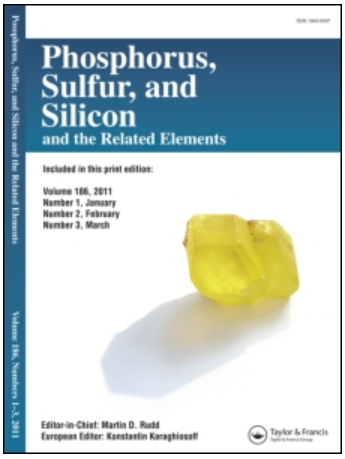

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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To cite this Article Jain, Renuka and Vajpei, Shipra(1992) 'REACTION OF SCHIFF'S BASES WITH MERCAPTO ACIDS. SYNTHESIS OF SPIRO [2H-1,3-BENZOTHIAZINE-2,3'-[3H]INDOLE]-2',4(1'H,3H)-DIONES AND SPIRO[3H-INDOLE-3,2'-THIAZOLIDINE]-2,4'(1H)-DIONES', Phosphorus, Sulfur, and Silicon and the Related Elements, 70: 1, 63 — 66
To link to this Article: DOI: 10.1080/10426509208049152
URL: http://dx.doi.org/10.1080/10426509208049152

Phosphorus, Sulfur, and Silicon, 1992, Vol. 70, pp. 63–66
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REACTION OF SCHIFF'S BASES WITH MERCAPTO ACIDS. SYNTHESIS OF SPIRO [2H-1,3-BENZOTHIAZINE-2,3'-[3H]INDOLE]-2',4(1'H,3H)-DIONES AND SPIRO[3H-INDOLE-3,2'-THIAZOLIDINE]-2,4'(1H)-DIONES

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(Received December 26, 1991; in final form March 30, 1992)

The synthesis of some new sulfur containing spiroindole derivatives is reported. Spiro[2H-1,3-benzothiazine-2,3'-[3H]indole]-2',4(1'H,3H)-diones and spiro[3H-indole-3,2'-thiazolidine]-2,4'(1H)-diones were prepared by the reaction of 3-[2-(4-arylthiazolylimino)]-1,3-dihydro-2H-indol-2-one with o-mercaptobenzoic acid and mercaptoacetic acid respectively. Such spiro benzothiazineindoles are being reported for the first time. The compounds have been characterised on the basis of elemental and spectral studies.

Key words: Spiroindole derivatives; mercapto acids; NMR; IR.

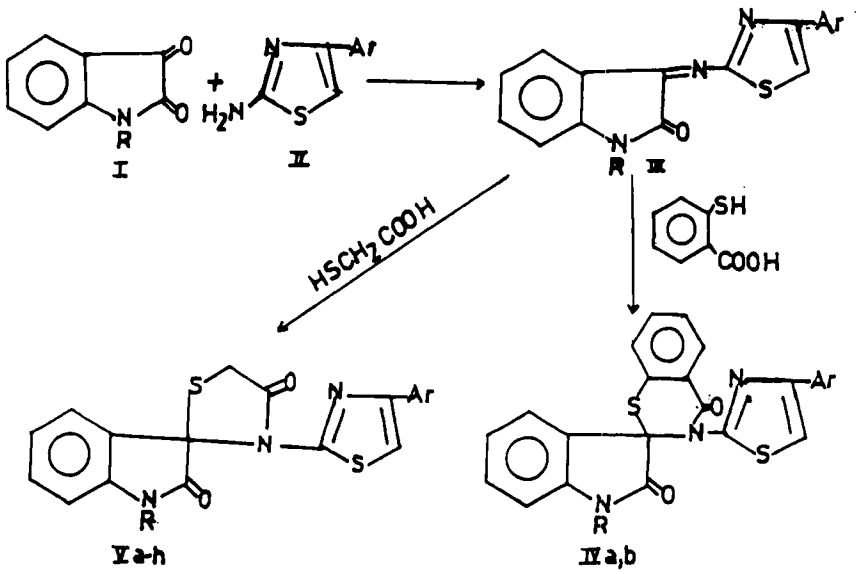
INTRODUCTION

Heterocyclic compounds possessing a spiro carbon atom find useful applications in medicinal chemistry.[1-3] The bioactivity of benzothiazines,[4-6] thiazoles[7-9] and indoles[10-12] is well established. In continuation with our earlier work on the synthesis of novel bioactive spiro derivatives[13,14] and in keeping with the above observations the synthesis of some novel spiro derivatives incorporating these nuclei was undertaken. This work reports the synthesis and characterization of some spiro-[2H-1,3-benzothiazine-2,3'-[3H]indole]-2',4(1'H,3H)-diones and spiro[3H-indole-3,2'-thiazolidine]-2,4'-(1H)diones. The spiro benzothiazineindole system has not been reported so far.

DISCUSSION

Condensation of indole-2,3-dione(**I**) with appropriate 2-thiazole amine (**II**) in dry benzene under reflux yielded 3-[2-(4-arylthiazolylimino)]-2H-indol-2-ones(**III**). Compound (**III**) were cyclized with o-mercaptobenzoic acid and mercaptoacetic acid to give spiro[2H-1,3-benzothiazine-2,3'-[3H]indole]-2',4(1'H,3H)-diones and spiro[3H-indole-3,2'-thiazolidine]-2,4'(1H)-diones respectively (Scheme I).

The structure of the synthesized compounds were established by analytical and spectral studies. Elemental and physical data of the synthesized compounds are given in Table I.



