C. R. Chimie 14 (2011) 556–562

Contents lists available at ScienceDirect

Comptes Rendus Chimie

www.sciencedirect.com

Full paper/Mémoire

A simple and catalyst-free three-component method for the synthesis of spiro[indenopyrazolopyridine indoline]diones and spiro[indenopyridopyrimidine indoline]triones

Ghazaleh Imani Shakibaei, Afsaneh Feiz, Ayoob Bazgir *

Department of Chemistry, Shahid Beheshti University, G.C, 1983963113 Tehran, Iran

ARTICLE INFO

Article history:
Received 5 July 2010
Accepted after revision 4 October 2010
Available online 11 November 2010

Keywords:
Isatin
Spirooxindole
Amino pyrazole
Spiroindenopyrazolopyridine indoline

ABSTRACT

An efficient, simple and catalyst-free synthesis of spiro[indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridine indoline]diones and spiro[acenaphthylene-indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridine]diones by the three-component reaction of 1,3-indandione, pyrazol-5-amines and isatins or acenaphthylene-1,2-dione in refluxing ethanol is reported. Reaction of 2,6-diaminopyrimidin-4(3*H*)-one with 1,3-indandione and isatins resulted in the formation of 1*H*-spiro[indeno[1,2-*b*]pyrido[2,3-*d*]pyrimidine-5,3′-indoline]-2′,4,6(11*H*)-triones.

1. Introduction

In the past few years, combinatorial methods using multi-component reactions (MCRs) have been closely examined as a fast and convenient solution for the synthesis of diverse classes of compounds [1]. MCRs, defined as one-pot reactions in which at least three molecule groups join through covalent bonds, have been steadily gaining importance in synthetic organic chemistry [1,2]. In the current work, we have elaborated a new MCR which gives wide access to annulated indenopyrazolopyridine *joined to oxindole units through a spiro junction* production.

Indole and indoline fragments are important moieties of a large number of natural biologically active compounds [3], and some indolines, spiro-annulated with heterocycles in the 3-position, have shown high biological activity [4]. The spirooxindole system is the core structure of many pharmacological agents and natural alkaloids [5]. For example, spirotryprostatin A and B, two natural alkaloids isolated from the fermentation broth of *Aspergillus fumigatus*, have been identified as novel inhibitors of microtubule assembly [5d], and pteropodine and isoptheropodine have been shown to modulate the function of muscarinic serotonin receptors (Fig. 1) [5a]. Indenone-fused heterocycles represent important biological and medicinal scaffolds. The indenopyridine skeleton is present in the 4-azafluorenone group of alkaloids, represented by its simplest member onychnine (Fig. 1) [6]. Indenopyrazoles **I** and indenopyridazines **II** have been investigated as cyclin-dependent kinase [7] and selective monoamine oxidase B (MAO-B) [8] inhibitors, respectively. Indenopyridines **III** exhibit cytotoxic [9a], phosphodiesterase inhibitory [9b], adenosine A_{2A} receptor antagonistic [9c], antiinflammatory/antiallergic [9d], coronary dilating [9e] and calcium modulating activities [9f]. These compounds have also been investigated for the treatment of hyperlipoproteinemia and arteriosclerosis [9g] as well as neurodegenerative diseases [9h].

As part of our program aimed at developing new methodologies for the preparation of heterocyclic compounds [10], very recently, we have reported the synthesis of spiro[diindenopyridine indoline]triones [11]. Herein, we describe an efficient and catalyst-free synthetic approach to spiro[indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridine indoline]-diones and spiro[indeno[1,2-*b*]pyrido[2,3-*d*]pyrimidine-

* Corresponding author.
E-mail address: a_bazgir@sbu.ac.ir (A. Bazgir).

1631-0748/$ – see front matter © 2010 Académie des sciences. Published by Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.crci.2010.10.001

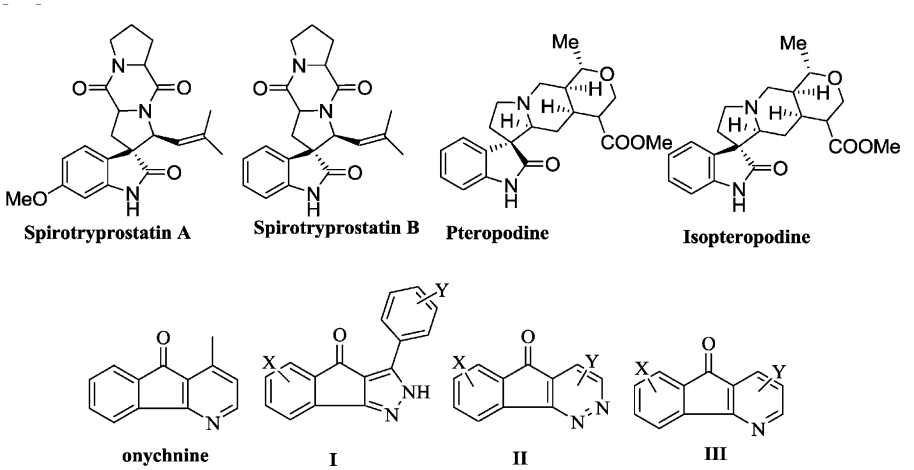
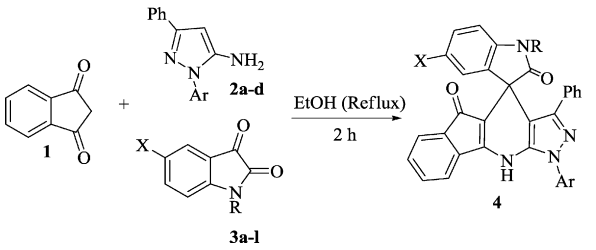


Figure 1. Representatives of important spirooxindoles and indenone-fused heterocycles.



Scheme 1.

5,3′-indoline]-2′,4,6(11*H*)-triones based on a one-pot methodology.

