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Short Communication

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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'-substitutedphenyl-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)**.

KEYWORDS

Spiro-indole;
Thiazolidine.

INTRODUCTION

Spiro-indole derivatives are associated with many biological activites[1,2] and also used as a dye developer in photographic diffusion transfer system[3] and as photochemic agents[4]. 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[5], antiviral[6], antitumar[7] etc. activities. These encourage synthesizing some novel spiro-indole derivatives **(7a-i)**. The title compounds and It's analogs were prepared by method outlined in the Scheme 1 and summarized in TABLE 1. Following the literature procedure[8] 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 (^{1}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, ^{1}H NMR was recorded in DMSO-d6 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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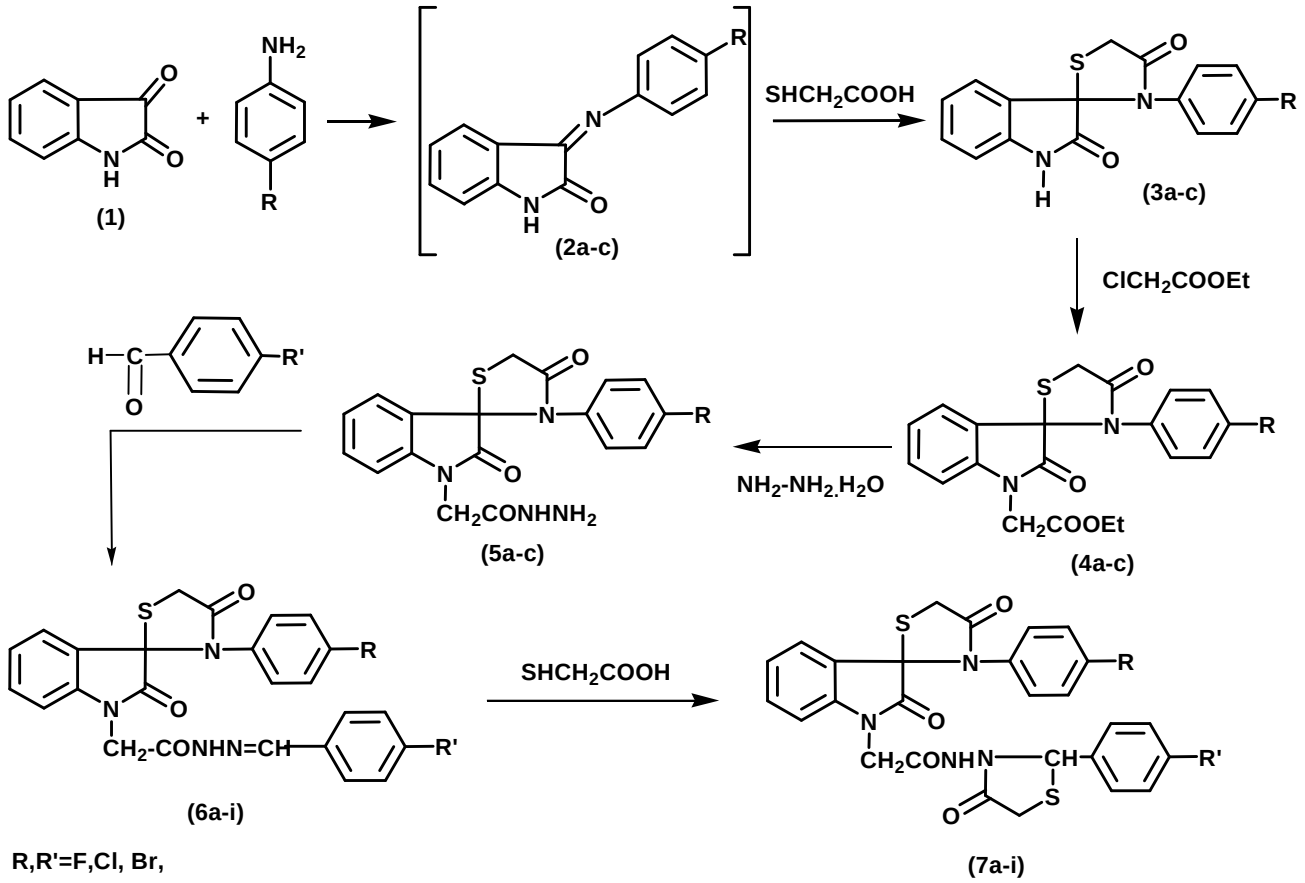

