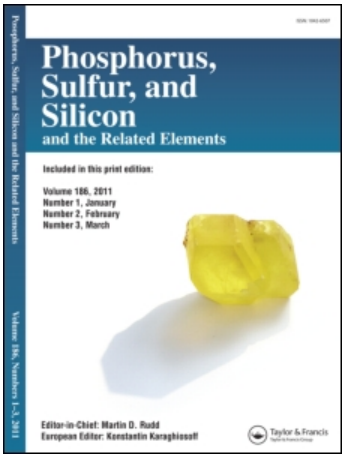

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Thiocarbamoyl in Organic Synthesis: Synthesis of Some New Arylazothiophene and Arylazopyrazole Derivatives

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Thiocarbamoyl in Organic Synthesis: Synthesis of Some New Arylazothiophene and Arylazopyrazole Derivatives

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*Arylazothiocarbamoyl derivatives **4a–e** were utilized for the synthesis of several new thiophene and pyrazole derivatives. Compound **4** reacted with phenacyl bromide, ethyl bromoacetate, chloroacetonitrile, chloroacetone and hydrazine hydrate to yield thiophene and pyrazole derivatives **7**, **10**, **12**, **14**, and **16**, respectively.*

Keywords Benzoylacetone; phenylisothiocyanate; pyrazole; thiophene

INTRODUCTION

Aryl isothiocyanates are versatile reagents, which have been used as synthetic intermediate to prepare biologically active heterocyclic compounds.[1] As a part of our program of developing new, simple, and efficient procedures for the synthesis of new aromatic compounds using readily available aryl isothiocyanates, we have recently affected recyclization of thiocarbamoyl in pyrazoles and thiazoles.[2–5] This procedure appears to be a fundamental type of thiocarbamoyl-into- pyrazole ring transformation.

RESULTS AND DISCUSSION

We have been particularly interested in studying if reactions of such thiocarbamoyl might be extended to include more general synthesis of other classes of organic compounds and its utility as synthetic intermediate for the synthesis of new heterocyclic compounds. The present work reports on the synthesis of several new arylazothiophene and arylazopyrazole derivatives by the reaction of thiocarbamoyl of the type **4** with compounds containing an active methylene group in the presence of a base. Reactions of this type have not been reported previously, but

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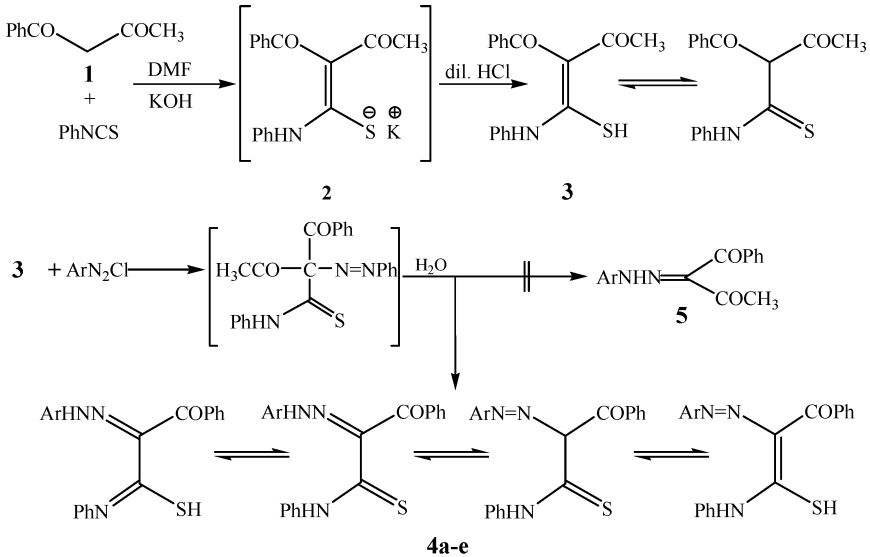
they were found to give products in excellent yields under very mild conditions. Moreover, the resulting thiophene and pyrazole derivatives have latent functional substituents, which have potential for further chemical transformations and new routes for the preparation of substituted thiophene and pyrazole derivatives with possible biological activity. Now, we have extended our synthetic program to the synthesis of otherwise inaccessible heterocyclic ring system utilizing phenyl isothiocyanate as a key starting material. It is known that a great variety of reactants bearing the N=C=S fragment undergoes cyclization on reaction with α-halocarbonyl compounds to afford thiazoles, 2,3-dihydrothiazoles,[6] which have been shown to exhibit antiprotozoal,[7] and fungicidal properties.[8]

Thus, the base-prompted reaction of the acidic methylene compound **1** with phenyl isothiocyanate in dry DMF at room temperature in basic medium led to the formation of the non-isolable intermediate **2** which gave thiocarbamoyl derivative **3** upon treatment with dilute HCl. Treatment of **3** with aromatic diazonium salts in the presence of sodium acetate affected acetyl cleavage with the formation of arylazothiocarbamoyl derivatives **4a–e** rather than the expected product **5**. This result is in agreement with the previously reported work[9–14] (Scheme 1).



