Tautomerism and Autoxidation of Indoline-2-thiones

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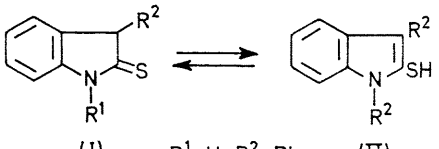
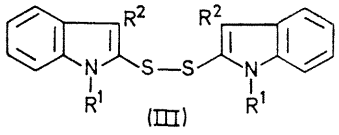
Summary 3-Arylindoline-2-thiones (Ia, c) are present as a tautomeric mixture of (I) and (II) in solution; autoxidation of some indolinethiones (I) gave disulphides (III), but the 1-methyl compound gave the oxo-indolinethione (IV).

IN our previous report[1] methyl-substituted indoline-2-thiones (I;R^1, R^2 = H or Me), prepared by the thiation of the corresponding oxindoles, were shown to exist mostly as the thione form (I) in solution. We have now prepared indoline-2-thiones (Ia—f) by the reduction with $NaBH_4$ of

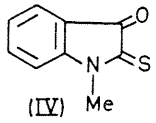


(I) (II)

a; R^1=H, R^2=Ph
b; R^1=Me, R^2=Ph
c; R^1=H, R^2=*p*-MeO·C_6H_4
d; R^1=Me, R^2=*p*-MeO·C_6H_4
e; R^1=H, R^2=$PhCH_2$
f; R^1=H, R^2=Bu^t



(III)



(IV)

the disulphides (III), which were obtained by the reaction of indoles with S_2Cl_2.[2] The u.v. spectra of (Ia) in various solvents are shown in the Figure. In 95% EtOH (Ia) exists as a tautomeric mixture of (Ia) and (IIa), in contrast to methyl substituted indoline-2-thiones. In methanol, the thiol form (IIa) is favoured. The u.v. spectrum of (Ia) immediately after dissolution in $CHCl_3$ was typical of the thione form (Ia), but the maximum at 320 nm decreased with concomitant increase in the maximum at *ca.* 290 nm after 30 min, indicating an increasing predominance of the thiol form (II). This was also observed in benzene. The spectral behaviour of (Ic) in various solvents was similar to that of (Ia). The spectra of the *N*-methylated derivatives (Ib and d), however, showed the thione form (I) as the predominant tautomer in both 95% EtOH and $CHCl_3$, and solvent dependency was not observed (see Table 1).

The n.m r. spectra (Table 2) of (Ia—d) in $CDCl_3$ clearly reveals the presence of the tautomeric forms (I) and (II). The ratio of the intensity of signals for (I) and (II) indicated the thiol form (II) is favoured in (Ia and c), but the thione form (I) is preferred in the *N*-methylated compounds (Ib and d). In benzene these signals (Table 2) are shifted to higher field without causing significant changes in the ratio of the tautomers.

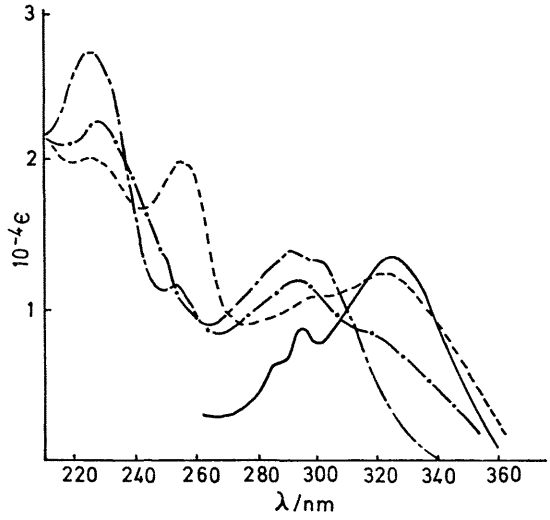


FIGURE. *U.v. spectra of* (Ia); – – – – – (Ia) in 95% EtOH; —·—·— (Ia) in MeOH; ———— (Ia) in $CHCl_3$; — — — - 2-Ethylthio-3-phenylindole in 95% EtOH.

These results suggest that the effect of the *p*-methoxy-group on tautomerism is not great, but *N*-methylation causes a considerable effect. The presence of the tautomeric mixture in solution of (Ia) and (Ic) shows that relative stability of the thiol form (II) is greater than that of the enol form of 3-phenyloxindole which is known to exist as the oxo-form in solution.[3] The u.v. and n.m.r. spectra showed that (Ie) and (If) are present as the thione form (I).

TABLE 1[a]

U.v. spectra of indoline-2-thiones; λ_{max}/nm ($10^{-3}\epsilon$)

(Ia)	226(20·2),	255(19·7),	297sh(11·0),	320(12·5)
(Ib)	228(17·0),	260(16·5),	295sh(10·5),	322(15·0)
(Ic)	229(22·0),	256(21·0),	296sh(11·8),	315(11·6)
(Id)	230(22·8),	261(15·4),	296sh(10·9),	321(13·7)
(Ie)	230(15·8),	284sh(6·5),	294(9·2),	321(13·8)
(If)	235(16·3),	296(9·5)	328(17·0),	

[a] In 95% EtOH.

When an ethanolic solution of these indoline-2-thiones (I) was left at room temperature for 24 h, autoxidation took place to produce the corresponding disulphides (III).[4] The autoxidation can be followed by the increase in absorption at 360 nm. The approximate speed of the autoxidation is, in decreasing order: (Ic) > (Ia), (I; R^1 = H, R^2 = Me), (Id), (Ie) > (Ib) ≫ (I; R^1, R^2 = H), (I; R^1 = Me, R^2 = H), (If). Indoline-2-thione, 1-methylindoline-2-thione, and 3-t-butylindoline-2-thione are stable to autoxidation and their u.v. spectra did not change significantly after 24 h. This order does not parallel the stability of the thiol

form of indoline-2-thiones. The autoxidation of (I) is slower in $CHCl_3$ or dichloroethane.

TABLE 2[a]

N.m.r. spectra of indoline-2-thiones

	(II)			(I)			
	NH	SH	NMe OMe	NH	3-H	NMe OMe	(II) : (I)
(Ia)	8·10	3·41		10·01	4·89		2:1
(Ib)		3·20	3·85		4·90	3·65	1:10
(Ic)	8·05	3·38	3·83	9·97	4·83	3·75	2:1
(Id)		3·26	3·70		4·92	3·70	1:8
			3·90			3·80	

[a] P.p.m. from tetramethylsilane in $CDCl_3$.

When an ethanolic solution of 1-methylindoline-2-thione was kept under oxygen for 2 weeks, a small amount of an oxidised compound (IV), m.p. 168—171°, was isolated besides the starting material. The structure of (IV) was confirmed by its spectra; λ_{max} (EtOH) 264, 271, 293sh, and 475 nm, ν_{max} (KBr 1730 cm^{-1} (C=O), *m/e* 177(M^+, 100%), 162(M − Me, 6%), 148(M − HCO, 9%), and 132(M − HCS, 10%).

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