Biomass Conversion

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Butenolide Derivatives of Biobased Furans: Sustainable Synthetic Dyes

*Jan Saska, Zheng Li, Andrew L. Otsuki, Jiahui Wei, James C. Fettinger, and Mark Mascal**

Abstract: *The dye and pigment manufacturing industry is one of the most polluting in the world. Each year, over one million tons of petrochemical colorants are produced globally, the synthesis of which generates a large amount of waste. Naturally occurring, plant-based dyes, on the other hand, are resource intensive to produce (land, water, energy), and are generally less effective as colorants. Between these two extremes would be synthetic dyes that are fully sourced from biomass-derived intermediates. The present work describes the synthesis of such compounds, containing strong chromophores that lead to bright colors in the yellow to red region of the visible spectrum. The study was originally motivated by an early report of an unidentified halomethylfurfural derivative which resulted from hydrolysis in the presence of barium carbonate, now characterized as a butenolide of 5-(hydroxymethyl)furfural (HMF). The method has been generalized for the synthesis of dyes from other biobased platform molecules, and a mechanism is proposed.*

Industrial dyes and pigments are almost exclusively derived from petrochemicals. The production for example of azo dyes, the largest class of organic colorants, relies on polyaromatic scaffolds from coal tar refining. Although many petroleum-based materials can be recycled, 100% of dyes end up in landfills, with all of their fossil carbon, ca. one million tons globally per annum, ultimately emerging as CO_2 in the atmosphere.[1] An answer to this issue from the sustainability movement has been to promote the use of plant-based dyes.[2] However, these products are expensive, suffer from generally inferior coloring performance, and many have poor substantivity, requiring metal mordants as fixatives, most of which ends up as effluent. Finally, natural dyes are low-yield crops with consequent land, water, energy, and agrochemical burdens. Alternative microbiologically-produced and waste-based colorants embody creative alternatives to botanical dyes,[3,4] although production limitations would suggest this is not a comprehensive solution to the problem.

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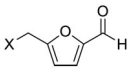
Despite the large market for organic dyes, sustainable chemistry research has primarily targeted fuels and polymers, and virtually no reports of renewable synthetic colorants have appeared to date. The present work thus represents an approach to introducing a new major chemical commodity to sustainable practice, that is, biobased synthetic dyes.

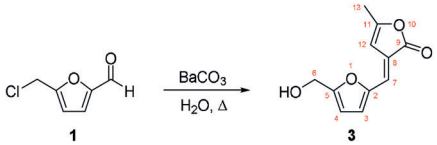
5-(Chloromethyl)furfural (CMF) **1** is a carbohydrate-derived renewable platform molecule that is considered to be a disruptive innovation in the field of green chemistry.[5,6] Equivalent to 5-(hydroxymethyl)furfural (HMF) **2** in its synthetic versatility, CMF **1** can be produced in high yield directly from raw biomass, while HMF **2** is only practically derived from fructose.[7]



1 (X=Cl)
2 (X=OH)

CMF first appeared in the literature in 1901, when Henry Fenton (of Fenton's reagent fame)[8] described its production in low yields by treatment of sugars or cellulose with HCl.[9] We were intrigued by the description of an early investigation into the chemistry of halomethylfurfurals that borrowed from Fenton's work, in which treatment of 5-(bromomethyl)furfural (BMF) with barium carbonate in hot water resulted in the isolation of "a beautiful yellow … compound, which usually crystallizes in canary-yellow needles."[10] The proposed formula was $C_{11}H_{10}O_4$, and yields were described as variable without being specified. No structural assignment was made, although it was suggested that the product could be the result of the reaction of BMF with levulinic acid, the latter of which is a known decomposition product of HMF. With the benefit of modern analytical techniques, we set out to determine the structure of this compound and investigate the chemistry of its formation.