Scheme 1

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

Compound	R	R^1	Molecular Formula	M.P. °C	Yield %	Compound	R	R^1	Molecular Formula	M.P. °C	Yield %
5a	F	--	$C_{18}H_{15}FN_4O_3S$	260°C	91%	6h	Br	Cl	$C_{25}H_{18}BrClN_4O_3S_2$	208°C	76%
5b	Cl	--	$C_{18}H_{15}ClN_4O_3S$	192°C	90%	6i	Br	Br	$C_{25}H_{18}Br_2N_4O_3S_2$	221°C	78%
5c	Br	--	$C_{18}H_{15}ClN_4O_3S$	181°C	89%	7a	F	F	$C_{27}H_{20}F_2N_4O_4S_2$	251°C	71%
6a	F	F	$C_{25}H_{18}F_2N_4O_3S$	280°C	74%	7b	F	Cl	$C_{27}H_{20}ClFN_4O_4S_2$	223°C	70%
6b	F	Cl	$C_{25}H_{18}ClFN_4O_3S_2$	225°C	79%	7c	F	Br	$C_{27}H_{20}BrFN_4O_4S_2$	243°C	69%
6c	F	Br	$C_{25}H_{18}BrFN_4O_3S_2$	244°C	77%	7d	Cl	F	$C_{27}H_{20}ClFO_4N_4S_2$	208°C	67%
6d	Cl	F	$C_{25}H_{18}ClFN_4O_3S_2$	256°C	78%	7e	Cl	Cl	$C_{27}H_{20}Cl_2N_4O_4S_2$	235°C	65%
6e	Cl	Cl	$C_{25}H_{18}Cl_2N_4O_3S_2$	205°C	81%	7f	Cl	Br	$C_{27}H_{20}BrClN_4O_4S_2$	260°C	68%
6f	Cl	Br	$C_{25}H_{18}BrClN_4O_3S_2$	254°C	82%	7g	Br	F	$C_{27}H_{20}BrFN_4O_4S_2$	217°C	73%
6g	Br	F	$C_{25}H_{18}BrFN_4O_3S_2$	261°C	75%	7h	Br	Cl	$C_{27}H_{20}BrClN_4O_4S_2$	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[8].

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-indole-3,2'-thiazolidine]-2,4'(1H)-dione-1-yl)-acetohydrazide(3.0gm, 0.0067mole), 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 mixtured was cooled at room temperature and poured into cold water. The light yellow solid precipi-

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^{-1}): 3300 (N-H), 3054 (C-H, Ar-H), 2972, 2930 (C-H, Alkyl), 1581, 1471 (C=C, aromatic). ^1H NMR: δ 4.00 –4.18 (dd, 2H-SCH_2), 4.85-4.92 (dd,2H, -NCH_2), 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'-4-chlorobenzyldine-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-freez for 8 hrs. Filter the pure crystallize product and wash with cold toluene gave (7h) in 70% yield, M.P.209°C

IR (cm^{-1}): 3274 (N-H), 3054 (C-H, Ar-H), 2978, 2940 (C-H), 1725, 1695 (C=O). ^1H NMR : δ 3.99-4.15 (dd, 2H,-SCH_2), 4.41-4.45 (dd, 2H, -SCH_2), 4.87-4.89 (dd, 2H, -NCH_2), 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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