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Tetracyanoethylene as a building block in the facile synthesis of heteroyl-tetrasubstituted thiazoles

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Abstract The transformation of *N*-substituted 2-heteroylthiosemicarbazides to *N*-(2-substituted imino)-4-amino-5-cyanothiazol-3(2*H*)-3-yl)-heteroyl-2-carboxamides was achieved *via* the reaction with tetracyanoethylene (TCNE). In this transformation; TCNE is used as a building block. The structures of the products have been confirmed unambiguously by single-crystal X-ray structure analysis. A rationale for the formation of the products is presented.

Keywords 2,3,4,5-Tetra-substituted thiazoles • *N*-substituted 2-heteroylthiosemicarbazides • Heterocycles • Donor-acceptor effects • NMR spectroscopy • X-ray structure determination.

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Introduction

Due to the accessibility and ability of carbothioamides and their analogs to act as bifunctional nucleophiles [1-6], they play a significant role among other nitrogen and sulfur-containing compounds. Carbothioamides contain several nucleophilic centers and used as building blocks for the synthesis of different heterocyclic rings [7-9].

Tetracyanoethylene (TCNE) is utilized as a part of a wide range of reactions either as a building block or as a reaction mediator [10]. The addition of nucleophiles to the double bond of TCNE followed by loss of cyanated fragments was considered as the most common reaction [11-13]. Direct nucleophilic addition to the nitrile can also occur but is less common [14, 15].

Thiosemicarbazide is one of the carbothioamide derivatives. Due to the presence of several nucleophilic centers in thiosemicarbazides, they are also ideal candidates and valuable building blocks for the synthesis of different heterocyclic rings.

Different families of heterocyclic compounds such as thiadiazoles, thiadiazines, thiadiazepines, and pyrazoles were prepared upon the reaction of TCNE with 2,4-disubstituted thiosemicarbazides [16].

N-substituted-2-phenyl thiosemicarbazides **1a-c** reacted with TCNE **2** in dry ethyl acetate afforded mesoionic-1,2,4-triazolium-3-thiolate derivatives **3a-c** in 67-76 % yields (Scheme 1) [6], whereas upon the reaction of 2-substituted hydrazinecarbothioamides with TCNE, 2-{amino-[5-amino-2-substituted hydrazinecarbothioamides were isolated [17].

Scheme 1

1,3: a, R = C₂H₅; b, R = CH₂-CH=CH₂; c, R = C₆H₅

New substituted (Z)-4-amino-3-(substituted amino)-2-(substituted imino)-2,3-dihydrothiazole-5-carbonitriles and (Z)-(4-amino-5-cyano-3-thiazol-2-ylidene)carbonohydrazonoyl dicyanides were synthesized *via* the reaction of TCNE with *N*-substituted alkenylidene hydrazinecarbothioamides [18].

The interaction between TCNE and (1-aryl ethylidene)hydrazine-carbothioamides afforded 1,3-thiazine-5,6,6-tricarbonitriles and 2-thioxo-2,3-dihydropyrimidine-4,5-dicarbonitriles [19]. Also, it has been reported that the addition of one mole of bis-thiosemicarbazones to doubled molar amounts of TCNE in dioxane gave bis-1,3-thiazines in high yields [13].

Tetracyanoethylene reacted with 1-acylthiosemicarbazides in ethyl acetate with the formation of *N'*-(4-amino-5,6-dicyano-1,3-thiazine-2-ylidene)substituted hydrazide, *N*-(5-amino-3,4-dicyanopyrrol-2-ylidene)-2-substituted imidazo[2,1-*b*][1,3,4]oxadiazole-5,6-dicarbonitriles [20].

