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THE REACTIONS OF INTERMEDIATES DERIVED FROM THE CHLORINATION OF INDOLES

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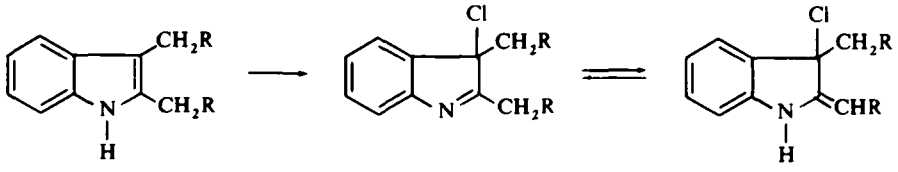
Abstract—The various steps involved in the reaction of indoles with sodium hypochlorite have been studied. At low temperatures, these reactions lead to the formation of 3-chloroindolenine. The 3-chloroindolenines have been found to be thermally labile. For example, 2,3-dimethyl-3-chloroindolenine rapidly rearranges to an isomeric compound at 15°. Selective reactions of 3-chloroindolenines with silver ion in methanol have been shown to produce 3-methoxyindolenines in high yield. In contrast, the rearranged isomer of 2,3-dimethyl-3-3-chloroindolenine has been shown to give high yields of indole derivatives which are functionalized in the 2-position.

The rearrangements of the tosylate or *p*-nitrobenzoate of 1-hydroxyindoles have been found to result in the formation of the respective tosylate or *p*-nitrobenzoate of the 3-hydroxyindolenine.

THE reactions of indole derivatives with various halogenating agents, such as bromine,[2] N-bromosuccinimide,[3-5] and t-butyl hypochlorite,[6, 14] have been discussed in detail in relation to various transformations of the indole alkaloids. Although much has been published in the way of mechanistic speculation, relatively little has appeared in the way of definitive evidence for the proposed mechanistic intermediates. In general, it has been suggested that indole derivatives of the general type **1** react with halogenating agents such as t-butyl hypochlorite to yield 3-haloindolenines (**2**). Also, it has been indicated

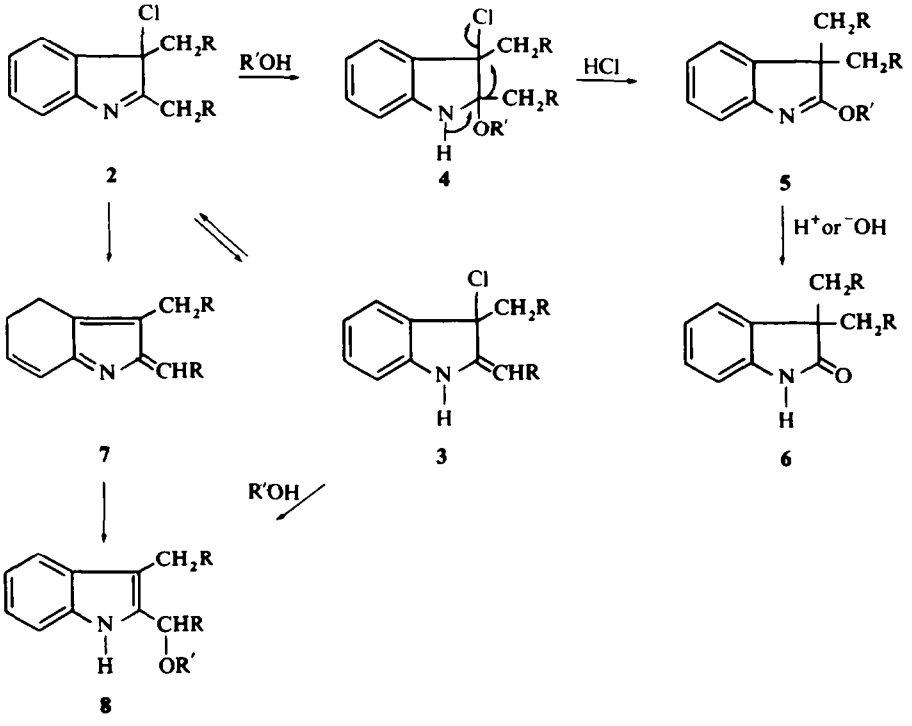


1 **2** **3**

that **2** equilibrates with the corresponding 2-alkylidene-3-chloroindolines (**3**) with ease under the reaction conditions. Starting with **2** and **3**, a variety of reaction paths have been described to explain a variety of products. Some of these reactions are summarized in Chart 1. Several workers[7-12] have invoked **2** as the first intermediate in the oxidative conversion of indoles into oxindoles (**6**) *via* the initial addition of the solvent to **2** to yield **4**, followed by concerted loss of hydrogen chloride and rearrangement to yield **5**. On hydrolysis **5** is postulated to give the oxindole, **6**. The formation of the oxygenated indoles represented by **8** has been discussed in terms of both the **2** → **7** → **8** and the **2** → **3** → **8** routes.[10, 12]

