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A novel system 2-oxo-1',2',4',5'-tetrahydrospiro[3*H*-indole-3,3'-1,2,4,5-tetrazine]-6'-thione has been synthesized by the treatment of fluorinated isatins with thiocarbohydrazide in aqueous ethanolic medium. Under exactly similar conditions, *N*-acetylisatin gave exclusively thiocarbohydrazone. The spiro product, on treatment with acetic acid, gave fluorinated isoindigo. Characterization of these products have been done by elemental analyses, ir, pmr and mass spectral studies.

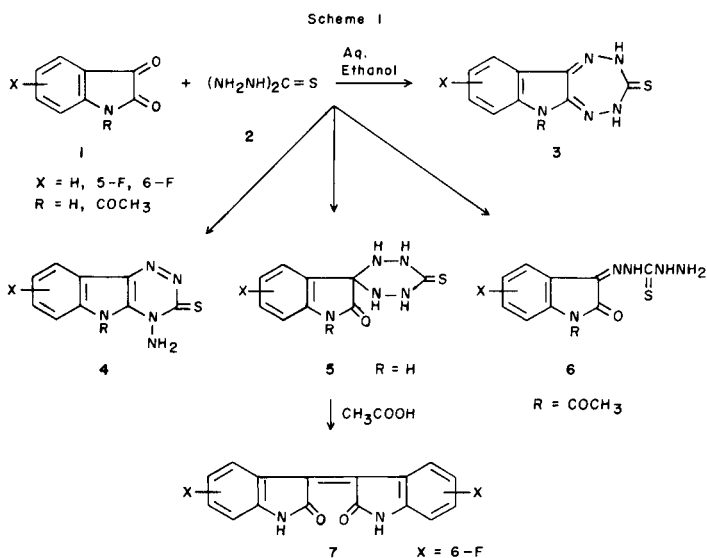
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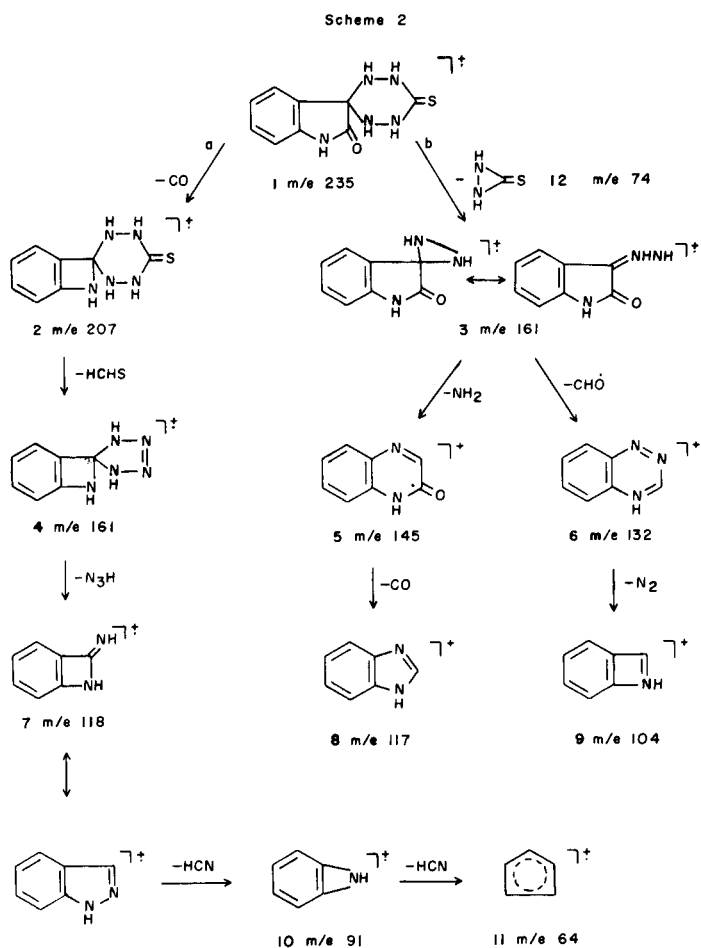
In an attempt to prepare some novel pharmacologically active heterocycles containing indole ring system [2-4], an interesting reaction was noticed when isatin and *N*-acetylisatin were allowed to react with thiocarbohydrazide. A literature survey revealed various interesting reactions of thiocarbohydrazide with cyclic ketones [5], cyclic *ortho*-diketones [6] and isatin [7,8,9]. Keeping in view the various possibilities offered by these reactions (Scheme 1) in investigating new systems and by our previous work on reactions of isatin and *N*-acetylisatin with *o*-phenylenediamine [10], this reaction was further investigated. Isatin, when treated with thiocarbohydrazide in aqueous ethanolic medium, gave a novel spiro compound 2-oxo-1',2',4',5'-tetrahydrospiro[3*H*-indole-3,3'-1,2,4,5-tetrazine]-6'-thione (**5**) in 65-75% yield whereas *N*-acetylisatin, on similar treatment, afforded only a thiocarbohydrazone **6**. Further, it was observed that fluorinated spiro compound **5a**, on treatment with acetic acid, gave a product **7** which was identified as 6,6'-difluoroisoindigo on the basis of comparative spectral studies with isoindigo [11].

