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Palladium-catalyzed, unsymmetrical homocoupling of thiophenes *via* carbon–sulfur bond activation: a new avenue to homocoupling reactions†

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The Pd-catalyzed, CN-directed unsymmetrical synthesis of 2,4′-bithiophenes *via* an unprecedented homocoupling reaction is described. The NH_2/CN/SMe arrangement breaks the routine. The cooperative performance of the functional groups in thiophenes would open up a new vision in the field of metal catalysis homocoupling reactions by joining the electrophilic and nucleophilic motifs of the substrate. Furthermore, it is found that the α-chelating effect of the carbonyl group in amino thiophene offers a new class of synthetic protocols for C–N cross-coupling with arylboronic acids. The bidentate *N*,*O*-chelation provides a series of advantages such as copper-catalyzed, ligand- and base-free under open-flask conditions. Interestingly, the combination of the C–N cross-coupling/homocoupling reactions in a domino fashion led to the bithiophene adducts featuring the C(Ar)–N bond cleavage in the nitrogen that bridged between the two thiophene units.

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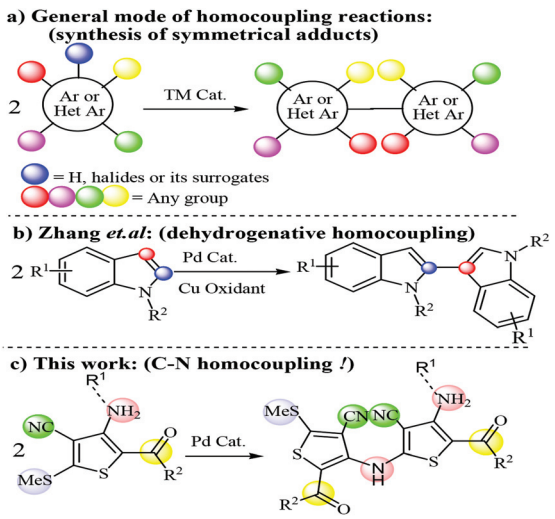
Introduction

Homocoupling reactions are the operators of the symmetrical compound productions within the synthetic chemist's repertoire. Typically, the metal-catalyzed synthesis of these reactions involves the reaction of (hetero)aryl halides or pseudohalides (Ullmann type reaction), oxidative-homocoupling of organometallic reagents such as B, Si, Sn, *etc.*,[1] and direct C–H bond functionalization (dehydrogenative homocoupling).[2] Generally, the formation of symmetrical adducts is a part of the characteristics of the homocoupling reactions (Scheme 1a). In 2010, Zhang *et al.* violated this general principle by synthesizing 2,3′-biindolyls through Pd-catalyzed unsymmetrical oxidative cross-dimerization (Scheme 1b).[2b]

The development of the organosulfur coupling reactions has lagged behind despite its wide existence in natural products, pesticides and proteins. This is mainly due to a slow oxidative addition as a result of the strength of the C_{sp^2}–S bond and the strong binding affinity of the sulfur atom to transition metal, which poisons the catalyst and leads to deactivation.[3]



Scheme 1 Homocoupling reactions.

In line with our previous efforts to synthesize thiophene-containing scaffolds,[4] herein, we disclosed the breakthrough in homocoupling reactions. Accordingly, the Pd-catalyzed C–S bond activation of thiophenes, which is assisted by an *ortho*-directing effect of the cyanide group conjoins two monomers

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†Electronic supplementary information (ESI) available: Copies of ^{1}H NMR and ^{13}C NMR spectra for all synthesized compounds and crystallography data for **4a** and **10a**. CCDC 1551355 and 1551356. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ob01923h

unsymmetrically (C(heteroaryl)–NH_2 bond formation) (Scheme 1c). We further report a one-pot domino procedure through the Chan–Lam (CEL)[5] C–N cross-coupling reaction and a desired homocoupling reaction. The overall process resulted in bithiophene adducts, featuring the C_{Ar}–N bond cleavage.

Results and discussion

Our study commenced with a three-component reaction of 2-imidazolinethione **1**, 2-di(methylsulfanyl)methylene malononitrile **2**, and 2-bromoacetophenone **3** as a model reaction in the presence of various Pd-catalysts such as Pd/C, $PdCl_2$ and $Pd(OAc)_2$. Cs_2CO_3 was used as a base in DMF/EtOH as a selected solvent[4a] at 80 °C (Table 1, entries 1–3). As shown in Table 1, the best result was obtained by using $Pd(OAc)_2$ (entry 3), and no reaction occurred in the absence of the catalyst (entry 4). Performing several experiments at different temperatures led to the inferior results relative to 80 °C (entries 5–8). There was a dramatic decrease in the yield when the reaction was performed at room temperature (entry 8). It was realized that the presence of the base is critical for this reaction to occur (entry 9). The use of three alternative bases, including K_2CO_3, Na_2CO_3 and K_3PO_4 demonstrated to be less effective than Cs_2CO_3 (entries 10–12), while no reaction occurred by using NaOAC, pyridine, and Et_3N (entries 13–15). It was found that lowering the loading amount of $Pd(OAc)_2$ from 5 mol% to 2.5 mol% decreased the isolated yield from 79% to 43% (entry 16). However, increasing the amount from 5 mol% to 7.5 mol% did not affect the reactivity (entry 17).

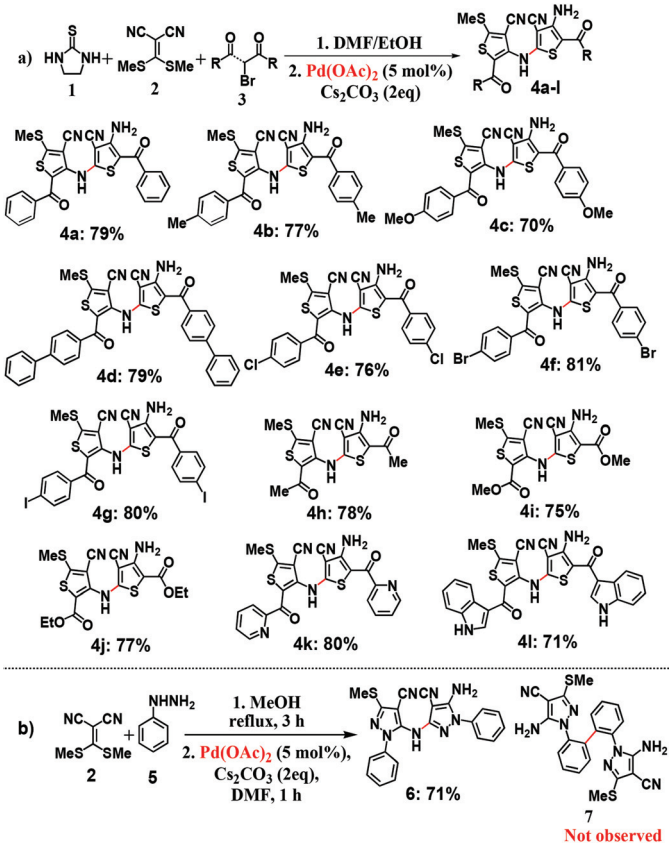
Having the optimal conditions in hand (Table 1, entry 3), we sought to further explore the reaction scope with a broad range of α-bromoketones (Table 2, part a). Both electron-rich and electron-poor aryl α-haloketones gave the homocoupling products **4a–g** in good yields (Table 2). The selective C–N bond formation in 4-Br and 4-I α-bromoarylketones (**4f**, **g**) without losing their efficiency is a remarkable result. Moreover, no competitive side-products were obtained, despite the fact that the activation of C–Br and C–I bonds is easier than the C–S bond.[3c] Similarly, α-haloketones containing alkyl and ester fragments (R = Me, OMe and OEt) underwent this reaction cleanly giving the corresponding products in good yields (**4h–j**). Interestingly, the ability to furnish **4k** and **4l** containing pyridine and indole segments, respectively, indicated that the presence of strong nitrogen donors did not lead to deactivation of the catalyst.[6] A limitation was met when ethyl 3-bromo-2-oxopropanoate, methyl 4-bromo-3-oxobutanoate, and α-haloketones bearing nitroarenes were used. In these cases, no trace of the desired adducts was observed. To find out if we could generalize the results to other compounds with the

Table 1 Optimization of reaction conditions[a]

Entry	Catalyst (mol%)	Base	Yield[b] (%)
1	Pd/C(5)	Cs_2CO_3	38
2	$PdCl_2$ (5)	Cs_2CO_3	71
3	$Pd(OAc)_2$ (5)	Cs_2CO_3	79
4	None	Cs_2CO_3	—
5[c]	$Pd(OAc)_2$ (5)	Cs_2CO_3	75
6[d]	$Pd(OAc)_2$ (5)	Cs_2CO_3	73
7[e]	$Pd(OAc)_2$ (5)	Cs_2CO_3	71
8[f]	$Pd(OAc)_2$ (5)	Cs_2CO_3	14
9	$Pd(OAc)_2$ (5)	None	—
10	$Pd(OAc)_2$ (5)	K_2CO_3	73
11	$Pd(OAc)_2$ (5)	Na_2CO_3	70
12	$Pd(OAc)_2$ (5)	K_3PO_4	75
13	$Pd(OAc)_2$ (5)	NaOAC	—
14	$Pd(OAc)_2$ (5)	Pyridine	—
15	$Pd(OAc)_2$ (5)	Et_3N	—
16	$Pd(OAc)_2$ (2.5)	Cs_2CO_3	43
17	$Pd(OAc)_2$ (7.5)	Cs_2CO_3	79

[a] Unless otherwise stated, reaction conditions: One-pot, **1** (0.25 mmol), **2** (0.25 mmol), 1 mL of DMF, 120 °C, 3 h; next **3** (0.14 mmol), 1 mL of EtOH, rt, 10 min (see ref. 4*a*); next 80 °C, 1 h. [b] Isolated yield. [c] Reaction performed at 60 °C. [d] Reaction performed at 100 °C. [e] Reaction performed at 120 °C. [f] Reaction performed at room temperature.

Table 2 Scope of the homocoupling reaction[a]



[a] For part a: same as for **4a** (Table 1, entry 3). For part b: one-pot, **2** (0.25 mmol), **5** (0.25 mmol), 1 mL of MeOH, 65 °C, 3 h; next $Pd(OAc)_2$ (5 mol%), Cs_2CO_3 (2 eq.), 1 mL of DMF, 80 °C, 1 h.

same pattern as NH_2/CN/SMe, we examined the reactivity of the pyrazole, which was *in situ* formed by the reaction of **2** and **5** (Table 2, part b). Similar to the reactivity pattern of thiophenes, the reaction furnished bis-pyrazole **6** in good yield through the C–N homocoupling reaction, and the homo-dimerization product **7** was not observed at all. Recently, however, Batra and co-workers reported a homo-dimerization reaction through C–H bond activation for the synthesis of bis-pyrazoles.[2c] In comparison, the cooperative performance of the functional groups in the current study accounts for the high selectivity in the production of **6** over **7** (Table 2, part b).

Apart from CHN, IR, mass, ^{1}H NMR, ^{13}C NMR analyses of all compounds, the structure of **4a** as a representative example is further confirmed by X-ray crystallography (Fig. 1).

