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Synthesis of Some New Spiro[indoline-3-heterocycle]-2-one Derivatives

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ABSTRACT

*Indole-2,3-dione was treated with malonic acid in a mixture of ethanol/pyridine to afford 1-[3-(2-oxoindolinylidene)]acetic acid (**3**), which was then reacted with thionyl chloride to give the corresponding acid chloride (**4**). The acid chloride **4** reacted with arenes in the presence of $AlCl_3$ to yield substituted 3-(2-oxoindolinylidene)acetophenones* **5a–c**. *Compounds* **5a–c** *were alkylated with methyl iodide to afford* **6a–c**. *Compounds* **6a–c** *were treated with hydrazine derivatives, hydroxylamine hydrochloride, urea, and thiourea to yield the complex spiro compounds* **7a–i**, **8a–c**, *and* **9a–f**, *respectively.*

INTRODUCTION

Certain spiro compounds are showing anticancer [1], central nervous system activity [2], anti-inflammatory activity [3], and antibiotic aranorosim [4]. Also, spiro compounds were used as starting materials for the preparation of N-(biphenylylmethyl)imidazolines as angiotensin II antagonists [5], for heterocyclic spiroannulation of 5α-cholestan-3-one [6], for the synthesis of spirofused β-lactam oxadiazolines [7], and for the preparation of various complex heterocycles [8–10]. Kinetic studies of solvent and pressure effects on thermal isomerization of spiro compounds [11], studies of light-induced change of the molecular charge in spironaphthoxazine compounds [12,13], and electrochemical studies on nitrospiro[indoline-naphthopyran] and 9,9′-spirobifluorene derivatives [14,15] have been investigated. Diverse biological activities have been encountered in compounds having the indole ring system [16–19].

As a continuation of our previous work [20,21], the syntheses of some new spiro[indoline-3-heterocycle]-2-one derivatives are reported.

RESULTS AND DISCUSSION

The syntheses of spiro compounds containing nitrogen have gained importance because of their biological activity, but, in some cases, the preparations of these compounds required many steps. For example, the preparation of spiro[indan-1,1′-[1H]-3-benzazepine] derivatives required seven steps [22]. Also, the preparation of the well-known spiro derivative, Fredericamycin A, required eight steps [23].

We report herein a facile synthesis of some spiro[indoline-3-heterocycle]-2-one derivatives analogous to spiro[indan-1,1′-[1H]-3-benzazepine] derivatives [22] and fredericamycin A [23]. The advantages of our syntheses were the use of inexpensive precursors such as indole-2,3-dione (**1**) and malonic acid (**2**), facile reactions, readily available reagents, and simple techniques.

As the first step to reach our goal, indole-2,3-dione (**1**) was reacted with malonic acid (**2**) in an ethanol/pyridine mixture to yield (Z)-1-[3-(2-oxoindolinylidene)]acetic acid (**3**). The reaction of the acid **3** with thionyl chloride in chloroform afforded the corresponding acid chloride **4**. Reaction of **4** with arenes in the presence of aluminum chloride gave 3-(2-oxoindolinylidene)acetophenones **5a–c** (Scheme 1). The structure of compound **3** was established from its elemental analysis and spectroscopic data. The IR spectrum of compound **3** showed a characteristic broad absorption band at 2600–3400 cm^{-1} corresponding to the stretching

