Synthesis of Tridentate [1,2,4] Triazinyl-Pyridin-2-yl Indole Lewis Basic Complexants via Pd-Catalyzed Suzuki–Miyaura Cross-Coupling

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Supporting Information

ABSTRACT: Full closure of the nuclear fuel cycle is predicated, in part, on defining efficient separations processes for the effective speciation of the neutron-absorbing lanthanides from the minor actinides post-PUREX. Pursuant to the aforementioned, a class of tridentate, Lewis basic procomplexants have been prepared leveraging a Pd-catalyzed Suzuki–Miyaura cross-coupling between 6-bromo-[1,2,4]-triazinylpyridine derivatives and various protected indole-boronic acids to afford functionalized 2-6-(5,6-diphenyl-[1,2,4]triazin-3-yl)-pyridin-2-yl]-1H-indoles. A highly active catalyst/ligand system with low loadings was employed rapidly affording 26 examples in yields as high as 85%. Method optimization, substrate and indole scope, comparative analysis between coupling reagents, and a scale-up experiment are reported.

INTRODUCTION

Heteroarene constructs bearing the indole functionality are ubiquitous in biologically active natural products, medicinal chemistry, synthesis, and related areas. Use of complexant scaffolds with the indole moiety in the context of radiochemical liquid–liquid separations of actinides from lanthanides has yet to appear. Sequestration of the minor actinides from the lanthanides is necessary for the use of these radionuclides in advanced fuels for further transmutation toward diminishing radiotoxicity, heat load, and long-term storage requirements of spent nuclear fuel in a geologic repository. Lewis basic scaffolds with soft donor atoms, specifically, N, and based on the CHON principle, have demonstrated effective performance in this area since Kolarik’s disclosure of alkyl bis-triazinyl-1,2,4-triazine complexants (BTPs) for minor actinide separations. In an effort to further define structure–activity relationships to potentially improve complexant performance, our lab has been engaged in the pursuit of scaffolds, which afford opportunities to leverage modular concepts for complexant construction.

We were interested in exploring the potential of tridentate, soft-Lewis basic [1,2,4] triazinyl-pyridin-2-yl complexants with an indole appendage in separations. A primary challenge in this area of separation science is to design a complexant, which displays significant binding affinity for the minor actinides over lanthanides while maximizing the covalency of the f-orbital interaction of the metal–ligand complex to afford selective speciation, while at the same time providing an opportunity for subsequent stripping and reuse of the complexant for additional separations. Further issues include dissolution of a relatively planar, polar heteroaromatic scaffold in diluents with low polarity and facilitating good kinetics of complexation.

RESULTS AND DISCUSSION

Table 1 describes selected efforts toward optimization of the desired Pd-catalyzed bond formation between 3-(6-bromo-pyridin-2-yl)-5,6-diphenyl-[1,2,4]triazine (1) and (1-(tert-butylcarbonyl)-5-(methoxy)-indol-2-yl)boronic acid utilizing Suzuki–Miyaura cross-coupling11 as the model system. The overarching goal was to develop a method that utilized the absolute minimum of all reagents necessary. Initial definition of reaction conditions began with the evaluation of previously disclosed transformations described by us for sp² C–sp³ N
Table 1. Indole-Boronic Acid Coupling Development

| entry | catalyst (mol %) | ligand (mol %) | base (equiv) | solvent system | temp (°C) | time (h) | conv (%) |
|-------|------------------|----------------|-------------|---------------|-----------|----------|----------|
| 1     | Pd(dba)2 (5%)    | CyPF-tBu (10%) | Cs2CO3 (3 equiv) | Toluene: H2O (4:1) | 115       | 16       | 76       |
| 2     | Pd(OAc)2 (5%)   | RuPhos (5%)    | Cs2CO3 (3 equiv) | Toluene: H2O (4:1) | 115       | 16       | 75       |
| 3     | Pd(dppp)Cl2 (5%) | [BuPd2]HI (5%) | Cs2CO3 (3 equiv) | Toluene: H2O (4:1) | 115       | 16       |          |
| 4     | Pd(OAc)2 (5%)   | XPhos (5%)     | Cs2CO3 (3 equiv) | Toluene: H2O (4:1) | 115       | 16       |          |
| 5     | Pd(dba)2 (5%)    | Xantphos (5%)  | Cs2CO3 (3 equiv) | Toluene: H2O (4:1) | 115       | 16       | 66       |
| 6     | Pd(PPh3)2Cl2 (5%) | XPhos (5%)     | Cs2CO3 (3 equiv) | Toluene: H2O (4:1) | 115       | 16       | 60       |
| 7     | Pd(OAc)2 (5%)   | XPhos (5%)     | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       | 93       |
| 8     | Pd(dba)2 (5%)    | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |
| 9     | XPhos-tBu Pd G3 (5%) | PPh3 (5%)     | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |
| 10    | Pd(OAc)2 (5%)   | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |
| 11    | Pd(dba)2 (2.5%)  | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 19       |          |
| 12    | Pd(dba)2 (2.5%)  | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |
| 13    | Pd(dba)2 (2.5%)  | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |
| 14    | Pd(dba)2 (2.5%)  | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |
| 15    | Pd(dba)2 (2.5%)  | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |
| 16    | Pd(dba)2 (2.5%)  | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |
| 17    | Pd(dba)2 (2.5%)  | Xantphos (5%)  | Cs2CO3 (1 equiv) | MTBE : H2O (4:1) | 115       | 16       |          |

a(1-(tert-Butylcarbonyl)-5-(methoxy)-indol-2-yl{boronic acid (1.05 equiv). bReaction concentration at 0.2 M (total). cConversion determined from the integration of select resonances in the 1H NMR spectrum without internal standard. dIsolated, purified yield. CyPF-tBu = 1-dicyclohexylphosphino-2-di-tert-butylphosphinothiylferrocene, CPME = cyclopentyl methyl ether, MTBE = methyl-tert-butyl ether.

Bond formation via Buchwald–Hartwig amination (entry 1) without success (Table 1). Modest conversion was realized for reagents from prior Suzuki–Miyaura (entry 2) and Sonogashira cross-couplings (entry 3) methods previously disclosed by us for similar substrates. Interested in improving conversion performance, additional catalyst/ligand combinations were evaluated. Entries 4–6 with Pd2+ and Pd0 sources, respectively, did not improve upon entry 2. Combining Pd(OAc)2 with the alkylbaryl phosphine XPhos, developed by Buchwald, afforded 93% conversion after 16 h (entry 7). Transitioning to Pd(dba)2 (entry 8), as well as the matched XPhos (entry 9), afforded 0 and 40% conversion, respectively. Expansion of ligand diversity to Xantphos with a large 108° bite angle to accelerate reductive elimination, in combination with Pd(dba)2, afforded 99% conversion of the starting material after just 1 h at 115 °C (entry 10). Minimal Boc deprotection of the product was observed in this case. Decrease of the base loading to 1 equiv did not result in the exclusion of Boc deprotection but still maintained excellent conversion (entry 11). Lowering the temperature to 55 °C in toluene extended the reaction time (16 h), as expected, but did not improve the impurity profile of the crude reaction mixture. Improving the efficiency of the transformation was, subsequently, attempted employing a solvent screen with ethereal solvents methyl-tert-butyl ether (MTBE) and cyclopentyl methyl ether (CPME) at their respective boiling points (entries 12 and 13). Entry 12 produced the cleanest transformation overall, but at lower conversion, whereas entry 13 afforded high conversion, no Boc deprotection in the proof of concept example, and a manageable impurity profile affording the desired product 2 in 73% isolated yield in an expeditious reaction time of 45 min. Reduction of the catalyst and ligand loading to 1 and 2%, respectively (entry 14), resulted in longer reaction time, lower conversion, and a worse impurity profile. The requisite control experiments were performed to underscore the necessity of all reagents to afford 2 (entries 15–17). With a viable procedure for the construction of the critical pyridin-2-yl-indole C=C bond defined, focus shifted toward the evaluation of the indole scope of the transformation (Table 2). Experiments were performed to understand the electronic preferences of the catalyst/ligand system.

