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Extending the Carbon Chain Length of Carbohydrate-Derived 5-Substituted-2-furaldehydes by Condensing with Active Methylene Compounds under Organocatalytic Conditions

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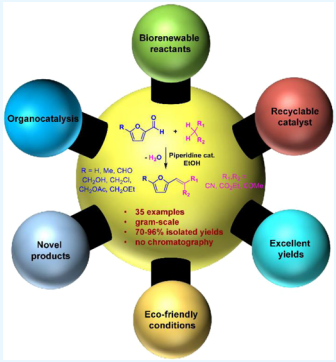
ABSTRACT: This work reports a high-yielding, organic solvent-free, gram-scale synthesis of novel Knoevenagel condensation products by reacting carbohydrate-derived 5-substituted-2-furaldehydes (SFLs) with active methylene compounds (AMCs) using various organic amines and inorganic bases as catalysts. Among the base catalysts examined, piperidine performed best, affording satisfactory selectivity and yield of the targeted Knoevenagel condensation products owing to the subtle balance between its nucleophilicity and basicity. The reaction was optimized on various reaction parameters, such as temperature, duration, solvent, catalyst loading, and molar ratio of the reactants. Even though the SFLs exhibited significantly different reactivity, a general synthetic protocol was developed successfully, affording good to excellent isolated yields (70−96%) of the novel Knoevenagel condensation products at ambient temperature. Moreover, the Knoevenagel products were purified by triturating with eco-friendly solvents (e.g., ethyl acetate and *n*-heptane) without chromatographic purification.



1. INTRODUCTION

The valorization of biomass in a biorefinery setting promises to solve many economic, societal, and environmental complications ensuing from our overdependence on fossilized carbon-based resources.[1] Over the past three decades, numerous journal publications and patents have been dedicated to producing furanic chemical platforms from biomass-derived carbohydrates and their synthetic value addition into organic chemicals of commercial significance.[2] Two of the most crucial carbohydrate-derived furaldehydes are furfural (FUR, **1a**) and 5-(hydroxymethyl)furfural (HMF, **1e**) (Scheme 1A). FUR is typically produced by the acid-catalyzed dehydration of pentose sugars (e.g., xylose), whereas HMF is produced by the dehydration of hexose sugars (e.g., fructose, glucose). Both **1a** and **1e** can be produced directly from polymeric carbohydrates in the presence of appropriate acid catalysts and reaction media that promote depolymerization, hydrolysis, and dehydration reactions.[3] The biorenewable 5-substituted-2-furaldehydes (SFLs) **1a** and **1e** have derivative chemistry that encompasses virtually all major classes of organic chemicals of industrial significance, including fuels, fuel additives, solvents, fragrances, monomers, plasticizers, dyes, surfactants, agrochemicals, and pharmaceuticals.[4] The hydroxymethyl group in **1e** can be synthetically modified selectively to produce a series of SFLs. 5-(Chloromethyl)furfural (CMF, **1f**) can be produced by reacting **1e** with a chlorinating reagent or directly from carbohydrates using hydrochloric acid.[5,6] 5-Methylfurfural (MF, **1b**) can be produced by dehydrating hexose sugars like L-rhamnose or by partially reducing **1e** and **1f**.[7,8] 5-(Ethoxymethyl)furfural (EMF, **1c**), a promising biofuel candidate, can be produced by etherification of **1e** or by acid-catalyzed ethanolysis of hexose sugars and polymeric carbohydrates.[9] 5-(Acetoxymethyl)furfural (AcMF, **1d**) can be produced from isolated **1e** and **1f** or directly from sugars by Fischer esterification or nucleophilic substitution reaction.[10] Although **1b**−**1f** are congeners, they differ noticeably in physicochemical properties (e.g., solubility, hydrolytic stability) and reactivity.[11]

A major technical challenge for expanding the derivative chemistry of the furanic platform chemicals is to develop economically attractive and environmentally acceptable synthetic strategies. The chemical reactivity patterns of the biomass-derived furaldehydes must be understood well by synthesizing their derivatives using innocuous reagents.[12,13] Even though the substitution is distant from the aldehyde moiety in the SFLs, the reactivity is markedly different in some organic transformations. Many of the FUR and HMF derivatives reported in the literature involve the aldehyde group selectively without involving the furan ring and substitution at the C-5 carbon atom. In this regard, Knoevenagel condensation is one of the most established

