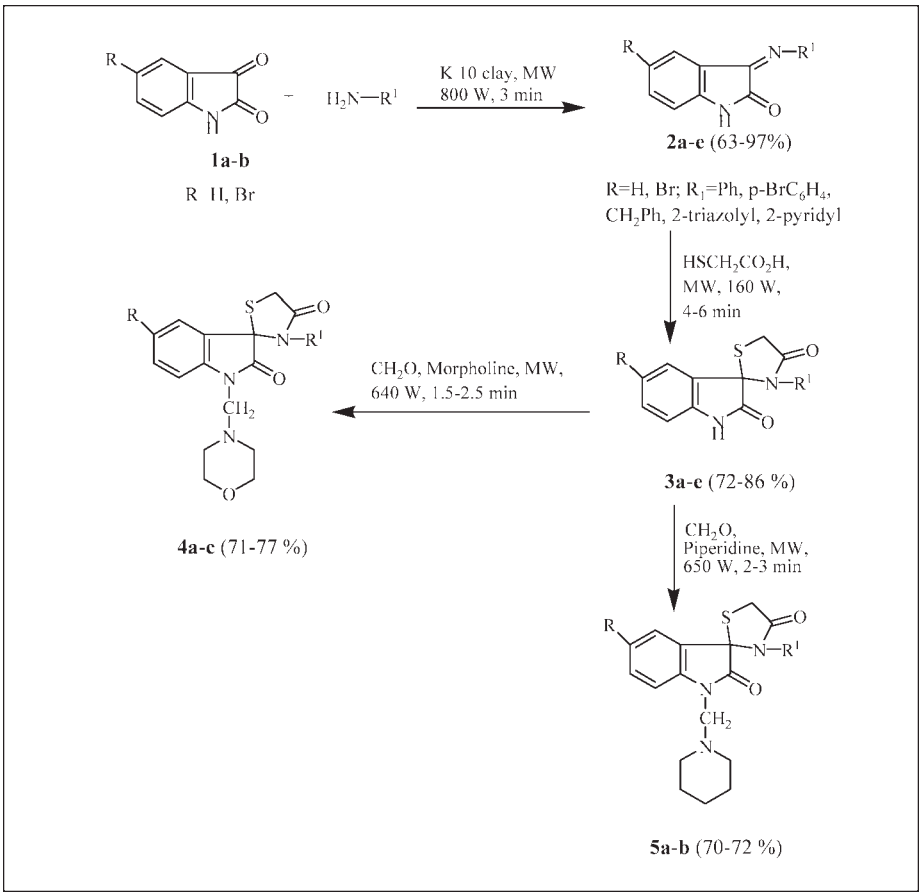
Microwave-Assisted, Solvent-Free Synthesis of 3′-(Aryl/Heteroaryl)-1-morpholinomethyl/piperidinomethylspiro[3*H*-indole-3,2′-thiazolidine]-2,4′(1*H*)-diones *via* 3-Isatinimines

Manju Pandey, Dushyant Singh Raghuvanshi, and Krishna Nand Singh*

Department of Chemistry, Banaras Hindu University, Varanasi 221005, India
*E-mail: knsinghbhu@yahoo.co.in

Received February 21, 2007
DOI 10.1002/jhet.12
Published online 5 February 2009 in Wiley InterScience (www.interscience.wiley.com).



The solvent-free, microwave (MW)-assisted synthesis of a new series of 3′-(aryl/heteroaryl)-1-morpholinomethyl/piperidinomethylspiro[3*H*-indole-3,2′-thiazolidine]-2,4′(1*H*)-diones has been achieved in an open vessel. Isatins **1** undergo an easy condensation with various aryl/heteroaryl amines by MW using montmorillonite K10 clay as a solid support to afford Schiff bases **2**, which subsequently undergo smooth cyclization with TGA under neat MW conditions to afford the spiro thiazolidinones **3**. The spiro-compounds are made to react with morpholine/piperidine and formaldehyde to give the corresponding Mannich bases **4/5** in reasonably good yield.

