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COMMUNICATION

Benzotrifuran (BTFuran): a building block for π-conjugated systems†

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Reported here is the first synthesis, X-ray crystal structure, and derivatization of benzotrifuran (BTFuran). Single crystal X-ray analysis of BTFuran shows a tight hexagonal packing stabilized by π-stacking interactions and C–H···O contacts. α-Lithiation of BTFuran enables the preparation of reactive intermediates suitable for cross-coupling reactions, allowing access to representative BTFuran-containing π-conjugated systems.

Fused C_{3h}-symmetric (hetero)aromatic molecules are highly sought building blocks for π-conjugated materials since their delocalized π-surfaces and "star" or "propeller" shapes can confer useful optoelectronic and self-assembly properties.[1] Notable members of this class include the benzotrithiophenes (BTTs),[2-6] triazacoronenes,[7] and triazatruxenes (TATs).[8-12] BTT (**1**, Fig. 1), for example, constitutes π-conjugated systems covering a broad functional spectrum: columnar liquid crystals with high charge carrier mobilities,[5, 13] small molecules[14] and mesoporous polymers[15] as photoactive layers in organic photovoltaic devices, hole-transporting materials for perovskite solar cells with power conversion efficiencies up to 18.2%,[6] and metal-organic frameworks with molecular adsorption and sensing properties.[4, 16]

Furan-based π-conjugated building blocks have emerged over the past decade as useful complements to thiophene derivatives.[17-21] Despite an often higher-lying highest occupied molecular orbital (HOMO) and increased propensity for air oxidation, furan derivatives can present superior solubility and processability, more rigid planar structures, tighter packing in the solid phase, and sustainable access from biomass precursors compared to their thiophene counterparts.[22-24] The synthesis and functionalization of parent benzotrifuran (BTFuran, **2**, Fig. 1), the oxygen analog of BTT, is reported here for the first time.

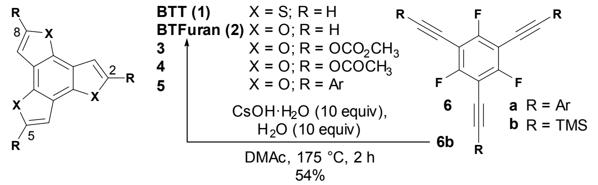

Fig. 1 Structures of benzotrithiophene (BTT, **1**) and benzotrifuran (BTFuran, **2**). The optimized synthesis of BTFuran as reported in this work is also shown.

The production of hexafunctionalized BTFurans from condensation reactions with phloroglucinol was first reported by Lang in 1886[25] and revisited later by other groups.[26-29] While we introduced the first 2,5,8-trifunctionalized benzotrifurans (**3** and **4**, Fig. 1) in 2009,[30] it was not until later, compliments of Nakamura and coworkers, that the first *π-conjugated* trifunctionalized BTFuran derivatives (**5**) appeared.[31] The molecules display enhanced octopolar properties as well as good 2D and 3D organization on surfaces and in the crystalline phase, respectively.[31] Synthesis of the targets came not from parent **2**, but from appropriately functionalized 1,3,5-triethynyl-2,4,6-trifluorobenzenes **6a**. Given the relatively harsh cyclization conditions required (10 equivalents of CsOH in DMAc at 175 °C), we imagined that parent BTFuran **2** might serve as a versatile building block for accessing broader classes of BTFuran-containing π-conjugated materials moving forward, by analogy to BTT. Toward this goal, reported here is the first synthesis and X-ray crystal structure of **2**. Also described are representative symmetric and desymmetrization functionalization reactions of **2** together with photophysical and computational characterization of various targets to highlight the system's relevance to organic π-conjugated materials.

