

# Studies in Spiroheterocycles. Part V. Synthesis of New Fluorinated Spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones

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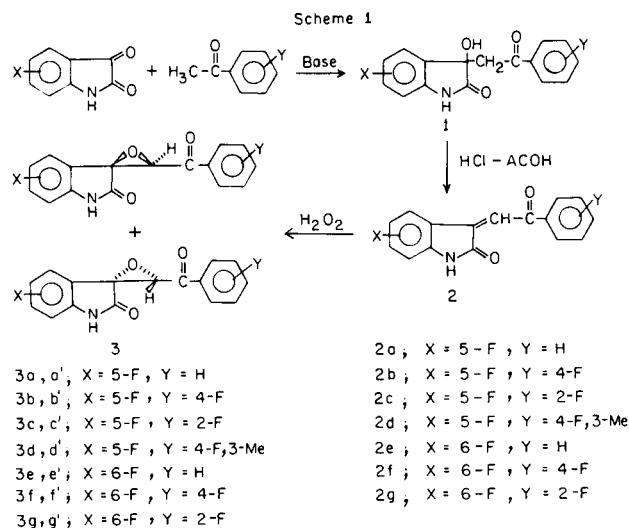
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Received November 17, 1983

Reinvestigation of the reaction of 3-arylmethyleneindol-2-ones with hydrogen peroxide has revealed that a 1:1 isomeric mixture of spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones is formed. The structures of the two isomers have been confirmed by their ir, pmr and mass spectral studies. Mass fragmentation patterns of these compounds are discussed.

*J. Heterocyclic Chem.*, **21**, 977 (1984).

Epoxidation of 3-arylmethyleneindol-2-ones with hydrogen peroxide was earlier reported to give spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones [1-4]. Theoretically, it appeared that such compounds could exist in the form of two isomers differing in the stereochemical arrangement of the hydrogen atom of oxirane ring. No such reports have appeared so far concerning these compounds. Also, the mass fragmentation studies of such compounds have not been reported earlier. These considerations, and the fact that the earlier literature reports concerning non-fluorinated analogs are patents with no specific details, led us to reinvestigate this reaction. During the course of this investigation, the product was found to be a mixture of two compounds in the ratio of 1:1 and was separated by plc using uv lamp. The two compounds were found to give identical mass spectrum although in the pmr, the peak due to CH was at a slightly different position in the two cases. The synthesis of these fluorine containing spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones is summarized in Scheme 1.



Reactions of fluorinated isatins with methyl ketones in presence of diethylamine yielded 3-hydroxy-3-phenacylindol-2-ones **1**, which on dehydration in hydrochloric acid-acetic acid gave the corresponding 3-arylmethyleneindol-

2-ones **2**. Epoxidation of **2** with hydrogen peroxide and sodium carbonate, in methanol, gave a 1:1 isomeric mixture of the corresponding spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones **3**.

The isomeric mixture gave two spots on tlc (benzene:ethyl acetate, 1:1) as observed under an ultraviolet lamp. Furthermore, two sharp signals of equal intensity were observed in the pmr spectrum (deuteriochloroform) for CH proton at  $\delta$  5.0 and 5.1 ppm. This provided support for the formation of 1:1 isomeric mixture of **3**. The two isomers were separated by preparative tlc over silica gel G using benzene-ethyl acetate (1:1) under an ultraviolet lamp. The pmr spectra of these isomers in deuteriochloroform show characteristic signals for NH at  $\delta$  7.7 and CH at 5.1 ppm (**3b**), NH at  $\delta$  7.7 and CH at 5.2 ppm (**3b'**). Position of NH was confirmed by deuteration. Appearance of oxirane CH signal and disappearance of original (CH) resonance signal of **2** at  $\delta$  7.15 ppm provides support for the epoxidation of **2** by hydrogen peroxide. In the ir spectrum, appearance of absorption band at  $1050\text{ cm}^{-1}$  demonstrates the pre-