On the other hand, the heterocyclization of 4-substituted-1-benzoylthiosemicarbazides using TCNE afforded two kinds of ring-forming reactions, i) By using DMF as a solvent of reaction, cyclization by intramolecular nucleophilic attack on either the carbonyl or thiocarbonyl carbon atom may be activated by TCNE to synthesize 2,5-disubstituted thiadiazoles or 2,5-disubstituted oxadiazoles [11]. ii) In the less polar chlorobenzene as a solvent, several possible types of tetracyanoethylation adducts may be formed followed by formation pyrazole, thiadiazole, and oxadiazine derivatives and TCNE reacted as a building block [11]. This unique reactivity has no precedence and warrants further study. In the present investigation, we undertook the preparation of less nucleophilicity and electron poorer analogs of **1a-c**, namely, *N*-substituted 2-

heteroylhydrazinecarbothioamides **4a-f** and investigated their behavior towards TCNE **2**.

Results and Discussion

Upon addition doubled molar amounts of TCNE, **2** to solutions of **4a-f** in dry THF with the admission of air at room temperature, the green color of the transient complex was observed which gradually gives away to brown and finally to a characteristic yellow color. This behavior may be explained due to the initial formation of the unstable CT-complexes, followed by a chemical reaction. The mixture was stirred and then left to stand for 72 h at room temperature. After complete, the reaction concentrated the residue was subjected to chromatographic separation. From the one significant zone and by crystallization, yellow to orange crystals of *N*-(2-substituted imino)-4-amino-5-cyanothiazol-3(2*H*)-3-yl)-heteroyl-2-carboxamides **5a-f** were obtained in 79-68 % (Scheme 2).

The structure assignments of **5a-f** were delineated from their spectroscopic properties, elemental analyses, and single-crystal X-ray crystallography. The molecular structure of **5a**, as an example, was supported by the following findings: the molecular formula of **5a** (C₁₇H₁₄N₆OS) represented a product from one molecule of **4a** and one molecule of TCNE (**2**) with loss one molecule of malononitrile with

abstraction two hydrogens from the start **4a** and giving rise to the ion m/z 350.

Scheme 2

The IR spectrum of **5a** shows characteristic absorption bands for the NH_2 and amide-NH groups at 3187-3305 and 2189 for cyano group, 1701 and 1633 cm^{-1} for amide C=O and C=N groups, The 1H NMR spectra of **5a** clearly shows the presence of NH_2 group by broad signal at 7.45 for two protons. Compound **5a** clearly shows the presence of broad amide-NH at 11.30 ppm (one proton) and two protons for benzyl- CH_2 as a singlet signal at 4.21 ppm, in addition to nine aryl protons as multiplets in the range 7.12-8.76 ppm. In the ^{13}C NMR spectrum of **5a** the thiazole C-4, C-5 resonated at 161.65, and 55.83 were by the observed trends for chemical shifts values of carbon atoms in push-pull alkenes [21, 22]. The presence of a Ph- CH_2 group is also evident from the ^{13}C -DEPT-NMR spectrum exhibiting a negative signal at 57.7 ppm. Whereas, thiazole-C5 in compound **5a** was evident from the ^{13}C NMR-DEPT spectra exhibiting positive signals at $\delta_C =$

55.58 ppm. The presence of an isothioureia carbon at 153.6 and amide C=O at 163.88 ppm was supported by ^{13}C - NMR.

The structure of **5a-f** was confirmed by single-crystal X-ray crystallography. The structure of *N*-(2-allyl imino)-4-amino-5-cyanothiazol-3(2*H*)-3-yl)-furan-2-carboxamide (**5d**) was determined by X-ray analysis and crystallized from ethanol in triclinic space group P-1 (Fig. 1, Tables S2-S8 in supplementary data).

The C(2)-S(1) and C(5)-S(1) bond lengths of 1.7684(12) Å and 1.7717(13)Å respectively due to C-S σ -bond. The C(2)-N(21) bond length of 1.2605 (17) Å and C(4)-C(5) bond length of 1.3730 (17) Å are closed to C/C double bonds, the thiazole ring is planar (mean deviation from the thiazole plane 0.017 Å). The same structures were assumed for other derivatives based on their NMR spectroscopic similarities.

