

**182. The Mechanism of Heterocyclic Ring Expansions. Part II.¹
The Reaction of Methylindoles with Halogenocarbenes.**

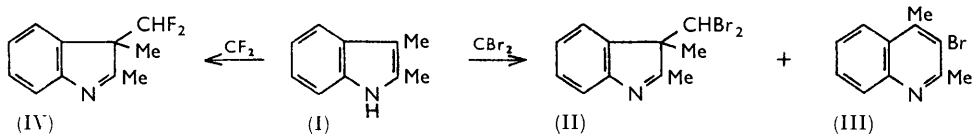
By C. W. REES and C. E. SMITHEN.

2,3-Dimethylindole reacts with dibromocarbene to give 3-dibromo-methyl-2,3-dimethyl-3*H*-indole (II) and 3-bromo-2,4-dimethylquinoline (III), but with difluorocarbene to give only the corresponding 3*H*-indole (IV), and with monochlorocarbene to give only the corresponding quinoline. With ethyl trichloroacetate and potassium *t*-butoxide, 3-methylindole gives 3-chloro-4-methylquinoline and ethyl 3-methylindole-1-carboxylate (VI), whilst 1,3-dimethylindole gives polymeric material only. 1,2,3-Trimethylindole gives 3-dichloromethyl-1,3-dimethyl-2-methyleneindoline (VIII) and, if the carbene is generated in overall neutral conditions, 3-chloro-1,2-dihydro-1,4-dimethyl-2-methylenequinoline (X) also, and 1,2,3,4-tetrahydro-9-methylcarbazole gives 4*a*-dichloromethyl-2,3,4,4*a*-tetrahydro-9-methylcarbazole (XVI). The mechanism of these reactions, which follow the pattern described in Part I, are briefly discussed.

Pyrolysis of sodium tribromoacetate and alkaline hydrolysis of ethyl chlorodifluoroacetate are useful sources of dibromo- and difluoro-carbene, respectively.

THE reactions of 2,3-dimethylindole with dichlorocarbene, considered in detail in Part I, have now been extended to other halogenocarbenes and other methylindoles, to test and, if possible, extend the previous conclusions about reaction mechanism.

Reaction of 2,3-Dimethylindole with Halogenocarbenes other than Dichlorocarbene.—With dibromocarbene, obtained from bromoform and ethanolic sodium ethoxide, 2,3-dimethylindole (I) gave two basic products, C₁₁H₁₁Br₂N, m. p. 92–93°, and C₁₁H₁₀BrN, m. p. 69–70°, assigned the structures 3-dibromomethyl-2,3-dimethyl-3*H*-indole (II) and 3-bromo-2,4-dimethylquinoline (III), respectively, on the basis of their chemical and spectral



properties which were entirely analogous to those of the dichlorocarbene reaction products.¹ The same two products were obtained from the thermal decomposition of sodium tribromoacetate in 1,2-dimethoxyethane containing dimethylindole. This appears to be the first use of tribromoacetic acid derivatives as a source of dibromocarbene, and the ease with which the sodium salt decomposed makes this an attractive route to dibromocarbene under overall neutral conditions. As described before for the thermal decomposition of trichloroacetate ions,¹ the strongly basic tribromomethyl anion should undergo proton-abstraction in competition with its heterolysis into dibromocarbene and bromide ion; the formation of bromoform in the present reaction confirms this. The ratio of the bromoquinoline (III) to the dibromomethyl-3*H*-indole (II) increased from 1:2 in ethanolic sodium ethoxide to 6:4 in the thermal decarboxylation reaction, thus following the same trend as for the dichlorocarbene reactions¹ in which more strongly basic conditions favoured 3*H*-indole formation.

With difluorocarbene, generated by base-catalysed cleavage of ethyl chlorodifluoroacetate for the first time, dimethylindole (I) gave only one basic product, C₁₁H₁₁F₂N, whose properties were exactly analogous to those of the other dihalogenomethyl-3*H*-indoles. The structure, 3-difluoromethyl-2,3-dimethyl-3*H*-indole (IV), assigned to it was confirmed by

¹ Part I, preceding paper.

the proton magnetic resonance spectrum (see Experimental section), and hence the structures of the other halogeno-3*H*-indoles are indirectly confirmed. Ethyl 2,3-dimethylindole-1-carboxylate was isolated from the acid-insoluble fraction. Careful examination of the acid-soluble fraction from this reaction failed to reveal any other product, particularly the difluorocarbene adduct (V), which was expected to be the most stable of the dihalogeno-compounds of this structure, or the ring-expanded quinoline. The absence of these products and the formation of the difluoromethyl-3*H*-indole (IV) in moderate yield lessens the possibility that the 3*H*-indoles arise from the dihalogenocyclopropane intermediates (e.g., V), in agreement with the mechanism proposed before.¹ Further support for this was found in the thermal decomposition of sodium chlorodifluoroacetate in boiling 1,2-dimethoxyethane containing the indole (I). Although decarboxylation under these conditions was slow (40% in 72 hours), the yield of basic products was negligible. The absence of the difluoromethyl-3*H*-indole (IV) may be explained by the absence of a strongly



basic carbanion, CClF_2^- , in the decarboxylation of the chlorodifluoroacetate anion which proceeds by a concerted α -elimination.² Thus the dimethylindolyl anion, required for the formation of the dihalogenomethyl-3*H*-indoles in our mechanism, would not be formed. Apparently difluorocarbene is not sufficiently electrophilic to react with neutral dimethylindole (I) under present conditions, in agreement with other reports on the relative unreactivity of this carbene.³

With monochlorocarbene, 2,3-dimethylindole gave a small yield of 2,4-dimethylquinoline, analogous to the recent⁴ ring-expansions of pyrrole and indole to pyridine and quinoline, respectively; no 3*H*-indole derivative could be isolated.

