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Synthesis of 2,6′-Dioxo-1′,5′,6′,7′-tetrahydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-5′-carbonitriles via a One-Pot, Three-Component Reaction in Water

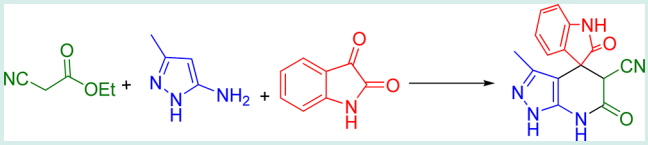
Abbas Rahmati,*[,†] Tahmineh Kenarkoohi,[†] and Hamid Reza Khavasi[‡]

[†]Department of Chemistry, University of Isfahan, P.O. Box 81746-73441, Isfahan, Iran

[‡]Departement of Chemistry, Shahid Beheshti University, General Campus, Evin, Tehran 1983963113, Iran

Supporting Information

ABSTRACT: A one-pot, three-component condensation reaction of an isatin, aminopyrazole, and alkyl cyanoacetate in water to give 2,6′-dioxo-1′,5′,6′,7′-tetrahydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-5′-carbonitrile with good yields, at 90 °C, using a Et_3N as catalyst, is described.



KEYWORDS: *spirooxindole, isatin, 1,4-dihydropyridines*

INTRODUCTION

Multicomponent reactions (MCRs) are chemical transformations in which three or more different starting materials combine together via a one-pot procedure to give a final complex product. Such reactions are one of the best tools in modern organic synthesis because they can generate a product with most of the atoms incorporating in the starting materials (this is important from the atom economic standpoint).[1] Also these reactions have received considerable attention in synthetic chemistry for the production of a broad spectrum of organic molecules. Water has emerged as a versatile solvent for organic reactions in the past two decades since it is available, inexpensive, environmentally benign, neutral, and natural solvent.[2] For these reasons, water has been used for MCRs as well.[3] MCRs in water are of outstanding value in organic synthesis and green chemistry.

Pyrazolo[3,4-*b*]pyridines and pyrazolo[3,4-*b*]pyridinones are attractive condensed heterocyclic compounds and are being extensively investigated because of their wide range of biological and pharmaceutical activities such as hypotensives,[4] antitumor,[5] antibacterial,[6] anti-inflammatory against TNF-α and IL-6,[7] antichagasic new drugs against *Trypanosoma cruzi*,[8] inhibitors of protein kinase,[9] cyclin-dependent kinase 1 (CDK1),[10] p38α Kinase,[11] glycogen synthase kinase-3 (GSK-3),[12] PDE4B[13] and HIV reverse transcriptase.[14]

Spirooxindoles have received more attention because of the wide range of useful pharmacological properties and biological activities such as antimicrobial,[15] antitumoral,[16] antibiotic agents,[17] inhibitors of human NK-1 receptor,[18] CRTH2 receptor antagonist[19] and microtubule assembly.[20] Also, in some of bioactive naturally alkaloids, the spirooxindole ring is the main core of structure.[21] For these reasons, there have been numerous investigations on the synthesis of spirooxindoles annulated in the 3-position with different fused-heterocyclic rings such as spiro[oxindole-3:4́-dihydropyridines] (**A,B**) and spiro[oxindole-3:4′-pyrans] (**C,D**) via various three and four component reactions (Figure 1).[22] The substructures (**I**) and (**II**) in Scheme 1 may be homocyclic and/or heterocyclic rings as well as substituents. Although many structures like A–D have been synthesized by various groups, there are no reports for the preparation of spirooxindoles like E.

In continuation of our previous work and the preparation of new heterocyclic compounds, we have utilized isatins instead of aldehydes;[23] therefore we wish to report the synthesis of 2,6′-dioxo-1′,5′,6′,7′-tetrahydrospiro[indoline-3,4′-pyrazolo[3,4-b]-pyridine]-5′-carbonitriles **4** via one-pot three-component condensation reaction.