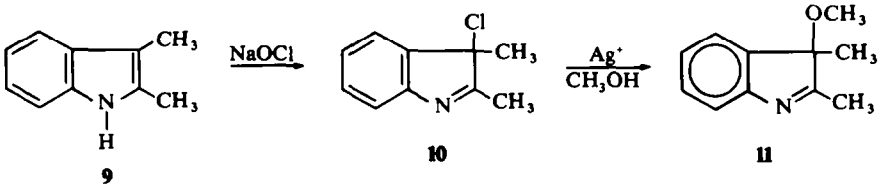
In line with our long-standing interest in the reaction of amines with hypohalite[14] and in view of the recently reported reactions of N-chloroanilines,[15] we decided to investigate the reaction of simple indole derivatives with hypohalite. We were intrigued by several

CHART I



aspects of the reaction of indoles with hypochlorite. One question was whether initial chlorination occurred at the 1-position or the 3-position of the indole nucleus. By analogy with the chlorination of anilines[15]* it might have been anticipated that the initial attack would be on nitrogen, followed by rapid migration of the chlorine from the nitrogen to the 3-position. The widespread reports of the extreme instability of the 3-chloroindolenines also represented a curiosity. Of particular interest were the nature of decomposition products and the mechanism of the decomposition. This paper presents the details of our studies related to these questions.

Our initial investigation was concerned with the model compound 2,3-dimethylindole (**9**). Reaction of **9** with aqueous sodium hypochlorite solution† at −5 to −10° gave the very unstable 3-chloro-2,3-dimethylindolenine (**10**). The structure of **10** was substan-



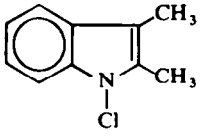
* We have recently shown that the chlorination of anilines involves initial N-chlorination followed by heterolytic cleavage of the N-Cl bond to yield chloride anion and a positively charged nitrogen species (anilenium ion). With simple N-alkyl-N-chloroanilines this heterolysis-recombination occurs rapidly in the vicinity of room temperature even in non-polar solvents.[15]

† Commercial bleach was used as the source of hypochlorite.

tiated on the basis of several pieces of evidence. The NMR spectrum of **10** taken at −25° in methylene chloride showed two sharp three proton singlets at τ 7·74 and 8·35, assigned to the C-2 and C-3 Me groups, respectively. This is to be contrasted with the Me groups of 2,3-dimethylindole (**9**) which appeared as sharp singlets at τ 7·83 and 7·76. Additional NMR evidence was provided by the NMR spectrum of 2,3-dimethyl-3-methoxyindolenine (**11**) which showed the C-2 and C-3 Me groups at τ 7·82 and 8·64, respectively (*vide post*). As expected, chlorine was slightly more deshielding than methoxyl.

The UV spectrum of **10** in methylene chloride showed a maximum at 266 nm with a shoulder at 292 nm. 2,3,3-Trimethylindolenine and **11** show maxima in alcoholic solvents at 265 and 256 nm, respectively.[16] These values are to be contrasted with the characteristic UV absorption of 2,3-dimethylindole which appears at 280 nm.

When the reaction of **9** with hypochlorite was followed by NMR spectroscopy at less than −5°, no trace of the intermediacy of N-chloro-2,3-dimethylindole (**12**) could be detected. Thus, if the formation of **12** preceded the formation of **10**, the lifetime of **12** must have been extremely short. The *feasibility* that **12** might actually be an extremely



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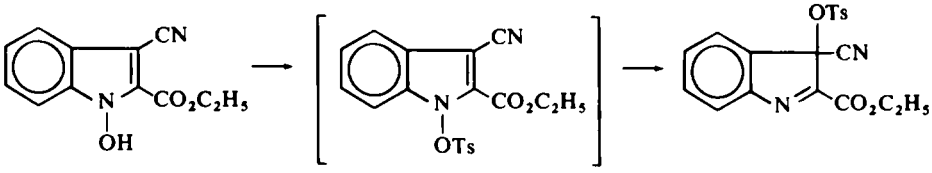
short-lived intermediate was supported by our observations of the thermal stability of derivatives of certain 1-hydroxyindoles. When **13**[17] was treated with *p*-toluenesulfonyl chloride in triethylamine, no trace of **14** could be found. Instead, we observed that the conversion of the OH function of **13** into a good leaving group resulted in the formation of **15** below room temperature.* In similar fashion we found that the reaction of the 1-



