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1-(3-METHYL-2-INDOLYL)PYRIDINIUM BROMIDE
SYNTHESIS AND AUTO-OXIDATION OF ITS CATALYTIC HYDROGENATION PRODUCT

T. HINO and M. NAKAGAWA
Department of Pharmaceutical Sciences,
National Institute of Radiological Sciences, Anagawa, Chiba-shi
T. WAKATSUKI, K. OGAWA and S. YAMADA
Faculty of Pharmaceutical Sciences, University of Tokyo, Hongo, Tokyo, Japan

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Abstract—1-(3-Methyl-2-indolyl)pyridinium bromide (I) was prepared by the bromination of skatole with dioxan–dibromide in dioxan in the presence of pyridine. The compound (I) gave II on catalytic hydrogenation. The free base of II was unstable and easily autoxidized to the 3-hydroxy compound IV. The mechanism of the formation of I is discussed.

THE bromination of indoles with N-bromosuccinimide (NBS) has been reported.[1-3] Indole and 3-alkylated indoles, with one mole of NBS under anhydrous conditions yield 3-bromoindole and 2-bromo-3-alkylindoles respectively. In contrast, oxindole derivatives are obtained in a solvent containing a small amount of water. The reaction of 3-alkylindoles with two moles of NBS in t-butanol yield 3-bromooxindole derivatives and in aqueous media 5-bromooxindoles are formed. The bromination of indole itself with dioxan-dibromide[4-6] or pyridinium bromide hydrobromide[5] has been reported to furnish 3-bromoindole.

During the course of the studies on indoles,[7] in an attempt to brominate skatole an unexpected product (I), m.p. 257–258°, which was neither a simple brominated skatole nor an oxindole derivative, was obtained in quantitative yield when skatole in dioxan was treated with an equimolar amount of dioxan–dibromide in the presence of an excess pyridine.

The structure of this compound was confirmed as I by the following facts: The compound (I) gave 3-methyloxindole on hydrolysis with hydrobromic acid and gave skatole and piperidine hydrobromide on the catalytic hydrogenation over Adams' catalyst. The NMR spectrum of I in heavy water showed a singlet for the methyl group at 2·36 ppm and multiplets for aromatic protons at between 7·15 to 8·89 ppm. The methyl signal appeared at 2·38 ppm in deuterochloroform and this value was close to the chemical shift of the methyl group in skatole, indicating an indolic structure in I.

During the course of this work, Kobayashi[8] reported that skatole with NBS in the presence of pyridine yielded a quaternary salt to which he assigned the same

[1] W. B. Lawson, O. Patchornik and B. Witkop, *J. Amer. Chem. Soc.* **82**, 5918 (1960); W. B. Lawson and B. Witkop, *J. Org. Chem.* **26**, 263 (1961).
[2] R. L. Hinman and C. P. Bauman, *J. Org. Chem.* **29**, 1206 (1964).
[3] T. Kobayashi and N. Inokuchi, *Tetrahedron* **20**, 2055 (1964).
[4] L. A. Yanowskaya, *Dolk. Akad. Nauk, SSSR* **71**, 693 (1950), *Chem. Abstr.* **44**, 8354.
[5] K. Piers, G. Meimaroglow, R. V. Jardine and R. K. Brown, *Canad. J. Chem.* **41**, 2399 (1963).
[6] M. Kunori, *Nippon Kagaku Zasshi* **83**, 836 (1962).
[7] T. Hino and S. Yamada, *Tetrahedron Letters* 1757 (1963).

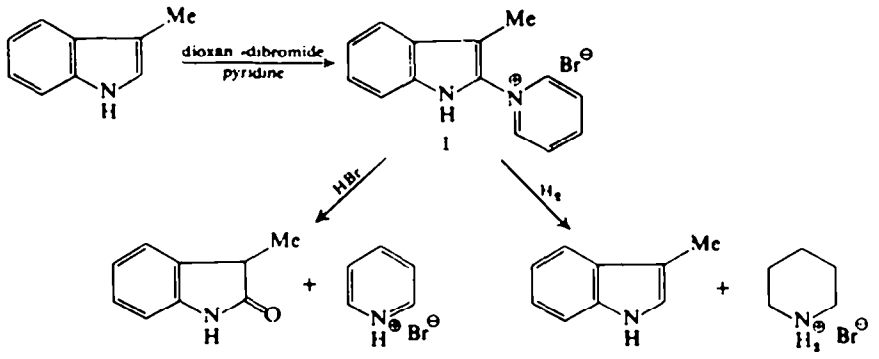

Chart I

structure I. Identity of his compound, prepared by our hands, with ours was confirmed by the direct comparison.