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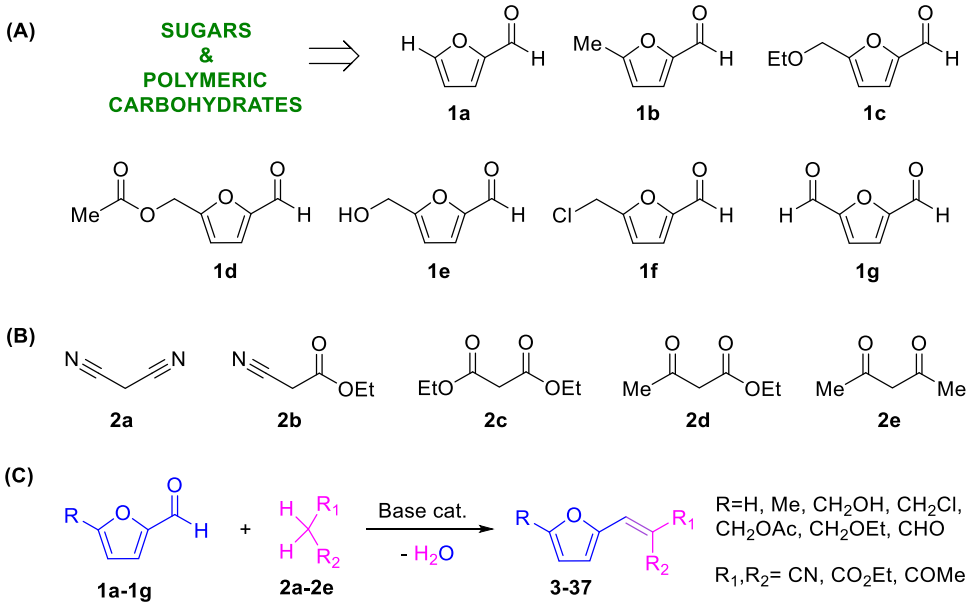
Scheme 1. (A) Carbohydrate-Derived 5-Substituted-2-furaldehydes, (B) Active Methylene Compounds, and the (C) Knoevenagel Condensation Products Reported in This Study



and efficient carbon-carbon bond-forming reactions in the synthetic organic chemistry literature, affording products of academic importance and industrial significance.[14] The Knoevenagel condensation reaction between aromatic aldehydes and active methylene compounds (AMCs) works under mild reaction conditions using an organic or inorganic base as the catalyst. The reaction has a high atom economy, low *E*-factor, and 100% carbon economy, producing water as an innocuous byproduct. The Knoevenagel condensation products often show promising bioactive properties (e.g., antiviral, antibacterial, anticancer).[15] They also act as chemical intermediates in downstream value-addition pathways for synthesizing therapeutic drugs, natural products, functional polymers, fine chemicals, herbicides, and insecticides.[16] Numerous publications have reported Knoevenagel condensation of alkyl or aryl aldehydes (and ketones) with a range of AMCs, and these works have been reviewed.[17] The preparative strategies vary on the type of catalyst, reaction media, and process conditions employed. Numerous acid and base catalysts (homogeneous and heterogeneous) have been employed for the Knoevenagel condensation reaction. However, the search for superior catalysts in terms of high catalytic efficiency (activity, selectivity), easy availability, low cost, eco-friendly nature, and convenient recoverability continues.[18] In this regard, organocatalysts have received significant interest in biorefinery research due to their eco-friendly characteristics.[19] Organic amines (primary, secondary, tertiary) are frequently used as base catalysts and organocatalysts in various organic transformations since they are inexpensive, commercially available in pure form, chemically stable, and recyclable via distillation.[20,21] Piperidine is an efficient organocatalyst in Knoevenagel condensation and Knoevenagel−Doebner reactions.[22] The mechanistic insights of piperidine-catalyzed Knoevenagel condensation reaction between substituted benzaldehydes and AMCs have been demonstrated, and the roles of iminium and enolate ions have been examined.[23] FUR **1a** has long been used as a substrate in many Knoevenagel condensation processes to demonstrate the wide substrate scope but is rarely depicted from the perspective of the renewability of the substrate used.[24,25] On the contrary, the recent publications on Knoevenagel condensation reaction using HMF **1e** as the substrate emphasize its biorenewable nature.[26,27] A systemic study has never been performed on the Knoevenagel condensation reaction between various biorenewable SFLs and AMCs. Such a study will not only furnish novel and biorenewable Knoevenagel condensation products with hitherto unknown physicochemical and biological properties but also help to widen the product portfolios of SFLs as chemical building units in a carbohydrate-centric biorefinery and improve its commercial feasibility. This work reports the Knoevenagel condensation between SFLs (**1a−1g**) with malononitrile (**2a**), ethyl cyanoacetate (**2b**), diethyl malonate (**2c**), ethyl acetoacetate (**2d**), and acetylacetone (**2e**) as the AMCs (Scheme 1B,C). Among the thirty-five Knoevenagel condensation products synthesized in this study, seventeen have never been reported in the literature.

