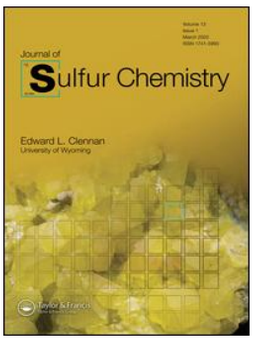

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An efficient synthesis of novel spiro[indole-3,8′-pyrano[2,3-*d*][1,3,4]thiadiazolo[3,2-*a*]pyrimidine derivatives *via* organobase-catalyzed three-component reaction of malononitrile, isatin and heterocyclic-1,3-diones

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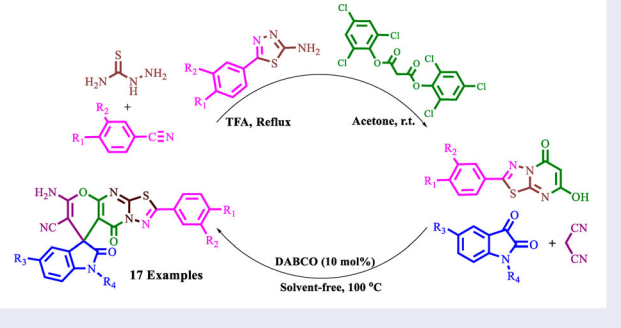
ABSTRACT

In this research, firstly, some derivatives of sulfur containing [1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one have been synthesized and then they were used for the synthesis of novel derivatives of 6′-amino-2,9′-dioxo-2′-phenyl-9′*H*-spiro[indoline-3,8′-pyrano[2,3-*d*][1,3,4]thiadiazolo[3,2-*a*]pyrimidine]-7′-carbonitriles *via* a one-pot three-component condensation reaction of 7-hydroxy-2-phenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one derivatives, malononitrile and isatin compounds in the presence of DABCO as a organocatalyst and under solvent-free conditions. In this report, a new family of spiro-pyrano-thiadiazolo-pyrimidine derivatives have been synthesized in short reaction times (10–60 min) and good to excellent yields (80–96%). The structures of all synthesized products have been confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectrometry, and the structure of one selected product was characterized by single-crystal X-ray diffraction studies as well.



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7-hydroxy-2-phenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one; spirooxindole; thiadiazolopyrimidine; organobase-catalyzed; multi-component reactions

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1. Introduction

Recently, one of the main challenges in organic synthesis and medicinal chemistry is the synthesis of novel heterocyclic systems with potential of biological activity [1–3]. Until now, different approaches have been developed for the synthesis of these valuable compounds [4–7]. Among them, multicomponent reactions (MCRs) have emerged as a powerful tool for the synthesis of a wide variety of biologically active heterocyclic compounds and provide significant advantages over traditional methods such as high efficiency, high selectivity, straightforward reaction design, mild reaction condition, environmental friendliness and high atom economy [8–10]. These reactions in which several easily available starting materials combine into a single synthetic operation to form complex organic structures that are widely used in chemicals and pharmaceuticals [11–17]. Also, during the past decade, solvent-free reactions have been attracted widespread retention, because they are in agreement with principle of green and sustainable chemistry [18–22]. Hence, development and design of efficient and green approaches for synthesis of new biological compounds is the endless task for chemists and pharmacists.

It is well known that spirooxindole compounds are considered as attractive synthetic targets in organic chemistry due to the unique conformational and interesting three-dimensional structural features that are existed in a couple of bioactive compounds as well as naturally occurring substances [23–25]. In addition, these valuable materials have big potential in synthetic medicinal chemistry owing to their privileged scaffolds and various biological activities and pharmacological properties including antimalarial, antimicrobial, antifungal, antitubercular, antioxidant, and anticancer activities [26–29]. Besides, the spiropyran heterocyclic compounds are a core of a wide variety of biologically active compounds and extensively found in nature and show different physiological applications such as anticancer [30], antimicrobial [31], antibacterial [32,33], and antifungal activities [34]. Representative examples of naturally obtained spirooxindoles are the NITD609 (antibacterial agent, Figure 1, **I**) [35], the MDM2-P53 interaction inhibitor (Figure 1, **II**) [36], and MI-77301 (anticancer activity, Figure 1, **III**) [37].

On the other hand, the heterocyclic systems including pyrimidine ring display interesting biological properties such as antimicrobial, antibacterial, antifungal, antiviral, anticancer activities [38–44], and additionally, high biological activity was also discovered at annulated derivatives of pyrimidine. On this basis, thiazolopyrimidine derivatives exhibit a bunch range of biological and pharmaceutical activities such as antibacterial [45], antimicrobial [46], anti-inflammatory [47, 48], antihypertensive [49], antinociceptive [50], and anticancer [51]. For example, the compounds **IV** and **V** have been used as anti-HIV-1 and anti-cancer drugs (Figure 1, **IV** and **V**) [52,53]. Thereby, based on these excellent and diverse applications of spirooxindole and thiazolopyrimidine heterocyclic compounds, the development and introduction of new approaches for the synthesis of these molecules is a pressing need in modern chemistry [54,55].

Thus, in continuation of our extensive attempts for the synthesis of novel heterocyclic molecules from readily available starting materials [56–63] in this study, firstly, some [1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one derivatives (**3a-d**) have been synthesized based on heteroatom chemistry (Scheme 1) and then, they were employed for the synthesis of novel 6′-amino-2,9′-dioxo-2′-phenyl-9′*H*-spiro[indoline-3,8′-pyrano[2,3-*d*][1,3,4]thiadiazolo[3,2-*a*]pyrimidine]-7′-carbonitrile derivatives (**6a-q**) *via* a one-pot

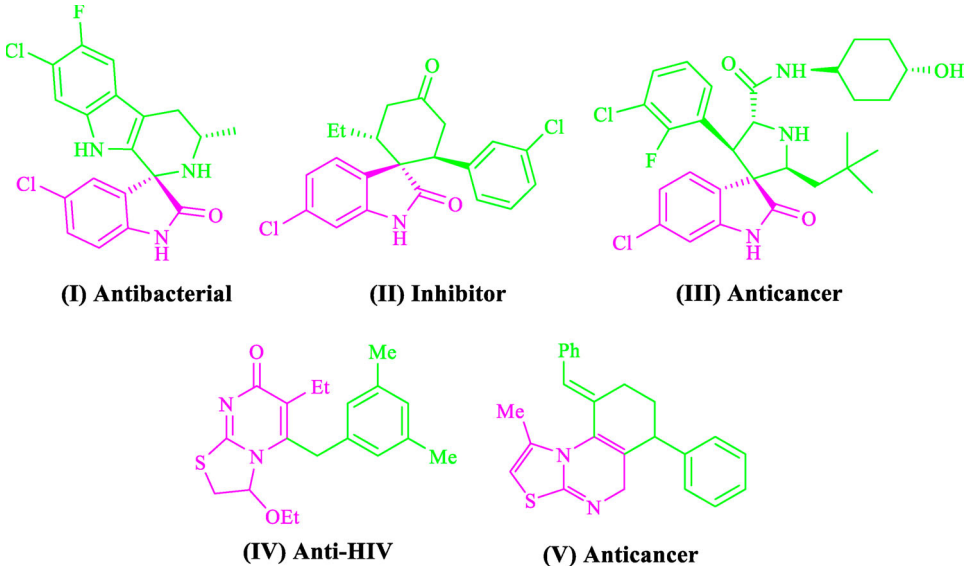
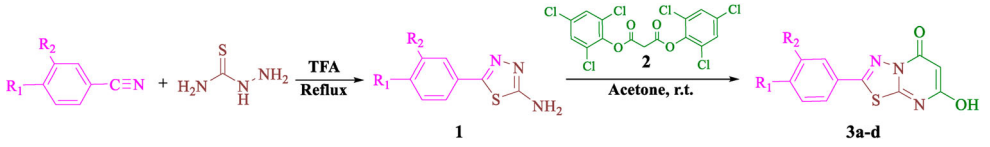
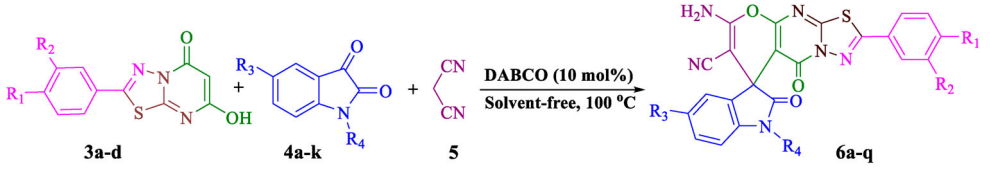


Figure 1. Selected biologically active compounds containing spirooxindole and thiazolopyrimidine moiety.



