



Communication

Synthesis of bis(amino)furans from biomass based 5-hydroxymethyl furfural

Xiaoyu Wang^a, Wei Chen^a, Zheng Li^a, Xianhai Zeng^{a,b,*}, Xing Tang^{a,b}, Yong Sun^{a,b}, Tingzhou Lei^c, Lu Lin^{a,b,*}

^a College of Energy, Xiamen University, Xiamen 361102, Fujian, China

^b Xiamen Key Laboratory of High-valued Conversion Technology of Agricultural Biomass, Xiamen University, Xiamen 361102, Fujian, China

^c Henan Key Laboratory of Biomass Energy, Zhengzhou 450008, Henan, China

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ABSTRACT

In this study we report a new reaction pathway in which the hydroxyl and the aldehyde groups of 5-hydroxymethyl furfural were aminated respectively. Hydroxyl group was aminated via Ritter reaction followed by direct reductive amination of aldehyde group. For the Ritter reaction of 5-hydroxymethyl furfural, mixture of trifluoromethane sulfonic acid and phosphoric anhydride showed good performance and the intermediate *N*-acyl-5-aminomethyl furfural with the highest yield of 89.1 wt% was obtained. Optimization of direct reductive amination of 2,5-bis(aminomethyl) furan was conducted and a yield of 45.7 wt% was achieved. This study presents a simple way for preparing bis(amino)furans from renewable biomass based 5-hydroxymethyl furfural, which enriches the biorefinery concept from biomass.

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As an important platform chemical derived from biomass, 5-hydroxymethyl furfural (HMF) is attracting increasing attention owing to the unique chemical structure containing both hydroxyl and aldehyde groups. It can be converted to a variety of value-added furan compounds such as 2,5-dimethylfuran (DMF), 2,5-diformylfuran (DFF), 2,5-furandimethanol (FDM), 2,5-furandicarboxylic acid (FDCA), 5-chloromethylfurfural (CMF), and 5-acetoxymethylfurfural (AMF) [1–6]. Moreover, HMF has attracted attention in the synthesis of polymers as it contains similar structure as aromatics. It is reported that HMF has been used for the production of special phenolic resins with phenol [7].

Amines, especially primary amines and di-amines, are important intermediates in chemical industry for polymerization reactions [8,9]. As a new type of 2,5-disubstituted furan derivative, 2,5-bis(aminomethyl)furan (BAF) is considered as a monomer for polymers such as polyamides and polyurethanes [10–12]. Generally, various types of amines are assembled with the reduction of aldehyde amine compounds [13,14]. BAF can be generated by the further reduction of DFF, which is obtained via direct processes from carbohydrates or HMF [15]. Haas et al. described a two-step pathway for preparing BAF from DFF in the presence of Raney-Ni cat-

alyst with a yield of 76% [16]. Most recently, Le et al. claimed the direct reductive amination of DFF to BAF with Raney-Ni catalysts under mild conditions and the yield of BAF is 42.6%. However, by-products of secondary, tertiary and polymeric amine species were generated due to the condensation of the reactive di-aldehyde and di-amines groups [17].

We describe a new reaction pathway in which the hydroxyl and the aldehyde groups of HMF were aminated successively (Scheme 1). N atoms were introduced into HMF in two steps separately, during which the hydroxylmethyl group was converted to amide group by Ritter reaction followed by the reductive amination of the aldehyde group to primary amine. Subsequently, BAF was obtained by simple hydrolysis. This special reaction pathway got rid of the formation of DFF and thus, the generation of polymers in further reductive amination was avoided.

5-Hydroxymethyl furfural, trifluoromethane sulfonic acid, Raney-Ni were purchased from Aladdin Chemical Reagent (Shanghai, China). All other chemicals were supplied by Sinopharm Chemical Reagent Co. Ltd. (Shanghai, China) and used without further purification.

In a typical reaction, trifluoromethane sulfonic acid (0.45 g, 3.0 mmol) was added dropwise to HMF (1 g, 1.62 mmol) in 20 mL acetonitrile, and kept at 100 °C. The solution was neutralized with sodium bicarbonate after 3 h and then 10 mL deionized water was added. Then the product was extracted by 20 mL chloroform for

* Corresponding authors.

E-mail addresses: xianhai.zeng@xmu.edu.cn (X. Zeng), lulin@xmu.edu.cn (L. Lin).

