Stereospecific Reduction of 3-Hydroxy-3*H*-indoles and of their Corresponding *N*-Oxides with $NaBH_4$ and $LiAlH_4$. Synthesis of True 1-Hydroxy-2,3-disubstituted Indoles. Crystal and Molecular Structure of 3-Hydroxy-2,3-diphenylindoline

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3-Hydroxy-3*H*-indoles (1) and their corresponding *N*-oxides (5) undergo stereospecific reduction at the double C=N bond giving the indoline derivatives (2) and (6) respectively, which, in acidic medium, lose water to give the 2,3-disubstituted indoles (3) and (7) whose physical and spectroscopic data are not in agreement with those reported previously. The structure of 3-hydroxy-2,3-diphenylindoline, one of the reduction products, was determined by *X*-ray diffraction, and it was shown that hydrogen adds at C-2 *cis* to the hydroxy-group on C-3. 3,3-Disubstituted-3*H*-indoles with two organic radicals on C-3 give a mixture of stereoisomers.

HYDRIDE reduction of carbonyl and azomethyne groups has been widely studied and recently the factors which influence the stereochemistry of this type of reaction have been rationalized.[1,2] However when the molecules, which are mainly rigid, have the groups OH, OR, NH_2, or halogen [3-5] α or β with respect to the reduction centre (C=O or C=N) the stereochemistry of the reaction is strongly influenced by these groups and, in most cases, became stereospecific. We have studied the reduction by $NABH_4$ and $LiAlH_4$ of some 3-hydroxy-3*H*-indoles, their corresponding *N*-oxides, and analogues without a 3-hydroxy-group. The results demonstrate the role played by the 3-hydroxy-group in the saturation of the double C=N bond α to the hydroxy-group.

RESULTS

When the 2,3-substituted-3-hydroxy-3*H*-indoles (1; a, R = Me; b, R = Et; c, R = Ph), are reduced with an excess of $NaBH_4$ in methanol at room temperature the corresponding indolines are obtained (Scheme 1), in the cases of (1a) and (1c) almost quantitatively. Their i.r. spectra show a band near 1 610 cm^{-1} due to the PhN–C– group.[6,7] Their ^1H n.m.r. spectra show a sharp signal near δ 4.2 due to the hydrogen on C-2 and, for (2a), a singlet at δ 1.0 due to the hydrogens of the methyl group on C-3. These signals show the presence of only one of the two possible diastereoisomers which, by analogy with (2c), has hydrogen on C-2 *cis* to the 3-hydroxy-group.

Analytical and spectroscopic data for (2a) and (2c) are given in Table 1.

When compounds (1a) and (1c), are reduced with $LiAlH_4$ in tetrahydrofuran at room temperature, compounds (2a) and (2c), respectively, are formed quantitatively. The indolines (2a—c) lose the elements of water easily. Treatment with ethanol saturated with hydrogen chloride gives the corresponding indoles (3a—c) quantitatively and attempted chromatography of (2a—c) results in conversion, to some extent, into the corresponding indole. Reduction of (1b) gives indole (3b) together with indoline (2b), which cannot be separated from the mixture because indolines (2a—c) lose water during chromatography on silica. Exposure to air of benzene solutions of indoles (3a) and (3b) results in the production of some of the corresponding 3-hydroperoxide, a type of autoxidation reported previously;[8,9] catalytic oxidation gives a quantitative conversion.

The 3-hydroxy-2-phenyl-3*H*-indole *N*-oxides (5a—c) undergo reduction at room temperature with $NaBH_4$ or $LiAlH_4$ to give the *N*-hydroxyindolines (6a—c) almost quan-

TABLE 1

Analytical and spectroscopic data

Compound	M.p. (°C)	Formula	Analyses, Found (Calc.) C	H	N	I.r.[g] (ν/cm^{-1})	U.v. [λ_{max}/nm (log ε)[n]]	^1H N.m.r. (δ: $CDCl_3$)	Mass M^+: found (m.w.)
(2a)	81[a]	$C_{15}H_{15}NO$	79.7 (79.97)	6.8 (6.71)	6.45 (6.22)	1 615[h] 3 300 3 350		1.0 (3 H, s, CH_3), 2.32 (1 H, broad, OH), 4.1 (1 H, broad, NH), 4.74 (1 H, s, CH), 6.62—7.62 (9 H, m, arom.)	
(2b)	Oil					1 610[h] 3 400 3 540			
(2c)	111[a]	$C_{20}H_{17}NO$	83.95 (83.59)	5.9 (5.96)	4.95 (4.87)	1 610[h] 3 345 3 375		2.77 (1 H, broad, OH), 4.12 (1 H, broad, NH), 4.21 (1 H, s, CH), 6.65—7.40 (14 H, m, arom)	
(3a)	Ref. 20					1 605[i] 3 325[j]	229 (4.36)[o] 310 (4.30)	2.44 (3 H, s, CH_3), 7.1—7.74 (9 H, arom.), 7.94 (1 H, broad, NH)	

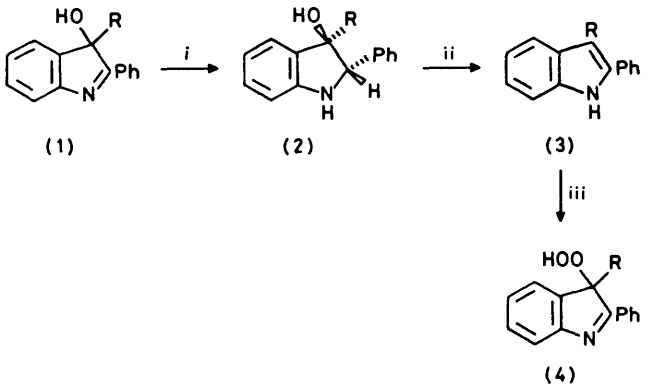
TABLE 1 (*Continued*)

