Synthesis of Functionalized *Hemi*-1,2,4-triazinyl-[2,2′]-bipyridines *via* Telescoped Condensation of [2,2′]-bipyridinyl-6-carbonitrile

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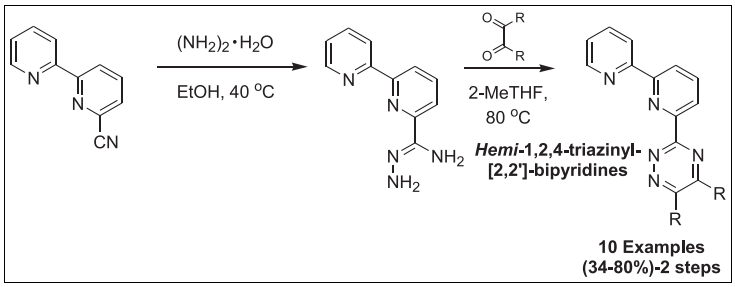

Partitioning of neutron-poisoning lanthanides from minor actinides in used nuclear fuel using liquid–liquid separation techniques with moderately soft Lewis basic heterocyclic scaffolds is an area of intense research focus. Nitrogen heterocycles have demonstrated potential for the selective separation of Am^{3+} from Eu^{3+} in separations processes. Improved synthetic strategies are required to access more diversified complexant scaffolds for further study. The present work describes an efficient synthetic strategy for the preparation of functionalized [2,2′]-bipyridinyl scaffolds using Pd catalysis to prepare the requisite starting material and telescoped condensation to afford direct access to *hemi*-1,2,4-triazinyl-[2,2′]-bipyridines with aliphatic character and potentially greater solubility in less polar diluents. Synthetic method development, optimization, and substrate scope are reported herein.

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INTRODUCTION

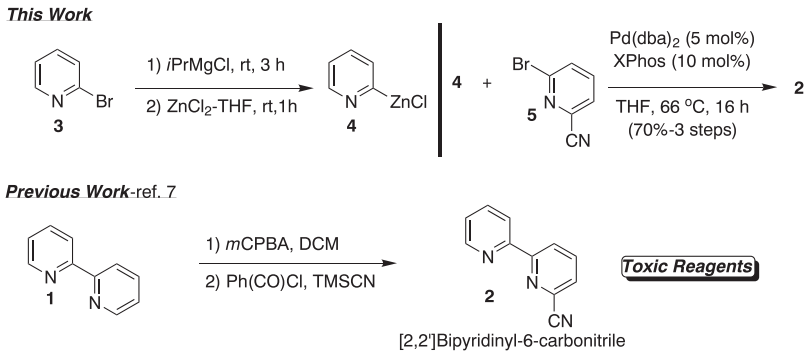
Transmutation and recovery of radionuclides intrinsic to used nuclear fuel continues to inspire significant effort. The fundamental impetus for our interest in this area is grounded in the hypothesis that moderately soft Lewis basic complexants with the appropriate physical properties can achieve selective separation of An(III) over Ln(III) from used nuclear fuel on a kinetically viable time scale with suitable distribution values [1]. While previously prepared complexants successfully address some important challenges, work over the last three decades has yet to identify the ideal complexant [2]. Efforts in this laboratory seek to develop streamlined synthetic methods [3] to address complexant solubility challenges, in addition to employing modular concepts for the rapid, convergent construction of novel scaffolds [4].

The present study describes the preparation of *hemi*-1,2,4-triazinyl-[2,2′]-bipyridine (*hemi*-TBP) complexant scaffolds as potential complexants for future investigation in liquid–liquid separations. While the utilization of the aforementioned scaffold has been described in separation studies [5], a general synthetic approach has not been disseminated. Highlights of the presented work include Pd-catalyzed coupling of 6-bromo-2-pyridinecarbonitrile and 2-bromopyridine using the Negishi coupling to afford the requisite 2,2′-bipyridinylcarbonitrile and subsequent telescoping of an intermediary hydrazonamide to afford **10** functionalized *hemi*-TBP complexants (six novel) in the polar aprotic solvent 2-methyltetrahydrofuran.