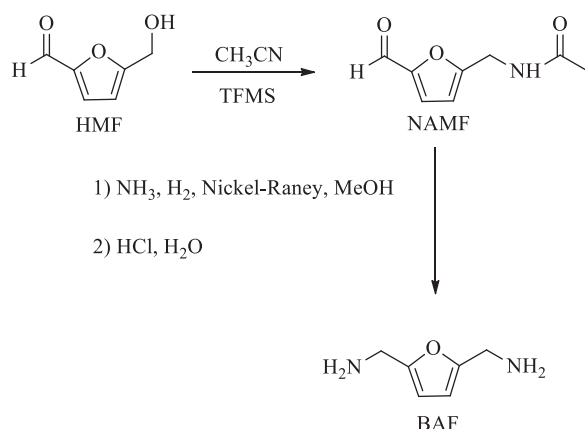
Abbreviations

HMF	5-Hydroxymethyl furfural
NAMF	<i>N</i> -Acyl-5-aminomethyl furfural
NBAF	<i>N</i> -Acyl-2,5-bis(aminomethyl)furan
BAF	2,5-bis(Aminomethyl)furan
DFF	2,5-Diformylfuran
OMBF	5,5'-Oxydimethylenebis (2-furfural)
MHP	5-Methyl-2-hydroxypyridine
TFMS	Trifluoromethane sulfonic acid

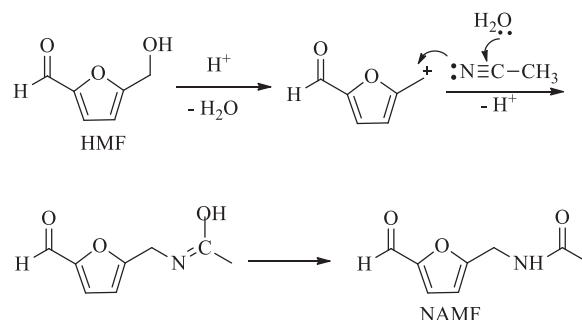
five times. The organic phase was evaporated at 45 °C under vacuum and the obtained NAMF raw product was dried with sodium sulfate. The raw product was then purified by silica gel column ($\text{CHCl}_3:\text{CH}_3\text{COOCH}_2\text{CH}_3 = 2:1$). After that, brown NAMF oil was finally obtained.

The NAMF raw product was dissolved in methanol to make a 30 wt% solution. The experiments were performed in a 50 mL cylindrical stainless steel high-pressure reactor (PARR 4848, instrument company, USA). In a typical reductive amination reaction, the reactor was loaded with NAMF solution (20 mL), Raney-Ni (0.05 g), ammonia (5 mL), and then hydrogen was introduced for several times to remove air. Thereafter, hydrogen was charged into the reactor with a pressure of 15 bar (at room temperature). After cooling down, the gaseous phase was released, and the catalyst was removed with centrifugation from the solution, whilst the supernatant is collected. Hydrochloric acid was added into the supernatant to hydrolyze NBAF, and then $\text{BAF}\cdot\text{HCl}$ was obtained. Subsequently, the pH of the solution was adjusted to 13 with 40 wt% sodium hydroxide solution to give BAF, which was then extracted with 20 mL ethyl acetate for five times. The organic phase was evaporated under vacuum and dried over sodium sulfate. The product was distilled under vacuum and BAF as colorless liquid was obtained with high purity at 115–120 °C.

The raw products from reaction were identified by Shimadzu GCMS-QP2010SE instrument with Rtx-5MS column (length 30 m, inner diameter 0.20 mm, film thickness 0.33 μm) and electron impact ionization (EI), with a 25 μA emission current and electron energy of 70 eV. Carrier gas was He with an elution rate of 1.00 mL/min and a split ratio of 5:1. Samples were injected (1 μL) from the auto sampler and the temperature program was as follows: initial oven temperature was set to 40 °C for 1 min, and then heated to 280 °C at 10 °C/min and held at 280 °C for 1 min. Quantitation by GC–MS was carried out using internal standards. Determination of the products (by-products) was performed us-



Scheme 1. Synthetic pathway for preparing BAF from HMF.