The catalytic hydrogenation of I over Adams' catalyst proceeded rapidly at room temperature until the uptake of three moles of hydrogen. TLC of the crude reaction mixture as well as its NMR spectrum showed the presence of skatole and piperidine hydrobromide besides the other hydrogenated products. The yield of skatole and piperidine hydrobromide was increased to 44% when the hydrogenation was carried out until the hydrogen uptake apparently ceased. However, skatole was scarcely detected by TLC or in the NMR spectrum of the crude reaction mixture obtained on the hydrogenation of I over Pd–C. To isolate the hydrogenated product, the crude mixture obtained by the hydrogenation of I over Adams catalyst was taken up in water and extracted with benzene to remove skatole. The aqueous solution was basified with sodium hydrogen carbonate and extracted with methylene chloride. A compound, m.p. 206–207°, was obtained from the extract in high yield, and its structure was confirmed as IV by the spectral data and the chemical evidence as well as elemental analysis. The IR spectrum of IV (KBr) showed strong bands at 1565 and 1555 cm^{-1} due to the C=N double bond and a medium band at 1095 cm^{-1} corresponding to C—O stretching vibration. The presence of an OH group was confirmed by a broad absorption band at about 3060 cm^{-1} in a solid phase and by a sharp band at 3580 cm^{-1} in a dilute solution.

The NMR spectrum of IV is shown in Fig. 1. The signal for nine protons corresponding to one methyl group and three methylenes in the piperidine ring appeared at 1·58 ppm as a broad singlet and the signals at about 3·55 ppm have been assigned to four protons in α-position of the piperidine ring, and four aromatic protons appeared at 6·90–7·25 ppm.

In order to prove the position of the OH group in IV, the latter was hydrolysed by heating with 10% aqueous sodium hydroxide to furnish 3-hydroxy-3-methyloxindole (VI) in low yield, which was raised to 70% when IV in methylene chloride was filtered slowly through an alumina column. The compound IV was found to be identical in all respects with an authentic sample,[8,9] prepared from isatin and methylmagnesium iodide.

[8] M. Kohn and A. Ostersetzer, *Monatsh.* 32, 905 (1911); E. Giovannini and J. Rosales, *Helv. Chim. Acta* 46, 1338 (1963).

[9] H. H. Wasserman and M. B. Floyd, *Tetrahedron Letters* 2009 (1963).

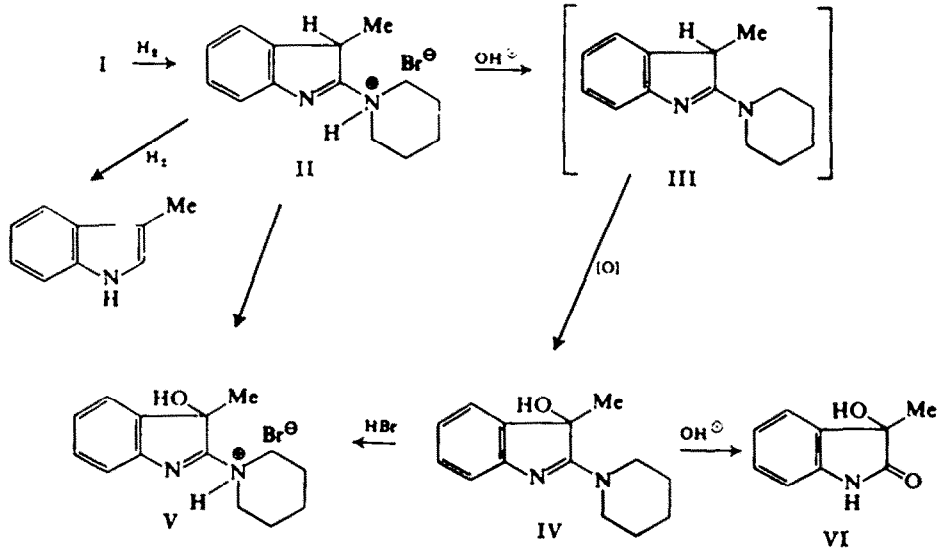

Chart 2

The conclusive evidence of the molecular formula and the presence of skatole and piperidine moieties was provided from the mass spectrum (Fig. 2) beside elemental analysis. The fragmentation pattern for the main peaks of this compound could be suggested as shown in Chart 3.*

The same structure as IV was proposed[10] for the compound obtained by the reaction of piperidine with the intermediate in the oxidation of skatole with NBS. Although the m.p. and other preperties were not reported the UV spectrum was very close to that of ours.