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vibrations for the hydroxyl group of a carboxylic acid, 3150 cm^{-1} for the NH group of the indoline moiety, and a broad absorption at 1705–1725 cm^{-1} for the carbonyl group in the indole ring and the carbonyl group of the carboxylic acid. The ^1H NMR spectrum of **3** (DMSO-d_6/TMS) showed the following signals: δ 6.65 (1H, s) for the methine proton, 7.00–7.50 (4H, m) for the aromatic protons of the benzene ring, 10.20 (1H, s) for the NH proton, and 12.20 (1H, s) for the proton of the carboxylic acid. Also, the structures of compounds **5a–c** were elaborated on the basis of their elemental analyses and spectroscopic data (Table 1). The IR spectrum of compound **5a** showed the following absorption bands: 3180 cm^{-1} for the NH of the indole ring, 3050 cm^{-1} for the aromatic CH groups, 1700 cm^{-1} for the amidic carbonyl group, and 1685 cm^{-1} for the α, β-unsaturated carbonyl moiety. The ^1H NMR spectrum of **5a** (DMSO-d_6/TMS) showed the following signals: δ 6.26 (1H, s) for the methine proton, 700–7.40 (9H, m) for the aromatic protons, and 10.28 (1H, s) for the NH proton. Alkylation of **5a–c** with methyl iodide in the presence of anhydrous potassium carbonate in dry acetone yielded compounds **6a–c**, these alkylation reactions being carried out in order to prevent the enolization of the carbonyl group at C_2 of the indole ring and subsequent reaction with the cyclizing reagents [24]. Compounds **6a–c** were identified by conventional methods, such as elemental and spectral analyses (IR and ^1H NMR spectra). The ^1H NMR spectrum of **6a** (DMSO-d_6/TMS) showed the following signals: δ 3.90 (3H, s) for the methyl group of N–CH_3, 6.10 (1H, s) for the methine proton, and 7.00–7.50 (9H, m) for the aromatic protons. For the synthesis of the new target spiro[indoline-3-heterocycle]-2-one derivatives, compounds **6a–c** were treated with hydrazine hydrate, phenylhydrazine, and *p*-nitrophenylhydrazine to yield the respective 3′-aryl-1-methylspiro[indoline-3,5′-pyrazoline]-2-one derivatives **7a–i**. The structures of compounds **7a–i** were established from their elemental analyses and spectroscopic data. The IR spectrum of **7a** showed characteristic strong absorption bands at 3200 cm^{-1} corresponding to the stretching vibration of the NH group of the pyrazoline ring, 3050 cm^{-1} for aromatic carbon–hydrogen stretching, 2920 cm^{-1} for aliphatic carbon–hydrogen, 1710 cm^{-1} for the amidic carbonyl at C_2 of the indole ring and at 1620 cm^{-1} for the C=N bond of the pyrazoline moiety. The ^1H NMR spectrum of **7a** (DMSO-d_6) showed the following signals: δ 3.39 (2H, s) for the methylene protons at C_4 of the pyrazoline ring, 3.93 (3H, s) for the methyl protons at N–CH_3 of the indole ring, 7.00–7.70 (9H, m) for the aromatic protons and 8.20 (1H, s) for the NH proton of the pyrazoline ring. Reactions of compounds **6a–c** with hydroxyamine hydrochloride in ethanol/pyridine mixture afforded 3′-aryl-1-methylspiro[indoline-3,5′-isoxazoline]-2-one derivatives **8a–c**. The structures of compounds **8a–c** were confirmed on the basis of their elemental analyses and spectroscopic data (Table 1). The ^1H NMR spectrum of **8a** (DMSO-d_6/TMS) showed the following signals: δ 3.39 (2H, s) for the methylene protons at C_4 of the isoxazoline ring, 3.90 (3H, s) for the three protons of the N-methyl group of the indole ring, and 7.00–7.85 (9H, m) for the aromatic protons of the indole ring and the phenyl group at C_3 of the isoxazoline ring. Reaction of compounds **6a–c** with urea and/or thiourea yielded 4′-aryl-1′,5′-dihydro-1-methylspiro[indoline-3,6′-pyrimidine]-2-one derivatives **9a–c** and 4′-aryl-1′,5′-dihydro-1-methylspiro[indoline-3,6′-thiopyrimidine]-2-one derivatives **9d–f** respectively, in good yields (Scheme 2). The structure assignments of compounds **9a–f** were based on their elemental and spectral analyses (Table 1). The IR spectrum of **9a** showed characteristic absorption bands at 3250 cm^{-1} corresponding to the stretching vibrations of the enolic OH at C_2 of the pyrimidine ring, 3180 cm^{-1} for the NH of the pyrimidine ring, 3045 cm^{-1} for the aromatic carbon–hydrogen stretching, 2890 cm^{-1} for the aliphatic carbon–hydrogen stretching, 1680 cm^{-1} and 1705 cm^{-1} for the two carbonyl groups of the pyrimidine moiety and the indole ring, and 1630 cm^{-1} for the C=N stretching of the pyrimidine ring. The ^1H NMR spectrum of **9a** (DMSO-d_6) showed the following signals: δ 3.38 (2H, s) for the methylene protons at C_6 of the pyrimidine ring, 3.90 (3H, s) for the protons of the methyl group of N–CH_3 of the indole ring, 6.80–7.60 (9H, m) for the aromatic protons of the indole ring and the phenyl group at C_4 of the pyrimidine ring, and 8.30 (1H, s) for the NH proton of the pyrimidine moiety.

