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The Synthesis and Transformations of Some 3-Chloro- and 3-Nitroindolenines

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3-Substituted indole-2-carboxylic acid esters and amides are readily converted to the corresponding 3-chloroindolenines by reaction with *tert*-butyl hypochlorite. These compounds rearrange in protic solvents to oxindoles with migration of the ester or amide function into the 3 position. 3-Substituted 2-acetylindoles and indole-2-carboxylic acids are converted to the oxindoles with loss of the carbonyl function. The intermediate 2-alkoxyindoles may be isolated. Nitration of 3-substituted indole-2-carboxylates yields the corresponding 3-nitroindolenines. The structure of ethyl 5-chloro-3-nitro-3-phenyl-3*H*-indole-2-carboxylate was determined by X-ray analysis. Ethyl 3-nitroindolenine-2-carboxylates also undergo acid-catalyzed rearrangement to ethyl oxindolecarboxylates. Treatment of 2-acetyl-3-nitroindolenines with trifluoroacetic acid results in the formation of 2-nitroindoles.

The oxidative rearrangement of indoles to oxindoles during halogenation is by now a common reaction.[1,2] It has been demonstrated in the alkaloid field[3,4] that 3-haloindolenines are the key intermediates in this overall transformation. With few exceptions,[5,6] however, 3-chloroindolenines have seldom been properly characterized, and until recently[7] no simple analog was disclosed in the literature.

We have obtained crystalline 3-chloroindolenines of formula **2** (Scheme I) by treating indole derivatives of structure **1** with *tert*-butyl hypochlorite in aprotic solvents. These 3-chloroindolenines were found to be of limited stability and to convert exothermally and in high yields to oxindoles **3** in protic solvents such as alcohol. The structure of these compounds was derived from their spectroscopic data and confirmed by conversion of ethyl 3-phenyloxindole-3-carboxylate (**3a**) to the known 3-phenyloxindole **4**.

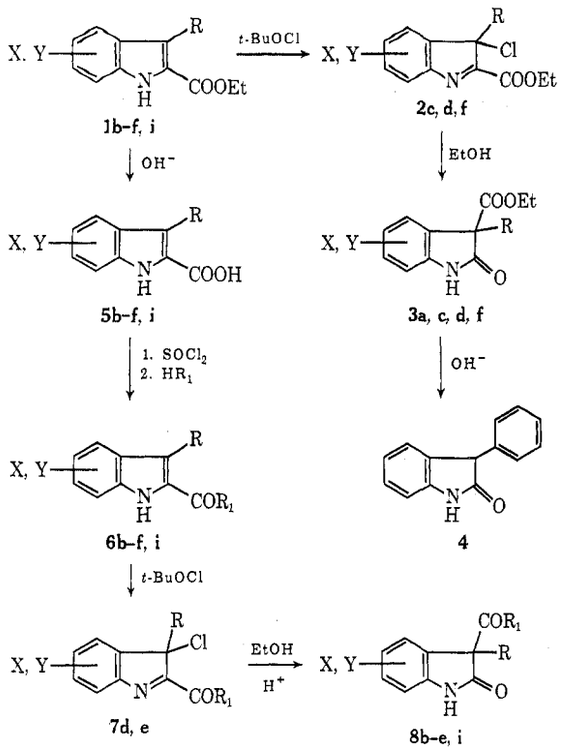
We have successfully extended this reaction to the indole-2-carboxamides **6**, which were prepared by standard methods *via* the indole-2-carboxylic acids **5**. Reaction of the indole-2-carboxamides with *tert*-butyl hypochlorite again produced the crystalline 3-chloroindolenines **7**. These compounds underwent the same transformation to the oxindoles **8** when subjected to protic solvents. The fact that even the primary amide **6d** rearranged in the same manner as the ester indicates that the carbonyl group migrates with its electrons. We believe that the mechanism of the reaction is best represented by the sequence of steps shown in Scheme II.

The protonated chlorindolenine A is assumed to be transformed to the carbonium ion C *via* a cyclic chloronium ion B. Migration of the carbonyl function with elimination of a proton leads to the imino chloride D, hydrolysis of which yields the oxindole **3**. Ethanolysis would convert the imino chloride to the oxindole **3** *via* the imino ether E. As illustrated by examples in Scheme III, the 2-acetylindole **9c** and the indole-2-carboxylic acids **5** undergo similar reactions. In both cases the carbonyl function was lost during the conversion of the 3-chloroindolenine to the oxindole. Thus refluxing 2-acetyl-3,5-dichloro-3-phenyl-3*H*-indole (**10**) in ethanol yielded 5-chloro-3-phenyloxindole (**12**). The intermediate 2-ethoxyindole **11** could be isolated under milder reaction conditions. According to the mechanism proposed in Scheme II, the 2-ethoxyindole would originate from deacetylation of the imino ether E. This would require migration of the carbonyl function prior to deacetylation. Possible deacetylation of the carbonium ion C was excluded by showing that the 2-chloroindole **13**, which would result from this deacetylation, does not convert to the 2-ethoxyindole **11** under reaction conditions. The 3-chloroindolenines derived from the indole-2-carboxylic acids **5c** and **5i** were not isolated but directly treated with ethanol and methanol, respectively, to afford **11** and the 2-methoxyindole **15**.

Reaction of the 3-chloroindolenine **10** with trifluoroacetic acid produced mainly a mixture of compounds **13** and **14** (separated by chromatography). For comparison the 2,5-dichloroindole **13** was prepared

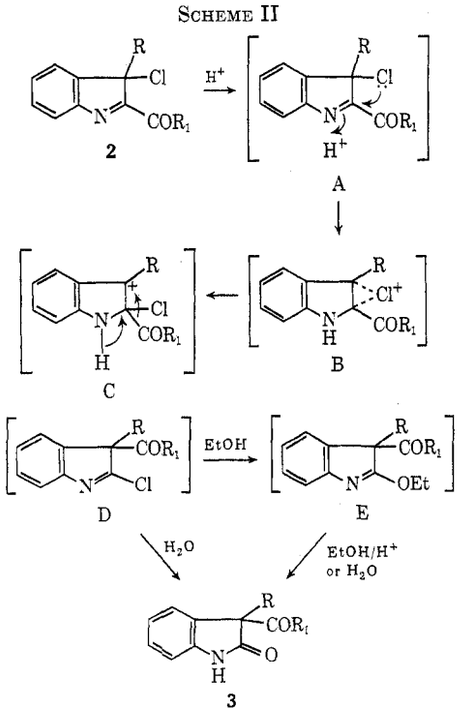
(1) J. M. Muchowski, *Can. J. Chem.*, **48**, 422 (1970).
(2) R. M. Acheson, R. W. Snaith, and J. M. Vernon, *J. Chem. Soc.*, 3229 (1964).
(3) N. Finch and W. I. Taylor, *J. Amer. Chem. Soc.*, **84**, 3871 (1962).
(4) K. V. Lichman, *J. Chem. Soc.*, 2539 (1971).
(5) N. O. Godtfredsen and S. Vangedal, *Acta Chem. Scand.*, **10**, 1414 (1956).
(6) H. Finnes and J. Shavel, Jr., *J. Org. Chem.*, **31**, 1765 (1966).
(7) While this manuscript was in preparation the synthesis and transformations of 3-chloro-2,3-dimethylindolenine have been reported by P. G. Gassman, G. A. Campbell, and G. Mehta, *Tetrahedron*, **28**, 2749 (1972).

SCHEME I



Compd	X, Y	R	R_1
a		C_6H_5	
b		CH_3	1-Pyrrolidino
c	5-Cl	C_6H_5	$N(Et)_2$
d	5-Cl	2-FC_6H_4	NH_2
e	5-Cl	2-FC_6H_4	NHEt
f	5-Cl	CH_3	1-Aziridino
g	5,7-di-Cl	C_6H_5	
h	4,7-di-Cl	C_6H_5	
i	6,7-di-Cl	C_6H_5	1-Morpholino
k	5,7-di-CH_3	C_6H_5	

SCHEME II



by heating the oxindole **12** with phosphorus oxychloride. Acetylation of **13** with acetic anhydride in boiling pyridine yielded **14** which in turn was hydrolyzed with alkali to give **13**. Formation of compounds **13** and **14** may follow the same mechanistic scheme. In this case nothing speaks against deacetylation of the carbonium ion C leading to the 2-chloroindole **13** and the mixed anhydride of trifluoroacetic and acetic acids, which is probably responsible for the formation of the acetyl derivative **14**.

To further explore the limitations of this reaction we prepared the vinylogous ester **17** as outlined in Scheme IV. The indole-2-carboxylic acid **5f** was converted to the aziridide **6f**, the reduction of which with lithium aluminum hydride yielded the aldehyde **16**. Treatment of **16** with ethyl diethylphosphonoacetate and base led to **17**. The crystalline 3-chloroindolenine **18** was readily formed but failed to undergo the rearrangement to the oxindole. Two products were isolated instead. Based on spectroscopic data we have assigned structure **19** to the major product and structure **20** to the minor component. Again, a cyclic chloronium ion such as G may be postulated. Removal of a proton from the α position of G leads to **20**; addition of ethoxide results in formation of **19**.