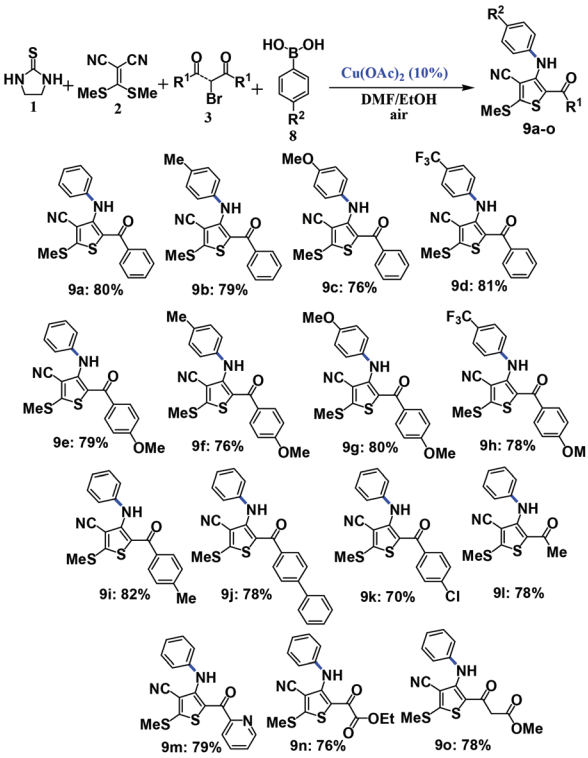
Next, we were interested to see whether the *N*-functionalization of the amino-2 (methylthio)thiophenes can have an impact on the applicability of this reaction. Therefore, we first established an *N*-arylation reaction. Accordingly, among the various conditions tested to manage the *N*-arylation of the substrate with $PhB(OH)_2$ (Table S1 in the ESI†), an efficient four-component reaction was selected (Table 3).

As seen in Table 3, a variety of *N*-aryl thiophenes **9a–o** were obtained in good yields. The reaction is prominent in terms of the simultaneous presence of catalytic, ligand-and base-free conditions for NH_2 (heteroaryl)–C(boronic acid) coupling. The electronic nature of $ArB(OH)_2$ and α-bromoketones showed to have little effect on the reactivity of the substrates. The presence of a pyridine moiety in **9m** as a strong metal coordinator did not interfere with the reaction system.[6] Major drawbacks were encountered when α-haloketones containing esters and indoles were employed. In these cases, several modifications, such as adding a base or using excessive amounts of $Cu(OAc)_2$ and $ArB(OH)_2$ were made. However, these modifications were unfruitful, and only the starting materials were recovered.

Then, the capability of the *N*-arylated thiophenes in homo-coupling reaction was examined. 2-Bromoacetophenone was maintained as a constant, and $ArB(OH)_2$, containing both electron-donating and electron-withdrawing groups, was changed (Table 4). As seen in Table 4, $PhB(OH)_2$ and its electron donating derivatives were smoothly involved in the reaction (**10a–c**), while $ArB(OH)_2$, containing an electron withdrawing CF_3 group did not undergo the desired reaction and only the *N*-arylated adduct was obtained. This observation revealed the significance of the electronic nature of $ArB(OH)_2$ on the applicability of this reaction. The structure of **10a** was unambiguously confirmed by X-ray crystallography analysis (Fig. 2).

To gain further knowledge on the mechanism of these reactions, several controlling experiments were designed (Scheme 2). First, to probe the effects of carbonyl and cyanide, as *ortho*-directing groups, on the syntheses of **4** and **9**, we simulated the reactivity template of thiophene functional groups by employing pyrazole **11**. Interestingly, among the different functional groups in C[4], only the pyrazole compound that contained the CN group successfully responded to the homocoupling reaction by affording **6** with 71% yield (Scheme 2, entry 1). Also, when the CN functional group was replaced by $CONH_2$ in thiophene **12**, the desired homo-coupling reaction did not take place (Scheme 2, entry 2). The results so far indicate the critical role of CN in the synthesis of **4** as a directing group (entries 1 and 2). Then, the effect of the carbonyl group on the *N*-arylation reaction was investigated. Unlike thiophenes, pyrazoles that lack a C=O group did not bear any reaction with $PhB(OH)_2$ (entry 3). Therefore, it was found that the carbonyl group is necessary for the *N*-arylation

Table 3 Scope of the *N*-arylation reaction[a]



[a] Reaction conditions: After execution the required conditions for synthesis of thiophene (as for **4a** in Table 1): $ArB(OH)_2$ (2 eq.) and $Cu(OAc)_2$ (10 mol%) at 70 °C in air for 1 h.

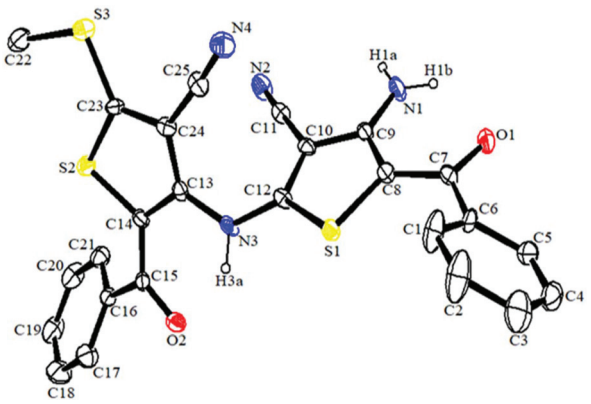
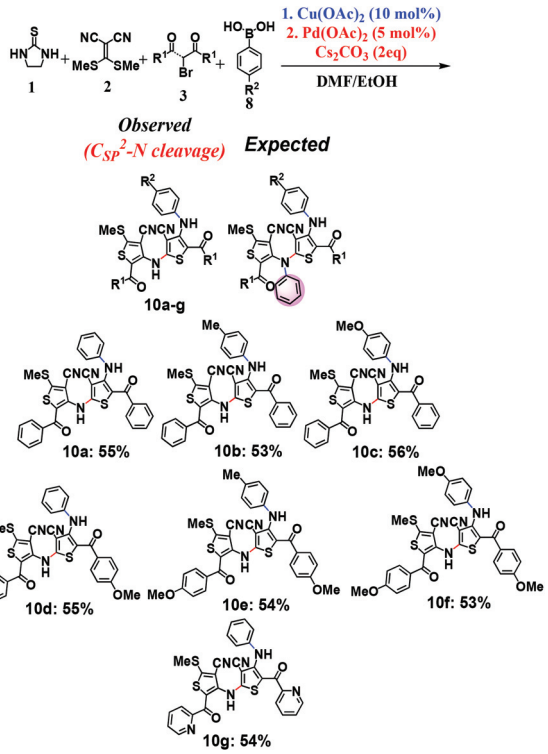


Fig. 1 Ortep diagram of compound **4a**.

Table 4 Domino *N*-arylation/homocoupling reaction[a]



[a] Reaction conditions: After execution the required conditions for synthesis of **9** (see Tables 1 and 4): $Pd(OAc)_2$ (5 mol%) and Cs_2CO_3 (2 eq.) at 80 °C for 1 h.

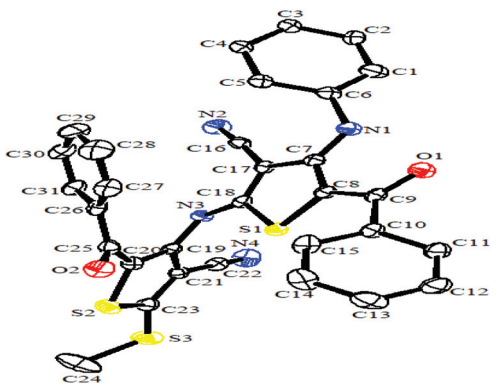
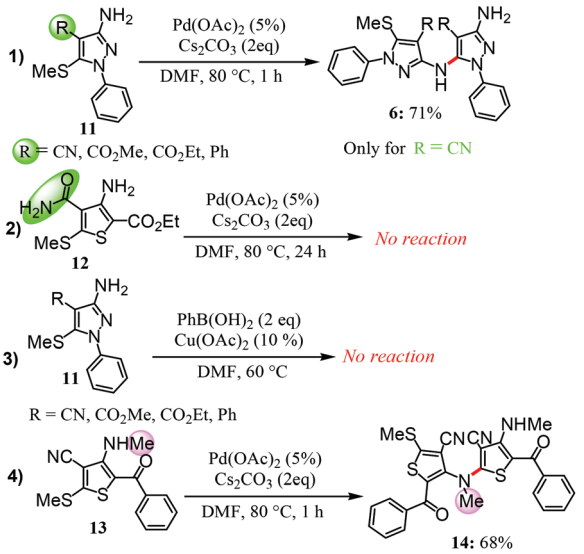
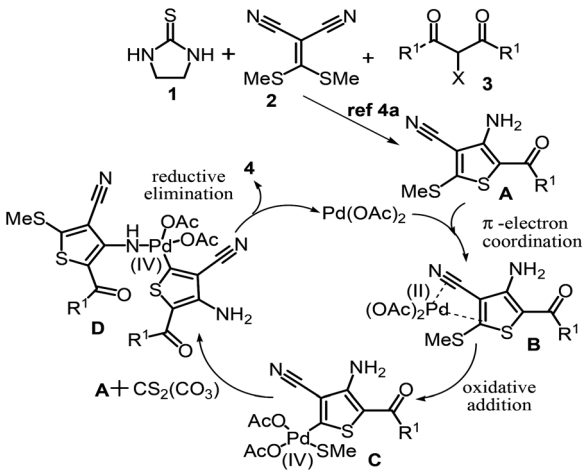


Fig. 2 Ortep diagram of compound **10a**.



Scheme 2 Control experiments.

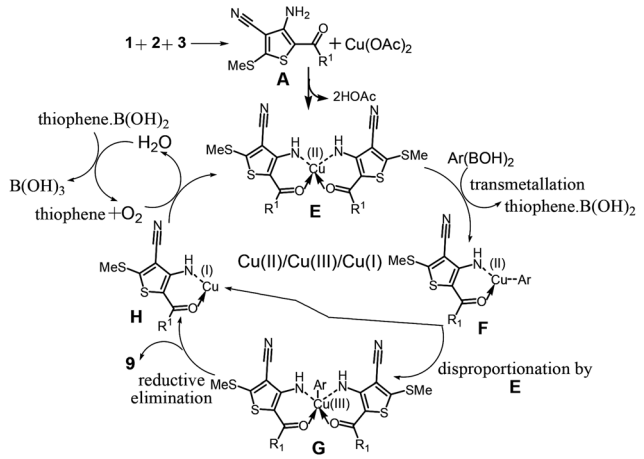


Scheme 3 Proposed mechanism for the synthesis of **4**.

reaction. In contrast to the reactivity of *N*-arylated thiophenes, the *N*-methylated thiophene **13** did not bear the C–N bond cleavage in the nitrogen that bridged between the two thiophene units (entry 4). This observation disclosed the mechanistic clues for the C_{sp^2}–N bond cleavage in **10** series.