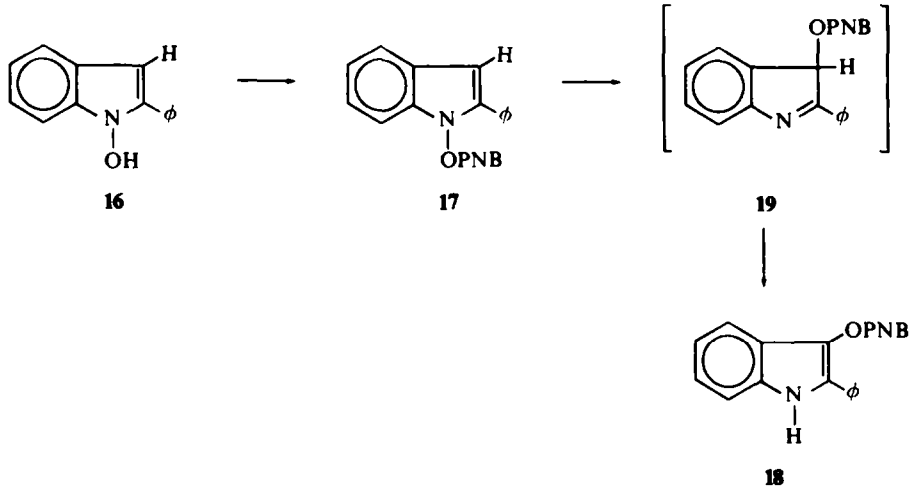
13 **14** **15**

hydroxyindole, **16**,[18] with *p*-nitrobenzoyl chloride resulted in the formation of the relatively unstable intermediate **17**. When **17** was warmed in methanol it was slowly transformed into **18**, presumably *via* the initial rearrangement of **17** to **19**, followed by a proton shift and rearomatization. The well-established ease of N-chlorination combined with the observed facile nature of the rearrangement of **14** to **15** and of **17** to **19** indicates that **12** could not be ruled out as a precursor of **10**.

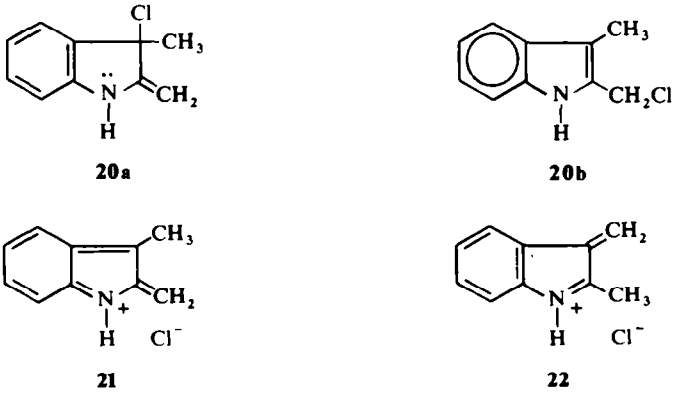
Although methylene chloride solutions of **10** were stable for several hours when kept at −25°, both spectroscopic and titrimetric analysis† of the solution showed that **10**

* The structure of **15** was established on the basis of its spectroscopic properties. For details see the Experimental.

† It is interesting to note that **10** retained its oxidizing properties. Thus, **10** could be titrated for active chlorine. Initially, this led us to suspect that we had **12** and not **10**. However, the various spectroscopic studies established the nature of **10**.

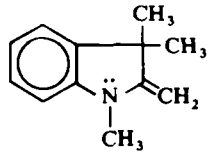


underwent a dramatic change upon warming to room temperature. As the temperature was elevated from −25° to 15°, the amount of active chlorine rapidly decreased. In addition the NMR spectrum completely changed. On standing at room temperature, the solution rapidly darkened and intractable material was produced. If the methylene chloride solution of **10** was warmed rapidly to 15° followed by immediate cooling to −25°, a solution of a new compound was obtained.* The NMR spectrum of this solution showed that only trace amounts of **10** remained. In place of the two Me absorptions of **10**, there appeared two new absorptions as singlets at τ 5·26 and 7·68. These absorptions had relative integrated intensities of 2 : 3, respectively. Thus, the NMR spectrum confirmed that **10** had undergone a spontaneous change at room temperature. Since no hydrogen chloride gas was given off by the reaction mixture, it was felt that the rearrangement product must have one of the structures **20–22**. The ionic nature of both **21** and **22** makes these structures unlikely since neither their solubility in methylene chloride nor their NMR spectra were consistent with what might be expected of such salts. Thus, it seemed probable that the rearranged material had either structure **20a** or



* NMR spectroscopy showed that this compound was formed in *ca* 75% yield from **10**. The spectrum indicated the presence of small amounts of several impurities. Chemical transformations of the rearrangement product indicated that the isomerization had occurred in much better than 75% yield (*vide post*).