RESULTS AND DISCUSSION

For the synthesis of 2,6′-dioxo-1′,5′,6′,7′-tetrahydrospiro-[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-5′-carbonitriles **4**, the ethyl cyanoacetate **1{1}**, 3-amin-5-methylpyrazole **2{1}**, and simple isatin **3{1}** were selected as model reactants during the optimization process. Initially, this transformation was carried out in methanol under reflux conditions in the absence of catalyst. It was found that no product was detected even after 72 h (entry 1, Table 1). Different acidic and basic catalysts (40 mol %) were screened. Results showed that reaction proceeds in the presence of both series of catalysts and also reaction yields were better with basic catalysts (entries 2–9, Table 1) and with Et_3N proved better than the others. To increase the yield, different solvents were tested at reflux (entries 10–15, Table 1). Water at 90 °C proved to be the best solvent. It is important to note that in nonprotic solvents, compound **5{-,1,1}** formed in 20 min as major product. Also, after 24 h this product did not change. However, after isolation of compound **5{-,1,1}** and treating with ethyl cyano acetate in water and/or ethanol, it was transformed to compound

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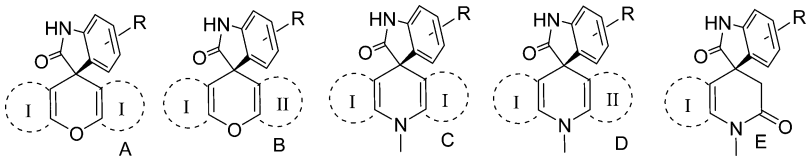
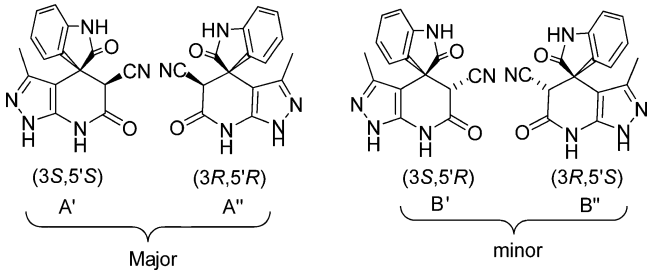


Figure 1. Various structures of spirooxindoles.

Scheme 1. Two Different Diastereomers (Each of Products as One Pair of Enantiomers)

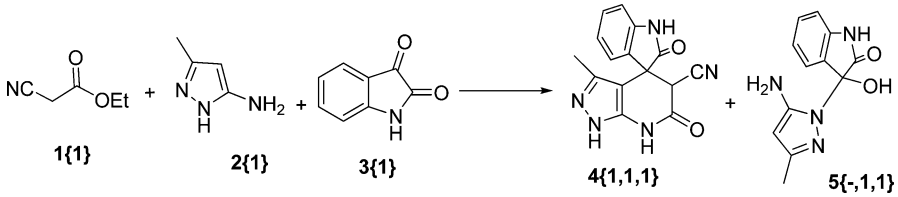


4{**1,1,1**}. In addition, it was found that compound **5**{**-,1,1**} in the absence of ethyl cyanoacetate converted to the starting materials in protic solvents. When **2**{**3**} was used instead of **2**{**1**} the corresponding product was not observed. The ^{1}H NMR spectrum of compound **5**{**-,1,1**} clearly showed that ethyl cyanoacetate was not incorporated in its structure. Subsequently, we further turned to testing the effect of catalyst loading with values of 10, 20, 30, and 40 mol % of catalyst, respectively. The results indicated that 20 mol % of catalyst was optimal. Higher amounts of catalyst did not lead to a significant change in yield.

To explore the scope and limitations of this reaction, the optimized reaction conditions (water solvent, Et_3N catalyst, 90 °C) were used for the construction of a library from two alkyl cyanoacetates **1** {**1**−**2**}, four aminopyrazoles **2** {**1**−**4**}, and six isatins **3** {**1**−**6**} (Figure 2 and Table 2).

The reaction proceeded equally well with either electron-withdrawing or electron-donating substituted isatins (entries1−4 also 6 and 7, Table 2). Similar to the isatins, the reaction was performed with various aminopyrazoles. The effect of pyrazole structure was more pronounced compared to substituted isatins. We concluded that the reaction yields were better in the presence of aryl pyrazoles compared to alkyl pyrazoles. Also, 5-hydroxy-3-amino pyrazole **2**{**4**} afforded no product. Finally, the effect of alkyl cyanoacetate stucture was investigated in this process. Although, final reaction products using ethyl