Scheme 1. Synthesis of 7-hydroxy-2-phenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one (**3a-d**).



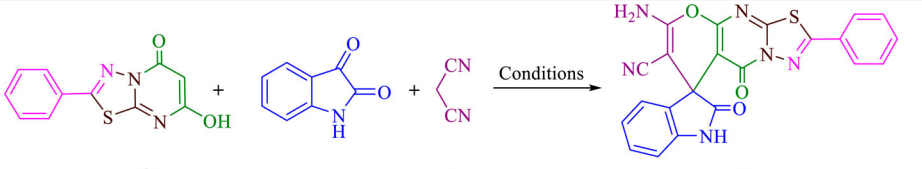
Scheme 2. Synthesis of 6′-amino-2,9′-dioxo-2′-phenyl-9′*H*-spiro[indoline-3,8′-pyrano[2,3-*d*][1,3,4] thiadiazolo[3,2-*a*]pyrimidine]-7′-carbonitrile derivatives (**6a-q**).

three-component reaction of different 7-hydroxy-2-phenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one (**3a-d**), isatin derivatives (**4a-k**), and malononitrile (**5**) in the presence of DABCO under solvent-free conditions. To the best of our knowledge, this is the first report for the synthesis of this kinds of products using 7-hydroxy-2-phenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one as an effective heterocyclic 1,3-dicarbonyl compound (Scheme 2).

2. Results and discussions

At the outset and to find the optimized reaction conditions, the three-component reaction of heterocyclic-1,3-dione (**3a**), isatin (**4a**), and malononitrile (**5**) was selected as a model reaction to synthesis of product **6a** (Table 1). Then, in the first experiment, the model reaction has been performed in the absence of catalyst under solvent-free condition at 100°C. The yield of the reaction was trace even after 24 h running the reaction (Table 1, entry 1). Afterwards and in the second experiment, the model reaction was examined in different catalysts including K_2CO_3, pipyridine, *N*,*N*-dimethylaminopyridine (DMAP), 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU), diisopropylethylamine (DIPEA) and 1,4-diazabicyclo[2.2.2]octane (DABCO) (Table 1, entries 2–7). The highest yield of product **6a** was obtained in the presence of DABCO as a Lewis basic catalyst (Table 1, entry 7). After finding the best catalyst, in the next experiment, its amount has been optimized (Table 1, entries 7–9). Surprisingly, the highest amount of product **6a** was prepared in the presence of 10 mol% of DABCO (93%) and the yields of the reaction were decreased to 85 and 87% in the lower and upper amount of DABCO, respectively (Table 1, entries 8 and 9). Evaluation of the effect of solvent was the next experiment. As a result, the model reaction was carried out in the presence of different polar and nonpolar solvents like H_2O, EtOH, MeOH, MeCN, THF and DMF, and more importantly solvent-free condition (Table 1, entries 1–15). Among these, the best condition was solvent-free in term of yield and time of the reaction. The last experiment was the optimization of temperature. So, the model reaction was tested in various temperatures including 80°C, 100°C and 120°C (Table 1, entries 16 and 17). 100°C was the best temperature and with decrease the temperature to

Table 1. Optimization of reaction conditions for the synthesis of compound **6a**.



3a **4a** **5** **6a**

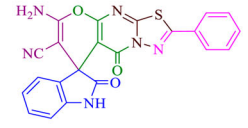
Entry	Catalyst (mol%)	Condition	Temperature (°C)	Yield (%)[a]	Time (h)
1	–	Solvent-free	100	trace	24
2	K_2CO_3	Solvent-free	100	86	5.0
3	Bipyridine	Solvent-free	100	47	2.0
4	DMAP	Solvent-free	100	89	4.0
5	DBU	Solvent-free	100	57	2.0
6	DIPEA	Solvent-free	100	85	3.0
7	**DABCO (10)**	**Solvent-free**	**100**	**93**	**25 (min)**
8	DABCO (5)	Solvent-free	100	85	25 (min)
9	DABCO (20)	Solvent-free	100	87	25 (min)
10	DABCO (10)	H_2O	reflux	52	3.0
11	DABCO (10)	EtOH	reflux	84	1.0
12	DABCO (10)	MeOH	reflux	85	2.0
13	DABCO (10)	MeCN	reflux	86	7.0
14	DABCO (10)	THF	reflux	82	1.0
15	DABCO (10)	DMF	80	84	1.0
16	DABCO (10)	Solvent-free	80	82	25 (min)
17	DABCO (10)	Solvent-free	120	93	25 (min)

[a]Isolated yield.

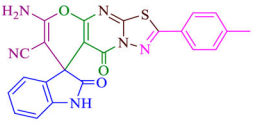
80°C, the yield of the reaction was reduced to 82 after 25 min running the reaction (Table 1, entry 16). Therefore, the optimized reaction condition for the synthesis of product **6a** was the use of 10 mol% DABCO under solvent-free condition at 100°C (Table 1, entry 7).

Thereupon, the scope of the reaction has been investigated for the synthesis of a number of spiro-pyrano-thiadiazolo-pyrimidine derivatives (**6a-q**) *via* a one-pot three-component condensation reaction of different 1,3-dicarbonyl compounds (**3a-d**), various isatin derivatives (**4a-k**), and malononitrile (**5**) under solvent-free condition at 100°C (Table 2). All

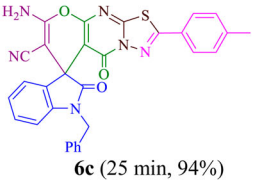
Table 2. Synthesis of different 6′-amino-2,9′-dioxo-2′-phenyl-9′*H*-spiro[indoline-3,8′-pyrano[2,3-*d*][1,3,4]thiadiazolo[3,2-*a*]pyrimidine]-7′-carbonitrile derivatives **6a-q.**[a]



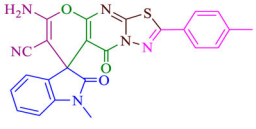
6a (25 min, 93%)



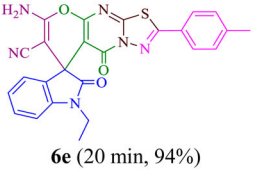
6b (30 min, 94%)



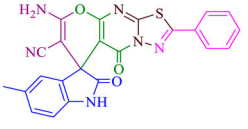
6c (25 min, 94%)



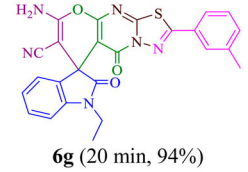
6d (30 min, 89%)



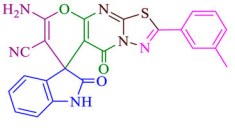
6e (20 min, 94%)



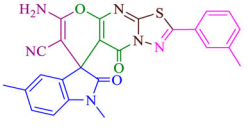
6f (20 min, 89%)



