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## Synthesis of N-(4-oxo-4,5-dihydro-2-substituted phenyl-3H-thiazolidine-3-yl)-2-(3'-substituted phenyl spiro [3H-indole-3,2'-thiazolidine]-2,4'(1H)-dione-1-yl)-acetamide

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### ABSTRACT

Starting material 2-(3'-substituted phenyl spiro [3H-indole-3,2'-thiazolidine-1-yl)acetohydrazide have been synthesized according to reported literature which react with different aromatic aldehyde to give N'-substituted benzylidene-2(3'-substituted phenyl-spiro[3H-indole-3,2'-thiazolidine]-2,4'(1H)-dione-1-yl)acetohydrazide (**6a-i**). These finally undergo cyclization with thioglycolic acid to give desired compound (**7a-i**).

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### KEYWORDS

Spiro-indole;  
Thiazolidine.

### INTRODUCTION

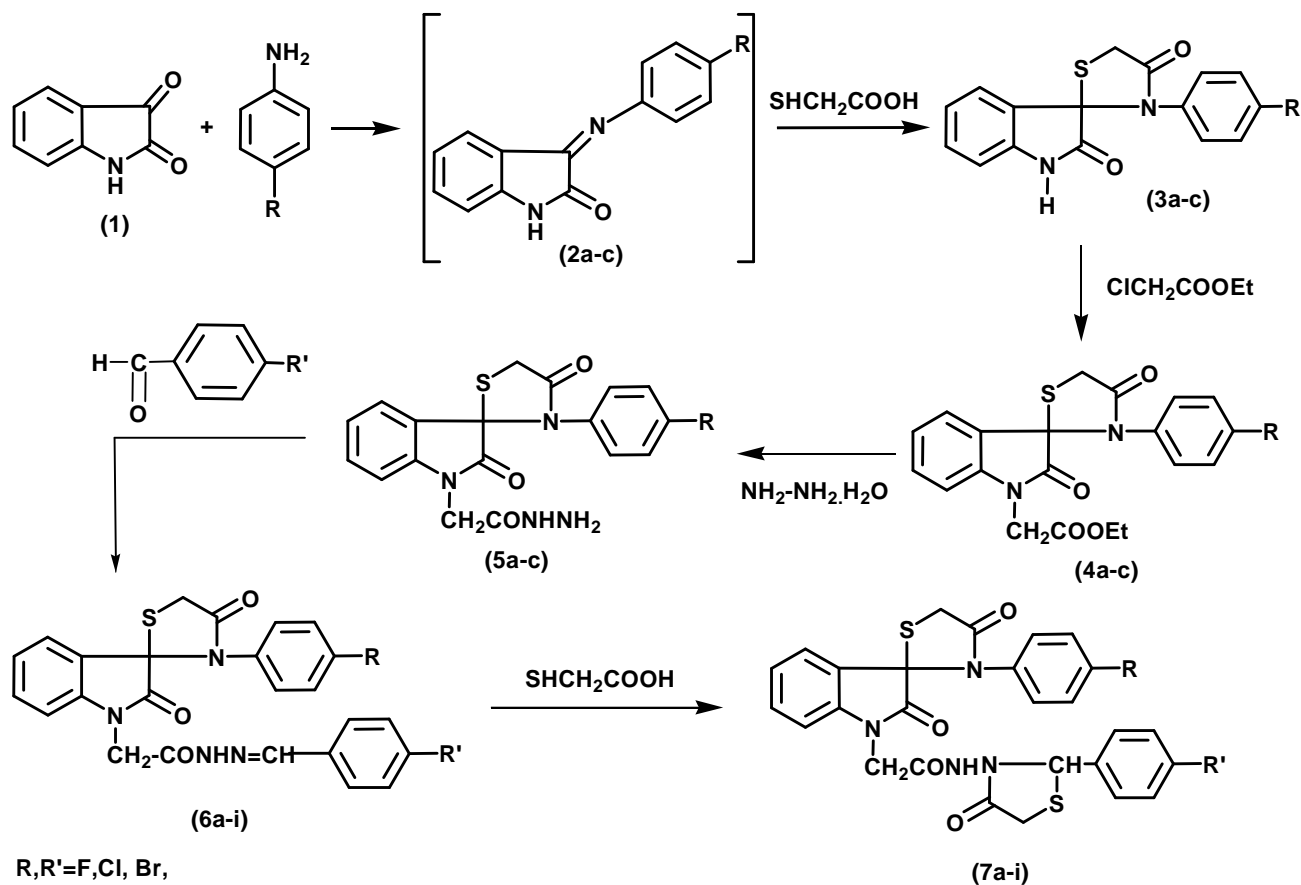
Spiro-indole derivatives are associated with many biological activities<sup>[1,2]</sup> and also used as a dye developer in photographic diffusion transfer system<sup>[3]</sup> and as photochemic agents<sup>[4]</sup>. Thiazolidinones, belongs to an important group of heterocyclic compound have been extensively explored for their application in the field of medicine. They have possessed cardiovascular<sup>[5]</sup>, anti-viral<sup>[6]</sup>, antitumor<sup>[7]</sup> etc. activities. These encourage synthesizing some novel spiro-indole derivatives (**7a-i**). The title compounds and its analogs were prepared by method outlined in the Scheme 1 and summarized in TABLE 1. Following the literature procedure<sup>[8]</sup> 2-(3'-substituted phenyl-spiro[3H-indole-3,2'-thiazolidine]-2,4'(1H)-dione-1-yl) acetohydrazide (**5a-c**) was prepared which under goes schiff's base reaction with different aromatic aldehyde gave N'-substituted benzylidene-2-(3'-substituted phenyl-spiro[3H-indole-