Compound	M.p. (°C) Ref. 20	Formula	Analyses: Found (Calc.) C	H	N	I.r.[g] (ν/cm^{-1})	U.v. [$\lambda_{max.}$/nm (log ε) [n]]	^{1}H N.m.r. (δ; $CDCl_3$)	Mass M^+: found (m.w.)
(3a) (*Continued*)							207 (4.46)	1.22 (3 H, t, CH_2CH_3, J = 7.6 Hz); 2.90 (2 H, q, CH_2CH_3, J = 7.6 Hz), 7.08—7.76 (9 H, m, arom.),. 7.9 (1 H, broad, NH)	221 (221)
(3b)	67	$C_{16}H_{15}N$	86.55 (86.83)	6.8 (6.83)	6.25 (6.33)	1 610 [f] 3 395 [j]	228 (4.40) 308 (4.26) 212 (4.41)		
(3c)	Ref. 21					1 603 [f] 3 415 [j]	225 (4.40) 250 (4.36) 309 (4.24)		
(4a) [r]	141 [b] (decomp.)	$C_{15}H_{13}NO_2$	75.15 (75.30)	5.7 (5.47)	5.85 (5.85)	1 545 [k] 3 060 [l]		1.6 (3 H, s, CH_3), 2.87 (1 H, broad, OOH), 7.12—7.77 (7 H, m, arom.), 8.4—8.6 (2 H, m, arom.) [p]	239 (239)
(4b)	137 [b] (decomp.)	$C_{16}H_{15}NO_2$	76.0 (75.86)	6.05 (5.97)	5.7 (5.53)	1 550 [k] 3 060 [l]		0.45 (3 H, t, CH_2CH_3, J = 7.3 Hz), 2.1 (3 H, m, CH_2CH_3 + OOH), 7.3—7.8 (7 H, m, arom.), 8.35—8.6 (2 H, m, arom.) [p]	253 (253)
(6a)	142 [c]	$C_{15}H_{15}NO_2$	74.6 (74.66)	6.25 (6.26)	5.9 (5.81)	1 605 [h] 3 380 3 540		0.94 (3 H, s, CH_3), 2.47 (1 H, s, OH), 4.45 (1 H, s, CH), 6.04 (1 H, s, N–OH), 6.88—7.62 (9 H, m, arom.)	
(6b)	131 [a]	$C_{16}H_{17}NO_2$	75.55 (75.27)	6.8 (6.71)	5.65 (5.48)	1 600 [h] 3 360		0.7 (3 H, s, CH_2CH_3, J = 7.1 Hz), 1.19 (2 H, m, CH_2CH_3), 2.33 (1 H, s, OH), 4.46 (1 H, s, CH), 6.03 (1 H, s, N–OH), 6.87—7.47 (9 H, m, arom.)	
(6c)	175 [a]	$C_{20}H_{17}NO_2$	78.95 (79.18)	5.5 (5.65)	4.85 (4.61)	1 600 [h] 3 490 3 520		2.59 (1 H, s, OH), 4.54 (1 H, s, CH), 5.47 (1 H, s, N–OH), 6.24—7.1 (14 H, m, arom.)	
(7a)	131 [d]	$C_{15}H_{13}NO$	80.0 (80.69)	5.9 (5.87)	6.25 (6.27)	1 605 [f] 3 420 [m]	232 (4.37) 304 (4.22) 212 (4.33)		223 (223)
(7c)	140 [d]	$C_{20}H_{15}NO$	83.9 (84.18)	5.25 (5.30)	4.85 (4.91)	1 605 [f] 3 340 [m]	228 (4.36) 252 (4.33) 308 (4.12)		285 (285)
(11a) [f]	83 [d]	$C_{17}H_{19}N$	86.4 (86.03)	8.05 (8.07)	5.8 (5.90)	1 605 [h] 3 340 [j]		1.18 (3 H, s, CH_3), 1.29 (3 H, d, CH_3, J = 7.0 Hz), 2.61 (2 H, AB q, CH_2Ph), 3.65 (1 H, q, CH, J = 7.0 Hz), 6.1—7.4 (10 H, m, arom. + NH)	
(12a)	Ref. 18							0.99 (3 H, d, CH_3, J = 7.0 Hz), 1.2 (3 H, s, CH_3), 3.0 (2 H, s, CH_2Ph), 4.21 (1 H, q, CH, J = 7.0 Hz), 6.1—7.4 (10 H, m, arom. + NH)	
(11b) [q]	Oil					1 610 [h] 3 375 [j]		0.78 (3 H, d, CH_3, J = 6.9 Hz), 1.77 (3 H, s, CH_3), 3.58 (1 H, broad, NH), 3.87 (1 H, q, CH, J = 6.9 Hz), 6.7—7.5 (9 H, m, arom.)	
(12b) [q]	Oil							1.15 (3 H, d, CH_3, J = 6.9 Hz), 1.45 (3 H, s, CH_3), 3.58 (1 H, broad, NH), 3.9 (1 H, q, CH, J = 6.9 Hz), 6.7—7.6 (9 H, m, arom.)	