RESULTS AND DISCUSSION

Initial efforts sought to form the desired C–C bond between a preactivated and unactivated derivative of 3-(6-bromopyridin-2-yl)-5,6-diphenyl-[1,2,4]-triazine to afford symmetric and unsymmetric bis-1,2,4-triazinyl-[2,2′]-bipyridines. This end goal proved elusive. A related goal focused on the synthesis of *hemi*-TBP complexants leveraging the synthesis of carbonitrile **2** while incorporating less toxic reagents derived from the pyridinyl zinc reagent **4**, obtained from 2-bromopyridine, via Negishi coupling with **5** (Scheme 1) [6]. The exorbitant cost of **2** from commercial sources rendered its synthesis of paramount importance on the path to functionalized *hemi*-TBPs. Previous approaches to the construction of the desired *hemi*-TBP scaffolds using [2,2′]bipyridinyl-6-carbonitrile routinely employ oxidation of a pyridinyl *N* to the corresponding *N*-oxide followed by functional group interconversion, and cyanation with trimethylsilyl cyanide [7]. Alternative

Scheme 1. Synthetic approaches to the construction of [2,2′]-bipyridinyl-2-carbonitrile.



procedures to the construction of **2** utilizing the Stille coupling have also been reported [8]. The formation of **2** has also been accomplished by Duan [9] using reductive Ni catalysis in the absence of ligand. We sought a direct method leveraging Pd catalysis that did not involve challenging reagent preformation [10] prior to execution of the desired transformation. Inspired by the work of Luzung and Yin [11], who demonstrated the formation of various aryl heterocycles via Negishi coupling of premetalated 2-bromopyridine and suitable aryl chlorides, we sought to define or apply the aforementioned reaction conditions toward the formation of **2**.

Treatment of 2-bromopyridine (**3**) with isopropylmagnesium chloride facilitated a metal-halogen exchange reaction to afford a pyridinyl Grignard reagent, which was transmetallated to the zinc reagent **4**. Negishi coupling of **5** using Dipalladium-*tris*-dibenzylideneacetone [$Pd_2(dba)_3$] with XPhos afforded 60% conversion to the desired 2,2′-bipyridine **2**. Additional optimization attempts through catalyst and/or ligand screening did not improve reaction outcome toward the production of **2**. Further optimization of the candidate system through solvent screening, reactant concentration, order of addition, or reaction temperature did not afford substantive advantages over the listed conditions. Contemporary approaches to the construction of **2** using *N*-methyliminodiacetic acid (MIDA) reagents for the formation of the desired [2,2′]-bipyridine substrate were also unsuccessful [12].

With a defined catalytic method in place for the formation of the desired carbon–carbon bond in the *hemi*-TBP starting material (**2**), we sought to evaluate the formation of the requisite hydrazonamide and preliminary heterocycle formation conditions. Entry into these diversified *hemi*-TBP scaffolds beyond those accessible from commercially available 1,2-dicarbonyls was predicated on preparation of the novel benzil reagents from 4,4′-dibromobenzil leveraging our recently published method for double Suzuki–Miyaura cross-coupling of such substrates (Scheme 2) [13]. The requisite 4,4′-dialkylbenzils, including novel examples **6**, **8**–**9**, were afforded in good to excellent isolated yields over two steps in one reaction pot from 4,4′-dibromobenzil (Supporting Information).

With a viable synthetic pathway for the production of **2** and **6**–**9** realized, our focus shifted to optimizing access to various *hemi*-TBP scaffolds. Thus, treatment of **2** with hydrazine hydrate afforded the desired [2,2′]-bipyridinyl hydrazonamide **10**. Analysis of **10** via ^{1}H NMR confirmed high levels of conversion in excess of 93 mol% via integration of selected resonances. Hydrazonamide **10** was directly telescoped to the condensation reaction without further purification. An initial solvent screen for *hemi*-TBP preparation was undertaken including THF, DMF, NMP, and 2-MeTHF pursuant to our previously published work using polar aprotic solvents, with 2-MeTHF emerging as the ideal candidate solvent for this system. Dissolution of **10** and the requisite 1,2-dicarbonyl in 2-MeTHF at 80°C afforded a homogeneous mixture, which was refluxed for 16 h to afford the desired complexants (**11**–**20**) (Table 1). Complexants **11**–**14** and **19** were accessed from commercially available 4,4′-benzil reagents. Di-4-alkylphenyl-1,2,4-triazinyl-[2,2′]-bipyridines **15**–**18** as well as **20** [3] required preparation of the 1,2-dicarbonyl (Scheme 2). Isolated, purified yields ranged from 34% to 80% over two steps from **2** (entries **1**–**10**). Interestingly,

Scheme 2. Preparation of requisite 4,4′-dialkyl benzils by Suzuki–Miyaura cross-coupling.