2. Results and discussion

We found that a mixture of 1,3-indandione **1**, pyrazol-5-amines **2** and isatins **3** in the absence of any catalyst in refluxing ethanol, afforded spiro[indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridine indoline]diones **4** in good yields for 2 h (Scheme 1).

To obtain spirooxindole annulated indenopyrazolopyridine, we used four pyrazol-5-amines **2a-d** and a wide diversity of isatins **3a-l**, substituted both in aromatic nucleus and at N-1. In this method, twenty-four new compounds **4a-x** were selectively synthesized by the one-pot, three-component condensation of 1,3-indandione **1**, 1*H*-pyrazol-5-amines **2** and isatins **3** in good yields without using any catalyst. The results are summarized in Table 1.

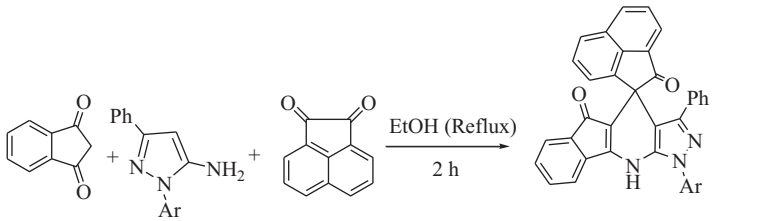
Recently, we have reported several isatin based three components reactions for the synthesis of spirooxindole in the presence of *p*-TSA as a catalyst [12]. Herein, we used *p*-TSA as a catalyst in the reaction but we did not observe the significant effect of catalyst on the yields and reaction times. In the previous work the catalyst had a significant effect on the reaction but it must be emphasized that the substrate used was also different from the present work. Thus, meaningful comparison (structural etc.) is not straightforward. To the best of our knowledge, this new procedure provides the first example of a catalyst-free synthesis of spirooxindole annulated indenopyrazolopyridine. The reactions in ethanol under catalyst-free are considerably safe, nontoxic, environmentally friendly, and inexpensive. The absence of catalyst for the reaction allows avoiding the use of moisture-sensitive and heavy metal-containing Lewis acids. This method is simple and convenient and would be applicable for the synthesis of different types of spiroindoline-pyrazolopyridopyrimidine derivatives. In addition, the workup of these very clean reactions involves only a filtration and simple washing step with EtOH. Using this simple purification protocol the desired products are obtained in high purity.

As expected, when the isatin **3** was replaced by acenaphthylene-1,2-dione **5**, 1′-aryl-3′-phenyl-1′*H*,2*H*-spiro[acenaphthylene-1,4′-indeno[1,2-*b*]pyrazolo[4,3-

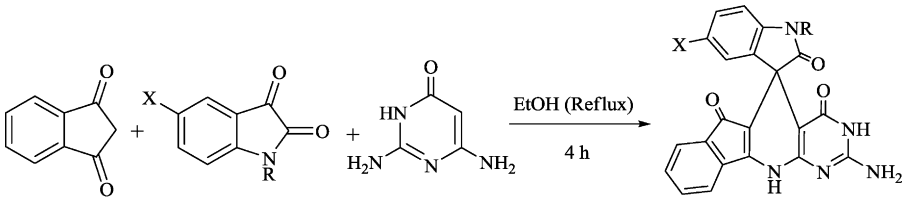
Table 1
Synthesis of spiro[indoline-pyrazolopyridopyrimidine] derivatives **4**.

Product **4**	Ar	X	R	Yield (%)[a]
a	C_6H_5	H	H	85
b	C_6H_5	Br	H	87
c	C_6H_5	NO_2	H	91
d	C_6H_5	Me	H	80
e	C_6H_5	F	H	92
f	C_6H_5	H	Me	75
g	C_6H_5	H	Et	76
h	C_6H_5	H	$PhCH_2$	73
i	C_6H_5	Br	Me	84
j	C_6H_5	Br	Et	85
k	C_6H_5	NO_2	Me	87
l	C_6H_5	NO_2	Et	82
m	4-NO_2-C_6H_4	H	H	91
n	4-NO_2-C_6H_4	Br	H	93
o	4-NO_2-C_6H_4	NO_2	H	94
p	4-NO_2-C_6H_4	H	Me	89
q	4-NO_2-C_6H_4	H	Et	87
r	4-MeO-C_6H_4	H	H	80
s	4-MeO-C_6H_4	NO_2	H	91
t	4-MeO-C_6H_4	H	Et	88
u	4-Br-C_6H_4	H	H	80
v	4-Br-C_6H_4	Br	H	82
w	4-Br-C_6H_4	NO_2	H	91
x	4-Br-C_6H_4	H	Me	88

[a] Isolated yields



Scheme 2.



Product **8**	X	R	Yield (%)[a]
a	H	H	82
b	Br	H	77
c	NO_2	H	81
d	Me	H	79
e	F	H	80
f	H	Me	78
g	H	Et	77
h	Br	Me	78
i	Br	Et	73
j	NO_2	Me	76

[a] Isolated yields

Scheme 3.

e]pyridine]-2,5′(10′*H*)diones **6** were obtained in good yields under the same reaction conditions (Scheme 2).

To further explore the potential of this protocol for spirooxindole synthesis, we investigated the reaction of 1,3-indandione **1** and isatin **3** with 2,6-diaminopyrimidin-4(3*H*)-one **7** and obtained 2-amino-1*H*-spiro[indeno[1,2-*b*]pyrido[2,3-*d*]pyrimidine-5,3′-indoline]-2′,4,6(11*H*)-triones **8a-j** in 73–82% yields under the same reaction conditions (Scheme 3).

Compounds **4**, **6** and **8** are stable solids whose structures were established by IR, ^{1}H, and ^{13}C NMR spectroscopy and elemental analysis.

3. Conclusions

In conclusion, we have described a facile, catalyst-free and three-component method for the synthesis of spiro[indenopyrazolopyridine indoline]diones, spiro[acenaphthylene-indenopyrazolopyridine]diones and spiro[indenopyridopyrimidine indoline]triones in ethanol using readily available starting materials. Prominent among the advantages of this new method are operational simplicity, good yields in short reaction times and easy work-up procedures employed.