Analogous to the chlorination, nitration of unprotonated 2,3-disubstituted indoles has been thoroughly studied[8,9] but no 3-nitroindolenines have been described.

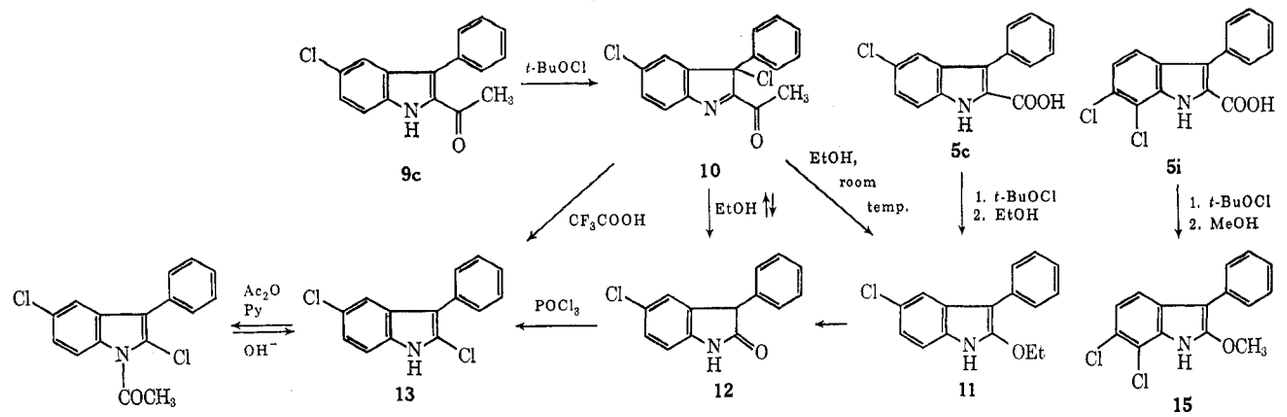
We obtained the crystalline 3-nitroindolenines **21** and **23** (Scheme V) by treating the 2,3-disubstituted indoles **1** and **9** with fuming nitric acid at low temperatures. Since the alternate 1-nitroindole structure **22** could not be excluded based on spectral and chemical data, the 3-nitroindolenine structure was confirmed by the single-crystal X-ray diffraction of ethyl 5-chloro-3-nitro-3-phenyl-3*H*-indole-2-carboxylate (**21c**).

The preparation of 3-nitroindolenines seems to be limited to indoles which are not susceptible to electrophilic attack in the benzene moiety. For example, we were unsuccessful in preparing 5-methoxy-3-nitroindolenines. It was found that 3-nitroindolenines are more stable than the corresponding 3-chloroindolenines. In analogy to the 3-chloroindolenines, ethyl 3-nitro-3-phenyl-3*H*-indole-2-carboxylates **21** were found to undergo an acid-catalyzed rearrangement to the oxindoles **3**. The reaction was slower and less clean than with the 3-chloroindolenines and the yields were inferior. Mechanistically, the reaction can be visualized as proceeding *via* a cyclic nitronium ion analogous to that proposed by Berti[9] and his coworkers. In the hydrogen chloride catalyzed reaction, however, the possibility of formation of the intermediate 3-chloroindolenines cannot be ruled out.

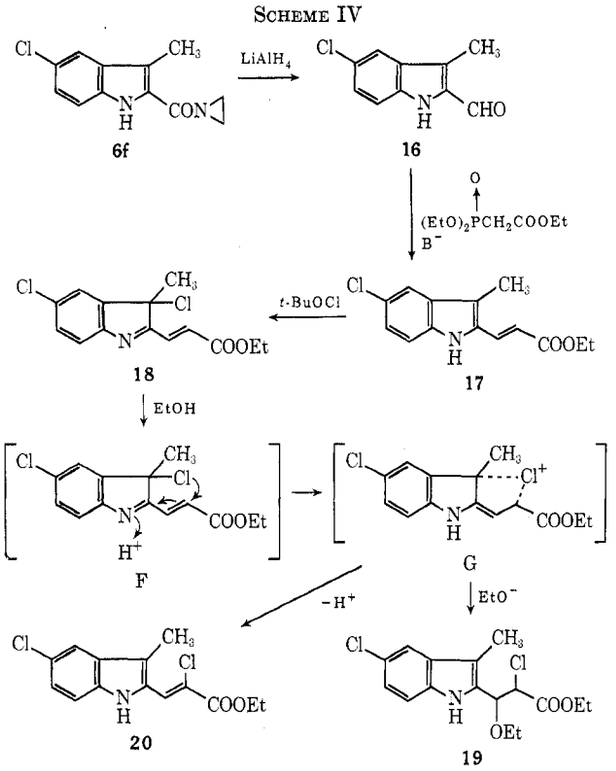
Treatment of the 2-acetyl-3-nitroindolenines **23** with trifluoroacetic acid resulted in a clean conversion to the 2-nitroindoles **24**. Berti and coworkers[9] have described the only 2-nitroindole that we could find in the literature. These authors treated 3-methylindole with benzoyl nitrate and obtained 3-methyl-2-nitroindole in 4.5% yield. The spectroscopic properties of 5-chloro-3-methyl-2-nitroindole (**24f**) are in agreement with the data reported by Berti and coworkers for 3-methyl-2-nitroindole. The formation of 2-nitroindoles from 2-acetyl-3-nitroindolenines is mechanistically difficult to explain. If a cyclic nitronium ion would be involved in this reaction we would

(8) W. E. Noland, K. R. Rush, and L. R. Smith, *J. Org. Chem.*, **31**, 65 (1966); W. E. Noland and K. R. Rush, *ibid.*, **31**, 70, (1966).
(9) G. Berti, A. DaSettimo, and E. Nannipieri, *J. Chem. Soc.*, 2145 (1968).

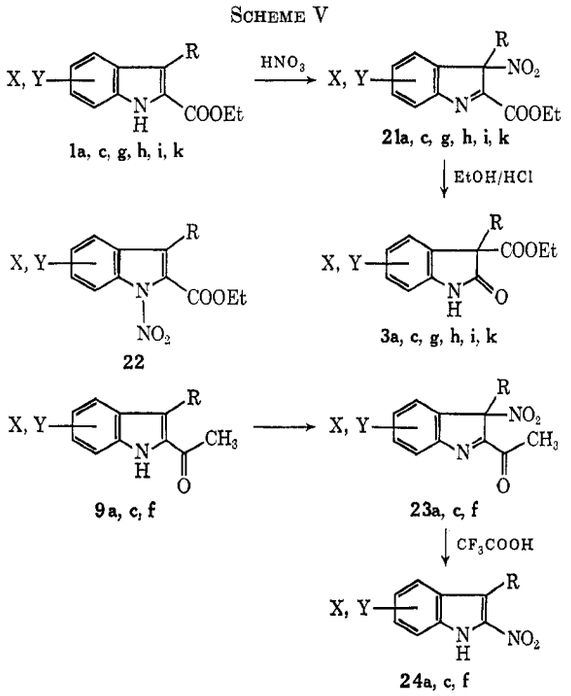
SCHEME III



SCHEME IV



SCHEME V



obtain the indole-2-nitrite rather than the 2-nitroindole. The 1,2 migration of a nitro group is more likely the result of dissociation and renitration together with displacement of the acetyl group. Nitration of 5-nitro-3-formylindole with replacement of the formyl group has been reported by Noland and Rush.[8]

Crystallography.—Crystals of **21c** are monoclinic, space group $P2_1/c$. The crystal data are a = 7.746 (3), b = 15.053 (5), c = 13.898 (5) Å, β = 100.23 (2)°, Z = 4, d_{obsd} = 1.44, d_{calcd} = 1.435 g cm^{-3}, μ (Cu K$_\alpha$) = 23.5 cm^{-1}. Despite the fact that **21c** crystallizes from CH_2Cl_2–Et_2O as elongated prisms with well-defined faces, many of the crystals failed to extinguish properly under crossed polarizing filters. Most crystals which were examined with a polarizing microscope could be considered as composed of two parts, one which extinguished properly and another which never extinguished. The boundary between these two parts was always sharp and ran parallel to the length of the crystal. No difference could be detected between Weissenberg photographs of crystals for which the whole crystal extinguished and those for which only one part of the crystal extinguished. The crystals used for data collection were those for which almost the entire crystal extinguished under crossed polaroids.

The intensity data were measured on a Hilger-Watts Model Y290 four-circle diffractometer by θ–2θ scans. Nickel-filtered Cu K$_\alpha$ radiation and pulse height discrimination were used. The crystals deteriorated slowly upon exposure to X-rays (25% decrease in the intensity of the three standard reflections over a 3-day period). Intensity data were collected from two crystals, one approximately 0.09 × 0.09 × 0.45 mm (used for $2\theta < 107°$) and the other 0.12 × 0.14 × 0.35 mm (used for $85 < 2\theta < 127°$). The intensity data were corrected for crystal deterioration, then placed on a common scale; no absorption correction was made.

The structure was solved by standard Patterson and Fourier methods. The hydrogen atoms were located from a difference Fourier calculated after partial refinement of the structure. The final refinement was by block-diagonal least squares with the matrix partitioned into five blocks. Anisotropic thermal parameters were used for all atoms except the hydrogens; the hydrogen atom parameters were not refined.

