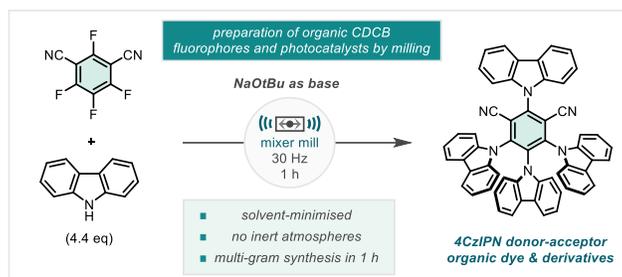# Solvent-Minimized Synthesis of 4CzIPN and Related Organic Fluorophores *via* Ball Milling

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ABSTRACT: The mechanochemical synthesis of 2,4,5,6-tetra(9H-carbazol-9-yl)isophthalonitrile (4CzIPN) and related organic fluorophores / photocatalysts *via* a solvent-minimized four-fold S_NAr pathway is herein described. Employing sodium *tert*-butoxide as base – and negating the need for any air/moisture sensitive reaction set-ups – a selection of organic dyes was synthesized in just one hour using this ball-milling technique. Furthermore, the transformation was then showcased on multi-gram scale.

INTRODUCTION

The use of mechanical force to induce a material change has been established for millennia.[1] Within this context, mechanochemical manipulations using ball-milling technology have been commonplace in crystallization, formulation chemistry, and engineering science for a number of years.[2] Despite this, recently a resurgence in the application of mechanochemical techniques towards organic synthesis has been witnessed.[3] This is primarily due to increased appreciation of the sustainable properties that can be harnessed through this strategy, especially in the use of solvent-free and solvent-minimized reaction environments (Scheme 1B).[4] Further to this, mechanochemical techniques also offer unique benefits in often negating the need for inert air/moisture-sensitivity precautions.[5] To this end, mechanochemistry can offer potent alternatives to solution-phase chemistry, with improved translational applications to industrial settings.[6]

In 2012, a pioneering report by Adachi and co-workers detailed the synthesis and development of a selection of donor-acceptor carbazolyl dicyanobenzene (CDCB) organic dyes including 4CzIPN (1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene, Scheme 1A).[7] Through rational design, these metal-free organic electroluminescent molecules were hypothesized and realized to possess a small singlet-triplet (S_1-T_1) energy gap, to enable – on thermal activation – reverse intersystem crossing (RISC), leading to enhanced intrinsic fluorescence properties. These initial discoveries have since launched research programs into CDCB design and synthesis as temperature activated delayed fluorescence (TDAF) materials for application in OLED technology.[8]

In parallel to these discoveries, the renaissance of visible light photoredox catalysis in organic synthesis has reaffirmed the opportunities that light-mediated transformations offer on the generation of efficient and often-unique disconnections in synthetic route design.[9] For these reasons, contemporary photoredox catalysis has been widely adopted in the synthesis of building blocks, pharmaceutical synthesis, and also as key steps in the total synthesis of complex natural product architectures.[10] Despite this, a significant proportion of these transformations rely on the use of precious-metal-based ruthenium(II) and iridium(III) complexes as photocatalysts to enable the electron transfer events. In the search for more environmentally and economically sustainable alternatives, and due to their established electronic properties, synthetic chemists saw the opportunity that organic fluorophores such as 4CzIPN could hold. To this end, since the initial report by Zhang and co-workers in 2016,[11] use of CDCB fluorophores has surged in popularity in photocatalytic methodology advances (Scheme 1A).[12] Furthermore, elegant reports – such as those by Zeitler and co-workers[13] – have demonstrated that libraries of derivatives 4CzIPN-type photocatalysts have been shown to possess diverse electrochemical properties and hold potential for unique future reaction discovery and development.