2. MATERIALS AND METHODS

2.1. Materials. Furfural (99%), ethyl acetoacetate (99%), ethyl cyanoacetate (98%), and silica gel (60−120 mesh) were purchased from Spectrochem Pvt., Ltd. Piperidine (98%), diethyl malonate (98%), acetylacetone (98%), and chloroform (99%) were purchased from Loba Chemicals Pvt., Ltd. Malononitrile (98%) was purchased from Sisco Research Laboratories Pvt., Ltd. Ethanol (99.8%) was purchased from Aqlivia Pvt., Ltd. 5-Methylfurfural (MF, 99%) was purchased from Sigma. Ethyl acetate (99%) was purchased from Finar Limited. *n*-Heptane (99%) was purchased from Molychem. 5-(Hydroxymethyl)furfural (HMF), 5-(chloromethyl)furfural (CMF), 5-(acetoxymethyl)furfural (AcMF), 5-(ethoxymethyl)furfural (EMF), and 2,5-diformylfuran (DFF) were synthesized and purified following literature procedures.[10,28−30] Ethanol was dried over preactivated molecular sieves (4 Å) for 12 h before use. Furfural was distilled and refrigerated in an airtight, amber-colored glass container. All other chemicals were used as received.

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2.2. Characterization Methods. The synthesized compounds were characterized using Fourier transform infrared (FTIR) spectra using a Bruker FTIR 4000 instrument equipped with a zinc selenide (ZnSe) ATR. The FTIR spectra were collected by performing 16 scans at a scanning rate of 4 scans/s in the range between 500 and 4000 cm^{-1}. Nuclear magnetic resonance (NMR) spectra of the synthesized compounds were collected in a Bruker NanoBay NMR instrument. The ^{1}H NMR spectra were collected at the operating frequency of 400 MHz, whereas the ^{13}C NMR spectra were collected in the same instrument at a calculated frequency of 100 MHz. Elemental analyses of the synthesized novel compounds were collected using Elementar, Germany (Model: vario MICRO select). The melting point of the solid compounds was checked in a Stuart digital melting point apparatus (Model: SMP3).

2.3. Typical Procedure for Preparing the Knoevenagel Condensation Products. Furfural **1a** (0.500 g, 5.20 mmol) was introduced in a 50 mL round-bottomed flask. Malononitrile **2a** (0.343 g, 5.20 mmol), piperidine (0.042 g, 0.49 mmol), and ethanol (5 mL) were added. A magnetic stirring bead was introduced, and the reaction mixture was stirred continuously on a magnetic stirrer for 30 min at room temperature. The progress of the reaction was monitored by thin-layer chromatography till the disappearance of **1a**. Upon completion, ethanol was removed in a rotary evaporator under reduced pressure. The residue was diluted with ethyl acetate (10 mL) and washed with deionized water (20 mL × 3) in a separatory funnel. The ethyl acetate layer was separated, dried over anhydrous Na_2SO_4, and evaporated in a rotary evaporator under reduced pressure to produce crude 2-(furan-2-ylmethylene)malononitrile (**3**) as a red solid. The product from the crude was triturated with 5 vol % ethyl acetate in *n*-heptane to remove colored impurities. Evaporation of the solvent in a rotary evaporator under reduced pressure afforded pure 2-(furan-2-ylmethylene)malononitrile (**3**) (0.645 g, 86%) as a yellow solid.

The optimized synthetic protocol was extended to SFLs and other AMCs. When **1d** and **1f** were used as reactants, cyclohexane (5 mL) was used as a solvent instead of ethanol to avoid the formation of **1e** and **1c** during the reaction, respectively, by ethanolysis reaction.