[a] Benzene–light petroleum. [b] Ethyl acetate. [c] Benzene–ligroin. [d] Washed with Et_2O. [e] n-Heptane. [f] Ref. 18. [g] Nujol. [h] Ph–N–C. [i] >C=C–N–. [j] NH. [k] Ph–N=C–Ph. [l] OOH, broad. [m] OH. [n] EtOH. [o] M. Nakazaki, *Bull. Chem. Soc. Japan*, 1960, 461. [p] In CD_3COCD_3. [q] I.r. spectrum was recorded on the pure mixture of the two diastereoisomers. [r] Ref. 20.

titatively. In this case also, only one of the diastereoisomers has been isolated. The i.r. and ^{1}H n.m.r. spectra (Table 1) of compounds (6a—c) confirm their indoline structure. Compounds (6a—c) when treated under nitrogen with ethanol saturated with hydrogen chloride lose water to give the corresponding 1-hydroxyindoles (7a—c) of which (7a) and (7c) were isolated; their analyses are given in Table 1. The hydroxyindoles (7a—c) easily autoxidize in solution in air giving the initial 3-hydroxy-3*H*-indole *N*-oxides (5a—c); in fact in the case of (6b), only compounds (5b) was

isolated. The formation of compound (7b) was shown by e.s.r. spectroscopy (see later). We think that compounds (5a—c) come from hydroxyindoles (7a—c) by autoxidation which involves first the formation of hydroperoxides (as described previously for indoles) which give, as previously



SCHEME 1 Compounds: a, R = Me; b, R = Et; c, R = Ph. Reagents: i, $NaBH_4$ or $LiAlH_4$; ii, HCl + EtOH; iii, O_2

reported,[10] the 3-hydroxy-compounds (5a—c). The chemical and physical properties we report for the hydroxyindoles (7a) and (7c) differ from those reported in ref. 11. We have repeated the syntheses of those compounds described there, and have found the products, purified to constant m.p.s, to be the corresponding 3-hydroxy-3*H*-indole *N*-oxides, (5a) and (5c). We therefore consider that the compounds isolated by Hill and his co-workers [11] are mixtures of hydroxyindoles (7) and of the corresponding 3-hydroxy-compounds (5) formed by an autoxidation process. The hydroxyindoles (7a) and (7c) in air autoxidize giving quantitatively the corresponding 3-hydroxy-3*H*-indole *N*-oxides (5a) and (5c) (see Experimental section). The u.v. spectra of compounds (7a) and (7c) are particularly interesting: as seen in Figure 1, the spectrum of 1-hydroxy-2,3-diphenylindole (7c) is similar to that of the corresponding

for which the value of the coupling constant at the nitrogen (a^N *ca.* 6 G, Table 2) is consistent with the indole struc-

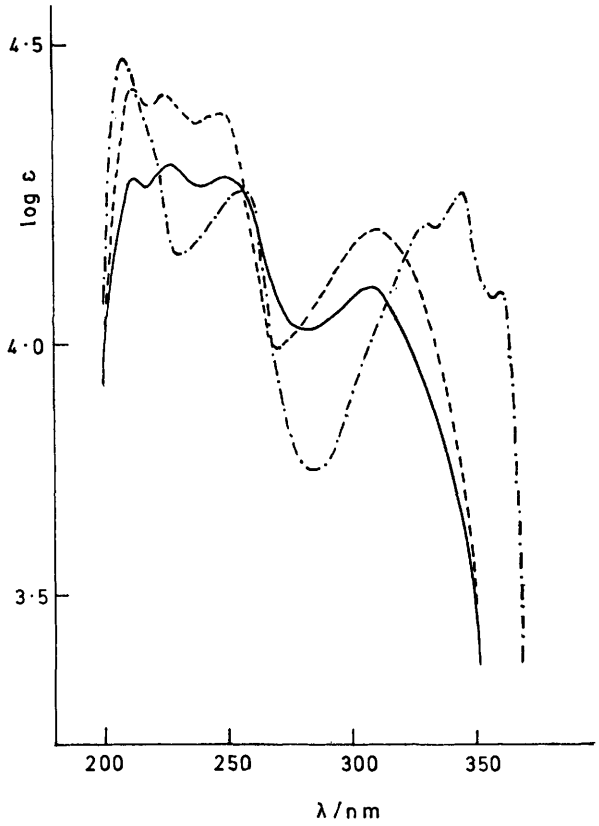
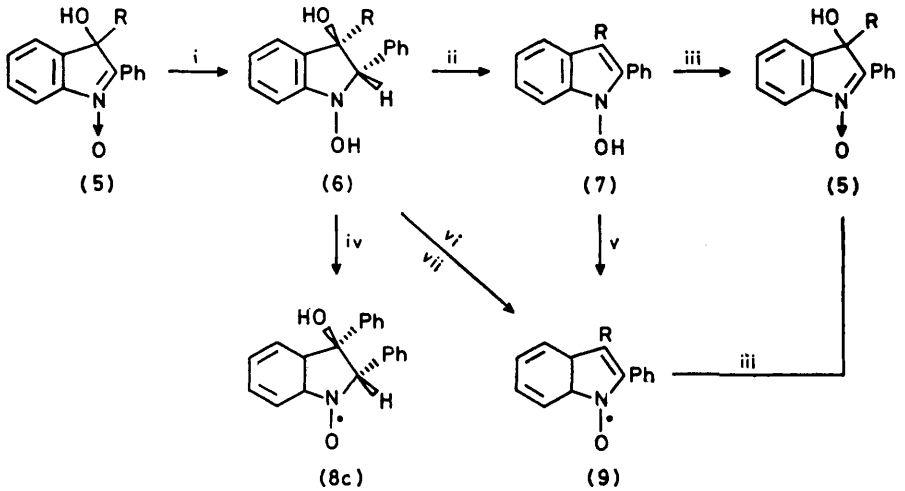


FIGURE 1 U.v. spectra: —— 1-hydroxy-2,3-diphenylindole (7c); – – – – 2,3-diphenylindole; —·—·— 3-hydroxy-2,3-diphenyl-3*H*-indole *N*-oxide (5c)

ture.[12,13] The same nitroxides have been obtained directly in the e.s.r. cavity by treatment of a chloroform solution



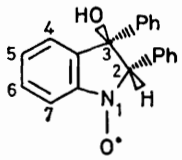
SCHEME 2 Compounds: a, R = Me; b, R = Et; c, R = Ph. Reagents: i, $NaBH_4$; ii, HCl + EtOH; iii, O_2; iv, choranil; v, PbO_2; vi, CF_3CO_2H–$CHCl_3$; vii, chloranil