Introduction of an OH group into 3-position of indole to form IV during the hydrogenation of I appeared remarkable. As the introduction of an OH group

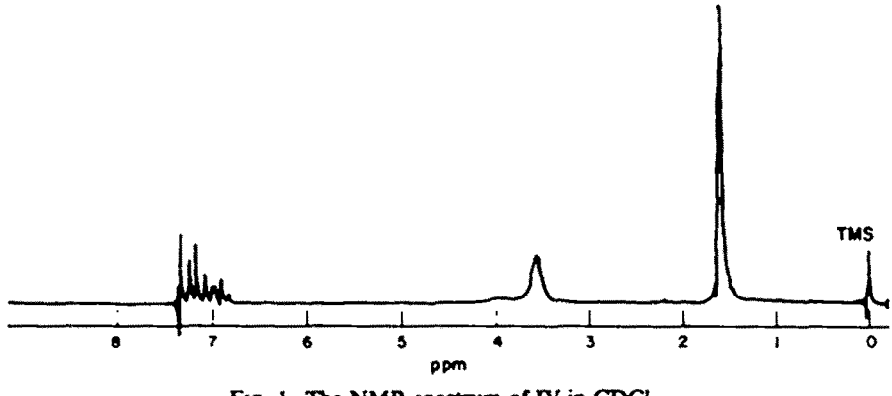

FIG. 1. The NMR spectrum of IV in $CDCl_3$.

* The structures of *m/e* 187 and 146 in Chart 3 are revised by the suggestion of the referee to whom the authors thanks are due.

[10] N. M. Green and B. Witkop, *Trans. N.Y. Acad. Sci.* **26**, 659 (1964).

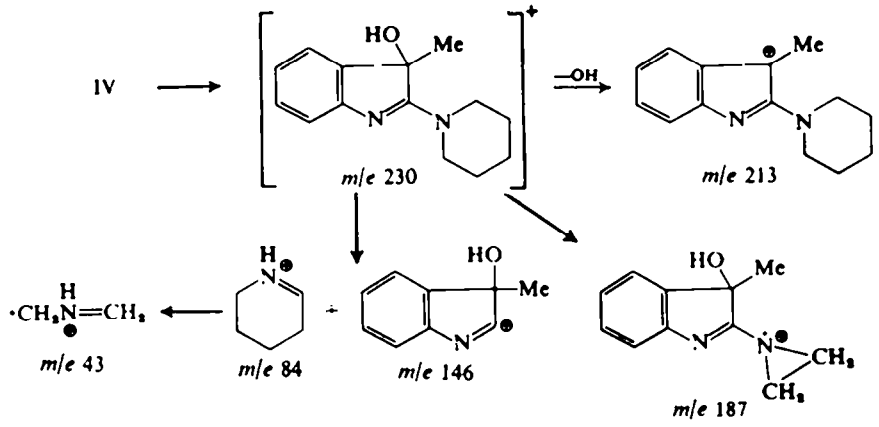

Chart 3

during the catalytic hydrogenation was unlikely, the hydrogenation product was isolated as a hydrobromide directly from the reaction mixture without using a base.

Attempted isolation of the hydrogenation product by crystallizing the crude reduction product from various solvents invariably gave only tarry substances. When, however, the crude product was covered with benzene for some time, followed by recrystallization of the deposit from water, compound II, m.p. 188–189° was

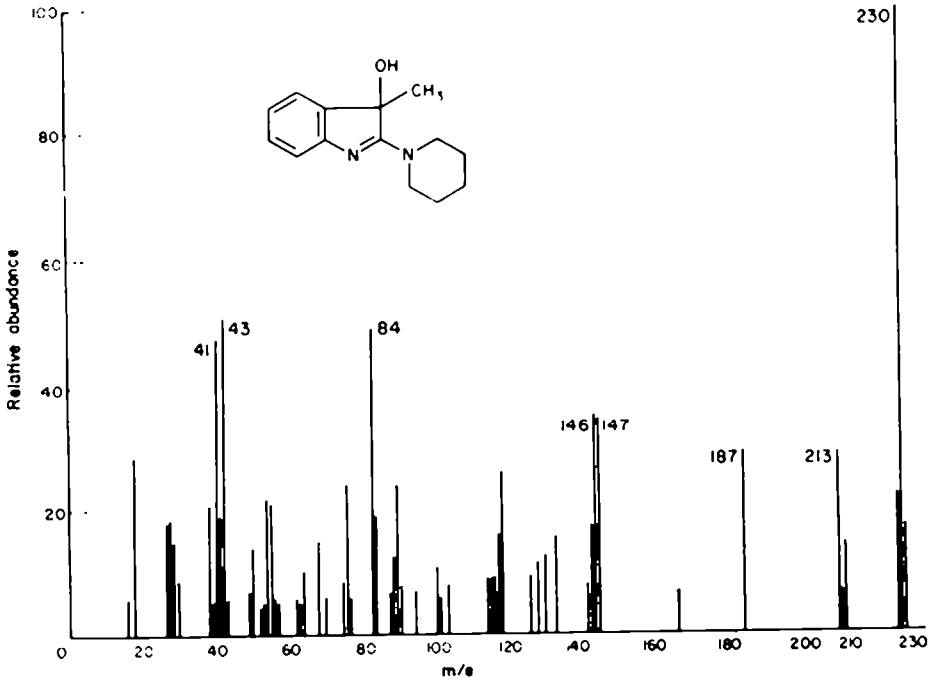

FIG. 2. The mass spectrum of IV.