4. Experimental

4.1. Materials and techniques

Melting points were measured on an Elecrtothermal 9100 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer at 300.13 and 75.47 MHz, respectively. ^{1}H and ^{13}C NMR spectra were obtained on solutions in DMSO-d_6 using TMS as internal standard. Due to very low solubility of the products **4u-x, 8d,e** and **8g-i** we cannot report the ^{13}C NMR data for these products. IR spectra were recorded using an FTIR apparatus. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer.

The chemicals used in this work were obtained from Fluka and Merck and were used without purification.

4.2. General procedure for preparation of spiro[indenopyrazolopyridine indoline]diones(4), spiro[acenaphthylene-1,4′-indenopyrazolopyridine]diones (6) and spiro[indenopyridopyrimidine indoline]triones (7)

A mixture of 1,3-indandione **1** (1 mmol), 1,3-diphenyl-1*H*-pyrazol-5-amine **2** or 2,6-diaminopyrimidin-4(3*H*)-

one **7** (1 mmol) and isatin **3** or acenaphthylene-1,2-dione **5** (1 mmol) in refluxing ethanol (5 mL) was stirred for 2 h. After completion of the reaction confirmed by TLC (eluent: EtOAc/*n*-hexane, 2:1), the reaction mixture was cooled to room temperature. Then, the precipitated product was filtered and washed with water (10 mL) and methanol (5 mL) to afford the pure product.

4.3. Spectral data

1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo [4,3-e]pyridine-4,3′-indoline]-2′,5(10H) -dione (4a): orange powder (yield 85%). m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3435, 3164, 1680, 1669. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.70–7.84 (18H, m, H-Ar), 10.32 (1H, s, NH), 11.22 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.8, 103.1, 106.9, 109.7, 120.7, 121.1, 122.2, 124.9, 126.0, 128.1, 128.5, 128.7, 130.1, 130.9, 132.2, 133.0, 134.1, 136.6, 136.7, 138.2, 139.4, 142.4, 150.2, 156.7, 178.8, 189.5. Anal. Calcd for $C_{32}H_{20}N_4O_2$: C, 78.03; H, 4.09; N, 11.38%. Found: C, 77.92; H, 4.01; N, 11.30%.

5′-Bromo-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline] -2′,5(10H)-dione (4b). Orange powder (yield 87%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3461, 3195, 1701, 1674. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.61–7.84 (17H, m, H-Ar), 10.46 (1H, s, NH), 11.30 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.9, 102.5, 106.1, 111.6, 113.9, 120.8, 121.2, 125.0, 127.6, 128.2, 128.5, 128.6, 128.7, 130.0, 131.0, 131.4, 132.2, 132.9, 134.1, 136.6, 138.2, 138.8, 139.5, 141.7, 150.1, 157.0, 178.6, 189.4. Anal. Calcd for $C_{32}H_{19}BrN_4O_2$: C, 67.26; H, 3.35; N, 9.80. Found: C, 67.25; H, 3.44; N, 9.72.

5′-Nitro-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4c). Orange powder (yield 91%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3482, 3153, 1680, 1627. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.81–8.08 (17H, m, H-Ar), 11.06 (1H, s, NH), 11.44 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.7, 102.1, 105.3, 109.7, 120.5, 120.9, 121.5, 125.1, 126.1, 128.2, 128.5, 128.7, 130.0, 131.1, 132.3, 132.7, 134.0, 136.5, 137.1, 138.1, 139.6, 142.9, 148.9, 150.1, 157.4, 179.6, 189.4. Anal. Calcd for $C_{32}H_{19}N_5O_4$: C, 71.50; H, 3.56; N, 13.03% Found: C, 71.59; H, 3.49; N, 12.96.

5′-Methyl-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline] -2′,5(10H)-dione (4d). Orange powder (yield 80%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3540, 3148, 1695, 1680. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.19 (3H, s, CH_3), 6.58–7.81 (17H, m, H-Ar), 10.21 (1H, s, NH), 11.20 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 21.1, 47.8, 103.1, 107.1, 109.5, 120.7, 121.0, 124.9, 125.3, 128.0, 128.5, 129.0, 130.1, 131.1, 132.2, 133.1, 134.1, 136.6, 136.9, 138.2, 139.4, 139.4, 140.0, 150.1, 156.6, 178.7, 189.5. Anal. Calcd for $C_{33}H_{22}N_4O_2$: C, 78.25; H, 4.38; N, 11.06% Found: C, 78.11; H, 4.32; N, 10.96.

5′-Fluoro-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline] -2′,5(10H)-dione (4e). Orange powder (yield 92%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3420, 3231, 1721, 1701. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.63–7.85 (17H, m, H-Ar), 10.32 (1H, s, NH), 11.25 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 48.3, 102.7, 106.2, 110.3, 120.8, 121.2, 124.9, 128.1, 128.5, 128.6, 130.1, 130.9, 132.2, 132.9, 134.1, 136.6, 138.0, 138.2, 138.6, 139.5, 150.1, 157.0, 179.0, 189.4. Anal. Calcd for $C_{32}H_{19}FN_4O_2$: C, 75.28; H, 3.75; N, 10.97% Found: C, 75.15; H, 3.82; N, 11.04.

1′-Methyl-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline] -2′,5(10H)-dione (4f). Orange powder (yield 75%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3164, 1685, 1622. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.87 (3H, s, NCH_3), 6.72–7.83 (18H, m, H-Ar), 11.30 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 26.4, 47.2, 103.3, 106.5, 108.5, 120.7, 121.2, 123.0, 124.5, 124.9, 128.0, 128.4, 128.6, 128.8, 130.1, 130.9, 132.2, 132.8, 134.1, 135.7, 136.7, 138.2, 139.3, 143.4, 150.1, 157.0, 177.2, 189.4. Anal. Calcd for $C_{33}H_{22}N_4O_2$: C, 78.25; H, 4.38; N, 11.06% Found: C, 78.15; H, 4.30; N, 10.96.