Reaction of Other Indoles with Dichlorocarbene.—3-Methylindole and dichlorocarbene, from ethyl trichloroacetate and potassium *t*-butoxide, gave 3-chloro-4-methylquinoline as the only identified basic product. 3-Dichloromethyl-3-methyl-3*H*-indole could only have been formed in very small amount and no products of its rearrangement or hydrolysis were detected. The major component of the acid-insoluble reaction product was ethyl 3-methylindole-1-carboxylate (VI).⁵ This ester could not be completely separated from 3-methylindole but its identity was established by elemental analysis, infrared spectrum [$\nu(\text{C}=\text{O})$ 1722 cm^{-1}], and boiling point; its rearrangement,⁵ on heating, to ethyl 3-methylindole-2-carboxylate may have contributed to the difficulty of purification. The formation of ethyl 3-methylindole-1-carboxylate (VI) in this reaction indicates participation by the 3-methylindolyl anion, so that the absence of products of reaction of this anion with dichlorocarbene is unexpected and contrasts with the related reaction of 2,3-dimethylindole. However, the 2-methyl group of the latter is known⁶ to increase the nucleophilicity of the 3-position considerably and it may be that the 3-methylindolyl anion is insufficiently nucleophilic to compete effectively with the *t*-butoxide ions for dichlorocarbene.

1,3-Dimethylindole with ethyl trichloroacetate and potassium *t*-butoxide gave an amorphous halogen-free polymer as the major product; much ethyl trichloroacetate was

² Hine and Duffey, *J. Amer. Chem. Soc.*, 1959, **81**, 1131.

³ Hine and Ehrenson, *J. Amer. Chem. Soc.*, 1958, **80**, 824; Simons and Yarwood, *Nature*, 1961, **192**, 943; Knox, Verlade, Berger, and Cuadriello, *Chem. and Ind.*, 1962, 860.

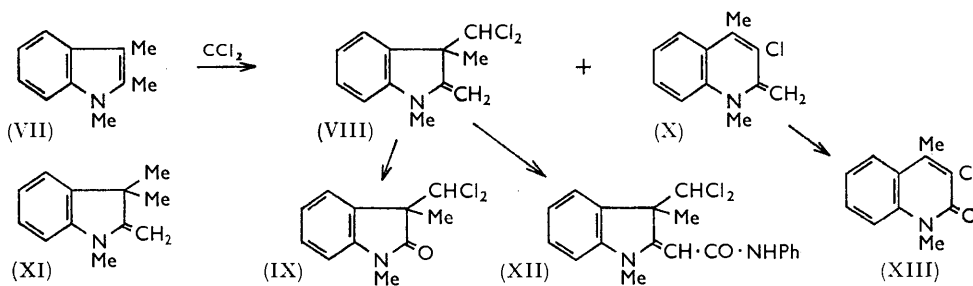
⁴ Closs and Schwartz, *J. Org. Chem.*, 1961, **26**, 1924.

⁵ Oddo, *Gazzetta*, 1912, **42**, 361.

⁶ Noland and Robinson, *Tetrahedron*, 1958, **3**, 68; Hinman and Shull, *J. Org. Chem.*, 1961, **26**, 2339; Hinman and Lang, *Tetrahedron Letters*, 1960, No. 21, 12; Kamlet and Dacons, *J. Org. Chem.*, 1961, **26**, 220; Hinman and Whipple, *J. Amer. Chem. Soc.*, 1962, **84**, 2534.

recovered and no other chlorine-containing material could be isolated. The lack of reactivity of 1,3-dimethylindole towards dichlorocarbene may be due to reduced nucleophilicity of the 2,3-double bond for the same reasons as in 3-methylindole; furthermore 1,3-dimethylindole cannot give rise to a stable anion.

The nucleophilicity of the 2,3-bond of 1,2,3-trimethylindole (VII) should be similar to that of 2,3-dimethylindole, and its reaction with dichlorocarbene was therefore investigated. The conversion of trimethylindole into the unstable 3-dichloromethyl-1,3-dimethyl-2-methyleneindoline (VIII) under Reimer-Tiemann conditions had been claimed by Plancher and Carrasco.⁷ Under various basic conditions we isolated the same compound, as the only product, and confirmed its structure. Its picrate was identical with the methopicrate of 3-dichloromethyl-2,3-dimethyl-3*H*-indole,¹ its ultraviolet and infrared spectra agreed well with those of Fischer's base (XI), and it exhibited the characteristic reactivity of 2-methyleneindolines towards electrophilic substitution at the methylene group. For example, it condensed readily with phenyl isocyanate to give the anilide (XII). The dichlorinated base (VIII), colourless when pure, darkened rapidly, especially in the presence of light and air. Recently Robinson⁸ reported the formation of 1,3,3-trimethyl-oxindole in the autoxidation of Fischer's base. The analogous 3-dichloromethyl-1,3-dimethyl-oxindole (IX) would be expected in the present case and, although not isolated



as an autoxidation product, its presence was indicated by strong carbonyl absorption at 1704 cm⁻¹. The oxindole (IX), m. p. 45°, was obtained in good yield from the indoline (VIII) by oxidation with Lemieux and von Rudloff's reagent,⁹ and had the expected properties.