2,3-diphenylindole but completely different from that of 3-hydroxy-2-phenyl-3H-indole *N*-oxide (5c). Oxidation of the hydroxyindoles (7a) and (7c) with PbO_2 gives the corresponding nitroxide radicals (9a) and (9c) (Scheme 2), of compounds (6a—c), acidified with trifluoroacetic acid, with chloranil (see Experimental section), while a chloroform solution of (6c) treated with chloranil in the e.s.r. cavity gives the nitroxide radical (8c) (Scheme 2). The structure

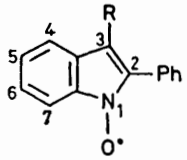
of the nitroxide radical (8c) is in agreement with the values of the observed coupling constants (Table 2 and Figure 2); the coupling constant a^N 10.5 g is in agreement with the indoline structure [14] and so the high value of the coupling constant (a^H 13.75; ref. 15) of the hydrogen at C-2 is justified. The nitroxide (8c) is rather unstable, as has been observed in other nitroxides having hydrogen α to the nitroxide functional group: [16] it was not possible to observe the e.s.r. signals of the possible nitroxides (8a) and (8b).

TABLE 2

Hyperfine coupling constants (in gauss) of the nitroxide radicals (8c) and (9a—c) *



(8c)



(9a—c)

Compound	R	a^N	$a^{H\cdot2}$	$a^{R\cdot3}$	$a^{H\cdot5} = a^{H\cdot7}$	$a^{H\cdot6} = a^{H\cdot8}$
(8c)		10.50	13.75 (1 H)		3.32 (2 H)	1.0 (2 H)
(9a)	Me	6.61		7.0 (3 H)	1.70 (2 H)	
(9b)	Et	6.00		4.11 (2 H)	1.87 (2 H)	
(9c)	Ph	6.00				

* All spectra were recorded in $CHCl_3$ solution.

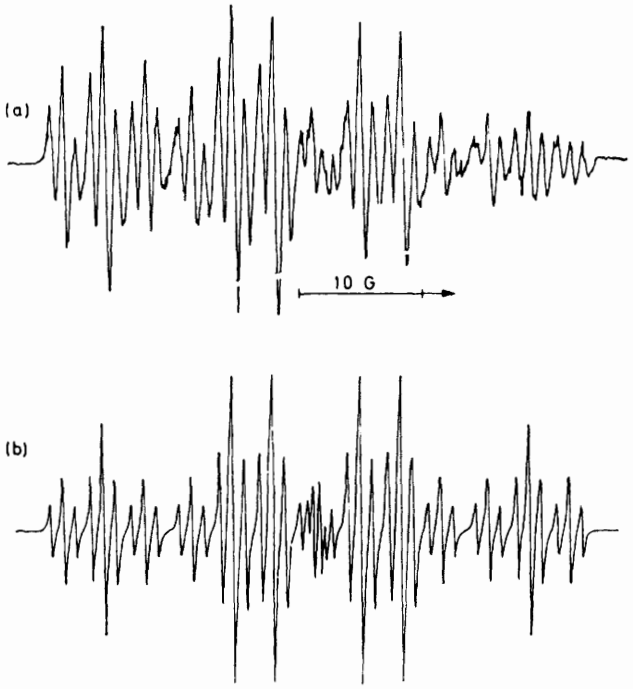


FIGURE 2 (a) E.s.r. first-derivative spectrum of nitroxide radical (8c); (b) calculated spectrum of (8c) with Lorentzian line width of 0.20 G.

Molecular Geometry of 3-Hydroxy-2,3-diphenylindoline.—Bond distances and angles are reported in Table 3 and a drawing of the structure showing the arbitrary crystallographic atom numbering scheme is shown in Figure 3. Bond distances are mainly as expected apart from small deformations within the pyrroline ring which are due to the overcrowding of the substituents. The conformation of the five-membered ring is intermediate between twist and envelope with the amplitude-phase puckering co-ordinates [17] Q 0.162 Å and ϕ 10.8°. The ring is thus rather flattened and the main deformations concern C(3) and C(4). The H and OH substituents are *cis*-pseudoaxial and -pseudoequatorial respectively. The torsion angles which define the orientation of the substituents at C(3) and C(4) are O(1)–C(4)–C(5)–C(6) −52.2(5), C(11)–C(4)–C(5)–C(6) 70.4(5), C(10)–N(2)–C(3)–H(3) −98.2(2.3), C(10)–N(2)–C(3)–C(17) 146.6 (4), C(10)–N(2)–C(3)–C(4) 15.7(5), and N(2)–C(3)–C(4)–C(5) −16.1 (4)°. A sub-structure similar to that of a substituted pyrroline has been found in 4-hydroxy-4,5-dimethyl-3,5-diphenylpyrrolidin-2-one [18] and 5-ethyl-5-hydroxy-1,4-dimethyl-Δ²-1,2,3-triazoline [19] where the configuration concerning the H and OH is *trans*-diaxial. The differences

TABLE 3

(*a*) Intermolecular distances (Å)

O(1)–C(4)	1.438(4)	C(11)–C(12)	1.384(5)
N(2)–C(3)	1.439(7)	C(11)–C(16)	1.378(5)
N(2)–C(10)	1.378(5)	C(12)–C(13)	1.402(6)
C(3)–C(4)	1.578(5)	C(13)–C(14)	1.373(7)
C(3)–C(17)	1.499(4)	C(14)–C(15)	1.365(7)
C(4)–C(5)	1.514(5)	C(15)–C(16)	1.388(6)
C(4)–C(11)	1.533(5)	C(17)–C(18)	1.367(6)
C(5)–C(6)	1.379(5)	C(17)–C(22)	1.381(5)
C(5)–C(10)	1.394(6)	C(18)–C(19)	1.396(7)
C(6)–C(7)	1.394(7)	C(19)–C(20)	1.362(9)
C(7)–C(8)	1.369(8)	C(10)–C(21)	1.354(9)
C(8)–C(9)	1.364(6)	C(21)–C(22)	1.362(7)
C(9)–C(10)	1.388(6)		

