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CYANOACETANILIDE INTERMEDIATE IN HETEROCYCLIC SYNTHESIS, PART 8 : PREPARATION OF THIAZOLIDINE, BENZO[*d*][1,3]OXAZINE,4-AMINOTHIOPHENE AND 4-AMINOTHIAZOLE DERIVATIVES STRATING FROM 2-(2-CYANOACETAMIDO)-BENZOATE

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Abstract: Cyclocondensation of compound (**1**) with sulfanylacetic acid under reflux in acetic acid furnished the novel 4-thiazolidinone derivative (**2**). The novel benzo[*d*][1,3]benzoxazin-4-one (**3**) was obtained by the reaction of compound (**2)** with 4-methoxybenzaldehyde at reflux temperature in ethanol and piperidine. The non-isolable intermediate(**4**) was exploited to synthesize some novel aminothiophene (**6** and **7**), thiazolidine (**10** and **11**), and aminothiazole (**12** and **13**) derivatives. The reaction of compound (**1**) with isothiocyanates in the presence of elemental sulfur was investigated. The structure of the newly synthesized compounds was confirmed on the basis of analytical and spectral data.

Keywords*:* Cyanoacetanilide, thiazolidine, benzo[*d*][1,3]oxazine, aminothiophene, and aminothiazole.

Introduction

4-Thiazolidinones are a class of important heterocycles that have attracted considerable attention because of their biological properties. They are represented in a well-known group of patented drugs and substances which possess hypoglycaemic, antiviral, antiasthmatic, anti-inflammatory, choleretic, antitumor, diuretic, antiproliferative and immunostimulant amongst other activities [1-12].Aminothiophenes are known to exhibit various biological and pharmaceutical activities such as potential antioxidant and anti-inflammatory agents[13,14], anti-HIV PR inhibitors[15], anti-breast cancer [16], anthelmintic activity against haemonchuscontortus[17], anti-avian influenza virus (H5N1)[18], a multitargeted kinase inhibitor[19], AMPK activators[20], antitubercular agent[21]. In addition, the aminothiazole scaffold was served as a privileged structure due to their prevalence in antibacterial agents and other biologically active molecules[22-25].Cyanoacetanilide derivatives are important and versatile reagents which have especially used for the synthesis of polyfunctionalized three, five and six

membered rings and condensed heterocycles[26,27]. Cyanoacetanilides are polyfunctional compounds possess both electrophilic and nucleophilic properties[28]. Two nucleophilic centers in cyanoacteanilides are localized on NH and C-2. Also, cyanoacetanilide possess two electrophilic positions[15] which are associated with C-1 and C-3, Figure 1. In view of the above mentioned benefits and in continuation of our previous work on the chemistry of cyanoacetanilides[29-35], we report here the synthesis of versatile 4-thiazolidinone, multi-substituted thiophene, and aminothiazole derivatives utilizing inexpensive cyanoacetanilide intermediate **1** as starting material.

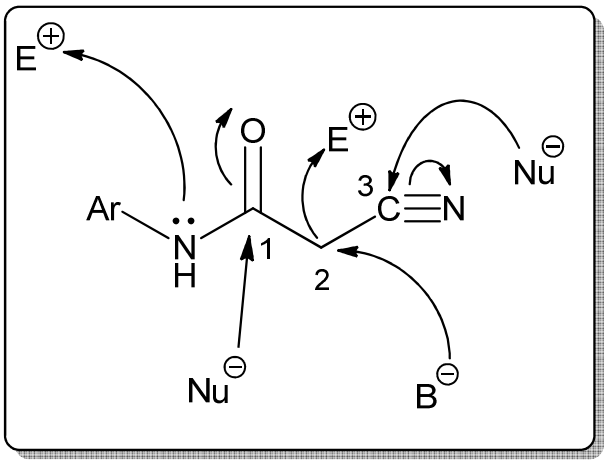
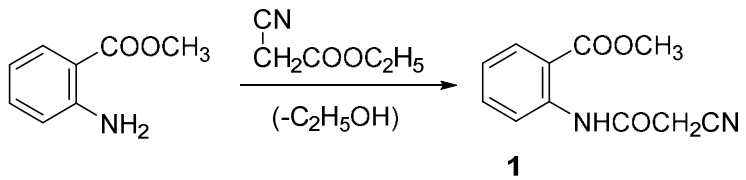