Structure assignment to the products formed is based on ir, pmr and mass spectral studies. The ir spectrum of the product formed by reaction of isatin and thiocarbohydrazide revealed C=O absorption at 1650 cm<sup>-1</sup> eliminating the possibility of the formation of products **3** and **4**; absence of peaks due to C=N and primary NH<sub>2</sub> group also eliminates the possibility of product **6**. The pmr spectrum exhibits characteristic tetrazine >NH signals at δ 11.1 (s, 2H, NH and N<sup>5</sup>H), δ 12.4 (s, 1H, N<sup>2</sup>H) and δ 14.2 ppm (s, 1H, N<sup>4</sup>H, which is hydrogen bonded to the carbonyl group) supporting the formation of the novel spiro system **5**. This is further supported by the mass spectrum of **5c** in which the M<sup>+</sup> peak appears at m/e 235 (97%). Differentiation between the spiro product and thiocarbohydrazone is again confirmed on the basis of the fragmentation pattern (Scheme 2).

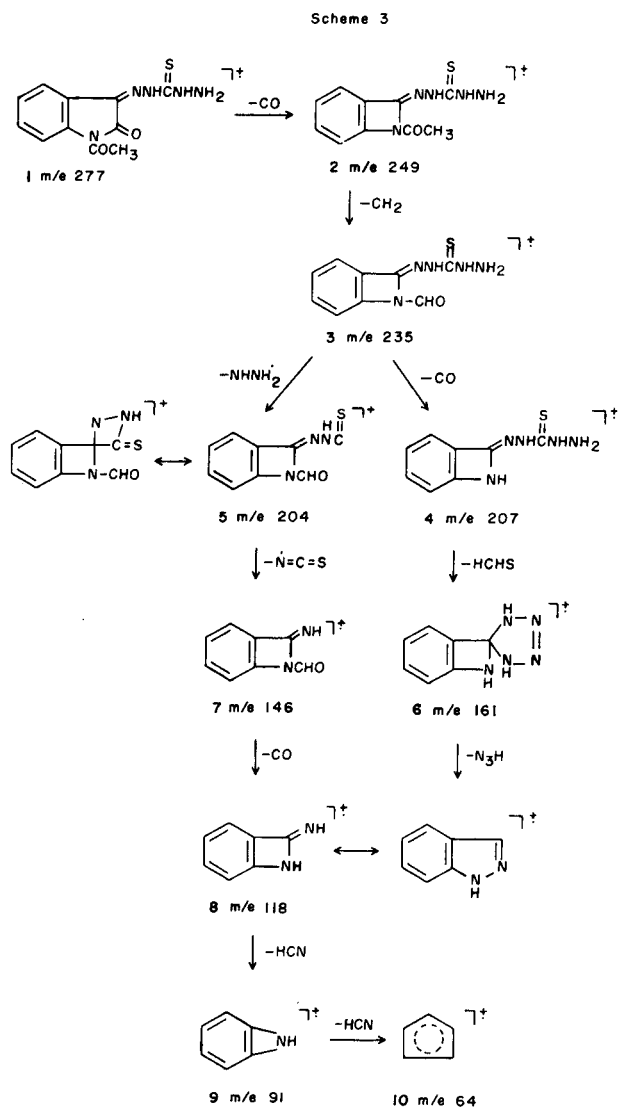
The molecular ion **1** of 2-oxo-1',2',4',5'-tetrahydrospiro[3*H*-indole-3,3'-1,2,4,5-tetrazine]-6'-thione under electron impact may decompose following path **a** or **b**. In path **a** molecular ion **1** eliminates neutral CO molecule and gives cation radical **2** (m/e 207, 100%) which constitutes the base peak. Further elimination of HCHS from **2** yields cation radical **4** (m/e 161, 30%) which in turn loses N<sub>3</sub>H giving cation radical **7** (m/e 118, 18%) which may exist in the form of either of the two isomeric structures. This eliminates two HCN fragments successively giving the cation radical **10** (m/e 191, 28%) and finally the cyclopentadienyl cation radical **11** (m/e 64, 10%).