3. RESULTS AND DISCUSSION

The compounds **1a** and **2a** were chosen as model reactants to form 2-(furan-2-ylmethylene)malononitrile (**3**) by the Knoevenagel condensation reaction. The Knoevenagel condensation reaction was performed at room temperature using ethanol as the biorenewable solvent and anhydrous sodium carbonate as a heterogeneous base catalyst. The reaction completed within 15 min at RT and **3** was obtained in an 86% isolated yield using only 10 mol% (calculated based on the amount of **1a**) Na_2CO_3 (entry 1, Table 1). A major concern in the process is the efficient recovery and recyclability of the catalyst. The Knoevenagel condensation reaction produces water as the byproduct, which dissolves the catalyst and makes its recovery by filtration less efficient. Moreover, using Na_2CO_3 as a catalyst led to significant decomposition of **1d** and **1f** during the reaction. When $CaCO_3$ was used as a heterogeneous inorganic base, catalyst recovery was convenient even though the reaction took significantly longer to complete (entry 2). However, $CaCO_3$ had negligible catalytic activity when other AMCs, such as **2c** and **2d**, were employed. This can be explained by the diminished acidity of the methylene protons in **2c** and **2d** when compared to **2a**.[31] Various secondary and tertiary amines effectively catalyzed the Knoevenagel condensation reaction and exhibited comparable catalytic activity. When diazabicyclo[2.2.2]octane (DABCO) was used as the catalyst for the reaction, the product yielded an 83% yield in 15 min. Triethylamine (TEA) afforded an 86% isolated yield of **3** after only 15 min at RT. Imidazole gave 82% yield in 30 min. When piperidine was used as the base and organocatalyst, the conversion of **1a** was complete within 30 min at RT, and an 86% isolated yield of **3** was obtained. 1,8-Diazabicyclo(5.4.0)-undec-7-ene (DBU) (entry 6) and pyrrolidine (entry 8) afforded noticeably lower yields of **3** due to partial decomposition of **1a**. In the control reaction (without catalyst), only a trace **3** was formed after 120 min at RT (entry 9). Evidently, the yields of **3** for TEA, DABCO, diisopropylethylamine (DIPEA), and piperidine were comparable. However, TEA and DABCO were not chosen as catalysts since they react with some SFLs, such as **1f**, by nucleophilic substitution. The central idea of this work was to develop a general synthetic strategy that works well for all commonly encountered carbohydrate-derived SFLs. Considering the above observations and results, piperidine was chosen as the most efficient base and organocatalyst to catalyze the Knoevenagel condensation reaction between SFLs and AMCs.

Table 1. Effect of Various Inorganic Bases and Organic Amines as Catalysts on the Yield of 2-(Furan-2-ylmethylene)malononitrile (3)[a]

entry	catalyst	duration (min)	yield (%)[b]
1	Na_2CO_3	15	86
2	$CaCO_3$	120	84
2	DABCO	15	83
3	TEA	15	86
4	imidazole	30	82
5	piperidine	30	86
6	DBU	30	71
7	DIPEA	30	85
8	pyrrolidine	30	50
9	no catalyst	12	trace

[a]Reaction conditions: furfural (5.2 mmol), malononitrile (5.2 mmol), catalyst (0.5 mmol), ethanol (5 mL), RT. [b]Isolated yield.

The loading of the catalyst plays a crucial role in reaction kinetics, selectivity, and process economics. Generally, a minimum loading of a homogeneous catalyst is warranted for cost minimization, easy recycling, and keeping the reaction volume low for maximum product density without compromising the reaction kinetics and product selectivity. A 10 mol% loading of piperidine, with respect to the initial amount of **1a**, allowed the reaction to complete within 30 min at RT and afforded an 83% isolated yield of **3**. Increasing the catalyst loading to 20 mol% did not improve the reaction kinetics or the yield of **3** to any significant extent. When the loading of piperidine was reduced to 5 mol%, the reaction required 4 h to complete, and only a 78% yield of **3** was obtained (Figure 1). In Figures 1 and 2, the percentage yield of the product is shown after ensuring quantitative conversion of the starting material. Different catalyst loadings needed different durations for the complete conversion of **1a**. The reaction between **1a** and a highly active methylene compound

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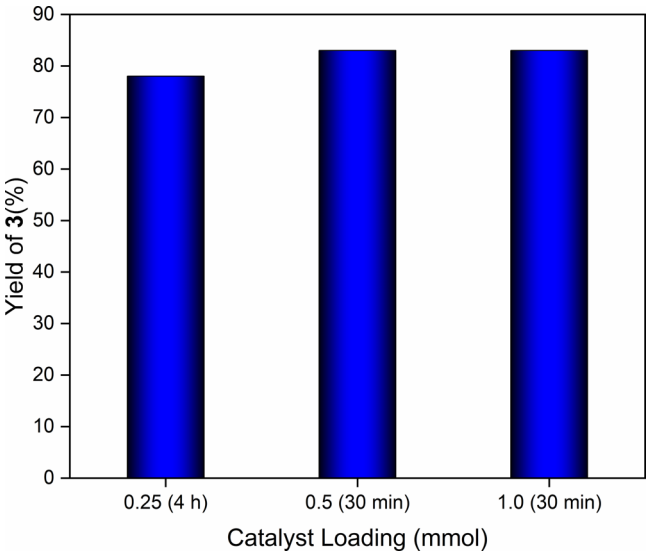

Figure 1. Effect of piperidine loading on yield of **3**. Reaction conditions: **1a** (5.20 mmol), **2a** (5.20 mmol), ethanol (5 mL), RT.