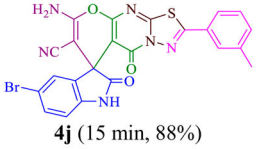
6g (20 min, 94%)



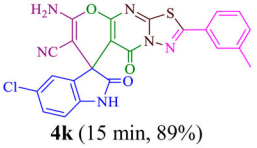
6h (55 min, 96%)



6i (20 min, 95%)

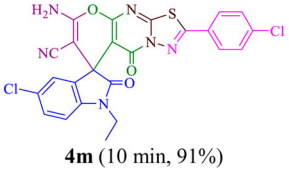


4j (15 min, 88%)

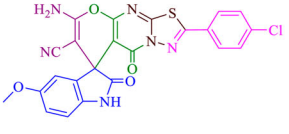


4k (15 min, 89%)

4l (15 min, 86%)

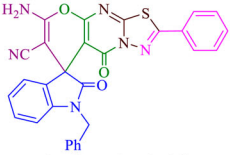


4m (10 min, 91%)

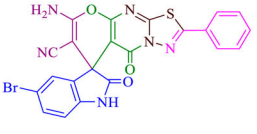


4n (60 min, 87%)

4o (35 min, 82%)

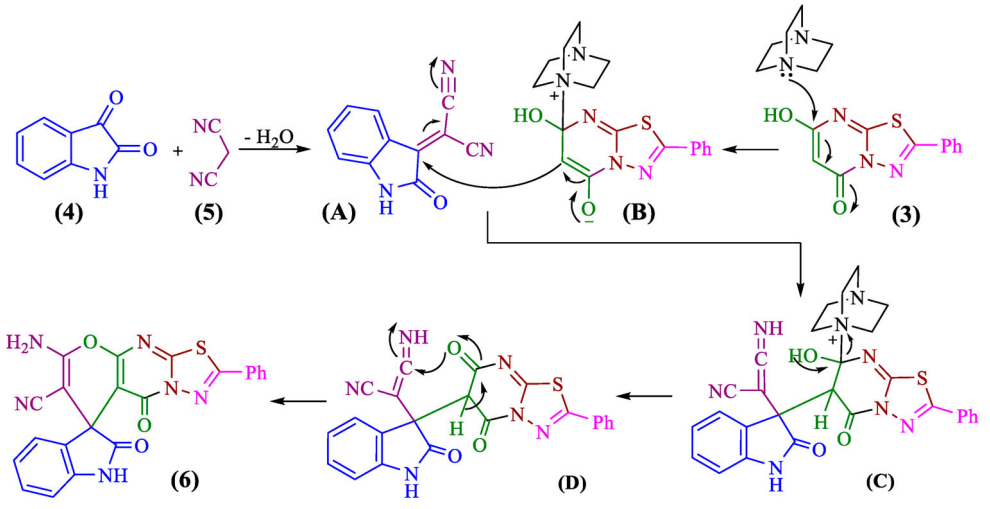


4p (25 min, 85%)



4q (20 min, 80%)

[a]Reaction condition: 7-hydroxy-2-phenyl-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidin-5-one derivatives **3a-d** (1.0 mmol), isatin derivatives **4a-k** (1.0 mmol), malononitrile **5** (1.2 mmol) and DUBCO (10 mol%) at 100°C under solvent-free condition



Scheme 3. Proposed mechanism for the synthesis of spiro-pyrano-thiadiazolo-pyrimidine derivatives in the presence of DABCO as a Lewis base catalyst.

isatin derivatives and heterocyclic1,3-diones with electron-withdrawing and electron-donating groups gave the desired products with high yields (80–96%) in short reaction times (10 to 60 min) (Table 2).

To better understanding the reaction mechanism and effect of DABCO as a Lewis base catalyst on this reaction [64], a plausible mechanism has been proposed for the synthesis of spiro-pyrano-thiadiazolo-pyrimidine derivatives (Scheme 2). As can be seen in this scheme, in the first step, from the condensation reaction of isatin (**4**) and malononitrile (**5**), the intermediate **(A)** was formed. On the other hand, the DABCO can act as a strong nucleophile and attacks to heterocyclic-1,3dione (**3**) to produce the active intermediate (**B**). Next, this active intermediate is ready to react with intermediate **(A)** *via* Michael addition to generate the intermediate (**C**). Finally, after remove the DABCO and 6-exo-dig-cyclization reaction of intermediate (**C**) and (**D**), respectively, the desired product **(6)** was generated (Scheme 3).

An ORTEP diagram of **6c** characterized by single crystal X-ray analysis (Figure 2). As depicted in this figure, the chemical structure and the stereochemistry of product **6c** confirmed successfully (CCDC 1527745): $C_{30}H_{20}N_6O_3S$: MW = 545. For more information about X-ray crystallographic data of compound **6c**, please see the supporting file.

3. Conclusion

In summary, in this study an efficient and fast procedure has been described for the synthesis of novel derivatives of spiro-pyrano-thiadiazolo-pyrimidine through one-pot three-component assembly of isatin derivatives, malononitrile, and some heterocyclic-1,3-dione in the presence of DABCO as a catalyst and under solvent-free condition. Simple and fast synthetic procedure, short reaction times, high to excellent isolated yields and carry out the reactions without using any hazardous solvents are the most advantages of present research.

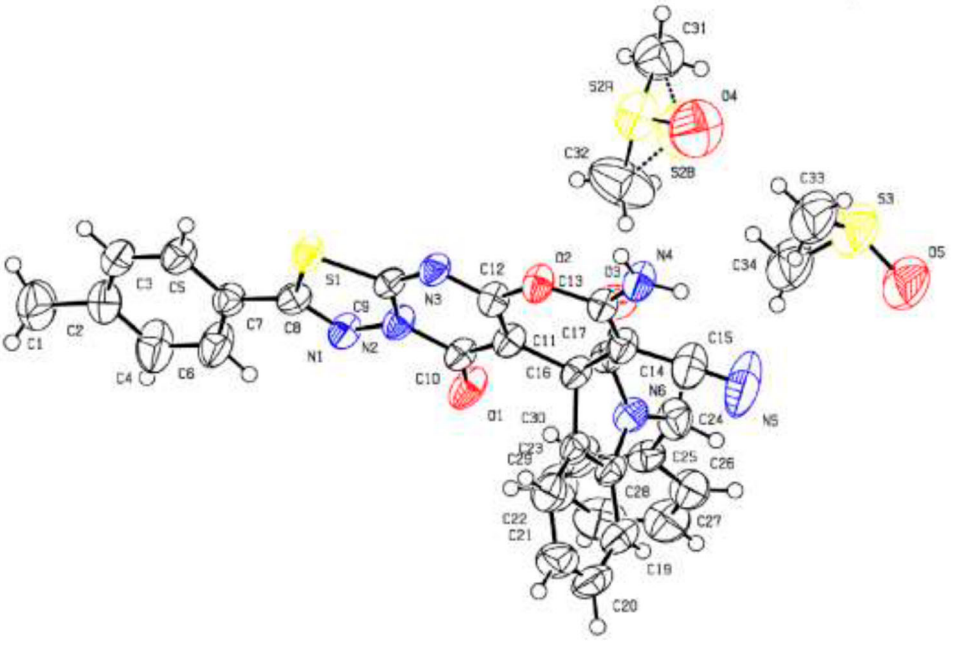


Figure 2. ORTEP structures of compound **6c.**

4. Experimental

4.1. Materials

All the starting materials have been purchased from Sigma-Aldrich and Merck companies without any further purification. Melting points were recorded on an Electrothermal-type 9100 melting point apparatus and are uncorrected. The IR spectra were obtained on an Avatar 370 FT-IR Thermo-Nicolet spectrometer. ^{1}H and ^{13}C NMR spectra were run on BRUKER DRX-300 AVANCE spectrometer at 300 for ^{1}H NMR, and 75 MHz for ^{13}C NMR DMSO-d_6 was used as solvent. The mass spectra were scanned on a Varian Mat CH-7 at 70 eV. Elemental analysis was performed on a Thermo Finnigan Flash EA microanalyser. X-ray crystal structure data were collected on a Bruker D8 VENTURE PHOTON 100 CMOS diffractometer with graphite monochromated Cu Kα radiation at 296(2) K. Isatin derivatives were prepared by known methods [65,66].