4a, Ar= C_6H_5; **b**, Ar= C_6H_4-CH_3-*p*; **c**, Ar= C_6H_4-OCH_3-*p*
d, Ar= C_6H_4-NO_2-*p*; **e**, Ar= C_6H_4-Cl-*p*

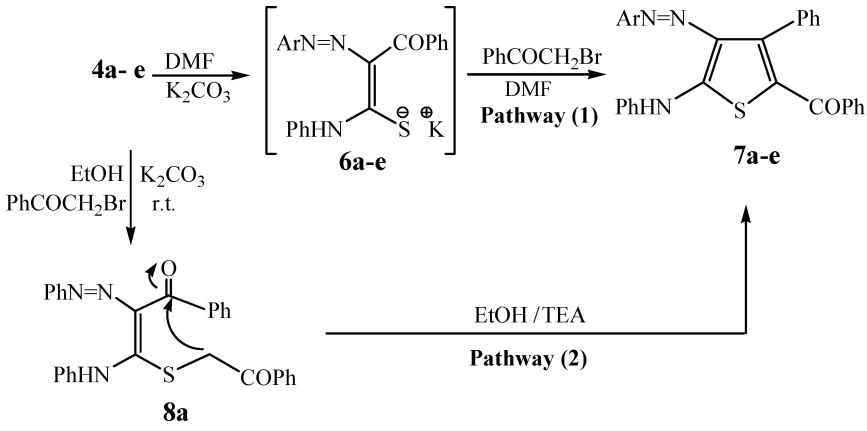
SCHEME 1

Assignment of the product **3** was based on elemental analysis, IR and ^{1}H-NMR spectral data. The IR spectrum showed absorption bands at 3229, 3125, 1600, and 1283 cm^{-1} attributable to the enolic OH, NH, C=O, C=S, functions, respectively. ^{1}H NMR spectrum of **3** displayed multiplet signals at σ 7.1–7.5 ppm for aromatic protons and exchangeable proton at 11.9 ppm for NH proton. Its mass spectrum showed molecular ion peak m/z = 297 (M^+, 14%). On the other hand, the structure of the newly prepared hydrazone derivatives **4a–e** was based on their correct elemental analysis and spectral data. In general, the IR spectra showed absorption bands due to C=O, C=S and NH at 1640, 1280, and 3250 cm^{-1}, respectively. The ^{1}H NMR spectrum of compound **4a** displayed multiplet signals at σ 6.8–7.8 ppm for aromatic protons and two exchangeable protons at σ 13.9 and 16.4 ppm for two NH protons. An additional conformation for the correct structure was supported by its mass spectroscopic measurements. The mass spectrum showed the molecular ion peak (m/z = 359, M^+).

In this paper, we describe a generally applicable extension of this synthetic approach, first reported by Hantzsch and Weber.[15] Thus, the base-prompted reaction of compounds **4a** with potassium carbonate in dry DMF at room temperature affords the non-isolable intermediate **6a**. Stirring of **6** with phenacyl bromide in DMF overnight yielded a product **7a**, which analyzed correctly for $C_{29}H_{21}N_3OS$. The structure **7a** was inferred from its spectral data. Thus, the IR spectrum showed absorption bands at 3150, 1660, and 1600 cm^{-1} corresponding to NH, CO, and N=N functions. Its ^{1}H-NMR spectrum showed two multiplet signals integrated for (20H) centered at 7.4 and 8.0 (aromatic protons) and a singlet (1H) at σ 10.2. On shaking the compound with D_2O, the broad band signal at σ 10.2 disappeared. Based on the foregoing data, structure **7a** was assigned to this product. The structure **7a** was further confirmed by alternative synthesis. Thus, it was found that stirring of **4a** with phenacyl bromide in the presence of potassium carbonate in ethanol at room temperature produced acyclic intermediate **8a**. Structure **8a** was suggested for the reaction product based on both elemental and spectral analyses. The IR spectrum showed the presence of carbonyl absorption bands at 1640 and 1623 cm^{-1}, N = N function at 1600 cm^{-1}, respectively.

Refluxing **8a** in ethanol with few drops of TEA led to the formation of a product identical in all respects (m.p. mixed m.p., IR) to **7a**. Similarly, compounds **7b–e** were synthesized by pathway (1) (Scheme 2).

