1058. *The Protonation of Tryptamine Derivatives in Acidic Media.*

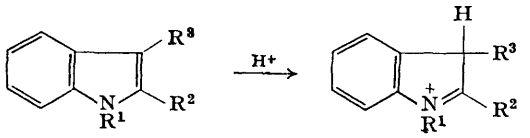
By A. H. Jackson and A. E. Smith.

Spectroscopic evidence shows that tryptamine and several of its *N*- and *C*-methyl derivatives are protonated at the 3-position of the indole nucleus in strongly acidic media to give the corresponding 3*H*-indolium salts (VI). Physostigmine and a number of related compounds also form 3*H*-indolium salts in acidic media (but at a much higher pH), by a ring-opening reaction, *e.g.* (VII) → (VIII). The latter observation has already proved to be a useful criterion for the presence of the Ph·N·C·N and Ph·N·C·O systems in certain indole alkaloids.

Recent spectroscopic studies[1,2] have shown that protonation of indoles in strongly acidic media occurs exclusively in the 3-position (even when this is already substituted), with formation of the corresponding 3*H*-indolium (or indolenine) salt, *e.g.* (I). By the use of

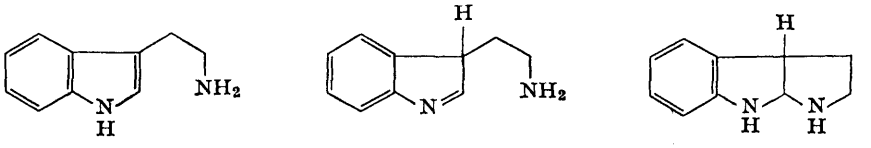
[1] R. L. Hinman and E. B. Whipple, *J. Amer. Chem. Soc.*, 1962, **84**, 2534.
[2] G. Berti, A. de Settimo, and D. Segnini, *Gazzetta*, 1961, **91**, 571.

deuterated sulphuric acid it has further been shown that the 1- and 3-hydrogens of the indole nucleus are rapidly exchanged in strong acid, whereas the 2-hydrogen is only exchanged slowly. In contrast, pyrroles usually undergo protonation at the α-position in acidic media, although in some instances competitive β-protonation may also occur simultaneously.[3]



(I)

In connection with other work on electrophilic substitution in indoles it was of interest to extend these studies to the protonation of tryptamine and its derivatives including physostigmine. The proton magnetic resonance (p.m.r.) spectra of tryptamine (II) and its *N*(a)- and *N*(b)-methyl derivatives[4] in deuterochloroform clearly indicate that there is no measurable amount of the tautomeric indolenine form (III), nor indeed of the ring-closed indoline form (IV) which is the basic ring system of the physostigmine group of alkaloids. The ultraviolet (u.v.) spectra of these tryptamines in neutral or dilute acid solutions are also fully consistent with the normal indole formulation (II). However, in concentrated sulphuric



(II) (III) (IV)

acid the indole nucleus in each of the various tryptamines studied was completely protonated at the 3-position with formation of the 3*H*-indolium salt (VI), as shown by the changes in their u.v. spectra, which are compared with those of some simple alkylindoles and 2,3,3-trimethylindolenine in Table 1. Tryptophan also underwent similar spectral shifts in

TABLE 1.

Ultraviolet spectra of tryptamine hydrochlorides and related compounds in ethanol and in concentrated sulphuric acid.