J. Heterocyclic Chem., **46**, 49 (2009).

INTRODUCTION

Microwave-assisted organic synthesis (MAOS) has been recognized as one of the most fascinating areas of current research [1–3]. Coupling of microwave (MW) irradiation with the use of catalysts or mineral supported reactions, under solvent-free conditions, provides a clean chemical process with an advantageous merit of enhanced reaction rates, higher yields, greater selectivity, and ease of manipulation [4–7]. Isatin Mannich bases are found to have cytotoxicity against a panel of human cancer cells [8]. They also possess antibacterial, antifungal, antiviral, anti-HIV, anti-protozoal, and anthelmintic activities. Indole ring, when joined to the other aryl/heteroaryl systems through a spiro carbon atom at C-3, the resulting spiroindoles exhibit an

Table 1

Physical and analytical data of compounds **2**.

Compound	R	R^1	Time (min)	Mp (°C)	Yield (%)	Molecular formula
2a	H	p-BrC_6H_4	3	242	94	$C_{14}H_9BrN_2O$
2b	H	Ph	3	183	97	$C_{14}H_{10}N_2O$
2c	Br	$CH_2C_6H_5$	3	105	90	$C_{15}H_{11}BrN_2O$
2d	Br	2-thiazolyl	2.5	120	63	$C_{11}H_6BrN_3OS$
2e	Br	2-pyridinyl	2	190	65	$C_{13}H_8BrN_3O$

increased spectrum of biological activities [9–11]. Further, spiro[indole-thiazolidine]-diones show a wide range of pharmacological properties as anticonvulsant, anti-inflammatory, antibacterial, and anti-fungal [12–14]. *N*-Piperidino-(or morpholino-) methylisatin-3-anils possess potential biological activity and have been prepared by the condensation of isatin with arylamines followed by the Mannich reaction with piperidine or morpholine [15]. Some new spiro[indoline-3,2′-thiazolidine]-2,4′-(1*H*)-diones and bis[spiro[indoline-3,2′-thiazolidine]-2,4′(1*H*)-diones] have been obtained thermally and under MW irradiation by the condensation of isatin, aromatic amines, and mercaptoacetate without isolating the imine intermediates [16]. 3′-Substituted phenylspiro[3*H*-indole-3,2′-thiazolidine]-2,4′-(1*H*)-diones are reported to have significant antimicrobial activity [17]. A convenient synthesis of spiro[3*H*-indole-3,2′thiazolidine]-2,4′(1*H*)-diones has also been carried out by the condensation and cyclization of isatin with various aromatic amines [18]. In view of the above and prompted by the solvent-free MAOS, we describe herein a MW-assisted regioselective synthesis of 3′-(aryl/heteroaryl)-1-morpholinomethyl/piperidinomethylspiro[3*H*-indole-3,2′-thiazolidine]-2,4′(1*H*)-diones under solvent-free conditions.

RESULTS AND DISCUSSION

The reaction sequence involves MW-induced preparation of Schiff bases **2a–e** (Table 1) from isatins **1a–b** and amines (R^2-NH_2) using montmorillonite K10 clay as a solid support, followed by the cyclocondensation of Schiff bases **2a–e** and mercaptoacetic acid under neat MW irradiation conditions to achieve the synthesis of spiro[indole-thiazolidine]-diones **3a–e** (Table 2). The resulting compounds **3a–e** are then allowed to react with either morpholine or piperidine and 37% formaldehyde, under solvent-free MW irradiation conditions, to afford the corresponding Mannich bases **4a–c** and **5a**,**b** (Table 3) in reasonably good yields (Scheme 1).