EXPERIMENTAL

The time required for completion of each reaction was monitored by thin layer chromatography (TLC). Melting points are uncorrected. ^1H NMR spectra were measured on an EM-360 90-MHz spectrophotometer. IR spectra were recorded on a Pye-Unicam SP 200-G spectrophotometer. Elemental analyses were determined on a Perkin-Elmer 240 C microanalyzer.

Synthesis of 1-[3-(2-Oxoindolinylidine)]acetic Acid (**3**)

A mixture of indole-2,3-dione **1** (14.7 g, 0.1 mol) and malonic acid (10.4 g, 0.1 mol) in ethanol/pyridine mixture (150 mL, 4:1) was refluxed for 48 hours. The solvents were removed by distillation to afford the crude product. The crude product was crystallized from water to give 14.7 g (78% yield) of the pure compound **3**, mp 262–264°C. Anal. calcd (found) for $C_{10}H_7NO_3$: C, 63.49 (63.32); H, 3.70 (3.52); N, 7.40 (7.20). IR (KBr), 2600–3400 (OH), 3150 (NH), 3040 (CH arom.), and 1705–1725 cm^{-1} (C=O); ^1H

TABLE 1 Physical Data of 3-(2-Oxoindolinylidene)acetophenone **5a–c**, **6a–c**, and Spiro[indoline-3-heterocycle]-2-one derivatives **7a–i**, **8a–c**, and **9a–f**

