A Green Synthesis of 2-Amino-4-(9*H*-carbazole-3-yl)thiophene-3-carbonitriles by a Step-wise and One-pot Three-component Gewald Reaction

Vijay Kumar Reddy Avula,[a,b] Swetha Vallela,[b] Jaya Shree Anireddy,[b] and Naga Raju Chamarthi[a]*

[a]Department of Chemistry, Sri Venkateswara University, Tirupati 517 502, Andhra Pradesh, India
[b]Centre for Chemical Science and Technological, IST, Jawaharlal Nehru Technological University, Kukatpally, Hyderabad 500 085, Telangana, India
*E-mail: rajuchamarthi10@gmail.com

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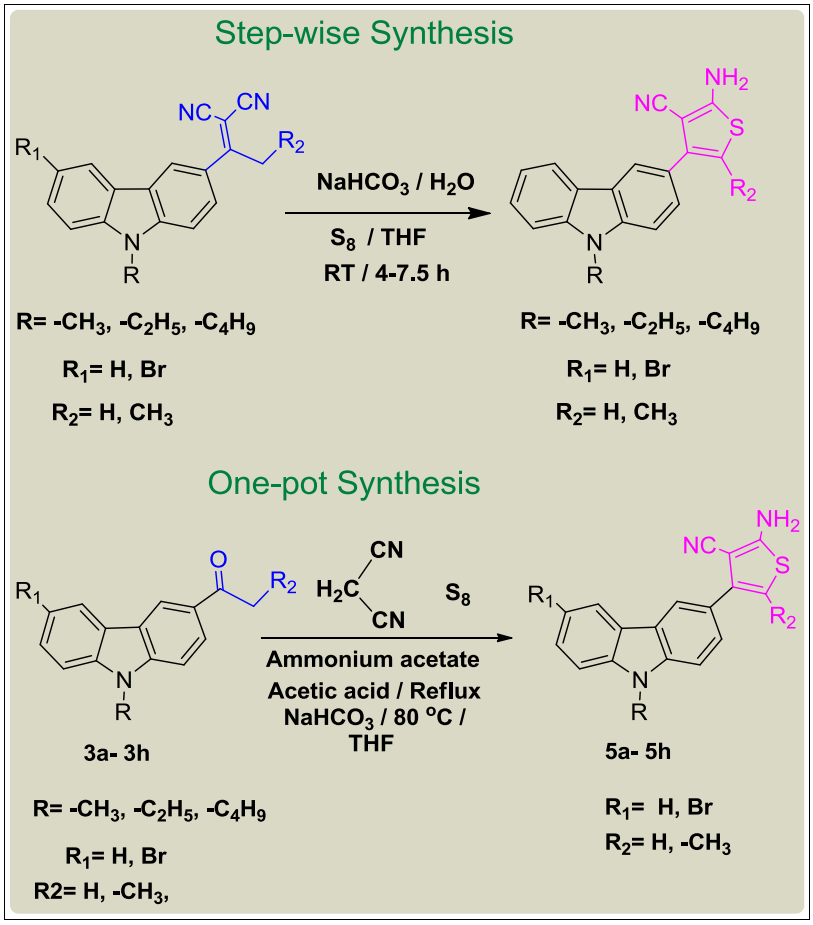


An eco-friendly method has been developed for the synthesis of 2-amino-4-(9*H*-carbazole-3-yl)thiophene-3-carbonitriles from preliminary carbazole (**1**) through an intermediate of 2-(1-(9*H*-carbazole-3-yl) ethylidene)malononitriles using the Knoevenagel condensation followed by the Gewald reaction. On the other hand, the target compounds could also be prepared in a one-pot three-component manner by treating equimolar quantities of 1-(9*H*-carbazole-3-yl)ethanone (**3**), malononitrile, and elemental sulfur. The merits of this preparation are mild reaction conditions. The Gewald reaction is executed with inorganic base $NaHCO_3$ (H_2O) in tetrahydrofuran, easy work-up procedure with good yields.

INTRODUCTION

Carbazoles display a wide range of biological activities, making them attractive compounds to synthetic and medicinal chemists [1–6]. Carbazole and its derivatives are important type of nitrogen-containing heterocyclic compounds that are widespread in nature. The chemistry and biology of carbazole have attracted an increasing interest over the last 50 years because it possesses a desirable electronic and charge transport properties, as

well as large π-conjugated system, so various functional groups are easily introduced into structurally rigid carbazolyl ring. These characteristics result in the extensive potential application of carbazole in the field of chemistry (photoelectrical material, dyes, and supramolecular recognition) and medicinal chemistry (antitumor, anti-inflammatory, antimicrobial, psychotropic, and antioxidative) [7,8]. First, carbazole alkaloids were isolated as natural products from *Murraya koenigii* that exhibited good antimicrobial activity [9]. They exhibited potent biological activity particularly against clinical antibiotic-resistant bacteria [10]. Several carbazoles are known for their potent antibacterial, antituberculosis, and antihistaminic properties [11–14]. Furthermore, sulfur-containing heterocycles have paved way for active research in medicinal chemistry [15]. Thiophene derivatives in combination with other ring systems have been used extensively in pharmaceutical applications such as antidepressant [16], analgesic [17], anti-inflammatory [18], and antimicrobial activities [19]. 2-Aminothiophenes have demonstrated a broad spectrum of uses, including pharmaceuticals, dyes, and agrochemical applications [20]. Conceptually, the simplest and most convergent preparation of this class of compounds is the condensation of ketones with an activated nitrile and elemental sulfur, which was first described in the 1960s by Gewald and coworkers [21].

Although a one-pot procedure is well established, the two-step procedure in which an α,β-unsaturated nitrile is first prepared by Knoevenagel condensation of a ketone or aldehyde with an activated acetonitrile, followed by base-promoted reaction with sulfur, has generally been found to result in higher yields [20]. Wahab et al. reported [22] the reaction of 3-acetyl-6,8-diiodo-2*H*-chromen-2-one with malononitrile to yield a mixture of 2-(1-(6,8-diiodo-2-oxo-2*H*-chromen-3-yl)ethylidene) malononitrile and the cyclized product, that is, 2-(6,8-diiodo-2-oxo-2*H*-chromen-3-yl)-7,9-diiodo-4-methyl-5*H*-chromeno[4,3-*b*]pyridin-5-one. Daniel Vegh et al. reported [23] the synthesis of p-conjugated thiophenes starting from substituted 3-oxopropanenitriles via the Gewald reaction. On the synthesis of nitrogen-containing heterocycles, Srikrishna et al. reported [24] the synthesis of 2-amino-4-(2-oxo-2*H*-chromen-3-yl)thiophene-3-carbonitriles using L-proline as a catalyst in PEG-600 solvent at 100°C for 1–2 h via Knoevenagel condensation followed by the Gewald reaction. Taking into account of valuable inputs, results of key empirical observations and scientific information are available that inspired the authors to further extend the work that would give high-quality innovative framework-containing compounds having both the carbazole ring and thiophene ring.

RESULTS AND DISCUSSION

1-(9*H*-Carbazole-3-yl)ethanone on reaction with malononitrile, using L-proline as a catalyst in ethanol at r.t. for 12 h, did not yield desired products of **4a**–**4h**. On the other hand, when we carried out this reaction with **3a**–**3h** using ammonium acetate as a base catalyst, acetic acid in toluene solvent under reflux conditions afforded products of **4a**–**4h**. In this manner, we have established our new synthetic method (Table 1, Scheme 1).

