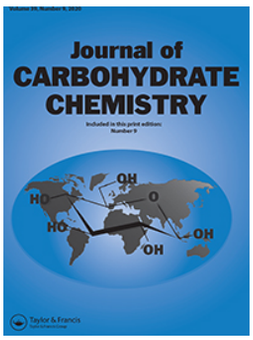

Journal of Carbohydrate Chemistry

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/lcar20

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To cite this article: Zhi-ling Cao, Cong Zhu, Wen-ying Wu, Dan-dan Zhu, Dong Qian, Jian Zhu, Tian-ge Chang, Mei Sheng, Xiu-li Yang & Wei-wei Liu (2020) Synthesis of β-acylamino furans from glucosamine, Journal of Carbohydrate Chemistry, 39:9, 472-484, DOI: 10.1080/07328303.2021.1895195

To link to this article: https://doi.org/10.1080/07328303.2021.1895195

Published online: 10 Mar 2021.

JOURNAL OF CARBOHYDRATE CHEMISTRY
2020, VOL. 39, NO. 9, 472–484
https://doi.org/10.1080/07328303.2021.1895195

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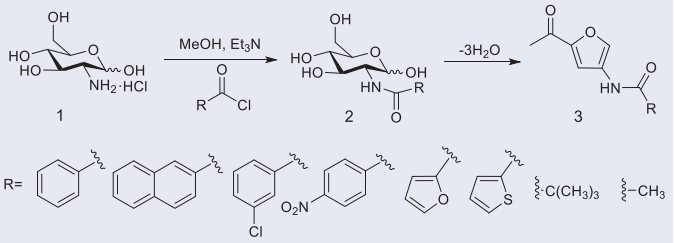
Jiangsu Key Laboratory of Marine Pharmaceutical Compound Screening, Jiangsu Institute of Marine Resources, Co-Innovation Center of Jiangsu Marine Bio-Industry Technology, Jiangsu Ocean University, Lianyungang, China

ABSTRACT

A facile method for the synthesis of a series of novel *β*-acylamino furans stating from renewable monosaccharide was achieved. Glucosamine hydrochloride was selectively *N*-acylated with acyl chlorides in methanol/triethylamine to yield *N*-acyl-D-glucosamines, which were subsequently converted into *β*-acylamino furans through dehydration and cyclization under microwave irradiation.

GRAPHICAL ABSTRACT



ARTICLE HISTORY
Received 18 November 2020
Accepted 21 February 2021

KEYWORDS
Glucosamine; amino furan; synthesis; acylation; dehydration

Introduction

The utilization of renewable resources as raw materials to synthesize organic compounds has increased over the past few decades. For example, carbohydrates can be converted into various compounds, such as levulinic acid, 5-hydroxymethylfurfural, and lactic acid, by acid and/or base catalysis.[1–4] Glucosamine is a natural amino sugar widely found in animals and microorganisms. As a renewable monosaccharide containing an amino group, glucosamine has been converted into α-amino acids and other heterocyclic chemicals including furan derivatives, pyrazine, and substituted pyrroles compounds.[5–8]

Amino-substituted furans are important structural units in many natural and pharmaceutical products.[9–12] Amino-substituted furans also represent

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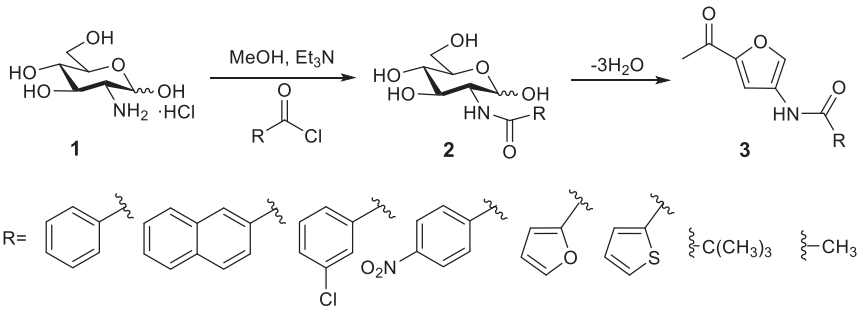


Scheme 1. Route for the synthesis of β-acylamino furans.

valuable building blocks for organic synthesis.[13] Literature searches revealed numerous syntheses of β-amino-substituted furans from acyclic precursors.[14–17] Several groups have reported the preparation of β-amino-furan derivatives by methods, e.g. reduction of 3-nitrofurans 3-furoyl azide to the amines, curtius rearrangement of furoyl azides, and copper-catalysed amidation of 3-bromofuran using CuI and different amides.[18] Another interesting and green approach for the preparation of 3-acetamido furan was based on renewable natural amino sugar. Kerton et al. previously developed an efficient process for converting *N*-acetyl-D-glucosamine into 3-acetamido-5-acetylfuran (3A5AF) in medium yield.[5] Chen et al. described the direct conversion of chitin into a 3A5AF for the first time.[19–21] 3A5AF is an exciting platform and other green methods for its synthesis are also developed.[22] However, this single product cannot meet the need of structural and functional diversity.