Scheme 1. Electronic properties of 4CzIPN and mechanochemical synthesis of organic fluorophores
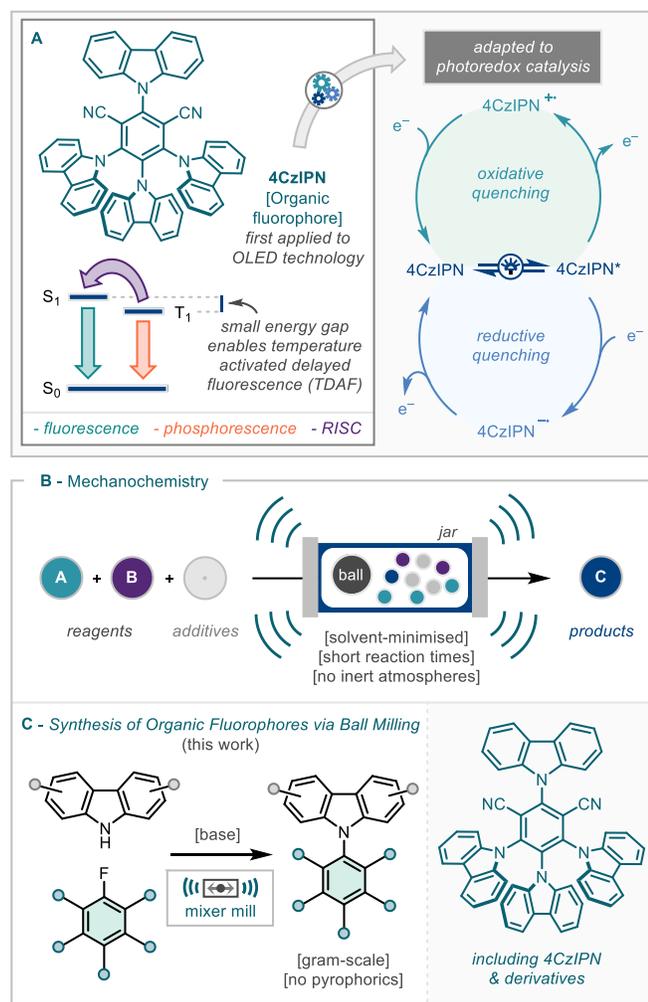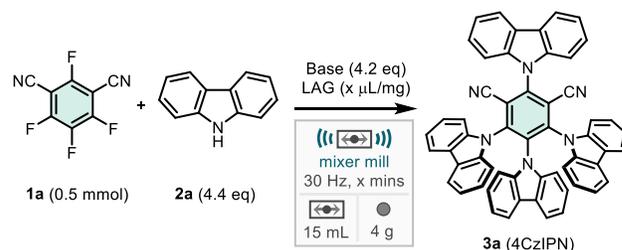

Despite the increasing importance of this family of organic fluorophores in OLED technology and as photocatalysts, current synthetic routes rely on the use of strong inorganic bases ($pK_a > 29$), large quantities of reaction solvent, and often require long reaction times (24 h+) coupled with increased temperatures.[14] Several of these reaction criteria can potentially be addressed by aforementioned ball milling techniques, where it appears that in the absence of a reaction solvent, bases with lower than typical pK_a values are still effective[15] and rigorously inert reaction conditions are not always necessary. For these reasons, mild, efficient, and sustainable synthetic strategies towards valuable 4CzIPN and 4CzIPN-type systems exploiting ball milling techniques via a solvent-minimized S_NAr pathway[16] would be of interest to academic and industrial teams alike, and herein we wish to report our findings (Scheme 1C).

RESULTS & DISCUSSION

Initial optimization studies were conducted with tetra-fluoroisophthalonitrile (**1a**, 0.5 mmol) and carbazole (**2a**, 4.4 eq),[17] using a mechanochemical mixer mill at 30 Hz for

60 minutes (Table 1). As previously stated, the synthesis of CDCB-type structures has relied on strong inorganic bases such as sodium hydride (NaH, $pK_{BH+} = 35.0$)[18] or sodium bis(trimethylsilyl)amide (NaHMDS, $pK_{BH+} = 29.5$)[18] to solicit formal deprotonation of the carbazole unit prior to addition to the fluoroarene. In our study, the use of milder bases was initially prioritized. To this end, a survey of a small subset of bases (K_2CO_3, $pK_{BH+} = 9.1$; KOtBu, $pK_{BH+} = 19.2$; NaOtBu, $pK_{BH+} = 19.2$)[18] uncovered promising reactivity when sodium *tert*-butoxide was employed as base (4.2 eq, 37% yield, entry 3).

Table 1. Optimization of Mechanochemical Synthesis of 4CzIPN

entry	Base	LAG (x μL/mg)	Pre-Mill[a]	Time (x mins)[b]	3a[c]
1	K_2CO_3	-	No	60	0
2	KOtBu	-	No	60	3
3	NaOtBu	-	No	60	37
4	NaOtBu	THF (0.1)	No	60	50
5	NaOtBu	THF (0.2)	No	60	61
6	NaOtBu	THF (0.4)	No	60	58
7	NaOtBu	THF (0.6)	No	60	65
8	NaOtBu	THF (0.8)	No	60	76
9	NaOtBu	THF (1.0)	No	60	80
10	NaOtBu	THF (1.0)	Yes	60	69
11	NaOtBu	THF (1.0)	Yes	45	82
12	**NaOtBu**	**THF (1.0)**	**Yes**	**30**	**92**
13	NaOtBu	THF (1.0)	Yes	15	80
14	NaOtBu	MeCN (1.0)	Yes	30	32
15	NaOtBu	DCM (1.0)	Yes	30	26
16	NaOtBu	DMA (1.0)	Yes	30	92
17	NaOtBu	2-MeTHF (1.0)	Yes	30	59
18	NaOtBu	THF (1.0)[d]	Yes	30	73
	change from entry 12				
19	in Schlenk tube as a slurried mixture				66
20	in Schlenk tube as a slurried mixture (24 h reaction time)				64
21	3 g ball used				81
22	2 x 2 g ball used				76

General Conditions: tetrafluoroisophthalonitrile **1a** (0.5 mmol), carbazole **2a** (2.2 mmol), base (2.1 mmol), under air atmosphere, agitated at 30 Hz for 1 hour, in a 15 mL stainless steel jar with a 4 g stainless steel ball. [a] Carbazole (**2a**) and sodium *tert*-butoxide were milled for 30 mins at 30 Hz prior to addition of **1a** and LAG. [b] Reaction time after addition of **1a**. [c] Yield after silica gel column chromatography. [d] Winchester grade THF used.

