Published in final edited form as:

Tetrahedron Lett. 2014 July 23; 55(30): 4141–4145. doi:10.1016/j.tetlet.2014.05.043.

Bio-Based Bisfuran: Synthesis, Crystal Structure and Low Molecular Weight Amorphous Polyester

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Abstract

Discovery of renewable monomer feedstocks for fabrication of polymeric demand is critical in achieving sustainable materials. In the present work we have synthesized bisfuran diol (BFD) monomer from furfural, over four steps. BFD was examined via X-ray crystallography to understand the molecular arrangement in space, hydrogen bonding and packing of the molecules. This data was further used to compare BFD with structurally related Bisphenol A (BPA), and its known derivatives to predict the potential estrogenic or anti-estrogenic activities in BFD. Further, BFD was reacted with succinic acid to generate polyester material, bisfuran polyester (BFPE-1). MALDI characterization of BFPE-1 indicates low molecular weight polyester and thermal analysis reveals amorphous nature of the material.

Keywords

Biomass; Furfural; Bisfuran diol (BFD); Bisfuran polyester (BFPE-1); Bisphenol A (BPA); X-ray crystallography.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at

The use of lignocellulose plays a central role in the potential of renewable resources contributing to a self-sustained model, for future polymer material demand.^{1, 2} A significant percentage of biomass consists of non-food-source material like grass, wood, straw, etc., which can be utilized for producing value-added chemicals and polymers.³⁻⁵ Research in the extraction and the development of raw materials from biomass for polymer synthesis is a field of growing interest. Polymer industry is one of the ever growing sectors, and biomass-derived polymers are attracting the attention of academic and industrial researchers alike.⁵

The molecular framework of furan has been fascinating to chemists. This is evident from the fact that some of the groundwork involving the construction of furan-based compounds as industrial commodities was envisaged as far back as the mid last century.⁶ Alessandro Gandini explained the use of furan containing moieties in the preparation of various polymers.⁷ The efforts of Moore and coworkers in producing furan polyesters are also recognized as a significant contribution in the field.⁸⁻¹¹ Furan-based compounds have also been explored as monomeric units for creation of polyamides, polyurethanes, polyesters, and polyethers by Gandini and coworkers.^{7, 12-30} Generation of furanic polyester material via, polymerization of diacid chlorides, and diester derivatives with a variety of diols has also been reported.^{10, 21, 29}

Encouraged by these reports we designed an efficient gram scale synthesis of bisfuran (BF) monomer, BFD, Scheme 1, compound **5**, from commercially available furfural, employing minimal chemical transformations.³¹ The low melting BFD compound was crystallized and examined via X-ray crystallography to understand the molecular structure, hydrogen bonding, and packing of the crystalline monomer. The crystal structure of BFD was compared with BPA and its derivatives. BPA is a ubiquitous molecule in polymer industry known to exhibit estrogenic activity.³²⁻³⁴ BFD was further studied in a bench scale polyester polymerization using classical step-growth polymerization which resulted in low molecular weight linear polyester, BFPE-1, with average molecular weight of 5 kDa, determined using MALDI-TOF/TOF analysis. TGA and DSC experiments revealed amorphous nature of the polyester material. IR, ¹H and ¹³C – NMR experiments were performed to establish the identity of the synthesized polyester, BFPE-1.

We envisioned the synthesis of BFD, compound **5**, Scheme 1, as a potential monomer to undertake a polymerization study. Starting with commercially available furfural, we protected the aldehyde functionality to afford 1,3-dithiolane protected compound **2**. Compound **2**, was subjected to Friedel-Crafts alkylation, to yield dimerized product, compound **3**. The dedithioacetalization of compound **3** led to the desired deprotected dialdehyde product, compound **4**. In the last step, reduction of dialdehyde to the diol was accomplished to yield target compound **5**, BFD. We note that we did attempt condensation of furfural **1** with acetone under acidic conditions. This reaction failed and rapidly produced red colored side products which we did not characterize.

The BFD compound was crystallized and examined via X-ray crystallography to understand the molecular structure, hydrogen bonding, and packing of the crystalline monomer. Further, we compared the structure of BFD with BPA and its known derivatives with estrogenic

activities to understand the molecular features that may be involved in possible estrogenic or anti-estrogenic activities.