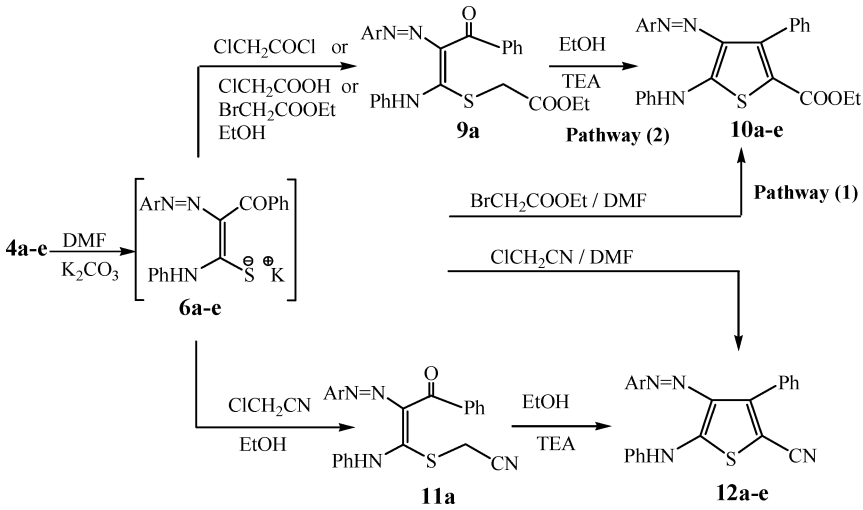
The addition of two or more equivalents of ethyl bromoacetate, chloroacetonitrile, chloroacetone leads only to thiophenes**10**, **12**, and **14** in good yields. Thus, condensation of the intermediate salt with an equimolar amount of chloroacetyl chloride or with chloroacetic acid in



SCHEME 2

ethanol, a product that analyzed for $C_{25}H_{23}N_3O_3S$ was isolated in each case in good yield. The acyclic structure **9a** was established based on its IR spectrum that showed bands related to NH and CO functions. Its ^1H NMR spectrum reveals a multiplet at (σ ppm) 6.8–7.7 (15H, aromatic), a triplet signal at σ 1.3 (3H, CH_3), singlet at σ 3.7 (2H), quartet at σ 4.3 (2H, CH_2) and a D_2O exchangeable NH at σ 12.9 ppm. Alternatively, treatment of the intermediate **6a** with ethyl bromoacetate in ethanol gives a single product, which is identical in all respects to **9a** (m.p. mixed m.p. and IR spectrum). The mass spectrum of **9a** showed a molecular formula $C_{25}H_{23}N_3O_3S$ ($M^+ = 445$). Refluxing of **9a** in ethanol with a catalytic amount of TEA or leaving it in DMF containing potassium carbonate at room temperature overnight afforded the corresponding thiophene derivative **10a**. In a similar manner, **10a**–**e** were prepared by pathway (1).

Similarly, when the intermediate potassium salt **6a** is stirred with chloroacetonitrile in ethanol at room temperature, the corresponding acyclic intermediate **11a** is exclusively isolated in good yield. The structure **11** has been confirmed based on elemental and spectral data, e.g. the IR spectrum exhibits bands at 3200 (NH), 2220, and 1695 cm^{-1} (cyano and carbonyl group). Its ^1H NMR spectrum reveals CH_2 signals at σ 3.23 ppm. Furthermore, heating of the intermediate **11a** in ethanol containing a catalytic amount of TEA affords the thiophene derivative **12a**. The thiophene structure **12a** was established based on its IR spectrum, which showed bands related to NH and CN functions. Its ^1H NMR spectrum reveals a multiplet at (σ ppm) 7.31–7.56 (15H,

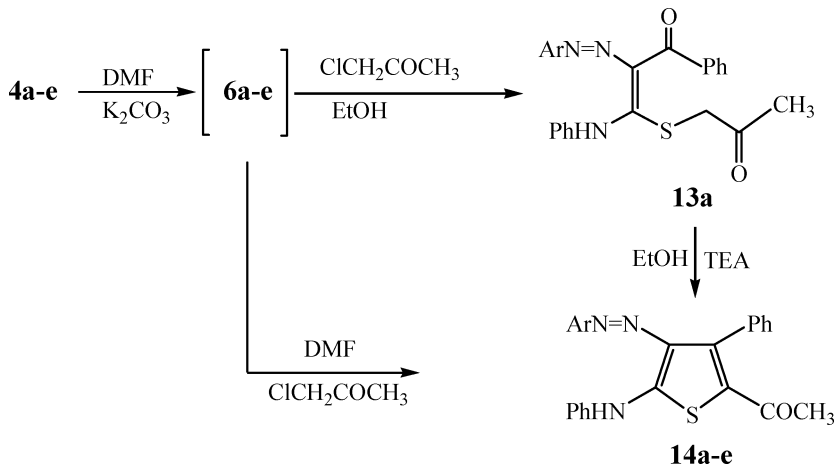


SCHEME 3

aromatic), broad signals at σ 14.2 ppm (1H, NH). On the other hand, it has been found that compounds **12a–e** are directly formed by treatment of **6a–e** with chloroacetonitrile in dimethylformamide and in the presence of potassium carbonate at room temperature overnight by pathway (1) (Scheme 3).

Compound **6a** reacted readily with chloroacetone in the presence of ethanol at room temperature to afford the acyclic intermediate **13a** by KCl elimination. Refluxing **13** in ethanol with a catalytic amount of TEA gave the thiophene derivative **14a** whose structure was confirmed by its alternative synthesis. Thus, stirring **6a–e** with chloroacetone in DMF overnight affords the thiophene derivative **14a–e** in reasonably good yield (Scheme 4).