(*b*) Bond angles (°)

C(3)–N(2)–C(10)	111.0(6)	N(2)–C(10)–C(9)	129.5(8)
N(2)–C(3)–C(4)	104.9(5)	C(5)–C(10)–C(9)	120.1(6)
N(2)–C(3)–C(17)	113.6(5)	C(4)–C(11)–C(12)	119.2(4)
C(4)–C(3)–C(17)	118.5(4)	C(4)–C(11)–C(16)	121.7(4)
O(1)–C(4)–C(3)	109.1(4)	C(12)–C(11)–C(16)	119.1(5)
O(1)–C(4)–C(5)	113.1(4)	C(11)–C(12)–C(13)	119.7(5)
O(1)–C(4)–C(11)	107.6(4)	C(12)–C(13)–C(14)	120.3(6)
C(3)–C(4)–C(5)	101.1(4)	C(13)–C(14)–C(15)	119.9(6)
C(3)–C(4)–C(11)	113.0(4)	C(14)–C(15)–C(16)	120.4(5)
C(5)–C(4)–C(11)	113.0(4)	C(11)–C(16)–C(15)	120.7(5)
C(4)–C(5)–C(6)	129.4(6)	C(3)–C(17)–C(18)	119.7(5)
C(4)–C(5)–C(10)	109.9(5)	C(3)–C(17)–C(22)	121.7(5)
C(6)–C(5)–C(10)	120.7(5)	C(18)–C(17)–C(22)	118.6(5)
C(5)–C(6)–C(7)	118.6(7)	C(17)–C(18)–C(19)	120.5(7)
C(6)–C(7)–C(8)	119.9(6)	C(18)–C(19)–C(20)	119.1(7)
C(7)–C(8)–C(9)	122.3(6)	C(19)–C(20)–C(21)	120.7(7)
C(8)–C(9)–C(10)	118.4(7)	C(20)–C(21)–C(22)	120.3(6)
N(2)–C(10)–C(5)	110.4(5)		

(*c*) Bond distances involving hydrogen atoms

O(1)–H(1)	0.85(3)	C(14)–H(14)	1.03(5)
N(2)–H(2)	0.96(4)	C(15)–H(15)	1.03(4)
C(3)–H(3)	0.99(4)	C(16)–H(16)	1.00(5)
C(6)–H(6)	1.12(5)	C(18)–H(18)	0.87(4)
C(7)–H(7)	1.03(4)	C(19)–H(19)	0.96(5)
C(8)–H(8)	0.93(5)	C(20)–H(20)	0.94(5)
C(9)–H(9)	0.91(5)	C(21)–H(21)	1.00(5)
C(12)–H(12)	0.97(4)	C(22)–H(22)	1.01(4)
C(13)–H(13)	0.87(5)		

in the steric and electronic natures of the other substituents could be a factor which stabilizes one or other configuration. The orientation of the two phenyl groups is mainly determined by steric interactions and the dihedral angles they form with the mean pyrroline plane are 74.9 and 113.6° for

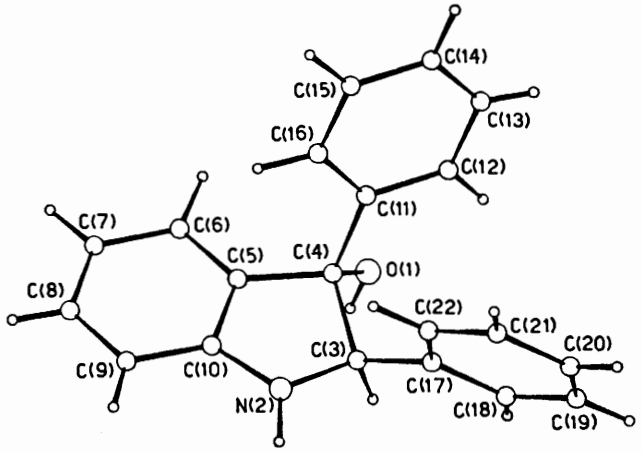


FIGURE 3 Projection of the molecule with the arbitrary numbering scheme used in the *X*-ray analysis

the rings containing C(11) and C(17) respectively. Steric effects are also responsible for the significant out-of-plane deviations of C(4) 0.034(4) and N(2) −0.053(6) Å from the indoline benzene ring.

A short O(1)...O(1′) (at $1-x, 1-y, 1-z$) contact of 2.896(8) Å suggests the presence of hydrogen bonding between the hydroxy-groups. The final ΔF map showed a significant residual peak of *ca.* 0.85(9) e Å^{-3} interpreted as being due to the hydrogen atom of the hydroxy-group which refined at a reasonable geometry: O(1)–H(1) 0.85(3) Å, C(4)–O(1)–H(1) 117.8(2)°. The angles C(4)–O(1) . . . O(1′)