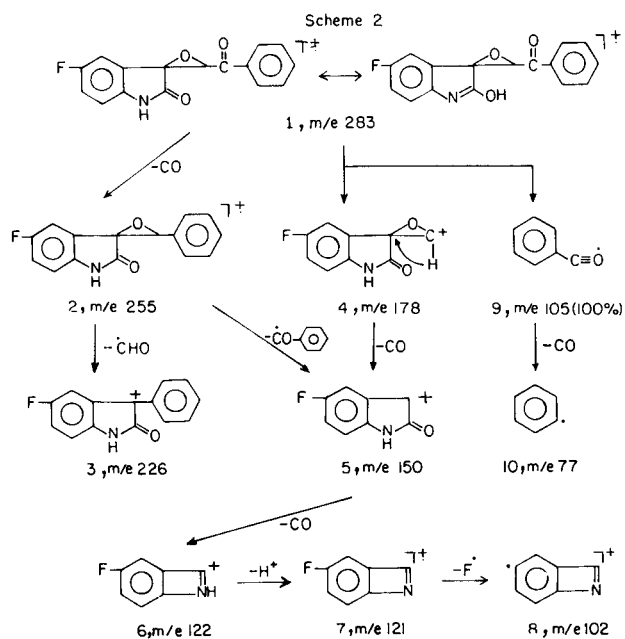
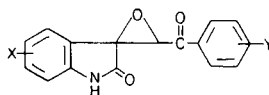


Table I

Analytical Data of Spiro[3*H*-indole-3,2'-oxirane]-2(1*H*)-ones

Compound No.	X	Y	Colour	Yield %	Mp °C	Formula	C	Calcd. H	Analysis %			Found H	N
									N	C	N		
<b>3a</b>	5-F	H	White	15	330	C <sub>16</sub> H <sub>10</sub> FNO <sub>3</sub>	67.84	3.52	4.91	67.74	3.50	5.07	
<b>3a'</b>	5-F	H	Brown	15	210					67.51	3.52	5.05	
<b>3b</b>	5-F	4-F	White	15	230	C <sub>16</sub> H <sub>9</sub> F <sub>2</sub> NO <sub>3</sub>	63.78	3.00	4.65	63.58	3.12	5.05	
<b>3b'</b>	5-F	4-F	Brown	15	180					63.81	3.08	4.60	
<b>3c</b>	5-F	2-F	White	15	225	C <sub>16</sub> H <sub>9</sub> F <sub>2</sub> NO <sub>3</sub>	63.78	3.00	4.65	64.02	3.09	4.68	
<b>3c'</b>	5-F	2-F	Brown	15	195					63.80	3.10	4.55	
<b>3d</b>	5-F	4-F, 2-Me	White	10	300	C <sub>17</sub> H <sub>11</sub> F <sub>2</sub> NO <sub>3</sub>	64.76	3.50	4.44	64.80	3.52	4.46	
<b>3d'</b>	5-F	4-F, 2-Me	Brown	10	242					64.68	3.48	4.45	
<b>3e</b>	6-F	H	White	10	280 dec	C <sub>16</sub> H <sub>10</sub> FNO <sub>3</sub>	67.84	3.52	4.91	67.78	3.48	5.01	
<b>3e'</b>	6-F	H	Brown	10	> 300					67.80	3.50	5.05	
<b>3f</b>	6-F	4-F	White	10	226	C <sub>16</sub> H <sub>9</sub> F <sub>2</sub> NO <sub>3</sub>	63.78	3.00	4.65	64.00	3.15	4.70	
<b>3f'</b>	6-F	4-F	Brown	10	245 dec					63.92	3.05	4.58	
<b>3g</b>	6-F	2-F	White	15	225	C <sub>16</sub> H <sub>9</sub> F <sub>2</sub> NO <sub>3</sub>	63.78	3.00	4.65	63.92	3.20	4.70	
<b>3g'</b>	6-F	2-F	Brown	15	245					63.85	3.18	4.71	

Table II

PMR Data for the Spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones

Compound No.	X	Y	NH	Chemical Shift, ppm (δ)			Aromatic protons
				CH	CH <sub>3</sub>		
<b>3a</b>	5-F	H	7.7	5.2	—	6.2-8.1	
<b>3a'</b>	5-F	H	7.7	5.9	—	6.2-8.1	
<b>3b</b>	5-F	4-F	7.4	5.1	—	6.6-8.2	
<b>3b'</b>	5-F	4-F	7.4	5.2	—	6.6-8.2	
<b>3c</b>	5-F	2-F	7.4	5.1	—	6.6-8.1	
<b>3c'</b>	5-F	2-F	7.4	5.2	—	6.6-8.1	
<b>3d</b>	5-F	4-F, 3-Me	7.4	5.1	3.3	6.6-8.2	
<b>3d'</b>	5-F	4-F, 3-Me	7.4	5.2	3.3	6.6-8.2	
<b>3e</b>	6-F	H	7.6	5.2	—	6.5-8.1	
<b>3e'</b>	6-F	H	7.6	6.0	—	6.5-8.1	
<b>3f</b>	6-F	4-F	7.4	5.1	—	6.6-8.2	
<b>3f'</b>	6-F	4-F	7.4	5.2	—	6.6-8.2	
<b>3g</b>	6-F	2-F	7.4	5.1	—	6.6-8.2	
<b>3g'</b>	6-F	2-F	7.4	5.2	—	6.6-8.2	

sence of oxirane ring system. Molecular weight was confirmed by mass spectra M<sup>+</sup> at m/z 301 (**3b** and **3b'**).

