KO(t)Bu-Initiated Aryl C−H Iodination: A Powerful Tool for the Synthesis of High Electron Affinity Compounds

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S *Supporting Information*

ABSTRACT: An efficient iodination reaction of electron-deficient heterocycles is described. The reaction utilizes KO(t)Bu as an initiator and likely proceeds by a radical anion propagation mechanism. This new methodology is particularly effective for functionalization of building blocks for electron transport materials. Its utility is demonstrated with the synthesis of a new perylenediimide−thiazole non-fullerene acceptor capable of delivering a power conversion efficiency of 4.5% in a bulk-heterojunction organic solar cell.

The extraordinary development of cross-coupling reaction technology has revolutionized the synthesis of both pharmaceutical and optically and electronically active materials.[1] Nonetheless, robust methods to introduce the necessary functional groups for the cross-coupling of electron-poor aromatic heterocycles remain scarce.[2] With their low-lying frontier molecular orbitals, these molecules are inherently resistant to electrophilic reagents and are also susceptible to reduction or nucleophilic decomposition pathways when exposed to strong bases, limiting deprotonative strategies for their functionalization. These limitations have created the need for new synthetic strategies to facilitate the development of electron-accepting building blocks used in organic electronic materials, such as electron transport materials and other acceptor-containing molecules and polymers. Here we describe an efficient aryl C−H iodination reaction that is capable of functionalizing a variety of electron-deficient heterocycles and highlight the utility of this methodology with the synthesis of a non-fullerene acceptor material.

Our investigation was initiated when we observed a significant aryl iodide byproduct (**1**, 47%, Figure 1) in the attempted C−H arylation of the perylenediimide (PDI)−thiazole TsCDI with pentafluoroiodobenzene (PFIB) (eq 1). This observation was of particular interest, as our previous attempts to halogenate this material under a range of standard conditions had all failed.[3] Control experiments indicated that while the Cu and Pd cocatalysts were required to obtain C−H arylation product **2**,[4] aryl iodide **1** was obtained in improved
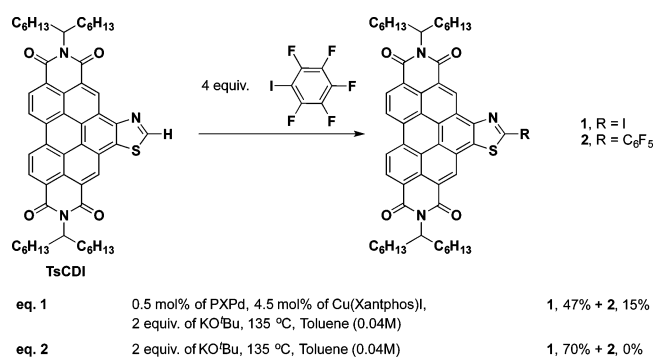

Figure 1. Discovery of a new C−H iodination reaction.

yield (70%) when TsCDI was treated solely with PFIB and potassium *tert*-butoxide (eq 2).[5]
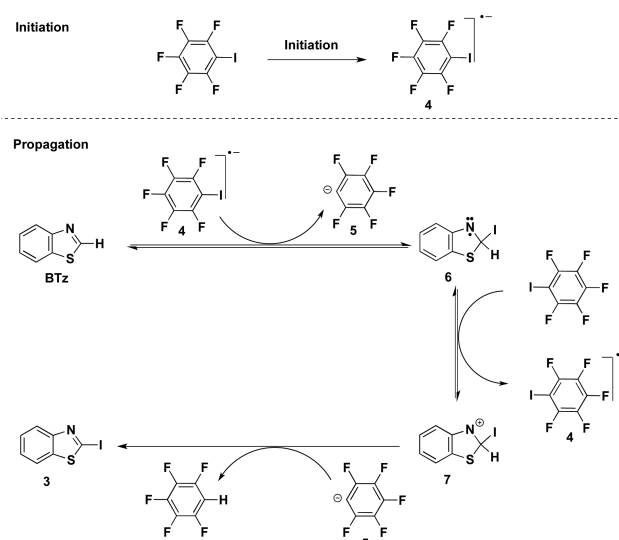

Figure 2. Proposed reaction mechanism.

