DBU-mediated [4 + 2] annulations of donor–acceptor cyclopropanes with 3-aryl-2-cyanoacrylates for the synthesis of fully substituted anilines†

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A facile synthesis of fully substituted anilines by the DBU-mediated [4 + 2] annulation of donor–acceptor 1,1-dicyano-cyclopropanes with 3-aryl-2-cyanoacrylate has been developed. This reaction involves a highly efficient multiple domino sequence consisting of ring opening of donor–acceptor cyclopropanes, regioselective intermolecular Michael addition, intramolecular nucleophilic addition and aromatization as key unit steps. This transformation provides a straightforward synthetic protocol for constructing fully substituted aniline derivatives. The structure of two typical products was confirmed by X-ray crystallography.

Polysubstituted benzenes are very valuable intermediates in the synthesis of numerous natural products and synthetic pharmaceuticals. Among polysubstituted benzene derivatives, those containing nitrogen-substituted benzene derivatives as a privileged scaffold have attracted more attention recently and serve as the central pharmacophore in drug discovery. These molecules were investigated extensively as neuraminidase inhibitors, antimicrobial agents, and biochemical fluorescent agents.

As a result of the unique photophysical and electronic properties, polysubstituted benzenes also were utilized as a versatile synthetic building block in materials science and continue to draw the interest of a large segment of the scientific community. Researchers have shown that polysubstituted benzenes have important fluorescence properties in solution and in the solid state which can play a significant role in optical and electronic devices such as organic lasers, light-emitting diodes (OLEDs), and organic field-effect transistors (OFET). Additionally, polysubstituted benzene derivatives also were used to construct the molecular architecture of MOF family and liquid crystals. Given their immense pharmaceutical and material usefulness, the development of efficient syntheses of these polysubstituted benzene derivatives has thus attracted many medicinal and material chemists for decades. Traditionally, there were several methods for the preparation of the polysubstituted benzene derivatives including electrophilic or nucleophilic substitutions of the benzene ring, coupling reactions catalyzed by transition metals, and metalation functionalization reactions.

Later, cycloaddition or annulation of suitable acyclic precursors has drawn great attention for the structure of polysubstituted benzenes such as the [3 + 2 + 1] Dötz reaction, [3 + 3] cyclocondensation, [4 + 2] annulations, [5 + 1] benzannulation of alkenoyl ketene-acetals and nitroalkane. Recently, Xin and co-workers described an appealing strategy to directly construct polysubstituted benzenes via sequential Michael addition, Knoevenagel condensation and nucleophilic cyclization reactions of chalcones with active methylene compounds in guanidinium ionic liquids. In the same way, using L-proline as a catalyst in an ionic liquid, the sequential Michael addition and cyclocondensation of arylethynylidenemalononitriles with arylenedimalononitriles also afforded polynuclearized benzenes. In addition, multicomponent reactions as an efficient synthetic strategy have drawn considerable attention over the past decades, because complex products are formed in a one-pot reaction and diversity can be simply attained by relatively simple starting materials. One-pot multicomponent reactions for the construction of structurally and stereochemically diverse polysubstituted benzenes has been developed using varied catalysts such as biodegradable cellulose sulfuric acid, reusable silica nanoparticles, N,N-dimethyl-4-aminopyridine (DMAP).

In recent years, as useful three-carbon synthons, cyclopropanes with donor and acceptor substituents in the vicinal positions (D–A cyclopropanes) have drawn considerable attention from synthetic chemists. D–A cyclopropanes easily underwent a variety of ring-opening reactions under the influence of a variety of conditions to form 1,3-dipolarophiles, which were
employed to react with a variety of dipolarophiles such as carbonyls, alkenes, imines, nitriles, and nitrones to construct varied important heterocycles. In addition, D–A cyclopropanes as appropriate candidates also underwent cyclodimerization in the absence of dipolarophiles or other reagents. Very recently, our group disclosed an efficient and straightforward synthetic protocol for the preparation of fully substituted benzenes via a [3 + 3]-cyclodimerization reaction of 1-cyanocyclopropane-1-esters.