Liquid-assisted grinding (LAG) agents are common additives to facilitate reactivity in "all-solid" mechanochemical reactions.[19] Accordingly, addition of THF (0.1 μL/mg) to the reaction mixture demonstrated an improvement in reaction efficiency (50% yield, entry 4), and increased

quantities augmented this further (80% yield when using 1.0 μL/mg, entry 9). We were then intrigued to see whether pre-milling the base and carbazole together before the addition of the fluoroarene (**1a**) and LAG agent (THF) could boost reactivity further. Pleasingly, whilst pre-milling for 30 minutes and reaction for 1 hour gave comparable yields to previous, 30-minute reaction times were shown to deliver **3a** in an excellent 92% yield (entry 12). A survey of further polar aprotic solvents demonstrated that DMA proved as effective as THF in the mechanochemical procedure (entry 16), that sustainable alternative 2-MeTHF gave the product in good yield (entry 17),[20] and that using Winchester grade THF only resulted in a modest drop in reaction efficiency (entry 18). Interestingly, when the slurried reaction mixture was stirred in a Schlenk tube, conversion to the organic dye was still observed (entry 19). Despite this after 24 hours of reaction time, there was shown to be no further improvement in reaction efficiency (entry 20). Considering the low solubility of **3a** in THF (0.088 g/mL)[14] as the reaction proceeded the reaction mixture becomes less mobile and the transformation may become mixing-limited. This feature has been previously observed by our group in a prior study[21] and is circumvented by the mixer mill reaction environment, leading to effective mass transfer throughout and leads to high isolated yield (92%) in just half an hour after addition of **1a**. Further studies also demonstrated that using varying ball sizes/number (entries 21-22) showed no improvement vs. the optimized conditions (entry 12).
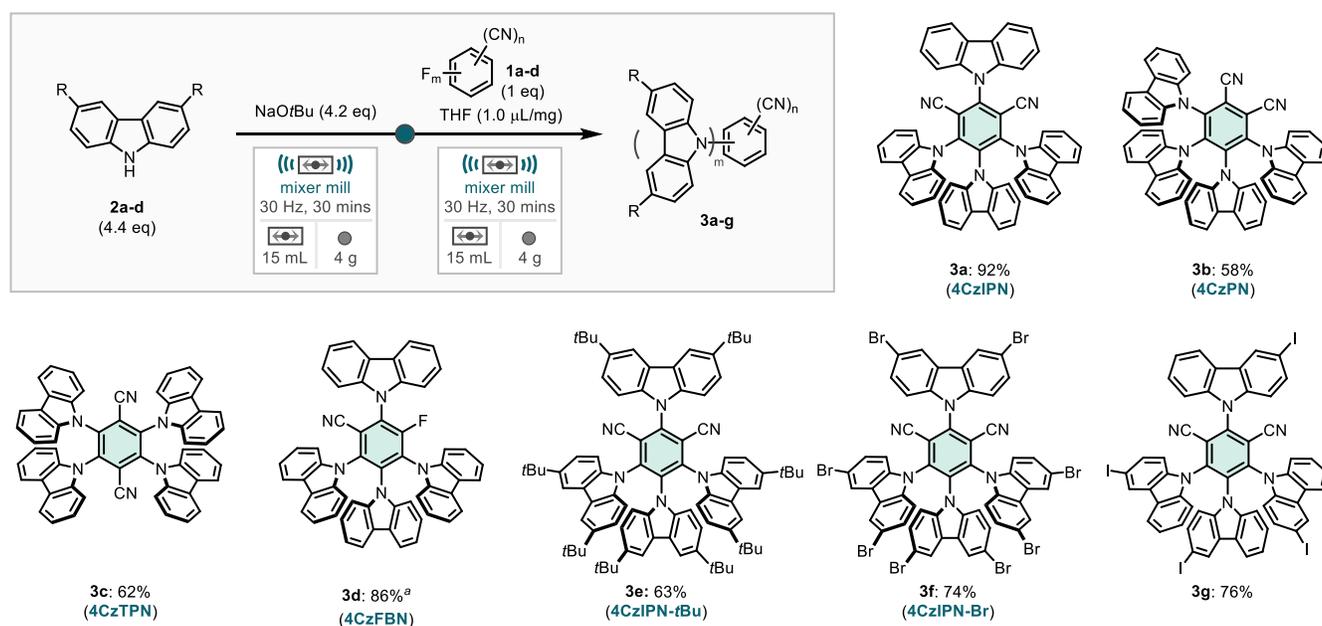
With optimal conditions in hand, this mechanochemical method was expanded to a small library of documented 4CzIPN-type fluorophores (Scheme 2). Phthalonitrile and teraphthalonitrile-derived isomers – whose photophysical properties were also explored in Adachi's initial report[7] – were shown to be compatible substrates in this methodology, delivering 4CzPN (**3b**, 58%) and 4CzTPN (**3c**, 62%) in good yields. Synthetic studies using penta-fluorobenzonitrile as the central core were then carried out. Interestingly, when using both 4.4 equivalents of carbazole (and 4.2 equivalents of base) and 5.5 equivalents of carbazole (and 5.25 equivalents of base), the 4-addition product (**4CzFBN**, **3d**) predominated, and excellent yields were achieved when using an average of these conditions (86%, 4.95 eq carbazole and 4.73 eq base).[22] Notably, even under forcing conditions – including further increases of equivalence of nucleophile and longer milling time, the penta-substituted structure – formed through a final fifth $S_{N}Ar$ reaction – was not observed in substantial quantities.