obtained in 60% yield. The mother liquor furnished IV in 30% yield on being basified.[11]

The spectrum of compound II was not identical with that of the hydrobromide V, m.p. 233–235°, prepared from IV. Absence of the OH group at 3-position of the indole in II was proved by the NMR spectrum in deuterochloroform (Fig. 3) which showed a doublet at 1·56 ppm (J = 7 c/s) corresponding to the Me group and a quartet at 4·32 ppm (J = 7 c/s) corresponding to the hydrogen at 3-position.[12] Furthermore, a comparison of the mass spectra of both hydrobromides of II and V showed that molecular ion peaks of both compounds were observed at *m/e* 214 and 230 respectively as base peaks, corresponding to those of the free bases and peaks of *m/e* 84 and 43 were observed as common peaks. A strong peak at *m/e* 146 in V was not prominent in II, instead *m/e* 130 which was 16 mass unit lower was prominent in II. This fact suggested that the difference between the two compounds was only due to the OH group in V. These facts suggest that the OH group at 3-position in IV was not introduced during the hydrogenation but after or during the work up by air oxidation. The possibility of hydroxylation with a hydroxide ion was excluded by the fact that only IV and not the ethoxylated compound was obtained, when II was treated with sodium ethoxide in anhydrous ethanol.

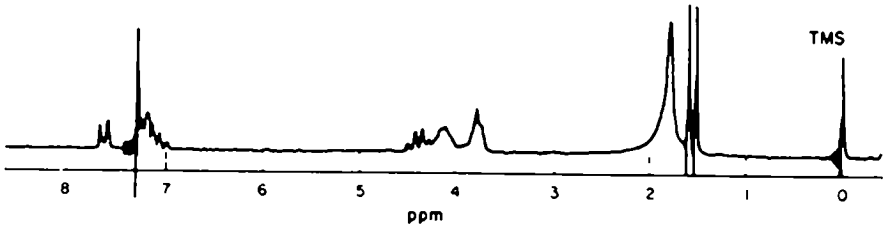

FIG. 3. The NMR spectrum of II in $CDCl_3$.

The first evidence for air oxidation came from an observation of the UV spectral change of II to that of IV when air was passed into the solution of II in ethanolic sodium hydroxide as shown in Fig. IV. The spectrum of II in ethanolic sodium hydroxide did not change on standing at room temperature for 6 hr, but on passing air into the solution the curve gradually changed to that of IV during 4 hr. In an attempt to isolate III a solution of II in methylene chloride was basified with triethylamine but the only product found was IV. It was considered that working up with an organic solvent had offered suitable conditions for the oxidation of III. Therefore, II was basified with sodium hydroxide in an aqueous solution under ice-cooling and the solution was decanted from a separated oil, which was rapidly washed with water, dried and its NMR spectrum taken in deuterochloroform. The

[11] The NMR spectrum of the crude product was nearly the same as that of II, suggesting the main hydrogenation product was II. However, the hydroxylated compound V was obtained when the crude product was shaken with a mixture of benzene and water and the aqueous layer was evaporated and the resulting residue chromatographed over silica gel (experimental).

[12] In heavy water the Me signal of II appeared at 1·54 ppm as a triplet having an intensity equal to that by which the quartet at 4·32 ppm had been decreased. This feature could be explained by the partial deuteration of the hydrogen at 3-position, since only a doublet was observed at 1·54 ppm in the spectrum taken in water.

oil was shown to contain the expected free base III as the major component accompanied with IV. Compound III had the expected doublet at 1·55 ppm (J 7 c/s) and a quartet at 4·36 ppm (J 7c/s), indicating the presence of the CH_3CH—group (Fig. 5). The NMR spectrum of the oil after standing in an open air indicated that the doublet for the methyl group had decreased as well as that of the quartet. Accordingly, it became clear that the base III was very susceptible to air oxidation. Although no attempt was made to purify it further due to its instability, its presence as the intermediate to form IV has been demonstrated.