Based on these findings, the proposed mechanism for the synthesis of **4** is depicted in Scheme 3. The *in situ* generated thiophene **A** involves the π-electron coordination of an anchoring cyanide group with $Pd(OAc)_2$ to produce palladacycle **B**.[7] The alternative end-on *n*-electron coordination scenario is ruled out, due to the formation of the strained cyclic transition state.[8] Next, the proximity-driven reactivity, prepared by the π-electron coordination of CN, ensures the regioselective oxidative-addition of C_{sp^2}–SMe to Pd(II) (**B**), which generates Pd(IV)[9] **C**. Subsequently, in the presence of CS_2CO_3 the *N*-coordination of the second thiophene to the Pd(IV) complex leads to **D**. Finally, the transient Pd(IV) **D** undergoes the reductive elimination to give **4**, along with the regeneration of Pd(II) species.

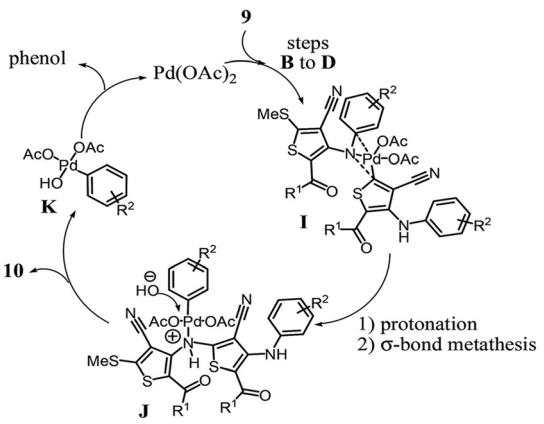
According to the mentioned control experiments and spectroscopic analyses (see in the ESI†), the rationalization for the synthesis of **9** is illustrated in Scheme 4. Accordingly, the first step involves a rapid coordination and dissolution of $Cu(OAc)_2$ by an α-carbonyl chelating effect of **A** to produce $Cu^{II}(thiophene)_2$ (**E**).[10] Next, the transmetalation of an aryl group from $ArB(OH)_2$ to **E** delivers $Cu^{II}(thiophene)(Ar)$ (**F**)



Scheme 4 Proposed mechanism for the synthesis of **9**.

along with thiophene-B(OH)$_2$. Then, **F** undergoes disproportionation by another equiv. of **E** to generate Cu^{III}(thiophene)$_2$(Ar) (**G**) and Cu^{I}(thiophene)(Ar) (**H**). The intermediate **G** readily undergoes facile reductive elimination to afford **5** along with another equiv. of **H**. Finally, in the presence of air, **E** is recycled through oxidative copper amination.[11] It is believed that thiophene can be injected into the cycle either by the incoming unreacted species or regeneration from the thiophene-B(OH)$_2$ species in the presence of water.[12]

Regarding the mechanism of **10**, the afforded *N*-arylated adduct **9** underwent the steps **B–D** (according to Scheme 3) to generate **I** (Scheme 5). It is assumed that the primary protonation of a tertiary amine in **I** may facilitate the concerted oxidative addition of C_{sp^2}–N to metal.[13] The process is followed by σ-bond metathesis[14] leading to **J**. Next, ligand exchange by an hydroxide ion affords target molecule **10** along with **K**. Complex **K** following the reductive elimination recycles Pd(II) species. The presence of phenol species as side-products was confirmed by spectroscopic analysis. The tendency of the electron-deficient Pd(IV) complex to undergo oxidative addition to the electron-rich bond (C_{aryl}–N) (steps **I** to **J**) could be



Scheme 5 Proposed mechanism for the synthesis of **10**.

considered a driving force for cleavage of the unreactive C_{sp^2}–N bond in the products **10**. This assumption was further reinforced by looking at the *N*-methylated thiophene product **13** (Scheme 2, entry 4), where involving the electron-poor C_{methyl}–N bond did not conclude the C_{sp^3}–N bond cleavage (see product **14**).

Conclusions

In summary, we devised an unprecedented pattern of reactivity, namely the C–N homocoupling in metal catalysis organic transformations where NH_2/CN/SMe functional groups are arranged next to one another. To the best of our knowledge, this ligandless transformation is the first catalytic conversion of C(heteroaryl)–S into C(heteroaryl)–N.[15] Moreover, this is the first example of CN-directed C–heteroatom bond activation. The bidentate *N*,*O*-chelation of the substrate avoids using a base, ligand, and other additives that are routinely used in CEL couplings, and, most importantly, it underpins the *de novo* design of new methods for copper-catalyzed C–N cross-coupling reactions.

Experimental

General information

Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were recorded using KBr pellets on a NICOLET FT-IR 100 spectrometer. ^{1}H NMR (300 and 500 MHz) and ^{13}C NMR (75 and 100 MHz) spectra were obtained using Bruker DRX-300 AVANCE and Bruker DRX-500 AVANCE spectrometers. All NMR spectra at room temperature were recorded in $CDCl_3$ and DMSO-d_6. Chemical shifts are reported in parts per million (δ) downfield from an internal tetramethylsilane reference. Coupling constants (*J* values) are reported in hertz (Hz), and spin multiplicities are indicated by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Elemental analyses of C, H and N were performed using a Heraeus CHN–O–Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. All chemicals were purchased from Merck or Aldrich and were used without further purification. Due to the very low solubility of the product **9h**, no ^{13}C NMR data were obtained for this product.

Experimental procedures and spectroscopic data for 4a–l

To a solution of 2-imidazolinethione **1** (0.025 g, 0.25 mmol) in DMF (1.0 mL) was added 2-di(methylsulfanyl)methylene malononitrile **2** (0.042 g, 0.25 mmol). The reaction mixture was stirred for three hours at 120 °C. Afterwards α-haloketones **3** (equivalent to the *in situ* generated thiolate anion, 0.14 mmol) and EtOH (1.0 mL) were added and the reaction mixture was stirred for another 20 min at room temperature. To this solution were added $Pd(OAc)_2$ (0.0016 g, 0.05 mmol) and CS_2CO_3 (0.163 g, 0.5 mmol). The reaction mixture was

heated to 80 °C for 1 h, and allowed to cool to room temperature. Then, the mixture was poured into water and extracted with chloroform. The combined organic layer after drying over magnesium sulfate was purified by silica gel flash chromatography (hexane : ethyl acetate = 3 : 1) to afford the desired adducts **4a–l**.

4-Amino-5-benzoyl-2-(2-benzoyl-4-cyano-5-methylsulfanyl-3-thienylamino)-3-thiophenecarbonitrile (4a). Yellow powder, mp: 173–174 °C, 0.055 g, yield: 79%. IR (KBr)(ν_{max}, cm^{-1}): 3423, 3313 (NH_2), 3190 (NH), 2216 (CN), 1604 (C═O), 1538 and 1451 (C═C). Anal. calcd for $C_{25}H_{16}N_4O_2S_3$ (500.61): C, 59.98; H, 3.22; N, 11.19%. Found C, 59.88; H, 3.15; N, 11.18. ^{1}H NMR (300 MHz, $CDCl_3$): 2.71 (3H, s, SMe), 6.91 (2H, brs, NH_2), 7.48 (1H, t, $^3J_{HH}$ = 6.9 Hz, CH_{para} of ph), 7.54 (4H, t, $^3J_{HH}$ = 7.5 Hz, $4CH_{meta}$ of Ph), 7.65 (1H, t, $^3J_{HH}$ = 6.9 Hz, CH_{para} of Ph), 7.77 (2H, d, $^3J_{HH}$ = 7.2 Hz, CH_{ortho} of Ph), 7.82 (2H, d, $^3J_{HH}$ = 7.5 Hz, CH_{ortho} of Ph), 10.56 (1H, s, NH). ^{13}C NMR (75.0 MHz, $CDCl_3$): 17.6, 93.5, 100.8, 102.3, 111.4, 111.9, 116.6, 127.7, 128.2, 128.5, 128.9, 131.4, 132.9, 138.3, 139.9, 148.7, 154.2, 157.5, 163.1, 187.4, 187.8. MS (EI, 70 eV): 500 (M^+, 14), 453 (5), 395 (6), 324 (8), 273 (6), 211 (5), 155 (7), 105 (100), 77 (84). Crystal data for **4a** $C_{25}H_{16}N_4O_2S_3$ (CCDC 1551355†): M_W = 500.63, triclinic, $P\bar{1}$, a = 6.4503(16) Å, b = 12.709(3) Å, c = 16.510(4) Å, α = 80.068(19), β = 88.626(19), γ = 82.085(19), V = 1320.4(5) Å^3, Z = 2, D_c = 1.259 mg m^{-3}, F(000) = 516, MoKα (λ = 0.71073 Å), intensity data were collected at 298(2) K with a STOE IPDS-II diffractometer with graphite monochromated radiation, and employing the $\omega/2\theta$ scanning technique, in the range of $-8 \le h \le 7$, $-16 \le k \le 14$, and $-21 \le l \le 21$; the structure was solved by direct methods, and all non-hydrogen atoms were positioned and anisotropic thermal parameters were refined from 5763 observed reflections with R(int) = 0.3047 by a full-matrix least-squares technique converged to R = 0.1350 and wR_2 = 0.2636 [$I > 2\sigma(I)$].

4-Amino-2-[4-cyano-2-(4-methylbenzoyl)-5-methylsulfanyl-3-thienylamino]-5-(4-methylbenzoyl)-3-thiophenecarbonitrile (4b). Red powder, mp: 115–116 °C, 0.057 g, yield: 77%. IR (KBr) (ν_{max}, cm^{-1}): 3416, 3304 (NH_2), 3185 (NH), 2216 (CN), 1595 (C═O), 1558 and 1451 (C═C). Anal. calcd for $C_{27}H_{20}N_4O_2S_3$ (528.66): C, 61.34; H, 3.81; N, 10.60%. Found C, 61.30; H, 3.86; N, 10.58. ^{1}H NMR (300 MHz, $CDCl_3$): 2.42 (3H, s, Me), 2.47 (3H, s, Me), 2.70 (3H, s, SMe), 6.86 (2H, brs, NH_2), 7.27 (2H, d, $^3J_{HH}$ = 6.9 Hz, 2CH of Ar), 7.34 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH of Ar), 7.67 (2H, d, $^3J_{HH}$ = 8.1 Hz, CH_{ortho} of Ar), 7.73 (2H, d, $^3J_{HH}$ = 8.1 Hz, CH_{ortho} of Ar), 10.54 (1H, s, NH). ^{13}C NMR (75.0 MHz, $CDCl_3$): 17.6, 21.6, 21.7, 93.1, 101.0, 102.1, 111.5, 112.0, 116.9, 127.8, 128.4, 129.2, 129.5, 135.6, 137.2, 142.0, 143.9, 148.4, 154.1, 157.6, 162.6, 187.2, 187.7. MS (EI, 70 eV): 528 (M^+, 6), 482 (7), 424 (6), 364 (8), 319 (19), 373 (28), 287 (17), 218 (19), 91 (84).