Fig. 1. Molecular structure of **5d** (displacement parameters are drawn at 50% probability level).

With the optimized reaction conditions in hand, an increased amount of the start **4a-f** was not necessary for the formation of high yields of the products **5a-f**, whereas upon addition two equivalents of TCNE, tetra-substituted thiazole derivatives **5a-f** were separated. Different solvents such as methylene chloride, benzene, acetonitrile, and 1,4-dioxane were studied but THF proved to be the best. The high yields of the products were obtained at room temperature and in the presence of air, where trace amounts of products were formed when the reaction subjected under nitrogen or argon.

Table1, Yields of synthetic products **5a-f** in different solvents.

Compound number	Structure	Yield of 5a-f (%)				
		THF	CH ₂ Cl ₂	Benzene	CH ₃ CN	1,4-dioxane
5a		79	36	33	40	56
5b		71	29	30	38	53

5c		74	34	31	39	54
5d		68	28	27	37	51
5e		77	34	31	39	54
5f		70	28	27	36	51

1

2 Mechanistic rationale for the formation of tetra-substituted thiazoles

3 **5a-f** as depicted in Scheme 3.

4 Charge transfer complexes may (but not necessarily have to) play an

5 intermediate role. Two routes may be suggested after the formation of the

6 radicals **4**[•] and 2[•]H. In the first route, the combination of the two radicals7 afforded the intermediate **6a-f**. Elimination of a molecule of CH₂(CN)₂8 with the abstraction of another hydrogen from **4** gave the intermediate **7a-f**

which abstracts another proton of **4** to give the imine **8**. Cyclization of the imine **8** *via* intramolecular nucleophilic attack of hydrazide NH on the imine C=NH afforded tetra-substituted thiazoles **5a-f**.

In the second route, the cyclizations involve intramolecular nucleophilic attacks on either a thiocarbonyl or carbonyl group (scheme 3). Since the aforementioned reactions do not take place when **2** are added to **4a-f**, this means that TCNE, **2** was used as a building block in this reaction and not a mediator.

Conclusion

In conclusion, novel heteroyl-tetrasubstituted thiazole derivatives containing aliphatic and aromatic substituents are presented *via* cyclization of *N*-substituted 2-heteroylhydrazinecarbothioamides by reaction with TCNE. Heteroylhydrazinecarbothioamides are multi-dentate nucleophiles allowing for various modes of heterocyclization with TCNE, providing several electrophilic sites.

Experimental

Melting points (mp's) were determined using open glass capillaries on a Gallenkamp melting point apparatus (Gallenkamp, UK) and are uncorrected. The IR spectra were recorded with alpha Bruker FT-IR a Bruker instrument using KBr pellets. 400 ¹H NMR and 100 ¹³C-NMR were determined on a Bruker AM400 spectrometer with tetramethylsilane as

1 *Scheme 3*

2

3 internal standard; s = singlet, m = multiplet, br = broad. The ^{13}C NMR
 4 signals were assigned based on DEPT 135/90 spectra, chemical shifts are
 5 expressed as δ . The mass spectra (70 eV, electron impact mode were
 6 recorded on a Finnigan MAT 312 instrument). The elemental analyses for
 7 C, H, N, and S were carried out on a Carlo Erba model 1106 C, H, N, and S
 8 analyzer. Preparative layer chromatography (Plc) used air-dried 1.0 mm

thick layer of slurry applied silica gel (Merck Pf₂₅₄) on 48 cm wide and 20 cm high glass plates using the solvent listed.

Starting materials

N-substituted 2-heteroylhydrazinecarbothioamides **4a-f** were prepared according to the literature. **4a**, **4b**, **4d**, **4f** [23], **4b**, **4c** [24]. Tetracyanoethylene (ethenetetracarbonitrile, **2**, Merck) was recrystallized from chlorobenzene and sublimed.