Derivatives of 4CzIPN-type fluorophores, notably 4CzIPN-*t*Bu have also found utility in photocatalytic methodology development, and, employing our mechanochemical system – 4CzIPN-*t*Bu (**3e**, 63%) was produced in good yield.[23] Moreover, halogenated analogues – which have also found utility in TDAF materials[24] – were compatible with this reaction system affording the dibrominated (4CzIPN-Br, **3f**, 74%) and mono-iodinated (**3g**, 76%) in impressive yields.[25,26]

Furthermore, the scalability of the reaction system was investigated. Pleasingly, using two 30 mL milling jars, larger stainless steel milling balls (9 g, 12.7 mm) and through running two 2.5 mmol reactions side by side, >3 g of the model 4CzIPN organic dye was afforded with excellent yield maintained (Scheme 3, 83%).

Scheme 2. Scope of the solvent-minimized synthesis of organic fluorophores via ball milling

3a: 92% (**4CzIPN**)

3b: 58% (**4CzPN**)

3c: 62% (**4CzTPN**)

3d: 86%[a] (**4CzFBN**)

3e: 63% (**4CzIPN-*t*Bu**)

3f: 74% (**4CzIPN-Br**)

3g: 76%

[a] Carbazole (**2a**, 4.95 eq), NaOtBu (4.73 eq).

Scheme 3. Gram-Scale Mechanochemical Synthesis of 4CzIPN

83% - 3.28 g[a]

before milling → after step 1 → after step 2 → after isolation
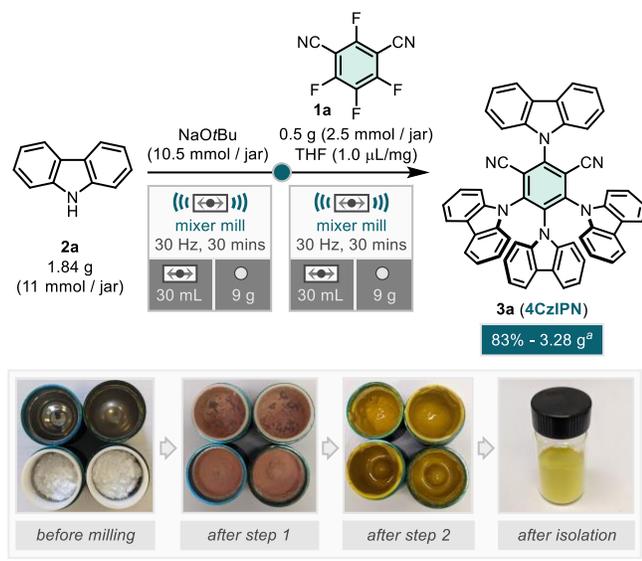
[a] Sum of two reaction jars

CONCLUSION

In conclusion we have demonstrated that the synthesis of 4CzIPN-type fluorophores can be achieved in a solvent-minimized mechanochemical environment. The newly developed process circumvents the need for air/moisture-sensitive reaction set-ups and pyrophoric bases; 4CzIPN and a selection of analogues have been prepared in only 1 hour using ball-milling technology. This system was then successfully adapted to multi-gram scale affording >3 g of the high-value organic fluorophore in a single two-jar run.

EXPERIMENTAL SECTION

Reagents: 2,4,5,6-tetrafluoroisophthalonitrile (**1a**) was purchased from Fluorochem Ltd. and used as received. Carbazole (**2a**) was purchased from Alfa Aesar or Fluorochem Ltd. and used as received. Sodium *tert*-butoxide was purchased from Sigma-Aldrich (Merck) and used as received. Tetrahydrofuran (anhydrous, 99.85%, Extra Dry, stabilized, AcroSeal) was purchased from Acros Organics and used as received. Substituted carbazoles (**2b-2d**) and fluoroarene derivatives (**1b-d**) were purchased from Fluorochem Ltd and used as received.