4-[4-Amino-3-cyano-5-(4-methoxybenzoyl)-2-thienylamino]-5-(4-methoxybenzoyl)-2-methylsulfanyl-3-thiophenecarbonitrile (4c). Red powder, mp: 125–126 °C, 0.055 g, yield: 70%. IR (KBr) (ν_{max}, cm^{-1}): 3426, 3310 (NH_2), 3196 (NH), 2215 (CN), 1602 (C═O), 1541 and 1451 (C═C). Anal. calcd for $C_{27}H_{20}N_4O_4S_3$ (560.66): C, 57.64; H, 3.60; N, 9.99%. Found C, 57.61; H, 3.66; N, 10.05. ^{1}H NMR (300 MHz, $CDCl_3$): 2.70 (3H, s, SMe), 3.86 (3H, s, OMe), 3.90 (3H, s, OMe), 6.88 (2H, brs, NH_2), 6.94 (2H, d, $^3J_{HH}$ = 8.4 Hz, CH of Ar), 6.99 (2H, d, $^3J_{HH}$ = 8.4 Hz, CH of Ar), 7.74 (2H, d, $^3J_{HH}$ = 8.1 Hz, CH of Ar), 7.82 (2H, d, $^3J_{HH}$ = 8.1 Hz, CH of Ar), 10.52 (1H, s, NH). ^{13}C NMR (75.0 MHz, $CDCl_3$): 17.6, 55.4, 55.6, 91.6, 101.1, 101.8, 111.6, 112.2, 113.7, 114.1, 118.7, 129.8, 130.4, 130.7, 132.5, 147.2, 154.3, 158.5, 162.1, 162.7, 163.5, 185.9, 186.6. MS (EI, 70 eV): 560 (M^+, 13), 500 (9), 460 (5), 451 (11), 366 (6), 303 (5), 275 (3), 231 (4), 191 (10), 150 (21), 135 (60), 105 (100), 77 (95).

4-[4-Amino-3-cyano-5-(4-phenylbenzoyl)-2-thienylamino]-2-methylsulfanyl-5-(4-phenylbenzoyl)-3-thiophenecarbonitrile (4d). Red powder, mp: 276–277 °C, 0.072 g, yield: 79%. IR (KBr) (ν_{max}, cm^{-1}): 3420, 3300 (NH_2), 3185 (NH), 2218 (CN), 1600 (C═O), 1552 and 1451 (C═C). Anal. calcd for $C_{37}H_{24}N_4O_2S_3$ (652.80): C, 68.08; H, 3.71; N, 8.58%. Found C, 68.05; H, 3.80; N, 8.52. ^{1}H NMR (300 MHz, DMSO-d_6): 2.82 (3H, s, SMe), 7.41 (1H, t, $^3J_{HH}$ = 7.8 Hz, CH_{para} of Ph), 7.49 (4H, t, $^3J_{HH}$ = 6.9 Hz, $4CH_{meta}$ of Ph), 7.56 (2H, d, $^3J_{HH}$ = 8.7 Hz, $2CH_{ortho}$ of Ph), 7.62 (1H, t, $^3J_{HH}$ = 7.5 Hz, CH_{para} of Ph), 7.67 (2H, d, $^3J_{HH}$ = 7.5 Hz, $2CH_{ortho}$ of Ph), 7.74 (4H, d, $^3J_{HH}$ = 9 Hz, 4CH of Ar), 7.79 (4H, d, $^3J_{HH}$ = 8.4 Hz, 4CH of Ar), 7.93 (2H, brs, NH_2), 10.93 (1H, brs, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.6, 82.6, 95.6, 105.1, 112.6, 112.8, 127.0, 127.2, 127.5, 128.0, 128.5, 128.9, 129.5, 129.6, 135.7, 139.3, 139.4, 139.6, 142.7, 144.9, 157.2, 161.1, 165.2, 185.3. MS (EI, 70 eV): 652 (M^+, 11), 647 (16), 591 (5), 535 (7), 489 (6), 443 (7), 367 (5), 316 (27), 253 (10), 191 (21), 147 (15), 119 (13), 105 (12), 95 (20), 57 (100).

4-Amino-5-(4-chlorobenzoyl)-2-[2-(4-chlorobenzoyl)-4-cyano-5-methylsulfanyl-3-thienylamino]-3-thiophenecarbonitrile (4e). Yellow powder, mp: 214–215 °C, 0.060 g, yield: 76%. IR (KBr) (ν_{max}, cm^{-1}): 3415, 3302 (NH_2, NH), 2213 (CN), 1603 (C═O), 1535 and 1446 (C═C). Anal. calcd for $C_{25}H_{14}Cl_2N_4O_2S_3$ (569.49): C, 52.73; H, 2.48; N, 9.84%. Found C, 52.75; H, 2.44; N, 9.79. ^{1}H NMR (300 MHz, DMSO-d_6): 2.82 (3H, s, SMe), 7.53–7.55 (6H, m, CH of Ar), 7.63 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH of Ar), 7.98 (2H, brs, NH_2), 10.95 (1H, brs, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.5, 82.5, 82.5, 95.4, 104.9, 112.5, 112.7, 129.1, 129.1, 129.2, 130.6, 135.6, 135.9, 138.3, 139.5, 157.3, 161.7, 165.1, 184.7. MS (EI, 70 eV): 569 (M^+, 6), 568 (5), 522 (7), 476 (6), 429 (8), 357 (5), 307 (14), 261 (7), 197 (5), 139 (100), 134 (34), 119 (62), 91 (29), 75 (17).

4-Amino-5-(4-bromobenzoyl)-2-[2-(4-bromobenzoyl)-4-cyano-5-methylsulfanyl-3-thienylamino]-3-thiophenecarbonitrile (4f). Yellow powder, mp: 138–139 °C, 0.075 g, yield: 81%. IR (KBr) (ν_{max}, cm^{-1}): 3412, 3310 (NH_2), 3195 (NH), 2217 (CN), 1587 (C═O), 1555 and 1447 (C═C). Anal. calcd for $C_{25}H_{14}Br_2N_4O_2S_3$ (658.40): C, 45.61; H, 2.14; N, 8.51%. Found C, 45.60; H, 2.12; N, 8.52. ^{1}H NMR (300 MHz, DMSO-d_6): 2.81 (3H, s, SMe), 7.46 (2H, d, $^3J_{HH}$ = 9.9 Hz, CH_{ortho} of Ar), 7.55 (2H, d, $^3J_{HH}$ = 8.1 Hz, CH of Ar), 7.66 (2H, d, $^3J_{HH}$ = 6.6 Hz, CH of Ar), 7.68 (2H, d, $^3J_{HH}$ = 8.1 Hz, CH of Ar), 7.98 (2H, brs, NH_2), 10.95 (1H, brs, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.5, 82.5, 89.8, 95.4, 104.9, 112.5, 124.8, 127.4, 129.3, 130.6, 132.0, 132.1, 136.0, 139.8, 157.3, 157.3, 161.7, 165.1, 184.8. MS (EI, 70 eV): 658 (M^+, 11), 613 (6), 568 (12), 522 (5), 475 (6), 429

(7), 351 (5), 273 (7), 185 (100), 155 (71), 139 (97), 91 (67), 75 (37).

4-Amino-2-[4-cyano-2-(4-iodobenzoyl)-5-methylsulfanyl-3-thienylamino]-5-(4-iodobenzoyl)-3-thiophenecarbonitrile (4g). Red powder, mp: 204–205 °C, 0.084 g, yield: 80%. IR (KBr) (ν_{max}, cm^{-1}): 3462, 3290 (NH_2, NH), 2212 (CN), 1578 (C═O), 1508 and 1452 (C═C). Anal. calcd for $C_{25}H_{14}I_2N_4O_2S_3$ (752.40): C, 39.91; H, 1.88; N, 7.44%. Found C, 39.88; H, 1.94; N, 7.39. ^{1}H NMR (300 MHz, DMSO-d_6): 2.82 (3H, s, SMe), 7.31 (2H, d, $^3J_{HH}$ = 7.2 Hz, CH of Ar), 7.39 (2H, d, $^3J_{HH}$ = 7.5 Hz, CH of Ar), 7.84 (2H, d, $^3J_{HH}$ = 6.6 Hz, CH of Ar), 7.86 (2H, d, $^3J_{HH}$ = 7.2 Hz, CH of Ar), 7.95 (2H, brs, NH_2), 10.90 (1H, brs, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.5, 79.7, 82.5, 95.4, 98.6, 101.8, 105.0, 112.4, 129.2, 130.3, 136.3, 137.8, 137.9, 140.1, 157.2, 157.3, 161.5, 165.0, 185.1. MS (EI, 70 eV): 752 (M^+, 5), 647 (16), 568 (12), 467 (6), 399 (19), 316 (21), 250 (23), 231 (39), 203 (22), 139 (100), 111 (20), 77 (28).

5-Acetyl-4-(5-acetyl-4-amino-3-cyano-2-thienylamino)-2-methylsulfanyl-3-thiophenecarbonitrile (4h). Red powder, mp: 231–232 °C, 0.041 g, yield: 78%. IR (KBr)(ν_{max}, cm^{-1}): 3429, 3320 (NH_2, NH), 2217 (CN), 1620 (C═O), 1601 (C═O), 1554 and 1460 (C═C). Anal. calcd for $C_{15}H_{12}N_4O_2S_3$ (376.46): C, 47.86; H, 3.21; N, 14.88%. Found C, 47.91; H, 3.16; N, 14.77. ^{1}H NMR (300 MHz, DMSO-d_6): 2.01 (3H, s, Me), 2.44 (3H, s, Me), 2.81 (3H, s, SMe), 7.65 (2H, brs, NH_2), 10.89 (1H, brs, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.5, 28.5, 82.0, 94.8, 96.9, 105.6, 112.4, 113.3, 153.4, 154.7, 161.2, 163.3, 188.4. MS (EI, 70 eV): 376 (M^+, 100), 319 (16), 299 (12), 264 (7), 239 (12), 212 (11), 197 (26), 139 (6), 94 (24).

Methyl 3-(4-amino-3-cyano-5-methyloxycarbonyl-2-thienylamino)-4-cyano-5-methylsulfanyl-2-thiophenecarboxylate (4i). Yellow powder, mp: 217–218 °C, 0.043 g, yield: 75%. IR (KBr) (ν_{max}, cm^{-1}): 3428, 3335 (NH_2, NH), 3250 (NH), 2215 (CN), 16 800 (C═O), 1621 (C═O), 1590 and 1437 (C═C). Anal. calcd for $C_{15}H_{12}N_4O_4S_3$ (408.46): C, 44.11; H, 2.96; N, 13.72%. Found C, 44.09; H, 2.95; N, 13.72. ^{1}H NMR (300 MHz, $CDCl_3$): 2.72 (3H, s, SMe), 3.82 (3H, s, OMe), 3.92 (3H, s, OMe), 5.86 (2H, s, NH_2), 8.78 (1H, s, NH). ^{13}C NMR (75.0 MHz, $CDCl_3$): 17.4, 51.5, 53.1, 83.8, 104.9, 107.2, 112.3, 113.2, 119.2, 143.3, 154.0, 159.5, 159.9, 162.7, 163.5. MS (EI, 70 eV): 408 (M^+, 17), 376 (24), 348 (12), 308 (29), 226 (55), 181 (44), 137 (100), 90 (44), 59 (77).