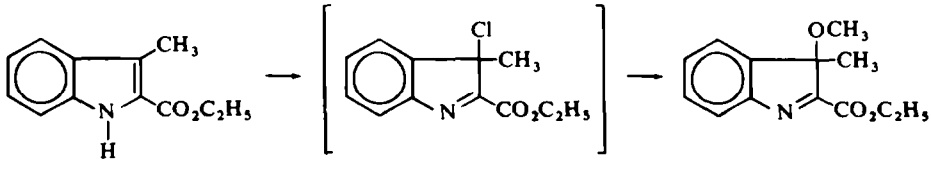
20b. The UV spectrum of the methylene chloride solution at −10° provided support for structure **20a.** After the methylene chloride solution of **10** had been warmed to 15° and recooled, the UV spectrum of **10** had completely disappeared.* A new absorption appeared at λ_{max} 285 nm with an intensity approximately five times as strong as that of the solution of **10.** Although the extinction coefficient of the rearranged material could not be accurately determined, it was estimated to be *ca* 20,000. These spectral properties are in good agreement with those reported[19] for Fischer's base, **23** (λ_{max} 283, ε 22,400), which should be a satisfactory model for UV spectral comparison purposes. The



23

position of the absorption was also consistent with the presence of the indole nucleus of **20b.** However, the extinction coefficient was about three times too large. For comparison, the UV spectrum of 2,3-dimethylindole (**9**) shows λ_{max} 280 (ε 7080).[20] Thus, on the basis of the UV spectrum, **20a** would seem to be preferred over **20b** as the structure of the intermediate.[2] Unfortunately, the NMR spectrum of the intermediate seemed more consistent with **20b** than with **20a.** The two-proton absorption at τ 5·26 was consistent with either the terminal methylene of **20a** or the methylene unit of **20b.** However, the three-proton singlet at τ 7·68 was more in line with the Me groups of **9** (τ 7·76 and 7·83), than with the 3-Me groups of **10** or **11** (τ 8·35 and 8·64, respectively). Thus, we were not able to definitively determine whether this very unstable intermediate had structure **20a** or that of the allylic rearrangement product **20b.**†...

An interesting and useful aspect of this investigation was associated with the finding that **10** and its isomer **20** showed completely different chemical behavior. When a methanolic solution of **10** was treated with silver trifluoroacetate at −10° an immediate formation of silver chloride was noted. On workup the reaction mixture gave a 94% yield of **11** (based on starting 2,3-dimethylindole). The NMR spectrum of **11** showed singlets at τ 8·64 (3H), 7·82(3H), 7·21 (3H), and a four proton multiplet at τ 2·64. The IR spectrum showed a characteristic indolenine imine stretch at 6·23 μ, while the UV spectrum showed $\lambda_{max}^{CH_3OH}$ 256 nm (ε 3870). In similar fashion, when **24**[21] was treated with hypochlorite, followed by addition of silver trifluoroacetate in methanol, we again noted precipitation of silver chloride and the formation of **25** in 74% yield based on **24.**



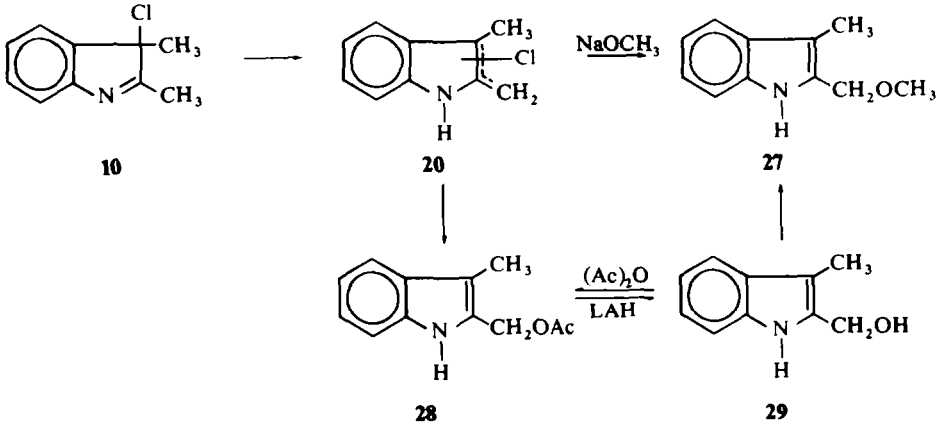
24 **26** **25**

* Any absorption due to the traces of **10** which remained would have been completely hidden by the much more intense absorptions of the rearrangement product.