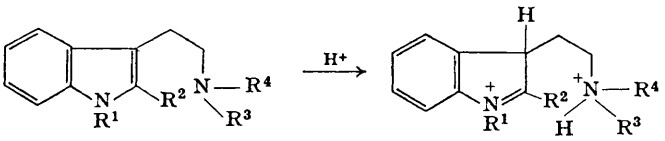
	95% Ethanol $\lambda_{max.}$ (mμ) (log ε)	Conc. H_2SO_4 $\lambda_{max.}$ (mμ) (log ε)	$[H_2SO_4]$*
Tryptamine	220 (4·56), 281 (3·78), 290 (3·71)	236 (3·63), 241 (3·60), 295 (3·68)	12M
N(a)-Methyltryptamine	223 (4·58), 287 (3·77)	233 (3·63), 240 (3·62), 288 (3·68)	10M
2-Methyltryptamine	224 (4·57), 281 (3·89), 288 (3·82)	233 (3·77), 241 (3·76), 289 (3·75)	6M
N(b)-Methyltryptamine	220 (4·57), 280 (3·79), 290 (3·72)	236 (3·62), 241 (3·58), 294 (3·64)	11M
N(b)-Dimethyltryptamine	223 (4·49), 282 (3·76), 291 (3·69)	236 (3·59), 242 (3·57), 295 (3·64)	9M
N(a)*N*(b)-Dimethyltryptamine	223 (4·55), 287 (3·74)	235 (3·50), 241 (3·49), 290 (3·64)	8M
Tryptophan	228 (4·17), 278 (3·72)	234 (3·73), 240† (3·65), 290 (3·64) inf.	12M
3-Methylindole[1,2]	222 (4·51), 284 (3·73), 291 (3·70)	236 (3·59), 241 (3·56), 290 (3·67)	9M[2]
2,3-Dimethylindole[1,2]	228 (4·50), 284 (3·83), 293 (3·79)	235 (3·70), 241 (3·68), 286 (3·74)	5M[2]
1,3-Dimethylindole	226 (4·50), 292 (3·78)	235 (3·58), 240 (3·59), 286 (3·67)	8M
2,3,3-Trimethylindolenine[2]		229 (4·00), 235 (3·95), 275 (3·91)‡	

* Minimum concentration required to completely protonate the 3-position of the indole nucleus.
† Inflection.
‡ In 0·1M-hydrochloric acid.

[3] E. B. Whipple, Y. Chiang, and R. L. Hinman, *J. Amer. Chem. Soc.*, 1963, **85**, 26.
[4] L. A. Cohen, J. W. Daly, H. King, and B. Witkop, *J. Amer. Chem. Soc.*, 1960, **82**, 2184.

concentrated sulphuric acid, and, as with the tryptamines, the shifts were reversible on dilution.

These observations were confirmed by study of the p.m.r. spectra of some of the tryptamines in strong sulphuric acid, *e.g.* *N*(a)-methyltryptamine in 12M-sulphuric acid gave a poorly resolved spectrum but a singlet resonance was clearly seen at 0·43 τ (area 1 proton) corresponding to the α-proton in the indolium-salt form (VI; R^1 = Me, $R^2 = R^3 = R^4$ = H).



(V) (VI)

1,3-Dimethylindole in 18M-sulphuric acid gives rise to a singlet at −1·2 τ corresponding to the α-proton of the indolium salt form (I; $R^1 = R^3$ = Me, R^2 = H), whilst the α-proton in 3,3-dimethylindolenine gives rise to a peak at 0·82 τ in trifluoroacetic acid solution; the α-proton in simple indoles and tryptamines in neutral solution normally gives a peak at *ca.* 3·0—3·3 τ.[4] Trifluoroacetic acid was not a sufficiently strong acid to effect complete conversion of any of the tryptamines in Table 1 into their 3*H*-indolium salts.

The minimum concentration of sulphuric acid needed to effect complete conversion of the tryptamines (V) into their conjugate acids (VI) is shown in Table 1, and this gives a semi-quantitative measure[2] of the relative basicities of the indole nucleus in the various tryptamines. Fig. 1 shows a typical series of spectra of one of the tryptamines in different concentrations of acid. Table 1 shows that the basicity is dependent both upon the position of