Figure 1: Reactivity of cyanoacetanilide

Results and discussion

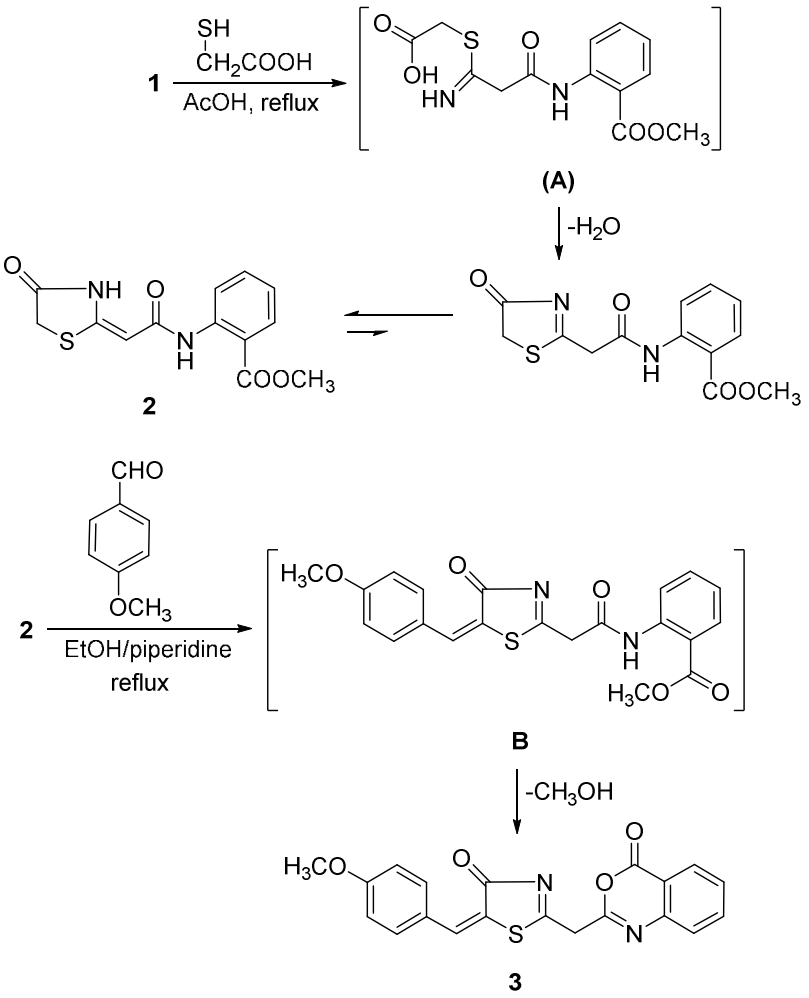
The key intermediate in the present investigation is methyl 2-(2-cyanoacetamido)-benzoate **(1)**[36] which was obtained from the solvent free reaction of ethyl cyanoacetate with methyl anthranilate, Scheme 1.



Scheme 1: Synthesis of 2-(2-cyanoacetamido)-benzoate **(1)**

4-Thiazolidinone derivative **2** was achieved in good yield by cyclocondensation of compound **1** with sulfanylacetic acid by refluxing in glacial acetic, Scheme 2. Assignment of structure **2** was confirmed on the basis of analytical and spectral data. The infrared spectrum of compound **2** revealed the lack of the absorption band which belong to C≡N function and presence of the characteristic absorption bands at 1724, 1700 and 1652 cm^{-1} for the three carbonyl groups. Also, the ^{1}HNMR spectrum (DMSO-d_6) was in accordance with the proposed structure. Formation of the latter product is assumed to proceed through the intermediacy of **(A)** followed by intramolecular cyclization via loss of water[37].The reaction of compound **2** with 4-methoxybenzaldehyde under reflux in ethanol in the presence of piperidine gave the novel benzo[*d*][1,3]oxazin-4-one **(3)**, via intermediacy **(B)** followed by loss of methanol, Scheme 2. The infrared spectrum of compound **3** showed two strong absorption bands at 1696 and 1666 cm^{-1} for two carbonyl groups and revealed the absence of absorption band assignable to NH function. Its ^{1}HNMR spectrum (DMSO-d_6) displayed