In order to develop more amino furan derivatives using ammonia sugar, we investigated the selective *N*-acylation of glucosamine (**1**) to prepare a series of *N*-acyl-D-glucosamine derivatives (**2**). They were then used for the facile synthesis of β-acylamino furans (**3**) employing boric acid as the dehydration catalyst (Scheme 1).

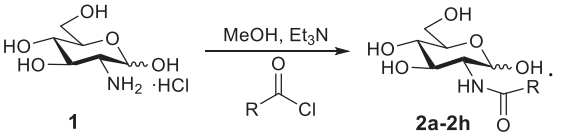
Results and discussion

First, we investigated the selective *N*-acylation of 2-amino group in D-glucosamine **1** to afford *N*-acyl-D-glucosamine compounds (**2**) as shown in Scheme 1. In literature,[23,24] glucosamine hydrochloride was usually *N*-acetylated with acetic anhydride in 10% methanol or pyridine. However, these methods sometimes give low yields and involve expensive reagents or tedious work-up procedures.

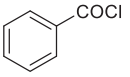
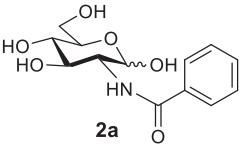
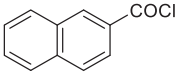
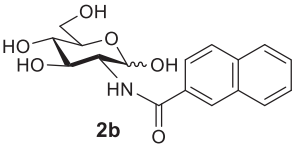
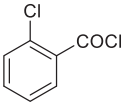
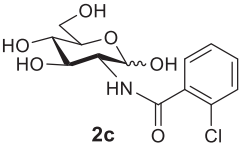
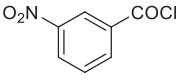
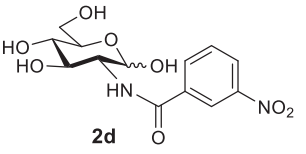
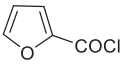
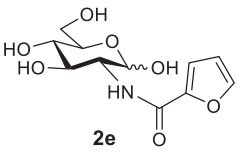
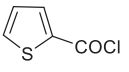
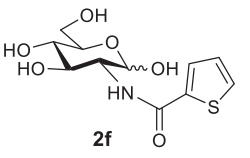
Glucosamine salts are soluble in water but difficult to dissolve in ordinary organic solvents. When water was used as a solvent, the *N*-acylated product was difficult to be isolated because *N*-acyl-D-glucosamine can

dissolve in both water and common organic solvents. We found that triethylamine could both promote the solubility of glucosamine in methanol and act as an acid-scavenging reagent, and we decide to use a mixture of methanol and triethylamine for this reaction. After optimization, the synthesis of various *N*-acyl-D-glucosamine compounds **2a**–**2h** was carried out in methanol containing 3.0 equivalents of triethylamine in good (49–70%) overall isolated yields using various acyl chlorides as acylation reagent (Table 1).

Table 1. Synthesis of *N*-acyl-D-glucosamines **2**

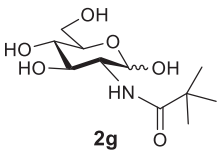
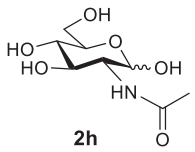


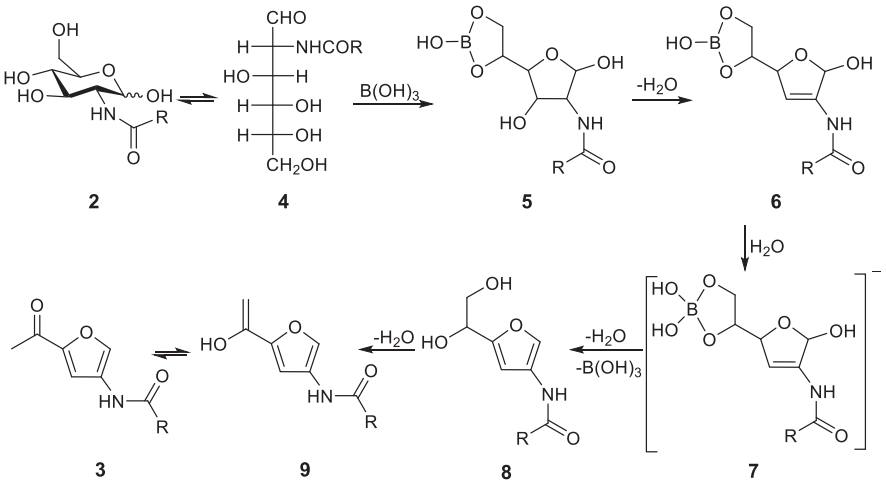
1 **2a-2h**

Entry	Acylation reagent	Product	Yield (%)
1		 **2a**	71
2		 **2b**	73
3		 **2c**	60
4		 **2d**	54
5		 **2e**	49
6		 **2f**	58
7			69

(*continued*)

Table 1. Continued.