When 1,2,3-trimethylindole (VII) reacted with dichlorocarbene generated by thermal decarboxylation of sodium trichloroacetate, under overall neutral conditions, a second acid-soluble product, 3-chloro-1,2-dihydro-1,4-dimethyl-2-methylenequinoline (X) was obtained as an unstable yellow crystalline solid, m. p. 75° (decomp.). Its structure followed from spectral properties, the identity of its picrate with the methopicrate of 3-chloro-2,4-dimethylquinoline, oxidation to a neutral product, C₁₁H₁₀ClNO, having the characteristic 2-quinolone chromophore and formulated as 3-chloro-1,4-dimethyl-2-quinolone (XIII), and finally from its synthesis from 3-chloro-2,4-dimethylquinoline methiodide and alkali. The unchlorinated analogue of the base (X) is a yellow crystalline compound, m. p. 60° (decomp.),¹⁰ and several related bases have been described.¹¹ This monochlorinated base (X) was shown not to survive strongly basic conditions or prolonged chromatography on neutral alumina, and this presumably explains the failure to detect this product in the earlier reactions of dichlorocarbene with trimethylindole in the presence of alkoxide ions.

The isolation of the ring-expanded product (X), together with the methyleneindoline (VIII), completes the analogy between the reactions of 2,3-di- and 1,2,3-tri-methylindole

⁷ Plancher and Carrasco, *Atti Accad. naz. Lincei*, 1904, **13**, I, 575.

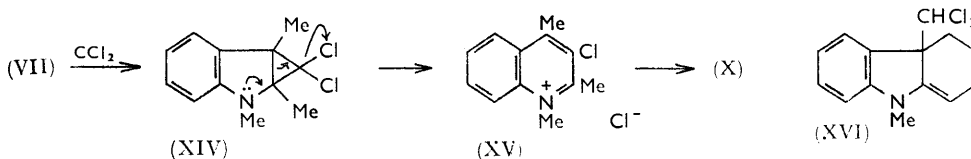
⁸ Robinson, *Chem. and Ind.*, 1962, 1291.

⁹ Lemieux and von Rudloff, *Canad. J. Chem.*, 1955, **33**, 1710.

¹⁰ Rosenhauer, Hoffmann, and Unger, *Ber.*, 1926, **59**, 946.

¹¹ Mills and Raper, *J.*, 1925, **127**, 2466; Hamer, Rathbone, and Winton, *J.*, 1947, 954.

with dichlorocarbene. On the basis of this analogy ring-expansion should proceed by addition of dichlorocarbene to trimethylindole (VII) to give the adduct (XIV) which rearranges to the 1-methylquinolinium chloride (XV); this is isolated as the methylene-dihydroquinoline (X) by the procedure used. As before, the intermediate adduct (XIV) could not be isolated. Formation of the methyleneindoline (VIII) may involve attack by



dichlorocarbene upon 1,2,3-trimethylindole, followed by loss of a proton from the then activated 2-methyl group. However, the reverse sequence is also possible and more evidence is required to settle this point. When sodium trichloroacetate was used to generate dichlorocarbene a substantial amount of chloroform was produced by reaction between trichloromethyl anions and a proton-donor, *e.g.*, the 1-methylquinolinium ion in (XV).

The conversion of 1,2,3,4-tetrahydrocarbazole by dichlorocarbene into 4a-dichloromethyl-1,2,3,4-tetrahydro-4aH-carbazole has been described.¹² The reaction between 1,2,3,4-tetrahydro-9-methylcarbazole and dichlorocarbene, under basic conditions, has now been investigated, and the only isolable product, an unstable base, $\text{C}_{14}\text{H}_{15}\text{Cl}_2\text{N}$, m. p. 82–84° (decomp.), assigned the structure 4a-dichloromethyl-2,3,4,4a-tetrahydro-9-methylcarbazole (XVI) on the basis of its chemical and spectral properties. It was presumably formed in the same way as the analogous methyleneindoline (VIII) and, like it, decomposed spontaneously with the development of carbonyl absorption at 1710 cm^{-1} , consistent with the formation of an oxindole derivative by autoxidation.

EXPERIMENTAL

For general directions, and for preparations and purifications not given, see Part I.¹

Materials.—3-Methylindole, chlorodifluoroacetic acid, and bromoform were good commercial specimens used without further purification. Ethyl chlorodifluoroacetate, b. p. 97–99°, n_D^{20} 1.3620 (lit.,¹³ b. p. 97°, n_D^{20} 1.3525), was prepared (92%) by the method of Bergmann *et al.*¹³ Sodium chlorodifluoroacetate and tribromoacetate were prepared from the acids, and dried as described for sodium trichloroacetate in Part I.¹ Tribromoacetic acid, m. p. 130° (lit.,¹⁴ 127°), was prepared by Woods and Spinks's method.¹⁴ 1,2,3-Trimethylindole, b. p. 140–141°/18 mm. (lit.,¹⁵ 283–284°/762 mm.), was prepared (90%) by Janetsky and Verkade's method,¹⁵ and 1,2,3,4-tetrahydro-9-methylcarbazole, m. p. 46–47° (lit.,¹⁶ 50°) was prepared (86%) by Nakazaki and Isoe's method.¹⁶