1′-Ethyl-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4 g). Orange powder (yield 76%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3174, 1685, 1622. ^{1}HNMR (300 MHz, DMSO-d_6): δ_H (ppm) 0.87 (3H, t, $^3J_{HH}$ = 6.9 Hz, CH_3), 3.42–3.52 (2H, m, CH_2), 6.70–7.85 (18H, m, H-Ar), 11.27 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 12.3, 34.7, 47.3, 103.0, 106.7, 108.6, 120.8, 121.1, 122.8, 124.8, 124.9, 128.1, 128.5, 128.6, 128.9, 130.1, 130.9, 132.2, 133.0, 134.1, 136.1, 136.6, 138.2, 139.4, 142.9, 150.1, 156.8, 176.6, 189.4. Anal. Calcd for $C_{34}H_{24}N_4O_2$: C, 78.44; H, 4.65; N, 10.76% Found: C, 78.35; H, 4.59; N, 10.69.

1′-Benzyl-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline] -2′,5(10H)-dione (4 h). Orange powder (yield 73%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3174, 1701, 1690. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm), 4.18 and 4.90 (2H, AB_q, $^2J_{HH}$ = 15.2 Hz, CH_2), 6.47–7.85 (24H, m, H-Ar), 11.36 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 44.0, 47.4, 103.2, 106.3, 109.2, 120.9, 121.2, 123.1, 124.7, 124.9, 127.4, 127.5, 128.1, 128.5, 128.9, 130.1, 132.3, 132.7, 134.1, 135.7, 136.3, 136.6, 138.2, 142.7, 150.2, 157.2, 177.6, 189.6. Anal. Calcd for $C_{39}H_{26}N_4O_2$: C, 80.39; H, 4.50; N, 9.62% Found: C, 80.50; H, 4.58; N, 9.55.

5′-Bromo-1′-methyl-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4i). Orange powder (yield 84%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3169, 1695, 1622. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.87 (3H, s, NCH_3), 6.76–7.87 (17H, m, H-Ar) 11.37 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 26.6, 47.3, 102.7, 105.7, 110.4, 114.7, 120.8, 121.4, 125.0, 127.3, 128.1, 128.4, 128.7, 130.0, 131.0, 131.5, 132.3, 132.7, 134.1, 136.6, 137.7, 138.1, 139.4, 142.8, 150.0, 157.3, 176.9, 189.4. Anal. Calcd for $C_{33}H_{21}BrN_4O_2$: C, 67.70; H, 3.62; N, 9.57% Found: C, 67.61; H, 3.56; N, 9.50.

5′-Bromo-1′-ethyl-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4j). Orange powder (yield 85%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3169, 1715, 1685. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 0.86 (3H, t, $^3J_{HH}$ = 6.9 Hz, CH_3), 3.42–3.52 (2H, m, CH_2), 6.74–7.84 (17H, m, H-Ar) 11.35 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 12.2, 34.8, 47.4, 102.3, 105.9, 110.6, 114.5, 120.8, 121.3, 125.0, 127.6, 128.2, 128.4, 128.6, 128.7, 130.0, 131.0, 131.6, 132.3, 132.8, 134.0, 136.6, 138.2, 139.6, 142.2, 150.0,

157.1, 176.3, 189.4. Anal. Calcd for $C_{34}H_{23}BrN_4O_2$: C, 68.12; H, 3.87; N, 9.35% Found: C, 68.23; H, 3.79; N, 9.46.

1′-Methyl-5′-nitro-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4k). Orange powder (yield 87%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3174, 1701, 1685. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.98 (3H, s, NCH_3), 6.76–7.14 (17H, m, H-Ar) 11.51 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 26.9, 47.0, 102.2, 108.7, 120.1, 120.9, 121.6, 125.1, 126.1, 128.2, 128.5, 128.7, 130.0, 131.1, 132.5, 136.2, 136.6, 138.1, 143.4, 149.3, 150.1, 178.1. Anal. Calcd for $C_{33}H_{21}N_5O_4$: C, 71.86; H, 3.84; N, 12.70% Found: C, 71.94; H, 3.76; N, 12.62.

1′-Ethyl-5′-nitro-1,3-diphenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4l). Orange powder (yield 82%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3174, 1695, 1664. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 0.91 (3H, bs, CH_3), 3.48–3.61 (2H, m, CH_2), 6.74–8.21 (17H, m, H-Ar) 11.48 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 12.2, 35.3, 47.2, 101.9, 105.2, 108.8, 120.3, 120.9, 121.6, 125.1, 126.2, 128.3, 128.5, 128.7, 130.0, 131.1, 132.3, 132.6, 134.0, 136.6, 138.1, 139.7, 143.3, 148.9, 150.1, 157.4, 177.6, 189.4. Anal. Calcd for $C_{34}H_{23}N_5O_4$: C, 72.20; H, 4.10; N, 12.38% Found: C, 72.09; H, 4.03; N, 12.49.

1-(4-Nitrophenyl)-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4m). Orange powder (yield 91%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3409, 3137, 1711, 1706. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.66–8.49 (17H, m, H-Ar), 10.37 (1H, s, NH), 11.30 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.8, 94.6, 104.1, 107.1, 109.8, 120.9, 122.3, 125.0, 125.5, 128.1, 128.5, 128.8, 131.0, 132.3, 132.4, 132.8, 136.4, 136.5, 140.0, 142.3, 143.1, 146.5, 151.7, 156.7, 178.7, 189.5. Anal. Calcd for $C_{32}H_{19}N_5O_4$: C, 71.50; H, 3.56; N, 13.03% Found: C, 71.63; H, 3.64; N, 13.11.