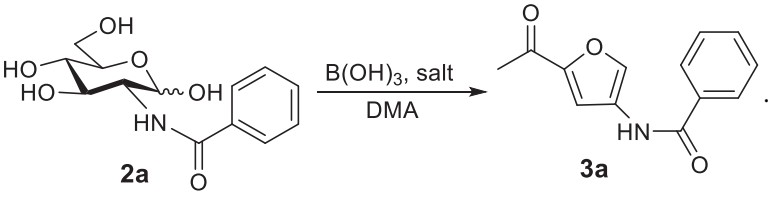
Entry	Acylation reagent	Product	Yield (%)
		 **2g**	
8	CH_3COCl	 **2h**	63



Scheme 2. Possible mechanism involved in the dehydration of glucosamine for the formation of β-acylamino furans.

Boric acid was an efficient catalyst for the dehydration of pyranose to furan compounds.[25] Compared to glucose, the dehydration of *N*-acyl-D-glucosamine and furan ring formation is different.[26] The proposed reaction pathway for the formation of furan derivatives **3** is shown in Scheme 2. The borate formation of the C-5 OH group with boric acid prevented the conversion of the open chain tautomer **4** into a six-membered ring form, thus facilitating the formation of a furan ring intermediate **5**. Due to the conjugation effect with the C-2 *N*-acetyl group, the first dehydration proceeds between H-2-H and C-3-OH in **5** to give **6**. Subsequent dehydration involving the C-1-OH group leads to 3-acylamino-5-(1′,2′-dihydroxyethyl) furan **8**.[6] Finally, higher temperature (220 °C) induced the elimination of water from C-6-OH and C-5-H to form an enol intermediate **9**, which undergoes tautomerization to give ketones **3**. In our

Table 2. Effect of salts on the yield of **3a**[a]



Entry	Catalyst/Salt	Yield/%
1	$B(OH)_3/VB_1$	50
2	B_2O_3/VB_1	42
3	$B(OH)_3/KH_2PO_4$	37
4	$B(OH)_3/H_3PO_4$	22
5	$B(OH)_3/Na_2SO_4$	30
6	$B(OH)_3/CaSO_4$	34
7	$B(OH)_3$	15
8	$B(OH)_3$/NaCl	55
9	B_2O_3/NaCl	51

[a]Conditions: **2a** (0.57 g) in DMA (10 mL); **2a**:$B(OH)_3$ or B_2O_3:salt = 1:1.5:2; MW 220 °C for 15 min.

study, microwave (MW) heating in dimethylacetamide (DMA) was found to obviously promote dehydration and shorten the reaction time.

However, when only boric acid was used as the catalyst, the yield of the acylamino furans was relatively low ($< 15\%$). We found that the addition of a salt with $B(OH)_3$ could significantly increase the yield of target compounds, suggesting that the inorganic salts stabilized one or more of the charged intermediates or the final product.[25,27] This may also be due to the salting effect, which results in increased solvent polarity and decreased degradation of furan product. The experimental results of the influence of different salts on the reaction yields are presented in Table 2. Clearly, sodium chloride gave the highest yield (Table 2, entry 8). In comparison with most inorganic salts, experiments with thiamin hydrochloride (VB_1) also resulted in higher yields, indicating that the chloride anion might have an influence on the catalytic performance. Furthermore, boric anhydride (B_2O_3) appeared to be slightly less effective to promote the formation of **3a** as compared to boric acid (entries 2 and 9).

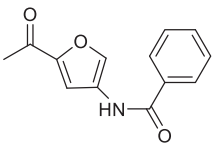
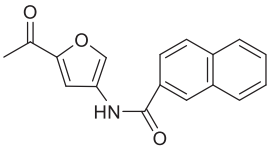
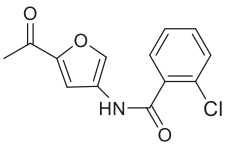
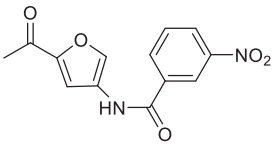
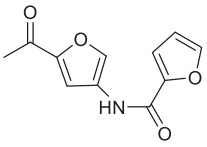
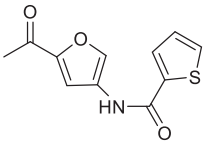
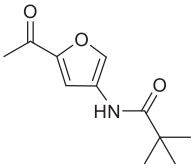
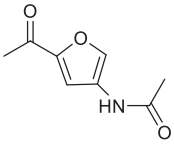
Eventually, the synthesis of β-acylamino furans was performed with $B(OH)_3$-NaCl using DMA as solvent and MW at 220 °C for 15 min, and the results are listed in Table 3. β-Acylamino furan derivatives **3a**–**3h** were prepared in yield around 27–62%. Further studies are necessary to evaluate the biological activity of these compounds and their chemical applications.

Experimental section

General procedures

All reagents were provided by the J&K Scientific Co. unless otherwise specified. All MW reactions were carried out with a Discover SP (CEM)

Table 3. Reactions to convert *N*-acetyl-D-glucosamines **2a**–**h** into **3a**–**h**.