Owing to that 2,6-dicyanoanilines belong to typical acceptor–donor–acceptor (A–D–A) systems, which are the basis for artificial photosynthetic systems, materials possessing semiconducting or nonlinear properties, and molecular electronic devices. The development of methodologies for a direct access to highly substituted and specifically functionalized 2,6-dicyanoanilines is a continuing challenge in modern synthetic organic chemistry.

In continuation of our interests in D–A cyclopropanes and constructing cyclic compounds, based on our studies on the reactivity of 2-aroyl-3-aryl-1-cyanocyclopropane-1-carboxylates, we envisioned that the reaction of D–A 1,1-dicyanocyclopropanes which supply three carbons from the skeleton of cyclopropane and other carbon from its cyano group with substituted 3-aryl-2-cyanoacrylates may offer an efficient approach to benzene skeletons via [4 + 2] annihilations and aromatization. To the best of our knowledge, no example using [4 + 2] annihilations of D–A 1,1-dicyanocyclopropanes as starting materials to construct the 2,6-dicyanoaniline core were reported. In this context, the [4 + 2] annihilations of D–A 1,1-dicyanocyclopropanes with substituted 3-aryl-2-cyanoacrylates could provide an easy access to highly substituted 2,6-dicyanoaniline frameworks.

Based on our more recent results, the donor–acceptor 1,1-dicyanocyclopropanes was easily promoted by basic agents to form a 1,3-dipole, the following 2-aryloxy-1,1-dicyanocyclopropane-1-carboxylates was firstly by stirring the mixture of 2-benzoyl-3-(4-methoxyphenyl)cyclopropane-1,1-dicarbonitrile (1a), ethyl 2-cyano-3-(m-tolyl)acrylate (2a) and Et_3N in dichloromethane at 20 °C for 24 h, the desired product was not obtained (Table 1, entry 1). Then, reaction of cyclopropane-1,1-dicarbonitrile 1a and 2-cyanoacrylate 2a using Et_3N in dichloromethane resulted in the formation of 2,6-dicyanoaniline 3a in only 29% at 40 °C after 24 h (Table 1, entry 2). Exploring the effect of various bases, DBU, DABCO, piperidine, and NaOH were employed under similar reaction conditions (entries 3–6). Pleasingly, DBU and DABCO gave decent yields of 2,6-dicyanoaniline 3a (entries 3–4). Using piperidine as a base, only 5% of 2,6-dicyanoaniline 3a were obtained (entry 5), and in the presence of NaOH, no reaction took place (entry 6). Considering the replacement of dichloromethane by 1,2-DCE, toluene, and DMF for the raising of reaction temperature, the changing the solvent to 1,2-DCE instead of dichloromethane at 40 °C, 70 °C and 80 °C, respectively, did not have a significant improvement (entries 7–9), however, the results indicated the important role of the reaction temperature, the higher temperature was propitious to the formation of 2,6-dicyanoaniline 3a. The aforementioned experiments showed that both toluene and DMF play crucial roles in generating the 1,3-dipole from donor–acceptor cyclopropanes. In order to improve the yield of product 3a, switching the solvent to toluene or DMF did not give the best yields of the desired product 3a under high-temperature conditions, indicating the important role of the solvent and reaction temperature (entries 10–14). It was worth mentioning at this point that in DMF, the desired product 3a was obtained hardly any, but the formation of 3,6-bisbenzoyl-4,5-bis(4-methoxyphenyl) phthalonitrile was observed via [3 + 3] dimerization of cyclopropane-1,1-dicarbonitrile 1a, which was consistent with our previous reports. However, higher loading of DBU (to 1.25 equiv.) under otherwise identical conditions did not significantly improve the yield of 2,6-dicyanoaniline 3a, the reaction time was shortened slightly (entry 15). Subsequently, reducing the amount of DBU from 1.0 equiv. to 0.75 equiv. gave the expected product 3a in 85% yield (Table 1, entry 16), lower than that yield of product 3a using 1.0 equiv. DBU, furthermore the longer reaction time was needed.