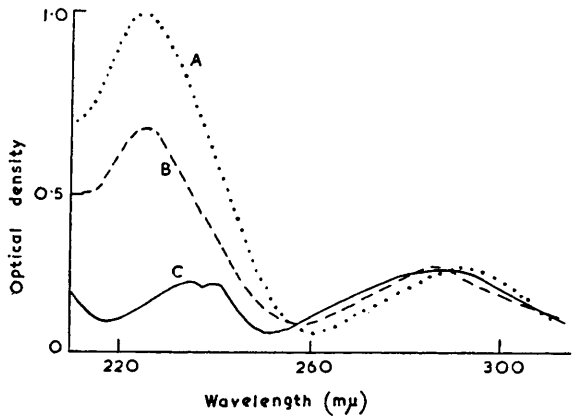


FIG. 1. Ultraviolet spectrum of *N*(a)-methyltryptamine in (A) 6M-, (B) 8M-, and (C) 10—18M-sulphuric acid.

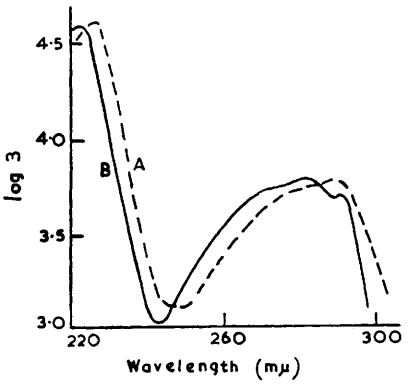


FIG. 2. Ultraviolet spectra of (A) *N*(a)-methyltryptamine and (B) *N*(b)-methyltryptamine in 95% ethanol.

methyl substitution in the indole nucleus (unsubstituted < 1-methyl < 2-methyl), and upon the degree of substitution of the side-chain amino-group (NH_2 < NHMe < NMe_2). The base-strengthening effects of nuclear methyl groups parallel those observed with simple alkylated indoles, although the basicities of the indole nuclei of the tryptamines are slightly lower than those of similarly substituted alkylindoles [*e.g.*, *N*(a)-methyltryptamine is less basic than 1,3-dimethylindole]. However, this is almost certainly due to the inhibiting effect of the positively charged aminoethyl side-chain in acidic solutions of the tryptamines. The reason for the increase in basicity of the indole nucleus on methylation of the side-chain

nitrogen is less obvious, but it may be due to the steric effect of the methyl groups in preventing close approach of the protonated amino-function to the indole nucleus, and hence diminishing any field effects.

An interesting feature of the u.v. spectra of *N*(a)-methyltryptamines and -indoles in ethanol is that they do not show the small peak or inflection *ca.* 290 mμ which appears to be characteristic of indoles unsubstituted on the nuclear nitrogen, but they do of course show the typically indolic absorptions *ca.* 220 mμ and *ca.* 280—290 mμ (rather broad) (cf. Table 1 and Fig. 2).

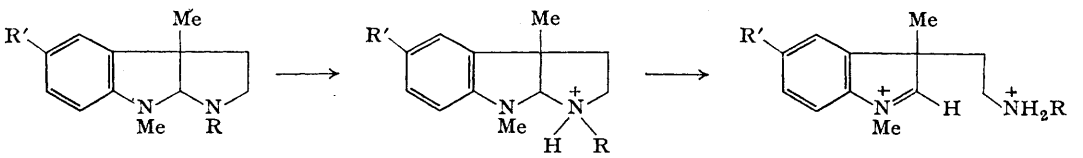
In contrast to the tryptamines described above, physostigmine and its analogues containing the tricyclic pyrroloindole system (IV) all show modified indoline-type u.v. spectra in neutral solution (Table 2), with $\lambda_{max.}$ *ca.* 250 and 310 mμ. The biogenetically related alkaloids chimonanthine, folicanthine, and calycanthine also give very similar u.v. spectra in

TABLE 2.

Ultraviolet spectra of physostigmine and some analogues in neutral and acidic media.