Ethyl 3-(4-amino-3-cyano-5-ethyloxycarbonyl-2-thienylamino)-4-cyano-5-methylsulfanyl-2-thiophenecarboxylate (4j). Yellow powder, mp: 209–210 °C, 0.047 g, yield: 77%. IR (KBr) (ν_{max}, cm^{-1}): 3446, 3340 (NH_2), 3243 (NH), 2218 (CN), 1685 (C═O), 1668 (C═O), 1616 and 1563 (C═C). Anal. calcd for $C_{17}H_{16}N_4O_4S_3$ (436.52): C, 46.78; H, 3.69; N, 12.83%. Found C, 46.89; H, 3.58; N, 12.81. ^{1}H NMR (300 MHz, $CDCl_3$): 1.34 (3H, t, $^3J_{HH}$ = 7.2 Hz, OCH_2CH_3), 1.40 (3H, t, $^3J_{HH}$ = 7.2 Hz, OCH_2CH_3), 2.72 (3H, s, SMe), 4.28 (2H, q, $^3J_{HH}$ = 6.9 Hz, OCH_2CH_3), 4.38 (2H, q, $^3J_{HH}$ = 6.9 Hz, OCH_2CH_3), 5.84 (2H, brs, NH_2), 8.80 (1H, s, NH). ^{13}C NMR (75.0 MHz, $CDCl_3$): 14.3, 14.4, 17.6, 60.6, 61.9, 85.8, 93.0, 101.1, 109.4, 111.5, 112.1, 147.0, 156.6, 160.6, 162.0, 163.4. MS (EI, 70 eV): 436 (M^+, 14), 390 (100), 344 (11), 316 (9), 290 (7), 273 (9), 214 (11), 197 (13), 149 (14), 138 (27), 78 (71).

4-[4-Amino-3-cyano-5-(2-pyridylcarbonyl)-2-thienylamino]-2-methylsulfanyl-5-(2-pyridylcarbonyl)-3-thiophenecarbonitrile (4k). Red powder, mp: 268–269 °C, 0.056 g, yield: 80%. IR (KBr) (ν_{max}, cm^{-1}): 3378, 3278 (NH_2, NH), 2215 (CN), 1601 (C═O), 1578 (C═O), 1544 and 1448 (C═C). Anal. calcd for $C_{23}H_{14}N_6O_2S_3$ (502.58): C, 54.97; H, 2.81; N, 16.72%. Found C, 54.95; H, 2.84; N, 16.72. ^{1}H NMR (300 MHz, DMSO-d_6): 2.84 (3H, s, SMe), 7.57 (1H, d, $^3J_{HH}$ = 4.1 Hz, CH^3 of Py), 7.71 (1H, d, $^3J_{HH}$ = 5.1 Hz, CH^3 of Py), 8.01 (1H, t, $^3J_{HH}$ = 7.2 Hz, CH^5 of Py), 8.05 (1H, t, $^3J_{HH}$ = 7.5 Hz, CH^5 of Py), 8.09–8.11 (2H, m, $2CH^4$ of Py), 8.62 (1H, s, CH^6 of Py), 8.79 (1H, s, CH^6 of Py), 11.17 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 16.9, 83.7, 95.2, 103.1, 112.6, 113.3, 121.1, 126.8, 128.5, 138.9, 139.0, 146.5, 148.3, 152.2, 154.0, 159.6, 164.7, 166.8, 179.4, 179.9. MS (EI, 70 eV): 502 (M^+, 14), 469 (6), 441 (7), 396 (15), 368 (8), 332 (7), 297 (5), 269 (6), 259 (6), 200 (8), 139 (6), 119 (31), 78 (100).

4-[4-Amino-3-cyano-5-(1*H*-3-indolylcarbonyl)-2-thienylamino]-5-(1*H*-3-indolylcarbonyl)-2-methylsulfanyl-3-thiophenecarbonitrile (4l). Red powder, mp: 130–131 °C, 0.057 g, yield: 71%. IR (KBr)(ν_{max}, cm^{-1}): 3249, 3303 (NH_2, NH), 2207 (CN), 1638 (C═O), 1606 (C═O), 1558 and 1448 (C═C). Anal. calcd for $C_{29}H_{18}N_6O_2S_3$ (578.68): C, 60.19; H, 3.14; N, 14.52%. Found C, 60.27; H, 3.07; N, 14.44. ^{1}H NMR (300 MHz, DMSO-d_6): 2.70 (3H, s, SMe), 6.69 (2H, brs, NH_2), 7.05 (1H, brs, NH of indole), 7.19–7.28 (4H, m, CH of Ar), 7.46 (1H, brs, NH of indole), 7.61 (1H, d, $^3J_{HH}$ = 7.5 Hz, CH of Ar), 7.74–7.77 (4H, m, CH of Ar), 7.93 (1H, d, $^3J_{HH}$ = 7.5 Hz, CH of Ar), 10.85 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.6, 94.8, 98.9, 102.2, 102.7, 106.8, 109.7, 113.1, 113.1, 113.6, 114.9, 117.1, 118.1, 120.8, 121.3, 122.6, 123.9, 124.6, 124.6, 125.7, 125.7, 126.3, 129.7, 132.6, 136.4, 154.7, 162.0, 162.4, 166.2, 170.4, 172.3. MS (EI, 70 eV): 575 (5), 592 (6), 438 (5), 366 (21), 303 (7), 242 (12), 197 (100), 170 (26), 142 (29), 117 (31), 94 (19), 89 (27).

Experimental procedures and spectroscopic data for 6

A solution of 2-di(methylsulfanyl)methylene malononitrile **2** (0.043 g, 0.25 mmol) and phenylhydrazine **5** (0.027 g, 0.25 mmol) in 1 mL of MeOH was refluxed for 3 h. Then, $Pd(OAc)_2$ (0.0016 g, 0.05 mmol), CS_2CO_3 (0.163 g, 0.5 mmol), and DMF (1 mL) were added to this solution. The reaction mixture was heated to 80 °C for 1 h, and allowed to cool to room temperature. Then, the mixture was poured into water and extracted with ethyl acetate. The combined organic layer after drying over magnesium sulfate was purified by silica gel flash chromatography (hexane : ethyl acetate = 3 : 1) to afford the desired adduct **6**.

3-(3-Amino-4-cyano-1-phenyl-1*H*-5-pyrazolylamino)-5-methylsulfanyl-1-phenyl-1*H*-4-pyrazolecarbonitrile (6). White powder, mp: 195–196 °C, 0.073 g, yield: 71%. IR (KBr)(ν_{max}, cm^{-1}). Anal. calcd for $C_{21}H_{16}N_8S$ (412.47): C, 61.15; H, 3.91; N, 27.17%. Found C, 61.02; H, 3.98; N, 27.19. ^{1}H NMR (300 MHz, DMSO-d_6): 2.72 (3H, s, SMe), 7.06 (2H, brs, NH_2), 7.29 (1H, t, $^3J_{HH}$ = 7.5 Hz, CH of Ph), 7.38 (1H, t, $^3J_{HH}$ = 7.2 Hz, CH of Ph), 7.52–7.57 (5H, m, 4CH of Ph and 1H of NH), 7.65 (2H, d, $^3J_{HH}$ = 7.5 Hz, CH of Ph), 8.48 (2H, d, $^3J_{HH}$ = 7.8 Hz, CH of Ph). ^{13}C NMR (75.0 MHz, DMSO-d_6): 14.8, 97.4, 99.4, 120.3, 123.7,

125.7, 127.2, 129.4, 129.4, 139.0, 139.4, 142.2, 148.6, 150.1, 155.3, 157.4, 160.6. MS (EI, 70 eV): 412 (M^+, 7), 339 (19), 275 (8), 230 (16), 184 (14), 134 (12), 105 (82), 77 (100).

Experimental procedures and spectroscopic data for 9a–o

After implementing the required conditions for the preparation of thiophene (as for **4**), arylboronic acid (2 eq.: 0.5 mmol) and $Cu(OAc)_2$ (0.005 g, 0.1 mmol) were added to the mixture. The reaction mixture was stirred for 1 h at 70 °C under open-flask conditions. After that, the reaction mixture was poured into water and the resulting precipitates were filtered. The obtained solid after dissolving in acetone was passed through a thin pad of Celite on sintered glass. The residue after evaporation of the solvent was further purified by washing with ether to afford the desired adducts **9a–o**.

4-Anilino-5-benzoyl-2-methylsulfanyl-3-thienyl cyanide (9a). Yellow powder, mp: 110–111 °C, 0.039 g, yield: 80%. IR (KBr) (ν_{max}, cm^{-1}): 3429 (NH), 2209 (CN), 1585 (C═O), 1544 and 1443 (C═C). Anal. calcd for $C_{19}H_{14}N_2OS_2$ (350.45): C, 65.12; H, 4.03; N, 7.99%. Found C, 65.14; H, 4.03; N, 7.98. ^{1}H NMR (300 MHz, DMSO-d_6): 2.72 (3H, s, SMe), 7.19 (1H, t, $^3J_{HH}$ = 7.2 Hz, CH_{para} of Ph), 7.25 (2H, d, $^3J_{HH}$ = 7.2 Hz, $2CH_{ortho}$ of Ph), 7.36 (2H, t, $^3J_{HH}$ = 7.8 Hz, $2CH_{meta}$ of Ph), 7.53 (2H, t, $^3J_{HH}$ = 7.5 Hz, $2CH_{meta}$ of Ph), 7.61 (1H, t, $^3J_{HH}$ = 7.2 Hz, CH_{para} of Ph), 7.75 (2H, d, $^3J_{HH}$ = 7.2 Hz, $2CH_{ortho}$ of Ph), 10.22 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.1, 98.5, 112.3, 112.4, 123.6, 125.6, 128.0, 129.1, 129.4, 132.2, 139.7, 139.8, 152.3, 171.0, 186.4. MS (EI, 70 eV): 349 (M^+ − 1, 100), 283 (7), 234 (18), 203 (19), 171 (38), 149 (41), 121 (52), 77 (84).

5-Benzoyl-2-methylsulfanyl-4-(4-toluidino)-3-thienyl cyanide (9b). Yellow powder, mp: 184–185 °C, 0.040 g, yield: 80%. IR (KBr)(ν_{max}, cm^{-1}): 3396 (NH), 2209 (CN), 1584 (C═O), 1563 and 1364 (C═C). Anal. calcd for $C_{20}H_{16}N_2OS_2$ (364.48): C, 65.91; H, 4.42; N, 7.69%. Found C, 65.96; H, 4.47; N, 7.66. ^{1}H NMR (300 MHz, DMSO-d_6): 2.31 (3H, s, Me), 2.71 (3H, s, SMe), 7.18–7.20 (5H, m, CH of Ar and Ph), 7.54–7.61 (3H, m, CH of Ar), 7.68 (2H, d, $^3J_{HH}$ = 6.9 Hz, $2CH_{ortho}$ of Ph), 10.29 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.0, 21.0, 97.8, 111.0, 112.3, 124.3, 127.9, 129.1, 129.9, 132.1, 135.4, 136.8, 138.9, 140.0, 153.2, 186.3. MS (EI, 70 eV): 363 (M^+ − 1, 52), 317 (5), 272 (7), 243 (6), 212 (15), 174 (5), 190 (5), 105 (49), 77 (100).