Entry	Compound 2	Product		Yield/%
1	R = Ph		**3a**	55
2	R = 2-naphthyl		**3b**	62
3	R = 2-chlorophenyl		**3c**	51
4	R = 3-nitrophenyl		**3d**	43
5	R = furan-2-yl		**3e**	27
6	R = thiophen-2-yl		**3f**	45
7	R = *t*-butyl		**3g**	49
8	R = methyl		**3h**	53

MW reactor. NMR data were obtained using a Bruker Avance 500 MHz nuclear magnetic resonance instrument with internal TMS as standard. Infrared (IR) data were measured using a NICOLET IS5 Fourier transform infrared spectrometer. Mass spectra were performed with an Agilent MSD SL Trap mass spectrometer with an ESI source. Elemental analysis was performed with the Perkin-Elmer 24 elemental analyzer. Flash chromatography (FC) was carried out with silica gel (200 − 400 mesh) as the stationary phase.

Synthesis of N-acyl-D-glucosamines (2)

Glucosamine hydrochloride (11.6 mmol) was suspended in methanol (30 mL) containing triethylamine (34.8 mmol). The mixture was vigorously stirred at room temperature for 0.5 h, and then cooled to 5 °C before the precipitates of triethylamine hydrochloride were filtered off. Acyl chloride (15.0 mmol) was slowly added dropwise into the filtrate over 0.5 h, and diethyl ether (50 mL) was then added. The mixture was vigorously stirred in an ice bath to rapidly precipitate. After chilling for 2 h, the solid material was filtered, washed with ether and dichloromethane, and dried to give products **2a**–**2h**.

Synthesis of β-acylamino furans (3)

N-Acyl-D-glucosamines (**2**) (2.0 mmol) and boric acid (3.0 mmol) were dissolved in DMA (10 mL), and then sodium chloride (4.0 mmol) was added. The mixture was heated at 220 °C by MW irradiation at 100 W for 15 min. The reaction mixture was cooled to room temperature, quenched with a saturated Na_2CO_3 solution, and extracted with ethyl acetate. The combined organic phase was washed with water, brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the resulting solid was purified by column chromatography to afford products **3a**–**3h**.

N-Benzoyl-D-glucosamine (2a)

White solid; 71% yield; m.p. 197 − 200 °C (lit.[28] 198 ∼ 200 °C); ^{1}H NMR (500 MHz, D_2O) δ 7.71 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 6.8 Hz, 2H), 5.26 (d, J = 3.5 Hz, 0.5 H, H-1 of α anomer), 4.79 (d, J = 8.5 Hz, 0.5 H, H-1 of β anomer), 4.07 − 3.41 (m, 6H); ^{13}C NMR (126 MHz, D_2O) δ 171.7, 171.4, 133.6, 133.4, 132.3, 132.2, 128.8, 128.7, 127.3, 127.1, 94.9, 90.9, 76.0, 73.9, 71.6, 70.6, 70.2, 70.0, 60.8, 60.6, 57.2, 54.7; IR ν: 3424, 3424, 1603, 1467, 1072 cm^{-1}.

N-(2-Naphthylacetyl)-D-glucosamine (2b)

White solid; 73% yield; m.p. 187 − 188 °C; ^{1}H NMR (500 MHz, D_2O) δ 8.43 (d, J = 7.1 Hz, 1H), 7.98 − 7.90 (m, 4H), 7.57 (td, J = 12.9, 6.8 Hz, 2H), 5.30 (d, J = 3.5 Hz, 0.7 H, H-1 of α anomer), 4.81 (d, J = 8.4 Hz, 0.3 H, H-1 of β anomer), 4.19 − 3.36 (m, 6H); IR ν: 3334, 3334, 2928, 1636, 1503, 1432, 1081(C − O) cm^{-1}. ESI-MS m/z: 356 $[M + Na]^+$; Anal. calcd. for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.75; N, 4.20. Found: C, 60.86; H, 5.96; N, 4.33.

N-(2-Chlorine-benzoyl)-D-glucosamine (2c)

White solid, 60% yield; m.p. 204 − 205 °C; ^{1}H NMR (500 MHz, D_2O) δ 7.49 − 7.32 (m, 4H), 5.30 (d, J = 3.5 Hz, 0.6 H, H-1 of α anomer), 4.74 (d, J = 8.5 Hz, 0.4 H, H-1 of β anomer), 4.06 − 3.37 (m, 6H); IR ν: 3373, 3373, 1644, 1594, 1433, 1080 cm^{-1}. ESI-MS m/z: 340 $[M + Na]^+$; Anal. calcd. for $C_{13}H_{16}ClNO_6$: C, 49.14; H, 5.08; N, 4.41. Found: C, 50.17; H, 5.18; N, 4.30.

N-(3-Nitro-benzoyl)-D-glucosamine (2d)

White solid, 54% yield; m.p. 171 − 173 °C; ^{1}H NMR (500 MHz, D_2O) δ 8.57 (dd, J = 4.0, 2.2 Hz, 1H), 8.39 − 8.34 (m, 1H), 8.10 (d, J = 7.8 Hz, 1H), 7.68 (td, J = 8.0, 3.5 Hz, 1H), 5.28 (d, J = 3.5 Hz, 0.7 H, H-1 of α anomer), 4.81 (d, J = 8.5 Hz, 0.3 H, H-1 of β anomer), 4.11 − 3.43 (m, 6H); IR ν: 3374, 3374, 2926, 1634, 1532, 1080 cm^{-1}; ESI-MS m/z: 329 $[M + H]^+$; Anal. calcd. for $C_{13}H_{16}N_2O_8$: C, 47.56; H, 4.91; N, 8.53. Found: C, 47.98; H, 5.00; N, 8.63.