1,3-Dimethylindole (cf. ref. 17).—Chloroacetone (36 g.) was added dropwise with stirring to *N*-methylaniline (90 ml.), and the mixture was stirred overnight at room temperature and slowly heated to 150°. 10*N*-Hydrochloric acid (1 ml.) was added and the mixture heated at 150° for a further 6 hr. When cool, the dark red viscous oil was dissolved in 20% hydrochloric acid (500 ml.) and extracted with ether (5 × 10 ml.). The ethereal solution was washed with 20% hydrochloric acid (3 × 50 ml.) and water (3 × 100 ml.), dried, and the solvent removed. The crude product (35 g.) was distilled in a stream of nitrogen to give 1,3-dimethylindole (28 g., 50%), b. p. 72–73°/0.4 mm. (lit.,¹⁷ 120°/7 mm.), n_D^{23} 1.5930, which was stored in the dark under nitrogen. Its infrared spectrum showed no N–H absorption.

Reaction of 2,3-Dimethylindole with Dibromocarbene.—(a) *Under basic conditions.* 2,3-Dimethylindole (10 g.) was dissolved in absolute ethanol (50 ml.) containing sodium ethoxide

¹² Plancher and Carrasco, *Atti. Accad. naz. Lincei*, 1904, **13**, I, 632; Bartlett, Dickel, and Taylor, *J. Amer. Chem. Soc.*, 1958, **80**, 126.

¹³ Bergmann, Moses, Neeman, Cohen, Kaluszyner, and Reuter, *J. Amer. Chem. Soc.*, 1957, **79**, 4174.

¹⁴ Woods and Spinks, *Canad. J. Chem.*, 1960, **38**, 79.

¹⁵ Janetsky and Verkade, *Rec. Trav. chim.*, 1946, **65**, 691.

¹⁶ Nakazaki and Isoe, *J. Chem. Soc. Japan*, 1955, 1159.

¹⁷ Meisenheimer, *Ber.*, 1924, **57**, 1744.

[from sodium (1.52 g.), and the mixture stirred at 50–55°. A solution of bromoform (20 g.) in ethanol (7 ml.) was added dropwise during 1 hr., and the stirring was continued at this temperature overnight. Volatile material was removed at 50°/15 mm., and the residue dissolved in ether (150 ml.) and extracted with ice-cold 10% hydrochloric acid (10 × 50 ml.), to give a basic fraction (4.20 g.) and a non-basic fraction (12.9 g.). The basic fraction was adsorbed on neutral alumina (2 × 38 cm.) and eluted as follows. (i) Ether (2%) in light petroleum (500 ml.) gave crystals (1.43 g.) of 3-bromo-2,4-dimethylquinoline, m. p. 69–70° (from hexane) (Found: C, 55.9; H, 4.3; N, 5.5. C₁₁H₁₀BrN requires C, 55.95; H, 4.3; N, 5.9%) [*picrate*, fine yellow needles sparingly soluble in ethanol, m. p. 213° (decomp.) (Found: C, 44.2; H, 2.85. C₁₇H₁₃BrN₄O₇ requires C, 43.9; H, 2.8%)], which showed typical quinoline absorption: λ_{\max} . 279 (3.64), 294sh (3.59), 307 (3.57), 321 (3.62); λ_{\min} . 251 (3.44), 304 (3.45), 317 (3.36) m μ . (ii) Ether (20%) in light petroleum (500 ml.) then ether (50%) in light petroleum (200 ml.) yielded a crystalline solid (1.50 g.) which gave 3-dibromomethyl-2,3-dimethyl-3H-indole as pale yellow prisms, m. p. 92–93° (from hexane) (Found: C, 41.6; H, 3.4; N, 4.2. C₁₁H₁₁Br₂N requires C, 41.7; H, 3.5; N, 4.4%) [*picrate*, deep yellow needles from ethanol, m. p. 168–169° (decomp.) (Found: C, 38.2; H, 2.6. C₁₇H₁₄Br₂N₄O₇ requires C, 37.4; H, 2.6%)], which showed typical 3H-indole absorption: λ_{\max} . 266 (3.64); λ_{\min} . 244 (3.48) m μ ; ν_{\max} . 1618w, 1587 (aryl-N=C), 769m, 752 (o-disubstituted benzene), 712w, and 697 cm⁻¹. Each of these bases had a characteristic smell and crystalline form like the corresponding chloro-compounds.

The non-basic fraction was chromatographed on active alumina (3.5 × 20 cm.), as described¹ for the dichlorocarbene reactions, to give 2,3-dimethylindole (5.8 g.), the dibromomethyl-3H-indole (0.17 g.), and 2-acetamidoacetophenone (0.50 g.). Thus the total yields of the recovered indole, the bromoquinoline, and the 3H-indole were 58, 9.2, and 8.0%, respectively, and the molar ratio of quinoline to 3H-indole was 1.15.