Treatment of 1 with the unfunctionalized, indole-boronic acid resulted in the desired complexant 3 in 78% yield (entry 1). The weakly electron-donating methyl substituent in 4 afforded the lowest yield (47%) of the indole boron reagent examples evaluated in Table 2 (entry 2) due, in part, to purification challenges. The method was tolerant of inductive electron-withdrawing (entries 3 and 4) as well as resonance-donating substituents (entry 5), on the indole-boronic acid with the substituent in the 5-position. Substituent transposition to the 6-position in the case of resonance-donating groups afforded the desired products 7 and 8. The success of the transmetallating indole boron species was not limited to boronic acids. Treatment of 1 with the pinacol ester indole derivative afforded the desired product 10 in good yield. Employment of this reagent in the context of a double cross-coupling experiment with 2,6-dibromopyridine (entry 11) was also successful leading to the formation of 12 in 85% yield over two steps from 1. Exchange of the heteroatom in the boronic acid to the more electron-withdrawing oxygen atom in the case...
of entry 10 was successful but afforded 11 in a modest 37% yield. It is also noteworthy that when the boronic acid functional group was located in the 5-position of the indole, successful coupling was not realized suggesting that effective transmetallation and/or reductive elimination of the desired product were predicated on the boronic acid being present in the 2-position relative to the indole.

Having ascertained that the desired substrates were tolerant of electronically diverse indole coupling reagents, efforts shifted to the variation of the electrophile and cross-coupling reagent toward potentially improving complexant solubility and separations outcomes in process-relevant diluents (Table 3).

Table 3 highlights the diversified combination of the substrate and indole-boronic acids. Interestingly, when a weakly electron-donating substituent is placed on the electrophile and paired with the same functionality on the indole-

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**Table 2. Indole-Boronic Acid Scope**

| Entry | Product | Yield (%) |
|-------|---------|-----------|
| 1     | R = Boc | 3 (78%)   |
| 2     | R = Boc | 4 (47%)   |
| 3     | R¹ = Boc; R² = F | 5 (62%) |
| 4     | R² = Boc; R² = Br | 6 (72%) |
| 5     | R² = Boc; R² = OCH₃ | 2 (73%) |
| 6     | R¹ = Boc; R² = OSi(CH₃)₂Bu | 7 (69%) |
| 7     | R¹ = Boc; R² = OCH₃Ph | 8 (82%) |
| 8     | R = Boc | 9 (58%)   |
| 9     | R² = NH | 10 (82%) |
| 10    | X = O   | 11 (37%) |
| 11    |         | 12 (85%) |

**Table 3. Scaffold Diversification Scope**

| Entry | Product | Yield (%) |
|-------|---------|-----------|
| 1     | R¹ = Boc; R² = CH₃ | 13 (77%) |
| 2     | R¹ = Boc; R² = H | 14 (38%) |
| 3     | R¹ = Boc; R² = F; R³ = H | 15 (63%) |
| 4     | R¹ = Boc; R² = OSi(CH₃)₂Bu; R³ = H | 16 (58%) |
| 5     | R² = Boc | 17 (61%) |
| 6     | R² = R² = CH₃ | 18 (64%) |
| 7     | R² = Boc; R² = H | 19 (61%) |
| 8     | R = Boc | 20 (56%) |
| 9     | R² = F | 21 (75%) |
| 10    | R² = OCH₃ | 22 (73%) |
| 11    |         | 23 (62%) |
| 12    | R¹ = H; R² = Boc | 24 (42%) |
| 13    | R¹ = CH₃; R² = Boc | 25 (12%) |

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Reaction Conditions: 1 (0.258 mmol), Pd(dba)₂ (0.006 mmol), Xantphos (0.013 mmol), indole-boronic acid (0.270 mmol), Cs₂CO₃ (0.774 mmol), CPME:H₂O (4:1) (0.20 M), and heated for time indicated. Isolated, purified yield over one synthetic step. Average yield from two experiments. Employed 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole as the indole boron reagent. Pd(dba)₂ (0.010 mmol) and Xantphos (0.019 mmol) utilized. 2,6-Dibromo-pyridine used as the substrate with described conditions and 2.10 equiv of coupling reagent; yield over 2 steps.
boronic acid (entry 1), a satisfactory coupling outcome (13) is afforded. However, when the same substrate is combined with an unfunctionalized-Boc-protected indole-boronic acid, a modest 38% yield (14) is afforded. The low yield in the case of 14 is primarily due to purification issues with this combination, which proved the most difficult in the entire project. Combining an electron-withdrawing functionality in the case of a F-substituent on the substrate with electron-withdrawing (entry 3) and electron-donating (entry 4) functionalities rendered little difference in the product formation. Complexants bearing the 3,3′-methylene substituent on the 1,2,4-triazinyl moiety have demonstrated acumen in separations processes.20 Evaluation of this synthon with the 5-methoxy- (entry 5) and 4-methyl-Boc-protected (entry 8) indole-boronic acids resulted in similar performance affording 17 and 20 in 61 and 56% isolated yield, respectively.

The study of complexant scaffolds with aliphatic functionality is an important area of focus for this laboratory. Entries 9–11 with butyl and 3-methylbutyl substituents on the arene moiety of the electrophile performed similarly with resonance-donating, neutral, and electron-withdrawing functionalities (22, 23, and 21, respectively). Entries 12 and 13 with the 6-benzyloxy-substituent on the Boc-protected indole-boronic acid were achievable, but yield issues were experienced in both cases (24 and 25) with two flash purifications on acidic Al2O3 required to obtain a spectroscopically clean material from 25.