A series of experiments revealed that the optimal results were obtained when the reaction of 2-benzoyl-3-(4-methoxyphenyl)cyclopropane-1,1-dicarbonitrile (1a) and 1.2 equiv. ethyl

| Entry | Base          | Solvent | T (°C) | t (h) | Yield (%) |
|-------|---------------|---------|--------|-------|-----------|
| 1     | Et_3N (1.0)   | DCM     | 20     | 24    | 0         |
| 2     | Et_3N (1.0)   | DCM     | 40     | 24    | 29        |
| 3     | DBU (1.0)     | DCM     | 40     | 10    | 90        |
| 4     | DABCO (1.0)   | DCM     | 40     | 12    | 75        |
| 5     | Piperidine (1.0)| DCM  | 40     | 24    | <5        |
| 6     | NaOH (1.0)    | DCM     | 40     | 12    | 0         |
| 7     | DBU (1.0)     | 1,2-DCE | 40     | 12    | 48        |
| 8     | DBU (1.0)     | 1,2-DCE | 70     | 10    | 75        |
| 9     | DBU (1.0)     | 1,2-DCE | 80     | 10    | 86        |
| 10    | DBU (1.0)     | Toluene | 40     | 12    | 43        |
| 11    | DBU (1.0)     | Toluene | 100    | 10    | 85        |
| 12    | DBU (1.0)     | Toluene | 110    | 9     | 83        |
| 13    | DBU (1.0)     | DMF     | 40     | 24    | Trace     |
| 14    | DBU (1.0)     | DMF     | 100    | 24    | Trace     |
| 15    | DBU (1.25)    | DCM     | 40     | 9     | 90        |
| 16    | DBU (0.75)    | DCM     | 40     | 14    | 85        |

*Reaction conditions: 1 mmol of 1a, 1.2 equiv. of 2a, appropriate basic reagent, 15 mL solvent. Isolated yield.
2-cyano-3-(m-tolyl)acrylate (2a) together with 1.0 equiv. DBU was carried out in dichloromethane, the resultant mixture was stirred for 10 h at 40 °C, whereby the yield of product 3a reached 90% (Table 1, entry 3).

Under the optimized conditions as described in entry 3, Table 1, the generality of the reaction was examined in Table 2. The reaction tolerates different substituents on the 1,1-dicyanocyclopropanes and substituted 3-aryl-2-cyanoacrylates, generally, 1,1-dicyanocyclopropanes with a range of substituents at aryl such as methoxy, methyl, chloro, and bromo groups all worked well to give 2,6-dicyanoaniline derivatives. Substrate 3-aryl-2-cyanoacrylates at aryl with electron-withdrawing group such as chloro, bromo, fluoro and ester gave the products in higher yields than the aryl with electron-donating methoxy and methyl. The electronic properties and positions of the

substituents on the benzene ring of 3-aryl-2-cyanoacrylates had a slight effect on the reaction. Additionally, substrate 3-aryl-2-cyanoacrylate with a heterocycle such as thiophene also worked well to give the corresponding products. The molecular structures of all 2,6-dicyanoanilines 3a-x were elucidated from their spectroscopic analyses as described herein for 3a. In the IR spectrum of 3a, two sharp absorption bands at 2221 and 1665 cm⁻¹ could be related to CN and PhCOAr stretching frequencies. The high-resolution mass spectrum of 3a displayed the molecular ion peak at m/z = 466.1530 [(M + Na)+], which is in good agreement with the proposed structure. The ¹H NMR spectrum of 3a exhibited three sharp singlet signals at 5.31 ppm (bs, 2H), 3.52 ppm (s, 3H), 2.17 ppm (s, 3H) for Ar-NH₂, ArOCH₃ and ArCH₃, respectively. Characteristic ¹H chemical shift of Ar-NH₂, ArOCH₃ and ArCH₃ unequivocally indicated the exclusive chemical environment of 2,6-dicyanoaniline 3a protons. The ¹H-Decoupled ¹³C NMR spectrum of 3a showed 24 distinct signals in agreement with the suggested structure. The important peaks were related to the ArCO, COCH₃, and PhCH₃ groups which appeared at = 193.4, 54.1, and 20.4 ppm (see ESIF).