† Attempts to synthesize **20b** were unsuccessful in our laboratory. We wish to thank a referee for pertinent and perceptive comments concerning the structure of **20.**

It is presumed that **26** was the chlorine containing intermediate which led to **25**.

When a solution of **10** was rapidly warmed to 25° and immediately cooled to −25°, the solution of **20**, which was formed, was very reactive. Addition of sodium methoxide

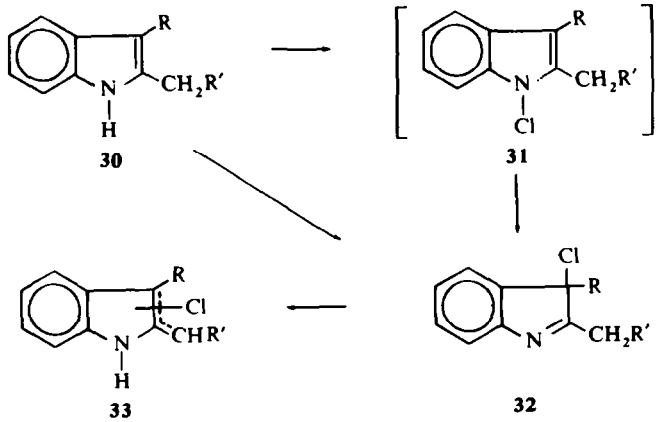


10 **20** **27** **28** **29**

gave an 80% yield* of **27**, while addition of thallium acetate resulted in the formation of **28** in 88% yield.* The structure of **27** was based on consistent spectral properties and on its comparison with an authentic sample synthesized from **29**.[2] Reduction of **24** with lithium aluminum hydride gave **29** which was converted to the methyl ether **27** utilizing diazomethane in the presence of borontrifluoride-etherate. Esterification of **29** with acetic anhydride in pyridine gave an authentic sample of **28** which was identical to that obtained from **20**.

DISCUSSION

The results reported in this paper are consistent with the general scheme outlined below for the conversion of indoles into the various products which have been observed on reaction of hypochlorite with indoles. By analogy to the facile N-chlorination of anilines[15] we feel that the first step *could* involve either the conversion of **30** into **31** or the direct conversion of **30** to **32**. The failure to detect or isolate **14** from the tosylation of



30 **31** **32** **33**

* Both yields are based on starting 2,3-dimethylindole.

13 indicates that **14** must be exceptionally prone to rearrangement. In this regard, **31**, if formed as an intermediate, might also be expected to spontaneously rearrange to **32** even at relatively low temperatures.* As long as the solution is kept cold, chemical reactions can be carried out on **32**. However, if the solution is warmed to room temperature, **32** isomerizes to **33** which undergoes its set of chemical reactions.

On the basis of this mechanistic scheme, it can be seen that a variety of different substitution reactions can be accomplished with chlorinated indoles. The exact nature of these transformations will depend on which chlorinated species is present. This, in turn, will depend critically on the thermal history of the chlorinated indole. Of course, it should be noted that the ease of these rearrangements will be a function of nature of R and R of **30**.

EXPERIMENTAL†

3-Chloro-2,3-dimethylindolenine (**10**). A soln of **9** (1·45 g) in CH_2Cl_2 (50 ml) was added under N_2 to a vigorously agitated mixture of 6% NaOCl aq (150 ml) and CH_2Cl_2 (100 ml) at −8°. After being stirred for 30 min, the organic layer was separated, washed with 30 ml cold sat NaCl aq, dried over $MgSO_4$ in the cold, and filtered. The filtrate showed the presence of 85% active chlorine as determined by a low temperature iodometric titration.‡ When the solvent was removed *in vacuo* only a dark intractable material was obtained. However, **10** was stable in solution for several hours at −25°. The NMR spectrum of **10** taken at −25° showed three-proton singlets at τ 7·74 and 8·35. The UV spectrum determined at −30° showed $\lambda_{max}^{CH_2Cl_2}$ 266 nm ($\varepsilon = ca$ 5000) with a shoulder at 292 nm.

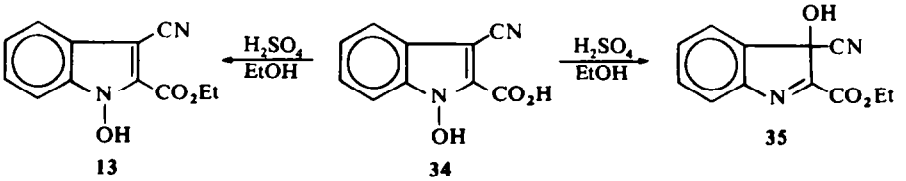
2-Carboethoxy-3-cyano-1-hydroxyindole (**13**).§ A soln of **34** (3·0 g; 15·1 mmoles) in 10% ethanolic

* It is interesting to speculate that the possible **31** to **32** isomerization could involve the formation of chloride anion and a delocalized nitrenium ion, as has recently been demonstrated for the rearrangement of N-chloroanilines.[14] In this regard the electron-withdrawing nitrile function would slow the rearrangement of the tosylate, **14**, while an alkyl substituent, such as is present in **12**, would greatly facilitate the formation of **10**. *It should be stressed that we have no evidence for the actual intermediary of* **31**. The point which we wish to emphasize is that the intermediacy of **31** cannot be *unequivocally* eliminated in favor of the direct chlorination of **30** to give **32**.

