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Six substituted 6*H*-indolo[2,3-*b*]quinoxalines were synthesized by the interaction of *o*-phenylenediamine with substituted isatins. The uv, ir and nmr spectral data for the compounds synthesized are presented and discussed.

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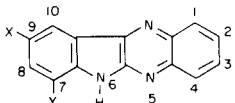
In common with other nitrogen heterocycles, quinoxaline and indole compounds show marked activity in many biological systems (1). A great number of compounds containing these ring systems were prepared and found to have antitumor and antimicrobial activities (2,3). It was therefore thought worthwhile to prepare a series of 6*H*-indolo[2,3-*b*]quinoxalines, study their spectroscopic properties and biological activities. Six substituted 6*H*-indolo[2,3-*b*]quinoxalines were synthesized by the interaction of *o*-phenylenediamine with isatin, 5-bromo-, 7-chloro-, 5-nitro-, 5,7-dichloro-, and 5,7-dibromoisatin (4,5). The structures and physical properties of these compounds are given in Table 1. The uv, ir and nmr spectral data are presented in Tables 2 and 3.

The uv absorption spectra of the compounds synthesized are given in Table 2. Compound 1 shows a red shift and an increase in absorption intensity in comparison with quinoxaline [232 (log 4.51), 312 (log 3.81), 340 nm (log 2.84)]. Compound 1 also shows uv spectral data similar to indole [220 (log 4.15), 262 (log 3.80), 280 (log 3.75), 288 nm (log 3.62)], but with higher absorption intensity (10). The effect of the indole nucleus in compound 1 is to increase the conjugation of the lone-pair of electrons on nitrogen through the quinoxaline ring system, thus increasing the length of the chromophore and, leading to a longer wave-

length and higher absorption intensity. Substitution in the benzene ring of indole by halogens causes only a slight shift in the K-band but a marked hypsochromic shift in the B-band with an increase in absorption intensity, with the exception of compound 5, where the uv exhibits a hypsochromic effect due to a break in the long conjugated system. In compound 6, the presence of a nitro group in the indole nucleus, which is complemented by the lone-pair of electrons on the nitrogen atom, causes a bathochromic shift of both the K- and B-bands. The condensed indole-quinoxaline system has a marked effect on $n \rightarrow \pi^*$ transitions. In this system, 2-3 bands in the $n \rightarrow \pi^*$ region, due to the presence of three nitrogen atoms (15) were noticed. This system leads to a red shift in the $n \rightarrow \pi^*$ bands with an increase in absorption intensity relative to both quinoxaline and indole (4,13). When halogen atoms are introduced into the indole nucleus of the molecule, a red shift in the $n \rightarrow \pi^*$ band is produced.

The ir absorption spectra of the indolo[2,3-*b*]quinoxaline compounds studied here, show vibrational stretching frequencies characteristic of this ring system at 1653-1420 cm^{-1} . Earlier studies on quinoxaline derivatives showed the presence of four bands within this region (6,7). The additional two bands of variable intensity found at about 1555 and 1510 cm^{-1} may be attributed to pyrrole C=C

Table I

Physical Properties of Substituted 6*H*-Indolo[2,3-*b*]quinoxalines


Compound No.	X	Y	M.p. °C	Yield %	Formula	Calcd.			Found		
						C	H	N	C	H	N
1	H	H	294-295 (a)	100	C ₁₄ H ₉ N ₃	76.71	4.11	19.18	76.76	3.94	18.98
2	Br	Br	289-290	84	C ₁₄ H ₇ Br ₂ N ₃	44.58	1.86	11.14	44.61	1.84	11.10
3	Cl	Cl	298-299	83	C ₁₄ H ₇ Cl ₂ N ₃	58.35	2.43	14.59	58.37	2.39	14.52
4	Br	H	157-158	97	C ₁₄ H ₈ BrN ₃	56.39	2.68	14.10	56.41	2.63	13.94
5	H	Cl	286-288	80	C ₁₄ H ₈ ClN ₃	66.28	3.15	16.57	66.31	3.13	16.21
6	NO ₂	H	320	92	C ₁₄ H ₈ N ₄ O ₂	63.64	3.03	21.20	63.69	2.98	21.17

(a) Reference 14, m.p. 295-297°.

Table 2

Characteristic Ir and Uv Absorption of 6*H*-Indolo[2,3-*b*]quinoxalines (a)

Compound No.	NH Stretching Vibration	Ring Stretching Vibration	C-H In-Plane Deformation	C-H Out-of-Plane Deformation	λ Max (nm) (Log ϵ)
1	3365 m	1650 s, 1605 s, 1558 s, 1518 m, 1465 m, 1428 m	1398 s, 1332 m, 1232 m, 1203 s, 1120 s, 1101 s	938 m, 871 m, 818 m, 742 s	222 (4.513), 265 (4.454), 334 (4.102), 350 (4.134)
2	3368 m	1647 s, 1585 s, 1555 m, 1510 m, 1472 s, 1421 s	1251 s, 1225 w, 1200 s, 1122 w, 1020 w	895 m, 862 m, 825 m, 758 m, 743 s, 720 m	228 (4.619), 244 (4.506), 299 (4.251), 357 (4.186), 372 (4.196)
3	3402 m	1653 s, 1604 m, 1546 m, 1470 m, 1452 m, 1422 w	1270 m, 1202 m, 1075 m, 1032 m	880 w, 856 m, 840 m, 754 s, 742 m	225 (4.567), 244 (4.474), 299 (4.167), 354 (4.126), 371 (4.135)
4	3360 m	1650 s, 1595 m, 1555 s, 1515 m, 1473 s, 1420 m	1390 s, 1272 m, 1250 m, 1202 s, 1155 s, 1120 m, 1020 m	934 m, 898 m, 810 s, 750 s, 740 s, 688 m	223 (4.440), 249 (4.485), 299 (4.215), 352 (4.109), 360 (4.052)
5	3400 m	1650 s, 1620 s, 1583 s, 1532 m, 1488 m, 1445 s, 1420 s	1288 s, 1268 s, 1245 s, 1151 m, 1090 s, 1030 s, 1015 s	960 m, 940 m, 880 s, 852 m, 765 s, 728 s, 665 s	225 (4.345), 244 (4.219), 302 (3.973), 352 (3.980), 370 (3.966)
6	3370 m	1633 s, 1605 s, 1575 s, 1478 m, 1462 m	1318 s, 1292 s, 1260 s, 1214 m, 1103 s, 1000 m	830 m, 820 m, 754 s, 747 s, 695 m, 625 s	240 (3.976), 301 (3.885), 357 (3.956)