Mechanochemistry equipment (see supporting information for further details): The reactions were conducted using 15 mL SMARTSNAP™ stainless steel grinding jars with Teflon seals purchased from Formtech Scientific (formtechscientific.com). Stainless steel balls were purchased from Bearing Boys Ltd (bearingboys.co.uk) and used as received - 4 g ball refers to 10 mm (4.18 g) and 9 g ball refers to 12.7 mm (8.56 g). The mechanochemical reactions were conducted using an IST636 mixer mill (for general use, insolidotech.org) and a Retsch MM400 Mixer Mill (for large-scale synthesis, retsch.com).

Analytical equipment: Proton and carbon NMR spectra were recorded on Bruker Avance 400 MHz (^{1}H NMR at 400 MHz, ^{13}C NMR at 101 MHz) spectrometer equipped with a broadband and selective (^{1}H and ^{13}C) inverse probes or Bruker Avance 500 MHz (^{1}H NMR at 500 MHz, ^{13}C NMR at 126 MHz) spectrometer equipped with a QNP (^{31}P, ^{13}C, ^{15}N, ^{1}H) cryoprobe. Chemical shifts for protons are reported in parts per million downfield from $Si(CH_3)_4$ and are referenced to residual protium in the deuterated solvent ($CHCl_3$ at 7.26 ppm, DMSO at 3.31 (H_2O), 2.50, Acetone-d_6 depending on solvent used). NMR data are presented in the following format: chemical shift (multiplicity [app = apparent, br = broad, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, ddd = doublet of doublet of doublets, m = multiplet], coupling constant [in Hz], number of equivalent nuclei by integration). Analytical thin-layer chromatography (TLC) was performed on Merck silica gel 60zf F254 plates and visualised with UV light (254 or 365 nm). Flash chromatography was performed on a Biotage Selekt. Samples were dried onto silica gel prior to addition to column. Solvents were removed under reduced pressure using Heidolph Rotavapor apparatus.

Synthetic Procedures and Characterization Data

General procedure for the synthesis of 4CzIPN-based organic fluorophores. To a 15 mL stainless steel milling jar was charged a 4.18 g (10 mm) stainless steel ball, relevant carbazole (2.2 mmol, 4.4 eq) and sodium *tert*-butoxide (202 mg, 2.1 mmol, 4.2 eq). The jar was sealed tightly and connected to an In Solid Technologies 636 mixer mill and agitated at 30 Hz for 30 minutes. After this time, the jar was removed and carefully opened to reveal a light pink powder. To the jar was added relevant fluoroarene (0.5 mmol, 1 eq), and THF (anhydrous, 1.0 μL/mg of sum of all reaction components). The jar was resealed, reconnected, and agitated for a further 30 mins. After this time the jar was again removed from the mill and carefully opened. To the golden paste was added CH_2Cl_2 (2 mL) and H_2O (2 mL) and using a spatula and further aliquots of CH_2Cl_2 the contents of the jar was decanted into a separating funnel. Note: 4CzIPN organic dyes have very low solubility in EtOAc (0.002 g/mL) and Et_2O (0.002 g/mL).[14] To the separating funnel was added H_2O (20 mL) and brine (20 mL). The organic phase was then separated and the aqueous phase then re-extracted with CH_2Cl_2 (2 x 50 mL). The combined organics were then dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was then purified *via* silica gel column chromatography (CH_2Cl_2 : Hexane – 10:90 – 50:50 v:v) to give the pure organic dye.

Note 1: the organic dyes are relatively insoluble in most organic solvents. However, they generally show good solubility in CH_2Cl_2 and modest solubility in $CHCl_3$ and Acetone.[14]

Note 2: It is often challenging to remove all residual solvent from 4CzIPN and related fluorophores, even after sustained drying procedures.[14]

Synthesis of 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (**4CzIPN**, **3a**).

The general procedure was followed using 2,4,5,6-tetrafluoroisophthalonitrile (**1a**, 100 mg, 0.5 mmol, 1 eq), 9*H*-carbazole (**2a**, 368 mg, 2.2 mmol, 4.4 eq), and THF (0.67