Table 1. Solvent, Catalyst, and Temperature Optimization for the One-Pot Synthesis of 4 {1,1,1}[a]



entry	solvent	catalyst[b]	time/temperature	yield (%)[c]	yield (%)[d]
1	MeOH		24,72 h/reflux		
2	MeOH	*p*-TsOH	24 h/reflux	21	
3	MeOH	H_2SO_4	24 h/reflux	22	
4	MeOH	AcOH	24 h/reflux	10	
5	MeOH	Et_3N	24 h/reflux	70	
6	MeOH	NaOH	24 h/reflux	61	
7	MeOH	Na_2CO_3	24 h/reflux	61	
8	MeOH	$NaHCO_3$	24 h/reflux	52	
9	MeOH	pyridine	24 h/reflux	69	
10	ethanol	Et_3N	24 h/reflux	61	
11	water	Et_3N	24 h/reflux	89	
12	ethyl acetate	Et_3N	24 h/reflux	15	40
13	CH_3CN	Et_3N	24 h/reflux	12	72
14	water/ethanol(1:1)	Et_3N	24 h/reflux	73	
15	Choline chloride[e]	Et_3N	24 h/90 °C	59	
16	water	Et_3N	48 h/90 °C	89	
17	water	Et_3N	24 h/90 °C	89	
18	water	Et_3N	18 h/90 °C	89	
19	water	Et_3N	12 h/90 °C	88	
20	water	Et_3N	6 h/90 °C	84	
21	water	Et_3N	24 h/70 °C	37	
22	water		24 h/90 °C	25	

[a]Isatin (1 mmol), ethyl cyanoacetate (1 m mol), 3-amin-5-methylpyrazole (1 m mol) in solvent (5 mL). [b]40 mol % of catalyst. [c]Isolated yield of 4{1,1,1}. [d]Isolated yield of 5{-,1,1}. [e]RTIL.

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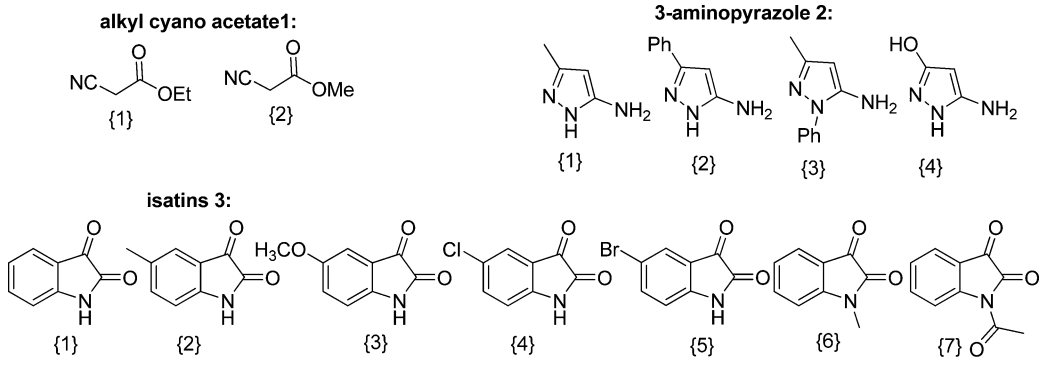
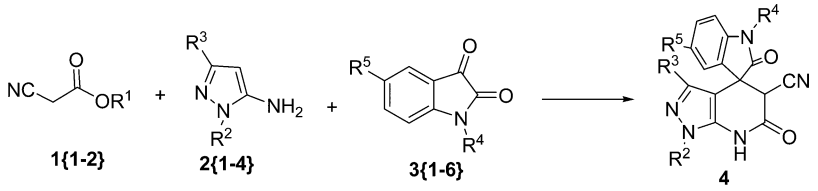


Figure 2. Diversity of reagents.

Table 2. One-Pot Synthesis of 2,6′-Dioxo-1′,5′,6′,7′-tetrahydrospiro[indoline-3,4′-pyrazolo[3,4-b]pyridine]-5′-carbonitrile[a]



entry	alkyl cyanoacetate	aminopyrazole	isatin	product	yield(%)[b]	major:minor[c]
1	1{1}	2{1}	3{1}	4{1,1,1}	89	79:21
2	1{1}	2{1}	3{7}	4{1,1,1}[d]	92	81:19
3	1{1}	2{1}	3{2}	4{1,1,2}	57	76:24
4	1{1}	2{1}	3{3}	4{1,1,3}	56	85:15
5	1{1}	2{1}	3{4}	4{1,1,4}	67	83:17
6	1{1}	2{1}	3{6}	4{1,1,5}	63	82:18
7	1{1}	2{2}	3{1}	4{1,2,1}	83	66:34
8	1{1}	2{2}	3{2}	4{1,2,2}	89	62:38
9	1{1}	2{3}	3{1}	4{1,3,1}	83	76:24
10	1{1}	2{3}	3{2}	4{1,3,2}	71	72:28
11	1{1}	2{3}	3{3}	4{1,3,3}	78	81:19
12	1{1}	2{3}	3{4}	4{1,3,4}	72	77:23
13	1{1}	2{3}	3{5}	4{1,3,5}	72	77:23
14	1{1}	2{3}	3{6}	4{1,3,6}	74	75:25
15	1{2}	2{1}	3{1}	4{2,1,1}[e]	61	82:18
16	1{2}	2{1}	3{7}	4{2,1,7}[e]	62	81:19