Reactions of *N*-substituted 2-heteroylthiosemicarbazides **4a-f** with TCNE **2**

General procedure: A solution of *N*-substituted 2-heteroylthiosemicarbazides **4a-f** (1.0 mmol) in dry THF (25ml) was added dropwise with stirring at room temperature to 2.0 mmol of TCNE **2** in (20 ml) THF. The reaction mixture was stirred followed by TLC for 72 hrs at room temperature which caused a spontaneous change of color from green to brown and finally to yellow with consuming all the start materials and complete the reaction. After concentration to dryness, the residue was sublimed at 80 °C under vacuum to remove the excess of TCNE and then subjected to preparative thin-layer chromatography using toluene /ethyl acetate (1:1) in case of the reaction with (**4c**, **4d**, **4e**, and **4f**) and toluene/ethyl acetate (1:2) in case of (**4a** and **4b**) as eluent to give numerous colored zones. Only one high intense zone was removed and

1 extracted with acetone then recrystallized to give pure crystals of **5a-f**. The
2 other colored zones were very small.

3 **(Z)-N-(4-Amino-2-(benzylimino)-5-cyanothiazol-3(2H)-yl)picolinamide**
4 **(5a, C₁₇H₁₄N₆OS)**

5 Yellow crystals (acetonitrile), (*R_f* = 0.27), m.p.: 124–125 °C; yield: 276 mg
6 (79 %); IR (KBr) $\bar{\nu}$ = 3305 (NH₂), 3187 (NH), 3082 (Ar-CH), 2189
7 (C≡N), 1701 (C=O), 1623 (C=N), 1585 (Ar-C=C) cm⁻¹; ¹H NMR (400
8 MHz, DMSO-*d*₆): δ = 11.30 (s, 1H, amide- NH), 8.76–8.66 (m, 1H, Pyr-
9 H), 8.10–7.99 (m, 2H, Pyr-H), 7.70–7.66 (m, 1H, Pyr-H), 7.45 (s, 2H, NH₂
10 attached to thiazole), 7.35–7.12 (m, 5H, Ph-H), 4.21 (s, 2H, CH₂Ph) ppm;
11 ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 163.88 (amide-CO), 161.65
12 (thiazole-C4), 153.6 (thiazole-C2), 150.6 (Pyr-C), 148.8 (Pyr-CH), 139.5
13 (Pyr-CH), 138.0 (Ph-C), 128.3 (Ph-2CH), 127.7 (Ph-CH), 127.3 (Ph-2CH),
14 126.7, 123.0 (Pyr-CH), 116.8 (C≡N), 57.7 (CH₂Ph), 55.83 (thiazole-C5)
15 ppm; MS (FAB) *m/z* (%) = 350 (M⁺, 100); Calcd: C, 58.27; H, 4.03; N,
16 23.98; S, 9.15.

17 **(Z)-N-(2-(Allylimino)-4-amino-5-cyanothiazol-3(2H)-yl)picolinamide**
18 **(5b, C₁₃H₁₂N₆OS)**

19 Yellow crystals (acetonitrile) , (*R_f* = 0.29), m.p.: 170–171 °C; yield: 213
20 mg (71%); IR (KBr) $\bar{\nu}$ = 3284 (NH₂), 3185 (NH), 3066 (Ar-CH), 2191
21 (C≡N), 1700 (C=O), 1630 (C=N), 1589 (Ar-C=C) cm⁻¹; ¹H NMR (400