mL). Silica gel column chromatography (CH$_2$Cl$_2$: Hexane 20:80 – 70:30 v:v) gave **3a** as a vibrant yellow solid, 92% (363 mg). **mp** (from CH$_2$Cl$_2$ / Hexane): >300 °C. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.23 (d, J = 7.7 Hz, 2H), 7.76 – 7.65 (m, 8H), 7.54 – 7.46 (m, 2H), 7.34 (t, J = 10.4 Hz, 2H), 7.25 – 7.21 (m, 4H), 7.15 – 7.05 (m, 8H), 6.83 (dd, J = 13.0, 7.7 Hz, 4H), 6.70 – 6.58 (m, 2H). **^{13}C{^{1}H} NMR** (126 MHz, CDCl$_3$) δ 145.3, 144.7, 140.1, 138.3, 137.1, 134.8, 127.1, 125.9, 125.1, 124.9, 124.7, 124.0, 122.5, 122.1, 121.6, 121.1, 120.6, 119.8, 116.4, 111.8, 110.1, 109.6, 109.5. **IR (neat): ν$_{max}$** 3049, 2154, 2024, 1599, 1543, 1443, 1300, 1215, 738, 716. **HRMS** (ESI-TOF) m/z: [M + H$^+$] Calcd for C$_{56}$H$_{33}$N$_6$ 789.2767; found 789.2750. R$_f$ (CH$_2$Cl$_2$:Hexane 70:30) = 0.38. Data is consistent with literature precedent.[11]

Note 3: *4CzIPN can be further purified recrystallization if required.* A sample of **3a** (2.86 g) was dissolved in hot CH$_2$Cl$_2$ (~40 mL) and to the solution was added MeOH until crystals started to appear. At that point, the flask was placed in a freezer at -20 °C for 2-4 hours. After this time, the precipitate (4CzIPN, **3a**) was filtered, washing with cold MeOH. The resulting microcrystals were decanted into a vial and dried *in vacuo* in an oil bath at 70 °C for 2 hours, to give 4CzIPN as vibrant yellow microcrystals (2.05 g, first crop + 0.37 g second crop).

Synthesis of 3,4,5,6-tetra(9H-carbazol-9-yl)phthalonitrile (**4CzPN**, **3b**). The general procedure was followed using 3,4,5,6-tetrafluorophthalonitrile (**1b**, 100 mg, 0.5 mmol, 1 eq), 9H-carbazole (**2a**, 368 mg, 2.2 mmol, 4.4 eq), and THF (0.67 mL). Silica gel column chromatography (CH$_2$Cl$_2$: Hexane 20:80 – 70:30 v:v) gave **3b** as a yellow solid, 58% (229 mg). **mp** (from CH$_2$Cl$_2$ / Hexane): >300 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.91 – 7.84 (m, 4H), 7.71 (d, J = 7.3 Hz, 4H), 7.39 (t, J = 8.1 Hz, 8H), 7.18 – 7.05 (m, 8H), 6.74 (t, J = 7.4 Hz, 4H), 6.59 (t, J = 7.7 Hz, 4H). **^{13}C{^{1}H} NMR** (126 MHz, DMSO-d_6) δ 141.6, 141.1, 138.8, 137.6, 125.2, 124.1, 123.1, 122.8, 121.1, 120.5, 120.2, 119.4, 119.0, 113.50, 111.2, 111.1. **IR (neat): ν$_{max}$** 3060, 2154, 2020, 1587, 1443, 1334, 1304, 1279, 1219, 738, 719. **HRMS** (ESI-TOF) m/z: [M + H$^+$] Calcd for C$_{56}$H$_{33}$N$_6$ 789.2767; found 789.27. R$_f$ (CH$_2$Cl$_2$:Hexane 70:30) = 0.26. Data is consistent with literature precedent.[7]

Synthesis of 3,4,5,6-tetra(9H-carbazol-9-yl)terephthalonitrile (**4CzTPN**, **3c**). The general procedure was followed using 2,3,5,6-tetrafluoroterephthalonitrile (**1b**, 100 mg, 0.5 mmol, 1 eq), 9H-carbazole (**2a**, 368 mg, 2.2 mmol, 4.4 eq), and THF (0.67 mL). Silica gel column chromatography (CH$_2$Cl$_2$: Hexane 20:80 – 100:0 v:v) gave **3c** as a bright orange solid, 62% (244 mg). **mp** (from CH$_2$Cl$_2$ / Hexane): >300 °C. **^{1}H NMR** (500 MHz, CD$_2$Cl$_2$) δ 7.83 – 7.80 (m, 8H), 7.33 (d, J = 7.7 Hz, 8H), 7.21 (dtd, J = 18.5, 7.3, 1.1 Hz, 16H). **^{13}C{H} NMR** (126 MHz, CD$_2$Cl$_2$) δ 140.4, 139.0, 126.5, 124.8, 123.2, 122.4, 121.0, 112.7, 110.3. **IR (neat): ν$_{max}$** 3034, 2158, 2020, 1599, 1449, 1330, 1312, 1282, 1218, 1028, 741, 715. **HRMS** (ESI-TOF) m/z: [M + H$^+$] Calcd for C$_{56}$H$_{33}$N$_6$ 789.2767; found 789.2797. R$_f$ (CH$_2$Cl$_2$:Hexane 70:30) = 0.39. Data is consistent with literature precedent.[7]