4.2. Typical procedure for the synthesis of heterocyclic-1,3dione (3)

In order to synthesis of compound **3**, initially, the enamine **1** was prepared according to the following procedure; 9.0 mL trifluoroacetic acid was added to a mixture of 3.0 g thiosemicarbazide and 3.06 g benzonitrile derivatives, and then the mixture was refluxed at 75°C for 6 h. After completion the reaction, the reaction was permitted to cool to room temperature and next, 10 mL ammonium hydroxide solution was added droppingly and the mixture was stirred constantly. The formed resulting precipitate was separated from the reaction mixture by simple filtration and washed many times with hot EtOH and after recrystallization with EtOH, it was dried in vacuum oven to afford the enamine **1** [67]. Afterwards, in order

to synthesis of heterocyclic-1,3-dione, the prepared enamine **1** (5.0 mmol) was added to a solution of bis(2,4,6-trichlorophenyl) malonate **2** (5.0 mmol) in 10 mL acetone and this mixture was stirred at room temperature for 3 h. After completion the reaction the resulting precipitate has been separated from the reaction mixture by simple filtration and finally it was recrystallized with the mixture of chloroform/ethanol (10:10 mL) to afford the final product of heterocyclic-1,3-dione (**3**).

Spectral data for compound (3):
White powder; Mp: 274–277°C, 0.2 g, yield 81%; R_f (1:1 n-hexane/EtOAc) 0.68; IR (KBr) (υ_{max}/cm^{-1}): 3076, 2869, 2745, 2657, 2568, 2504 (OH), 1661.38 (1C = O); ^{1}H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 5.44 (1H, s, CH), 7.58–7.67 (3H, m, CH_{arom}), 7.93 (2H, d, $^3J_{H,H}$ = 6.016 Hz, CH_{arom}), 11.95 (1H, br, s, OH); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 86.10 (CH– C = O), 127.64, 128.72, 130.03 (5CH_{arom} of phenyl), 133.07 (C_{arom}), 157.93 (N = C–N), 157.24 (N–C = O), 168.39 (N–C–OH), 162.35 (N = C–S); MS: (m/z, %), 245 (M^+, 28), 242, (100), 202 (99), 120 (88), 104 (87), 77 (92), 69 (95), 51 (87), 39 (49), 29 (87).

4.3. Typical procedure for the spiro-pyrano-thiadiazolo-pyrimidine derivatives 4a-q

A mixture of heterocyclic-1,3-diones **3a-d** (1.0 mmol), isatin derivatives **4a-k** (1.0 mmol) and malononitrile **5** (1.2 mmol) was stirred under solvent-free condition at 100°C for 10 to 60 min. The progress of the reaction was monitored by TLC. After finalization of the reaction, the reaction mixture was cooled to room temperature and thereafter the precipitated product was separated from the reaction mixture by simple filtration and washed three times with EtOH (20 mL). The obtained crude products were more purified by crystallization (EtOH) to afford the final product **6a-q**. The structures of all synthesized products have been confirmed by IR, ^{1}H NMR, ^{13}C NMR, mass spectrometry, CHN analysis, and also a structure of one selected product has been characterized by single-crystal X-ray diffraction studies as well.

The chemical structure of all prepared products have been characterized with mass, FT-IR, ^{1}H NMR, ^{13}C NMR, and CHN analysis (see Supporting Information). For example, the ^{1}H NMR spectrum of product (**6a)** exhibited two doublet and two triplet with four protons for the protons related to isatin ring at δ = 687–7.22, a singlet with two protons for NH_2 at δ = 7.49, one multiplet (3H) and one doublet (2H) for the protons related to phenyl ring of thiadiazolopyrimidine moiety at δ = 7.60–792, and finally a singlet with one proton for NH at δ = 10.66. Moreover, the FT-IR was another analysis to approve the structures of all synthesized products. In this regard, the IR absorption peak at 3429 cm^{-1} is assigned to the NH group, the peak at 2197 cm^{-1} is belongs to CN moiety and the peaks at 1723 and 1698 are attributed to the C = O functional groups. In addition, the carbon NMR spectrum of **6a** showed 20 distinct C NMR signal particularly carbonyls at δ = 158.9 and 177.8 ppm and cyanide at δ = 117.8 ppm. Besides, the mass spectrometry of all synthesized compounds exhibited the molecular ion peaks at relevant m/z values.

Spectral data for compound (6a):
Gray powder; Mp: 300°C, 0.41 g, yield 93%; R_f (1:3 n-hexane/EtOAc) 0.42; FT-IR (KBr) (υ_{max}/cm^{-1}): 3649, 3429, 3313, 3289, 3186, 2197 (CN), 1723, 1698 (2 C = O); ^{1}H NMR

(300.84 MHz, DMSO-d_6): δ (ppm): 10.66 (s, 1H, NH), 7.92 (d, 2H, $^3J_{HH}$ = 6.9 Hz, H_{Ar}), 7.71-7.60 (m, 3H, H_{Ar}), 7.49 (s, 2H, NH_2), 7.22 (t, 1H, $^3J_{HH}$ = 7.4 Hz, H_{Ar}), 7.10 (d, 1H, $^3J_{HH}$ = 7.2 Hz, H_{Ar}), 6.94 (t, 1H, $^3J_{HH}$ = 7.5 Hz, H_{Ar}), 6.87 (d, 1H, $^3J_{HH}$ = 7.5 Hz, H_{Ar}); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 48.7 (C_{spiro}), 57.0 (=*C*-CN), 96.5 (=*C*-C=O), 109.8 (CH_{Ar}), 117.8 (CN), 122.3, 124.4, 127.8, 128.3, 129.1, 130.1 (8 CH_{Ar}), 133.5, 133.7, 142.7 (3 C_{Ar}), 154.8 (N-*C*=N), 158.9 (C=O), 159.6 (=C-NH_2), 159.9 (N-N=C), 161.9 (CO-C=*C*-O), 177.8 (C=O_{isa}); MS: (m/z, %), 441 (M^+, 21), 194 (100), 28 (99), 202 (97), 77 (78), 167 (74), 243 (73), 103 (72), 139 (62), 334 (42), Anal. Calcd for $C_{22}H_{12}N_5O_3S$(440.43): C,60.00; H, 2.75; N,19.08%. Found: C, 60.28; H, 3.03; N, 18.95%.