To optimize the reaction conditions for the synthesis of target compounds in high yields, we examined them using different solvents and catalysts at different temperatures, to obtain **4a**–**4h**. Among all the conditions used (Table 1), toluene was found to be the best solvent and ammonium acetate as the best catalyst in terms of reaction time and yields of the products formed. The results of these studies are presented in Table 1, entry 6.

As exposed in Scheme 2, the commercially available carbazole (**1**) was treated in a pragmatic way with

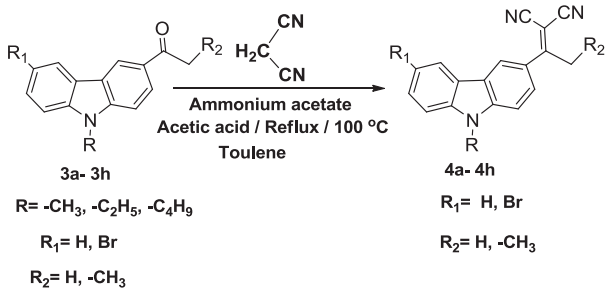
Table 1

Optimization of reaction conditions.

Entry	Solvent	Catalyst	Mol (%)	Time (h)	Temperature (°C)	Yield (%)[a]
1	PEG-200	Morpholine	10	14	65	32
2	Ethanol	Diethyl amine	10	8	60	25
3	Methanol	*N*-Methyl imidazole	10	6	60	30
4	Glycerol	Triethyl phosphite	10	8	70	10
5	THF	*N*-*N*-Dimethyl glycine	10	10	60	35
6	**Toluene**	**Ammonium acetate**	**10**	**3**	**105**	**80**
7	THF	L-Proline	10	10	65	50
8	Toluene	L-Proline	10	12	105	45
9	THF	Triethyl amine	10	10	60	20
10	THF	Piperidine	10	10	65	30
11	THF	Ammonium acetate	10	5	55	50
12	Glycerol	Sulfamic acid	10	4	70	10

Bold text identifies optimized conditions.
[a]Isolated yield.

Scheme 1. Knoevenagel condensation of 1-(9*H*-carbazole-3-yl)ethanone with malononitrile.



different alkylating agents such as methyl iodide, ethyl bromide, and *n*-butyl bromide in acetone at r.t. using K_2CO_3 as a base to give the corresponding *N*-alkylated carbazoles [25] (**2**). As reported earlier, on this Friedel–Craft acylation at r.t. for 24 h resulted in the formation of 1-(9*H*-carbazole-3-yl)ethanone (**3**). This, on reaction with malononitrile under refluxing conditions in acetic acid using ammonium acetate as a base for 2–3 h, yielded the 2-(1-(9*H*-carbazole-3-yl)ethylidene) malononitriles (**4a**–**4h**). In order to synthesize the target compounds, that is, thiophene, we have used the method of Chengyuan et al. [26], where they have synthesized the 2-aminothiophene by using a reaction of ketones and aldehydes, dicyanomethane, and elemental sulfur in PEG-200 in high yields under sonication. As a result, on reaction with **4a**–**c**, by the malononitrile, different catalysts and elemental sulfur in tetrahydrofuran (THF) solvent at different temperatures for 10–24 h resulted in the formation of *N*-alkylated-2-amino-4-(9*H*-carbazole-3-yl)thiophene-3-carbonitriles (**5a**–**c**) in low yields (Table 2). We used inorganic base $NaHCO_3$ as a catalyst to obtain excellent yields as given in Table 3. We have optimized the reaction conditions using different catalysts and in THF solvent. Among all the conditions worked out (Table 2), THF was found to be the best solvent and $NaHCO_3$ the best catalyst in terms of reaction time and yield of the product produced (Table 2, entry 12). Hence, using $NaHCO_3$–THF system, we have synthesized the title compounds in excellent yields.

As shown in Scheme 3 considering the aforementioned positive results, we have extended the same work to 1-(6-

Scheme 2. Synthesis of 2-amino-4-(9*H*-carbazole-3-yl)thiophene-3-carbonitriles (**5a**–**5c**).

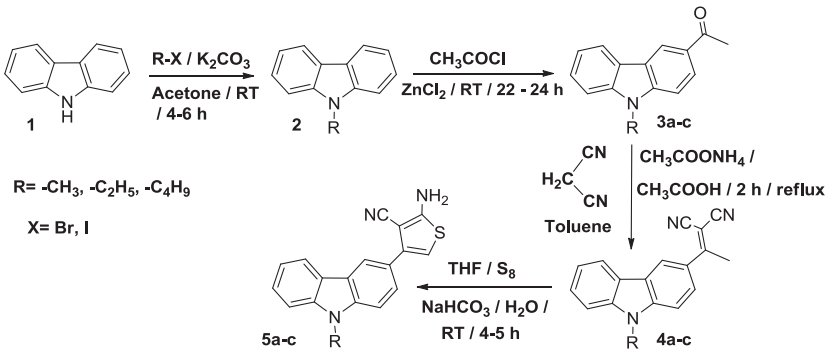


Table 2

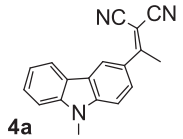
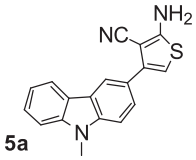
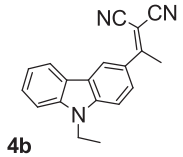
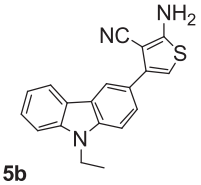
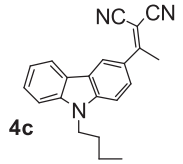
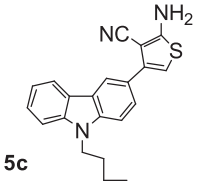
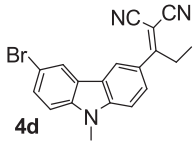
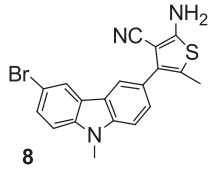
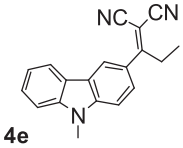
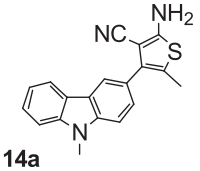
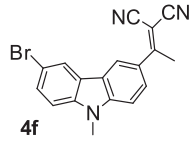
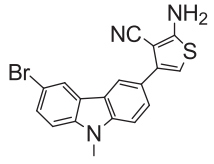
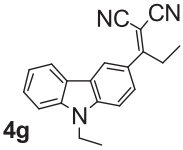
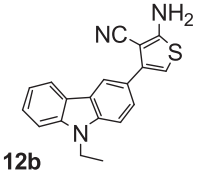
Optimization of reaction conditions.

Entry	Solvent[a]	Catalyst	Mol (%)	Time (h)	Yield (%)[b]
1	THF	Morpholine	10	10	20
2	THF	Diethyl amine	10	11	23
3	THF	*N*-Methyl imidazole	10	12	25
4	THF	Triethyl phosphite	10	10	Trace
5	THF	*N*-*N*-Dimethyl glycine	10	10	30
6	THF	D-Proline	10	11	40
7	THF	L-Proline	10	24	50
8	THF	L-Proline	10	12	40
9	THF	Triethyl amine	10	10	55
10	THF	Piperidine	10	10	30
11	THF	DABCO	10	12	40
12	**THF**	**Saturated $NaHCO_3$**	**10**	**4**	**90**

Bold text identifies optimized conditions.
[a]At reflux temperature.
[b]Isolated yield.