[a]Isatin (1 mmol), alkyl cyanoacetate (1 m mol), 3-aminpyrazole (1 m mol) in water (5 mL), Et_3N (20 mol %), 6−12 h. [b]Isolated yield. [c]Ratio of isomers based on average of CH_3, CH and NH groups signals in ^1H NMR. [d]Product obtained from *N*-acylisatin. [e]Products **4{2,1,1}** and **4{2,1,7}** obtained from methyl cyanoacetate are the same as **4{1,1,1}**.

cyanoacetate and methyl cyanoacetate were the same, the results revealed that ethyl cyanoacetate yields were better than methyl cyanoacetate (Table 2, entries1−2 also 15 and 16). Furthermore, the last column in Table 2 represents the ratio of the two diastereomers generated during the reaction. These were given as minor and major isomers, and the amount of them was obtained according to the CH_3, CH, and NH functional group signals in ^1H NMR. However, each of them exists as a pair of enantiomers (Scheme 1). It is worthy to mention that *N*-acylisatin products hydrolyzed during this process, and its products were similar to simple isatin (Table 2, entry 2). The same result was obtained under neutral conditions indicating the labiality of the *N*-acyl group.

The structures of all derivatives of compound **4** were deduced from their IR, ^1H NMR, ^{13}C NMR, mass spectra, and elemental analysis.

The IR spectrum of **4{1,1,4}** showed absorptions at 3633, 3418, 3322 (NH), 2906 (CH_3), 2254 (CN), 1716, 1690 (C═O), 1619 (bending NH), 1477 (bending CH_3), 1306, 1174 (C−N), and 708 (C−Cl) cm^{-1} indicating the presence of these functional groups at the proposed structure. The mass spectrum of **4{1,1,4}** displayed the molecular ion peaks at m/z = 329 (^{37}Cl) and 327 (^{35}Cl), which were in agreement with the 1:1:1 adduct of starting materials with loss of water and ethanol. The ^1H NMR and ^{13}C NMR spectra of **4{1,1,4}** exhibit duplication of signals because of the presence of one pair of diasteriomers. The ^1H NMR spectrum to major isomer exhibited a singlet for $-CH_3$ group at δ = 1.44 ppm and another singlet at δ = 5.38 ppm for the CH group. Two independent doublets for two aromatic hydrogens appeared at δ = 7.02 and 7.53 ppm with $^3J_{HH}$= 8.0 Hz and $^4J_{HH}$= 1.6 Hz, respectively, and a doublet of doublet for other aromatic hydrogen at δ = 7.43 ppm with $^3J_{HH}$ = 8.4 Hz and $^4J_{HH}$ = 2.0 Hz. Signals for the NH-group of amides and pyrazole ring appeared as three singlet at δ = 10.90, 11.01 and δ = 12.43 ppm, respectively. The ^1H decoupled ^{13}C NMR spectrum for major isomer of **4{1,1,4}** showed 15 distinct resonances in agreement with the suggested structures. Signals for the minor stereo-

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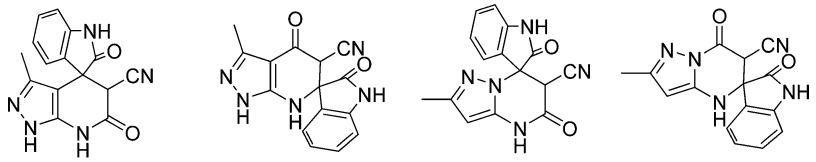
Scheme 2. Possible Four Different Products (Regioisomers) during the Reaction

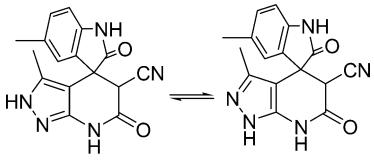


4 6 7 8

isomer in amount up to between 13 and 19% were observed as follows: two singlets for $-CH_3$ and CH groups corresponding at δ = 1.82 and 5.38 ppm. Two aromatic hydrogen appeared at δ = 6.94 and 7.04 ppm with $^4J_{HH}$ = 2.0 and $^3J_{HH}$ = 8.8 Hz; and a doublet of doublet for other aromatic hydrogen at δ = 7.38 ppm with $^3J_{HH}$ = 8.4 Hz and $^4J_{HH}$ = 2.0 Hz. One of the aromatic hydrogen signals from a minor isomer at δ = 7.04 was embedded at a major isomer signal. Signals for the NH-group of amides and pyrazole ring were similar to the signals of the major isomer and were appeared at δ = 11.24, 11.27 and δ = 12.28 ppm, respectively. The ^{1}H decoupled ^{13}C NMR spectrum for the minor isomer showed 15 distinct resonances. All *J* values were given as real values without correction and average.

