Synthesis Of Some Sulfur-Containing Spiroindole Derivatives

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INTRODUCTION

4-Thiazolidinone derivatives are an important class of bioactive compounds and are reported to be potent as pesticides,[1] anti-convulstants[2] and memory enhancers.[3] This class of compounds also exhibit antitubercular,[4] fungicidal[5,6] antibacterial[7] and anti-viral[*] activities. The pyrazolothiazole derivatives are used as antigungal agents.[8] Although the indole nucleus is recognised as an important bioactive centre,[9,10] yet spiroindole derivatives incorporating both thiazole and pyrazole moieties have not been synthesised. In continuation to our earlier work on the synthesis of spiroindole derivatives of thiazolidinones[11] and pyrazolones.[12]

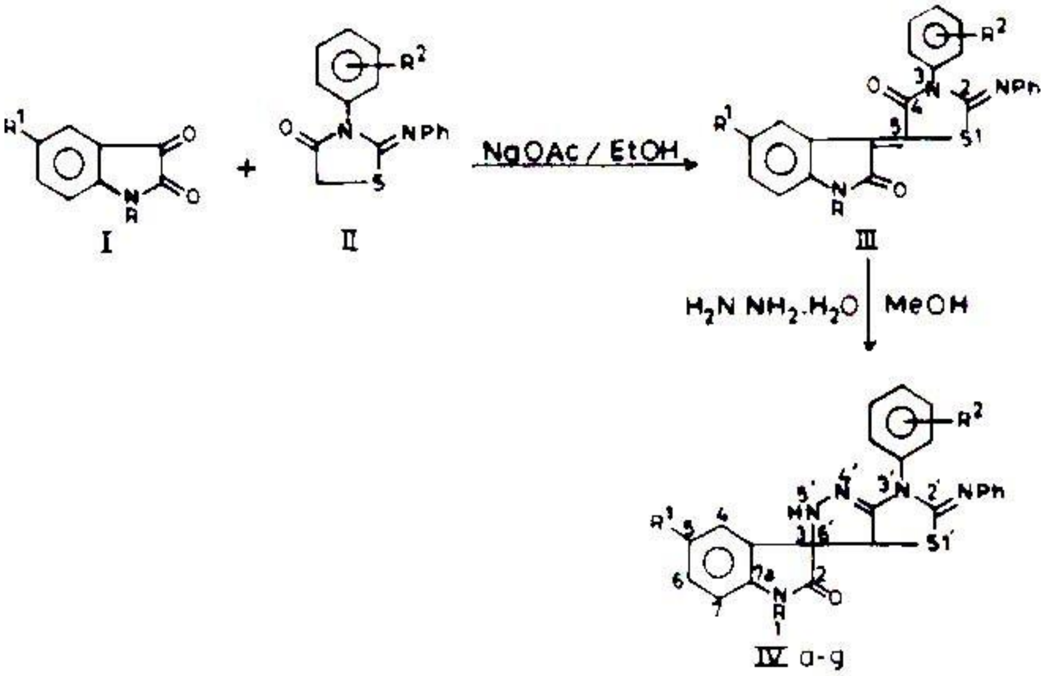
DISCUSSION

3' - Aryl-2' - phenylimino-spiro [3H-indole-3, 6' [4'5 - pyrazolin] [4,3-d] thiazolo]- 2 (1H)-ones (IV_{a-g}) were prepared by the reaction of hydrazine hydrate with equimolar amounts of 5(2-oxo-3-indolinyl-idene)-3-aryl-2- phenylimono-4- thiazolidinones (III) (Scheme 1). The latter compounds (III) were prepared by the reaction of dihydro-indole-2, 3-diones (I) with 4-thiazolidinones (II). The structures of the synthesized compounds (**IV_{a-g}**) were further established by IR, PMR, ^{13}C NMR and mass spectral studies. Elemental and physical data are given in Table I.

IR Spectra

The IR spectra of compounds **IV_{a-g}** show only one strong band in the region 1680 cm^{-1}, which can be attributed to the cyclic imido v C=O vibration.

A. doublet corresponding to the v C=N vibration is observed in the region 1510cm^{-1}. The N-H band is observed in the region 3340 cm^{-1}.



Scheme 1

^{1}H *and* ^{19}F NMR *Spectra*

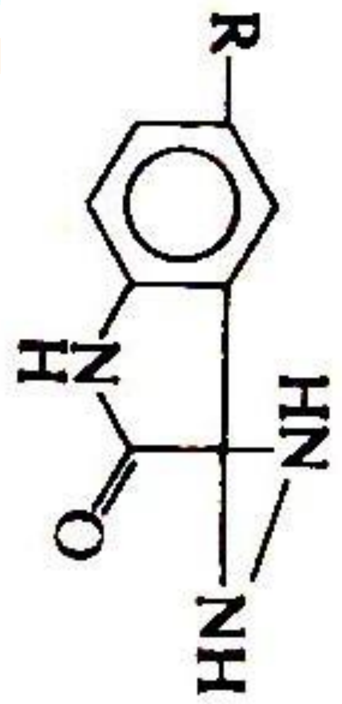
In the PMR spectra of the spiroindole derivatives (**IVa-g**), the signal of the indole ring was observed as a broad band in the region at δ 10.15 - 8.84ppm and as earlier reported, 13 the N-H signal of the pyrazoline ring was not observed. The aromatic proton signals were observed in the region at δ7.93-6.72 ppm and in the compounds **IVf** and **IVg** a characteristics doublet[14] of 4-H aromatic proton at δ 8.43 and 8.09 ppm could be distinguished. The –C–H proton signal was clearly observed in the region 5.69 - 4.10ppm. In compounds **IVd** & **IVE**, the ^{19}F signal for the $-CF_3$ group was observed at δ -62.49 & -56.48 ppm and in compound **IVc**, and **IVg**, the C–F signal was observed at δ-114.75 and – 123.36 ppm.

