Synthesis of 1,3-thiazole and 1,2,4-oxadiazole substituted spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-diones

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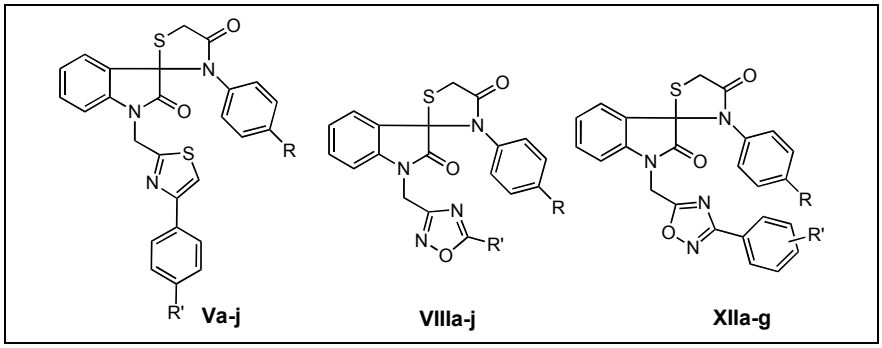

Some new derivatives of spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione with the heterocyclic ring such as substituted thiazole and 1,2,4-oxadiazole attached to the indolinone ring *via* CH_2 linkage has been synthesized in moderate yields. The synthesis have been carried out by making use of the reactivity of the NH group of the indolinone moiety present in spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione.

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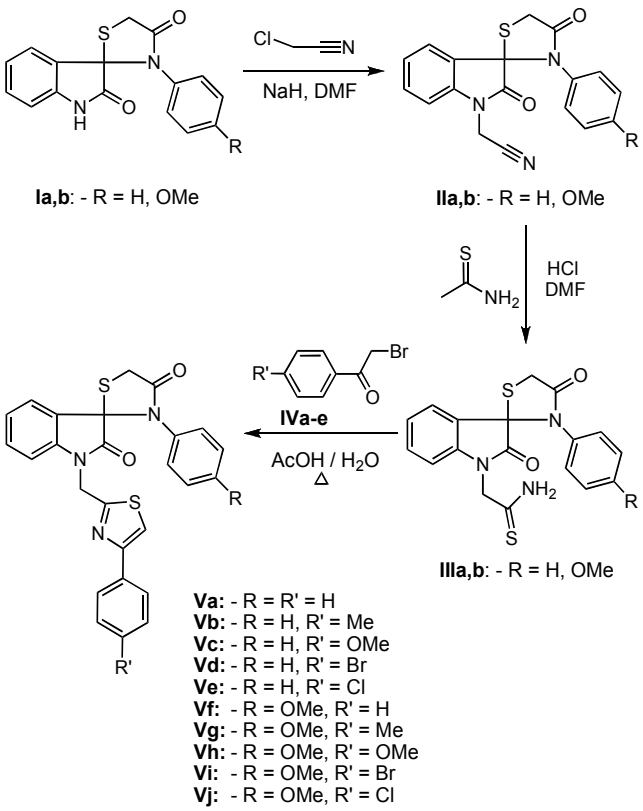
INTRODUCTION

The chemistry of spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione in which an indolinone ring is joined to sulfur and nitrogen containing thiazolidinone ring at the C-3 position through a spiro carbon atom is of great interest due to their antileukemic and anticonvulsant [1-3] and also for biological activities [4-5]. Even the spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-diones have been reported, where the phenyl ring attached to the thiazolidinone ring is replaced by other heterocycles such as coumarin [6] and 2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl [7] group. Some reports where the NH group of indolinone in spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-diones is subjected to Mannich reaction and acetylation is cited [8-9]. We in our earlier work have described the synthesis of spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones substituted with phenyl-1,3,4-oxadiazoles at the indolinone ring [10]. Owing to the paucity of work reported and by making use of the reactivity of NH the group, we have synthesized various thiazole and 1,2,4-oxadiazole substituted spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-diones. The synthesized compounds may be expected to possess biological activity.

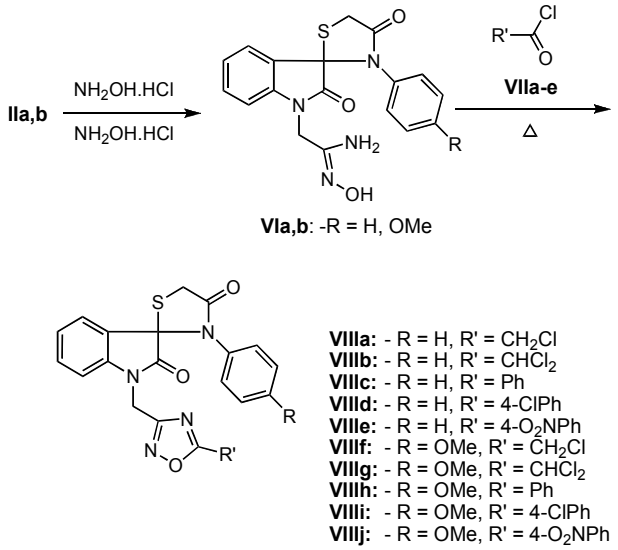
The title compounds 5-phenylthiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **Va-j** were synthesized as per the method depicted in Scheme 1. 3'-Aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **Ia-b** were reacted with chloroacetonitrile in the presence of sodium hydride under nitrogen atmosphere to give 3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione-1-ylacetonitriles **IIa-b**.



Scheme 1. Synthesis of 5-phenylthiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **Va-j**.

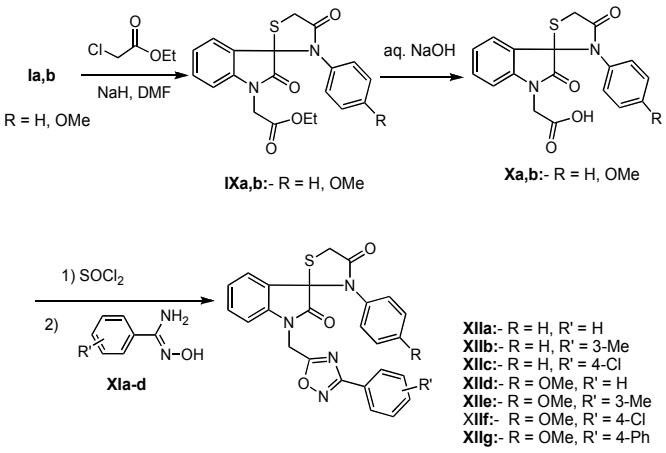
These acetonitrile derivatives **IIa-b** underwent rearrangement when treated with thioacetamide and dry hydrogen chloride gas to give 3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione-1-yl-thioacetamides **IIIa-b**. The synthetic methodology used for the conversion of a nitrile into thioacetamides using above methodology is reported in the literature [11]. The thioacetamides **IIIa-b** on refluxing with α-bromoacetophenones **IVa-e** in acetic acid and water mixture to give 5-phenylthiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **Va-j** in 43-76 percent yields.