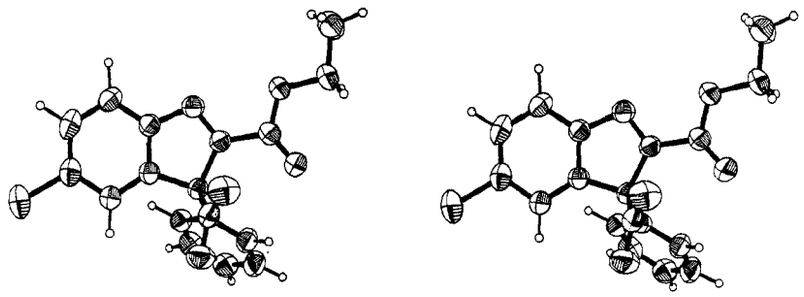


Figure 1.—Stereodrawing of **21c** showing its conformation in the solid state. The ellipsoids represent the thermal motions of each atom at the 50% probability level. The hydrogen atoms are represented as spheres of an arbitrary size.

The quantity minimized was

$$\Sigma w||F_o| - |F_c||^2$$

where $w = 1/(8.5 + |F_o| + 0.013 |F_o|^2)$. Standard scattering curves were used for Cl, O, N, C,[10] and H.[11] The Cl curve was corrected for the real and imaginary parts of the anomalous scattering.[12] The refinement was stopped when the shifts of all parameters were less than one fifth of the corresponding standard deviations. The difference Fourier based on the final parameters has no features >0.2 eÅ^{-3} in magnitude.

$$\text{final } R = \Sigma||F_o| - |F_c||/\Sigma|F_o| = 0.041$$

The bond lengths and angles in **11b** are in agreement with the expected values; the N_1–C_2 distance is 1.287 (5) Å. The conformation of the molecule is shown in Figure 1. The phenyl ring of the indolenine system is planar to within 0.006 Å. The indolenine nitrogen and the 2 and 3 position carbon atoms [C(2) and C(3)] are displaced 0.02, 0.06, and −0.02 Å, respectively, from the plane of the indolenine phenyl ring. The nitrogen of the 3-nitro group is 0.03 Å out of the plane of C(3) and the two oxygens. The displacement is toward the carboxyl oxygen (N···O distance, 3.20 Å). The final atomic parameters and the observed and calculated structure factors appear in the microfilm in edition of this journal.[13]

Experimental Section

Melting points were determined in a capillary melting point apparatus. The uv spectra were measured in 2-propanol on a Cary Model 14 spectrophotometer; nmr spectra were recorded with a Varian A-60 or Varian T-60 instrument. Ir spectra were determined on a Beckman IR-9 spectrometer. Silica gel Merck (70–325 mesh) was used for chromatography.

Ethyl indole-2-carboxylates (**1**) were prepared by the Japp–Klingemann reaction[14] following the procedure described by Hughes, *et al.*[15]

Ethyl 5,7-dichloro-3-phenylindole-2-carboxylate (**1g**) had mp 148–150°; ir ($CHCl_3$) 1705, 1740 cm^{-1} (COOEt); uv λ_{max} 238–239 mμ (ε 39,000), 298–299 (14,600), sh 320 (7300).

Anal. Calcd for $C_{17}H_{13}Cl_2NO_2$: C, 61.00; H, 3.92; N, 4.19. Found: C, 60.99; H, 3.86; N, 4.03.

Ethyl 4,7-dichloro-3-phenylindole-2-carboxylate (**1h**) had mp 130–132°; ir ($CHCl_3$) 1705, 1740 cm^{-1} (COOEt); uv λ_{max} 241 mμ (ε 38,200), 296–297 (16,300), 320 (8250).

Anal. Calcd for $C_{17}H_{13}Cl_2NO_2$: C, 61.00; H, 3.92; N, 4.19. Found: C, 60.49; H, 3.77; N, 4.09.

Ethyl 6,7-dichloro-3-phenylindole-2-carboxylate (**1i**) had mp 154–155°; ir ($CHCl_3$) 1700, 1730 cm^{-1}; uv λ_{max} 241 mμ (ε 38,600), 303 (18,000), infl 325 (8500).

Anal. Calcd for $C_{17}H_{13}Cl_2NO_2$: C, 61.00; H, 3.92; N, 4.19. Found: C, 61.11; H, 3.91; N, 4.18.

Ethyl 5,7-dimethyl-3-phenylindole-2-carboxylate (**1k**) had mp 126–128°; ir ($CHCl_3$) 1690, 1710 cm^{-1}; uv λ_{max} 225 mμ (ε 25,150), 242 (26,100), 302 (18,400), infl 335 (6800).

Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.50; H, 6.34; N, 4.62.

Indole-2-carboxylic acids **5** were accessible by alkaline hydrolysis of the corresponding ester according to the standard procedure.

5-Chloro-3-methylindole-2-carboxylic acid (**5f**) had mp 238–240° dec.

Anal. Calcd for $C_{10}H_8ClNO_2$: C, 57.29; H, 3.84; N, 6.68. Found: C, 57.37; H, 3.80; N, 6.51.

6,7-Dichloro-3-phenylindole-2-carboxylic acid (**5i**) had mp 219–221°.

Anal. Calcd for $C_{15}H_9Cl_2NO_2$: C, 58.85; H, 2.96; N, 4.58. Found: C, 58.77; H, 3.11; N, 4.32.

Indole-2-carboxamides were obtained by converting the indole-2-carboxylic acids with thionyl chloride or phosphorus pentachloride to the acid chlorides which were directly treated with the amines.

5-Chloro-3-(2-fluorophenyl)indole-2-carboxamide (**6d**).[14]—A mixture of 14.5 g (0.05 mol) of 5-chloro-3-(2-fluorophenyl)indole-2-carboxylic acid (**5d**),[14] 12 g of phosphorus pentachloride, and 400 ml of methylene chloride was stirred at room temperature for 30 min. Concentrated aqueous ammonia was added with ice cooling until the aqueous phase was strongly alkaline. The precipitated crystals were collected and recrystallized from methanol to yield 10.2 g of product, mp 209–212°. From the evaporated methylene chloride phase and the mother liquor, another 2 g of product was obtained, yield 12.2 g (84%).

1-(5-Chloro-3-methylindole-2-carbonyl)aziridine (**6f**).—A mixture of 42 g (0.2 mol) of 5-chloro-3-methylindole-2-carboxylic acid (**5f**), 100 ml of thionyl chloride, and 200 ml of methylene chloride was refluxed for 16 hr. The solvent and excess thionyl chloride were evaporated under reduced pressure, at the end azeotropically with benzene. The residue was dissolved in tetrahydrofuran and added to a solution of 25 ml of aziridine in 200 ml of methylene chloride cooled to 0°.

A 150-ml portion of 10% aqueous sodium carbonate solution was added at 0° and the two-phase mixture was stirred for 2 hr at room temperature. The methylene chloride layer was separated, dried over sodium sulfate, and evaporated. Crystallization of the residue from methylene chloride–hexane yielded 38 g (81%) of product, mp 140–142°.

The analytical sample was recrystallized from methylene chloride–ether: mp 145–146°; uv λ_{max} 235 mμ (ε 21,400), 310 (21,000).

Anal. Calcd for $C_{12}H_{11}ClN_2O$: C, 61.42; H, 4.72; N, 11.93. Found: C, 61.43; H, 4.88; N, 12.09.

The following amides were prepared in the same way.

5-Chloro-*N*,*N*-diethyl-3-phenylindole-2-carboxamide (**6c**) had mp 195–198°; uv λ_{max} 226 mμ (ε 35,000), sh 265 (11,050), 293–297 (11,400).

Anal. Calcd for $C_{19}H_{19}ClN_2O$: C, 69.83; H, 5.86; N, 8.57. Found: C, 69.69; H, 5.89; N, 8.61.

5-Chloro-*N*-ethyl-3-(2-fluorophenyl)indole-2-carboxamide (**6e**) had mp 248–250°; uv λ_{max} 233 mμ (ε 35,000), 300 (16,000).

Anal. Calcd for $C_{17}H_{14}ClFN_2O$: C, 64.40; H, 4.45; N, 8.84. Found: C, 64.40; H, 4.15; N, 8.78.

(10) D. T. Cromer and J. T. Waber, *Acta Crystallogr.*, **18**, 104 (1965).
(11) R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, **42**, 3175 (1965).
(12) D. T. Cromer, *Acta Crystallogr.*, **18**, 17 (1965).
(13) See paragraph at end of paper regarding supplementary material.
(14) R. R. Phillips, *Org. React.*, **10**, 143 (1959).
(15) G. K. Hughes, *et al.*, *J. Proc. Roy. Soc. N. S. W.*, **71**, 475 (1959).

1-(3-Methylindole-2-carbonyl)pyrrolidine (6b) had mp 232–234°; uv λ_{max} 222 mμ (ε 32,200), infl 242 (12,000), 293 (14,400).

Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.06; N, 12.27. Found: C, 73.84; H, 7.30; N, 12.28.