SCHEME I

TABLE 1
Physical and analytical data of the compounds

S. No.	Compound Ar	R	Yield %	M.P. (°C)	M.F.	Anals. % Found (Cal.) N	S
IVa	C_6H_5	H	58	206–8	$C_{24}H_{15}N_3O_2S_2$	9.53 (9.52)	14.49 (14.51)
IVb	C_6H_5	CH_3	70	196–7	$C_{25}H_{17}N_3O_2S_2$	9.20 (9.23)	14.02 (14.06)
Va	C_6H_5	H	62	189–90	$C_{19}H_{13}N_3O_2S_2$	11.10 (11.08)	16.85 (16.88)
Vb	4-F,C_6H_4	H	58	221	$C_{19}H_{12}N_3FO_2S_2$	10.62 (10.57)	16.07 (16.12)
Vc	4-F,3-CH_3,C_6H_3	H	72	205–6	$C_{20}H_{14}FN_3O_2S_2$	10.16 (10.21)	15.59 (15.57)
Vd	4-F,3-Cl,C_6H_3	H	60	190	$C_{19}H_{11}ClFN_3O_2S_2$	9.68 (9.73)	14.80 (14.83)
Ve	4-F,2-Cl,C_6H_3	H	64	>300	$C_{19}H_{11}ClFN_3O_2S_2$	9.72 (9.73)	14.86 (14.83)
Vf	4-F,3-OCH_3,C_6H_3	H	79	177–8	$C_{20}H_{14}N_3FO_3S_2$	9.81 (9.83)	14.91 (14.98)
Vg	2-F,C_6H_4	H	56	220	$C_{19}H_{12}FN_3O_2S_2$	10.51 (10.57)	16.05 (16.12)
Vh	4-F,C_6H_4	CH_3	50	202	$C_{20}H_{14}FN_3O_2S_2$	10.15 (10.21)	15.51 (15.57)

IR Spectra

The IR spectra of compounds **IVa,b** and **Va–h** showed two absorption bands in the region 1690–1660 cm^{-1} which can be attributed to the cyclic imido C=O vibration. The N—H band is observed at 3280–3320 cm^{-1}.

^1H NMR Spectra

In the PMR spectra of spiroindole derivatives **IV & V** the aromatic signals were observed as a multiplet in the region δ7.12–8.44. A singlet due to —NH was observed at δ10.22 in compound **IVa** and at δ9.86–10.32 in **Va–g**. The methyl group in compound **IVb** was observed as a singlet at δ3.82. Additional singlets were observed in **Va–h** due to —CN_2— at δ3.86–4.18, in **Vc** due to —CH_3 group attached to phenyl ring at δ2.22 and at δ3.96 in **Vh** due to N—CH_3 group.

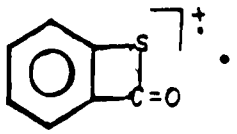
^{13}C NMR Spectra

The ^{13}C NMR spectra of **IVa** and **Va** have been recorded. In **IVa** two signals at δ172.26 and 172.68 corresponding to carbonyl groups of thiazine and indole ring were observed. The aromatic carbons were observed from δ153.68 to 121.62 and the spiro carbon appeared at δ110.62.

Compound **Va** displayed two characteristic signals at δ176.27 and 171.78 which are attributed to the carbonyl groups of thiazolidine and indole ring. Signal due to aromatic carbons is obtained from δ115.38 to 149.82. A signal at δ69.05 due to the methylene carbon and at δ111.26 for the spiro carbon were also obtained.

Mass Spectra

In the mass spectrum of compound **IVa** the molecular ion peak appeared at m/z 441 which corresponded to the molecular formula $C_{24}H_{15}N_3O_2S_2$. Other important peaks were observed at m/z 413, 385, 356, 342, 190, 189 and 145. The base peak appeared at m/z 136 due to the formation of



In compound **Va** the appearance of the parent peak at m/z 379 confirmed the structure assigned.

EXPERIMENTAL

Melting points, determined on a Toshniwal melting point 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 (ν_{max} in cm^{-1}), PMR spectra in $CDCl_3$ and DMSO-d_6 on Jeol FX 90Q (89.55 MHz) using TMS as internal standard and ^{13}C NMR in DMSO-d_6 on the same instrument at 22.49 MHz. Mass spectra were recorded on Kratos 30 and 50 mass spectrometer at 70 eV.

(i) *2-Thiazoleamine (**II**) and 3-[2-(4-arylthiazolylimino)]-1,3-dihydro-2H-indole-2-one (**III**).* These compounds were synthesized by literature methods.[15,16]

(ii) *Synthesis of spiro[2H-1,3-benzothiazines-2,3'-[3H]indole]-2',4(1'H,3H)-diones* (**IVa,b**): A mixture of 3-[2-(4-arylthiazolylimino)]-1,3-dihydro-2H-indole-2-one (0.01 mol) and o-mercaptobenzoic acid (0.011 mol) was refluxed in absolute ethanol-gl. acetic acid (5:1) for 10 hrs. The crystals obtained on cooling were filtered, washed successively with ethanol, water and ethanol, dried and crystallized from ethanol to give solid crystals.

(iii) *Synthesis of Spiro[3H-indole-3,2'-thiazolidine]-2,4'(1H)diones* (**Va–h**). 3-[2-(4-Arylthiazolylimino)]-1,3-dihydro-2H-indole-2-one (0.01 mol) and mercapto acetic acid (0.012 mol) in dry benzene were refluxed in a Dean-Stark apparatus with azeotropic removal of water; white crystals appeared during the progress of the reaction. When the formation of water ceased the reaction mixture was cooled, filtered and the crystals recrystallized with ethanol.

ACKNOWLEDGEMENT

Financial support from the University Grants Commission, New Delhi is gratefully acknowledged.

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