Spectral data for compound (6b):

Milky powder; Mp: 300°C, 0.42 g, yield 94%; R_f (1:3 n-hexane/EtOAc) 0.37; FT-IR (KBr)(υ_{max}/cm^{-1}): 3426, 3358, 3325, 3293, 3248, 3198, 3023, 2194 (CN), 1731, 1690 (2 C=O); ^{1}H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 10.65 (s, 1H, NH), 7.82 (d, 2H, $^3J_{HH}$ = 7.8 Hz, H_{Ar}), 7.48–7.43 (m, 4H, $H_{Ar,}$ NH_2), 7.21 (t, 1H, $^3J_{HH}$ = 7.7 Hz, H_{Ar}), 7.10 (d, 1H, $^3J_{HH}$ = 7.5 Hz, H_{Ar}), 6.93 (t, 1H, $^3J_{HH}$ = 7.5 Hz, H_{Ar}), 6.86 (d, 1H,$^3J_{HH}$ = 7.8 Hz, H_{Ar}), 2.41 (s, 3H, CH_3); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 21.6 (CH_3), 48.7 (C_{spiro}), 57.0 (=*C*-CN), 96.4(=*C*-C=O), 109.7 (CH_{Ar}), 117.7 (CN), 122.3, 124.4, 125.6, 127.7, 129.0 (7 CH_{Ar}), 130.7, 133.7, 142.7, 144.0 (4 C_{Ar}), 154.8 (N-C=N), 158.8 (C=O), 159.6 (=CNH_2), 159.8 (N-N=C), 161.8 (CO-C=*C*-O), 177.8 (C=O_{isa}); MS: (m/z, %), 453 (M^+, 5), 206 (100), 28 (97), 116 (57),192 (57), 133 (46), 331 (43), 215 (33), 65 (20), Anal. Calcd for $C_{23}H_{14}N_6O_3S$ (365.06): C, 60.79; H, 3.11; N,18.49%. Found: C, 60.62; H, 2.94; N, 18.65%.

Spectral data for compound (6c):

White powder; Mp: 300°C, 0.51 g, yield 94%; $R_{f=}$ 0.53 (1:3 n-hexane/EtOAc); FT-IR (KBr)(υ_{max}/cm^{-1}): 3485, 3381, 3183, 3060, 3036, 2917, 2200 (CN), 1710, 1654 (2 C=O), ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 7.83 (d, 2H,$^3J_{HH}$ = 8.1 Hz, H_{Ar}), 7.58–7.52 (m, 4H, $H_{Ar,}$ NH_2), 7.44 (d, 2H, $^3J_{HH}$ = 8.1 Hz, H_{Ar}), 7.38–7.29 (m, 3H, H_{Ar}), 7.23–7.19 (m, 2H, H_{Ar}), 7.00 (t, 1H, $^3J_{HH}$ = 7.5 Hz, H_{Ar}), 6.79 (d, 1H, $^3J_{HH}$ = 7.5 Hz, H_{Ar}), 5.04 (1H, d,$^2J_{HH}$ = 16.2 Hz, PhC$H_A$$H_B$), 4.94 (1H, d,$^2J_{HH}$ = 15.9 Hz, PhC$H_A$$H_B$), 2.41 (s, 3H, CH_3);^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 21.6 (CH_3), 44.0 (C_{spiro}), 48.5 (CH_2), 56.7 (=*C*-CN), 96.3 (=*C*-C=O), 109.4 (CN), 117.8, 123.2, 124.3, 125.6, 127.6, 127.7, 127.8, 128.9, 129.1 (13CH_{Ar}), 130.7, 132.9, 136.5, 143.3 (4 C_{Ar}), 144.1 (N-C=N), 154.9 (C=O), 158.9 (C_{Ar}), 159.7 (=CNH_2), 160.0 (N-N=C), 162.0 (CO-C=*C*-O), 176.5 (C=O_{isa}); MS: (m/z, %), 544 (M^+, 19), 90 (100), 280 (78), 64 (75), 253 (72), 451 (72), 39 (71), 215 (70), 116 (51), 133 (39). Anal. Calcd for $C_{30}H_{20}N_6O_3S$ (544.59): C, 66.17; H, 3.70; N, 15.43%. Found: C, 66.30; H, 3.54; N, 15.25%.

Spectral data for compound (6d):

White powder; Mp: 300°C, 0.42 g, yield 89%; R_f (1:3 n-hexane/EtOAc) 0.47; FT-IR (KBr)(υ_{max}/cm^{-1}): 3497, 3377, 3186, 3052, 3031, 2974, 2880, 2202 (CN), 1714, 1657 (2 C=O), ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 7.79 (d, 2H,$^3J_{HH}$ = 7.8 Hz, H_{Ar}), 7.55 (s, 2H, NH_2), 7.42 (d, 2H, $^3J_{HH}$ = 7.8 Hz, H_{Ar}), 7.33 (t, 1H, $^3J_{HH}$ = 7.7 Hz, H_{Ar}), 7.16 (d, 1H, $^3J_{HH}$ = 7.5 Hz, H_{Ar}), 7.10-7.00 (m, 2H, H_{Ar}), 3.23 (s, 3H, N-CH_3), 2.40 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 21.6 (CH_3), 27.0 (N-CH_3), 48.3 (C_{spiro}), 56.5 (=*C*-CN), 96.4 (=*C*-C=O), 108.7 (CH_{Ar}), 117.6 (CN), 123.0, 124.1, 125.6, 127.7, 129.3 (7 CH_{Ar}), 130.7, 132.9, 144.1, 144.3 (C_{Ar}), 154.7 (N-C=N), 158.7 (C=O), 159.6

(=CNH_2), 160.0 (N-N=C), 161.9 (CO-C=*C*-O), 176.3 (C=O $_{isa}$); MS: (m/z, %), 468 (M^+, 12), 206 (100), 220 (93), 28 (90), 152 (74), 255 (73), 116(56), 90(50), 133(42), 467(37), Anal. Calcd for $C_{24}H_{16}N_6O_3S$ (468.48): C, 61.53; H, 3.44; N, 17.94%. Found: C, 61.62; H, 3.24; N, 18.15%.

Spectral data for compound (6e):

White powder; Mp: 300°C, 0.45 g, yield 94%; R_f (1:3 n-hexane/EtOAc) 0.48; FT-IR (KBr)(υ_{max}/cm^{-1}): 3489, 33.77, 3190, 3064, 3032, 2984, 2937, 2880, 2199 (CN), 1709, 1656 (2 C=O); ^{1}H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 7.80 (d, 2H,$^3J_{HH}$ = 7.8 Hz, H_{Ar}), 7.53 (s, 2H, NH_2), 7.41 (d, 2H, $^3J_{HH}$ = 7.8 Hz, H_{Ar}), 7.32 (t, 1H, $^3J_{HH}$ = 7.5 Hz, H_{Ar}), 7.17 (d, 1H, $^3J_{HH}$ = 7.2 Hz, H_{Ar}), 7.12 (d, 1H, $^3J_{HH}$ = 7.8 Hz, H_{Ar}), 7.01 (t, 1H, $^3J_{HH}$ = 7.4 Hz, H_{Ar}), 3.80 (q, 2H, $^3J_{HH}$ = 13.8 Hz,$^3J_{HH}$ = 6.9 Hz,CH_2-CH_3), 2.39 (s, 3H, CH_3), 1.24 (t, 3H,$^3J_{HH}$ = 6.9 Hz, CH_2-CH_3); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 17.5 (CH_2-CH_3), 26.3 (CH_3), 39.8 (CH_2), 53.0 (C_{spiro}), 61.4 (=*C*-CN), 101.1 (=*C*-C=O), 113.5 (CN), 122.3, 127.6, 129.0, 130.3, 132.5, 134.0 (8 CH_{Ar}), 135.4, 137.9, 147.9 (3C_{Ar}), 148.9 (N-C=N), 159.5 (C=O), 163.5 (C_{Ar}), 164.3 (=CNH_2), 164.7 (CO-C=*C*-O), 166.6 (N-N=C), 180.5 (C=O $_{isa}$); MS: (m/z, %), 483 (M^+, 52), 206 (100), 221 (72), 454 (69), 29 (68), 426 (42), 117 (38), 179 (36), 91 (29), 256 (15), Anal. Calcd for $C_{25}H_{18}N_6O_3S$ (482.51): C, 62.23; H, 3.76; N, 17.42%. Found: C, 62.12; H, 3.94; N, 17.65%.