1 MHz, DMSO- d_6): δ = 11.25 (s, 1H, amide- NH), 8.83–8.62 (m, 1H, Pyr-
2 H), 8.21–7.92 (m, 2H, Pyr-H), 7.72–7.66 (m, 1H, Pyr-H), 7.43 (s, 2H, NH₂
3 attached to thiazole), 5.85–5.76 (m, 1H, allyl-CH=), 5.40–4.87 (m, 2H,
4 allyl-CH₂=), 3.66–3.62 (m, 2H, allyl-CH₂N) ppm; ¹³C NMR (100 MHz,
5 DMSO- d_6): δ = 164.1 (amide-CO), 153.6 (thiazole-C4) 150.3 (Pyr-C),
6 148.9 (Pyr-CH), 148.8 (thiazole-C2), 138.1 (Pyr-CH), 135.3 (allyl-CH=),
7 127.8, 123.1 (Pyr-CH), 116.9 (allyl-CH₂=), 115.4 (C≡N), 55.0 (thiazole-
8 C5), 43.6(allyl-CH₂) ppm; MS (FAB) m/z (%) = 300 (M⁺, 100); Calcd: C,
9 51.99; H, 4.03; N, 27.98; S, 10.68.

10 **(Z)-N-(4-Amino-2-(benzylimino)-5-cyanothiazol-3(2H)-yl)furan-2-**
11 **carboxamide (5c, C₁₆H₁₃N₅O₂S)**

12 Orange crystals (acetonitrile), (R_f = 0.44), m.p.: 180–181 °C ; yield: 250
13 mg (74%); IR (KBr) $\bar{\nu}$ = 3310 (NH₂), 3191 (NH), 3045 (Ar-CH), 2190
14 (C≡N), 1695 (C=O), 1627 (C=N), 1582 (Ar-C=C) cm⁻¹; ¹H NMR (400
15 MHz, DMSO- d_6): δ = 11.10 (s, 1H, amide-NH), 7.98–7.88 (m, 1H, Furan-
16 H), 7.75 (s, 2H, NH₂ attached to thiazole), 7.69–7.30 (m, 5H, Ph-H), 7.28–
17 7.10 (m, 2H, Furan-H), 4.32 (s, 2H, CH₂Ph) ppm; ¹³C NMR (100 MHz,
18 DMSO- d_6): δ = 157.3 (amide-CO), 153.3 (thiazole-C4), 145.5 (Furan-C2),
19 139.2 (Furan-CH), 146.3 (thiazole-C2), 139.0 (Ph-C), 128.1, 127.1 (Ph-
20 2CH), 126.5 (Ph-CH), 116.4 (C≡N), 116.1, 113.1 (Furan-CH), 57.6

(thiazole-C5), 55.8 (CH₂Ph) ppm; MS (FAB) m/z (%) = 339 (M⁺, 100);

Calcd: C, 56.63; H, 3.86; N, 20.64; S, 9.45.

(Z)-N-(2-(Allylimino)-4-amino-5-cyanothiazol-3(2H)-yl)furan-2-carboxamide (5d, C₁₂H₁₁N₅O₂S)

Yellow crystals (acetonitrile), (R_f = 0.42), m.p.: 130–131 °C; yield: 196 mg

(68%), IR (KBr) $\bar{\nu}$ = 3305 (NH₂), 3181 (NH), 3060 (Ar-CH), 2195 (C≡N),

1700 (C=O), 1623 (C=N), 1590 (Ar-C=C) cm⁻¹; ¹H NMR (400 MHz,

DMSO-*d*₆): δ = 11.20 (s, 1H, amide-NH), 8.28–8.02 (m, 1H, Furan-H),

7.58–7.30 (m, 2H, Furan-H), 7.25 (s, 2H, NH₂ attached to thiazole), 5.95–

5.73 (m, 1H, allyl-CH=), 5.47–4.80 (m, 2H, allyl-CH₂=), 3.96–3.61 (m,

2H, allyl-CH₂) ppm; ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 158.3 (amide-

CO), 154.3 ((thiazole-C4), 145.3 (Furan-C2), 139.3 (Furan-CH), 147.3

(thiazole-C2), 133.3 (allyl-CH=), 117.2 (allyl-CH₂=), 116.7 (C≡N), 116.2,

114.1 (Furan-CH), 56.8 (thiazole-C5), 48.6 (allyl-CH₂) ppm; MS (FAB)

m/z (%) = 289 (M⁺, 50); Calcd: C, 49.82; H, 3.83; N, 24.21; S, 11.08.