Compound No.	*Yield (%)*	*Mp (°C)*	*Molecular Formula[a] (Solvent of Crystallization)*	*IR (KBr), cm^{-1}*	*^1H NMR (DMSO-d_6), δ(TMS)*
5a	68	260–262	$C_{16}H_{11}NO_2$ (ethanol-water) 1:1	3180 (NH), 3050 (CH arom.), 1685 (C=O, α,β-unsaturated carbonyl), 1700 (amidic carbonyl), 1630 (C=C)	6.26 (1H, s), 7.00–7.40 (9H, m), 10.28 (1H, s)
5b	72	220–222	$C_{17}H_{13}NO_2$ (ethanol)	3200 (NH), 3030 (CH arom.), 2980 (CH aliph.), 1710, 1680 (C=O), 1625 (C=C)	2.30 (3H, s), 6.30 (1H, s), 7.00–7.50 (8H, m), 10.25 (1H, s)
5c	70	260–262	$C_{17}H_{13}NO_3$ (ethanol-water) 2:1	3200 (NH), 3030 (CH arom.) 1710, 1680 (C=O), 1630 (C=C)	3.20 (3H, s), 6.20 (1H, s), 7.00–7.40 (8H, m), 10.20 (1H, s)
6a	66	250–252	$C_{17}H_{13}NO_2$ (ethanol-water) 4:1	3040 (CH arom.), 2890 (CH aliph.), 1705, 1685 (C=O), 1630 (C=C)	3.90 (3H, s), 6.10 (1H, s), 7.00–7.50 (9H, m)
6b	66	180–182	$C_{18}H_{15}NO_2$ (ethanol-water) 2:1	3050 (CH arom.), 2890 (CH aliph.), 1700, 1680 (C=O), 1630 (C=C)	2.30 (3H, s), 3.93 (3H, s), 7.00–7.60 (8H, m), 6.20 (1H, s)
6c	70	>350	$C_{18}H_{15}NO_3$ (ethanol)	3040 (CH arom.), 2890 (CH aliph.), 1705, 1685 (C=O), 1630 (C=C)	3.20 (3H, s), 3.93 (3H, s), 7.00–7.50 (8H, m), 6.10 (1H, s)
7a	68	200–202	$C_{17}H_{15}N_3O$ (ethanol-water) 2:1	3200 (NH), 3050 (CH arom.), 2920 (CH aliph.), 1710 (C=O), 1620 (C=N)	3.39 (2H, s), 3.93 (3H, s), 7.00–7.70 (9H, m), 8.20 (1H, s)
7b	66	230–232	$C_{18}H_{17}N_3O$ (acetone-water) 4:1	3200 (NH), 3050 (CH arom.), 2920 (CH aliph.), 1700 (C=O), 1630 (C=N)	3.39 (2H, s), 3.93 (3H, s), 7.00–7.70 (8H, m), 8.20 (1H, s)
7c	62	245–247	$C_{18}H_{17}N_3O_2$ (acetone-water) 4:1	3200 (NH), 3050 (CH arom.), 2890 (CH aliph.), 1700 (C=O)	3.20 (3H, s), 3.39 (2H, s), 7.00–7.60 (8H, m), 8.30 (1H, s)
7d	65	166–168	$C_{27}H_{19}N_3O$ (ethanol-water) 4:1	3060 (CH arom.), 2870 (CH aliph.), 1700 (C=O), 1630 (C=N)	3.39 (2H, s), 3.93 (3H, s), 7.00–8.00 (14H, m)
7e	60	183–185	$C_{24}H_{21}N_3O$ (acetone-water) 2:1	3050 (CH arom.), 2890 (CH aliph.), 1700 (C=O), 1620 (C=N)	2.30 (3H, s), 3.39 (2H, s), 7.00–8.10 (13H, m), 3.93 (3H, s)
7f	57	280–282	$C_{24}H_{21}N_3O_2$ (ethanol)	3040 (CH arom.), 2890 (CH aliph.), 1705 (C=O), 1620 (C=N)	3.20 (3H, s), 3.39 (3H, s), 7.00–7.80 (13H, m), 3.93 (3H, s)
7g	55	215–217	$C_{23}H_{18}N_4O_3$ (ethanol)	3050 (CH arom.), 2890 (CH aliph.), 1700 (C=O), 1630 (C=N)	3.39 (2H, s), 3.93 (3H, s), 7.00–7.50 (13H, m)
7h	52	230–232	$C_{24}H_{20}N_4O_3$ (ethanol-water) 4:1	3050 (CH arom.), 2890 (CH aliph.), 1705 (C=O), 1630 (C=N), 1510 (NO_2)	2.30 (3H, s), 3.38 (2H, s), 7.00–7.60 (12H, m), 3.90 (3H, s)
7i	50	260–262	$C_{24}H_{20}N_4O_4$ (ethanol-water) 2:1	3040 (CH arom.), 2890 (CH aliph.), 1700 (C=O), 1620 (C=N), 1510 (NO_2)	3.20 (3H, s), 3.39 (2H, s), 7.00–7.65 (12H, m), 3.90 (3H, s)
8a	50	160–162	$C_{17}H_{14}N_2O_2$ (ethanol)	3045 (CH arom.), 2890 (CH aliph.), 1700 (C=O), 1620 (C=N)	3.39 (2H, s), 3.90 (3H, s), 7.00–7.85 (9H, m)
8b	54	220–222	$C_{18}H_{16}N_2O_2$ (ethanol)	3050 (CH arom.), 2890 (CH aliph.), 1705 (C=O), 1620 (C=N)	2.30 (3H, s), 3.39 (2H, s), 7.00–7.90 (8H, m), 3.90 (3H, s)
8c	58	226–228	$C_{18}H_{16}N_2O_3$ (ethanol)	3050 (CH arom.), 2890 (CH aliph.), 1700 (C=O), 1620 (C=N)	3.20 (3H, s), 3.38 (2H, s), 7.00–7.80 (8H, m), 3.90 (3H, s)
9a	55	220–222	$C_{18}H_{15}N_3O_2$ (ethanol-water) 2:1	3250 (OH), 3180 (NH), 3045 (CH arom.), 2890 (CH aliph.), 1680, 1705 (C=O), 1630 (C=N)	3.38 (2H, s), 3.90 (3H, s), 6.80–7.60 (9H, m), 8.30 (1H, s)