Table 3

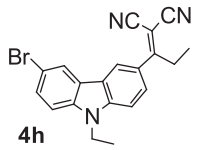
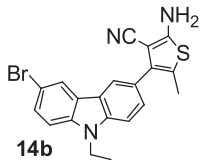
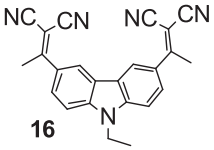
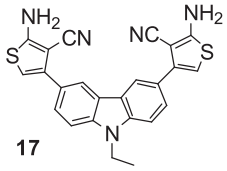
Reaction time and yields of the title compounds **5a–c**, **8**, **14a–b**, **12a–b**, and **17**.

S. no.	Starting materials	Product obtained	Time (h)	Yield (%)
1	 **4a**	 **5a**	4	90
2	 **4b**	 **5b**	4.5	89
3	 **4c**	 **5c**	5	85
4	 **4d**	 **8**	5	80
5	 **4e**	 **14a**	6	70
6	 **4f**		6.5	68
7	 **4g**	 **12b**	7	65

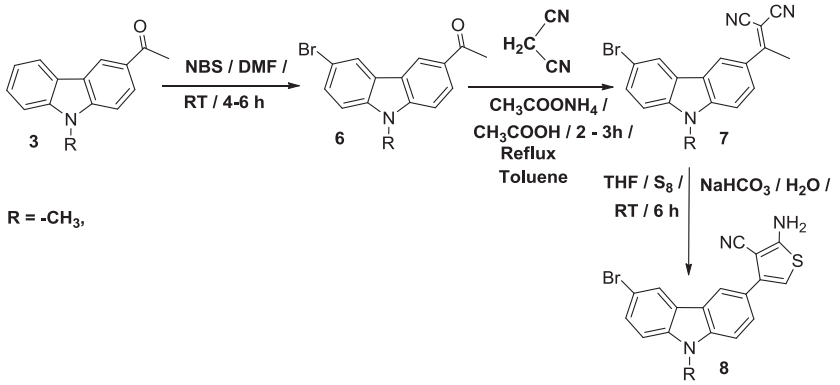
(*Continued*)

Table 3

(*Continued*)

S. no.	Starting materials	Product obtained	Time (h)	Yield (%)
8	 **4h**	 **14b**	7.5	60
9	 **16**	 **17**	6	55

Scheme 3. Synthesis of 2-amino-4-(6-bromo-9*H*-carbazole-3-yl)thiophene-3-carbonitrile (**8**).

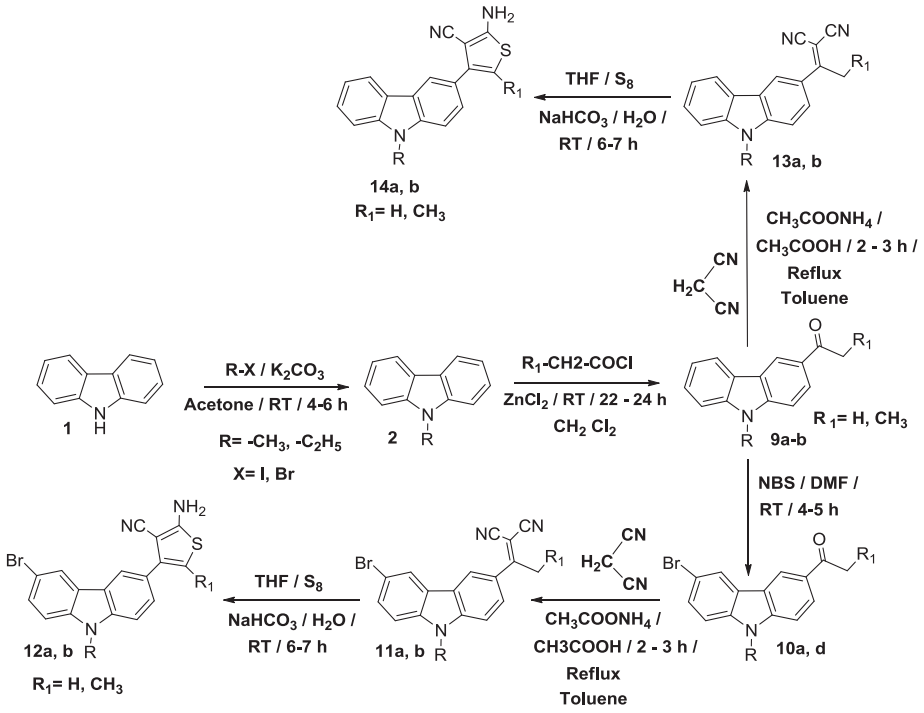


bromo-9*H*-carbazole-3-yl)ethanone **6** [27]. The compound **6** was prepared by bromination of **3** with *N*-bromosuccinimide in dimethylformamide at r.t. for 4–5 h. This, on reaction with malononitrile under refluxing conditions, acetic acid and ammonium acetate as a base in toluene for 2–3 h, yielded the 2-(1-(6-bromo-9*H*-carbazole-3-yl)ethylidene)malononitriles **7**. This, on further reaction with elemental sulfur (S_8) in THF solvent and $NaHCO_3$ as a base at r.t. for 4–6 h, resulted in the formation of 2-amino-4-(6-bromo-9*H*-carbazole-3-yl) thiophene-3-carbonitrile (**8**) in good yield (Table 3).

Carbazole **1**, on reaction with acetyl chloride/propionyl chloride and $ZnCl_2$ in dichloromethane at r.t. for 24 h, yielded 1-(9*H*-carbazole-3-yl)ethanone/propan-1-one (**9a**, **b**). **9a**, **b**, on reaction with *N*-bromosuccinimide n dimethylformamide at room temperature for 4–5 h, resulted in the formation of compounds **10a**, **b**, which, on further reaction with malononitrile under refluxing conditions in acetic acid, ammonium acetate as a base for 2–3 h, yielded 2-(1-(6-bromo-9*H*-carbazole-3-yl) propylidene)malononitriles (**11a**, **b**). They were further treated with elemental sulfur (S_8) in THF as a solvent and $NaHCO_3$ as a base at room temperature for 6–7 h to afford 2-amino-4-(6-bromo-9*H*-carbazole-3-yl)-5*H*/5-methylthiophene-3-carbonitriles (**12a**, **b**). **9a**, **b** on treatment with malononitrile under refluxing conditions in acetic acid using ammonium acetate as a base for 2–3 h afforded **13a**, **b**, which, on reaction with elemental sulfur (S_8) in THF as a solvent and $NaHCO_3$ as a base at r.t. for 6–7 h, yielded the thiophene products (**14a**, **b**) (Table 3; Scheme 4).

With the aforementioned results as an encouragement and considering the significance, it is designed to synthesize bis-thiophene containing carbazole moiety. Hence, the Friedel–Craft acylation (2 mol) of **2** furnished 1,1′-(9-ethyl-9*H*-carbazole-3,6-diyl)diethanone **15** [28]. On reaction of **15** with 2 mol of malononitrile under refluxing conditions in acetic acid–ammonium acetate as a base for 3 h yielded the 2,2″-((9-ethyl-9*H*-carbazole-3,6-diyl)bis(ethan-1-yl-1ylidene))dimalononitrile **16**. **16**,

Scheme 4. Synthesis of substituted thiophene derivatives.