1-(6,7-Dichloro-3-phenylindole-2-carbonyl)morpholine (6i) had mp 129–135°; uv λ_{max} 233 mμ (ε 32,500), 298 (11,500).

Anal. Calcd for $C_{19}H_{16}Cl_2N_2O_2$: C, 60.81; H, 4.30; N, 7.46. Found: C, 60.79; H, 4.44; N, 7.32.

2-Acetylindoles **9c** and **9f** were prepared by the modified Japp–Klingemann reaction following a procedure described by Manske, Perkin, and Robinson.[16]

2-Acetyl-5-chloro-3-phenylindole (9c) had mp 151–153°; ir ($CHCl_3$) 1650 cm^{-1}; uv λ sh 232 mμ (ε 21,000), max 244 (21,900), 313 (19,250), infl 345 (6600).

Anal. Calcd for $C_{16}H_{12}ClNO$: C, 71.25; H, 4.49; N, 5.19. Found: C, 71.48; H, 4.55; N, 5.18.

2-Acetyl-5-chloro-3-methylindole (9f) had mp 200–202°; ir ($CHCl_3$) 1655 cm^{-1}; uv λ_{max} 238 mμ (ε 9400), 312 (20,450).

Anal. Calcd for $C_{11}H_{10}ClNO$: C, 63.62; H, 4.85; N, 6.75. Found: C, 63.53; H, 4.74; N, 6.79.

3-Chloroindolenines (**10**) were obtained by reaction of the indoles with *tert*-butyl hypochlorite in methylene chloride or tetrahydrofuran. The reactions were followed by thin layer chromatography and were found to be in general complete within 15 min to a few hours at room temperature.

2-Acetyl-3,5-dichloro-3-phenyl-3*H*-indole (10).—A 15-ml portion of *tert*-butyl hypochlorite (14.3 g, 0.133 mol) was added to a solution of 27 g (0.1 mol) of 2-acetyl-5-chloro-3-phenylindole (**9c**) in 300 ml of methylene chloride. After sitting for 30 min at room temperature the solvent was removed under reduced pressure. The residue crystallized from methylene chloride–hexane to yield 27.5 g (90%) of product: mp 145–148° dec; nmr ($CDCl_3$) δ 2.6 (s, 3, $COCH_3$), 7.33 (s, 5, C_6H_5), 7.8 (d, 1, J = 8 Hz, C_7H), 7.25–7.7 (m, 2, C_4H and C_6H); uv (CH_2Cl_2) λ_{max} 251 mμ (ε 15,400) 322 (7100); ir ($CHCl_3$) 1700 cm^{-1} (CO).

Anal. Calcd for $C_{16}H_{11}Cl_2NO$: C, 63.18; H, 3.65; N, 4.60. Found: C, 63.30; H, 3.55; N, 4.60.

***N*-Ethyl-3,5-dichloro-3-(2-fluorophenyl)-3*H*-indole-2-carboxamide (7e).**—A 1.6-g (5 mmol) portion of *N*-ethyl-5-chloro-3-(2-fluorophenyl)indole-2-carboxamide (**6e**) was dissolved in 100 ml of tetrahydrofuran by warming. *tert*-Butyl hypochlorite (2 ml, 17.5 mmol) was added to the warm solution. After sitting for 10 min, the solvent was removed under reduced pressure and the residue was crystallized from methylene chloride–hexane to yield 1.6 g (91%) of product: mp 160–162°; nmr ($CDCl_3$) δ 1.2 (t, 3, J = 7 Hz, CH_3), 3.42 (quintuplet, 2, J = 7 Hz, CH_2), 6.6–8.2 (m, 8, NH and 7 aromatic H); uv λ_{max} 243 mμ (ε 19,900), infl 269 (5020), 320 (6980); ir ($CHCl_3$) 1680 cm^{-1} (CO).

Anal. Calcd for $C_{17}H_{13}Cl_2FN_2O$: C, 58.14; H, 3.73; N, 7.98. Found: C, 58.17; H, 3.66; N, 7.90.

As above the following were prepred.

Ethyl 3,5-dichloro-3-phenyl-3*H*-indole-2-carboxylate (2c) had mp 110–113°, crystallized from methylene chloride–hexane; uv (CH_2Cl_2) λ_{max} 246 mμ (ε 17,000), 325 (6420); ir ($CHCl_3$) 1725 cm^{-1} (CO); nmr ($CDCl_3$) δ 1.3 (t, 3, J = 7 Hz, CH_3), 4.36 (q, 2, J = 7 Hz, CH_2), 7.37 (s, 5, C_6H_5), 7.83 (d, 1, J = 8 Hz, C_7H), 7.25–7.7 (m, 2, C_4 and C_6 H).

Anal. Calcd for $C_{17}H_{13}Cl_2NO_2$: C, 61.10; H, 3.92; N, 4.19. Found: C, 61.46; H, 4.11; N, 4.15.

Ethyl 3,5-dichloro-3-(2-fluorophenyl)-3*H*-indole-2-carboxylate (2d) had mp 120–123°, crystallized from methylene chloride–hexane; uv (CH_2Cl_2) λ_{max} 245 mμ (ε 18,150) 322 (6580); ir ($CHCl_3$) 1735 cm^{-1} (CO); nmr ($CDCl_3$) δ 1.32 (t, 3, J = 7 Hz, CH_3), 4.4 (q, 2, J = 7 Hz, CH_2), 7.8 (d, 1, J = 8 Hz, C_7 H), 6.7–8.5 (m, 6, aromatic protons).

Anal. Calcd for $C_{17}H_{12}Cl_2FNO_2$: C, 57.98; H, 3.43; N, 3.97. Found: C, 58.08; H, 3.27; N, 3.93.

3,5-Dichloro-3-(2-fluorophenyl)-3*H*-indole-2-carboxamide (7d) had mp 186–188° dec, crystallized from tetrahydrofuran–hexane; uv λ_{max} 242 mμ (ε 18,800), 318 (6500); ir (KBr) 1680 cm^{-1} (CO).

Anal. Calcd for $C_{15}H_9Cl_2FN_2O$: C, 55.75; H, 2.81; N, 8.67. Found: C, 55.79; H, 2.72; N, 8.59.

***trans*-Ethyl 3-(3,5-dichloro-3-methyl-3*H*-indolyl)propenoate (18)** was obtained in 90% yield by treating 2.65 g (10 mmol) of *trans*-ethyl 3-(5-chloro-3-methyl-2-indolyl)propenoate (**17**) in 50 ml of methylene chloride with 2.5 ml (22 mmol) of *tert*-butyl hypochlorite for 3 hr at room temperature: mp 100–102°, crystallized from ether–hexane; uv λ_{max} 271 mμ (ε 12,800); ir ($CHCl_3$) 1720 cm^{-1} (CO); nmr ($CDCl_3$) δ 1.37 (t, 3, J = 7 Hz, CH_3), 1.97 (s, 3, CH_3), 4.33 (q, 2, J = 7 Hz, CH_2), 7.02 (d, 1, J = 17 Hz), and 7.64 (d, 1, J = 17 Hz, olefinic H), 7.2–7.7 (m, 3, aromatic H).

Anal. Calcd for $C_{14}H_{13}Cl_2NO_2$: C, 56.39; H, 4.39; N, 4.70. Found: C, 56.39; H, 4.33; N, 4.67.

5-Chloro-3-methylindole-2-carboxaldehyde (16).—A 23.5-g (0.1 mol) portion of 1-(5-chloro-3-methylindole-2-carbonyl)aziridine (**6f**) was added in portions at 0° to a suspension of 5.6 g (0.14 mol) of lithium aluminum hydride in 200 ml of ether. The mixture was stirred at 0° for 1 hr and at room temperature for another 1 hr. The hydride was hydrolyzed by addition of 30 ml of water. The inorganic material was filtered and washed well with tetrahydrofuran. The filtrate was concentrated and the residue was slurried with ether. The collected solid was recrystallized from tetrahydrofuran–ethanol to yield 8.5 g (44%) of product, mp 248–250°. The analytical sample was recrystallized from methylene chloride–methanol: mp 250–252°; uv λ_{max} 238 mμ (ε 18,800), 314 (23,150); ir (KBr) 1640 cm^{-1} (CO).

Anal. Calcd for $C_{10}H_8ClNO$: C, 62.03; H, 4.16; N, 7.24. Found: C, 62.17; H, 4.24; N, 7.08.

***trans*-Ethyl 3-(5-Chloro-3-methyl-2-indolyl)propenoate (17).**—A 6-g (53 mmol) portion of potassium *tert*-butoxide was added to a solution of 10.5 g (52.5 mmol) of ethyl diethylphosphonoacetate in 50 ml of tetrahydrofuran. After stirring for 15 min under nitrogen, a solution of 6 g (21 mmol) of 5-chloro-3-methylindole-2-carboxaldehyde (**16**) in 300 ml of tetrahydrofuran was added. The mixture was stirred for 2 hr at room temperature and partitioned between 200 ml of methylene chloride and 300 ml of hexane and water. The organic layer was separated, washed with water, dried, and evaporated. Crystallization of the residue from ethanol yielded 6.1 g (75%) of product, mp 178–183°. The analytical sample was recrystallized from ethanol: mp 183–184°; uv λ_{max} 239 mμ (ε 12,400), 254 (11,100), 345 (32,700); ir ($CHCl_3$) 1700 cm^{-1} (CO); nmr (DMSO) δ 1.29 (t, 3, J = 7 Hz, CH_3), 2.32 (s, 3, CH_3), 4.22 (q, 2, J = 7 Hz, CH_2), 6.52 (d, 1, J = 16 Hz, α proton), 7.2 (q, 1, J_{AB} = 8 Hz, J_{AX} = 2 Hz, C_6 H), 7.4 (d, 1, J_{AB} = 8 Hz, C_7 H), 7.64 (d, 1, J_{AX} = 2 Hz, C_4 H), 7.7 (d, 1, J = 16 Hz, β proton), 11.45 (broad s, 1, NH).