An issue among Suzuki–Miyaura cross-coupling methods is the performance variation of boron reagent within the confines of a specific catalyst–ligand combination. Diversity of the boron reagent can lead to substantive deviation in method performance.21 Interested in ascertaining the applicability of alternative boron reagents with 1,22 evaluations of the boronic acid, pinacol ester, potassium trifluoroborate, and MIDA23 ester of benzene were studied (Table 4). Results toward 26 sought to evaluate the performance differences between transmetallating reagents with 1 and the current catalyst/ligand system.24

Phenyl boronic acid (entry 1) afforded the highest conversion in the shortest period of time but profoundly slower than the comparable indole-boronic acids suggesting that the presence of the N atom on the arene had a marked influence in accelerating the rate of transmetalation or reductive elimination toward product formation. The case of potassium phenyltrifluoroborate (entry 3) afforded 85% conversion but a poor isolated yield. It is important to mention that 1 was successfully coupled and purified with other potassium aryl, and even alkyltrifluoroborates, in our previous work25 suggesting that this catalytic system is less effective for these reagents. Entry 3 with the phenyl pinacol ester afforded modest conversion even though the indole derivative performed well (Table 2, entry 12). Low conversion in the case of the phenyl MIDA reagent26 was observed (entry 4). In both of the aforementioned cases of low conversion, it is postulated that protodeboronation of the boron reagent occurred affording benzene, which, subsequently, boiled off of the reaction at the temperature performed.

Production of sufficient quantities of a given complexant scaffold for full solubility and separation efficacy via scale-up of a development scale transformation can frequently present challenges. With the aforementioned in mind, a 10-fold scale-up transformation of 1 to 2 (Table 2, Entry 5) was executed with equivalent stoichiometry to the development of scale transformation. Pleasingly, the conversion, purification, and isolation were commensurate with the development scale-approaching 2 in a slightly improved 78% yield over the development example described in Table 1 (Scheme 1).

![Scheme 1. Tenfold Scale-Up Experiment](image)

### Table 4. Boron Reagent Scope

| entry | R           | time (h) | conv (%) | yield (%) |
|-------|-------------|----------|----------|-----------|
| 1     | B(OH)₂      | 21       | 100      | 69        |
| 2     | BF₃         | 16       | 85       | 30        |
| 3     | B(OAc)₂     | 21       | 56       | ---       |
| 4     | BMIDA       | 16       | 28       | ---       |

| Reaction conditions: | 1 (0.258 mmol), Pd(dbas)₂ (0.006 mmol), Xantphos (0.013 mmol), Boron reagent (0.270 mmol), Cs₂CO₃ (0.774 mmol), CPME₃H₂O (4:1) (0.20 M), and heated for time indicated. | (1) | 100 | 69 |
| Percent conversion determined from integration of selected resonances in the ¹H NMR spectrum without internal standard. | (2) | 28 | --- |

**CONCLUSIONS**

In summary, we have disclosed a potent catalytic system for the construction of tridentate, semifrustrated 2-[(6-(5,6-diphenyl-[1,2,4]triazin-3-yl)-pyridin-2-yl]-1H-indole complexants and related derivatives with low catalyst/ligand loadings, wide substrate scope, and good functional group tolerance. This work bears relevance to the construction of the challenging pyridin-2-yl indole C–C bond and should find further applicability in medicinal chemistry and related areas. Exploration of this class of complexants for potential application in minor actinide separations as well as defining experimental conditions for Boc deprotection are currently ongoing in this laboratory and will be reported in due course.

**EXPERIMENTAL SECTION**

**General Considerations.** All reagents were purchased from US chemical suppliers, stored according to published protocols, and used as received unless indicated otherwise. All experiments were performed in an oven- or flame-dried glove box. Reaction progress was monitored using thin-layer chromatography on glass-backed basic Al₂O₃ plates and/or ¹H NMR analysis of crude reaction mixtures. Rₚ values for compounds that resulted in a concentrically observed spot on basic alumina TLC plates are reported using the conditions listed. Melting point data listed is for a single, uncorr...
experiment unless noted otherwise. All reported yields listed are for pure compounds and corrected for the residual solvent, if applicable, from 1H NMR spectroscopy unless otherwise indicated. Infrared spectral data were acquired using attenuated total reflectance (ATR) from the (form) listed. All 1H and 13C NMR data were acquired from a 500 MHz multinuclear spectrometer with a broadband N2 cryoprobe. Chemical shifts are reported using the δ scale and are referenced27 to the residual solvent signal: CDCl3 (δ 7.26), CD3CN (δ 1.94), (CD3)2C=O (δ 2.05), CD3CD3 (δ 6.97), and (CD3)2SO (δ 5.20) for 1H NMR and chloroform (δ 77.16), CD3CN (δ 1.32), (CD3)2C=O (δ 29.84), CD3CD3 (δ 137.48), and (CD3)2SO (δ 39.52) for 13C NMR. Splittings are reported as follows: (s) = singlet, (d) = doublet, (t) = triplet, (dd) = doublet of doublets, (dt) = doublet of triplets, (ddd) = doublet of doublet of doublets, (br) = broad, (br-m) = broad multiplet, and (m) = multiplet.13C NMR spectra were corrected for ringdown using linear back prediction. High-resolution mass spectrometry (HRMS) data were obtained utilizing electron impact ionization (EI) with a magnetic sector mass spectrometer equipped with a broadband N2 cryoprobe.

Special Instructions. It should be noted that products afforded in the context of the described method demonstrate significant sensitivity to the residual acidity in chloroform and dichloromethane, even when buffered. Pursuant to the aforementioned, these solvents should be avoided where possible for the purposes of chromatographic purification, transfer, and/or NMR analysis. Acetone and acetonitrile were suitable alternatives for this work. Most products display limited solubility in methanol. Additionally, prepared materials appear to readily incorporate the residual solvent into the crystal lattice, which is challenging to remove via standard reduced pressure techniques. Azeotropic removal of the residual acetone and/or ethyl acetate with acetonitrile afforded dry, residual solvent-free compounds at a much faster rate than freeze, pump, thaw strategies.

Starting Material Preparation. For a general procedure on the preparation of the requisite 3-(6-bromo-pyridin-2-yl)-5,6-diphenyl-[1,2,4]triazine starting materials see: refs28 below.

1,2-Bis-[4-(3-methyl-butyl)-phenyl]-ethane-1,2-dione, prepared as described above, (0.280 g, 0.80 mmol, 1.05 equiv) in one portion. The resulting mixture was heated to 66 °C for 12 h upon which the mixture was cooled to ambient temperature and directly absorbed onto normal phase silica gel under reduced pressure at ambient temperature. The crude material was purified using automated flash column chromatography to afford the title compound. Rf = 0.56, 20% EtOAc:hexanes; eluent, methyl-tert-butyl ether/ethyl acetate; gradient:

General Procedure for Indole-Boronic Acid Coupling. To an 8 mL reaction vial equipped with a magnetic stirring bar, ambient temperature was charged the requisite 3-(6-bromo-pyridine-2-yl)-5,6-diphenyl-[1,2,4]triazine (or derivative) (100 mg, 0.258 mmol, 1.00 equiv), followed by palladium dibenzylidene acetone (3.45 mg, 0.006 mmol, 0.025 equiv), 4,4′-dibromobenzil (0.500 g, 1.36 mmol, 1.00 equiv), Pd(OAc)2 (15.3 mg, 0.06 mmol, 0.05 equiv), RuPhos (67.5 mg, 0.14 mmol, 0.01 equiv), 3-methylbutylboronic acid (0.331 g, 2.85 mmol, 2.10 equiv), and Cs2CO3 (84 mg, 0.258 mmol, 1.00 equiv). The resulting mixture was heated to 66 °C for 12 h. The crude mixture was slurried in a 4:1 mixture of CPME:H2O (0.86 mL, 8 vol) at ambient temperature and treated with 1,2-bis-[4-(3-methyl-butyl)-phenyl]-ethane-1,2-dione, prepared as described above, (0.280 g, 0.80 mmol, 1.05 equiv) in one portion. The resulting mixture was heated to 66 °C for 12 h upon which the mixture was cooled to ambient temperature and directly absorbed onto normal phase silica gel under reduced pressure at ambient temperature. The crude material was purified using automated flash column chromatography to afford the title compound. Rf = 0.56, 20% EtOAc:hexanes; eluent, methyl-tert-butyl ether/ethyl acetate; gradient: 4,4′-dibromobenzil (0.500 g, 1.36 mmol, 1.00 equiv), Pd(OAc)2 (15.3 mg, 0.06 mmol, 0.05 equiv), RuPhos (67.5 mg, 0.14 mmol, 0.01 equiv), 3-methylbutylboronic acid (0.331 g, 2.85 mmol, 2.10 equiv), and Cs2CO3 (84 mg, 0.258 mmol, 1.00 equiv). The resulting mixture was slurried in 1H NMR spectroscopy unless otherwise indicated. Infrared spectral data were acquired using attenuated total reflectance (ATR) from the (form) listed. All 1H and 13C NMR data were acquired from a 500 MHz multinuclear spectrometer with a broadband N2 cryoprobe. Chemical shifts are reported using the δ scale and are referenced27 to the residual solvent signal: CDCl3 (δ 7.26), CD3CN (δ 1.94), (CD3)2C=O (δ 2.05), CD3CD3 (δ 6.97), and (CD3)2SO (δ 5.20) for 1H NMR and chloroform (δ 77.16), CD3CN (δ 1.32), (CD3)2C=O (δ 29.84), CD3CD3 (δ 137.48), and (CD3)2SO (δ 39.52) for 13C NMR. Splittings are reported as follows: (s) = singlet, (d) = doublet, (t) = triplet, (dd) = doublet of doublets, (dt) = doublet of triplets, (ddd) = doublet of doublet of doublets, (br) = broad, (br-m) = broad multiplet, and (m) = multiplet.13C NMR spectra were corrected for ringdown using linear back prediction. High-resolution mass spectrometry (HRMS) data were obtained utilizing electron impact ionization (EI) with a magnetic sector (EIE trisector), double focusing-geometry mass analyzer.

Special Instructions. It should be noted that products afforded in the context of the described method demonstrate significant sensitivity to the residual acidity in chloroform and dichloromethane, even when buffered. Pursuant to the aforementioned, these solvents should be avoided where possible for the purposes of chromatographic purification, transfer, and/or NMR analysis. Acetone and acetonitrile were suitable alternatives for this work. Most products display limited solubility in methanol. Additionally, prepared materials appear to readily incorporate the residual solvent into the crystal lattice, which is challenging to remove via standard reduced pressure techniques. Azeotropic removal of the residual acetone and/or ethyl acetate with acetonitrile afforded dry, residual solvent-free compounds at a much faster rate than freeze, pump, thaw strategies.

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1,2-Bis-[4-(3-methyl-butyl)-phenyl]-ethane-1,2-dione, prepared as described above, (0.280 g, 0.80 mmol, 1.05 equiv) in one portion. The resulting mixture was heated to 66 °C for 12 h. The crude mixture was slurried in a 4:1 mixture of CPME:H2O (0.86 mL, 8 vol) at ambient temperature and treated with 1,2-bis-[4-(3-methyl-butyl)-phenyl]-ethane-1,2-dione, prepared as described above, (0.280 g, 0.80 mmol, 1.05 equiv) in one portion. The resulting mixture was heated to 66 °C for 12 h. The crude mixture was slurried in a 4:1 mixture of CPME:H2O (0.86 mL, 8 vol) at ambient temperature and treated with 1,2-bis-[4-(3-methyl-butyl)-phenyl]-ethane-1,2-dione, prepared as described above, (0.280 g, 0.80 mmol, 1.05 equiv) in one portion. The resulting mixture was heated to 66 °C for 12 h. The crude mixture was slurried in a 4:1 mixture of CPME:H2O (0.86 mL, 8 vol) at ambient temperature and treated with 1,2-bis-[4-(3-methyl-butyl)-phenyl]-ethane-1,2-dione, prepared as described above, (0.280 g, 0.80 mmol, 1.05 equiv) in one portion. The resulting mixture was heated to 66 °C for 12 h. The crude mixture was slurried in a 4:1 mixture of CPME:H2O (0.86 mL, 8 vol) at ambient temperature and treated with 1,2-bis-[4-(3-methyl-butyl)-phenyl]-ethane-1,2-dione, prepared as described above, (0.280 g, 0.80 mmol, 1.05 equiv) in one portion. The resulting mixture was heated to 66 °C for 12 h.
using automated flash column chromatography on an acidic alumina stationary phase, with an isocratic mobile phase consisting of 8% [(3:1-ethyl acetate:acetone):hexanes] to afford the title compounds in the morphologies indicated. All yields reported are for pure materials and take into consideration the residual solvent, if applicable.

2-[6-(5,6-Diphenyl-[1,2,4]triazin-3-yl)-pyridin-2-yl]-5-methoxy-indole-1-carboxylic Acid tert-Butyl Ester (2). Prepared according to the general procedure discussed above with 3-[6-bromo-pyridin-2-yl]-5,6-diphenyl-[1,2,4]triazine (1) (0.1000 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.05 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), (1-tert-butylcarbonyl)-5-(methoxy)-indol-2-yl)boronic acid (0.0786 g, 0.270 mmol, 1.05 equiv), and Cs₂CO₃ (0.0838 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CPME:H₂O (1.29 mL, 0.20 M total), Rf = 0.34, 20% [(3:1ethyl acetate:acetone):hexanes; eluent, [(3:1) ethyl acetate:acetone]:hexanes, gradient then 8% isocratic hold; isolated yield 0.105 g, 73%; light yellow powder; melting point = 164.2–165.8 °C. ¹H NMR (500 MHz, (CD₃)₂C=O): δ = 9.09 (d, J = 7.8 Hz, 1H), 8.63 (t, J = 7.9 Hz, 1H), 8.57 (d, J = 9.1 Hz, 1H), 8.33 (d, J = 7.8 Hz, 1H), 8.16 (d, J = 7.7 Hz, 2H), 1.12 (d, J = 7.6 Hz, 2H), 7.99–7.82 (m, 6H), 7.64 (d, J = 2.2 Hz, 1H), 7.46 (dd, J = 2.3, 9.1 Hz, 1H), 7.38 (s, 4H), 1.34 (s, 3H), 1.72 (s, 9H); ¹³C NMR [¹H] (125 MHz, (CD₃)₂C=O): δ = 161.8, 157.4, 157.2, 156.8, 154.6, 153.7, 150.7, 140.9, 138.4, 136.9, 136.8, 133.3, 131.5, 130.9, 130.54, 130.55, 130.48, 130.47, 129.4, 129.3, 125.6, 123.4, 116.3, 114.5, 111.8, 104.1, 83.9, 55.9, 27.7; IR (ATR-(CD₃)₂C=O): νmax = 3055, 2977, 2930, 1731, 1588, 1570, 1492, 1445, 1412, 1316, 1141, 768, 694 cm⁻¹; HRMS (EI): m/z: [M⁺] Calcd for C₃₆H₂₉N₅O₅ 555.2270; Found: 555.2263.