(Z)-N-(4-Amino-2-(benzylimino)-5-cyanothiazol-3(2H)-yl)thiophene-2-carboxamide (5e, C₁₆H₁₃N₅OS₂)

Orange crystals (acetonitrile), (R_f = 0.51), m.p.: 140–141 °C; yield: 273 mg

(77 %); IR (KBr) $\bar{\nu}$ = 3308 (NH₂), 3171 (NH), 3070 (Ar-CH), 2186

(C≡N), 1690 (C=O), 1630 (C=N), 1562 (Ar-C=C) cm⁻¹; ¹H NMR (400

1 MHz, DMSO- d_6): δ = 11.25 (s, 1H, amide-NH), 8.01–7.78 (m, 3H,
2 Thiophene-H), 7.55 (s, 2H, NH₂ attached to thiazole), 7.42–7.02 (m, 5H,
3 Ph-H), 4.29 (s, 2H, CH₂Ph) ppm; ¹³C NMR (100 MHz, DMSO- d_6): δ =
4 161.1 (amide CO), 153.3 (thiazole-C4), 150.6 (thiazole-C2), 139.3
5 (thiophene-C2), 135.9 (Ph-C), 132.6, 130.5 (thiophene-CH), 128.1, 127.1
6 (Ph-2CH), 127.0 (Ph-CH), 126.5 (thiophene-CH), 116.4 (C≡N), 63.4
7 (thiazole-C5), 55.8 (CH₂Ph) ppm; MS (FAB) m/z (%) = 355 (M⁺, 80);
8 Calcd: C, 54.07; H, 3.69; N, 19.70; S, 18.04.
9 **(Z)-N-(2-(Allylimino)-4-amino-5-cyanothiazol-3(2H)-yl)thiophene-2-**
10 **carboxamide (5f, C₁₂H₁₁N₅OS₂)**
11 Yellowish orange crystals (acetonitrile), (R_f = 0.53), m.p.: 152–153 °C;
12 yield: 213 mg (70%); IR (KBr) $\bar{\nu}$ = 3295 (NH₂), 3180 (NH), 3058 (Ar-
13 CH), 2185 (C≡N), 1690 (C=O), 1625 (C=N), 1526 (Ar–C=C) cm⁻¹; ¹H
14 NMR (400 MHz, DMSO- d_6 , ppm) δ = 11.20 (br, 1H, amide- NH), 8.10–
15 7.82 (m, 3H, Thiophene-H), 7.55 (s, 2H, NH₂ attached to thiazole), 5.90–
16 5.74 (m, 1H, allyl-CH=), 5.21–4.99 (m, 2H, allyl-CH₂=), 3.81–3.68 (m,
17 2H, allyl-CH₂N). ¹³C NMR (100 MHz, DMSO- d_6 , ppm) δ = 160.1 (amide-
18 CO), 154.4 (thiazole-C4), 138.3 (thiazole-C2), 137.2 (thiophene-C2),
19 133.7, 132.2 (thiophene-CH), 131.3 (allyl-CH=), 129.3 (thiophene-CH),
20 117.4 (allyl-CH₂=), 114.6 (C≡N) 58.3 (thiazole-C5), 49.6 (allyl-CH₂N).

MS (FAB) m/z (%) = 305 (M^+ , 60); Calcd: C, 47.20; H, 3.63; N, 22.93; S, 21.00.

Crystal Structure Determination of **5d**

The single-crystal X-ray diffraction study was carried out on a Bruker D8 Venture diffractometer with PhotonII detector at 123 K using Cu-K α radiation ($\lambda = 1.54178$ Å). Dual space Methods (SHELXT) [25] were used for structure solution and refinement was carried out using SHELXL-2013 / 2014 (full-matrix least-squares on F^2) [26]. Hydrogen atoms were localized by difference Fourier synthesis map and refined using a model (H(N) free). Semi-empirical absorption correction was applied.