5-Benzoyl-4-(4-methoxyanilino)-2-methylsulfanyl-3-thienyl cyanide (9c). Yellow powder, mp: 149–150 °C, 0.040 g, yield: 76%. IR (KBr)(ν_{max}, cm^{-1}): 3396 (NH), 2209 (CN), 1588 (C═O), 1562 and 1361 (C═C). Anal. calcd for $C_{20}H_{16}N_2O_2S_2$ (380.48): C, 63.14; H, 4.24; N, 7.36%. Found C, 63.22; H, 4.19; N, 7.47. ^{1}H NMR (300 MHz, DMSO-d_6): 2.70 (3H, s, SMe), 3.78 (3H, s, OMe), 6.95 (2H, d, $^3J_{HH}$ = 8.1 Hz, $2CH_{meta}$ of Ar), 7.28 (2H, d, $^3J_{HH}$ = 7.8 Hz, $2CH_{ortho}$ of Ar), 7.57–7.58 (3H, m, $2CH_{meta}$ of Ar and CH_{para} of Ph), 7.76 (2H, d, $^3J_{HH}$ = 6.9 Hz, $2CH_{ortho}$ of Ph), 10.36 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 16.9, 55.7, 101.8, 112.1, 114.6, 127.4, 127.8, 129.2, 132.0, 137.1, 140.2, 146.0, 154.6, 158.3, 186.1. MS (EI, 70 eV): 380 (M^+, 28), 273 (55), 197 (12), 169 (6), 142 (8), 105 (60), 77 (100).

5-Benzoyl-2-methylsulfanyl-4-(4-trifluoromethylanilino)-3-thienyl cyanide (9d). Pale yellow powder, mp: 160–161 °C, 0.047 g, yield: 81%. IR (KBr)(ν_{max}, cm^{-1}): 3393 (NH), 2215 (CN), 1587 (C═O), 1554 and 1367 (C═C). Anal. calcd for $C_{20}H_{13}F_3N_2OS_2$ (418.45): C, 57.41; H, 3.13; N, 6.69%. Found C, 57.49; H, 3.11; N, 6.65. ^{1}H NMR (300 MHz, DMSO-d_6): 2.77 (3H, s, SMe), 7.16 (2H, d, $^3J_{HH}$ = 7.8 Hz, $2CH_{ortho}$ of Ar), 7.43 (2H, t, $^3J_{HH}$ = 7.2 Hz, $2CH_{meta}$ of Ph), 7.56 (3H, m, $2CH_{meta}$ of Ar and CH_{para} of Ph), 7.68 (2H, d, $^3J_{HH}$ = 7.2 Hz, $2CH_{ortho}$ of Ph), 9.70 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.3, 112.7, 112.7, 119.3, 119.7, 122.9, 123.1, 126.6, 127.5, 128.5, 128.9, 129.1, 131.8, 132.7, 138.8, 145.4, 147.7, 162.5, 186.3. MS (EI, 70 eV): 417 (M^+ − 1, 15), 273 (27), 227 (4), 197 (9), 149 (13), 105 (36), 77 (100).

4-Anilino-5-(4-methoxybenzoyl)-2-methylsulfanyl-3-thienyl cyanide (9e). Dim orange powder, mp: 138–139 °C, 0.042 g, yield: 79%. IR (KBr)(ν_{max}, cm^{-1}): 3409 (NH), 2223 (CN), 1600 (C═O), 1560 (C═C). Anal. calcd for $C_{20}H_{16}N_2O_2S_2$ (380.48): C, 63.14; H, 4.24; N, 7.36%. Found C, 63.15; H, 4.25; N, 7.34. ^{1}H NMR (300 MHz, DMSO-d_6): 2.72 (3H, s, SMe), 3.83 (3H, s, OMe), 7.05 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH of Ar), 7.15 (1H, t, $^3J_{HH}$ = 7.2 Hz, CH_{para} of Ph), 7.21 (2H, d, $^3J_{HH}$ = 7.8 Hz, $2CH_{ortho}$ of Ph), 7.34 (2H, t, $^3J_{HH}$ = 7.5 Hz, $2CH_{meta}$ of Ph), 7.66 (2H, d, $^3J_{HH}$ = 8.4 Hz, 2CH of Ar), 10.14 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.1, 55.9, 99.0, 112.5, 113.0, 114.4, 123.0, 125.2, 129.4, 129.8, 130.4, 132.0, 140.0, 151.6, 162.7, 185.3. MS (EI, 70 eV): 379 (M^+ − 1, 26), 303 (86), 272 (5), 238 (6), 197 (5), 135 (100), 107 (21), 92 (42), 77 (50).

5-(4-Methoxybenzoyl)-2-methylsulfanyl-4-(4-toluidino)-3-thienyl cyanide (9f). Yellow powder, mp: 184–185 °C, 0.042 g, yield: 76%. IR (KBr)(ν_{max}, cm^{-1}): 3220 (NH), 2216 (CN), 1588 (C═O), 1544 and 1413 (C═C). Anal. calcd for $C_{21}H_{18}N_2O_2S_2$ (394.50): C, 63.94; H, 4.60; N, 7.10%. Found C, 63.85; H, 4.53; N, 7.14. ^{1}H NMR (300 MHz, DMSO-d_6): 2.30 (Me), 2.72 (3H, s, SMe), 3.85 (3H, s, OMe), 7.07 (2H, d, $^3J_{HH}$ = 8.7 Hz, 2CH of Ar), 7.13–7.17 (4H, m, $2CH_{meta}$ and $2CH_{ortho}$ of Ar), 7.77 (2H, d, $^3J_{HH}$ = 8.7 Hz, 2CH of Ar), 10.21 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.1, 21.0, 55.9, 98.3, 111.5, 112.4, 114.4, 123.8, 129.9, 130.3, 132.2, 134.9, 137.1, 145.8, 152.6, 162.6, 185.3. MS (EI, 70 eV): 393 (M^+ − 1, 8), 303 (100), 261 (5), 229 (6), 197 (7), 135 (96), 107 (16), 92 (30), 77 (58).

4-(4-Methoxyanilino)-5-(4-methoxybenzoyl)-2-methylsulfanyl-3-thienyl cyanide (9g). Yellow powder, mp: 125–126 °C, 0.046 g, yield: 80%. IR (KBr)(ν_{max}, cm^{-1}): 3416 (NH), 2217 (CN), 1610 (C═O), 1590 and 1496 (C═C). Anal. calcd for $C_{21}H_{18}N_2O_3S_2$ (410.50): C, 61.44; H, 4.42; N, 6.82%. Found C, 61.40; H, 4.40; N, 6.89. ^{1}H NMR (300 MHz, DMSO-d_6): 2.69 (3H, s, SMe), 3.85 (6H, s, 2OMe), 6.93 (2H, d, $^3J_{HH}$ = 8.7 Hz, 2CH of Ar), 7.04 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH of Ar), 7.07 (2H, d, $^3J_{HH}$ = 7.5 Hz, 2CH of Ar), 7.24 (2H, d, $^3J_{HH}$ = 8.4 Hz, 2CH of Ar), 10.31 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.1, 55.8, 55.9, 97.4, 106.5, 112.9, 114.3, 114.4, 129.8, 130.1, 132.8, 154.2, 156.7, 158.1, 162.1, 162.2, 185.0. MS (EI, 70 eV): 303 (87), 257 (7), 197 (14), 135 (100), 92 (55), 77 (85).

5-(4-Methoxybenzoyl)-2-methylsulfanyl-4-(4-trifluoromethylanilino)-3-thienyl cyanide (9h). Yellow powder, mp: 156–157 °C, 0.035 g, yield: 78%. IR (KBr)(ν_{max}, cm^{-1}): 3417 (NH), 2219 (CN), 1615 (C═O), 1552 and 1495 (C═C). Anal.

calcd for $C_{21}H_{15}F_3N_2O_2S_2$ (448.48): C, 56.24; H, 3.37; N, 6.25%. Found C, 56.25; H, 3.36; N, 6.25. ^{1}H NMR (300 MHz, DMSO-d_6): 2.69 (3H, s, SMe), 3.83 (3H, s, OMe), 6.94 (2H, d, $^3J_{HH}$ = 8.4 Hz, 2CH$_{meta}$ of Ar), 7.05 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH$_{ortho}$ of Ar), 7.12 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH$_{meta}$ of Ar), 7.54 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH$_{ortho}$ of Ar), 9.61 (1H, s, NH). MS (EI, 70 eV): 447 ($M^+ - 1$, 6), 303 (93), 261 (5), 197 (6), 135 (100), 115 (17), 92 (56), 77 (85).

4-Anilino-5-(4-methylbenzoyl)-2-methylsulfanyl-3-thienyl cyanide (9i). Pale yellow powder, mp: 139–140 °C, 0.042 g, yield: 82%. IR (KBr)(ν_{max}, cm^{-1}): 3463 (NH), 2216 (CN), 1592 (C=O), 1549 (C=C). Anal. calcd for $C_{20}H_{16}N_2OS_2$ (364.48): C, 65.91; H, 4.42; N, 7.69%. Found C, 65.84; H, 4.48; N, 7.63. ^{1}H NMR (300 MHz, DMSO-d_6): 2.38 (3H, s, Me), 2.71 (3H, s, SMe), 7.18 (1H, t, $^3J_{HH}$ = 7.2 Hz, CH$_{para}$ of Ph), 7.24 (2H, d, $^3J_{HH}$ = 7.5 Hz, 2CH$_{ortho}$ of Ph), 7.35 (2H, t, $^3J_{HH}$ = 8.1 Hz, 2CH$_{meta}$ of Ph), 7.36 (2H, d, $^3J_{HH}$ = 7.5 Hz, 2CH of Ar), 7.66 (2H, d, $^3J_{HH}$ = 7.5 Hz, 2CH of Ar), 10.21 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.1, 21.5, 98.5, 112.4, 123.5, 125.5, 125.6, 128.2, 129.4, 129.6, 137.1, 139.7, 142.5, 152.1, 163.9, 186.2. MS (EI, 70 eV): 363 ($M^+ - 1$, 100), 349 (13), 287 (9), 258 (8), 229 (9), 198 (16), 174 (6), 145 (11), 119 (60), 91 (95), 77 (26).

4-Anilino-2-methylsulfanyl-5-(4-phenylbenzoyl)-3-thienyl cyanide (9j). Yellow powder, mp: 114–115 °C, 0.046 g, yield: 78%. IR (KBr)(ν_{max}, cm^{-1}): 3443 (NH), 2209 (CN), 1689 (C=O), 1600 and 1551 (C=C). Anal. calcd for $C_{25}H_{18}N_2OS_2$ (426.55): C, 70.40; H, 4.25; N, 6.57%. Found C, 70.41; H, 4.26; N, 6.57. ^{1}H NMR (300 MHz, DMSO-d_6): 2.74 (3H, s, SMe), 7.36 (1H, t, $^3J_{HH}$ = 7.5 Hz, CH$_{para}$ of Ph), 7.42–7.54 (5H, m, 2CH$_{ortho}$ of Ar, 1CH$_{para}$ and 2CH$_{meta}$ of Ph), 7.75–7.88 (6H, m, 2CH$_{ortho}$, 2CH$_{meta}$, and 2CH$_{ortho}$ of Ph), 8.07 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH$_{meta}$ of Ar), 10.26 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.2, 103.5, 115.6, 123.5, 127.3, 127.3, 127.4, 127.4, 128.8, 128.9, 129.5, 133.6, 138.6, 139.2, 145.6, 152.2, 163.5, 191.6. MS (EI, 70 eV): 425 ($M^+ - 1$, 23), 409 (31), 379 (15), 363 (4), 349 (88), 230 (6), 181 (100), 152 (62), 115 (4), 92 (9), 76 (26).