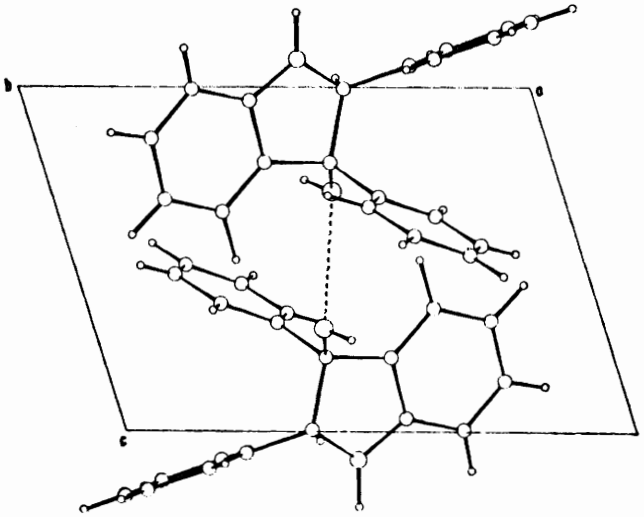
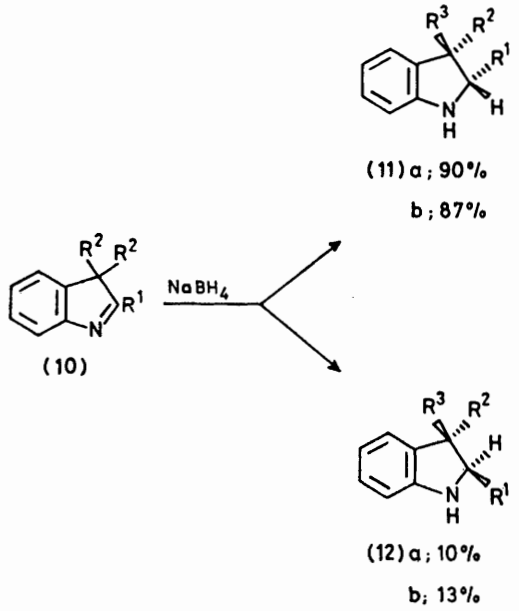


FIGURE 4 Projection of the structure on (0 1 0)

111.1 (4) and H(1)–O(1) . . . O(1′) 106.8 (9)°, which have close to tetrahedral values, suggests as geometrically possible the formation of dimers with one hydroxy-group pointing towards the hydrogen, along the dashed line of Figure 4, toward the centrosymmetric group whose hydrogen atom occupies the position given as H(1).

DISCUSSION

The *X*-ray analysis of compound (2c), confirming the stereospecificity of the reaction determined from the ^{1}H n.m.r. spectrum, shows that hydride ion attack has taken place on the same side of the hydroxy-group. This is not in agreement with previous reports [3,4] of $LiAlH_4$ reduction, which suggested that the reduction centres (C=O or C=N) undergo hydride attack on the opposite site with respect to the group containing a heteroatom with an unshared electron pair. Since we considered the stereospecificity of this reaction to be linked more to co-ordinative interactions between the hydroxy-group and $NaBH_4$ or $LiAlH_4$ than to steric or stability factors of the reaction products,[1b] we have attempted to verify this assumption by using different reduction methods. However, compounds (2a—c) lose water, leading to indoles (3a—c), so easily that all our attempts have been frustrated. In fact catalytic reduction of (2a—c) gives directly the corresponding indoles [20]



SCHEME 3 Compounds: a, $R^1 = R^3 = Me$, $R^2 = CH_2Ph$; b, $R^1 = R^3 = Me$, $R^2 = Ph$

and reduction with sodium in ethanol has not been possible because indolenines (1a—c) in alkaline medium undergo rearrangement.[9] In order to understand the role played by the hydroxy-group in making the reaction stereospecific, we have synthesized compounds (10a) and (10b) which are models similar to those under study and have no hydroxy-group α to the reduction centre. Compounds (10a) and (10b), when reduced with $NaBH_4$, give a mixture of two diastereoisomers (11a) and (12a) [21] and (11b) and (12b) respectively, whose ratio (Scheme 3) has been determined by ^{1}H n.m.r. spectroscopy (Figure 5), and whose formation stereochemistry depends upon the common factors which govern stereoselective reactions. The assignment of the structure of compounds (11) and (12) has been made on the basis of the proof reported by

Jackson and Smith [21] concerning diastereoisomers (11a) and (12a), which have been isolated (Table 1).

To sum up we think that the stereochemistry of the reduction reaction of compounds (1a—c) and (5a—c) with $NaBH_4$ or $LiAlH_4$ is determined by the presence of the hydroxy-group which influences, by a unimolecular mechanism according to the results of Cawley and his co-workers,[5] the formation of only one of the two possible diastereoisomers (2) and (6) (Schemes 1 and 2).

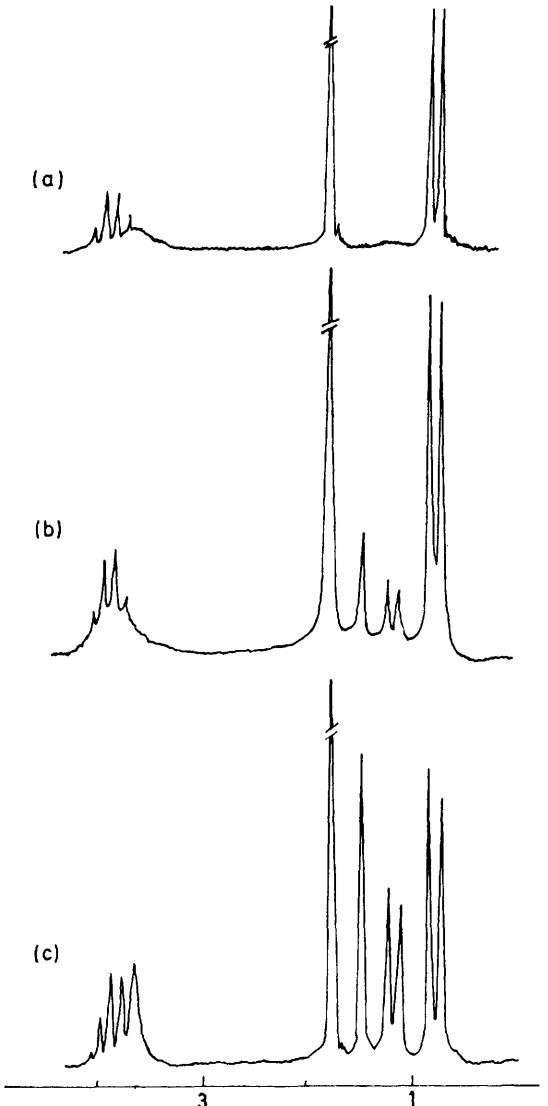


FIGURE 5 ^1H N.m.r. spectra of the diastereoisomeric 2,3-dimethyl-3-phenylindolines: (a) spectrum of pure (11b); (b) spectrum of the mixture of (11b) and (12b) obtained from the reduction of (10b); (c) spectrum of the mixture of (11b) and (12b) enriched in respect of (12b) by preparative t.l.c.