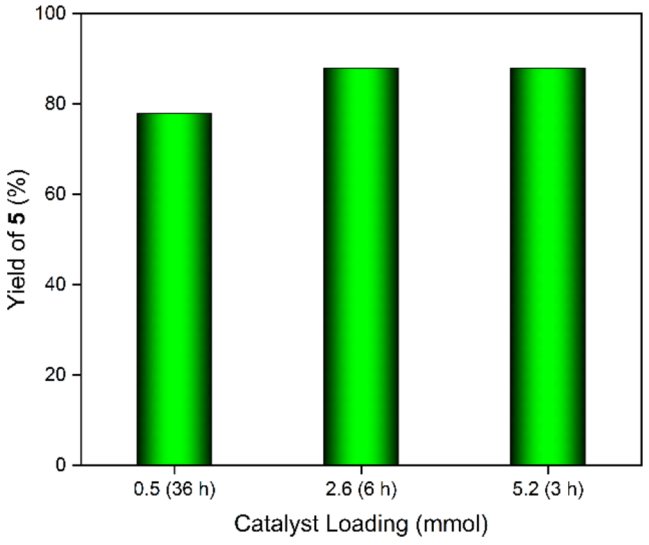

Figure 2. Effect of piperidine loading on the yield of **5**. Reaction conditions: **1a** (5.20 mmol), **2c** (5.20 mmol), ethanol (5 mL), RT.

2a gave only a 10% yield of **3** after 30 min using 5 mol% piperidine. However, increasing the catalyst loading to 10 mol % significantly improved the reaction kinetics and provided an 86% isolated yield of **3** in 30 min.

The reactions were carried out using equimolar amounts of **1a** and **2a**. Using a slight excess of **2a** had no noticeable impact on the duration of the reaction or the isolated yield of **3**. The optimized reaction protocol was extended to do the reaction with other SFLs (**1b**−**1g**). The Knoevenagel condensation reaction between **1a** and ethyl cyanoacetate **2b** was completed within 15 min, and ethyl (*E*)-2-cyano-3-(furan-2-yl)acrylate (**4**) was isolated in a 96% yield. Other organic amines, such as TEA and DABCO, took longer (30−90 min) and afforded slightly lower yields (88−92%) of **4**.

It is worth mentioning that mild bases like Na_2CO_3, $CaCO_3$, DABCO, imidazole, and triethylamine could not effectively catalyze the Knoevenagel condensation between **1a** and less active methylene compounds such as diethyl malonate **2c**, ethyl acetoacetate **2d**, and acetylacetone **2e**. A 50 mol% loading of piperidine allowed the reaction between **1a** and **2c** to complete within 6 h at RT and afforded an 88% yield of diethyl 2-(furan-2-ylmethylene)malonate (**5**) (Figure 2). Further lowering the loading to 10 mol% led to a significant increase in the reaction duration (36 h), giving only a 78% yield of **5** due to competing side reactions. Similarly, for the reaction between FUR **1a** and a less active methylene compound, diethyl malonate, a catalyst loading of 10 mol% gave only a trace yield (<10% yield) of **5** after 3 h. Increasing the catalyst loading to 50 and 100 mol% improved the isolated yield of **5** to 30 and 88%, respectively, after a reaction duration of 3 h. Lower yields of **5** using lower loadings of piperidine were due to incomplete conversion of **1a**. At 50 mol% loading of piperidine, the reaction took 6 h for the quantitative conversion of **1a** and afforded an 88% isolated yield of **5**.

When the reaction temperature was increased to 60 °C, the reaction kinetics got significantly faster, and the reaction was completed in 10 h. However, the yield of **5** did not improve further.