In the ^{1}H nmr spectra of acetonitriles **IIa-b,** thioacetamides **IIIa-b** and 3'-aryl-[2-(5-phenylthiazole)-methyl]spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **Va-j** the SCH_2 group showed AB splitting between δ 3.9 to δ 4.3 except for the compound **IIIb** which showed AX splitting. The NCH_2 group which appeared as a singlet between δ 4.8 to δ 5.0 in acetonitriles **IIa-b** showed AB splitting for thioacetamides **IIIa-b** and 3'-aryl-[2-(5-phenylthiazole)methyl]spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **Va-j** between δ 4.2 to δ 5.5, except for the compound **IIIb** which showed AX splitting. The AB or AX splitting of NCH_2 and SCH_2 group was due to geminal coupling.



Scheme 2. Synthesis of 3-Aryl/alkyl[1,2,4]oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **VIIIa-j**.

After successfully synthesizing various 5-phenyl-thiazole substituted spiro[3*H*-indole-3,2'-thiazol-idine]-2,4'(1*H*)dione **Va-j,** we utilized the spiroaceto-nitrile derivatives **IIa-b** for the synthesis of 5-aryl/alkyl-[1,2,4]oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione **VIIIa-j** as exemplified in Scheme 2. Compounds **IIa-b** on refluxing with hydroxyl aminehydrochloride in the presence of sodium carbonate as base give N-hydroxy-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione-1-yl-acetamidines **VIa-b**. Heating acetamidines **VIa-b** with various aliphatic and aromatic acid chlorides **VIIa-e** in the absence of any solvent at 100 °C resulted in the formation of 5-aryl/alkyl-[1,2,4]oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione **VIIIa-j**. The ^{1}H nmr spectra of the N-hydroxy acetamidines **VIa,b** and 5-aryl/alkyl-[1,2,4]oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **VIIIa-j** showed AB splitting between δ 3.9 to δ 5.5 for SCH_2 and NCH_2 group due to geminal coupling.



Scheme 3. Synthesis of 3-phenyl-1,2,4-oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **XIIa-g**.

In our third attempt we became interested in the synthesis of spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones with 3-phenyl-1,2,4-oxadiazol-5-yl methyl moiety. The schematic representation for the synthesis of 3-phenyl-1,2,4-oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **XIIa-g** is depicted in Scheme 3. The starting material ethyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione-1-yl-acetates **IXa-b** required for the synthesis were synthesized as per the method reported by us [12]. The ester derivatives were hydrolyzed using 2% aq. sodium hydroxide solution to give the corresponding 3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione-1-yl-acetic acids **Xa-b**. The compounds **Xa-b** were then converted into acid chlorides using thionyl chloride and reacted *in situ* with N-hydroxy phenylamidines **XIa-d** in acetic acid at reflux temperature to give the desired molecules **XIIa-g**. Even the ^{1}H nmr spectra of 3-phenyl-1,2,4-oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones **XIIa-g** showed AB splitting between δ 3.9 to δ 5.5 for SCH_2 and NCH_2 group as observed in earlier cases, except for the compound **XIIa-b** which showed AX splitting.

EXPERIMENTAL

3'-Aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*) diones **Ia-b** required for the synthesis were prepared as per the method reported in the literature [8-9]. The α-bromoacetophenones **IVa-e** and various aliphatic as well as aromatic acid chlorides **VIIa-e** were purchased from Aldrich or Lanchester chemical companies. The N-hydroxy phenylamidines **XIa-c** were synthesized as per the reported method [13-14]. Melting points are uncorrected. Ir spectra (ν_{max} in cm^{-1}) were recorded in KBr on a Shimadzu 8201 PC FTIR spectrophotometer. ^1H nmr spectra were recorded on Varian AX400 spectrophotometer at 400MHz using DMSO-d_6 or $CDCl_3$ as a solvent (chemical shifts in δ ppm).

3'-Phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione-1-yl acetonitriles IIa. Sodium hydride (50% in mineral oil) (4.8 g, 0.11mole) was added to suspension of 3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione **1a** (29.6 g, 0.10 mole) taken in 250 mL dry DMF at 0–5 °C under an inert atmosphere of nitrogen. After the mixture was stirred for 1 h, chloroacetonitrile (8.25 g, 0.11mole) was added drop wise at such a rate that the temperature of the reaction is maintained below 10 °C. The reaction was stirred at 5–10 °C for 30 min and at room temperature for 2.5 h. The reaction mixture was poured into ice water. The solid obtained was collected by filtration, washed with water and dried. It was further recrystallized from methanol. Yield: 25.0g (75%), mp 206 - 08 °C. Ir (KBr): 2925, 2382, 1732, 1691, 1608, 1475, 1353, 1253, 1105, 902, 833 and 765 cm^{-1}; ^1H nmr ($CDCl_3$): δ = 4.09 (center of AB quartet, 2H, SCH_2), 4.89 (s, 2H, NCH_2), 6.85-7.08 (m, 3H), 7.14-7.32 (m, 4H), 7.39 (t, *J* = 6.2 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H); Microanalysis calculated for $C_{18}H_{13}N_3O_2S$ (%): C, 64.46; H, 3.91; N, 12.53; S, 9.56. Found: C, 64.31; H, 4.11; N, 12.76; S, 9.43.

3'-(4-Methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione-1-yl acetonitriles IIb. Similarly was synthesized **IIb** from 3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione **Ib** (32.6g, 0.1mole) and chloroacetonitrile (8.25 g, 0.11mole) in 78 % yield using sodium hydride as base,mp 238-40°C. Ir (KBr): 2947, 2382, 1731, 1693, 1610, 1510, 1467,1363, 1249, 1180, 1031, 937, 900, 835 and 752 cm^{-1}; ^1H nmr (DMSO-d_6): δ = 3.64 (s, 3H), 4.10 (center of AB quartet, 2H, SCH_2), 4.97 (s, 2H, NCH_2), 6.78 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 7.14-7.20 (m, 2H), 7.39 (t, *J* = 6.2 Hz & *J* = 6.2 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H); Microanalysis calculated for $C_{19}H_{15}N_3O_3S$ (%) C, 62.45; H, 4.14; N, 11.50; S, 8.77. Found (%): C, 62.21; H, 4.41; N, 11.23; S, 8.93.