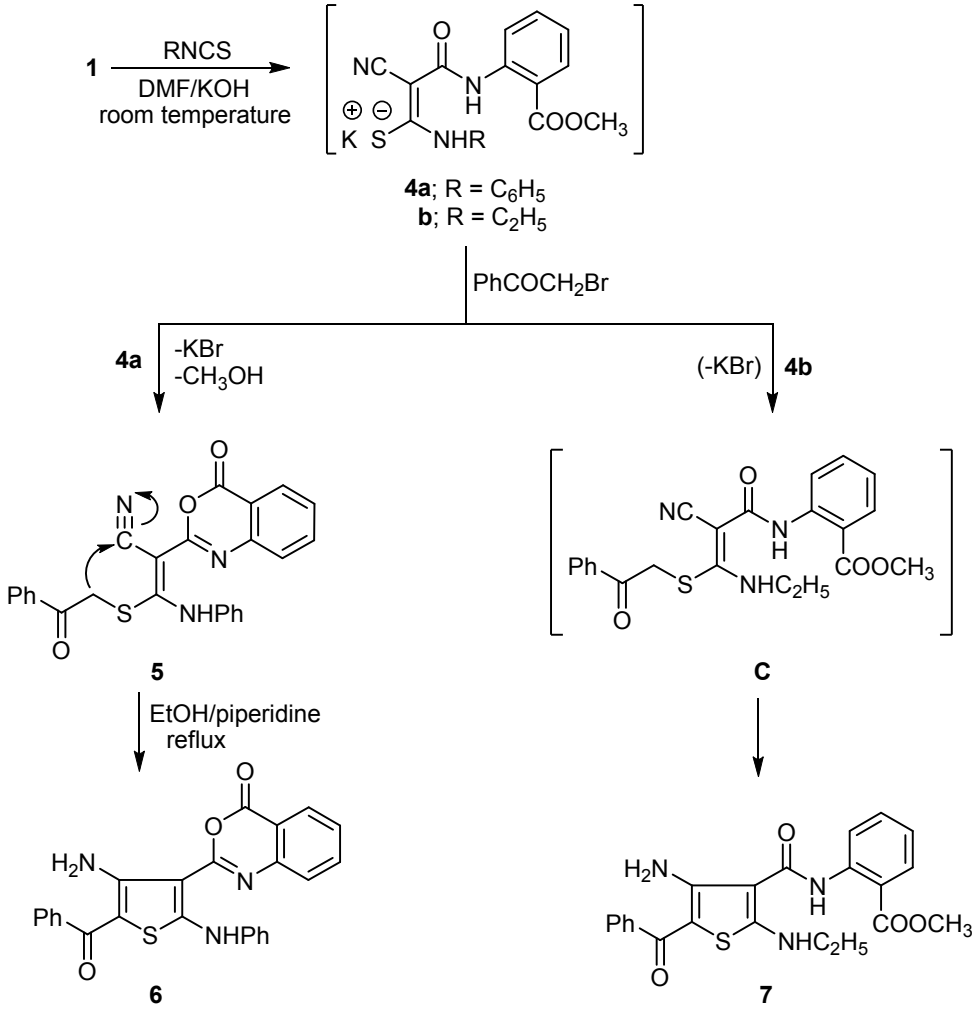
the absence of two signals characteristic to OCH_3 of ester and methylene of thiazolidinone protons.



Scheme 2 : Synthesis of 4-oxothiazolidin-2-ylidene **(2)** and 4-oxo-4,5-dihydrothiazol-2-yl **(3)** derivatives

The active methylene group in compound **1** was condensed with isothiocyanates in *N,N*-dimethylformamide in the presence of potassium hydroxide to furnish the non-isolable intermediate salts **4a,b**, Scheme 3. The intermediate salts **4** are versatile starting materials for the synthesis of some novel aminothiopheneand thiazolidinederivatives. Treatment of the intermediate salt **4a** with phenacyl bromide at room temperature afforded 2-(4-oxo-4*H*-benzo-[*d][*1,3]oxazin-2-yl)-3-(2-oxo-2-phenylethenyl-sulfanyl)-3-phenyl-amino-acrylonitrile **(5)**, Scheme 3. The infrared spectrum of the reaction product displayed absorption bands for the NH, C≡N and two carbonyl functions at 3180, 2222, 1688 and 1658 cm^{-1}, respectively. Also, the ^{1}HNMR spectrum (DMSO-d_6) showed the absence of signal characteristic for OCH_3 protons and exhibited singlet signal at 6.38 ppm assigned for CH_2 protons and a multiplet at 7.27-8.03 ppm assigned to aromatic protons and revealed downfield singlet signal at δ 12.10 ppm assigned to the NH proton (D_2O exchangeable). Refluxing of compound **5** in ethanol containing a catalytic amount of piperidine as a basic catalyst gave the corresponding 4-aminothiophene derivative **6**, via *Thorpe-Ziegler* cyclization[38]. The structure of compound **6** was supported on the basis of analytical and spectral data. Its infrared spectrum revealed the