In path **b**, the ion **1** decomposes giving out a neutral fragment **12** (m/e 74, 26%) and cation radical **3** (m/e 161, 30%) which may exist in two isomeric forms the spiro one or open chain one. This may further decompose *via* two paths. In the first path it loses the NH<sub>2</sub> radical and forms cation **5** (m/e 145, 37%) which further eliminates neutral CO molecule and gives cation **8** (m/e 117, 58%). In the second path **3** eliminates -CHO radical and gives cation **6** (m/e 132, 30%) which further eliminates nitrogen giving cation **9** (m/e 104, 40%).





In the ir spectra of product formed by reaction of *N*-acetyl-satin and thiocarbohydrazide under similar conditions, peaks at  $3400\text{--}3500\text{ cm}^{-1}$ ,  $1620\text{ cm}^{-1}$  and  $1650\text{ cm}^{-1}$  indicated the presence of primary amino, C=N and C=O groups respectively suggesting the formation of product **6** instead of spiro product **5**. The pmr (DMSO) spectra of product **6**



exhibits peaks at  $\delta$  6.5 due to  $\text{-NH}_2$  group and at 8.4 and 9.4 ppm corresponding to two NH groups. These data led

Table I

Analytical Data of 2-Oxo-1',2',4',5'-tetrahydrospiro[3*H*-indole-3,3'-1,2,4,5-tetrazine]-6'-thione and 1-Acetyl-2-oxo[3*H*]indole Thiocarbohydrazone

Compound No.	X	R	Yield %	Mp °C	Formula	Analysis %					
						Calcd. C	Calcd. H	N	C	Found H	N
<b>5a</b>	6-F	H	62	> 300	$\text{C}_9\text{H}_8\text{FN}_5\text{OS}$	42.68	3.16	27.66	42.61	3.13	27.57
<b>5b</b>	5-F	H	75	> 300	$\text{C}_9\text{H}_8\text{FN}_5\text{OS}$	42.68	3.16	27.66	42.64	3.10	27.59
<b>5c</b>	H	H	75	> 300	$\text{C}_9\text{H}_9\text{N}_5\text{OS}$	45.95	3.82	29.78	45.92	3.78	29.69
<b>6a</b>	6-F	$\text{COCH}_3$	67	282	$\text{C}_{11}\text{H}_{10}\text{FN}_5\text{O}_2\text{S}$	44.74	3.38	23.72	44.71	3.32	23.69
<b>6b</b>	5-F	$\text{COCH}_3$	55	294	$\text{C}_{11}\text{H}_{10}\text{FN}_5\text{O}_2\text{S}$	44.74	3.38	23.72	44.68	3.37	23.66
<b>6c</b>	H	$\text{COCH}_3$	66	232	$\text{C}_{11}\text{H}_{11}\text{N}_5\text{O}_2\text{S}$	47.65	3.97	25.27	47.59	3.92	25.23

to the conclusion that in this case only thiocarbohydrazone **6** is formed and not the spiro compound as in the case of non acetylated isatin. This is further supported by the mass spectra of **6c** which showed  $M^+$  at  $m/e$  277 (100%) and its fragmentation as given in Scheme 3.