To optimize the yield of products, the effect of various parameters such as MW power, irradiation time, and molar proportions of the reactants were investigated in detail. The preparation of **2a** as reference compound was observed under three different sets of reaction conditions. In the first run, isatin was refluxed with *p*-bromoaniline in absolute ethanol for 2 h, yielding the product **2a** (83%). In the second run, the reactants were refluxed in triply distilled water containing a few drops of glacial acetic acid for 30 min affording **2a** (82%). Finally, the reaction was carried out under MW-assisted (800 W) solvent free conditions using K10 clay as a solid support, to afford **2a** (94%) in just 3 min. Because of the unambiguous merits, MW method was adopted for the preparation of the rest of the compounds (Table 1). It is worthwhile to mention that in the case of compounds **2d** and **2e** (*cf*. Table 1); a 500-mL Borosil beaker containing 200 mL of water was kept as a heat sink to avoid the burning of the compound. For compound **3a**, a higher MW power (420 W and 320 W) resulted in reasonably poor yield of product probably due to the loss of low boiling mercaptoacetic acid.

However, 160 W irradiation using equimolar quantities of **2a** and mercaptoacetic acid gave rise to an enhanced yield (65%) of the product **3a**. The yields of **3a–e** were considerably increased (72–86%) when the molar ratio of the reactants **2a** and mercaptoacetic acid were kept to be 1:2. A trace of acidic compound was also observed in this run. To achieve the optimum yield of Mannich bases **4**/**5**,

Table 2

Physical and analytical data of compounds **3**.

Compound	R	R^1	Time (min)	Mp (°C)	Yield (%)	Molecular formula
3a	H	p-BrC_6H_4	6	90	72	$C_{16}H_{11}BrN_2O_2S$
3b	H	Ph	5	230	76	$C_{16}H_{12}N_2O_2S$
3c	Br	$CH_2C_6H_5$	5	125	75	$C_{17}H_{13}BrN_2O_2S$
3d	Br	2-thiazolyl	4	135	78	$C_{13}H_8BrN_3O_2S_2$
3e	Br	2-pyridinyl	4	120	87	$C_{15}H_{10}BrN_3O_2S$

Table 3

Physical and analytical data of compounds **4**/**5**.

Compound	R	R^1	X	Time (min)	Mp (°C)	Yield (%)	Molecular formula
4a	H	p-BrC_6H_4	O	2	114	71	$C_{21}H_{20}N_3O_3S$
4b	H	Ph	O	1.5	101	77	$C_{21}H_{21}N_3O_3S$
4c	Br	2-pyridinyl	O	2.5	70	74	$C_{20}H_{19}BrN_4O_3S$
5a	Br	$CH_2C_6H_5$	C	2	85	70	$C_{23}H_{24}BrN_3O_2S$
5b	Br	2-thiazolyl	C	3	120	72	$C_{19}H_{19}BrN_4O_2S_2$

the reaction mixture was irradiated intermittently (30 s/cycle) to avoid the loss of low boiling reactants.