N-Furoyl-D-glucosamine (2e)

White solid, 49% yield; m.p. 94 − 96 °C; ^{1}H NMR (500 MHz, D_2O) δ 7.59 − 7.56 (m, 1H), 7.08 (t, J = 3.1 Hz, 1H), 6.52 (dt, J = 3.7, 2.0 Hz, 1H), 5.22 (d, J = 3.5 Hz, 0.6 H, H-1 of α anomer), 4.78 (d, J = 8.4 Hz, 0.4 H, H-1 of β anomer), 4.04 − 3.39 (m, 6H); IR ν: 3413, 3413, 1631, 1596, 1075 cm^{-1}. ESI-MS m/z: 296 $[M + Na]^+$; Anal. calcd. for $C_{11}H_{15}NO_7$: C, 48.35; H, 5.53; N, 5.13. Found: C, 48.70; H, 5.66; N, 5.10.

N-(2-Thienylcarbonyl)-D-glucosamine (2f)

White solid, 58% yield; m.p. 139 − 141 °C; ^{1}H NMR (500 MHz, D_2O) δ 7.70 − 7.60 (m, 2H), 7.09 (dd, J = 6.0, 2.8 Hz, 1H), 5.21 (d, J = 3.4 Hz, 0.3 H, H-1 of α anomer), 4.76 (d, J = 8.4 Hz, 0.7 H, H-1 of β anomer), 4.02 − 3.37 (m, 6H); IR ν: 3425, 3425, 1609, 1469, 1072 cm^{-1}. ESI-MS m/z:

312 $[M+Na]^+$; Anal. calcd. for $C_{11}H_{15}NO_6S$: C, 45.67; H, 5.23; N, 4.84. Found: C, 45.34; H, 5.35; N, 4.95.

N-Trimethylacetyl-D-glucosamine (2 g)

White solid, 69% yield; m.p. 177 – 178 °C; ^{1}H NMR (400 MHz, D_2O) δ 5.08 (d, J = 3.5 Hz, 0.5 H, H-1 of α anomer), 4.66 (d, J = 8.5 Hz, 0.5 H, H-1 of β anomer), 3.84 – 3.33 (m, 6H), 1.09 – 1.10 (m, 9H); ^{13}C NMR (126 MHz, D_2O) δ 183.2, 182.9, 94.9, 90.8, 75.9, 73.6 71.5, 70.4, 70.0, 70.0, 60.7, 60.5, 56.7, 54.1, 38.63, 38.5, 26.5, 26.4; IR ν: 3376, 3376, 2964, 2914, 1646, 1086 cm^{-1}; ESI-MS: m/z $[M+H]^+$ Calcd for $C_{11}H_{22}N_2O_6^+$ 264.14, Found 264.21. ESI-MS m/z: 264 $[M+H]^+$; Anal. calcd. for $C_{11}H_{21}NO_6$: C, 50.18; H, 8.04; N, 5.32. Found: C, 49.93; H, 8.20; N, 5.41.

N-Acetyl-D-glucosamine (2 h)

White solid; 63% yield; m.p. 202 – 204 °C (lit.[25] 206 °C); ^{1}H NMR (500 MHz, D_2O) δ 5.15 (d, J = 3.5 Hz, 0.5 H, H-1 of α anomer), 4.66 (d, J = 8.5 Hz, 0.5 H, H-1 of β anomer), 3.9 – 3.4 (m, 6H), 2.00 (s, 3H) .

3-Benzamido-5-acetylfuran (3a)

Yellow solid, 55% yield; m.p.140 – 141 °C; ^{1}H NMR (500 MHz, DMSO) δ 10.70 (s, 1H), 8.40 (s, 1H), 7.98 (d, J = 7.2 Hz, 2H), 7.59 (dt, J = 29.7, 7.2 Hz, 3H), 7.42 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 186.5, 165.0, 150.3, 136.4, 133.8, 132.4, 129.0, 128.0, 127.7, 112.1, 26.3; IR ν: 3430, 1607, 1383, 1073 cm^{-1}. ESI-MS m/z: 252 $[M+Na]^+$; Anal. calcd. for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84; N, 6.11. Found: C, 68.68; H, 4.99; N, 6.00.

3-(Naphthalene-2-carboxamido)-5-acetylfuran (3 b)

Yellow solid, 62% yield; m.p.142 – 144 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.89 (s, 1H), 8.59 (s, 1H), 8.45 (s, 1H), 8.13 – 8.07 (m, 2H), 8.06 – 8.01 (m, 2H), 7.70 – 7.63 (m, 2H), 7.46 (s, 1H), 2.46 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 186.6, 165.0, 150.3, 136.5, 134.9, 132.6, 131.2, 129.4, 128.8, 128.5, 128.4, 128.2, 127.8, 127.5, 124.6, 112.1, 26.4; IR ν: 3426, 1606, 1467, 1385, 1071 cm^{-1}. ESI-MS m/z: 302 $[M+Na]^+$; Anal. calcd. for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.19; H, 4.85; N, 4.90.