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6-(tert-Butyl-dimethyl-silylamo)-2-[6-(5,6-diphenyl-[1,2,4]triazin-3-yl)-pyridin-2-yl]-indole-1,6-dicarboxylic Acid 1-tert-Butyl Ester (7). Prepared according to the general procedure above with 3-(6-bromo-pyridin-2-yl)-5,6-diphenyl-[1,2,4]triazine (1) (0.1000 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), and Cs2CO3 (0.0842 g, 0.258 mmol, 1.05 equiv), and Cs2CO3 (0.0842 g, 0.258 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CPM:MeOH (1.29 mL, 0.20 M total), Rf = 0.59, 20% [(3:1) ethyl acetate:acetone]; hexanes; eluent, [(3:1) ethyl acetate:acetone]; hexanes, gradient then 8% isocratic hold; isolated yield 0.090 g, 82%; medium brown powder; melting point = 184.6–186.2 °C; 1H NMR (500 MHz, (CD3)2CO): δ = 8.65 (d, J = 7.8 Hz, 1H), 8.18 (t, J = 7.8 Hz, 1H), 8.09 (d, J = 8.8 Hz, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.73–7.69 (m, 2H), 7.68–7.64 (m, 2H), 7.52–7.38 (m, 6H), 7.15 (d, J = 2.3 Hz, 1H), 6.97 (dd, J = 2.3, 9.0 Hz, 1H), 6.91 (s, 1H), 1.26 (s, 9H), 1.03 (s, 9H), 0.25 (s, 6H); 13C NMR (125 MHz, (CD3)2CO): δ = 161.8, 157.4, 156.8, 154.6, 153.7, 152.5, 150.7, 141.0, 134.8, 138.6, 138.6, 133.9, 131.5, 130.9, 130.7, 130.49, 129.4, 125.7, 120.8, 119.3, 119.3, 116.2, 111.8, 111.6, 83.9, 27.7, 26.1, 18.8, –43; IR ATR-(neat): vmax = 3061, 2955, 2929, 2886, 2856, 1732, 1615, 1589, 1571, 1471, 1446, 1347, 1225, 1158, 1125, 867, 857, 837, 695 cm⁻¹; HRMS (EI): m/z: [M⁺] Calcd for C35H27N5O4Si 583.2220; Found: 583.2212.

6-Benzyl-2-[6-(5,6-diphenyl-[1,2,4]triazin-3-yl)-pyridin-2-yl]-indole-1-carboxylic Acid tert-Butyl Ester (8). Prepared according to the general procedure discussed above with 3-(6-bromo-pyridin-2-yl)-5,6-diphenyl-[1,2,4]triazine (1) (0.1000 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.013 mmol, 0.05 equiv), and Cs2CO3 (0.0842 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CPM:MeOH (1.29 mL, 0.20 M total), Rf = 0.36, 20% [(3:1) ethyl acetate:acetone]; hexanes; eluent, [(3:1) ethyl acetate:acetone]; hexanes, gradient then 8% isocratic hold; isolated yield 0.090 g, 82%; medium brown powder; melting point = 211.6–213.2 °C; 1H NMR (500 MHz, (CD3)2CO): δ = 11.11 (br-s, 1H), 8.50 (dd, J = 0.9, 7.7 Hz, 1H), 8.22 (dd, J = 0.9, 8.0 Hz, 1H), 8.12 (t, J = 7.8 Hz, 1H), 7.79–7.76 (m, 2H), 7.72–7.69 (m, 2H), 7.66–7.61 (m, 2H), 7.56–7.43 (m, 6H), 7.30–7.28 (br-m, 1H), 7.19 (dd, J = 1.1, 7.0, 8.5 Hz, 1H), 7.06 (dd, J = 1.1, 7.0, 8.5 Hz, 1H); 13C NMR (125 MHz, (CD3)2CO): δ = 160.6, 156.4, 155.8, 152.6, 151.0, 132.7, 137.4, 136.6, 135.44, 135.38, 130.7, 129.9, 129.7, 119.4, 128.6, 128.5, 129.3, 126.2, 1439, 1438, 1432, 1378, 775, 701 cm⁻¹; HRMS (EI): m/z: [M⁺] Calcd for C28H21N5O3 425.1640; Found: 425.1623.

6-Benzofuran-2-[6-(5,6-diphenyl-[1,2,4]triazin-3-yl)-pyridin-2-yl]-indole-1-carboxylic Acid tert-Butyl Ester (9). Prepared according to the general procedure discussed above with 3-(6-bromo-pyridin-2-yl)-5,6-diphenyl-[1,2,4]triazine (1) (0.1000 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), (1-tert-butylcarbonyl)-6-(methoxyacarbonyl)-indol-2-yl)boronic acid (0.0868 g, 0.272 mmol, 1.05 equiv), and Cs2CO3 (0.0838 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CPM:MeOH (1.29 mL, 0.20 M total), Rf = 0.26, 20% [(3:1) ethyl acetate:acetone]; hexanes; eluent, [(3:1) ethyl acetate:acetone]; hexanes, gradient then 8% isocratic hold; isolated yield 0.087 g, 58%; pale green/yellow solid; melting point = 188.6–189.8 °C; 1H NMR (500 MHz, (CD3)2CO): δ = 8.95–8.94 (br-m, 1H), 8.70 (dd, J = 0.9, 8.0 Hz, 1H), 8.23 (t, J = 7.9 Hz, 1H), 7.97 (dd, J = 0.9, 7.9 Hz, 1H), 7.96 (dd, J = 1.5, 8.2 Hz, 1H), 7.79 (dd, J = 8.2 Hz, 1H), 7.74–7.70 (m, 2H), 7.68–7.65 (m, 2H), 7.53–7.39 (m, 6H), 7.10 (1H), 3.95 (s, 3H), 1.29 (s, 9H); 13C NMR (125 MHz, (CD3)2CO): δ = 167.7, 161.7, 157.5, 156.8, 154.0, 153.8, 150.4, 143.3, 138.7, 138.0, 136.8, 133.4, 131.5, 131.5X (overlaps with 131.54), 130.9, 130.5, 129.4, 129.3, 127.5, 125.7, 124.7, 123.9, 121.9, 117.2, 111.4, 84.8, 52.4, 27.7; IR ATR-(neat): vmax = 3099, 2952, 1727, 1714, 1611, 1585, 1489, 1439, 1409, 1393, 1375, 1334, 1298, 1219, 1093, 768, 705, 692 cm⁻¹; HRMS (EI): m/z: [M⁺] Calcd for C30H21N5O3 583.2220; Found: 583.2212.
palladium dibenzylidene acetone (5.6 mg, 0.010 mmol, 0.004 equiv), XantPhos (11.2 mg, 0.013 mmol, 0.008 equiv), Benzo[b]furan-2-ylboronic acid (0.0450 g, 0.277 mmol, 1.05 equiv), and Cs₂CO₃ (0.0838 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CMP:H₂O (1.29 mL, 0.20 M total), R₂ = 0.40, 20% [(3:1) ethyl acetate:acetone]:hexanes; gradient then 8% isocratic hold; isolated yield 0.040 g, 37%; bright yellow solid; melting point = 183.9–184.7 °C; ¹H NMR (500 MHz, (CD₃)₂C=O): δ = 8.60 (dd, J = 1.1, 7.6 Hz, 1H), 8.23 (t, J = 7.8 Hz, 1H), 8.22–8.18 (m, 1H), 7.80–7.76 (m, 3H), 7.75 (d, J = 0.9 Hz, 1H), 7.72–7.69 (m, 2H), 7.68–7.65 (m, 1H), 7.56–7.40 (m, 7H), 7.33 (dt, J = 1.0, 7.4 Hz, 1H); ¹³C NMR{¹H} (125 MHz, CDCl₃): δ = 160.7, 156.6, 156.3, 155.6, 155.0, 153.3, 151.0, 138.0, 135.8, 135.5, 131.0, 130.2, 130.0, 129.7, 129.0, 128.8, 127.5, 125.3, 122.0, 122.4, 111.7, 106.1, one carbon was phased out, or overlapped during acquisition, and was not observed; IR (ATR-solid): ν₃max = 3054, 2958, 2916, 1738, 1606, 1587, 1493, 1365, 1155, 1130, 846, 815, 800, 750 cm⁻¹; HRMS (EI): m/z: [M⁺] Calcd for C₁₃H₁₄N₂O₂: 226.34757; Found: 226.34732.