EXPERIMENTAL

I.r. spectra were recorded on Perkin-Elmer 257 spectrometer, and u.v. spectra on Perkin-Elmer 402 spectrometers. ^1H N.m.r. spectra were recorded on Perkin-Elmer R12 B and Varian FT 20 spectrometers (tetramethylsilane as internal standard). E.s.r. spectra were recorded on a Varian E4 apparatus. Compounds (1a—c),[22] (3a),[23] (5a—c),[24] (10),[21] and (13) [25] were prepared as described in the literature. Analytical and spectroscopic data are listed in Table 1.

Reduction of Indolenines (1a—c) *and the Corresponding* N-*Oxides* (5a—c) *by* $NaBH_4$.—$NaBH_4$ (2 g) was added to a solution of (1a—c) (3 mmol) in 50 ml of MeOH during 1.5 h at room temperature with stirring. After 2.5 h the reaction mixture was poured into 5% aqueous ammonium chloride and extracted with benzene. The organic layer was separated, dried (Na_2SO_4), and evaporated to dryness. The residue was recrystallized to give the indolines (2a) and (2c) in quantitative yields. *N*-Hydroxyindolines (6a—c) were obtained similarly from indolenine *N*-oxides (5a—c) Indoline (2b) was isolated as an oil, which rearranges easily to the corresponding indole (3b).

Reduction of the Indolenines (1a) *and* (2c) *by* $LiAlH_4$.—$LiAlH_4$ (300 mg) was added to (1a) or (1c) (250 mg) dissolved in tetrahydrofuran (20 ml) and the reaction mixture stirred for 2 h at room temperature. It was then poured into aqueous ammonium chloride (100 ml) and extracted with diethyl ether. The ethereal layer was separated, dried (Na_2SO_4), and evaporated to dryness; the ^1H n.m.r. spectrum of the residue showed the presence of either indoline (2a) or (2c); the residue was then recrystallized.

Indoles (3a—c) and N-*Hydroxyindoles* (7a—c) *from Indolines*.—Indolines (2a—c) (3 mmol) were dissolved in saturated with gaseous HCl at room temperature. After 2.5 h, the reaction solution was poured into 10% aqueous sodium hydrogen carbonate (100 ml) and extracted with benzene. The benzene layer was separated, dried (Na_2SO_4), and evaporated to dryness to give the indoles (3a—c) in quantitative yield. When the benzene solution was left in air for several hours, compounds (4a) and (4b) were also isolated. The *N*-hydroxyindoles (7a) and (7c) were obtained similarly from indolines (6a) and (6c) but under nitrogen. The residue from the benzene layer, was washed with ether, to give (7a) and (7c) in quantitative yield. Compounds (7a) and (7c) in solution undergo aerial autoxidation to give the corresponding 3-hydroxyindolenines (5a) and (5c); in the case of (6b) only (5b) was isolated.

Hydroperoxyindoles (4a) *and* (4b) *by Catalytic Oxidation*.—Compound (3a) or (3b) (6 mmol) and 10% Pt/C (400 mg) in benzene (30 ml) saturated with oxygen were stirred at room temperature for 3 days. Catalyst was filtered off and the filtrate evaporated to dryness giving hydroperoxyindoles (4a) or (4b) in quantitative yield.

3-*Hydroxyindolenine* N-*Oxides* (5a) *and* (5c) *by Autoxidation of* N-*Hydroxyindoles* (7a) *and* (7c). Either compound (7a) or (7c) (3 mmol) in benzene (20 ml) was stirred at room temperature for 12 h to give either (5a) or (5c); each was obtained in quantitative yield upon recrystallization.

Nitroxide Radicals (9a—c).—Nitroxide radicals (9a—c) were obtained in the e.s.r. cavity of a cell similar to that described by Russel.[26] Trifluoroacetic acid (2 ml; 4% v/v) in chloroform was placed in one leg of an inverted U cell, and the indoline (6a—c) (0.05 mmol) and chloranil (0.002 5 mmol) in the other. The chloroform solution, degassed with nitrogen, was allowed to mix with the indoline and chloranil, after which mixture was transferred to the e.s.r. cell; the latter was then placed in the e.s.r. cavity. All e.s.r. spectra corresponding to nitroxide radicals (9a—c) were easily recorded by this procedure. The nitroxide radicals (9a) and (9c) were also obtained from chloroform solutions of (7a) and (7c) respectively, by oxidation with

PbO_2. Hyperfine coupling constants are recorded in Table 2.

Nitroxide Radical (8c).—Compound (6c) (3.3 mg) in chloroform (1 ml) and chloranil (2.75 mg) in chloroform (1 ml) were each placed in the two legs of the inverted U cell already described. The two solutions, degassed with nitrogen, were mixed and from the new solution the e.s.r. spectrum of the nitroxide radical (8c) was recorded. Hyperfine coupling constants are recorded in Table 2.