(b) *Under neutral conditions.* Dry powdered 2,3-dimethylindole (10 g.) and sodium tri-bromoacetate (22 g.) were heated under reflux in anhydrous 1,2-dimethoxyethane (100 ml.) under nitrogen for 18 hr. Gas evolution began at ca. 60° and was quite vigorous near the b. p. The solvent was removed at 40°/12 mm. and the residue dissolved in ether (100 ml.) and extracted with acid as in (a) to give a basic fraction (4.6 g.) and a non-basic fraction (9.2 g.). The basic fraction was separated by chromatography on neutral alumina as in (a) to give 3-bromo-2,4-dimethylquinoline (3.33 g.) and 3-dibromomethyl-2,3-dimethyl-3H-indole (0.70 g.). The non-basic fraction was adsorbed on active alumina (3.5 × 20 cm.) and eluted as follows. (i) Light petroleum (500 ml.) gave semicrystalline material (3.9 g.) which was distilled at 30°/1 mm. and the volatile material collected in an ice-cold trap to give bromoform (1 g., 6%), m. p. and mixed m. p. ca. 5°, n_D^{20} 1.5940 (lit.,¹⁸ 1.598). The residue gave 2,3-dimethylindole, m. p. and mixed m. p. 102° (2.23 g.) (from light petroleum–ether). (ii) Ether (10%) in light petroleum (500 ml.) then ether (20%) in light petroleum (500 ml.) gave 2,3-dimethylindole (2.43 g.), m. p. 98–100°. Thus the total yields of the recovered indole, the bromoquinoline, and the 3H-indole were 47, 20.5, and 3.2%, respectively, and the molar ratio of quinoline to 3H-indole was 6.4.

Reaction of 2,3-Dimethylindole with Difluorocarbene.—(a) *One mole of difluorocarbene under basic conditions.* Dimethylindole (10 g.) and potassium t-butoxide (7.9 g.) were suspended by vigorous stirring in olefin-free light petroleum (b. p. 40–60°) (100 ml.) at room temperature. Ethyl chlorodifluoroacetate (11 g.) in the same solvent (30 ml.) was added dropwise during 1 hr. with ice-cooling, and the mixture then stirred at room temperature for a further 18 hr. Water (100 ml.) was added and the layers separated. The aqueous layer was extracted with ether (2 × 50 ml.) and the combined ether–light petroleum solution extracted with acid, as before, to give a basic oil (2.26 g.) and a non-basic solid (10.3 g.).

The basic oil was adsorbed on neutral alumina (2 × 22 cm.) and eluted as follows. (i) Ether (10%) in light petroleum (500 ml.) gave a pale yellow fluorine-containing oil (0.86 g.) which was unchanged by further chromatography on neutral alumina to give 3-difluoromethyl-2,3-dimethyl-3H-indole, n_D^{24} 1.5180 (Found: C, 67.0; H, 5.8; N, 7.2. C₁₁H₁₁F₂N requires C, 67.7; H, 5.7; N, 7.2%) [*picrate*, orange needles, m. p. 128–129° (Found: C, 47.7; H, 3.5; N, 13.3. C₁₇H₁₄F₂N₄O₇ requires C, 48.1; H, 3.3; N, 13.2%)], which showed typical 3H-indole absorption: λ_{\max} . 256 (3.73); λ_{\min} . 232 (3.48) m μ ; ν_{\max} . 1613w, 1582 (aryl-N=C), 1456, 1429, 1387 (C–CH₃),

¹⁸ Vogel, J., 1948, 1850.

1075vs, 1047vs (CF₂), 772, and 752 cm.⁻¹ (*o*-disubstituted benzene). (ii) Ether (20%) in light petroleum (200 ml.) then ether (500 ml.) gave a yellow oil (0.48 g.) which solidified to a glass, m. p. 77–80° (Found: C, 74.9; H, 6.3; N, 8.2%). This product was unchanged (infrared spectrum) on rechromatography but could not be recrystallised; the proton magnetic resonance spectrum in deuteriochloroform (cf. below) suggested that it was not a single compound.

The non-basic fraction (10.3 g.) was adsorbed on active alumina (3.5 × 22 cm.) and eluted as follows. (i) Light petroleum (200 ml.) eluted an oil (1.1 g.) which gave ethyl 2,3-dimethylindole-1-carboxylate¹ (0.5 g.), b. p. 120°/1 mm., and a residue of (mainly) 2,3-dimethylindole (infrared). (ii) Ether (10%) in light petroleum (500 ml.) gave 2-acetamidoacetophenone (0.3 g.), m. p. 60–65°.

The proton magnetic resonance spectra of the acid-soluble products of this reaction were examined at 60 Mc./sec.* The integrated spectrum of 3-difluoromethyl-2,3-dimethyl-3*H*-indole (in carbon tetrachloride) was in full agreement with this structure: τ 2.72, multiplet (4 aromatic protons); τ 4.52, triplet (CHF₂ proton; $J_{HF} = 56$ c./sec.);¹⁹ τ 7.75 (3 α -methyl protons);²⁰ and τ 8.62 (3 β -methyl protons).²⁰ The spectrum of the crude basic fraction (in deuteriochloroform) indicated the presence of no products additional to those described above.

(b) *Two moles of difluorocarbene under basic conditions.* The above reaction was repeated using two molar equivalents of the same difluorocarbene precursors, to give, in the usual manner, a basic product (3.1 g.) and a non-basic product (13.9 g.). Chromatography of the basic product gave the difluoromethyl-3*H*-indole (1.58 g.) and the glassy product, m. p. 77–80° (0.45 g.); distillation of the non-basic fraction gave a volatile colourless liquid (2 g.), considered to be chlorodifluoroacetic acid, and a yellow oil (2 g.), b. p. 140°/1 mm., consisting mainly of ethyl 2,3-dimethylindole-1-carboxylate with a little 2,3-dimethylindole (infrared spectrum).