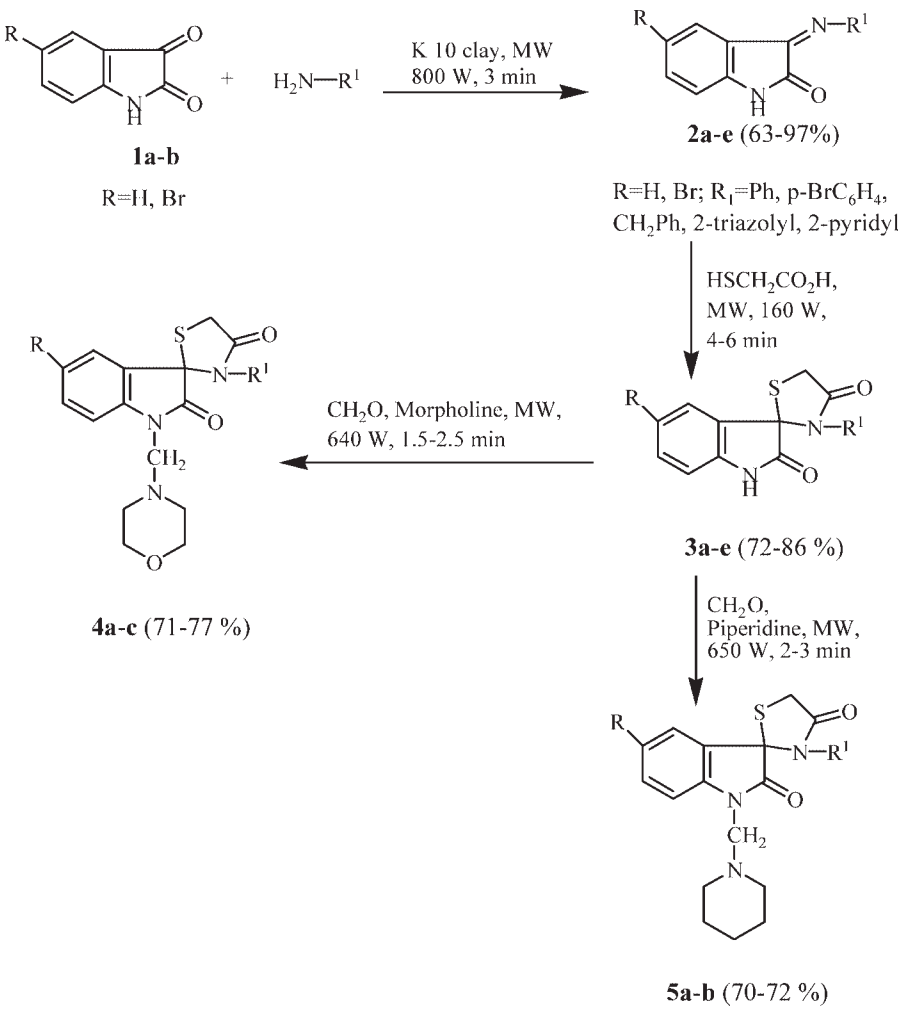
All the reactions were monitored by TLC and then worked up to afford the products, which exhibited physical and spectral data consistent with their structures.

EXPERIMENTAL

IR spectra were recorded on a JASCO FT/IR-5300 spectrophotometer, whereas NMR was run on a JEOL AL300 FTNMR spectrometer. The chemical shifts are given in δ ppm with respect to TMS as internal standard. The TLC spots were detected using iodine chamber. All commercially available chemicals were purchased from Aldrich and Merck.

General procedure for the synthesis of isatin Schiff bases (2). Equimolar quantities (1 mmole) of either isatin or 5-bromoisatin and corresponding amino reagent were blended with Montmorillonite K10 clay (20 mg) and heated for 2–3 min in a MW oven set (LG, Model MS-194W) for 900 W. Upon completion of the reaction, as checked by TLC, the product was extracted with CH_2Cl_2 (3 × 10 mL). After evaporation of

Scheme 1



the solvent under reduced pressure, the product was recrystallized from ethanol.

3-(p-Bromophenylimino)-isatin (2a). From *p*-bromoaniline, yellow crystals (94%), mp 242°C; ir (potassium bromide): NH 3236, C=O 1700, C=N 1619 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.2 (s, 1H, NH), 7.0–7.8 ppm (m, 8H, Ar—H); ^{13}C NMR (DMSO-d_6): 168 (C=O), 160 (C=N), 152 (C—N=C), 120–139 ppm (Ar—C's). Anal. Calcd. For $C_{14}H_9BrN_2O$: C, 55.84; H, 3.01; Br, 26.53; N, 9.30; O, 5.31. Found: C, 55.89; H, 3.06; Br, 26.48; N, 9.33; O, 5.28.

3-(Phenylimino)-isatin (2b). From aniline, yellow solid (97%), mp 183°C; ir (potassium bromide): NH 3260, C=O 1695, C=N 1612 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.3 (s, 1H, N—H,); 6.8–7.6 ppm (m, 9H, Ar—H); ^{13}C NMR (DMSO-d_6): 166 (C=O), 162 (C=N), 155 (C—N=C), 120–138 ppm (Ar—C's); Anal. Calcd. For $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60; O, 7.20. Found: C, 75.63; H, 4.55; N, 12.63; O, 7.18.