Scheme 5. Synthesis of 4,4′-(9-ethyl-9*H*-carbazole-3,6-diyl)bis(2-aminothiophene)-3-carbonitrile.

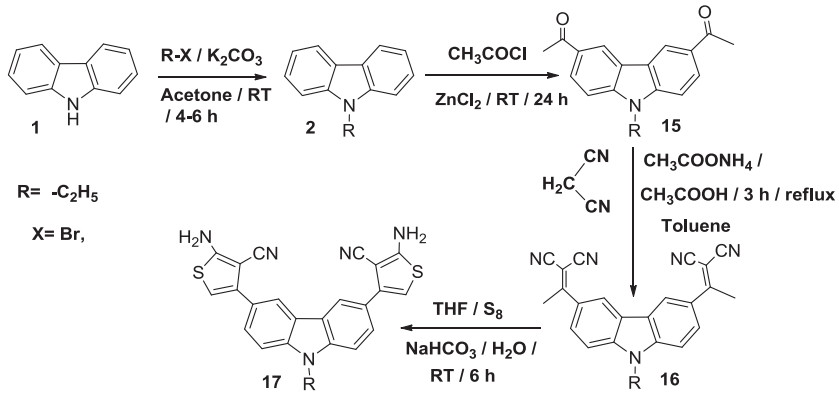


Table 4

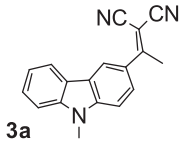
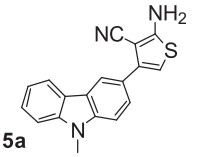
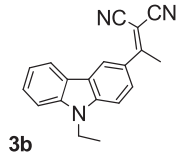
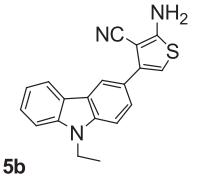
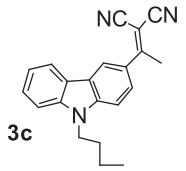
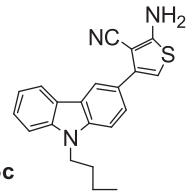
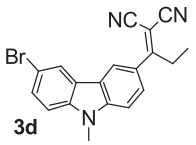
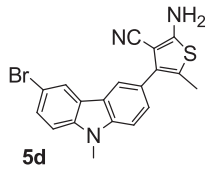
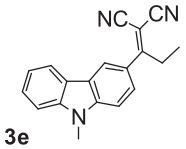
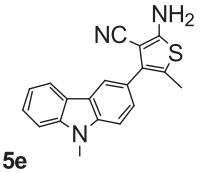
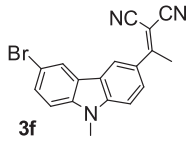
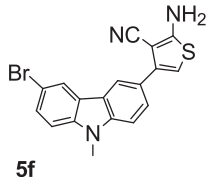
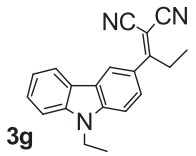
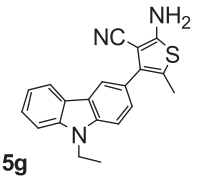
Optimizing the reaction conditions for the one-pot synthesis of **5a–5h**.

S. no.	Solvent	Catalyst	Mol (%)	Time (h)	Temperature (0°C)	Yield (%)[a]
1	Ethanol	l-Proline	10	8	80	10
2	Methanol	l-Proline	10	6	70	15
3	PEG-600	DABCO	10	12	80	25
4	**THF**	**$NaHCO_3$**	**10**	**10**	**70**	**70**
5	Ethanol	$NaHCO_3$	10	8	80	40
6	Glycerol	$NaHCO_3$	10	9	90	45

Bold text identifies optimized conditions.
[a]Isolated yield.

Table 5

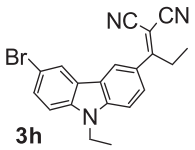
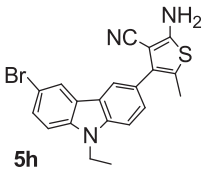
Reaction time and yields of the title compounds (one-pot method) **5a**–**h**.

S. no.	Starting materials	Product obtained	Time (h)	Yield (%)
1	 **3a**	 **5a**	10	70
2	 **3b**	 **5b**	10	68
3	 **3c**	 **5c**	11	65
4	 **3d**	 **5d**	12	60
5	 **3e**	 **5e**	10	60
6	 **3f**	 **5f**	12	55
7	 **3g**	 **5g**	10	58

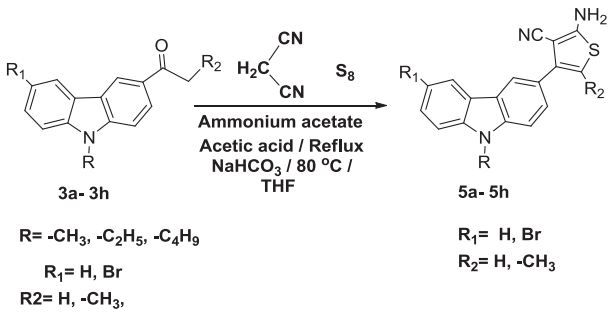
(*Continued*)

Table 5

(*Continued*)

S. no.	Starting materials	Product obtained	Time (h)	Yield (%)
8	 **3h**	 **5h**	11	55

Scheme 6. One-pot synthesis of *N*-alkylated-2-amino-4-(9*H*-carbazole-3-yl)thiophene-3-carbonitriles (**5a–5h**).



on further reaction with two equivalents of elemental sulfur in THF solvent and $NaHCO_3$ as a base catalyst, resulted in the formation of bis-thiophene, that is, 4,4″-(9-ethyl-9*H*-carbazole-3,6-diyl)bis(2-minothiophene-3-carbonitrile) **17** in good yield (Table 3) (Scheme 5).

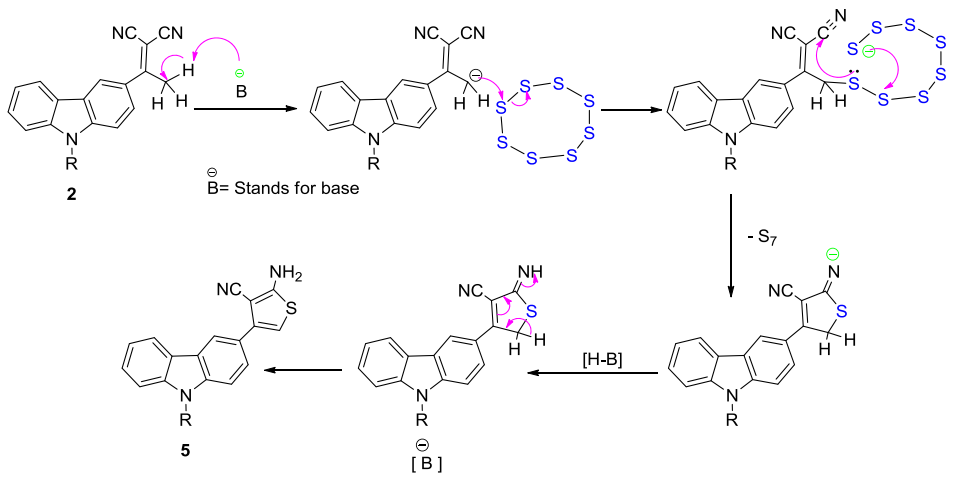
One-pot synthesis of title compounds (5a–5h). In consideration of curiosity to prepare the title compounds (**5a–5h**) via the one-pot method, **3a–3h** were treated with malononitrile, elemental sulfur, and L-proline as a base in ethanol at 80°C for 8 h to obtain target compound in very low yield as shown in Table 4, in order to optimize the reaction conditions to increase the yields, by screening the different catalysts and green solvents, and the results are summarized in Table 4. Among all conditions used (Table 4) and on observation, THF was found to be the best solvent and $NaHCO_3$ the best catalyst for the one-pot synthesis. Thus, this method was adopted for the synthesis of **5a–5h** from **3** in moderate yields. The reaction time, yield, and physical data of compounds **5a–5h** in the one-pot method are summarized in Table 5 (Scheme 6).