Spectral data for compound (6f):

Gray powder; Mp: 298°C, 0.39 g, yield 87%; R_f (1:3 n-hexane/EtOAc) 0.34; FT-IR (KBr)(υ_{max}/cm^{-1}): 3649, 3427, 3317, 3289, 3187, 2913, 2860, 2200 (CN), 1724, 1699 (2 C=O); ^{1}H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 10.56 (s, 1H, NH), 7.92 (d, 2H, $^3J_{HH}$ = 6.6 Hz, H_{Ar}), 7.71-7.60 (m, 3H, H_{Ar}), 7.48 (s, 2H, NH_2), 7.02 (d, 2H, $^3J_{HH}$ = 6.0 Hz, H_{Ar}), 6.93 (s, 1H, H_{Ar}), 6.76 (d, 1H,$^3J_{HH}$ = 7.8 Hz, H_{Ar}), 2.21 (s, 3H, CH_3); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 21.1 (CH_3), 48.7 (C_{spiro}), 57.2 (=*C*-CN), 96.6 (=*C*-C=O), 109.5 (CN), 117.8, 124.9, 127.8, 128.4, 129.3, 130.2 (8 CH_{Ar}), 131.1, 133.5, 133.8, 140.3 (4C_{Ar}), 154.8 (N-C=N), 158.8 (C=O), 159.6 (=CNH_2), 159.8 (N-N=C), 161.9 (CO-C=*C*-O), 177.7 (C=O $_{isa}$); MS: (m/z, %), 455 (M^+, 6), 176 (100), 207 (97), 243 (74), 28 (72), 153 (72), 126 (72), 102 (72), 66 (72), 44 (62), Anal. Calcd for $C_{23}H_{14}N_6O_3S$ (454.46):C, 60.70; H, 3.11; N, 18.49%. Found: C, 60.62; H, 2.94; N, 18.36%.

Spectral data for compound (6g):

White powder; Mp: 297°C, 0.45 g, yield 94%; R_f (1:3 n-hexane/EtOAc) 0.60; FT-IR (KBr)(υ_{max}/cm^{-1}): 3457, 3325, 3183, 3052, 2987, 2933, 2880, 2199 (CN), 1704, 1656 (2 C=O); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 7.74-7.70 (m, 2H, H_{Ar}), 7.52-7.48 (m, 4H, $H_{Ar,}$ NH_2), 7.32 (t, 1H, $^3J_{HH}$ = 7.4 Hz, H_{Ar}), 7.17 (d, 1H, $^3J_{HH}$ = 6.3 Hz, H_{Ar}), 7.11 (d, 1H, $^3J_{HH}$ = 7.82 Hz, H_{Ar}), 7.01 (t, 1H, $^3J_{HH}$ = 7.4 Hz, H_{Ar}), 3.80 (q, 2H, $^3J_{HH}$ = 14.1 Hz,$^3J_{HH}$ = 6.9 Hz, CH_2-CH_3), 2.40 (s, 3H, CH_3), 1.24 (t, 3H,$^3J_{HH}$ = 6.9 Hz, CH_2-CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 12.7 (CH_2-CH_3), 21.2 (CH_3), 35.0 (CH_2), 48.2 (C_{spiro}), 56.7 (=*C*-CN), 96.4 (=*C*-C=O), 108.7 (CN), 117.5, 122.8, 124.3, 125.0, 128.1, 128.3, 129.3, 130.0, (8 CH_{Ar}), 133.1, 134.2, (2C_{Ar}), 139.8 (N-C=N), 143.2 (C_{Ar}), 154.8 (C=O), 158.8 (C_{Ar}), 159.7 (=CNH_2), 159.9 (CO-C=*C*-O), 161.9 (N-N=C), 175.8 (C=O $_{isa}$); MS: (m/z, %), 483 (M^+, 23), 29 (99), 190 (97), 206 (74), 118 (81), 74 (80), 216 (68), 256 (60), 91 (51), 134 (50), Anal. Calcd for $C_{25}H_{18}N_6O_3S$ (482.51): C, 62.23; H, 3.76; N, 17.42%. Found: C, 62.32; H, 3.58; N, 17.15%.

Spectral data for compound (6h):
Milky powder; Mp: 293°C, 0.43 g, yield 96%; R_f (1:3 n-hexane/EtOAc) 0.43; FT-IR (KBr)(υ_{max}/cm^{-1}): 3649, 3501, 3444, 3375, 3187, 2199 (CN), 1725, 1651 (2 C = O); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 10.65 (s, 1H, NH),7.74-7.71 (m, 2H, H_{Ar}), 7.51-7.49 (m, 4H, $H_{Ar,}$ NH_2), 7.22 (t, 1H, $^3J_{HH}$ = 7.7 Hz, H_{Ar}), 7.10 (d, 1H, $^3J_{HH}$ = 7.22 Hz, H_{Ar}), 6.94 (t, 1H, $^3J_{HH}$ = 7.4 Hz, H_{Ar}), 6.87 (d, 1H, $^3J_{HH}$ = 7.5 Hz, $\underline{H_{Ar}}$), 2.40 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 21.2 (CH_3), 48.7 (C_{spiro}), 57.0 (= *C*-CN), 96.5 (= *C*-C = O), 109.7 (CH_{Ar}), 117.7 (CN), 122.3, 124.4, 125.0, 128.2, 128.3, 129.1, 130.1 (7CH_{Ar}), 133.7, 134.2, 139.8 (3C_{Ar}), 142.8 (N-C = N), 154.8 (C_{Ar}), 158.8 (C = O), 159.7 (= CNH_2), 159.8 (N-N = C), 161.9 (CO-C = *C*-O), 177.8 (C = O $_{isa}$); MS: (m/z, %), 454 (M^+, 2), 29 (100), 194 (80), 66 (57), 39 (56), 90 (50), 134 (47), 116 (33), 216 (31), 167 (31), Anal. Calcd for $C_{23}H_{14}N_6O_3S$ (454.46): C, 60.79; H, 3.11; N, 18.49%. Found: C, 60.82; H, 3.38; N, 18.31%.

Spectral data for compound (6i):
Milky powder; Mp: 281°C, 0.46 g, yield 95%; R_f (1:3 n-hexane/EtOAc) 0.59; FT-IR (KBr)(υ_{max}/cm^{-1}): 3489, 3369, 3187, 3015, 2962, 2917, 2872, 2201 (CN), 1716, 1703 (2 C = O); ^{1}H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 7.79-7.70 (m, 2H, H_{Ar}), 7.53-7.49 (m, 4H, H_{Ar}, NH_2), 7.13 (d, 1H, $^3J_{HH}$ = 6.3 Hz, $\underline{H_{Ar}}$), 6.99-6.95 (m, 2H, H_{Ar}), 3.20 (s, 3H, N-CH_3), 2.40 (s, 3H, CH_3), 2.24 (s, 3H,CH_3); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 21.1 (CH_3), 21.2 (CH_3), 26.9 (N-CH_3), 48.4 (C_{spiro}), 56.6 (= *C*-CN), 96.6 (= *C*-C = O), 108.4 (CN), 117.7, 124.8, 125.0, 128.2, 128.3 (5 CH_{Ar}), 129.5 (C_{Ar}), 130.1, 132.0 (2 CH_{Ar}), 134.2, 139.8 (2C_{Ar}), 142.0 (N-C = N), 154.8, 158.7 (2 C_{Ar}), 159.7 (C = O), 159.9 (= CNH_2), 160.0 (N-N = C), 162.0 (CO-C = *C*-O), 176.2 (C = O $_{isa}$); MS: (m/z, %), 482 (M^+, 21), 29 (100), 232 (100), 257 (51), 217 (50), 167 (36), 190 (25), 118 (22), 91 (18), 66 (15), 44 (13). Anal. Calcd for $C_{25}H_{18}N_6O_3S$ (482.51): C, 62.23; H, 3.76; N, 19.42%. Found: C, 62.42; H, 3.88; N, 19.15%