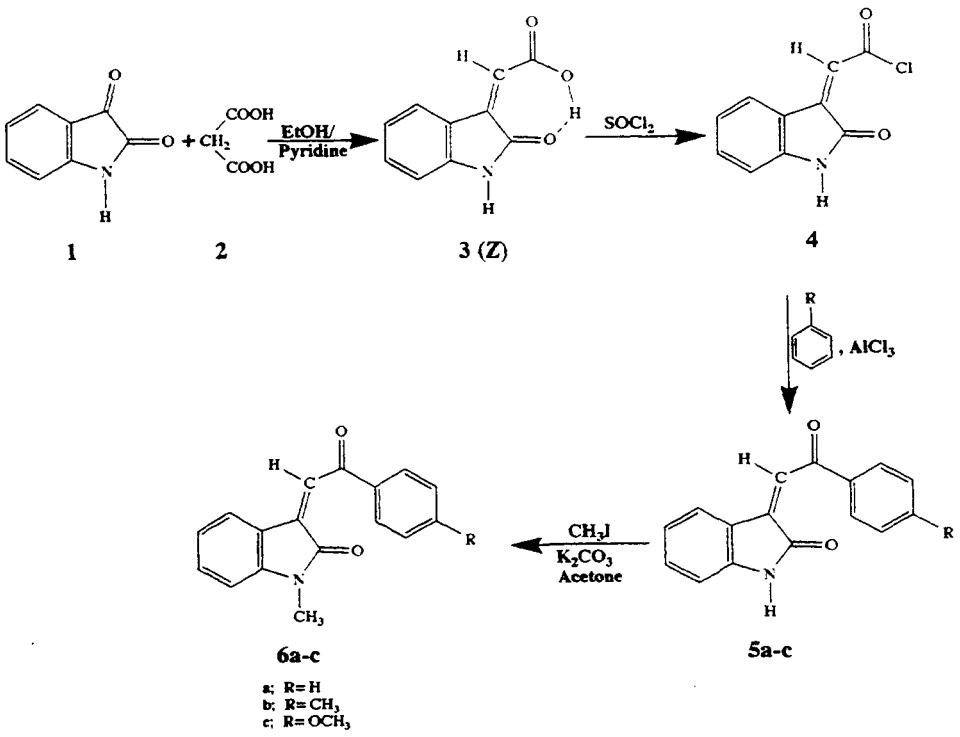
(*Continued*)

TABLE 1 (*Continued*) Physical Data of 3-(2-Oxoindolinylidene)acetophenone **5a–c**, **6a–c**, and Spiro[indoline-3-heterocycle]-2-one derivatives **7a–i**, **8a–c**, and **9a–f**