In this reaction besides the product **4**, compounds **6**, **7**, and **8** could potentially be formed because of the presence of two nucleophilic sites close to the amine group (nitrogen and carbon of pyrazole ring) (Scheme 2). However, the ^{1}H NMR spectrum of the product straightforwardly specified that the NH signal appeared while the CH signal of pyrazole ring did not appear. Therefore, these results indicated that products **7** and **8** were not generated. In addition, spectral data obtained for the product may correspond for two regioisomers **4** and **6** which is shown in Scheme 2. ROSEY and HMBC spectra of product (**4{1,1,2}**) proved that only **4** was generated. Also, the ROSEY spectrum indicated that in the minor isomer, the hydrogen of the pyrimidine ring was close to the aromatic hydrogen. In addition, the HMBC spectrum indicated that among the two tautomeric forms (**III**) and (**IV**) in Scheme 3 only form (**IV**) was generated.

Scheme 3. Two Tautomeric Forms 4{1,1,2}



(III) (IV)

The major isomer of product **4{1,1,1}** was separated by column chromatography and established by ^{1}H NMR. Then a single crystal of it was obtained from ethanol, and the stereochemistry of its structure was confirmed by a single crystal X-ray analysis (Figure 3).[24]

There is no established mechanism for the formation of 2,6′-dioxo-1′,5′,6′,7′-tetrahydrospiro[indoline-3,4′-pyrazolo[3,4-b]-pyridine]-5′-carbonitrile; a reasonable possibility is shown in Scheme 4. The reaction presumably proceeds via Knoevenagel condensation between ethyl cyanoacetate **1{1}** and the isatin **3{1}** to give *α*,*β*-unsaturated compound **11**. Then, compound **11** converts to intermediate **13** through a Michael addition of 5-aminopyrazole **2{1}**. Then, product **14** was obtained by a cyclization process from compound **13**. Finally, compound

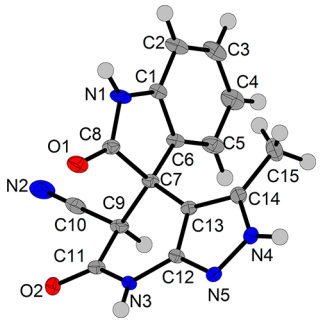


Figure 3. X-ray crystal structure of major isomer from **4{1,1,1}**.

4{1,1,1} was converted to final product via tautomerization (Scheme 4).

Interesting results were obtained by stopping the reaction of entry 7 in Table 2 after one hour. The reaction mixture was filtered immediately and the solid residue washed with water, and after drying, the ratio of A′,A′′ and B′,B′′ isomers (Scheme 1) in the products were determined by ^{1}H NMR spectrum. As a consequence, the amount of B′,B′′ isomers were higher than A′,A′′ isomers (Figures 4). Therefore, B′,B′′ isomers were kinetically products and A′,A′′ isomers were thermodynamically products. These results were confirmed by comparing the two spectra in Figures 4 and 5. B′,B′′ isomers were not observed upon heating of the isolated A′,A′′ isomers in the absence of catalyst in water. Meanwhile addition of triethylamine catalyst led to the production of B′,B′′ after 48 h. However, the equilibrium was established slowly. In addition, in a separate experiment the isolated product **4{1,2,1}** (after 1 h in Figure 4) was heated in water in the absence of catalyst. Results showed that the ratio of isomers remains unchanged during 24 h, whereas in the presence of catalyst the obtained isomer ratio was similar to that of obtained for the experimental condition of Figure 5. No further change of isomers ratio was observed with increasing heating time. Therefore, these results showed that these isomers were in equilibrium in the presence of catalyst, but were not in equilibrium in the absence of catalyst.