Scheme 2. Reaction mechanism for the conversion of HMF to NAMF by Ritter reaction.

ing full scan mode. Characteristic ions with the highest abundance were selected as the quantitative ion peak and product/by-product were identified and quantified. Typically, NAMF, OMBF and BAF were calculated as follows:

$$\text{NAMF yield (wt\%)} = \frac{\text{the weight of NAMF}}{\text{initial weight of HMF}} \times 100\%$$

$$\text{NAMF yield (mol\%)} = \frac{\text{mole of NAMF}}{\text{initial mole of HMF}} \times 100\%$$

$$\text{OMBF yield (wt\%)} = \frac{\text{the weight of OMBF}}{\text{initial weight of HMF}} \times 100\%$$

$$\text{BAF yield (wt\%)} = \frac{\text{the weight of BAF}}{\text{initial weight of NAMF}} \times 100\%$$

$$\text{BAF yield (mol\%)} = \frac{\text{mole of BAF}}{\text{initial mole of NAMF}} \times 100\%$$

In Ritter reaction, nitriles were converted to *N*-alkyl amides with alkylation agents such as isobutylene and alcohols [18,19]. The aldehyde group of HMF can be directly converted to primary amine by reductive amination. However, the hydroxymethyl group could be acylated instead of direct reductive amination [20]. In the presence of strong acids, HMF carbocation could be generated and attacked by nitrogen atom in nitrile (Scheme 2). Primary amine was obtained with further hydrolysis reaction unless a final product was reached, as primary amine was much more unstable than *N*-acyl-5-aminomethyl group [21]. Herein, the Ritter reaction not only introduced the N atom into hydroxyl group of HMF, but also the primary amino protector via the amide group generated during the reaction.

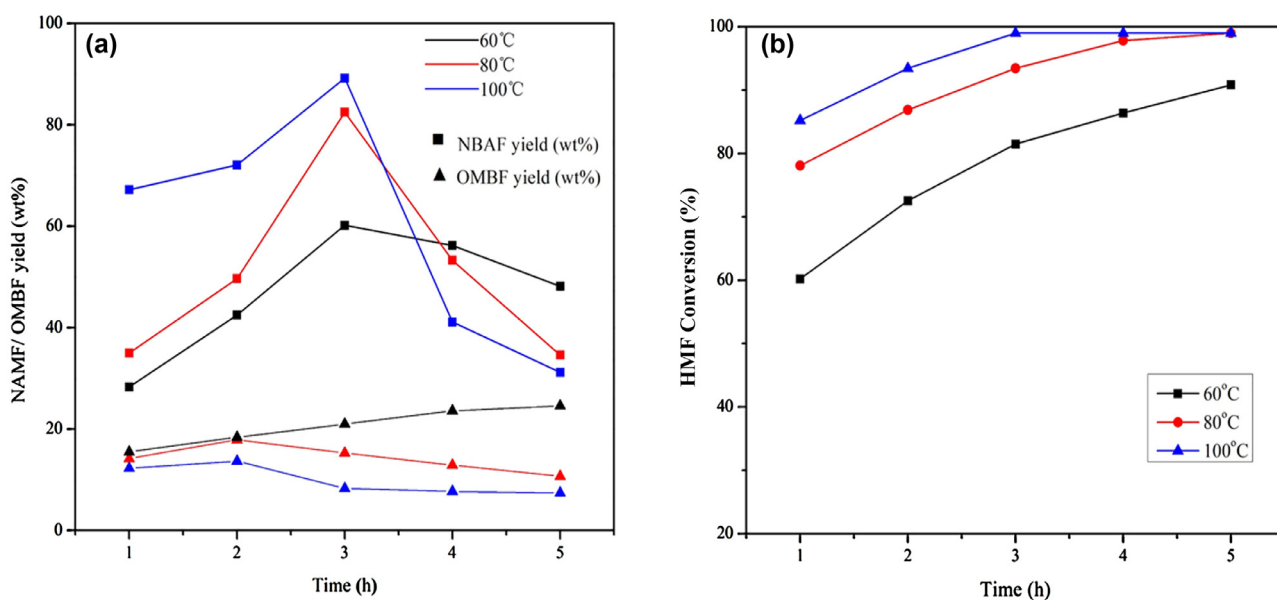
Considering that acetonitrile is the simplest nitrile molecule, it was applied as the solvent in this study. Strong acids such as sulfonic acid, trifluoromethane sulfonic acid ($\text{CHF}_3\text{O}_3\text{S}$), and especially, a mixture of $\text{CHF}_3\text{O}_3\text{S}$ and phosphoric anhydride, were preferred. HMF and acetonitrile solution were mixed and maintained at 100 °C for 3 h in the presence of $\text{CHF}_3\text{O}_3\text{S}$ and the highest yield of NAMF of 89.1 wt% (67.2 mol%) was obtained (Table 1). We observed that the yield of NAMF increased with the increase of acid loading (Table 1, Entries 1–5). 5,5'-Oxydimethylenebis (2-furfural) (OMBF) as the main by-product has been detected in the reaction, and the yield decreased with the increase of acid content. However, it dropped down once the $\text{CHF}_3\text{O}_3\text{S}$ content was as high as 6.7 mmol (Table 1, Entry 5), probably due to that more undesired by-products such as soluble polymers and insoluble humins were formed [22].