Compound 5d: $C_{12}H_{11}N_5O_2S$, Mr = 289.32 g mol⁻¹, yellow blocks, size 0.14 × 0.08 × 0.04 mm, triclinic, P-1 (no. 2), $a = 4.5032$ (1) Å, $b = 11.4730$ (4) Å, $c = 13.0278$ (4) Å, $\alpha = 80.483$ (1)°, $\beta = 84.692$ (1)°, $\gamma = 89.314$ (1)°, $V = 666.97$ (3) Å³, $Z = 2$, $D_{\text{calcd}} = 1.454$ Mg m⁻³, $F(000) = 300$, $\mu = 2.28$ mm⁻¹, $T = 123$ K 10950 measured reflections ($2\theta_{\text{max}} = 144.4^\circ$), 2601 independent reflections [$R_{\text{int}} = 0.025$], 190 parameters, 3 restraints, R_1 [for 2515 $I > 2\sigma(I)$] = 0.027, wR^2 (for all data) = 0.070, $S = 1.07$, largest diff. peak and hole = 0.25 e Å⁻³/- 0.21 e Å⁻³.

CCDC 1961343 (**5d**) contains the supplementary crystallographic data for this paper [27].

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Figure Captions

Fig. 1 Molecular structure of **5d** (displacement parameters are drawn at 50% probability level.

Scheme Captions

Scheme 1. Reactions of disubstituted thiosemicarbazids **1a-c** with TCNE **2** in ethyl acetate.

Scheme 2. Reactions of **4a-f** with TCNE **2** and formation of the products **5a-f**.

Scheme 3. Mechanistic rationale for the formation of compounds **5a-f**.

Figure 1

1

2 *Scheme 1*

3

1,3: a, R = C₂H₅; b, R = CH₂-CH=CH₂; c, R = C₆H₅4 *Scheme 2*

5

6

7

1 *Table1*, yields of synthetic products **5a-f** in different solvents.

Compound number	Structure	Yield 5a-f (%)				
		THF	CH ₂ Cl ₂	benzene	CH ₃ CN	1,4-dioxane
5a		79	36	33	40	56
5b		71	29	30	38	53
5c		74	34	31	39	54
5d		68	28	27	37	51
5e		77	34	31	39	54

5f		70	28	27	36	51
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1

2 *Scheme 3*

3

4

1 Graphical abstract

3 Elemental analyses

No.	Compounds	Chemical Formula	Calculated	Found
1	5a	C ₁₇ H ₁₄ N ₆ OS	C, 58.27; H, 4.03; N, 23.98; S, 9.15	C, 58.33; H, 4.10; N, 24.04; S, 9.22
2	5b	C ₁₃ H ₁₂ N ₆ OS	C, 51.99; H, 4.03; N, 27.98; S, 10.68	C, 52.05; H, 4.11; N, 28.04; S, 10.73
3	5c	C ₁₆ H ₁₃ N ₅ O ₂ S	C, 56.63; H, 3.86; N, 20.64; S, 9.45	C, 56.70; H, 3.92; N, 20.69; S, 9.51
4	5d	C ₁₂ H ₁₁ N ₅ O ₂ S	C, 49.82; H, 3.83; N, 24.21; S, 11.08	C, 49.88; H, 3.89; N, 24.26; S, 11.17
5	5e	C ₁₆ H ₁₃ N ₅ OS ₂	C, 54.07; H, 3.69; N, 19.70; S, 18.04	C, 54.12; H, 3.74; N, 19.74; S, 18.10
6	5f	C ₁₂ H ₁₁ N ₅ OS ₂	C, 47.20; H, 3.63; N, 22.93; S, 21.00	C, 47.25; H, 3.69; N, 22.98; S, 21.08

4