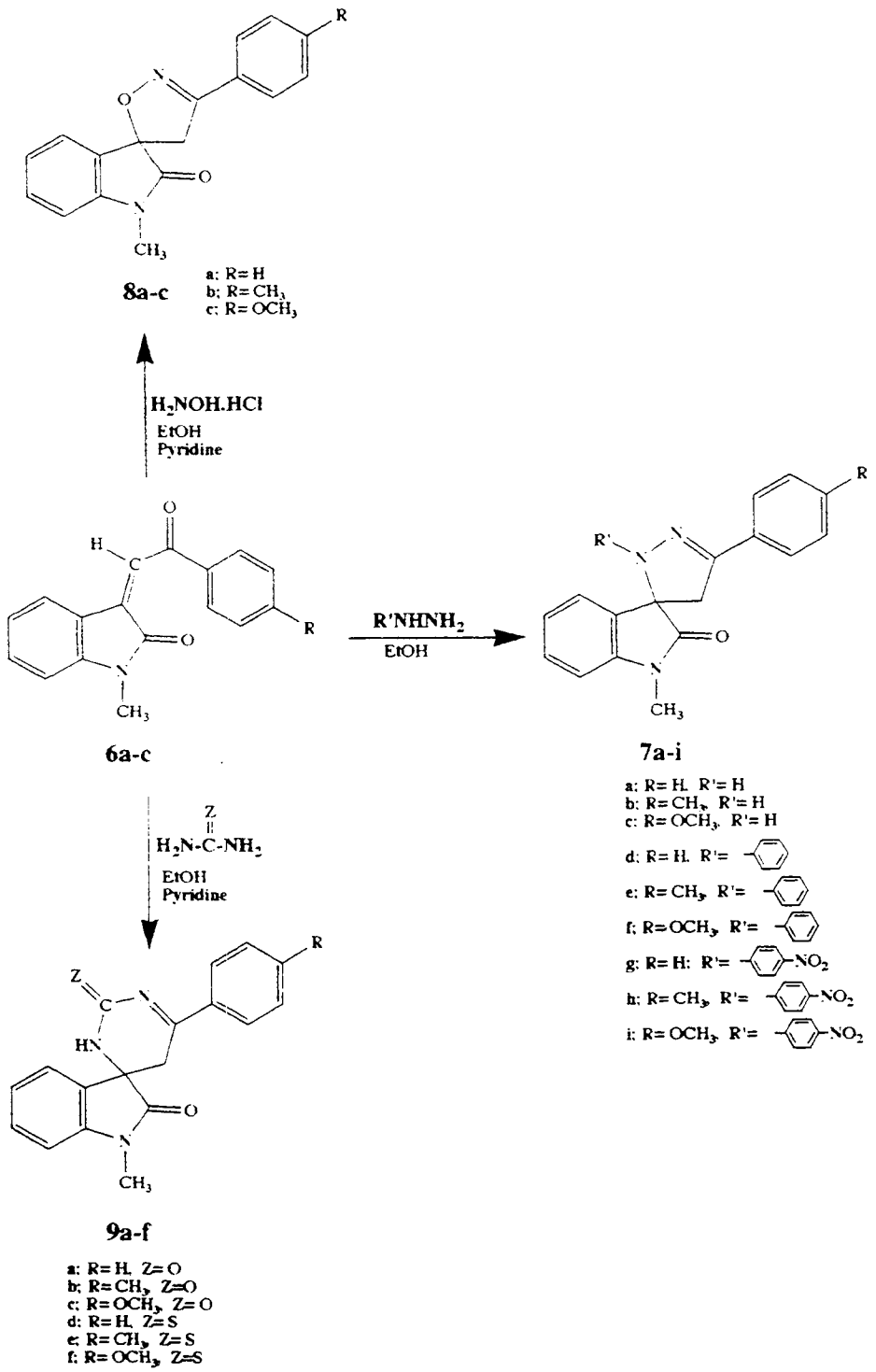
Compound No.	*Yield (%)*	*Mp (°C)*	*Molecular Formula[a] (Solvent of Crystallization)*	*IR (KBr), cm^{-1}*	*^{1}H NMR (DMSO-d_6), δ(TMS)*
9b	54	160–162	$C_{19}H_{17}N_3O_2$ (ethanol-water) 4:1	3250 (OH), 3180 (NH), 3050 (CH arom.), 2860 (CH aliph.), 1680, 1705 (C=O), 1620 (C=N)	2.30 (3H, s), 3.38 (2H, s), 6.90–7.60 (8H, m), 3.90 (3H, s), 8.30 (1H, s)
9c	56	195–197	$C_{19}H_{17}N_3O_3$ (acetone-water) 2:1	3270 (OH), 3180 (NH), 3050 (CH arom.), 2860 (CH aliph.), 1685, 1710 (C=O), 1620 (C=N)	3.20 (3H, s), 3.39 (2H, s), 7.00–7.85 (8H, m), 3.90 (3H, s), 8.30 (1H, s)
9d	50	168–170	$C_{18}H_{15}N_3OS$ (acetone-water) 2:1	3300 (SH), 3200 (NH), 3050 (CH arom.), 2860 (CH aliph.), 1710 (C=O), 1620 (C=N), 1110 (C=S)	3.38 (2H, s), 3.90 (3H, s), 7.00–7.60 (9H, m), 8.30 (1H, s)
9e	52	170–172	$C_{19}H_{17}N_3OS$ (acetone-water) 2:1	3300 (SH), 3200 (NH), 3050 (CH arom.), 2860 (CH aliph.), 1705 (C=O), 1630 (C=N), 1115 (C=S)	2.30 (2H, s), 3.38 (2H, s), 6.70–7.80 (8H, m), 3.90 (3H, s), 8.30 (1H, s)
9f	50	190–192	$C_{19}H_{17}N_3O_2S$ (acetone-water) 2:1	3300 (SH), 3180 (NH), 3050 (CH arom.), 2860 (CH aliph.), 1710 (C=O), 1620 (C=N), 1110 (C=S)	3.20 (3H, s), 3.39 (2H, s), 6.90–7.60 (8H, m), 3.85 (3H, s), 8.30 (1H, s)