5-Bromo-3-(benzylimino)-isatin (2c). From benzyl amine, shiny light brown solid (90%), mp 105°C, ir (potassium bromide): NH 3350, C=O 1690, C=N 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.1 (s, 1H, NH); 7.1–7.7 (m, 8H, Ar—H); 4.8 ppm (m, 2H, N—CH_2—C); ^{13}C NMR (DMSO-d_6): 168 (C=O), 161 (C=N), 152 (C—N=C), 118–137 (Ar—C's), 57 ppm (N—CH_2—C); Anal. Calcd. For $C_{15}H_{11}BrN_2O$: C, 57.16; H, 3.52; Br, 25.35; N, 8.89; O, 5.08. Found: C, 57.21; H, 3.57; Br, 25.27; N, 8.91; O, 4.91.

5-Bromo-3-(2-thiazolylimino)-isatin (2d). From 2-thiazolyl amine, dark brown solid (63%), mp 120°C; ir (potassium bromide): NH 3370, C=O 1692, C=N 1615 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.2 (s, 1H, NH); 7.4–7.8 (m, 3H, Ar—H); 7.3, 8.0 ppm (m, 2H, heteroAr—H); ^{13}C NMR (DMSO-d_6): 166 (C=O), 163 (C=N), 154 (C—N=C), 118–153 ppm (Ar and heteroAr C's); Anal. Calcd. For $C_{11}H_6BrN_3OS$: C, 42.87; H, 1.96; Br, 25.93; N, 13.64; O, 5.19; S, 10.41. Found: C, 42.79; H, 1.91; Br, 25.97; N, 13.60; O, 5.24; S, 10.50.

5-Bromo-3-(2-pyridinylimino)-isatin(2e). From 2-pyridinyl amine, yellow–orange solid (65%), mp 190°C; ir (potassium bromide): NH 3452, C=O 1685, C=N 1618 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.0 (s, 1H, NH); 7.4–7.8 (m, 3H, Ar—H); 7.2, 8.6 ppm (m, 2H, heteroAr—H); ^{13}C NMR (DMSO-d_6): 168 (C=O), 162 (C=N), 152 (C—N=C), 118–175 ppm (Ar and heteroAr C's); Anal. Calcd. For $C_{13}H_8BrN_3O$: C, 51.68; H, 2.67; Br, 26.45; N, 13.91; O, 5.30. Found: C, 51.61; H, 2.72; Br, 26.50; N, 13.85; O, 5.38.

General procedure for the synthesis of 3′-arylspiro[3*H*–indole-3,2′-thiazolidine]-2,4′(1*H*)-2,4-dione (3). A mixture of **2** (1 mmol) and mercaptoacetic acid (2 mmol) was heated for 4–6 min in a MW oven set for 160 W. The completion of the reaction was checked by TLC. The reaction content was then treated with 15 mL, 10% $NaHCO_3$ solution and stirred well. The resulting compound was filtered, washed with water, dried and recrystallized from ethanol to give the pure product.

3-(p-Bromophenyl)spiro[3H-indole-3,2′-thiazolidine]-2,4′(1H)-dione (3a). From **2a**, yellow solid (72%), mp 90°C; ir (potassium bromide): NH 3260, C=O 1720, 1690, C=N 1608 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.5 (s, 1H, NH), 6.8–7.5 ppm (m, 8H, Ar—H); ^{13}C NMR (DMSO-d_6): 77 (spiro C), 170,168 (2 C=O), 35 (S—CH_2—C), 118–141 ppm (Aromatic-C); Anal. Calcd. For $C_{16}H_{11}BrN_2O_2S$: C, 51.21; H, 2.95; Br, 21.29; N, 7.49; O, 8.53; S, 8.55. Found: C, 51.17; H, 3.09; Br, 21.37; N, 7.53; O, 8.44; S, 8.61.