For the different catalysts, the conversion increased with increasing acid strength (Table 1, Entries 4, 7, 10). When the mixture of two acids ($\text{CHF}_3\text{O}_3\text{S}$ or H_2SO_4 and P_2O_5) was applied, the yield of NAMF significantly increased. It was attributed to that

Table 1. NAMF preparation from HMF in the acetonitrile system.

Entry	Acid	Dosage (mmol)	Time (h)	Conversion (%)	NAMF yield (wt%)	NAMF yield (mol%)	OMBF yield (wt%)
1	CH ₃ CO ₃ S	1.0	3	83.3	30.9	23.3	46.0
2	CH ₃ CO ₃ S	1.7	3	90.3	54.3	40.9	34.6
3	CH ₃ CO ₃ S	2.3	3	96.2	69.8	52.6	13.8
4	CH ₃ CO ₃ S	3.0	3	100.0	82.6	62.3	8.2
5	CH ₃ CO ₃ S	6.7	3	100.0	70.3	52.7	6.7
6	H ₂ SO ₄	3.0	2	66.5	52.9	39.9	9.7
7	H ₂ SO ₄	3.0	3	78.7	70.1	52.9	7.2
8	H ₂ SO ₄	3.0	4	89.1	79.1	59.6	5.3
9	H ₂ SO ₄	3.0	5	100.0	75.5	56.9	4.8
10	P ₂ O ₅	3.0	3	41.3	18.5	13.9	20.1
11	CH ₃ CO ₃ S & P ₂ O ₅	3.0:3.0	2	93.2	81.3	61.3	9.5
12	CH ₃ CO ₃ S & P ₂ O ₅	3.0:3.0	3	100.0	88.5	66.7	5.2
13	H ₂ SO ₄ & P ₂ O ₅	3.0:3.0	2	89.5	65.1	49.1	15.2
14	H ₂ SO ₄ & P ₂ O ₅	3.0:3.0	3	92.1	77.9	58.7	10.8
15	H ₂ SO ₄ & P ₂ O ₅	3.0:3.0	4	100.0	81.7	61.6	6.5
16	CH ₃ CO ₃ S & P ₂ O ₅	3.0: 6.0	3	100.0	89.1	67.2	4.9

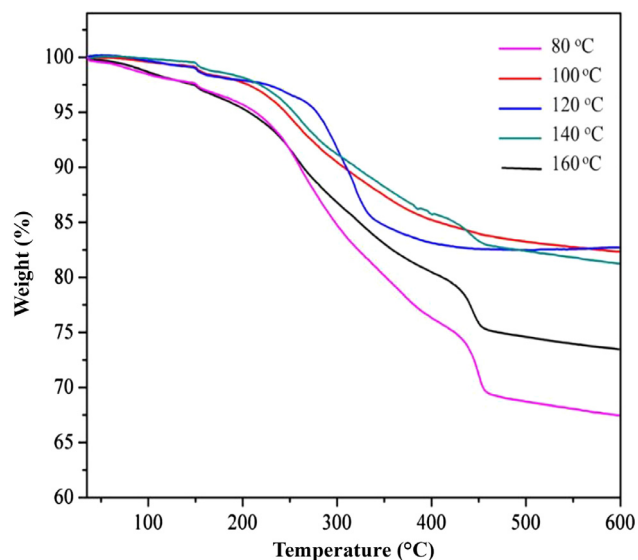
The reaction conditions: HMF: 1.0 g; acetonitrile: 20 mL; temperature: 100 °C.

**Fig. 1.** Optimization of reaction conditions on NAMF production. (a) The yield of NAMF and OMBF, (b) the conversion of HMF.

P₂O₅ with strong hygroscopicity promoted acid anhydride formation from CH₃CO₃S and H₂SO₄ (Table 1, Entries 4 and 12). However, the change of TMFS to P₂O₅ ratio showed almost no influence on the yield of NAMF (Table 1, Entries 4, 12 and 16).