3'-Phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione-1-yl-thioacetamide IIIa. A flask containing a mixture of **IIa** (15.0 g, 0.044 moles) and thioacetamide (9.9 g, 0.13 moles) dissolved in 75 mL of DMF was immersed in an ice bath and cooled to 0-5 °C. Freshly generated dry hydrogen chloride gas was bubbled into it for 1.5 h maintaining the reaction mixture at 0-5 °C. The cold solution was poured into ice-water mixture and the solid product was collected by filtration. It was further washed with 200 mL of ice-cold water and dried in air. Crude product was crystallized from methanol and afforded 16.2 g (85% yield) of **IIIa** as colourless crystals, mp. 212-14 °C. Ir (KBr): 3554, 3292, 3195, 1720, 1670, 1612, 1490, 1363, 1263, 1178, 910, 817 and 756 cm^{-1}; ^1H nmr (DMSO d_6) δ = 4.14 (center of AB quartet, 2H, SCH_2), 4.45 (center of AB quartet, 2H, NCH_2), 6.73-6.81 (m, 3H), 6.88 (d, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 8.5 Hz, 2H), 7.03 (t, *J* = 7.1 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.53 (d, *J* = 7.2 Hz, 1H), 9.39 (s, Br, 1H, $CSNH_2$), 9.72 (s, Br, 1H, $CSNH_2$). Microanalysis calculated for $C_{18}H_{15}N_3O_2S_2$ (%): C, 58.52; H, 4.09; N, 11.37; S, 17.36. Found (%): C, 58.49; H, 3.95; N, 11.51; S, 17.19.

3'-(4-Methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione-1-yl-thioacetamide IIIb. Similarly was synthesized **IIIb** from **IIb** (15.0 g, 0.041 mole) in 75% yield, mp.183-85°C. Ir (KBr): 3413, 3294, 1720, 1691, 1610, 1510, 1361, 1249, 1031,937, 783 and 752 cm^{-1}; ^1H nmr ($CHCl_3$) δ = 3.71 (s, 3H), 3.91 (AX splitting, 1H, SCH_2), 4.30 (AX splitting, 1H, SCH_2), 4.52 (AX splitting, 1H, NCH_2), 4.79 (AX splitting, 1H, NCH_2), 6.41 (s, Br, 1H, $CSNH_2$), 6.74 (d, *J* = 9.0 Hz, 2H), 7.82 (d, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 9.0 Hz, 2H), 7.07 (s, Br, 1H, $CSNH_2$), 7.21 (t, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H). Microanalysis calculated for $C_{19}H_{17}N_3O_3S_2$ (%) C, 57.13; H, 4.29; N, 10.52; S, 16.05. Found: C, 57.28; H, 4.18; N, 10.67; S, 15.93.

Procedure A: General procedure for the synthesis of (un)substituted 5-phenylthiazolemethyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones Va-j.

5-Phenylthiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Va. The synthesis of **Va** is representative. A mixture of **IIIa** (1.11 g, 0.003 moles) and α-bromoacetophenone **IVa** (0.6 g, 0.003 moles) was taken in 25 mL acetic acid/water (3:1) and heated to reflux for 45 min. The reaction mixture was cooled in ice-water at 5–10 °C. The precipitated solid was collected by filtration, washed with aqueous solution of Na_2CO_3 followed by water and dried. The crude product on crystallization from ethanol afforded 0.92 g (66% yield) of **Va**, mp. = 238-40 °C. Ir (KBr): 3058, 1730, 1697, 1610, 1510, 1492, 1350, 1249, 1029, 831 and 752 cm^{-1}, ^1H nmr (DMSO-d_6) δ = 4.14 (center of AB quartet, 2H, SCH_2), 5.30 (center of AB quartet, 2H, NCH_2), 6.95-7.90 (m, 4H), 7.14-7.22 (m, 3H), 7.25-7.35 (m, 2H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.89 (d, *J* = 7.3 Hz, 2H), 8.03 (s, 1H, Th H), ms: m/z 470(M^{+1}). Microanalysis calculated for $C_{26}H_{19}N_3O_2S_2$ (%): C, 66.50; H, 4.08; N, 8.95; S, 13.66. Found (%): C, 66.36; H, 4.17; N, 8.80; S, 13.82.

5-(4-methylphenyl)thiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Vb. Following general procedure A was synthesized **Vb** from **IIIa** (1.1 g, 0.003 mole) and α-bromo-4-methylacetophenone **IVb** (0.64 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 0.92 g (64% yield) of **Vb** as colourless crystals, mp = 210-12 °C. Ir (KBr): 3066, 1733, 1692, 1615, 1513, 1473, 1345, 1233, 1052, 830 and 732 cm^{-1}, ^1H nmr (DMSO-d_6) δ = 2.31 (s, 3H, CH_3), 4.14 (center of AB quartet, 2H, SCH_2), 5.29 (center of AB quartet, 2H, NCH_2), 6.98-7.10 (m, 4H), 7.15-7.30 (m, 6H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.94 (s, 1H, Th H). Microanalysis calculated for $C_{27}H_{21}N_3O_2S_2$ (%) C, 67.06; H, 4.38; N, 8.69; S, 13.26. Found: C, 67.23; H, 4.19; N, 8.55; S, 13.03.

5-(4'-Methoxyphenyl)thiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Vc. Following general procedure A was synthesized **Vc** from **IIIa** (1.1 g, 0.003 mole) and α-bromo-4-methoxyacetophenone **IVc** (0.69 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 0.93 g (64% yield) of **Vc** as colourless crystals, mp = 193-95 °C. Ir (KBr); 3059, 1722, 1697, 1509, 1345, 1278, 1027, 973, 832, 747 cm^{-1}.

^{1}H nmr (DMSO-d_6) δ = 3.8 (s, 3H, OCH_3), 4.11 (center of AB quartet, 2H, SCH_2), 5.30 (center of AB quartet, 2H, NCH_2), 6.96-7.10 (m, 6H), 7.15-7.20 (m, 3H), 7.28 (t, *J* = 7.1 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 2H), 7.86 (s, 1H, Th H). Microanalysis calculated for $C_{27}H_{21}N_3O_3S_2$ (%) C, 64.91; H, 4.24; N, 8.41; S, 12.84. Found: C, 64.72; H, 4.15; N, 8.63; S, 12.61.