3′-(Phenyl)spiro[3H-indole-3,2′-thiazolidine]-2,4′(1H)-dione (3b). From **2b**, dark brown solid (76%), mp 230°C; ir (potassium bromide): NH 3258, C=O 1730, 1695, C=N 1608 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.1 (s, 1H, NH), 6.8–7.5 (m, 9H, Ar—H), 3.5 ppm (S—CH_2—C); ^{13}C NMR (DMSO-d_6): 77 (spiro C), 170,168 (2 C=O), 35 (S—CH_2—C), 120–141 ppm (Aromatic-C); Anal. Calcd. For $C_{16}H_{12}N_2O_2S$: C, 64.85; H, 4.08; N, 9.45; O, 10.80; S, 10.82. Found: C, 64.91; H, 3.95; N, 9.52; O, 10.87; S, 10.90.

5-Bromo-3′-(benzyl)spiro[3H-indole-3,2′-thiazolidine]-2,4′(1H)-dione (3c). From **2c**, brown solid (75%), mp 125°C; ir (potassium bromide): NH 3345, C=O 1732, 1687 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.3 (s, 1H, NH), 7.1–7.4 (m, 8H, Ar—H), 3.4 (S—CH_2—C), 4.5 ppm (N—CH_2—C); ^{13}C NMR (DMSO-d_6): 74 (spiro C), 170,171 (2 C=O), 35 (S—CH_2—C), 47 (N—CH_2—C) 119–137 ppm (Aromatic-C), Anal. Calcd. For $C_{17}H_{13}BrN_2O_2S$: C, 52.45; H, 3.37; N, 7.20; O, 8.22; S, 8.24. Found: C, 52.39; H, 3.31; N, 7.14; O, 8.30; S, 8.38.

5-Bromo-3′-(2-thiazolyl)spiro[3H-indole-3,2′-thiazolidine]-2,4′(1H)-dione (3d). From **2d**, shiny blackish solid (78%), mp 135°C; ir (potassium bromide): NH 3360, C=O 1730, 1698 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.5 (s, 1H, NH), 7.2–7.4 (m, 3H, Ar—H), 3.5 (S—CH_2—C), 6.6–7.5 ppm (2H, thiazolyl), ^{13}C NMR (DMSO-d_6): 76 (spiro C), 170,168 (2 C=O), 35 (S—CH_2—C), 119–141 ppm (Aromatic-C), 108, 138, 172 (thiazolyl C), Anal. Calcd. For $C_{13}H_8BrN_3O_2S_2$: C, 40.85; H, 2.11; Br, 20.90; N, 10.99; O, 8.37; S, 16.78. Found: C, 40.91; H, 2.04; Br, 20.83; N, 11.03; O, 8.31; S, 16.84.

5-Bromo-3′-(2-piperidinyl)spiro[3H-indole-3,2′-thiazolidine]-2,4′(1H)-dione (3e). From **2e**, brown solid (87%), mp 120°C; ir (potassium bromide): NH 3450, C=O 1732, 1690 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.7 (s, 1H, NH), 7.2–7.4 (m, 3H, Ar—H), 7.1–8.5 (4H, pyridine), 3.5 ppm (S—CH_2—C), ^{13}C NMR (DMSO-d_6): 76 (spiro C), 170,168 (2 C=O), 35 (S—CH_2—C), 119–152 ppm (Aromatic-C and heteroAr-C), Anal. Calcd. for $C_{15}H_{10}BrN_3O_2S$: C, 47.89; H, 2.68; Br, 21.25; N, 11.17; O, 8.51; S, 8.52. Found: C, 47.95; H, 2.73; Br, 21.19; N, 11.11; O, 8.57; S, 8.46.