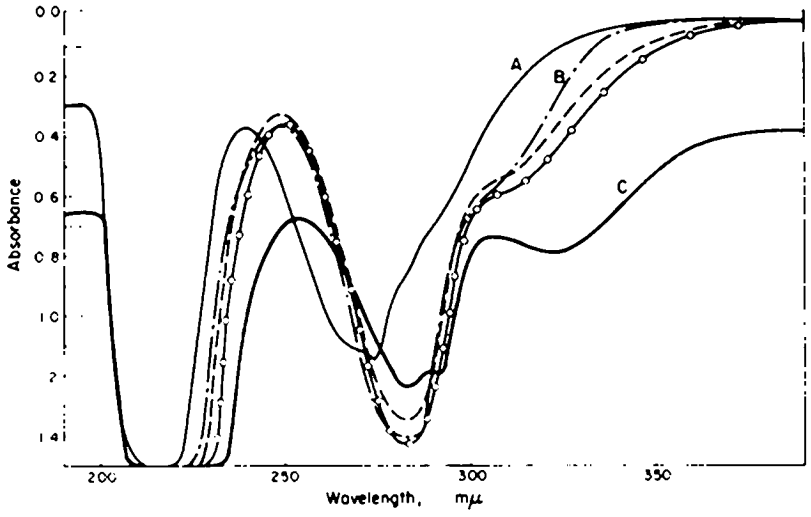

FIG. 4. Air oxidation of III
A: The UV spectrum of II in EtOH.
B: The UV spectrum of II in EtOH–NaOH.
C: The UV spectrum of IV in EtOH;
– – – The UV spectrum of II in EtOH–NaOH after 30 min air oxidation.
– o – The UV spectrum of II in EtOH–NaOH after 1 hr air oxidation.

It was shown by NMR spectroscopy that the salt II in heavy water or in ethanol at room temperature is stable to air oxidation without formation of V.

The autoxidation of 2,3-disubstituted indoles has been reported[9,13–15] to proceed via indolenine-3-hydroperoxide as the intermediate. Therefore, in the present case, IV would be formed from a hydroperoxide of III, though this could not be isolated.

As 3-methyl-2-bromoindole is obtained from skatole and NBS in acetic acid, it was first thought that the intermediate in the formation of I might be 3-methyl-2-bromoindole. However, 3-methyl-2-bromoindole[8] proved to be stable toward bases and the reaction with pyridine did not take place either in dioxan under cooling or at an elevated temperature without solvent. In fact the reaction did not take place

[13] B. Witkop, J. B. Patrick and M. Rosenblum, *J. Amer. Chem. Soc.* 73, 2641 (1951).
[14] E. Leete, *J. Amer. Chem. Soc.* 83, 3645; F. Y.-H. Chen and E. Leete, *Tetrahedron Letters* 2013 (1963).
[15] W. I. Taylor, *Proc. Chem. Soc.* 247 (1962); B. Robinson, *Chem. & Ind.* 1291 (1962); *J. Chem. Soc.* 586 (1963).

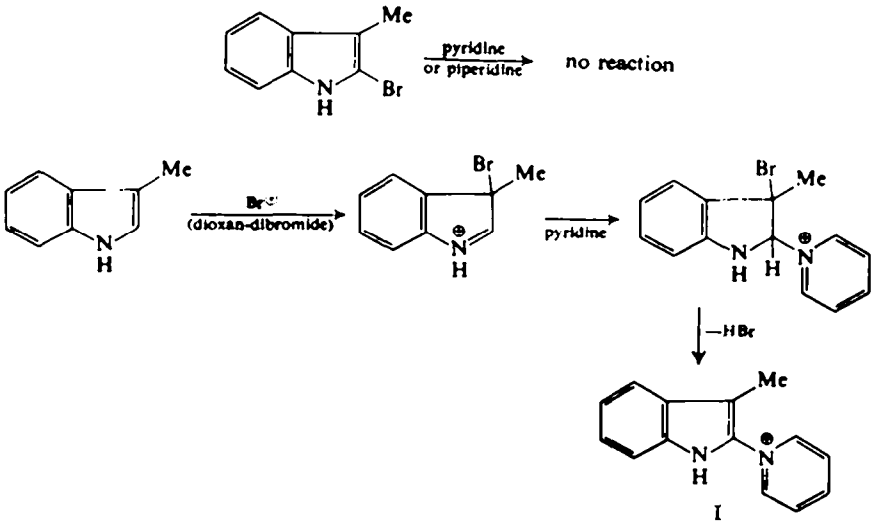

Chart 4

under any working conditions even with more nucleophilic piperidine. The mechanism for the reaction of skatole and dioxan–dibromide in the presence of an excess pyridine may, therefore, be proposed as shown in Chart 4. The mechanism is similar to that proposed for the bromination of indoles with NBS.[3]

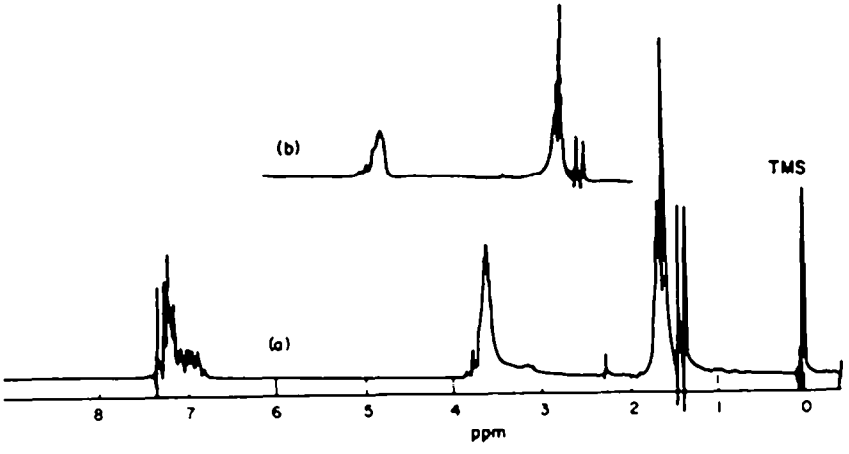

Fig. 5. a: The NMR spectrum of III (crude product; immediately after isolation).
b: The NMR spectrum of III (after standing in an open air).