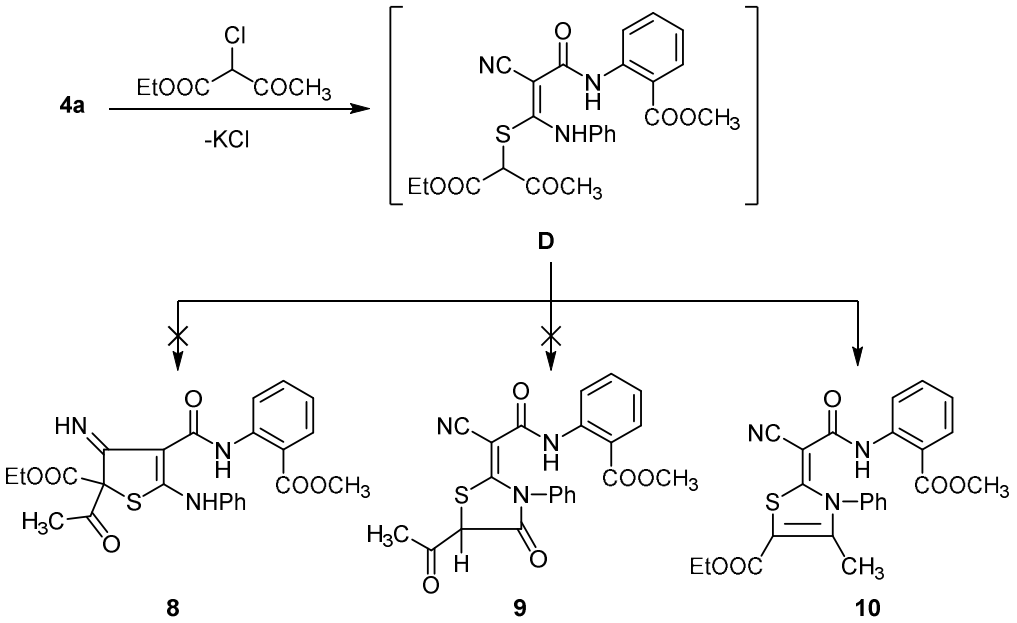
absence of absorption band which belong to cyano function and the presence of absorption bands for NH_2 at 3478 and 3358 cm^{-1}. On the other hand, 4-aminothiophene derivative **7** was obtained by treatment of non-isolable intermediate **4b** with phenacyl bromide at room temperature. Its ^{1}HNMR spectrum (DMSO-d_6) showed a triplet at δ 1.14 ppm and a quartet at δ 4.05 ppm assigned to the ethyl group, and singlet at δ 3.95 ppm assigned for the methoxy protons, and a singlet signal at 3.92 ppm assigned for the NH_2 group (D_2O exchangeable) and two downfield signals at δ 8.67, 11.75 (D_2O exchangeable) which were assigned for two NH groups. Formation of the thiophene ring **7** is assumed to proceed via the initial alkylation followed by intramolecular cyclization through *Thorpe-Ziegler* cyclization [38].



Scheme 3: Synthesis of 4-oxo-4H-benzo[d][1,3]oxazin-2-yl **(6)** and 4-aminothiophene **(7)** derivatives

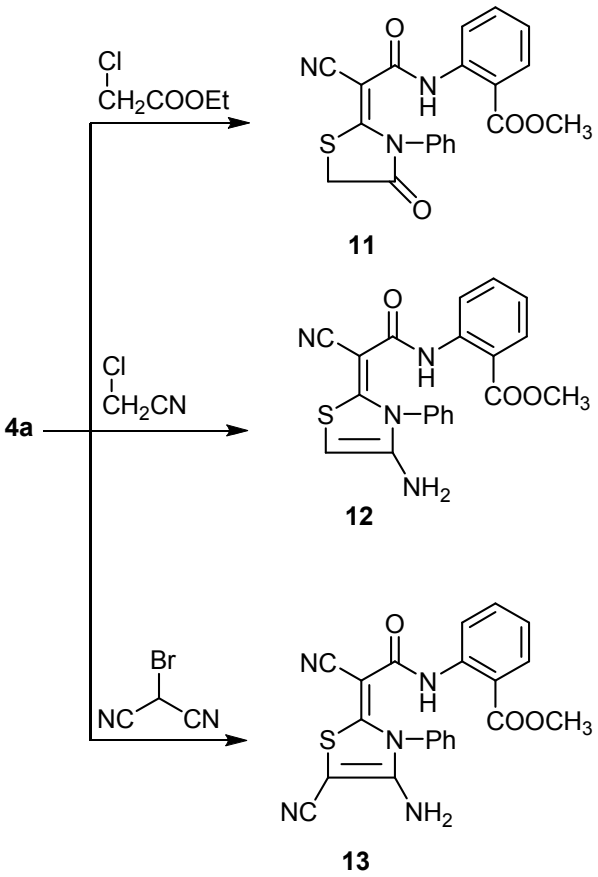
The 5-ethoxycarbonyl-4-methyl-3-phenyl-2,3-dihydrothiazole derivative **10** was obtained by treatment of the non-isolable intermediate **4a** with α-chloro ethyl acetoacetate at room temperature rather than the other possible structures **8** and **9**, Scheme 4. The infrared spectrum of the reaction product showed the characteristic absorption band at 2184 cm^{-1} for the C≡N group. In addition, the structure was supported by the ^{1}HNMR spectrum (DMSO-d_6) which revealed a triplet at δ 1.36 ppm and a quartet at δ 4.34 ppm assigned to the ethyl group, a singlet at δ 2.18 ppm for methyl protons, a singlet at δ 3.86 ppm for methoxyprotons, a multiplet at 7.05-8.01 ppm assigned to the aromatic protons and a singlet at 11.20 ppm assigned to the NH proton (D_2O exchangeable). Formation of 2,3-dihydrothiazole derivative **10** is assumed to proceed through the initial alkylation by loss of potassium chloride to form

the intermediate **D** , followed by intramolecular cyclization via water elimination[39], Scheme 4.