† M.ps are uncorrected. NMR spectra were measured on Varian Associates Model A-60A or HA-100 Spectrometers. Microanalyses were performed by the Scandinavian Microanalytical Laboratories, Herlev, Denmark.

‡ An aliquot of the cold methylene chloride solution of **10** was added to an excess methanolic solution of potassium iodide at −10°. The resulting solution was quickly acidified with acetic acid to liberate iodine which was titrated with aqueous sodium thiosulfate solution.

§ It was noted that the acid (**34**) might possibly undergo an acid-catalyzed rearrangement during the esterification to yield the indolenine **35** (however, see reference 20 for comments on the acid stability). This was shown not to occur by a comparison of the ester carbonyl IR absorption frequencies of **13** and **15** to those of the analogous compounds **24** and **25**. The indolenines **15** and **25** exhibit absorptions at 5·78 and 5·80 μ, respectively, while the indoles **13** and **24** have carbonyl absorptions at 5·90 and 5·95 μ,



13 **34** **35**

respectively. The aromatic nature of the 5-membered ring of the indoles, which is destroyed in going to compounds **15** and **25**, is responsible for the longer wavelength carbonyl absorptions of **13** and **24**. If the product of the esterification of **34** were actually **35**, a carbonyl absorption at shorter wavelength should have been observed.

$HgSO_4$ (100 ml) was refluxed for 3 hr. After cooling, the soln was added to 400 ml crushed ice. The product precipitated and was collected by filtration and dried *in vacuo* at room temp. Recrystallization from 1:1 benzene-hexane (20 ml) gave **13** (2·1 g; 62%), mp 119–120° (lit[17] mp 116°); IR (KBr) 2·99, 4·48, 5·90, 7·83, 13·34 μ.

Methanolysis of 2-*carboethoxy*-3-*cyanoindol*-1-*yl* p-*toluenesulfonate* (**14**). To a soln of **13** (500 mg. 2·42 mmoles) and Et_3N (300 mg) in dry THF (20 ml) at −78° was added a soln of tosyl chloride (462 mg; 2·42 mmoles) in THF (5 ml). Triethylamine hydrochloride immediately precipitated. After being stirred for 1 hr at −78°, MeOH (50 ml) was added and the resulting soln was allowed to warm to room temp. The solvents were removed *in vacuo*, leaving a residue, which was chromatographed on 25 g of silica gel. Elution with benzene gave **15** (590 mg; 64%), which was recrystallized from 1:1 benzene–hexane to give mp 108–110°; IR (KBr) 4·48, 5·78, 6·28, 8·39, 8·49, 13·40, 14·20 μ; NMR ($CDCl_3$) τ 8·53 (3H, t), 7·50 (3H, s), 5·58 (2H, q), 2·70 (4H, m), 2·38 (4H, q). Found C, 59·25; H, 4·24; N, 7·34; S, 8·53. Calcd for $C_{19}H_{16}N_2O_5S$: C, 59·37; H, 4·20; N, 7·29; S, 8·34%.

N-*Hydroxy*-2-*phenylindole* (**16**). This compound was prepared in 75% yield by the treatment of benzoin oxime with conc H_2SO_4 according to the method of Fischer.[18]

2-*Phenylindol*-1-*yl* p-*nitrobenzoate* (**17**). To a soln of **16** (500 mg; 2·39 mmoles) and Et_3N (300 mg) in dry ether (20 ml) at 0–5° was added a soln of *p*-nitrobenzoyl chloride (443 mg; 2·39 mmoles) in ether (10 ml). A ppt immediately came out of the soln. After being stirred for an additional 0·5 hr, the ether was removed *in vacuo*, leaving a damp solid. The solid was dissolved in 50 ml chloroform and the resulting soln was washed with sat $NaHCO_3$ aq (50 ml) and sat NaCl aq (50 ml). The organic layer was dried over $MgSO_4$, filtered, and the solvent evaporated, leaving an oil which slowly crystallized. Recrystallization from 1:1 benzene–hexane gave **17** (640 mg; 75%), mp 128° dec; IR (KBr) 5·70, 6·64, 7·52, 10·00, 13·34, 14·15 μ; NMR ($CDCl_3$) τ 3·30 (1H, s), 2·80 (9H, m), 1·80 (4H, s). Found: C, 70·37; H, 4·02; N, 7·77. Calcd for $C_{21}H_{14}N_2O_4$: C, 70·38; H, 3·94; N, 7·82.