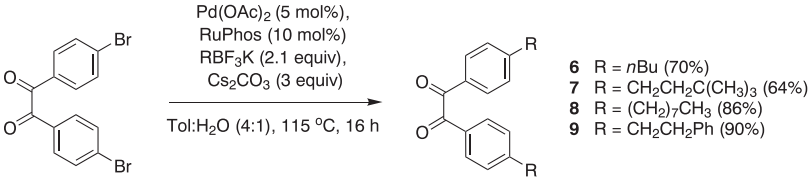
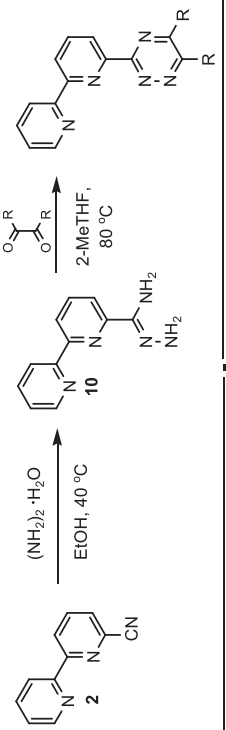
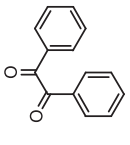
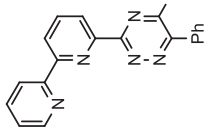
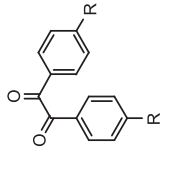
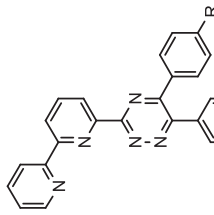
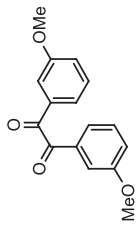
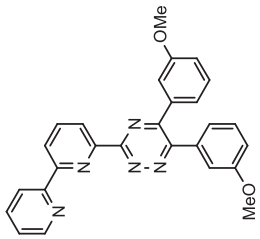
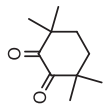
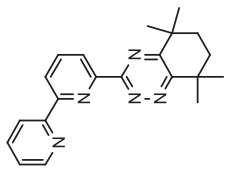


Table 1

Synthesis of *hemi*-1,2,4-triazinyl-[2,2′]-bipyridines via telescoped condensation.



Entry	Benzil	Product	Yield[a]
1			**11** (80)
2 3 4 5 6 7 8	 **12** R = F **13** R = Br **14** R = CH_3 **15** R = *n*Bu **16** R = $CH_2CH_2C(CH_3)_3$ **17** R = $(CH_2)_7CH_3$ **18** R = CH_2CH_2Ph		**12** (69)[b] **13** (48)[b] **14** (71)[b] **15** (63) **16** (34) **17** (47) **18** (58)
9			**19** (59)[b]
10			**20** (64)[c]

hemi-TBP complexants appear to display electronic environment sensitivity to heterocycle formation that was previously encountered in earlier work from this lab [3], whereby resonance donating substitutents, such as the 3,3′-OMe substituent in **19**, inhibited the condensation reaction leading to lower conversion of **10** and similarly lower isolated yields presumably via suppression of the electrophilicity of the 1,2-dione carbonyl. Synthesis of the 4,4′-OMe constitutional isomer of **19** was attempted, but resulted in incomplete conversion and a complex mixture of materials unable to be separated chromatographically. Although a decrease in efficiency of the heterocycle synthesis with 4,4′-alkyl benzils (**15**–**17**) beyond methyl (**14**) was observed, presumably because of the inductively electron-donating alkyl substituents, preparation of these completely novel complexants was possible. Isolation and purification of the complexant scaffolds was straightforward and involved direct absorption of the crude reaction mixture on silica gel followed by purification using automated flash chromatography.