(c) *Under neutral conditions.* 2,3-Dimethylindole (10 g.) and sodium chlorodifluoroacetate (15 g.) were heated under reflux in anhydrous 1,2-dimethoxyethane (100 ml.) for 72 hr. under nitrogen, during which time sodium chloride (2.2 g., 38%) separated. (Fluoride ions could not be detected.) The solvent was removed at 40°/12 mm. and the residue gave, in the usual manner, a small basic fraction (0.08 g.) almost identical (infrared spectra) with the glassy solid, m. p. 77–80°, obtained under basic conditions, and a non-basic fraction from which dimethylindole (9 g.) was recovered. None of the difluoromethyl-3*H*-indole was detected.

Reaction of 2,3-Dimethylindole with Monochlorocarbene.—The monochlorocarbene (*ca.* 4 moles) was generated by Closs and Closs's method.²¹ The dry powdered indole (7.5 g.) in anhydrous dichloromethane (100 ml.) was stirred at 0° under nitrogen. A solution of *n*-butyllithium in ether (130 ml.), prepared²² from butyl bromide (34 g.) and lithium (3.8 g.), was added dropwise during 2 hr., and the mixture stirred at room temperature for a further 15 hr. The mixture was poured with stirring into ice-water, the aqueous layer was extracted with ether (2 × 50 ml.), and the combined organic solutions were extracted with ice-cold 10% aqueous hydrochloric acid (10 × 50 ml.), to give a basic oil (1.43 g.) and a non-basic crystalline solid (7.30 g.). A portion (0.40 g.) of the basic oil and an excess of ethanolic picric acid gave, after fractional crystallisation from ethanol, 2,4-dimethylquinoline picrate (0.36 g., 6.3% overall), m. p. and mixed m. p. 180–185°. The remainder (1.03 g.) of the basic oil was chromatographed on neutral alumina to give, with ether (5%) in light petroleum (300 ml.), 2,4-dimethylquinoline (0.34 g., 5.8%) identical (infrared) with authentic material (picrate, m. p. and mixed m. p. 198–199°). The non-basic solid was largely unchanged 2,3-dimethylindole (infrared), and chromatography on deactivated alumina gave this indole (6.7 g., 88%), m. p. and mixed m. p. 99–100°.

Reaction of 3-Methylindole with Dichlorocarbene.—Dry powdered 3-methylindole (10 g.) and potassium *t*-butoxide (17 g.) were suspended by vigorous stirring in olefin-free light petroleum (b. p. 40–60°) (100 ml.) at room temperature. Ethyl trichloroacetate (30 g.) in the same solvent (20 ml.) was added dropwise during 1 hr., and the mixture stirred at room temperature for a further 18 hr. Water (100 ml.) was added and the layers separated. Extraction with

* Kindly measured by Dr. A. Melera of Varian A.G., Zurich, whose assistance with the interpretation of the spectra is gratefully acknowledged.

¹⁹ Arison, Shen, and Trenner, *J.*, 1962, 3828.

²⁰ "NMR Spectra Catalog," Varian Associates, Palo Alto, California, 1962, Spectrum No. 286.

²¹ Closs and Closs, *J. Amer. Chem. Soc.*, 1959, **81**, 4996; 1960, **82**, 5723.

²² Gilman, Beel, Brannen, Bullock, Dunn, and Miller, *J. Amer. Chem. Soc.*, 1949, **71**, 1499.

acid, as before, gave a basic fraction (0.88 g.) and a non-basic fraction (27 g.). Chromatography of the former gave 3-chloro-4-methylquinoline (0.61 g., 4.5%) as needles from hexane, m. p. 55° (lit.,²³ 54—55°) [picrate, m. p. 212° (lit.,²³ 208°)], and a red gum (0.1 g.) which did not yield a crystalline derivative with picric acid. The infrared spectrum (ν_{\max} , 1603, 780sh, 750 cm^{-1}) suggested that this might be 3-dichloromethyl-3-methyl-3*H*-indole. Distillation of the non-basic fraction gave ethyl trichloroacetate (14 g., 47% recovered), b. p. 63°/15 mm., n_D^{24} 1.4465. The residue was chromatographed on active alumina to give, with light petroleum and ether (2%) in light petroleum, a mixture (6 g.) with an infrared spectrum similar to that of 3-methylindole, with additional strong absorption at 1722 cm^{-1} [cf. ethyl 2,3-dimethylindole-1-carboxylate, $\nu(\text{C}=\text{O})$ 1727 cm^{-1}]. The ester component, ethyl 3-methylindole-1-carboxylate (1.5 g.), when distilled, had b. p. 105—110°/0.5 mm. (lit.,⁵ 289°/760 mm., 215°/11 mm.) (Found: N, 6.9. Calc. for $\text{C}_{12}\text{H}_{13}\text{NO}_2$: N, 6.9%), but was not completely separated from 3-methylindole.

Reaction of 1,3-Dimethylindole with Dichlorocarbene.—1,3-Dimethylindole (10 g.) was treated with dichlorocarbene (2 moles) generated from potassium *t*-butoxide (16 g.) and ethyl trichloroacetate (27.5 g.) as in the previous experiment. During the reaction an amorphous solid (8.5 g.) separated; this contained nitrogen but only traces of chlorine, was insoluble in water, and could not be crystallised from organic solvents; it was not investigated further. The remainder of the reaction mixture gave a negligible basic fraction (<0.10 g.), unchanged ethyl trichloroacetate (14 g.), and 1,3-dimethylindole (6 g.).