CONCLUSION

In summary, a novel, green, and efficient three-component domino reaction of some typical isatins, 3-aminopyrazoles, and alkyl cyanoacetate was developed for the synthesis of 2,6′-dioxo-1′,5′,6′,7′-tetrahydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]-pyridine]-5′-carbonitrile. The simple one-pot nature of the reaction makes it an interesting approach. One of the main advantages of the proposed method is its good reaction yields. Also, the reactions were carried out in water which is considerably safer, nontoxic, environmentally friendly, and inexpensive. Furthermore, the existence of three different important heterocyclic moieties such as oxindole, pyridinone, and pyrazole rings in one molecule is fantastic because of the

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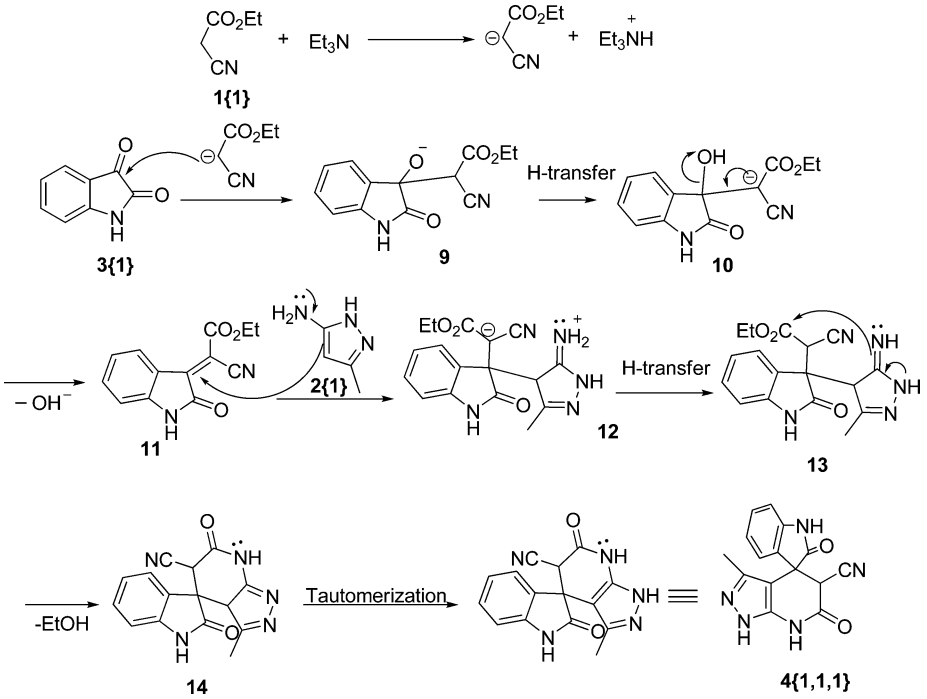
Scheme 4. Mechanism of Reaction



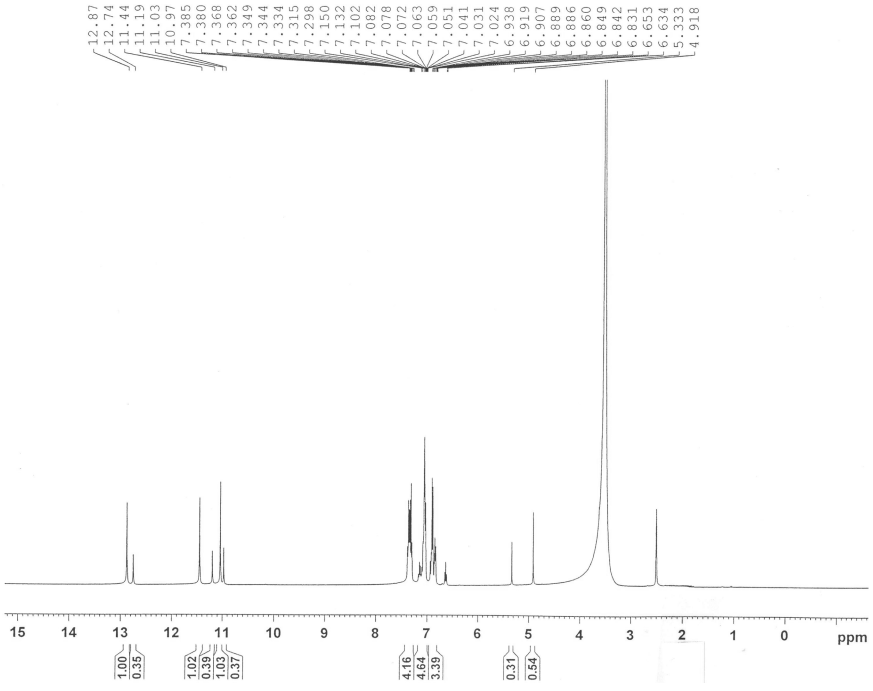


Figure 4. ^{1}H NMR of **4{1,2,1}** after 1 h.

potential applications of these rings in biological and pharmacological activities.