Inspired by Nakamura's synthetic approach to 2,5,8-trifunctionalized benzotrifurans,[31] we entertained **6b** (Fig. 1) bearing three trimethylsilyl (TMS) groups as an entry to BTFuran (**2**). The cyclization precursor could be prepared in two steps from 1,3,5-trifluorobenzene, first through modification of an exhaustive iodination procedure reported by Wenk and Sander (see the SI for details),[32] followed by

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† Electronic Supplementary Information (ESI) available: Experimental procedures, UV-Vis absorption and NMR spectra, computational data (energies and coordinates of geometry-minimized structures), and details of X-ray data collection and structure refinement. CCDC 1551219. See DOI: 10.1039/x0xx00000x

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Sonogashira coupling with TMS-acetylene as described by Fourmigué and coworkers.[33] Alkyne **6b** was first subjected to the conditions previously reported for the formation of aryl functionalized BTFurans.[31] Fortuitously, the strongly basic reaction medium and perhaps the generation of fluoride ions in solution led to in situ deprotection of the TMS groups and direct access to the BTFuran core **2** in up to 41% yield (Table S1). Different reaction times as well as additives as fluoride or proton sources were evaluated; an optimized yield of 54% was realized after two hours when 10 equivalents of water was used (Fig. 1). Other bases (e.g., LiOH, Cs_2CO_3, NaOAc, KOAc, NaOMe, and KOEt) were also evaluated (not shown) but failed to produce **2**, providing instead mixtures of partially cyclized compounds (e.g., benzodifurans). BTFuran (**2**) is isolated as a white powder and presents good solubility in common organic solvents. Also, while bench stable for several weeks (after which it shows some coloration), **2** remains stable for months if stored in the refrigerator.

Slow diffusion of water in a DMSO solution of BTFuran (**2**) provided crystals suitable for single crystal X-ray analysis (Fig. 2). The heterocycle is highly planar; the maximum deviation of any atom from the root mean square plane of the molecule is 0.02 Å (versus up to 0.09 Å for crystalline BTT[2]). Taken together with nearly identical C–C bond lengths within the core benzene ring (Fig. 2a), BTFuran can be considered aromatic. The same conclusion was reached in earlier work for **3** and **4** based on X-ray crystallographic analysis and DFT calculations, respectively.[30] The molecules of **2** further organize into helical columnar stacks (Fig. 2b-c), an arrangement dominated by parallel-displaced π-π stacking interactions and the partial overlap between benzene and furan rings. The π-stacking distances (3.38–3.42 Å) are at the van der Waals limit (2 × r_{vdW}(carbon) = 3.40 Å),[34] and about 0.1 Å *shorter* than those observed in the crystal structure of BTT (see Figs. S1–2 for additional details).[2] C–H···O interactions[35] define BTFuran's lateral interactions in the solid state and the intercolumnar associations (Fig. 2d). The O···H—Cα arrangement is only slightly distorted from linearity and the average intermolecular distance between the oxygen atom and the α-carbon is 3.44 Å, shorter than the sum of the C–H bond distance and the van der Waals radii of hydrogen and oxygen ($r(\text{C—H}) + r_{\text{vdW}}(\text{H}) + r_{\text{vdW}}(\text{O}) = (1.08+1.20+1.52) = 3.80$ Å).[34] Given the distances and angles of these interactions it is reasonable to conclude that hydrogen bonding influences molecular organization of BTFuran in the crystal. The combination of face-to-face π-π and lateral hydrogen bonding interactions leads to a tight hexagonal packing arrangement, very different from the packing structure of BTT that is dominated by edge-to-face interactions (Fig. S2). BTFuran's crystal packing features bode well for its usage in optoelectronic device settings where charge transport through π-stacks is important.

The synthesis of π-conjugated systems relies extensively on metal-mediated cross-coupling reactions due to their general efficiency, modularity, and availability of coupling partners. To establish BTFuran as a building block for π-conjugated materials, we have explored its derivatization to intermediates useful for cross-coupling reactions. Along these lines, deprotonation of BTFuran with a slight excess of *n*-BuLi followed by quenching with several common electrophiles successfully affords **7a–d**, equipped with halogen, trimethyltin, and boronic ester groups, in moderate to good yields (Scheme 1). Of note, attempts to purify **7a** and **7b** by column chromatography on silica led to recovery of non-functionalized **2**. Alternatively, simple crystallization from MeOH proved to be an easy and efficient way to obtain compounds **7a–d** in good purity.