Anal. Calcd for $C_{14}H_{14}ClNO_2$: C, 63.76; H, 5.35; N, 5.31. Found: C, 63.82; H, 5.37; N, 5.03.

Ethyl 5-Chloro-3-nitro-3-phenyl-3*H*-indole-2-carboxylate (21c).—A 10-ml portion of fuming nitric acid was added to a solution of 15 g of ethyl 5-chloro-3-phenylindole-2-carboxylate[17] in 300 ml of methylene chloride cooled to −50°. The temperature was allowed to reach −30° within 30 min. A 150-ml portion of 10% aqueous sodium carbonate solution was added with stirring. The methylene chloride layer was separated, washed with sodium carbonate solution and water, dried over sodium sulfate, and concentrated below 30°. The product crystallized upon addition of ether, yield 13.7 g (79%), mp 117–120° dec.

The analytical sample was recrystallized from methylene chloride–hexane: mp 120–124° dec; uv λ_{max} 238 mμ (ε 15,560), 321 (6800); ir (KBr) 1730 cm^{-1} (CO); nmr ($CDCl_3$) δ 1.33 (t, 3, J = 7 Hz, CH_3), 4.36 (q, 2, J = 7 Hz, CH_2), 7–7.7 (m, 7, aromatic H), 7.82 (d, 1, J = 8.5 Hz, C_7 H).

Anal. Calcd for $C_{17}H_{13}ClN_2O_4$: C, 59.23; H, 3.80; N, 8.13. Found: C, 59.41; H, 3.90; N, 8.13.

Ethyl 3-nitro-3-phenyl-3*H*-indole-2-carboxylate (21a) was obtained in 60% yield by treating 26.5 g (0.1 mol) of ethyl 3-phenylindole-2-carboxylate[15] in 300 ml of methylene chloride with 20 ml of fuming nitric acid at −50 to −38°: mp 79–81°, crystallized from ether–hexane; uv λ_{max} 233 mμ (ε 16,380), 311 (6020); ir (KBr) 1725 cm^{-1} (CO).

Anal. Calcd for $C_{17}H_{14}N_2O_4$: C, 65.80; H, 4.55; N, 9.03. Found: C, 65.85; H, 4.55; N, 8.92.

Ethyl 4,7-Dichloro-3-nitro-3-phenyl-3*H*-indole-2-carboxylate (21h).—A 17-g (0.05 mol) portion of ethyl 4,7-dichloro-3-phenylindole-2-carboxylate (**1h**) in 300 ml of methylene chloride was treated at −10 to 18° with 10 ml of fuming nitric acid to yield 14.2 g (75%) of product with mp 124–126° after recrystallization from acetone–ethanol: uv λ_{max} 240 mμ (ε 13,500), 294 (4900), 327 (4750); ir ($CHCl_3$) 1740 cm^{-1} (CO).

Anal. Calcd for $C_{17}H_{12}Cl_2N_2O_4$: C, 53.85; H, 3.19; N, 7.39. Found: C, 53.81; H, 3.46; N, 7.44.

Ethyl 5,7-Dichloro-3-nitro-3-phenyl-3*H*-indole-2-carboxylate

(16) R. H. F. Manske, W. H. Perkin, and R. Robinson, *J. Chem. Soc.*, 1 (1927).

(17) H. Yamamoto, *et al.*, *Chem. Ber.*, **101**, 4245 (1968).

(21g).—Reaction of 17 g (0.05 mol) of ethyl 5,7-dichloro-3-phenylindole-2-carboxylate (1g) in 300 ml of methylene chloride with 10 ml of nitric acid at −10 to 5° yielded after two recrystallizations from methylene chloride–ethanol 6 g (31.5%) of product: mp 107–109°; uv λ_{max} 244 mμ (ε 13,620), 323 (6720); ir ($CHCl_3$) 1750 cm^{-1} (CO).

Anal. Calcd for $C_{17}H_{12}Cl_2N_2O_4$: C, 53.85; H, 3.19; N, 7.39. Found: C, 53.76; H, 3.36; N, 7.28.

Ethyl 6,7-dichloro-3-nitro-3-phenyl-3*H*-indole-2-carboxylate (21i) was obtained in 71% yield by reaction of 17 g (0.05 mol) of 6,7-dichloro-3-phenylindole-2-carboxylate (1i) in 400 ml of methylene chloride with 10 ml of nitric acid at −20 to 0°: mp 109–112°, crystallized from acetone–ethanol; uv λ_{max} 242 mμ (ε 17,700), 309 (6000); ir ($CHCl_3$) 1740 cm^{-1} (CO).

Anal. Calcd for $C_{17}H_{12}Cl_2N_2O_4$: C, 53.85; H, 3.19; N, 7.39. Found: C, 53.67; H, 3.38; N, 7.32.

Ethyl 5,7-Dimethyl-3-nitro-3-phenyl-3*H*-indole-2-carboxylate (21k).—Treating 14.7 g (0.05 mol) of ethyl 5,7-dimethyl-3-phenylindole-2-carboxylate (1k) in 300 ml of CH_2Cl_2 with 10 ml nitric acid at −60 to −50° for 5 min yielded a mixture of mainly two compounds. By crystallization from ether the by-product crystallized. Crystallization of the mother liquor from ethanol yielded 8.1 g (46%) of product, which was recrystallized from acetone–ethanol: mp 119–121°; uv λ_{max} 245 mμ (ε 14,400), 338 (7250); ir ($CHCl_3$) 1730 cm^{-1} (CO); nmr ($CDCl_3$) δ 1.30 (t, 3, J = 7 Hz, CH_3), 2.36 (s, 3, CH_3), 2.63 (s, 3, CH_3), 4.33 (q, 2, J = 7 Hz, CH_2), 7–7.6 (m, 7, aromatic H).

Anal. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28. Found: C, 67.73; H, 5.40; N, 8.27.

2-Acetyl-3-nitro-3-phenyl-3*H*-indole (23a).—Reaction of 23.5 g (0.1 mol) of 2-acetyl-3-phenylindole[16] in 400 ml of methylene chloride with 20 ml of nitric acid at −50 to −25° (15 min) yielded 11.6 g (41%) of product, crystallized from ethanol: mp 122–124° dec; uv λ_{max} 235 mμ (ε 12,580), 315 (6480); ir ($CHCl_3$) 1700 cm^{-1} (CO); nmr ($CDCl_3$) δ 2.6 (s, 3, CH_3), 7–8 (m, 9, aromatic H).

Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.54; H, 4.32; N, 10.00. Found: C, 68.75; H, 4.19; N, 9.93.

2-Acetyl-5-chloro-3-nitro-3-phenyl-3*H*-indole (23c) was obtained in 38% yield by treating 27 g (0.1 mol) of 2-acetyl-5-chloro-3-phenylindole (9c) in 500 ml of methylene chloride with 20 ml of nitric acid at −30 to −5° for 15 min: mp 124–128° dec, crystallized from acetone–ethanol; uv λ_{max} 241 mμ (ε 13,400), 317 (7500); ir ($CHCl_3$) 1700 cm^{-1} (CO); nmr ($CDCl_3$) δ 2.6 (s, 3, CH_3), 7–8 (m, 8, aromatic H).

Anal. Calcd for $C_{16}H_{11}ClN_2O_3$: C, 61.06; H, 3.52; N, 8.90. Found: C, 60.93; H, 3.45; N, 9.13.

2-Acetyl-5-chloro-3-methyl-3-nitro-3*H*-indole (23f).—A 20.7-g (0.1 mol) portion of 2-acetyl-5-chloro-3-methylindole (9f) dissolved in 500 ml of methylene chloride was treated with 20 ml of fuming nitric acid at −30 to −5°. Crystallization from ether–ethanol yielded 10.2 g (40%) of product which was recrystallized twice from ether–ethanol: mp 93–94°; uv λ_{max} 240 mμ (ε 12,100), 324 (9140); ir ($CHCl_3$) 1690 cm^{-1} (CO); nmr ($CDCl_3$) δ 2.08 (s, 3, CH_3), 2.67 (s, 3, $COCH_3$), 7.3–7.7 (m, 3, aromatic H).

Anal. Calcd for $C_{11}H_9ClN_2O_3$: C, 52.29; H, 3.59; N, 11.00. Found: C, 52.09; H, 3.55; N, 10.78.