CONCLUSIONS

In conclusion, we have described an efficient preparation of various functionalized *hemi*-TBPs using a Negishi-coupling reaction to afford [2,2′] bipyridinyl-6-carbonitrile, which was transformed to the *hemi*-TBP via telescoped condensation to afford six novel (Supporting Information) complexants (10 total) over two steps via a unified approach without the use of anhydrous hydrazine, discrete purification of the intermediary hydrazonamide, or recrystallization protocols. Moreover, this general strategy was applicable to the production of *hemi*-TBPs with various substituents including those with resonance and inductive electron-donating properties. Future work will ascertain the solubility of prepared complexants in process-relevant diluents followed by evaluation of the most promising candidates in separation assays to study chemoselectivity for complexation of Am^{3+} over Eu^{3+}. Synthesis of these important scaffolds could provide additional insight into metal–ligand covalency related to the interaction of moderately soft-*N*-donor complexants with the *f*-orbitals of minor-actinide Lewis acids such as Am^{3+}. Additional efforts will center on defining experimental parameters for the direct formation of the 2,2′-bipyridine carbon–carbon of bis-1,2,4-triazinyl-[2,2′]-bipyridine bond via cross-coupling of the appropriately functionalized precursors in addition to the investigation of aryl–aryl couplings to 3-(6-bromopyridin-2-yl)-5,6-diphenyl-[1,2,4] triazine. Studies to address the current synthetic limitations of the method are ongoing in this laboratory and will be reported in due course.

EXPERIMENTAL

General. All reagents were purchased from the US chemical suppliers, stored according to published protocols, and used as received unless indicated otherwise. All experiments were performed in oven-dried or flame-dried glassware under an inert atmosphere of Ar except where indicated. Reaction progress was monitored using thin-layer chromatography on glass-backed silica gel plates and/or ^{1}H-NMR analysis of crude reaction mixtures. R_F values for compounds that resulted in a concentrically observed spot on normal phase silica gel are reported using the conditions listed. All reported yields listed are for pure compounds and corrected for residual solvent, if applicable, from ^{1}H NMR spectroscopy unless otherwise indicated. Infrared spectral data were acquired from the (form) listed. All ^{1}H and ^{13}C NMR chemical shifts are reported using the δ scale and are referenced to the residual solvent signal: $CDCl_3$ (δ 7.26) or DMSO-d_6 (δ 2.50) for ^{1}H-NMR and chloroform (δ 77.16), DMSO-d_6 (δ 39.52) for ^{13}C-NMR. Splittings are reported as follows: (s) = singlet, (d) = doublet, (t) = triplet, (dd) = doublet of doublets, (dt) = doublet of triplets, (br) = broad, and (m) = multiplet. High-resolution mass spectrometry (HRMS) data was obtained utilizing electron impact (EI) ionization with a magnetic sector (EBE trisector), double focusing-geometry mass analyzer unless indicated otherwise.

For a general experimental procedure on the preparation of **6**–**9**, see [13].

[2,2′]-Bipyridinyl-6-carbonitrile (2). An oven-dried 8-mL reaction vial equipped with a magnetic stir bar was treated with 2-bromopyridine (0.388 g, 2.46 mmol, 1.50 equiv) followed by dropwise addition of isopropylmagnesium chloride-2.0*M* in THF (1.35 mL, 2.70 mmol, 1.65 equiv) at ambient temperature and continued for 3 h upon which time a solution of $ZnCl_2$-2.0*M* in anhydrous THF (1.47 mL, 2.95 mmol, 1.80 equiv) was added followed by continuation at ambient temperature for an additional 2 h. A 25-mL round-bottom flask equipped with a magnetic stir bar was charged in sequential order the catalyst (5 mol%), ligand (10 mol%), and 6-bromopyridine-2-carbonitrile (0.300 g, 1.64 mmol, 1.00 equiv) in the listed solvent at 0.3*M*. The homogeneous mixture containing catalyst, ligand, and 6-bromopyridine-2-carbonitrile was allowed to precomplex for 0.5 hr upon which time the transmetallated material in the auxiliary flask was charged dropwise followed by reflux at the temperature listed for 16 h. Afterwards, the crude reaction mixture was filtered through Celite, and the cake was conditioned with copious amounts of EtOAc. The filtrate was transferred to a separatory funnel where the organic layer was washed successively with a saturated $NaHCO_3$

solution followed by a saturated NaCl solution, dried over anhydrous Na_2SO_4, filtered, and then concentrated to afford the crude compound, which was purified on silica gel using automated flash column chromatography with an EtOAc : hexanes gradient.