We first reproduced the method as described in the literature, but substituting the more practical CMF for BMF. Thus CMF was suspended in water and the mixture was heated from room temperature to 60 °C. Solid barium carbonate was introduced portionwise. Once a clear solution was obtained, an excess of $BaCO_3$ was added and the mixture was heated to near boiling and then filtered hot. The filtrate deposited a yellow oil which on cooling gradually solidified to a mass of deep yellow needles. We have now identified this product as **3** (Scheme 1), the apparent result of the reaction of



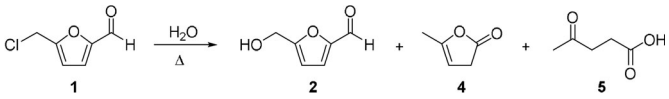
1 **3**

Scheme 1. Original synthesis of **3** from CMF and aq. barium carbonate.

1 with angelica lactone **4**, followed by hydrolysis of the chloromethyl group. The yield in our hands was 22%.

Compound **3** had in fact previously been reported as the product of the reaction of HMF with angelica lactone, which was first described in 1982,[11] and revisited more recently for the purposes of making biofuels.[12,13] Indeed, the condensation of butenolides with carbonyl groups is a well-known reaction.[14] The question here however is this: if angelica lactone **4** was involved in the process, how did it arise?

Angelica lactone **4** is known to be a dehydration product of levulinic acid **5**, and the derivation of levulinic acid in high yield from CMF in hot water has also been described.[15] However, the conversion of levulinic acid **5** to angelica lactone **4** requires the use of a dehydrating agent,[16] so it would be puzzling to see this transformation operating between **1** and **3**, particularly as the reaction takes place in aqueous solution. Proposing an alternative direct condensation between levulinic acid and CMF is equally problematic, in that it would involve exclusive attack of the enolate of the carboxylic acid of levulinic acid at the aldehyde function of **1** (or **2**) in preference to the more reactive positions α to the ketone. We therefore set out to obtain evidence of the intermediacy of angelica lactone in the reaction in Scheme 1. Interestingly, heating a mixture of CMF **1** and water to 60°C followed by immediate quenching gave a clear solution that was shown by NMR to be a mixture of HMF **2** (41%), angelica lactone **4** (22%), and levulinic acid **5** (5%) by integration against a dioxane internal standard (Scheme 2).

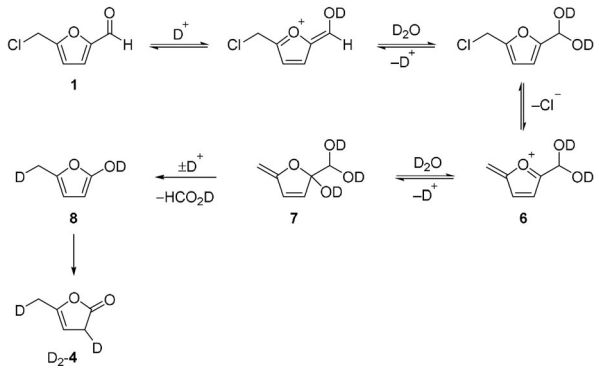


Scheme 2. Decomposition products of CMF **1** in water at 60°C.

The remaining mass balance was CMF, which collected as an oil at the bottom of the flask, and could be isolated by extraction with solvent.

Since this outcome could not have reasonably involved dehydration of levulinic acid, we sought a mechanism to link CMF directly with angelica lactone. Conducting the above reaction in D_2O gave angelica lactone mono-deuterated at both the 2- and 5-positions, as clearly shown by both the ^1H and ^{13}C NMR spectra (see SI).[17] This led us to propose the mechanism in Scheme 3 for the conversion of CMF **1** to angelica lactone **4**. The catalytic D^+ required derives from background hydrolysis of CMF to HMF.[15] Initial generation of the hydrate facilitates the expulsion of chloride to give key intermediate **6**. Addition of D_2O to **6** at the *exo* methylene would lead to HMF **2**, while addition to the C=O$^+$ function as shown provides a route to D_2-**4**. Computational modeling of the pathway in Scheme 3 fully supports the proposed mechanism (see SI for details).