Reaction of 1,2,3-Trimethylindole with Dichlorocarbene.—(a) *From chloroform and ethanolic sodium ethoxide.* To 1,2,3-trimethylindole (10 g.) in absolute ethanol (50 ml.) containing sodium ethoxide [from sodium (2.0 g.)] stirred at 45—50° (water-bath), a solution of chloroform (20 g.) in ethanol (10 ml.) was added during 2 hr. The dark green mixture was stirred at 45—50° for a further 4 hr. and then all volatile material was removed at 40°/15 mm. The oily residue, in ether (150 ml.), was extracted with ice-cold 5% aqueous hydrochloric acid (5 × 100 ml.). The red ethereal solution was washed with water, dried, and evaporated, to give a dark oil (6.5 g.) which was largely unchanged trimethylindole (infrared spectrum and picrate, m. p. and mixed m. p. 150°). The violet acidic extracts were filtered and basified at 0° with 10*N*-potassium hydroxide. Extraction with ether gave a dark green semi-solid (3.7 g.) which was separated by trituration with light petroleum into an insoluble blue amorphous solid (0.50 g.), m. p. *ca.* 50° (decomp.), and a red oil (3 g.). The latter was adsorbed on neutral alumina (2 × 20 cm.) and eluted with ether (10%) in light petroleum to give 3-dichloromethyl-1,3-dimethyl-2-methyleneindoline, as an oil (0.90 g.), n_D^{25} 1.5970 [picrate, needles from ethanol, m. p. 147—148° (decomp.) (lit.,²⁴ 146—147°) not depressed on admixture with 3-dichloromethyl-2,3-dimethyl-3*H*-indole methopicrate¹]. The base, which was unsaturated, reddened rapidly. The ultraviolet spectrum showed 2-methyleneindoline absorption: λ_{\min} , 241 (3.64); λ_{\max} , 280 (4.35); λ_{infl} 305 (3.41) μ . The infrared spectrum [ν_{\max} , 1653 (C=CH₂), 1610 (aromatic), 1493 (C—CH₃), 1464, 1377 (C—CH₃), 1340, 1309, 1284w, 1250m, 1212m, 1159m, 1129m, 1104, 1046w, 1022, 948 (C=CH₂), 868w, 844w, 777 (CHCl₂), 743 (*o*-disubstituted benzene), 727 cm^{-1}] was very similar to that of 1,3,3-trimethyl-2-methyleneindoline (ν_{\max} , 1650, 1610, 1493, 1456m, 1377, 1340, 1304, 1235, 1134, 1020m, 936, 766m, 738 cm^{-1}). Oxidation of the dichlorinated base (0.50 g.) with Lemieux and von Rudloff's⁹ reagent in 50% aqueous *t*-butyl alcohol containing sodium carbonate gave, after chromatography in benzene on active alumina 3-dichloromethyl-1,3-dimethyl-2-methyloxindole (0.18 g.) as prisms from hexane, m. p. 45°; ν_{\max} , 1724 (oxindole C=O), 1616m (aromatic), 787 (CHCl₂), 744 (*o*-disubstituted benzene); liquid film, 1704 cm^{-1} (oxindole C=O) (Found: C, 54.3; H, 4.0; Cl, 28.9; N, 5.8. $\text{C}_{11}\text{H}_{11}\text{Cl}_2\text{NO}$ requires C, 54.1; H, 4.5; Cl, 29.05; N, 5.7%). In a similar manner 1,3,3-trimethyl-2-methyleneindoline gave 1,3,3-trimethyl-2-methyloxindole (60%), b. p. 100° (bath)/0.5 mm. (lit.,²⁵ 131—132°/11 mm., m. p. 50°) (Found: N, 7.9. Calc. for $\text{C}_{11}\text{H}_{13}\text{NO}$: N, 8.0%), with a very similar infrared spectrum to that of the above oxindole, ν_{\max} (liquid film) 1705 cm^{-1} . The dichlorinated base (0.50 g.) was also treated with phenyl isocyanate (1 ml.) in toluene (10 ml.) at 100° for 2 hr. Evaporation at 80°/15 mm., followed by chromatography of the product on neutral alumina (light petroleum—benzene, 1:1), gave 3-dichloromethyl-1,3-dimethyl-2-phenylcarbamoyl-methyleneindoline (0.30 g.) as needles (from benzene), m. p. 167—168° (decomp.) (Found: C, 63.0; H, 4.5. $\text{C}_{19}\text{H}_{18}\text{Cl}_2\text{N}_2\text{O}$ requires C, 63.2; H, 5.0%).

²³ Magnanini, *Ber.*, 1887, **20**, 2608.

²⁴ Plancher and Carrasco, *Atti Accad. naz. Lincei*, 1905, **14**, I, 705.

²⁵ Julian, Piki, and Boggess, *J. Amer. Chem. Soc.*, 1934, **56**, 1797.

(b) From ethyl trichloroacetate and potassium *t*-butoxide. Trimethylindole (10 g.) was treated with dichlorocarbene (1 mole) generated in olefin-free light petroleum from potassium *t*-butoxide (7 g.) and ethyl trichloroacetate (12 g.) at 0°, and worked up, as before, to give a basic oil (2 g.) and a non-basic fraction (11 g.). The latter, on distillation, gave ethyl trichloroacetate (3.5 g.) and trimethylindole (7.5 g.) (infrared spectra). Chromatography of the basic oil gave only 3-dichloromethyl-1,3-dimethyl-2-methyleneindoline (0.74 g.).