	95% Ethanol $\lambda_{max.}$ (mμ) (log ε)	0·01M-Ethanolic HCl $\lambda_{max.}$ (mμ) (log ε)	6M-Ethanolic HCl $\lambda_{max.}$ (mμ) (log ε)
Physostigmine	254 (4·07), 312 (3·47)	246 (4·05), 303 (3·47)	237 (3·78), 294 (3·76)
Deoxynoreseroline	252 (4·02), 302 (3·44)	246 (3·97), 298 (3·40)	234 (3·67), 240 (3·63), 284 (3·58)
Esermethole	248 (4·02), 320 (3·52)	244 (4·04), 313 (3·53)	252 (3·66), 331 (3·74)
Physostigmine methiodide	245 (4·08), 303 (3·40)		

neutral solution,[5] as do the structurally related compounds echitinolide,[6] corymine,[7] and hodgkinsine.[8] In dilute acidic solution, however, the spectra of physostigmine and its congeners undergo a hypsochromic shift of 8—10 mμ,[5–8] and Hodson and Smith[5] have attributed this to protonation of N(b), the positive charge on which is then sufficiently close to partially inhibit the delocalisation of the lone pair of electrons on N(a) over the aromatic nucleus. We have confirmed these results for physostigmine (VIIa), and have also shown that the related compounds esermethole (VIIb) and deoxynoreseroline (VIIc) undergo similar shifts in 0·01M-hydrochloric acid; the spectrum of physostigmine methiodide (VIId) also shows a small hypsochromic shift relative to that of physostigmine (VIIa), and this clearly confirms Smith's interpretation of the reasons for the spectral shifts in dilute acid.



(VII) (VIII)

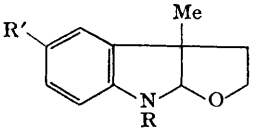
a: R = Me, R′ = O·CO·NHMe
b: R = Me, R′ = OMe
c: R=R′=H
d: >NR = >NMe_2^+ I^-, R′ = O·CO·NHMe

In more strongly acidic solution (> 1M-HCl) marked changes occur in the spectra of these physostigmine derivatives (cf. Table 2), and they become very similar to those of the tryptamines in strongly acidic solution, and of indolenines (cf. Table 1). This is clearly consistent with the opening of ring c to give the 3*H*-indolium salt (VII) → (VIII). Conversion of physostigmine (VIIa) into the ring-opened form (VIIIa) began in approximately 1M-hydrochloric acid and was essentially complete in 5M-acid, whilst esermethole (VIIb) and

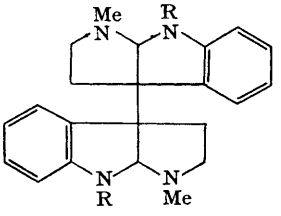
[5] H. F. Hodson and G. F. Smith, *J.*, 1957, 1877.
[6] A. J. Birch, H. F. Hodson, and G. F. Smith, *Proc. Chem. Soc.*, 1959, 224.
[7] A. K. Kiang and G. F. Smith, *Proc. Chem. Soc.*, 1962, 298.
[8] Cf. B. Robinson, *Chem. and Ind.*, 1963, 218.

deoxynoreseroline (VIIc) were fully converted into the indolium salts in 3M-acid. A noteworthy, but as yet unexplained, feature of the spectrum of esermethole in strong acid, *i.e.* (VIIIb), is that the long-wavelength absorption at 331 mμ is about 40 mμ higher than the corresponding bands in the spectra of all the other indolium salts (cf. Tables 1 and 2). It was thought that this might be due to the electron-releasing effect of the methoxyl substituent of esermethole (absent in deoxynoreseroline, and inhibited by urethane formation in physostigmine), but this was not borne out by the spectra, in 18M-sulphuric acid, of 5-methoxyindole (242 and 302 mμ) and 5-hydroxytryptamine (240 and 295 mμ) which are very similar to those of the other indolium salts.