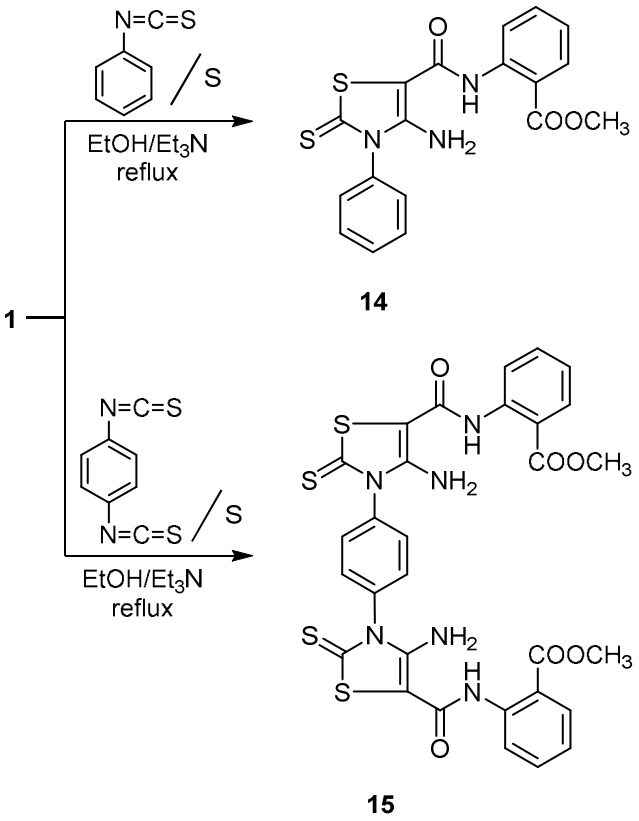
Scheme 4 : Synthesis of 2,3-dihydrothiazole **(10)** derivative

Cycloalkylation of the non-isolable intermediate **4a** with ethyl chloroacetate at room temperature afforded the novel 4-thiazolidinone derivative **11** in high yield, Scheme 5. The infrared spectrum of compound **11** showed the characteristic absorption band at 3456 cm^{-1} for the NH group and at 2200 cm^{-1} for the cyano group and three absorption bands corresponding to carbonyl groups at 1730, 1700 and 1654 cm^{-1}. Its ^{1}HNMR spectrum showed the lack of two signals characteristic to the ethyl protons and the presence of signals at δ3.6, 3.87, 7.13-8.05 and 11.60 ppm for CH_2, OCH_3, aromatic and NH protons, respectively. Formation of 4-thiazolidinone **11** is assumed to proceed through the initial alkylation followed by intramolecular cyclization via ethanol elimination. 4-Aminothiazolidine derivative **12** was achieved by cyclocondensation of the non-isolable intermediate **4a** with chloroacetonitrile. The structure of compound **12** was established on the basis of analytical and spectral data. The infrared spectrum showed absorption bands at 3434, 3196, 2194 cm^{-1} for amino and cyano groups in addition to strong absorption bands at 1684 and 1644 cm^{-1} for carbonyl groups. The ^{1}HNMR spectrum (DMSO-d_6) showed singlet signal at δ 6.95 ppm for the thiazolidinone proton at C-5 in addition to the presence of signals at δ 3.79, 7.09-8.51 and 10.94 ppm for methoxy, aromatic and NH protons. Formation of aminothiazolidine **12** is assumed to proceed through the initial alkylation followed by intramolecular cyclization via nucleophilic addition of the NH group to cyano group[39]. Under similar condition, treatment of the non-isolable intermediate **4a** with bromo-malononitrile furnished the corresponding enaminonitrile derivative **13,** Scheme 5.



Scheme 5 : Synthesis of 4-oxo-thiazolidin-2-ylidene **(11)** , 4-aminothiazol-2(3*H*)-ylidene **(12)** and 4-amino-5-cyano-thiazol-2(3*H*)-ylidene **(13)** derivatives

The reaction of compound **1** with elemental sulfur and phenyl isothiocyanate (1:1:1 molar ratio) in ethanol in the presence of triethylamine under reflux gave the aminothiazole derivative **14,** according to the reported *Hantzsch* reaction[40], Scheme 6. The infrared spectrum showed the lack of absorption band assignable to cyano group, and presence of strong bands at 3350, 3290 and 1624 cm^{-1} for amino and carbonyl groups, respectively. Also, the ^{1}HNMR spectrum revealed the lack of a signal characteristic to methylene protons. In a similar manner, the bis(dihydrothiazole) derivative **15** was synthesized by cyclization of compound **1** with 1,4-diisothiocyanatobenzene and elemental sulfur (2:1:2 molar ratio) in refluxing ethanol in the presence of triethylamine. Mass spectrum of the reaction product showed a molecular ion peak at m/z = 692 (10%) corresponding to the molecular formula ($C_{30}H_{24}N_6O_6S_6$)