Ethyl 3-Phenyloxindole-3-carboxylate (3a).—A solution of 31 g (0.1 mol) of ethyl 3-nitro-3-phenyl-3*H*-indole-2-carboxylate (23a) in 500 ml of methylene chloride and 250 ml of ethanol was treated with 100 ml of ethanol containing 5% of hydrogen chloride. After sitting at room temperature for 20 hr the solvents were evaporated and the residue was crystallized from ether to yield 17 g (60%) of product: mp 156–158°; uv λ_{max} 254 mμ (ε 7800), infl 265 (5600), 289 (1800); ir (KBr) 1740, 1720, 1684 cm^{-1} (CO); nmr ($CDCl_3$) δ 1.17 (t, 3, J = 7 Hz, CH_3), 4.21 (q, 2, J = 7 Hz, CH_2), 7.3 (s, 5, C_6H_5), 6.8–7.6 (m, 4, aromatic H).

Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.56; H, 5.44; N, 4.99.

Similarly the following were prepared.

Ethyl 5-chloro-3-phenyloxindole-2-carboxylate (3c) was obtained in 55% yield by crystallization and chromatography of the mother liquor on silica gel using 10% ethyl acetate in methylene chloride: mp 186–188°, crystallized from ethyl acetate–hexane; uv λ_{max} 259 mμ (ε 11,800), 300 (1800); ir (KBr) 1740, 1720, and 1680 cm^{-1} (CO).

Anal. Calcd for $C_{17}H_{14}ClNO_3$: C, 64.67; H, 4.50; N, 4.44. Found: C, 64.50; H, 4.41; N, 4.27.

Ethyl 5,7-dichloro-3-phenyloxindole-2-carboxylate (3g) (72.5% yield) had mp 182–183°, crystallized from methylene chloride–hexane; uv λ_{max} 258 mμ (ε 11,600), 303 (2200).

Anal. Calcd for $C_{17}H_{13}Cl_2NO_3$: C, 58.31; H, 3.74; N, 4.00. Found: C, 58.31; H, 3.78; N, 4.02.

Ethyl 6,7-dichloro-3-phenyloxindole-3-carboxylate (3i) (89% yield) had mp 238–239°, crystallized from ethanol–ethyl acetate; uv λ_{max} 257 mμ (ε 6300), infl 269 (4500), 294 (2100), sh 300 (2000).

Anal. Calcd for $C_{17}H_{13}Cl_2NO_3$: C, 58.31; H, 3.74; N, 4.00. Found: C, 58.07; H, 3.52; N, 4.02.

Ethyl 4,7-dichloro-3-phenyloxindole-3-carboxylate (3h) (43% yield) had mp 200–203°, crystallized from ethyl acetate; uv λ_{max} 248 mμ (ε 8250), 255 (8350), infl 268 (5000), 295 (1975), 301 (1950).

Anal. Calcd for $C_{17}H_{13}Cl_2NO_3$: C, 58.31; H, 3.74; N, 4.00. Found: C, 58.43; H, 3.61; N, 3.97.

Ethyl 5,7-dimethyl-3-phenyloxindole-3-carboxylate (3k) (55% yield) had mp 199–201°, crystallized from ethyl acetate–hexane; uv λ_{max} 259 mμ (ε 7300), 298 (2040).

Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.83; H, 6.19; N, 4.53. Found: C, 78.83; H, 6.25; N, 4.80.

Ethyl 5-Chloro-3-(2-fluorophenyl)oxindole-3-carboxylate (3d).—A 7.05-g (0.02 mol) portion of ethyl 3,5-dichloro-3-(2-fluorophenyl)-3*H*-indole-2-carboxylate (2d) was dissolved in 100 ml of ethanol by gentle warming. After the exothermic reaction, the solvent was evaporated and the residue was crystallized from ether to yield 6.4 g (95%) of product: mp 177–179°; uv λ_{max} 257 mμ (ε 10,980), 299 (1700).

Anal. Calcd for $C_{17}H_{13}ClFNO_3$: C, 61.18; H, 3.92; N, 4.20. Found: C, 60.99; H, 3.60; N, 4.09.

Ethyl 5-Chloro-3-methyloxindole-3-carboxylate (3f).—A 9-ml portion of *tert*-butyl hypochlorite was added to a solution of 12 g (0.05 mol) of ethyl 5-chloro-3-methylindole-2-carboxylate (1f). After sitting for 10 min the solvent was evaporated below 30°. Crystallization from ether–hexane yielded unstable ethyl 3,5-dichloro-3-methyl-3*H*-indole-2-carboxylate (2f): nmr ($CDCl_3$) δ 1.43 (t, 3, J = 7 Hz, CH_3), 2.0 (s, 3, CH_3), 4.46 (q, 2, J = 7 Hz, CH_2), 7.2–7.8 (m, 3, aromatic H).

The collected crystals were dissolved and refluxed for 10 min in 100 ml of ethanol. Chromatography of the residue obtained after evaporation on 200 g of silica gel using 10% ethyl acetate in methylene chloride yielded 5.5 g (43%) of product: mp 120–122°; uv λ_{max} 254 mμ (ε 12,980), 294 (1550); nmr ($CDCl_3$) δ 1.2 (t, 3, J = 7 Hz, CH_3), 1.7 (s, 3, CH_3), 4.2 (q, 2, J = 7 Hz, CH_2), 6.8–7.45 (m, 3, aromatic H), 9.65 (broad s, 1, NH).

Anal. Calcd for $C_{12}H_{12}ClNO_3$: C, 56.81; H, 4.77; N, 5.52. Found: C, 51.09; H, 4.70; N, 5.54.

Without characterization of the 3-chloroindolenines the following were similarly prepared.

***N*,*N*-Diethyl-5-chloro-3-phenyloxindole-3-carboxamide (8c)** was obtained in 80% yield by first treating 2.4 g (7.3 mmol) of *N*,*N*-diethyl-5-chloro-3-phenylindole-2-carboxylate (6c) in 50 ml of CH_2Cl_2 with 1.2 ml (10.5 mmol) of *tert*-butyl hypochlorite for 30 min at room temperature and then refluxing the residue obtained upon evaporation in 50 ml of ethanol for 1 hr. Evaporation of the ethanol and crystallization from acetone–hexane gave 2 g of product: mp 130–133°; uv λ_{max} 262 mμ (ε 9100), 300 (1700); nmr ($CDCl_3$) δ 1 (broad s, 6, 2 CH_3), 3.34 (broad s, 4, 2 CH_2), 6.74 (d, 1, J = 8 Hz, C_7 H), 7–7.6 (m, 7, C_6H_5 and C_4 H, C_6 H), 11.0 (broad s, 1, NH).

Anal. Calcd for $C_{19}H_{19}ClN_2O_2$: C, 66.57; H, 5.59; N, 8.17. Found: C, 66.59; H, 5.70; N, 8.19.

1-(6,7-Dichloro-3-phenyloxindole-3-carbonyl)morpholine (8i).—A solution of 3.75 g (0.01 mol) of 1-(6,7-dichloro-3-phenylindole-2-carbonyl)morpholine (6i) in 50 ml of methylene chloride was treated with 1.6 ml (0.014 mol) of *tert*-butyl hypochlorite for 30 min at room temperature. The residue obtained after evaporation was refluxed in 50 ml of ethanol for 1 hr. Removal of the solvent and crystallization of the residue from methylene chloride–ethyl acetate yielded 3.1 g (79%) of product: mp 241–243°; uv λ_{max} 216 mμ (ε 32,600), sh 260 (4600), 292 (1780).

Anal. Calcd for $C_{19}H_{16}Cl_2N_2O_3$: C, 58.33; H, 4.12; N, 7.16. Found: C, 58.61; H, 4.43; N, 7.12.

1-(3-Methyloxindole-3-carbonyl)pyrrolidine (8b) was obtained in 75% yield by first treating 4.6 g (0.02 mol) of 1-(3-methylindole-2-carbonyl)pyrrolidine (6b) in 60 ml of methylene chloride with 3 ml (0.026 mol) of *tert*-butyl hypochlorite for 30 min and then refluxing the crude 3-chloroindolenine in 50 ml of ethanol for 15 min. Evaporation and crystallization from ether yielded 3.7 g of product: mp 218–220°; uv λ_{max} 251 mμ (ε 8190), 282 (1560).

Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 69.01; H, 6.73; N, 11.62.

N-Ethyl-5-chloro-3-(2-fluorophenyl)oxindole-3-carboxamide (**8e**).—A mixture of 3.5 g (0.01 mol) of *N*-ethyl-3,5-dichloro-3-(2-fluorophenyl)-3*H*-indole-2-carboxamide (**7e**), 100 ml of ethanol, and 3 ml of 1.5 *N* ethanolic hydrogen chloride was heated to boiling. Evaporation and crystallization from ethyl acetate–methanol yielded 2.45 g (74%) of product: mp 228–230°; uv λ_{max} 260 mμ (ε 10,150), infl 269 (7850), 295 (1780); nmr (DMSO-d_6) δ 1.0 (t, 3, J = 7 Hz, CH_3), 3.16 (m, 2, $NHCH_2$–), 6.7–7.5 (m, 7, aromatic H), 7.7 (t, 1, J = 6 Hz, $NHCH_2$, exchanged slowly with D_2O), 11.0 (broad s, 1, NHCO).