Further optimization of the iodination protocol was conducted using benzothiazole (BTz) (Table 1). The reaction

Table 1. Reaction Optimization

entry	equiv of PFIB	base (equiv)	temp	solvent	yield (%)[a]
1	4	KO^{t}Bu (2)	135 °C	toluene	86
2	4	KO^{t}Bu (2)	RT	toluene	79
3	4	KO^{t}Bu (0.2)	RT	toluene	83
4	1	KO^{t}Bu (0.2)	RT	toluene	90/91[b]
5	1	NaO^{t}Bu (0.2)	RT	toluene	0.4
6	1	K$_2$CO$_3$ (0.2)	RT	toluene	0
7	1	KO^{t}Bu (0.2)	RT	hexanes	87
8	1	KO^{t}Bu (0.2)	RT	DCM	15
9	1	KO^{t}Bu (0.2)	RT	THF	0

[a]Based on GC analysis using anthracene as an internal standard. [b]Isolated yield (2.18 g scale).

proceeds at room temperature (entry 2) and most efficiently in nonpolar solvents (toluene, hexanes). Cognizant of the recent C–H silylation protocol reported by Stoltz, Grubbs, and co-workers,[6] we investigated the use of substoichiometric potassium tert-butoxide in this reaction and found that 20 mol % was sufficient to achieve an excellent yield (83%; entry 3). Alternative bases were not effective in the reaction (entries 5 and 6). Under the optimized conditions, only a single equivalent of PFIB was required to deliver a high yield (91%) of isolated product 3 on a 2.18 g scale (entry 4).

An investigation of alternative iodination reagents revealed that neither iodine nor N-iodosuccinamide were competent in the reaction, despite that fact that both compounds readily undergo homolytic bond cleavage to deliver iodine atoms in radical reactions (Table 2, entries 1 and 2). Aryl iodides bearing

Table 2. Investigation of Iodine Sources

entry	Iodine source[a]	% yield[b]	entry	Iodine Source[a]	% yield[b]
1	I$_2$	0	6		0
2	NIS	0	7		0
3		91	8		17
4		93	9		0
5		41/ 90[c]	10[d]		38

[a]All of the iodine sources were used at a stoichiometry of 1.1 equiv. [b]All yields are isolated yields. [c]Optimized yield with 0.5 equiv of base and 2.2 equiv of PFIB. [d]Iodine source was used at a stoichiometry of 0.95 equiv.

two o-fluorine atoms all were viable reagents (entries 3–5), but compounds containing a single o-fluorine were not (entries 6 and 7). o-Nitroiodobenzene was not an efficient iodination reagent (17% yield; entry 8), and 3,5-dinitroiodobenzene was not capable of transferring the iodine atom. We note that diiododifluorobenzothiadiazole, a compound obtained in this study, was also capable of transferring iodine to benzothiazole under the reaction conditions (38% yield; entry 10).

These observations are consistent with a radical mechanism in which the reaction is initiated by single electron transfer to PFIB,[7] possibly from the potassium tert-butoxide (Figure 2).[8] The resultant radical anion (4) is able to transfer the iodine atom to the substrate (BTz) with the o-fluorine atoms in the iodine transfer reagent essential for stabilizing the resulting aryl anion 5.[9] After iodine transfer, the iodinated substrate 6 is proposed to transfer an electron to PFIB, propagating the reaction and delivering cation 7. Deprotonation of 7 with the pentafluorophenyl anion completes the process.[10] Supporting a radical mechanism, an electron paramagnetic resonance (EPR) spectrum of the reaction mixture showed a signal with a g value of 2.00, consistent with the generation of an organic radical under the reaction conditions.[11] Additionally, we note that when 1 equiv of BHT was added to the reaction mixture, product formation was suppressed.