The Knoevenagel condensation reaction between **1a** and **2d** was then investigated. With a 25 mol% loading of piperidine, the conversion of **1a** was not complete even after 24 h reaction at RT. Hence, the amount of **2d** was slightly increased to 1.25 equiv based on the initial amount of **1a**. The reaction was completed in 4 h, providing a 78% isolated yield of ethyl 2-(furan-2-ylmethylene)-3-oxobutanoate (**6**). Furthermore, when the piperidine loading was increased to 50 mol% (i.e., 0.5 equiv of **1a**), the reaction duration was shortened to 3 h, but no improvement in the yield of **6** was observed. The use of Na_2CO_3, DABCO, triethylamine, and imidazole as base catalysts did not show appreciable conversion of **1a** even after 12 h. The reaction between **1a** and **2e** was then investigated using equimolar amounts and 100 mol% piperidine catalyst. The reaction required 90 min for complete conversion of **1a**, giving a 70% yield of **7**. Reducing the catalyst loading to 50 mol% of **1a** slowed down the reaction to some extent, but it was completed in 120 min. However, when the catalyst loading was further decreased to 25 mol%, the conversion of **1a** remained incomplete even after 24 h of reaction at RT. Hence, 50 mol% (0.5 equiv of starting **1a**) loading of piperidine was considered the optimum catalyst loading, providing a 70% yield of **7**. The optimized process was then extended to the Knoevenagel condensation between **2e** and other SFLs (**1b**−**1g**). Table 2 lists the molecular structure and yield of novel Knoevenagel condensation products (**3**−**37**). Slightly lower yields were obtained for Knoevenagel condensation products of **1e** (i.e., **23**−**27**). The observation may be explained by the inherent hydrolytic instability of **1e**. No apparent trend was observed in the case of a specific AMC, and the reactivity was mostly dependent on the reactivity of SFLs. In the case of derivatives of **2b** and **2d**, the formation of *E* and *Z* isomers was apparent from the ^{1}H NMR and ^{13}C NMR spectra, and the thermodynamically more stable *E*-isomer dominated (Supporting Information). Moreover, the synthesis of **3** was scaled up, starting with 10 g of **1a**. The yield of **3** marginally increased to 88%. After the reaction was complete, ethanol was evaporated in a rotary evaporator under reduced pressure. Piperidine was conveniently recovered by vacuum distillation of the crude mixture. The first recycling gave a 79% isolated yield of **3** after 6 h due to slight contamination of water in recycled piperidine.

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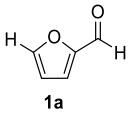
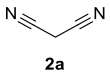
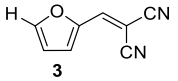
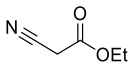
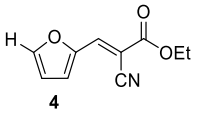
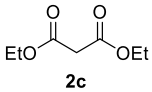
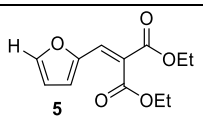
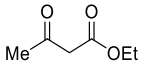
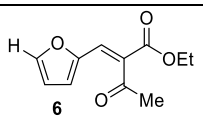
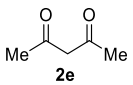
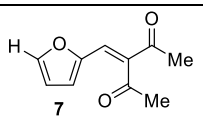
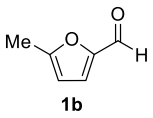
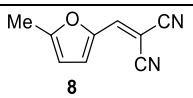
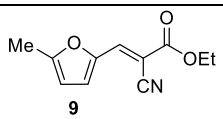
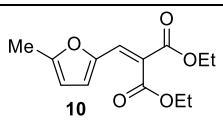
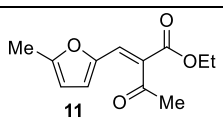
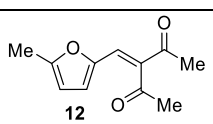
Table 2. Molecular Structure of 5-Substituted-2-furaldehydes, Active Methylene Compounds, and the Knoevenagel Condensation Products

Entry	*SFL*	*AMC*	*Knoevenagel product*	*Yield (%)*[a]
1	 **1a**	 **2a**	 **3**	86[#]
2		 **2b**	 **4**	96
3		 **2c**	 **5**	88
4[b]		 **2d**	 **6**	78
5		 **2e**	 **7**	70
6	 **1b**	**2a**	 **8**	87
7		**2b**	 **9**	70
8		**2c**	 **10**	77
9[c]*		**2d**	 **11**	80
10		**2e**	 **12**	85