5′-Bromo-1-(4-nitrophenyl)-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4n). Orange powder (yield 93%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3425, 3174, 1706, 1674. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.61–8.51 (16H, m, H-Ar), 10.53 (1H, s, NH), 11.40 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.9, 103.5, 106.4, 111.6, 113.9, 121.0, 125.2, 125.5, 127.8, 128.2, 128.4, 128.9, 131.1, 131.6, 132.3, 133.9, 136.5, 138.5, 140.2, 141.6, 143.1, 146.6, 151.5, 157.0, 178.4. Anal. Calcd for $C_{32}H_{18}BrN_5O_4$: C, 62.35; H, 2.94; N, 11.36% Found: C, 62.21; H, 2.83; N, 11.43.

5′-Nitro-1-(4-nitrophenyl)-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4o). Orange powder (yield 94%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3331, 2918, 2840, 1701, 1685. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.81–8.52 (16H, m, H-Ar), 11.09 (1H, s, NH), 11.51 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.7, 103.1, 109.8, 120.7, 121.1, 121.3, 125.4, 125.5, 126.2, 128.3, 128.5, 129.0, 131.2, 132.2, 132.5, 136.5, 136.8, 142.9, 143.1, 146.7, 148.8, 151.5, 179.4. Anal. Calcd for $C_{32}H_{18}N_6O_6$: C, 65.98; H, 3.11; N, 14.43% Found: C, 65.90; H, 3.05; N, 14.38.

1′-Methyl-1-(4-nitrophenyl)-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine -4,3′-indoline]-2′,5(10H)-dione (4p). Orange powder (yield 89%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3143, 1680, 1612. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.87 (3H, s, CH_3), 6.73–8.51 (17H, m, H-Ar), 11.38 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 26.5, 47.1, 104.3, 106.7, 108.5, 120.9, 121.0, 123.0, 124.5, 125.0, 125.5, 128.1, 128.4, 128.8, 129.0, 131.0, 132.2, 132.4, 133.8, 135.3, 136.6, 143.1, 143.4, 146.5, 151.6, 177.0. Anal. Calcd for $C_{33}H_{21}N_5O_4$: C, 71.86; H, 3.84; N, 12.70% Found: C, 71.73; H, 3.75; N, 12.60.

1′-Ethyl-1-(4-nitrophenyl)-3-phenyl-1*H*-spiro[indeno[1,2-*b*]pyrazolo[4,3-*e*]pyridine-

4,3′-indoline]-2′,5(10H)-dione (4q). Orange powder (yield 87%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3153, 1695, 1690. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 0.87 (3H,t, $^3J_{HH}$ = 6.3 Hz, CH_3), 3.41–3.54 (2H, m, CH_2), 6.70–8.51 (17H, m, H-Ar), 11.35 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 12.2, 34.7, 47.3, 103.9, 107.0, 108.7, 121.0, 122.9, 124.8, 125.0, 125.5, 128.2, 128.4, 128.8, 129.0, 131.0, 132.4, 133.8, 135.7, 136.5, 140.1, 142.8, 143.1, 146.5, 151.6, 156.8, 176.5, 189.5. Anal. Calcd for $C_{34}H_{23}N_5O_4$: C, 72.20; H, 4.10; N, 12.38% Found: C, 72.10; H, 4.17; N, 12.31.

1-(4-Methoxyphenyl)-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4r). Orange powder (yield 80%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3430, 3148, 1690, 1674. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.87 (3H, s, OCH_3), 6.68–7.84 (17H, m, H-Ar), 10.32 (1H, s, NH), 11.12 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.9, 56.1, 102.6, 106.8, 109.7, 115.1, 120.7, 121.0, 122.2, 124.8, 126.8, 128.0, 128.4, 128.5, 128.7, 130.8, 131.1, 132.1, 133.2, 134.2, 136.6, 136.8, 139.5, 142.4, 149.6, 156.7, 159.6, 178.9, 189.4. Anal. Calcd for $C_{33}H_{22}N_4O_3$: C, 75.85; H, 4.24; N, 10.72% Found: C, 75.77; H, 4.16; N, 10.84.

1-(4-Methoxyphenyl)-5′-nitro-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4s). Orange powder (yield 91%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3420, 3263, 1690, 1680. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.88 (3H, s, OCH_3), 6.81–8.08 (16H, m, H-Ar), 11.05 (1H, s, NH), 11.34 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.8, 56.1, 101.6, 105.2, 109.7, 115.1, 120.5, 120.9, 121.4, 126.1, 127.0, 128.2, 128.5, 128.6, 131.0, 131.1, 132.3, 132.8, 134.1, 136.5, 137.2, 139.7, 142.9, 148.9, 149.6, 157.4, 159.7, 179.7, 18.4. Anal. Calcd for $C_{33}H_{21}N_5O_5$: C, 69.84; H, 3.73; N, 12.34% Found: C, 69.71; H, 3.67; N, 12.25.

1′-Ethyl-1-(4-methoxyphenyl)-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e] pyridine-4,3′-indoline]-2′,5(10H)-dione (4t). Orange powder (yield 88%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3174, 1674, 1612. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 0.86 (3H, t, $^3J_{HH}$ = 6.9 Hz, CH_3), 3.44–3.57 (2H, m, CH_2), 3.87 (3H, s, OCH_3), 6.68–7.91 (17H, m, H-Ar), 11.17 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 12.3, 34.6, 47.3, 56.1, 102.4, 106.6, 108.6, 115.1, 120.7, 121.1, 122.7, 123.1, 124.7, 126.8, 128.1, 128.3, 128.4, 128.8, 130.8, 131.1, 132.1, 133.1, 134.1, 136.1, 136.6, 139.5, 142.9, 149.5, 156.7, 159.6, 174.1, 176.6, 189.4. Anal. Calcd for $C_{35}H_{26}N_4O_3$: C, 76.35; H, 4.76; N, 10.18% Found: C, 76.22; H, 4.69; N, 10.25.