(c) From sodium trichloroacetate in 1,2-dimethoxyethane. Trimethylindole (10 g.) and powdered sodium trichloroacetate (12 g.) were boiled under reflux under nitrogen in dry 1,2-dimethoxyethane (100 ml.) for 18 hr. Volatile material was removed at 40°/15 mm. and the chloroform content estimated to be 4.5 ± 0.5 g. (58%, based on the sodium salt) by gas-liquid chromatography as described in Part I.¹ Extraction of the residue with acid gave a non-basic fraction (7.5 g.), which was mainly unchanged trimethylindole (infrared), and a semi-solid basic fraction (2.7 g.). A portion (0.30 g.) of the latter was treated with excess of ethanolic picric acid and the product was fractionally crystallised from ethanol to give 3-chloro-2,4-dimethylquinoline methopicate (0.175 g., 4.6%), m. p. and mixed m. p. 193–194° (decomp.), and 3-dichloromethyl-2,3-dimethyl-3*H*-indole methopicate (0.19 g., 5.9%), m. p. and mixed m. p. 148–149° (decomp.). A second portion (1.00 g.) of this basic fraction was oxidised with Lemieux and von Rudloff's reagent, as described above, to give (i) 3-chloro-1,4-dimethyl-2-quinolone (0.20 g., 4.2% overall) as needles from ethanol, m. p. 187° (Found: C, 63.1; H, 4.9; N, 6.8. C₁₁H₁₀ClNO requires C, 63.6; H, 4.85; N, 6.75%), λ_{max} 277 (3.91), 286sh (3.84), 321sh (3.77), 331 (3.865) m μ ; ν_{max} 1642 (quinolone C=O), 1595m (aromatic), 748, 735m cm.⁻¹ (*o*-disubstituted benzene and aryl-Cl) (in agreement with the 4-methyl-2-quinolone rather than the 2-methyl-4-quinolone structure),²⁶ and (ii) 3-dichloromethyl-1,3-dimethylindole (0.23 g., 4.1% overall) as prisms from hexane, m. p. and mixed m. p. 43–44°, identical with the oxindole derivative described above. The remainder of the basic fraction was adsorbed on neutral alumina (1.5 × 20 cm.) and rapidly eluted with ether (10%) in light petroleum, the solvent being removed at 30°/15 mm., to give 3-dichloromethyl-1,3-dimethyl-2-methyleneindoline as an oil, n_D^{25} 1.5960, which rapidly reddened, and crystalline 3-chloro-1,2-dihydro-1,4-dimethyl-2-methylenequinoline, m. p. 75° (decomp.), ν_{max} 1626m (conj. C=C), 1587 (conj. aromatic), 1314, 946m (C=CH₂), 762m and 741 cm.⁻¹ (*o*-disubstituted benzene and aryl-Cl), identical with the following product. 3-Chloro-2,4-dimethylquinoline methoxide (1.0 g.) in water (50 ml.) was slowly treated with an excess of ice-cold 2*N*-aqueous sodium hydroxide and the yellow solid taken up in ether, dried, and recovered as yellow needles (0.60 g.), m. p. 75° (decomp.), which deteriorated on standing at room temperature for several days.

Reaction of 1,2,3,4-Tetrahydro-9-methylcarbazole with Dichlorocarbene.—The carbazole (10 g.) was treated with ethanolic sodium ethoxide (50 ml.) from sodium (1.27 g.) and chloroform (20 g.), as described for 1,2,3-trimethylindole in (a) above, and the products separated into a basic fraction (2.8 g.) and a non-basic fraction (8.2 g.). Chromatography of the latter in light petroleum on active alumina gave only the starting tetrahydrocarbazole (7.0 g., 70%), m. p. and mixed m. p. 46–47°. The basic fraction was adsorbed on neutral alumina (2 × 20 cm.) and eluted rapidly with light petroleum (300 ml.) then ether (10%) in light petroleum (200 ml.) the solvents being removed at 20°/15 mm., to give a solid, m. p. 76–78° (1.6 g.), which on rechromatography gave only 4*a*-dichloromethyl-2,3,4,4*a*-tetrahydro-9-methylcarbazole (1.3 g.) as almost colourless prisms, m. p. 82–84° (decomp.) (Found: C, 62.5; H, 5.4; Cl, 27.7; N, 5.5. C₁₄H₁₅Cl₂N requires C, 62.7; H, 5.6; Cl, 26.5; N, 5.2%). This compound, unsaturated to potassium permanganate, darkened rapidly to give an ether-insoluble solid; it did not yield a crystalline picrate. Its ultraviolet spectrum showed 2-methyleneindoline absorption: λ_{min} 239 (3.57); λ_{max} 278 (4.15), 310sh (3.36) m μ . The infrared spectrum showed ν_{max} 1672 (–CH=C), 1603 (aromatic), 1339, 1312, 1276m, 1224m, 1089m, 978m, 887m, 853m, 800 (–CH=C), 767 (–CHCl₂), 748 and 732sh cm.⁻¹ (*o*-disubstituted benzene), together with carbonyl absorption at 1710 cm.⁻¹ which increased with time and was presumably the result of autoxidation to a 1-methylindole derivative.

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²⁶ Grundon, McCorkindale, and Rodger, *J.*, 1955, 4284.