The title compound BFD, also referred to as 5'-(propane-2,2-diyl)bis(furan-2,5-diyl)dimethanol **5**, crystallized in the space group $P2_1/c$ with one molecule in the asymmetric unit. As shown in Figure 1A, the molecules exhibit an approximate non-crystallographic 2-fold symmetry through the central bridging C6 atom with the oxygen-atoms O1, O1' and O2, O2' pointing in opposite directions, respectively. The orientation of the two aromatic rings towards each other can be described by the dihedral angle between the mean planes of the two rings, which has a value of $80.15(5)^\circ$. This is within the broad range of equivalent angles in the solid state structures of BPA and its derivatives ($71.43 - 89.62^\circ$). Specifically, the three crystallographically independent molecules in the crystal structure of BPA possess dihedral angles of $79.7(2)$, $83.6(2)$ and $86.9(2)^\circ$.^{35, 36}

There is a significant difference in the conformation of the BPA and the currently discussed structure of BFD with respect to the propeller-like arrangement of the aromatic rings. A pitch angle, Ψ , can be used to describe the amount of rotation around the C6-C5 or C6-C5' bond, turning the respective aromatic ring in ($\Psi = 0^\circ$) and out of the central C5-C6-C5' plane.³⁶ The two rings in BFD are with pitch angles of $74.98(8)$ and $66.04(7)^\circ$ significantly more twisted toward a perpendicular arrangement than the ones in all three BPA molecules, whose pitch angles range from only $45.59(6)$ to $59.62(7)^\circ$. In 2007, Matsushima *et al.* have demonstrated the binding of BPA to human estrogen-related receptor γ (EER γ) and its activity as an endocrine disruptor.³⁷ The study reported the anchoring of the terminal hydroxyl groups on the two aromatic rings with i) Glu275 and Arg316, ii) Asn346, accompanied with hydrophobic interactions with Tyr326 to establish a good binding with ERR γ .³⁷ It has been documented that the estrogen receptor ligands possessing hydroxyl groups with O-O distance ranging from $9.7 - 12.3$ Å display a medium to strong endocrine receptor ligand capacity, and O-O distances outside of this range are expected to weakly interact with the receptor.³⁸ The O-O distance between the oxygen atoms of BPA is 9.404 Å. It has also been discussed that the planarity of the non-hydrogen atoms of the hydroxyphenol moieties in BPA (± 0.03 Å) is advantageous for its locking into the estrogen acceptor pocket of ERR γ . By replacing the hydroxyl group with a CH₂OH-group in BFD, the geometry of the substituent is distinctively non-planar with O2 and O2' being $1.050(3)$ and $1.210(3)$ Å above the respective aromatic ring moiety potentially hindering the binding of BFD, to the receptor. Also, the O-O distance between terminal hydroxy groups of BFD is $8.215(2)$ Å, which is substantially outside the range to be a xenoestrogen.

Further, the conformation of BFD in the solid state comes from steric hindrance of the two methyl groups (C7 and C7') and packing effects, especially hydrogen bonds. Although on initial inspection, molecules of BFD seem to exhibit a non-crystallographic 2-fold axis, closer examination reveals a quite different secondary coordination sphere for O1 and O1' as well as O2 and O2'. While the furan oxygen O1 is not involved in any hydrogen bonds, the other furan oxygen O1' acts as an acceptor with $O1' \cdots H2_C-O2_C$ ($\times, 0.5-y, 0.5+z$) = $2.05(3)$ Å. Concomitantly, the C2-O1 and C5-O1 bonds are with $1.380(2)$ and $1.378(2)$ Å shorter than the comparable C2'-O1' and C5'-O1' bonds of $1.386(2)$, respectively. In a similar way, the hydroxyl group O2'-H2' is acting as a hydrogen bond donor O2'-

$\text{H2}' \dots \text{O2_A}(-x, 2-y, 1-z) = 1.90(3) \text{ \AA}$, while the other hydroxyl group O2-H2 acts simultaneously as a hydrogen-bond acceptor ($\text{O2} \dots \text{H2}'_A - \text{O2}'_A(-x, 2-y, 1-z) = 1.90(3) \text{ \AA}$) and as hydrogen-bond donor to a furan oxygen ($\text{O2-H2} \dots \text{O1}'_B(x, 1.5-y, -0.5+z) = 2.05(3) \text{ \AA}$). Figure 1B shows how hydrogen bonds between two molecules of BFD with $\text{O2}'$ as a hydrogen bond donor and O2 as the acceptor forming a rectangular dimer of approximate dimensions $8 \times 12 \text{ \AA}^2$. The structure resembles the covalently bonded cyclic BPA-carbonate dimer, which shows a similar small ring structure with dimensions $9 \times 10 \text{ \AA}$.^{39, 40}