Final confirmation for the formation of the reaction products was obtained by X-ray crystal structure analysis of compounds 3b and 3i. The structures of 3b and 3i was unambiguously solved by X-ray crystallography (Fig. 1). X-ray crystallographic analysis determined that products 3b and 3i possess two aryl and an aryl contiguous substituents at C(3), C(4) and C(5) of 2,6-dicyanoaniline core.

Based on the above experimental results, a possible mechanism is proposed in Scheme 1. Initially, the cyclopropane was activated by base generated a zwitterions [A], which formed easily 2-aryl-1,1-dicyano-3-arylprop-2-en-1-ide [B]. The Michael addition of 2-aryl-1,1-dicyano-3-arylprop-2-en-1-ide [B] to the substrate ethyl 3-aryl-2-cyanoacrylate afforded the intermediate 5-aryl-2,6,6-tricyano-1-ethoxy-1-oxo-3,4-diarylhex-5-en-2-ide [C]. Subsequently, the intramolecular nucleophilic addition of intermediate [C] to C6-cyano group formed the intermediate 6'-aryl-3',5'-dicyano-4'-imino-1',2',3',4'-tetrahydro-[1',1',2',1',1'-terphenyl]-3'-carboxylate [D] again, which transferred easily to the intermediate enamine ethyl 4'-amino-6'-aryl-3',5'-dicyano-2',3'-dihydro-[1',1',2',1',1'-terphenyl]-3'-carboxylate [E] in the presence of base DBU via 1,5-H shift. The following base DBU-promoted the tautomerism of the intermediate [E] gave the intermediate 4'-amino-2',3'-dihydro-[1',1',2',1',1'-terphenyl]-3'-carboxylate [F],

![Fig. 1](image_url) Molecular structure of 2,6-dicyanoanilines 3b and 3i.

Table 2 Scope with respect to D-A cyclopropanes and 2-cyanoacrylatesα

| Entry | R¹ | R² | R³ | Yield (%) |
|-------|----|----|----|----------|
| 1     | p-CH₃H | m-CH₃ | m-CH₃ | 90 (3a) |
| 2     | m-CH₃ | p-Br | m-CH₃ | 90 (3b) |
| 3     | m-CH₃ | p-Br | p-CH₃O | 87 (3c) |
| 4     | m-CH₃ | p-Br | p-Cl | 91 (3d) |
| 5     | m-CH₃ | p-Br | p-Br | 92 (3e) |
| 6     | m-CH₃ | p-Br | o-CH₃ | 89 (3f) |
| 7     | p-Cl | H | m-CH₃ | 89 (3g) |
| 8     | p-Cl | H | p-Br | 92 (3h) |
| 9     | p-CH₃O | H | p-Cl | 90 (3i) |
| 10    | p-CH₃O | p-Br | p-Cl | 88 (3j) |
| 11    | m-Cl | m-CH₃ | m-Cl | 93 (3k) |
| 12    | m-Cl | m-CH₃ | p-Br | 92 (3l) |
| 13    | m-Cl | m-CH₃ | p-CH₃ | 89 (3m) |
| 14    | m-CH₃ | H | H | 91 (3n) |
| 15    | m-CH₃ | H | Thiophen-2 | 84 (3o) |
| 16    | m-CH₃ | H | m-Cl | 89 (3p) |
| 17    | m-CH₃ | m-CH₃ | m-Cl | 91 (3q) |
| 18    | p-CH₃O | m-CH₃ | o-CH₃ | 88 (3r) |
| 19    | m-CH₃ | m-CH₃ | p-Cl | 90 (3s) |
| 20    | m-Cl | m-CH₃ | Thiophen-2 | 86 (3t) |
| 21    | p-Cl | H | 3,5-Cl₂C₆H₄ | 93 (3u) |
| 22    | m-CH₃ | H | p-PhO | 88 (3v) |
| 23    | p-C₆H₄-CH₃ | m-CH₃O | m-CH₃ | 84 (3w) |
| 24    | p-F | m-CH₃O | m-CH₃ | 89 (3x) |