On the other hand, treatment of the key intermediate **4b** with hydrazine hydrate in DMF gave a single product, which analyzed correctly for $C_{22}H_{19}N_5$ **(16b)**. The structure of **16b** was inferred from its spectral data. Thus, the infrared spectrum of **16b** showed a band at 3189 and 3229 cm^{-1}, corresponding to the NH groups, and avoided a band due to the carbonyl group. The ^1H NMR spectrum revealed a singlet at σ 2.3 assigned for the methyl protons, a broad band located at σ 10.1 and 12.0 assignable to the NH protons, and a multiplet at σ 7.0–8.2, assigned for aromatic protons. The formation of **16a–e** is assumed to proceed via the replacement of the SH group by the hydrazine moiety to give the intermediate **15** which then cyclized via the carbonyl group



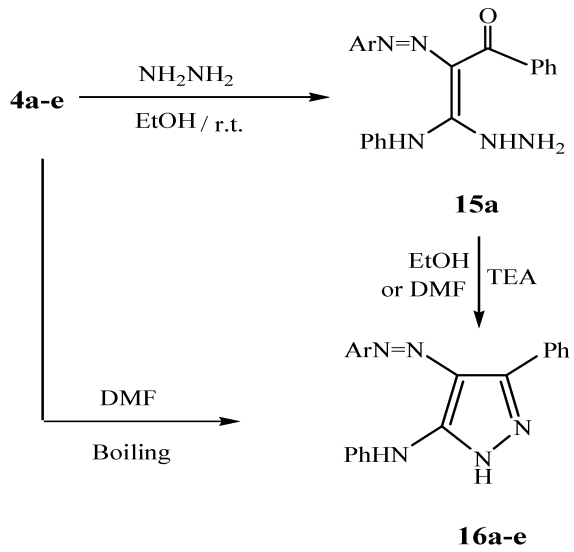
SCHEME 4

to afford the final isolable products **16a–e**. In fact, the structure of **16** was further confirmed by alternative synthesis. Thus, it has been found that treatment of **4a** with hydrazine hydrate for long time in ethanol produced the intermediate **15a**. Refluxing **15a** in ethanol containing a catalytic amount of TEA or in DMF lead to the formation of a product identical in all respects (m.p., mixed m.p., IR) with **16a**.[16] Structure **15a** is suggested for the reaction product based on both elemental and spectral analyses. The infrared spectrum of compound **15a** showed absorption at 1640 (CO), 3340 (NH), 3418, and 3550 $cm^{-1}(NH_2)$ groups, and the ^1H- NMR spectrum revealed a broad signal at σ 6.4 assigned for NH_2 protons, a multiplet at σ 7.2–7.8 for aromatic protons, and a singlet at σ 12.7 and 14.0 ppm for NH protons (Scheme 5).

These results indicate that the reaction of thiocarbamoyls and bifunctional reagents provides an excellent route for the synthesis of five—otherwise not easily accessible—arylazothiophenes and pyrazoles. The compounds synthesized will be subjected to biological testing.

EXPERIMENTAL

All melting points are uncorrected. FTIR spectra (KBr disk) were recorded on a Nicolet Magna. IR-Model 550 Spectrophotometers, ^1H NMR spectra in DMSO, were determined on Brucker Wpsy 200 MHZ spectrometer with TMS as internal standard and the chemical shifts are in σ ppm. Mass spectra were recorded at 70 eV with a Varian MAT 311.



8, **9**, **11**, **13**, **15a**, Ar= Ph

7, **10**, **12**, **14**, **16a**, Ar= C_6H_5; **b**, Ar= C_6H_4-CH_3-*p*; **c**, Ar= C_6H_4-OCH_3-*p*; **d**, Ar= C_6H_4-NO_2-*p*; **e**, Ar= C_6H_4-Cl-*p*

SCHEME 5

Synthesis of Thiocarbamoyl Derivative (3)

To a cold suspension of potassium hydroxide (1.4 g, 25 mmol) in DMF (30 ml) was added the benzoyl acetone (4.05 g, 25 mmol), followed by phenyl isothiocyanate (3.375 g, 25 mmol). The mixture was stirred overnight at room temperature and then poured onto ice-cold water. Acidification using dilute HCl until the medium becomes acidic gave solid product **3,** which was filtered off, washed with water, dried and crystallized from aqueous ethanol to give compound **3** (cf. Table I).

Coupling of (3) with Aromatic Diazonium Salts. Formation of Monoazothiocarbamoyl Derivatives (4a–e)—General Procedure

A well–stirred solution of aromatic amines (20 mmol) in concentrated HCl (6 ml) and water (4 ml) was cooled in an ice bath and diazotized with a solution of sodium nitrite (1.39 g, 20 mmol) in water (5 ml).