BFD was further utilized to develop a linear polyester material employing a classical step-growth polymerization via alcohol esterification, Scheme 2. Two co-monomeric units, diol **5** and succinic acid were used to generate poly (furan succinate) copolyester, BFPE-1, compound **6**. Succinic acid is a well established industrial commodity and identified as one of the top value added chemicals accessible from fermentable sugars, via biomass.^{41, 42}

The molar mass distribution of the synthesized BFPE-1 was determined using MALD-ITOF/TOF analysis. The spectrum of BFPE-1 illustrates mass distribution in the range of 3 – 7.5 kDa Figure 2, and 0.5 – 3.0 kDa, inset Figure 2. A repeat of 318 mass units and residue of 276 mass units was identified from the MALDI spectrum.

Thermal analysis of the synthesized BFPE-1 material was studied via TGA and DSC experiments. At 100 °C the material shows a weight loss of ~ 2 % which could be accounted for the loss of residual water, Figure 3. The start of thermal decomposition (T_{start}) between 100 to 225 °C, displays a weight loss of ~ 5 %. A plot of derivative weight (%/°C) vs. temperature (°C) reveals two stage degradation of the BFPE-1 material with two maximum (T_{max}), inset Figure 3. The T_{max} for first stage of degradation exhibits a value of 266 °C, and for the second stage 329 °C. The corresponding weight losses at the end (T_{end}) of the two degradation stage temperatures are ~ 52 % and ~ 80 %, respectively.

DSC analysis of BFPE-1 was performed to observe glass transition (T_g) between 15 – 25 °C and degradation temperature (T_d) of 260 °C. Absence of melt crystallization (T_c) and melting (T_m) suggests the amorphous nature of BFPE-1. The BFPE-1 sample was subjected to a heat-cool-reheat cycle from –10 to 150 °C, Figure 4, to record $T_g = 20 \text{ °C}$, and C_p of $0.676 \text{ J/g}^\circ\text{C}$.

At present polyethers, polyesters, polycarbonates and epoxy resins of significant commercial value are derived from non-renewable feedstock. Furfural can be readily accessed from renewable and non-food-source biomass. The use of renewable furfural to access furan based polymer, would aid in generating next-generation bio-based materials. We have demonstrated the gram-scale conversion of furfural to BFD, and an exploratory example as feedstock for polymer generation, accessing the BFPE-1 material. Characterization of BFPE-1 has displayed encouraging results for the application of BFD as monomeric unit in polymer synthesis. Based on this preliminary investigation we anticipate employing BFD in generating other classes of BF-based polymers. The X-ray crystallographic study provides insight to the molecular structure of BFD, which will be useful in future, polymerization studies. This data would also provide the basis for understanding the potential self-healing properties based on H-bonding and - stacking of the monomeric BFD molecules.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We are grateful to the University of Toledo for an Interdisciplinary Research Initiation Award to Professor Steven J. Sucheck for the financial support.

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Scheme 1.

Synthetic route to access BFD from furfural.

^aReagents and conditions: a) 1,2-Ethanedithiol, glycerol, overnight, 90 °C, 93 %; b)

Hydroquinone, acetone, aq. 50 % H₂SO₄, overnight, 65 °C, 58 %; c) SeO₂, AcOH, 24 h, rt,

90 %; d) NaBH₄, MeOH, N₂, 30 - 40 mins, rt, 96 %.

Figure 1.
A) ORTEP drawing of BFD with 50% probability ellipsoids and labeling scheme, and B)
Dimer of BFD created by strong H-bonds in the solid state.

Scheme 2.

Synthesis of BFPE-1 from BFD.

^aReagents and conditions: a) Succinic acid, *N,N*-dimethyl-4-aminopyridine, *N,N'*-diisopropylcarbodiimide, 1,2-dichloroethane, N₂, 15 h, rt.

Figure 2. MALDI-TOF/TOF mass spectrum of BFPE-1 with DHB matrix in range of 3 to 7.5 kDa. Inset shows an expanded region between 0.5 to 3 kDa. Structures of 318 mass units and 276 mass units of the BFPE-1 shown in inset picture.

Figure 3. TGA thermograms of BFPE-1 weight loss (%) vs. temperature (°C). Inset shows TGA thermograms of BFPE-1 derivative weight (%/°C) vs. temperature (°C).

Figure 4.

DSC thermograms of BFPE-1 obtained during heat-cool-reheat cycle from -10 to 150 °C.

Inset shows expanded glass transition (T_g) region from 2nd heat (reheat) curve.