General procedure for the synthesis of 3′-aryl-1-morpholino/piperidinomethylspiro[3*H*-indole-thiazolidine]-2,4′(1*H*)-dione (4/5). An equimolar quantity of **3** (5 mmol) and morpholine/piperidine (5 mmol) was blended with 37 % formaldehyde (0.5 mL) and then irradiated in a MW oven at 640 W with 30 s/cycle for 2–3 min, as checked by TLC. After cooling, the product mixture was recrystallized from aqueous ethanol to afford product.

3′-(p-Bromophenyl)-1-morpholinomethylspiro[3H-indole-thiazolidine]-2,4′(1H)-dione (4a). From **3a**, yellow solid (71%), mp 114°C; ir (potassium bromide): C=O 1720, 1690 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.9–7.5 (m, 8H, Ar—H), 2.4–3.7 (m, 10H, 5 × CH_2), 4.6 ppm (s, N—CH_2—N); ^{13}C NMR (DMSO-d_6): 74 (spiro C), 170,168 (2 C=O), 35 (—CH_2—), 70 (N—CH_2—N), 54–71 (4 × CH_2), 118–142 ppm (Aromatic-C); Anal. Calcd. for $C_{21}H_{20}BrN_3O_3S$: C, 53.17; H, 4.25; Br, 16.84; N, 8.86; O, 10.12; S, 6.76. Found: C, 53.26; H, 4.18; Br, 16.76; N, 8.80; O, 10.21; S, 6.82

3′-(Phenyl)-1-morpholinomethylspiro[3H-indole-thiazolidine]-2,4′(1H)-dione (4b). From **3b**, yellow solid (77%), mp 101°C; ir. (potassium bromide): C=O 1730, 1695 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.9–7.3 (m, 9H, Ar—H), 2.4–3.4 (m, 10H, 5 × CH_2), 4.6 (s, N—CH_2—N), 3.4 ppm (S—CH_2—C), ^{13}C NMR

(DMSO-d_6): 74 (spiro C), 169,168 (2 C=O), 33 (—CH_2—), 71 (N—CH_2—N), 54–71 (4 × CH_2), 120–140 ppm (Aromatic-C), Anal. Calcd. for $C_{21}H_{21}N_3O_3S$: C, 63.78; H, 5.35; N, 10.63; O, 12.14; S, 8.11. Found: C, 63.85; H, 5.28 N, 10.60; O, 12.08; S, 8.28.

5-Bromo-3′-(2-piperidinyl)-1-morpholinomethylspiro [3H-indole-thiazolidine]-2,4′(1H)-dione (4c). From **3e**, brown solid (74%), mp 70°C; ir (potassium bromide): C=O 1740, 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.9–7.3 (m, 3H, Ar—H), 2.3–3.7 (m, 8H, 4 × CH_2), 4.5 (s, N—CH_2—N), 3.3 (S—CH_2—C), 7.2–8.5 ppm (4H, pyridine), ^{13}C NMR (DMSO-d_6): 75 (spiro C), 170,168 (2 C=O), 33 (S—CH_2—C), 70 (N—CH_2—N), 54–71 (4 × CH_2), 119–142 (Aromatic-C), 115–153 ppm (pyridine C), Anal. Calcd. for $C_{20}H_{19}BrN_4O_3S$: C, 50.53; H, 4.03; Br, 16.81; N, 11.79; O, 10.10; S, 6.75. Found: C, 50.59; H, 4.11; Br, 16.77; N, 11.84; O, 10.17; S, 6.81.