5-(4'-Bromophenyl)thiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Vd. Following general procedure A was synthesized **Vd** from **IIIa** (1.1 g, 0.003 mole) and α-bromo-4-bromoacetophenone **IVd** (0.83 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 0.90 g (55% yield) of **Vd** as colourless crystals, mp = 228-30 °C. Ir (KBr); 3055, 1720, 1696, 1500, 1350, 1271, 1010, 934, 826, 755 cm^{-1}. ^{1}H nmr (DMSO-d_6) δ = 4.11 (center of AB quartet, 2H, SCH_2), 5.30 (center of AB quartet, 2H, NCH_2), 6.98-7.10 (m, 4H), 7.16-7.19 (m, 3H), 7.29 (t, *J* = 7.0 Hz, 1H), 7.59-7.64 (m, 3H), 7.84 (d, *J* = 8.0 Hz, 2H), 8.11 (s, 1H, Th H). Microanalysis calculated for $C_{26}H_{18}BrN_3O_2S_2$ (%) C, 56.94; H, 3.31; Br, 14.57; N, 7.66; S11.69. Found (%) C 57.15; H 3.49; Br, 13.71; N,7.80; S,11.54.

5-(4'-Chlorophenyl)thiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Ve. Following general procedure A was synthesized **Ve** from **IIIa** (1.1 g, 0.003mole) and α-bromo-4-chloroacetophenone **IVe** (0.70 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 1.0 g (68% yield) of **Ve** as colourless crystals,mp = 243-45 °C. Ir (KBr): 3066, 1708, 1610, 1492, 1350, 1271, 1010, 929, 844, 756 cm^{-1}. ^{1}H nmr (DMSO-d_6) δ = 4.14 (center of AB quartet, 2H, SCH_2), 5.31 (center of AB quartet, 2H, NCH_2), 6.98-7.11 (m, 4H), 7.14-7.20 (m, 1H), 7.28 (t, *J* = 6.9 Hz, 1H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 2H), 8.10 (s, 1H, Th H). Microanalysis calculated for $C_{26}H_{18}ClN_3O_2S_2$ (%): C, 61.96; H, 3.60; Cl, 7.03; N, 8.34; S, 12.72. Found (%) C, 61.77; H, 3.75; Cl, 7.24; N, 8.62; S, 12.57.

5-Phenylthiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Vf. Following general procedure A was synthesized **Vf** from **IIIb** (1.2 g, 0.003 mole) and α-bromoacetophenone **IVa** (0.60 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 0.64 g (43% yield) of **Vf** as colourless crystals,mp = 88-90 °C. Ir (KBr): 3056, 1728, 1697, 1611, 1510, 1490, 1249, 1029, 831, 755 cm^{-1}. ^{1}H nmr (DMSO-d_6) δ **=** 3.56 (s, 3H), 4.11 (center of AB quartet, 2H, SCH_2), 5.30 (center of AB quartet, 2H, NCH_2), 6.68 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 7.03-7.12 (m, 2H), 7.29-7.34 (m, 2H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.89 (d, *J* = 7.4 Hz, 2H), 8.03 (s, 1H, Th H). Microanalysis calculated for $C_{27}H_{21}N_3O_3S_2$ (%) C, 64.91; H, 4.24; N, 8.41; S, 12.84. Found (%): C, 65.11; H, 4.01; N, 8.68;S, 12.59.

5-(4-Methylphenyl)thiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Vg. Following general procedure A was synthesized **Vg** from **IIIb** (1.2 g, 0.003 mole) and α-bromo-4-methylacetophenone **IVb** (0.64 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 1.15 g (75% yield) of **Vg** as colourless crystals, mp = 175-77 °C. Ir (KBr): 3050, 1730, 1690, 1602, 1511, 1496, 1250, 1029, 833, 749 cm^{-1}. ^{1}H nmr (DMSO-d_6) δ **=** 2.31 (s, 3H), 3.56 (s, 3H), 4.10 (center of AB quartet, 2H, SCH_2), 5.27 (center of AB quartet, 2H, NCH_2), 6.68 (d, *J* = 9.0 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 7.04-7.13 (m, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.94 (s, 1H, Th H). Microanalysis calculated for $C_{28}H_{23}N_3O_3S_2$ (%): C, 65.48; H, 4.51; N, 8.18; S, 12.48. Found (%): C, 65.43; H, 4.24; N, 8.40;S, 12.25.

5-(4-methoxyphenyl)thiazolyl methyl-3'-(4-methoxyphen-yl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Vh. Following general procedure A was synthesized **Vh** from **IIIb** (1.2 g, 0.003mole) and α-bromo-4-methoxyacetophenone **IVc** (0.69 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 1.2 g (76% yield) of **Vh** as colourless crystals, mp = 178-80 °C. Ir (KBr):- 3055, 1728, 1691, 1610, 1496, 1250, 1023, 855, 756 cm^{-1}. ^{1}H nmr (DMSO-d_6) δ **=** 3.57 (s, 3H), 3.77 (s, 3H), 4.10 (center of AB quartet, 2H, SCH_2), 5.26 (center of AB quartet, 2H, NCH_2), 6.69 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 7.01-7.12 (m, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 2H), 7.85 (s, 1H, Th H). Microanalysis calculated for $C_{28}H_{23}N_3O_4S_2$ (%): C, 63.50; H, 4.38; N, 7.93; S, 12.11. Found (%): C, 63.29; H, 4.44; N, 7.72; S, 11.85.

5-(4-bromophenyl)thiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Vi. Following general procedure A was synthesized **Vi** from **IIIb** (1.2 g, 0.003mole) and α-bromo-4-bromoacetophenone **IVd** (0.83 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 1.1 g (63% yield) of **Vi** as colourless crystals, mp = 76-78 °C. Ir (KBr): 3066, 1728, 1690, 1495, 1350, 1271, 1014, 934, 826, 752 cm^{-1}. ^{1}H nmr (DMSO-d_6) δ **=** 3.57 (s, 3H), 4.10 (center of AB quartet, 2H, SCH_2), 5.27 (center of AB quartet, 2H, NCH_2), 6.68 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 7.04 (d, *J* = 7.2 Hz, 1H), 7.09(t, *J* = 7.4 Hz, 1H) 7.29 (t, *J* = 7.4 Hz, 1H), 7.60-7.68 (m, 3H), 7.83 (d, *J* = 8.5 Hz, 2H), 8.10 (s, 1H, Th H). Microanalysis calculated for $C_{27}H_{20}BrN_3O_3S_2$ (%): C, 56.06; H, 3.48; Br, 13.81; N, 7.26; S, 11.09. Found (%): C, 56.31; H, 3.40; Br, 14.05; N, 7.52; S, 10.95.