An investigation of the scope of the reaction revealed that the conditions are applicable to a wide variety of electron-deficient heterocycles (Figure 3). Thiazole, oxazole, and imidazole derivatives are all efficiently iodinated at their respective 2-positions (1, 3, 8–16).[12] 2-Bromothiazole, in which the 2-
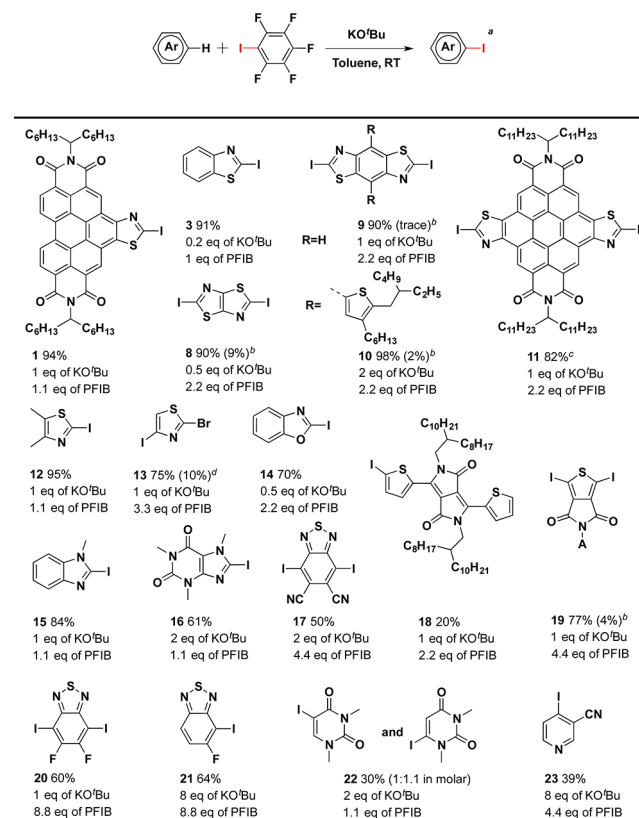

Figure 3. PFIB iodination of aromatic heterocycles. [a]All yields are isolated yields. [b]Yields in parentheses are for monosubstituted compounds. [c]The cis:trans molar ratio was 3:1. [d]Yield of 2-bromo-4,5-diiodothiazole.

position is blocked, is selectively iodinated at the 4-position (**13**, 75% yield). The electron-deficient thiazole ring is selectively iodinated in the presence of electron-rich thiophenes (**10**). However, in the absence of an electron-deficient heterocycle, thiophenes in conjugation with electron-withdrawing groups can be iodinated at the 2-position under these conditions (**18** and **19**). Dicyano-, difluoro-, and monofluorobenzothiadiazole all are competent substrates for this reaction, delivering the respective iodides in moderate to good yields (50–64%, **17**, **20**, and **21**). In these cases, excess PFIB is required to drive the reaction to completion. This observation suggests that the iodine transfer step in the reaction is under thermodynamic control, and when the energy of the product iodide is similar to that of the iodinating reagent, excess iodinating reagent can be utilized to drive the equilibrium to favor the desired product. Empirically we observed that additional potassium *tert*-butoxide can improve the reaction yield in these cases. The role of the excess potassium *tert*-butoxide remains unclear at this stage. *N,N*-Dimethylpyrimidinone is also iodinated, but no regioselectivity was observed (**22**). In contrast, 3-cyanopyridine is selectively iodinated at the 4-position (**23**, 39% yield).

The broad applicability of the iodination reaction to electron-deficient heterocycles suggests that this methodology may be of utility in constructing conjugated materials with strong electron acceptors for organic electronic applications. Recently several dimeric and trimeric PDI derivatives have been used as non-fullerene acceptors in bulk-heterojunction (BHJ) organic photovoltaic (OPV) systems, resulting in devices with power conversion efficiencies (PCEs) of 3–8%.[13] Inspired by these results, as a preliminary test of the utility of our iodination chemistry, we investigated whether compound **1** could be useful as a building block for a non-fullerene acceptor in organic BHJ solar cells.[14] Thus, we synthesized $(TsCDI)_2T$ (**24**) by Stille coupling of iodide TsCDI (**1**) and 2,5-bis(tributyltin)thiophene (90% yield).