2-[6-(5,6-Di-p-toly1)-1,2,4triazin-3-yl]-pyridin-2-yl]-5-fluoro-indole-1-carboxylic Acid tert-Butyl Ester (15). Prepared according to the general procedure discussed above with 3-(6-bromo-pyridin-2-yl)-5-fluoro-indole-1-carboxylic Acid tert-Butyl Ester (14). Prepared according to the general procedure discussed above with 3-(6-bromo-pyridin-2-yl)-5,6-di-p-toly1-[1,2,4]triazine (0.0109 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), (1-(tert-butylcarbonyl)-5-(fluoroo-indol-2-yl)boronic acid (0.0754 g, 0.270 mmol, 1.05 equiv), and Cs₂CO₃ (0.0838 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CMP:H₂O (1.29 mL, 0.20 M total), R₂ = 0.75, 20% [(3:1) ethyl acetate:acetone]:hexanes; gradient then 8% isocratic hold; isolated yield 0.093 g, 63%; bright yellow solid; melting point = 189.6–191.4 °C; 'H NMR (500 MHz, (CD₂)₂C=O): δ = 8.66 (dd, J = 0.9, 7.9 Hz, 1H), 8.24–8.21 (m, 2H), 7.92 (dd, J = 0.8, 7.7 Hz, 1H), 7.82–7.76 (m, 2H), 7.75–7.71 (m, 2H), 7.42 (dd, J = 2.6, 8.9 Hz, 1H), 7.29–7.17 (m, 5H), 7.00 (s, 1H), 1.27 (s, 9H); ¹³C NMR{¹H} (125 MHz, CDCl₃): δ = 164.2 (d, J = 250.7 Hz), 163.6 (d, J = 249.1 Hz), 160.8, 159.3 (d, J = 238.0 Hz), 155.6, 155.0, 153.4, 152.7, 149.6, 141.1, 137.7, 134.2, 132.5, 132.4, 132.1 (d, J = 3.0 Hz), 132.1 (overlaps with 132.1), 131.9 (d, J = 8.8 Hz), 129.7, 129.0 (d, J = 10.6 Hz), 124.8, 122.8, 115.7 (d, J = 9.2 Hz), 115.5 (d, J = 10.6 Hz), 112.6, 112.6, 112.0 (d, J = 25.7 Hz), 112.5, 110.5 (d, J = 3.9 Hz), 106.2 (d, J = 23.4 Hz), 83.5, 26.8; IR (ATR-neat): ν₃max = 3079, 2985, 1756, 1599, 1588, 1571, 1475, 1447, 1384, 1328, 1223, 1156, 1110, 843, 803 cm⁻¹; HRMS (EI): m/z: [M⁺] Calcd for C₁₃H₁₁FN₂O: 297.0882; Found: 297.0863.

2-[6-(5,6-Bis-(4-fluoro-phenyl)-1,2,4triazin-3-yl)-pyridin-2-yl]-5-(tert-butyl(dimethyl-silyl)-oxy)-indole-1-carboxylic Acid tert-Butyl Ester (16). Prepared according to the general procedure discussed above with 3-(6-bromo-pyridin-2-yl)-5,6-bis-(4-fluoro-phenyl)-[1,2,4]triazine (0.1091 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), 1-(tert-butylcarbonyl)-5-(fluoro-indol-2-yl)boronic acid (0.0754 g, 0.270 mmol, 1.05 equiv), and Cs₂CO₃ (0.0838 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CMP:H₂O (1.29 mL, 0.20 M total), R₂ = 0.60, 20% [(3:1) ethyl acetate:acetone]:hexanes; gradient then 8% isocratic hold; isolated yield 0.103 g, 58%; bright yellow solid; melting point = 157.8–158.9 °C; 'H NMR (500 MHz, (CD₂)₂C=O): δ = 6.86 (dd, J = 0.9, 7.9 Hz, 1H), 8.18 (t, J = 7.9 Hz, 1H), 8.10–8.08 (m, 1H), 7.88 (dd, J = 0.9, 7.8 Hz, 1H), 7.81–7.77 (m, 2H), 7.76–7.71 (m, 2H), 7.29–7.20 (m, 4H), 7.15 (br-d, J = 2.4 Hz, 1H), 6.97 (dd, J = 2.5, 9.0 Hz, 1H), 6.90 (br-s, 1H), 1.26 (s, 9H), 1.03 (s, 9H), 0.25 (9s, 6H); ¹³C NMR{¹H} (125 MHz, CDCl₃): δ = 165.1 (d, J = 249.6 Hz), 164.5 (d, J = 249.6 Hz), 161.8, 156.5, 155.8, 154.7.
1.35, 152.5, 150.7, 134.0, 133.9, 133.4 (d, J = 9.5 Hz), 133.1, 133.1X (overlaps with 133.1), 132.8 (d, J = 8.3 Hz), 130.7, 125.6, 123.5, 119.3, 116.6 (d, J = 9.1 Hz), 116.4 (d, J = 9.1 Hz), 116.2, 111.8, 111.6, 83.9, 27.7, 26.1, 18.8, −4.3; IR ATR-(neat): δmax = 3064, 2982, 2958, 2925, 2856, 1726, 1601, 1592, 1503, 1471, 1456, 1361, 1345, 1227, 1157, 1127, 841 cm−1; HRMS (EI): m/z: [M]+ Calcd for C98H48F2N8O8Si 691.2790; Found: 691.2769.