1,2-Bis-(4-butylphenyl)ethane-1,2-dione (6). R_F = 0.62, 5% EtOAc : hexanes; MTBE : hexanes (gradient); isolated yield 0.121 g, 70%; yellow-greenish oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (dt, *J* = 1.9, 8.4 Hz, 4H), 7.30 (Br–d, *J* = 8.4 Hz, 4H), 2.68 (t, *J* = 7.5 Hz, 4H), 1.64–1.58 (m, 4H), 1.36 (sextet, *J* = 7.5, 10.0 Hz, 4H), 0.93 (t, *J* = 7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.7, 151.1, 131.0, 130.2, 129.2, 36.0, 32.3, 22.4, 14.0; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3031, 2957, 2860, 1668, 1603, 1570, 1216, 1172, 845 cm^{-1}; HRMS (EI): *m*/*z* calculated for $C_{22}H_{26}O_2$: 322.1933; found 322.1935.

1,2-Bis-(4-octylphenyl)ethane-1,2-dione (8). R_F = 0.82, 10% MTBE : hexanes; MTBE/hexanes (gradient); isolated yield 0.150 g, 64%; yellow/green oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.4 Hz, 4H), 7.30 (d, *J* = 8.4 Hz, 4H), 2.67 (t, *J* = 7.5 Hz, 4H), 1.65–1.59 (m, 4H), 1.36–1.23 (m, 20H), 0.87 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.7, 151.1, 131.0, 130.2, 129.2, 36.4, 32.0, 31.2, 29.5, 29.4, 29.3, 22.8, 14.2; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3031, 2924, 2854, 1669, 1603, 1570, 1216, 1171, 886 cm^{-1}; HRMS (EI): *m*/*z* calculated for $C_{30}H_{42}O_2$: 434.1385; found: 434.1392.

1,2-Bis-(4-phenethylphenyl)ethane-1,2-dione (9). R_F = 0.42, 5% EtOAc : hexanes; MTBE/hexanes (gradient); isolated yield 0.240 g, 90%; pale yellow/green solid; mp = 81.3–83.7°C, ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.89 (dt, *J* = 1.8, 8.4 Hz, 4H), 7.31–7.26 (m, 8H), 7.22–7.18 (m, 2H), 7.17–7.14 (m, 4H), 3.03–2.98 (m, 4H), 2.96–2.92 (m, 4H), ^{13}C NMR (125 MHz, $CDCl_3$): δ = 194.5, 149.8, 141.0, 131.3, 130.3, 129.3, 128.6, 128.56, 126.35, 38.4, 38.2; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3027, 2926, 2858, 1667, 1602, 1570, 1217, 1172, 829, 748, 698 cm^{-1}; HRMS (EI): *m*/*z* calculated for $C_{30}H_{26}O_2$: 418.1933; found: 418.1927.

Hydrazonamide (10). To an 8-mL reaction vial equipped with a magnetic stirring bar at ambient temperature was charged **2** (0.100 g, 0.55 mmol, 1.00 equiv). After dissolution in anhydrous EtOH (57 µL, 9.60*M*), the clear solution was cooled to 0°C treated dropwise with hydrazine monohydrate (60–65% hydrazine) (0.24 mL, 2.76 mmol, 5.00 equiv) and continued for 1 h. The homogeneous mixture was allowed to gradually warm to ambient temperature and heated to 40°C for 12 h. Afterwards, the heterogeneous mixture was filtered under vacuum at ambient temperature to afford a white filter cake that was conditioned with a minimal amount of 0°C hexanes. The resulting solids were analyzed by ^{1}H NMR confirming consumption of the starting material and were telescoped directly to the condensation step in 2-methyl THF (0.5*M*) with the appropriate 1,2-dicarbonyl (1.05 equiv) without further purification. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.73–8.69 (m, 2H), 8.34 (dd, *J* = 1.0, 7.8 Hz, 1H), 8.01–7.96 (m, 2H), 7.91 (t, *J* = 7.8 Hz, 1H), 7.49 (ddd, *J* = 1.0, 4.5, 7.8 Hz, 1H).