Synthesis of 2,3,4,6-tetra(9H-carbazol-9-yl)-5-fluorobenzonitrile (**4CzFBN**, **3d**). The general procedure was followed using 2,3,4,5,6-pentafluorobenzonitrile (**1d**, 63 µL, 97 mg,

0.5 mmol, 1 eq), 9H-carbazole (**2a**, 414 mg, 2.2 mmol, 4.4 eq), sodium *tert*-butoxide (227 mg, 2.37 mmol, 4.73 eq) and THF (0.67 mL). Silica gel column chromatography (CH$_2$Cl$_2$: Hexane 20:80 – 60:40 v:v) gave **3d** as a vibrant green/yellow solid, 86% (335 mg). **mp** (from CH$_2$Cl$_2$ / Hexane): >300 °C. **^{1}H NMR** (400 MHz, CD$_2$Cl$_2$) δ 8.28 (d, J = 7.8 Hz, 2H), 7.87 – 7.78 (m, 4H), 7.73 (d, J = 5.9 Hz, 4H), 7.51 (ddd, J = 8.0, 5.9, 2.2 Hz, 2H), 7.43 (d, J = 7.7 Hz, 2H), 7.39 – 7.27 (m, 4H), 7.25 – 7.04 (m, 10H), 6.88 (t, J = 7.5 Hz, 2H), 6.76 (t, J = 7.7 Hz, 2H) **^{13}C{^{1}H} NMR** (101 MHz, CD$_2$Cl$_2$) δ = 157.4, 154.8, 140.4, 139.3, 139.0, 138.0, 137.7, 135.9, 132.1, 130.3, 130.1, 127.2, 126.2, 126.1, 125.3, 124.9, 124.5, 124.4, 124.1, 122.4, 121.8, 121.7, 121.4, 121.2, 120.7, 120.6, 120.0, 116.3, 112.6, 110.5, 110.4, 110.3, 110.2. **IR (neat): ν$_{max}$** 3049, 2922, 2158, 1975, 1599, 1453, 1308, 1222, 738, 716. **HRMS** (ESI-TOF) m/z: [M + Na$^+$] Calcd for C$_{55}$H$_{32}$N$_5$FNa 804.2540; found 804.2532. R$_f$ (CH$_2$Cl$_2$:Hexane 70:30) = 0.46. Data is consistent with literature precedent.[22]

Synthesis of 2,4,5,6-tetrakis(3,6-di-tert-butyl-9H-carbazol-9-yl)isophthalonitrile (**4CzIPN-tBu**, **3e**). The general procedure was followed using 2,3,5,6-tetrafluoroterephthalonitrile (**1b**, 100 mg, 0.5 mmol, 1 eq), 3,6-di-tert-butyl-9H-carbazole (**2b**, 615 mg, 2.2 mmol, 4.4 eq), and THF (0.92 mL). Silica gel column chromatography (CH$_2$Cl$_2$: Hexane 10:90 – 50:50 v:v) gave **3e** as a bright yellow solid, 63% (393 mg). **mp** (from CH$_2$Cl$_2$ / Hexane): >300 °C. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.20 (d, J = 1.7 Hz, 2H), 7.74 (dd, J = 8.6, 1.8 Hz, 2H), 7.62 – 7.57 (m, J = 8.6 Hz, 6H), 7.18 (d, J = 1.7 Hz, 2H), 7.05 – 6.99 (m, 8H), 6.50 (dd, J = 8.6, 1.8 Hz, 2H), 6.44 (d, J = 8.5 Hz, 2H), 1.53 (s, 18H), 1.29 (s, 36H), 1.22 (s, 18H). **^{13}C{^{1}H} NMR** (126 MHz, CDCl$_3$) δ 146.0, 145.1, 144.7, 144.5, 143.5, 138.6, 137.2, 135.6, 134.1, 125.1, 124.6, 124.2, 123.4, 122.2, 117.6, 116.2, 115.5, 115.1, 112.4, 109.9, 109.1, 109.0, 35.1, 34.7, 34.4, 32.2, 31.9, 31.7, 22.8, 14.3. **IR (neat): ν$_{max}$** 3052, 2955, 2903, 2862, 1535, 1468, 1364, 1297, 1259, 1218, 890, 805. **HRMS** (ESI-TOF) m/z: [M + H$^+$] Calcd for C$_{88}$H$_{97}$N$_6$ 1237.7775; found 1237.7731. R$_f$ (CH$_2$Cl$_2$:Hexane 70:30) = 0.74. Data is consistent with literature precedent.[23]