3-(2-Chlorobenzamido)-5-acetylfuran (3c)

Yellow solid, 51% yield; m.p.115 − 117 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.87 (s, 1H), 8.36 (d, J = 0.6 Hz, 1H), 7.63 − 7.58 (m, 2H), 7.54 (d, J = 1.7 Hz, 1H), 7.49 (dd, J = 7.4, 1.3 Hz, 1H), 7.29 (d, J = 0.6 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 186.5, 164.6, 150.4, 136.3, 136.1, 132.0, 130.5, 130.3, 129.5, 127.8, 127.2, 111.7, 26.4; IR ν: 3426, 1647, 1500, 1373, 1073 cm^{-1}. ESI-MS m/z: 286 $[M + Na]^+$; Anal. calcd. for $C_{13}H_{10}ClNO_3$: C, 59.22; H, 3.82; N, 5.31. Found: C, 59.48; H, 3.70; N, 5.22.

3-(3-Nitrobenzamido)-5-acetylfuran (3d)

Yellow solid, 43% yield; m.p.214 − 215 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.06 (s, 1H), 8.82 (t, J = 1.8 Hz, 1H), 8.47 (dd, J = 8.1, 1.7 Hz, 1H), 8.42 (d, J = 8.8 Hz, 2H), 7.88 (t, J = 8.0 Hz, 1H), 7.43 (s, 1H), 2.46 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 186.5, 162.8, 150.4, 148.3, 136.7, 135.1, 134.5, 130.9, 127.3, 127.0, 122.6, 112.0, 26.4 IR ν: 3425, 1655, 1603, 1375, 1073 cm^{-1}. ESI-MS m/z: 297 $[M + Na]^+$; Anal. calcd. for $C_{13}H_{10}N_2O_5$: C, 56.94; H, 3.68; N, 10.22. Found: C, 56.58; H, 3.75; N, 10.41.

3-(2-Furoylamido)-5-acetylfuran (3e)

Yellow solid, 27% yield; m.p.153 − 154 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.14 (s, 1H), 7.56 − 7.51 (m, 1H), 7.27 (d, J = 3.5 Hz, 1H), 7.22 (s, 1H), 6.59 (dd, J = 3.5, 1.7 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (126 MHz, DMSO) δ 187.2, 155.6, 150.9, 148.9, 144.6, 136.1, 125.8, 115.8, 112.8, 109.8, 25.9; IR ν: 3425, 1655, 1502, 1368, 1071 cm^{-1}. ESI-MS m/z: 242 $[M + Na]^+$; Anal. calcd. for $C_{11}H_9NO_4$: C, 60.28; H, 4.14; N, 6.39. Found: C, 60.32; H, 4.22; N, 6.25.

3-(Thiophene-2-carboxamido)-5-acetylfuran (3f)

Yellow solid, 45% yield; m.p.159 ∼ 160 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.71 (s, 1H), 8.31 (s, 1H), 7.93 (dd, J = 3.7, 0.9 Hz, 1H), 7.89 (dd, J = 5.0, 0.9 Hz, 1H), 7.39 (s, 1H), 7.26 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 186.5, 159.7, 150.3, 138.9, 136.3, 132.7, 129.7, 128.7, 127.30, 111.9, 26.3; IR ν: 3426, 1648, 1499, 1371, 1069 cm^{-1}. ESI-MS m/z: 258 $[M + Na]^+$; Anal. calcd. for $C_{11}H_9NO_3S$: C, 56.16; H, 3.86; N, 5.95. Found: C, 56.42; H, 4.01; N, 5.80.

3-Trimethylacetamido-5-acetylfuran (3g)

Yellow solid, 49% yield; m.p.126 − 127 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.68 (s, 1H), 8.23 (d, J = 0.7 Hz, 1H), 7.33 (d, J = 0.7 Hz, 1H), 2.40 (s, 3H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 186.4, 176.4, 149.9, 135.9, 127.8, 112.1, 39.0, 27.6, 26.3; IR ν: 3390, 1657, 1503, 1369, 1076 cm^{-1}. ESI-MS m/z: 232 $[M + Na]^+$; Anal. calcd. for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.22; H, 7.45; N, 6.85.

3-Acetamido-5-acetylfuran (3 h) [29,30]

Yellow solid, 53% yield; m.p.120 − 122 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.23 (s, 1H), 8.18 (s, 1H), 7.19 (s, 1H), 2.41 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 186.5, 168.1, 150.2, 135.71, 127.5, 111.4, 26.3, 23.3; IR ν: 3440(NH), 1631(C = O), 1488(C = C), 1045 (C − O) cm^{-1}.

Conclusion

Glucosamine hydrochloride was selectively *N*-acylated to yield *N*-acyl-D-glucosamines, which were transformed into a series of novel *β*-acylamino furans by cyclization and dehydration under MW irradiation. Glucosamine hydrochloride is industrially produced by the hydrolysis of chitin. Thus, synthesis of *β*-acylamino furans from glucosamine hydrochloride is preferable and convenient. This method will also help in the development of utilization of marine amino sugar for the synthesis of value-added products.