[a]All the prepared compounds gave satisfactory elemental analyses.

SCHEME 1



SCHEME 2



NMR (DMSO-d_6): δ 6.65 (1H, s), 7.00–7.50 (4H, m), 10.20 (1H, s), 12.20 (1H, s).

Preparation of 1-[3-(2-Oxoindolinylidene)]-acetyl chloride (**4**)

An 18.9 g (0.1 mol) amount of **3** was dissolved in 200 mL of carbon tetrachloride, and to this mixture was added 7 mL (0.1 mol) of thionyl chloride. The reaction mixture was then refluxed for 4 hours. The solvent was removed by distillation to afford the crude acid chloride as a residue, which was washed with petroleum ether 60–80°C to yield 15.5 g (75%) of the acid chloride **4**, mp 200–202°C decomp.

Synthesis of 3-(2-Oxoindolinylidene)acetophenone Derivatives (*5a–c*) General Procedure

The acid chloride **4** (0.01 mol) was added portionwise to a mixture of $AlCl_3$, (0.04 mol) in 50 mL of the arene, and the reaction mixture was stirred at room temperature for 5 hours, then heated at 70°C on a water bath for 1 hour. The reaction mixture was poured into 100 mL of cold 10% hydrochloric acid, whereby the crude product precipitated. It was filtered off, washed with water several times, and crystallized from the proper solvent (Table 1).

Preparation of 3-(2-Oxoindolinylidene)acetophenone (**5a**)

A 2.07 g (0.01 mol) amount of the acid chloride **4** was treated with benzene (50 mL) in the presence of $AlCl_3$ (5.28 g, 0.04 mol) according to the previous general procedure to give 1.85 g of crude **5a**. The crude product was crystallized from an ethanol/water mixture (1:1) to give 1.69 g (68% yield) of pure **5a**, mp 260–262°C. IR (KBr): 3180 (NH), 3050 (CH arom.), 1685, 1700 (C=O), 1630 (C=C); ^{1}H NMR (DMSO-d_6): δ 6.26 (1H, s), 7.00–7.40 (9H, m), 10.28 (1H, s).

Synthesis of 1-Methyl-3-(2-oxoindolinylidene)acetophenone Derivatives (**6a–c**) General Procedure

Each compound **5a–c** (0.01 mol) was dissolved in 50 mL of dry acetone, and to this solution 3 g of anhydrous potassium carbonate was added. Then, 1.42 g (0.01 mol) of methyl iodide was added dropwise. The reaction mixture was stirred at room temperature for 2 hours, then heated at 70°C for 3 hours. The solvent was removed by distillation, and the residue was diluted with cold water, whereby the crude product precipitated. It was filtered off and crystallized from the proper solvent (Table 1).