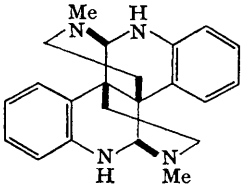
Some preliminary results of our work on physostigmine and esermethole were communicated privately to Dr. B. Robinson and discussed in his recent review[8] on alkaloids containing the Ph•N•C•N system, and he suggested that the ready conversion of physostigmine (VIIa) and esermethole (VIIb) into their indolium salts (VIIIa) and (VIIIb) in acidic solution might be due to the decreased electrophilic character of the 2-position in the indole nucleus owing to electron release from the O•CO•NHMe and OMe groups, respectively.[cf.18] However, since deoxynoreseroline (VIIc) is just as readily converted into its indolium salt (VIIIc), as physostigmine (VIIa) and esermethole (VIIb) are into theirs, it would seem that substituents in the aromatic nucleus of these physostigmine analogues exert at most only a minor influence on the opening of ring C in acidic solution. On the other hand, it has been reported that the oxygen analogue (IXa) of dinordeoxyeseroline shows a mixture of benzenoid and 3*H*-indolium-cation absorption in concentrated acid (although no details have been published),[9] whereas physovenine (IXb) is fully converted into the corresponding indolium salt in concentrated acid.[10] However the analogue (IXa) may behave differently because it is not *N*(a)-methylated.



(IX) a: R = R′ = H
b: R = Me, R′ = O•CO•NHMe



(X) a: R = Me
b: R = H



(XI)

Folicanthine (Xa) and chimonanthine (Xb) decompose rapidly in concentrated hydrochloric acid solution, but in the first few seconds show a clear Ph•N•C•N$^+$ type absorption.[11] Calycanthine (XI) shows only Ph•N•C•N$^+$ in both 0·1N- and 8N-hydrochloric acid,[12] and thus appears to be an exception to the general rule; however it is structurally rather dissimilar to the other compounds described in this Paper, particularly as both N(b)-atoms are in six-membered rings.

The p.m.r. spectra of physostigmine, esermethole, and deoxynoreseroline in deuterochloroform and in trifluoroacetic acid are shown in Table 3, together with the appropriate assignments, which are quite straightforward. The spectra in trifluoroacetic acid (and of deoxynoreseroline in 4M-HCl) clearly confirm that the three compounds have been converted into the ring-opened 3*H*-indolium salts (VIII) (cf. in particular the low-field resonances due to the α-protons).

Thus, both u.v. and p.m.r. evidence indicate that in moderately strong acid (*e.g.*, *ca.* 4N-HCl or trifluoroacetic acid) physostigmine and its derivatives exist in the ring-opened

[9] W. G. Bardsley, M.Sc. Thesis, Manchester 1961; see also ref. 10.
[10] B. Robinson, *J.*, 1964, 1503.
[11] G. F. Smith, personal communication.
[12] J. Harley-Mason, personal communication.

TABLE 3.

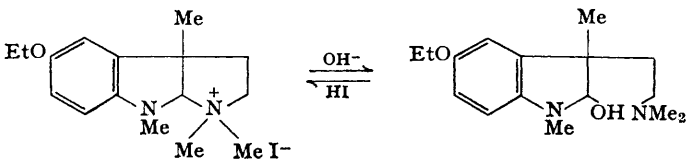
Proton magnetic resonance spectra (τ values) of physostigmine and analogues.

	Deuterochloroform			Trifluoroacetic acid			4M-Hydrochloric acid
Assignment	(VIIa)[a]	(VIIb)[b]	VIIc)	(VIIIa)[c]	(VIIIb)[d]	(VIIIc)	(VIIIc)
C_2H	5·95	5·98	5·60	0·71	0·92	1·08	0·69
N(a)-CH_3	7·13	7·13	7·24	5·67	5·70	5·66	5·73
N(b)-CH_3	7·50	7·49	—	6·96	*ca.* 7·1	—	—
C_6-CH_3	8·61	8·57	8·62	8·20	8·24	8·20	8·33
5-CH_2	8·06t	8·06t	*ca.* 8·1t	*ca.* 7·1m	*ca.* 7·0m	*ca.* 7·1m	*ca.* 7·3m
4-CH_2	*ca.* 7·3t	7·27t	*ca.* 7·2t				
7-H	3·23d	3·37d	2·85	2·0	2·5		
9-H	3·20d[e]	3·33d[e]	to	to	to	*ca.* 2·15	*ca.* 2·2
10-H	3·69d[e]	3·65d[e]	3·85m	2·8m	2·8m		
8-H	—	—		—	—		

d, doublet; t, triplet; m, multiplet.