5-(4-Chlorophenyl)thiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione Vj. Following general procedure A was synthesized **Vj** from **IIIb** (1.2 g, 0.003 mole) and α-bromo-4-chloroacetophenone **IVe** (0.70 g, 0.003 moles) by heating in acetic acid/water mixture. The crude product on crystallization from ethanol afforded 0.72 g (45% yield) of **Vj** as colourless crystals, mp = 152-54 °C. Ir (KBr): 3055, 1715, 1695, 1508, 1353, 1274, 1012, 929, 835, 750 cm^{-1}. ^{1}H nmr (DMSO-d_6) δ **=** 3.58 (s, 3H), 4.09 (center of AB quartet, 2H, SCH_2), 5.27 (center of AB quartet, 2H, NCH_2), 6.68 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 2H), 8.07 (s, 1H, Th H). Microanalysis calculated for $C_{27}H_{20}ClN_3O_3S_2$ (%): C, 60.72; H, 3.77; Cl, 6.64; N, 7.87; S, 12.01. Found (%): C, 60.44; H, 3.89; Cl, 6.43; N, 7.56; S, 11.86.

***N*-Hydroxy-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione-1-yl-acetamidine Via.** A mixture of **IIa** (16.75 g, 0.05 mole), 15.0 g of Na_2CO_3 and 21.0 g of hydroxylamine hydrochloride in 150 mL of 5:1 ethanol/water was refluxed for 45 min. The reaction mixture was cooled in ice-bath at 0-5 °C. The solid precipitated was collected by filtration, washed with ethanol/water (1:1) and dried at 50 °C afford 15.64 g (85% yield) of **VIa** as colourless amorphous powder, mp 129-31 °C. The compound obtained by this method was sufficiently pure

and was used as such for the next reaction. Ir (cm^{-1}): 3429, 3354, 1706, 1674, 1593, 1490, 1346, 1207, 1097, 939 and 756 CM^{-1}. ^1H nmr (DMSO-d_6): δ = 4.09 (center of AB quartet, 2H, SCH_2), 4.28 (center of AB quartet, 2H, NCH_2), 5.41 (s, 2H, NH_2), 6.90-7.05 (m, 4H), 7.10-7.31 (m, 4H), 7.46 (d, *J* = 7.5 Hz, 1H), 9.07 (s, 1H, OH). Microanalysis calculated for $C_{18}H_{16}N_4O_3S$ (%): 58.68; H, 4.38; N, 15.21; S, 8.70. Found (%): C, 58.49; H, 4.61; N, 15.04; S, 8.48.

***N*-Hydroxy-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione-1-yl-acetamidine VIb.** Similarly was synthesized **VIb** from **IIb** (17. g, 0.05 moles) in 85% yield, mp. 236-38°C. Ir (KBr): 3473, 3361, 1718, 1658, 1589, 1510, 1363, 1299, 1178, 1103, 945 and 754. ^1H nmr (DMSO-d_6): δ = 3.66 (s, 3H), δ = 4.07 (center of AB quartet, 2H, SCH_2), 4.26 (center of AB quartet, NCH_2), 5.41 (s, 2H, NH_2), 6.82 (d, *J* = 8.9 Hz, 2H), 6.97 (d, *J* = 9.5 Hz, 3H), 7.07 (t, *J* = 7.1 Hz, 1H), 7.30 (t, *J* = 7.0 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 9.10 (s, 1H, OH). Microanalysis calculated for $C_{19}H_{18}N_4O_4S$ (%): C, 57.28; H, 4.55; N, 14.06; S, 8.05. Found: C, 57.53; H, 4.37; N, 13.88; S, 8.21.

Procedure B: General procedure for the synthesis of (un)substituted 3-aryl/alkyl[1,2,4]oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones VIIIa-j.

5-Chloromethyl-[1,2,4]oxadiazolyl methyl-3'-phenyl-spiro-[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIa. The synthesis of **VIIIa** is representative. **VIa** (2.0 g, 0.0054 mole) and chloroacetyl chloride **VIIa** (0.68 g, 0.006 mole) were taken in 6 mL of acetic acid and heated at reflux temperature. After 30 min, reaction mixture was cooled down to room temperature and poured into ice water. The resulting solid was filtered, washed with aqueous solution of $NaHCO_3$, washed with water and dried. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.8 g (38% yield), mp 165-67 °C. Ir (KBr): 2991, 2964, 1730, 1693, 1610, 1508, 1357, 1251, 1178, 1031, 900 and 831 cm^{-1}. ^1H nmr (DMSO-d_6): δ = 4.11 (center of AB quartet, 2H, SCH_2), 5.08 (s, 2H), 5.16 (center of AB quartet, 2H, NCH_2), 6.95-7.08 (m, 4H), 7.15-7.32 (m, 4H), 7.52 (d, *J* = 7.4 Hz, 1H), ms: m/z 427(M^{+1}). Microanalysis calculated for $C_{20}H_{15}ClN_4O_3S$ (%) C, 56.27; H, 3.54; Cl, 8.31; N, 13.12; S, 7.51. Found (%): C, 56.08; H, 3.30; Cl, 8.10; N, 13.33; S, 7.29.

5-Dichloromethyl-[1,2,4]oxadiazolyl methyl-3'-phenyl-spiro-[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIb. Following general procedure B was synthesized **VIIIb** from **VIa** (2.0 g, 0.0054mole) and dichloroacetyl chloride **VIIb** (0.88 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 1.29 g (52% yield), mp. 135-37 °C. Ir (KBr): 2991, 1724, 1687, 1606, 1490, 1423, 1350, 1209, 1174, 1035, 906, 767 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 4.10 (center of AB quartet, 2H, SCH_2), 5.22 (center of AB quartet, 2H, NCH_2), 6.95-7.10 (m, 4H), 7.15-32 (m, 4H), 7.53 (d, *J* = 7.5 Hz, 1H), 7.93 (s, 1H, $CHCl_2$). Microanalysis calculated for $C_{20}H_{14}Cl_2N_4O_3S$ for C, 52.07, H, 3.06; Cl, 15.37; N, 12.14; S, 6.95. Found (%): C, 52.20; H, 3.21; Cl, 15.18; N, 12.40; S, 7.12.