Mechanism. The mechanism of this reaction has been considered by two possibilities. In the first possibility, the base abstracts a proton from **2** to form an anion that attacks elemental sulfur with subsequent cyclization to yield **5** as shown in Scheme 7.

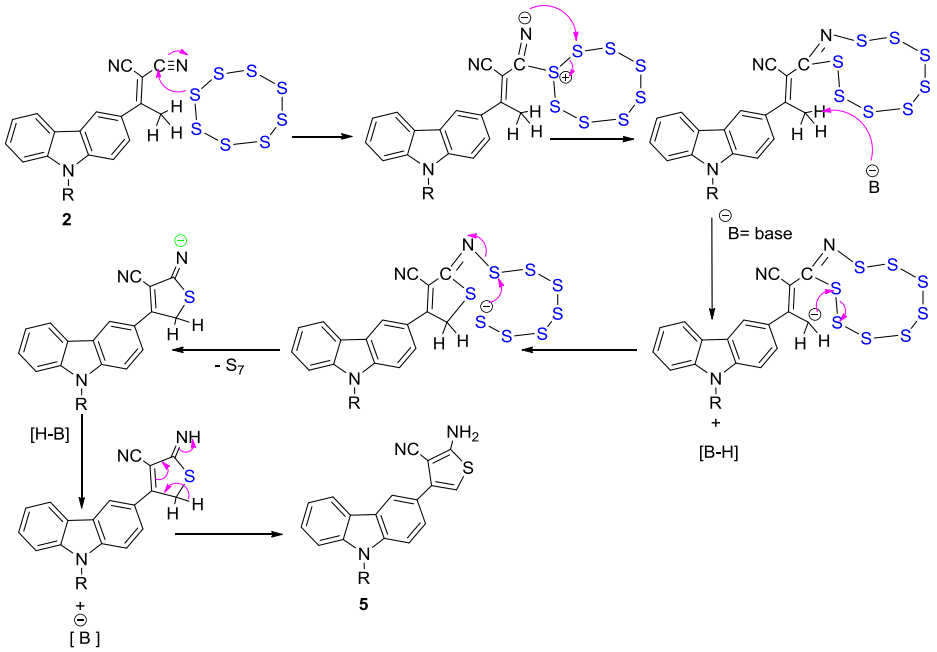
In the second possibility, the elemental sulfur first attacks the nitrile group of **2** with its lone pair of electrons followed by abstraction of proton by the base to generate the intermediate anion that undergoes cyclization to give product **5** as exposed in Scheme 8.

As per the mechanistic representation outlined, the stable S_7 allotrope formed after the cyclization has been

Scheme 7. Mechanism possibility 1.



Scheme 8. Mechanism possibility 2.



separated simply by filtration [24]. The sulfur (S_7) is soluble in benzene and was removed simply by filtration as filtrate, and the product (solid residue) was purified further.

CONCLUSIONS

We have developed novel synthetic methodologies for the Knoevenagel condensation and subsequent Gewald reaction. Hence, the designed compounds were prepared in step-wise manner and also in one-pot method. Of these methods described, one-pot three-component method appears to be convenient method in consideration of reaction times and less cumbersome. A significant enhancement in the rate of the reaction was observed in THF–$NaHCO_3$ (aq) when compared with other green solvents and catalysts. Furthermore, simple reaction conditions and easy work-up make this method facile and superior to reported method for the synthesis of 2-amino-4-(9*H*-carbazole-3-yl)thiophene-3-carbonitriles (**5a–5h**).

EXPERIMENTAL

All the commercially available starting materials, reagents, catalysts, and solvents were procured from Sigma-Aldrich (Hyderabad, India) and used without purification. All products were purified by silica gel (200–300) column chromatography. Melting points are uncorrected and were determined in open capillary tubes using Guna digital melting point apparatus (Hyderabad, India). Thin-layer chromatography (TLC) analyses were run on silica gel-G, and visualization was performed using UV lamp (Hyderabad, India) and iodine. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker 400-MHz instrument (Ettlingen, Germany) in $CDCl_3$ or DMSO-d_6 using tetramethylslane (TMS) as an internal standard at 400 and 100 MHz, respectively. Mass spectra were recorded on Agilent-LCMS instrument (Ettlingen, Germany). Chemical shifts were recorded on δ scale in parts per million, and multiplicities are represented as abbreviations: s (singlet), d (doublet), t (triplet), and m (multiplet). Elemental analysis was performed on Thermo Finnigan Instrument (Courtaboeuf, France).

General procedure for the preparation of 4 from 1-(9*H*-carbazole-3-yl)methanone (3). A mixture of 1-(9*H*-carbazole-3-yl)methanone (**3**) (5 mmol), malononitrile (10 mmol), ammonium acetate (10 mol%), and toluene (20 mL) was stirred and heated at 100°C for 3–4 h (Table 1). The reaction progress was monitored by TLC. After completion of reaction, as shown by the disappearance of **3** (TLC, hexane–ethyl acetate, 7:3), the solvent was evaporated *in vacuo*. The product was purified by column chromatography (hexane–ethyl acetate, 4:1), to yield 2-(1-(9*H*-carbazole-3-yl)ethylidene) malononitrile **4a** as a light yellow solids.

General procedure for the preparation of 5a from 4a. A mixture of **4a** (5 mmol), elemental sulfur (5 mmol), THF (20 mL), and saturated solution of sodium bicarbonate in water (5 mL) was stirred at r.t. for 4–7.5 h (Table 3). The completion of the reaction was monitored by TLC. After completion of the reaction, as shown by the disappearance

of **4a** (TLC, hexane–ethyl acetate, 4:2), the solvent was evaporated *in vacuo*. The product was purified by column chromatography (hexane–ethyl acetate, 9:1), to obtain 2-amino-4-(9*H*-carbazole-3-yl)thiophene-3-carbonitrile (**5a**).

One-pot method for the synthesis of 5a. A mixture of **3** (5 mmol), malononitrile (10 mmol), elemental sulfur (5 mmol), and saturated sodium bicarbonate (10 mol%) and THF (20 mL) was heated to 70°C and stirred for 6–10 h (Table 4). The reaction progress was monitored by TLC analysis. After completion of reaction, the mixture was cooled to r.t. and then poured into ice-cold water (40 mL). The organic layer was separated by a separating funnel, and the solvent was evaporated *in vacuo*. The product was purified by column chromatography (hexane–ethyl acetate, 9:1), to give 2-amino-4-(9*H*-carbazole-3-yl)thiophene-3-carbonitrile (**5a**).