Anal. Calcd for $C_{17}H_{14}ClFN_2O_2$: C, 61.36; H, 4.24; N, 8.42. Found: C, 61.41; H, 4.26; N, 8.42.

5-Chloro-3-(2-fluorophenyl)oxindole-3-carboxamide (**8d**) was obtained in 53% yield by refluxing 3.2 g of 3,5-dichloro-3-(2-fluorophenyl)-3*H*-indole-2-carboxamide (**7d**) with 100 ml of ethanol containing 3 ml of 1.5 *N* ethanolic hydrogen chloride for 10 min: mp 250–253°, crystallized from tetrahydrofuran–methanol; uv λ_{max} 260 mμ (ε 11,000), infl 270 (8300), 295 (1900); nmr (DMSO-d_6) δ 6.8–7.5 (m, 7, aromatic H), 7.76 (broad s, 2, NH_2, slowly exchanged with D_2O), 11.0 (s, 1, NHCO).

Anal. Calcd for $C_{15}H_{10}ClFN_2O_2$: C, 59.13; H, 3.31; N, 9.19. Found: C, 59.07; H, 3.75; N, 9.08.

5-Chloro-3-phenyloxindole[18] (**12**). A.—A mixture of 2 g of 2-acetyl-3,5-dichloro-3-phenyl-3*H*-indole (**10**) and 30 ml of methanol was refluxed for 10 min. Evaporation and crystallization from ether yielded 1.3 g (81%) of product, melting point and spectroscopic data in agreement with those reported in the literature.[18]

B.—A mixture of 0.5 g of ethyl 5-chloro-3-phenyloxindole-3-carboxylate (**3c**), 10 ml of ethanol, and 1 ml of 50% aqueous potassium hydroxide was heated to reflux for 20 min. The ethanol was evaporated and the residue was partitioned between methylene chloride and dilute hydrochloric acid. The organic layer was dried and evaporated. Crystallization from methylene chloride–ether yielded 0.2 g of 5-chloro-3-phenyloxindole.

5-Chloro-2-ethoxy-3-phenylindole (**11**). A.—A mixture of 2 g of 2-acetyl-3,5-dichloro-3-phenyl-3*H*-indole (**10**), 30 ml of methylene chloride, and 10 ml of ethanol was allowed to sit at room temperature for 15 min. The reaction mixture was washed with 10% aqueous sodium carbonate, dried, and evaporated. Crystallization from ethanol–water yielded 1.6 g (90%) of product, mp 124–127°. The analytical sample was recrystallized twice from EtOH–H_2O, mp 127–129°.

Anal. Calcd for $C_{16}H_{14}ClNO$: C, 70.72; H, 5.19; N, 5.16. Found: C, 71.04; H, 5.34; N, 5.09.

Uv λ_{max} 228 mμ (ε 30,700), 281 (17,900); nmr ($CDCl_3$) δ 1.27 (t, 3, J = 7 Hz, CH_3), 4.03 (q, 2, J = 7 Hz, OCH_2), 6.9–8.0 (m, 9, aromatic H and NH).

B.—A suspension of 1.35 g of 5-chloro-3-phenylindole-2-carboxylic acid[17] in 20 ml of methylene chloride was treated with 1 ml of *tert*-butyl hypochlorite. After 5 min, 10 ml of ethanol was added while the temperature was kept at 15–20° by cooling with ice water. After 15 min, the reaction mixture was washed with 10% aqueous sodium carbonate solution. The methylene chloride layer was dried and evaporated. Chromatography of the residue over 30 g of silica gel with benzene and crystallization from hexane yielded 0.5 g (37%) of product, mp 127–129°.

6,7-Dichloro-2-methoxy-3-phenylindole (**15**).—A 1-ml portion of *tert*-butyl hypochlorite was added to a suspension of 1.5 g of 6,7-dichloro-3-phenylindole-2-carboxylic acid (**5i**) in 30 ml of methylene chloride. After stirring for 5 min, 20 ml of methanol was added and stirring was continued for 10 min. Work-up as described above yielded after chromatography over 30 g of silica gel using benzene 0.4 g (27%) of product, mp 115–118°.

Anal. Calcd for $C_{15}H_{11}Cl_2NO$: C, 61.67; H, 3.80; N, 4.79. Found: C, 61.49; H, 3.62; N, 4.71.

Uv λ_{max} 234 mμ (ε 23,000), 277–278 (14,400); nmr ($CDCl_3$) δ 3.86 (s, 3, OCH_3), 7–7.8 (m, 7, aromatic H), 8.05 (broad s, 1, NH).

Reaction of 3-Acetyl-3,5-dichloro-3-phenyl-3*H*-indole (**10**) **with Trifluoroacetic Acid.**—A 2-ml portion of trifluoroacetic acid was added to a solution of 2 g of 2-acetyl-3,5-dichloro-3-phenyl-3*H*-indole (**10**) in 20 ml of methylene chloride. After standing at room temperature for 1 hr, the reaction mixture was evaporated, at the end azeotropically with benzene. The residue was chromatographed over 40 g of silica gel using methylene chloride–hexane (1:1). Crystallization of the less polar main component from hexane–ether yielded 0.86 g (50%) of 2,5-dichloro-3-phenylindole (**13**), mp 89–91°.

Anal. Calcd for $C_{14}H_9Cl_2N$: C, 64.15; H, 3.46; N, 5.34. Found: C, 64.35; H, 3.59; N, 5.28.

Uv λ_{max} 230 mμ (ε 31,800), 270 (11,600), infl 283 (10,750), infl 290 (9400), 301 (7250); ir ($CHCl_3$) 3460 cm^{-1} (NH); nmr ($CDCl_3$) δ 7.0–7.95 (m, 8, aromatic H).

Crystallization of the more polar component from ether yielded 0.18 g (9%) of 1-acetyl-2,5-dichloro-3-phenylindole (**14**), mp 153–154°.

Anal. Calcd for $C_{16}H_{11}Cl_2NO$: C, 63.18; H, 3.65; N, 4.61. Found: C, 62.87; H, 3.63; N, 4.63.

Uv λ_{max} 243 mμ (ε 23,100), 280 (11,500), 299 (8600), 309 (8050); ir ($CHCl_3$) 1700 cm^{-1} (CO); nmr ($CDCl_3$) δ 2.85 (s, 3, $COCH_3$), 7.1–7.7 (m, 7, aromatic H), 8.33 (d, 1, J = 9 Hz, C_7 H).

A 0.1-g portion of 1-acetyl-2,5-dichloro-3-phenylindole (**14**) was refluxed for 5 min in 5 ml of ethanol containing 1 ml of 1 *N* aqueous sodium hydroxide. Evaporation, extraction with ether, and crystallization from ether–hexane yielded 0.55 g of 2,5-dichloro-3-phenylindole (**13**).

A mixture of 0.3 g of 2,5-dichloro-3-phenylindole (**13**), 2 ml of pyridine, and 0.5 ml of acetic anhydride was heated to reflux for 10 min. The crystals separated from the cooled reaction mixture were collected and recrystallized from ethanol, melting point and mixture melting point identical with those of 1-acetyl-2,5-dichloro-3-phenylindole (**14**).

A mixture of 0.8 g of 5-chloro-3-phenyloxindole (**12**) and 10 ml of phosphorus oxychloride was refluxed for 4 hr. The reagent was removed under reduced pressure and the residue was partitioned between benzene and 1 *N* sodium hydroxide solution. The benzene layer was dried and evaporated. Chromatography of the residue on 10 g of silica gel with hexane–methylene chloride (1:1) yielded 0.179 g of 2,5-dichloro-3-phenylindole (**13**), melting point and mixture melting point identical with those of material obtained before.

2-Nitro-3-phenylindole (**24a**).—A 5-ml portion of trifluoroacetic acid was added to a solution of 10 g of 2-acetyl-3-nitro-3-phenyl-3*H*-indole (**23a**) in 100 ml of methylene chloride. After sitting for 1 hr at room temperature the mixture was evaporated under reduced pressure and the residue was crystallized from hexane to yield 6.8 g (80%) of yellow crystals. The analytical sample was recrystallized from acetone–hexane, mp 160–162°.

Anal. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.75. Found: C, 70.67; H, 4.29; N, 11.72.

Uv λ_{max} 237–238 mμ (ε 14,900), 351–352 (13,250); ir (KBr) 3250 (NH), 1555 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 7–8 (m, 9, aromatic H), 9.24 (broad s, 1, NH).

5-Chloro-2-nitro-3-phenylindole (**24c**).—A mixture of 2 g of 2-acetyl-5-chloro-3-nitro-3-phenyl-3*H*-indole (**23c**), 20 ml of methylene chloride, and 2 ml of trifluoroacetic acid was allowed to sit at room temperature for 1 hr. Crystals started to separate after 10 min. The suspension was diluted with hexane and the crystals were collected to yield 1.2 g (69%) of product, mp 201–203°.

Anal. Calcd for $C_{14}H_9ClN_2O_2$: C, 61.67; H, 3.33; N, 10.27. Found: C, 61.54; H, 3.21; N, 10.17.