2-*Phenylindol*-3-*yl* p-*nitrobenzoate* (**18**). A soln of **17** (10·0 g) in 1:1 MeOH-THF (250 ml) was refluxed for 2 days to precipitate a yellow solid. The solid was collected by filtration and the mother liquor concentrated to 50 ml in order to precipitate a second crop of yellow solid, which was collected by filtration. The solids were combined and recrystallized from 1:1 THF–EtOAc, yielding **18** (6·52 g; 65%), mp 284–285°; IR (KBr) 2·98, 5·75, 7·52, 8·00, 9·30 μ; NMR (DMSO-d_6) τ 2·55 (9H, m), 1·55 (4H, s). Found: C, 70·13; H, 4·06; N, 7·71. Calcd for $C_{21}H_{14}N_2O_4$: C, 70·38; H, 3·94; N, 7·82.

Conversion of **10** *into* **20**. A soln of **10**, about 1·45 g, in CH_2Cl_2 (100 ml) at −25° was rapidly warmed to 15° (3–4 min warming time) and immediately cooled again to −25°, yielding a soln of **20**. This soln showed only a trace of active chlorine, indicating that only small amounts of **10** remained in soln. The NMR spectrum of this sample showed two new singlets at τ 5·26 and 7·68 with relative intensities of 2:3, respectively. The UV spectrum of the soln of **20** at −10° exhibited a λ_{max} of 285 nm with an extinction coefficient of *ca* 20,000.

3-*Methoxy*-2,3-*dimethylindolenine* (**11**). A methylene chloride soln of **10** (4·35 g, 0·03 mole) at −10° was added to a stirred soln of silver trifluoroacetate (6·6 g, 0·03 mole) in MeOH (150 ml) at −10°. The mixture was stirred for 4 hr at −10° and then allowed to warm to room temp. The ppt of AgCl was removed by filtration and washed with 50 ml of CH_2Cl_2. The filtrate and washings were combined, washed with two 100 ml portions of 10% $NaHCO_3$ aq and two 100 ml portions of sat NaCl aq. The organic layer was dried over $MgSO_4$, filtered, and the solvent removed on the rotary evaporator, giving 5·1 g of a pale yellow oil. Distillation gave 4·9 g (94%) of pure **11**: bp 71–73° (1·5 mm); $n_D^{26} = 1·5338$; IR (neat) 6·20, 8·82, 9·42, 12·93, 13·22 μ; NMR (CCl_4) τ 8·64 (3H, s), 7·82 (3H, s), 7·21 (3H, s), 2·64 (4H, m); UV $\lambda_{max}^{CH_3OH}$ 256 nm (ε 3870). Analysis was carried out by high resolution mass spectrometry. *Mol wt:* Calcd for $C_{11}H_{13}NO$: 175·0997. Found: 175·0983.

2-*Carboethoxy*-3-*methoxy*-3-*methylindolenine* (**25**). A soln of **24** (1·0 g; 4·93 mmoles) in CH_2Cl_2 (100 ml) was cooled to −78° and chlorinated by dropwise addition of a soln of t-butyl hypochlorite (0·535 g; 4·93 mmoles) in CH_2Cl_2 (10 ml). After being stirred for 0·5 hr at −78°, the clear soln was added to a soln of silver trifluoroacetate (3·0 g) in MeOH (50 ml) at −78°. The soln was then allowed to warm to room temp to bring about the slow precipitation of AqCl. After being stirred for 24 hr, excess LiCl was added and the salts were removed by filtration. The filtrate was concentrated *in vacuo*, leaving a yellow residue, which was taken up in 10% $NaHCO_3$ aq (50 ml) and extracted with three 50 ml portions of CH_2Cl_2. The combined extracts were washed with sat NaCl aq (50 ml) and dried over $MgSO_4$. The desiccant was removed by filtration and the solvent evaporated, giving 1·20 g of crude product. Recrystallization from hexane gave **25** (0·85 g; 74%), mp 81–83°; IR (KBr) 5·88, 7·68, 8·97, 13·22 μ; NMR (CCl_4) τ 8·55 (3H, t), 8·38 (3H,

s), 7·13 (3H, s), 5·60 (2H, q), 2·72 (4H, m). Found: C, 66·90; H, 6·46; N, 6·13. Calcd for $C_{13}H_{15}NO_3$: C, 66·93; H, 6·48; N, 6·01.