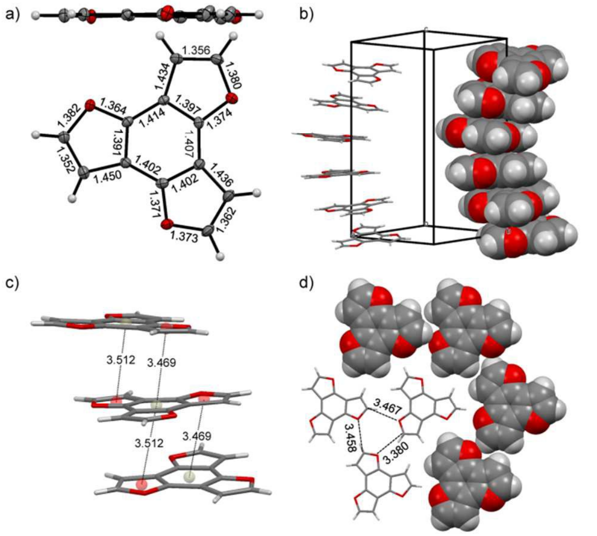
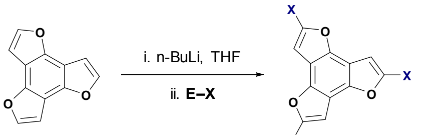


Fig. 2 X-ray crystal structure of BTFuran (**2**): (a) ORTEP plot of BTFuran (thermal ellipsoids shown at the 50% probability level); (b) the packing structure contains 6_5 screw axes localized in each vertex of the unit cell (only two columnar stacks are shown for clarity); (c) the slipped stacking favors the partial overlap between benzene and furan rings among the planar units that are not perfectly parallel (centroids indicated by a sphere, distances in Å); (d) lateral packing of the molecules is directed by intermolecular O···H—Cα hydrogen bonding interactions, as observed by the intermolecular distances (in Å) and the superposition of H and O atoms in the space-filling model.

To evaluate the fitness of the reactive intermediates shown in Scheme 1 to produce BTFuran-containing π-conjugated systems, Pd-catalyzed cross-coupling reactions were attempted using appropriate thiophene partners to obtain novel tris(2-hexylthiophenyl) derivative **8** (Scheme 2). After routine optimization of the reaction conditions, **8** could be obtained in good yields for all combinations of **7a–c** and the thiophene derivatives in both Stille and Suzuki coupling reactions (Scheme 2a). Compound **8** is a furan/thiophene hybrid π-system, a new entry in a class of materials that has



BTFuran (2)

7a: E–X = *i*-PrOBPin, X = BPin, 45%
7b: E–X = Me_3SnCl, X = $SnMe_3$, 69%
7c: E–X = CBr_4, X = Br, 70%
7d: E–X = I_2, X = I, 46%

Scheme 1 α-Lithiation of BTFuran (**2**) to create cross-coupling precursors **7a–d**.

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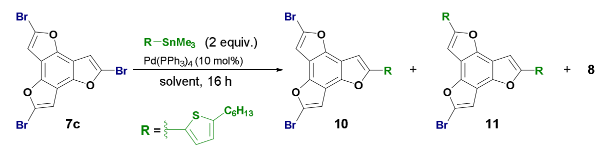
been receiving increasing attention given combination of the superior optical/electronic properties of thiophenes and improved packing of furans.[21, 36-38] Additionally, halogenated **7c–d** function well in Sonogashira reactions with terminal acetylenes to afford trialkynes **9a–b**. Of note, a copper-free methodology was used in reactions of phenylacetylene[39] to afford **9a** in moderate yields with no sign of homocoupling by-product. While the same methodology failed with TMS-acetylene, **9b** was successfully prepared using standard Sonogashira conditions (Scheme 2b).

