmol), $AgNO_3$ (1.7mg, 0.01mmol), $(NH_4)_2S_2O_8$ (0.50g, 2.2mmol) and water (3ml).Then, the solution was stirred at room temperature for 2h. After sufficient reaction, the solvent was removed under reduced pressure. The product was analyzed by ^{1}HNMR spectrum and HPLC to determine the pyroglutamic acid yield (>99%). HPLC apparatus: Hitachi L2000 HPLC; Column: Alltima C18(5µ*250mm*4.6mm); mobile phase: methanol : water = 10 : 90 (v / v, containing 0.1% phosphoric acid); flow rate: 1.0mL/min; column temperature: 30°C; detector: diode array; detection wavelength: 204nm

Under the same conditions described above, with $AgNO_3$ as the catalyst, the kinds and amount of the oxidizing agents were replaced, the reaction time (stirring time) and the present or absence of catalyst were described in Table 1. According to the method as above, the product was tested by HPLC. The conversion rate of pyroglutamic acid and yield of pyroglutamic acid were listed in Table 1.

Under the same conditions described above, with $(NH_4)_2S_2O_8$ as the oxidant, the catalyst was replaced as described in Table 2 and Table 3. According to the method as above, the product was tested by HPLC. The conversion rate of pyroglutamic acid and yield of pyroglutamic acid were listed in Table 2 and Table 3 respectively.

Acknowledgements

Notes and references

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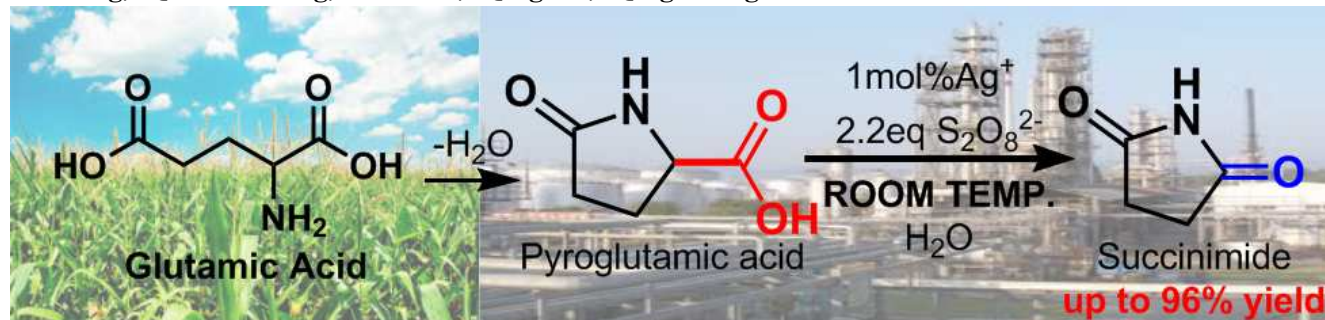
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