EXPERIMENTAL PROCEDURES

General Procedure for the Synthesis of 2,6′-Dioxo-1′,5′,6′,7′-tetrahydrospiro[indoline-3,4′-pyrazolo[3,4-*b*]-pyridine]-5′-carbonitriles 4. A solution of isatin (1 mmol), ethyl cyanoacetate (1 mmol), and Et_3N (0.1 mmol) in water (10 mL) in a balloon (25 mL) was stirred for 1 h at 60−70 °C in an oil bath. After production of intermediate 3-amin-pyrazole (1 mmol) was added in a balloon and stirred for 5−12 h at 90 °C in an oil bath. After the completion of the reactions, which has been followed by TLC (EtOAc:*n*-hexene, 1:2), the reaction mixture was filtered while warm. The residue was washed with water and then recrystallized from ethanol, and pure product was obtained.

3′,5-Dimethyl-2,6′-dioxo-1′,5′,6′,7′-tetrahydrospiro-[indoline-3,4′-pyrazolo[3,4-*b*]pyridine]-5′-carbonitrile 4-{1,1,2}. White powder (57%); IR (KBr): 3639, 3313, 3256, 3039, 2912, 2254, 1707, 1605, 1530 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 307 (M^+, 100), 280 (49), 252 (82), 77 (75), 63 (53), 42

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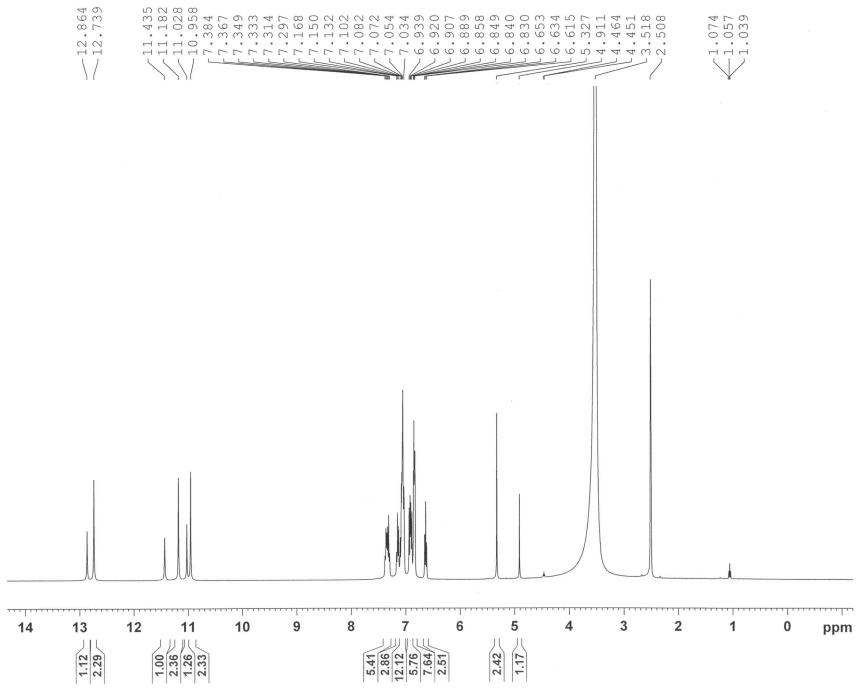

Figure 5. ^{1}H NMR of **4{1,2,1}** after completion.

(61); Anal. Calcd for $C_{16}H_{13}N_5O_2$: C 60.53, H 4.26, N 22.79; Found: C 60.29, H 4.29, N 22.65. (major isomer)) ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.38 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 5.31(s, 1H, CH), 6.87 (d, ^{3}J = 7.6 Hz, 1H, CH_{arom}), 7.16 (d, ^{3}J = 7.6 Hz, 1H, CH_{arom}), 7.24 (s, 1H, CH_{arom}), 10.64 (s, 1H, NH_{amide}), 10.97 (s, 1H, NH_{amide}), 12.11 (s, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 8.90, 20.73, 42.54, 48.88, 97.39, 109.96, 115.24, 125.06, 127.57, 130.05, 131.36, 134.96, 140.12, 148.15, 162.15, 176.04 ppm. (minor isomer) ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.82 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 4.88 (s, 1H, CH), 6.79 (s, 1H, CH_{arom}), 6.89 (d, ^{3}J = 7.6 Hz, 1H, CH_{arom}), 7.10 (d, ^{3}J = 7.6 Hz, 1H, CH_{arom}), 11.01 (s, 1H, NH_{amide}), 11.23 (s, 1H, NH_{amide}), 12.22 (s, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 9.07, 20.61, 43.41, 48.41, 98.61, 110.28, 114.74, 123.45, 129.19, 129.96, 131.61, 134.18, 138.35, 147.57, 161.74, 175.27 ppm.