We then studied the conversion of HMF to NAMF at 60, 80, and 100 °C with different reaction durations. As shown in Fig. 1(a), the yield of NAMF was increased with prolonged reaction time from 1 to 3 h under different reaction temperatures. Raising the reaction temperature showed a considerably positive effect on the formation of NAMF with the reaction duration of no more than 3 h. The NAMF yield decreased quickly once the reaction time extended to 5 h, which indicated the occurrence of side reactions. At 60 °C, the yield of OMBF gradually increased with the increase of reaction time, while it increased first and then decreased at 80 and 100 °C, probably due to the polymerization of OMBF to humins.

The direct reductive amination of aldehyde group to primary amine using ammonia in THF-water mixed medium has been reported by Le and co-workers [17]. In our study, the direct reductive amination of NAMF with ammonia to NBAF with Raney-Ni catalysts under mild conditions in methanol-ammonia system was applied. BAF was obtained by hydrolysis of NBAF. The effect of temperature on the BAF yield was studied in a temperature range of 80–160 °C (Table 2). The yield of BAF was obviously affected by

**Fig. 2.** The weight loss of used Raney-Ni at different temperatures.

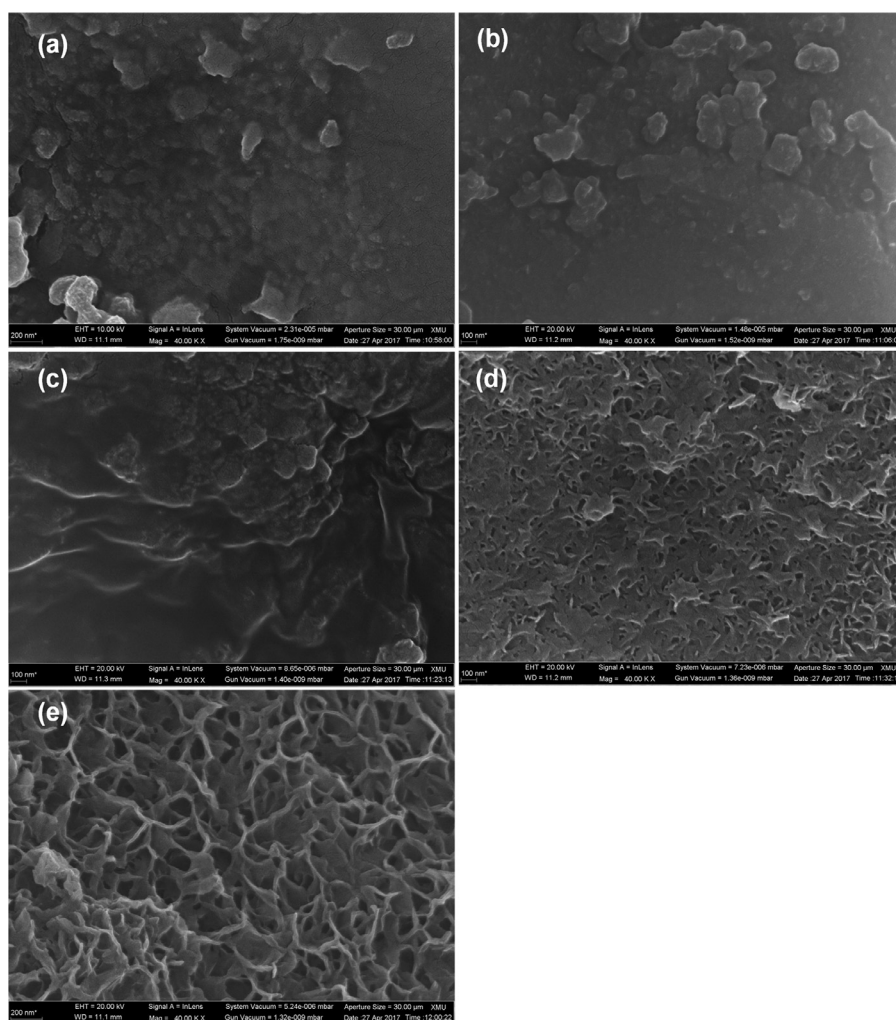


Fig. 3. SEM images of spent Raney-Ni at different temperatures. (a) 80 °C, (b) 100 °C, (c) 120 °C, (d) 140 °C, (e) 160 °C.

Table 2. BAF production from NAMF in CH₃OH–ammonia system.