6-(5,6-Diphenyl-[1,2,4]triazin-3-yl)-[2,2′]bipyridinyl (11). EtOAc/hexanes (gradient), yellow solid; mp = 172.8–176.4°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.81 (Br–d, *J* = 7.8 Hz, 1H), 8.75–8.70 (m, 3H), 8.11–8.06 (m, 1H), 7.95–7.89 (Br–m, 1H), 7.77–7.73 (m, 2H), 7.70–7.66 (m, 2H), 7.50–7.37 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.8, 156.5, 156.1, 155.5, 152.6, 148.72, 148.7X (overlaps with 148.72), 138.3, 137.8, 135.9, 135.5, 131.0, 130.1, 130.0, 129.7, 128.83, 128.76, 124.5, 124.4, 123.1, 122.3; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3059, 2930, 2855, 1580, 1561, 1493, 1382, 1361, 768, 697 cm^{-1}; HRMS (EI): *m*/*z* calculated for $C_{25}H_{17}N_5$: 387.1484; found: 387.1494.

6-[5,6-Bis-(4-fluorophenyl)-[1,2,4]triazin-3-yl]-[2,2′]bipyridinyl (12). EtOAc/hexanes (gradient); pale green powder; mp = 193.4–197.6°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 8.0 Hz, 1H), 8.78–8.73 (m, 2H), 8.71 (dd, *J* = 1.0, 8.0 Hz, 1H), 8.11 (t, *J* = 8.0 Hz, 1H), 7.99–7.94 (m, 1H), 7.79–7.44 (m, 2H); C–F coupling = 2.5 Hz, 7.70–7.65 (m, 2H); C–F coupling = 2.5 Hz, 7.45–7.41 (Br–m, 1H), 7.16–7.09 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.6, 165.0, 163.6, 163.0, 160.8, 155.4, 154.9, 152.4, 148.6, 138.45, 138.4X (overlaps with 138.45), 132.3, 131.6, 131.4, 131.35, 124.7, 124.6, 123.4, 122.5, 116.3, 116.2; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3062, 2932, 3855, 1603, 1581, 1514, 1493, 1382, 1362, 1232, 1160, 841, 783 cm^{-1}; HRMS (EI): *m*/*z* calculated for $C_{25}H_{15}F_2N_5$: 423.1296; found: 423.1294.

6-[5,6-Bis-(4-bromophenyl)-[1,2,4]triazin-3-yl]-[2,2′]bipyridinyl (13). MeOH/DCM (gradient); brown solid; mp = 202.0–206.0°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.86–8.75 (m, 3H), 8.72 (d, *J* = 8.0 Hz, 1H), 8.15–8.10 (Br–m, 1H), 8.05–7.97 (Br–m, 1H), 7.65–7.54 (m, 8H), 7.52–7.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.0, 155.6, 155.2, 154.9, 152.1, 149.0, 148.9X (overlaps with 149.0), 138.3, 137.49, 134.4, 134.1, 132.3, 132.27, 131.6, 131.1, 126.2, 125.0, 124.4, 124.36, 123.2, 122.0; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3058, 1582, 1563, 1487, 1471, 1380, 1360, 904, 727 cm^{-1}; HRMS (EI): *m*/*z* calculated for $C_{25}H_{15}Br_2N_5$: 542.9694; found: 542.9706.

6-(5,6-Di-p-tolyl-[1,2,4]triazin-3-yl)-[2,2′]bipyridinyl (14). EtOAc/hexanes (gradient); green-yellow solid; mp = 198.4–204.0°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.80 (d, *J* = 8.0 Hz, 1H), 8.73–8.71 (m, 1H), 8.70–8.65 (m, 2H), 8.07 (t, *J* = 8.0 Hz, 1H), 7.92–7.88 (m,

1H), 7.67 (d, J = 8.2 Hz, 2H), 7.59 (d, J = 8.2 Hz, 2H), 7.39–7.35 (Br–m, 1H), 7.22 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 8.2 Hz, 2H), 2.46 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.5, 156.3, 155.9, 155.64, 155.6X (overlaps with 155.64), 152.7, 149.0, 141.5, 140.0, 138.2, 137.7, 133.1, 132.8, 130.0, 129.53, 129.5X (overlaps with 129.53), 129.46, 124.4, 124.3, 122.9, 122.2, 21.7, 21.6; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3058, 3025, 2921, 2863, 1675, 1607, 1581, 1561, 1493, 1381, 1361, 821, 782 cm^{-1}; HRMS (EI): m/z calculated for $C_{27}H_{21}N_5$: 415.1797; found: 415.1791.