4-Anilino-5-(4-chlorobenzoyl)-2-methylsulfanyl-3-thienyl cyanide (9k). Yellow powder, mp: 148–149 °C, 0.038 g, yield: 70%. IR (KBr)(ν_{max}, cm^{-1}): 3443 (NH), 2211 (CN), 1605 (C=O), 1585 and 1491 (C=C). Anal. calcd for $C_{19}H_{13}ClN_2OS_2$ (384.90): C, 59.29; H, 3.40; N, 7.28%. Found C, 59.36; H, 3.33; N, 7.29. ^{1}H NMR (300 MHz, DMSO-d_6): 2.72 (3H, s, SMe), 7.17 (1H, t, $^3J_{HH}$ = 7.2 Hz, CH$_{para}$ of Ph), 7.22 (2H, d, $^3J_{HH}$ = 7.8 Hz, 2CH$_{ortho}$ of Ph), 7.34 (2H, t, $^3J_{HH}$ = 7.5 Hz, 2CH$_{meta}$ of Ph), 7.57 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH of Ar), 7.75 (2H, d, $^3J_{HH}$ = 8.1 Hz, 2CH$_{ortho}$ of Ar), 10.14 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.1, 98.6, 112.3, 112.5, 123.4, 125.6, 129.2, 129.4, 130.0, 137.0, 138.3, 139.8, 152.2, 164.6, 185.0. MS (EI, 70 eV): 383 ($M^+ - 1$, 78), 349 (6), 307 (11), 258 (11), 229 (12), 198 (32), 139 (79), 111 (100), 77 (57).

5-Acetyl-4-anilino-2-methylsulfanyl-3-thienyl cyanide (9l). Orange powder, mp: 159–160 °C, 0.031 g, yield: 78%. IR (KBr) (ν_{max}, cm^{-1}): 3411 (NH), 2212 (CN), 1612 (C=O), 1551 and 1498 (C=C). Anal. calcd for $C_{14}H_{12}N_2OS_2$ (288.38): C, 58.31; H, 4.19; N, 9.71%. Found C, 58.30; H, 4.19; N, 9.72. ^{1}H NMR (300 MHz, DMSO-d_6): 2.38 (3H, s, Me), 2.75 (3H, s, SMe), 7.12 (1H, t, $^3J_{HH}$ = 6.9 Hz, CH$_{para}$ of Ph), 7.13 (2H, d, $^3J_{HH}$ = 7.5 Hz, 2CH$_{ortho}$ of Ph), 7.32 (2H, t, $^3J_{HH}$ = 6.9 Hz, 2CH$_{meta}$ of Ph), 9.62 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.2, 28.8, 99.8, 112.4, 122.2, 124.1, 124.7, 129.5, 140.5, 149.6, 161.9, 189.0. MS (EI, 70 eV): 288 (M^+, 72), 258 (11), 236 (9), 215 (14), 197 (45), 167 (12), 149 (46), 112 (5), 82 (12), 78 (13), 71 (36), 43 (100).

4-Anilino-2-methylsulfanyl-5-(2-pyridylcarbonyl)-3-thienyl cyanide (9m). Yellow powder, mp: 181–182 °C, 0.039 g, yield: 79%. IR (KBr)(ν_{max}, cm^{-1}): 3392 (NH), 2210 (CN), 1594 (C=O), 1578 and 1493 (C=C). Anal. calcd for $C_{18}H_{13}N_3OS_2$ (351.44): C, 61.52; H, 3.73; N, 11.96%. Found C, 61.44; H, 3.76; N, 11.88. ^{1}H NMR (300 MHz, DMSO-d_6): 2.77 (3H, s, SMe), 7.26 (1H, t, $^3J_{HH}$ = 6.9 Hz, CH$_{para}$ of Ph), 7.33 (2H, d, $^3J_{HH}$ = 7.2 Hz, 2CH$_{ortho}$ of Ph), 7.40 (2H, t, $^3J_{HH}$ = 7.5 Hz, 2CH$_{meta}$ of Ph), 7.60–7.68 (4H, m, 4CH of pyridine), 11.01 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 16.4, 95.5, 103.8, 113.2, 122.6, 125.0, 127.2, 129.5, 138.5, 148.0, 153.4, 159.2, 167.1, 179.9. MS (EI, 70 eV): 351 (M^+, 6), 288 (53), 275 (44), 258 (32), 229 (10), 197 (87), 154 (19), 142 (27), 106 (24), 94 (26), 78 (96), 43 (100).

Methyl 2-(3-anilino-4-cyano-5-methylsulfanyl-2-thienyl)-2-oxoacetate (9n). Yellow powder, mp: 164–165 °C, 0.035 g, yield: 76%. IR (KBr)(ν_{max}, cm^{-1}): 3368 (NH), 2218 (CN), 1713 (CO_2Et), 1600 (C=O), 1581 and 1539 (C=C). Anal. calcd for $C_{16}H_{14}N_2O_3S_2$ (346.42): C, 55.48; H, 4.07; N, 8.09%. Found C, 55.47; H, 4.08; N, 8.09. ^{1}H NMR (300 MHz, DMSO-d_6): 1.32 (3H, t, $^3J_{HH}$ = 6.6 Hz, OCH$_2$CH_3), 2.78 (3H, s, SMe), 4.30 (2H, q, $^3J_{HH}$ = 6.6 Hz, OCH_2CH$_3$), 7.31 (1H, t, $^3J_{HH}$ = 5.7 Hz, 2CH$_{para}$ of Ph), 7.34 (2H, d, $^3J_{HH}$ = 6.9 Hz, 2CH$_{ortho}$ of Ph), 7.42 (2H, t, $^3J_{HH}$ = 7.5 Hz, 2CH$_{ortho}$ of Ph), 10.64 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 14.2, 16.4, 62.8, 95.3, 111.9, 112.6, 125.7, 125.8, 127.4, 129.5, 138.2, 156.5, 162.7. MS (EI, 70 eV): 346 (M^+, 26), 273 (88), 258 (55), 229 (11), 197 (100), 154 (12), 142 (16), 135 (12), 109 (18), 77 (44).

Methyl 3-(3-anilino-4-cyano-5-methylsulfanyl-2-thienyl)-3-oxopropanoate (9o). Pale yellow powder, mp: 144–145 °C, 0.038 g, yield: 78%. IR (KBr)(ν_{max}, cm^{-1}): 3389 (NH), 2215 (CN), 1741 (CO_2Me), 1605 (C=O), 1552 and 1502 (C=C). Anal. calcd for $C_{16}H_{14}N_2O_3S_2$ (346.42): C, 55.48; H, 4.07; N, 8.09%. Found C, 55.40; H, 4.12; N, 8.08. ^{1}H NMR (300 MHz, DMSO-d_6): 2.77 (3H, s, SMe), 3.57 (3H, s, OMe), 3.72 (2H, s, CH_2CO$_2$Me), 7.14 (1H, t, $^3J_{HH}$ = 7.2 Hz, CH$_{para}$ of Ph), 7.15 (2H, d, $^3J_{HH}$ = 7.5 Hz, 2CH$_{ortho}$ of Ph), 7.34 (2H, t, $^3J_{HH}$ = 8.1 Hz, 2CH$_{meta}$ of ph), 9.63 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.2, 47.3, 52.51, 107.4, 112.2, 112.7, 122.4, 125.0, 129.5, 140.2, 150.4, 167.8, 183.0, 183.8. MS (EI, 70 eV): 346 (M^+, 12), 313 (10), 270 (15), 238 (22), 197 (100), 169 (8), 142 (19), 94 (17), 109 (11), 77 (28), 43 (96).

Experimental procedures and spectroscopic data for 10a–g

After performing the required conditions for synthesis **9**, Pd(OAc)$_2$ (0.0016 g, 0.05 mmol) and CS_2CO_3 (0.163 g, 0.5 mmol) were added to the mixture. The mixture was stirred at 80 °C for 1 h (similar to synthesis **4**). Then, the mixture was poured into water and extracted with chloroform. The combined organic layer after drying over magnesium sulfate

was purified by silica gel flash chromatography (hexane : ethyl acetate = 3 : 1) to afford the desired adducts **10a–g**.

4-(4-Anilino-5-benzoyl-3-cyano-2-thienylamino)-5-benzoyl-2-methylsulfanyl-3-thiophenecarbonitrile (10a). Yellow powder, mp: 154–155 °C, 0.044 g, yield: 55%. IR (KBr)(ν_{max}, cm^{-1}): 3440 (NH), 2215 (CN), 1620 (C═O), 1548 and 1363 (C═C). Anal. calcd for $C_{31}H_{20}N_4O_2S_3$ (576.70): C, 64.56; H, 3.50; N, 9.72%. Found C, 64.55; H, 3.51; N, 9.70. ^{1}H NMR (300 MHz, DMSO-d_6): 2.8 (3H, s, SMe), 7.07–7.17 (3H, m, 2CH of Ph), 7.29 (2H, t, $^3J_{HH}$ = 7.5 Hz, CH of Ph), 7.47–7.59 (7H, m, 4CH of Ph), 7.68–7.74 (3H, m, 2CH of Ph), 10.4 (1H, s, NH), 10.90 (1H, brs, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.5, 84.1, 100.8, 104.7, 112.2, 112.6, 123.3, 125.4, 127.6, 129.0, 129.0, 129.0, 129.1, 129.3, 131.7, 133.4, 137.0, 139.4, 140.2, 152.3, 161.3, 166.2, 185.6, 185.7. MS (EI, 70 eV): 576 (M^+, 15), 529 (6), 471 (8), 425 (7), 368 (7), 323 (16), 273 (21), 197 (21), 150 (19), 105 (96), 77 (100). Crystal data for **10a** $C_{31}H_{20}N4O_2S_3$ (CCDC 1551356†): M_W = 576.72, monoclinic, $P12/n$, a = 12.844(4) Å, b = 13.059(3) Å, c = 17.671(6) Å, α = 90.00, β = 109.17(3), γ = 90.00, V = 2799.6(14) Å^3, Z = 4, D_c = 1.368 mg m^{-3}, F(000) = 1192, MoKα (λ = 0.71073 Å), intensity data were collected at 298(2) K with a STOE IPDS-II diffractometer with graphite monochromated radiation, and employing the $\omega/2\theta$ scanning technique, in the range of $-16 \le h \le 16$, $-16 \le k \le 16$, and $-22 \le l \le 22$; the structure was solved by direct methods, and all non-hydrogen atoms were positioned and anisotropic thermal parameters were refined from 6110 observed reflections with R(int) = 0.2212 by a full-matrix least-squares technique converged to R = 0.0907 and wR_2 = 0.1091 [$I > 2\sigma(I)$].