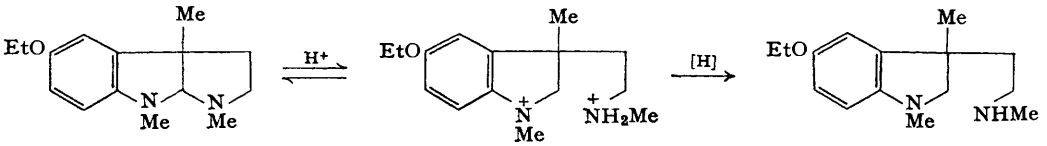
[a] 5-Urethane, CH_3 at 7·30d, NH at 4·00q. [b] 5-CH_3O at 6·29. [c] 5-Urethane, CH_3 at 7·08, [d] 5-CH_3O at 5·97. [e] AB-quartet, J = 9·5 c./sec.; 9-H coupled with 7H, J = 2 c./sec.

indolenine form (VIII), and it is interesting to note that this transformation takes place at much lower acid strengths than those required for conversion of tryptamine and its derivatives into their indolium salts (*i.e.*, 6—12M-H_2SO_4). Trifluoroacetic acid (as has already been mentioned) is not a sufficiently strong acid to fully protonate the indole nucleus of any of the simple tryptamines investigated; similarly we have also found that it is not strong enough to fully protonate either indole or 3-methylindole, *e.g.* the 3-methyl group of 3-methylindole in trifluoroacetic acid gives rise to both a singlet resonance at 7·53 τ, (corresponding to the free base), and a quadruplet (J = 7 c./sec.) at 8·48 τ, [corresponding to the 3H-indolium salt (I; $R^1 = R^2 = H$, R^3 = Me)]. On the other hand the more basic 2-methylindole is completely converted into the 3H-indolium salt (I; $R^1 = R^3 = H$, R^2 = Me) in trifluoroacetic acid, and shows resonances at 6·97 (2-CH_3), 5·5 (3-CH_2), and 2·3 τ (4,5,6,7-H). [In deuterochloroform 2-methylindole gives resonances at 7·75 (2-CH_3), 3·83 (3-H), *ca.* 2·9 (4,5,6-H), and *ca.* 2·6 τ (7-H and NH)].



(XII) (XIII)

The ease with which ring-opening of the various physostigmine analogues occurs in acidic solution is reminiscent of the ease with which ring-opening of eserethole methiodide (XII) occurs in alkaline solution to give eserethole methine (XIII), and highlights the reactivity and versatility of the pyrroloindole ring system. This reactivity can now be seen to provide an explanation for the facts that eserethole (XIV) and its analogues are readily reduced by zinc and hydrochloric acid,[13] or by hydrogenation over platinum in glacial acetic acid,[14] to the ring-opened indoline, *e.g.* (XV), whereas no reduction occurs in neutral or



(XIV) (XV)

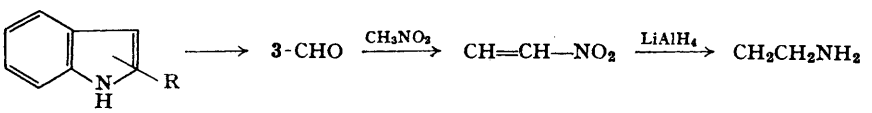
[13] M. Polonovski and M. Polonovski, *Bull. Soc. chim. France.*, 1924, **35**, 1492.
[14] E. Stedman and G. Barger, *J.*, 1925, 247.