Scheme 6 : Synthesis of 4-amino-2-thioxo-2,3-dihydrothiazole **(14)** and bis(4-amino-2-thioxo-2,3-dihydrothiazole-3,5-diyl-5-carbonyl)) bis (azanediyl))dibenzoate **(15)** derivatives

Experimental

Melting points were determined on a digital Gallen-Kamp MFB-595 instrument and are uncorrected. IR spectra (KBr) were measured on a Shimadzu 440 spectrometer. ^{1}HNMR spectra were recorded in deuterated dimethylsulfoxide (DMSO-d_6) on a Varian Gemini 300 (300 MHz) spectrometer using tetramehylsilane (TMS) as an internal standard; chemical shifts are reported as δ units. Mass spectra were performed on a Shimadzu GSMS-QP 1000 Ex mass spectrometer at 70eV. The elemental analyses were carried out at the Microanalytical Center, Cairo University, Cairo (Egypt).

Methyl 2-(2-(4-oxothiazolidin-2-ylidene)acetamido)benzoate (2).

A mixture of **1** (0.01 mol) and sulfanylacetic acid (0.01 mol) in acetic acid (20 mL) was heated under reflux for 3 hours. The solid product was collected and crystallized to give **2**. This compound was obtained in 75% as a yellow crystals (from EtOH), mp. 182-183ºC; IR (KBr, cm^{-1}): 3258 (NH), 2900 (CH-aliph.), 1724, 1700, 1652 (3C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 3.73 (s, 2H, CH_2), 3.84 (s, 3H, OCH_3), 5.71 (s, 1H, methylidene-H), 7.10-8.20 (m, 4H, Ar-H), 10.45, 11.30 (2s, 2H, 2NH, exchangeable with D_2O);^{13}CNMR (75 MHz, DMSO-d_6, δ/ppm): 173.19, 167.15, 166.44 (3CO), 155.18 (C-2 thiazolidinone), 88.23 (CH-methylidene), 50.28(CH_3), 34.56 (CH_2), 139.92, 133.64, 130.21, 123.77, 118.68, 116.24 (aromatic)**;**Anal. Calcd. For $C_{13}H_{12}N_2O_4S$: C, 53.42; H, 4.14; N, 9.58. Found: C, 53.30; H, 4.10; N, 9.42.

2-((5-(4-Methoxybenzylidene)-4-oxo-4,5-dihydrothiazol-2-yl)methyl)-4*H*-benzo[*d*][1,3]oxazin-4-one (3).

To a solution of **2** (0.01 mol) in absolute ethanol (30 mL) containing piperidine (0.1 mL), 4-methoxybenzaldehyde (0.01 mol) was added. The reaction mixture was heated under reflux for 1 hour, and the solid product obtained after cooling was collected by filtration and crystallized to give **3**. This compound was obtained in 70% yield as a yellow crystals (from

EtOH), m.p. 270-271ºC; IR (KBr, cm^{-1}): 2996 (CH-aliph.), 1696, 1666 (2C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 3.71 (s, 2H, CH_2), 3.83 (s, 3H, OCH_3), 6.86-8.03 (m, 9H, Ar-H and methylidene-H); ^{13}CNMR (75 MHz, DMSO-d_6, δ/ppm): 169.32, 160.81 (2CO), 162.42 (C-2 thiazolidinone), 161.53 (C-2, oxazine), 151.72 (CH-benzylidene), 38.42 (CH_2-methylidene), 54.67(OCH_3), 133.68 (C-5 thiazolidinone), 157.64, 143.15, 135.92, 130.11, 130.74, 128.46, 127.12, 124.25, 114.87, 114.41 (aromatic)**;**Anal. Calcd. For $C_{20}H_{14}N_2O_4S$: C, 63.48; H, 3.73; N, 7.40. Found: C, 63.40; H, 3.60; N, 7.28.

General procedure for the preparation of compounds 5, 7, 10, 11, 12 and 13*;*A 100 mL three-necked round-bottomed flask equipped with a magnetic stirrer, condenser and septumwas charged with a solution of compound 1 (0.01 mol) in *N,N*-dimethylformamide (20 mL). Dried potassium carbonate (0.01mol) was added and the mixture was stirred for 1 hour at room temperature. Isothiocyanate (0.01 mol) was then added drop wise and the mixture was stirred for 2 hours at room temperature before adding the appropriate halo-compound (0.01 mol) and dried potassium carbonate (0.01 mol). The reaction mixture was quenched with 100 mL of water after having stirred for 2 hours at room temperature. The crude product precipitated and was purified by filtration followed by crystallization.