A parallel experiment involving the submission of HMF to the exact same reaction conditions (time, temperature and pH gradient) resulted in the observation of < 10% conversion levulinic acid **5**, with no trace of angelica lactone **4**. We also subjected 5-(ethoxymethyl)furfural (EMF), which has (poor)

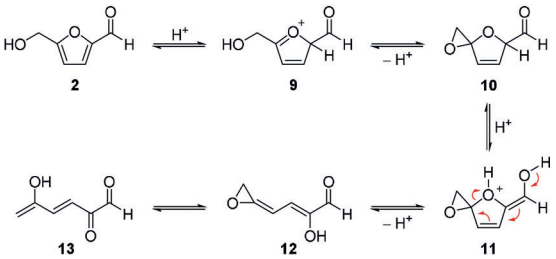


Scheme 3. Proposed mechanism for the conversion of CMF to angelica lactone in D_2O.

solubility in water similar to that of CMF, to these same conditions, and likewise observed < 10% conversion to levulinic acid, but again no angelica lactone. These results indicate the reaction in Scheme 2 is unique to halomethylfurfurals.

Several literature interpretations of the mechanism of the hydrolysis of HMF to levulinic acid invoke an intermediate like **7**, which ring opens to give levulinic acid after deformylation and hydration.[18–20] Our results however indicate that the activation barrier to ring opening of **7** is higher than that which leads to **8**. Li et al. also found this to be the case when they modeled the rehydration of HMF in the presence of an ionic liquid catalyst, where the more energetically favorable pathway to levulinic acid was found to go via **8** (non-deuterated).[21] Yang and co-workers came to the same general conclusion, where levulinic acid was proposed to result from the hydrolysis of an angelica lactone intermediate.[22] Our findings here however suggest that this cannot be the case, since only the hydrolysis of CMF, not HMF, leads to angelica lactone **4**. If an intermediate akin to **7** is not present in the hydrolysis of HMF, what then is the mechanism?

We approached this question by considering that the only difference between CMF **1** and HMF **2** is that the latter incorporates an oxygen that can potentially act as a nucleophile. Starting from this premise, the only reasonable intramolecular attack of OH group on the furan ring involves the formation of spiro acetal **10** (Scheme 4), which was found to have a moderate activation barrier of 16.6 kcal mol^{-1} (see SI). This versatile intermediate could in principle directly deformylate to furfuryl alcohol, which is a known precursor to



Scheme 4. Alternative mechanism for cleavage of the HMF ring in aqueous acid.

levulinic acid by acid-catalyzed hydrolysis.[23] We did not however observe furfuryl alcohol in the course of the hydrolysis of HMF, and we thus looked to the outcomes of protonation of **10** at the acetal oxygen sites. Protonation of the oxirane leads back to HMF **2**, as expected. Protonation however at the dihydrofuran oxygen results in ring opening as indicated in structure **11** to give **12**, which rearranges to **13**. Compound **13** then enolizes, decarbonylates, and hydrates to levulinic acid as described by previous mechanistic studies.[20] The above results suggest that literature proposals for the mechanism of HMF rehydration to LA may only be partially correct.

The intermediacy of angelica lactone in this reaction suggested that the addition of external **4** to the reaction mixture should improve the selectivity for product **3**. Indeed, the yield of **3** ultimately rose to 46% in the presence of three added equivalents of angelica lactone. The mass balance of the reaction was shown to be levulinic acid, derived mainly from the competing hydrolysis of angelica lactone. It was also found that $CaCO_3$ was equally effective as $BaCO_3$ in this reaction. The attempted use of a soluble base (K_2CO_3) or nucleophilic catalysts (piperidine, proline) resulted in little or no yield of **3**.