α Reaction conditions: substituted 1,1-dicyanocyclopropanes 1a-k (1 mmol), substituted 3-aryl-2-cyanoacrylates 2a-k (1.2 mmol), DBU (152 mg, 1.0 mmol), dichloromethane (15 mL), 40 °C, 10 h. Isolated yield.
The fully substituted benzenes were finally obtained through the aromatization of the intermediate 4'-amino-2',3'-dihydro-[1,1'-2',1''-terphenyl]-3'-carboxylate [F] by removal of ethyl formate in the presence of base DBU.\textsuperscript{11,23}

**Conclusions**

In conclusion, we have developed an efficient DBU-mediated [4 + 2] annulations of donor-acceptor 1,1-dicyanocyclopropanes with ethyl 3-aryl-2-cyanoacrylate for the preparation of fully substituted anilines which are a wide range of structurally interesting and pharmacologically significant compounds. This reaction involves a highly efficient multiple domino sequence consisting of ring opening of donor-acceptor cyclopropanes, regioselective intermolecular Michael addition, intramolecular nucelophilic addition and aromatization as key unit steps. The reaction appears to be general for a variety of 1,1-dicyanocyclopropanes and 3-aryl-2-cyanoacrylate and tolerates the presence of aromatic moieties with electron-withdrawing and electron-donating substituents. It should be pointed out that this transformation presents a novel synthetic protocol, which is complementary and superior to previous synthetic methods for the formation of fully substituted aniline derivatives.

**Experimental section**

All melting points were determined in a Yanaco melting point apparatus and are uncorrected. IR spectra were recorded in a Nicolet FT-IR 5DX spectrometer. The \( ^1H \) NMR (400 MHz) and \( ^13C \) NMR (100 MHz) spectra were recorded in a Bruker AV-400 spectrometer with TMS as internal reference in CDCl\(_3\) solutions. The \( J \) values are given in hertz. Only discrete or characteristic signals for the \( ^1H \) NMR are reported. High-resolution ESI mass spectra were obtained on a UHR-TOF maXis (ESI) mass spectrometer. X-ray crystallographic analysis was performed with a SMART APEX-II diffractometer. Flash chromatography was performed on silica gel (230–400 mesh) eluting with ethyl acetate-hexanes mixture. All reactions were monitored by thin layer chromatography (TLC). All reagents and solvents were purchased from commercial sources and purified commonly before used.

The standard procedure for the synthesis of fully substituted anilines via [4 + 2] reaction between substituted 2-aryl-3-arylcyclopropane-1,1-dicarbonitriles and 3-aryl-2-cyanoacrylates as follows.

To the mixture of 2-aryl-3-arylcyclopropane-1,1-dicarbonitriles 1a-k (1.0 mmol) and 3-aryl-2-cyanoacrylates 2a-k (1.2 mmol) in dichloromethane (15 mL) was added DBU (152 mg, 1.0 mmol) at room temperature, and the resultant mixture was stirred at room temperature for 5 min. The resulting mixture was stirred at 40 °C for 10 h, and the completion of reaction was confirmed by TLC (hexanes/EtOAc 6/1). Subsequently, the resultant mixture was added with water (10 mL) and the water phase was extracted with dichloromethane (15 mL). The combined organic phase was washed with water (5 mL) and brine (5 mL), and dried over anhydride sodium sulfate. After removal of dichloromethane, the crude product was purified by flash chromatography (silica gel, EtOAc/hexanes, 1/10) to give the desirable products 3a-x.
Yellow solid, yield: 92%; mp 250.2–250.8 °C (EA/PE); IR (KBr, cm⁻¹): ν 3441, 3332, 3225, 2216, 1670, 1638, 1437, 1244, 909, 846, 745; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.53 (d, J = 7.8 Hz, 2H), 7.45 (dd, J = 7.2 Hz and 7.2 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.28 (dd, J = 7.6 Hz and 7.6 Hz, 2H), 6.91 (d, J = 7.7 Hz, 2H), 6.85 (d, J = 8.0 Hz, 2H), 6.62 (d, J = 7.2 Hz, 2H), 5.39 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 192.5, 150.0, 148.2, 147.3, 134.0, 133.5, 133.4, 132.9, 132.0, 131.0, 130.9, 129.9, 128.7, 127.9, 127.2, 126.9, 122.7, 113.7, 112.7, 108.9, 98.2, 93.6; HR-MS (ESI) calcld for C₂₉H₂₂BrN₃O₂ [M + Na]⁺: 533.9985; found: 533.9982.