Spectral data for 2-(1-(9*H*-carbazole-3-yl)ethylidene) malononitriles (4a–4h). ***2-(1-(9-Methyl-9H-carbazole-3-yl) ethylidene)malononitrile (4a).*** Light yellow solid; yield (80%); m.p. 100–102°C; IR (KBr): 2948, 2851, 2230, 1715, 1588, 1447, 1366, 1215, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 2.76 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 7.29–7.27 (m, 2H, Ar-H), 7.45–743 (d, 1H, Ar-H), 7.62–7.59 (m, 1H, Ar-H), 7.82–7.80 (m, 1H, Ar-H), 8.30–8.20 (m, 2H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 24.2, 29.5 (aliphatic C) 81.6, 109.1, 110.7, 113.3, 113.7, 114.2, 120.9, 122.0, 123.4, 124.0, 126.2, 126.6, 129.7, 140.2, 143.2, 174.8. (Aromatic C): mass spectrometry (MS) (positive mode): m/z = 272 $[M + H]^+$. *Anal*. Calcd (%) for $C_{18}H_{13}N_3$; C, 79.68. H, 4.83. N, 15.59. Found: C, 79.64. H, 4.85. N, 15.61.

2-(1-(9-Ethyl-9H-carbazole-3-yl)ethylidene)malononitrile (4b). Light yellow solid; yield (76%); m.p. 98–100°C; IR (KBr): 3010, 2958, 2851, 2230, 1715, 1588, 1457, 1346, 1215, 815; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.30–1.21 (t, 3H, CH_3), 3.18–3.12 (m, 2H, CH_2), 3.89 (s, 3H, CH_3) 7.37–7.34 (t, 1H, Ar-H), 7.50–745 (t, 2H, Ar-H), 7.60–7.56 (t, 1H, Ar-H), 7.75–7.73 (d, 1H, Ar-H), 8.17–8.54 (d, 1H, Ar-H), 8.36 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.6, 29.3, 31.0 (aliphatic C) 80.8, 108.1, 109.0, 109.2, 113.6, 114.3, 120.4, 120.8, 122.4, 123.1, 124.7, 125.8, 127.0, 141.6, 143.1, 181.7. (Aromatic C): MS (positive mode): m/z = 286 $[M + H]^+$. *Anal.* Calcd (%) for $C_{19}H_{15}N_3$; C, 79.98. H, 5.30. N, 14.73. Found: C, 79.94. H, 5.32. N, 14.75.

2-(1-(9-Butyl-9H-carbazole-3-yl)ethylidene)malononitrile (4c). Light yellow solid; yield (75%); m.p. 90–92°C; IR (KBr): 3048, 2921, 2851, 2230, 1615, 1568, 1457, 1366, 1215, 810; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.10–1.7 (t, 3H, CH_3), 1.44–1.40 (m, 2H, CH_2), 1.89–1.80 (m, 2H, CH_2), 2.75–2.70 (m, 2H, CH_2), 4.32 (s, 3H, CH_3), 7.57–7.35 (m, 4H, Ar-H), 7.82–781 (d, 1H, Ar-H), 8.17–8.16 (d, 2H, Ar-H), 8.43 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.9, 20.5, 24.2, 31.0, 43.2 (aliphatic C) 80.7, 109.0, 109.5, 114.0, 114.5, 120.2, 120.7, 120.9, 122.6, 123.1, 125.6, 126.0, 127.0, 141.2, 142.8 175.0. (Aromatic C): MS (positive mode): m/z = 314 $[M + H]^+$. *Anal.* Calcd (%) for $C_{21}H_{19}N_3$; C, 80.48. H, 6.11. N, 13.41. Found: C, 80.50 H, 6.13 N, 13.45.

2-(1-(6-Bromo-9-methyl-9H-arbazol-3-yl)propylidene) malononitrile (4d). Yellow solid; yield (68%); m.p. 200–202°C; IR (KBr): 2998, 2891, 2230, 1715, 1688, 1449, 1366, 1255, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.30–1.21 (t, 3H, CH_3), 3.18–3.12 (m, 2H, CH_2), 3.89 (s, 3H, CH_3) 7.37–7.34 (t, 1H, Ar-H), 7.50–745 (t, 2H, Ar-H), 7.60–7.56 (t, 1H, Ar-H), 7.75–7.73 (d, 1H, Ar-H), 8.17–8.54 (d, 1H, Ar-H), 8.36 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.5, 29.3, 30.10 (aliphatic C) 80.8, 108.2, 109.1, 109.2, 113.6, 114.4, 120.4, 120.8, 122.5, 123.2, 124.7, 125.8, 127.3, 141.7, 143.1, 183.7. (Aromatic C): MS (positive mode): m/z = 365 $[M + H]^+$. *Anal*. Calcd (%) for $C_{19}H_{14}BrN_3$; C, 62.65. H, 3.87. N, 11.54. Found: C, 62.63. H, 3.83. N, 11.60.

2-(1-(9-Methyl-9H-carbazole-3-yl)propylidene)malononitrile (4e). Light yellow solid; yield (70%); m.p. 100–102°C IR (KBr): 2948, 2851, 2230, 1715, 1588, 1447, 1366, 1215, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.31–1.21 (t, 3H, CH_3), 3.17–3.12 (m, 2H, CH_2), 3.89 (s, 3H, CH_3), 7.35–7.34 (t, 1H, Ar-H), 7.52–745 (t, 2H, Ar-H), 7.60–7.57 (t, 1H, Ar-H), 7.75–7.73 (d, 1H, Ar-H), 8.54–8.17 (d, 1H, Ar-H), 8.38 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.6, 29.3, 30.1 (aliphatic C) 82.8, 108.1, 109.0, 109.2, 113.6, 114.4, 120.4, 120.8, 122.4, 123.2, 123.7, 125.9, 127.0, 141.6, 142.1, 181.1. (Aromatic C): MS (positive mode): m/z = 286 $[M + H]^+$. *Anal*. Calcd (%) for $C_{19}H_{15}N_3$; C, 79.98. H, 5.30. N, 14.73. Found: C, 79.94. H, 5.32. N, 14.75.

2-(1-(6-Bromo-9-methyl-9H-carbazole-3-yl)ethylidene) malononitrile (4f). Yellow solid; yield (72%); m.p. 170–172°C; IR (KBr): 2978, 2881, 2230, 1715, 1688, 1547, 1366, 1215, 735; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 2.75 (s, 3H, CH_3), 3.83 (s, 3H, CH_3), 7.28–7.26 (m, 2H, Ar-H), 7.45–743 (d, 1H, Ar-H), 7.60–7.58 (m, 1H, Ar-H), 7.82–7.80 (m, 1H, Ar-H), 8.32–8.22 (m, 2H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 24.2, 29.5 (aliphatic C) 81.6, 109.1, 111.6, 113.3, 113.7, 114.2, 120.9, 121.9, 123.4, 124.0, 126.2, 126.6, 129.8, 140.2, 143.2, 175.8. (Aromatic C): MS (positive mode): m/z = 351 $[M + H]^+$. *Anal*. Calcd (%) for $C_{18}H_{12}BrN_3$; C, 61.73. H, 3.45. N, 12.00. Found: C, 61.75 H, 3.46. N, 12.01.