EXPERIMENTAL[10]

1-(3-Methyl-2-indolyl)pyridinium bromide (I)

(i) *With dioxan–dibromide.* A soln of 6·5 ml (0·12 mole) Br_2 in 250 ml dioxan was added dropwise over a period of 2·5 hr to a stirred soln of 16·5 g (0·12 mole) skatole in 65 ml pyridine and 150 ml

[10] All m.ps are uncorrected. The IR spectra were taken with a JASCO-DS-301 spectrophotometer; UV spectra with a Cary Model 14 or Perkin–Elmer 202 spectrometer, and NMR spectra with a Varian Associates HR-100 spectrometer. The chemical shifts were expressed by the δ-values in ppm from internal standards, TMS in organic solvents and DSS in heavy water.

dioxan at 0–3° under a stream of N_2. The soln was allowed to warm up to 25–27° and the stirring continued for 2 hr. The yellow ppt was filtered off, washed with 1 l. dioxan, and dried *in vacuo* at 50°. Recrystallization from 1·5 l. EtOH gave 3 crops of I as yellow needles, (33·6 g; 97%), m.p. 243–244° (dec.). Additional recrystallizations from EtOH raised the m.p. to 257–258°. The IR, UV, NMR spectra and *Rf* value on TLC were identical with those of the sample made by the Kobayashis procedure and no depression was observed in a mixed m.p. with the specimen prepared in (ii). UV λ_{max}^{EtOH} mμ (log ε) 253 (4·08), 355 (3·76). IR ν_{max}^{KBr} cm^{-1} 1630, 1480, 1455, 775, 765, 755 (indole and pyridinium). NMR (in D_2O, ppm from DSS) 2·36 (s, CH_3), 7·15–8·87 (m, aromatic H). (Found: Cl, 57·78; H, 4·31; N, 9·69; Br, 27·71. Calc. for $C_{14}H_{12}N_2Br$: Cl, 58·14; H, 4·53; N, 9·69; Br, 27·64%.) The chloride was prepared from the bromide using an ion exchange resine (Amberlite-400 Cl form) in EtOH, yellow needles, m.p. 261–262·5° (dec). (Found: C, 68·76; H, 5·41; N, 11·14; Cl, 14·57. Calc. for $C_{14}H_{13}N_2Cl$: C, 68·78: H, 5·35; N, 11·45; Cl, 14·49%.)

Upon basification with NaOHaq, I in water afforded red needles which were very susceptible to air oxidation and could not be isolated as a crystalline form, but only as a dark-colored oil.

(ii) *With NBS.*[8] To a stirred soln of 790 mg skatole and 640 mg pyridine in 16 ml anhyd. dioxan was added in a small portion 1·076 g NBS at 12–15°. The yellow ppt of I was collected, washed with dioxan and then ether, and dried *in vacuo* (1·47 g; 84%) m.p. 211–219°. Recrystallizations from EtOH–ether gave yellow needles, m.p. 257–258° (dec) (reported m.p. 230° [8]).

Hydrolysis of I *with* HBr: *Formation of* 3-*methyloxindole*

A soln of 500 mg of I in 15% HBr was refluxed for 10 hr. The reaction mixture was extracted with benzene several times. The benzene extracts were washed with water, dried and evaporated *in vacuo*. The residue (100 mg, 40%) was recrystallized from toluene–hexane to give 3-methyloxindole as colorless needles, m.p. 119–120°. The sample showed no depression of the m.p. on admixture with the authentic specimen prepared from skatole.[17] The IR spectra of both samples were superimposable. The aqueous soln was concentrated to dryness leaving 230 mg (83%) pyridine HBr which was recrystallized from EtOH–ether, m.p. 223–224°, and showed no depression of the m.p. on admixture with an authentic specimen. The IR spectra of both samples were superimposable.

3-*Hydroxy*-3-*methyl*-2-*piperidino*-3H-*indole* (IV)