Table 1 Screening of Stille coupling conditions to produce desymmetrized **10** and **11**.

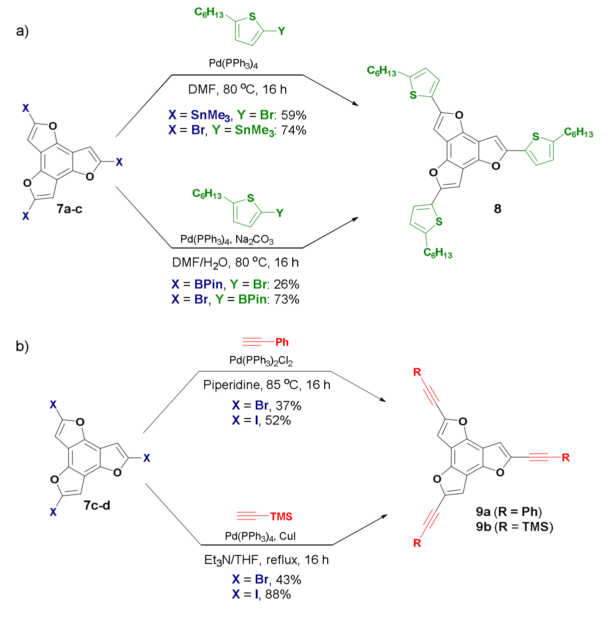


Entry	Solvent	T (°C)	**7c** (%)[a,b]	**10** (%)[b]	**11** (%)[c]	**8** (%)[c]
1	DMF	80	-	16	37	38
2	DMF	60	1	26	44	19
3	DMF	50	1	23	39	14
4	DMF	40	4	31	37	11
5	DMF	30	4	33	19	7
6	PhMe	110	12	16	33	15
7	PhMe	100	32	48	10	-
8	PhMe	90	52	31	-	-
9	PhMe	80	71	8	-	-
10	THF	66	74	26	-	-

[a] Recovery yield. [b] Yield calculated based on NMR integration of the isolated mixture of **7c** and **10**. [c] Isolated yield after purification.

Desymmetrizing otherwise C_{3h}-symmetric heteroaromatics is one way to access more exotic structures, like dendrimers and donor-acceptor constructs, with unique structural and electronic features. The approach has been exploited with BTT, where dendritic oligomers were synthesized and applied as p-channel semiconductors in OFET devices.[40] With this goal in mind, we have explored ways to mono- and di-functionalize BTFuran. Initially attempts to produce desymmetrized BTFuran derivatives through selective lithiation (by controlling temperature and reagent stoichiometry) led to a mixture of products requiring difficult purification. We turned to a strategy described by Takimiya *et al.* in the synthesis of BTT-containing materials[40] involving the control of the stoichiometry of the cross-coupling reactions as an alternative way to create desymmetrized molecules. One advantage of this approach is that the mono- and di-functionalized products produced still contain reactive groups which can subsequently engage in cross-coupling reactions with different reaction partners. As proof-of-principle, Stille coupling of tribromo species **7c** was selected due to the stability of the bromides **10** and **11** upon purification by column chromatography (Table 1). As expected, higher temperatures favored the production of the byproduct **8**. Decreasing the temperature to favor formation of incomplete coupling products also led to slower reaction rates and lower conversion, causing the increasing recovery of the starting material **7c**. We also observed that DMF favored the coupling reactions compared to toluene and THF. By screening several conditions we could successfully obtain **10** and **11** in modest yields (entries 2 and 7, Table 1).