(a) Abbreviations: s = strong, m = medium, w = weak.

bond stretching vibrations in the indole ring system (8). The ir spectra of these molecules show an NH absorption at 3402-3365 cm^{-1} due to the free indole NH stretching vibration. Table 2 shows marked variations in both frequency and intensity of this band in the compounds which were studied. Both properties of this band were found to be very sensitive to the surrounding structure.

The chemical shifts and coupling constants in the nmr spectra of the indoloquinoxaline derivatives are summarized in Table 3. The assignments were as follows. In compound 1, a triplet was observed at 8.5 ppm ($J = 7.2$ Hz), which integrated for two protons. This triplet was assigned to H_2 and H_5 . A double-doublet centered at 8.16 ppm, which integrated for two protons, was assigned to H_7 and H_{10} ($J_{9,10} = 7.5$ Hz, $J_{8,10} = 3$ Hz). A singlet at 7.91 ppm was assigned to the NH proton of the pyrrole ring. A partially resolved quartet at 7.76 ppm, which integrated for four protons, was assigned to H_3 , H_4 , H_8 and H_9 . The chemical shifts and coupling constants are not significantly different from those reported for 2,3-dimethylquinoxaline (11,12). The most interesting feature in the nmr spectrum of 3 is a double-doublet centered at 8.2 ppm, inte-

grating for one proton, which was assigned to H_{10} . This proton is coupled to H_8 ($J_{8,10} = 3$ Hz) and possibly to H_6 , through long-range coupling. This long-range coupling has been observed in the nmr spectra of substituted indoles, where the NH proton is coupled to the olefinic proton of the pyrrole ring (13). This coupling was conformed by deuteration.

EXPERIMENTAL

Melting points were determined on a Kofler Hot Bench and are uncorrected. Elemental analyses were performed by Alfred Bernhardt Laboratories, Ruhr, Germany. Uv absorption spectra were measured as solutions in dioxane with a Unicam SP 800B uv spectrophotometer. Ir absorption spectra were recorded on a Beckman IR 12 spectrophotometer as potassium bromide wafers. Nmr spectra were measured on a Varian EM 390 spectrometer operating at 90 MHz as solutions in trifluoroacetic acid (TFA) with tetramethylsilane (TMS) as an internal reference.

General Procedure for the Preparation of Quinoxaline Derivatives.

The diketone (0.03 mole) was added to *o*-phenylenediamine (0.03 mole) in dioxane (20 ml.); the mixture was refluxed for 15 minutes. The reaction mixture was then cooled and filtered. Recrystallization of the product from glacial acetic acid afforded the pure 6*H*-indolo[2,3-*b*]quinoxaline derivatives. Physical properties for these compounds are given in Table 1.

Table 3
Nmr Spectral Data for Substituted 6*H*-Indolo[2,3-*b*]quinoxalines (a)

Compound No.	Chemical Shifts (Ppm)	Proton Assignment	J _{1,2}	J _{7,8}	J _{8,10} (Hz)	J _{9,10}
1	7.76 q, 7.91 s, 8.16 dd, 8.50 t	H-2, H-3, H-8, H-9, (4H); H-6 (1H); H-7, H-10 (2H); H-1, H-4 (2H)			3	7.5
2	7.66 c, 8.10 s, 8.13 s, 8.46 d	H-1, H-2, H-3, H-4 (4H); H-6 (1H); H-10 (1H); H-8 (1H)			3	
3	7.66 s, 7.73 s, 7.86 d, 8.20 dd, 8.43 d	H-6 (1H); H-2, H-3 (2H); H-1, H-4 (2H); H-10 (1H); H-8 (1H)			3	
4	7.63 q, 7.83 q, 7.90 d, 8.10 d, 8.33 d	H-2, H-3 (2H); H-1, H-4 (2H); H-7 (1H); H-8 (1H); H-10 (1H)		7.8	3	
5	7.73 s, 7.83 d, 7.90 dd, 8.16 dd, 8.30 dd	H-2, H-3 (2H); H-1, H-4 (2H); H-9 (1H); H-10 (1H); H-8 (1H)		7.5		7.5
6	7.73 t, 8.10 d, 8.23 d, 8.66 dd, 9.40 d, 9.73 bm	H-2, H-3 (2H); H-1, H-4 (2H); H-7 (1H); H-8 (1H); H-10 (1H); H-6 (1H)	9	9	3	

(a) Abbreviations: s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, bm = broad multiplet.

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