Uv λ_{max} 234–235 mμ (ε 18,150), infl 253 (12,800), 349–350 (1400); ir ($CHCl_3$) 3450 (NH), 1520 cm^{-1} (NO_2); nmr ($CDCl_3$) δ 7.2–7.8 (m, 8, aromatic H), 9.4 (broad s, 1, NH).

5-Chloro-3-methyl-2-nitroindole (**24f**).—A solution of 5 g of 2-acetyl-5-chloro-3-methyl-3-nitro-3*H*-indole (**23f**) in 20 ml of trifluoroacetic acid was allowed to sit at room temperature for 15 min. The separated crystals were collected and washed with acetic acid and methanol to leave 3.9 g (93%) of yellow crystals, mp 220–222°. The analytical sample was recrystallized from acetone–methylene chloride, mp 224–226°.

Anal. Calcd for $C_9H_7ClN_2O_2$: C, 51.32; H, 3.35; N, 13.29. Found: C, 51.25; H, 3.42; N, 13.19.

Uv λ_{max} 246 mμ (ε 8700), 346 (16,560); ir (KBr) 3400 (NH), 1560 cm^{-1} (NO_2); nmr (DMSO-d_6) δ 2.53 (s, 3, CH_3), 7.32 (s with fine structure, 2, C_6 H and C_7 H), 7.65 (s with fine structure, 1, C_4 H), 12.4 (broad s, 1, NH).

Reaction of *trans*-Ethyl 3-(3,5-Dichloro-3-methyl-3*H*-2-indolyl)propenoate (**18**) **with Ethanol.**—A mixture of 2 g of *trans*-ethyl 3-(3,5-dichloro-3-methyl-3*H*-2-indolyl)propenoate (**18**), 20 ml of methylene chloride, and 10 ml of ethanol was allowed to sit at room temperature for 2 hr. The solvents were removed under reduced pressure and the residue was chromatographed over 60 g of silica gel using methylene chloride–hexane (2:1,

(18) H. Kuch, G. Seidl, and K. Schmitt, *Arch. Pharm. (Weinheim)*, **300**, 299 (1967).

v/v). Crystallization of the first eluted compound from ethanol yielded 0.2 g (10%) of ethyl 2-chloro-3-(5-chloro-3-methyl-2-indolyl)propenoate (**20**) as yellow crystals, mp 155–157°.

Anal. Calcd for $C_{14}H_{13}Cl_2NO_2$: C, 56.40; H, 4.40; N, 4.70. Found: C, 56.26; H, 4.28; N, 4.65.

Uv λ_{max} 262 mμ (ε 9670), 355–357 (ε 33,200); ir (KBr) 3440 (NH), 1710 cm^{-1} (CO); nmr ($CDCl_3$) δ 1.4 (t, 3, J = 7 Hz, CH_3), 2.4 (s, 3, CH_3), 4.45 (q, 2, J = 7 Hz, CH_2), 7.28 (s with fine structure, 2, C_6 H and C_7 H), 7.55 (s with fine structure, 1, C_4 H), 7.99 (s, 1, β proton).

Crystallization of the later eluted second component from hexane yielded 0.9 g (39%) of ethyl 2-chloro-3-(5-chloro-3-methyl-2-indolyl)-3-ethoxypropanoate (**19**), mp 81–83°.

Anal. Calcd for $C_{16}H_{19}Cl_2NO_3$: C, 55.83; H, 5.56; N, 4.07. Found: C, 55.60; H, 5.48; N, 4.19.

Uv λ_{max} 230 mμ (ε 38,000), 286–287 (8100), 294 (8100), infl 304 (5850); ir ($CHCl_3$) 3470 (NH), 1750 cm^{-1} (CO); nmr ($CDCl_3$) δ 1.13 (t, 3, J = 7 Hz, CH_3), 1.3 (t, 3, J = 7 Hz, CH_2), 2.34 (s, 3, CH_3), 3.52 (q, 2, J = 7 Hz, OCH_2), 4.33 (q, 2, J = 7 Hz, $COOCH_2$–), 4.5 (d, 1, J = 9 Hz), and 5.05 (d, 1, J = 9 Hz) (AB system, α and β proton), 7–7.5 (m, 2, C_6 H and C_7 H), 7.53 (s with fine structure, 1, C_4 H), 8.33 (broad s, 1, NH).

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Registry No.—**1g**, 40735-51-1; **1h**, 40735-52-2; **1i**, 40735-53-3; **1k**, 40735-54-4; **2c**, 40735-55-5; **2d**, 40735-56-6; **2f**, 40735-57-7; **3a**, 40735-58-8; **3c**, 40735-59-9; **3d**, 40735-60-2; **3f**, 40735-61-3; **3g**, 40735-62-4; **3h**, 40735-63-5; **3i**, 40735-64-6; **3k**, 40827-74-5; **5d**, 40731-34-8; **5f**, 16381-47-8; **5i**, 40731-36-0; **6b**, 40731-37-1; **6c**, 40731-38-2; **6d**, 24106-90-9; **6e**, 40730-98-1; **6f**, 40730-99-2; **6i**, 40731-00-8; **7d**, 40731-01-9; **7e**, 40731-02-0; **8b**, 40731-03-1; **8c**, 40731-04-2; **8d**, 40731-05-3; **8e**, 40731-06-4; **8i**, 40731-07-5; **9c**, 40731-08-6; **9f**, 40731-09-7; **10**, 40731-10-0; **11**, 40731-11-1; **12**, 15815-97-1; **13**, 40731-13-3; **14**, 40731-14-4; **15**, 40731-15-5; **16**, 40731-16-6; **17**, 40731-17-7; **18**, 40827-72-3; **19**, 40731-18-8; **20**, 40731-19-9; **21a**, 40731-20-2; **21c**, 40731-21-3; **21g**, 40827-73-4; **21h**, 40731-22-4; **21i**, 40731-23-5; **21k**, 40731-24-6; **23a**, 40731-25-7; **23c**, 40731-26-8; **23f**, 40731-27-9; **24a**, 40731-28-0; **24c**, 40731-29-1; **24f**, 40731-30-4; phosphorus pentachloride, 10026-13-8; methylene chloride, 75-09-2; thionyl chloride, 7719-09-7; *tert*-butyl hypochlorite, 507-40-4; ethyl 5-chloro-3-phenylindole-2-carboxylate, 21139-32-2; ethyl 3-phenylindole-2-carboxylate, 37129-23-0; 2-acetyl-3-phenylindole, 36015-23-3; trifluoroacetic acid, 76-05-1; ethanol, 64-17-5.

Supplementary Material Available.—Listings of structure factors coordinates, and thermal parameters for **21c** will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20 × reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JOC-73-3077.

Synthesis of 1,2-Diaminobenzimidazole, 1*H*-*s*-Triazolo[1,5-*a*]benzimidazoles, and *as*-Triazino[2,3-*a*]benzimidazoles

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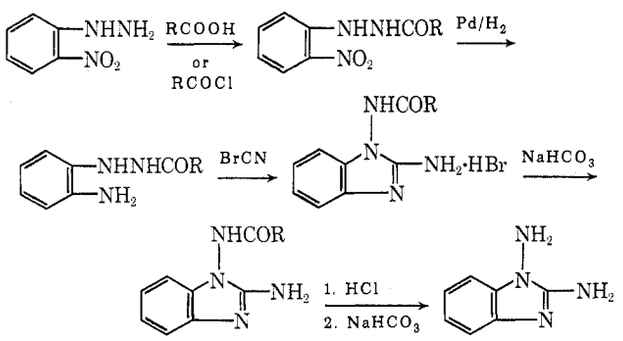
The preparations of 1,2-diaminobenzimidazole, a new compound, and of two new ring systems, 1*H*-*s*-triazolo[1,5-*a*]benzimidazole and *as*-triazino[2,3-*a*]benzimidazole, are reported.

Although 1-aminobenzimidazoles are relatively well-known compounds[1] and 2-aminobenzimidazoles have been known for a longer period of time,[2] nothing has been reported on 1,2-diaminobenzimidazole and its derivatives. The 1,2-diaminobenzimidazoles are readily obtained from *o*-acylhydrazidoanilines and cyanogen bromide.



The *o*-nitrophenylhydrazines were obtained from the corresponding *o*-nitroanilines by diazotization followed by reduction with sodium bisulfite.[3] The catalytic hydrogenation proceeded smoothly as long as the *o*-acylhydrazidonitrobenzene was pure. The ring-closure step was carried out by adding the cyanogen bromide to a suspension of the *o*-acylhydrazidoaniline in water. All of the ring compounds, isolated from the cyanogen bromide reactions, had the uv absorptions characteristic of benzimidazoles, namely 240–250 mμ for the amidine group and 280–300 mμ for the benzenoid portion.[4]

Heating the 1-acylamido-2-aminobenzimidazoles with acid anhydrides or acid chlorides produced 1*H*-*s*-triazolo[1,5-*a*]benzimidazoles (a new ring system). The R groups at positions 1 and 2 were always found to be identical with the R group of the acid anhydride or chloride.[1b] It would appear from this observation that ring closure is slow compared to the rate of trans acylation. It is interesting to note that the action of hydrochloric acid on the 1-acylamido-2-aminobenzimidazoles did not bring about the formation of the triazolo compound (Phillips method).[5]

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