3,2'-thiazolidine]-2,4'(1H)-dione-1-yl)acetahydrazides (**6a-i**). These further undergo cyclization with thioglycolic acid yielded desired products (**7a-i**). The structure of the products (**7a-i**) was confirmed on the basis of their spectral (<sup>1</sup>H NMR & IR) data and purity was established on the basis of TLC.

### EXPERIMENTAL

Melting points were determined on Buchi B-545 melting point apparatus and are uncorrected. IR spectrum was recorded in KBr on a Perkin Elmer spectrometer, <sup>1</sup>H NMR was recorded in DMSO-d<sub>6</sub> using 300MHz brucker spectrometer (Chemical shift in δ ppm).with TMS as internal standard. The TLC was performed on precoated Silica-gel sheets obtained from Merck & Co., Germany, which were visualizing using UV light. The analytical Research Department of Ipca Labs. Ltd. (Kandivali, Mumbai) carried out all analytical work.

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Scheme 1

TABLE 1 : Characterization data of compound (5a-c), (6a-i) &amp; (7a-i)

Compound	R	R <sup>1</sup>	Molecular Formula	M.P. °C	Yield %	Compound	R	R <sup>1</sup>	Molecular Formula	M.P. °C	Yield %
5a	F	--	C <sub>18</sub> H <sub>15</sub> FN <sub>4</sub> O <sub>3</sub> S	260°C	91%	6h	Br	Cl	C <sub>25</sub> H <sub>18</sub> BrClN <sub>4</sub> O <sub>3</sub> S <sub>2</sub>	208°C	76%
5b	Cl	--	C <sub>18</sub> H <sub>15</sub> ClN <sub>4</sub> O <sub>3</sub> S	192°C	90%	6i	Br	Br	C <sub>25</sub> H <sub>18</sub> Br <sub>2</sub> N <sub>4</sub> O <sub>3</sub> S <sub>2</sub>	221°C	78%
5c	Br	--	C <sub>18</sub> H <sub>15</sub> BrN <sub>4</sub> O <sub>3</sub> S	181°C	89%	7a	F	F	C <sub>27</sub> H <sub>20</sub> F <sub>2</sub> N <sub>4</sub> O <sub>4</sub> S <sub>2</sub>	251°C	71%
6a	F	F	C <sub>25</sub> H <sub>18</sub> F <sub>2</sub> N <sub>4</sub> O <sub>3</sub> S	280°C	74%	7b	F	Cl	C <sub>27</sub> H <sub>20</sub> ClFN <sub>4</sub> O <sub>4</sub> S <sub>2</sub>	223°C	70%
6b	F	Cl	C <sub>25</sub> H <sub>18</sub> ClFN <sub>4</sub> O <sub>3</sub> S <sub>2</sub>	225°C	79%	7c	F	Br	C <sub>27</sub> H <sub>20</sub> BrFN <sub>4</sub> O <sub>4</sub> S <sub>2</sub>	243°C	69%
6c	F	Br	C <sub>25</sub> H <sub>18</sub> BrFN <sub>4</sub> O <sub>3</sub> S <sub>2</sub>	244°C	77%	7d	Cl	F	C <sub>27</sub> H <sub>20</sub> ClFO <sub>4</sub> N <sub>4</sub> S <sub>2</sub>	208°C	67%
6d	Cl	F	C <sub>25</sub> H <sub>18</sub> ClFN <sub>4</sub> O <sub>3</sub> S <sub>2</sub>	256°C	78%	7e	Cl	Cl	C <sub>27</sub> H <sub>20</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>4</sub> S <sub>2</sub>	235°C	65%
6e	Cl	Cl	C <sub>25</sub> H <sub>18</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>3</sub> S <sub>2</sub>	205°C	81%	7f	Cl	Br	C <sub>27</sub> H <sub>20</sub> BrClN <sub>4</sub> O <sub>4</sub> S <sub>2</sub>	260°C	68%
6f	Cl	Br	C <sub>25</sub> H <sub>18</sub> BrClN <sub>4</sub> O <sub>3</sub> S <sub>2</sub>	254°C	82%	7g	Br	F	C <sub>27</sub> H <sub>20</sub> BrFN <sub>4</sub> O <sub>4</sub> S <sub>2</sub>	217°C	73%
6g	Br	F	C <sub>25</sub> H <sub>18</sub> BrFN <sub>4</sub> O <sub>3</sub> S <sub>2</sub>	261°C	75%	7h	Br	Cl	C <sub>27</sub> H <sub>20</sub> BrClN <sub>4</sub> O <sub>4</sub> S <sub>2</sub>	209°C	70%