5-Phenyl-[1,2,4]oxadiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIc. Following general procedure B was synthesized **VIIIc** from **VIa** (2.0 g, 0.0054 mole) and benzoyl chloride **VIIc** (0.84 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.73 g (30% yield), mp. 200-02 °C. Ir (KBr): 2983, 1735, 1710, 1604, 1475, 1213, 1176, 1099, 1008, 912, 754. ^1H nmr (DMSO-d_6) δ = 4.13 (center of AB quartet, 2H, SCH_2), 5.20 (center of AB quartet, 2H, NCH_2), 7.00-7.21 (m, 7H), 7.29 (t, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 2H), 7.71 (t, *J* = 7.8 Hz, 1H), 8.04 (d, *J* = 7.4 Hz, 1H). Microanalysis calculated for $C_{25}H_{18}N_4O_3S$ (%): C, 66.07; H, 3.99; N, 12.33; S, 7.05. Found (%): C, 65.85; H, 4.19; N, 12.09; S, 7.23.

5-(4-Chlorophenyl)-[1,2,4]oxadiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIId. Following general procedure B was synthesized **VIIId** from **VIa** (2.0 g, 0.0054 mole) and 4-chlorobenzoyl chloride **VIId** (1.05 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 1.3 g (50% yield), mp. 129-31 °C. Yield was 50% (1.3g). mp:- 131°C. Ir (KBr): 2987, 1730, 1715, 1604, 1562, 1470, 1340, 1210, 1008, 750 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 4.12 (center of AB quartet, 2H, SCH_2), 5.20 (center of AB quartet, 2H, NCH_2), 6.96-7.09 (m, 4H), 7.11-7.22 (m, 3H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 2H), 8.04 (d, *J* = 7.5 Hz, 2H). Microanalysis calculated for $C_{25}H_{17}ClN_4O_3S$ (%): C, 61.41; H, 3.50; Cl, 7.25; N, 11.46; S, 6.56. Found (%): C, 61.25; H, 3.66; Cl, 7.47; N, 11.63; S, 6.39.

5-(4-Nitrophenyl)-[1,2,4]oxadiazolyl methyl-3'-phenyl-spiro-[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIe. Following general procedure B was synthesized **VIIIe** from **VIa** (2.0 g, 0.0054 mole) and 4-nitrobenzoyl chloride **VIIe** (1.11 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 1.4 g (53% yield), mp. 177-79 °C. Ir (KBr): 2980, 1725, 1710, 1608, 1470, 1345, 1215, 1002, 933, 743 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 4.11 (center of AB quartet, 2H, SCH_2), 5.24 (center of AB quartet, 2H, NCH_2), 6.98-7.20 (m, 7H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.57 (d, *J* = 7.5 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 2H), 8.44 (d, *J* = 7.8 Hz, 2H). Microanalysis calculated for $C_{25}H_{17}N_5O_5S$ (%): C, 60.11; H, 3.43; N, 14.02; S, 6.42. Found (%): C, 59.93; H, 3.35; N, 14.20; S, 6.27.

5-Chloromethyl-[1,2,4]oxadiazolyl methyl-3'-(4-methoxy-phenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIf. Following general procedure B was synthesized **VIIIf** from **VIb** (2.15 g, 0.0054mole) and chloroacetylchloride **VIIa** (0.68 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.8 g (35% yield), mp 151-53 °C. Ir (KBr): 2975, 1720, 1715, 1610, 1465, 1340, 1223, 1002, 944, 750 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 3.66 (s, 3H, OCH_3), 4.08 (center of AB quartet, 2H, SCH_2), 5.07 (s, 2H), 5.13 (center of AB quartet, 2H, NCH_2), 6.78 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4Hz, 2H), 7.00 (d, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.58 (d, *J* = 7.5 Hz, 1H). Microanalysis calculated for $C_{21}H_{17}ClN_4O_4S$ (%): C, 55.20; H, 3.75; Cl, 7.76; N, 12.26; S, 7.02. Found (%): C, 55.03, H, 3.67; Cl, 7.52; N, 12.02; S, 6.87.

5-Dichloromethyl-[1,2,4]oxadiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIg. Following general procedure B was synthesized **VIIIg** from **VIb** (2.15 g, 0.0054mole) and dichloroacetylchloride **VIIb** (0.88 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 1.1 g (45% yield), mp 157-59 °C. Ir (KBr): 2989, 1730, 1695, 1608, 1508, 1031, 933, 752 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 3.65 (s, 3H, OCH_3), 4.08 (center of AB quartet, 2H, SCH_2), 5.20 (center of AB quartet, 2H, NCH_2), 6.78 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.5 Hz, 2H), 7.02 (d, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.93 (s, 1H). Microanalysis calculated for $C_{21}H_{16}Cl_2N_4O_4S$ (%): C, 51.33; H, 3.28; Cl, 14.43; N, 11.40; S, 6.53. Found (%): C, 51.21, H, 3.19; Cl, 14.64; N, 11.51; S, 6.40.

5-Phenyl-[1,2,4]oxadiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIh. Following general procedure B was synthesized **VIIIh** from **VIb** (2.15 g, 0.0054 mole) and benzoylchloride **VIIc** (0.84 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.96 g (40% yield), mp 176-78 °C. Ir (KBr): 2997, 1732, 1701, 1610, 1562, 1417, 1180, 1039, 933, 823 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 3.50 (s, 3H, OCH_3), 4.09 (center of AB quartet, 2H, SCH_2), 5.17 (center of AB quartet, 2H, NCH_2), 6.67 (d, *J* = 8.0 Hz, 2H), 6.94 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 7.4 Hz, 1H), 7.08 (t, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.58-7.65 (m, 3H), 7.72 (t, *J* = 7.2 Hz, 1H), 8.03 (d, *J* = 7.9 Hz, 2H). Microanalysis calculated for $C_{26}H_{20}N_4O_4S$ (%): C, 64.45; H, 4.16; N, 11.56; S, 6.62. Found (%): C, 64.62, H, 4.01; N, 11.29; S, 6.47.