Spectral data for compound (6j):
Gray powder; Mp: 300°C, 0.47 g, yield 88%; R_f (1:3 n-hexane/EtOAc) 0.55; FT-IR (KBr)(υ_{max}/cm^{-1}): 3481, 3448, 3352, 3268, 3183, 3068, 2198 (CN), 1743, 1724 (2 C = O); ^{1}H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 10.81 (s, 1H, NH), 7.74-7.72 (m, 2H, H_{Ar}), 7.58 (s, 2H, NH_2), 7.54-7.49 (m, 2H, H_{Ar}), 7.42-7.35 (m, 2H, H_{Ar}), 6.84 (d, 1H, $^3J_{HH}$ = 8.1 Hz, H_{Ar}), 2.40 (s, 3H,CH_3); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 21.2 (CH_3), 49.0 (C_{spiro}), 56.2 (= *C*-CN), 95.9 (= *C*-C = O), 111.7 (CH_{Ar}), 114.0 (C_{Ar}), 117.6 (CN), 125.0, 127.3, 128.2, 128.3, 130.1, 131.8 (6 CH_{Ar}), 134.2, 136.0 (2 C_{Ar}), 139.8 (N-C = N), 142.1, 155.0 (2 C_{Ar}), 158.9 (C = O), 159.7 (= CNH_2), 160.0 (CO-C = *C*-O), 162.1 (N-N = C),177.5 (C = O $_{isa}$); MS: (m/z, %), 534 (M^+, 3), 114 (100), 138 (90), 272 (85), 69 (83), 216 (82), 91 (80), 29 (80), 245 (78), 165 (76), Anal. Calcd for $C_{23}H_{13}BrN_6O_3S$ (533.36): C, 51.79; H, 2.46; N, 15.76%. Found: C, 51.82; H, 2.38; N, 15.55%.

Spectral data for compound (6k):
Gray powder; Mp: 300°C, 0.43 g, yield 89%; R_f (1:3 n-hexane/EtOAc) 0.47; FT-IR (KBr)(υ_{max}/cm^{-1}): 3436, 3330, 3186, 3076, 3019, 2207 (CN), 1730, 1701 (2 C = O); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 10.80 (s, 1H, NH), 7.81 (d, 2H,$^3J_{HH}$ = 7.8 Hz, H_{Ar}), 7.58 (s, 2H, NH_2), 7.43 (d, 2H,$^3J_{HH}$ = 7.8 Hz, H_{Ar}), 7.29-7.23 (m, 2H, H_{Ar}), 6.89 (d, 1H, $^3J_{HH}$ = 8.4 Hz, H_{Ar}), 2.40 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm): 21.6 (CH_3), 49.0 (C_{spiro}), 56.2 (= *C*-CN), 95.9 (= *C*-C = O), 111.1 (CH_{Ar}), 117.6 (CN), 124.7

(CH_{Ar}), 125.6 (C_{Ar}), 126.3, 127.7, 129.0 (5 CH_{Ar}), 130.7, 135.7, 141.7, 144.1 (4 C_{Ar}), 154.9 (N-C = N), 158.9 (C = O), 159.6 (= CNH_2), 160.0 (N-N = C), 162.0 (CO-C = *C*-O), 177.6 (C = O $_{isa}$); MS: (m/z, %), 489 (M^+, 28), 227 (100), 29 (75), 257 (68), 216 (56), 190 (35), 368 (33), 118 (22), 461 (20), 66 (18), Anal. Calcd for $C_{23}H_{13}ClN_6O_3S$ (488.90): C, 56.50; H, 2.68; N, 17.19%. Found: C, 56.72; H, 2.36; N, 17.07%.

Spectral data for compound (6l):
Brick powder; Mp: 280 °C, 0.42 g, yield 86%; R_f (1:3 n-hexane/EtOAc) 0.46; FT-IR (KBr)(υ_{max}/cm^{-1}): 3534, 3444, 3324, 3193, 2200 (CN), 1737, 1697 (2 C = O); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm): 11.43 (s, 1H, NH),8.23 (dd, 1H, $^3J_{HH}$ = 8.4 Hz,$^3J_{HH}$ = 2.4 Hz, H_{Ar}), 8.13 (d, 1H, $^3J_{HH}$ = 2.4 Hz, H_{Ar}), 7.94-7.91 (m, 2H, H_{Ar}), 7.71-7.60 (m, 4H, H_{Ar}, NH_2), 7.11 (d, 1H, $^3J_{HH}$ = 8.4 Hz, H_{Ar}); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm):48.9 (C_{spiro}), 55.5 (= *C*-CN), 95.5 (= *C*-C = O), 110.0(CH_{Ar}), 117.5 (CN), 120.4, 126.6, 127.8, 128.3, 130.2 (7 CH_{Ar}), 133.6, 134.6 (2 C_{Ar}), 143.0 (N-C = N), 149.3 (C_{Ar}), 155.1 (C = O), 159.1 (C_{Ar}), 159.8 (= CNH_2), 160.2 (N-N = C), 162.4 (CO-C = *C*-O), 178.5 (C = O $_{isa}$); MS: (m/z, %), 486 (M^+, 5), 29 (100), 196 (74), 97 (28), 202 (26), 243 (26), 131 (18), 468 (17), 208 (14), 66 (12), Anal. Calcd for $C_{22}H_{11}N_7O_5S$ (485.43): C, 54.43; H, 2.28; N, 20.20%. Found: C, 54.62; H, 2.44; N, 19.95%.

Spectral data for compound (6m):
White powder; Mp: 300°C, 0.49 g, yield 91%; R_f (1:3 n-hexane/EtOAc) 0.63; FT-IR (KBr)(υ_{max}/cm^{-1}): 3322, 3293, 3252, 3178, 2987, 2946, 2876, 2198(CN), 1710, 1659 (2 C = O); ^{1}H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 7.96 (d, 2H, $^3J_{HH}$ = 8.7 Hz, HAr), 7.71 (d, 2H, $^3J_{HH}$ = 8.4 Hz, HAr), 7.62 (d, 2H, NH2), 7.35 (dd,$^3J_{HH}$ = 2.1 Hz, $^3J_{HH}$ = 8.1 Hz,1H, HAr), 7.32 (d, 1H, $^3J_{HH}$ = 2.4 Hz, $\underline{H_{Ar}}$), 7.17 (d, 1H, $^3J_{HH}$ = 8.4 Hz, $\underline{H_{Ar}}$), 3.79 (q, $^3J_{HH}$ = 13.8 Hz, $^3J_{HH}$ = 6.6 Hz, 2H,CH_2), 1.21 (t, 3H,$^3J_{HH}$ = 6.9 Hz, CH_3); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 12.6 (CH_3), 35.2 (CH_2), 48.4 (C_{spiro}), 55.9 (= *C*-CN), 95.9 (= *C*-C = O), 110.3 (CN), 117.4, 124.6, 126.9, 127.2 (6 CH_{Ar}), 129.1 (C_{Ar}), 129.6 (CH_{Ar}), 130.3, 135.0, 138.3 (3C_{Ar}), 142.1 (N-C = N), 154.9 (C = O), 158.6 (C_{Ar}), 158.9 (= CNH_2), 160.0 (CO-C = *C*-O), 162.2 (N-N = C), 175.6 (C = O $_{isa}$); MS: (m/z, %), 537 (M^+, 41), 29 (92), 511 (89), 115 (31), 235 (26), 209 (20), 254 (18), 44 (11), 482 (11). Anal. Calcd for $C_{24}H_{14}Cl_2N_6O_3S$ (537.37): C, 53.64; H, 2.63; N, 15.64%. Found: C, 53.82; H, 2.38; N, 15.75%