Entry	Temperature (°C)	Time (h)	Hydrogen pressure (bar)	Conversion (%)	BAF yield (wt%)	BAF yield (mol%)
1	80	3	15	100	12.8	17.0
2	100	3	15	100	34.0	45.2
3	120	3	15	100	45.7	60.8
4	140	3	15	100	43.1	57.3
5	160	3	15	100	42.4	56.4
6	120	1	15	100	31.6	42.0
7	120	2	15	100	36.3	48.3
8	120	4	15	100	33.8	45.0
9	120	5	15	100	33.2	44.1
10	120	3	5	100	30.5	40.6
11	120	3	10	100	36.9	49.1
12	120	3	20	100	45.1	60.0

The reaction conditions: NAMF 0.6 g, methanol 20 mL, ammonia 5 mL, Raney-Ni 0.05 g.

temperature, which was found to be really low at 80 °C and maximized at 120 °C. With the increase of temperature, there was a slight decrease of BAF yield after the maximum yield (45.7 wt%, 60.8 mol%, Entry 3) was reached (Table 2, Entries 2–5). The spent catalyst was filtered and dried and the thermogravimetric analysis showed that there were much more insoluble by-products observed at 80 or 160 °C than that at 100–140 °C (Fig. 2).

The SEM images of used Raney-Ni at different temperatures were represented in Fig. 3. The surface morphology of these catalysts was significantly different. Large particles were accumulated on the spent catalyst surface at the reaction temperature of 80 °C

while floccule or unshaped films were observed on the spent catalysts surface at 140 and 160 °C. The weight loss curves of 80, 140 and 160 °C showed a visible weight drop at ca. 450 °C because of the difference in composition. These particles, floccule or unshaped films were considered to be humins loaded to the catalyst surface, and the burning of humins at ca. 450 °C resulted in the weight drop. Appropriate temperature could reduce the formation of insoluble by-products and was beneficial to the accumulation of the products.

Although the conversion NAMF was totally converted after 1 h, the extension of reaction time was beneficial to the accumulation

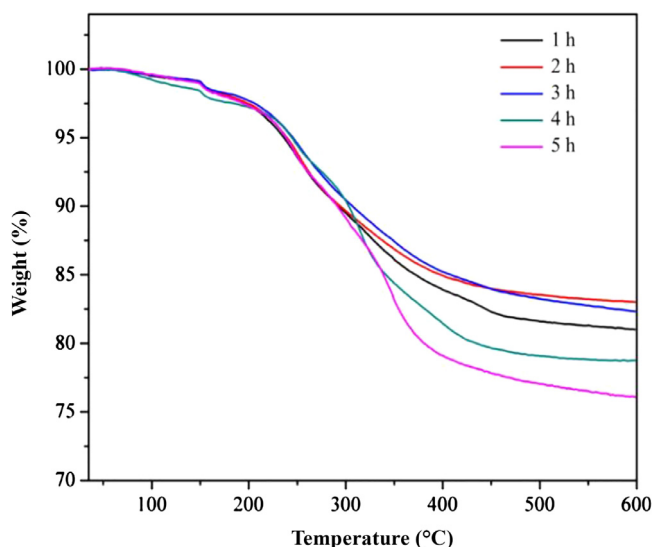


Fig. 4. The weight loss of used Raney-Ni at different times.

of BAF. The yield of BAF reached the maximum value of 45.7% (60.8 mol%) after 3 h, and then decreased with 4 h or longer reaction time (Table 2, Entries 3 and 6–9). The thermogravimetric analysis of spent Raney-Ni illustrated that the insoluble by-products (such as polymers) accumulation had a positive correlation of reaction time (Fig. 4). The SEM images of spent Raney-Ni at different times were shown in Fig. 5. The surface morphology of these spent catalysts was similar, which led to similar profiles of the weight loss curve. The similar morphology of humins was loaded to the catalyst surface which led to similar profiles of the weight loss curve.

The initial increase of hydrogen pressure from 5 to 10 bar significantly promoted the BAF accumulation, which meant hydrogen with enough dosage was essential for the reductive amination of NAMF (Table 2, Entries 3 and 10–12).

As described above, the reductive amination could be divided into amination and reduction sections. As shown in Scheme 3, the aldehyde group of NAMF first reacted with ammonia to form terminal imine with reversible reactions, which was then hydrogenated to NBAF over Raney-Ni. At the beginning of the reaction, NAMF was converted into imine, and part of the imine was hydrogenated to form NBAF. This explained why the conversion of NAMF was 100% and the yield of BAF was low after 1 h.

There might be a series of secondary reactions in the reaction. NAMF, imine and NBAF might polymerize to cyclic trimer, linear oligomeric or polymeric imine species. These imine intermediates were further subjected to transamination to NBAF with ammonia, followed by hydrogenation of the furanic imine, which formed NBAF (Scheme 3, route 1). Furthermore, BAF hydrochloride was obtained with hydrochloric acid hydrolysis of NBAF. On the other hand, the polymeric imine intermediates could be reduced by the direct hydrogenation to polyamines (Scheme 3, route 2) [17].