Figure 4a,b shows the chemical structure of **24** and its optical absorption spectra in solution and in a thin film (other data are summarized in Table S23). **24** has good solubility in most common solvents and good thermal stability (Figure S6). The UV–vis absorption spectrum in chloroform (Figure 4b)
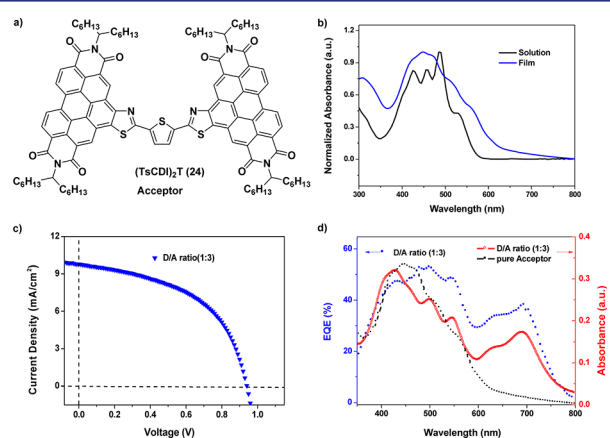
exhibits a vibronically structured band, ($\lambda_{max} \approx 485$ nm, $\varepsilon = 10.3 \times 10^4$ M^{-1} cm^{-1}). This absorption is slightly bathochromically shifted and broadened in the thin film and complements that of the well-known OPV polymer donor PBDTT-F-TT, which absorbs from 500 to 780 nm (Figure 4d).[15] Cyclic voltammetry (Figure S4, right) showed two reversible reductions at −1.18 and −1.38 V vs Fc$^+$/Fc, and thus, we expected the excited state of PBDTT-F-TT to be able to transfer an electron to $(TsCDI)_2T$.[15] To investigate the potential application of $(TsCDI)_2T$ as a non-fullerene acceptor in solution-processed BHJ organic solar cells, the device performance was tested in both inverted and conventional structures (Tables S24 and S25), and the former one proved to have better performance. This observation is consistent with the literature results for other non-fullerene systems.[15b] Optimized results are summarized in Table S24 with additives, donor/acceptor (D/A) ratio, and spin-coating speed applied to optimize the device performance. Solar cells with a 1:3 D/A blend ratio showed the best performance, with $V_{oc} = 0.94$ V, $J_{sc} = 9.74$ A/cm^2, FF = 49.6%, and average PCE = 4.54 ± 0.12% (4.7% best). The accuracy of the photovoltaic measurements was confirmed by the external quantum efficiency (EQE) of the same devices. Both the acceptor and donor contribute to the photon-to-electron conversion, yielding a broad EQE band from 350 to 800 nm. The higher EQE is mainly due to the absorption of the acceptor ranging from 350 to 600 nm. The estimated electron mobility (μ_e) and hole mobility (μ_h) were 2.27×10^{-5} and 2.89×10^{-4} cm^2 V^{-1} s^{-1}, respectively, from the J–V curve characteristics (Figure S7), indicative of relatively balanced electron and hole mobilities. Further device optimization of $(TsCDI)_2T$ as an acceptor is underway.

In conclusion, we have described a novel method for the iodination of a broad array of aromatic heterocycles under mild conditions, and we anticipate that this methodology will be particularly useful for the synthesis of highly electron-deficient compounds.

Figure 4. (a) Chemical structure of $(TsCDI)_2T$, (b) its UV–vis absorption spectra in chloroform solution and in a thin film, and (c, d) the J–V curve (c) and the EQE and film absorption spectra of blend and pure acceptor (d) for PBDTT-F-TT/$(TsCDI)_2T$ BHJ-based inverted structure devices with the optimized composites.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b12259.

> Experimental procedures and analytical data (PDF)
> Crystallographic data for 5-fluoro-4-iodo-2,1,3-benzothiadiazole (CIF)
> Crystallographic data for 2-bromo-4,5-diiodothiazole (CIF)

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Notes

The authors declare no competing financial interest.

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