6-[5,6-Bis-(4-butylphenyl)-[1,2,4]triazin-3-yl]-[2,2′]bipyridinyl (15). MeOH/DCM (gradient); yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.84 (d, J = 8.0 Hz, 1H), 8.77–8.69 (m, 3H), 8.09 (t, J = 8.0 Hz, 1H), 7.99–7.93 (Br–s, 1H), 7.70–7.66 (m, 2H), 7.62–7.58 (m, 2H), 7.45–7.39 (m, 1H), 7.24–7.18 (m, 4H), 2.69–2.63 (m, 4H), 1.67–1.58 (m, 4H), 1.42–1.32 (m, 4H), 0.98–0.91 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.5, 156.4, 156.0, 155.4, 152.8, 148.3, 146.5, 145.1, 138.3, 133.3, 133.0, 130.1, 129.6, 128.9, 128.8, 124.5, 124.5X (overlaps with 124.5), 124.4, 124.4X (overlaps with 124.4), 123.1, 123.0, 35.72, 35.67, 33.5, 33.4, 22.50, 22.46, 14.11, 14.08; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3060, 3027, 2956, 2930, 2859, 1609, 1581, 1493, 1467, 1381, 1360, 834, 782, 732 cm^{-1}; HRMS (EI): m/z calculated for $C_{33}H_{33}N_5$: 499.2736; found: 499.2730.

6-{5,6-Bis-[4-(3,3-dimethylbutyl)phenyl]-[1,2,4]triazin-3-yl}-[2,2′]bipyridinyl (16). MeOH/DCM (gradient); yellow solid; mp = 125.6–130.6°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.82 (Br–d, J = 8.0 Hz, 1H), 8.76–8.67 (m, 3H), 8.08 (t, J = 8.0 Hz, 1H), 7.96–7.91 (m, 1H), 7.71–7.67 (m, 2H), 7.62–7.59 (m, 2H), 7.42–7.37 (m, 1H), 7.25–7.20 (m, 4H), 2.67–2.59 (m, 4H), 1.58–1.49 (m, 4H), 0.98 (s, 9H), 0.97 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.1, 156.5, 156.0, 153.16, 153.1X (overlaps with 153.16), 147.3, 145.9, 138.76, 138.7X (overlaps with 138.76), 133.1, 132.8, 130.1, 129.6, 128.82, 128.77, 125.3, 124.9, 123.89, 123.8X (overlaps with 123.89), 46.02, 46.01, 31.4, 31.3, 30.77, 30.7X, 29.50, 29.48; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3060, 3027, 2953, 2865, 1610, 1581, 1562, 1493, 1472, 1382, 1364, 844, 823, 783 cm^{-1}; HRMS (EI): m/z calculated for $C_{37}H_{41}N_5$: 555.3362; found: 555.3372.

6-[5,6-Bis-(4-octylphenyl)[1,2,4]triazin-3-yl]-[2,2′]bipyridinyl (17). MeOH/DCM (gradient); yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.80 (Br–d, J = 8.0 Hz, 1H), 8.74–8.71 (m, 1H), 8.71–8.65 (m, 2H), 8.07 (t, J = 8.0 Hz, 1H), 7.94–7.88 (m, 1H), 7.70–7.67 (m, 2H), 7.61–7.58 (m, 2H), 7.40–7.36 (m, 1H), 7.23–7.18 (m, 4H), 2.68–2.62 (m, 4H), 1.68–1.59 (m, 4H), 1.37–1.22 (m, 20H), 0.91–0.86 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.6, 156.4, 156.0, 155.8, 152.7, 148.9, 146.5, 145.1, 138.2, 137.5, 133.3, 133.0, 130.1, 129.6, 128.9, 128.8, 124.32, 124.26, 122.8, 122.2, 36.01, 35.96, 32.02, 32.01, 31.31, 31.25, 29.61, 29.58, 29.5X (overlaps with 29.58), 29.43, 29.40, 29.4X (overlaps with 29.40), 22.82, 22.81, 14.26, 14.2X (overlaps with 14.26); IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3056, 2926, 2854, 1610, 1581, 1493, 1468, 1431, 1381, 782 cm^{-1}; HRMS (EI): m/z calculated for $C_{41}H_{45}N_5$: 611.3988; found: 611.3998.