5-Chloro-3′-methyl-2,6′-dioxo-1′,5′,6′,7′-tetrahydrospiro[indoline-3,4′-pyrazolo[3,4-b]pyridine]-5′-carbonitrile 4{1,1,4}. White powder (57%); IR (KBr): 3633, 3418, 3323, 2906, 2254, 1716, 1690, 1619, 1529, 1477, 1306, 1174, 708 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 329 (M^{+}+2, 31), 327 (M^{+}, 79), 166 (91), 75 (93), 69(95), 67 (90), 57 (100), 44 (87). Anal. Calcd for $C_{15}H_{10}ClN_5O_2$: C 54.97, H 3.08, N 21.37; Found: C 55.09, H 4.11, N 21.26. (major isomer) ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.44 (s, 3H, CH_3), 5.38 (s, 1H, CH), 7.02 (d, ^{3}J = 8.0 Hz, 1H, CH_{arom}), 7.43 (dd, ^{3}J = 8.4 Hz, ^{4}J = 2.0 Hz, 1H, CH_{arom}), 7.54 (d, ^{4}J = 1.6 Hz, 1H, CH_{arom}), 10.90 (s, 1H, NH_{amide}), 11.01 (s, 1H, NH_{amide}), 12.16 (s, 1H, $NH_{pyrazole}$)ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 8.94, 42.22, 49.09, 96.66, 111.86, 114.95, 154.80, 126.48, 129.44, 129.89, 134.99, 141.49, 148.04, 161.77, 175.74 ppm. (minor isomer): ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.82 (s, 3H, CH_3), 4.92 (s, 1H, CH), 6.94 (d, ^{4}J = 2.0 Hz, 1H, CH_{arom}), 7.04 (d, ^{3}J = 8.8 Hz, 1H, CH_{arom}), 7.38 (dd, ^{3}J = 8.4 Hz, ^{4}J = 2.0 Hz, 1H, CH_{arom}), 11.24 (s, 1H, NH_{amide}), 11.26 (s, 1H, NH_{amide}), 12.28 (s, 1H, $NH_{pyrazole}$) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ: 9.04, 43.17, 48.43, 97.69, 112.26, 114.57, 122.85, 126.48, 129.77, 130.81, 134.99, 139.84, 148.04, 161.42, 174.93 ppm.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedure, IR, ^{1}H NMR, ^{13}C NMR, mass spectra, and elemental analysis data to all products; also IR, ^{1}H NMR, ^{13}C NMR, mass spectra for all products presented. Only the ^{1}H NMR spectrum is given for the repetitive product. In addition, ROSEY and HMBC spectra of product **4{1,1,2}**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: a.rahmati@sci.ui.ac.ir or abbass_rahmati@yahoo.com.

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Notes

The authors declare no competing financial interest.

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(24) X-ray data for 4{1,1,1}: ($C_{15}H_{11}N_5O_2$), M = 293.29 g/mol, monoclinic system, space group *C*2/*c*, *a* = 24.154(8) Å, *b* = 7.5150(15) Å, *c* = 16.506(5) Å, β = 110.27(2)°, *V* = 2810.6(14) Å^3, *Z* = 8, *Dc* = 1.386 g cm^{-3}, μ(Mo Kα)= 0.097 mm^{-1}, crystal dimension:

0.22 × 0.21 × 0.20 mm. The structure was solved by using SHELXS. The structure refinement and data reduction was carried out with SHELXL of the X-Step32 suite of programs. (REF: X-STEP32, version 1.07b, X-ray structure evaluation package; Stoe & Cie: Darmstadt, Germany, 2000). The non-hydrogen atoms were refined anisotropically by full matrix least-squares on F^2 values to final R_1 = 0.0847, wR_2 = 0.1777, and S = 1.084 with 199 parameters using 2768 independent reflection (θ range = 2.62−26.00°). Hydrogen atoms were located from expected geometry and were not refined. Crystallographic data for 4{1,1,1} have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to The Director, CCDC 904326, Union Road, Cambridge CB2 1EZ, U.K. Fax: +44 1223 336033. E-mail: deposit@ccdc.cam.ac.uk.