2-[6-[5,6-Bis(3-methoxy-phenyl)-1,2,4]triazin-3-yl]-pyridin-2-yl]-5-methoxy-indole-1-carboxylic Acid tert-Butyl Ester (17). Prepared according to the general procedure discussed above with 3-(6-bromo-pyridin-2-yl)-5,6-bis-(3-methoxy-phenyl)-[1,2,4]triazine (0.1150 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), 1-(tert-butyl-10-foldcarbonyl)-5-(methoxy)-indol-2-yl)boronic acid (0.0786 g, 0.270 mmol, 1.0 equiv), and Cs2CO3 (0.0838 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurred in a 4:1 mixture of CPME:H2O (1.29 mL, 0.20 M total), Rf = 0.52, 20% [(3:1) ethyl acetate:acetone]; hexanes; eluent, [(3:1) ethyl acetate:acetone]; hexanes; isolated yield 0.083 g, 61%; bright yellow powder; melting point = 242.5–243.7 °C; 1H NMR (500 MHz, (CD3)2C6D6): δ = 11.10 (br-s, 1H), 8.47 (dd, J = 1.0, 7.8 Hz, 1H), 8.20 (dd, J = 1.0, 8.0 Hz, 1H), 8.10 (t, J = 7.8 Hz, 1H), 7.70–7.67 (m, 2H), 7.66–7.62 (m, 2H), 7.61–7.58 (m, 2H), 7.29–7.23 (br-m, 1H), 7.21–7.14 (m, 5H), 7.08–7.04 (m, 1H), 2.04–1.97 (m, 2H), 1.08–1.02 (m, 4H), 0.81–0.76 (m, 4H); 13C NMR ([H] (125 MHz, (CD3)2C6D6): δ = 160.2, 156.0, 155.2, 152.7, 151.0, 145.9, 138.2, 137.4, 136.7, 132.4, 132.3, 129.8, 129.2, 128.3, 125.5, 125.3, 122.6, 122.3, 121.6, 120.8, 119.6, 112.3, 107.1, 15.2, 15.1, 10.3, 10.1; IR (ATR-neat)): δmax = 3318, 3080, 3056, 1609, 1590, 1488, 1396, 1356, 1338, 1148, 899, 817, 787 cm−1; HRMS (EI): m/z: [M]+ Calcd for C40H37N5O2 619.2947; Found: 619.2945.

2-[6-[5,6-Bis(3-methoxy-phenyl)-1,2,4]triazin-3-yl]-pyridin-2-yl]-4-methyl-indole-1-carboxylic Acid tert-Butyl Ester (20). Prepared according to the general procedure discussed above with 3-(6-bromo-pyridin-2-yl)-5,6-bis-(3-methoxy-phenyl)-[1,2,4]triazine (0.1150 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), 1-(tert-butylcarbonyl)-4-(methyl)-indol-2-yl)boronic acid (0.0742 g, 0.270 mmol, 1.05 equiv), and Cs2CO3 (0.0838 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurred in a 4:1 mixture of CPME:H2O (1.29 mL, 0.20 M total), Rf = 0.36, 20% [(3:1) ethyl acetate:acetone]; hexanes; eluent, [(3:1) ethyl acetate:acetone]; hexanes; isolated yield 0.083 g, 61%; bright yellow powder; melting point = 242.5–243.7 °C; 1H NMR (500 MHz, (CD3)2C6D6): δ = 11.10 (br-s, 1H), 8.47 (dd, J = 1.0, 7.8 Hz, 1H), 8.20 (dd, J = 1.0, 8.0 Hz, 1H), 8.10 (t, J = 7.8 Hz, 1H), 7.70–7.67 (m, 2H), 7.66–7.62 (m, 2H), 7.61–7.58 (m, 2H), 7.29–7.23 (br-m, 1H), 7.21–7.14 (m, 5H), 7.08–7.04 (m, 1H), 2.04–1.97 (m, 2H), 1.08–1.02 (m, 4H), 0.81–0.76 (m, 4H); 13C NMR ([H] (125 MHz, (CD3)2C6D6): δ = 160.2, 156.0, 155.2, 152.7, 151.0, 145.9, 138.2, 137.4, 136.7, 132.4, 132.3, 129.8, 129.2, 128.3, 125.5, 125.3, 122.6, 122.3, 121.6, 120.8, 119.6, 112.3, 107.1, 15.2, 15.1, 10.3, 10.1; IR (ATR-neat)): δmax = 3318, 3080, 3056, 1609, 1590, 1488, 1396, 1356, 1338, 1148, 899, 817, 787 cm−1; HRMS (EI): m/z: [M]+ Calcd for C40H37N5O2 619.2945; Found: 619.2943.

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XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), total (1-(tert-
butylcarbonyl)-5-(fluoro)-2-indol-2-yl)boronic acid (0.0754 g, 0.270 mmol, 1.05 equiv), and Cs$_2$CO$_3$ (0.0838 g, 0.258 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CPMe$_2$H$_2$O (1.29 mL, 0.20 M total), $R_p$ = 0.68, 20% [(3:1) ethylacetate:acetone]; hexanes; eluent, [(3:1) ethyl acetate:aceto-
ne]; hexanes; isolated yield 0.127 g, 75%; bright yellow solid; melting point = 81.3–82.4 °C; $^1$H NMR (500 MHz, CD$_3$CN): δ = 8.60 (d, $J$ = 8.0 Hz, 1H), 8.16 (dd, $J$ = 4.5, 8.9 Hz, 1H), 8.10 (t, $J$ = 8.0 Hz, 1H), 7.81 (d, $J$ = 7.8 Hz, 1H), 7.54–7.48 (m, 4H), 7.38 (dd, $J$ = 2.6, 9.1 Hz, 1H), 7.27–7.24 (m, 2H), 7.23–7.20 (m, 2H), 7.17 (dt, $J$ = 2.6, 9.3 Hz, 1H), 6.92 (s, 1H), 2.70–2.61 (m, 4H), 1.65–1.54 (m, 4H), 1.40–1.29 (m, 4H), 0.94 (t, $J$ = 7.3 Hz, 3H), 0.91 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR ($^1$H) (125 MHz, CD$_3$CN): δ = 161.5, 161.2, 159.3, 157.7, 157.2, 154.1, 153.7, 147.1, 145.9, 141.9, 138.7, 135.0, 134.4, 134.3, 130.7, 130.6 (d, $J$ = 130.6 Hz), 130.4, 129.5, 129.4, 125.9, 123.8, 116.9 (d, $J$ = 9.3 Hz), 113.6 (d, $J$ = 25.4 Hz), 111.5 (d, $J$ = 4.4 Hz), 107.3 (d, $J$ = 4.4 Hz), 84.9, 35.95, 35.93, 34.2, 34.1, 27.7, 22.99, 22.96, 14.19, 14.16; IR (ATR-(neat)): $\nu_{max}$ = 3050, 2956, 2929, 2858, 1758, 1609, 1508, 1486, 1366, 1325, 1158, 820 cm$^{-1}$; HRMS (EI): $m/z$: [M]$^+$ Calcd for C$_{41}$H$_{45}$NO$_5$: 655.3326; Found: 653.3282.