https://doi.org/10.1021/acsomega.4c04261
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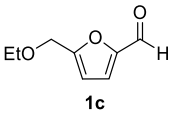
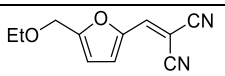
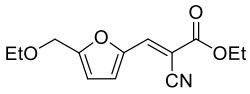
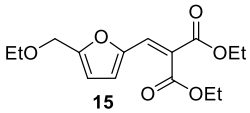
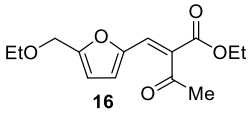
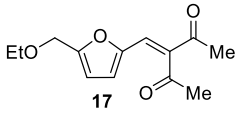
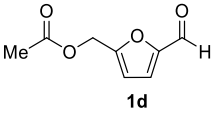
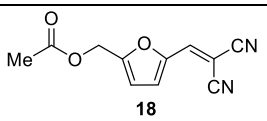
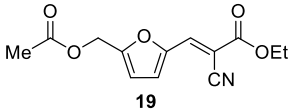
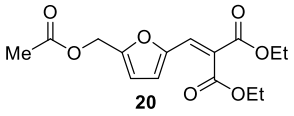
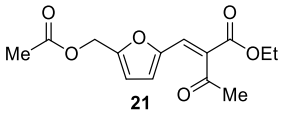
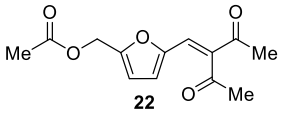
Table 2. continued

Entry	*SFL*	*AMC*	*Knoevenagel product*	*Yield (%)*[a]
11*	 **1c**	**2a**	 **13**	77
12*		**2b**	 **14**	73
13*		**2c**	 **15**	92
14[d]*		**2d**	 **16**	78
15*		**2e**	 **17**	75
16	 **1d**	**2a**	 **18**	70
17*		**2b**	 **19**	95
18*		**2c**	 **20**	96
19[e]*		**2d**	 **21**	83
20*		**2e**	 **22**	80

https://doi.org/10.1021/acsomega.4c04261
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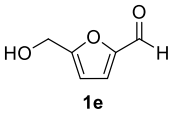
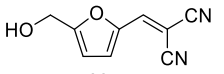
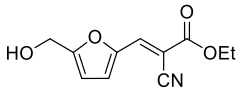
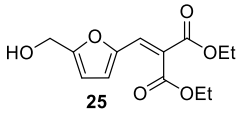
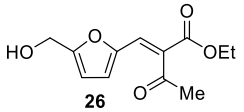
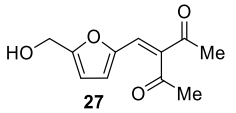
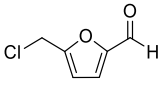
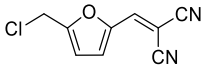
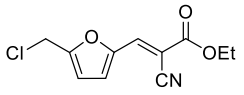
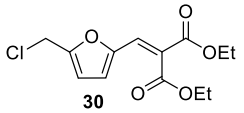
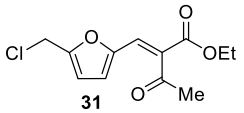
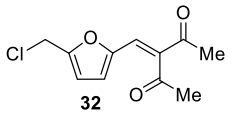
Table 2. continued

Entry	*SFL*	*AMC*	*Knoevenagel product*	*Yield (%)*[a]
21	 **1e**	**2a**	 **23**	65
22		**2b**	 **24**	60
23		**2c**	 **25**	75
24[f]*		**2d**	 **26**	78
25		**2e**	 **27**	60
26*	 **1f**	**2a**	 **28**	85
27*		**2b**	 **29**	70
28*		**2c**	 **30**	76
29[g]*		**2d**	 **31**	84
30*		**2e**	 **32**	75