1-(4-Bromophenyl)-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine-4,3′-indoline]-2′,5(10H)-dione (4u). Orange powder (yield 80%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3440, 3143, 1691, 1621. ^{1}H NMR

(300 MHz, DMSO-d_6): δ_H (ppm) 6.66–7.83 (17H, m, H-Ar), 10.13 (1H, s, NH), 10.91 (1H, s, NH). Anal. Calcd for $C_{32}H_{19}BrN_4O_2$: C, 67.26; H, 3.35; N, 9.80;% Found: C, 67.35; H, 3.28; N, 9.74.

5′-Bromo-1-(4-bromophenyl)-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine -4,3′-indoline]-2′,5(10H)-dione (4v). Orange Powder (yield 82%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3425, 3130, 1687, 1629. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.68–7.98 (16H, m, H-Ar), 11.02 (1H, s, NH), 11.30 (1H, s, NH). Anal. Calcd for $C_{32}H_{18}Br_2N_4O_2$: C, 59.10; H, 2.79; N, 8.62;% Found: C, 59.18; H, 2.70; N, 8.68

1-(4-Bromophenyl)-5′-nitro-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e]pyridine -4,3′-indoline]-2′,5(10H)-dione (4w). Orange Powder (yield 91%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3430, 3137, 1685, 1627. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.69–8.01 (16H, m, H-Ar), 11.07 (1H, s, NH), 11.35 (1H, s, NH). Anal. Calcd for $C_{32}H_{18}BrN_5O_4$: C, 62.35; H, 2.94; N, 11.36;% Found: C, 62.44; H, 2.99; N, 11.31.

1-(4-Bromophenyl)-1′-methyl-3-phenyl-1H-spiro[indeno[1,2-b]pyrazolo[4,3-e] pyridine-4,3′-indoline]-2′,5(10H)-dione (4x). Orange Powder (yield 88%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3420, 1711, 1695. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 2.87 (3H, s, CH_3), 6.72–7.91 (17H, m, H-Ar), 11.12 (1H, s, NH). Anal. Calcd for $C_{33}H_{21}BrN_4O_2$: C, 67.70; H, 3.62; N, 9.57% Found: C, 67.56; H, 3.53; N, 9.50.

1′,3′-diphenyl-1′H,2H-spiro[acenaphthylene-1,4′-indeno[1,2-b]pyrazolo[4,3-e]pyridine]-2,5′(10′H)-dione (6a). Orange Powder (yield 88%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3174, 1714, 1690. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.36–8.17 (20H, m, H-Ar), 11.36 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 52.5, 104.7, 108.2, 120.7, 121.2, 121.4, 121.9, 124.9, 127.3, 128.0, 128.2, 128.6, 128.8, 129.4, 130.0, 130.1, 131.8, 132.3, 133.3, 136.8, 138.2, 141.4, 145.0, 150.3, 157.1, 189.8, 205.2. Anal. Calcd for $C_{36}H_{21}N_3O_2$: C, 81.96; H, 4.01; N, 7.96% Found: C, 81.85; H, 4.07; N, 7.89.

1′-(4-nitrophenyl)-3′-phenyl-1′H,2H-spiro[acenaphthylene-1,4′-indeno[1,2-b]pyrazolo[4,3-e]pyridine]-2,5′(10′H)-dione (6b). Orange Powder (yield 89; m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3190, 1685, 1648. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.36–8.52 (19H, m, H-Ar), 11.42 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 52.4, 105.7, 108.5, 121.1, 121.6, 12.0, 125.0, 127.4, 128.2, 128.3, 128.8, 129.4, 130.1, 131.0, 131.7, 131.8, 133.2, 136.7, 141.4, 143.2, 143.2, 144.7, 146.5, 151.7, 204.9. Anal. Calcd for $C_{36}H_{20}N_4O_4$: C, 75.52; H, 3.52; N, 9.79% Found: C, 75.40; H, 3.44; N, 9.71.

2-Amino-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine-5,3′-indoline]-2′,4,6(11H)-triones (8a). Light orange powder (yield 82%); m.p. 268–270 °C. IR (KBr) (ν_{max}/cm^{-1}): 3461, 3336, 3195, 1701, 1648, 1627. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.50–7.77 (10H, m, H-Ar, NH_2), 10.23 (1H, s, NH), 10.56 (1H, s, NH), 10.92 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 47.7, 93.1, 106.5, 108.8, 120.4, 120.6, 121.4, 123.6, 127.7, 128.6, 130.8, 132.2, 133.6, 136.4, 136.5, 143.0, 154.8, 155.6, 156.1, 161.1, 179.5, 189.6. Anal. Calcd for $C_{21}H_{13}N_5O_3$: C, 65.79; H, 3.42; N, 18.27%. Found: C, 65.70; H, 3.37; N, 18.19.

2-Amino-5′-bromo-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine-5,3′-indoline]-2′,4,6(11H)-triones (8b). Light orange Powder (yield 77%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3456, 3184, 1706, 1648, 1633. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.57–7.82 (9H, m, H-Ar, NH_2), 10.41 (1H, s, NH), 10.62 (1H, s, NH), 11.01 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 48.0, 92.6, 105.6, 110.8, 113.1, 120.8, 126.3, 130.5, 131.0, 132.3, 133.6, 136.3, 138.9, 142.5, 154.9, 155.7, 156.5, 161.1, 179.2, 189.6. Anal. Calcd for $C_{21}H_{12}BrN_5O_3$: C, 54.56; H, 2.62; N, 15.15%;. Found: C, 54.46; H, 2.68; N, 15.09.

2-Amino-5′-nitro-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine-5,3′-indoline]-2′,4,6(11H)-triones (8c). Orange Powder (yield 81%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3649, 3435, 3326, 1716, 1690, 1643. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.64–8.11 (9H, m, H-Ar, NH_2), 10.69 (1H, s, NH), 11.05 (1H, s, NH), 11.16 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) Anal. 47.8, 92.0, 104.9, 108.9, 119.0, 120.9, 125.6, 131.1, 132.4, 133.5, 136.3, 137.4, 142.4, 149.8, 155.1, 156.0, 157.0, 161.3, 180.2, 189.6. Calcd for $C_{21}H_{12}N_6O_5$: C, 58.88; H, 2.82; N, 19.62% Found: C, 58.76; H, 2.90; N, 19.53.