5-Benzoyl-4-[5-benzoyl-3-cyano-4-(4-toluidino)-2-thienylamino]-2-methylsulfanyl-3-thiophenecarbonitrile (10b). Dim red, mp: 165–166 °C, 0.044 g, yield: 53%. IR (KBr)(ν_{max}, cm^{-1}): 3444 (NH), 2209 (CN), 1636 (C═O), 1558 and 1363 (C═C). Anal. calcd for $C_{32}H_{22}N_4O_2S_3$ (590.73): C, 65.06; H, 3.75; N, 9.48%. Found C, 65.14; H, 3.64; N, 9.33. ^{1}H NMR (300 MHz, $CDCl_3$): 2.4 (3H, s, Me), 2.69 (3H, s, SMe), 7.15–7.28 (5H, m, CH of Ar), 7.45–7.62 (6H, m, CH of Ar), 7.76–7.80 (3H, m, CH of Ar), 10.48 (1H, s, NH), 10.74 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.1, 19.3, 84.0, 101.2, 104.7, 112.5, 123.5, 127.3, 128.5, 128.7, 129.0, 129.4, 129.6, 129.8, 131.1, 133.3, 133.5, 137.2, 137.8, 140.2, 160.9, 167.7, 186.5. MS (EI, 70 eV): 590 (M^+, 16), 500 (14), 454 (8), 395 (19), 323 (15), 273 (13), 223 (14), 155 (18), 105 (100), 77 (83).

5-Benzoyl-4-[5-benzoyl-3-cyano-4-(4-methoxyanilino)-2-thienylamino]-2-methylsulfanyl-3-thiophenecarbonitrile (10c). Red powder, mp: 122–123 °C, 0.047 g, yield: 56%. IR (KBr)(ν_{max}, cm^{-1}): 3422 (NH), 2216 (CN), 1600 (C═O), 1562 and 1365 (C═C). Anal. calcd for $C_{32}H_{22}N_4O_4S_3$ (606.73): C, 63.35; H, 3.65; N, 9.23%. Found C, 63.44; H, 3.68; N, 9.27. ^{1}H NMR (300 MHz, DMSO-d_6): 2.73 (3H, s, SMe), 3.76 (3H, s, SMe), 6.88 (2H, t, $^3J_{HH}$ = 8.4 Hz, 2CH of Ph), 7.08 (1H, t, $^3J_{HH}$ = 8.1 Hz, CH of Ph), 7.44–7.54 (7H, m, CH of Ar), 7.28–7.72 (4H, m, CH of Ar), 10.82 (2H, brs, 2NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.3, 55.7, 86.2, 109.8, 112.9, 113.0, 113.7, 114.3, 114.4, 127.2, 127.3, 128.84, 128.9, 131.9, 136.9, 137.2, 143.4, 157.6, 157.7, 160.9, 162.7, 185.8. MS (EI, 70 eV): 606 (M^+, 8), 560 (9), 500 (13), 454 (16), 395 (17), 323 (14), 273 (15), 227 (15), 171 (13), 105 (100), 77 (79).

4-[4-Anilino-3-cyano-5-(4-methoxybenzoyl)-2-thienylamino]-5-(3-methoxybenzoyl)-2-methylsulfanyl-3-thiophenecarbonitrile (10d). Yellow powder, mp: 130–131 °C, 0.049 g, yield: 55%. IR (KBr)(ν_{max}, cm^{-1}): 3436 (NH), 2216 (CN), 1635 (C═O), 1598 (C═O), 1558 and 1452 (C═C). Anal. calcd for $C_{33}H_{24}N_4O_4S_3$ (636.76): C, 62.25; H, 3.80; N, 8.80%. Found C, 62.32; H, 3.77; N, 8.71. ^{1}H NMR (300 MHz, DMSO-d_6): 2.74 (3H, s, SMe), 3.78 (3H, s, OMe), 3.84 (3H, s, OMe), 6.91–7.10 (7H, m, CH of Ar), 7.29 (2H, t, $^3J_{HH}$ = 7.8 Hz, 2CH of Ph), 7.48 (2H, d, $^3J_{HH}$ = 8.4 Hz, 2CH of Ar), 7.64 (2H, d, $^3J_{HH}$ = 8.7 Hz, 2CH of Ar), 11.61 (2H, brs, 2NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.2, 55.7, 55.9, 88.9, 110.7, 113.6, 113.8, 114.2, 116.2, 121.5, 122.9, 124.3, 129.0, 129.4, 131.2, 131.7, 137.4, 140.0, 145.7, 155.6, 160.9, 162.7, 162.8, 185.2. MS (EI, 70 eV): 636 (M^+, 6), 606 (5), 590 (7), 500 (7), 454 (5), 379 (8), 303 (16), 246 (6), 185 (9), 150 (19), 135 (100), 107 (31), 92 (35), 77 (85).

4-[3-Cyano-5-(4-methoxybenzoyl)-4-(4-toluidino)-2-thienylamino]-5-(3-methoxybenzoyl)-2-methylsulfanyl-3-thiophenecarbonitrile (10e). Dim red powder, mp: 125–126 °C, 0.049 g, yield: 54%. IR (KBr)(ν_{max}, cm^{-1}): 3444 (NH), 2210 (CN), 1615 (C═O), 1558 and 1430 (C═C). Anal. calcd for $C_{34}H_{26}N_4O_4S_3$ (650.78): C, 62.75; H, 4.03; N, 8.61%. Found C, 62.76; H, 4.02; N, 8.61. ^{1}H NMR (300 MHz, DMSO-d_6): 2.29 (3H, s, Me), 2.77 (3H, s, SMe), 3.80 (3H, s, OMe), 3.86 (3H, s, OMe), 6.92–7.16 (8H, m, CH of Ar), 7.52 (2H, d, $^3J_{HH}$ = 8.4 Hz, 2CH of Ar), 7.66 (2H, d, $^3J_{HH}$ = 8.4 Hz, 2CH of Ar). ^{13}C NMR (100.0 MHz, DMSO-d_6): 16.9, 20.5, 55.2, 55.3, 96.6, 104.5, 113.5, 113.6, 113.7, 113.9, 114.8, 123.0, 122.9, 128.6, 129.1, 129.8, 130.9, 136.6, 144.1, 162.7, 166.9, 179.2. MS (EI, 70 eV): 650 (M^+, 12), 559 (14), 515 (17), 473 (19), 385 (22), 303 (14), 265 (27), 179 (32), 156 (43), 105 (77), 93 (66), 82 (100).

4-[3-Cyano-4-(4-methoxyanilino)-5-(4-methoxybenzoyl)-2-thienylamino]-5-(4-methoxybenzoyl)-2-methylsulfanyl-3-thiophenecarbonitrile (10f). Red powder, mp: 141–142 °C, 0.049 g, yield: 53%. IR (KBr)(ν_{max}, cm^{-1}): 3416 (NH), 2223 (CN), 1599 (C═O), 1550 and 1362 (C═C). Anal. calcd for $C_{34}H_{26}N_4O_5S_3$ (666.78): C, 61.25; H, 3.93; N, 8.40%. Found C, 61.19; H, 3.86; N, 8.49. ^{1}H NMR (300 MHz, DMSO-d_6): 2.80 (3H, s, SMe), 3.78–3.86 (9H, m, 3OMe), 6.96–7.06 (6H, m, 6CH of Ar), 7.50–7.58 (4H, m, 4CH of Ar), 7.67 (2H, d, $^3J_{HH}$ = 8.4 Hz, 2CH of Ar), 10.64 (1H, brs, NH), 10.83 (1H, brs, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.6, 55.7, 55.8, 56.1, 82.7, 95.3, 105.3, 112.6, 114.1, 114.2, 114.4, 126.6, 129.3, 129.6, 131.4, 131.5, 133.3, 156.8, 157.8, 160.0, 161.7, 161.9, 163.7, 184.3, 184.3. MS (EI, 70 eV): 647 (8), 575 (7), 523 (9), 459 (11), 410 (5), 364 (10), 316 (15), 257 (9), 191 (8), 154 (41), 135 (66), 84 (62), 66 (100).

4-[4-anilino-3-cyano-5-(2-pyridylcarbonyl)-2-thienylamino]-2-methylsulfanyl-5-(2-pyridylcarbonyl)-3-thiophenecarbonitrile (10g). Red powder, mp: 152–153 °C, 0.043 g, yield: 54%. IR (KBr)(ν_{max}, cm^{-1}): 3417 (NH), 2209 (CN), 1630 (C═O), 1560 and 1444 (C═C). Anal. calcd for $C_{29}H_{18}N_6O_2S_3$ (578.80): C, 60.19; H, 3.14; N, 14.52%. Found C, 60.20; H, 3.16; N, 14.55. ^{1}H NMR (300 MHz, DMSO-d_6): 7.34 (3H, s, SMe), 7.18–7.32 (2H, m, CH of Ar), 7.57–7.76 (2H, m, CH of Ar), 8.10–8.14 (7H,

m, CH of Ar), 8.64–8.81 (2H, m, CH of Ar), 11.20 (1H, brs, NH), 11.51 (1H, brs, NH). ^{13}C NMR (100.0 MHz, DMSO-d_6): 16.5, 83.3, 94.9, 102.8, 112.1, 112.8, 120.7, 122.0, 123.1, 126.3, 128.0, 128.8, 137.8, 138.4, 146.0, 147.3, 147.9, 151.7, 153.7, 159.0, 164.1, 166.2, 184.3, 184.3. MS (EI, 70 eV): 578 (M^+, 7), 502 (9), 441 (8), 396 (17), 353 (8), 297 (6), 246 (6), 200 (5), 135 (18), 105 (34), 78 (100).

Experimental procedures and spectroscopic data for 14

To a solution of 5-benzoyl-4-methylamino-2-methylsulfanyl-3-thienyl cyanide **13** (0.072 g, 0.25 mmol) in DMF (1 mL) were added $Pd(OAc)_2$ (0.0016 g, 0.05 mmol) and CS_2CO_3 (0.163 g, 0.5 mmol). The mixture was stirred at 80 °C for 1 h (similar to syntheses of **4** and **10**). Then, the mixture was poured into water and extracted with chloroform. The combined organic layer after drying over magnesium sulfate was purified by silica gel flash chromatography (hexane : ethyl acetate = 3 : 1) to afford the desired adducts **14**.

5-Benzoyl-4-[5-benzoyl-3-cyano-4-methylamino-2-thienyl(methyl) amino]-2-methylsulfanyl-3-thiophenecarbonitrile (14). Red powder, mp: 75–76 °C, 0.090 g, yield: 68%. IR (KBr)(ν_{max}, cm^{-1}): 3453 (NH), 2221 (CN), 1644 (C═O), 1544 and 1440 (C═C). Anal. calcd for $C_{27}H_{20}N_4O_2S_3$ (528.66): C, 61.34; H, 3.81; N, 10.60%. Found C, 61.35; H, 3.83; N, 10.62. ^{1}H NMR (300 MHz, $CDCl_3$): 2.70 (3H, s, SMe), 2.90 (3H, s, NMe), 2.97 (3H, s, NHMe), 7.46–7.56 (5H, m, CH of Ph), 7.62–7.71 (2H, m, CH of Ph), 7.74–7.77 (1H, m, CH of Ph), 7.81 (2H, $^3J_{HH}$ = 7.2 Hz, CH of Ph), 9.39 (1H, s, NH). ^{13}C NMR (75.0 MHz, DMSO-d_6): 17.6, 31.5, 36.5, 93.1, 100.8, 102.1, 111.5, 112.0, 116.9, 127.6, 128.2, 128.5, 128.9, 131.4, 132.9, 138.2, 139.9, 148.5, 154.2, 156.3, 163.1, 187.3, 187.4. MS (EI, 70 eV): 514 (14), 500 (16), 409 (9), 319 (7), 273 (22), 239 (10), 197 (9), 151 (16), 121 (14), 121 (14), 105 (100), 77 (73).

Conflicts of interest

There are no conflicts to declare.

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