Reduction of the Indolenines (10a) *and* (10b) *by* $NaBH_4$.—The reactions were carried out as already described, using the same quantities and the same procedure. From (10a) an oily mixture of two diastereoisomers (11a) (90%) and (12a) (10%) was isolated as described by Jackson [21] and the ratio was determined by ^1H n.m.r. integration. Diastereoisomer (11a) was also isolated by SiO_2 preparative t.l.c. using cyclohexane–ethyl acetate 95 : 5 as the eluant (Table 1). From (10b) an oily mixture of the two diastereoisomers (11b) (87%) and (12b) (13%) was obtained. Isomer (11b) was isolated by chromatography (see earlier) as a pure oil which could not be crystallized owing to its high solubility in all organic solvents. By chromatography a mixture enriched in isomer (12b) (the minor product) was isolated (Figure 5). Both indolenines (10a) and (10b) were hydrogenated quantitatively.

TABLE 4

Fractional co-ordinates ($\times 10^4$ for non-hydrogen atoms and $\times 10^3$ for hydrogen) with standard deviations in parentheses

	x/a	*y/b*	*z/c*
O(1)	4 501(2)	4 950(2)	6 990(3)
N(2)	4 372(4)	2 731(6)	10 819(6)
C(3)	3 650(3)	3 547(4)	9 951(5)
C(4)	4 364(3)	3 578(3)	7 818(4)
C(5)	5 643(3)	3 098(3)	7 830(5)
C(6)	6 770(3)	3 109(4)	6 394(6)
C(7)	7 822(4)	2 576(5)	6 752(7)
C(8)	7 720(4)	2 057(4)	8 500(8)
C(9)	6 619(4)	2 054(4)	9 941(8)
C(10)	5 563(3)	2 581(4)	9 605(5)
C(11)	3 624(3)	2 657(3)	6 822(4)
C(12)	2 630(3)	3 144(4)	6 275(5)
C(13)	1 913(4)	2 294(5)	5 427(6)
C(14)	2 186(4)	980(5)	5 152(6)
C(15)	3 162(4)	500(4)	5 701(6)
C(16)	3 878(3)	1 332(4)	6 543(5)
C(17)	2 215(3)	3 133(3)	10 635(4)
C(18)	1 391(4)	4 108(5)	11 092(6)
C(19)	52(5)	3 742(7)	11 724(7)
C(20)	−423(5)	2 399(8)	11 895(7)
C(21)	388(5)	1 427(6)	11 453(6)
C(22)	1 695(4)	1 782(4)	10 828(5)
H(1)	497(3)	556(3)	733(4)
H(2)	410(4)	253(4)	1 218(5)
H(3)	374(3)	450(4)	1 027(5)
H(6)	680(4)	355(4)	500(6)
H(7)	868(4)	261(4)	571(5)
H(8)	847(4)	176(4)	866(5)
H(9)	652(4)	177(4)	1 113(6)
H(12)	244(3)	407(3)	647(4)
H(13)	129(4)	269(4)	519(5)
H(14)	166(4)	35(4)	453(6)
H(15)	344(4)	−46(4)	546(2)
H(16)	461(4)	96(5)	687(5)
H(18)	173(4)	495(4)	1 096(5)
H(19)	−53(5)	443(5)	1 201(6)
H(20)	−132(5)	213(4)	1 231(6)
H(21)	1(4)	45(5)	1 163(6)
H(22)	230(4)	106(4)	1 052(5)

X-*Ray Structure Analysis of* 3-*Hydroxy*-2,3-*diphenylindoline* (2c).—Crystals were obtained as colourless prisms from benzene–light petroleum. Preliminary cell dimensions and symmetry informations were obtained from rotation and Weissenberg photographs. Lattice parameters were refined by least-squares by use of fourteen $(\theta,\chi,\phi)_{hkl}$ measurements taken on a Siemens single-crystal diffractometer.

Crystal data. $C_{20}H_{17}NO$, $M = 287.4$. Triclinic, $a = 10.873(5)$, $b = 9.879(5)$, $c = 7.619(5)$ Å; $\alpha = 86.78(5)$, $\beta = 72.80(5)$, $\gamma = 95.45(5)°$; $U = 775.1$ Å^3, $Z = 2$, $D_c = 1.23$ g cm^{-3}. Cu-K_α radiation, $\bar{\lambda} = 1.541\,8$ Å; μ(Cu-K_α) = 5.1 cm^{-1}. Space group $P\bar{1}$ from structure determination.

Intensity data were collected up to θ 70° by use of the ω—2θ scan method and the five-points technique [27] with nickel-filtered Cu-K_α radiation on a Siemens AED single-crystal diffractometer. Of 2 927 independent reflections measured 656, having intensities $I \leqslant 2\sigma(I)$, were not used in the crystal analysis. The crystal used had dimensions *ca.* 0.31 × 0.52 × 0.62 mm in the *x*, *y*, *z* directions, respectively. No absorption correction was applied.

Structure analysis and refinement. The structure was solved by direct methods by use of the SHELX system of computer programs.[28] An *E* map computed using 433 reflections with $|E| > 1.2$ revealed the position of all non-hydrogen atoms in the molecule. A structure-factor calculation based on the co-ordinates derived from the *E* map at this stage gave *R* 0.20. Refinement was carried out by several cycles of full-matrix least-squares first with isotropic and then with anisotropic thermal parameters reducing *R* to 0.10. A difference-Fourier synthesis revealed significant peaks near the positions where the hydrogen atoms were expected to occur. Further least-squares cycles were then computed, including the hydrogen atoms with isotropic thermal parameters, which gave a final *R* index of 0.065.

Final positional parameters together with their standard deviations are given in Table 4.

Atomic scattering factors used throughout the calculations were from ref. 29 for non-hydrogen atoms and from ref. 30 for hydrogen.

Thermal parameters and observed and calculated structure factors are listed in Supplementary Publication SUP 22642 (9 pp).*

All the calculations were carried out on a CDC Cyber 76 at the Consorzio per la Gestione del Centro di Calcolo Interuniversitario dell'Italia Nord-Orientale, Casalecchio, Bologna (Italy).

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