A soln of 5·8 g of I in 230 ml anhyd. EtOH was hydrogenated over 620 mg PtO_2. After H_2 up-take ceased (ca. 4·5 moles) the catalyst and the solvent were removed. The residue (6·4 g) was taken up in warm water and washed with benzene. The benzene layer was evaporated to dryness leaving 780 mg skatole. The aqueous soln was made alkaline with $NaHCO_3$aq at below 0°, giving an oil which was extracted with methylene chloride, and dried. The residue (3·1 g) obtained on evaporation of methylene chloride was crystallized from acetone to give 2·46 g (60%) of IV, colorless needles, m.p. 202–205°. Recrystallizations from acetone gave m.p. 206–207°. UV λ_{max}^{EtOH} mμ (log ε): 317 (3·82), 289 (4·13), 280 (4·14) 224 (4·30); λ_{min}^{EtOH} 302 (3·75), 248 (3·23). IR ν_{max}^{KBr} cm^{-1} 3060 (broad, OH) 1565, 1555 (C=N), 1095 (C—O), 755 (*o*-disubstituted benzene); ν_{max}^{chf} cm^{-1} 3580, 3200 (OH). NMR (Fig. 1). Mass spectrum (Fig. 2). (Found: C, 73·25; H, 7·55; N, 11·99. Calc. for $C_{14}H_{18}N_2O$: C, 73·01; H, 7·88; N, 12·17%.)

3-*Hydroxy*-3-*methyl*-2-*piperidino*-3H-*indole hydrobromide* (V)

(i) *From* IV. The hydrobromide V was prepared by adding an ethanolic HBr solution to the free base IV in EtOH, colorless needles, m.p. 233·5–235·5° (recrystallized from EtOH–ether). (Found: C, 53·72; H, 6·01; N, 9·17; Br, 26·01. Calc. for $C_{14}H_{19}N_2OBr$: C, 54·02; H, 6·15; N, 9·00; Br, 25·68%.) UV λ_{max}^{EtOH} mμ (ε) 292 (7000), 278 (8700), 224 (18500); λ_{min} 287 (6600) 244 (2200). IR ν_{max}^{KBr} cm^{-1} 3230 (OH), 1670 (C=N). NMR (in $CDCl_3$ ppm from TMS): 1·68 (s, broad, 9H, CH_3 and three β and γ methylenes in the piperidine), 3·61–4·41 (m, 4H, α-methylene in the piperidine), 7·06–8·23 (m, aromatic H).

(ii) *Direct isolation from the hydrogenation products of* I. A soln of 6·0 g of I in 250 ml EtOH was hydrogenated over 700 mg of PtO_2 for 17 hr until H_2 uptake ceased (ca. 4·5 moles). Filtration and evaporation of the solvent yielded 6·3 g of a residue which was taken up in warm water. The aqueous

[17] C. E. Dalgiesh and W. Keely, *J. Chem. Soc.* 3726 (1958).

soln was extracted with benzene. The extracts were concentrated to dryness to give 1·13 g (43%) skatole. The aqueous layer was concentrated *in vacuo* at a bath temp not exceeding 40°. The residue (4·4 g) was chromatographed over 150 g silica gel prepared in methylene chloride. The 10% MeOH in methylene chloride elute furnished 2·4 g (90%, based on non-fissioned product) of V, m.p. 230–235°, which was identified by its undepressed mixed m.p. with an authentic specimen and by comparison of IR, UV and NMR spectra. TLC was also carried out using an authentic sample of V and the reaction product both giving a spot of the same *Rf* value. Further elution of the column with 20% MeOH in methylene chloride afforded 765 mg of a crystalline residue which on recrystallization from EtOH–ether gave piperidine HBr, colorless needles, m.p. 239–240°.

3-*Methyl*-2-*piperidino*-3H-*indole* (II)

(i) *By the catalytic hydrogenation of* I *over* PtO_2. An ethanolic soln of 2·9 g of I was hydrogenated over PtO_2 until 3 moles of H_2 was absorbed. Removal of the catalyst and the solvent left 3·1 g of a semi-solid which crystallized partially on contact with dry benzene. The crystals were collected and washed with acetone (800 mg), slightly colored needles, m.p. 130–180°. Recrystallizations from H_2O gave colorless needles, m.p. 131–132°, which on heating at 80° *in vacuo* for 12 hr gave II H_2O, m.p. 187–188°. UV λ_{max}^{EtOH} mμ (ε); 274 (13500), 214 (18540); λ_{min} 237 (2460). IR ν_{max}^{KBr} cm^{-1}; 3400 (broad, crystalline water), 1660–1670 (strong, C=N). NMR (Fig. 3). (Found: C, 54·08; H, 6·43; N, 8·71; Br, 26·05. Calc. for $C_{14}H_{19}N_2BrH_2O$: C, 53·68; H, 6·77; N, 8·95; Br, 25·51%.)

This monohydrate gave an anhydrous compound when it was heated at 130° over P_2O_5 *in vacuo*, colorless needles, m.p. 188–189°. (Found: C, 56·56; H, 6·82; N, 9·29. Calc. for $C_{14}H_{19}N_2Br$: C, 56·38; H, 6·42; N, 9·40%.)

The non crystalline portion was separated from the benzene and crystallized from H_2O to give two crops of II, totaling 970 mg, whose NMR spectrum was identical with that of the analysis sample and no significant evidence of V contamination was observed. Total yield of II, 1·77 g (56%). The mother liquor was made basic with $NaHCO_3$aq, yielding a crystalline ppt which was filtered off dried and recrystallized from acetone to give 690 mg (30%) of IV, m.p. 202–203°, identical with a specimen prepared in the previous manner.