3-((2-Oxo-2-phenylethyl)thio)-2-(4-oxo-4H-benzo[*d*][1,3]oxazin-2-yl)-3-(phenylamino)acrylonitrile (5). This compound was obtained in 74% yield as a yellow crystals (from AcOH), mp 220-221ºC; IR (KBr, cm^{-1}): 3180 (NH), 3002 (CH-arom.), 2946 (CH-aliph.), 2222 (C≡N), 1688, 1658 (2C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 6.38 (s, 2H, CH_2), 7.27-8.03 (m, 14H, Ar-H), 12.10 (s, 1H, NH, exchangeable with D_2O); Anal. Calcd. For $C_{25}H_{17}N_3O_3S$: C, 68.32; H, 3.90; N, 9.56. Found: C, 68.20; H, 3.79; N, 9.47.

Methyl 2-(4-amino-5-benzoyl-2-(ethylamino) thiophene-3-carboxamido) benzoate (7). This compound was obtained in 60% yield as a yellow crystals (from AcOH), mp 210-211ºC; IR (KBr, cm^{-1}): 3350, 3308, 3230 (NH/NH_2), 3040 (CH-arom.), 2998 (CH-aliph.), 1690, 1678, 1664 (3 C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 1.14 (t, 3H, CH_3, J = 1.72 Hz), 3.92 (s, 2H, NH_2, exchangeable with D_2O), 3.95 (s, 3H, OCH_3), 4.05 (q, 2H, CH_2, J= 1.80 Hz), 7.46-8.15 (m, 9H, Ar-H), 8.67, 11.75 (2s, 2H, 2NH, exchangeable with D_2O); ^{13}CNMR (75 MHz, DMSO-d_6, δ/ppm): 181.73, 167.21, 162.16 (3CO), 35.61 (CH_2-ethyl), 16.14 (CH_3-ethyl), 52.26(OCH_3), 170.68, 140.64, 137.81, 133.05, 132.58, 131.09, 129.64, 128.82, 128.35, 126.71, 124.12, 118.06, 103.16, 93.81 (aromatic)**;**Anal. Calcd. For $C_{22}H_{21}N_3O_4S$: C, 62.40; H, 5.00; N, 9.92. Found: C, 62.27; H, 4.87; N, 9.76.

Ethyl 2-(1-cyano-2-((2-(methoxycarbonyl)phenyl)amino)-2-oxoethylidene)-4-methyl-3-phenyl-2,3-dihydrothiazole-5-carboxylate (10). This compound was obtained in 70% yield as a brown crystals (from AcOH), mp 290-291ºC; IR (KBr, cm^{-1}): 3338 (NH), 3058 (CH-arom.), 2966 (CH-aliph.), 2184 (C≡N), 1716, 1690, 1632 (3 C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 1.36 (t, 3H, CH_3, J = 1.70 Hz), 2.18 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 4.34 (q, 2H, CH_2, J = 1.81 Hz), 7.05-8.01 (m, 9H, Ar-H), 11.26 (s, 1H, NH, exchangeable with D_2O);^{13}CNMR (75 MHz, DMSO-d_6, δ/ppm):170.19 (C-2 thiazolidine), 169.17, 166.08, 163.78 (3CO),146.67 (C-4thiazolidine), 101.85 (C-5 thiazolidine), 114.29 (CN), 81.04 (C-methylidene), 59.36 (CH_2-ester), 51.46 (OCH_3), 15.25 (CH_3-ester), 14.5 (CH_3), 141.51, 139.95, 132.58, 129.41, 128.82, 124.21, 122.36, 121.08, 120.18, 115.82 (aromatic**);** Anal. Calcd. For $C_{24}H_{21}N_3O_5S$: C, 62.19; H, 4.57; N, 9.07. Found: C, 62.10; H, 4.45; N, 8.95.

Methyl 2-(2-cyano-2-(4-oxo-3-phenylthiazolidin-2-ylidene)acetamido)benzoate (11). This compound was obtained in 75% yield as a browncrystals (from AcOH), mp 220-221ºC; IR (KBr, cm^{-1}): 3456 (NH), 2930 (CH-aliph.), 2200 (C≡N), 1730, 1700, 1654 (3 C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 3.60 (s, 2H, CH_2), 3.87 (s, 3H, OCH_3), 7.13-8.05 (m, 9H, Ar-H), 11.60 (s, 1H, NH, exchangeable with D_2O); ^{13}CNMR (75 MHz, DMSO-d_6, δ/ppm): 169.84, 167.53, 165.42 (3CO), 173.51 (C-2 thiazolidinone), 114.13 (CN), 76.10 (C-methylidene), 31.71 (C-5 thiazolidinone), 54.67 (OCH_3), 140.14, 139.77, 132.16, 129.05,

128.63, 124.42, 122.67, 121.51, 120.25, 115.43 (aromatic);Anal. Calcd. For $C_{20}H_{15}N_3O_4S$: C, 61.06; H, 3.84; N, 10.68. Found: C, 60.89; H, 3.78; N, 10.53.