Funding

The work described in this article was supported by the Natural Science Foundation of Jiangsu Province [BK20141246], the PAPD Program (A Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions), the Postgraduate Research and Practice Innovation Program of Jiangsu Province [SJCX20-1220, SJCX20-1225, SJCX20-1232] and the Open-end Funds of Jiangsu Institute of Marine Resources [JSIMR201513].

References

[1] Hegner, J.; Pereira, K. C.; DeBoef, B.; Lucht, B. L. Conversion of cellulose to glucose and levulinic acid via solid-supported acid catalysis. *Tetrahedron Lett.* **2010**, *51*(17), 2356–2358. DOI: 10.1016/j.tetlet.2010.02.148.

[2] Yong, G.; Zhang, Y.; Ying, J. Y. Efficient catalytic system for the selective production of 5-hydroxymethylfurfural from glucose and fructose. *Angew. Chem. Int. Ed. Engl.* **2008**, *47*(48), 9345–9348. DOI: 10.1002/anie.200803207.

[3] Onda, A.; Ochi, T.; Yanagisawa, K. Selective hydrolysis of cellulose into glucose over solid acid catalysts. *Green Chem.* **2008**, *10*(10), 1033–1037. DOI: 10.1039/b808471h.

[4] Holm, M. S.; Saravanamurugan, S.; Taarning, E. Conversion of sugars to lactic acid derivatives using heterogeneous zeotype catalysts. *Science* **2010**, *328*(5978), 602–605. DOI: 10.1126/science.1183990.

[5] Drover, M. W.; Omari, K. W.; Murphy, J. N.; Kerton, F. M. Formation of a renewable amide, 3-acetamido-5-acetylfuran, via direct conversion of N-acetyl-D-glucosamine. *RSC Adv.* **2012**, *2*(11), 4642–4644. DOI: 10.1039/c2ra20578e.

[6] Osada, M.; Kikuta, K.; Yoshida, K.; Totani, K.; Ogata, M.; Usui, T. Non-catalytic synthesis of chromogen I and III from N-acetyl-D-glucosamine in high-temperature water. *Green Chem.* **2013**, *15*(10), 2960–2966. DOI: 10.1039/c3gc41161c.

[7] Rohovec, J.; Kotek, J.; Peters, J. A.; Maschmeyer, T. A clean conversion of d-glucosamine hydrochloride to a pyrazine in the presence of phenylboronate or borate. *Eur. J. Org. Chem.* **2001**, *2001*(20), 3899–3901. DOI: 10.1002/1099-0690(200110)2001:20<3899::AID-EJOC3899>3.0.CO;2-G.

[8] Li, B.; Wang, G.; Li, Z.; Meng, X. $InCl_3$-catalyzed synthesis of C-pyrrolyl glycosides via tandem condensation of aminosugars and 1, 3-dicarbonyl compounds in water. *Tetrahedron Lett.* **2011**, *52*(30), 3891–3894. DOI: 10.1016/j.tetlet.2011.05.083.

[9] Sugiyama, H.; Yoshida, M.; Mori, K.; Kawamoto, T.; Sogabe, S.; Takagi, T.; Oki, H.; Tanaka, T.; Kimura, H.; Ikeura, Y. Synthesis and structure activity relationship studies of benzothieno [3, 2-b] furan derivatives as a novel class of IKKβ inhibitors. *Chem. Pharm. Bull.* **2007**, *55*(4), 613–624. 55(4), 613-624. DOI: 10.1248/cpb.55.613.

[10] Zhou, L.; Stewart, G.; Rideau, E.; Westwood, N. J.; Smith, T. K. A class of 5-nitro-2-furancarboxylamides with potent trypanocidal activity against trypanosoma brucei in vitro. *J. Med. Chem.* **2013**, *56*(3), 796–806. DOI: 10.1021/jm301215e.

[11] Tsuji, E.; Ando, K.; Kunitomo, J. I.; Yamashita, M.; Ohta, S.; Kohno, S.; Ohishi, Y. Preparation of 3-acetoacetylaminobenzo [b] furan derivatives with cysteinyl leukotriene receptor 2 antagonistic activity. *Org. Biomol. Chem.* **2003**, *1*(18), 3139–3141. DOI: 10.1039/b307468d.

[12] Wolter, F. E.; Schneider, K.; Davies, B. P.; Socher, E. R.; Nicholson, G.; Seitz, O.; SüSsmuth, R. D. Total Synthesis of proximicin A − C and synthesis of new furan-based DNA binding agents. *Org. Lett.* **2009**, *11*(13), 2804–2807. DOI: 10.1021/ol901003p.

[13] Padwa, A.; Dimitroff, M.; Waterson, A. G.; Wu, T. Diels − Alder reaction of 2-amino-substituted furans as a method for preparing substituted anilines. *J. Org. Chem.* **1997**, *62*(12), 4088–4096. DOI: 10.1021/jo9702599.