The above cold diazonium solution was added drop wise to a well stirred cold solution of **3** in ethanol (10 ml) containing sodium acetate (1.75 g, 20 mmol). The reaction mixture was stirred for 1–2 h until

TABLE I Characterization Data of Compounds (3–16)

Compound No	M.P °C	Yield %	Mol. formula	Microanalysis calculated found C	Microanalysis calculated found H	Characterization
3	140	100	$C_{17}H_{15}NO_2S$ (297.4)	68.66 68.50	5.08 4.90	IR: 3229, 3125, 1600, 1283 cm^{-1} (OH, NH, C=O, C=S); ^1H NMR: (DMSO), σ 2.5 (s, 3H, CH_3), 7.1–7.5 (m, 10H, Ar), 11.9 (s, 1H, NH); MS: (m/z) 297 (M^+, 14%), 255 (17%), 222 (25%).
4a	140	80	$C_{21}H_{17}N_3OS$ (359.4)	70.17 70.00	4.77 4.60	IR: 3250, 1640, 1280 cm^{-1} (NH, C=O, C=S); ^1H NMR: ($CDCl_3$), σ 6.8–7.8 (m, 15H, Ar), 13.9 and 16.4 (s, 2H, 2NH); MS: (m/z) 359 (M^+, 19%), 239 (13%), 161 (4.5%), 105 (80%), 77 (100%).
b	174	88	$C_{22}H_{19}N_3OS$ (373.5)	70.75 70.75	5.13 5.08	IR: 3250, 2919, 1640, 1280 cm^{-1} (NH, CH_3, C=O, C=S); ^1H NMR: (DMSO), σ 2.3 (s, 3H, CH_3), 7.1–8.2 (m, 14H, Ar), 10.7 and 12.3 (s, 2H, 2NH); MS: (m/z) 373 (M^+, 15%), 239 (12%), 105 (73%), 77 (96%).
c	172	85	$C_{22}H_{19}N_3O_2S$ (389.5)	67.84 67.83	4.92 4.80	IR: 3250, 2937, 1640, 1280 cm^{-1} (NH, CH_3, C=O, C=S); ^1H NMR: (DMSO), σ 4.0 (s, 3H, CH_3), 7.0–8.7 (m, 14H, Ar), 12.6 and 16.4 (s, 2H, 2NH); MS: (m/z) 389 (M^+, 24%), 239 (15%), 161 (18%), 105 (80%), 77 (100%).
d	218	78	$C_{21}H_{16}N_4O_3S$ (404.4)	62.36 62.30	3.99 3.99	IR: 3250, 1640, 1550, 1280 cm^{-1} (NH, C=O, NO_2, C=S); ^1H NMR: (DMSO), σ 6.8–7.9 (m, 14H, Ar), 12.5 and 14.8 (s, 2H, 2NH); MS: (m/z) 404 (M^+, 18%), 402 (7%), 239 (30%), 161 (10%), 105 (100%), 77 (97%).
e	200	72	$C_{21}H_{16}N_3OSCl$ (393.9)	64.03 64.00	4.09 4.03	IR: 3250, 1640, 1280 cm^{-1} (NH, C=O, C=S); ^1H NMR: ($CDCl_3$), σ 7.0–7.6 (m, 14H, Ar), 10.2 and 14.6 (s, 2H, 2NH); MS: (m/z) 393 (M^+, 17%), 239 (20%), 125 (10%), 105 (75%), 77 (100%).
7a	180	68	$C_{29}H_{21}N_3OS$ (459.6)	75.79 75.79	4.61 4.59	IR: 3150, 1660, 1600 cm^{-1} (NH, C=O, N=N); ^1H NMR: ($CDCl_3$), σ 7.4–8.0 (m, 20H, Ar), 10.2 (s, 1H, NH); MS: (m/z) 459 (M^+, 10%), 428 (18%), 105(20%), 77 (80%).

(*continues on next page*)

TABLE I Characterization Data of Compounds (3–16) (*Continued*)