Methanolysis of **20**. To a stirred soln of 2,3-dimethylindole (1·45 g; 0·01 mole) in CH_2Cl_2 (130 ml) at −78° was added dropwise a soln of t-butyl hypochlorite (1·19 g; 0·011 mole) in CH_2Cl_2 (10 ml). The soln was stirred at −78° for 15 min and then quickly warmed to 15° with an oil bath (3–4 min warming time). A freshly prepared soln of methanolic NaOMe made from 0·23 g Na metal and 50 ml MeOH was immediately added. NaCl precipitated. After being stirred at room temp for 5 hr, the NaCl was removed by filtration and the filtrate was washed with 100 ml water and then 100 ml sat NaCl aq and dried over $MgSO_4$. The desiccant was removed by filtration and the solvent evaporated, leaving 2·10 g of a light red oil. The oil was distilled in a molecular still, yielding **27** (1·43 g; 82%) as a pale yellow semi-solid material: $n_D^{26} = 1·5933$; IR (neat) 2·90, 6·12, 9·38, 13·50 μ; NMR (CCl_4) τ 7·75 (3H, s), 6·7 (3H, s), 5·45 (2H, s), 2·84 (4H, m); UV $\lambda_{max}^{CH_3OH}$ 283 nm (ε = 6400). Since the compound slowly decomposed to a red oil on standing, analysis was carried out by high resolution mass spectrometry. *Mol wt:* Calcd for $C_{11}H_{13}NO$: 175·0997. Found: 175·0999.

Acetolysis of **20**. To a stirred soln of 2,3-dimethylindole (1·45 g; 0·01 mole) in CH_2Cl_2 (130 ml) at −78° was added dropwise a soln of t-butyl hypochlorite (1·19 g; 0·11 mole) in CH_2Cl_2 (10 ml). The soln was stirred at −78° for 15 min and then quickly warmed to 15° with an oil bath (3–4 min warming time). A soln of thallium acetate (2·63 g; 0·01 mole) in glacial AcOH (50 ml) was then immediately added. Thallium chloride precipitation began at once. After being stirred at room temp for 5 hr, the salts were removed by filtration and the pale yellow filtrate was added to 500 ml water. Excess $NaHCO_3$ was slowly added to neutralize the AcOH. The organic layer was separated, washed with sat NaCl aq, and dried over $MgSO_4$. The drying agent was removed by filtration and the solvents evaporated *in vacuo* giving 1·80 g of a pale yellow oil. A 500 mg sample of the oil was sublimed yielding 452 mg of **28**. Recrystallization from Skellysolve B gave **28** (430 mg; 76·5%) from 2,3-dimethylindole; mp 90–92°; IR (CH_2Cl_2) 2·76, 5·70, 8·07 μ; NMR (CCL_4) τ 7·95 (3H, s), 7·6 (3H, s), 4·79 (2H, s), 2·70 (4H, m); UV $\lambda_{max}^{CH_3OH}$ 279 nm (ε = 6300). Found: C, 70·89; H, 6·55; N, 6·97. Calcd for $C_{12}H_{13}NO_2$: C, 70·91; H, 6·45; N, 6·89.

2-Methoxymethyl-3-methylindole (**27**). To a soln of **29**[22] (1·00 g; 6·20 mmoles) in dry ether (30 ml) at room temp was added a soln of BF_3 etherate (87 mg) in dry ether (10 ml). Immediately a soln of diazomethane (800 mg; 19 mmoles) in dry ether (30 ml) was added dropwise. N_2 was vigorously evolved. After 10 min, 10% NaOH aq (50 ml) was added and the mixture stirred for 0·5 hr. The mixture was decanted from precipitated polymethylene and the organic layer was separated and dried over $MgSO_4$. The desiccant was removed by filtration and the solvent evaporated, yielding 1·00 g of a pale yellow oil which partially solidified on standing. The oil was distilled in a molecular still, giving **27** (781 mg; 72%) which was a semi-solid colorless compound at room temp: $n_D^{25} = 1·5910$. The IR, NMR, and UV spectra of this sample were identical to those of **27** obtained from the methanolysis of **20**.

3-Methylindol-2-ylmethyl acetate (**28**). To a soln of **29** (500 mg) in dry pyridine (5 ml) was added Ac_2O (316 mg). After being stirred overnight at room temp, the soln was poured into water (20 ml). An oil, which slowly crystallized, came out of soln. After the mixture was cooled in an ice bath, the solid was collected by filtration, dried, and the product was recrystallized from Skellysolve B to give **28** (492 mg; 78%): mp 91·0–93·5°. The IR, NMR, and UV spectra of this sample were identical to those of **28** which was obtained from the acetolysis of **20**. A mixture mp determination showed no depression.

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