5-Bromo-3′-(benzyl)-1-piperidinomethylspiro[3H-indole-thiazolidine]-2,4′(1H)-dione (5a). From **3c**, brown solid (70%), mp 85°C; ir (potassium bromide): C=O 1728, 1695 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.9–7.5 (m, 8H, Ar—H), 1.5–3.3 (m, 12H, 6 × CH_2), 4.6 (s, N—CH_2—N), 4.5 (N—CH_2—C), 3.3 ppm (S—CH_2—C), ^{13}C NMR (DMSO-d_6): 68 (spiro C), 171,168 (2 C=O), 35 (S—CH_2—C), 70 (N—CH_2—N), 54–71 (4 × CH_2), 125–141 ppm (Aromatic-C), Anal. Calcd. for $C_{23}H_{24}BrN_3O_3S$: C, 56.79; H, 4.97; Br, 16.43; N, 8.64; O, 6.58; S, 6.59. Found: C, 56.67; H, 5.08; Br, 16.49; N, 8.70; O, 6.49; S, 6.50.

5-Bromo-3′-(2-thiazolyl)-1-piperidinomethylspiro[3H-indole-thiazolidine]-2,4′(1H)-dione (5b). From **3d**, coffee colored shiny powder (72%), mp 120°C; ir (potassium bromide): C=O 1735, 1692 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.8–7.3 (m, 3H, Ar—H), 1.5–2.4 (m, 10H, 5 × CH_2), 4.5 (s, N—CH_2—N), 6.5,7.5 (2H, thiazole), 3.3 ppm (S—CH_2—C), ^{13}C NMR (DMSO-d_6): 74 (spiro C), 173,172 (2 C=O), 35 (S—CH_2—C), 70 (N—CH_2—N), 54–71 (5 × CH_2), 119–141 (Aromatic-C), 138,168,171 ppm (thiazole), Anal. Calcd. for $C_{19}H_{19}BrN_4O_2S_2$: C, 47.60; H, 3.49; Br, 16.67; N, 11.69; O, 6.67; S, 13.38. Found: C, 47.51; H, 3.56; Br, 16.71; N, 11.75; O, 6.59; S, 13.47

Acknowledgment. The authors are thankful to the Department of Biotechnology, New Delhi for financial assistance.

REFERENCES AND NOTES

[1] Lidstrom, P.; Tierney, J.; Wathey, B.; Westman, J. Tetrahedron 2001, 57, 9225.

[2] Perrux, L.; Loupy, A. Tetrahedron 2001, 57, 9199.

[3] Caddick, S. Tetrahedron 1995, 51, 10403.

[4] Loupy, A. C. R. Chimie 2004, 7, 103.

[5] Lerestif, J. M.; Toupet, L.; Sun-bandhit, S.; Tonnard, F.; Bazureau, J. P.; Hamelin, J. Tetrahedron 1997, 53, 635.

[6] Varma, R. S.; Dahiya, R.; Kumar, S. Tetrahedron Lett 1997, 38, 2039.

[7] Varma, R. S. Tetrahedron 2002, 58, 1235.

[8] Karah, N. Eur J Med Chem 2002, 37, 909.

[9] Joshi, K. C.; Jain, R.; Chand, P. Heterocycles 1985, 23, 957.

[10] Azizian, J.; Morady, A. V.; Soozangarzarzadeh, S.; Asadi, A. Tetrahedron Lett 2002, 43, 9721.

[11] Saxena, A.; Khanna, P.; Bhagat, S.; Gupta, A.; Jain, S. C. Indian J Chem B 2006, 45, 1504.

[12] Sweetman, B. J.; Bellas, M.; Field, L. J Med Chem 1963, 12, 888.

[13] Rajopadhye, M.; Popp, F. D. J Heterocycl Chem 1987, 24, 1637.

[14] Rajopadhye, M.; Popp, F. D. J Heterocycl Chem 1984, 21, 28.

[15] Varma, R. S. Pol. J Pharmacol Pharm 1975, 27, 641.

[16] Azizian, J.; Morady, A. V.; Jadidi, K.; Mehrdad, M.; Sarrafi, Y. Synth Commun 2000, 30, 537.

[17] Diurno, M. V.; Mazzoni, O.; Piscopo, E.; Bolognese, A. Farmaco 1993, 48, 435.

[18] Joshi, K. C.; Patni, R.; Chand, P. Heterocycles 1981, 16, 1555.