alkaline solution. In the earlier literature it was implied that these reductions must have involved direct rupture of the C_2–N(b) bond,[14] but this seems rather unlikely as this is not activated, *e.g.* benzylically or allylically. However, a more logical explanation is that in acidic media the eserethole is partly or fully ring-opened, and it is the N(a)-C_2 double bond thus formed which is reduced. In agreement with this hypothesis we have found that simple 3,3-dialkylindolenines are not reduced catalytically in neutral or alkaline solution, but in acidic media hydrogenation occurs very rapidly and the corresponding indolines are formed.[15]

Other indole derivatives which give 3*H*-indolium salts on treatment with acid are those with the Ph•N•C•O system, *e.g.* the simple indolines, 2-hydroxy-1,3,3-trimethylindoline[16] and 2-hydroxy-1-methylindoline-3-spirocyclopentane,[17] and the more complex indole alkaloids, ψ-akuammigine,[18,19] *O*-methylakuammine,[18] picraline,[20] and deacetylpicraline.[20] It is clear that formation of these indolium salts has been, and will continue to be, a useful diagnostic test for the presence of the Ph•N•C•N and Ph•N•C•O systems in newly discovered indole alkaloids. The two systems can be distinguished from each other by the fact that only the former can undergo quaternisation in dilute acids, and hence give the characteristic small hypsochromic shift first observed by Smith. A cogent recent example is the utilisation of our observations on physostigmine and the earlier data in the proof of the presence of the Ph•N•C•O system in the alkaloid physovenine.[8]

Most of the tryptamines used in this work were prepared by well-known methods as indicated by the references in the following list: tryptamine,[21] *N*(b)-methyltryptamine,[4] *N*(b)*N*(b)-dimethyltryptamine,[22] and *N*(a)*N*(b)-dimethyltryptamine.[23] Esermethole (VIIb) was prepared from physostigmine,[24] and deoxynoreseroline (VIIc) from 1,3-dimethyloxindole.[25]

Both *N*(a)- and 2-methyltryptamines were prepared from the indoles by the following well-established sequence (see ref. 20), a route which does not hitherto appear to have been used for these compounds:



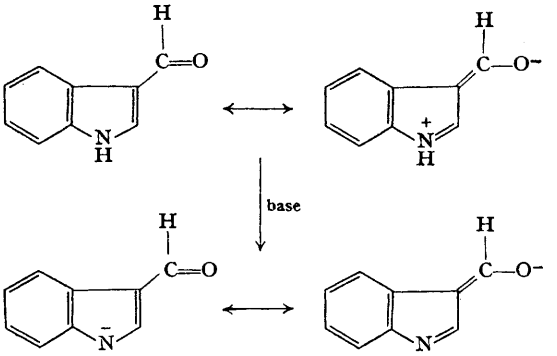
One notable feature is that 3-formyl-*N*-methylindole can be prepared by a remarkably easy methylation of 3-formylindole with methyl iodide in acetone over potassium carbonate. This may be contrasted with the *N*-alkylation of indole or *C*-alkylindoles which requires the use of much stronger bases such as sodamide or potassium t-butoxide. This ready alkylation of 3-formylindole can be attributed to its mesomeric nature as illustrated.

Experimental

Ultraviolet absorption spectra were determined with Perkin–Elmer 137 and Unicam SP 500 spectrometers, and p.m.r. spectra were measured with a Varian A-60 spectrometer.

2-*Methyltryptamine.*—Phosphorous oxychloride (5 ml.) was added slowly with stirring to dimethylformamide (16·8 ml.), the temperature of the mixture being kept between 10 and 20°.