**4'-Amino-6'-bromo-4'-chloro-4'-methoxy-[1,1',2',1'-terphenyl]-3',5'-dicarbonitrile (3i)**

Yellow solid, yield: 90%; mp 244.4–245.0 °C (EA/PE); IR (KBr, cm⁻¹): ν 3449, 3336, 3236, 2225, 1671, 1634, 1442, 1264, 931, 843, 749; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.53 (d, J = 7.8 Hz, 2H), 7.36 (dd, J = 7.3 Hz and 7.3 Hz, 1H), 7.20 (dd, J = 7.5 Hz and 7.5 Hz, 2H), 7.16 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 7.2 Hz, 2H), 6.58 (d, J = 6.8 Hz, 2H), 6.38 (d, J = 8.0 Hz, 2H), 5.36 (s, 2H), 3.53 (s, 3H); ¹¹C NMR (100 MHz, CDCl₃) δ (ppm): 193.1, 157.9, 150.0, 148.6, 147.6, 143.4, 134.2, 133.4, 133.2, 133.1, 130.0, 129.7, 128.9, 128.7, 128.3, 127.7, 125.8, 114.2, 113.2, 112.5, 98.3, 93.6, 54.1; HR-MS (ESI) calcld for C₂₉H₁₈BrCN₃O [M + Na]⁺: 486.0985; found: 486.0991.

**4'-Amino-6'-bromomethyl-4'-chloro-4'-methyl-[1,1',2',1'-terphenyl]-3',5'-dicarbonitrile (3j)**

Yellow solid, yield: 88%; mp 236.8–237.2 °C (EA/PE); IR (KBr, cm⁻¹): ν 3442, 3334, 3237, 2223, 1675, 1649, 1482, 1254, 941, 826, 750; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.39 (s, 4H), 7.17 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 6.7 Hz, 2H), 6.57 (d, J = 6.7 Hz, 2H), 6.41 (d, J = 7.9 Hz, 2H), 5.35 (s, 2H), 3.56 (s, 3H); ¹¹C NMR (100 MHz, CDCl₃) δ (ppm): 193.1, 153.0, 150.0, 147.1, 137.2, 132.4, 135.0, 134.4, 134.2, 131.8, 130.6, 130.2, 129.9, 129.4, 129.1, 128.4, 127.5, 125.5, 114.5, 114.0, 100.2, 94.4, 21.0, 19.7; HR-MS (ESI) calcld for C₂₉H₁₈BrCN₃O [M + Na]⁺: 593.9966; found: 593.9630.
(ESI) calef for C_{28}H_{12}Cl_{2}N_{8}O [(M + Na)^+] : 504.0646; found: 504.0645.