2-Amino-5′-methyl-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine-5,3′-indoline]-2′,4,6(11H)-triones (8d). Light orange Powder (yield 79%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3602, 3430, 3383, 1695, 1648, 1627. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.14 (3H, s, CH_3), 6.56–7.81 (9H, m, H-Ar, NH_2), 10.49 (1H, s, NH), 11.00 (1H, s, NH). Anal. Calcd for $C_{22}H_{15}N_5O_3$: C, 66.49; H, 3.80; N, 17.62% Found: C, 66.38; H, 3.73; N, 17.54.

2-Amino-5′-fluoro-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine-5,3′-indoline]-2′,4,6(11H)-triones (8e). Red Powder (yield 80%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3639, 3514, 3378, 3158, 1789, 1721, 1638. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 6.55–7.79 (9H, m, H-Ar, NH_2), 10.27 (1H, s, NH), 10.60 (1H, s, NH), 10.99 (1H, s, NH). Anal. Calcd for $C_{21}H_{12}FN_5O_3$: C, 62.84; H, 3.01; N, 17.45% Found: C, 62.70; H, 3.08; N, 17.53.

2-Amino-1′-methyl-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine-5,3′-indoline]-2′,4,6(11H)-triones (8f). Orange Powder (yield 78%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3382, 3174, 1704, 1648, 1630. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.13 (3H, s, CH_3). 6.55–7.80 (9H, m, H-Ar, NH_2), 10.48 (1H, s, NH), 10.99 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 26.7, 47.2, 107.7, 120.5, 120.6, 122.1, 123.3, 128.0, 130.9, 132.3, 133.5, 135.7, 136.4, 154.9, 155.6, 156.2, 178.0, 189.5. Anal. Calcd for $C_{22}H_{15}N_5O_3$: C, 66.49; H, 3.80; N, 17.62% Found: C, 66.56; H, 3.85; N, 17.51.

2-Amino-1′-ethyl-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine-5,3′-indoline]-2′,4,6(11H)-triones (8 g). Orange Powder (yield 77%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3446, 3336, 1701, 1680, 1648. ^{1}HNMR (300 MHz, DMSO-d_6): δ_H (ppm) 1.23 (3H, bs, CH_3), 3.65–3.78 (2H, m, CH_2), 6.57–7.81 (10H, m, H-Ar, NH_2), 10.49 (1H, s, NH), 10.99 (1H, s, NH). Anal. Calcd for $C_{23}H_{17}N_5O_3$: C, 67.15; H, 4.16; N, 17.02% Found: C, 67.01; H, 4.07; N, 16.91.

2-Amino-5′-bromo-1′-methyl-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine -5,3′-indoline]-2′,4,6(11H)-triones (8 h). Light orange Powder (yield 78%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3479, 3382, 17014,

1648, 1630, 1603. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.12 (3H, s, CH_3), 6.61–7.81 (9H, m, H-Ar, NH_2), 10.53 (1H, s, NH), 11.07 (1H, s, NH). Anal. Calcd for $C_{22}H_{14}BrN_5O_3$: C, 55.48; H, 2.96; N, 14.70% Found: C, 55.40; H, 3.02; N, 14.77.

2-Amino-5′-bromo-1′-ethyl-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine -5,3′-indoline]-2′,4,6(11H)-triones (8i). Yellow Powder (yield 73%); m.p. > 300 °C. IR (KBr) (ν_{max}/cm^{-1}): 3446, 3336, 1701, 1680, 1648. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 1.19 (3H, bs, CH_3), 3.70 (2H, bs, CH_2), 6.61–7.81 (9H, m, H-Ar, NH_2), 10.51 (1H, s, NH), 11.04 (1H, s, NH). Anal. Calcd for $C_{23}H_{16}BrN_5O_3$: C, 56.34; H, 3.29; N, 14.28% Found: C, 56.23; H, 3.21; N, 14.22.

2-Amino-1′-methyl-5′-nitro-1H-spiro[indeno[1,2-b]pyrido[2,3-d]pyrimidine-5,3′-indoline]-2′,4,6(11H)-triones (8j). Orange Powder (yield 76%); m.p. 270–272 °C. IR (KBr) (ν_{max}/cm^{-1}): 3566, 3346, 3211, 1701, 1669, 1643. ^{1}H NMR (300 MHz, DMSO-d_6): δ_H (ppm) 3.25(3H, s, CH_3), 6.68–8.19 (10H, m, H-Ar, NH_2), 10.65 (1H, s, NH), 11.22 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ_C (ppm) 27.32, 47.2, 91.8, 104.7, 107.9, 118.7, 120.9, 121.0, 125.7, 131.2, 132.5, 133.4, 136.2, 136.6, 142.9, 150.7, 155.1, 156.1, 157.1, 161.2, 178.9, 189.6. Anal. Calcd for $C_{22}H_{14}N_6O_5$: C, 59.73; H, 3.19; N, 19.00% Found: C, 59.92; H, 3.11; N, 19.09.

Acknowledgements

We gratefully acknowledge financial support from the Research Council of Shahid Beheshti University.