https://doi.org/10.1021/acsomega.4c04261
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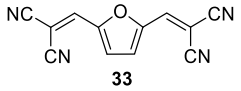
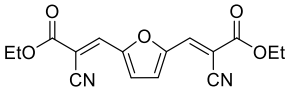
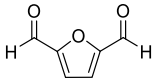
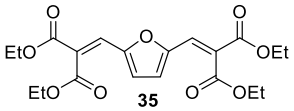
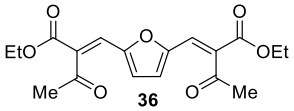
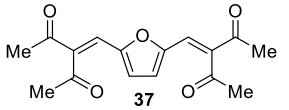
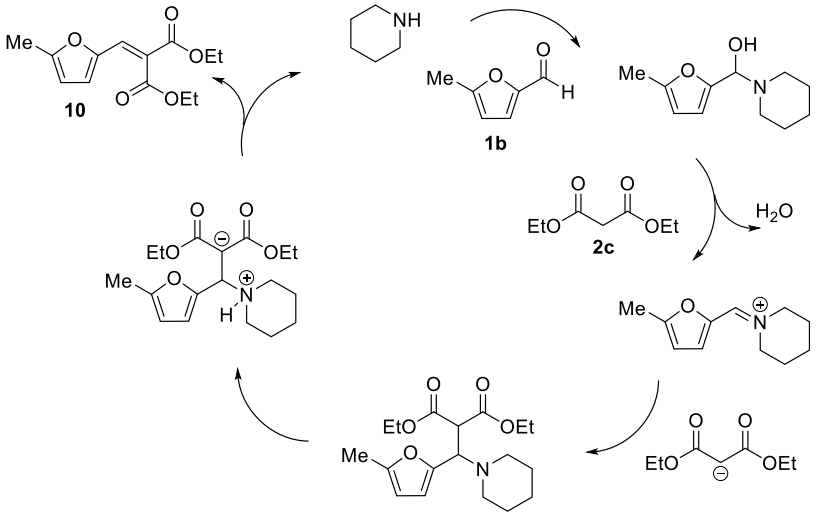
Table 2. continued

Entry	*SFL*	*AMC*	*Knoevenagel product*	*Yield (%)*[a]
31		**2a**	 **33**	84
32		**2b**	 **34**	86
33	 **1g**	**2c**	 **35**	90
34[h]		**2d**	 **36**	80
35*		**2e**	 **37**	80

[a]Isolated yield of spectroscopically pure compounds. [b]*E*:*Z* ratio 3:1. [c]*E*:*Z* ratio 7:3. [d]*E*:*Z* ratio 4:1. [e]*E*:*Z* ratio 9:1. [f]*E*:*Z* ratio 7:3. [g]*E*:*Z* ratio 4:1. [h](2*E*,2′*E*):(2*Z*,2′*E*):(2*Z*,2′*Z*) ratio 6.5:2.2:1.3. [#]A scale-up of the reaction using 10 g of FUR **1a** gave an 88% isolated yield of **3**. [*]Novel compounds.

Scheme 2. Proposed Mechanism of Piperidine-Catalyzed Synthesis of Knoevenagel Condensation Products from 5-Methylfurfural and Diethyl Malonate (Adapted from Reference 23)



A general reaction mechanism has been proposed for the piperidine-catalyzed Knoevenagel reaction between MF **1b** and **2c**, which agrees with a published work (Scheme 2).[23] Initially, **1b** condenses with piperidine to form an iminium ion, which then reacts with the deprotonated **2c**. The adduct then undergoes a proton transfer process followed by elimination of the piperidine molecule, leading to the Knoevenagel condensation product **10**. The ^{1}H NMR spectrum of the incomplete reaction mixture showed the iminium proton around 8 ppm.

It must be noted that the reaction gets accelerated at elevated temperatures, allowing a significantly lesser amount of piperidine catalyst to be used. However, elevated temperature leads to side reactions when **1d**, **1e**, and **1f** are used as substrates.

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4. CONCLUSIONS

In conclusion, a piperidine-catalyzed general synthetic protocol was developed for preparing several novel Knoevenagel condensation products by reacting carbohydrate-derived 5-substituted-2-furaldehydes with active methylene compounds. The reaction was performed in the aqueous medium or under organic solvent-free conditions to improve the eco-friendly characteristics of the synthetic protocol. The gram-scale reaction afforded satisfactory yields of the targeted compounds at room temperature. The compounds were isolated and purified by solvent-solvent extraction and trituration using eco-friendly solvents, such as ethyl acetate and *n*-heptane. The biorenewable aldehydes as substrates, ambient temperature, a metal-free recyclable catalyst, convenient purification of products, and satisfactory yield of products, make this process an economically amenable and environmentally acceptable process of extending the carbon chain of 5-substituted-2-furaldehydes for downstream value addition pathways. All the synthesized compounds were characterized by FTIR, NMR (^{1}H, ^{13}C), and elemental analysis. Future studies will focus on the biological activities of these renewable compounds.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c04261.

FTIR, ^{1}H NMR, and ^{13}C NMR, characterization data, spectra, elemental analysis data, and melting points of all synthesized Knoevenagel condensation products (PDF)

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Author Contributions

P.S.P. performed the experiments and analyzed the spectroscopic data. A.H.S. and M.R.K. acquired research funding and edited the manuscript. S.D. conceptualized the work, supervised the progress, and wrote the original manuscript.

Notes

The authors declare no competing financial interest.

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