2-(1-(9-Ethyl-9H-carbazole-3-yl)propylidene)malononitrile (4g). Light yellow solid; yield (70%); m.p. 120–122°C; IR (KBr): 2959, 2891, 2230, 1715, 1688, 1547, 1366, 1215, 825; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.34–1.22 (t, 3H, CH_3), 1.60–1.47 (t, 3H, CH_3), 3.18–3.12 (m, 2H, CH_2), 4.42–4.37 (m, 2H, CH_2), 7.35–729 (t, 1H, Ar-H), 7.52–7.49 (d, 1H, Ar-H), 7.67–7.64 (m, 1H, Ar-H), 7.75–7.73 (m, 1H, Ar-H), 8.30–8.29 (m, 2H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.6, 13.9, 30.1, 37.9 (aliphatic) 81.3, 108.08, 108.1, 109.3, 113.7, 114.3,

120.3, 120.7, 120.9, 122.7, 123.4, 124.7, 125.8, 127.0, 140.7, 142.2, 181.7. (Aromatic C): MS (positive mode): m/z = 300 $[M + H]^+$. *Anal*. Calcd (%) for $C_{20}H_{17}N_3$; C, 80.24. H, 5.72. N, 14.04. Found: C, 80.28. H, 5.70. N, 14.02.

2-(1-(6-Bromo-9-ethyl-9H-carbazole-yl)propylidene) malononitrile (4h). Yellow solid; yield (68%); m.p. 198–200°C; IR (KBr): 3048, 2950, 2851, 2230, 1715, 1588, 1447, 1366, 1215, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.32–1.20 (t, 3H, CH_3), 1.59–1.46 (t, 3H, CH_3), 3.17–3.11 (m, 2H, CH_2), 4.41–4.36 (m, 2H, CH_2), 7.36–728 (t, 1H, Ar-H), 7.51–7.49 (d, 1H, Ar-H), 7.65–7.62 (m, 1H, Ar-H), 7.75–7.73 (m, 1H, Ar-H), 8.29–8.27 (m, 2H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.6, 13.8, 30.1, 37.9 (aliphatic) 80.7, 108.1, 108.9, 109.2, 113.6, 114.3, 120.3, 120.8, 120.9, 122.6, 123.3, 124.7, 125.8, 127.0, 140.6, 142.1, 181.7. (Aromatic C): MS (positive mode): m/z = 379 $[M + H]^+$. *Anal*. Calcd (%) for $C_{20}H_{16}BrN_3$; C, 63.50. H, 4.26. N, 11.11. Found: C, 63.54. H, 4.28. N, 11.13.

2,2′-(1,1-(9-Ethyl-9H-carbazole-3,6-diyl)bis(ethan-1-yl-1-ylidene))dimalononitrile (16). Yellow solid; yield (65%); m.p. 170–172°C; IR (KBr): 3084, 2948, 2851,2230, 2158, 1715, 1688, 1447, 1366, 1215, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.02–1.00 (t, 3H, CH_3), 2.86 (s, 6H, CH_3, CH_3), 4.06–4.01 (m, 2H, CH_2), 7.28–726 (d, 2H, Ar-H), 7.45–7.43 (d, 2H, Ar-H), 7.53 (s, 1H, Ar-H), 8.15 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.2, 23.4, 39.3 (aliphatic C) 80.2, 110.4, 115.4, 118.5, 127.5, 119.2, 138.5, 148.7, 180.0. (Aromatic C): MS (positive mode): m/z = 376 $[M + H]^+$. *Anal*. Calcd (%) for $C_{24}H_{17}N_5$; C, 76.78. H, 4.56. N, 18.65. Found: C, 76.74. H, 4.58. N, 18.67.

Spectral data for title compounds. ***2-Amino-4-(9-methyl-9H-carbazole-3-yl)thiophene-3-carbonitrile (5a).*** Dark blue solid; yield (90%); m.p. 110–112°C; IR (KBr): 3420, 3330, 3284, 2948, 2851, 2158, 1715, 1588, 1447, 1366, 1215, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 3.86 (s, 3H, CH_3), 4.91 (s, 2H, NH_2), 6.38 (s, 1H, Ar-H), 7.30–721 (t, 1H, Ar-H), 7.45–7.41 (m, 2H, Ar-H), 7.54–7.50 (t, 1H, Ar-H), 7.73–7.71 (m, 1H, Ar-H), 8.16–8.14 (d, 1H, Ar-H), 8.31 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 29.20 (aliphatic C) 89.2, 104.7, 108.7, 116.2, 119.1, 119.2, 120.5, 122.7, 123.0, 125.1, 125.3, 126.1, 140.8, 141.1, 141.4, 163.4. (Aromatic C): MS (positive mode): m/z = 304 $[M + H]^+$. *Anal*. Calcd (%) for $C_{18}H_{13}N_3S$; C, 71.26. H, 4.32. N, 13.85. Found: C, 71.15. H, 4.41. N, 13.72.

2-Amino-4-(9-ethyl-9H-carbazole-3-yl)thiophene-3-carbonitrile (5b). Dark blue solid; yield (89%); m.p. 112–114°C; IR (KBr): 3410, 3340, 3184, 2958, 2851, 2177, 1715, 1564, 1437, 1376, 1205, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.49–1.45 (t, 3H, CH_3), 4.43–4.32 (m, 2H, CH_2), 4.92 (s, 2H, NH_2), 6.39 (s, 1H, Ar-H), 7.29–7.26 (m, 1H, Ar-H), 7.52–7.44 (m, 3H, Ar-H), 7.73–7.71 (m, 1H, Ar-H), 8.17–8.15 (d, 1H, Ar-H), 8.35–8.32 (d, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.9, 37.7 (aliphatic C) 89.3, 104.7, 108.7, 116.2, 119.1, 119.3, 120.7, 122.9, 123.2, 125.1, 125.3, 126.0, 139.8, 140.4, 141.1, 163.3. (Aromatic C): MS (positive mode): m/z = 318 $[M + H]^+$. *Anal*. Calcd (%) for $C_{19}H_{15}N_3S$; C, 71.90. H, 4.76. N, 13.24. Found: C, 71.82. H, 4.81. N, 13.15.

2-Amino-4-(9-butyl-9H-carbazole-3-yl)thiophene-3-carbonitrile (5c). Dark blue solid; yield (85%); m.p. 98–100°C; IR (KBr): 3430, 3320, 3194, 2958, 2871, 2197, 1715, 1594, 1457, 1386, 1205, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.00–0.96 (t, 3H, CH3), 1.46–1.43 (t, 2H, CH_2), 1.19–1.89 (d, 2H, CH_2), 4.35–4.33 (d, 2H, CH_2), 4.94 (s, 2H, NH_2), 6.38 (s, 1H, Ar-H), 7.29–7.28 (s, 1H, Ar-H), 7.51–7.47 (m, 3H, Ar-H), 7.72–7.70 (s, 1H, Ar-H), 8.17–8.15 (d, 1H, Ar-H), 8.32 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.9, 20.6, 31.2, 42.9 (aliphatic C) 89.2, 104.7, 108.9, 116.2, 119.1, 119.2, 120.6, 122.8, 123.1, 125.1, 125.22, 125.98, 140.29, 140.91, 141.08, 163.4. (Aromatic C): MS (positive mode): m/z = 346 $[M + H]^+$. *Anal*. Calcd (%) for $C_{21}H_{19}N_3S$; C, 73.01. H, 5.54. N, 12.16. Found: C, 73.12. H, 5.48. N, 12.26.