References

[1] (a) L.F. Tietze, Chem. Rev 96 (1996) 115;
(b) A. Dömling, Chem. Rev 106 (2006) 17.
[2] (a) A. Dömling, I. Ugi, Angew. Chem., Int. Ed 39 (2000) 3168;
(b) I. Ugi, Angew. Chem., Int. Ed. Engl 21 (1982) 810.
[3] R.J. Sundberg, The Chemistry of Indoles, Academic, New York, NY, 1996
[4] (a) K.C. Joshi, P. Chand, Pharmazie 37 (1982) 1;
(b) J.F.M. Da-Silva, S.J. Garden, A.C. Pinto, J. Braz. Chem. Soc 12 (2001) 273;
(c) A.H. Abdel-Rahman, E.M. Keshk, M.A. Hanna, S.M. El-Bady, Bioorg. Med. Chem 12 (2004) 2483;
(d) S.-L. Zhu, S.-J. Ji, Z. Yong, Tetrahedron 63 (2007) 9365.
[5] (a) T.-H. Kang, K. Matsumoto, Y. Murakami, H. Takayama, M. Kitajima, N. Aimi, H. Watanabe, Eur. J. Pharmacol 444 (2002) 39;
(b) J. Ma, S.M. Hecht, Chem. Commun (2004) 1190;
(c) T. Usui, M. Kondoh, C.B. Cui, T. Mayumi, H. Osada, Biochem. J 333 (1998) 543;
(d) M.M. Khafagy, A.H.F.A. El-Wahas, F.A. Eid, A.M. El-Agrody, Farmaco 57 (2002) 715.
[6] J. Zhang, A.-R.O. El-Shabrawy, M.A. El-Shanawany, P.L. Schiff, D.J. Slatkin, J. Nat. Prod 50 (1987) 800.
[7] D.A. Nugiel, A.-M. Etzkorn, A. Vidwans, P.A. Benfield, M. Boisclair, C.R. Burton, S. Cox, P.M. Czerniak, D. Doleniak, S.P. Seitz, J. Med. Chem 44 (2001) 1334.
[8] R. Fréderick, W. Dumont, F. Ooms, L. Aschenbach, C.J. Van der Schyf, N. Castagnoli, J. Wouters, A.J. Krief, Med. Chem 49 (2006) 3743.
[9] (a) R. Miri, K. Javidnia, B. Hemmateenejad, A. Azarpira, Z. Amirghofran, Bioorg. Med. Chem 12 (2004) 2529;
(b) Heintzelman, G. R. Averill K. M.; Dodd, J. H. PCT Int. Appl. WO 2002085894 A1 20021031, (2002);
(c) G.R. Heintzelman, K.M. Averill, J.H. Dodd, K.T. Demarest, Y. Tang, P.F. Jackson, Pat. Appl. Publ. US 2004082578 A1 20040429 (2004);
(d) K. Cooper, M.J. Fray, P.E. Cross, K. Richardson, Eur. Pat. Appl. EP 299727 A1 19890118 (1989);
(e) Vigante B, Ozols, J. Sileniece, G. Kimenis A. Duburs, G. U. S. S. R. SU, 794006 19810107, (1989);
(f) C. Safak, R. Simsek, Y. Altas, S. Boydag, K. Erol, Boll. Chim. Farm 136 (1997) 665;
(g) A. Brandes, M. Loegers, G. Schmidt, R. Angerbauer, C. Schmeck, K.-D. Bremm, H. Bischoff, D. Schmidt, Schuhmacher, J. Ger. Offen. DE 19627430 A1 19980115 (1998);
(h) Heintzelman G. R.; Averill, K. M.; Dodd, J. H.; Demarest, K. T.; Tang Y.; Jackson, P. F. PCT Int. Appl. WO 2003088963 A1 20031030, 2003..
[10] (a) A. Bazgir, M. Seyyedhamzeh, Z. Yasaei, P. Mirzaei, Tetrahedron Lett 48 (2007) 8790;
(b) M. Sayyafi, M. Seyyedhamzeh, H.R. Khavasi, A. Bazgir, Tetrahedron 64 (2008) 2375;
(c) M. Dabiri, H. Arvin-Nezhad, H.R. Khavasi, A. Bazgir, J. Heterocycl. Chem 44 (2007) 1009;
(d) M. Dabiri, S.C. Azimi, H. Arvin-Nezhad, A. Bazgir, Heterocycles 75 (2008) 87;
(e) M. Dabiri, A.S. Delbari, A. Bazgir, Synlett (2007) 821;
(f) M. Dabiri, H. Arvin-Nezhad, H.R. Khavasi, A. Bazgir, Tetrahedron 63 (2007) 1770;
(g) M. Dabiri, A.S. Delbari, A. Bazgir, Heterocycles 71 (2007) 543;
(h) R. Ghahremanzadeh, G. Imani Shakibaei, A. Bazgir, Synlett (2008) 1129;
(i) G. Imani Shakibaei, H.R. Khavasi, P. Mirzaei, A. Bazgir, J. Heterocycl. Chem 45 (2008) 1481;
(j) A. Bazgir, Z. Noroozi Tisseh, P. Mirzaei, Tetrahedron Lett 49 (2008) 5165;
(k) K. Jadidi, R. Ghahremanzadeh, A. Bazgir, Tetrahedron 65 (2009) 2005;
(l) M. Dabiri, S.C. Azimi, H.R. Khavasi, A. Bazgir, Tetrahedron 64 (2008) 7307;
(m) S. Ahadi, H.R. Khavasi, A. Bazgir, Chem. Pharm. Bull 56 (2008) 1328.
[11] (a) R. Ghahremanzadeh, S. Ahadi, G. Imani Shakibaei, A. Bazgir, Tetrahedron Lett 51 (2010) 499;
(b) R. Ghahremanzadeh, G. Imani Shakibaei, S. Ahadi, A. Bazgir, J. Comb. Chem 12 (2010) 191.
[12] (a) R. Ghahremanzadeh, M. Sayyafi, S. Ahadi, A. Bazgir, J. Comb. Chem 11 (2009) 393;
(b) K. Jadidi, R. Ghahremanzadeh, A. Bazgir, J. Comb. Chem 11 (2009) 341;
(c) A. Bazgir, S. Ahadi, R. Ghahremanzadeh, H.R. Khavasi, P. Mirzaei, Ultrason. Sonochem 17 (2010) 447;
(d) S. Ahadi, R. Ghahremanzadeh, P. Mirzaei, A. Bazgir, Tetrahedron 65 (2009) 9316;
(e) R. Ghahremanzadeh, F. Fereshtehnejad, Z. Yasaei, T. Amanpour, A. Bazgir, J. Heterocycl. Chem 47 (2010) 967.