A two-step procedure for BAF synthesis via Ritter reaction and direct reductive amination of biomass derived HMF has been developed. Besides Ritter reaction, the process involves imine formation from the direct reductive amination of HMF with amines followed by hydrogenation. The method presented in this study is feasible for the preparation of BAF as well as several intermediates and other bis(amino)furans. Although further optimization is still needed, this method provides a new pathway for synthesizing amino-hydroxymethylfurans for the pharmaceutical and polymer industries.

Acknowledgments

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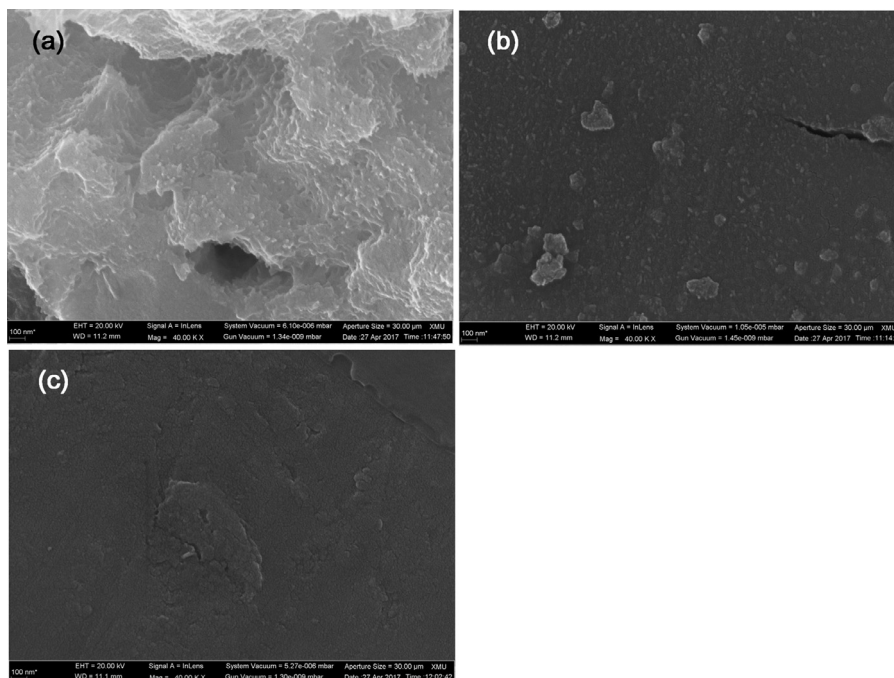
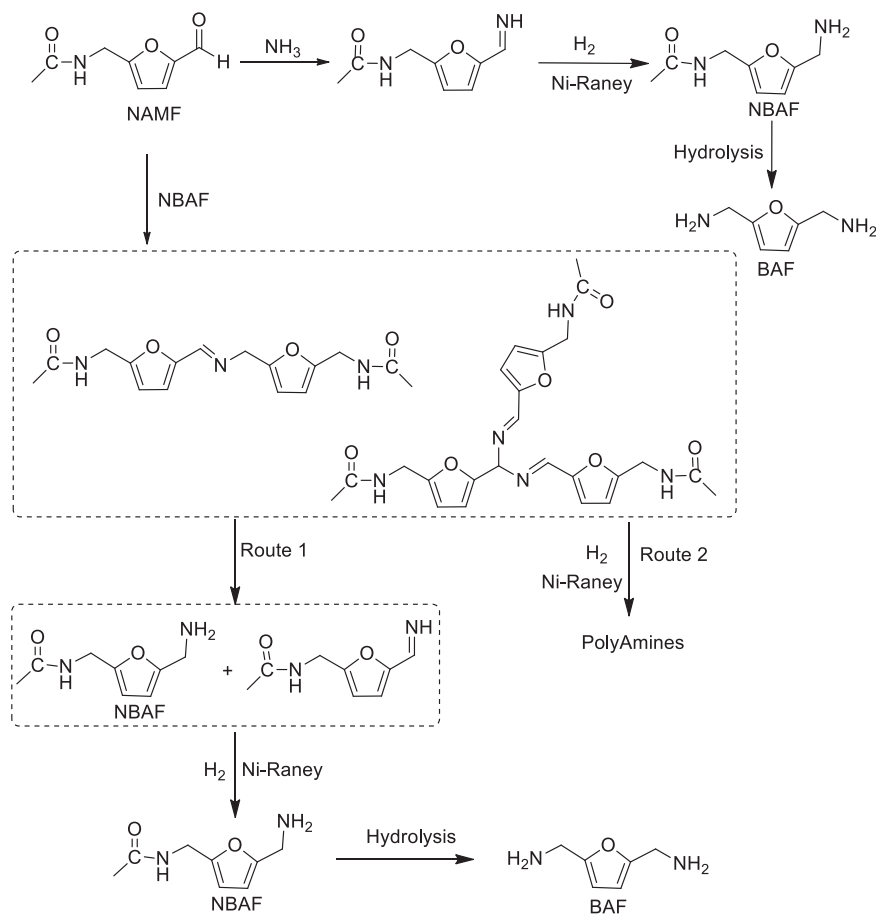