Spectral data for compound (6n):
Gray powder; Mp: 300°C, 0.44 g, yield 87%; R_f (1:3 n-hexane/EtOAc) 0.30; FT-IR (KBr)(υ_{max}/cm^{-1}): 3489, 3377, 3299, 3186, 3027, 2945, 2847, 2202 (CN), 1725, 1657 (2 C = O); ^{1}H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 10.47 (s, 1H, NH),7.96 (d, 2H, $^3J_{HH}$ = 8.7 Hz, $\underline{H_{Ar}}$), 7.72 (d, 2H, $^3J_{HH}$ = 8.7 Hz, $\underline{H_{Ar}}$), 7.48 (d, 2H, NH_2), 7.76 (d, 2H, $^3J_{HH}$ = 7.5 Hz, $\underline{H_{Ar}}$), 3.67 (s, 2H,CH_3); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 49.2 (C_{spiro}), 55.9 (CH_3), 57.1 (= *C*-CN), 96.5 (= *C*-C = O), 110.1, 111.2 (2 CH_{Ar}), 113.8 (CN), 117.7, 127.3, 129.6 (5 CH_{Ar}), 130.3, 134.9, 136.0, 138.3 (4 C_{Ar}), 154.8 (N-C = N), 155.6 (C = O), 158.5 (= CNH_2), 158.9 (C_{Ar}), 159.8 (N-N = C), 161.9 (CO-C = *C*-O), 177.6 (C = O $_{isa}$); MS: (m/z, %), 505 (M^+, 11), 223 (100), 29 (99), 208 (83), 236 (30), 153 (30), 136 (25), 276 (24), 66 (23), 322 (8). Anal. Calcd for $C_{23}H_{13}ClN_6O_4S$ (504.90): C, 54.71; H, 2.60; N, 16.65%. Found: C, 54.82; H, 2.39; N, 16.39%

Spectral data for compound (6o):
Gray powder; Mp: 300°C, 0.39 g, yield 82%; R_f (1:3 n-hexane/EtOAc) 0.43; FT-IR (KBr)(υ_{max}/cm^{-1}): 3440, 3329, 3191, 3076, 3019, 2202 (CN), 1727, 1702 (2 C=O); ^1H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 10.81 (s, 1H, NH), 7.91 (d, 2H, $^3J_{HH}$ = 6.9 Hz, H_{Ar}), 7.70-7.58 (m, 5H, H_{Ar}, NH_2), 7.29-7.26 (m, 2H, H_{Ar}), 6.90 (d, 1H,$^3J_{HH}$ = 8.1 Hz, H_{Ar}); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 49.0 (C_{spiro}), 56.3 (=*C*-CN), 96.0 (=*C*-C=O), 111.2 (CH_{Ar}), 117.7 (CN), 124.7 (CH_{Ar}), 126.3 (C_{Ar}), 127.8, 128.3, 129.0, 130.2 (6 CH_{Ar}), 133.6, 135.7, 141.7 (3 C_{Ar}), 155.0 (N-C=N), 159.0 (C=O), 159.7 (=CNH_2), 160.0 (N-N=C), 162.1 (CO-C=*C*-O), 177.6 (C=O $_{isa}$); MS: (m/z, %), 475 (M^+, 2), 29 (98), 44 (85), 66 (73), 227 (67), 36 (61), 103 (56), 201 (55), 77 (54), 121 (43), Anal. Calcd for $C_{22}H_{11}ClN_6O_3S$ (474.88): C, 55.64; H, 2.33; N, 17.70%. Found: C, 55.72; H, 2.14; N, 17.95%.

Spectral data for compound (6p):
Karami powder; Mp: 300°C, 0.45 g, yield 85%; R_f (1:3 n-hexane/EtOAc) 0.65; FT-IR (KBr)(υ_{max}/cm^{-1}): 3464, 3329, 3174, 3064, 3027, 2913, 2202 (CN), 1705, 1653 (2 C=O); ^1H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 7.93 (d, 2H,$^3J_{HH}$ = 6.9 Hz, H_{Ar}), 7.71–7.57 (m, 4H, $H_{Ar,}$ NH_2), 7.51 (d, 2H, $^3J_{HH}$ = 6.9 Hz, H_{Ar}), 7.37-7.26 (m, 3H, H_{Ar}), 7.23-7.19 (m, 2H, H_{Ar}), 7.01 (t, 1H, $^3J_{HH}$ = 7.3 Hz, H_{Ar}), 6.78 (d, 1H, $^3J_{HH}$ = 7.8 Hz, H_{Ar}), 5.05 (1H, d,$^2J_{HH}$ = 16.2 Hz, phCH_AH$_B$), 4.95 (1H, d,$^2J_{HH}$ = 16.2 Hz, phCH_AH$_B$); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 44.0 (C_{spiro}), 48.5 (CH_2),56.7 (=*C*-CN), 96.3 (=*C*-C=O), 109.4 (CN), 117.8, 123.2, 124.3, 127.6, 127.7, 127.9, 128.3, 128.9, 129.2, 130.2 (14 CH_{Ar}), 132.9, 133.6, 136.5 (3 C_{Ar}), 143.3 (N-C=N), 154.9 (C=O), 158.9 (C_{Ar}), 159.7 (=CNH_2), 160.0 (N-N=C), 162.1 (CO-C=*C*-O), 176.6 (C=O $_{isa}$); MS: (m/z, %), 531 (M^+, 10), 90(100), 281 (85), 242 (78), 202 (78), 175 (78), 102 (78), 51 (78), 28 (77), 120 (63). Anal. Calcd for $C_{29}H_{18}N_6O_3S$ (530.56): C, 65.65; H, 3.42; N, 15.84%. Found: C, 65.62; H, 3.24; N, 15.95%.

Spectral data for compound (6q):
Karami powder; Mp: 300°C, 0.41 g, yield 80%; R_f (1:3 n-hexane/EtOAc) 0.46; FT-IR (KBr)(υ_{max}/cm^{-1}): 3599, 3468, 3339, 3239, 3192, 3031, 2831, 2201 (CN), 1737, 1702 (2 C=O); ^1H NMR (300.84 MHz, DMSO-d_6): δ (ppm): 10.82 (s, 1H, NH), 7.91 (d, 2H, $^3J_{HH}$ = 6.9 Hz, H_{Ar}), 7.70–7.58 (m, 5H, H_{Ar}, NH_2), 7.41 (dd, 1H, $^3J_{HH}$ = 1.8 Hz,$^3J_{HH}$ = 8.1 Hz, H_{Ar}), 7.36 (d, 1H, $^3J_{HH}$ = 1.8 Hz, H_{Ar}), 6.85 (d, 1H,$^3J_{HH}$ = 8.1 Hz, H_{Ar}); ^{13}C NMR (75.65 MHz, DMSO-d_6): δ (ppm): 49.0 (C_{spiro}), 56.3 (=*C*-CN), 96.0 (=*C*-C=O), 111.7 (CH_{Ar}), 114.1 (C_{Ar}), 117.7 (CN), 127.4, 127.8, 128.3, 130.2, 131.8 (7 CH_{Ar}), 133.6, 136.0 (2 C_{Ar}), 142.1 (N-C=N), 155.0 (C_{Ar}), 159.0 (C=O), 159.7 (=CNH_2), 160.0 (N-N=C), 162.1 (CO-C=*C*-O), 177.5 (C=O $_{isa}$); MS: (m/z, %), 519 (M^+, 6),28 (100), 102 (75), 76 (56), 202 (54), 44 (42), 120 (38), 271 (37), 242 (37), 138 (32), Anal. Calcd for $C_{22}H_{11}BrN_6O_3S$ (519.33): C, 50.88; H, 2.14; N, 16.18%. Found: C, 50.62; H, 2.41; N, 15.95%.

Disclosure statement

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