Compound No	M.P °C	Yield %	Mol. formula	Microanalysis calculated found C	H	Characterization
b	200	60	$C_{30}H_{23}N_3OS$ (473.6)	76.08 76.00	4.90 4.80	IR: 3321, 2919, 1660, 1602 cm^{-1}(NH, CH_3, C=O, N=N); ^1H NMR: (DMSO), σ 2.3 (s, 3H, CH_3), 7.0–7.8 (m, 19H, Ar), 14.2 (s, 1H, NH); MS: (m/z) 473 (M^+, 70%), 472 (18%), 239 (20%), 105 (25%), 77 (80%).
c	210	64	$C_{30}H_{23}N_3O_2S$ (489.6)	73.60 73.60	4.74 4.60	IR: 3344, 2923, 1684, 1598 cm^{-1} (NH, CH_3, C=O, N=N); ^1H NMR: (DMSO), σ 3.9 (s, 3H, CH_3), 6.9–7.5 (m, 19H, Ar), 12.3 (s, 1H, NH); MS: (m/z) 489 (M^+, 68%), 458 (40%), 368 (20%), 105 (28%), 77 (100%),
d	226	74	$C_{29}H_{20}N_4O_3S$ (504.6)	69.30 69.00	4.00 4.00	IR: 3342, 1680, 1549, 1590 cm^{-1} (NH, C=O, NO_2, N=N); ^1H NMR: ($CDCl_3$), σ 7.0–8.4 (m, 19H, Ar), 10.8 (s, 1H, NH); MS: (m/z) 504 (M^+, 80%), 501 (24%), 456 (16%), 105 (70%), 77 (90%).
e	160	55	$C_{29}H_{20}N_3OSCl$ (494)	70.51 70.51	4.08 4.08	IR: 3320, 1660, 1600 cm^{-1} (NH, C=O, N=N); ^1H NMR: (DMSO), σ (7.0–7.6) (m, 19H, Ar), 14.2 (s, 1H, NH); MS: (m/z) 494 (M^+, 60%), 492 (18%), 105 (70%).
8a	153	58	$C_{29}H_{23}N_3O_2S$ (477.5)	72.94 72.94	4.85 4.79	IR: 3150, (1640 and 1623), 1600 cm^{-1} (NH, two C=O, N=N); ^1H NMR: (DMSO): σ 4.2 (s, 2H, CH_2), 6.8–7.9 (m, 20H, Ar), 10.5 (s, 1H, NH).
9a	170	60	$C_{25}H_{23}N_3O_3S$ (445.5)	67.40 67.30	5.20 5.00	IR: 3150, (170 and 1625), 1600 cm^{-1} (NH, two C=O, N=N); ^1H NMR: (DMSO), σ 1.3 (t, 3H, CH_3), 3.7 (s, 2H, CH_2), 4.3 (q, 2H, CH_2), 6.8–7.7 (m, 15H, Ar), 12.9 (s, 1H, NH); MS: (m/z) 445 (M^+, 10%).
10a	180	55	$C_{25}H_{21}N_3O_2S$ (427.5)	70.24 70.19	4.95 4.95	IR: 3327, 1700, 1594 cm^{-1} (NH, C=O, N=N); ^1H NMR: ($CDCl_3$), σ 1.1 (t, 3H, CH_3), 4.1 (q, 2H, CH_2), 7.0–7.6 (m, 15H, Ar), 14.3 (s, 1H, NH); MS: (m/z) 427 (M^+, 80%), 105 (70%), 77 (90%).

b	170	75	$C_{26}H_{23}N_3O_2S$ (441.5)	70.72 70.72	5.25 5.25	IR: 3427, 1734, 1580 cm^{-1}(NH, C=O, N=N); ^1H NMR: ($CDCl_3$), σ 1.1(t, 3H, CH_3), 2.3 (s, 3H, CH_3), 4.2 (q, 2H, CH_2), 7.0–7.6 (m, 14H, Ar), 14.1 (s, 1H, NH); MS: (m/z) 441 (M^+, 50%), 105 (M^+, 70%).
c	140	62	$C_{26}H_{23}N_3O_3S$ (457.5)	68.25 68.25	5.07 5.07	IR: 3344, 1684, 1608 cm^{-1} (NH, C=O, N=N); ^1H NMR: (DMSO), σ 1.3 (t, 3H, CH_3), 3.9 (s, 3H, CH_3), 4.2 (q, 2H, CH_2), 7.0–7.6 (m, 14H, Ar), 14.2 (s, 1H, NH); MS: (m/z) 457 (M^+, 10%), 426 (12%), 105 (70%).
d	190	70	$C_{25}H_{20}N_4O_4S$ (472.5)	63.55 63.55	4.27 4.00	IR: 3345, 1718, 1540, 1594 cm^{-1} (NH, C=O, NO_2, N=N); ^1H NMR: ($CDCl_3$), σ 1.1(t, 3H, CH_3), 4.1 (q, 2H, CH_2), 7.3–8.4 (m, 14H, Ar), 14.9 (s, 1H, NH); MS: (m/z) 472 (M^+, 10%), 426 (24%), 105 (77%), 77 (89%).
e	180	57	$C_{25}H_{20}N_3O_2SCl$ (462)	65.00 65.00	4.36 4.30	IR: 3316, 1715, 1690 cm^{-1}(NH, C=O, N=N); ^1H NMR: ($CDCl_3$), σ 1.1(t, 3H, CH_3), 4.1 (q, 2H, CH_2), 7.2–7.6 (m, 14H, Ar), 14.1 (s, 1H, NH); MS: (m/z) 462 (M^+, 80%).
11a	160	60	$C_{23}H_{18}N_4OS$ (398.48)	69.33 69.33	4.55 4.55	IR: 3200, 2220, 1695 cm^{-1} (NH, CN, C=O); ^1H NMR: (DMSO), σ 3.23 (s, 2H, CH_2), 7.5–8.0 (m, 15H, Ar), 14.2 (s, 1H, NH); MS: (m/z) 398 (M^+, 90%).
12a	204	52	$C_{23}H_{16}N_4S$ (380.5)	72.61 72.61	4.24 4.00	IR: 3327, 2196, 1595 (NH, CN, N=N); ^1H NMR: (DMSO), σ 7.31–7.56 (m, 15H, Ar), 14.2 (s, 1H, NH); MS: (m/z) 380 (M^+, 86%), 365 (15%), 105 (77%), 77 (100%).
b	176	58	$C_{24}H_{18}N_4S$ (394.3)	73.07 73.00	4.60 4.50	IR: 3324, 2199 cm^{-1}(NH, CN);^1H NMR: (DMSO), σ 2.3 (s, 3H, CH_3), 7.3–7.6 (m, 14H, Ar), 13.8 (s, 1H, NH); MS: (m/z) 394 (M^+, 88%), 379(18%), 105 (78%).