^{13}C NMR Spectra

The ^{13}C NMR spectra of **IVa** and its precursor (**IIIa**) have been recorded. In **IIIa**, two characteristics signals are observed at δ 184.32 and 169.46 ppm which are attributed to the carbonyl groups of the thiazolidinone ring and cyclic imide group respectively. Compound IVa displayed only one signal at δ170.90 ppm corresponding to the imido carbonyl group, and the signal due to the carbonyl group of the thiazolidinone ring disappeared. The methine carbon was clearly observed at δ 110.70ppm and the signals of other carbon atoms were observed in the expected region.

Mass Spectra

The mass spectra of the compounds **IVa** & **IVg** show modes of framentation. The [M$^+$] peaks were not observed in the mass spectra of these compounds and their precursors. According to literature information,[13] this is not unusual with spirocyclic compounds. The spectraum shows peaks corresponding to M$^+$ – PhN≡C ion. The ion at *m/z*, 161 and 179 corresponding to the



cations forms of the base peak in the spectrum.

TABLE I

Physical and analytical data of the compounds IVa–g

S.No.	Compound			% Yield	M.p. (°C)	M.F.	Anals. % Found (Cal.)		
	R	*R*^{1}	*R*^{2}				*C*	*H*	*S*
IVa	H	H	H	45	223	$C_{23}H_{17}ON_5S$	67.48 (67.15)	4.21 (4.13)	7.35 (7.78)
IVb	$COCH_3$	H	H	62	228	$C_{25}H_{19}O_2N_5S$	66.35 (66.22)	4.26 (4.19)	7.01 (7.06)
IVc	H	5-F	H	50	237	$C_{23}H_{16}ON_5FS$	64.55 (64.33)	3.90 (3.72)	7.24 (7.43)
IVd	H	H	4-CF_3	60	235	$C_{24}H_{16}ON_5F_3S$	60.04 (60.12)	3.39 (3.34)	6.75 (6.68)
IVe	$COCH_3$	H	4-CF_3	50	183	$C_{26}H_{18}O_2N_5F_3S$	59.72 (59.88)	3.40 (3.45)	6.25 (6.14)
IVf	H	H	0-Cl	51	218	$C_{23}H_{16}ON_5ClS$	61.73 (61.88)	3.52 (3.58)	7.26 (7.17)
IVg	H	5-F	0-Cl	60	267	$C_{23}H_{15}ON_5FClS$	59.62 (59.48)	3.28 (3.23)	6.79 (6.89)

EXPERIMENTAL

Melting points, determined on a Toshniwal melting points apparatus, (capillary method) are uncorrected. The purity of the synthesized compounds was tested by thin layer chromatography on silica gel in various nonaqueous solvents. IR spectra were recorded in KBr on a Perkin-Elmer 577 grating spectrophotometer (*v* max in cm^{-1}), PMR spectra in $CDCl_3$ and DMSO-d_6 onJeol FX 90 Q (89.55 MHz) using TMS as internal standard (^{19}F and ^{13}C NMR on the same instrument), and mass spectra were recorded on Kratz 30 and 50 mass spectrometer at 70 eV.

(i) 5-(2-Oxo-3-indolinylidene)-3-aryl-2-phenylimino-4-thiazolidinones (III). These compounds were synthesized by a reported method[14] with some modification. 3-Aryl-2-phenylimino-4-thiazolidinone (II, 0.016 mole), dihydroindole -2, 3-diones (1, 0.015 mole), finely-grounded fused anhydrous sodium acetate (0.04 mole) and absolute ethanol (50ml) were heated under reflux for 4-5 hr.; a dark precipitate appeared during the progress of the reaction. At the end, the reaction mixture was poured into crushed ice and the brownish-red precipitate, which separated was filtered, washed with water and ethanol and dried, to give the little compounds. Yields, 60-70%; m.p.>300º.

(ii) Synthesis of 3'-aryl-2'-phenylimino-spiro[3H-indole-3, 6'-[4',5'- pyrazolin] [4,3-d] thiazolo] -2(1H)-ones (**IVa-g**) 5-(2-Oxo-e- indolinylidene)-3-aryl-2-phenylimino-4-thiazolidinone (III, 0.01 mole) and hydrazine hydrate (0.012 mole) were heated under reflux in methanol (25ml) for 5-6 hrs. On cooling, crystals of the title compounds
(IV) separated which were filtered and recrystallized from a mixture of methanol and chloroform.

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