5-(4-Chlorophenyl)-[1,2,4]oxadiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIi. Following general procedure B was synthesized **VIIIi** from **VIb** (2.15 g, 0.0054 mole) and 4-chlorobenzoylchloride **VIId** (1.05 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.77 g (30% yield), mp 206-08 °C. Ir (KBr): 2983, 1725, 1701, 1610, 1570, 1420, 1180, 1039, 940, 824 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 3.56 (s, 3H, OCH_3), 4.10 (center of AB quartet, 2H, SCH_2), 5.17 (center of AB quartet, 2H, NCH_2), 6.67 (d, *J* = 8.2 Hz, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 7.02 (d, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.1 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 2H), 8.03 (d, *J* = 7.9 Hz, 2H). Microanalysis calculated for $C_{26}H_{19}ClN_4O_4S$ (%): C, 60.17; H, 3.69; Cl, 6.83; N, 10.80; S, 6.18. Found (%): C, 60.32, H, 3.84; Cl, 6.67; N, 10.57; S, 6.35.

5-(4-Nitrophenyl)-[1,2,4]oxadiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione VIIIj. Following general procedure B was synthesized **VIIIj** from **VIb** (2.15 g, 0.0054 mole) and 4-nitrobenzoylchloride **VIIe** (1.11 g, 0.006 mole) in acetic acid. The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.92 g (35% yield),mp 178-80 °C. Ir (KBr): 2990, 1730, 1712, 1698, 1608, 1570, 1420, 1180, 1030, 936, 855 $cm.^{-1}$ ^1H nmr (DMSO-d_6) δ = 3.56 (s, 3H, OCH_3), 4.10 (center of AB quartet, 2H, SCH_2), 5.21 (center of AB quartet, 2H, NCH_2), 6.69 (d, *J* = 8.2 Hz, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 7.04 (d, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.1 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 8.28 (d, *J* = 8.2 Hz, 2H), 8.42 (d, *J* = 8.2 Hz, 2H). Microanalysis calculated for $C_{26}H_{19}N_5O_6S$ (%): C, 58.97; H, 3.62; N, 13.23; S, 6.06. Found (%): C, 60.13; H, 3.47; N, 13.03; S, 6.19.

3'-Phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)-dione-1-yl-acetic acid (Xa). A suspension of **IXa** (15.3 g, 0.04 mole) in a 50mL of 2% aqueous solution of sodium hydroxide, was heated with vigorous stirring on water-bath for 1 h. After cooling the reaction mixture at room temperature, it was slowly poured into ice cold 10% dilute HCl with vigorous stirring. The resulted solid was collected by filtration, washed with water and dried. Crude product on crystallization from methanol afforded colourless crystals of **Xa**, 11.3 g (80% yield) mp 125-27 °C. Ir (KBr): 2976, 1712, 1691, 1612, 1510, 1411, 1247, 1022, 831 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 4.09 (center of AB quartet, 2H, SCH_2), 4.48 (center of AB quartet, 2H, NCH_2), 6.9-7.06 (m, 4H), 7.12-7.30 (m, 4H), 7.45 (d, *J* = 7.8 Hz, 1H), 13.23 (s, 1H, OH). Microanalysis calculated for $C_{18}H_{14}N_2O_4S$ (%) C, 61.01; H, 3.98; N, 7.90; S, 9.05. Found: C, 60.87; H, 3.91; N, 7.66; S, 8.95.

3'-(4-Methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione-1-yl-acetic acid Xb. Similarly was synthesized **Xb** from **IXb** (16.0 g, 0.04 moles) using 2% aqueous sodium hydroxide solution. The product on crystallization from methanol afforded **Xb**, 12 g (78% yield); mp 223-25 °C. Ir (KBr) 2985, 17202, 1695, 1604, 1510, 1411, 1250, 1022, 825 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 3.72 (s, 3H, OCH_3), 4.11 (center of AB quartet, 2H, SCH_2), 4.46 (center of AB quartet, 2H, NCH_2), 6.84 (d, *J* = 8.2 Hz, 2H), 6.93-7.00 (m, 3H), 7.09 (t, *J* = 6.5 Hz, 1H), 7.30 (t, *J* = 6.4 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 13.25 (s, 1H, OH). Microanalysis calculated for $C_{19}H_{16}N_2O_5S$ (%) C, 59.37; H, 4.20; N, 7.29; S, 8.34. Found (%): C, 59.51; H, 4.11; N, 7.35; S, 8.18.

Procedure C: General procedure for the synthesis of (un)substituted 3-phenyl-1,2,4-oxadiazolyl methyl-3'-aryl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)diones XIIa-g.

3-Phenyl-1,2,4-oxadiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione XIIa. Xa (1.5 g, 0.0042 mole) and 3mL thionyl chloride were refluxed together for 1 h. Excess of thionyl chloride was distilled off completely under reduced pressure and reaction mixture was cooled at room temperature. The resulting acid chloride was diluted with 3 mL glacial acetic acid and preformed *N*-hydroxybenzene-carboximidamide **XIa** (0.63 g, 0.0046 moles) was added to same flask. The reaction mixture was heated on oil-bath at 160°C for 30 min. On completion, the reaction mixture was cooled to room temperature, poured into ice-water and extracted with ethyl acetate (2 X 25 mL). Organic phase was thoroughly washed with 2% aqueous NaOH, and with water, followed by drying over anhydrous Na_2SO_4. After evaporation of the organic phase, the resulting crude product was further purified by column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.63 g (33% yield), mp 170-72 °C. Ir (KBr) 2927, 1739, 1691, 1612, 1587, 1514, 1209, 1170, 1014, 941, 893, 765 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 4.13 (center of AB quartet, 2H, SCH_2), 5.44 (center of AB quartet, 2H, NCH_2), 7.00-7.15 (m, 4H), 7.18-7.25 (m, 3H), 7.31 (t, *J* = 7.2 Hz, 1H),

7.52-7.63 (m, 4H), 7.91 (d, *J* = 8.2 Hz, 2H), ms: m/z 455(M^{+1}). Microanalysis calculated for $C_{25}H_{18}N_4O_3S$ (%) C, 66.07; H, 3.99; N, 12.33; S, 7.05. Found (%): C, 66.29; H, 4.12; N, 12.17; S, 7.28.

3-(3-Methylphenyl)-1,2,4-oxadiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione XIIb. Following general procedure C was synthesized **XIIb** from **Xa** (1.5 g, 0.0042 mole) and N-hydroxy-3-methylbenzenecarboximidamide **XIb** (0.69 g, 0.0046 moles). The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.7 g (36% yield), mp 102-04 °C. Ir (KBr): 2934, 1730, 1692, 1605, 1590, 1515, 1470, 1257, 1355, 1023, 935, 810, 760 cm^{-1}. ^1H nmr ($CDCl_3$) δ = 2.54 (s, 3H, CH_3), 3.88 (AX splitting, 1H, SCH_2), 4.40 (AX splitting, 1H, SCH_2), 5.03 (AX splitting, 1H, NCH_2), 5.28 (AX splitting, 1H, NCH_2), 6.74 (d, *J* = 7.8 Hz, 1H), 7.00-7.30 (m, 9H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.86 (d, *J* = 7.5 Hz, 1H). Microanalysis calculated for $C_{26}H_{20}N_4O_3S$ (%) C, 66.65; H, 4.30; N, 11.96; S, 6.84. Found (%): C, 66.43; H, 4.57; N, 12.13; S, 6.61.