(*continues on next page*)

Characterization Data of Compounds (3–16) (*Continued*)

Compound No	M.P °C	Yield %	Mol. formula	Microanalysis calculated found C	H	Characterization
c	184	53	$C_{24}H_{18}N_4OS$ (410.5)	70.22 70.00	4.42 4.00	IR: 3345, 2201cm^{-1} (NH, CN);^{1}H NMR: (DMSO), σ 4.2 (s, 3H, CH_3), 7.2–8.0 (m, 14H, Ar), 14.2 (s, 1H, NH); MS: (m/z) 410 (M^+, 88%), 381 (70%), 105 (70%).
d	210	57	$C_{23}H_{15}N_5O_2S$ (425.5)	64.93 64.80	3.55 3.40	IR: 3319, 2202, 1593, 1531 cm^{-1}(NH, CN, N=N, NO_2); ^{1}H-NMR: ($CDCl_3$), σ 7.3–8.0 (m, 14H, Ar), 14.3 (s, 1H, NH); MS: (m/z) 425 (M^+, 100%), 379 (24%), 105 (70%).
e	190	83	$C_{23}H_{15}N_4SCl$ (414.9)	66.58 66.58	3.55 3.50	IR: 3420, 2198, 1568 cm^{-1} (NH, CN, N=N); ^{1}H-NMR: ($CDCl_3$), σ 7.2–8.5 (m, 14H, Ar), 14.3 (s, 1H, NH); MS: (m/z) 414 (M^+, 68%).
13a	178	76	$C_{23}H_{19}N_3O_2S$ (401.49)	68.81 68.80	4.77 4.76	IR: 3250, 1660, 1600 cm^{-1} (NH, C=O, N=N); ^{1}H-NMR: (DMSO), σ 2.5 (s, 3H, CH_3), 3.2 (s, 2H, CH_2), 7.5–8.0 (m, 15H, Ar), 14.5 (s, 1H, NH).
14a	140	74	$C_{24}H_{19}N_3OS$ (397.5)	72.52 72.40	4.82 4.70	IR: 3337, 1645, 1597 cm^{-1} (NH, C=O, N=N); ^{1}H-NMR: ($CDCl_3$), σ 2.1 (s, 3H, CH_3), 7.3–7.8 (m, 15H, Ar), 14.2 (s, 1H, NH); MS: (m/z) 397 (M^+, 78%).
b	140	50.5	$C_{25}H_{21}N_3OS$ (411.5)	72.97 72.97	5.14 5.00	IR: 3345, 1645, 1598 (NH, C=O, N=N); ^{1}H-NMR ($CDCl_3$), σ 1.9 (s, 3H, CH_3), 2.3 (s, 3H, CH_3), 7.1–7.6 (m, 14H, Ar), 14.1 (s, 1H, NH); MS: (m/z) 411 (M^+, 15%).
c	192	63	$C_{25}H_{21}N_3O_2S$ (427.5)	70.24 70.24	4.95 4.95	IR: 3345, 1643, 1600 cm^{-1} (NH, C=O, N=N); ^{1}H-NMR ($CDCl_3$), σ 1.9 (s, 3H, CH_3), 4.2 (s, 3H, CH_3), 7.2–8.0 (m, 14H, Ar), 14.1 (s, 1H, NH); MS: (m/z) 427 (M^+, 25%).
d	160	86	$C_{24}H_{18}N_4O_3S$ (442.5)	65.14 65.14	4.10 4.00	IR: 3445, 1645, 1515 cm^{-1} (NH, C=O, NO_2); ^{1}H-NMR: ($CDCl_3$), σ 1.9 (s, 3H, CH_3), 7.3–7.58 (m, 14H, Ar), 14.7 (s, 1H, NH); MS: (m/z) 442 (M^+, 12%).
e	140	69.5	$C_{24}H_{18}N_3OSCl$ (431.9)	66.74 66.74	4.20 4.00	IR: 3321, 1622, 1594 cm^{-1}(NH, C=O, N=N); ^{1}H-NMR: ($CDCl_3$), σ 1.9 (s, 3H, CH_3), 7.2–7.6 (m, 14H, Ar), 13.85 (s, 1H, NH); MS: (m/z) 431 (M^+, 78%).