2-Amino-4-(6-bromo-9-methyl-9H-carbazole-3-yl)thiophene-3-carbonitrile (8). Brown solid; yield (80%); m.p. 258–260°C; IR (KBr): 3320, 3205, 2197, 1621, 1506, 1452, 1380, 1287, 1238, 1145, 854, 783, 706; ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ 3.88 (s, 3H, CH_3), 6.51 (s, 1H, Ar-H), 7.26 (s, 2H, NH_2), 7.68–7.59 (m, 4H, Ar-H), 8.39–8.38 (t, 2H, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6): 29.7 (aliphatic C) 84.4, 109.9, 111.5, 111.9, 117.4, 119.8, 121.6, 123.4, 124.3, 126.3, 162.5, 128.8, 139.9, 140.2, 140.9, 166.7. (Aromatic C): MS (positive mode): m/z = 381 $[M + H]^+$. *Anal*. Calcd (%) for $C_{18}H_{12}BrN_3S$; C, 56.55. H, 3.16. N, 10.99. Found: C, 56.48. H, 3.23. N, 10.85.

2-Amino-5-methyl-4-(9-methyl-9H-carbazole-3-yl)thiophene-3-carbonitrile (14a). Brown solid; yield (75%); m.p. 190–192°C; IR (KBr): 3320, 3240, 3124, 2958, 2841, 2167, 1715, 1584, 1437, 1356, 1226, 809; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 2.30 (s, 3H, CH_3), 3.87 (s, 3H, CH_3), 7.28–7.26 (m, 1H, Ar-H), 7.53–742 (m, 4H, Ar-H), 8.08–8.07 (d, 1H, Ar-H), 8.13–8.12 (d, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.5, 29.2 (aliphatic C) 90.6, 108.5, 108.6, 116.2, 118.5, 119.1, 120.5, 121.0, 122.7, 122.8, 124.5, 125.9, 126.8, 136.1, 140.5, 141.4, 159.57. (Aromatic C): MS (positive mode): m/z = 318 $[M + H]^+$. *Anal*. Calcd (%) for $C_{19}H_{15}N_3S$; C, 71.90. H, 4.76. N, 13.24. Found: C, 71.95. H, 4.82. N, 13.15.

2-Amino-4-(6-bromo-9-methyl-9H-carbazole-3-yl)-5-methylthiophene-3-carbonitrile (12a). Light yellow solid; yield (70%); m.p. 242–244°C; IR (KBr): 3430, 3298, 3205, 2197, 1621, 1512, 1446, 1282, 1137, 1019, 783; ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ 2.17 (s, 3H, CH_3), 3.88 (s, 3H, CH_3), 7.06 (s, 1H, Ar-H), 7.46–

743 (m, 1H, Ar-H), 7.58 (s, 1H, Ar-H), 7.67–7.65 (d, 1H, Ar-H), 8.18–8.17 (d, 1H, Ar-H), 8.45 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6): 13.5, 29.7 (aliphatic C) 85.8, 109.8, 111.5, 111.8, 115.6, 117.3, 121.4, 121.8, 123.5, 124.3, 125.5, 128.0, 128.7, 135.3, 140.1, 140.7, 162.9. (Aromatic C): MS (positive mode): m/z = 395 $[M + H]^+$. *Anal*. Calcd (%) for $C_{19}H_{14}BrN_3S$; C, 57.58. H, 3.56. N, 10.60. Found: C, 57.48. H, 3.51. N, 10.52.

2-Amino-4-(6-bromo-9-ethyl-9H-carbazole-3-yl)-5-methylthiophene-3-carbonitrile (12b). Brown solid; yield (68%); m.p. 160–162°C; IR (KBr); 3330, 3215, 2197, 1621, 1516, 1452, 1350, 1287, 1238, 1155, 854, 773, 716; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.45–1.43 (t, 3H, CH_3), 2.30 (s, 3H, CH_3) 4.37–4.32 (m, 2H, CH_2), 7.30–7.27 (d, 1H, Ar-H), 7.57–7.44 (m, 3H, Ar-H), 8.01–8.00 (d, 1H, Ar-H), 8.22–8.21 (d, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.5, 13.8, 37.8 (aliphatic C) 90.5, 108.8, 110.1, 111.8, 116.2, 118.7, 121.3, 121.3, 121.9, 123.3, 124.6, 124.9, 127.6, 128.6, 135.8, 138.9, 139.7, 159.6. (Aromatic C): MS (positive mode): m/z = 409 $[M + H]^+$. *Anal*. Calcd (%) for $C_{20}H_{16}BrN_3S$; C, 58.54. H, 3.93. N, 10.24. Found: C, 58.42. H, 3.31. N, 10.41.

2-Amino-4-(9-ethyl-9H-carbazole-3-yl)-5-methylthiophene-3-carbonitrile (14b). Light pink solid; yield (70%); m.p. 203–205°C; IR (KBr): 3320, 3140, 3084, 2958, 2871, 2157, 1715, 1534, 1457, 1346, 1205, 805; ^{1}H-NMR (400 MHz, $CDCl_3$/TMS): δ 1.46–1.42 (t, 3H, CH_3), 2.27 (s, 2H, CH_3), 4.39–4.35 (t, 2H, CH_2), 4.70 (s, 2H, NH_2), 7.25–7.21 (m, 1H, Ar-H), 7.49–7.40 (m, 4H, Ar-H), 78.09–8.05 (d, 1H, Ar-H), 8.11 (s, 1H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 13.5, 13.9, 37.7 (aliphatic C) 90.6, 108.5, 108.6, 116.2, 118.5, 119.0, 120.6, 121.1, 122.8, 122.9, 124.4, 125.9, 126.8, 136.1, 139.4, 140.3, 159.6. (Aromatic C): MS (positive mode): m/z = 332 $[M + H]^+$. *Anal*. Calcd (%) for $C_{20}H_{17}N_3S$; C, 72.48. H, 5.17. N, 12.68. Found: C, 72.37. H, 5.23. N, 12.56.

4,4"-(9-Ethyl-9H-carbazole-3,6-diyl)bis(2-aminothiophene-3-carbonitrile) (17). Dark blue solid; yield (55%); m.p. 104–106°C; IR (KBr): 3415, 3340, 3154, 2954, 2841, 2166, 1715, 1664, 1437, 1356, 1256, 805; ^{1}H-NMR (400 MHz, DMSO-d_6/TMS): δ 1.35 (s, 3H, CH_3), 3.34 (s, 2H, CH_2), 4.49 (s, 2H, NH_2), 6.54 (s, 2H, Ar-H), 7.29 (s, 3H, Ar-H), 7.68 (s, 3H, Ar-H), 8.35 (s, 2H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$): 14.3, 37.7 (aliphatic C) 84.3, 104.2, 109.9, 117.5, 119.4, 122.7, 125.8, 126.3, 139.9, 140.0, 166.8. (Aromatic C): MS (positive mode): m/z = 440 $[M + H]^+$. *Anal.* Calcd (%) for $C_{24}H_{17}N_5S$; C, 65.58 H, 3.90. N, 15.93. Found: C, 65.48 H, 3.96. N, 15.82.

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