Fig. 5. SEM images of used Raney-Ni at different times. (a) 2 h, (b) 3 h, (c) 4 h.



Scheme 3. Proposed reaction mechanism for the conversion of NAMF to BAF.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jechem.2017.06.015](https://doi.org/10.1016/j.jechem.2017.06.015).

References

- [1] A.S. Nagpure, N. Lucas, S.V. Chilukuri, *ACS Sustainable Chem. Eng.* 3 (11) (2015) 2909–2916.
- [2] N.T. Le, P. Lakshmanan, K. Cho, Y. Han, H. Kim, *Appl. Catal. A* 464–465 (2013) 305–312.
- [3] W. Hao, W. Li, X. Tang, X. Zeng, Y. Sun, S. Liu, L. Lin, *Green Chem.* 18 (4) (2016) 1080–1088.
- [4] A. Jain, S.C. Jonnalagadda, K.V. Ramanujachary, A. Mugweru, *Catal. Commun.* 58 (2015) 179–182.
- [5] M. Mascal, E.B. Nikitin, *ChemSusChem* 2 (9) (2009) 859–861.
- [6] E.S. Kang, Y.W. Hong, W. Chae da, B. Kim, B. Kim, Y.J. Kim, J.K. Cho, Y.G. Kim, *ChemSusChem* 8 (7) (2015) 1179–1188.
- [7] H. Koch, J. Pein, *Polym. Bull.* 13 (6) (1985) 525–532.
- [8] K. Kruger, A. Tillack, M. Beller, *ChemSusChem* 2 (8) (2009) 715–717.
- [9] O. Kreye, H. Mutlu, M.A.R. Meier, *Green Chem.* 15 (6) (2013) 1431.
- [10] F.W. Lichtenthaler, *Acc. Chem. Res.* 35 (9) (2002) 728–737.
- [11] C. Moreau, M.N. Belgacem, A. Gandini, *Top. Catal.* 27 (1–4) (2004) 11–30.
- [12] A. Gandini, M.N. Belgacem, *Prog. Polym. Sci.* 22 (6) (1997) 1203–1379.
- [13] E.J. Molitor, T.W. Toyzan, U.S. Patent Application 2007, 11/957,165.
- [14] D. Talwar, N.P. Salguero, C.M. Robertson, J. Xiao, *Chem. Eur. J.* 20 (1) (2014) 245–252.
- [15] Q. Girka, B. Estrine, N. Hoffmann, J. Le Bras, S. Marinković, J. Muzart, *React. Chem. Eng.* 1 (2) (2016) 176–182.
- [16] T. Haas, T. Tacke, J.C. Pfeffer, F. Klasovky, M. Rimbach, M. Volland, M. Ortel, WO Patent No. 004069A1, 2012.
- [17] N.T. Le, A. Byun, Y. Han, K.-I. Lee, H. Kim, *Green Sustainable Chem.* 05 (03) (2015) 115–127.
- [18] B.J.J. Ritter, P.P. Inieri, *J. Am. Chem. Soc.* 70 (12) (1948) 4045–4048.
- [19] A.G. Martinez, R.M. Alvarez, E.T. Vilar, A.G. Fraile, M. Hanack, L.R. Subramanian, *Tetrahedron Lett.* 30 (5) (1989) 581–582.
- [20] G. Descotes, L. Cottier, L. Eymard, K.M. Rapp, U.S. Patent 5,344,974. 1994.
- [21] P.J. Scheuer, H.C. Botelho, C. Pauling, *J. Org. Chem.* 22 (6) (1957) 674–676.
- [22] S.K.R. Patil, C.R.F. Lund, *Energy Fuels* 25 (10) (2011) 4745–4755.