In the mass spectrum of 1-acetyl-2-oxo[3H]indole thiocarbohydrazone, the parent peak, as well as the base peak was observed at  $m/e$  277, which correspond to the molecular weight of the compound. The molecular ion **1** of 1-acetyl-2-oxo[3H]indole thiocarbohydrazone under electron impact decomposes, eliminating a neutral CO molecule and giving cation radical **2** ( $m/e$  249, 9.6%) which further loses a neutral  $CH_2$  molecule giving **3** ( $m/e$  235, 24.1%). The cation radical **3** may decompose along two pathways. In the first pathway, it eliminates radical  $-NHNH_2$  and gives cation **5** ( $m/e$  204, 23%) which may exist in two isomeric forms. Further elimination of NCS radical from this gives **7** ( $m/e$  146, 31%). The cation radical **7** eliminates a neutral CO molecule giving **8** ( $m/e$  118, 45%) which further loses a neutral HCN molecule giving **9** ( $m/e$  91, 13%). Cation radical **9** eliminates a neutral HCN molecule giving the cyclopentadienyl cation radical **10** ( $m/e$  64, 8%).

In the second pathway **3** eliminates a neutral CO molecule giving **4** ( $m/e$  207, 40%) which further loses a neutral HCHS molecule giving **6** ( $m/e$  161, 23%). The cation radical **6** loses radical  $N_3H$  molecule, giving **8** ( $m/e$  118), thus joining the first pathway.

It is interesting to note that the spiro compound **5a** on treatment with acetic acid give a product showing  $M^+$  at  $m/e$  298 (70%). Other important peaks were observed at  $m/e$  270 (52%), 249 (45%), 235 (38%), 221 (48%), 179 (100%), 162 (27%), 122 (66%), 108 (37%), 94 (18%) *etc.* The ir spectrum of this compound showed NH absorptions at  $3120-3320\text{ cm}^{-1}$  and C=O absorption at  $1670\text{ cm}^{-1}$ . The pmr spectrum showed signals at  $\delta$  8.2 and  $\delta$  6.5-6.9 ppm attributed to two indolyl  $>NH$  and aromatic protons respectively. On the basis of spectral studies and comparing these with isoindigo, the compound was identified as 6,6'-difluoroisoindigo [11,12].

#### EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were recorded using a Perkin-Elmer 577 spectrophotometer. Proton magnetic resonance spectra were recorded on Perkin-Elmer RB-12 using TMS as internal stan-

dard. Mass spectra were recorded using MS-30 and MS-50 Kratos mass spectrometer.

2-Oxo-1',2',4',5'-tetrahydrospiro[3H-indole-3,3'-1,2,4,5-tetrazine]-6'-thione **5a-c**.

Thiocarbohydrazone **2** (0.01 mole) was dissolved in 20 ml of hot water. The solution was stirred without further heating and treated dropwise over 15 minutes with isatin (0.01 mole) in 25 ml of ethanol. The product began to precipitate during the course of addition. The mixture was allowed to stand overnight and then was filtered, washed with dilute ethanol and dried. The compound was recrystallized from ethanol. Analytical data for all of the compounds which were synthesized are recorded in Table I.

1-Acetyl-2-oxo [3H]indole Thiocarbohydrazones **6a-c**.

It was synthesized from thiocarbohydrazone (0.01 mole) and *N*-acetyl-isatin (0.01 mole) in a similar manner in aqueous ethanol medium. It was recrystallized from ethanol. The analytical data of other compounds are recorded in Table I.

6,6'-Difluoroisoindigo.

6'-Fluoro-2-oxo-1',2',4',5'-tetrahydrospiro[3H-indole-3,3'-1,2,4,5-tetrazine]-6'-thione was heated with acetic acid and left overnight. It was filtered and recrystallized from acetic acid, mp  $> 300^\circ$ , yield 40%.

*Anal.* Calcd. for  $C_{16}H_8F_2N_2O_2$ : C, 64.42; H, 2.68; N, 9.39. Found: C, 64.38; H, 2.65; N, 9.30.

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