According to DFT modeling (B3LYP/6-31 + G(d,p)), the C2–C7 bond in **3**, while formally single, is short (1.43 Å) and has a computed rotational barrier of 11.5 kcal mol^{-1}. This lack of free rotation on the NMR time scale, along with the *cis-trans* isomers of the double bond, leads to a total of four distinguishable stereoisomers: *trans s-trans*, *trans s-cis*, *cis s-trans*, and *cis s-cis*. Optimization of each of these structures showed that the *trans s-cis* stereoisomer (as drawn in Scheme 1) was the lowest in energy, and included a weak hydrogen bond between C12–H and O1. Furthermore, modeling of the ^{13}C-NMR shielding tensors of the stereoisomers of **3** using the gauge-independent atomic orbital (GIAO) ab initio method showed that *trans s-cis* **3** gave the best agreement with the experimental data (RMS deviation 1.4 ppm, maximum error 2.3 ppm; see SI for comparisons with other structures). Finally, an X-ray crystal structure of **3** confirmed that the same isomer was also present in the solid state (Figure 1). The agreement between the modeled and experimental structures of **3** is excellent.

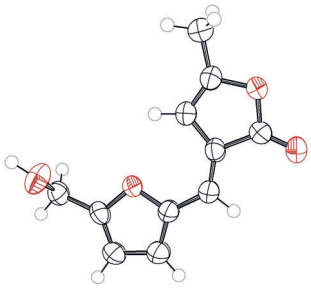


Figure 1. X-ray crystal structure of **3**.

The intense yellow color of crystals of **3** and its solutions led us to a closer investigation of the nature of the chromophore, which was evaluated by UV/Vis spectroscopy

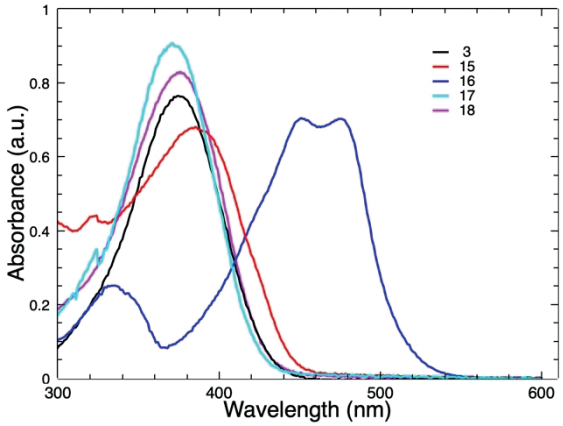
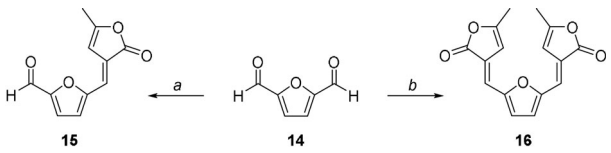


Figure 2. UV/Vis curves of **3** (black), **15** (red), **16** (blue), **17** (cyan), and **18** (magenta) in ethanol with maxima at 9.22×10^{-2}, 7.68×10^{-2}, 3.88×10^{-2}, 2.22×10^{-2} and 4.90×10^{-2} mmol L^{-1}, respectively.

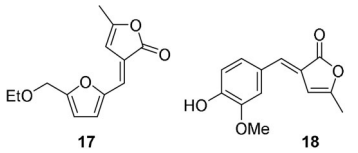
(Figure 2). The peak at 374 nm has a molar absorptivity of 1.254×10^4 M^{-1} cm^{-1}. In an attempt to intensify absorption, we oxidized CMF to 2,5-diformylfuran (DFF) **14** in a single step by Kornblum reaction[24] and condensed **14** directly with angelica lactone. Under mild conditions this led to a mono-adduct of the angelica lactone nucleophile, giving derivative **15**, while under more forcing conditions, twofold reaction was observed, giving **16** as a red solid (Scheme 5). While **15** had a similar absorption spectrum to that of **3**, its TLC spot showed evidence of fluorescence under UV light. Indeed, excitation at 389 nm gave a strong fluorescence peak at 497 nm (see SI). The more extensive conjugation in **16** led to bathochromic and hyperchromic shifts, with molar absorptivity of 3.086 and 3.097×10^4 M^{-1} cm^{-1} at 451 and 475 nm, respectively, values well within the range of commercial disperse dyes.[25] As was the case for **3**, the most stable stereoisomers of **15** and **16** were determined by energy minimization and comparison of calculated and experimental ^{13}C NMR shifts, and are as shown in the structures in Scheme 5 (see SI for details).