1-Methyl-3-(2-oxoindolinylidene)acetophenone (**6a**)

A 2.49 g (0.01 mol) amount of **5a** was treated with 1.42 g (0.01 mol) of methyl iodide in 50 mL of dry acetone in the presence of 3 g of anhydrous potassium carbonate, according to the previous general procedure, to yield 1.73 g (66% yield) of **6a**, mp 250–252°C, IR (KBr), 3040 (CH arom.), 2890 (CH aliph.), 1705, 1685 (C=O); 1630 (C=C); ^{1}H NMR (DMSO-d_6): δ 3.90 (3H, s), 6.10 (1H, s), 7.00–7.50 (9H, m).

Synthesis of Spiro[indoline-3-heterocycle]-2-one Derivatives **7a–i**, **8a–c**, *and* **9a–f** *General Procedure*

A solution of each 3-(2-oxoindolinylidene)-acetophenone derivative **6a–c** (0.001 mol) was dissolved in 25 mL of an ethanol/pyridine mixture (4:1). To this solution, hydrazine hydrate, or phenylhydrazine, or *p*-nitrophenylhydrazine, or hydroxylaminehydrochloride, or urea, and/or thiourea (0.001 mol) was added portionwise. The reaction mixture was heated at 70°C for 3 hours, then cooled to room temperature, whereby the target product precipitated. It was filtered off and crystallized from the proper solvent (Table 1).

1-Methyl-3'-phenylspiro[indoline-3,5'-pyrazoline]-2-one (**7a**)

A 0.263 g (0.01 mol) amount of **6a** was treated with 0.05 g (0.01 mol) of hydrazine hydrate in 25 mL of an ethanol/pyridine mixture (4:1), according to the previous general procedure, to yield 0.19 g (68% yield) of **7a**, mp 200–202°C, IR (KBr) 3200 (NH), 3050 (CH arom.), 2920 (CH aliph.), 1710 (C=0), 1620 (C=N); ^{1}H NMR (DMSO-d_6): δ 3.39 (2H, s), 3.93 (3H, s), 7.00–7.70 (9H, m), 8.20 (1H, s).

1-Methyl-3'-phenylspiro[indoline-3,5'-isoxazoline]-2-one (**8a**)

The reaction of 0.263 g (0.01 mol) of **6a** with 0.07 g (0.01 mol) of hydroxylamine hydrochloride in an ethanol/pyridine mixture, according to the previous general procedure, gave 0.14 g (50% yield) of **8a**, mp 160–162°C, IR (KBr): 3045 (CH arom.), 2890 (CH aliph.), 1700 (C=O), 1620 (C=N); ^{1}H NMR (DMSO-d_6): δ 3.39 (2H, s), 3.90 (3H, s), 7.00–7.85 (9H, m).

1',5'-Dihydro-1-methyl-3'-phenylspiro[indoline-3,6'-pyrimidine]-2,2'-dione (**9a**)

Compound **6a** (0.263 g, 0.01 mol) was treated with 0.06 g (0.01 mol) of urea in an ethanol/pyridine mixture, according to the previous general procedure, to yield 0.167 g (55% yield) of **9a**, mp 220–222°C, IR (KBr): 3250 (OH), 3180 (NH), 3045 (CH arom.), 2890 (CH aliph.), 1680 and 1705 (C=O), 1630 (C=N); ^{1}H NMR (DMSO-d_6): δ 3.38 (2H, s), 3.90 (3H, s), 6.80–7.60 (9H, m), 8.30 (1H, s).

1',5'-Dihydro-1-methyl-3'-phenyl-2'-thioxospiro[indoline-3,6'-pyrimidine]-2-one (**9d**)

The reaction of 0.263 g (0.01 mol) of **6a** with 0.067 g (0.01 mol) of thiourea according to the previous general procedure yielded 0.16 g (50% yield) of **9d**, mp 168–170°C, IR (KBr): 3300 (SH), 3200 (NH), 3050 (CH arom.), 2860 (CH aliph.), 1710 (C=O), 1620 (C=N), 1110 (C=S). ^{1}H NMR (DMSO-d_6): δ 3.38 (2H, s), 3.90 (3H, s), 7.00–7.60 (9H, m), 8.30 (1H, s).

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