15a	168	65	$C_{21}H_{19}N_5O$ (357.4)	70.57 70.50	5.35 5.30	IR: 3550, 3340, 1640 cm^{-1} (NH_2, NH, C=O); ^{1}H-NMR: (DMSO), σ 6.4 (s, 2H, NH_2), 7.2–7.8 (m, 15H, Ar), 12.7 and 14.0 (s, 2H, 2NH).
16a	256	48	$C_{21}H_{17}N_5S$ (339.4)	74.32 74.32	5.05 5.00	IR: 3235 and 3192, 1595 cm^{-1}(two NH, N=N); ^{1}H-NMR: (DMSO), σ 7.3–8.0 (m, 15H, Ar), 10.0 and 12.0 (s, 2H, 2NH); MS: (m/z) 339 (M^+, 12%).
b	228	38	$C_{22}H_{19}N_5$ (353.4)	74.77 74.77	5.42 5.42	IR: 3229 and 3189, 1597 cm^{-1} (two NH, N=N); ^{1}H-NMR: (DMSO), σ 2.3 (s, 3H, CH_3), 7.0–8.2 (m, 14H, Ar), 10.1 and 12.0 (s, 2H, 2NH); MS: (m/z) 353 (M^+, 21%).
c	210	40	$C_{22}H_{19}N_5O$ (369.4)	71.53 71.53	5.18 5.00	IR: 3230 and 3195, 1597 (two NH, N=N); ^{1}H-NMR: ($CDCl_3$), σ 4.1 (s, 3H, CH_3), 7.0–7.7 (m, 14H, Ar), 10.2, 13.1 (s, 2H, 2NH).
d	200	43	$C_{21}H_{16}N_6O_2$ (384.4)	63.62 63.62	4.20 4.20	IR: 3343 and 3231, 1597cm^{-1} (two NH, N=N); ^{1}H-NMR: (DMSO), 7.3–7.8 (m, 14H, Ar), 13.8 and 14.2 for two (s, 1H, NH); MS: (m/z) 384 (M^+, 24%).
e	230	33	$C_{21}H_{16}N_5Cl$ (373.8)	67.47 67.47	4.31 4.31	IR: 3187 and 3117, 1594cm^{-1} (two NH, N=N); ^{1}H-NMR: (DMSO), 7.3–8.0 (m, 14H, Ar), 13.7 and 13.9 (s, 2H, 2NH); MS: (m/z) 373 (M^+, 37%).

reach complete coupling reaction. The crude product was filtered off, dried well, and recrystallized from ethanol. The results are given in Table I.

Synthesis of the Acyclic Intermediate 8a, 9a, 11a, and 13a

Equimolecular quantities of **4a** (3.59 g, 10 mmol) in ethanol containing potassium carbonate (1.39 g, 10 mmol) and phenacyl bromide and/or ethyl bromoacetate and/or chloroacetonitrile and/or chloroacetone were stirred for 6 h at room temperature, then left to stand at the same temperature for 24 h. The separated solid product was washed with water, dried, and crystallized from ethanol to give **8a**, **9a**, **11a**, and **13a,** respectively (cf. Table I).

Synthesis of Thiophene Derivatives

Pathway (1)

A mixture of equimolecular amounts of **4a– e** and α-halo compounds (10 mmol) was stirred in DMF (20 ml) containing potassium carbonate (1.39 g, 10 mmol) overnight. The reaction mixture was poured onto ice-cold water, acidified by dilute HCl, filtered off, and recrystallized from ethanol to give the corresponding thiophene derivatives (cf. Table I).

Pathway (2)

Refluxing the acyclic intermediate **8a**, **9a**, **11a,** and **13a** in ethanol (20 ml) containing a catalytic amount of TEA for 3 h afforded the corresponding thiophene derivatives **7a**, **10a**, **12a**, and **14a**.

1-Phenylamino-1-hydrazone-2-(arylazo)-2-benzoylethylene (15a). A mixture of **4a** (3.55 g, 50 mmol) and hydrazine hydrate (1.6 g, 50 mmol) in ethanol was stirred for 4 h at room temperature. The reaction mixture was then cooled and the solid product was filtered off and recrystallized from ethanol to give compound **15a** (cf. Table I).

Synthesis of Arylazopyrazoles (16a–e)

Method A

A mixture of **4a–e** (50 mmol), hydrazine hydrate (1.6 g, 50 mmol) in DMF was refluxed for 4 h. The reaction mixture then poured onto ice water (200 ml). The solid product was filtered off and recrystallized from ethanol:DMF (1:1) to give the corresponding derivatives **16a–e**, respectively (cf. Table I).

Method B

Refluxing the acyclic intermediate **15a** in ethanol (20 ml) containing a catalytic amount of TEA for 3h gave the pyrazole derivative **16a**.

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