Synthesis of 2,4,5,6-tetrakis(3,6-di-bromo-9H-carbazol-9-yl)isophthalonitrile (**4CzIPN-Br**, **3f**). The general procedure was followed using 2,3,5,6-tetrafluoroterephthalonitrile (**1b**, 100 mg, 0.5 mmol, 1 eq), 3,6-dibromo-9H-carbazole (**2c**, 715 mg, 2.2 mmol, 4.4 eq), and THF (1.02 mL). Silica gel column chromatography (CH$_2$Cl$_2$: Hexane 0:100 – 60:40 v:v) gave **3f** as a bright yellow solid, 74% (525 mg). **mp** (from CH$_2$Cl$_2$ / Hexane): >300 °C. **^{1}H NMR** (500 MHz, Acetone-d_6) δ 8.66 (d, J = 0.7 Hz, 2H), 8.22 (d, J = 1.9 Hz, 4H), 7.93 – 7.85 (m, 6H), 7.60 (d, J = 8.8 Hz, 4H), 7.43 – 7.38 (m, 6H), 7.04 (dd, J = 8.7, 1.9 Hz, 2H). **^{13}C{^{1}H} NMR** (126 MHz, Acetone-d_6) δ 146.2, 146.0, 140.0, 138.8, 137.8, 136.9, 131.5, 130.3, 129.3, 126.2, 125.8, 125.4, 125.4, 124.8, 124.2, 118.7, 116.1, 115.7, 115.0, 113.4, 113.21, 113.17, 112.4. **IR (neat): ν$_{max}$** 3369, 3075, 2158, 2027, 1539, 1539, 1464, 1427, 1297, 1278, 1218, 1058, 1021, 872, 827, 790. R$_f$ (CH$_2$Cl$_2$:Hexane 70:30) = 0.51. Data is consistent with literature precedent.[24]

Synthesis of 2,4,5,6-tetrakis(3-iodo-9H-carbazol-9-yl)isophthalonitrile (**3g**). The general procedure was followed using 2,3,5,6-tetrafluoroterephthalonitrile (**1b**, 100 mg, 0.5 mmol, 1 eq), 3-iodo-9H-carbazole (**2d**, 645 mg, 2.2

mmol, 4.4 eq), and THF (0.95 mL). Silica gel column chromatography (CH_2Cl_2 : Hexane 0:100 –60:40 v:v) gave **3g** as a pale orange solid, 76% (491 mg). **mp** (from CH_2Cl_2 / Hexane): 275-280 °C (decomp). **¹H NMR** (400 MHz, CD_2Cl_2) δ 8.60 (d, J = 1.7 Hz, 1H), 8.21 (d, J = 7.8 Hz, 1H), 8.11 (ddd, J = 7.0, 5.2, 1.6 Hz, 2H), 8.04 (d, J = 8.5 Hz, 1H), 7.79 (t, J = 7.8 Hz, 1H), 7.77 – 7.63 (m, 4H), 7.59 – 7.46 (m, 2H), 7.46 – 7.38 (m, 1H), 7.38 – 7.25 (m, 4H), 7.19 (dddd, J = 16.0, 8.9, 6.6, 3.2 Hz, 4H), 7.10 – 6.98 (m, 2H), 7.00 – 6.71 (m, 4H), 6.67 (td, J = 8.3, 3.0 Hz, 1H). **¹³C{¹H} NMR** (101 MHz, CD_2Cl_2) δ = 145.3, 145.2, 144.8, 140.2, 139.5, 138.7, 138.6, 138.6, 137.9, 137.8, 137.5, 136.8, 135.8, 135.2, 134.7, 134.6, 134.6, 134.5, 133.7, 130.8, 130.0, 130.0, 129.9, 129.4, 129.4, 128.2, 127.6, 127.3, 127.3, 127.2, 127.2, 127.1, 126.8, 126.3, 123.9, 123.6, 123.5, 123.4, 123.1, 123.1, 123.0, 122.9, 122.3, 122.0, 121.3, 121.2, 120.6, 117.1, 112.2, 112.1, 112.1, 112.0, 111.9, 111.7, 111.5, 110.4, 110.3, 110.3, 110.1, 109.9, 109.8, 85.9, 85.6, 85.5, 84.7, 84.6. **IR (neat): v_{max}** 3052, 2154, 2027, 1546, 1438, 1293, 1218, 1025, 875, 790, 738. R_f (CH_2Cl_2:Hexane 70:30) = 0.47. Data is consistent with literature precedent.[24]

ASSOCIATED CONTENT

The supporting information is available free of charge at:

Further details on mechanochemistry equipment, copies of NMR spectra

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ABBREVIATIONS

4CzIPN = 2,4,5,6-tetra(9*H*-carbazol-9-yl)isophthalonitrile
OLED = organic light-emitting diode
4CzPN = 3,4,5,6-tetra(9*H*-carbazol-9-yl)phthalonitrile.
4CzTPN = 2,3,5,6-tetra(9*H*-carbazol-9-yl)terephthalonitrile
4CzFBN = 2,3,4,6-tetra(9H-carbazol-9-yl)-5-fluorobenzonitrile

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(26) Simple S$_N$Ar systems such as 4-fluoronitrobenzene led to low yields in this reaction methodology.