3-(4-Chlorophenyl)-1,2,4-oxadiazolyl methyl-3'-phenyl-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione XIIc. Following general procedure C was synthesized **XIIc** from **Xa** (1.5 g, 0.0042 mole) and N-hydroxy-4-chlorobenzenecarboximidamide **XIc** (0.78 g, 0.0046 moles). The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.63 g (31% yield), mp 194-96 °C. Ir (KBr): 2930, 1721, 1700, 1611, 1592, 1504, 1475, 1360, 1255, 1033, 950, 895, 756 cm^{-1}. ^1H nmr ($CDCl_3$) δ = 3.89 (AX splitting, 1H, SCH_2), 4.40 (AX splitting, 1H, SCH_2), 5.01 (AX splitting, 1H, NCH_2), 5.26 (AX splitting, 1H, NCH_2), 6.71 (d, *J* = 7.8 Hz, 1H), 7.02-7.29 (m, 7H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 2H). Microanalysis calculated for $C_{25}H_{17}ClN_4O_3S$ (%) C, 61.41; H, 3.50; Cl, 7.25; N, 11.46; S, 6.56. Found (%): C, 61.59; H, 3.24; Cl, 7.48; N, 11.31; S, 6.76.

3-Phenyl-1,2,4-oxadiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione XIId. Following general procedure C was synthesized **XIId** from **Xb** (1.6 g, 0.0042 mole) and *N*-hydroxybenzenecarboximidamide **XIa** (0.63 g, 0.0046 moles). The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.71 g (38% yield), mp 160-62 °C. Ir (KBr): 2932, 1730, 1695, 1610, 1510, 1245, 1004, 910, 843 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 3.61 (s, 3H, OCH_3), 4.12 (center of AB quartet, 2H, SCH_2), 5.43(center of AB quartet, 2H, NCH_2), 6.75 (d, *J* = 9.0 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.52-7.65 (m, 3H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 2H). Microanalysis calculated for $C_{26}H_{20}N_4O_4S$ (%) C, 64.45; H, 4.16; N, 11.56; S, 6.62. Found (%): C, 64.21; H, 3.98; N, 11.73; S, 6.49.

3-(3-Methylphenyl)-1,2,4-oxadiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione XIIe. Following general procedure C was synthesized **XIIe** from **Xb** (1.6 g, 0.0042 mole) and N-hydroxy-3-methylbenzenecarboximidamide **XIb** (0.69 g, 0.0046 moles). The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.64 g (33% yield), mp 163-65 °C. Ir (KBr): 2930, 1721, 1697, 1612, 1513, 1350, 1249, 1170, 1011, 901, 841, 760 cm^{-1} .^1H nmr (DMSO-d_6) δ = 2.45 (s, 3H, CH_3), 3.58 (s, 3H, OCH_3), 4.11 (center of AB quartet, 2H, SCH_2), 5.43 (center of AB quartet, 2H, NCH_2), 6.69 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 7.02-7.18 (m, 2H), 7.26-7.42 (m, 3H), 7.46 (t, *J* = 7.0 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H). Microanalysis calculated for $C_{27}H_{22}N_4O_4S$ (%) C, 65.05; H, 4.45; N, 11.24; S, 6.43. Found (%): C, 65.19; H, 4.30; N, 11.07; S, 6.29.

3-(4-Chlorophenyl)-1,2,4-oxadiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione XIIf. Following general procedure C was synthesized **XIIf** from **Xb** (1.6 g, 0.0042mole) and N-hydroxy-4-chlorobenzenecarboximidamide **XIc** (0.78 g, 0.0046 moles). The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.82 g (41% yield), mp 183-85 °C. Ir (KBr): 2927, 1728, 1697, 1610, 1514, 1469, 1353, 1257, 1176, 1014, 900, 833, 766 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 3.58 (s, 3H, OCH_3), 4.09 (center of AB quartet, 2H, SCH_2), 5.40 (center of AB quartet, 2H, NCH_2), 7.06 (d, *J* = 7.9 Hz, 1H), 7.13 (t, *J* = 7.1 Hz, 1H), 7.32 (t, *J* = 7.1 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.90 (d, *J* = 8.8 Hz, 2H). Microanalysis calculated for $C_{26}H_{19}ClN_4O_4S$ (%) C, 60.17; H, 3.69; Cl, 6.83; N, 10.80; S, 6.18. Found (%): C, 60.33; H, 3.88; Cl, 6.59; N, 11.01; S, 6.02.

3-(4-Biphenyl)-1,2,4-oxadiazolyl methyl-3'-(4-methoxyphenyl)-spiro[3*H*-indole-3,2'-thiazolidine]-2,4'(1*H*)dione XIIg. Following general procedure C was synthesized **XIIg** from **Xb** (1.6 g, 0.0042 mole) and *N*-hydroxy-4-biphenylcarboximidamide **XId** (0.975 g, 0.0046 moles). The crude product was purified using column chromatography [Stationary phase Silica gel (120-200 mesh), Mobile phase hexane:ethyl acetate (70:30)]. The pure product was obtained as colourless solid, 0.82 g (41% yield), mp 183-85 °C. Ir (KBr): 2927, 1728, 1697, 1610, 1514, 1469, 1353, 1257, 1176, 1014, 900, 833, 766 cm^{-1}. ^1H nmr (DMSO-d_6) δ = 3.58 (s, 3H, OCH_3), 4.10 (center of AB quartet, 2H, SCH_2), 5.43 (center of AB quartet, 2H, NCH_2), 6.74 (d, *J* = 8.6 Hz, 2H), 6.94 (d, *J* = 8.6 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 1H), 7.13 (t, *J* = 7.1 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 7.9 Hz, 2H), 7.85 (d, *J* = 7.3 Hz, 2H), 7.98 (d, *J* = 7.8 Hz, 2H). Microanalysis calculated for $C_{32}H_{24}N_4O_4S$ (%) C, 68.56; H, 4.31; N, 9.99; S, 5.72. Found (%): C, 68.33; H, 4.10; N, 9.76; S, 5.50.

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