[15] A. H. Jackson and A. E. Smith, unpublished results; cf. A. E. Smith, Ph.D. Thesis, Liverpool, 1963.
[16] G. Ciamician and A. Piccinini, *Ber.*, 1896, **29**, 2467; *Gazzetta*, 1897, **271**, 341.
[17] B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, 1953, **75**, 2572.
[18] J. A. Joule and G. F. Smith, *J.*, 1962, 312.
[19] A. Z. Britten, P. N. Edwards, J. A. Joule, G. F. Smith, and G. Spiteller, *Chem. and Ind.*, 1963, 1120.
[20] A. Z. Britten, G. F. Smith, and G. Spiteller, *Chem. and Ind.*, 1963, 1492.
[21] E. H. P. Young, *J.*, 1958, 3493.
[22] M. E. Speeter, U.S.P. 2,825,734; (*Chem. Abs.*, 1958, **52**, 12,923).
[23] H. F. Hodson and G. F. Smith, *Chem. and Ind.*, 1956, 740.
[24] F. E. King and R. Robinson, *J.*, 1932, 326.
[25] P. L. Julian, J. Pikl, and D. Boggess, *J. Amer. Chem. Soc.*, 1934, **56**, 1797.



2-Methylindole (6·60 g.) in dimethylformamide (4 ml.) was then added slowly to the well-stirred mixture, the temperature being kept below 30°. Finally, the mixture was warmed to 35° for 45 min. before being poured on to crushed ice (100 g.). Sodium hydroxide (9·5 g.) in water (50 ml.) was added cautiously to the aqueous solution, the mixture heated to boiling for 2 min., and allowed to cool. The 3-formyl-2-methylindole (7·3 g., 91%) was precipitated as colourless needles, which on recrystallisation from aqueous ethanol had m. p. 202° (lit.,[26] 202—203°).

The foregoing aldehyde (5·0 g.), nitromethane (10 ml.), and ammonium acetate (1 g.) were boiled together under reflux for 30 min. On cooling the dark brown solution in ice 2-*methyl*-3-(2-*nitrovinyl*)*indole* crystallised as reddish-brown prisms (4·2 g., 65%), m. p. 197° (from methanol) (Found: C, 65·0; H, 5·0; N, 13·6. $C_{11}H_{10}N_2O_2$ requires C, 65·3; H, 5·0; N, 13·9%).

The finely powdered nitrovinylindole (5 g.) was extracted slowly (Soxhlet) into dry ether (300 ml.) containing lithium aluminium hydride (5 g.). When the extraction was complete (6—10 hr.) the excess of hydride was cautiously decomposed by the slow addition of water (30 ml.). Saturated Rochelle salt solution (150 ml.) was added and the product isolated in the usual manner as an ethereal extract which was dried (Na_2SO_4). On evaporation of the extracts under reduced pressure, 2-methyltryptamine was obtained (3·5 g., 63%) as needles, m. p. 81—83° (lit.,[27] 83°) from ether. The hydrochloride was not obtained crystalline, but the oxalate crystallised from ethanol–ether as tiny needles, m. p. 219°.

N(a)-*Methyltryptamine*.—This synthesis closely paralleled that described above for the 2-methyl isomer. 3-Formyl-1-methylindole was obtained in 87% yield from 1-methylindole as pale yellow rhombs, m. p. 67° (from ether) (lit.,[28] m. p. 65°). It was also obtained in 92% yield by boiling 3-formylindole and a two-fold excess of methyl iodide in acetone in presence of anhydrous potassium carbonate for 3 hr. under reflux. N(a)-*Methyl*-3-(2-*nitrovinyl*)*indole* (72%) formed yellow needles, m. p. 162° (from methanol) (Found: C, 65·6; H, 5·1; N, 14·1. $C_{11}H_{10}N_2O_2$ requires C, 65·3; H, 5·0; N, 13·9%).

N(a)-Methyltryptamine was obtained as an oil in 80% yield. The hydrochloride crystallised from ethanol–ethyl acetate as needles, m. p. 198° (lit.,[29] 198—199°), and the picrate crystallised from ethanol as red needles, m. p. 178° (lit.,[29] 178—179°).

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