Methyl 2-(2-(4-amino-3-phenylthiazol-2(3H)-ylidene)-2-cyanoacetamido)benzoate (12). This compound was obtained in 60% yield as a faint yellowcrystals (from AcOH), mp 268-269ºC; IR (KBr, cm^{-1}): 3434, 3300, 3196 (NH/NH_2), 2196 (C≡N), 1684, 1644 (2 C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 3.79 (s, 3H, OCH_3), 6.95 (s, 1H, thiazole-H), 7.09-8.51 (m, 11H, Ar-H + NH_2), 11.94 (s, 1H, NH, exchangeable with D_2O). Anal. Calcd. For $C_{20}H_{16}N_4O_3S$: C, 61.21; H, 4.11; N, 14.28. Found: C, 61.10; H, 4.02; N, 14.12.

Methyl 2-(2-(4-amino-5-cyano-3-phenylthiazol-2(3*H*)-ylidene)-2-cyanoacetamido)-benzoate (13). This compound was obtained in 65% yield as a red crystals (from AcOH), mp 254-255ºC; IR (KBr, cm^{-1}): 3272, 3200, 3176 (NH/NH_2), 3058 (CH-arom.), 2950 (CH-aliph.), 2224 (C≡N), 1688, 1628 (2 C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 3.71 (s, 2H, NH_2, exchangeable with D_2O), 3.78 (s, 3H, OCH_3), 7.14-8.32 (m, 9H, Ar-H), 12.18 (s, 1H, NH, exchangeable with D_2O). Anal. Calcd. For $C_{21}H_{15}N_5O_3S$: C, 60.42; H, 3.62; N, 16.78. Found: C, 60.29; H, 3.52; N, 16.62.

2-(4-Amino-5-benzoyl-2-phenylamino-thiophen-3-yl)-benzo[*d*][1,3]oxazin-4-one (6). A solution of compound **5** (0.01 mol) in absolute ethanol (30 mL) containing a catalytic amount of piperidine was refluxed for 3 hours. The solid product that formed on heating was filtered off, and crystallized to give **6**. This compound was obtained in 70% yield as a brown crystals (from EtOH), mp>300ºC; IR (KBr, cm^{-1}): 3478, 3358, 3310 (NH/NH_2), 1710, 1684 (2 C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 6.94 (s, 2H, NH_2, exchangeable with D_2O), 7.33-8.16 (m, 14H, Ar-H), 11.87 (s, 1H, NH, exchangeable with D_2O). Anal. Calcd. For $C_{25}H_{17}N_3O_3S$: C, 68.32; H, 3.90; N, 6.56. Found: C, 68.21; H, 3.81; N, 6.42.

Methyl 2-(4-amino-3-phenyl-2-thioxo-2,3-dihydrothiazole-5-carboxamido)benzoate (14). A mixture of **1** (0.01 mol), phenyl isothiocyanate (0.01 mol) and elemental sulfur (0.01 mol) in ethanol (30 mL) containing few drops of piperidine was refluxed for 3 hours. The solid product so formed on heating was collected and crystallized to give **14**. This compound was obtained in 73% yield as a faint yellow crystals (from AcOH), mp287-288ºC; IR (KBr, cm^{-1}): 3350, 3290, 3168 (NH/NH_2), 2848 (CH-aliph.), 1690, 1624 (2 C=O); ^{1}HNMR (300 MHz, DMSO-d_6, δ/ppm): 3.94 (s, 3H, OCH_3), 6.96 (s, 2H, NH_2, exchangeable with D_2O), 6.98-8.01 (m, 9H, Ar-H), 10.67 (s, 1H, NH, exchangeable with D_2O); ^{13}CNMR (75 MHz, DMSO-d_6, δ/ppm):182.16 (CS), 168.47, 162.39 (2CO), 158.25 (C-4 thiazolidine), 74.33 (C-5 thiazolidine), 52.44(OCH_3), 140.61, 133.64, 132.16, 130.25, 129.41, 128.13, 124.43, 121.42, 119.75, 114.88 (aromatic);Anal. Calcd. For $C_{18}H_{15}N_3O_3S_2$: C, 56.09; H, 3.92; N, 10.90. Found: C, 55.92; H, 3.85; N, 10.73.

Dimethyl 2,2'-((3,3'-(1,4-phenylene)bis(4-amino-2-thioxo-2,3-dihydrothiazole-3,5-diyl-5-carbonyl))bis(azanediyl))dibenzoate (15). This compound was synthesized from **1** (0.02 mol), 1,4-bis(isothiocyanato)benzene (0.01 mol) and elemental sulfur (0.02 mol) in a manner similar to that described for the preparation of 14. This compound was obtained in 65% yield as a brown crystals (from EtOH/DMF), mp>300ºC; IR (KBr, cm^{-1}): 3334, 3246, 3198 (NH/NH_2), 2958 (CH-aliph.), 1694, 1648 (2 C=O); ^{1}HNMR: insoluble; MS: 692 (10.14%). Anal. Calcd. For $C_{30}H_{24}N_6O_6S_4$: C, 52.01; H, 3.49; N, 12.13. Found: C, 51.91; H, 3.38; N, 12.20.

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