[14] Mageswaran, S.; Ollis, W. D.; Southam, D. A.; Sutherland, I. O.; Thebtaranonth, Y. Base catalysed rearrangements involving ylide intermediates. Part 11. Rearrangements of 3-phenylprop-2-ynylammonium ylides. *J. Chem. Soc. Perkin Trans. I* **1981**, *12*(7), 1969–1980.

[15] Erdenebileg, U.; Høstmark, I.; Polden, K.; Sydnes, L. K. Synthesis and reactivity of 4-amino-substituted furfurals. *J. Org. Chem.* **2014**, *79*(3), 1213–1221. DOI: 10.1021/jo4026308.

[16] Ma, C.; Yang, Y. Thiazolium-mediated multicomponent reactions: a facile synthesis of 3-aminofuran derivatives. *Org. Lett.* **2005**, *7*(7), 1343–1345. DOI: 10.1021/ol0501368.

[17] Granik, V. G.; Kadushkin, A. V.; Liebscher, J. Synthesis of amino derivatives of five-membered heterocycles by Thorpe-Ziegler cyclization. *Adv Heterocyclic Chem.* 1998, 72, 79–125.

[18] Ramsden, C. A.; Milata, V. 2-Aminofurans and 3-aminofurans. *Adv. Heterocycl. Chem.* **2006**, *92*, 1–54.

[19] Pham, T. T.; Lindsay, A. C.; Kim, S. W.; Persello, L.; Chen, X.; Yan, N.; Sperry, J. Two-step preparation of diverse 3-amidofurans from chitin. *Chem. Select* **2019**, *4*(34), 10097–10099. DOI: 10.1002/slct.201902765.

[20] Chen, X.; Gao, Y.; Wang, L.; Chen, H.; Yan, N. Effect of treatment methods on chitin structure and its transformation into nitrogen-containing chemicals. *Chempluschem*. **2015**, *80*(10), 1565–1572. DOI: 10.1002/cplu.201500326.

[21] Chen, X.; Liu, Y.; Kerton, F. M.; Yan, N. Conversion of chitin and N-acetyl-d-glucosamine into a N-containing furan derivative in ionic liquids. *RSC Adv*. **2015**, *5*(26), 20073–20080. DOI: 10.1039/C5RA00382B.

[22] Wang, J.; Zang, H.; Jiao, S.; Wang, K.; Shang, Z.; Li, H.; Lou, J. Efficient conversion of N-acetyl-D-glucosamine into nitrogen-containing compound 3-acetamido-5-acetylfuran using amino acid ionic liquid as the recyclable catalyst. *Sci Total Environ*. **2020**, *710*, 136293 DOI: 10.1016/j.scitotenv.2019.136293.

[23] Dang, C. H.; Nguyen, C. H.; Nguyen, T. D.; Im, C. Synthesis and characterization of N-acyl-tetra-O-acyl glucosamine derivatives. *RSC Adv*. **2014**, *4*(12), 6239–6245. DOI: 10.1039/c3ra46007j.

[24] Brockhausen, I.; Carran, J.; McEleney, K.; Lehotay, M.; Yang, X.; Yin, L.; Anastassiades, T. N-Acyl derivatives of glucosamine as acceptor substrates for galactosyltransferase from bone and cartilage cells. *Carbohydr. Res*. **2005**, *340*(12), 1997–2003. DOI: 10.1016/j.carres.2005.06.002.

[25] Hansen, T. S.; Mielby, J.; Riisager, A. Synergy of boric acid and added salts in the catalytic dehydration of hexoses to 5-hydroxymethylfurfural in water. *Green Chem*. **2011**, *13*(1), 109–114. DOI: 10.1039/C0GC00355G.

[26] Johnson, S.; Tanaka, F. Direct synthesis of C-glycosides from unprotected 2-N-acyl-aldohexoses via aldol condensation-oxa-Michael reactions with unactivated ketones . *Org. Biomol. Chem*. **2016**, *14*(1), 259–264. DOI: 10.1039/c5ob02094h.

[27] Fedorov, M. V.; Arif, R. N.; Frolov, A. I.; Kolar, M.; Romanova, A. O.; Rozhin, A. G. Salting out in organic solvents: a new route to carbon nanotube bundle engineering. *Phys. Chem. Chem. Phys*. **2011**, *13*(27), 12399–12402. DOI: 10.1039/c1cp21440c.

[28] Mukerjee, H.; Pal, P. R. N-acylation of D-glucosamine by a new method. *J. Org. Chem*. **1970**, *35*(6), 2042–2043. DOI: 10.1021/jo00831a080.

[29] Omari, K. W.; Dodot, L.; Kerton, F. M. A Simple one-pot dehydration process to convert N-acetyl-D-glucosamine into a nitrogen-containing compound, 3-acetamido-5-acetylfuran. *Chem. Sus. Chem*. **2012**, *5*(9), 1767–1772. DOI: 10.1002/cssc.201200113.

[30] Liu, Y.; Stähler, C.; Murphy, J. N.; Furlong, B. J.; Kerton, F. M. Formation of a renewable amine and an alcohol via transformations of 3-acetamido-5-acetylfuran. *ACS Sustainable Chem. Eng*. **2017**, *5*(6), 4916–4922. DOI: 10.1021/acssuschemeng.7b00323.