2-(3'-(4-bromophenyl)-spiro[3H-indole-3,2'-thiazolidine]-2,4'-(1H)-dione-1-yl)-acetohydrazide (5c) was prepared as per the reported literature<sup>[8]</sup>.

**N'-(4-Chlorobenzylidene)-2-(3'-(4-bromophenyl)spiro[3H-indole-3,2'-thiazolidine]-2,4-(1H)-dione-1-yl) acetohydrazide (6h)**

A mixture of 2-[3'-(4-bromophenyl)-spiro[3H-in-

dole-3,2'-thiazolidine]-2,4'-(1H)-dione-1-yl)-acetohydrazide (3.0gm, 0.0067 mole), 4-chlorobenzaldehyde (0.94gm, 0.0067 mole), and few drops of gl. acetic acid in ethanol (30ml) was refluxed for 8 hrs. Reaction was monitoring by TLC (Solvent system = Methanol: toluene; 30% : 70%). After completion, reaction mixture was cooled at room temperature and poured into cold water. The light yellow solid precipi-

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tated was isolated by filtration & dried. Further purification of product by crystallization from mixture of solvents chloroform/ methanol afford (**6a-i**) pure form in 77 yield, M.P.208°C

IR (cm<sup>-1</sup>): 3300 (N-H), 3054 (C-H, Ar-H), 2972, 2930 (C-H, Alkyl), 1581, 1471 (C=C, aromatic). <sup>1</sup>H NMR: δ 4.00–4.18 (dd, 2H-SCH<sub>2</sub>), 4.85-4.92 (dd, 2H, -NCH<sub>2</sub>), 7.00-8.11 (m-12H, Ar-H), 11.75 (S, 1H—NH)

Similar procedure was followed to synthesized other derivatives (**6a-i**).

### **N-(4-oxo-4,5-dihydro-2-(4-chlorophenyl)-3H-thiazolidine-3-yl)-2-(3'-(4-bromophenyl)-spiro[3H-indole-3,2'-thiazolidine]-2,4'-(1H)-dione-1-yl)-acetamide (7h)**

A mixture of N<sup>2</sup>-4-chlorobenzylidene-2-(3'-(4-bromophenyl)-spiro[3H-indole-3,2'-thiazolidine]-2,4'-(1H)-dione-1-yl) acetohydrazide (2.0gm 0.0037mole) and thioglycolic acid (0.51gm 0.0055mole) in dry toluene (30ml) was reflux for 12 hrs. Collect the water azeotropically with dean-stark assembly. Monitoring the reaction by TLC (Solvent system= Methanol: Toluene; 30%: 70%). After completion, distilled out half of toluene. Keep the reaction mass in deep-freeze for 8 hrs. Filter the pure crystallize product and wash with cold toluene gave (7h) in 70% yield, M.P.209°C

IR (cm<sup>-1</sup>): 3274 (N-H), 3054 (C-H, Ar-H), 2978, 2940 (C-H), 1725, 1695 (C=O). <sup>1</sup>H NMR : δ 3.99-

4.15 (dd, 2H,-SCH<sub>2</sub>), 4.41-4.45 (dd, 2H, -SCH<sub>2</sub>), 4.87-4.89 (dd, 2H, -NCH<sub>2</sub>), 7.01-8.16 (m, 12H, Ar-H), 11.83 (S,-1H,NH)

Similar procedure was followed to synthesized other derivatives (**7a-i**).

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