2-(6-[5,6-Bis-(4-butyl-phenyl)-yl]-5-methoxy-1-carboxylic Acid tert-Butyl Ester (22). Prepared according to the general procedure discussed above with 3-((6-bromo-pyridin-2-yl)-5-bis-(3-methoxy-phen-
yl)-1,2,4)triazine (0.01286 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), total (1-((tert-butylcarbonyl)-5-(methoxy)-indol-2-yl)boronic acid (0.0786 g, 0.208 mmol, 1.05 equiv), and Cs$_2$CO$_3$ (0.1525 g, 0.468 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CPMe$_2$H$_2$O (3.24 mL, 0.20 M total), $R_p$ = 0.30, 5% [(3:1) ethyl acetate:acetone]; hexanes; eluent, [(3:1) ethyl acetate:acetone]; hexanes, gradient then 4% isocratic hold; isolated yield 0.163 g, 61%; pale-yellow solid; melting point = 195.1–196.4 °C; $^1$H NMR (500 MHz, CD$_3$CN): δ = 11.11 (br-s, 1H), 8.48 (dd, $J$ = 0.9, 7.7 Hz, 1H), 8.20 (dd, $J$ = 0.9, 8.0 Hz, 1H), 8.10 (t, $J$ = 7.9 Hz, 1H), 7.72–7.68 (m, 2H), 7.66–7.60 (m, 4H), 7.34–7.31 (m, 2H), 7.30–7.27 (m, 3H), 7.19 (ddd, $J$ = 1.1, 7.6, 8.7 Hz, 1H), 7.06 (ddd, $J$ = 1.1, 7.4, 8.5 Hz, 1H), 2.75–2.67 (m, 4H), 1.67–1.50 (m, 6H), 0.97 (d, $J$ = 6.5 Hz, 6H), 0.95 (d, $J$ = 6.6 Hz, 6H); $^{13}$C NMR ($^1$H) (125 MHz, CD$_3$CN): δ = 161.4, 157.3, 156.4, 154.0, 152.2, 147.1, 145.7, 138.7, 134.8, 137.8, 134.3, 131.0, 131.4, 129.4, 129.3, 127.1, 123.1, 122.3, 121.8, 120.7, 113.0, 102.1, 41.4, 31.3, 34.25, 34.21, 28.4, 28.4$\times$ (overlaps with 28.4), 22.82, 22.78; IR (ATR-(neat)): $\nu_{max}$ = 3435, 3053, 2954, 2928, 2967, 1609, 1591, 1568, 1496, 1467, 1382, 1365, 820, 783 cm$^{-1}$; HRMS (EI): $m/z$: [M]$^+$ Calcd for C$_{69}$H$_{77}$N$_5$: 965.3190; Found: 965.3190.

6-Benzoxly-2-(6-[5,6-bis-(4-[3,3-dimethyl-butyl]-phenyl]-
[1,2,4]triazin-3-yl)-pyridin-2-yl)-1H-indole (25). Prepared according to the general procedure discussed above with 3-(6-bromo-pyridin-2-yl)-5-bis-(4-[3,3-dimethyl-butyl]-phenyl]-1,2,4)triazine (0.1430 g, 0.218 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv), XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), (1-(tert-butylcarbonyl)-6-(benzoxly)-indol-2-yl)boronic acid (0.0992 g, 0.264 mmol, 1.05 equiv), and Cs$_2$CO$_3$ (0.0838 g, 0.257 mmol, 1.00 equiv). The resulting mixture was slurried in a 4:1 mixture of CPMe$_2$H$_2$O (1.29 mL, 0.20 M total), Two purifications were required to obtain material pure enough for characterization, $R_p$ = 0.26 5% [(3:1) ethyl acetate:acetone]; hexanes; eluent, [(3:1) ethyl acetate:acetone]; hexanes; isolated yield 0.025 g, 12%; bright yellow solid; melting point = 158.9–160.1 °C; $^1$H NMR (500 MHz, CD$_3$CN): δ =
1.05 equiv, and Cs2CO3 (0.0838 g, 0.257 mmol, 1.00 equiv).

C26H18N4 386.1531; Found: 386.1531.

J = 7.55, 7.96 = 7.6 Hz, 1H), 8.24

acetate:hexanes; eluent, [(3:1) ethyl acetate:acetone]:hexanes;

The resulting mixture was slurried in a 4:1 mixture of

boron reagent (PhB(OH)2, PhBF3K, PhBpin, or PhB-MIDA)

XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), the requisite
dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv),
above with 3-(6-bromo-pyridin-2-yl)-5,6-diphenyl-[1,2,4]
triazine. Prepared according to the general procedure discussed
above with 3-(6-bromo-pyridin-2-yl)-5,6-diphenyl-[1,2,4]triazine
(1) (0.1000 g, 0.257 mmol, 1.00 equiv), palladium dibenzylidene acetone (3.7 mg, 0.006 mmol, 0.025 equiv),
XantPhos (7.4 mg, 0.013 mmol, 0.05 equiv), the requisite boron reagent (PhB(OH)2, PhBF3K, PhBpin, or PhB-MIDA)
1.05 equiv, and Cs2CO3 (0.0838 g, 0.257 mmol, 1.00 equiv).

The resulting mixture was slurried in a 4:1 mixture of

CPME:H2O (1.29 mL, 0.20 M total, R9 = 0.51 20% ethyl acetate:hexanes; eluent, [(3:1) ethyl acetate:acetone]:hexanes;

isolated yield 0.069 g, 69%; bright yellow solid; melting point = 164.5–167.2 °C; 1H NMR (500 MHz, CDCl3): δ = 8.61 (d, J = 7.6 Hz, 1H), 8.24–8.21 (m, 2H), 8.00 (t, J = 7.7 Hz, 1H),
7.96–7.94 (m, 1H), 7.76–7.73 (m, 2H), 7.69–7.66 (m, 2H),
7.55–7.50 (m, 2H), 7.49–7.37 (m, 7H); 13C NMR (125 MHz, CDCl3): δ = 161.0, 158.0, 156.4, 151.2, 150.5, 150.9,
147.6, 136.9, 139.4, 138.4, 138.3, 133.4, 134.2, 134.0,
129.4, 129.27, 129.25, 128.6, 128.5, 125.0, 123.8, 123.0,
122.6, 113.7, 111.8, 100.8, 84.0, 70.9, 46.8, 46.7, 31.8, 31.7, 31.1,
31.1X (overlaps with 31.1), 29.62, 29.59, 27.7; IR (ATR-
( neat)): u max = 3062, 3032, 2952, 2907, 2865, 1732, 1611,
1585, 1486, 1365, 1327, 844, 820 cm −1; HRMS (EI): m/z: [M]+
Calcld for C26H18N4 386.1531; Found: 386.1531.

The authors dedicate this work in memory of the TN Tech College of Arts and Sciences Associate Dean Dr. Kurt R. Eisen (1958–2019).

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(30) Repeated experiment on 0.259 g (1.21 mmol) scale afforded 0.247 g, 39%.