6-[5,6-Bis-(4-phenethylphenyl)[1,2,4]triazin-3-yl]-[2,2′]bipyridinyl (18). EtOAc/hexanes (gradient); pale-yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.98 (Br–s, 1H), 8.83 (Br–s, 1H), 8.76 (d, J = 8.0 Hz, 1H), 8.16 (Br–t, J = 8.0 Hz, 1H), 7.66–7.63 (m, 2H), 7.59–7.56 (m, 2H), 7.29–7.24 (m, 7H), 7.21–7.13 (m, 10H), 3.00–2.91 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.6, 156.3, 155.9, 155.6, 152.7, 148.69, 148.6X (overlaps with 148.69), 145.12, 143.8, 141.5, 141.3, 138.2, 137.8, 133.6, 133.2, 130.1, 129.6, 129.0, 128.9, 128.7, 128.6, 128.51, 128.49, 126.2, 124.4, 124.3, 123.0, 122.3, 37.91, 37.87, 37.7, 37.6; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3056, 3026, 2924, 2859, 1609, 1580, 1562, 1495, 1382, 1361, 825, 783, 748, 699 cm^{-1}; HRMS (EI): m/z calculated for $C_{41}H_{33}N_5$: 595.2736; found: 595.2728.

6-[5,6-Bis-(3-methoxy-phenyl)-[1,2,4]triazin-3-yl]-[2,2′]bipyridinyl (19). EtOAc/hexanes (gradient); yellow solid; mp = 134.2–138.8°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.92–8.77 (m, 3H), 8.73 (d, J = 8.0 Hz, 1H), 8.13 (t, J = 8.0 Hz, 1H), 8.06–7.99 (Br–m, 1H), 7.54–7.45 (m, 1H), 7.35–7.28 (m, 5H), 7.20–7.15 (m, 1H), 7.05–6.97 (m, 2H), 3.79 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.8, 159.9, 159.7, 156.8, 156.2, 155.88, 155.81, 152.31, 149.16, 138.1, 137.1, 137.0, 136.7, 129.74, 129.7X (overlaps with 129.74), 124.23, 124.2, 122.8, 122.5, 122.2, 121.9, 117.2, 116.3, 114.9, 114.4, 55.45, 55.38; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 3065, 3003, 2966, 2835, 1601, 1581, 1502, 1487, 1465, 1379, 908, 781, 731 cm^{-1}; HRMS (EI): m/z calculated for $C_{27}H_{21}N_5O_2$: 447.1695; found: 447.1701.

3-[2,2′]Bipyridinyl-6-yl-5,5,8,8-tetramethyl-5,6,7,8-tetrahydrobenzo[1,2,4]triazine (20). EtOAc/hexanes (gradient); pale-yellow solid; mp = 196.7–200.8°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.77 (d, J = 8.0 Hz, 1H), 8.71–8.69 (m, 1H), 8.61 (d, J = 8.0 Hz, 1H), 8.52 (d, J = 8.0 Hz, 1H), 8.02 (t, J = 8.0 Hz, 1H), 7.90–7.85 (m, 1H), 7.38–7.33 (m, 1H), 1.87 (s, 4H), 1.51 (s, 6H), 1.45 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 164.5, 163.1, 160.9, 156.3, 155.8, 153.0, 149.0, 138.0, 137.2, 124.1, 123.8, 122.3, 121.9, 37.4, 36.6, 33.8, 33.3, 29.9, 29.3; IR (ATR-$CDCl_3$): $\bar{\upsilon}_{max}$ = 2966, 2928, 2854, 1582, 1560, 1520, 1474, 1423, 1369, 794 cm^{-1}; HRMS (EI): m/z calculated for $C_{21}H_{35}N_5$: 345.1953; found: 345.1957.

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