4’-Amino-4’-bromo-3-chloro-6’-(3-methylbenzoyl)-[1,1’;2’,1’’-terphenyl]-3’,5’dicarbonitrile (3l)
White solid, yield: 92%; mp 227.5–228.7 °C (EA/PE); IR (KBr, cm⁻¹): v 3434, 3331, 3238, 2223, 1670, 1643, 1449, 1216, 939, 825, 769; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.36 (s, 2H), 7.30 (d, J = 7.7 Hz, 1H), 7.26 (d, J = 7.6 Hz, 1H), 7.22–7.09 (m, 2H), 6.96–6.85 (m, 3H), 6.81 (dd, J = 7.6 Hz and 7.6 Hz, 1H), 6.68 (s, 1H), 6.58 (d, J = 7.1 Hz, 1H), 5.38 (s, 2H), 2.25 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 192.7, 150.3, 148.3, 137.6, 135.6, 134.6, 134.2, 133.6, 130.9, 130.1, 129.9, 128.9, 128.3, 128.1, 127.7, 127.1, 126.2, 122.9, 113.9, 110.3, 98.3, 93.9, 20.3; HR-MS (ESI) calef for C_{28}H_{12}BrCl_{2}N_{8}O [(M + Na)^+] : 548.0141; found: 548.0148.

4’-Amino-4-chloro-4’-methyl-6’-(3-methylbenzoyl)-[1,1’;2’,1’’-terphenyl]-3’,5’-dicarbonitrile (3m)
Yellow solid, yield: 89%; mp 232.9–233.6 °C (EA/PE); IR (KBr, cm⁻¹): v 3455, 3319, 3233, 2209, 1671, 1645, 1489, 1295, 903, 829, 752; ¹H NMR (400 MHz, CDCl₃) δ (ppm): 7.52 (d, J = 7.9 Hz, 2H), 7.41 (dd, J = 7.4 Hz and 7.4 Hz, 1H), 7.25 (dd, J = 7.7 Hz and J = 7.7 Hz, 2H), 7.18 (d, J = 2.9 Hz, 1H), 7.11 (dd, J = 7.8 Hz and 7.8 Hz, 1H), 7.06 (s, 1H), 6.94 (d, J = 7.5 Hz, 1H), 6.76–6.64 (m, 2H), 6.53–6.42 (m, 2H), 5.34 (s, 2H), 1.93 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm): 192.8, 149.8, 147.8, 147.2, 136.6, 136.4, 134.3, 133.2, 133.1, 130.0, 128.4, 127.9, 127.4, 127.3, 126.8, 126.6, 126.6, 113.8, 113.0, 98.1, 93.6, 19.9; HR-MS (ESI) calef for C_{28}H_{12}BrCl_{2}N_{8}O [(M + Na)^+] : 470.1036; found: 470.1034.
δ (ppm): 193.2, 150.1, 148.3, 147.6, 137.5, 136.6, 134.4, 134.2, 133.7, 133.6, 130.7, 130.0, 128.9, 128.7, 127.6, 127.5, 127.0, 126.9, 126.2, 114.2, 93.8, 93.7, 90.2, 20.2; HR-MS (ESI) calcd for C23H26ClN4O [M + Na]+: 484.1193; found: 484.1187.

4-Amino-3’-chloro-2-(3-methylbenzoyl)-6-(thiophen-2-yl)[1,1’-biphenyl]-3,5-dicarbonitrile (3f)

White solid, yield: 86%; mp 246.8–247.4 °C (EA/PE); IR (KBr, cm−1): ν 3439, 3328, 3236, 2226, 1669, 1643, 1461, 1229, 946, 859, 746; 1H NMR (400 MHz, CDCl3) δ (ppm): 7.43–7.44 (m, 4H), 7.28–7.24 (m, 1H), 7.07–7.02 (m, 1H), 6.92–6.86 (m, 1H), 6.80 (d, J = 7.7 Hz and 7.8 Hz, 2H), 6.60–6.50 (m, 2H), 5.34 (s, 2H), 2.00 (s, 3H); 13C NMR (100 MHz, CDCl3) δ (ppm): 192.3, 149.7, 147.3, 145.8, 135.0, 134.0, 133.6, 133.2, 132.4, 132.3, 131.6, 130.3, 128.7, 128.5, 127.7, 127.1, 126.4, 113.0, 112.6, 98.8, 94.3; HR-MS (ESI) calcd for C23H18ClN4O [M + Na]+: 476.0600; found: 476.0613.

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