The mass spectral fragmentation patterns were studied for further confirmation of the structures of these compounds and some of the typical ions that occur in the majority of the spectra are discussed.

The appearance of a reasonably intense molecular ion peak in the mass spectra of spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones established the molecular weights (Table III). In a typical mass spectrum of **3a,a'** (Scheme 2), an intense molecular ion peak **1** at m/e 283 was observed. This may lose a neutral fragment CO to give a peak at m/e 255, **2** or

generate a radical at m/e 105, **9**, which forms the base peak along with a cation **4** at m/e 178. Fragment **5** at m/e 150 can be obtained by two different pathways *i.e.* from fragment **2** as well as **4**. This successively loses neutral fragments and ions to give peaks at m/e 150, **5**, 122, **6**, 121, **7** and 102, **8**. The peak **2** and **9** lose formyl free radical and neutral CO to give fragments of m/e 226, **3** and 77, **10**, respectively.

The mass spectrum of **3b,b'** and **3c,c'**, having fluorine in place of hydrogen, confirmed the fragmentation pattern depicted for **3a,a'**. All the fragments for compounds

Table III

Mass Fragments of Spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones

Fragment No.	<b>3a,a'</b>		<b>3b,b'</b>		<b>3c,c'</b>	
	m/e	% ab	m/e	% ab	m/e	% ab
<b>1</b>	283	19.6	301	16.6	301	15.5
<b>2</b>	255	78.6	273	100	273	56.6
<b>3</b>	226	20.9	244	25.5	244	22.2
<b>4</b>	178	3.3	178	3.3	178	3.3
<b>5</b>	150	5.5	150	4.4	150	4.4
<b>6</b>	122	10.0	122	7.7	122	8.8
<b>7</b>	121	5.5	121	5.5	121	5.5
<b>8</b>	102	3.0	102	7.7	102	7.7
<b>9</b>	105	100	123	72.15	123	100
<b>10</b>	77	78.6	95	44.0	95	64.4
<b>11</b>	—	—	75	16.65	75	11.1

**3a,a'**, **3b,b'** and **3c,c'** are listed in Table III along with their percentage abundance.

## EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were recorded using a Perkin Elmer Model 337 spectrophotometer. Proton magnetic resonance spectra were recorded on a Perkin Elmer Model R 32 spectrometer in deuteriochloroform using tetramethylsilane (TMS) as internal standard. The chemical shifts are reported in ten parts per million.

3-Aroylmethyleneindol-2-ones **2**.

5-Fluoro-3-benzoylmethyleneindol-2-one, 5-fluoro-3-(4'-fluorobenzoyl)-

methyleneindol-2-one, 5-fluoro-3-(2'-fluorobenzoyl)methyleneindol-2-one, 5-fluoro-3-(4'-fluoro-3'-methylbenzoyl)methyleneindol-2-one, 6-fluoro-3-benzoylmethyleneindol-2-one, 6-fluoro-3-(4'-fluorobenzoyl)methyleneindol-2-one and 6-fluoro-3-(2'-fluorobenzoyl)methyleneindol-2-one were prepared by the method of Joshi *et al.* [5].

Spiro[3*H*-indole-3,2'-oxiran]-2(1*H*)-ones **3**.

To a solution of appropriate 3-arylmethyleneindol-2-one (1.0 g) in methanol (50 ml), was added a solution of sodium carbonate (5 ml, 5%) and hydrogen peroxide (4 ml, 15%) with stirring. The stirring was further continued for 6 hours. The resultant solid mass was filtered, and the filtrate concentrated to give a second crop of compound. The two crops were mixed and isomers were separated by preparative tlc over silica gel G using benzene-ethyl acetate (1:1) under ultraviolet lamp. Both isomers were finally recrystallized from methanol. All synthesised compounds along with their analytical data are given in Table I, pmr and mass spectral data are reported in Tables II and III.

## Acknowledgement.

The authors are thankful to the Indian Council of Medical Research, New Delhi, for financial support.

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