UV analysis of BTFuran (**2**), **7c**, and derivatives **8–11** expectedly show bathochromic shifts in λ_{max} with increasing conjugation (e.g., **8** > **9a** > **9b**), a trend generally mirrored in the HOMO–LUMO gaps obtained through electronic structure calculations at the B3LYP/6-31+G* level (Fig. 3 and Table S2). Comparing the BTFuran-based compounds with their published BTT-based congeners reveals higher energy λ_{max} values for the former,[2, 3] again consistent with theoretical calculations that indicate slightly smaller HOMO-LUMO gaps for the thiophenes (Table S2). Nonetheless, the absorption differences are relatively small and the BTFuran derivatives are typified by high molar extinction coefficients common to organic π-systems. Perhaps most interestingly, comparison of



Scheme 2 Pd-catalyzed cross-coupling reactions of BTFuran derivatives.

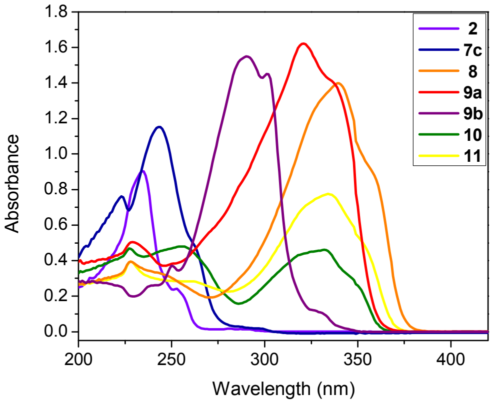


Fig. 3. Absorption spectra of BTFuran and its derivatives (15 µM solutions in CH_2Cl_2). Bathochromic shifts are observed upon increasing π-conjugation.

the calculated HOMO and LUMO energy levels of BTT **1** vs. BTFuran **2** (or alternatively **8** versus its BTT derivative, Table S2) shows comparable HOMO energies and modulated LUMO energies. To follow up on this comparison experimentally, electrochemical measurements were performed. Electrochemical analysis of BTFuran (Fig. S3) revealed an irreversible oxidation, E_{pa} = 1.61 V (corresponding to an estimated E_{HOMO} of –6.1 eV), only slightly higher than that determined for BTT, E_{pa} = 1.55 V, under similar electrochemical conditions.[2] Currently we are exploring the consequences of the improved solid-state packing ability of the benzotrifurans on solid-state absorption and charge transport properties.

In conclusion, parent, C_{3h}-symmetric BTFuran (**2**) has been prepared for the first time. The molecule presents a tight hexagonal packing arrangement in the solid state, with structural features (e.g., short π-stacking distances) that are attractive for downstream π-conjugated materials applications. Lithiation of BTFuran followed by quenching with various electrophiles readily generates reactive intermediates for a range of Pd-catalyzed cross-coupling reactions. Sample BTFuran-containing π-conjugated molecules were produced in moderate to good yields and show, based on UV-Vis absorption measurements, electrochemistry, and DFT calculations, comparable optical and electronic properties to their BTT congeners. The protocols developed in this work are expected to encourage the development of BTFuran-based π-conjugated systems for solid-state optoelectronic applications.

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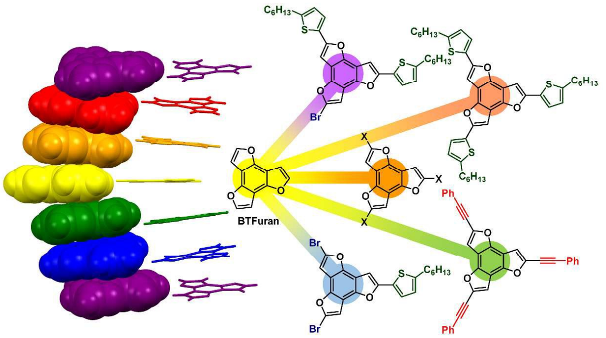

Reported here is the first synthesis, X-ray crystal structure, and derivatization of C_{3h}-symmetric benzotrifuran (BTFuran), oxygen analog of the widely exploited benzotrithiophene.