A synthetically more useful route to **3** employed dioxane as solvent instead of water (to suppress competing hydrolysis of **4**) and Mn_2O_3 as catalyst, which outperforms $CaCO_3$.[12,13] The yield of **3** under these conditions improved to 87%. Using ethanol as the solvent gave the corresponding ethoxy derivative **17**, also in high yield (85%). Condensation of DFF **14** with angelica lactone in dioxane gave **16** with no trace of **15**, and in much improved yield (82%) over the reaction in aqueous solution.



Scheme 5. Synthesis of dyes **15** and **16** via CMF-derived DFF **14**. Reagents and conditions: a) **4**, H_2O, 90 °C, 1 h. b) **4**, $CaCO_3$, H_2O, 100 °C, 2 h.

In order to generalize the concept of installing the angelica lactone-derived methylbutenolide chromophore onto biobased aldehydes to produce synthetic dyes, we extended the reaction to vanillin, a cheap commodity chemical isolated from processed lignin.[26] Under the same general conditions (**4**, Mn_2O_3, dioxane, reflux 14 h), **18** was obtained as a bright yellow solid in 84% yield.



17 **18**

We carried out preliminary dyeing tests of **3**, **15**, **16**, **17**, and **18** using a fabric strip consisting of cellulose diacetate, cotton, Nylon 6-6, Dacron 54 polyester, Dralon polyacrylic, silk, viscose, and wool. A standard aqueous dyeing procedure was used, involving the dyes (1 mg mL^{-1}), a dispersing agent (formalin), accelerator (phenol), and fixative (ammonium sulfate). The detailed procedure is given in the SI. The dyes colored all of the fabrics except cellulose and viscose (regenerated cellulose), with colors that varied from yellow (**3**, **17**, and **18**) to canary (**15**) to orange (**16**). Standard wash testing demonstrated excellent substantivity.

In summary, although various classes of sustainably sourced industrial products have been described in the literature, to our knowledge, no synthetic dyes produced entirely from biomass-derived platform molecules[27] have been reported. It is our intention to introduce here the concept of biobased synthetic dyes that bear neither the stigma of derivation from petrochemicals nor the drawbacks of natural colorants. The method described here is versatile and can in principle be applied to any naturally occurring aromatic aldehyde. Preliminary analysis shows good color performance and substantivity and, combined with more sustainably produced synthetic fabrics, such as poly(ethylene terephthalate) from biomass,[28] the potential to unlock new markets in 100% sustainable wearables is in view.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: biomass conversion · chromophores · dyes/pigments · furans · sustainable chemistry

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Communications

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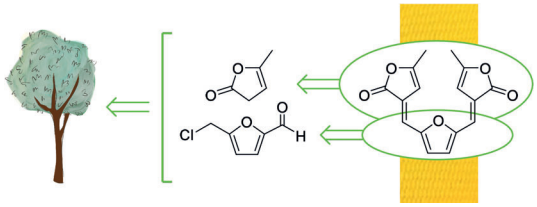

To dye for: Synthetic dyes are yet another industrial commodity that can be sustainably produced wholly from biomass-derived platform molecules. The synthesis of biobased dyes containing strong chromophores that lead to bright colors in the yellow to red region of the visible spectrum is described.