All attempts to isolate II by crystallization of the crude hydrogenation product from a variety of solvents and solvent mixtures failed, as it seemed to decompose in organic solvents to a dark-colored oil.

(ii) *By the catalytic hydrogenation of* I *over* Pd–C. A soln of 6·0 g of I in 300 ml EtOH was hydrogenated over 30% Pd–C at room temp. Removal of the catalyst and the solvent left a residue in which skatole could not be detected by TLC or in the NMR spectrum. The residue was crystallized from H_2O to afford 3·45 g (57%) of II, m.p. 128–130°. Its IR and NMR spectra were identical with an authentic specimen. On basification of the aqueous soln with $NaHCO_3$ 1·9 g (40%) of IV was obtained.

A soln of 100 mg of II in 20 ml 95% EtOH was hydrogenated over PtO_2 at atm press for 1 hr (H_2-uptake, 12 ml). Removal of the catalyst and the solvent left 92 mg of a residue which was extracted with benzene and H_2O. The benzene extract gave 31 mg of skatole on evaporation of the solvent.

Treatment of II *with* Et_3N: *A formation of* IV

To a soln of 300 mg of II in 5 ml methylene chloride was added 2 ml Et_3N, giving a crystalline ppt. The mixture was filtered and the filtrate evaporated to dryness to give a residue which was extracted with ether several times. The ethereal soln was evaporated to dryness leaving 200 mg (98%) of semi-solid. Its NMR spectrum showed that the crude product essentially consisted of IV. Recrystallization from Me_2CO gave 160 mg (80%) of IV, colorless needles, m.p. 201–202°.

Treatment of II *with* NaOEt: *a formation of* IV

The hydrobromide II (220 mg) was dissolved in anhyd. EtOH and basified with EtONa in EtOH. The solvent was removed to give a semi-solid which was extracted with methylene chloride, dried and concentrated to dryness. The residue was confirmed as IV by its spectral properties. TLC was also carried out using an authentic sample of IV and the reaction product both giving a spot of the same *Rf* value. Recrystallizations of the residue from acetone gave 130 mg (80%) of IV, m.p. 199–204°.

Treatment of II *with* NaOH; *Formation of a mixture of* III *and* IV

An aqueous soln of 96 mg of II in 3·5 ml H_2O was made basic with NaOHaq, with separation of an oil. The aqueous soln was decanted from the oil, which was rapidly washed with water and dried *in vacuo* at 70–80° to give a colorless glassy residue. The residue was shown to contain the expected free base III as the main component accompanied with IV in the NMR spectrum taken in $CDCl_3$ (Fig. 5). The instability of the compound (III) precluded further purification.

Air oxidation of III

An ethanolic soln of II (about 10^{-4} molar) was basified with a small amount of ethanolic NaOHaq. The soln was oxidized by passing air for 4 hr. Its UV spectrum was essentially the same as that of IV. Spectral change during the oxidation was shown in Fig. 4.

The air oxidation of the hydrobromide II in D_2O for 53 hr and in EtOH for 24 hr by passing air into each soln at room temp was carried out. Neither the NMR spectra of the air oxidation product in D_2O or EtOH showed the presence of V in the reaction mixture.

Hydrolysis of IV: *Formation of* 3-*hydroxy*-3-*methyloxindole* (VI)

(i) *With* NaOH. A mixture of 110 mg of V and 5 ml 10% NaOH was gently heated at 95° for 2 hr. The soln was neutralized with dil HCl, extracted with methylene chloride, washed with H_2O, dried and evaporated to dryness leaving 10 mg residue which was identified as VI by NMR, IR and UV spectra and *Rf* value on TLC.

(ii) *With* Al_2O_3. To a soln of 500 mg of IV in methylene chloride was added 10 g Al_2O_3 and the solvent removed. The Al_2O_3 was left overnight and then put on 150 g of Al_2O_3 column prepared in methylene chloride. The 10% MeOH in methylene chloride elute furnished 340 mg (67%) of VI, which on recrystallization from acetone gave colorless needles, m.p. 161–162° (reported m.p. 161·5–162·5° [8], 160° [8]). A mixed m.p. with the specimen[8] prepared from isatin and MeMgI gave no depression and their IR, UV and NMR spectra and *Rf* value on TLC were identical.

Reaction of 2-*bromoskatole with pyridine or piperidine*

Pyridine did not react with 2-bromoskatole in either anhydr. dioxan at temps from 0° to the b.p. or without solvent at 100–180° for 12 hr under a stream of N_2. The UV spectra and TLC of the reaction mixtures showed no appreciable change.

A few experiments were also carried out in an attempt to prepare III directly from 2-bromoskatole and piperidine, using the similar conditions. The UV spectra as well as TLC failed to show formation of III or IV in the reaction mixtures.

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